# Efficient and Selective Synthesis of Multifunctional Organoboron Compounds Promoted by Cu-Based N-Heterocyclic Carbene Complexes

Author: Hwanjong Jang

Boston College

The Graduate School of Arts and Sciences

Department of Chemistry

# EFFICIENT AND SELECTIVE SYNTHESIS OF MULTIFUNCTIONAL ORGANOBORON COMPOUNDS PROMOTED BY Cu-BASED *N*-HETEROCYCLIC CARBENE COMPLEXES

A Dissertation

By

HWANJONG JANG

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# EFFICIENT AND SELECTIVE SYNTHESIS OF MULTIFUNCTIONAL ORGANOBORON COMPOUNDS PROMOTED BY Cu-BASED *N*-HETEROCYCLIC CARBENE COMPLEXES

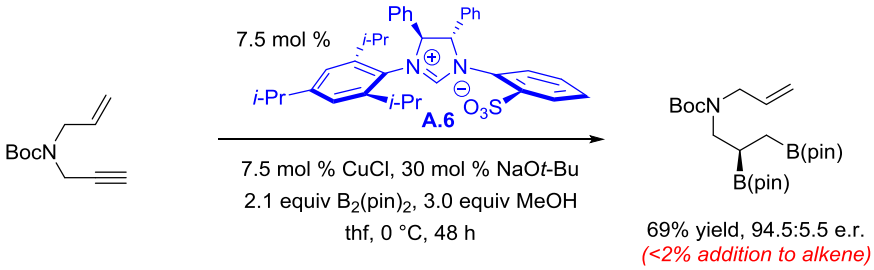
**Hwanjong Jang**

**Thesis Advisor: Professor Amir H. Hoveyda**

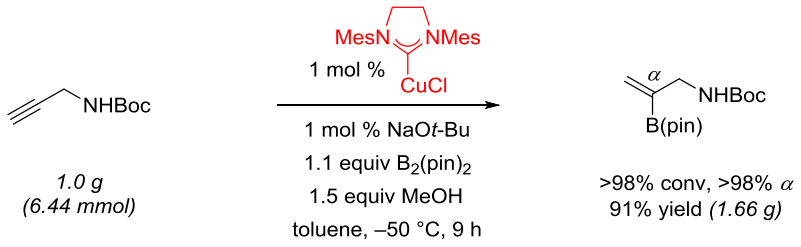
**Abstract**

■ **Chapter 1.** We have developed a single-vessel catalytic protocol for double protoboryl additions to terminal alkynes with $B_2(pin)_2$ promoted by Cu complex derived from chiral *N*-heterocyclic carbene (NHC), to achieve enantiomerically enriched versatile vicinal diborons. Since an alkenyl(pinacolato)boron, which was *in situ* generated by the first protoboration of a terminal alkyne, can serve as an effective substrate for the second protoboration (alkenylboron can allow delocalization of π electrons of olefin to a partially vacant p orbital on boron), single-vessel catalytic process with 2 equiv. of $B_2(pin)_2$ in the presence of sulfonate-bearing chiral NHC–Cu complex, affords enantiomerically enriched 1,2-diborons in up to 93% yield and 97.5:2.5 enantiomeric ratio (e.r.). Site-selective Pd-catalyzed cross-coupling with alkenyl bromide shows the versatility of the resulting diboron compounds, which delivers the coupling product efficiently.

Interestingly, only the less hindered, primary C–B bond on vicinal diboron compound participates in the cross coupling.

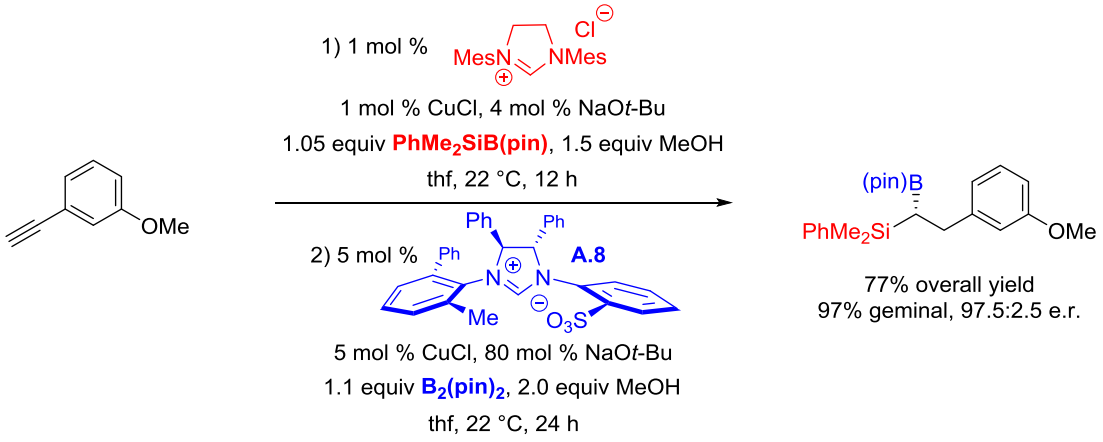



■ **Chapter 2.** Cu-catalyzed protocol for selective formation of $\alpha$-alkenylborons has been demonstrated. With achiral NHC–Cu complex, readily prepared from commercially available imidazolinium salt, various terminal alkynes are converted to internal alkenylborons in up to 93% yield with high to exclusive $\alpha$ selectivity. Propargyl ethers, amides and aryl alkynes are proved to be suitable substrates. Utility of $\alpha$-alkenylborons is demonstrated by conversion to methyl ketone and synthesis of cyclic alkenylboron compound. In addition, when Cu complex bearing a stronger electron-donating NHC is used, the site selectivity of protoboration reaction becomes reversed, which delivers the alternative isomer, $\beta$-alkenylboron efficiently. By altering the steric and electronic nature of NHC, site selectivity is dramatically changed. Mechanistic basis for site selectivity is presented.

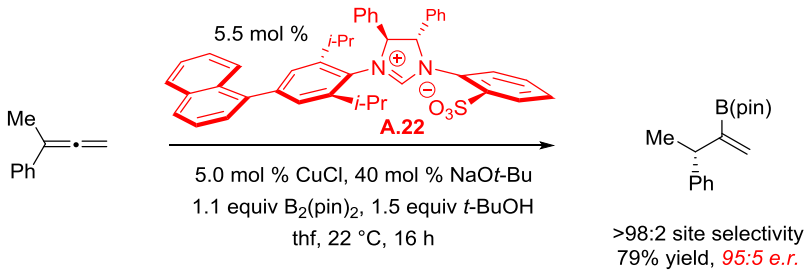


■ **Chapter 3.** Efficient and selective protocol for synthesis of enantiomerically enriched silylborons is described. In the presence of achiral NHC–Cu complex, site- and stereoselective protosilyl additions to terminal alkynes afford a wide range of alkyl- and aryl-substituted (*E*)-*β*-alkenylsilanes. Chiral monodentate NHC−Cu complex promotes enantioselective protoboration of alkyl- or alkenyl-bearing alkenylsilanes, delivering vicinal borosilanes with up to 96.5:3.5 e.r. When an alkene bearing both silyl and aryl groups is utilized, on the other hand, geminal silylboron is obtained with high enantio- (93:7–98.5:1.5 e.r.) and site selectivity (up to >98% geminal). In this case, we have reasoned that the electronic attribute of aryl unit is more dominant than the silyl group to control site selectivity.

To demonstrate the utility of the Cu-catalyzed transformation, we have illustrated the formal synthesis of bruguierol A, natural product active against Gram-positive and also Gram-negative bacteria. The key intermediate geminal borosilane is provided by sequential NHC–Cu-catalyzed protosilylation and protoboration of terminal alkyne in 77% overall yield with 97.5:2.5 e.r. and 97% site selectivity. Additionally, stereochemical models to account for levels and trends in site- and enantioselectivity are proposed.

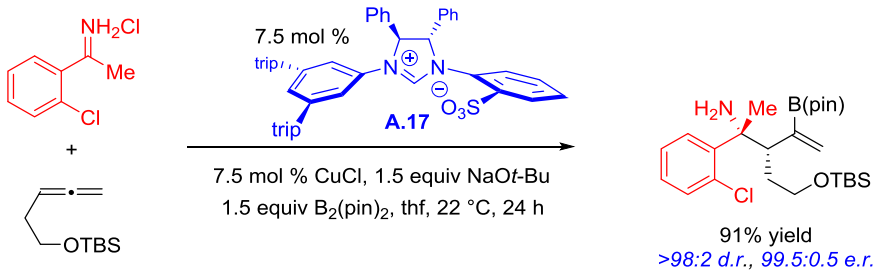


■ **Chapter 4.** New methods for enantioselective protonation of 2-B(pin)-bearing allylcopper, which is *in situ* generated by site-selective Cu–B addition to 1,1-disubstituted allene, are presented. Transformations are promoted by a chiral NHC–Cu complex, affording an alkenylboron containing $\alpha$-carbon stereogenic center. Enantiomerically enriched aryl-, heteroaryl- and silyl-bearing alkenylborons are generated in high yield (up to 98%) and selectivities (up to >98% site selectivity and 96.5:3.5 e.r.). To explore the utility of enantiomerically enriched alkenylborons, we have developed Cu-catalyzed enantioselective allylic alkenyl addition to allylic phosphate. A chiral NHC–Cu complex promotes the allylic substitution of enantiomerically enriched alkenylboronic acid with ally phosphate to deliver 1,4-diene in 62% yield with 96:4 d.r. (>98% stereoselectivity).

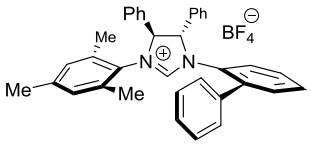



■ **Chapter 5.** We have developed a single-vessel, multicomponent process to synthesize *N*-bearing quaternary carbon stereogenic centers with exceptional diastereo- (>98:2 d.r. for all cases) and high enantioselectivity (88:12 to >99:1 e.r. except one case). Especially, protecting group-free ketoimine ("N–H" ketoimine), which can be prepared by alkylation of a readily available nitrile, has been utilized for the study. The transformation of "N–H" ketoimine is very useful because the obtained amine has no protecting group, which allows us to avoid the deprotection step as well as to be able to choose appropriate

protecting group for subsequent chemical reactions. By oxidation of $\alpha$-tertiary carbamine with $NaBO_3$, $\beta$-amino ketones (Mannich reaction product) are obtained in up to 83% yield. A stereochemical model to account for the level of diastereo- and enantioselectivity are presented using DFT calculations. To show the utility of the present method, we have synthesized a medicinally active compound, which was studied for Alzheimer's disease. The Cu-catalyzed protocol delivers the core structure of the target molecule with exclusive diastereo- and enantioselectivity (>98:2 d.r. and 99.5:0.5 e.r.).



# Index of Imidazolinium Salts



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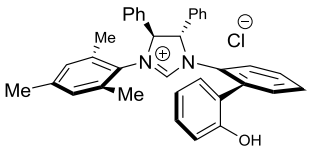

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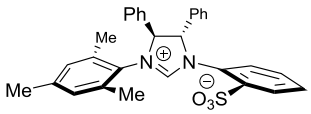

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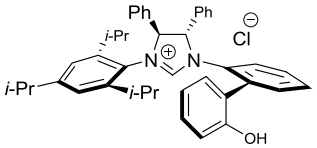

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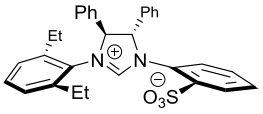

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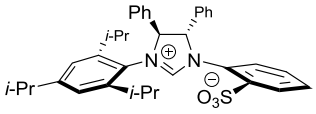

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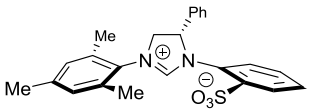

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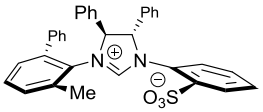

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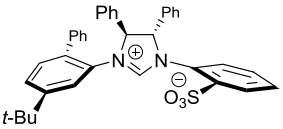

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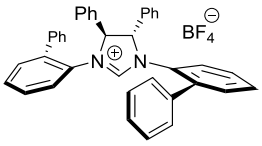

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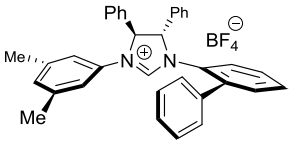

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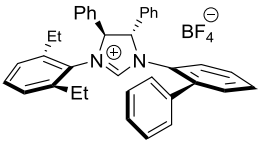

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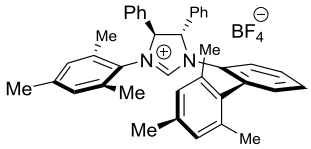

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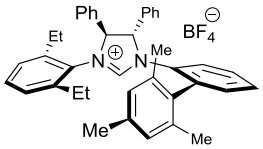

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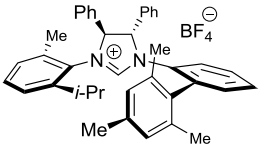

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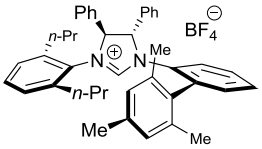

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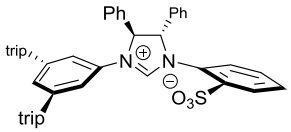

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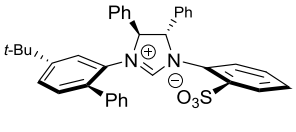

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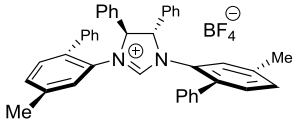

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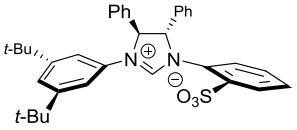

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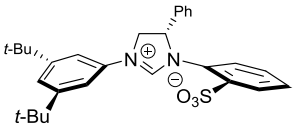

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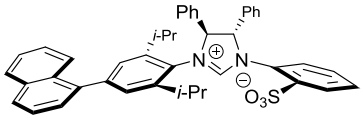

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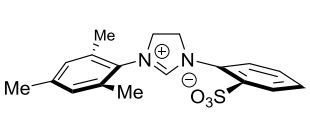

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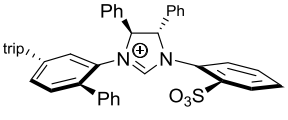

**A.24**

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I would like to express my sincere appreciation to my advisor Prof. Amir H. Hoveyda for all of his supports, advices, and encouragements. I was very lucky to join his group. He is passionate about thinking of, talking about, and teaching all kinds of chemistry. He has been leading me to be a better chemist and group members. In addition, he has given great advices for my future career. I'll keep in mind them all the time. I would also thank Prof. Mark L. Snapper and Prof. Masayuki Wasa for kindly accepting to serve as members of my doctoral committee, spending time to read this document, and giving me valuable suggestions.

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## Table of Contents

## *Chapter One*

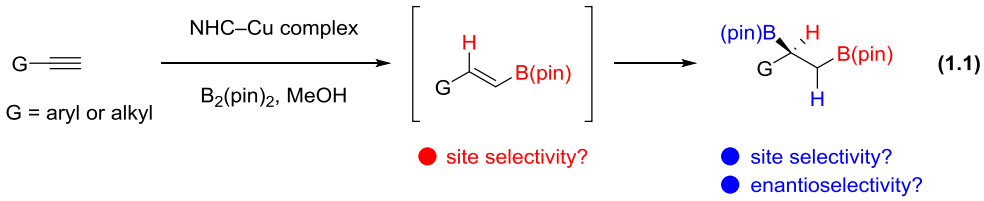
# Tandem Site- and Enantioselective NHC–Cu-Catalyzed Double Protoboryl Additions to Terminal Alkynes to Generate Enantiomerically Enriched Vicinal Diborons

### *1.1. Introduction*

Organoboron compounds are one of the most useful intermediates in the field of organic synthetic chemistry due to the versatility of the carbon–boron bond.[1] Stereoselective metal-catalyzed hydroboration has been widely studied for the synthesis of organoboron compounds.[2] There are, however, still a number of challenges that remain to be addressed. In most of previous examples, precious metals such as Rh, Ir, or Pd have been utilized. In 2009, our group reported first enantioselective NHC–Cu-catalyzed protoboryl addition to styrenes (site-selective boron–copper addition to aryl alkene followed by protonation of *in situ* generated carbon–copper bond by MeOH).[3] It was

(1) For reviews on functionalizations of organoboron compounds, see: (a) Brown, H. C.; Singaram, B. *Pure & Appl. Chem.* **1987**, *59*, 879–894. (b) Brown, H. C.; Singaram, B. *Acc. Chem. Rec.* **1988**, *21*, 287–293. (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483. (d) Miyaura, N. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1535–1553.
(2) For reviews on metal-catalyzed hydroborations, see: (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179–1191. (b) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957–5026. For reviews on enantioselective hydroboration of olefins, see: (c) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695–4712. (d) Carroll, A. -M.; O'Sullivan, T. P.; Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609–631. (e) Thomas, S. P.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 1896–1898.
(3) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161.

shown that aryl group is required to achieve high efficiency since it lowers the olefin's LUMO energy, which promotes olefin–Cu coordination. We reasoned that if alkenylborons, which contain boron, allowing delocalization of π electrons of olefin to a partially vacant p orbital on boron, can be induced to undergo site-selective protoborations, an efficient Cu-catalyzed protocol for enantioselective synthesis of the highly versatile vicinal diboron compounds would be accomplished. Since alkenylborons can be prepared by another protoboryl addition to terminal alkynes, we examined a single-vessel Cu-catalyzed process for double protoborations of terminal alkynes to achieve enantiomerically enriched versatile vicinal diborons (eq 1.1).




(1.1)

Vicinal diborons are versatile building blocks for organic syntheses. A lot of efforts have been made to develop efficient procedure for preparation of 1,2-diboron compounds, the majority of which is metal-catalyzed diboration of alkenes.[4] A number of metal-catalyzed protocols for diboration of alkenes,[5] alkynes,[6] enones,[7] and allenes[8] have

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(4) For reviews on metal-catalyzed diboration, see: (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63–73. (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392–402. (c) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271–280. (d) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320–2354. (e) Burks, H. E.; Morken, J. P. *Chem. Commun.* **2007**, 4717–4725. (f) Ramirez, J.; Lillo, V.; Segarra, A. M.; Fernandez, E. *Comp. Rend. Chim.* **2007**, *10*, 138–151.

(5) For selected recent reports regarding catalytic enantioselective diboration of terminal alkenes, see: Rh-catalyzed: (a) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702–8703. (b) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538–9544. Pt-catalyzed: (c) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210–13211.

(6) (a) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115,* 11018–11019. (b) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713–720.

(7) (a) Ito, H.; Yamanaka, H.; Tateiwa, J.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821–6825. (b) Mun, S.; Lee, J.-E.; Yun, J. *Org. Lett.* **2006**, *8*, 4887–4889.

(8) (a) Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357–2360. (b) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328–16329.

been extensively reported through the use of Rh, Ir, Pt, Pd or Au catalysts, however, few of which demonstrate dihydroboration of alkynes to generate 1,2-diborated compounds and enantioselectivities reported for dihydroboration are low (65:35–67.5:32.5 e.r.).[9] Moreover, the more practical Cu-catalyzed variant of these reactions has been underdeveloped. Thus, an efficient and enantioselective Cu-catalyzed double protoborations of alkynes would thus constitute an important contribution. Herein, we have disclosed tandem site- and enantioselective NHC–Cu-catalyzed double protoboryl additions to terminal alkynes to achieve enantiomerically enriched vicinal diboron compounds.

### *1.2. Background*

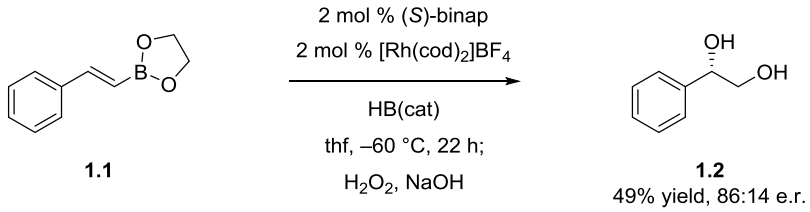
Enantiomerically enriched vicinal diboron compounds are key intermediates in chemical synthesis since two C–B bonds can be converted to synthetically useful C–O, C–N, C–C or C–H bonds independently. Therefore, efficient and selective protocols for preparing this class of molecules have been developed. In this section, we will summarize the advances regarding catalytic synthesis of enantiomerically enriched 1,2-diboron compounds, which includes (1) metal-catalyzed enantioselective hydroboration of alkenylboron compounds, (2) metal-catalyzed diboration with chiral diboron reagents, (3) metal-catalyzed enantioselective diboration of olefins, and (4) metal-catalyzed enantioselective hydrogenation of alkenyldiborons.

(9) 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*, 77-85. Ramirez, J.; Segarra, A. M.; Fernandez, E. *Tetrahedron: Asymmetry* **2005**, *16*, 1289–1294.

### *1.2.1. Metal-Catalyzed Enantioselective Hydroboration of Alkenylborons*

In 1996, Weissensteiner and coworkers reported that enantioselective hydroboration of (*E*)-alkenylboronic ester **1.1** in the presence of 2 mol % of (*S*)-binap–Rh complex with catecolborane affords 1,2-diol **1.2** in 49% yield and 86:14 e.r. after oxidation (Scheme 1.1).[10] Several bisphosphine–rhodium complexes were investigated, and they obtained the highest efficiency and enantioselectivity with (*S*)-binap–Rh complex. Substrate scope is, however, extremely limited; they only showed one example of the desired diol product **1.2**.

***Scheme 1.1.*** Rh-Catalyzed Enantioselective Hydroboration of Alkenylboron




**1.1** **1.2** 49% yield, 86:14 e.r.

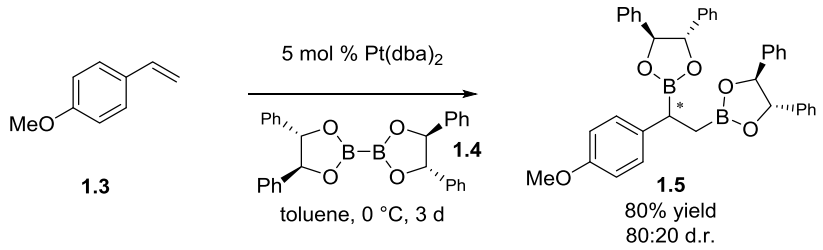
### *1.2.2. Metal-Catalyzed Diboration with Chiral Diboron Reagents*

An alternative strategy for optically active vicinal diboron compounds is diboration of terminal alkenes. Norman and coworkers developed Pt-catalyzed diboration of terminal olefins with chiral diboron reagent (Scheme 1.2).[11] With 5 mol % of $Pt(dba)_2$, diboration of styrenyl olefin **1.3** in the presence of chiral diboron reagent **1.4** affords vicinal diboron compound **1.5** in 80% yield and 80:20 d.r. There are several limitations for the aforementioned transformation. The reaction requires stoichiometric amounts of expensive chiral diboron **1.4**, and also a long reaction time (3 days) to achieve high

(10) Wiesauer, C.; Weissensteiner, W. *Tetrahedron: Asymmetry* **1996**, *7*, 5–8.
(11) Marder, T. B.; Norman, N. C.; Rice, C. R. *Tetrahedron Lett.* **1998**, *39*, 155–158.

efficiency. In addition, they only demonstrated three substrates, which are all styrenyl olefins, showed moderate selectivities (55:45–80:20 d.r.).

***Scheme 1.2.*** Pt-Catalyzed Diboration of Terminal Alkenes with Chiral Diboron **5.4**

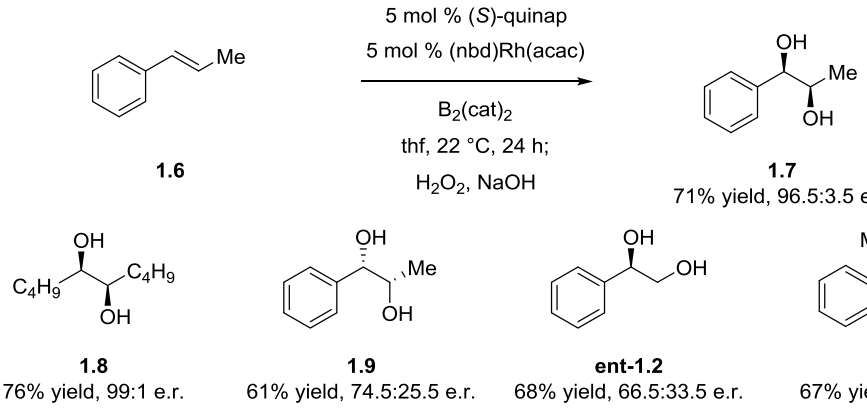



### *1.2.3. Metal-Catalyzed Enantioselective Diboration of Alkenes*

The first catalytic enantioselective diboration of olefins with chiral ligand was disclosed by Morken and coworkers in 2003.[12] The authors utilized commercially available $B_2(cat)_2$ reagent. As illustrated in Scheme 1.3, reaction of various alkenes is promoted by 5 mol % of rhodium salt and chiral bisphosphine (*S*)-quinap. When they use (*E*)-disubstituted olefin **1.6**, after oxidation with $H_2O_2$, desired diol **1.7** is obtained with high efficiency (71% yield) and enantioselectivity (96.5:3.5 e.r.). Transformation of symmetric disubstituted olefin is highly selective to deliver the corresponding diol **1.8** in 76% yield and 99:1 e.r. (*S*)-Quinap–Rh-catalyzed diboration of (*Z*)-disubstituted alkene, however, is significantly less enantioselective, providing diol **1.9** in 74.5:25.5 e.r. (96.5:3.5 e.r. for **1.7** from (*E*)-alkene). Additionally, enantioselective diboration of terminal or 1,1-disubstituted olefin does not proceed with high levels of selectivity (66.5:33.5 e.r. for **ent-1.2** and 73:27 e.r. for **1.10**).

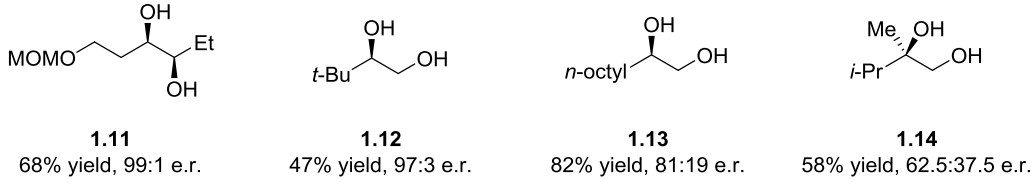
(12) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702–8703.

***Scheme 1.3.*** Rh-Catalyzed Enantioselective Diboration of Alkenes




In subsequent studies, Morken and coworkers demonstrated that Rh-catalyzed enantioselective diboration of a broad range of alkenes is efficient and selective (Scheme 1.4).[13] Reaction of desymmetrized dialkyl-substituted olefin shows high selectivity (99:1 e.r. for **1.11**). Several alkyl-substituted terminal alkenes were investigated; sterically demanding *t*-butyl-bearing **1.12** was obtained with high enantioselectivity, but moderate yield (97:3 e.r. and 47% yield). On the other hand, when *n*-octyl-alkene was utilized, diol **1.13** was isolated with higher efficiency, but reduced selectivity (82% yield and 81:19 e.r.). Reaction of 1,1-dialkyl-olefin provides diol **1.14** in 58% yield and 62.5:37.5 e.r. Even though the authors illustrated that phosphine–Rh-catalyzed diboration reaction can be applied to wide range of simple alkenes, there are still unsolved limitations including low selectivities for terminal and 1,1-disubstituted olefins.

***Scheme 1.4.*** Representative Substrate Scope for Rh-Catalyzed Enantioselective Diboration




(13) (a) Miller, S. P.; Morgan, J. B.; Nepveux, F. J.; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133. (b) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538–9544.

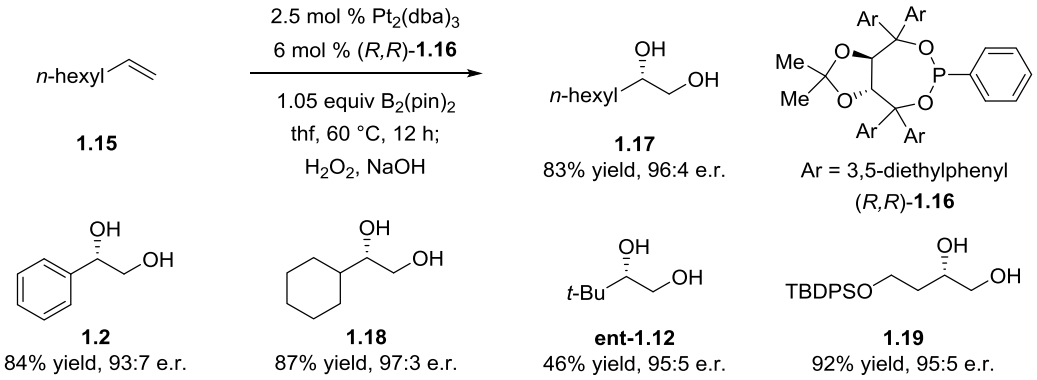
Fernández and coworkers studied chiral phosphine–Rh- or NHC–Ag-catalyzed complex to promote transformations of styrene to diboryl compound.[14] They observed, however, minimal enantioselectivities.

Recently, Morken and coworkers reported Pt-catalyzed enantioselective diboration of terminal olefins (Scheme 1.5).[15] In this report, the low selectivity issue for terminal olefins was addressed. At the same time, they also introduced less expensive and more robust reagent, $B_2(pin)_2$ for their enantioselective diboration reaction. They found that taddol-derived phosphonite–Pt complex promotes diboration of various monosubstituted olefins with $B_2(pin)_2$ to generate corresponding vicinal diols after oxidation. Reaction of 1-octene **1.15** with $B_2(pin)_2$ in the presence of 5 mol % of chiral (*R*,*R*)-**1.16**−Pt complex affords 1,2-diol **1.17** in 83% yield and 96:4 e.r. In their previous Rh-catalyzed protocol, transformation of *n*-alkyl-olefin showed moderate selectivity (81:19 e.r. for **1.13** in Scheme 1.4). In addition, Pt-catalyzed diboration of styrene delivers vicinal diol **1.2** more efficiently with much higher enantioselectivity compared to Rh-catalyzed protocol (84% yield and 93:7 e.r. vs 68% yield and 66.5:33.5 e.r. in Scheme 1.3). Cyclohexyl- and *t*-butyl-bearing olefins are utilized as substrates for Pt-catalyzed diboration, and both are converted to vicinal diols efficiently and enantioselectively (87% yield, 97:3 e.r. for **1.18** and 46% yield, 95:5 e.r. for **ent-1.12**). Additionally, catalytic transformation tolerates silyl ether moiety in **1.19** (92% yield and 95:5 e.r.).

(14) (a) Ramírez, J.; Segarra, A. M.; Fernández, E. *Tetrahedron: Asymmetry* **2005**, *16*, 1289–1294. (b) Corberán, R.; Ramírez, J.; Poyatos, M.; Peris, E.; Fernández, E. *Tetrahedron: Asymmetry* **2006**, *17*, 1759–1762.

(15) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210–13211.

***Scheme 1.5.*** Pt-Catalyzed Enantioselective Diboration of Terminal Alkenes

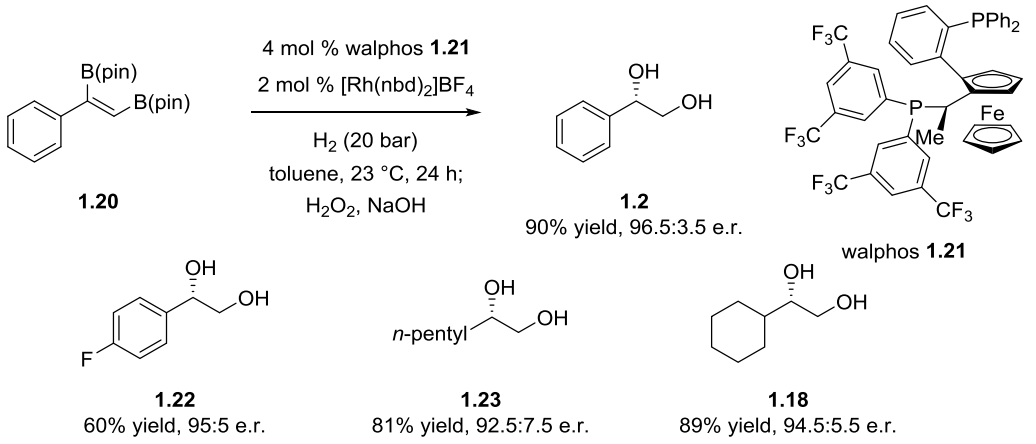



### *1.2.4. Metal-catalyzed Enantioselective Hydrogenation of Alkenyldiborons*

In 2004, Morken and coworkers reported another approach to reach enantiomerically enriched 1,2-diborons through Rh-catalyzed hydrogenation of alkenyldiborons (Scheme 1.6).[16] In the presence of walphos **1.21**–Rh complex, hydrogenation of alkenyl bis(boronates) proceed efficiently with high enantioselectivity. Aryl-bearing olefins are converted to diols after oxidative work-up with up to 96.5:3.5 e.r. (**1.2** and **1.22**). Alkyl-substituted vicinal diols are also successfully obtained efficiently with similar levels of selectivity (92.5:7.5 e.r. for **1.23** and 94.5:5.5 e.r. for **1.18**).

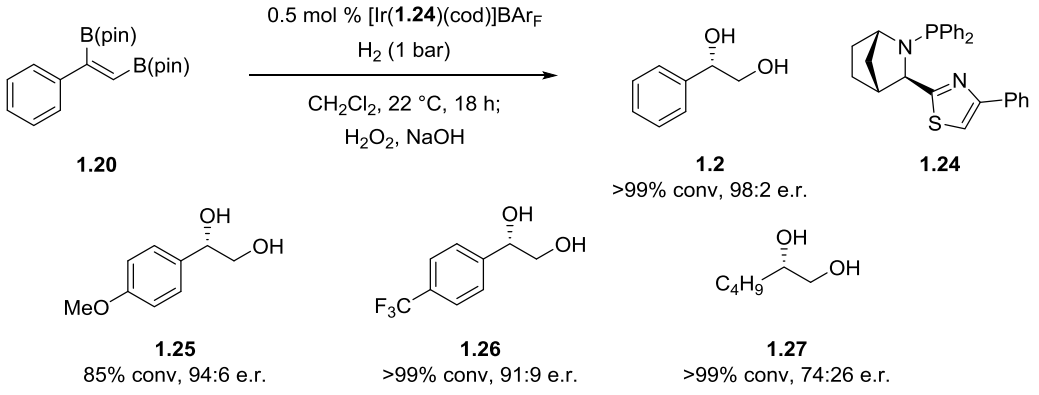
(16) Morgan, J. B.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 15338–15339.

***Scheme 1.6.*** Rh-Catalyzed Enantioselective Hydrogenation of Alkenyl Bis(boronates)




In a related report, Andersson and coworkers developed enantioselective hydrogenation of bis(boryl)alkenes catalyzed by chiral ligand–Ir complex (Scheme 1.7).[17] The Ir complex derived from Ir salt and chiral N,P ligand **1.24** promotes the hydrogenation of aryl-bearing alkenyldiborons to afford corresponding 1,2-diols with high enantioselectivities (91:9–98:2 e.r. for **1.2**, **1.25** and **1.26**). When the authors used alkyl-substituted olefin, however, the selectivity of reaction was reduced (74:26 e.r. for **1.27**).

***Scheme 1.7.*** Ir-Catalyzed Enantioselective Hydrogenation of Alkenyl Bis(boronates)



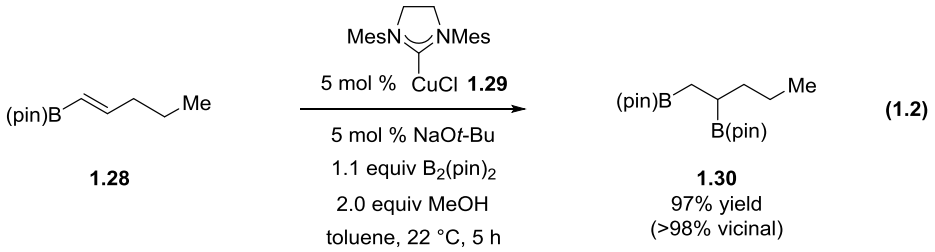

(17) Paptchikhine, A.; Cheruku, P.; Engman, M.; Andersson, P. G. *Chem. Commun.* **2009**, 5996–5998.

Herein, we have disclosed efficient and selective protocol for enantiomerically enriched vicinal diboron compounds through tandem NHC–Cu-catalyzed protoborations to readily accessible terminal alkynes.

## *1.3. NHC–Cu-Catalyzed Enantioselective Double Protoborations of Terminal Alkynes*

### *1.3.1. Initial Obervations*

We began by examining the efficiency and site selectivity of protoboration of alkenylboronic pinacol ester under the identical conditions that are optimal for the previously disclosed styrene protoboration reactions.[3] We investigated the Cu-catalyzed protoboryl addition to alkenylboron **1.28** in the presence of 5 mol % of NHC–Cu complex **1.29**, NaO*t*-Bu, and MeOH (eq 1.2). After 5 h, we obtained the desired vicinal diboron **1.30** in 97% yield and exclusive site selectivity (<2% geminal diboron).

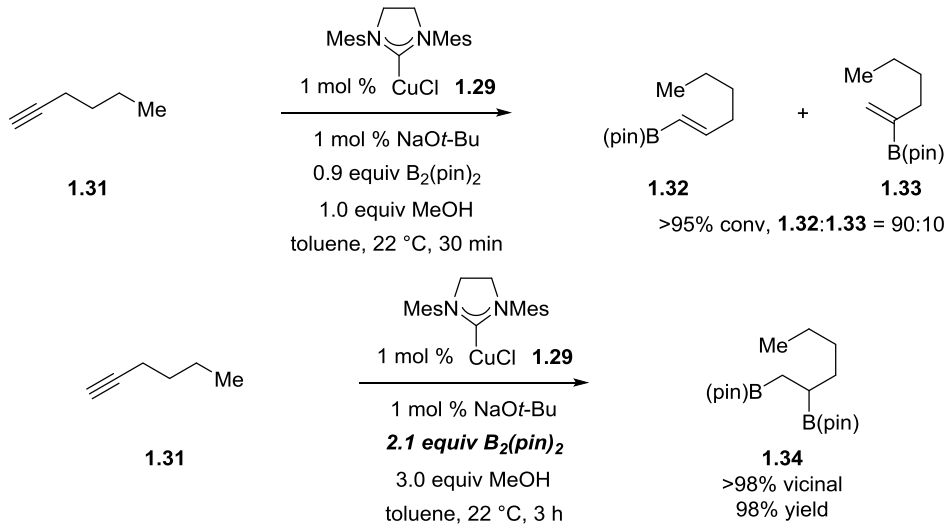



(1.2)

Alkenylborons might be prepared by Cu-catalyzed protoboration of terminal alkynes. Thus, we explored to utilize an NHC–Cu complex **1.29** for double protoborations, which could deliver 1,2-diboron compound from the corresponding alkyne in a single-vessel process. As illustrated in Scheme 1.8, we examined Cu-catalyzed protoboration of 1-hexyne **1.31** with 0.9 equiv. of $B_2(pin)_2$ in the presence of 1 mol % of NHC–Cu complex **1.29** and NaO*t*-Bu to obtain alkenylboron compound. After

30 min, a 90:10 mixture of terminal (**1.32**) and internal (**1.33**) alkenylboron isomers are obtained with complete conversion. Then, we tested to realize the above strategy; with 2.1 equiv. of $B_2(pin)_2$ and 3 equiv. of MeOH, 1-hexyne **1.31** was completely converted to vicinal diboron compound **1.34** with exclusive site selectivity (<2% geminal), which can be isolated by silica gel column chromatography in 98% yield. It is worth mentioning that isolated diboron compounds have been reported scarcely due to the instability of organoboron species with catechol.

***Scheme 1.8.*** Initial Observations for Cu-Catalyzed Double Protoborations




### *1.3.2. Examination of Various Chiral NHC–Cu Complexes*

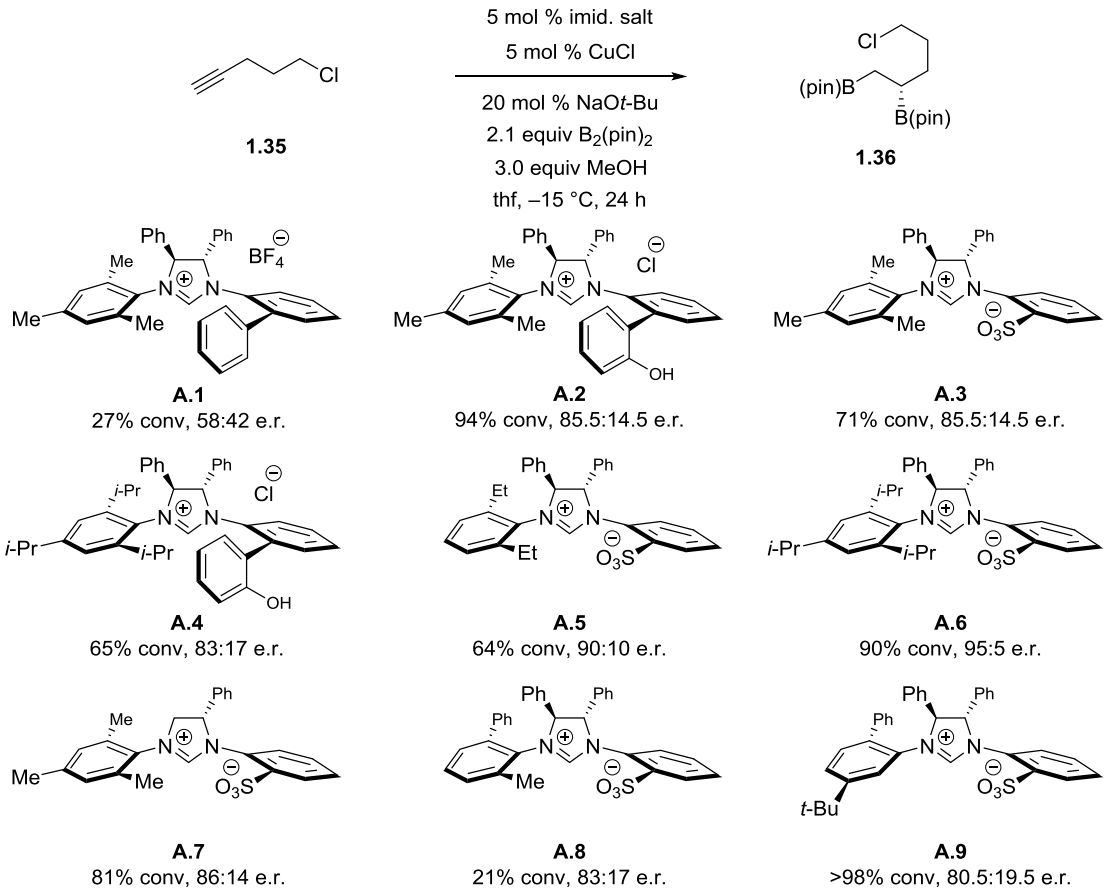
Since we succeeded to obtain vicinal diboron compound selectively with achiral NHC–Cu complex **1.29**, we investigated chiral NHCs our laboratory developed[18] for efficient and enantioselective double protoborations of terminal alkynes under conditions that might be optimal for the second enantioselective process (–15 °C, thf).[3] As shown in

(18) (a) Larsen, A. O.; Liu, W.; Nieto-Oberhuber, C.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 11130–11131. (b) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877–6882. (c) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100.

Scheme 1.9, reaction of 5-chloropentyne **1.35** was examined in the presence of 5 mol % chiral imidazolinium salt, CuCl and 20 mol % NaO*t*-Bu. Initially, three types of NHCs derived from **A.1**–**A.3** were investigated. Monodentate NHC from **A.1** provides 1,2-diboron **1.36** in only 27% conversion and 58:42 e.r., which leads us to rule out this type of NHC for further investigation. With phenoxy-bearing **A.2**, reaction of **1.35** proceeds much more efficiently and selectively (94% conv and 85.5:14.5 e.r.). When NHC–Cu complex generated from sulfonate-containing **A.3** is used, we observed a similar level of selectivity (85.5:14.5 e.r.). Based on these preliminary observations, we decided to examine more chiral Cu complexes bearing these types of NHCs (bidentate phenoxy- or sulfonate-containing). With sterically more demanding, triisopropylphenyl-bearing **A.4**, however, we could not improve enantioselectivity (83:17 e.r.). Interestingly, in the case with sulfonate-containing bidentate NHCs, as the size of substituents on *N*-Ar is increased, enantioselectivity is also enhanced (85.5:14.5 e.r. with **A.3**, 90:10 e.r. with **A.5**, and 95:5 e.r. with **A.6**) without deterioration of the efficiency (90% conv with **A.6**). Double protoborations of **1.35** with a chiral imidazolinium salt **A.7** containing a monophenyl backbone delivers diboron **1.36** with a similar level of enantioselectivity to the result with corresponding diphenyl backbone bearing **A.3** (86:14 e.r. with **A.7** vs 85.5:14.5 e.r. with **A.3**). To improve the enantioselectivity further, we prepared structurally modified imidazolinium salts **A.8** and **A.9** bearing *o*-phenyl substituent on *N*-aryl group, which might make more severe sterically demanding environment around Cu center. With 5 mol % of Cu complex with **A.8**, reaction becomes sluggish (21% conv) without improved enantioselectivity (83:17 e.r.) mainly due to the severe sterics on *o*-position (2-phenyl and 6-methyl) interrupting the association of Cu with substrate. When

we moved one of the *o*-substituent to *m*-position (6-methyl to 5-*tert*-butyl; **A.9**), complete conversion was achieved with moderate selectivity (80.5:19.5 e.r.). Based on the chiral NHC screening results, we chose the chiral imidazolinium salt **A.6**, which contains a sulfonate group on *N*-Ar and triisopropyl substituents on the other *N*-Ar unit at the same time as an optimal NHC precursor.

***Scheme 1.9.*** Ligand Screen for Cu-Catalyzed Enantioselective Double Protoborations

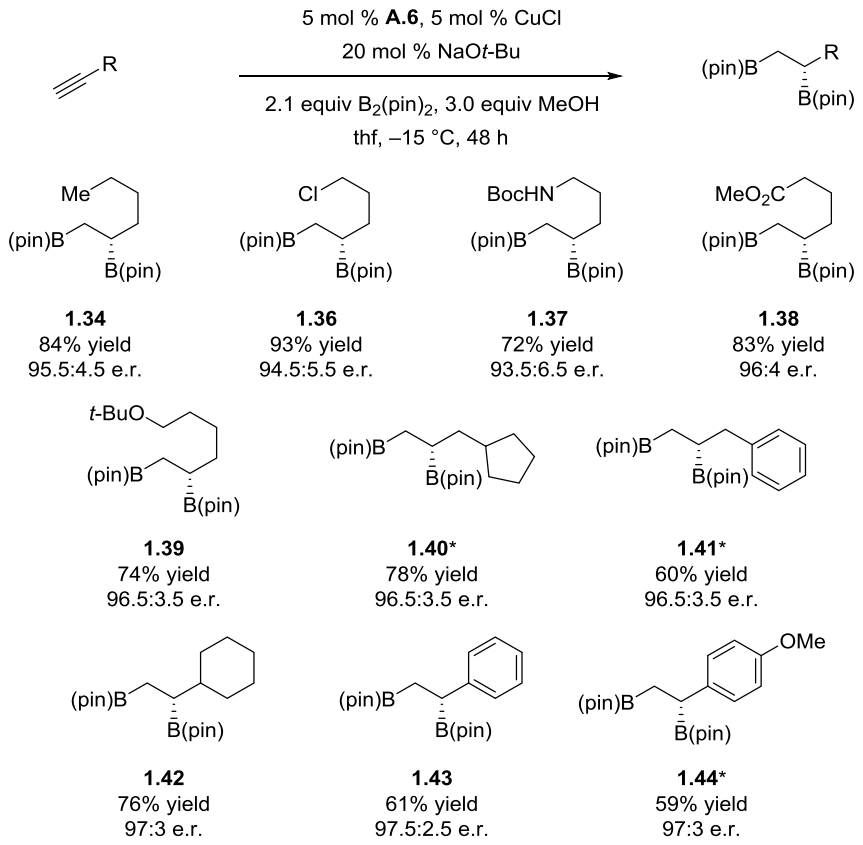



### *1.3.3. Substrate Scope of NHC–Cu-Catalyzed Enantioselective Double Protoborations of Terminal Alkynes*

As summarized in Scheme 1.10, a wide range of terminal alkynes are examined for enantioselective double protoborations with 2.1 equiv. of $B_2(pin)_2$ and 3 equiv. of

MeOH in the presence of 5 mol % of NHC–Cu complex generated from chiral imidazolinium salt **A.6**, CuCl and NaO*t*-Bu. An alkyne **1.31**, bearing *n*-alkyl unit, which was originally examined for achiral reaction in the presence of NHC–Cu complex **1.29** (Scheme 1.8) undergo diprotoboration to provide vicinal diboron **1.34** in 84% yield and 95.5:4.5 e.r. at –15 °C in 48 h. Since we elongate the reaction time to 48 h (vs 24 h in Scheme 1.9) to achieve optimal efficiency, chlorine-containing diboron **1.36** is isolated in 93% yield. Terminal alkynes bearing functional group such as amide, ester, or ether have been utilized, affording corresponding 1,2-diborons efficiently and selectively (72% yield and 93.5:6.5 e.r. for **1.37**; 83% yield and 96:4 e.r. for **1.38**; 74% yield and 96.5:3.5 e.r. for **1.39**). In addition, *β*-branched chain-bearing vicinal diboron compounds **1.40** and **1.41** are obtained through Cu-catalyzed transformation in 60−78% yield and 96.5:3.5 e.r. For these alkynes, 7.5 mol % of **A.6** and CuCl are required for high conversion due to the sterics of *β*-branched chain. On the other hand, when *α*-branched chain-bearing alkynes are used, we obtain similar level of efficiency with only 5 mol % of NHC−Cu complex (61–76% yield for **1.42** and **1.43**). Reaction of terminal alkynes bearing aryl group proceed more enantioselectively, but less efficiently (61% yield and 97.5:2.5 e.r. for **1.43**; 59% yield and 97:3 e.r. for **1.44**). Electronics on aryl group might play an important role in diprotoboration reaction. *p*-MeO-containing phenylacetylene undergo transformation in the presence of 7.5 mol % Cu–NHC derived from **A.6** to afford the desired product **1.44** in 59% yield. Comparison of this data with that in **1.43** (product from phenylacetylene; 61% yield with 5 mol % **A.6**) indicates that transformation of alkynes containing an electron-donating group proceed slower.

***Scheme 1.10.*** Cu-Catalyzed Enantioselective Diprotoboration of Terminal Alkynes




**1.34**
84% yield
95.5:4.5 e.r.

**1.36**
93% yield
94.5:5.5 e.r.

**1.37**
72% yield
93.5:6.5 e.r.

**1.38**
83% yield
96:4 e.r.

**1.39**
74% yield
96.5:3.5 e.r.

**1.40***
78% yield
96.5:3.5 e.r.

**1.41***
60% yield
96.5:3.5 e.r.

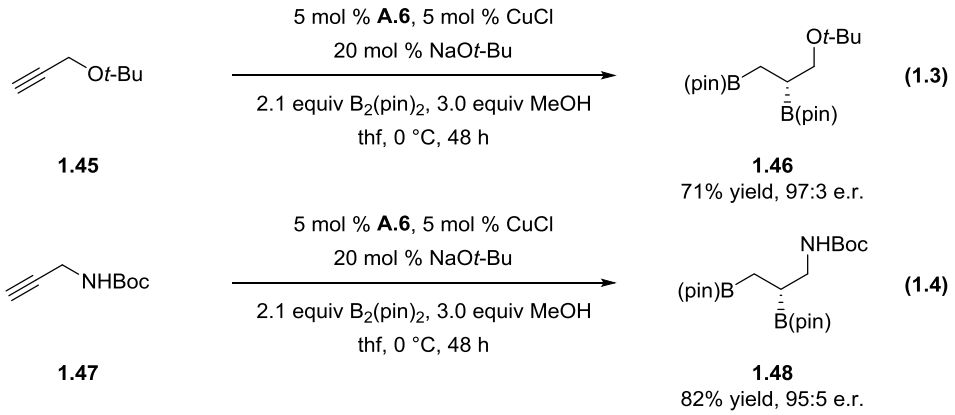
**1.42**
76% yield
97:3 e.r.

**1.43**
61% yield
97.5:2.5 e.r.

**1.44***
59% yield
97:3 e.r.

* 7.5 mol % of **A.6** and CuCl were used

Additionally, two interesting terminal alkynes **1.45** and **1.47** bearing a propargylic heteroatom are examined. The Cu-catalyzed double protoborations presented in eqs 1.3 and 1.4 demonstrate that the reaction can be carried out with these types of terminal alkynes, affording **1.46** and **1.48** in 71% and 82% yield and 97:3 and 95:5 e.r., respectively. This type of vicinal diboron compounds is not easy to be prepared through metal-catalyzed diboration of alkene because when transition metal adds to $\alpha$-carbon to the propargylic heteroatom, facile elimination reaction becomes competitive. Therefore, Cu-catalyzed protocol is exceptionally useful reaction for propargylic heteroatom-containing compounds.

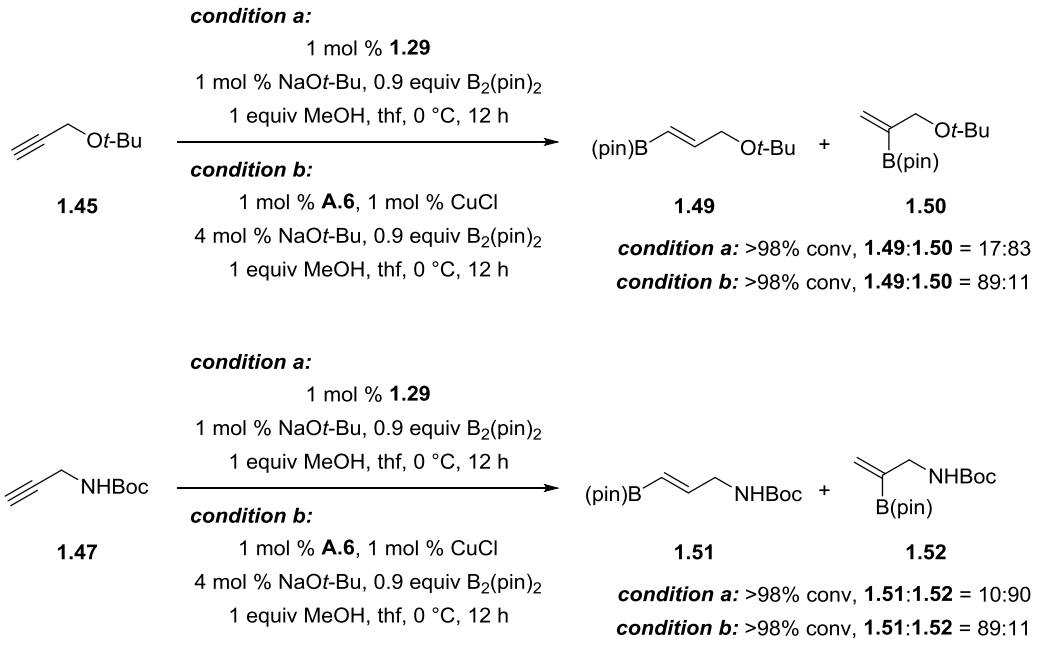



During this study, we found a critical attribute of the sulfonate group-containing NHC−Cu complex derived from **A.6**: high site selectivity in alkyne protoboration. As illustrated in Scheme 1.11, Protoboryl addition to propargyl ether **1.45** with 0.9 equiv. of $B_2(pin)_2$ and 1 equiv. of MeOH in the presence of 1 mol % achiral NHC−Cu complex **1.29** (*condition a*) proceeds to internal alkenylboron isomer **1.50** predominantly (**1.49**:**1.50** = 17:83). In contrast, when 1 mol % of imidazolinium salt **A.6** is utilized for an NHC precursor (*condition b*), terminal alkenylboron **1.49** is provided selectively (**1.49**:**1.50** = 89:11).[19] Control experiments indicate that protoboration of internal alkenylborons (e.g., **1.50**) catalyzed by NHC–Cu complex derived from **A.6** delivers vicinal diborons with substantially lower enantiomeric purity. For example, after isolation of a pure sample of **1.50**, we carry out transformation of **1.50** under the identical condition as previously described. The reaction is sluggish and much less selective (13% conversion to **1.46**, and 55:45 e.r.). Thus, high level of enantioselectivity we achieved with chiral NHC–Cu complex from **A.6** is mainly due to its ability to control the site selectivity of the first stage protoboration of terminal alkyne for generation of the terminal alkenylboron isomer selectively (e.g., **1.49**). In addition, propargyl amide **1.47** is

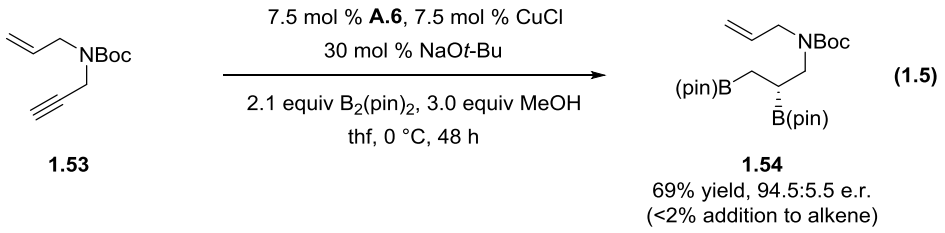
(19) For a study regarding variations in the site selectivity of boron–copper additions to terminal alkynes (not catalytic), see: Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47–53.

also investigated, affording internal alkenylboron **1.52** as a major isomer with the achiral NHC–Cu complex **1.29** (**1.51**:**1.52** = 10:90; *condition a*), and delivering terminal isomer **1.51** with 89:11 selectivity with **A.6** (*condition b*), which is consistent with the above findings with propargyl ether **1.45**.

***Scheme 1.11.*** Influence of NHC Structure on Site Selectivity of Copper–Boron Addition




Furthermore, our own Cu-catalyzed protoboration has another essential property: high chemoselectivity. When we use a molecule containing both terminal alkyne and terminal alkene **1.53** for catalytic enantioselective double protoborations in the presence of 7.5 mol % NHC–Cu derived from **A.6**, reaction proceeds to afford olefin-bearing diboron compound **1.54** in 69% yield and 94.5:5.5 e.r. (eq 1.5), which means that Cu–B addition to alkene is not favored (<2% conversion to alkene). The Cu-catalyzed reaction, thus, allows for chemoselective diprotoboration of an alkyne in the presence of an olefin.

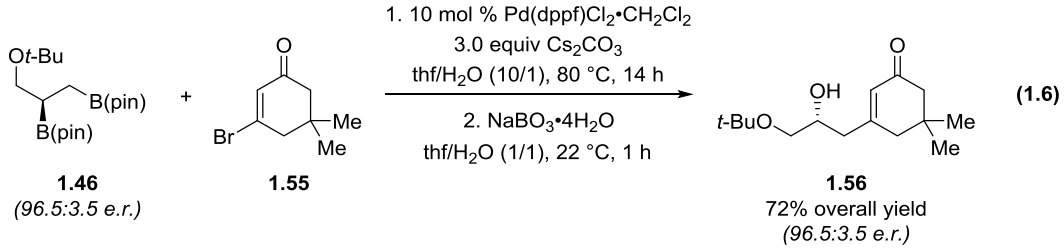



**1.53**

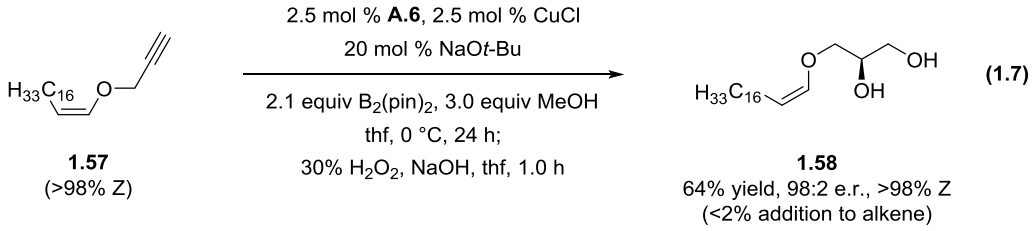
**1.54**
69% yield, 94.5:5.5 e.r.
(<2% addition to alkene)

### *1.3.4. Functionalization of Enantiomerically Enriched Vicinal Diborons and Utility in Chemical Synthesis*

The enantiomerically enriched vicinal diborons obtained through the present method are versatile, providing access to other useful molecules since functionalization of C–B bonds is already well developed. 1,2-Diboron compound has two distinctive C–B bonds (primary and secondary), which can be independently functionalized. Pd-catalyzed selective cross-coupling of *in situ* generated diboron catechol ester with aryl halides was reported by Morken and coworkers.[13a] In their work, they obtained sterically less hindered, primary C–B bond coupled only product selectively. They only showed, however, aryl halides as a cross partner, and alkenyl halides have not been studied. Thus, we investigate the development of site selective cross coupling of vicinal diboron compound with alkenyl halides. As demonstrated in eq 1.6, with 10 mol % of $Pd(dppf)Cl_2$ and 3 equiv. of $Cs_2CO_3$, cross-coupling reaction of enantiomerically enriched vicinal diboron **1.46** (96.5:3.5 e.r.) and commercially available alkenyl bromide **1.55** is performed, generating desired primary C–B bond only coupled product **1.56** in 72% yield after oxidative work-up without loss of enantiomeric purity (96.5:3.5 e.r. for **1.56**).




Moreover, the utility of NHC–Cu-catalyzed enantioselective double protoborations of terminal alkyne has been demonstrated by one of colleagues in our group.[20] *Z*-Alkenyl ether-bearing 1,2-diol **1.58** is obtained in 64% overall yield and 98:2 e.r. after oxidation (<2% reaction of alkene) through Cu-catalyzed diprotoboration of corresponding terminal alkyne containing Z-olefin **1.57** in the presence of 2.5 mol % of NHC−Cu complex derived from **A.6** without loss of olefin stereochemistry (high chemoselectivity; eq 1.7). Optically active diol **1.58** has been used further for the stereoselective synthesis of an anti-oxidant plasmalogen phospholipid C18 (plasm)-16:0 (PC).




## *1.4. Conclusions*

We have developed an efficient and enantioselective NHC–Cu-catalyzed double protoboryl addition to various terminal alkynes with readily accessible $B_2(pin)_2$ and MeOH to afford vicinal diboron compounds in up to 93% yield with high enantioselectivity (93.5:6.5–97.5:2.5 e.r.). In a single-vessel, two reactions occurred; (1) a

(20) Meek, S. J.; O'Brien, R. V.; Llaveria, J.; Schrock, R. R.; Hoveyda, A. H. *Nature* **2011**, *471*, 461–466.

site-selective protoboration of terminal alkynes to afford alkenylboron, (2) a site- and enantioselective protoboration of the derived alkenylboron to generate enantiomerically enriched vicinal diboron compound. Various functional group-bearing alkynes are investigated, delivering desired vicinal diborons with high efficiency and selectivity.

The site selectivity for the first protoboration is reversed by altering the NHC–Cu complexes. With *N*-mesityl-bearing NHC–Cu complex, unusual α-selectivity is observed, which forms internal alkenylboron preferentially. In addition, catalytic process of the molecule containing both alkene and alkyne generates 1,2-diboron compound with exceptional site selectivity (<2% alkene addition) and high enantioselecitvity (94.5:5.5 e.r.). Moreover, selective functionalization of primary C–B bond of vicinal diboron is illustrated; Pd-catalyzed cross-coupling with alkenyl bromide followed by oxidation generates the primary C–B bond coupled only product in 72% yield without diminution of enantiomeric enrichment.

## *1.5. Experimentals*

**General.** Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, $\lambda_{max}$ in $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). $^{1}H$ NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet app = apparent), and coupling constants (Hz). $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Elemental microanalyses were performed at Robertson Microlit Laboratories (Madison, NJ). Enantiomeric ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralcel OD (4.6 x 250 mm), Chiral Technologies Chiralcel OB-H (4.6 x 250 mm), Chiral Technologies Chiralcel OJ-H (4.6 x 250 mm), or Chiral Technologies Chiralpak AS (4.6 x 250 mm)) in comparison with authentic racemic materials. Optical rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry $N_2$ in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Dichloromethane (Fisher Scientific, Inc.) was purified by being passed

through two alumina columns under a positive pressure of dry argon by a modified Innovative Technologies purification system. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over $CaH_2$. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Doe & Ingalls) under air.

### *1.5.1. Reagents and Ligands*

**Benzoyl Chloride:** purchased from Aldrich Chemical Co. and used as received.

**Bis(pinacolato)diboron:** purchased from Frontier Scientific, Inc. and recrystallized from pentane.

***N*-Boc-propargylamine (1.47):** purchased from Aldrich Chemical Co. and purified by flash silica gel chromatography (hexanes:EtOAc = 10:1).

**3-Bromo-5,5-dimethylcyclohex-2-enone (1.55):** prepared according to previously reported procedures.[21]

**6-*tert*-Butoxyhex-1-yne:** prepared according to a previously reported procedure.[22]

**3-*tert*-Butoxyprop-1-yne (1.45):** prepared according to a previously reported procedure.[23]

***tert*-Butyl allyl(but-3-ynyl)carbamate (1.53):** prepared according to previously reported procedures.[24]

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(21) Mewshaw, R. E. *Tetrahedron Lett.* **1989**, *30*, 3753–3756.
(22) Mansurova, M.; Klusák, V.; Nešněrová, P.; Muck, A.; Doubský, J.; Svatoš, A. *Tetrahedron* **2009**, *65*, 1069–1076.
(23) Alexakis, A.; Gardette, M.; Colin, S. *Tetrahedron Lett.* **1988**, *29*, 2951–2954.
(24) Becker, D. P.; Flynn, D. L. *Tetrahedron* **1993**, *49*, 5047–5054.

***tert*-Butyl pent-4-ynylcarbamate:** prepared according to a previously reported procedure.[25]

**Cesium carbonate:** purchased from Aldrich Chemical Co. and used as received.

**5-Chloro-1-pentyne (1.35):** purchased from Aldrich Chemical Co. and purified by distillation over $CaCl_2$.

**Copper (I) chloride:** purchased from Aldrich Chemical Co. and used as received.

**Cu−NHC complex (1.29):** prepared according to previously reported procedures.[26]

**Cyclohexylacetylene:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ under reduced pressure.

**3-Cyclopentyl-1-propyne:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$.

**Dichloro 1,1'-bis(diphenylphosphino)ferrocene palladium (II) dichloromethane adduct:** purchased from Strem Chemicals Inc. and used as received.

**1-Hexyne:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$.

**Hydrogen peroxide (35 wt. % solution in water):** purchased from Aldrich Chemical Co. and used as received.

**Imidazolinium salt (A.1):** prepared according to previously reported procedures.[27]

**Imidazolinium salt (A.6):** prepared according to previously reported procedures.[28]

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(25) Saito, Y.; Matsumoto, K.; Bag, S. S.; Ogasawara, S.; Fujimoto, K.; Hanawa, K.; Saito, I. *Tetrahedron* **2008**, *64*, 3578–3588.
(26) Díez-González, S.; Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *J. Org. Chem*. **2005**, *70*, 4784–4796.
(27) (a) Chaulagain, M. R.; Sormunen, G. J.; Montgomery, J. *J. Am. Chem. Soc.* **2007**, *129*, 9568–9569. (b) Lillo, V.; Prieto, A.; Bonet, A.; Díaz-Requejo, M. M.; Ramírez, J.; Pérez, P. J.; Fernández, E. *Organometallics*, **2009**, 28, 659–662. (c) Lee, K-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74,* 4455–4462.
(28) (a) Brown, M. K.; May, T. L.; Baxter, C. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 1097–1100. (b) May, T. L.; Brown, M. K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7468–7472.

**Phenylacetylene:** purchased from Aldrich Chemical Co. and purified by distillation and passed through activated neutral alumina prior to use.

**3-Phenyl-1-propyne:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ under reduced pressure.

**Pyridine (anhydrous):** purchased from Aldrich Chemical Co. and used as received.

**Sodium *tert*-butoxide** (98%)**:** purchased from Strem Chemicals Inc. and used as received.

**Sodium perborate tetrahydrate:** purchased from Aldrich Chemical Co. and used as received.

### *1.5.2. Experimental Procedure and Characterization Data*

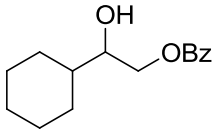
■ **Representative Experimental Procedure for Enantioselective Cu-Catalyzed Double Protoborations of 6-*tert*-Butoxyhex-1-yne:** In a $N_2$-filled glovebox, an oven-dried vial (4 mL, 17 x 38 mm) with magnetic stir bar was charged with imidazolinium salt **A.6** (5.80 mg, 0.0100 mmol, 5.0 mol %), CuCl (1.00 mg, 0.0100 mmol, 5.0 mol %), NaO*t*-Bu (3.80 mg, 0.0400 mmol, 20 mol %)[29] and thf (0.5 mL). The mixture was sealed with a cap (phenolic open top cap with red PTFE/white silicone) and allowed to stir for 30 min. Bis(pinacolato)diboron (107 mg, 0.420 mmol, 2.1 equiv.) was added to the solution. The color of the solution immediately turned dark brown. The vial was resealed with a cap (phenolic open top cap with red PTFE/white silicone) and removed from the glovebox. After 30 min, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) under $N_2$ atm. A solution of 6-*tert*-butoxyhex-1-yne (30.8 mg, 0.200 mmol, 1.0 equiv.) in thf (0.3 mL) and MeOH (24.0 μL, 0.600 mmol, 3.0 equiv.) were added by syringes. The

(29) Since NaO*t*-Bu does not promote protoboration, four equivalents of NaO*t*-Bu per CuCl are used for reproducible conversions to afford the desired diborons.

vial was transferred to a –30 °C cryocool. After 48 h, the solution was allowed to cool to –78 °C and quenched by passing through a short plug of celite and silica gel and washed with $Et_2O$ (3 x 2 mL). The filtrate was concentrated *in vacuo* to provide dark brown oil, which was purified by silica gel column chromatography (hexanes:EtOAc=10:1) to afford the desired product **1.39** as a colorless oil (60.5 mg, 0.147 mmol, 74% yield).

■ **Representative Experimental Procedure for Oxidation[30]/Monobenzoylation of Diboron 1.42 to Determine the Enantiomeric Purity:**

**1-Cyclohexylethane-1,2-diol.** To a solution of **1.42** (163 mg, 0.447 mmol) in thf (1 mL) at 0 °C (ice bath) were added $H_2O_2$ (217 μL, 2.23 mmol) and 2 N NaOH (1.12 mL, 2.23 mmol). The resulting solution was allowed to stir for 20 min. After this time, the mixture was diluted with water (2 mL), washed with EtOAc (3 x 1 mL), and filtered through a plug of $MgSO_4$. The filtrate was concentrated *in vacuo* to provide colorless oil, which was purified by silica gel chromatography (hexanes:EtOAc=1:2) to afford the derived diol as a colorless oil (62.1 mg, 0.430 mmol, 96% yield). (This compound has been previously reported and spectra data match those described).[31] $^1$H NMR (400 MHz, $CDCl_3$): δ 3.65 (1H, m), 3.47 (1H, m), 3.39 (1H, t, *J* = 7.2 Hz), 2.95 (2H, s), 1.86–1.80 (1H, m), 1.74–1.67 (2H, m), 1.64–1.58 (2H, m), 1.40–1.31 (1H, m), 1.25–0.95 (5H, m); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 76.6, 64.8, 40.8, 29.0, 28.7, 26.4, 26.1, 26.1.

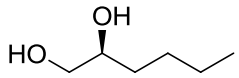



**2-Cyclohexyl-2-hydroxyethyl benzoate.** To a solution of diol (24 mg, 0.17 mmol) in $CH_2Cl_2$ (1 mL) were added pyridine (27 μL, 0.33 mmol)

(30) Oxidation of diborons could be carried out in the presence of $NaBO_3$•$4H_2O$. See: Lee, J.-E.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 145–147.
(31) Miller, S. P.; Morgan, J. B.; Nepveux V, F. J.; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133.

and benzoyl chloride (25 μL, 0.21 mmol). The resulting mixture was allowed to stir at 22 °C for 1 hour. After this time, the mixture was quenched through the addition of a saturated aqueous solution of $NH_4Cl$ (2 mL), washed with $CH_2Cl_2$ (3 x 1 mL), and filtered through a plug of $MgSO_4$. The filtrate was concentrated *in vacuo* to provide a colorless oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=3:1) to afford the monobenzoyl alcohol as a white solid (28 mg, 0.11 mmol, 68% yield). mp: 65 °C; IR (neat): 3480 (br), 2923 (m), 2851 (w), 1717 (m), 1701 (m), 1449 (m), 1268 (s), 1176 (w), 1115 (m), 1096 (m), 1068 (m), 1025 (m), 708 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 8.06–8.03 (2H, m), 7.59–7.54 (1H, m), 7.46–7.41 (2H, m), 4.46 (1H, dd, *J* = 11.6, 3.2 Hz), 4.29 (1H, dd, *J* = 11.6, 7.6 Hz), 3.76–3.71 (1H, m), 2.26 (1H, br s), 1.93–1.90 (1H, m), 1.80–1.66 (4H, m), 1.58–1.49 (1H, m), 1.32–1.07 (5H, m); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 166.9, 133.2, 130.0, 129.7, 128.5, 74.3, 67.9, 41.1, 29.0, 28.3, 26.4, 26.2, 26.1; HRMS ($ESI^+$): Calcd for $C_{15}H_{21}O_3$ $[M+H]^+$: 249.14907, Found: 249.14860.

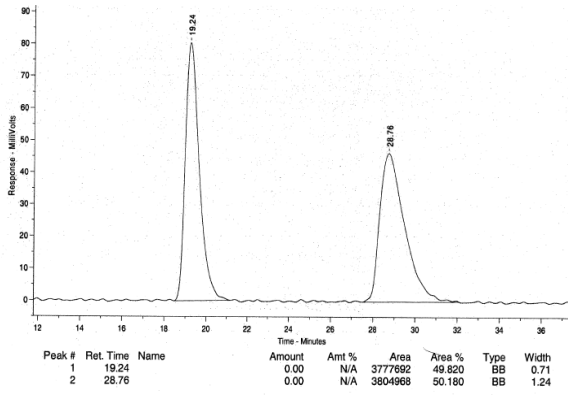
**(*R*)-2,2'-(Hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.34).** IR (neat): 2977 (w), 2925 (w), 2858 (w), 1369 (s), 1309 (s), 1271 (w), 1249 (w), 1229 (w), 1139 (s), 967 (m), 845 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 1.45–1.36 (1H, m), 1.33–1.23 (5H, m), 1.21 (6H, s), 1.21 (6H, s), 1.20 (6H, s), 1.20 (6H, s), 1.12–1.04 (1H, m), 0.85 (1H, dd, *J* = 15.6, 9.6 Hz), 0.84 (3H, t, *J* = 6.8 Hz), 0.77 (1H, dd, *J* = 15.6, 6.0 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 82.8, 82.8, 33.6, 31.2, 25.0, 24.9, 24.8, 24.8, 23.0, 18.5, 14.2, 12.8; HRMS ($ESI^+$): Calcd for $C_{18}H_{37}B_2O_4$ $[M+H]^+$: 339.28779, Found: 339.28856. Elemental Analysis: Calcd for $C_{18}H_{36}B_2O_4$: C, 63.94; H, 10.73; Found: C, 64.21; H, 11.00. Specific Rotation: $[\alpha]_D^{20}$ +0.47 (*c* 2.38, $CHCl_3$) for an enantiomerically enriched sample of 95.5:4.5 e.r.

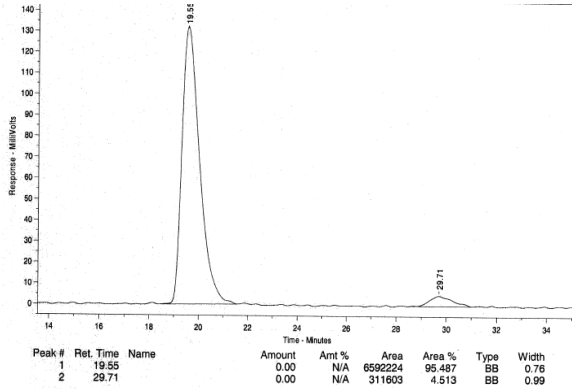


**(*S*)-Hexane-1,2-diol** (**Oxidation of 1.34**, This compound has been previously reported and spectra data match those described).[32] $^1$H NMR (400 MHz, $CDCl_3$): δ 3.69–3.63 (1H, m), 3.60 (1H, dd, *J* = 11.2, 2.8 Hz), 3.39 (1H, dd, *J* = 11.2, 8.0 Hz), 3.24 (2H, s), 1.44–1.24 (6H, m), 0.88 (3H, t, *J* = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 72.4, 66.8, 32.9, 27.8, 22.8, 14.1. Specific Rotation: $[\alpha]_D^{20}$ –9.21 (*c* 0.73, EtOH) for an enantiomerically enriched sample of 95.5:4.5 e.r.

**Proof of Stereochemistry:** Literature value ($[\alpha]_D^{20}$ –22.1 (*c* 1.00, EtOH), >99:1 e.r.) is assigned to the (*S*) enantiomer.[32a]

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralpak AS column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 19.24 | 3777692 | 49.820 |
| 2 | 28.76 | 3804968 | 50.180 |

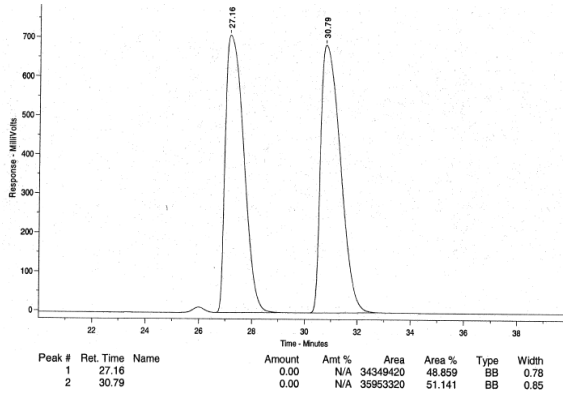
| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 19.55 | 6592224 | 95.487 |
| 2 | 29.71 | 311603 | 4.513 |

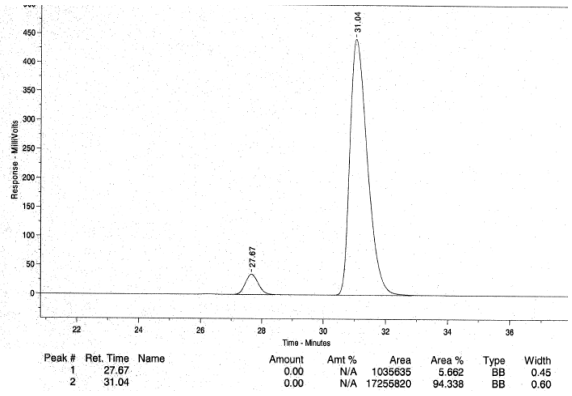
**(*R*)-2,2'-(5-Chloropentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.36).** IR (neat): 2977 (w), 2929 (w), 1459 (w), 1369 (s), 1310 (s), 1267 (m), 1139 (s), 967 (m), 860 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.47 (2H, dt, *J* = 6.8, 1.6 Hz),

(32) (a) Hasegawa, J.; Ogura, M.; Tsuda, S.; Maemoto, S.; Kutsuki, H.; Ohashi, T. *Agric. Biol. Chem.* **1990**, *54*, 1819. (b) Brown, S. P.; Brochu, M. P.; Sinz, C. J.; MacMillan, D. W. *J. Am. Chem. Soc.* **2003**, *125*, 10808–10809.

1.79–1.72 (2H, m), 1.57–1.49 (1H, m), 1.48–1.35 (1H, m), 1.20 (6H, s), 1.20 (6H, s), 1.20 (6H, s), 1.19 (6H, s), 1.12–1.04 (1H, m), 0.89–0.79 (2H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 83.0, 45.4, 32.1, 31.0, 24.9, 24.9, 24.8, 24.8, 17.8, 12.8; HRMS ($ESI^+$): Calcd for $C_{17}H_{34}B_2Cl_1O_4$ $[M+H]^+$: 359.23317, Found: 359.23455. Elemental Analysis: Calcd for $C_{17}H_{33}B_2Cl_1O_4$: C, 56.95; H, 9.28; Found: C, 57.22; H, 9.54. Specific Rotation: $[\alpha]_D^{20}$ –1.45 (*c* 3.30, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralcel OJ-H column, 92:8 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



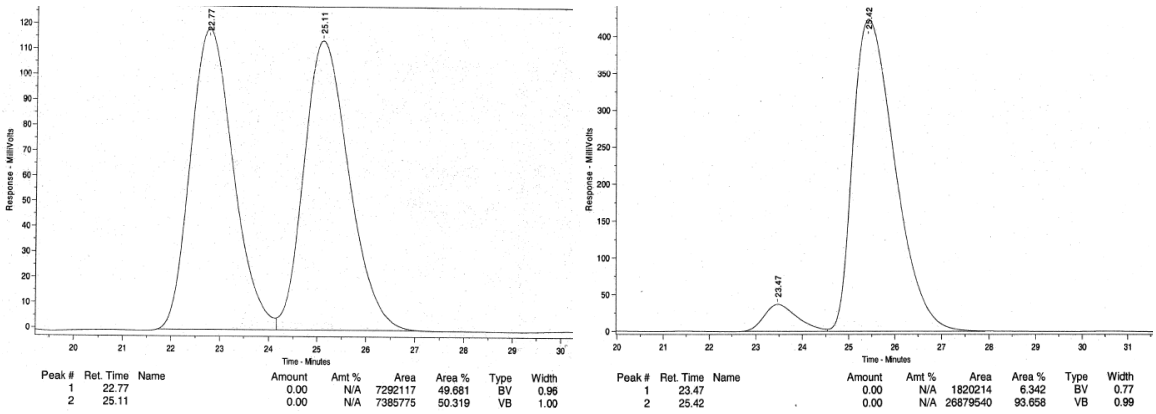

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 27.16 | 34349420 | 48.859 |
| 2 | 30.79 | 35953320 | 51.141 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 27.67 | 1035635 | 5.662 |
| 2 | 31.04 | 17255820 | 94.338 |

**(*R*)-*tert*-Butyl 4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentylcarbamate (1.37)**. IR (neat): 3370 (br), 2977 (m), 2929 (w), 1703 (m), 1512 (m), 1366 (s), 1311 (s), 1270 (m), 1248 (m), 1215 (m), 1165 (s), 1139 (s), 967 (m), 846 (m), 732 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.67 (1H, br s), 3.07 (2H, s), 1.46–1.43 (2H, m), 1.41 (9H, s), 1.38–1.29 (1H, m), 1.21 (24H, s), 1.13–1.04 (2H, m), 0.86 (1H, dd, *J* = 16.0, 9.2 Hz), 0.76 (1H, dd, *J* = 15.6, 6.4 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 156.1, 83.0, 83.0, 78.7, 40.7, 30.6, 28.6, 25.1, 25.0, 25.0, 24.9, 24.9, 18.1, 12.7; HRMS ($ESI^+$): Calcd for

$C_{22}H_{44}B_2N_1O_6$ $[M+H]^+$: 440.33547, Found: 440.33376. Specific Rotation: $[\alpha]_D^{20}$ –3.82 (*c* 2.09, $CHCl_3$) for an enantiomerically enriched sample of 93.5:6.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived tri-Boc protected derivative, which was prepared by monobenzoylation of the diol, followed by Boc-protection with $Boc_2O$ (Chiralpak OD column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

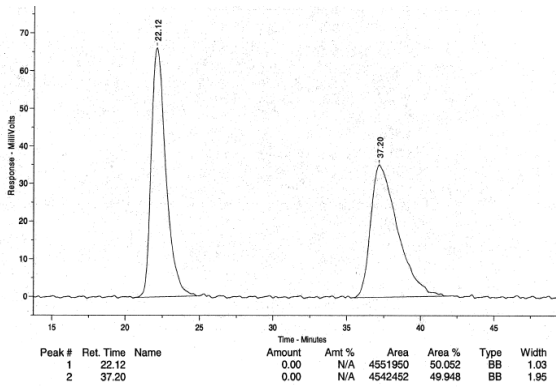



| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 22.77 | 7292117 | 49.681 |
| 2 | 25.11 | 7385775 | 50.319 |

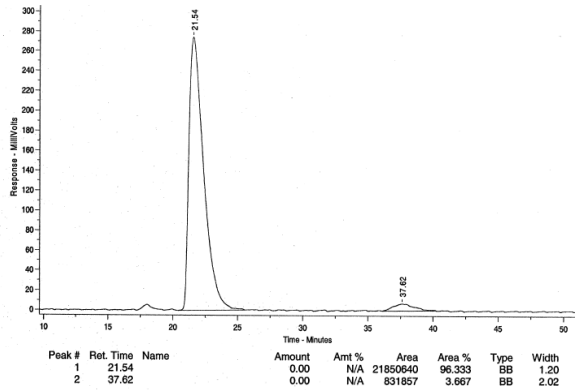
| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 23.47 | 1820214 | 6.342 |
| 2 | 25.42 | 26879540 | 93.658 |

**(*R*)-2,2'-(6-*tert*-Butoxyhexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.39).** IR (neat): 2975 (m), 2930 (w), 2864 (w), 1361 (s), 1310 (s), 1268 (w), 1231 (w), 1198 (s), 1140 (m), 1080 (m), 967 (m), 845 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 3.27 (2H, t, *J* = 6.4 Hz), 1.49–1.40 (3H, m), 1.35–1.23 (3H, m), 1.21 (12H, s), 1.19 (12H, s), 1.13 (9H, s), 1.10–1.03 (1H, m), 0.83 (1H, dd, *J* = 15.6, 9.6 Hz), 0.76 (1H, dd, *J* = 15.6, 6.0 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 82.8, 82.8, 72.3, 61.6, 33.7, 31.0, 27.6, 25.6, 24.9, 24.9, 24.8, 24.8, 18.5, 12.7; HRMS ($ESI^+$): Calcd for $C_{22}H_{45}B_2O_5$ $[M+H]^+$: 411.34531, Found: 411.34620. Elemental Analysis: Calcd for $C_{22}H_{44}B_2O_5$: C, 64.42; H, 10.81; Found: C, 64.68; H, 11.07. Specific Rotation: $[\alpha]_D^{20}$ –0.51 (*c* 2.15, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralpak AS column, 99/1 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).



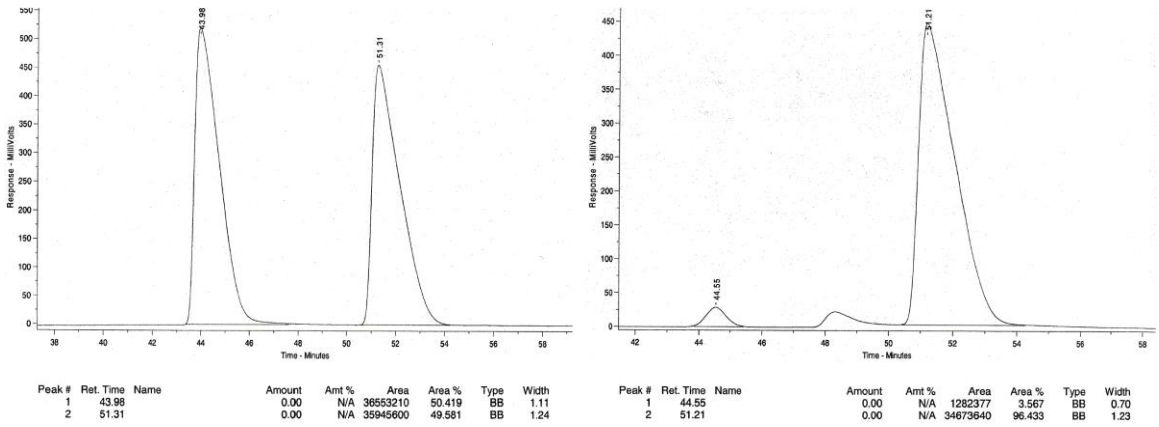

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 22.12 | 4551950 | 50.052 |
| 2 | 37.20 | 4542452 | 49.948 |




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 21.54 | 21850640 | 96.333 |
| 2 | 37.62 | 831857 | 3.667 |

**(*R*)-2-(3-Cyclopentyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)-4,4,5,5-tetra-methyl-1,3,2-dioxaborolane (1.40).** IR (neat): 2977 (m), 2946 (m), 2867 (w), 1369 (s), 1309 (s), 1268 (m), 1213 (m), 1139 (s), 967 (m), 847 (m), 671 (w), 578 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 1.83–1.76 (1H, m), 1.76–1.67 (2H, m), 1.57–1.42 (5H, m), 1.31–1.26 (1H, m), 1.23 (12H, s), 1.21 (12H, s), 1.17–1.12 (1H, m), 1.08–1.00 (2H, m), 0.85 (1H, dd, $J$ = 16.0, 8.4 Hz), 0.81 (1H, dd, $J$ = 15.6, 6.4 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 82.9, 82.8, 40.3, 39.4, 32.9, 32.9, 25.4, 25.2, 25.0, 24.9, 24.9, 24.9, 17.5, 13.2; HRMS ($ESI^+$): Calcd for $C_{20}H_{39}B_2O_4$ $[M+H]^+$: 365.30344, Found: 365.30443. Elemental Analysis: Calcd for $C_{20}H_{38}B_2O_4$: C, 65.97; H, 10.52; Found: C, 65.99; H, 10.78. Specific Rotation: $[\alpha]_D^{20}$ –3.09 (*c* 2.00, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

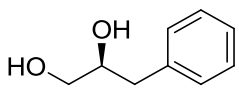
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralpak OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 43.98 | 36553210 | 50.419 |
| 2 | 51.31 | 35945600 | 49.581 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 44.55 | 1282377 | 3.567 |
| 2 | 51.21 | 34673640 | 96.433 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)-1,3,2-dioxaborolane (1.41).** IR (neat): 2977 (m), 2928 (w), 1369 (s), 1311 (s), 1269 (m), 1214 (m), 1139 (s), 967 (m), 846 (m), 698 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.24–7.17 (4H, m), 7.13–7.09 (1H, m), 2.79 (1H, dd, *J* = 13.2, 7.6 Hz), 2.59 (1H, dd, *J* = 13.2, 8.0 Hz), 1.47–1.43 (1H, m), 1.21 (12H, s), 1.17 (6H, s), 1.15 (6H, s), 0.81 (2H, d, *J* = 7.6 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 142.4, 129.2, 128.0, 125.6, 83.0, 82.9, 39.6, 25.0, 24.9, 24.9, 24.8 20.7, 12.4; HRMS ($ESI^+$): Calcd for $C_{21}H_{35}B_2O_4$ $[M+H]^+$: 373.27214, Found: 373.27372. Elemental Analysis: Calcd for $C_{21}H_{34}B_2O_4$: C, 67.78; H, 9.21; Found: C, 68.03; H, 9.58. Specific Rotation: $[\alpha]_D^{20}$ +6.48 (*c* 2.00, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

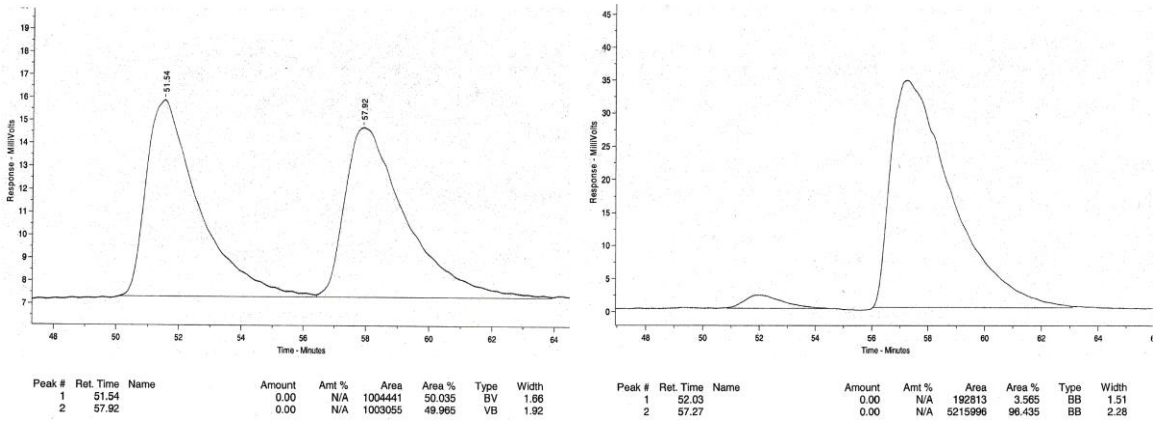



**(*S*)-3-Phenylpropane-1,2-diol** (**Oxidation of 1.41**, This compound has been previously reported and spectra data match those

described).[33] $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.33–7.29 (2H, m), 7.26–7.21 (3H, m), 3.96–3.91 (1H, m), 3.67 (1H, dd, *J* = 11.2, 3.2 Hz), 3.50 (1H, dd, *J* = 11.2, 6.8 Hz), 2.79 (1H, dd, *J* = 13.6, 5.6 Hz), 2.74 (1H, dd, *J* = 13.6, 8.0 Hz), 2.22 (2H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 137.9, 129.5, 128.8, 126.8, 73.2, 66.2, 40.0. Specific Rotation: $[\alpha]_D^{20}$ –13.4 (*c* 1.81, EtOH) for an enantiomerically enriched sample of 95:5 e.r.

**Proof of Stereochemistry:** Literature value ($[\alpha]_D^{20}$ +33.2 (*c* 1.00, EtOH), 97.5:2.5 e.r.) is assigned to the (*R*) enantiomer.[33]

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived diol (Chiralpak OD-R column, 98/2 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 51.54 | 1004441 | 50.035 |
| 2 | 57.92 | 1003055 | 49.965 |

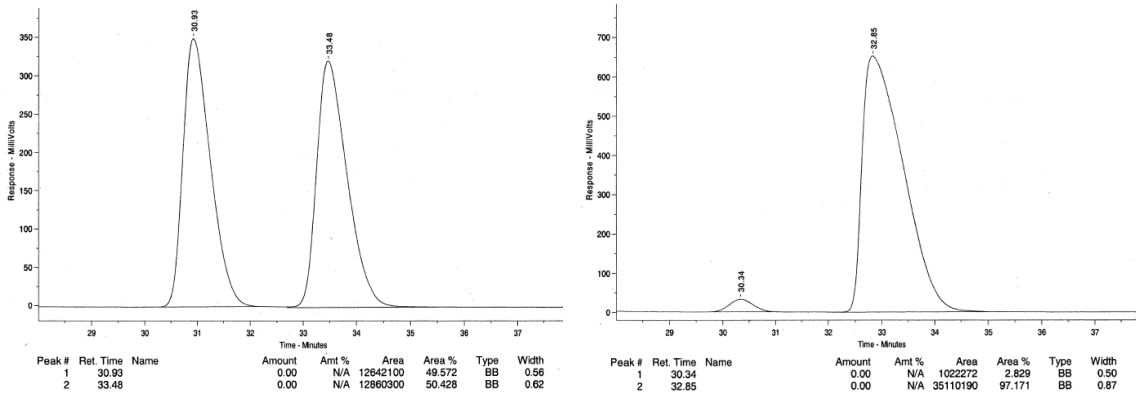
| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 52.03 | 192813 | 3.0565 |
| 2 | 57.27 | 5215996 | 96.435 |

**(*R*)-2,2'-(1-Cyclohexylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.42).** IR (neat): 2977 (w), 2921 (w), 2850 (w), 1368 (s), 1307 (s), 1271 (w), 1237 (w), 1214 (w), 1140 (s), 1105 (w), 969 (m), 845 (m) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 1.68–1.57 (5H, m), 1.37–1.26 (1H, m), 1.23 (12H, s), 1.22 (12H, s), 1.20–0.95 (6H, m),

(33) Cardillo, G.; Orena, M.; Romero, M.; Sandri, S. *Tetrahedron* **1989**, *45*, 1501–1508.

0.86 (1H, dd, $J$ = 16.0, 11.2 Hz), 0.76 (1H, dd, $J$ = 15.6, 5.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 82.8, 82.8, 41.6, 32.2, 32.0, 27.0, 26.9, 26.8, 25.0, 25.0, 24.9, 24.8, 9.6; HRMS ($ESI^+$): Calcd for $C_{20}H_{39}B_2O_4$ $[M+H]^+$: 365.30344, Found: 365.30358. Elemental Analysis: Calcd for $C_{20}H_{38}B_2O_4$: C, 65.97; H, 10.52; Found: C, 66.33; H, 10.92. Specific Rotation: $[\alpha]_D^{20}$ –4.73 (*c* 2.44, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralcel OJ-H column, 98/2 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).

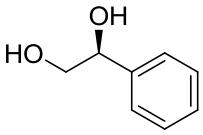



| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 30.93 | 12642100 | 49.572 |
| 2 | 33.48 | 12860300 | 50.428 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 30.34 | 1022272 | 2.829 |
| 2 | 32.85 | 35110190 | 97.171 |

**(*R*)-2,2'-(1-Phenylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.43)**. IR (neat): 2977 (w), 2929 (w), 1492 (w), 1467 (w), 1354 (s), 1313 (s), 1264 (m), 1213 (m), 1164 (m), 1139 (s), 966 (m), 843 (m), 731 (m), 699 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.20 (4H, d, $J$ = 4.0 Hz), 7.10–7.05 (1H, m), 2.50 (1H, dd, $J$ = 11.2, 5.6 Hz), 1.36 (1H, dd, $J$ = 16.0, 10.8 Hz), 1.18 (12H, s), 1.17 (6H, s), 1.15 (6H, s), 1.09 (1H, dd, $J$ = 15.6, 6.0 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 145.5, 128.2, 128.0, 125.0, 83.2, 83.1, 26.7, 25.0, 24.8, 24.7, 24.5, 14.6; HRMS ($ESI^+$): Calcd for $C_{20}H_{33}B_2O_4$ $[M+H]^+$:

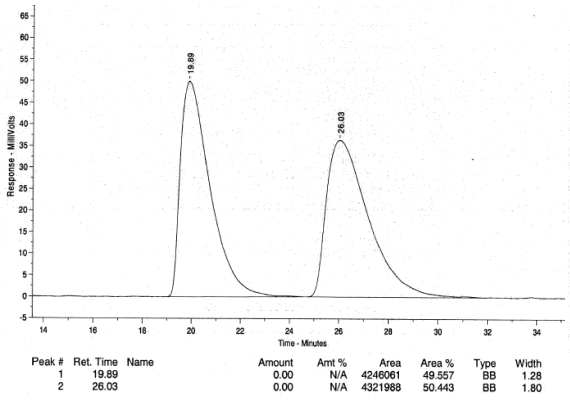
359.25649, Found: 359.25766. Elemental Analysis: Calcd for $C_{20}H_{32}B_2O_4$: C, 67.08; H, 9.01; Found: C, 67.24; H, 9.27. Specific Rotation: $[\alpha]_D^{20}$ –24.2 (*c* 2.80, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

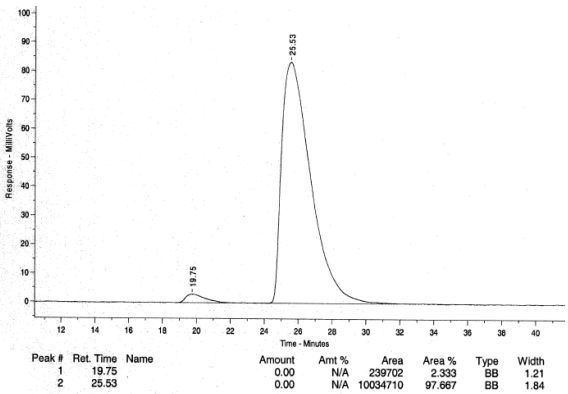


**(*S*)-1-Phenylethane-1,2-diol** (**Oxidation of 1.43**, This compound has been previously reported and spectra data match those described).[34] $^1$H NMR (400 MHz, $CDCl_3$): δ 7.38–7.26 (5H, m), 4.84 (1H, dt, *J* = 8.4, 3.2 Hz), 3.78 (1H, ddd, *J* = 11.2, 7.6, 4.0 Hz), 3.68 (1H, ddd, *J* = 11.2, 8.0, 4.4 Hz), 2.43 (1H, d, *J* = 3.2 Hz), 1.97 (1H, dd, *J* = 7.6, 4.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.6, 128.5, 128.0, 126.1, 74.7, 68.1. Specific Rotation: $[\alpha]_D^{20}$ +68.1 (*c* 0.50, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

**Proof of Stereochemistry:** Literature value ($[\alpha]_D^{20}$ –63.7 (*c* 5.45, $CDCl_3$), >99:1 e.r.) is assigned to the (*R*) enantiomer.[35]

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived diol (Chiralcel OB-H column, 93/7 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



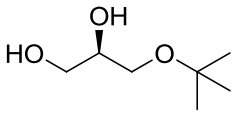




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 19.89 | 4246061 | 49.557 |
| 2 | 26.03 | 4321988 | 50.443 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 19.75 | 239702 | 2.333 |
| 2 | 25.53 | 10034710 | 97.667 |

(34) Miller, S. P.; Morgan, J. B.; Nepveux V, F. J.; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133.
(35) Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1970**, *35*, 4002–4003.

**(*R*)-2-(3-*tert*-Butoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)-4,4,5,5-tetra-methyl-1,3,2-dioxaborolane (1.46).** IR (neat): 2975 (m), 1366 (s), 1311 (s), 1199 (m), 1141 (s), 1075 (m), 968 (m), 846 (m), 734 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 3.37 (1H, dd, *J* = 8.0, 6.4 Hz), 3.32 (1H, dd, *J* = 8.0, 7.6 Hz), 1.37–1.32 (1H, m), 1.22 (12H, s), 1.20 (12H, s), 1.13 (9H, s), 0.92 (1H, dd, *J* = 16.0, 9.2 Hz), 0.84 (1H, dd, *J* = 16.0, 5.6 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 82.9, 82.8, 72.1, 65.0, 27.7, 25.0, 24.9, 20.5, 9.7; HRMS ($ESI^+$): Calcd for $C_{19}H_{39}B_2O_5$ $[M+H]^+$: 369.29836, Found: 369.30005. Specific Rotation: $[\alpha]_D^{20}$ +3.85 (*c* 2.41, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.




**(*R*)-3-*tert*-Butoxypropane-1,2-diol** (**Oxidation of 1.46**, This compound has been previously reported and spectra data match those described).[36] $^1H$ NMR (400 MHz, $CDCl_3$): δ 3.79 (1H, m), 3.72–3.66 (2H, m), 3.50 (1H, dd, *J* = 9.2, 4.0 Hz), 3.45 (1H, dd, *J* = 9.2, 5.6 Hz), 2.69 (1H, br s), 2.34 (1H, br s), 1.20 (9H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 73.7, 70.6, 64.7, 64.0, 27.6. Specific Rotation: $[\alpha]_D^{20}$ +8.5 (*c* 0.20, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

**Proof of Stereochemistry:** Literature value ($[\alpha]_D^{20}$ –1.00 (*c* 0.76, $CHCl_3$), 87:13 e.r.) is assigned to the (*S*) enantiomer.[36a]

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralpak AS column, 99.5/0.5 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).

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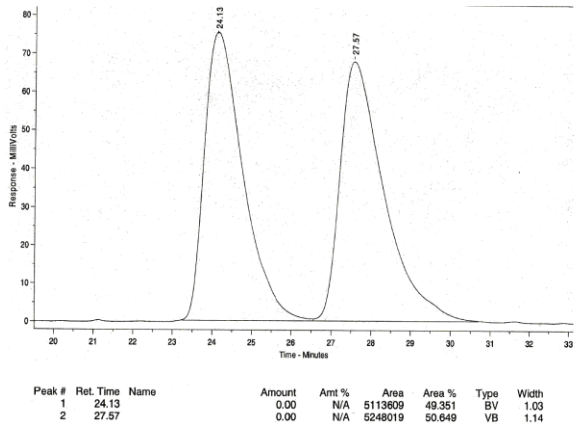
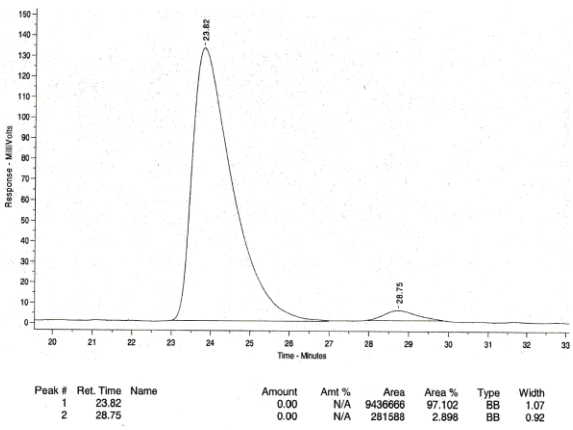
(36) (a) Zhao, Y.; Mitra, A. W.; Hoveyda, A. H.; Snapper, M. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8471–8474. (b) Verheij, H. M.; Bonsen, P. P. M.; van Deenen, L. L. M. *Chem. Phys. Lipids*. **1971**, *6*, 46–57.



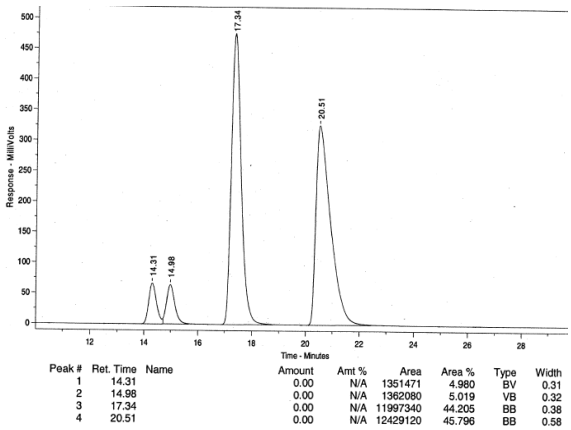



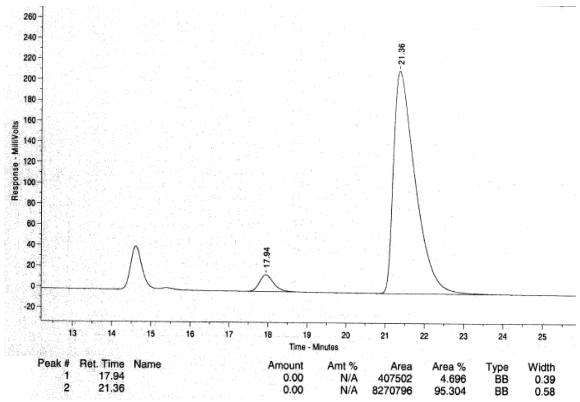

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 24.13 | 5113609 | 49.351 |
| 2 | 27.57 | 5248019 | 50.649 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 23.82 | 9436666 | 97.102 |
| 2 | 28.75 | 281588 | 2.898 |

**(*R*)-*tert*-Butyl 2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propylcarbamate (1.48)**. IR (neat): 3379 (w), 2977 (w), 2930 (w), 1713 (m), 1506 (w), 1365 (m), 1313 (m), 1247 (m), 1212 (w), 1165 (m), 1139 (s), 1109 (w), 966 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 4.92 (1H, s), 3.13 (2H, dd, $J$ = 6.4, 5.6 Hz), 1.37 (9H, s), 1.31–1.21 (1H, m), 1.18 (12H, s), 1.18 (12H, s), 0.84 (1H, dd, $J$ = 16.4, 8.4 Hz), 0.77 (1H, dd, $J$ = 16.0, 6.4 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 156.1, 83.3, 83.2, 78.6, 43.9, 28.6, 25.0, 24.9, 19.4, 10.5; HRMS ($ESI^+$): Calcd for $C_{20}H_{40}B_2N_1O_6$ $[M+H]^+$: 412.30417, Found: 412.30305. Specific Rotation: $[\alpha]_D^{20}$ –1.28 (*c* 2.50, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralcel OJ-H column, 90/10 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Four peaks from two rotamers of the carbamate are shown below:




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 14.31 | 1351471 | 4.980 |
| 2 | 14.98 | 1362080 | 5.019 |
| 3 | 17.34 | 11997340 | 44.205 |
| 4 | 20.51 | 12429120 | 45.796 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 17.94 | 407502 | 4.696 |
| 2 | 21.36 | 8270796 | 95.304 |

**(*E*)-2-(3-*tert*-Butoxyprop-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**1.49,** This compound has been previously reported and spectra data match those described).[37] $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 6.64 (1H, dt, *J* = 18.0, 4.4 Hz), 5.69 (1H, dt, *J* = 18.0, 1.6 Hz), 3.95 (2H, dd, *J* = 4.8, 4.0 Hz), 1.22 (12H, s), 1.17 (9H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 151.0, 118.5, 83.1, 73.2, 63.8, 27.6, 24.8.

**2-(3-*tert*-Butoxyprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.50).** IR (neat): 2975 (m), 2871 (w), 1625 (w), 1364 (s), 1344 (s), 1307 (s), 1196 (m), 1142 (s), 1074 (s), 946 (m), 863 (m), 743 (w), 672 (w) $cm^{-1}$; $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 5.95–5.94 (1H, m), 5.86–5.85 (1H, m), 3.99–3.98 (2H, m), 1.24 (12H, s), 1.20 (9H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 139.5, 128.3, 83.4, 73.0, 63.3, 27.8, 24.9; HRMS ($ESI^+$): Calcd for $C_{13}H_{26}B_1O_3$ $[M+H]^+$: 241.18968, Found: 241.24772.

(37) Pandya, S. U.; Pinet, S. Chavant, P. Y.; Vallée, Y. *Eur. J. Org. Chem*. **2003**, 3621–3627.

**(*E*)-*tert*-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allylcarbamate (1.51,** This compound has been previously reported and spectra data match those described)**.**[38] IR (neat): 3357 (br), 2977 (w), 2931 (w), 1698 (m), 1643 (w), 1512 (m), 1364 (s), 1320 (s), 1269 (m), 1246 (m), 1165 (s), 1140 (s), 970 (m), 849 (m), 731 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 6.49 (1H, dt, *J* = 18.0, 4.4 Hz), 5.49 (1H, dt, *J* = 18.0, 2.0 Hz), 4.80 (1H, br s), 3.74 (2H, br s), 1.35 (9H, s), 1.17 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 155.8, 149.5, 118.4, 83.3, 79.3, 44.0, 28.4, 24.9, 24.8.

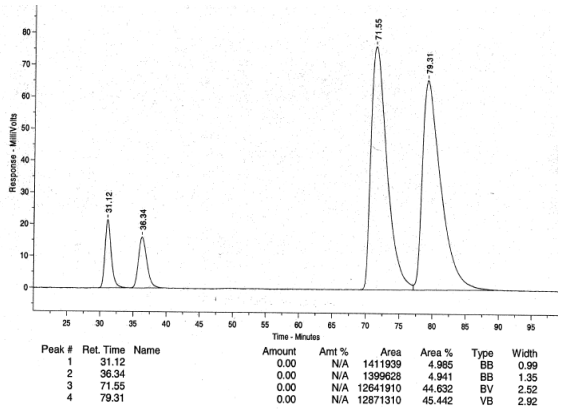
***tert*-Butyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allylcarbamate (1.52)**. IR (neat): 3358 (br), 2977 (m), 1705 (m), 1366 (m), 1311 (m), 1247 (m), 1140 (s), 1047 (w), 949 (m), 860 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.81 (1H, t, *J* = 1.4 Hz), 5.70 (1H, s), 4.80 (1H, s), 3.78 (2H, d, *J* = 4.4 Hz), 1.39 (9H, s), 1.21 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 155.9, 137.6, 129.1, 83.6, 78.9, 44.4, 28.4, 25.0, 24.8; HRMS ($ESI^+$): Calcd for $C_{14}H_{27}B_1N_1O_4$ $[M+H]^+$: 284.20331, Found: 284.20343.

**(*R*)-*tert*-Butyl allyl(2,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)carbamate (1.54)**. IR (neat): 2976 (w), 2929 (w), 1692 (s), 1643 (w), 1458 (w), 1405 (w), 1364 (s), 1314 (s), 1245 (s), 1163 (s), 1139 (s), 968 (w), 876 (w), 850 (w) $cm^{-1}$; $^1H$ NMR spectrum exists as a 10:1 mixture of rotamers. $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.74 (1H, m), 5.08 (2H, m), 3.89 (1H, br s), 3.76 (dd, *J* = 16.0, 5.6 Hz), 3.21 (2H, br s), 1.41–1.36 (10H, m), 1.20 (12H, s), 1.19 (12H, s), 0.79 (1H, dd, *J* = 6.0, 6.0 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 148.7, 134.5, 115.9, 83.3, 83.1, 83.0, 79.7, 49.2, 28.6, 25.0, 24.9, 18.2, 10.1; HRMS ($ESI^+$): Calcd for $C_{23}H_{44}B_2N_1O_6$ $[M+H]^+$: 452.33547, Found:

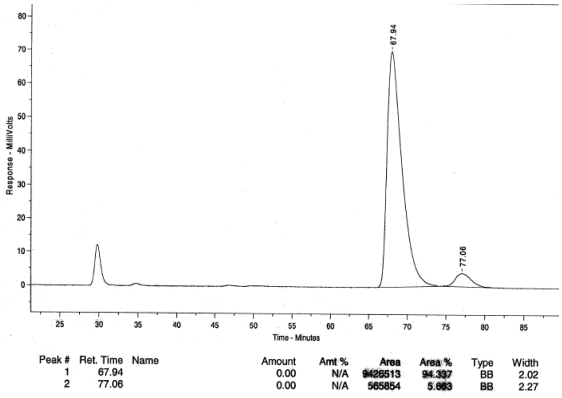
(38) Berrée, F.; Bleis, P. G-L.; Carboni, B. *Tetrahedron Lett.* **2002**, *43*, 4935–4938.

452.33386. Specific Rotation: $[\alpha]_D^{20}$ +5.80 (*c* 2.70, $CHCl_3$) for an enantiomerically enriched sample of 93.5:6.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived monobenzoyl-alcohol (Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm). Four peaks from two rotamers of the carbamate are shown below:




| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 31.12 | 1411939 | 4.985 |
| 2 | 36.34 | 1399628 | 4.941 |
| 3 | 71.55 | 12641910 | 44.632 |
| 4 | 79.31 | 12871310 | 45.442 |



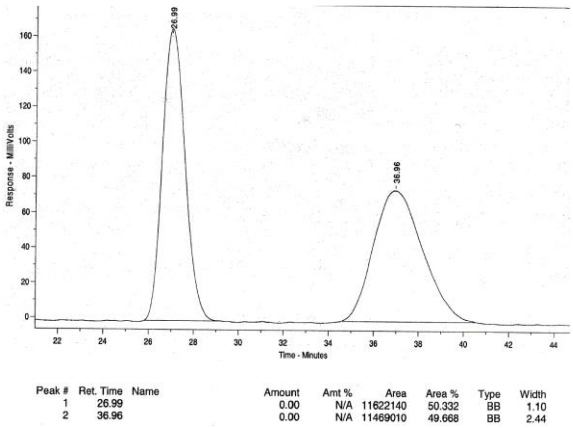

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 67.94 | 9426513 | 94.337 |
| 2 | 77.06 | 565854 | 5.663 |

■ **Experimental procedures for Pd-catalyzed cross-coupling:** To a flame-dried round bottom flask equipped with reflux condenser were added diboron **1.46** (50.0 mg, 0.135 mmol), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (9.80 mg, 0.0135 mmol, 10 mol %), $Cs_2CO_3$ (132 mg, 0.405 mmol, 3.0 equiv.) and 3-bromo-5,5-dimethylcyclohex-2-enone **1.55** (54.8 mg, 0.270 mmol, 2.0 equiv.). The vessel was purged under $N_2$ atm for 10 min. To the mixture were added thf (5 mL) and $H_2O$ (0.5 mL), which was allowed to stir at 80 °C for 14 h. After this time, the solution was allowed to cool to 22 °C, diluted with $Et_2O$ (10 mL), dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* to provide a bright red

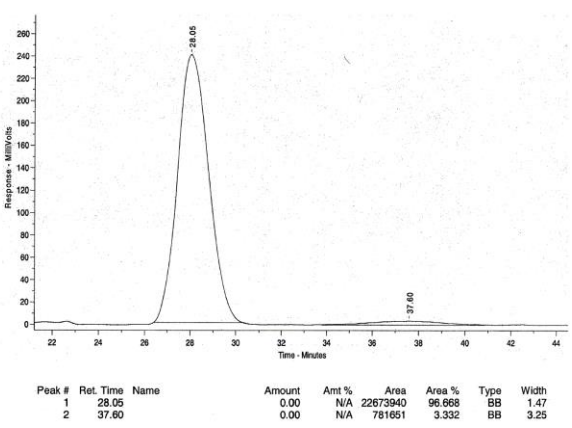
oil, which was purified by silica gel chromatography (hexanes:EtOAc=10:1) to afford the diboron product as a pale yellow oil (37.2 mg, 0.102 mmol, 76% yield). To a solution of diboron (37.2 mg, 0.102 mmol) in thf (1 mL) and $H_2O$ (1 mL) at 22 °C was added $NaBO_3 \cdot 4H_2O$ (78.5 mg, 0.511 mmol, 5.0 equiv.). The resulting solution was allowed to stir for one hour. After this time, the mixture was diluted with water (2 mL), washed with $Et_2O$ (3 x 1 mL), and filtered through a plug of $MgSO_4$. The filtrate was concentrated *in vacuo* to provide a colorless oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=3:1) to afford the desired product **1.56** as a colorless oil (24.8 mg, 0.0975 mmol, 95% yield).

**(*R*)-3-(3-*tert*-Butoxy-2-hydroxypropyl)-5,5-dimethylcyclohex-2-enone (1.56).** IR (neat): 3438 (br), 2972 (m), 2869 (w), 1656 (s), 1365 (s), 1194 (s), 1084 (s), 903 (m), 731 (s), 525 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.93 (1H, s), 3.92 (1H, m), 3.37 (1H, dd, $J$ = 8.8, 3.2 Hz), 3.21 (1H, dd, $J$ = 8.8, 7.2 Hz), 2.55 (1H, s), 2.36–2.33 (2H, m), 2.26 (2H, s), 2.21 (2H, s), 1.18 (9H, s), 1.03 (3H, s), 1.02 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 200.0, 160.6, 126.7, 73.6, 68.8, 65.5, 51.1, 44.3, 42.0, 33.8, 28.5, 28.3, 27.6; HRMS ($ESI^+$): Calcd for $C_{15}H_{27}O_3$ $[M+H]^+$: 255.19602, Found: 255.19701. Specific Rotation: $[\alpha]_D^{20}$ +0.635 (*c* 1.44, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralcel OJ-H column, 98/2 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).



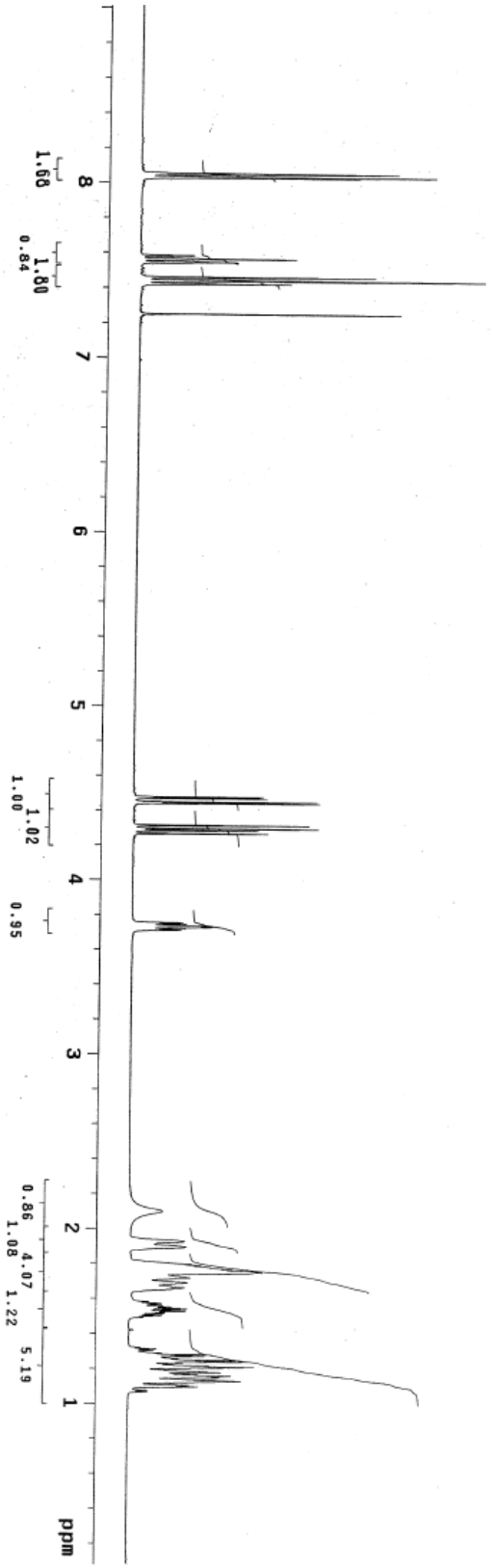

| Peak # | Ret. Time | Name | Amount | Amt % | Area | Area % | Type | Width |
|---|---|---|---|---|---|---|---|---|
| 1 | 26.99 | | 0.00 | N/A | 11622140 | 50.332 | BB | 1.10 |
| 2 | 36.96 | | 0.00 | N/A | 11469010 | 49.668 | BB | 2.44 |




| Peak # | Ret. Time | Name | Amount | Amt % | Area | Area % | Type | Width |
|---|---|---|---|---|---|---|---|---|
| 1 | 28.05 | | 0.00 | N/A | 22673940 | 96.668 | BB | 1.47 |
| 2 | 37.60 | | 0.00 | N/A | 781651 | 3.332 | BB | 3.25 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 26.99 | 11622140 | 50.332 |
| 2 | 36.96 | 11469010 | 49.668 |

| Peak # | Ret. Time | Area | Area % |
|---|---|---|---|
| 1 | 28.05 | 22673940 | 96.668 |
| 2 | 37.60 | 781651 | 3.332 |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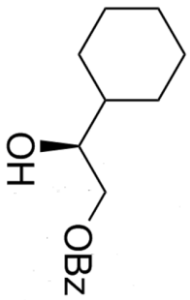
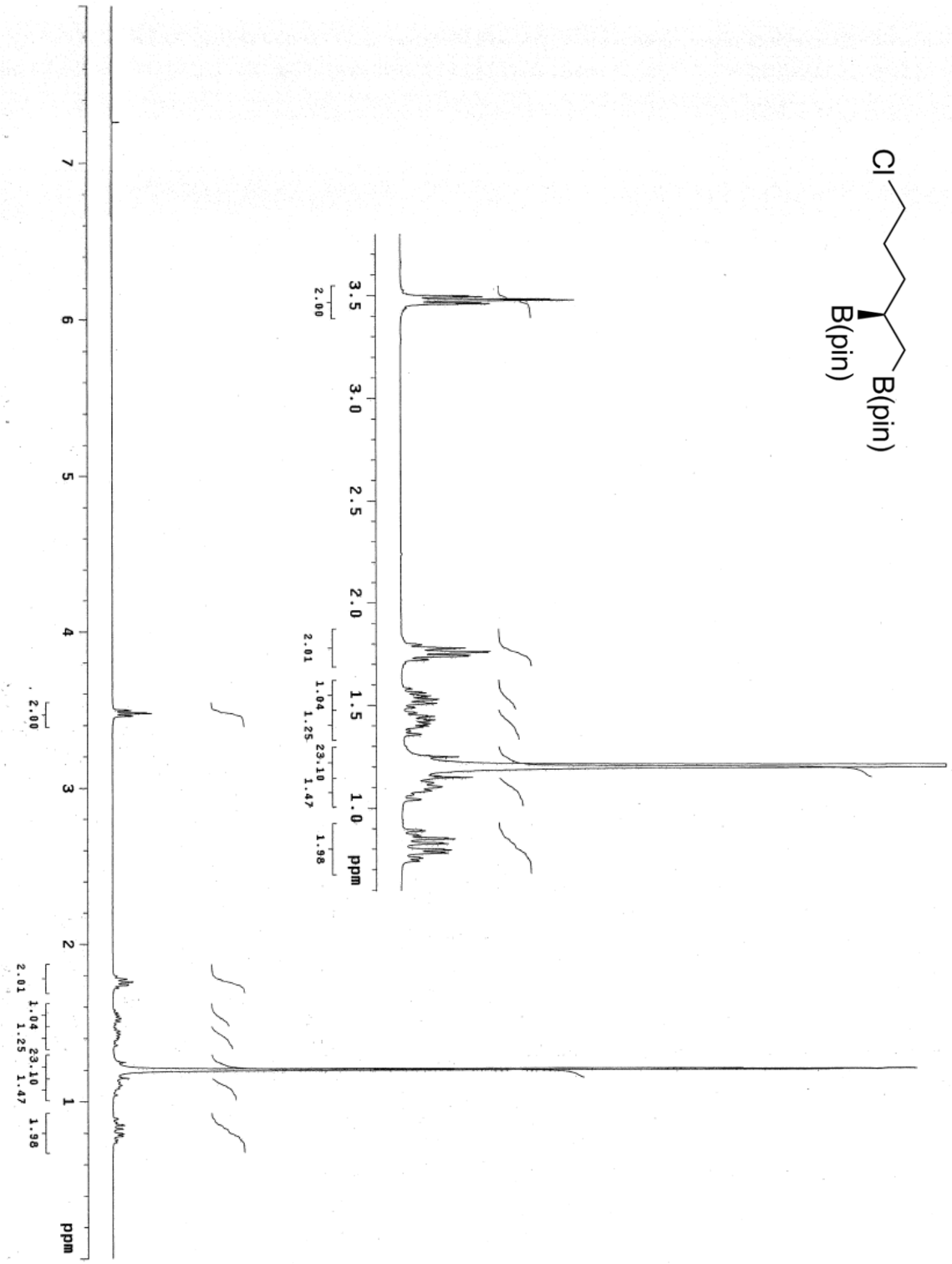
1.80
0.84
1.00
1.02
0.95
0.86
4.07
1.08
1.22
5.19
8
7
6
5
4
3
2
1
ppm


OH
OBz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B(pin)
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2.5
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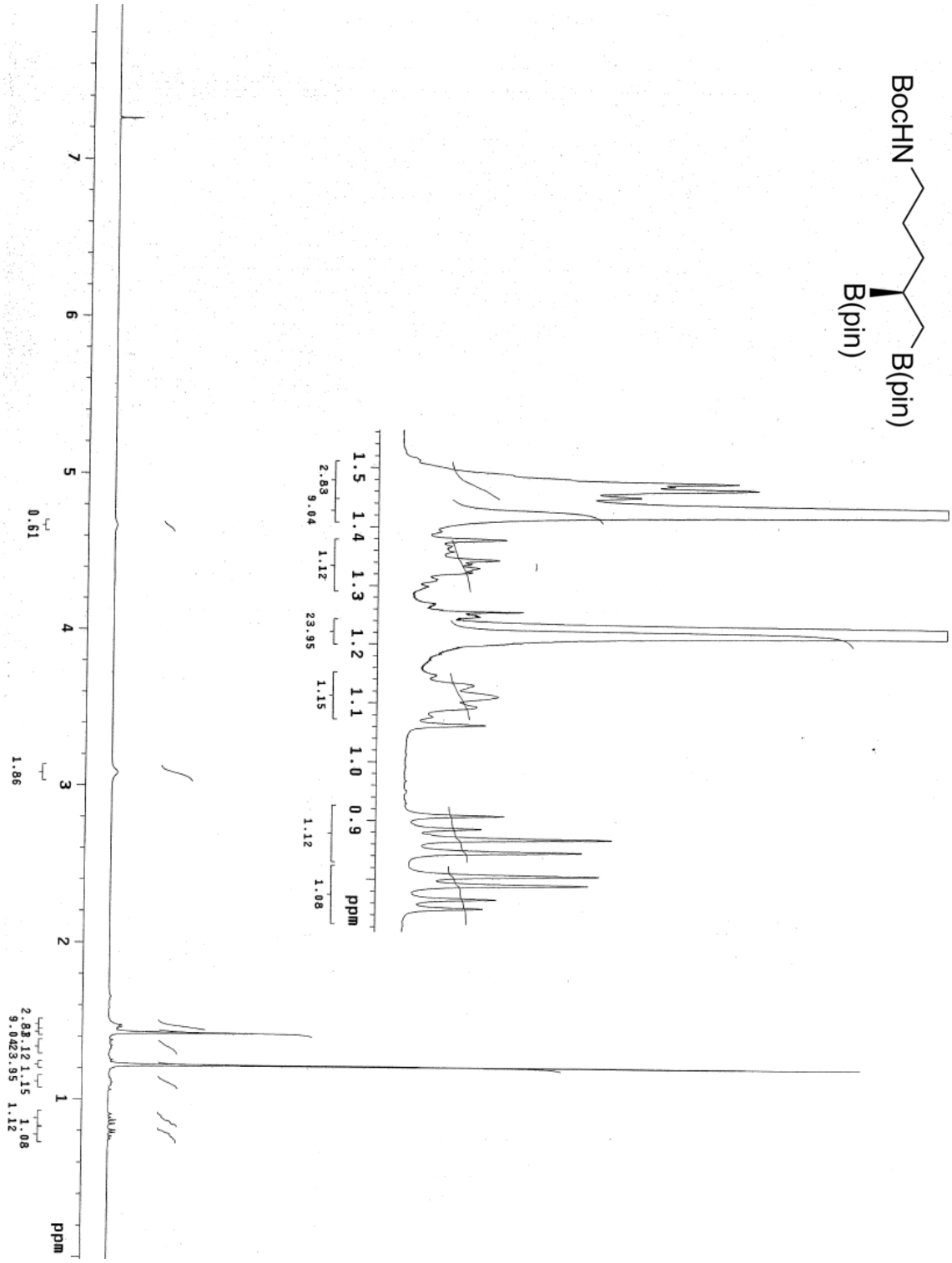
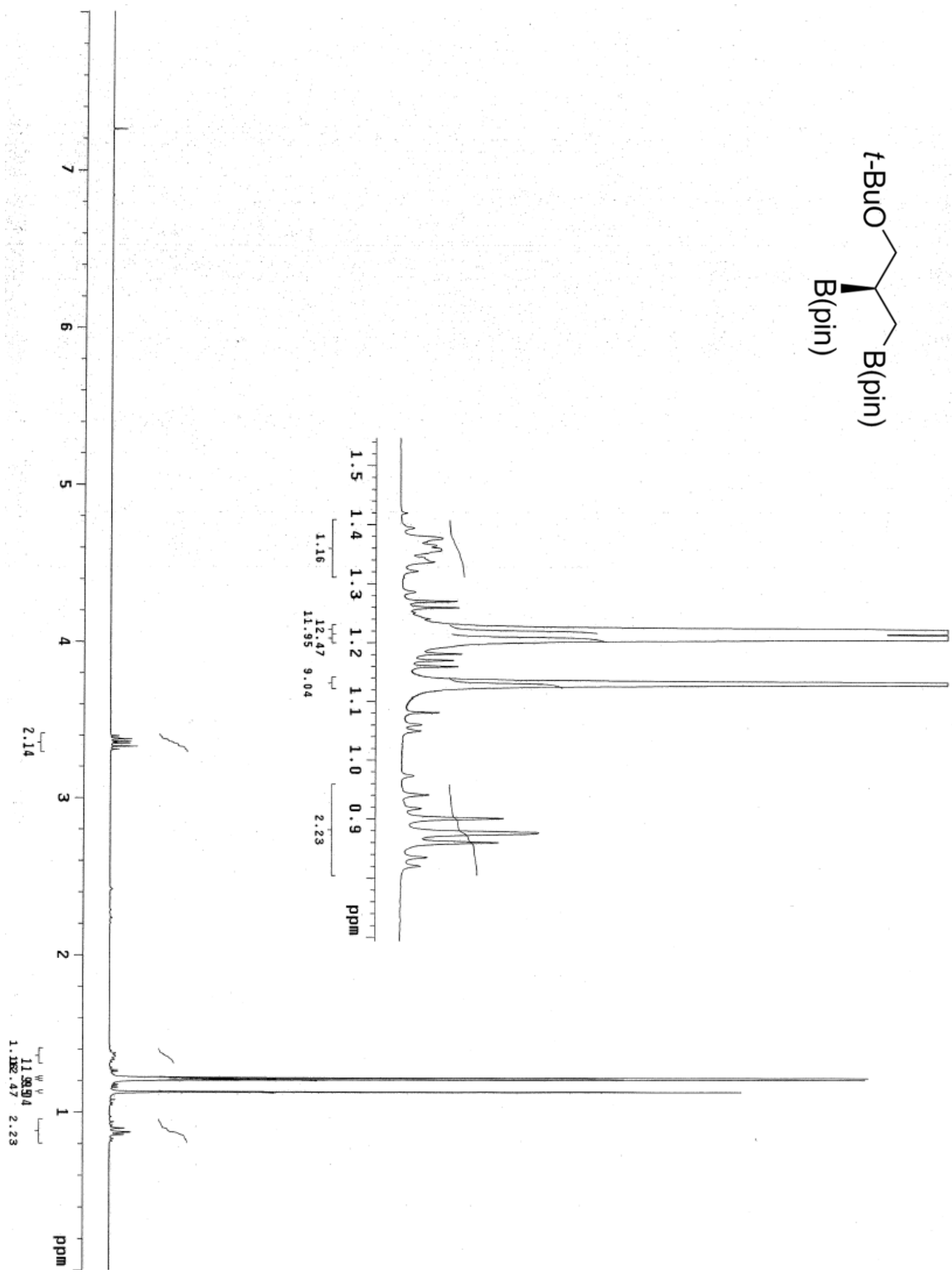
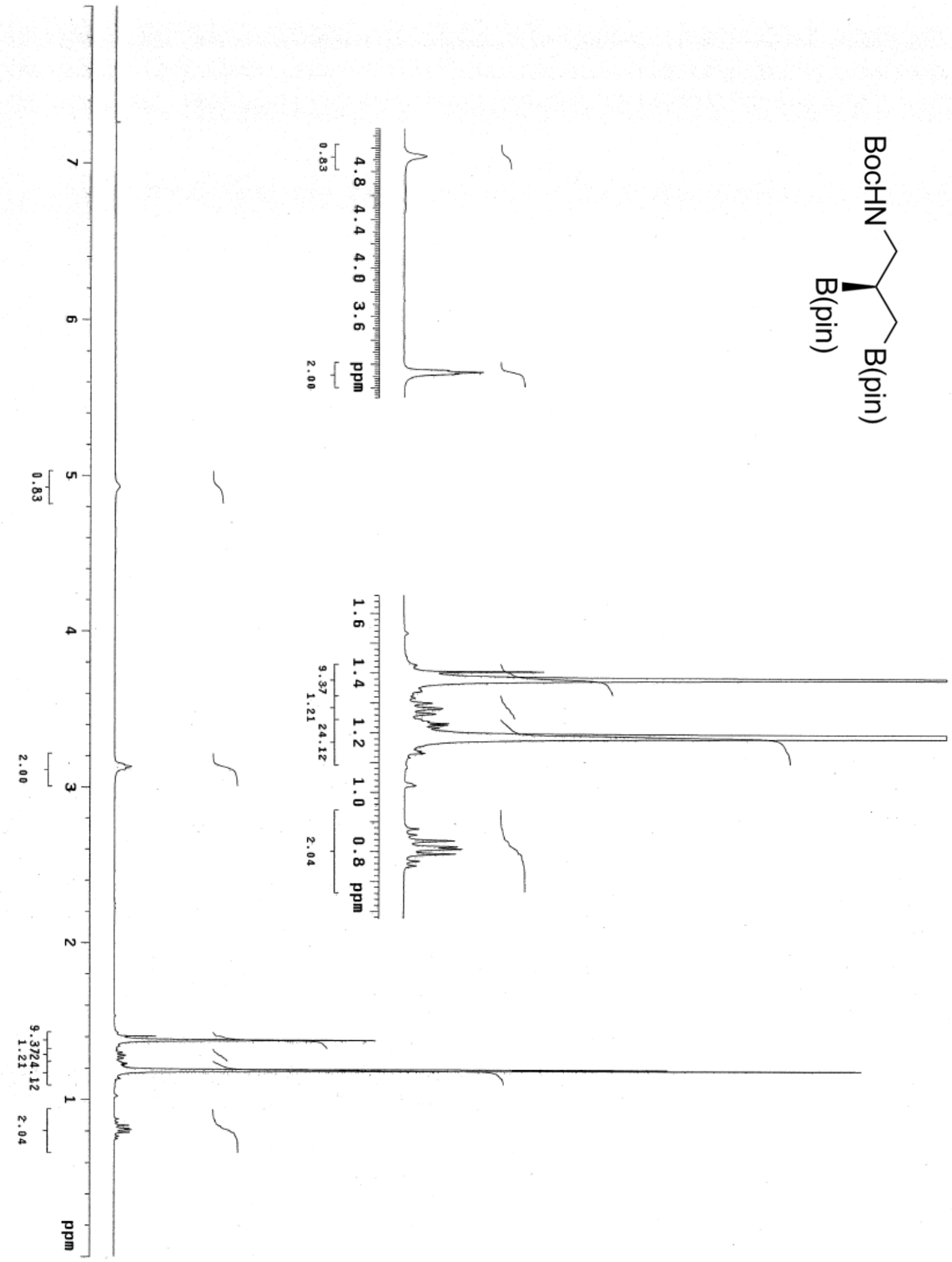
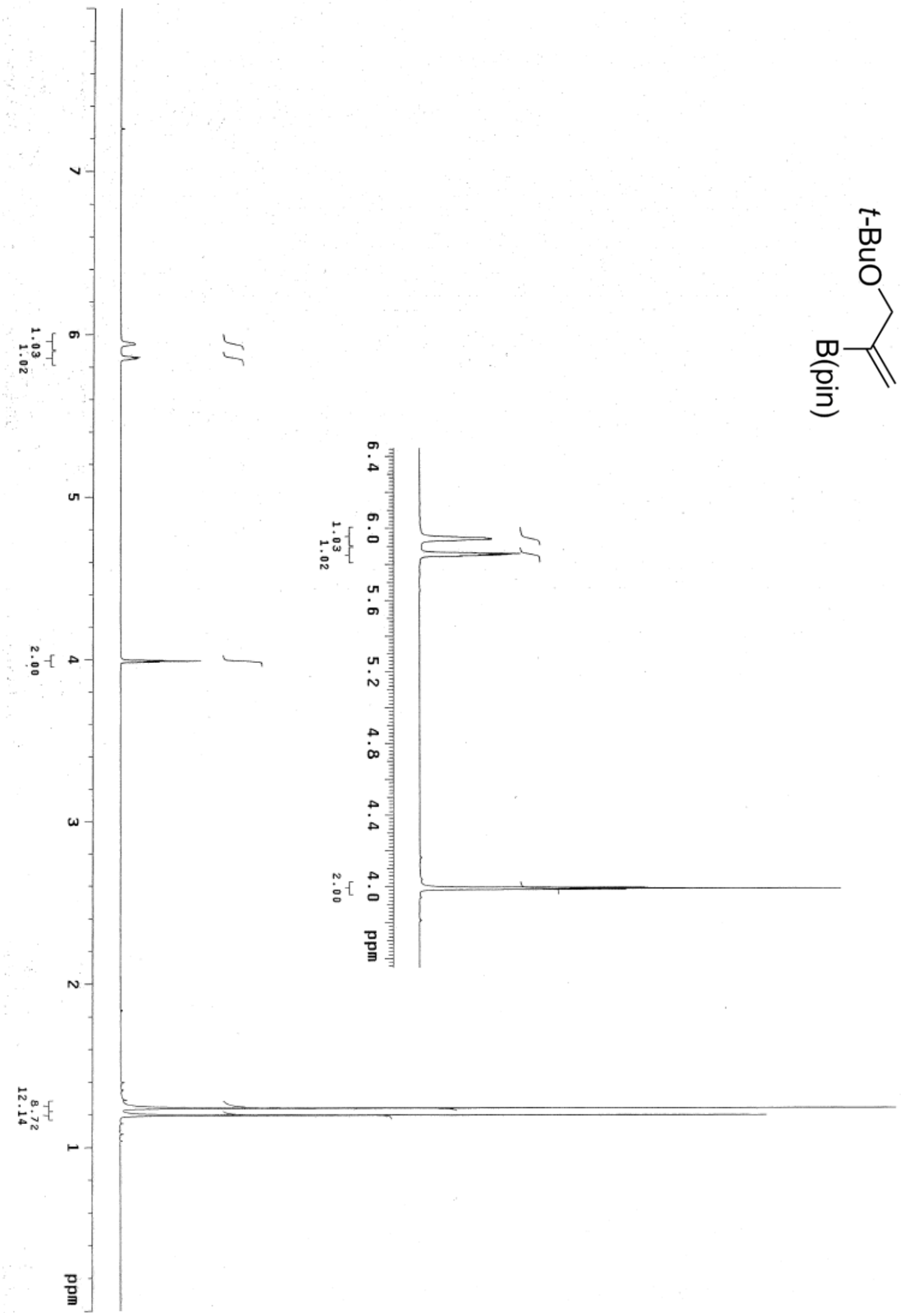
1.5
1.0
ppm
2.00
2.01
1.04
1.25
23.10
1.47
1.98
7
6
5
4
3
2
1
ppm
2.00
2.01
1.04
1.25
23.10
1.47
1.98


BocHN
B(pin)
B(pin)
1.5 1.4 1.3 1.2 1.1 1.0 0.9 ppm
2.83 9.04 1.12 23.95 1.15 1.12 1.08
0.61
1.86
2.88 12.12 1.15 1.08
9.04 23.95 1.12
7 6 5 4 3 2 1 ppm


t-BuO
B(pin)
B(pin)
1.5 1.4 1.3 1.2 1.1 1.0 0.9 ppm
1.16
12.47
11.95 9.04
2.23
7 6 5 4 3 2 1 ppm
2.14
11.95
12.47 2.23


BocHN
B(pin)
B(pin)
4.8 4.4 4.0 3.6 ppm
0.83
2.00
1.6 1.4 1.2 1.0 0.8 ppm
9.37 24.12
1.21 2.04
7 6 5 4 3 2 1 ppm
0.83
2.00
9.37 24.12
1.21 2.04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4.4
4.0
ppm
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7
6
5
4
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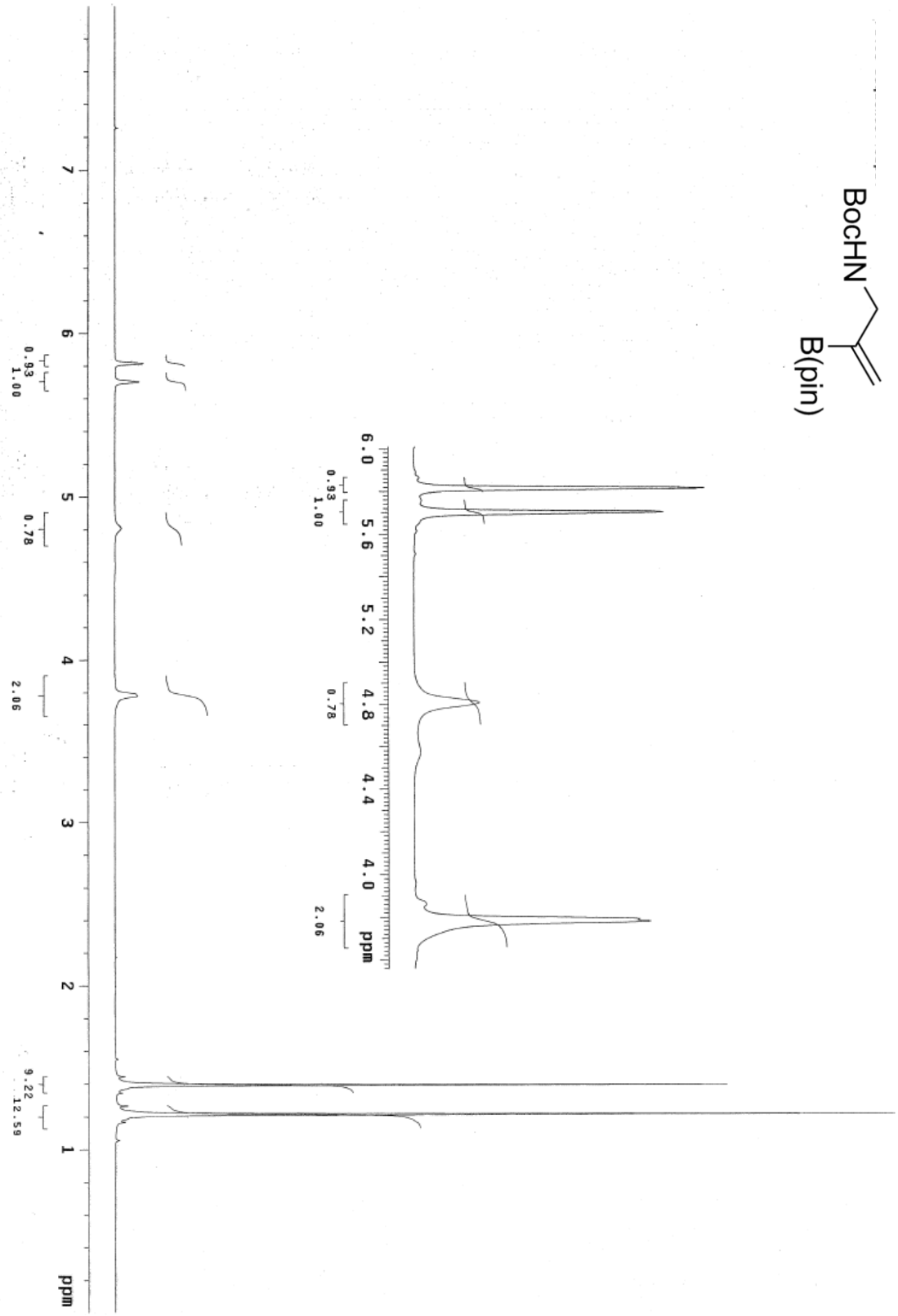
ppm
1.03
1.02
2.00
8.72
12.14


BocHN
B(pin)
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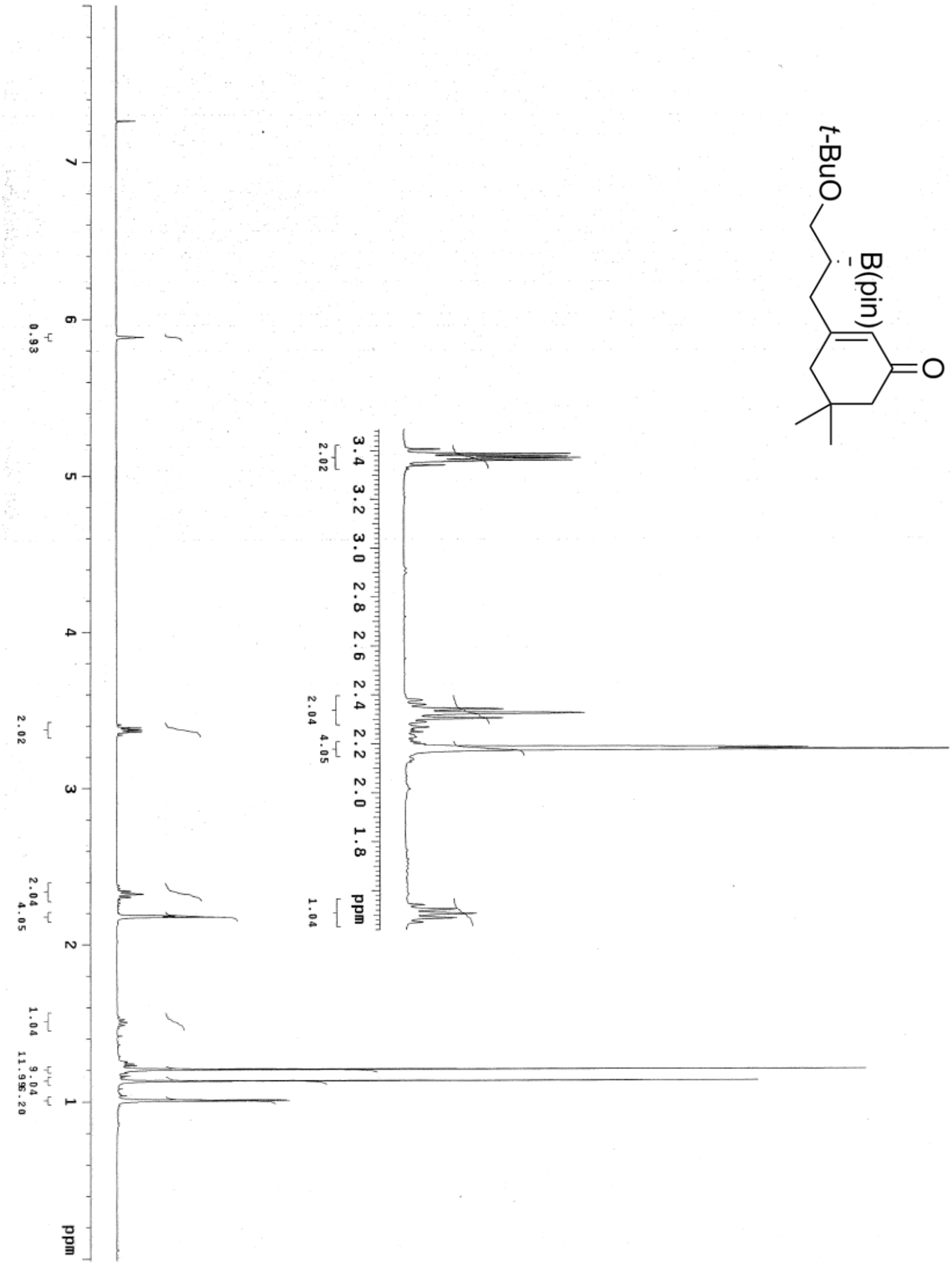
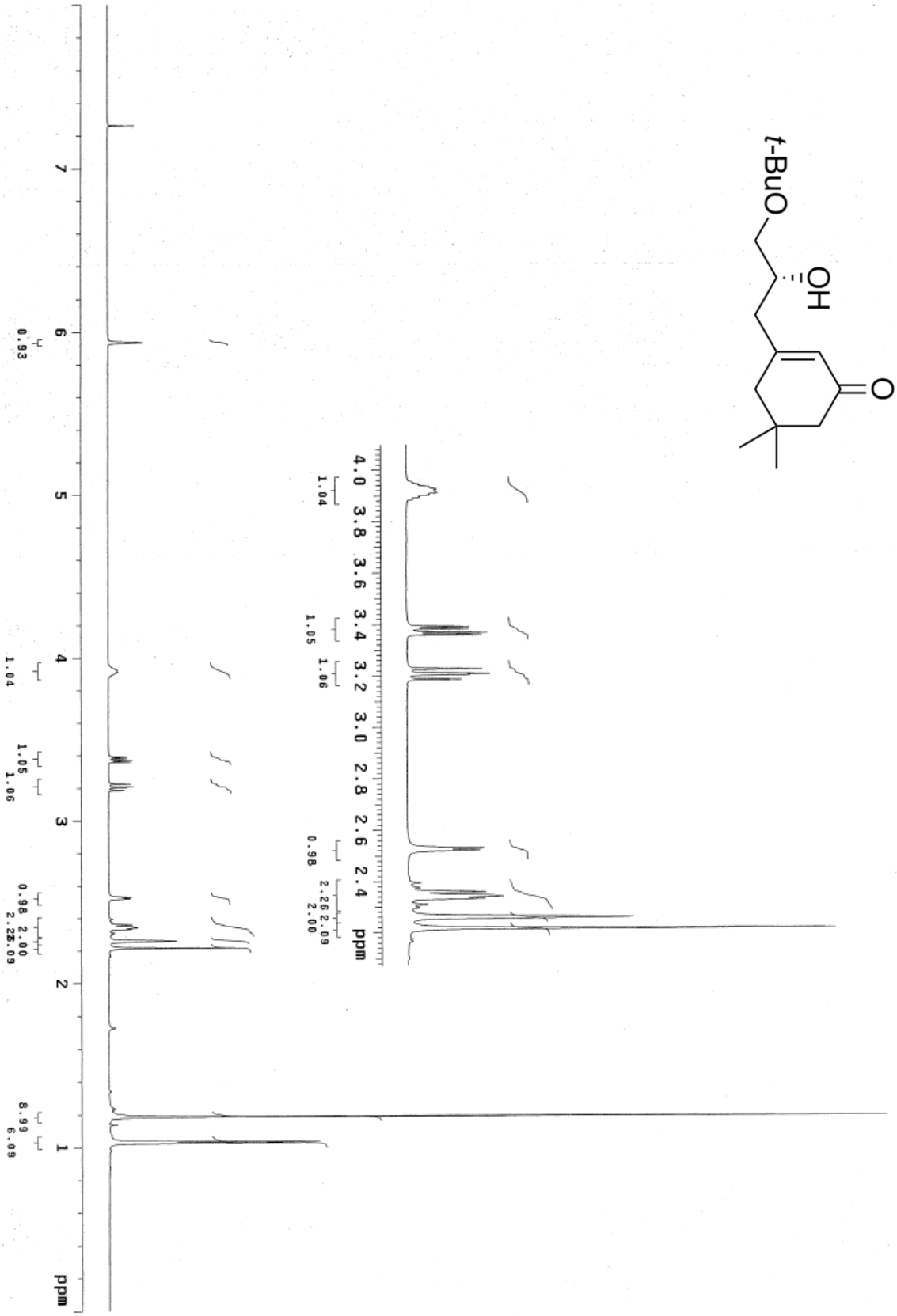
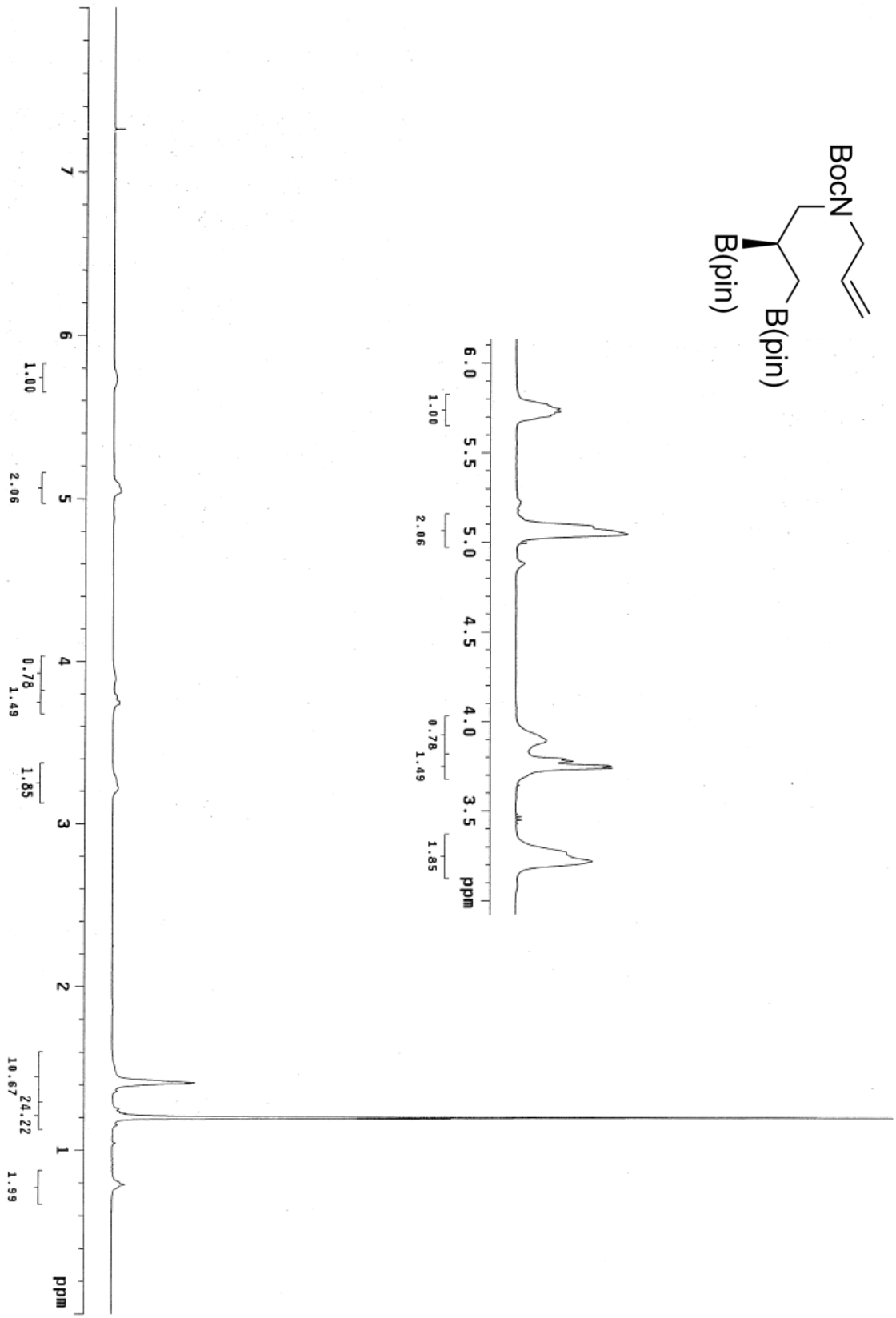
5.2
4.8
4.4
4.0
ppm
0.93
1.00
0.78
2.06
7
6
5
4
3
2
1
ppm
0.93
1.00
0.78
2.06
9.22
12.59


t-BuO
B(pin)
O
3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 ppm
2.02
2.04
4.05
1.04
7 6 5 4 3 2 1 ppm
0.93
2.02
2.04
4.05
1.04
9.04
11.96
6.20


t-BuO
OH
O
4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 ppm
1.04 1.05 1.06 0.98 2.26 2.09 2.00
7 6 5 4 3 2 1 ppm
0.93 1.04 1.05 1.06 0.98 2.00 2.25 2.09 8.99 6.09


BocN
B(pin)
B(pin)
6.0
5.5
5.0
4.5
4.0
3.5
ppm
1.00
2.06
0.78
1.49
1.85
7
6
5
4
3
2
1
ppm
1.00
2.06
0.78
1.49
1.85
10.67
24.22
1.99

## *Chapter Two*

# Site-Selective NHC–Cu-Catalyzed Protoboryl Addition to Terminal Alkynes for Synthesis of Internal (*α*-) or Terminal (*β*-) Alkenylborons. Utility in Chemical Synthesis and Mechanistic Basis for Site Selectivity

### *2.1. Introduction*

Alkenylboron reagents are useful key intermediates in chemical synthesis.[1] The C–B bond of an alkenylboron can be easily transformed into a variety of other chemical bonds: C–H, C–O, C–N, C–X, and C–C.[2,3] While terminal (*β*-) alkenylborons are readily

(1) (a) Brown, H. C.; Campbell, J. B., Jr. *Aldrichimica Acta* **1981**, *14*, 3–11. (b) Matteson, D. S. *Tetrahedron* **1989**, *45*, 1859–1885.

(2) For applications of alkenylborons in C–C bond formation, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147–168. (c) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695. (d) Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 3565–3568. For syntheses of various cyclic and acyclic alkenylborons through Pd-catalyzed cross-coupling reactions involving the corresponding alkenyl bromides and triflates, see: (e) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006. For a review regarding applications of alkenyltrifluoroborates, which can be accessed via alkenylborons, in C–C bond forming reactions, see: (f) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286.

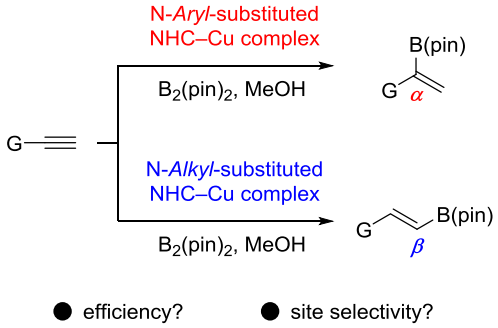
(3) For examples of C–C bond forming methods that utilize alkenylborons but are not considered cross-coupling reactions, see: (a) Batey, R. A.; Quach, T. D.; Shen, M.; Thadani, A. N.; Smil, D. V.; Li, S.-W.; MacKay, D. B. *Pure Appl. Chem.* **2002**, *74*, 43–55. and references cited therein. (b) Sasaki, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 8145–8147.

accessible through simple processes such as hydroboration,[4] haloboration,[5] and organometal synthesis,[6] protocols for synthesis of internal ($\alpha$-) alkenylborons in high site selectivity is severely underdeveloped and the existing approaches involve stepwise and requiring relatively harsh reaction conditions. Especially, hydroborations of readily accessible terminal alkynes cannot be performed with effective control of site selectivity leading to afford internal alkenylborons predominantly.[4] Internal alkenylborons can be prepared by a three-step, two-vessel process including synthesis of an $\alpha$-alkenyl halide, converting to the corresponding $\alpha$-alkenyllithium species, and treatment of isopropoxy(pinacolato)boron reagent.[7] Pd-catalyzed cross-coupling of an internal alkenyl halide with $B_2(pin)_2$ can be an alternative method to generate an $\alpha$-alkenylborons.[2e] The preparation of the internal alkenyl halides, however, is necessary for both approaches and requires strongly acidic conditions. For instance, $\alpha$-alkenyl bromides may be synthesized by selective B–Br addition to an alkyne with $BBr_3$, followed by protonation of the C–B bond with excess amount of acetic acid.[8] Alternatively, Ishii group prepared internal alkenyl iodides through site-selective hydroiodination of an alkyne and HI was generated *in situ* from TMSCl/NaI in the presence of water.[9] Furthermore, synthesis of internal alkenyl metals from the corresponding $\alpha$-alkenyl halides bearing an allylic nitrogen or

(4) (a) Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981–990. (b) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485. (c) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127–3128. (d) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991. (e) PraveenGanesh, N.; d'Hondt, S.; Chavant, P. Y. *J. Org. Chem.* **2007**, *72*, 4510–4514. (f) Karamov, D. M.; Rosen, E. L.; Er, J. A. V.; Vu, P. D.; Lynch, V. M.; Bielawski, C. W. *Tetrahedron* **2008**, *64*, 6853–6862.
(5) (a) Suzuki, A. *Pure & Appl. Chem.* **1986**, *58*, 629–638. (b) Satoh, Y.; Serizawa, H.; Miyaura, N.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1988**, *29*, 1811–1814.
(6) (a) Matteson, D. S.; Liedtke, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 1526–1531. (b) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316–1319.
(7) (a) Morrill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, *45*, 7733–7736. (b) Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415.
(8) Hara, S.; Dojo, H.; Takinami, S.; Suzuki, A. *Tetrahedron Lett.* **1983**, *24*, 731–734.
(9) Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675–676.

oxygen atom is challenging due to the elimination reactions.[10] To avoid these limitations, the site-selective hydroboration of a terminal alkyne would be the most direct route for synthesis of an internal alkenyl boron compound. However, efficient and catalytic protocols for hydroboration of a terminal alkyne to deliver $\alpha$-alkenylboron have not been disclosed yet.[11,12] Thus, the development of efficient and selective process for generating $\alpha$-alkenylboron compounds is of high value.

***Scheme 2.1.*** Control of Site Selectivity in NHC–Cu-Catalyzed Protoboration of Terminal Alkynes




As discussed in Chapter 1, we observed that site selectivity can be controlled to achieve either $\alpha$- or $\beta$-alkenylborons efficiently and selectively by altering the structure of NHC–Cu complex. Herein, we have disclosed site-selective protoboryl additions to a wide array of terminal alkynes to provide $\alpha$-alkenylborons in the presence of *N*-aryl-substituted NHC–Cu complex. In addition, by changing the electronic attributes of the NHC–Cu complexes, preparation of $\beta$-alkenyl–B(pin) compounds will be illustrated (Scheme 2.1).

