Carbohydrate-Catalyzed Enantioselective Alkene Diboration and Its Synthetic Application:

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Advisor: Professor James P. Morken

Abstract: This dissertation will present four main projects that I have been working on since January 2015. The first two chapters will be focusing on the developments of the carbohydrate-catalyzed enantioselective alkene diboraiton. The exchange catalysis between carbohydrate-derived diol catalyst and diboron starting material renders the alkene diboration reaction possible without the aid from transition metals. This successfully brought down the cost for the enantioselective alkene diboration, making it an appealing tool for alkene transformation. Detailed mechanistic study that leads to the reaction efficiency improvements were discussed in chapter 2. The third chapter of this dissertation is about the developments of site-selective oxidation of 1,2-bis(boronate). This is a new type of a reaction motif that the alkene diboration product can undergo. The secondary boronic ester of the 1,2-bis(boronate) was selectively oxidized to hydroxyl group while leaving the primary boronic ester untouched. This new reaction opens up a variety of opportunities to transform 1,2-bis(boronate) into different functional groups. Lastly, in the fourth chapter, recent synthetic methods developed in the Morken group was used in the total synthesis study of complex natural product Amphidinolide C. As it is disclosed, the carbohydrate-catalyzed enantioselective alkene diboration proved to be a powerful transformation either in early stage starting material preparation or in late stage complex structure motif functionalization.

Dedicated to

My parents Chuanhai Yan and Xia Chen for 28 years' love, support and guidance.

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Lastly, I have to thank my dear parents Chuanhai Yan and Xiachen for their greatest support and unconditional love through in my life. I also would like to thank Chaofan Xu, for five years company, support and friendship. I feel fortunate that we met each other in Boston College and get through all the difficulty together in our Ph.D study. Thank you for your patience and love.

List of Abbreviations

Å: angstrom

Ac: acetyl

acac: acetylacetonyl

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

$B_2(eg)_2$: bis(ethyleneglycolato)diboron

$B_2(neo)_2$: bis(neopentylglycolato)diboron

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

$B_2(pro)_2$: Propanediol diboron

Bn: benzyl

cat: catechol

cod: 1,5-cyclooctadiene

DART: direct analysis in real time

dba: dibenzylideneacetone

DCM: dichloromethane

DFT: density functional theory

DHR: (2S,3R,4S)-2-methyltetrahydro-2H-pyran-3,4-diol

DMF: N,N-dimethylformamide

dmp: 2,4-dimethylpenane-2,4-diol

DMSO: dimethyl sulfoxide

d.r.: diastereomeric ratio

e.e.: enantiomeric excess

equiv.: equivalent(s)

e.r.: enantiomeric ratio

ESI: electrospray ionization

EtOAc: ethyl acetate

GC: gas chromatography

h: hour(s)

HRMS: high resolution mass spectrometry

IR: infrared spectroscopy

LDA: lithium diisopropylamide

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

M: molar

MeCN: acetonitrile

min: minutes

MS: molecular sieves

NMO: N-methylmorpholine N-oxide

NMR: nuclear magnetic resonance

neo: neopentylglycol

pin: pinacol

ppm: parts per million

Pyr: pyrimidine

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

rac: racemic

RCM: ring-closing metathesis

rt: room temperature

SFC: supercritical fluid chromatography

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

TBAF: tetrabutylammonium fluoride

TBDPS: t-butyldiphenylsilyl

TBS: t-butyldimethylsilyl

TBS-DHG: (2R,3S,4R)-2-(((tert-butyldimethylsilyl)oxy)methyl)tetrahydro-2H-pyran-3,4-diol

TCD: trans-cyclohexanediol

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

TES: triethylsilyl

Tf: trifluoromethanesulfonyl

THF: tetrahydrofuran

TLC: thin layer chromatography

TMS: trimethylsilyl

tol: toluene

TS: transition state

Ts: p-toluenesulfonyl

UV: ultraviolet

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Chapter 1. Developments of the Carbohydrate-Catalyzed Enantioselective Alkene Diboration

1.1 Introduction

Alkenes are inexpensive, abundant feedstock chemicals, making them ideal starting materials for chemical synthesis. However, there are a limited number of methods that allow enantioselective transformations of alkenes in literature. To address this short coming, the Morken group has been developing enantioselective diboration reaction of alkenes. The diboration reaction can serve as a powerful tool for chemical synthesis, so long as it can be done with broad substrate scope and high selectivity. A significant feature of the diboration is that two boronic esters in the product can be easily transformed to a variety of functional groups such as alcohols, amines.

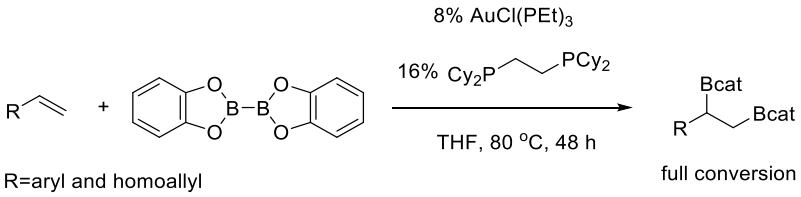
Compared to nonselective alkene diboration reaction, the catalytic enantioselective diboration reactions using terminal alkenes are even more valuable. Firstly, there are fewer reports of enantioselective transformations of terminal alkenes. Secondly, many asymmetric reactions with terminal alkenes do not provide the products in high enantioselectivities. For example, the well-known Sharpless asymmetric dihydroxylation reaction, while selective with a variety of disubstituted and trisubstituted alkenes, only affords terminal alkene dihydroxylation products with moderate enantioselectivity.[1] Therefore, a highly enantioselective terminal alkene diboration reaction is worth developing.

[1] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.

1.2 Backgrounds – History of Alkene Diboration

In 1995, Baker, Marder and Westcott reported the first example of the alkene diboration reaction.[2] As shown in Scheme 1.1, when alkene substrates were treated with a (dCyPE)Au and the diboron reagent $B_2(cat)_2$ at 80 ^oC in THF, the diboration product was formed efficiently. Activated olefins such as vinylarenes and allylbenzene were found to react well.

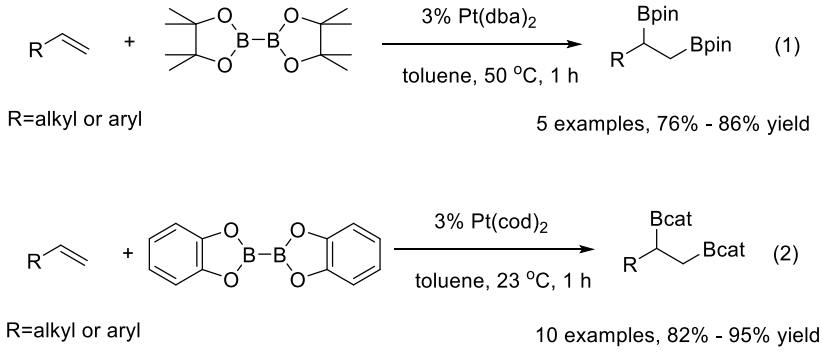
Scheme 1.1 The First Catalytic Diboration of Alkenes



Shortly after this first report, Miyaura and coworkers investigated the alkene diboration reaction catalyzed by platinum.[3] As shown in Scheme 1.2 (equation 1), terminal alkenes and activated internal alkenes such as norbornene were found to undergo diboration reaction smoothly with the diboron reagent B_2pin_2 when $Pt(dba)_2$ was applied as catalyst. Around the same time, Iverson and Smith also studied the platinum catalyzed alkene diboration reaction.[4] As shown in Scheme 1.2 (equation 2), the diboration of terminal alkenes and norbornene was achieved by using $Pt(cod)_2$ as catalyst and $B_2(cat)_2$ as diboron reagent.

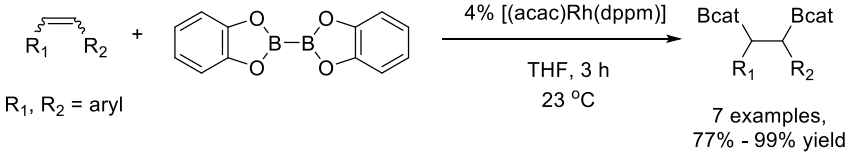
[2] Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. *Angew. Chem. Int. Ed.* **1995**, *34*, 1336.
[3] Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1997**, 689.
[4] Iverson, C. N.; Smith, M. R. III. *Organometalllics.* **1997**, *16*, 2757

Scheme 1.2 Alkene Diboration catalyzed by Platinum



In 1998, Marder found that other than platinum complexes, rhodium complexes were also able to catalyze the alkene diboration reaction.[5] Both aryl-substituted terminal alkenes and disubstituted alkenes afforded diboration products when [(acac)Rh(dppm)] was used as catalyst and $B_2(cat)_2$ was used as diboron starting material (Scheme 1.3).

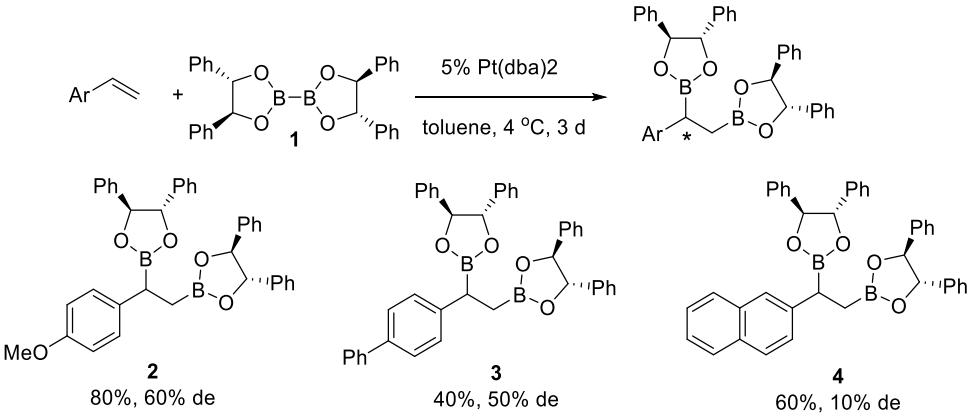
Scheme 1.3 Alkene Diboration catalyzed by Rhodium



The first example of catalytic diastereoselctive alkene diboration reaction was reported in 1998 by Marder and Norman.[6] As depicted in Scheme 1.4, when chiral diboron **1** was used as diboron reagent and $Pt(dba)_2$ was used as the catalyst, the diastereoselective diboration was achieved on substrates **2**, **3**, and **4** albeit with low diastereoselectivity.

[5] Dai, C.; Robins, E. G.; Scott, A. J.; Clegg, W.; Yufit, D. S.; Howard, J. A. K.; Marder, T. B. *Chem. Commun.* **1998**, 1983.
[6] Marder, T. B.; Norman, N. C.; Rice, C. R. *Tetrahedron Letters.***1998**, *39*, 155.

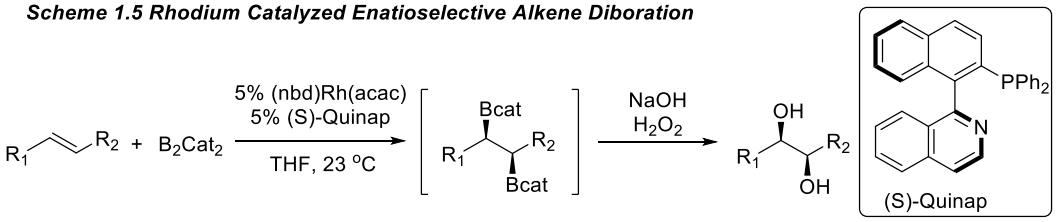
Scheme 1.4 Diastereoselective Alkene Diboration Catalyzed by Platinum.



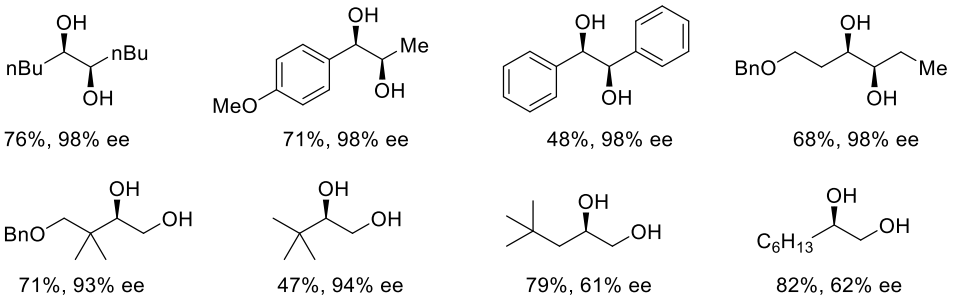
Using the previous work on catalytic alkene diboration reaction as precedent, the Morken group developed the first example of catalytic enantioselective alkene diboration.[7] Thus, as shown in Scheme 1.5, (nbd)Rh(acac) and Quinap[8] were used as the catalyst and $B_2(cat)_2$ was used as diboron reagent. The bis(boronates) products were directly oxidized to afford stable and isolable 1,2-diols in one pot. According to the initial report, only *trans* alkenes afforded products in good yields and good enantioselectivities. Most terminal alkenes only afforded diboration products in low enantioselectivities. Later, the group found that specialized terminal alkenes bearing α-quaternary center also reacted selectively in the diboration reaction.[9]

[7] Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702.
[8] Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron Asymmetry*, **1993**, *4*, 743.
[9] Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538.

Scheme 1.5 Rhodium Catalyzed Enatioselective Alkene Diboration



SELECTED EXAMPLES

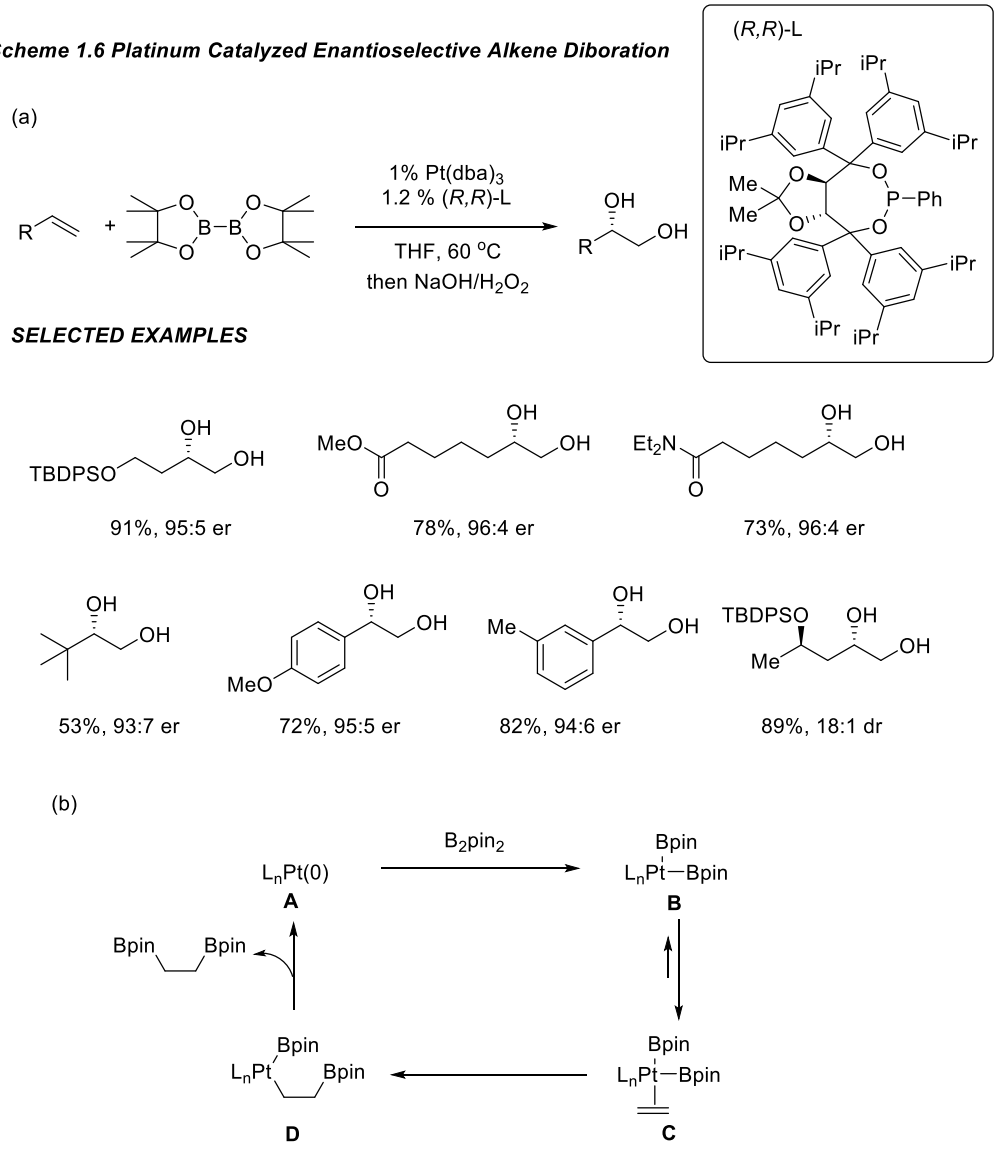


To further expand the scope of the enantioselective alkene diboration reaction from *trans* alkenes to terminal alkenes, Morken group developed the platinum-catalyzed enantioselective alkene diboration, which can successfully convert terminal alkenes into enantio enriched 1,2-bis(boronates).[10] As shown in Scheme 1.6 (a), a combination of $Pt(dba)_3$ and TADDOL derived phosphonite ligand[11] were used as the catalyst, and $B_2(pin)_2$ was used as the diboron reagent. Terminal alkenes bearing various functional groups underwent diboration reaction smoothly. The 1,2-bis(boronates) products were oxidized to 1,2-diols by treating with 3 M sodium hydroxide and 30% H_2O_2 in a one pot fashion. Mechanistic studies helped elucidate the reaction mechanism, and it is as depicted in Scheme 1.6 (b). The phosphonite-platinum complex was proposed to undergo oxidative addition with $B_2(pin)_2$ to afford the diboron adduct **B**. Adduct **B** can associate with the alkene substrate to afford complex **C**. After migratory insertion, complex **D** was

[10] (a) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210.
(b) Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222
[11] Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta.* **1987**, *70*, 954.

formed. Complex **D** then undergoes reductive elimination to regenerate catalyst **A** and afford the 1,2-bis(boronates) product.

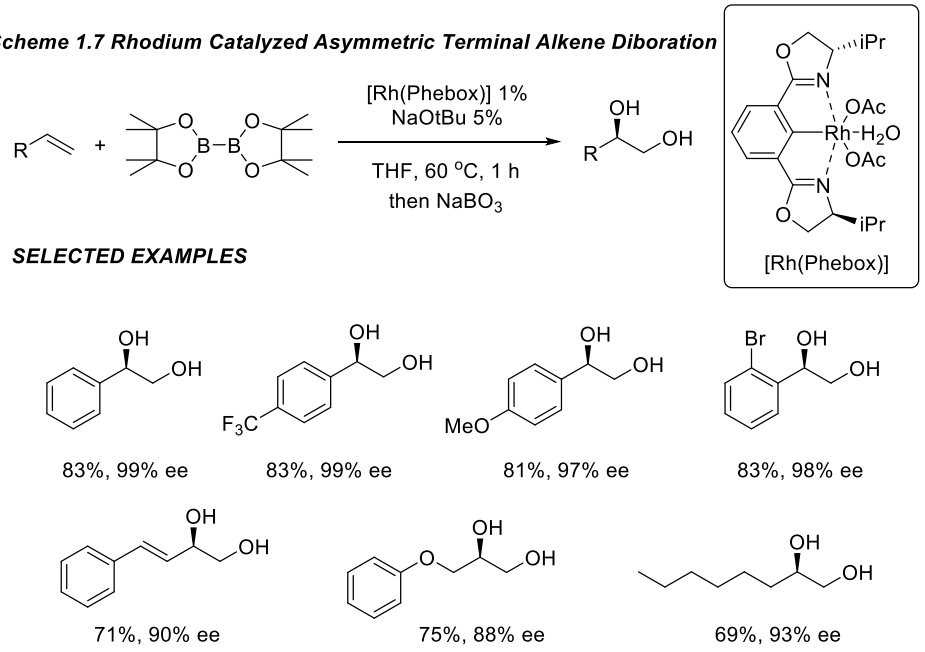
Scheme 1.6 Platinum Catalyzed Enantioselective Alkene Diboration



Later on, Nishiyama and coworkers reported another example of an asymmetric terminal alkene diboration reaction. As depicted in Scheme 1.7, when chiral rhodium Phebox complex was used as catalyst, a variety of activated and unactivated terminal

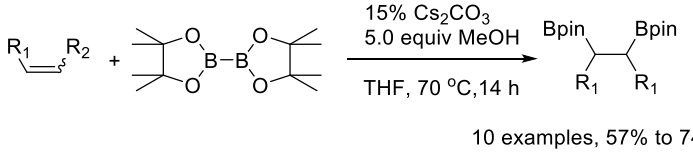
alkenes smoothly underwent the diboration reaction with $B_2(pin)_2$.[12] After basic oxidation, the 1,2-diol products were afforded in good yields and good enantioselectivities.

Scheme 1.7 Rhodium Catalyzed Asymmetric Terminal Alkene Diboration



Up until 2010, transition metal catalysts were always required to accomplish the alkene diboration reactions. The first example of non-transition-metal catalyzed alkene diboration was reported in 2010 by the Fernandez group[13]. As shown in Scheme 1.8, both activated and unactivated alkenes can react with $B_2(pin)_2$, in the presence of alkoxide catalysts, generating diboration products. Ten examples were included in this seminal report, with product yields ranging from 57% to 74%.

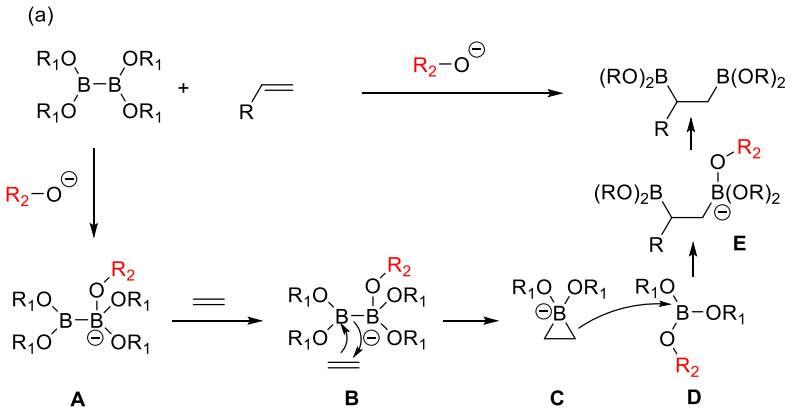
Scheme 1.8 Transition Metal Free Alkene Diboration



[12] Toribatake, K.; Nishiyama, H. *Angew. Chem. Int. Ed.* **2013**, *52,* 11011.
[13] Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Cluyas, H.; Fernanadez, E. *Angew. Chem. Int. Ed.* **2011**, *50*, 7158.

Fernandez and coworkers also proposed a mechanism for the alkoxide catalyzed alkene diboration reaction. As depicted in Scheme 1.9, the diboron starting material was proposed to be activated by catalyst alkoxide to form the polarized "ate" complex **A**.[14] The "ate" complex **A** can associate with the alkene substrate through the use of its empty p orbital. Because the "ate" complex has high energy B-B bond electrons, these can simultaneously donate to the empty π* orbital of the alkene substrate. Following this pair of filled/unfilled orbital interactions, two species were afforded: an anionic borocycle **C**, and the trivalent borate **D**. Species **C** and **D** then further react with each other to form the diboration adduct **E**. After further exchange, the bis(boronates) product was formed and the alkoxide base was regenerated.

Scheme 1.9 Proposed Mechanism for Transition Metal Free Alkene Diboration



Although, the proposed reactive intermediate anionic borocyle **C** is a quite unusual structure, there are literature precedents of similar structural motifs. As displayed in Scheme 1.10, the earliest report of an anionic borocycle was in 1975 by the Eisch group (equation 1).[15] Thirteen years later, Schuster and coworkers successfully obtained the X-

[14] Lee, K-S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253.
[15] Eisch, J. J.; Tamao, K.; Wilcsek, R. J. *J. Am. Chem. Soc.* **1975**, *97*, 895.

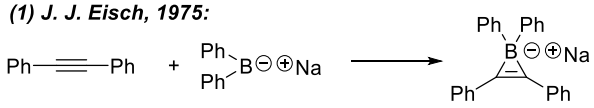
Ray crystal structure of an anionic borocycle (equation 2).[16] Denmark's group also synthesized a similar anionic borocycle following Schuster's procedure.[17] The compound was shown to be configurationally stable even at elevated temperature (equation 3). Most recently, Denmark and coworkers found that compound **A** underwent an interesting rearrangement when treated with LDMAN [lithium 1-(dimethylamino)napthalenide]. The anionic borocyle **B** was proposed to be the reactive intermediate for the rearrangement (equation 4).[18]

Other than the examples listed in Scheme 1.10, Professor Wang[19] and Professor Braunschweig[20] also studied NHC-stabilized borocycles.

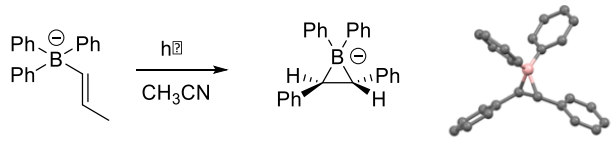
[16] (a) Kropp, M. A; Bhamidapaty, K.; Schuster, G. B. *J. Am Chem. Soc.* **1988**, *110*, 6252. (b) Kropp, M. A.; Ballargeon, M.; Park, K. M.; Bhamidapaty, K.; Schuster, G. B. *J. Am. Chem. Soc.* **1991**, *113*, 2155.
[17] Denmark, S. E.; Nishide, K.; Faucher, A. *J. Am. Chem. Soc.* **1991**, *113*, 6675.
[18] Tao, Z.; Robb, K. A.; Panger, J. L.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 15621.
[19] Rao, Y.; Chen, L. D.; Mosey, N. J.; Wang, S. *J. Am. Chem. Soc.* **2012**, *134*, 11026.
[20] Braunschweig, H.; Claes, C.; Damme, A.; Deibenberger, A.; Dewhurst, R. D.; Hori, C.; Kramer, T.; *Chem. Commun.* **2015**, *51*, 1627.

Scheme 1.10 Precedents for anionic borocyles.

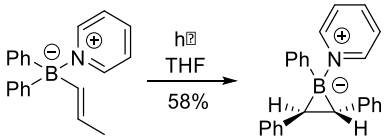
(1) J. J. Eisch, 1975:



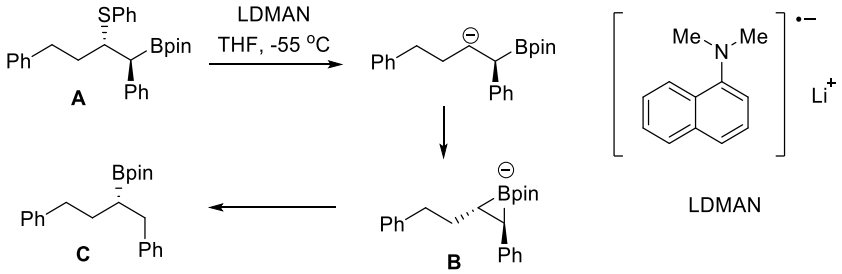
(2) G. B. Schuster, 1988:



(3) S. E. Denmark, 1991:



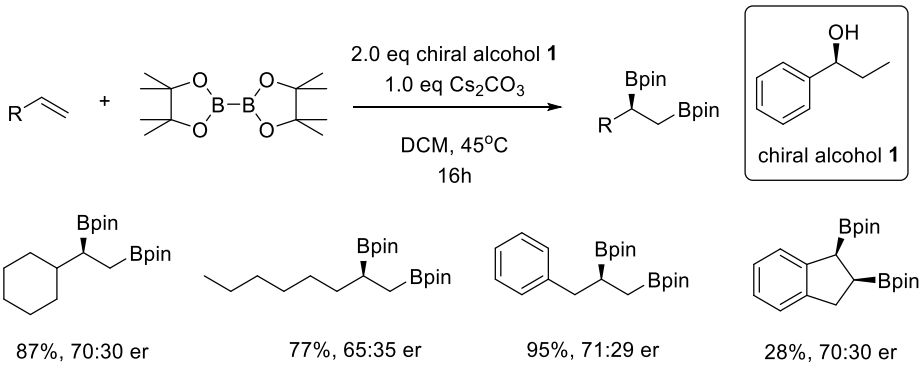
(4) S. E. Denmark, 2019:



Fernandez and coworkers also tried to render the alkoxide catalyzed diboration reaction enantioselective.[21] As shown in Scheme 1.11, super-stoichiometric amounts of chiral alcohols were used instead of methanol. Unfortunately, the diol products were afforded in low enantioselectivities.

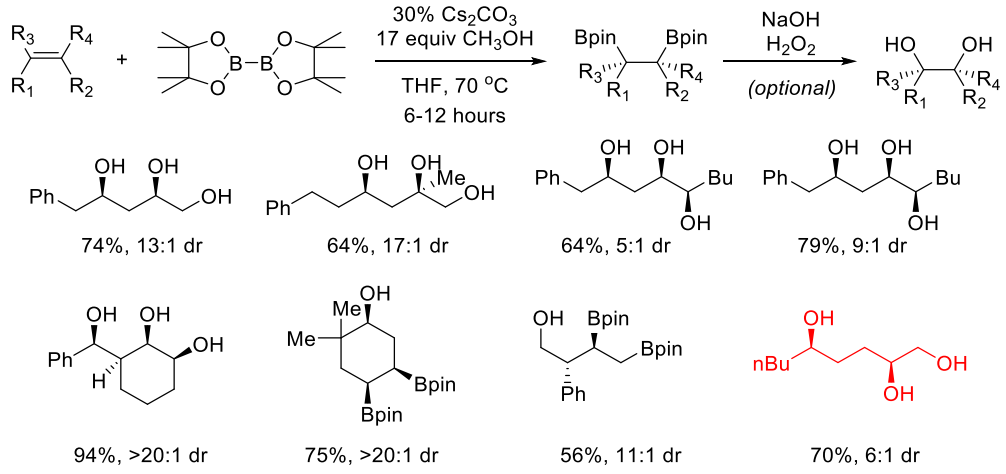
[21] Bonet, A.; Sole, C. Gulyas, H.; Fernandez, E. *Org. Biomol. Chem.* **2012**, *10*, 6621.

Scheme 1.11 Chiral Alcohol Promoted Alkene Diboration



Inspired by the seminal reports from Professor Fernandez and coworkers, the Morken group developed a hydroxyl-directed stereoselective diboration of alkenes.[22] As shown in Scheme 1.12, various kinds of homoallylic alcohols were diborated in good diastereoselectivities by treating with 30% cesium carbonate, 2 equivalents of B_2pin_2, and 17 equivalents of methanol. The hydroxyl group could be moved one carbon further away from the alkene and still have a significant impact on reaction selectivity (highlighted in red).

Scheme 1.12 Hydroxyl-Directed Stereoselective Diboration of Alkenes

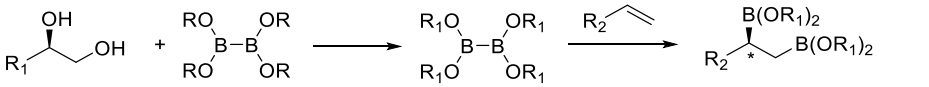


[22] Blaisdell, T. P.; Caya, T. C.; Zhang, L.; Sanz-Marco, A.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 9264.

1.3 Reaction Optimization

We proposed a possible mechanism for rendering the non-transition metal catalyzed alkene diboration reaction enantioselective. As depicted in Scheme 1.13, if a chiral alcohol could exchange with the diboron reagent to generate a chiral diboron which is more reactive then the achiral precursor, then the bis(boronates) products might be generated in enantioselective fashion.

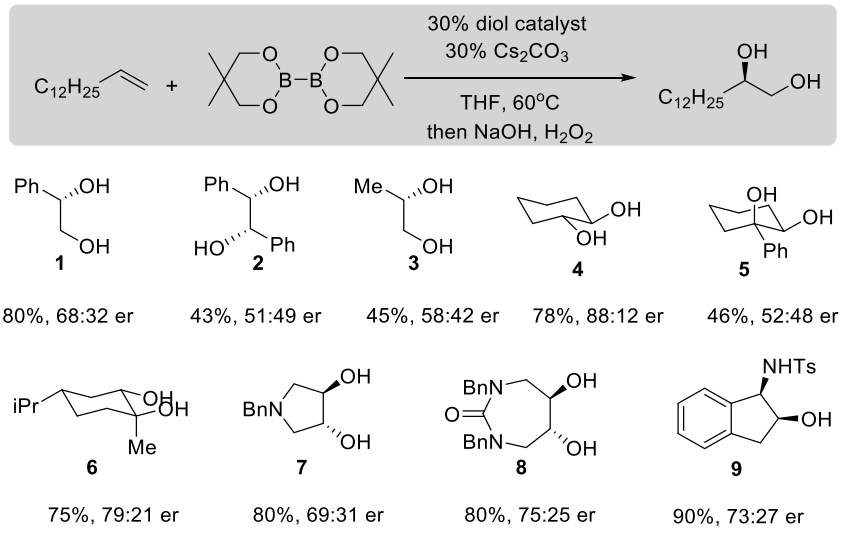
Scheme 1.13 Proposed Mechanism for Non-metal Catalyzed Enantioselective Alkene Diboration



Chiral, More Reactive ***Enantioenriched Product***

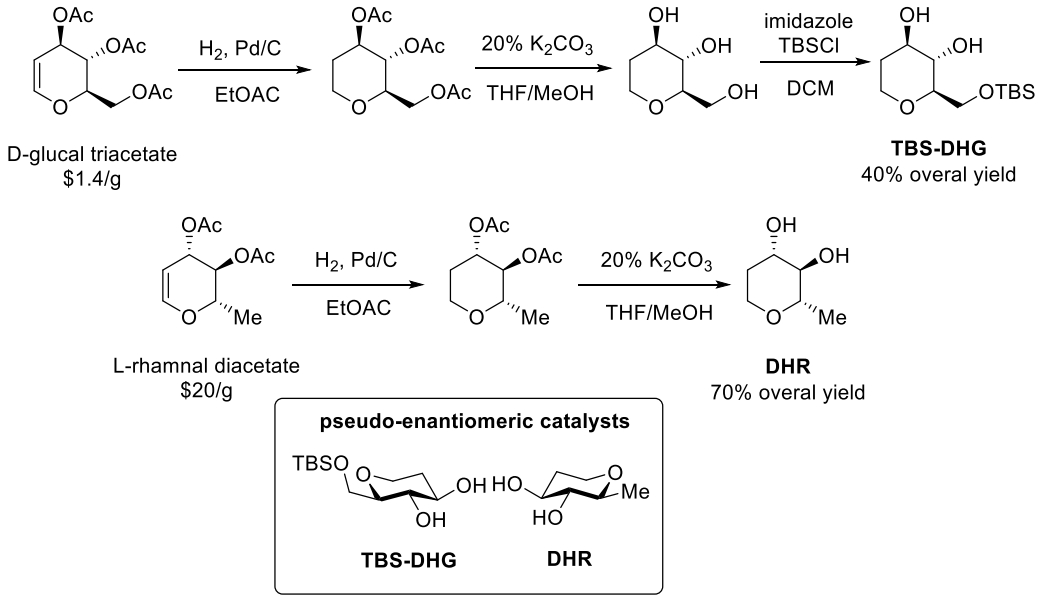
Based on this proposal, we first investigated different diols, combined with 30% cesium carbonate and 1.0 equivalent $B_2(neo)_2$ in the alkene diboration reaction. Rather than mono-alcohols, diols were chosen as catalysts because they might be more prone to exchange with the diboron reagent, forming thermodynamically favored cyclic diboron complexes. Similarly, $B_2(neo)_2$ was chosen as the diboron starting material because it is less hindered than widely used B_2pin_2, so it might be more prone to exchange with the catalyst. As shown in Scheme 1.14, acyclic diols **1**, **2**, and **3** afforded the product non-selectively. *trans*-Cyclohexanediol **4** gave more promising results. The product was formed in 78% yield, and 88:12 er. In contrast, *cis*-cyclohexanediol derivative **5** gave almost racemic product. The substituted *trans*-cyclohexanediol derivative **6** afforded the product in much diminished enantioselectivity. Additionally, five-membered and seven-membered vicinal *trans*-diol derivatives **7** and **8** also gave the products in lower enantioselectivities. The *cis*-aminoindanol derivative **9** afforded the product in moderate enantioselectivity.

Scheme 1.14 Catalyst Investigation of Enantioselective Diboration



Although *trans*-cyclohexanediol **4** gave very exciting results in the enantioselective alkene diboration reaction, it is too expensive ($300/g) to be practical. Therefore, the structure motif was selected as a lead for further catalyst development. Upon broader investigation, carbohydrate derivatives were considered as a pool of readily available nonracemic *trans*-cyclohexyl diols. These studies led to the finding of similarly effective alkene diboration catalysts TBS-DHG and DHR. As depicted in Scheme 1.15, TBS-DHG was synthesized from inexpensive carbohydrate starting material D-glucal triacetate ($1.4/g) in three steps (hydrogenation, deacylation, TBS protection). The DHR catalyst was derived from L-rhamnal diacetate ($20/g) in two steps (hydrogenation, deacylation). Importantly, TBS-DHG catalyst and DHR catalyst are pseudo-enantiomers of each other, such that both enantiomers of products can be readily obtained from the enantioselective alkene diboration reaction.

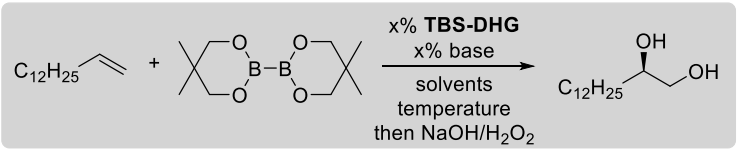
Scheme 1.15 Preparation of catalysts TBS-DHG and DHR



With the best catalysts in hand, various other reaction conditions such as temperature, solvents and bases were then studied for further improvement of reactivity and enantioselectivity. As shown in Scheme 1.16, 1-tetradecene, $B_2(neo)_2$ and TBS-DHG catalyst were chosen for the reaction optimization. When operating the carbohydrate-catalyzed diboration reaction with 30% cesium carbonate at 60 ^oC, an appreciable amount of product (47%) was formed even when no catalyst was used in the reaction. This indicates that background reaction is a possible reason for the erosion of the product enantioselectivity (entry 1 and entry 2). When using an organic base DBU, a diminished amount of background reaction (18%) was observed. At the same time, the product was afforded in higher enantioselectivity (94:6 er, entry 3 and 4). Further lowering the reaction temperature to room temperature appeared to completely suppress the background reaction. In this case, the product enantioselectivity was enhanced to 96:4 er (entry 5, 6). As shown in entry 7, the loading of the TBS-DHG catalyst can be lowered from 30% to 10% but requires prolonged reaction time (48 hours instead of 16 hours).

Although the reaction works well in THF, reactions in other solvents such as DCM, toluene and ethyl acetate are not as efficient (entry 8, 9, 10). In conclusion, the conditions shown in entry 7 were chosen as the standard reaction conditions for the rest of this preliminary study.

Scheme 1.16 Condition Optimization for Carbohydrate Catalyzed Alkene Diboration



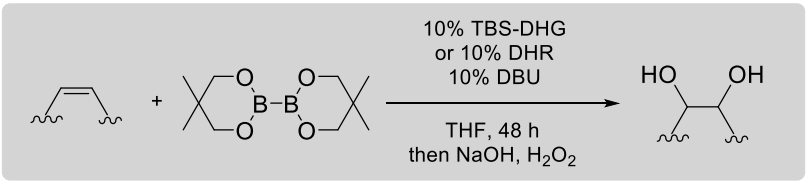
entry	catalyst(%)	time	solvent	temperature	base	conversion	er
1	30%	16h	THF	60°C	Cs_2CO_3	90%	90:10 er
2	0%	16h	THF	60°C	Cs_2CO_3	47%	n.r.
3	30%	16h	THF	60°C	DBU	85%	94:6 er
4	0%	16h	THF	60°C	DBU	18%	n.r
5	30%	16h	THF	22°C	DBU	80%	96:4 er
6	0%	16h	THF	22°C	DBU	0%	n.r.
7	10%	48h	THF	22°C	DBU	77%	96:4 er
8	10%	24h	DCM	22°C	DBU	15%	90:10 er
9	10%	24h	toluene	22°C	DBU	<2% yield	
10	10%	24h	EtOAc	22°C	DBU	<2% yield	

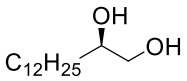
1.4 Substrate Scope

With the optimized reaction condition in hand, we studied the substrate scope of the carbohydrate catalyzed enantioselective alkene diboration. As depicted in Scheme 1.17, a number of terminal alkenes were tested in the standard reaction conditions. Generally, unactivated terminal alkenes reacted smoothly, affording products in synthetically useful yields and good enantioselectivities (**10**, **11**, **12**, **13**, **16**). Styrenes appeared to pose a challenge (**14**); the corresponding diol was afforded in much lower enantioselectivity.

Functional groups such as protected alcohols and esters were well tolerated (**15**, **17**, **19**). Internal alkenes were also tested in the carbohydrate catalyzed alkene diboration. They underwent the diboration reaction only under more forcing conditions (10% Cs_2CO_3, 60 ^oC). Thus, products from internal alkene diboration were generated in lower enantioselectivities (**20**, **21**), possibly because of the competing background reaction.

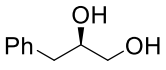
Scheme 1.17 Substrate Scope of Carbohydrate Catalyzed Alkene Diboration





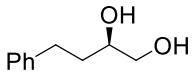
10

TBS-DHG:
70%, 96:4 er



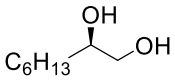
11

TBS-DHG:
74%, 96:4 er



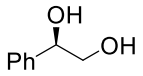
12

TBS-DHG:
47%, 96:4 er



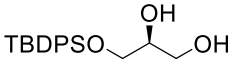
13

TBS-DHG: 79%, 96:4 er
DHR: 81%, 5:95 er



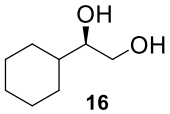
14

TBS-DHG:
54%, 61:39 er



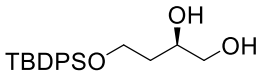
15

TBS-DHG:
47%, 96:4 er



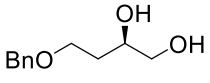
16

TBS-DHG: 68%, 97:3 er
DHR: 50%, 4:96 er



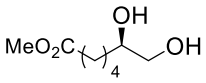
17

TBS-DHG: 74%, 96:4 er
DHR: 60%, 3:97 er



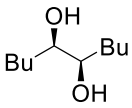
18

TBS-DHG: 74%, 96:4 er
DHR: 69%, 4:96 er



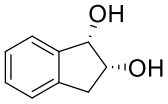
19

TBS-DHG:
72%, 97:3 er



20[a]

TBS-DHG: 61%, 86:14 er
DHR: 60%, 15:85 er



21[a]

TBS-DHG:
30%, 88:12 er

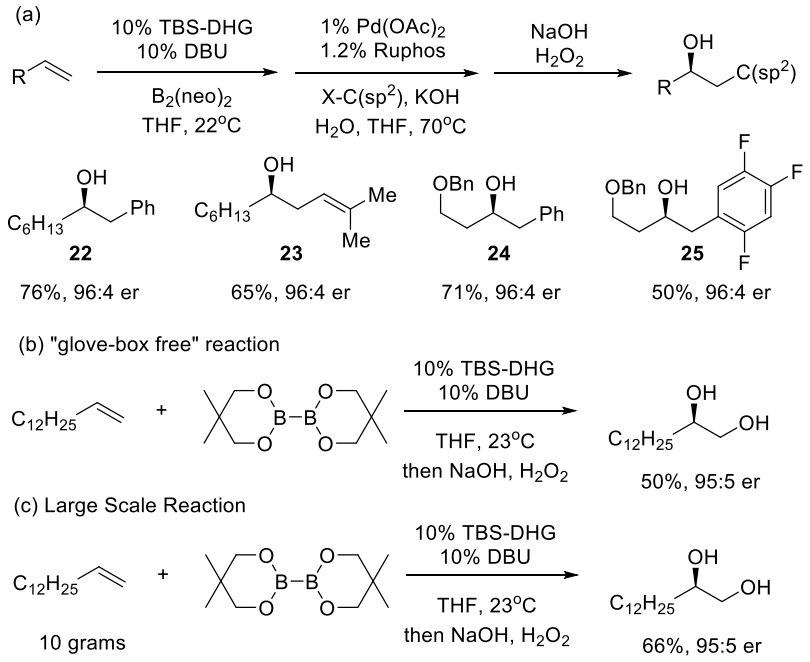
a. Reaction conducted at 60 ^oC with 10% of TBS-THG and 10% Cs_2CO_3

To further demonstrate the synthetic applications of the carbohydrate catalyzed alkene diboration, we studied the cascade diboration/selective Suzuki cross-coupling reaction. This cascade reaction was developed by the Morken group in 2014.[23] However, pinacol boronic esters were studied in this previous paper. Transformations employing the

[23] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature*, **2014**, *16*, 386.

neopentyl glycolato boronic esters has much less precedent in literature. As depicted in Scheme 1.18 (a), the primary boronic ester of the diboration product was selectively cross-coupled with various types of aryl or alkenyl eletrophiles. The untouched secondary boronic ester was then oxidized to form an alcohol. This cascade sequence builds up the molecular complexity very efficiently. Of note, the carbohydrate catalyzed alkene diboration reaction is less sensitive to air and moisture compared to the previous methods using transition metal catalysis, and as a result, the reaction can be performed without a glovebox and still affords the product in good enantioselectivity and yield (Scheme 1.18, (b)). Furthermore, the reaction can also be conducted on large scale (10 gram) while still generates product in good yield (66%) and high enantioselectivity (95:5 er) (Scheme 1.18, (c)).

Scheme 1.18 Product Functionalization (a) and Large Scale Reaction (b)

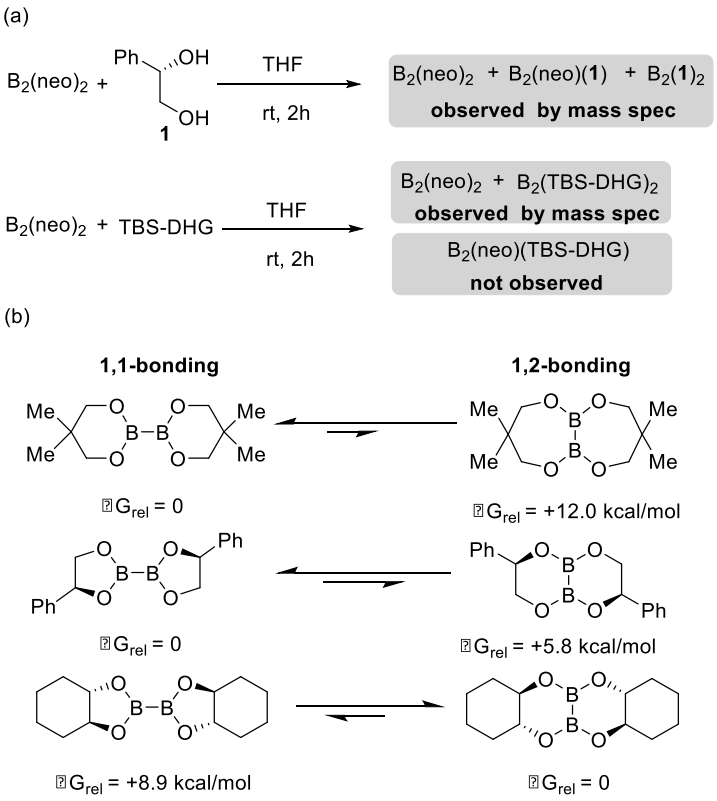


1.5 **Mechanistic Studies**

To further probe the reaction mechanism, several experiments were performed. As shown in Scheme 1.19 (a), when diboron starting material $B_2(neo)_2$ and styrene derived diol **1** were mixed together for 2 hours, both mono exchanged species $B_2(neo)$(**1**) and doubly exchanged species B_2(**1**)$_2$ were detected by mass spectrometry. However, when $B_2(neo)_2$ and TBS-DHG catalyst were mixed together for 2 hours, only the doubly exchanged species B_2(TBS-DHG)$_2$ was detected by mass spectrometry. The mono exchanged species B_2(neo)(TBS-DHG) was not detected. These interesting results made us suspect that B_2(TBS-DHG)$_2$, the reactive chiral intermediate for the carbohydrate catalyzed alkene diboration, is bonded differently from common diboron structures. As shown in Scheme 1.19 (b), common diboron compounds are bonded in 1,1-bonding mode. Diboron compounds can also exist in 1,2-bonding mode, which is uncommon, but has been addressed for several compounds.[24] According to the DFT calculations (M06-2X/6-31+G*; PCM solvation model with THF), for acyclic diol ligands such as neopentyl glycol and styrenediol, the 1,1-bonding diboron is energetically favored compared to the 1,2-bonding diboron. However, for trans-cyclohexanediol, the 1,2-bonded diboron is much more favored energetically than the 1,1,-bonded diboron.

[24] (a) Clegg, W.; Johann, T. R.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. *J. Chem. Soc., Dalton Trans*. **1998**, 1431
(b) Alibadi, M. A. M.; Batsanov, A. S.; Bramham, G.; Charmant, J. P. J.; Haddow, M. F.; Mackay, L.; Mansell, S. M.; McGrady, J. E.; Norman, N. C.; Roffey, A.; Russell, C. A. *Dalton Trans.* **2009**, 5348.
(c) Lesley, M. J. G.; Norman, N. C.; Orpen, A. G.; Starbuck, J. *New. J. Chem.* **2000**, *24*, 115
(d) Cade, I. A.; Chau, W. Y.; Victorica-Yrezabal, I.; Ingleson, M. J. *Dalton Trans.* **2015**, *44,* 7506.

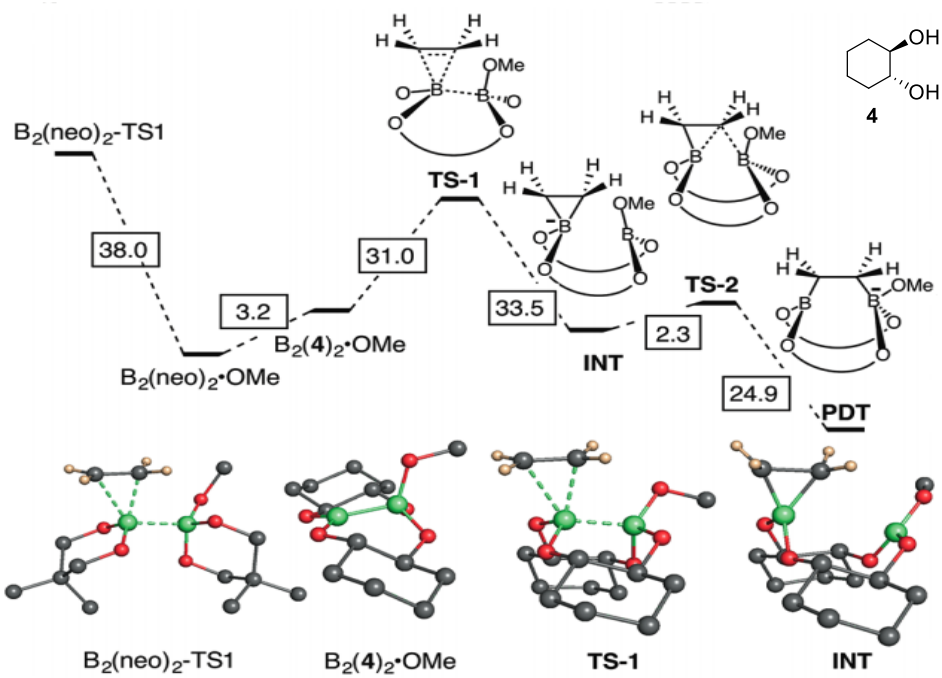
Scheme 1.19 Mechanistic Studies of Carbohydrate Catalyzed Alkene Diboration



With this piece of information in hand, the reaction pathway for the carbohydrate-catalyzed enantioselective diboration was investigated by DFT calculations (Figure 1, M06-2X/6-31+G*; PCM solvation model with THF, IRC analysis to confirm transition structures connect with correct ground state). Simplified reagents 1,2-*trans*-cyclohexldiol (catalyst), ethylene (substrate), and methoxide (base) were used in the DFT calculations. As depicted in Figure 1, the activation energy for activated $B_2(neo)_2$*OMe to react with ethylene is 7.0 kcal/mol higher than the activation energy for chiral reactive intermediate $B_2(\mathbf{4})_2$*OMe reacting with ethylene. This means that under standard reaction conditions, background reaction is not a huge problem for the carbohydrate-catalyzed diboration. Secondly, the diboration reaction occurs in a stepwise manner between ethylene and the activated chiral complex $B_2(\mathbf{4})_2$*OMe. The first step is the rupture of the B-B bond (**TS-1**,

Figure 1) and the formation of an anionic boracycle tethered with a trivalent borate. Mechanistically, this first step appears to be isoelectronic with cyclopropanation involving singlet carbenes, and it is related to the mechanism proposed by Fernandez and coworkers.[10] The second step is the intramolecular reaction between anionic boracycle and trivalent borate to afford the macrocyclic adduct. This step happens in a stereoretentive fashion and after further exchange with neopentyl glycol exiting in the reaction media, the 1,2-bis(boronates) was formed and the chiral diol catalyst was regenerated.

Figure 1. Calculated Reaction Mechanism for Carbohydrate Catalyzed Alkene Diobration



1.6 Conclusions

We developed the carbohydrate-catalyzed enantioselective alkene diboration after investigating a variety of chiral diols as catalysts. The catalysts used in this method can be easily accessed from inexpensive carbohydrates. Both terminal alkenes and internal

alkenes underwent the diboration reaction in a selective fashion. The diol products obtained after oxidation, were afforded in synthetically useful yields and enantioselectivities. The reaction can be conducted without a glovebox in as large as 10 gram scale. Additionally, preliminary mechanistic studies suggest that the 1,2-bonded chiral diboronate is the potential reactive intermediate for the carbohydrate catalyzed alkene diboration reaction.

1.7 Experimental Section

1.7.1 General Information

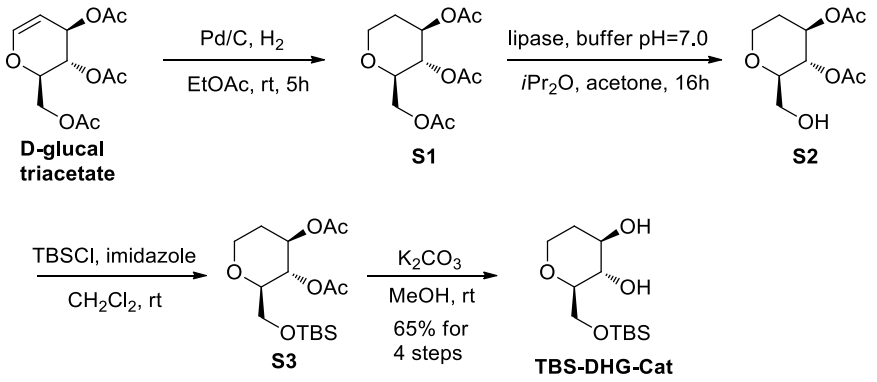
^{1}H NMR spectra were measured using a Varian Unity Inova 500 MHz or a Varian Gemini 400 MHz spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and assignment. ^{13}C NMR spectra were recorded on Varian Unity Inova 500 MHz (125 MHz) or a Varian Gemini 400 MHz (100 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.00 ppm). Infrared (IR) spectra were recorded on a Bruker α-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High resolution mass spectrometry (HRMS) was performed at Boston College, Chestnut Hill, MA.

Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA), and potassium

permanganate (KMnO4). Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization detector, and a Supleco β-Dex 120 column with helium as the carrier gas. Analytical chiral gas-liquid chromatography (GLC) was also performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β -Dex 120 column with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Thar Supercritical Chromatograph equipped with an auto sampler and a Waters photoiodide array detector with isopropanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Bis(neopentyl glycolato)diboron was purchased from Oakwood Chemicals. D-glucal triacetate and L-rhamnal triacetate were purchased from Alfa Aesar. 5-Hexenoic acid was purchased from TCI America. (1S, 2S)-*trans*-1,2-cyclohexanediol and (1R, 2R)-trans-1,2-cyclohexanediol were purchased from Acros Organics. Tetradecene, octene, 4-phenyl-1-butene, vinyl cyclohexane, allylbenzene, indene, trans-5-decene, styrene, 3-buten-1-ol and DBU were purchased from Aldrich. Phosphate buffer solution (PH = 7.0) was purchased from Fisher Scientific. Palladium Acetate and palladium on carbon were purchased from Strem Chemicals. Ruphos was purchased from Acros Organics. Bromobenzene was purchased from Aldrich. Potassium hydroxide was purchased from Fisher Scientific. All chemicals were used as received.

1.7.2 Synthesis of TBS-DHG and DHR catalysts



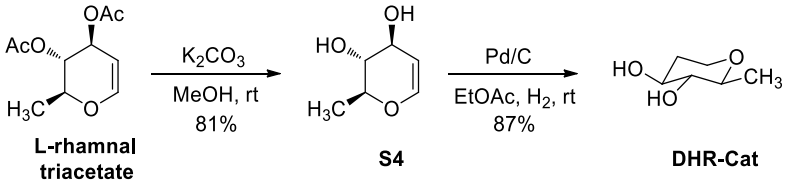
A flame-dried round bottom flask equipped with a stir bar was charged with D-glucal triacetate (4.36 g, 16.0 mmol), palladium on carbon (5%, 0.80 mmol, 852.0 mg) and ethyl acetate (30 mL). The vessel was purged with hydrogen gas and the reaction mixture was allowed to stir at room temperature under balloon pressure of hydrogen for 5 hours. The mixture was then filtered through a pad of silica gel. The filtrate was concentrated by rotary evaporation to give crude oil **S1**. The crude product was used for next step without further purification.

A round bottom flask was equipped with stir bar and a solution of the crude product **S1** in acetone (17.6 mL) and isopropyl ether (30.0 mL) was added to the flask. To the reaction mixture was then added Lipase from *Candida rugosa* (1.54 g) and phosphate buffer (pH = 7.0, 180 mL). The reaction mixture was stirred at room temperature for 16 h and was then filtered through a pad of Celite. After separating the organic layer, the aqueous layer was washed four times with dichloromethane and the combined organics layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford crude oil **S2**. The crude product **S2** was used for next step without further purification.

A flame-dried round bottom flask equipped with a stir bar was charged with imidazole (2.0 equiv., 32.0 mmol, 2.18 g), sealed with a septum, and the flask flushed with nitrogen

gas for 5 minutes. To the round bottom flask was then added the crude oil **S2** dissolved in THF (40 mL), follwed by *tert*-butyldimethylsilyl chloride (1.5 equiv., 24.0 mmol, 3.60 g) dissovled in THF (30 mL). The reaction mixture was allowed to stir at room temperature under nitrogen for 20 h. After this time, saturated aqueous ammonium chloride (10 mL) and water (20 mL) were added to the reaction mixture. After separating the organic layer, the aqueous layer was washed three times with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford crude oil **S3**. The crude product **S3** was used for next step without further purification.

To a round bottom flask equipped with a stir bar was added the crude product **S3** and methanol (90 mL), followed by potassium carbonate (1.5 equiv., 24.0 mmol, 3.31 g). The reaction mixture was stirred at room temperature for 3 hours. After this time period, the reaction was slowly quenched with saturated aqueous NH_4Cl (15.0 mL). The methanol solvent was removed by rotary evaporation and the remaining aqueous phase washed with ethyl acetate (3 x 30 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford the crude oil. The crude product was purified through silica gel column (50% ethyl acetate in hexane) to afford the DHG catalyst as white solid (2.73 g, 65% yield over 4 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s,1H), 0.10(s, 1H) 0.91 (s, 9H), 1.68 (ddq, 1H, J = 1.0, 5.0, 12.5 Hz), 1.90-1.95 (m, 1H), 3.18-3.22 (m, 1H), 3.42-3.48 (m, 2H), 3.63-3.68 (m, 1H), 3.73 (dd, 1H, J = 7.5, 10.0 Hz), 3.92-3.95 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ -5.3, -5.4, 18.4, 26.0, 32.9, 65.7, 65.8, 73.1, 76.2, 77.9; IR (film) cm^{-1} 3365w, 2952m, 2855m, 1463w, 1251m, 1093s; HRMS-(DART+) for C12H27O4Si$[M+H]^+$: calculated: 263.1679, found: 263.1681. Optical rotation: $[\alpha]_D^{25}$ = -19.4 [c=1.0, $CHCl_3$].



Diol S4. L-rhamnal diacetate (642.7 mg, 3.0 mmol) and methanol (30.0 mL) were added to a 100-mL round bottom flask. Then at room temperature, K_2CO_3 (621.9 mg, 4.5 mmol) was added to the solution. The mixture was stirred at room temperature for another 2 hours, followed by slow addition of saturated aqueous NH_4Cl (10.0 mL). The methanol solvent was then removed by rotary evaporation, the crude product extracted from the aqueous phase by washing with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude residue was used without further purification. (314.0 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (d, 3H, *J* = 6.5 Hz), 3.42 (t, 1H, *J* = 9.0 Hz), 3.84-3.89 (m, 1H), 4.21 (d, 1H, *J* = 6.0 Hz), 4.71 (d, 1H, *J* = 5.5 Hz), 6.31 (d, 1H, *J* = 6.0 Hz);^{13}C NMR (150 MHz, $CDCl_3$) δ 17.4, 70.4, 74.7, 75.3, 102.9, 145.0; IR (film) cm^{-1} 3243m, 2895w, 2890w, 1642s, 1387m, 1149s; HRMS-(DART+) for C6H9O2 $[M+H-H_2O]^+$: calculated: 113.0603, found: 113.0599. Optical rotation: $[\alpha]_D^{25}$ = +26.2 [c=1.3, $CHCl_3$].

DHR catalyst. The above compound **S4** (130.1 mg, 1.0 mmol) and ethyl acetate (10.0 mL) were added to a 25-mL round bottom flask. Then Pd/C (10% Pd on carbon, 106.4 mg, 0.1 mmol) was added to the solution at room temperature. The flask was sealed with a rubber septum and flushed with a balloon pressure of H_2 atmosphere. The reaction was stirred at room temperature under a balloon atmosphere of H_2 for 3 h before it was filtered through a pad of silica gel and washed with EtOAc (2 × 20 mL). The filtrate was concentrated by rotary evaporation, then the crude residue was purified on silica gel (60%

ethyl acetate in hexanes, stain in CAM) to afford the **DHR catalyst** as a white solid (115.0 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, 3H, *J* = 6.0 Hz), 1.72 (dq, 1H, *J* = 5.0, 12.5 Hz), 1.94-1.98 (m, 1H), 3.08 (t, 1H, *J* = 9.0 Hz), 3.19-3.24 (m, 1H), 3.45 (dt, 1H, *J* = 2.0, 12.0 Hz), 3.56-3.61 (m, 1H), 3.92 (ddd, 1H, *J* = 1.5, 5.0, 12.5 Hz);^{13}C NMR (150 MHz, $CDCl_3$) δ 18.3, 34.0, 65.7, 73.3, 76.4, 78.2; IR (film) cm^{-1} 3364m, 2933w, 2858w, 1379w, 1085s, 1056s; HRMS-(DART+) for C12H13O3 $[M+H]^+$: calculated: 133.0864, found: 133.0866. Optical rotation: $[\alpha]_D^{25}$ = +2.9 [c=1.4, $CHCl_3$].

1.7.3 General Experimental Procedure for Alkene Diboration/Oxidation

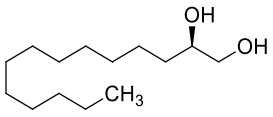
A. General Procedure with DHG catalyst.

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (0.05 mmol, 0.1 equiv), bis(neopentylglycolato)diboron (0.50 mmol, 1.0 equiv), the alkene substrate (0.50 mmol, 1.0 equiv) and THF (0.50 mL). Then DBU (0.05 mmol, 0.1 equiv) was added to the solution. The vial was sealed with a rubber septum, removed from the glove box, and the mixture was stirred at room temperature for 24-48 hours. Then the reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give crude reaction mixture.

B. General Procedure with DHR catalyst.

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with DHR catalyst (0.10 mmol, 0.2 equiv), bis(neopentylglycolato)diboron (0.50 mmol, 1.0 equiv), the alkene substrate (0.50 mmol, 1.0 equiv) and THF (0.50 mL). Then DBU (0.05 mmol, 0.1 equiv) was added to the solution. The vial was sealed with rubber septum, removed from the glove box, placed in an oil bath which was preheated to 35 ^{o}C, and stirred at 35 ^{o}C for 48 hours. Then the reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give crude reaction mixture.

1.7.4 Full Characterization and Proof of Stereochemistry

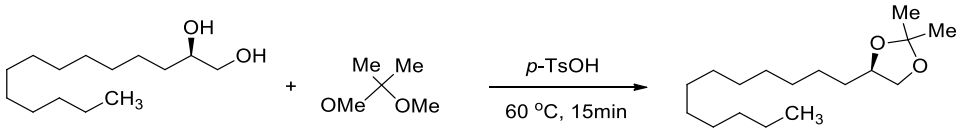


***(R)*-tetradecane-1,2-diol (10)**. The diboration was performed for 48 hours according to the general procedure with 1-tetradecene substrate (94%, 104.5 mg, 0.50 mmol, 0.13 mL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (1.00 mL, 0.5 M). After oxidation, the crude reaction mixture was purified on silica gel (40% ethyl acetate in

hexanes, stain in CAM) to afford the product as a white solid (90.0 mg, 78% yield). Spectral data and optical rotation are in accordance with the literature[25]. HRMS-(DART+) for C14H34NO2 $[M+NH4]^+$: calculated: 248.2590, found: 248.2583.

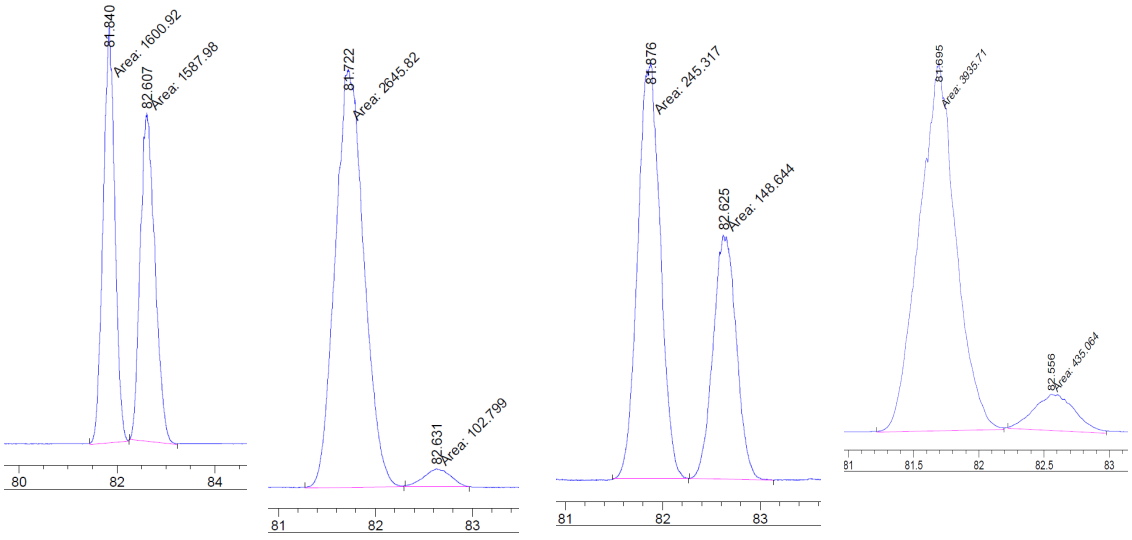
Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid (below). The resulting ketal was compared to the racemic ketal of tetradecane-1,2-diol prepared from dihydroxylation of 1-tetradecene with ruthenium trichloride and sodium periodiate[26]. The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-tetradecene utilizing AD-mix-β[27].



Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.

[25] Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Eric N. Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.
[26] Shing, T. K. M.; Tam, E. K. W.; Tai, V. W.-F.; Chung, I. H. F.; Jiang, Q. *Chem. Eur. J.* **1996**, *2*, 50.
[27] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.



racemic product diboration product coinjection of diboration product + racemic authentic product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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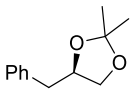
2	82.631	MM	0.3142	102.79861	5.45218	3.74001



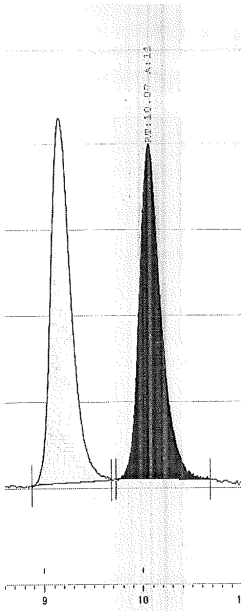
(R)-4-benzyl-2,2-dimethyl-1,3-dioxolane (11). The diboration was performed for 48 hours according to the general procedure with allyl benzene (59.1 mg, 0.50 mmol, 66.4 µL), DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 µL) in THF (0.50 mL, 1.0 M). After oxidation, the crude reaction mixture was dissolved in EtOAc (5 mL) and filtered through a short pad of silica gel. Elution with EtOAc followed by concentration. Because the product diol co-eluted with neopentyl glycol, the resulting residue was treated with 2,2-

dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, then stirred at 60 ^{o}C for 30 min. Then the mixture was filtered through a short pad of silica gel. Elution with hexanes/EtOAc (3/1) followed by concentration furnished the crude product which was purified on silica gel (4% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (60.0 mg, 63% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.44 (s, 3H), 2.77 (dd, 1H, *J* = 7.2, 13.8 Hz), 3.02 (dd, 1H, *J* = 6.6, 13.8 Hz), 3.65 (dd, 1H, *J* = 6.6, 7.8 Hz), 3.96 (dd, 1H, *J* = 6.0, 7.8 Hz), 4.31-4.35 (m, 1H), 7.21-7.24 (m, 3H), 7.29-7.31 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.9, 27.2, 40.3, 69.2, 76.9, 109.3, 126.7, 128.7, 129.3, 137.7; HRMS-(DART+) for C12H17O2 $[M+H]^{+}$: calculated: 193.1229, found: 193.1226. Optical rotation: $[\alpha]_D^{25} = -8.2^{o}$ [c=1.4, $CHCl_3$].

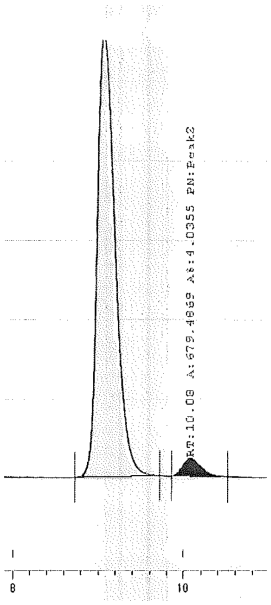
Analysis of Stereochemistry:

The acetonide product was treated with methanol and catalytic toluenesulfonic acid. The resulting diol was compared to the racemic 3-phenylpropane-1,2-diol prepared from dihydroxylation of allylbenzene with ruthenium trichloride and sodium periodiate[22]. The absolute stereochemistry was assigned by analogy.