---

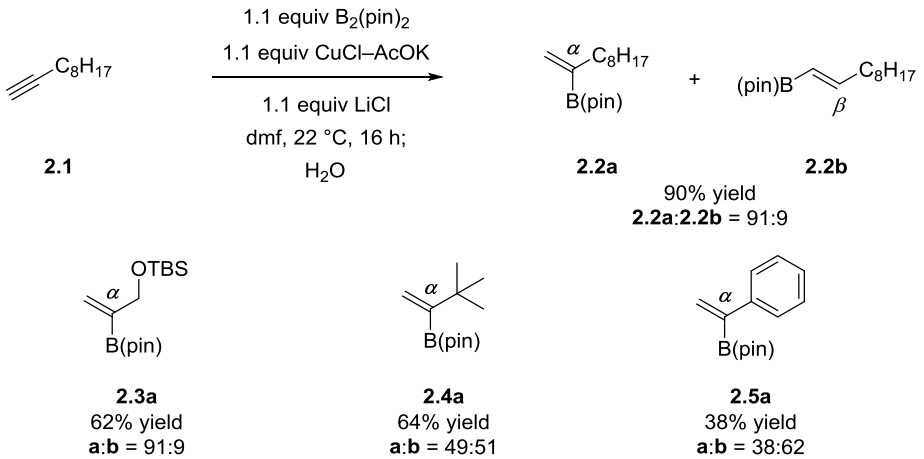
(10) Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961–10963.
(11) For a Cu-catalyzed hydroboration of phenylacetylene that affords the terminal alkenylboron, see: Lee, J. E.; Kwon, J.; Yun, J. *Chem. Commun.* **2008**, 733–734. This procedure is ineffective with alkylsubstituted alkynes.
(12) Alkyl-substituted $\alpha$-alkenylborons can be accessed through hydroborations that require stoichiometric amounts of a Cu complex (1.1 equiv. of CuCl, KOAc, and LiCl or a phosphine), and only in up to 91% selectivity (typically 9–71%). See: Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47–53.

## *2.2. Background*

Efficient and selective protocols for preparation of terminal alkenylborons have been developed by a lot of chemists. However, there are no catalytic methods for selective generation of internal alkenylboron products. Thus, in this section, we will summarize the advances regarding selective synthesis for *α*-alkenylborons.

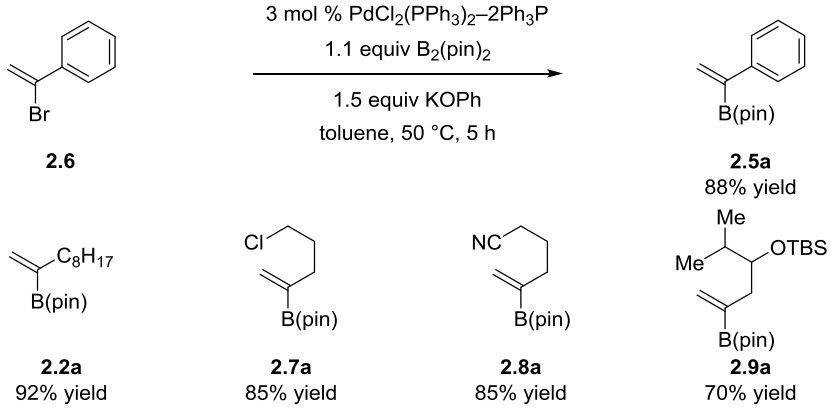
In 2001, Miyaura and coworkers reported selective addition of borylcopper species, *in situ* generated from CuCl and $B_2(pin)_2$, to terminal alkyne **2.1**, delivering a 91:9 mixture of internal- (**2.2a**) and terminal- (**2.2b**) alkenylborons after work-up in 90% yield (Scheme 2.2).[12] Reaction of propargyl *tert*-butyl ether proceeded with the same level of selectivity (**2.3a**:**2.3b** = 91:9). When they utilized sterically more hindered *t*-Bu-bearing-alkyne, however, reaction underwent with minimal selectivity (**2.4a**:**2.4b** = 49:51). Furthermore, reaction of phenylacetylene afforded *β*-alkenylboron product as a major regioisomer with a moderate selectivity (**2.5a**:**2.5b** = 38:62). There are several drawbacks in this transformation; (1) stoichiometric amount of CuCl salt is necessary (non-catalytic), (2) substrate scope is extremely limited (only four substrates illustrated), (3) the level of selectivity is not ideal (up to 91% to internal isomer).

***Scheme 2.2.*** Addition of Borylcopper Species to Terminal Alkynes



Ishiyama, Miyaura, and coworkers demonstrated that $\alpha$-alkenylboron **2.5a** is obtained efficiently (88% yield) by phosphine–Pd-catalyzed cross-coupling of alkenyl bromide **2.6** with 1.1 equiv. of $B_2(pin)_2$ (Scheme 2.3).[13] Internal alkenyl (pinacolato) boron compounds **2.2a** and **2.7a**–**2.9a**, which are bearing an alkyl chain, are prepared in 70–92% yield. Since they used internal alkenyl bromide as a cross-coupling partner, the alkenylboron product is also obtained as pure internal isomeric form. Although relatively wide range of $\alpha$-alkenylborons can be generated through the aforementioned transformation, several issues need to be addressed. First, the synthesis of internal alkenyl bromide is not trivial, which can be synthesized by selective B–Br addition to an alkyne with $BBr_3$, followed by protodeboration with AcOH. Additionally, the use of precious metal (Pd salt) is required for the cross-coupling reaction.

***Scheme 2.3.*** Pd-Catalyzed Cross-Couplings of Alkenyl Bromide with $B_2(pin)_2$

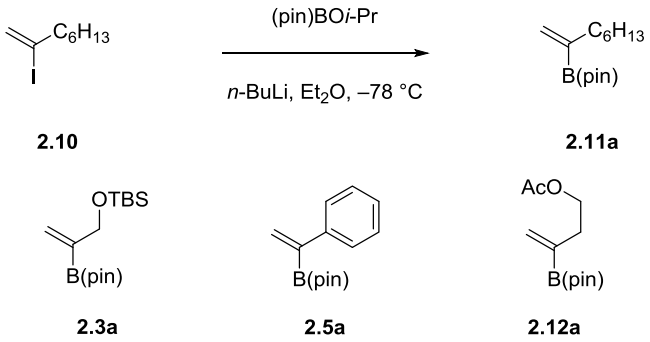



Another indirect method to prepare internal alkenylboron compounds was illustrated by Grubbs and coworkers in 2004.[14] The authors developed Pd-catalyzed cross-coupling of internal alkenyl–B(pin) with monosubstituted olefin to afford trisubstituted alkenylboron compound. In their study, they provided the protocol to

(13) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006.
(14) Morrill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, *45*, 7733–7736.

synthesize $\alpha$-alkenyl–B(pin) compound, which included preparation of alkenyl iodide, transformation to alkenyllithium species, and treatment of (pin)BO*i*-Pr (Scheme 2.4). Internal alkenyl iodides were prepared by a previously reported method by Ishii,[9] which is site-selective hydroiodination of terminal alkyne with HI, which was generated *in situ* from TMSCl/NaI in the presence of water. Various internal (pinacolato) alkenylborons are prepared by the aforementioned process, although no isolated product yields are reported.[15]

***Scheme 2.4.*** Synthesis of Internal Alkenylborons




Both of above methods to synthesize internal alkenylboron compounds require initial preparation of corresponding alkenyl halides. Either $BBr_3$ and acetic acid or HI is included in the reaction solution during the preparation of alkenyl halides. Thus, the synthesis of acid-sensitive substituent-bearing alkenylboron compound might not be effective by these methods. Herein, we present a catalytic selective protocol for synthesis of various $\alpha$-alkenylborons from readily available terminal alkynes.

(15) The authors mentioned that they obtained with moderate to high yields.

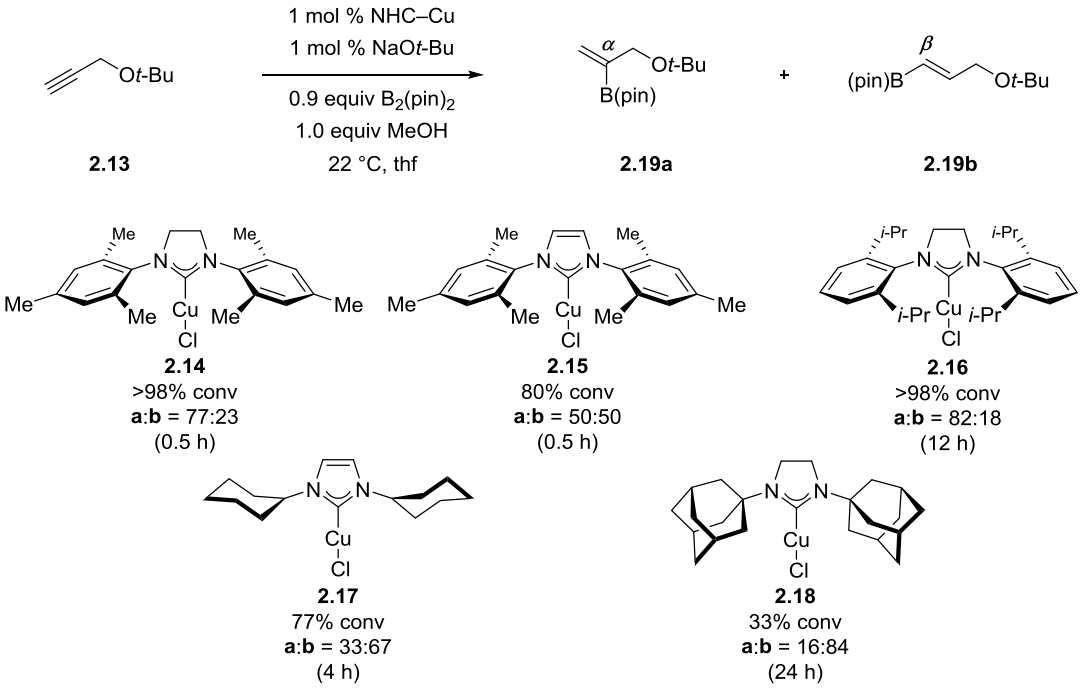
## *2.3. NHC–Cu-Catalyzed α-Selective Protoborations of Terminal Alkynes*

### *2.3.1. Examination of Various NHC–Cu Complexes*

Preliminary observations, which are mentioned in Section 1.3.3 allow us to begin our studies regarding site-selective NHC–Cu-catalyzed protoborations of terminal alkynes. As shown in Scheme 1.11, with bis-*N*-mesityl-NHC–Cu complex **1.29**, reaction of propargyl *t*-butyl ether **1.45** proceeds to internal alkenylboron **1.50** with 83% site selectivity. In contrast, when chiral bidentate NHC–Cu complex derived from **A.6** is utilized, terminal alkenylboron **1.49** becomes a major product (89:11 **1.49**:**1.50**). To further explore the preference for generation of the *α*-alkenylborons, we investigated a number of achiral monodentate NHC–Cu complexes for reaction of propargyl ether **2.13** (Scheme 2.5). *N*-Mesityl-containing NHC–Cu **2.14** promotes the reaction with 77:23 site selectivity at 22 ˚C, which is slightly lower than that obtained at 0 ˚C (83:17 **2.19a**:**2.19b**; Scheme 1.11). With unsaturated backbone-bearing NHC–Cu complex **2.15**, on the other hand, same amount of two regioisomers **2.19a** and **2.19b** are afforded (50:50 **2.19a**:**2.19b**). In the presence of sterically congested 2,6-(*i*-Pr)$_2$-phenyl-bearing complex **2.16**, reaction of **2.13** undergoes with higher site selectivity (82% of **2.19a**), although much longer reaction time is required for reaction completion (12 h vs 0.5 h for **2.14**). In contrast, *N*-alkyl-containing NHC–Cu complexes **2.17** and **2.18** deliver *β*-alkenylboron **2.19b** preferentially (67–84% of **2.19b**). Especially, bis-adamantyl-based complex **2.18** promotes reaction of **2.13**, affording **2.19b** with 84% selectivity, which is totally reversed to that with complex **2.16** (82% of **2.19a**). Even though we obtained higher level of selectivity with **2.16** (vs **2.14**), when we lowered the reaction temperature to –50 ˚C to improve selectivity, which is guided by the above observation (**2.19a**:**2.19b** = 77:23 at 22

˚C vs 83:17 at 0 ˚C), reaction with complex **2.16** becomes sluggish (only 14% conv in 21 h). On the other hand, reaction with NHC–Cu **2.14** proceeds with 89:11 site selectivity and 96% conversion in 21 hours at –50 ˚C. Thus, we chose the complex **2.14** as an optimal catalyst for further study.

***Scheme 2.5.*** Screen of Various NHC–Cu Complexes

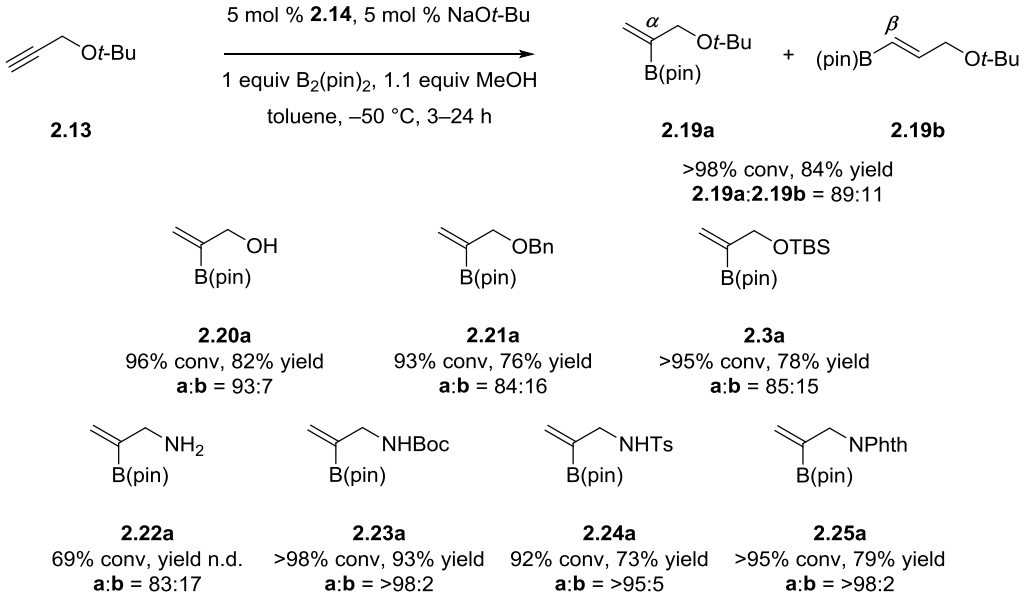



### *2.3.2. α-Selective Protoborations of Propargyl Alcohols, Amines and Derivatives*

With 5 mol % of NHC–Cu complex **2.14**, we obtained desired internal alkenylboron compound **2.19a** in 84% yield at –50 ˚C, isolated from a 89:11 mixture of **2.19a** and **2.19b** (Scheme 2.6). We have examined different protecting group-containing propargyl alcohols as well as unprotected ones. Reaction of propargyl alcohol affords corresponding *α*-alkenylboron **2.20a** in 82% yield (93:7 **2.20a**:**2.20b**). In this reaction, since the substrate propargyl alcohol can serve as the proton source, we do not need to use MeOH. Internal alkenylborons containing a benzyloxy (**2.21a**) or a *tert*-

butyldimethylsiloxy (**2.3a**) are isolated in 76–78% yield from a 84:16 or a 85:15 mixture of $\alpha$- and $\beta$-isomers by silica gel chromatography. Then, propargyl amine and amides are investigated for $\alpha$-selective protoboryl addition reaction. When propargyl amine is used, similar level of site selectivity (83:17 **a**:**b**) relative to propargyl ethers is obtained. Because of its instability on silica gel, however, purification and isolation of **2.22a** was not successful. Unlike the case with propargyl alcohol, when we performed the reaction of propargyl amine without addition of MeOH, reaction becomes sluggish, which means that an amine might not be acidic enough to protonate the C–Cu bond in the intermediate. Several different protecting group-containing propargyl amides are prepared. Site selectivities for propargyl amides are exclusive (>98% $\alpha$) and corresponding alkenylborons are obtained in up to 93% yield. The products formed in $\alpha$-selective protoboration reactions illustrated in Scheme 2.6 are not able to be easily prepared by other methods. For instance, as we mentioned in Section 2.1, Ni-catalyzed hydroalumination of propargyl ether or amide to generate $\alpha$-alkenyl–Al species, followed by treatment of methoxy(pinacolato)boron, cannot afford the desired product, because of competitive elimination.[10] And also previously developed protocols as depicted in Scheme 2.3 and 2.4, might not be operative, because either an alkenyl–Pd or an alkenyl–Li is generated *in situ* from alkenylhalide, which can suffer from the aforementioned elimination.

***Scheme 2.6.*** $\alpha$-Selective Protoborations of Propargyl Alcohols, Amines and Derivatives

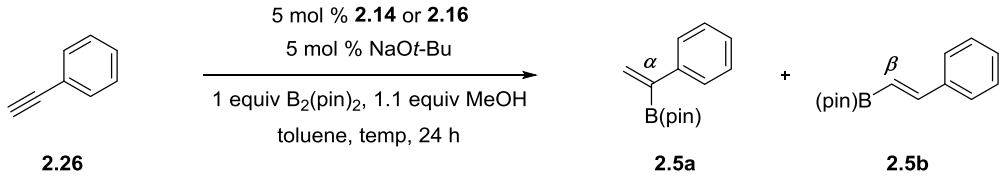



### *2.3.3. α-Selective Protoborations of Aryl- and Heteroaryl-Substituted Terminal Alkynes*

To expand the substrate scope, we investigated different types of alkynes bearing an aryl- or a heteroaryl unit as substrates for $\alpha$-selective protoborations. Initially, we examined reaction temperature with 5 mol % of NHC–Cu complex **2.14** (Table 2.1). Reaction of phenylacetylene **2.26** at 0 ˚C proceeded with moderate site selectivity favoring $\beta$-alkenylboron isomer (**2.5a**:**2.5b** = 33:67; entry 1). When we lowered the reaction temperature to –15 ˚C and –30 ˚C, $\alpha$-selectivity is slightly increased to 38% and 44%, respectively (entries 2 and 3). Lowering temperature to –50 ˚C, however, did not give high site selectivity (53:47 **a**:**b**; entry 4). The above results led us to utilize the less active but more sterically hindered 2,6-($i$-Pr)$_2$-phenyl-substituted NHC–Cu complex **2.16** for reaction of aryl-bearing alkyne. Interestingly, with 5 mol % of **2.16**, 79:21 site selectivity favoring to $\alpha$-alkenylboron **2.5a** was obtained (entry 5). After further temperature screening, we found that at lower temperature (–15 ˚C), NHC–Cu complex

**2.16** promoted reaction of **2.26** in 94% conv with 88:12 site selectivity (entry 6). The latter condition was chosen as optimal one for reactions of aryl alkynes.

***Table 2.1.*** Temperature Screening for Reaction of Phenylacetylene **2.26**



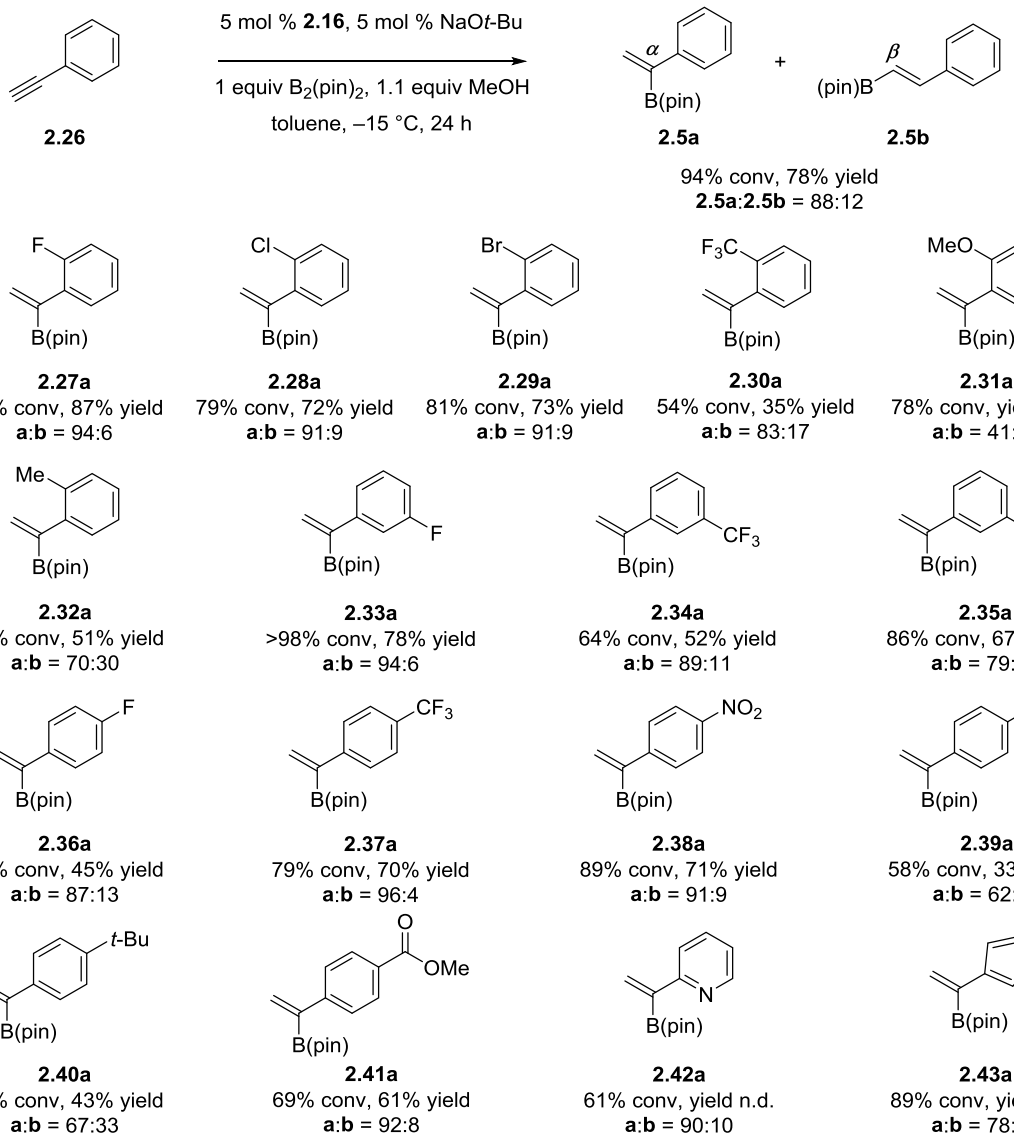

**2.26** **2.5a** **2.5b**

| entry | NHC–Cu complex | temp | conv | **2.5a**:**2.5b** |
|---|---|---|---|---|
| 1 | **2.14** | 0 °C | 99% | 33:67 |
| 2 | **2.14** | –15 °C | 96% | 38:62 |
| 3 | **2.14** | –30 °C | 96% | 44:56 |
| 4 | **2.14** | –50 °C | 96% | 53:47 |
| 5 | **2.16** | 22 °C (6 h) | 77% | 79:21 |
| 6 | **2.16** | –15 °C | 94% | 88:12 |

Various aryl and heteroaryl alkynes are examined, which undergo *α*-selective protoboryl addition in up to 96:4 site selectivity (Scheme 2.7). Pure *α*-alkenylborons (>98% *α*) are isolated by silica gel chromatography in up to 87% yield. Reactions of *ortho*-halogen-bearing phenylacetylenes (**2.27a**, **2.28a**, and **2.29a**) are more selective (91:9–94:6 **a**:**b** vs 88:12 for **2.5a**) and efficient (72–87% yield). It seems that electron-withdrawing substituted aryl alkynes undergo protoboration reaction with higher *α* selectivity. In addition, reactions of alkynes bearing a *meta*-F and a *para*-F unit proceed with 94% and 87% *α* selectivity, respectively (**2.33a** and **2.36a**). When fluorine atom is placed more proximal to the alkyne, higher site selectivity was obtained, which shows the importance of the inductive effect. Then, electron-withdrawing, trifluoromethyl-substituted phenyl acetylenes are investigated, that are converted to *α*-alkenylborons bearing an *ortho*-$CF_3$ (**2.30a**), a *meta*-$CF_3$ (**2.34a**), or a *para*-$CF_3$ (**2.37a**) in 35–70%

yield. Interestingly, we observed completely reversed selectivity trend compare to F-containing substrates. When we locate $CF_3$ unit close to the alkyne, $\alpha$ selectivity is decreased (83% $\alpha$ for **2.30a**, 89% $\alpha$ for **2.34a**, and 96% $\alpha$ for **2.37a**). This unexpected trend might be explained as follows; (1) since trifluoromethyl group attracts electrons through σ-bond framework as well as those that do so through resonance, the electron-withdrawing ability of *m*-$CF_3$-bearing substrate is weaker (no resonance effects are possible), (2) although *o*-$CF_3$-containing substrate might have stronger ability to attract electrons through σ-bond framework, it also might have negative steric effect (with *o*-Me-phenylacetylene, only 70% $\alpha$ selectivity is obtained; **2.32a**). Phenylacetylenes bearing other electron-withdrawing group, such as a nitro or a methyl ester unit were subjected to the $\alpha$-selective protoboration reaction, both of which gave higher $\alpha$ selectivity (91% $\alpha$ for **2.38a** and 92% $\alpha$ for **2.41a**). In contrast, reactions of electron-donating, methoxy-containing aryl alkynes proceed with lower site selectivity (41% $\alpha$ for **2.31a**, 79% $\alpha$ for **2.35a**, and 62% $\alpha$ for **2.39a**). As we mentioned above, *meta*-substituted phenylacetylene has weaker electronic effect compared to *ortho*- or *para*-substituted one, which might be a reason why **2.35a** is obtained with relatively higher $\alpha$ selectivity. Additionally, heteroaryl-bearing substrates were utilized, and moderate to high site selectivity is obtained (90% $\alpha$ for **2.42a** and 78% $\alpha$ for **2.43a**). However, because of instability of these alkenylboron compounds **2.42a** and **2.43a**, we fail to isolate them. It should be noted that, based on the above observations, there is a general trend that electron-withdrawing groups prefer $\alpha$ selectivity and more $\beta$-alkenylborons are generated with electron-donating substituents.

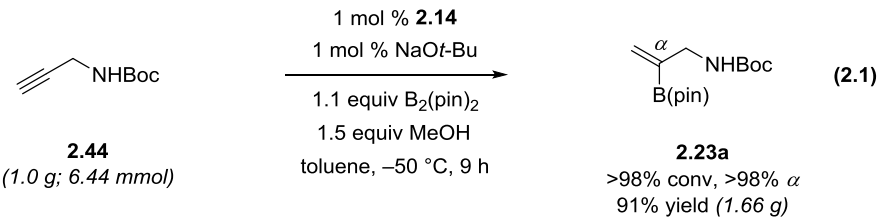
***Scheme 2.7.*** $\alpha$-Selective Protoborations of Aryl- and Heteroaryl-Substituted Terminal Alkynes




### *2.3.4. The Utility of Cu-Catalyzed α-Selective Protoboration of Terminal Alkyne*

The utility of NHC–Cu-catalyzed process is illustrated by gram scale procedure (eq 2.1). Reaction of propargyl Boc amide **2.44** (1.0 gram; 6.44 mmol) with 1.1 equiv. of $B_2(pin)_2$ and 1.5 equiv. of MeOH in the presence of only 1 mol % of NHC–Cu complex **2.14**, which can be prepared readily from CuCl, commercially available *N*-Mes imidazolinium salt, and NaO*t*-Bu, delivers affording $\alpha$-alkenylboron product **2.23a** in

91% yield (1.66 gram) after purification with perfect site selectivity (>98% $\alpha$). Internal alkenylboron **2.23a** can be utilized for metal-catalyzed cross-coupling reaction, and also recently, was used for NHC–Cu-catalyzed enantioselective allylic alkenyl addition to allylic phosphate.[16]

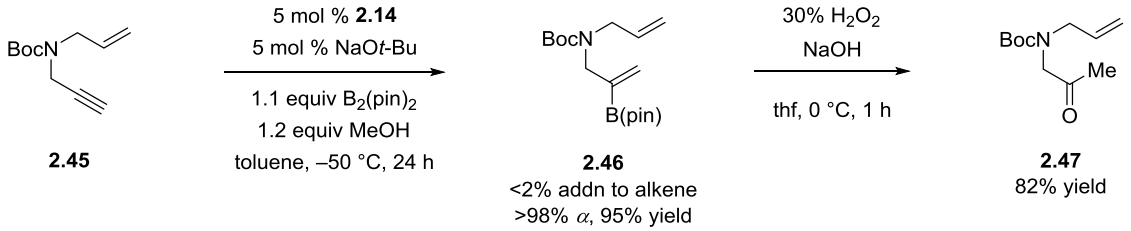



(2.1)

In addition, since the conversion of C–B bond to C–O bond is widely used and very efficient, through the present Cu-catalyzed protocol, a methyl ketone might be synthesized from the corresponding terminal alkyne. Although a methyl ketone can be accessed by Pd-catalyzed Wacker oxidation of terminal alkene,[17] our strategy has still a significant advantage, which is high chemoselectivity. As illustrated in Scheme 2.8, enyne **2.45** is subjected to Cu-catalyzed protoboration, affording internal alkenylboron compound **2.46** in 95% yield with complete $\alpha$ selectivity (>98% $\alpha$) and perfect chemoselectivity (<2% addition to alkene). The corresponding methyl ketone **2.47** is obtained in 82% yield by $H_2O_2$-mediated oxidation. The alternative pathway, which includes Wacker oxidation, might not operative due to low chemoselectivity.

(16) Gao, F.; Carr, J. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 2149−2161.
(17) (a) Smidt, J.; Hafner, W.; Jira, R.; Sieber, R.; Sedlmeier, J.; Sabel, A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 80–88. (b) Muzart, J. *Tetrahedron* **2007**, *63*, 7505–7521.

***Scheme 2.8.*** Site- and Chemoselective NHC–Cu-Catalyzed Protoboration of an Enyne. Conversion of a Terminal Alkyne to a Methyl Ketone



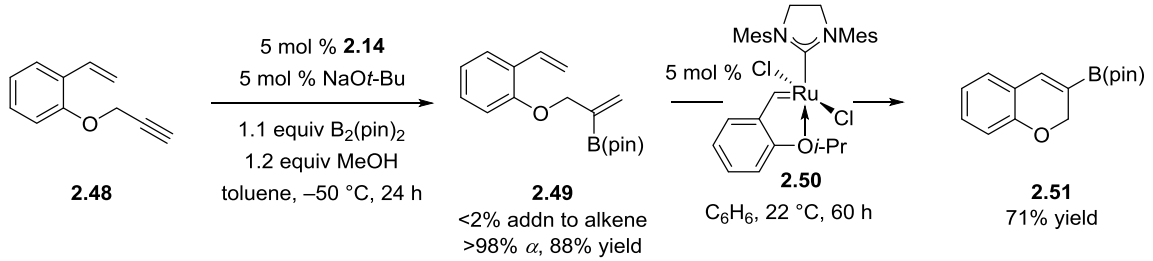

**2.45**

**2.46**
<2% addn to alkene
>98% $\alpha$, 95% yield

**2.47**
82% yield

Synthetically useful intermediate, cyclic alkenylboron compounds [18] can be prepared through the Cu-catalyzed $\alpha$-selective protoboration of terminal alkynes. As shown in Scheme 2.9, cyclic alkenylboron **2.51** was obtained in 71% yield by ring-closing metathesis of $\alpha$-alkenylboron bearing terminal alkene **2.49** in the presence of 5 mol% of Ru complex **2.50**.[19] The desired diene compound **2.49** was synthesized in 88% yield through Cu-catalyzed protoboration of enyne **2.48** with exceptional site- and chemoselectivity (>98% $\alpha$ and <2% addition to alkene). Because of the allylic oxygen atom on compound **2.49**, the synthesis of **2.49** might not be possible by other methods we mentioned above (Section 2.2).

***Scheme 2.9.*** Synthesis of Cyclic Alkenylboron Compound




**2.48**

**2.49**
<2% addn to alkene
>98% $\alpha$, 88% yield

**2.50**
$C_6H_6$, 22 °C, 60 h

**2.51**
71% yield

(18) For a method for synthesis of cyclic alkenylborons through the use of $\beta$-borylallylsilanes, prepared by Pd-catalyzed silaboration of allenes, see: (a) Suginome, M.; Ohmori, Y.; Ito, Y. *J. Am. Chem. Soc.* **2001**, *123*, 4601–4602. For synthesis of cyclic alkenylborons through Pd-catalyzed C–H borylation, see: (b) Olsson, V. J.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 6891–6893. (c) Selander, N.; Willy, B.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4051–4053. Cyclic alkenylborons have also been prepared through Ni-catalyzed borylation processes that involve C–O activation: (d) Huang, K.; Yu, D.-G.; Zheng, S.-F.; Wu, Z.-H.; Shi, Z.-J. *Chem. –Eur. J.* **2011**, *17*, 786–791.

(19) (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179. For an early report regarding the synthesis of cyclic alkenylborons through catalytic RCM of dienes, see: (b) Renaud, J.; Ouellet, S. G. *J. Am. Chem. Soc.* **1998**, *120*, 7995–7996.

### *2.4. NHC–Cu-Catalyzed β-Selective Protoborations of Terminal Alkynes*

Various synthetic strategies for selective preparation of *β*-alkenylboron compounds have been reported including the most straightforward method, hydroboration of terminal alkynes.[20] Metal-catalyzed variants have been also developed with a variety of metals including Rh, Ir,[21] Ti,[22] and Zr.[23] Although there are plenty of methods regarding synthesis of *β*-alkenylborons, no Cu-catalyzed protocol has been reported yet. Moreover, mechanistically, the present study might be useful for establishing the origins of *α* selectivity obtained with *N*-aryl-bearing NHC–Cu complexes **2.14** and **2.16**. As we illustrated in Scheme 2.5, *N*-alkyl-substituted NHC–Cu complexes **2.17** and **2.18** generate the terminal alkenylboron isomer as a major product (67% and 84% of *β*, respectively). With Cu complex **2.18** as an optimal catalyst for *β*-selective protoboration of terminal alkynes, we investigated wide array of alkynes.

As shown in Scheme 2.10, reaction of propargyl *tert*-butyl ether **2.13** with 5 mol % of **2.18** at ambient temperature in 12 h affords terminal alkenylboron **2.19b** in 80% yield with high *β* selectivity (88%). Propargyl alcohol was converted to *β*-alkenylboron product **2.20** in 65% yield with 87% of selectivity. Although the level of selectivity is

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(20) For protocols with catecholborane, see: (a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249–5255. (b) Hoffmann, R. W.; Dresely, S. *Synthesis* **1988**, 103–106. (c) Arase, A.; Hoshi, M.; Mijin, A.; Nishi, K. *Synth. Commun.* **1995**, *25*, 1957–1962. For protocols with di(isocamphenyl)borane, see: (d) Martinez-Fresneda, P.; Vaultier, M. *Tetrahedron Lett.* **1989**, *30*, 2929–2932. (e) Kamabuchi, A.; Moriya, T.; Miyaura, N.; Suzuki, A. *Synth. Commun.* **1993**, *23*, 2851–2859. (f) Gravel, M.; Toure, B. B.; Hall, D. G. *Org. Prep. Proced. Int.* **2004**, *36*, 573–579. For a protocol with pinacolborane, see: (g) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485. For a protocol with di(isopropylprenyl)borane, see: (h) Kalinin, A. V.; Scherer, S.; Snieckus, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 3399–3404.

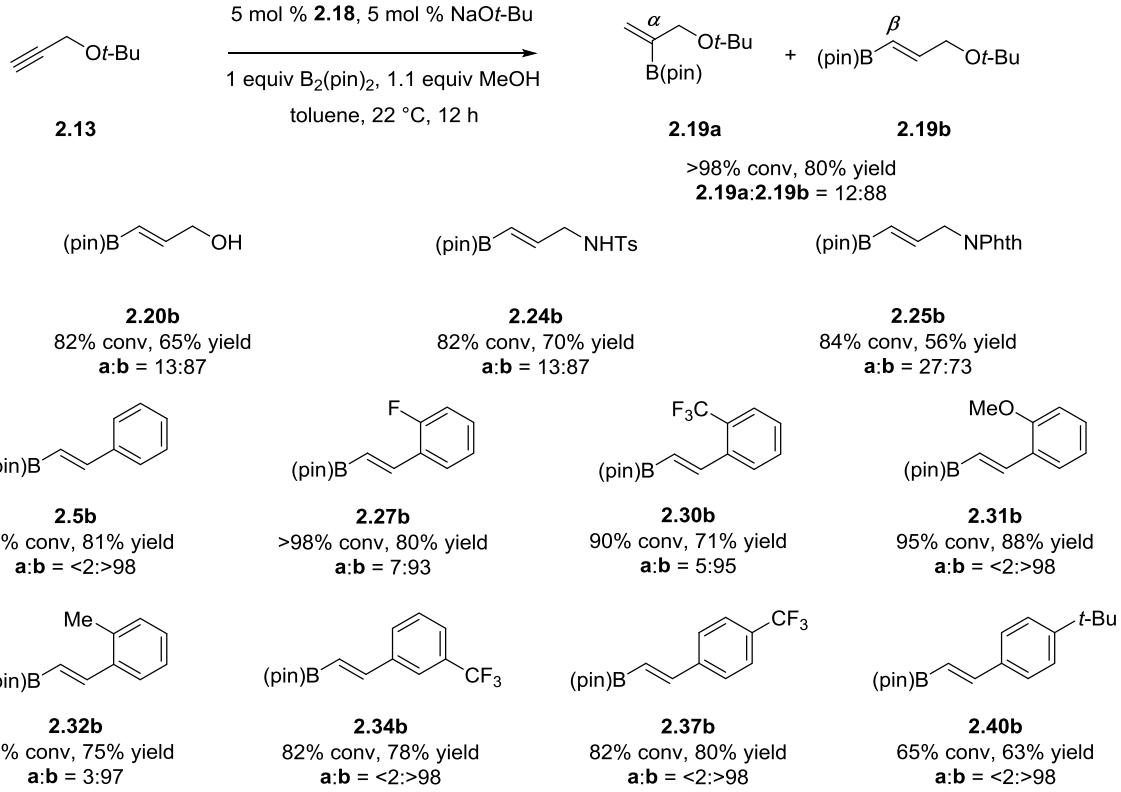
(21) (a) Pereira, S.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 3283–3286. (b) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990–4991. (c) Khramov, D. M.; Rosen, E. L.; Er, J. A. V.; Vu, P. D.; Lynch, V. M.; Bielawski, C. W. *Tetrahedron* **2008**, *64*, 6853–6862.

(22) He, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 1696–1702.

(23) (a) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127–3128. (b) Wang, Y. D.; Kimball, G.; Prashad, A. S.; Wang, Y. *Tetrahedron Lett.* **2005**, *46*, 8777–8780. (c) PraveenGanesh, N.; d'Hondt, S.; Chavant, P. Y. *J. Org. Chem.* **2007**, *72*, 4510–4514.

somewhat lower than $\alpha$-selective variants, reactions of propargyl amides undergo $\beta$-selective protoboration to afford terminal B(pin)-substituted allylic amides **2.24b** and **2.25b** in 56–70% yield with 73–87% $\beta$ selectivity. With aryl-bearing terminal alkynes, on the other hand, we obtained higher site selectivities regardless of electronic nature of substituents for $\beta$-selective protoboration compared to $\alpha$-selective variants. For instance, although only 41% of $\alpha$-selectivity is obtained from reaction of *ortho*-MeO-phenylacetylene with NHC–Cu **2.16** (**2.31a**; Scheme 2.7), $\beta$-selective protoboration of the same substrate in the presence of Cu complex **2.18** proceeds with exclusive $\beta$ selectivity (**2.31b**; >98% $\beta$). There might be minor steric effects for $\beta$-selective protoboration since we obtained slightly decreased site selectivity with some of *ortho*-substituted phenylacetylenes (93% $\beta$ for **2.27b**, 95% $\beta$ for **2.30b**, and 97% $\beta$ for **2.32b**).

***Scheme 2.10.*** $\beta$-Selective Protoborations of Terminal Alkynes



## *2.5. Mechanistic Basis for Site Selectivity in NHC–Cu-Catalyzed Protoboration of Terminal Alkynes*

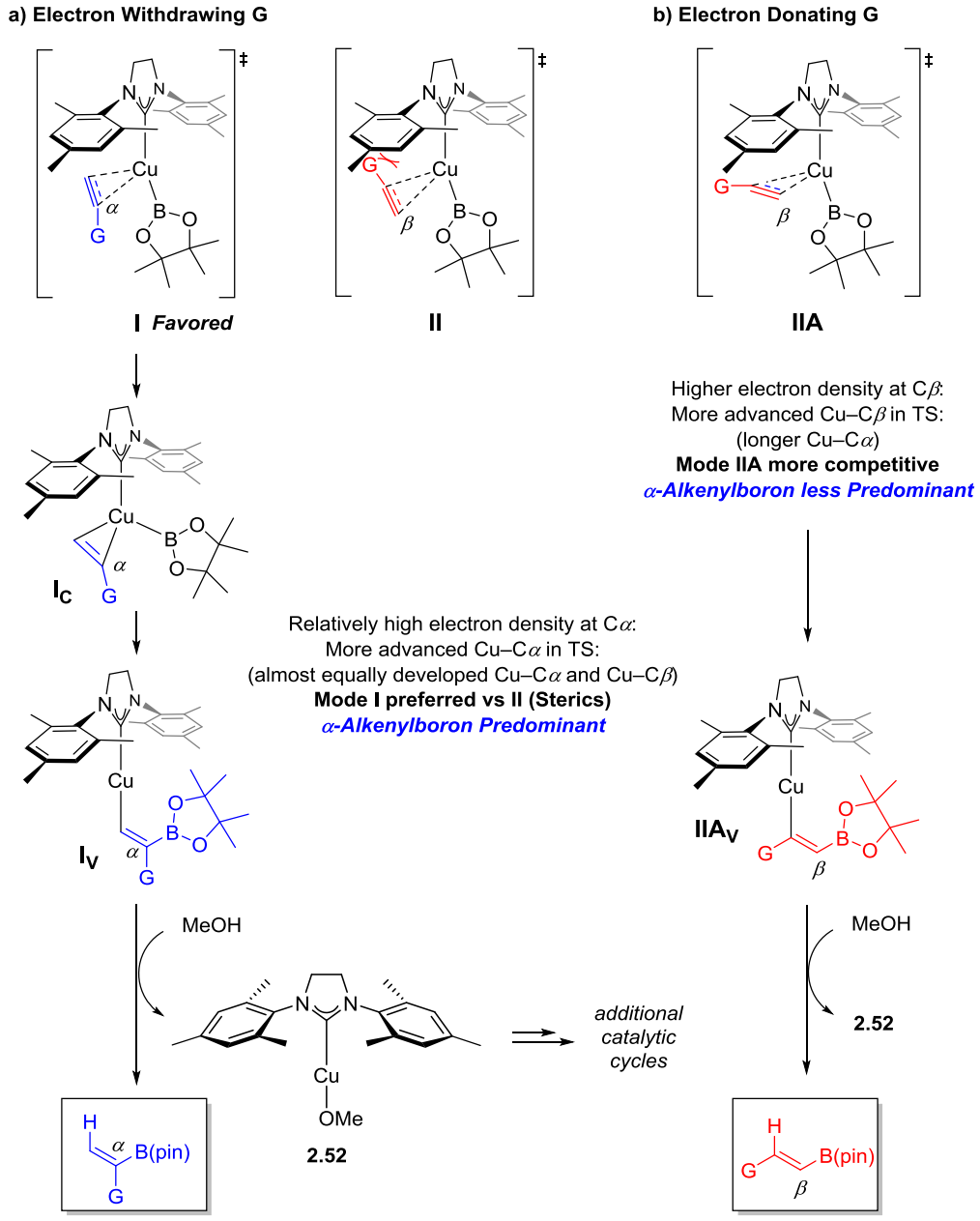
Based on above observations, we suggest plausible pathways for the generation of *α*-alkenylboron products in reactions catalyzed by *N*-aryl-NHC–Cu complex **2.14** or **2.16** (Scheme 2.11), and also for the synthesis of *β*-alkenylborons in reactions promoted by *N*-alkyl-NHC–Cu complex **2.18** (Scheme 2.12). Generally, since the electron-donating ability of an *N*-aryl-bearing NHC is weaker than that of an *N*-alkyl-containing NHC ligand based on Tolman electronic parameter (TEP),[24] structure of an NHC–Cu–B(pin) species is more linear with an *N*-aryl-bearing NHC. Therefore, when it is approaching to the Cu center, terminal alkyne substrate is placed parallel to NHC–Cu–B(pin) ("syn-to-NHC" mode). When a terminal alkyne bearing electron-withdrawing unit (Scheme 2.11a), the coordination mode I is preferred (vs II), mainly due to steric repulsion between substituent of alkyne (G) and *N*-aryl moiety of the NHC in mode II, which is consistent with our previous observation in Scheme 2.5; when we use more sizeable aryl-bearing NHC, higher *α* selectivity we obtained. The transformation might proceed to metallacyclopropene $I_C$, which is converted to copper–boron addition species $I_V$ through B(pin) unit migration to adjacent *α* carbon. Subsequent protonation of C–Cu bond in $I_V$ generates the *α*-alkenylboron product, and at the same, catalytic active NHC–Cu–OMe species **2.52** is regenerated.

In general, the HOMO coefficient of *β* carbon on terminal alkynes is larger than *α* carbon. Thus, a more advanced C*β*–Cu bond is expected than C*α*–Cu bond (shorter

(24) For a review of the Tolman electronic parameter (TEP) for phosphine ligands, see: (a) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313–348. The TEP values for NHC ligands were obtained from: (b) Kelly, R. A., III; Clavier, H.; Giudice, S.; Scott, N. M.; Stevens, E. D.; Bordner, J.; Samardjiev, I.; Hoff, C. D.; Cavallo, L.; Nolan, S. P. *Organometallics* **2008**, *27*, 202–210.

distance) in the transition state (mode I). However, as depicted in Scheme 2.11, two bonds are similarly advanced in transition state (mode I), because with an electron-withdrawing substituent, the electron density at *α* carbon is increased, which causes more similar HOMO coefficients at the two alkynyl carbons. On the other hand, the electron-donating substituent may enhance the electron density at *β* carbon, which causes the less advanced C*α*–Cu bond (mode IIA in Scheme 2.11). With this electronic effect, the distance of C*α*–Cu bond becomes relatively longer, which makes the steric repulsion between *N*-aryl unit and substituent on alkyne (G) weaker. Thus, with electron-donating substrates such as *o*-MeO-bearing phenylacetylene, mode IIA may be more competitive, which lowers the *α* selectivity (41:59 α:β for **2.31a**; Scheme 2.7).

***Scheme 2.11.*** Elelctonic and Steric Effects Influence the Sense and Level of Selectivity Less Donating NHC: More Linear C–Cu–B: ***"Syn-to-NHC"*** Alkyne Approach




When the more electron-donating alkyl-substituted NHC–Cu complex **2.18** is used, because of stronger trans effect by NHC ligand, the conformation of NHC–Cu–B(pin) may be bent from the linear structure (Scheme 2.12),[25] compare to that with less

(25) For computational studies regarding the connection between substrate coordination to distortion of $d^{10}$ metal complexes [Cu(I), Ag(I), and Au(I)] from linearity, see: (a) Carvajal, M. A.; Novoa, J. J.; Alvarez, S. *J. Am. Chem. Soc.* **2004**, *126*, 1465–1477. These investigations indicate that the barrier to distortion in

electron-donation aryl-bearing NHC–Cu complex (Scheme 2.11). This distortion would make an available coordination site more trans-to-NHC direction, which allows alkyne substrates to approach the NHC–Cu–B(pin) with "anti-to-NHC" mode. Since alkyne approaches from an angle, which positions it more distal to NHC, steric factors become less dominant in mode III and IV (Scheme 2.12). Therefore, in this case of a more electron-donating NHC, electronic effects are the key factors to determine site selectivity. When more electron donating NHC–Cu–B(pin) reacts with an alkyne, mode IV would be more favored because in mode IV, C$\beta$ (larger LUMO coefficient) is located trans to the NHC ligand, which allows more effective hyperconjugation. Therefore, $\beta$-alkenylboron compounds are afforded through metallacyclopropene $IV_C$, and B(pin)-substituted alkenylcopper species $IV_V$. The lower selectivity with propargyl heteroatom-bearing substrates (73–88% $\beta$ in Scheme 2.10), compare to those with aryl alkynes (93 to >98% $\beta$ in Scheme 2.10), might be because resonance-based effects (aryl alkynes) is more dominant than inductive effects by an electronegative heteroatom (O or N).

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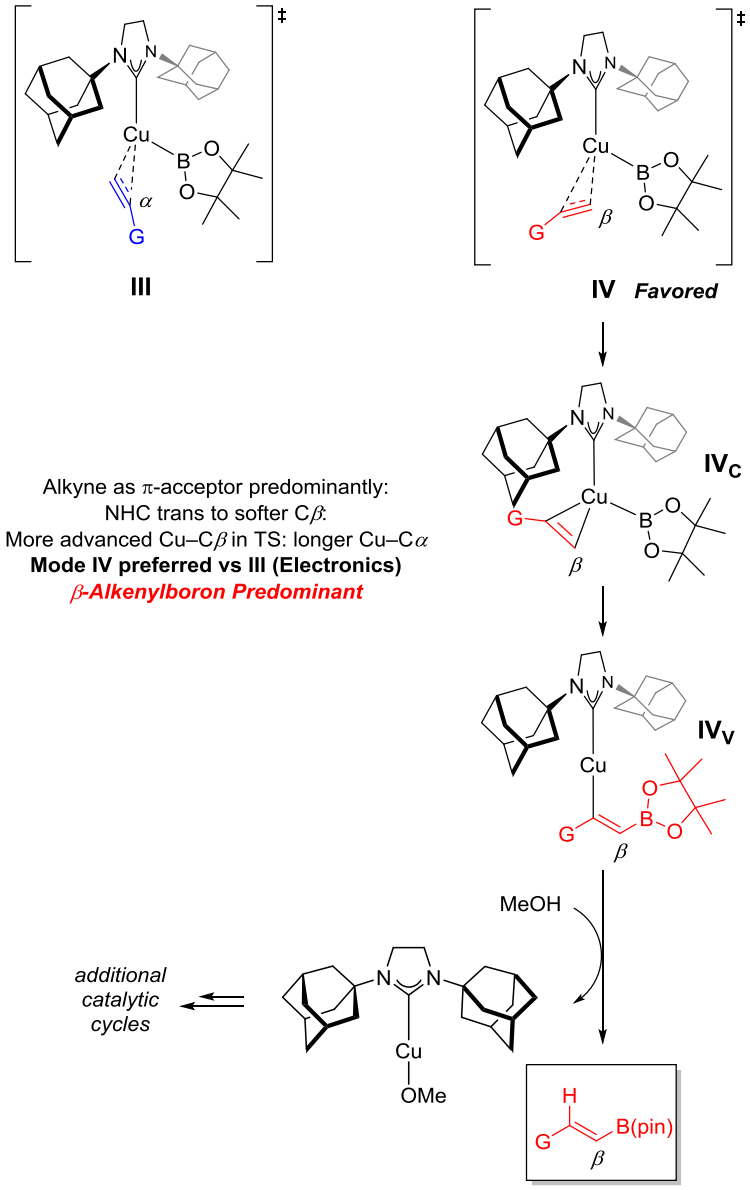
Cu(I) complexes, much of which is due to the bending in L–Cu–L' systems, is diminished with the more strongly donating ligands. For examples of distortion from linearity in an NHC–metal–ligand bond and related discussions, see: (b) Poater, A.; Ragone, F.; Correa, A.; Szadkowska, A.; Barbasiewicz, M.; Grela, K.; Cavallo, L. *Chem. –Eur. J.* **2010**, *16*, 14354–14364. For examples of structural distortion as a result of trans-influence, see: (c) Lövqvist, K. C.; Wendt, O. F.; Leipoldt, J. G. *Acta Chem. Scand.* **1996**, *50*, 1069–1073. (d) Wendt, O. F.; Elding, L. I. *J. Chem. Soc., Dalton Trans.* **1997**, 4725–4731. (e) Fernández, D.; García-Seijo, I.; Sevillano, P.; Castineiras, A.; García-Fernández, M. E. *Inorg. Chim. Acta* **2005**, *358*, 2575–2584.

***Scheme 2.12.*** Elelctonic and Steric Effects Influence the Sense and Level of Selectivity
More Donating NHC: Bent C–Cu–B: ***"Anti-to-NHC"*** Alkyne Approach




## *2.6. Conclusions*

We have developed an efficient and practical protocol for selective synthesis of internal alkenylboron compounds. Reactions of a wide range of terminal alkynes with readily available $B_2(pin)_2$ and MeOH, catalyzed by 5 mol % NHC–Cu complexes derived from commercially available imidazolinium salt, CuCl, and NaO*t*-Bu, deliver *α*-

alkenylborons with high site selectivity (up to >98% *α*). The present method is amenable to gram scale process with only 1 mol % of NHC–Cu complex, affording *α*-alkenylboron without diminution of site selectivity. The efficient syntheses of useful intermediates such as a methyl ketone and a cyclic alkenylboron compound are accomplished by chemo- and site-selective protoboryl addition to alkene-bearing terminal alkynes. With *N*-adamantyl-NHC–Cu complex, site selectivity of reactions of terminal alkynes is reversed. By changing the NHC–Cu complex, various *β*-alkenylborons are provided by catalytic protoboration method with high selectivity (73–>98% *β*).

To account for the sense and the level of site selectivity, we propose plausible pathways, which show the steric and electronic effects from the NHC ligands and the alkyne substrates. Based on proposed stereochemical models, with less electron-donating NHC–Cu complex, steric repulsion between aryl groups on NHC and substituent of alkyne is a key factor to determine the site selectivity. In the case of electron-donating group-containing alkynes, the aforementioned steric repulsion is relieved to lower the selectivity for generation of *α*-alkenylboron compounds. On the other hand, with more electron-donating NHC–Cu complex, because of the stronger trans effect, the structure of NHC–Cu–B(pin) is bended, which weakens the steric repulsion between *N*-alkyl unit and alkyne substituent. Thus electronic factor becomes more dominant to control site selectivity to afford *β*-alkenylborons. The investigations presented above illustrate that, by altering the electronic nature of the NHC ligand, high level of site selectivity can be achieved for either *α*-alkenylborons, which are not easy to prepare by other methods, or alternative *β*-alkenylborons.

## *2.7. Experimentals*

**General.** Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, $\lambda_{max}$ in $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). $^{1}H$ NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sb = sebtet, br s = broad singlet, m = multiplet), and coupling constant (Hz). $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry $N_2$ in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; $CH_2Cl_2$ and $Et_2O$ were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over $CaH_2$. All work-up and purification procedures

were carried out with reagent grade solvents (purchased from Fisher Scientific, Inc.) in air.

### *2.7.1. Reagents and Ligands*

**Aryl-substituted terminal alkynes:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

**Bis(pinacolato)diboron:** purchased from Frontier Scientific, Inc. and recrystallized from pentane.

**(1,3-Bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxyphenylmethylene)ruthenium (2.50):** obtained from Materia, Inc. and purified by silica gel column chromatography and recrystallization ($CH_2Cl_2$/*n*-pentane) prior to use.[26]

**3-*tert*-Butoxyprop-1-yne (2.13):** prepared according to a previously reported procedure.[27]

***tert*-Butyldimethyl(prop-2-yn-1-yloxy)silane:** prepared according to a previously reported procedure.[28]

***tert*-Butyl allyl(prop-2-yn-1-yl)carbamate (2.45):** prepared according to previously reported procedures.[29]

***tert*-Butyl pent-4-ynylcarbamate:** prepared according to a previously reported procedure.[30]

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(26) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.
(27) Alexakis, A.; Gardette, M.; Colin, S. *Tetrahedron Lett.* **1988**, *29*, 2951–2954.
(28) Falck, J. R.; He, A.; Fukui, H.; Tsutsui, H.; Radha, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4527–4529.
(29) Becker, D. P.; Flynn, D. L. *Tetrahedron* **1993**, *49*, 5047–5054.
(30) Saito, Y.; Matsumoto, K.; Bag, S. S.; Ogasawara, S.; Fujimoto, K.; Hanawa, K.; Saito, I. *Tetrahedron* **2008**, *64*, 3578–3588.

***tert*-Butyl prop-2-yn-1-ylcarbamate (2.44):** purchased from Aldrich Chemical Co. and purified by flash silica gel chromatography (hexanes:EtOAc = 10:1).

**5-Chloro-1-pentyne:** purchased from Aldrich Chemical Co. and purified by distillation over $CaCl_2$ prior to use.

**6-Chloro-1-pentyne:** purchased from Aldrich Chemical Co. and purified by distillation over $CaCl_2$ prior to use.

**Copper (I) chloride:** purchased from Strem Chemicals Inc. and used as received.

**Cu−NHC complex (2.14−2.18):** prepared according to previously reported procedures.[31]

**Ethynylcyclohexane:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ under reduced pressure.

**Hydrogen peroxide (35 wt. % solution in water):** purchased from Aldrich Chemical Co. and used as received.

**Methyl 4-ethynylbenzoate:** prepared according to previously reported procedures.[32]

**Methyl hex-5-ynoate:** purchased from Acros Organics Co. and purified by distillation over $CaCl_2$ prior to use.

**4-Methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide:** prepared according to a previously reported procedure.[33]

**Prop-2-yn-1-amine:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

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(31) Díez-González, S.; Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *J. Org. Chem.* **2005**, *70*, 4784–4796.
(32) Niamnont, N.; Siripornnoppakhun, W.; Rashatasakhon, P.; Sukwattanasinitt, M. *Org. Lett.* **2009**, *11*, 2768–2771.
(33) Lo, M. M. -C.; Neumann, C. S.; Nagayama, S.; Perlstein, E. O.; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 16077–16086.

**Prop-2-yn-1-ol:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

**Prop-2-yn-1-ylbenzene:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ under reduced pressure.

**Prop-2-yn-1-ylcyclopentane:** purchased from Aldrich Chemical Co. and purified by distillation over $CaCl_2$ prior to use.

**2-(Prop-2-yn-1-yl)isoindoline-1,3-dione:** purchased from Aldrich Chemical Co. and purified by flash silica gel chromatography (hexanes:EtOAc = 10:1).

**((Prop-2-yn-1-yloxy)methyl)benzene:** prepared according to a previously reported procedure.[34]

**1-(Prop-2-yn-1-yloxy)-2-vinylbenzene (2.48):** prepared according to previously reported procedures.[35]

**Sodium *tert*-butoxide** (98%)**:** purchased from Strem Chemicals Inc. and used as received.

### *2.7.2. Experimental Procedure and Characterization Data*

■ **Representative Experimental Procedure for α-Selective NHC−Cu-catalyzed Protoboration of *tert*-Butyl prop-2-yn-1-ylcarbamate 2.44:** In an $N_2$-filled glove-box, an oven-dried vial (4 mL, 17 x 38 mm) with magnetic stir bar was charged with NHC–Cu complex **2.14** (4.1 mg, 0.0100 mmol, 5.0 mol %), NaO*t*-Bu (1.0 mg, 0.0100 mmol, 5.0 mol %) and thf (0.3 mL). The mixture was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and allowed to stir for 10 min. Bis(pinacolato)diboron (50.8 mg, 0.200 mmol, 1.0 equiv.) was added to the solution, causing it to turn dark

(34) Fischer, D. F.; Xin, Z-q.; Peters, R. *Angew. Chem., Int. Ed.* **2007**, *46*, 7704–7707.
(35) Pérez-Serrano, L.; Blanco-Urgoiti, J.; Casarrubios, L.; Domínguez, G.; Pérez-Castells, J. *J. Org. Chem.* **2000**, *65*, 3513–3519.

brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of $N_2$. After this time, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) under atmosphere of $N_2$. A solution of *tert*-butyl prop-2-yn-1-ylcarbamate **2.44** (31.0 mg, 0.200 mmol, 1.0 equiv.) in thf (0.2 mL) and MeOH (8.9 μL, 0.220 mmol, 1.1 equiv.) were added (syringe). The vial was placed in a –50 °C cryocool. After 9 h, the solution was allowed to cool to –78 °C and the reaction was quenched by passing the mixture through a short plug of celite and silica gel and washed with $Et_2O$ (3 x 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=10:1) to afford the desired product **2.23a** as colorless oil (52.7 mg, 0.186 mmol, 93% yield).

**2-(3-*tert*-Butoxyprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.19a,** This compound has been previously reported and spectra data match those described**).**[36] $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.95–5.94 (1H, m), 5.86–5.85 (1H, m), 3.99–3.98 (2H, m), 1.24 (12H, s), 1.20 (9H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 139.5, 128.3, 83.4, 73.0, 63.3, 27.8, 24.9.

**2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (2.20a).** IR (neat): 3431 (br), 2979 (m), 2929 (w), 1624 (w), 1372 (s), 1307(s), 1214 (m), 1139 (s), 1033 (s), 968 (m), 905(m), 859 (s), 730 (s) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.83 (1H, s), 5.80 (1H, s), 4.18 (2H, d, *J* = 1.6 Hz), 2.36 (1H, s**)**, 1.23 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 128.7, 83.7, 65.6, 24.8; HRMS (ESI$^+$): Calcd for $C_9H_{18}B_1O_3$ $[M+H]^+$: 185.13490, Found: 185.13456.

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(36) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235.

**2-(3-(Benzyloxy)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.21a).** IR (neat): 2978 (m), 2852 (w), 1623 (w), 1420 (s), 1369 (s), 1310 (s), 1142 (s), 1093 (s), 1028 (m), 948 (s), 862 (s), 735 (s), 697 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.37–7.26 (5H, m), 5.98 (1H, br s), 5.95 (1H, d, *J* = 1.2 Hz), 4.55 (2H, s), 4.15 (2H, t, *J* = 1.2 Hz), 1.26 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 138.9, 129.6, 128.4, 127.6, 127.5, 83.6, 72.3, 72.0, 24.9; HRMS ($ESI^+$): Calcd for $C_{16}H_{24}B_1O_3$ $[M+H]^+$: 275.18185; Found: 275.18211.

***tert*-Butyldimethyl((2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)oxy)silane (2.3a,** This compound has been previously reported and spectra data match those described**).**[37] $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.96–5.95 (1H, m), 5.88–5.86 (1H, m), 4.28–4.27 (2H, m), 1.25 (12H, s), 0.91 (9H, s), 0.60 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 127.1, 83.3, 64.5, 25.9, 24.7, 18.4, –5.4.

***tert*-Butyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allylcarbamate (2.23a,** This compound has been previously reported and spectra data match those described**).**[35] $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.81 (1H, t, *J* = 1.4 Hz), 5.70 (1H, s), 4.80 (1H, s), 3.78 (2H, d, *J* = 4.4 Hz), 1.39 (9H, s), 1.21 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 155.9, 137.6, 129.1, 83.6, 78.9, 44.4, 28.4, 25.0, 24.8.

**4-Methyl-*N*-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)benzenesulfonamide (2.24a).** IR (neat): 3285 (br), 2978 (w), 2927 (w), 1372 (m), 1315 (s), 1139 (s), 1093 (m), 969 (w), 859 (m), 814 (m), 664 (s), 550 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.72 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.4 Hz), 5.78 (1H, t, *J* = 1.2 Hz), 5.72 (1H, d, *J* = 1.2 Hz), 4.97 (1H, t, *J* = 6.4 Hz), 3.68 (2H, dt, *J* = 6.4, 1.2 Hz),

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(37) Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47–53.

2.40 (3H, s), 1.21 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 143.3, 137.5, 131.5, 129.6, 127.4, 84.0, 47.8, 24.8, 21.6; HRMS ($ESI^+$): Calcd for $C_{16}H_{25}B_1N_1O_4S_1$ $[M+H]^+$: 338.15973; Found: 338.16078.

**2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)isoindoline-1,3-dione (2.25a).** IR (neat): 2979 (w), 1772 (w), 1712 (s), 1370 (s), 1314 (s), 1136 (s), 1112 (m), 955 (m), 907 (m), 859 (m), 712 (s), 529 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.84 (2H, dd, *J* = 5.6, 2.8 Hz), 7.70 (2H, dd, *J* = 5.6, 2.8 Hz), 5.88 (1H, d, *J* = 2.0 Hz), 5.55 (1H, d, *J* = 2.0 Hz), 4.41 (2H, t, *J* = 2.0 Hz), 1.20 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 168.3, 133.9, 132.4, 129.0, 123.3, 83.8, 41.1, 24.8; HRMS ($ESI^+$): Calcd for $C_{17}H_{21}B_1N_1O_4$ $[M+H]^+$: 314.15636; Found: 314.15650.

**4,4,5,5-Tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (2.5a).** IR (neat): 2978 (m), 1371 (s), 1306 (s), 1210 (s), 1142 (s), 1095 (m), 966 (m), 887 (m), 849 (s), 781 (m), 730 (m), 698 (m), 512 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.48 (2H, m), 7.34–7.30 (2H, m), 7.27–7.23 (1H, m), 6.09 (1H, d, *J* = 2.8 Hz), 6.07 (1H, d, *J* = 2.8 Hz), 1.33 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 141.5, 131.0, 128.3, 127.3, 127.1, 83.9, 24.9; HRMS ($ESI^+$): Calcd for $C_{14}H_{20}B_1O_2$ $[M+H]^+$: 231.15564; Found: 231.15565.

**2-(1-(2-Fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.27a).** IR (neat): 2979 (m), 1487 (m), 1413 (m), 1372 (s), 1319 (s), 1266 (m), 1196 (m), 1144 (s), 1104 (m), 967 (m), 852 (m), 827 (m), 753 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.29 (1H, ddd, *J* = 7.6, 7.6, 2.0 Hz), 7.21–7.17 (1H, m), 7.08 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.01 (1H, ddd, *J* = 10.4, 8.4, 1.2 Hz), 6.10 (1H, d, *J* = 3.2 Hz), 6.01 (1H, d, *J* = 2.8 Hz), 1.30 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 160.0 (d, *J* = 245 Hz), 132.6 (d, *J* = 2.3 Hz), 129.9 (d, *J* = 14.1 Hz), 129.7 (d, *J* = 3.8 Hz), 128.8 (d, *J* = 8.2 Hz), 124.2 (d, *J* = 3.0

Hz), 115.4 (d, $J$ = 22.3 Hz), 84.0, 24.8; HRMS (ESI$^+$): Calcd for $C_{14}H_{19}B_1F_1O_2$ $[M+H]^+$: 249.14621; Found: 249.14681.

**2-(1-(2-Chlorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.28a).** IR (neat): 2979 (m), 1471 (m), 1369 (s), 1316 (s), 1261 (m), 1209 (m), 1143 (s), 1100 (s), 1045 (m), 966 (m), 889 (w), 849 (m), 744 (s), 697 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.32 (1H, dd, $J$ = 8.0, 1.2 Hz), 7.24–7.16 (3H, m), 6.11 (1H, d, $J$ = 3.2 Hz), 5.84 (1H, d, $J$ = 3.2 Hz), 1.29 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 141.8, 132.7, 132.6, 129.8, 129.1, 128.4, 127.1, 84.0, 24.9; HRMS (ESI$^+$): Calcd for $C_{14}H_{19}B_1Cl_1O_2$ $[M+H]^+$: 265.11666; Found: 265.11782.

**2-(1-(2-Bromophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.29a).** IR (neat): 2978 (m), 1468 (m), 1369 (s), 1317 (s), 1259 (m), 1212 (m), 1144 (s), 1099 (m), 1024 (m), 966 (m), 849 (m), 742 (m), 689 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.51 (1H, dd, $J$ = 8.0, 1.2 Hz), 7.26 (1H, ddd, $J$ = 7.6, 7.6, 1.2 Hz), 7.20 (1H, dd, $J$ = 7.6, 2.0 Hz), 7.09 (1H, ddd, $J$ = 8.0, 8.0, 2.0 Hz), 6.10 (1H, d, $J$ = 3.6 Hz), 5.78 (1H, d, $J$ = 3.2 Hz), 1.29 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 143.9, 132.6, 132.2, 129.8, 128.5, 127.7, 123.0, 84.1, 24.9; HRMS (ESI$^+$): Calcd for $C_{14}H_{19}B_1Br_1O_2$ $[M+H]^+$: 309.06615; Found: 309.06523.

**4,4,5,5-Tetramethyl-2-(1-(2-(trifluoromethyl)phenyl)vinyl)-1,3,2-dioxaborolane (2.30a).** IR (neat): 2980 (w), 1369 (m), 1313 (s), 1212 (w), 1124 (s), 1052 (m), 1035 (m), 966 (w), 850 (m), 766 (m), 697 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.61 (1H, d, $J$ = 7.6 Hz), 7.47 (1H, ddd, $J$ = 7.6, 7.6, 0.4 Hz), 7.33 (1H, dd, $J$ = 7.6, 7.6 Hz), 7.16 (1H, d, $J$ = 7.6 Hz), 6.20 (1H, d, $J$ = 3.6 Hz), 5.76 (1H, d, $J$ = 3.2 Hz), 1.26 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 142.3, 133.6 (q, $J$ = 3.6 Hz), 131.6, 130.5, 127.8 (q, $J$ = 29.0 Hz),

126.7, 125.9 (q, $J$ = 3.0 Hz), 124.6 (q, $J$ = 266 Hz), 84.1, 24.8; HRMS ($ESI^+$): Calcd for $C_{15}H_{22}B_1F_3N_1O_2$ $[M+NH_4]^+$: 316.16957; Found: 316.17040.

**4,4,5,5-Tetramethyl-2-(1-(*o*-tolyl)vinyl)-1,3,2-dioxaborolane (2.32a).** IR (neat): 2978 (m), 2926 (w), 1367 (s), 1312 (s), 1216 (m), 1143 (s), 1087 (m), 966 (m), 889 (w), 850 (m), 772 (m), 737 (m), 688 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.17–7.14 (3H, m), 7.11–7.08 (1H, m), 6.16 (1H, d, $J$ = 4.0 Hz), 5.80 (1H, d, $J$ = 3.6 Hz), 2.27 (3H, s), 1.28 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 142.8, 135.1, 133.1, 129.8, 128.5, 127.0, 125.9, 83.9, 24.9, 20.4; HRMS ($ESI^+$): Calcd for $C_{15}H_{22}B_1O_2$ $[M+H]^+$: 245.17129; Found: 245.17158.

**2-(1-(3-Fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.33a).** IR (neat): 2979 (m), 1577 (m), 1371 (s), 1314 (s), 1237 (s), 1140 (s), 932 (m), 867 (s), 843 (m), 787 (m), 735 (m), 672 (m), 521 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.30–7.24 (2H, m), 7.22–7.19 (1H, m), 6.95–6.90 (1H, m), 6.09 (2H, s), 1.32 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 163.0 (d, $J$ = 243 Hz), 143.7 (d, $J$ = 8.2 Hz), 132.0, 129.6 (d, $J$ = 8.2 Hz), 122.9 (d, $J$ = 3.0 Hz), 114.2 (d, $J$ = 21.6 Hz), 113.9 (d, $J$ = 20.8 Hz), 84.1, 24.9; HRMS ($ESI^+$): Calcd for $C_{14}H_{19}B_1F_1O_2$ $[M+H]^+$: 249.14621; Found: 249.14641.

**4,4,5,5-Tetramethyl-2-(1-(3-(trifluoromethyl)phenyl)vinyl)-1,3,2-dioxaborolane (2.34a).** IR (neat): 2980 (w), 1371 (m), 1324 (s), 1204 (m), 1121 (s), 1073 (s), 966 (w), 901 (w), 855 (m), 806 (m), 742 (w), 696 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.75–7.74 (1H, m), 7.67 (1H, dd, $J$ = 8.0, 1.2 Hz), 7.51 (1H, dd, $J$ = 7.6, 0.8 Hz), 7.43 (1H, ddd, $J$ = 7.2, 7.2, 0.8 Hz), 6.16 (1H, d, $J$ = 2.8 Hz), 6.14 (1H, d, $J$ = 2.4 Hz), 1.34 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 142.3, 132.6, 130.7 (d, $J$ = 1.5 Hz), 130.6 (q, $J$ = 31.3 Hz),

128.7, 124.5 (q, $J$ = 271 Hz), 124.1 (q, $J$ = 3.7 Hz), 123.8 (q, $J$ = 3.7 Hz), 84.2, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{19}B_1F_3O_2$ $[M+H]^+$: 299.14302; Found: 299.14410.

**2-(1-(3-Methoxyphenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.35a).** IR (neat): 2977 (m), 1598 (m), 1574 (m), 1371 (s), 1311 (s), 1285 (m), 1244 (s), 1195 (m), 1142 (s), 1048 (m), 967 (m), 863 (m), 786 (m), 743 (m), 682 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.23 (1H, m, $J$ = 8.0, 8.0, 1.2 Hz), 7.09–7.04 (2H, m), 6.80 (1H, ddd, $J$ = 8.0, 2.4, 0.8 Hz), 6.08 (1H, d, $J$ = 3.2 Hz), 6.05 (1H, d, $J$ = 2.8 Hz), 3.80 (3H, s), 1.32 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 159.6, 142.9, 131.1, 129.2, 119.8, 113.0, 112.7, 83.9, 55.3, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{22}B_1O_3$ $[M+H]^+$: 261.16620; Found: 261.16634.

**2-(1-(4-Fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.36a).** IR (neat): 2979 (w), 1508 (s), 1371 (s), 1315 (s), 1298 (m), 1207 (s), 1142 (s), 1084 (m), 966 (m), 889 (w), 840 (s), 751 (w), 670 (w), 586 (w), 515 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.46 (2H, dd, $J$ = 8.8, 5.6 Hz), 7.01 (2H, dd, $J$ = 8.8, 8.8 Hz), 6.05 (2H, m), 1.33 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 162.4 (d, $J$ = 244 Hz), 137.5, 130.9 (d, $J$ = 1.5 Hz), 128.9 (d, $J$ = 8.2 Hz), 115.1 (d, $J$ = 20.8 Hz), 84.0, 24.9; HRMS ($ESI^+$): Calcd for $C_{14}H_{19}B_1F_1O_2$ $[M+H]^+$: 249.14621; Found: 249.14663.

**4,4,5,5-Tetramethyl-2-(1-(4-(trifluoromethyl)phenyl)vinyl)-1,3,2-dioxaborolane (2.37a).** IR (neat): 2980 (w), 1372 (m), 1320 (s), 1213 (m), 1113 (s), 1090 (s), 1065 (s), 1017 (m), 966 (m), 849 (s), 743 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.58 (4H, s), 6.18 (1H, d, $J$ = 2.4 Hz), 6.13 (1H, d, $J$ = 2.4 Hz), 1.34 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 145.2, 133.1, 129.1 (q, $J$ = 32 Hz), 127.6, 125.2 (q, $J$ = 4.0 Hz), 124.5 (q, $J$ = 270 Hz), 84.2, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{19}B_1F_3O_2$ $[M+H]^+$: 299.14302; Found: 299.14348.

**4,4,5,5-Tetramethyl-2-(1-(4-nitrophenyl)vinyl)-1,3,2-dioxaborolane (2.38a,** This compound has been previously reported and spectra data match those described**).**[38] $^1$H NMR ($CDCl_3$, 400 MHz): δ 8.17 (2H, dd, *J* = 7.2, 2.0 Hz), 7.62 (2H, dd, *J* = 7.2, 2.0 Hz), 6.25 (1H, d, *J* = 2.4 Hz), 6.19 (1H, d, *J* = 2.4 Hz), 1.33 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 148.3, 147.0, 134.5, 128.1, 123.6, 84.4, 24.9.

**Methyl 4-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzoate (2.41a).** IR (neat): 2978 (w), 1719 (s), 1607 (w), 1434 (m), 1370 (s), 1319 (m), 1273 (s), 1210 (s), 1143 (s), 1106 (s), 1019 (m), 966 (m), 850 (s), 785 (m), 734 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.98 (2H, dd, *J* = 6.8, 1.6 Hz), 7.54 (2H, dd, *J* = 6.8, 2.0 Hz), 6.15 (2H, d, *J* = 1.6 Hz), 3.90 (3H, s), 1.32 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 167.2, 146.2, 132.9, 129.7, 128.7, 127.3, 84.1, 52.1, 24.9; HRMS ($ESI^+$): Calcd for $C_{16}H_{22}B_1O_4$ $[M+H]^+$: 289.16111; Found: 289.16028.

■ **Experimental Procedure for α-Selective NHC−Cu-Catalyzed Protoboration of *tert*-Butyl prop-2-yn-1-ylcarbamate 2.44 on Gram Scale:** In an $N_2$-filled glove-box, an oven-dried round-bottom flask (50 mL) with magnetic stir bar was charged with NHC–Cu complex **2.14** (26.1 mg, 0.0644 mmol, 1.0 mol %), NaO*t*-Bu (6.2 mg, 0.0644 mmol, 1.0 mol %) and toluene (10 mL). The vessel was sealed with a septum and allowed to stir for 10 min. Bis(pinacolato)diboron (1.80 g, 7.09 mmol, 1.1 equiv.) was added to the solution, causing to turn dark brown immediately. The flask was resealed with a septum and removed from the glovebox. The mixture was allowed to stir at 22 °C for 30 min under $N_2$ atm. After that, it was allowed to cool to –78 °C (dry ice/acetone bath) under $N_2$

(38) Khramov, D. M.; Rosen, E. L.; Er, J. A. V.; Vu, P. D.; Lynch, V. M.; Bielawski, C. W. *Tetrahedron* **2008**, *64*, 6853–6862.

atm. A solution of *tert*-butyl prop-2-yn-1-ylcarbamate **2.44** (1.00 g, 6.44 mmol, 1.0 equiv.) in toluene (5 mL) and MeOH (392 μL, 9.67 mmol, 1.5 equiv.) were added (syringe). The flask was placed in a –50 °C cryocool. After nine hours, the solution was allowed to cool to –78 °C and the reaction was quenched by passing through a short plug of celite and silica gel and washed with $Et_2O$ (3 x 20 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel column chromatography (hexanes:$Et_2O$=10:1) to afford the desired product **2.23a** as colorless oil (1.66 g, 5.85 mmol, 91% yield).

***tert*-Butyl allyl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate (2.46,** This compound has been previously reported and spectra data match those described**).**[39] $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.85–5.84 (1H, m), 5.74–5.70 (1H, m), 5.60 (1H, d, *J* = 2.8 Hz), 5.07 (1H, br s), 5.04 (1H, br s), 3.92–3.71 (4H, m), 1.41 (9H, s), 1.22 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 155.8 (155.6), 148.6, 134.2 (133.9), 128.8 (128.5), 116.3 (115.8), 83.6 (83.3), 79.3 (79.7), 49.6 (48.9), 28.5, 24.8.

■ **Experimental Procedure for Oxidation of Alkenylboron 2.46:** To a solution of vinylboronate **14** (119 mg, 0.368 mmol) in thf (2 mL) at 0 °C (ice bath) were added $H_2O_2$ (179 μL, 1.84 mmol, 5.00 equiv.) and 2 N NaOH (921 μL, 1.84 mmol, 5.00 equiv.). The resulting solution was allowed to stir at 22 °C for one hour. After this time, the mixture was diluted with water (4 mL), washed with $Et_2O$ (3 x 2 mL). Combined organic layers were filtered through a plug of $MgSO_4$. The filtrate was concentrated *in vacuo* to provide

(39) Renaud, J.; Ouellet, S. G. *J. Am. Chem. Soc.* **1998**, *120*, 7995–7996.

brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=10:1) to afford the desired product **2.47** as a pale yellow oil (64.5 mg, 0.302 mmol, 82% yield).

***tert*-Butyl allyl(2-oxopropyl)carbamate (2.47).** IR (neat): 2979 (w), 2929 (w), 1688 (s), 1454 (m), 1393 (m), 1366 (m), 1247 (s), 1164 (s), 910 (s), 728 (s), 647 (m), 568 (w), 529 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.77–5.69 (1H, m), 5.12–5.04 (2H, m), 3.94 (1H, s), 3.89 (1H, d, *J* = 6.0 Hz), 3.82 (1H, s), 3.81 (1H, d, *J* = 6.0 Hz), 2.08 (3H, d, *J* = 4.8 Hz), 1.41 (9H, d, *J* = 16.4 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 204.6 (204.5), 155.7 (155.1), 133.8 (133.7), 117.7 (116.9), 80.4, 56.2 (55.9), 50.9 (50.6), 28.4 (28.3), 27.0 (26.8); HRMS ($ESI^+$): Calcd for $C_{11}H_{20}N_1O_3$ $[M+H]^+$: 214.14432; Found: 214.14369.

**4,4,5,5-Tetramethyl-2-(3-(2-vinylphenoxy)prop-1-en-2-yl)-1,3,2-dioxaborolane (2.49).** IR (neat): 2979 (w), 1626 (w), 1598 (w), 1486 (m), 1450 (m), 1422 (m), 1381 (m), 1372 (m), 1350 (s), 1314 (s), 1242 (s), 1141 (m), 1035 (m), 951 (w), 907 (w), 864 (w), 749 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.49 (1H, dd, *J* = 7.6, 1.6 Hz), 7.21–7.19 (1H, m), 7.16 (1H, dd, *J* = 17.6, 11.2 Hz), 6.95–6.89 (2H, dd, *J* = 13.6, 7.2 Hz), 6.08 (1H, s), 6.04 (1H, dd, *J* = 3.2, 1.6 Hz), 5.75 (1H, dd, *J* = 18.0, 1.6 Hz), 5.25 (1H, dd, *J* = 11.2, 1.6 Hz), 4.68 (2H, t, *J* = 1.6 Hz), 1.30 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 156.0, 131.9, 130.1, 128.8, 127.1, 126.4, 120.7, 114.2, 112.7, 83.8, 69.9, 24.9; HRMS ($ESI^+$): Calcd for $C_{17}H_{24}B_1O_3$ $[M+H]^+$: 287.18185; Found: 287.18252.

■ **Experimental Procedure for Ru-Catalyzed Ring-closing Metathesis of Alkenylboron 2.49:** To a solution of alkenylboron **2.49** (28.6 mg, 0.100 mmol, 1.0 equiv.) in anhydrous benzene (9 mL) was added a solution of the Ru carbene **2.50** (3.1 mg, 0.00500 mmol, 5.0 mol %) in benzene (1 mL) via syringe. The mixture was allowed to

stir at 22 °C under $N_2$ atm. After 60 h, the reaction was quenched by passing through a short plug of celite and silica gel and the mixture was washed with $Et_2O$ (3 x 10 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=20:1) to afford the desired product **2.51** as a pale yellow oil (18.2 mg, 0.0705 mmol, 71% yield).

**2-(2*H*-Chromen-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.51).** IR (neat): 2977 (w), 1627 (m), 1485 (w), 1355 (s), 1309 (m), 1211 (m), 1141 (s), 987 (m), 847 (m), 754 (m), 662 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.14 (1H, ddd, *J* = 8.0, 7.2, 1.6 Hz), 7.10 (1H, s), 7.01 (1H, dd, *J* = 7.6, 1.6 Hz), 6.86 (1H, ddd, *J* = 7.2, 1.2, 1.2 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 4.87 (2H, d, *J* = 1.6 Hz), 1.30 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 155.4, 137.4, 130.6, 127.7, 122.6, 121.4, 116.0, 83.9, 67.1, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{20}B_1O_3$ $[M+H]^+$: 259.15055; Found: 259.15032.

■ **Representative Experimental Procedure for *β*-Selective NHC−Cu-Catalyzed Protoboration of Phenylacetylene 2.26:** In an $N_2$-filled glovebox, an oven-dried vial (4 mL, 17 x 38 mm) with magnetic stir bar was charged with NHC–Cu complex **2.18** (4.4 mg, 0.0100 mmol, 5.0 mol %), NaO*t*-Bu (1.0 mg, 0.0100 mmol, 5.0 mol %) and thf (0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and allowed to stir for 10 min. Bis(pinacolato)diboron (50.8 mg, 0.200 mmol, 1.0 equiv.) was added, causing the solution to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under $N_2$ atm. At this time, phenylacetylene **2.26** (22.0 μL, 0.200 mmol, 1.0 equiv.) and MeOH (8.9 μL, 0.220 mmol, 1.1 equiv.) were added (syringe). The solution was allowed to stir

at 22 °C for 12 h. After 12 h, the reaction was quenched by passing through a short plug of celite and silica gel and washed with $Et_2O$ (3 x 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=50:1) to afford the desired product **2.5b** as pale yellow oil (37.1 mg, 0.161 mmol, 81% yield).

**(*E*)-2-(3-*tert*-Butoxyprop-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.19b,** This compound has been previously reported and spectra data match those described**).**[40] $^1$H NMR ($CDCl_3$, 400 MHz): δ 6.64 (1H, dt, *J* = 18.0, 4.4 Hz), 5.69 (1H, dt, *J* = 18.0, 1.6 Hz), 3.95 (2H, dd, *J* = 4.8, 4.0 Hz), 1.22 (12H, s), 1.17 (9H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 151.0, 118.5, 83.1, 73.2, 63.8, 27.6, 24.8.

**(*E*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (2.20b).** IR (neat): 3426 (br), 2979 (m), 2929 (w), 1643 (m), 1359 (s), 1317 (s), 1141 (s), 1088 (m), 1003 (m), 970 (s), 921 (m), 849 (s), 732 (s), 627 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 6.68 (1H, dt, *J* = 18.4, 4.0 Hz), 5.65 (1H, dt, *J* = 18.4, 2.0 Hz), 4.17 (2H, m), 2.36 (1H, br s), 1.22 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 152.1, 83.4, 64.4, 24.8; HRMS ($ESI^+$): Calcd for $C_9H_{18}B_1O_3$ $[M+H]^+$: 185.13490; Found: 185.13563.

**(*E*)-4-Methyl-*N*-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)benzenesulfonamide (2.24b).** IR (neat): 3275 (br), 2978 (m), 2928 (w), 1644 (m), 1364 (s), 1322 (s), 1143 (s), 1094 (s), 971 (s), 848 (s), 663 (s), 550 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.70 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.0 Hz), 6.39 (1H, dt, *J* = 18.0, 5.2 Hz), 5.50 (1H, dt, *J* = 18.0, 1.6 Hz), 4.74 (1H, t, *J* = 6.4 Hz), 3.62 (2H, m), 2.38 (3H, s), 1.19 (12H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 146.8, 143.5, 137.1,

(40) Pandya, S. U.; Pinet, S.; Chavant, P. Y.; Vallée, Y. *Eur. J. Org. Chem*. **2003**, 3621–3627.

129.8, 127.3, 83.5, 46.8, 24.8, 21.6; HRMS ($ESI^+$): Calcd for $C_{16}H_{28}B_1N_2O_4S_1$ $[M+NH_4]^+$: 355.18628; Found: 355.18570.

**(*E*)-2-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)isoindoline-1,3-dione (2.25b).** IR (neat): 2978 (m), 2928 (w), 1773 (m), 1712 (s), 1645 (m), 1326 (s), 1143 (s), 955 (m), 850 (m), 714 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.84 (2H, dd, *J* = 5.6, 2.8 Hz), 7.71 (2H, dd, *J* = 5.6, 2.8 Hz), 6.58 (1H, dt, *J* = 18.0, 4.4 Hz), 5.47 (1H, dt, *J* = 18.0, 1.6 Hz), 4.37 (2H, dd, *J* = 4.4, 2.0 Hz), 1.22 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 167.9, 145.3, 134.1, 132.2, 123.4, 83.5, 41.0, 24.9; HRMS ($ESI^+$): Calcd for $C_{17}H_{21}B_1N_1O_4$ $[M+H]^+$: 314.15636; Found: 314.15697.

**(*E*)-4,4,5,5-Tetramethyl-2-styryl-1,3,2-dioxaborolane (2.5b,** This compound has been previously reported and spectra data match those described**).**[41] $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.49–7.47 (2H, m), 7.40 (1H, d, *J* = 18.4 Hz), 7.35–7.27 (3H, m), 6.17 (1H, d, *J* = 18.4 Hz), 1.30 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 149.6, 137.6, 129.0, 128.7, 127.2, 83.4, 24.9.

**(*E*)-2-(2-Fluorostyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.27b).** IR (neat): 2979 (w), 1625 (m), 1486 (m), 1349 (s), 1227 (w), 1144 (s), 970 (w), 849 (w), 755 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.59 (1H, d, *J* = 18.4 Hz), 7.56 (1H, dt, *J* = 7.6, 1.6 Hz), 7.26 (1H, m), 7.11 (1H, dt, *J* = 7.6, 0.8 Hz), 7.03 (1H, ddd, *J* = 10.4, 8.4, 1.2 Hz), 6.24 (1H, d, *J* = 18.8 Hz), 1.32 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 160.9 (d, *J* = 250 Hz), 141.4 (d, *J* = 3.7 Hz), 130.3 (d, *J* = 8.2 Hz), 127.5 (d, *J* = 3.0 Hz), 125.5 (d, *J* = 11.1 Hz), 124.2 (d, *J* = 3.8 Hz), 115.9 (d, *J* = 21.5 Hz), 83.6, 25.0; HRMS ($ESI^+$): Calcd for $C_{14}H_{19}B_1F_1O_2$ $[M+H]^+$: 249.14621; Found: 249.14654.

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(41) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485.

**(*E*)-4,4,5,5-Tetramethyl-2-(2-(trifluoromethyl)styryl)-1,3,2-dioxaborolane (2.30b).** IR (neat): 2980 (w), 1625 (w), 1484 (w), 1349 (s), 1311 (s), 1270(m), 1208 (w), 1121(s), 1060 (m), 1036 (m), 996 (m), 969 (m), 850 (m), 764 (m), 744 (m), 647 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.74 (1H, d, *J* = 18.4 Hz), 7.71 (1H, d, *J* = 8.0 Hz), 7.63 (1H, dd, *J* = 8.0, 0.8 Hz), 7.52 (1H, dd, *J* = 7.6, 7.6 Hz), 7.38 (1H, dd, *J* = 7.6, 7.6 Hz), 6.16 (1H, d, *J* = 18.4 Hz), 1.31 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.9 (d, *J* = 1.5 Hz), 137.1, 132.0, 128.3, 127.9 (q, *J* = 29.8 Hz), 127.6, 125.8 (q, *J* = 6.0 Hz), 124.3 (q, *J* = 272 Hz), 83.7, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{19}B_1F_3O_2$ $[M+H]^+$: 299.14302; Found: 299.14395.

**(*E*)-2-(2-Methoxystyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.31b,** This compound has been previously reported and spectra data match those described**).**[42] $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.76 (1H, d, *J* = 18.4 Hz), 7.53 (1H, dd, *J* = 7.6, 1.6 Hz), 7.25 (1H, ddd, *J* = 8.4, 7.6, 2.0 Hz), 6.92 (1H, dd, *J* = 7.6, 7.6 Hz), 6.85 (1H, dd, *J* = 8.4, 0.8 Hz), 6.17 (1H, d, *J* = 18.4 Hz), 3.83 (3H, s), 1.30 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 157.5, 144.2, 130.1, 127.2, 126.7, 120.7, 111.0, 83.3, 55.5, 24.9.

**(*E*)-4,4,5,5-Tetramethyl-2-(2-methylstyryl)-1,3,2-dioxaborolane (2.32b).** IR (neat): 2977 (w), 1620 (m), 1483 (w), 1345 (s), 1203 (w), 1143 (s), 996 (m), 970 (m), 850 (m), 749 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.66 (1H, d, *J* = 18.4 Hz), 7.58–7.55 (1H, m), 7.21–7.18 (2H, m), 7.17–7.14 (1H, m), 6.09 (1H, d, *J* = 18.4 Hz), 2.43 (3H, s), 1.33 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 147.3, 136.8, 136.4, 130.5, 128.7, 126.2, 125.9, 83.4, 25.0, 19.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{22}B_1O_2$ $[M+H]^+$: 245.17129; Found: 245.17119.

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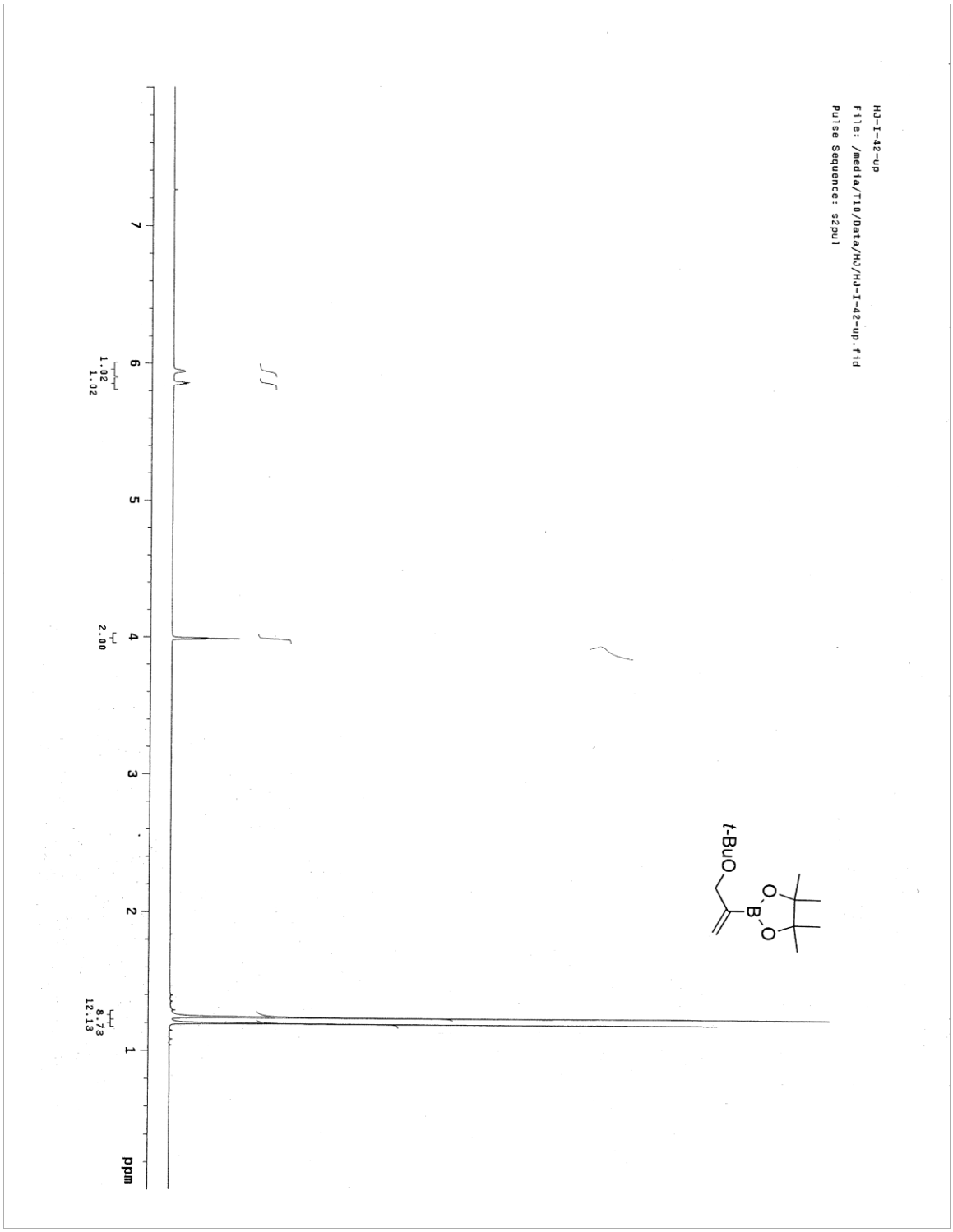
(42) Stewart, S. K.; Whiting, A. *J. Organomet. Chem.* **1994**, *482*, 293–300.

**(*E*)-4,4,5,5-Tetramethyl-2-(3-(trifluoromethyl)styryl)-1,3,2-dioxaborolane (2.34b).** IR (neat): 2980 (w), 1627 (m), 1438 (w), 1350 (s), 1329 (s), 1206 (m), 1128 (s), 1074 (m), 995 (w), 970 (w), 849 (m), 795 (m), 697 (w), 665 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.72 (1H, s), 7.64 (1H, d, $J$ = 8.0 Hz), 7.53 (1H, d, $J$ = 8.0 Hz), 7.46 (1H, d, $J$ = 8.0 Hz), 7.40 (1H, d, $J$ = 18.4 Hz), 6.24 (1H, d, $J$ = 18.4 Hz), 1.31 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 147.8, 138.4, 131.2 (q, $J$ = 32 Hz), 130.1 (d, $J$ = 1.5 Hz), 129.2, 125.4 (q, $J$ = 4.0 Hz), 124.1 (q, $J$ = 272 Hz), 123.9 (q, $J$ = 3.7 Hz), 83.7, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{19}B_1F_3O_2$ $[M+H]^+$: 299.14302; Found: 299.14400.

**(*E*)-4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)styryl)-1,3,2-dioxaborolane (2.37b).** IR (neat): 2980 (w), 1628 (w), 1351 (m), 1322 (s), 1126 (m), 1067 (m), 970 (w), 816 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.60–7.55 (4H, m), 7.40 (1H, d, $J$ = 18.4 Hz), 6.26 (1H, d, $J$ = 18.4 Hz), 1.32 (12H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 147.8, 140.9, 130.6 (q, $J$ = 32 Hz), 127.3, 125.7 (q, $J$ = 4.0 Hz), 124.2 (q, $J$ = 271 Hz), 83.8, 24.9; HRMS ($ESI^+$): Calcd for $C_{15}H_{19}B_1F_3O_2$ $[M+H]^+$: 299.14302; Found: 299.14311.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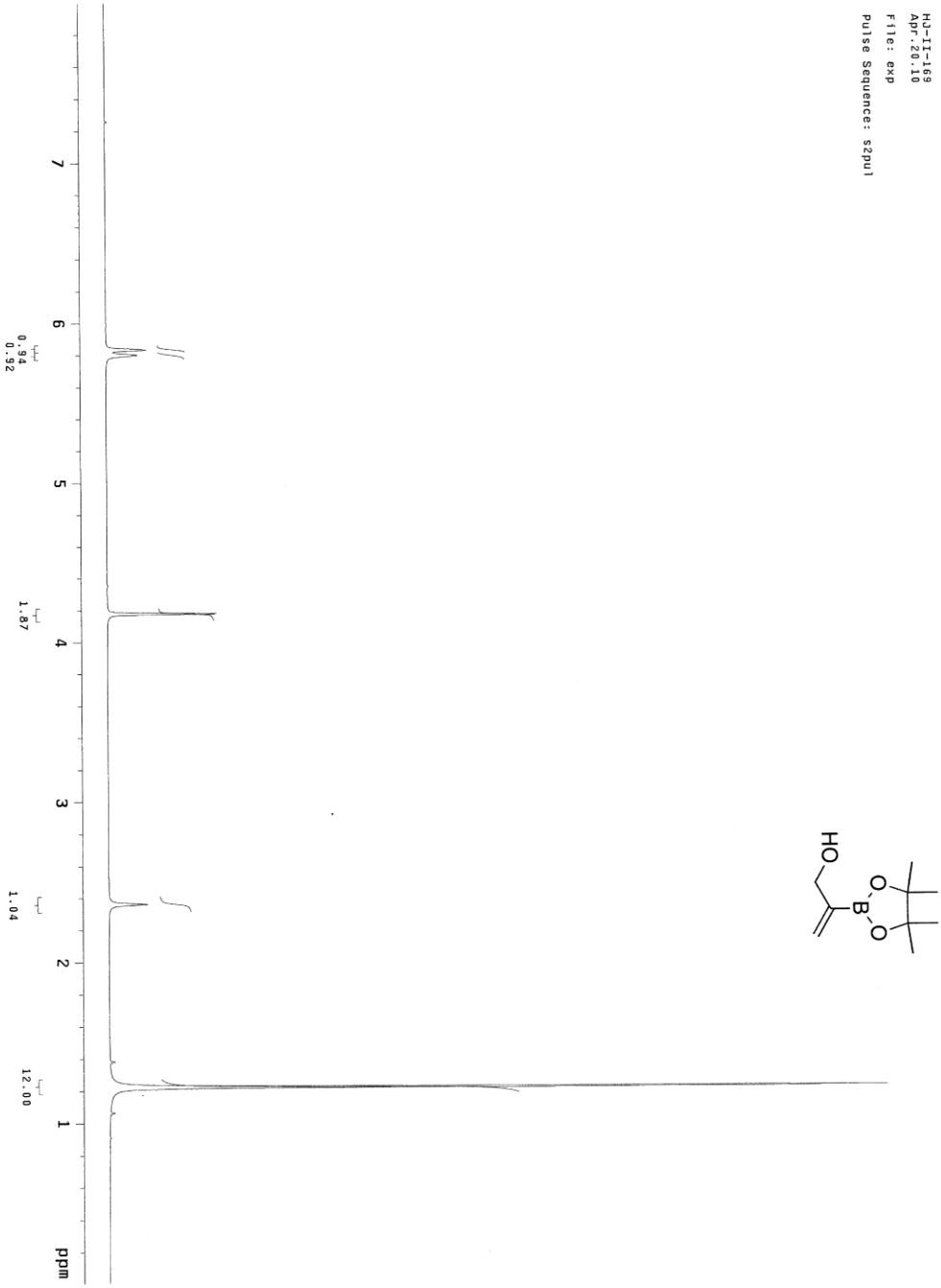
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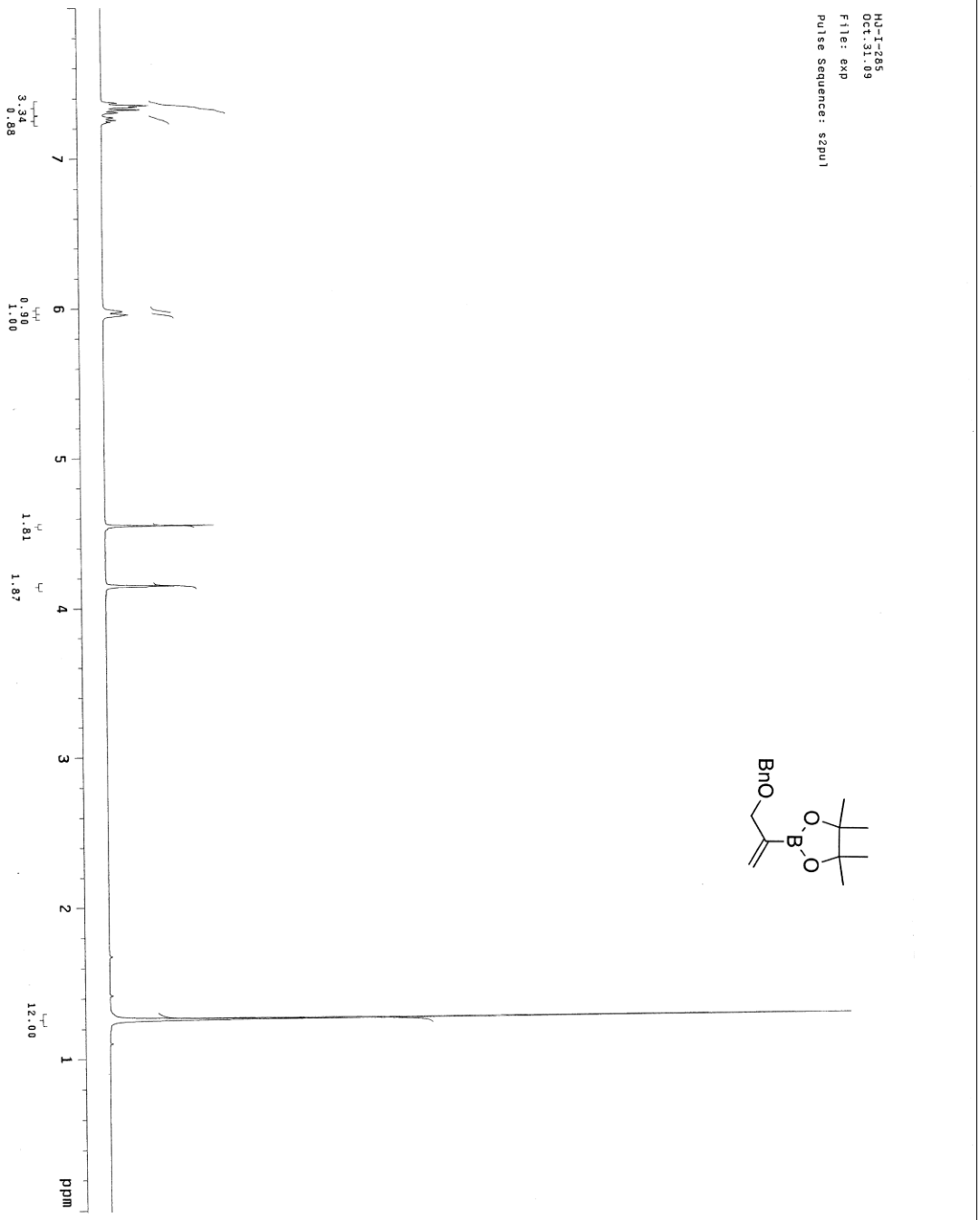
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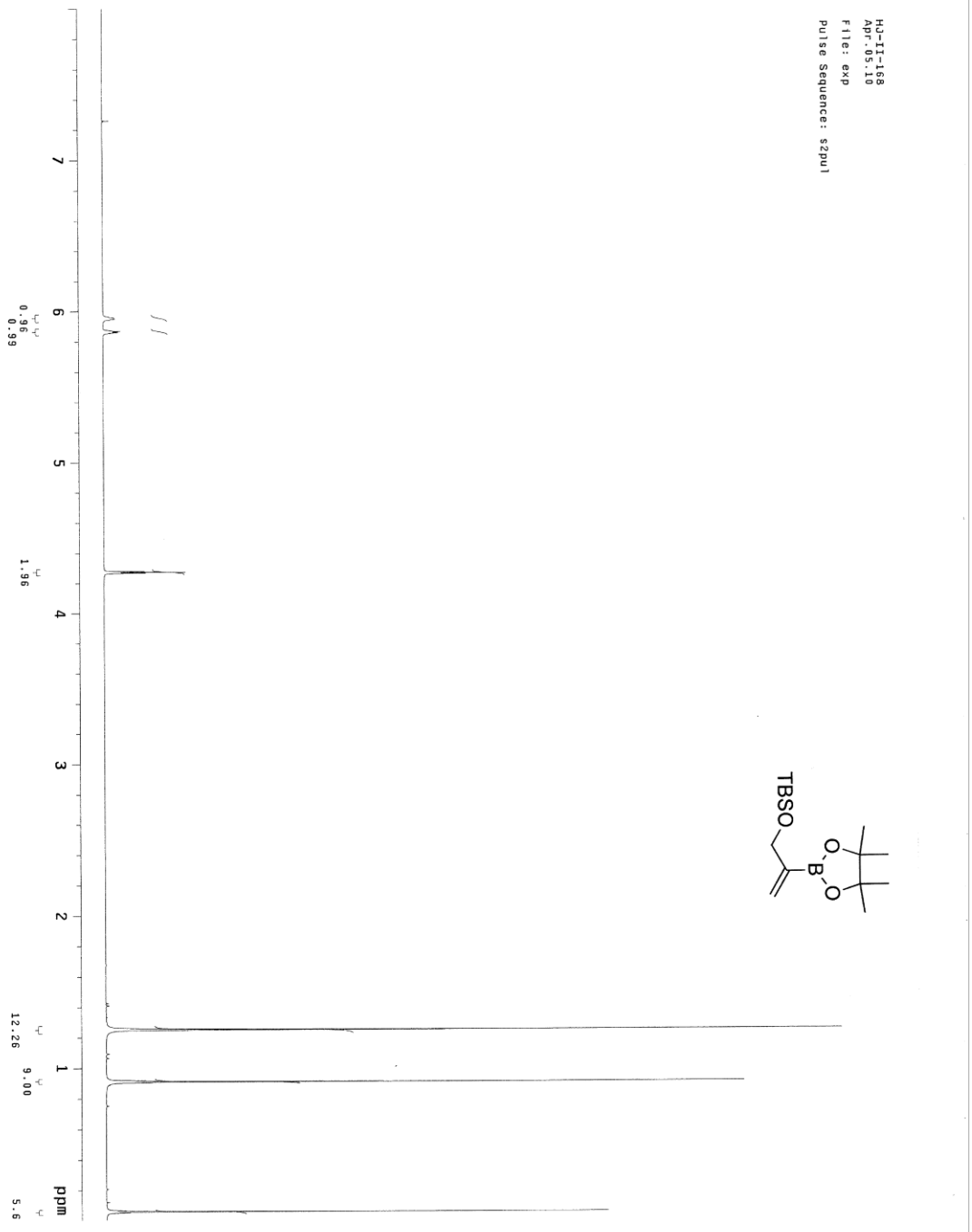
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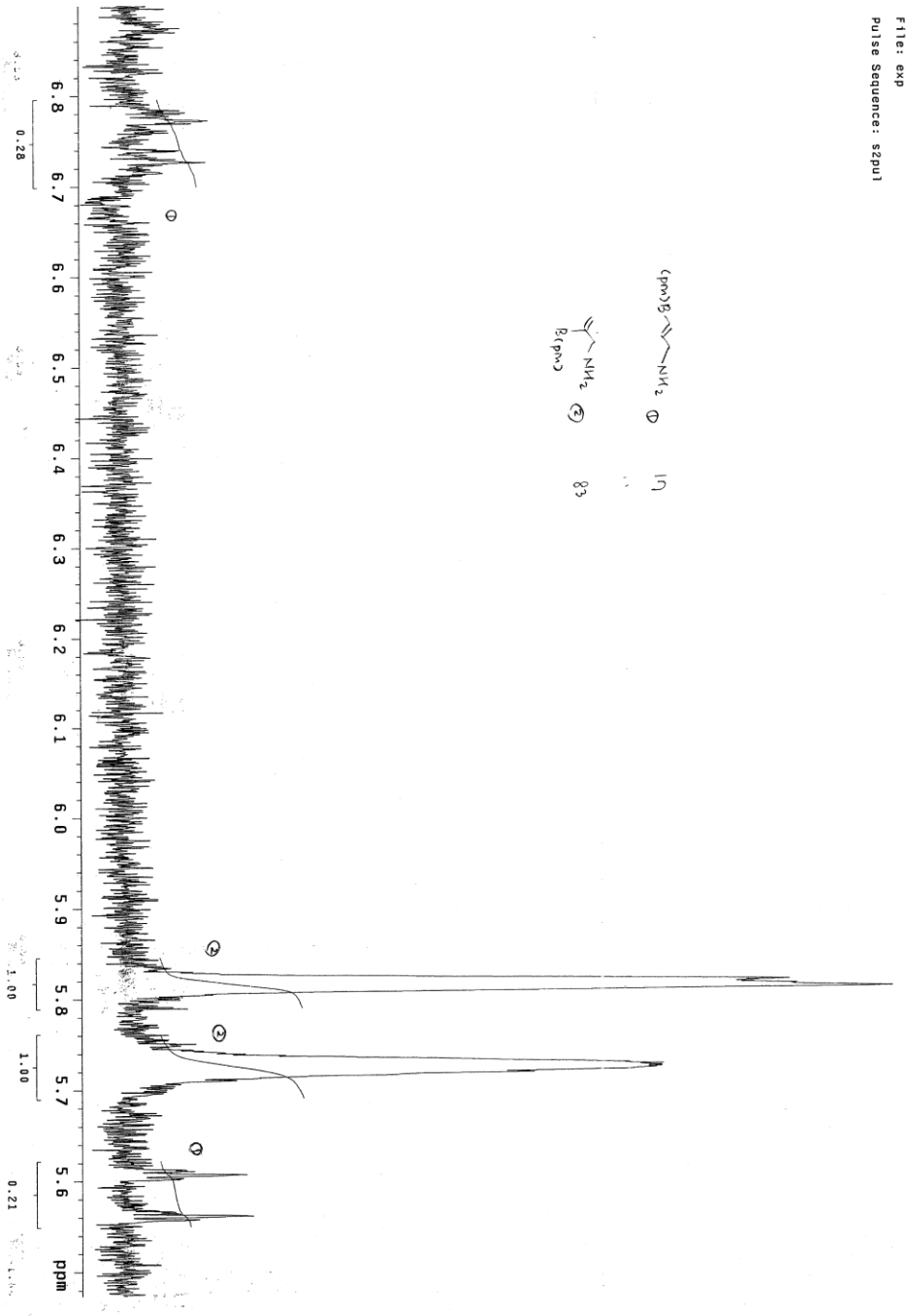
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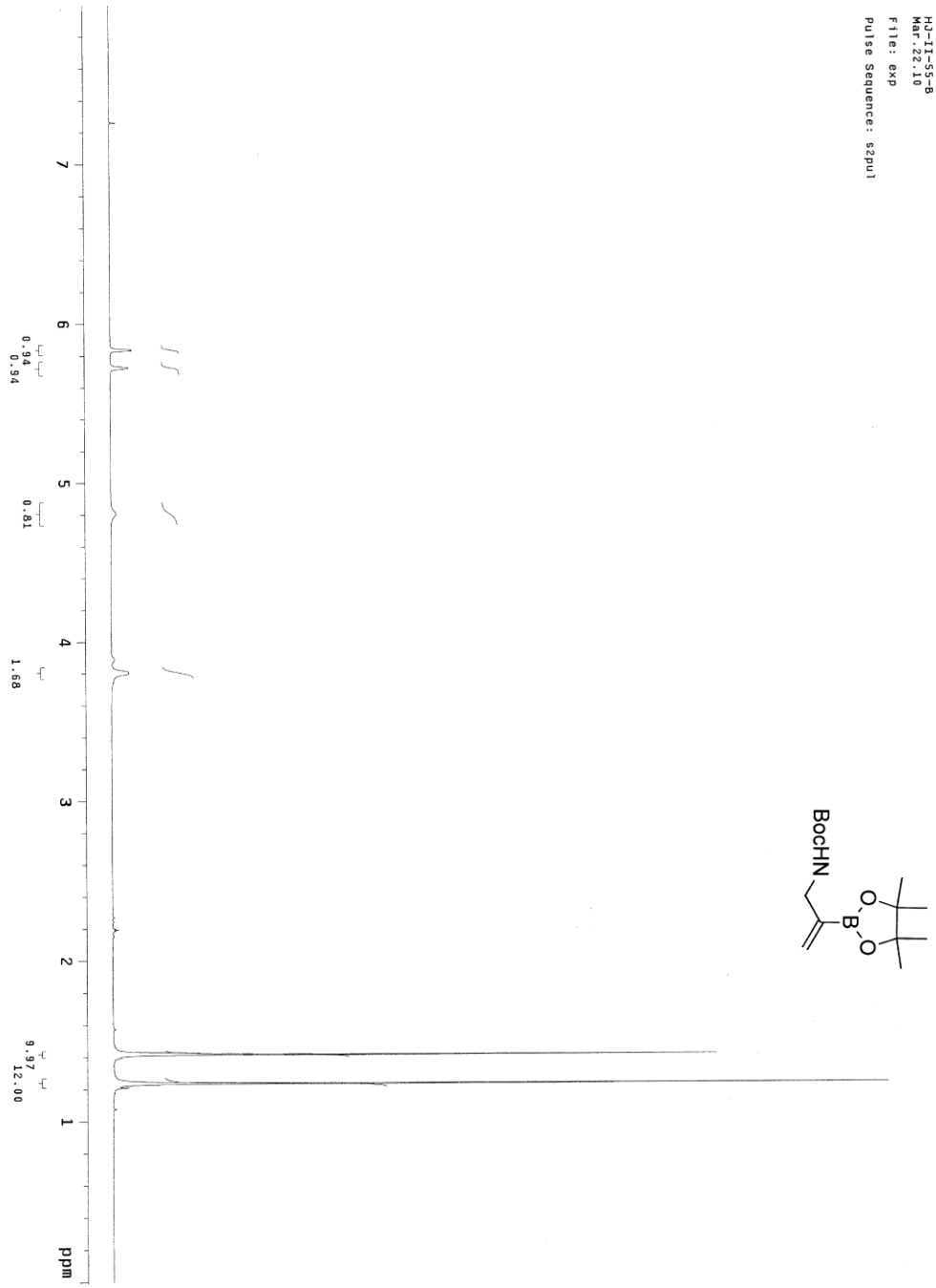
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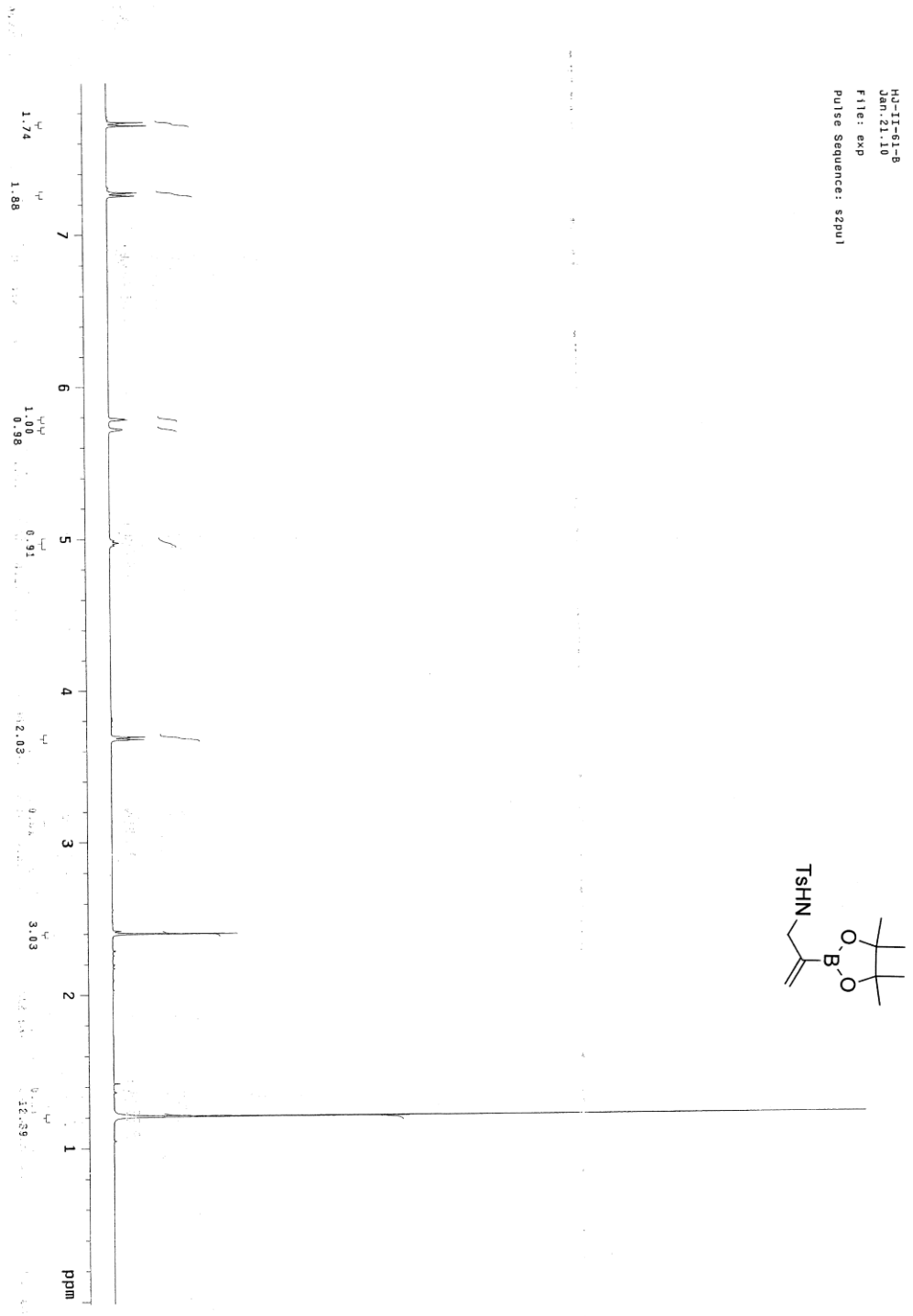
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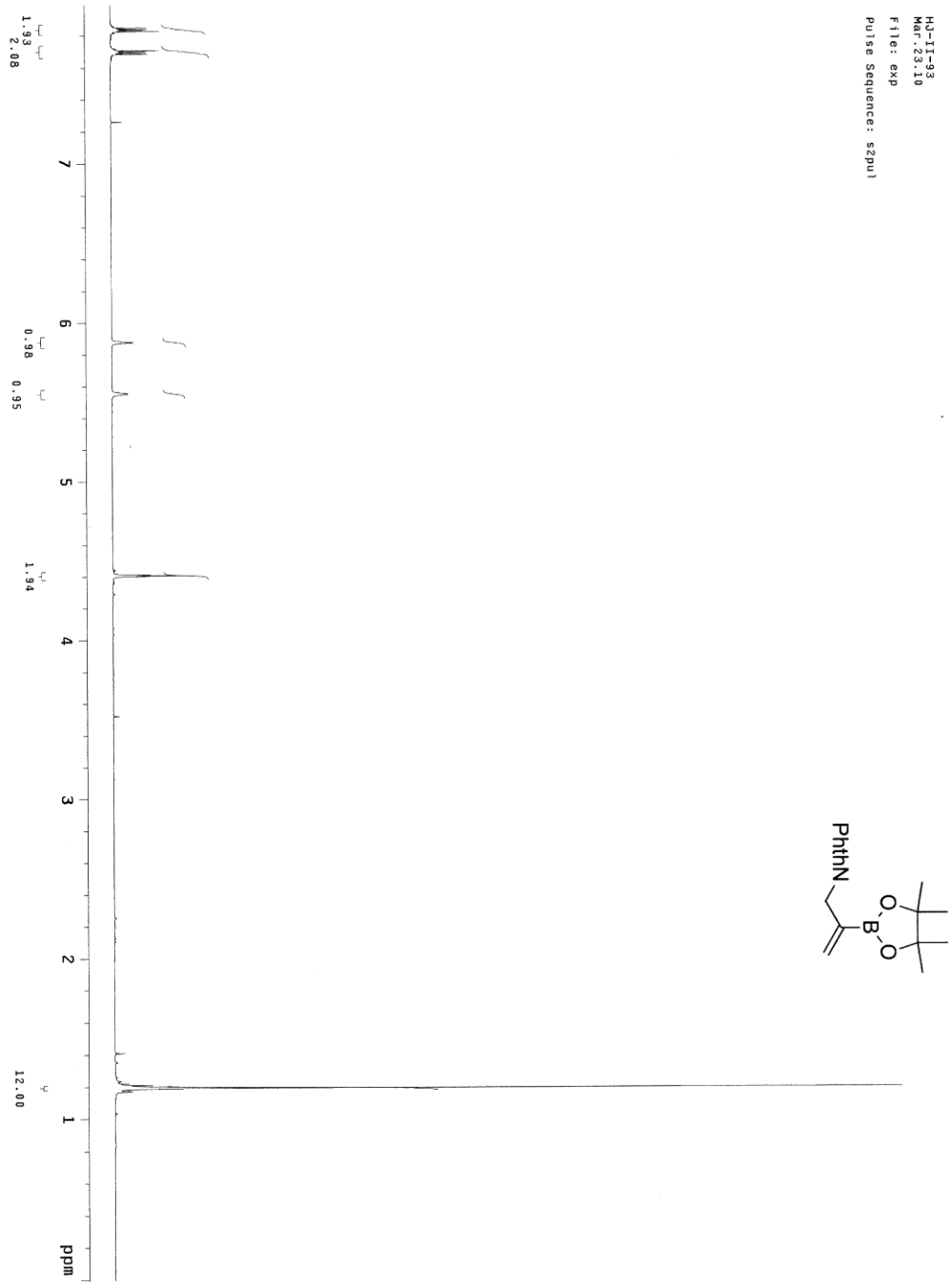
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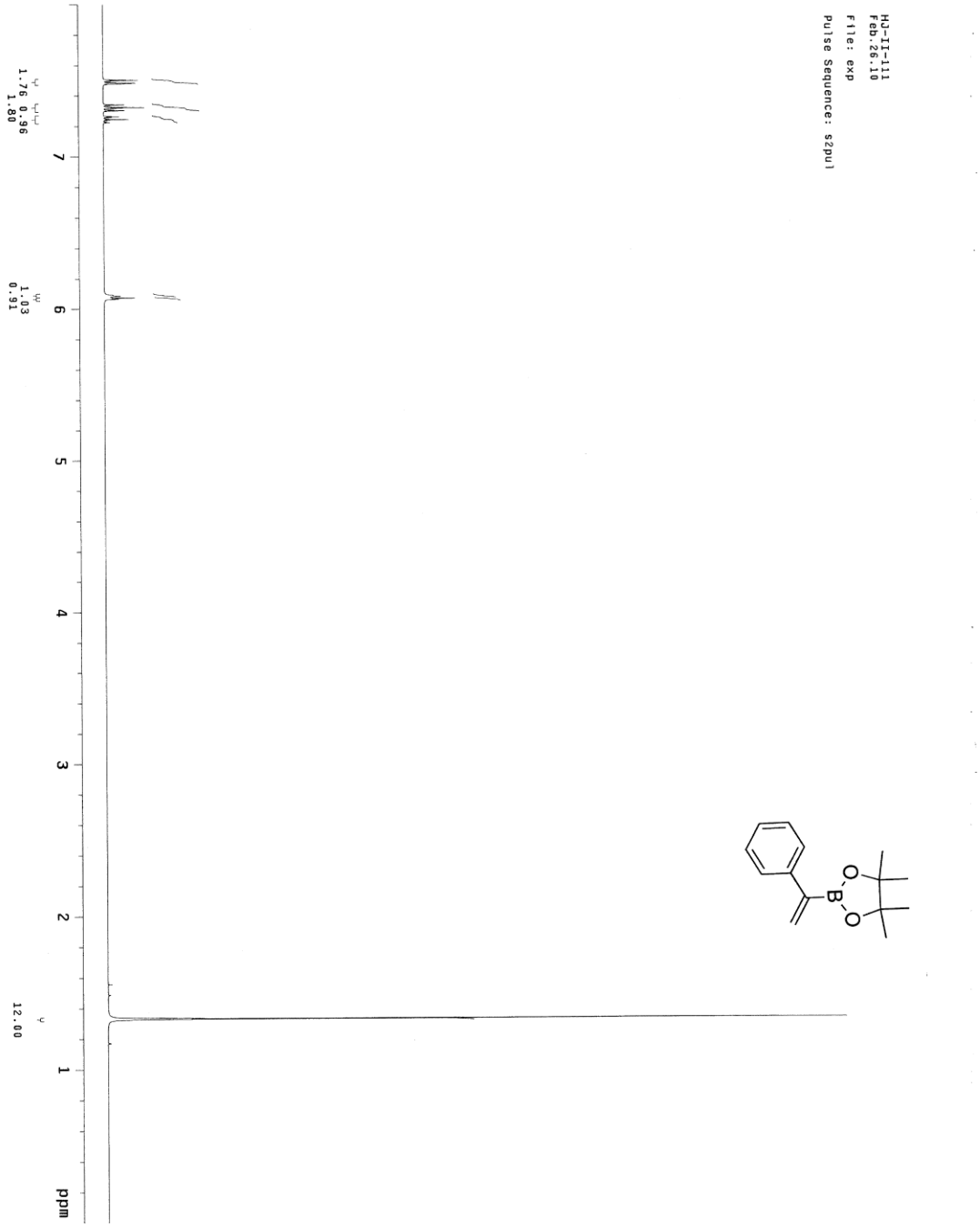
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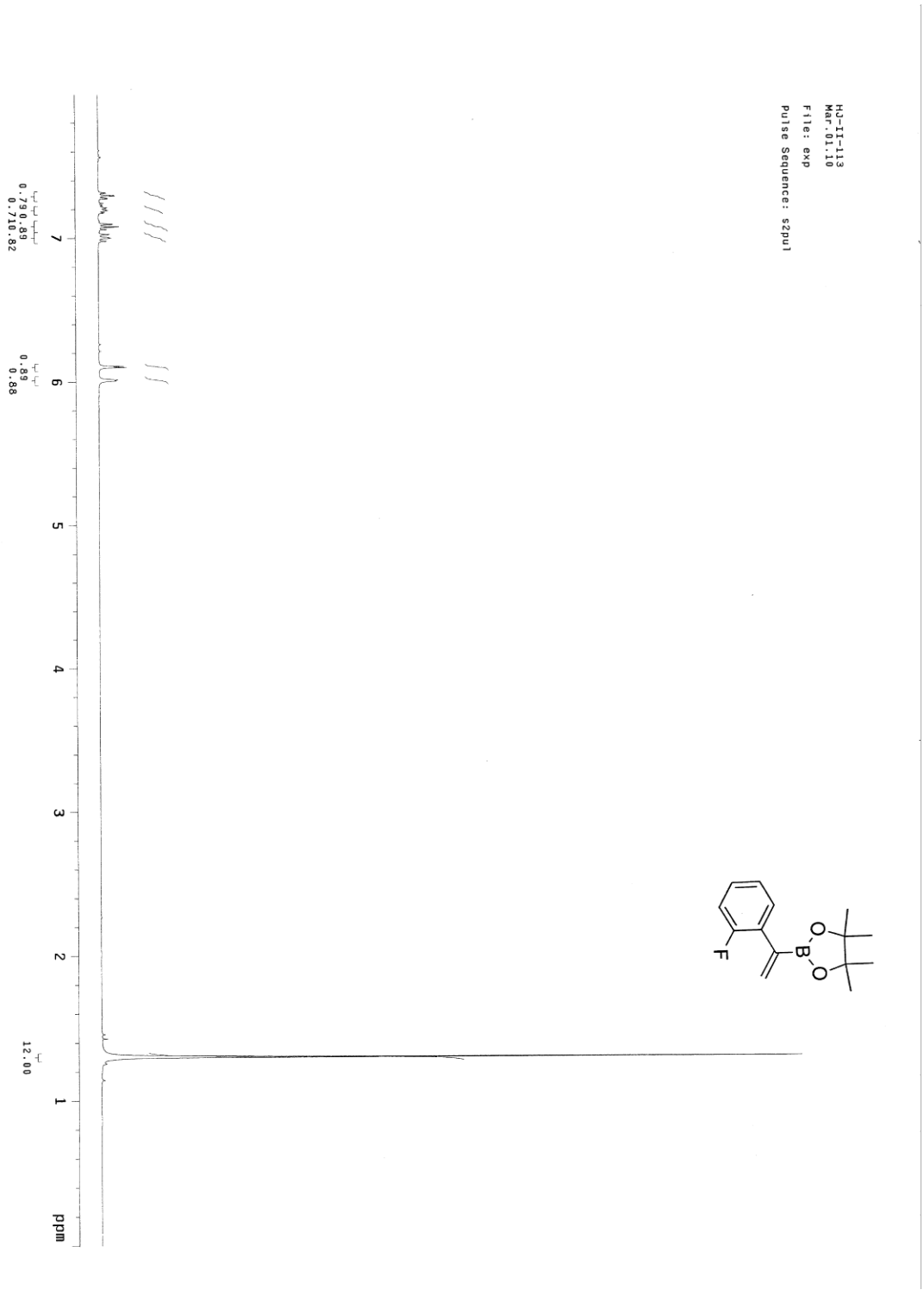
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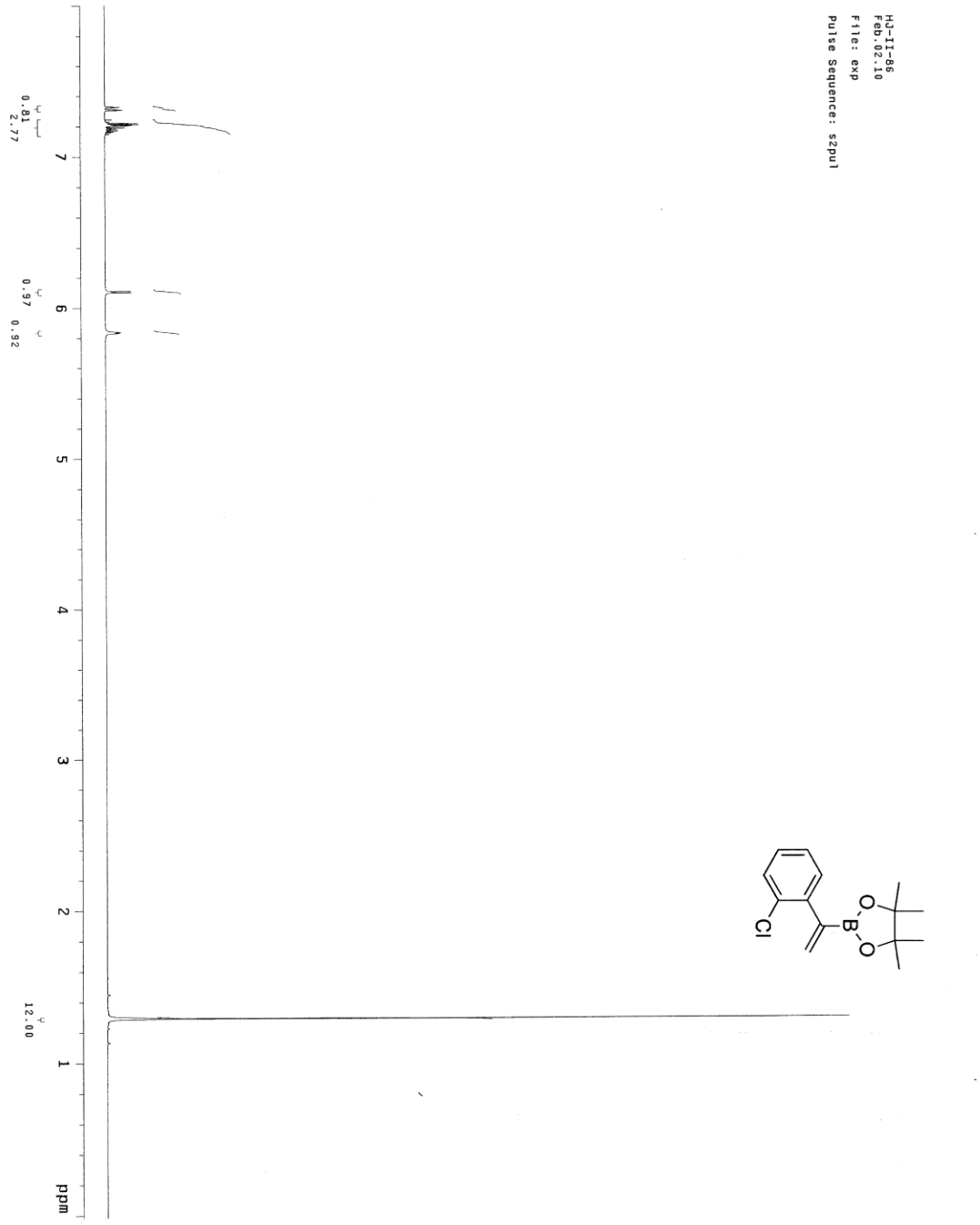
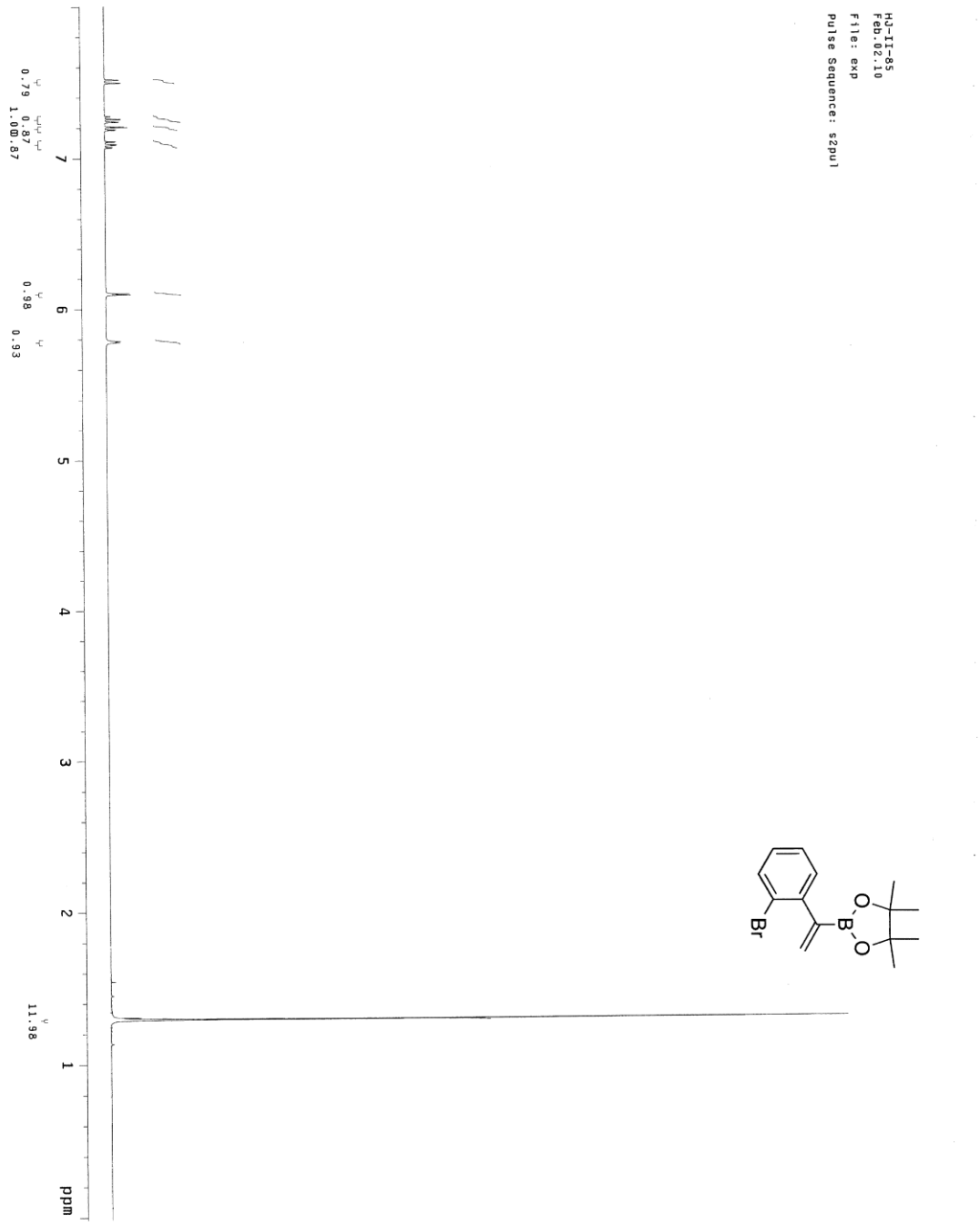
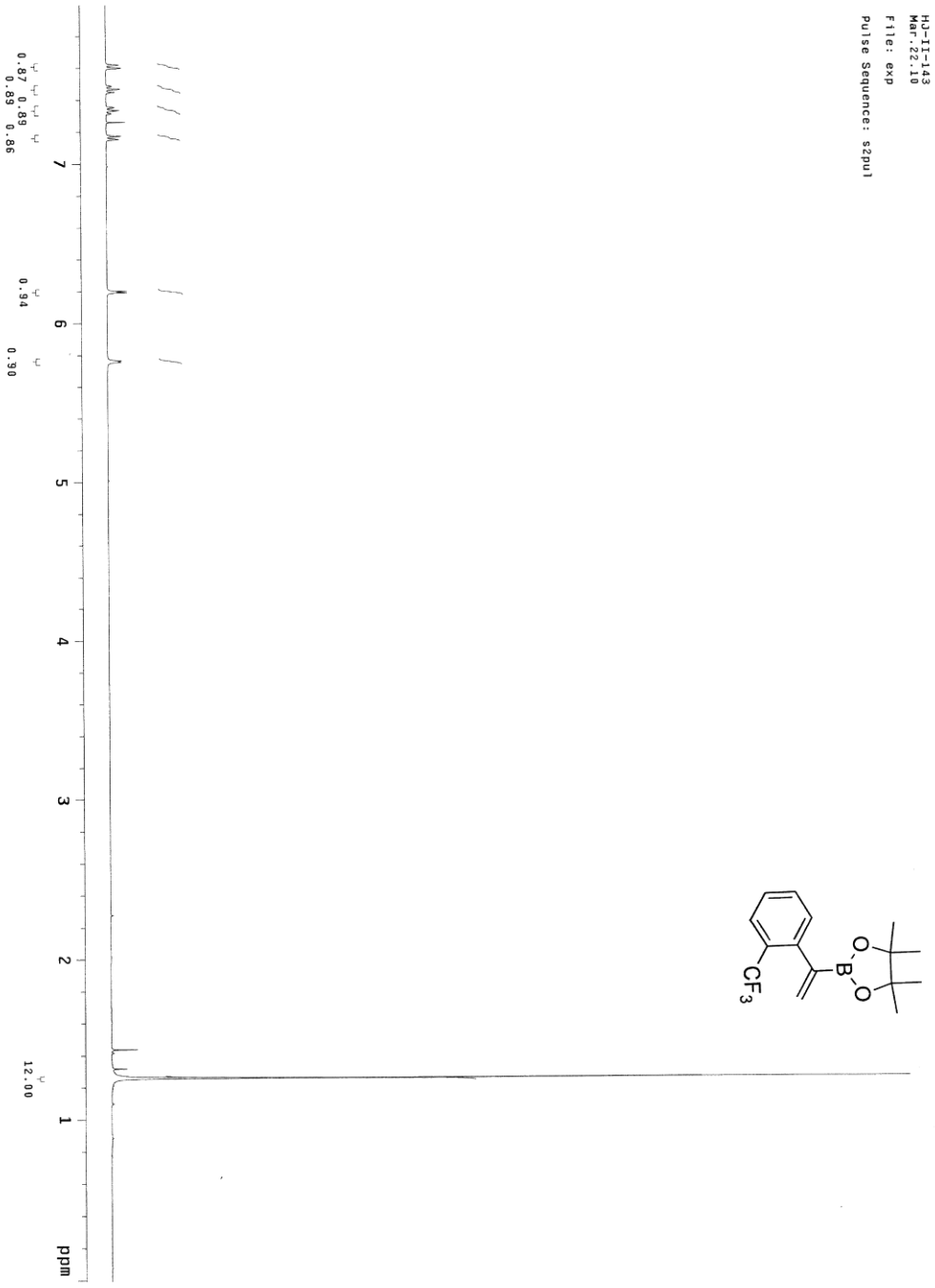
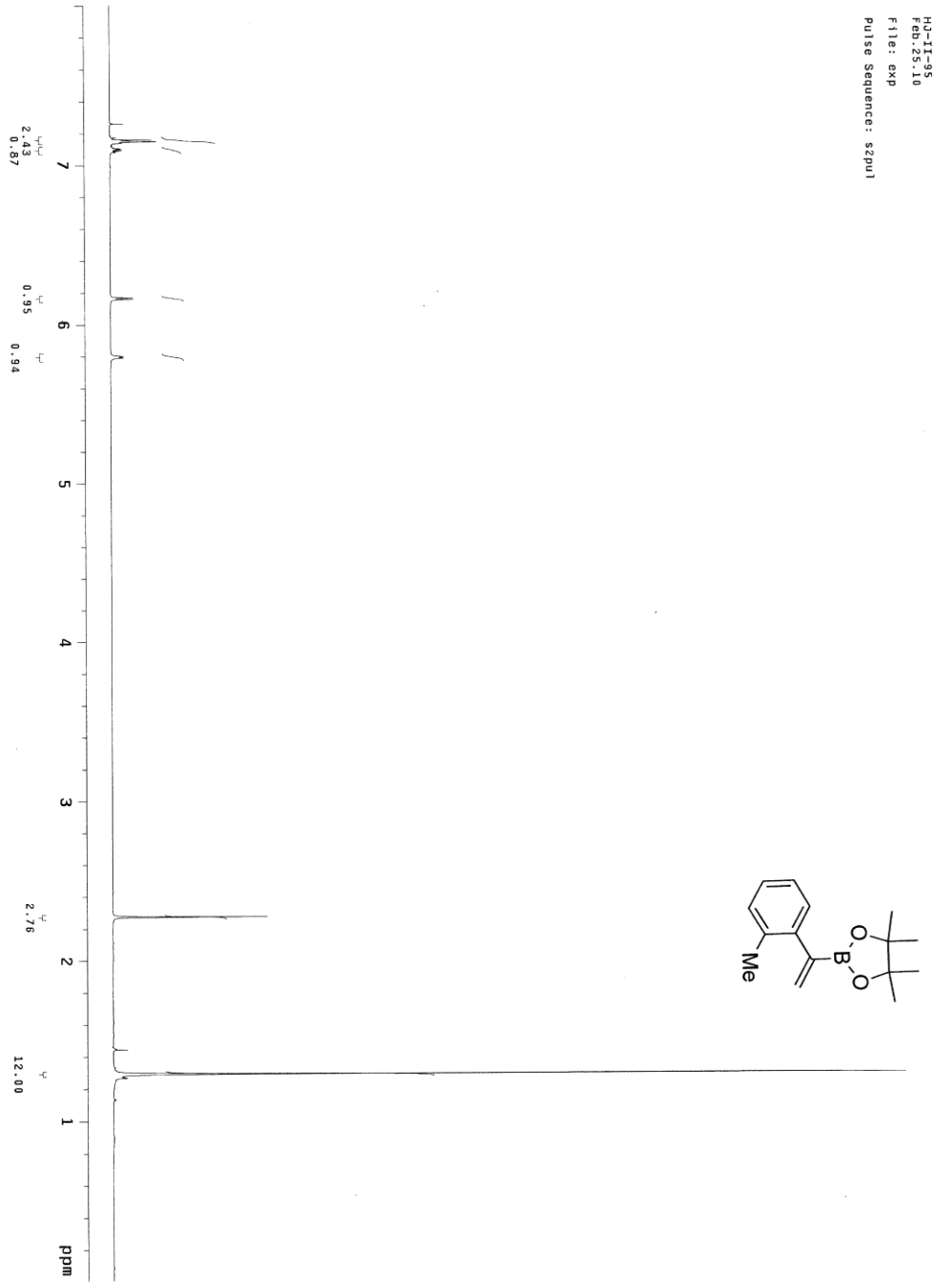
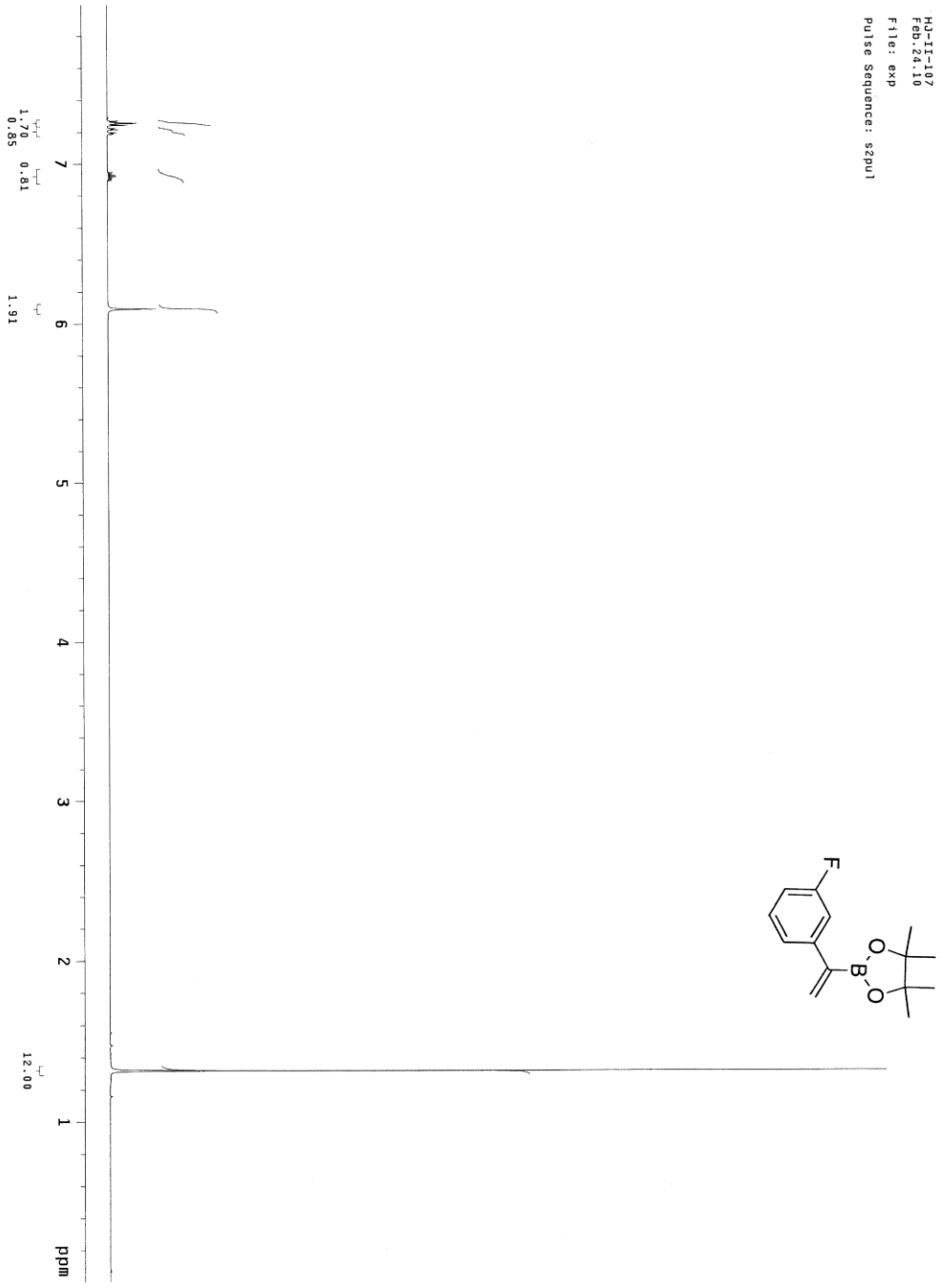
1
ppm

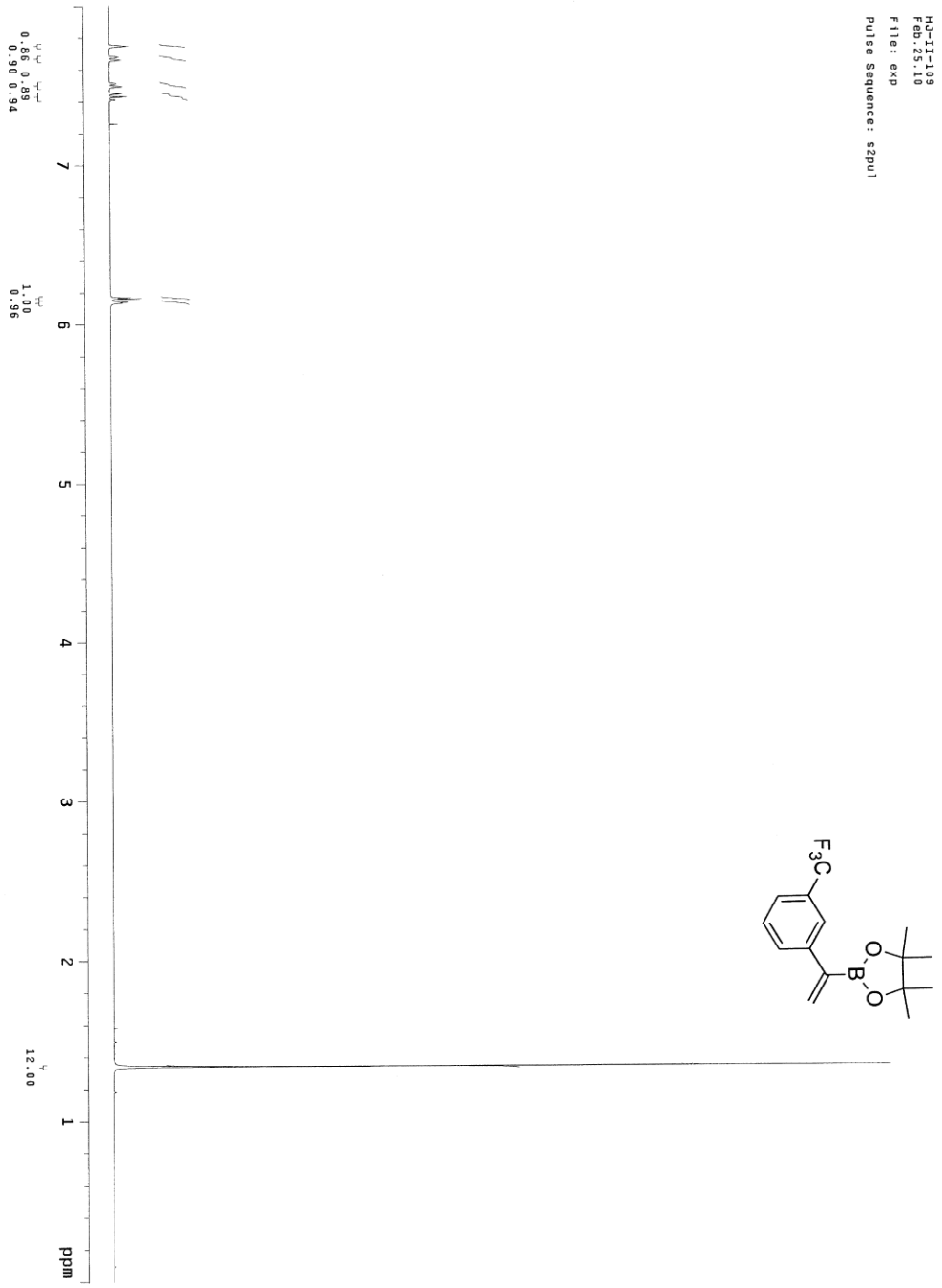

HJ-I-86
Feb.02.10
File: exp
Pulse Sequence: s2pul
0.81
2.77
0.97
0.92
12.00
ppm
Cl
O
B
O

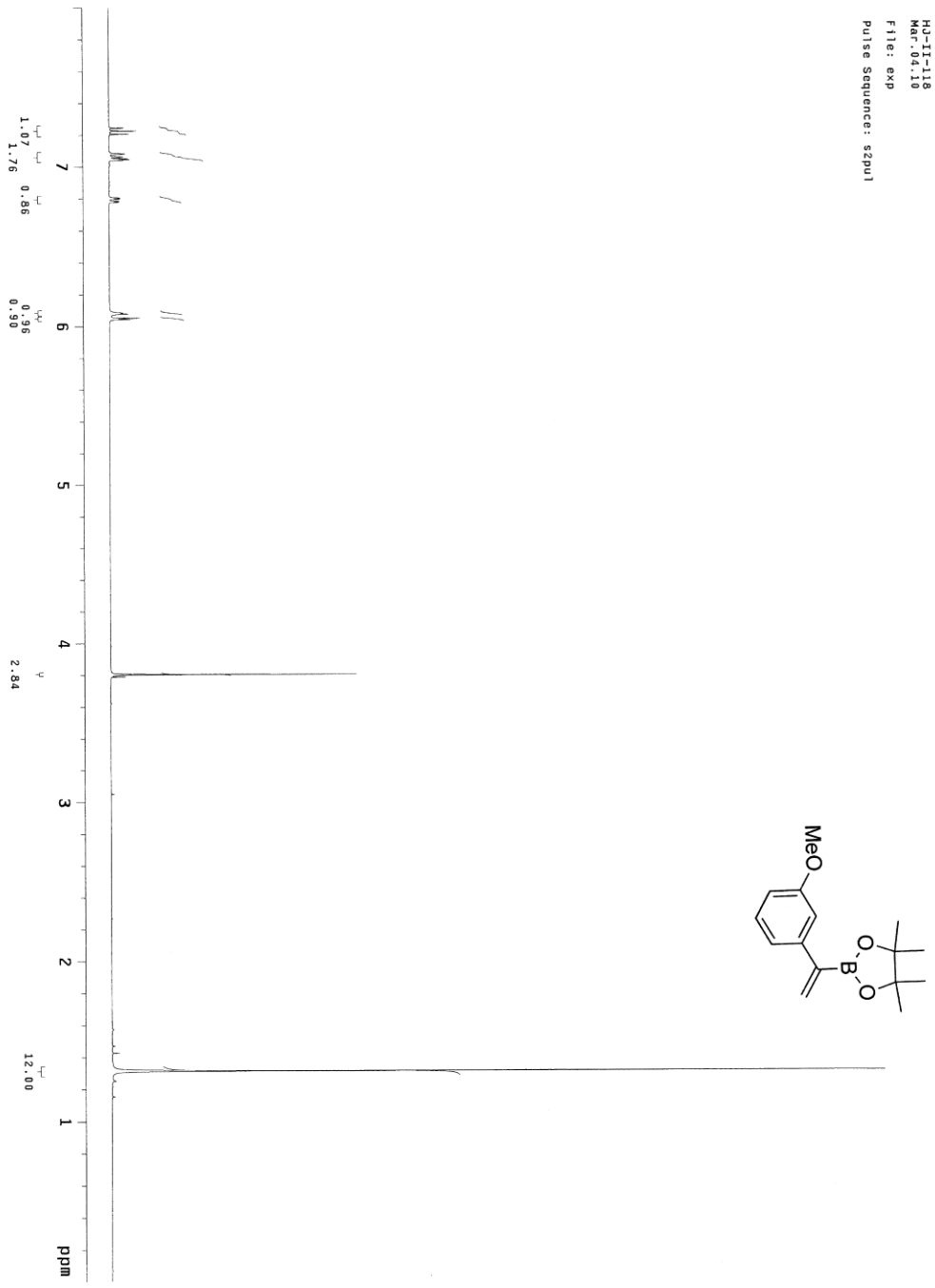

HJ-II-85
Feb.02.10
File: exp
Pulse Sequence: s2pul
Br
O
B
O
0.79
0.87
1.00
0.87
0.98
0.93
11.98
7
6
5
4
3
2
1
ppm

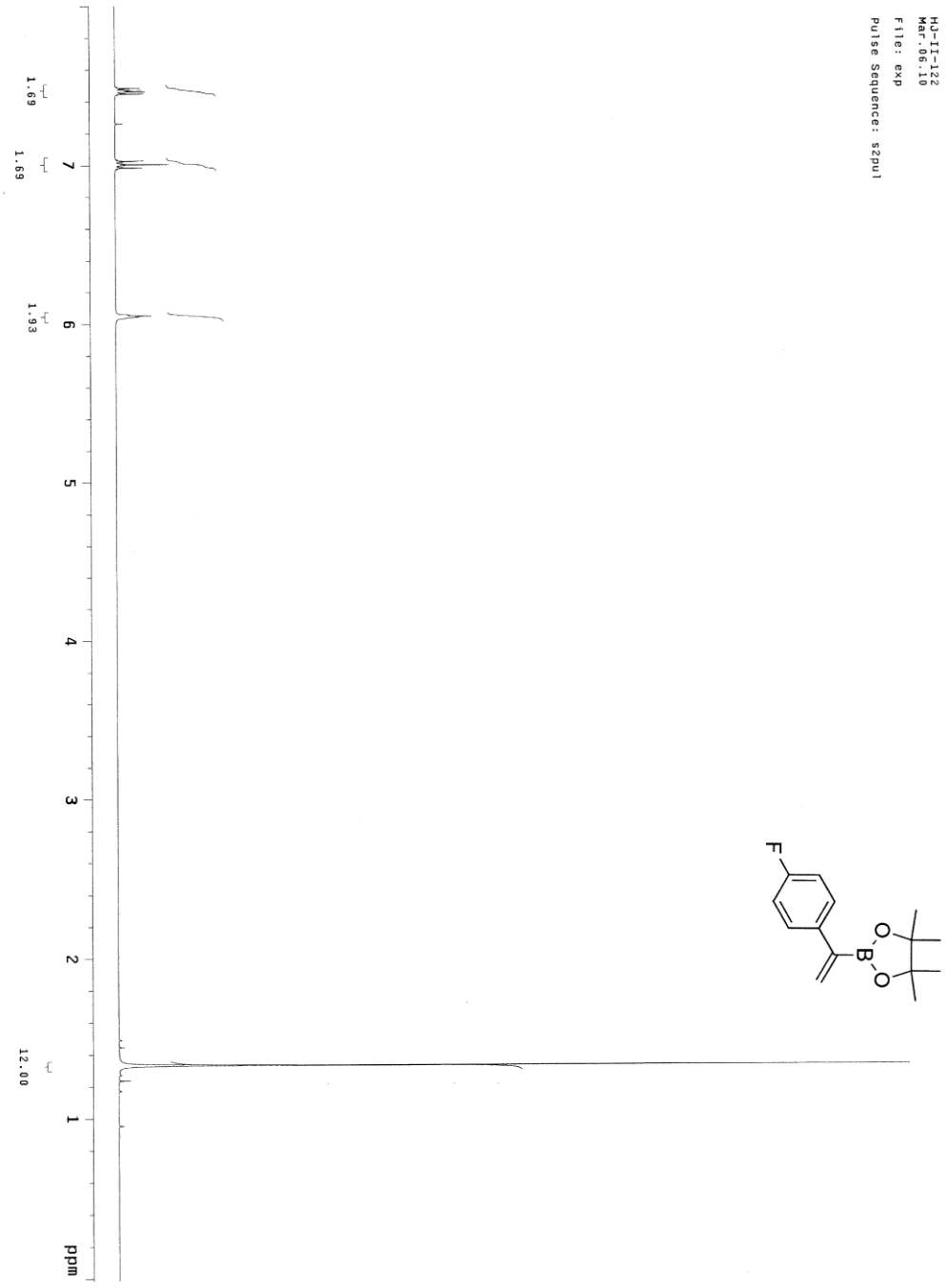

HJ-II-143
Mar.22.10
File: exp
Pulse Sequence: s2pul
CF3
O
B
O
O
0.87
0.89
0.86
0.94
0.90
12.00
7
6
5
4
3
2
1
ppm

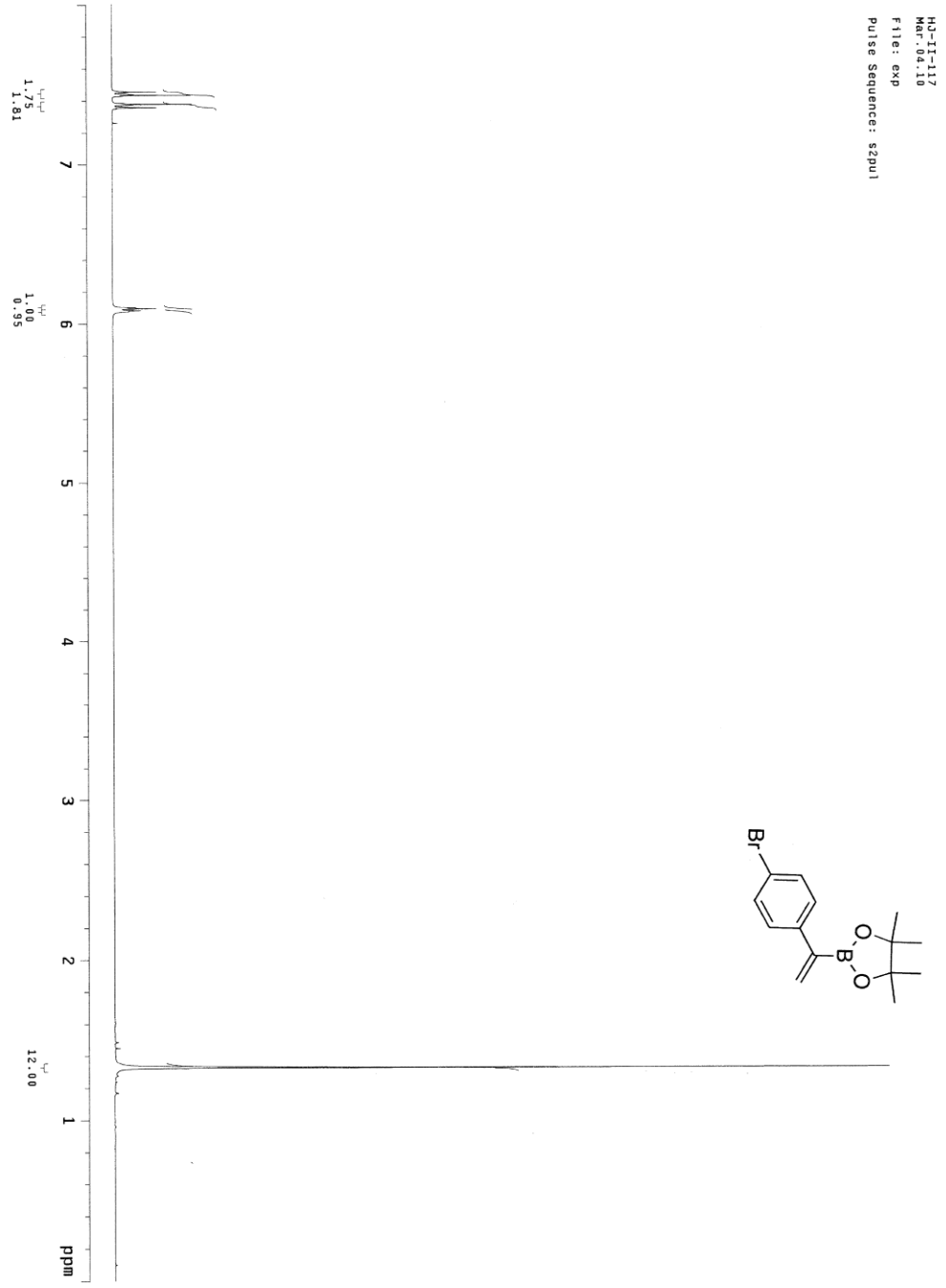

HJ-II-95
Feb.25.10
File: exp
Pulse Sequence: s2pul
Me
B
O
O
ppm
12.00
2.76
0.94
0.95
2.43
0.87

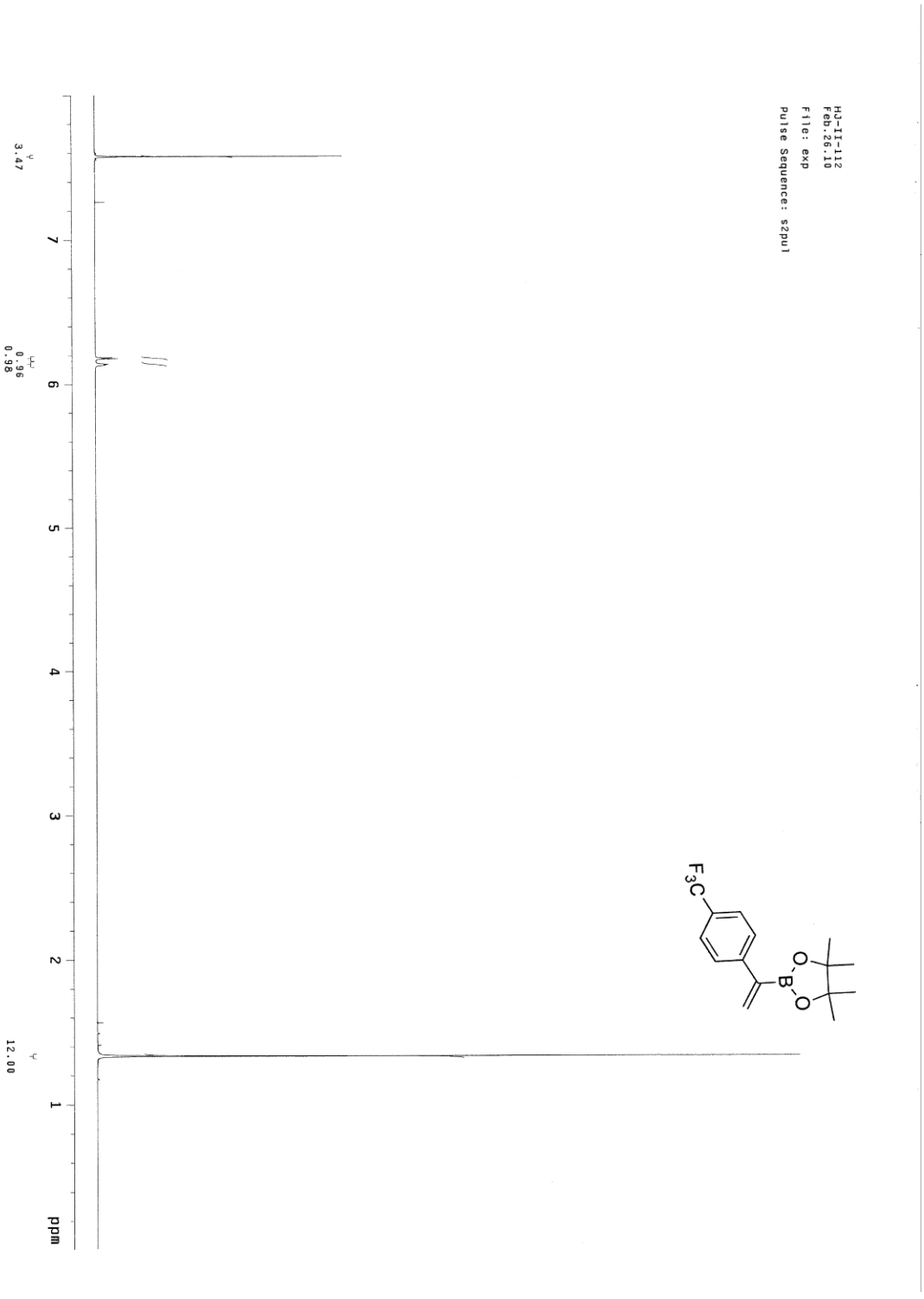

HJ-II-107
Feb.24.10
File: exp
Pulse Sequence: s2pul
F
O
B
O
1.70
0.85
0.81
1.91
12.00
7
6
5
4
3
2
1
ppm

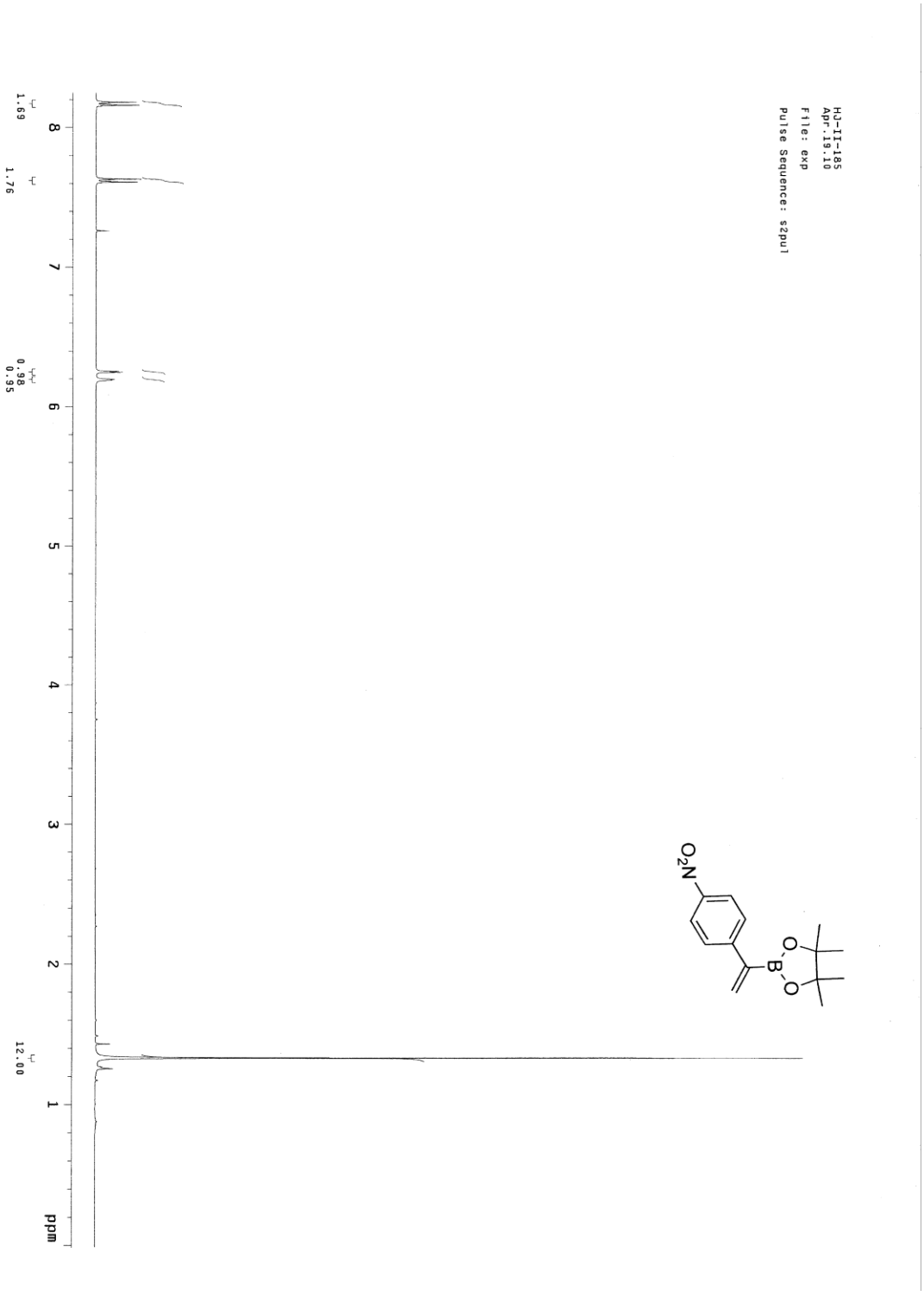

Hd-II-109
Feb.25.10
File: exp
Pulse Sequence: s2pul
F3C
O
B
O
ppm
12.00
1.00
0.96
0.86 0.89
0.90 0.94

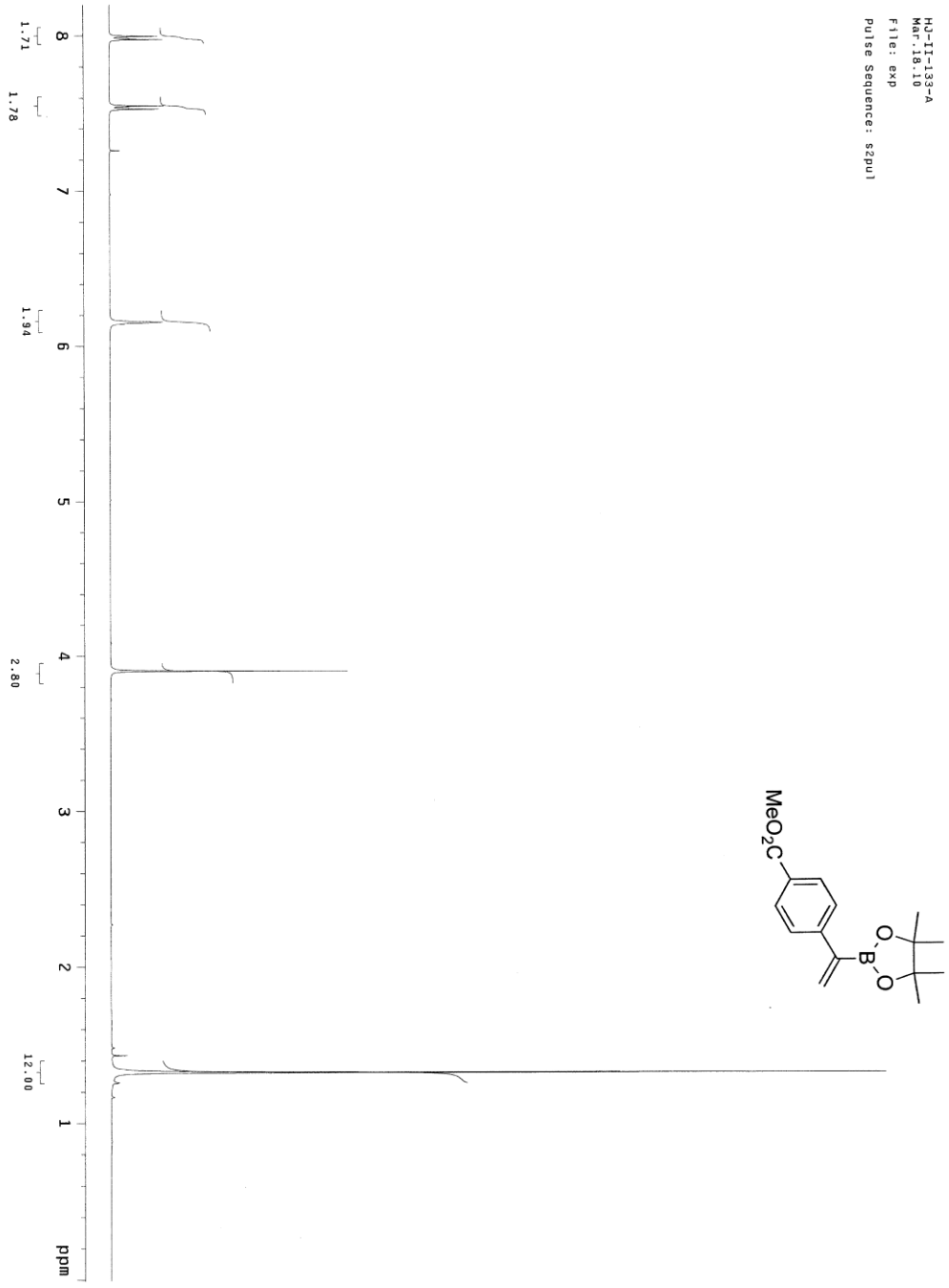

HJ-II-118
Mar.04.10
File: exp
Pulse Sequence: s2pul
MeO
O
B
O
ppm
12.00
2.84
0.96
0.90
0.86
1.07
1.76

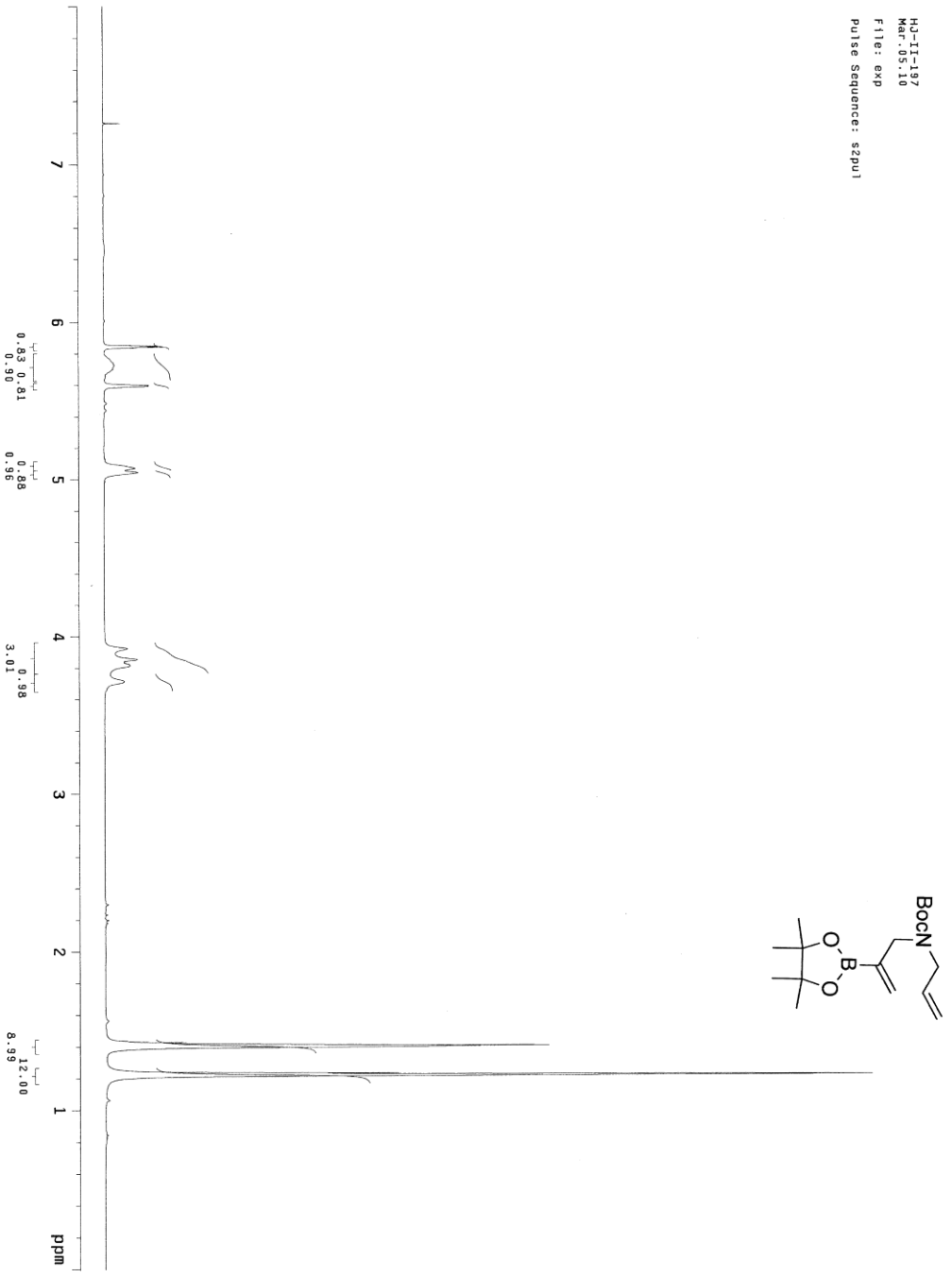

HJ-II-122
Mar.06.10
File: exp
Pulse Sequence: s2pul
F
O
B
O
1.69
1.69
1.93
12.00
7
6
5
4
3
2
1
ppm

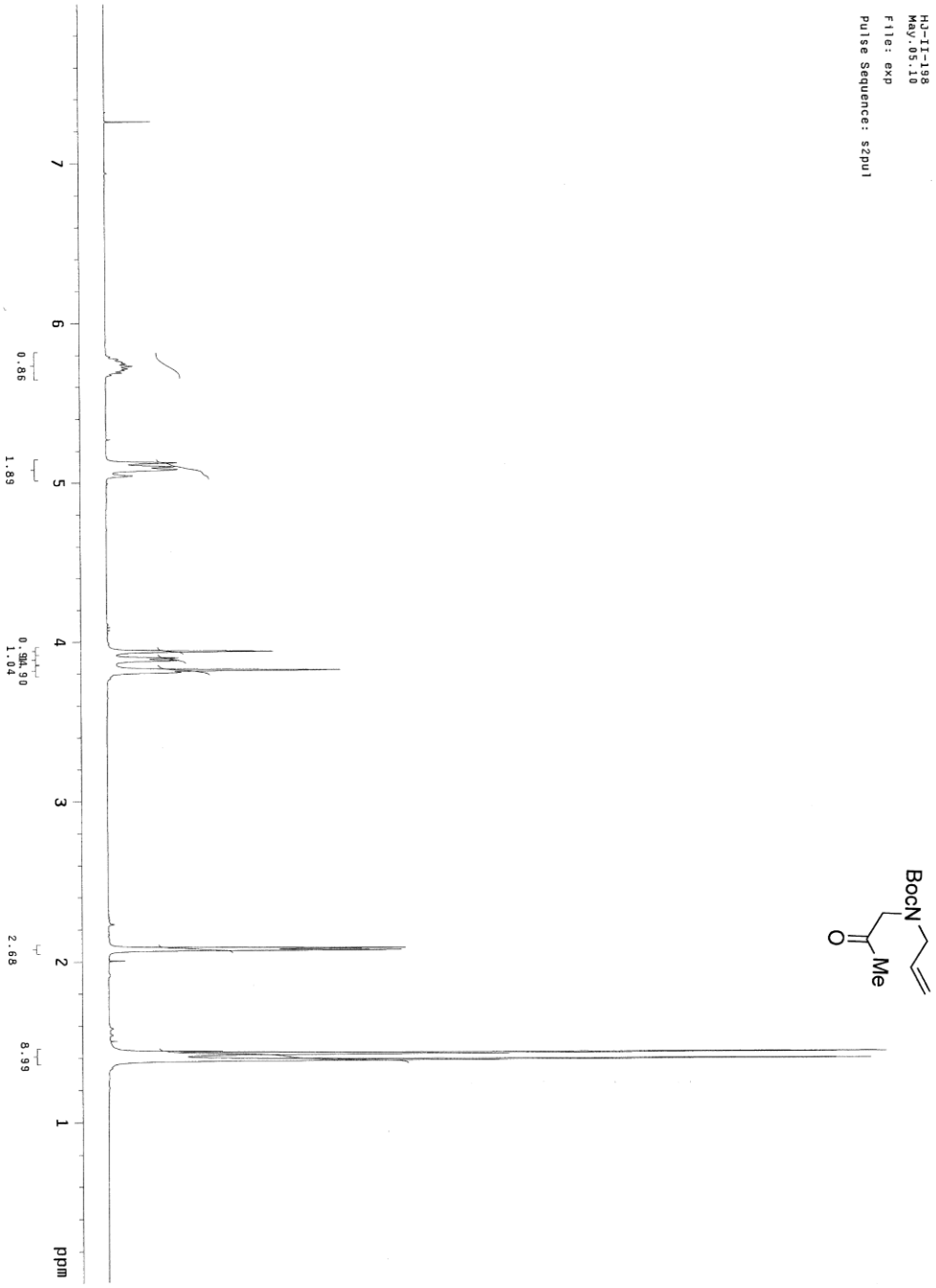

HJ-II-117
Mar.04.10
File: exp
Pulse Sequence: s2pul
Br
O
B
O
1.75
1.81
1.00
0.95
12.00
7
6
5
4
3
2
1
ppm

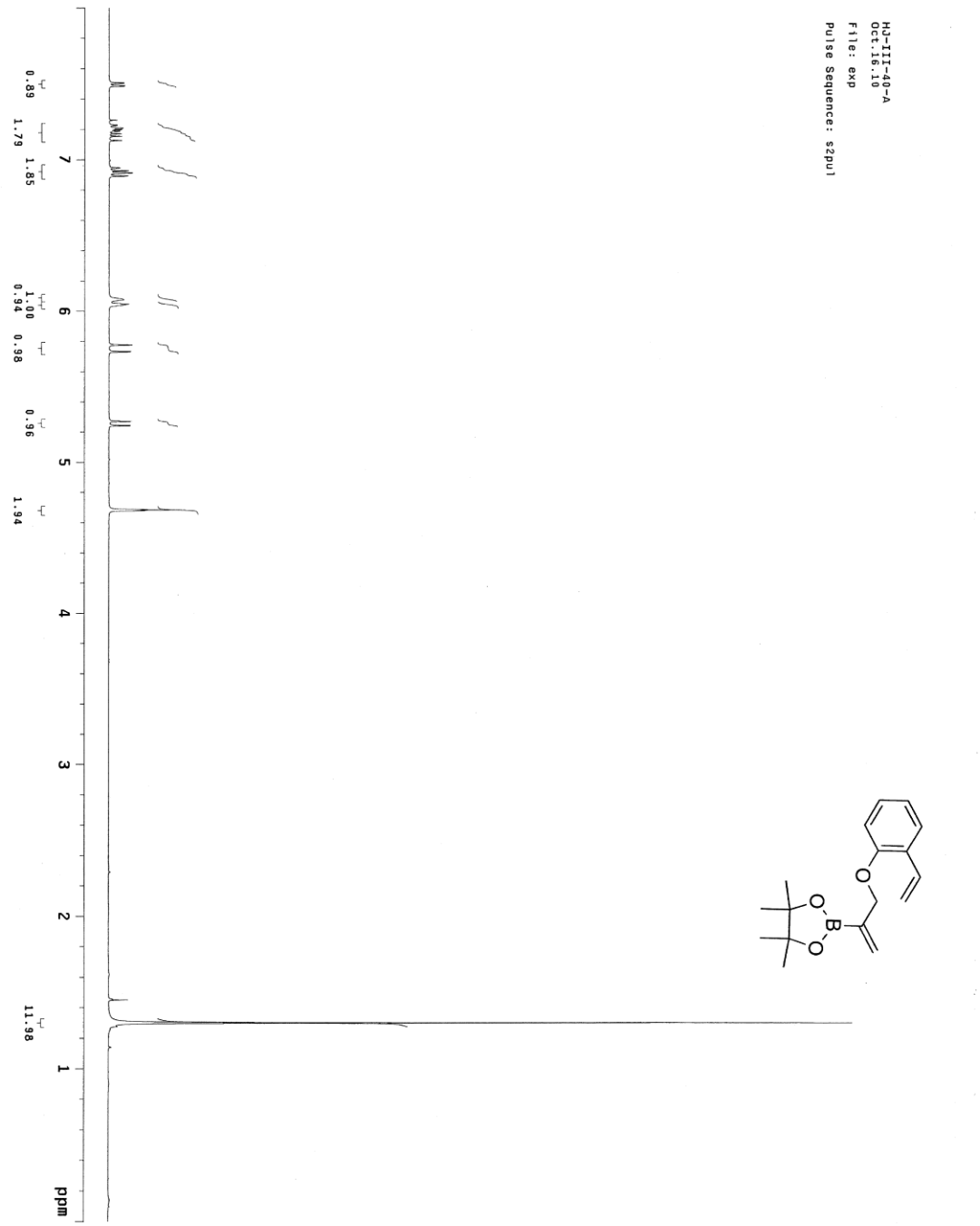

HJ-II-112
Feb.26.10
File: exp
Pulse Sequence: s2pul
F3C
O
B
O
3.47
0.96
0.98
12.00
7
6
5
4
3
2
1
ppm

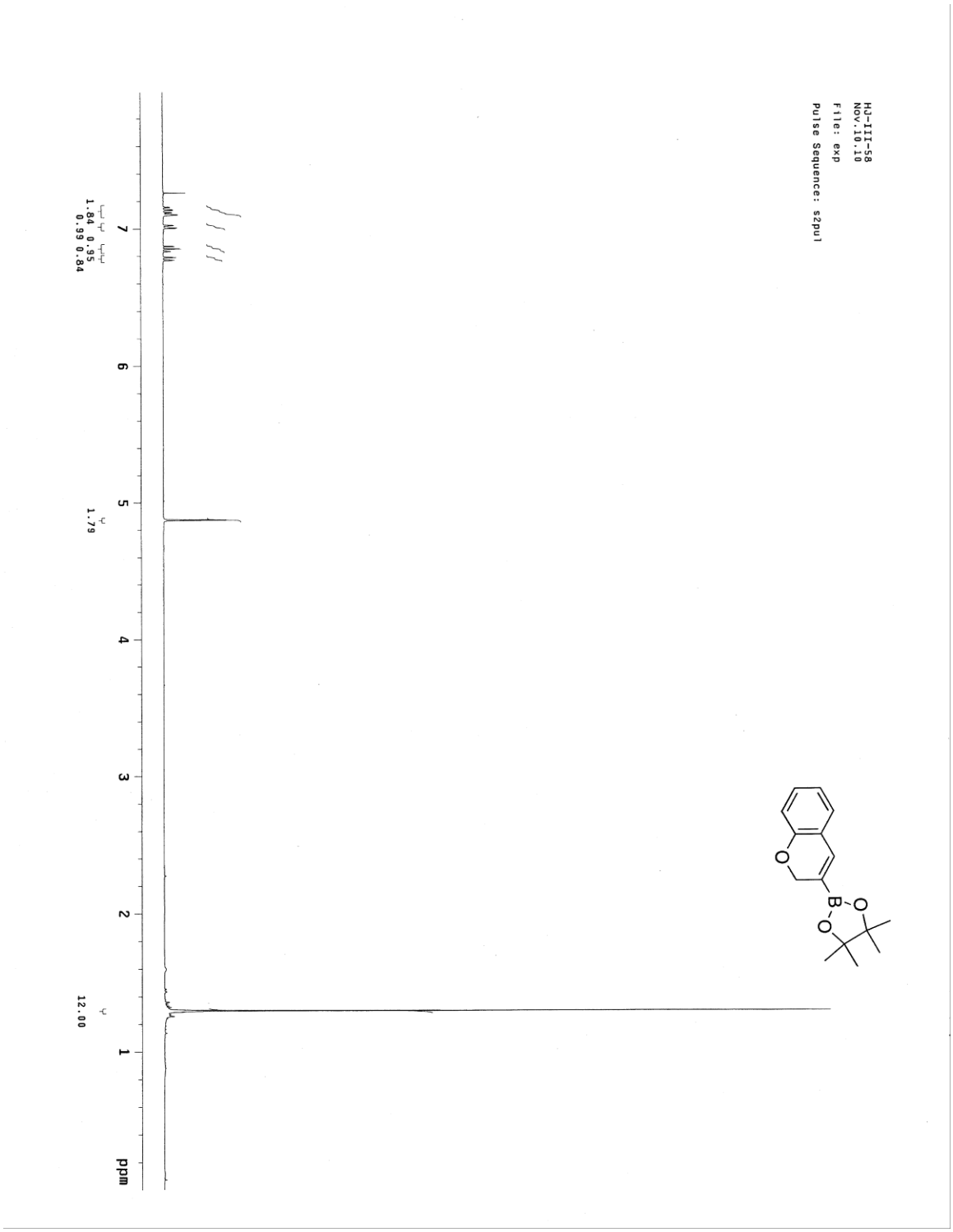

HJ-II-185
Apr.19.10
File: exp
Pulse Sequence: s2pul
O2N
B
O
O
ppm
1.69
1.76
0.98
0.95
12.00

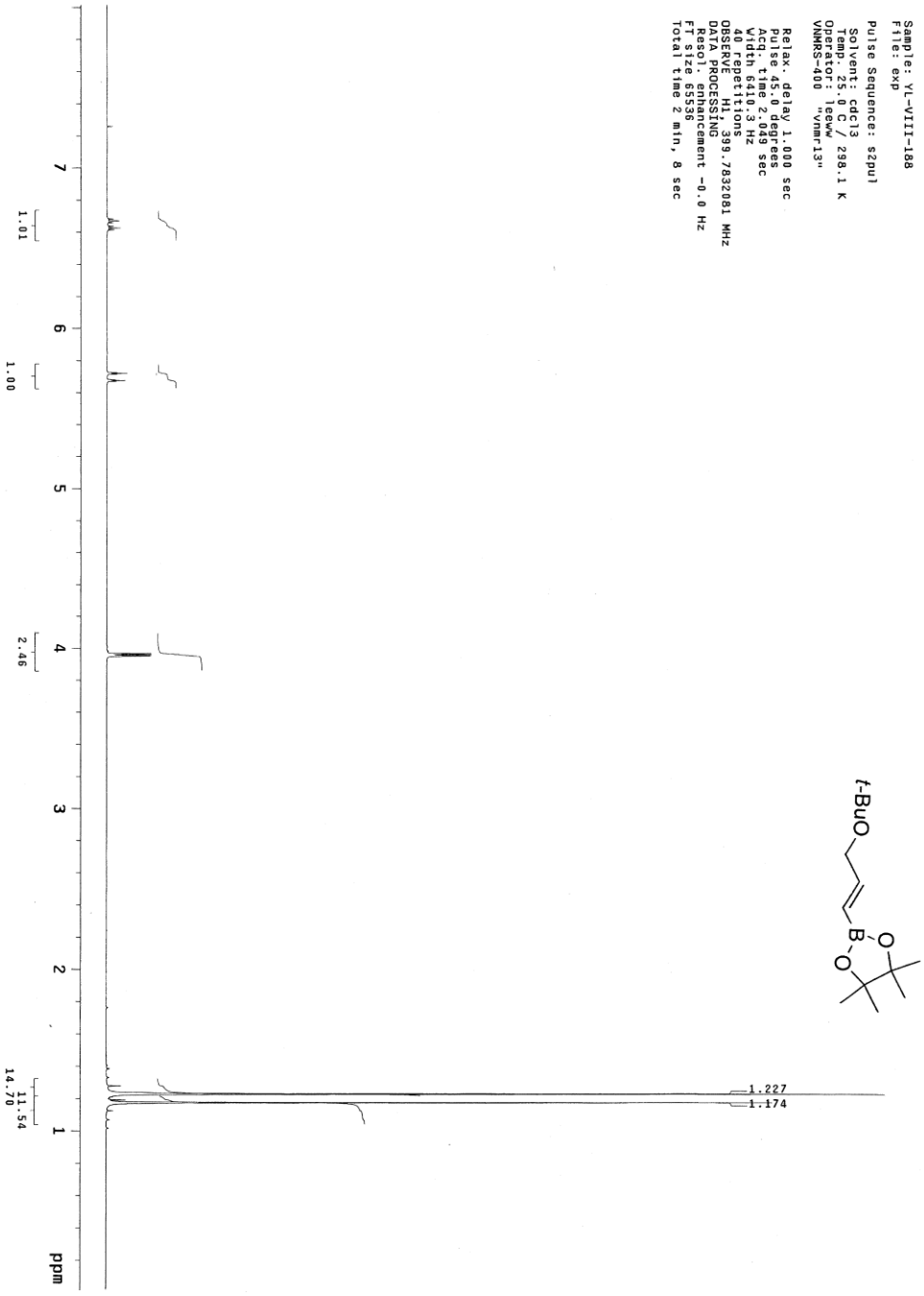

HJ-II-133-A
Mar.18.10
File: exp
Pulse Sequence: s2pul
MeO2C
O
B
O
8
7
6
5
4
3
2
1
ppm
1.71
1.78
1.94
2.80
12.00

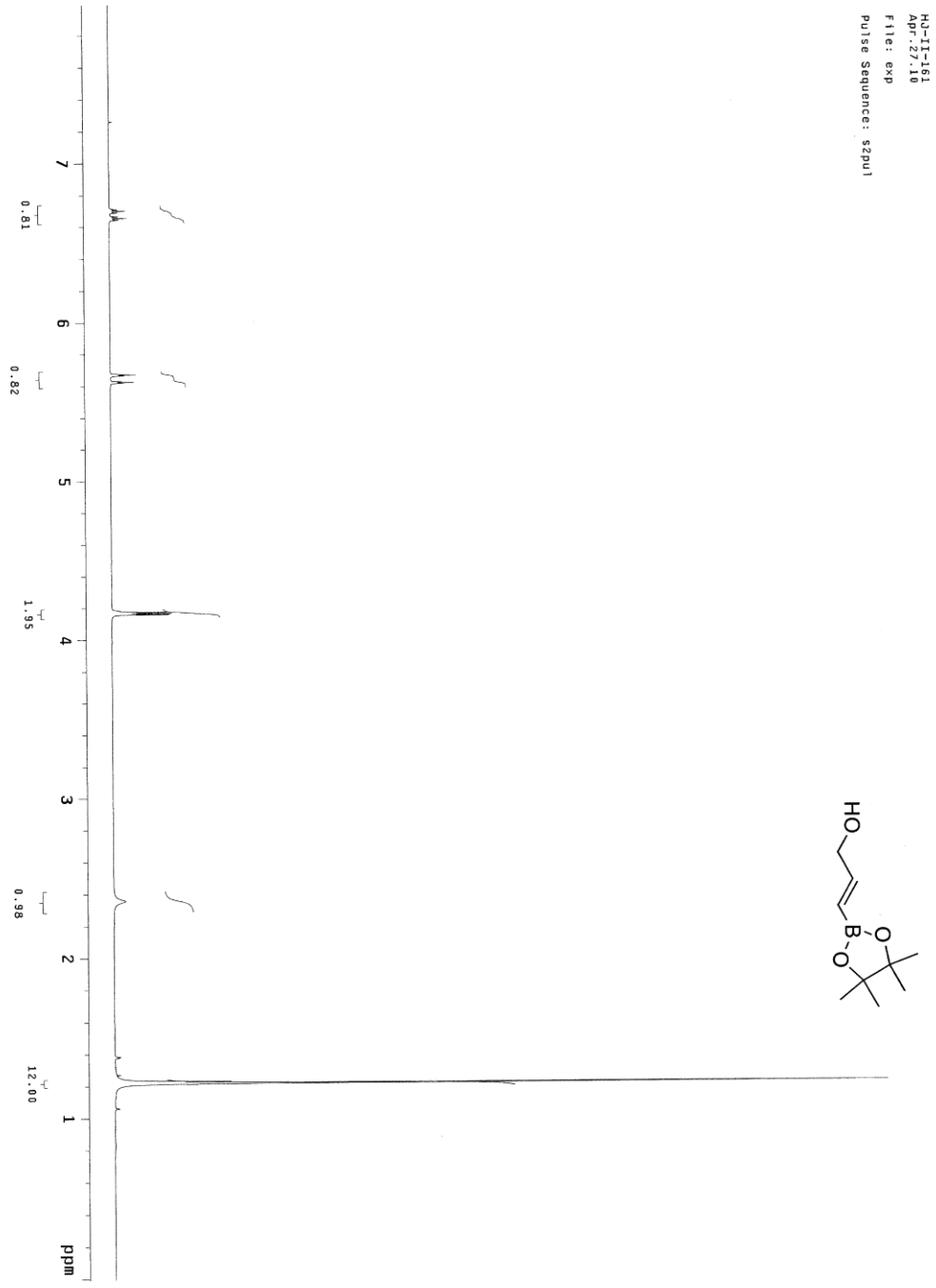

HJ-II-197
Mar.05.10
File: exp
Pulse Sequence: s2pul
BocN
O
B
O
7
6
5
4
3
2
1
ppm
0.83
0.81
0.90
0.88
0.96
0.98
3.01
12.00
8.99

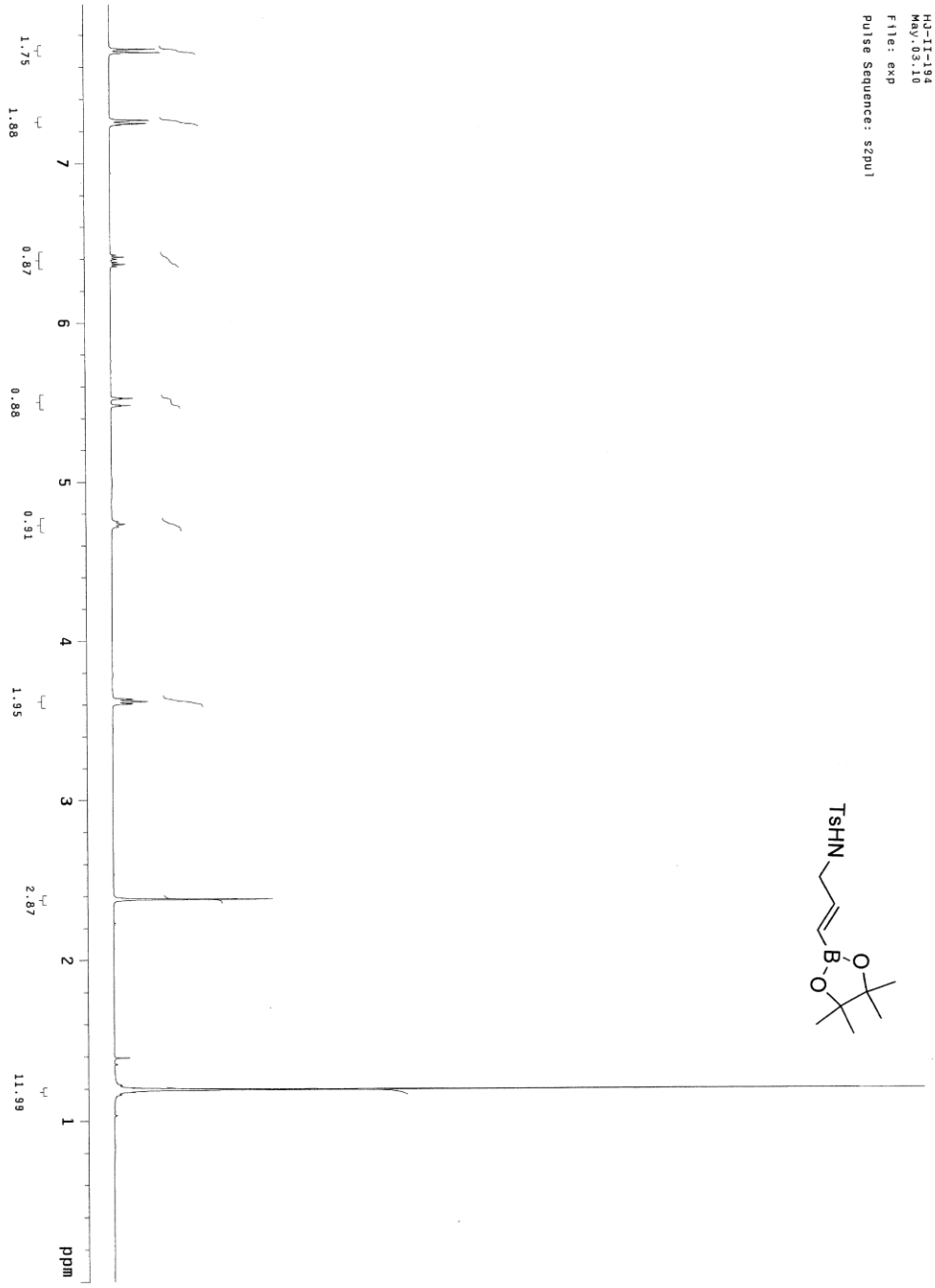

HJ-II-198
May.05.10
File: exp
Pulse Sequence: s2pul
BocN
O
Me
7
6
5
4
3
2
1
ppm
0.86
1.89
0.90
0.90
1.04
2.68
8.99

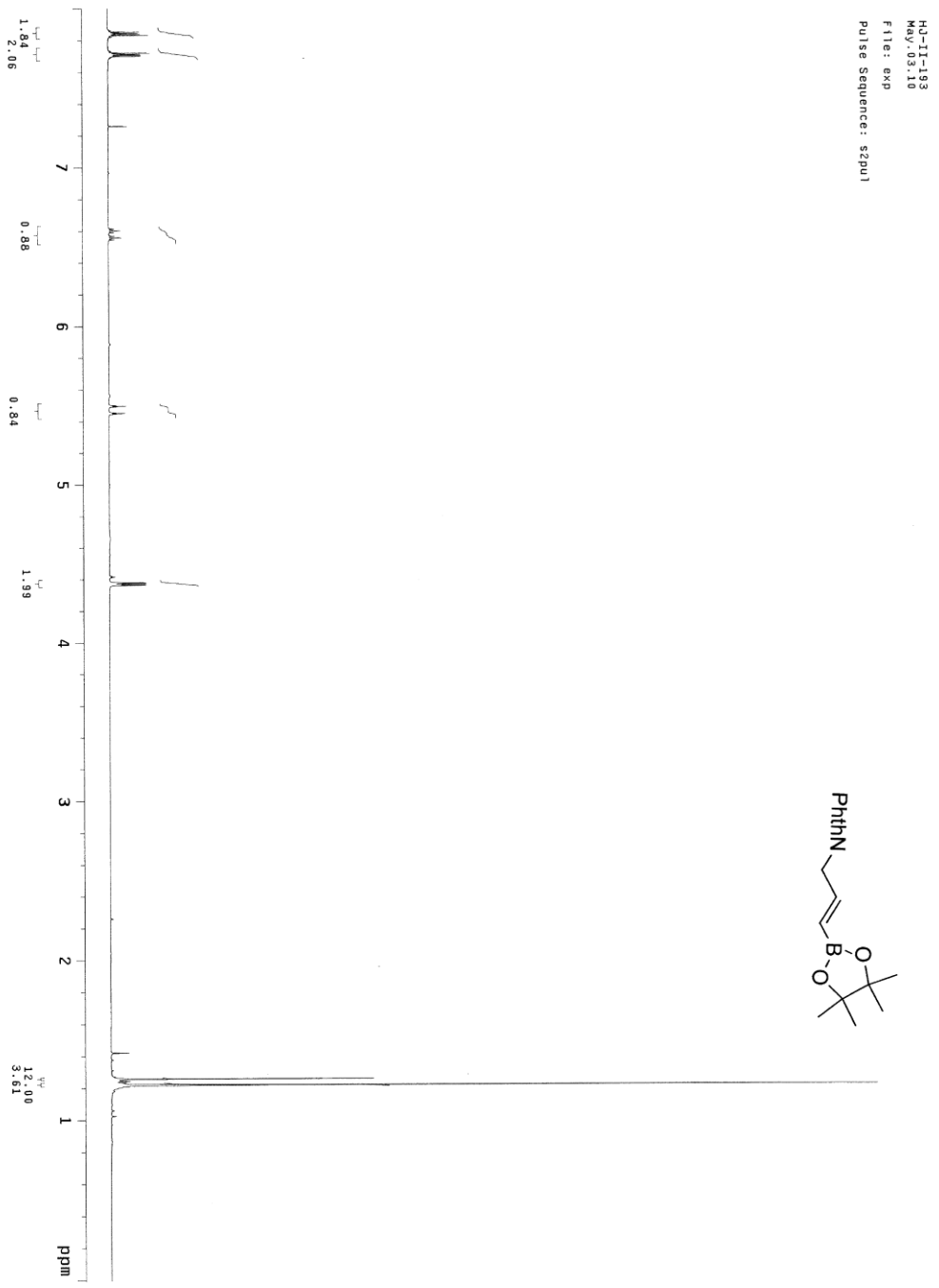

HJ-III-40-A
Oct.16.10
File: exp
Pulse Sequence: s2pul
O
O
B
O
O
0.89
1.79
1.85
1.00
0.94
0.98
0.96
1.94
11.98
7
6
5
4
3
2
1
ppm

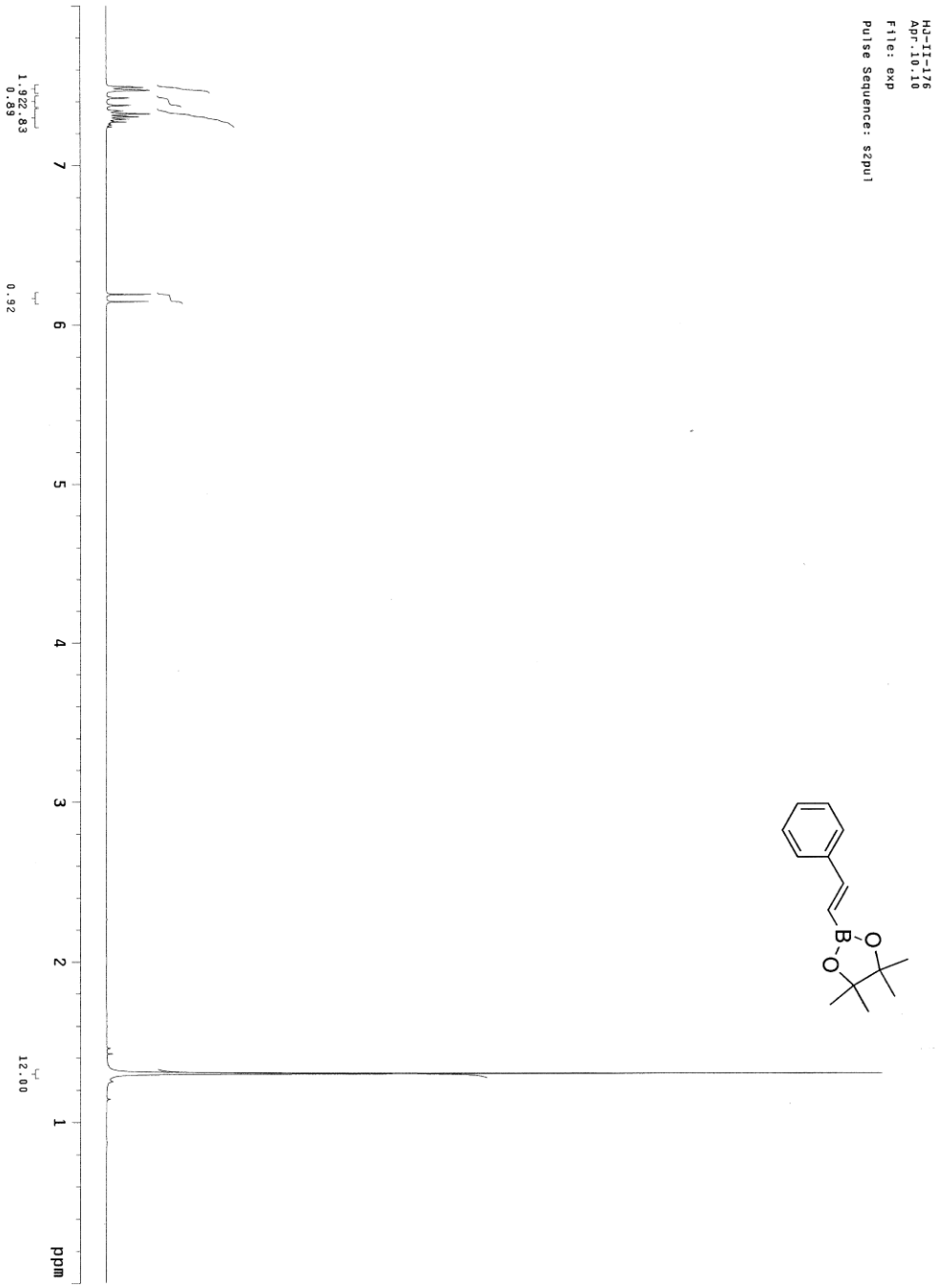

HJ-III-58
Nov.10.10
File: exp
Pulse Sequence: s2pul
ppm
12.00
1.79
1.84 0.95
0.99 0.84

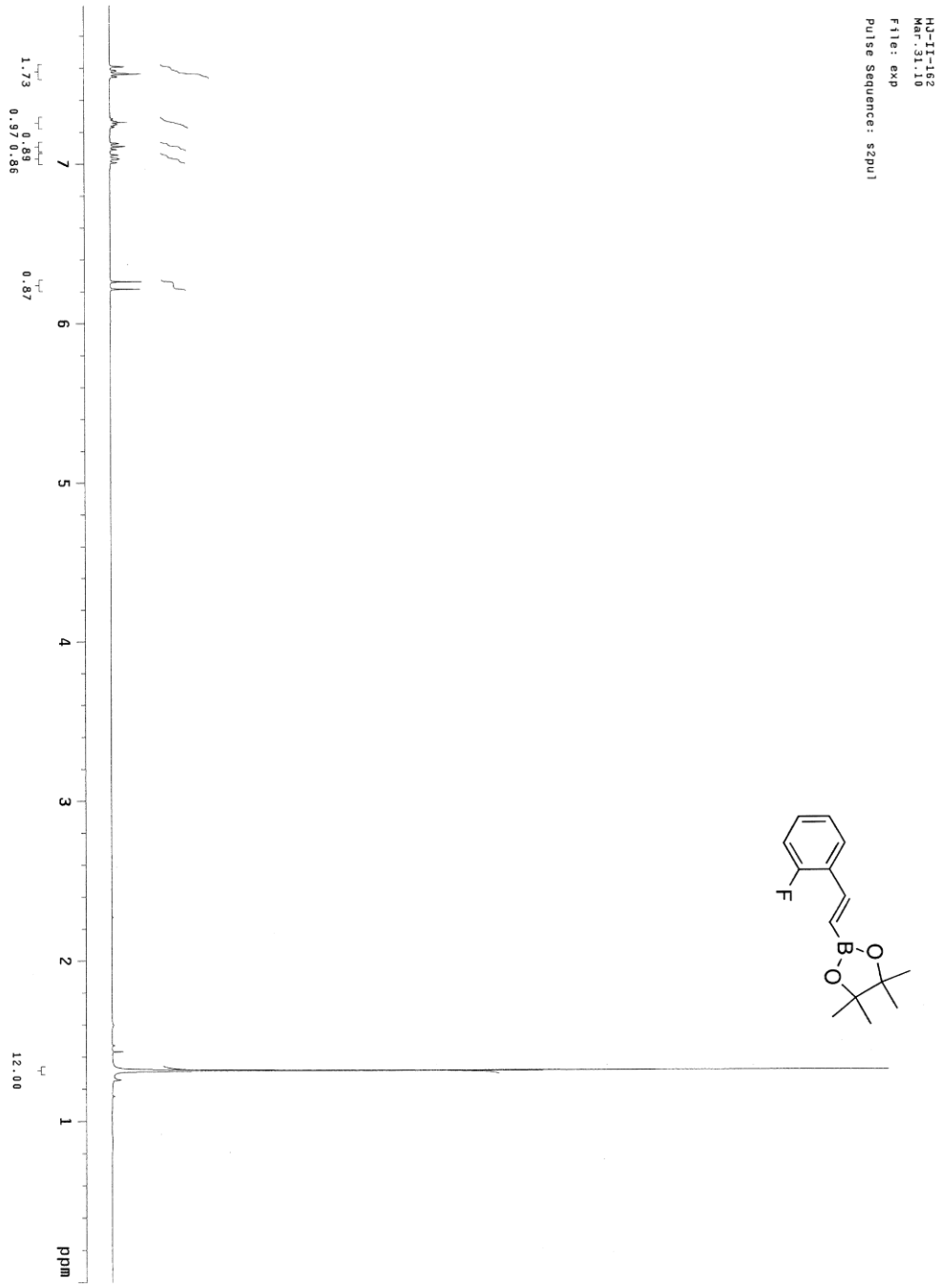

YL-VIII-188
Sample: YL-VIII-188
File: exp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: tcsw
VNMRS-400 "vnmr13"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.000 sec
Width 6410.3 Hz
40 repetitions
OBSERVE H1, 399.7832081 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 2 min, 8 sec
t-BuO
O
B
O
1.227
1.174
1.01
1.00
2.46
11.54
14.70
7
6
5
4
3
2
1
ppm

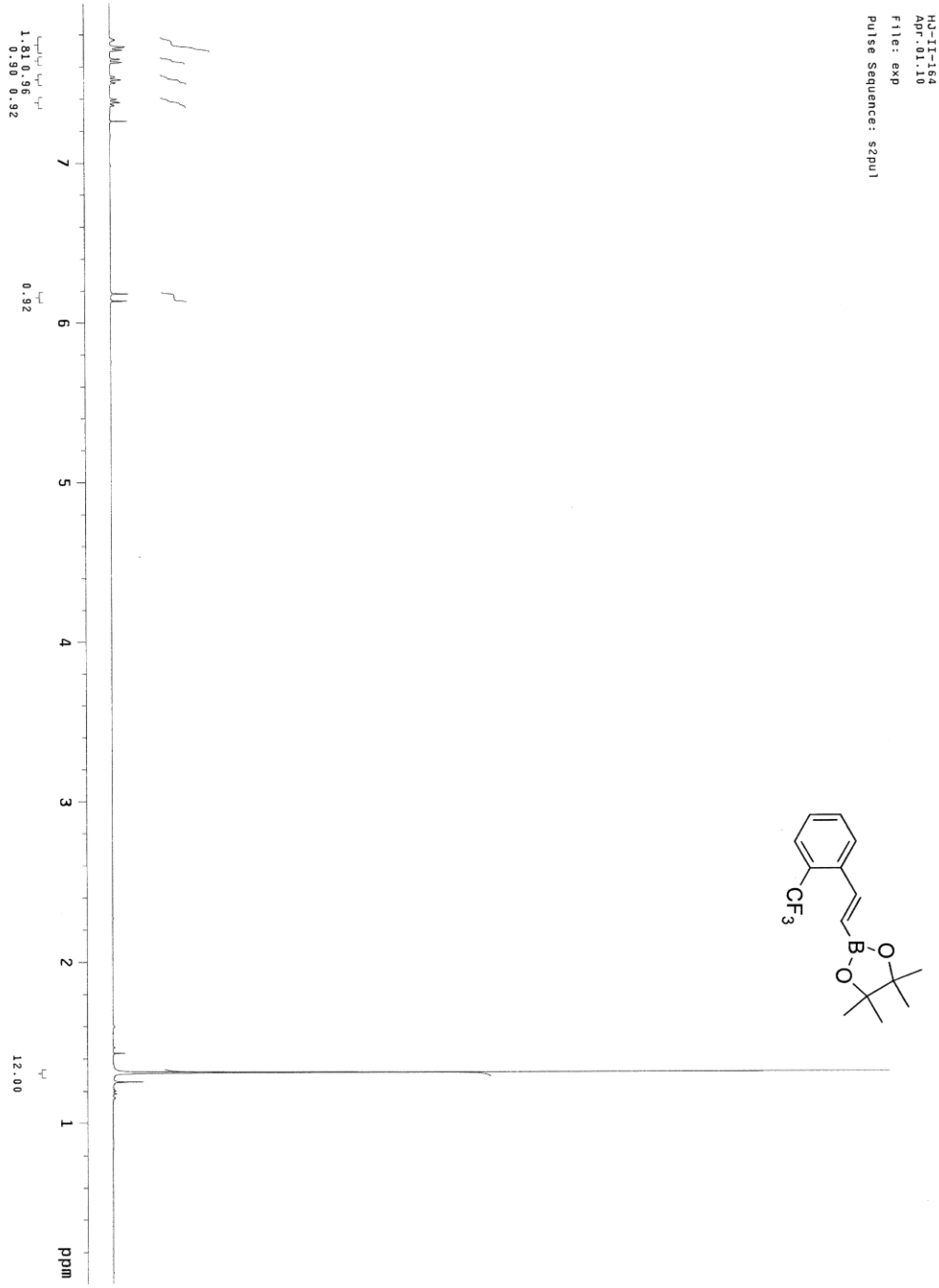

HJ-II-161
Apr.27.10
File: exp
Pulse Sequence: s2pul
HO
B
O
O
7
6
5
4
3
2
1
ppm
0.81
0.82
1.95
0.98
12.00

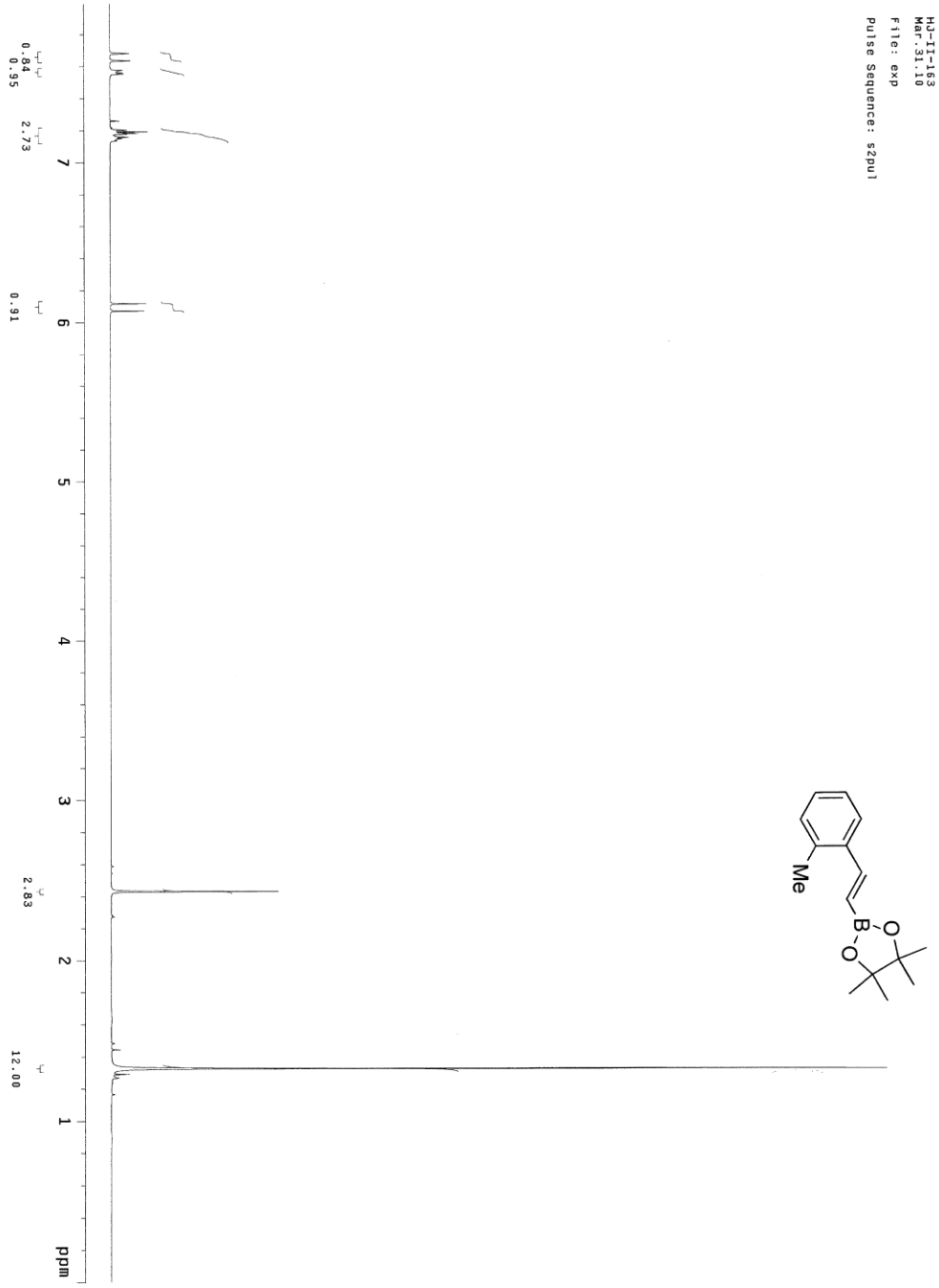

HJ-II-194
May.03.10
File: exp
Pulse Sequence: s2pul
TsHN
B
O
O
1.75
1.88
0.87
0.88
0.91
1.95
2.87
11.99
7
6
5
4
3
2
1
ppm

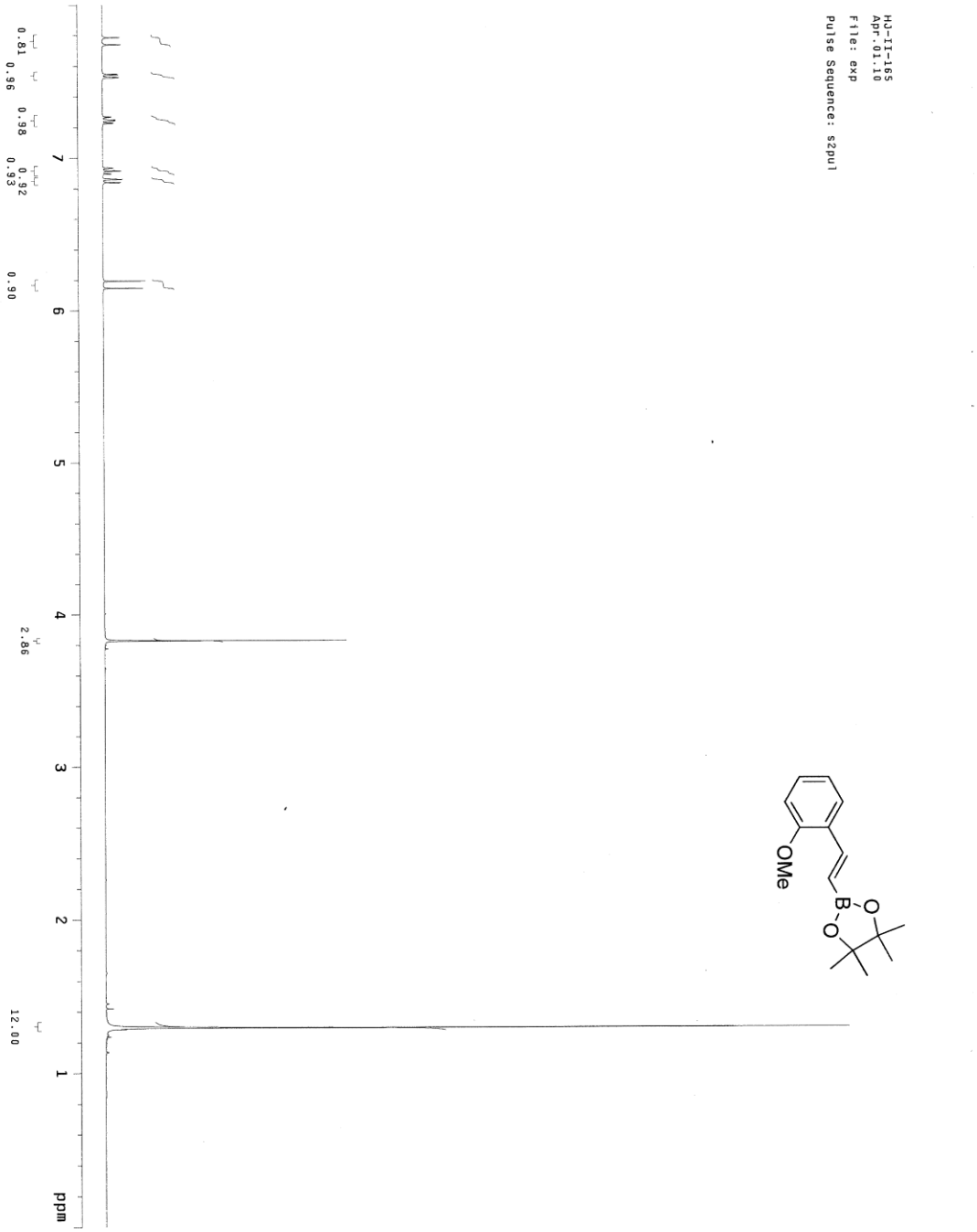

HJ-II-193
May.03.10
File: exp
Pulse Sequence: s2pul
PhthN
B
O
O
1.84
2.06
0.88
0.84
1.99
12.00
3.61
7
6
5
4
3
2
1
ppm

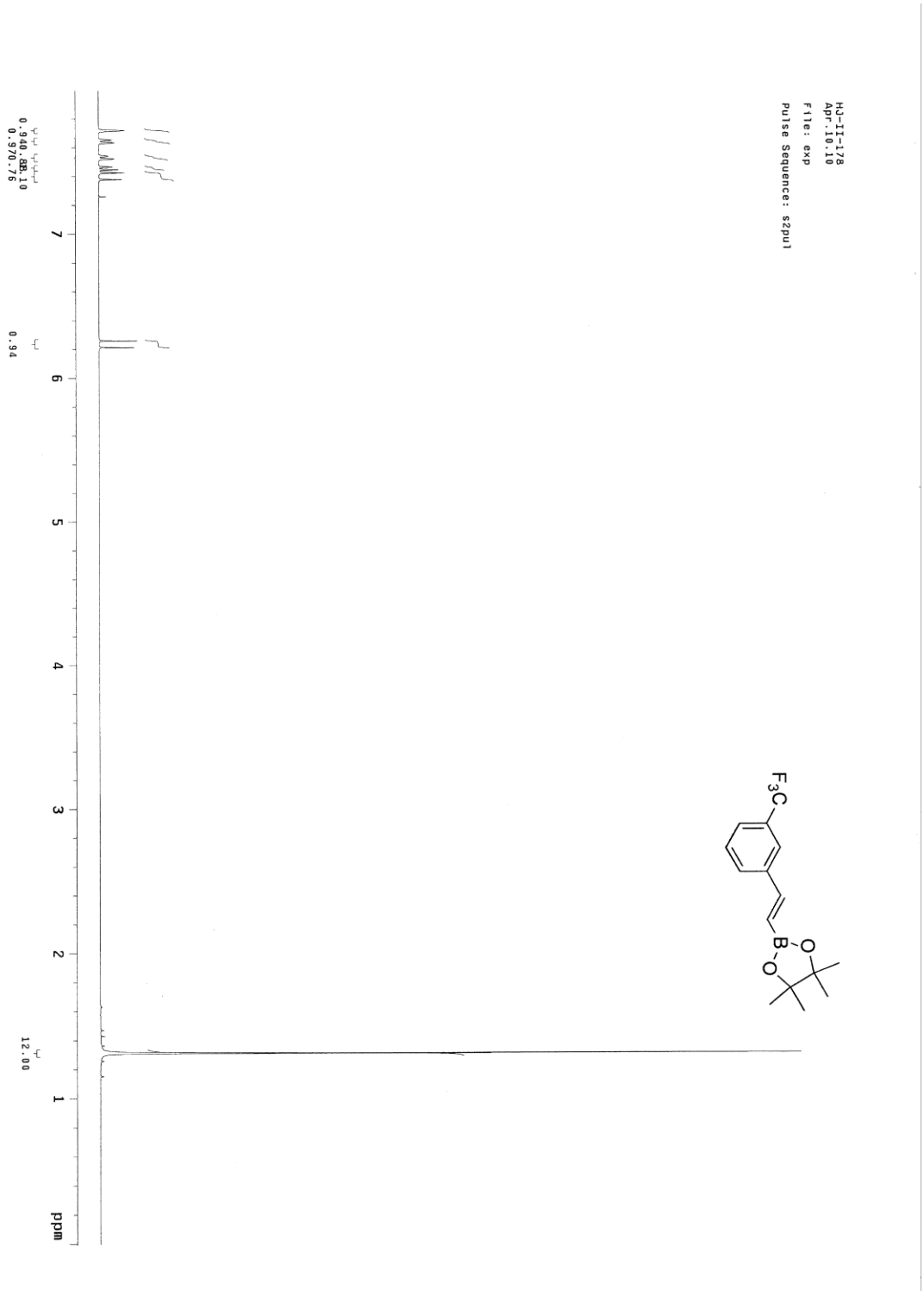

HJ-II-176
Apr.10.10
File: exp
Pulse Sequence: s2pul
1.922.83
0.89
0.92
12.00
7
6
5
4
3
2
1
ppm
B
O
O

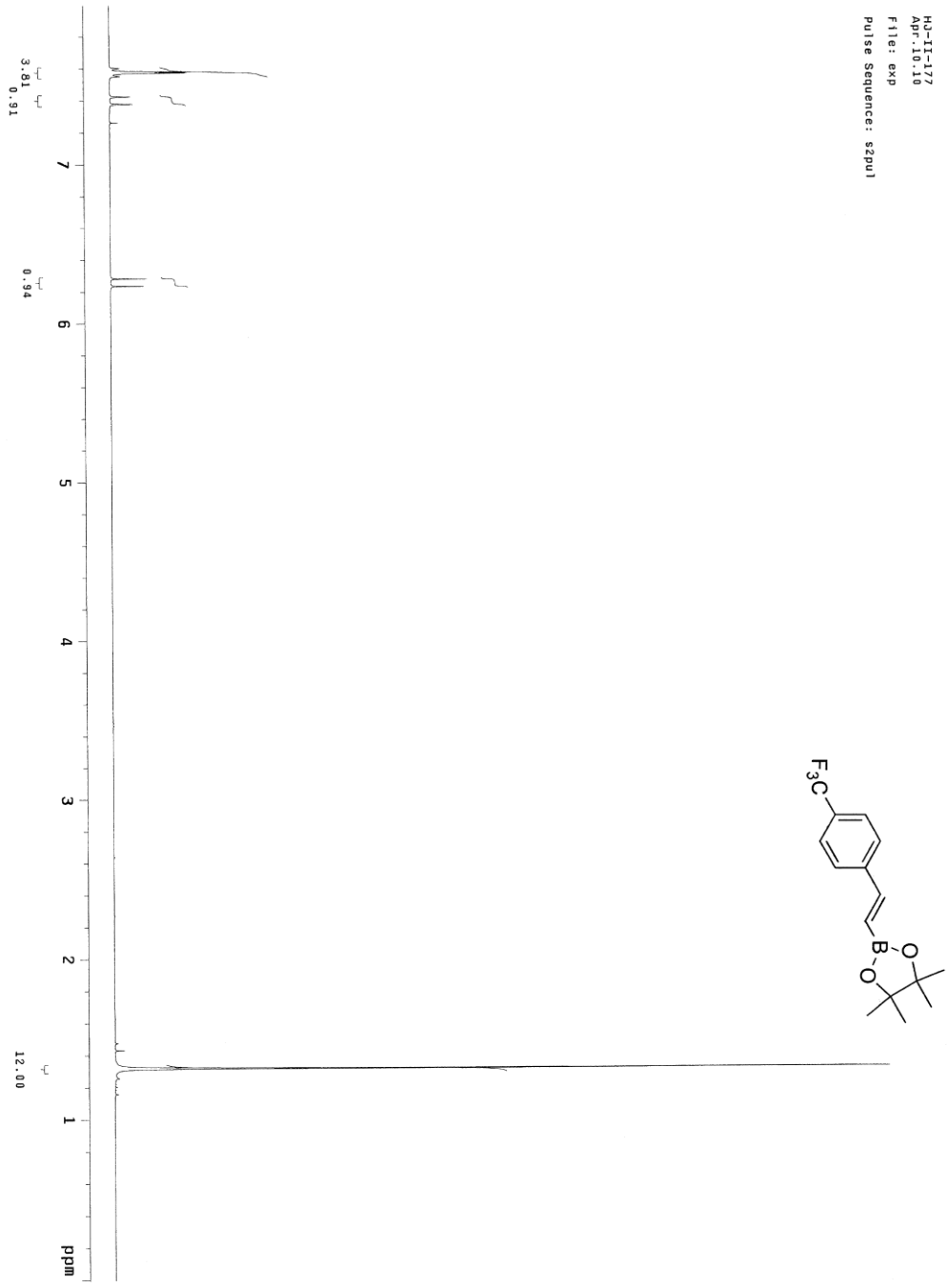

HJ-II-162
Mar.31.10
File: exp
Pulse Sequence: s2pul
F
B
O
O
ppm
1.73
0.89
0.97
0.86
0.87
12.00


HJ-II-164
Apr.01.10
File: exp
Pulse Sequence: s2pul
CF3
B
O
O
1.81 0.96
0.90 0.92
0.92
12.00
7
6
5
4
3
2
1
ppm


HJ-II-163
Mar.31.10
File: exp
Pulse Sequence: s2pul
Me
B
O
O
7
6
5
4
3
2
1
ppm
0.84
0.95
2.73
0.91
2.83
12.00


HJ-II-165
Apr.01.10
File: exp
Pulse Sequence: s2pul
OMe
B
O
O
0.81
0.96
0.98
0.92
0.93
0.90
2.86
12.00
7
6
5
4
3
2
1
ppm


HJ-II-178
Apr.10.10
File: exp
Pulse Sequence: s2pul
F3C
B
O
O
0.940.88.10
0.970.76
0.94
12.00
7
6
5
4
3
2
1
ppm


HJ-II-177
Apr.10.10
File: exp
Pulse Sequence: s2pul
F3C
B
O
O
3.81
0.91
0.94
12.00
7
6
5
4
3
2
1
ppm

## *Chapter Three*

# (*E*)- and *β*-Selective NHC–Cu-Catalyzed Protosilyl Addition to Terminal Alkynes and Site- and Enantioselective Protoboryl Addition to the Resulting Alkenylsilanes: Synthesis of Enantiomerically Enriched Vicinal and Geminal Borosilanes

### *3.1. Introduction*

Borosilanes are useful intermediates in chemical synthesis[1] since both boron and silicon form stable bonds to carbon, which can be readily elaborated into a variety of other chemical bonds.[1,2] Vicinal or geminal enantiomerically enriched borosilanes can be accessed through metal-catalyzed silaboration of alkenes;[3] however, there are no reports for methods that efficiently deliver these synthetically useful structural units in high

(1) (a) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29−49. (b) Burks, H. E.; Morken, J. P. *Chem. Commun.* **2007**, 4717−4725.
(2) For transformations of C−B bonds, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013−2030. (c) Brown, H. C.; Singh, S. M.; Rangaishenvi, M. V. *J. Org. Chem.* **1986**, *51*, 3150−3155. For transformations of C−Si bonds, see: (d) Miura, K.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *Org. Lett.* **2000**, *2*, 385−388. (e) Heitzman, C. L.; Lambert, W. T.; Mertz, E.; Shotwell, J. B.; Tinsley, J. M.; Va, P.; Roush, W. R. *Org. Lett.* **2005**, *7*, 2405−2408.
(3) (a) Suginome, M.; Nakamura, H.; Ito, Y. *Angew. Chem. Int., Ed. Engl.* **1997**, *36*, 2516−2518. (b) Ohmura, T.; Furukawa, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366−13367.

enantiomeric purity. Recently, Ito, Toyoda, and Sawamura reported a protocol for preparation of cyclic 1,2-silylborylalkanes through phosphine–Cu-catalyzed boron–copper addition to aliphatic alkenylsilanes followed by cyclization.[4] More recently, Ito and coworkers developed the efficient and highly site-selective transformation of aryl olefins to the corresponding borosilanes by activation of a B–Si bond with KO*t*-Bu.[5] Although several catalytic enantioselective methods for preparation of borosilanes have been disclosed,[6] protocols leading to the synthesis of products of the type in Scheme 3.1 have not been described. Although silaboration is less efficient than the corresponding diboration, one significant merit silylboranes hold over diboranes is that the C–B bond and C–Si bond can be differentially functionalized easily, whereas differentiation of two C–B bonds is potentially more challenging. Therefore, development of an efficient and enantioselective protocol to achieve silylboranes is an attractive objective in chemical synthesis.

Previously, we have reported that styrenes[7] and alkenylborons[8] undergo highly enantioselective protoborations with chiral NHC–Cu–B(pin) complexes, leading to the formation of the corresponding organoboron products in high enantiomeric purity. A key attribute of the above transformations is their exceptional site selectivity. Selective addition of the NHC–Cu occurs at the carbon bearing the aryl or the B(pin) unit, which

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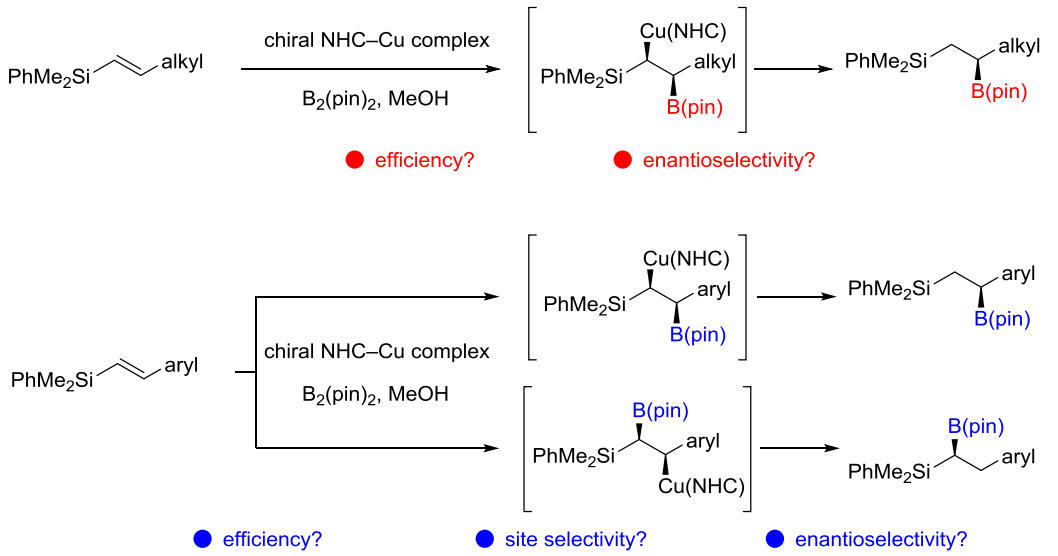
(4) Ito, H.; Toyoda, T.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 5990−5992.
(5) Ito, H.; Horita, Y.; Yamamoto, E. *Chem. Commun.* **2012**, *48*, 8006–8008.
(6) (a) Ohmura, T.; Furukawa, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366−13367. (b) Ohmura, T.; Suginome, M. *Org. Lett.* **2006**, *8*, 2503–2506. (c) Ito, H.; Kosaka, Y.; Nonoyama, K.; Sasaki, Y.; Sawamura, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7424–7427. (d) Park, J. K.; McQuade, D. T. *Synthesis* **2012**, *44*, 1485–1490. For an efficient (non-catalytic) method for enantioselective synthesis of geminal borosilanes, see: (e) Aggarwal, V. K.; Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vázquez-Romero, A.; Webster, M. P. *Org. Lett.* **2011**, *13*, 1490–1493.
(7) (a) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161. (b) Corberán, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079–7082.
(8) (a) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235.

can stabilize the incipient C–Cu bond due to the adjacent aryl or B(pin) group (hyperconjugation with aryl π* or boron p orbital, respectively). Since silyl groups can also lower the LUMO energy of the adjacent olefin through hyperconjugation of the π electron density of the alkene with the low lying Si–C σ* orbital, we have investigated alkenylsilanes as suitable substrates for the enantioselective protoboration reaction.

Mechanistically, the study for protoboration of alkenylsilanes would have several interesting aspects. Based on previous studies, as illustrated in Scheme 3.1, we predicted that in reactions of alkyl-substituted alkenylsilanes, vicinal borosilyl products would be generated with high site selectivity due to the stabilization of C–Cu bond by silyl group. Although we might be able to achieve high site selectivity, it was still unclear whether transformations would take place with high efficiency and enantioselectivity. On the other hand, when we utilize aryl-substituted silyl olefins, since the olefin contains two functional groups (silyl and aryl), both of which can stabilize the incipient C–Cu bond, an additional site selectivity issue presents itself.

***Scheme 3.1.*** NHC–Cu-Catalyzed Cu–B Additions to Alkyl- and Aryl-Substituted Alkenylsilanes



In addition, since alkenylsilanes can be prepared by site- and stereoselective protosilylation (Si–Cu addition followed by C–Cu protonation) of terminal alkynes, we examined a Cu-catalyzed process for preparation of alkenylsilanes and another Cu-catalyzed transformation for synthesis of enantiomerically enriched vicinal or geminal borosilanes selectively. Herein, we have disclosed a protocol for an efficient, general and exceptionally site- and stereoselective protosilylation of terminal alkynes bearing an alkyl or an aryl group. Substantial quantities of (*E*)-*β*-alkenylsilanes are obtained through the use of a readily available $PhMe_2SiB(pin)$ reagent with exclusive stereo- and site selectivity (>98:2 *E*:*Z* and *β*:*α* for all the cases). We then have disclosed NHC–Cu-catalyzed site- and enantioselective protoboration of (*E*)-*β*-alkenylsilanes,[9] affording enantiomerically enriched vicinal or geminal borosilanes in up to >98% site selectivity and 98.5:1.5 e.r. In the presence of 5 mol % monodentate chiral NHC–Cu complex, alkyl- and alkenyl-containing alkenylsilanes are successfully converted to vicinal silylboryl products efficiently and selectively. Additions to aryl-bearing alkenylsilanes require bidentate chiral sulfonate-bearing NHC ligands for optimal selectivity, which react with the opposite sense of site selectivity and generate geminal silylborons predominantly with high enantioselectivity. We will demonstrate representative functionalizations to show the utility of the aforementioned protocol, including a formal enantioselective synthesis of antibacterial agent bruguierol A. Furthermore, stereochemical models will be presented to account for the levels and trends in site- and enantioselectivities we observed.

(9) Enantioselective hydroboration reactions of alkenyl(trimethyl)silanes in the presence of stoichiometric amounts of a chiral borohydride reagent have been reported (up to >98% geminal selectivity and 70:30 e.r.). See: Soderquist, J. A.; Lee, S. -J. H. *Tetrahedron* **1988**, *44*, 4033–4042.

## *3.2. Background*

Enantiomerically enriched silylboryl compounds are useful intermediates in chemical synthesis since we can easily functionalize C–B and C–Si bonds independently. Thus, protocols for either vicinal or geminal borosilanes enantioselectively have been developed. In this section, we will introduce the advances regarding catalytic synthesis of vicinal borosilanes and also approaches to prepare geminal silylborylalkanes.

### *3.2.1. Metal-Catalyzed Silaborations of Terminal Alkenes*

In 1997, a pioneering work was reported by Suginome, Nakamura, and Ito, involving Pt-catalyzed site-selective silaboration of terminal olefins.[10] Reactions are promoted by 2 mol % of Pt salt in the presence of $PhMe_2SiB(pin)$ reagent (Scheme 3.2). Conversion of styrene **3.1** to the corresponding 1,2-borosilane **3.2** is highly selective (>98% vicinal). The authors utilized aryl- or alkyl-substituted olefins, both of which undergo boron–silicon addition catalyzed by Pt catalyst to afford vicinal borosilyl products with similar level of efficiency (53% yield for **3.3** and **3.4**). Reaction of *n*-hexyl-bearing alkene is, however, less site-selective than those of aryl-olefins (87% vicinal for **3.4** vs >98% vicinal for **3.2** and **3.3**). Additionally, the borosilylation of ethylene with 2 mol % $Pt(CH_2{=}CH_2)(PPh_3)_2$ delivers 1,2-borylsilylethane **3.5** in 73% yield with perfect site selectivity.

(10) Suginome, M.; Nakamura, H.; Ito, Y. *Angew. Chem. Int., Ed. Engl.* **1997**, *36*, 2516−2518.

***Scheme 3.2.*** Pt-Catalyzed Site-Selective Silaboration of Terminal Alkenes


**3.1**

**3.2**
51% yield
>98% vicinal

**3.3**
53% yield
>98% vicinal

**3.4**
53% yield
87% vicinal

**3.5**
73% yield
>98% vicinal

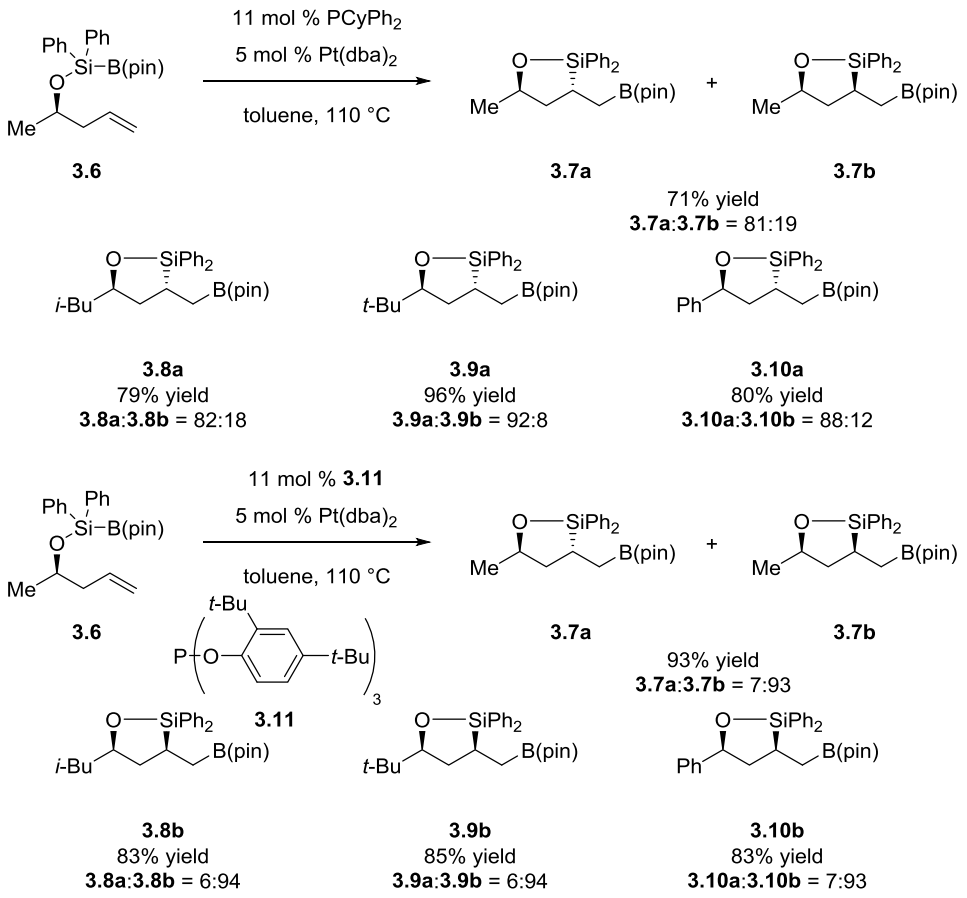
Suginome and coworkers described intramolecular boron–silicon addition to tethered terminal olefins catalyzed by Pt–phosphine complex.[11] As illustrated in Scheme 3.3, silicon-tethered olefin **3.6**, which is prepared by the reaction of homoallylic alcohol with $ClPh_2SiB(pin)$ reagent in the presence of pyridine, undergoes $Ph_2CyP$–Pt-catalyzed intramolecular silaboration to afford a 81:19 mixture of two stereoisomers **3.7a** and **3.7b** in 71% yield. Reactions of *i*-Bu- and *t*-Bu-bearing substrates are investigated, delivering anti-addition products **3.8a** and **3.9a** as major isomers with 82–92% selectivity. Intramolecular borosilylation of phenyl-containing silicon-tethered olefin, promoted by Pt complex derived from $Pt(dba)_2$ and $PCyPh_2$, proceed to furnish *trans* isomer **3.10a** with 88% selectivity in 80% yield. Thus, *trans*/*cis* selectivity is not affected by whether substituent is alkyl or aryl unit.

Interestingly, high *cis*-selectivity is observed when reaction is carried out with sterically more hindered phosphine ligand **3.11**. Under identical reaction conditions to the above mentioned transformation except with the use of 11 mol % **3.11**, intramolecular silaborations are performed, resulting in complete reversal of *trans*/*cis* selectivity. The

(11) Ohmura, T.; Furukawa, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366−13367.

major products are *cis*-isomers with higher levels of selectivity (*trans*/*cis* = 7:93–6:94 for **3.7b**–**3.10b**).

***Scheme 3.3.*** Pt-Catalyzed Intramolecular Silaboration of Terminal Alkenes



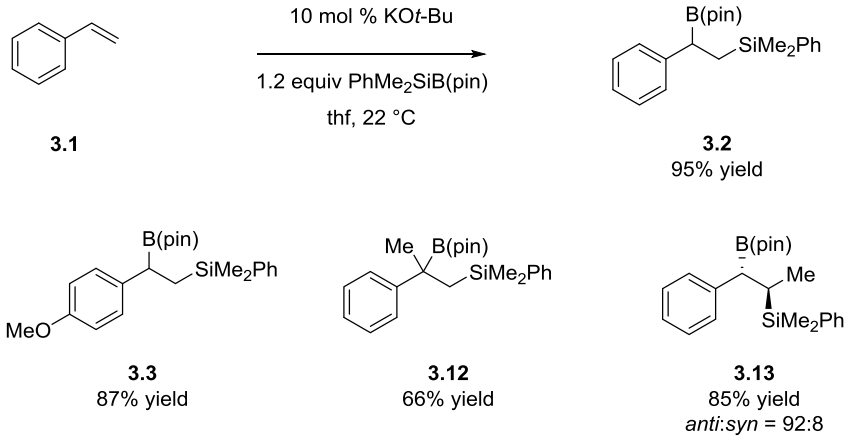

### *3.2.2. Base-Mediated Selective Silaboration of Aryl Alkenes*

Ito and coworkers demonstrated that efficient and site-selective borosilylation of aryl olefins can be achieved by use of potassium alkoxide base for activation of boron–silicon bond.[12] As described in Scheme 3.4, site-selective B–Si addition to styrene **3.1** in the presence of 10 mol % of KO*t*-Bu proceeds to deliver vicinal silylborane **3.2** efficiently (95% yield). Then, methyl-substituted styrenes are investigated, affording

(12) Ito, H.; Horita, Y.; Yamamoto, E. *Chem. Commun.* **2012**, *48*, 8006–8008.

B(pin)-bearing quaternary center **3.12** in 66% yield from *α*-methyl styrene, and a 92:8 mixture of *anti*- and *syn*-isomers of **3.13** in 85% yield from *β*-methyl styrene. Although readily accessible alkoxide base, KO*t*-Bu was utilized as a catalyst (non-transition metal catalyst), silaborations of aryl alkenes are relatively efficient (up to 95% yield) and highly selective (<2% geminal) in mild condition, which makes this transformation practical and useful. However, substrate scope is limited; only aryl-bearing olefins are investigated, and an enantioselective variant is not presented.

***Scheme 3.4.*** Potassium *tert*-Butoxide-Catalyzed Silaboration of Aromatic Alkenes

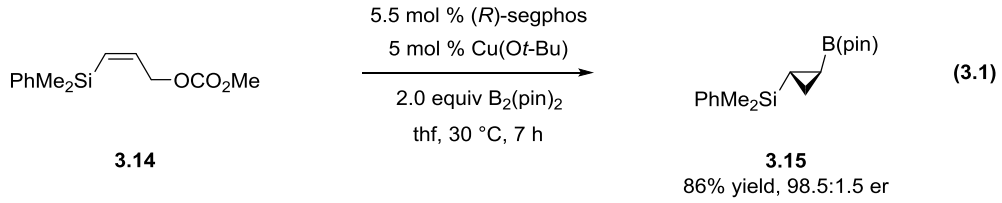



### *3.2.3. Cu-Catalyzed Selective Synthesis of Cyclic Vicinal Borosilanes*

Ito, Sawamura, and coworkers reported phosphine–Cu-catalyzed Cu–B addition to alkenylsilanes followed by Cu–alkoxide elimination to generate cyclic 1,2-borosilanes.[13] As illustrated in eq 3.1, in the presence of 5 mol % of (*R*)-segphos–Cu complex, reaction of (*Z*)-silyl-olefin **3.14**, which bearing an allylic carbonate, with 2 equiv. of $B_2(pin)_2$ furnishes *trans*-1,2-boryl,silyl-cyclopropane **3.15** in 86% yield and 98.5:1.5 e.r. The (*Z*)-olefin geometry is essential for high efficiency and selectivity; when

(13) Ito, H.; Kosaka, Y.; Nonoyama, K.; Sasaki, Y.; Sawamura, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7424–7427.

(*E*)-isomeric **3.14** is utilized instead, *trans*-silylborane **3.15** is obtained in much lower yield along with a significant amount of *cis*-isomer.




**3.14**

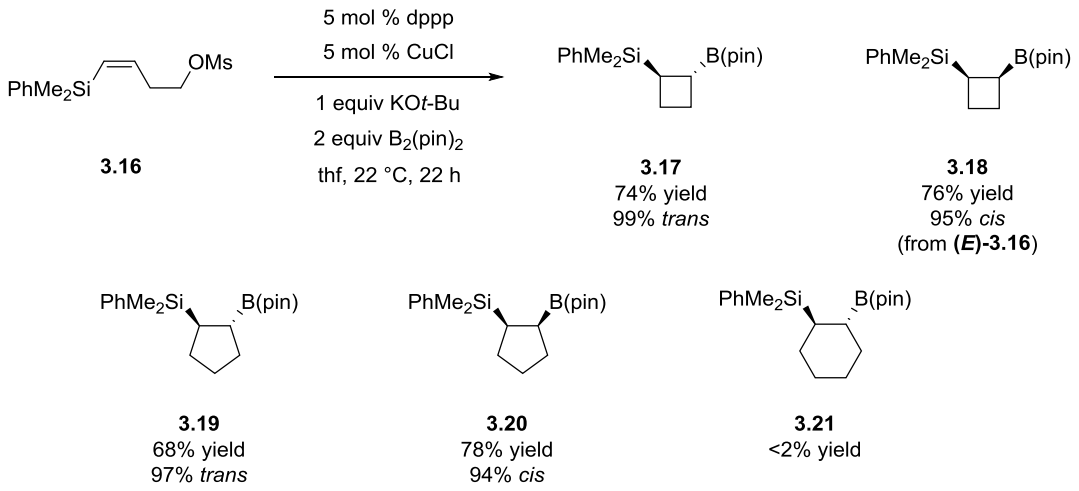
**3.15**
86% yield, 98.5:1.5 er

**(3.1)**

Another noteworthy advance was illustrated by Ito, Toyoda, and Sawamura in 2010.[14] With 5 mol % of achiral bidentate 1,3-bis(diphenylphosphino)propane (dppp), 5 mol % of CuCl, and 1 equiv. of KO*t*-Bu, (*Z*)-homoallylic sulfonate **3.16** was successfully converted to *trans*-1-boryl-2-silylcyclobutane **3.17** in 74% yield and 99% *trans* selectivity (Scheme 3.5). In contrast, when (*E*)-stereoisomer of **3.16** was utilized, *cis*-cyclobutylborosilane **3.18** was obtained in 76% yield and 95% *cis* selectivity. The reactions of (*Z*)- and (*E*)-bis-homoallylic sulfonates provided five-membered-borosilanes with high stereoselectivity (97% *trans* selectivity for **3.19** and 94% *cis* selectivity for **3.20**). When the authors tried to achieve 1-boryl-2-silylcyclohexane **3.21**, however, they only observed trace amounts of the products.

(14) Ito, H.; Toyoda, T.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 5990−5992.

***Scheme 3.5.*** Stereospecific Synthesis of Cyclic Silylborylalkanes




Although the transformations for cyclic vicinal borosilanes developed by Ito, Sawamura, and coworkers are efficient and highly stereoselective, there are limitations. First, substrate scope is limited. Only certain sized cyclic products (3-, 4-, and 5-membered) are provided and no functional groups (such as halogens, ethers, amides, etc.)-bearing products are shown. In addition, enantioselective variants are not described yet.

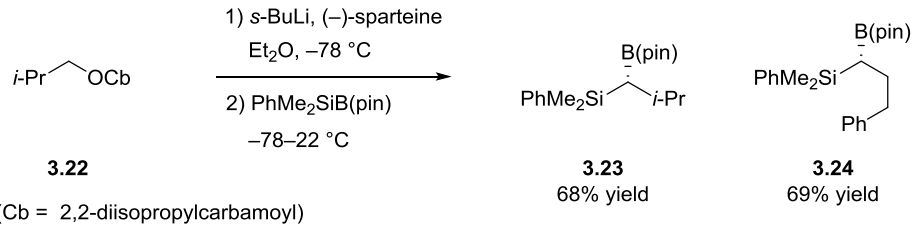
### *3.2.4. Non-Catalytic Synthesis of Enantiomerically Enriched Geminal Borosilanes*

In 2011, Aggarwal and coworkers reported enantioselective synthesis of allyl- and crotylsilanes. [15] Their substrates for the aforementioned transformation are 1,1-borosilanes, which are prepared through a single-vessel protocol described in Scheme 3.6. Conversion of *i*-propyl-bearing carbamate **3.22** to corresponding geminal silylborane **3.23** is effective (68% yield). With a similar efficiency, 1,1-silylborane **3.24** is also prepared in 69% yield. Even though this transformation requires the use of a

(15) Aggarwal, V. K.; Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vázquez-Romero, A.; Webster, M. P. *Org. Lett.* **2011**, *13*, 1490–1493.

stoichiometric amount of expensive (–)-sparteine, enantiomerically enriched geminal borosilanes, not easily prepared by other methods, can be obtained efficiently.

***Scheme 3.6.*** Enantioselective Synthesis of Geminal Borosilanes




**3.22** (Cb = 2,2-diisopropylcarbamoyl)

**3.23** 68% yield

**3.24** 69% yield

Since there have been no reports for efficient and catalytic enantioselective synthesis of vicinal or geminal borosilanes, development of protocols for the site- and enantioselective catalysis to afford either isomeric borosilane is very attractive.

## *3.3. Site- and Stereoselective Synthesis of alkenylsilanes by NHC–Cu-Catalyzed Protosilylation of Terminal Alkynes*

Before beginning our investigation into NHC–Cu-catalyzed protoboration of alkenylsilanes, we focused on the development of an efficient and selective protocol for preparation of alkenylsilanes.[16] Although there are protocols for (*E*)- and *β*-selective hydrosilylation of terminal alkynes,[17] most of them require the use of precious metals such as Rh,[18] Pt,[19] or Ru.[20] In addition, selective hydrosilylation of terminal alkynes with

(16) For selected reviews regarding the utility of alkenylsilanes, see: (a) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857–873. (b) Curtis-Long, M. J.; Aye, Y. *Chem. –Eur. J.* **2009**, *15*, 5402–5416. (c) Denmark, S. E.; Liu, J. H.-C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2978–2986.
(17) For a review regarding catalytic hydrosilylation reactions of alkynes, see: (a) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853–887. For an *α*-selective catalytic hydrosilylation of terminal alkynes, see: (b) Wang, P.; Yeo, X.-L.; Loh, T.-P. *J. Am. Chem. Soc.* **2011**, *133*, 1254–1256.
(18) For examples of Rh-catalyzed hydrosilylation of terminal alkynes, see: (a) Faller, J. W.; D'Alliessi, D. G. *Organometallics* **2002**, *21*, 1743–1746. (b) Mori, A.; Takahisa, E.; Yamamura, Y.; Kato, T.; Mudalige, A. P.; Kajiro, H.; Hirabayashi, K.; Nishihara, Y.; Hiyama, T. *Organometallics* **2004**, *23*, 1755–1765.
(19) For examples of Pt-catalyzed hydrosilylation of terminal alkynes, see: (a) Aneetha, H.; Wu, W.; Verkade, J. G. *Organometallics* **2005**, *24*, 2590–2596. (b) Berthon-Gelloz, G.; Schumers, J-M.; De Bo, G.;

stoichiometric amounts of Cr salts[21] and Ti-catalyzed transformation for alkyl-substituted alkynes[22] are also illustrated. Thus, development of selective Cu-catalyzed protocol for alkenylsilanes with a broad substrate scope is highly attractive.

As illustrated in Scheme 3.7, alkyl- or aryl-substituted (*E*)-*β*-alkenylsilanes are obtained efficiently (79–98% yield) with complete stereo- and site selectivity (>98% (*E*) and *β*) for all cases through NHC–Cu-catalyzed protosilylation of alkynes. Reactions of terminal alkynes with commercially available $PhMe_2SiB(pin)$, which can be prepared through a simple procedure,[23] in the presence of 1 mol % NHC–Cu complex derived from achiral imidazolinium salt **3.26**, CuCl, and NaO*t*-Bu undergo Cu–Si addition followed by C–Cu bond protonation by MeOH. Reactions of linear or *α*-branched alkyl chain-bearing terminal alkynes, containing functional group (halide, ester, or silyl ether) deliver desired alkenylsilanes **3.27**–**3.32** efficiently (up to 98% yield) with perfect selectivities (>98% (*E*)- and *β*-selectivity). A variety of electronically and/or sterically different aryl-alkynes are examined, affording (*E*)-*β*-silyl-styrenes **3.33**–**3.40** exclusively in 79–93% yield. Noticeably, we observe exclusive site selectivity for all the terminal alkyne substrates (>98% *β*-selectivity), which suggests that a large $PhMe_2Si$ unit is placed at the terminal carbon preferentially regardless of the substituent of the alkyne substrate. Then, C–Cu bond is protonated by MeOH to form C–H bond, which

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Markó, I. E. J. Org. Chem. 2008, 73, 4190–4197. For related catalytic silaboration of alkynes, see: (c) Suginome, M.; Matsuda, T.; Nakamura, H.; Ito, Y. *Tetrahedron* **1999**, *55*, 8787–8800.

(20) For Ru-catalyzed hydrosilylation of terminal alkynes, see: Katayama, H.; Taniguchi, K.; Kobayashi, M.; Sagawa, T.; Minami, T.; Ozawa, F. *J. Organomet. Chem.* **2002**, *645*, 192–200.

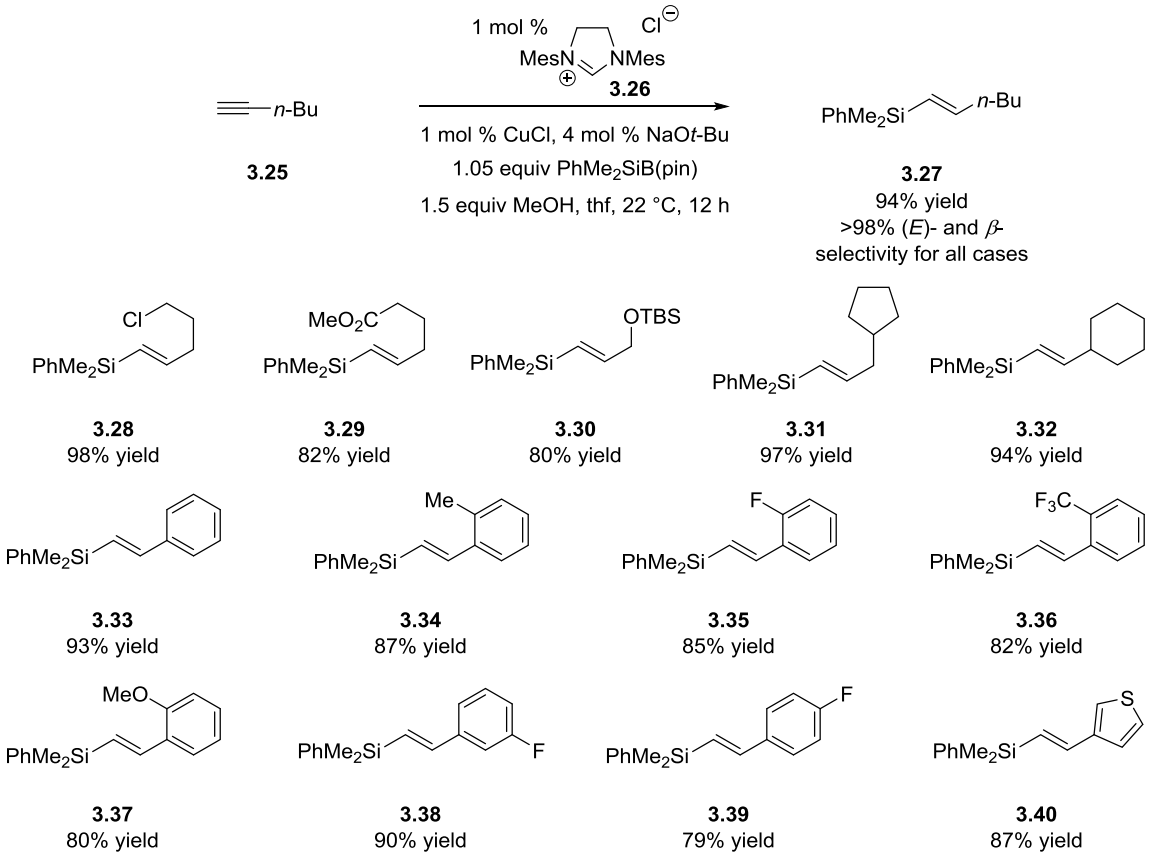
(21) Lim, D. S. W.; Anderson, E. A. *Org. Lett.* **2011**, *13*, 4806–4809.

(22) Takahashi, T.; Bao, F.; Gao, G.; Ogasawara, M. *Org. Lett.* **2003**, *5*, 3479–3481.

(23) For a procedure for preparation of $PhMe_2SiB(pin)$, see: Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **2000**, *19*, 4647–4649.

regenerates the catalytic active NHC–Cu–OMe species and provides the protosilylation product.

***Scheme 3.7.*** Selective NHC–Cu-Catalyzed Protosilylation of Terminal Alkynes



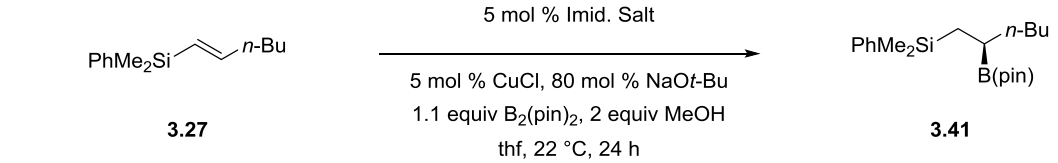

## *3.4. Site- and Enantioselective NHC–Cu-Catalyzed Protoboration of Alkenylsilanes*

### *3.4.1. Examination of Various Chiral NHC–Cu Complexes*

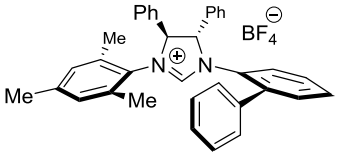
We investigated the ability of chiral Cu–NHC complexes to promote efficient site- and enantioselective protoborations. Initially, we examined the reactions of alkyl-bearing alkenylsilane **3.27** in the presence of 5 mol % various chiral NHC–Cu complexes to obtain vicinal borosilane **3.41** (Scheme 3.7). As we predicted above, Cu–B addition occurs such that the copper is located at the carbon bearing silicon unit (Section 3.1). We

began the screening by examination of three representative NHCs derived from **A.1**–**A.3**. Among them, monodentate NHC–Cu complex derived from **A.1** shows promising efficiency and selectivity (61% conv, 56% yield, and 79.5:80.5 e.r.). When we utilize $C_2$-symmetric monodentate NHC–Cu complex, both efficiency and enantioselectivity are reduced (32% conv, 30% yield, and 57:43 e.r. for **A.10**). Thus, we decide to modify the structure of $C_1$-symmetric monodentate NHC (**A.1**), preparing di-*m*-methyl-substituted *N*-phenyl imidazolinium salt **A.11** and sterically more hindered **A.12**, *o*-$Et_2$-phenyl variant of **A.1**. Both of them, however, do not promote reaction of **3.27** with high efficiency and/or enantioselectivity (52% conv, 51% yield, and 51:49 e.r. for **A.11**; 56% conv, 54% yield, and 81.5:18.5 e.r. for **A.12**). Since reaction with bidentate sulfonate **A.3** is efficient, affording **3.41** in 78% yield, although selectivity is moderate (60:40 e.r.), we examine chiral sulfonates **A.6** and **A.8** for NHC precursors. Unfortunately, selectivities obtained by both NHC–Cu complexes are moderate (34.5:65.5 e.r. for **A.6** and 45:55 e.r. for **A.8**). The observations with **A.6** and **A.8** led us to focus on further modification of $C_1$-symmetric monodentate NHCs. Interestingly, when we introduce sterically demanding mesityl unit on the *ortho* position of *N*-phenyl moiety (**A.13**), complete consumption of **3.27** is observed (93% yield) with slightly higher enantioselectivity (85:15 e.r.). For further enhancement of selectivity, we prepared three modified imidazolinium salts **A.14**, **A.15**, and **A.16**, all of which contain *o*-mesityl-phenyl substituent. An NHC–Cu generated from 2,6-$Et_2$-phenyl-variant **A.14** catalyzes boron–copper addition with higher enantioselectivity (87:13 e.r. vs 85:15 e.r. for **A.13**). With an NHC–Cu complex derived from even longer, *n*-propyl-containing variant **A.16**, however, enantioselectivity is lower (82:18 e.r.). Thus, we chose **A.14** as an optimal NHC precursor for further study.

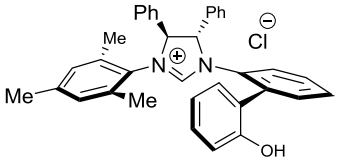
***Scheme 3.8.*** Evaluation of Chiral NHC–Cu Complexes for Alkyl-Substituted Alkenylsilane



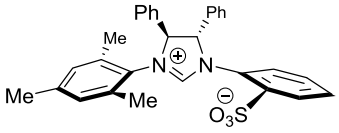

**3.27** **3.41**



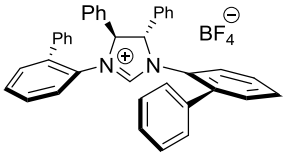
**A.1**
61% conv, 56% yield
79.5:20.5 e.r.



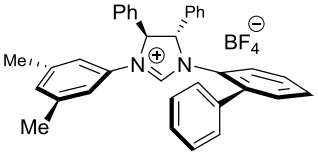
**A.2**
74% conv, 61% yield
78.5:21.5 e.r.



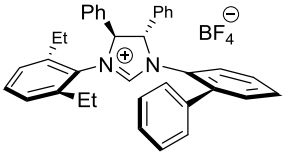
**A.3**
92% conv, 78% yield
60:40 e.r.



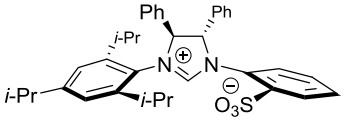
**A.10**
32% conv, 30% yield
57:43 e.r.



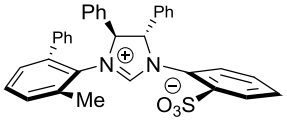
**A.11**
52% conv, 51% yield
51:49 e.r.



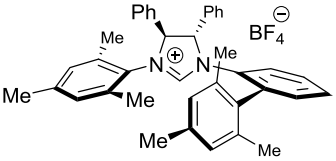
**A.12**
56% conv, 54% yield
81.5:18.5 e.r.



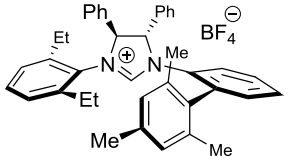
**A.6**
53% conv, 44% yield
34.5:65.5 e.r.



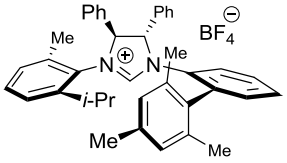
**A.8**
87% conv, 84% yield
45:55 e.r.



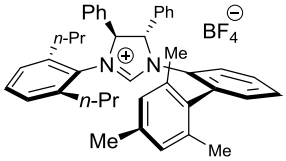
**A.13**
>98% conv, 93% yield
85:15 e.r.



**A.14**
98% conv, 85% yield
87:13 e.r.



**A.15**
88% conv, 81% yield
80.5:19.5 e.r.

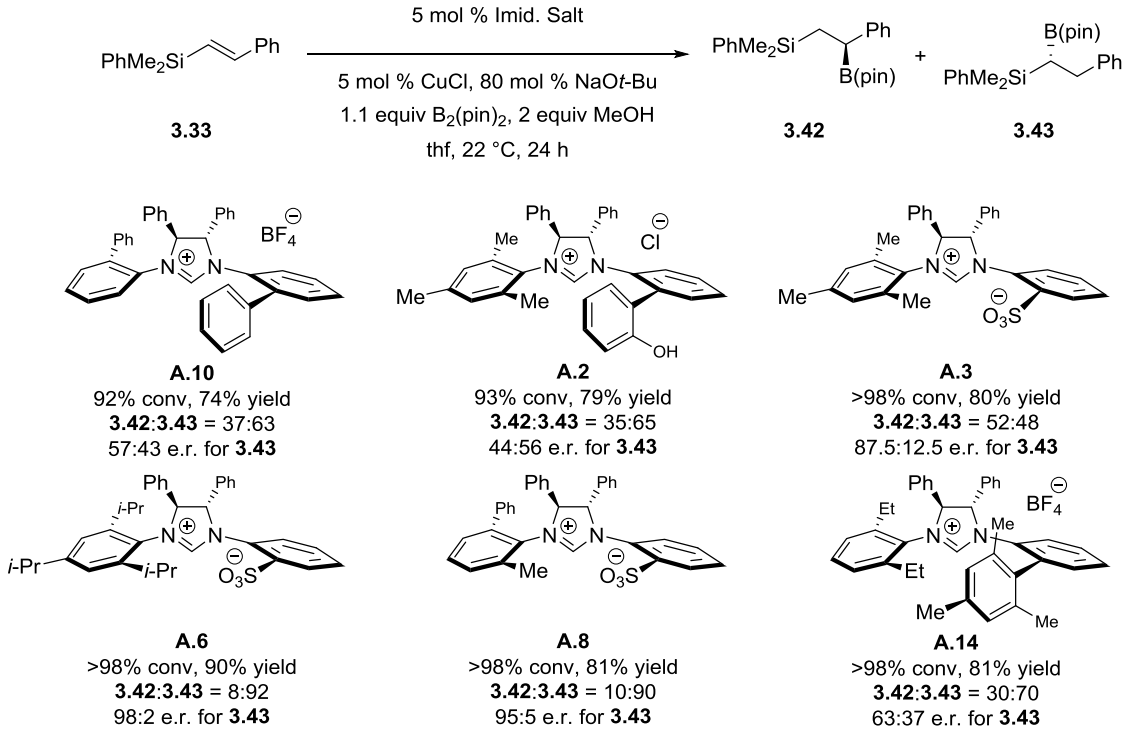


**A.16**
>98% conv, 88% yield
82:8 e.r.

Next, we have investigated reactions of aryl-alkenylsilane **3.33**, which cause additional site selectivity issues. Since both aryl and silyl groups can stabilize adjacent C–Cu bond, achievement of high site-selective boron–copper addition might not be trivial. As illustrated in Scheme 3.9, the trends in site selectivity and the most effective chiral catalysts are totally different. Site selectivity for protoboration of silyl olefin **3.33** in the

presence of monodentate or phenoxy-bidentate NHC–Cu complex is moderate (**3.42**:**3.43** = 37:63 for **A.10** and 35:65 for **A.2**). With a sulfonate salt **A.3**, reaction takes place with minimal selectivity (**3.42**:**3.43** = 52:48), with relatively high enantioselectivity for geminal borosilane **3.43** (87.5:12.5 e.r.). Interestingly, slightly modified sulfonate salts **A.6** and **A.8** promote Cu–B additions, providing 1,1-silylborane **3.43** predominantly (92% and 90% respectively). Moreover, Cu–NHC complexes generated from imidazolinium salts **A.6** and **A.8** deliver products with higher enantioselectivities (95:5–98:2 e.r.). Since we obtained high efficiency and selectivity for the reaction of alkyl-bearing alkenylsilane **3.29** with monodentate NHC–Cu derived from **A.14**, we tested the same complex for the reaction of aryl-alkenylsilane **3.33**, unfortunately, delivering a 30:70 mixture of vicinal (**3.42**) and geminal borosilanes (**3.43**) with low enantioselectivity (63:37 e.r.).

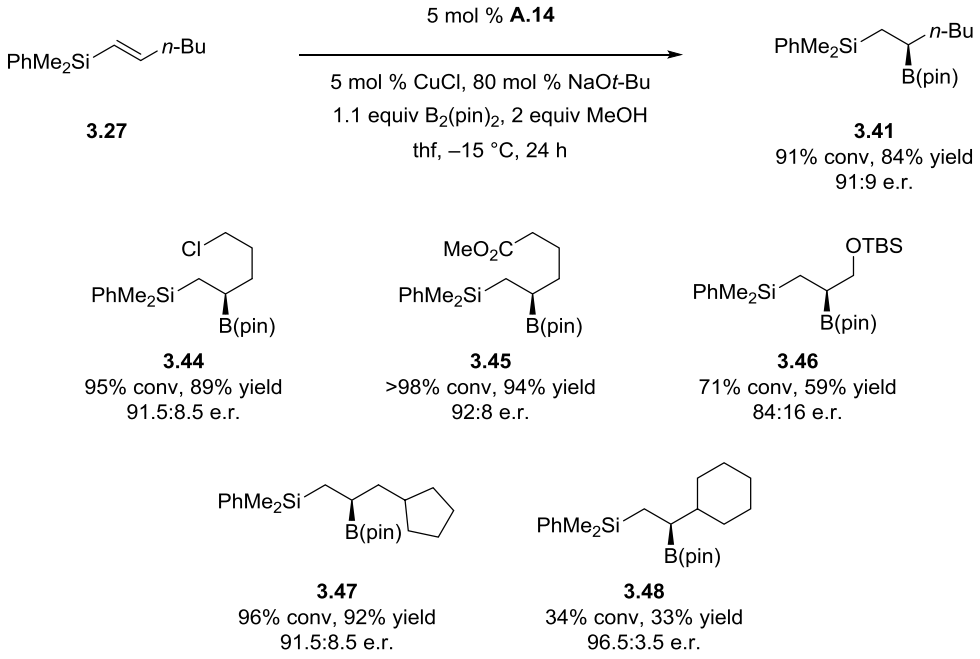
***Scheme 3.9.*** Evaluation of Chiral NHC–Cu Complexes for Aryl-Substituted Alkenylsilane



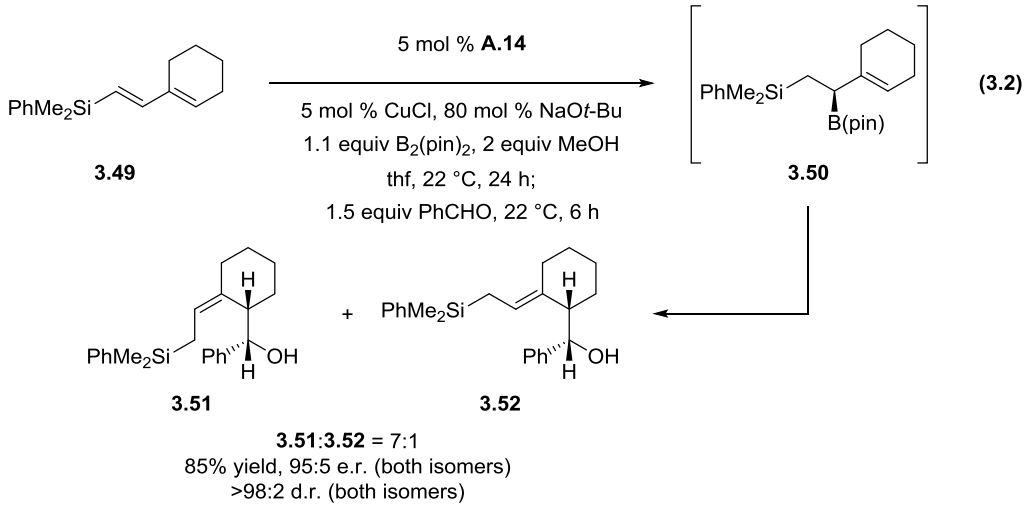
### *3.4.2. NHC–Cu-Catalyzed Enantioselective Protoborations of Alkyl- and Alkenyl-Substituted Alkenylsilanes*

With the optimal NHC–Cu complex, which is derived from chiral imidazolinium **A.14**, for enantioselective protoboration of alkyl-substituted alkenylsilanes in hand, we performed reactions of alkenylsilanes containing an alkyl group at –15 ˚C to achieve the maximum enantioselectivity (91:9 e.r. for **3.41** vs 87:13 e.r. at 22 ˚C; Scheme 3.8). Chlorine- or methyl ester-bearing substrates are converted to vicinal borosilane efficiently and enantioselectively (89–95% yield and 91.5:8.5 to 92:8 e.r. for **3.44** and **3.45**). When silyl ether-containing alkenylsilane is used, however, desired product **3.46** is obtained in only 59% yield and 84:16 e.r., probably due to the sterics of bulky TBS group. We also observe low efficiency for cyclohexyl-containing substrate (33% yield for **3.48**), which has $\alpha$-branched alkyl group causing steric repulsion with the sizeable B(pin) unit.

***Scheme 3.10.*** Enantioselective Protoboration of Alkyl-Substituted Alkenylsilanes



In addition to alkyl-bearing substrates, catalytic protoboration of alkene-substituted alkenylsilane **3.49** is performed with 5 mol % **A.14** and CuCl. NHC–Cu-catalyzed copper–boron addition/protonation of silyl-diene **3.49** followed by treatment with excess amount of benzaldehyde affords a 7:1 mixture of trisubstituted allylsilanes **3.51** and **3.52** (85% combined overall yield, 95:5 e.r. and >98:2 e.r. for both isomers; eq 3.2). Based on isolated products **3.51** and **3.52**, we suggest that the transformation proceeds through the intermediate **3.50**, which has C–B bond at the carbon carrying an alkene. This indicates that initial C–Cu bond formation happens at the carbon bearing the silicon group although alkene might be able to stabilize C–Cu bond as well. Thus, in contrast to an aryl group, an alkenyl substituent does not compete with a silyl group.

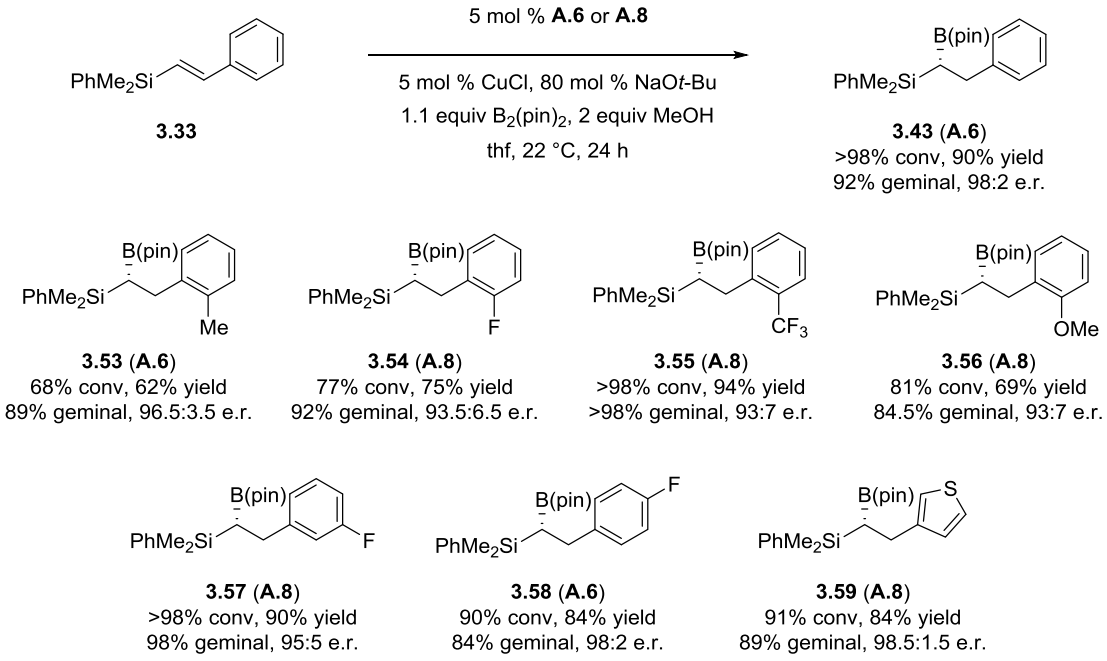



### *3.4.3. NHC–Cu-Catalyzed Enantioselective Protoborations of Aryl-Substituted Alkenylsilanes*

As illustrated in Scheme 3.11, NHC–Cu-catalyzed enantioselective protoborations of aryl- and heteroaryl-containing alkenylsilanes with sulfonate salt **A.6** or **A.8** provide geminal borosilanes preferentially (up to >98%) with high enantioselectivities at 22 ˚C

(93:7–98.5:1.5 e.r.). For these substrates, lowering of reaction temperature does not enhance enantioselectivities. Although enantioselectivities for aryl- or heteroaryl-containing substrates is relatively higher than those for alkyl,silyl-olefins (84:16–96.5:3.5 e.r.), site selectivities are not exclusive (84.5–>98%). Since both aryl and silyl group can stabilize the incipient C–Cu bond, they compete with each other, which lowers the site selectivity. Consistent with the above rationale, reaction of substrates with aryl units that carry an electron-withdrawing group such as trifluoromethyl unit leads to higher degree of site selectivity (>98% geminal for **3.55**). In contrast, when we utilize electron-donating, MeO-substituted phenyl-alkenylsilane, site selectivity is reduced (84.5% geminal for **3.56**).

***Scheme 3.11.*** Enantioselective Protoboration of Aryl-Substituted Alkenylsilanes




**3.33**

**3.43** (**A.6**)
>98% conv, 90% yield
92% geminal, 98:2 e.r.

**3.53** (**A.6**)
68% conv, 62% yield
89% geminal, 96.5:3.5 e.r.

**3.54** (**A.8**)
77% conv, 75% yield
92% geminal, 93.5:6.5 e.r.

**3.55** (**A.8**)
>98% conv, 94% yield
>98% geminal, 93:7 e.r.

**3.56** (**A.8**)
81% conv, 69% yield
84.5% geminal, 93:7 e.r.

**3.57** (**A.8**)
>98% conv, 90% yield
98% geminal, 95:5 e.r.

**3.58** (**A.6**)
90% conv, 84% yield
84% geminal, 98:2 e.r.

**3.59** (**A.8**)
91% conv, 84% yield
89% geminal, 98.5:1.5 e.r.

### *3.4.4. Functionalization and Utility in Chemical Synthesis*

To show the utility of the aforementioned protocol, we examined other methods to prepare borosilanes selectively. Vicinal borosilanes that carry an alkyl group can be synthesized by the Cu-catalyzed protocol detailed above efficiently and selectively. When we use common hydroboration methods, however, a mixture of geminal and vicinal isomers are generated; reaction of **3.29** with $BH_3$·thf at 22 ˚C in three hours or with 9-BBN at 60 ˚C in two hours proceeds to a 1:1 or 2:1 mixture of geminal:vicinal borosilanes, respectively. Thus, the site selectivity of Cu-catalyzed protoboration is unique and can be used to prepare silylboranes that cannot be prepared efficiently or selectively through the use of traditional methods. Furthermore, when phenyl-bearing alkenylsilane **3.33** is subjected to the hydroboration reaction under the same conditions, we obtain a 4:1 mixture of the two isomers ($BH_3$·thf at 22 ˚C) or recovered starting material completely (<2% conv with 9-BBN). To further demonstrate the utility of the Cu-catalyzed method, we have examined the possibility of applying sequential NHC–Cu-catalyzed protosilylation/protoboration transformations towards enantioselective formal synthesis of bruguierol A. Bruguierols A–C[24] are members of a family of natural products which have activity against both Gram-positive and Gram-negative bacteria, and were isolated in 2005 from the stem of the *Bruguiera gymmorrhiza* tree.[25]

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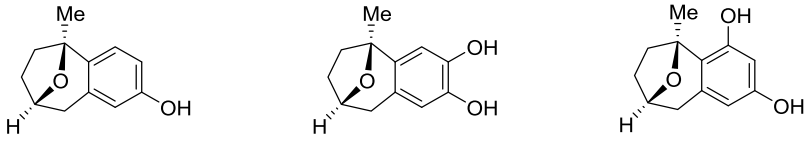
(24) For previous enantioselective synthesis of bruguierols, see: (a) Ramana, C. V.; Salian, S. R.; Gonnade, R. G. *Eur. J. Org. Chem.* **2007**, 5483–5486. (b) Solorio, D. M.; Jennings, M. P. *J. Org. Chem.* **2007**, *72*, 6621–6623. (c) Fananás, F. J.; Fernández, A.; Cevic, D.; Rodríguez, F. *J. Org. Chem.* **2009**, *74*, 932–934.
(25) Han, L.; Huang, X.; Sattler, I.; Moellmann, U.; Fu, H.; Lin, W. Grabley, S. *Planta Med.* **2005**, *71*, 160–164.

***Figure 3.1.*** Antibacterial Natural Products Bruguierol A–C



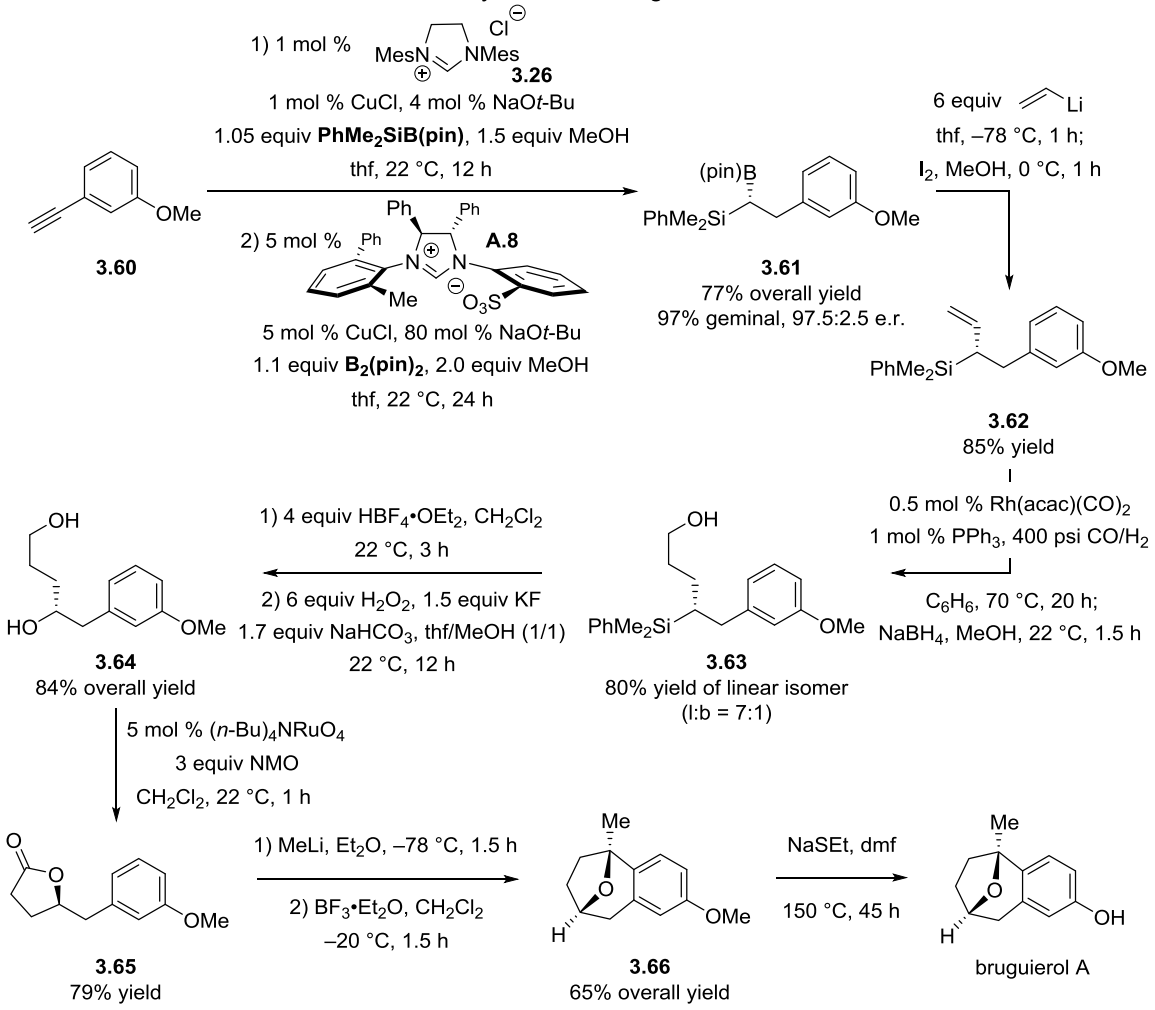

Our synthetic route for enantioselective preparation of bruguierol A is depicted in Scheme 3.12. Site-selective NHC–Cu-catalyzed protosilylation of *m*-MeO-phenylacetylene **3.60**, followed by site- and enantioselective NHC–Cu-catalyzed protoboration of the resulting alkenylsilane proceeds to the formation of geminal borosilane **3.61** in 77% overall yield (two steps), 97% site selectivity and 97.5:2.5 e.r. Then, selective functionalization of the C–B bond over the C–Si bond is examined. An efficient protocol for conversion of geminal borosilanes to synthetically useful allylsilanes[26] was reported by Aggarwal and coworkers.[27] Enantiomerically enriched allylsilane **3.62** is synthesized in 85% yield by the use of Aggarwal's procedure. Linear-selective Rh-catalyzed hydroformylation[28] of terminal alkene followed by $NaBH_4$-reduction delivers primary alcohol as a 7:1 mixture of linear and branched isomers. Pure linear product **3.63** is isolated in 80% yield by column chromatography. Next, Fleming–Tamao oxidation of C–Si bond[29] is performed based on a reported procedure,[30] which

(26) For reviews on the utility of allylsilanes in organic synthesis, see: (a) Masse, C. E.; Panek, J. C. *Chem. Rev.* **1995**, *95*, 1293–1316. (b) Barbero, A.; Pulido, F. J. *Acc. Chem. Res.* **2004**, *37*, 817–825. (c) Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, 3173–3199.
(27) (a) Ref 6e. For other relevant procedures, see: (b) Tsai, D. J. S.; Matteson, D. S. *Organometallics* **1983**, *2*, 236–241. (c) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron Lett.* **2005**, *46*, 8981–8985.
(28) For representative reviews on catalytic hydroformylation reactions, see: (a) Ojima, I.; Tsai, C.-Y.; Tzamarioudaki, M.; Bonafoux D. in *Organic Reactions, Vol. 50* (Ed.: Overman, L. E.), Wiley, New York, **2000**, pp. 1–354. (b) Diéguez, M.; Pàmies, O.; Claver, C. *Tetrahedron:Asymmetry* **2004**, *15*, 2113–2122. (c) Klozin, J.; Landis, C. R. *Acc. Chem. Res.* **2007**, *40*, 1251–1259. (d) Gual, A.; Godard, C.; Castillón, S.; Claver, C. *Tetrahedron:Asymmetry* **2010**, *21*, 1135–1146.
(29) For a review on oxidation of C–Si bonds, see: Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.
(30) (a) Krohn, K.; Khanbabaee, K. *Liebigs Ann. Chem.* **1994**, 1109–1112. (b) Krohn, K.; Khanbabaee, K. *Liebigs Ann. Chem.* **1995**, 1529–1537.

affords diol **3.64** efficiently (84% overall yield). Ru-catalyzed oxidative cyclization[31] of diol delivers lactone **3.65** in 79% yield. To construct tricyclic core structure, methyl addition to lactone followed by cyclization is performed, which leads to the desired product **3.66** in 65% overall yield. Transformation of tricycle **3.66** to the natural product is previously reported.[32] Although the synthetic route illustrated in Scheme 3.12 has a slightly longer sequence than a previously reported approach,[18c] there are several advantages compare to other methods. Our sequence is the first catalytic enantioselective approach for introducing enantiomerically enrichment (vs. the use of chiral pool as the substrate source) and utilizes minimal amount of precious metal (0.5 mol % Rh salt).

(31) For a review on catalytic procedures involving ruthenium oxo complexes, see: (a) Griffith, W. P. *Chem. Soc. Rev.* **1992**, *21*, 179–185. For a review on oxidation reactions catalyzed by tetrapropylammonium perruthenate, see: (b) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639–666.
(32) Hu, B.; Xing, S.; Ren, J.; Wang, Z. *Tetrahedron* **2010**, *66*, 5671–5674.

***Scheme 3.12.*** Enantioselective Formal Synthesis of Bruguierol A



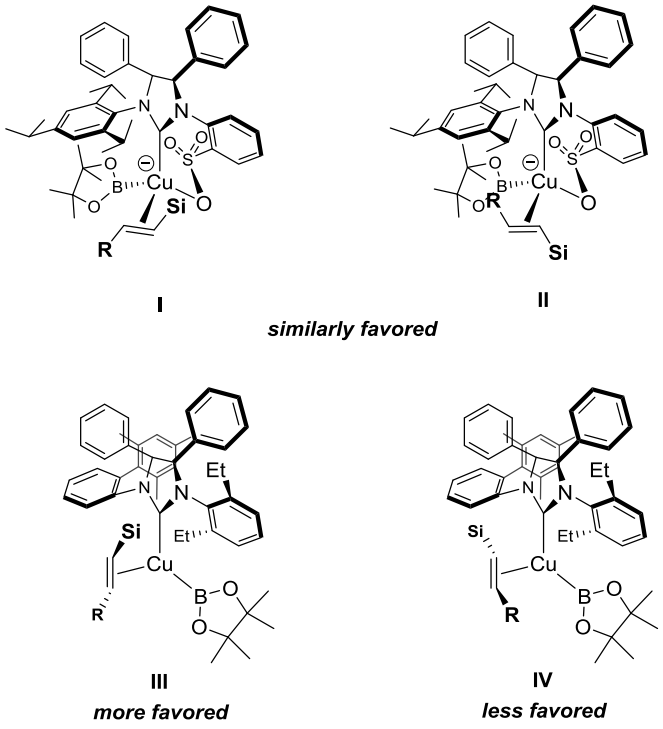

### *3.4.5. Stereochemical Models to Account for Levels and Trends in Site- and Enantioselectivity*

We built up the stereochemical models[33] in order to rationalize the levels and trends in site- and enantioselectivity for Cu-catalyzed protoborations of alkenylsilanes. As illustrated in Scheme 3.13 and 3.14, we propose that the association of alkenylsilane

(33) The stereochemical models represented for the chiral NHC–Cu complexes are based on the strong structural preferences indicated by spectroscopic as well as crystallographic data available for sulfonate-bridged bidentate and monodentate complexes and/or ligands. For sulfonate-bridged bidentate complex, see: (a) Lee, Y.; Li, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 11625–11633. For monodentate complex, see: (b) Lee, K-s.; Hoveyda, A. H. *J. Org. Chem.* **2009**, *74*, 4455–4462. (c) Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332–3335.

with the chiral cuprate occurs through the manner in mode I, II, V, and VI. Because of the *syn*-orientation for the sulfonate bridge and the phenyl unit of the NHC backbone, a relatively spacious binding pocket might be generated, which allows the sterically demanding, silyl group-bearing olefin substrate to be accommodated, as shown in modes I, II, V, and VI. For alkyl-substituted substrates, regardless of NHC–Cu complex used (either monodentate or bidentate), we obtain complete site selectivity (>98% vicinal) for all the cases because of stabilization of C–Cu bond by silicon unit. As illustrated in Scheme 3.8, with the monodentate NHC–Cu complex derived from **A.14**, maximum enantioselectivity was achieved (87:13 e.r.). We believe that the major enantiomer of product is generated preferentially through mode III since there is a significant energetic difference between modes III and IV, which arises from the severe steric repulsion between sizeable dimethylphenylsilyl group and phenyl group on NHC backbone in mode IV (Scheme 3.13). In contrast, when sulfonate-containing bidentate complex was used (**A.3**, **A.6**, or **A.8**), two possible modes I and II seem to be similarly preferred because similar unfavorable steric interactions are present in both modes I and II (Scheme 3.13). Thus, we obtain moderate enantioselectivities (34.5:65.5–60:40 e.r.) Moreover, with sterically demanding *ortho*-substituent, *i*-propyl-containing complex (**A.6**), reactivity of the reaction suffered due to these steric interactions (53% conv; Scheme 3.8), supporting the above contention.

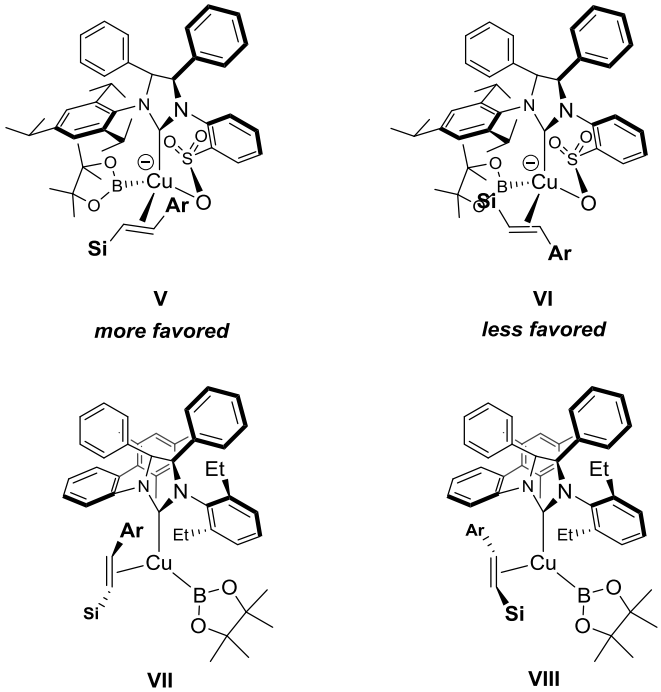
***Scheme 3.13.*** Stereochemical Models for Alkyl-Substituted Alkenylsilanes




In the case of aryl-bearing alkenylsilanes, on the other hand, since either the silyl or the aryl group can control site selectivity, only certain sulfonate-bridged bidentate NHC–Cu complexes deliver the geminal borosilanes with a relatively strong preference (Scheme 3.9). In catalytic protoborations of aryl-substituted alkenylsilanes, copper–boron addition can occur via modes V or VI (Scheme 3.14). The steric repulsion between the *ortho*-substituent of *N*-Ar moiety and sizeable dimethylphenylsilyl group in mode VI is severe, making mode VI less favorable than mode V. Based on this model, lower enantioselectivity obtained with **A.3** (*o*-methyl) than with **A.6** (*o*-isopropyl) can be explained (87.5:12.5 e.r. with **A.3** vs 98:2 e.r. with **A.6**; Scheme 3.9). Significant energetic difference between III and IV is mainly due to the steric repulsion of backbone phenyl group with the large dimethylphenylsilyl unit in mode IV. In modes VII and VIII, however, the preference for VII is minimized because the aforementioned steric repulsion

is less severe with relatively smaller aryl group of substrate (vs dimethylphenylsilyl unit). Thus, with monodentate NHC–Cu complexes, we obtained borosilane products of low enantiomeric purity.

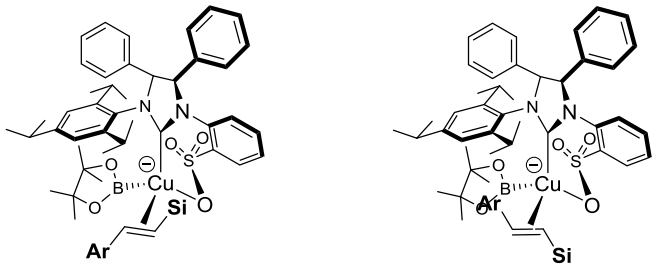
***Scheme 3.14.*** Stereochemical Models for Aryl-Substituted Alkenylsilanes




For aryl-bearing alkenylsilane substrates, there is an additional site selectivity issue. Since either the silyl or the aryl group can serve to stabilize the C–Cu bond, when monodentate salts **A.10** and **A.14** are used, we obtain moderate site selectivities (63–70% geminal; Scheme 3.9). With bidentate sulfonate-containing NHC–Cu complex derived from **A.3**, almost equal amount of the two isomers is obtained (52:48 vicinal:geminal; Scheme 3.9). The sterically more demanding 2,4,6-triisopropyl- (**A.6**) or 2-methyl-6-phenyl- (**A.8**) substituted bidentate salt promotes reaction of silyl-bearing styrene with high level of site selectivity (92% and 90% geminal, respectively). To explain these observations, we introduce additional stereochemical models, which can generate vicinal

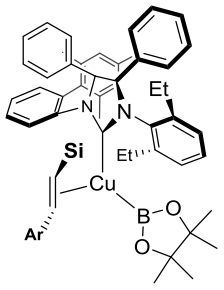
borosilane products (Scheme 3.15). Because of severe steric interactions between *ortho*-substituent on *N*-Ar and either the large silyl group (mode IX) or the aryl unit (mode X), with **A.6** or **A.8**, mode V might be the most favorable, affording geminal product with high site selectivity. When sulfonate salt **A.3** is utilized as an NHC precursor, the smaller *ortho* methyl substituent does not present the same degree of steric hindrance as is observed with **A.6** or **A.8** and site selectivity suffers (modes IX and X become more competitive). In cases of monodentate NHC–Cu complexes, the size difference between the aryl and the silyl groups is not large enough (compare to that between the alkyl and the silyl units), the alternative pathway via mode XI would be similarly preferred, which leads to low site selectivity.

***Scheme 3.15.*** Rationale for High Site Selectivity in Reactions of Aryl-Substituted Alkenylsilanes




**IX** **X**

***less favored than V***




**XI**

***similarly favored as VII or VIII: low site selectivity***

### *3.5. Conclusions*

We have developed efficient and selective NHC–Cu-catalyzed protosilyl addition to various terminal alkynes to afford (*E*)-*β*-alkenylsilanes with an exceptional selectivity (>98% *E* and *β*). A number of functional group-bearing alkyl-, aryl-, and heteroaryl-substituted alkenylsilanes are prepared in up to 97% yield. Site- and enantioselective protoboryl addition to alkenylsilanes promoted by chiral NHC–Cu complexes are illustrated as well. With chiral monodentate NHC–Cu complex, alkyl- or alkenyl-substituted alkenylsilanes are converted to corresponding vicinal borosilanes with high enantioselectivity (84:16–96.5:3.5 e.r.). In contrast, protoborations of aryl-bearing alkenylsilanes generate geminal borosilanes predominantly (84–>98% geminal) in the presence of bidentate sulfonate-bridged NHC–Cu complex with high enantioselectivity (93:7–98:2 e.r.). Since C–Si bond is more robust, C–B bond can be converted to C–H, C–C, C–O or C–N bonds by well-established procedures, then C–Si bond also might be converted to C–H, C–C, of C–O bonds. By use of this strategy, we illustrate the enantioselective formal synthesis of natural product bruguierol A from enantiomerically enriched geminal borosilane, which is prepared by Cu-catalytic process. Furthermore, we propose plausible stereochemical models to account for site- and/or enantioselectivities with two different types of NHC–Cu complexes.

### *3.6. Experimentals*

**General.** Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, $\lambda_{max}$ in $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). $^{1}H$ NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, app = apparent), and coupling constant (Hz). $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Enantiomeric ratios were determined by high-performance liquid chromatography (HPLC) with a Shimadzu chromatograph (Chiral Technologies Chiralpak AD-H (4.6 x 250 mm), Chiralcel OD-H (4.6 x 250 mm), Chiralcel OJ-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Optical rotations were measured on a Rudolph Research Analytical Autopol IV Polarimeter. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry $N_2$ in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; $CH_2Cl_2$ and $Et_2O$ were purged with Ar and purified by passage

through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. Methanol (Aldrich Chemical Co.) was distilled over $CaH_2$. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific, Inc.) in air.

### *3.6.1. Reagents and Ligands*

**Aryl-substituted terminal alkynes:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

**Benzaldehyde:** purchased from Aldrich Chemical Co. and purified by bulb to bulb distillation prior to use.

**Bis(pinacolato)diboron:** purchased from Frontier Scientific, Inc. and recrystallized from pentane.

**1,3-Bis-(2,4,6-trimethylphenyl)imidazolinium chloride (3.26):** purchased from Aldrich Chemical Co. and used as received.

**Boron trifluoride diethyl etherate:** purchased from Aldrich Chemical Co. and used as received.

***n*-Butyllithium, 15% in hexane (1.6 M):** purchased from Strem Chemicals Inc. and titrated prior to use.

**Copper (I) chloride:** purchased from Strem Chemicals Inc. and used as received.

**Dicarbonylacetylacetonato rhodium(I):** purchased from Strem Chemicals Inc. and used as received.

**Dimethyl(phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)silane:** prepared according to previously reported procedure.[34]

**Hex-1-yne (3.25):** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

**Hydrogen peroxide solution (35 wt. % in $H_2O$):** purchased from Aldrich Chemical Co. and used as received.

**Imidazolinium salt A.2,[35] A.3,[30] A.6,[36] A.8,[37] A.10,[38] and A.13[39]:** prepared according to previously reported procedures.

**Methyllithium, 1.6 M solution in diethyl ether:** purchased from Acros Organics Co. and titrated prior to use.

**4-Methylmorpholine *N*-oxide:** purchased from Aldrich Chemical Co. and used as received.

**Potassium fluoride:** purchased from Aldrich Chemical Co. and used as received.

**Prop-2-yn-1-ol:** purchased from Aldrich Chemical Co. and purified by distillation over $CaH_2$ prior to use.

**Sodium borohydride:** purchased from Aldrich Chemical Co. and used as received.

**Sodium *tert*-butoxide** (98%)**:** purchased from Strem Chemicals Inc. and used as received.

**Sodium perborate:** purchased from Aldrich Chemical Co. and used as received.

**Sodium thiosulfide:** purchased from Aldrich Chemical Co. and used as received.

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(35) Lee, K-s.; Brown, M. K.; Hird, A. W.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2006**, *128*, 7182–7184.
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(38) (a) Chaulagain, M. R.; Sormunen, G. J.; Montgomery, J. *J. Am. Chem. Soc.* **2007**, *129*, 9568–9569. (b) Lillo, V.; Prieto, A.; Bonet, A.; Diaz-Requejo, M. M.; Ramirez, J.; Perez, P. J.; Fernandez, E. *Organometallics* **2009**, *28*, 659–662.
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**Tetrafluoroboric acid dimethyl ether complex:** purchased from Aldrich Chemical Co. and used as received.

**Tetrapropylammonium perruthenate:** purchased from TCI Chemical Co. and used as received.

**Tetravinyltin:** purchased from Aldrich Chemical Co. and used as received.

**Triphenylphosphine:** purchased from Aldrich Chemical Co. and used as received.

### *3.6.2. Experimental Procedure and Characterization Data*

■ **Experimental Procedure for Preparation of Borosilane Reagent:** A 100 mL flame-dried Schlenk flask equipped with a magnetic stir bar was charged with Li (4.2 g, 600 mmol, 6.0 equiv.) and mineral oil (20 mL) under argon. The mixture was heated to 180 °C under vigorous stirring. The suspension was allowed to cool to 22 °C. The Li particles were washed with thf (3 × 20 mL). Then, 100 mL of thf was added to the Li particles. To the suspension, chlorodimethylphenylsilane (16.8 mL, 100 mmol, 1.0 equiv.) was added at 0 °C. The resulting suspension was allowed to stir at 0 °C for 6 h. To a stirred solution of pinacolborane (29.0 mL, 200 mmol, 2.0 equiv.) in hexanes (100 mL) in another flame-dried Schlenk flask was added the dimethylphenylsilyllithium solution slowly at 0 °C. The resulting solution was allowed to stir at 22 °C for 12 h. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. To the resulting light yellow oil were added 50 mL of hexanes. After the precipitate was filtered, the filtrate was concentrated *in vacuo*. The resulting light yellow oil (24.5 g, 93.4 mmol, 93% yield) was used directly without any further purification.

■ **Representative Experimental Procedure for Protosilylation of Terminal Alkynes:** In a $N_2$-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolinium salt **3.26** (30.8 mg, 0.0900 mmol, 1.0 mol %), CuCl (9.0 mg, 0.090 mmol, 1.0 mol%), NaO*t*-Bu (34.6 mg, 0.360 mmol, 4.0 mol %) and thf (10 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for two hours. Borosilane (2.478 g, 9.450 mmol, 1.05 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was resealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of $N_2$. Phenylacetylene (988 μL, 9.00 mmol, 1.0 equiv.) and MeOH (547 μL, 12.5 mmol, 1.5 equiv.) were added through syringes. The resulting mixture was allowed to stir at 22 °C for 12 h before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=80:1) to afford the desired product **3.33** as colorless oil (1.988 g, 0.927 mmol, 93% yield).

**(*E*)-Hex-1-en-1-yldimethyl(phenyl)silane (3.27).** The title compound has been previously reported and spectra data match those described.[40] $^1$H NMR (400 MHz, $CDCl_3$): δ 7.54–7.51 (2H, m), 7.37–7.34 (3H, m), 6.12 (1H, dt, *J* = 18.4, 6.4 Hz), 5.75 (1H, dt, *J* = 18.4, 1.6 Hz), 2.15 (2H, tdd, *J* = 6.4, 6.4, 1.6 Hz), 1.44–1.30 (4H, m), 0.91 (3H, t, *J* = 7.6 Hz), 0.32 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 149.6, 139.6, 134.0, 128.9, 127.8, 127.3, 36.7, 31.0, 22.4, 14.1, –2.3.

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**(*E*)-(5-Chloropent-1-en-1-yl)dimethyl(phenyl)silane (3.28).** The title compound has been previously reported and spectra data match those described.[41] $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.56–7.54 (2H, m), 7.40–7.37 (3H, m), 6.11 (1H, dt, *J* = 18.4, 6.4 Hz), 5.87 (1H, dt, *J* = 18.4, 1.6 Hz), 3.56 (2H, t, *J* = 6.8 Hz), 2.34 (2H, tdd, *J* = 6.8, 6.8, 1.6 Hz), 1.93 (2H, tt, *J* = 6.8, 6.8 Hz), 0.37 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 147.0, 139.1, 133.9, 129.3, 129.0, 127.9, 44.5, 33.9, 31.6, –2.4.

**(*E*)-Methyl 6-(dimethyl(phenyl)silyl)hex-5-enoate (3.29).** IR (neat): 3069 (w), 2952 (m), 1738 (s), 1616 (m), 1428 (m), 1364 (w), 1316 (w), 1247 (s), 1203 (m), 1172 (m), 1141 (m), 1112 (m), 1078 (w), 989 (m), 837 (s), 821 (s), 784 (m), 730 (s), 699 (s), 638 (w), 470 (m) $cm^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.52–7.50 (2H, m), 7.37–7.33 (3H, m), 6.07 (1H, dt, *J* = 18.4, 6.0 Hz), 5.79 (1H, dt, *J* = 18.8, 1.2 Hz), 3.67 (3H, s), 2.32 (2H, t, *J* = 7.6 Hz), 2.19 (2H, tdd, *J* = 7.6, 7.6, 1.6 Hz), 1.76 (2H, tt, *J* = 7.6, 7.6 Hz), 0.31 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.2, 147.8, 139.2, 133.9, 129.0, 128.8, 127.9, 51.7, 36.1, 33.6, 23.9, –2.4; HRMS ($ESI^+$): Calcd for $C_{15}H_{23}O_2Si_1$ $[M+H]^+$: 263.1467; Found: 263.1469.

**(*E*)-*tert*-Butyl((3-(dimethyl(phenyl)silyl)allyl)oxy)dimethylsilane (3.30).** IR (neat): 2955 (w), 2929 (w), 2894 (w), 2856 (w), 1471 (w), 1428 (w), 1361 (w), 1249 (m), 1195 (w), 1113 (m), 1097 (m), 1049 (w), 987 (w), 939 (w), 909 (w), 857 (m), 832 (s), 774 (s), 728 (s), 697 (s), 666 (m), 522 (m), 469 (m) $cm^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (2H, m), 7.36–7.33 (3H, m), 6.17 (1H, dt, *J* = 18.8, 4.0 Hz), 6.04 (1H, dt, *J* = 18.4, 1.6 Hz), 4.23 (2H, dd, *J* = 4.0, 1.6 Hz), 0.92 (9H, s), 0.34 (6H, s), 0.07 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 147.3, 139.0, 134.0, 129.0, 127.9, 126.0, 65.9, 26.1, 18.6, –2.4, –5.0; HRMS ($ESI^+$): Calcd for $C_{17}H_{34}N_1O_1Si_2$ $[M+NH_4]^+$: 324.2179; Found: 324.2181.

(41) Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2004**, *126*, 11146–11147.

**(*E*)-(3-Cyclopentylprop-1-en-1-yl)dimethyl(phenyl)silane (3.31).** IR (neat): 3068 (w), 3050 (w), 2950 (m), 2866 (m), 1615 (m), 1451 (w), 1427 (m), 1313 (w), 1247 (m), 1112 (m), 990 (m), 926 (w), 880 (w), 816 (s), 780 (s), 727 (s), 697 (s), 638 (m), 469 (m), 417 (m) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.55–7.51 (2H, m), 7.37–7.34 (3H, m), 6.12 (1H, dt, *J* = 18.4, 6.4 Hz), 5.75 (1H, dt, *J* = 18.8, 1.6 Hz), 2.17 (2H, dt, *J* = 6.4, 1.6 Hz), 1.91 (1H, septet, *J* = 7.6 Hz), 1.78–1.71 (2H, m), 1.63–1.49 (4H, m), 1.19–1.10 (2H, m), 0.32 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 149.0, 139.6, 134.0, 128.9, 128.0, 127.8, 43.6, 39.5, 32.4, 25.3, –2.2; HRMS ($ESI^+$): Calcd for $C_{16}H_{28}N_1Si_1$ $[M+NH_4]^+$: 262.1991; Found: 262.1985.

**(*E*)-(2-Cyclohexylvinyl)dimethyl(phenyl)silane (3.32).** The title compound has been previously reported and spectra data match those described.[36] $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (2H, m), 7.43–7.40 (3H, m), 6.17 (1H, dd, *J* = 18.8, 6.0 Hz), 5.80 (1H, dd, *J* = 18.8, 1.6 Hz), 2.16–2.07 (1H, m), 1.86–1.79 (4H, m), 1.76–1.71 (1H, m), 1.38–1.16 (5H, m), 0.40 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 155.0, 139.7, 134.0, 128.9, 127.8, 124.0, 44.2, 32.5, 26.4, 26.2, –2.2.

**(*E*)-Dimethyl(phenyl)(styryl)silane (3.33).** IR (neat): 3067 (w), 2995 (w), 2955(w), 1947 (w), 1604 (m), 1427 (m), 1301 (m), 1112 (m), 1027 (w), 989 (m), 827 (s), 726 (s), 688 (s) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.46–7.40 (2H, m), 7.38–7.36 (3H, m), 7.35–7.31 (3H, m), 6.94 (1H, d, *J* = 19.2 Hz), 6.59 (1H, d, *J* = 19.2 Hz), 0.44 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 145.5, 138.7, 138.3, 134.1, 129.2, 128.7, 128.3, 128.0, 127.2, 126.6, –2.4; HRMS ($ESI^+$): Calcd for $C_{16}H_{22}N_1Si_1$ $[M+NH_4]^+$: 256.1521, Found: 256.1519.

**(*E*)-Dimethyl(2-methylstyryl)(phenyl)silane (3.34).** IR (neat): 3067 (w), 3017 (w), 2955 (w), 1597 (w), 1479 (w), 1427 (m), 1288 (m), 1248 (w), 1113 (m), 989 (m), 841 (s), 829 (s), 699 (s), 644 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (2H, m), 7.56–7.54 (1H, m), 7.39–7.37 (3H, m), 7.21 (1H, d, $J$ = 19.2 Hz), 7.19–7.12 (3H, m), 6.50 (1H, d, $J$ = 19.2 Hz), 2.36 (3H, s), 0.45 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 143.3, 138.9, 137.6, 135.5, 134.1, 130.5, 129.2, 129.0, 128.0, 127.9, 126.2, 125.5, 19.7, –2.3; HRMS ($ESI^+$): Calcd for $C_{17}H_{20}Si_1$ $[M]^+$: 252.1334, Found: 252.1338.

**(*E*)-(2-Fluorostyryl)dimethyl(phenyl)silane (3.35).** IR (neat): 3068 (w), 3020 (w), 2957 (w), 1601 (w), 1482 (m), 1456 (m), 1279 (m), 1248 (m), 1150 (m), 1093 (w), 843 (s), 753 (s), 731 (s), 699 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.54 (3H, m), 7.38–7.37 (3H, m), 7.24–7.20 (1H, m), 7.17 (1H, d, $J$ = 19.6 Hz), 7.12–7.09 (1H, m), 7.05–7.01 (1H, m), 6.66 (1H, d, $J$ = 19.2 Hz), 0.45 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 161.7, 138.5, 137.1 (d, $J$ = 4.4 Hz), 134.0, 130.3 (d, $J$ = 3.7 Hz), 129.6, 129.5, 129.3, 128.0, 127.0 (d, $J$ = 3.0 Hz), 124.2 (d, $J$ = 3.0 Hz), 115.9 (d, $J$ = 22.4 Hz), –2.5; HRMS ($ESI^+$): Calcd for $C_{16}H_{21}F_1N_1Si_1$ $[M+NH_4]^+$: 274.1427, Found: 274.1438.

**(*E*)-Dimethyl(phenyl)(2-(trifluoromethyl)styryl)silane (3.36).** IR (neat): 3070 (w), 2958 (w), 1481 (w), 1312 (s), 1250 (m), 1158 (s), 1116 (s), 1037 (m), 831 (s), 764 (s), 730 (m), 698 (m), 655 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.71 (1H, d, $J$ = 7.6 Hz), 7.63 (1H, d, $J$ = 8.0 Hz), 7.59–7.57 (2H, m), 7.51 (1H, t, $J$ = 7.6 Hz), 7.39–7.33 (5H, m), 6.60 (1H, d, $J$ = 19.2 Hz), 0.46 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 140.7 (app. d, $J$ = 2.2 Hz), 138.2, 137.8 (app. d, $J$ = 1.5 Hz), 134.0, 133.0, 131.9, 129.3, 128.1 (q, $J$ = 231.0 Hz), 128.0, 127.7, 127.4, 125.6 (q, $J$ = 5.8 Hz), 123.1, –2.6; HRMS ($ESI^+$): Calcd for $C_{17}H_{17}F_3Si_1$ $[M]^+$: 306.1052, Found: 306.1045.

**(*E*)-(2-Methoxystyryl)dimethyl(phenyl)silane (3.37).** IR (neat): 3068 (w), 2955 (w), 2836 (w), 1597 (m), 1485 (m), 1288 (w), 1243 (s), 1113 (m), 1050 (w), 842 (s), 766 (s), 700 (m), 434 (w) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.60–7.55 (3H, m), 7.41–7.35 (4H, m), 7.25–7.22 (1H, m), 6.92 (1H, t, $J$ = 7.2 Hz), 6.87 (1H, d, $J$ = 8.4 Hz), 6.57 (1H, d, $J$ = 19.2 Hz), 3.85 (3H, s), 0.44 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 156.9, 139.7, 139.2, 134.1, 129.3, 129.1, 127.9, 127.5, 126.5, 120.7, 111.1, 55.6, –2.3; HRMS ($ESI^+$): Calcd for $C_{17}H_{21}O_1Si_1$ $[M+H]^+$: 269.1362, Found: 269.1372.

**(*E*)-(3-Fluorostyryl)dimethyl(phenyl)silane (3.38).** IR (neat): 3068 (w), 2996 (w), 2957 (w), 1609 (w), 1577 (m), 1484 (w), 1249 (s), 1199 (w), 1073 (m), 986 (m), 841 (s), 825 (s), 730 (s), 677 (m) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.40–7.38 (3H, m), 7.32–7.28 (1H, m), 7.21–7.15 (1H, m), 6.96 (1H, td, $J$ = 8.4, 1.6 Hz), 6.90 (1H, d, $J$ = 19.2 Hz), 6.61 (1H, d, $J$ = 19.6 Hz), 0.45 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 162.1(d, $J$ = 260.0 Hz), 144.1 (d, $J$ = 2.2 Hz), 140.7 (d, $J$ = 7.5 Hz), 138.3, 134.1, 130.1 (d, $J$ = 8.2 Hz), 129.3, 129.2, 128.0, 122.6 (d, $J$ = 3.0 Hz), 115.1 (d, $J$ = 21.6 Hz), 112.9 (d, $J$ = 21.6 Hz), –2.5; HRMS ($ESI^+$): Calcd for $C_{16}H_{17}F_1Si_1$ $[M]^+$: 256.1084, Found: 256.1067.

**(*E*)-(4-Fluorostyryl)dimethyl(phenyl)silane (3.39).** IR (neat): 3068 (w), 2957 (w), 1601 (m), 1506 (s), 1427 (w), 1248 (m), 1156 (m), 1114 (m), 987 (m), 841 (s), 821 (s), 732 (m), 699 (m), 471 (w) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.44–7.37 (5H, m), 7.04–7.00 (2H, m), 6.89 (1H, d, $J$ = 19.2 Hz), 6.49 (1H, d, $J$ = 19.2 Hz), 0.44 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 162.8 (d, $J$ = 245.5 Hz), 144.1, 138.6, 134.6 (d, $J$ = 3.7 Hz), 134.0, 129.2, 128.2 (d, $J$ = 7.4 Hz), 128.0, 127.0 (d, $J$ = 2.2 Hz), 115.6 (d, $J$ = 21.6 Hz), –2.4; HRMS ($ESI^+$): Calcd for $C_{16}H_{17}F_1Si_1$ $[M]^+$: 256.1084, Found: 256.1098.