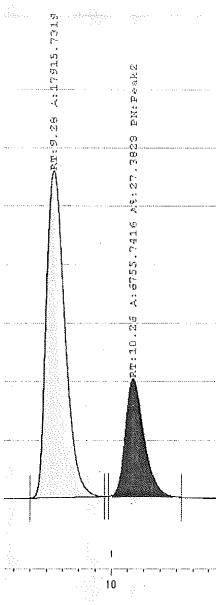
Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-phenylpropane-1,2-diol.



racemic product

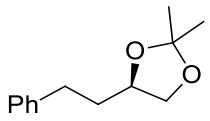


diboration product



coinjection

Peak Info						
Peak No	% Area	Area	RT (min)		Height (mV)	K'
1	95.9645	16158.4394	9.07		1115.6597	0.008
2	4.0355	679.4869	10.08		45.0861	0.0089
Total:	100	16837.9263				



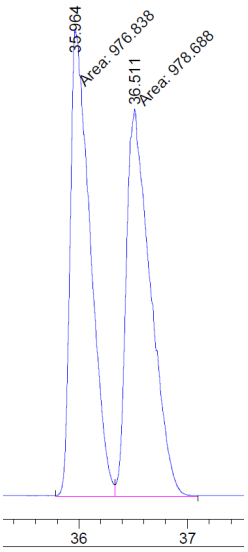
(R)-2,2-dimethyl-4-phenethyl-1,3-dioxolane (12). The diboration was performed for 24 hours according to the general procedure with 4-phenyl-1-butene (66.1 mg, 0.50 mmol, 75.1 μL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). After oxidation, the crude reaction mixture was dissolved in EtOAc (5 mL) and filtered through a short pad of silica gel with elution with EtOAc followed by concentration. The

resulting residue was treated with 2,2-dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, then stirred at 60 ^{o}C for 30 min. Then the mixture was filtered through a short pad of silica gel with elution by hexanes/EtOAc (3/1), followed by concentration. The crude product was purified on silica gel (4% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (80.0 mg, 78% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.37 (s, 3H), 1.44 (s, 3H), 1.81-1.85 (m, 1H), 1.94-2.00 (m, 1H), 2.63-2.68 (m, 1H), 2.75-2.80 (m, 1H), 3.53 (dd, 1H, *J* = 7.2, 15.0 Hz), 4.02 (dd, 1H, *J* = 6.6, 7.8 Hz), 4.09-4.13 (m, 1H), 7.19-7.21 (m, 3H), 7.26-7.30 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.9, 27.2, 32.2, 35.5, 69.5, 75.6, 108.9, 126.1, 128.5, 128.6, 141.7; HRMS-(DART+) for C13H19O2 $[M+H]^{+}$: calculated: 207.1385, found: 207.1389. Optical rotation: $[\alpha]_D^{25} = -4.1^{o}$ [c=3.2, $CHCl_3$].

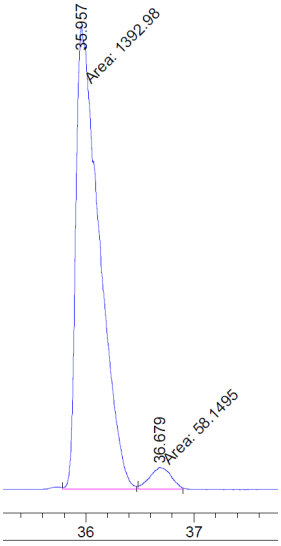
Analysis of Stereochemistry:

The ketal product was compared to the racemic ketal of 4-phenylbutane-1,2-diol prepared from dihydroxylation of 4-phenyl-1-butene with ruthenium trichloride and sodium periodiate[22]. The absolute stereochemistry was assigned by analogy.

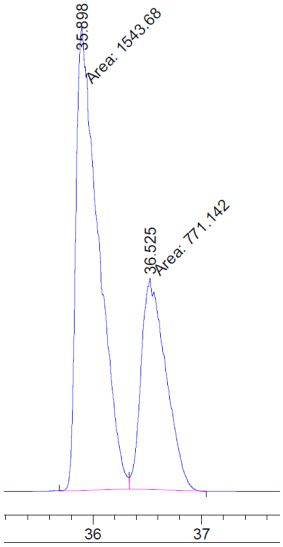
Chiral GLC (β-dex, Supelco, 120 °C 5min, then 0.5°C /min to 140°C, 20 psi)- analysis of the acetonide of 4-phenylbutane-1,2-diol



racemic product

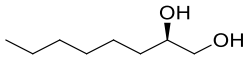


diboration product



coinjection of diboration product + racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.957	MM	0.2510	1392.98035	92.48728	95.99281
2	36.679	MM	0.2272	58.14952	4.26476	4.00719



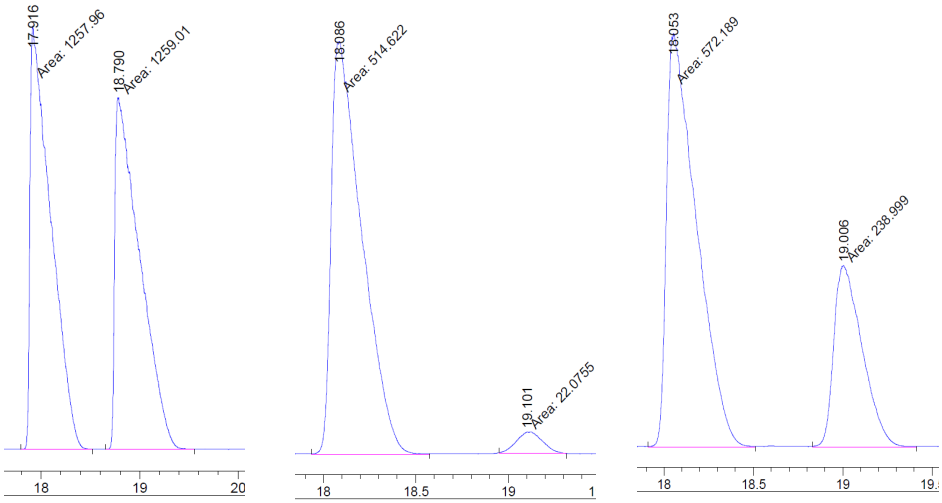
***(R)*-octane-1,2-diol (13)**. The diboration was performed for 24 hours according to the general procedure with 1-octene (56.1 mg, 0.50 mmol, 78.5 µL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 µL) in THF (0.50 mL, 1.0 M). To facilitate removal of catalyst, after oxidation the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 2h. Then the solution was concentrated by rotary

evaporation, and the resulting crude product was purified on silica gel (40% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (58.0 mg, 79% yield). Spectral data and optical rotation are in accordance with the literature[28]. HRMS-(DART+) for C8H22NO2 $[M+NH_4]^+$: calculated: 164.1651, found: 164.1655.

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate[22]. The absolute stereochemistry was assigned by analogy.

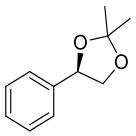
Chiral GLC (β-dex, Supelco, 100 °C 30min, 20 psi)- analysis of the acetonide of octane-1,2-diol.



racemic product diboration product coinjection of diboration product + racemic

[28] Toribatake, K.; Nishiyama, H. *Angew. Chem. Int. Ed.* **2013**, *52,* 11011.

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	18.086	MM	0.1920	514.62189	44.68312	95.88678
2	19.101	MM	0.1620	22.07553	2.27065	4.11322

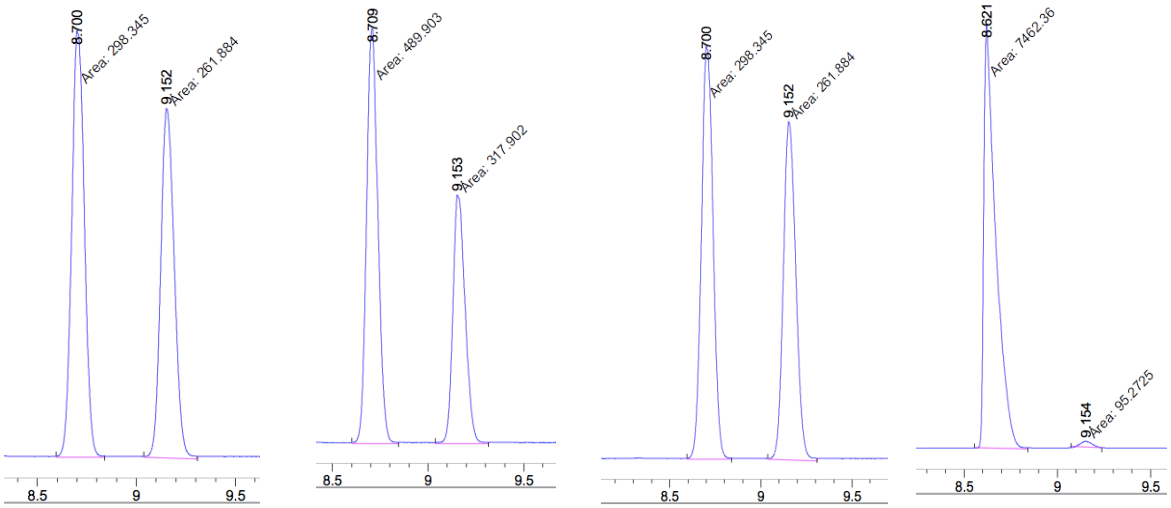


(*R*)-2,2-dimethyl-4-phenyl-1,3-dioxolane (14). The diboration was performed for 48 hours according to the general procedure with styrene (52.1 mg, 0.50 mmol, 57.3 μL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.5 mL, 1.0 M). After oxidation, the crude reaction mixture was dissolved in EtOAc (5 mL) and filtered through a short pad of silica gel. The resulting residue was treated with 2,2-dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, then stirred at 60 ^{o}C for 30 min, and filtered through a short pad of silica gel eluting with hexanes/EtOAc (3/1), followed by concentration. The crude product was purified on silica gel (4% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (48.0 mg, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 3H), 1.57 (s, 3H), 3.72 (t, 1H, J = 8.0 Hz), 4.31 (dd, 1H, J = 6.0, 8.0 Hz), 5.08 (dd, 1H, J = 6.0, 8.0 Hz), 7.31-7.33 (m, 1H), 7.35-7.39 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.1, 26.8, 71.9, 78.1, 109.9, 126.4, 128.2, 128.7, 139.2; HRMS-(DART+) for C11H13O2 $[M-H]^-$: calculated: 177.0916, found: 177.0909. Optical rotation: $[\alpha]_D^{25}$ = -12.9^{o} [c 2.3 $CHCl_3$].

Analysis of Stereochemistry:

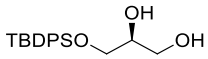
The ketal product was compared to the racemic ketal of 1-phenylethane-1,2-diol prepared from dihydroxylation of styrene with ruthenium trichloride and sodium periodiate[22]. The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of styrene utilizing AD-mix-β[23].

Chiral GLC (β-dex, Supelco, 140 °C 20 min)- analysis of the acetonide of (R)-1-phenylethane-1,2-diol



racemic product | diboration product | coinjection of diboration product + racemic | authentic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.709	MM	0.0687	489.90314	118.90469	60.64622
2	9.153	MM	0.0744	317.90179	71.21526	39.35378



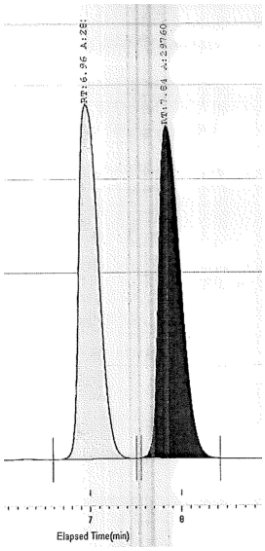
(*S*)-3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol (15). The diboration was performed according to the general procedure for 48 hours at 60 ^{o}C with (allyloxy)(tert-butyl)diphenylsilane (148.25mg, 0.50 mmol), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.5 mL, 1.0 M). Due to the propensity for intramolecular silyl migration, neutral oxidation is required for this substrate. The reaction mixture was cooled to 0 °C (ice/water) and charged with phosphate buffer (pH = 7.0, 2.0 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The crude reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (77.7 mg, 47% yield). Spectral data and optical rotation are in accordance with the literature[29]. HRMS-(DART+) for C19H27O3Si $[M+H]^{+}$: calculated: 331.1730, found: 331.1731.

Analysis of Stereochemistry:

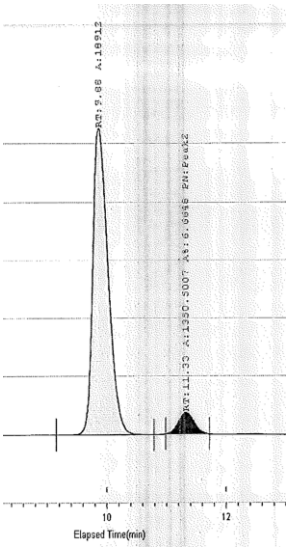
The 1,2-diol was compared to the racemic 3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol prepared from dihydroxylation of (allyloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate[22].

[29] Liang, C.; Lee, D. W.; Newton, M. G.; Chu, C. K. *J. Org. Chem.* **1995**, *60*, 1546.

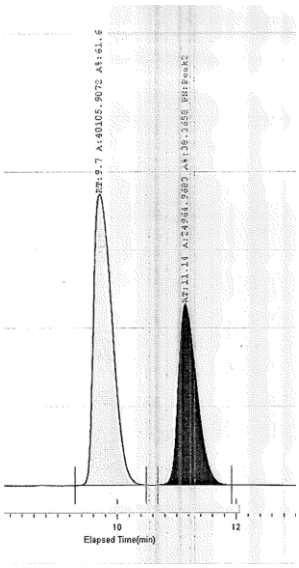
Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol



racemic product

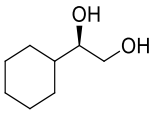


diboration product



coinjection of racemic and diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.3352	18912.6377	9.88	1053.8936	0.0091
2	6.6648	1350.5007	11.33	73.1425	0.0105
Total:	100	20263.1384			



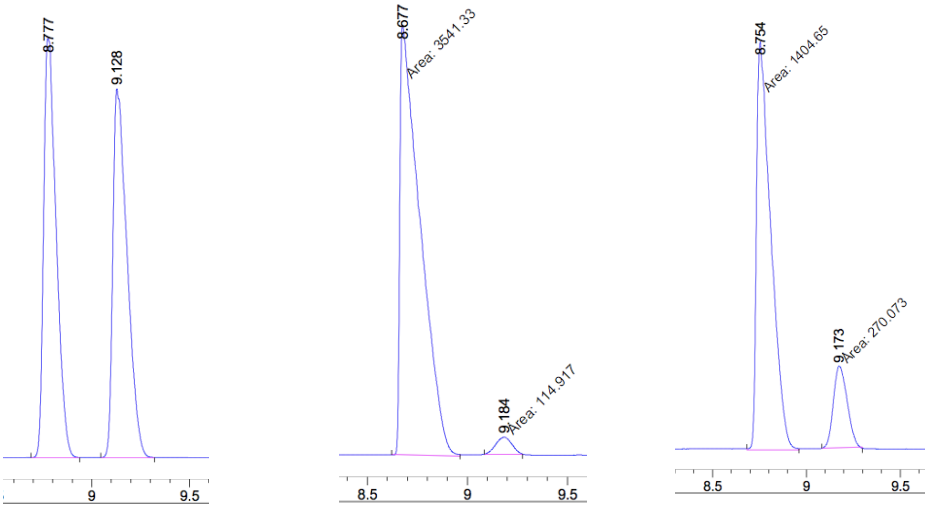
(*R*)-1-cyclohexylethane-1,2-diol (16). The diboration was performed according to the general procedure for 48 hours with vinyl cyclohexane (55.1 mg, 0.50 mmol, 68.5 µL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 µL) in THF (0.5 mL, 1.0 M). The crude

reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (50.0 mg, 68% yield). Spectral data is in accordance with the literature[30]. HRMS-(DART+) for $C_8H_{15}O$ $[M+H-H_2O]^+$: calculated: 127.1123, found:127.1117. Optical rotation: $[\alpha]_D^{25} = -5.2$ [c=0.5 $CHCl_3$].

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from dihydroxylation of vinyl cyclohexane with ruthenium trichloride and sodium periodiate[22].

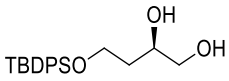
Chiral GLC (β-dex, Supelco, 130 °C 20 min)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol.



[30] Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538.

racemic product diboration product coinjection of diboration product + racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.677	MM	0.1174	3541.33301	502.56915	96.85698
2	9.184	MM	0.0940	114.91650	20.36620	3.14302



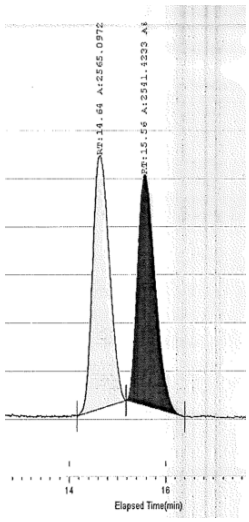
(*R*)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol (17). The diboration was performed according to the general procedure for 48 hours at 60 ^{o}C with (but-3-en-1-yloxy)(tert-butyl)diphenylsilane (155.3 mg, 0.50 mmol), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.5 mL, 1.0 M). Due to the capacity for silyl migration, neutral oxidation was employed for this substrate. The reaction mixture was cooled to 0 °C (ice/water) and charged with phosphate buffer (pH = 7, 2.0 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The crude reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (127.5 mg, 74% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.64-1.68 (m, 1H), 1.75-1.81 (m, 1H), 3.53 (dd, 1H, J = 6.6, 10.8 Hz), 3.65 (dd, 1H, J = 2.4, 10.8 Hz), 3.87 (s, 1H), 4.01 (s, 1H), 4.13 (q, 1H, J = 7.2 Hz), 7.39-7.44 (m, 6H), 7.68-7.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.0, 26.8, 34.7,

62.7, 66.7, 71.7, 127.8, 130.0, 135.5; HRMS-(DART+) for $C_{20}H_{29}O_3Si[M+H]^+$: calculated: 345.1886, found: 345.1895. Optical rotation: $[\alpha]_D^{25} = -2.9$ [c=3.6 $CHCl_3$].

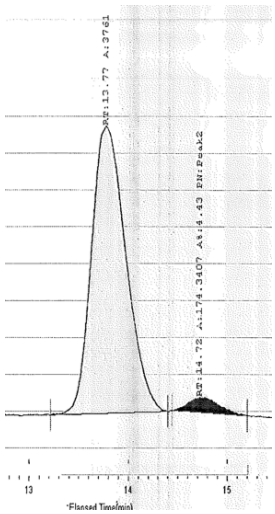
Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol prepared from dihydroxylation of (but-3-en-1-yloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[22]

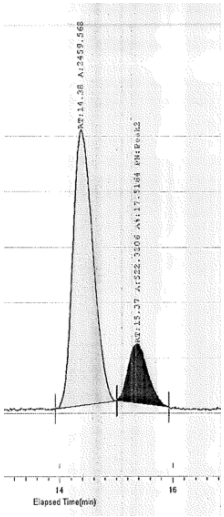
Chiral SFC (Chiracel OD-H, 7% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol



racemic product

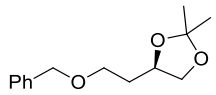


diboration product



coinjection of diboration product + racemic

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	95.57	3761.1062	13.77	155.8105	0.011
2	4.43	174.3407	14.72	8.1677	0.0118
Total:	100	3935.4469			

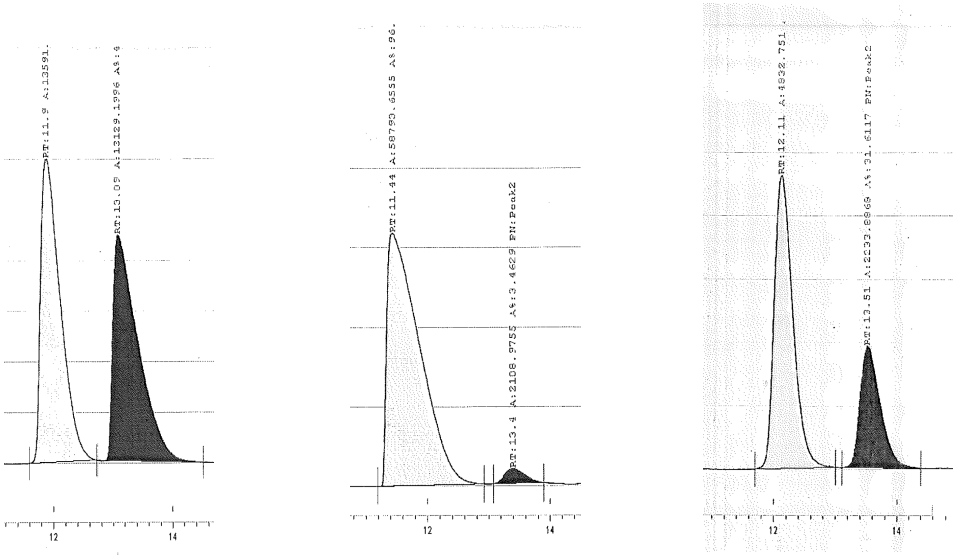


(R)-4-(2-(benzyloxy)ethyl)-2,2-dimethyl-1,3-dioxolane (18). The diboration was performed for 48 hours according to the general procedure with ((but-3-en-1-yloxy)methyl)benzene (81.1 mg, 0.50 mmol), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). After oxidation, the crude reaction mixture was dissolved in EtOAc (5 mL) and filtered through a short pad of silica gel. The resulting residue was treated with 2,2-dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, stirred at 60 ^{o}C for 30 min, and then filtered through a short pad of silica gel eluting with hexanes/EtOAc (3/1), followed by concentration. The crude product was purified on silica gel (4% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (87.0 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.40 (s, 3H), 1.83-1.89 (m, 1H), 1.91-1.96 (m, 1H), 3.55-3.61 (m, 3H), 4.05 (dd, 1H, *J* = 6.0, 7.8 Hz), 4.20-4.24 (m, 1H), 4.50 (d, 1H, *J* = 14.4 Hz), 4.52 (d, 1H, J=12.0 Hz) 7.27-7.29 (m, 1H), 7.29-7.36 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.9, 27.1, 34.0, 67.2, 69.8, 73.3, 74.1, 108.7, 127.8, 128.5, 138.5; HRMS-(DART+) for C14H21O3 $[M+H]^+$: calculated: 237.1491, found: 237.1489. Optical rotation: $[\alpha]_D^{25}$ = +0.7 [c=4.3, $CHCl_3$].

Analysis of Stereochemistry:

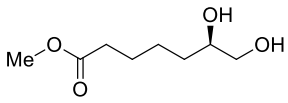
The acetonide product was treated with methanol and catalytic toluenesulfonic acid. The resulting diol was compared to the racemic 4-(benzyloxy)butane-1,2-diol prepared from dihydroxylation of ((but-3-en-1-yloxy)methyl)benzene with ruthenium trichloride and sodium periodiate.[22] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OD-H, 7% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-(benzyloxy)butane-1,2-diol.



racemic product | diboration product | coinjection of diboration product + racemic

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	96.5371	58793.6555	11.44	1591.7406	0.0145
2	3.4629	2108.9755	13.4	91.434	0.017
Total:	100	60902.631			



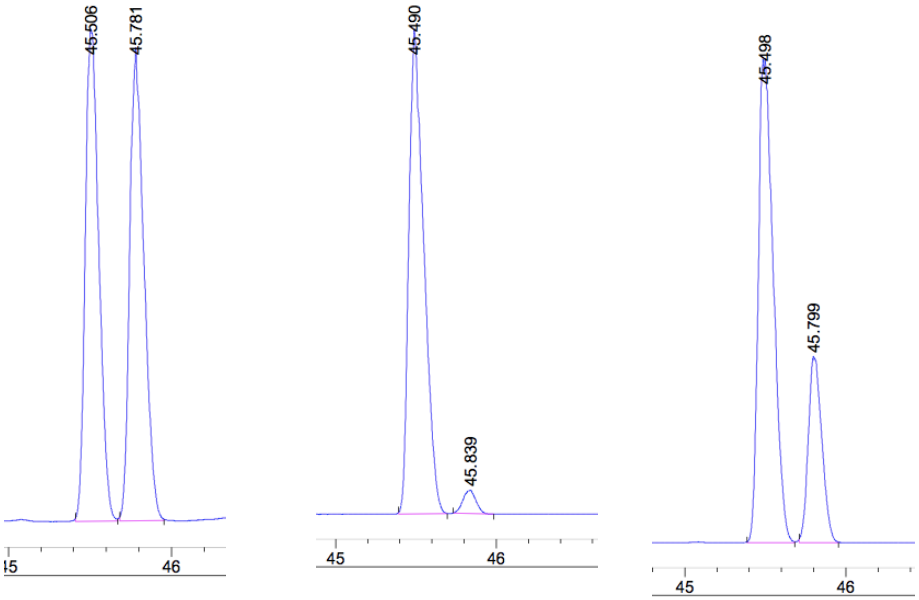
(*R*)-methyl 6,7-dihydroxyheptanoate (19). The diboration was performed according to the general procedure for 48 hours with methyl hept-6-enoate[7] (71.1 mg, 0.50 mmol), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.5 mL, 1.0 M). Due to the capacity for ester hydrolysis, neutral oxidation condition was employed for this substrate. The reaction mixture was cooled to 0 °C (ice/water) and charged with phosphate buffer

(pH = 7, 2.0 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes to pure ethyl acetate, stain in CAM) to afford the product as a white solid (63.0 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.33-1.49 (m, 4H), 1.59-1.62 (m, 2H), 2.31 (t, 2H, *J* = 7.3 Hz), 2.98 (s, 1H), 3.07 (s, 1H), 3.44 (dd, 1H, *J* = 7.8, 11.4 Hz), 3.58 (m, 1H), 3.65 (s, 3H), 3.68 (dd, 1H, *J* = 3.0, 11.4 Hz); ^{13}C NMR (125 MHz, CDCl3): δ 24.7, 25.0, 32.6, 33.8, 51.5, 66.7, 71.9, 174.3; HRMS-(DART+) for $C_8H_{17}O_4$ $[M+H]^+$: calculated:177.1127, found: 177.1129. Optical rotation: $[\alpha]_D^{25} = +2.6^o$ [c=0.76 $CHCl_3$].

Analysis of Stereochemistry:

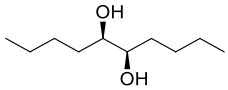
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of methyl 6,7-dihydroxyheptanoate prepared from dihydroxylation of hept-6-enoate with ruthenium trichloride and sodium periodiate.[22]

Chiral GLC (β-dex, Supelco, 70 °C 5 min, 2°C/min to 180 °C)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol.



racemic product diboration product coinjection

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	45.368	MM	0.1595	2483.64771	259.47623	97.05970
2	45.787	MM	0.1307	75.23882	9.59074	2.94030



(5R,6R)-decane-5,6-diol (20). In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar was charged with TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol), trans-5-decene (70.1 mg, 0.50 mmol, 94.8 μL), Cs_2CO_3 (16.3 mg, 0.05 mmol) and THF (0.50 mL). The vial was sealed with rubber septum, removed from the glove box, and put in a oil bath which was

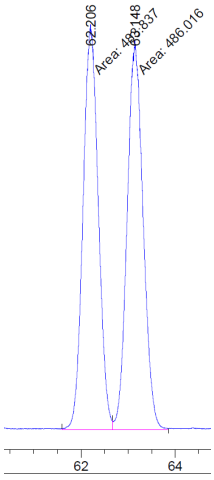
preheated to 60 ^{o}C, then sitrred for 24 hours. Then the reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The resulting crude product was purified on silica gel (30% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (53.0 mg, 61% yield). Spectral data and optical rotation are in accordance with the literature[31]. HRMS-(DART+) for C10H21O1 $[M+H-H_2O]^+$: calculated: 157.1592, found: 157.1589.

Analysis of Stereochemistry:

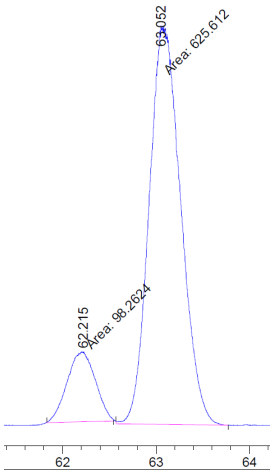
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of decane-5,6-diol prepared from dihydroxylation of trans-5-decene with ruthenium trichloride and sodium periodiate.[22] The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of trans-5-decene utilizing AD-mix-β.[23]

Chiral GLC (β-dex, Supelco, 70 °C 15min, then 0.25 °C/min to 90 °C, 20 psi)- analysis of the acetonide of decane-5,6-diol

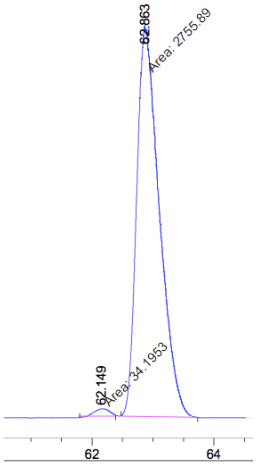
[31] Huang, J.; Corey, E. J. *Org. Lett.* **2003**, *5*, 3455.



racemic product

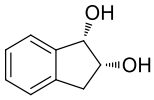


diboration product



authentic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.215	MM	0.3493	98.26236	4.68885	13.57451
2	63.052	MM	0.3919	625.61176	26.60573	86.42549

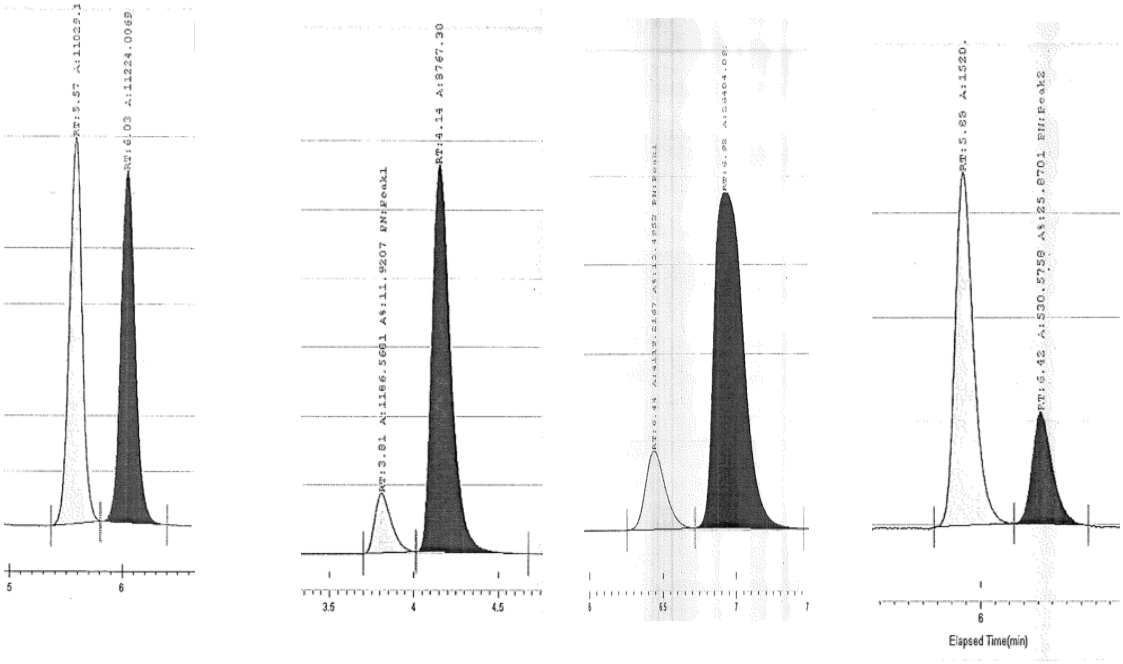


(1*S*,2*R*)-2,3-dihydro-1H-indene-1,2-diol. The diboration was performed for 48 hours according to the general procedure with indene (58.1 mg, 0.50 mmol, 58.3 µL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentyl glycolato)diboron (112.9 mg, 0.50 mmol) and cesium carbonate (16.3 mg, 0.05 mmol) in THF (0.5 mL, 1.0 M). The crude reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (22.5 mg, 30% yield). Spectral data and optical

rotation are in accordance with the literature[32]. HRMS-(DART+) for C_9H_9O [M+H-H_2O]$^+$: calculated:133.0653, found:133.0659.

Analysis of Stereochemistry:

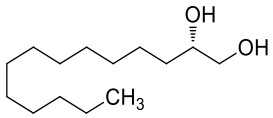
The 1,2-diol was compared to the racemic 2,3-dihydro-1H-indene-1,2-diol prepared from dihydroxylation of indene with ruthenium trichloride and sodium periodiate.[22] The authentic (1*R*, 2*S*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-tetradecene utilizing AD-mix-β.[23]



racemic product diboration product coinjection authentic

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	11.9207	1186.5681	3.81	174.4625	0.0046
2	88.0793	8767.3036	4.14	1126.0676	0.005
Total:	100	9953.8717			

[32] Fernandez, R.; Ros, A.; Magriz, A.; Dietrichc, H.; Lassalettab, J. M. *Tetrahedron,* **2007**, *63*, 6755.



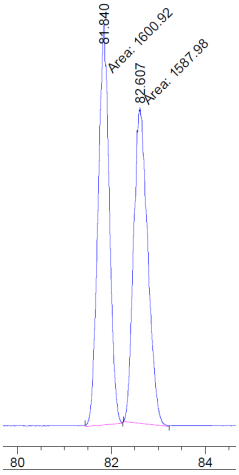
***(S)*-tetradecane-1,2-diol (10')**. The diboration was performed for 48 hours according to the general procedure with 1-tetradecene (94%, 104.5 mg, 0.50 mmol, 0.13 mL), DHR catalyst (13.2 mg, 0.10 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (1.00 mL, 0.5 M). After oxidation, the crude reaction mixture was purified on silica gel (40% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (80.0 mg, 70% yield). Spectral data and optical rotation are in accordance with the literature[33]. HRMS-(DART+) for $C_{14}H_{34}NO_2$ $[M+NH4]^+$: calculated: 248.2590, found: 248.2601.

Analysis of Stereochemistry:

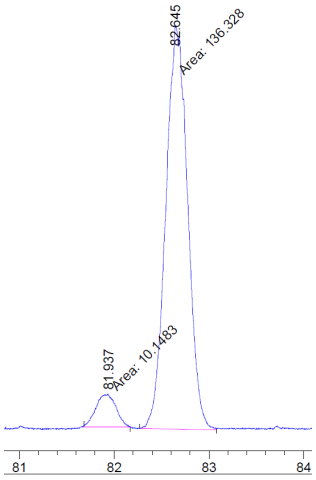
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of tetradecane-1,2-diol prepared from dihydroxylation of 1-tetradecene with ruthenium trichloride and sodium periodiate.[22] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.

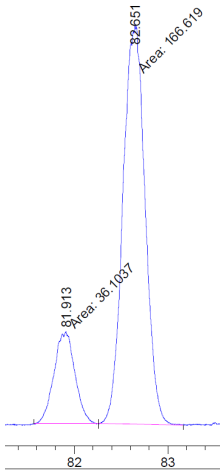
[33] Stallforth, P.; Adibekian, A.; Seeberger, P.H. *Org. Lett.* **2008**, *10*, 1573.



racemic product

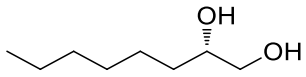


diboration product



coinjection of diboration product + racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.937	MM	0.2418	10.14835	6.99506e-1	6.92834
2	82.645	MM	0.2671	136.32758	8.50809	93.07166



***(S)*-octane-1,2-diol (13')**. The diboration was performed for 48 hours according to the general procedure with 1-octene (56.1 mg, 0.50 mmol, 78.5 µL), DHR catalyst (13.2 mg, 0.10 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 µL) in THF (0.50 mL, 1.0 M). After oxidation, the crude reaction mixture was purified on silica gel (40% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (59.0 mg, 81% yield). Spectral data and optical rotation are in

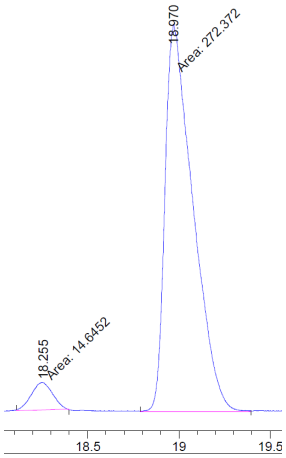
accordance with the literature[34]. HRMS-(DART+) for $C_8H_{17}O$ $[M+H-H2O]^+$: calculated: 129.1279, found: 129.1278.

Analysis of Stereochemistry:

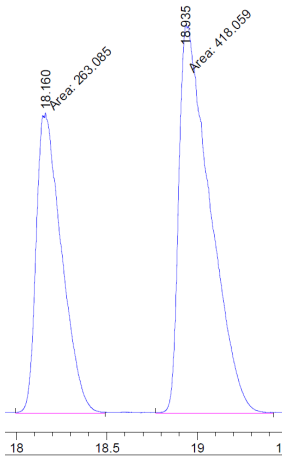
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate.[22] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 100 °C 30min, 20 psi)- analysis of the acetonide of octane-1,2-diol.

racemic product



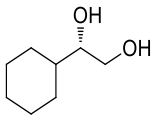
diboration product



coinjection of diboration product + racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	18.255	MM	0.1353	14.64524	1.80436	5.10256
2	18.970	MM	0.1776	272.37225	25.56671	94.89744

[34] Emmanuvel, L.; Shaikh, T. M. A.; Sudalai, A. *Org. Lett.* **2005**, *7*, 5071.



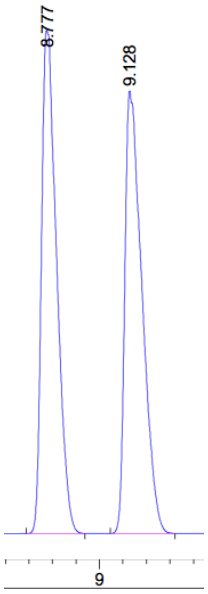
(*S*)-1-cyclohexylethane-1,2-diol (16'). The diboration was performed for 48 hours according to the general procedure with vinyl cyclohexane (55.1 mg, 0.50 mmol, 68.5 μL), DHR catalyst (13.1 mg, 0.10 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (15.2 mg, 0.1 mmol, 14.9 μL) in THF (0.5 mL, 1.0 M). The crude reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (36.1 mg, 50% yield). Spectral data and optical rotation are in accordance with the literature[35]. HRMS-(DART+) for $C_8H_{17}O_2$ $[M+H]^+$: calculated:145.1229, found:145.1222.

Analysis of Stereochemistry:

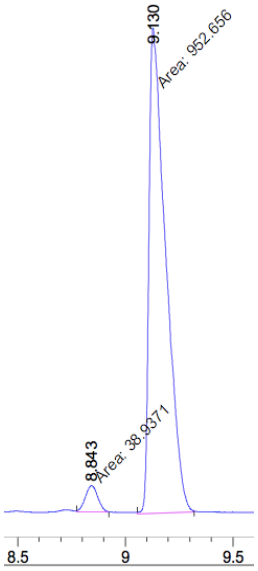
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from dihydroxylation of vinyl cyclohexane with ruthenium trichloride and sodium periodiate.[22]

Chiral GLC (β-dex, Supelco, 130 °C 20 min)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol.

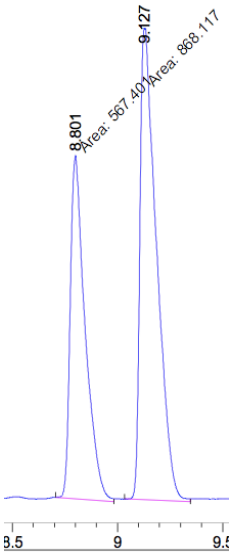
[35] Miller, S. P.; Morgan, J. B.; Nepveux, F. J.; Morken, J. P. *Org. Lett.* **2004**, *6*, 131.



racemic product

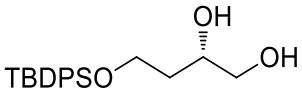


diboration product



coinjection of diboration product + racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.843	MM	0.0671	38.93710	9.66645	3.92672
2	9.130	MM	0.0899	952.65637	176.52306	96.07328



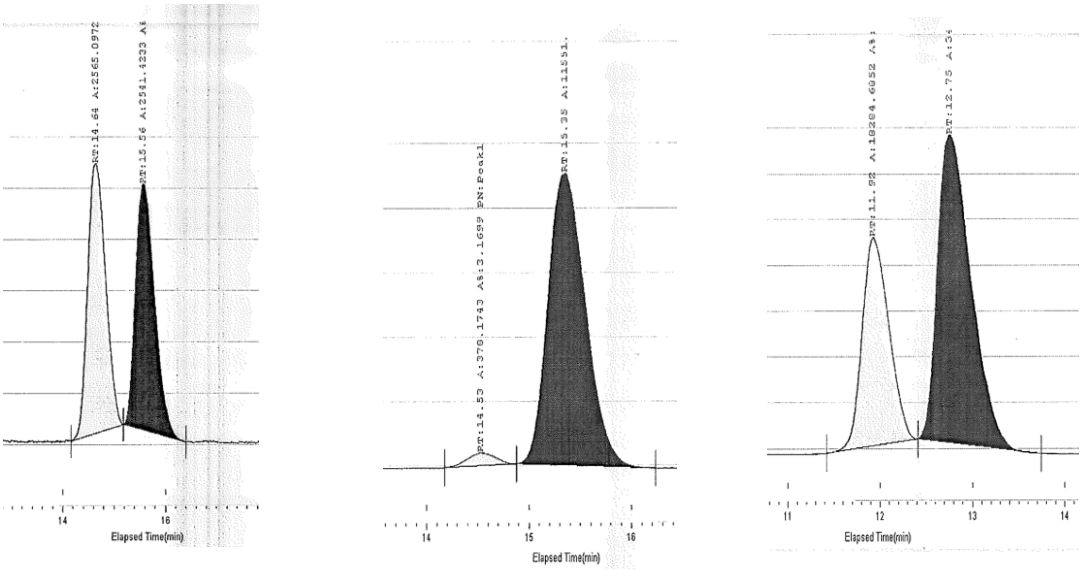
(*S*)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol (17'). The diboration was performed according to the general procedure for 48 hours at 60 °C with (but-3-en-1-yloxy)(tert-butyl)diphenylsilane (155.25 mg, 0.50 mmol), DHR catalyst (13.1 mg, 0.10 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (15.2 mg, 0.10 mmol, 14.9 μL) in THF (0.5 mL, 1.0 M). Neutral oxidation is required for this substrate. After the diboration, the reaction mixture was cooled to 0 °C (ice/water) and charged

with phosphate buffer (pH = 7.0, 2.0 mL), followed by dropwise addition of 30% hydrogen peroxide (1.0 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4.0 mL) was added dropwise over 5 minutes. The crude reaction mixture was purified on silica gel (33% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (103.0 mg, 60% yield). Spectral data and optical rotation are in accordance with the literature[36]. HRMS-(DART+) for $C_{20}H_{29}O_3Si$ [M+H]: calculated: 345.1886, found: 345.1878.

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol prepared from dihydroxylation of (but-3-en-1-yloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[22]

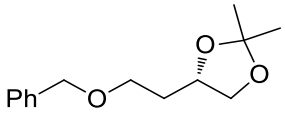
Chiral SFC (Chiracel OD-H, 7% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol



[36] Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210.

racemic product diboration product coinjection of diboration product + racemic

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	3.1699	378.1743	14.53	20.2396	0.014
2	96.8301	11551.811	15.35	453.664	0.0148
Total:	100	11929.9853			



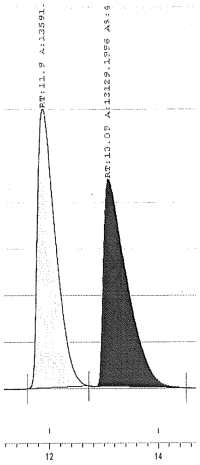
(S)-4-(2-(benzyloxy)ethyl)-2,2-dimethyl-1,3-dioxolane (12'). The diboration was performed for 48 hours according to the general procedure with ((but-3-en-1-yloxy)methyl)benzene (81.1 mg, 0.50 mmol), DHR catalyst (13.2 mg, 0.10 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). After oxidation, the crude reaction mixture was dissolved in EtOAc (5 mL) and filtered through a short pad of silica gel. Elution with EtOAc followed by concentration. The resulting residue was treated with 2,2-dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, then stirred at 60 ^{o}C for 30 min. Then the mixture was filtered through a short pad of silica gel eluting with hexanes/EtOAc (3/1) followed by concentration. The crude product was purified on silica gel (4% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (82.0 mg, 69% yield). Spectral data and optical rotation are in accordance with the literature[37]. HRMS-(DART+) for $C_{14}H_{19}O_3$ $[M+H]^+$: calculated: 235.1334, found: 235.1335.

[37] Takaoka, L. R.; Buckmelter, A. J.; LaCruz, T. E.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2005**, *127*, 528.

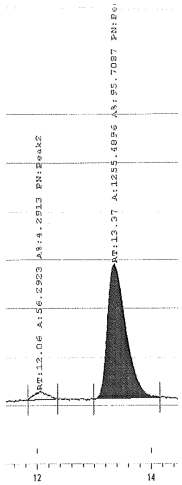
Analysis of Stereochemistry:

The acetonide product was treated with methanol and catalytic toluenesulfonic acid. The resulting diol was compared to the racemic 4-(benzyloxy)butane-1,2-diol prepared from dihydroxylation of ((but-3-en-1-yloxy)methyl)benzene with ruthenium trichloride and sodium periodiate.[22] The absolute stereochemistry was assigned by analogy.

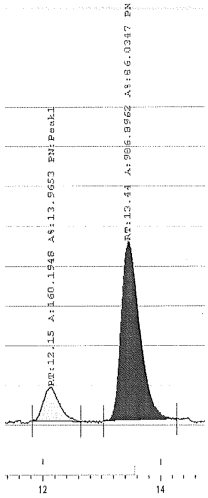
Chiral SFC (Chiracel OD-H, 7% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-(benzyloxy)butane-1,2-diol.



racemic product

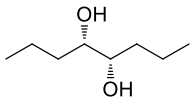


diboration product



coinjection of diboration product + racemic

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.2913	56.2923	12.06	3.4396	0.0176
2	95.7087	1255.4896	13.37	55.5085	0.0196
Total:	100	1311.7819			



(5S,6S)-decane-5,6-diol (20'). In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar was charged with DHR catalyst (13.1 mg, 0.10 mmol),

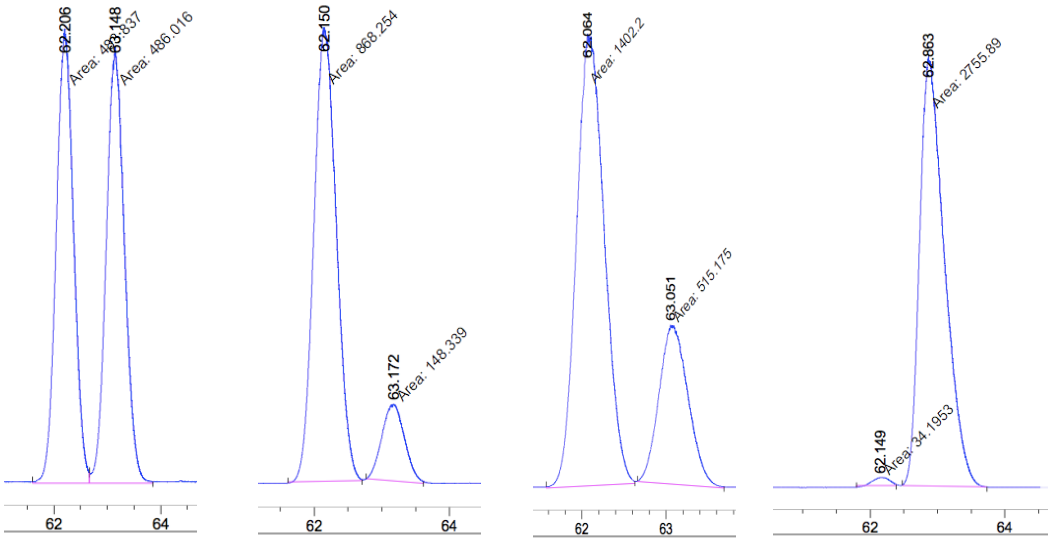
bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol), trans-5-decene (70.1 mg, 0.50 mmol, 94.8 μL), Cs_2CO_3 (32.6 mg, 0.10 mmol) and THF (0.50 mL). The vial was sealed with a rubber septum, removed from the glove box, and placed in a oil bath which was preheated to 60 ^oC, then sitrred for 48 hours. Then the reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2.0 mL), followed by dropwise addition of 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation. The resulting crude product was purified on silica gel (30% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (52.0 mg, 60% yield). Spectral data and optical rotation are in accordance with the literature[38]. HRMS-(DART+) for $C_{10}H_{21}O$ $[M+H-H_2O]^+$: calculated: 157.1592, found: 157.1599.

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of decane-5,6-diol prepared from dihydroxylation of trans-5-decene with ruthenium trichloride and sodium periodiate.[22] The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of trans-5-decene utilizing AD-mix-β.[23]

[38] Cheng, S. K.; Zhang, S. Y.; Wang, P. A.; Kuang, Y. Q.; Sun, X. L. *Appl. Organomet. Chem.* **2005**, *19,* 975.

Chiral GLC (β-dex, Supelco, 70 °C 15min, then 0.25 °C/min to 90 °C, 20 psi)- analysis of the acetonide of decane-5,6-diol.

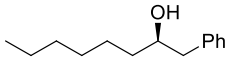


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.150	MM	0.3844	868.25366	37.64571	85.40823
2	63.172	MM	0.3870	148.33890	6.38813	14.59177

1.7.5 Experimental Procedure and Characterization of Alkene Diboration/Cross Coupling/Oxidation Cascade

In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar was charged with TBS-DHG catalyst (0.05 mmol, 0.1 equiv), bis(neopentylglycolato)diboron (0.50 mmol, 1.0 equiv), alkene substrate (0.50 mmol, 1.0 equiv) and THF (0.50 mL). Then DBU (0.05 mmol, 0.1 equiv) was added into the solution. The vial was sealed with rubber septum, removed from the glove box, and the mixture was sitrred at room

temperature for 24-48 hours. The vial was cooled to room temperature, and returned to the dry box. The reaction mixture and magnetic stir bar were transferred to an oven-dried 16-mL vial. Then the following were added: solid potassium hydroxide (84.2 mg, 1.5 mmol, 3.0 equiv), RuPhos (11.7 mg, 0.025 mmol, 0.05 equiv), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 0.05 equiv), THF (2.0 mL) and electrophile (0.75 mmol, 1.5 equiv). The vial was sealed, removed from the dry box, and H_2O (sparged with N_2 for 30 min, 0.25 mL) was added through the teflon septum cap. The vial was heated to 70 ºC and stirred for 12 h. The reaction mixture was transferred to a 50-mL round bottom flask and cooled to 0 ºC (ice/water) and charged with 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the flask was cooled to 0ºC and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 20 mL) and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation.



22

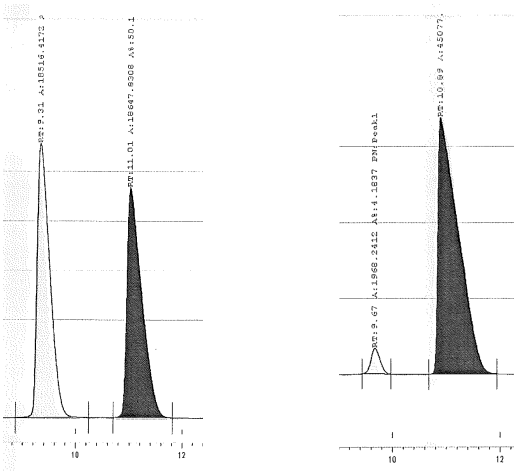
(*R*)-1-phenyloctan-2-ol (22). The diboration was performed for 24 hours according to the general procedure with 1-octene (56.1 mg, 0.50 mmol, 78.5 μL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). The cross-coupling was performed according to the general procedure with bromobenzene (117.8 mg, 0.75 mmol,

78.5 μL). The crude product was purified on silica gel (8% ethyl acetate in hexanes, stain in CAM) to afford the product as pale yellow oil (78.0 mg, 76% yield). Spectral data and optical rotation are in accordance with the literature[39]. HRMS-(DART+) for $C_{14}H_{21}O$ $[M+H-H_2O]^+$: calculated: 189.1643, found: 189.1638.

Analysis of Stereochemistry:

The product was compared to the racemic 1-phenyloctan-2-ol prepared from diboration of 1-octene with B_2Pin_2, Cs_2CO_3 and MeOH[40] followed by coupling with bromobenzene.

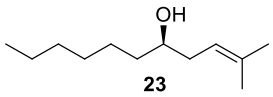
Chiral SFC (Chiracel OD-H, 2% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-phenyloctan-2-ol.



racemic product DCC product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.1837	1968.2412	9.67	167.7336	0.0114
2	95.8163	45077.1354	10.89	1685.725	0.0128
Total:	100	47045.3766			

[39] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature*, **2014**, *505*, 386.
[40] Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyas, H.; Fernandez, E. *Angew. Chem. Int. Ed.* **2011**, *50*, 7158.

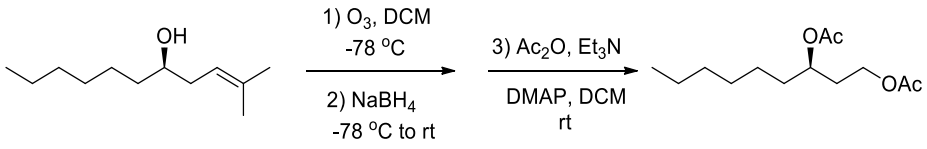


23

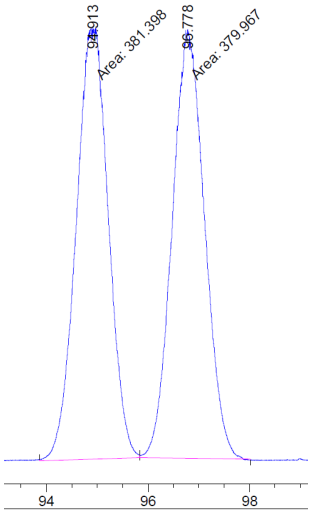
(*R*)-2-methylundec-2-en-5-ol (23). The diboration was performed for 24 hours according to the general procedure with 1-octene (56.1 mg, 0.50 mmol, 78.5 μL), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). The cross-coupling was performed according to the general procedure with 1-chloro-2-methylpropene (67.9 mg, 0.75 mmol, 73.8 μL). The crude product was purified on silica gel (8% ethyl acetate in hexanes, stain in CAM) to afford the product as pale yellow oil (60.0 mg, 65% yield). Spectral data is in accordance with the literature.[16] IR (film) cm^{-1} 3331w, 2925s, 2856s, 1453m, 1377m, 1051m; HRMS-(DART+) for $C_{12}H_{23}O$ $[M+H-H_2O]^+$: calculated: 167.1800, found: 167.1806. Optical rotation: $[\alpha]_D^{25} = -6.0$ [c=1.7, $CHCl_3$].

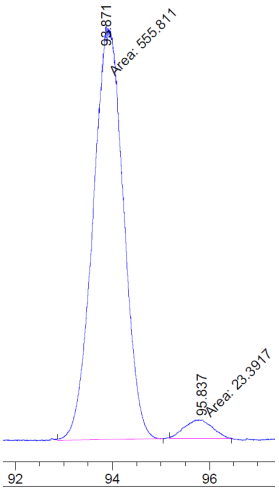
Analysis of Stereochemistry:

The title compound was converted to the corresponding bis-acetate as shown below. The resulting bis-acetate was compared to racemic material prepared from diboration/cross-coupling with B_2Pin_2, Cs_2CO_3 and MeOH[36] for diboration. Absolute stereochemistry was assigned by analogy.



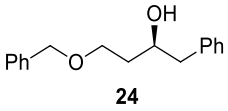
Chiral GLC (β-dex, Supelco, 115 °C 120min, 20 psi)- analysis of bis-acetate of nonane-1,3-diol derived from 2-methylundec-2-en-5-ol.





racemic product DCC product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	93.871	MM	0.7242	555.81079	12.79143	95.96139
2	95.837	MM	0.6662	23.39174	5.85222e-1	4.03861



24

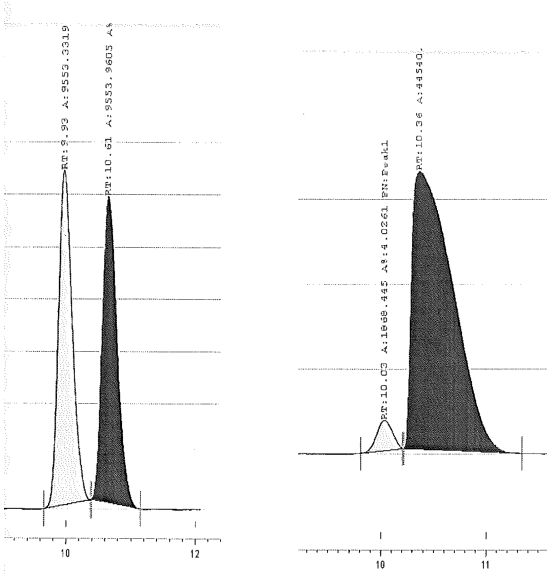
(S)-4-(benzyloxy)-1-phenylbutan-2-ol (24). The diboration was performed for 48 hours according to the general procedure with ((but-3-en-1-yloxy)methyl)benzene (81.1 mg, 0.50 mmol), TBS-DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 µL) in THF (0.50 mL, 1.0 M). The cross-coupling was performed according to the general procedure with bromobenzene (117.8 mg, 0.75 mmol, 78.5 µL). The crude product was purified on silica gel (15% ethyl acetate in hexanes, stain in CAM) to afford the product as pale yellow oil

(91.0 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.78-1.81 (m, 2H), 2.76 (dd, 1H, *J* = 6.0, 13.2 Hz), 2.81 (dd, 1H, *J* = 7.8, 13.2 Hz), 2.87 (s, 1H), 3.62-3.66 (m, 1H), 3.71-3.74 (m, 1H), 4.05-4.07 (m, 1H), 4.52 (s, 2H), 7.22-7.24 (m, 3H), 7.28-7.36 (m, 7H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 35.9, 44.1, 69.2, 72.3, 73.5, 126.5, 127.8, 127.9, 128.6, 128.7, 129.6, 138.1, 138.8; IR (film) cm^{-1} 3443w, 2917w, 2859w, 1495m, 1453m, 1078s; HRMS-(DART+) for $C_{17}H_{21}O_2$ $[M+H]^+$: calculated: 257.1542, found: 257.1551. Optical rotation: $[\alpha]_D^{25} = -14.5^o$ [c=3.8, $CHCl_3$].

Analysis of Stereochemistry:

The product was compared to the racemic 4-(benzyloxy)-1-phenylbutan-2-ol from diboration of ((but-3-en-1-yloxy)methyl)benzene with B_2Pin_2, Cs_2CO_3 and MeOH[36] followed by coupling with bromobenzene.

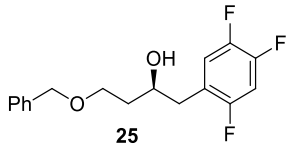
Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-(benzyloxy)-1-phenylbutan-2-ol.



racemic product DCC product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.0261	1868.445	10.03	181.2271	0.0098
2	95.9739	44540.285	10.36	1636.902	0.0102
Total:	100	46408.73			



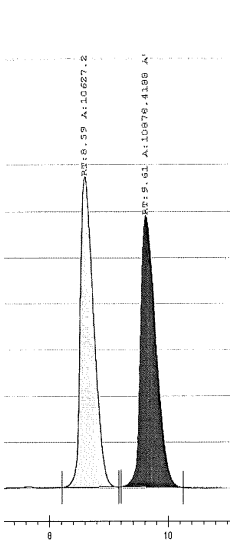
25

(*S*)-4-(benzyloxy)-1-(2,4,5-trifluorophenyl)butan-2-ol (25). The diboration was performed for 48 hours according to the general procedure with ((but-3-en-1-yloxy)methyl)benzene (81.1 mg, 0.50 mmol), DHG catalyst (13.1 mg, 0.05 mmol), bis(neopentylglycolato)diboron (112.9 mg, 0.50 mmol) and DBU (7.6 mg, 0.05 mmol, 7.45 μL) in THF (0.50 mL, 1.0 M). The cross-coupling was performed according to the general procedure with 1-bromo-2,4,5-trifluorobenzene (158.2 mg, 0.75 mmol, 87.9 μL). The crude product was purified on silica gel (15% ethyl acetate in hexanes, stain in CAM) to afford the product as pale yellow oil (78.0 mg, 50% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.76-1.80 (m, 2H), 2.71-2.78 (m, 2H), 3.16 (s, 1H), 3.64-3.68 (m, 1H), 3.73-3.76 (m, 1H), 4.05-4.07 (m, 1H), 4.52 (s, 2H), 6.88 (dt, 1H, J = 6.6, 9.6 Hz), 7.09-7.13 (m, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 35.9, 36.2, 69.3, 71.4, 73.6, 105.3, 119.4, 122.1, 127.9, 128.0, 128.7, 137.8, 145.8, 147.5, 147.9, 149.6, 155.4, 157.0; IR (film) cm^{-1} 3451w, 2923w, 2864w, 1516s, 1423m, 1210m, 1150m, 1095s; HRMS-(DART+) for $C_{17}H_{18}F_3O_2$ $[M+H]^+$: calculated: 311.1259, found: 311.1244. Optical rotation: $[\alpha]_D^{25}$ = -20.6 [c=2.5, $CHCl_3$].

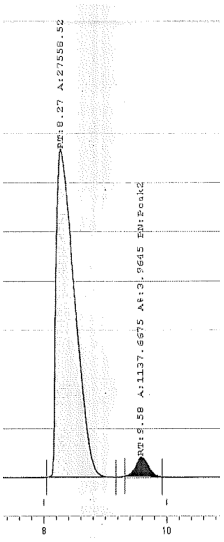
Analysis of Stereochemistry:

The product was compared to the racemic 4-(benzyloxy)-1-(2,4,5-trifluorophenyl)butan-2-ol from diboration of ((but-3-en-1-yloxy)methyl)benzene with B_2Pin_2, Cs_2CO_3 and MeOH[36] followed by coupling with 1-bromo-2,4,5-trifluorobenzene.

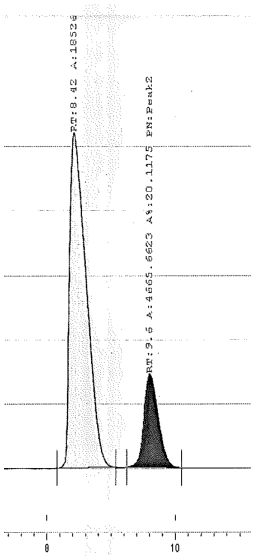
Chiral SFC (Chiracel OJ-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-(benzyloxy)-1-phenylbutan-2-ol.



racemic product



DCC product



coinjection of DCC product + racemic

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	96.0355	27558.5287	8.27	1333.2067	0.008
2	3.9645	1137.6675	9.58	78.3219	0.0092
Total:	100	28696.1962			

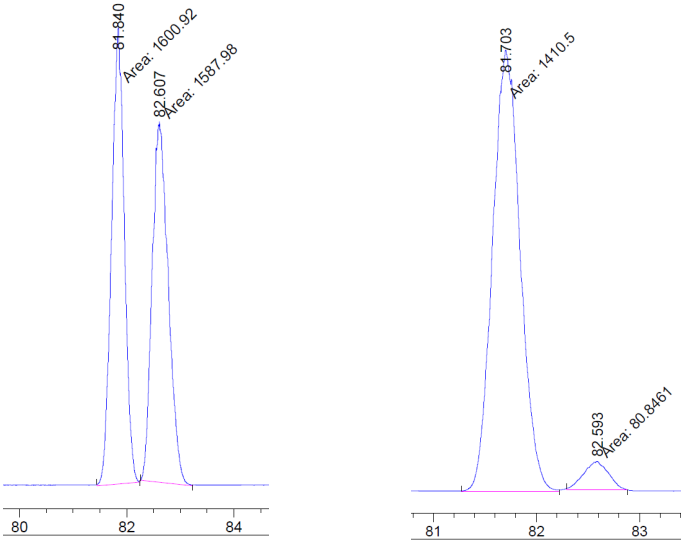
1.7.6 Glovebox-Free Alkene Diboration Procedure

A flame-dried two-dram vial equipped with a magnetic stir bar was charged with Magnesium Sulfate (300.1mg, 2.5mmol), $B_2(neo)_2$ (112.7mg, 0.5mmol), TBS-DHG

catalyst (13.1mg, 0.05mmol), The vial was then sealed with a rubber septum and purged with nitrogen. THF (1ml), 1-tetradecene (0.13ml, 0.5mmol) and DBU (7.5 µL) was added to the reaction vial after 10 minutes. The reaction mixture was allowed to stir under nitrogen for 48h. Then the reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (1 mL), followed by dropwise addition of 30% hydrogen peroxide (0.5 mL). The reaction was gradually warmed to room temperature and stirred 4 hours at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 10 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give crude reaction mixture. The crude reaction mixture was purified on silica gel (40% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (57.5mg, 50% yield).

Analysis of Stereochemistry:

Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.



Racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.703	MM	0.3100	1410.50049	75.84548	94.57898
2	82.593	MM	0.2755	80.84614	4.89055	5.42102

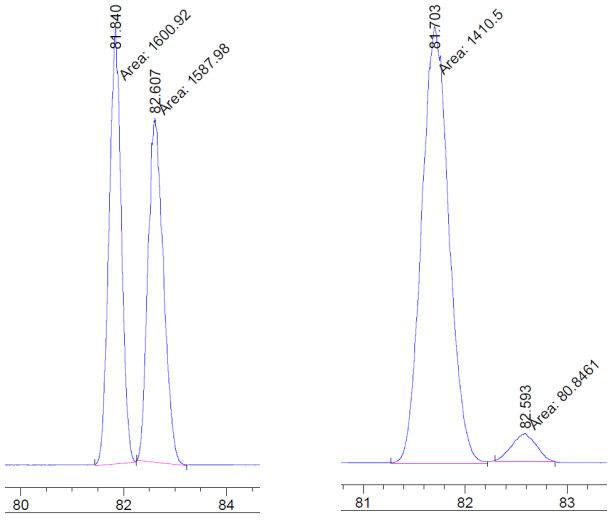
1.7.7 Experimental Procedure for 10g-Scale Alkene Diboration

In the glove box, a flame-dried 250 mL round flask equipped with magnetic stir bar was charged with TBS-DHG catalyst (5.0 mmol, 1.31 g, 0.1 equiv), bis(neopentyl glycolato)diboron (50.0 mmol, 11.29 g, 1.0 equiv), 1-tetradecene (94%, 50.0 mmol, 10.45 g, 13.4 mL, 1.0 equiv) and THF (100 mL). Then DBU (5.0 mmol, 761.2 mg, 7.5 mL, 0.1 equiv) was added into the solution. The flask was sealed with rubber septum, removed from the glove box, and the mixture was sitrred at room temperature for 60 hours. Then the reaction mixture was transferred to a 500 mL round flask, then cooled to 0 °C (ice/water) and slowly charged with 3 M sodium hydroxide (80 mL), followed by slow addition of 30% hydrogen peroxide (40 mL) over 30 minutes. The reaction was gradually warmed to room temperature and stirred 12 hours at which time the flask was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (60 mL) was added dropwise over 30 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 150 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give crude reaction mixture. The crude reaction mixture was treated with $TBAF{\cdot}3H_2O$ (20.0 mmol, 6.31 g) at room

temperature and stirred for 12 h. Then the solution was concentrated by rotary evaporation, the resulting crude product was purified on silica gel (40% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (7.56 g, 66% yield).

Analysis of Stereochemistry:

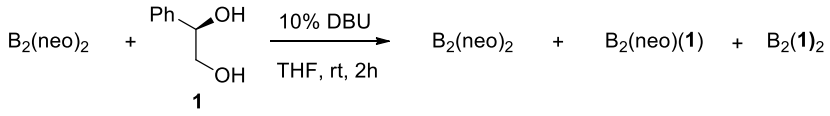
Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.703	MM	0.3100	1410.50049	75.84548	94.57898
2	82.593	MM	0.2755	80.84614	4.89055	5.42102

1.7.8 Experiment Procedure for Diol Exchange Reaction

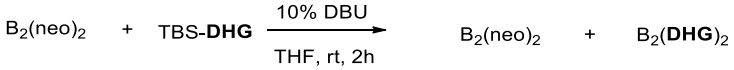


In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar was charged with $B_2(neo)_2$ (22.6 mg, 0.1 mmol), (s)-(+)-1-phenyl-1 2-ethanediol (13.8 mg, 0.1 mmol), DBU (1.5 mg, 0.01 mmol, 1.5 μL) and THF (0.2 mL). The vial was sealed with rubber septum, removed from the glove box, and stirred at room temperature for 2 hours. Then the reaction mixture was directly used for HRMS analysis.

For $B_2(neo)_2$: HRMS-(DART) for $C10H21B_2O4$ $[M+H]^+$: calculated: 227.1626, found: 227.1635.

For $B_2(neo)(\mathbf{1})$: HRMS-(DART) for $C13H19B_2O4$ $[M+H]^+$: calculated: 261.1469, found: 261.1461.

For $B_2(\mathbf{1})_2$: HRMS-(DART) for $C16H17B_2O4$ $[M+H]^+$: calculated: 295.1313, found: 295.1321.



In the glove box, an oven-dried 2-dram vial equipped with magnetic stir bar was charged with $B_2(neo)_2$ (22.6 mg, 0.1 mmol), TBS-DHG (2.6 mg, 0.01 mmol), DBU (1.5 mg, 0.01 mmol, 1.5 μL) and THF (0.2 mL). The vial was sealed with rubber septum, removed from the glove box, and stirred at room temperature for 2 hours. Then the reaction mixture was directly used for HRMS spectrum test.

For $B_2(neo)_2$: HRMS-(DART) for $C_{10}H_{21}B_2O4$ $[M+H]^+$: calculated: 227.1626, found: 227.1631.

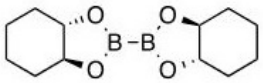
For $B_2(\mathbf{TBS\text{-}DHG})_2$: HRMS-(DART) for $C24H49B_2O8$ $Si_2[M+H]^+$: calculated: 543.3152, found: 543.3167.

1.7.9 DFT Calculations

All calculations were carried out with the M06-2X density functional and the 6-31+G* basis set using the Gaussian 09 program.18 THF-solvation was simulated using the PCM solvation model. Frequency calculations were carried out on all fully geometry optimized structures to make sure the transition states have one imaginary frequency and all other structures have only real frequencies. Gibbs free energies were computed using these normal mode frequencies at 298.15 K and 1 atm.

The reaction coordinate was followed using the intrinsic reaction coordinate (IRC) method to verify that TS-1 and TS-2 connect with the correct ground states. A maximum of 20 steps of integration were carried out in forward and reverse directions from the transition state. The local quadratic approximation (LQA) method was used to integrate the reaction coordinate with a step size of 0.3 Bohr.