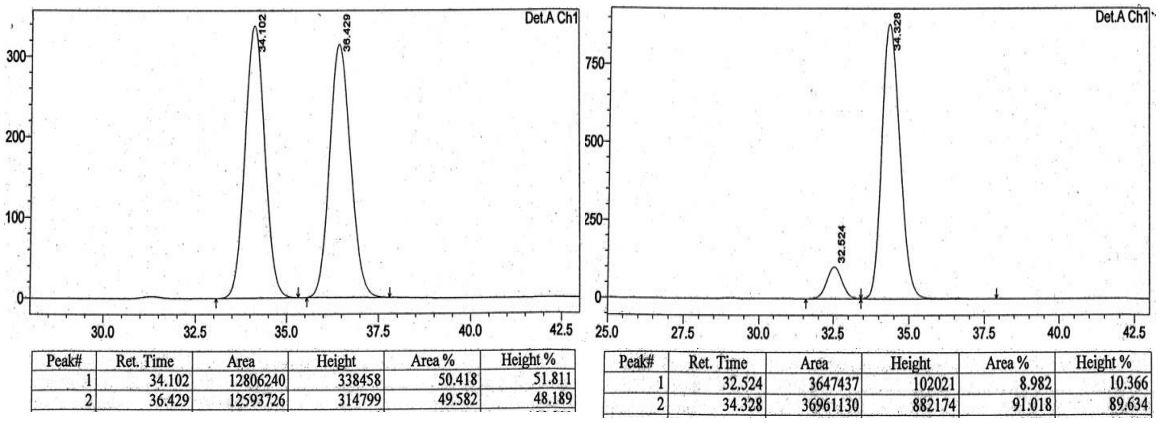
**(*E*)-Dimethyl(phenyl)(2-(thiophen-3-yl)vinyl)silane (3.40).** IR (neat): 3067 (w), 2955 (w), 1601 (m), 1427 (m), 1245 (m), 1198 (w), 1156 (w), 1113 (m), 984 (m), 830 (s), 729 (s), 698 (s), 606 (w) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.38–7.37 (3H, m), 7.30–7.25 (2H, m), 7.22–7.21 (1H, m), 6.94 (1H, d, $J$ = 18.8 Hz), 6.36 (1H, d, $J$ = 19.2 Hz), 0.42 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 142.1, 139.2, 138.7, 134.1, 129.2, 128.0, 126.9, 126.1, 125.1, 123.1, –2.4; HRMS ($ESI^+$): Calcd for $C_{14}H_{17}S_1Si_1$ $[M+H]^+$: 245.0820, Found: 245.0826.

■ **Representative Experimental Procedure for Site- and Enantioselective NHC–Cu-Catalyzed Protoboration of Alkyl-substituted Alkenylsilanes:** In a $N_2$-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolinium salt **A.14** (3.2 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.0050 mmol, 5.0 mol%), NaO*t*-Bu (7.7 mg, 0.0800 mmol, 80.0 mol %) and thf (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for two hours. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The resulting mixture was allowed to stir at 22 °C for 30 min under an atmosphere of $N_2$. At this time, the mixture was allowed to cool to –78 °C (dry ice/acetone bath) and a solution of (*E*)-hex-1-en-1-yldimethyl(phenyl)silane **3.27** (21.8 mg, 0.100 mmol, 1.0 equiv.) in thf (0.2 mL) followed by MeOH (8.2 μL, 0.200 mmol, 2.0 equiv.) were added through a syringe. The vial was placed in a –15 °C cryocool. After 24 h, the solution was

allowed to cool to –78 °C and the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=50:1) to afford the desired product **3.41** as colorless oil (29.1 mg, 0.0840 mmol, 84% yield).

**(*R*)-Dimethyl(phenyl)(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)silane (3.41).** IR (neat): 2977 (w), 2956 (w), 2925 (w), 2857 (w), 1377 (m), 1315 (m), 1247 (m), 1143 (s), 1112 (m), 968 (w), 829 (s), 727 (s), 699 (s), 468 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.55–7.52 (2H, m), 7.35–7.32 (3H, m), 1.43–1.33 (1H, m), 1.29–1.22 (5H, m), 1.21 (12H, s), 1.08–1.06 (1H, m), 1.05–0.97 (1H, m), 0.85 (3H, t, $J$ = 6.8 Hz), 0.76 (1H, dd, $J$ = 14.4, 5.2 Hz), 0.28 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 140.3, 133.8, 128.7, 127.7, 82.9, 34.7, 31.3, 25.0, 24.9, 23.0, 16.7, 14.2, –2.1, –2.3; HRMS ($ESI^+$): Calcd for $C_{20}H_{39}B_1N_1O_2Si_1$ $[M+NH_4]^+$: 364.2843; Found: 364.2860. Specific Rotation: $[\alpha]_D^{20}$ –7.61 (*c* 1.96, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borosilane product with $NaBO_3$•$4H_2O$ (Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 34.102 | 12806240 | 338458 | 50.418 | 51.811 |
| 2 | 36.429 | 12593726 | 314799 | 49.582 | 48.189 |

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 32.524 | 3647437 | 102021 | 8.982 | 10.366 |
| 2 | 34.328 | 36961130 | 882174 | 91.018 | 89.634 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 34.102 | 50.418 | 1 | 32.524 | 8.982 |
| 2 | 36.429 | 49.582 | 2 | 34.328 | 91.018 |

**(*R*)-Hexane-1,2-diol** (Synthesized by oxidation of **3.41** with $NaBO_3$•$4H_2O$ followed by another oxidation with KBr, $AcO_2H$ and NaOAc.[42] The title compound has been previously reported and spectra data match those described).[43] $^1$H NMR (400 MHz, $CDCl_3$): δ 3.73–3.69 (1H, m), 3.66 (1H, dd, *J* = 10.8, 3.2 Hz), 3.44 (1H, dd, *J* = 11.2, 7.6 Hz), 2.01 (2H, br s), 1.47–1.25 (6H, m), 0.91 (3H, t, *J* = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 72.5, 67.0, 33.1, 27.8, 22.9, 14.1; Specific Rotation: $[\alpha]_D^{20}$ +4.51 (*c* 1.25, EtOH) for an enantiomerically enriched sample of 91:9 e.r.

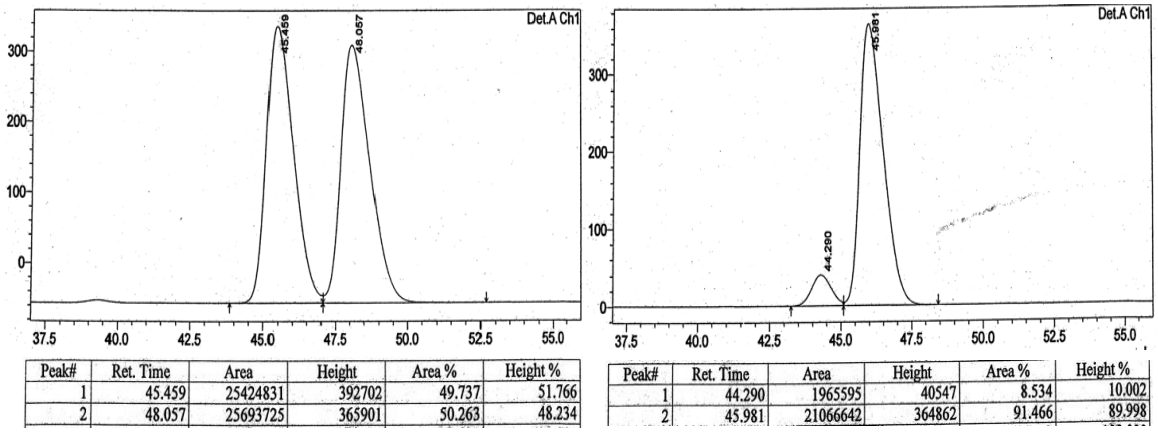
**Proof of Stereochemistry:** Literature value ($[\alpha]_D^{20}$ +14.8 (*c* = 0.76, EtOH), 98:2 e.r.) is assigned to the (*R*) enantiomer.[38c]

**(*R*)-(5-Chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)dimethyl(phenyl)silane (3.44).** IR (neat): 2977 (w), 1379 (m), 1317 (m), 1247 (m), 1142 (s), 1112 (m), 968 (w), 828 (s), 727 (s), 699 (s), 468 (w) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.54–7.51 (2H, m), 7.36–7.33 (3H, m), 3.43 (2H, t, *J* = 6.8 Hz), 1.78–

(42) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229–4232.
(43) (a) Hasegawa, J.; Ogura, M.; Tsuda, S.; Maemoto, S.-i.; Kutsuki, H.; Ohashi, T. *Agric. Biol. Chem.* **1990**, *54*, 1819–1827. (b) Brown, S. P.; Brochu, M. P.; Sinz, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 10808–10809. (c) Notte, G. T.; Sammakia, T.; Steel, P. J. *J. Am. Chem. Soc.* **2005**, *127*, 13502–13503.

1.69 (2H, m), 1.54–1.45 (2H, m), 1.21 (12H, s), 1.11–1.00 (2H, m), 0.73 (1H, dd, $J$ = 14.4, 5.2 Hz), 0.29 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 139.9, 133.8, 128.9, 127.8, 83.2, 45.3, 32.1, 25.0, 24.9, 16.7, –2.1, –2.4; HRMS ($ESI^+$): Calcd for $C_{19}H_{36}B_1Cl_1N_1O_2Si_1$ $[M+NH_4]^+$: 384.2297; Found: 384.2313. Specific Rotation: $([\alpha]_D^{20}$ –4.64 (*c* 2.43, $CHCl_3$) for an enantiomerically enriched sample of 91.5:8.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borylsilane product with $NaBO_3$•$4H_2O$ (Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 45.459 | 25424831 | 392702 | 49.737 | 51.766 |
| 2 | 48.057 | 25693725 | 365901 | 50.263 | 48.234 |

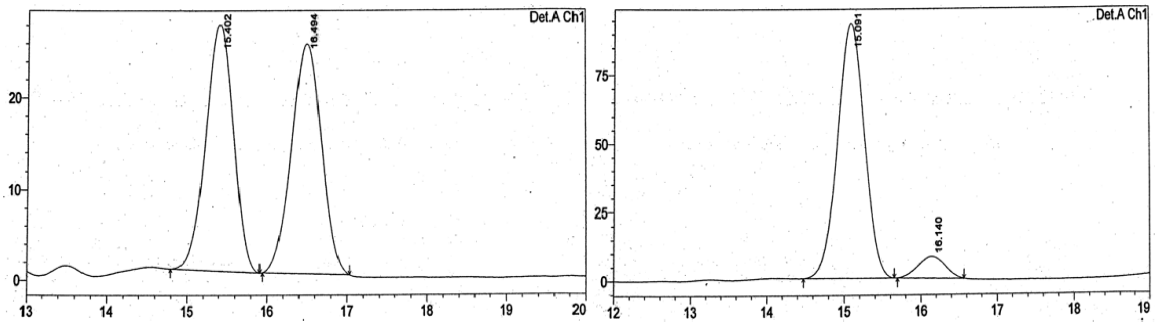
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 44.290 | 1965595 | 40547 | 8.534 | 10.002 |
| 2 | 45.981 | 21066642 | 364862 | 91.466 | 89.998 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 45.459 | 49.737 | 1 | 44.290 | 8.534 |
| 2 | 48.057 | 50.263 | 2 | 45.981 | 91.466 |

**(*R*)-Methyl 6-(dimethyl(phenyl)silyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate (3.45).** IR (neat): 2977 (w), 2951 (w), 1739 (s), 1427 (w), 1379 (m), 1371 (m), 1317 (m), 1247 (m), 1212 (m), 1166 (m), 1142 (s), 1112 (m), 970 (w), 829 (s), 728 (m), 700 (m), 469 (w) $cm^{-1}$; $^1$H NMR (400MHz, $CDCl_3$): δ 7.52–7.50 (2H, m), 7.33–7.32 (3H, m), 3.64 (3H, s), 2.21 (2H, t, $J$ = 7.6 Hz), 1.60–1.56 (2H, m), 1.44–1.24 (2H, m), 1.19 (12H, s), 1.08–0.97 (2H, m), 0.73 (1H, dd, $J$ = 14.4, 5.2 Hz),

0.27 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.3, 140.0, 133.8, 128.8, 127.8, 83.1, 51.5, 34.4, 34.3, 25.0, 24.9, 24.3, 16.6, –2.2, –2.4; HRMS ($ESI^+$): Calcd for $C_{21}H_{39}B_1N_1O_4Si_1$ $[M+NH_4]^+$: 408.2741; Found: 408.2747. Optical Rotation: $[\alpha]_D^{20}$ +3.12 (*c* 0.87, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borylsilane product with $NaBO_3$•$4H_2O$ (Chiralcel OJ-H column, 92/8 hexanes/*i*-PrOH, 1.0 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 15.402 | 654186 | 27078 | 49.813 | 51.731 |
| 2 | 16.494 | 659097 | 25266 | 50.187 | 48.269 |

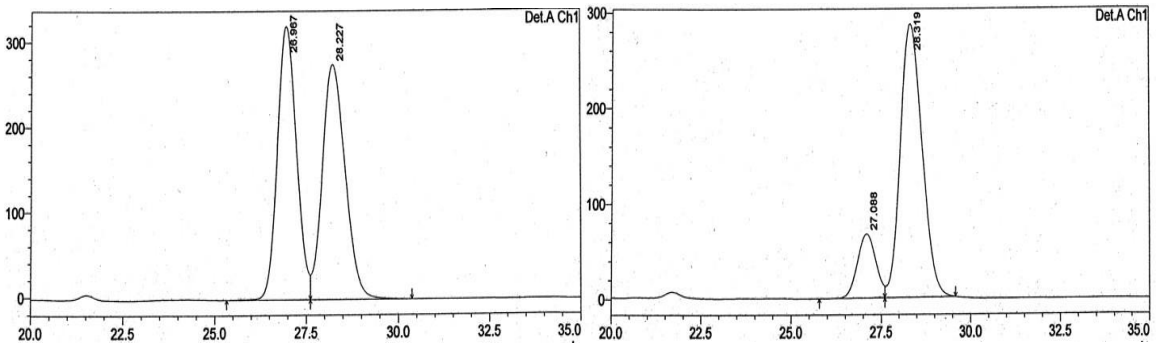
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 15.091 | 2238072 | 93071 | 91.971 | 92.118 |
| 2 | 16.140 | 195393 | 7964 | 8.029 | 7.882 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 15.402 | 49.813 | 1 | 15.091 | 91.971 |
| 2 | 16.494 | 50.187 | 2 | 16.140 | 8.029 |

**(*R*)-*tert*-Butyl(3-(dimethyl(phenyl)silyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propoxy)dimethylsilane (3.46).** IR (neat): 2955 (w), 2930 (w), 2857 (w), 1471 (w), 1389 (m), 1371 (m), 1319 (m), 1254 (m), 1144 (m), 1083 (m), 906 (s), 832 (s), 776 (m), 727 (s), 700 (s), 649 (m), 578 (w), 469 (w) $cm^{-1}$; $^1$H NMR (400MHz, $CDCl_3$): δ 7.54–7.51 (2H, m), 7.34–7.31 (3H, m), 3.57 (2H, d, $J$ = 7.2 Hz), 1.35–1.28 (1H, m), 1.20 (12H, s), 0.94–0.88 (1H, m), 0.87 (9H, s), 0.83–0.78 (1H, m), 0.28 (6H, s), 0.00 (3H, s), –0.01 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.0, 133.8, 128.8, 127.8, 83.1, 67.5, 26.1,

25.0, 18.5, 12.8, –2.1, –2.4, –5.2, –5.3; HRMS (ESI$^+$): Calcd for $C_{17}H_{38}B_1O_3Si_2$ [M–$C_6H_5$]$^+$: 357.2452; Found: 357.2435. Specific Rotation: $[\alpha]_D^{20}$ –5.87 (*c* 2.15, $CHCl_3$) for an enantiomerically enriched sample of 84:16 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borylsilane product with $NaBO_3$•$4H_2O$ (Chiralcel OJ-H column, 99/1 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 26.967 | 11655105 | 321164 | 49.399 | 53.794 |
| 2 | 28.227 | 11938832 | 275856 | 50.601 | 46.206 |

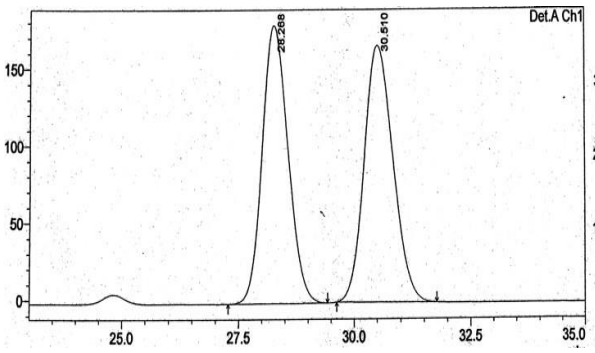
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 27.088 | 2376356 | 66968 | 16.293 | 18.977 |
| 2 | 28.319 | 12209137 | 285918 | 83.707 | 81.023 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 26.967 | 49.399 | 1 | 27.088 | 16.293 |
| 2 | 28.227 | 50.601 | 2 | 28.319 | 83.707 |

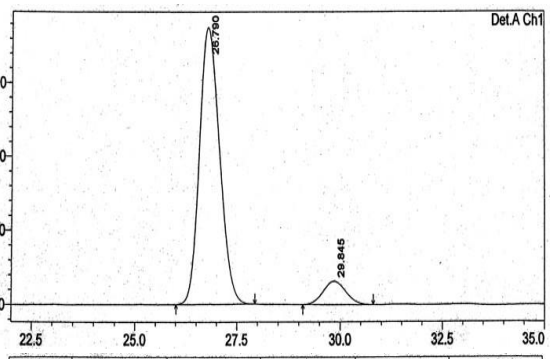
**(*R*)-(3-Cyclopentyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)dimethyl(phenyl)silane (3.47).** IR (neat): 2977 (w), 2949 (w), 2908 (w), 2866 (w), 1377 (m), 1315 (m), 1246 (m), 1213 (w), 1142 (s), 1112 (m), 966 (w), 828 (s), 727 (s), 698 (s), 467 (w) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.54–7.52 (2H, m), 7.35–7.32 (3H, m), 1.78–1.61 (3H, m), 1.58–1.44 (5H, m), 1.31–1.24 (1H, m), 1.21 (12H, s), 1.11 (1H, tt, *J* = 6.4, 6.4 Hz), 1.05–0.93 (3H, m), 0.78 (1H, dd, *J* = 14.4, 5.6 Hz), 0.29 (6H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.2, 133.8, 128.8, 127.7, 82.9, 41.2, 39.5, 33.0, 32.8, 25.4, 25.2, 25.0, 24.9, 16.8, –2.1, –2.2; HRMS (ESI$^+$): Calcd for $C_{22}H_{41}B_1N_1O_2Si_1$

$[M+NH_4]^+$: 390.3000; Found: 390.2994. Specific Rotation: $[\alpha]_D^{20}$ –12.61 (*c* 1.76, $CHCl_3$) for an enantiomerically enriched sample of 91.5:8.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borylsilane product with $NaBO_3 \bullet 4H_2O$ (Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.6 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 28.268 | 7022232 | 180471 | 49.422 | 51.995 |
| 2 | 30.510 | 7186490 | 166620 | 50.578 | 48.005 |

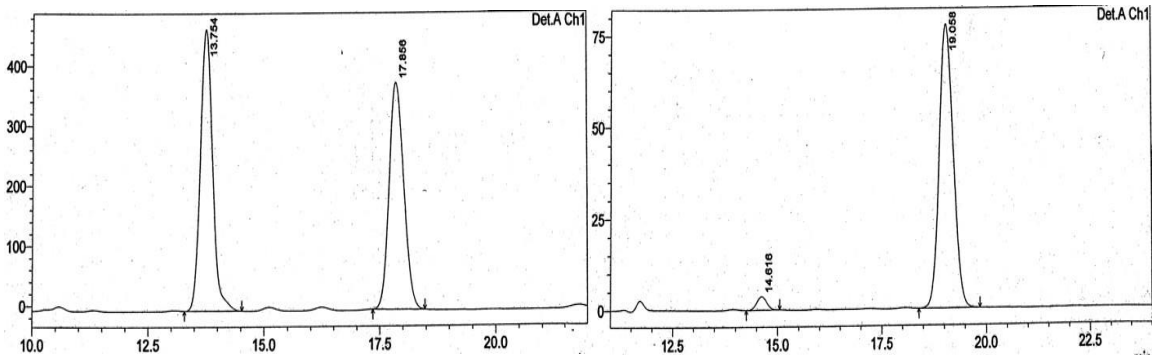



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 26.790 | 12949844 | 374603 | 91.491 | 92.223 |
| 2 | 29.845 | 1204401 | 31589 | 8.509 | 7.777 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 28.268 | 49.422 | 1 | 26.790 | 91.491 |
| 2 | 30.510 | 50.578 | 2 | 29.854 | 8.509 |

**(*R*)-(2-Cyclohexyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.48).** IR (neat): 2977 (w), 2923 (s), 2851 (m), 1448 (w), 1427 (w), 1371 (m), 1313 (m), 1246 (m), 1214 (w), 1144 (s), 1112 (m), 970 (w), 832 (s), 728 (m), 699 (m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.53–7.50 (2H, m), 7.33–7.31 (3H, m), 1.69–1.61 (5H, m), 1.38–1.25 (1H, m), 1.19 (12H, s), 1.18–0.94 (7H, m), 0.75 (1H, d, *J* = 11.2), 0.25 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 140.2, 133.8, 128.7, 127.7, 83.0, 42.8, 32.3, 31.5, 27.1, 27.0, 26.8, 25.2, 25.1, 13.5, –2.2, –2.6; HRMS ($ESI^+$): Calcd for $C_{22}H_{41}B_1N_1O_2Si_1$ $[M+NH_4]^+$: 390.3000; Found: 390.2996. Optical Rotation: $[\alpha]_D^{20}$ –24.63 (*c* 1.03, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material obtained from the derived alcohol, which was synthesized by oxidation of the borylsilane product with $NaBO_3 \bullet 4H_2O$ (Chiralcel OD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.6 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 13.754 | 8603528 | 469679 | 50.649 | 55.403 |
| 2 | 17.856 | 8382889 | 378078 | 49.351 | 44.597 |

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 14.616 | 62476 | 3733 | 3.343 | 4.581 |
| 2 | 19.058 | 1806547 | 77772 | 96.657 | 95.419 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 13.754 | 50.649 | 1 | 14.616 | 3.343 |
| 2 | 17.856 | 49.351 | 2 | 19.058 | 96.657 |

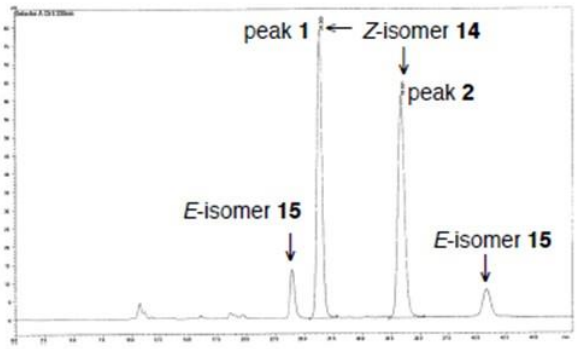
■ **Experimental Procedure for NHC–Cu-Catalyzed Site- and Enantioselective Protoboration of a Si-Substituted Diene (3.49):** In a $N_2$-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolinium salt **A.14** (3.2 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.0050 mmol, 5.0 mol %), NaO*t*-Bu (7.7 mg, 0.080 mmol, 80.0 mol %) and thf (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the mixture was allowed to stir at 22 °C for two hours. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min

under an atmosphere of $N_2$. (*E*)-(2-(Cyclohex-1-en-1-yl)vinyl)dimethyl(phenyl)silane **3.49** (24.2 mg, 0.100 mmol, 1.0 equiv.) followed by MeOH (8.2 μL, 0.200 mmol, 2.0 equiv.) were added through a syringe. The mixture was allowed to stir at 22 °C for 24 h, after which, benzaldehyde (15.3 μL, 0.150 mmol, 1.5 equiv.) was added through a syringe. The mixture was allowed to stir for an additional 12 h. Then the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=15:1 to 10:1) to afford a 7:1 mixture of **3.51** and **3.52** as colorless oil (29.9 mg, 0.0853 mmol, 85% yield).

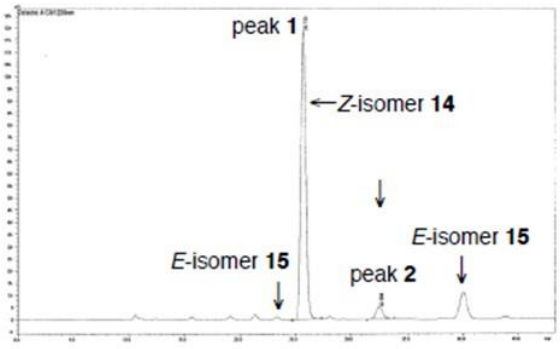
**(*E*)-(2-(Cyclohex-1-en-1-yl)vinyl)dimethyl(phenyl)silane (3.49).** IR (neat): 2926 (w), 2858 (w), 1633 (w), 1427 (w), 1246 (m), 1203 (w), 1112 (m), 985 (m), 860 (s), 841 (s), 728 (s), 697 (s), 513 (m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.56–7.53 (2H, m), 7.37–7.35 (3H, m), 6.60 (1H, d, $J$ = 18.8 Hz), 5.84–5.79 (2H, m), 2.19–2.15 (4H, m), 1.69–1.60 (4H, m), 0.37 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 149.2, 139.4, 137.5, 134.0, 131.8, 129.0, 127.9, 122.1, 26.1, 24.2, 22.7, 22.6, –2.2; HRMS ($ESI^+$): Calcd for $C_{16}H_{23}Si_1$ $[M+H]^+$: 243.1569, Found: 243.1565.

**3.51** and **3.52** are not separable on silica gel. Characterization data for **3.51** and **3.52** are not shown. $^1H$ NMR of mixture of **3.51** and **3.52** is provided.

Enantiomeric purity of **3.51** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



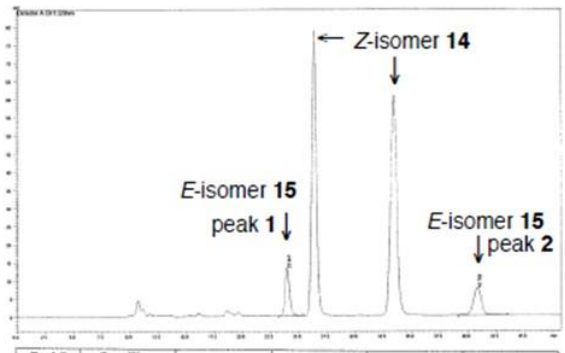

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 26.305 | 2427713 | 78778 | 49.918 | 56.419 |
| 2 | 33.351 | 2435653 | 60852 | 50.082 | 43.581 |



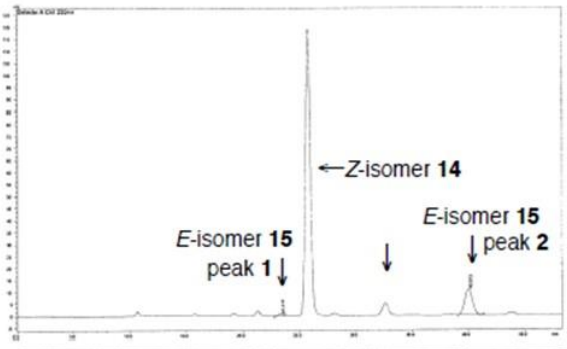

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 25.725 | 3616934 | 119141 | 95.259 | 96.080 |
| 2 | 32.586 | 179996 | 4861 | 4.741 | 3.920 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 26.305 | 49.918 | 1 | 25.725 | 95.259 |
| 2 | 33.351 | 50.082 | 2 | 32.586 | 4.741 |

Enantiomeric purity of **3.52** was determined by HPLC analysis in comparison with authentic racemic material (95:5 e.r. shown; Chiralcel OD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 23.941 | 382475 | 13228 | 50.298 | 63.548 |
| 2 | 40.769 | 377938 | 7588 | 49.702 | 36.452 |




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 23.319 | 28861 | 1011 | 5.172 | 8.422 |
| 2 | 40.013 | 529122 | 10989 | 94.828 | 91.578 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 23.941 | 50.298 | 1 | 23.319 | 5.172 |
| 2 | 40.769 | 49.702 | 2 | 40.013 | 94.828 |

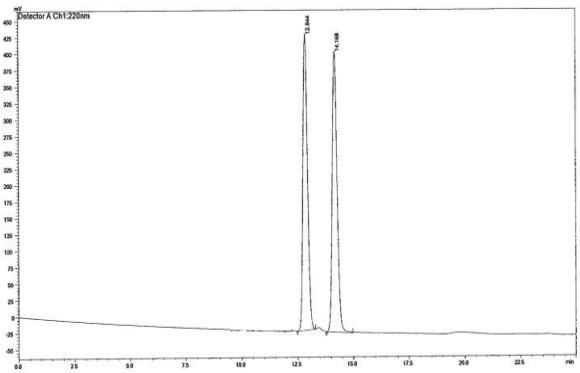
**Proof of Stereochemistry:** (*S*)-((*R*)-2-Oxocyclohexyl)(phenyl)methyl 4-bromobenzoate, the spectroscopic data of which match those reported previously,[44] was obtained through ozonolysis of mixture of **3.51** and **3.52**, followed by benzoylation with *para*-

(44) Denmark, S. E.; Stavenger, R. A.; Wong, K.; Su, X. *J. Am. Chem. Soc.* **1999**, *121,* 4982–4991.

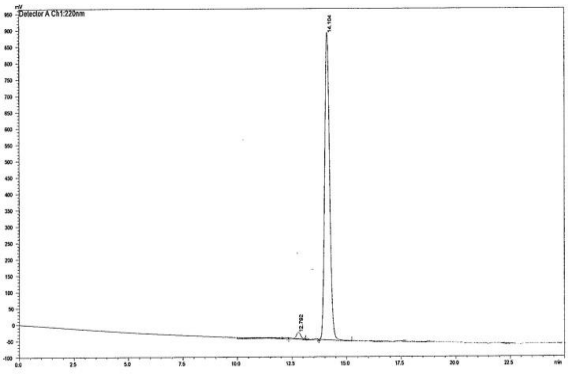
bromobenzoyl chloride. Specific rotation of (*S*)-((*R*)-2-oxocyclohexyl)(phenyl)methyl 4-bromobenzoate : $[\alpha]_D^{20}$ +92.4 (*c* 0.251, $CHCl_3$), 95:5 e.r. Literature value ($[\alpha]_D^{20}$ +111.6 (*c* 1.21, $CHCl_3$), >98:2 e.r.) is assigned to (*S*)-((*R*)-2-oxocyclohexyl)(phenyl)methyl 4-bromobenzoate.

■ **Representative Experimental Procedure for Site- and Enantioselective NHC–Cu-Catalyzed Protoboration of Aryl-Substituted Alkenylsilanes:** In a $N_2$-filled glove-box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolinium salt **A.6** (2.9 mg, 0.0050 mmol, 5.0 mol %), CuCl (0.5 mg, 0.0050 mmol, 5.0 mol %), NaO*t*-Bu (7.7 mg, 0.080 mmol, 80.0 mol %) and thf (0.5 mL). The reaction vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the mixture was allowed to stir at 22 °C for two hours. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol, 1.1 equiv.) was added to the above solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove-box. The mixture was allowed to stir at 22 °C for 30 min under an atmosphere of $N_2$. After this time, (*E*)-dimethyl(phenyl)(styryl)silane **3.33** (23.8 mg, 0.100 mmol, 1.0 equiv.) followed by MeOH (8.2 μL, 0.200 mmol, 2.0 equiv.) were added via syringes. The mixture was allowed to stir at 22 °C for 24 h. The reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide brown oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=80:1) to afford a mixture of **3.43** as colorless oil (33.0 mg, 0.0901 mmol, 90% yield).

**(*R*)-Dimethyl(phenyl)(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)silane (3.43).** IR (neat): 3067 (w), 3025 (w), 2977 (m), 1494 (m), 1351 (s), 1248 (m), 1143 (s), 1113 (m), 837 (m), 814 (m), 774 (m), 730 (s) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (2H, m), 7.38–7.36 (3H, m), 7.21–7.16 (4H, m), 7.11–7.09 (1H, m), 2.78 (1H, dd, $J$ = 14.0, 12.0 Hz), 2.68 (1H, dd, $J$ = 14.0, 3.2 Hz), 1.09–1.05 (7H, m), 1.02 (6H, s), 0.39 (3H, s), 0.37 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 144.9, 138.7, 134.0, 129.1, 128.3, 128.1, 127.8, 125.5, 83.0, 31.7, 25.0, 24.8, 16.2, –2.2, –3.3; HRMS ($ESI^+$): Calcd for $C_{22}H_{35}B_1N_1O_2Si_1$ $[M+NH_4]^+$: 384.2530, Found: 384.2523. Specific Rotation: $[\alpha]_D^{20}$ +14.8 (*c* 1.73, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.844 | 6373385 | 452600 | 49.666 | 51.415 |
| 2 | 14.168 | 6459178 | 427680 | 50.334 | 48.585 |



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.792 | 273162 | 20227 | 1.818 | 2.106 |
| 2 | 14.104 | 14754936 | 940087 | 98.182 | 97.894 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 12.844 | 49.666 | 1 | 12.792 | 1.818 |
| 2 | 14.168 | 50.334 | 2 | 14.104 | 98.182 |

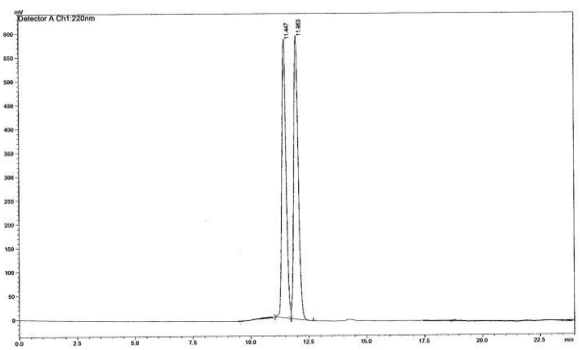
**Proof of stereochemistry:** The corresponding (*R*)-1-phenylbutan-2-ol was obtained after olefination, reduction and oxidation of **3.43**.[45] Specific Rotation of (*R*)-1-phenylbutan-2-ol: $[\alpha]_D^{20}$ –14.2 (*c* 0.52, $CHCl_3$). Literature value ($[\alpha]_D^{20}$ –8.3 (*c* 1.02, $CHCl_3$), 71:29 e.r.)

(45) Aggarwal, V. K.; Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vázquez-Romero, A.; Webster, M. P. *Org. Lett.* **2011**, *13*, 1490–1493.

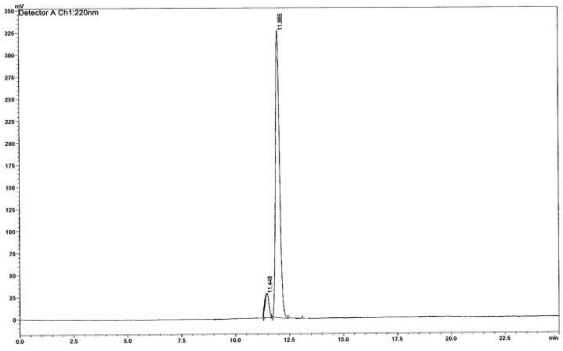
is assigned to the (*R*) enantiomer.[46]

**(*R*)-Dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(*o*-tolyl)ethyl)silane (3.53).** IR (neat): 3068 (w), 2876 (w), 1603 (w), 1348 (s), 1309 (m), 1213 (m), 1142 (s), 1112 (m), 969 (w), 833 (s), 731 (s), 698 (s), 635 (w), 468 (m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.62–7.59 (2H, m), 7.38–7.35 (3H, m), 7.22–7.21 (1H, m), 7.05–7.01 (3H, m), 2.78 (1H, dd, *J* = 14.0, 12.0 Hz), 2.64 (1H, dd, *J* = 14.0, 3.2 Hz), 2.13 (3H, s), 1.09 (6H, s), 1.07 (6H, s), 1.02 (1H, dd, *J* = 12.0, 3.2 Hz), 0.43 (3H, s), 0.41 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 142.9, 138.7, 135.8, 134.1, 130.0, 129.1, 128.6, 127.8, 125.6, 83.0, 28.8, 25.03, 24.96, 19.3, 14.8, –2.4, –3.4; HRMS ($ESI^+$): Calcd for $C_{23}H_{37}B_1N_1O_2Si_1$ $[M+NH_4]^+$: 398.2687, Found: 398.2696. Specific Rotation: $[\alpha]_D^{20}$ +12.7 (*c* 1.13, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.447 | 7445566 | 585158 | 48.161 | 49.573 |
| 2 | 11.963 | 8014181 | 595249 | 51.839 | 50.427 |




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.448 | 152596 | 16008 | 3.450 | 4.677 |
| 2 | 11.965 | 4270317 | 326238 | 96.550 | 95.323 |

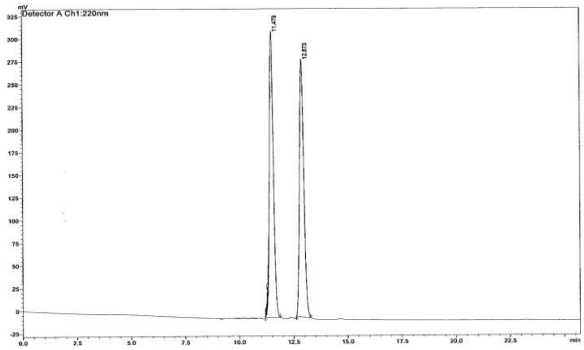
| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 11.447 | 48.161 | 1 | 11.448 | 3.450 |
| 2 | 11.963 | 51.839 | 2 | 11.965 | 96.550 |

**(*R*)-(2-(2-Fluorophenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.54).** IR (neat): 3068 (w), 2976 (w), 2927 (w), 1583

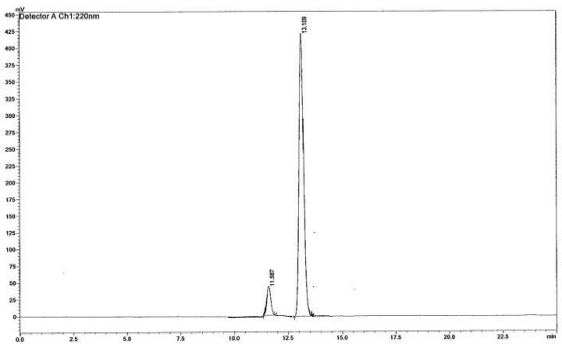
(46) Matsunaga, H.; Ishizuka, T.; Kunieda, T. *Tetrahedron Lett.* **2005**, *46*, 3645–3648.

(m), 1352 (s), 1313 (m), 1248 (m), 1143 (s), 1113 (w), 865 (m), 755 (m), 733 (w), 700 (w), 502 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (2H, m), 7.37–7.34 (3H, m), 7.21 (1H, td, *J* = 7.6, 1.6 Hz), 7.11–7.05 (1H, m), 6.98–6.89 (2H, m), 2.82–2.71 (2H, m), 1.11 (1H, dd, *J* = 11.6, 4.4 Hz), 1.08 (6H, s), 1.03 (6H, s), 0.40 (3H, s), 0.38 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 161.1 (d, *J* = 244.1 Hz), 138.5, 134.0, 131.7 (d, *J* = 15.7 Hz), 130.3 (d, *J* = 5.2 Hz), 129.1, 127.8, 127.0 (d, *J* = 8.2 Hz), 123.5 (d, *J* = 3.7 Hz), 115.0 (d, *J* = 21.6 Hz), 83.0, 30.5, 25.1, 24.8, 14.3, –2.3, –3.3; HRMS ($ESI^+$): Calcd for $C_{22}H_{34}B_1F_1N_1O_2Si_1$ $[M+NH_4]^+$: 402.2436, Found: 402.2443. Specific Rotation: $[\alpha]_D^{20}$ +13.7 (*c* 1.33, $CHCl_3$) for an enantiomerically enriched sample of 93.5:6.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.479 | 4332793 | 316253 | 51.984 | 52.619 |
| 2 | 12.873 | 4002141 | 284775 | 48.016 | 47.381 |



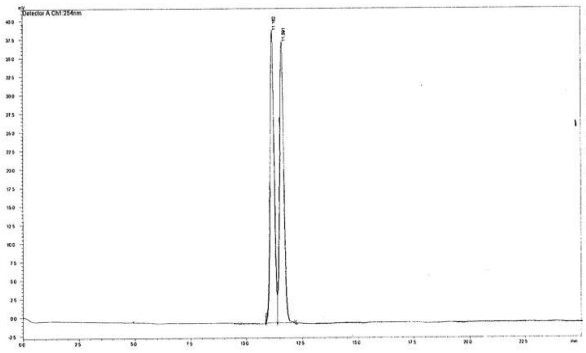

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.587 | 407632 | 36633 | 6.450 | 8.028 |
| 2 | 13.109 | 5912126 | 419702 | 93.550 | 91.972 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 11.479 | 51.984 | 1 | 11.587 | 6.450 |
| 2 | 12.873 | 48.016 | 2 | 13.109 | 93.550 |

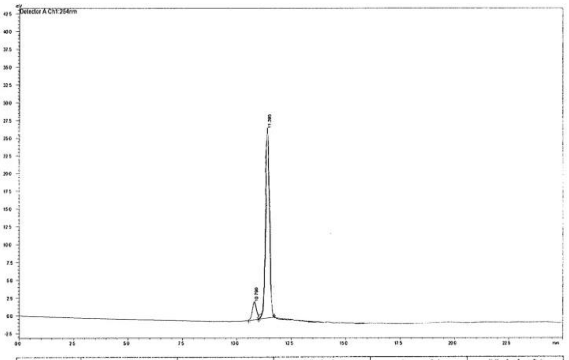
**(*R*)-Dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(2-(trifluoromethyl)phenyl)ethyl)silane (3.55).** IR (neat): 3071 (w), 2978 (w), 1483 (w), 1352 (m), 1249 (s), 1142 (s), 1116 (s), 1037 (m), 815 (m), 766 (m), 732 (m), 699 (m), 634 (m), 469 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (2H, m), 7.52 (2H, dd, *J* =

14.0, 8.0 Hz), 7.39–7.35 (4H, m), 7.21 (1H, t, $J$ = 7.6 Hz), 2.97–2.95 (2H, m), 1.11 (1H, dd, $J$ = 9.2, 6.0 Hz), 1.08 (6H, s), 1.03 (6H, s), 0.42 (3H, s), 0.41 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 143.6 (app. d, $J$ = 1.5 Hz), 138.3, 134.1, 131.4, 130.7, 129.1, 128.1, 127.8, 125.9 (q, $J$ = 5.9 Hz), 125.7, 124.8 (q, $J$ = 272.3 Hz), 83.1, 28.3, 25.1, 25.0, 15.7, –2.8, –3.0; HRMS (ESI$^+$): Calcd for $C_{23}H_{34}B_1F_3N_1O_2Si_1$ $[M+NH_4]^+$: 452.2404, Found: 452.2425. Specific Rotation: $[\alpha]_D^{20}$ +5.62 (*c* 1.99, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.162 | 469592 | 38491 | 49.493 | 50.732 |
| 2 | 11.591 | 479211 | 37380 | 50.507 | 49.268 |



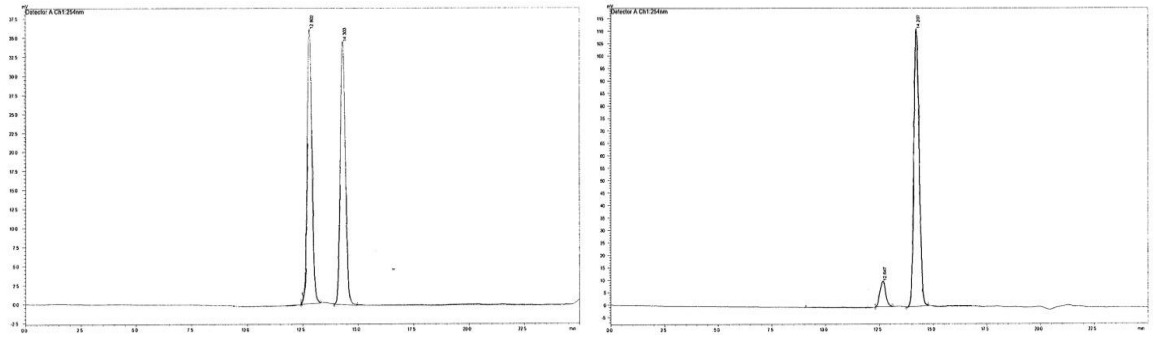
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 10.799 | 24754 | 2198 | 7.000 | 7.670 |
| 2 | 11.395 | 328854 | 26466 | 93.000 | 92.330 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 11.162 | 49.493 | 1 | 10.799 | 7.000 |
| 2 | 11.591 | 50.507 | 2 | 11.395 | 93.000 |

**(*R*)-(2-(2-Methoxyphenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.56).** IR (neat): 3069 (w), 2976 (w), 2835 (w), 1492 (m), 1350 (s), 1240 (s), 1143 (s), 1112 (m), 996 (w), 835 (m), 750 (m), 699 (m), 521 (w) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.64–7.61 (2H, m), 7.37–7.34 (3H, m), 7.19 (1H, dd, $J$ = 7.2, 1.6 Hz), 7.09 (1H, td, $J$ = 8.0, 1.6 Hz), 6.81–6.73 (2H, m), 3.74 (3H, s), 2.80

(1H, dd, $J$ = 14.0, 3.2 Hz), 2.71–2.65 (1H, m), 1.18 (1H, dd, $J$ = 12.0, 3.2 Hz), 1.09 (6H, s), 1.06 (6H, s), 0.40 (3H, s), 0.37 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.4, 139.1, 134.1, 133.2, 129.5, 128.9, 127.6, 126.7, 119.9, 109.9, 82.9, 55.1, 26.3, 25.1, 24.9, 13.8, –2.2, –3.1; HRMS ($ESI^+$): Calcd for $C_{23}H_{37}B_1N_1O_3Si_1$ $[M+NH_4]^+$: 414.2636, Found: 414.2620. Specific Rotation: $[\alpha]_D^{20}$ +18.0 (*c* 1.58, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99.5/0.5 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.802 | 557573 | 36169 | 49.537 | 51.080 |
| 2 | 14.303 | 567986 | 34639 | 50.463 | 48.920 |

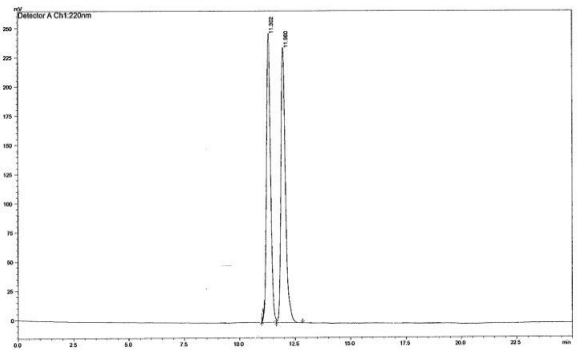
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.647 | 137316 | 8572 | 6.539 | 7.124 |
| 2 | 14.207 | 1962744 | 111759 | 93.461 | 92.876 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 12.802 | 49.537 | 1 | 12.647 | 6.539 |
| 2 | 14.303 | 50.463 | 2 | 14.207 | 93.461 |

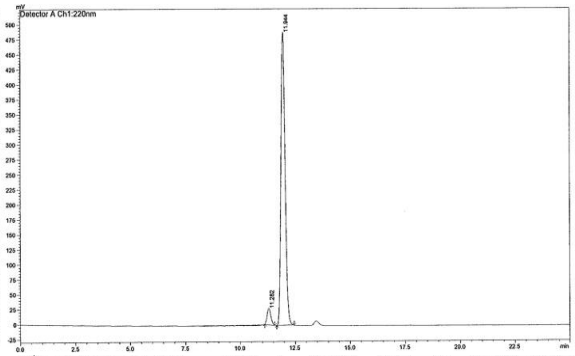
**(*R*)-(2-(3-Fluorophenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.57).** IR (neat): 3070 (w), 2977 (w), 2929 (w), 1615 (w), 1349 (s), 1307 (m), 1249 (m), 1142 (s), 1113 (m), 971 (w), 836 (m), 778 (m), 731 (m), 699 (m) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.60–7.57 (2H, m), 7.39–7.36 (3H, m), 7.17–7.12 (1H, m), 6.93–6.87 (2H, m), 6.79 (1H, td, $J$ = 8.4, 2.4 Hz), 2.81–2.74 (1H, m), 2.65 (1H, dd, $J$ = 14.0, 3.2 Hz), 1.08 (6H, s), 1.05 (7H, m), 0.40 (3H, s), 0.38 (3H, s);

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.9 (d, *J* = 243.3 Hz), 147.7 (d, *J* = 7.5 Hz), 138.5, 134.1, 129.4 (d, *J* = 8.2 Hz), 129.2, 127.9, 123.9 (d, *J* = 2.2 Hz), 115.2 (d, *J* = 20.8 Hz), 112.3 (d, *J* = 20.8 Hz), 83.1, 31.5, 25.0, 24.8, 16.4, –2.2, –3.4; HRMS (ESI$^+$): Calcd for $C_{22}H_{34}B_1F_1N_1O_2Si_1$ $[M+NH_4]^+$: 402.2436, Found: 402.2430. Specific Rotation: $[\alpha]_D^{20}$ +15.1 (*c* 1.82, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.302 | 3212978 | 247883 | 49.408 | 51.209 |
| 2 | 11.960 | 3289961 | 236180 | 50.592 | 48.791 |



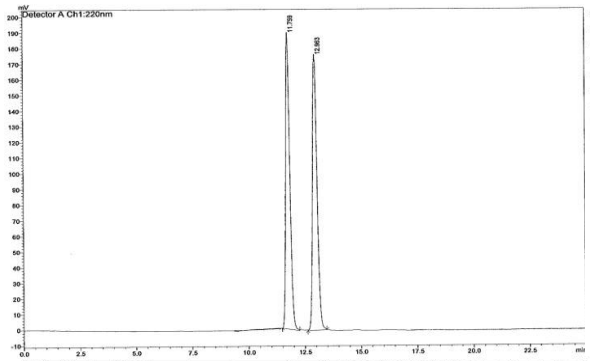

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.282 | 333463 | 27643 | 4.884 | 5.340 |
| 2 | 11.944 | 6493504 | 490056 | 95.116 | 94.660 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 11.302 | 49.408 | 1 | 11.282 | 4.884 |
| 2 | 11.960 | 50.592 | 2 | 11.944 | 95.116 |

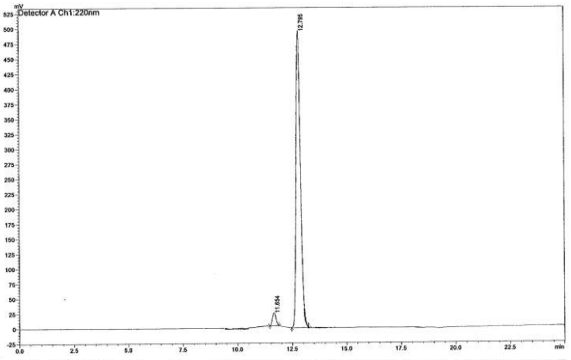
**(*R*)-(2-(4-Fluorophenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.58).** IR (neat): 3069 (w), 2977 (w), 2928 (w), 1508 (s), 1348 (s), 1312 (m), 1220 (m), 1141 (s), 1112 (m), 970 (w), 840 (s), 731 (s), 700 (m), 502 (w) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (2H, m), 7.37–7.35 (3H, m), 7.10 (2H, dd, *J* = 8.8, 6.0 Hz), 6.87 (2H, t, *J* = 8.8 Hz), 2.78–2.71 (1H, m), 2.63 (1H, dd, *J* = 14.0, 3.6 Hz), 1.08 (6H, s), 1.06–1.01 (7H, m), 0.39 (3H, s), 0.36 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 161.2 (d, *J* = 241.1 Hz), 140.6 (d, *J* = 3.8 Hz), 138.6, 134.0, 129.6 (d, *J* = 7.4 Hz), 129.1, 127.9, 114.7 (d, *J* = 20.8 Hz), 83.0, 30.9, 25.0, 24.8, 16.6, –2.2, –

3.4; HRMS (ESI$^+$): Calcd for $C_{22}H_{34}B_1F_1N_1O_2Si_1$ $[M+NH_4]^+$: 402.2436, Found: 402.2445. Specific Rotation: $[\alpha]_D^{20}$ +15.7 (*c* 1.62, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).




| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.759 | 2455479 | 189898 | 49.650 | 51.787 |
| 2 | 12.963 | 2490142 | 176795 | 50.350 | 48.213 |

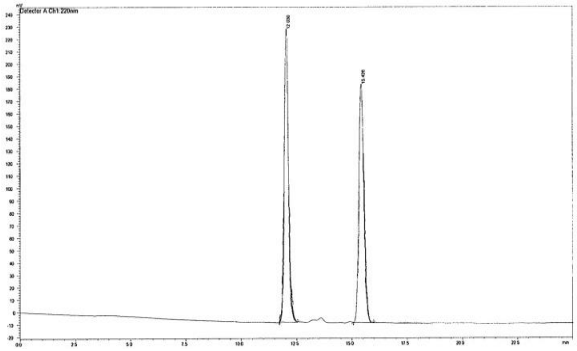



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.494 | 153378 | 12525 | 2.233 | 2.569 |
| 2 | 12.546 | 6715742 | 475017 | 97.767 | 97.431 |

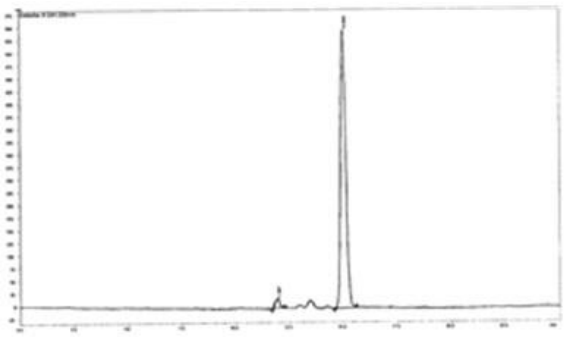
| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 11.759 | 49.650 | 1 | 11.494 | 2.233 |
| 2 | 12.963 | 50.350 | 2 | 12.546 | 97.767 |

**(*R*)-Dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(thiophen-3-yl)ethyl)silane (3.59).** IR (neat): 3069 (w), 2976 (w), 2957 (w), 1427 (w), 1347 (s), 1303 (m), 1248 (s), 1142 (s), 1112 (m), 1007 (w), 908 (w), 814 (s), 771 (m), 730 (s), 699 (s), 578 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.55 (2H, m), 7.37–7.34 (3H, m), 7.16–7.14 (1H, m), 6.90–6.89 (2H, m), 2.85 (1H, dd, *J* = 14.8, 12.8 Hz), 2.65 (1H, dd, *J* = 14.8, 3.6 Hz), 1.11 (6H, s), 1.07–1.03 (7H, m), 0.38 (3H, s), 0.36 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 145.5, 138.6, 134.0, 129.1, 128.4, 127.8, 124.9, 119.6, 83.0, 30.5, 25.0, 24.8, 15.5, –2.3, –3.3; HRMS (ESI$^+$): Calcd for $C_{20}H_{33}B_1N_1O_2S_1Si_1$ $[M+NH_4]^+$: 390.2094, Found: 390.2096. Specific Rotation: $[\alpha]_D^{20}$ +20.5 (*c* 1.56, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.030 | 3040885 | 233381 | 49.309 | 54.824 |
| 2 | 15.426 | 3126056 | 192313 | 50.691 | 45.176 |



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 11.887 | 140256 | 12568 | 1.487 | 2.234 |
| 2 | 14.953 | 9289539 | 550116 | 98.513 | 97.766 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 12.030 | 49.309 | 1 | 11.887 | 1.487 |
| 2 | 15.426 | 50.691 | 2 | 14.953 | 98.513 |

## ■ Enantioselective Synthesis of Bruguierol A

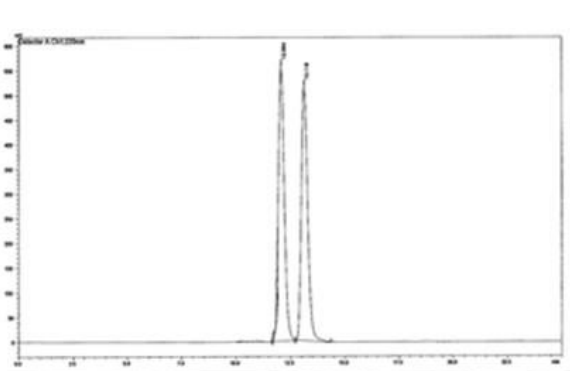
**Procedure for Synthesis of Alkenylsilane 3.60a from Protosilylation of Alkyne 3.60:** The experimental procedure for synthesis of compound **3.60a** is the same as described above in the representative experimental procedure.

**(*E*)-(3-Methoxystyryl)dimethyl(phenyl)silane (3.60a).** IR (neat): 2921 (w), 2851 (w), 1737 (s), 1446 (w), 1364 (m), 1219 (s), 1084 (m), 1024 (m), 965 (m), 834 (w), 762 (w), 738 (w), 672 (w) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.57 (2H, m), 7.38–7.36 (3H, m), 7.25 (1H, t, $J$ = 8.0 Hz), 7.05–7.03 (1H, m), 7.00–6.99 (1H, m), 6.92 (1H, d, $J$ = 19.2 Hz), 6.84–6.81 (1H, m), 6.58 (1H, d, $J$ = 18.8 Hz), 3.82 (3H, s), 0.44 (6H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 160.0, 145.3, 139.8, 138.7, 134.1, 129.6, 129.2, 128.0, 127.6, 119.4, 114.3, 111.5, 55.4, –2.4; HRMS ($ESI^+$): Calcd for $C_{17}H_{21}O_1Si_1$ $[M+H]^+$: 269.1385, Found: 269.1380.

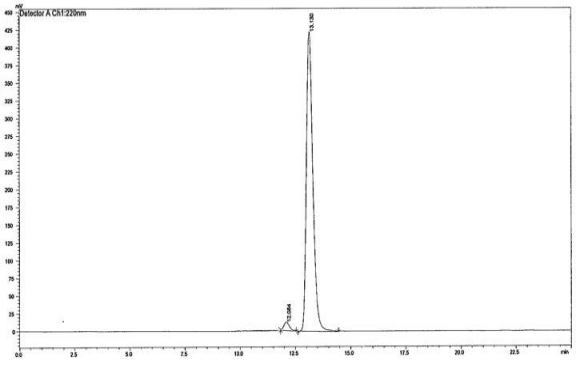
**Procedure for Enantioselective Protoboration of Alkenylsilane 3.60a:** The experimental procedure for synthesis of compound **3.61** is the same as described above in the representative experimental procedure.

**(*R*)-(2-(3-Methoxyphenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)dimethyl(phenyl)silane (3.61).** IR (neat): 3068 (w), 2977 (w), 1600 (w), 1488 (w), 1379 (m), 1349 (s), 1308 (m), 1259 (m), 1143 (s), 1113 (w), 1049 (w), 838 (m), 698 (m) $cm^{-1}$; $^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.59–7.57 (2H, m), 7.37–7.36 (3H, m), 7.12 (1H, t, $J$ = 8.0 Hz), 6.78–6.65 (3H, m), 3.77 (3H, s), 2.83–2.76 (1H, m), 2.68 (1H, dd, $J$ = 14.0, 3.2 Hz), 1.12–1.09 (7H, m), 1.04 (6H, s), 0.39 (3H, s), 0.36 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 159.5, 146.6, 138.7, 134.0, 129.1, 129.0, 127.8, 120.7, 113.7, 111.2, 83.0, 55.2, 31.7, 25.0, 24.8, 16.2, –2.2, –3.3; HRMS (ESI+): Calcd for $C_{23}H_{37}B_1N_1O_3Si_1$ $[M+NH_4]^+$: 414.2636, Found: 414.2646. Specific Rotation: $[\alpha]_D^{20}$ +17.5 (*c* 2.20, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material (Chiralpak AD-H column, 99/1 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm).



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.064 | 10641647 | 571742 | 50.118 | 51.923 |
| 2 | 13.118 | 10591420 | 529390 | 49.882 | 48.077 |



| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.084 | 220868 | 12032 | 2.483 | 2.764 |
| 2 | 13.130 | 8673045 | 423324 | 97.517 | 97.236 |

| Peak # | Time (min) | Area (%) | Peak # | Time (min) | Area (%) |
|---|---|---|---|---|---|
| 1 | 12.064 | 50.118 | 1 | 12.084 | 2.483 |

| | | | | | |
|---|---|---|---|---|---|
| 2 | 13.118 | 49.882 | 2 | 13.130 | 97.517 |

**Procedure for Synthesis of Allylsilane 3.62:** The experimental procedure has been reported previously.[47]

**(*S*)-(1-(3-Methoxyphenyl)but-3-en-2-yl)dimethyl(phenyl)silane (3.62).** IR (neat): 2956 (w), 2916 (w), 1625 (m), 1488 (m), 1428 (m), 1257 (s), 1190 (m), 1083 (m), 833 (s), 775 (s), 699 (s) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.55–7.52 (2H, m), 7.39–7.34 (3H, m), 7.13 (1H, t, *J* = 8.0 Hz), 6.69–6.63 (3H, m), 5.65 (1H, td, *J* = 17.2, 10.0 Hz), 4.86–4.84 (1H, m), 4.76–4.72 (1H, m), 3.76 (3H, s), 2.79 (1H, dd, *J* = 14.8, 3.6 Hz), 2.59 (1H, dd, *J* = 14.4, 11.2 Hz), 2.17–2.10 (1H, m), 0.32 (3H, s), 0.31 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 159.5, 144.0, 139.0, 137.5, 134.2, 129.2, 129.1, 127.9, 121.2, 114.5, 113.4, 111.0, 55.2, 36.0, 34.9, –4.3, –5.0; HRMS ($ESI^+$): Calcd for $C_{19}H_{25}O_1Si_1$ $[M+H]^+$: 297.1675, Found: 297.1676. Specific Rotation: $[\alpha]_D^{20}$ –13.5 (*c* 0.99, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

**Procedure for Hydroformylation/Reduction:** Compound **3.63** was prepared according to a known procedure.[48]

**(*R*)-4-(Dimethyl(phenyl)silyl)-5-(3-methoxyphenyl)pentan-1-ol (3.63).** IR (neat): 3359 (br), 2924 (s), 2853 (m), 1600 (m), 1454 (m), 1258 (s), 1190 (m), 1048 (s), 814 (s), 733 (s), 699 (s), 472 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.54–7.51 (2H, m), 7.37–7.34 (3H, m), 7.15 (1H, t, *J* = 8.0 Hz), 6.73–6.66 (3H, m), 3.77 (3H, s), 3.43–3.40 (2H, m), 2.78 (1H, dd, *J* = 14.0, 4.8 Hz), 2.44 (1H, dd, *J* = 14.0, 10.4 Hz), 1.57 (1H, s), 1.48–1.33 (4H, m), 1.32–1.22 (1H, m), 0.31 (3H, s), 0.29 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 159.7, 144.5, 138.7, 134.0, 129.2, 129.1, 127.9, 121.4, 114.8, 111.0, 63.2, 55.3, 36.3,

(47) Aggarwal, V. K.; Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vázquez-Romero, A.; Webster, M. P. *Org. Lett.* **2011**, *13*, 1490–1493.
(48) (a) Lightburn, T. E.; Dombrowski, M. T.; Tan, K. L. *J. Am. Chem. Soc.* **2008**, *130*, 9210–9211. (b) Sun, X.; Frimpong, K.; Tan, K. L. *J. Am. Chem. Soc.* **2010**, *132*, 11841–11843.

32.3, 27.2, 25.5, –3.7, –3.8; HRMS ($ESI^+$): Calcd for $C_{20}H_{32}N_1O_2Si_1$ $[M+NH_4]^+$: 346.2202, Found: 346.2206. Specific Rotation: $[\alpha]_D^{20}$ +7.1 (*c* 0.16, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

**Procedure for Fleming Oxidation of 3.63:** To a solution of **3.63** (358.1 mg, 1.090 mmol, 1.0 equiv.) in $CH_2Cl_2$ (3 mL) was added $HBF_4 \cdot OEt_2$ (598 μL, 4.360 mmol, 4.0 equiv.) at 22 °C. The mixture was allowed to stir at 22 °C for 3.0 h. A saturated aqueous solution of sodium bicarbonate (5 mL) was added to quench the reaction. Layers were separated and the organic layer was washed with a saturated aqueous solution of sodium bicarbonate. The aqueous layer was extracted by diethyl ether (3 × 3 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The yellow oil was dissolved in thf/MeOH (1/1) (6 mL). $NaHCO_3$ (137.5 mg, 1.635 mmol, 1.5 equiv.), KF (107.7 mg, 1.835 mmol, 1.7 equiv.) and $H_2O_2$ (744 μL, 6.540 mmol, 6.0 equiv.) were added sequentially at 22 °C. The resulting mixture was allowed to stir at 22 °C for 12 h. The reaction was quenched by passing the mixture through a short plug of silica gel and eluting with $CH_2Cl_2$. The filtrate was concentrated *in vacuo* and the crude product was purified by silica gel chromatography (hexanes:EtOAc=1:1) to afford the desired diol **3.64** as colorless oil (192.5 mg, 0.915 mmol, 84% yield over two steps).

**(*R*)-5-(3-Methoxyphenyl)pentane-1,4-diol (3.64).** IR (neat): 3328 (br), 2922 (s), 2852 (m), 1713 (w), 1584 (m), 1488 (m), 1436 (m), 1258 (s), 1153 (m), 1044 (s), 780 (m), 697 (m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.23 (1H, t, *J* = 8.0 Hz), 6.81–6.76 (3H, m), 3.90–3.84 (1H, m), 3.80 (3H, s), 3.68–3.63 (2H, m), 2.80 (1H, dd, *J* = 13.6, 4.4 Hz), 2.68 (1H, dd, *J* = 13.2, 8.4 Hz), 2.28 (2H, br s), 1.76–1.67 (3H, m), 1.62–1.56 (1H, m); $^{13}C$

NMR (100 MHz, $CDCl_3$): δ 159.9, 140.2, 129.7, 121.8, 115.2, 112.0, 72.7, 63.0, 55.3, 44.3, 33.9, 29.4; HRMS ($ESI^+$): Calcd for $C_{12}H_{19}O_3$ $[M+H]^+$: 211.1334, Found: 211.1340. Specific Rotation: $[\alpha]_D^{20}$ –4.5 (*c* 0.28, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

**Procedure for Synthesis of Lactone 3.65:** To a solution of diol **3.64** (205.0 mg, 0.975 mmol, 1.0 equiv.) in $CH_2Cl_2$ (10 mL) was added TPAP (17.1 mg, 0.049 mmol, 0.05 equiv.) and NMO (342.7 mg, 2.925 mmol, 3.0 equiv.) at 22 °C. The mixture was allowed to stir at 22 °C for 1.0 h. The reaction was quenched by passing the mixture through a short plug of silica gel and eluting with $CH_2Cl_2$. The filtrate was concentrated *in vacuo* and the crude product was purified by silica gel chromatography (hexanes:EtOAc=4:1) to afford the desired lactone **3.65** (160.9 mg, 0.780 mmol, 80% yield) as colorless oil.

**(*R*)-5-(3-Methoxybenzyl)dihydrofuran-2(3*H*)-one (3.65).** IR (neat): 2945 (w), 1769 (s), 1601 (m), 1490 (w), 1437 (w), 1259 (m), 1175 (s), 1040 (m), 918 (w), 783 (w), 699 (w), 649 (w) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.23 (1H, t, *J* = 8.0 Hz), 6.84–6.76 (3H, m), 4.77–4.70 (1H, m), 3.79 (3H, s), 3.05 (1H, dd, *J* = 14.0, 6.0 Hz), 2.90 (1H, dd, *J* = 14.0, 6.0 Hz), 2.51–2.36 (2H, m), 2.29–2.21 (1H, m), 2.00–1.90 (1H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 177.1, 159.9, 137.5, 129.8, 121.9, 115.3, 112.4, 80.8, 55.3, 41.5, 28.8, 27.3; HRMS ($ESI^+$): Calcd for $C_{12}H_{15}O_3$ $[M+H]^+$: 207.1021, Found: 207.1014. Specific Rotation: $[\alpha]_D^{20}$ –5.1 (*c* 0.34, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.

**Procedure for Synthesis of 3.66:** The experimental procedure has been reported previously.[49]

(49) Solorio, D. M.; Jennings, M. P. *J. Org. Chem.* **2007**, *72*, 6621–6623.

**(5*R*,8*S*)-2-Methoxy-5-methyl-6,7,8,9-tetrahydro-5*H*-5,8-epoxybenzo[7]annulene (3.66).** IR (neat): 2935 (m), 1607 (m), 1577 (m), 1496 (s), 1375 (w), 1274 (w), 1248 (s), 1082 (s), 999 (s), 843 (m), 741 (w), 601 (w), 547 (m) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.07 (1H, d, *J* = 8.4 Hz), 6.69 (1H, dd, *J* = 8.4, 2.4 Hz), 6.18–6.12 (1H, m), 4.74–4.70 (1H, m), 3.77 (3H, s), 3.35 (1H, dd, *J* = 16.4, 5.2 Hz), 2.49 (1H, d, *J* = 16.4 Hz), 2.29–2.20 (1H, m), 2.03–1.97 (1H, m), 1.86–1.80 (1H, m), 1.75–1.67 (4H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ 158.4, 136.6, 133.5, 123.9, 114.4, 111.7, 80.4, 74.4, 55.3, 43.1, 37.9, 30.6, 23.0; HRMS ($ESI^+$): Calcd for $C_{13}H_{17}O_2$ $[M+H]^+$: 205.1229, Found: 205.1225. Specific Rotation: $[\alpha]_D^{20}$ +25.0 (*c* 1.48, $CHCl_3$) for an enantiomerically enriched sample of 97.5:2.5 e.r.


HJ-II-205
May.20.10
File: exp
Pulse Sequence: s2pul
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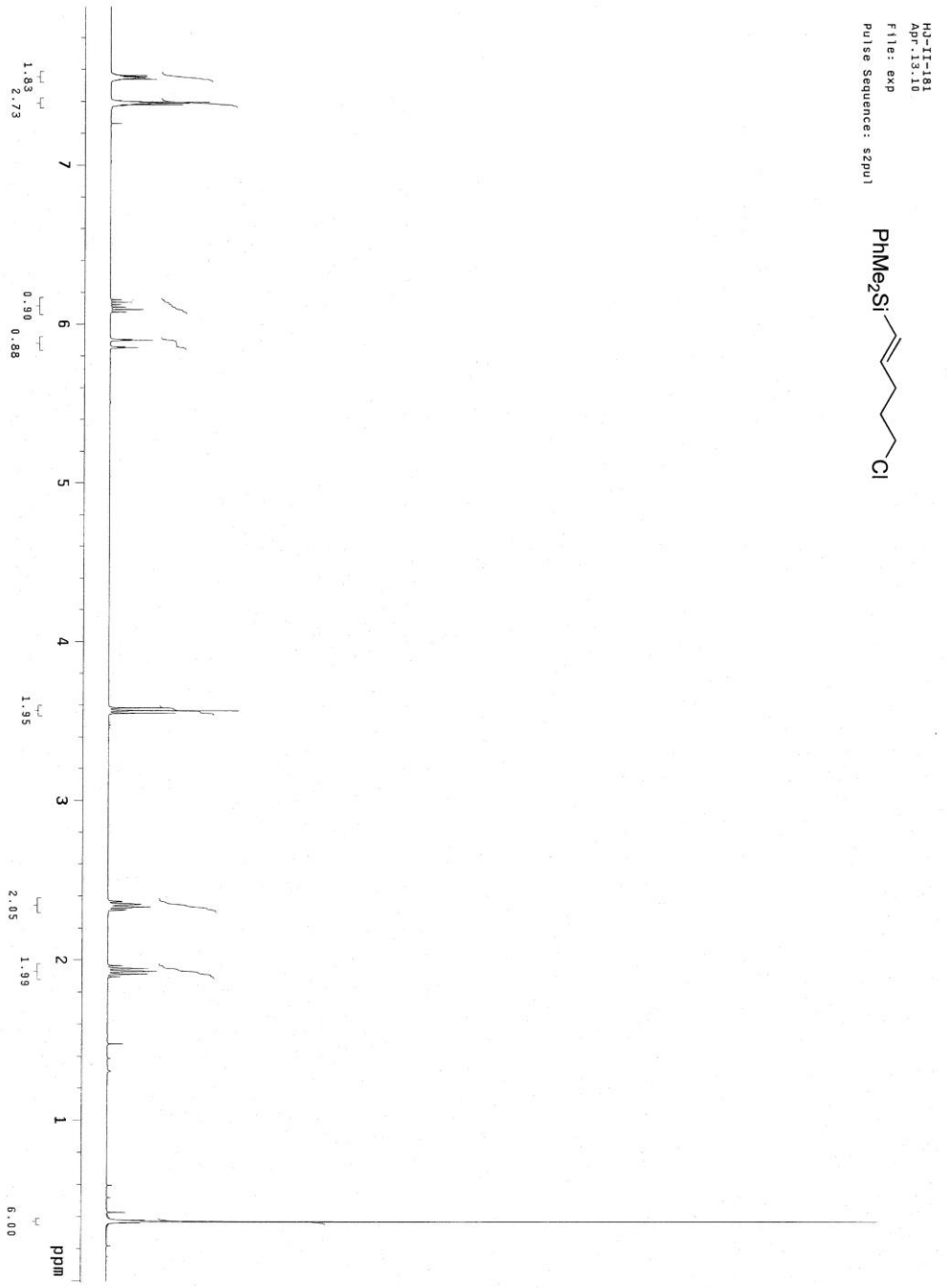
Me
1.88
2.81
0.91
0.89
2.06
4.36
3.00
5.22
ppm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Apr.13.10
File: exp
Pulse Sequence: s2pul
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Cl
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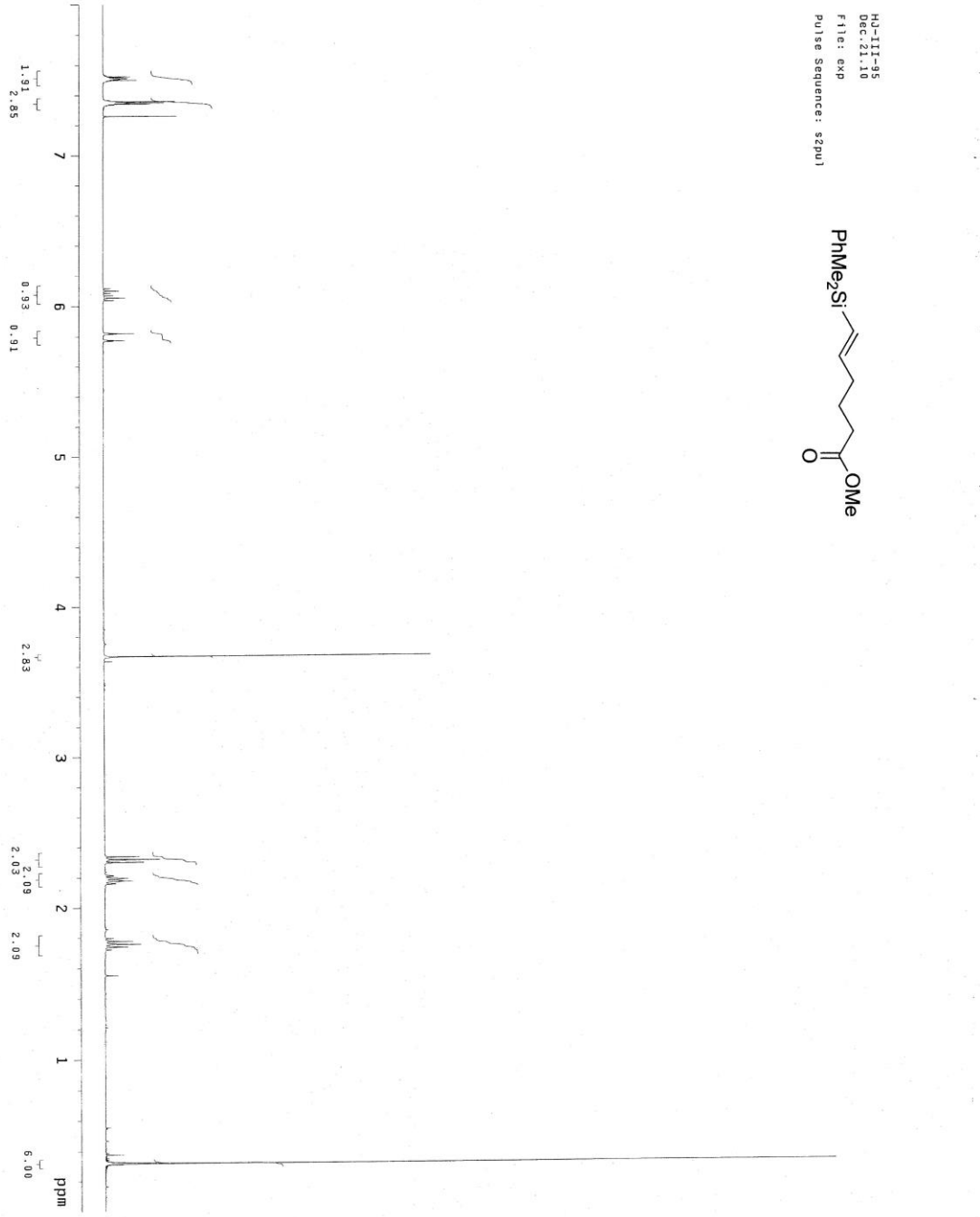
2.73
0.90
0.88
1.95
2.05
1.99
6.00
ppm


HJ-III-95
Dec.21.10
File: exp
Pulse Sequence: s2pul
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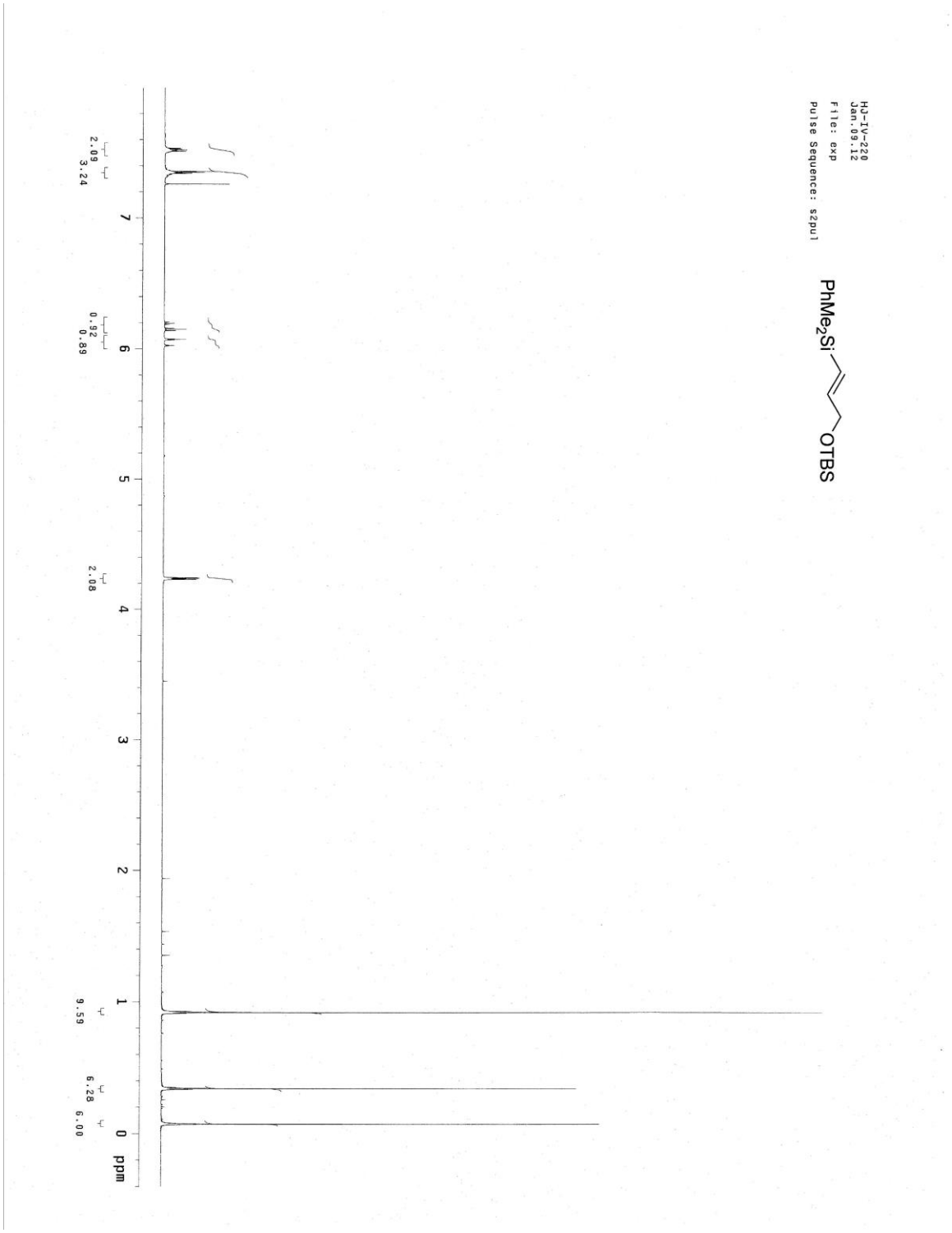
OMe
O
ppm
7
6
5
4
3
2
1
1.91
2.85
0.93
0.91
2.83
2.03
2.09
2.09
6.00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Jan.09.12
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OTBS
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3.24
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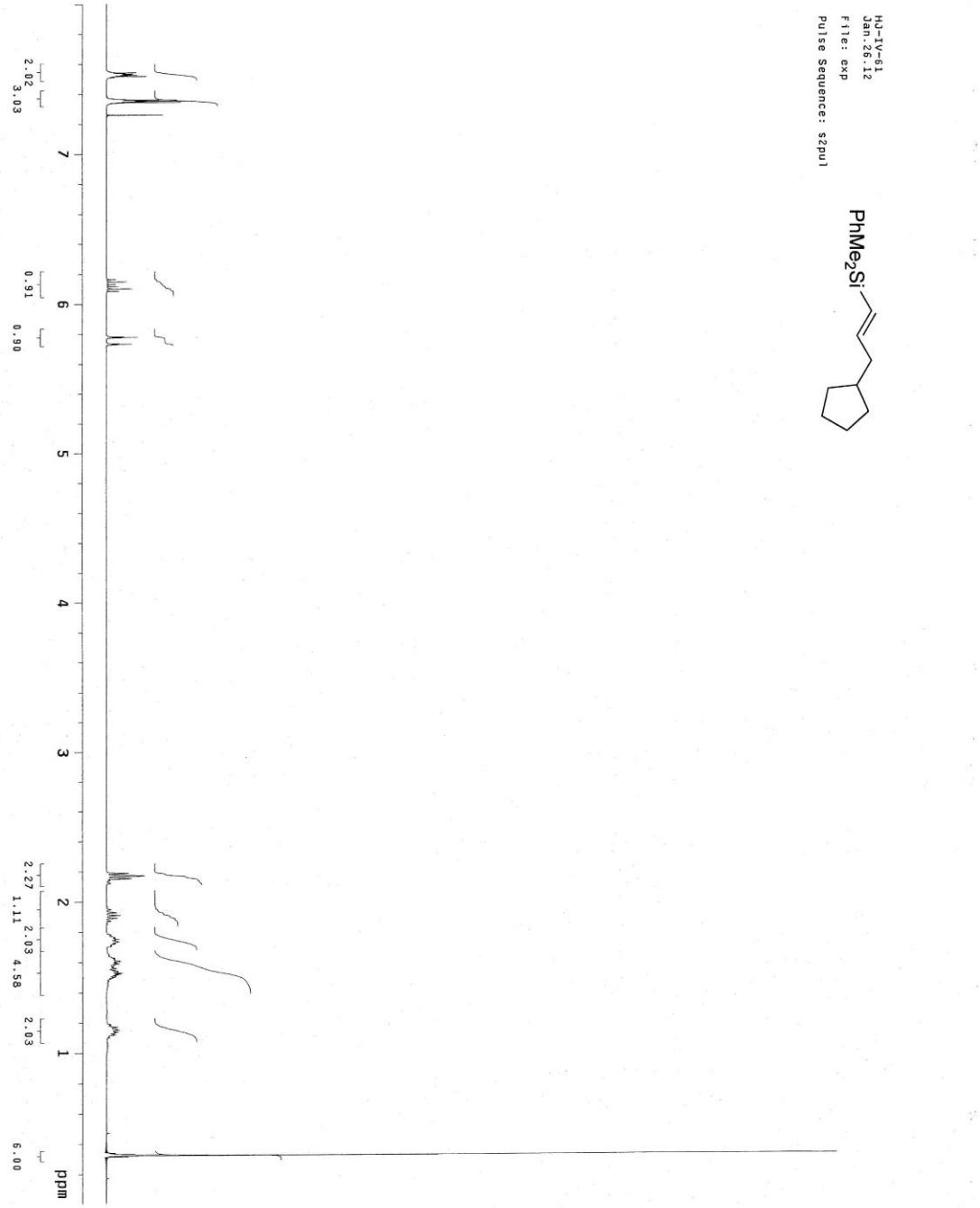
2.08
9.59
6.28
6.00
7
6
5
4
3
2
1
0
ppm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Jan.26.12
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Pulse Sequence: s2pul
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3.03
0.91
0.90
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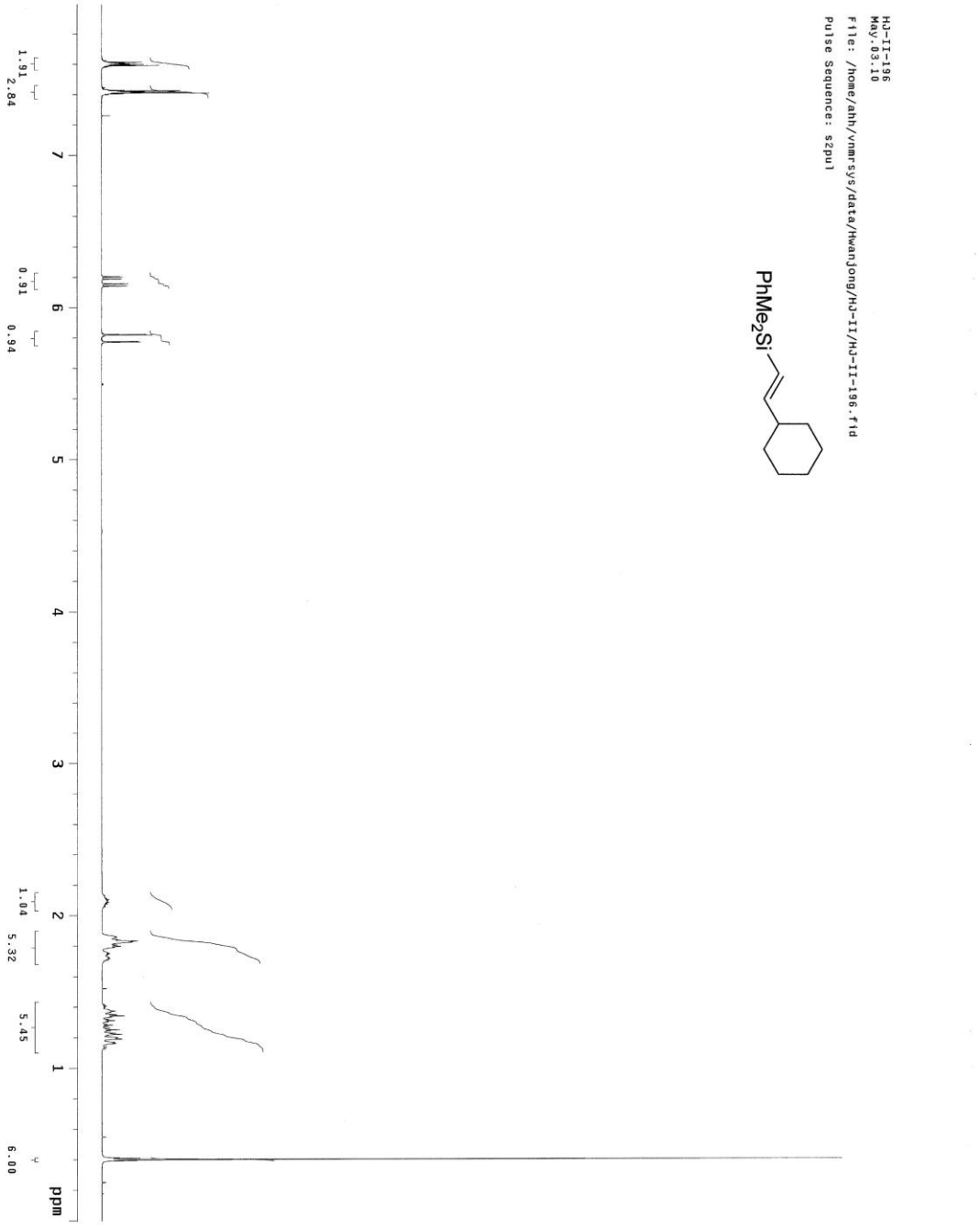
1.11
2.03
4.58
2.03
6.00
7
6
5
4
3
2
1
ppm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May.03.10
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Pulse Sequence: s2pul
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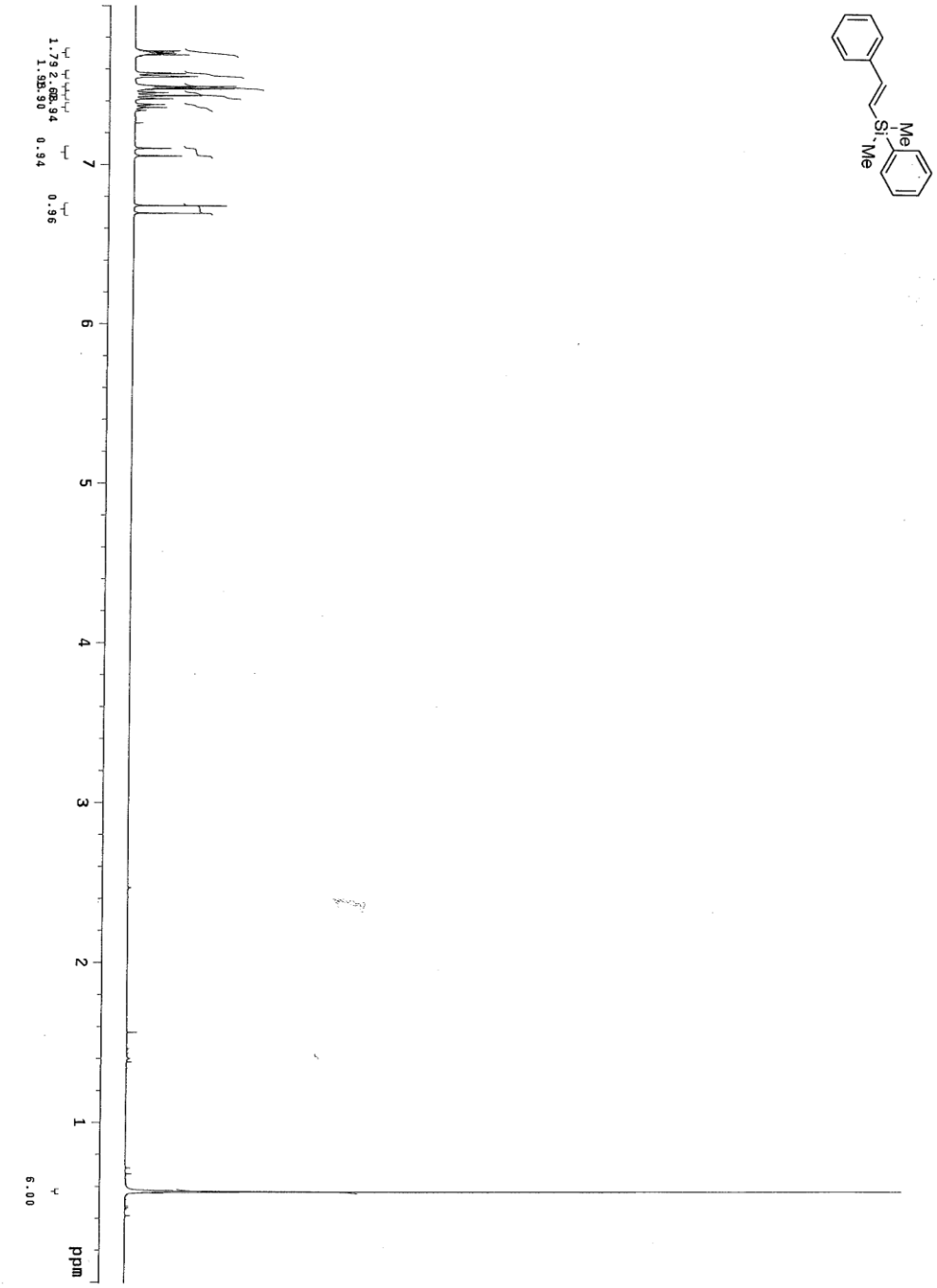
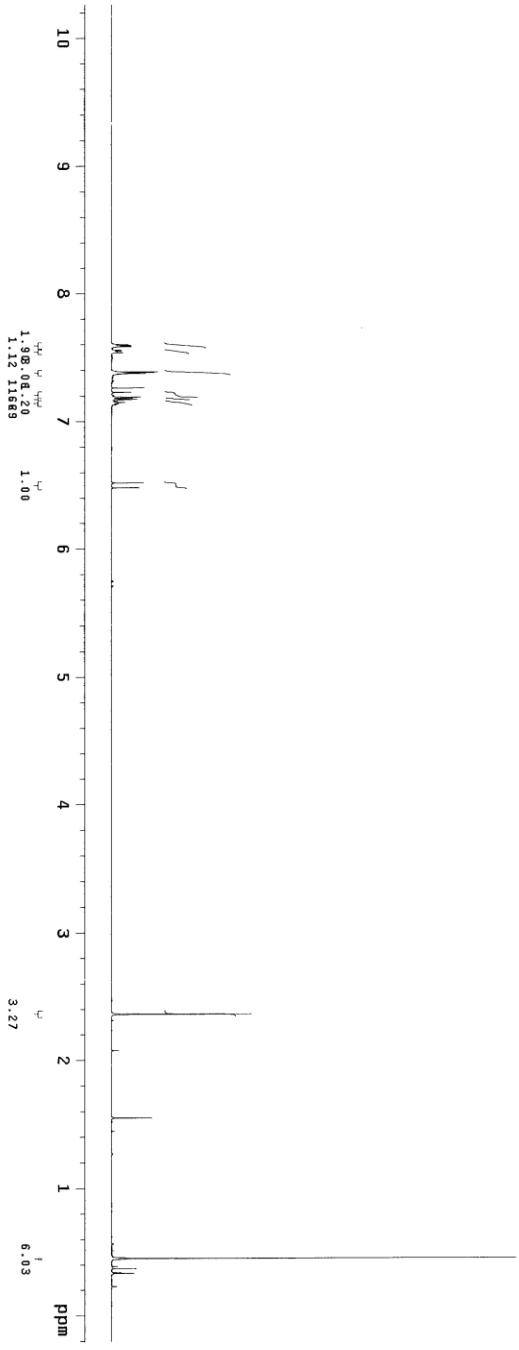
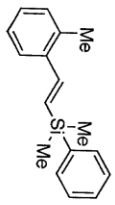
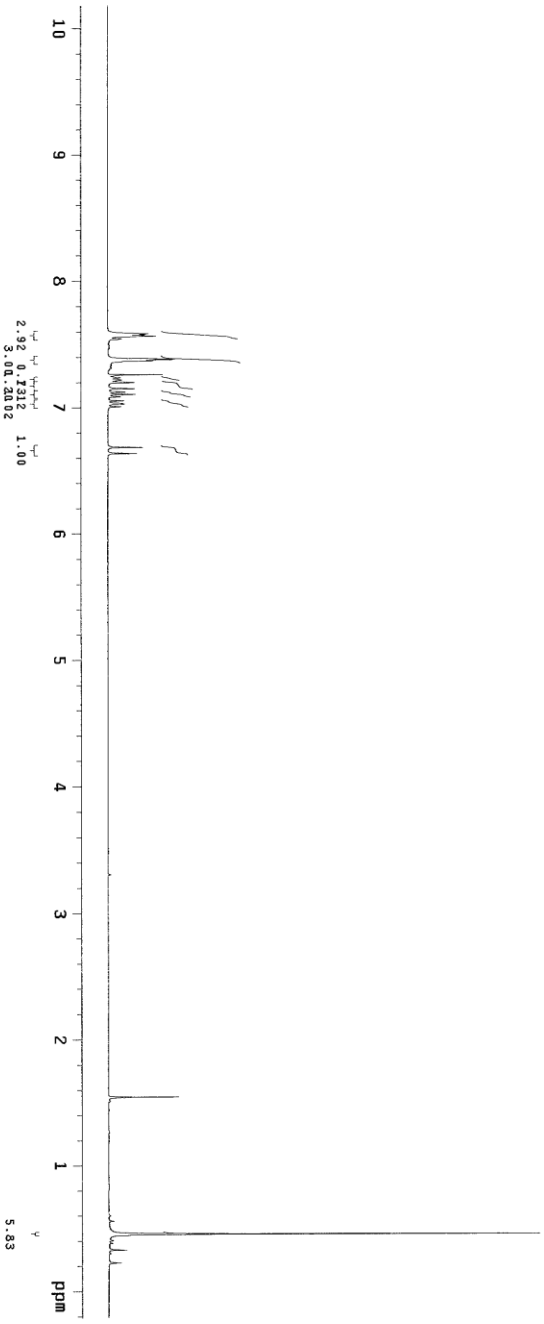
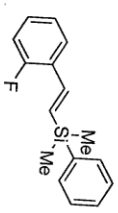
2.84
0.91
0.94
1.04
5.32
5.45
6.00
ppm

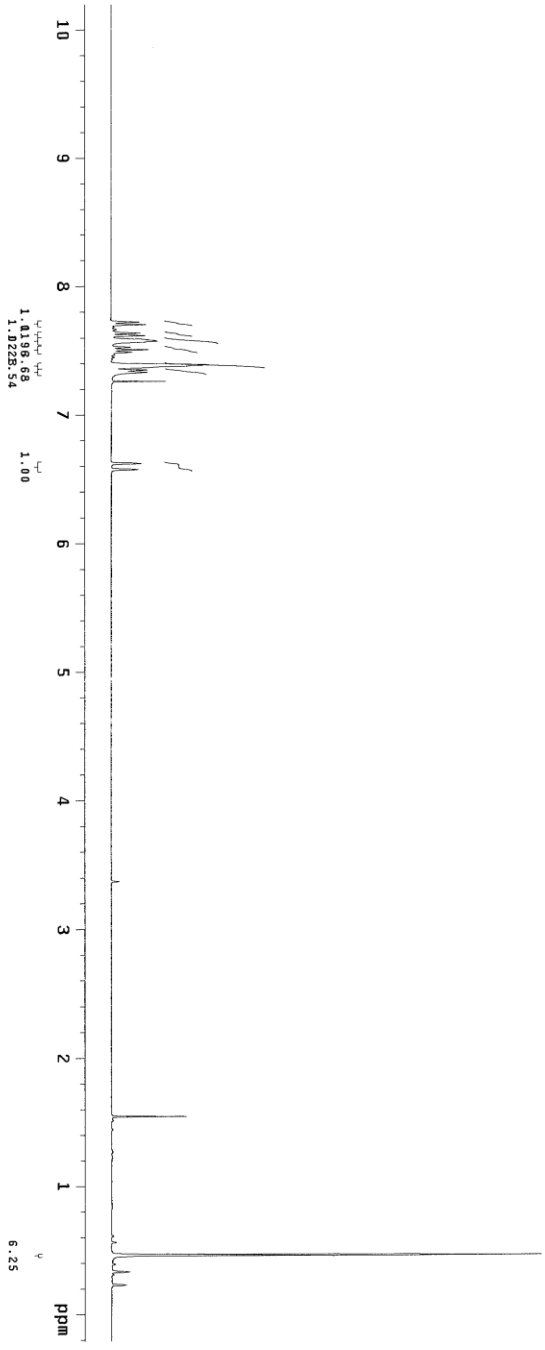

Me
Si
Me
1.79
2.68
2.94
1.93
5.90
0.94
0.96
7
6
5
4
3
2
1
ppm
6.00

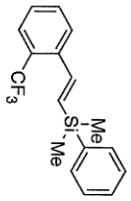

10
9
8
7
6
5
4
3
2
1
ppm
1.98
8.04
4.20
1.12
11.69
1.00
3.27
6.03

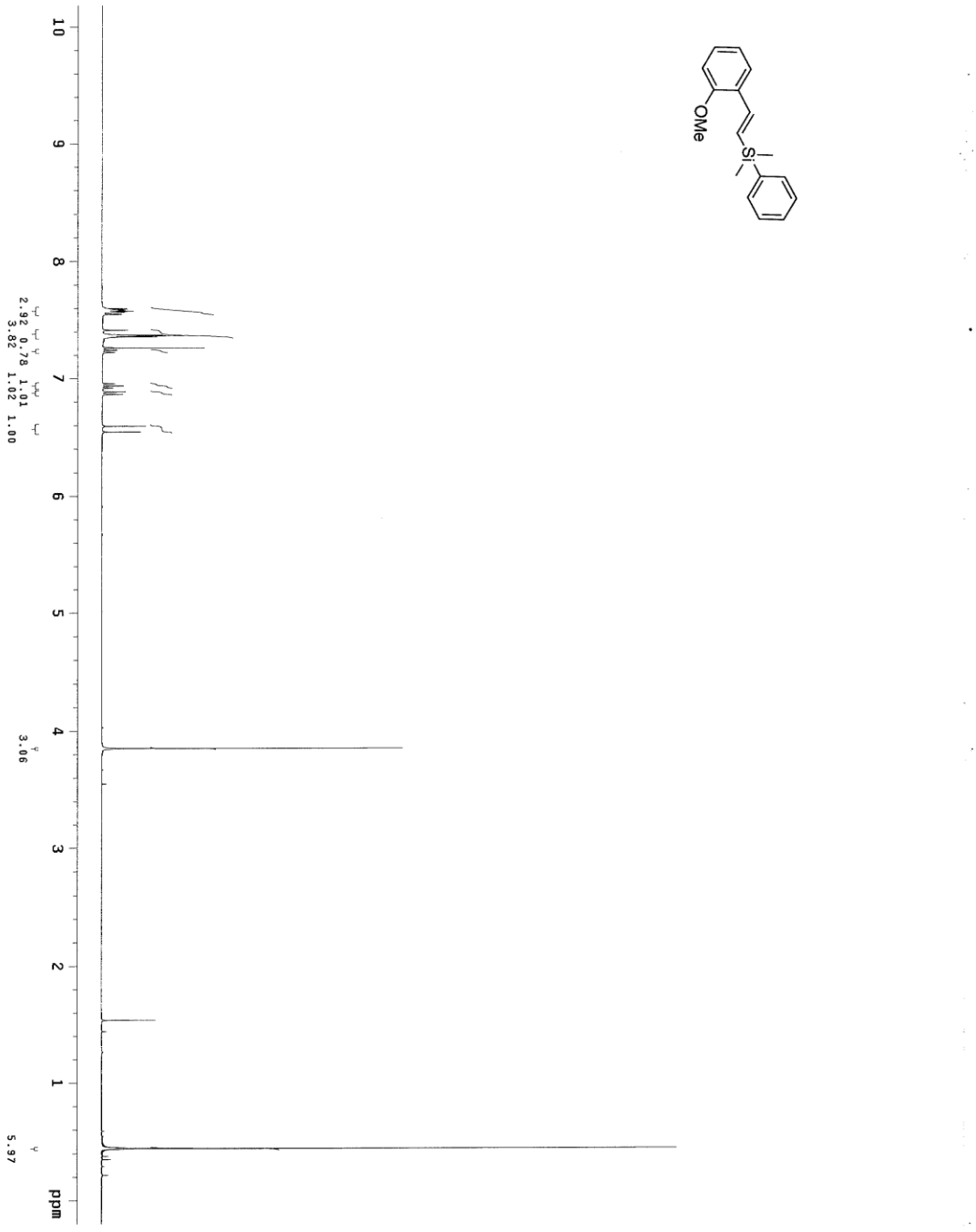

Me
Me
Si
Me

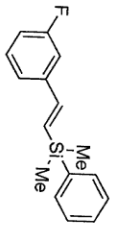

10
9
8
7
6
5
4
3
2
1
ppm
5.83
1.00
2.92
0.73
12
3.00
2.00
2

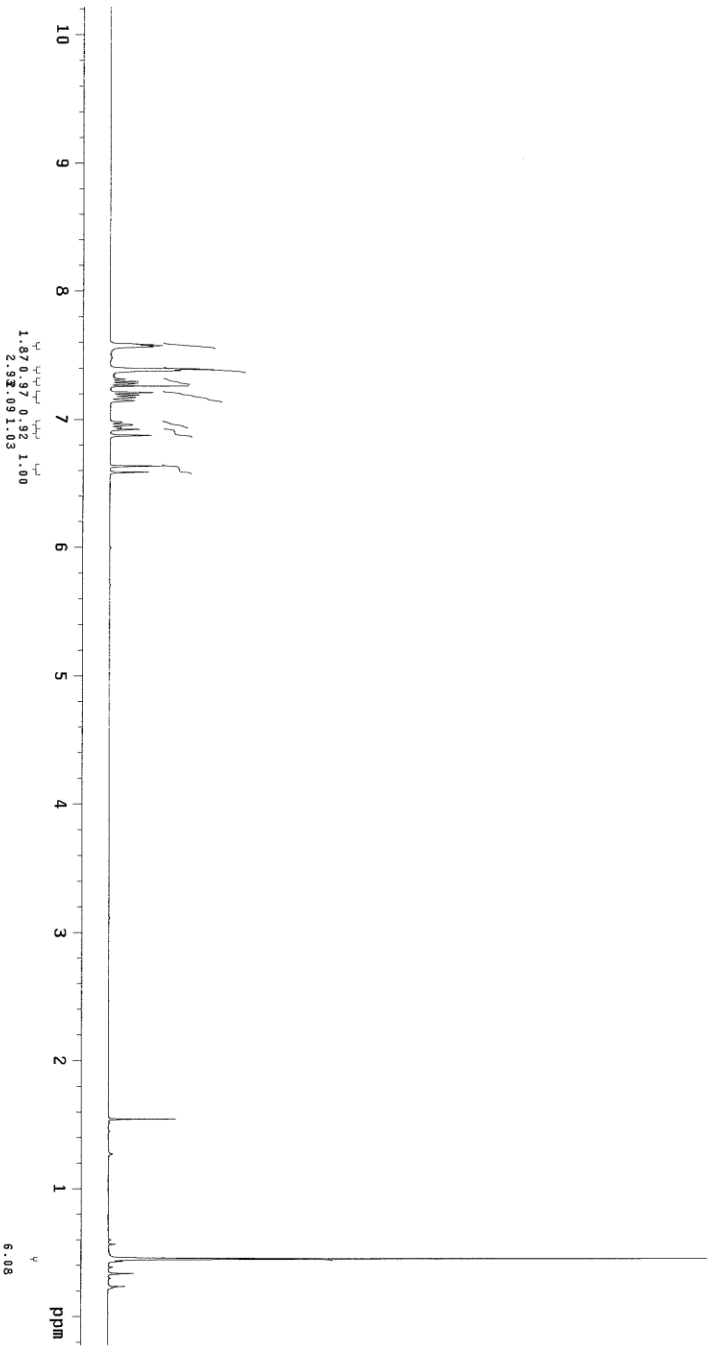

F
Si
Me
Me
Me

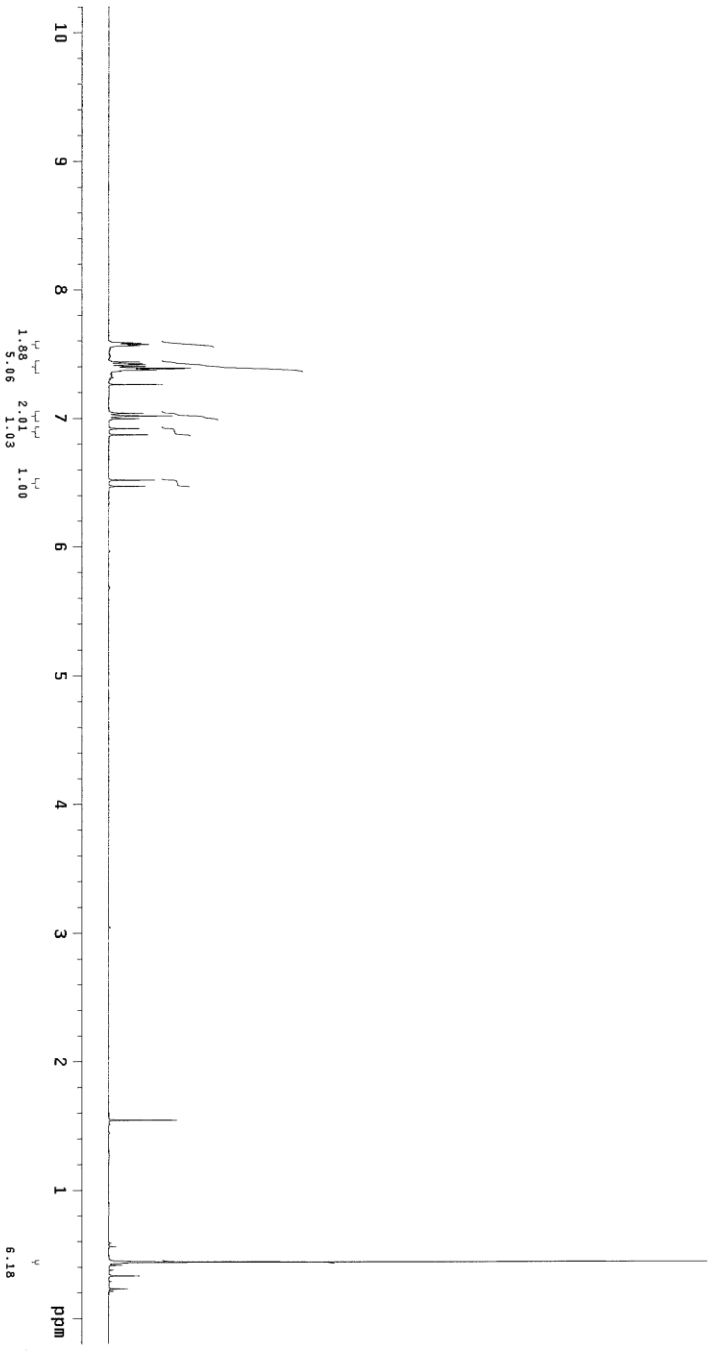

10
9
8
7
6
5
4
3
2
1
ppm
1.00
6.25

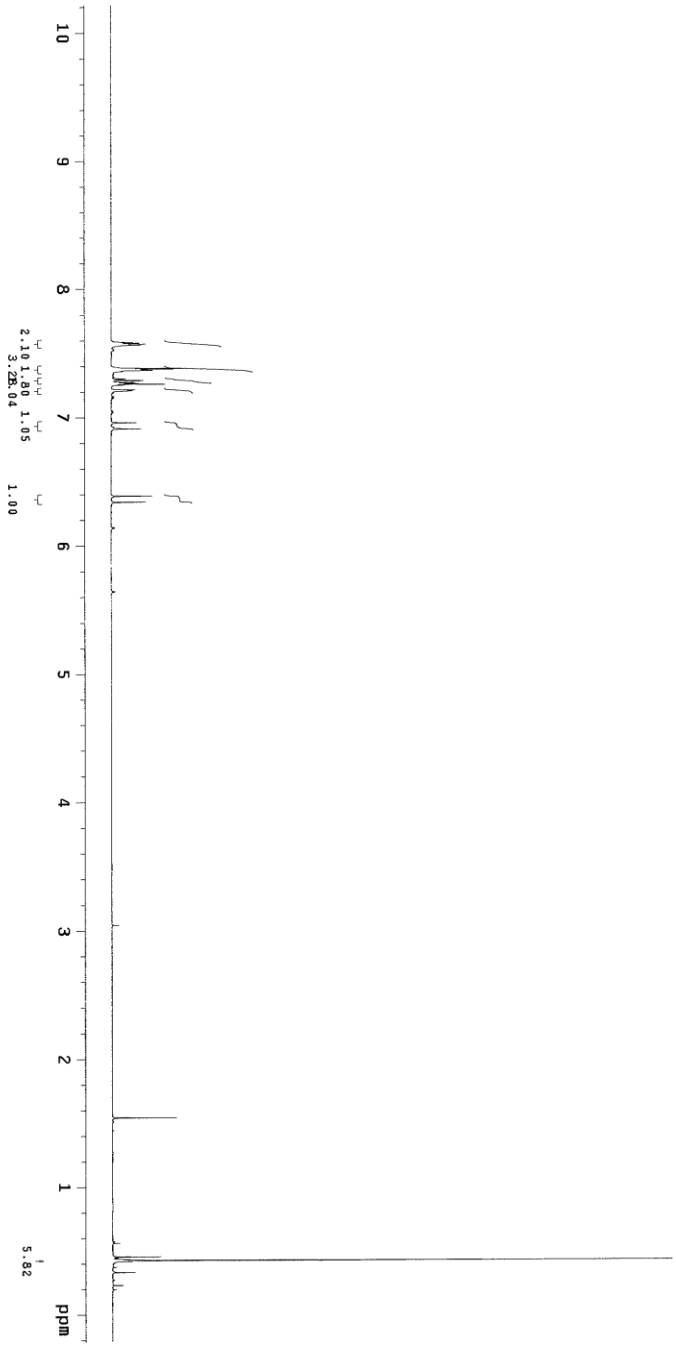

CF3
Si
Me
Me

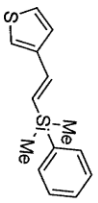

OMe
Si
10
9
8
7
6
5
4
3
2
1
ppm
2.92
0.78
1.01
3.82
1.02
1.00
3.06
5.97

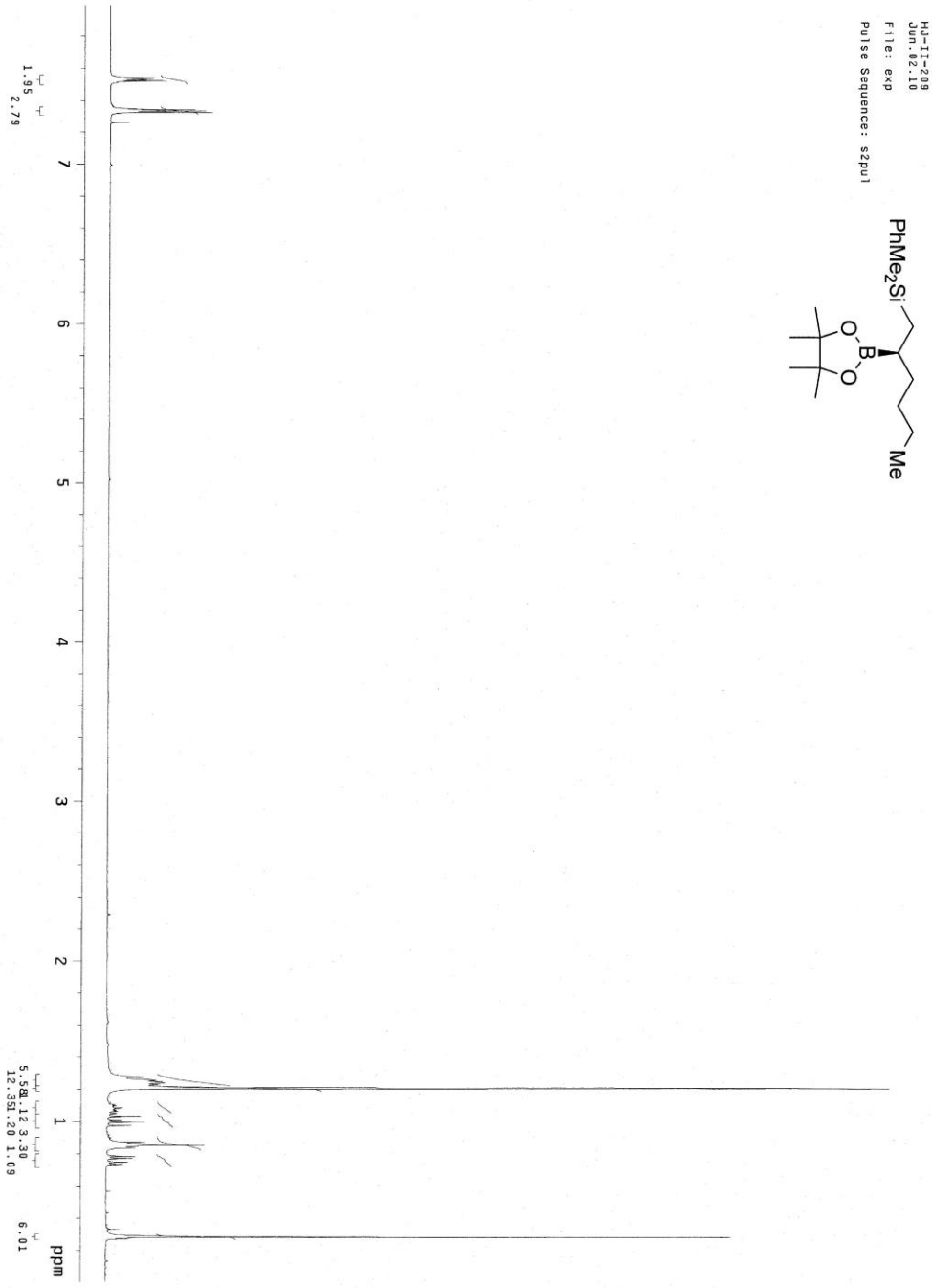

F
Me
Si
Me

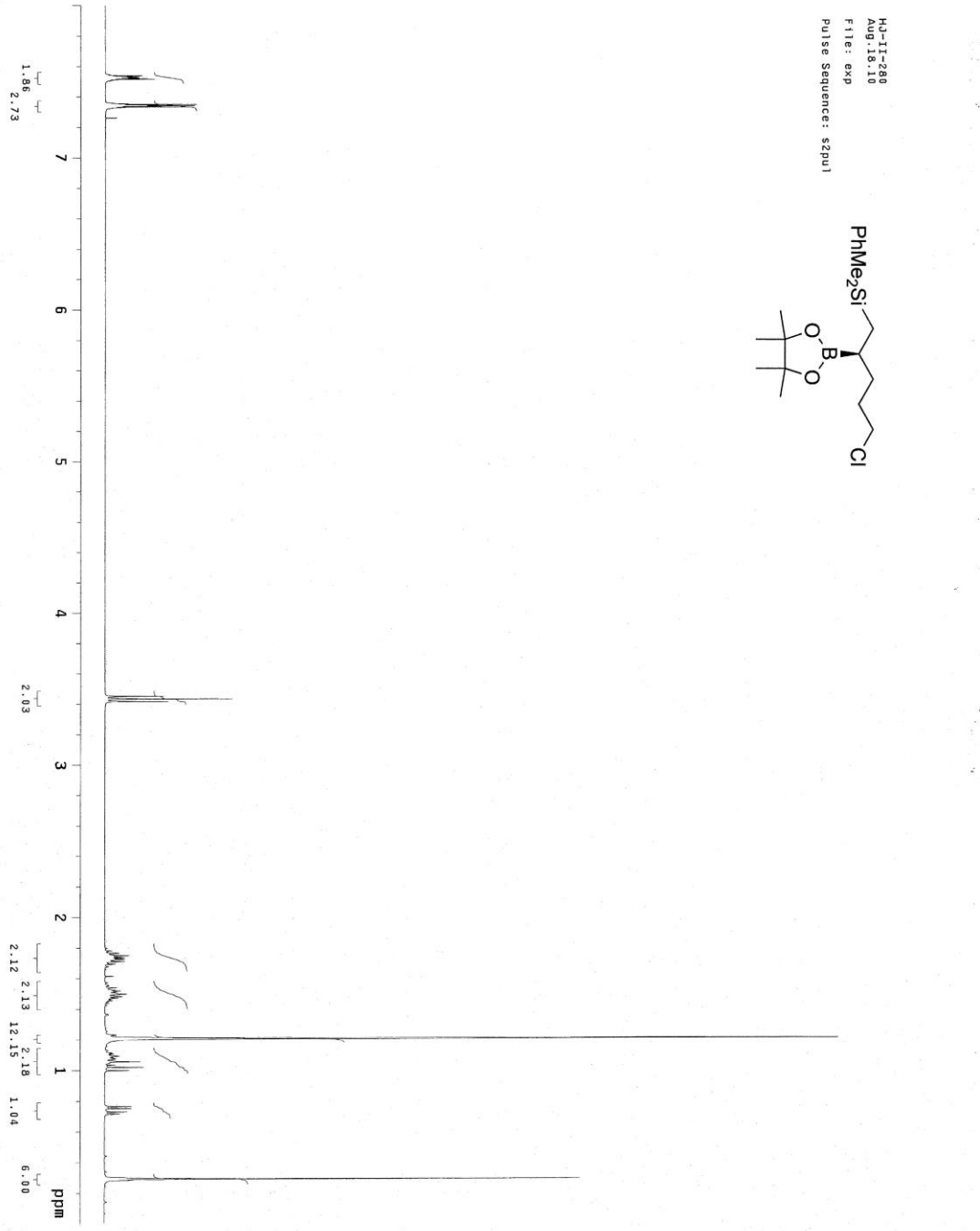

10
9
8
7
6
5
4
3
2
1
ppm
1.87 0.97 0.92 1.00
2.93 2.09 1.03
6.08

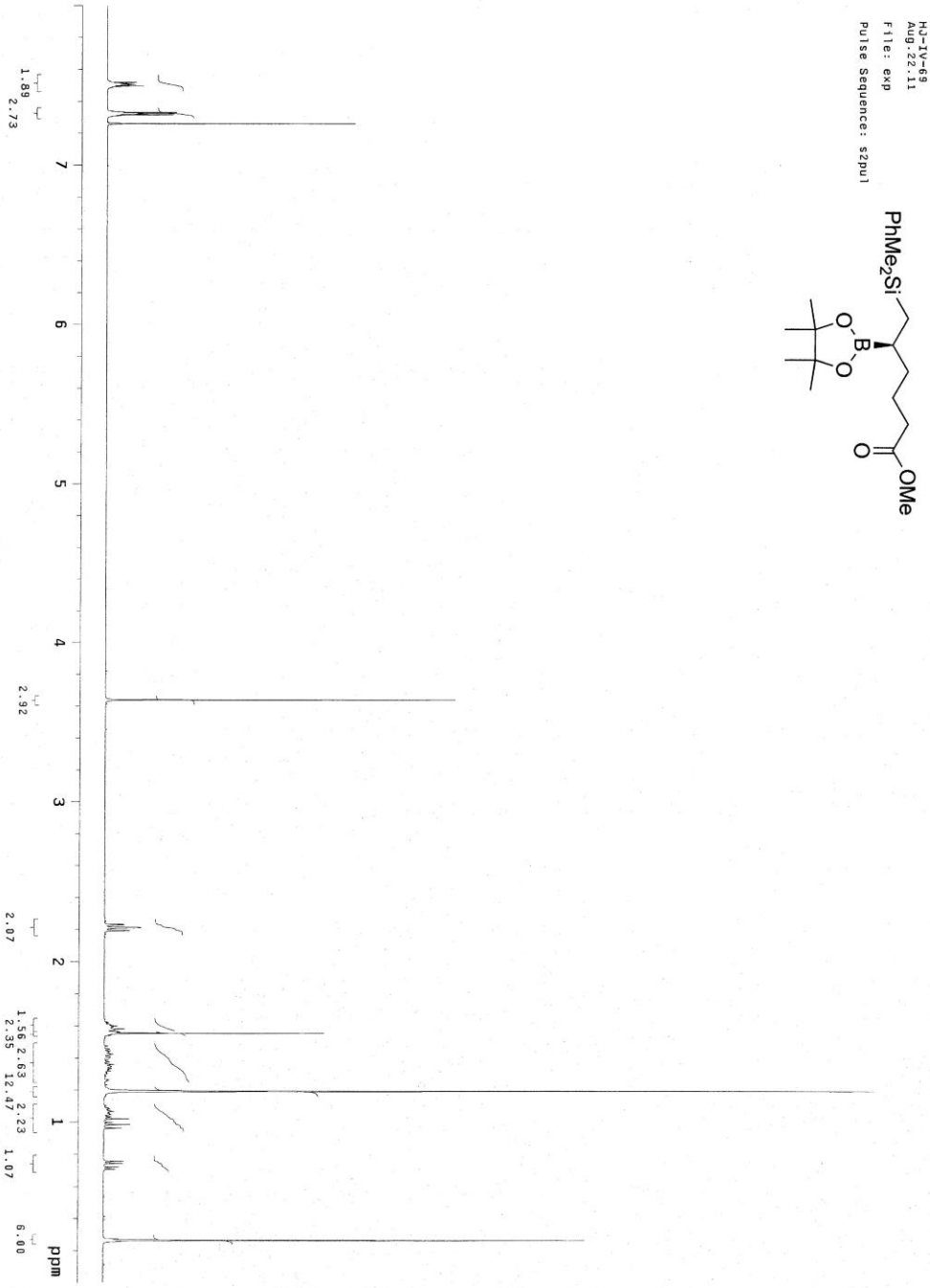

F
Me
Si
Me
10
9
8
7
6
5
4
3
2
1
ppm
1.88
5.06
2.01
1.03
1.00
6.18


10
9
8
7
6
5
4
3
2
1
ppm
2.10
1.80
1.05
3.22
2.04
1.00
5.82


S
Me
Si
Me


HJ-II-209
Jun.02.10
File: exp
Pulse Sequence: s2pul
PhMe2Si
Me
O
B
O
O
1.95
2.79
5.58
12.35
12.30
1.20
1.09
6.01
7
6
5
4
3
2
1
ppm


HJ-II-280
Aug.16.10
File: exp
Pulse Sequence: s2pul
PhMe2Si
O
B
O
Cl
ppm
1.86
2.73
2.03
2.12
2.13
12.15
2.18
1.04
6.00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Aug.22.11
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Pulse Sequence: s2pul
PhMe2Si
OMe
O
B
O
O
ppm
7
6
5
4
3
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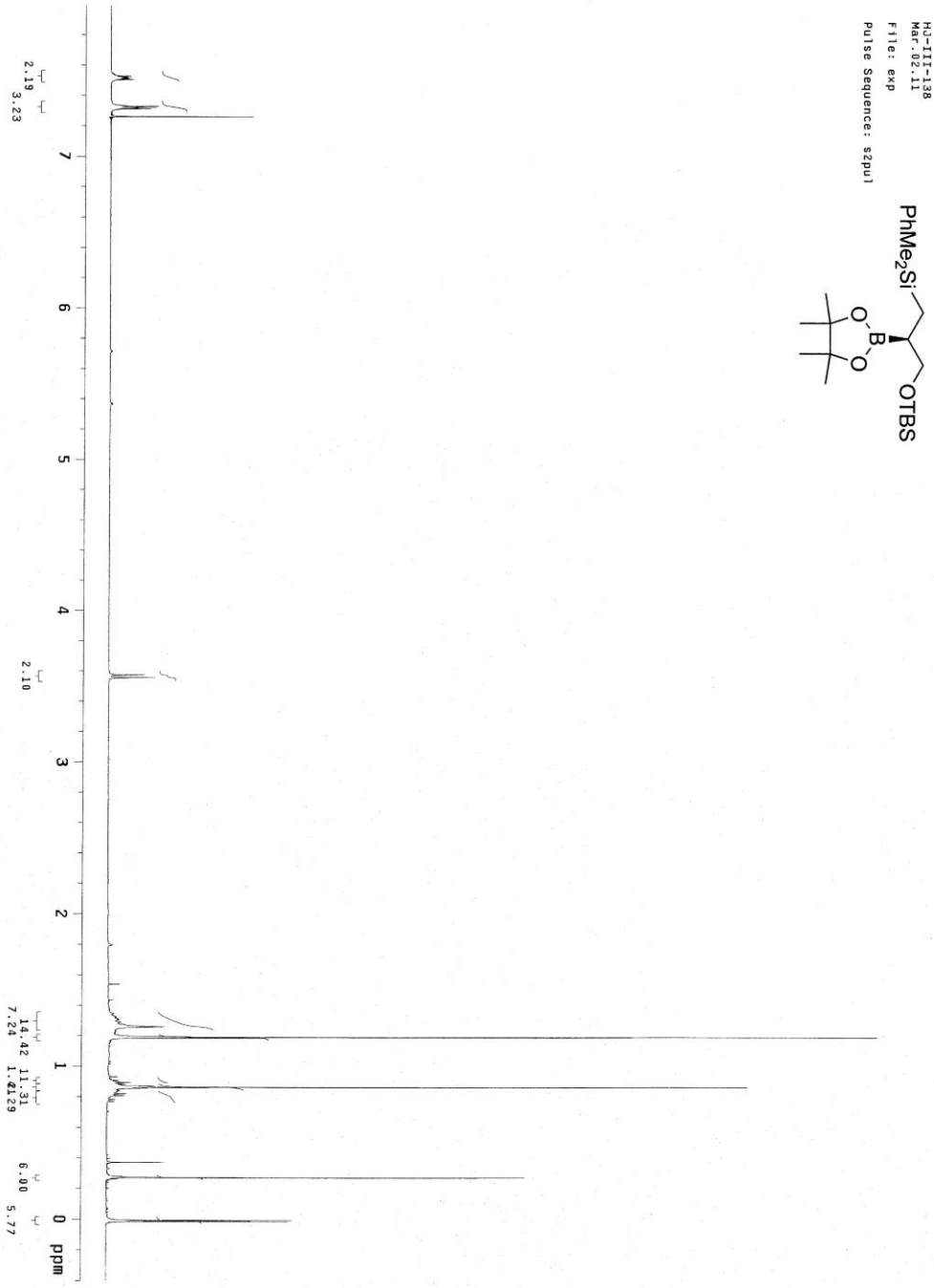
2.63
2.23
2.35
12.47
1.07
6.00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Mar.02.11
File: exp
Pulse Sequence: s2pul
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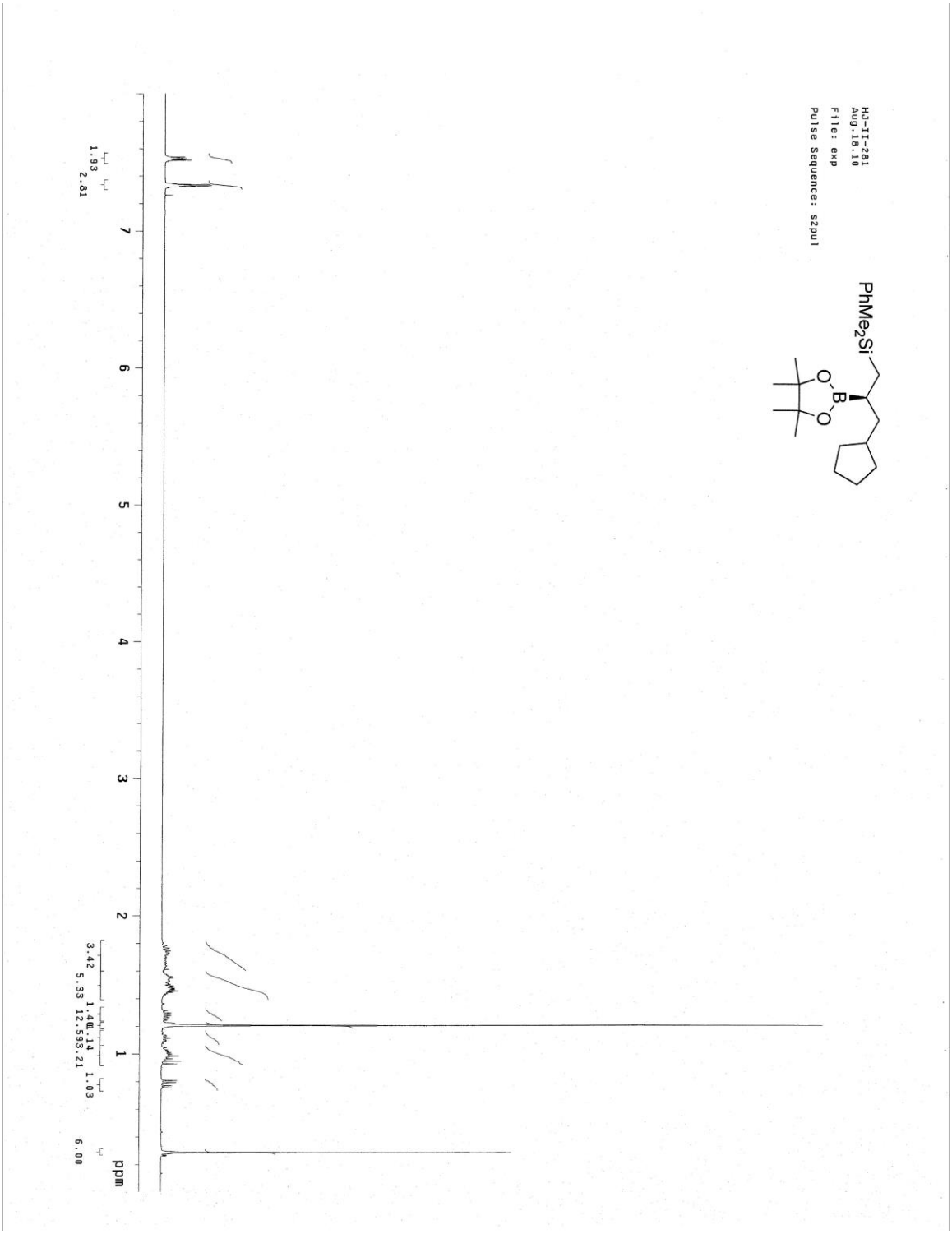
OTBS
B
O
O
7
6
5
4
3
2
1
0 ppm
2.19
3.23
2.10
14.42
11.31
7.24
1.41
29
6.00
5.77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Aug-18-10
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O
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1.40
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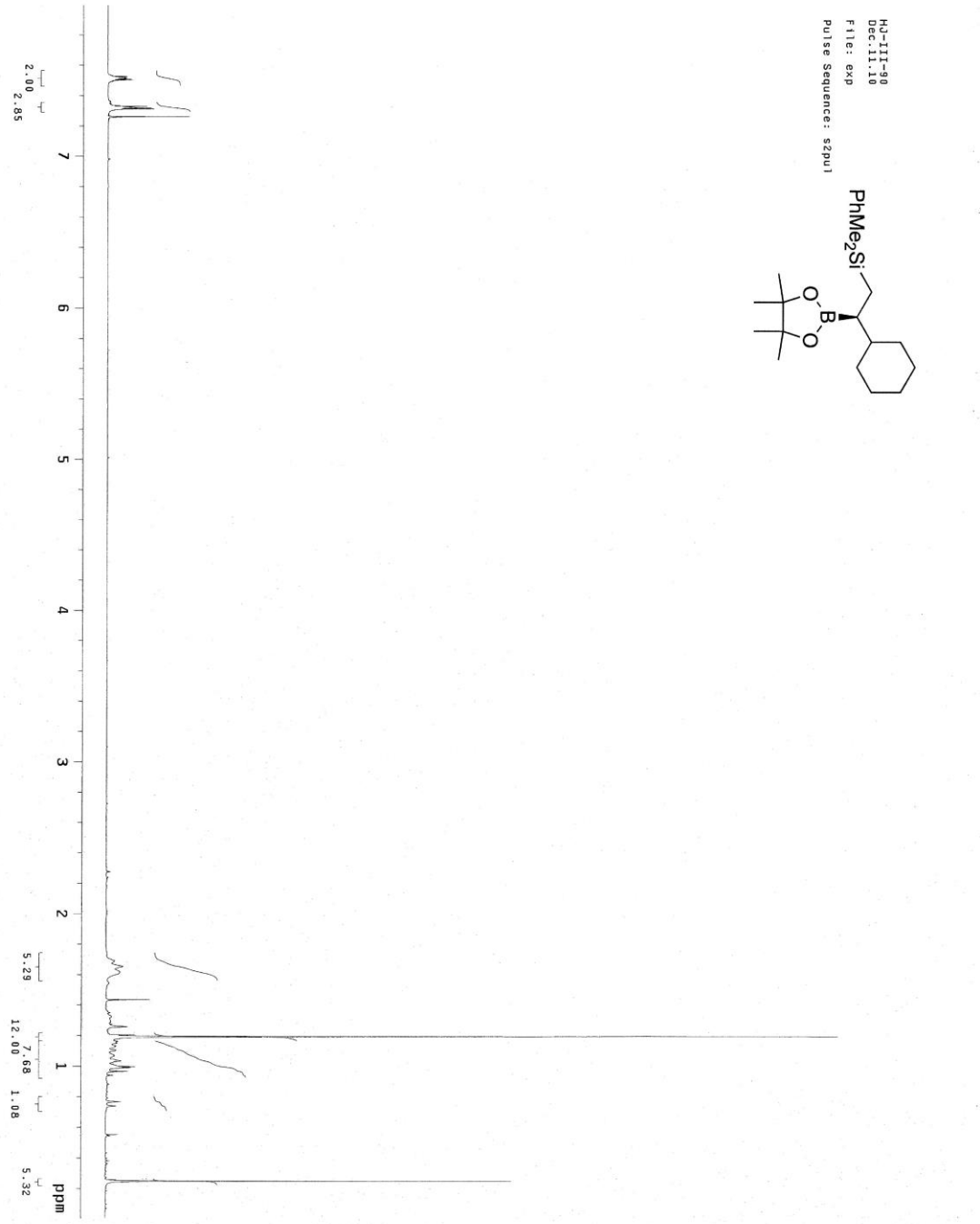
5.33
12.59
3.21
1.03
6.00


HJ-III-90
Dec-11-10
File: exp
Pulse Sequence: s2pul
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O
B
O
O
7
6
5
4
3
2
1
ppm
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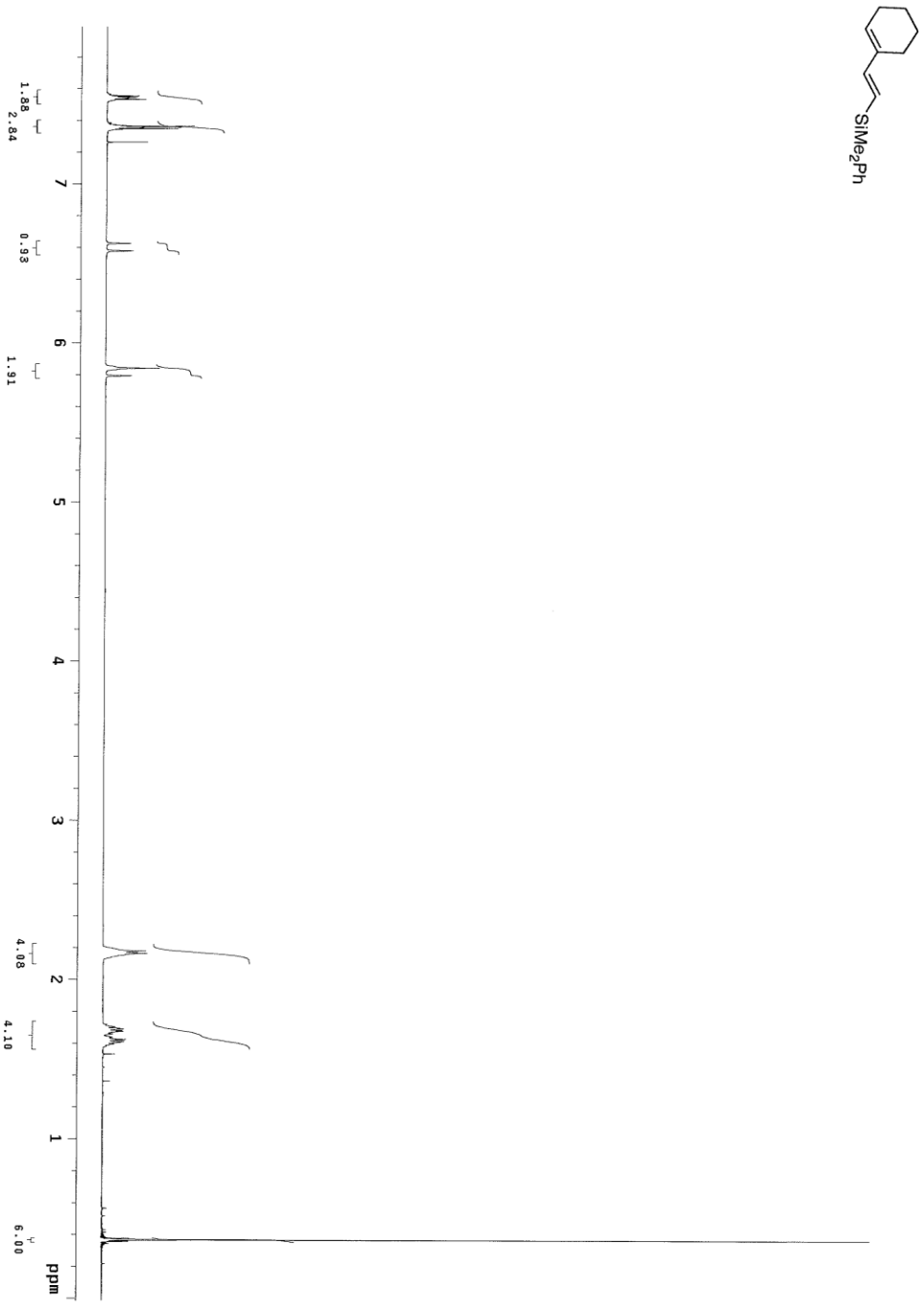
2.85
5.29
12.00
7.68
1.08
5.32


SiMe2Ph
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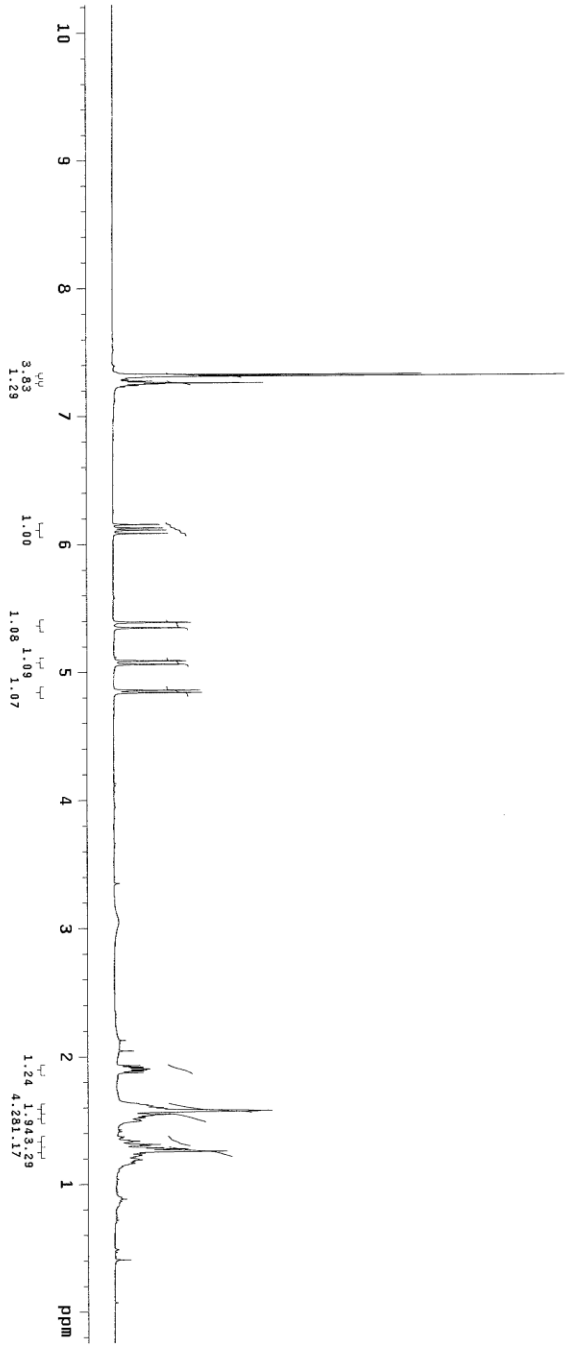
1.91
4.08
4.10
6.00
7
6
5
4
3
2
1
ppm


10
9
8
7
6
5
4
3
2
1
ppm
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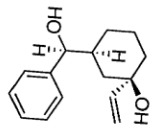
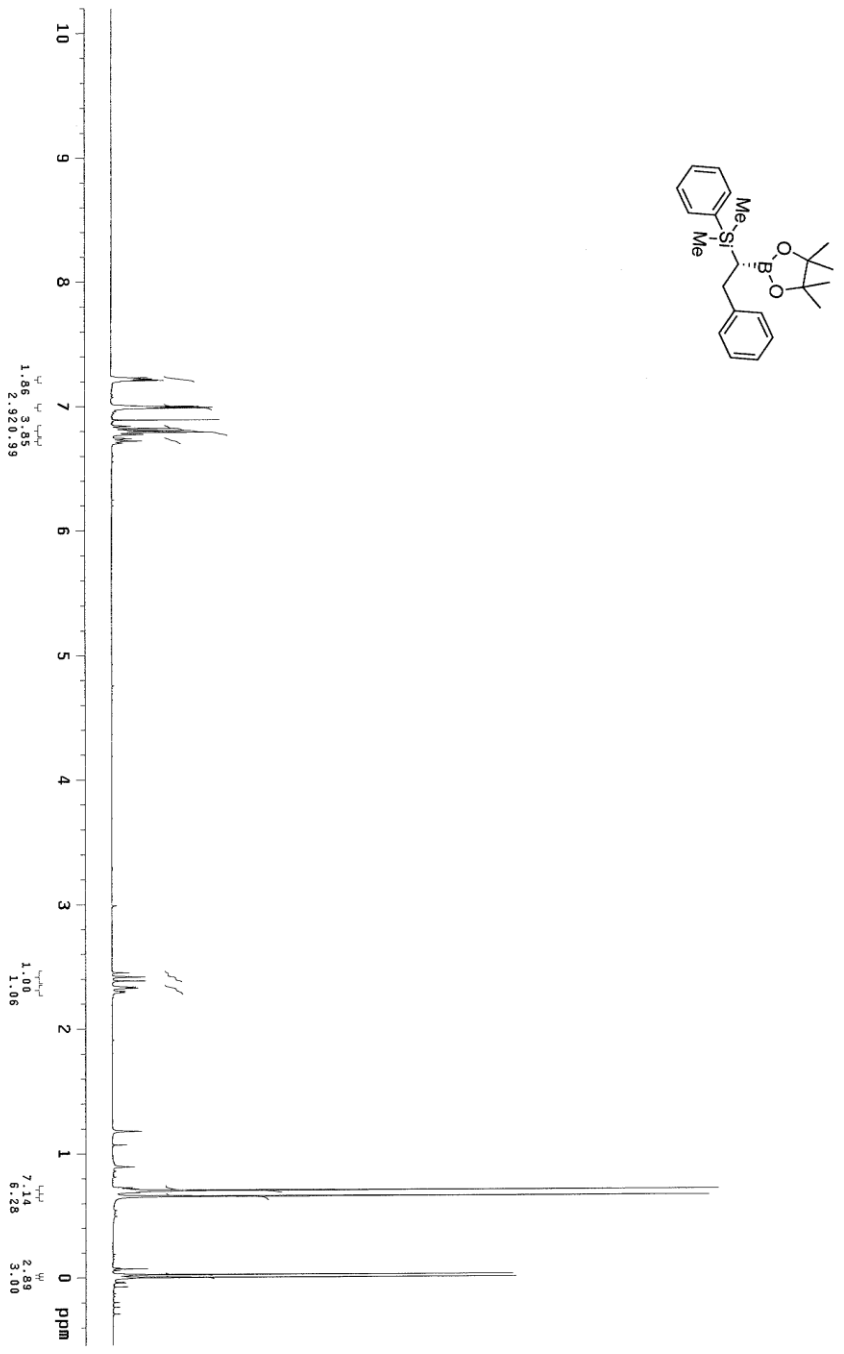
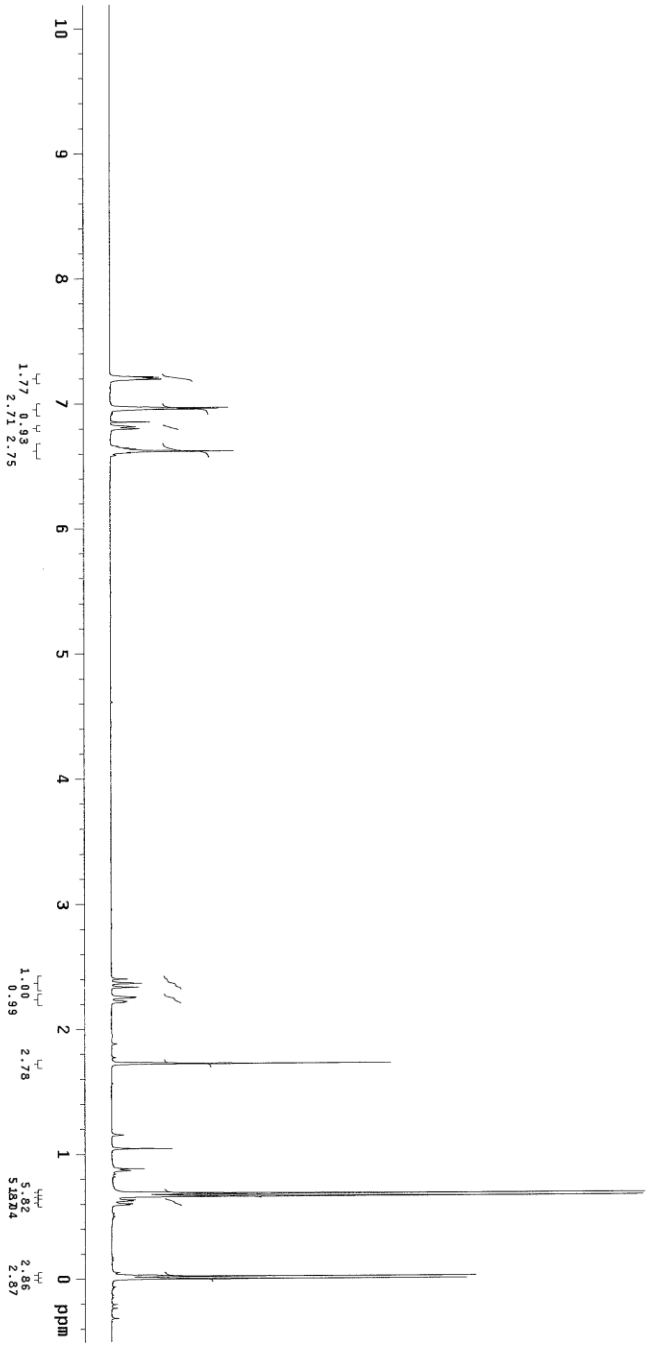
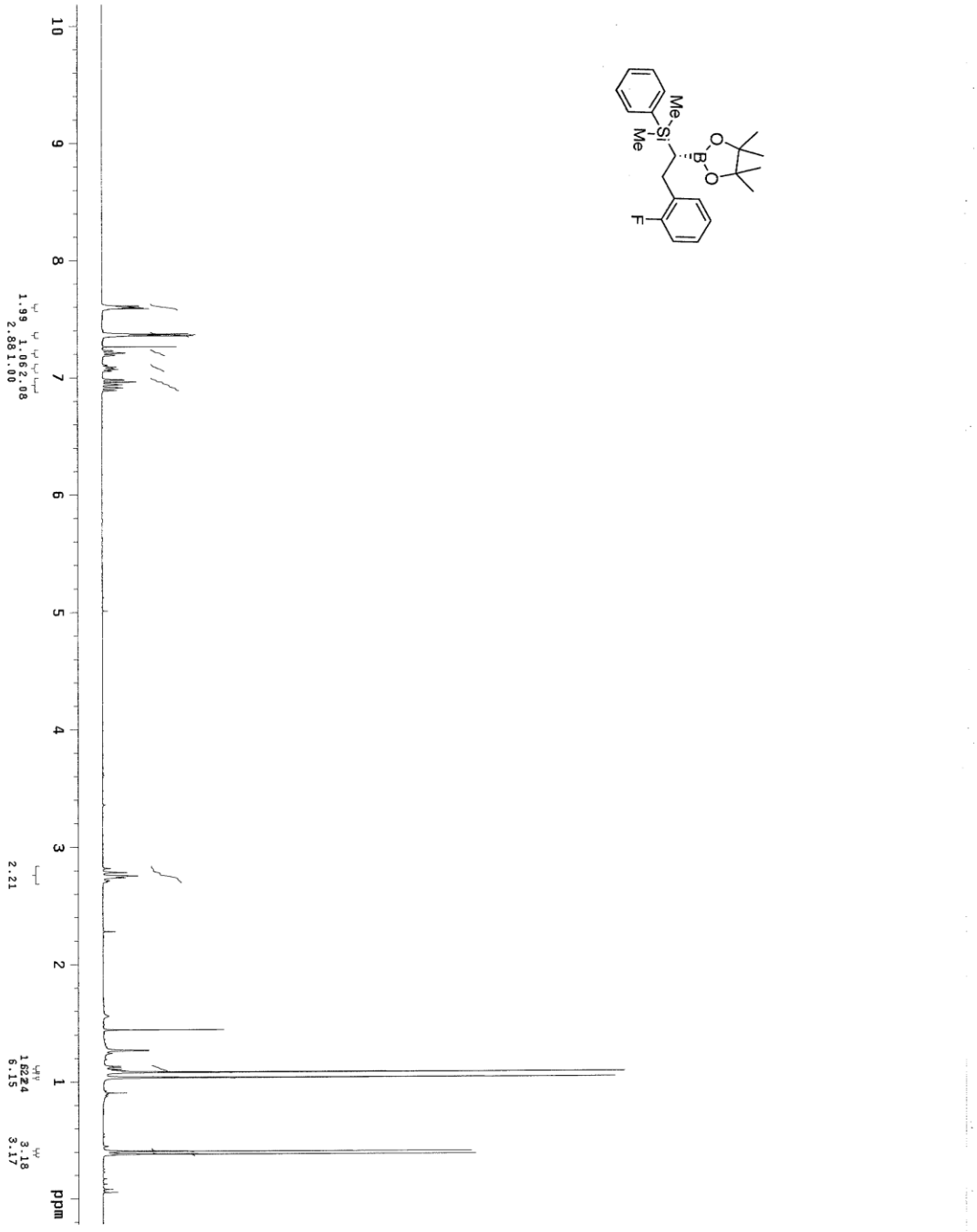
1.29
1.00
1.08
1.09
1.07
1.24
1.94
3.29
4.28
1.17


HO
H
H
OH


Me
Si
Me
B
O
O
10
9
8
7
6
5
4
3
2
1
0
ppm
1.86
3.85
2.92
0.99
1.00
1.06
7.14
6.28
2.89
3.00


10
9
8
7
6
5
4
3
2
1
0 ppm
1.77
0.93
2.71
2.75
1.00
0.99
2.78
5.82
5.84
2.86
2.87
Me
Si
Me
B
O
O
Me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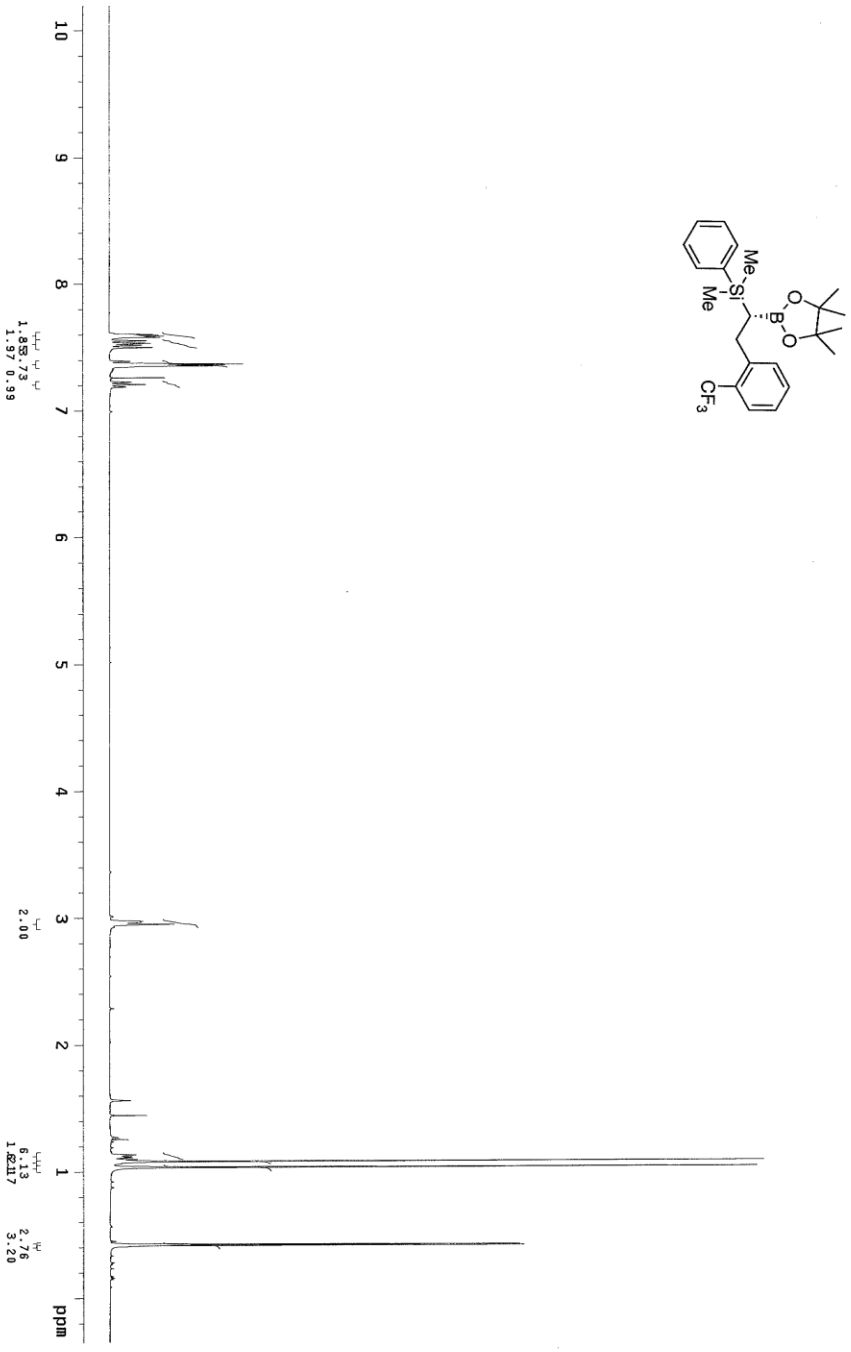
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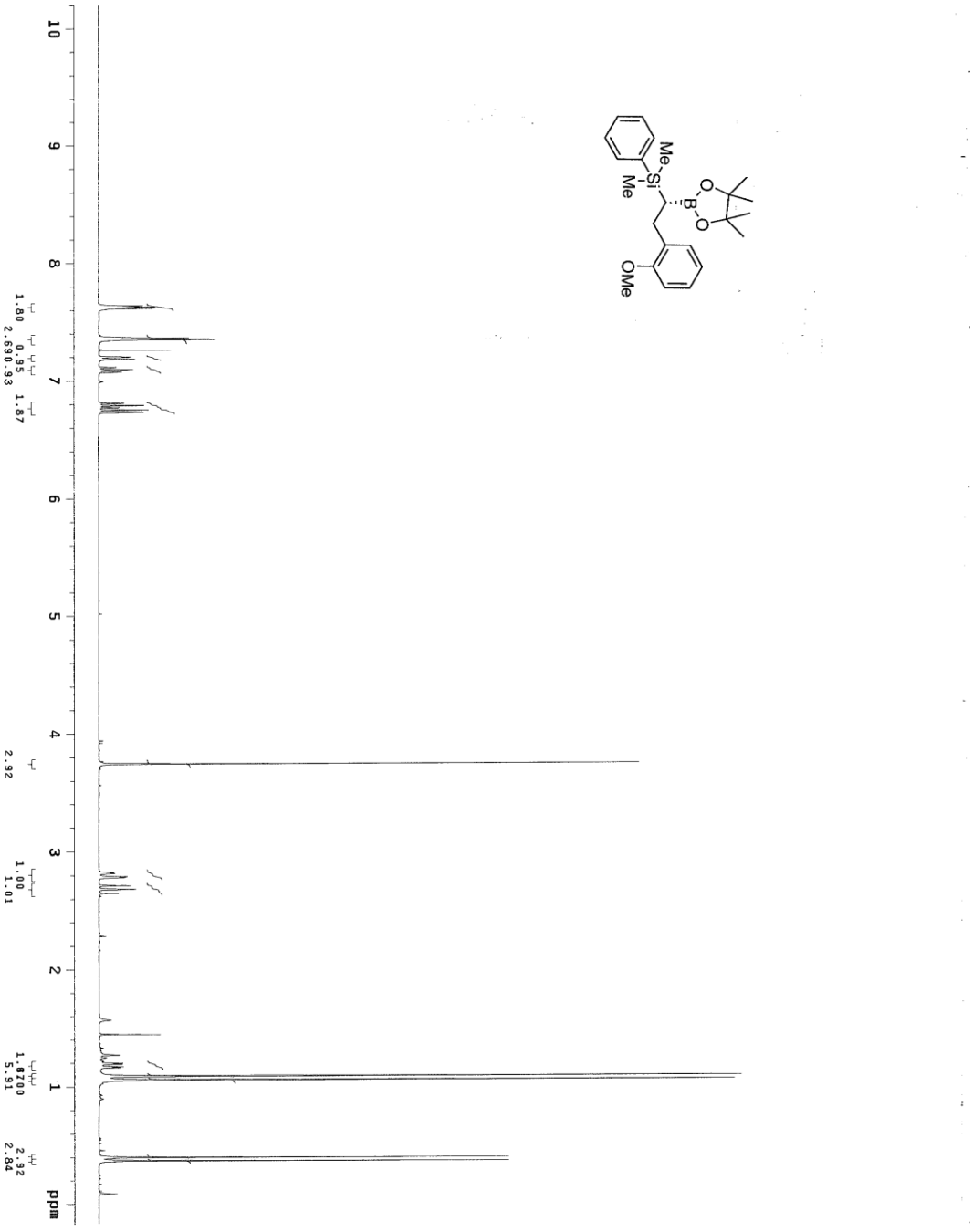
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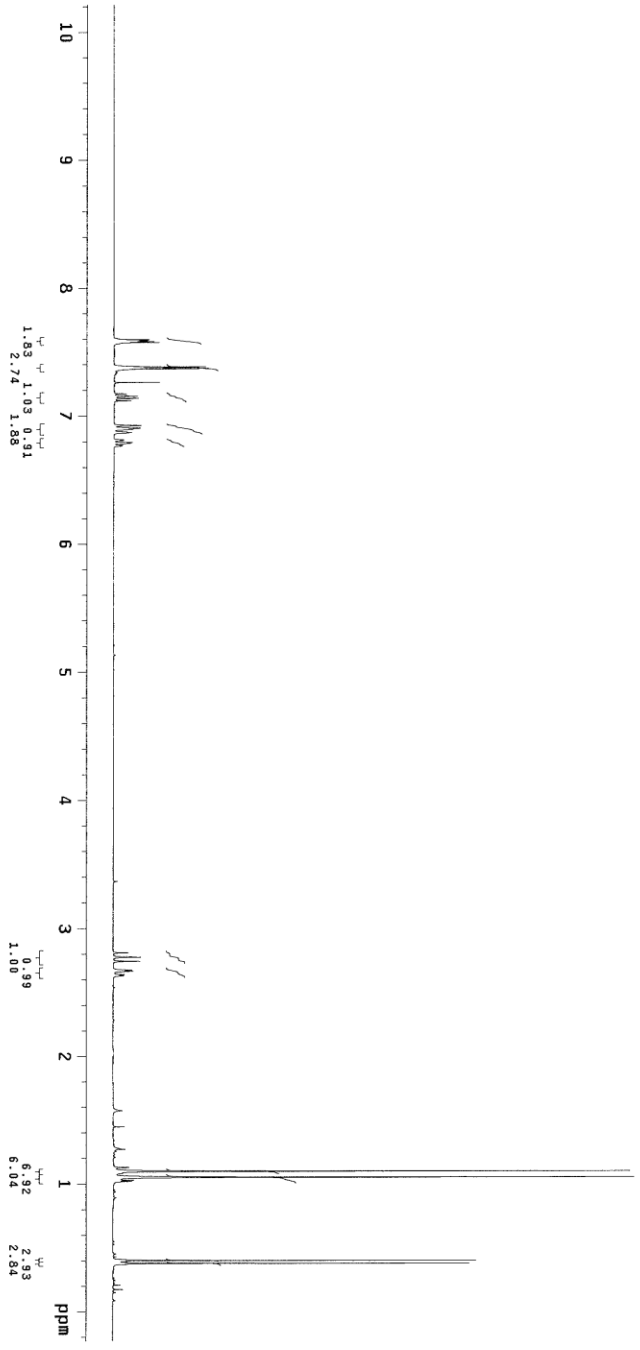
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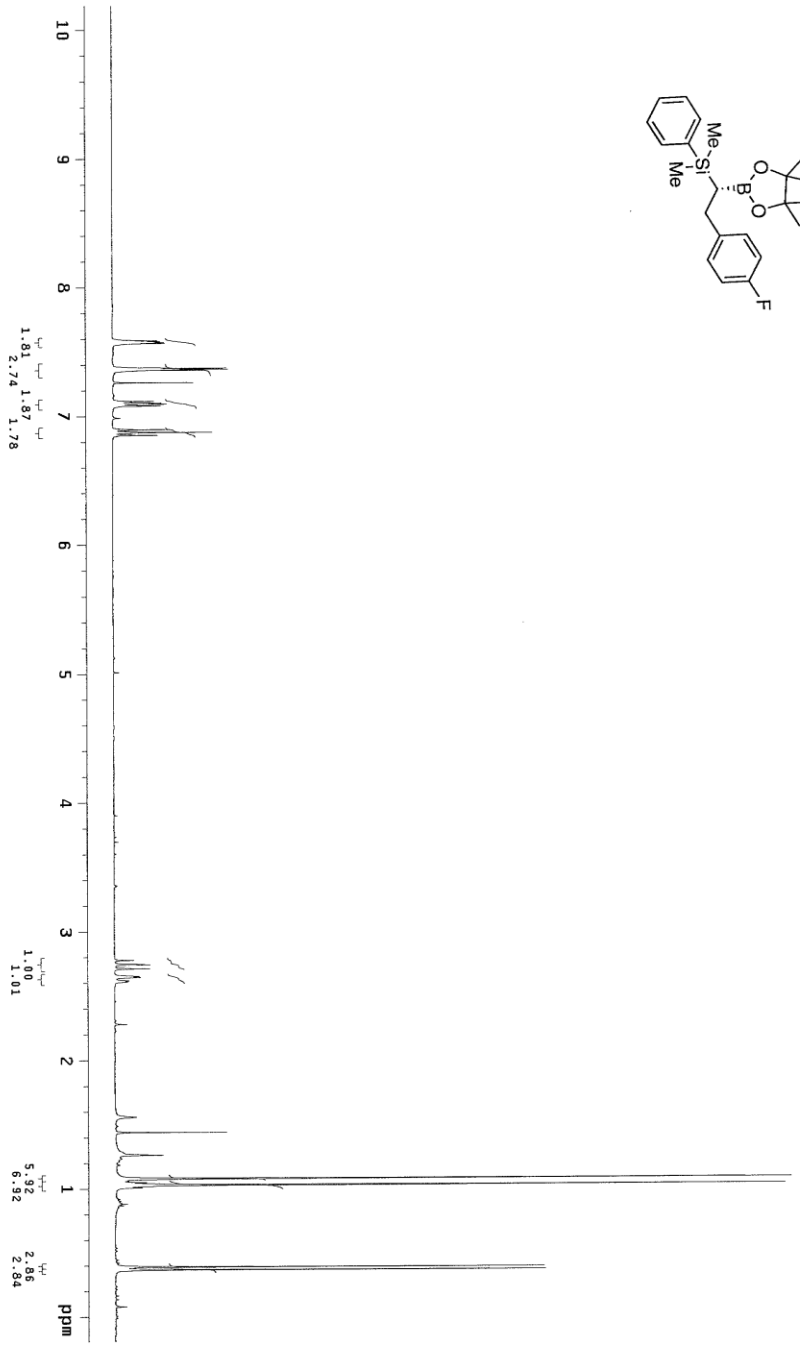
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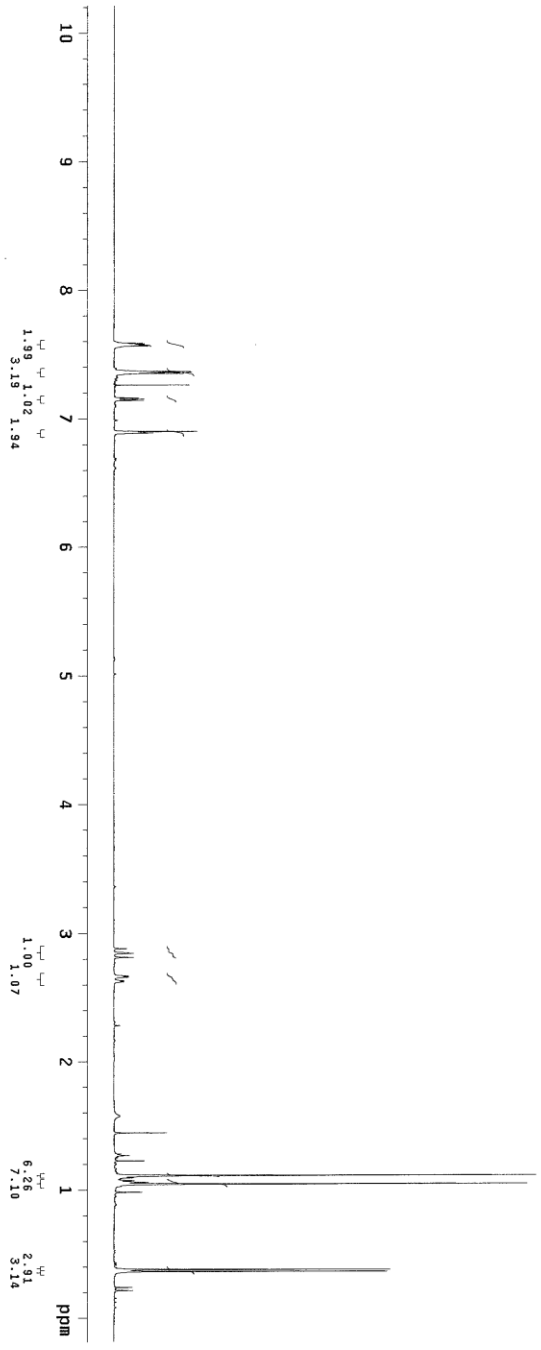
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1.94
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3.14

## *Chapter Four*

# Site- and Enantioselective NHC–Cu-Catalyzed Protoboryl Additions to Disubstituted Allenes: Access to Enantiomerically Enriched Alkenylborons

### *4.1. Introduction*

Allylmetal complexes have been utilized widely in organic chemistry field.[1] Nucleophilic additions of these nucleophilic agents to electrophiles such as carbonyl- and imine-containing compounds are powerful methods of chemical synthesis. Enantioselective protonation[2] of allylmetal species, however, are rare.[3] In 2013, site-selective NHC–Cu-catalyzed protoboration of monosubstituted allenes was reported by our group.[4] In this transformation, with a sterically demanding NHC–Cu complex, Cu–B is inserted into the less hindered olefin of the allene to generate an allylcopper bearing a B(pin) unit at the center carbon, which is protonated γ-selectively by MeOH to generate 1,1-disubstituted alkenylboron. Since protoboration of 1,1-disubstituted allene can deliver

(1) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595–5698.
(2) For recent reviews on enantioselective protonations, see: (a) Blanchet, J.; Baudoux, J.; Amere, M.; Lasne, M.-C.; Rouden, J. *Eur. J. Org. Chem.* **2008**, 5493–5506. (b) Mohr, J. T.; Hong, A. Y.; Stoltz, B. M. *Nat. Chem.* **2009**, *1*, 359–369. For a recent relevant report, see: (c) Cheon, C. H.; Kanno, O.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 13248–13251.
(3) (a) Nishimura, T.; Hirabayashi, S.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2556–2557. (b) Sawano, T.; Ou, K.; Nishimura, T.; Hayashi, T. *J. Org. Chem.* **2013**, *78*, 8986–8993.
(4) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417.

alkenylboron containing stereogenic carbon center, we have probed the transformation of 1,1-disubstituted allenes to achieve enantiomerically enriched alkenylboron. The identification of a proper chiral ligand–Cu complex has challenges: (1) Initial copper–boron addition to 1,1-disubstituted allene needs to be highly site selective. (2) The chiral ligand–Cu complex requires containing sufficient bulk to cause stereochemical differentiation for high enantioselectivity. As illustrated in Scheme 1, we wondered that if a 1,1-disubstituted allene (i) could undergo site-selective reaction with a chiral ligand–Cu–B(pin) complex,[5] and the resulting 2-B(pin)-substituted allylcopper (ii) could be protonated γ- and enantioselectively through a chair-like transition state (iii),[6] enantiomerically enriched alkenylboron compounds (iv) would be obtained efficiently. Since the enantioselective protonation of C–Cu bond would proceed γ-selectively, which is distinct from other catalytic protoborations (direct Cu–C bond protonation), the resulting organoboron compounds might not be able to be accessed by traditional metal-catalyzed hydroboration reactions.[7]

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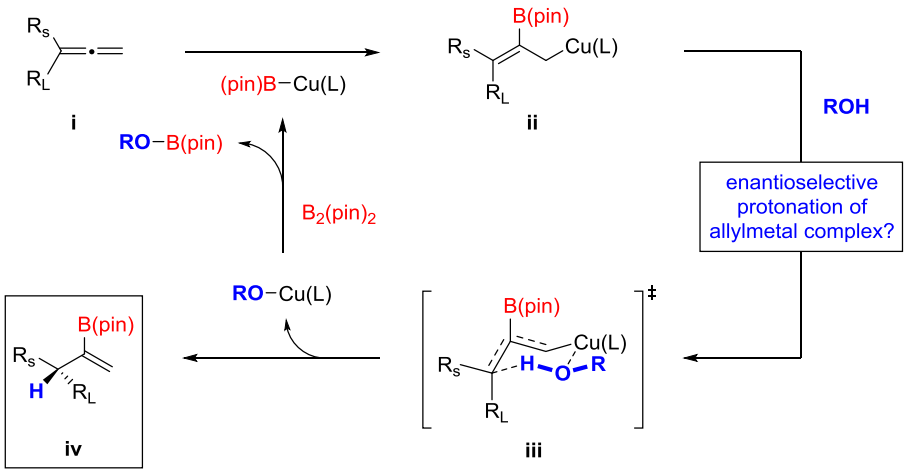
(5) (a) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 3160–3161. (b) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235. (c) Coberán, R.; Mszar, N. M.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079–7082. (d) Meng, F.; Jang, H.; Hoveyda, A. H. *Chem. Eur. J.* **2013**, *19*, 3204–3214. See also: (e) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2013**, *135*, 4934–4937. (f) Meng, F.; Haeffner, J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 11304–11307.

(6) (a) Meng, F.; Jung, B.; Haeffner, F.; Hoveyda, A. H. *Org. Lett.* **2013**, *15*, 1414–1417. For related studies, see: (b) Yuan, W.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1867–1872. (c) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. –Eur. J.* **2013**, *19*, 7125–7132.

(7) *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials*, Vol. 2; Hall, D. G., Ed.; Wiley-VCH: Weinheim, Germany, 2011.

***Scheme 4.1.*** Proposed Catalytic Cycle




Enantiomerically enriched α-stereogenic center-containing alkenylboron product is a synthetically useful intermediate, since C–B bond can be readily functionalized to other bonds. After simple oxidation, we can obtain corresponding methyl ketone, and also another synthetically useful alkenyl bromide might be afforded through Cu-mediated conversion of C–B bond to C–Br bond. Catalytic direct oxidation to carboxylic acid may illustrate further utility of alkenylboron product. In addition, alkenylboron has been utilized as an alkenyl-metal precursor for a wide range of C–C bond forming reactions such as allylic substitution. Herein, we have disclosed Cu-catalyzed enantioselective protoboryl addition to 1,1-disubstituted allenes to afford enantiomerically enriched alkenylboron products, and also describe the transformation of them to other useful intermediates including methyl ketones, alkenyl bromides, and carboxylic acids. Moreover, we illustrate NHC–Cu-catalyzed allylic substitution with an alkenylboron to introduce another stereogenic center.

## *4.2. Background*

In this section, we will summarize the advances regarding catalytic synthesis of optically active $\alpha$-stereogenic center-containing ketones as well as the protocol for preparation of corresponding alkenyl bromides. Additionally, we will introduce catalytic enantioselective allylic substitutions with alkenylboron reagent as well.

### *4.2.1. Catalytic Enantioselective Synthesis of α-Stereogenic Center-bearing Ketones*

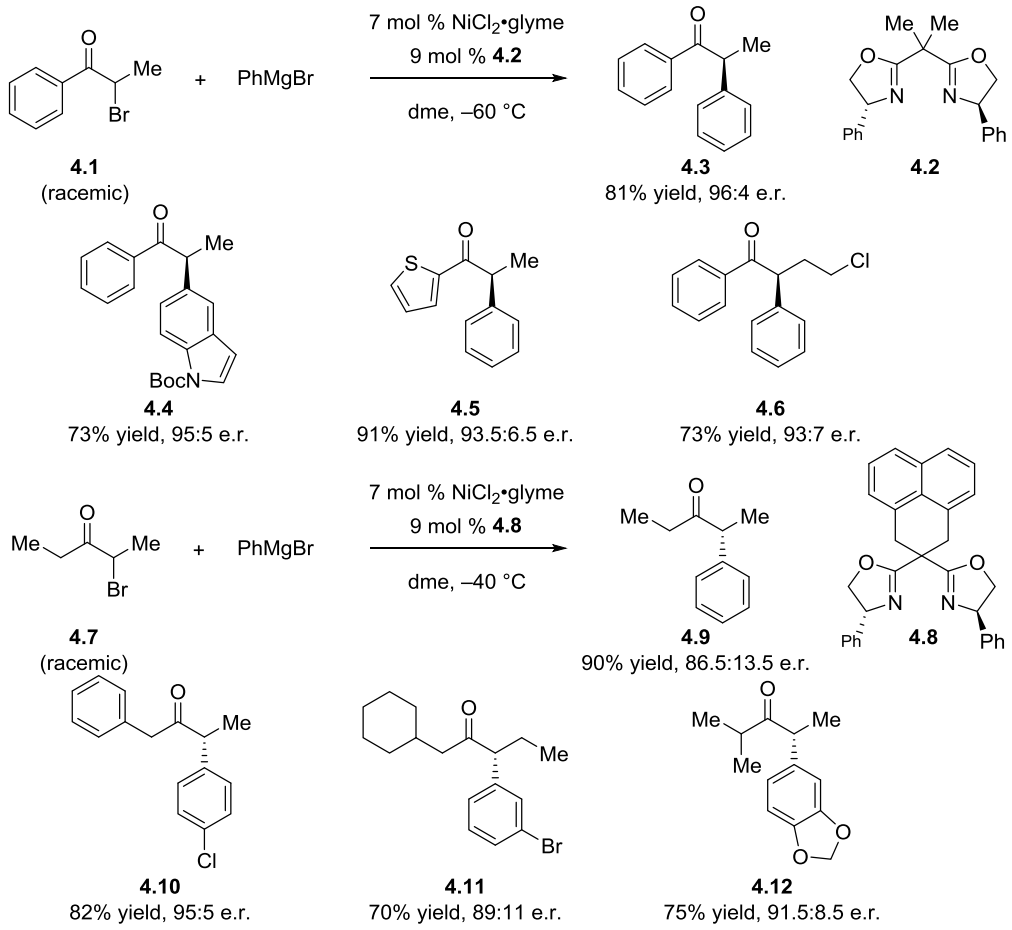
Catalytic enantioselective protocols for synthesis of $\alpha$-tertiary stereogenic center-bearing ketones have been the subject of synthetic chemistry field due to the versatility of them for the natural product and pharmaceutical syntheses.[8] We will summarize recent advances regarding catalytic enantioselective methods for preparing ketones containing $\alpha$-tertiary stereogenic center.

In 2010, Fu and coworkers described enantioselective Kumada coupling of $\alpha$-bromo ketones with aryl–Grignard reagents catalyzed by 7 mol % of a chiral Ni–bis(oxazoline) complex to afford a wide range of coupled products with high enantioselectivities (up to 97.5:2.5 e.r.).[9] Coupling of racemic $\alpha$-bromo ketone **4.1** with phenyl magnesium bromide in the presence of 7 mol % of a chiral Ni complex derived from $NiCl_2$·glyme and chiral bis(oxazoline) **4.2** furnishes $\alpha,\alpha$-phenyl,methyl-bearing phenyl ketone **4.3** in 81% yield and 96:4 e.r. (Scheme 4.2). To expand the substrate scope, they examine various aryl Grignard reagents as coupling partner, one of which is Boc-

(8) (a) Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 17180−17181. (b) Yan, X.-X.; Liang, C.-G.; Zhang, Y.; Hong, W.; Cao, B.-X.; Dai, L.-X.; Hou, X.-L. *Angew. Chem., Int. Ed.* **2005**, *44*, 6544−6546. (c) Zheng, W.-H.; Zheng, B.-H.; Zhang, Y.; Hou, X.-L. *J. Am. Chem. Soc.* **2007**, *129*, 7718−7719. (d) Lundin, P. M.; Esquivias, J.; Fu, G. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 154−156. (e) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264−1266. (f) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442−7445.
(9) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264−1266.

protected indole magnesium bromide, delivering desired product **4.4** efficiently and selectively (73% yield and 95:5 e.r.). Heterocycle-containing ketone **4.5** can be accessed through Ni-catalyzed Kumada coupling without reduced selectivity (93.5:6.5 e.r.). In addition, $\alpha$-bromo ketone containing longer chain with a halide group is subjected to the coupling reaction, and successfully converted to $\alpha,\alpha$-aryl,alkyl-phenyl ketone **4.6** with similar level of efficiency and selectivity (73% yield and 93:7 e.r.). When the authors utilize dialkyl ketones (e.g., **4.7**), the use of structurally modified bis(oxazoline) ligand **4.8** is required for maximum efficiency and enantioselectivity. They obtained $\alpha$-stereogenic center-bearing alkyl ketones **4.9**–**4.12** with slightly lower selectivities (86.5:13.5–95:5 e.r.), but high efficiency (70–90% yield). The above transformation has a broad substrate scope including aryl- or alkyl-ketones bearing two substituents on $\alpha$-carbon. They haven't report, however, corresponding methyl ketones.

***Scheme 4.2.*** Ni-Catalyzed Enantioselective Kumada Reactions with Grignard Reagent

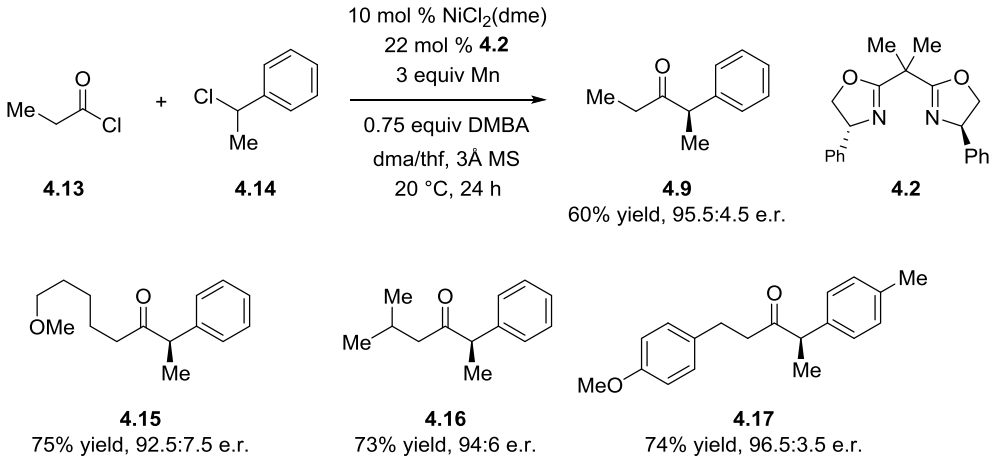



Recently, Reisman and coworkers reported that reaction of acyl chloride **4.13** and alkyl chloride **4.14** with 10 mol % Ni complex, derived from bis(oxazoline) **4.2** and Ni(II) salt, and 3 equiv. of reductant Mn(0), proceeds to reductive cross-coupling product **4.9** in 60% yield and 95.5:4.5 e.r. (Scheme 4.3).[10] Various *α,α*-disubstituted ketones bearing linear (**4.15** and **4.17**) and *β*-branched (**4.16**) alkyl chains are provided with high selectivity (92.5:7.5–96.5:3.5 e.r.). In comparison with previous Kumada coupling to afford alkyl ketones,[11] the aforementioned process can deliver *α,α*-disubstituted alkyl ketones with higher level of enantioselectivity. However, no aryl ketones as well as no

(10) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442−7445.
(11) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264−1266.

methyl ketones are reported. Thus, although lots of efforts by various organic chemists have been made, there are still some unsolved problems such as efficient and selective synthesis of methyl ketone containing *α*-tertiary stereogenic center.

***Scheme 4.3.*** Ni-Catalyzed Enantioselective Reductive Acyl Cross-Couplings



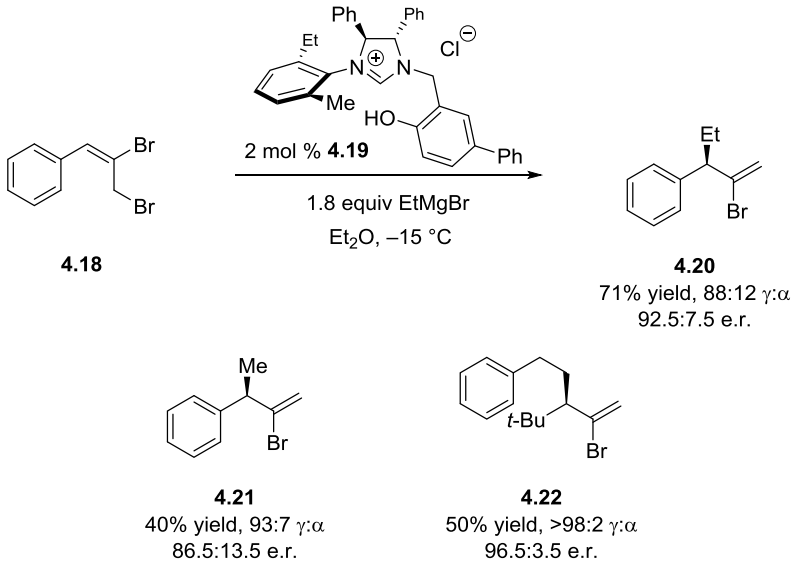

### *4.2.2. Preparation of α-Stereogenic Center-containing Alkenyl Bromides*

Since alkenyl bromides have been utilized widely for a lot of transformations to build a C–C bond such as metal-catalyzed cross-coupling reactions. Thus, development of efficient protocol for synthesis of bromo alkenes is of high value. Especially, *α*-stereogenic center-bearing alkenyl bromides might be useful, can be applied to various transformations. However, only one example has been reported to generate this class of alkenyl bromide by Alexakis and coworkers in 2012.[12] As described in Scheme 4.4, enantioselective allylic ethyl addition to bromo-substituted allylic bromide **4.18** with ethyl Grignard reagent in the presence of 2 mol % of chiral imidazolinium salt **4.19** delivers desired internal alkenyl bromide **4.20** in 70% yield with 88% $S_N2'$ selectivity and 92.5:7.5 e.r. When they introduce methyl magnesium bromide, unfortunately,

(12) Grassi, D.; Alexakis, A. *Org. Lett.* **2012**, *14*, 1568−1571.

reaction becomes less efficient (40% yield for **4.21**). With a Grignard reagent carrying a longer alkyl chain, similar level of efficiency is obtained (50% yield for **4.22**). Both of them afford *α,α*-disubstituted alkenyl bromides with high site- and enantioselectivities (93–>98% γ and 86.5:13.5–96.5:3.5 e.r.). Their substrate scope is, however, very limited; less than ten examples are reported. Thus, the aforementioned protocol cannot be a general method to provide this type of alkenyl bromide.

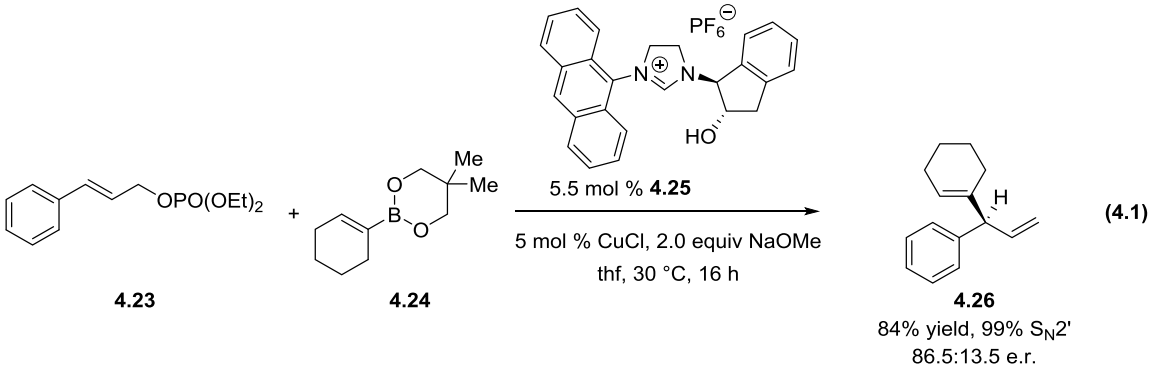
***Scheme 4.4.*** Enantioselective Allylic Alkylations with Grignard Reagents




### *4.2.3. Catalytic Enantioselective Allylic Substitutions with Alkenylboron Reagent*

Development of catalytic enantioselective allylic substitution reactions with alkenylboron compounds have been interested by organic chemists because boron reagents are robust and have functional group compatibility. In comparison with other alkenylmetal reagents, however, alkenylboron reagents are far less reactive. Because of poor reactivity of alkenylboron compounds, there have been rarely developed catalytic protocols for allylic substitution with this type of alkenyl-group source. In 2011, Shintani, Hayashi, and coworkers described NHC–Cu-catalyzed allylic aryl additions to allylic

phosphate to achieve enantiomerically enriched terminal olefins.[13] Addition to their aryl boronate cases, they examine an alkenyl boronate (cyclohexenyl; **4.24**) as a substrate for allylic alkenyl addition with allylic phosphate **4.23** in the presence of Cu–NHC complex generated from chiral salt **4.25**, delivering product **4.26** in 84% yield and 86.5:13.5 e.r. with high site selectivity (99% $S_N2'$). Although the aforementioned reaction is highly efficient and selective, they only illustrated a single example.




(4.1)

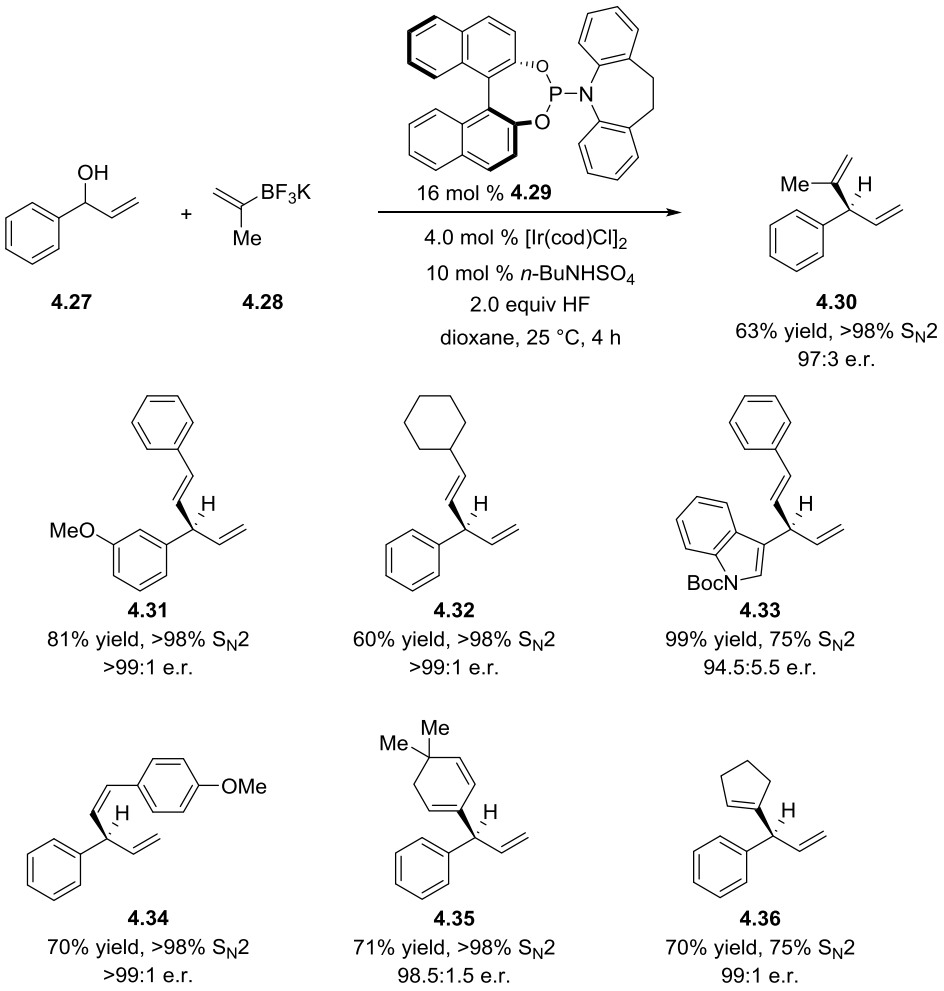
NHC–Cu-catalyzed enantioselective allylic alkenyl additions to trisubstituted allylic phosphate by the use of alkenylboron pinacol esters, generating quaternary stereogenic centers are illustrated by our laboratory in 2012.[14] No example for the preparation of tertiary center, however, is addressed.

In 2013, Carreira and coworkers reported that coupling of secondary alcohols and alkenyltrifluoroborates with catalytic amount of a chiral phosphoramidite–Ir complex affords desired products efficiently and highly selectively (Scheme 4.5).[15] When they utilize secondary alcohol **4.27** and internal alkenyl (trifluoro)boron potassium salt **4.46** in the presence of 8 mol % Ir complex derived from $[Ir(cod)Cl]_2$ salt and a chiral phosphoramidite **4.29**, allylic substitution product **4.30** is obtained in 63% yield and 97:3

(13) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 8656−8659.
(14) Gao, F.; Carr, J. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 6613−6617.
(15) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 994−997.

e.r. with exclusive site selectivity (>98% $S_N2$). The authors demonstrate that wide range of (*E*)-alkenylboron salts can be used for alkenyl-group transferring reagents. Phenyl- or cyclohexyl-bearing (*E*)-alkene addition products **4.31** and **4.32** are furnished by the aforementioned transformation in 60–81% yield and perfect site- and enantioselectivity (>98% $S_N2$ and >99:1 e.r.). Reaction of secondary allylic alcohol with either (Z)-alkenyl- or trisubstituted-trifluoroborate undergoes Ir-catalyzed allylic substitution to deliver desired product **4.34** or **4.35** as a single regioisomer (>98% $S_N2$) efficiently (70–71% yield) with high enantioselectivity (>99:1 and 98.5:1.5 e.r., respectively). In some cases (e.g., indole-substituted, **4.33** and cyclopentenyl-bearing, **4.36**), they observe significant decrease of site selectivity (75:25 $S_N2$:$S_N2$' for both **4.33** and **4.36**). A significant advantage of their approach is that unactivated secondary allylic alcohol can be used for the catalysis. There are several points, however, they cannot address; (1) only aryl-bearing allylic alcohols are utilized, (2) preparation of trifluoroboron reagent from another boron compound [e.g., (pinacolato)boron] is required, (3) the use of precious metal, Ir, is necessary.

***Scheme 4.5.*** Ir-Catalyzed Enantioselective Allylic Alkenyl Addition with Alkenyltrifluoroborates

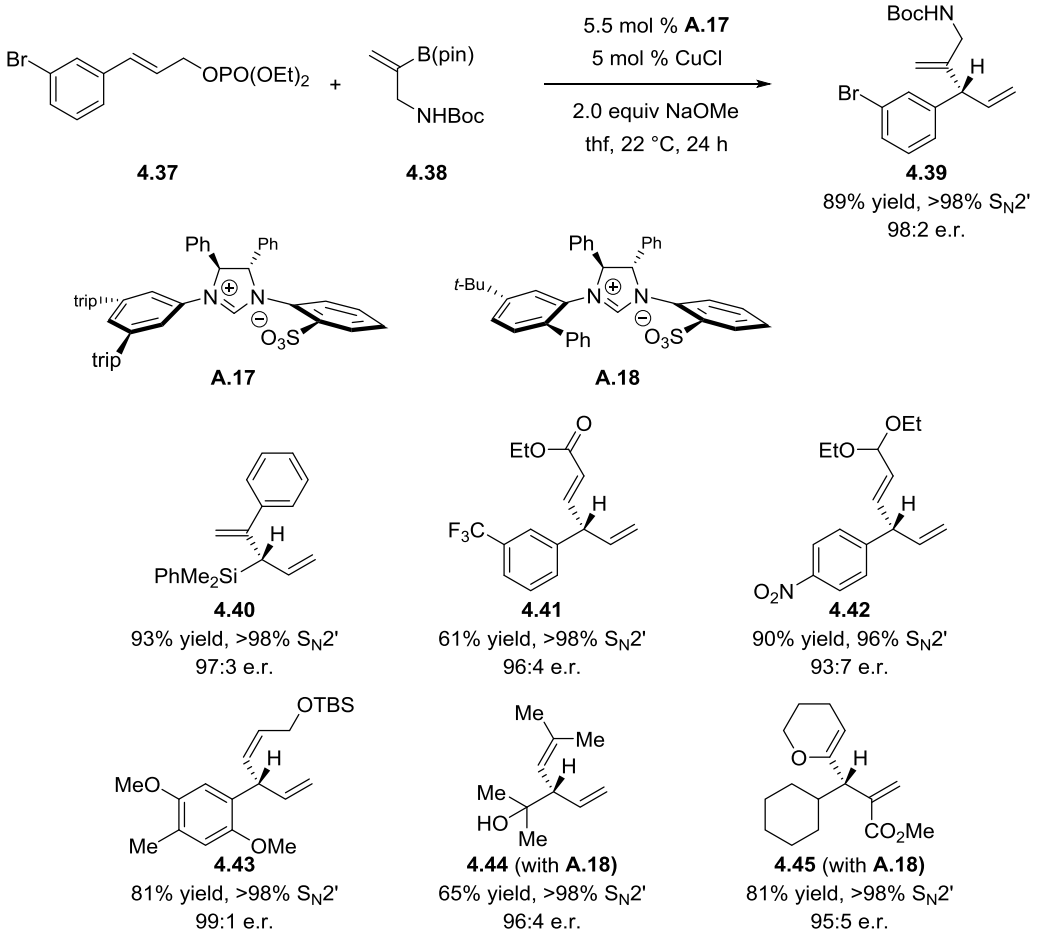



A year later, our laboratory developed NHC–Cu-catalyzed enantioselective allylic substitution of allylic phosphate with an alkenyl (pinacolato)boron compound.[16] With 5 mol % of NHC–Cu complex derived from CuCl, chiral imidazolinium salt **A.17**, and NaOMe, allylic phosphate **4.37** is coupled with internal (pinacolato) alkenylboron **4.38**, prepared vis *α*-selective protoboration of terminal alkyne,[17] to afford allylic substitution product **4.39** in 89% yield, >98% $S_N2'$ and 98:2 e.r. (Scheme 4.6). When silyl-substituted allylic phosphate serves as a substrate, allylic substitution with phenyl-bearing internal alkenylboron proceeds to provide desired product **4.40** in 93% yield and 97:3 e.r. as a

(16) Gao, F.; Carr, J. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2014**, *136*, 2149−2161.
(17) Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859−7871.

single regioisomer (>98% $S_N2'$). Both (*E*)- and (*Z*)-alkenyl groups are successfully added to an allylic phosphate to achieve corresponding diol products **4.41**–**4.43** efficiently (61–90% yield) and selectively (96–>98% $S_N2'$ and 93:7–99:1 e.r.). It is worth mentioning that enantiomerically enriched products **4.41** and **4.42** are obtained, which are carrying a relatively acidic proton, although stoichiometric amount of base is used in the reaction solution. Reactions of alkyl-substituted allylic phosphate with trisubstituted alkenylboron in the presence of slightly modified NHC–Cu complex derived from **A.18** afford products **4.44** and **4.45** with high level of selectivities (>98% $S_N2'$ and up to 96:4 e.r.).

***Scheme 4.6.*** NHC–Cu-Catalyzed Enantioselective Allylic Alkenyl Additions with (Pinacolato) Alkenylboron Compounds



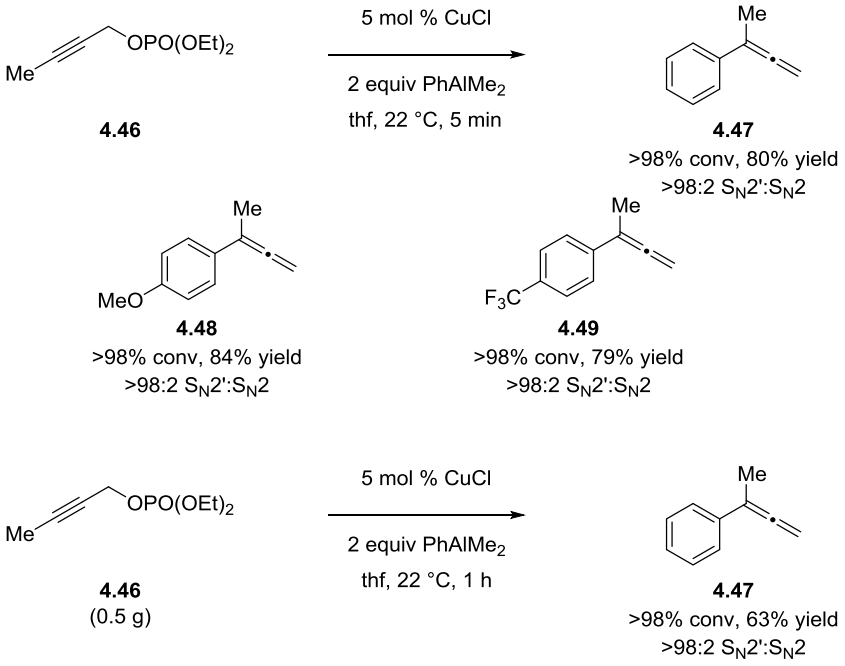
As shown in Scheme 4.5 and 4.6, a variety of alkenylboron reagents can be utilized for catalytic processes such as allylic alkenyl addition reactions. There are, however, still unsolved problems need to be addressed. One of them is that there is no example to utilize alkenylboron reagent which carries a stereogenic center already. Thus, we will address this issue by the use of protoboration of 1,1-disubstituted allene, bearing an *α*-stereogenic center for Cu-catalyzed enantioselective allylic alkenyl addition reactions to afford synthetically useful 1,4-diol compounds.

### *4.3. Practical Method for Preparation of 1,1-Disubstituted Allenes*

First, we developed a Cu-catalyzed protocol to prepare 1,1-disubstituted allenes efficiently. The representative examples are illustrated in Scheme 4.7. Reaction of a propargylic phosphate **4.46** with a phenylaluminum species, prepared *in situ* by reaction of an dimethyl aluminum chloride and a phenyl–Li reagent, in the presence of 5 mol % CuCl, affords 1,1-disubstituted allene **4.47** in 80% yield with a perfect site selectivity (>98% $S_N2'$) in only five minute.[18] The efficiency and site selectivity of the aforementioned reaction is not affected by electronic nature of aryl substituent. We successfully synthesized *p*-MeO-phenyl- and *p*-$CF_3$-phenyl-containing 1,1-disubstituted allenes **4.48** and **4.49** in 79–84% yield as a single regioisomer (>98% $S_N2'$) under the same condition. Transformation proceeds to completion in one hour for a one half gram scale, providing allene **4.47** in 63% yield.

(18) For a related catalytic protocol involving $Ni(acac)_2$ and Grignard reagents, see: Li, Q.; Gau, H. *Synlett* **2012**, *23*, 747–750.

***Scheme 4.7.*** Cu-Catalyzed Synthesis of 1,1-Disubstituted Allenes



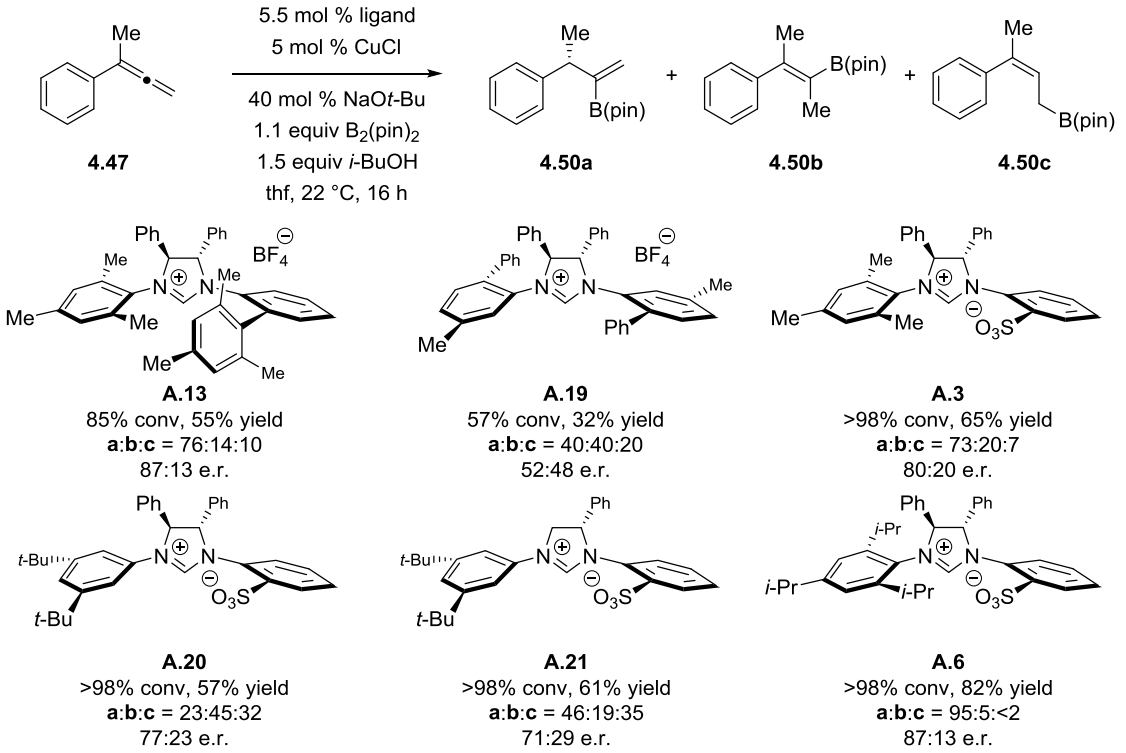

## *4.4. Catalytic Enantioselective Protoboration of 1,1-Disubstituted Allenes*

### *4.4.1. Evaluation of Chiral NHC–Cu and Bisphosphine–Cu Complexes*

We began by examining various chiral NHC–Cu complexes for protoboryl addition to phenyl,methyl-allene **4.47** with 1.5 equiv. of *i*-BuOH as a proton source (Scheme 4.8). With 5 mol % of monodentate NHC–Cu complex derived from **A.13**, we obtained a mixture of three regioisomers **4.50a**, **4.50b**, and **4.50c** (76:14:10) in 55% yield and 87:13 e.r. Encouraged by the result with **A.13**, we examined another monodentate NHC–Cu complex generated from C2-symmetric salt **A.19**, proceeding to moderate site selectivity (40:40:20) and low enantioselectivity (52:48 e.r.). Since the isolation of pure **4.48a** isomer from a mixture of three isomers is not trivial, the achievement of high site selectivity is significant. We turned our attention to bidentate sulfonate-bridging NHC–Cu complexes. Reaction of **4.47** in the presence of *N*-Mes-bearing sulfonate salt **A.3**,

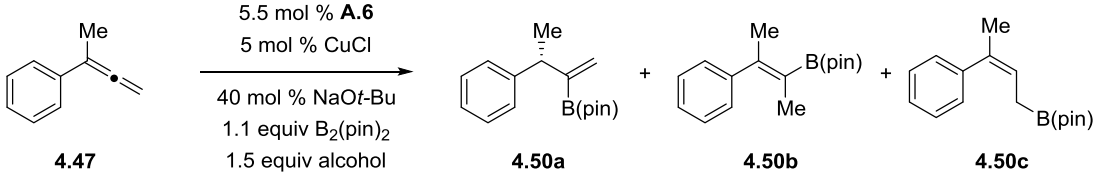
delivered a mixture of products in 65% yield with 73% selectivity for **4.50a** and 80:20 e.r. We prepared *N*-3,5-(*t*-Bu)$_2$-phenyl-containing imidazolinium salt **A.20** to investigate the effect of substitution pattern to site- and/or enantioselectivities. Since the ratio of **4.50a**:**b**:**c** is 23:45:32, Cu–NHC complex with *m*-substituted phenyl unit seems not suitable to achieve high site selectivity for this transformation. In addition, mono phenyl backbone-bearing variant of **A.20** was also tested, giving a similar level of site selectivity (**4.50a**:**b**:**c** = 46:19:35 for **A.21**). Based on these observations, we decided to examine reaction of **4.47** with Cu complex carrying sterically more demanding, 1,3,5-(*i*-Pr)$_3$-phenyl-bearing NHC (**A.6**), delivering 82% yield of 95:5 mixture of **4.50a** and **4.50b** (<2% of **4.50c**) with 87:13 e.r. Thus, we chose a chiral imidazolinium **A.6** as an optimal NHC precursor for further study.

***Scheme 4.8.*** Evaluation of Chiral NHC–Cu Complexes



To improve site- and enantioselectivity, we have investigated the proton source for the reaction (Table 4.1). We reasoned that use of a more sterically hindered alcohol might exacerbate the steric interactions with *in situ* generated allylcopper species in the competing transition states for enantioselective protonation, leading to a rise in enantioselectivity (see section 4.4.3 for detailed analysis). We therefore examined protoboration of 1,1-disubstituted allene **4.47** with various alcohols in the presence of NHC–Cu complex derived from **A.6**. As shown in entry 1, with a small methyl-bearing alcohol, much lower enantioselectivity (63:37 e.r.), and also lower site selectivity (**4.50a**:**b**:**c** = 86:14:<2) are obtained. On the other hand, with $\alpha$-branched *i*-PrOH, as we expected, the enantioselectivity is slightly increased (90:10 vs 87:13 e.r.; entry 3 vs entry 2). When sterically more demanding *t*-butanol was utilized as a proton source, reaction of **4.47** proceeded to 97.5% of **4.50a** isomer in 77% yield with 93:7 e.r. (entry 4).

***Table 4.1.*** Evaluation of Alcohols as a Proton Source[a]




**4.47** **4.50a** **4.50b** **4.50c**

| entry | alcohol | conv (%)[b] | yield (%)[c] | **a**:**b**:**c**[b] | e.r.[d] |
|---|---|---|---|---|---|
| 1 | MeOH | >98 | 89 | 86:14:<2 | 63:37 |
| 2 | *i*-BuOH | >98 | 82 | 95:5:<2 | 87:13 |
| 3 | *i*-PrOH | >98 | 94 | 97:3:<2 | 90:10 |
| 4 | *t*-BuOH | >98 | 77 | 97.5:2.5:<2 | 93:7 |

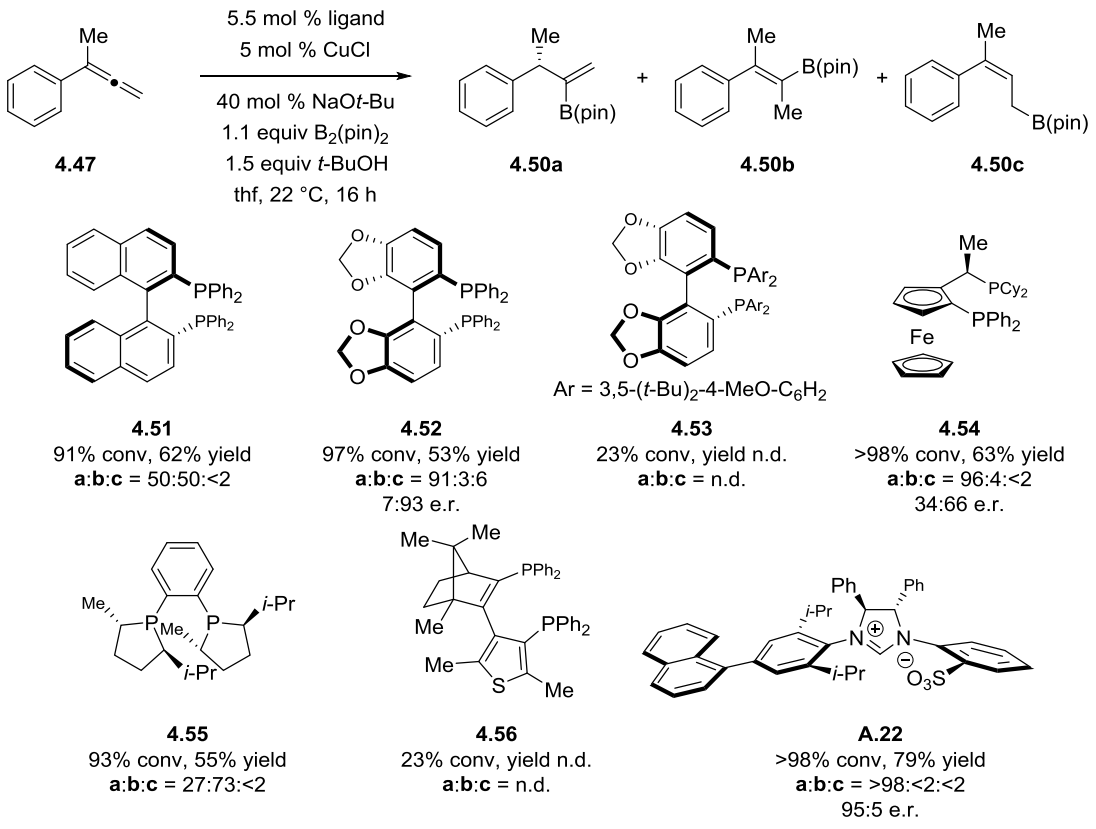
[a]Reactions were performed under $N_2$ atm. [b]Determined by analysis of $^1$H NMR spectra of unpurified mixture. [c]Yields of isolated and purified products. [d]Determined by GLC analysis.

Since we observed that chiral bisphosphine–Cu complex can promote Cu–B addition to monosubstituted allene followed by addition to aldehyde with high

enantioselectivity,[19] these complexes are also examined for catalytic protoboration of disubstituted allenes. As illustrated in Scheme 4.9, with 1.5 equiv. of *t*-BuOH, we examined NHC–Cu-catalyzed protoboration of **4.47** in the presence of commercially available chiral phosphine ligands (**4.51**–**4.56**) and a further structurally modified imidazolinium salt **A.22**. Based on our screening results, generally, chiral bisphosphine–Cu complexes catalyze protoboration reaction with either low efficiency (23% conv for **4.53** and **4.56**) or minimal site selectivity (50:50:<2 for **4.51**). On the other hand, with a phosphine ligand **4.55**, tetrasubstituted alkenylboron compound **4.50b** was generated as a major regioisomer (27:73:<2). Reaction with bisphosphine **4.52** [(*R*)-segphos] generated **4.50a** in 53% yield and 93:7 e.r. along with 9% of byproducts (**4.50b** and **4.50c**). Although the level of enantioselectivity is compatible, site selectivity with **4.52** is lower than that with **A.6** (91% vs 97.5% of **4.50a**), and significantly lower yield (53% vs 77%) is obtained with **4.52**. Further efforts to improve site- and enantioselectivities lead us to prepare a chiral imidazolinium sulfonate **A.22**, *p*-naphthyl-bearing variant of **A.6**, which providing even higher enantioselectivity (95:5 e.r.) and a perfect site selectivity (>98% **4.50a**). Based on the chiral Cu complex screening results, we chose the chiral imidazolinium salt **A.22**, which contains a large naphthyl unit on the *para* position of *N*-Ar group as an optimal NHC precursor.

(19) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046−5051.

***Scheme 4.9.*** Evaluation of Chiral Bisphosphine–Cu and NHC–Cu Complexes

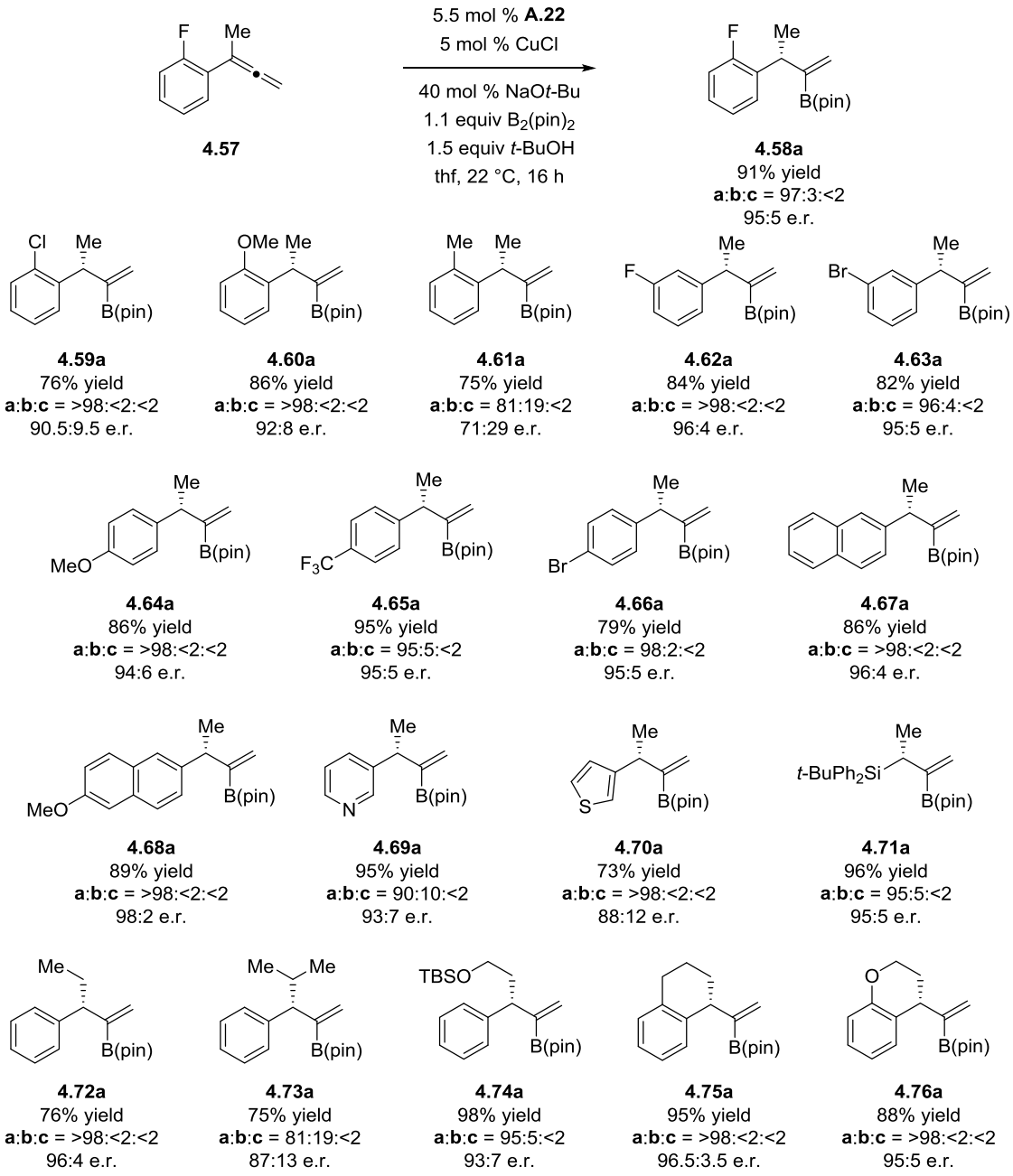



### *4.4.2. Cu-Catalyzed Enantioselective Protoboration of 1,1-Disubstituted Allenes*

A wide array of 1,1-disubstituted allenes serve as substrates for Cu-catalyzed enantioselective protoboration reaction to deliver *α*-tertiary stereogenic center-bearing internal alkenylboron products efficiently and highly selectively (Scheme 4.10). When *o*-Cl-containing allene is used, alkenylboron **4.59a** is provided with lower enantioselectivity (90.5:9.5 e.r.). Since we obtain even lower enantioselectivity (71:29 e.r.) with *o*-Me-bearing substrate (**4.61a**), the diminution of selectivity might be due to a steric effect. Especially, in the latter case, site selectivity for the reaction is low as well (81:19:<2 **a**:**b**:**c**). With sterically less demanding fluorine-bearing substrate, on the other hand, **4.58a** is achieved without diminution of enantioselectivity (95:5 e.r.), which is consistent

with the above hypothesis. Since the structure of NHC derived from **A.22** is sterically congested, especially near Cu center, when sterically demanding substrate is used, severe interaction might occur to allow the competing other pathways to become more dominant. Allenes containing a *meta*-, or *para*-substituted aryl group are suitable substrates, leading to corresponding alkenylborons **4.62a**–**4.66a** with high levels of selectivities (95–>98% site selectivity and 94:6–96:4 e.r.). Additionally, heterocycle-bearing alkenylboron products **4.69a** and **4.70a** are delivered through Cu-catalyzed protoboration reaction with up to <98% site selectivity and 93:7 e.r. Similar efficiency and stereoselectivity levels are observed with substrates with an alkyl and a silyl substituent (96% yield, 95% site selectivity, and 95:5 e.r. for **4.71a**). Then, NHC–Cu-catalyzed enantioselective protoboration of Et- and *i*-Pr-substituted allenes is probed. Reaction of Et-substutitued allene is more selective than *i*-Pr-bearing one (95% vs 81% site selectivity and 96:4 vs 87:13 e.r.; **4.72a** vs **4.73a**). This observation is consistent with the results from reaction of *o*-Me-containing allene (**4.61a**). Moreover, we examine enantioselective protoboration of exocyclic 1,1-disubstituted allenes, furnishing desired alkenylboron **4.75a** or **4.76a** efficiently, site- and enantioselectively (88–95% yield, >98% site selectivity and up to 96.5:3.5 e.r.).

***Scheme 4.10.*** Enantioselective Protoborations of 1,1-Disubstituted Allenes




Since we obtained similar level of enantioselectivity with chiral NHC–Cu complex derived from **A.6** or bisphosphine–Cu complex from (*R*)-segphos **4.52**, Cu-catalyzed process in the presence of either one of these Cu complexes is also examined for the cases in Scheme 4.10 to compare efficiency and selectivity to those obtained with **A.22**-mediated Cu complex. In many instances, the phosphine–Cu complex provided

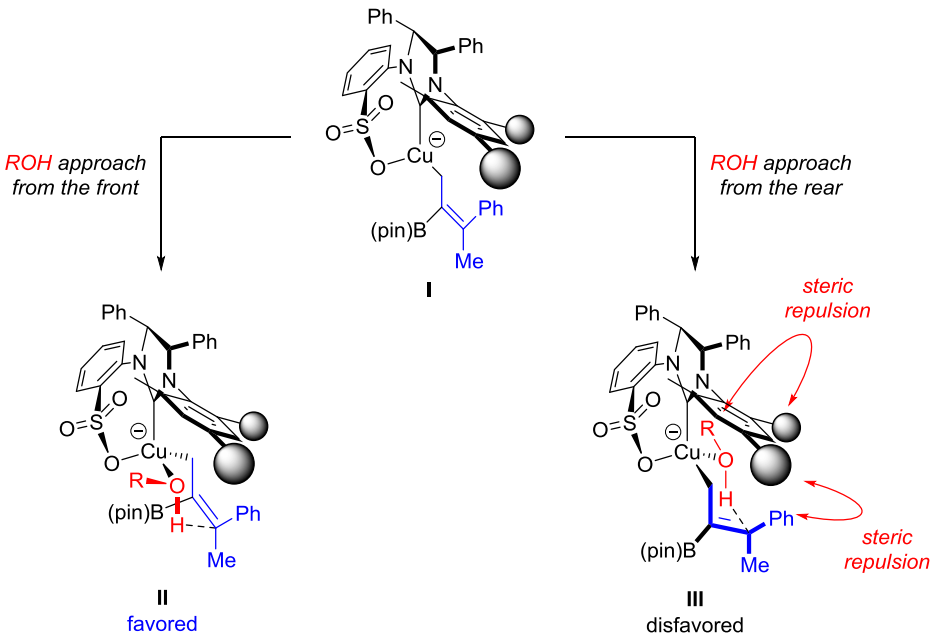
substantial amounts of inseparable isomeric products. The worst case is that with *o*-methoxy-substituted **4.60a**, only 5% of the product mixture is desired isomer (**a**:**b**:**c** = 5:80:15). Moreover, in many cases, the use of bisphosphine **4.52** resulted in low enantioselectivity (e.g., 33:67 e.r. for **4.60a** and 23.5:76.5 e.r. for **4.71a**). Although reaction of **4.47** with either **A.6** or **A.22** results in similar efficiency and selectivity [77% yield, 97.5% site selectivity, and 93:7 e.r. for **A.6** (Table 4.1) vs 79% yield, >98% site selectivity, and 95:5 e.r. for **A.22** (Scheme 4.9)], in some cases, the latter afforded significantly higher site selectivities. For instance, pyridine-bearing alkenylboron product **4.69a** was generated less site-selectively with **A.6** (**a**:**b**:**c** = 77:23:<2 vs 90:10:<2 for **A.22**).

### *4.4.3. Stereochemical Models to Account for Enantioselectivity*

As illustrated in Scheme 4.11, we build up the stereochemical models to account for the selectivity trends with various NHC–Cu complexes and influence of different alcohols. Allylcopper bearing B(pin) unit (I), generated through site-selective copper–boron addition to 1,1-disubstituted allene, reacts with alcohol either by front- (mode II) or rear-face approach (mode III). There are two steric interactions can make mode III less preferred than mode II, one of which is the interaction between alcohol substituent (R) and *ortho*-substituent on *N*-Ar of the NHC. Because of the tilt of the *N*-Ar, this interaction is more severe in mode III than in mode II, which render III less favorable. This point led us to screen various alcohols, and to observe increased enantioselectivity with sterically more demanding alcohol [93:7 e.r. with *t*-BuOH vs 63:37 e.r. with MeOH (Table 4.1)). Another factor can control the enantioselectivity is the interaction between

*para*-substituent on *N*-Ar of the NHC and aryl unit of substrate. This repulsive interaction might make mode III less dominant. With a large *p*-naphthyl-containing **A.22**, we obtained slightly higher enantioselecitivity (95:5 e.r.) compared to one (93:7 e.r.) with *p*-isopropyl **A.6**, which is consistent with our hypothesis.

***Scheme 4.11.*** Stereochemical Models

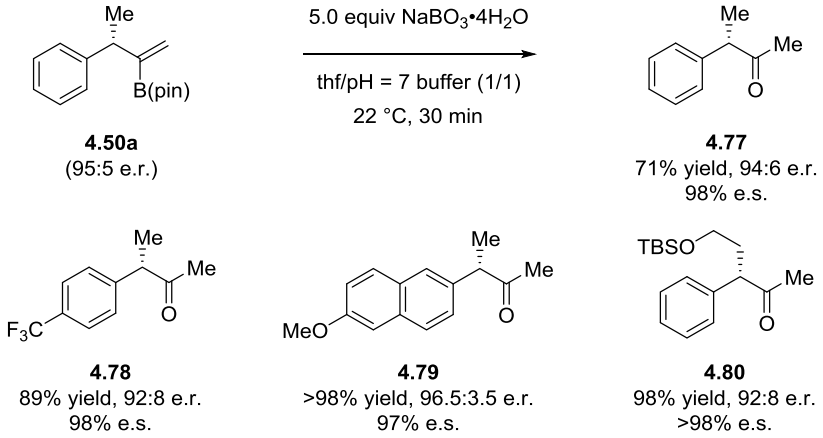



### *4.4.4. Representative Functionalizations*

Since C–B bond in alkenylboron product is readily converted to other useful bonds, we have focused on development of functionalization methods to synthesize synthetically useful molecules. First, as illustrated in Scheme 4.12, the mild oxidation of enantiomerically enriched alkenylboron **4.50a** (95:5 e.r.) is complete in 30 min with 5 equiv. of sodium perborate in a 1:1 mixture of thf and buffered water (pH = 7) to afford corresponding methyl ketone **4.77** in 94:6 e.r. (98% e.s.). As we mentioned in Section 4.2.1, synthesis of enantiomerically enriched $\alpha$-tertiary stereogenic center-containing

methyl ketone is not presented yet.[20] Thus, Cu-catalyzed enantioselective protoboration of 1,1-disubstituted allene can be a unique strategy to access those types of compounds. Three different substituent-bearing methyl ketones **4.78**–**4.80** are achieved under the same oxidation condition without significant diminution of enantioselectivity (97–>98% e.s.) with high efficiency (89–>98% yield).

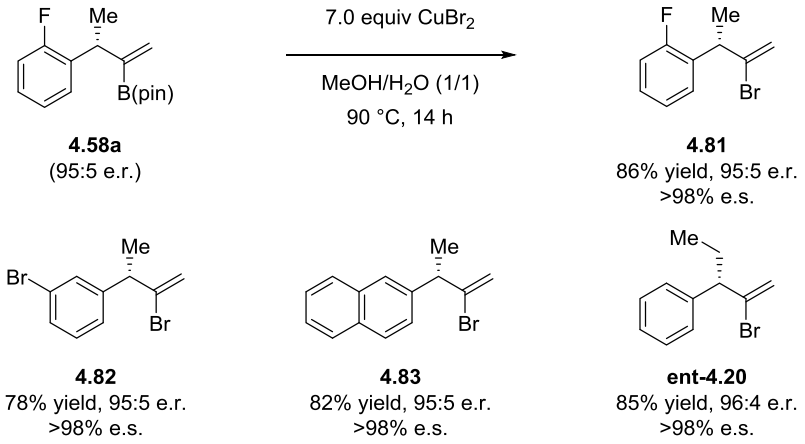
***Scheme 4.12.*** Synthesis of Enantiomerically Enriched Methyl Ketones




Next, the transformation of alkenyl–B(pin) to alkenyl bromide, which has been widely utilized for various C–C bond forming reactions such as metal-catalyzed cross-coupling reaction, is demonstrated in Scheme 4.13. With 7 equiv. of $CuBr_2$, enantiomerically enriched $\alpha,\alpha$-disubstituted alkenyl bromides **4.81**–**4.83** and **ent-4.20** are successfully synthesized with a perfect enantiospecificity (>98% e.s. for all cases) under the reflux condition in 14 hours. As we also mentioned in Section 4.2.1, catalytic enantioselective protocol for prepare this type of product is rare.

(20) For enzyme-catalyzed enantioselective synthesis of 2-arylsubstituted butanones, see: Rodríguez, C.; de Gonzalo, G.; Pazmiño, D. E. T.; Fraaije, M. W.; Gotor, V. *Tetrahedron: Asymmetry* **2009**, *20*, 1168−1173.

***Scheme 4.13.*** Synthesis of Enantiomerically Enriched Alkenyl Bromides




**4.58a**
(95:5 e.r.)

**4.81**
86% yield, 95:5 e.r.
>98% e.s.

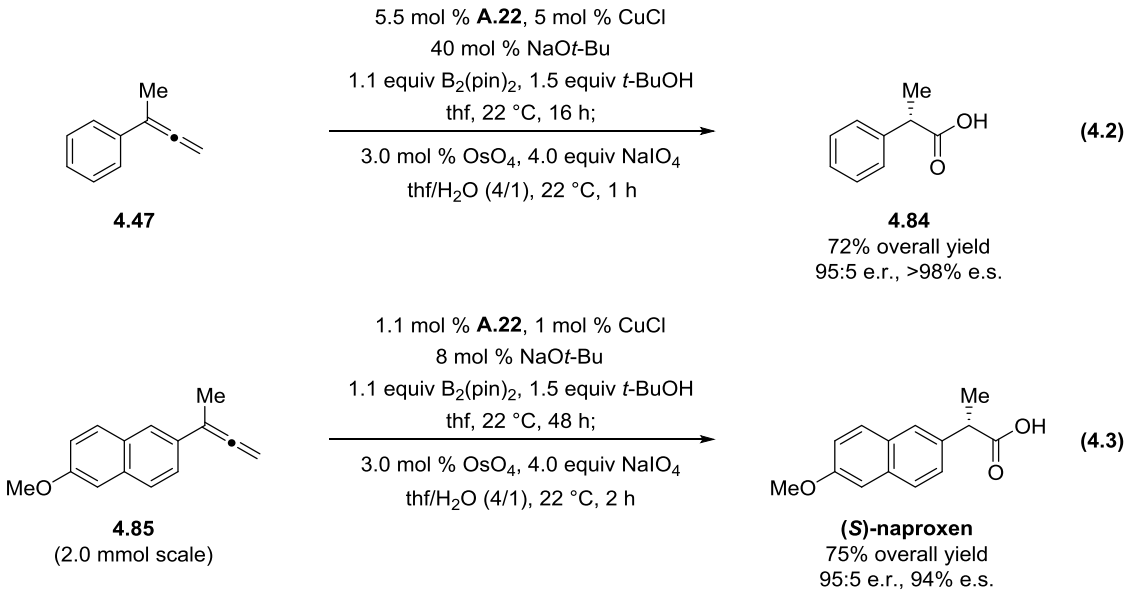
**4.82**
78% yield, 95:5 e.r.
>98% e.s.

**4.83**
82% yield, 95:5 e.r.
>98% e.s.

**ent-4.20**
85% yield, 96:4 e.r.
>98% e.s.

In addition, direct oxidation of alkenylboron product to corresponding carboxylic acid with a catalytic amount of $OsO_4$ is examined. Enantiomerically enriched *α*,*α*-disubstituted carboxylic acid **4.84** is obtained in 72% overall yield with high enantioselectivity (95:5 e.r.) by the sequential NHC–Cu-catalyzed protoboration of **4.47** and the aforementioned process (eq 4.2).[21] Enantioselective synthesis of nonsteroidal anti-inflammatory agent (*S*)-naproxen is illustrated in eq 4.3 by use of this strategy. With only 1 mol % of NHC–Cu complex from **A.22**, the sequential transformation underwent to deliver (*S*)-naproxen in 75% overall yield and 95:5 e.r. (94% e.s.).

(21) For recent catalytic enantioselective synthesis of *α*,*α*-disubstituted carboxylic acids, see: (a) Bigot, A.; Williamson, A. E.; Gaunt, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 13778−13781. (b) Harvey, J. S.; Simonovich, S. P.; Jamison, C. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 13782−13785. (c) Huang, Z.; Liu, Z.; Zhou, J. *J. Am. Chem. Soc.* **2011**, *133*, 15882−15885.



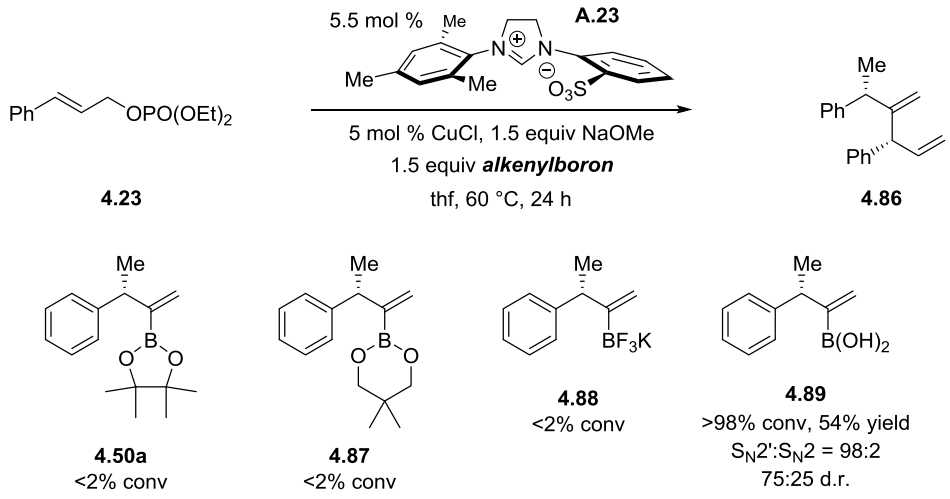

### *4.4.5. Catalytic Allylic Substitutions with Enantiomerically Enriched Alkenylboron*

Alkenylboron reagents have been used for catalytic enantioselective allylic substitution reactions. However, chiral nucleophiles have not been utilized. Thus, we tried to develop this class of reaction by direct use of enantiomerically enriched alkenyl–B(pin), the protoboration product. Initially, we performed reaction of **4.50a** with allylic phosphate **4.23** in the presence of achiral sulfonate-bearing salt **A.23**, CuCl, and NaOMe, proceeded to <2% conversion (Scheme 4.14). To facilitate transmetallation of C–B bond to C–Cu bond, more accessible alkenylboron reagents such as neopentyl glycol ester **4.87** and the trifluoroborate **4.88** were prepared. However, no desired products are observed with these alkenylboron reagents (<2% conv). Then, we prepared sterically less hindered alkenylboronic acid **4.89** by previously reported simple transformation of alkenylboron pinacol ester **4.50a** (83% yield).[22] When we subjected **4.89** to the reaction with **4.23**,

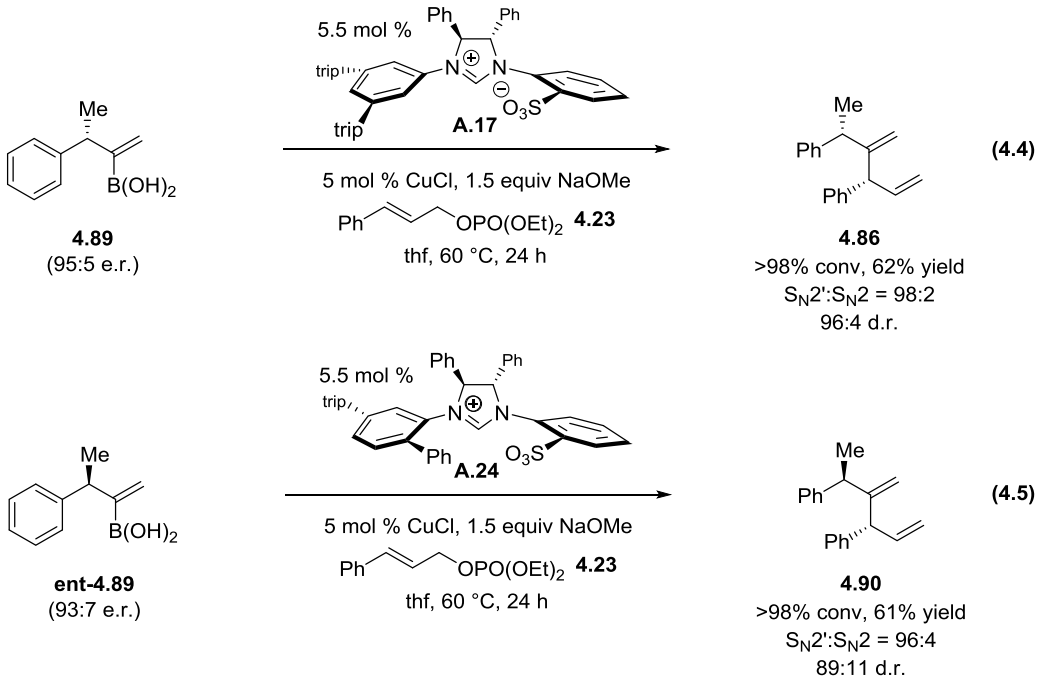
(22) Wang, H.-Y.; Anderson, L. L. *Org. Lett.* **2013**, *15*, 3362−3365.

desired allylic alkenyl addition product **4.86** was delivered with >98% conv, 54% yield, 98:2 site selectivity, and 75:25 d.r. (Scheme 4.14).

***Scheme 4.14.*** Initial Observation for Allylic Substitution with Alkenylborons




To improve selectivity, various chiral NHC–Cu complexes are investigated, and as shown in eq 4.4, we found that the complex derived from imidazolinium salt **A.17** promotes allylic alkenyl addition reaction with enantiomerically enriched alkenylboronic acid **4.89** (95:5 e.r.), to afford 1,4-diene **4.86** in 62% yield with 98% $S_N2$' selectivity and 96:4 d.r. Since we use alkenylboronic acid **4.89** as a 95:5 mixture of enantiomers, the stereoselectivity for the allylic substitution reaction is exclusive. With **ent-4.89**, an opposite enantiomer, diastereoisomer **4.90** was generated with similar efficiency and site selectivity (62% yield and 96% $S_N2$') in the presence of NHC–Cu derived from different sulfonate salt **A.24** (eq 4.5). The stereoselectivity for allylic substitution reaction is slightly reduced in the latter case (95%) because an alkenylboron reagent might be mismatched with the chiral Cu complex.




## *4.5. Conclusions*

We have demonstrated site- and enantioselective protonation of B(pin)-substituted allylcopper species, which is *in situ* generated from 1,1-disubstituted allene promoted by chiral NHC–Cu complex in a single vessel process. A wide assortment of allenes is utilized, affording α-stereogenic center-bearing alkenylboron compounds in up to 98% yield and 98:2 e.r. Based on proposed stereochemical models, we successfully found an optimal NHC and alcohol source to achieve high efficiency and enantioselectivity. To show the utility of aforementioned transformation, we illustrate simple and practical methods to convert alkenylboron product to corresponding methyl ketone, alkenyl bromide, or carboxylic acid efficiently without diminution of enantiomeric enrichment (>94% e.s.). We also have developed NHC–Cu-catalyzed enantioselective allylic alkenyl addition to allylic phosphate with alkenylboronic acid, which is prepared from

alkenyl(pinacolato)boron product, providing 1,4-diene with high selectivity (61–62% yield, 96–98% $S_N2'$, and 89:11–96:4 d.r.).

### *4.6. Experimentals*

**General.** Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, $\lambda_{max}$ in $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). $^{1}H$ NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, app = apparent), and coupling constant (Hz). $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry $N_2$ in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; $CH_2Cl_2$ and $Et_2O$ were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific, Inc.) under air atmosphere. Enantiomeric ratios were determined by GC

analysis (Alltech Associated Chiraldex B-DM (30 m x 0.25 mm), Chiraldex G-TA (30 m x 0.25 mm), and β-dex 120 column (30 m x 0.25 mm)), or HPLC analysis (Chiral Technologies Chiralpak® AD-H (4.6 x 250 mm), Chiralcel® OD-H (4.6 x 250 mm), OJ-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Specific rotations were measured on a ATAGO® AP-300 Automatic Polarimeter. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected.

### *4.6.1. Reagents and Ligands*

**Acetyl chloride:** purchased from Aldrich Chemical Co. and used as received.

**Ammonium acetate:** purchased from Aldrich Chemical Co. and used as received.

**Bis(dibenzylideneacetone)palladium(0):** purchased from Strem Chemicals Inc. and used as received.

**Bis(pinacolato)diboron [$B_2(pin)_2$]:** purchased from Frontier Scientific Inc., recrystallized from pentane and dried under vacuum prior to use.

**Bis(triphenylphosphine)palladium (II) dichloride:** purchased from Aldrich Chemical Co. and used as received.

**4-Bromoanisole:** purchased from Aldrich Chemical Co. and distilled from $CaH_2$ prior to use.

**Bromobenzene:** purchased from Aldrich Chemical Co. and distilled from $CaH_2$ prior to use.

**4-Bromobenzotrifluoride:** purchased from Aldrich Chemical Co. and distilled from $CaH_2$ prior to use.

**3-Bromo-3-buten-1-ol:** purchased from Aldrich Chemical Co. and used as received.

**1-Bromo-2-butyne:** purchased from Aldrich Chemical Co. and used as received.

**2-Bromo-5-iodo-1,3-diisopropylbenzene:** prepared according to a previously reported procedure.[23]

***n*-Butyllithium:** purchased from Strem Chemicals Inc. and used as received.

**2-Butyn-1-ol:** purchased from Aldrich Chemical Co. and used as received.

**2-Butyn-1-yl diethyl phosphate:** prepared according to a previously reported procedure.[24]

**Chiral bis-phosphines:** purchased from Strem Chemicals Inc. and used as received.

**Copper (II) bromide:** purchased from Strem Chemicals Inc. and used as received.

**Copper (I) chloride:** purchased from Strem Chemicals Inc. and used as received.

**Diethyl chlorophosphate:** purchased from Aldrich Chemical Co. and used as received.

**Dimethylaluminum chloride (**neat**):** purchased from Aldrich Chemical Co. and used as received.

***N*,*N*-Dimethylformamide (**99.8% purity**):** purchased from Acros Organics Co. and used as received.

**Dimethylmethylideneammonium iodide (Eschenmoser's salt):** purchased from Aldrich Chemical Co. and used as received.

**Dioxane:** purchased from Acros Organics Co. and used as received.

**(–)-(*S*,*S*)-Diphenylethylenediamine (**99% purity**):** purchased from Ivy Chemical Company and used as received.

**Glacial acetic acid:** purchased from Aldrich Chemical Co. and used as received.

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(23) Cheng, X.; Goddard, R.; Buth, G.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 5079–5081.
(24) Sanders, T. C.; Hammond, G. B. *J. Org. Chem.* **1993**, *58*, 5598–5599.

**Methanol:** purchased from Acros and purified by distillation from Na (Aldrich Chemical Co.) prior to use.

**Methylmagnesium bromide (3.0 M in $Et_2O$):** purchased from Aldrich Chemical Co. and used as received.

**2-Methyl-1-propanol (**99.5% purity, ***i*-BuOH):** purchased from Aldrich Chemical Co. and used as received.

**2-Methyl-2-propanol (*t*-BuOH):** purchased from Aldrich Chemical Co. and purified by distillation from Na (Aldrich Chemical Co.) prior to use.

**1-Naphthalenylboronic acid:** purchased from Aldrich Chemical Co. and used as received.

**Osmium tetroxide (**4 wt % in $H_2O$ solution**):** purchased from Aldrich Chemical Co. and used as received.

**Palladium (II) acetate:** purchased from Strem Chemicals Inc. and used as received.

**Phenylboronic acid:** purchased from Aldrich Chemical Co. and used as received.

**Phenylmagnesium bromide (3.0 M in $Et_2O$):** purchased from Aldrich Chemical Co. and used as received.

**Potassium phosphate tribasic:** purchased from Aldrich Chemical Co. and used as received.

**Sodium borohydride ($NaBH_4$):** purchased from Aldrich Chemical Co. and used as received.

**Sodium *t*-butoxide (NaO*t*-Bu):** purchased from Strem Chemicals Inc. and used as received.

**Sodium hydroxide (NaOH):** purchased from Fischer Scientific, Inc. and used as received.

**Sodium methoxide (NaOMe):** purchased from Strem Chemicals Inc. and used as received.

**Sodium perborate tetrahydrate ($NaBO_3 \cdot 4H_2O$):** purchased from Aldrich Chemical Co. and used as received.

**Sodium periodate ($NaIO_4$):** purchased from Acros Organics Co. and used as received.

**Tetrabutylammonium fluoride:** purchased from Aldrich Chemical Co. and used as received.

**Tetrakis(triphenylphosphine)palladium(0):** purchased from Strem Chemicals Inc. and used as received.

**Triethylamine ($Et_3N$):** purchased from Fisher Scientific, Inc. and distilled over $CaH_2$ prior to use.

**Triphenylphosphine:** purchased from Aldrich Chemical Co. and used as received.

### *4.6.2. Experimental Procedure and Characterization Data*

■ **Representative Procedure for Preparation of 1,1-Disubstituted Allenes:**[25] To a flame-dried 10 mL round bottom flask equipped with a stir bar was added bromobenzene (0.42 mL, 4.00 mmol) and thf (2 mL). The mixture was allowed to cool to –78 °C before *n*-BuLi (2.52 mL, 4.00 mmol) was added drop-wise by a syringe and the solution was allowed to stir at –78 °C for one hour. At this point, $Me_2AlCl$ (0.37 mL, 4.00 mmol) was added drop-wise by a syringe and the solution was allowed to warm to 22 °C and stir for

(25) Dabrowski, J. A.; Villaume, M. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 8156–8159.

12 h. Pentane (2 mL) was added and the solution was allowed to stir for an additional hour. The mixture was then allowed to stand for approximately one hour before removal and use of the top pentane layer in reactions. (The lower thf layer contains LiCl salts, which are detrimental to the site selectivity ($S_N2'$) of the reaction significantly.) A flame-dried 50 mL round bottom flask equipped with a stir bar was charged with CuCl (13.1 mg, 0.130 mmol) in an $N_2$ filled glove box. The flask was capped with a septum and removed from the glove box. Tetrahydrofuran (15 mL) was added to the flask and the previously prepared solution of dimethylphenylaluminum (0.581 M, 6.8 mL, 4.00 mmol) was added slowly and the resulting solution was allowed to stir for five minutes at 0 °C. A solution of 2-butyn-1-yl diethylphosphate **4.46** (536 mg, 2.60 mmol) in thf (6 mL) was added drop-wise through cannula and the solution was allowed to warm to 22 °C and stir for one hour. The reaction was quenched by addition of saturated solution of sodium potassium tartrate (30 mL, added slowly). The solution was diluted with $Et_2O$ and the mixture was allowed to stir at 22 °C until the layers were separated clearly. The aqueous layer was washed with $Et_2O$ (3 × 10 mL) and the combined organic layer was dried over $MgSO_4$, concentrated *in vacuo* (caution: The product is volatile. Use house-vacuum only) and purified by silica gel chromatography (100% pentane) to afford 212 mg of 1-(buta-2,3-dien-2-yl)benzene **4.47** as colorless oil (1.63 mmol, 63% yield).

The following substrates were prepared according to the above procedure. Characterization data match the reported ones: **1-(Buta-2,3-dien-2-yl)benzene** (**4.47**),[26] **1-(Buta-2,3-dien-2-yl)-4-methoxybenzene** (**4.48**),[27] **Buta-2,3-dien-2-yl(*tert*-butyl)**

(26) (a) Ngai, M.-Y.; Skucas, E.; Krische, M. J. *Org. Lett.* **2008**, *10*, 2705–2708. (b) Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2002**, *124*, 11566–11567. (c) Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1593.

(27) Schmittel, M.; Wöhrle, C.; Bohn, I. *Chem. Eur. J.* **1996**, *2*, 1031–1040.

**diphenylsilane** (substrate for **4.71a**),[28] **Penta-1,2-dien-3-ylbenzene** (substrate for **4.72a**).[29]

**1-(Buta-2,3-dien-2-yl)-4-trifluoromethylbenzene** (**4.49**): IR (neat): 2987 (w), 2929 (w), 1943 (w), 1616 (m), 1577 (w), 1458 (w), 1441 (w), 1426 (w), 1409 (w), 1322 (s), 1277 (w), 1233 (w), 1163 (w), 1108 (s), 1073 (s), 1058 (m), 1015 (m), 953 (w), 927 (w), 839 (s), 778 (w), 706 (m), 618 (m), 581 (w), 526 (w), 498 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.56 (2H, app d, $J$ = 8.0 Hz), 7.49 (2H, app d, $J$ = 8.0 Hz), 5.09 (2H, q, $J$ = 3.2 Hz), 2.11 (3H, t, $J$ = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.6, 140.7, 129.1 (q, $J_{CF}$ = 133 Hz), 128.7, 125.8 (d, $J_{CF}$ = 15.2 Hz), 125.3 (d, $J_{CF}$ = 3.8 Hz), 123.1, 77.4, 99.3, 16.6; HRMS: Calcd for $C_{11}H_{10}F_3$ $[M+H]^+$: 199.0734; Found: 199.0739.

**1-(Buta-2,3-dien-2-yl)-2-fluorobenzene** (**4.57**): IR (neat): 2960 (w), 2929 (w), 2872 (w), 1945 (w), 1576 (w), 1490 (s), 1448 (m), 1373 (w), 1301 (w), 1278 (w), 1260 (w), 1223 (m), 1106 (w), 1063 (w), 1034 (w), 937 (w), 849 (m), 818 (m), 753 (s), 606 (w), 554 (w), 543 (w), 489 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.30 (1H, dt, $J$ = 8.0, 1.6 Hz), 7.21–7.17 (1H, m), 7.09 (1H, dt, $J$ = 7.6, 1.6 Hz), 7.03 (1H, ddd, $J$ = 11.2, 8.0, 1.6 Hz), 4.91 (2H, q, $J$ = 3.2 Hz), 2.12 (3H, dt, $J$ = 3.2, 1.6 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 210.1, 160.4 (d, $J_{CF}$ = 248 Hz), 129.1 (d, $J_{CF}$ = 3.8 Hz), 128.4 (d, $J_{CF}$ = 8.3 Hz), 124.1 (d, $J_{CF}$ = 3.8 Hz), 116.1 (d, $J_{CF}$ = 22.0 Hz), 116.0, 95.7, 75.1 (d, $J_{CF}$ = 2.2 Hz), 18.8 (d, $J_{CF}$ = 3.0 Hz); HRMS: Calcd for $C_{10}H_{10}F_1$ $[M+H]^+$: 149.0767; Found: 149.0766.

**1-(Buta-2,3-dien-2-yl)-2-chlorobenzene** (substrate for **4.59a**): IR (neat): 3059 (w), 2982 (w), 2922 (w), 2856 (w), 1953 (w), 1701 (w), 1591 (w), 1565 (w), 1474 (m), 1432 (m),

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(28) (a) Kim, Y.; George, D.; Prior, A. M.; Prasain, K.; Hao, S.; Le, D. D.; Hua, D. H.; Chang, K.-O. *Eur. J. Med. Chem.* **2012**, *50*, 311–318. (b) Evans, D. A.; Sweeney, Z. K.; Rovis, T.; Tedrow, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 12095–12096.

(29) (a) Kobayashi, K.; Naka, H.; Wheatley, A. E. H.; Kondo, Y. *Org. Lett.* **2008**, *10*, 3375–3377. (b) Li, J.; Zhou, C.; Fu, C.; Ma, S. *Tetrahedron* **2009**, *65*, 3695–3703.

1370 (w), 1296 (w), 1125 (w), 1084 (m), 1038 (s), 943 (w), 848 (s), 755 (s), 739 (m), 730 (m), 666 (w), 607 (m), 547 (w), 464 (w), 448 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.37 (1H, dd, *J* = 7.6, 1.6 Hz), 7.29 (1H, dd, *J* = 7.6, 1.6 Hz), 7.25–7.16 (2H, m), 4.83 (2H, q, *J* = 3.2 Hz), 2.08 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 208.3, 137.6, 133.0, 130.2, 129.9, 128.4, 126.9, 98.5, 75.2, 19.8; HRMS: Calcd for $C_{10}H_{10}Cl_1$ $[M+H]^+$: 165.0471; Found: 165.0474.

**1-(Buta-2,3-dien-2-yl)-2-methoxybenzene** (substrate for **4.60a**): IR (neat): 2955 (w), 2834 (w), 1946 (w), 1594 (w), 1578 (w), 1490 (m), 1461 (m), 1433 (m), 1367 (w), 1301 (m), 1268 (s), 1241 (m), 1179 (w), 1161 (m), 1117 (m), 1063 (m), 1042 (s), 1026 (w), 930 (w), 843 (m), 794 (m), 746 (s), 690 (w), 581 (w), 539 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.22 (1H, d, *J* = 7.6 Hz), 7.21 (1H, dd, *J* = 8.8, 7.6 Hz), 6.91 (1H, dd, *J* = 7.6, 7.6 Hz), 6.87 (1H, d, *J* = 8.8 Hz), 4.78 (2H, q, *J* = 3.2 Hz), 3.82 (3H, s), 2.08 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.4, 157.0, 129.3, 128.3, 127.3, 120.8, 111.4, 97.9, 73.6, 55.6, 19.3; HRMS: Calcd for $C_{11}H_{13}O_1$ $[M+H]^+$: 161.0966; Found: 161.0977.

**1-(Buta-2,3-dien-2-yl)-3-fluorobenzene** (substrate for **4.62a**): IR (neat): 3063 (w), 2985 (w), 2952 (w), 2927 (w), 2859 (w), 1943 (m), 1610 (m), 1583 (m), 1523 (w), 1486 (s), 1461 (m), 1437 (m), 1371 (w), 1304 (w), 1286 (w), 1266 (w), 1239 (m), 1224 (m), 1178 (m), 1157 (m), 1080 (w), 1062 (w), 951 (m), 853 (s), 778 (s), 691 (s), 634 (w), 615 (m), 605 (m), 566 (w), 522 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.28–7.23 (1H, m), 7.20 (1H, s), 7.09 (1H, d, *J* = 10.4 Hz), 6.88 (1H, dd, *J* = 8.4, 8.4 Hz), 5.04 (2H, q, *J* = 3.2 Hz), 2.06 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.2, 163.2 (d, $J_{CF}$ = 244 Hz), 139.5 (d, $J_{CF}$ = 7.6 Hz), 129.7 (d, $J_{CF}$ = 8.4 Hz), 121.3 (d, $J_{CF}$ = 2.3 Hz), 113.4 (d, $J_{CF}$ =

21.3 Hz), 112.7 (d, $J_{CF}$ = 22 Hz), 99.3 (d, $J_{CF}$ = 2.2 Hz), 77.5, 16.7; HRMS: Calcd for $C_{10}H_{10}F_1$ $[M+H]^+$: 149.0767; Found: 149.0759.

**1-(Buta-2,3-dien-2-yl)-3-bromobenzene** (substrate for **4.63a**): IR (neat): 3060 (w), 2983 (w), 2950 (w), 2924 (w), 2860 (w), 1941 (m), 1589 (m), 1559 (m), 1473 (s), 1440 (w), 1424 (m), 1371 (w), 1299 (w), 1281 (w), 1271 (w), 1250 (w), 1079 (w), 1065 (m), 994 (m), 932 (w), 850 (s), 778 (s), 749 (s), 689 (s), 659 (s), 607 (s), 440 (w), 417 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.54 (1H, t, *J* = 1.6 Hz), 7.32 (2H, dd, *J* = 7.2, 1.6 Hz), 7.18 (1H, dd, *J* = 8.4, 7.2 Hz), 5.07 (2H, q, *J* = 3.2 Hz), 2.07 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.1, 139.3, 129.9, 129.6, 128.8, 124.3, 122.8, 99.1, 77.7, 16.7; HRMS: Calcd for $C_{10}H_{10}Br_1$ $[M+H]^+$: 208.9966; Found: 208.9966.

**1-(Buta-2,3-dien-2-yl)-4-bromobenzene** (substrate for **4.66a**): IR (neat): 2954 (w), 2924 (m), 2854 (w), 1941 (w), 1485 (m), 1456 (w), 1420 (w), 1395 (w), 1367 (w), 1293 (w), 1206 (w), 1103 (w), 1075 (m), 1005 (m), 924 (w), 851 (m), 822 (s), 755 (w), 725 (m), 715 (m), 699 (w), 630 (w), 612 (m), 547 (m), 528 (m), 490 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.42 (2H, app d, *J* = 6.8 Hz), 7.25 (2H, app d, *J* = 6.8 Hz), 5.01 (2H, q, *J* = 3.2 Hz), 2.06 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.0, 135.8, 131.4, 127.4, 120.5, 99.2, 77.4, 16.7; HRMS: Calcd for $C_{10}H_{10}Br_1$ $[M+H]^+$: 208.0966; Found: 208.0969.

**2-(Buta-2,3-dien-2-yl)naphthalene** (substrate for **4.67a**): white solid, mp = 65–67 °C, IR (neat): 3052 (m), 3018 (w), 2983 (w), 2957 (m), 2925 (w), 2857 (w), 1937 (m), 1626 (w), 1596 (w), 1501 (m), 1438 (m), 1373 (w), 1351 (w), 1278 (w), 1127 (m), 1065 (w), 950 (w), 888 (m), 857 (s), 824 (s), 770 (w), 743 (s), 620 (w), 594 (m), 477 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.81 (1H, dd, *J* = 8.8, 2.0 Hz), 7.79 (1H, dd, *J* = 8.4, 2.0 Hz),

7.76 (1H, app d, $J$ = 8.8 Hz), 7.72 (1H, s), 7.64 (1H, dd, $J$ = 8.4, 1.2 Hz), 7.48–7.40 (2H, m), 5.11 (2H, q, $J$ = 3.2 Hz), 2.22 (3H, t, $J$ = 3.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 209.8, 134.2, 133.7, 132.4, 128.0, 127.8, 127.6, 126.2, 125.7, 125.0, 123.4, 100.2, 77.3, 16.8; HRMS: Calcd for $C_{14}H_{13}$ $[M+H]^+$: 181.1017; Found: 181.1014.

**3-(Buta-2,3-dien-2-yl)pyridine** (substrate for **4.69a**): [Note: 3-(Buta-2,3-dien-2-yl)pyridine is unstable even at –30 °C. 3-(Buta-2,3-dien-2-yl)pyridine is colorless oil, but it becomes yellowish after one hour at ambient temperature. For this reason, it is imperative that this material is used immediately after preparation.] IR (neat): 3397 (br), 3033 (w), 2984 (w), 2949 (w), 2923 (w), 2860 (w), 1941 (m), 1569 (w), 1479 (m), 1458 (w), 1424 (m), 1408 (m), 1373 (w), 1332 (w), 1289 (w), 1242 (w), 1183 (w), 1123 (w), 1101 (w), 1076 (m), 1034 (w), 1020 (m), 989 (w), 946 (w), 923 (w), 851 (s), 805 (s), 706 (s), 625 (m), 606 (s), 533 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 8.64 (1H, d, $J$ = 2.4 Hz), 8.43 (1H, dd, $J$ = 4.4, 1.6 Hz), 7.66 (1H, d, $J$ = 8.4 Hz), 7.24–7.21 (1H, m), 5.08 (2H, q, $J$ = 3.2 Hz), 2.10 (3H, t, $J$ = 3.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 208.7, 147.6, 147.2, 132.7, 132.4, 123.0, 97.3, 77.6, 16.2; HRMS: Calcd for $C_9H_{10}N_1$ $[M+H]^+$: 132.0813; Found: 132.0818.

**3-(Buta-2,3-dien-2-yl)thiophene** (substrate for **4.70a**): [Note: 3-(Buta-2,3-dien-2-yl)thiophene is unstable even at –30 °C. For this reason, it is recommended that protoboration reaction is performed as soon as 3-(buta-2,3-dien-2-yl)thiophene is prepared.] IR (neat): 3109 (w), 2919 (w), 1942 (w), 1621 (m), 1493 (w), 1398 (w), 1353 (m), 1249 (w), 1195 (w), 1074 (w), 1085 (m), 951 (w), 880 (m), 845 (s), 797 (w), 760 (s), 677 (m), 612 (m), 584 (s), 484 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.26–7.24 (1H, m), 7.12 (1H, dd, $J$ = 5.2, 1.2 Hz), 7.04 (1H, dd, $J$ = 2.8, 1.2 Hz), 4.97 (2H, qd, $J$ = 3.2,

0.8 Hz), 2.07 (3H, t, *J* = 3.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 209.1, 126.4, 126.2, 119.8, 109.5, 96.2, 76.4, 17.0; HRMS: Calcd for $C_8H_9S_1$ $[M+H]^+$: 137.0425; Found: 137.0418.

**(4-Methylpenta-1,2-dien-3-yl)benzene** (substrate for **4.73a**): IR (neat): 3058 (w), 3031 (w), 2963 (m), 2929 (w), 2869 (w), 1942 (w), 1596 (w), 1494 (m), 1451 (m), 1383 (w), 1364 (w), 1075 (w), 1056 (w), 1033 (w), 965 (w), 909 (w), 847 (s), 763 (s), 794 (s), 639 (m), 609 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.41 (2H, d, *J* = 8.4 Hz), 7.33 (2H, dd, *J* = 8.4, 7.2 Hz), 7.20 (1H, t, *J* = 7.2 Hz), 5.09 (2H, d, *J* = 2.8 Hz), 2.85–2.78 (1H, m), 1.15 (6H, d, *J* = 6.8 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 207.8, 136.6, 128.5, 126.6, 126.5, 112.3, 79.2, 27.5, 22.3; HRMS: Calcd for $C_{12}H_{15}$ $[M+H]^+$: 159.1174; Found: 159.1173.

**5-(*tert*-Butyldimethylsilyloxy)-3-phenyl-penta-1,2-diene** (substrate for **4.74a**): IR (neat): 2953 (w), 2928 (w), 2885 (w), 2855 (w), 1940 (w), 1597 (w), 1494 (w), 1471 (w), 1462 (w), 1452 (w), 1387 (w), 1360 (w), 1253 (m), 1216 (w), 1095 (s), 1030 (w), 1005 (w), 982 (w), 937 (w), 907 (w), 832 (s), 773 (s), 760 (s), 717 (w), 692 (s), 664 (m), 636 (w), 606 (w), 573 (w), 525 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.40 (2H, app d, *J* = 8.0 Hz), 7.31 (2H, dd, *J* = 8.0, 7.2 Hz), 7.19 (1H, t, *J* = 7.2 Hz), 5.06 (2H, t, *J* = 3.2 Hz), 3.81 (2H, app t, *J* = 7.2 Hz), 2.65 (2H, tt, *J* = 7.2, 3.2 Hz), 0.89 (9H, s), 0.04 (6H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 208.7, 136.0, 128.3, 126.6, 125.9, 101.6, 78.0, 62.0, 32.8, 25.9, 18.2, –5.3; HRMS: Calcd for $C_{17}H_{27}O_1Si_1$ $[M+H]^+$: 275.1831; Found: 275.1820.

**1-Vinylidene-1,2,3,4-tetrahydronaphthalene** (substrate for **4.75a**): IR (neat): 3059 (w), 3020 (w), 2932 (s), 2862 (w), 2838 (w), 1940 (m), 1745 (w), 1719 (w), 1684 (m), 1599 (w), 1489 (s), 1452 (s), 1284 (m), 1014 (w), 849 (s), 760 (s), 728 (s), 577 (m), 482 (w),

437 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.49 (1H, d, *J* = 8.4 Hz), 7.16–7.12 (1H, m), 7.10 (2H, dd, *J* = 5.2, 1.2 Hz), 5.07 (2H, t, *J* = 3.2 Hz), 2.81 (2H, t, *J* = 6.4 Hz), 2.60–2.56 (2H, m), 1.93–1.87 (2H, m); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 206.7, 136.5, 131.3, 129.3, 127.0, 126.6, 126.2, 101.1, 78.1, 30.2, 28.8, 22.9; HRMS: Calcd for $C_{12}H_{13}$ $[M+H]^+$: 157.1017; Found: 157.1020.

**4-Vinylidenechroman** (substrate for **4.76a**): IR (neat): 3068 (w), 3036 (w), 2962 (w), 2930 (w), 2874 (w), 1944 (w), 1688 (w), 1603 (m), 1577 (m), 1486 (s), 1452 (s), 1293 (m), 1252 (m), 1219 (s), 1116 (m), 1042 (s), 867 (m), 803 (m), 753 (s), 580 (w), 507 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.37 (1H, dd, *J* = 7.6, 1.6 Hz), 7.10 (1H, td, *J* = 7.2, 1.6 Hz), 6.89 (1H, td, *J* = 7.6, 1.2 Hz), 6.83 (1H, dd, *J* = 8.4, 1.2 Hz), 5.16 (2H, t, *J* = 3.2 Hz), 4.24 (2H, t, *J* = 5.6 Hz), 2.76–2.72 (2H, m); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 205.1, 154.1, 128.4, 127.3, 121.1, 118.5, 117.5, 96.1, 79.6, 66.0, 27.9; HRMS: Calcd for $C_{11}H_{11}O_1$ $[M+H]^+$: 159.0810; Found: 159.0803.

**2-(Buta-2,3-dien-2-yl)-6-methoxynaphthalene** (**4.85**): yellow solid, mp = 113–115 °C. IR (neat): 3054 (m), 3006 (m), 2958 (m), 2933 (w), 2836 (w), 1936 (m) 1625 (m), 1598 (m), 1499 (m), 1481 (m), 1453 (m), 1438 (m), 1389 (m), 1369 (m), 1336 (w), 1276 (m), 1250 (m), 1223 (m), 1199 (m), 1186 (m), 1162 (m), 1150 (m), 1121 (m), 1064 (w), 1026 (m), 991 (w), 958 (w), 938 (w), 898 (w), 884 (m), 852 (s), 811 (s), 761 (w), 733 (w), 678 (m), 655 (w), 617 (m), 546 (m), 522 (w), 476 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.71 (1H, d, *J* = 8.8 Hz), 7.66 (1H, d, *J* = 8.4 Hz), 7.65 (1H, s), 7.60 (1H, app dd, *J* = 8.4, 1.6 Hz), 7.14 (1H, app dd, *J* = 8.8, 2.8 Hz), 7.11 (1H, s), 5.09 (2H, q, *J* = 3.2 Hz), 3.92 (3H, s), 2.20 (3H, t, *J* = 3.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.5, 157.7, 133.5,

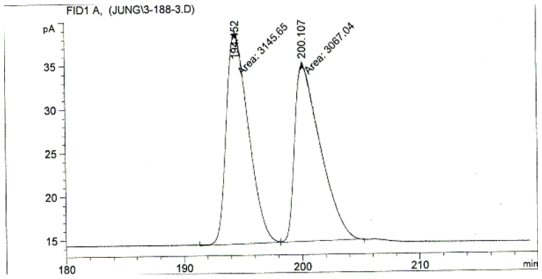
131.9, 129.6, 129.1, 126.7, 125.5, 123.3, 118.8, 105.9, 100.1, 77.3, 55.4, 16.9; HRMS: Calcd for $C_{15}H_{15}O_1$ $[M+H]^+$: 211.1122; Found: 211.1126.

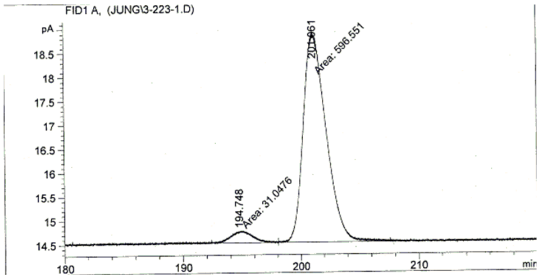
■ **Representative Procedure for NHC–Cu-Catalyzed Enantioselective Protoboration of 1,1-Disubstituted Allenes:** An oven-dried vial equipped with a stir bar was charged with imidazolinium salt **A.22** (3.4 mg, 5.50 μmol), NaO*t*-Bu (3.8 mg, 0.0400 mmol), CuCl (0.5 mg, 5.00 μmol) and thf (0.3 mL) in a $N_2$ filled glove box. The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol) was added to the solution, which turned dark brown immediately and the wall of a reaction vial was rinsed with additional thf (0.2 mL). The vial was resealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The solution was allowed to stir at 22 °C for 30 min under a $N_2$ atmosphere. Buta-2,3-dien-2-ylbenzene **4.47** (13.1 mg, 0.100 mmol) and *t*-BuOH (14.3 μL, 0.150 mmol) were added through a syringe. The resulting solution was allowed to stir at 22 °C for 16 hours before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to afford yellow oil, which was purified by silica gel chromatography (hexanes:$Et_2O$ = 50:1) to afford **4.50a** as colorless oil (20.4 mg, 0.0790 mmol, 79% yield).

**(*R*)-4,4,5,5-Tetramethyl-2-(3-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane** (**4.50a**): IR (neat): 3062 (w), 3026 (w), 2976 (m), 2931 (w), 2876 (w), 1613 (w), 1492 (w), 1451 (w), 1414 (m), 1370 (m), 1358 (m) 1306 (s), 1270 (w), 1214 (w), 1164 (w), 1138 (s), 1111 (w),

1068 (w), 1053 (w), 1029 (w), 1004 (w), 992 (m), 967 (m), 941 (w), 907 (w), 856 (s), 834 (w), 822 (w), 785 (w), 757 (m), 734 (m), 698 (s), 670 (w), 644 (w), 613 (w), 579 (w), 562 (w), 539 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.26–7.22 (3H, m), 7.14 (1H, t, *J* = 6.4 Hz), 5.81 (1H, dd, *J* = 2.8, 1.2 Hz), 5.56 (1H, d, *J* = 2.8 Hz), 3.70 (1H, q, *J* = 7.2 Hz), 1.40 (3H, d, *J* = 7.2 Hz), 1.17 (6H, s), 1.12 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 145.9, 128.1, 128.0, 126.8, 125.8, 83.4, 43.8, 24.7, 24.6, 20.3; HRMS: Calcd for $C_{16}H_{24}B_1O_2$ $[M+H]^+$: 259.1869; Found: 259.1862; specific rotation: $[\alpha]_D^{22}$ +8.33 (*c* 1.20, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 90 °C, 15 psi.



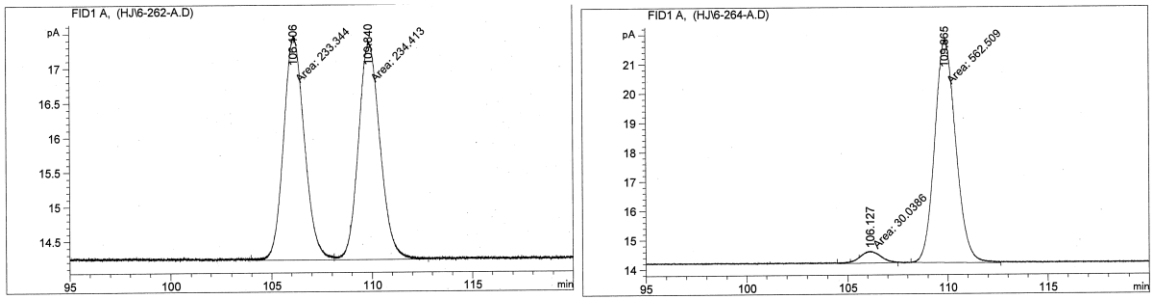




| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 194.452 | 3145.64 | 50.632 | 194.748 | 31.04 | 4.947 |
| 200.107 | 3067.04 | 49.368 | 201.061 | 596.55 | 95.053 |

**(*R*)-2-(3-(2-Fluorophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**4.58a**): IR (neat): 3068 (w), 2977 (m), 2932 (w), 2875 (w), 1617 (w), 1584 (w), 1489 (m), 1452 (m), 1423 (m), 1371 (s), 1358 (s), 1309 (s), 1270 (m), 1227 (s), 1138 (s), 1111 (m), 1070 (m), 967 (m), 943 (m), 858 (s), 834 (m), 753 (s), 689 (m), 580 (w), 521 (w), 483 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.21–7.11 (2H, m), 7.04 (1H, dt, *J* = 7.6, 1.2 Hz), 6.97 (1H, ddd, *J* = 10.4, 8.0, 1.2 Hz), 5.86 (1H, dd, *J* = 2.4, 1.6 Hz), 5.57 (1H, br s), 4.04 (1H, q, *J* = 7.2 Hz), 1.38 (3H, d, *J* = 7.2 Hz), 1.19 (6H, s), 1.12 (6H, s); $^{13}C$ NMR

($CDCl_3$, 100 MHz): δ 160.8 (d, $J_{CF}$ = 244 Hz), 132.9 (d, $J_{CF}$ = 15.2 Hz), 129.1 (d, $J_{CF}$ = 4.6 Hz), 127.4, 127.3 (d, $J_{CF}$ = 5.3 Hz), 123.7 (d, $J_{CF}$ = 3.8 Hz), 115.1 (d, $J_{CF}$ = 22.8 Hz), 83.5, 36.2 (d, $J_{CF}$ = 3.1 Hz), 24.8, 24.6, 19.3; HRMS: Calcd for $C_{16}H_{23}B_1F_1O_2$ $[M+H]^+$: 277.1775; Found: 277.1781; specific rotation: $[\alpha]_D^{20}$ –4.46 (*c* 2.24, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 100 °C, 15 psi.

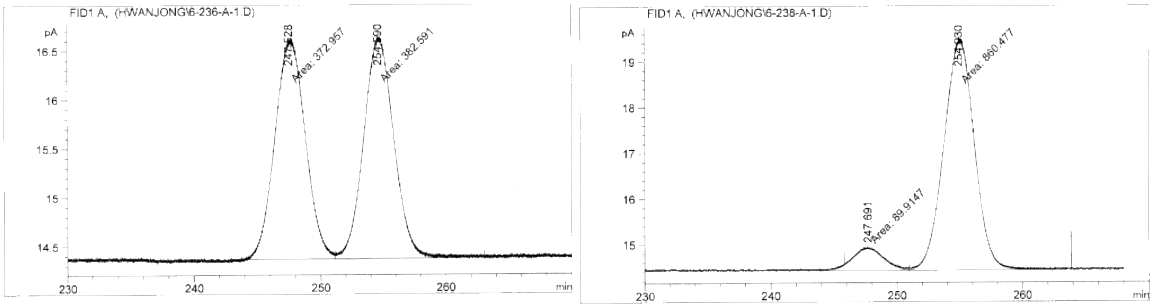



| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 106.106 | 233.34 | 49.886 | 106.127 | 30.04 | 5.069 |
| 109.840 | 234.41 | 50.114 | 109.865 | 562.51 | 94.931 |

**(*R*)-2-(3-(2-Chlorophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**4.59a**): IR (neat): 3068 (w), 2976 (w), 2931 (w), 2874 (w), 1617 (w), 1472 (m), 1423 (m), 1371 (s), 1356 (s), 1309 (s), 1271 (m), 1214 (m), 1139 (s), 1034 (m), 967 (m), 943 (m), 857 (s), 751 (s), 675 (m), 579 (w), 460 (w), 417 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.32 (1H, dd, *J* = 7.6, 1.2 Hz), 7.20 (1H, dt, *J* = 8.0, 2.0 Hz), 7.17 (1H, dt, *J* = 8.0, 1.6 Hz), 7.09 (1H, ddd, *J* = 7.6, 6.8, 2.0 Hz), 5.87 (1H, dd, *J* = 2.8, 1.2 Hz), 5.54 (1H, br s), 4.19 (1H, q, *J* = 7.2 Hz), 1.36 (3H, d, *J* = 6.8 Hz), 1.19 (6H, s), 1.10 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 143.5, 134.2, 129.4, 128.8, 127.4, 127.1, 126.6, 83.5, 39.7, 24.8, 24.5, 19.3; HRMS: Calcd for $C_{16}H_{23}B_1Cl_1O_2$ $[M+H]^+$: 293.1480; Found: 293.1481;

specific rotation: $[\alpha]_D^{20}$ +13.4 (*c* 1.49, $CHCl_3$) for an enantiomerically enriched sample of 90.5:9.5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 100 °C, 15 psi.

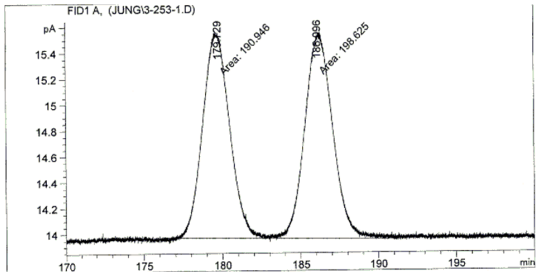


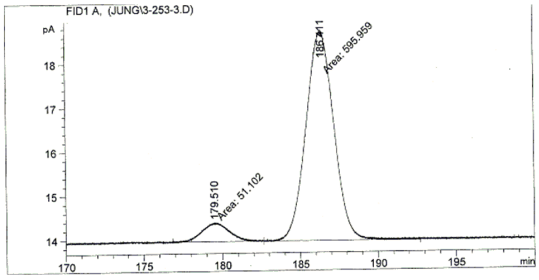

!

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 247.528 | 372.96 | 49.362 | 247.691 | 89.91 | 9.461 |
| 254.590 | 382.59 | 50.638 | 254.930 | 860.48 | 90.539 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(2-methoxyphenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.60a**): IR (neat): 3066 (w), 2976 (m), 2932 (w), 2835 (w), 1614 (w), 1598 (w), 1585 (w), 1490 (m), 1458 (w), 1413 (w), 1370 (m), 1356 (m), 1305 (s), 1271 (w), 1238 (s), 1214 (w), 1163 (m), 1138 (s), 1110 (m), 1070 (m), 1049 (m), 1030 (m), 998 (m), 967 (w), 939 (m), 907 (w), 858 (w), 828 (m), 796 (w), 750 (w), 691 (s), 670 (m), 644 (w), 619 (w), 579 (w), 521 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.14 (1H, dd, *J* = 7.6, 7.2 Hz), 7.12 (1H, d, *J* = 7.6 Hz), 6.87 (1H, ddd, *J* = 7.6, 7.2, 1.2 Hz), 6.83 (1H, d, *J* = 7.6 Hz), 5.79 (1H, dd, *J* = 3.2, 1.2 Hz), 5.52 (1H, d, *J* = 3.2 Hz), 4.14 (1H, q, *J* = 7.2 Hz), 1.33 (3H, d, *J* = 7.2 Hz), 1.18 (6H, s), 1.10 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 156.9, 134.5, 127.9, 126.6, 126.3, 120.2, 110.5, 83.1, 55.5, 35.7, 24.6, 24.3, 19.2; HRMS: Calcd for $C_{17}H_{25}B_1Na_1O_3$ $[M+Na]^+$: 311.1794; Found: 311.1798; specific rotation: $[\alpha]_D^{24}$ +8.32 (*c* 1.32, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 110 °C, 15 psi.

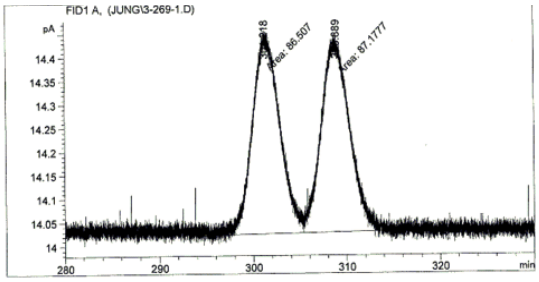


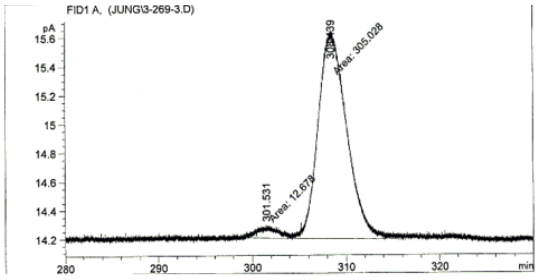




| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 179.729 | 190.94 | 49.014 | 179.510 | 51.10 | 7.897 |
| 186.096 | 198.62 | 50.986 | 186.411 | 595.95 | 92.103 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(3-fluorophenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.62a**): IR (neat): 2977 (w), 2932 (w), 2876 (w), 1612 (w), 1588 (w), 1485 (w), 1420 (w), 1371 (m), 1357 (m), 1308 (s), 1271 (w), 1261 (w), 1241 (w), 1227 (w), 1215 (w), 1165 (m), 1139 (s), 1112 (w), 1068 (w), 1055 (w), 1005 (w), 967 (m), 945 (m), 925 (m), 888 (m), 871 (m), 853 (s), 834 (w), 808 (w), 783 (m), 745 (m), 729 (m), 698 (w), 670 (w), 622 (w), 579 (w), 521 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.20 (1H, app q, $J$ = 7.2 Hz), 6.98 (1H, d, $J$ = 7.6 Hz), 6.94 (1H, d, $J$ = 10.8 Hz), 6.84 (1H, dd, $J$ = 10.8, 7.6 Hz), 5.84 (1H, d, $J$ = 2.4 Hz), 5.59 (1H, d, $J$ = 2.4 Hz), 3.69 (1H, q, $J$ = 7.2 Hz), 1.38 (3H, d, $J$ = 7.2 Hz), 1.17 (6H, s), 1.12 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 162.9 (d, $J_{CF}$ = 244 Hz), 148.7 (d, $J_{CF}$ = 6.8 Hz), 129.3 (d, $J_{CF}$ = 8.4 Hz), 127.4, 123.6 (d, $J_{CF}$ = 2.2 Hz), 114.8 (d, $J_{CF}$ = 20.5 Hz), 112.6 (d, $J_{CF}$ = 20.5 Hz), 83.5, 43.7, 24.7, 24.5, 20.0; HRMS: Calcd for $C_{16}H_{23}B_1F_1O_2$ $[M+H]^+$: 277.1775; Found: 277.1768; specific rotation: $[\alpha]_D^{23}$ +8.69 (*c* 2.30, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 83 °C, 15 psi.

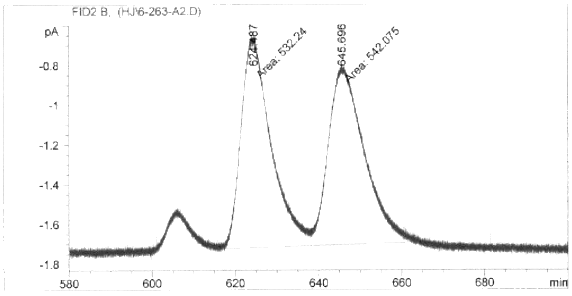


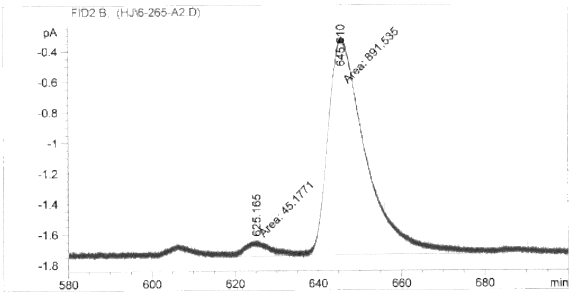




| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 301.218 | 86.50 | 49.807 | 301.531 | 12.67 | 3.990 |
| 308.889 | 87.17 | 50.193 | 308.439 | 305.02 | 96.010 |

**(*R*)-2-(3-(3-Bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**4.63a**): IR (neat): 3063 (w), 2976 (w), 2931 (w), 2874 (w), 1615 (w), 1592 (w), 1566 (w), 1420 (m), 1371 (s), 1357 (s), 1308 (s), 1271 (m), 1138 (s), 1074 (m), 997 (w), 966 (m), 945 (m), 858 (s), 831 (m), 779 (m), 716 (s), 690 (s), 579 (w), 438 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.39 (1H, d, $J$ = 2.0 Hz), 7.28 (1H, dt, $J$ = 6.8, 2.0 Hz), 7.16–7.09 (2H, m), 5.84 (1H, dd, $J$ = 2.8, 1.2 Hz), 5.60 (1H, br s), 3.65 (1H, q, $J$ = 7.2 Hz), 1.38 (3H, d, $J$ = 7.2 Hz), 1.18 (6H, s), 1.13 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 148.5, 131.1, 129.7, 128.9, 127.5, 126.7, 122.2, 83.6, 43.8, 24.8, 24.6, 20.0; HRMS: Calcd for $C_{16}H_{23}B_1Br_1O_2$ $[M+H]^+$: 337.0975; Found: 337.0988; specific rotation: $[\alpha]_D^{20}$ +6.28 (*c* 3.18, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDG-TA column, 90 °C, 15 psi.

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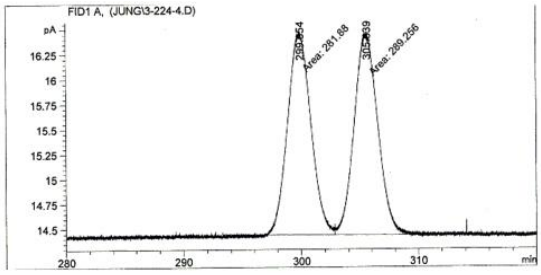
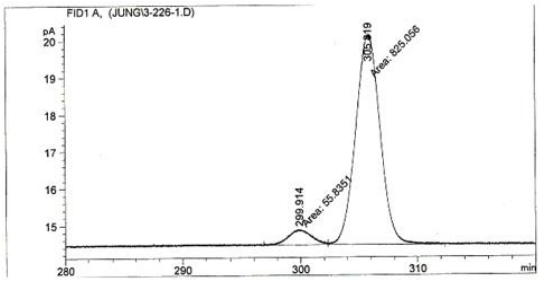
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 624.487 | 532.24 | 49.542 | 625.165 | 45.18 | 4.823 |
| 645.696 | 542.08 | 50.458 | 645.610 | 891.54 | 95.177 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(4-methoxyphenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.64a**): IR (neat): 2976 (w), 2932 (w), 2834 (w), 1610 (w), 1582 (w), 1509 (s), 1459 (w), 1441 (w), 1417 (w), 1370 (m), 1355 (m), 1306 (s), 1242 (s), 1214 (w), 1176 (m), 1138 (s), 1110 (m), 1068 (w), 1055 (w), 1035 (m), 995 (w), 967 (m), 942 (m), 906 (w), 857 (m), 830 (s), 800 (w), 733 (w), 719 (w), 680 (w), 666 (w), 640 (w), 612 (w), 578 (w), 549 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.13 (2H, d, *J* = 9.2 Hz), 6.81 (2H, d, *J* = 9.2 Hz), 5.78 (1H, d, *J* = 2.8 Hz), 5.53 (1H, d, *J* = 2.8 Hz), 3.77 (3H, s), 3.64 (1H, q, *J* = 7.2 Hz), 1.37 (3H, d, *J* = 7.2 Hz), 1.17 (6H, s), 1.13 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 157.8, 138.1, 128.9, 126.4, 113.5, 83.4, 55.3, 43.0, 24.8, 24.6, 20.4; HRMS: Calcd for $C_{17}H_{26}B_1O_3$ $[M+H]^+$: 289.1975; Found: 289.1986; specific rotation: $[\alpha]_D^{25}$ +4.34 (*c* 2.30, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 100 °C, 60 min, 0.1 °C/min to 115 °C, 15 psi.

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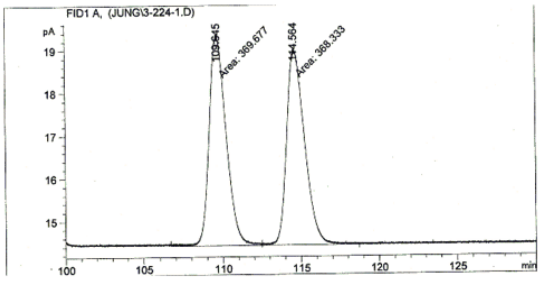
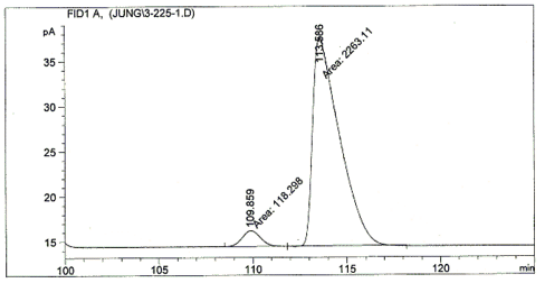
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 299.954 | 281.87 | 49.354 | 299.914 | 55.83 | 6.338 |
| 305.639 | 289.25 | 50.646 | 305.819 | 825.05 | 93.662 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(4-trifluoromethylphenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.65a**): IR (neat): 2978 (w), 2932 (w), 1616 (w), 1416 (w), 1371 (w), 1354 (w), 1322 (s), 1267 (w), 1213 (w), 1162 (m), 1120 (s), 1069 (s), 1016 (s), 967 (m), 947 (w), 907 (w), 857 (m), 842 (s), 728 (w), 689 (w), 670 (w), 645 (w), 607 (w), 578 (w), 528 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.50 (2H, d, $J$ = 8.0 Hz), 7.33 (2H, d, $J$ = 8.0 Hz), 5.87 (1H, d, $J$ = 2.8 Hz), 5.60 (1H, d, $J$ = 2.8 Hz), 3.75 (1H, q, $J$ = 7.2 Hz), 1.41 (3H, d, $J$ = 7.2 Hz), 1.16 (6H, s), 1.11 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 150.2, 128.3, 128.1 (q, $J_{CF}$ = 19.8 Hz), 127.7, 125.0 (q, $J_{CF}$ = 3.8 Hz), 124.6 (q, $J_{CF}$ = 270 Hz), 83.5, 43.8, 24.6, 20.0; HRMS: Calcd for $C_{17}H_{23}B_1F_3O_2$ $[M+H]^+$: 327.1743; Found: 327.1749; specific rotation: $[\alpha]_D^{22}$ +8.81 (*c* 3.40, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 100 °C, 15 psi.

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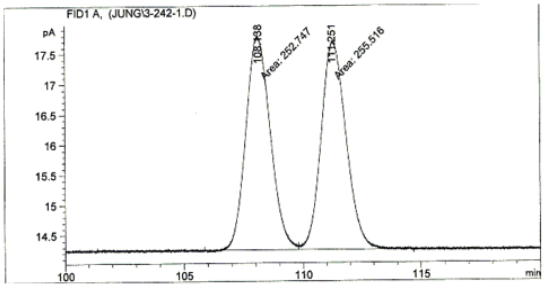
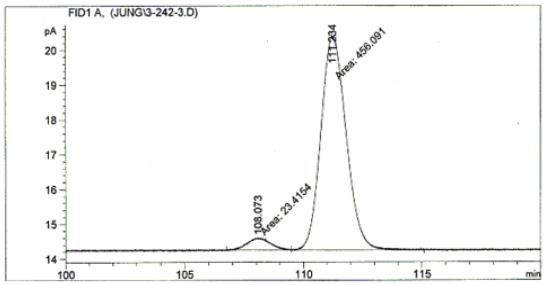
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 109.645 | 369.67 | 50.091 | 109.859 | 118.29 | 4.967 |
| 114.564 | 368.33 | 49.909 | 113.586 | 2263.10 | 95.033 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(4-bromophenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.66a**): IR (neat): 2976 (w), 2931 (w), 2875 (w), 1613 (w), 1487 (w), 1459 (w), 1415 (w), 1370 (m), 1356 (w), 1307 (s), 1270 (w), 1213 (w), 1164 (w), 1137 (s), 1111 (w), 1074 (m), 1009 (m), 966 (m), 944 (m), 906 (w), 856 (m), 828 (m), 778 (w), 736 (w), 722

(w), 695 (w), 670 (w), 638 (w), 592 (w), 578 (w), 536 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.36 (2H, d, *J* = 8.4 Hz), 7.09 (2H, d, *J* = 8.4 Hz), 5.83 (1H, dd, *J* = 2.8, 1.2 Hz), 5.57 (1H, d, *J* = 2.8 Hz), 3.65 (1H, q, *J* = 7.2 Hz), 1.36 (3H, d, *J* = 7.2 Hz), 1.17 (6H, s), 1.13 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 145.0, 131.1, 129.8, 127.3, 119.5, 83.5, 43.3, 24.8, 20.1; HRMS: Calcd for $C_{16}H_{23}B_1Br_1O_2$ $[M+H]^+$: 337.0974; Found: 337.0982; specific rotation: $[\alpha]_D^{23}$ +5.00 (*c* 4.00, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 130 °C, 15 psi.

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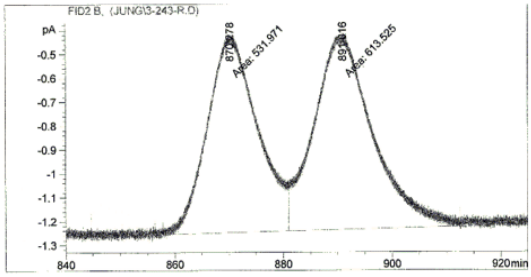
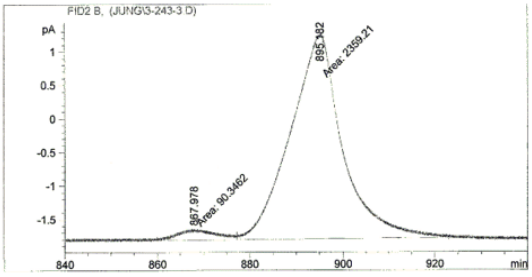
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 108.138 | 252.74 | 49.727 | 108.073 | 23.41 | 4.883 |
| 111.251 | 255.51 | 50.273 | 111.234 | 456.09 | 95.117 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(2-naphthyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.67a**): IR (neat): 3054 (w), 2975 (w), 2931 (w), 2873 (w), 1632 (w), 1613 (w), 1600 (w), 1506 (w), 1418 (w), 1370 (m), 1353 (m), 1306 (s), 1270 (w), 1213 (w), 1164 (w), 1137 (s), 1069 (m), 1018 (w), 1004 (w), 966 (m), 946 (m), 909 (w), 892 (w), 893 (w), 851 (s), 818 (m), 771 (w), 744 (s), 724 (m), 677 (w), 619 (w), 578 (w), 543 (w), 520 (w), 475 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.81 (1H, d, *J* = 2.4 Hz), 7.79 (1H, d, *J* = 2.4 Hz), 7.76 (1H, d, *J* = 8.8 Hz), 7.69 (1H, s), 7.46–7.38 (3H, m), 5.90 (1H, d, *J* = 2.8 Hz), 5.64 (1H, d,

*J* = 2.8 Hz), 3.90 (1H, q, *J* = 7.2 Hz), 1.52 (3H, d, *J* = 7.2 Hz), 1.17 (6H, s), 1.11 (6H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 143.4, 133.6, 132.2, 127.7, 127.6, 127.5, 127.3, 127.2, 125.9, 125.7, 125.1, 83.4, 43.9, 24.7, 24.6, 20.2; HRMS: Calcd for $C_{20}H_{26}B_1O_2$ $[M+H]^+$: 309.2025; Found: 309.2024; specific rotation: $[\alpha]_D^{22}$ +4.00 (*c* 5.00, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDG-TA column, 110 °C, 15 psi.

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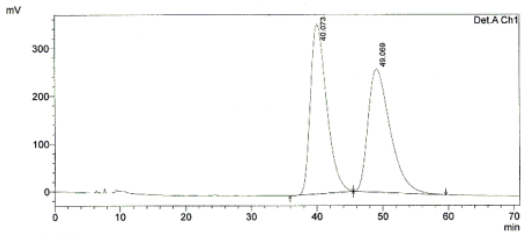
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 870.278 | 531.97 | 46.440 | 867.978 | 90.34 | 3.688 |
| 891.016 | 613.52 | 53.560 | 895.182 | 2359.20 | 96.312 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(6-methoxy-2-naphthyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.68a**): IR (neat): 3058 (w), 2975 (w), 2934 (w), 1633 (w), 1604 (m), 1504 (w), 1482 (w), 1462 (w), 1416 (w), 1389 (w), 1370 (w), 1356 (w), 1307 (s), 1263 (s), 1229 (w), 1213 (m), 1162 (m), 1137 (s), 1070 (w), 1033 (m), 966 (w), 944 (w), 927 (m), 907 (w), 852 (s), 808 (m), 730 (s), 672 (m), 647 (w), 622 (w), 578 (w), 521 (w), 474 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.67 (1H, d, *J* = 10.0 Hz), 7.64 (1H, d, *J* = 8.4 Hz), 7.59 (1H, s), 7.33 (1H, dd, *J* = 8.4, 2.0 Hz), 7.10 (1H, dd, *J* = 8.4, 2.8 Hz), 7.09 (1H, s), 5.85 (1H, dd, *J* = 2.8, 1.6 Hz), 5.60 (1H, dd, *J* = 2.8, 1.6 Hz), 3.90 (3H, s), 3.84 (1H, q, *J* = 7.2 Hz), 1.48 (3H, d, *J* = 7.2 Hz), 1.15 (6H, s), 1.10 (6H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 157.1, 141.1, 133.1, 129.2, 129.1, 127.6, 127.0, 126.4, 125.8, 118.4, 105.6, 83.4,

55.3, 43.7, 24.7, 20.2; HRMS: Calcd for $C_{21}H_{28}B_1O_3$ $[M+H]^+$: 339.2131; Found: 339.2132; specific rotation: $[\alpha]_D^{21}$ +3.43 (*c* 1.06, $CHCl_3$) for an enantiomerically enriched sample of 98:2 e.r.

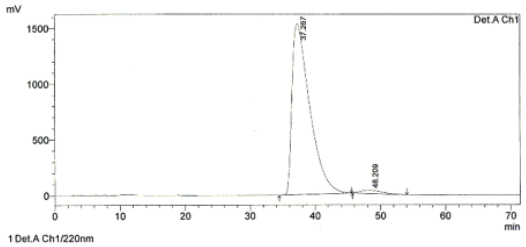
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OJ-H column, 100% hexanes, 0.5 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 40.073 | 61056897 | 355447 | 50.252 | 57.912 |
| 2 | 49.069 | 60445037 | 258328 | 49.748 | 42.088 |
| Total | | 121501934 | 613775 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 37.267 | 291823527 | 1534186 | 97.949 | 98.134 |
| 2 | 48.209 | 6110078 | 29175 | 2.051 | 1.866 |
| Total | | 297933605 | 1563362 | 100.000 | 100.000 |

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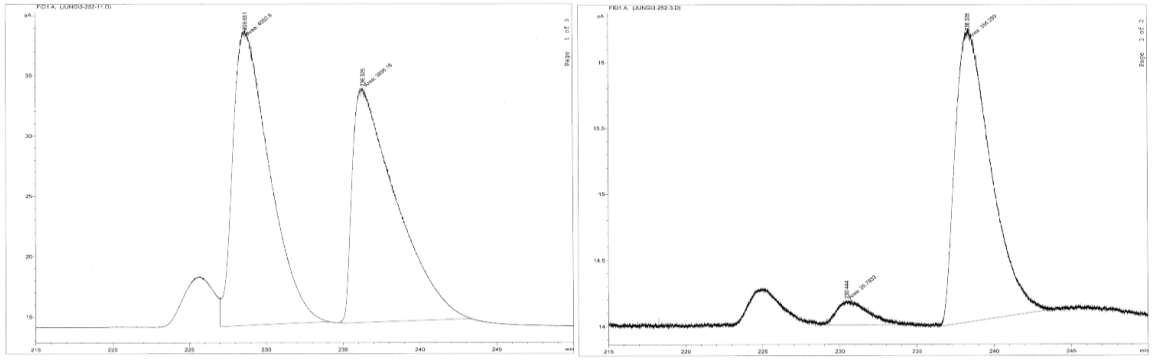
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 40.073 | $6.10 \times 10^7$ | 50.252 | 37.267 | $2.91 \times 10^8$ | 97.949 |
| 49.069 | $6.04 \times 10^7$ | 49.748 | 48.209 | $6.11 \times 10^6$ | 2.051 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(3-pyridyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.69a**): IR (neat): 3297 (br), 2976 (w), 2931 (w), 1617 (w), 1574 (w), 1473 (w), 1457 (w), 1419 (m), 1370 (s), 1352 (s), 1304 (s), 1270 (m), 1213 (w), 1139 (s), 1110 (m), 1071 (w), 1024 (w), 967 (m), 949 (m), 885 (m), 857 (w), 831 (w), 809 (w), 715 (s), 688 (m), 670 (m), 621 (w), 578 (w), 549 (w), 520 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 8.48 (1H, s), 8.39 (1H, s), 7.50 (1H, dt, *J* = 8.0, 1.6 Hz), 7.16 (1H, dd, *J* = 7.6, 4.8 Hz), 5.86 (1H, d, *J* = 2.8 Hz), 5.61 (1H, d, *J* = 2.8 Hz), 3.69 (1H, q, *J* = 7.2 Hz), 1.39 (3H, d, *J* = 7.2 Hz), 1.24 (6H, s), 1.22 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 149.6, 146.9, 135.2, 127.6, 83.4, 76.6, 74.9, 41.3, 24.6, 19.7; HRMS: Calcd for $C_{15}H_{23}B_1N_1O_2$ $[M+H]^+$: 260.1821; Found: 260.1821; specific rotation: $[\alpha]_D^{23}$ +9.99 (*c* 2.00, $CHCl_3$) for an enantiomerically enriched sample of 93:7 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDG-TA column, 100 °C, 15 psi.



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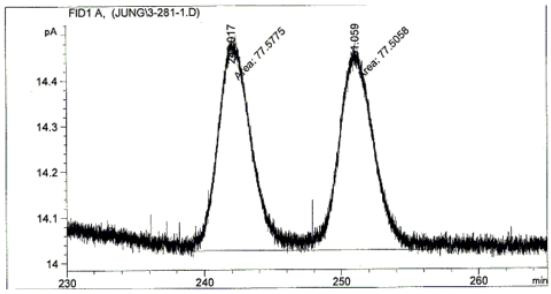
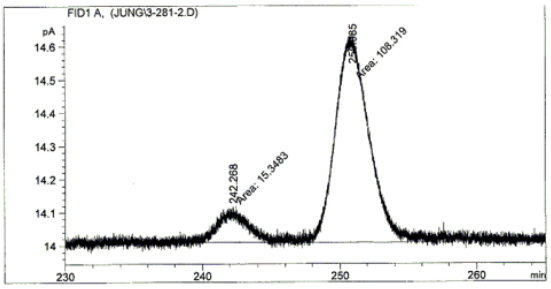
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 228.651 | 4184.22 | 49.943 | 230.380 | 28.77 | 7.174 |
| 236.325 | 4153.76 | 50.057 | 238.369 | 372.32 | 92.826 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(3-thiophenyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.70a**): IR (neat): 3068 (w), 2976 (w), 2931 (w), 2875 (w), 1614 (w), 1422 (w), 1371 (m), 1355 (s), 1307 (s), 1271 (w), 1213 (w), 1182 (w), 1165 (w), 1139 (s), 1111 (w), 1070 (w), 1005 (w), 967 (w), 945 (w), 895 (w), 853 (m), 832 (w), 806 (w), 779 (m), 723 (w), 671 (w), 649 (w), 579 (w), 518 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.20 (1H, dd, *J* = 4.8, 2.8 Hz), 6.96 (1H, d, *J* = 4.8 Hz), 6.94 (1H, d, *J* = 2.8 Hz), 5.78 (1H, d, *J* = 2.8 Hz), 5.53 (1H, d, *J* = 2.8 Hz), 3.76 (1H, q, *J* = 7.2 Hz), 1.41 (3H, d, *J* = 7.2 Hz), 1.20 (6H, s), 1.19 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 146.7, 127.9, 127.0, 124.5, 119.7, 83.2, 39.6, 24.5, 20.2; HRMS: Calcd for $C_{14}H_{22}B_1O_2S_1$ $[M+H]^+$: 265.1433; Found: 265.1442; specific rotation: $[\alpha]_D^{23}$ +10.9 (*c* 0.92, $CHCl_3$) for an enantiomerically enriched sample of 88:12 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 90 °C, 15 psi.

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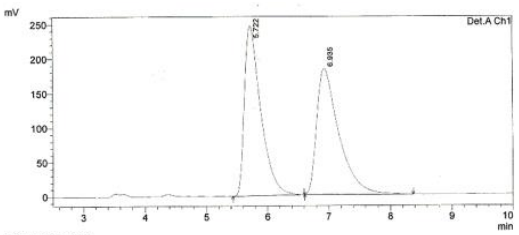
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 242.017 | 77.57 | 50.023 | 242.268 | 15.34 | 12.410 |
| 251.059 | 77.50 | 49.977 | 250.985 | 108.31 | 87.590 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-(*tert*-butyldiphenylsilyl)but-1-en-2-yl)-1,3,2-dioxaborolane** (**4.71a**): IR (neat): 3070 (w), 2976 (w), 2930 (w), 2857 (w), 1599 (w), 1460 (m), 1426 (w), 1389 (m), 1372 (m), 1352 (w), 1306 (m), 1270 (w), 1212 (w), 1186 (w), 1131 (s), 1102 (s), 1000 (m), 966 (m), 933 (m), 907 (s), 857 (m), 818 (m), 731 (s), 698 (s), 671 (w), 635 (s), 617 (w) 598 (m), 578 (w), 492 (s) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.65 (4H, dd, *J* = 16.4, 7.6 Hz), 7.41–7.30 (6H, m), 5.76 (1H, d, *J* = 2.8 Hz), 4.98 (1H, d, *J* = 2.8 Hz), 2.81 (1H, q, *J* = 7.2 Hz), 1.26 (12H, s), 1.14 (3H, d, *J* = 7.2 Hz), 1.06 (9H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 137.2, 136.8, 135.3, 133.7, 129.2, 128.8, 127.0, 83.4, 28.7, 25.0, 20.8, 19.0, 18.6; HRMS: Calcd for $C_{26}H_{37}B_1Na_1O_2Si_1$ $[M+Na]^+$: 443.2554; Found: 443.2559; specific rotation: $[\alpha]_D^{23}$ +36.4 (*c* 3.75, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

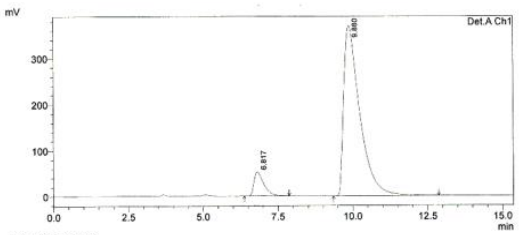
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H column, 100% hexanes, 1.0 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 5.722 | 4610752 | 247035 | 50.054 | 57.449 |
| 2 | 6.935 | 4600839 | 182976 | 49.946 | 42.551 |
| Total | | 9211592 | 430011 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 6.817 | 1177015 | 52285 | 7.844 | 12.358 |
| 2 | 9.880 | 13828246 | 370816 | 92.156 | 87.642 |
| Total | | 15005261 | 423102 | 100.000 | 100.000 |

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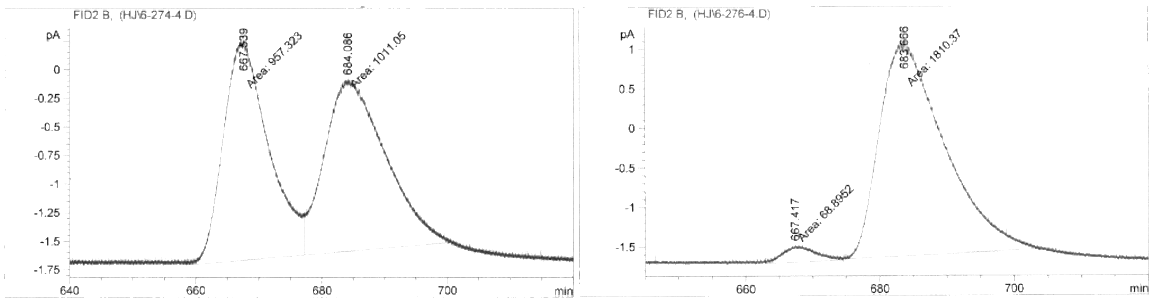
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 5.722 | $4.61 \times 10^6$ | 50.054 | 6.817 | $1.17 \times 10^6$ | 7.844 |
| 6.935 | $4.60 \times 10^6$ | 49.946 | 9.880 | $1.38 \times 10^7$ | 92.156 |

**(*R*)-4,4,5,5-Tetramethyl-2-(3-phenylpent-1-en-2-yl)-1,3,2-dioxaborolane** (**4.72a**): IR (neat): 3062 (w), 3027 (w), 2976 (m), 2930 (w), 2873 (w), 1602 (w), 1414 (m), 1361 (s), 1306 (s), 1262 (m), 1214 (m), 1139 (s), 1028 (w), 969 (m), 942 (m), 902 (w), 865 (s), 839 (m), 768 (m), 748 (m), 700 (s), 671 (m), 579 (w), 541 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.27–7.21 (4H, m), 7.16–7.13 (1H, m), 5.82 (1H, dd, $J$ = 2.8, 0.8 Hz), 5.61 (1H, d, $J$ = 1.6 Hz), 3.38 (1H, t, $J$ = 6.8 Hz), 1.98–1.91 (1H, m), 1.81–1.73 (1H, m), 1.18 (6H, s), 1.14 (6H, s), 0.85 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.5, 128.6, 128.1, 127.4, 125.8, 83.4, 52.3, 26.8, 24.8, 24.6, 12.8; HRMS: Calcd for $C_{17}H_{26}B_1O_2$ $[M+H]^+$: 273.2026; Found: 273.2016; specific rotation: $[\alpha]_D^{20}$ +16.6 (*c* 2.40, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDG-TA column, 70 °C, 15 psi.

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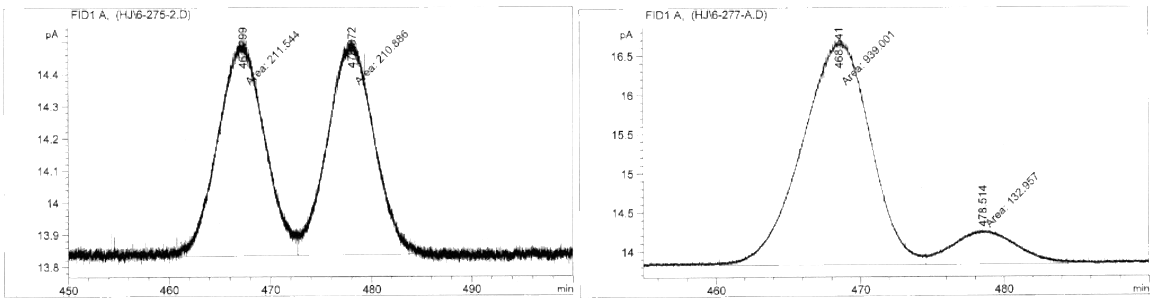
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 667.539 | 957.32 | 48.635 | 667.417 | 68.90 | 3.666 |
| 684.086 | 1011.05 | 51.365 | 683.666 | 1810.37 | 96.334 |

**(*R*)-4,4,5,5-Tetramethyl-2-(4-methyl-3-phenylpent-1-en-2-yl)-1,3,2-dioxaborolane** (**4.73a**): IR (neat): 3062 (w), 3026 (w), 2975 (m), 2868 (w), 1601 (w), 1428 (m), 1413 (m), 1379 (s), 1357 (s), 1305 (m), 1165 (s), 966 (m), 942 (m), 865 (s), 839 (m), 758 (m), 701 (s), 591 (m), 522 (w), 496 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.29 (1H, dd, *J* = 8.0, 1.6 Hz), 7.23 (1H, dt, *J* = 6.4, 1.6 Hz), 7.17 (1H, tt, *J* = 7.2, 1.6 Hz), 5.80 (1H, d, *J* = 3.2 Hz), 5.69 (1H, d, *J* = 2.8 Hz), 3.02 (1H, d, *J* = 10.4 Hz), 2.48–2.42 (1H, m), 1.23 (6H, s), 1.19 (6H, s), 0.95 (3H, d, *J* = 6.4 Hz), 0.73 (3H, d, *J* = 6.4 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 145.0, 128.9, 128.7, 128.1, 125.7, 83.4, 61.0, 30.2, 24.8, 24.7, 22.2, 21.7; HRMS: Calcd for $C_{18}H_{28}B_1O_2$ $[M+H]^+$: 287.2182; Found: 287.2179; specific rotation: $[\alpha]_D^{20}$ +4.66 (*c* 2.14, $CHCl_3$) for an enantiomerically enriched sample of 88:12 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 85 °C, 15 psi.




!

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 467.299 | 211.54 | 50.078 | 468.541 | 939.00 | 87.597 |
| 478.072 | 210.89 | 49.922 | 478.514 | 132.957 | 12.403 |

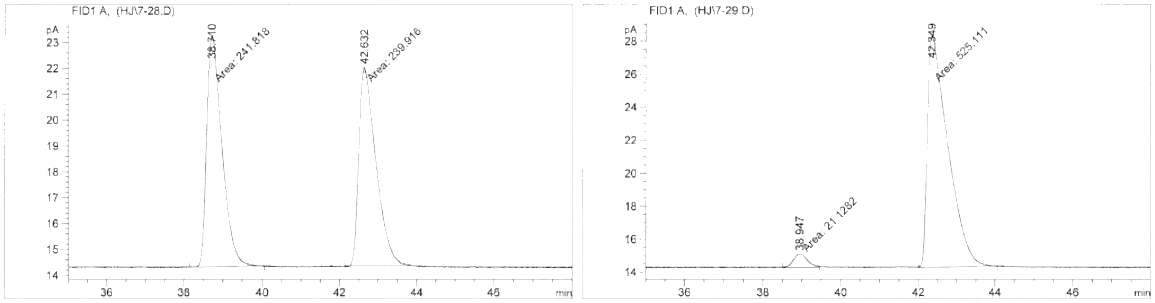
**(*R*)-4,4,5,5-Tetramethyl-2-(1-(1,2,3,4-tetrahydronaphthalen-1-yl)vinyl)-1,3,2-dioxaborolane** (**4.75a**): IR (neat): 3059 (w), 2977 (m), 2931 (m), 2861 (w), 1613 (w), 1449 (m), 1429 (m), 1412 (m), 1359 (s), 1306 (s), 1272 (m), 1214 (m), 1134 (s), 966 (m), 946 (m), 865 (m), 851 (m), 737 (s), 687 (m), 671 (m), 579 (w), 444 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.07–7.03 (3H, m), 7.02–6.99 (1H, m), 5.91 (1H, d, $J$ = 2.8 Hz), 5.25 (1H, d, $J$ = 2.8 Hz), 3.77 (1H, t, $J$ = 6.4 Hz), 2.83–2.69 (2H, m), 1.93–1.77 (3H, m), 1.71–1.64 (1H, m), 1.25 (6H, s), 1.17 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 139.1, 137.9, 130.1, 128.8, 125.6, 125.4, 83.4, 44.3, 29.8, 29.4, 25.1, 24.4, 20.0; HRMS: Calcd for $C_{18}H_{26}B_1O_2$ $[M+H]^+$: 285.2026; Found: 285.2012; specific rotation: $[\alpha]_D^{20}$ +4.36 (*c* 1.53, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material of the ketone (oxidation product of **4.75a**) obtained through sodium perborate-mediated oxidative work-up.

**(*S*)-1-(1,2,3,4-Tetrahydronaphthalen-1-yl)ethanone** (Oxidation product of **4.75a**): IR (neat): 3060 (w), 3017 (w), 2934 (m), 2864 (w), 1702 (s), 1493 (m), 1450 (m), 1355 (s), 1227 (m), 1188 (m), 1037 (w), 970 (w), 818 (w), 740 (s), 551 (m), 498 (w), 441 (w) $cm^{-1}$;

$^1$H NMR ($CDCl_3$, 400 MHz): δ 7.20–7.11 (3H, m), 7.00–6.97 (1H, m), 3.83 (1H, t, *J* = 6.8 Hz), 2.80 (2H, q, *J* = 6.0 Hz), 2.12 (3H, s), 2.09–1.87 (3H, m), 1.78–1.70 (1H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 211.0, 137.5, 133.8, 129.7, 129.4, 127.0, 126.1, 53.9, 29.4, 27.9, 26.3, 21.0; HRMS: Calcd for $C_{12}H_{15}O_1$ $[M+H]^+$: 175.1123; Found: 175.1129; specific rotation: $[\alpha]_D^{20}$ –15.6 (*c* 1.92, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 120 °C, 15 psi.

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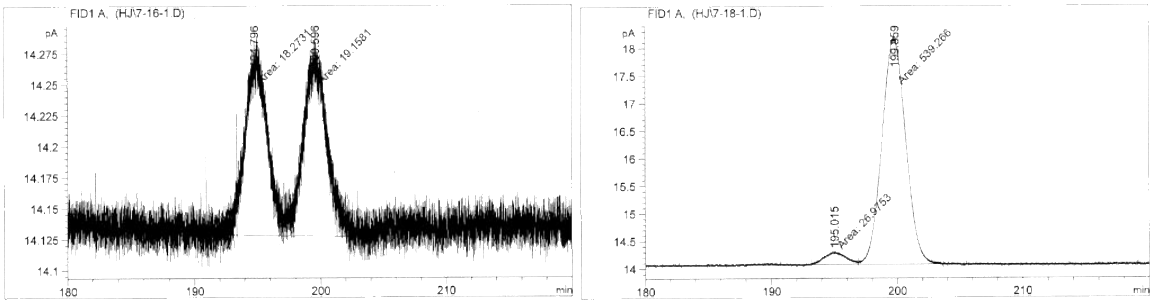
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 38.710 | 241.82 | 50.197 | 38.947 | 21.13 | 3.868 |
| 42.632 | 239.92 | 49.803 | 42.349 | 525.11 | 96.132 |

**(*R*)-2-(1-(Chroman-4-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.76a)**: IR (neat): 2975 (w), 2927 (w), 2874 (w), 1607 (w), 1580 (w), 1487 (m), 1450 (m), 1361 (m), 1304 (s), 1268 (m), 1248 (m), 1221 (s), 1136 (s), 1113 (m), 1062 (m), 1017 (w), 967 (w), 950 (w), 855 (w), 833 (w), 752 (s), 722 (w), 687 (w), 579 (w), 468 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.08 (1H, t, *J* = 8.0 Hz), 6.95 (1H, d, *J* = 7.2 Hz), 6.81 (2H, t, *J* = 8.0 Hz), 6.01 (1H, d, *J* = 3.2 Hz), 5.34 (1H, d, *J* = 2.0 Hz), 4.13–4.10 (2H, m), 3.75 (1H, t, *J* = 5.6 Hz), 2.12–2.07 (1H, m), 2.02–1.97 (1H, m), 1.26 (6H, s), 1.20 (6H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 155.3, 132.3, 130.7, 127.6, 124.1, 120.0, 116.6, 83.7, 63.1, 39.8,

28.1, 25.1, 24.5; HRMS: Calcd for $C_{17}H_{24}B_1O_3$ $[M+H]^+$: 287.1819; Found: 287.1824; specific rotation: $[\alpha]_D^{20}$ +3.98 (*c* 2.51, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 120 °C, 15 psi.

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| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 194.796 | 18.27 | 48.818 | 195.015 | 26.98 | 4.764 |
| 199.596 | 19.16 | 51.182 | 199.859 | 539.27 | 95.236 |

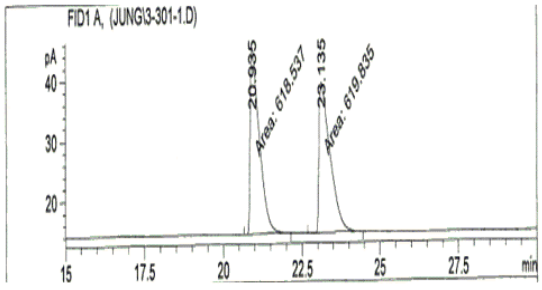
■ **Representative Procedure for Conversion of Alkenylborons to Methyl Ketones:** (*R*)-4,4,5,5-Tetramethyl-2-(3-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane **4.50a** (25.8 mg, 0.100 mmol) was dissolved in a mixture of thf (0.5 mL) and pH = 7 buffer (0.5 mL). $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol) was added to the mixture and it was allowed to stir at 22 °C for 30 min. The reaction was quenched by addition of $H_2O$ (2 mL) and water layer was washed with $Et_2O$ (3 x 2 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure (Note: Most of methyl ketones are quite volatile. It is recommended not to dry the unpurified mixture under high-vacuum. House-vacuum was used exclusively for concentrating the products). The product **4.77** was

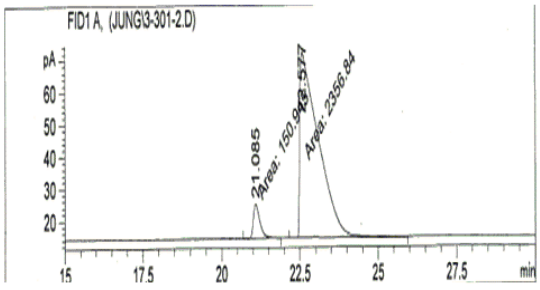
isolated by silica gel chromatography (hexanes:$Et_2O$=20:1) as colorless oil (10.5 mg, 0.07080 mmol, 71% yield).

**(*S*)-3-Phenylbuta-2-one** (**4.77**): [Note: The analytical data are fully consistent with those reported previously.][30] IR (neat): 3061 (w), 3027 (w), 2976 (w), 2932 (w), 1710 (s), 1600 (w), 1583 (w), 1493 (m), 1452 (m), 1372 (m) 1354 (w), 1317 (w), 1248 (w), 1195 (w), 1164 (m), 1068 (m), 1024 (w), 949 (w), 912 (w), 804 (w), 765 (m), 738 (w), 698 (s), 635 (w), 591 (w), 541 (s), 472 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.35–7.34 (2H, m), 7.32–7.31 (1H, m), 7.21 (2H, d, $J$ = 7.2 Hz), 3.74 (1H, q, $J$ = 7.2 Hz), 2.04 (3H, s), 1.39 (3H, d, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 208.8, 140.5, 128.9, 127.7, 127.1, 53.7, 28.3, 17.1; HRMS: Calcd for $C_{10}H_{13}O_1$ $[M+H]^+$: 149.0966; Found: 149.0972; specific rotation: $[\alpha]_D^{21}$ +212.9 (*c* 0.61, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 90 °C, 15 psi.

**Stereochemistry Proof** is based on the optical rotation for the *R* enantiomer: $[\alpha]_D^{20}$ –234 (*c* 1.0, $CHCl_3$) for a 83.5:16.5 e.r. sample.[27]

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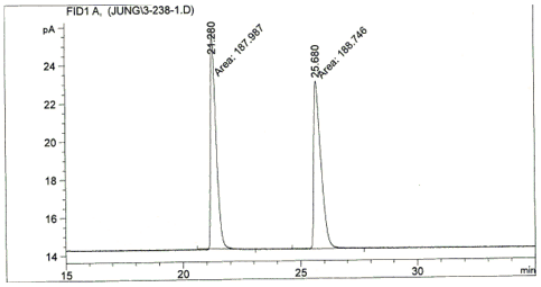
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 20.935 | 618.53 | 49.947 | 21.085 | 150.94 | 6.019 |

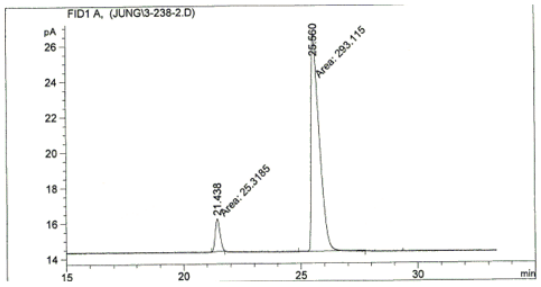
(30) Roy, O.; Riahi, A.; Hénin, F.; Muzart, J. *Eur. J. Org. Chem.* **2002**, 3986–3994.

| | | | | | |
|---|---|---|---|---|---|
| 23.135 | 619.83 | 50.053 | 22.577 | 2356.84 | 93.981 |

**(*S*)-3-(4-Trifluoromethylphenyl)buta-2-one** (**4.78**): IR (neat): 2981 (w), 2937 (w), 1715 (s), 1618 (w), 1455 (w), 1418 (w), 1356 (w), 1322 (s), 1250 (w), 1161 (s), 1113 (s), 1067 (s), 1017 (m), 952 (w), 843 (s), 776 (w), 750 (w), 729 (w), 654 (w), 635 (w), 603 (m), 535 (w), 505 (w), 452 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.59 (2H, d, $J$ = 8.0 Hz), 7.34 (2H, d, $J$ = 8.0 Hz), 3.82 (1H, q, $J$ = 7.2 Hz), 2.07 (3H, s), 1.41 (3H, d, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 207.8, 172.4 (d, $J_{CF}$ = 0.7 Hz), 144.6, 128.2 (d, $J_{CF}$ = 10.6 Hz), 126.0 (d, $J_{CF}$ = 3.0 Hz), 124.2 (q, $J_{CF}$ = 271 Hz), 53.5, 28.6, 17.4; HRMS: Calcd for $C_{11}H_{12}F_3O_1$ $[M+H]^+$: 217.0840; Found: 217.0849; specific rotation: $[\alpha]_D^{22}$ +135.1 (*c* 2.44, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 100 °C, 15 psi.