B_2(*trans*-1,2-cyclohexanediol)$_2$ 1,1-bonded



Cartesian coordinates (Angstroms):

38

C	-5.342	-0.943	-0.612
C	-5.356	0.597	-0.688
C	-4.087	1.197	-1.330
C	-2.924	0.605	-0.569
C	-2.909	-0.903	-0.702
C	-4.069	-1.518	0.046
H	-5.422	-1.352	-1.629
H	-6.227	-1.286	-0.067
H	-5.457	1.004	0.327
H	-6.241	0.923	-1.244
H	-4.099	2.289	-1.259
H	-4.020	0.927	-2.392
H	-3.025	0.872	0.495
H	-2.993	-1.171	-1.767
H	-4.020	-1.247	1.108
H	-4.058	-2.611	-0.026
O	-1.584	0.965	-0.958
B	-0.810	-0.130	-0.625
B	0.894	-0.118	-0.617

O	-1.567	-1.238	-0.298
C	4.166	-1.576	-0.220
C	2.999	-0.630	-0.058
C	3.000	0.413	-1.156
C	4.156	1.370	-0.983
C	5.432	0.505	-1.076
C	5.433	-0.700	-0.115
H	4.114	-2.075	-1.197
H	4.167	-2.349	0.555
H	3.088	-0.125	0.917
H	3.102	-0.091	-2.131
H	4.158	2.143	-1.758
H	4.090	1.868	-0.007
H	5.528	0.139	-2.107
H	6.313	1.125	-0.880
H	5.515	-0.333	0.918
H	6.322	-1.311	-0.302
O	1.656	0.929	-1.098
O	1.661	-1.158	-0.129

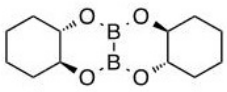
	1	2	3
	A	A	A
Frequencies --	28.1230	33.6575	38.5711
Red. masses --	3.6109	4.8164	5.1549

Zero-point correction= 0.332144 (Hartree/Particle)
Thermal correction to Energy= 0.347241
Thermal correction to Enthalpy= 0.348185
Thermal correction to Gibbs Free Energy= 0.288594
Sum of electronic and zero-point Energies= -819.469727
Sum of electronic and thermal Energies= -819.454630
Sum of electronic and thermal Enthalpies= -819.453686
Sum of electronic and thermal Free Energies= -819.513277

Item	Value	Threshold	Converged?
Maximum Force	0.000096	0.000450	YES
RMS Force	0.000014	0.000300	YES

SCF: -819.801871431

B_2(*trans*-1,2-cyclohexanediol)$_2$ 1,2-bonded



Cartesian coordinates (Angstroms):

38

C	-4.796	-0.880	-0.912
C	-4.808	0.548	-0.362
C	-3.545	1.298	-0.787
C	-2.282	0.568	-0.348
C	-2.271	-0.862	-0.914
C	-3.525	-1.611	-0.482
H	-4.847	-0.848	-2.009
H	-5.677	-1.433	-0.569
H	-4.863	0.515	0.735
H	-5.695	1.089	-0.709
H	-3.522	2.309	-0.365
H	-3.519	1.405	-1.880
H	-2.259	0.500	0.751
H	-2.243	-0.793	-2.013
H	-3.503	-1.717	0.612
H	-3.485	-2.621	-0.904
O	-1.153	1.365	-0.761
B	0.036	0.697	-0.775
B	0.047	-0.959	-0.474
O	-1.133	-1.643	-0.496
C	3.626	-1.523	-0.245
C	2.362	-0.685	-0.101
C	2.358	0.454	-1.135
C	3.609	1.309	-0.982
C	4.884	0.474	-1.116
C	4.888	-0.670	-0.102
H	3.609	-2.005	-1.233
H	3.598	-2.321	0.504
H	2.330	-0.235	0.903
H	2.338	0.003	-2.139
H	3.575	2.106	-1.732
H	3.578	1.792	0.004
H	4.946	0.060	-2.132
H	5.762	1.114	-0.980
H	4.937	-0.256	0.915
H	5.776	-1.298	-0.232
O	1.217	1.331	-1.026

O 1.235 -1.577 -0.217

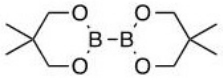
	1	2	3
	A	A	A
Frequencies --	37.5111	73.6518	95.5107
Red. masses --	4.4421	2.9129	4.4420

Zero-point correction= 0.332044 (Hartree/Particle)
Thermal correction to Energy= 0.346932
Thermal correction to Enthalpy= 0.347877
Thermal correction to Gibbs Free Energy= 0.290618
Sum of electronic and zero-point Energies= -819.486108
Sum of electronic and thermal Energies= -819.471220
Sum of electronic and thermal Enthalpies= -819.470275
Sum of electronic and thermal Free Energies= -819.527534

Item	Value	Threshold	Converged?
Maximum Force	0.000033	0.000450	YES
RMS Force	0.000006	0.000300	YES

SCF: -819.818152118

B_2neo_2 1,1-bonded



Cartesian coordinates (Angstroms):

36

B	-11.644	-9.277	-3.310
B	-10.372	-8.208	-2.879
O	-11.562	-9.970	-4.489
O	-12.721	-9.404	-2.472
O	-10.456	-7.511	-1.702
O	-9.293	-8.083	-3.714
C	-13.800	-10.278	-2.809
C	-12.608	-10.861	-4.877
C	-13.966	-10.431	-4.321
C	-14.999	-11.520	-4.609
C	-14.408	-9.105	-4.950
C	-9.411	-6.619	-1.315
C	-8.215	-7.209	-3.378
C	-8.051	-7.051	-1.866
C	-7.019	-5.961	-1.579
C	-7.612	-8.374	-1.231
H	-13.684	-8.303	-4.772

H	-15.371	-8.787	-4.535
H	-14.524	-9.218	-6.034
H	-14.704	-12.479	-4.169
H	-15.117	-11.663	-5.689
H	-15.977	-11.242	-4.199
H	-8.336	-9.177	-1.408
H	-7.498	-8.258	-0.147
H	-6.648	-8.694	-1.642
H	-7.313	-5.004	-2.023
H	-6.041	-6.241	-1.986
H	-6.904	-5.815	-0.499
H	-14.706	-9.859	-2.360
H	-13.609	-11.257	-2.349
H	-12.627	-10.879	-5.972
H	-12.355	-11.868	-4.522
H	-9.395	-6.596	-0.220
H	-9.663	-5.613	-1.676
H	-7.307	-7.630	-3.823
H	-8.403	-6.232	-3.842

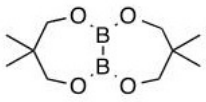
	1	2	3
	A	A	A
Frequencies --	18.5247	37.6035	58.3708
Red. masses --	3.5005	3.9825	4.2770

Zero-point correction= 0.313720 (Hartree/Particle)
Thermal correction to Energy= 0.330509
Thermal correction to Enthalpy= 0.331453
Thermal correction to Gibbs Free Energy= 0.268998
Sum of electronic and zero-point Energies= -743.298363
Sum of electronic and thermal Energies= -743.281573
Sum of electronic and thermal Enthalpies= -743.280629
Sum of electronic and thermal Free Energies= -743.343085

Item	Value	Threshold	Converged?
Maximum Force	0.000023	0.000450	YES
RMS Force	0.000005	0.000300	YES

SCF: -743.612082683

B_2neo_2 1,2-mode



Cartesian coordinates (Angstroms):

36

H	-13.713	-7.240	-2.755
H	-12.076	-5.722	-1.922
O	-12.927	-9.144	-2.773
C	-13.486	-8.058	-2.057
H	-14.157	-5.942	-0.596
H	-14.439	-8.434	-1.670
O	-10.498	-7.008	-2.087
C	-11.593	-6.517	-1.338
C	-13.640	-6.712	-0.010
C	-12.661	-7.516	-0.880
H	-11.152	-6.050	-0.450
H	-14.397	-7.374	0.422
H	-13.115	-6.215	0.813
C	-12.053	-8.647	-0.048
H	-11.286	-9.206	-0.591
H	-12.830	-9.357	0.256
H	-11.588	-8.237	0.856
H	-10.971	-9.716	-6.862
H	-9.736	-8.441	-6.933
C	-10.346	-9.050	-6.256
H	-11.012	-8.373	-5.713
H	-9.016	-11.332	-6.873
H	-10.521	-11.712	-5.117
H	-7.796	-10.053	-6.747
C	-9.441	-9.862	-5.327
C	-8.465	-10.699	-6.169
C	-10.245	-10.864	-4.483
O	-11.466	-10.395	-3.942
H	-7.918	-8.364	-5.120
C	-8.565	-8.952	-4.460
H	-7.848	-11.350	-5.538
O	-9.205	-8.009	-3.622
H	-9.611	-11.250	-3.672
H	-7.916	-9.577	-3.832
B	-11.645	-9.238	-3.237
B	-10.408	-8.046	-2.973

1 2 3

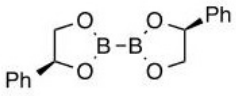
	A	A	A
Frequencies --	33.7874	52.9825	94.6061
Red. masses --	2.9669	3.8523	4.8194

Zero-point correction= 0.314771 (Hartree/Particle)
Thermal correction to Energy= 0.331267
Thermal correction to Enthalpy= 0.332211
Thermal correction to Gibbs Free Energy= 0.272006
Sum of electronic and zero-point Energies= -743.281242
Sum of electronic and thermal Energies= -743.264746
Sum of electronic and thermal Enthalpies= -743.263802
Sum of electronic and thermal Free Energies= -743.324006

Item	Value	Threshold	Converged?
Maximum Force	0.000129	0.000450	YES
RMS Force	0.000016	0.000300	YES

SCF: -743.596012302

B_2(styrenediol)$_2$ 1,1-bonded



Cartesian coordinates (Angstroms):

38

C	-9.520	-7.991	-1.171
O	-12.653	-10.036	-4.452
O	-10.782	-8.665	-1.260
C	-14.021	-10.423	-4.635
B	-11.035	-8.929	-2.579
B	-12.482	-9.620	-3.155
C	-14.583	-10.481	-3.189
C	-8.898	-8.127	-2.588
O	-9.994	-8.571	-3.399
O	-13.602	-9.805	-2.390
C	-16.666	-8.941	-6.922
C	-16.219	-7.628	-7.078
C	-15.935	-9.840	-6.149
C	-14.752	-9.437	-5.520
C	-14.306	-8.125	-5.682
C	-15.037	-7.224	-6.458
H	-16.284	-10.864	-6.035
H	-17.581	-9.267	-7.408
H	-13.377	-7.809	-5.217
H	-14.678	-6.206	-6.581

H	-16.785	-6.927	-7.684
C	-7.742	-9.102	-2.646
C	-7.888	-10.394	-3.151
C	-6.500	-8.700	-2.145
C	-5.421	-9.579	-2.137
C	-5.572	-10.874	-2.639
C	-6.805	-11.277	-3.146
H	-6.376	-7.689	-1.759
H	-4.461	-9.253	-1.747
H	-4.730	-11.560	-2.638
H	-6.929	-12.279	-3.545
H	-8.843	-10.708	-3.561
H	-15.542	-9.968	-3.090
H	-14.677	-11.508	-2.827
H	-14.037	-11.413	-5.100
H	-8.571	-7.153	-2.964
H	-9.701	-6.947	-0.902
H	-8.912	-8.468	-0.399

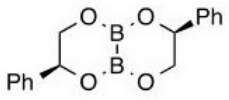
	1	2	3
	A	A	A
Frequencies --	10.9960	19.0358	23.4007
Red. masses --	5.9321	5.8073	5.0846

Zero-point correction= 0.306240 (Hartree/Particle)
Thermal correction to Energy= 0.324362
Thermal correction to Enthalpy= 0.325306
Thermal correction to Gibbs Free Energy= 0.254511
Sum of electronic and zero-point Energies= -969.454337
Sum of electronic and thermal Energies= -969.436215
Sum of electronic and thermal Enthalpies= -969.435271
Sum of electronic and thermal Free Energies= -969.506066

Item	Value	Threshold	Converged?
Maximum Force	0.000005	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF: -969.760576977

B_2(styrenediol)$_2$ 1,2-bonded



Cartesian coordinates (Angstroms):

38

C	-10.348	-8.667	-5.438
O	-13.335	-9.573	-2.816
O	-9.882	-8.511	-4.093
C	-13.106	-8.893	-1.575
B	-10.821	-8.842	-3.160
B	-12.276	-9.521	-3.678
C	-11.693	-9.152	-1.017
C	-11.154	-9.954	-5.699
O	-12.379	-9.998	-4.954
O	-10.628	-8.636	-1.825
C	-13.733	-5.276	-0.575
C	-13.890	-4.642	-1.810
C	-13.496	-6.646	-0.519
C	-13.408	-7.407	-1.692
C	-13.583	-6.769	-2.921
C	-13.819	-5.393	-2.979
H	-13.384	-7.130	0.449
H	-13.797	-4.703	0.345
H	-13.560	-7.338	-3.846
H	-13.951	-4.914	-3.945
H	-14.074	-3.573	-1.856
C	-10.321	-11.207	-5.478
C	-10.580	-12.116	-4.452
C	-9.246	-11.451	-6.341
C	-8.437	-12.569	-6.172
C	-8.694	-13.469	-5.135
C	-9.768	-13.240	-4.280
H	-9.044	-10.763	-7.160
H	-7.609	-12.743	-6.853
H	-8.066	-14.344	-5.003
H	-9.984	-13.939	-3.477
H	-11.429	-11.970	-3.790
H	-11.609	-8.680	-0.036
H	-11.555	-10.232	-0.893
H	-13.800	-9.339	-0.854
H	-11.447	-9.912	-6.754
H	-10.968	-7.802	-5.702
H	-9.468	-8.668	-6.085

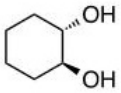
	1	2	3
	A	A	A
Frequencies --	15.0583	32.4244	34.2648
Red. masses --	5.4119	5.0601	4.3983

Zero-point correction= 0.307708 (Hartree/Particle)
Thermal correction to Energy= 0.324846
Thermal correction to Enthalpy= 0.325790
Thermal correction to Gibbs Free Energy= 0.260439
Sum of electronic and zero-point Energies= -969.449503
Sum of electronic and thermal Energies= -969.432365
Sum of electronic and thermal Enthalpies= -969.431421
Sum of electronic and thermal Free Energies= -969.496772

Item	Value	Threshold	Converged?
Maximum Force	0.000019	0.000450	YES
RMS Force	0.000005	0.000300	YES

SCF: -969.757210867

trans-Cyclohexan-1,2-diol



Cartesian coordinates (Angstroms):

20

O	-10.141	-8.017	-4.459
O	-10.769	-8.543	-1.836
C	-9.323	-7.453	-3.436
C	-10.230	-7.289	-2.226
C	-9.469	-6.691	-1.054
C	-8.707	-6.119	-3.844
H	-11.051	-6.610	-2.515
H	-8.527	-8.167	-3.168
H	-9.516	-5.445	-4.159
C	-7.935	-5.503	-2.673
H	-8.052	-6.265	-4.711
H	-8.689	-7.401	-0.746
H	-10.152	-6.572	-0.205
C	-8.835	-5.352	-1.443
H	-9.628	-4.624	-1.662
H	-8.263	-4.952	-0.599
H	-7.522	-4.532	-2.967
H	-7.082	-6.149	-2.420
H	-9.581	-8.339	-5.180

H -11.107 -8.965 -2.643
YYY

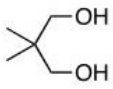
	1	2	3
	A	A	A
Frequencies --	141.2957	196.1327	268.2647
Red. masses --	3.6350	2.2629	2.2013

Zero-point correction= 0.181093 (Hartree/Particle)
Thermal correction to Energy= 0.188897
Thermal correction to Enthalpy= 0.189841
Thermal correction to Gibbs Free Energy= 0.149521
Sum of electronic and zero-point Energies= -385.974341
Sum of electronic and thermal Energies= -385.966538
Sum of electronic and thermal Enthalpies= -385.965594
Sum of electronic and thermal Free Energies= -386.005914

Item	Value	Threshold	Converged?
Maximum Force	0.000042	0.000450	YES
RMS Force	0.000009	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-386.155434428', 'A.U.', 'after', '1', 'cycles']
MP2: no data
G_corr: 93.82592271 kcal/mol
H_corr: 119.12712591 kcal/mol
S_corr: 25.30130715 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 11.97459845 kcal/mol
S_rot: 8.4215449 kcal/mol
S_vib: 4.90546195 kcal/mol

Neopentandiol



Cartesian coordinates (Angstroms):

19

O -11.475 -10.294 -4.102
O -13.260 -8.844 -2.527
C -14.144 -9.898 -2.874
C -12.583 -11.148 -4.399
C -13.944 -10.447 -4.295
C -15.026 -11.498 -4.559
C -14.047 -9.318 -5.324
H -13.304 -8.534 -5.146
H -15.035 -8.847 -5.275

H -13.907 -9.708 -6.340
H -14.982 -12.310 -3.824
H -14.908 -11.936 -5.556
H -16.023 -11.046 -4.506
H -15.157 -9.490 -2.781
H -14.050 -10.727 -2.154
H -12.461 -11.587 -5.398
H -12.528 -11.959 -3.664
H -11.298 -9.726 -4.866
H -12.364 -9.133 -2.776
YYY

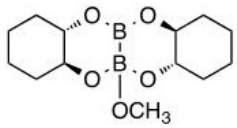
	1	2	3
	A	A	A
Frequencies --	113.0811	191.6810	216.4340
Red. masses --	2.2762	3.1390	1.1439

Zero-point correction= 0.172738 (Hartree/Particle)
Thermal correction to Energy= 0.181203
Thermal correction to Enthalpy= 0.182148
Thermal correction to Gibbs Free Energy= 0.140850
Sum of electronic and zero-point Energies= -347.875459
Sum of electronic and thermal Energies= -347.866993
Sum of electronic and thermal Enthalpies= -347.866049
Sum of electronic and thermal Free Energies= -347.907347

Item	Value	Threshold	Converged?
Maximum Force	0.000037	0.000450	YES
RMS Force	0.000009	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-348.048196822', 'A.U.', 'after', '1', 'cycles']
MP2: no data
G_corr: 88.3847835 kcal/mol
H_corr: 114.29969148 kcal/mol
S_corr: 25.9146017 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 11.87740155 kcal/mol
S_rot: 8.23758635 kcal/mol
S_vib: 5.79931565 kcal/mol

1,2-Bonded B_2(*trans*-1,2-cyclohexanediol)$_2$-OMe



Cartesian coordinates (Angstroms):

43

C	-4.755	-0.941	-0.958
C	-4.825	0.517	-0.497
C	-3.567	1.284	-0.915
C	-2.292	0.623	-0.395
C	-2.239	-0.832	-0.897
C	-3.474	-1.609	-0.457
H	-4.774	-0.972	-2.057
H	-5.633	-1.498	-0.611
H	-4.917	0.544	0.599
H	-5.720	1.004	-0.902
H	-3.596	2.316	-0.545
H	-3.509	1.339	-2.013
H	-2.349	0.588	0.711
H	-2.215	-0.792	-1.999
H	-3.480	-1.659	0.642
H	-3.397	-2.639	-0.825
O	-1.169	1.366	-0.793
B	0.039	0.892	-0.038
B	0.043	-0.814	-0.152
O	-1.074	-1.556	-0.485
C	3.603	-1.543	-0.298
C	2.382	-0.677	-0.007
C	2.306	0.524	-0.972
C	3.623	1.303	-0.938
C	4.842	0.429	-1.233
C	4.905	-0.742	-0.251
H	3.478	-1.983	-1.298
H	3.622	-2.375	0.416
H	2.438	-0.284	1.021
H	2.183	0.087	-1.985
H	3.547	2.132	-1.653
H	3.721	1.753	0.061
H	4.775	0.036	-2.258
H	5.759	1.027	-1.181
H	5.062	-0.354	0.765
H	5.755	-1.395	-0.479
O	1.256	1.421	-0.710
O	1.231	-1.522	-0.121

C	-0.118	2.767	1.511
H	0.681	3.289	0.961
H	-0.028	3.026	2.574
H	-1.083	3.152	1.145
O	-0.021	1.376	1.368

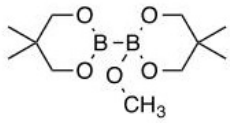
	1	2	3
	A	A	A
Frequencies --	25.7022	53.2089	77.8867
Red. masses --	4.4420	3.3083	3.1192

Zero-point correction= 0.372941 (Hartree/Particle)
Thermal correction to Energy= 0.390853
Thermal correction to Enthalpy= 0.391797
Thermal correction to Gibbs Free Energy= 0.327540
Sum of electronic and zero-point Energies= -934.653207
Sum of electronic and thermal Energies= -934.635296
Sum of electronic and thermal Enthalpies= -934.634352
Sum of electronic and thermal Free Energies= -934.698609

Item	Value	Threshold	Converged?
Maximum Force	0.000065	0.000450	YES
RMS Force	0.000007	0.000300	YES

SCF: -935.026148562

1,1-$B_2(neo)_2$-OMe



Cartesian coordinates (Angstroms):

41

B	-11.382	-9.591	-3.349
B	-10.118	-8.659	-2.588
O	-11.762	-9.315	-4.658
O	-12.091	-10.557	-2.643
O	-9.007	-8.440	-3.566
O	-10.706	-7.357	-2.169
C	-13.195	-11.242	-3.218
C	-12.865	-9.962	-5.274
C	-13.924	-10.397	-4.262
C	-14.984	-11.245	-4.960
C	-14.572	-9.174	-3.605
C	-8.049	-7.519	-3.123

C	-9.764	-6.409	-1.739
C	-8.670	-6.153	-2.789
C	-7.605	-5.224	-2.215
C	-9.289	-5.542	-4.047
H	-13.833	-8.542	-3.101
H	-15.313	-9.489	-2.861
H	-15.083	-8.562	-4.358
H	-14.539	-12.125	-5.439
H	-15.500	-10.662	-5.733
H	-15.738	-11.592	-4.243
H	-10.065	-6.203	-4.447
H	-8.527	-5.392	-4.823
H	-9.743	-4.567	-3.824
H	-7.146	-5.654	-1.315
H	-8.037	-4.253	-1.941
H	-6.808	-5.041	-2.947
H	-13.876	-11.513	-2.401
H	-12.838	-12.173	-3.682
H	-13.295	-9.262	-6.001
H	-12.501	-10.841	-5.828
H	-7.288	-7.395	-3.911
H	-7.532	-7.894	-2.218
H	-10.291	-5.465	-1.524
H	-9.279	-6.738	-0.802
O	-9.570	-9.289	-1.349
C	-8.852	-10.465	-1.560
H	-8.655	-10.949	-0.594
H	-7.885	-10.281	-2.056
H	-9.411	-11.180	-2.190

	1	2	3
	A	A	A
Frequencies --	39.3933	46.1050	59.7255
Red. masses --	3.5913	3.7395	4.0587

Zero-point correction= 0.354594 (Hartree/Particle)
Thermal correction to Energy= 0.374119
Thermal correction to Enthalpy= 0.375063
Thermal correction to Gibbs Free Energy= 0.307765
Sum of electronic and zero-point Energies= -858.459316
Sum of electronic and thermal Energies= -858.439791
Sum of electronic and thermal Enthalpies= -858.438846
Sum of electronic and thermal Free Energies= -858.506144

Item	Value	Threshold	Converged?
Maximum Force	0.000098	0.000450	YES
RMS Force	0.000014	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-858.813909562', 'A.U.', 'after', '1', 'cycles']
MP2: no data
G_corr: 193.12561515 kcal/mol
H_corr: 235.35578313 kcal/mol
S_corr: 42.229966 kcal/mol

S_elec: 0.0 kcal/mol
S_trans: 12.6815121 kcal/mol
S_rot: 9.93823395 kcal/mol
S_vib: 19.61021995 kcal/mol

C_2H_4

ethylene

Cartesian coordinates (Angstroms):

6

H	-1.445	-2.371	2.424
C	-0.930	-1.417	2.488
H	-1.542	-0.523	2.399
H	1.001	-2.237	2.758
C	0.388	-1.344	2.669
H	0.902	-0.388	2.733

1	2	3
	A	A	A
Frequencies --	831.8093	984.8869	994.0695
Red. masses --	1.0423	1.1603	1.5169

Zero-point correction= 0.051423 (Hartree/Particle)
Thermal correction to Energy= 0.054461
Thermal correction to Enthalpy= 0.055405
Thermal correction to Gibbs Free Energy= 0.029240
Sum of electronic and zero-point Energies= -78.491082
Sum of electronic and thermal Energies= -78.488045
Sum of electronic and thermal Enthalpies= -78.487101
Sum of electronic and thermal Free Energies= -78.513266

Item	Value	Threshold	Converged?
Maximum Force	0.000088	0.000450	YES
RMS Force	0.000046	0.000300	YES

SCF: -78.5425055126

TS1

Cartesian coordinates (Angstroms):

49

C	-4.340	-1.644	-0.596
C	-4.351	-0.427	-1.525
C	-2.925	-0.004	-1.883
C	-2.084	0.270	-0.639
C	-2.071	-0.958	0.275
C	-3.491	-1.373	0.649
H	-3.925	-2.506	-1.138
H	-5.362	-1.915	-0.305
H	-4.862	0.406	-1.020
H	-4.924	-0.644	-2.434
H	-2.923	0.892	-2.515
H	-2.434	-0.803	-2.459
H	-2.549	1.099	-0.067
H	-1.598	-1.777	-0.299
H	-3.943	-0.563	1.240
H	-3.447	-2.257	1.297
O	-0.782	0.624	-1.025
B	0.046	1.201	0.073
B	-0.009	-0.175	1.261
O	-1.333	-0.735	1.460
C	3.040	-1.983	0.046
C	2.216	-0.753	0.417
C	2.104	0.208	-0.775
C	3.496	0.586	-1.279
C	4.326	-0.643	-1.654
C	4.431	-1.605	-0.468
H	2.495	-2.537	-0.733
H	3.108	-2.642	0.920
H	2.744	-0.205	1.226
H	1.567	-0.333	-1.577
H	3.388	1.265	-2.133
H	4.006	1.150	-0.484
H	3.848	-1.162	-2.497
H	5.324	-0.340	-1.993
H	4.999	-1.121	0.340
H	4.988	-2.507	-0.750
O	1.413	1.381	-0.439
O	0.957	-1.184	0.882
C	-0.767	3.395	-0.554
H	0.081	3.499	-1.247
H	-0.986	4.381	-0.126
H	-1.641	3.072	-1.142

O	-0.482	2.504	0.491
C	0.474	-0.084	3.321
H	-0.431	-0.451	3.791
H	1.366	-0.696	3.408
C	0.476	1.077	2.593
H	-0.374	1.750	2.611
H	1.405	1.521	2.244

	1	2	3
	A	A	A
Frequencies --	-314.1151	39.7981	69.3340
Red. masses --	10.1863	4.1789	3.2853

Zero-point correction= 0.426166 (Hartree/Particle)
Thermal correction to Energy= 0.446613
Thermal correction to Enthalpy= 0.447557
Thermal correction to Gibbs Free Energy= 0.379130
Sum of electronic and zero-point Energies= -1013.115443
Sum of electronic and thermal Energies= -1013.094995
Sum of electronic and thermal Enthalpies= -1013.094051
Sum of electronic and thermal Free Energies= -1013.162478

Item	Value	Threshold	Converged?
Maximum Force	0.000019	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF: -1013.54160836

INT

Cartesian coordinates (Angstroms):

49

C	-4.106	-1.812	-0.990
C	-4.272	-0.374	-1.481
C	-2.900	0.264	-1.688
C	-2.023	0.229	-0.435
C	-1.891	-1.190	0.139
C	-3.275	-1.831	0.290
H	-3.606	-2.404	-1.770
H	-5.084	-2.277	-0.815
H	-4.841	0.200	-0.735
H	-4.845	-0.340	-2.414
H	-2.991	1.305	-2.024
H	-2.362	-0.276	-2.480
H	-2.456	0.856	0.356
H	-1.295	-1.769	-0.590
H	-3.809	-1.283	1.080

H	-3.133	-2.854	0.658
O	-0.746	0.721	-0.827
B	0.057	1.642	-0.206
B	0.054	-0.738	1.638
O	-1.302	-1.236	1.409
C	3.141	-1.788	-0.095
C	2.196	-0.657	0.326
C	2.105	0.400	-0.787
C	3.486	0.866	-1.245
C	4.382	-0.294	-1.676
C	4.521	-1.301	-0.535
H	2.661	-2.327	-0.925
H	3.213	-2.495	0.740
H	2.613	-0.157	1.221
H	1.561	-0.058	-1.627
H	3.360	1.596	-2.054
H	3.958	1.398	-0.406
H	3.942	-0.795	-2.551
H	5.364	0.084	-1.986
H	5.032	-0.819	0.311
H	5.143	-2.151	-0.840
O	1.421	1.569	-0.357
O	0.953	-1.231	0.596
C	-1.700	3.257	0.396
H	-2.259	2.968	-0.502
H	-1.709	4.348	0.476
H	-2.196	2.839	1.279
O	-0.355	2.845	0.332
C	0.486	-0.632	3.168
H	-0.205	-0.849	3.987
H	1.529	-0.774	3.463
C	0.222	0.687	2.378
H	-0.669	1.241	2.688
H	1.086	1.345	2.269

	1	2	3
	A	A	A
Frequencies --	43.9244	57.6908	71.0497
Red. masses --	3.7879	3.1200	3.1763

Zero-point correction= 0.428002 (Hartree/Particle)
Thermal correction to Energy= 0.448573
Thermal correction to Enthalpy= 0.449517
Thermal correction to Gibbs Free Energy= 0.380814
Sum of electronic and zero-point Energies= -1013.168603
Sum of electronic and thermal Energies= -1013.148032
Sum of electronic and thermal Enthalpies= -1013.147088
Sum of electronic and thermal Free Energies= -1013.215791

Item	Value	Threshold	Converged?
Maximum Force	0.000034	0.000450	YES
RMS Force	0.000005	0.000300	YES

SCF: -1013.59660517

TS2

Cartesian coordinates (Angstroms):

49

C	-4.106	-1.938	-0.747
C	-4.247	-0.588	-1.451
C	-2.868	0.010	-1.722
C	-2.025	0.152	-0.455
C	-1.911	-1.175	0.298
C	-3.295	-1.780	0.538
H	-3.600	-2.646	-1.419
H	-5.092	-2.363	-0.522
H	-4.827	0.094	-0.812
H	-4.803	-0.694	-2.390
H	-2.947	0.992	-2.206
H	-2.314	-0.640	-2.415
H	-2.499	0.868	0.234
H	-1.315	-1.854	-0.335
H	-3.836	-1.121	1.235
H	-3.166	-2.742	1.048
O	-0.748	0.606	-0.860
B	0.071	1.532	-0.201
B	0.038	-0.496	1.651
O	-1.303	-1.019	1.556
C	3.125	-1.832	0.136
C	2.201	-0.645	0.423
C	2.123	0.283	-0.795
C	3.514	0.682	-1.289
C	4.398	-0.528	-1.587
C	4.514	-1.413	-0.345
H	2.640	-2.449	-0.635
H	3.185	-2.446	1.042
H	2.615	-0.058	1.265
H	1.592	-0.270	-1.587
H	3.401	1.319	-2.174
H	3.987	1.298	-0.510
H	3.959	-1.113	-2.408
H	5.388	-0.199	-1.924
H	5.028	-0.852	0.450
H	5.124	-2.299	-0.555
O	1.438	1.485	-0.510
O	0.938	-1.160	0.741
C	-1.672	3.263	-0.057
H	-2.209	2.831	-0.913

H	-1.708	4.354	-0.143
H	-2.195	2.975	0.866
O	-0.325	2.875	-0.034
C	0.444	0.044	3.056
H	-0.244	-0.008	3.902
H	1.488	0.037	3.374
C	0.130	1.178	2.016
H	-0.796	1.708	2.255
H	0.961	1.875	1.914

	1	2	3
	A	A	A
Frequencies --	-250.8197	34.7261	62.9033
Red. masses --	7.0705	4.1129	2.8753

Zero-point correction= 0.427083 (Hartree/Particle)
Thermal correction to Energy= 0.447053
Thermal correction to Enthalpy= 0.447997
Thermal correction to Gibbs Free Energy= 0.380595
Sum of electronic and zero-point Energies= -1013.165639
Sum of electronic and thermal Energies= -1013.145669
Sum of electronic and thermal Enthalpies= -1013.144724
Sum of electronic and thermal Free Energies= -1013.212127

Item	Value	Threshold	Converged?
Maximum Force	0.000017	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF: -1013.59272174

PDT

Cartesian coordinates (Angstroms):

49

C	-4.238	-1.383	-1.170
C	-4.178	0.116	-1.477
C	-2.730	0.617	-1.504
C	-2.001	0.296	-0.199
C	-2.077	-1.211	0.091
C	-3.515	-1.706	0.140
H	-3.765	-1.938	-1.993
H	-5.280	-1.722	-1.119
H	-4.736	0.662	-0.702
H	-4.673	0.329	-2.432
H	-2.689	1.699	-1.677
H	-2.184	0.138	-2.331
H	-2.513	0.819	0.628

H	-1.530	-1.731	-0.713
H	-4.025	-1.213	0.979
H	-3.527	-2.784	0.342
O	-0.655	0.655	-0.267
B	0.041	1.558	0.697
B	-0.105	-1.104	1.469
O	-1.444	-1.461	1.339
C	2.829	-2.099	-0.516
C	2.080	-1.081	0.341
C	2.031	0.306	-0.334
C	3.455	0.737	-0.709
C	4.190	-0.282	-1.577
C	4.241	-1.637	-0.871
H	2.252	-2.254	-1.440
H	2.847	-3.059	0.013
H	2.594	-0.962	1.309
H	1.434	0.192	-1.254
H	3.389	1.711	-1.210
H	4.017	0.899	0.223
H	3.668	-0.396	-2.538
H	5.203	0.073	-1.805
H	4.840	-1.545	0.047
H	4.736	-2.388	-1.499
O	1.500	1.304	0.490
O	0.780	-1.621	0.556
C	0.075	3.406	-0.876
H	1.159	3.326	-1.057
H	-0.217	4.458	-0.990
H	-0.437	2.819	-1.655
O	-0.265	2.973	0.411
C	0.245	-0.151	2.676
H	-0.227	-0.513	3.602
H	1.321	-0.074	2.866
C	-0.313	1.244	2.264
H	-1.398	1.262	2.449
H	0.115	2.023	2.913

	1	2	3
	A	A	A
Frequencies --	50.6611	69.4880	76.7805
Red. masses --	4.0720	2.7489	3.2085

Zero-point correction= 0.429520 (Hartree/Particle)
Thermal correction to Energy= 0.449421
Thermal correction to Enthalpy= 0.450365
Thermal correction to Gibbs Free Energy= 0.383300
Sum of electronic and zero-point Energies= -1013.205731
Sum of electronic and thermal Energies= -1013.185829
Sum of electronic and thermal Enthalpies= -1013.184885
Sum of electronic and thermal Free Energies= -1013.251951

Item	Value	Threshold	Converged?

Maximum Force	0.000040	0.000450	YES
RMS Force	0.000005	0.000300	YES

SCF: -1013.63525054

1,1-$B_2(neo)_2$-OMe TS1

Cartesian coordinates (Angstroms):

47

H	-9.710	-11.743	-2.616
H	-11.561	-12.730	-3.944
C	-9.878	-11.415	-3.637
C	-10.850	-12.049	-4.397
H	-9.024	-10.947	-4.119
H	-10.899	-11.915	-5.472
B	-11.211	-10.199	-3.532
B	-9.906	-9.164	-2.623
O	-11.555	-9.447	-4.708
O	-12.266	-10.538	-2.612
O	-8.892	-8.728	-3.592
O	-10.803	-8.080	-2.213
C	-13.535	-10.774	-3.169
C	-12.822	-9.694	-5.262
C	-13.928	-9.710	-4.201
C	-15.259	-10.086	-4.847
C	-14.014	-8.342	-3.524
C	-8.218	-7.551	-3.225
C	-10.140	-6.902	-1.834
C	-9.187	-6.398	-2.926
C	-8.412	-5.184	-2.422
C	-9.981	-6.052	-4.186
H	-13.052	-8.090	-3.064
H	-14.789	-8.345	-2.746
H	-14.271	-7.565	-4.257
H	-15.204	-11.067	-5.337
H	-15.548	-9.346	-5.603
H	-16.058	-10.128	-4.096
H	-10.520	-6.936	-4.541
H	-9.311	-5.702	-4.983
H	-10.707	-5.255	-3.979
H	-7.840	-5.423	-1.517
H	-9.094	-4.358	-2.182
H	-7.707	-4.824	-3.182
H	-14.268	-10.791	-2.349
H	-13.556	-11.766	-3.659
H	-13.027	-8.910	-6.005
H	-12.822	-10.668	-5.790
H	-7.544	-7.268	-4.049

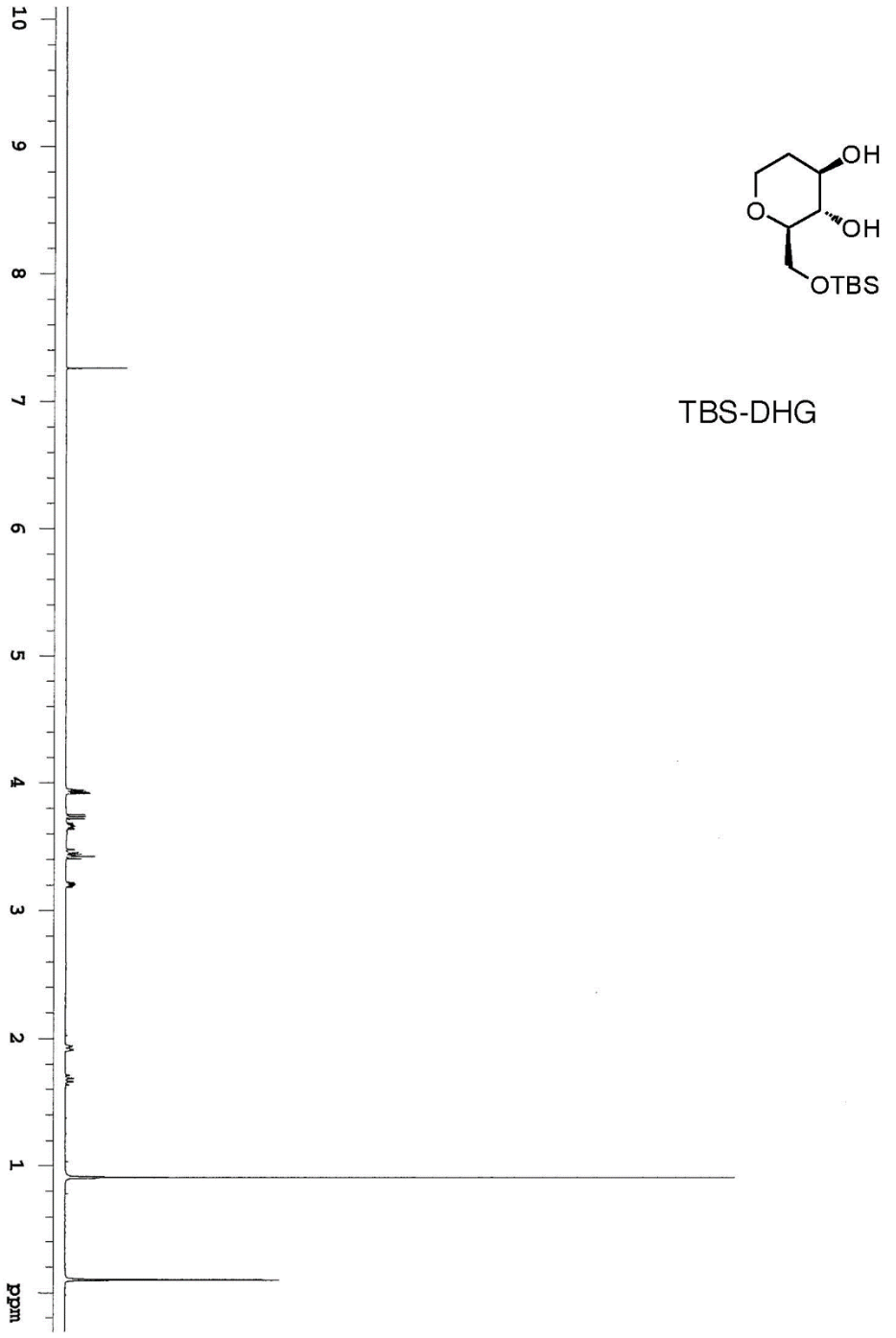
H	-7.590	-7.722	-2.328
H	-10.900	-6.133	-1.623
H	-9.561	-7.061	-0.905
O	-9.296	-9.715	-1.396
C	-8.007	-10.258	-1.388
H	-8.028	-11.325	-1.114
H	-7.384	-9.742	-0.640
H	-7.511	-10.165	-2.363

	1	2	3
	A	A	A
Frequencies --	-388.3046	45.4172	58.3107
Red. masses --	10.2966	3.7769	3.6487

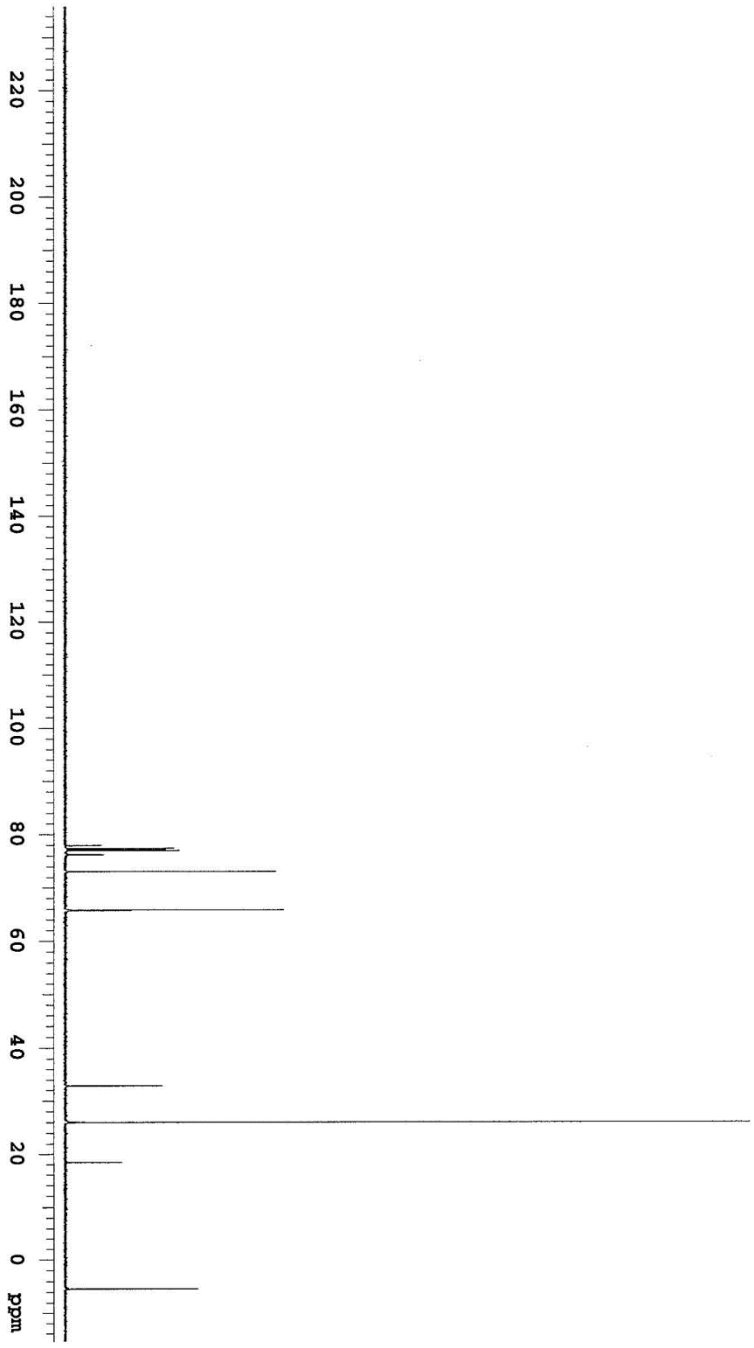
Zero-point correction= 0.408658 (Hartree/Particle)
Thermal correction to Energy= 0.430098
Thermal correction to Enthalpy= 0.431042
Thermal correction to Gibbs Free Energy= 0.361292
Sum of electronic and zero-point Energies= -936.911556
Sum of electronic and thermal Energies= -936.890116
Sum of electronic and thermal Enthalpies= -936.889172
Sum of electronic and thermal Free Energies= -936.958922

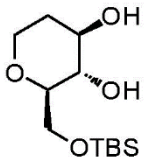
Item	Value	Threshold	Converged?
Maximum Force	0.000018	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-937.320213920', 'A.U.', 'after', '1', 'cycles']
MP2: no data
G_corr: 226.71434292 kcal/mol
H_corr: 270.48316542 kcal/mol
S_corr: 43.76842 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 12.7733423 kcal/mol
S_rot: 10.023803 kcal/mol
S_vib: 20.9712747 kcal/mol



TBS-DHG





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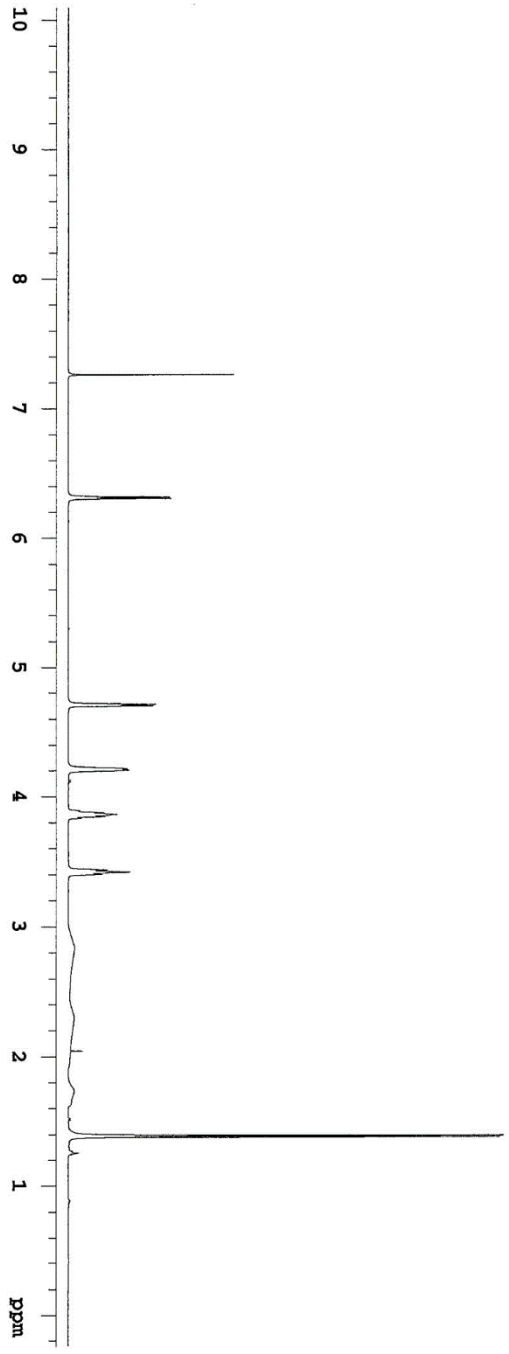
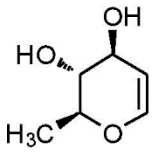
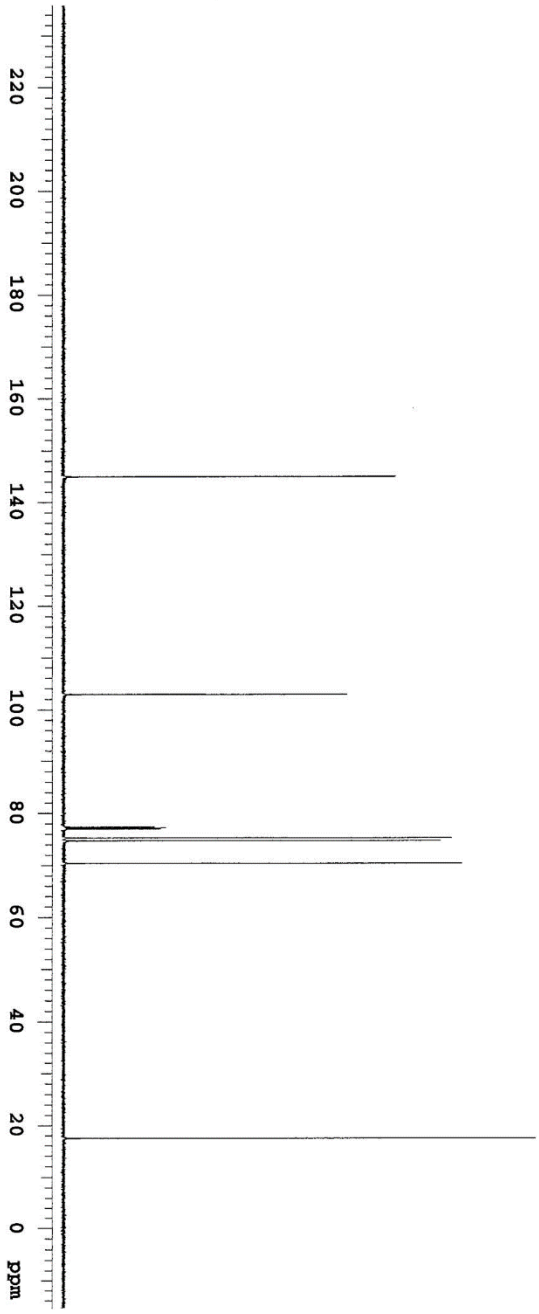
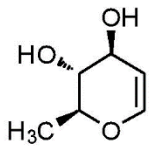


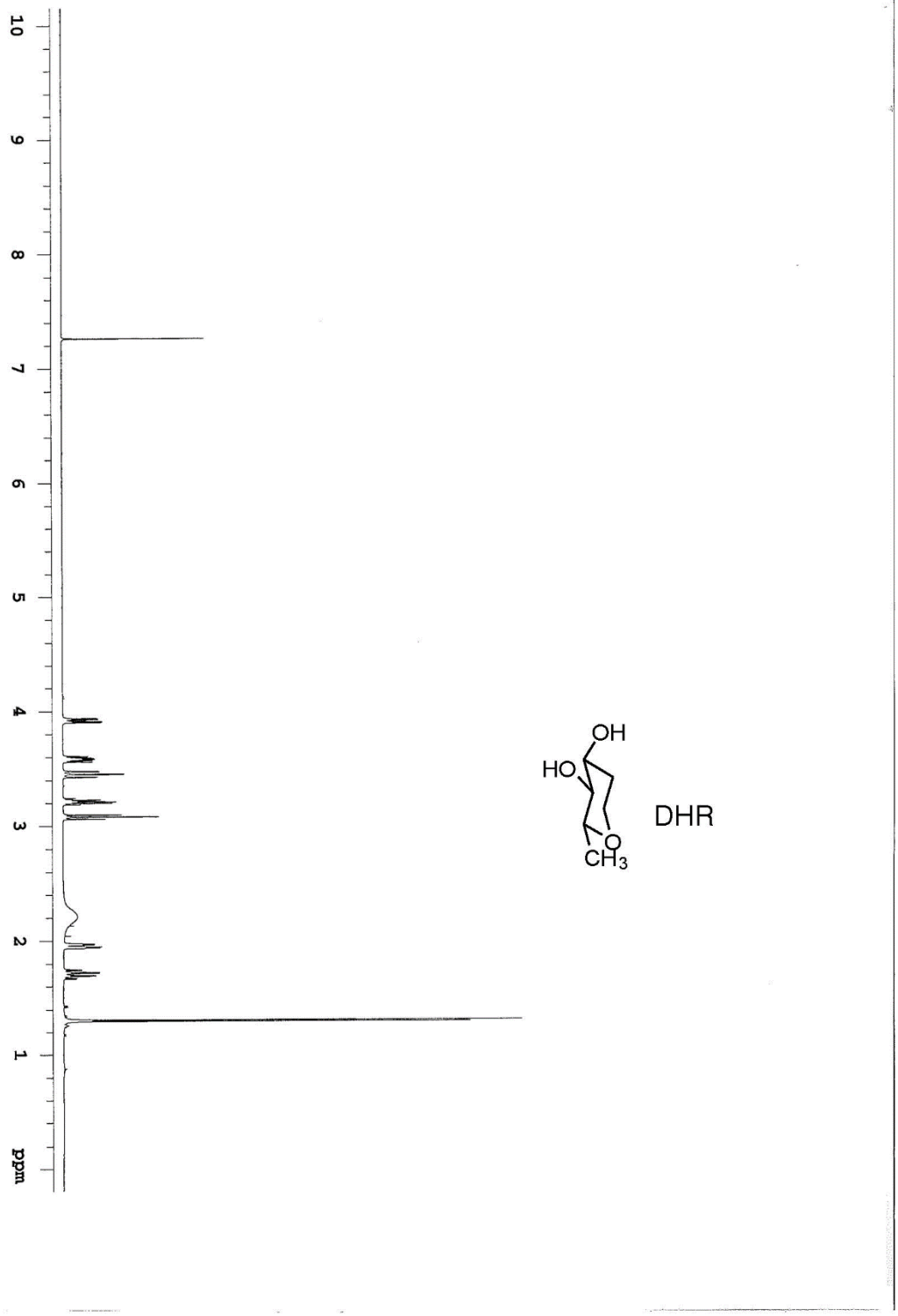


S4





S4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9
8
7
6
5
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3
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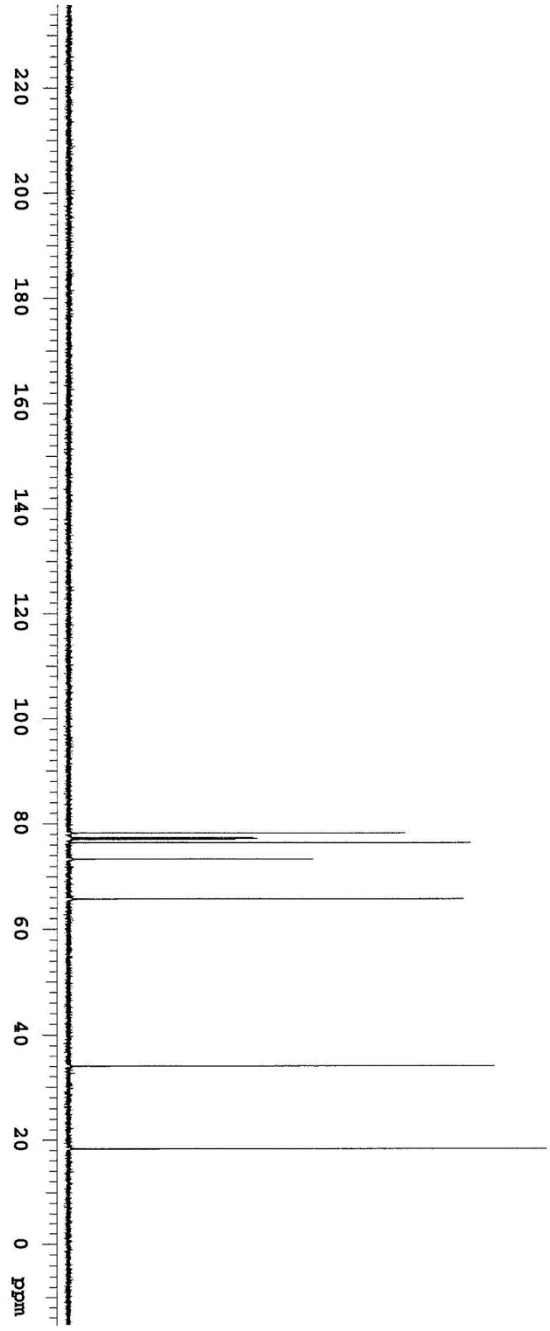

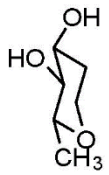

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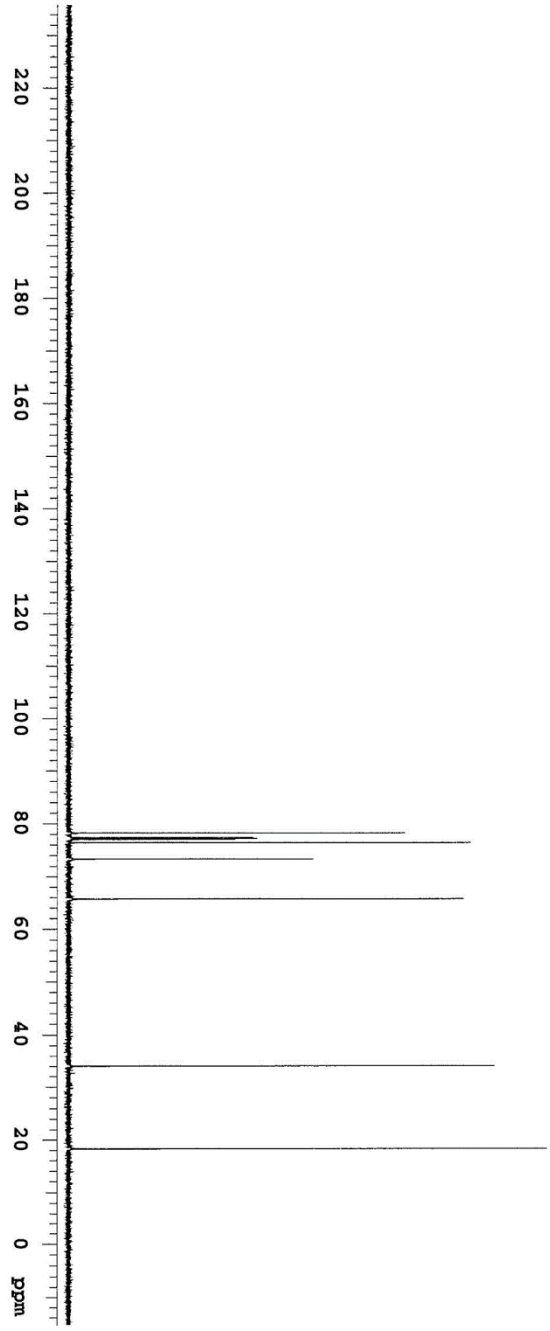

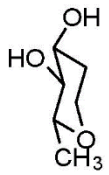

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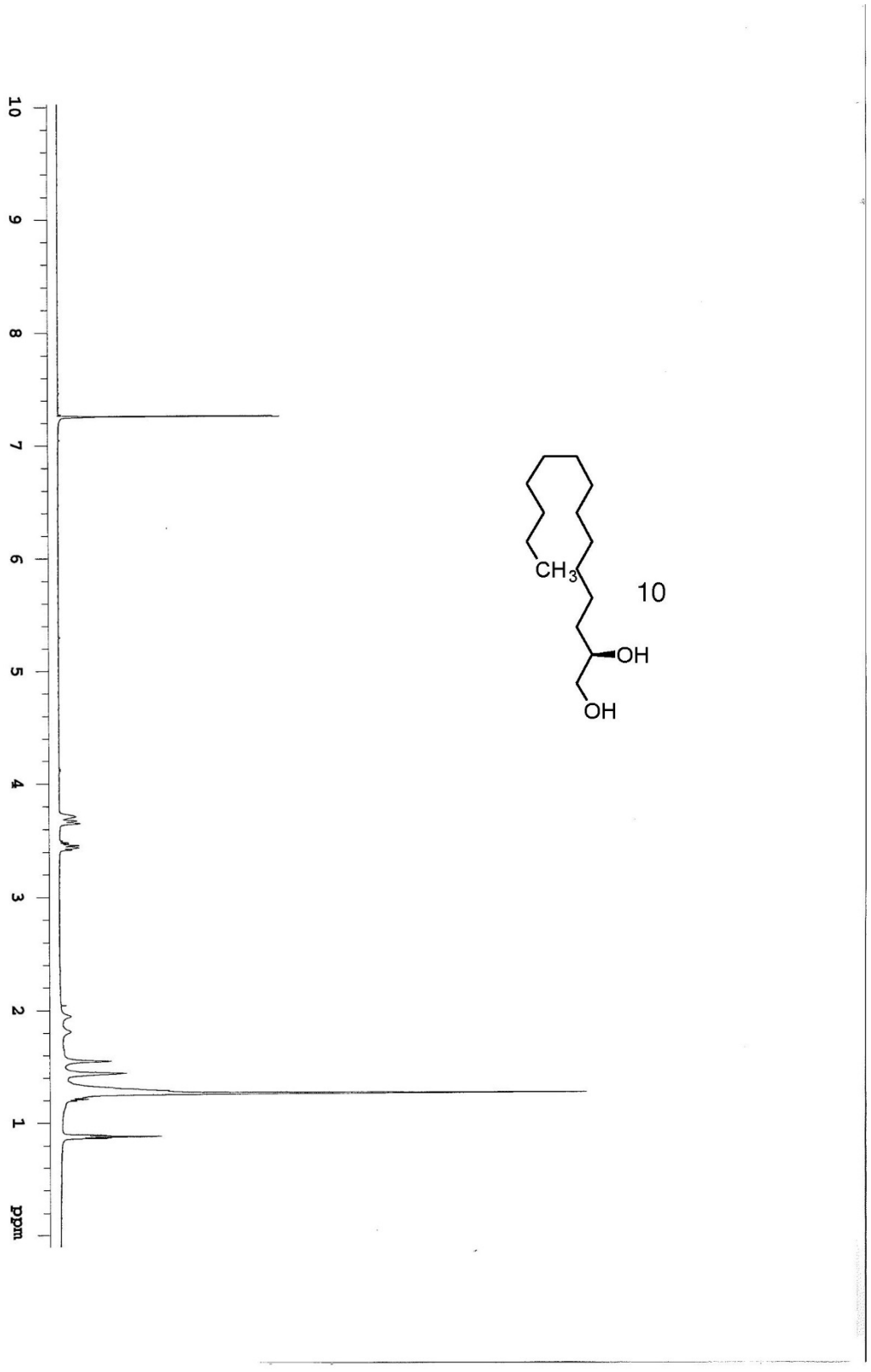
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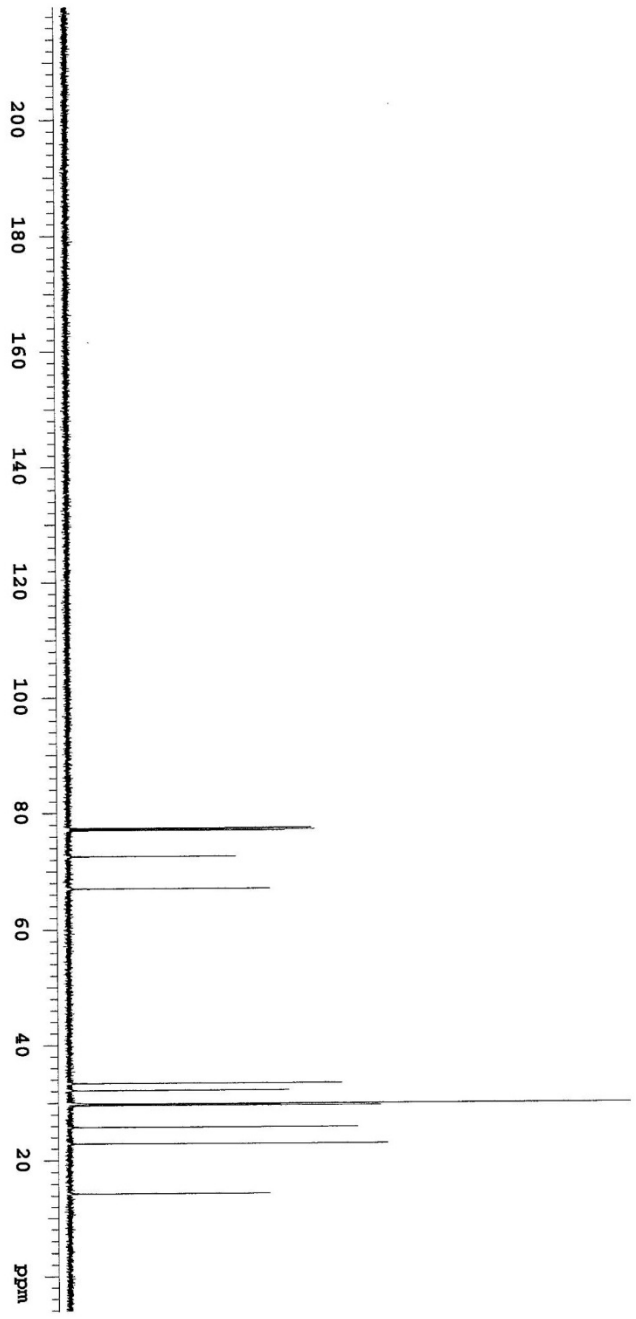

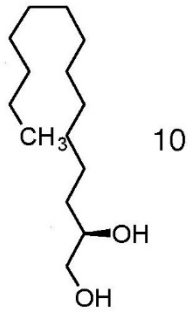

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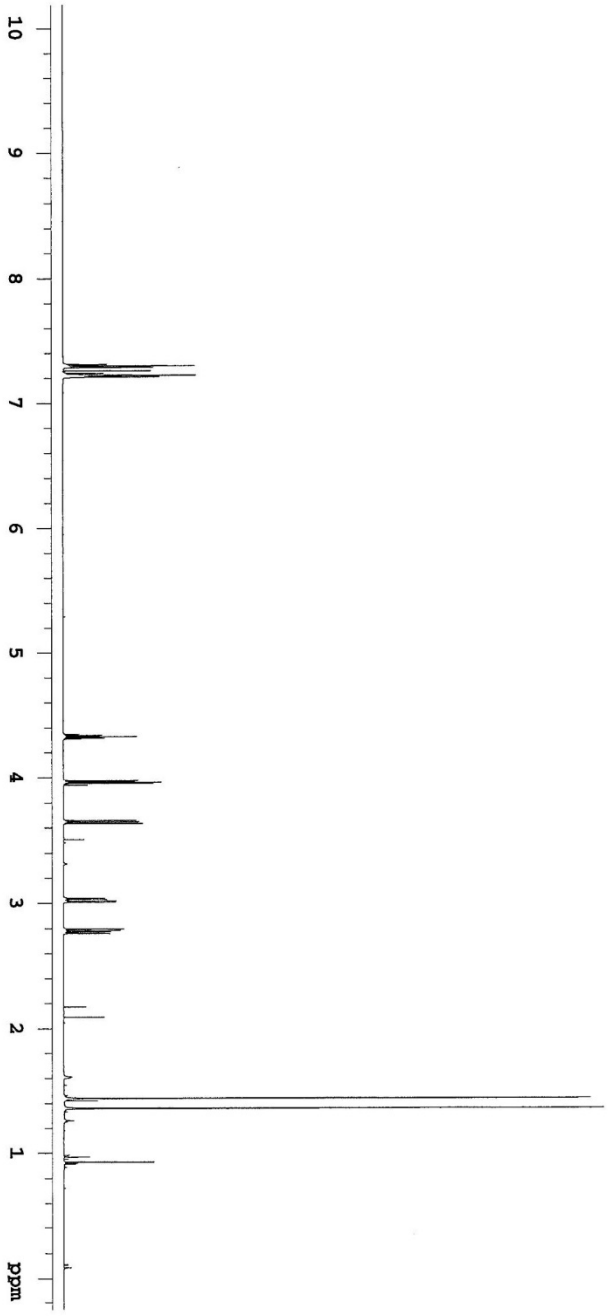

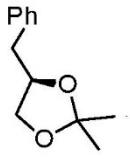

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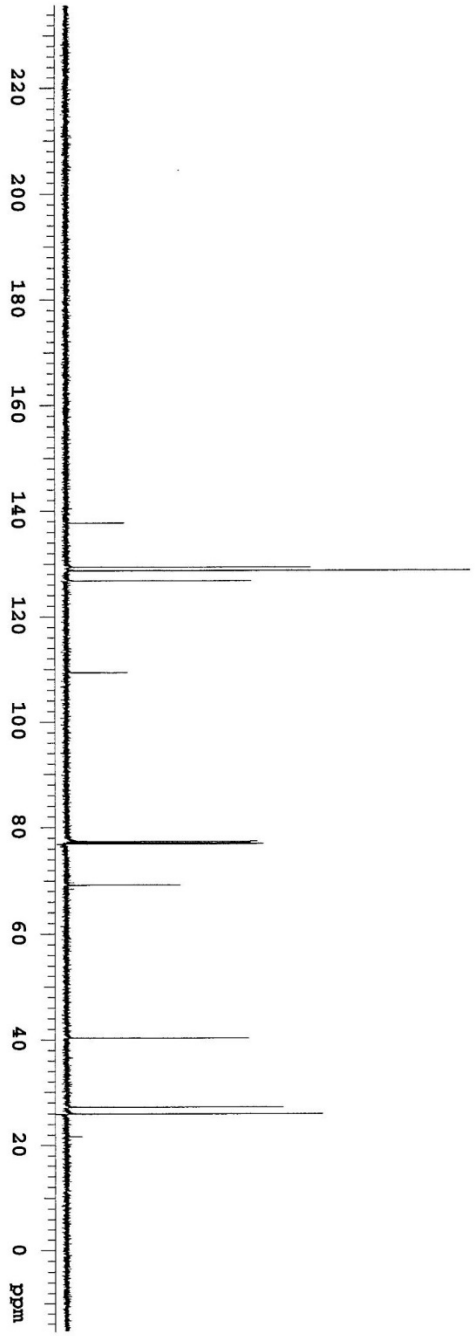

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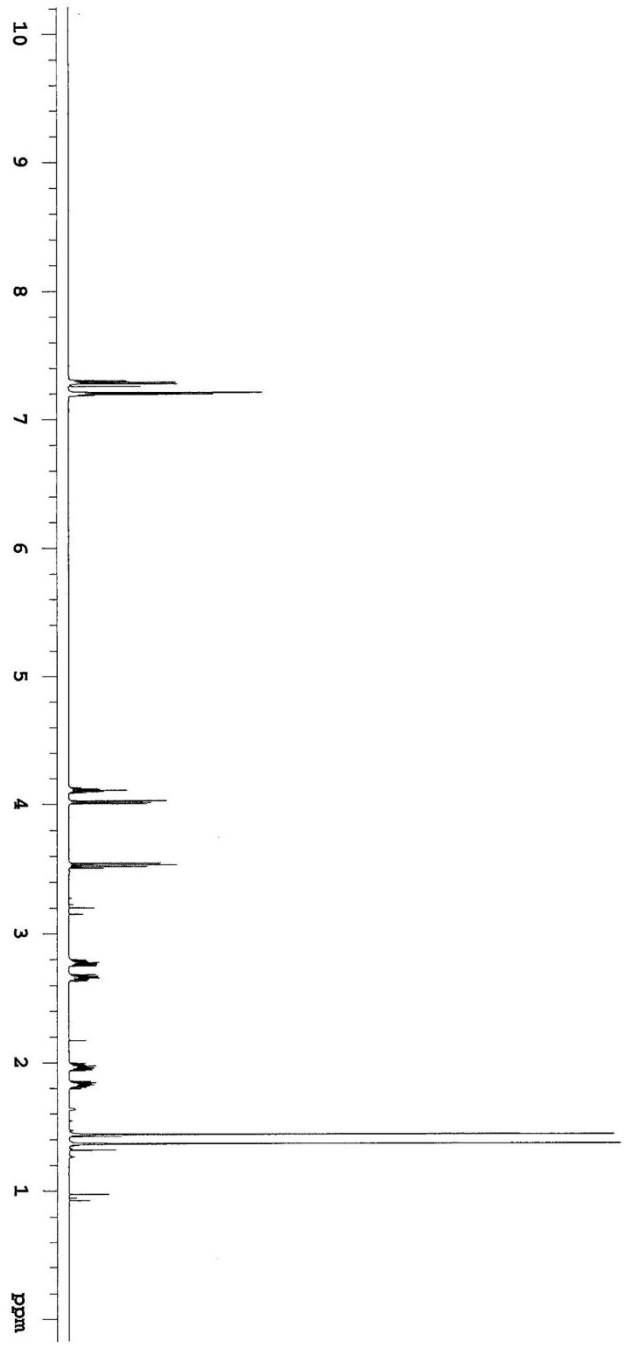

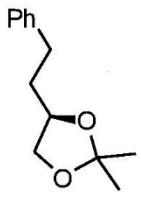

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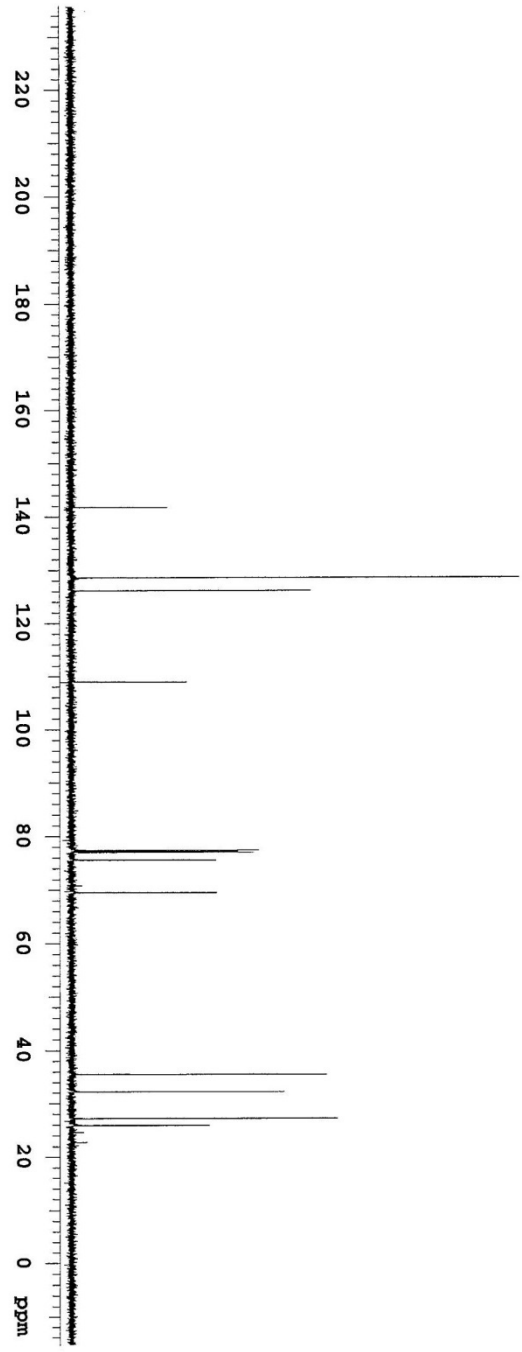

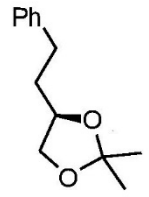

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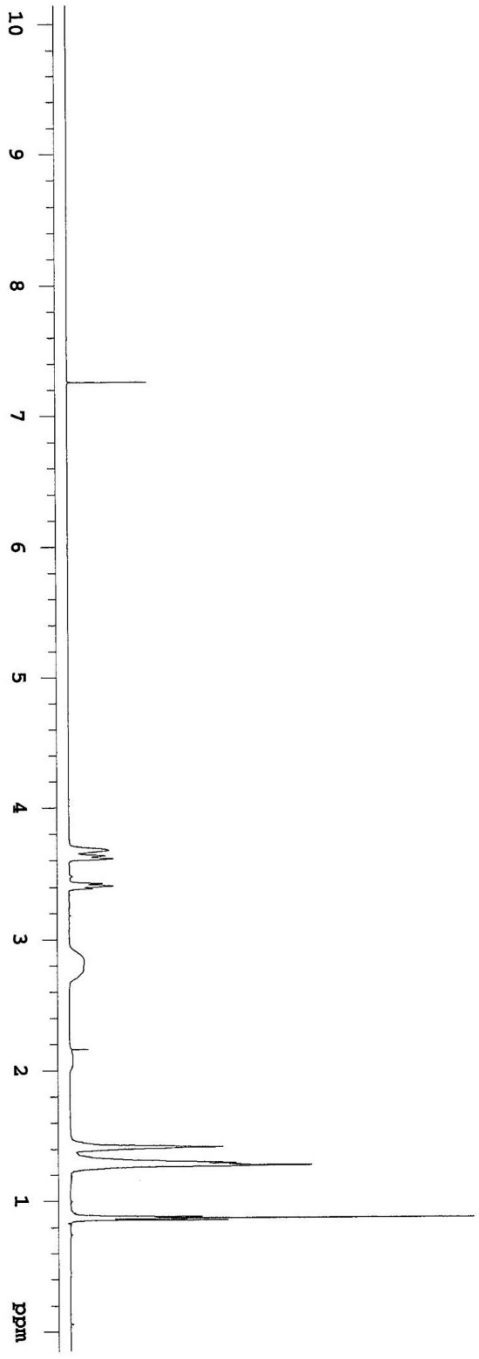

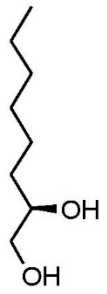

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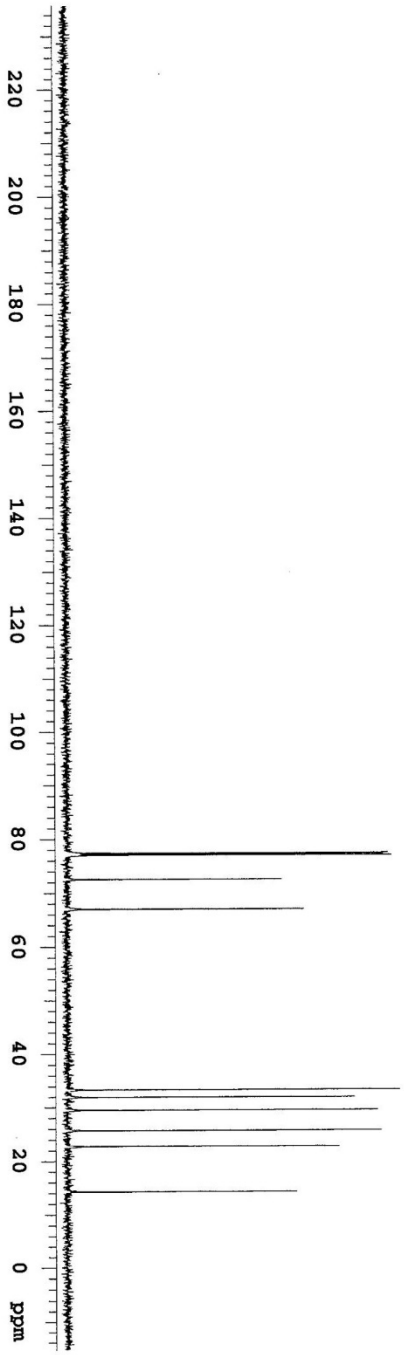

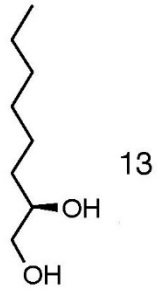

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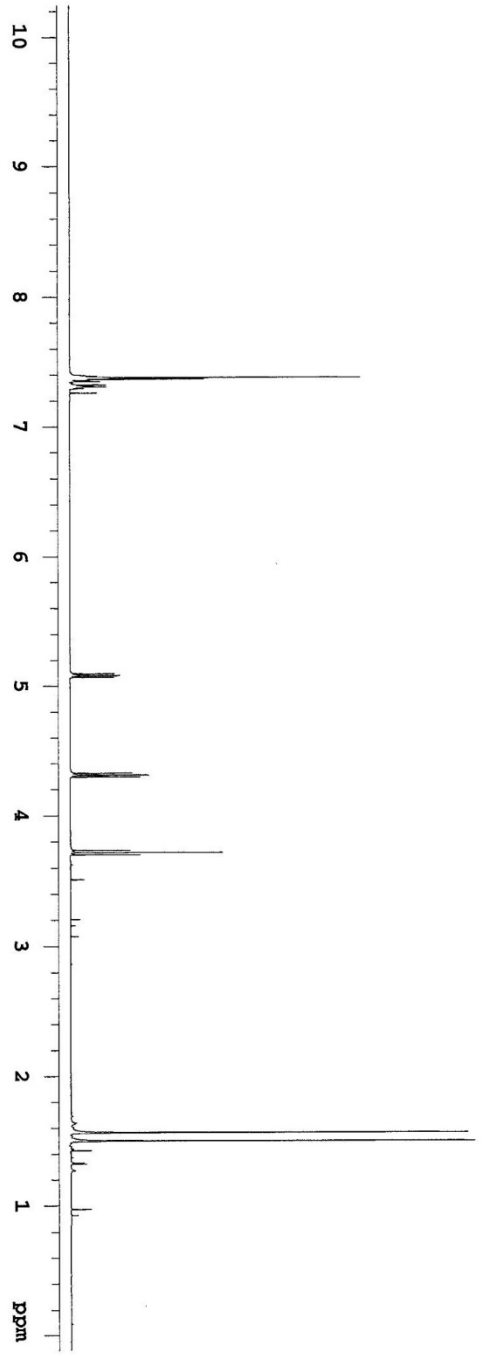

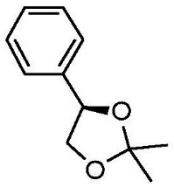

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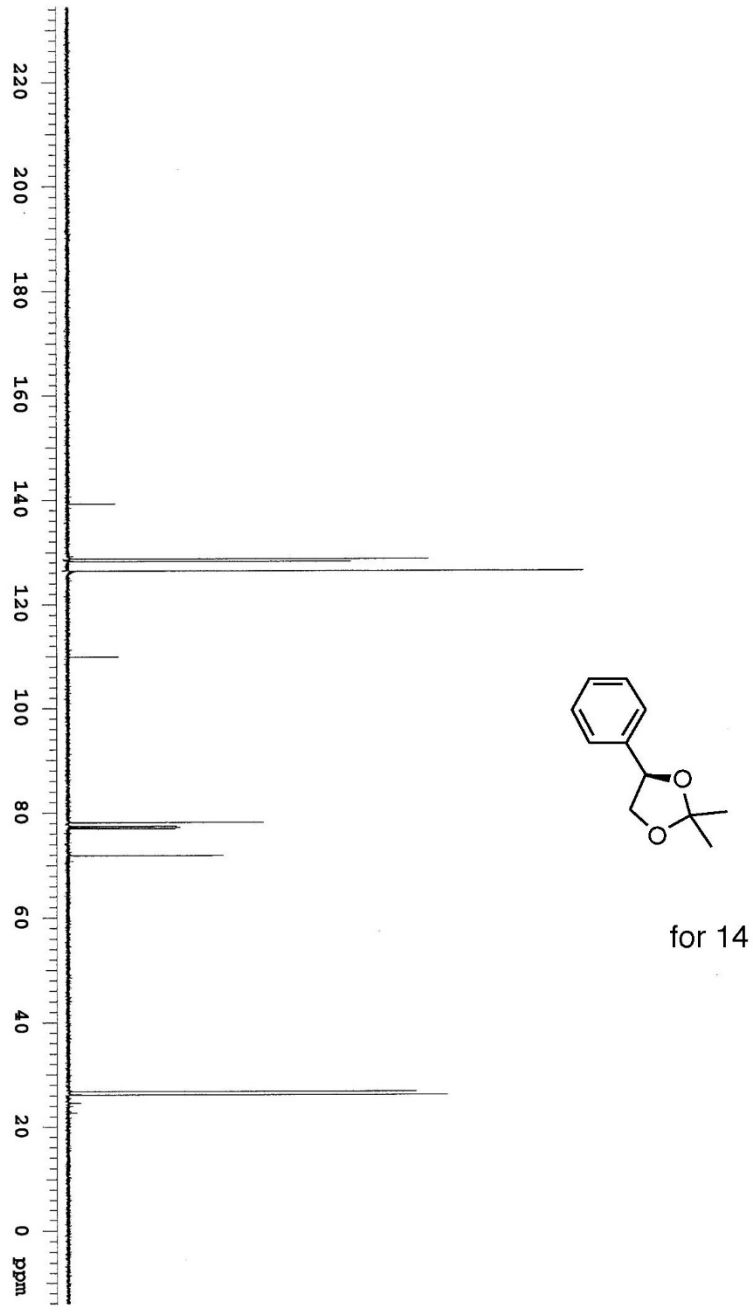

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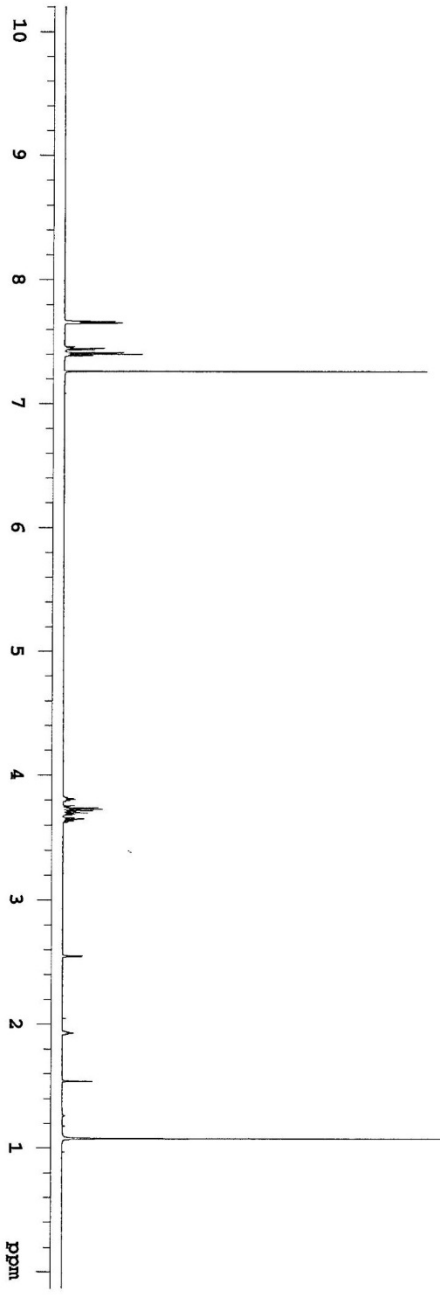

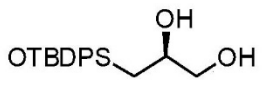

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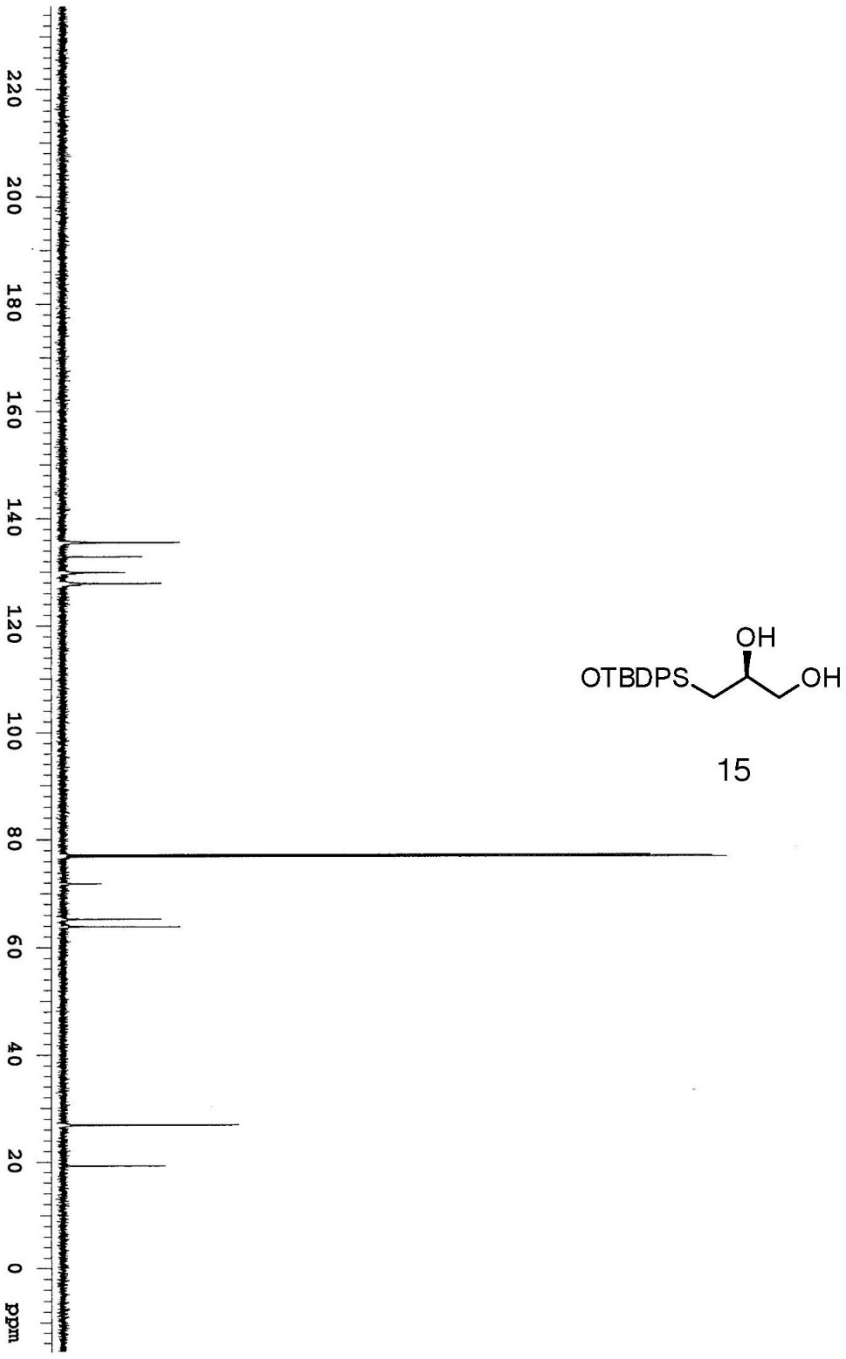

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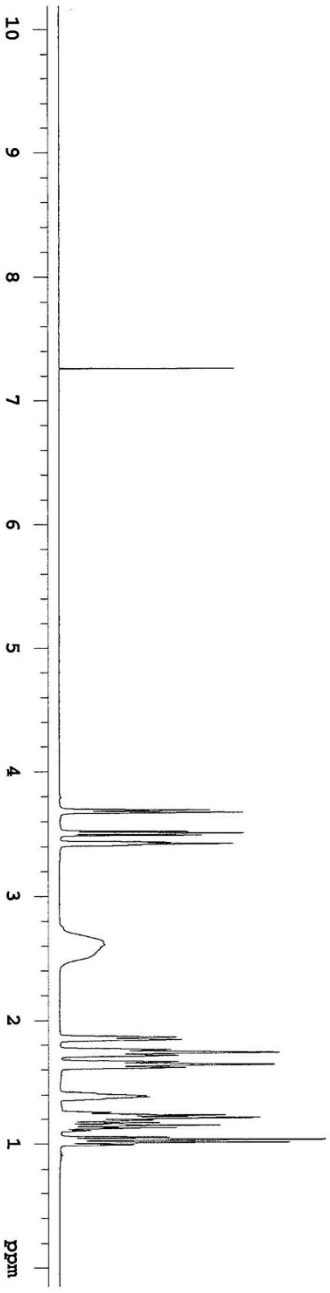

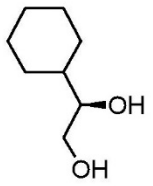

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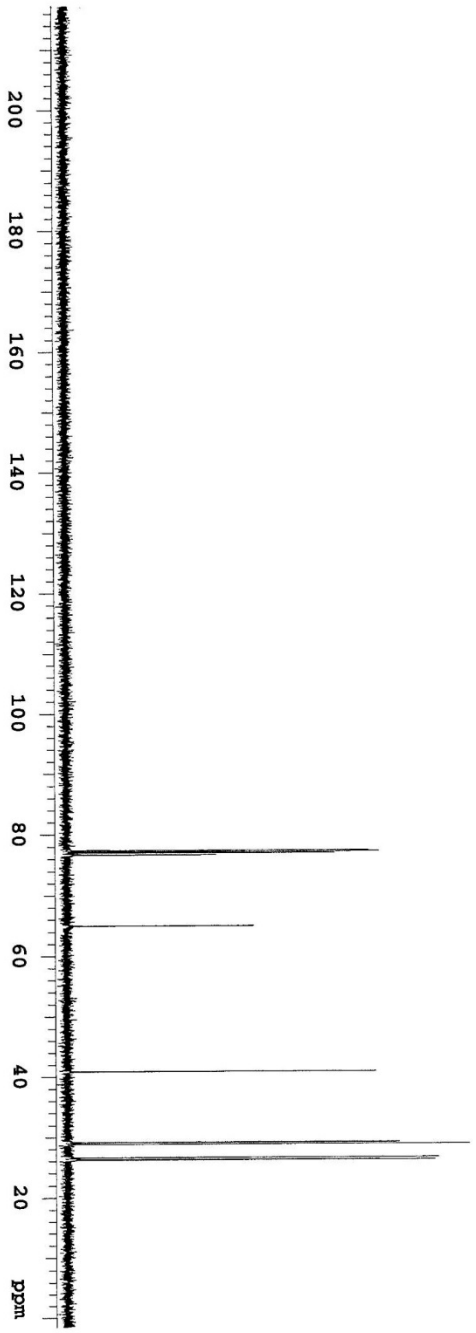

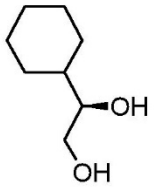

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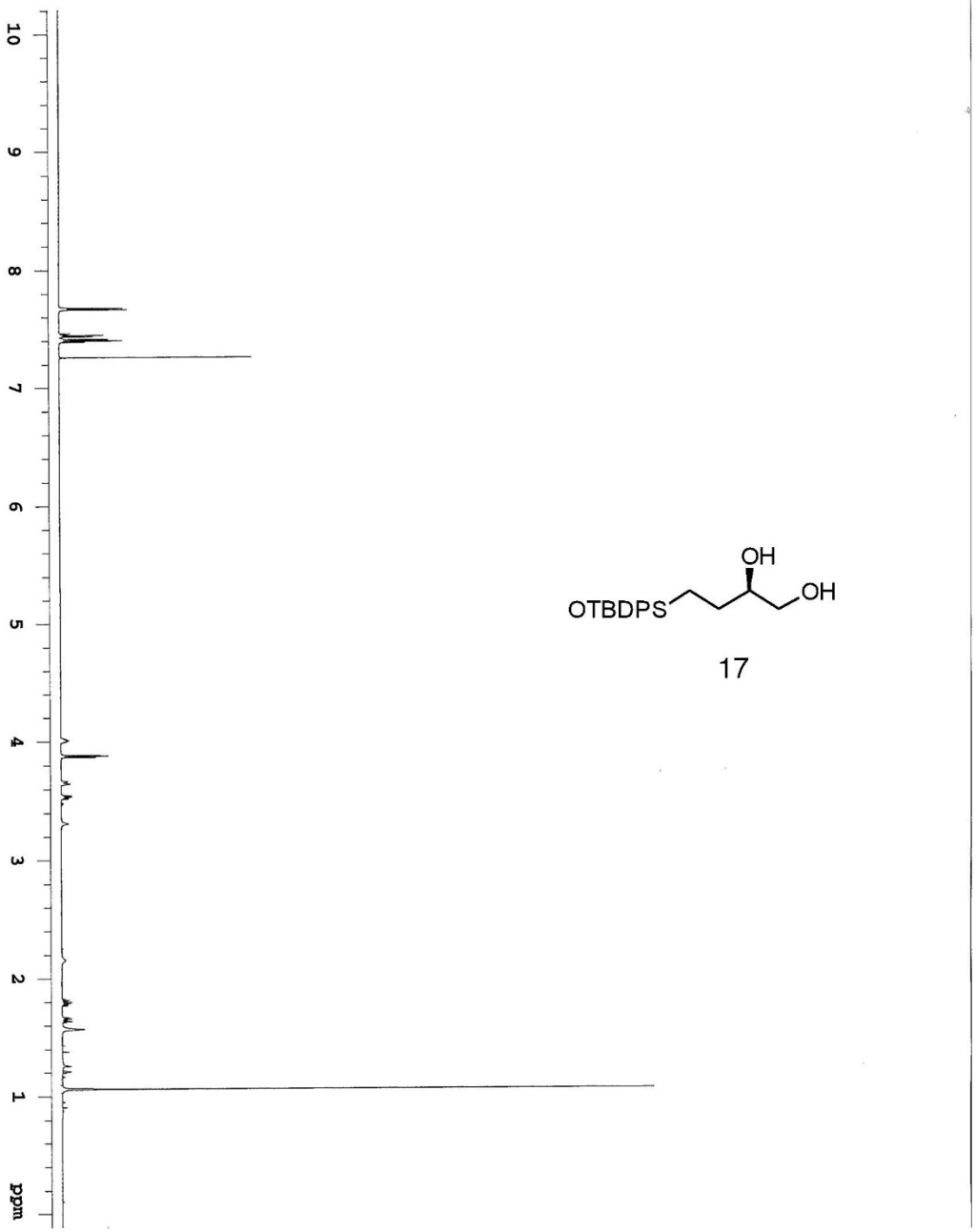

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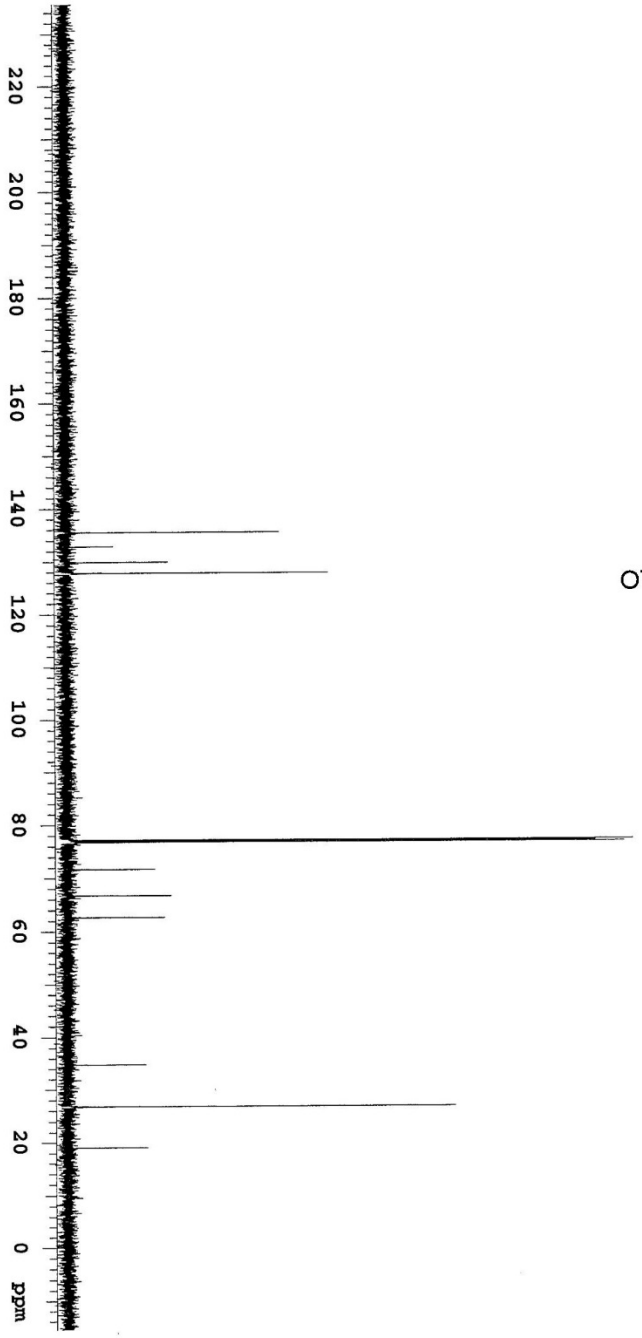

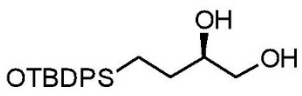

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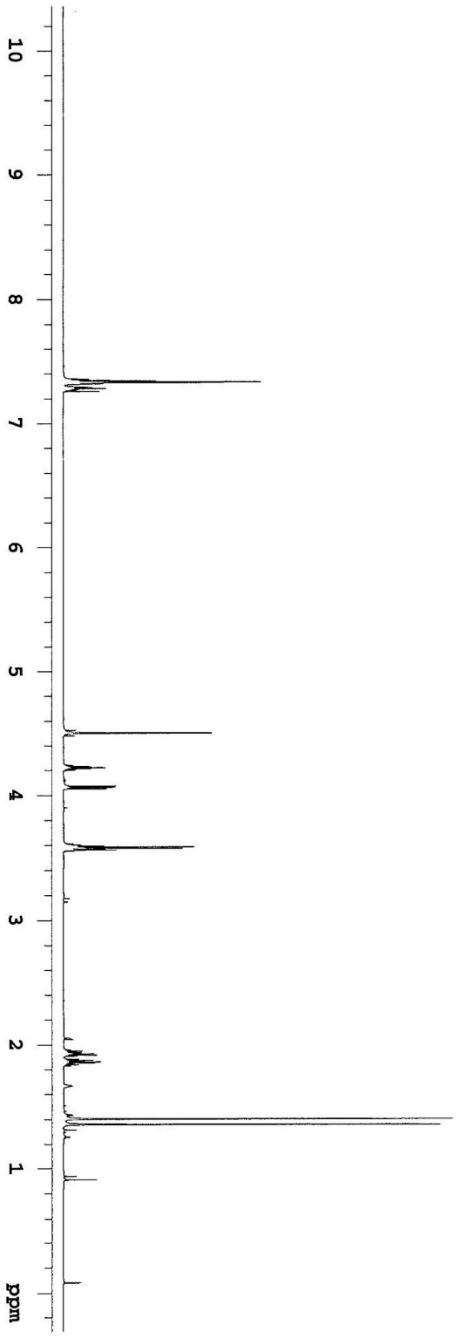

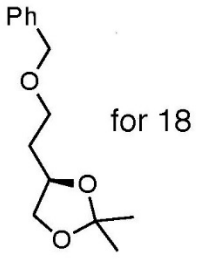

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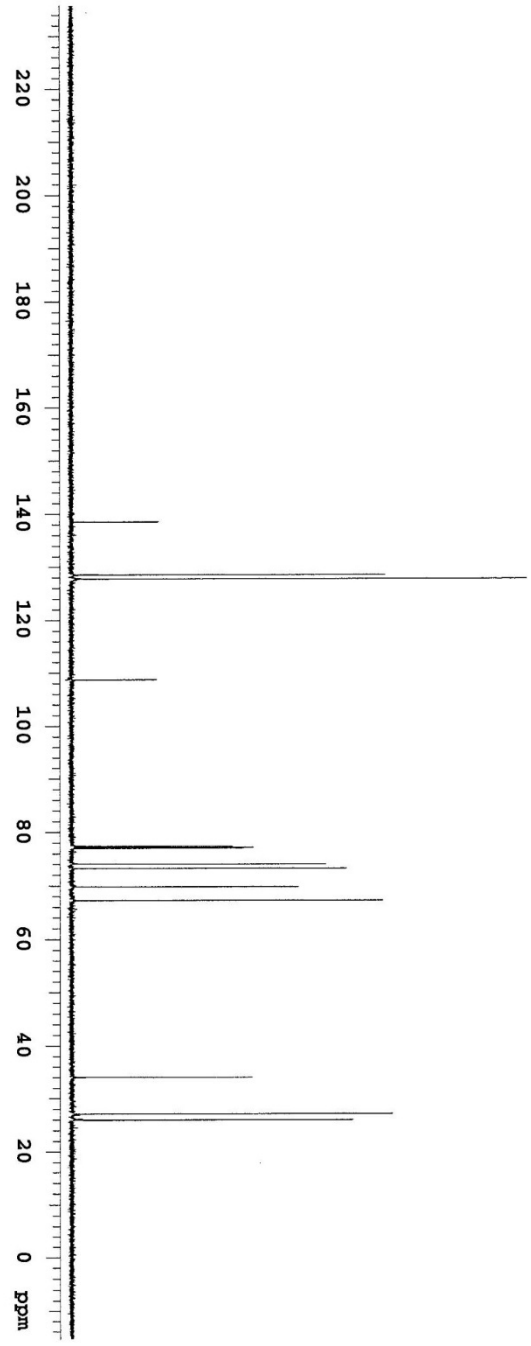

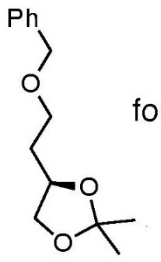

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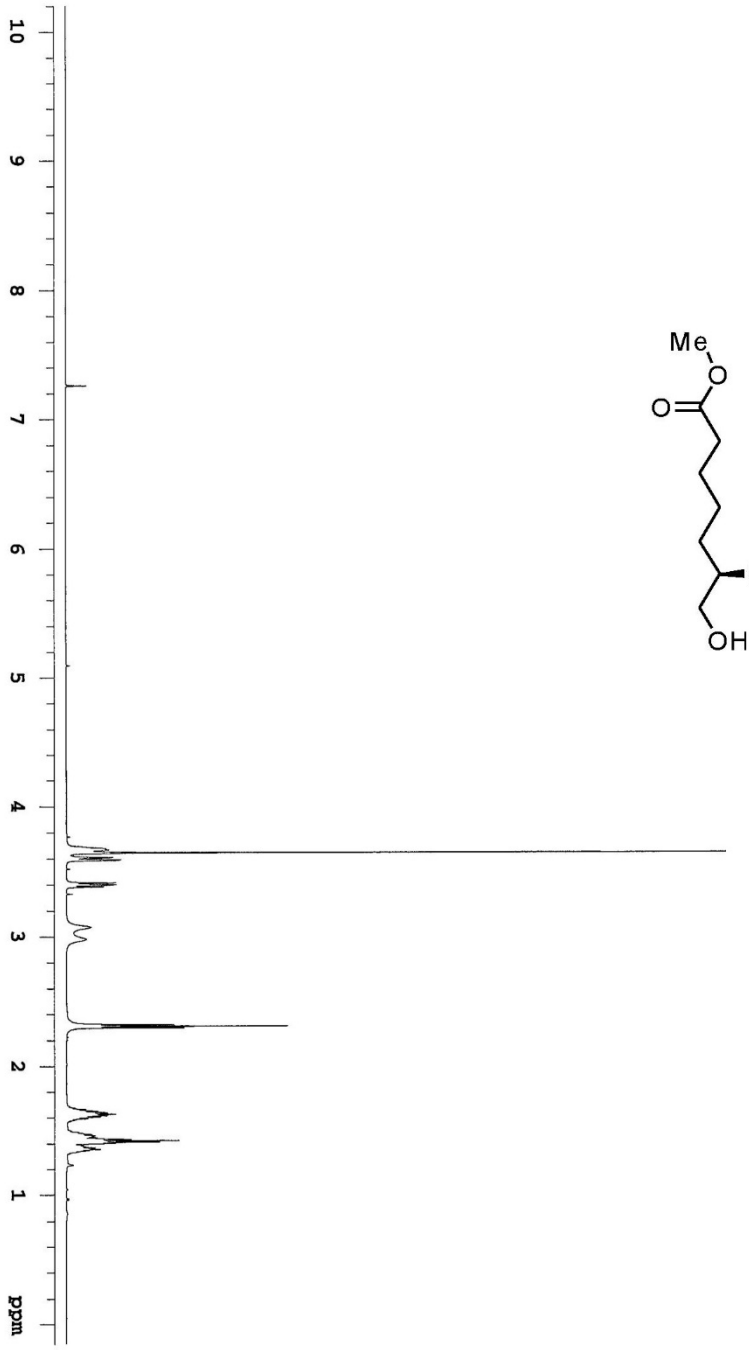

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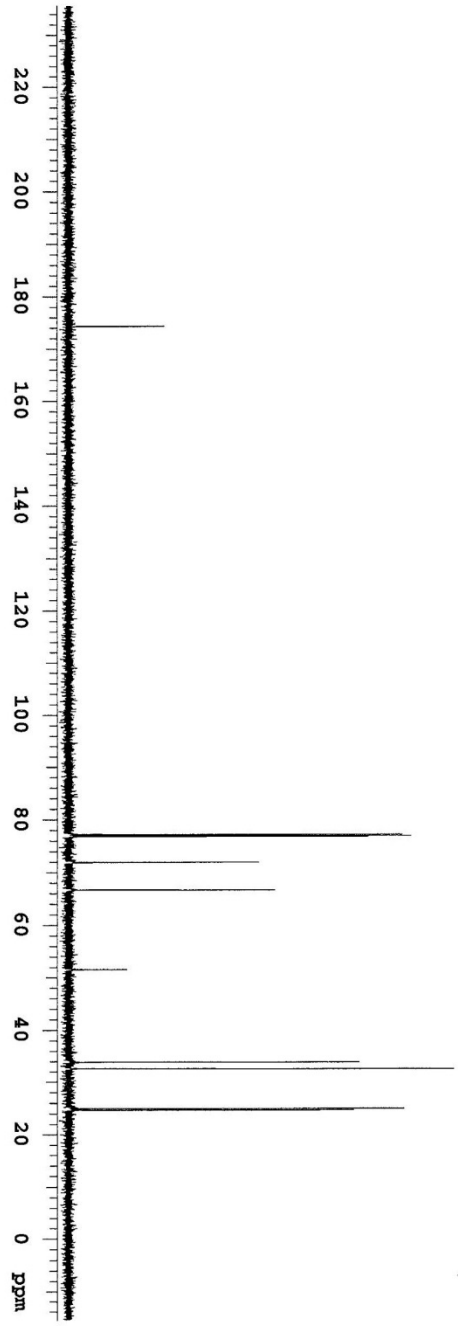

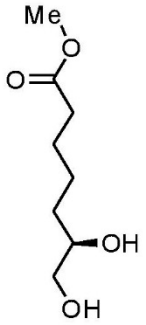

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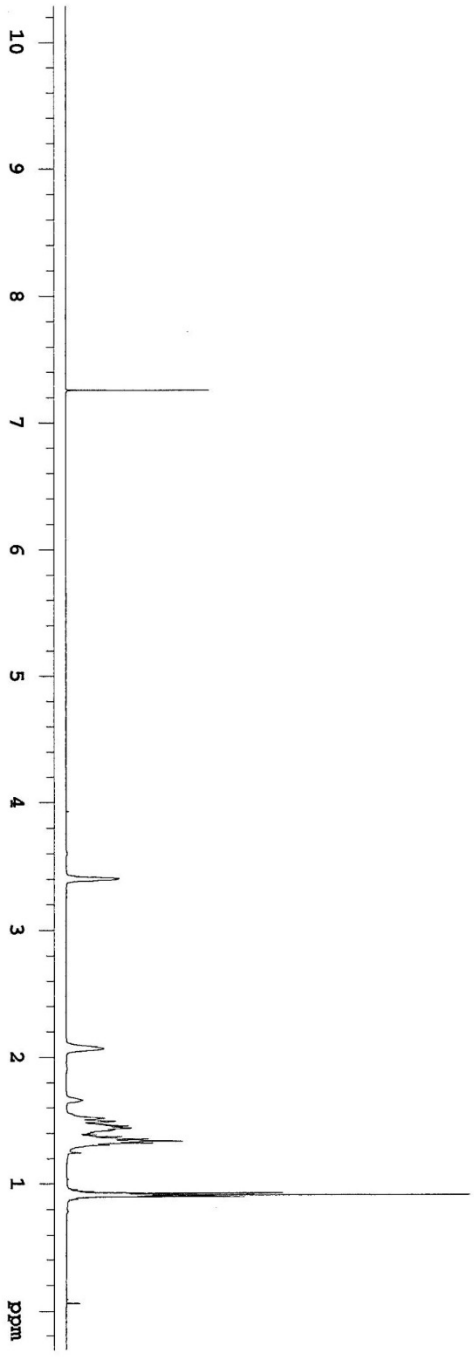

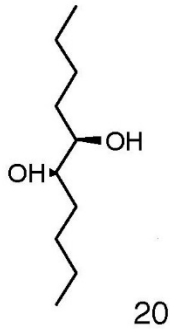

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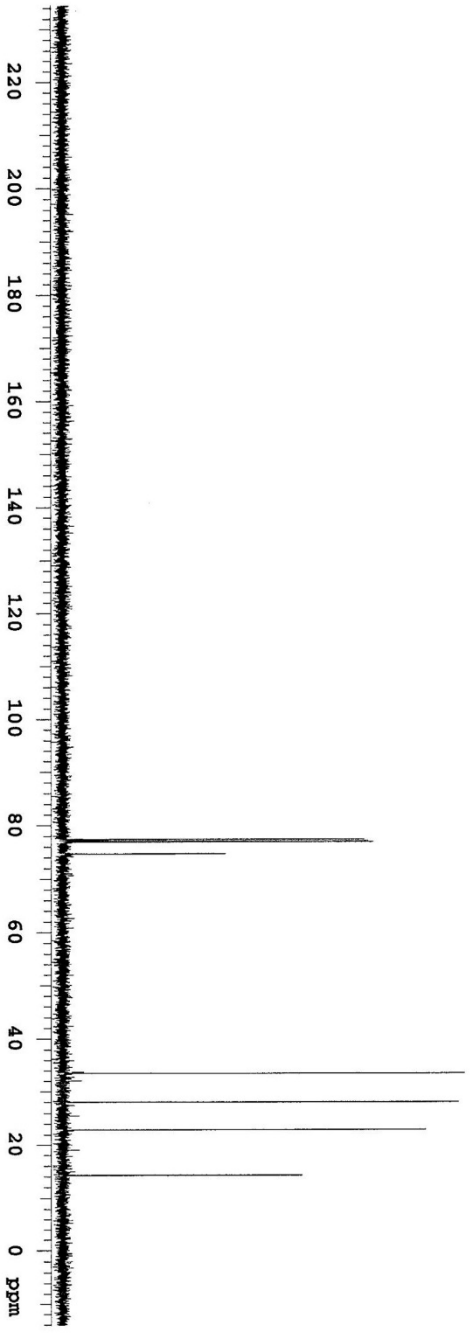

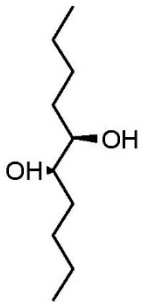

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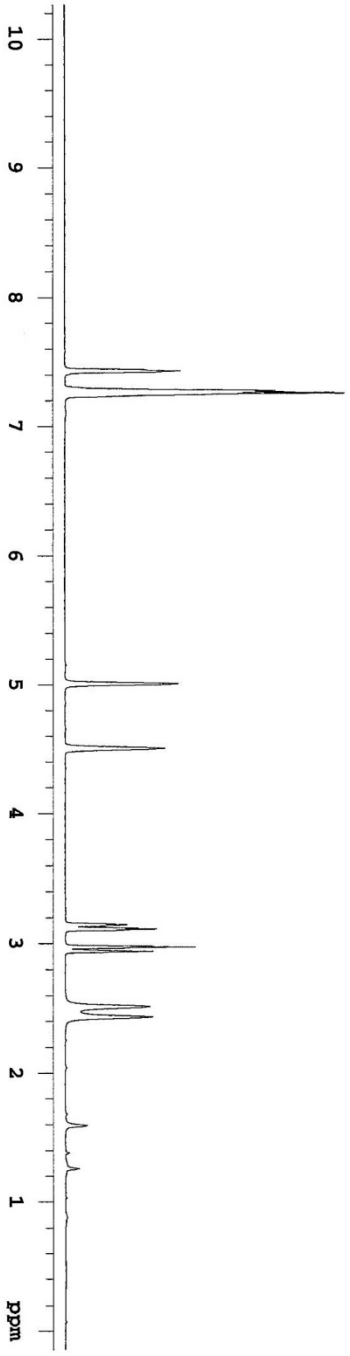

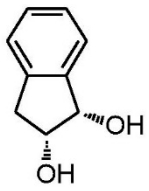

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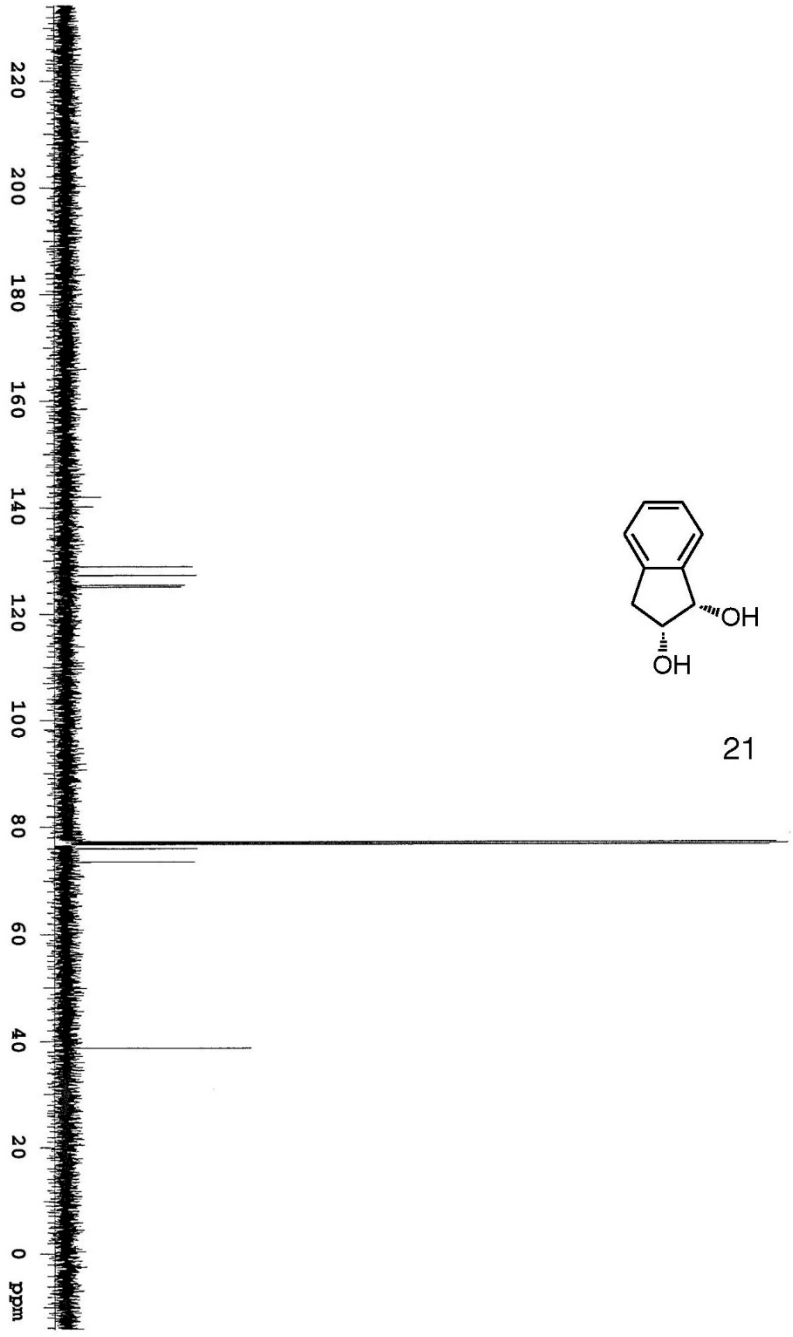

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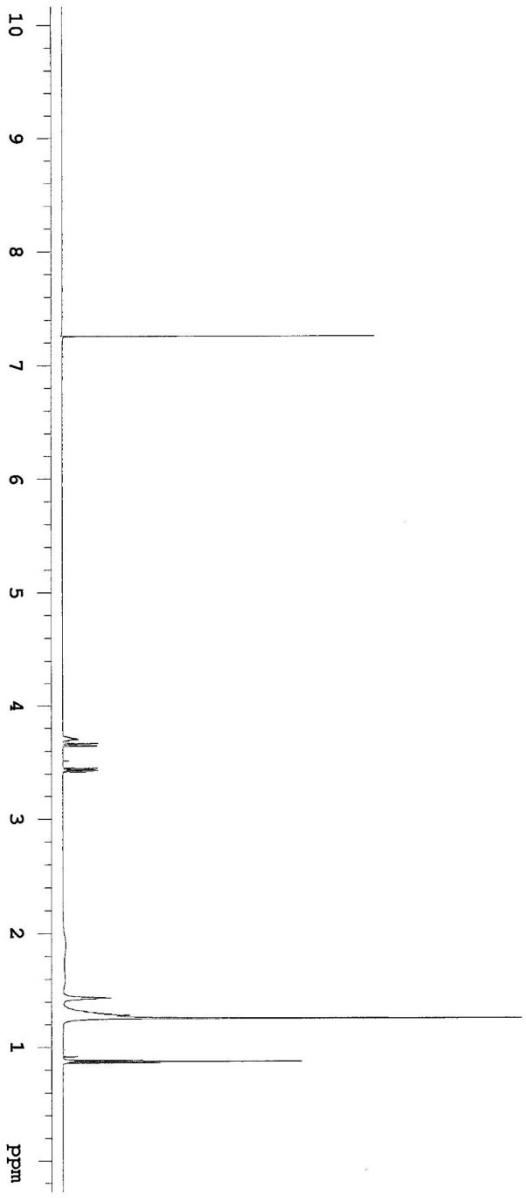

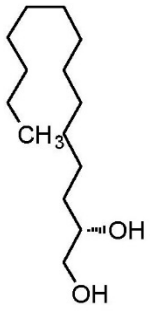

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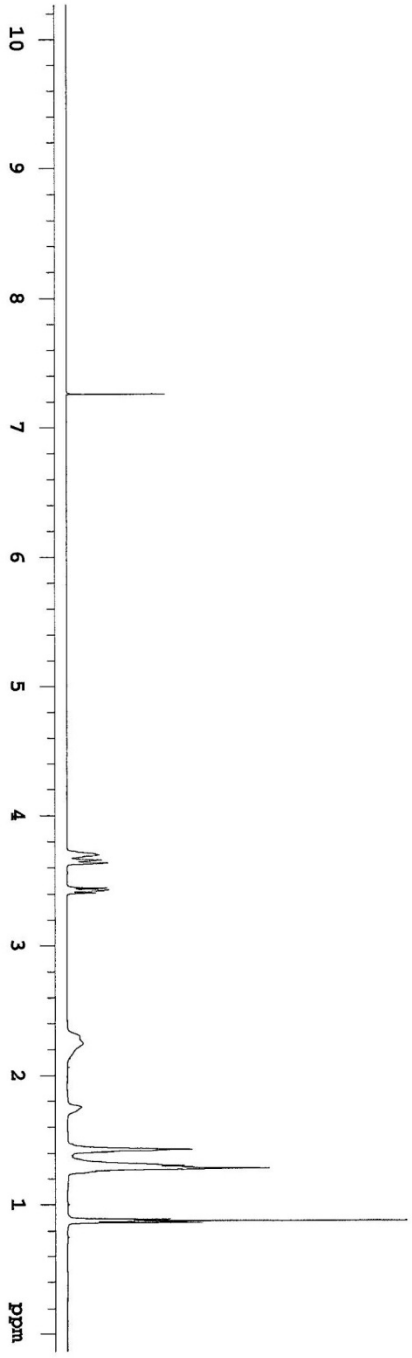

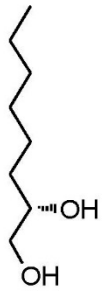

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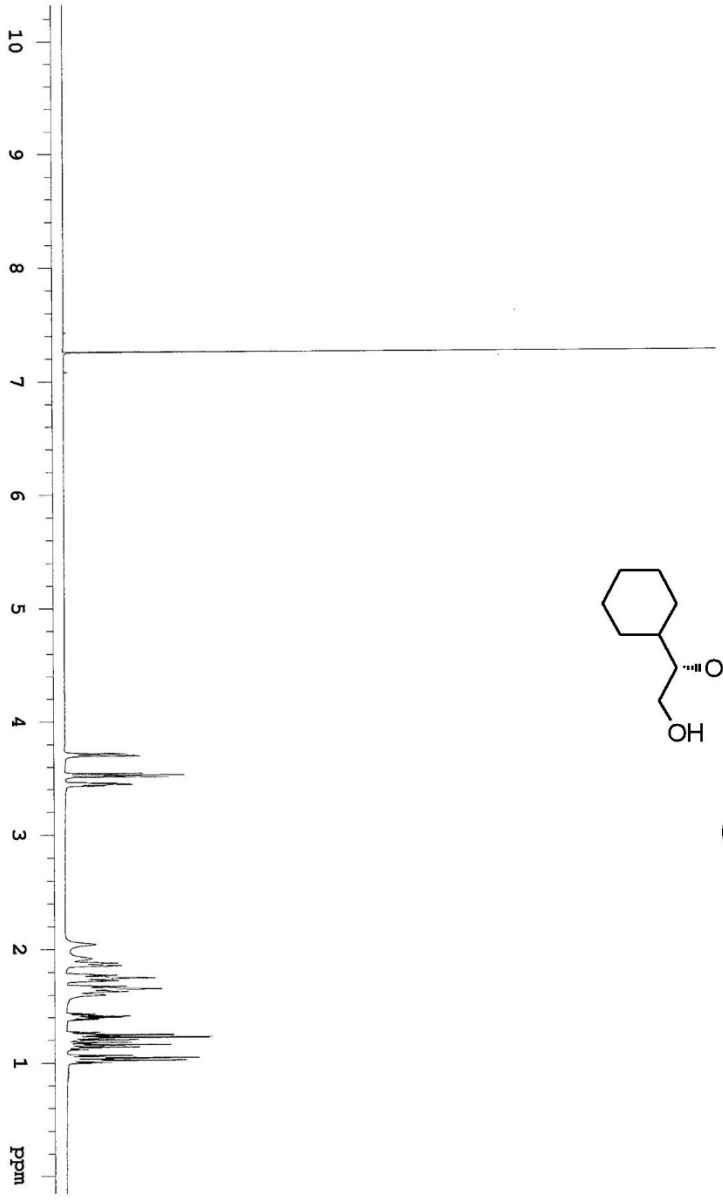

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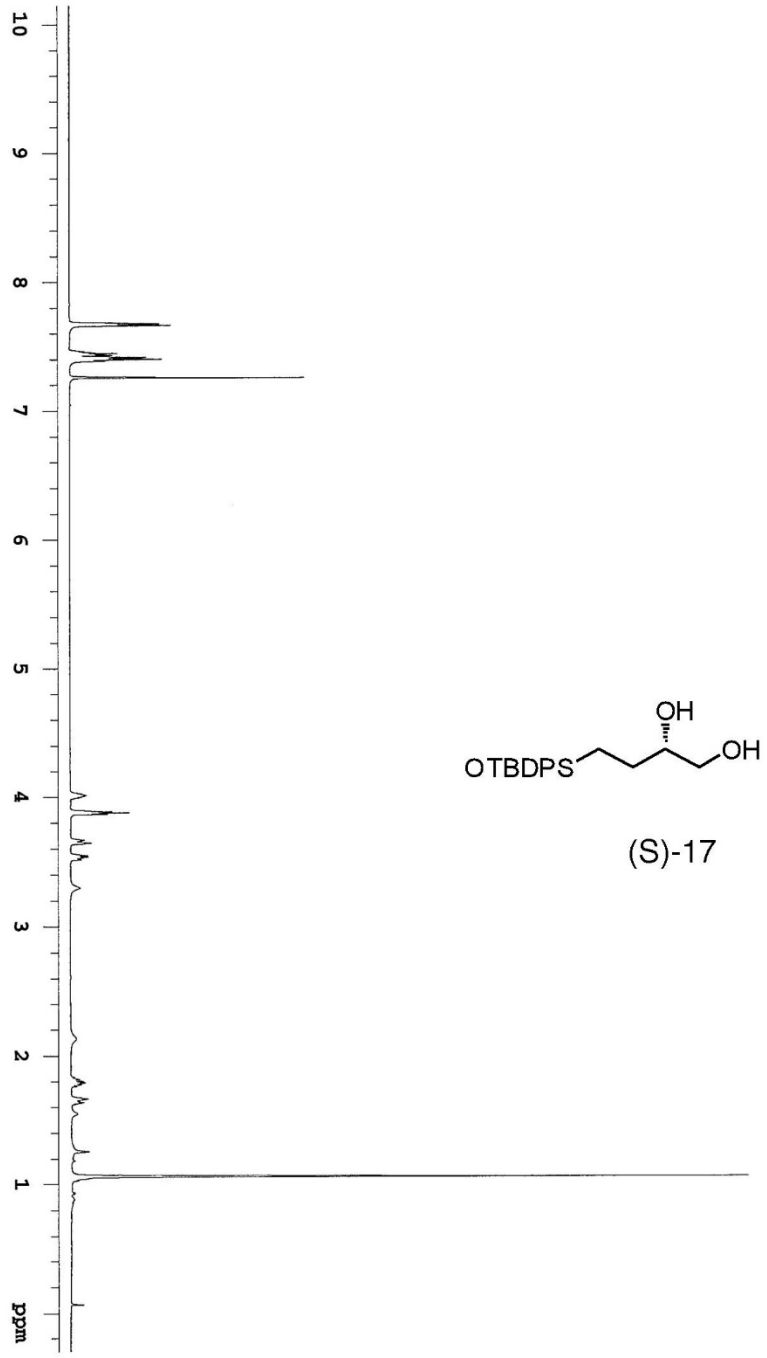

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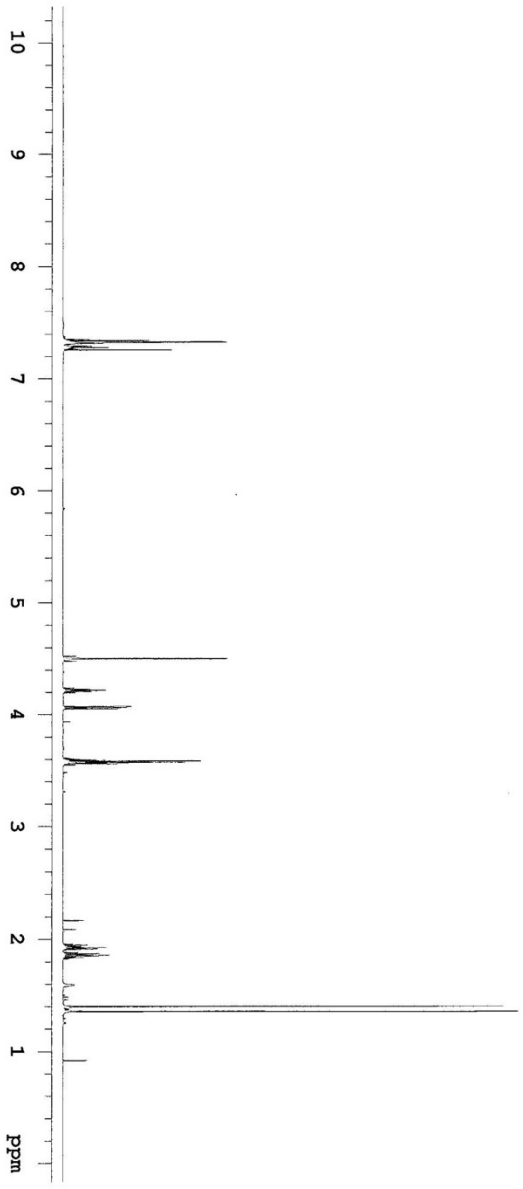
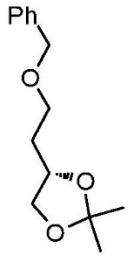
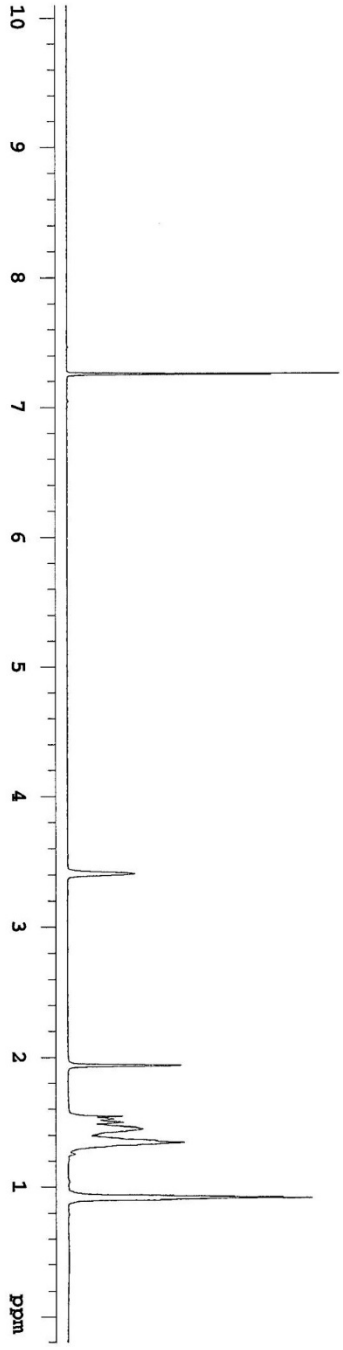
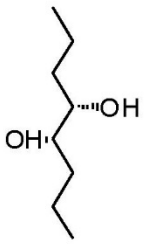


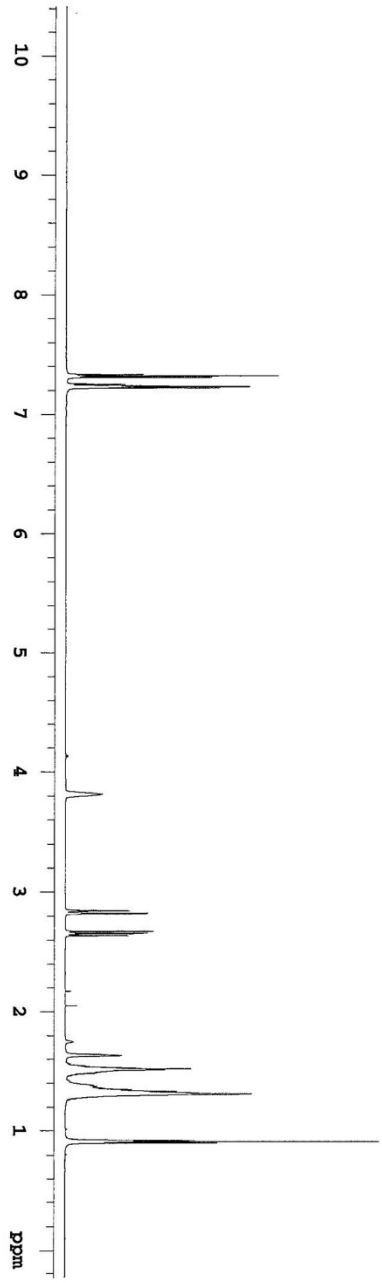


for (S)-18





(*S,S*)-20



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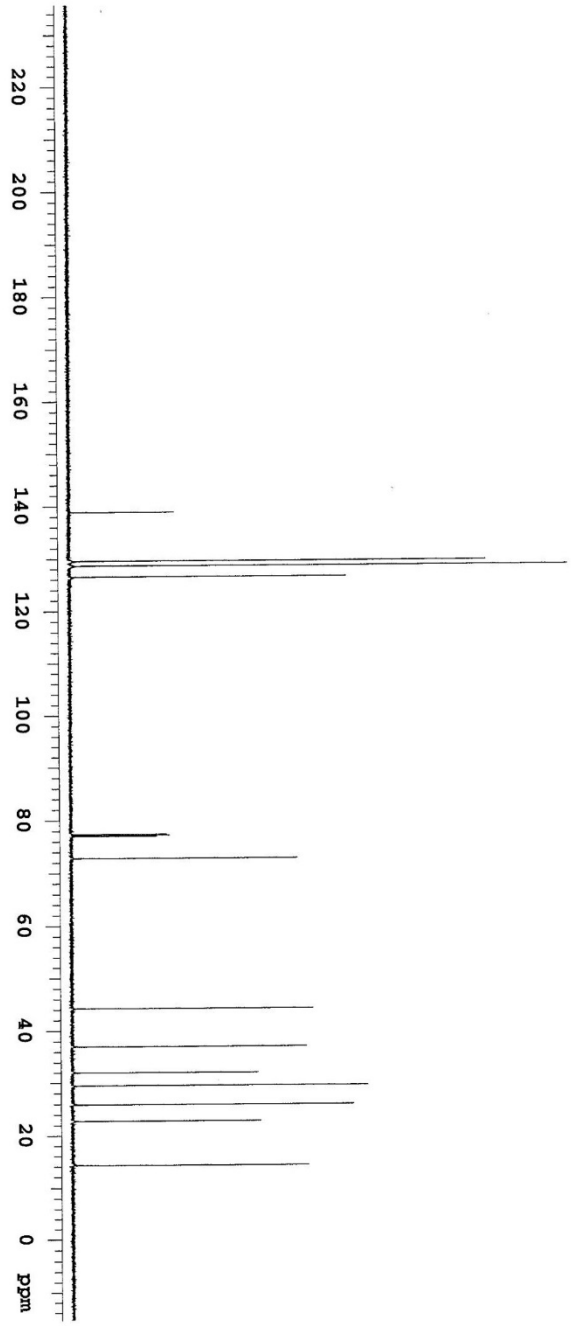

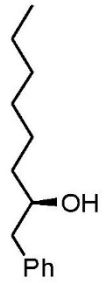

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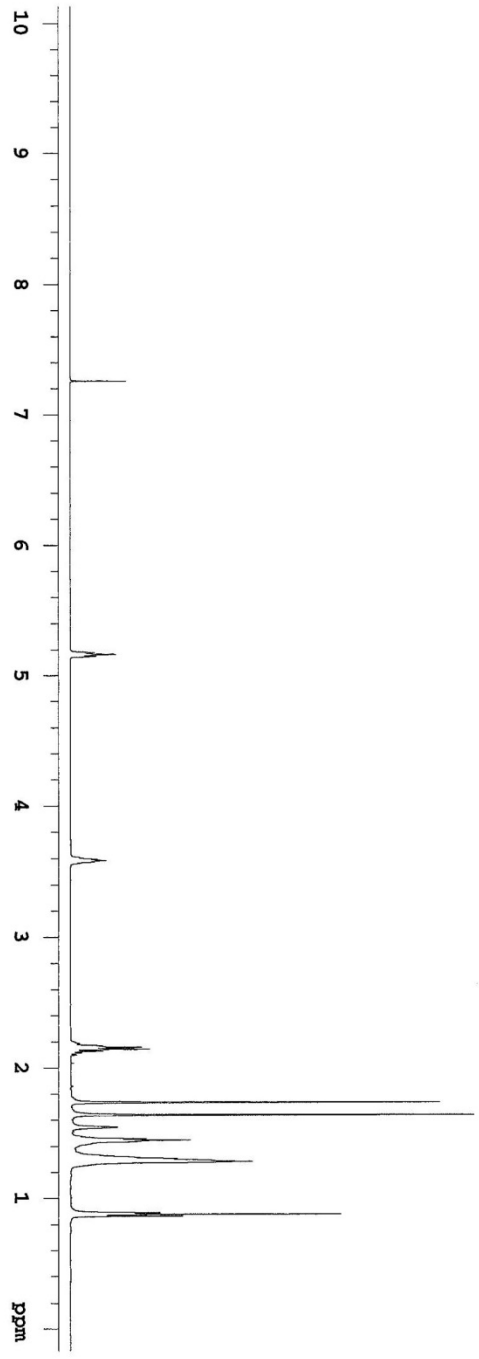

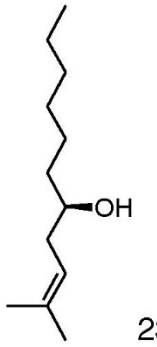

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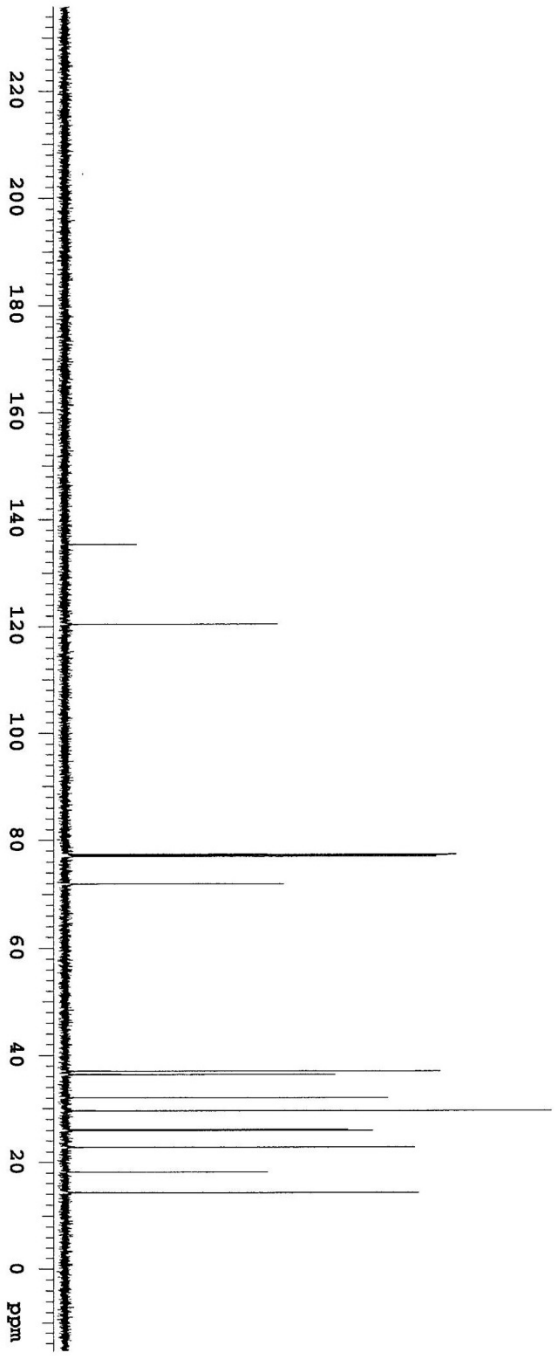

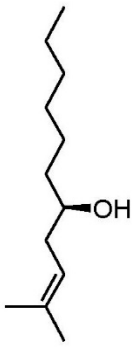

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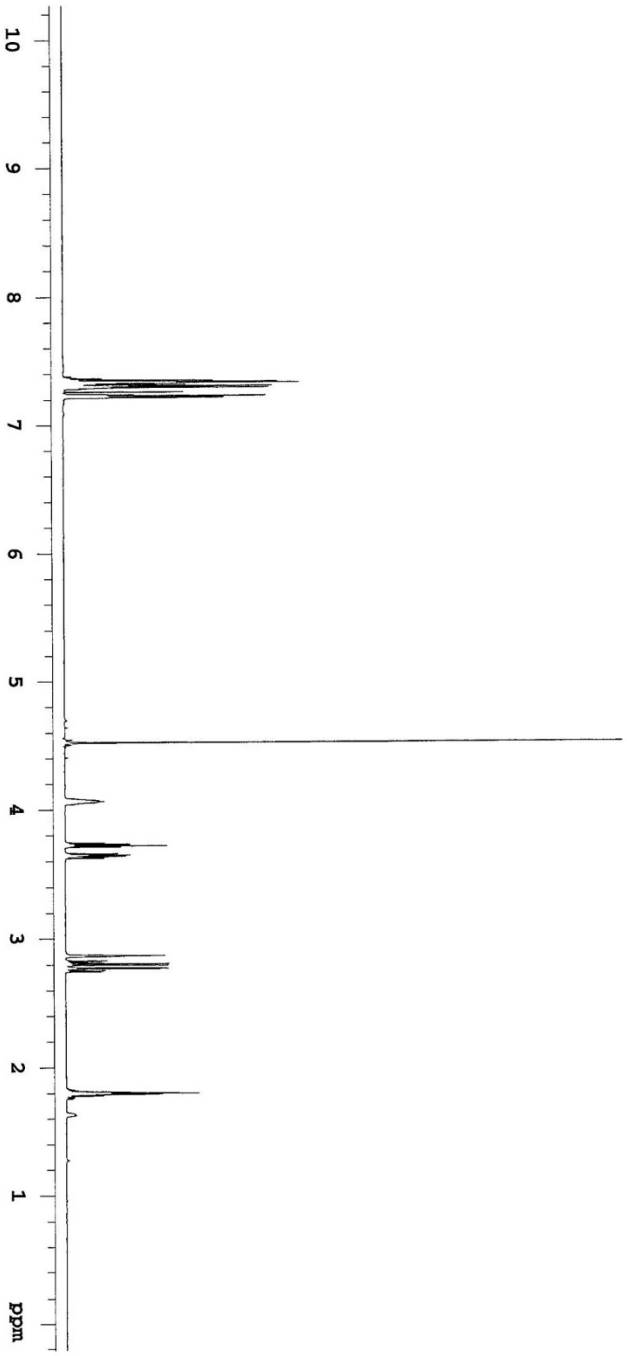