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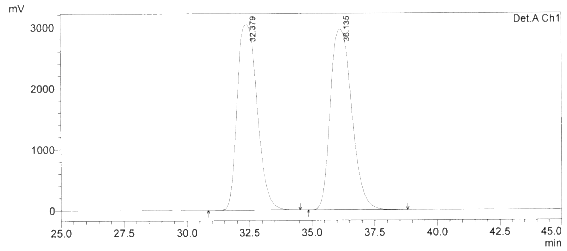
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 21.280 | 187.98 | 49.899 | 21.438 | 25.31 | 7.950 |
| 25.680 | 188.74 | 50.101 | 25.560 | 293.11 | 92.050 |

**(*S*)-3-(6-Methoxy-2-naphthyl)buta-2-one** (**4.79**): [Note: The synthesis of racemic **4.79** is already reported, but the analytical data of **4.79** is not reported.] IR (neat): 2984 (w), 2960 (w), 2938 (w), 2886 (w), 1712 (s), 1703 (s), 1629 (w), 1601 (m), 1503 (w), 1483 (w), 1457 (w), 1437 (w), 1414 (w), 1390 (w), 1372 (w), 1353 (m), 1311 (w), 1265 (m), 1224 (m), 1194 (w), 1169 (s), 1121 (w), 1065 (m), 1025 (s), 959 (w), 943 (w), 921 (w),

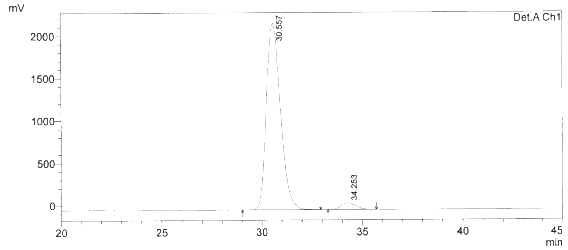
890 (m), 854 (s), 815 (s), 765 (w), 742 (w), 691 (w), 672 (w), 631 (w), 600 (w), 586 (w), 533 (w), 520 (w), 477 (s), 456 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.71 (1H, d, $J$ = 4.4 Hz), 7.69 (1H, d, $J$ = 4.4 Hz), 7.60 (1H, d, $J$ = 1.2 Hz), 7.28 (1H, dd, $J$ = 8.4, 2.0 Hz), 7.15 (1H, dd, $J$ = 8.4, 2.0 Hz), 7.11 (1H, d, $J$ = 2.0 Hz), 3.92 (3H, s), 3.87 (1H, q, $J$ = 7.2 Hz), 2.06 (3H, s), 1.46 (3H, d, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 209.1, 157.8, 135.8, 133.8, 129.3, 129.2, 127.6, 126.5, 126.4, 119.3, 105.7, 55.4, 53.8, 28.5, 17.3; HRMS: Calcd for $C_{15}H_{16}Na_1O_2$ $[M+Na]^+$: 251.1048; Found: 251.1041; specific rotation: $[\alpha]_D^{20}$ +343 (*c* 1.66, $CHCl_3$) for an enantiomerically enriched sample of 96.5:3.5 e.r. Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralpak AD-H column, 99:1 hexanes:*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 32.379 | 169677393 | 3048853 | 49.109 | 50.726 |
| 2 | 36.135 | 175834269 | 2961608 | 50.891 | 49.274 |
| Total | | 345511662 | 6010461 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 30.557 | 108492943 | 2204073 | 96.454 | 96.621 |
| 2 | 34.253 | 3988911 | 77069 | 3.546 | 3.379 |
| Total | | 112481854 | 2281141 | 100.000 | 100.000 |

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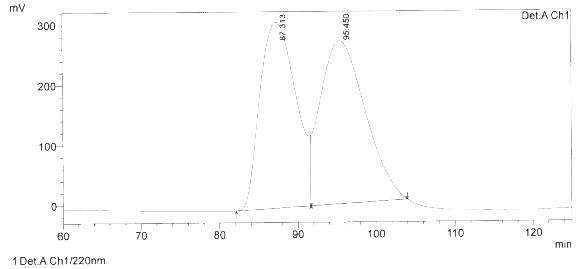
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 32.379 | $1.69 \times 10^8$ | 49.109 | 30.557 | $1.08 \times 10^8$ | 96.454 |
| 36.135 | $1.75 \times 10^8$ | 50.891 | 34.253 | $3.98 \times 10^6$ | 3.546 |

**(*S*)-5-(*tert*-Butyldimethylsilyloxy)-3-phenylpenta-2-one** (**4.80**): IR (neat): 2953 (w), 2928 (w), 2884 (w), 2856 (w), 1713 (s), 1493 (w), 1471 (w), 1454 (w), 1431 (w), 1387 (w), 1355 (m), 1252 (m), 1159 (w), 1100 (s), 1064 (m), 1030 (w), 1006 (w), 969 (w), 926 (w), 830 (s), 811 (m), 774 (s), 699 (s), 663 (w), 593 (w), 548 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.34–7.30 (2H, m), 7.27–7.25 (1H, m), 7.22–7.19 (2H, m), 3.89 (1H, t, $J$ =

7.2 Hz), 3.59–3.54 (2H, m), 3.45–3.40 (2H, m), 2.30–2.24 (1H, m), 2.06 (3H, s), 1.86–1.78 (1H, m), 0.88 (9H, s), 0.00 (6H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 208.4, 138.9, 129.0, 128.5, 127.3, 60.5, 55.7, 34.9, 29.3, 26.0, 18.4, –5.2; HRMS: Calcd for $C_{17}H_{28}Na_1O_2Si_1$ $[M+Na]^+$: 315.1756; Found: 315.1759; specific rotation: $[\alpha]_D^{22}$ +149.9 (*c* 2.00, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

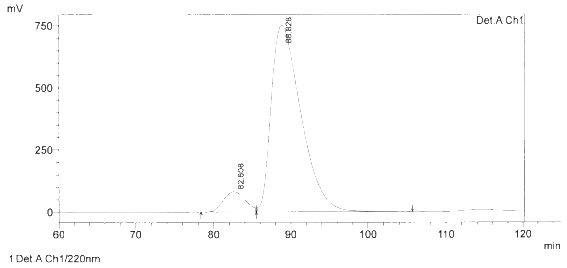
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralcel OD-H column, 100% hexanes, 0.1 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 87.313 | 99339633 | 308864 | 47.891 | 53.266 |
| 2 | 95.450 | 108087609 | 270984 | 52.109 | 46.734 |
| Total | | 207427242 | 579848 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 82.608 | 16318152 | 81709 | 7.477 | 9.797 |
| 2 | 88.828 | 201937746 | 752290 | 92.523 | 90.203 |
| Total | | 218255898 | 833999 | 100.000 | 100.000 |

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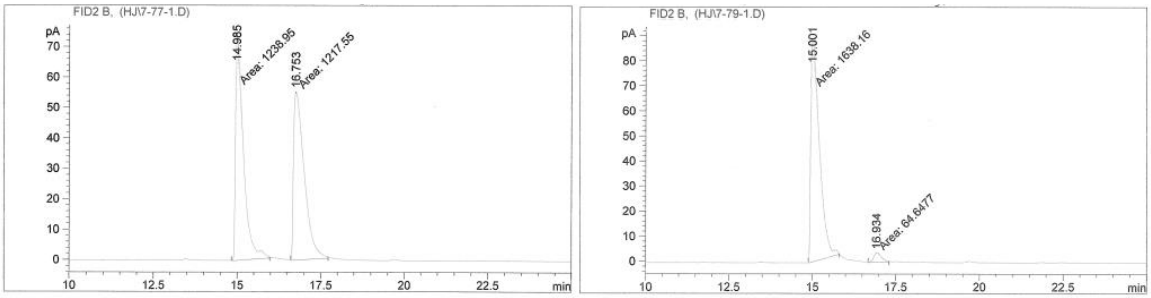
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 87.313 | $9.93 \times 10^7$ | 47.891 | 82.608 | $1.63 \times 10^7$ | 7.477 |
| 95.450 | $1.08 \times 10^8$ | 52.109 | 88.828 | $2.02 \times 10^8$ | 92.523 |

■ **Representative Procedure for Synthesis of Alkenyl Bromides:** A vial was charged with $CuBr_2$ (156.3 mg, 0.700 mmol), (*R*)-4,4,5,5-tetramethyl-2-(3-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane **4.58a** (27.6 mg, 0.100 mmol) and MeOH/$H_2O$ (1 mL/1 mL). The mixture was sealed with a cap and allowed to stir at 90 °C for 14 h. After cooling to 22 °C, the mixture was diluted with water (5 mL) and washed with $Et_2O$ (3 x 2 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The unpurified material was purified by silica gel chromatography

(hexanes:$Et_2O$=50:1) to afford the desired product **4.81** as colorless oil (19.7 mg, 0.0860 mmol, 86% yield).

**(*S*)-1-(3-Bromobut-3-en-2-yl)-2-fluorobenzene** (**4.81**): IR (neat): 2976 (w), 2928 (w), 1627 (m), 1586 (w), 1490 (s), 1453 (m), 1401 (w), 1375 (w), 1264 (w), 1229 (s), 1131 (m), 1111 (m), 1067 (m), 938 (w), 891 (s), 820 (s), 752 (s), 644 (m), 580 (m), 537 (m), 484 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.31–7.22 (2H, m), 7.13 (1H, td, $J$ = 7.6, 1.2 Hz), 7.03 (1H, ddd, $J$ = 10.0, 7.6, 1.2 Hz), 5.74 (1H, dd, $J$ = 3.2, 1.6 Hz), 5.57 (1H, d, $J$ = 2.0 Hz), 4.12 (1H, q, $J$ = 6.8 Hz), 1.48 (3H, d, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 160.8 (d, $J_{CF}$ = 245 Hz), 137.3, 129.7 (d, $J_{CF}$ = 14.4 Hz), 128.6 (d, $J_{CF}$ = 8.3 Hz), 128.5 (d, $J_{CF}$ = 4.6 Hz), 124.3 (d, $J_{CF}$ = 3.8 Hz), 117.0, 115.6 (d, $J_{CF}$ = 22.8 Hz), 42.7 (d, $J_{CF}$ = 3.0 Hz), 19.8; HRMS: Calcd for $C_{10}H_{11}Br_1F_1$ $[M+H]^+$: 229.0028; Found: 229.0032; specific rotation: $[\alpha]_D^{20}$ –6.57 (*c* 1.52, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDG-TA column, 100 °C, 15 psi.

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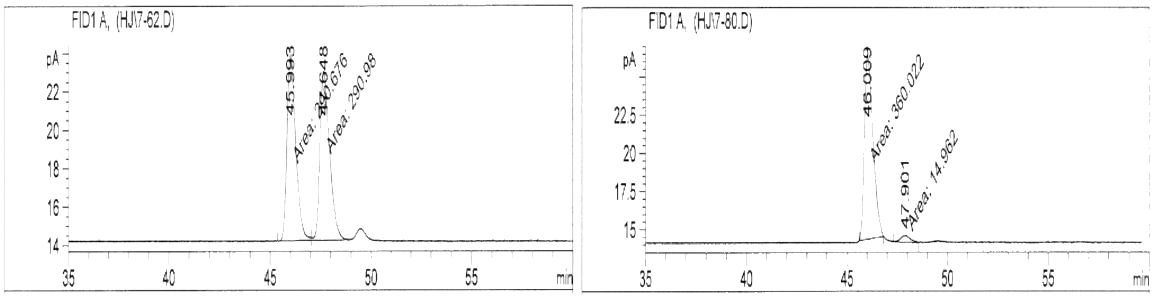
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 14.985 | 1238.95 | 50.436 | 15.001 | 1638.16 | 96.203 |
| 16.753 | 1217.55 | 49.564 | 16.934 | 64.65 | 3.797 |

**(*S*)-1-Bromo-3-(3-bromobut-3-en-2-yl)benzene** (**4.82**): IR (neat): 3060 (w), 2974 (w), 2933 (w), 2873 (w), 1624 (m), 1592 (m), 1568 (m), 1475 (m), 1424 (m), 1372 (w), 1192 (w), 1159 (w), 1127 (m), 1074 (m), 997 (m), 884 (s), 802 (m), 780 (s), 709 (s), 691 (s), 666 (s), 640 (m), 605 (m), 577 (m), 554 (m), 435 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.41–7.38 (2H, m), 7.23–7.19 (2H, m), 5.75 (1H, dd, *J* = 2.0, 1.2 Hz), 5.57 (1H, d, *J* = 2.0 Hz), 3.73 (1H, q, *J* = 6.8 Hz), 1.47 (3H, d, *J* = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 145.0, 138.1, 130.7, 130.2, 130.1, 126.3, 122.7, 117.0, 49.6, 20.5; HRMS: Calcd for $C_{10}H_{11}Br_2$ $[M+H]^+$: 288.9228; Found: 288.9222; specific rotation: $[\alpha]_D^{20}$ –7.62 (*c* 1.31, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 120 °C, 15 psi.

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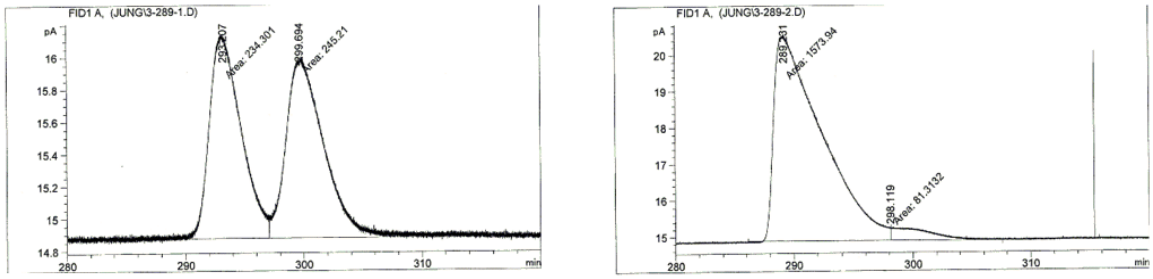
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 45.993 | 290.68 | 49.974 | 46.009 | 360.02 | 96.010 |
| 47.648 | 290.98 | 50.026 | 47.901 | 14.96 | 3.990 |

**(*R*)-3-(2-Naphthyl)-2-bromobut-1-ene** (**4.83**): IR (neat): 3052 (w), 3020 (w), 2972 (w), 2933 (w), 2874 (w), 1622 (m), 1599 (w), 1506 (w), 1450 (w), 1390 (w), 1374 (w), 1270 (w), 1242 (w), 1200 (w), 1172 (w), 1155 (w), 1125 (m), 1048 (w), 1018 (w), 988 (w), 949 (w), 889 (s), 855 (s), 815 (s), 769 (w), 747 (s), 658 (w), 640 (w), 622 (w), 568 (w), 539 (w), 516 (w), 475 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.83–7.80 (3H, m), 7.81

(1H, d, $J$ = 4.0 Hz), 7.71 (1H, s), 7.50–7.45 (2H, m), 7.39 (1H, dd, $J$ = 8.4, 2.0 Hz), 5.78 (1H, d, $J$ = 1.2 Hz), 5.60 (1H, d, $J$ = 1.2 Hz), 3.93 (1H, q, $J$ = 7.2 Hz), 1.58 (3H, d, $J$ = 7.2 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 140.0, 139.0, 133.6, 132.6, 128.2, 127.9, 127.7, 126.2, 126.1, 125.9, 125.8, 116.7, 50.0, 20.6; HRMS: Calcd for $C_{14}H_{14}Br_1$ $[M+H]^+$: 261.0278; Found: 261.0287; specific rotation: $[\alpha]_D^{23}$ –13.1 (*c* 1.52, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 115 °C, 15 psi.

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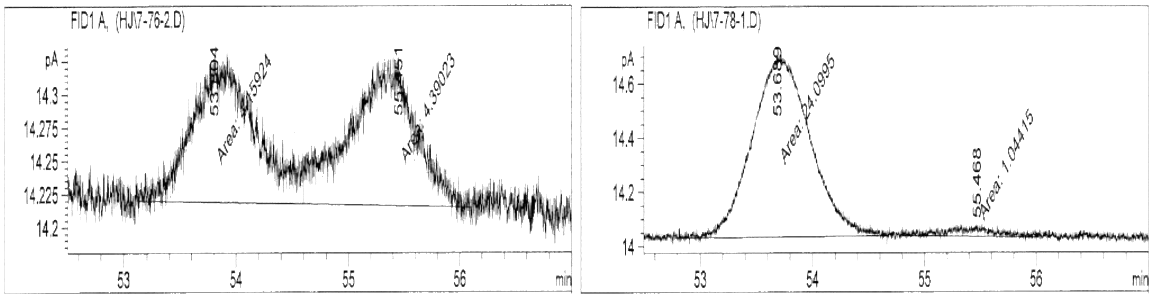
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 293.207 | 234.30 | 48.862 | 289.231 | 1573.94 | 95.088 |
| 299.694 | 245.20 | 51.138 | 298.119 | 81.31 | 4.912 |

**(*S*)-(2-Bromopent-1-en-3-yl)benzene** (**ent-4.20**): IR (neat): 3062 (w), 3028 (w), 2963 (m), 2929 (m), 2874 (w), 1621 (m), 1601 (w), 1493 (m), 1453 (m), 1379 (w), 1155 (m), 1143 (m), 1129 (m), 1064 (w), 1029 (w), 888 (s), 842 (w), 769 (m), 744 (m), 698 (s), 655 (w), 566 (m), 542 (m), 498 (w) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.35–7.31 (2H, m), 7.27–7.24 (3H, m), 5.76 (1H, dd, $J$ = 2.0, 0.8 Hz), 5.53 (1H, d, $J$ = 2.0 Hz), 3.43 (1H, t, $J$ = 7.6 Hz), 2.02 (1H, dq, $J$ = 20.4, 7.6 Hz), 1.79 (1H, dq, $J$ = 20.8, 7.6 Hz), 0.91 (3H, t, $J$ = 7.6 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 141.3, 138.5, 128.5, 128.1, 127.1, 116.9, 57.5, 26.6, 12.3; HRMS: Calcd for $C_{11}H_{13}$ $[M–Br]^+$: 145.1027; Found: 145.1020; specific rotation: $[\alpha]_D^{20}$ –6.24 (*c* 1.60, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by GC analysis in comparison with authentic racemic material; CDB-DM column, 120 °C, 15 psi.

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| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 53.804 | 4.16 | 48.649 | 53.689 | 24.10 | 95.847 |
| 55.451 | 4.39 | 51.351 | 55.468 | 1.04 | 4.153 |

■ **Representative Procedure for NHC–Cu-Catalyzed Enantioselective Protoboration of 1,1-Disubstituted Allenes Followed by Conversion to Carboxylic Acids:** An oven-dried vial equipped with a stir bar was charged with imidazolinium salt **A.22** (3.4 mg, 5.50 μmol), NaO*t*-Bu (3.8 mg, 0.0400 mmol), CuCl (0.5 mg, 5.00 μmol) and thf (0.3 mL) in a $N_2$-filled glove box. The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (27.9 mg, 0.110 mmol) was added to the solution, which turned dark brown immediately and the wall of a reaction vial was rinsed with additional thf (0.2 mL). The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. The mixture was allowed to stir at 22 °C for 30 min under a $N_2$ atmosphere. 2-(Buta-2,3-dien-2-yl)-6-methoxynaphthalene **4.85** (13.1 mg, 0.100 mmol) and *t*-BuOH (14.3 μL, 0.150 mmol) were added through syringes. The resulting solution was allowed to stir at 22 °C for 16 h

before the reaction was quenched by passing the mixture through a short plug of celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was dissolved in mixture of thf (0.5 mL) and pH = 7 buffer (0.5 mL). $NaIO_4$ (86.0 mg, 0.400 mmol) and $OsO_4$ (1 drop of 4 wt % $H_2O$ solution) was added to the mixture and it was allowed to stir at 22 °C for 8 h. The reaction was quenched by addition of saturated aqueous solution of $Na_2SO_3$ (1 mL) and the mixture was allowed to stir for an additional hour to complete quenching $OsO_4$. The water layer was washed with $Et_2O$ (2 x 2 mL; recovery of remained starting material for determination of the conversion of the transformation) and acidified with 3N HCl solution until pH<3. Water layer was washed with EtOAc (3 x 2 mL) and the combined organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The product (*S*)-naproxen was isolated by silica gel chromatography (hexanes:$Et_2O$=2:1) as colorless oil (17.3 mg, 0.0750 mmol, 75% yield).

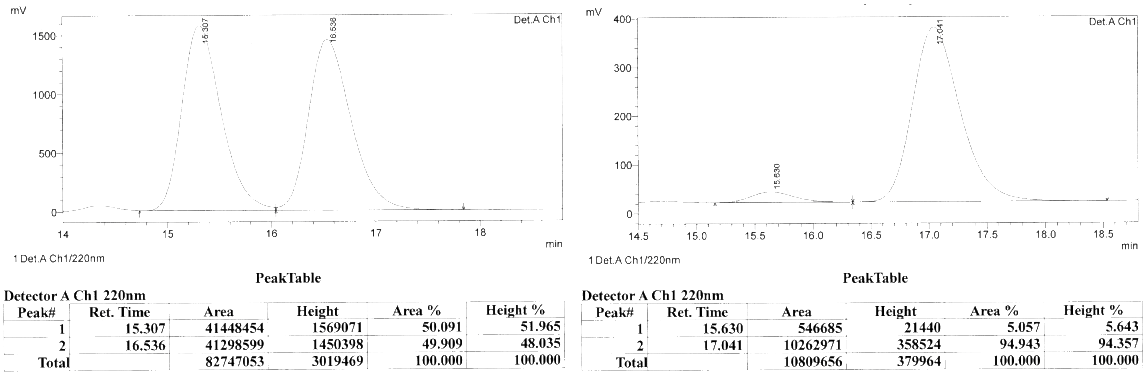
**(*S*)-2-(6-Methoxy-2-naphthyl)propinoic acid, (*S*)-Naproxen**: [Note: The analytical data are fully consistent with those reported previously.][31] IR (neat): 3097 (br), 2973 (w), 2938 (w), 1708 (s), 1685 (s), 1629 (w), 1602 (s), 1504 (w), 1480 (w), 1459 (w), 1435 (w), 1418 (w), 1391 (s), 1345 (w), 1262 (s), 1225 (s), 1191 (s), 1174 (s), 1156 (s), 1120 (w), 1090 (m), 1070 (m), 1027 (s), 962 (w), 924 (m), 895 (m), 854 (s), 817 (s), 793 (m), 761 (w), 741 (m), 673 (m), 642 (m), 600 (w), 568 (w), 522 (w), 482 (s), 472 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.72 (1H, s), 7.69 (2H, s), 7.43 (1H, dd, *J* = 8.4, 2.0 Hz), 7.15 (1H, dd, *J* = 8.4, 2.0 Hz), 7.11 (1H, d, *J* = 2.0 Hz), 3.91 (3H, s), 3.88 (1H, q, *J* = 7.2 Hz), 1.60 (3H, d, *J* = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 181.0, 157.8, 134.9, 133.9,

(31) (a) Frank, A.; Rüchardt, C. *Chem. Lett.* **1984**, *13*, 1431–1434. (b) Boyd E.; Coulbeck E.; Coumbarides G. S.; Chavda S.; Dingjan M.; Eames J.; Flinn A.; Motevalli M.; Northen J.; Yohannes Y. *Tetrahedron: Asymmetry* **2007**, *18*, 2515–2530.

129.4, 129.0, 127.3, 126.3, 126.2, 119.1, 105.7, 55.4, 45.4, 18.2; specific rotation: $[\alpha]_D^{21}$ +55.5 (*c* 1.87, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralpak AD-H column, 95:5 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm.

**Stereochemistry Proof** is based on the optical rotation for the *S* enantiomer: $[\alpha]_D^{20}$ +65.0 (*c* 1.00, $CHCl_3$) for a >99:1 e.r.[31]

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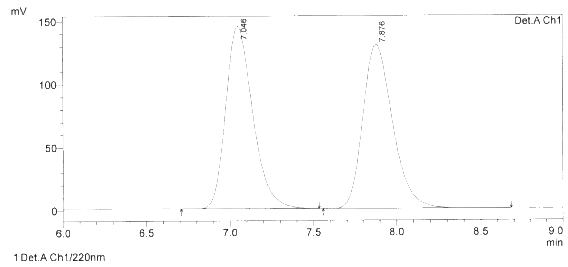
| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 15.307 | $4.14 \times 10^7$ | 50.091 | 15.630 | $5.46 \times 10^5$ | 5.057 |
| 16.536 | $4.12 \times 10^7$ | 49.909 | 17.041 | $1.02 \times 10^7$ | 94.943 |

**(*S*)-2-Phenylpropinoic acid** (**4.84**): [Note: The analytical data are fully consistent with those reported previously.][32] IR (neat): 3029 (w), 2978 (br), 2936 (w), 1700 (s), 1601 (w), 1496 (w), 1453 (w), 1412 (w), 1378 (w), 1261 (w), 1227 (m), 1181 (w), 1095 (w), 1065 (w), 1030 (w), 1006 (w), 992 (w), 911 (w), 858 (w), 759 (w), 726 (m), 695 (s), 658 (w), 614 (w), 575 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.32–7.30 (4H, m), 7.27–7.25 (1H, m), 3.72 (1H, q, *J* = 7.2 Hz), 1.50 (3H, d, *J* = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 180.8, 139.8, 128.8, 127.7, 127.5, 45.4, 18.2; specific rotation: $[\alpha]_D^{21}$ +59.7 (*c* 0.81, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

(32) Shaye, N. A.; Chavda, S.; Coulbeck, E.; Eames, J.; Yohannes, Y. *Tetrahedron: Asymmetry* **2011**, *22*, 439–463.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material; Chiralpak AD-H column, 95:5 hexanes:*i*-PrOH, 1.0 mL/min, 220 nm.

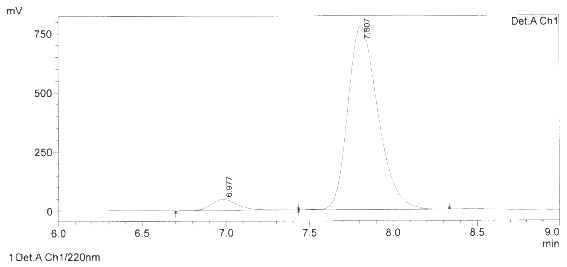
**Stereochemistry Proof** is based on the optical rotation for the *S* enantiomer: $[\alpha]_D^{20}$ +72.0 (*c* 0.61, $CHCl_3$) for a 99:1 e.r.[32]




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 7.046 | 1632138 | 144690 | 50.118 | 52.666 |
| 2 | 7.876 | 1624454 | 130043 | 49.882 | 47.334 |
| Total | | 3256592 | 274733 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 6.977 | 516046 | 46354 | 5.036 | 5.642 |
| 2 | 7.807 | 9731008 | 775287 | 94.964 | 94.358 |
| Total | | 10247054 | 821641 | 100.000 | 100.000 |

!

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 7.046 | $1.63 \times 10^6$ | 50.118 | 6.997 | $5.16 \times 10^5$ | 5.036 |
| 7.876 | $1.62 \times 10^6$ | 49.882 | 7.807 | $9.73 \times 10^6$ | 94.964 |

■ **Representative Procedure for Preparation of Chiral Alkenylboronic Acids:**[33] An oven-dried vial equipped with a stir bar was charged with (*R*)-4,4,5,5-tetramethyl-2-(3-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane **4.58a** (100 mg, 0.380 mmol), $NH_4OAc$ (107.4 mg, 1.39 mmol), $NaIO_4$ (298 mg, 1.39 mmol) and the mixture of acetone (0.35 mL) and water (0.35 mL) in ambient atmosphere. The vial was sealed with a cap and the solution was allowed to stir at 22 °C for 12 h. The slurry was filtered by passing it through a short plug of celite (4 cm × 1 cm) eluted with acetone and the volatiles were removed from the filtrate *in vacuo*. The aqueous solution was washed with $Et_2O$ (3 × 10 mL) and the combined organic layer was washed with water, brine and dried over $MgSO_4$, filtered and

(33) Wang, H.-Y.; Anderson, L. L. *Org. Lett.* **2013**, *15*, 3362–3365.

concentrated under vacuum to afford the unpurified product, which was purified by silica gel chromatography (hexanes:$Et_2O$=3:1) to afford 55.5 mg of **4.89** as colorless oil (0.315 mmol, 83% yield). IR (neat): 3215 (br), 3061 (w), 3026 (w), 2966 (w), 2931 (w), 2874 (w), 1754 (w), 1738 (w), 1602 (w), 1492 (m), 1451 (m), 1409 (s), 1355 (s), 1234 (m), 1214 (m), 1140 (s), 1068 (s), 1029 (m), 951 (s), 907 (m), 857 (m), 763 (s), 731 (s), 697 (s), 606 (w), 536 (s), 465 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.29–7.15 (5H, m), 6.19 (1H, d, $J$ = 2.4 Hz), 5.80 (1H, dd, $J$ = 2.4, 1.2 Hz), 3.77 (1H, q, $J$ = 7.2 Hz), 1.36 (3H, d, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 131.6, 129.1, 128.3, 127.8, 127.5, 125.9, 42.6, 20.9; HRMS: Calcd for $C_{10}H_{12}B_1O_2$ $[M–H]^+$: 175.0930; Found: 175.0958.

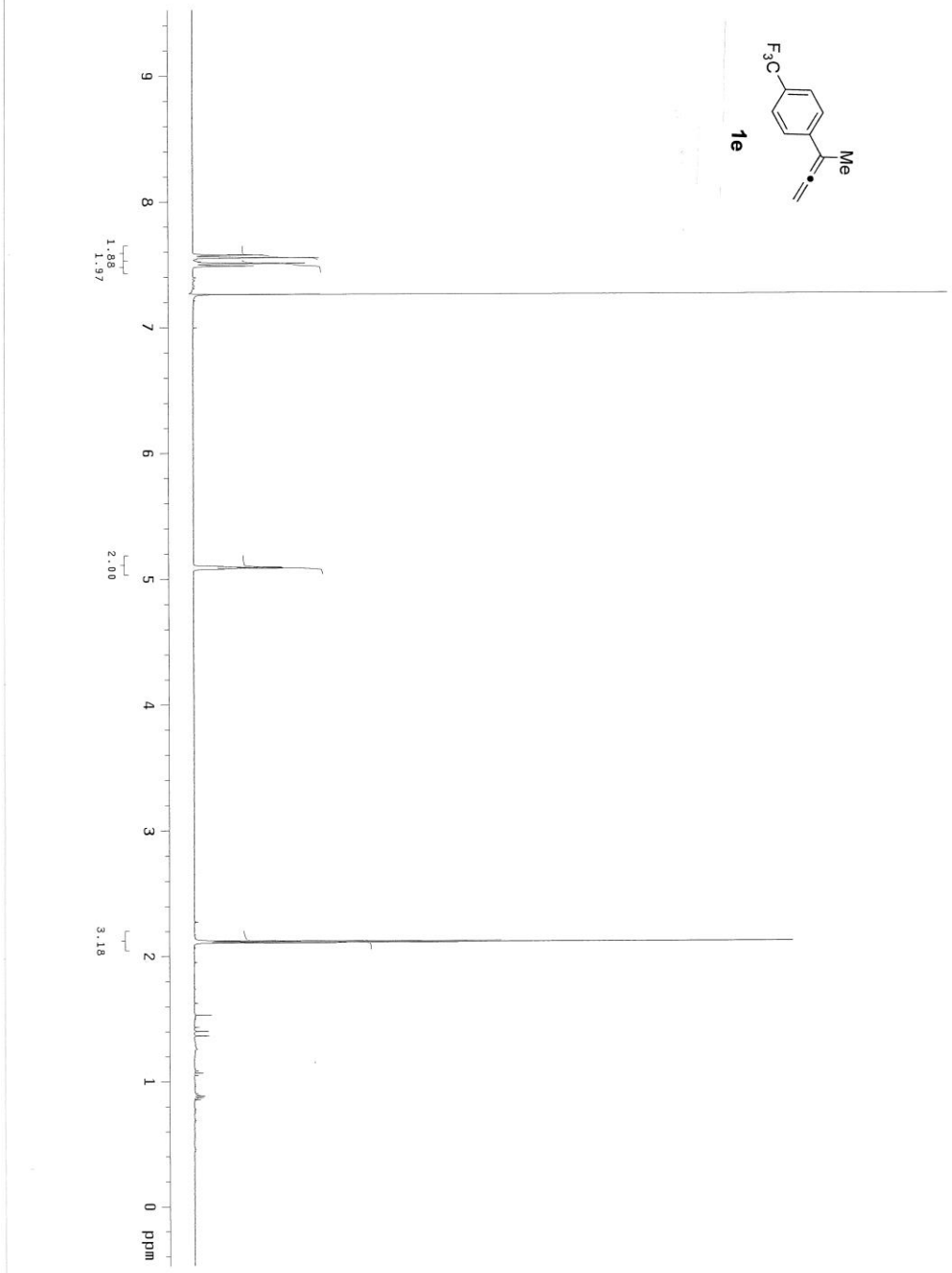
■ **Representative Procedure for NHC–Cu-Catalyzed Diastereoselective Allylic Substitution with Alkenylboronic Acids:** An oven dried vial equipped with a stir bar was charged with chiral imidazolinium salt **A.17** (4.7 mg, 5.50 μmol), CuCl (0.5 mg, 5.00 μmol) and NaOMe (8.1 mg, 0.150 mmol) in a $N_2$ filled glove-box. The vial was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and removed from the glove box. Tetrahydrofuran (0.5 mL) was added to the vial and the resulting solution was allowed to stir at 22 °C for one hour. A solution of (*E*)-diethyl 3-phenylprop-2-enyl phosphate **4.23** (27 mg, 0.100 mmol) and alkenylboronic acid **4.89** (26.4 mg, 0.150 mmol) in thf (0.5 mL) was added to the reaction vial through syringe and the mixture was allowed to stir at 60 °C for 24 h. The reaction was quenched by passing through a short plug of silica gel (4 cm × 1 cm) and eluted with $Et_2O$ (10 mL). The organic layer was concentrated *in vacuo* and purified by silica gel chromatography (100%

pentane) to afford 15.2 mg of ((2*R*,4*S*)-3-methylenehex-5-ene-2,4-diyl)dibenzene **4.86** as colorless oil (0.0620 mmol, 62% yield, 96:4 d.r.).

**((2*R*,4*S*)-3-Methylenehex-5-ene-2,4-diyl)dibenzene** (**4.86**): IR (neat): 3081 (w), 3060 (w), 3025 (w), 2966 (w), 2931 (w), 2874 (w), 1634 (w), 1599 (w), 1491 (m), 1450 (m), 1405 (w), 1370 (w), 1338 (w), 1290 (w), 1254 (w), 1180 (w), 1155 (w), 1071 (w), 1029 (w), 995 (w), 906 (s), 837 (w), 781 (w), 760 (s), 696 (s), 621 (w), 606 (w), 584 (w), 548 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.30–7.24 (2H, m), 7.22–7.17 (6H, m), 7.04–7.02 (2H, m), 6.01 (1H, ddd, *J* = 17.2, 9.8, 7.2 Hz), 5.13 (1H, d, *J* = 9.8 Hz), 5.09 (1H, s), 4.97 (1H, d, *J* = 17.2 Hz), 4.76 (1H, s), 3.91 (1H, d, *J* = 7.2 Hz), 3.48 (1H, q, *J* = 7.2 Hz), 1.35 (3H, d, *J* = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 155.2, 145.2, 142.3, 139.9, 128.7, 128.4, 128.3, 128.0, 126.4, 126.3, 116.0, 112.2, 54.3, 44.6, 21.1; HRMS: Calcd for $C_{19}H_{21}$ $[M+H]^+$: 249.1643; Found: 249.1638; specific rotation: $[\alpha]_D^{24}$ +102.3 (*c* 1.30, $CHCl_3$).

**((2*S*,4*S*)-3-Methylenehex-5-ene-2,4-diyl)dibenzene** (**4.90**): IR (neat): 3081 (w), 3060 (w), 3025 (w), 2965 (w), 2931 (w), 2874 (w), 1636 (w), 1599 (w), 1490 (m), 1451 (m), 1406 (w), 1369 (w), 1338 (w), 1295 (w), 1255 (w), 1199 (w), 1155 (w), 1071 (w), 1029 (w), 995 (w), 906 (s), 836 (w), 761 (s), 697 (s), 611 (w), 548 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.42–7.38 (2H, m), 7.35–7.28 (6H, m), 7.27–7.22 (2H, m), 6.16 (1H, ddd, *J* = 15.6, 10.8, 7.2 Hz), 5.43 (1H, s), 5.34 (1H, d, *J* = 1.2 Hz), 5.14 (1H, dt, *J* = 10.8, 1.6 Hz), 4.77 (1H, dt, *J* = 15.6, 1,6 Hz), 3.90 (1H, d, *J* = 6.8 Hz), 3.32 (1H, q, *J* = 7.2 Hz), 1.43 (3H, d, *J* = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 154.4, 145.6, 141.8, 140.9, 128.8, 128.5, 128.4, 128.1, 126.5, 126.3, 115.4, 110.7, 54.3, 44.3, 21.5; HRMS: Calcd for

$C_{19}H_{21}$ $[M+H]^+$: 249.1643; Found: 249.1635; specific rotation: $[\alpha]_D^{22}$ –182.1 (*c* 1.70, $CHCl_3$).


F3C
Me
1e
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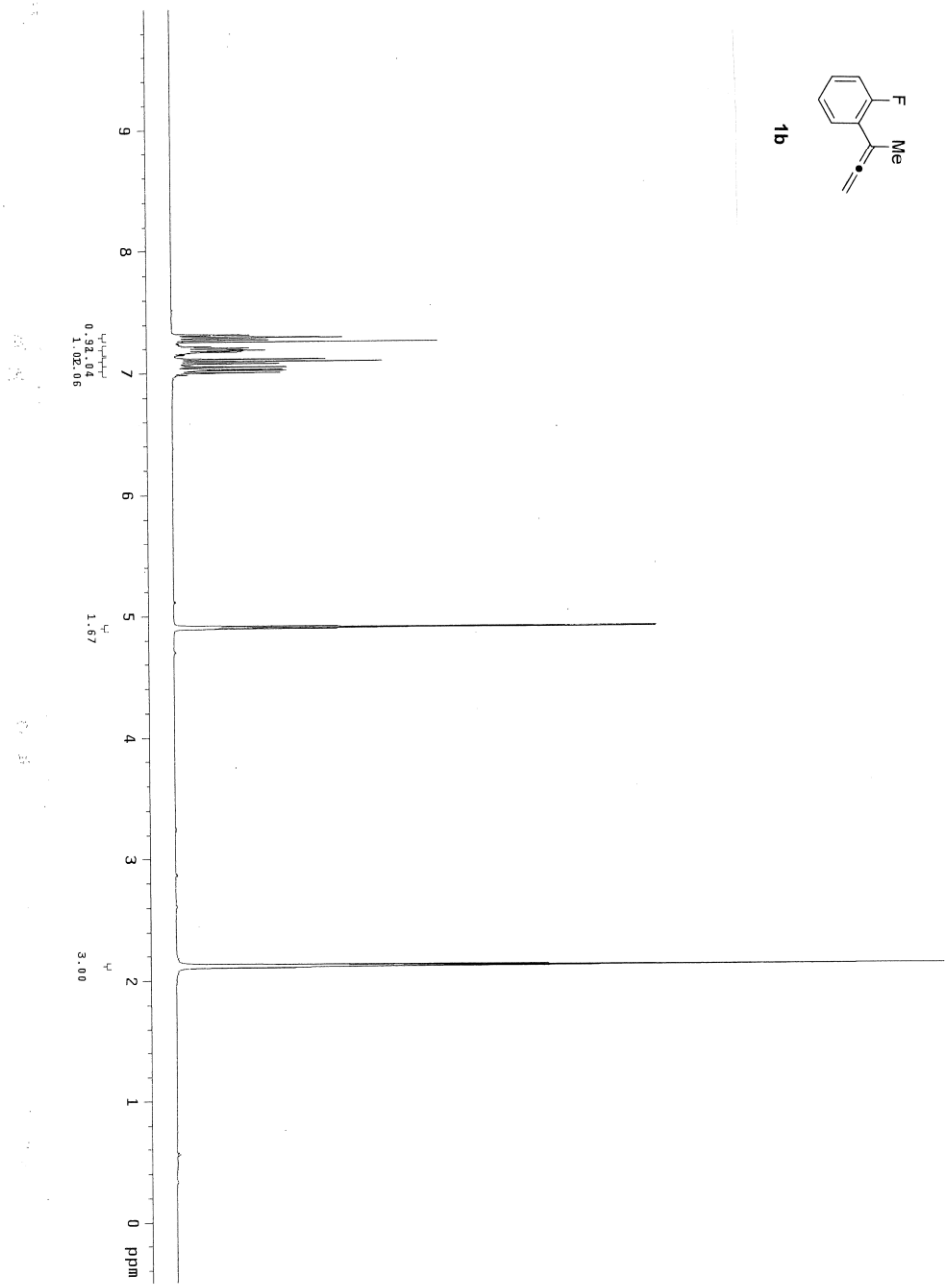
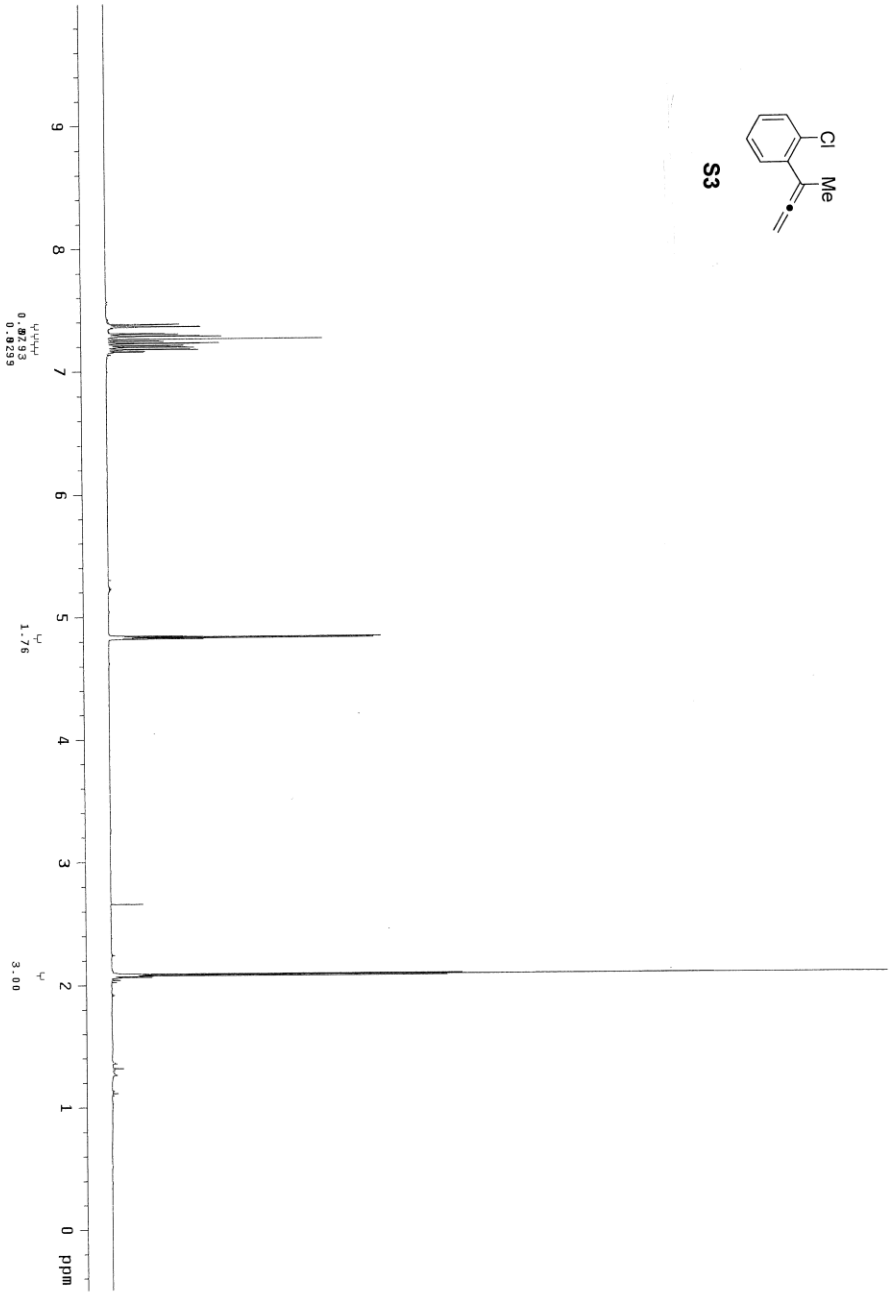
1.97
2.00
3.18
9
8
7
6
5
4
3
2
1
0
ppm


F
Me
1b
9
8
7
6
5
4
3
2
1
0
ppm
0.92
1.02
1.67
3.00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Me
S3
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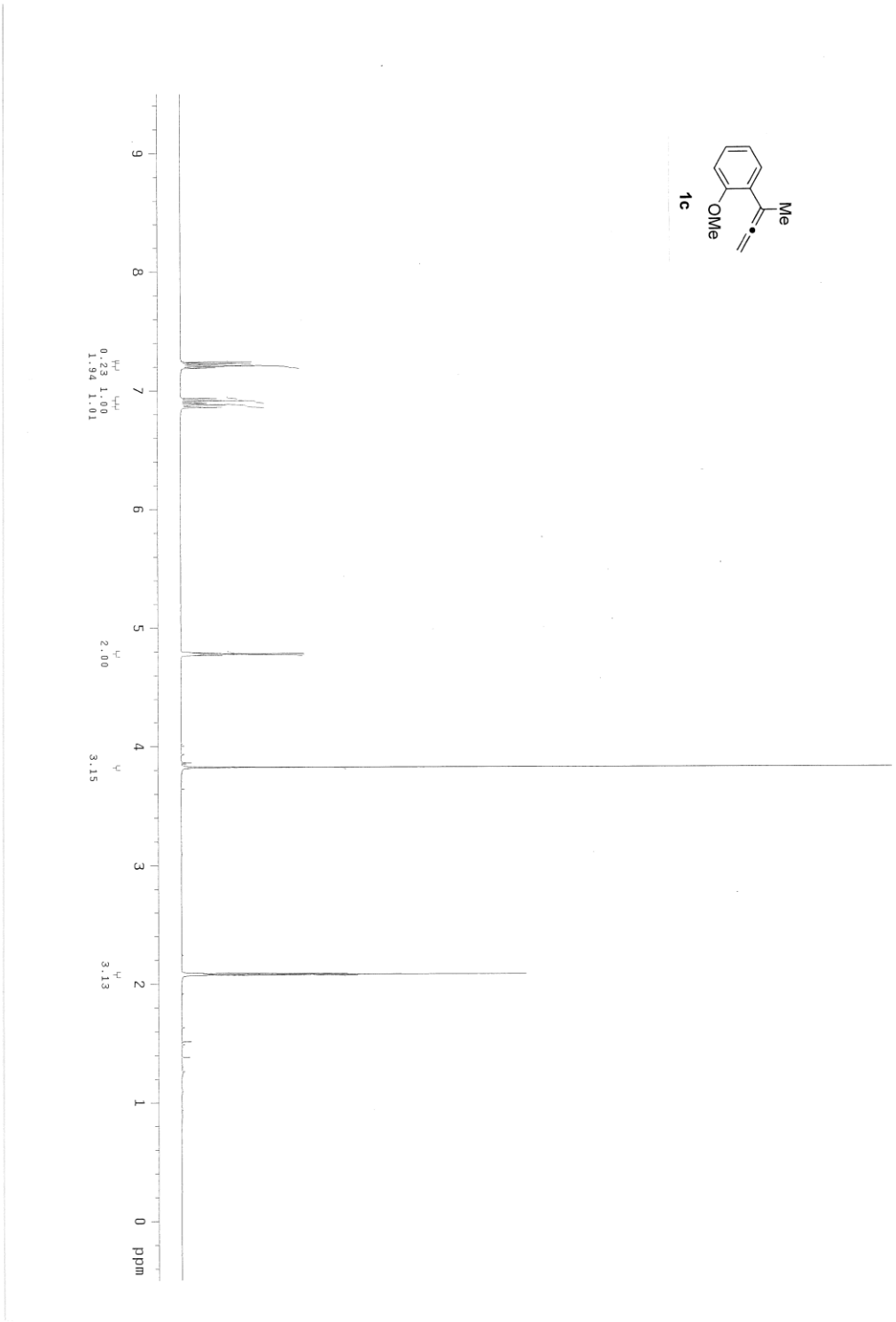
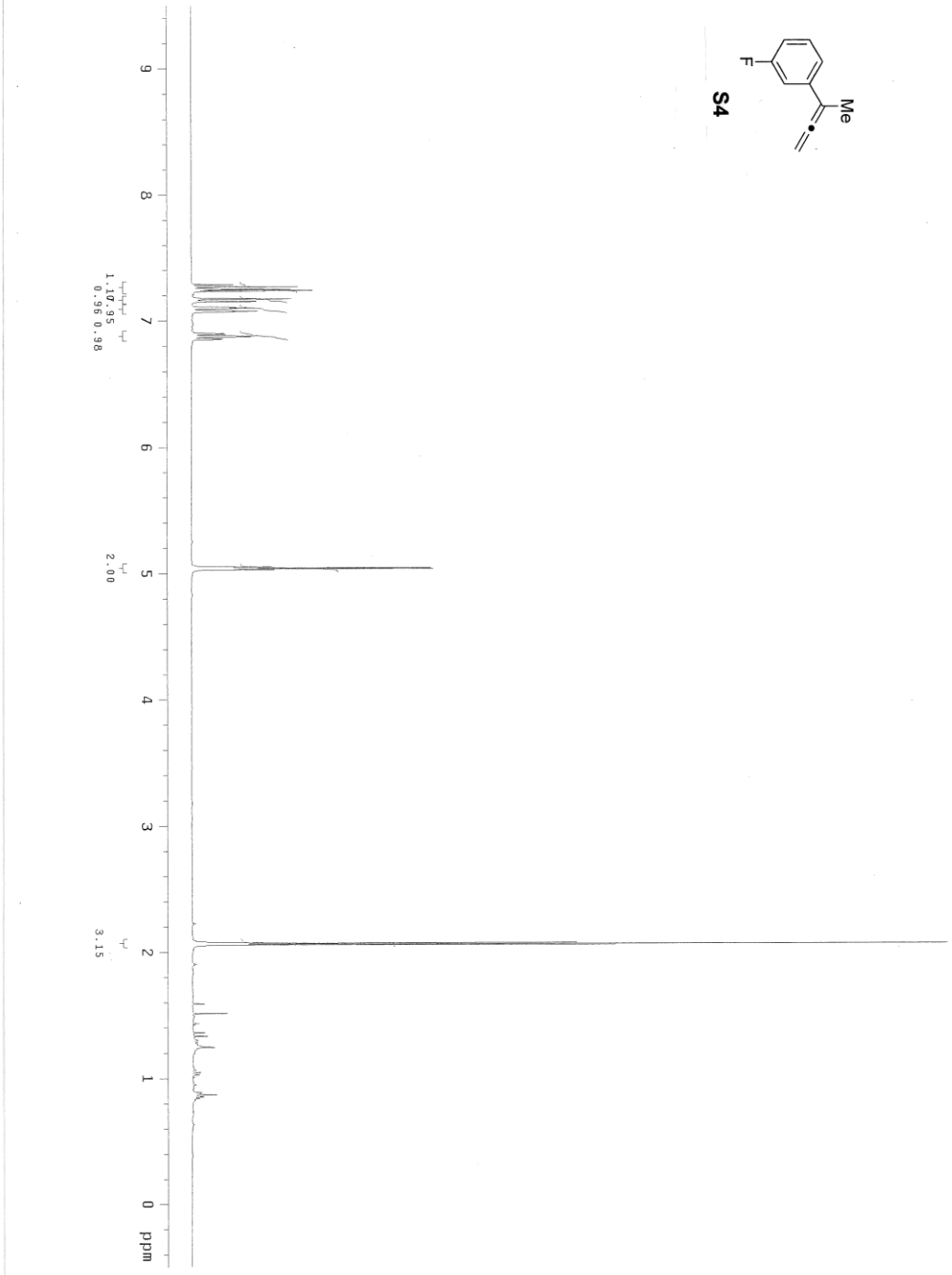
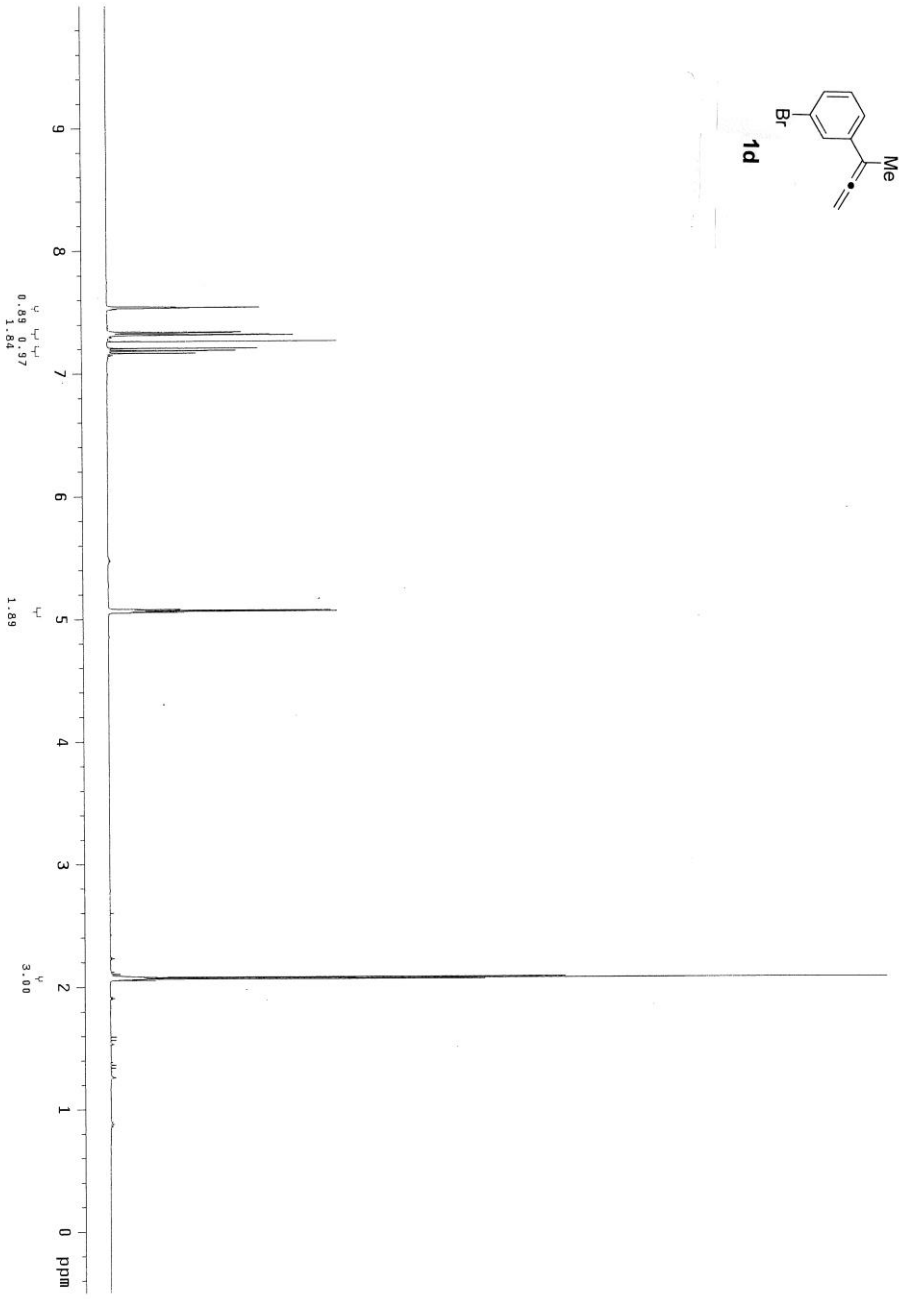
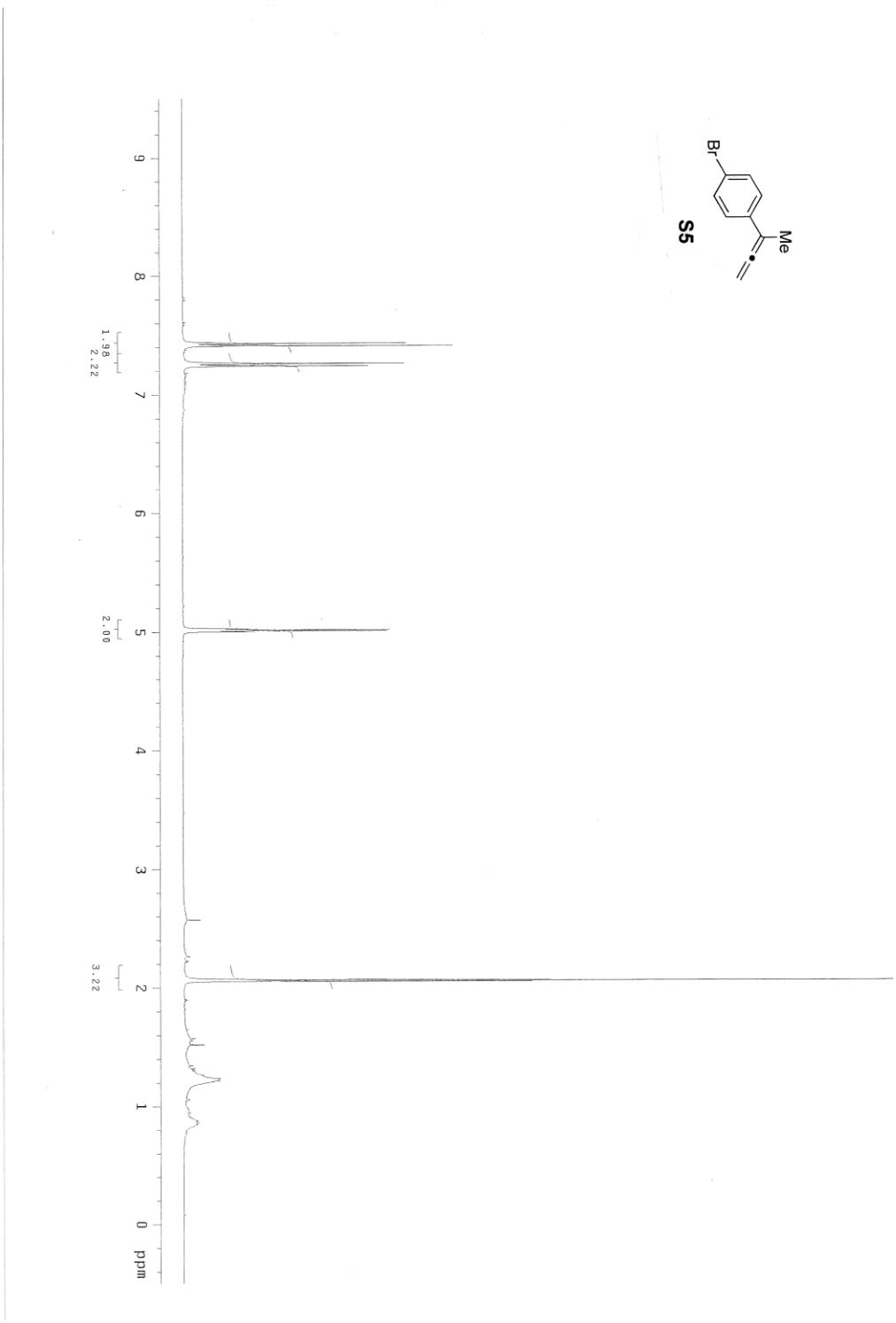
8
7
6
5
4
3
2
1
0
ppm
1.76
3.00


Me
OMe
1c
9
8
7
6
5
4
3
2
1
0
ppm
0.23 1.00 1.94 1.01
2.00
3.15
3.13


S4
F
Me
9
8
7
6
5
4
3
2
1
0
ppm
1.10
0.96
0.98
2.00
3.15


Br
Me
1d
9
8
7
6
5
4
3
2
1
0 ppm
1.89
3.00
0.89
0.97
1.84


Br
Me
S5
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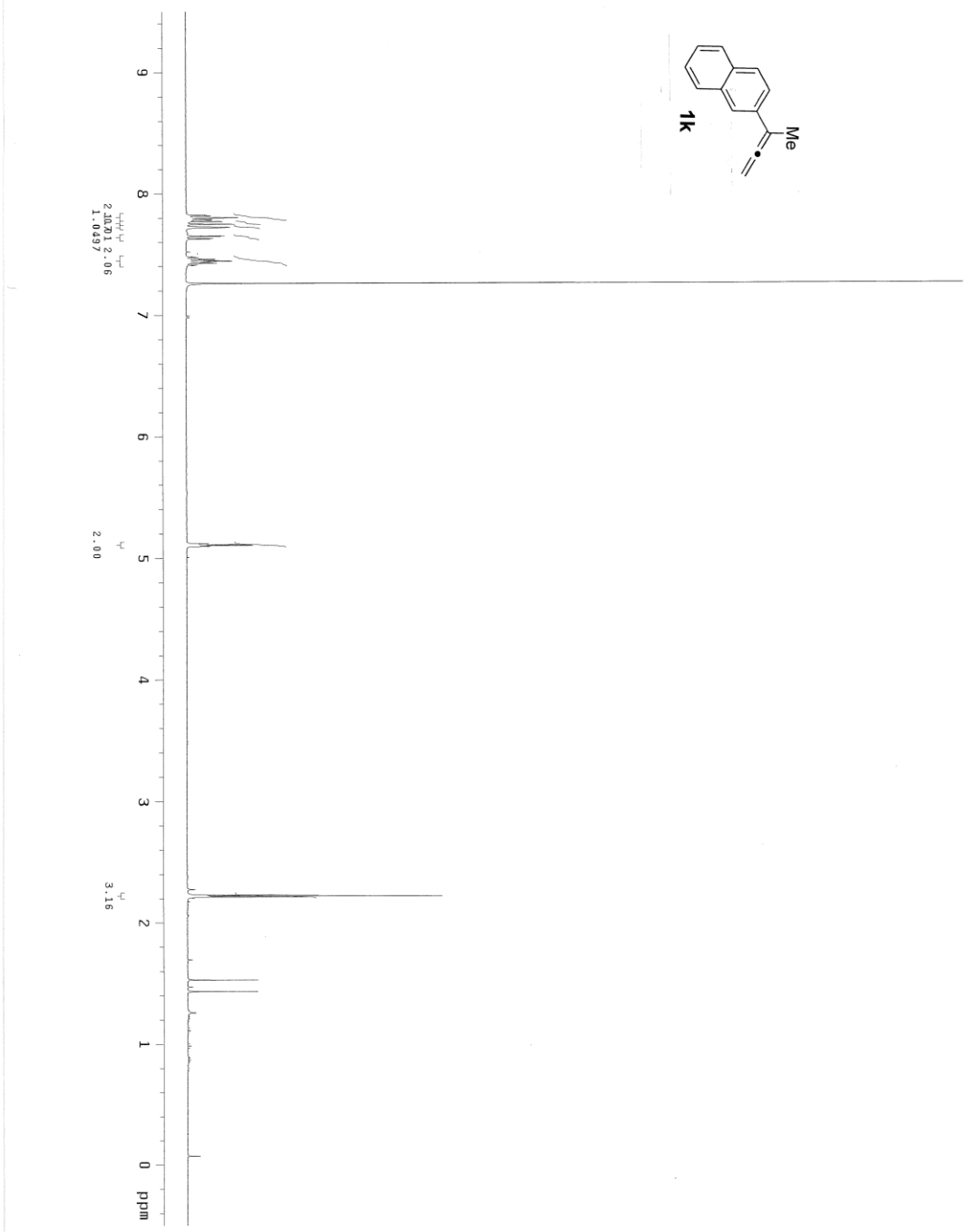
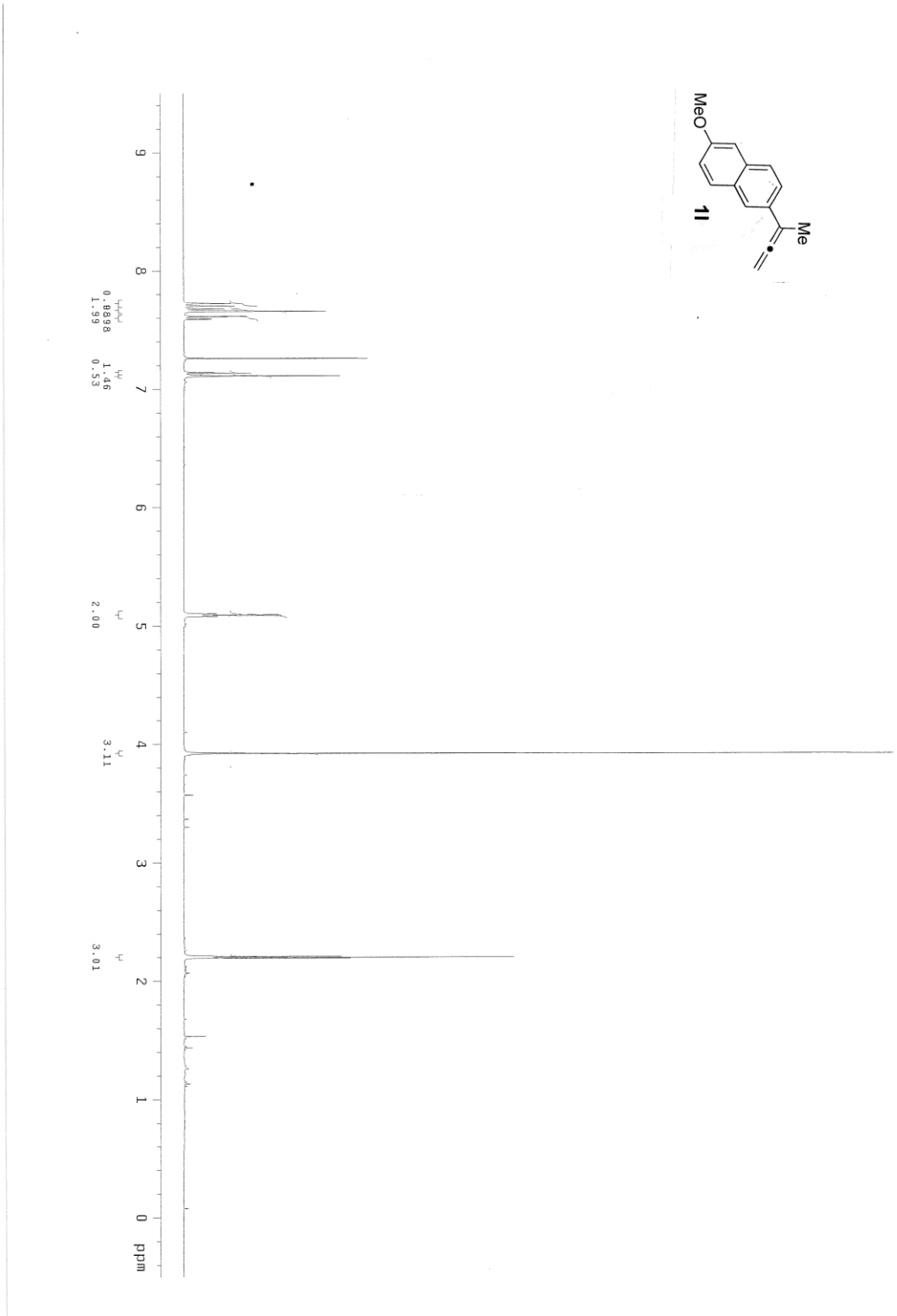
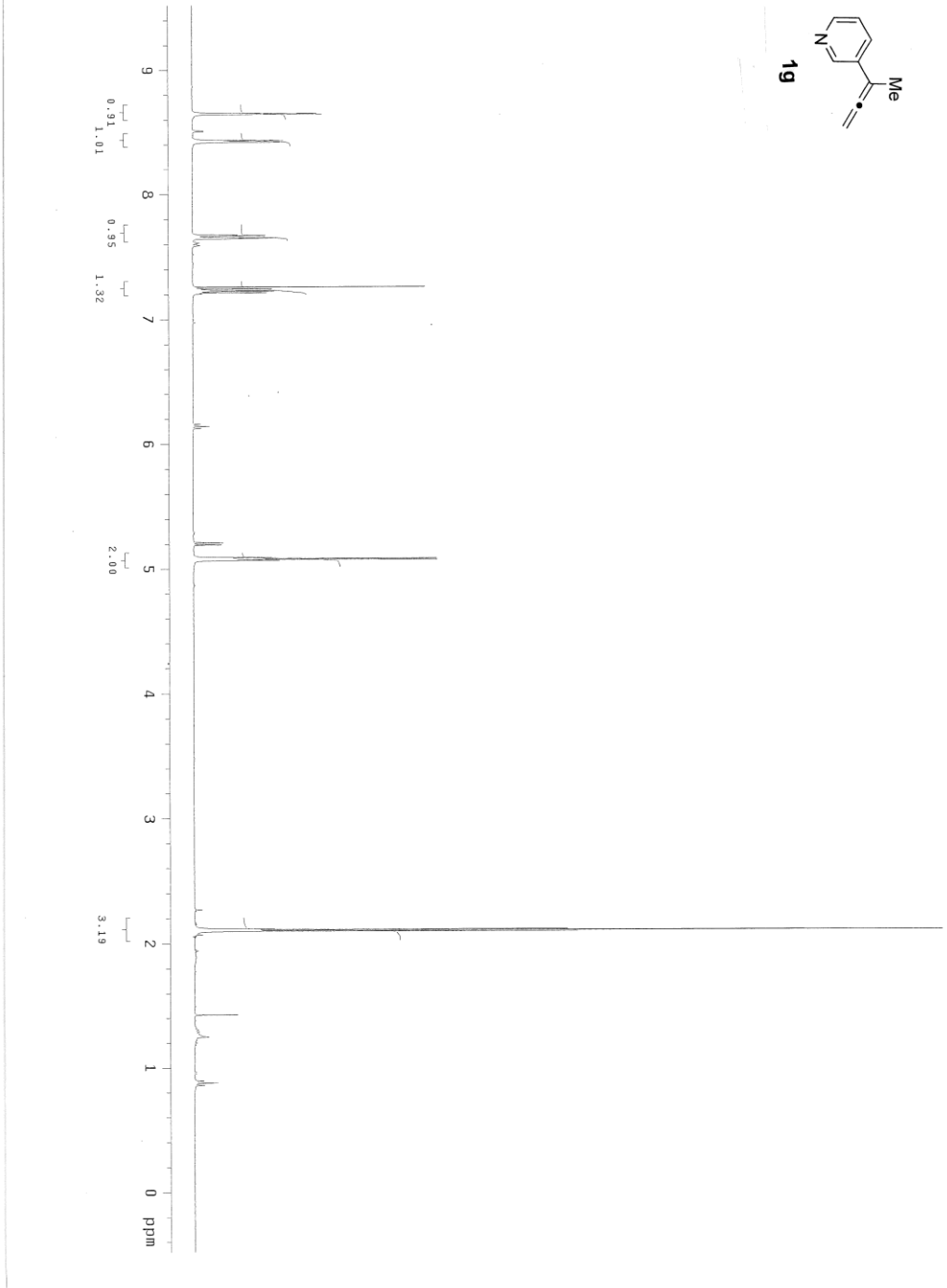
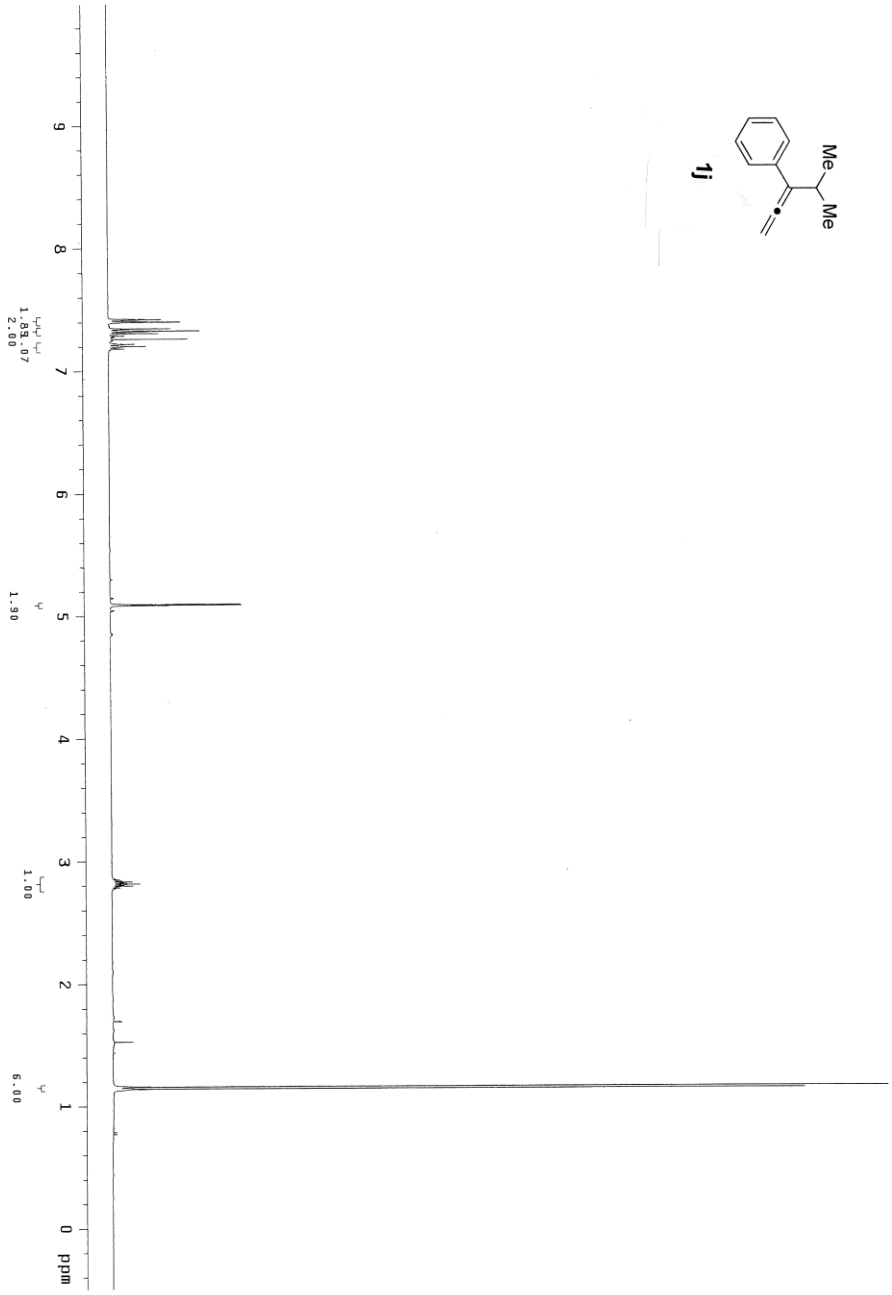
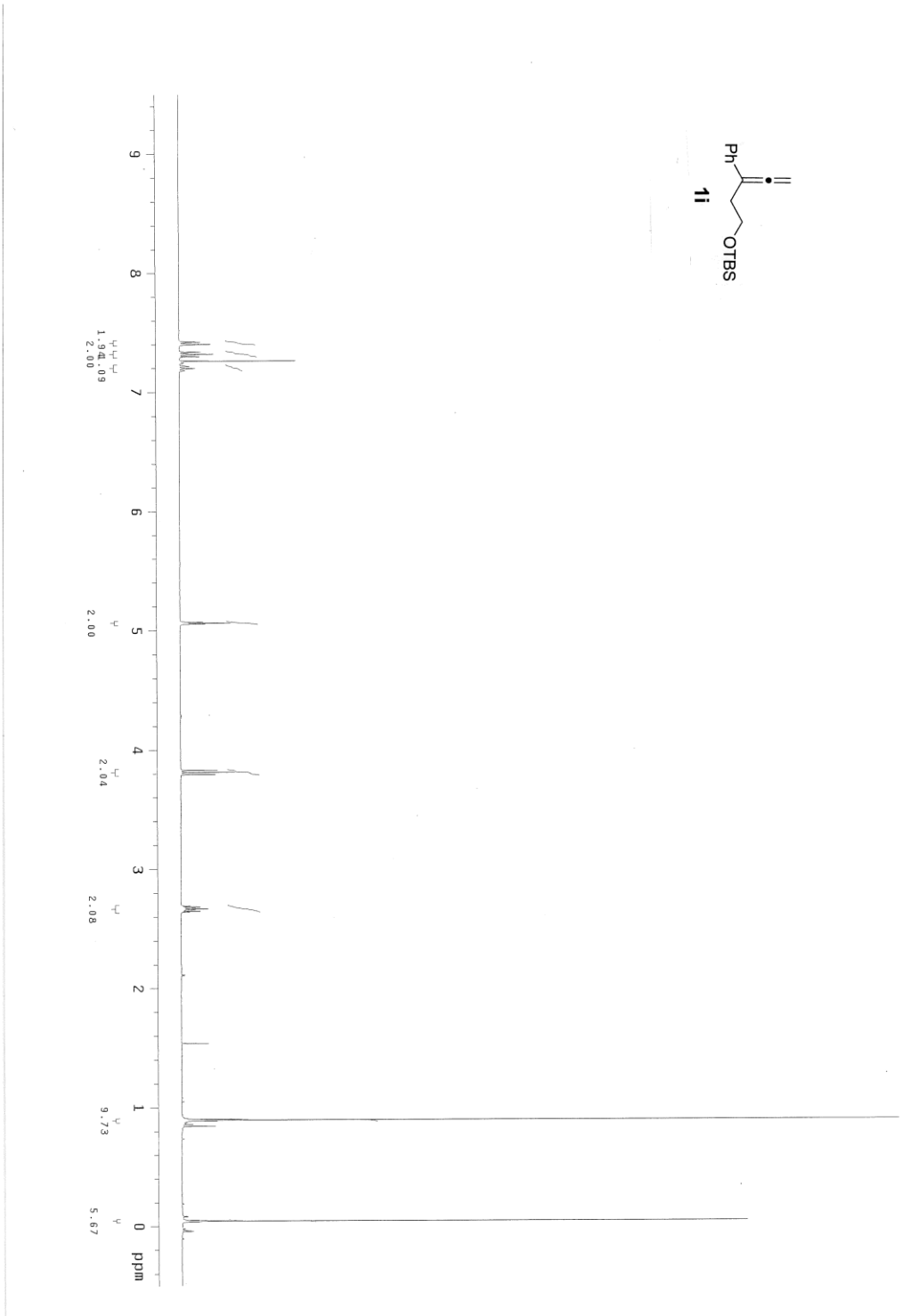
8
7
6
5
4
3
2
1
0
ppm
1.98
2.22
2.00
3.22

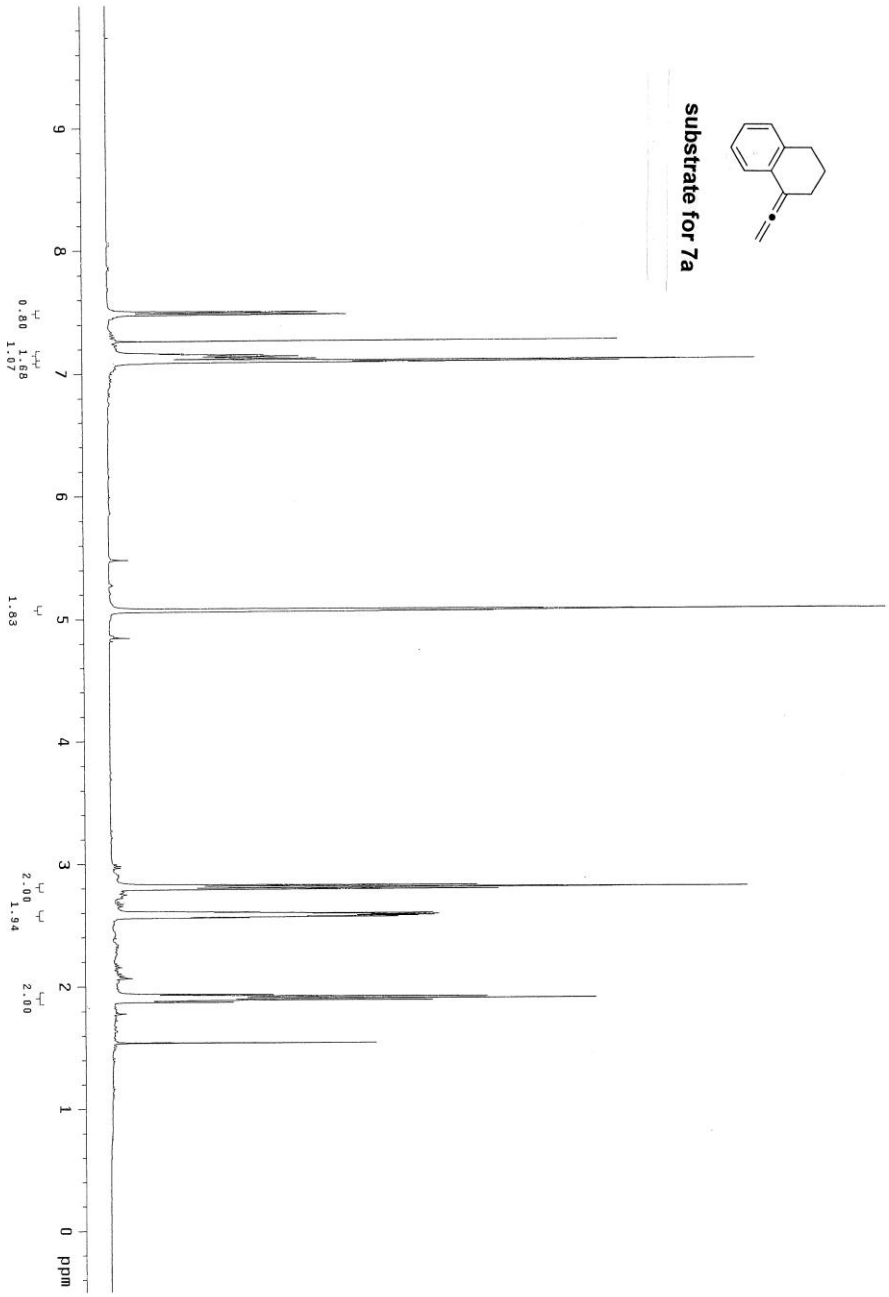

1k
Me
9
8
7
6
5
4
3
2
1
0
ppm
2.06
2.01
1.04
1.00
2.06
1.04
97
2.00
3.16

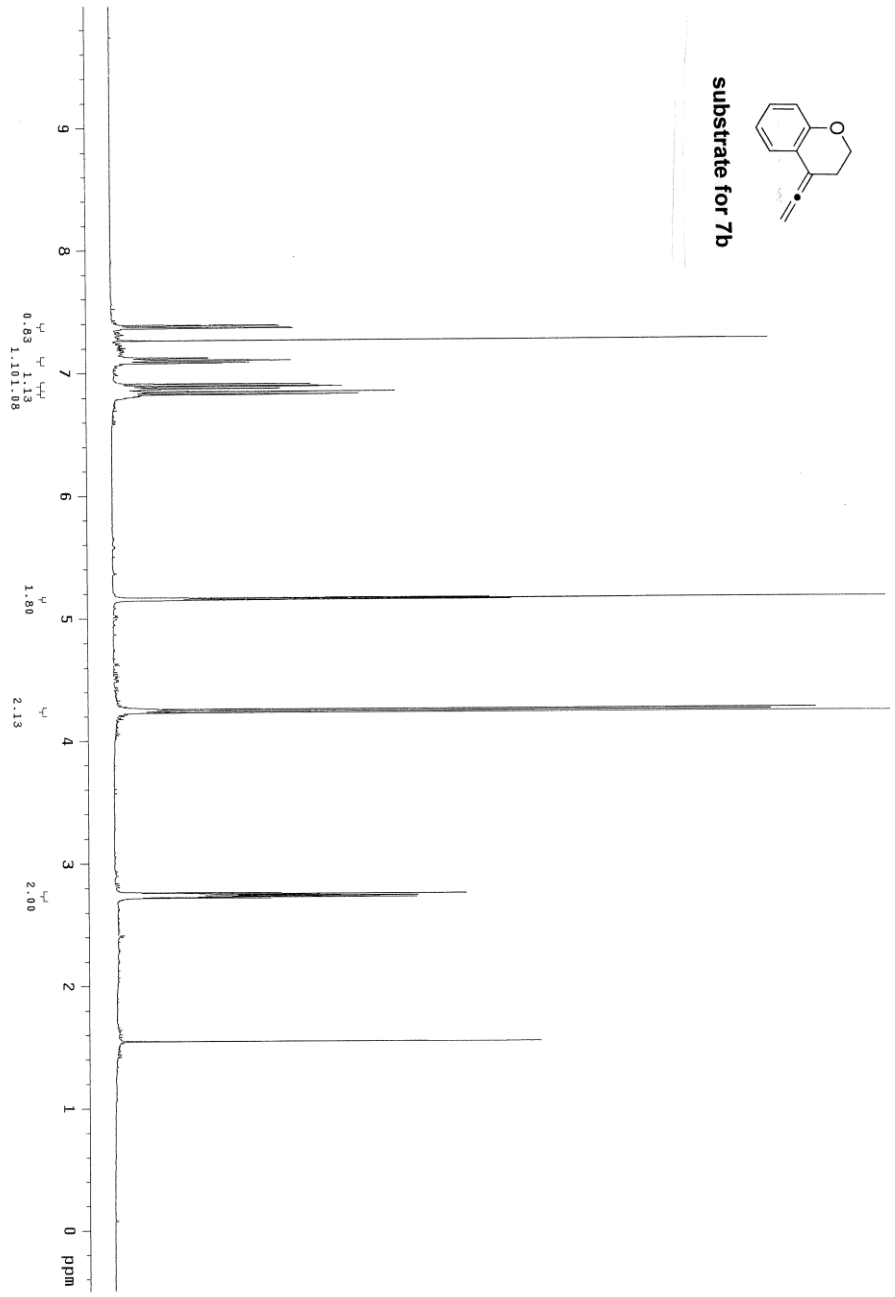

MeO
Me
11
ppm
0
1
2
3
4
5
6
7
8
9
3.01
2.00
3.11
1.46
0.93
0.8898
1.99

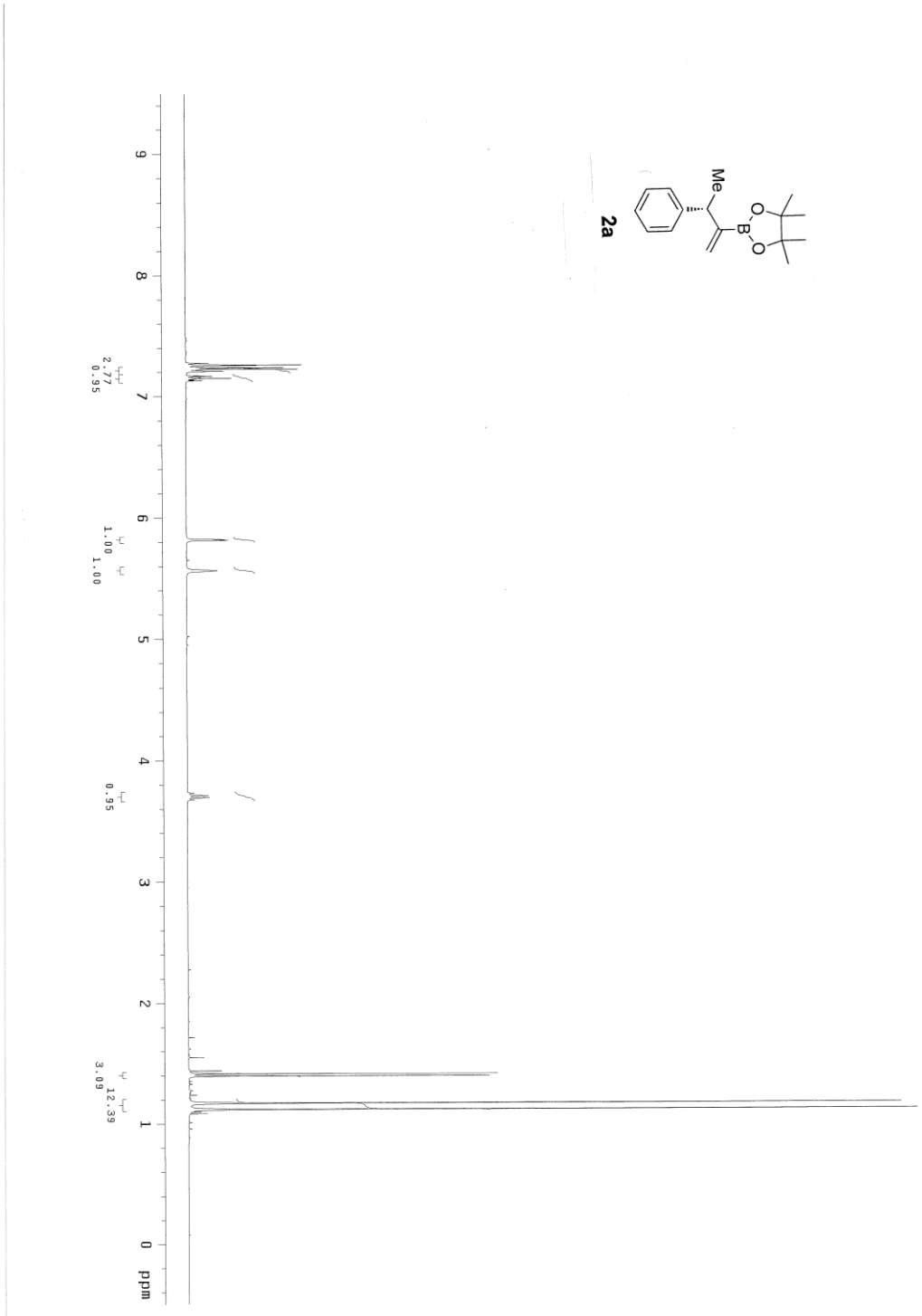

N
Me
1g
9
8
7
6
5
4
3
2
1
0
ppm
0.91
1.01
0.95
1.32
2.00
3.19

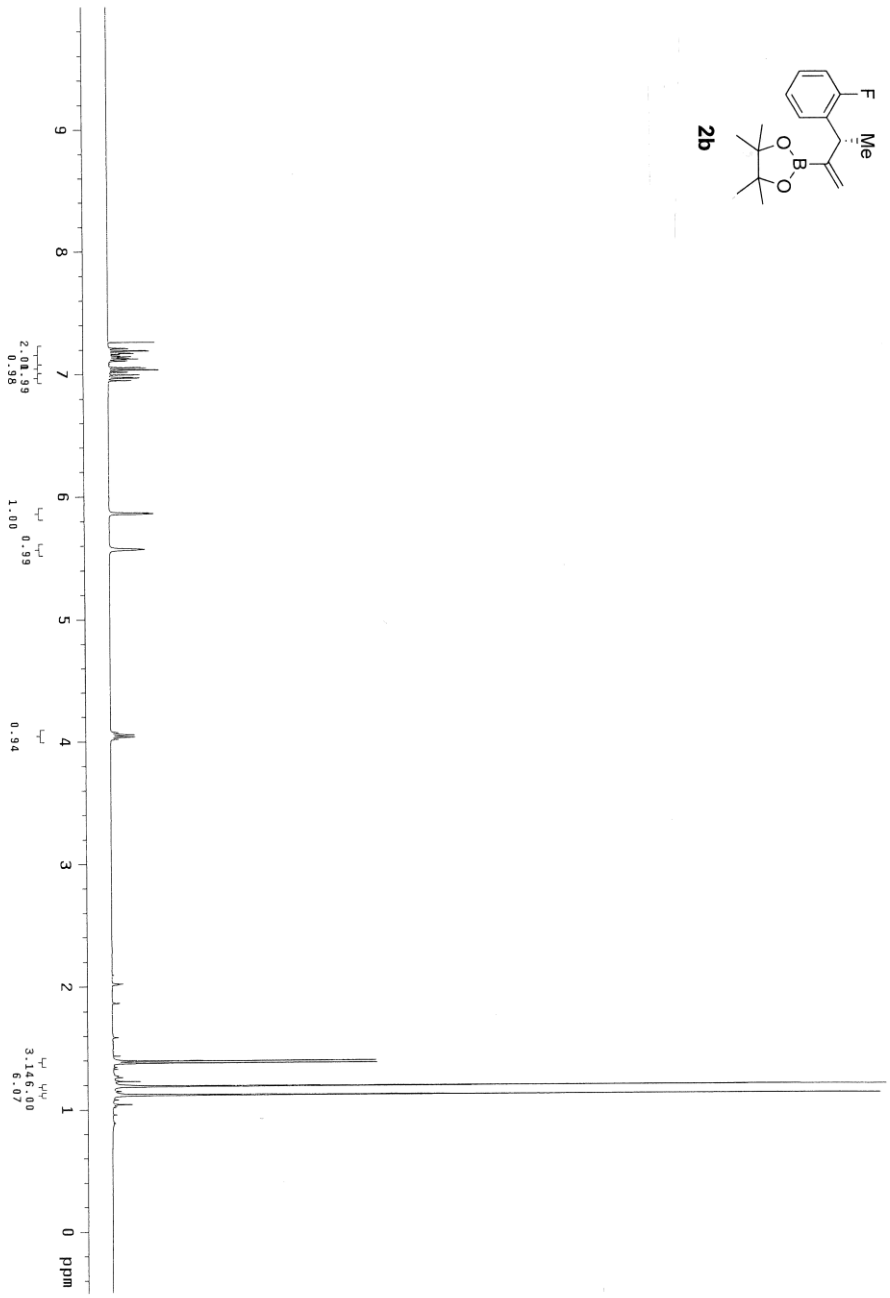

Me
Me
1j
9
8
7
6
5
4
3
2
1
0
ppm
1.83
1.07
2.00
1.90
1.00
6.00

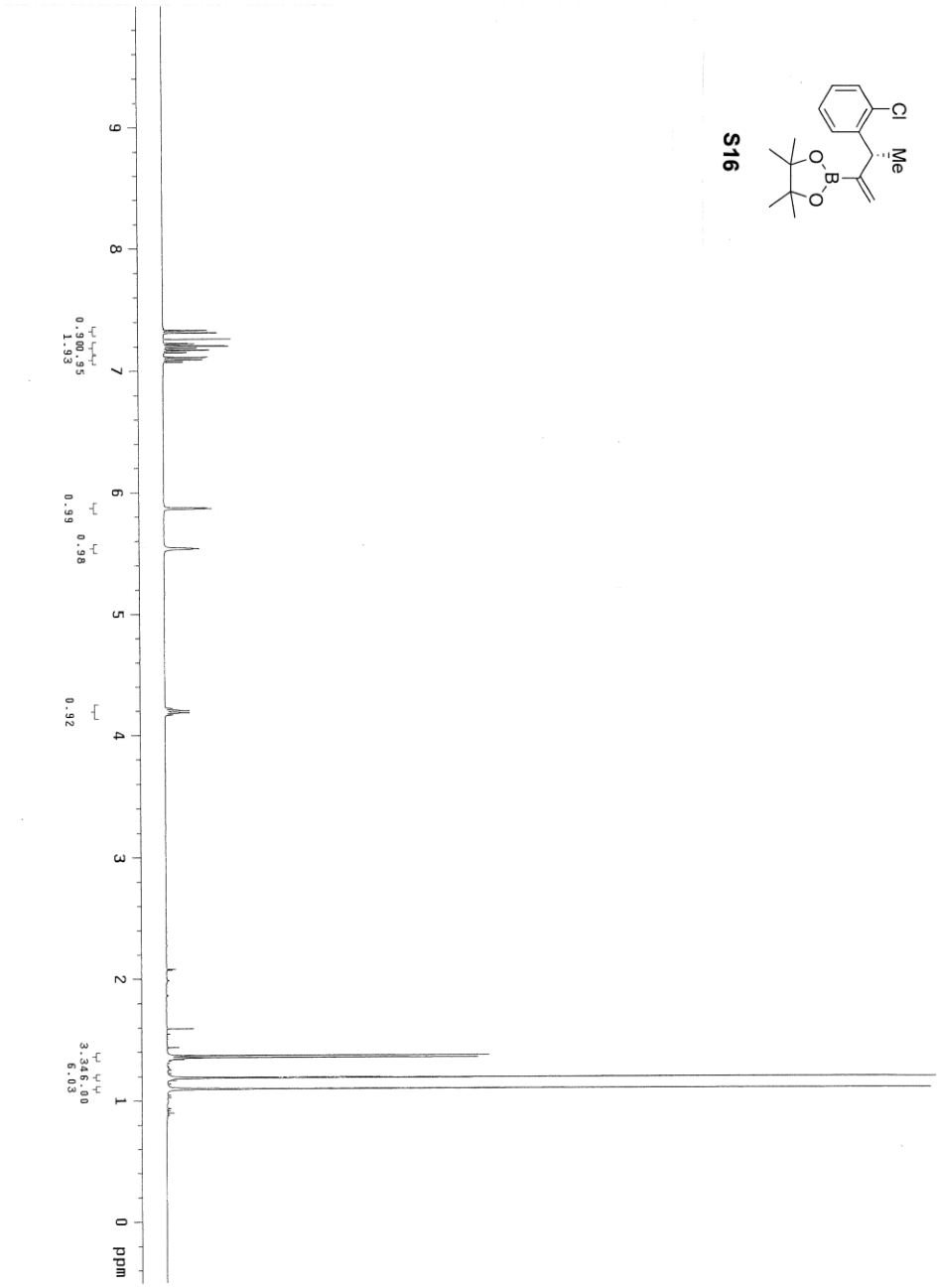

Ph
OTBS
1i
9
8
7
6
5
4
3
2
1
0
ppm
5.67
9.73
2.08
2.04
2.00
1.94
4.09
2.00


substrate for 7a
0.80
1.68
1.07
1.83
2.00
1.94
2.80
9
8
7
6
5
4
3
2
1
0
ppm


substrate for 7b
9
8
7
6
5
4
3
2
1
0
ppm
1.13
1.10
1.08
0.83
1.80
2.13
2.00


Me
O
B
O
2a
9
8
7
6
5
4
3
2
1
0
ppm
2.77
0.95
1.00
1.00
0.95
12.39
3.09


F
Me
O
B
O
O
2b
9
8
7
6
5
4
3
2
1
0
ppm
2.08
0.98
1.00
0.99
0.94
3.14
6.00
6.07


S16
Cl
Me
B
O
O
9
8
7
6
5
4
3
2
1
0
ppm
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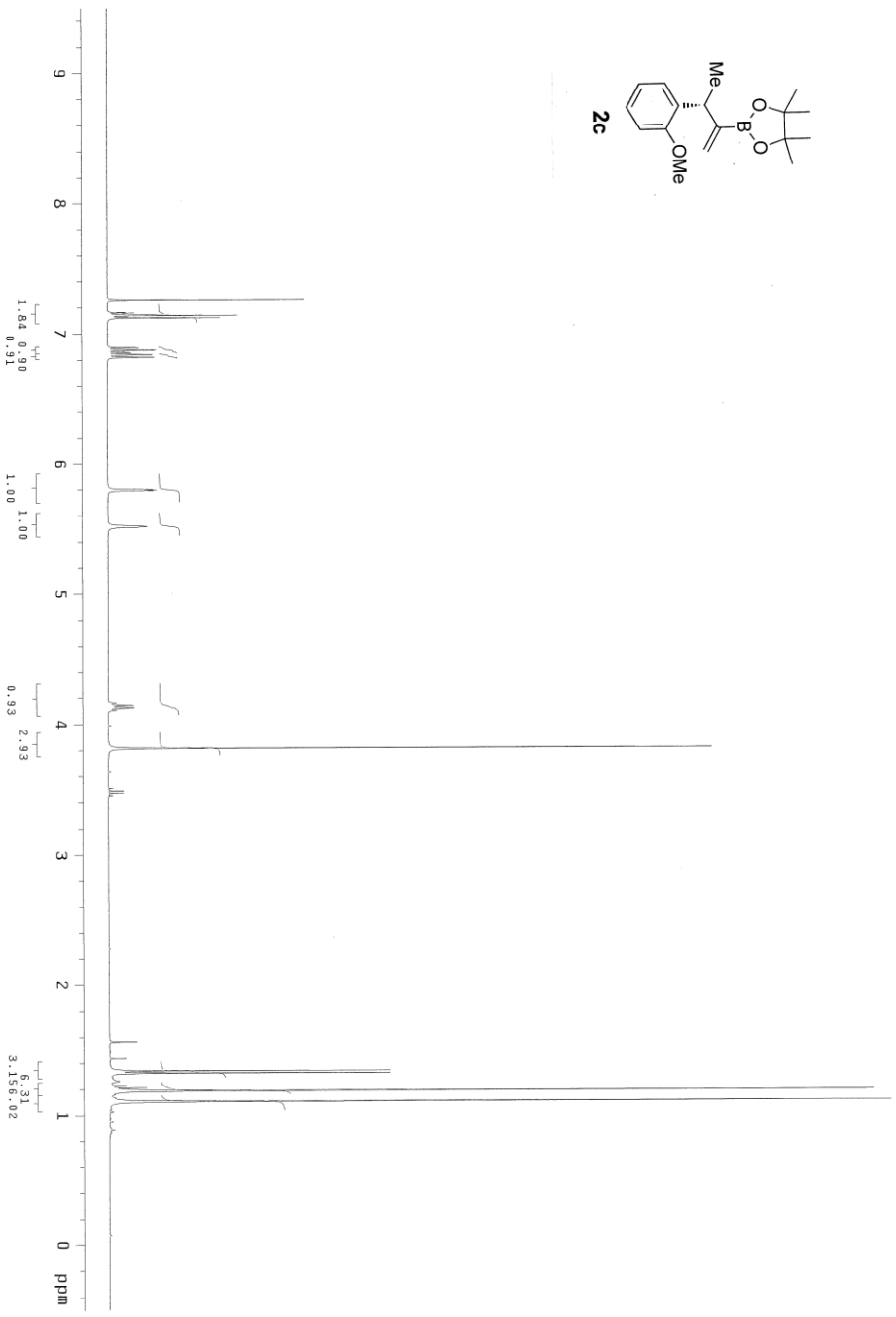
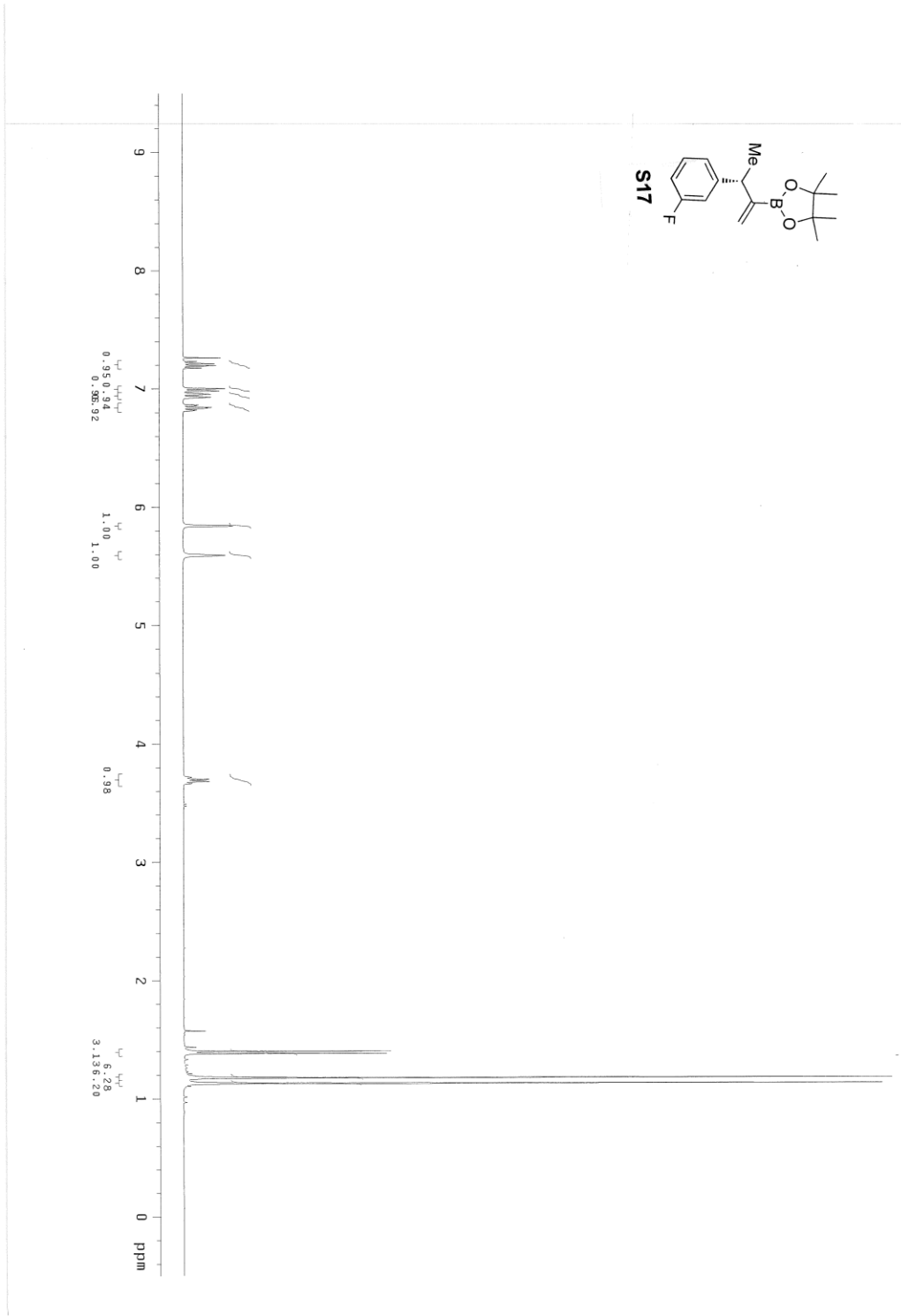
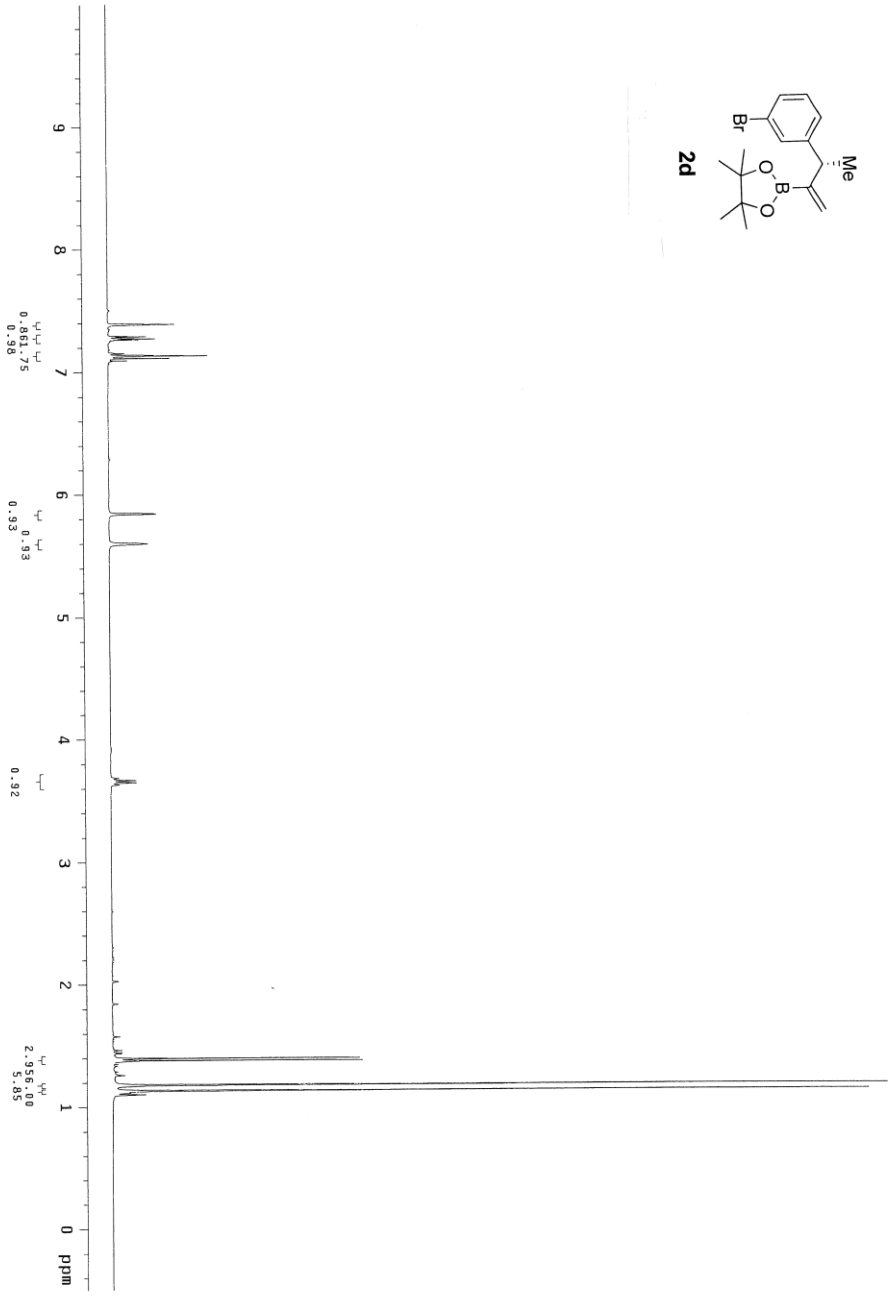
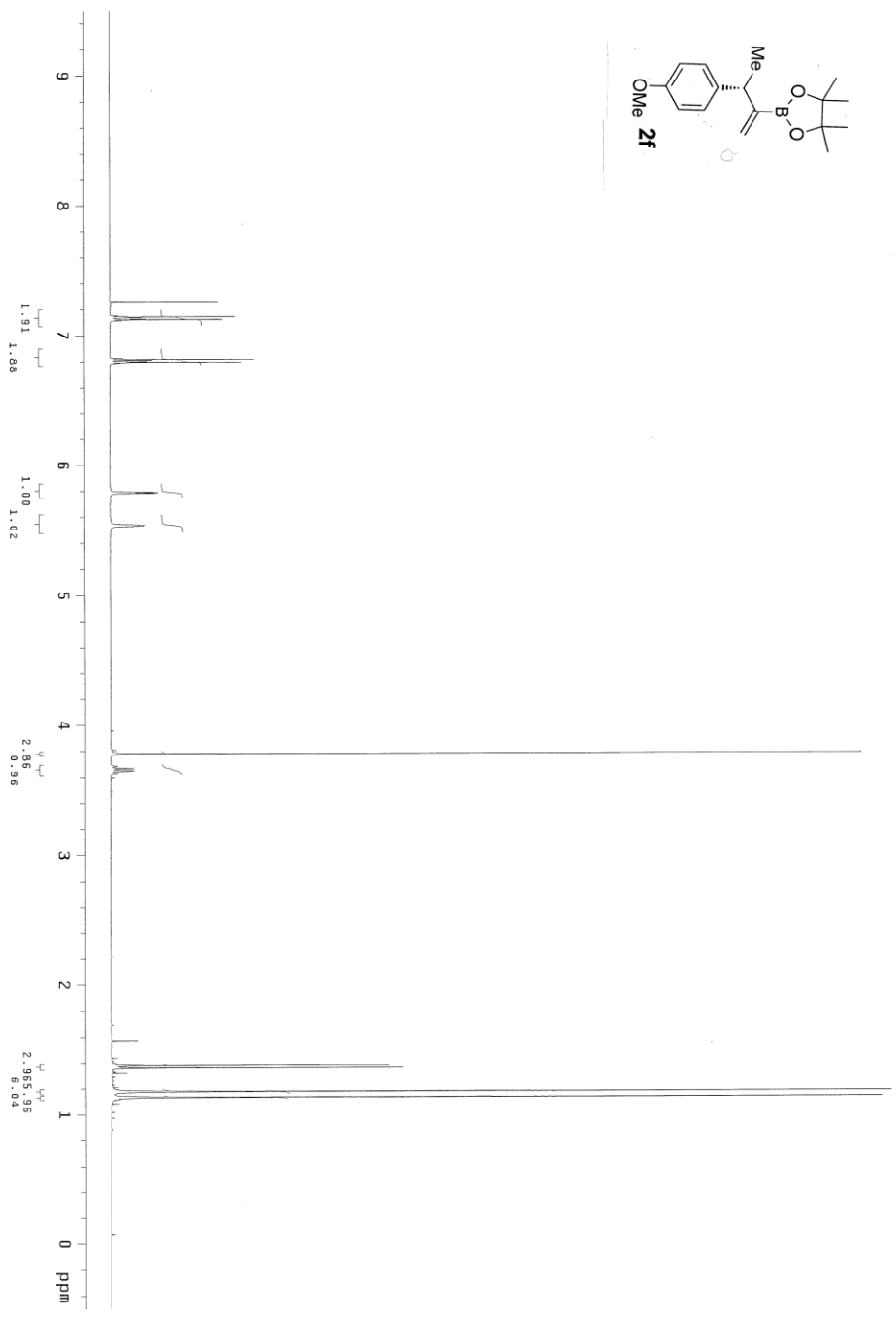
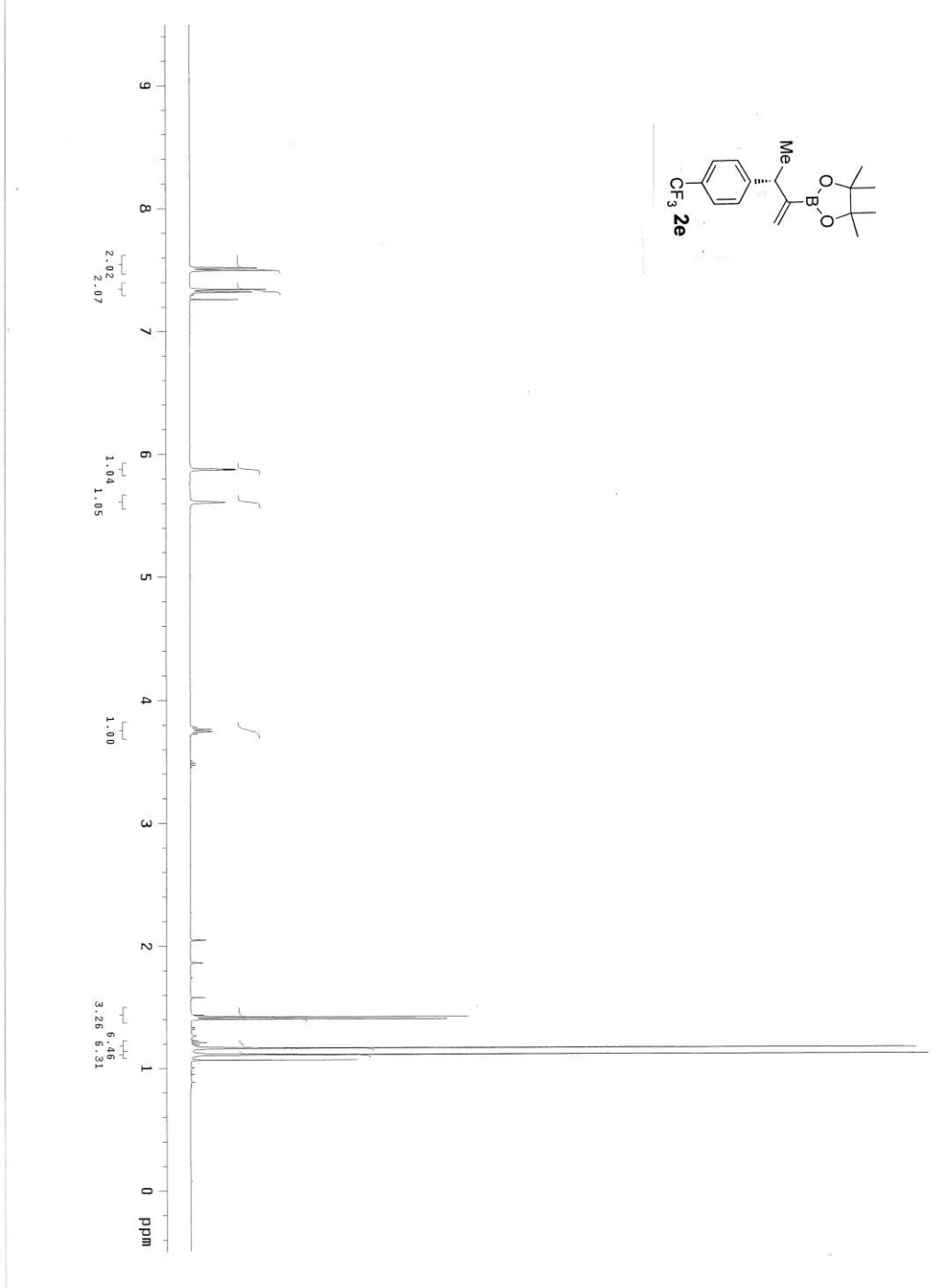
0.95
1.93
0.99
0.98
0.92
3.34
6.00
6.03

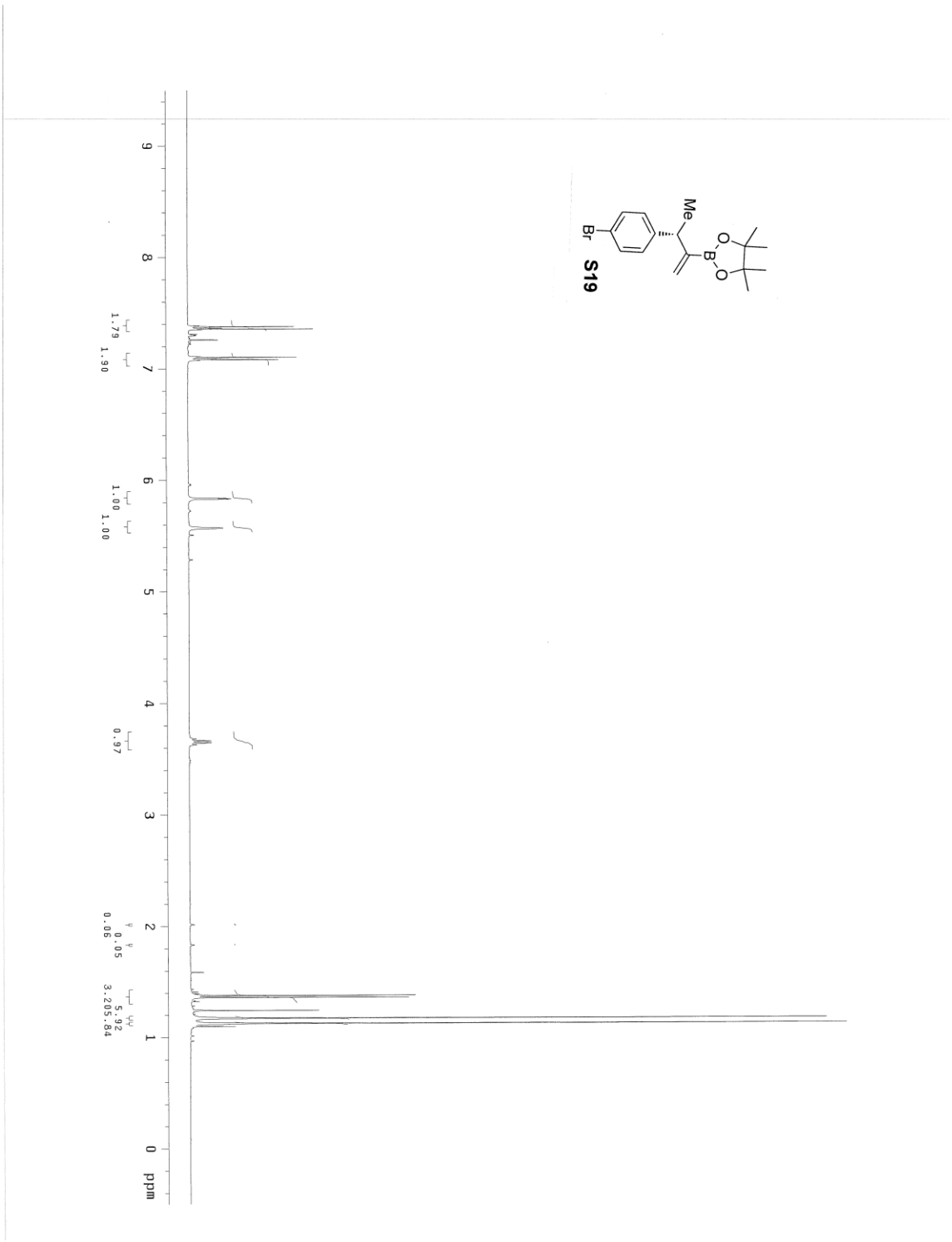

Me
OMe
O
B
O
2c
9
8
7
6
5
4
3
2
1
0
ppm
1.84
0.90
0.91
1.00
1.00
0.93
2.93
6.31
3.15
6.02


Me
F
B
O
O
O
S17
9
8
7
6
5
4
3
2
1
0
ppm
0.95
0.94
0.96
0.92
1.00
1.00
0.98
6.28
3.13
6.20


Br
Me
B
O
O
2d
9
8
7
6
5
4
3
2
1
0
ppm
0.98
0.93
0.93
0.92
5.85


Me
OMe
2f
O
B
O
O
9
8
7
6
5
4
3
2
1
0
ppm
1.91
1.88
1.00
1.02
2.86
0.96
2.965.96
6.04


Me
$CF_3$ **2e**
O
B
O
O
9
8
7
6
5
4
3
2
1
0
ppm
2.02
2.07
1.04
1.05
1.00
3.26
6.46
6.31


Me
Br
O
B
O
S19
9
8
7
6
5
4
3
2
1
0
ppm
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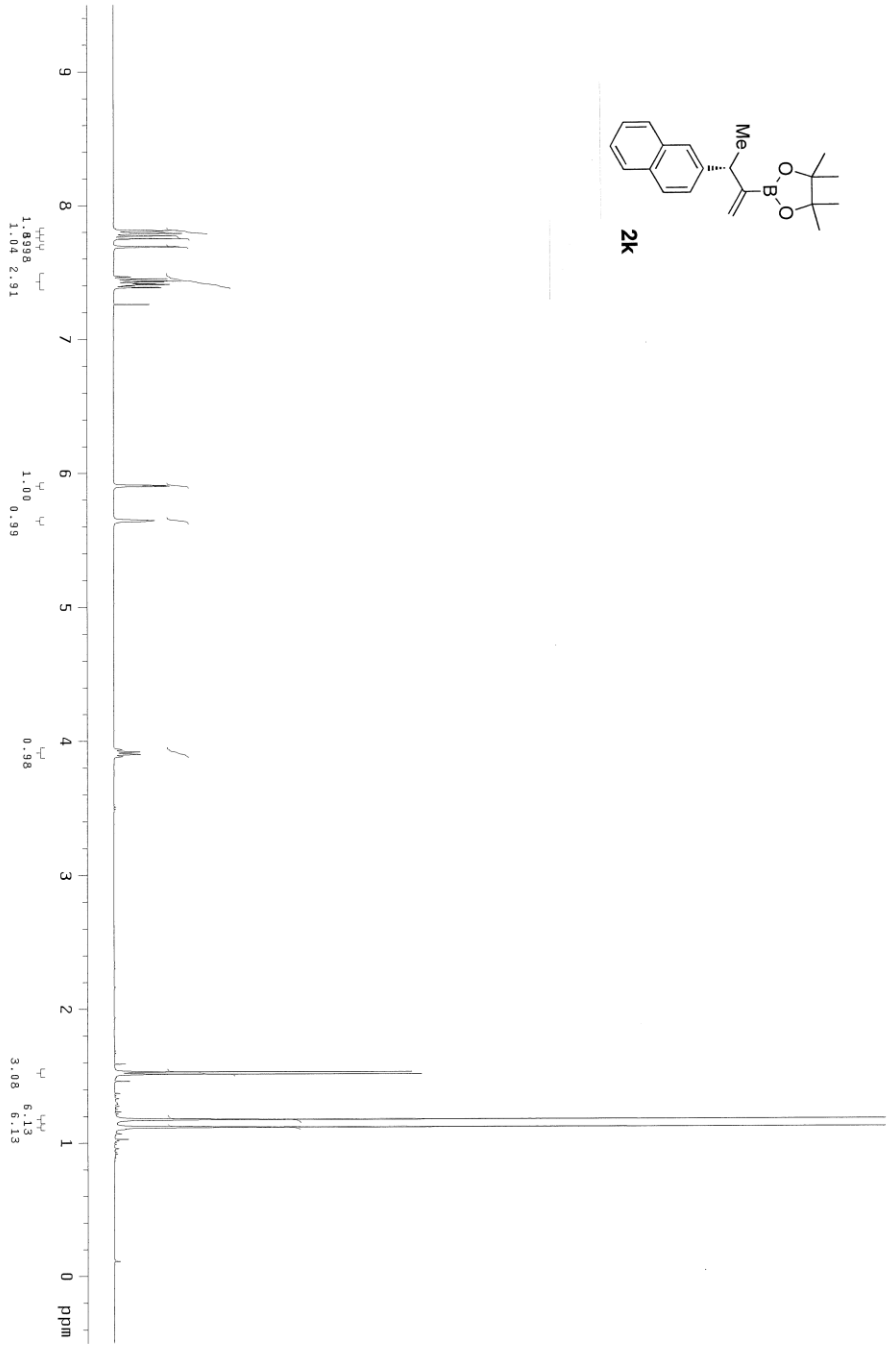
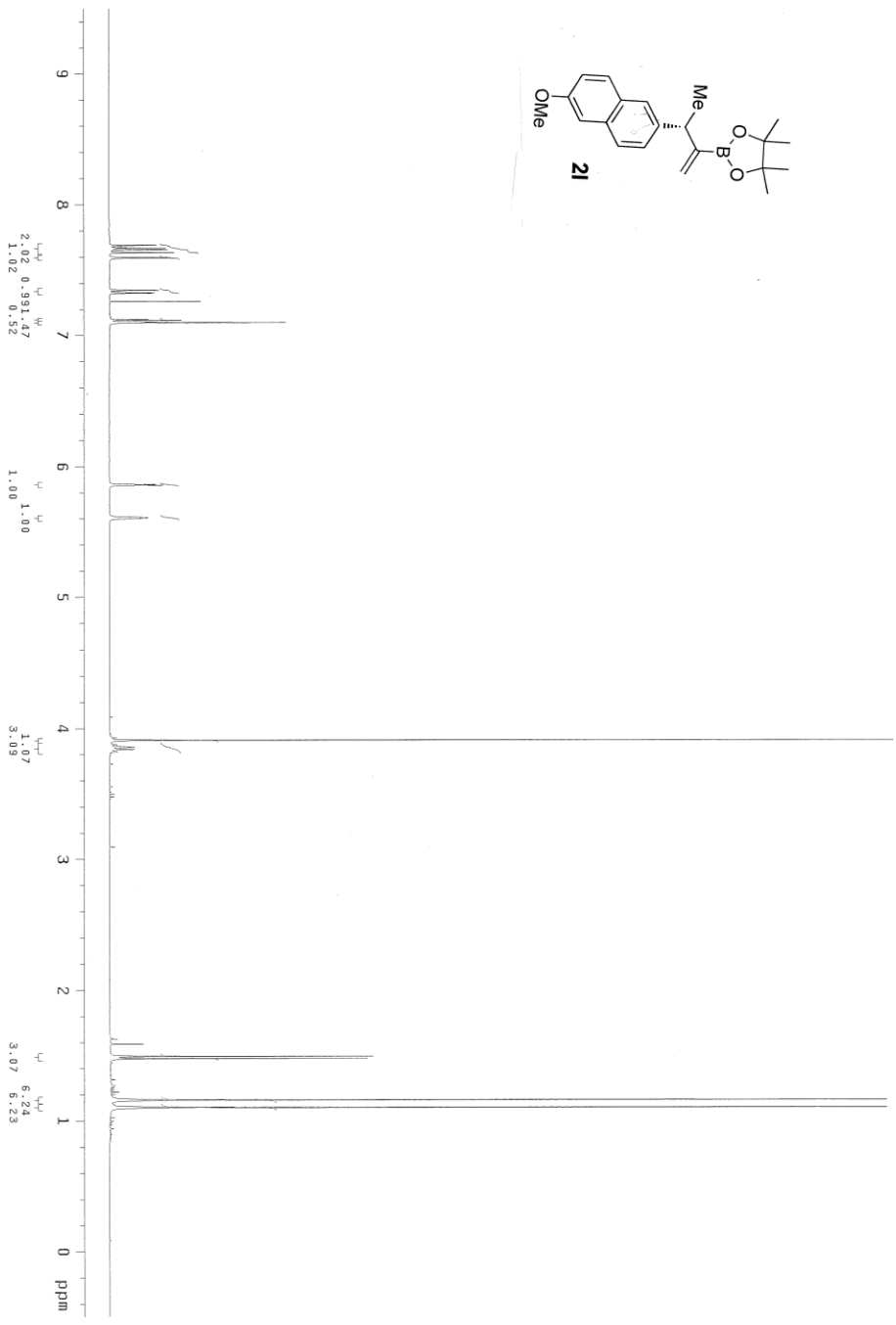
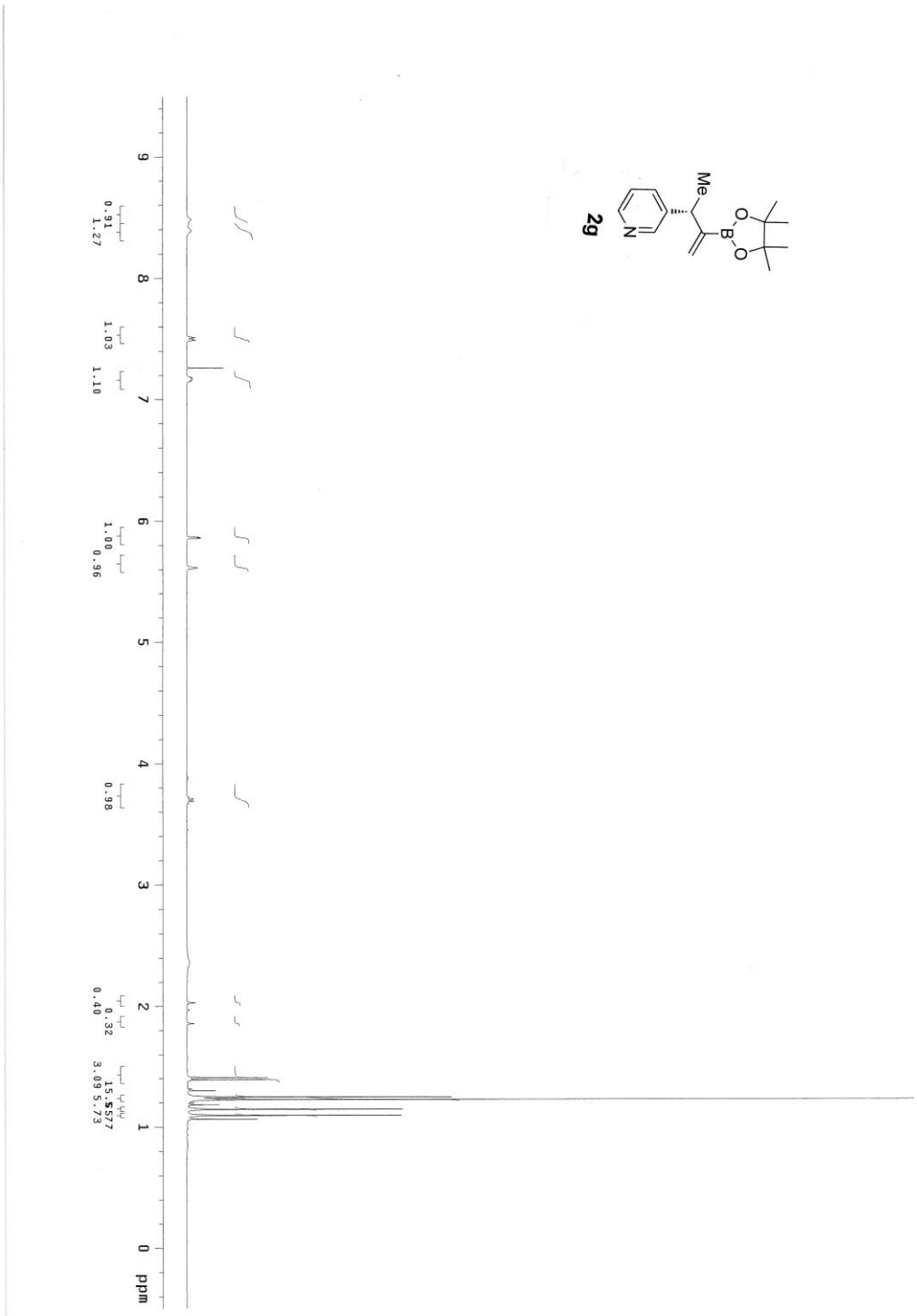
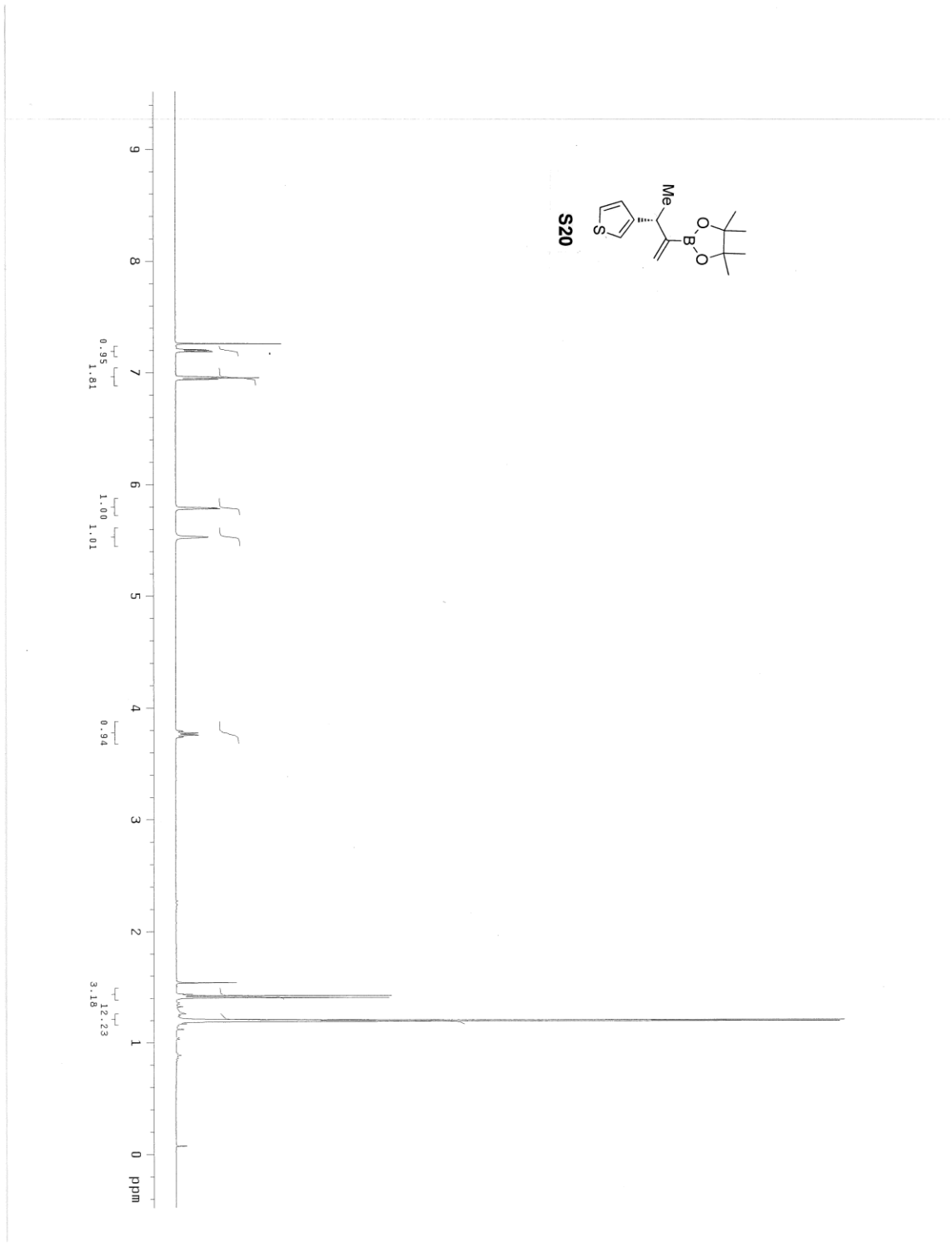
1.90
1.00
1.00
0.97
0.06
0.05
5.92
3.20
5.84


Me
O
B
O
2k
9
8
7
6
5
4
3
2
1
0
ppm
1.04
2.91
1.00
0.99
0.98
3.08
6.13
6.13


OMe
Me
O
B
O
O
2l
9
8
7
6
5
4
3
2
1
0
ppm
2.02
0.99
1.47
1.02
0.52
1.00
1.00
1.07
3.09
3.07
6.24
6.23


Me
B
O
O
O
N
2g
9
8
7
6
5
4
3
2
1
0
ppm
0.91
1.27
1.03
1.10
1.00
0.96
0.98
0.32
0.40
15.57
3.09
5.73


S20
Me
S
B
O
O
9
8
7
6
5
4
3
2
1
0
ppm
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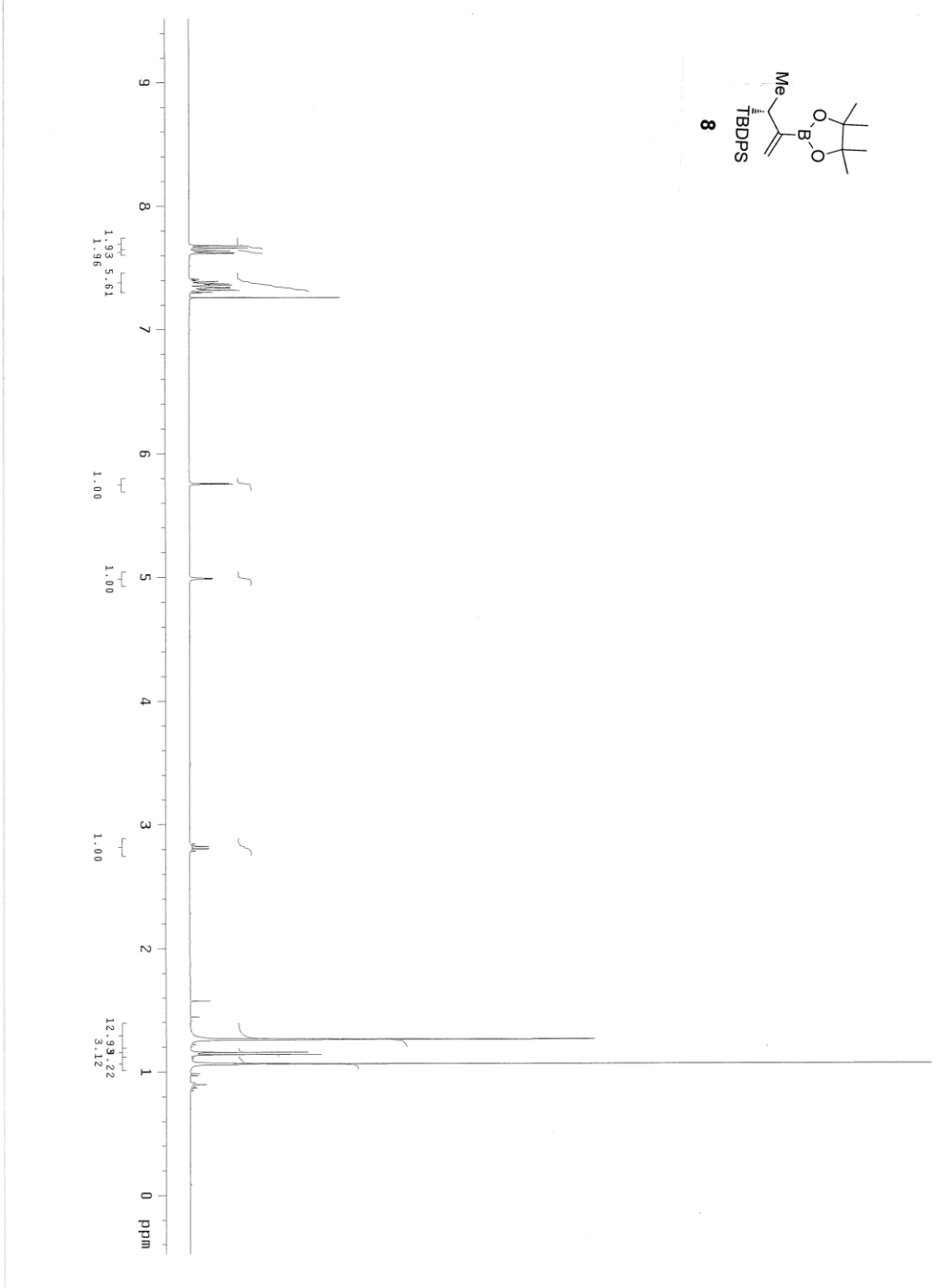
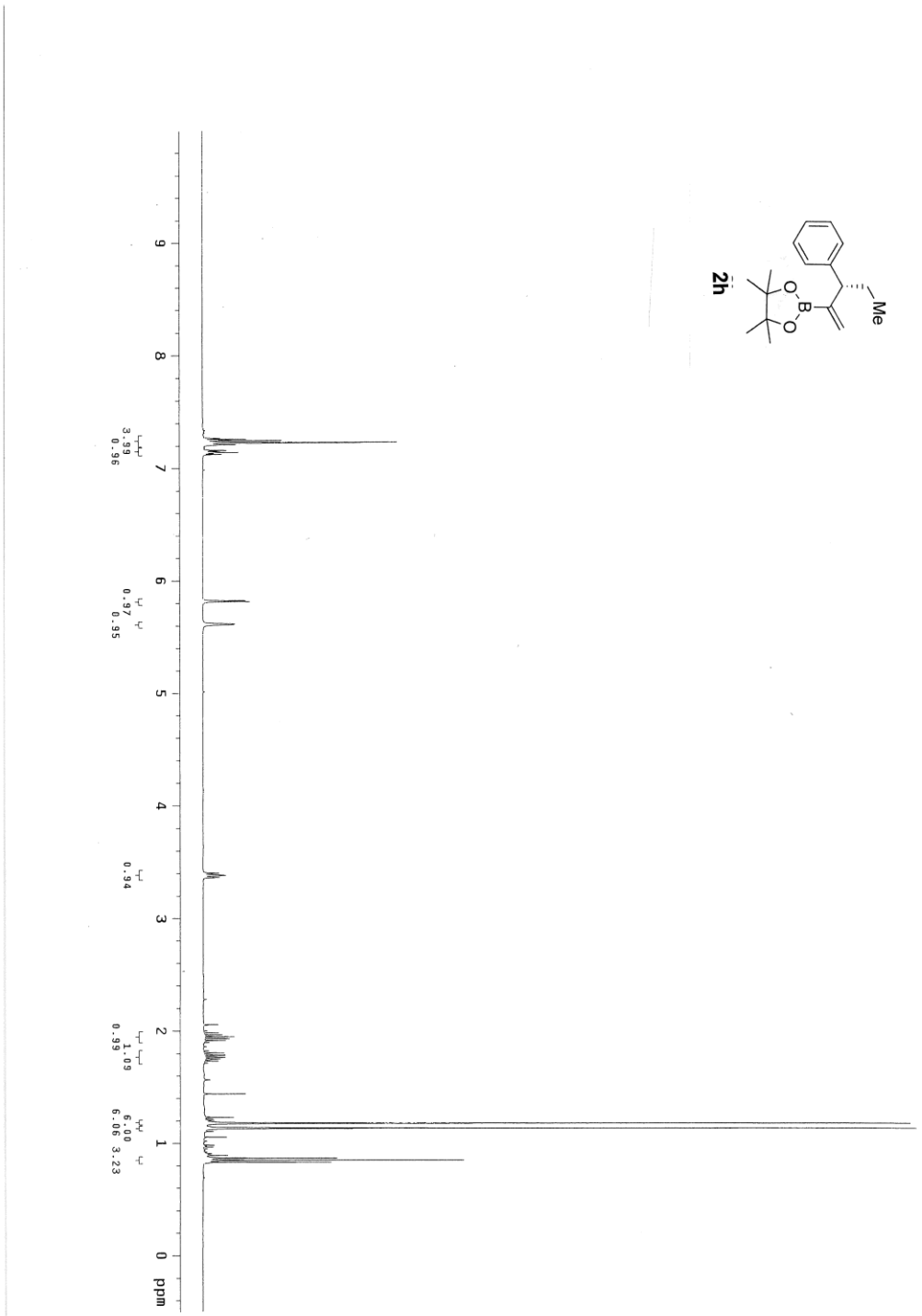
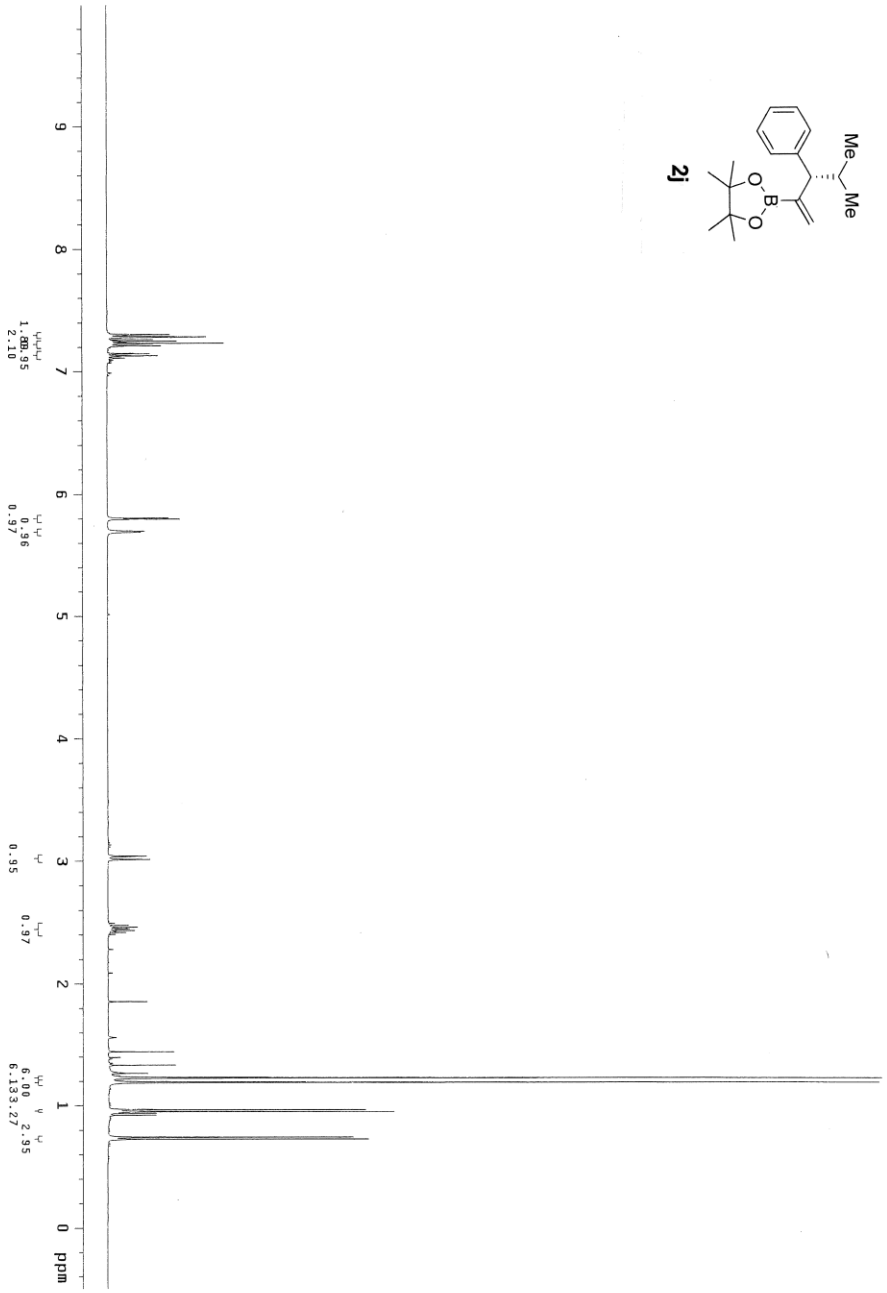
1.81
1.00
1.01
0.94
12.23
3.18


Me
TBDPS
O
B
O
8
9
8
7
6
5
4
3
2
1
0
ppm
1.93
1.96
5.61
1.00
1.00
1.00
12.93
3.12
4.22


2h
Me
3.99
0.96
0.97
0.95
0.94
1.09
0.99
6.00
6.06
3.23
9
8
7
6
5
4
3
2
1
0
ppm


Me
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O
B
O
O
2j
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7
6
5
4
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2
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0.97
0.95
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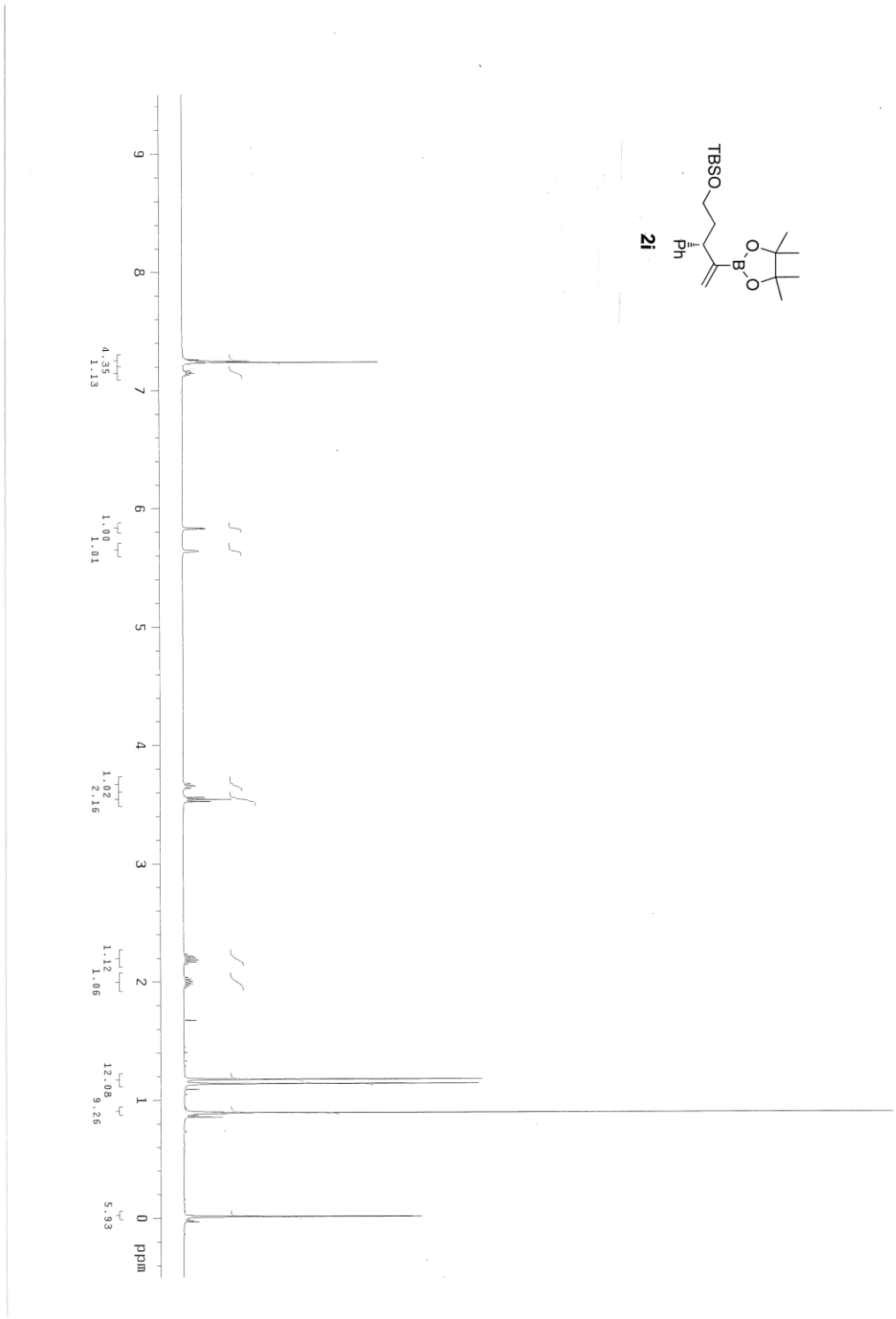
2.95
6.13
3.27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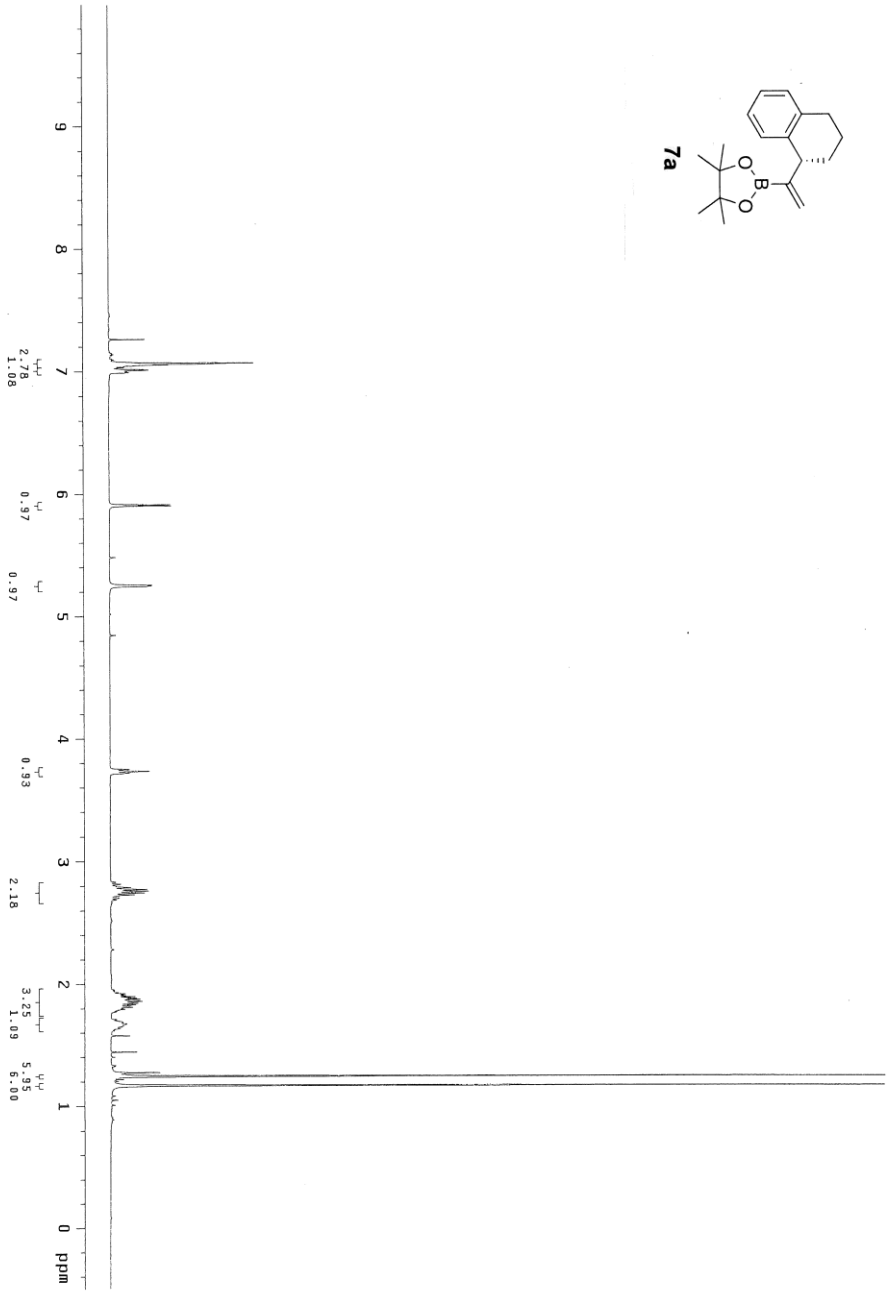
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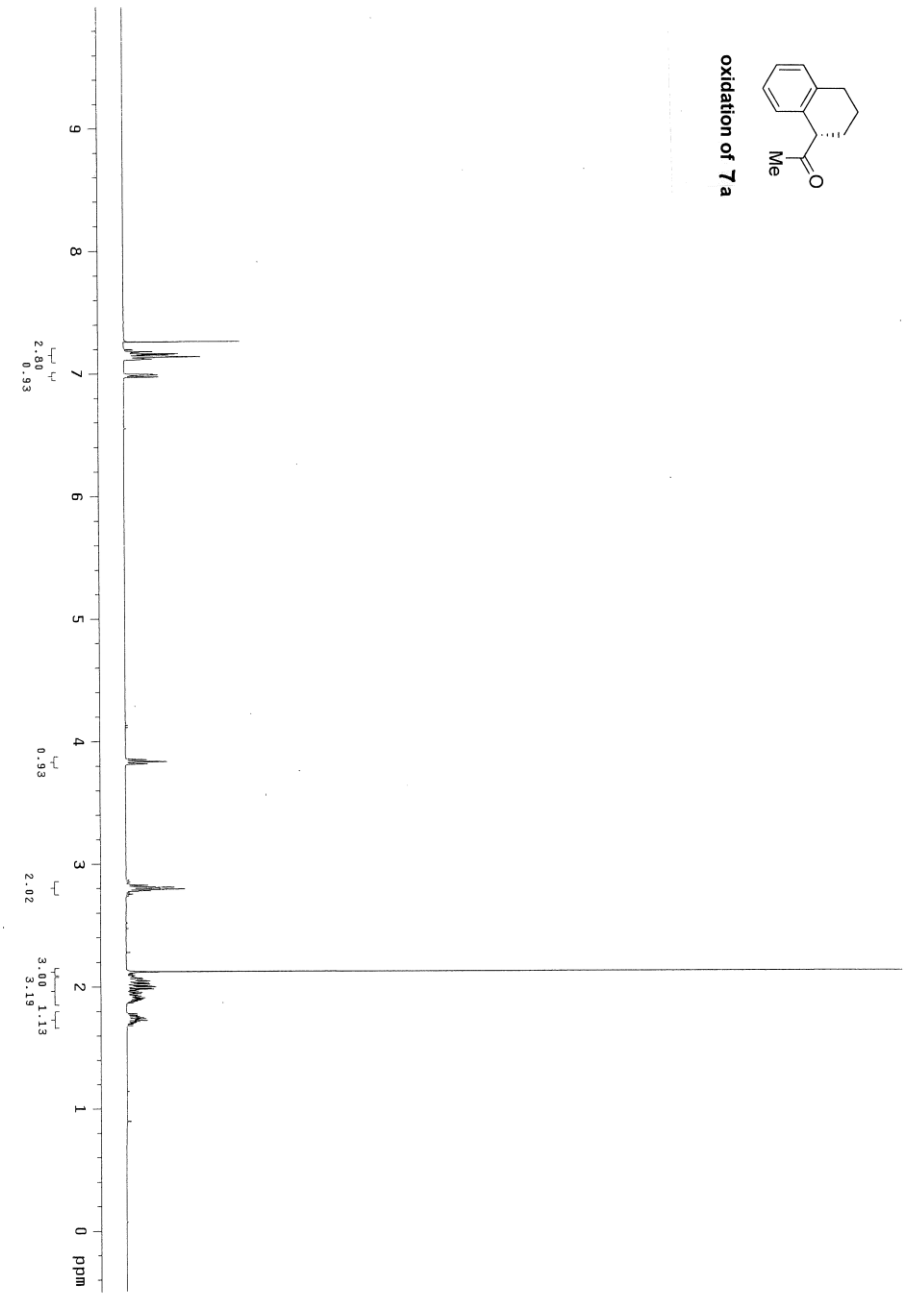
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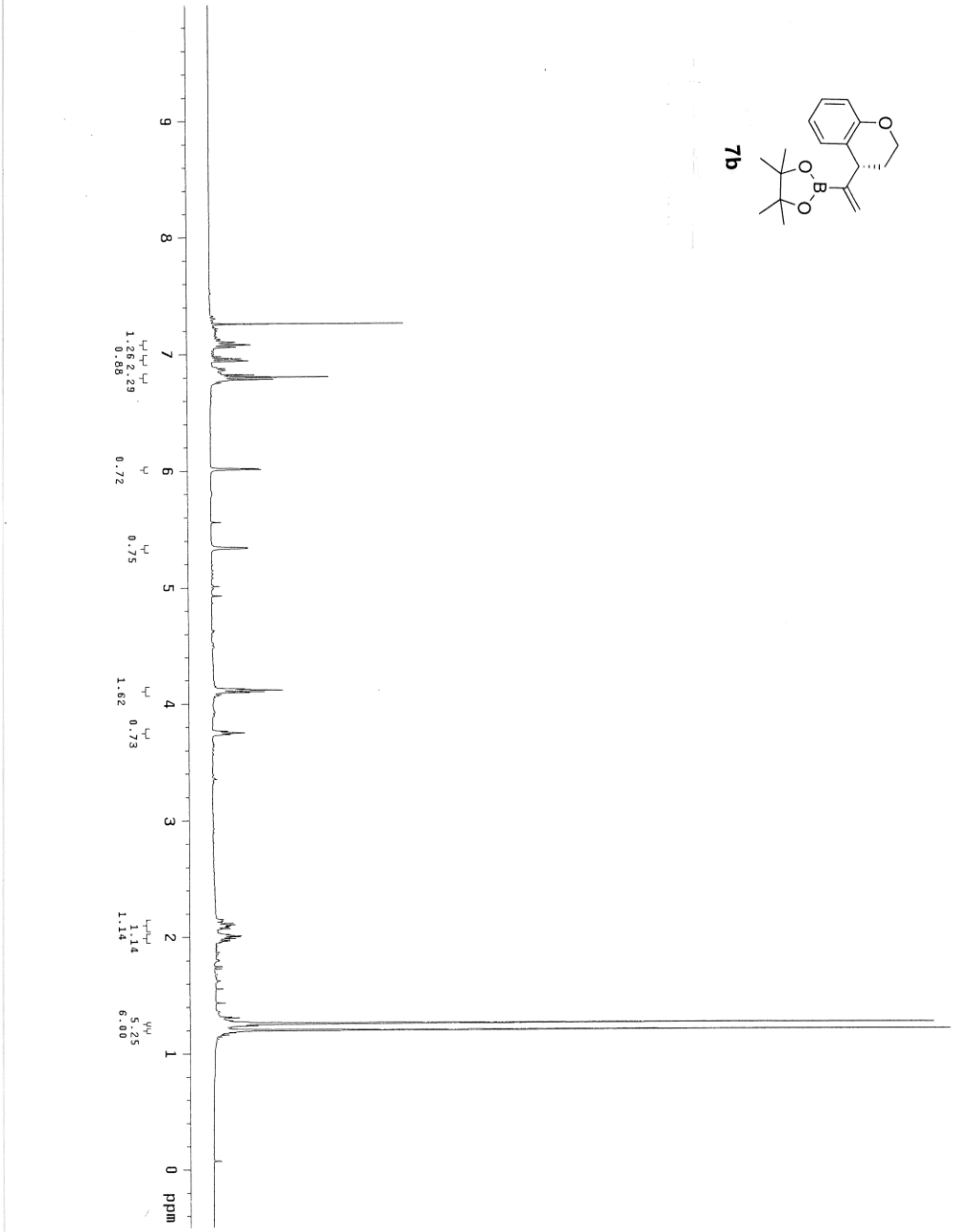
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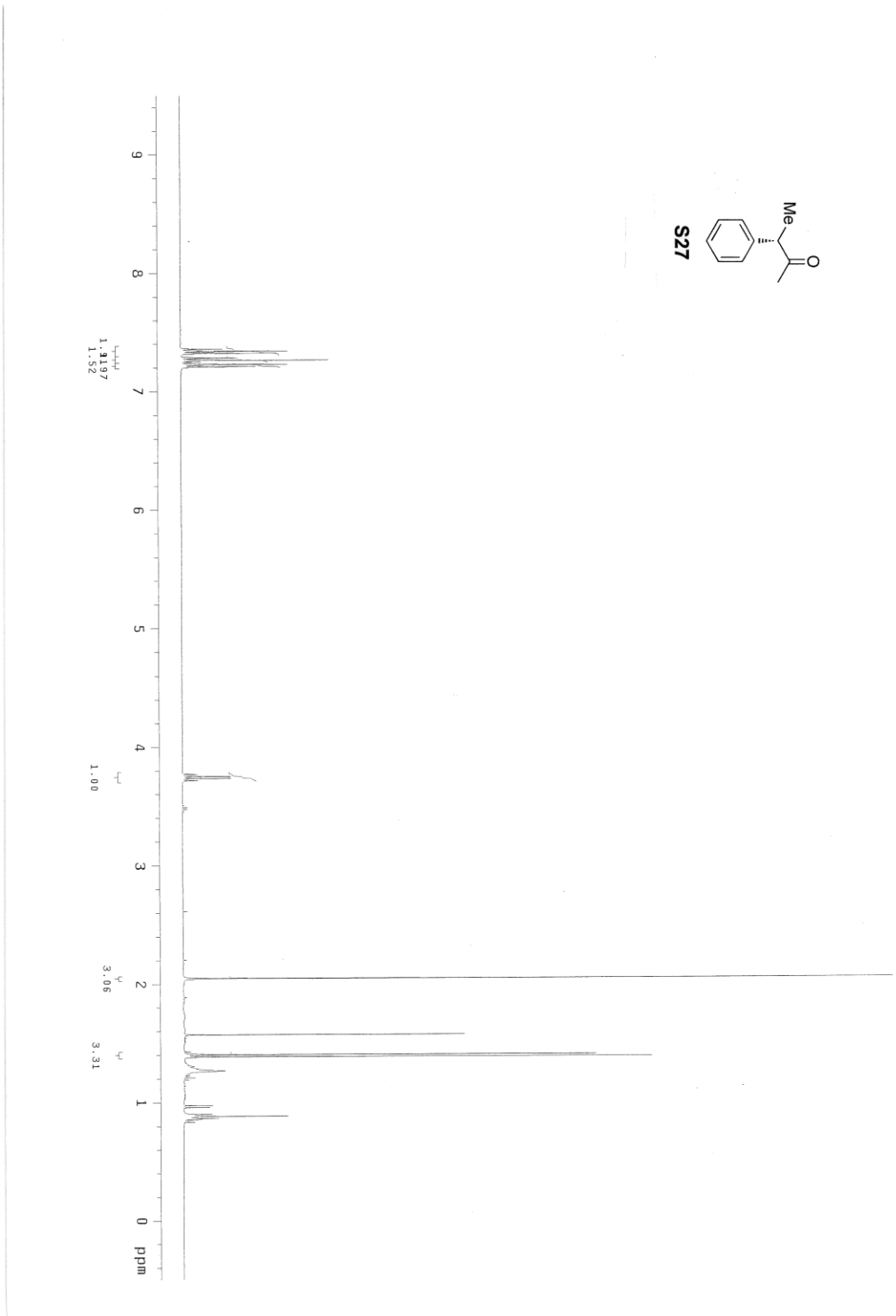
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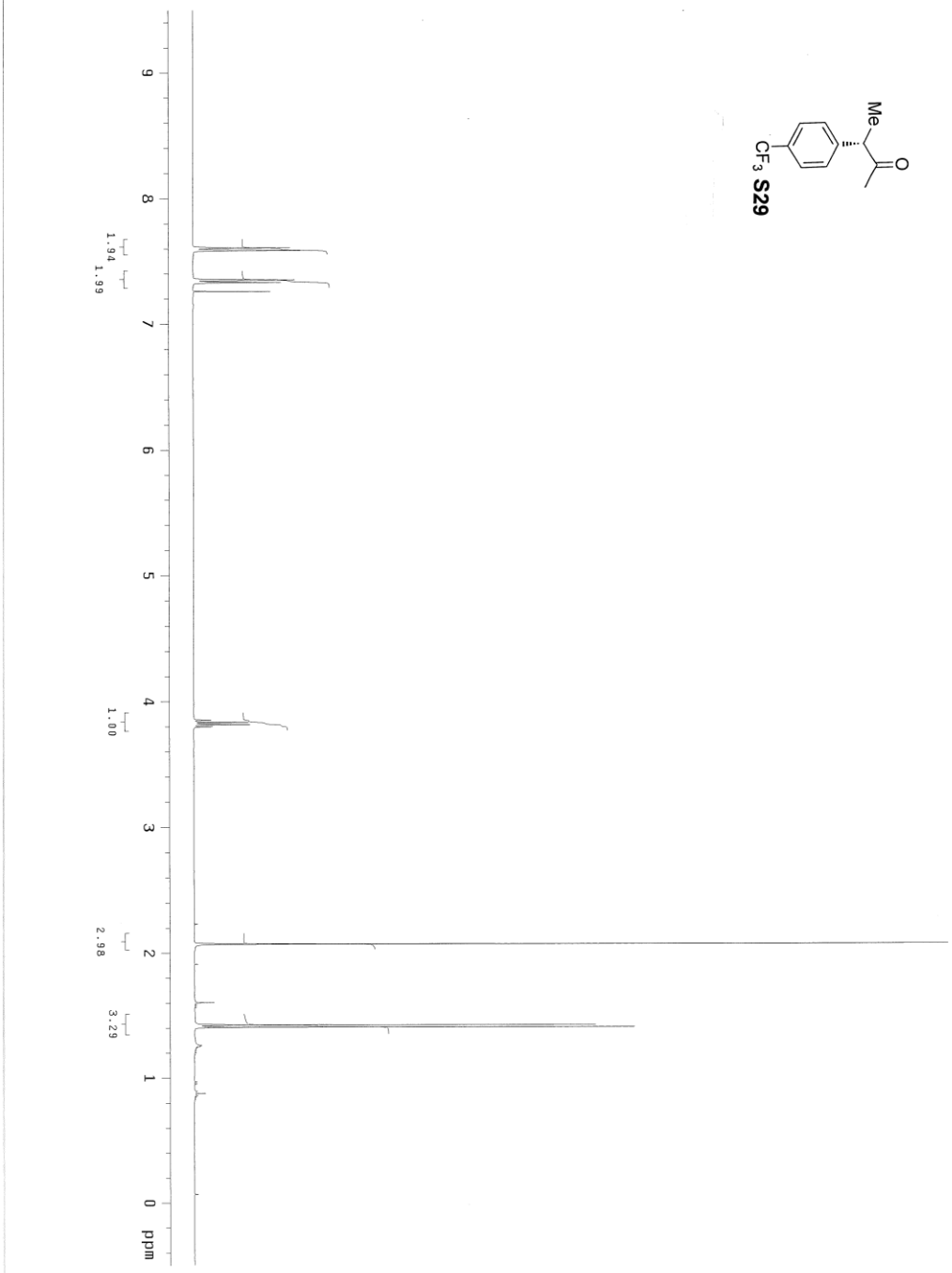
ppm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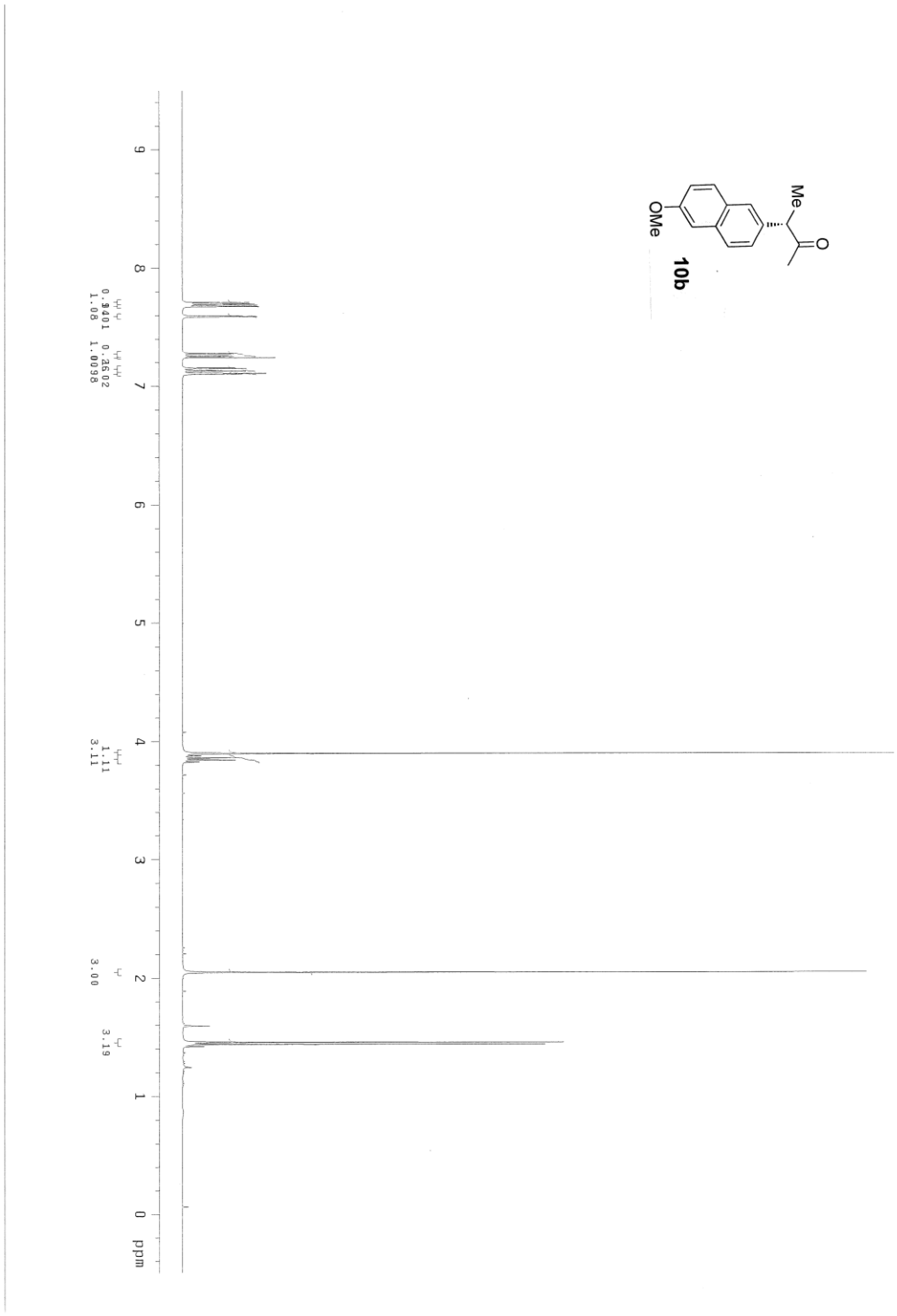
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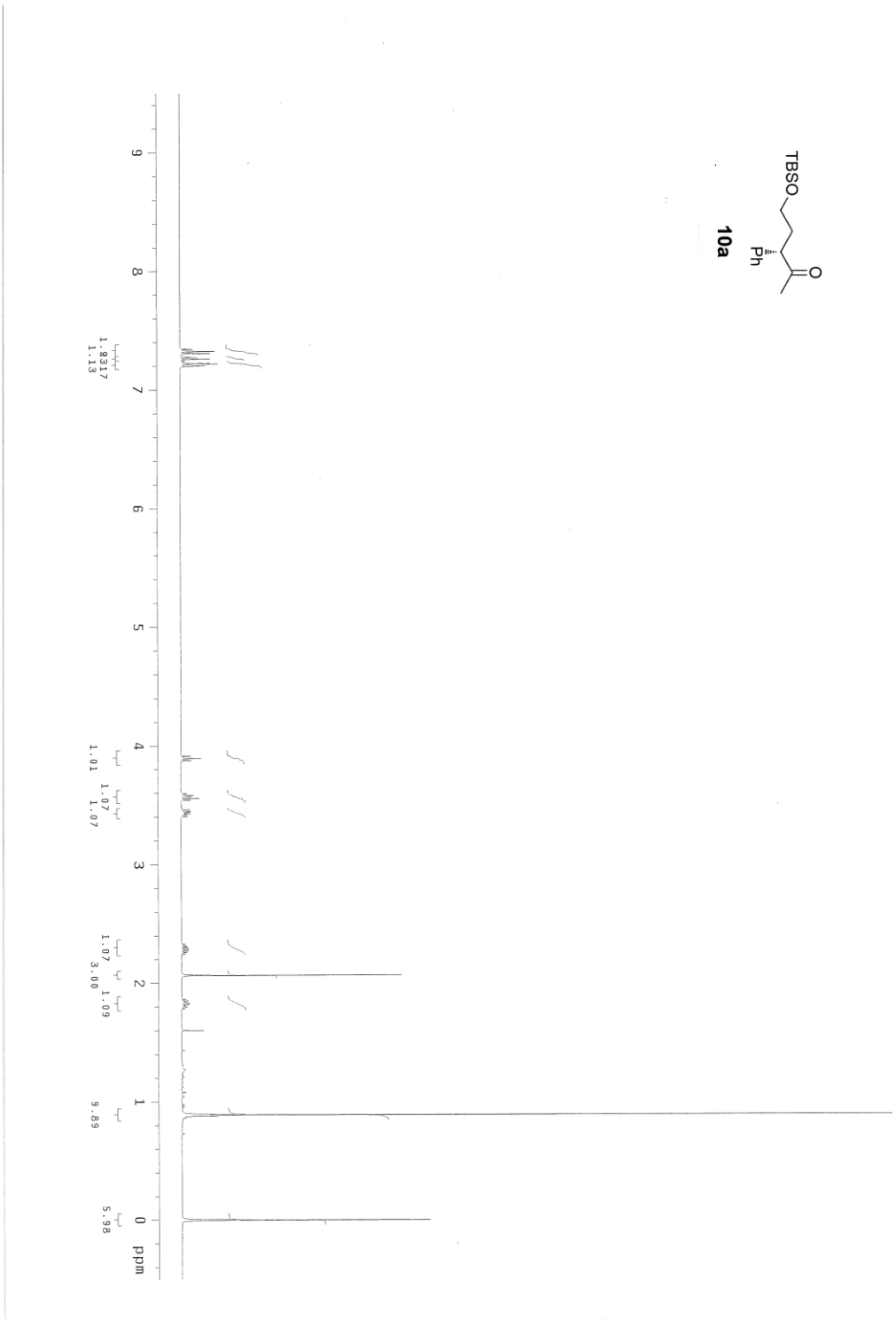
3.00
3.19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ppm
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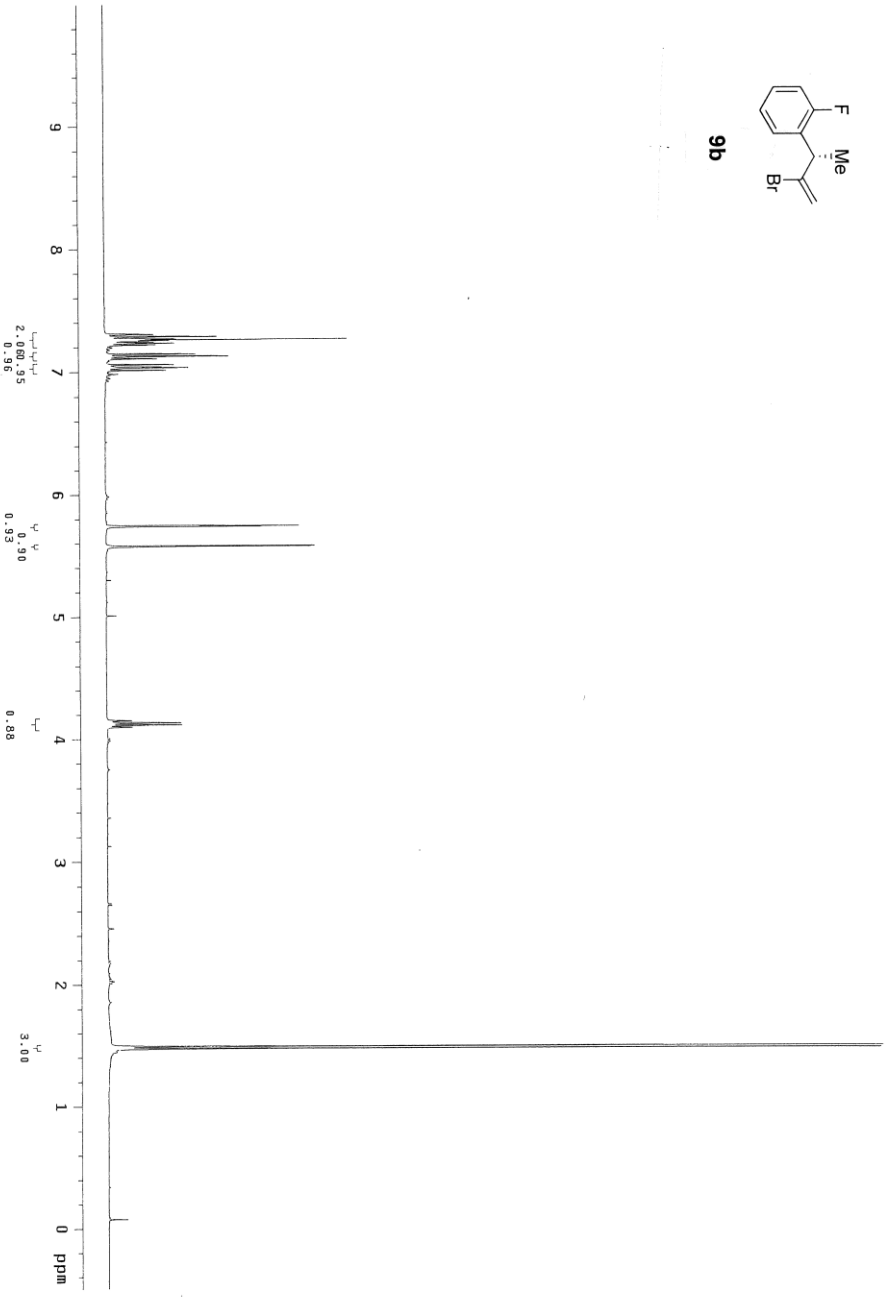
1.07
3.00
9.89
5.98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0.90
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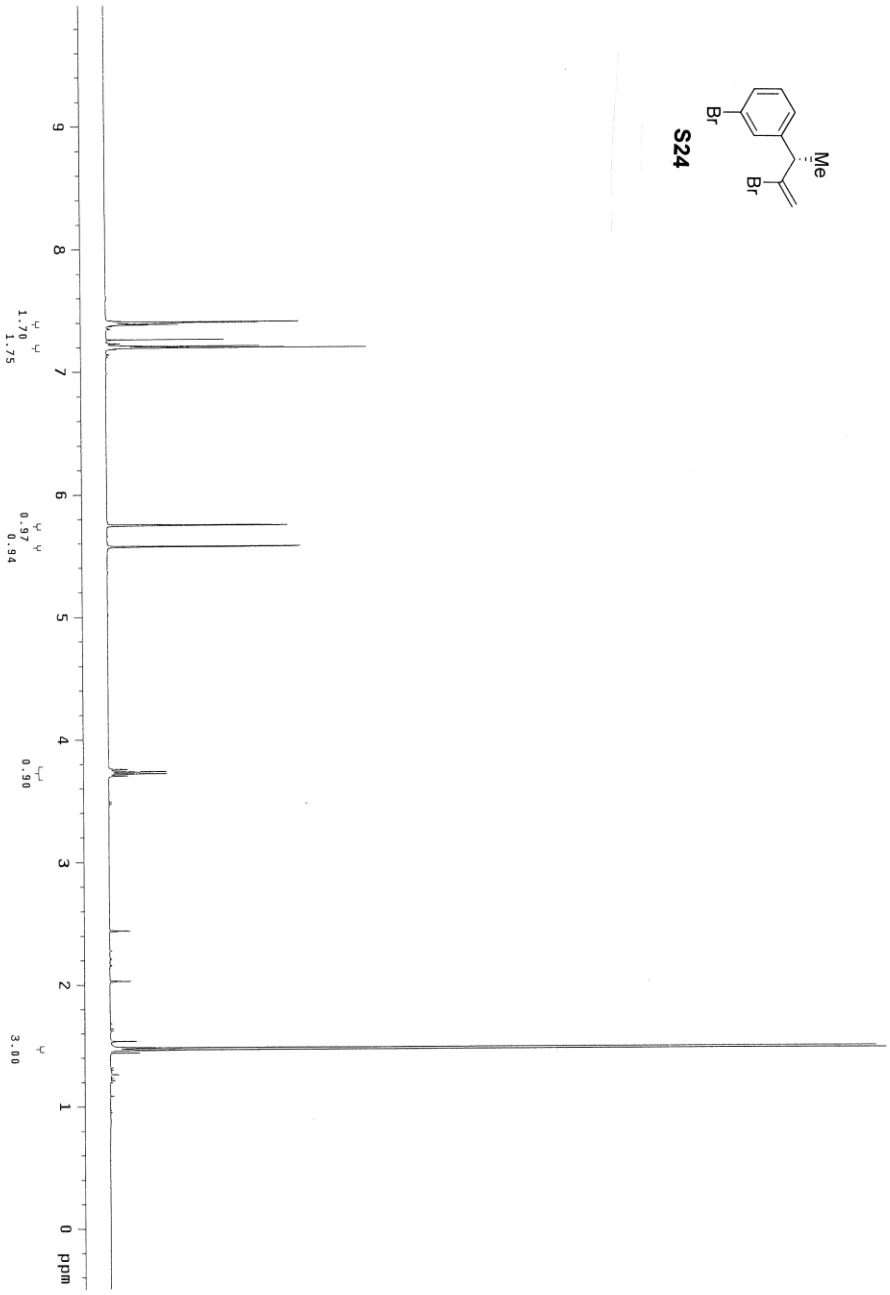
0.95
0.96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ppm
1.70
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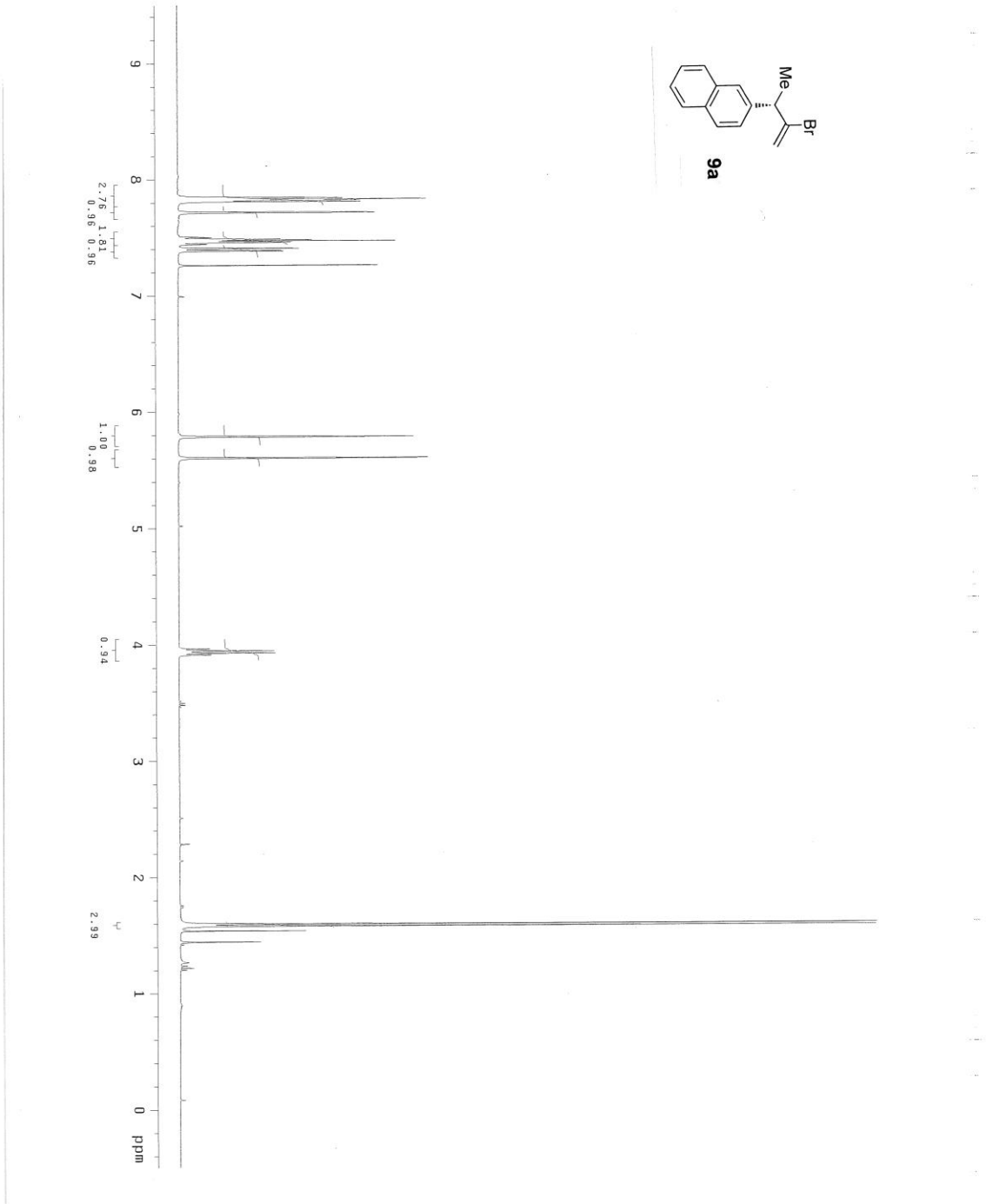
0.97
0.94
0.90
3.00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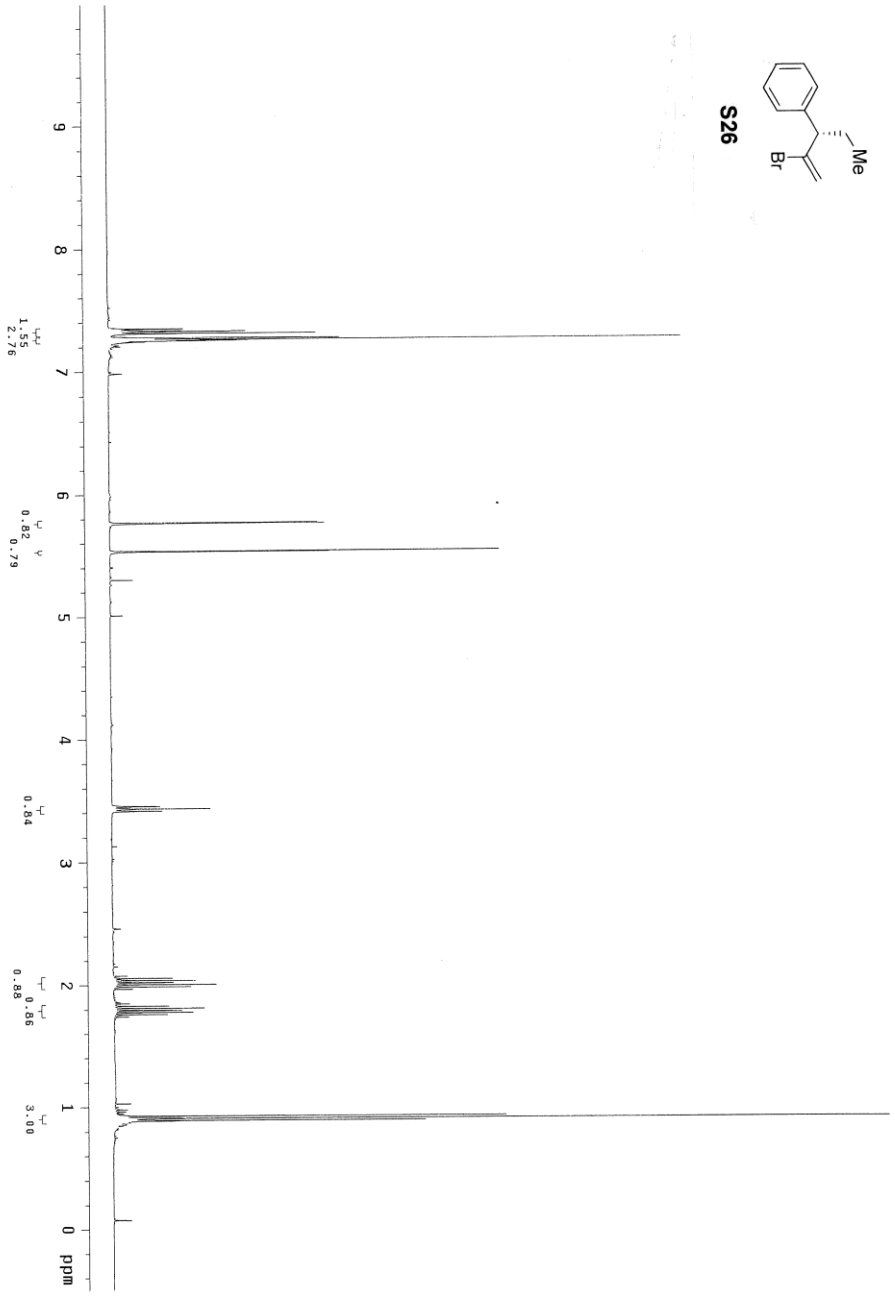
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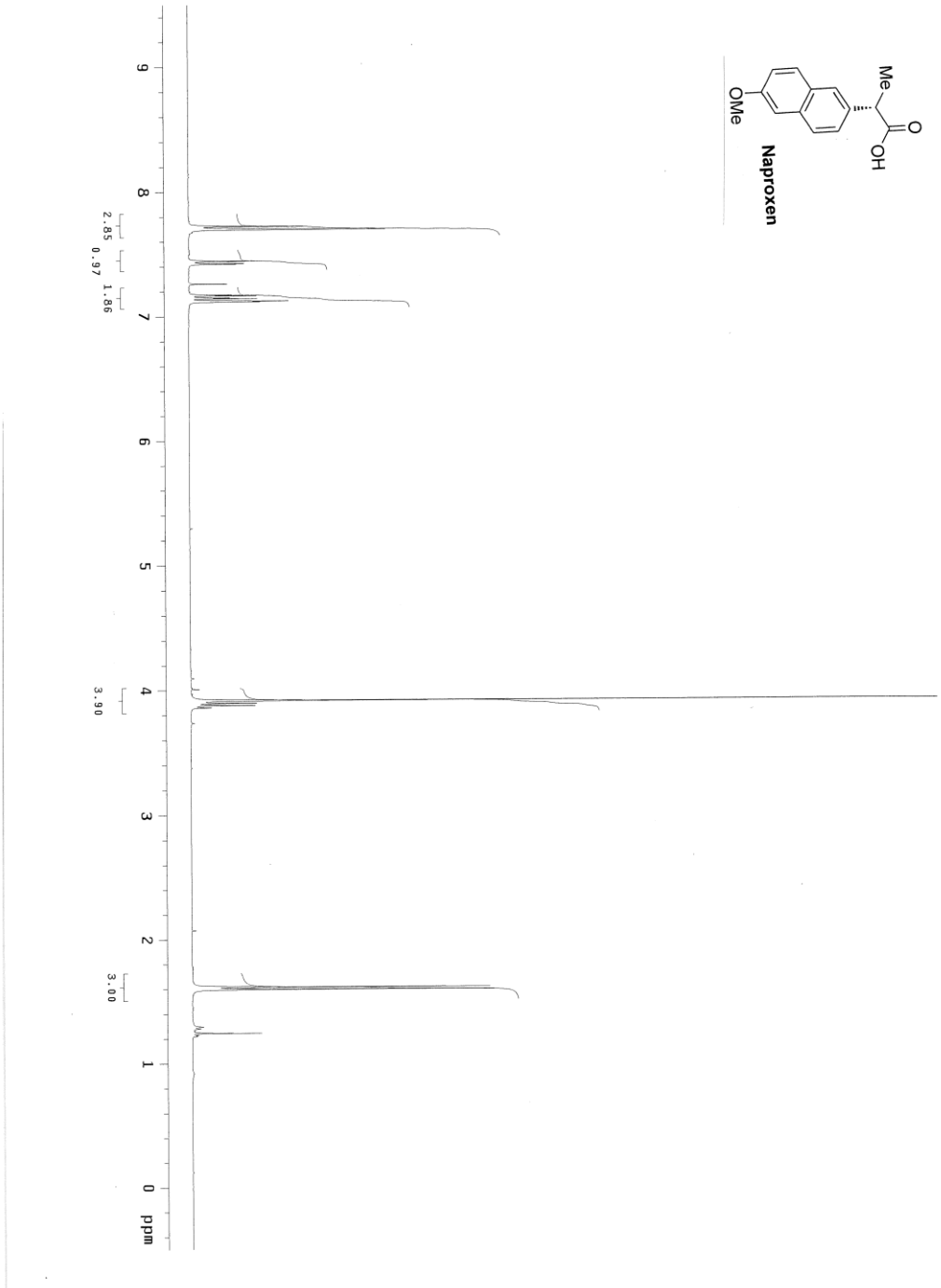
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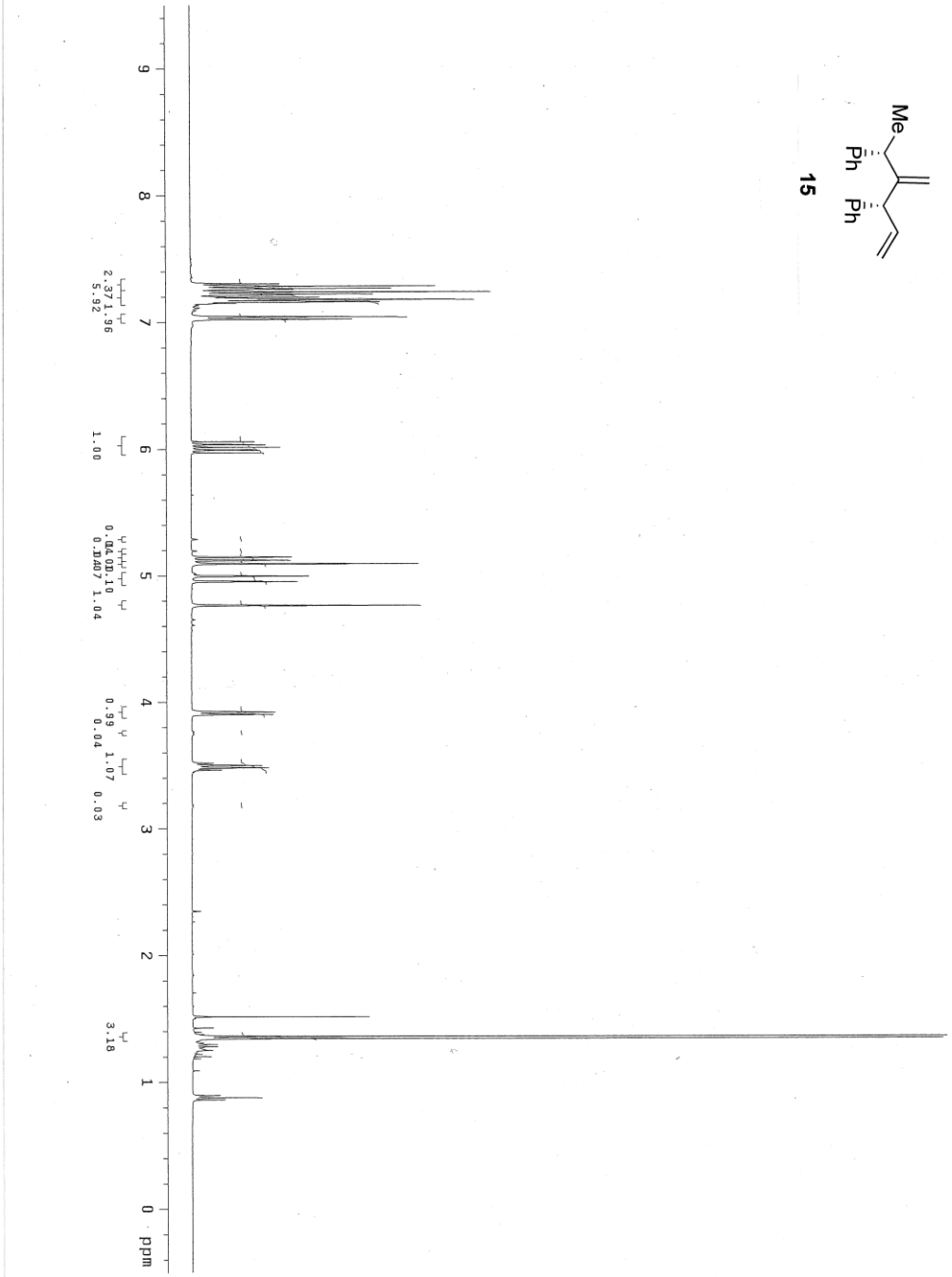
3.90
3.00


Me
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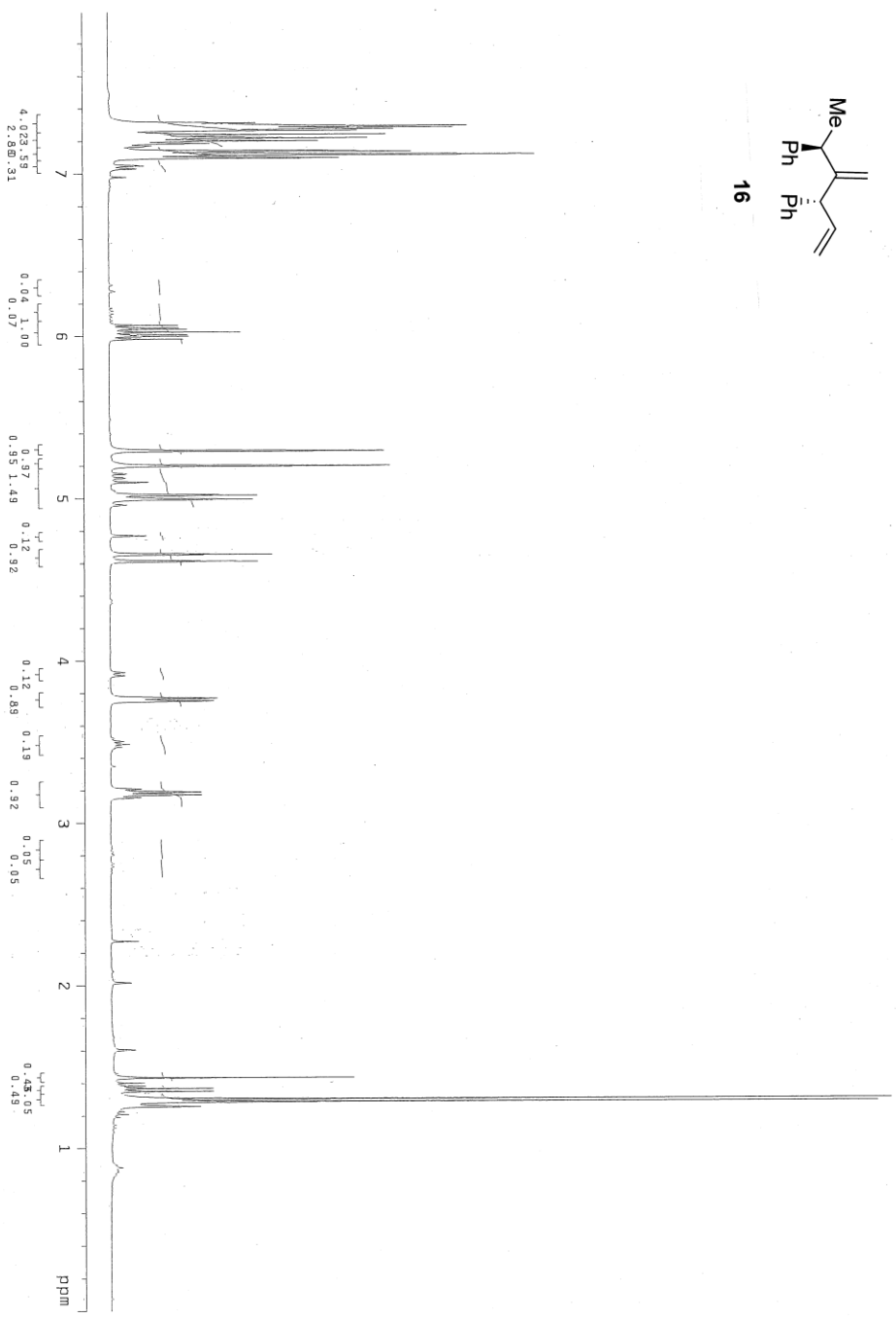
0.99
1.07
0.04
0.03
3.18


Me
Ph
Ph
16
ppm

## *Chapter Five*

# NHC–Cu-Catalyzed Chemoselective Boron–Copper Addition to Monosubstituted Allenes followed by Diastereo- and Enantioselective Additions to Protecting Group-Free Ketoimines: Three-Component, Single-Vessel Catalytic Protocol for 2-B(pin)-Substituted Homoallylic Tertiary Carbamines

### *5.1. Introduction*

Enantiomerically enriched molecules that contain stereogenic carbon center bearing a nitrogen atom are useful intermediates in organic synthesis. Therefore, much attention has been devoted to the development of catalytic enantioselective C–C bond formations by addition of C-based nucleophiles to nitrogen-containing electrophiles.[1] Mannich reactions[2] and allyl addition to imines[3] are two representative methods for

(1) For reviews, see: (a) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407–1438. (b) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069–1094. (c) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853–2873. (d) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. *Chem. Rev.* **2011**, *111*, 2626–2704.
(2) For a review, see: Arend, M.; Westermann, B.; Risch, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 1044–1070.
(3) (a) Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332–3335. For a

building of C–C bond by addition of C-based nucleophiles to C=N bonds. However, protocols for catalytic enantioselective additions to ketoimines have been rarely developed.[4] The differentiation of two substituents on ketoimine may be more difficult (vs aldimines) because of the smaller size difference of them. In addition, since the electrophilicity of a ketoimine is low than a ketone, development of catalytic process with ketoimines would be challenging.

One desirable, but underdeveloped set of transformations would be the addition of allyl groups to ketoimines, which can afford quaternary carbon stereogenic center-bearing homoallylic amines. In 2006, Shibasaki, Kanai, and coworkers reported catalytic enantioselective allyl additions to benzyl-protected ketoimines promoted by chiral bisphosphine–Cu complex.[4l] Two years later, Shibasaki, Kumagai, and coworkers demonstrated Cu-catalyzed additions of allylic cyanides to *N*-phosphinoyl-ketoimines.[4m] Enantioselective additions of functionalized allylic silanes to *N*-tosyl-ketoimines, followed by cyclization, catalyzed by chiral phosphoramidite–Pd catalysts were developed by Trost and coworkers in 2010.[4n] The ketoimines they utilized are protected and activated by benzyl, phosphinoyl, or tosyl group, which needs to be detached

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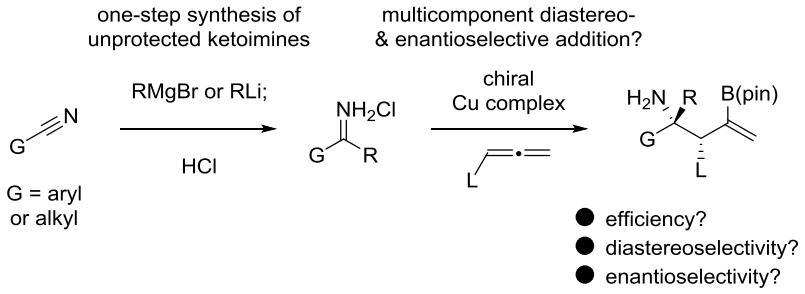
review, see: (b) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774–7854.
(4) For catalytic enantioselective Mannich-type additions to ketoimines, see: (a) Saaby, S.; Nakama, K.; Alstrup Lie, M.; Hazell, R. G.; Jørgensen, K. A. *Chem. Eur. J.* **2003**, *9*, 6145–6154. (b) Zhuang, W.; Saaby, S.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 4476–4478. (c) Suto, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2007**, *129*, 500–501. (d) Du, Y.; Xu, L.-W.; Shimizu, Y.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 16146–16147. (e) Wieland, L. C.; Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 570–576. (f) Lu, G.; Yoshino, T.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4382–4385. (g) Kano, T.; Song, S.; Kubota, Y.; Maruoka, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 1191–1194. (h) Hayashi, M.; Sano, M.; Funahashi, Y.; Nakamura, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 5557–5560. (i) Yin, L.; Takada, H.; Kumagai, N.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 7310–7313. (j) Hayashi, M.; Iwanaga, M.; Shiomi, N.; Nakane, D.; Masuda, H.; Nakamura, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 8411–8415. (k) Nakamura, S.; Yamaji, R.; Hayashi, M. *Chem. –Eur. J.* **2015**, *21*, 9615–9618. For catalytic enantioselective allyl addition to ketoimines, see: (l) Wada, R.; Shibuguchi, T.; Makino, S.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 7687–7691. (m) Yazaki, R.; Nitabaru, T.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 14477–14479. (n) Trost, B. M.; Silverman, S. M. *J. Am. Chem. Soc.* **2010**, *132*, 8238–8240.

afterward. Thus, we are particularly interested in utilization of a protecting group-free ketoimine, which was reported by Zhang's group in their Ir-catalyzed enantioselective hydrogenation of "N–H" ketoimines.[5] In their study, they introduced a novel class of imine, "N–H" ketoimine, which has no protecting group on the nitrogen atom. This type of ketoimine is prepared through a simple process, addition of an organolithium or a Grignard reagent to a nitrile, followed by treatment of MeOH. The transformation of "N–H" ketoimine is very useful because the obtained amine has no protecting group, which allows us to avoid the deprotection step as well as to be able to choose appropriate protecting group for subsequent chemical reactions. For the above reasons, we envisioned the sequence shown in Scheme 5.1. Herein, we have disclosed NHC–Cu-catalyzed diastereo- and enantioselective additions of 2-B(pin)-substituted allyl groups to unprotected ketoimines to afford homoallylic amides containing carbon quaternary stereogenic center and alkenylboron moiety.

***Scheme 5.1.*** Diastereo- and Enantioselective Addition of Allyl Unit to Unprotected Ketoimines

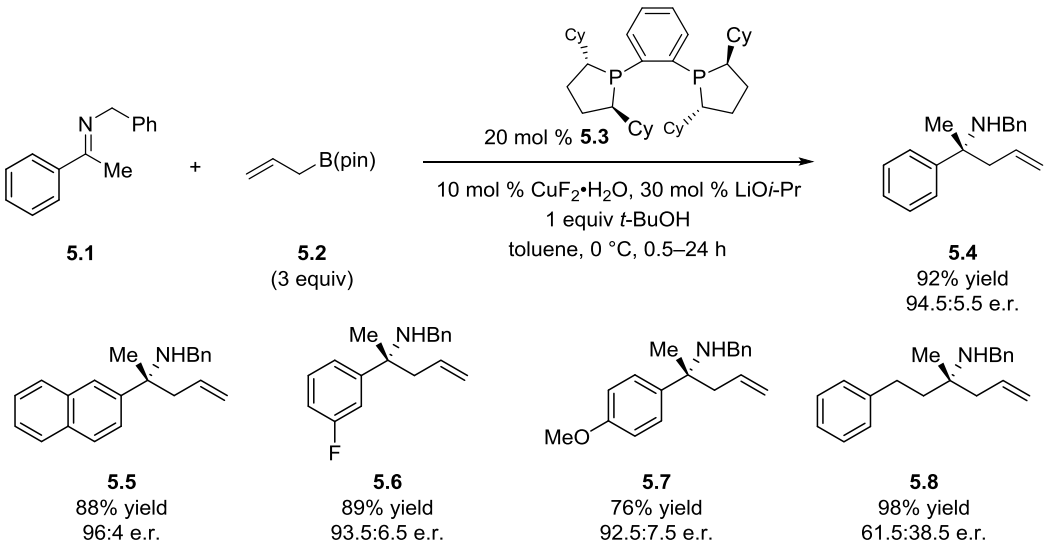



(5) (a) Hou, G.; Gosselin, F.; Li, W.; McWilliams, J. C.; Sun, Y.; Weisel, M.; O'Shea, P. D.; Chen, C.-y.; Davies, I. W.; Zhang, X. *J. Am. Chem. Soc.* **2009**, *131*, 9882–9883. (b) Hou, G.; Tao, R.; Sun, Y.; Zhang, X.; Gosselin, F. *J. Am. Chem. Soc.* **2010**, *132*, 2124–2125. For diastereoselective coupling of unprotected ketoimines prepared by the same method and monosubstituted allenes, catalyzed by bisphosphine–Rh complexes (one enantioselective example shown with selectivity of 84:16 e.r.), see: (c) Tran, D. N.; Cramer, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 8181–8184.

## *5.2. Background*

In this section, we will introduce previously reported catalytic protocols for enantioselective additions of allyl unit to acyclic ketoimines. The pioneering work by Shibasaki, Kanai, and coworkers was disclosed in 2006, which is catalytic enantioselective allyl addition to *N*-benzyl-ketoimines.[6] As illustrated in Scheme 5.2, reaction of acetophenone-derived ketoimine **5.1** with 3 equiv. of allyl–B(pin) **5.2** in the presence of 10 mol % of Cu complex, derived from chiral bisphosphine **5.3** and $CuF_2$ salt, affords homoallylic amide **5.4** in 92% yield with 94.5:5.5 e.r. The level of enantioselectivity for reactions of various aryl-bearing ketoimines is high (92.5:7.5–96:4 e.r. for **5.5**–**5.7**). However, dialkyl-substituted ketoimine was converted to desired homoallylic benzyl amide **5.8** with low enantioselectivity (61.5:38.5 e.r.), mainly due to the difficulty of differentiation of methyl and *n*-alkyl unit on ketoimine.

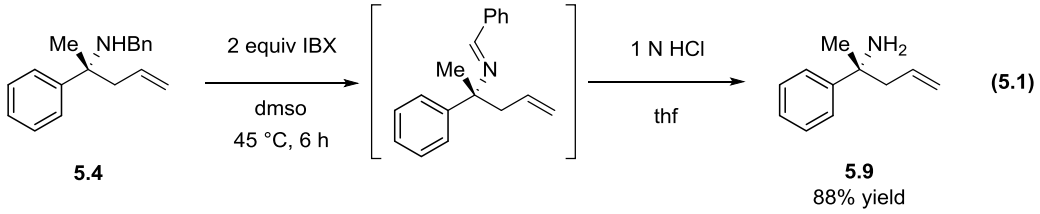
***Scheme 5.2.*** Cu-Catalyzed Enantioselective Allyl Additions to N-Benzyl-Ketoimines




This is the first catalytic enantioselective allyl addition to ketoimines including reasonable substrate scope for methyl ketones bearing various aryl groups with high

(6) Wada, R.; Shibuguchi, T.; Makino, S.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 7687–7691.

eanatioselectivity. There are, however, several limitations. First, two-step sequence of deprotection of a benzyl group is required to achieve homoallylamines. Oxidation of **5.4** by use of 2 equiv. of IBX followed by the treatment of HCl afforded the corresponding homoallylamine **5.9** in 88% yield (2 steps; eq 5.1). In some cases, the removal of a benzyl group might not be effective because a nitrogen atom in **5.4** has actually two different benzyl groups, and differentiation of them would be difficult. In addition, only one example of dialkyl ketoimine is illustrated with moderate enantioselectivity (61.5:38.5 e.r. for **5.8**).

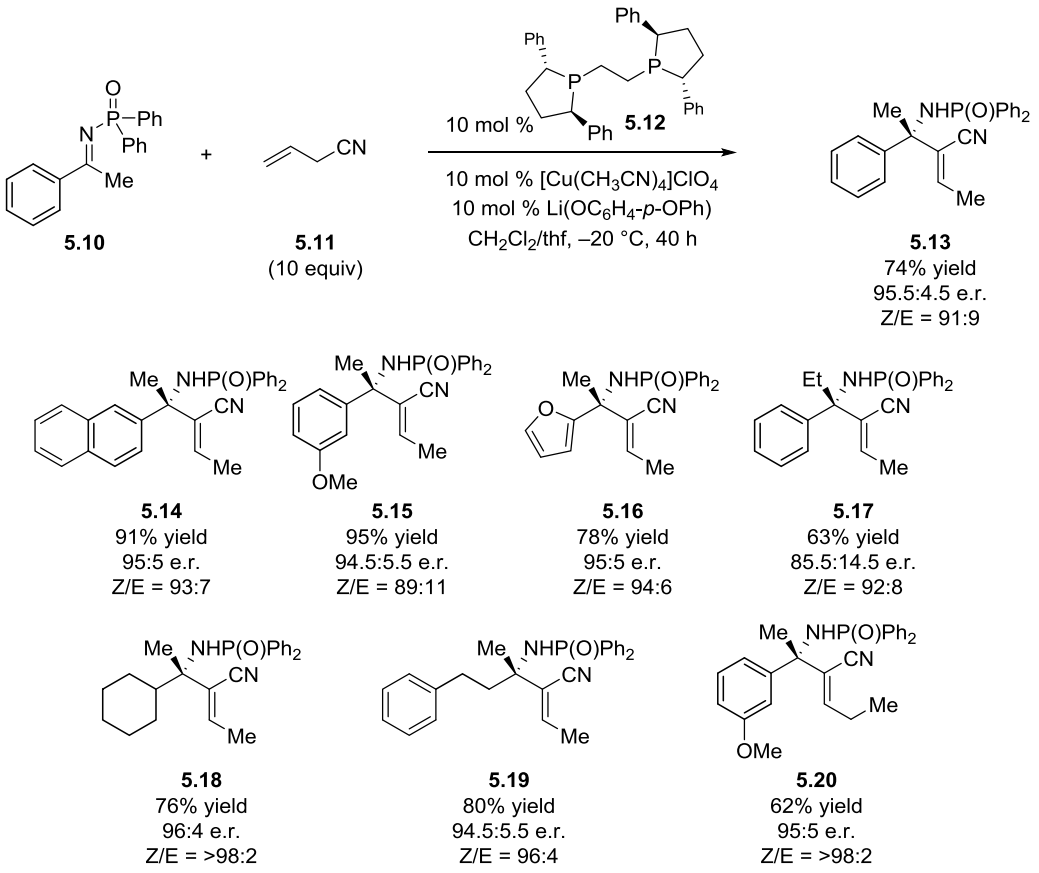



In 2008, Shibasaki, Kumagai, and coworkers developed enantioselective additions of allylic cyanides to *N*-phosphinoyl-ketoimines promoted by bisphosphine–Cu complex.[7] With 10 mol % of $[Cu(CH_3CN)_4]ClO_4$, chiral bisphosphine **5.12**, $Li(OC_6H_4$-*p*-OPh) and 10 equiv. of allylcyanide **5.11**, phosphinoyl ketoimine **5.10** was converted to *α*,*β*-unsaturated cyanide bearing quaternary carbon stereogenic center **5.13** in 74% yield with 95.5:4.5 e.r. and 91% *Z* selectivity (Scheme 5.2). A wide range of *N*-phosphinoyl-ketoimines were utilized, affording *α*-addition followed by isomerization products **5.13**–**5.20** in up to 95% yield with high enantio- and stereoselectivity (85.5:14.5–96:4 e.r. and 89–>98% *Z*). Aryl- and heteroaryl-bearing ketoimines as well as dialkyl ketoimines underwent Cu-catalytic transformation to deliver alkenyl cyanides without diminution of both efficiency and selectivity. When (*E*)-methyl-substituted allylcyanide was used,

(7) Yazaki, R.; Nitabaru, T.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2008**, *130*, 14477–14479.

desired product **5.20** was afforded in 62% yield with high selectivities (95:5 e.r. and >98% *Z*). Although initial product would be homoallylic amide, subsequent isomerization was fast to generate functionalized allylamide (loss of one stereogenic center).

***Scheme 5.3.*** Cu-Catalyzed Enantioselective Additions of Allylic Cyanide to Ketoimines

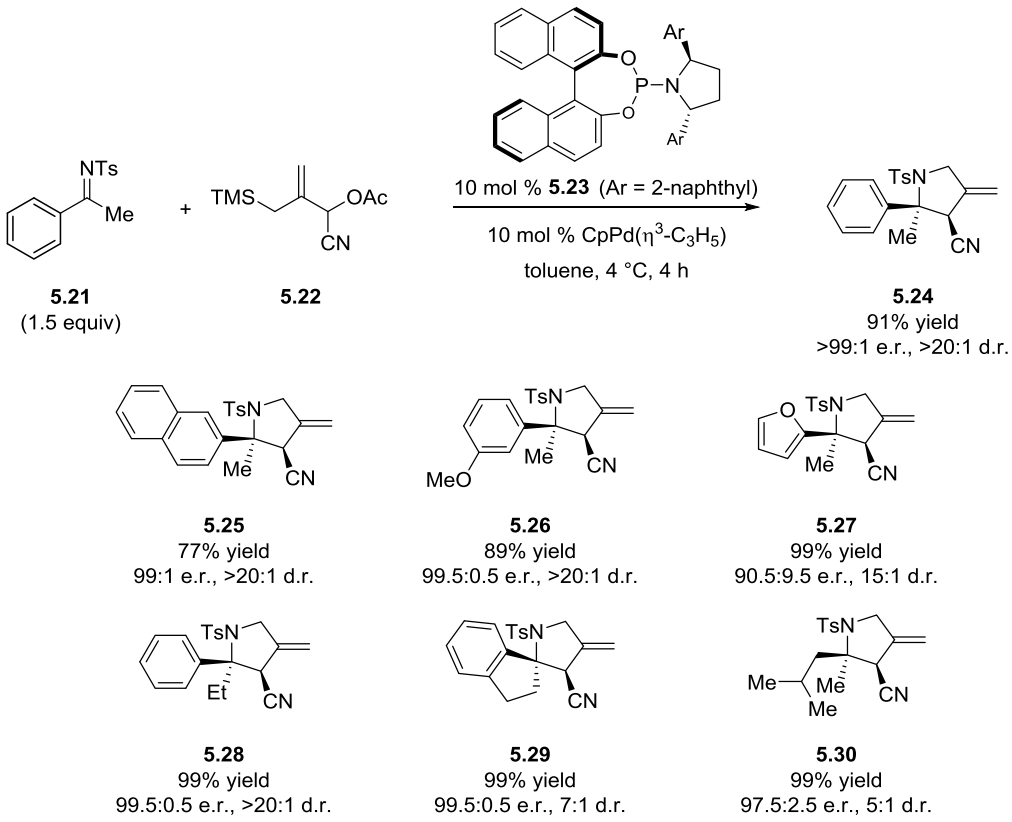



More recently, Trost and coworkers described Pd-catalyzed enantioselective additions of functionalized allylsilanes to *N*-tosyl-ketoimines, followed by cyclization, providing pyrrolidines.[8] As shown in Scheme 5.4, chiral Pd complex derived from phosphoramidite **5.23** promotes cycloaddition type reaction of tosyl-protected ketoimine **5.21** and cyano-trimethylenemethane donor **5.22**, delivering highly substituted pyrrolidine **5.24** in 91% yield and exclusive selectivities (>99:1 e.r. and >20:1 d.r.).

(8) Trost, B. M.; Silverman, S. M. *J. Am. Chem. Soc.* **2010**, *132*, 8238–8240.

Reactions of various ketoimines are examined, including aryl- (**5.25** and **5.26**) and heteroaryl- (**5.27**) bearing methyl ketoimines as well as cyclic- (**5.29**) and dialkyl- (**5.30**) ketoimines, proceed efficiently (77–99% yield) with high enantioselectivity (90.5:9.5–>99:1 e.r.). However, for cyclic and dialkyl ketoimine cases, diastereoselectivity for the present reaction is moderate (5:1 for **5.29** and 7:1 for **5.30**). Moreover, the use of highly activated *N*-tosyl-ketoimine is necessary to achieve high efficiency and selectivity, which arises the difficulty for applying the present approach to the synthesis of complex molecule (deprotection of tosyl unit needs a harsh condition).

***Scheme 5.4.*** Enantioselective Cycloadditions of Trimethylenemethane with Ketoimines




Herein, we have disclosed efficient and highly selective catalytic process for single vessel, multicomponent reaction of monosubstituted allene, unprotected ketoimine, and $B_2(pin)_2$ promoted by chiral NHC–Cu complex, affording a quaternary carbon

stereogenic center-containing homoallylic amine with high diastereo- and enantioselectivity.

## *5.3. Diastereoselective Additions of 2-B(pin)-Substituted Allyl Groups to Unprotected Ketoimines*

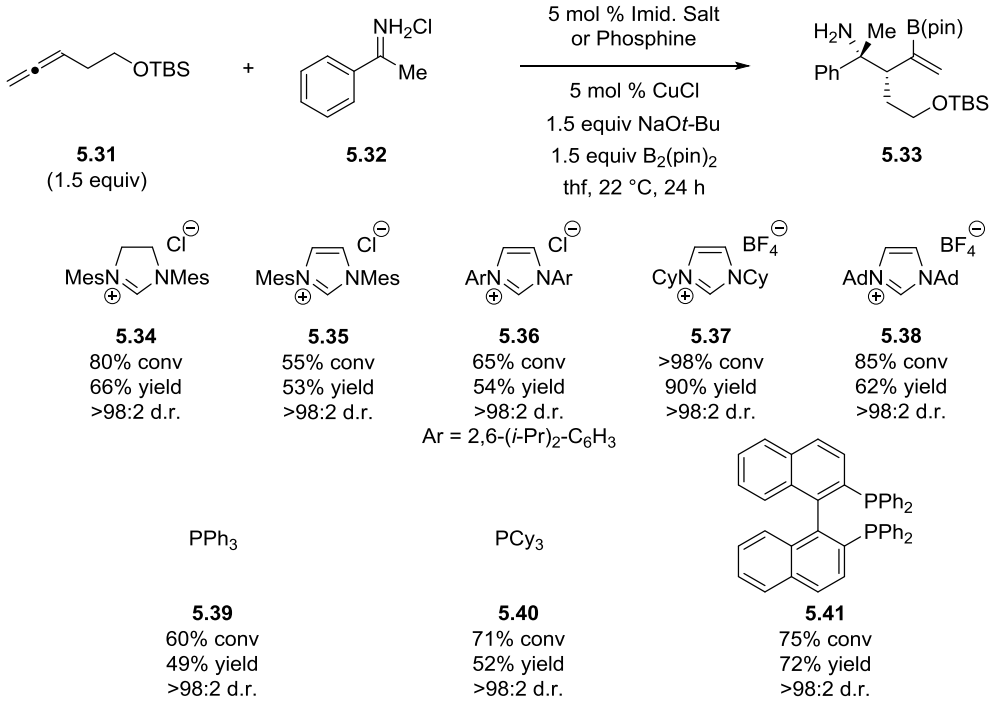
### *5.3.1. Search for Optimal Conditions*

Based on our previous report about the diastereo-, and enantioselective additions of 2-B(pin)-substituted allylcopper to carbonyls,[9] we began our investigation involving a monosubstituted allene **5.31**, $B_2(pin)_2$, and the ketoimine **5.32**, which was prepared from the reaction of benzonitrile with MeLi followed by the treatment of HCl solution.[5] As illustrated in Scheme 5.5, we have examined various imidazolinium (**5.34**) and imidazolium salts (**5.35**–**5.38**) as NHC ligand precursors as well as phosphine ligands (**5.39**–**5.41**). Interestingly, complete diastereoselectivity was observed regardless of the ligand we used (>98:2 d.r.), but diverse level of efficiency was obtained. With *N*-mesityl-bearing NHCs, moderate yields are observed (66% for **5.34** and 53% for **5.35**), and with sterically more demanding imidazolium **5.36** proceeded to similar level of efficiency as well (54% yield). Reaction with 5 mol % *N*-cyclohexyl-containing imidazolium salt **5.37** as an NHC precursor was performed, leading to the desired product **5.33** most efficiently (>98% conversion and 90% yield). Additionally, three representative phosphine ligands were evaluated, none of which proceeded with high level of efficiency (49–72% yield for **5.39**–**5.41**), but with perfect diastereoselectivity (>98:2 d.r.). Based on above

(9) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046–5051.

observations, we chose the imidazolium salt **5.37** as an optimal NHC precursor for further study.

***Scheme 5.5.*** Evaluation of NHC–Cu and Phosphine–Cu Complexes

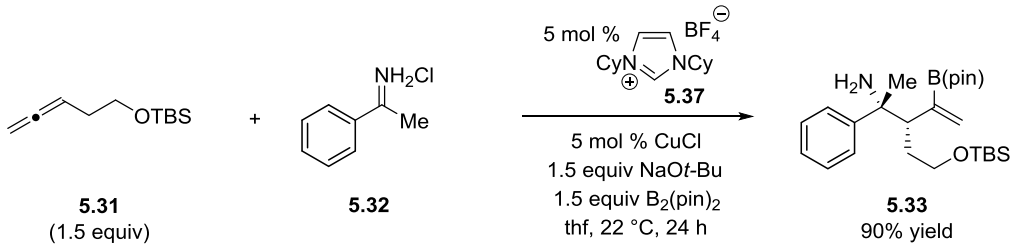



### *5.3.2. Substrate Scope of Diastereoselective Cu–B Addition/Allyl Addition to Unprotected Ketoimines*

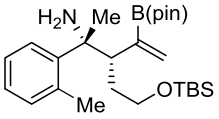
With an optimal condition (Section 5.3.1) we have evaluated the substrate scope of diastereoselective copper–boron addition to monosubstituted allene followed by addition to unprotected ketoimine. As illustrated in Scheme 5.6, a wide range of ketoimines, prepared through reaction of various nitriles with alkyllithium reagent, are examined, affording desired products in up to 94% yield. It is worth to mention that exclusive diastereoseletivity was observed for all substrates we investigated (>98:2 d.r.). Reactions of 1.5 equiv. of monosubstituted allene **5.31** and aryl-bearing methyl ketoimine in the presence of 5–10 mol % of NHC–Cu complex derived from imidazolium salt **5.37**

and CuCl, proceed to quaternary stereogenic center-containing alkenylboron **5.33** and **5.42**–**5.52** with moderate to high efficiently (57–90% yield). Heteroaryl-substituted methyl ketoimines are converted to desired products **5.53**–**5.55** in 41–49% yield, probably because of instability of alkenylboron products (see below). When dialkyl ketoimines are subjected to the catalytic process, 10 mol % of Cu complex is required for high yields of products **5.56** and **5.57** (76% and 56% yield, respectively). In addition, monosubstituted allenes bearing a different alkyl group are utilized, delivering alkenylboron products **5.59**–**5.61** efficiently (68–78% yield).

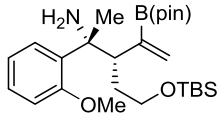
***Scheme 5.6.*** Substrate Scope of Catalytic Diastereoselective Process[a]



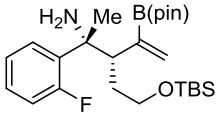

**5.31** (1.5 equiv) + **5.32** → **5.33** 90% yield



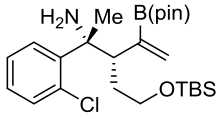

**5.42** (7.5 mol %) 57% yield



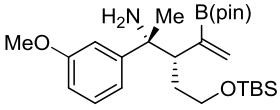

**5.43** (10 mol %) 89% yield



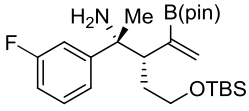

**5.44** (5 mol %) 63% yield



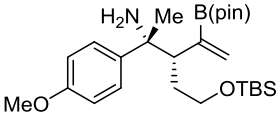

**5.45** (5 mol %) 82% yield



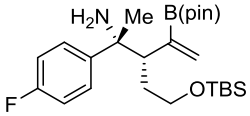

**5.46** (7.5 mol %) 59% yield



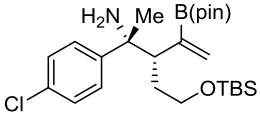

**5.47** (7.5 mol %) 63% yield



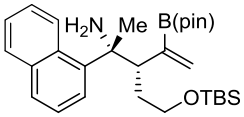

**5.48** (5 mol %) 77% yield



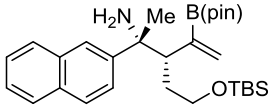

**5.49** (5 mol %) 68% yield



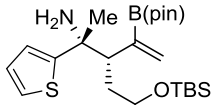

**5.50** (7.5 mol %) 72% yield



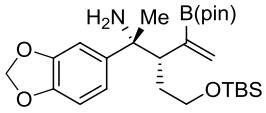

**5.51** (10 mol %) 90% yield



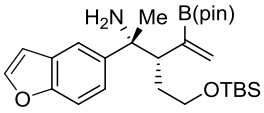

**5.52** (5 mol %) 75% yield



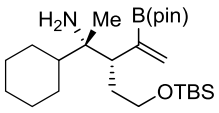

**5.53** (7.5 mol %) 41% yield



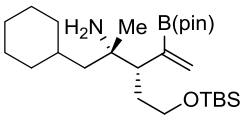

**5.54** (10 mol %) 49% yield



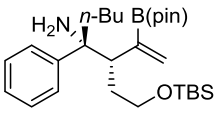

**5.55** (10 mol %) 48% yield



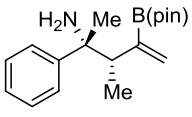

**5.56** (10 mol %) 76% yield



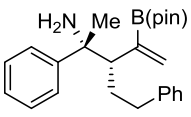

**5.57** (10 mol %) 56% yield



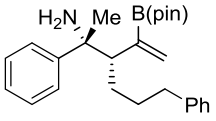

**5.58** (10 mol %) 94% yield




**5.59** (5 mol %) 78% yield




**5.60** (5 mol %) 68% yield



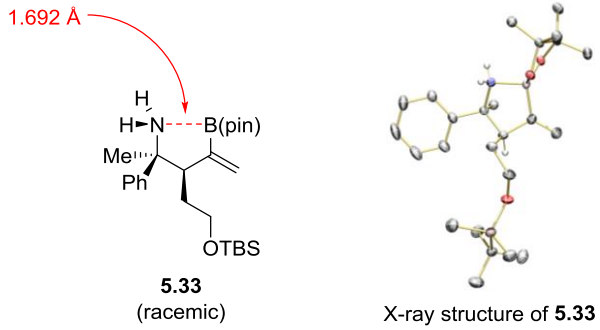

**5.61** (5 mol %) 74% yield

[a] >98:2 d.r. for all cases

### *5.3.3. Stereochemical Models to Account for Levels in Diastereoselectivity*

The relative stereochemical identity of alkenylboron product **5.33** (racemic) was established by the X-ray crystallography (Figure 5.1). Based on the X-ray structure of **5.33**, it seems that there is an association between the boron and the nitrogen atoms; the distance of which in the X-ray structure is 1.692 Å. In addition, we obtained a signal at δ 22.11 ppm in the $^{11}$B NMR spectrum of **5.33**, relatively upfield signal compare to δ 29.4 ppm in the $^{11}$B NMR spectrum of vinyl–B(pin), which supports the aforementioned hypothesis of an association between B and N atoms. This association might be caused by the coordination of electron lone pair on nitrogen atom to partially empty p orbital on boron atom,[10] which would weaken a carbon–boron bond. For this reason, the latter bond is relatively sensitive to hydrolysis during silica gel column chromatography, leading relatively low yields of the organoboron products in some cases (e.g., **5.54** and **5.55**; Scheme 5.6).

***Figure 5.1.*** Stereochemical Identity of Alkenylboron Product




**5.33**
(racemic)

X-ray structure of **5.33**

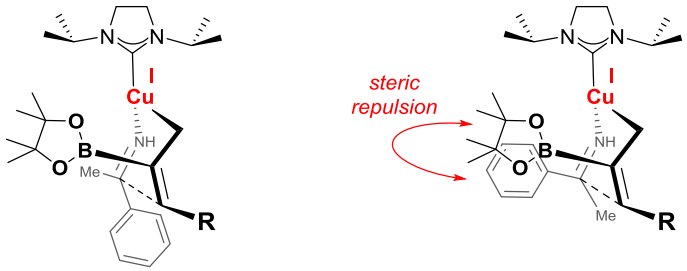
$^{11}$B NMR = δ 22.11 ppm [cf. δ 29.4 ppm for vinyl–B(pin)]

Another interesting aspect of the X-ray structure of **5.33** is that the C–N bond and the C–$(CH_2)_2$OTBS bond are *syn* relationship to each other. Based on DFT calculation for

(10) For detailed analysis and discussions regarding the impact of coordination of a Lewis basic group to the boron atom of a B(pin) moiety, see: Wu, H.; Garcia, J. M.; Haeffner, F.; Radomkit, S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2015**, *137*, 10585–10602.

possible stereochemical models (Figure 5.2), the pathway through mode I, which provides major *syn* diastereomer, is 3.7 kcal/mol lower than one through mode II, which leads to minor *anti* isomer. The energy difference between two modes is due to severe steric repulsion between a B(pin) and a phenyl groups, both of which are pointing axial direction, on mode II. In the favored mode I, a phenyl unit is located on equatorial position, which releases the repulsion in mode II. Since the selectivity is controlled by the interaction between two units on substrates, not between substrate and ligand, complete diastereoselectivity was obtained regardless of the ligand structure (Scheme 5.5).

***Figure 5.2.*** Stereochemical Models with Achiral NHC Ligand




*DFT calculations (M06/Def2TZVPP with solvation in thf)*

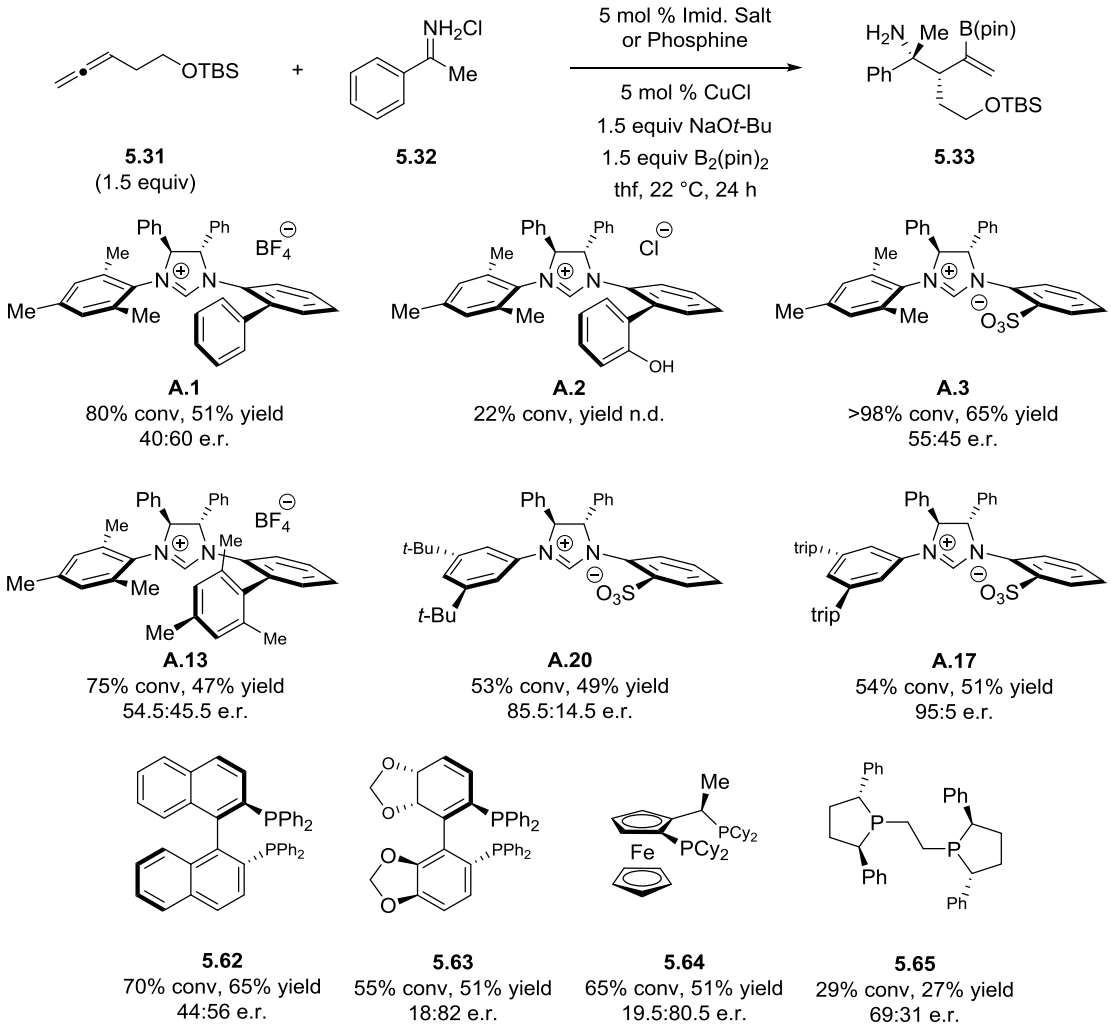
## *5.4. Diastereo- and Enantioselective Additions of 2-B(pin)-Substituted Allyl Groups to Unprotected Ketoimines*

### *5.4.1. Study of Chiral Cu Complexes*

To find a chiral Cu complex, promoting reaction of monosubstituted allene, $B_2(pin)_2$, and unprotected ketoimine to afford diastereo- and enantiomerically enriched quaternary carbon stereogenic center bearing a nitrogen atom, several NHC–Cu and phosphine–Cu complexes have been screened. As depicted in Scheme 5.7, reaction of

**5.31** with phenyl,methyl-ketoimine **5.32** in the presence of monodentate NHC–Cu complex derived from **A.1** proceeded with low enantioselectivity (40:60 e.r.). With sterically more congested monodentate NHC–Cu complex generated from **A.13**, alkenylboron product **5.33** was obtained as almost racemic mixture (54.5:45.5 e.r.). The reaction became sluggish when phenol-bearing **A.2** was utilized (22% conversion). Then, we turned to probe a number of sulfonate-bridged NHC–Cu complexes. *N*-mesityl-substituted **A.3** promoted multicomponent reaction efficiently, but with minimal enantioselectivity (>98% conv and 55:45 e.r.). However, when we altered the mesityl unit to 3,5-(*t*-Bu)$_2$-phenyl group, there was a significant enhancement of enantioselectivity (85.5:14.5 e.r. for **A.20**). For further improvement of selectivity, we replaced 3,5-substituents from *t*-Bu group to sterically more demanding, 2,4,6-triisopropylphenyl moiety, and obtained 95:5 e.r. (**A.17**). Several representative bisphosphine–Cu complexes were investigated as well. As shown in Scheme 5.7, reasonably high level of enantioselectivity was achieved with segphos **5.63** or josiphos **5.64** (18:82 and 19.5:80.5 e.r., respectively). Remarkable point is that, in all cases, we obtained the product **5.33** as a single *syn* diastereomer (>98:2 d.r.). Based on the screening of chiral Cu complexes, we identified the sulfonate-bearing **A.17** as an optimal NHC precursor.

***Scheme 5.7.*** Study of Chiral NHC–Cu and Phosphine–Cu Complexes[a]



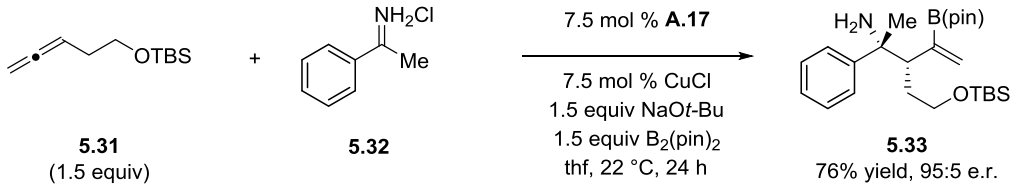

[a] >98:2 d.r. for all cases

### *5.4.2. Substrate Scope of Diastereo- and Enantioselective Cu–B Addition/Allyl Addition to Unprotected Ketoimines*

The catalytic process, promoted by NHC–Cu complex generated from **A.17**, has a considerable substrate scope. We examined various substrates, which were utilized in Scheme 5.6 (the catalytic process with achiral Cu complex derived from **5.37**). One thing we have to mention again is that complete diastereoselectivity was observed for all cases. Substantially high enantioselectivity was achieved with ketoimines containing an *ortho*

substituent-bearing phenyl unit (98.5:1.5–99.5:0.5 e.r. for **5.42**, **5.43**, and **5.45**; Scheme 5.8). However, with 2-F-phenyl-bearing ketoimine, the catalytic reaction was much less selective and lower yielding (66:34 e.r. and 30% yield for **5.44**), one possible explanation of which is that there might be an association between a fluorine atom and the Cu center. When the F atom is placed in *meta* or *para* position on phenyl ring, the distance of a fluorine and the Cu center would be too far to have an association with each other. For the above reason, in cases of **5.47** and **5.49**, the level of enantioselectivity was much higher (93.5:6.5 and 94.5:5.5 e.r., respectively vs 66:34 e.r. for **5.44**). Reactions of heteroaryl-bearing ketoimine were lower yielding although enantioselectivity was high (42–60% yield and 94.5:5.5–96.5:3.5 e.r. for **5.53**–**5.55**). Some of the alkenylboron products might be hydrolyzed during the silica gel chromatography due to the possible association between N and B atoms, which can facilitate hydrolysis. Dialkyl ketoimines were also examined, delivering desired products **5.56** and **5.57** with moderate efficiency (38–48% yield). For this class of ketoimines, the enamine formation might become competitive. Several different alkyl-bearing allenes were utilized for the multicomponent process with $B_2(pin)_2$ and acetophenone-derived ketoimine, leading to alkenylboron compounds containing a quaternary stereogenic center **5.59**–**5.61** with high selectivity (up to >99:1 e.r.). The level of enantioselectivity was similar with either shorter alkyl chain-bearing (5.59) or longer chain-containing allenes, which means that the steric interaction between the substituent of allene and NHC ligand might not play an important role in the stereochemistry-determining step.

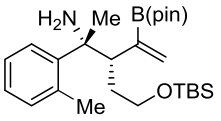
***Scheme 5.8.*** Substrate Scope of Catalytic Diastereo- and Enantioselective Process[a]



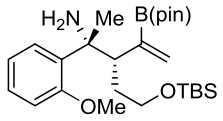

**5.31** (1.5 equiv)

**5.32**

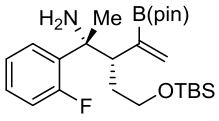
**5.33**
76% yield, 95:5 e.r.



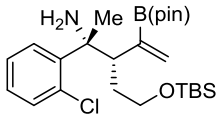
**5.42**
(7.5 mol %)
59% yield, 99.5:0.5 e.r.



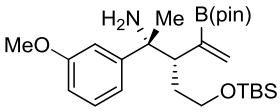
**5.43**
(10 mol %)
95% yield, 98.5:1.5 e.r.



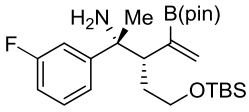
**5.44**
(7.5 mol %)
30% yield, 66:34 e.r.



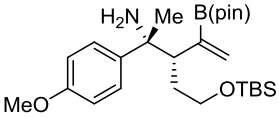
**5.45**
(7.5 mol %)
91% yield, 99.5:0.5 e.r.



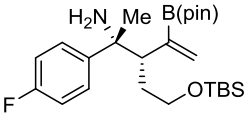
**5.46**
(7.5 mol %)
57% yield, 98.5:1.5 e.r.



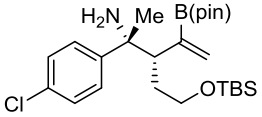
**5.47**
(7.5 mol %)
64% yield, 93.5:6.5 e.r.



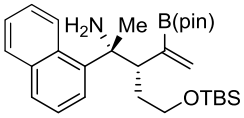
**5.48**
(7.5 mol %)
39% yield, 92.5:7.5 e.r.



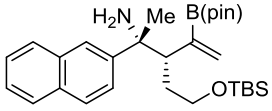
**5.49**
(7.5 mol %)
71% yield, 94.5:5.5 e.r.



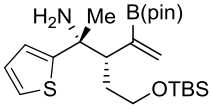
**5.50**
(7.5 mol %)
56% yield, 92:8 e.r.



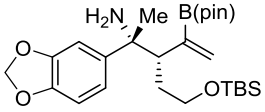
**5.51**
(10 mol %)
66% yield, 98.5:1.5 e.r.



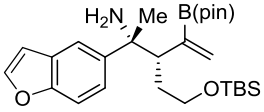
**5.52**
(7.5 mol %)
81% yield, 94:6 e.r.



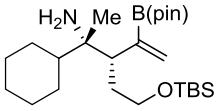
**5.53**
(7.5 mol %)
49% yield, 96.5:3.5 e.r.



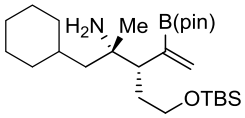
**5.54**
(10 mol %)
42% yield, 94.5:5.5 e.r.



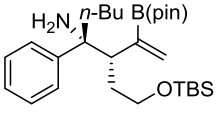
**5.55**
(10 mol %)
60% yield, 94.5:5.5 e.r.



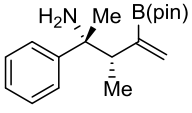
**5.56**
(10 mol %)
48% yield, 95:5 e.r.



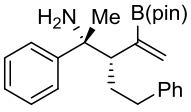
**5.57**
(10 mol %)
38% yield, 91:9 e.r.



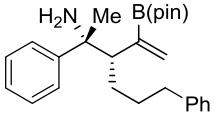
**5.58**
(10 mol %)
94% yield, 88:12 e.r.



**5.59**
(5 mol %)
78% yield, 96:4 e.r.



**5.60**
(5 mol %)
41% yield, 97:3 e.r.



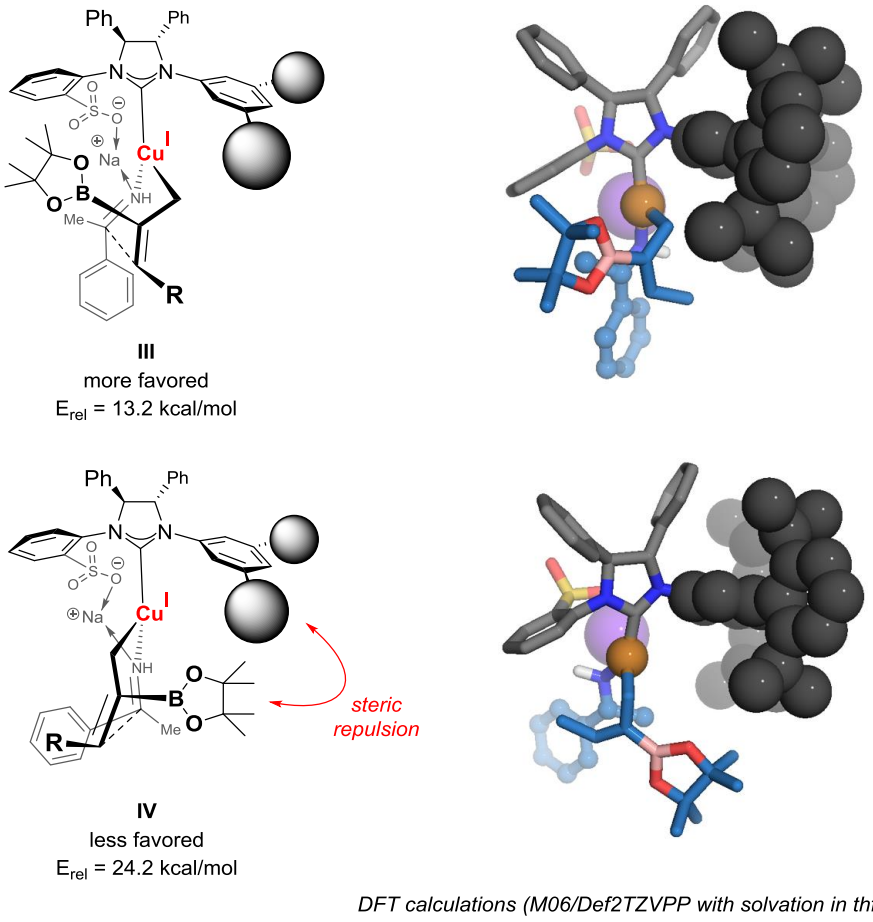
**5.61**
(5 mol %)
41% yield, >99:1 e.r.

[a] >98:2 d.r. for all cases

### *5.4.3. Stereochemical Models to Account for Levels in Enantioselectivity*

We have tried to build up stereochemical models by DFT calculation, to account for high selectivities (Figure 5.3). The relative energy level of the transition state mode III, which delivers the major enantiomer, is much lower than that of mode IV (13.2 vs 24.2 kcal/mol). Based on the proposed stereochemical models, there is a severe steric repulsion between the bulky substituent on *N*-aryl unit of NHC ((*i*-Pr)$_3$C$_6$H$_2$) and a B(pin) moiety in mode IV (Figure 5.3), which makes mode IV less favored. In addition, in both modes III and IV, sodium cation-bridge between a sulfonate unit and a nitrogen atom on ketoimine is significant for formation of organized, chair-like transition state, which might be one of the reasons why sulfonate-bearing NHC–Cu complexes **A.20** and **A.17** showed dramatic boost in enantioselectivity (Scheme 5.7). In addition, as we expected above, the steric repulsion between *N*-aryl group and the substituent of allene (R) is not severe for both modes III and IV, so it cannot play a significant role to determine the face selectivity. This is consistent with the observation above (high enantioselectivities for **5.59**–**5.61**).

***Figure 5.3.*** Stereochemical Models with Chiral, Sulfonate-Based NHC Ligand



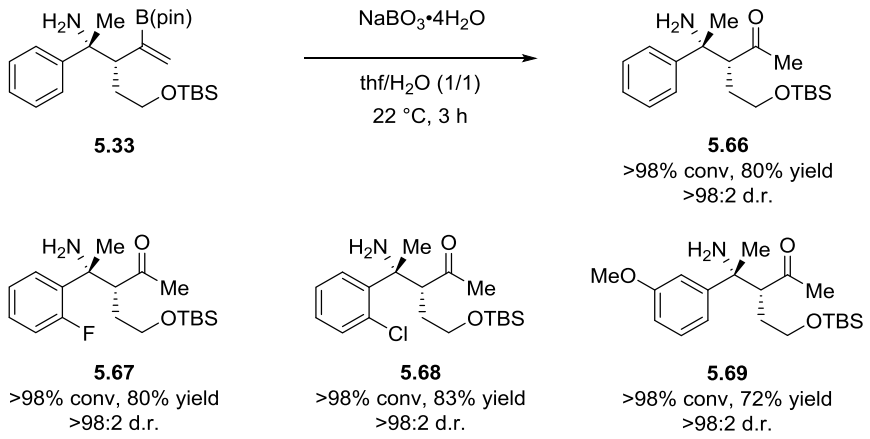

*DFT calculations (M06/Def2TZVPP with solvation in thf)*

### *5.4.4. Functionalization and Utility in Chemical Synthesis*

The utility of the aforementioned catalytic method is illustrated by transformations to *β*-amino methyl ketones or allyl addition product, and an application toward the synthesis of a medicinally active agent. Simple sodium perborate-mediated oxidation of alkenylboron compound **5.33** provided methyl ketone containing *β*-amine unit **5.66**, which is identical to Mannich reaction product, in 80% yield without diminution of enantiomeric enrichment (Scheme 5.9). Three more *β*-amino methyl ketones **5.67**–**5.69** are afforded as illustrated in Scheme 5.9, which contain *ortho*-

halogen- or *meta*-methoxy-bearing phenyl unit. Considerable yields of products **5.67**–**5.69** are obtained (72–83% yield).

***Scheme 5.9.*** Synthesis of *β*-Amino Carbonyl Compounds




**5.33**

**5.66**
>98% conv, 80% yield
>98:2 d.r.

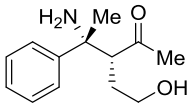
**5.67**
>98% conv, 80% yield
>98:2 d.r.

**5.68**
>98% conv, 83% yield
>98:2 d.r.

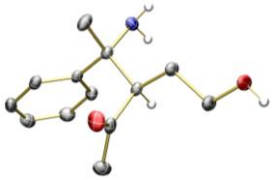
**5.69**
>98% conv, 72% yield
>98:2 d.r.

Next, we have made efforts on the determination of the absolute and relative configuration of the alkenylboron product. Unfortunately, we failed to obtain pure crystal structure of enantiomerically enriched alkenylborons, which lead us to synthesize derivatives of them (only X-ray structure of *racemic* sample of alkenylboron **5.33** was obtained; Figure 5.1). Enantiomerically enriched alkenylboron **5.33** (95:5 e.r.) is oxidized to **5.66** with sodium perborate efficiently (80% yield) as illustrated in Scheme 5.9. Subsequent desilylation by tetra-*n*-butylammonium fluoride delivers primary alcohol-bearing methyl ketone **5.70**, X-ray structure of which is shown in Figure 5.4. Based on this X-ray structure, we confirmed the absolute stereochemistry for two continuative stereogenic centers (*R* configuration for both centers), the relative stereochemistry for which matches with that in X-ray structure of from *rac*-**5.33** (*syn* diastereomer; Figure 5.1).

***Figure 5.4.*** X-ray Structure for Stereochemistry Proof

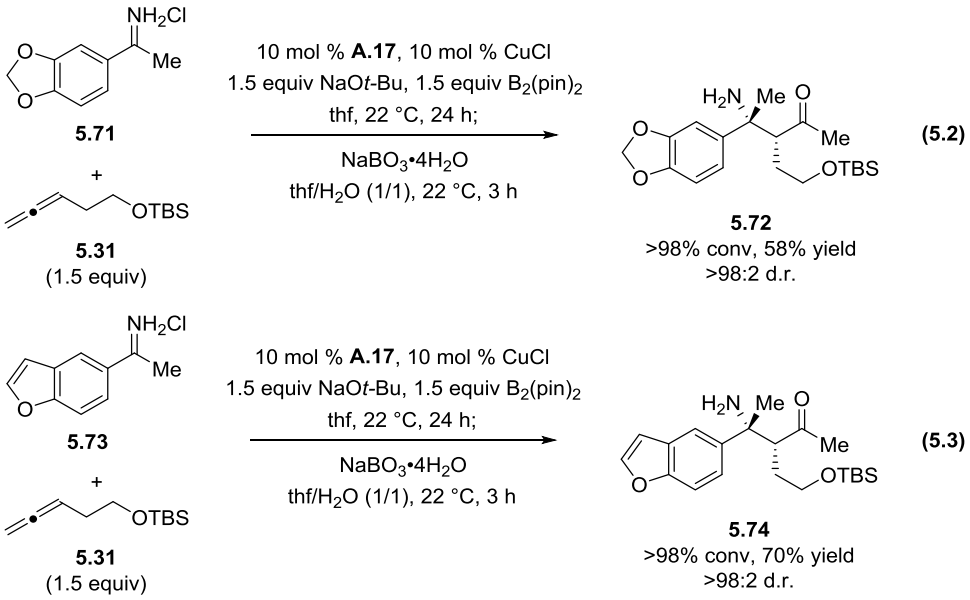



**5.70**

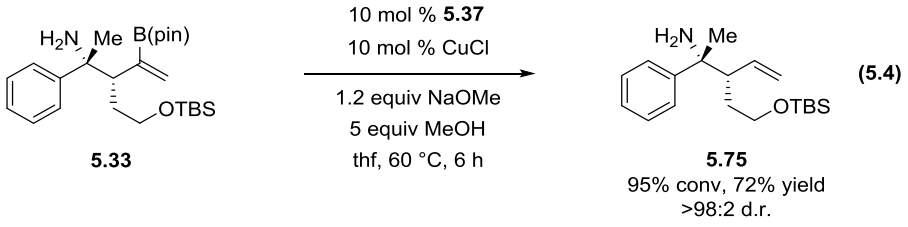


X-ray structure of **5.70**

As we mentioned above, in some cases, the product of catalytic process, alkenylboron compound, might not be stable enough to be purified by silica gel chromatography. Especially, when we utilized heteroaryl-substituted ketoimines, relatively lower yields were observed (e.g., 42% yield for **5.54** and 60% yield for **5.55**; Scheme 5.8). To address this issue, as illustrated in eqs 5.2 and 5.3, we performed Cu-catalyzed multicomponent reaction of allene **5.31** and ketoimine **5.71** or **5.73** in the presence of 10 mol % of chiral imidazolinium salt **A.17**, and directly utilized the alkenylboron product without the purification step for the subsequent oxidation with sodium perborate. We isolated *β*-amino methyl ketones **5.72** and **5.74** by silica gel column chromatography in 58% and 70% yield, respectively. Noticeably, although we performed an additional oxidation reaction, higher yields of methyl ketone products were obtained compare to those of alkenylboron products (58% for **5.72** vs 42% for **5.54** and 70% for **5.74** vs 60% for **5.55**).




Cu-catalyzed protodeboration of the alkenylboron **5.33**, promoted by 10 mol % Cu complex derived from achiral imidazolium salt **5.37**, delivers homoallylic amine **5.75** in 72% yield, which is identical to product of allyl addition to ketoimine (eq 5.4). Although protodeboration reaction was performed at 60 °C in six hours, no epimerization was observed (>98:2 d.r.).




Then, we have investigated the synthesis of biologically active molecule to further demonstrate the utility of the aforementioned protocol. BMS research group synthesized a series of the compounds containing tertiary carbamine, which were related to inhibitors of *β*-amyloid peptide (A*β*) production.[11] They obtained an enantiomerically enriched product from the racemic mixture by the use of chiral HPLC. We tested to utilize the

(11) Thompson, III, L. A. et al. Compounds for the reduction of beta-amyloid production. United States Patent US 2013/0131051 Al

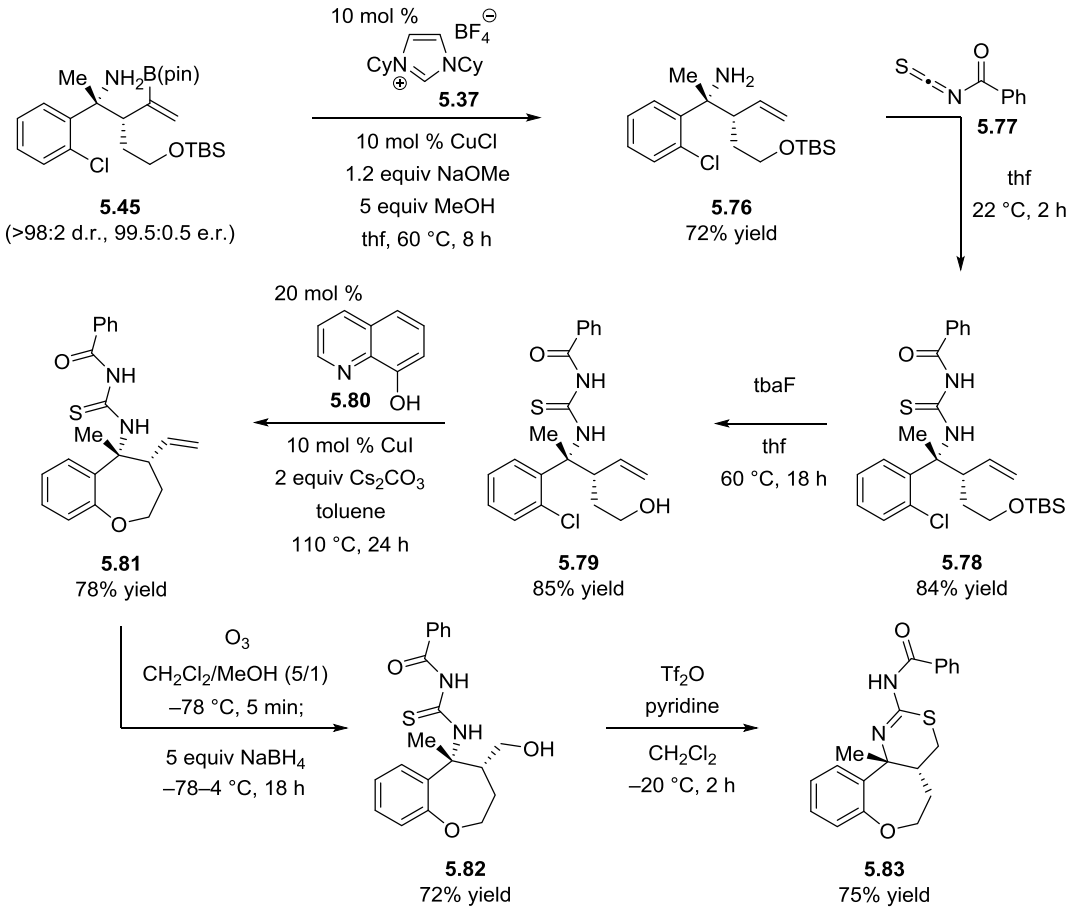
single-vessel, multicomponent process for the generation of the core structure of the target molecule. To construct the quaternary carbon stereogenic center bearing a nitrogen atom, we utilize the present NHC–Cu-catalyzed transformation of monosubstituted allene with *ortho*-chloro-phenyl ketoimine, which affords alkenylboron compound **5.45** in 91% yield with >98:2 d.r. and 99.5:0.5 e.r. (Scheme 5.8). As illustrated in Scheme 5.10, Cu-catalyzed protodeboration of **5.45** is examined in the presence of 10 mol % of NHC–Cu complex derived from imidazolium salt **5.37**, delivering homoallylic amine **5.76** in 72% yield at 60 °C after eight hours. Since the product **5.76** has no protecting group on a nitrogen atom, deprotection step is not necessary, and directly used for the next transformation. With 2 equiv. of commercially available isothiocyanate **5.77**, thiourea **5.78** is successfully generated in 84% yield from unprotected homoallylic amine **5.76**. Subsequent desilylation of silyl ether **5.78** is performed with 2 equiv. of tetra-*n*-butylammonium fluoride at elevated temperature (60 °C), providing primary alcohol **5.79** in 85% yield.

The next step was the challenging transformation to form seven-membered ether through an intramolecular cross-coupling of aryl chloride with alcohol moiety on compound **5.79**. First, we investigated the phoshpine–Pd-catalyzed etherification reaction developed by Buchwald and coworkers in 2000.[12] With 3 mol % Pd complex derived from *rac*-trixiephos **5.84** and $Pd(OAc)_2$, desired aryl ether **5.81** was isolated in 68% yield after purification by silica gel chromatography (eq 5.5). The reaction was clean, and we did not detect a significant amount of any byproducts. At the same time, we also probed Cu-catalyzed Ullmann-type intramolecular coupling, which was reported by Xu, Hu, and

(12) Torraca, K. E.; Kuwabe, S. -I.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12907–12908.

coworkers in 2009.[13] Cu-catalytic cyclization of **5.79** was performed in the presence of 10 mol % CuI, 20 mol % 8-hydroxyquinoline **5.80** as a ligand, and 2 equiv. of $Cs_2CO_3$, furnishing 78% yield of seven-membered ether **5.81** (Scheme 5.10). Since copper (I) salt is much more abundant and cheap metal, the strategy for utilizing Ullmann coupling seems more attractive method for the medicinally active molecule synthesis.

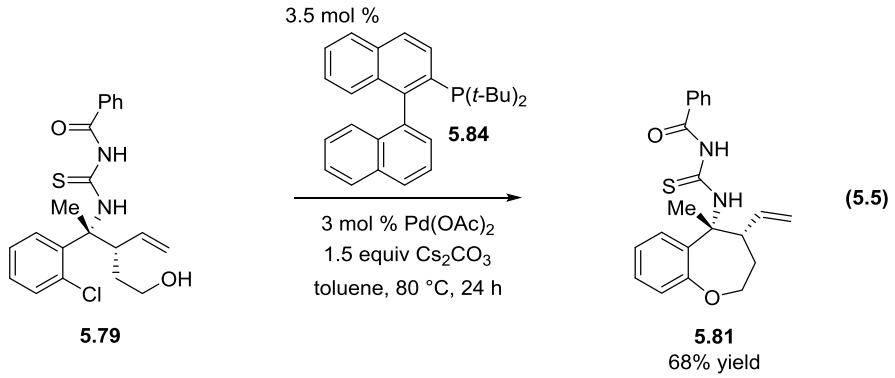
***Scheme 5.10.*** Application to Synthesis of a Medicinally Active Agent (Alzheimer)




Conversion of a terminal olefin **5.81** to a primary alcohol **5.82** was proceeded by ozonolysis followed by $NaBH_4$-mediated reduction sequence. After careful study of aforementioned sequential procedure, we obtain the desired primary alcohol **5.82** in 72% yield without decomposition of a thiourea moiety. Then, the target compound **5.83** was

(13) Niu, J.; Guo, P.; Kang, J.; Li, Z.; Xu, J.; Hu, S. *J. Org. Chem.* **2009**, *74*, 5075–5078.

obtained through cyclization of **5.82** by activation of the primary alcohol with triflic anhydride (75% yield).[14]




## *5.5. Conclusions*

We have described the Cu-catalyzed protocol for multicomponent reaction involving a monosubstituted allene, $B_2(pin)_2$, and unprotected ketoimine, promoted by chiral NHC–Cu complex. The practical and efficient preparation of unprotected ketoimine as a bench-stable powder is accomplished through a simple transformation with a readily available nitrile and an alkyl–Li or an alkyl–Grignard reagent. Various ketoimines are proved to serve as substrate for the present multicomponent reaction, affording diastereo- and enantiomerically enriched quaternary carbon stereogenic center-bearing homoallylic amines, which are not possible to be prepared by other methods. To show the utility of the aforementioned transformation, we have demonstrated several functionalization methods including oxidation to generate corresponding methyl ketones (Mannich reaction product) and Cu-catalyzed protodeboration to achieve allyl addition product. The diastereo- and enantioselective synthesis of biologically active compound has been illustrated. The Cu-catalyzed multicomponent reaction delivers the core

(14) Butler, C. R. et al. *J. Med. Chem.* **2015**, *58*, 2678–2702.

structure of the target molecule with exclusive diastereo- and enantioselectivity (>98:2 d.r. and 99.5:0.5 e.r.), which allows us to utilize this information for further transformations toward the target compound synthesis.

## *5.6. Experimentals*

**General.** Infrared (IR) spectra were recorded on a Bruker FT-IR Alpha (ATR mode) spectrophotometer, $\lambda_{max}$ in $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). $^{1}H$ NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet, app = apparent), and coupling constant (Hz). $^{13}C$ NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a JEOL AccuTOF DART (positive mode) at the Mass Spectrometry Facility, Boston College. Unless otherwise noted, all reactions were carried out with distilled and degassed solvents under an atmosphere of dry $N_2$ in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum-line techniques. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system: toluene, benzene and hexanes were purified through a copper oxide and alumina column; $CH_2Cl_2$ and $Et_2O$ were purged with Ar and purified by passage through two alumina columns. Tetrahydrofuran (Aldrich Chemical Co.) was purified by distillation from sodium benzophenone ketyl immediately prior to use unless otherwise specified. All work-up and purification procedures were carried out with reagent grade solvents (purchased from Fisher Scientific, Inc.) under air atmosphere. Enantiomeric ratios were determined by

HPLC analysis (Chiral Technology Chiralcel® OD-H (4.6 x 250 mm)) in comparison with authentic racemic materials. Specific rotations were measured on a ATAGO® AP-300 Automatic Polarimeter. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected.

### *5.6.1. Reagents and Ligands*

**Allene (5.31):** prepared according to previously reported procedures.[15]

**Benzoyl isothiocyanate (5.77):** purchased from Alfa Aesar and used as received.

**Bis(pinacolato)diboron [$B_2(pin)_2$]:** purchased from Frontier Scientific Inc., recrystallized from pentane and dried under vacuum prior to use.

**Cesium carbonate:** purchased from Aldrich Chemical Co. and used as received.

**Chiral bis-phosphines:** purchased from Strem Chemicals Inc. and used as received.

**Copper (I) chloride:** purchased from Strem Chemicals Inc. and used as received.

**Copper (I) Iodide:** purchased from Strem Chemicals Inc. and used as received.

**8-Hydroxyquinoline (5.80):** purchased from Alfa Aesar and used as received.

**Imidazolinium or imidazolium salts (5.34–5.38):** purchased from Aldrich Chemical Co. and used as received.

**Ketoimines:** prepared according to a previously reported procedure.[16]

**Methanol:** purchased from Acros and purified by distillation from Na (Aldrich Chemical Co.) prior to use.

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(15) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859–860. (b) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 747–751. (c) Inoue, A. Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740. (d) Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1588.
(16) Hou, G.; Gosselin, F.; Li, W.; McWilliams, J. C.; Sun, Y.; Weisel, M.; O'Shea, P. D.; Chen, C.-y.; Davies, I. W.; Zhang, X. *J. Am. Chem. Soc.* **2009**, *131*, 9882–9883.

**2-Methyl-2-propanol (*t*-BuOH):** purchased from Aldrich Chemical Co. and purified by distillation from Na (Aldrich Chemical Co.) prior to use.

**Pyridine:** purchased from Aldrich Chemical Co. and used as received.

**Palladium (II) acetate:** purchased from Strem Chemicals Inc. and used as received.

**Sodium borohydride ($NaBH_4$):** purchased from Aldrich Chemical Co. and used as received.

**Sodium *t*-butoxide (NaO*t*-Bu):** purchased from Strem Chemicals Inc. and used as received.

**Sodium methoxide (NaOMe):** purchased from Strem Chemicals Inc. and used as received.

**Sodium perborate tetrahydrate ($NaBO_3 \cdot 4H_2O$):** purchased from Aldrich Chemical Co. and used as received.

**Tetra-*n*-butylammonium fluoride solution (1.0 M in thf):** purchased from Aldrich Chemical Co. and used as received.

**Trifluoromethanesulfonic anhydride:** purchased from Aldrich Chemical Co. and used as received.

### *5.6.2. Experimental Procedure and Characterization Data*

■ **Representative Experimental Procedure for NHC–Cu-Catalyzed Cu–B Addition/Addition to Ketoimines:** In a $N_2$-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolium salt **5.37** (1.6 mg, 0.00500 mmol, 5.0 mol %), CuCl (0.5 mg, 0.00500 mmol, 5.0 mol %), NaO*t*-Bu (14.4 mg, 0.150 mmol, 1.5 equiv.) and thf (0.5 mL). The vessel was sealed with a cap (phenolic

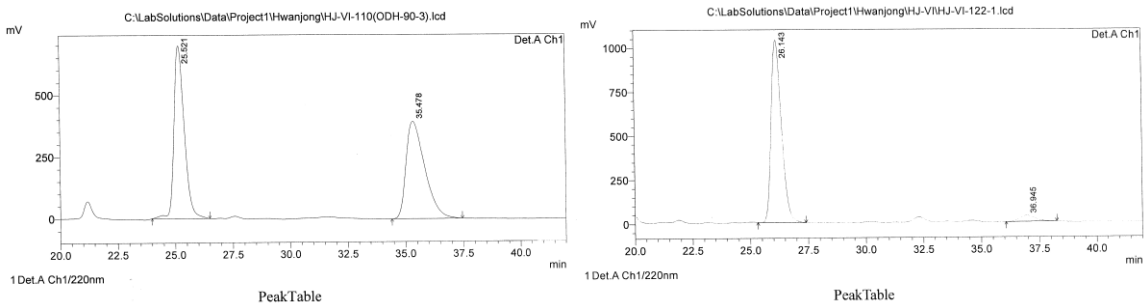
open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (38.1 mg, 0.150 mmol, 1.5 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and allowed to stir at 22 °C for one hour. Allene **5.31** (29.8 mg, 0.150 mmol, 1.5 equiv.) and ketoimine **5.32** (15.6 mg, 0.100 mmol, 1.0 equiv.) were added to the solution, and the vial was removed from the glove box. The resulting solution was allowed to stir at 22 °C for 24 hours before the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo* to provide yellow oil, which was purified by silica gel chromatography (hexanes:$Et_2O$=1:1 to 1:5) to afford **5.33** as a white solid (40.1 mg, 0.0900 mmol, 90% yield).

■ **Representative Experimental Procedure for Enantioselective NHC–Cu-Catalyzed Cu–B Addition/Addition to Ketoimines:** In a $N_2$-filled glove box, an oven-dried vial (4 mL, 17 × 38 mm) with a magnetic stir bar was charged with imidazolinium salt **A.17** (6.4 mg, 0.00750 mmol, 7.5 mol %), CuCl (0.7 mg, 0.00750 mmol, 7.5 mol %), NaO*t*-Bu (14.4 mg, 0.150 mmol, 1.5 equiv.) and thf (0.5 mL). The vessel was sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and the solution was allowed to stir at 22 °C for one hour. Bis(pinacolato)diboron (38.1 mg, 0.150 mmol, 1.5 equiv.) was added to the solution, causing it to turn dark brown immediately. The vial was re-sealed with a cap (phenolic open top cap with red PTFE/white silicone septum) and allowed to stir at 22 °C for one hour. Allene **5.31** (29.8 mg, 0.150 mmol, 1.5 equiv.) and ketoimine **5.32** (15.6 mg, 0.100 mmol, 1.0 equiv.) were added to the solution, and the

vial was removed from the glove box. The resulting solution was allowed to stir at 22 °C for 24 hours before the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with $Et_2O$ (3 × 2 mL). The filtrate was concentrated *in vacuo*. The crude product was purified by silica gel chromatography (hexanes:$Et_2O$=1:1 to 1:5) to afford **5.33** as a white solid (33.9 mg, 0.0761 mmol, 76% yield).

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.33):** IR ($CH_2Cl_2$): 3237 (w), 3149 (w), 3043 (w), 2975 (m), 2929 (m), 2857 (w), 1520 (w), 1474 (m), 1457 (m), 1372 (m), 1328 (m), 1254 (m), 1141 (s), 1095 (s), 1051 (m), 982 (m), 835 (s), 774 (m), 735 (m), 699 (m), 674 (m), 578 (m) 522 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.35–7.32 (2H, m), 7.28–7.21 (3H, m), 5.49 (1H, d, *J* = 2.8 Hz), 5.30 (1H, d, *J* = 2.8 Hz), 3.58–3.53 (1H, m), 3.49–3.43 (1H, m), 2.76 (1H, t, *J* = 6.8 Hz), 1.49 (3H, s), 1.29–1.22 (2H, m), 1.21 (12H, s), 0.84 (9H, s), –0.03 (3H, s), –0.05 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.9, 128.6, 126.9, 125.2, 119.7, 104.8, 82.7, 80.8, 75.2, 61.9, 61.1, 52.8, 30.7, 26.1, 25.2, 25.1, 24.7, 24.6, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{25}H_{45}B_1N_1O_3Si_1$ $[M+H]^+$: 446.32617; Found: 446.32608; specific rotation: $[\alpha]_D^{20}$ –10.86 (*c* 1.84, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 25.521 | 15007961 | 697828 | 49.668 | 63.920 |
| 2 | 35.478 | 15208417 | 393887 | 50.332 | 36.080 |
| Total | | 30216379 | 1091715 | 100.000 | 100.000 |

PeakTable

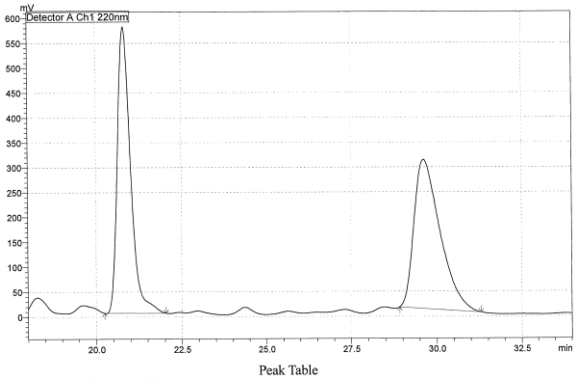
Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 26.143 | 32409594 | 1036241 | 95.265 | 96.863 |
| 2 | 36.945 | 1610912 | 33564 | 4.735 | 3.137 |
| Total | | 34020506 | 1069804 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 25.521 | 15007961 | 49.668 | 26.143 | 32409594 | 95.265 |
| 35.478 | 15208417 | 50.332 | 36.945 | 1610912 | 4.735 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(*o*-tolyl)pent-4-en-2-amine (5.42):** IR ($CH_2Cl_2$): 3234 (w), 3138 (w), 2956 (m), 2929 (m), 2857 (w), 1686 (w), 1600 (w), 1471 (m), 1449 (m), 1379 (m), 1254 (m), 1154 (s), 1096 (s), 1058 (s), 1005 (m), 983 (m), 968 (m), 952 (m), 912 (m), 876 (m), 834 (s), 775 (s), 760 (s), 735 (s), 702 (s), 677 (m), 448 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.21–7.17 (3H, m), 7.12–7.09 (1H, m), 5.43 (1H, d, $J$ = 3.2 Hz), 5.31 (1H, d, $J$ = 2.8 Hz), 3.60–3.55 (2H, m), 3.14 (1H, dd, $J$ = 12.0, 2.4 Hz), 2.50 (3H, s), 1.52 (3H, s), 1.30–1.26 (2H, m), 1.21 (12H, s), 0.86 (9H, s), 0.01 (3H, s), –0.02 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 142.5, 135.1, 133.4, 127.4, 126.5, 124.2, 118.4, 82.7, 79.9, 75.2, 64.6, 60.1, 51.6, 27.2, 26.1, 25.4, 25.3, 25.0, 24.8, 22.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{26}H_{47}B_1N_1O_3Si_1$ $[M+H]^+$: 460.34182; Found: 460.34336; specific rotation: $[\alpha]_D^{20}$ –3.83 (*c* 2.61, $CHCl_3$) for an enantiomerically enriched sample of 99.5:0.5 e.r.

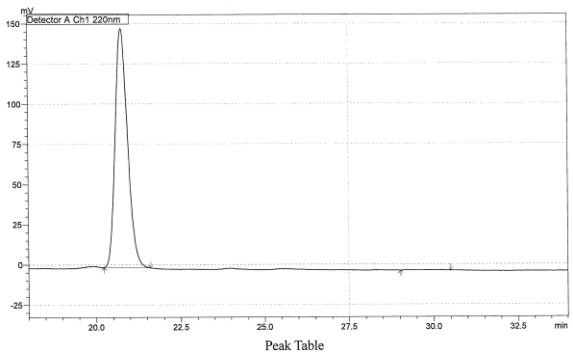
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.




Peak Table

Detector A Channel 1 220nm

| Peak# | Ret. Time | Area | Area% | Height | Height% |
|---|---|---|---|---|---|
| 1 | 20.814 | 15448219 | 49.424 | 575330 | 65.784 |
| 2 | 29.624 | 15808355 | 50.576 | 299239 | 34.216 |
| Total | | 31256574 | 100.000 | 874569 | 100.000 |




Peak Table

Detector A Channel 1 220nm

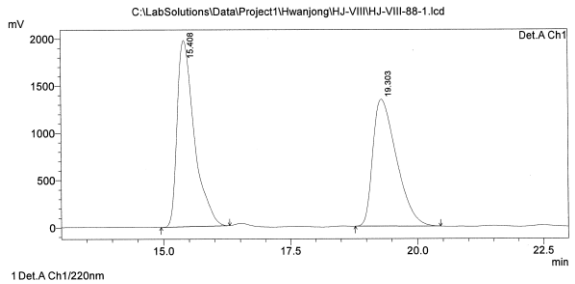
| Peak# | Ret. Time | Area | Area% | Height | Height% |
|---|---|---|---|---|---|
| 1 | 20.759 | 3771880 | 99.747 | 148604 | 99.857 |
| 2 | 29.909 | 9580 | 0.253 | 213 | 0.143 |
| Total | | 3781460 | 100.000 | 148817 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 20.814 | 15448219 | 49.424 | 20.759 | 3771880 | 99.747 |
| 29.624 | 15808355 | 50.576 | 29.909 | 9580 | 0.253 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(2-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.43):** IR ($CH_2Cl_2$): 3239 (br), 2975 (m), 2930 (m), 2857 (w), 1600 (w), 1473 (s), 1458 (s), 1372 (m), 1330 (m), 1295 (m), 1249 (s), 1145 (s), 1094 (s), 1053 (s), 1028 (m), 1007 (m), 982 (m), 967 (m), 951 (m), 910 (m), 877 (m), 833 (s), 775 (s), 752 (s), 699 (m), 675 (s), 578 (w), 551 (w), 519 (w), 496 (w), 447 (w), 417 (w), 404 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.25–7.20 (2H, m), 6.95–6.88 (2H, m), 5.33 (1H, d, $J$ = 3.2 Hz), 5.23 (1H, d, $J$ = 2.8 Hz), 3.83 (3H, s), 3.61–3.54 (2H, m), 2.82 (1H, d, $J$ = 10.4 Hz), 1.48 (3H, s), 1.30–1.27 (2H, m), 1.17 (12H, s), 0.86 (9H, s), –0.01 (3H, s), –0.02 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 157.2, 131.0, 128.6, 127.9, 121.2, 116.5, 111.8, 82.6, 79.7, 75.2, 62.9, 60.7, 55.4, 52.6, 28.4, 26.1, 25.3, 25.2, 25.0, 24.6, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{26}H_{47}B_1N_1O_4Si_1$

$[M+H]^+$: 476.3367; Found: 476.3383; specific rotation: $[\alpha]_D^{20}$ –15.54 (*c* 2.70, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

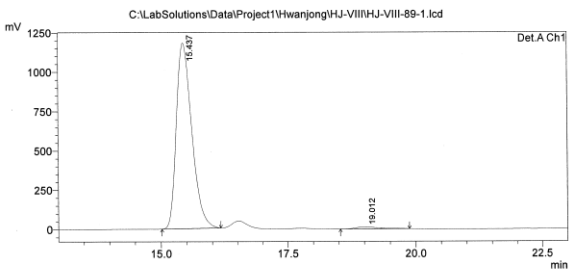
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 15.408 | 45883540 | 1974345 | 51.393 | 59.503 |
| 2 | 19.303 | 43395471 | 1343725 | 48.607 | 40.497 |
| Total | | 89279011 | 3318070 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

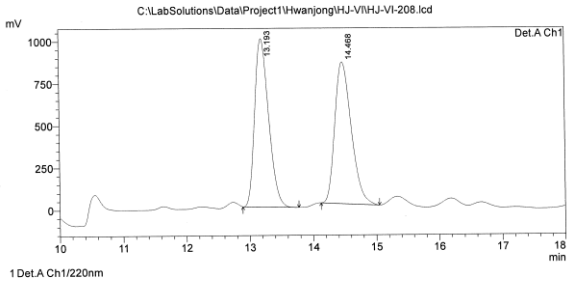
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 15.437 | 24661867 | 1179084 | 98.410 | 98.946 |
| 2 | 19.012 | 398543 | 12561 | 1.590 | 1.054 |
| Total | | 25060410 | 1191645 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 15.408 | 45883540 | 51.393 | 15.437 | 24661867 | 98.410 |
| 19.303 | 43395471 | 48.607 | 19.012 | 398543 | 1.590 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(2-fluorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.44):** IR ($CH_2Cl_2$): 3235 (br), 2976 (m), 2930 (m), 2858 (w), 1474 (s), 1449 (s), 1371 (s), 1331 (m), 1254 (m), 1206 (m), 1144 (s), 1096 (s), 1067 (m), 1008 (m), 982 (m), 967 (m), 951 (m), 925 (w), 881 (w), 850 (s), 834 (s), 758 (m), 735 (m), 699 (m), 675 (s), 578 (w), 552 (w), 518 (w), 496 (w), 452 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.31–7.22 (2H, m), 7.12 (1H, t, *J* = 8.0 Hz), 7.03 (1H, dd, *J* = 12.8, 6.8 Hz), 5.48 (1H, d, *J* = 2.8 Hz), 5.36 (1H, d, *J* = 2.8 Hz), 3.64–3.59 (1H, m), 3.53–3.47 (1H, m), 2.93–2.90 (1H, m), 1.49 (3H, s), 1.28–1.21 (2H, m), 1.20 (12H, s), 0.85 (9H, s), –0.01 (3H, s), –0.03 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 160.4 (d, *J* = 243 Hz), 131.8, 128.9 (d, *J* = 8.4 Hz), 127.7 (d, *J* = 4.6 Hz), 124.4 (d, *J* =

3.0 Hz), 120.4, 116.8 (d, $J$ = 23.5 Hz), 82.8, 80.7, 75.2, 61.2, 60.9, 52.3, 29.0, 26.1, 25.2, 25.1, 25.0, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{25}H_{44}B_1F_1N_1O_3Si_1$ $[M+H]^+$: 464.31675; Found: 464.31536; specific rotation: $[\alpha]_D^{20}$ –4.09 (*c* 3.42, $CHCl_3$) for an enantiomerically enriched sample of 66:34 e.r.

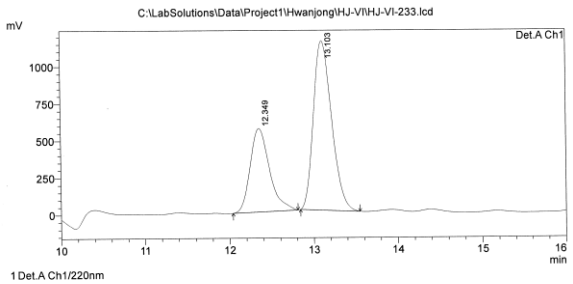
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 13.193 | 15306517 | 998397 | 50.039 | 54.248 |
| 2 | 14.468 | 15282929 | 842041 | 49.961 | 45.752 |
| Total | | 30589445 | 1840438 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

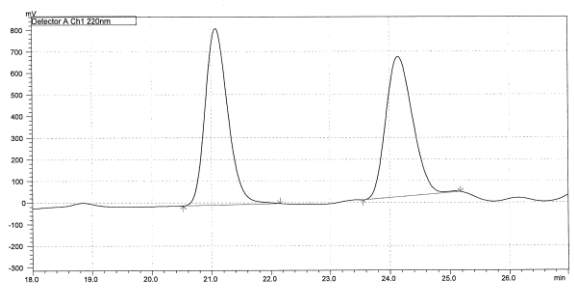
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 12.349 | 8958464 | 563687 | 34.117 | 32.988 |
| 2 | 13.103 | 17299501 | 1145068 | 65.883 | 67.012 |
| Total | | 26257965 | 1708755 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 13.193 | 15306517 | 50.039 | 12.349 | 8958464 | 34.117 |
| 14.468 | 15282929 | 49.961 | 13.103 | 17299501 | 65.883 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(2-chlorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.45):** IR ($CH_2Cl_2$): 3232 (br), 2929 (w), 2856 (w), 1661 (w), 1472 (w), 1380 (w), 1362 (w), 1253 (m), 1156 (m), 1139 (s), 1096 (s), 1038 (s), 1005 (w), 982 (w), 967 (w), 949 (m), 910 (w), 885 (w), 833 (s), 774 (s), 754 (s), 729 (m), 675 (m), 616 (w), 575 (w), 547 (w), 522 (w), 495 (w), 451 (w), 430 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.40 (1H, d, $J$ = 8.0 Hz), 7.36 (1H, dd, $J$ = 8.0, 1.6 Hz), 7.25 (1H, dt, $J$ = 7.6, 1.6 Hz), 7.19 (1H, dt, $J$ = 7.6, 1.6 Hz), 5.44 (1H, d, $J$ = 3.2 Hz), 5.34 (1H, d, $J$ = 3.2 Hz), 3.67–3.62 (1H, m), 3.59–3.47 (1H, m), 3.22 (1H, d, $J$ =

10.4 Hz), 1.56 (3H, s), 1.38–1.32 (2H, m), 1.22 (6H, s), 1.19 (6H, s), 0.86 (9H, s), 0.01 (3H, s), 0.00 (3H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 141.2, 132.2, 132.1, 128.6, 128.6, 127.2, 119.1, 82.5, 80.3, 75.1, 63.3, 60.7, 51.7, 27.4, 26.1, 25.2, 25.0, 24.6, 24.5, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{25}H_{44}B_1Cl_1N_1O_3Si_1$ $[M+H]^+$: 480.28720; Found: 480.28648; specific rotation: $[\alpha]_D^{20}$ –6.42 (*c* 2.49, $CHCl_3$) for an enantiomerically enriched sample of 99.5:0.5 e.r.

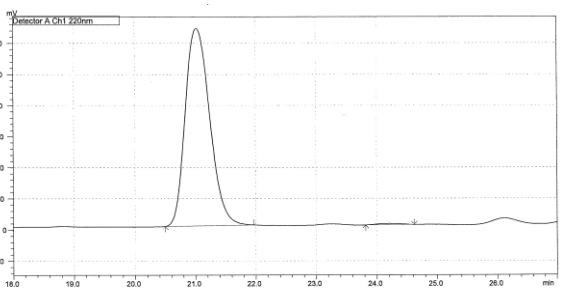
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.




PeakTable

Detector A Channel 1 220nm

| Peak# | Ret. Time | Area | Area % | Height | Height% |
|---|---|---|---|---|---|
| 1 | 21.072 | 21626503 | 51.870 | 818002 | 55.705 |
| 2 | 24.140 | 20067467 | 48.130 | 650449 | 44.295 |
| Total | | 41693970 | 100.000 | 1468451 | |




PeakTable

Detector A Channel 1 220nm

| Peak# | Ret. Time | Area | Area % | Height | Height% |
|---|---|---|---|---|---|
| 1 | 21.018 | 45038852 | 99.413 | 1586486 | 99.374 |
| 2 | 24.198 | 265964 | 0.587 | 10002 | 0.626 |
| Total | | 45304817 | 100.000 | 1596488 | |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 21.072 | 21626503 | 51.870 | 21.018 | 45038852 | 99.374 |
| 24.140 | 20067467 | 48.130 | 24.198 | 265964 | 0.626 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(3-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.46):** IR ($CH_2Cl_2$): 3238 (w), 3149 (w), 2976 (m), 2930 (m), 2857 (m), 1585 (m), 1474 (s), 1456 (s), 1372 (m), 1328 (m), 1254 (m), 1141 (s), 1095 (s), 1049 (s), 1008 (m), 982 (s), 951 (m), 834 (s), 775 (s), 701 (m), 675 (m), 577 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.25 (1H, t, *J* = 8.0 Hz), 6.85–6.83 (2H, m), 6.77 (1H, d, *J* = 9.2 Hz), 5.51 (1H, d, *J* = 3.2 Hz), 5.32 (1H, d, *J* = 3.2

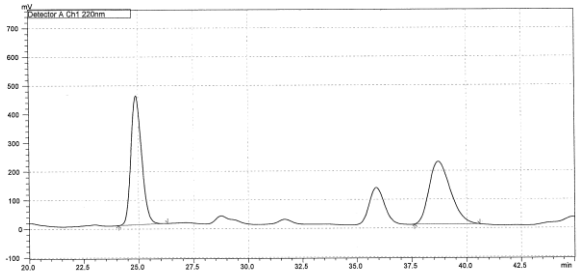
Hz), 3.80 (3H, s), 3.58–3.53 (1H, m), 3.50–3.42 (1H, m), 2.73 (1H, t, $J$ = 6.8 Hz), 1.47 (3H, s), 1.32–1.26 (2H, m), 1.21 (6H, s), 1.20 (6H, s), 0.85 (9H, s), –0.03 (3H, s), –0.05 (3H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 159.9, 146.7, 129.6, 120.2, 117.5, 111.9, 111.7, 82.9, 80.9, 75.2, 61.8, 61.1, 55.4, 52.9, 30.6, 26.1, 25.2, 25.1, 25.0, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{26}H_{47}B_1N_1O_4Si_1$ $[M+H]^+$: 476.33674; Found: 476.33517; specific rotation: $[\alpha]_D^{20}$ –11.83 (*c* 1.36, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(3-fluorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.47):** IR ($CH_2Cl_2$): 3263 (w), 3151 (w), 2977 (m), 2930 (m), 2858 (m), 1615 (m), 1590 (m), 1473 (m), 1451 (m), 1372 (m), 1338 (m), 1254 (m), 1140 (s), 1096 (s), 1061 (s), 1007 (m), 982 (m), 968 (m), 952 (m), 835 (s), 807 (m), 774 (s), 700 (s), 674 (s), 578 (m), 520 (m) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.29 (1H, dt, $J$ = 8.4, 6.0 Hz), 7.12 (1H, d, $J$ = 8.0 Hz), 7.06 (1H, d, $J$ = 10.8 Hz), 6.92 (1H, d, $J$ = 8.0 Hz), 5.65 (1H, d, $J$ = 3.2 Hz), 5.43 (1H, d, $J$ = 2.8 Hz), 3.55–3.51 (1H, m), 3.43–3.39 (1H, m), 2.77 (1H, d, $J$ = 10.4 Hz), 1.41 (3H, s), 1.30–1.25 (2H, m), 1.23 (12H, s), 0.85 (9H, s), –0.04 (3H, s), –0.06 (3H, s); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 160.7 (d, $J$ = 235 Hz), 130.0 (d, $J$ = 8.4 Hz), 128.0, 121.3, 121.1, 113.6 (d, $J$ = 21.2 Hz), 112.8 (d, $J$ = 22.8 Hz), 171.3, 144.1, 128.5, 128.0, 127.7, 125.9, 83.0, 81.7, 75.2, 61.1, 60.5, 31.5, 30.9, 26.1, 25.1, 25.1, 24.9, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd

for $C_{25}H_{44}B_1F_1N_1O_3Si_1$ $[M+H]^+$: 464.31675; Found: 464.31699; specific rotation: $[\alpha]_D^{20}$ –8.04 (*c* 1.49, $CHCl_3$) for an enantiomerically enriched sample of 93.5:6.5 e.r.

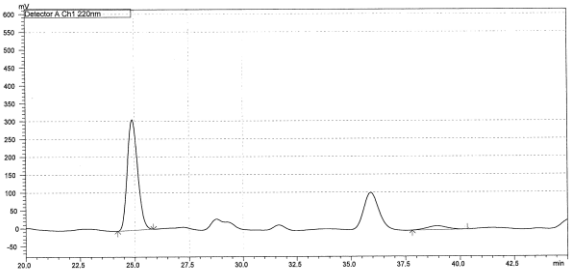
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.




Peak Table

Detector A Channel 1 220nm

| Peak# | Ret. Time | Area | Area% | Height | Height% |
|---|---|---|---|---|---|
| 1 | 24.891 | 15187285 | 50.670 | 449514 | 67.246 |
| 2 | 38.709 | 14785426 | 49.330 | 218947 | 32.754 |
| Total | | 29972710 | 100.000 | 668462 | 100.000 |




Peak Table

Detector A Channel 1 220nm

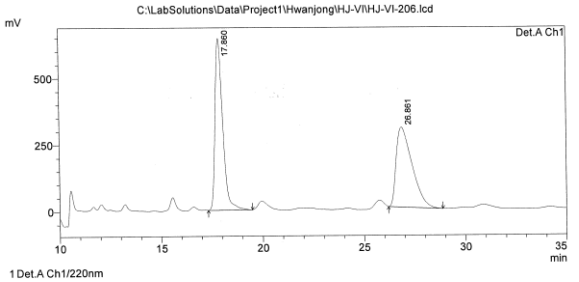
| Peak# | Ret. Time | Area | Area% | Height | Height% |
|---|---|---|---|---|---|
| 1 | 24.891 | 10208352 | 93.821 | 309418 | 96.690 |
| 2 | 38.935 | 672282 | 6.179 | 10592 | 3.310 |
| Total | | 10880635 | 100.000 | 320010 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 24.891 | 15187285 | 50.670 | 24.891 | 10208352 | 93.821 |
| 38.709 | 14785426 | 49.330 | 38.935 | 672282 | 6.179 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(4-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.48):** IR ($CH_2Cl_2$): 3242 (w), 3150 (w), 2975 (m), 2930 (m), 2857 (m), 1605 (m), 1517 (m), 1474 (s), 1457 (s), 1372 (m), 1327 (m), 1254 (s), 1141 (s), 1094 (s), 1050 (m), 1008 (m), 982 (s), 952 (m), 832 (s), 774 (s), 675 (s), 622 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.22 (2H, d, *J* = 8.8 Hz), 6.86 (2H, d, *J* = 9.2 Hz), 5.52 (1H, d, *J* = 3.2 Hz), 5.31 (1H, d, *J* = 2.8 Hz), 3.79 (3H, s), 3.59–3.53 (1H, m), 3.47–3.41 (1H, m), 2.72 (1H, dd, *J* = 8.8, 4.4 Hz), 1.47 (3H, s), 1.33–1.27 (2H, m), 1.21 (12H, s), 0.85 (9H, s), –0.03 (3H, s), –0.05 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 172.6, 158.4, 134.8, 126.5, 113.9, 83.0, 80.8, 75.2, 66.0, 61.3, 55.4, 31.7,

30.7, 26.1, 25.2, 25.0, 24.7, 24.2, 18.4, –5.1, –5.2; specific rotation: $[\alpha]_D^{20}$ –14.60 (*c* 0.82, $CHCl_3$) for an enantiomerically enriched sample of 92.5:7.5 e.r.

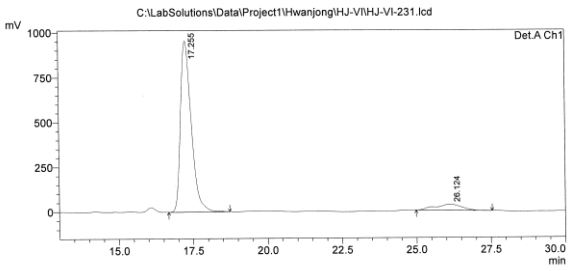
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 17.860 | 16897534 | 645009 | 50.811 | 68.216 |
| 2 | 26.861 | 16358259 | 300524 | 49.189 | 31.784 |
| Total | | 33255794 | 945533 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 17.255 | 24088189 | 954602 | 92.348 | 96.638 |
| 2 | 26.124 | 1995838 | 33210 | 7.652 | 3.362 |
| Total | | 26084027 | 987812 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 17.860 | 16897534 | 50.811 | 17.255 | 24088189 | 92.348 |
| 26.861 | 16358259 | 49.189 | 26.124 | 1995838 | 7.652 |

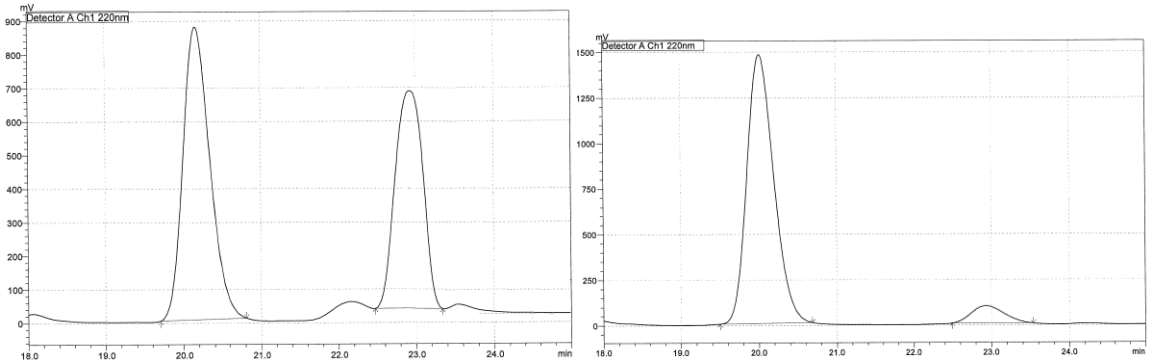
**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(4-fluorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.49):** IR ($CH_2Cl_2$): 3234 (w), 2976 (m), 2930 (m), 2858 (m), 1604 (m), 1514 (m), 1474 (s), 1455 (s), 1372 (m), 1329 (m), 1253 (m), 1141 (s), 1094 (s), 1050 (s), 1008 (m), 982 (s), 968 (m), 951 (m), 924 (m), 911 (m), 878 (m), 833 (s), 775 (s), 756 (s), 674 (s), 578 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.31 (2H, dd, *J* = 8.8, 5.6 Hz), 7.00 (2H, dd, *J* = 8.8, 8.8 Hz), 5.62 (1H, d, *J* = 2.8 Hz), 5.38 (1H, d, *J* = 3.2 Hz), 3.54–3.49 (1H, m), 3.43–3.37 (1H, m), 2.75 (1H, d, *J* = 8.4 Hz), 2.10 (3H, s), 1.28–1.24 (2H, m), 1.22 (12H, s), 0.84 (9H, s), –0.04 (3H, s), –0.06 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 161.6 (d, *J* = 244 Hz), 141.8, 127.1 (d, *J* = 7.5 Hz), 122.8, 115.1 (d, *J* = 21.3 Hz), 81.5, 75.1, 61.3, 60.3, 52.7, 31.5, 26.1, 25.2, 25/1,

24.9, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{25}H_{44}B_1F_1N_1O_3Si_1$ $[M+H]^+$: 464.31675; Found: 464.31758; specific rotation: $[\alpha]_D^{20}$ –14.16 (*c* 1.39, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(4-chlorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.50):** IR ($CH_2Cl_2$): 3285 (br), 2929 (w), 2856 (w), 1686 (w), 1590 (w), 1472 (m), 1448 (s), 1371 (m), 1334 (m), 1302 (w), 1255 (m), 1217 (w), 1146 (s), 1093 (s), 1010 (m), 982 (m), 952 (m), 924 (w), 883 (w), 830 (s), 776 (s), 723 (w), 700 (w), 675 (s), 622 (w), 577 (w), 523 (w), 468 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.29 (4H, s), 5.64 (1H, d, *J* = 2.8 Hz), 5.40 (1H, d, *J* = 2.8 Hz), 3.56–3.51 (1H, m), 3.43–3.37 (1H, m), 2.76 (1H, dd, *J* = 11.2, 2.0 Hz), 1.42 (3H, s), 1.22 (12H, s), 1.20–1.14 (2H, m), 0.85 (9H, s), –0.03 (3H, s), –0.05 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.6, 132.6, 128.6, 127.0, 106.2, 83.0, 81.7, 75.2, 61.2, 60.5, 52.6, 26.1, 25.1, 25.0, 24.7, 24.6, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{25}H_{44}B_1Cl_1N_1O_3Si_1$ $[M+H]^+$: 480.28720; Found: 480.28949; specific rotation: $[\alpha]_D^{20}$ –18.16 (*c* 1.32, $CHCl_3$) for an enantiomerically enriched sample of 92:8 e.r.

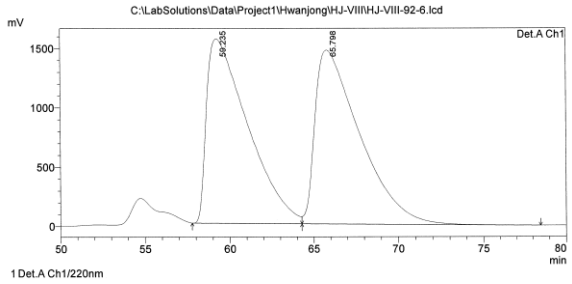
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.




| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 20.159 | 21056770 | 49.513 | 20.010 | 35520207 | 92.308 |
| 22.921 | 21470574 | 50.487 | 22.926 | 2772334 | 7.692 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(naphthalen-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.51):** IR ($CH_2Cl_2$): 3359 (br), 2956 (m), 2930 (m), 2858 (w), 1685 (w), 1598 (w), 1471 (s), 1447 (s), 1371 (s), 1336 (m), 1302 (m), 1253 (m), 1215 (w), 1148 (s), 1095 (s), 1007 (m), 982 (m), 952 (m), 924 (m), 832 (s), 779 (s), 728 (m), 700 (s), 675 (s), 578 (m), 518 (m), 448 (m), 434 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 8.31 (1H, d, *J* = 9.2 Hz), 7.89–7.87 (1H, m), 7.79 (1H, d, *J* = 7.6 Hz), 7.52–7.49 (2H, m), 7.42 (1H, t, *J* = 7.6 Hz), 7.32 (1H, d, *J* = 7.6 Hz), 5.55 (1H, d, *J* = 3.2 Hz), 5.44 (1H, d, *J* = 2.8 Hz), 3.53 (1H, d, *J* = 11.6 Hz), 3.48–3.43 (2H, m), 1.78 (3H, s), 1.26 (6H, s), 1.24 (6H, s), 1.07–1.01 (2H, m), 0.77 (9H, s), –0.12 (3H, s), –0.18 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 140.9, 135.0, 130.3, 129.6, 129.1, 126.2, 125.8, 125.7, 124.8, 121.9, 119.5, 82.6, 80.2, 75.2, 64.5, 60.4, 53.0, 28.2, 26.1, 25.7, 25.4, 25.0, 24.7, 18.3, –5.3, –5.4; HRMS: Calcd for $C_{29}H_{47}B_1N_1O_3Si_1$ $[M+H]^+$: 496.3418; Found: 496.3437; specific rotation: $[\alpha]_D^{20}$ –2.91 (*c* 3.43, $CHCl_3$) for an enantiomerically enriched sample of 98.5:1.5 e.r.

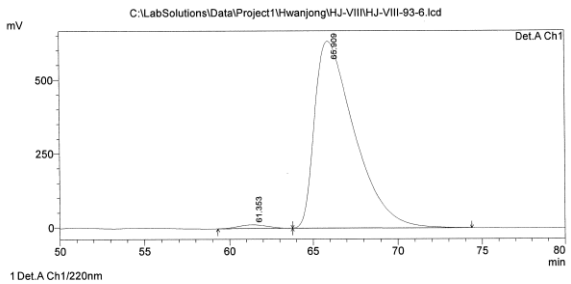
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 98:2 hexanes/*i*-PrOH, 0.4 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 59.235 | 264275233 | 1555719 | 49.261 | 51.471 |
| 2 | 65.798 | 272203167 | 1466768 | 50.739 | 48.529 |
| Total | | 536478400 | 3022487 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

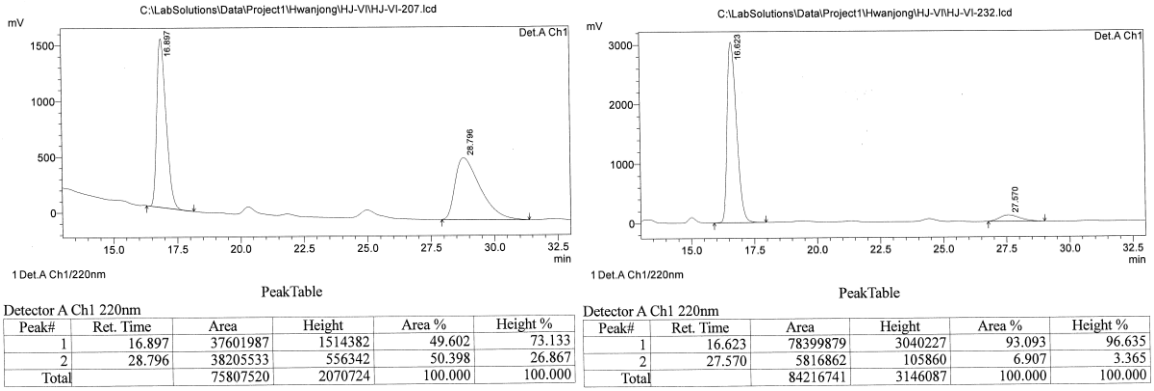
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 61.353 | 1488378 | 12530 | 1.411 | 1.941 |
| 2 | 65.909 | 104018457 | 632972 | 98.589 | 98.059 |
| Total | | 105506835 | 645501 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 59.235 | 264275233 | 49.261 | 61.353 | 1488378 | 1.411 |
| 65.798 | 272203167 | 50.739 | 65.909 | 104018457 | 98.589 |

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(naphthalen-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.52):** IR ($CH_2Cl_2$): 3399 (br), 2976 (m), 2954 (m), 2929 (m), 2857 (w), 1709 (w), 1678 (m), 1628 (w), 1598 (w), 1471 (s), 1438 (s), 1369 (s), 1301 (m), 1282 (m), 1253 (m), 1228 (w), 1192 (m), 1147 (s), 1103 (s), 1007 (m), 982 (m), 951 (s), 884 (m), 857 (s), 830 (s), 780 (s), 747 (s), 701 (m), 675 (s), 617 (w), 577 (m), 553 (m), 520 (m), 476 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.83–7.80 (3H, m), 7.70 (1H, s), 7.50–7.43 (3H, m), 5.61 (1H, d, $J$ = 3.2 Hz), 5.42 (1H, d, $J$ = 3.2 Hz), 3.54–3.50 (1H, m), 3.46–3.43 (1H, m), 2.91 (1H, dd, $J$ = 9.2, 2.0 Hz), 1.53 (3H, s), 1.43–1.35 (2H, m), 1.23 (12H, s), 0.84 (9H, s), –0.04 (3H, s), –0.07 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 143.4, 133.2, 132.3, 128.5, 128.0, 127.6, 126.4, 126.0, 124.2, 123.1, 121.7, 82.7, 81.1, 75.2, 61.5, 61.0, 52.6, 30.9, 26.1, 25.2, 25.1, 25.0, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{29}H_{47}B_1N_1O_3Si_1$ $[M+H]^+$: 496.34182; Found: 496.34110;

specific rotation: $[\alpha]_D^{20}$ –17.08 (*c* 2.34, $CHCl_3$) for an enantiomerically enriched sample of 94:6 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 16.897 | 37601987 | 1514382 | 49.602 | 73.133 |
| 2 | 28.796 | 38205533 | 556342 | 50.398 | 26.867 |
| Total | | 75807520 | 2070724 | 100.000 | 100.000 |

PeakTable

Detector A Ch1 220nm

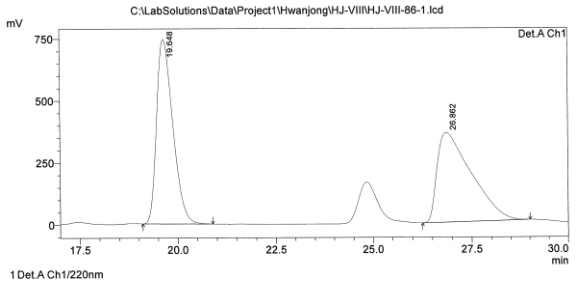
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 16.623 | 78399879 | 3040227 | 93.093 | 96.635 |
| 2 | 27.570 | 5816862 | 105860 | 6.907 | 3.365 |
| Total | | 84216741 | 3146087 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 16.897 | 37601987 | 49.602 | 16.623 | 78399879 | 93.093 |
| 28.796 | 38205533 | 50.398 | 27.570 | 5816862 | 6.907 |

**(2*R*,3*S*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.54):** IR ($CH_2Cl_2$): 3055 (w), 2980 (w), 1505 (m), 1473 (m), 1440 (m), 1370 (m), 1335 (m), 1264 (s), 1143 (s), 1095 (s), 1040 (s), 1007 (m), 981 (m), 951 (m), 882 (m), 836 (s), 812 (m), 777 (m), 732 (s), 702 (s), 675 (s), 577 (w), 553 (w), 522 (w), 454 (w), 435 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 6.80–6.72 (3H, m), 5.94 (2H, s), 5.52 (1H, d, *J* = 2.8 Hz), 5.32 (1H, d, *J* = 2.8 Hz), 3.60–3.54 (1H, m), 3.51–3.43 (1H, m), 2.68 (1H, t, *J* = 6.8 Hz), 1.43 (3H, s), 1.38–1.32 (2H, m), 1.23 (12H, s), 0.85 (9H, s), –0.01 (3H, s), –0.03 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 148.1, 146.4, 118.8, 118.0, 108.0, 106.8, 106.4, 101.2, 82.9, 81.0, 75.2, 61.4, 61.3, 31.6, 30.9, 26.1, 25.2, 25.1, 25.0, 24.7, 18.4, –5.1, –5.2; HRMS: Calcd

for $C_{26}H_{45}B_1N_1O_5Si_1$ $[M+H]^+$: 490.3160; Found: 490.3137; specific rotation: $[\alpha]_D^{20}$ +6.99 (*c* 1.43, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

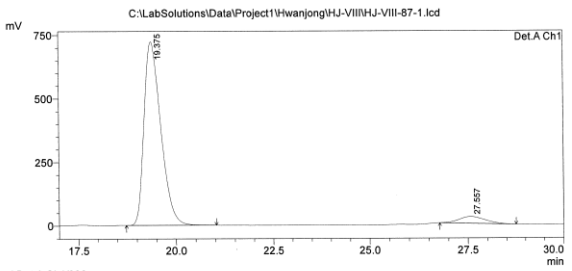
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 19.648 | 21534978 | 744466 | 49.743 | 67.291 |
| 2 | 26.862 | 21757196 | 361869 | 50.257 | 32.709 |
| Total | | 43292174 | 1106335 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

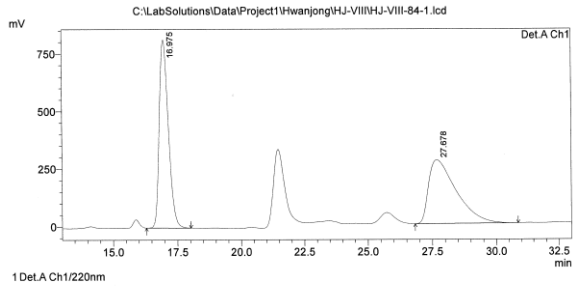
| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 19.375 | 21468166 | 722221 | 94.578 | 96.461 |
| 2 | 27.557 | 1230723 | 26499 | 5.422 | 3.539 |
| Total | | 22698888 | 748720 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 19.648 | 21534978 | 49.743 | 19.375 | 21468166 | 94.578 |
| 26.862 | 21757196 | 50.257 | 27.557 | 1230723 | 5.422 |

**(2*R*,3*S*)-2-(Benzofuran-5-yl)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.55):** IR ($CH_2Cl_2$): 3238 (br), 2974 (m), 2929 (m), 2887 (w), 2856 (w), 1518 (w), 1474 (s), 1458 (s), 1378 (m), 1330 (m), 1255 (m), 1196 (s), 1144 (s), 1095 (m), 1051 (w), 1007 (m), 982 (m), 968 (m), 952 (w), 879 (w), 836 (s), 810 (m), 775 (s), 739 (m), 699 (w), 675 (m), 422 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.60 (1H, d, *J* = 10.0 Hz), 7.51–7.41 (2H, m), 7.22 (1H, d, *J* = 8.4 Hz), 6.74 (1H, s), 5.52 (1H, d, *J* = 2.8 Hz), 5.33 (1H, d, *J* = 2.8 Hz), 3.56–3.52 (1H, m), 3.39–3.34 (1H, m), 2.82 (1H, t, *J* = 6.4 Hz), 1.53 (3H, s), 1.32–1.27 (2H, m), 1.23 (12H, s), 0.85 (9H, s), –0.03 (3H, s), –0.06 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 172.5, 153.9, 145.7, 145.2, 127.6, 122.0, 117.7, 111.4, 106.8, 82.9, 80.9, 75.2, 61.9, 61.1, 31.7,

31.3, 26.1, 25.2, 25.1, 25.0, 24.7, 18.4, –5.2, –5.3; HRMS: Calcd for $C_{27}H_{45}B_1N_1O_4Si_1$ $[M+H]^+$: 486.3211; Found: 486.3220; specific rotation: $[\alpha]_D^{20}$ –6.48 (*c* 1.85, $CHCl_3$) for an enantiomerically enriched sample of 94.5:5.5 e.r.

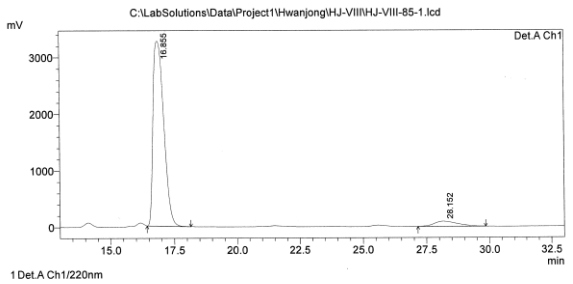
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 16.975 | 19949090 | 815861 | 49.172 | 74.720 |
| 2 | 27.678 | 20621055 | 276023 | 50.828 | 25.280 |
| Total | | 40570146 | 1091884 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 16.855 | 95589785 | 3267929 | 94.260 | 97.314 |
| 2 | 28.152 | 5821179 | 90205 | 5.740 | 2.686 |
| Total | | 101410964 | 3358134 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 16.975 | 19949090 | 49.172 | 16.855 | 95589785 | 94.260 |
| 27.678 | 20621055 | 50.828 | 28.152 | 5821179 | 5.740 |

**(2*S*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-cyclohexyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.56):** IR ($CH_2Cl_2$): 3398 (br), 3061 (w), 3028 (w), 2944 (w), 2827 (w), 1705 (s), 1666 (m), 1625 (w), 1605 (w), 1576 (m), 1494 (m), 1451 (m), 1415 (w), 1357 (m), 1329 (w), 1256 (m), 1226 (w), 1206 (m), 1169 (m), 1074 (w), 1025 (s), 976 (m), 912 (w), 843 (w), 752 (s), 698 (s), 558 (m), 547 (m), 517 (m), 482 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.29 (1H, br s), 5.13 (1H, br s), 3.77–3.72 (1H, m), 3.59–3.53 (1H, m), 2.24 (1H, d, *J* = 8.4 Hz), 1.84–1.50 (7H, m), 1.47–1.38 (1H, m), 1.25–1.16 (4H, m), 1.14 (6H, s), 1.11 (6H, s), 1.04 (3H, s), 0.99–0.90 (1H, m), 0.88 (9H, s), 0.04 (3H, s), 0.03 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 82.8, 79.7, 75.2,

61.6, 60.9, 51.4, 43.5, 30.0, 27.7, 27.4, 26.6, 26.4, 26.1, 25.3, 25.0, 24.8, 24.7, 20.4, 18.4, –5.1, –5.2; HRMS: Calcd for $C_{25}H_{51}B_1N_1O_3Si_1$ $[M+H]^+$: 452.37312; Found: 452.37187; specific rotation: $[\alpha]_D^{20}$ –15.88 (*c* 1.51, $CHCl_3$) for an enantiomerically enriched sample of 95:5 e.r.

Enantiomeric purity was determined by $^1H$ NMR analysis of derived Mosher's amide.

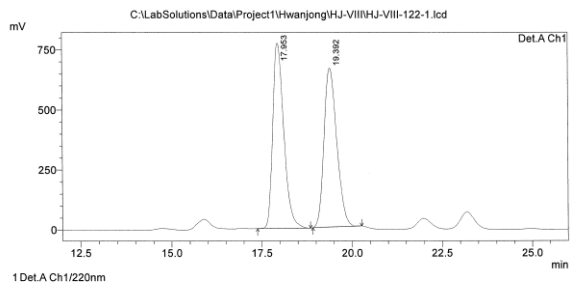
**(2*S*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-1-cyclohexyl-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.57):** IR ($CH_2Cl_2$): 3238 (br), 2976 (w), 2926 (m), 2854 (w), 1707 (w), 1473 (s), 1449 (s), 1370 (s), 1330 (s), 1253 (m), 1216 (w), 1145 (s), 1095 (s), 982 (m), 951 (s), 924 (s), 883 (w), 833 (s), 775 (s), 732 (w), 700 (w), 674 (s), 577 (w), 551 (w), 521 (w), 494 (w), 451 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 5.32 (1H, br s), 5.14 (1H, br s), 3.77–3.73 (1H, m), 3.56–3.52 (1H, m), 2.29–2.21 (1H, m), 1.80–1.53 (11H, m), 1.40–1.31 (3H, m), 1.21 (6H, s), 1.18 (6H, s), 1.14 (3H, s), 1.03–0.98 (1H, m), 0.88 (9H, s), 0.03 (6H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 107.5, 82.9, 79.9, 75.2, 62.0, 60.2, 42.1, 35.2, 35.1, 33.8, 32.9, 30.9, 30.4, 29.8, 26.1, 25.2, 25.1, 24.9, 24.7, 18.4, –5.1, –5.2; HRMS: Calcd for $C_{26}H_{53}B_1N_1O_3Si_1$ $[M+H]^+$: 466.38877; Found: 466.39005; specific rotation: $[\alpha]_D^{20}$ –8.68 (*c* 1.61, $CHCl_3$) for an enantiomerically enriched sample of 91:9 e.r.

Enantiomeric purity was determined by $^1H$ NMR analysis of derived Mosher's amide.

**(3*S*,4*R*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-1-en-4-amine (5.58):** IR ($CH_2Cl_2$): 3238 (br), 2975 (w), 2929 (w), 2857 (w), 1603 (w), 1506 (w), 1473 (m), 1438 (m), 1371 (m), 1334 (m), 1297 (w), 1247 (m), 1143 (s), 1093 (s), 1038 (s), 1007 (m), 982 (m), 967 (m), 950 (m), 925 (m), 881 (m), 833 (s), 807 (m), 774 (s), 727 (m), 698 (m), 674 (s), 645 (w), 618 (m), 577 (w),

555 (w), 521 (w), 496 (w), 428 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.33 (2H, t, *J* = 7.6 Hz), 7.23 (1H, t, *J* = 7.6 Hz), 7.18 (2H, d, *J* = 7.2 Hz), 5.45 (1H, d, *J* = 3.2 Hz), 5.29 (1H, d, *J* = 2.8 Hz), 3.58–3.52 (1H, m), 3.50–3.44 (1H, m), 2.79 (1H, d, *J* = 7.6 Hz), 1.94–1.86 (1H, m), 1.79–1.71 (1H, m), 1.21 (12H, s), 1.19–0.94 (6,m), 0.85 (9H, s), 0.83–0.78 (3H, m), –0.03 (3H, s), –0.05 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 142.7, 128.5, 126.8, 125.9, 119.0, 82.6, 80.5, 75.1, 65.2, 60.8, 52.3, 40.7, 31.5, 26.1, 25.4, 25.0, 24.9, 24.7, 22.7, 18.4, 14.1, –5.2, –5.3; specific rotation: $[\alpha]_D^{20}$ –18.29 (*c* 1.42, $CHCl_3$) for an enantiomerically enriched sample of 88:12 e.r.

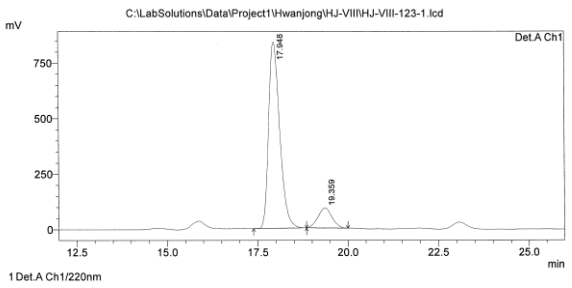
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 17.953 | 16546365 | 772136 | 50.460 | 53.839 |
| 2 | 19.392 | 16244594 | 662013 | 49.540 | 46.161 |
| Total | | 32790958 | 1434148 | 100.000 | 100.000 |




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 17.948 | 17946169 | 839300 | 88.016 | 90.293 |
| 2 | 19.359 | 2443568 | 90235 | 11.984 | 9.707 |
| Total | | 20389737 | 929535 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 17.953 | 16546365 | 50.460 | 17.948 | 17946169 | 88.016 |
| 19.392 | 16244594 | 49.540 | 19.359 | 2443568 | 11.984 |

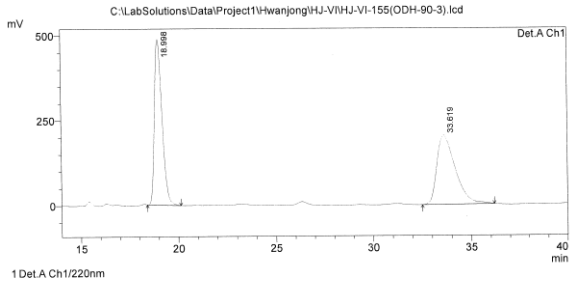
**(2*R*,3*S*)-3-Methyl-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.59):** IR ($CH_2Cl_2$): 3236 (w), 3151 (w), 2976 (m), 2929 (m), 1519 (m), 1474 (s), 1448 (s), 1371 (s), 1325 (s), 1270 (m), 1217 (m), 1142 (s), 1105 (s), 1069 (m), 1050 (m), 1008 (m), 981 (s), 968 (m), 951 (m), 850 (s), 762 (m), 737 (m), 700 (s), 674 (s), 578

(m), 519 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.45–7.42 (1H, m), 7.37–7.31 (2H, m), 7.28–7.23 (1H, m), 7.19–7.17 (1H, m), 5.42 (1H, dd, *J* = 2.0, 2.0 Hz), 5.16 (1H, br s), 2.79 (1H, q, *J* = 6.8 Hz), 1.65 (3H, s), 1.18 (12H, s), 0.68 (3H, d, *J* = 6.8 Hz); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 146.5, 128.4, 127.2, 125.7, 124.4, 83.0, 80.8, 75.2, 62.0, 30.5, 25.2, 25.1, 24.9, 24.7, 14.4; HRMS: Calcd for $C_{18}H_{29}B_1N_1O_2$ $[M+H]^+$: 302.22913; Found: 302.23074; specific rotation: $[\alpha]_D^{20}$ –7.99 (*c* 1.50, $CHCl_3$) for an enantiomerically enriched sample of 96:4 e.r.

Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.2 mL/min, 220 nm.

**(2*R*,3*S*)-3-Phenethyl-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine (5.60):** IR ($CH_2Cl_2$): 3370 (br), 3060 (w), 3026 (w), 2976 (m), 2929 (w), 1685 (w), 1600 (w), 1517 (m), 1473 (s), 1449 (s), 1371 (s), 1330 (s), 1266 (m), 1217 (w), 1144 (s), 1076 (m), 1029 (w), 1007 (m), 981 (s), 952 (m), 922 (m), 850 (s), 757 (m), 731 (m), 698 (s), 673 (s), 617 (w), 587 (w), 496 (w), 450 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.33–7.28 (2H, m), 7.25–7.16 (5H, m), 7.13–7.09 (1H, m), 7.05–7.03 (2H, m), 5.59 (1H, d, *J* = 3.2 Hz), 5.38 (1H, d, *J* = 2.8 Hz), 2.73–2.65 (1H, m), 2.56 (1H, dd, *J* = 10.8, 2.4 Hz), 2.40–2.32 (1H, m), 1.46 (3H, s), 1.42–1.37 (1H, m), 1.34–1.29 (1H, m), 1.23 (12H, s); HRMS: Calcd for $C_{25}H_{35}B_1N_1O_2$ $[M+H]^+$: 392.27608; Found: 392.27612; specific rotation: $[\alpha]_D^{20}$ –6.14 (*c* 2.60, $CHCl_3$) for an enantiomerically enriched sample of 97:3 e.r.