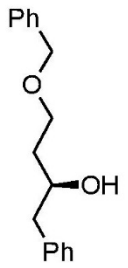

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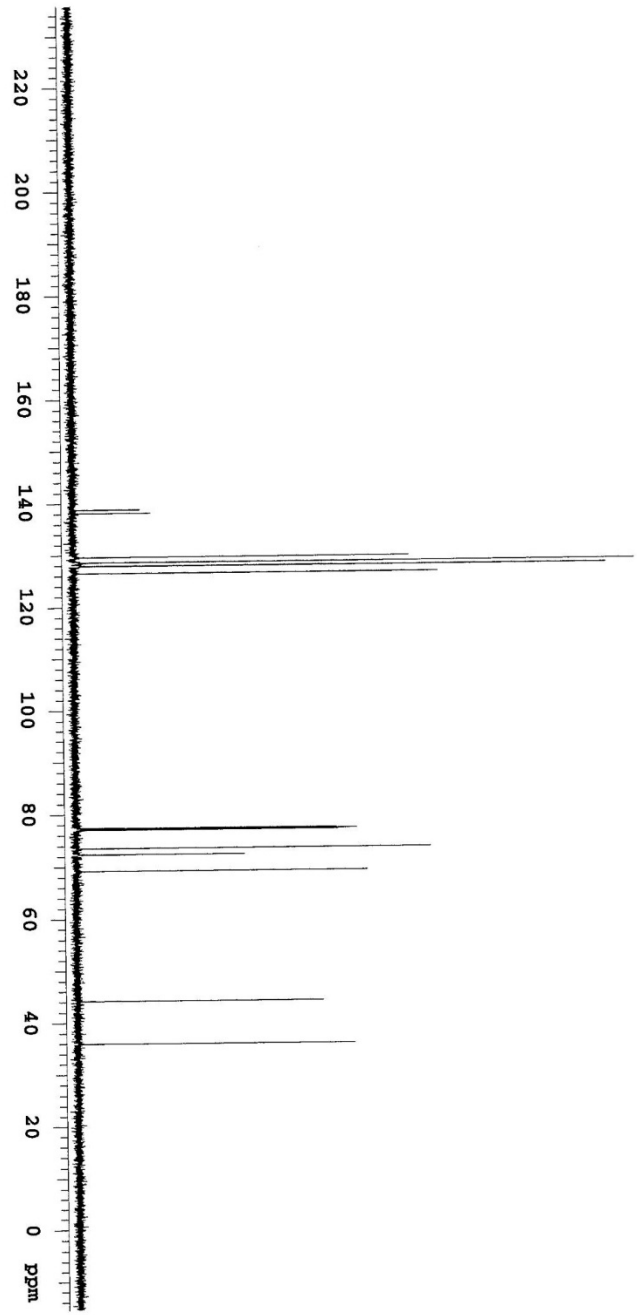

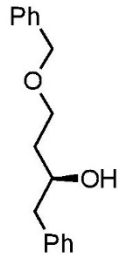

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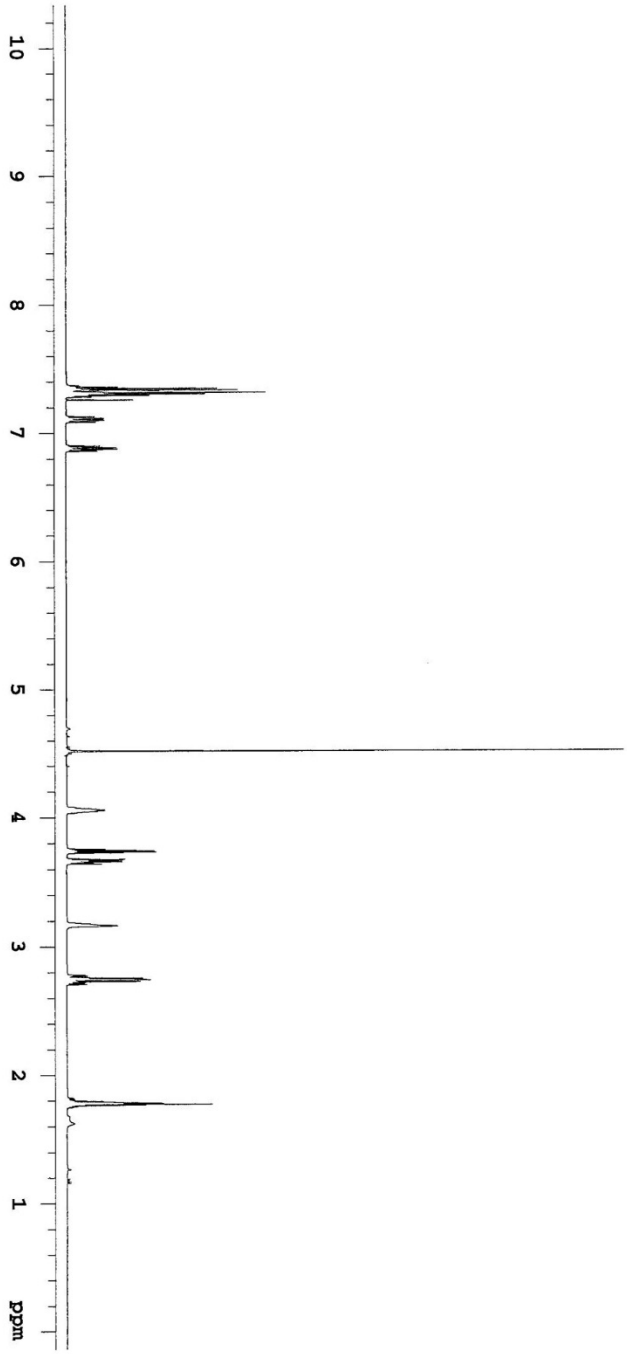

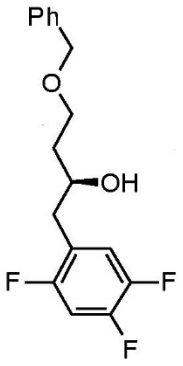

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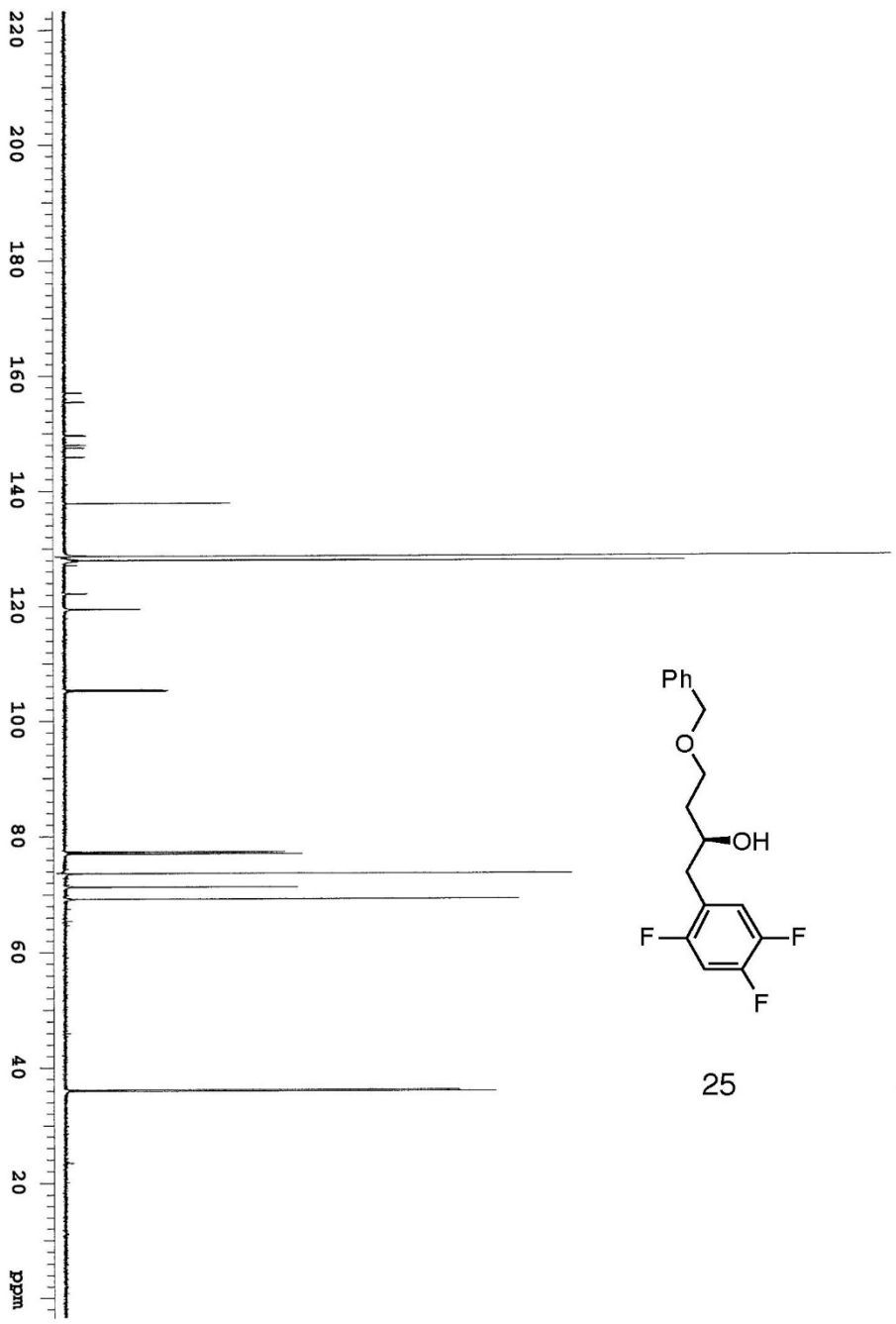

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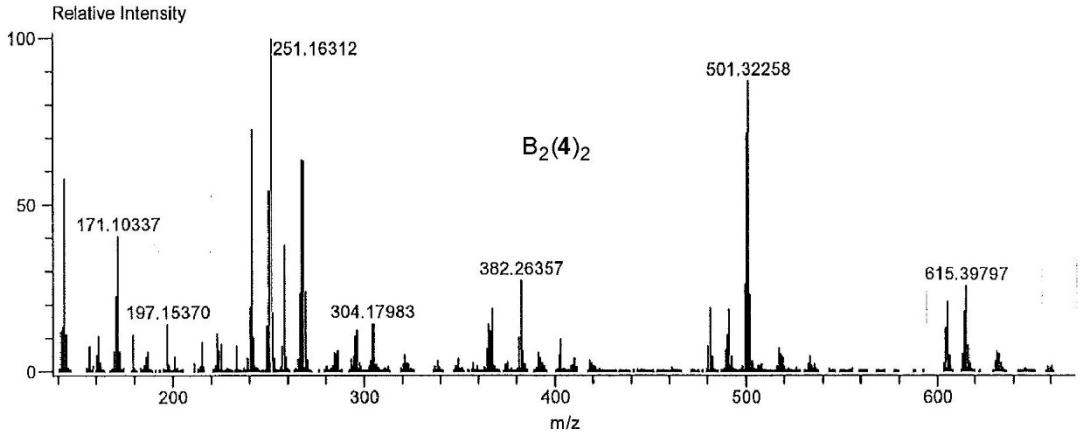
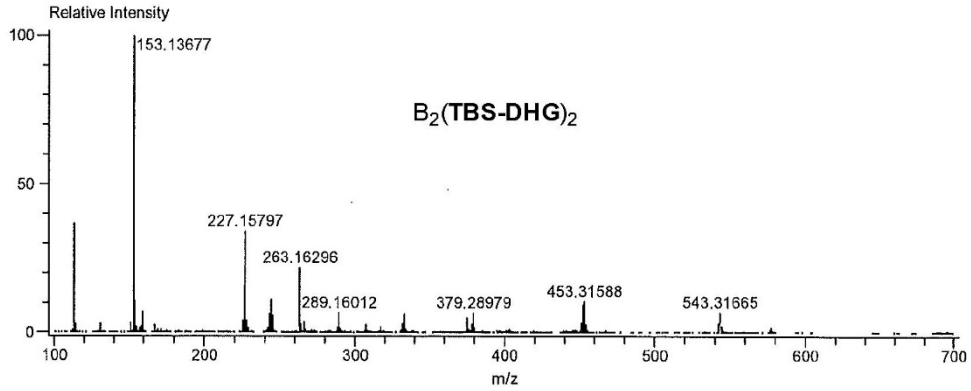


Mass	Calc. Mass	Mass Difference (mmu)	Mass Difference (ppm)	Possible Formula	Unsaturation Number
251.16312	251.16259	0.53	2.10	$^{12}C_{12}{}^{1}H_{21}{}^{11}B_2{}^{16}O_4$	3.5
	251.16072	2.40	9.56	$^{12}C_{17}{}^{1}H_{20}{}^{11}B_1{}^{16}O_1$	8.5



Mass	Calc. Mass	Mass Difference (mmu)	Mass Difference (ppm)	Possible Formula	Unsaturation Number
543.31665	543.31521	1.45	2.66	$^{12}C_{24}{}^{1}H_{49}{}^{11}B_2{}^{16}O_8{}^{28}Si_2$	3.5
	543.31333	3.32	6.11	$^{12}C_{29}{}^{1}H_{48}{}^{11}B_1{}^{16}O_5{}^{28}Si_2$	8.5

Chapter 2. Mechanistic Studies of the Carbohydrate-Catalyzed Enantioselective Alkene Diboration: Improved Reaction Efficiency and Subtrate Scope

2.1 Introduction

The platinum-catalyzed enantioselective alkene diboration reaction developed in the Morken group provided a powerful method for transforming feedstock chemicals into useful building blocks. However, the high cost of the platinum catalyst greatly limits the application of this methodology in both industrial and academic research. Other than the expense, it is also complicated to set up the the platinum-catalyzed diboration reaction, because a glovebox is needed to handle the air and moisture-sensitive TADDOL-derived phosphonite ligand. Additionally, the substrate scope of the platinum catalyzed diboration is limited to terminal alkenes: disubstituted alkenes are unreactive under the reaction conditions.

The Morken group has been working on developing new generations of asymmetric alkene diboration catalysts to make the process more user friendly. One such example is the carbohydrate catalyzed enantioselective alkene diboration. This new generation of diboration reaction successfully minimized the cost of the diboration process by using catalysts derived from inexpensive carbohydrates rather than precious metals. The carbohydrate-catalyzed reaction is not sensitive to air and moisture such that it can be set up on a large scale without the aid of a glovebox. However, there are new problems associated with this new diboration reaction. First, the catalyst efficiency is relatively low. A long reaction time (48 hours) was needed for most substrates to attain synthetically useful conversions, and the yields were moderate with an averagely 50% being observed. Secondly, although disubstituted alkenes can react in the carbohydrate catalysis,

moderate enantioselectivities were observed for those substrates. Consequently, finding ways to improve the reaction efficiency of the carbohydrate catalyzed alkene diboration is crucial for the synthetic applications of this reaction.

2.2 Overview of Mechanistic Studies

We envisioned that mechanistic studies could help guide reaction optimization, so detailed studies of the inner workings of this process were undertaken.

Firstly, according to the preliminary mechanistic studies for the carbohydrate catalyzed alkene diboration, the possible reactive intermediate for alkene diboration might be a 1,2-bonded bis(boronate) generated from boronic ester exchange between the diboron starting material $B_2(neo)_2$ and the diol catalyst. However, there was not sufficient experimental evidence supporting the unprecedented boronic ester exchange process with a *trans*-diol under the reaction conditions. Therefore, various NMR experiments were designed in order to study both the boronic ester exchange, and the structure of reactive intermediate. Details of those experiments will be discussed later in this chapter.

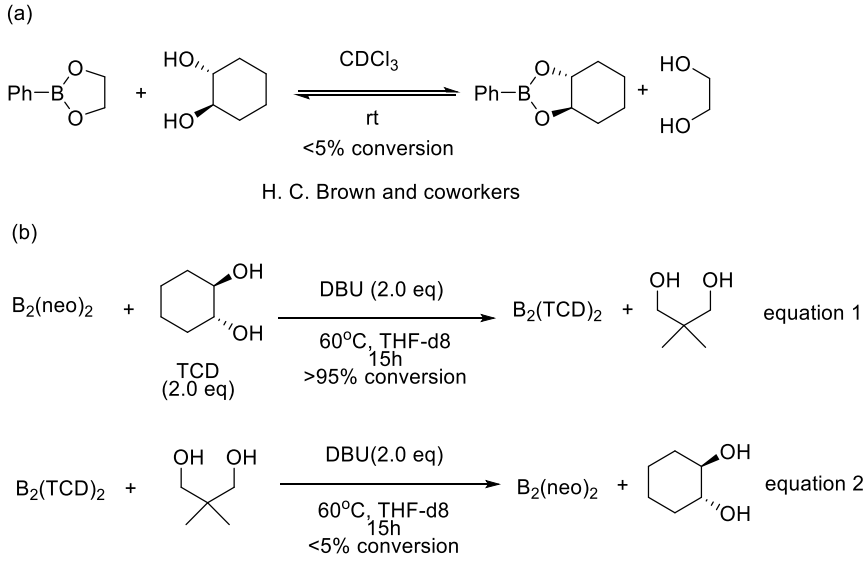
In addition, to improve the catalytic efficiency of the carbohydrate catalyzed alkene diboration, the turn-over limiting step of the catalysis needed to be identified, since accelerating the turn-over limiting step would lead to the enhanced overall reaction rate. As a result, reaction kinetics were conducted and proved to be helpful in the reaction optimization.

Finally, DFT calculations were conducted to explain the mechanism of boronic ester exchange and allowed us to propose a stereochemical model for the enantioselectivity of carbohydrate catalyzed asymmetric alkene diboration.

2.3 Characterization of the Reactive Intermediate

Transesterification between diols and boronic esters has been reported in the literature. As shown in Scheme 2.1a, in 2007, Professor H. C. Brown and coworkers reported the transesterification reaction between ethylene glycolato phenyl boronic ester and *trans*-1,2-cyclohexane diol.[41] According to their report, this exchange occurs in less than 5% conversion at room temperature presumably because of the strain engendered in the trans-fused 5,6-bicyclic ring framework of the product. However, we found out that the transesterification reaction between $B_2(neo)_2$ and 1,2-*trans*-cyclohexane diol proceeds to full conversion at 60 ^oC under basic reaction condition (Scheme 2.1b, equation 1). Importantly, when the chiral diboron $B_2(TCD)_2$ was treated with neopentyl glycol and DBU, the transesterification product $B_2(neo)_2$ was not observed (Scheme 2.1b, equation 2). These results suggested that the chiral diboron $B_2(TCD)_2$ is the thermodynamically more favored compound.

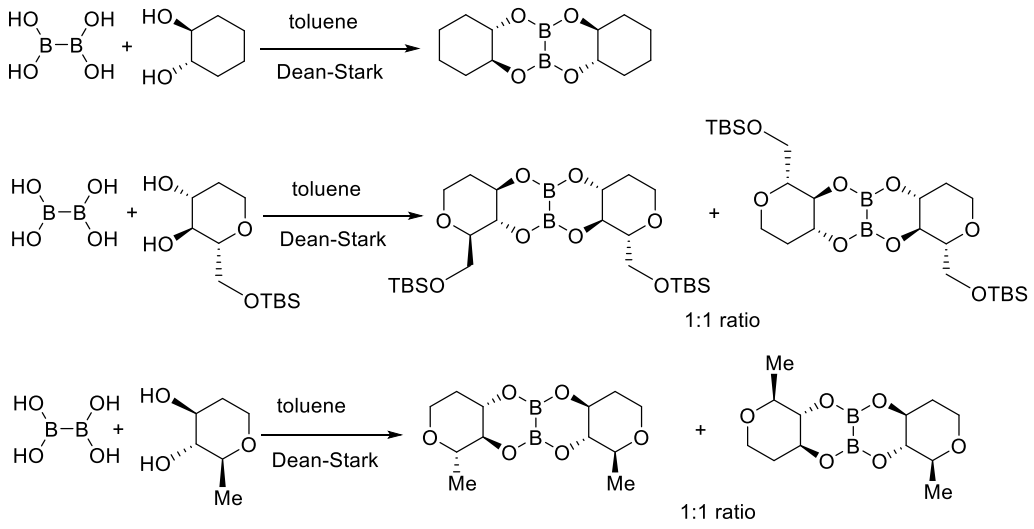
Scheme 2.1 Study of transesterification between boronic esters



[41] Roy, C. D.; Brown, H. C. *J. Organomet. Chem.* **2007**, *692*, 784.

To further elucidate the structure of chiral diboron $B_2(TCD)_2$, we prepared the chiral diboron compounds $B_2(TCD)_2$, $B_2(TBS\text{-}DHG)_2$ and $B_2(DHR)_2$ through a different route. As depicted in Scheme 2.2, TCD, TBS-DHG and DHR were each treated with $B_2(OH)_4$ under dehydrating reaction conditions (refluxing toluene, Dean-Stark trap), which furnished the corresponding chiral diborons. Upon characterizing these chiral diborons, it was found that the spectral features of these compounds are consistent with 1,2-bonded diboron complexes. Due to the C_2 symmetry axis in *trans*-1,2-cyclohexanediol, the ^{13}C NMR spectrum of $B_2(TCD)_2$ (^{13}C δ: 81.8, 32.9, 24.3 ppm) is consistent with both 1,1-bonded and 1,2-bonded diboron complexes. However, due to the lack of the symmetry element in TBS-DHG and DHR, 1,2-bonded chiral diboron $B_2(TBS\text{-}DHG)_2$ and $B_2(DHR)_2$ should be mixtures of two regioisomers. In contrast, the 1,1-bonded $B_2(TBS\text{-}DHG)_2$ and $B_2(DHR)_2$ would exist as single compounds. The fact that we observed two sets of ^{13}C resonances for both $B_2(TBS\text{-}DHG)_2$ and $B_2(DHR)_2$ suggested that these compounds were bonded in 1,2-bonding mode.

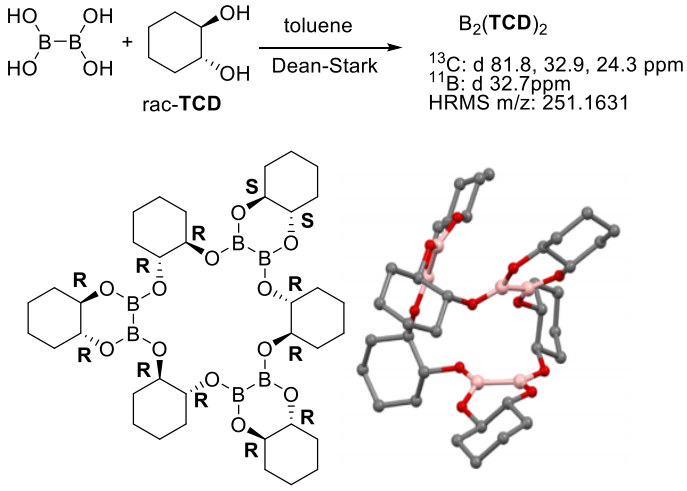
Scheme 2.2 Chacterization of Chiral Diboron Compounds



Although, significant effort was invested in preparing X-ray quality crystals of 1,2-bonded diboron complexes derived from TBS-DHG, DHR and nonracemic TCD, diffraction-quality crystals were not obtained. In contrast, we did obtain X-ray quality crystals from the dehydration product of $B_2(OH)_4$ and racemic *trans*-1,2-cyclohexandiol. As shown in Scheme 2.3, the solution stated dehydration product has ^{13}C NMR and HRMS spectra consistent with a dimer. However, the crystal structure shows a solid state compound that is more complex and includes two enantiomeric molecules of $B_2(TCD)_5$(*ent*-TCD) per unit cell. Each molecule in the unit cell has three diboron subunits tethered by *trans*-1,2-cyclohexanediol. In each diboron subunit, there are six 1,2-bonded *trans*-cyclohexanediol molecules, and of the six diol ligands in the molecule structure, five are (*R, R*) isomers, while the other one is the (*S, S*) isomer. Although this species is clearly unavailable when using a enantiopure ligand, the bonding motif present in the trimeric structure gave evidence to the existence 1,2-bonded chiral diboron. Furthermore, the crystal structure revealed that even in the 1,2-bonding mode, the B-B bond distances (1.706, 1.721 and 1.724 Å) are not substantially distorted relative to other diboron compounds (1.720 Å for $B_2(OMe)_4$[42]; 1.711 Å for B_2pin_2[43]).

[42] Brain, P. T.; Downs, A. J.; MacCallum, P.; Rankin, D. W. H.; Robertson, H. E.; Forsyth, G. A. *J. Chem. Soc., Dalton Trans.* **1991**, 1195.
[43] Noth, H. Z. *Naturforsch, Teil. B.* **1984**, *39*, 1463.

Scheme 2.3 X-ray Structure of $B_6(TCD)_5$(ent-TCD)

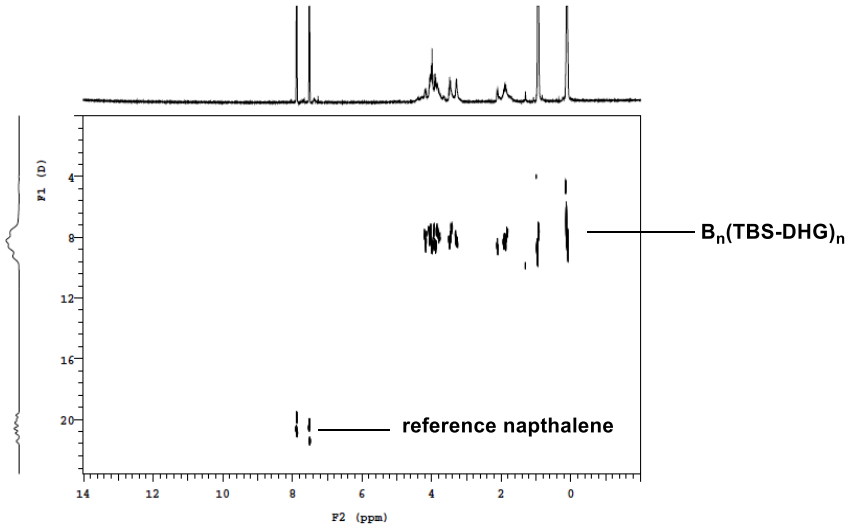


The presence of oligomeric species in *rac*-TCD-derived diboron structures suggests higher-order aggregation states of chiral reactive species might be both accessible and relevant to the carbohydrate catalyzed alkene diboration. As a consequence, we decided to use diffusion ordered two dimensional nuclear magnetic resonance spectroscopy (DOSY NMR) analysis to study the aggregation states of B_2(TBS-DHG)$_2$ in solution. DOSY NMR was first introduced by Professor Charles S. Johnson in 1992.[44] The analytical method was developed to identify molecular components of mixtures and characterize the sizes of aggregates. Later on, in 1995, Barjat and Morris were able to improve the resolution of the DOSY NMR technique.[45] Since then, many researchers have used the method to study complex mixtures of polymers, vesicles, and organometallic complexes.[46] In theses experiments, the diffusion constant of a given species is correlated with the molecular weight of the complexes in solution. Figure 1 shows the DOSY NMR spectrum of B_2(TBS-DHG)$_2$. $CDCl_3$ was employed as solvent,

[44] Morris, K. F.; Johnson, C. S. *J. Am. Chem. Soc.* **1992**, *114*, 3139.
[45] Barjat, H.; Morris, G. A.; Swanson, A. G.; Williams, S. C. R. *J. Magn. Reson. Spectrosc.* **1994**, *34*, 203.
[46] (a) Cohen, Y.; Avram, L. Frish. L. *Angew. Chem. Int. Ed.* **2005**, *44*, 520. (b) Johnson, C. Jr. *Prog. Nucl. Magn. Reson. Spectrosc.* **1999**, *34*, 203.

and naphthalene was used as the internal standard for molecular weight calculation. As shown in this 2D NMR, only one species exists in the solution of $B_2(TBS\text{-}DHG)_2$, and it exhibits an average diffusion constant of 8.805. To derive the molecular weight of the species observed, we used the external calibration curve method developed by Stalke and coworkers.[47] According to this correlation curve, the calculated molecular weight for the $B_n(TBS\text{-}DHG)_n$ in $CDCl_3$ from DOSY NMR is 536.4 g/mol. Considering that the theoretical molecular weight for dimeric $B_2(TBS\text{-}DHG)_2$ is 543.3 g/mol, this study suggested that the dimeric $B_2(TBS\text{-}DHG)_2$ predominates over higher order aggregates in solution state.

Figure 1. DOSY NMR analysis of $B_2(TBS\text{-}DHG)_2$



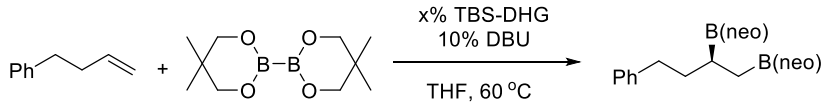
[47] (a) Neufeld, R.; Stalke, D. *Chem. Sci.* **2015**, *6*, 3354. (b) Bachmann, S.; Neufeld, R.; Dzemski, M.; Stalke, D. *Chem. Eur. J.* **2016**, *22*, 8462. (c) Neufeld, R.; Teuteberg, T. L.; Herbst-Irmer, R.; Mata, R. A.; Stalke, D. *J. Am. Chem. Soc.* **2016**, *138*, 4796. (d) Neufeld, R.; John, M.; Stalke, D. *Angew. Chem. Int. Ed.* **2015**, *54*, 6994.

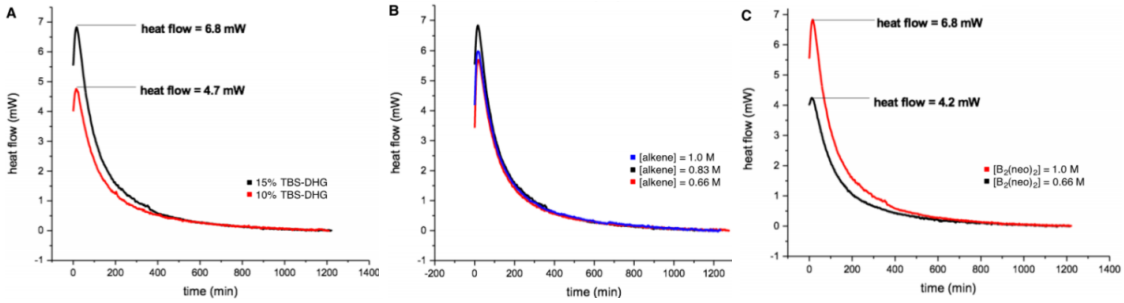
2.4 Reaction Kinetics

After identifying that the structure of the reactive intermediate B_2(TBS-DHG)$_2$ is a 1,2-bonded chiral diboron, we were interested in studying the kinetics of the carbohydrate catalyzed alkene diboration in order to identify the turn-over limiting step of the catalysis, and hopefully find an approach to improve the reaction efficiency.

Calorimetry was chosen as the approach for kinetic studies because it is convenient to use and it collects data continuously throughout the entire cause of the reaction. As shown in Scheme 2.4A, the diboration of 4-phenyl-1-butene (0.83 M) with B_2(neo)$_2$ (1.0 M) in the presence of either 10% or 15% TBS-DHG catalyst was monitored by calorimeter. Because these two reactions did not achieve full conversion, it is difficult to process the whole data file generated throughout the entire reaction. As a result, only initial rates of these two reactions were compared. As indicated in graph A, a 45% increase in the initial rate was observed when TBS-DHG catalyst loading increases from 10 mol% to 15 mol%, suggesting that the carbohydrate catalyzed alkene diboration is first order in catalyst concentration. Shown in scheme 2.4B, different alkene concentrations (0.66 M, 0.83 M, 1.0 M) were examined in the kinetic study, and no significant reaction rate changes were observed, suggesting that the reaction rate has a zero order dependence on alkene concentration. Depicted in Scheme 2.4C, different B_2(neo)$_2$ concentrations (1.0 M and 0.66 M) were studied. The initial rates increased about 60% when diboron concentration increased from 0.66 M to 1.0 M, suggesting that the rate of the diboration reaction is close to first order in diboron concentration.

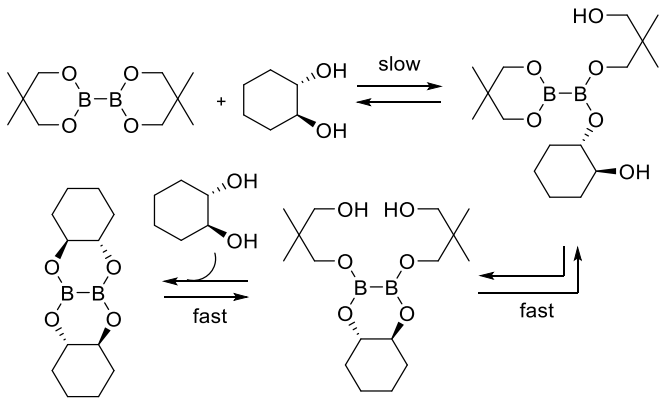
Scheme 2.4 Reaction Kinetics Study-1





The zero order dependence of reaction rate on alkene concentration suggested that steps involving boronic ester exchange, and not the diboration step itself is rate limiting. With the reaction rate being first order in catalyst concentration and first order in diboron concentration, it was suspected that the first association of TCD with $B_2(neo)_2$ is slow step in the exchange (Scheme 2.5). This hypothesis is reasonable since initially displacing a bidentate primary alcohol (neopentyl glycol) from $B_2(neo)_2$ with secondary alcohol TCD is likely to be slower compared to subsequent intramolecular transesterification and displacement of monodentate neopentyl glycol with TCD.

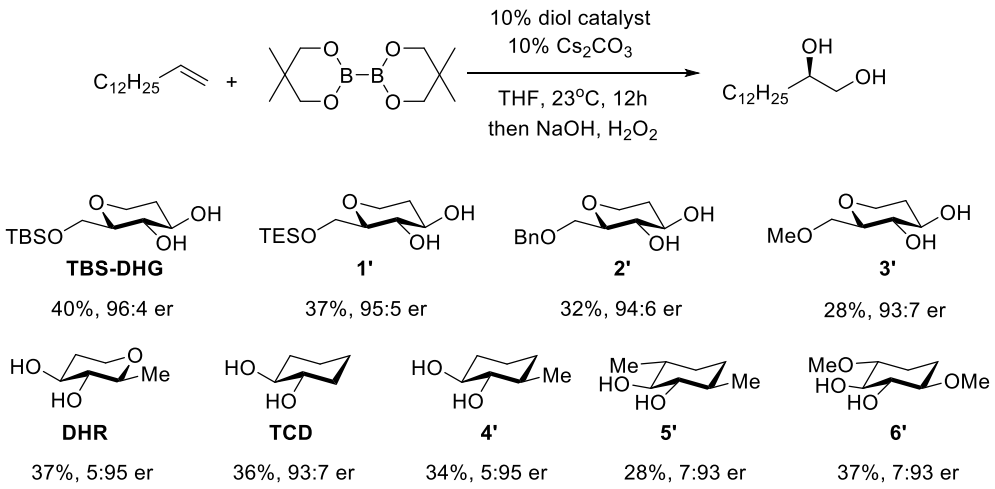
Scheme 2.5 Proposed Mechanism for Diboron-Catalyst Transesterification



According to the reaction kinetic study, in order to improve the reaction efficiency of the carbohydrate catalyzed alkene diboration reaction, the turn-over limiting step of the catalysis, the transesterification between $B_2(neo)_2$ and the diol catalyst needs to be accelerated. Two ways were proposed to improve the rate of transesterification: First, designing a new catalyst that is more reactive in the exchange with $B_2(neo)_2$, and second, developing a new diboron reagent that can exchange with TBS-DHG, DHR and TCD faster.

As shown in Scheme 2.6, a small library of 1,2-*trans*-cyclohexanediol derivatives were synthesized and tested in the carbohydrate catalyzed alkene diboration. Catalysts **1'**, **2'** and **3'** have different protecting groups on the primary alcohol side chain compared to TBS-DHG catalyst. Catalyst **4'** has an all carbon backbone instead of a carbohydrate backbone. Catalysts **5'** and **6'** have different substituents on the 1,2-*trans*-cyclohexanediol backbone. Unfortunately, none of these catalysts gave better results than the current catalysts TBS-DHG, DHR and TCD. All of the catalysts afforded the product in similar yields and enantioselectivities. In summary, new catalyst design was not an effective way for the reaction optimization.

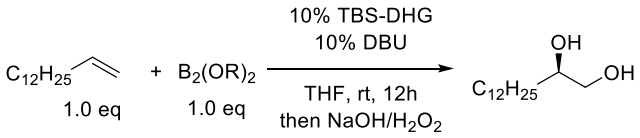
Scheme 2.6 Catalysts Investigation for Carbohydrate Catalyzed Alkene Diboration

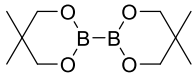
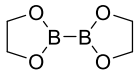
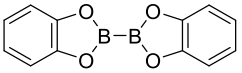
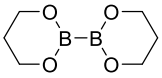
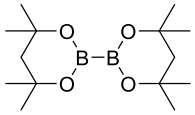
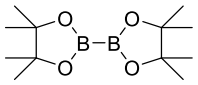


Next, we decided to study different diboron reagents in the carbohydrate catalyzed alkene diboration in order to find a diboron starting material that is more prone to exchange with the catalyst. As shown in Scheme 2.7, diboration reaction with $B_2(neo)_2$ only achieved moderate conversion (40%) at room temperature over 12 hours (entry 1). When $B_2(neo)_2$ was replaced with $B_2(eg)_2$, a compound that should undergo faster transesterification because of decreased steric encumbrance and increased ring strain, a significant improvement in the reaction efficiency was observed, however, a measurable diminished enantioselectivity was also observed (entry 2). Similar to $B_2(eg)_2$, the catechol group in $B_2(cat)_2$ is also more labile. Electronically, catechol is a better leaving group compared to other alkyl diols because of its oxy-anion stabilization. However, presumably because of the facile background reaction, $B_2(cat)_2$ afforded racemic product (entry 3). In entry 4, the reagent $B_2(pro)_2$ provided the optimal combination of both enhanced efficiency while maintaining high enantioselectivity. As expected, more hindered diboron reagents such as $B_2(dmp)_2$ and $B_2(pin)_2$ reacted with the alkene

substrate in severely diminished efficiency, possibly because of sterically-inhibited transesterification (entry 5 and entry 6).

Scheme 2.7 Diboron Reagents Investigation of Carbohydrate Catalyzed Diboration

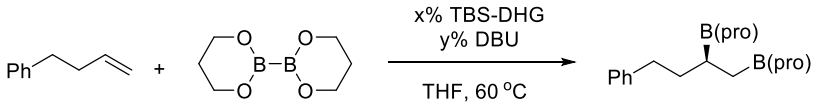


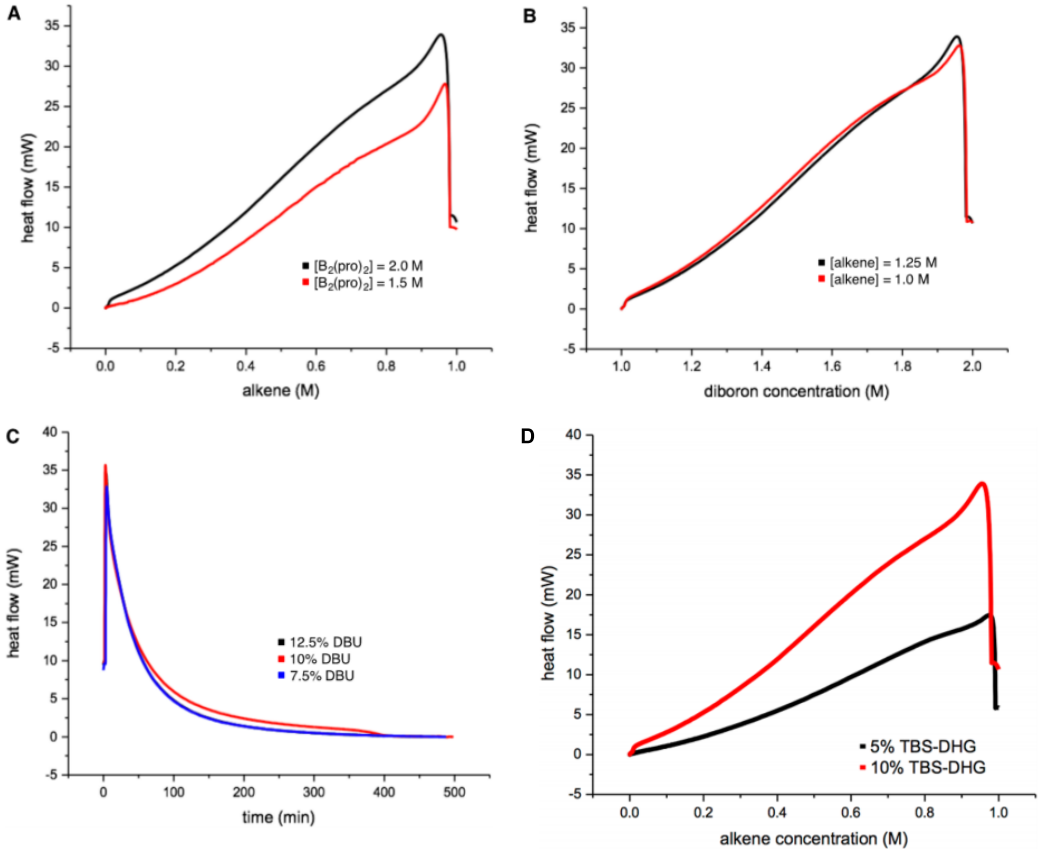
entry	diboron	abbrev	yield (%)	er
1		$B_2(neo)_2$	40	96:4
2		$B_2(eg)_2$	75	91:9
3		$B_2(eg)_2$	98	51:49
4		$B_2(pro)_2$	56	95:5
5		$B_2(dmp)_2$	15	81:19
6		B_2pin_2	10	69:31

We finally decided to use $B_2(pro)_2$ (entry 4) for further study, not only because $B_2(pro)_2$ exhibted enhanced reactivity, but also since it is more soluble in THF than most of the diboron compounds studied, more diboron reagent can be added to the reaction to realize further reaction rate acceleration. As a next step, $B_2(pro)_2$ was subjected to kinetic analysis. As depicted in Scheme 2.8, the following reaction conditions: [4-phenyl-1-butene] = 1.0 M, [B_2pro_2] = 2.0 M, 10 mol% DBU, and 10 mol% TBS-DHG were chosen as the reference set of reaction conditions. When heat flow versus time data was integrated, it becomes obvious that the carbohydrate catalyzed alkene diboration reaction

behaves like an overall first-order reaction over the entire course of the reaction. The two plots in Scheme 2.7A showed the effect of diboron concentration on reaction rate. As a 1.33-fold increase in diboron concentration leads to a 1.30-fold increase in reaction rate, it is clear that the rate of diboration reaction is first order in $B_2(pro)_2$ concentration. Plots in Scheme 2.7B and 2.7C showed that changing alkene concentration and DBU concentration do not have significant effect on diboration reaction rate. The dependence of reaction rate upon catalyst concentration was also analyzed (Scheme 2.7D). As the reaction rate with 5 mol% catalyst loading is approximately half of the reference reaction (10 mol% catalyst loading), the reaction appears to be first-order in catalyst concentration. The overall rate law of carbohydrate catalyzed alkene diboraiton is $\text{rate}=[\text{diboron}]^1\times[\text{catalyst}]^1$.

Scheme 2.7 Reaction Kinetics Study-2



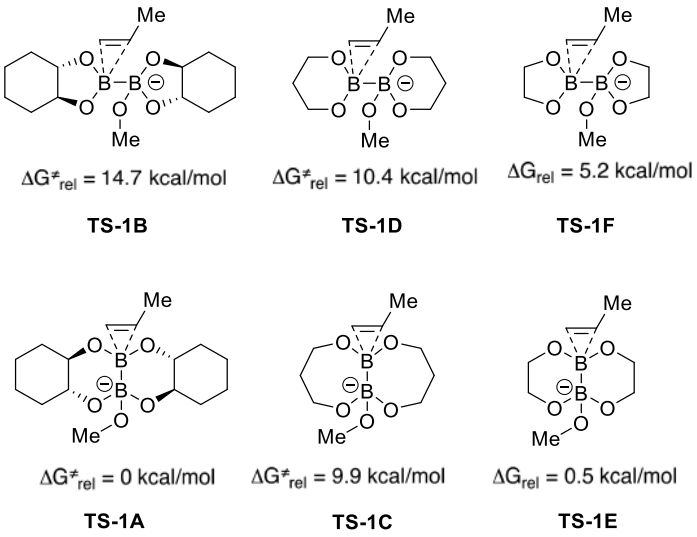


2.5 DFT Calculations for Studying the Reaction Pathway.

After identifying that the reactive intermediate of the carbohydrate-catalyzed diboration is the 1,2-bonded chiral diboron, and that the turn-over limiting step of the catalysis is the boronic ester exchange, we became interested in the mechanistic origin for rate acceleration with TBS-DHG, DHR and TCD in the diboration reaction. Previous DFT calculations suggest that the activation energy of $B_2(TCD)_2$ reacting with alkene is much lower than the activation of $B_2(neo)_2$ reacting with alkene. To study the transition state energies of 1,1-bonded and 1,2-bonded diboron in detail, more DFT calculations

were performed with Gaussian 09 and optimized with the M06-2X density functional with 6-31+G* as the basis set. The PCM solvation model was used (THF). Of note, these calculations were performed in collaboration with Dr. Fredrik Haeffner. As depicted in Scheme 2.9, the transition state energies were calculated for 1,1-bonded and 1,2-bonded diboron derived from TCD, 1,3-propanediol and ethylene glycol. The energy of transition state **TS-1A** (derived from 1,2-bonded TCD diboron) was set as 0 kcal/mol, serving as a reference for all the transition state energies. The relative transition state energy of 1,2-bonded TCD (**TS-1A**) is far lower than the relative transition state energy of 1,1-bonded TCD (**TS-1B**, $\Delta G^{\neq}_{rel}$ = 14.7 kcal/mol). **TS-1A** is also lower in energy than the transition state derived from both 1,1-bonded and 1,2-bonded $B_2(pro)_2$ (**TS-1C**, $\Delta G^{\neq}_{rel}$ = 9.9 kcal/mol and **TS-1D**, $\Delta G^{\neq}_{rel}$ = 10.4 kcal/mol), indicating that the background reaction is not competitive in the carbohydrate-catalyzed diboration reaction. Of note, the energy difference between **TS-1A** and transition states of 1,1-bonded and 1,2-bonded $B_2(eg)_2$ (**TS-1E**, $\Delta G^{\neq}_{rel}$ = 0.5 kcal/mol and **TS-1F**, $\Delta G^{\neq}_{rel}$ = 5.2 kcal/mol) are smaller. And this is in line with the experimental result that when $B_2(eg)_2$ was used as the stoichiometric diboron reagent, products were generated in lower enantioselectivities because of the competing backgrounds reaction.

Scheme 2.9 DFT caculations of transition states for 1,1 and 1,2-bonded diborons

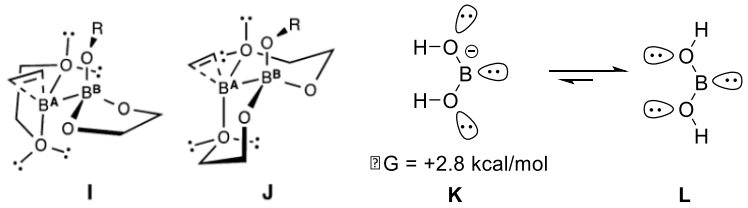


The six-membered ring in TCD imposes significant ring strain that severely penalizes the 1,1-bonding mode in transition state (**TS-1B**), thereby the 1,2-bonded transition state **TS-1A** is much more favored. However, when this ring strain element is removed such as in case of the $B_2(eg)_2$, the 1,2-bonded **TS-1E** is still favored over 1,1-bonded **TS-1F**, suggesting a general preference for 1,2-bonded transition states for alkoxide promoted diboration.

The origin of transition state stabilization with 1,2-bonded versus 1,1-bonded diboron is proposed below. As shown in Scheme 2.10, abbreviated transition state **I** and **J** revealed a substantial difference in the orientation of lone pair electrons on the oxygen atoms. For the 1,2-bonded transition state **J**, much of the oxygen lone pair electron density is directed away from the breaking B-B bond, whereas in the 1,1-bonded complex **I**, the breaking B-B bond bisects the oxygen lone pairs. According to the previous DFT calculation studies, during the first step of diboration reaction, π electrons from alkene donate to the boron atom B^A, while the B-B electrons then donate back to the π* orbital

of alkene to realize the rupture of the B-B bond. So, during the transition state of diboration reaction, there is an increase in electron density on boron atom $\mathbf{B^A}$, and due to the different oxygen lone pair orientation, the 1,1-bonding mode might suffer enhanced electron-electron repulsion compared to the 1,2-bonding mode. To gain an understanding of the magnitude of this effect, the energy difference between two conformers of the boryl anion $^{\ominus}B(OH)_2$ was studied by DFT calculations. Structure **K** is reflective of 1,1-bonding mode, and structure **L** is reflective of 1,2-bonding mode. **K** is 2.8 kcal/mol higher in energy than **L** which is consistent with destabilization of the 1,1-bonded transition state relative to 1,2-bonded transition state.

Scheme 2.10 General Comparision of 1,1- and 1,2-Bonded Transition States

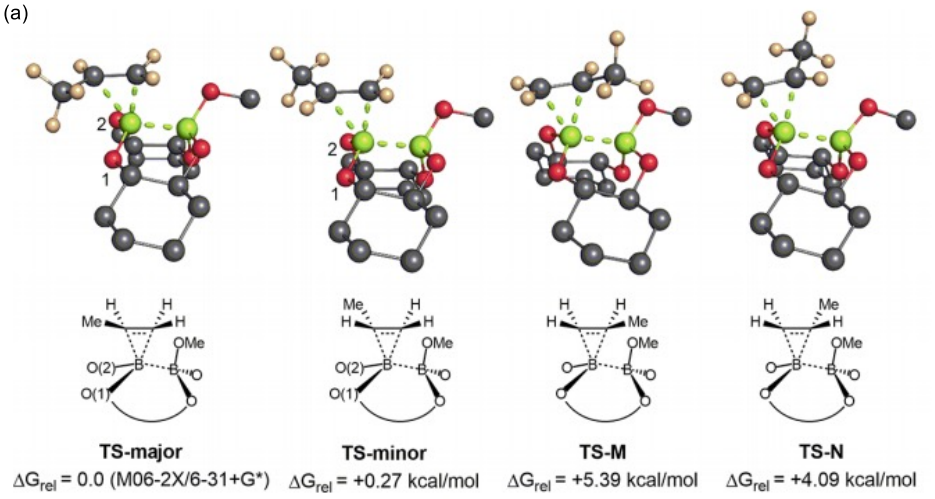


2.6 DFT Calculations for the Stereochemical Model

The stereochemical outcome of the carbohydrate catalyzed alkene diboration reaction would arise from the facial selectivity with which a prochiral alkene engages in **TS-1A** (shown in Scheme 2.8). Thus, four different reaction pathways were studied by DFT calculations. As shown in Scheme 2.11 (a), **TS-M** and **TS-N** are higher in energy as the alkene substituent is directed toward the activating alkoxy group, causing disfavored sterics repulsions. Two lower energy transition states **TS-major** and **TS-minor** do not have a clear difference in steric effects. The key distinguishing feature is that the O(2) oxygen atom in **TS-minor** is positioned in such a way that its lone pair electrons are

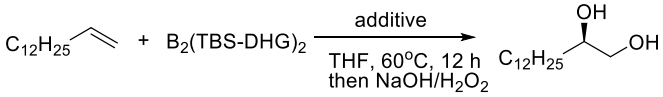
directed toward the alkene substituent, whereas for **TS-major**, the alkene substituent is situated near O(1) oxygen atom whose lone pair electrons are directing away from the olefin substituent. This difference in lone pair electrons orientation can be discerned from the electrostatic potential surface calculated for the most favored transition state (scheme 2.11 (b)). The electron density associate with O(2) oxygen atom is believed to provide an energetic preference for locating the small vinylic H over O(2) and the large alkyl group over O(1).

Scheme 2.11 DFT Calculations for Stereochemical Model



Of note, the energy difference between TS-major and TS-minor is only 0.27 kcal/mol, which is far off from the product enantioselectivity (95:5 er, ΔG_{rel} = 1.74 kcal/mol) generally obtained from carbohydrate catalyzed alkene diboration reaction. To test the reliability of the DFT calculation studies, a series of experiments were designed. As depicted in Scheme 2.12, 1-tetradecene was treated with prepared B_2(TBS-DHG)$_2$ and various alkoxide activators. Products from these stoichiometric experiments were then analyzed. It was found out that when different activators were used, the product was formed in different enantioselectivities. For example, when tert-butanol or isopropanol were used together with DBU as activators, the product was formed in much lower enantioselectivity (entry 1 and entry 2), whereas when n-butanol and 1,3-propanediol were used as activators, the product was formed in high enantioselectivities similar to the catalytic reaction (entry 3 and entry 4). To mimic the condition used in DFT calculations, potassium methoxide was applied to this stoichiometric experiment as the activator. In this case, the product was formed in 81: 19 er (ΔG_{rel} = 0.82 kcal/mol), which is closer to the theoretical energy difference calculated by DFT studies.

Scheme 2.12 Additive Effects in the Diboration Reaction



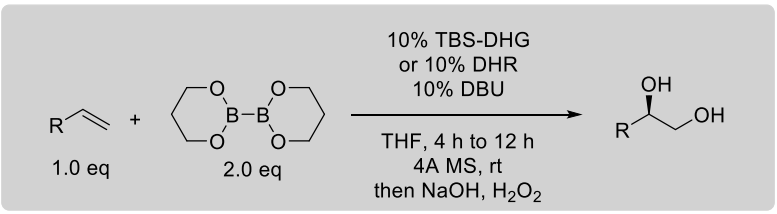
entry	additive	yield (%)	er
1	20% DBU, 20% t-BuOH	30%	80:20
2	20% DBU, 20% i-PrOH	25%	86:14
3	20% DBU, 20% n-BuOH	40%	90:10
4	20% DBU, 20%, 1,3-propanediol	43%	92:8
5	20% KOMe	46%	81:19

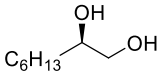
2.7 Substrate Scope

With a better understanding of reaction mechanism and a strategy for enhancing reaction rates by employing $B_2(pro)_2$, we explored the scope of the carbohydrate-catalyzed enantioselective diboration with both TBS-DHG and DHR catalysts. Two equivalents of $B_2(pro)_2$ were employed in order to obtain consistently high reaction efficiency. As shown in Scheme 2.13, generally, high enantioselectivities and high yields were observed regardless of alkyl substituents. 1-octene, 1-tetradecene, and vinylcyclohexane furnished the corresponding diols in similar yields and enantioselectivities (products **1**, **2**, **3**). Allyl and homoallyl benzene derivatives also underwent the diboration reaction smoothly (products **4-7**). Heterocycle-containing terminal alkenes, such as furan, Boc-protected indole, thiophene, and pyridine-containing substrates, afforded diol products in similarly good yields and good enantioselectivities (products **8-11**). To test out the functional group tolerance of the carbohydrate-catalyzed alkene diboration reaction, substrates bearing functional groups such as TBDPS-protected alcohols (**12** and **13**), ketone (**14**), ester (**15**) and alkyl bromide (**16**) were studied. All of these functional groups were well tolerated. Also, when substrates containing nearby stereocenters were applied to the diboration reaction, the products were formed in good diastereoselectivity thoroughly controlled by the catalyst (**17**, **18**). However, as depicted in product **19**, aromatic alkenes appear to be one type of substrates that do not react with high selectivity. In addition, it should be noted that DHR catalyzed reactions are generally as efficient as the TBS-DHG catalyzed process. Diol **1**, **3**, **5**, **7**, **10**, **13**, and **16** were obtained in similar yields and enantioselectivities. Finally, a comparison of reaction efficiency with $B_2(neo)_2$ was also included in Scheme 2.14. Diol **2**, **4** and **12** were

obtained in much higher yields and similar enantioselectivities by using the newly optimized reaction conditions.

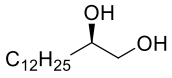
Scheme 2.13 Substrate Scope with terminal Alkenes





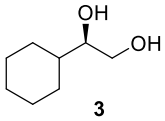
1

TBS-DHG: 97%, 95:5 er
DHR: 97%, 6:94 er



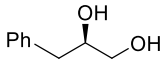
2

TBS-DHG: 95%, 96:4 er
with $B_2(neo)_2$: 65%, 96:4 er



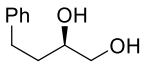
3

TBS-DHG:84%, 95:5 er
DHR: 90%, 5:95 er



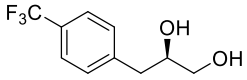
4

TBS-DHG:73%, 95:5 er
with $B_2(neo)_2$: 47%, 95:5 er



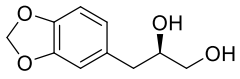
5

TBS-DHG: 92%, 95:5 er
DHR: 97%, 5:95 er



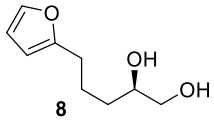
6

TBS-DHG:75%, 95:5 er



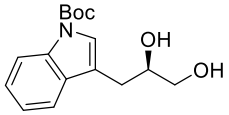
7

TBS-DHG:88%, 95:5 er
DHR: 90%, 5:95 er



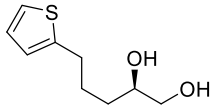
8

TBS-DHG:97%, 92:8 er



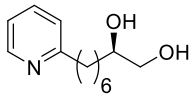
9

TBS-DHG:85%, 97:3 er



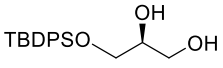
10

TBS-DHG:92%, 95:5 er



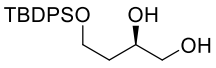
11

TBS-DHG: 70%, 95:5 er



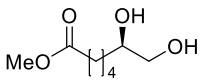
12

TBS-DHG:79%, 93:7 er
with $B_2(neo)_2$: 36%, 97:3 er



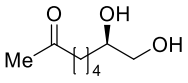
13

TBS-DHG: 89%, 97:3 er
DHR: 96%, 4:96 er



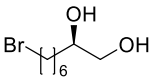
14

TBS-DHG:95%, 92:8 er



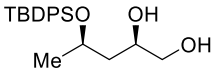
15

TBS-DHG:70%, 92:8 er



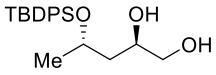
16

TBS-DHG:70%, 93:7 er
DHR: 90%, 7:93 er



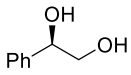
17

TBS-DHG: 78%, 14:1 dr



18

TBS-DHG: 73%, 15:1 dr



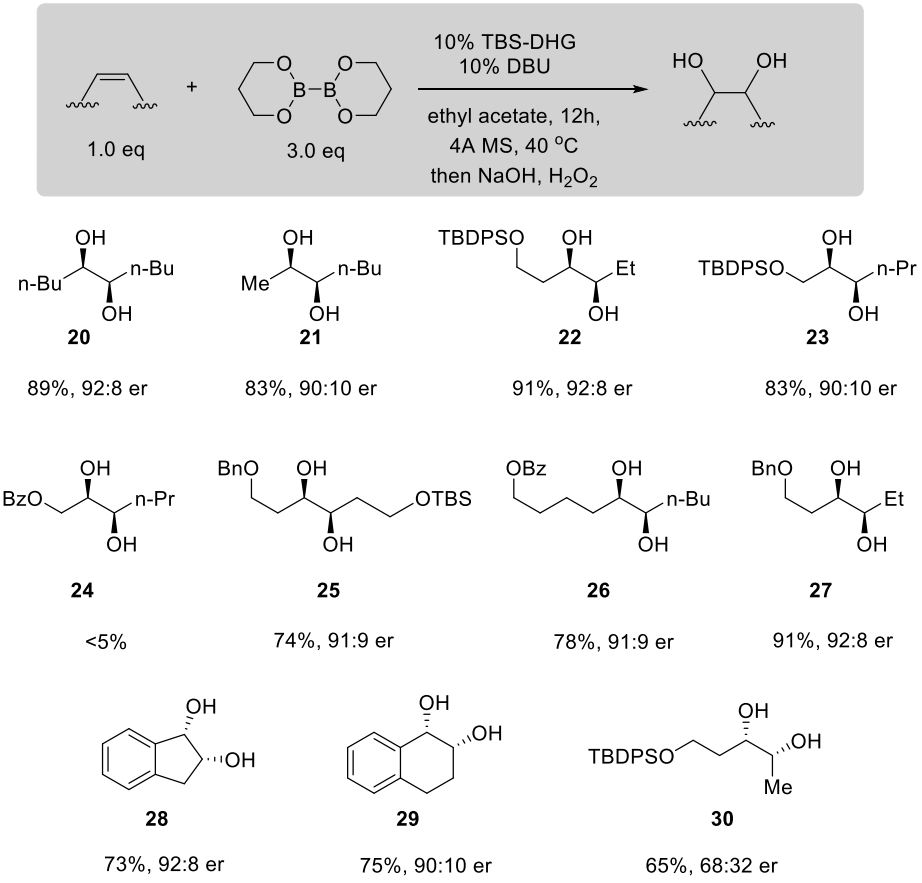
19

TBS-DHG: 73%, 55:45 er

Internal alkenes are less reactive than terminal alkenes under carbohydrate-catalyzed diboration reaction conditions, mainly because they are more sterically hindered. Previously when $B_2(neo)_2$ was used as the diboron reagent, harsher conditions such as elevated temperature (60 ^oC instead of room temperature) and stronger base (cesium carbonate instead of DBU) were needed to obtain the products in synthetically useful yields. However, in those reaction conditions, products were formed in lower enantioselectivity due to the competing background reaction. When the more reactive reagent $B_2(pro)_2$ was used, the reaction could be conducted at lower temperature and with DBU as base. It appears that the reaction suffers less nonselective background reaction under these milder condition, and products can be afforded in synthetically useful yields and enantioselectivity. As depicted Scheme 2.14, standard conditions for carbohydrate catalyzed enantioselective internal alkene diboration is 10 mol% TBS-DHG catalyst, 3.0 equivalents of $B_2(pro)_2$ at 40 ^oC. A modest improvement in yield was obtained when the reaction was conducted in ethyl acetate instead of THF. A collection of functionalized disubstituted alkenes were examined under the standard reaction conditions. As the results showed in Scheme 2.14 suggest, these reaction conditions operate well on non-functionalized hydrocarbons (**20**, **21**) as well as on substrates bearing adjacent oxygenated functional groups (**22**, **23**, **25**, **26**, **27**). However, electron withdrawing allylic substituents decrease alkene reactivity (**20**, **23**, **24**). When a substrate with an allylic benzoate (**24**) was tested in the diboration reaction, the product was not detected. Specialized *cis*-alkenes such as indene and dihydronaphthalene were also examined in the diboration reaction. Products **28** and **29** were formed in synthetically useful yields and

enantioselectivities. However, when acyclic *cis*-alkene **30** was tested, the product was formed in poor enantioselectivity.

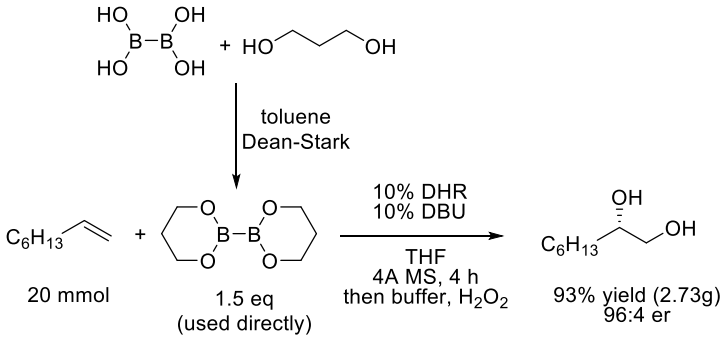
Scheme 2.14 Substrate Scope with Internal Alkenes



As shown by all the examples included in the substrate scope, the carbohydrate-catalyzed diboration reaction is remarkably accelerated by the use of $B_2(pro)_2$ instead of $B_2(neo)_2$. Additionally, it must be noted that due to the high solubility of 1,3-propanediol in water, removing it from the reaction products is easily achieved by aqueous wash. This makes the product purification far easier than when neopentyl glycol or pinacol-derived diboron reagents were used. To further demonstrate the robustness of carbohydrate catalyzed enantioselective alkene diboration reaction, we conducted a 20 mmol 1-octene diboration reaction by using 1.5 equivalents of crude diboron generated directly from

dehydration reaction between $B_2(OH)_4$ and 1,3-propanediol (no recrystallization). The "Green" solvent ethyl acetate was employed. The reaction was allowed to stir at room temperature for 12 hours. Subsequent buffered (pH = 7) oxidation with H_2O_2 and purification provided the product 1,2-diol in 93% yield.

Scheme 2.15 Large Scale Cabohydrate Catalyzed Alkene DIboration



2.8 Conclusions

The carbohydrate catalyzed enantioselective alkene diboration reaction is an efficient reaction that employs simple catalysts and reagents to convert unsaturated hydrocarbons into useful chiral building blocks. Detailed mechanistic studies suggested that the crucial reactive intermediate is a 1,2-bonded chiral diboron and the boronic ester exchange between diboron starting material and diol catalyst is the turn-over limiting step of the catalysis. These mechanistic insights helped us find a more reactive diboron starting material $B_2(pro)_2$ that significantly improved the catalysis efficiency. With $B_2(pro)_2$ as the reagent, the reaction occurs in a reasonable time course and works well for both terminal and internal alkenes. Of note, the waste streams arising from the diboration/oxidation are 1,3-propanediol and boric acid, both of which are relatively non-toxic. Thus, the carbohydrate-catalyzed diboration of alkenes is an appealing method for the enantioselective transformation of olefins.

2.9 Experimental Section

2.9.1 General Information

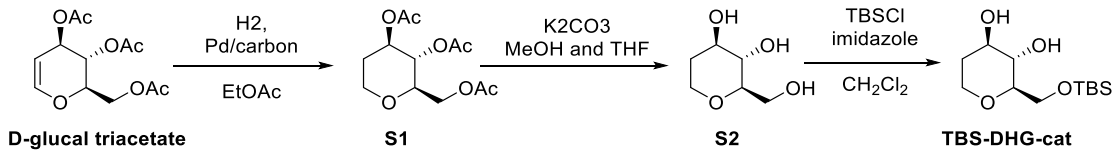
^{1}H NMR spectra were recorded on Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz) or Varian Gemini 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: integration, chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz) or a Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (160 MHz). Chemical shifts are reported in ppm with an external standard ($BF_3 \cdot Et_2O$: 0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol, or potassium permanganate.

Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier. Analytical chiral gas-liquid chromatography (GLC) was performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β -Dex 120 column with helium as the carrier gas.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Tetrahydroxydiboron was purchased from Frontier Scientific. It was recrystallized by water before use. Bis(neopentyl glycolato)diboron was purchased from Oakwood Chemicals. D-glucal triacetate was purchased from Alfa Aesar. (1S, 2S)-trans-1,2-cyclohexanediol and (1R, 2R)-trans-1,2-cyclohexanediol were purchased from Acros Organics. Phosphate buffer solution (PH = 7.0) was purchased from Fisher Scientific. Tris(dibenzylideneacetone)dipalladium(0) and Ruphos were purchased from Strem Chemicals. Activated 4A Molecular Seives was bought from Sigma-Aldrich. All other reagents were purchased either from Aldrich, Alfa Aesar, Acros, Oakwood Chemicals, Combi Blocks, or TCI and were used without further purification.

2.9.2 Catalysts Preparation

A. Synthesis of TBS-DHG catalyst.



A flame-dried round bottom flask equipped with a stir bar was charged with D-glucal triacetate (4.36 g, 16.0 mmol), palladium on carbon (5%, 0.85g, 0.80 mmol) and ethyl acetate (30 mL). The vessel was purged with hydrogen gas and the reaction mixture was allowed to stir at room temperature under balloon pressure of hydrogen for 5 hours. The mixture was then filtered through a pad of silica gel. The filtrate was concentrated by rotary evaporation to afford crude oil **S1**. The crude product was used for next step without further purification.

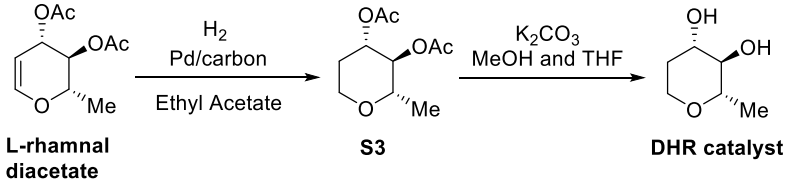
A round bottom flask was equipped with stir bar and a solution of the crude product **S1** (1.00g, 3.65 mmol) in tetrahydrofuran (10 mL) and methanol (10 mL) was added to the flask. To the reaction mixture was then added potassium carbonate (0.13 g, 0.91mmol). The reaction was allowed to stir at room temperature for 16 h. 2.6 g of silica gel was then added to the reaction. Solvents were removed by rotary evaporation. The crude was purified through silica gel column (hexane: acetone: methanol=10:10:2) to afford the product **S2** as white solid. (0.50g, 92% yield). Spectral data and physical data are in accordance with literature report[48]. ^{1}H NMR (600 MHz, Methanol-d4) δ 3.95 (ddd, J = 11.7, 4.9, 1.6 Hz, 1H), 3.87 (dd, J = 11.8, 2.3 Hz, 1H), 3.66 (dd, J = 11.7, 5.7 Hz, 1H), 3.58 – 3.50 (m, 1H), 3.47 (td, J = 12.2, 2.1 Hz, 1H), 3.22 – 3.12 (m, 2H), 2.04 – 1.81 (m,

[48] Kikuo, I.; Tsunetoshi, H. *J. Org. Chem.* **1970**, *35*, 606.

1H), 1.63 (tdd, J = 12.9, 11.4, 5.0 Hz, 1H). ^{13}C NMR (151 MHz, Methanol-d4) δ 83.7, 75.3, 74.9, 67.8, 64.5, 36.4. HRMS-(DART+) for $C_6H_{13}O_4$ $[M+H]^+$: calculated: 149.0814. found: 149.0806.

A flame-dried round bottom flask equipped with a stir bar was charged with imidazole (0.34g, 5.06 mmol) and product **S2** (0.50g, 3.37 mmol). The flask was sealed with a septum, and flushed with nitrogen gas for 5 minutes. To the round bottom flask was then added *tert*-butyldimethylsilyl chloride (0.61g, 4.05 mmol) dissolved in dichloromethane (6 mL). The reaction mixture was allowed to stir at room temperature under nitrogen for 6 h. The reaction mixture was then treated with water (10 mL). The layers were separated and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford crude product. The crude product was purified through silica gel column (50% ethyl acetate in hexane) to afford the TBS-DHG catalyst as white solid (0.64g, 71% yield). Spectral data was in accordance with literature report[49].

B. Synthesis of DHR catalyst.



L-rhamnal diacetate **S3** **DHR catalyst**

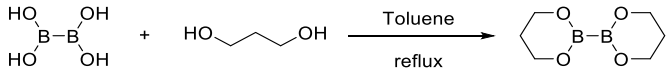
A round bottom flask equipped with a stir bar was charged with L-rhamnal diacetate (2.14 g, 10.0 mmol), palladium on carbon (5%, 0.53g, 0.50 mmol) and ethyl acetate (20 mL). The vessel was purged with hydrogen gas and the reaction mixture was allowed to

[49] Fang, L. C.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508.

stir at room temperature under balloon pressure of hydrogen for 5 hours. The mixture was then filtered through a pad of silica gel. The filtrate was concentrated by rotary evaporation to afford crude oil **S3**. The crude product was used for next step without further purification.