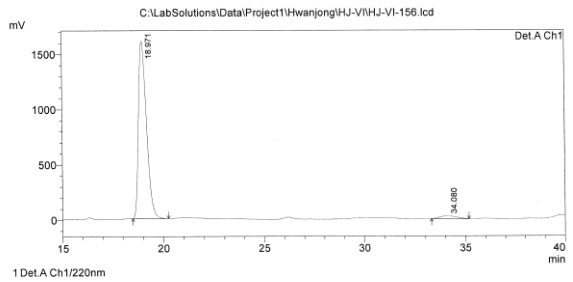
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.3 mL/min, 220 nm.




PeakTable

Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 18.998 | 13082825 | 487209 | 49.743 | 70.534 |
| 2 | 33.619 | 13218029 | 203538 | 50.257 | 29.466 |
| Total | | 26300855 | 690747 | 100.000 | 100.000 |




PeakTable

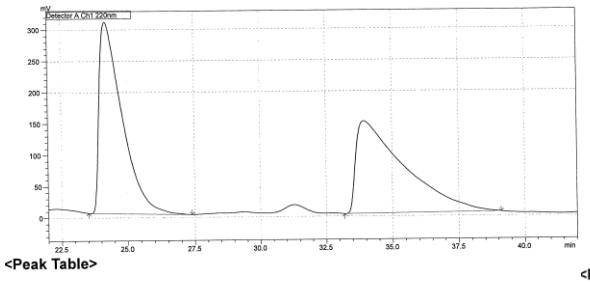
Detector A Ch1 220nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 18.971 | 44341680 | 1607176 | 97.113 | 98.530 |
| 2 | 34.080 | 1318230 | 23986 | 2.887 | 1.470 |
| Total | | 45659910 | 1631162 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 18.998 | 13082825 | 49.743 | 18.971 | 44341680 | 97.113 |
| 33.619 | 13218029 | 50.257 | 34.080 | 1318230 | 2.887 |

**(2*R*,3*S*)-2,6-Diphenyl-3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)hexan-2-amine (5.61):** IR ($CH_2Cl_2$): 3381 (br), 3029 (w), 2976 (m), 2931 (m), 2860 (w), 1708 (w), 1685 (w), 1601 (m), 1517 (m), 1474 (s), 1450 (s), 1372 (s), 1266 (m), 1217 (m), 1146 (s), 1066 (s), 1008 (m), 982 (s), 951 (m), 924 (m), 851 (m), 748 (m), 699 (s), 674 (s), 578 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.35–7.31 (2H, m), 7.26–7.24 (3H, m), 7.23–7.18 (2H, m), 7.13–7.09 (1H, m), 7.07–7.05 (2H, m), 5.53 (1H, d, $J$ = 2.8 Hz), 5.31 (1H, d, $J$ = 2.8 Hz), 2.58 (1H, dd, $J$ = 12.0, 3.2 Hz), 2.47–2.40 (2H, m), 1.72–1.62 (1H, m), 1.50 (3H, s), 1.45–1.37 (2H, m), 1.22 (12H, s), 1.07–1.00 (1H, m); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.9, 142.9, 128.6, 128.4, 128.2, 126.9, 125.5, 125.1, 120.3, 82.8, 80.9, 61.8, 56.5, 35.7, 30.5, 29.6, 28.2, 25.1, 25.0, 24.9, 24.7; specific rotation: $[\alpha]_D^{20}$ –10.83 (*c* 1.66, $CHCl_3$) for an enantiomerically enriched sample of >99:1 e.r.

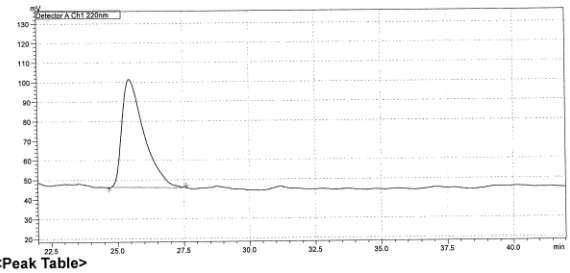
Enantiomeric purity was determined by HPLC analysis in comparison with authentic racemic material derived from acetyl-amine; Chiralcel OD-H column, 90:10 hexanes/*i*-PrOH, 0.5 mL/min, 220 nm.



<Peak Table>

Detector A Channel 1 220nm

| Peak# | Ret. Time | Height | Area | Height% | Area% |
|---|---|---|---|---|---|
| 1 | 24.188 | 305376 | 18294690 | 67.448 | 49.604 |
| 2 | 33.936 | 147380 | 18586427 | 32.552 | 50.396 |
| Total | | 452756 | 36881117 | 100.000 | 100.000 |



<Peak Table>

Detector A Channel 1 220nm

| Peak# | Ret. Time | Height | Area | Height% | Area% |
|---|---|---|---|---|---|
| 1 | 25.474 | 55268 | 3179514 | 100.000 | 100.000 |
| Total | | 55268 | 3179514 | 100.000 | 100.000 |

| Retention Time | Area | Area% | Retention Time | Area | Area% |
|---|---|---|---|---|---|
| 24.188 | 18294690 | 49.604 | 25.474 | 3179514 | 100.000 |
| 33.936 | 18586427 | 50.396 | | | |

■ **Representative Procedure for Synthesis of *β*-Amino Methyl Ketones:** (2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine **5.33** (44.6 mg, 0.100 mmol, 1.0 equiv.) was dissolved in a mixture of thf (0.5 mL) and $H_2O$ (0.5 mL). $NaBO_3$•$4H_2O$ (76.9 mg, 0.500 mmol, 5.0 equiv.) was added to the mixture and it was allowed to stir at 22 °C for three hours. The reaction was quenched by addition of $H_2O$ (5 mL) and aqueous layer was washed with $Et_2O$ (3 x 5 mL). The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (hexanes:$Et_2O$=1:1) to afford (3*R*,4*R*)-4-amino-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-phenylpentan-2-one **5.66** as colorless oil (26.9 mg, 0.0802 mmol, 80% yield).

**(3*R*,4*R*)-4-Amino-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-phenylpentan-2-one (5.66).** IR ($CH_2Cl_2$): 2954 (w), 2928 (w), 2884 (w), 2856 (w), 1703 (m), 1600 (w), 1494

(w), 1471 (w), 1462 (w), 1445 (w), 1358 (w), 1254 (m), 1166 (w), 1093 (s), 1042 (w), 1006 (w), 938 (w), 832 (s), 812 (m), 775 (s), 700 (s), 661 (w), 645 (w), 568 (w), 535 (w) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$, 400 MHz): δ 7.49 (2H, d, *J* = 7.2 Hz), 7.33 (2H, t, *J* = 7.6 Hz), 7.22 (1H, t, *J* = 7.6 Hz), 3.40 (2H, t, *J* = 5.6 Hz), 3.25 (1H, d, *J* = 10.4 Hz), 2.17 (3H, s), 1.90–1.80 (1H, m), 1.43–1.36 (1H, m), 1.26 (3H, s), 0.85 (9H, s), –0.04 (3H, s), –0.07 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 214.0, 147.5, 128.4, 126.7, 125.5, 61.8, 58.9, 57.1, 34.4, 31.8, 30.3, 26.0, 18.4, –5.3, –5.4; HRMS: Calcd for $C_{19}H_{34}N_1O_2Si_1$ $[M+H]^+$: 336.23588; Found: 336.23634.

■ **Pepresentative Experimental Procedure for Cu-Catalyzed Protodeboration of Alkenylboron:** In a $N_2$-filled glove box, an oven-dried vial with a magnetic stir bar was charged with imidazolium salt **5.37** (16.0 mg, 0.0501 mmol, 10.0 mol %), CuCl (5.0 mg, 0.0501 mmol, 10.0 mol %), NaOMe (32.5 mg, 0.601 mmol, 1.2 equiv.) and thf (2.0 mL). The vessel was sealed with a cap and the solution was allowed to stir at 22 °C for one hour. (2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(2-chlorophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-2-amine **5.45** (240.5 mg, 0.501 mmol, 1.0 equiv.) and MeOH (101.4 μL, 2.51 mmol, 5.0 equiv.) were added to the solution, and the vial was re-sealed and removed from the glove box. The resulting solution was allowed to stir at 60 °C for eight hours before the reaction was quenched by passing the mixture through a short plug of Celite and silica gel and eluted with $Et_2O$ (3 × 5 mL). The filtrate was concentrated *in vacuo*. The crude product was purified by silica gel chromatography (hexanes:$Et_2O$=2:1 to 1:5) to afford (2*R*,3*S*)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-

(2-chlorophenyl)pent-4-en-2-amine **5.76** as colorless oil (127.7 mg, 0.361 mmol, 72% yield).

**(2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-phenylpent-4-en-2-amine (5.75).** IR ($CH_2Cl_2$): 3354 (br), 2928 (m), 2856 (m), 1664 (m), 1599 (w), 1551 (w), 1462 (m), 1446 (m), 1377 (m), 1252 (m), 1143 (m), 1094 (s), 1030 (m), 1005 (m), 949 (m), 917 (m), 881 (m), 833 (s), 773 (s), 700 (s), 665 (m), 566 (w), 496 (w), 475 (w), 451 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.43–7.41 (2H, m), 7.35–7.29 (2H, m), 7.20 (1H, t, *J* = 6.8 Hz), 5.61 (1H, dt, *J* = 17.2, 10.4 Hz), 5.18 (1H, dd, *J* = 10.4, 2.0 Hz), 5.08 (1H, dd, *J* = 17.6, 2.0 Hz), 3.53–3.47 (1H, m), 3.40–3.34 (1H, m), 2.47 (1H, t, *J* = 10.0 Hz), 2.27 (3H, s), 1.48–1.45 (1H, m), 1.35–1.32 (1H, m), 0.84 (9H, s), –0.05 (3H, s), –0.07 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 144.6, 141.5, 141.0, 131.9, 128.1, 107.0, 56.8, 51.8, 46.1, 32.9, 31.8, 30.5, 25.7, –5.3; HRMS: Calcd for $C_{19}H_{34}N_1O_1Si_1$ $[M+H]^+$: 320.24097; Found: 320.24125.

■ **Synthesis of Medicinally Active Molecule**

**Experimental Procedure for Synthesis of Thiourea 5.78 from 5.76:** To a solution of **5.76** (522 mg, 1.48 mmol, 1.0 equiv.) in thf (10 mL) was added benzoyl isothiocyanate **5.77** (298 μL, 2.21 mmol, 1.5 equiv.) in one portion. The solution was allowed to stir at 22 °C for two hours. Water (10 mL) was added to quench the reaction. The organic layer was separated and the aqueous layer was extracted by EtOAc (3 × 5 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (hexanes:$Et_2O$=10:1 to 5:1) to afford the desired product **5.78** as pale yellow oil (643 mg, 1.243 mmol, 84% yield).

***N*-(((2*R*,3*S*)-3-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2-(2-chlorophenyl)pent-4-en-2-yl)carbamothioyl)benzamide (5.78).** IR ($CH_2Cl_2$): 3258 (br), 3066 (w), 2952 (m), 2925 (m), 2854 (m), 2262 (w), 1724 (m), 1694 (s), 1599 (m), 1544 (s), 1504 (m), 1469 (s), 1430 (m), 1376 (m), 1362 (m), 1250 (s), 1095 (s), 1034 (s), 1002 (m), 922 (m), 881 (m), 834 (s), 807 (m), 773 (s), 757 (s), 708 (s), 675 (m), 666 (m), 617 (m), 574 (m), 459 (w), 441 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 11.74 (1H, br s), 8.80 (1H, br s), 7.84 (2H, d, *J* = 7.6 Hz), 7.60 (1H, t, *J* = 7.6 Hz), 7.50 (2H, t, *J* = 7.6 Hz), 7.32 (2H, dd, *J* = 21.2, 8.0 Hz), 7.17 (2H, dt, *J* = 21.2, 7.6 Hz), 5.44–5.35 (1H, m), 4.90 (1H, d, *J* = 10.0 Hz), 4.80 (1H, d, *J* = 16.8 Hz), 3.76–3.71 (1H, m), 3.64–3.57 (1H, m), 3.49 (1H, t, *J* = 10.0 Hz), 2.13 (3H, s), 0.93 (9H, s), 0.90–0.80 (2H, m), 0.09 (3H, s), 0.07 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 177.8, 166.6, 139.4, 135.8, 133.4, 132.1, 131.5, 131.4, 130.7, 129.1, 128.3, 127.6, 126.2, 119.0, 64.7, 46.9, 32.1, 32.0, 29.8, 26.1, 18.4, –5.3; HRMS: Calcd for $C_{27}H_{38}Cl_1N_2O_2S_1Si_1$ $[M+H]^+$: 517.21118; Found: 517.21210.

**Experimental Procedure for TBS-Deprotection of 5.78:** To a solution of *N*-(((2*R*,3*S*)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-(2-chlorophenyl)pent-4-en-2-yl)carbamothioyl)benzamide **5.78** (611 mg, 1.18 mmol, 1.0 equiv.) in thf (10 mL) was added 1.0 M solution of tetra-*n*-butylammonium fluoride in thf (2.23 mL, 2.23 mmol, 2.0 equiv.) slowly through a syringe. The solution was allowed to stir at 60 °C for 18 hours. The reaction was quenched by the addition of $H_2O$ (50 mL) and the organic layer was extracted with EtOAc (3 × 50 mL) and washed with brine. The organic layer was dried over $Na_2SO_4$, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography (hexanes:$Et_2O$=2:1 to 1:5) to afford *N*-(((2*R*,3*S*)-2-(2-

chlorophenyl)-3-(2-hydroxyethyl)pent-4-en-2-yl)carbamothioyl)benzamide **5.79** as colorless oil (404.4 mg, 1.00 mmol, 85% yield).

***N*-(((2*R*,3*S*)-2-(2-Chlorophenyl)-3-(2-hydroxyethyl)pent-4-en-2-yl)carbamothioyl)benzamide (5.79).** IR ($CH_2Cl_2$): 3234 (w), 3067 (w), 2925 (w), 1671 (w), 1588 (s), 1567 (s), 1504 (w), 1471 (m), 1446 (m), 1428 (s), 1348 (s), 1292 (m), 1268 (m), 1140 (s), 1110 (w), 1059 (m), 1034 (s), 1017 (s), 994 (m), 915 (w), 826 (w), 757 (m), 714 (s), 689 (m), 617 (w), 574 (w), 461 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 11.4 (1H, br s), 8.21 (2H, d, *J* = 8.0 Hz), 7.50–7.38 (5H, m), 7.27–7.25 (2H, m), 5.74–5.65 (1H, m), 5.06 (1H, d, *J* = 11.2 Hz), 5.05 (1H, d, *J* = 16.4 Hz), 4.46–4.41 (1H, m), 4.35–4.29 (1H, m), 3.96 (1H, dd, *J* = 10.0, 7.6 Hz), 2.17–2.10 (1H, m), 2.03–1.99 (1H, m), 1.78 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 168.6, 166.8, 150.1, 140.7, 137.0, 132.9, 132.1, 131.8, 129.5, 129.4, 128.9, 128.1, 127.3, 118.7, 69.9, 64.9, 45.1, 31.4, 24.3; HRMS: Calcd for $C_{21}H_{24}Cl_1N_2O_2S_1$ $[M+H]^+$: 403.12470; Found: 403.12444.

**Experimental Procedure for Cu-Catalyzed Intramolecular Ullmann Coupling of 5.79:** To a vial were added CuI (9.5 mg, 0.0496 mmol, 10 mol %), 8-hydroxyquinoline **5.80** (14.4 mg, 0.0993 mmol, 20 mol %), and $Cs_2CO_3$ (323.4 mg, 0.993 mmol, 2.0 equv.) under $N_2$ atm. The vial was then evacuated and backfilled with $N_2$ atm. *N*-(((2*R*,3*S*)-2-(2-Chlorophenyl)-3-(2-hydroxyethyl)pent-4-en-2-yl)carbamothioyl)benzamide **5.79** (200 mg, 0.496 mmol, 1.0 equiv.) and toluene (10 mL) were added by syringe at 22 °C. The solution was allowed to stir at 110 °C for 24 hour. The solution was allowed to reach 22 °C and then diluted with $CH_2Cl_2$ (50 mL). The slurry was filtered and washed with $CH_2Cl_2$ (3 × 50 mL). The solvent was removed *in vacuo*, and the residue was purified by

silica gel column chromatography to afford *N*-(((4*S*,5*R*)-5-methyl-4-vinyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide **5.81** (141.8 mg, 0.387 mmol, 78% yield).

***N*-(((4*S*,5*R*)-5-Methyl-4-vinyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide (5.81).** IR ($CH_2Cl_2$): 3241 (w), 3066 (w), 2923 (m), 2852 (w), 1695 (m), 1666 (m), 1591 (s), 1568 (s), 1504 (w), 1468 (s), 1447 (m), 1429 (s), 1350 (s), 1291 (w), 1266 (s), 1204 (m), 1140 (s), 1059 (s), 1034 (s), 1017 (s), 994 (s), 913 (s), 802 (m), 756 (s), 712 (s), 689 (s), 646 (m), 617 (w), 574 (w), 497 (w), 460 (w), 434 (w), 418 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): δ 11.46 (1H, br s), 8.22 (2H, d, $J$ = 7.2 Hz), 7.49–7.44 (2H, m), 7.43–7.39 (3H, m), 7.28–7.25 (2H, m), 5.71–5.67 (1H, m), 5.06 (1H, d, $J$ = 10.2 Hz), 5.05 (1H, d, $J$ = 17.4 Hz), 4.45–4.42 (1H, m), 4.32 (1H, ddd, $J$ = 12.0, 9.0, 3.0 Hz), 3.97 (1H, dd, $J$ = 12.6, 7.8 Hz), 2.18–2.12 (1H, m), 2.07–2.02 (1H, m), 1.78 (3H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 188.3, 166.9, 140.7, 137.1, 137.0, 134.4, 132.9, 132.1, 129.5, 129.4, 128.9, 128.1, 127.3, 118.7, 69.9, 64.9, 45.1, 37.3, 31.4.

**Experimental Procedure for Ozonolysis/Reduction of 5.81:** *N*-(((4*S*,5*R*)-5-Methyl-4-vinyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide **5.81** (47.5 mg, 0.130 mmol, 1.0 equiv.) was dissolved in a 5:1 mixture of $CH_2Cl_2$ (2 mL) and MeOH (0.4 mL) and $NaHCO_3$ (87.1 mg, 1.04 mmol, 8.0 equiv.) was added. The solution was allowed to cool to –78 °C, then ozone was bubbled through the solution until it turned to blue for about five minutes. To the solution was added $NaBH_4$ (24.5 mg, 0.648 mmol, 5.0 equiv.) and it was allowed to warm to 4 °C slowly for 18 hours. The reaction was quenched by the addition of $H_2O$ (5 mL) and the organic layer was extracted with $CH_2Cl_2$

(3 × 5 mL) and washed with brine. The organic layer was dried over $Na_2SO_4$, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography (hexanes:EtOAc=1:1 to EtOAc 100%) to afford *N*-(((4*R*,5*R*)-4-(hydroxymethyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide **5.82** as white solid (34.7 mg, 0.0937 mmol, 72% yield).

***N*-(((4*R*,5*R*)-4-(Hydroxymethyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide (5.82).** IR ($CH_2Cl_2$): 3406 (w), 3067 (w), 2928 (w), 1597 (s), 1586 (s), 1565 (s), 1490 (m), 1460 (m), 1445 (m), 1356 (s), 1271 (w), 1191 (m), 1136 (m), 1097 (w), 1046 (m), 1035 (m), 1007 (m), 947 (w), 826 (w), 758 (m), 715 (m), 687 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 12.0 (1H, br s), 8.3 (2H, d, *J* = 8.0 Hz), 7.70 (1H, dd, *J* = 8.0, 1.6 Hz), 7.49 (1H, tt, *J* = 7.2, 1.6 Hz), 7.44–7.39 (3H, m), 7.36 (1H, dd, *J* = 8.0, 1.6 Hz), 7.28 (1H, td, *J* = 7.6, 1.6 Hz), 4.65 (1H, dd, *J* = 12.4, 1.2 Hz), 4.55 (1H, dd, *J* = 12.4, 1.6 Hz), 3.65 (2H, dd, *J* = 7.2, 4.4 Hz), 3.25–3.20 (1H, m), 2.00 (3H, s), 1.39–1.29 (1H, m), 1.26–1.16 (1H, m); $^{13}C$ NMR ($CDCl_3$, 100 MHz): δ 179.5, 162.3, 139.0, 137.2, 132.5, 132.0, 131.3, 129.4, 129.3, 128.2, 128.1, 127.3, 64.8, 60.8, 59.9, 34.7, 29.3; HRMS: Calcd for $C_{20}H_{23}N_2O_3S_1$ $[M+H]^+$: 371.14239; Found: 371.13653.

**Experimental Procedure for Cyclization of 5.81:** To a solution of *N*-(((4*R*,5*R*)-4-(hydroxymethyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-5-yl)carbamothioyl)benzamide **5.82** (11.3 mg, 0.0305 mmol, 1.0 equiv.) in $CH_2Cl_2$ (1 mL) at –20 °C was added pyridine (7.4 μL, 0.0915 mmol, 3.0 equiv.), followed by dropwise addition of trifluoromethanesulfonic anhydride (7.7 μL, 0.0458 mmol, 1.5 equiv.). After the addition, the solution was allowed to stir at –20 °C for two hours. The reaction was

quenched by the addition of saturated aq. Solution of $NaHCO_3$ (5 mL) and the organic layer was extracted with $CH_2Cl_2$ (3 × 5 mL) and washed with brine. The organic layer was dried over $Na_2SO_4$ and concentrated *in vacuo* to afford *N*-((4a*R*,11b*R*)-11b-methyl-4a,5,6,11b-tetrahydro-4H-benzo[2,3]oxepino[4,5-*d*][1,3]thiazin-2-yl)benzamide **5.83** as yellow solid (8.1 mg, 0.0230 mmol, 75% yield).

## ■ X-Ray Crystal Structure of *rac*-5.33

**Table 1.** Crystal data and structure refinement for *rac*-**5.33**.

| | | |
|---|---|---|
| Identification code | $C_{25}H_{44}BNO_3Si(C_6H_{13}BO_3)$ | |
| Empirical formula | $C_{31}\ H_{57}\ B_2\ N\ O_6\ Si$ | |
| Formula weight | 589.48 | |
| Temperature | 100(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Triclinic | |
| Space group | P-1 | |
| Unit cell dimensions | a = 6.7751(10) Å | α= 100.057(2)°. |
| | b = 10.8228(15) Å | β= 95.125(3)°. |
| | c = 24.618(4) Å | γ = 100.679(2)°. |
| Volume | 1732.7(4) $Å^3$ | |
| Z | 2 | |
| Density (calculated) | 1.130 $Mg/m^3$ | |
| Absorption coefficient | 0.107 $mm^{-1}$ | |
| F(000) | 644 | |
| Crystal size | 0.380 x 0.220 x 0.100 $mm^3$ | |
| Theta range for data collection | 1.952 to 28.424°. | |
| Index ranges | -9<=h<=9, -14<=k<=14, -32<=l<=32 | |
| Reflections collected | 60094 | |
| Independent reflections | 8614 [R(int) = 0.1048] | |
| Completeness to theta = 25.242° | 100.0 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7457 and 0.7033 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 8614 / 0 / 393 | |
| Goodness-of-fit on $F^2$ | 1.002 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0502, wR2 = 0.0921 | |
| R indices (all data) | R1 = 0.1046, wR2 = 0.1113 | |
| Extinction coefficient | na | |
| Largest diff. peak and hole | 0.329 and -0.279 $e.Å^{-3}$ | |

**Table 2.** Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for *rac*-**5.33**. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Si(1) | 1074(1) | 2844(1) | 5976(1) | 24(1) |
| O(1) | 6496(2) | 5783(1) | 8586(1) | 19(1) |
| O(2) | 9852(2) | 6364(1) | 8433(1) | 18(1) |
| O(3) | 3015(2) | 3300(1) | 6467(1) | 26(1) |
| O(4) | 14484(2) | 10081(1) | 8432(1) | 21(1) |
| O(5) | 13183(2) | 7832(1) | 8227(1) | 21(1) |
| O(6) | 11060(2) | 9377(1) | 8424(1) | 21(1) |
| N(1) | 7236(2) | 7249(1) | 7887(1) | 17(1) |
| B(1) | 7759(3) | 5994(2) | 8157(1) | 18(1) |
| B(2) | 12909(3) | 9040(2) | 8353(1) | 18(1) |
| C(1) | 7045(3) | 6879(2) | 7263(1) | 18(1) |
| C(2) | 6070(3) | 5426(2) | 7156(1) | 20(1) |
| C(3) | 7253(3) | 4929(2) | 7593(1) | 20(1) |
| C(4) | 9194(3) | 7074(2) | 7098(1) | 22(1) |
| C(5) | 5870(3) | 7687(2) | 6967(1) | 21(1) |
| C(6) | 5645(3) | 8890(2) | 7219(1) | 25(1) |
| C(7) | 4686(3) | 9640(2) | 6922(1) | 34(1) |
| C(8) | 3922(3) | 9182(2) | 6370(1) | 41(1) |
| C(9) | 4130(3) | 7983(2) | 6116(1) | 40(1) |
| C(10) | 5107(3) | 7244(2) | 6407(1) | 31(1) |
| C(11) | 3807(3) | 5157(2) | 7222(1) | 23(1) |
| C(12) | 2833(3) | 3746(2) | 7039(1) | 26(1) |
| C(13) | -396(3) | 4132(2) | 5977(1) | 39(1) |
| C(14) | -618(3) | 1368(2) | 6091(1) | 34(1) |
| C(15) | 2251(3) | 2556(2) | 5315(1) | 26(1) |
| C(16) | 3666(3) | 3794(2) | 5258(1) | 35(1) |
| C(17) | 3484(3) | 1504(2) | 5321(1) | 36(1) |
| C(18) | 619(4) | 2166(2) | 4808(1) | 44(1) |
| C(19) | 7736(3) | 3782(2) | 7501(1) | 26(1) |
| C(20) | 7665(3) | 6376(2) | 9114(1) | 20(1) |

| | | | | |
|---|---|---|---|---|
| C(21) | 9829(3) | 6201(2) | 9004(1) | 21(1) |
| C(22) | 7542(3) | 7792(2) | 9250(1) | 22(1) |
| C(23) | 6795(3) | 5694(2) | 9555(1) | 25(1) |
| C(24) | 10159(3) | 4851(2) | 9024(1) | 27(1) |
| C(25) | 11520(3) | 7177(2) | 9380(1) | 28(1) |
| C(26) | 13719(3) | 11191(2) | 8691(1) | 23(1) |
| C(27) | 11399(3) | 10779(2) | 8499(1) | 24(1) |
| C(28) | 14277(3) | 11344(2) | 9313(1) | 33(1) |
| C(29) | 14765(3) | 12353(2) | 8486(1) | 34(1) |
| C(30) | 10784(3) | 11086(2) | 7937(1) | 36(1) |
| C(31) | 10076(3) | 11239(2) | 8925(1) | 36(1) |

**Table 3.** Bond lengths [Å] and angles [°] for *rac*-**5.33**.

| | |
|---|---|
| Si(1)-O(3) | 1.6433(14) |
| Si(1)-C(13) | 1.857(2) |
| Si(1)-C(14) | 1.866(2) |
| Si(1)-C(15) | 1.879(2) |
| O(1)-C(20) | 1.435(2) |
| O(1)-B(1) | 1.441(2) |
| O(2)-C(21) | 1.448(2) |
| O(2)-B(1) | 1.468(2) |
| O(3)-C(12) | 1.430(2) |
| O(4)-B(2) | 1.373(2) |
| O(4)-C(26) | 1.464(2) |
| O(5)-B(2) | 1.342(2) |
| O(5)-H(5O) | 0.83(2) |
| O(6)-B(2) | 1.385(2) |
| O(6)-C(27) | 1.468(2) |
| N(1)-C(1) | 1.505(2) |
| N(1)-B(1) | 1.692(2) |
| N(1)-H(1NA) | 0.884(19) |
| N(1)-H(1NB) | 0.901(19) |
| B(1)-C(3) | 1.607(3) |

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|---|---|
| C(1)-C(5) | 1.519(2) |
| C(1)-C(4) | 1.533(2) |
| C(1)-C(2) | 1.555(2) |
| C(2)-C(3) | 1.516(2) |
| C(2)-C(11) | 1.536(2) |
| C(2)-H(3) | 1.0000 |
| C(3)-C(19) | 1.329(2) |
| C(4)-H(5A) | 0.9800 |
| C(4)-H(5B) | 0.9800 |
| C(4)-H(5C) | 0.9800 |
| C(5)-C(6) | 1.383(3) |
| C(5)-C(10) | 1.395(3) |
| C(6)-C(7) | 1.392(3) |
| C(6)-H(7) | 0.9500 |
| C(7)-C(8) | 1.379(3) |
| C(7)-H(8) | 0.9500 |
| C(8)-C(9) | 1.376(3) |
| C(8)-H(9) | 0.9500 |
| C(9)-C(10) | 1.380(3) |
| C(9)-H(10) | 0.9500 |
| C(10)-H(11) | 0.9500 |
| C(11)-C(12) | 1.517(2) |
| C(11)-H(12A) | 0.9900 |
| C(11)-H(12B) | 0.9900 |
| C(12)-H(13A) | 0.9900 |
| C(12)-H(13B) | 0.9900 |
| C(13)-H(14A) | 0.9800 |
| C(13)-H(14B) | 0.9800 |
| C(13)-H(14C) | 0.9800 |
| C(14)-H(15A) | 0.9800 |
| C(14)-H(15B) | 0.9800 |
| C(14)-H(15C) | 0.9800 |
| C(15)-C(16) | 1.532(3) |
| C(15)-C(17) | 1.534(3) |
| C(15)-C(18) | 1.535(3) |
| C(16)-H(17A) | 0.9800 |

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|---|---|
| C(16)-H(17B) | 0.9800 |
| C(16)-H(17C) | 0.9800 |
| C(17)-H(18A) | 0.9800 |
| C(17)-H(18B) | 0.9800 |
| C(17)-H(18C) | 0.9800 |
| C(18)-H(19A) | 0.9800 |
| C(18)-H(19B) | 0.9800 |
| C(18)-H(19C) | 0.9800 |
| C(19)-H(20A) | 0.9500 |
| C(19)-H(20B) | 0.9500 |
| C(20)-C(23) | 1.520(2) |
| C(20)-C(22) | 1.531(2) |
| C(20)-C(21) | 1.553(2) |
| C(21)-C(25) | 1.518(2) |
| C(21)-C(24) | 1.527(2) |
| C(22)-H(23A) | 0.9800 |
| C(22)-H(23B) | 0.9800 |
| C(22)-H(23C) | 0.9800 |
| C(23)-H(24A) | 0.9800 |
| C(23)-H(24B) | 0.9800 |
| C(23)-H(24C) | 0.9800 |
| C(24)-H(25A) | 0.9800 |
| C(24)-H(25B) | 0.9800 |
| C(24)-H(25C) | 0.9800 |
| C(25)-H(26A) | 0.9800 |
| C(25)-H(26B) | 0.9800 |
| C(25)-H(26C) | 0.9800 |
| C(26)-C(29) | 1.515(3) |
| C(26)-C(28) | 1.516(3) |
| C(26)-C(27) | 1.558(3) |
| C(27)-C(30) | 1.518(3) |
| C(27)-C(31) | 1.518(3) |
| C(28)-H(29A) | 0.9800 |
| C(28)-H(29B) | 0.9800 |
| C(28)-H(29C) | 0.9800 |
| C(29)-H(30A) | 0.9800 |

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|---|---|
| C(29)-H(30B) | 0.9800 |
| C(29)-H(30C) | 0.9800 |
| C(30)-H(31A) | 0.9800 |
| C(30)-H(31B) | 0.9800 |
| C(30)-H(31C) | 0.9800 |
| C(31)-H(32A) | 0.9800 |
| C(31)-H(32B) | 0.9800 |
| C(31)-H(32C) | 0.9800 |

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|---|---|
| O(3)-Si(1)-C(13) | 110.22(9) |
| O(3)-Si(1)-C(14) | 110.18(9) |
| C(13)-Si(1)-C(14) | 108.97(10) |
| O(3)-Si(1)-C(15) | 104.21(8) |
| C(13)-Si(1)-C(15) | 110.86(10) |
| C(14)-Si(1)-C(15) | 112.34(9) |
| C(20)-O(1)-B(1) | 108.01(13) |
| C(21)-O(2)-B(1) | 107.99(13) |
| C(12)-O(3)-Si(1) | 123.46(11) |
| B(2)-O(4)-C(26) | 106.65(13) |
| B(2)-O(5)-H(5O) | 110.9(14) |
| B(2)-O(6)-C(27) | 106.96(13) |
| C(1)-N(1)-B(1) | 108.13(13) |
| C(1)-N(1)-H(1NA) | 110.5(12) |
| B(1)-N(1)-H(1NA) | 107.5(12) |
| C(1)-N(1)-H(1NB) | 112.1(12) |
| B(1)-N(1)-H(1NB) | 111.7(12) |
| H(1NA)-N(1)-H(1NB) | 106.8(17) |
| O(1)-B(1)-O(2) | 106.24(15) |
| O(1)-B(1)-C(3) | 116.23(14) |
| O(2)-B(1)-C(3) | 118.66(15) |
| O(1)-B(1)-N(1) | 109.31(14) |
| O(2)-B(1)-N(1) | 107.62(13) |
| C(3)-B(1)-N(1) | 97.99(14) |
| O(5)-B(2)-O(4) | 122.29(17) |
| O(5)-B(2)-O(6) | 124.65(16) |
| O(4)-B(2)-O(6) | 113.06(16) |

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|---|---|
| N(1)-C(1)-C(5) | 113.20(14) |
| N(1)-C(1)-C(4) | 107.26(14) |
| C(5)-C(1)-C(4) | 108.26(14) |
| N(1)-C(1)-C(2) | 102.33(13) |
| C(5)-C(1)-C(2) | 115.16(14) |
| C(4)-C(1)-C(2) | 110.30(14) |
| C(3)-C(2)-C(11) | 110.09(14) |
| C(3)-C(2)-C(1) | 103.58(14) |
| C(11)-C(2)-C(1) | 113.44(14) |
| C(3)-C(2)-H(3) | 109.9 |
| C(11)-C(2)-H(3) | 109.9 |
| C(1)-C(2)-H(3) | 109.9 |
| C(19)-C(3)-C(2) | 123.06(17) |
| C(19)-C(3)-B(1) | 127.92(17) |
| C(2)-C(3)-B(1) | 109.02(14) |
| C(1)-C(4)-H(5A) | 109.5 |
| C(1)-C(4)-H(5B) | 109.5 |
| H(5A)-C(4)-H(5B) | 109.5 |
| C(1)-C(4)-H(5C) | 109.5 |
| H(5A)-C(4)-H(5C) | 109.5 |
| H(5B)-C(4)-H(5C) | 109.5 |
| C(6)-C(5)-C(10) | 118.35(18) |
| C(6)-C(5)-C(1) | 122.49(17) |
| C(10)-C(5)-C(1) | 119.01(17) |
| C(5)-C(6)-C(7) | 120.79(19) |
| C(5)-C(6)-H(7) | 119.6 |
| C(7)-C(6)-H(7) | 119.6 |
| C(8)-C(7)-C(6) | 120.1(2) |
| C(8)-C(7)-H(8) | 120.0 |
| C(6)-C(7)-H(8) | 120.0 |
| C(9)-C(8)-C(7) | 119.6(2) |
| C(9)-C(8)-H(9) | 120.2 |
| C(7)-C(8)-H(9) | 120.2 |
| C(8)-C(9)-C(10) | 120.5(2) |
| C(8)-C(9)-H(10) | 119.7 |
| C(10)-C(9)-H(10) | 119.7 |

| | |
|---|---|
| C(9)-C(10)-C(5) | 120.7(2) |
| C(9)-C(10)-H(11) | 119.7 |
| C(5)-C(10)-H(11) | 119.7 |
| C(12)-C(11)-C(2) | 112.25(15) |
| C(12)-C(11)-H(12A) | 109.2 |
| C(2)-C(11)-H(12A) | 109.2 |
| C(12)-C(11)-H(12B) | 109.2 |
| C(2)-C(11)-H(12B) | 109.2 |
| H(12A)-C(11)-H(12B) | 107.9 |
| O(3)-C(12)-C(11) | 110.90(15) |
| O(3)-C(12)-H(13A) | 109.5 |
| C(11)-C(12)-H(13A) | 109.5 |
| O(3)-C(12)-H(13B) | 109.5 |
| C(11)-C(12)-H(13B) | 109.5 |
| H(13A)-C(12)-H(13B) | 108.0 |
| Si(1)-C(13)-H(14A) | 109.5 |
| Si(1)-C(13)-H(14B) | 109.5 |
| H(14A)-C(13)-H(14B) | 109.5 |
| Si(1)-C(13)-H(14C) | 109.5 |
| H(14A)-C(13)-H(14C) | 109.5 |
| H(14B)-C(13)-H(14C) | 109.5 |
| Si(1)-C(14)-H(15A) | 109.5 |
| Si(1)-C(14)-H(15B) | 109.5 |
| H(15A)-C(14)-H(15B) | 109.5 |
| Si(1)-C(14)-H(15C) | 109.5 |
| H(15A)-C(14)-H(15C) | 109.5 |
| H(15B)-C(14)-H(15C) | 109.5 |
| C(16)-C(15)-C(17) | 108.72(17) |
| C(16)-C(15)-C(18) | 108.02(17) |
| C(17)-C(15)-C(18) | 109.38(17) |
| C(16)-C(15)-Si(1) | 109.37(13) |
| C(17)-C(15)-Si(1) | 110.53(13) |
| C(18)-C(15)-Si(1) | 110.76(15) |
| C(15)-C(16)-H(17A) | 109.5 |
| C(15)-C(16)-H(17B) | 109.5 |
| H(17A)-C(16)-H(17B) | 109.5 |

| | |
|---|---|
| C(15)-C(16)-H(17C) | 109.5 |
| H(17A)-C(16)-H(17C) | 109.5 |
| H(17B)-C(16)-H(17C) | 109.5 |
| C(15)-C(17)-H(18A) | 109.5 |
| C(15)-C(17)-H(18B) | 109.5 |
| H(18A)-C(17)-H(18B) | 109.5 |
| C(15)-C(17)-H(18C) | 109.5 |
| H(18A)-C(17)-H(18C) | 109.5 |
| H(18B)-C(17)-H(18C) | 109.5 |
| C(15)-C(18)-H(19A) | 109.5 |
| C(15)-C(18)-H(19B) | 109.5 |
| H(19A)-C(18)-H(19B) | 109.5 |
| C(15)-C(18)-H(19C) | 109.5 |
| H(19A)-C(18)-H(19C) | 109.5 |
| H(19B)-C(18)-H(19C) | 109.5 |
| C(3)-C(19)-H(20A) | 120.0 |
| C(3)-C(19)-H(20B) | 120.0 |
| H(20A)-C(19)-H(20B) | 120.0 |
| O(1)-C(20)-C(23) | 108.31(14) |
| O(1)-C(20)-C(22) | 109.68(14) |
| C(23)-C(20)-C(22) | 109.63(15) |
| O(1)-C(20)-C(21) | 102.11(14) |
| C(23)-C(20)-C(21) | 114.89(15) |
| C(22)-C(20)-C(21) | 111.86(14) |
| O(2)-C(21)-C(25) | 110.34(14) |
| O(2)-C(21)-C(24) | 107.26(14) |
| C(25)-C(21)-C(24) | 109.46(15) |
| O(2)-C(21)-C(20) | 101.97(13) |
| C(25)-C(21)-C(20) | 114.34(15) |
| C(24)-C(21)-C(20) | 113.01(14) |
| C(20)-C(22)-H(23A) | 109.5 |
| C(20)-C(22)-H(23B) | 109.5 |
| H(23A)-C(22)-H(23B) | 109.5 |
| C(20)-C(22)-H(23C) | 109.5 |
| H(23A)-C(22)-H(23C) | 109.5 |
| H(23B)-C(22)-H(23C) | 109.5 |

| | |
|---|---|
| C(20)-C(23)-H(24A) | 109.5 |
| C(20)-C(23)-H(24B) | 109.5 |
| H(24A)-C(23)-H(24B) | 109.5 |
| C(20)-C(23)-H(24C) | 109.5 |
| H(24A)-C(23)-H(24C) | 109.5 |
| H(24B)-C(23)-H(24C) | 109.5 |
| C(21)-C(24)-H(25A) | 109.5 |
| C(21)-C(24)-H(25B) | 109.5 |
| H(25A)-C(24)-H(25B) | 109.5 |
| C(21)-C(24)-H(25C) | 109.5 |
| H(25A)-C(24)-H(25C) | 109.5 |
| H(25B)-C(24)-H(25C) | 109.5 |
| C(21)-C(25)-H(26A) | 109.5 |
| C(21)-C(25)-H(26B) | 109.5 |
| H(26A)-C(25)-H(26B) | 109.5 |
| C(21)-C(25)-H(26C) | 109.5 |
| H(26A)-C(25)-H(26C) | 109.5 |
| H(26B)-C(25)-H(26C) | 109.5 |
| O(4)-C(26)-C(29) | 108.00(15) |
| O(4)-C(26)-C(28) | 106.31(15) |
| C(29)-C(26)-C(28) | 110.59(16) |
| O(4)-C(26)-C(27) | 102.67(13) |
| C(29)-C(26)-C(27) | 114.71(16) |
| C(28)-C(26)-C(27) | 113.74(16) |
| O(6)-C(27)-C(30) | 106.90(15) |
| O(6)-C(27)-C(31) | 107.60(14) |
| C(30)-C(27)-C(31) | 111.12(17) |
| O(6)-C(27)-C(26) | 102.32(13) |
| C(30)-C(27)-C(26) | 113.25(16) |
| C(31)-C(27)-C(26) | 114.80(16) |
| C(26)-C(28)-H(29A) | 109.5 |
| C(26)-C(28)-H(29B) | 109.5 |
| H(29A)-C(28)-H(29B) | 109.5 |
| C(26)-C(28)-H(29C) | 109.5 |
| H(29A)-C(28)-H(29C) | 109.5 |
| H(29B)-C(28)-H(29C) | 109.5 |

| | |
|---|---|
| C(26)-C(29)-H(30A) | 109.5 |
| C(26)-C(29)-H(30B) | 109.5 |
| H(30A)-C(29)-H(30B) | 109.5 |
| C(26)-C(29)-H(30C) | 109.5 |
| H(30A)-C(29)-H(30C) | 109.5 |
| H(30B)-C(29)-H(30C) | 109.5 |
| C(27)-C(30)-H(31A) | 109.5 |
| C(27)-C(30)-H(31B) | 109.5 |
| H(31A)-C(30)-H(31B) | 109.5 |
| C(27)-C(30)-H(31C) | 109.5 |
| H(31A)-C(30)-H(31C) | 109.5 |
| H(31B)-C(30)-H(31C) | 109.5 |
| C(27)-C(31)-H(32A) | 109.5 |
| C(27)-C(31)-H(32B) | 109.5 |
| H(32A)-C(31)-H(32B) | 109.5 |
| C(27)-C(31)-H(32C) | 109.5 |
| H(32A)-C(31)-H(32C) | 109.5 |
| H(32B)-C(31)-H(32C) | 109.5 |

Symmetry transformations used to generate equivalent atoms:

**Table 4.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for *rac*-**5.33**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| Si(1) | 21(1) | 21(1) | 27(1) | -1(1) | 0(1) | 1(1) |
| O(1) | 16(1) | 20(1) | 18(1) | 4(1) | -1(1) | -1(1) |
| O(2) | 15(1) | 19(1) | 21(1) | 7(1) | 0(1) | 2(1) |
| O(3) | 22(1) | 31(1) | 22(1) | -4(1) | 2(1) | 1(1) |
| O(4) | 18(1) | 17(1) | 27(1) | 2(1) | 4(1) | 1(1) |
| O(5) | 16(1) | 17(1) | 29(1) | 4(1) | 5(1) | 2(1) |
| O(6) | 17(1) | 14(1) | 32(1) | 5(1) | 4(1) | 2(1) |
| N(1) | 16(1) | 18(1) | 18(1) | 2(1) | 2(1) | 3(1) |
| B(1) | 16(1) | 16(1) | 22(1) | 6(1) | 2(1) | 5(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| B(2) | 18(1) | 19(1) | 17(1) | 4(1) | 1(1) | 2(1) |
| C(1) | 18(1) | 21(1) | 15(1) | 1(1) | 3(1) | 4(1) |
| C(2) | 18(1) | 20(1) | 19(1) | -1(1) | 3(1) | 2(1) |
| C(3) | 16(1) | 19(1) | 24(1) | 6(1) | 6(1) | 1(1) |
| C(4) | 21(1) | 24(1) | 21(1) | 3(1) | 5(1) | 5(1) |
| C(5) | 17(1) | 29(1) | 21(1) | 8(1) | 4(1) | 6(1) |
| C(6) | 23(1) | 30(1) | 24(1) | 11(1) | 6(1) | 7(1) |
| C(7) | 37(1) | 38(1) | 38(1) | 19(1) | 12(1) | 18(1) |
| C(8) | 38(1) | 61(2) | 37(1) | 29(1) | 9(1) | 24(1) |
| C(9) | 38(1) | 64(2) | 24(1) | 15(1) | 1(1) | 19(1) |
| C(10) | 32(1) | 43(1) | 21(1) | 6(1) | 2(1) | 14(1) |
| C(11) | 18(1) | 27(1) | 21(1) | 0(1) | 3(1) | 2(1) |
| C(12) | 21(1) | 31(1) | 22(1) | 3(1) | 4(1) | -2(1) |
| C(13) | 35(1) | 38(1) | 45(1) | 3(1) | 3(1) | 13(1) |
| C(14) | 29(1) | 29(1) | 38(1) | 0(1) | 6(1) | -2(1) |
| C(15) | 29(1) | 22(1) | 24(1) | 2(1) | -1(1) | 2(1) |
| C(16) | 41(1) | 27(1) | 34(1) | 5(1) | 9(1) | 0(1) |
| C(17) | 47(1) | 30(1) | 37(1) | 9(1) | 17(1) | 13(1) |
| C(18) | 47(1) | 45(1) | 30(1) | 2(1) | -5(1) | -4(1) |
| C(19) | 26(1) | 24(1) | 29(1) | 5(1) | 6(1) | 4(1) |
| C(20) | 18(1) | 21(1) | 18(1) | 6(1) | -1(1) | 0(1) |
| C(21) | 18(1) | 21(1) | 22(1) | 7(1) | -1(1) | 1(1) |
| C(22) | 22(1) | 24(1) | 22(1) | 5(1) | 4(1) | 4(1) |
| C(23) | 24(1) | 26(1) | 25(1) | 10(1) | 2(1) | 2(1) |
| C(24) | 24(1) | 27(1) | 33(1) | 12(1) | 1(1) | 7(1) |
| C(25) | 22(1) | 32(1) | 27(1) | 8(1) | -3(1) | 1(1) |
| C(26) | 21(1) | 17(1) | 32(1) | 1(1) | 4(1) | 4(1) |
| C(27) | 21(1) | 14(1) | 37(1) | 7(1) | 4(1) | 3(1) |
| C(28) | 30(1) | 32(1) | 33(1) | -3(1) | 4(1) | 4(1) |
| C(29) | 25(1) | 20(1) | 55(2) | 6(1) | 7(1) | -1(1) |
| C(30) | 29(1) | 27(1) | 53(2) | 17(1) | -5(1) | 1(1) |
| C(31) | 26(1) | 21(1) | 59(2) | 1(1) | 12(1) | 6(1) |

**Table 5.** Hydrogen coordinates (x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for *rac*-**5.33**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(5O) | 12150(30) | 7311(19) | 8258(8) | 31 |
| H(1NA) | 6080(30) | 7400(17) | 7994(8) | 21 |
| H(1NB) | 8180(30) | 7969(18) | 8020(8) | 21 |
| H(3) | 6278 | 5004 | 6776 | 24 |
| H(5A) | 9859 | 7979 | 7216 | 33 |
| H(5B) | 9128 | 6821 | 6694 | 33 |
| H(5C) | 9969 | 6546 | 7280 | 33 |
| H(7) | 6152 | 9208 | 7601 | 30 |
| H(8) | 4557 | 10470 | 7099 | 41 |
| H(9) | 3256 | 9689 | 6167 | 49 |
| H(10) | 3597 | 7663 | 5737 | 48 |
| H(11) | 5261 | 6424 | 6224 | 37 |
| H(12A) | 3640 | 5442 | 7617 | 28 |
| H(12B) | 3103 | 5660 | 6998 | 28 |
| H(13A) | 3495 | 3243 | 7272 | 31 |
| H(13B) | 1384 | 3617 | 7093 | 31 |
| H(14A) | -945 | 4292 | 6332 | 59 |
| H(14B) | -1510 | 3865 | 5672 | 59 |
| H(14C) | 493 | 4918 | 5928 | 59 |
| H(15A) | 149 | 685 | 6093 | 50 |
| H(15B) | -1752 | 1093 | 5791 | 50 |
| H(15C) | -1140 | 1552 | 6449 | 50 |
| H(17A) | 4284 | 3645 | 4914 | 52 |
| H(17B) | 4729 | 4058 | 5577 | 52 |
| H(17C) | 2890 | 4470 | 5248 | 52 |
| H(18A) | 4137 | 1393 | 4981 | 54 |
| H(18B) | 2582 | 696 | 5340 | 54 |
| H(18C) | 4521 | 1749 | 5646 | 54 |
| H(19A) | -136 | 2852 | 4795 | 66 |
| H(19B) | -311 | 1377 | 4836 | 66 |

| | | | | |
|---|---|---|---|---|
| H(19C) | 1263 | 2019 | 4468 | 66 |
| H(20A) | 7336 | 3231 | 7148 | 32 |
| H(20B) | 8479 | 3512 | 7788 | 32 |
| H(23A) | 8256 | 8252 | 8993 | 34 |
| H(23B) | 8170 | 8163 | 9632 | 34 |
| H(23C) | 6119 | 7869 | 9214 | 34 |
| H(24A) | 5427 | 5844 | 9594 | 37 |
| H(24B) | 7658 | 6026 | 9911 | 37 |
| H(24C) | 6737 | 4771 | 9446 | 37 |
| H(25A) | 9017 | 4220 | 8803 | 41 |
| H(25B) | 10256 | 4730 | 9410 | 41 |
| H(25C) | 11415 | 4736 | 8872 | 41 |
| H(26A) | 12832 | 7013 | 9282 | 42 |
| H(26B) | 11416 | 7105 | 9768 | 42 |
| H(26C) | 11406 | 8042 | 9332 | 42 |
| H(29A) | 13570 | 10591 | 9440 | 50 |
| H(29B) | 13880 | 12114 | 9506 | 50 |
| H(29C) | 15742 | 11425 | 9397 | 50 |
| H(30A) | 16208 | 12554 | 8630 | 51 |
| H(30B) | 14156 | 13086 | 8617 | 51 |
| H(30C) | 14609 | 12170 | 8079 | 51 |
| H(31A) | 11610 | 10738 | 7665 | 54 |
| H(31B) | 10993 | 12018 | 7969 | 54 |
| H(31C) | 9351 | 10700 | 7815 | 54 |
| H(32A) | 8647 | 10914 | 8776 | 53 |
| H(32B) | 10356 | 12179 | 9008 | 53 |
| H(32C) | 10371 | 10923 | 9267 | 53 |

**Table 6.** Torsion angles [°] for *rac*-**5.33**.

| | |
|---|---|
| C(13)-Si(1)-O(3)-C(12) | 54.51(16) |
| C(14)-Si(1)-O(3)-C(12) | -65.79(16) |
| C(15)-Si(1)-O(3)-C(12) | 173.50(14) |
| C(20)-O(1)-B(1)-O(2) | 17.23(17) |
| C(20)-O(1)-B(1)-C(3) | 151.68(15) |
| C(20)-O(1)-B(1)-N(1) | -98.63(15) |
| C(21)-O(2)-B(1)-O(1) | 7.49(17) |
| C(21)-O(2)-B(1)-C(3) | -125.65(16) |
| C(21)-O(2)-B(1)-N(1) | 124.48(14) |
| C(1)-N(1)-B(1)-O(1) | -134.31(14) |
| C(1)-N(1)-B(1)-O(2) | 110.72(15) |
| C(1)-N(1)-B(1)-C(3) | -12.84(16) |
| C(26)-O(4)-B(2)-O(5) | -166.39(17) |
| C(26)-O(4)-B(2)-O(6) | 12.9(2) |
| C(27)-O(6)-B(2)-O(5) | -174.23(18) |
| C(27)-O(6)-B(2)-O(4) | 6.5(2) |
| B(1)-N(1)-C(1)-C(5) | 159.38(14) |
| B(1)-N(1)-C(1)-C(4) | -81.27(16) |
| B(1)-N(1)-C(1)-C(2) | 34.82(16) |
| N(1)-C(1)-C(2)-C(3) | -44.07(16) |
| C(5)-C(1)-C(2)-C(3) | -167.31(14) |
| C(4)-C(1)-C(2)-C(3) | 69.80(17) |
| N(1)-C(1)-C(2)-C(11) | 75.26(17) |
| C(5)-C(1)-C(2)-C(11) | -48.0(2) |
| C(4)-C(1)-C(2)-C(11) | -170.87(15) |
| C(11)-C(2)-C(3)-C(19) | 95.0(2) |
| C(1)-C(2)-C(3)-C(19) | -143.36(17) |
| C(11)-C(2)-C(3)-B(1) | -84.50(17) |
| C(1)-C(2)-C(3)-B(1) | 37.11(17) |
| O(1)-B(1)-C(3)-C(19) | -78.3(2) |
| O(2)-B(1)-C(3)-C(19) | 50.3(3) |
| N(1)-B(1)-C(3)-C(19) | 165.48(17) |
| O(1)-B(1)-C(3)-C(2) | 101.17(17) |
| O(2)-B(1)-C(3)-C(2) | -130.18(16) |

| | |
|---|---|
| N(1)-B(1)-C(3)-C(2) | -15.02(16) |
| N(1)-C(1)-C(5)-C(6) | 21.8(2) |
| C(4)-C(1)-C(5)-C(6) | -96.9(2) |
| C(2)-C(1)-C(5)-C(6) | 139.10(17) |
| N(1)-C(1)-C(5)-C(10) | -162.77(16) |
| C(4)-C(1)-C(5)-C(10) | 78.5(2) |
| C(2)-C(1)-C(5)-C(10) | -45.5(2) |
| C(10)-C(5)-C(6)-C(7) | -0.2(3) |
| C(1)-C(5)-C(6)-C(7) | 175.25(17) |
| C(5)-C(6)-C(7)-C(8) | 0.8(3) |
| C(6)-C(7)-C(8)-C(9) | -0.5(3) |
| C(7)-C(8)-C(9)-C(10) | -0.4(3) |
| C(8)-C(9)-C(10)-C(5) | 1.1(3) |
| C(6)-C(5)-C(10)-C(9) | -0.8(3) |
| C(1)-C(5)-C(10)-C(9) | -176.36(18) |
| C(3)-C(2)-C(11)-C(12) | -72.29(19) |
| C(1)-C(2)-C(11)-C(12) | 172.18(15) |
| Si(1)-O(3)-C(12)-C(11) | -112.93(15) |
| C(2)-C(11)-C(12)-O(3) | -59.7(2) |
| O(3)-Si(1)-C(15)-C(16) | -58.95(15) |
| C(13)-Si(1)-C(15)-C(16) | 59.60(16) |
| C(14)-Si(1)-C(15)-C(16) | -178.22(14) |
| O(3)-Si(1)-C(15)-C(17) | 60.72(14) |
| C(13)-Si(1)-C(15)-C(17) | 179.27(14) |
| C(14)-Si(1)-C(15)-C(17) | -58.54(16) |
| O(3)-Si(1)-C(15)-C(18) | -177.89(13) |
| C(13)-Si(1)-C(15)-C(18) | -59.34(16) |
| C(14)-Si(1)-C(15)-C(18) | 62.85(16) |
| B(1)-O(1)-C(20)-C(23) | -154.74(14) |
| B(1)-O(1)-C(20)-C(22) | 85.66(16) |
| B(1)-O(1)-C(20)-C(21) | -33.10(16) |
| B(1)-O(2)-C(21)-C(25) | -148.64(15) |
| B(1)-O(2)-C(21)-C(24) | 92.20(16) |
| B(1)-O(2)-C(21)-C(20) | -26.77(16) |
| O(1)-C(20)-C(21)-O(2) | 36.32(15) |
| C(23)-C(20)-C(21)-O(2) | 153.31(14) |

| | |
|---|---|
| C(22)-C(20)-C(21)-O(2) | -80.88(16) |
| O(1)-C(20)-C(21)-C(25) | 155.40(14) |
| C(23)-C(20)-C(21)-C(25) | -87.61(19) |
| C(22)-C(20)-C(21)-C(25) | 38.2(2) |
| O(1)-C(20)-C(21)-C(24) | -78.49(17) |
| C(23)-C(20)-C(21)-C(24) | 38.5(2) |
| C(22)-C(20)-C(21)-C(24) | 164.31(15) |
| B(2)-O(4)-C(26)-C(29) | -146.86(16) |
| B(2)-O(4)-C(26)-C(28) | 94.43(16) |
| B(2)-O(4)-C(26)-C(27) | -25.29(18) |
| B(2)-O(6)-C(27)-C(30) | 97.74(17) |
| B(2)-O(6)-C(27)-C(31) | -142.82(16) |
| B(2)-O(6)-C(27)-C(26) | -21.51(18) |
| O(4)-C(26)-C(27)-O(6) | 28.25(17) |
| C(29)-C(26)-C(27)-O(6) | 145.12(16) |
| C(28)-C(26)-C(27)-O(6) | -86.17(17) |
| O(4)-C(26)-C(27)-C(30) | -86.44(17) |
| C(29)-C(26)-C(27)-C(30) | 30.4(2) |
| C(28)-C(26)-C(27)-C(30) | 159.15(17) |
| O(4)-C(26)-C(27)-C(31) | 144.47(15) |
| C(29)-C(26)-C(27)-C(31) | -98.6(2) |
| C(28)-C(26)-C(27)-C(31) | 30.1(2) |

Symmetry transformations used to generate equivalent atoms:

**Table 7.** Hydrogen bonds for *rac*-**5.33** [Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(5)-H(5O)...O(2) | 0.83(2) | 1.83(2) | 2.6516(17) | 170(2) |
| N(1)-H(1NA)...O(5)#1 | 0.884(19) | 2.20(2) | 3.084(2) | 177.1(17) |
| N(1)-H(1NB)...O(6) | 0.901(19) | 2.268(19) | 3.1425(19) | 163.8(16) |

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z

## ■ X-Ray Crystal Structure of 5.70

**Table 1.** Crystal data and structure refinement for **5.70**.

| | | |
|---|---|---|
| Identification code | $C_{13}H_{19}NO_2$ | |
| Empirical formula | $C_{13}\ H_{19}\ N\ O_2$ | |
| Formula weight | 221.29 | |
| Temperature | 100(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 7.8093(10) Å | α= 90°. |
| | b = 11.0945(15) Å | β= 90°. |
| | c = 14.1156(19) Å | γ = 90°. |
| Volume | 1223.0(3) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.202 $Mg/m^3$ | |
| Absorption coefficient | 0.642 $mm^{-1}$ | |
| F(000) | 480 | |
| Crystal size | 0.440 x 0.320 x 0.250 $mm^3$ | |
| Theta range for data collection | 5.070 to 66.891°. | |
| Index ranges | -9<=h<=9, -13<=k<=13, -16<=l<=16 | |
| Reflections collected | 8468 | |
| Independent reflections | 2150 [R(int) = 0.0326] | |
| Completeness to theta = 66.891° | 98.8 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7528 and 0.6456 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 2150 / 2 / 159 | |
| Goodness-of-fit on $F^2$ | 1.097 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0301, wR2 = 0.0792 | |
| R indices (all data) | R1 = 0.0301, wR2 = 0.0793 | |
| Absolute structure parameter | -0.01(6) | |
| Extinction coefficient | na | |
| Largest diff. peak and hole | 0.233 and -0.130 $e.Å^{-3}$ | |

**Table 2.** Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for **5.70**. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 8740(2) | 2934(2) | 735(1) | 31(1) |
| O(2) | 5599(2) | 5512(1) | 2495(1) | 31(1) |
| N(1) | 2229(2) | 2562(2) | 1210(1) | 20(1) |
| C(1) | 7642(2) | 2978(2) | 1534(1) | 25(1) |
| C(2) | 5929(2) | 3488(2) | 1245(1) | 20(1) |
| C(3) | 4684(2) | 3520(2) | 2082(1) | 16(1) |
| C(4) | 2742(2) | 3625(2) | 1775(1) | 17(1) |
| C(5) | 1650(2) | 3627(2) | 2675(1) | 16(1) |
| C(6) | 1429(2) | 2560(2) | 3185(1) | 20(1) |
| C(7) | 504(2) | 2538(2) | 4020(1) | 25(1) |
| C(8) | -218(2) | 3589(2) | 4375(1) | 27(1) |
| C(9) | -21(3) | 4652(2) | 3877(1) | 26(1) |
| C(10) | 899(2) | 4676(2) | 3033(1) | 21(1) |
| C(11) | 5190(2) | 4517(2) | 2776(1) | 19(1) |
| C(12) | 5216(3) | 4223(2) | 3808(1) | 30(1) |
| C(13) | 2437(2) | 4732(2) | 1156(1) | 24(1) |

**Table 3.** Bond lengths [Å] and angles [°] for **5.70**.

| | |
|---|---|
| O(1)-C(1) | 1.418(2) |
| O(1)-H(3N) | 0.80(3) |
| O(2)-C(11) | 1.215(2) |
| N(1)-C(4) | 1.479(2) |
| N(1)-H(1N) | 0.87(2) |
| N(1)-H(2N) | 0.873(19) |
| C(1)-C(2) | 1.509(2) |
| C(1)-H(1A) | 0.9900 |
| C(1)-H(1B) | 0.9900 |

| | |
|---|---|
| C(2)-C(3) | 1.530(2) |
| C(2)-H(2A) | 0.9900 |
| C(2)-H(2B) | 0.9900 |
| C(3)-C(11) | 1.530(2) |
| C(3)-C(4) | 1.582(2) |
| C(3)-H(3) | 1.0000 |
| C(4)-C(13) | 1.527(2) |
| C(4)-C(5) | 1.529(2) |
| C(5)-C(6) | 1.397(2) |
| C(5)-C(10) | 1.398(2) |
| C(6)-C(7) | 1.383(3) |
| C(6)-H(6) | 0.9500 |
| C(7)-C(8) | 1.389(3) |
| C(7)-H(7) | 0.9500 |
| C(8)-C(9) | 1.381(3) |
| C(8)-H(8) | 0.9500 |
| C(9)-C(10) | 1.392(3) |
| C(9)-H(9) | 0.9500 |
| C(10)-H(10) | 0.9500 |
| C(11)-C(12) | 1.492(3) |
| C(12)-H(12A) | 0.9800 |
| C(12)-H(12B) | 0.9800 |
| C(12)-H(12C) | 0.9800 |
| C(13)-H(13A) | 0.9800 |
| C(13)-H(13B) | 0.9800 |
| C(13)-H(13C) | 0.9800 |

| | |
|---|---|
| C(1)-O(1)-H(3N) | 112(2) |
| C(4)-N(1)-H(1N) | 111.7(17) |
| C(4)-N(1)-H(2N) | 110.5(16) |
| H(1N)-N(1)-H(2N) | 105(2) |
| O(1)-C(1)-C(2) | 109.52(15) |
| O(1)-C(1)-H(1A) | 109.8 |
| C(2)-C(1)-H(1A) | 109.8 |
| O(1)-C(1)-H(1B) | 109.8 |
| C(2)-C(1)-H(1B) | 109.8 |

| | |
|---|---|
| H(1A)-C(1)-H(1B) | 108.2 |
| C(1)-C(2)-C(3) | 111.31(14) |
| C(1)-C(2)-H(2A) | 109.4 |
| C(3)-C(2)-H(2A) | 109.4 |
| C(1)-C(2)-H(2B) | 109.4 |
| C(3)-C(2)-H(2B) | 109.4 |
| H(2A)-C(2)-H(2B) | 108.0 |
| C(2)-C(3)-C(11) | 110.35(13) |
| C(2)-C(3)-C(4) | 113.57(13) |
| C(11)-C(3)-C(4) | 111.70(13) |
| C(2)-C(3)-H(3) | 106.9 |
| C(11)-C(3)-H(3) | 106.9 |
| C(4)-C(3)-H(3) | 106.9 |
| N(1)-C(4)-C(13) | 106.92(14) |
| N(1)-C(4)-C(5) | 107.34(13) |
| C(13)-C(4)-C(5) | 112.81(15) |
| N(1)-C(4)-C(3) | 110.37(14) |
| C(13)-C(4)-C(3) | 111.42(14) |
| C(5)-C(4)-C(3) | 107.91(13) |
| C(6)-C(5)-C(10) | 117.88(15) |
| C(6)-C(5)-C(4) | 119.70(15) |
| C(10)-C(5)-C(4) | 122.39(15) |
| C(7)-C(6)-C(5) | 121.22(16) |
| C(7)-C(6)-H(6) | 119.4 |
| C(5)-C(6)-H(6) | 119.4 |
| C(6)-C(7)-C(8) | 120.38(18) |
| C(6)-C(7)-H(7) | 119.8 |
| C(8)-C(7)-H(7) | 119.8 |
| C(9)-C(8)-C(7) | 119.18(17) |
| C(9)-C(8)-H(8) | 120.4 |
| C(7)-C(8)-H(8) | 120.4 |
| C(8)-C(9)-C(10) | 120.65(17) |
| C(8)-C(9)-H(9) | 119.7 |
| C(10)-C(9)-H(9) | 119.7 |
| C(9)-C(10)-C(5) | 120.69(17) |
| C(9)-C(10)-H(10) | 119.7 |

| | |
|---|---|
| C(5)-C(10)-H(10) | 119.7 |
| O(2)-C(11)-C(12) | 120.87(17) |
| O(2)-C(11)-C(3) | 120.99(16) |
| C(12)-C(11)-C(3) | 118.12(16) |
| C(11)-C(12)-H(12A) | 109.5 |
| C(11)-C(12)-H(12B) | 109.5 |
| H(12A)-C(12)-H(12B) | 109.5 |
| C(11)-C(12)-H(12C) | 109.5 |
| H(12A)-C(12)-H(12C) | 109.5 |
| H(12B)-C(12)-H(12C) | 109.5 |
| C(4)-C(13)-H(13A) | 109.5 |
| C(4)-C(13)-H(13B) | 109.5 |
| H(13A)-C(13)-H(13B) | 109.5 |
| C(4)-C(13)-H(13C) | 109.5 |
| H(13A)-C(13)-H(13C) | 109.5 |
| H(13B)-C(13)-H(13C) | 109.5 |

Symmetry transformations used to generate equivalent atoms:

**Table 4.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **5.70**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 9(1) | 58(1) | 25(1) | -11(1) | 0(1) | 4(1) |
| O(2) | 30(1) | 20(1) | 42(1) | -2(1) | 2(1) | -6(1) |
| N(1) | 14(1) | 27(1) | 20(1) | -4(1) | 1(1) | -1(1) |
| C(1) | 14(1) | 38(1) | 23(1) | -3(1) | 0(1) | 4(1) |
| C(2) | 11(1) | 27(1) | 20(1) | -1(1) | 0(1) | 0(1) |
| C(3) | 11(1) | 15(1) | 21(1) | 2(1) | 0(1) | 0(1) |
| C(4) | 12(1) | 18(1) | 20(1) | 2(1) | 0(1) | 0(1) |
| C(5) | 9(1) | 18(1) | 21(1) | -1(1) | -3(1) | 0(1) |
| C(6) | 17(1) | 18(1) | 25(1) | -1(1) | 0(1) | -1(1) |
| C(7) | 23(1) | 27(1) | 24(1) | 3(1) | 1(1) | -8(1) |
| C(8) | 18(1) | 41(1) | 21(1) | -5(1) | 3(1) | -2(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(9) | 19(1) | 30(1) | 28(1) | -10(1) | -2(1) | 7(1) |
| C(10) | 17(1) | 18(1) | 26(1) | -2(1) | -5(1) | 2(1) |
| C(11) | 10(1) | 20(1) | 28(1) | -3(1) | 1(1) | 0(1) |
| C(12) | 22(1) | 41(1) | 26(1) | -5(1) | -3(1) | -6(1) |
| C(13) | 17(1) | 28(1) | 29(1) | 9(1) | 2(1) | 5(1) |

**Table 5.** Hydrogen coordinates (x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for **5.70**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(3N) | 9690(40) | 2750(30) | 880(20) | 46(8) |
| H(1N) | 2730(30) | 2550(20) | 661(15) | 30(6) |
| H(2N) | 2550(30) | 1898(19) | 1491(16) | 29(6) |
| H(1A) | 8158 | 3491 | 2032 | 30 |
| H(1B) | 7489 | 2157 | 1796 | 30 |
| H(2A) | 5437 | 2987 | 732 | 23 |
| H(2B) | 6088 | 4315 | 996 | 23 |
| H(3) | 4811 | 2737 | 2425 | 19 |
| H(6) | 1923 | 1835 | 2953 | 24 |
| H(7) | 361 | 1801 | 4352 | 30 |
| H(8) | -840 | 3577 | 4953 | 32 |
| H(9) | -519 | 5373 | 4113 | 31 |
| H(10) | 1018 | 5413 | 2697 | 25 |
| H(12A) | 6104 | 3619 | 3932 | 45 |
| H(12B) | 4098 | 3903 | 3997 | 45 |
| H(12C) | 5464 | 4955 | 4172 | 45 |
| H(13A) | 3038 | 4633 | 551 | 37 |
| H(13B) | 2871 | 5451 | 1480 | 37 |
| H(13C) | 1207 | 4824 | 1038 | 37 |

**Table 6.** Torsion angles [°] for **5.70**.

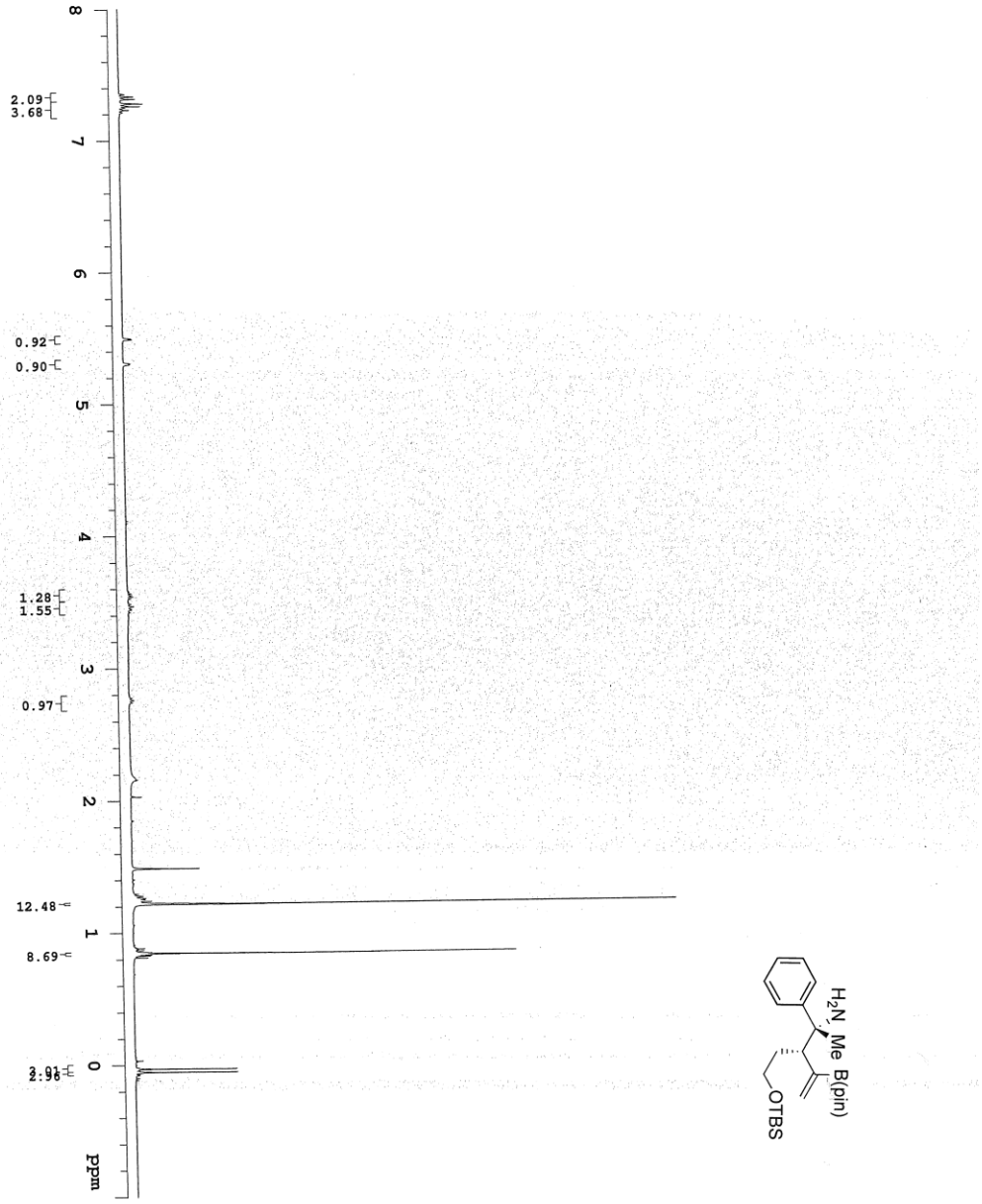
| | |
|---|---|
| O(1)-C(1)-C(2)-C(3) | 178.48(15) |
| C(1)-C(2)-C(3)-C(11) | 72.82(19) |
| C(1)-C(2)-C(3)-C(4) | -160.87(15) |
| C(2)-C(3)-C(4)-N(1) | 62.09(19) |
| C(11)-C(3)-C(4)-N(1) | -172.31(14) |
| C(2)-C(3)-C(4)-C(13) | -56.5(2) |
| C(11)-C(3)-C(4)-C(13) | 69.06(19) |
| C(2)-C(3)-C(4)-C(5) | 179.10(14) |
| C(11)-C(3)-C(4)-C(5) | -55.30(18) |
| N(1)-C(4)-C(5)-C(6) | 45.61(19) |
| C(13)-C(4)-C(5)-C(6) | 163.13(15) |
| C(3)-C(4)-C(5)-C(6) | -73.35(18) |
| N(1)-C(4)-C(5)-C(10) | -136.63(16) |
| C(13)-C(4)-C(5)-C(10) | -19.1(2) |
| C(3)-C(4)-C(5)-C(10) | 104.42(17) |
| C(10)-C(5)-C(6)-C(7) | -0.3(2) |
| C(4)-C(5)-C(6)-C(7) | 177.56(16) |
| C(5)-C(6)-C(7)-C(8) | -0.5(3) |
| C(6)-C(7)-C(8)-C(9) | 0.9(3) |
| C(7)-C(8)-C(9)-C(10) | -0.5(3) |
| C(8)-C(9)-C(10)-C(5) | -0.3(3) |
| C(6)-C(5)-C(10)-C(9) | 0.7(3) |
| C(4)-C(5)-C(10)-C(9) | -177.08(16) |
| C(2)-C(3)-C(11)-O(2) | 44.2(2) |
| C(4)-C(3)-C(11)-O(2) | -83.17(19) |
| C(2)-C(3)-C(11)-C(12) | -134.11(17) |
| C(4)-C(3)-C(11)-C(12) | 98.54(18) |

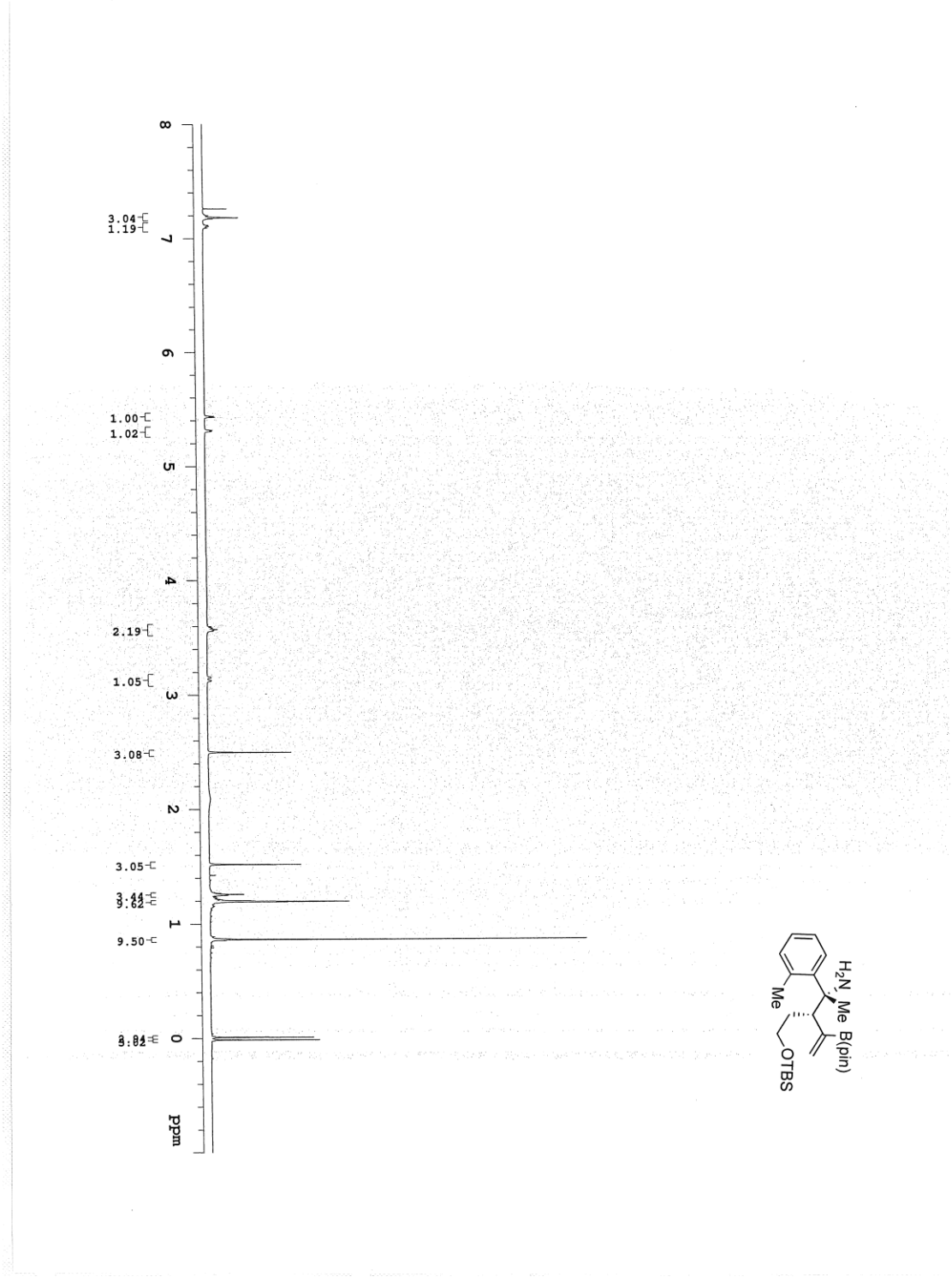
Symmetry transformations used to generate equivalent atoms:

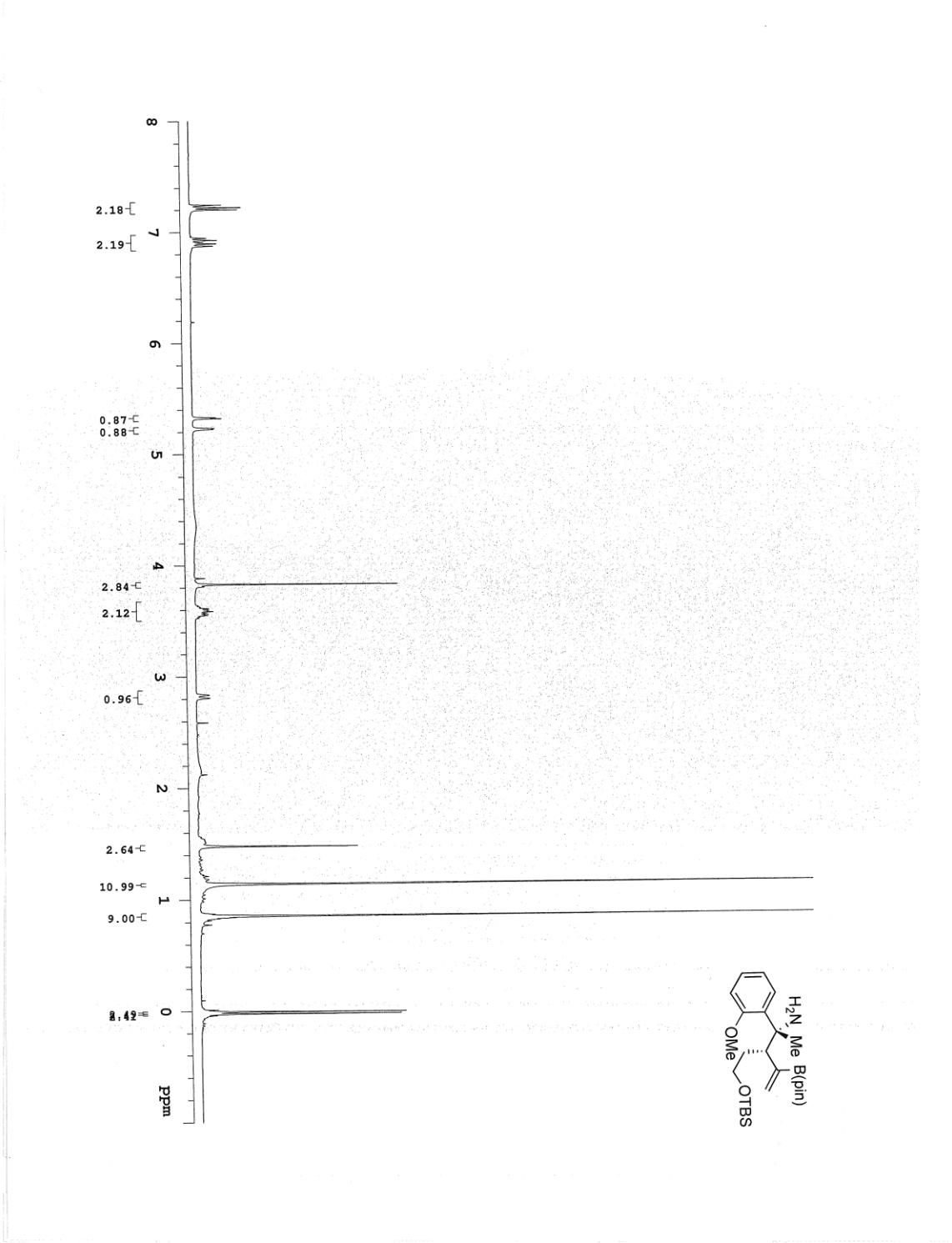
**Table 7.** Hydrogen bonds for **5.70** [Å and °].

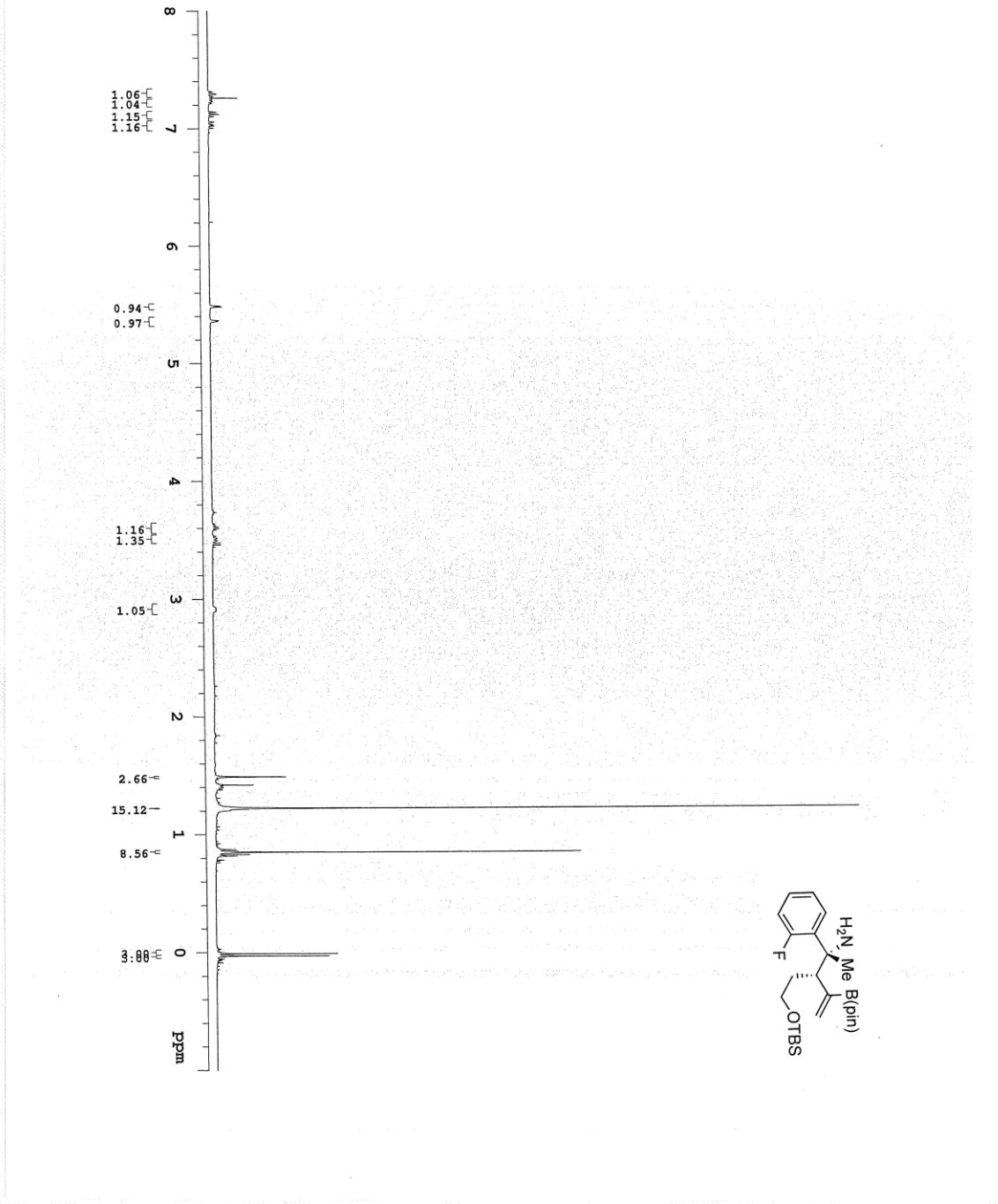
| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(1)-H(3N)...N(1)#1 | 0.80(3) | 2.05(3) | 2.837(2) | 171(3) |
| N(1)-H(1N)...O(1)#2 | 0.87(2) | 2.19(2) | 3.039(2) | 166(2) |
| N(1)-H(2N)...O(2)#3 | 0.873(19) | 2.55(2) | 3.374(2) | 158(2) |

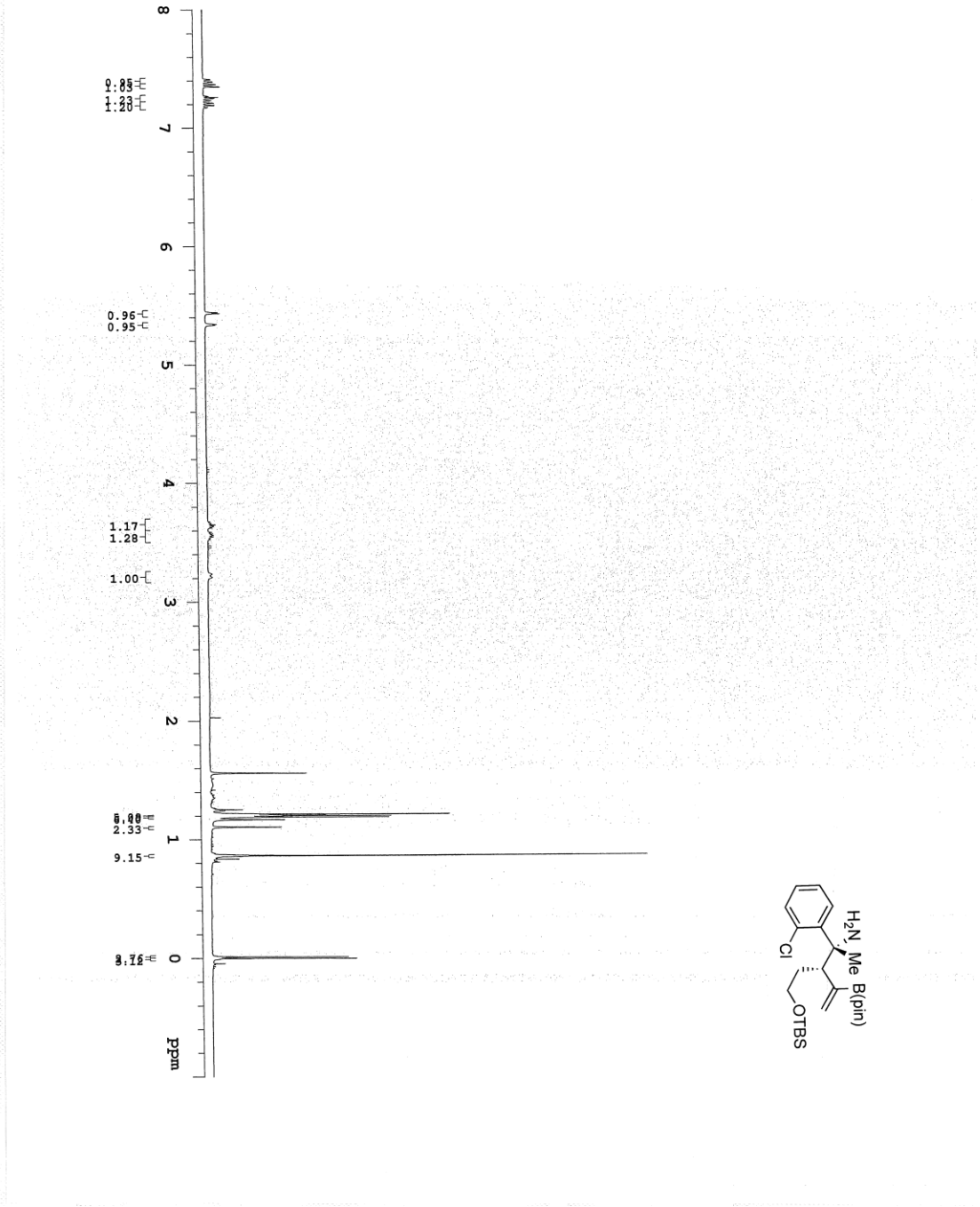
Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z  #2 x-1/2,-y+1/2,-z  #3 -x+1,y-1/2,-z+1/2

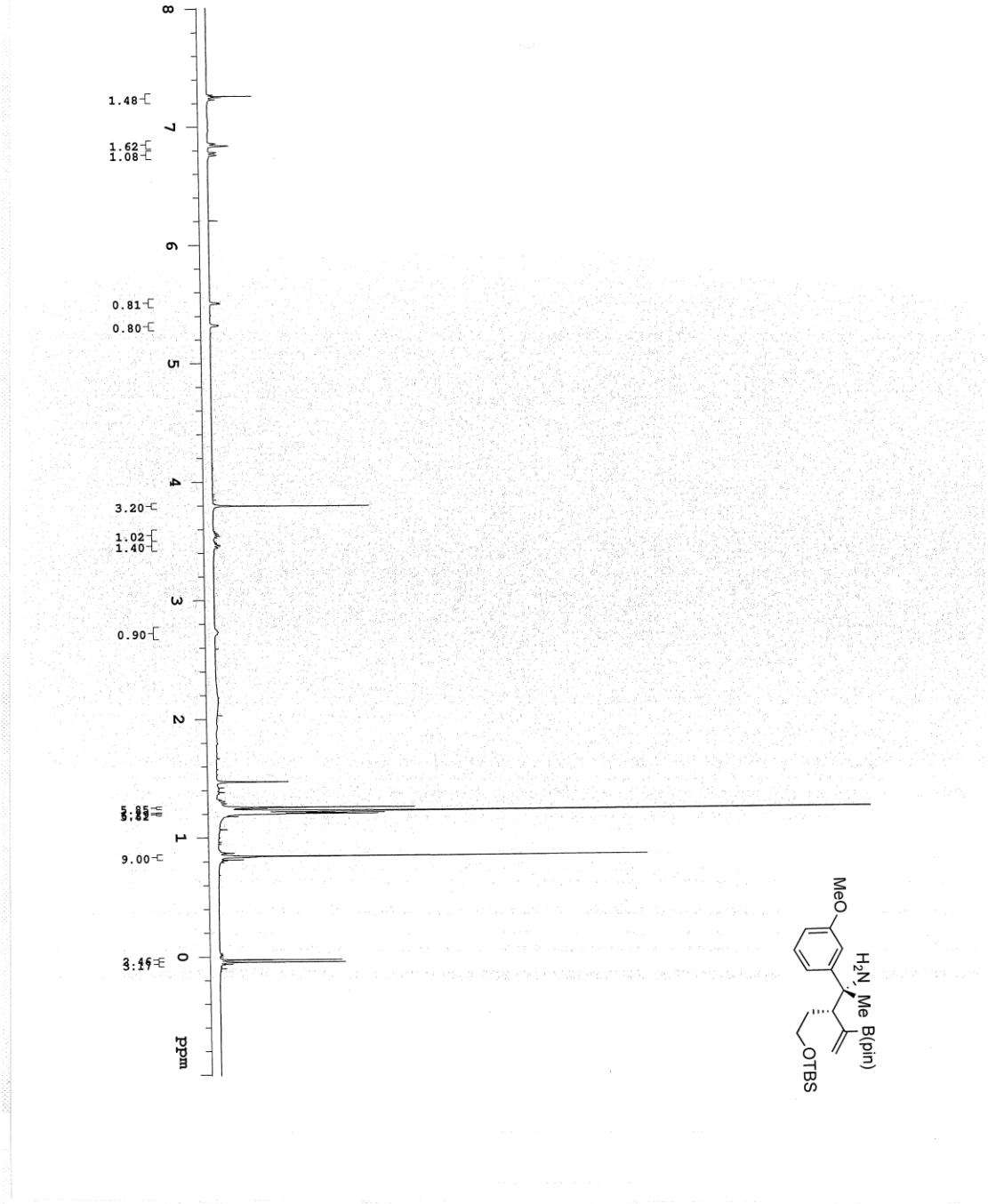

2.09
3.68
0.92
0.90
1.28
1.55
0.97
12.48
8.69
2.91
2.96
ppm
H2N
Me
B(pin)
OTBS

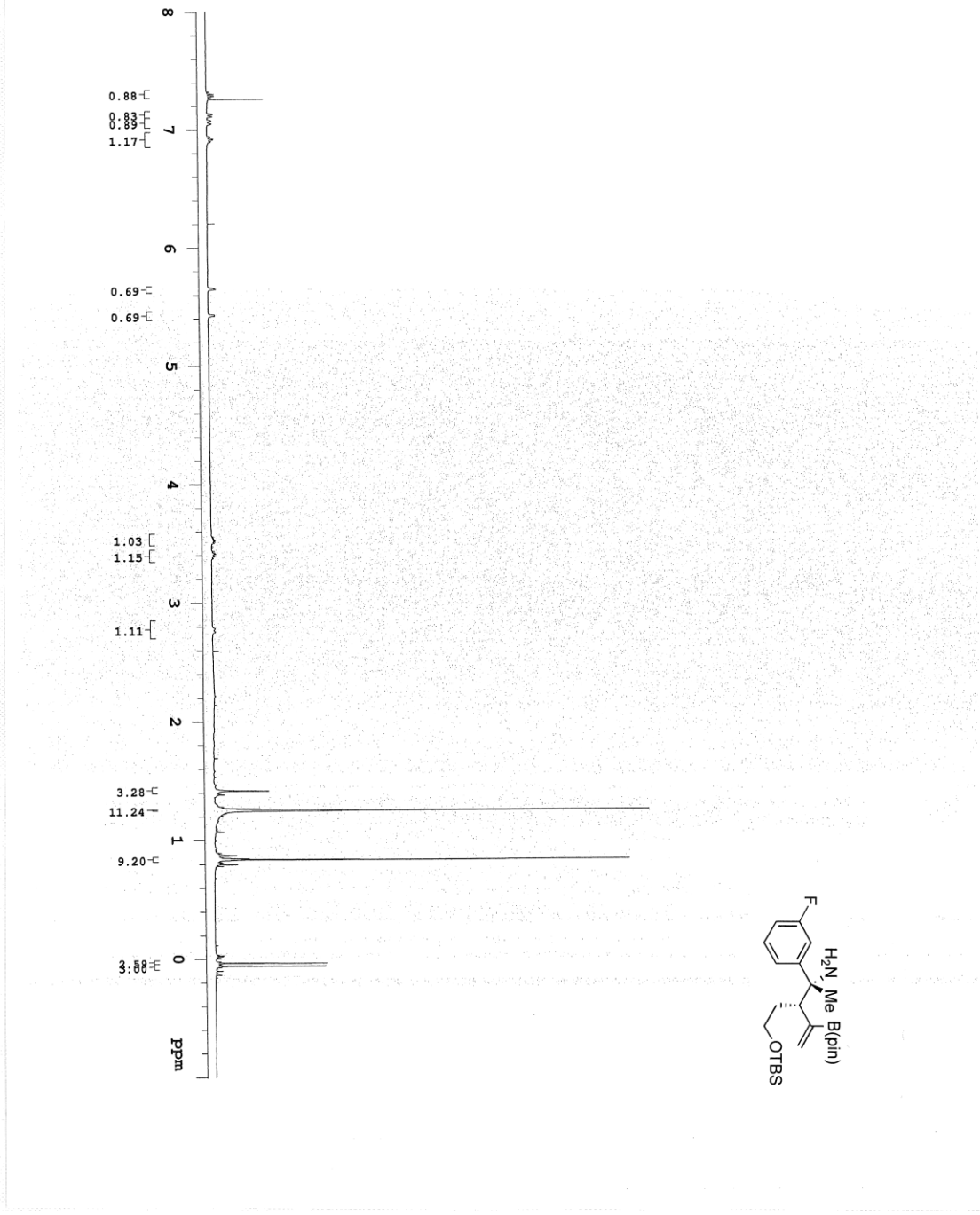

3.04
1.19
1.00
1.02
2.19
1.05
3.08
3.05
3.44
9.62
9.50
8
7
6
5
4
3
2
1
0
ppm
H2N
Me
B(pin)
Me
OTBS

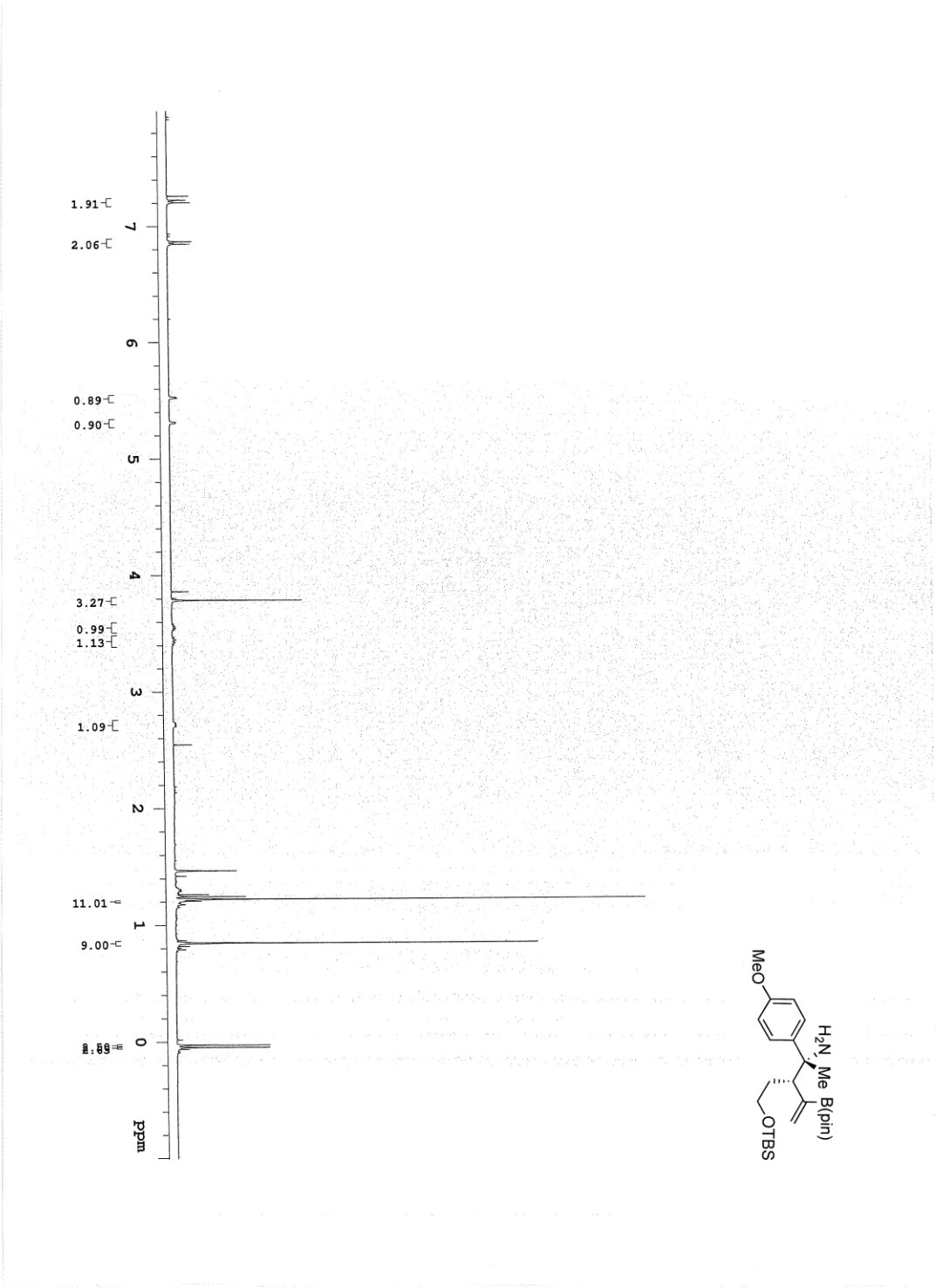

2.18
2.19
0.87
0.88
2.84
2.12
0.96
2.64
10.99
9.00
8
7
6
5
4
3
2
1
0
ppm
H2N
Me
B(pin)
OMe
OTBS

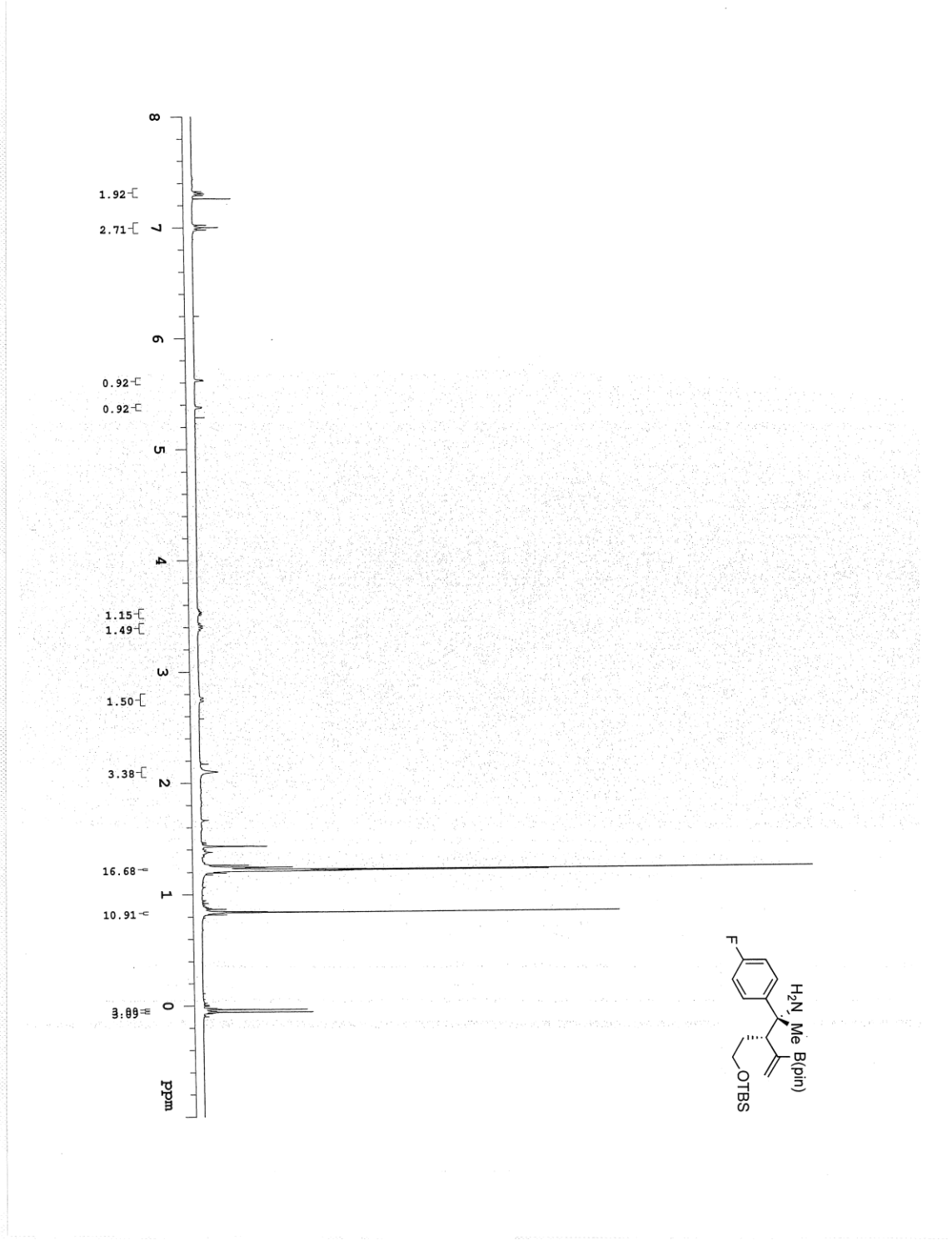

8
7
6
5
4
3
2
1
0
ppm
1.06
1.04
1.15
1.16
0.94
0.97
1.16
1.35
1.05
2.66
15.12
8.56
3.00
F
H2N
Me
B(pin)
OTBS

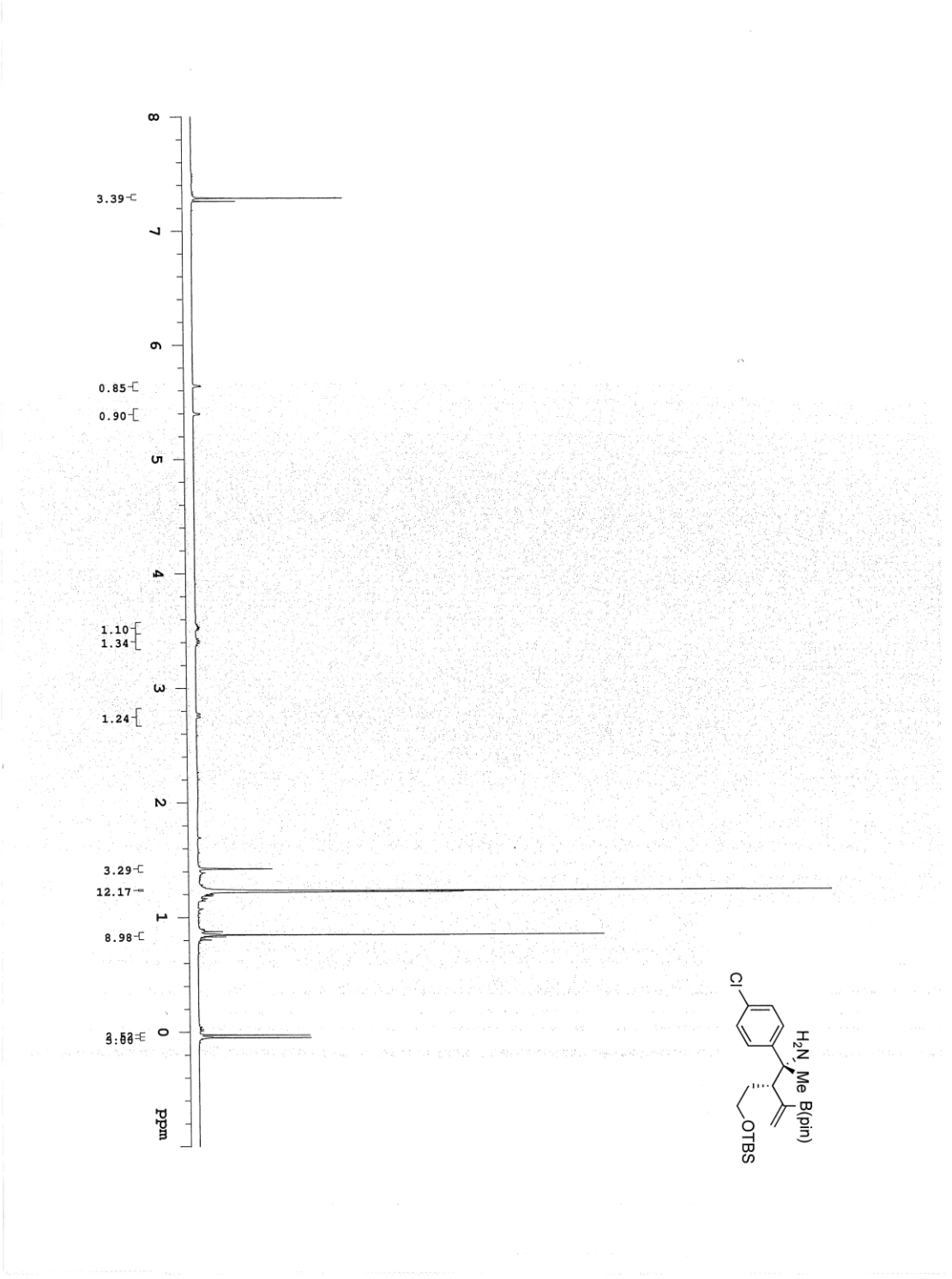

0.85
1.03
1.23
1.20
0.96
0.95
1.17
1.28
1.00
2.33
9.15
8
7
6
5
4
3
2
1
0
ppm
H2N
Me
B(pin)
Cl
OTBS

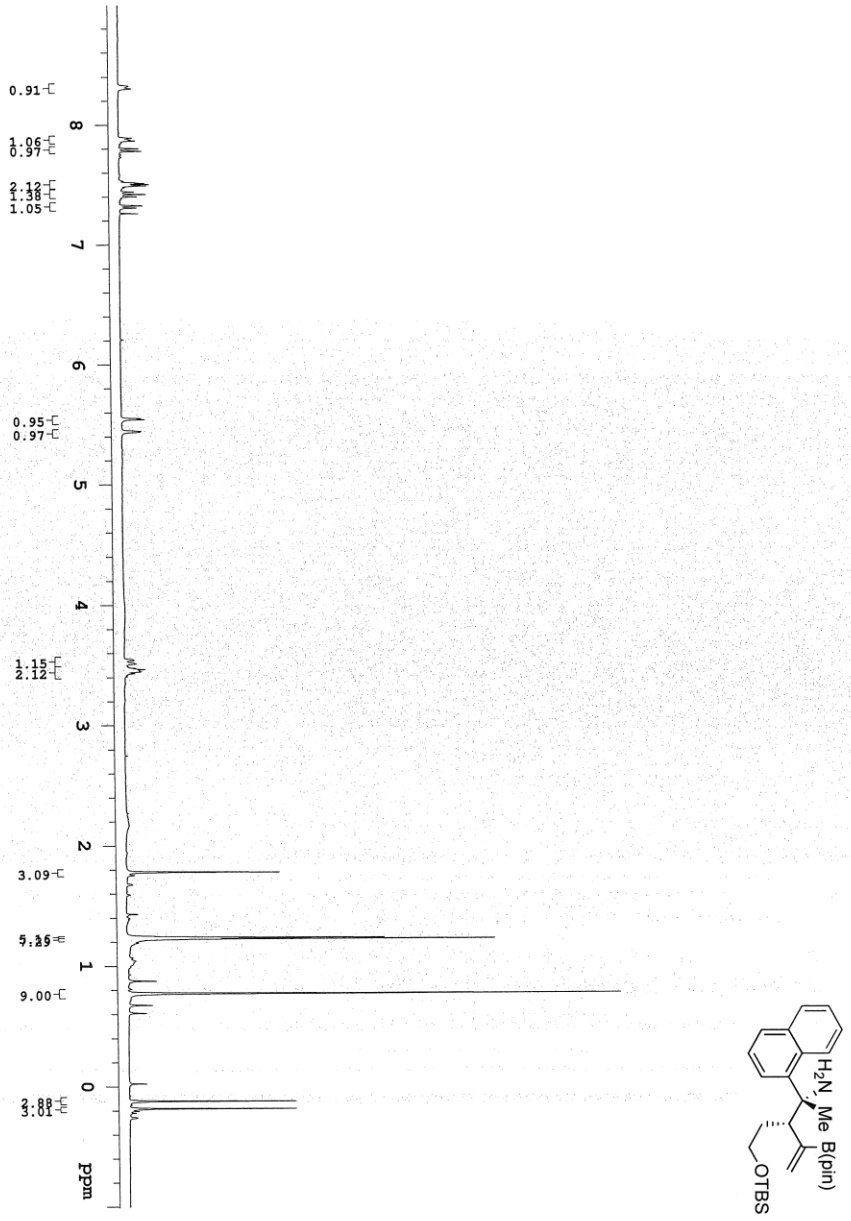

1.48
1.62
1.08
0.81
0.80
3.20
1.02
1.40
0.90
9.00
3.45
3.17
ppm
MeO
$H_2N$
Me
B(pin)
OTBS

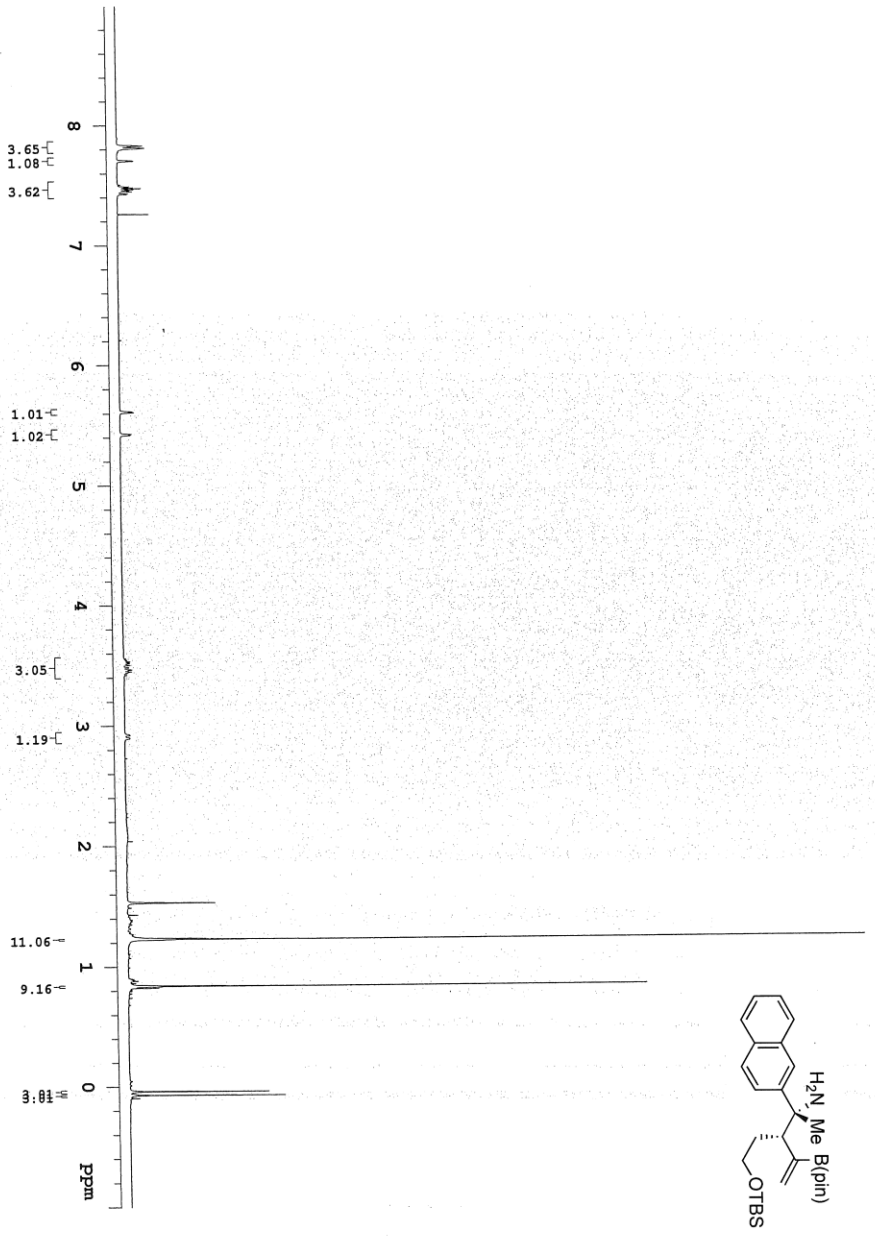

0.88
0.83
0.89
1.17
0.69
0.69
1.03
1.15
1.11
3.28
11.24
9.20
3.58
3.60
8
7
6
5
4
3
2
1
0
ppm
F
H2N
Me
B(pin)
OTBS

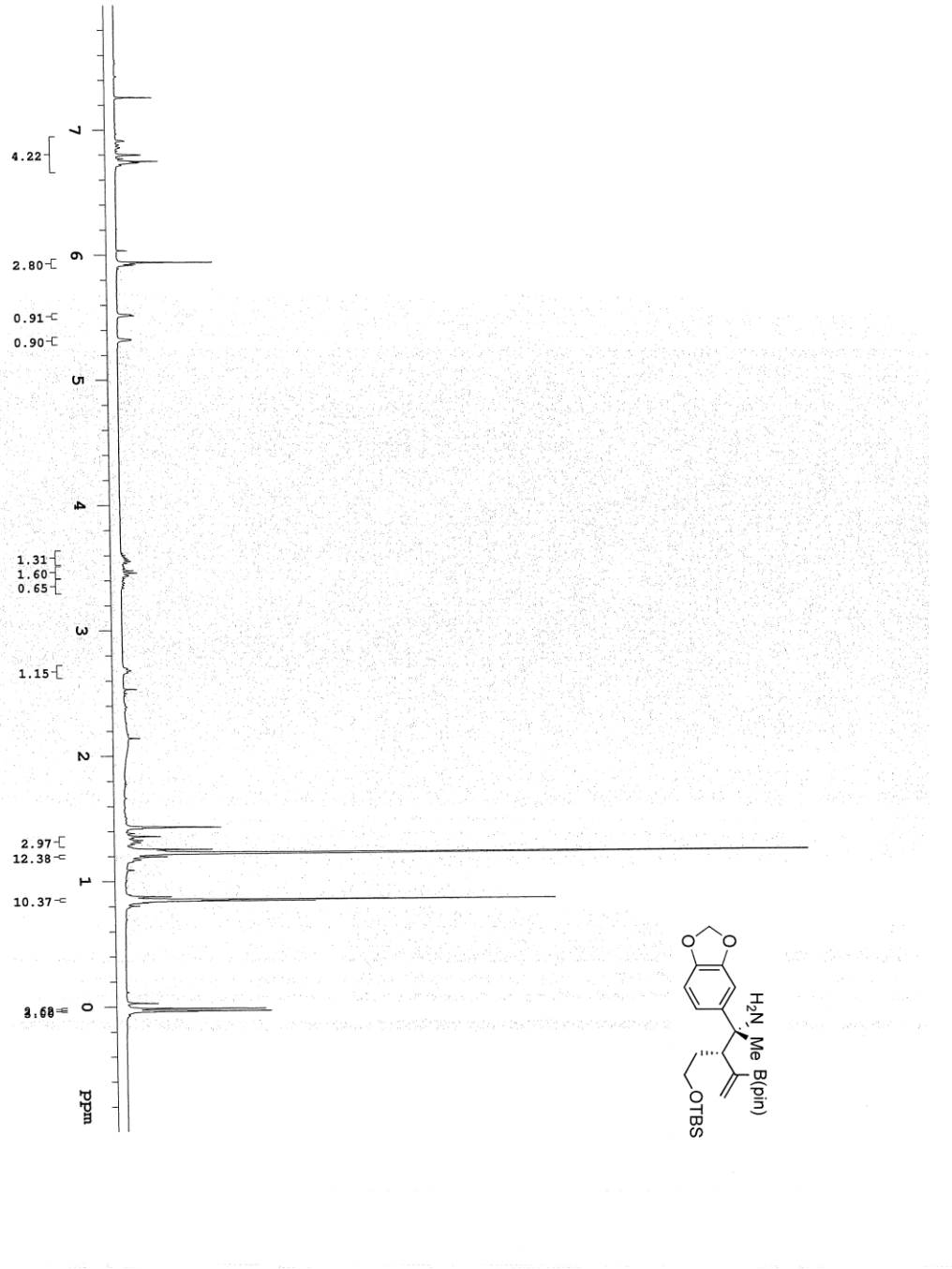

1.91
2.06
0.89
0.90
3.27
0.99
1.13
1.09
11.01
9.00
ppm
MeO
H2N
Me
B(pin)
OTBS

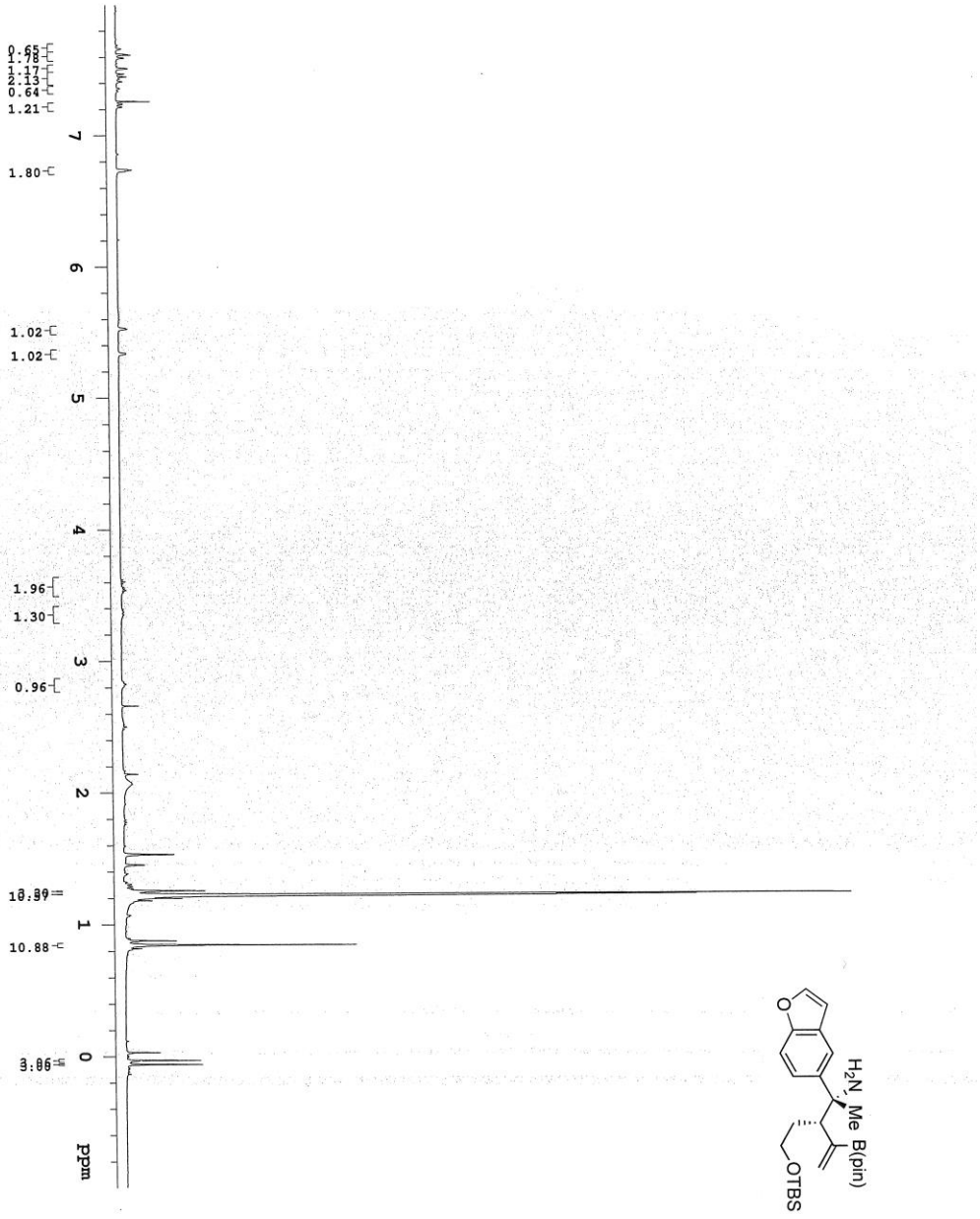

1.92
2.71
0.92
0.92
1.15
1.49
1.50
3.38
16.68
10.91
3.00
8
7
6
5
4
3
2
1
0
ppm
F
H2N
Me
B(pin)
OTBS

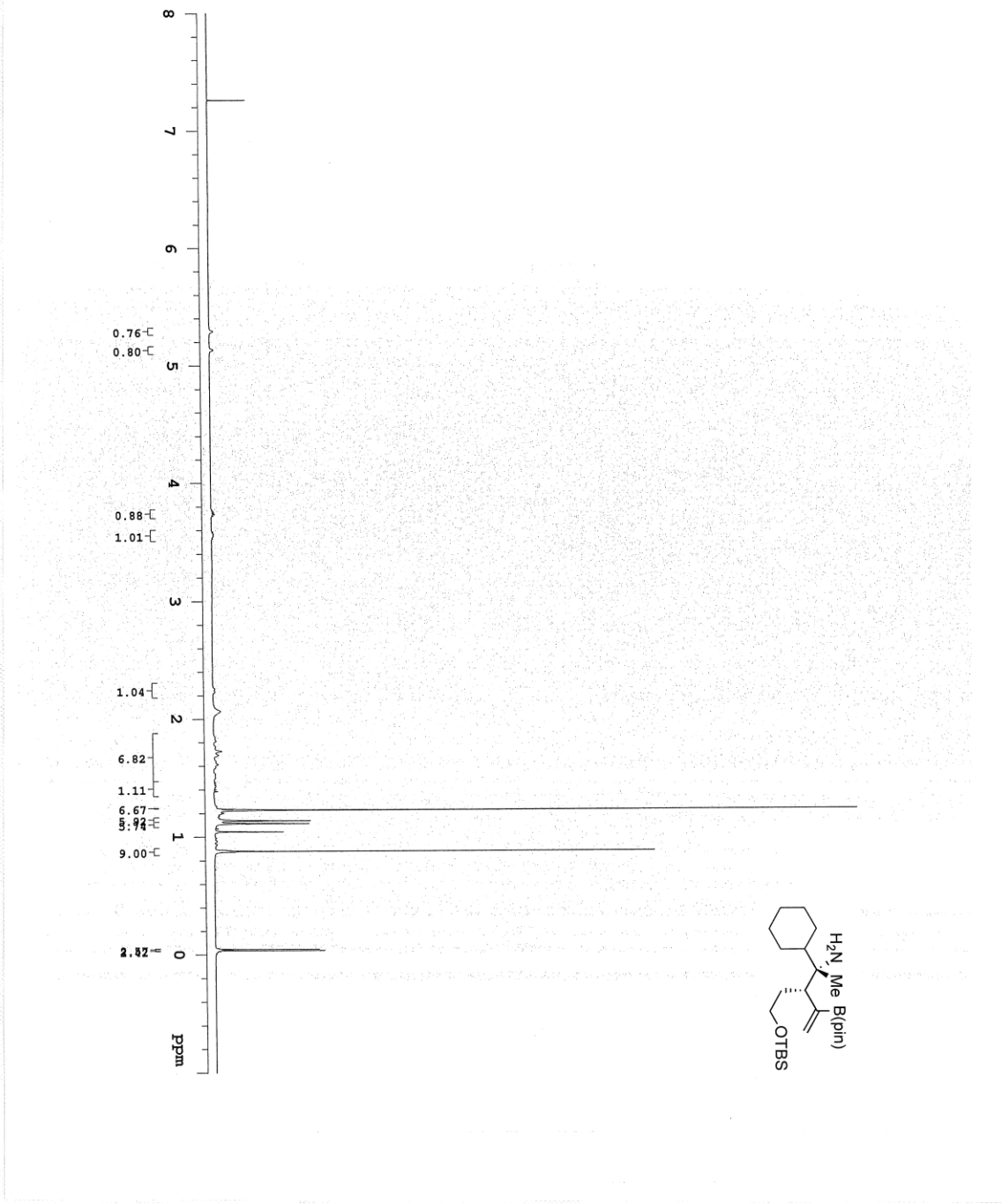

3.39
0.85
0.90
1.10
1.34
1.24
3.29
12.17
8.98
8
7
6
5
4
3
2
1
0
ppm
Cl
H2N
Me
B(pin)
OTBS

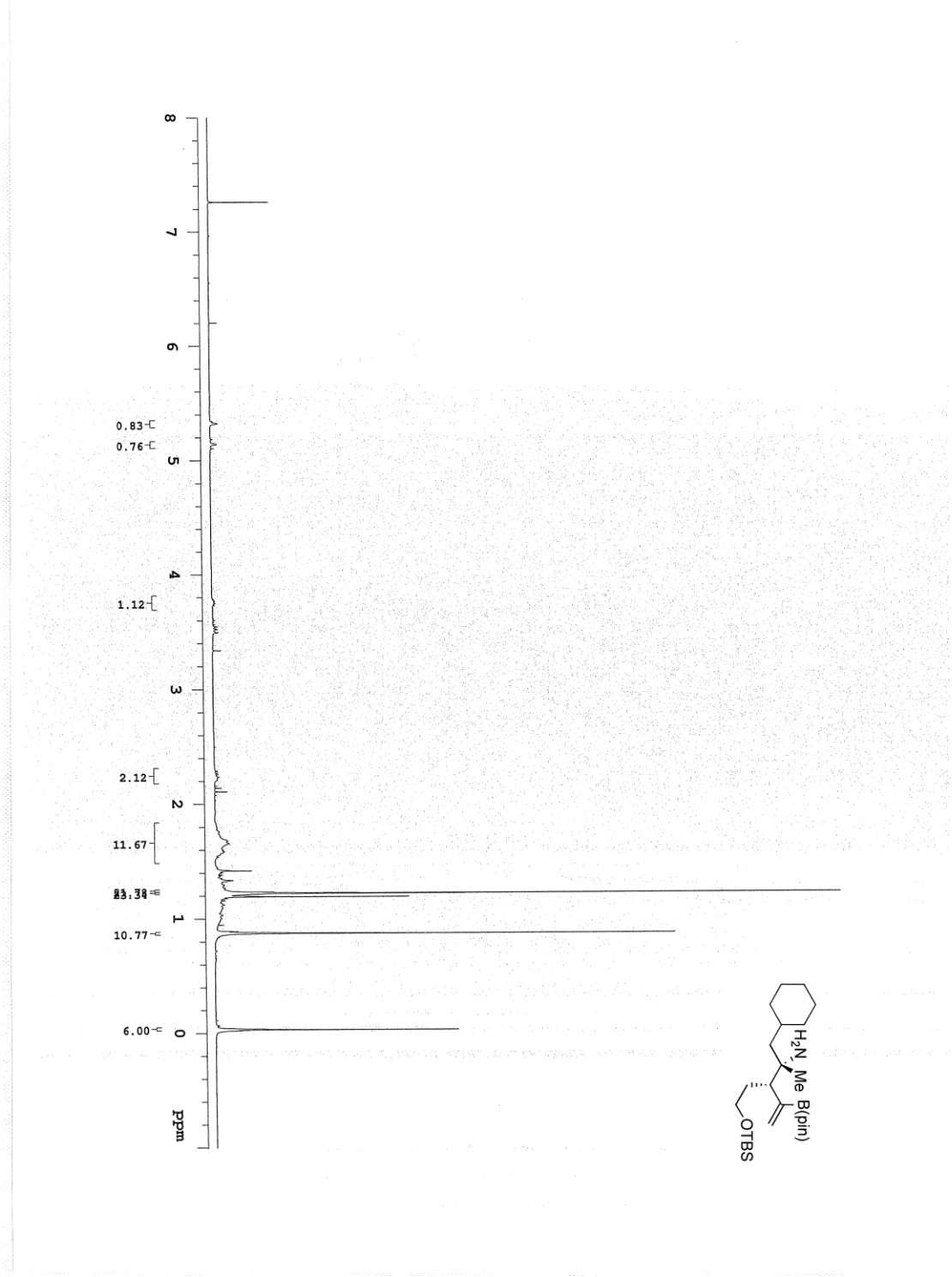

0.91
1.06
0.97
2.12
1.38
1.05
0.95
0.97
1.15
2.12
3.09
9.00
2.88
3.01
ppm
H2N
Me
B(pin)
OTBS

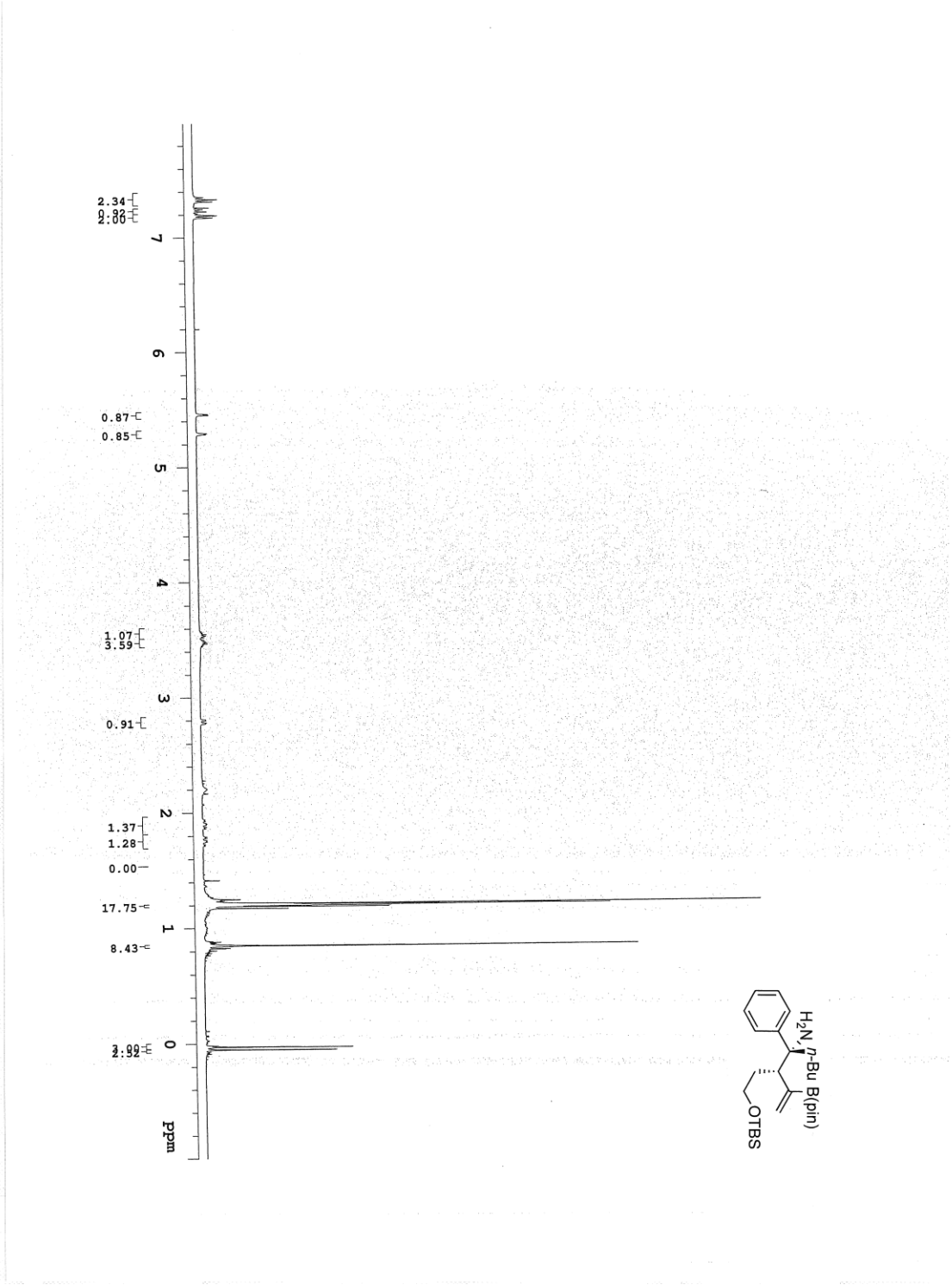

3.65
1.08
3.62
1.01
1.02
3.05
1.19
11.06
9.16
3.01
8
7
6
5
4
3
2
1
0
ppm
H2N
Me
B(pin)
OTBS

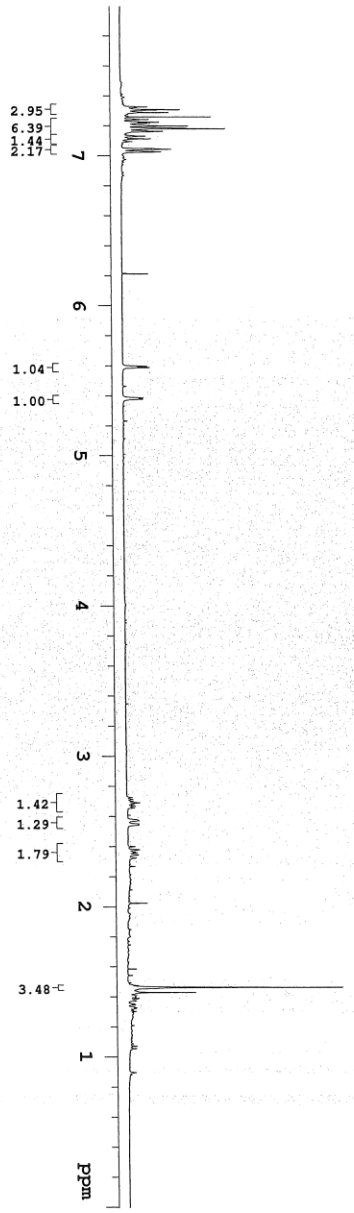

4.22
2.80
0.91
0.90
1.31
1.60
0.65
1.15
2.97
12.38
10.37
PPm
H2N
Me
B(pin)
OTBS

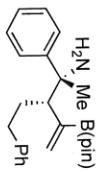

0.65
1.78
1.17
2.13
0.64
1.21
1.80
1.02
1.02
1.96
1.30
0.96
10.88
3.06
ppm
H2N
Me
B(pin)
OTBS

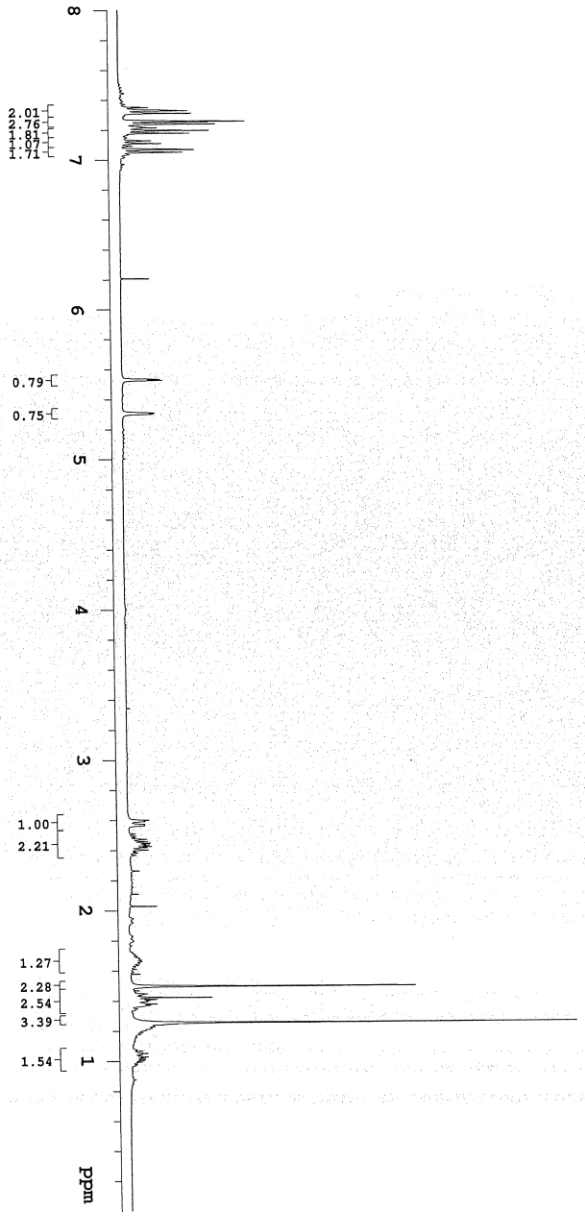

8
7
6
5
4
3
2
1
0
ppm
0.76
0.80
0.88
1.01
1.04
6.82
1.11
6.67
5.92
5.74
9.00
2.52
H2N
Me
B(pin)
OTBS

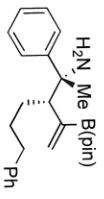

8
7
6
5
4
3
2
1
0
ppm
0.83
0.76
1.12
2.12
11.67
10.77
6.00
H2N
Me
B(pin)
OTBS

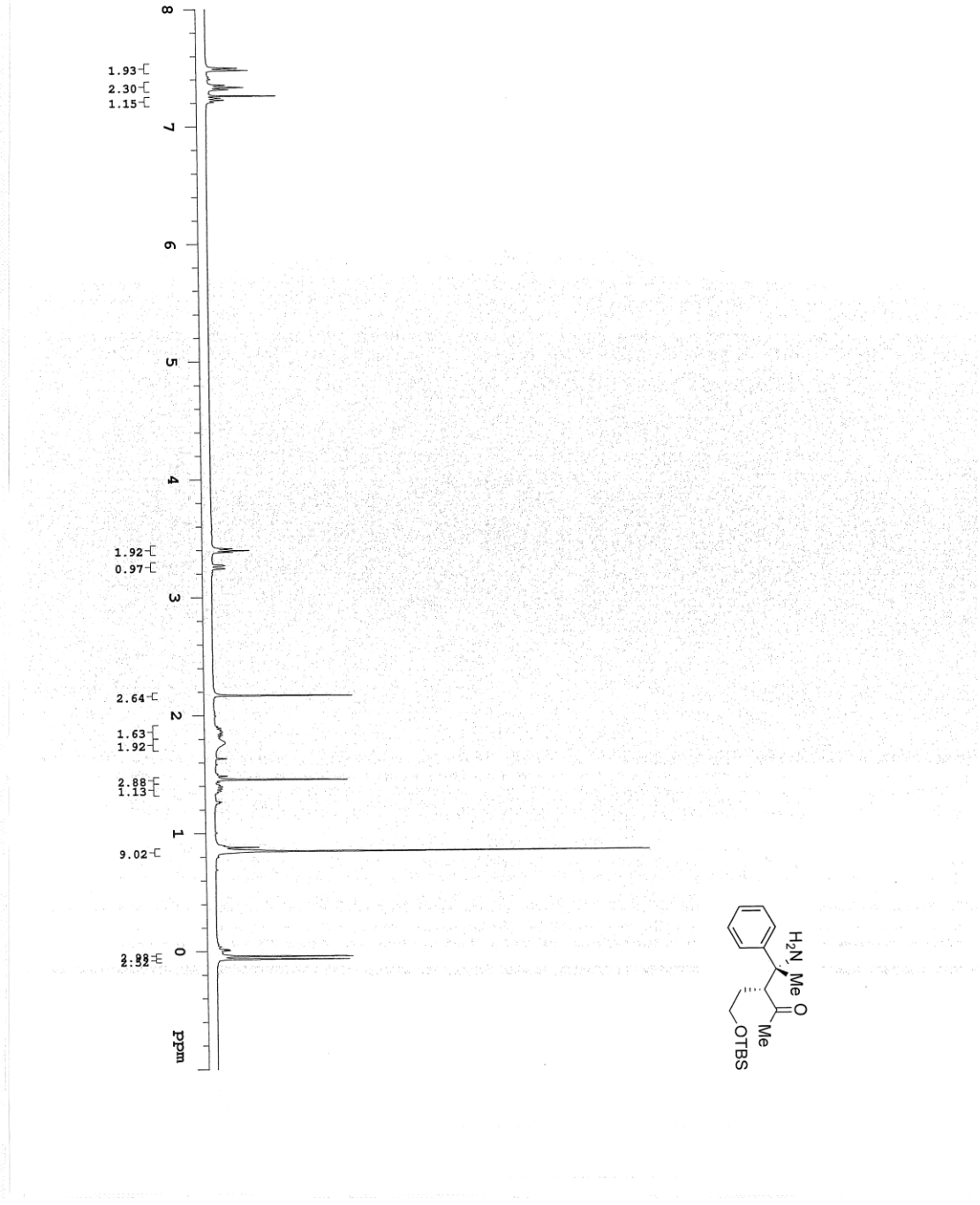

2.34
0.87
0.85
1.07
3.59
0.91
1.37
1.28
0.00
17.75
8.43
2.52
ppm
H2N
n-Bu
B(pin)
OTBS

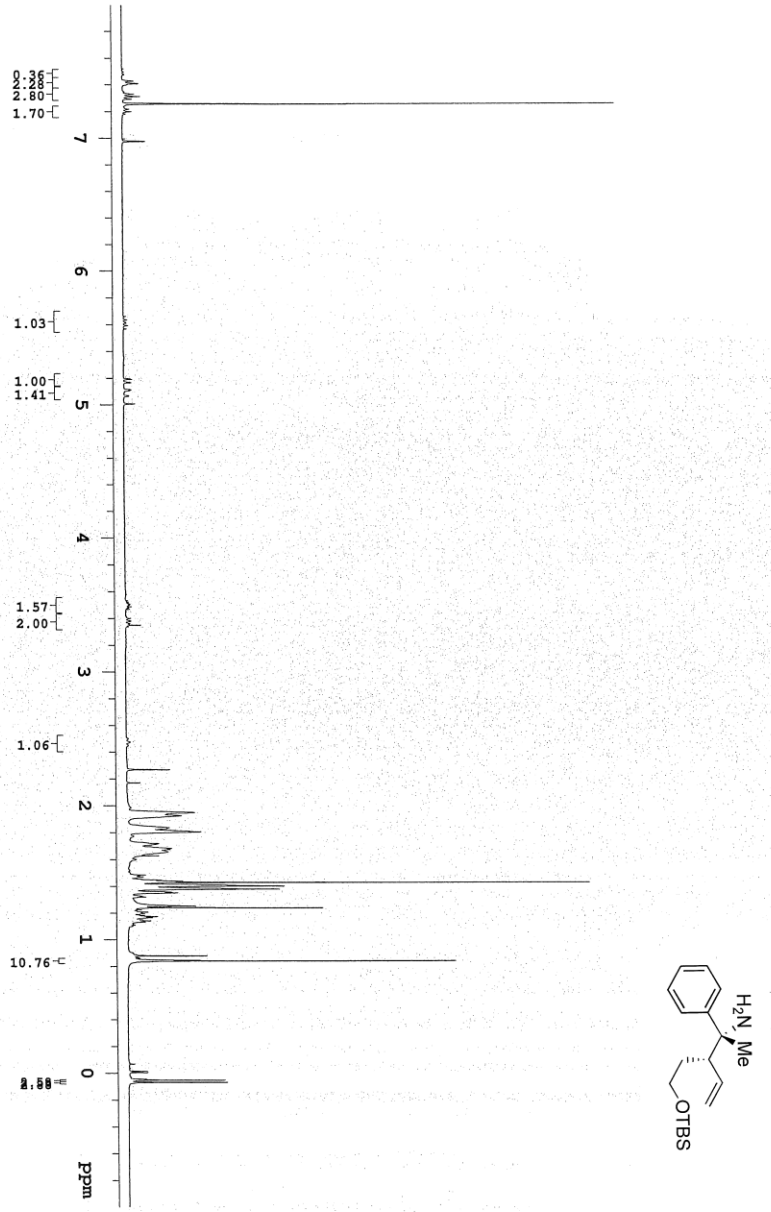

2.95
6.39
1.44
2.17
1.04
1.00
1.42
1.29
1.79
3.48
7
6
5
4
3
2
1
ppm

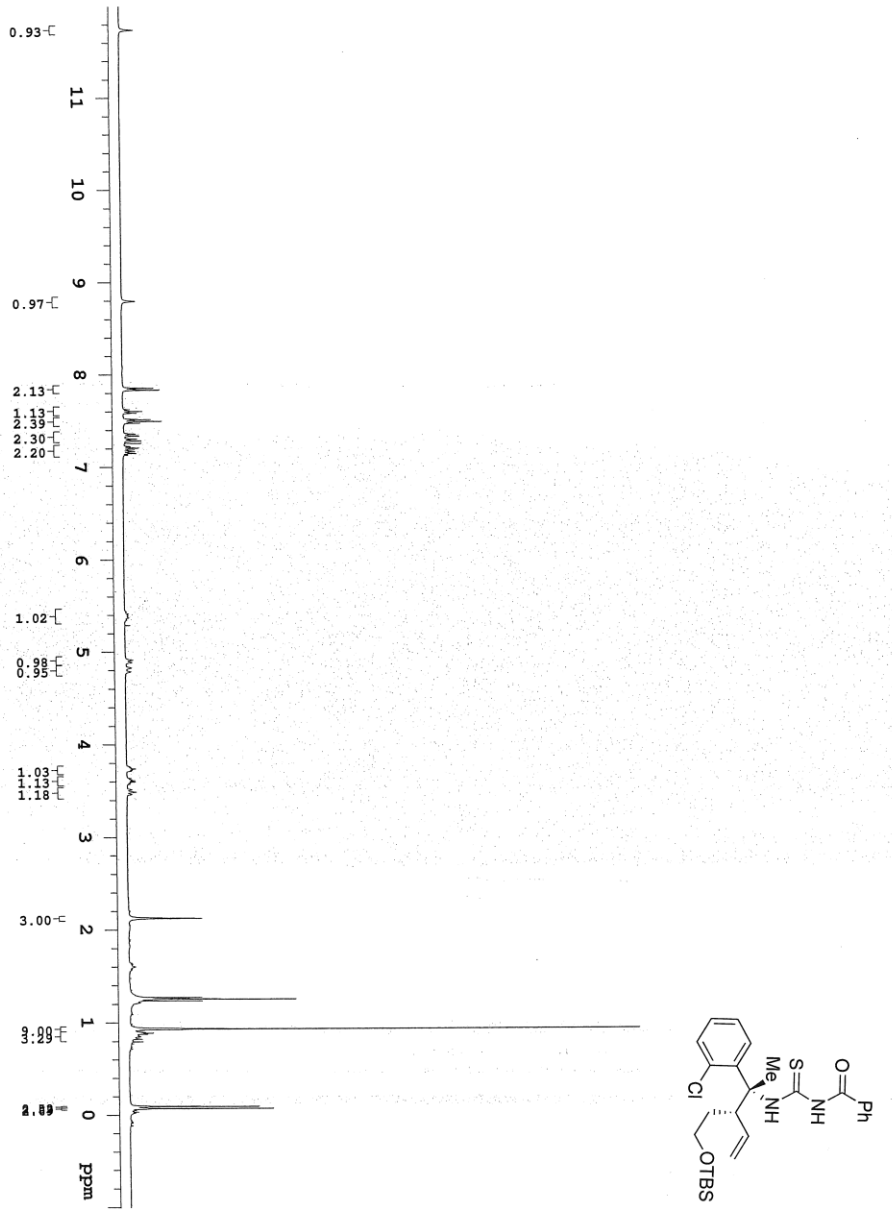

H2N
Me
B(pin)
Ph

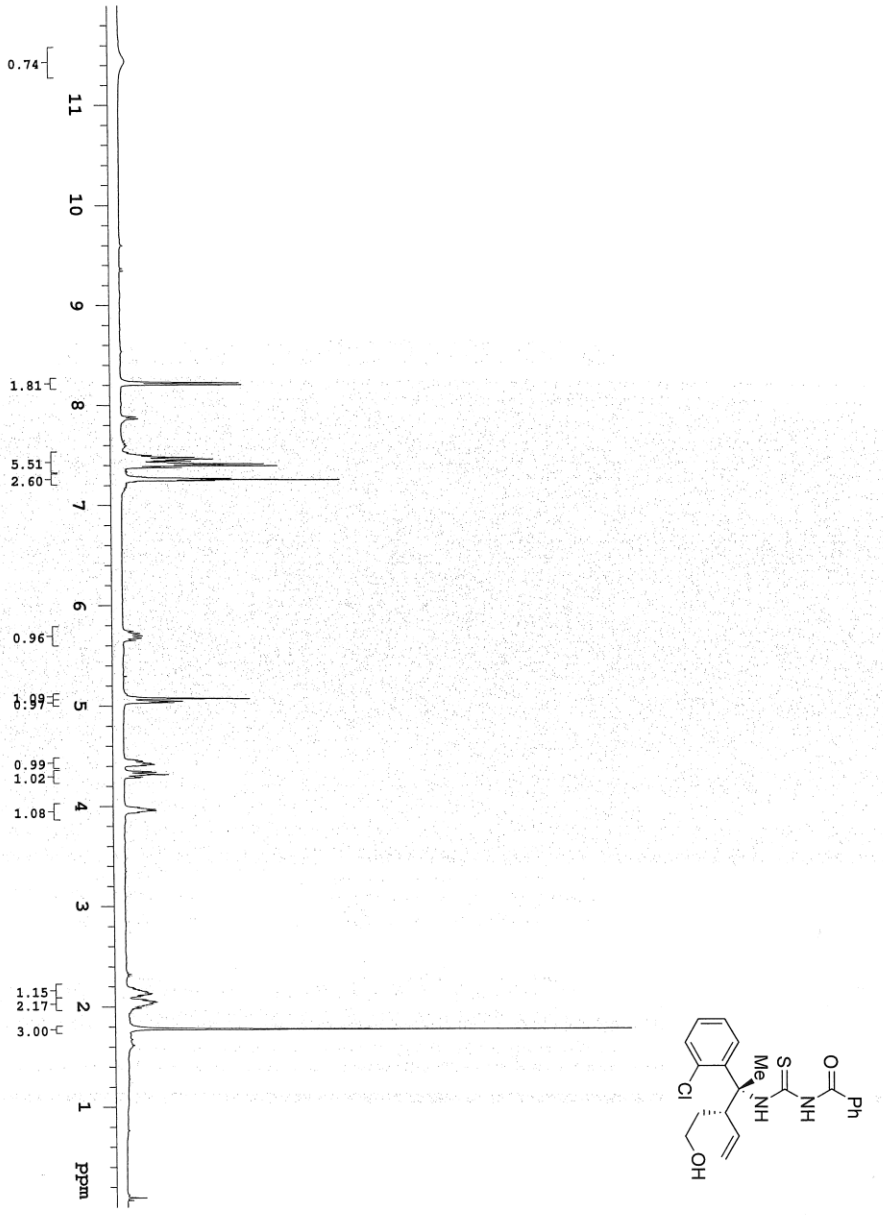

8
7
6
5
4
3
2
1
PPm
2.01
2.76
1.81
1.07
1.71
0.79
0.75
1.00
2.21
1.27
2.28
2.54
3.39
1.54

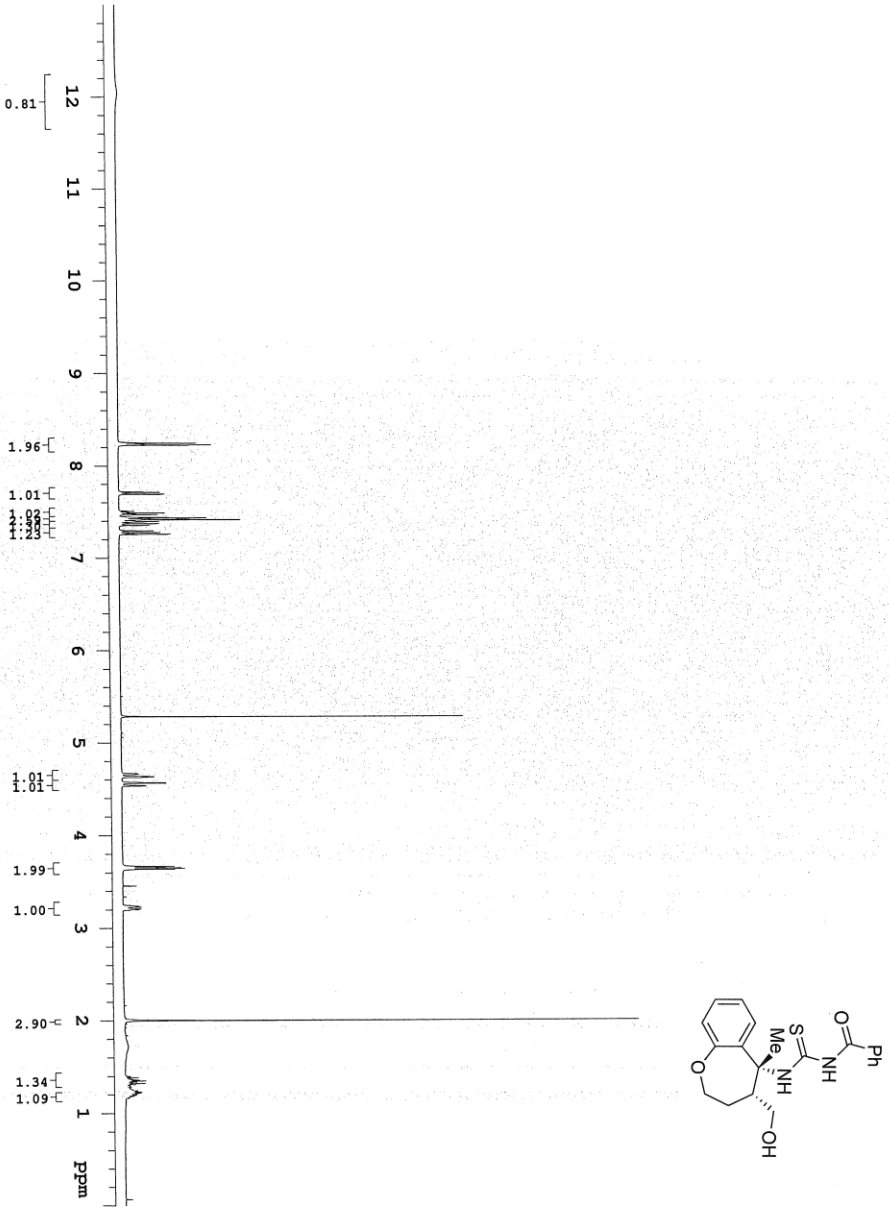

H2N
Me
B(pin)
Ph

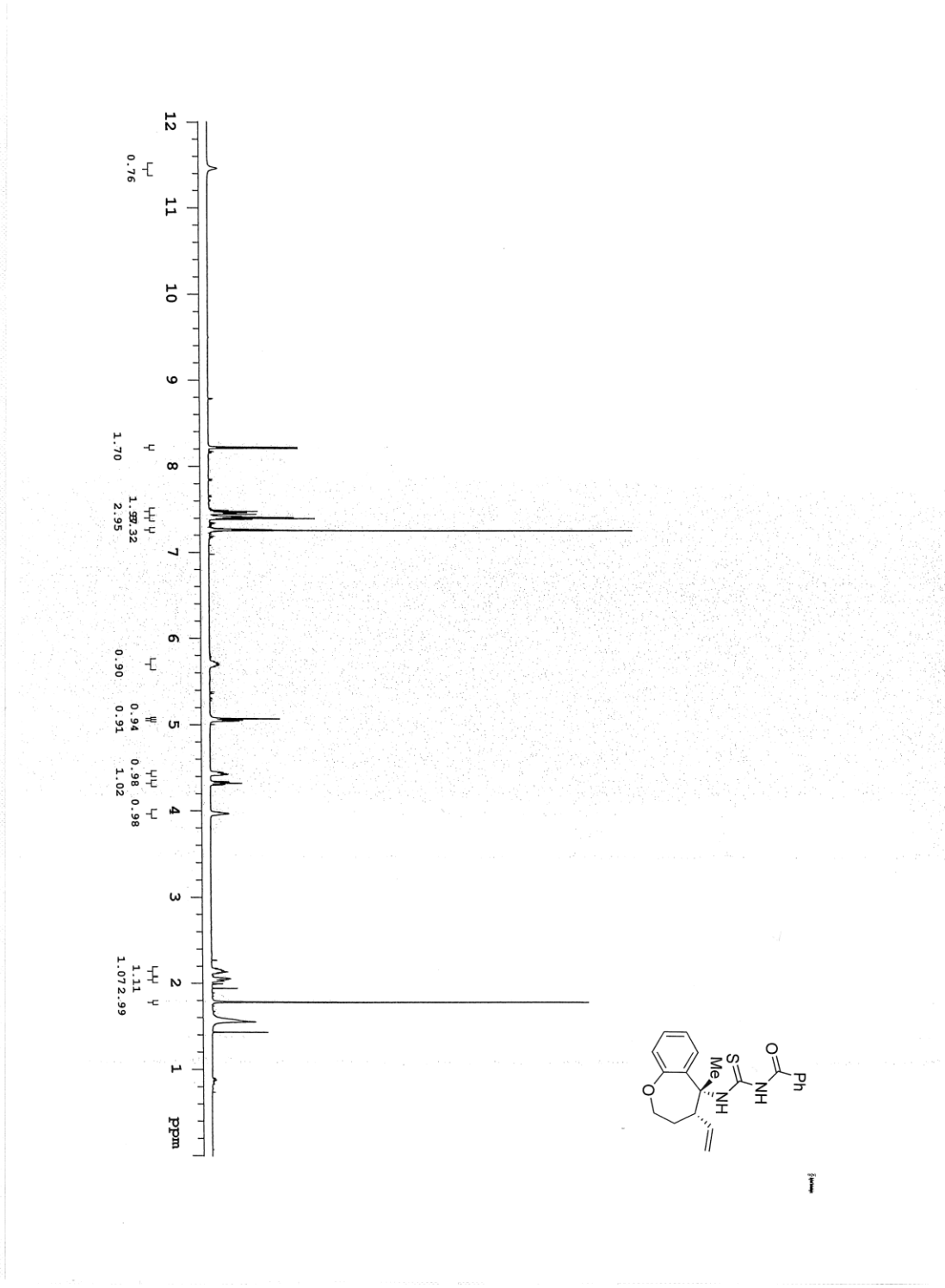

1.93
2.30
1.15
1.92
0.97
2.64
1.63
1.92
2.88
1.13
9.02
2.98
2.32
8
7
6
5
4
3
2
1
0
Ppm
H2N
Me
O
Me
OTBS


0.36
2.28
2.80
1.70
1.03
1.00
1.41
1.57
2.00
1.06
10.76
7
6
5
4
3
2
1
0
ppm
H2N
Me
OTBS


0.93
0.97
2.13
1.13
2.39
2.30
2.20
1.02
0.98
0.95
1.03
1.13
1.18
3.00
9.00
3.29
11
10
9
8
7
6
5
4
3
2
1
0
ppm
Cl
Me
NH
S
NH
O
Ph
OTBS


0.74
1.81
5.51
2.60
0.96
1.09
0.97
0.99
1.02
1.08
1.15
2.17
3.00
11
10
9
8
7
6
5
4
3
2
1
ppm
Cl
Me
NH
S
NH
O
Ph
OH


0.81
1.96
1.01
1.01
1.99
1.00
2.90
1.34
1.09
ppm
Ph
O
NH
S
NH
Me
OH
O


12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.76
1.70
2.95
1.32
0.90
0.94
0.91
0.98
0.98
1.02
1.11
1.07
2.99
O
NH
Ph
S
Me
NH