A round bottom flask was equipped with stir bar and a solution of the crude product **S3** (1.08g, 5 mmol) in tetrahydrofuran (10 mL) and methanol (10 mL). To the reaction mixture was then added potassium carbonate (0.13 g, 1.25 mmol). The reaction was allowed to stir at room temperature for 16 h and was then added 2.6g silica gel. The reaction was concentrated by rotary evaporation. The crude was purified through silica gel column (70% ethyl acetate in hexane) to afford the product **DHR catalyst** as white solid. (463 mg, 70% yield). Spectral data was in accordance with literature report.[9]

2.9.3 Preparation of B_2pro_2

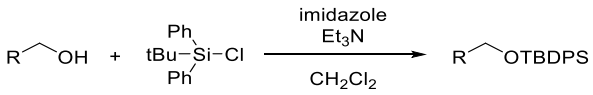


A round bottom flask equipped with a magnetic stir bar was added tetrahydoxydiboron (1.91g, 21.27 mmol), 1,3-propanediol (3.04 ml, 41.91mmol), and toluene (25 ml). A Dean-Stark distillation head was then equipped. The reaction was refluxing at 160 ^oC for 6h. Toluene was then removed by rotary evaporation to afford crude product. The crude product was recrystallized by hexane and dichloromethane to afford the propanediol diboron as white solid (2.50g, 70% yield). Spectral data was in accordance with literature report[50]. HRMS-(DART+) for $C_6H_{13}B_2O_4$ $[M+H]^+$: calculated: 171.1, found:171.1008.

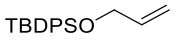
[50] Zaidlewicz, M.; Wolan, A. *Journal of Organometallic Chemistry*. **2002**, 657, 129.

2.9.4 Preparation of Alkenes

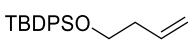
A. General Procedure for silyl protection of alkenes.



To a flame-dried round bottom flask equipped with stir bar was added imidazole (1.02g, 15mmol). The flask was purged with nitrogen for 5 min. Dichloromethane (20 ml), alcohol substrate (10 mmol), Et_3N (2.09 ml, 15 mmol) was then added. tert-Butyl (chloro)diphenylsilane (2.57ml, 10 mmol) was added to the reaction mixture in drop. The reaction was allowed to stir at room temperature for 16h. Water (20 ml) was then added to the reaction. The layers were separated. The aqueous layer was extracted by dichloromethane twice. The organic layers were combined, dried over sodium sulfate, filtered, and condensed under vacuum to afford the crude product.



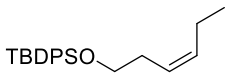
(allyloxy)(tert-butyl)diphenylsilane. The title compound was prepared by the representative procedure without modification. The crude product was purified by silica gel column with hexane to afford the product as colorless oil (2.61g, 88% yield). Spectral data was in accordance with the literature report[51]. HRMS-(DART+) for $C_{19}H_{24}OSi$ $[M+H]^+$: calculated: 297.1675, found:297.1662.



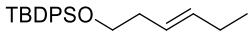
(but-3-en-1-yloxy)(tert-butyl)diphenylsilane. The title compound was prepared by the representative procedure without modification. The crude product was purified by silica

[51] Kliman, L. K. ; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210.

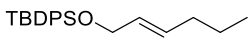
gel column with hexane to afford the product as colorless oil (2.95g, 95% yield). Spectral data was in accordance with the literature report.[11] HRMS-(DART+) for $C_{20}H_{26}OSi$ $[M+H]^+$: calculated: 311.1831, found: 311.1815.



(Z)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane. The title compound was prepared by the representative procedure without modification. The crude product was purified by silica gel column with hexane to afford the product as colorless oil (3.12g, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.60 (m, 4H), 7.50 – 7.31 (m, 6H), 5.48 – 5.39 (m, 1H), 5.38 – 5.29 (m, 1H), 3.65 (t, J = 7.0 Hz, 2H), 2.31 (q, J = 7.1 Hz, 2H), 2.06 – 1.91 (m, 2H), 1.05 (dd, J = 2.1, 0.7 Hz, 9H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 134.0, 133.5, 129.5, 127.6, 124.9, 76.7, 63.8, 30.7, 26.8, 20.6, 19.2, 14.3. HRMS-(DART+) for $C_{22}H_{30}OSi$ $[M+H]^+$: calculated:339.2144, found: 339.2160. IR(neat): 3071.27(w), 3050.30(w), 3010.25(w), 2960.51(m), 2931.33(m), 2892.88(m), 2858.24(m), 1462.68(m), 1188.08(s), 1091.21(s), 700.85(s), 504.80(m), cm^{-1} .



(E)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane. The title compound was prepared by the representative procedure without modification. The crude product was purified by silica gel column with hexane to afford the product as colorless oil (3.01g, 88% yield). Spectral data was in accordance with the literature.[52] HRMS-(DART+) for $C_{22}H_{30}OSi$ $[M+H]^+$: calculated:339.2144, found: 339.2152.

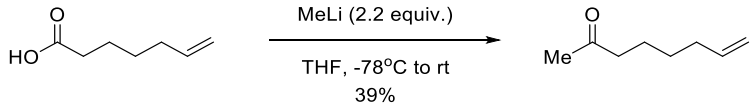


[52] Nishioka, Y.; Uchida, T.; Katsuki, T. *Angew. Chem. Int. Ed.* **2013**, *52*, 1739.

(E)-tert-butyl(hex-2-en-1-yloxy)diphenylsilane. The title compound was prepared by the representative procedure without modification. The crude product was purified by silica gel column with hexane to afford the product as colorless oil (3.20g, 95% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.56 (m, 4H), 7.55 – 7.30 (m, 6H), 5.65 (dtt, *J* = 14.9, 6.6, 1.5 Hz, 1H), 5.55 (dtt, *J* = 15.3, 5.2, 1.4 Hz, 1H), 4.17 (dd, *J* = 5.1, 1.4 Hz, 2H), 2.28 – 1.79 (m, 2H), 1.39 (h, *J* = 7.4 Hz, 2H), 1.06 (s, 9H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 136.6, 133.9, 132.2, 131.5, 130.2, 67.4, 37.0, 29.5, 25.0, 21.9, 16.3. HRMS-(DART+) for $C_{22}H_{30}OSi$ $[M+H]^+$: calculated:337.1988, found: 337.1987. IR(neat): 2957.87(m), 2929.83(m), 2857.54(m), 1462.35(m), 1427.69(m), 1110.55(s), 700.97(s), 504.60(s), cm^{-1}.

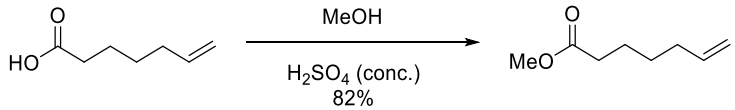
B. Preparation of oct-7-en-2-one.

The title compound was prepared by literature procedure. The spectral data was in accordance with the literature reference.[53]



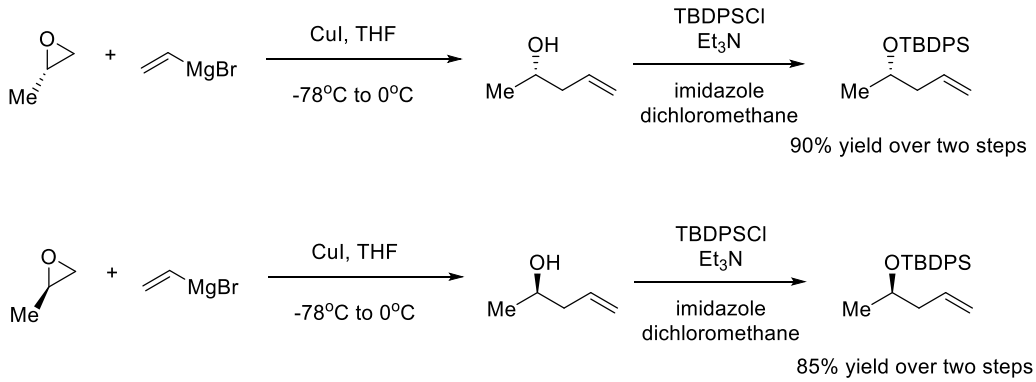
C. Preparation of methyl hept-6-enoate.

The title compound was prepared by literature procedure. The spectral data was in accordance with the literature reference.[13]



[53] Rosillo, M.; Arnáiz, E.; Abdi, D.; Blanco-Urgoiti, J.; Domínguez, G.; and Pérez-Castells, J. *Eur. J. Org. Chem.* **2008**, *23*, 3917.

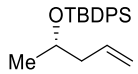
D. Preparation of (R)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane and (S)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane.



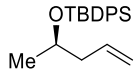
To a flame-dried round bottom flask equipped with stir bar was added CuI (381mg, 2 mmol) in the glovebox. The flask was sealed by rubber septa and removed from the glovebox. The flask was charged with tetrahydrofuran (30 ml) under nitrogen. The reaction was cooled down to -78 ^{o}C by dry ice/ acetone bath. Vinyl magnesium bromide (1M in THF, 20ml, 20 mmol) was then added dropwise. The reaction was allowed to stir at -78 ^{o}C for another 15 min, and then the propylene oxide (0.70 ml, 10 mmol) was added in one shot. The reaction was then allowed to stir at -78^{o}C for one hour and room temperature for another one hour. Upon the completion of the reaction, water and ammonium chloride were added to the reaction mixture. Layers were separated. The aqueous layer was extracted by diethyl ether twice. The organic layers were combined, dried over sodium sulfate, filtered. Diethyl ether was removed by atmospheric distillation. The residue was taken to next step without further purification.

To a flame-dried round bottom flask equipped with stir bar was added imidazole (1.02g, 15 mmol). The flask was then purged with nitrogen for 10 min. Crude product dissolved in dichloromethane (15ml) and trimethylamine (2.09ml, 15 mmol) was then

added. To the reaction mixture above was added tert-butyl(chloro)diphenylsilane (2.60ml, 10 mmol) in drop. The reaction was allowed to stir at room temperature for 12h. Water was then added to the reaction and layers were separated. The aqueous layer was extracted by dichloromethane twice. The organic layers were combined, dried over sodium sulfate, filtered and condense to crude.



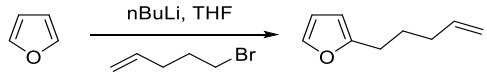
(R)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane. The crude was purified through silica gel column (pure hexane) to afford product as yellow oil (2.93g, 90% yield over 2 steps). Spectra data were in accordance with literature report.[54]

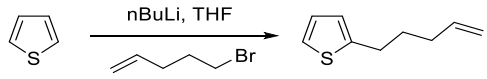


(S)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane. The crude was purified through silica gel column (pure hexane) to afford product as yellow oil (2.76g, 85% yield over 2 steps). Spectra data were in accordance with literature report.[55]

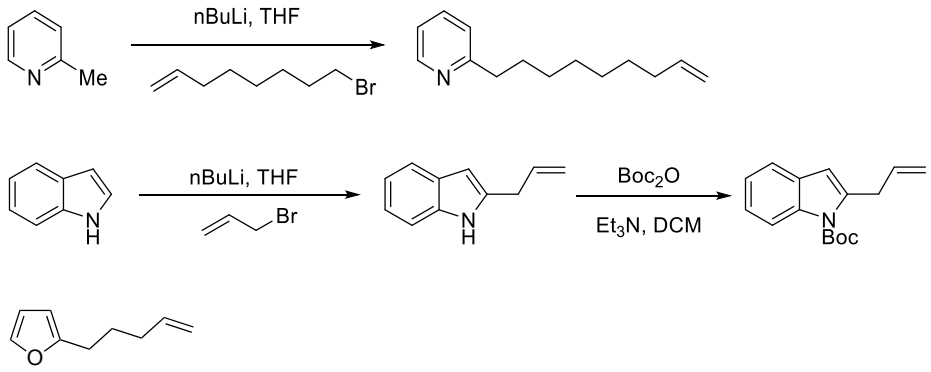
E. Preparation of heteroaryl substituted terminal alkenes.

The following alkenes were prepared according to literature procedure[56].

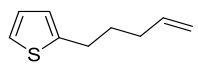




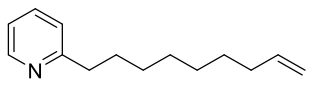
[54] Bujaranipalli, S.; Das, S.; *Tetrahedron Letters,* **2015**, *56*, 3747.
[55] Fuwa, H.; Sasaki, M. *Org. Lett.* **2008**, *10*, 2549.
[56] Kalaitzakis, D.; Antonatou, E.; Vassilikogiannakis, G. *Chem. Commun.* **2014**, *50*, 400.



2-(pent-4-en-1-yl)furan. Spectral data is in accordance with literature report.[16] HRMS-(DART+) for $C_9H_{13}O$ $[M+H]^+$: calculated: 137.0966, found: 137.0972. IR(neat): 3074.91(w), 2931.49(m), 1640.38(m), 1438.92(m), 990.79(m), 910.58(s), 850.40(s), 688.71(s), cm^{-1}.

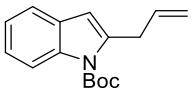


2-(pent-4-en-1-yl)thiophene. ^1H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, 1H), 6.92 (dd, *J* = 5.2, 3.1 Hz, 1H), 6.79 (d, *J* = 3.4 Hz, 1H), 5.83 (ddt, *J* = 18.8, 10.2, 5.7 Hz, 1H), 5.04 (d, *J* = 17.1 Hz, 1H), 4.99 (d, *J* = 12.0 Hz, 1H),2.85 (t, *J* = 7.6 Hz, 2H), 2.13 (q, *J* = 7.0 Hz, 2H), 1.79 (p, *J* = 7.5, 2H).. ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.0, 140.9, 129.3, 126.8, 125.5, 117.7, 35.7, 33.5, 31.9. HRMS-(DART+) for $C_9H_{13}S$ $[M+H]^+$: calculated: 153.0738, found: 153.0742. IR(neat): 3074.90(w), 2976.43(w), 2931.72(m), 2855.96(w), 1640.42(m), 1438.99(m), 1239.25(m), 910.51(s), 688.57(s), cm^{-1}.



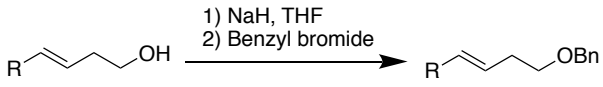
2-(non-8-en-1-yl)pyridine. ^1H NMR (600 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.9 Hz, 1H), 7.57 (td, *J* = 7.7, 1.9 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.08 (dd, *J* = 7.3, 5.1 Hz, 1H), 5.80 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 4.98 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.92 (dt, *J* = 10.2, 1.6

Hz, 1H), 2.77 (t, *J* = 7.9 Hz, 2H), 2.07 – 1.98 (m, 2H), 1.81 – 1.65 (m, 3H), 1.49 – 1.16 (m, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 151.9, 141.8, 138.8, 125.3, 123.5, 116.8, 41.1, 36.4, 32.6, 31.99, 31.97, 31.8, 31.5. . HRMS-(DART+) for $C_{14}H_{22}N$ $[M+H]^+$: calculated: 204.1752, found: 204.175. IR(neat): 3075.46(w), 3006.84(w), 2924.45(s), 2853.67(s), 1589.37(m), 1473.65(m), 1433.62(m), 908.13(s), 747.12(s), cm^{-1}.



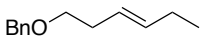
tert-butyl 2-allyl-1H-indole-1-carboxylate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.39 (s, 1H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 6.05 (ddt, *J* = 16.7, 10.0, 6.4 Hz, 1H), 5.19 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.13 (dd, *J* = 9.9, 1.2 Hz, 1H), 3.46 (dd, *J* = 6.4, 1.2 Hz, 2H), 1.68 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.5, 138.5, 133.2, 127.0, 125.5, 125.0, 121.9, 121.7, 118.8, 117.9, 86.0, 32.2, 31.0, 30.8. HRMS-(DART+) for $C_{16}H_{20}NO_2$ $[M]^+$: calculated: 258.1494, found: 258.1489. IR(neat): 2978.63(w), 1730.85(s), 1452.63(s), 1367.49(s), 1254.90(s), 1158.46(s), 1075.68(s), 744.59(m), cm^{-1}.

F. General Procedure for Benzyl protection of alkenes.

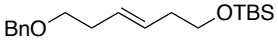


To a flame-dried round bottom flask equipped with stir bar was added sodium hydride (144 mg, 6mmol) in the glove box. The flask was sealed with a rubber septa and then removed from the box. A nitrogen inlet was then applied. THF (20 ml) was added under nitrogen. The reaction flask was cooled down to 0^{o}C by ice bath. Alcohol substrate (5

mmol) was then added dropwise. The reaction mixture was allowed to stir at room temperature for 30 minutes. Benzyl bromide (0.714 ml, 5 mmol) was then added to the reaction. The reaction mixture was allowed to stir at room temperature for 12h. The reaction was then cooled down to 0^{o}C by ice bath. 10ml of water was added to the reaction. The mixture was then transferred to a supranational funnel. Layers were then separated. The aqueous layer was extracted by dichloromethane (2*15ml). The organic layers were combined, dried over sodium sulfate, filtered and condense to crude.



(E)-((hex-3-en-1-yloxy)methyl)benzene. The title compound was prepared according to the standard procedure. The crude was purified through silica gel column (3% ethyl acetate in hexane) to afford the product as clear oil (818 mg, 86% yield). Spectral data are in accordance with literature report[57].



(E)-((6-(benzyloxy)hex-3-en-1-yl)oxy)(tert-butyl)dimethylsilane. The title compound was prepared according to the standard procedure. The starting material was synthesized according to the literature procedure[11]. The crude was purified through silica gel column (2% ethyl acetate in hexane) to afford the product as clear oil (1.36g, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 4.6 Hz, 4H), 7.30 – 7.25 (m, 1H), 5.52 – 5.45 (m, 2H), 4.50 (s, 2H), 3.60 (t, J = 7.0 Hz, 2H), 3.47 (d, J = 7.0 Hz, 2H), 2.31 (dtd, J = 8.6, 4.9, 2.3 Hz, 2H), 2.21 (tdd, J = 6.4, 4.4, 1.4 Hz, 2H), 0.87 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 128.9, 128.7, 128.6, 127.9, 127.7, 73.1, 70.4, 63.4, 36.6, 33.4,

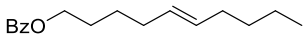
[57] Movassaghi, M.; Ahmad, K. O. *Angew. Chem. Int. Ed.* **2008**, *47*, 8909 –8912.

26.2, 18.6, -5.0. HRMS-(DART+) for $C_{19}H_{36}O_2SiN[M+NH_4]^+$: calculated: 338.2515, found: 338.2528.

G. General Procedure for Benzoyl Protection.

To a flame dried round bottom flask with stir bar was added DMAP (61.09 mg, 0.5 mmol). The flask was then purged with nitrogen. DCM (20 ml), trans-5-decen-1-ol (0.594 ml, 5 mmol), trimethylamine (1.39 ml, 10 mmol) and benzoyl chloride (1.16 ml, 10 mmol) was then added. The reaction was allowed to stir at room temparature for 14h.

The reaction was then quenched by water (10 ml). The reaction mixture was transferred to a sep funnel. The layers were separated. The auqeous layer was extracted by dichloromethane for 3 times (20 ml per time). Organic layers were combined and dry over sodium sulfate, filtered and condense to crude. The crude mixture was purified on silica gel column by 5% ethyl acetate in hexane to afford the product as yellow oil.(1.30g, 86% yield)



(E)-dec-5-en-1-yl benzoate. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 7.1 Hz, 2H), 7.55 (d, J = 7.4 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 5.54 – 5.19 (m, 2H), 4.32 (t, J = 6.6 Hz, 2H), 2.30 – 1.85 (m, 4H), 1.77 (dt, J = 15.2, 6.8 Hz, 2H), 1.63 – 1.39 (m, 2H), 1.39 – 1.26 (m, 3H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8, 132.9, 131.3, 129.7, 129.7, 128.5, 65.1, 32.4, 32.3, 31.9, 28.3, 26.2, 22.4, 14.1. HRMS-(DART+) for C17H25O6 [M+H]+: calculated: 261.1855, found: 261.186.

2.9.5 Experimental Procedure for Alkene Diboration/Oxidation and Product Characterization.

A. General Procedure for terminal alkenes with TBS-DHG catalyst.

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (5.25 mg, 0.02 mmol, 0.1 equiv), propanediol diboron (67.91mg, 0.40 mmol, 2.0 equiv), 4A molecular sieves (20 mg), the alkene substrate (0.20 mmol, 1.0 equiv) and THF (0.20 mL). DBU (3.00ml, 0.02 mmol, 0.1 equiv) was then added to the solution. The vial was sealed with a Teflon septum, removed from the glove box. The reaction mixture was stirred at room temperature for 12 hours. The reaction was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (0.6 mL), followed by dropwise addition of 30% hydrogen peroxide (0.3 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over sodium sulfate, filtered, and concentrated by rotary evaporation to afford crude reaction mixture.

B. General Procedure for terminal alkenes with DHR catalyst.

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with DHR catalyst (2.6 mg, 0.02 mmol, 0.1 equiv), propanediol diboron (67.91mg, 0.40 mmol, 2.0 equiv), 4A molecular sieves (20 mg), the alkene substrate

(0.20 mmol, 1.0 equiv) and THF (0.20 mL). DBU (3.00 μl, 0.02 mmol, 0.1 equiv) was then added to the solution. The vial was sealed with a Teflon septum, removed from the glove box. The reaction mixture was stirred at room temperature for 12 hours. The reaction was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (0.6 mL), followed by dropwise addition of 30% hydrogen peroxide (0.3 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over sodium sulfate, filtered, and concentrated by rotary evaporation to afford crude reaction mixture.

C. General Procedure for internal alkenes with TBS-DHG catalyst.

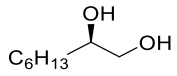
In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (7.87 mg, 0.03 mmol, 0.15 equiv), propanediol diboron (101.89 mg, 0.60 mmol, 2.0 equiv), 4A molecular sieves (30 mg), the alkene substrate (0.20 mmol, 1.0 equiv) and ethyl acetate (0.20 mL). DBU (4.50 μl, 0.03 mmol, 0.15 equiv) was then added to the solution. The vial was sealed with a Teflon septum, removed from the glove box. The reaction mixture was allowed to stir at 40^{o}C for 12 hours. The reaction was then cooled to 0 °C (ice/water) and charged with THF (0.2 ml), 3 M sodium hydroxide (0.6 mL), followed by dropwise addition of 30% hydrogen peroxide (0.3 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and

saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford crude reaction mixture.

D. General Procedure for terminal alkenes with TBS-DHG catalyst.

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (5.25 mg, 0.02 mmol, 0.1 equiv), Bis(neopentyl glycolato)diboron (90.35 mg, 0.40 mmol, 2.0 equiv), 4A molecular sieves (20 mg), the alkene substrate (0.20 mmol, 1.0 equiv) and THF (0.20 mL). DBU (3.00 ml, 0.02 mmol, 0.1 equiv) was then added to the solution. The vial was sealed with a Teflon septum, removed from the glove box. The reaction mixture was stirred at room temperature for 12 hours. The reaction was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (0.6 mL), followed by dropwise addition of 30% hydrogen peroxide (0.3 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over sodium sulfate, filtered, and concentrated by rotary evaporation to afford crude reaction mixture.

E. Full Characterizations and Proof of Stereochemistry (with TBS-DHG catalyst)



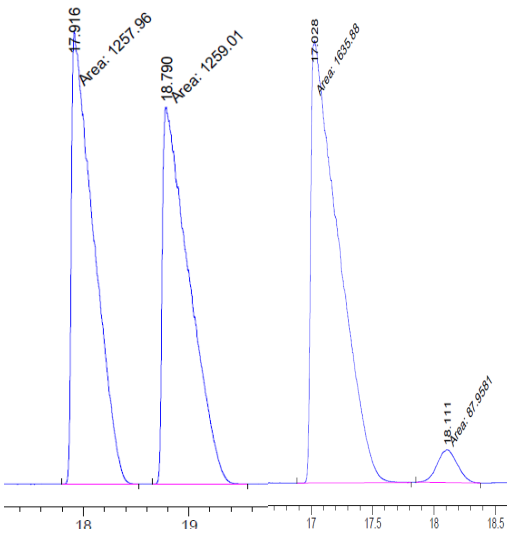
(R)-octane-1,2-diol (1). The diboration was performed according to the general procedure A with 1-octene (22.44 mg, 0.20 mmol, 32.4 μL). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (28.30 mg, 97% yield). Spectral data and optical rotation are in accordance with the literature report.[58] HRMS-(DART+) for C8H22NO2 $[M+NH_4]^+$: calculated: 164.1651, found: 164.1655.

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate.[59] The absolute stereochemistry was assigned by analogy.

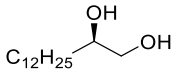
Chiral GLC (β-dex, Supelco, 100 °C 30min, 20 psi)- analysis of the acetonide of octane-1,2-diol.

[58] Toribatake, K.; Nishiyama, H; *Angew. Chem. Int. Ed.* **2013**, *52*, 11011.
[59] Shing, T. K. M.; Tam, E. K. W.; Tai, V. W.-F.; Chung, I. H. F.; Jiang, Q. *Chem. Eur. J.* **1996**, *2*, 50.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	17.028	MM	0.2614	1635.88281	104.29852	94.89755
2	18.111	MM	0.1889	87.95814	7.76046	5.10245



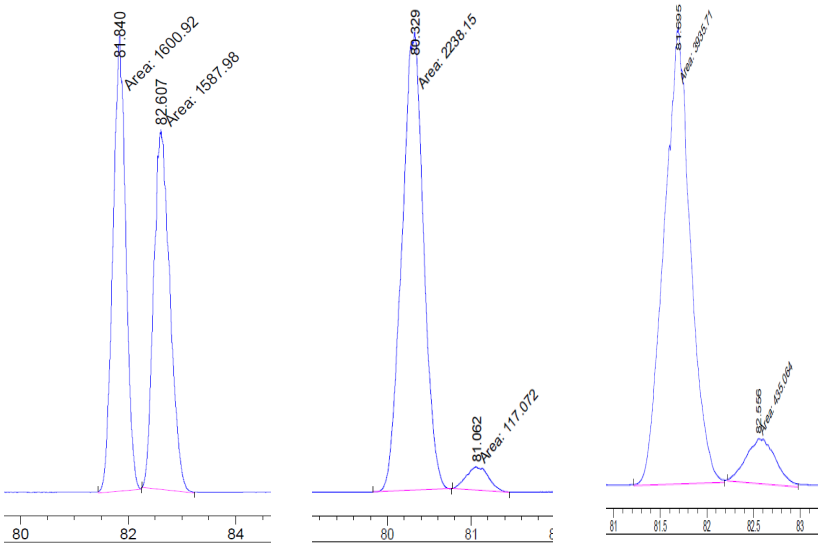
(R)-tetradecane-1,2-diol (2). The diboration was performed according to the general procedure A with 1-tetradecene substrate (94%, 41.78 mg, 0.20 mmol, 54 µL). The crude reaction mixture was purified on silica gel (40% ethyl acetate in hexanes) to afford the product as white solid (43.7 mg, 95% yield). Spectral data and optical rotation are in accordance with the literature report.[60] HRMS-(DART+) for C14H34NO2 $[M+NH4]^+$: calculated: 248.2590, found: 248.2583.

Analysis of Stereochemistry:

[60] Stallforth, P.; Adibekian, A.; Seeberger, H. P. *Org. Lett.,* **2008,** *10,* 1573.

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of tetradecane-1,2-diol prepared from dihydroxylation of 1-tetradecene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy. The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-tetradecene utilizing AD-mix-β.[61]

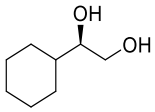
Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.



racemic product diboration product authentic product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	80.329	MM	0.2978	2238.15308	125.27486	95.02927
2	81.062	MM	0.3038	117.07190	6.42210	4.97073

[61] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem*. **1992**, *57*, 2768.



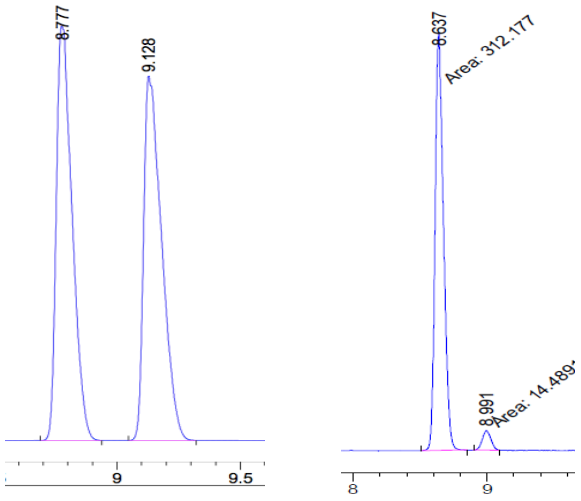
(R)-1-cyclohexylethane-1,2-diol (3). The diboration was performed according to the general procedure A with vinyl cyclohexane (22.04 mg, 0.20 mmol, 27.4 μL). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (24.2 mg, 84% yield). Spectral data and optical rotation are in accordance with the literature report.[62] HRMS-(DART+) for $C_8H_{15}O$ $[M+H-H_2O]^+$: calculated:127.1123, found:127.1117.

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from dihydroxylation of vinyl cyclohexane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy

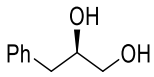
Chiral GLC (β-dex, Supelco, 130 °C 20 min)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol

[62] Gally, C.; Nestl, B. M.; Hauer, B. *Angew. Chem. Int. Ed.* **2015,** *54,* 12952.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.637	MM	0.0728	312.17676	71.49557	95.56456
2	8.991	MM	0.0726	14.48905	3.32531	4.43544



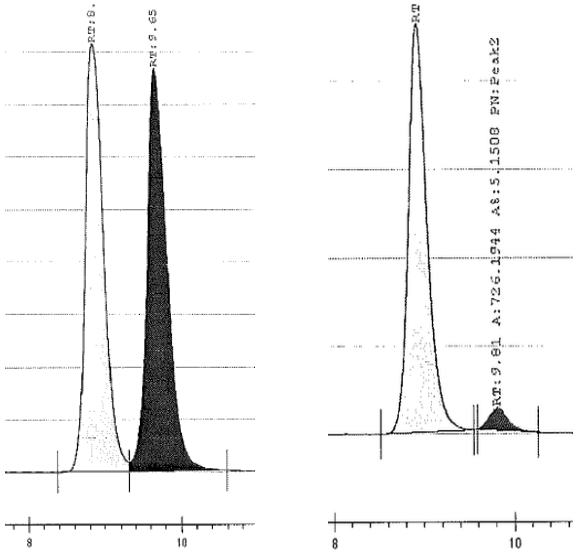
(R)-3-phenylpropane-1,2-diol (4). The diboration was performed according to the general procedure A with allyl benzene (23.64 mg, 0.50 mmol, 26.56µL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (28.2 mg, 73% yield). Spectral data and optical rotation are in accordance with the literature report.[63] HRMS-(DART+) for $C_9H_{11}O$ $[M\text{-}H_2O+H]^+$: calculated: 135.081, found: 135.0804.

Analysis of Stereochemistry:

[63] Toribatake, K.; Nishiyama, H.; *Angew. Chem. Int. Ed.* **2013**, *52*, 11011.

The 1,2-diol was compared to the racemic 3-phenylpropane-1,2-diol prepared from dihydroxylation of allyl benzene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

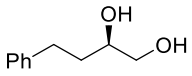
Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-phenylpropane-1,2-diol.



racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.8492	13372.3692	8.93	927.252	0.0068
2	5.1508	726.1944	9.81	50.3872	0.0074
Total:	100	14098.5636			



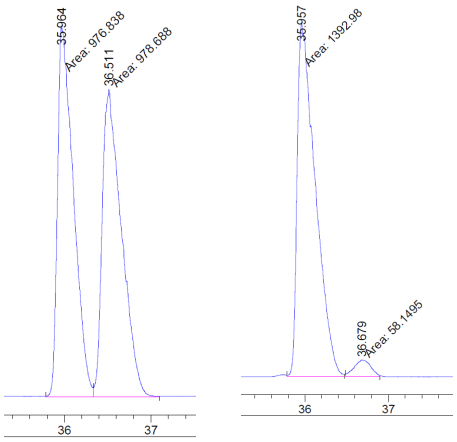
(R)-4-phenylbutane-1,2-diol (5). The diboration was performed according to the general procedure A with 4-phenyl-1-butene (26.44 mg, 0.20 mmol, 30.04 μL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as clear oil (29.9 mg, 92% yield). Spectral data and optical rotation are in

accordance with the literature report.[23] HRMS-(DART+) for C10H15O2 $[M+H]^+$: calculated: 167.1072, found: 167.108.

Analysis of Stereochemistry:

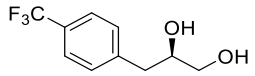
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 4-phenylbutane-1,2-diol prepared from dihydroxylation of 4-phenyl-1-butene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 120 °C 5min, then 0.5°C /min to 140°C, 20 psi)- analysis of the acetonide of 4-phenylbutane-1,2-diol.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.228	MM	0.2604	2155.20508	137.93863	96.27333
2	35.995	MM	0.2186	83.42645	6.36162	3.72667

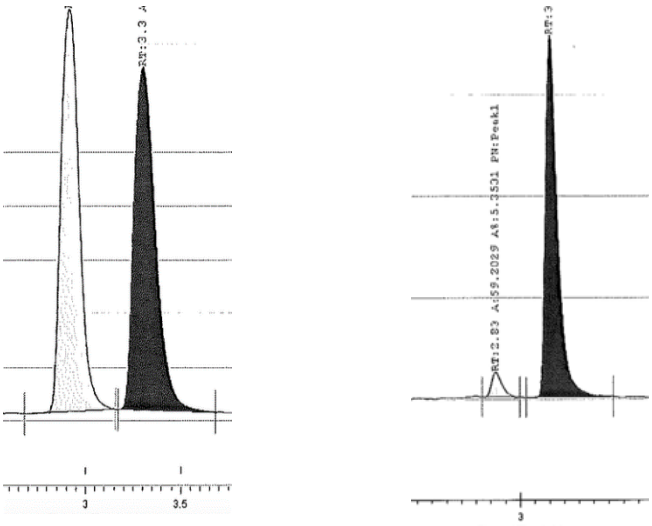


(R)-3-(4-(trifluoromethyl)phenyl)propane-1,2-diol (6). The diboration was performed according to the general procedure A with 1-allyl-4-(trifluoromethyl)benzene (37.24 mg, 0.20 mmol, 33.48 μL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (33.03 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.02 – 3.90 (m, 1H), 3.71 (d, *J* = 11.3 Hz, 1H), 3.52 (dd, *J* = 10.8, 7.1 Hz, 1H), 2.95 – 2.74 (m, 2H), 2.17 (s, 1H), 1.96 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.7, 132.3, 128.2, 128.1, 128.1, 128.1, 75.3, 68.6, 42.1. HRMS-(DART+) for $C_{10}H_{10}F_3O$ $[M\text{-}H_2O+H]^+$: calculated: 203.0684, found: 203.0691. IR (neat): 3353.92 (w), 2927.94(w), 1325.19(s), 1161.95(m), 1110.74(s), 1066.81(s), 1019.48(m). $[\alpha]_D^{20}$= +13.045 (c=1.0725, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

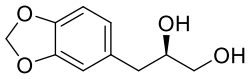
The 1,2-diol was compared to the racemic 3-(4-(trifluoromethyl)phenyl)propane-1,2-diol prepared from dihydroxylation of 1-allyl-4-(trifluoromethyl)benzene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel AS-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-(4-(trifluoromethyl)phenyl)propane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	5.3531	59.2029	2.83	12.2273	0.0027
2	94.6469	1046.7511	3.2	178.6614	0.003
Total:	100	1105.954			



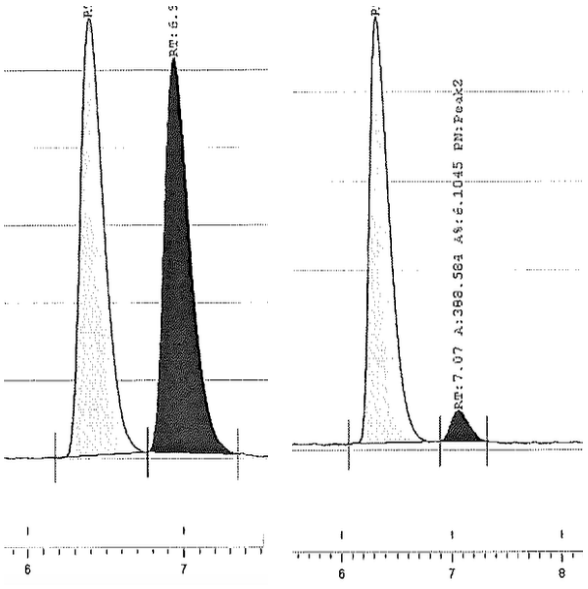
(R)-3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol (7). The diboration was performed according to the general procedure A with safrole (32.44 mg, 0.20 mmol, 29.60 μL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (34.53 mg, 88% yield). Spectral data and optical rotation are in accordance with the literature report.[64] HRMS-(DART+) for $C_{10}H_{11}O_3$ $[M\text{-}H_2O+H]^+$: calculated: 179.0708, found: 179.0715.

Analysis of Stereochemistry:

[64] Sawant, R. T.; Waghmode, S. B. *Synthetic Communications.* **2010**, *40*, 2269.

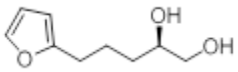
The 1,2-diol was compared to the racemic 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol prepared from dihydroxylation of safrole with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.8955	5976.94	6.31	475.5711	0.0084
2	6.1045	388.584	7.07	33.6678	0.0094
Total:	100	6365.524			



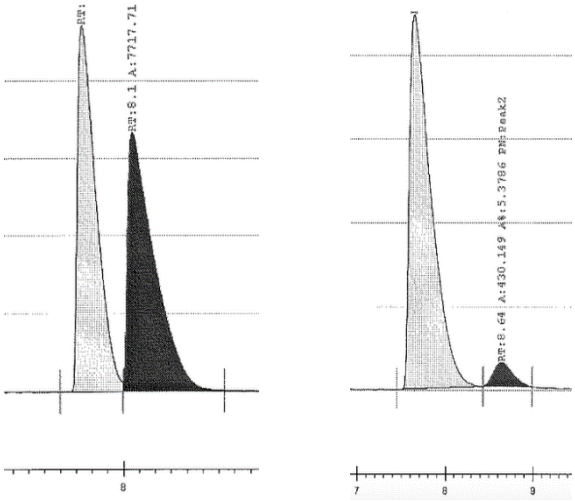
(R)-5-(furan-2-yl)pentane-1,2-diol (8). The diboration was performed according to the general procedure A with 2-(pent-4-en-1-yl)furan (27.22 mg, 0.20 mmol). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at

room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as clear oil (32.98 mg, 97% yield). Spectral data is in accordance with the literature report.[16] HRMS-(DART+) for C9H15O3 $[M+H]^+$: calculated: 171.1021, found: 171.1016. IR(neat): 3388.02(m), 2936.59(m), 2871.32(m), 1146.36(s), 1089.11(s), 1046.01(s), 600.19(w). $[\alpha]_D^{20}$= -11.958 (c=1.02, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

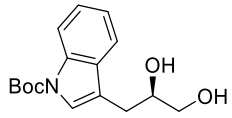
The 1,2-diol was compared to the racemic 5-(furan-2-yl)pentane-1,2-diol prepared from dihydroxylation of 2-(pent-4-en-1-yl)furan with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 5-(furan-2-yl)pentane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.6214	7567.2424	7.64	446.8813	0.0087
2	5.3786	430.149	8.64	28.7569	0.0098
Total:	100	7997.3914			

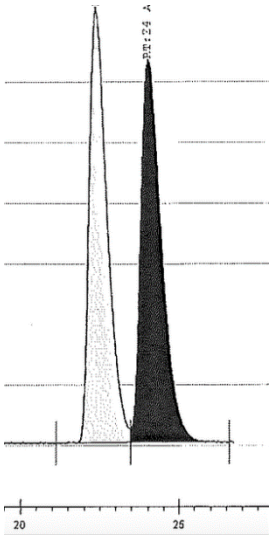


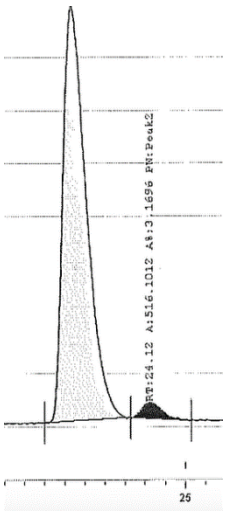
tert-butyl (R)-3-(2,3-dihydroxypropyl)-1H-indole-1-carboxylate (9). The diboration was performed according to the general procedure A with tert-butyl 3-allyl-1H-indole-1-carboxylate (51.47 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (49.50 mg, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* =7.7 Hz, 1H), 4.18 – 3.99 (m, 1H), 3.77 (ddd, *J* = 11.1, 6.4, 3.3 Hz, 1H), 3.59 (ddd, *J* = 11.1, 6.8, 5.4 Hz, 1H), 2.92 (ddd, *J* = 14.6, 5.3, 1.1 Hz, 1H), 2.87 (ddd, *J* = 14.6, 7.9, 0.9 Hz, 1H), 2.11 (s, 1H), 1.87 (s, 1H), 1.67 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.3, 138.3, 133.1, 127.2, 126.7, 125.2, 121.6, 119.0, 118.0, 86.3, 74.1, 68.9, 31.7, 30.9. HRMS-(DART+) for $C16H22NO_4$ $[M+H]^+$: calculated: 292.1549, found: 292.1541. IR (neat): 3349.53(br), 2977.24(w), 2930.89(w), 1726.44(s), 1451.24(s), 1308.41(s), 1225.24(s), 1024.74(s), 856.53(s), 766.87(s), 745.67(s). $[\alpha]_D^{20}$= +3.498 (c=1.086, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic tert-butyl-3-(2,3-dihydroxypropyl)-1H-indole-1-carboxylate prepared from dihydroxylation of tert-butyl 3-allyl-1H-indole-1-carboxylate with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl-3-(2,3-dihydroxypropyl)-1H-indole-1-carboxylate.

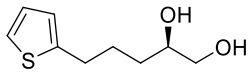




racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	96.8304	15766.7729	22.16	396.0168	0.0212
2	3.1696	516.1012	24.12	15.3297	0.0231
Total:	100	16282.8741			



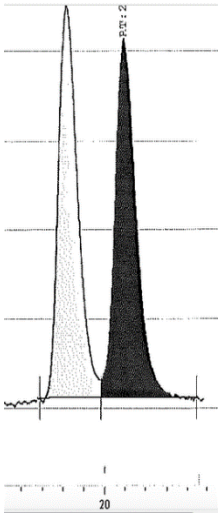
(R)-5-(thiophen-2-yl)pentane-1,2-diol (10). The diboration was performed according to the general procedure A with 2-(pent-4-en-1-yl)thiophene (30.45 mg, 0.20 mmol). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as clear oil (34.27 mg, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, J = 5.1, 1.2 Hz, 1H), 6.91 (dd, J = 5.1, 3.3 Hz, 1H), 6.79 (dt, J = 3.4, 1.0 Hz, 1H), 3.74 (dtd, J = 9.8, 6.5, 3.0 Hz, 1H), 3.65 (dd, J =

11.0, 3.1 Hz, 1H), 3.44 (dd, J = 11.0, 7.6 Hz, 1H), 2.87 (t, J = 7.5 Hz, 2H), 2.27 – 1.59 (m, 3H), 1.59 – 1.45 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 126.7, 124.2, 123.0, 72.0, 66.8, 32.4, 29.8, 27.7. HRMS-(DART+) for $C_9H_{13}OS$ $[M-H_2O+H]^+$: calculated: 169.0687, found: 169.0693. IR (neat): 3346.03(br), 2934.55(m), 2861.76(w), 1428.62(w), 1050.73(s), 870.95(w), 849.36(m), 823.85(w). $[\alpha]_D^{20}$= -1.598 (c=0.685, $CHCl_3$, l=50 mm).

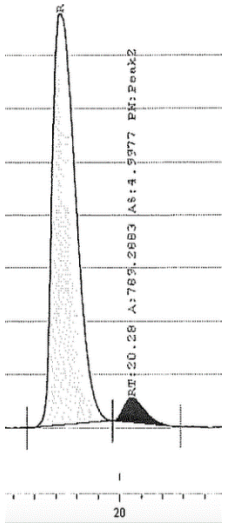
Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 5-(thiophen-2-yl)pentane-1,2-diol prepared from dihydroxylation of 2-(pent-4-en-1-yl)thiophene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 5-(thiophen-2-yl)pentane-1,2-diol.

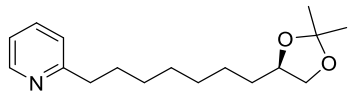


racemic product



diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	95.0023	15003.6324	18.6	386.6355	0.0262
2	4.9977	789.2883	20.28	23.4958	0.0286
Total:	100	15792.9207			

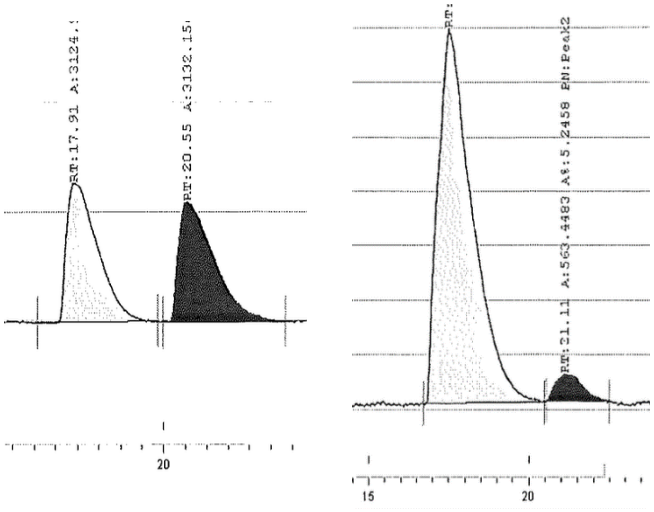


(R)-2-(7-(2,2-dimethyl-1,3-dioxolan-4-yl)heptyl)pyridine (11). The diboration was performed according to the general procedure A with 2-(non-8-en-1-yl)pyridine (40.67 mg, 0.20 mmol). The crude reaction mixture was dissolved in ethyl acetate (5 mL) and filtered through a short pad of silica gel with ethyl acetate (10ml). Solvent was then removed by rotatory evaporation. Because the product diol co-eluted with 1,3-propanediol, the resulting residue was treated with 2,2-dimethoxypropane (0.50 mL) and catalytic toluenesulfonic acid, then stirred at 60 ^{o}C for 30 min. Reaction mixture was filtered through a short pad of silica gel with 30% ethyl acetate in hexane. Solvents were removed by rotatory evaporation to afford the crude acetal product. The crude acetal product was purified on silica gel (10% ethyl acetate in hexanes) to afford the product as colorless oil (38.84 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.56 (td, *J* = 7.6, 1.9 Hz, 1H), 7.11 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 4.14 – 3.93 (m, 2H), 3.50 – 3.43 (m, 1H), 2.81 – 2.70 (m, 2H), 1.77 – 1.55 (m, 4H), 1.38 (s, 3H), 1.37 – 1.26 (m, 13H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 151.8, 138.8, 125.3, 123.5, 111.2, 78.8, 72.2, 41.1, 36.2, 32.5, 32.2, 32.0, 31.9, 29.6, 28.41, 28.37. HRMS-(DART+) for $C_{14}H_{22}NO$ $[M\text{-}H_2O+H]^+$: calculated: 220.1701, found: 220.1705. IR (neat): 2984.46(w), 2928.68(s), 2855.59(m), 1589.88(m), 1568.79(w), 1473.87(m), 1434.04(m), 1377.75(m), 1368.34(m), 1213.79(m), 1058.04(s). $[\alpha]_D^{20}$= -10.870 (c=1.02, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

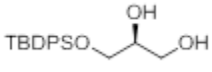
The acetal was compared to the racemic 2-(7-(2,2-dimethyl-1,3-dioxolan-4-yl)heptyl)pyridine prepared from dihydroxylation of 2-(non-8-en-1-yl)pyridine with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel AD-H, 3% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 2-(7-(2,2-dimethyl-1,3-dioxolan-4-yl)heptyl)pyridine.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.7542	10177.4096	17.48	137.4022	0.0185
2	5.2458	563.4483	21.11	9.7609	0.0223
Total:	100	10740.8579			



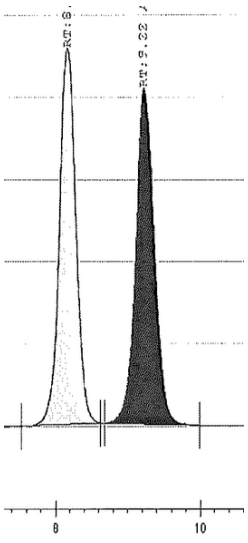
(S)-3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol (12). The diboration was performed according to the general procedure A with (allyloxy)(tert-butyl)diphenylsilane (59.30 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as white solid (52.22 mg, 79% yield). ^{1}H NMR

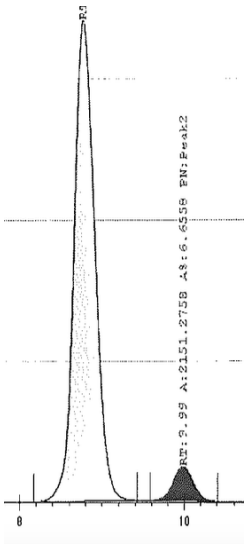
(600 MHz, $CDCl_3$) δ 7.69 – 7.62 (m, 4H), 7.47 – 7.42 (m, 2H), 7.42 – 7.38 (m, 4H), 3.87 – 3.58 (m, 5H), 2.55 (d, J = 5.3 Hz, 1H), 1.93 (t, J = 6.1 Hz, 1H), 1.07 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.5, 135.5, 132.9, 132.8, 129.9, 129.9, 127.9, 127.8, 71.9, 71.8, 65.2, 63.8, 26.9, 26.9, 26.8, 19.2. HRMS-(DART+) for $C_{19}H_{27}O_3Si$ $[M+H]^+$: calculated: 331.1730, found: 331.1731. IR (neat):3392.72(br), 3071.05(w), 3048.48(w), 2999.17(m), 2930.34(m), 2857.66(m), 1427.57(m), 1112.13(s), 823.82(m), 740.33(m), 701.55(s), 613.59(m). $[\alpha]_D^{20}$= -4.650 (c=1.213, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol prepared from dihydroxylation of (allyloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol.

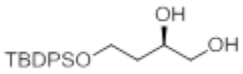




racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.7193	14564.0959	8.16	914.0679	0.0136
2	50.2807	14728.5662	9.22	815.9865	0.0154
Total:	100	29292.6621			

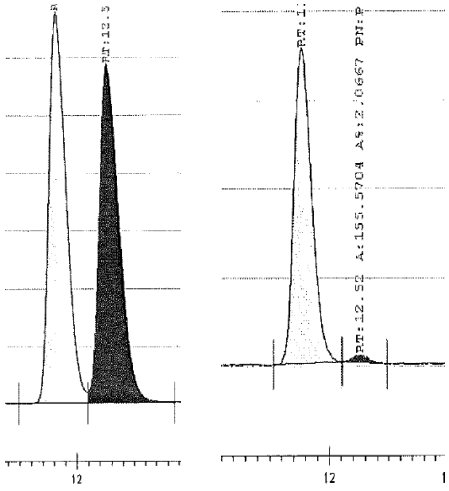


(R)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol (13). The diboration was performed according to the general procedure A with (but-3-en-1-yloxy)(tert-butyl)diphenylsilane (62.10 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as white solid (61.33 mg, 89% yield). Spectral data and optical rotation are in accordance with literature report.[23] HRMS-(DART+) for $C_{20}H_{29}O_3Si$ $[M+H]^+$: calculated: 345.1886, found: 345.1895. IR (neat): 3392.72(br), 3071.05(w), 3048.48(w), 2999.17(m), 2930.34(m), 2857.66(m), 1471.82(m), 1112.13(s), 823.82(m), 740.33(m), 701.55(s), 613.59(m), 505.32(m), 489.90(m).

Analysis of Stereochemistry:

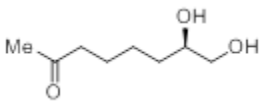
The 1,2-diol was compared to the 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol prepared from dihydroxylation of (but-3-en-1-yloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[13] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	97.9333	7371.9665	11.54	353.533	0.0092
2	2.0667	155.5704	12.52	8.819	0.01
Total:	100	7527.5369			



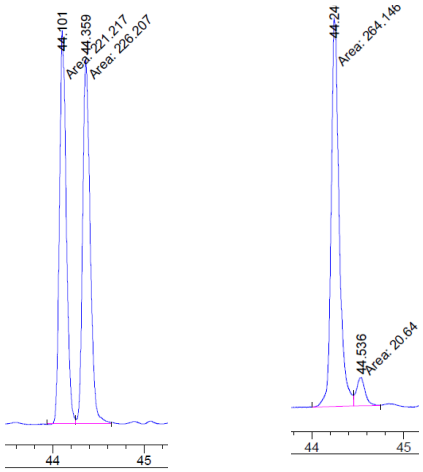
(R)-7,8-dihydroxyoctan-2-one (14). The diboration was performed according to the general procedure A with oct-7-en-2-one (25.24 mg, 0.20 mmol). The crude reaction

mixture was purified on silica gel (80% ethyl acetate in hexanes) to afford the product as clear oil (22.43 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 – 3.68 (m, 1H), 3.64 (dd, J = 11.1, 3.1 Hz, 1H), 3.43 (dd, J = 11.0, 7.6 Hz, 1H), 2.45 (t, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.68 – 1.50 (m, 2H), 1.51 – 1.28 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.1, 76.7, 71.9, 66.8, 43.5, 32.8, 29.9, 25.0, 23.5. HRMS-(DART+) for $C_8H_{15}O_3$ $[M+H]^+$: calculated: 159.1021, found: 159.1017. IR (neat): 3398.9 (br s), 2926.2 (s), 2858.8 (m), 1706.4 (s), 1459.5 (w), 1408.9 (w), 1363.0 (m), 1163.4 (w), 1054.2 (m), 599.8 (w). $[\alpha]_D^{20}$= -3.587 (c=1.150, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

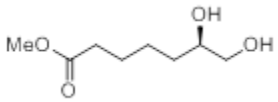
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 7,8-dihydroxyoctan-2-one prepared from dihydroxylation of oct-7-en-2-one with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 70 °C 5min, 2°C/min to 180°C, 20 psi)- analysis of the acetonide of 7,8-dihydroxyoctan-2-one.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	44.240	MF	0.1013	264.14587	43.46013	92.75245
2	44.536	FM	0.1091	20.64001	3.15330	7.24755



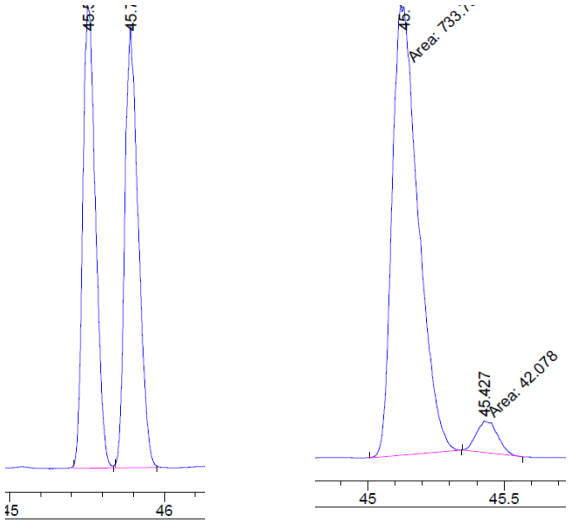
methyl (R)-6,7-dihydroxyheptanoate (15). The diboration was performed according to the general procedure A with methyl hept-6-enoate (28.44 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (ethyl acetate) to afford the product as clear oil (33.48 mg, 95% yield). Spectral data and optical rotation are in accordance with literature report.[65] HRMS-(DART+) for $C_8H_{17}O_4$ $[M+H]^+$: calculated: 177.1127, found: 177.1129. IR (neat): 3376.11(br), 2936.54(m), 2864.97(m), 1734.23(s), 1437.01(m), 1200.46(s), 1174.54(s), 1104.72(s), 1052.86(s), 1016.51(s).

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 6,7-dihydroxyheptanoate prepared from dihydroxylation of methyl hept-6-enoate with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

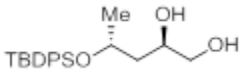
Chiral GLC (β-dex, Supelco, 70 °C 5min, 2°C/min to 180°C, 20 psi)- analysis of the acetonide of 6,7-dihydroxyheptanoate.

[65] Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	45.132	MM	0.1115	733.78345	109.71555	94.57661
2	45.427	MM	0.0911	42.07802	7.70144	5.42339

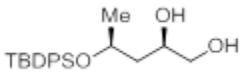


(2R,4R)-4-((tert-butyldiphenylsilyl)oxy)pentane-1,2-diol (17). The diboration was performed according to the general procedure A with (R)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane (64.91 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexane) to afford the product as clear oil (52.35 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 4H), 7.48 – 7.35 (m, 6H), 4.28 – 4.17 (m, 1H), 4.12 – 4.03 (m, 1H), 3.57 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.41 (dd, *J* = 11.1, 6.6 Hz, 1H), 1.77 (ddd, *J* = 14.4, 10.4, 4.0 Hz, 1H), 1.44 (dddd, *J* = 14.4, 5.3, 2.5, 1.1 Hz,

1H), 1.14 (d, *J* = 6.3 Hz, 3H), 1.07 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6, 138.53, 138.49, 138.45, 136.43, 135.9, 132.6, 132.5, 130.43, 130.42, 130.3, 130.2, 71.6, 71.2, 70.0, 43.0, 29.71, 29.65, 29.62, 25.3, 21.8. HRMS-(DART+) for $C_{21}H_{31}O_3Si$ $[M+H]^+$: calculated: 359.2042, found: 359.205. IR (neat): 3364.08(br), 3070.82(w), 3049.21(w), 2960.86(m), 2930.57(m), 2857.04(m), 1427.21(m), 1108.09(s), 1065.27(m), 1037.05(m), 1006.08(m), 821.74(s), 701.38(m), 611.06(s). $[a]_D^{20}$= -1.406 (c=0.972, $CHCl_3$, l=50 mm).

Proof of stereochemistry:

The relative configuration was assigned by comparison of the ^{13}C NMR and ^{1}H NMR spectrum with that reported in the literature.[66]



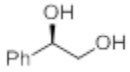
(2R,4S)-4-((tert-butyldiphenylsilyl)oxy)pentane-1,2-diol (18). The diboration was performed according to the general procedure A with (S)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane (64.91 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexane) to afford the product as clear oil (55.94 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.65 (m, 4H), 7.54 – 7.32 (m, 6H), 4.19 – 4.09 (m, 1H), 3.93 (ddt, *J* = 8.9, 6.8, 3.5 Hz, 1H), 3.57 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.41 (dd, *J* = 11.1, 6.5 Hz, 1H), 1.74 (ddd, *J* = 14.3, 8.9, 8.1 Hz, 1H), 1.55 (ddd, *J* = 14.3, 4.5, 3.5 Hz, 1H), 1.05 (s, 9H), 1.03 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6, 138.50, 138.48, 138.44, 136.9, 136.1, 132.5, 132.3, 130.43, 130.42, 130.3, 130.2, 73.5, 72.5, 69.5, 44.8, 29.6, 29.1, 26.6, 21.8. HRMS-(DART+) for $C_{21}H_{31}O_3Si$ $[M+H]^+$: calculated: 359.2042, found: 359.2043. IR (neat): 3364.08(br), 3070.82(w), 3049.21(w),

[66] Kumar, P.; Gupta, P.; Vasudeva Naida, S.; *Chem. Eur. J.* **2006**, *12*, 1397.

2960.86(m), 2930.57(m), 2857.04(m), 1427.21(m), 1108.09(s), 1065.27(m), 1037.05(m), 1006.08(m), 821.74(s), 701.38(m), 611.06(s). $[\alpha]_D^{20}$= -16.026 (c=0.967, $CHCl_3$, l=50 mm).

Proof of stereochemistry:

The relative configuration was assigned by comparison of the ^{13}C NMR and ^{1}H NMR spectrum with that reported in the literature[26].



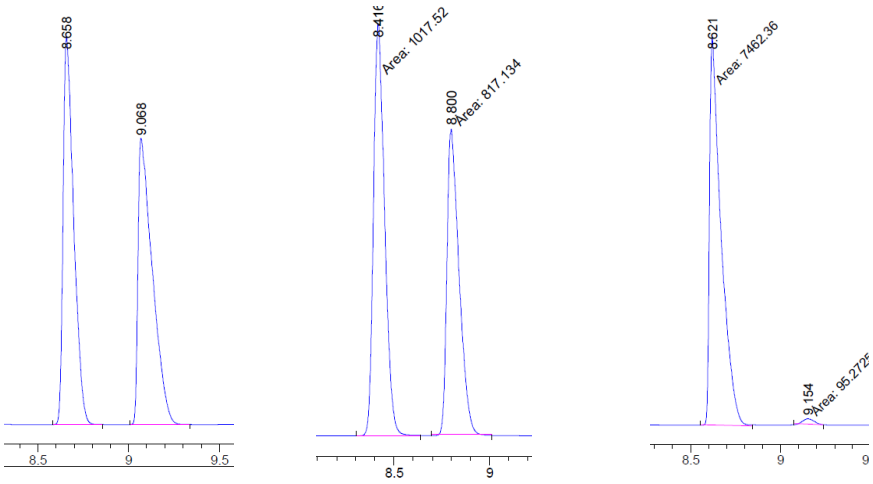
(R)-1-phenylethane-1,2-diol (19). The diboration was performed according to the general procedure A with styrene (20.83 mg, 0.20 mmol). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (16.58 mg, 60% yield). Spectral data is in accordance with literature report.[18] HRMS-(DART+) for C_8H_9O $[M-H_2O+H]^+$: calculated: 121.0653, found: 121.0659.

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-phenylethane-1,2-diol prepared from dihydroxylation of styrene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy. The authentic (*R*)-

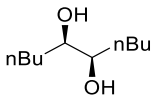
isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-tetradecene utilizing AD-mix-β.[21]

Chiral GLC (β-dex, Supelco, 140 °C 15min, 20 psi)- analysis of the acetonide of 1-phenylethane-1,2-diol



racemic product diboration product sharpless dihydroxylation product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.416	MM	0.0673	1017.51855	251.94304	55.46110
2	8.800	MM	0.0729	817.13422	186.89059	44.53890



(5R,6R)-decane-5,6-diol (20). The diboration was performed according to the general procedure C with (E)-dec-5-ene (28.05 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (25% ethyl acetate in hexanes) to afford the product as white solid (31.0 mg, 89% yield). Spectral data is in accordance with literature report.[67] HRMS-

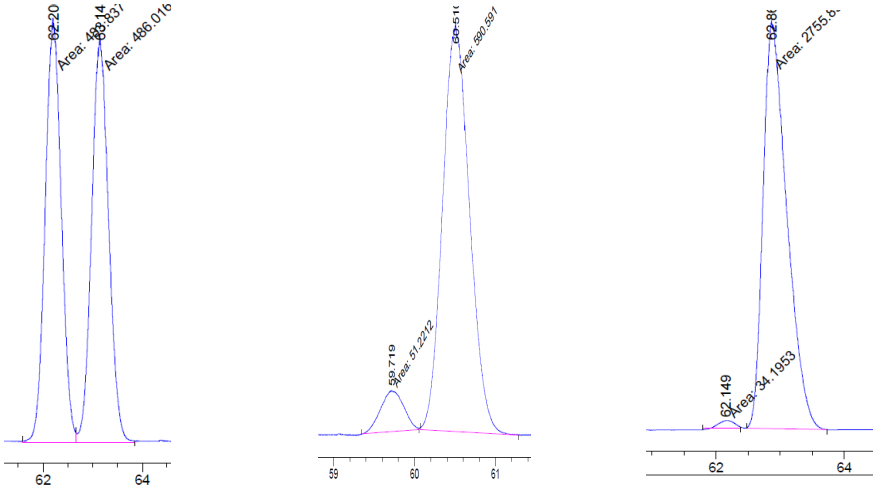
[67] Dobler, C.; Mehltretter, G. M.; Sundermeier, U.; Beller, M. *J. Am. Chem. Soc.* **2000**, *122*, 10289.

(DART+) for $C_{10}H_{21}O$ $[M\text{-}H_2O+H]^+$: calculated: 157.1592, found: 157.1589. IR (neat): 3347.86(br), 2955.18(s), 2929.84(s), 2858.41(s), 14.63.88(m), 1144.86(m), 1117.08(m), 1069.11(m), 1048.42(s), 1001.50(m). $[\alpha]_D^{20}$= +24.662 (c=1.195, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

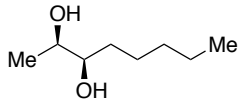
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of decane-5,6-diol prepared from dihydroxylation of (E)-dec-5-ene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy. The authentic (*R*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of (E)-dec-5-ene utilizing AD-mix-β.[21]

Chiral GLC (β-dex, Supelco, 70 °C 15min, 0.25°C/min to 90 °C 20 psi)- analysis of the acetonide of decane-5,6-diol.



racemic product diboration product sharpless dihydroxylation product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	59.719	MM	0.3277	51.22122	2.60471	7.98071
2	60.510	MM	0.3821	590.59149	25.76274	92.01929

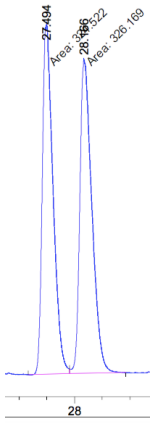


(2R,3R)-octane-2,3-diol (21). The diboration was performed according to the general procedure C with (E)-oct-2-ene (22.4 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as clear oil (24.2 mg, 83% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.58 (p, J = 6.3 Hz, 1H), 3.37 – 3.29 (m, 1H), 2.11 (s, 2H), 1.56 – 1.44 (m, 2H), 1.44 – 1.22 (m, 6H), 1.18 (d, J = 6.3 Hz, 3H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 76.5, 71.1, 33.6, 32.1, 25.5, 22.8, 19.7, 14.2. HRMS-(DART+) for $C_8H_{19}O_2$ $[M+H]^+$: calculated: 147.1385, found: 147.1379. IR (neat): 3356.13(br), 2955.49(s), 2928.07(s), 2858.13(s), 1458.61(m), 1375.80(m), 1057.67(s). $[\alpha]_D^{20}$= +14.579 (c=1.135, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

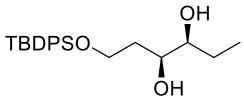
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-2,3-diol prepared from dihydroxylation of (E)-oct-2-ene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 70 °C 15min, 0.25°C/min to 90 °C 20 psi)- analysis of the acetonide of (2R,3R)-octane-2,3-diol.



Racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	27.436	MF	0.1790	246.94102	22.99488	10.15166
2	27.796	FM	0.3999	2185.57837	91.07913	89.84834



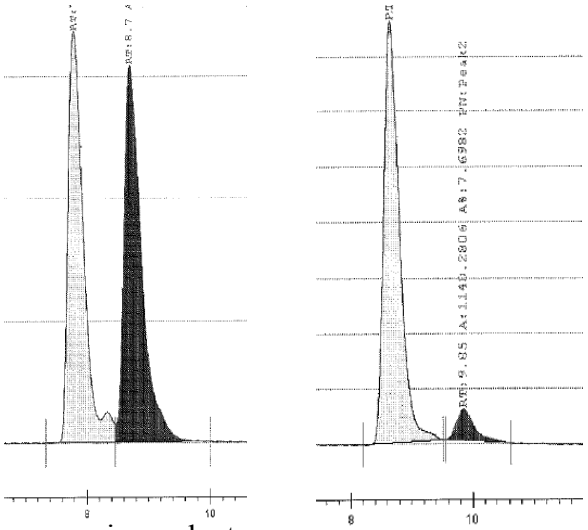
(3S,4S)-1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol (22). The diboration was performed according to the general procedure C with (E)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane (67.71 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (25% ethyl acetate in hexanes) to afford the product as clear oil (52.91 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 4H), 7.52 – 7.35 (m, 6H), 3.89 (d, J = 6.2 Hz, 2H), 3.77 (ddd, J = 9.0, 4.8, 2.9 Hz, 1H), 3.38 (dt, J = 8.8, 4.5 Hz, 1H), 1.83 (ddt, J = 15.3, 9.1, 6.3 Hz, 1H), 1.69 (dtd, J = 14.4, 4.7, 2.9 Hz, 1H), 1.65 – 1.40 (m, 2H), 1.06 (s, 9H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.20, 138.17,

135.6, 135.5, 132.6, 132.54, 130.48, 78.4, 76.2, 65.5, 37.8, 29.5, 29.0, 21.7, 12.8. HRMS-(DART+) for $C_{22}H_{33}O_3Si$ $[M+H]^+$: calculated: 373.2199, found: 373.2202. IR (neat): 3380.43(br), 3070.65(w), 3049.63(w), 2930.36(m), 2857.15(m), 1471.68(w), 1427.52(m), 1390.03(w), 1361.20(w), 1110.38(s), 701.43(s), 504.73(s). $[\alpha]_D^{20}$= -5.074 (c=1.0, $CHCl_3$, l=50 mm).

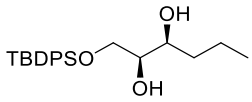
Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol prepared from dihydroxylation of (E)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol.



Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	92.3018	13672.0097	8.64	759.236	0.007
2	7.6982	1140.2806	9.85	56.7644	0.008
Total:	100	14812.2903			

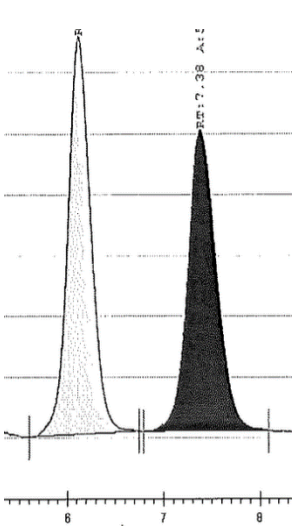


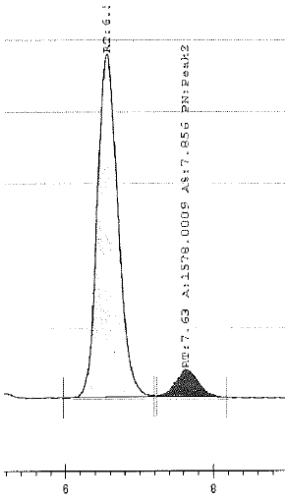
(2S,3S)-1-((tert-butyldiphenylsilyl)oxy)hexane-2,3-diol (23). The diboration was performed according to the general procedure C with (E)-tert-butyl(hex-2-en-1-yloxy)diphenylsilane (67.71 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (25% ethyl acetate in hexanes) to afford the product as clear oil (37.26 mg, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 4H), 7.50 – 7.36 (m, 6H), 3.79 (dd, *J* = 10.5, 4.0 Hz, 1H), 3.73 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.69 – 3.63 (m, 1H), 3.56 – 3.48 (m, 1H), 2.69 (d, *J* = 6.0 Hz, 1H), 2.59 (d, *J* = 4.3 Hz, 1H), 1.58 – 1.28 (m, 4H), 1.08 (s, 9H), 0.91 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ135.6, 135.5, 132.7, 130.0, 127.9, 73.4, 71.7, 66.3, 35.6, 26.9, 19.2, 18.7,14.0. HRMS-(DART+) for $C_{22}H_{33}O_3Si$ $[M+H]^+$: calculated: 373.2199, found: 373.2178. IR (neat): 3395.09(br), 3070.93(w), 2957.15(s), 2930.68(s), 2858.00(s), 1471.90(w), 1427.90(s), 1113.87(s), 708.13(s). $[\alpha]_D^{20}$= +1.2890 (c=1.26, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic1-((tert-butyldiphenylsilyl)oxy)hexane-2,3-diol prepared from dihydroxylation of (E)-tert-butyl(hex-2-en-1-yloxy)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

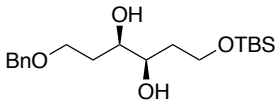
Chiral SFC (Chiracel OJ-H, 3% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-((tert-butyldiphenylsilyl)oxy)hexane-2,3-diol.





racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	92.144	18508.5084	6.57	954.7038	0.0095
2	7.856	1578.0009	7.63	75.3119	0.0111
Total:	100	20086.5093			



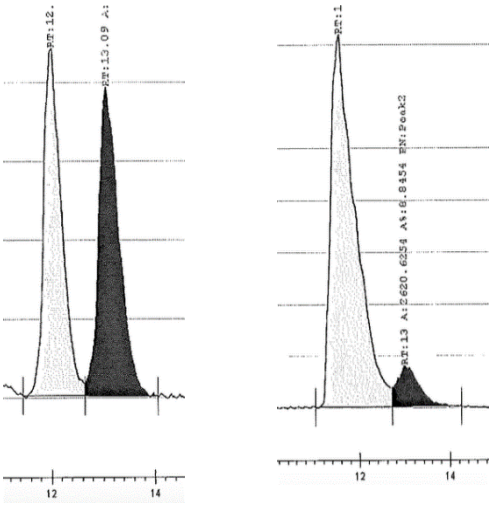
(3R,4R)-1-(benzyloxy)-6-((tert-butyldimethylsilyl)oxy)hexane-3,4-diol (25). The diboration was performed according to the general procedure C with (E)-((6-(benzyloxy)hex-3-en-1-yl)oxy)(tert-butyl)dimethylsilane (64.11 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as clear oil (52.4 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 (s, 2H), 3.91 – 3.77 (m, 2H), 3.76 – 3.60 (m, 4H), 3.45 (s, 1H), 3.09 (s, 1H), 1.96 – 1.61 (m, 4H), 0.88 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.3, 128.6, 127.9, 73.8, 73.5, 73.0, 68.4, 61.9, 35.4, 33.3, 26.0, 18.3, -5.3, -5.3. HRMS-(DART+) for $C_{19}H_{35}O_4Si$ $[M+H]^+$: calculated: 355.2305, found: 355.2318. IR (neat): 3424.04(br), 2952.80(m),

2927.46(m), 2856.16(m), 1253.92(m), 1090.05(s), 834.88(s), 811.67(s). $[\alpha]_D^{20}$= -1.002 (c=1.000, $CHCl_3$, l=50 mm)

Analysis of Stereochemistry:

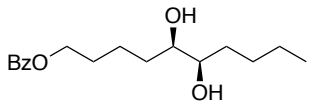
The 1,2-diol was compared to the racemic (3R,4R)-1-(benzyloxy)-6-((tert-butyldimethylsilyl)oxy)hexane-3,4-diol prepared from dihydroxylation of (E)-((6-(benzyloxy)hex-3-en-1-yl)oxy)(tert-butyl)dimethylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OJ-H, 2% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (3R,4R)-1-(benzyloxy)hexane-3,4-diol.



Racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	91.1546	27006.4746	11.61	716.8822	0.0121
2	8.8454	2620.6254	13	77.8071	0.0136
Total:	100	29627.1			

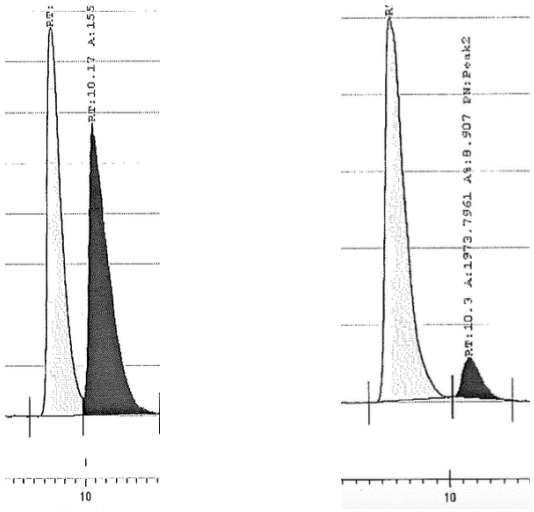


(5R,6R)-5,6-dihydroxydecyl benzoate (26). The diboration was performed according to the general procedure C with (E)-dec-5-en-1-yl benzoate (52.76 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as clear oil (45.9 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.2 Hz, 2H), 7.56 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 7.5 Hz, 2H), 4.35 (t, J = 6.6 Hz, 2H), 3.58 – 3.30 (m, 2H), 2.06 (d, J = 4.1 Hz, 1H), 1.93 (s, 1H), 1.82 (tdd, J = 12.8, 7.4, 5.6 Hz, 2H), 1.74 – 1.27 (m, 10H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 133.1, 130.6, 129.7, 128.5, 74.7, 74.5, 65.1, 33.5, 33.4, 29.0, 28.0, 22.9, 22.5, 14.2. HRMS-(DART+) for $C_{17}H_{27}O_4$ $[M+H]^+$: calculated: 295.1909, found: 295.1905. IR (neat): 3356.13(br), 2928.07(s), 2858.13(s), 1458.61(m), 1375.80(m), 1057.67(s). $[\alpha]_D^{20}$= +14.676 (c=1.09, $CHCl_3$, l=50 mm)

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic (5R,6R)-5,6-dihydroxydecyl benzoate prepared from dihydroxylation of (E)-dec-5-en-1-yl benzoate with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

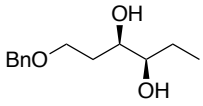
Chiral SFC (Chiracel ODR-H, 7% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (5R,6R)-5,6-dihydroxydecyl benzoate.



Racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	91.093	20186.277	9.15	997.1616	0.0101
2	8.907	1973.7961	10.3	104.7765	0.0114
Total:	100	22160.0731			



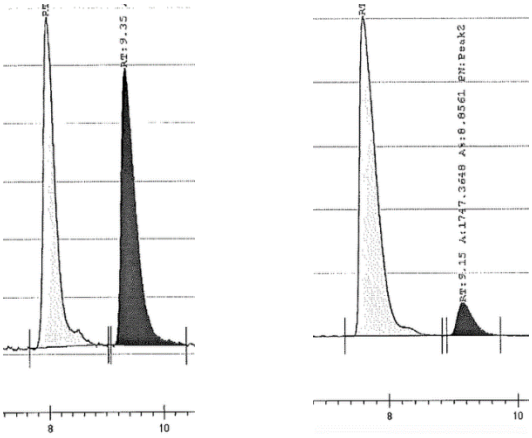
(3R,4R)-1-(benzyloxy)hexane-3,4-diol (27). The diboration was performed according to the general procedure C with (E)-((hex-3-en-1-yloxy)methyl)benzene (38.06 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as clear oil (41.3 mg, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 4H), 4.52 (s, 1H), 3.90 – 3.55 (m, 3H), 3.48 – 3.23 (m, 1H), 3.13 (s, 1H), 2.47 (s, 1H), 2.05 – 1.69 (m, 2H), 1.66 – 1.36 (m, 2H), 0.97 (d, J = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.4, 131.1, 130.5, 130.4, 78.4, 76.03, 76.01, 71.1,

35.9, 29.0, 12.8. HRMS-(DART+) for $C_{13}H_{21}O_3$ $[M+H]^+$: calculated: 225.1491, found: 225.1501. IR (neat): 3424.04(br), 2952.79(s), 2927.45(s), 2856.16(m), 1253.94(m), 1090.08(s), 834.88(s), 811.68(s). $[\alpha]_D^{20}$= +1.086 (c=1.105, $CHCl_3$, l=50 mm)

Analysis of Stereochemistry:

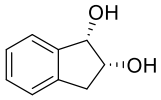
The 1,2-diol was compared to the racemic (3R,4R)-1-(benzyloxy)hexane-3,4-diol prepared from dihydroxylation of (E)-((hex-3-en-1-yloxy)methyl)benzene with ruthenium trichloride and sodium periodiate.[13] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (3R,4R)-1-(benzyloxy)hexane-3,4-diol.



Racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	91.1439	17983.244	7.61	1002.8404	0.0074
2	8.8561	1747.3648	9.15	101.161	0.0089
Total:	100	19730.6088			

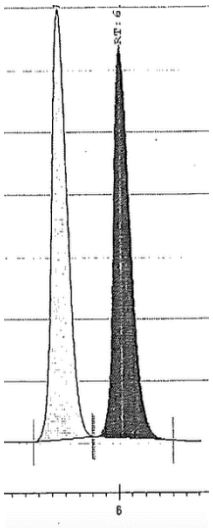


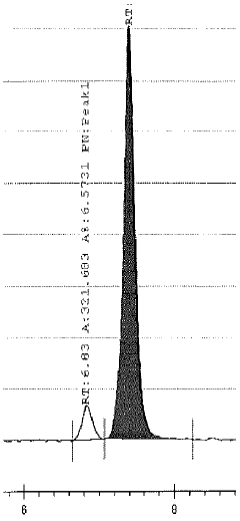
(1S,2R)-2,3-dihydro-1H-indene-1,2-diol (28). The diboration was performed according to the general procedure C with indene (23.23 mg, 0.20 mmol). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (15.02 mg, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dt, *J* = 5.7, 3.2 Hz, 1H), 7.35 – 7.20 (m, 3H), 5.00 (d, *J* = 5.0 Hz, 1H), 4.51 (s, 1H), 3.13 (ddd, *J* = 16.3, 5.9, 3.7 Hz, 1H), 2.96 (dt, *J* = 16.4, 3.6 Hz, 1H), 2.51 (s, 1H), 2.43 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 128.9, 127.2, 125.4, 125.0, 76.0, 73.5, 38.7. HRMS-(DART+) for C_9H_9O $[M\text{-}H_2O+H]^+$: calculated: 133.0653, found: 133.0659. IR (neat): 3314.86(br), 3070.24(w), 3046.34(w), 3023.68(w), 2950.25(w), 2927.07(w), 1404.80(w), 1260.64(m), 1154.55(m), 1110.66(s), 1069.97(s), 1045.31(m), 734.37(s). $[\alpha]_D^{20}$= -35.252 (c=1.115, $CHCl_3$, l=50 mm).

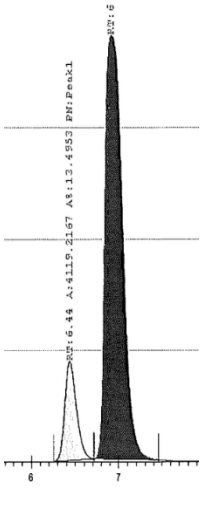
Analysis of Stereochemistry:

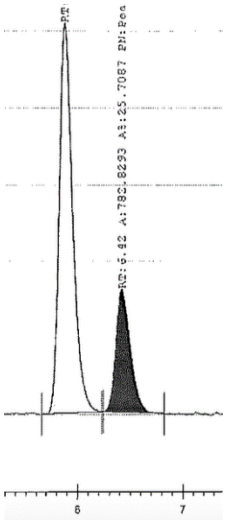
The 1,2-diol was compared to the racemic 2,3-dihydro-1H-indene-1,2-diol prepared from dihydroxylation of indene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy. The authentic (*1R, 2S*)-isomer was prepared from the Sharpless asymmetric dihydroxylation of indene utilizing AD-mix-β.[21]

Chiral SFC (Chiracel OJ-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 2,3-dihydro-1H-indene-1,2-diol.



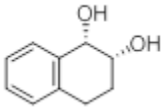






Racemic product diboration product coinjection sharpless dihyroxylation

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	6.5731	321.683	6.83	33.3762	0.0058
2	93.4269	4572.2383	7.4	401.4721	0.0063
Total:	100	4893.9213			



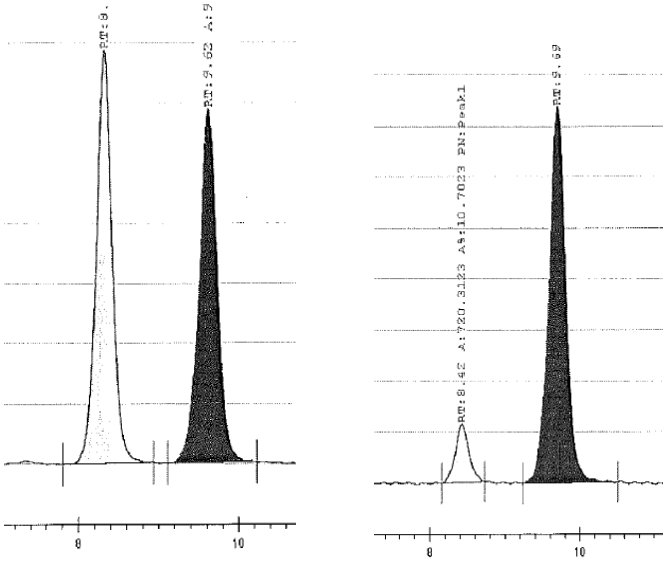
(1S,2R)-1,2,3,4-tetrahydronaphthalene-1,2-diol (29). The diboration was performed according to the general procedure C with 1,2-dihydronaphthalene (26.04 mg, 0.20 mmol). To remove the catalyst, the crude reaction mixture was treated with TBAF (1.0 M in THF, 0.20 mL) at room temperature and stirred for 0.5h. The reaction mixture was then concentrated by rotary evaporation, and the resulting crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (18.06 mg,

55% yield). Spectral data and optical rotation are in accordance with literature report.[68] HRMS-(DART+) for $C_{10}H_{11}O$ $[M\text{-}H_2O+H]^+$: calculated: 147.081, found: 147.0811.

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 1,2,3,4-tetrahydronaphthalene-1,2-diol prepared from dihydroxylation of 1,2-dihydronaphthalene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

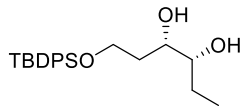
Chiral SFC (Chiracel OJ-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1,2,3,4-tetrahydronaphthalene-1,2-diol



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	10.7023	720.3123	8.42	56.6425	0.0075
2	89.2977	6010.142	9.69	368.5802	0.0087
Total:	100	6730.4543			

[68] Zang, C.; Liu, Y.; Xu, Z.; Tse, C.; Guan, X.; Wei, J.; Huang, J.; Che, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 10253.

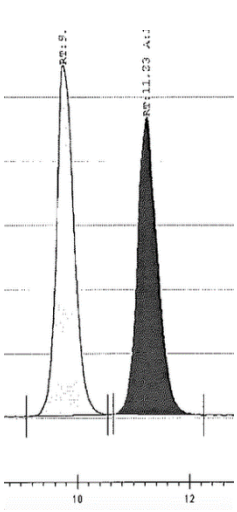


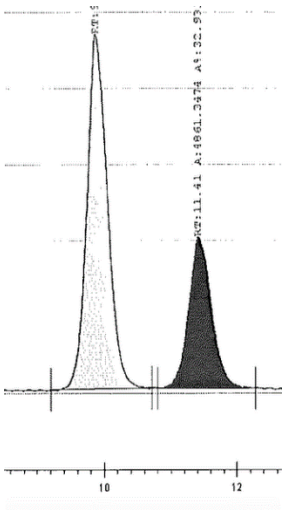
(3R,4S)-1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol (30). The diboration was performed according to the general procedure C with (Z)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane (67.71 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (25% ethyl acetate in hexanes) to afford the product as clear oil (43.22 mg, 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 – 7.62 (m, 4H), 7.56 – 7.31 (m, 6H), 4.06 – 3.77 (m, 3H), 3.71 – 3.42 (m, 2H), 2.30 (d, *J* = 4.2 Hz, 1H), 1.92 – 1.77 (m, 1H), 1.65 (dddd, *J* = 14.6, 4.9, 3.4, 2.4 Hz, 1H), 1.55 – 1.42 (m, 2H), 1.06 (s, 9H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.2, 135.5, 135.4, 132.57, 132.55, 130.5, 79.3, 78.4, 77.0, 66.1, 34.7, 29.4, 27.7, 21.7, 13.0. HRMS-(DART+) for $C_{22}H_{33}O_3Si$ $[M+H]^+$: calculated: 373.2199, found: 373.221. IR (neat): 3384.76(br), 2958.53(m), 2930.28(m), 2856.85(m), 1471.75(w), 1427.68(m), 1390.09(w), 1361.33(w), 1112.05(s), 1079.47(s), 704.14(s).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol prepared from dihydroxylation of (Z)-tert-butyl(hex-3-en-1-yloxy)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OJ-H, 3% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-((tert-butyldiphenylsilyl)oxy)hexane-3,4-diol.



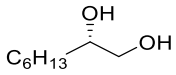


racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	67.0682	9900.5327	9.85	465.3841	0.0101
2	32.9318	4861.3474	11.41	198.0105	0.0117
Total:	100	14761.8801			

F. Full Characterizations and Proof of Stereochemistry (with DHR catalyst)

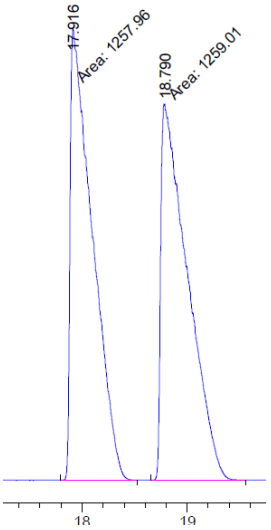


(S)-octane-1,2-diol (1). The diboration was performed according to the general procedure B with 1-octene (22.44 mg, 0.20 mmol, 32.4 μL). The crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (28.30 mg, 97% yield). Spectral data and optical rotation are in accordance with the literature report.[18] HRMS-(DART+) for C8H22NO2 $[M+NH_4]^+$: calculated: 164.1651, found: 164.1655.

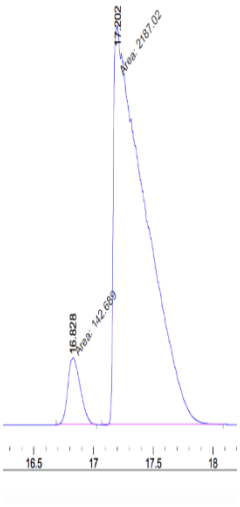
Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 100 °C 30min, 20 psi)- analysis of the acetonide of octane-1,2-diol.

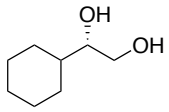


racemic product



diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	16.828	MM	0.1204	142.68919	19.75522	6.12477
2	17.202	MM	0.3076	2187.01807	118.51307	93.87523
Totals :				2329.70726	138.26829	

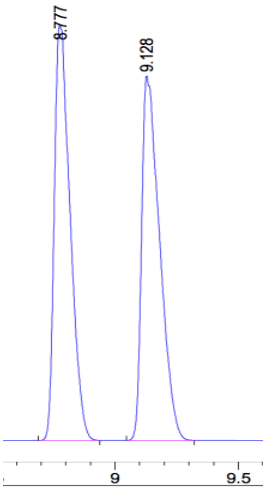


(S)-1-cyclohexylethane-1,2-diol (3). The diboration was performed according to the general procedure B with vinyl cyclohexane (22.04 mg, 0.20 mmol, 27.4 μL). The crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (23.9 mg, 83% yield). Spectral data and optical rotation are in accordance with the literature report.[22] HRMS-(DART+) for $C_8H_{15}O$ $[M+H-H_2O]^+$: calculated:127.1123, found:127.1117.

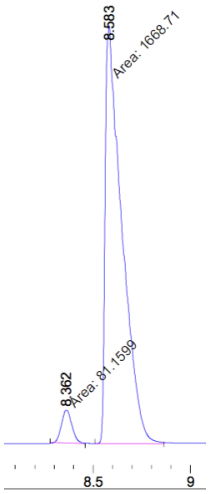
Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from dihydroxylation of vinyl cyclohexane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy

Chiral GLC (β-dex, Supelco, 130 °C 20 min)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol

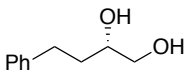


racemic product



diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.362	MM	0.0616	81.15990	21.95622	4.63806
2	8.583	MM	0.0996	1668.70691	279.33691	95.36194

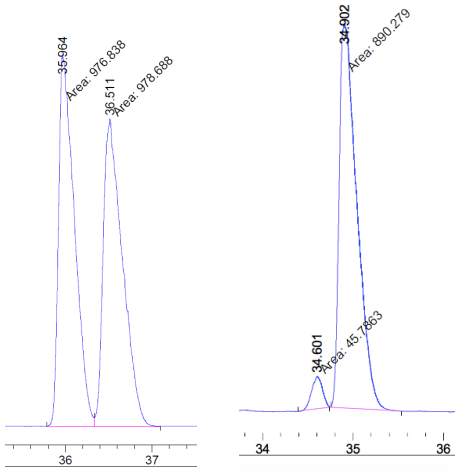


(S)-4-phenylbutane-1,2-diol (5). The diboration was performed according to the general procedure B with 4-phenyl-1-butene (26.44 mg, 0.20 mmol, 30.04 µL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as clear oil (31.54 mg, 97% yield). Spectral data and optical rotation are in accordance with the literature report.[23] HRMS-(DART+) for C10H15O2 $[M+H]^+$: calculated: 167.1072, found: 167.108.

Analysis of Stereochemistry:

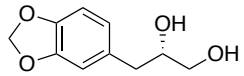
The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 4-phenylbutane-1,2-diol prepared from dihydroxylation of 4-phenyl-1-butene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 120 °C 5min, then 0.5°C /min to 140°C, 20 psi)- analysis of the acetonide of 4-phenylbutane-1,2-diol.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	34.601	MM	0.1379	45.78631	5.53192	4.89136
2	34.902	MM	0.2266	890.27930	65.47097	95.10864

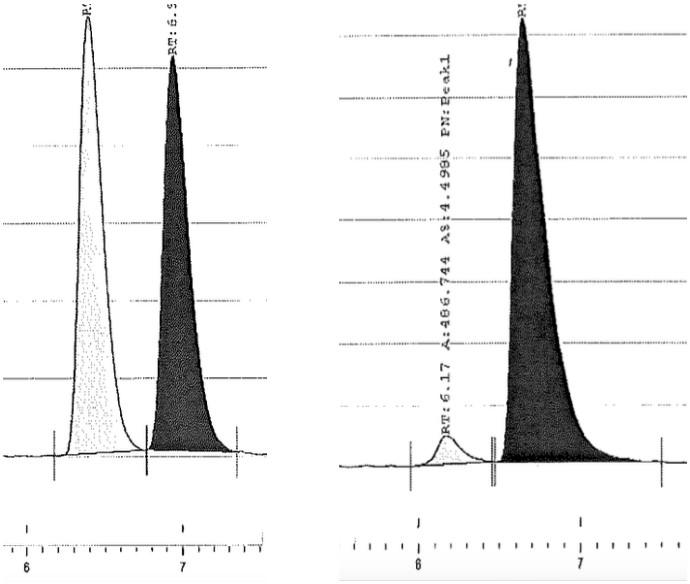


(S)-3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol (7). The diboration was performed according to the general procedure B with safrole (32.44 mg, 0.20 mmol, 29.60 μL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (38.8 mg, 99% yield). Spectral data and optical rotation are in accordance with the literature report.[24] HRMS-(DART+) for C10H11O3 $[M\text{-}H_2O+H]^+$: calculated: 179.0708, found: 179.0715.

Analysis of Stereochemistry:

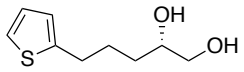
The 1,2-diol was compared to the racemic 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol prepared from dihydroxylation of safrole with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.4985	486.744	6.17	46.8535	0.0054
2	95.5015	10333.3923	6.64	719.9659	0.0058
Total:	100	10820.1363			

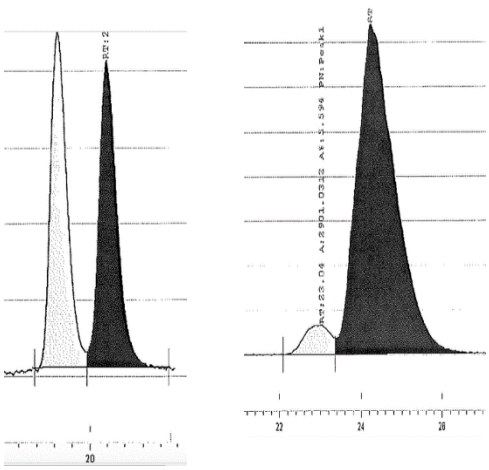


(S)-5-(thiophen-2-yl)pentane-1,2-diol (10). The diboration was performed according to the general procedure A with 2-(pent-4-en-1-yl)thiophene (30.45 mg, 0.20 mmol). The crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as clear oil (29.8 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, J = 5.1, 1.2 Hz, 1H), 6.91 (dd, J = 5.1, 3.3 Hz, 1H), 6.79 (dt, J = 3.4, 1.0 Hz, 1H), 3.74 (dtd, J = 9.8, 6.5, 3.0 Hz, 1H), 3.65 (dd, J = 11.0, 3.1 Hz, 1H), 3.44 (dd, J = 11.0, 7.6 Hz, 1H), 2.87 (t, J = 7.5 Hz, 2H), 2.27 – 1.59 (m, 3H), 1.59 – 1.45 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 126.7, 124.2, 123.0, 72.0, 66.8, 32.4, 29.8, 27.7. HRMS-(DART+) for $C_9H_{13}OS$ $[M\text{-}H_2O+H]^+$: calculated: 169.0687, found: 169.0693. IR (neat): 3346.03(br), 2934.55(m), 2861.76(w), 1428.62(w), 1050.73(s), 870.95(w), 849.36(m), 823.85(w). $[\alpha]_D^{20}$= -1.598 (c=0.685, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

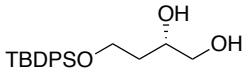
The 1,2-diol was compared to the racemic 5-(thiophen-2-yl)pentane-1,2-diol prepared from dihydroxylation of 2-(pent-4-en-1-yl)thiophene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 5-(thiophen-2-yl)pentane-1,2-diol.



racemic product diboration product

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	5.594	2901.0312	23.04	64.7142	0.0179
2	94.406	48958.6678	24.23	738.6956	0.0189
Total:	100	51859.699			

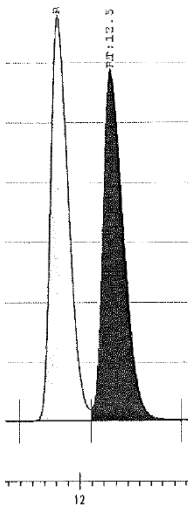


(S)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol (13). The diboration was performed according to the general procedure B with (but-3-en-1-yloxy)(tert-butyl)diphenylsilane (62.10 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as white solid (66.14 mg, 96% yield). Spectral data and optical rotation are in accordance with literature report.[23] HRMS-(DART+) for $C_{20}H_{29}O_3Si$ $[M+H]^+$: calculated: 345.1886, found: 345.1895. IR (neat): 3392.72(br), 3071.05(w), 3048.48(w), 2999.17(m), 2930.34(m), 2857.66(m), 1471.82(m), 1112.13(s), 823.82(m), 740.33(m), 701.55(s), 613.59(m), 505.32(m), 489.90(m).

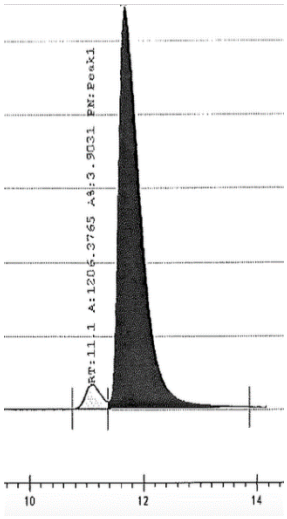
Analysis of Stereochemistry:

The 1,2-diol was compared to the 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol prepared from dihydroxylation of (but-3-en-1-yloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol.



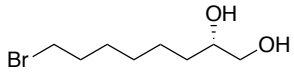
racemic product



diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	3.9031	1206.3765	11.1	65.307	0.0117
2	96.0969	29701.8286	11.68	1085.8772	0.0123
Total:	100	30908.2051			

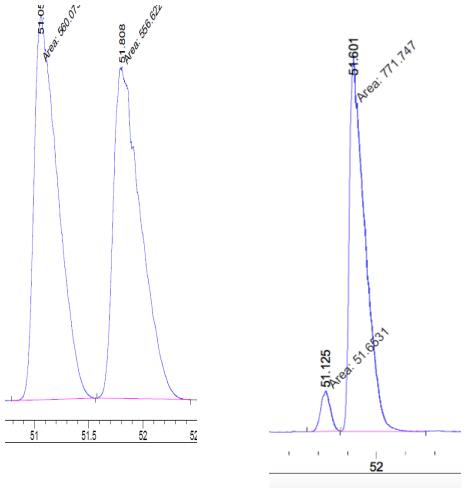


(S)-8-bromooctane-1,2-diol (16). The diboration was performed according to the general procedure A with 8-bromooct-1-ene (38.02 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexane) to afford the product as clear oil (40.52 mg, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.73 – 3.67 (m, 1H), 3.65 (dd, J = 11.0, 3.1 Hz, 1H), 3.47 – 3.35 (m, 3H), 1.85 (dd, J = 1059.8, 7.4 Hz, 2H), 1.52 – 1.39 (m, 5H), 1.39 – 1.28 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 74.9, 69.4, 36.6, 35.7, 35.3, 31.4, 30.7, 28.0. HRMS-(DART+) for $C_8H_{18}BrO_2$ $[M+H]^+$: calculated: 225.049, found: 225.0484. IR (neat): 3347.12(br), 2930.22 (s), 2856.22 (m), 1462.14(m), 1429.61(m), 1255.16(m), 1140.02(m), 1054.50(s), 868.96 (m). $[\alpha]_D^{20}$= -2.066 (c=1.215, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 8-bromooctane-1,2-diol prepared from dihydroxylation of 8-bromooct-1-ene with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

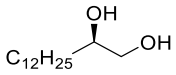
Chiral GLC (β-dex, Supelco, 120 °C 10min, 0.5^{o}C/min to 180^{o}C, 20 psi)- analysis of the acetonide of 8-bromooctane-1,2-diol.



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	51.125	MM	0.1915	51.65312	4.49532	6.27315
2	51.601	MM	0.3092	771.74683	41.59966	93.72685

F. Proof of Stereochemistry (with Bis(neopentyl glycolato)diboron)



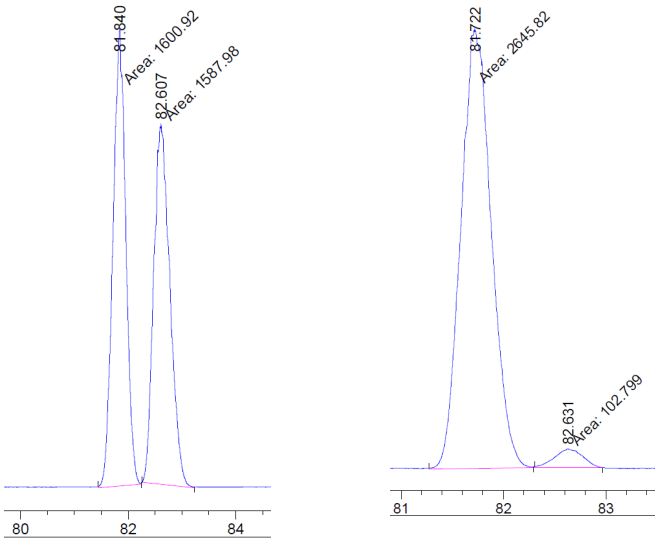
(R)-tetradecane-1,2-diol (2). The diboration was performed according to the general procedure D with 1-tetradecene substrate (94%, 41.78 mg, 0.20 mmol, 54 µL). The crude reaction mixture was purified on silica gel (40% ethyl acetate in hexanes) to afford the product as white solid (30.0 mg, 65% yield).

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of tetradecane-1,2-diol prepared

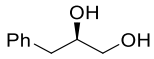
from dihydroxylation of 1-tetradecene with ruthenium trichloride and sodium periodiate.[19]

Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180°C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol



racemic product diboration product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.722	MM	0.3444	2645.81689	128.05505	96.25999
2	82.631	MM	0.3142	102.79861	5.45218	3.74001

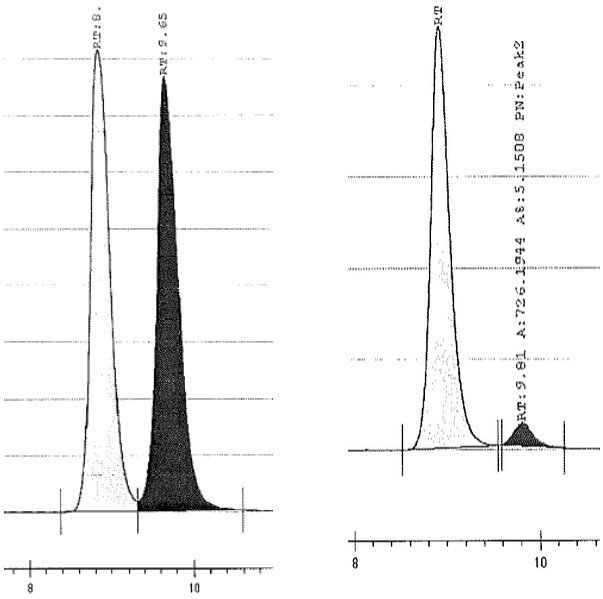


(R)-3-phenylpropane-1,2-diol (4). The diboration was performed according to the general procedure D with allyl benzene (23.64 mg, 0.50 mmol, 26.56µL). The crude reaction mixture was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (14.4 mg, 47% yield).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 3-phenylpropane-1,2-diol prepared from dihydroxylation of allyl benzene with ruthenium trichloride and sodium periodiate.[13] The absolute stereochemistry was assigned by analogy.

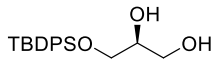
Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-phenylpropane-1,2-diol.



racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	95.3829	25442.9155	8.91	1088.8435	0.0074
2	4.6171	1231.6012	9.77	48.5118	0.0081
Total:	100	26674.5167			

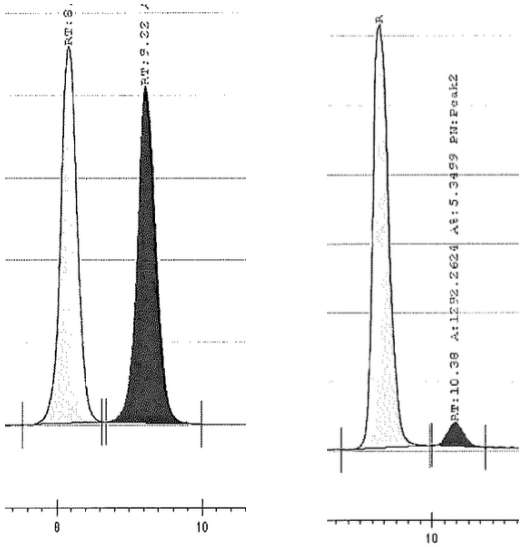


(S)-3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol (12). The diboration was performed according to the general procedure D with (allyloxy)(tert-butyl)diphenylsilane (59.30 mg, 0.20 mmol). The crude reaction mixture was purified on silica gel (30% ethyl acetate in hexanes) to afford the product as white solid (24.0 mg, 36% yield).

Analysis of Stereochemistry:

The 1,2-diol was compared to the racemic 3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol prepared from dihydroxylation of (allyloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate.[19] The absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((tert-butyldiphenylsilyl)oxy)propane-1,2-diol.



racemic product diboration product

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.6501	22862.5521	9.16	1226.6073	0.0074
2	5.3499	1292.2624	10.38	70.3645	0.0084
Total:	100	24154.8145			

2.9.6 Experimental Procedure for Large Scale Reaction.

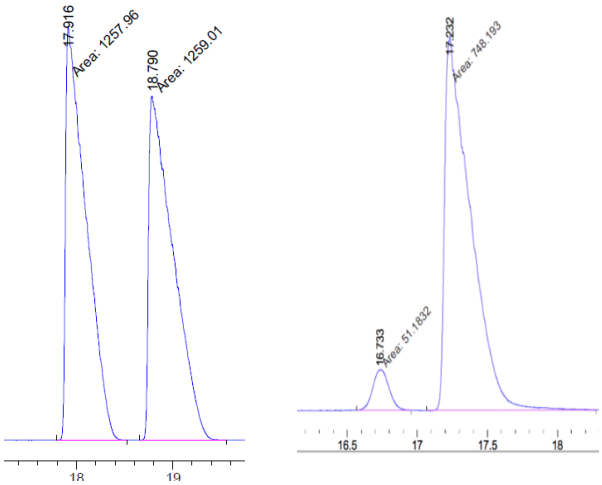
A round bottom flask equipped with a magnetic stir bar was added tetrahydoxydiboron (2.76g, 30.8 mmol), 1,3-propanediol (4.45 ml, 61.6 mmol), and toluene (70 ml). A Dean-Stark distillation head was then equipped. The reaction was refluxing at 160^{o}C for 6h. Toluene was then removed by rotary evaporation to afford crude product as white solid. The crude product was used directly in the diboration reaction without further purification.

To the 250 ml round bottom flask with crude propanediol diboron and stir bar was added DHR catalyst (264.31 mg, 2 mmol), 4A molecular sieves (1.0 g), anhydrous ethyl acetate (20 ml) 1-octene (3.23 ml, 20 mmol) and DBU (304.48 mg, 2 mmol). The flask was sealed with rubber septa and was then removed from the glove box. The reaction was allowed to stir at room temperature for 12h. The reaction was cooled to 0 °C (ice/water) and charged with pH=7 buffer solution (40 mL), followed by slow addition of 30% hydrogen peroxide (20 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (40 mL) was added slowly over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 50 mL). The combined organics were dried over sodium sulfate, filtered, and concentrated by rotary evaporation to afford crude reaction mixture. The crude product was purified on silica gel (50% ethyl acetate in hexanes) to afford the product as white solid (2.73, 93% yield).

Analysis of Stereochemistry:

The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate.[13] The absolute stereochemistry was assigned by analogy.

Chiral GLC (β-dex, Supelco, 100 °C 30min, 20 psi)- analysis of the acetonide of octane-1,2-diol.

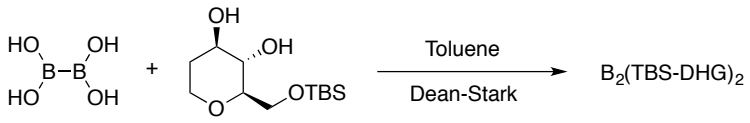


Racemic product diboration product

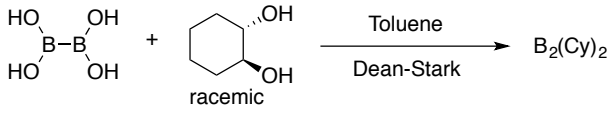
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	16.733	MM	0.1345	51.18321	6.34325	6.40289
2	17.232	MM	0.2117	748.19299	58.91286	93.59711

2.9.7. Experimental Procedure for $B_2(TBS\text{-}DHG)_2$, $B_2(TCD)_2$, and $B_2(DHR)_2$.

A. Preparation of $B_2(TBS\text{-}DHG)_2$, $B_2(TCD)_2$ and $B_2(DHR)_2$

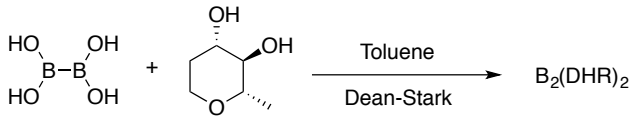


A round bottom flask equipped with a magnetic stir bar was added tetrahydoxydiboron (44.5 mg, 0.5mmol), TBS-DHG catalyst (262.4 mg, 1 mmol), and toluene (10ml). A Dean-Stark distillation head was then equipped. The reaction was refluxing at 160°C for 12h. Toluene was then removed by rotary evaporation to afford the crude product as white product.^{1}H NMR (600 MHz, $CDCl_3$) δ 4.52 – 3.54 (m, 10H), 3.58 – 2.99 (m, 4H), 2.25 – 1.49 (m, 4H), 1.07 – 0.70 (m, 18H), 0.26 – -0.14 (m, 12H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 80.3, 79.7, 79.6, 65.6, 62.8, 62.8, 33.2, 26.3, 26.2, 18.8, 18.7, -4.97, -5.02, -5.03, -5.1.^{11}B NMR (160 MHz, $CDCl_3$) δ 32.05. HRMS-(DART+) for $C_{24}H_{49}B_2O_8Si_2[M+H]^+$: calculated: 543.31521, found: 543.31748. Stereoisomers were observed through carbon NMR.



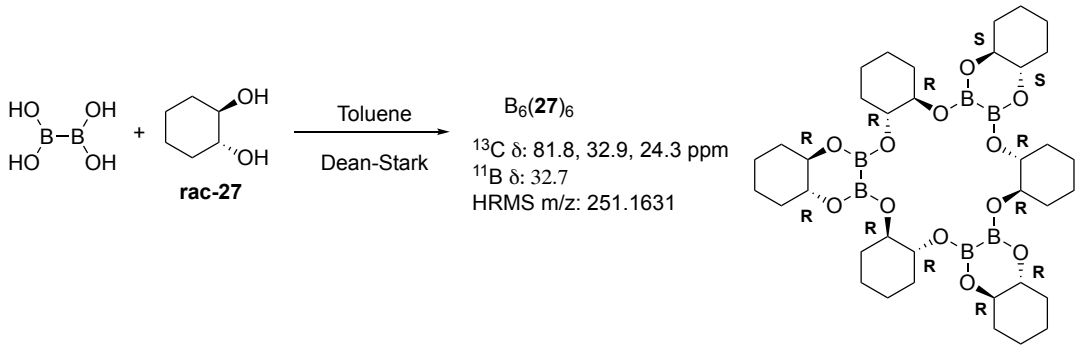
A round bottom flask equipped with a magnetic stir bar was added tetrahydoxydiboron (44.5 mg, 0.5mmol), (S,S)-1,2-transcyclohexanediol (116.6 mg, 1 mmol), and toluene (10ml). A Dean-Stark distillation head was then equipped. The reaction was refluxing at 160°C for 12h. Toluene was then removed by rotary evaporation to afford the crude product as white product. ^{13}C NMR (150 MHz, $CDCl_3$) δ 24.3, 32.9,

81.8; ^{13}B NMR (160 MHz, $CDCl_3$) δ 32.7; HRMS-(DART+) for C12H21B$_2$O4 $[M+H]^+$: calculated: 251.1626, found: 251.1631.



A round bottom flask equipped with a magnetic stir bar was added tetrahydoxydiboron (44.5 mg, 0.5mmol), DHR catalyst (132.1 mg, 1 mmol), and toluene (10ml). A Dean-Stark distillation head was then equipped. The reaction was refluxing at 160^{o}C for 12h. Toluene was then removed by rotary evaporation to afford the crude product as white product. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.24 – 4.07 (m, 1H), 4.07 – 3.76 (m, 3H), 3.73 – 3.56 (m, 1H), 3.54 – 3.39 (m, 3H), 3.39 – 3.10 (m, 2H), 2.15 – 1.94 (m, 2H), 1.93 – 1.69 (m, 2H), 1.38 – 1.14 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 83.6, 83.4, 79.4, 79.3, 65.6, 33.5, 18.1, 18.0. ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.34. HRMS-(DART+) for C12H21B$_2$O4 $[M+H]^+$: calculated: 253.15089, found: 283.15290. Stereoisomers were observed through carbon NMR.

B. Crystal structure of B_6(27)$_6$



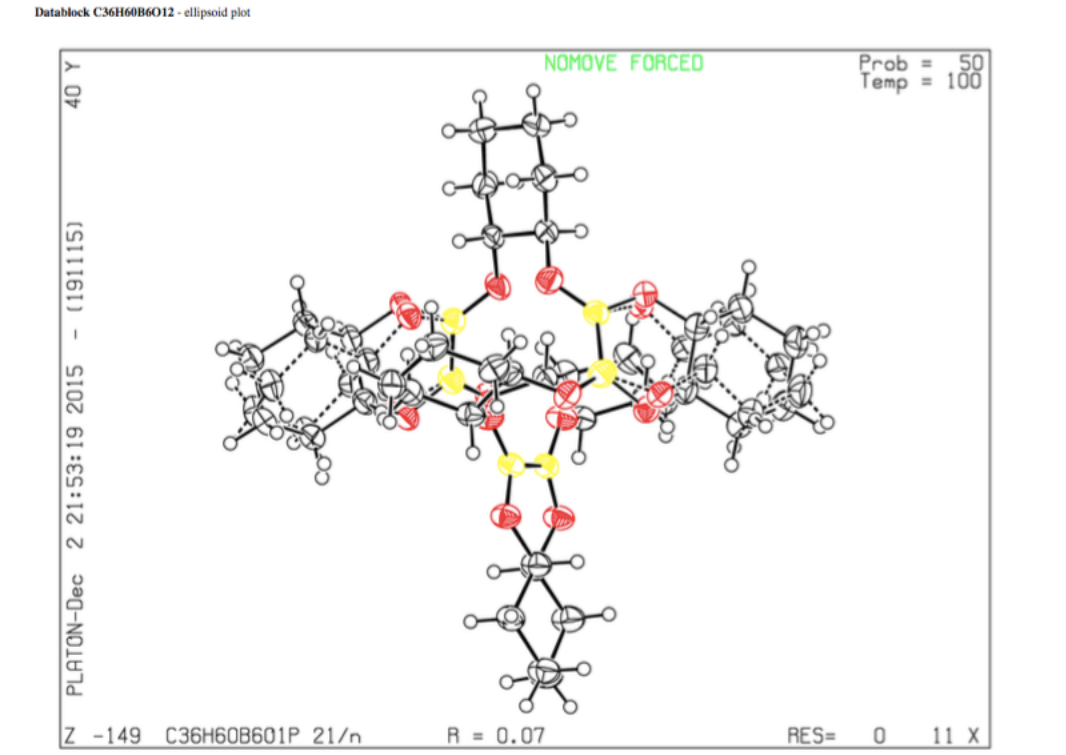


Table 1. Crystal data and structure refinement for C36H60B6O12.

Identification code	C36H60B6O12
Empirical formula	C36 H60 B6 O12
Formula weight	749.70
Temperature	100(2) K
Wavelength	1.54178 ≈
Crystal system	Monoclinic
Space group	$P2_1/n$

Unit cell dimensions a = 10.9587(4) ≈ α= 90∞.

b = 19.3545(7) ≈ β= 96.063(2)∞.

c = 19.5983(9) ≈ γ= 90∞.

Volume 4133.6(3) ≈3

Z 4

Density (calculated) 1.205 Mg/m3

Absorption coefficient 0.694 mm-1

F(000) 1608

Crystal size 0.150 x 0.100 x 0.050 mm3

Theta range for data collection 3.218 to 66.853∞.

Index ranges -13<=h<=13, -23<=k<=22, -23<=l<=23

Reflections collected 53394

Independent reflections 7313 [R(int) = 0.0930]

Completeness to theta = 66.853∞ 99.8 %

Absorption correction Semi-empirical from equivalents

Max. and min. transmission 0.7528 and 0.6732

Refinement method Full-matrix least-squares on F2

Data / restraints / parameters 7313 / 651 / 633

Goodness-of-fit on F2 1.026

Final R indices [I>2sigma(I)] R1 = 0.0667, wR2 = 0.1701

R indices (all data) R1 = 0.1049, wR2 = 0.1951

Extinction coefficient na

Largest diff. peak and hole 0.571 and -0.273 e.≈-3

C. Sample Preparation and data processing -- DOSY NMR.

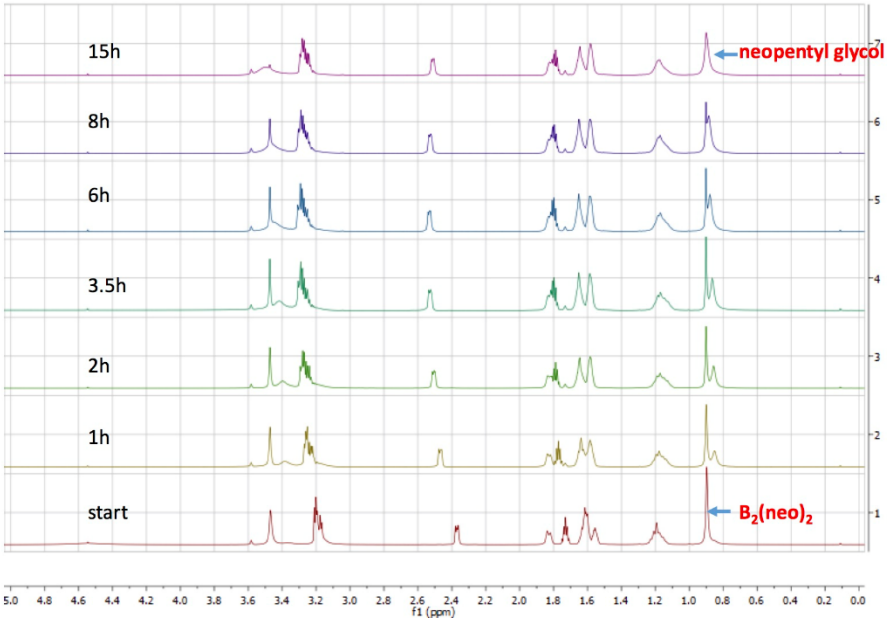
B_2(TBS-DHG)$_2$ (30 mg) and naphthalene (15mg) were dissolved in anhydrous deuterochloroform. The solution was then transferred to a NMR tube. The tube was sealed by a NMR cap and removed from the glovebox. DOSY NMR was taken on Varian Gemini-600 (600 MHz). The data processing was done according to the literature report.[69] The DSE model was adopted. $LogK = -7.59, a = -0.572$, $LogDref, fix = -8.7453$. Diffusion number of naphthalene reference = 20.59, diffusion number of B_2(TBS-DHG)$_2$= 8.085. Calculated molecular weight= 536.4189.

D. Equilibria between B_2(neo)$_2$ and (1S,2S)-trans-cyclohexanediol.

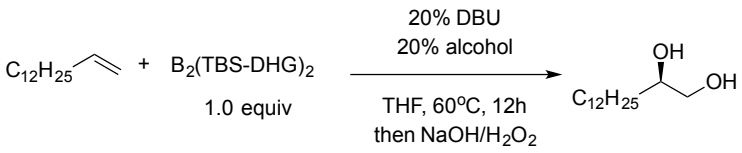
To an oven dried 2-dram vial was added B_2(neo)2 (11.3 mg, 0.05 mmol), (1S,2S)-trans-cyclohexanediol (11.6 mg, 0.1 mmol) and DBU (15.2 mg, 0.1 mmol) and tetrahydrofuran-d8 (0.7 ml) in the glovebox. The solution was then transferred to a NMR tube. The NMR tube was sealed with a NMR cap and removed from the glovebox. The NMR tube was heated in the oil bath at 60oC. Proton NMR was taken occasionally over

[69] Neufeld, R.; Stalke, D. *Chem. Sci.* **2015**, *6*, 3354.

15h. The combined NMR data was shown below. The exchange was completed within 15h.

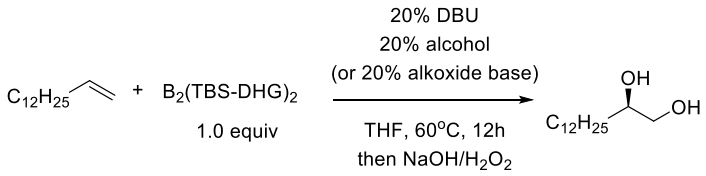


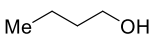
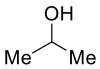
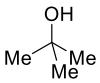
E. Experimental Procedure for B_2(TBS-DHG)$_2$ reactions



In the glove box, an oven-dried 1-dram vial equipped with a magnetic stir bar was charged with B_2(TBS-DHG)$_2$ (54.3 mg, 0.1mmol, 1.0 equiv), , 1-tetradecene (19.6 mg, 0.10 mmol, 1.0 equiv) and THF (0.1 mL). DBU (3.0 ml, 0.02 mmol, 0.2 equiv) and alcohol (0.02 mmol, 0.2 equiv) or alkoxide base (0.02 mmol, 0.2 equiv)was then added to the solution. The vial was sealed with a cap, removed from the glove box. The reaction mixture was stirred at 60^{o}C for 12 hours. The reaction was cooled to 0 °C (ice/water) and

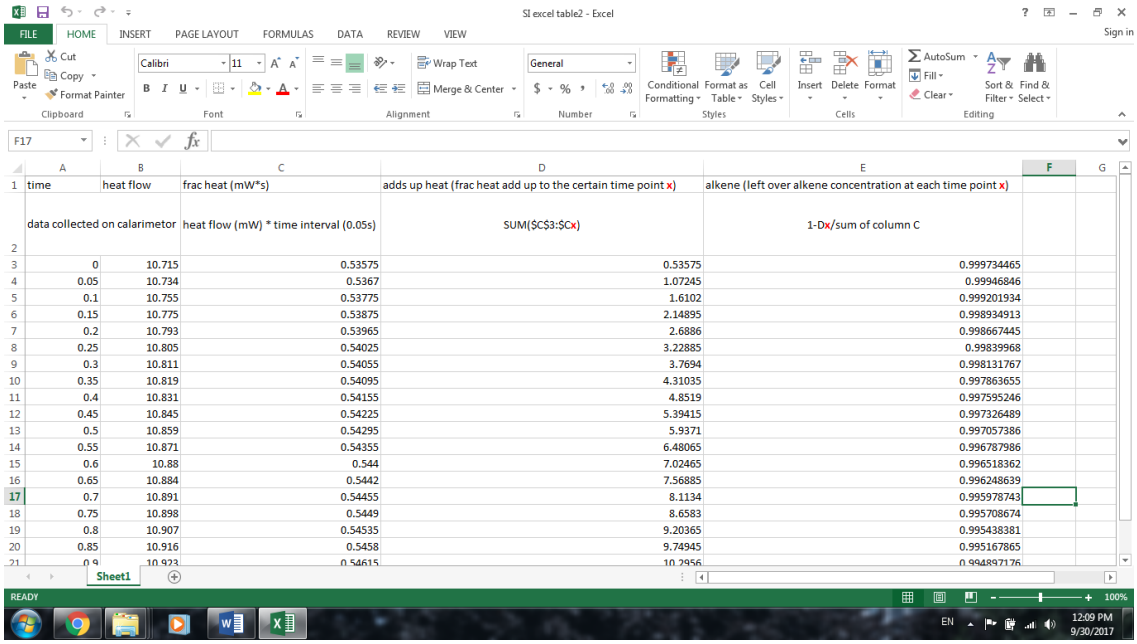
charged with 3 M sodium hydroxide (0.6 mL), followed by dropwise addition of 30% hydrogen peroxide (0.3 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours at room temperature. The reaction was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (4 mL) was added dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to afford crude reaction mixture. The crude mixture was purified through silica gel column (30% ethyl acetate in hexane) to afford the product as white solid. The product was then treated with catalytic amount of p-toluenesulfonic acid and 1 ml of acetone dimethyl acetal and heated to 70^{o}C for 15 minutes. The mixture was filtered through silica gel by ether and the solution was injected on chiral GC to find out the enantioselectivity.



entry	alcohol	yield	selectivity
1	no alcohol	0%	n.r.
2	DBU	0%	n.r.
3		43%	92:8
4		40%	90:10
5		27%	86:14
6		30%	80:20
7	KO^{t}Bu	52%	73:27
8	KOMe	46%	81:19

2.9.8. Experimental Procedure for Kinetic Study.

To a flame-dried reaction calorimeter vial equipped with stir bar was added TBS-DHG catalyst (20.99 mg, 0.08 mmol), propanediol diboron (272 mg, 1.6 mmol), 4A Molecular Seives (80 mg), DBU (12.00 mg, 0.08 mmol), tetrahydrofuran (0.8 ml). The vial was sealed with a teflon septa. To the reference vial equipped with stir bar was added propanediol diboron (272 mg, 1.6 mmol), 4A Molecular Seives (80 mg), DBU (12.00 mg, 0.08 mmol), tetrahydrofuran (0.8 ml). The vial was sealed with a teflon speta. Two vials were removed from the glovebox and put into the Omnical SuperCRC calorimeter. 4-phenyl-1 butene (160 μL, 0.8 mmol) was taken up in a 250 μL gas-tight glass syringe, and the syringe was placed into the sample syringe inlet. Another sample of 4-phenyl-1-butene (160 μL, 0.8 mmol) was taken up in a 250 μL gas-tight glass syringe, and the syringe was placed into the reference syringe inlet. The system was then thermostated to 30 °C and was allowed to stand for 1 hour to reach thermal equilibrium. The reaction was initiated by addition of 4-phenyl-1-butene to both the reaction vial and the reference vial simultaneously and all at once via microsyringe. Microsyringes were quickly removed from the synringe inlets. The top of the calorimeter was then fully insulated, and the reaction was allowed to run without disturbance until the heat evolved from the reaction returned to baseline. Data from the calorimeter was then analyzed by Excel and Origin. Excel data processing was shown below.



SI excel table2 - Excel

	A	B	C	D	E	F	G
1	time	heat flow	frac heat (mW*s)	adds up heat (frac heat add up to the certain time point x)	alkene (left over alkene concentration at each time point x)		
2	data collected on calarimetor		heat flow (mW) * time interval (0.05s)	SUM(C3:$Cx)	1-Dx/sum of column C		
3	0	10.715	0.53575	0.53575	0.999734465		
4	0.05	10.734	0.5367	1.07245	0.99946846		
5	0.1	10.755	0.53775	1.6102	0.999201934		
6	0.15	10.775	0.53875	2.14895	0.998934913		
7	0.2	10.793	0.53965	2.6886	0.998667445		
8	0.25	10.805	0.54025	3.22885	0.99839968		
9	0.3	10.811	0.54055	3.7694	0.998131767		
10	0.35	10.819	0.54095	4.31035	0.997863655		
11	0.4	10.831	0.54155	4.8519	0.997595246		
12	0.45	10.845	0.54225	5.39415	0.997326489		
13	0.5	10.859	0.54295	5.9371	0.997057386		
14	0.55	10.871	0.54355	6.48065	0.996787986		
15	0.6	10.88	0.544	7.02465	0.996518362		
16	0.65	10.884	0.5442	7.56885	0.996248639		
17	0.7	10.891	0.54455	8.1134	0.995978743		
18	0.75	10.898	0.5449	8.6583	0.995708674		
19	0.8	10.907	0.54535	9.20365	0.995438381		
20	0.85	10.916	0.5458	9.74945	0.995167865		
21	0.9	10.923	0.54615	10.2956	0.994897176		

Sheet1

READY

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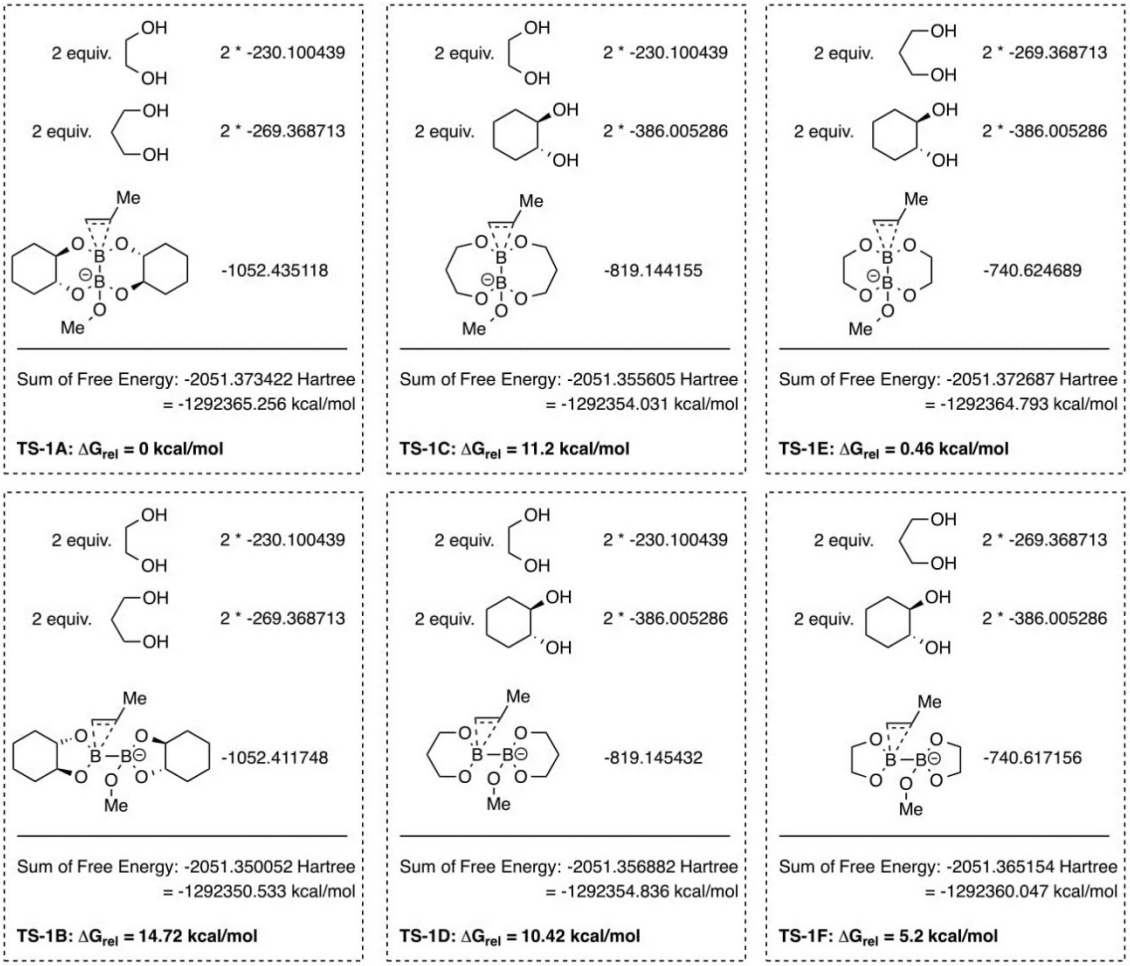
12:09 PM
9/30/2017

2.9.9 DFT Calculations

All calculations were carried out with the M06-2X density functional and the 6-31+G* basis set using the Gaussian 09 program.25 THF solvation was simulated using the PCM solvation model. Frequency calculations were carried out on all fully geometry optimized structures to make sure the transition states have one imaginary frequency and all other structures have only real frequencies. Gibbs free energies were computed using these normal mode frequencies at 298.15 K and 1 atm. The reaction coordinate was followed using the intrinsic reaction coordinate (IRC) method to verify that TS-1 and TS-2 connect with the correct ground states. A maximum of 20 steps of integration were carried out in forward and reverse directions from the transition state. The local quadratic approximation (LQA) method was used to integrate the reaction coordinate with a step size of 0.3 Bohr.

Calculations for scheme 2.9: The relative energies of transition states were calculated by considering the relative energies of the six systems below that are all interconverted by exchanging either the diol ligand or the bonding mode of the reagent.



charge= 0 multiplicity= 1

Cartesian coordinates (Angstroms):

10

O	0.884	-1.080	0.847
O	1.443	1.365	-0.297
C	2.198	-0.729	0.443
C	2.165	0.219	-0.737
H	2.742	-0.258	1.274
H	1.652	-0.257	-1.582
H	2.710	-1.656	0.172
H	3.185	0.486	-1.038
H	0.393	-0.248	0.947
H	1.234	1.930	-1.054

	1	2	3
	A	A	A
Frequencies --	168.9039	267.5372	334.1100
Red. masses --	3.2090	1.1306	1.8936

Zero-point correction= 0.086540 (Hartree/Particle)
Thermal correction to Energy= 0.091546
Thermal correction to Enthalpy= 0.092490
Thermal correction to Gibbs Free Energy= 0.059326
Sum of electronic and zero-point Energies= -230.073225
Sum of electronic and thermal Energies= -230.068218
Sum of electronic and thermal Enthalpies= -230.067274
Sum of electronic and thermal Free Energies= -230.100439

Item	Value	Threshold	Converged?
Maximum Force	0.000034	0.000450	YES
RMS Force	0.000012	0.000300	YES

SCF: -230.159764324 A.U.

charge= 0 multiplicity= 1

Cartesian coordinates (Angstroms):

13

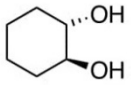
O	-1.310	0.187	-1.376
O	-1.546	0.735	1.318
C	-2.675	-0.244	-1.409
C	-2.907	0.456	1.017
C	-3.070	-0.666	-0.005
H	-3.316	0.583	-1.744
H	-2.787	-1.078	-2.112
H	-3.410	1.364	0.650
H	-3.376	0.176	1.965
H	-2.468	-1.529	0.308
H	-4.119	-0.986	-0.027
H	-1.062	0.546	-2.239
H	-1.081	0.802	0.466

	1	2	3
	A	A	A
Frequencies --	84.5275	234.0255	311.9412
Red. masses --	2.5866	4.0151	1.3574

Zero-point correction= 0.116022 (Hartree/Particle)
Thermal correction to Energy= 0.121993
Thermal correction to Enthalpy= 0.122937
Thermal correction to Gibbs Free Energy= 0.086891
Sum of electronic and zero-point Energies= -269.339582
Sum of electronic and thermal Energies= -269.333611
Sum of electronic and thermal Enthalpies= -269.332667
Sum of electronic and thermal Free Energies= -269.368713

Item	Value	Threshold	Converged?
Maximum Force	0.000015	0.000450	YES
RMS Force	0.000004	0.000300	YES

SCF: -269.455604120 A.U.



charge= 0 multiplicity= 1

Cartesian coordinates (Angstroms):

20

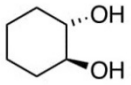
C	-4.798	-0.897	-0.728
C	-4.827	0.631	-0.620
C	-3.590	1.256	-1.275
C	-2.315	0.675	-0.674
C	-2.290	-0.845	-0.799
C	-3.508	-1.466	-0.131
H	-4.870	-1.187	-1.786
H	-5.667	-1.330	-0.221
H	-4.857	0.919	0.440
H	-5.736	1.031	-1.083
H	-3.584	2.345	-1.153
H	-3.602	1.048	-2.356
H	-2.256	0.930	0.392
H	-2.302	-1.098	-1.876
H	-3.462	-1.248	0.945
H	-3.466	-2.555	-0.244
O	-1.128	1.226	-1.244
O	-1.114	-1.369	-0.204
H	-1.203	1.192	-2.211
H	-0.378	-0.805	-0.497

	1	2	3
	A	A	A
Frequencies --	143.7296	195.8343	270.0270
Red. masses --	3.6146	2.2392	3.6942

Zero-point correction= 0.181324 (Hartree/Particle)
Thermal correction to Energy= 0.189061
Thermal correction to Enthalpy= 0.190005
Thermal correction to Gibbs Free Energy= 0.149815
Sum of electronic and zero-point Energies= -385.973777
Sum of electronic and thermal Energies= -385.966040
Sum of electronic and thermal Enthalpies= -385.965096
Sum of electronic and thermal Free Energies= -386.005286

Item	Value	Threshold	Converged?
Maximum Force	0.000061	0.000450	YES
RMS Force	0.000009	0.000300	YES

SCF: -386.155100802 A.U.



charge= 0 multiplicity= 1

Cartesian coordinates (Angstroms):

20

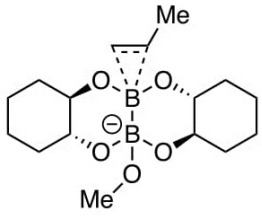
C	-4.798	-0.897	-0.728
C	-4.827	0.631	-0.620
C	-3.590	1.256	-1.275
C	-2.315	0.675	-0.674
C	-2.290	-0.845	-0.799
C	-3.508	-1.466	-0.131
H	-4.870	-1.187	-1.786
H	-5.667	-1.330	-0.221
H	-4.857	0.919	0.440
H	-5.736	1.031	-1.083
H	-3.584	2.345	-1.153
H	-3.602	1.048	-2.356
H	-2.256	0.930	0.392
H	-2.302	-1.098	-1.876
H	-3.462	-1.248	0.945
H	-3.466	-2.555	-0.244
O	-1.128	1.226	-1.244
O	-1.114	-1.369	-0.204
H	-1.203	1.192	-2.211
H	-0.378	-0.805	-0.497

	1	2	3
	A	A	A
Frequencies --	143.7296	195.8343	270.0270
Red. masses --	3.6146	2.2392	3.6942

Zero-point correction= 0.181324 (Hartree/Particle)
Thermal correction to Energy= 0.189061
Thermal correction to Enthalpy= 0.190005
Thermal correction to Gibbs Free Energy= 0.149815
Sum of electronic and zero-point Energies= -385.973777
Sum of electronic and thermal Energies= -385.966040
Sum of electronic and thermal Enthalpies= -385.965096
Sum of electronic and thermal Free Energies= -386.005286

Item	Value	Threshold	Converged?
Maximum Force	0.000061	0.000450	YES
RMS Force	0.000009	0.000300	YES

SCF: -386.155100802 A.U.



$\Delta G^{\neq}_{rel}$ = 0 kcal/mol

TS-1A

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

52

C	-4.307	-1.652	-0.620
C	-4.320	-0.426	-1.539
C	-2.893	0.005	-1.885
C	-2.065	0.272	-0.632
C	-2.048	-0.958	0.275
C	-3.468	-1.388	0.633
H	-3.883	-2.507	-1.167
H	-5.330	-1.932	-0.339
H	-4.836	0.400	-1.029
H	-4.887	-0.639	-2.453
H	-2.890	0.906	-2.511
H	-2.395	-0.788	-2.462
H	-2.535	1.097	-0.059
H	-1.562	-1.770	-0.299
H	-3.931	-0.587	1.229
H	-3.423	-2.277	1.273
O	-0.760	0.627	-1.004
B	0.063	1.221	0.072
B	0.015	-0.177	1.318
O	-1.328	-0.727	1.466
C	3.025	-1.990	-0.011
C	2.221	-0.752	0.378
C	2.093	0.213	-0.805
C	3.475	0.581	-1.339
C	4.283	-0.655	-1.738
C	4.406	-1.623	-0.559
H	2.457	-2.543	-0.773
H	3.108	-2.645	0.865
H	2.773	-0.208	1.170
H	1.527	-0.309	-1.599
H	3.355	1.266	-2.186
H	4.009	1.135	-0.552
H	3.779	-1.166	-2.572
H	5.275	-0.361	-2.100
H	4.999	-1.148	0.237
H	4.948	-2.529	-0.858

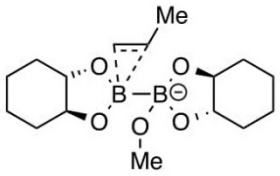
O	1.425	1.389	-0.430
O	0.969	-1.171	0.870
C	-0.768	3.403	-0.547
H	0.073	3.511	-1.248
H	-0.989	4.387	-0.117
H	-1.646	3.074	-1.125
O	-0.467	2.514	0.496
C	0.451	-0.111	3.321
H	-0.497	-0.434	3.744
C	1.653	-0.946	3.633
C	0.462	1.038	2.541
H	-0.376	1.726	2.574
H	1.412	1.499	2.270
H	2.583	-0.391	3.467
H	1.687	-1.846	2.999
H	1.634	-1.271	4.680

	1	2	3
	A	A	A
Frequencies --	-309.9100	39.6829	67.2106
Red. masses --	9.4203	4.1260	2.6117

Zero-point correction= 0.455010 (Hartree/Particle)
Thermal correction to Energy= 0.476696
Thermal correction to Enthalpy= 0.477640
Thermal correction to Gibbs Free Energy= 0.406568
Sum of electronic and zero-point Energies= -1052.386676
Sum of electronic and thermal Energies= -1052.364990
Sum of electronic and thermal Enthalpies= -1052.364046
Sum of electronic and thermal Free Energies= -1052.435118

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF: -1052.84168581 A.U.



$\Delta G^{\neq}_{rel}$ = 14.72 kcal/mol

TS-1B

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

52

H	0.209	-1.574	-2.149
H	-2.225	-1.748	-2.634
C	-0.397	-0.680	-2.267
C	-1.734	-0.780	-2.690
H	0.168	0.205	-2.554
C	-2.495	0.350	-3.317
C	-5.356	-0.949	1.308
C	-5.213	0.578	1.440
C	-4.313	1.191	0.351
C	-2.989	0.451	0.391
C	-3.196	-1.036	0.131
C	-3.998	-1.675	1.247
H	-5.915	-1.175	0.388
H	-5.953	-1.336	2.141
H	-4.781	0.809	2.424
H	-6.206	1.042	1.417
H	-4.174	2.265	0.524
H	-4.774	1.070	-0.639
H	-2.559	0.561	1.405
H	-3.772	-1.135	-0.813
H	-3.463	-1.563	2.200
H	-4.141	-2.748	1.072
O	-2.015	0.826	-0.557
B	0.521	-0.130	-0.034
B	-1.253	-0.403	-0.816
O	-1.885	-1.509	-0.087
C	3.803	-1.577	-0.865
C	2.705	-0.727	-0.257
C	2.471	0.524	-1.087
C	3.683	1.436	-1.036
C	4.876	0.639	-1.599
C	5.080	-0.716	-0.896
H	3.514	-1.876	-1.883
H	3.970	-2.492	-0.285
H	3.036	-0.409	0.752
H	2.338	0.205	-2.141
H	3.519	2.350	-1.621

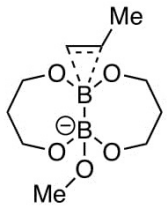
H	3.874	1.737	0.003
H	4.702	0.461	-2.670
H	5.795	1.232	-1.527
H	5.402	-0.533	0.139
H	5.894	-1.263	-1.386
O	1.253	1.029	-0.592
O	1.418	-1.296	-0.168
O	0.143	0.174	1.330
C	-0.112	-0.863	2.240
H	0.371	-0.622	3.198
H	0.281	-1.822	1.883
H	-1.189	-0.980	2.418
H	-2.874	0.068	-4.309
H	-1.855	1.231	-3.439
H	-3.351	0.664	-2.704

	1	2	3
	A	A	A
Frequencies --	-445.8394	23.5485	36.2182
Red. masses --	9.4398	1.3801	3.1018

Zero-point correction= 0.454305 (Hartree/Particle)
Thermal correction to Energy= 0.476550
Thermal correction to Enthalpy= 0.477495
Thermal correction to Gibbs Free Energy= 0.403358
Sum of electronic and zero-point Energies= -1052.360801
Sum of electronic and thermal Energies= -1052.338555
Sum of electronic and thermal Enthalpies= -1052.337611
Sum of electronic and thermal Free Energies= -1052.411748

Item	Value	Threshold	Converged?
Maximum Force	0.000228	0.000450	YES
RMS Force	0.000022	0.000300	YES

SCF: -1052.81510581 A.U.



$\Delta G^{\neq}_{rel}$ = 11.2 kcal/mol

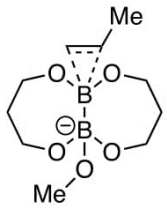
TS-1C

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

38

H	-1.730	-0.563	3.705
H	-0.537	-1.455	4.663
C	-0.812	-1.164	3.642
H	-1.075	-2.090	3.096
H	-0.801	1.081	1.900
C	0.305	-0.414	2.990
C	0.149	0.551	1.963
B	0.182	-0.772	0.859
O	-0.193	2.011	-0.220
H	-0.434	3.960	-0.773
O	-1.010	0.131	-1.530
H	1.310	-0.760	3.223
C	-0.233	2.986	-1.234
B	0.032	0.670	-0.705
H	-1.026	2.777	-1.968
H	0.975	1.232	1.770
O	1.383	-1.530	0.630
H	0.723	3.046	-1.775
O	1.251	0.472	-1.430
C	2.655	-0.980	0.850
C	3.271	-0.312	-0.374
C	2.472	0.884	-0.878
C	-2.352	0.302	-1.161
C	-2.907	-0.943	-0.482
C	-2.256	-1.231	0.866
H	-2.338	-0.330	1.493
O	-0.924	-1.672	0.779
H	-2.823	-2.022	1.376
H	3.045	1.403	-1.660
H	2.312	1.607	-0.061
H	2.635	-0.247	1.672
H	3.310	-1.800	1.176
H	-2.464	1.169	-0.491
H	-2.929	0.512	-2.073
H	-2.777	-1.808	-1.144
H	-3.986	-0.808	-0.320
H	4.287	0.015	-0.109



$\Delta G^{\neq}_{rel}$ = 11.2 kcal/mol

TS-1C

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

38

H	-1.730	-0.563	3.705
H	-0.537	-1.455	4.663
C	-0.812	-1.164	3.642
H	-1.075	-2.090	3.096
H	-0.801	1.081	1.900
C	0.305	-0.414	2.990
C	0.149	0.551	1.963
B	0.182	-0.772	0.859
O	-0.193	2.011	-0.220
H	-0.434	3.960	-0.773
O	-1.010	0.131	-1.530
H	1.310	-0.760	3.223
C	-0.233	2.986	-1.234
B	0.032	0.670	-0.705
H	-1.026	2.777	-1.968
H	0.975	1.232	1.770
O	1.383	-1.530	0.630
H	0.723	3.046	-1.775
O	1.251	0.472	-1.430
C	2.655	-0.980	0.850
C	3.271	-0.312	-0.374
C	2.472	0.884	-0.878
C	-2.352	0.302	-1.161
C	-2.907	-0.943	-0.482
C	-2.256	-1.231	0.866
H	-2.338	-0.330	1.493
O	-0.924	-1.672	0.779
H	-2.823	-2.022	1.376
H	3.045	1.403	-1.660
H	2.312	1.607	-0.061
H	2.635	-0.247	1.672
H	3.310	-1.800	1.176
H	-2.464	1.169	-0.491
H	-2.929	0.512	-2.073
H	-2.777	-1.808	-1.144
H	-3.986	-0.808	-0.320
H	4.287	0.015	-0.109

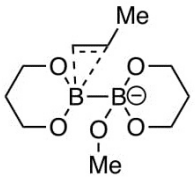
H 3.360 -1.041 -1.190

	1	2	3
	A	A	A
Frequencies --	-447.2880	34.4631	80.7907
Red. masses --	9.9193	3.2637	2.0338

Zero-point correction= 0.324554 (Hartree/Particle)
Thermal correction to Energy= 0.342111
Thermal correction to Enthalpy= 0.343056
Thermal correction to Gibbs Free Energy= 0.281017
Sum of electronic and zero-point Energies= -819.100617
Sum of electronic and thermal Energies= -819.083060
Sum of electronic and thermal Enthalpies= -819.082116
Sum of electronic and thermal Free Energies= -819.144155

Item	Value	Threshold	Converged?
Maximum Force	0.000013	0.000450	YES
RMS Force	0.000003	0.000300	YES

SCF: -819.425171513 A.U.



$\Delta G^{\neq}_{rel}$ = 10.4 kcal/mol

TS-1D

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

38

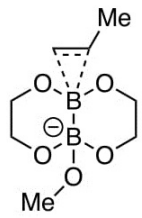
B	-1.082	0.541	-0.769
C	0.403	2.286	0.633
B	0.762	0.628	0.023
C	1.676	2.245	1.199
O	0.913	-0.422	0.994
O	1.653	0.626	-1.106
C	-0.736	2.272	-2.486
O	-0.988	0.941	-2.149
H	0.325	2.528	-2.348
H	-0.983	2.416	-3.546
H	-1.347	2.972	-1.896
O	-1.308	-0.895	-0.785
O	-2.120	1.296	-0.075
C	-2.573	0.735	1.131
C	-1.852	-1.502	0.362
C	2.180	-1.023	1.137
C	2.923	0.041	-0.956
H	-0.461	2.254	1.292
H	0.229	2.877	-0.258
C	1.882	1.891	2.644
H	2.944	1.787	2.892
H	1.383	0.942	2.886
H	1.460	2.655	3.314
C	-3.028	-0.704	0.919
H	-1.078	-1.591	1.138
H	-2.171	-2.515	0.083
H	-3.391	1.361	1.512
H	-1.768	0.739	1.891
C	2.834	-1.285	-0.213
H	2.846	-0.363	1.721
H	2.047	-1.954	1.703
H	3.585	0.721	-0.387
H	3.355	-0.091	-1.955
H	2.538	2.520	0.597
H	3.832	-1.718	-0.075
H	2.227	-1.993	-0.792
H	-3.866	-0.719	0.210
H	-3.370	-1.144	1.865

	1	2	3
	A	A	A
Frequencies --	-507.2638	46.2910	69.3546
Red. masses --	10.0312	2.9262	3.3594

Zero-point correction= 0.324789 (Hartree/Particle)
Thermal correction to Energy= 0.342329
Thermal correction to Enthalpy= 0.343273
Thermal correction to Gibbs Free Energy= 0.281064
Sum of electronic and zero-point Energies= -819.101707
Sum of electronic and thermal Energies= -819.084168
Sum of electronic and thermal Enthalpies= -819.083223
Sum of electronic and thermal Free Energies= -819.145432

Item	Value	Threshold	Converged?
Maximum Force	0.000011	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF: -819.426496325 A.U.



ΔG_{rel} = 0.5 kcal/mol

TS-1E

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

32

H	-1.568	0.279	4.114
H	-3.069	-1.201	0.427
H	-0.500	-0.677	5.166
C	-0.795	-0.495	4.124
H	-1.247	-1.416	3.733
H	-2.549	1.143	-0.196
C	-2.035	-0.908	0.201
O	-1.381	-0.668	1.427
C	-2.029	0.313	-0.705
H	-2.580	0.081	-1.628
H	-0.334	1.807	2.611
C	0.392	-0.082	3.310
H	-1.550	-1.742	-0.330
C	0.459	1.068	2.540
B	-0.035	-0.138	1.316
O	-0.484	2.552	0.488
H	-0.932	4.442	-0.131
O	-0.718	0.680	-1.044
H	1.267	-0.726	3.359
C	-0.708	3.458	-0.560
B	0.059	1.260	0.077
H	-1.559	3.153	-1.189
H	1.418	1.469	2.217
O	0.915	-1.161	0.891
H	0.173	3.555	-1.212
O	1.446	1.429	-0.369
C	2.181	-0.730	0.456
C	2.105	0.240	-0.715
H	2.732	-0.245	1.284
H	1.595	-0.257	-1.556
H	2.753	-1.619	0.157
H	3.127	0.490	-1.035

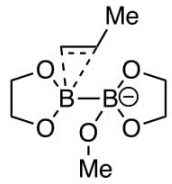
	1	2	3
	A	A	A
Frequencies --	-314.3864	61.8963	89.2515
Red. masses --	9.5419	2.3992	2.6043

Zero-point correction= 0.266813 (Hartree/Particle)

Thermal correction to Energy= 0.282055
Thermal correction to Enthalpy= 0.282999
Thermal correction to Gibbs Free Energy= 0.225759
Sum of electronic and zero-point Energies= -740.583634
Sum of electronic and thermal Energies= -740.568393
Sum of electronic and thermal Enthalpies= -740.567448
Sum of electronic and thermal Free Energies= -740.624689

Item	Value	Threshold	Converged?
Maximum Force	0.000014	0.000450	YES
RMS Force	0.000002	0.000300	YES

SCF: -740.850447507 A.U.



ΔG_{rel} = 5.2 kcal/mol

TS-1F

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

32

O	1.002	-1.232	0.073
C	1.686	-1.602	-1.107
B	0.735	0.201	-0.033
C	2.219	-0.282	-1.679
O	1.242	0.669	-1.316
H	-3.519	1.538	0.479
B	-1.168	0.355	-0.040
C	0.634	1.266	1.318
C	2.000	0.951	1.252
C	-2.976	1.880	-0.415
O	-1.588	1.721	-0.265
H	-3.356	1.316	-1.280
H	-3.195	2.943	-0.568
O	-1.513	-0.519	-1.171
O	-1.780	-0.291	1.140
C	-2.537	-1.398	0.707
C	-1.937	-1.758	-0.656
C	2.652	-0.118	2.079
H	2.645	1.576	0.640
H	0.028	0.840	2.116
H	0.282	2.227	0.957
H	-1.081	-2.437	-0.535
H	-2.670	-2.217	-1.332
H	-3.599	-1.118	0.597
H	-2.470	-2.217	1.434
H	2.486	-2.318	-0.879
H	0.983	-2.072	-1.813
H	2.346	-0.302	-2.767
H	3.188	-0.031	-1.211
H	3.100	-0.905	1.458
H	1.921	-0.606	2.732
H	3.445	0.302	2.714

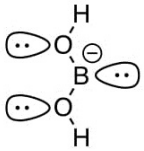
	1	2	3
	A	A	A
Frequencies --	-417.1815	10.7393	58.4169
Red. masses --	9.1637	3.0447	2.8935

Zero-point correction= 0.265896 (Hartree/Particle)
Thermal correction to Energy= 0.281726
Thermal correction to Enthalpy= 0.282671
Thermal correction to Gibbs Free Energy= 0.221933
Sum of electronic and zero-point Energies= -740.573193
Sum of electronic and thermal Energies= -740.557362
Sum of electronic and thermal Enthalpies= -740.556418
Sum of electronic and thermal Free Energies= -740.617156

Item	Value	Threshold	Converged?
Maximum Force	0.000202	0.000450	YES
RMS Force	0.000041	0.000300	YES

SCF: -740.839088474 A.U.

Calculations for Figure 8:



L

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

5

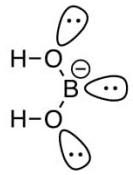
B	-2.147	10.229	-1.319
O	-2.188	9.775	-2.653
O	-2.875	9.295	-0.555
H	-2.861	9.577	0.366
H	-1.699	10.398	-3.202

	1	2	3
	A	A	A
Frequencies --	500.0354	538.5006	598.3531
Red. masses --	4.7850	1.1744	1.0912

Zero-point correction= 0.031067 (Hartree/Particle)
Thermal correction to Energy= 0.034613
Thermal correction to Enthalpy= 0.035557
Thermal correction to Gibbs Free Energy= 0.006785
Sum of electronic and zero-point Energies= -176.529588
Sum of electronic and thermal Energies= -176.526043
Sum of electronic and thermal Enthalpies= -176.525098
Sum of electronic and thermal Free Energies= -176.553870

Item	Value	Threshold	Converged?
Maximum Force	0.000122	0.000450	YES
RMS Force	0.000070	0.000300	YES

SCF: -176.560655343 A.U.



ΔG = +2.8 kcal/mol

K

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

5

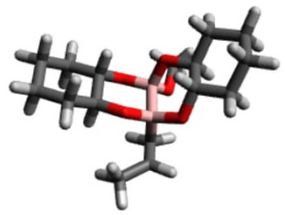
B	-2.149	10.179	-1.331
O	-2.119	9.774	-2.675
O	-2.949	9.364	-0.515
H	-3.375	8.621	-1.004
H	-2.666	8.973	-2.852

	1	2	3
	A	A	A
Frequencies --	419.5954	535.9608	576.5149
Red. masses --	1.0538	3.3783	1.5534

Zero-point correction= 0.028860 (Hartree/Particle)
Thermal correction to Energy= 0.032486
Thermal correction to Enthalpy= 0.033430
Thermal correction to Gibbs Free Energy= 0.004453
Sum of electronic and zero-point Energies= -176.524943
Sum of electronic and thermal Energies= -176.521318
Sum of electronic and thermal Enthalpies= -176.520374
Sum of electronic and thermal Free Energies= -176.549351

Item	Value	Threshold	Converged?
Maximum Force	0.000089	0.000450	YES
RMS Force	0.000038	0.000300	YES

SCF: -176.553803586 A.U.



TS-major

#p m062x/6-31+G* freq geom=check guess=check scrf=(pcm,solvent=thf) nosym

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

XXX
52

C	-4.307	-1.652	-0.620
C	-4.320	-0.426	-1.539
C	-2.893	0.005	-1.885
C	-2.065	0.272	-0.632
C	-2.048	-0.958	0.275
C	-3.468	-1.388	0.633
H	-3.883	-2.507	-1.167
H	-5.330	-1.932	-0.339
H	-4.836	0.400	-1.029
H	-4.887	-0.639	-2.453
H	-2.890	0.906	-2.511
H	-2.395	-0.788	-2.462
H	-2.535	1.097	-0.059
H	-1.562	-1.770	-0.299
H	-3.931	-0.587	1.229
H	-3.423	-2.277	1.273
O	-0.760	0.627	-1.004
B	0.063	1.221	0.072
B	0.015	-0.177	1.318
O	-1.328	-0.727	1.466
C	3.025	-1.990	-0.011
C	2.221	-0.752	0.378
C	2.093	0.213	-0.805
C	3.475	0.581	-1.339
C	4.283	-0.655	-1.738
C	4.406	-1.623	-0.559
H	2.457	-2.543	-0.773
H	3.108	-2.645	0.865
H	2.773	-0.208	1.170
H	1.527	-0.309	-1.599
H	3.355	1.266	-2.186

H 4.009 1.135 -0.552
H 3.779 -1.166 -2.572
H 5.275 -0.361 -2.100
H 4.999 -1.148 0.237
H 4.948 -2.529 -0.858
O 1.425 1.389 -0.430
O 0.969 -1.171 0.870
C -0.768 3.403 -0.547
H 0.073 3.511 -1.248
H -0.989 4.387 -0.117
H -1.646 3.074 -1.125
O -0.467 2.514 0.496
C 0.451 -0.111 3.321
H -0.497 -0.434 3.744
C 1.653 -0.946 3.633
C 0.462 1.038 2.541
H -0.376 1.726 2.574
H 1.412 1.499 2.270
H 2.583 -0.391 3.467
H 1.687 -1.846 2.999
H 1.634 -1.271 4.680
YYY

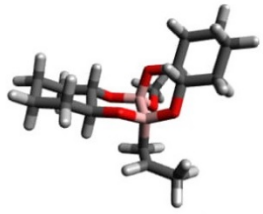
	1	2	3
	A	A	A
Frequencies --	-309.9100	39.6829	67.2106
Red. masses --	9.4203	4.1260	2.6117

Zero-point correction= 0.455010 (Hartree/Particle)
Thermal correction to Energy= 0.476696
Thermal correction to Enthalpy= 0.477640
Thermal correction to Gibbs Free Energy= 0.406568
Sum of electronic and zero-point Energies= -1052.386676
Sum of electronic and thermal Energies= -1052.364990
Sum of electronic and thermal Enthalpies= -1052.364046
Sum of electronic and thermal Free Energies= -1052.435118

Item	Value	Threshold	Converged?
Maximum Force	0.000007	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-1052.84168581', 'A.U.', 'after', '1', 'cycles']
MP2: no data
Temperature: 298.15
G_corr: 255.12548568 kcal/mol
H_corr: 299.7238764 kcal/mol
S_corr: 44.59876775 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 12.88455225 kcal/mol
S_rot: 10.2754416 kcal/mol
S_vib: 21.43847575 kcal/mol

TS-minor



#p m062x/6-31+G* freq geom=check guess=check scrf=(pcm,solvent=thf) nosym

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

XXX
52

C	-4.319	-1.659	-0.660
C	-4.319	-0.446	-1.595
C	-2.888	-0.017	-1.928
C	-2.080	0.270	-0.666
C	-2.073	-0.950	0.255
C	-3.496	-1.377	0.601
H	-3.886	-2.521	-1.190
H	-5.345	-1.936	-0.390
H	-4.844	0.386	-1.104
H	-4.874	-0.672	-2.514
H	-2.879	0.876	-2.566
H	-2.381	-0.817	-2.488
H	-2.563	1.098	-0.110
H	-1.578	-1.769	-0.302
H	-3.967	-0.570	1.181
H	-3.458	-2.259	1.252
O	-0.771	0.629	-1.021
B	0.028	1.221	0.077
B	-0.030	-0.162	1.310
O	-1.368	-0.705	1.452
C	2.993	-1.992	0.019
C	2.188	-0.757	0.417
C	2.084	0.223	-0.760
C	3.477	0.596	-1.262
C	4.290	-0.636	-1.662
C	4.387	-1.623	-0.495
H	2.436	-2.524	-0.767
H	3.057	-2.668	0.880
H	2.733	-0.230	1.228
H	1.537	-0.296	-1.568
H	3.373	1.292	-2.103
H	3.997	1.140	-0.459
H	3.803	-1.133	-2.514
H	5.291	-0.339	-1.998
H	4.965	-1.162	0.319
H	4.930	-2.526	-0.798
O	1.403	1.396	-0.398

O 0.927 -1.174 0.883
C -0.782 3.404 -0.567
H 0.075 3.501 -1.249
H -1.002 4.393 -0.145
H -1.650 3.081 -1.163
O -0.513 2.517 0.487
C 0.425 -0.089 3.314
C -0.750 -0.490 4.150
C 0.483 1.052 2.534
H -0.306 1.795 2.610
H 1.437 1.443 2.185
H -1.524 0.283 4.136
H -0.442 -0.653 5.191
H -1.205 -1.418 3.781
H 1.297 -0.739 3.351
YYY

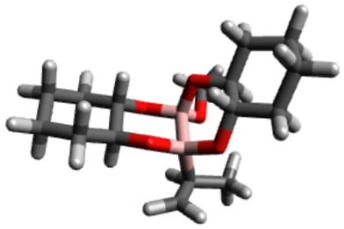
	1	2	3
	A	A	A
Frequencies --	-300.5235	39.0027	46.2469
Red. masses --	9.6446	4.0225	2.3049

Zero-point correction= 0.454635 (Hartree/Particle)
Thermal correction to Energy= 0.476558
Thermal correction to Enthalpy= 0.477502
Thermal correction to Gibbs Free Energy= 0.405511
Sum of electronic and zero-point Energies= -1052.385563
Sum of electronic and thermal Energies= -1052.363641
Sum of electronic and thermal Enthalpies= -1052.362696
Sum of electronic and thermal Free Energies= -1052.434687

Item	Value	Threshold	Converged?
Maximum Force	0.000008	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-1052.84019805', 'A.U.', 'after', '1', 'cycles']
MP2: no data
Temperature: 298.15
G_corr: 254.46220761 kcal/mol
H_corr: 299.63728002 kcal/mol
S_corr: 45.17479355 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 12.88455225 kcal/mol
S_rot: 10.28408795 kcal/mol
S_vib: 22.0058552 kcal/mol

TS-M



#p m062x/6-31+G* freq geom=check guess=check scrf=(pcm,solvent=thf) nosym

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

XXX

52

C	-4.370	-1.567	-0.559
C	-4.360	-0.358	-1.500
C	-2.927	0.023	-1.880
C	-2.061	0.286	-0.650
C	-2.068	-0.934	0.274
C	-3.495	-1.305	0.669
H	-3.985	-2.445	-1.098
H	-5.395	-1.807	-0.253
H	-4.842	0.492	-0.997
H	-4.949	-0.569	-2.401
H	-2.911	0.913	-2.521
H	-2.465	-0.793	-2.454
H	-2.491	1.136	-0.081
H	-1.627	-1.769	-0.305
H	-3.916	-0.475	1.257
H	-3.467	-2.182	1.328
O	-0.754	0.594	-1.058
B	0.074	1.231	-0.004
B	0.003	-0.131	1.273
O	-1.312	-0.730	1.446
C	3.044	-1.991	0.022
C	2.229	-0.745	0.361
C	2.142	0.196	-0.839
C	3.539	0.562	-1.333
C	4.361	-0.681	-1.681
C	4.443	-1.630	-0.482
H	2.502	-2.553	-0.753
H	3.097	-2.636	0.908
H	2.755	-0.188	1.167
H	1.607	-0.345	-1.642
H	3.448	1.230	-2.199
H	4.046	1.133	-0.540
H	3.888	-1.206	-2.523
H	5.367	-0.393	-2.012
H	5.006	-1.141	0.326

H 4.997 -2.539 -0.748
O 1.449 1.366 -0.502
O 0.958 -1.141 0.804
C -0.620 3.394 -0.832
H 0.256 3.416 -1.496
H -0.823 4.418 -0.492
H -1.482 3.050 -1.425
O -0.408 2.583 0.292
C 0.613 -0.060 3.143
C 0.286 1.163 2.586
C -1.018 1.819 2.975
H 1.075 1.828 2.243
H 1.624 -0.451 3.112
H -0.133 -0.636 3.681
H -1.485 2.311 2.123
H -0.804 2.574 3.743
H -1.701 1.079 3.398
YYY

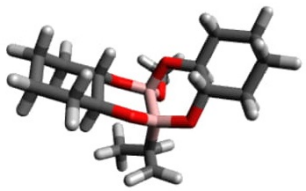
	1	2	3
	A	A	A
Frequencies --	-374.2569	37.2159	60.9849
Red. masses --	8.9423	4.1235	3.5954

Zero-point correction= 0.454803 (Hartree/Particle)
Thermal correction to Energy= 0.476455
Thermal correction to Enthalpy= 0.477399
Thermal correction to Gibbs Free Energy= 0.406486
Sum of electronic and zero-point Energies= -1052.378223
Sum of electronic and thermal Energies= -1052.356571
Sum of electronic and thermal Enthalpies= -1052.355627
Sum of electronic and thermal Free Energies= -1052.426540

Item	Value	Threshold	Converged?
Maximum Force	0.000006	0.000450	YES
RMS Force	0.000001	0.000300	YES

SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-1052.83302594', 'A.U.', 'after', '1', 'cycles']
MP2: no data
Temperature: 298.15
G_corr: 255.07402986 kcal/mol
H_corr: 299.57264649 kcal/mol
S_corr: 44.4982912 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 12.88455225 kcal/mol
S_rot: 10.2659008 kcal/mol
S_vib: 21.34783815 kcal/mol

TS-N



#p m062x/6-31+G* freq geom=check guess=check scrf=(pcm,solvent=thf) nosym

charge= -1 multiplicity= 1

Cartesian coordinates (Angstroms):

XXX

52

C	-4.278	-1.675	-0.613
C	-4.294	-0.468	-1.556
C	-2.869	-0.036	-1.909
C	-2.045	0.260	-0.659
C	-2.027	-0.949	0.273
C	-3.445	-1.379	0.638
H	-3.846	-2.537	-1.141
H	-5.300	-1.955	-0.330
H	-4.816	0.366	-1.064
H	-4.859	-0.702	-2.467
H	-2.870	0.852	-2.553
H	-2.366	-0.838	-2.470
H	-2.519	1.096	-0.107
H	-1.535	-1.771	-0.281
H	-3.914	-0.569	1.215
H	-3.398	-2.256	1.295
O	-0.739	0.605	-1.030
B	0.087	1.211	0.049
B	0.041	-0.138	1.307
O	-1.309	-0.688	1.459
C	2.986	-2.046	-0.063
C	2.234	-0.784	0.351
C	2.094	0.170	-0.841
C	3.474	0.507	-1.402
C	4.248	-0.745	-1.815
C	4.366	-1.722	-0.641
H	2.381	-2.574	-0.814
H	3.070	-2.712	0.805
H	2.834	-0.257	1.119
H	1.511	-0.365	-1.616
H	3.351	1.193	-2.250
H	4.033	1.054	-0.628
H	3.722	-1.241	-2.644
H	5.243	-0.474	-2.189
H	4.990	-1.268	0.142
H	4.872	-2.643	-0.955

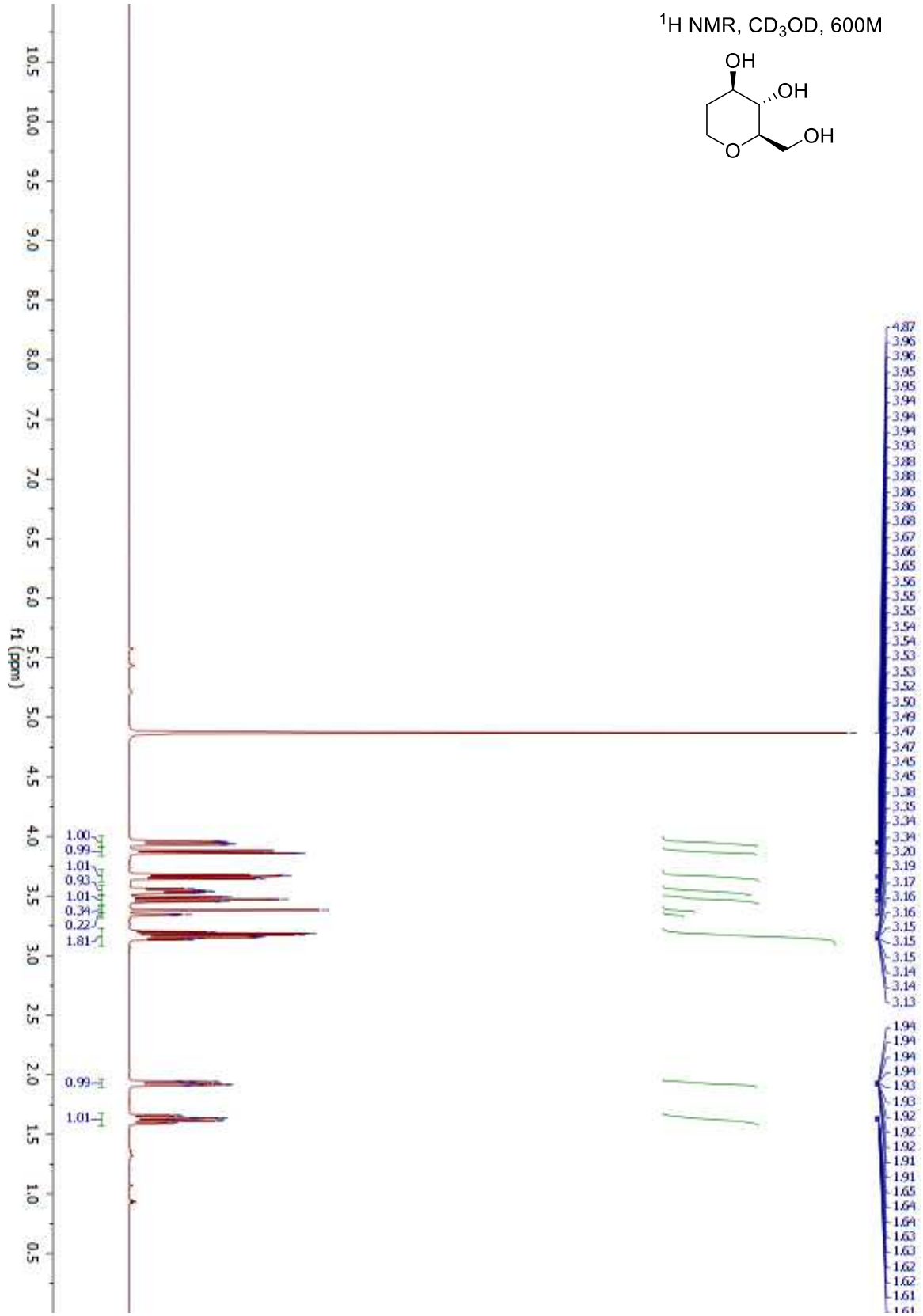
O 1.445 1.361 -0.488
O 0.992 -1.164 0.897
C -0.722 3.379 -0.655
H 0.117 3.433 -1.364
H -0.912 4.387 -0.265
H -1.613 3.054 -1.217
O -0.445 2.525 0.422
C 0.400 -0.069 3.261
C 0.394 1.156 2.629
C 1.644 1.993 2.525
H 1.343 -0.575 3.453
H -0.505 -0.539 3.621
H 1.648 2.598 1.619
H 2.543 1.369 2.546
H 1.674 2.655 3.400
H -0.537 1.716 2.579
YYY

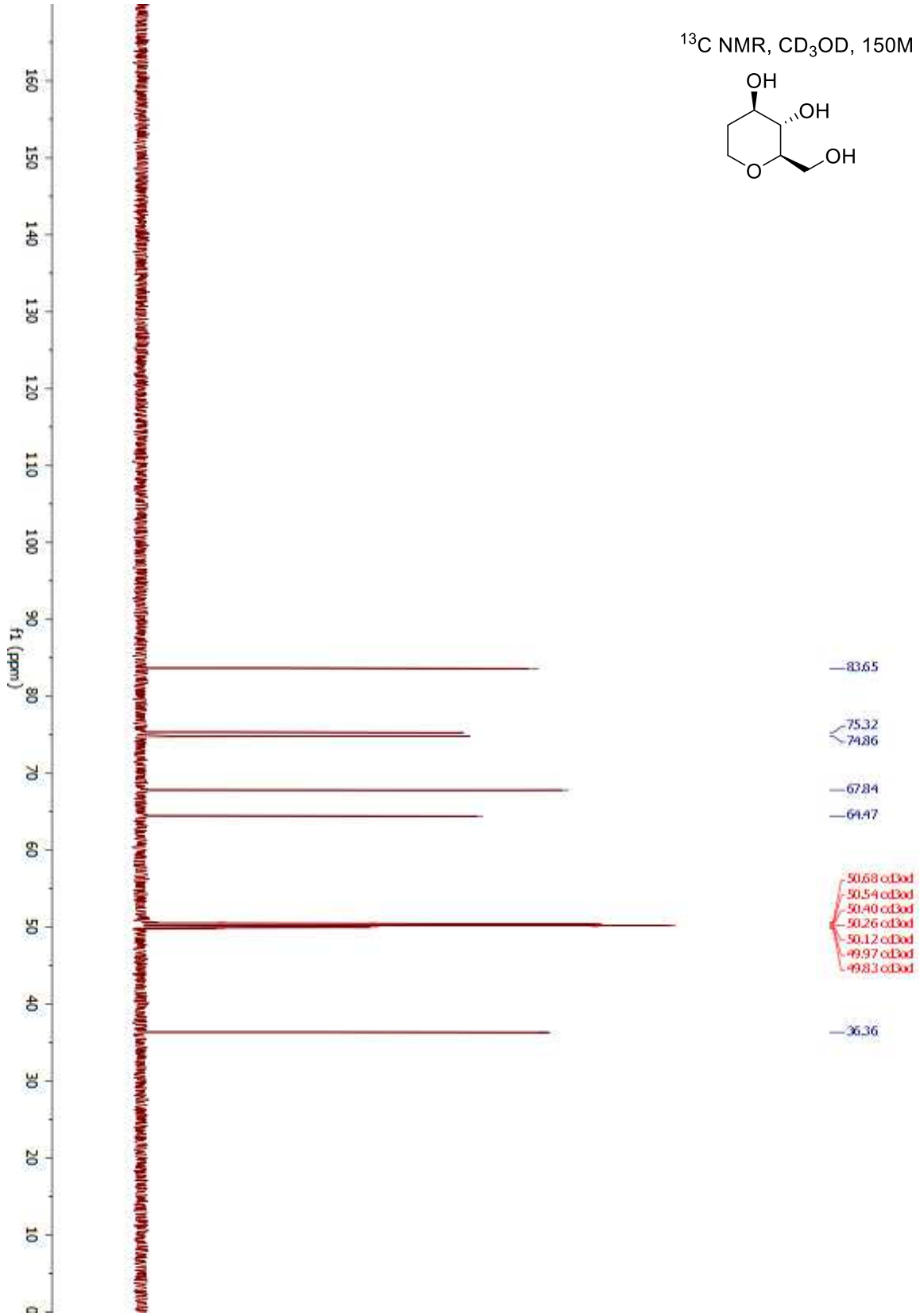
	1	2	3
	A	A	A
Frequencies --	-348.5850	35.7389	69.5284
Red. masses --	8.7344	4.1168	3.7207

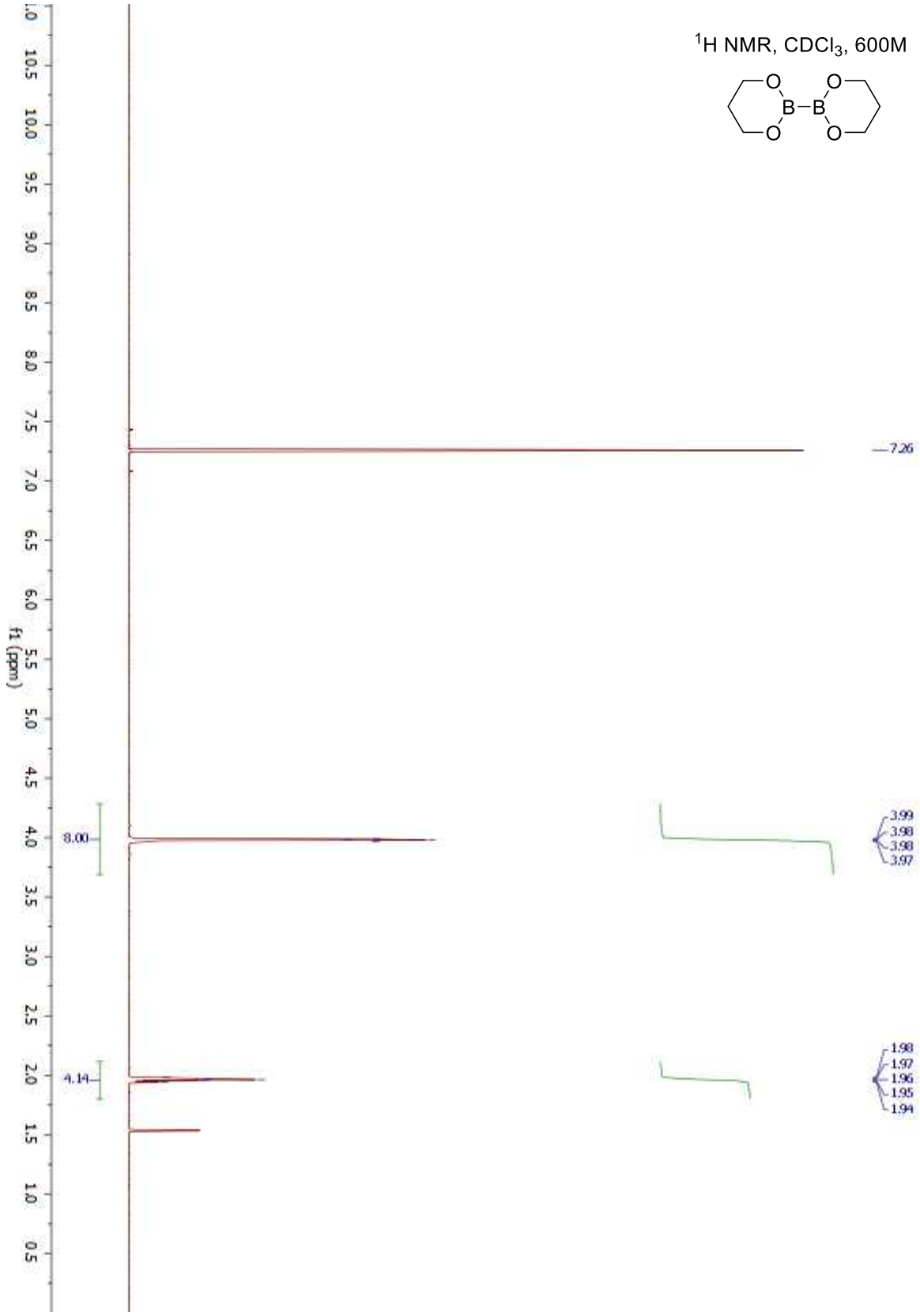
Zero-point correction= 0.455254 (Hartree/Particle)
Thermal correction to Energy= 0.476808
Thermal correction to Enthalpy= 0.477752
Thermal correction to Gibbs Free Energy= 0.407246
Sum of electronic and zero-point Energies= -1052.380582
Sum of electronic and thermal Energies= -1052.359028
Sum of electronic and thermal Enthalpies= -1052.358084
Sum of electronic and thermal Free Energies= -1052.428590

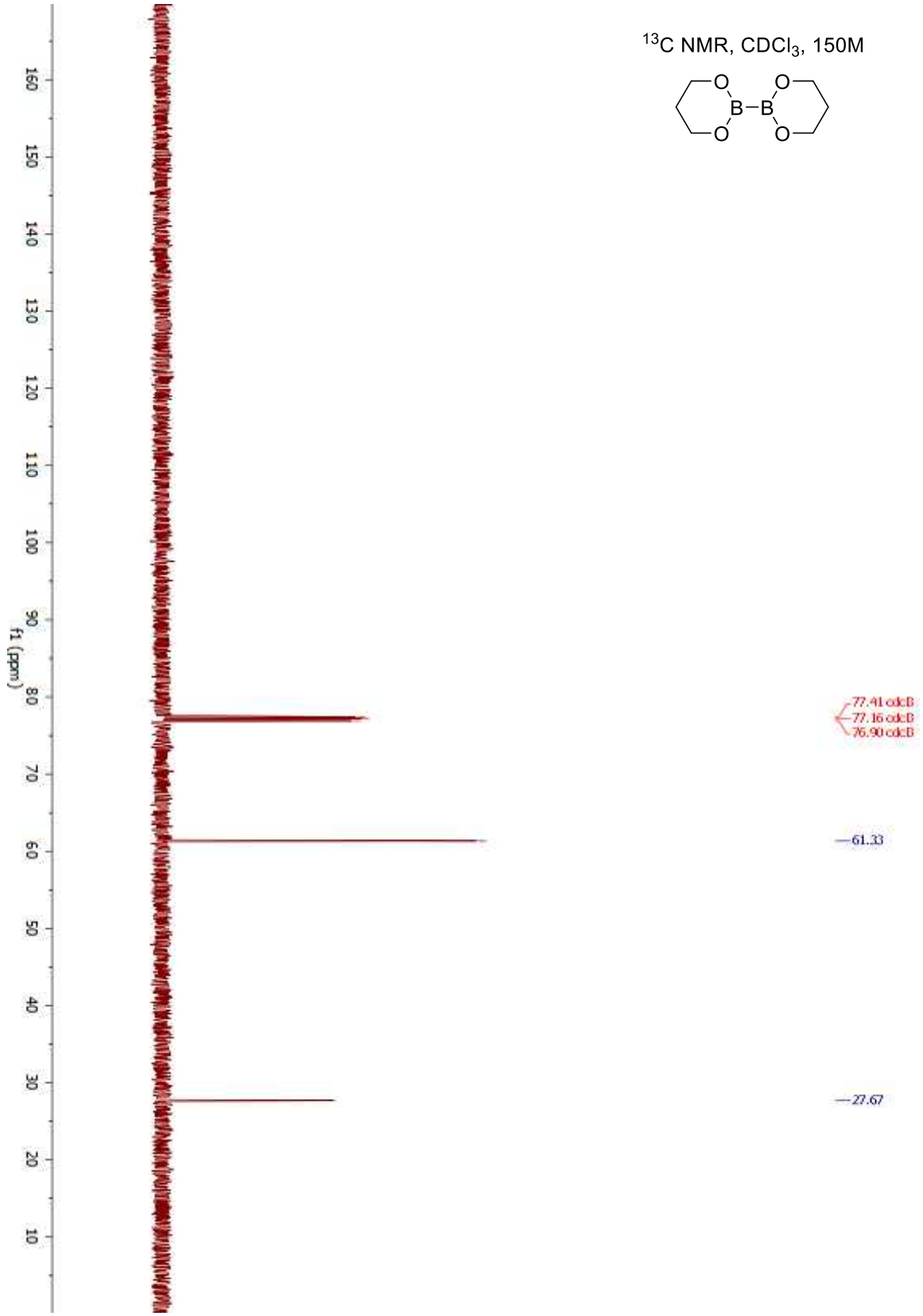
Item	Value	Threshold	Converged?
Maximum Force	0.000027	0.000450	YES
RMS Force	0.000004	0.000300	YES

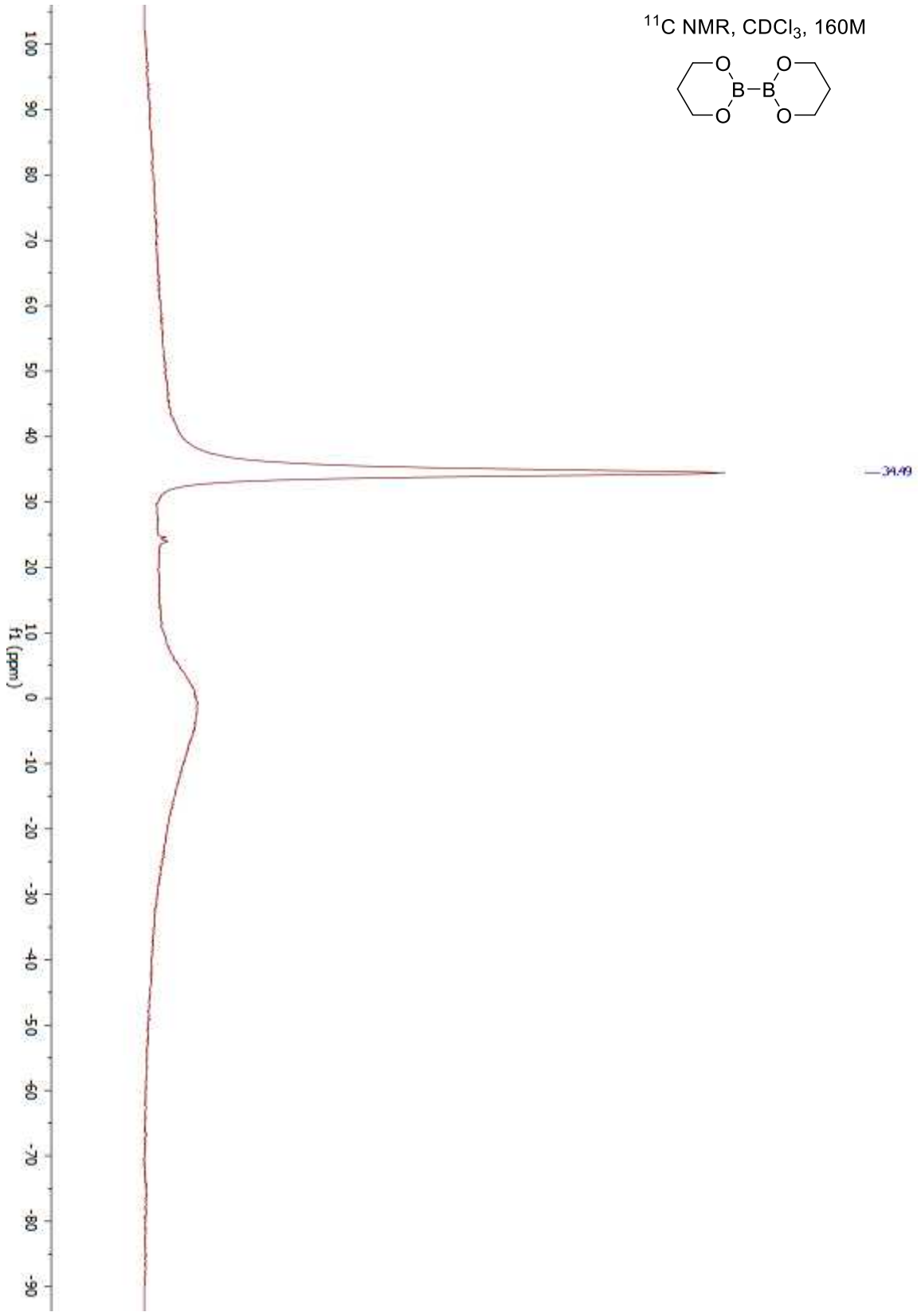
SCF: ['SCF', 'Done:', 'E(RM062X)', '=', '-1052.83583618', 'A.U.', 'after', '1', 'cycles']
MP2: no data
Temperature: 298.15
G_corr: 255.55093746 kcal/mol
H_corr: 299.79415752 kcal/mol
S_corr: 44.2436711 kcal/mol
S_elec: 0.0 kcal/mol
S_trans: 12.88455225 kcal/mol
S_rot: 10.2617267 kcal/mol
S_vib: 21.09739215 kcal/mol

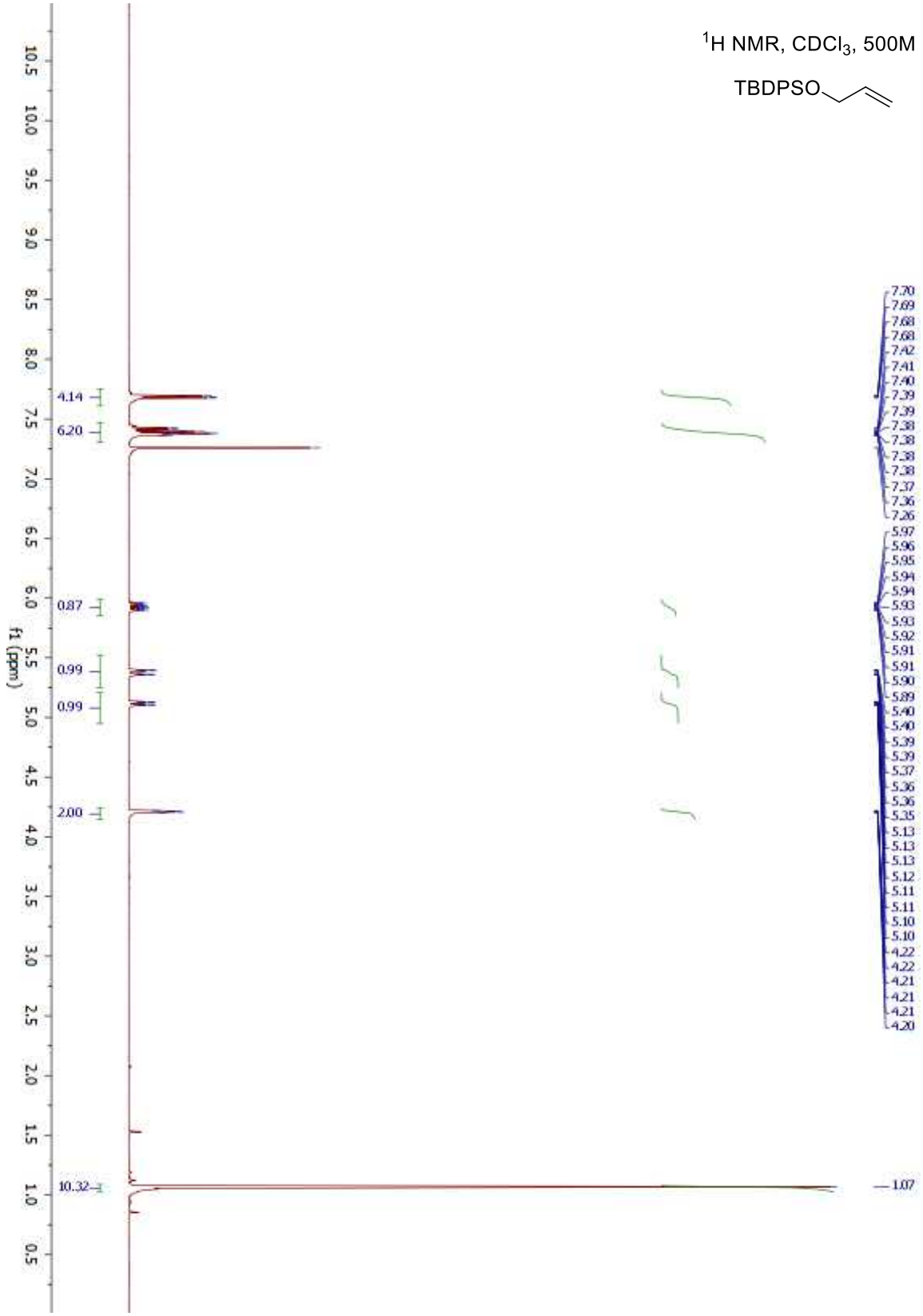

^{1}H NMR, CD_3OD, 600M
OH
OH
OH
O
f1 (ppm)
1.00
0.99
1.01
0.93
1.01
0.34
0.22
1.81
0.99
1.01

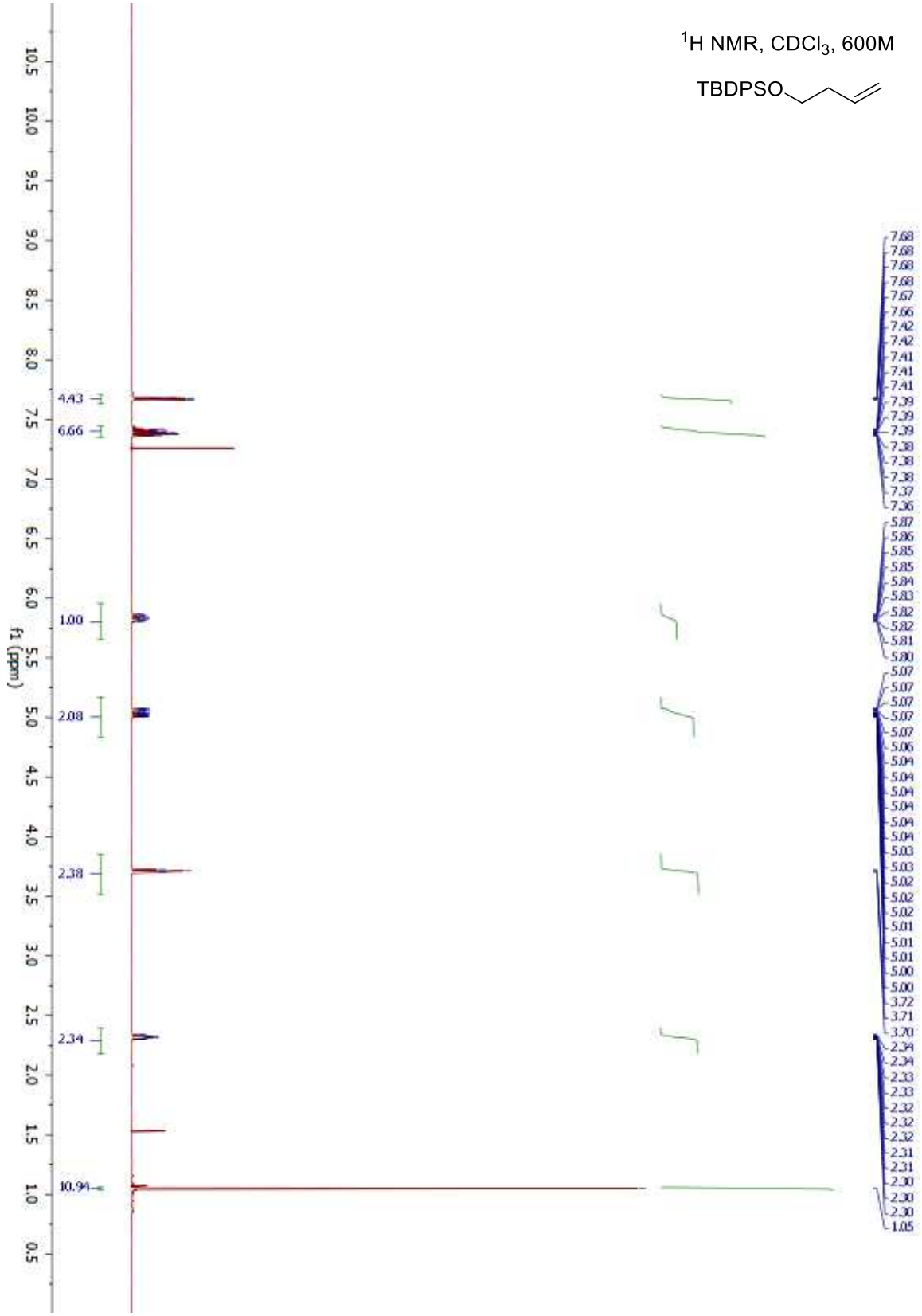

^{13}C NMR, CD_3OD, 150M
OH
OH
OH
O
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
83.65
75.32
74.86
67.84
64.47
50.68 cd3od
50.54 cd3od
50.40 cd3od
50.26 cd3od
50.12 cd3od
49.97 cd3od
49.83 cd3od
36.36

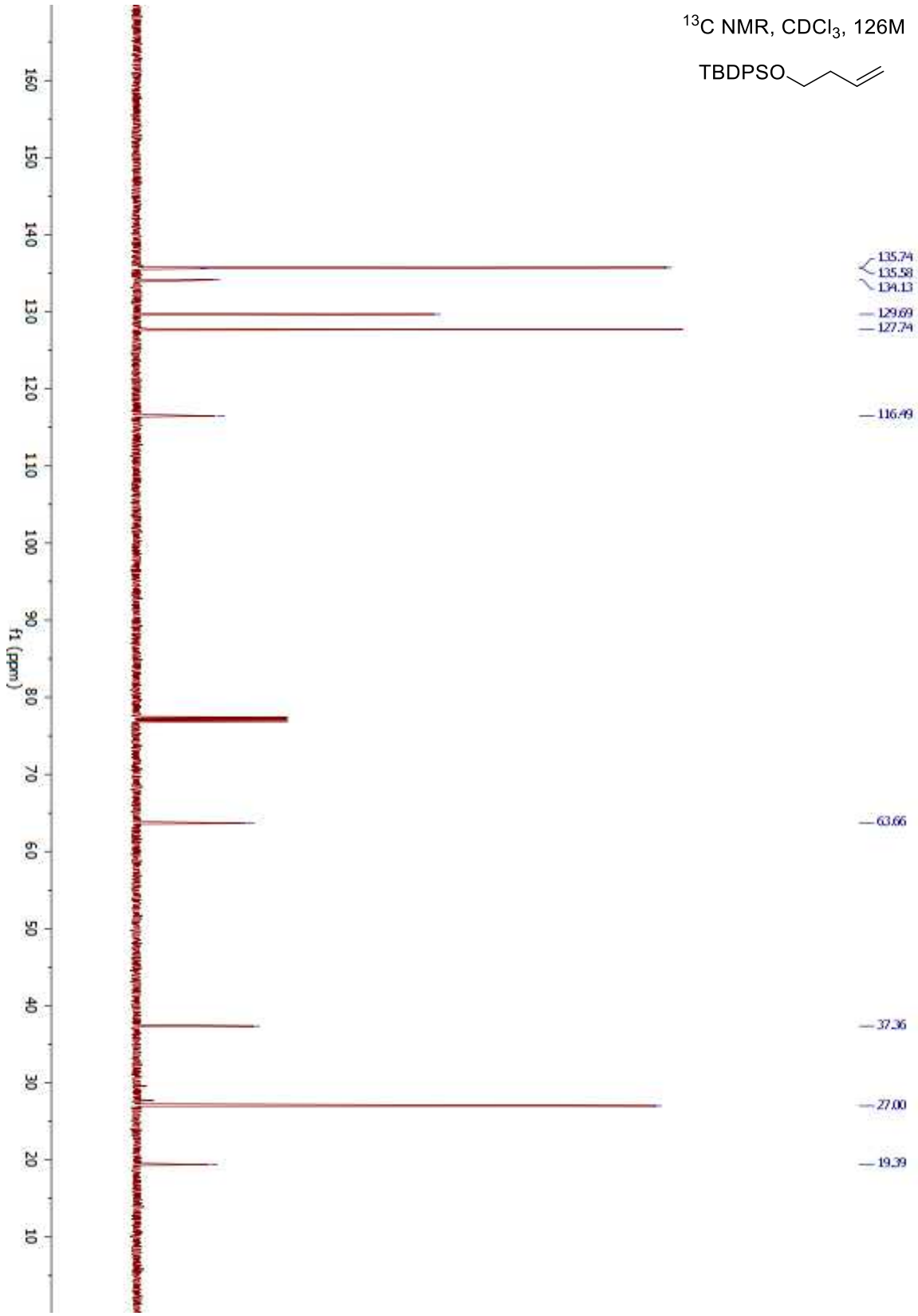

^{1}H NMR, $CDCl_3$, 600M
O
O
B
B
O
O
7.26
3.99
3.98
3.98
3.97
8.00
1.98
1.97
1.96
1.95
1.94
4.14
f1 (ppm)

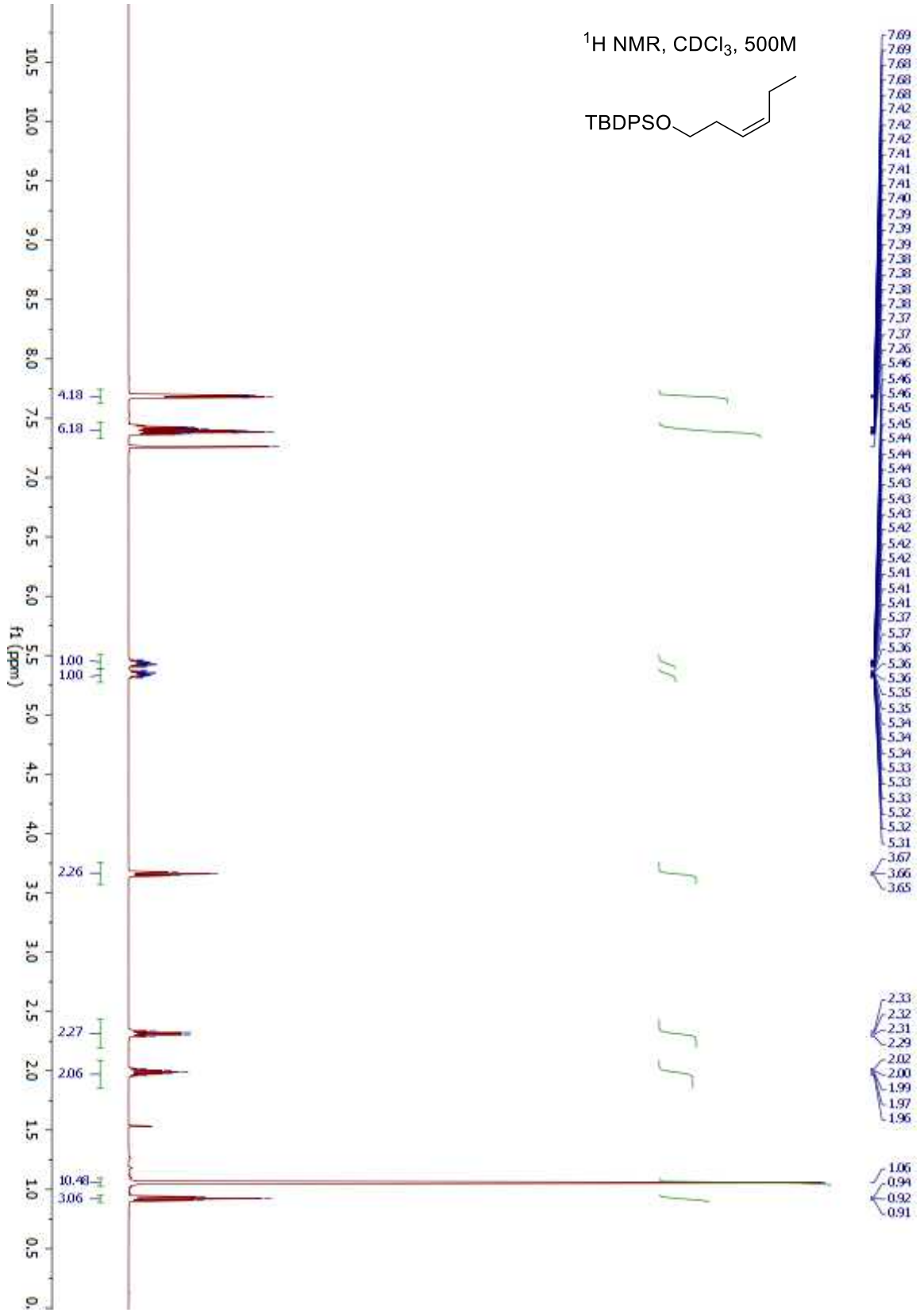

^{13}C NMR, $CDCl_3$, 150M
O
O
B
B
O
O
77.41 cdcl3
77.16 cdcl3
76.90 cdcl3
61.33
27.67
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

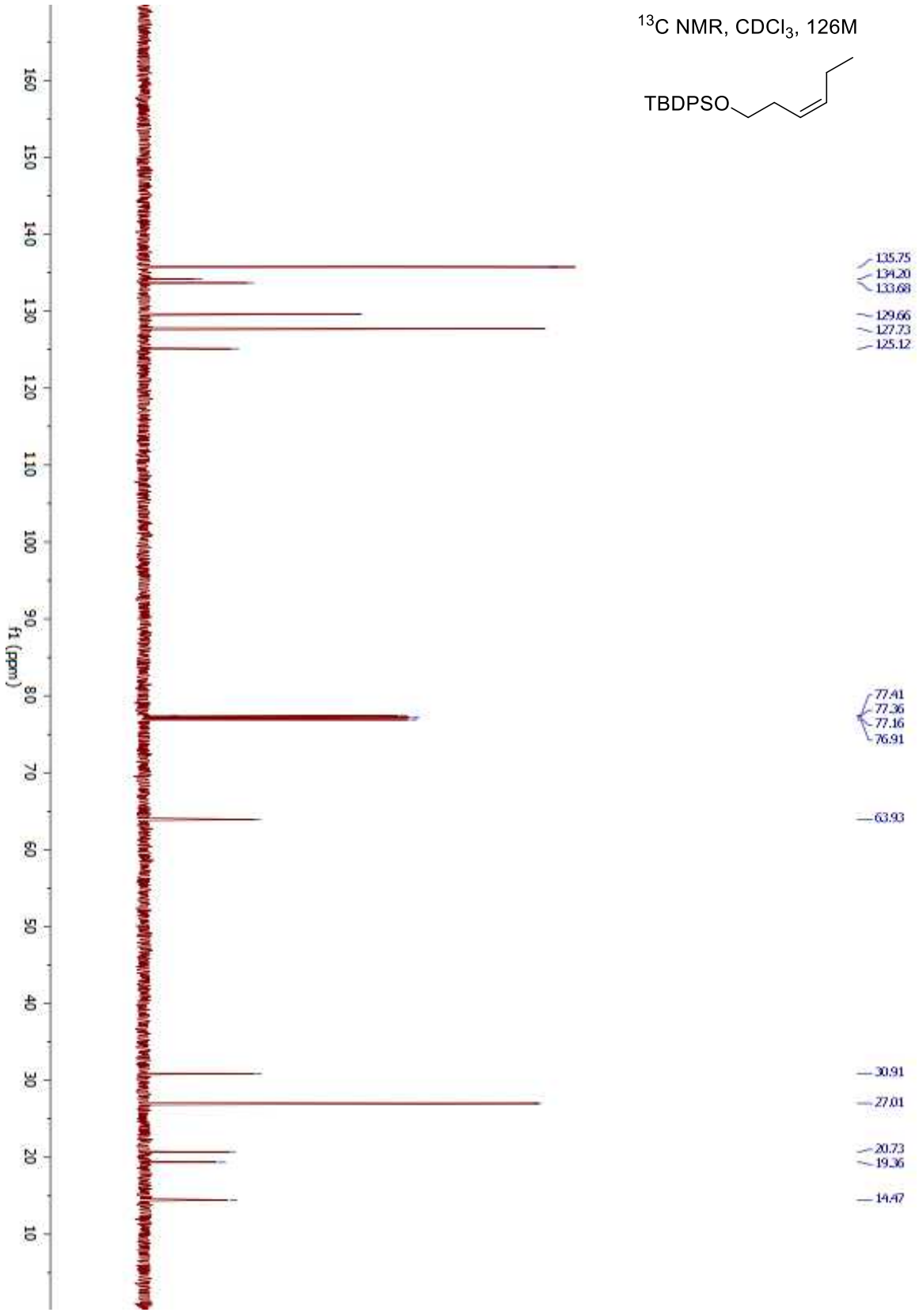

^{11}C NMR, $CDCl_3$, 160M
O
O
B
B
O
O
34.49
f1 (ppm)
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90

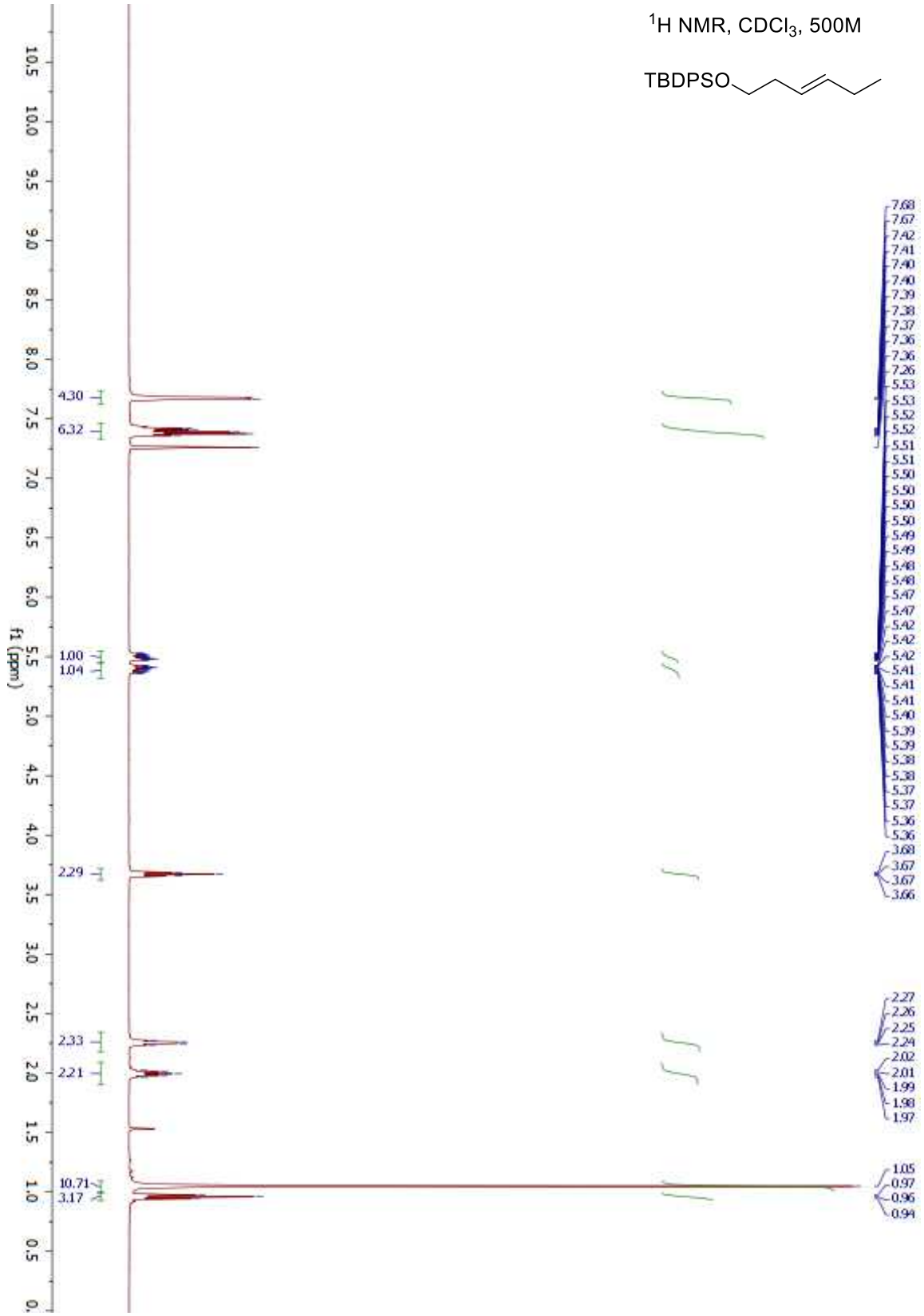

^{1}H NMR, $CDCl_3$, 500M
TBDPSO
f1 (ppm)
4.14
6.20
0.87
0.99
0.99
2.00
10.32
1.07

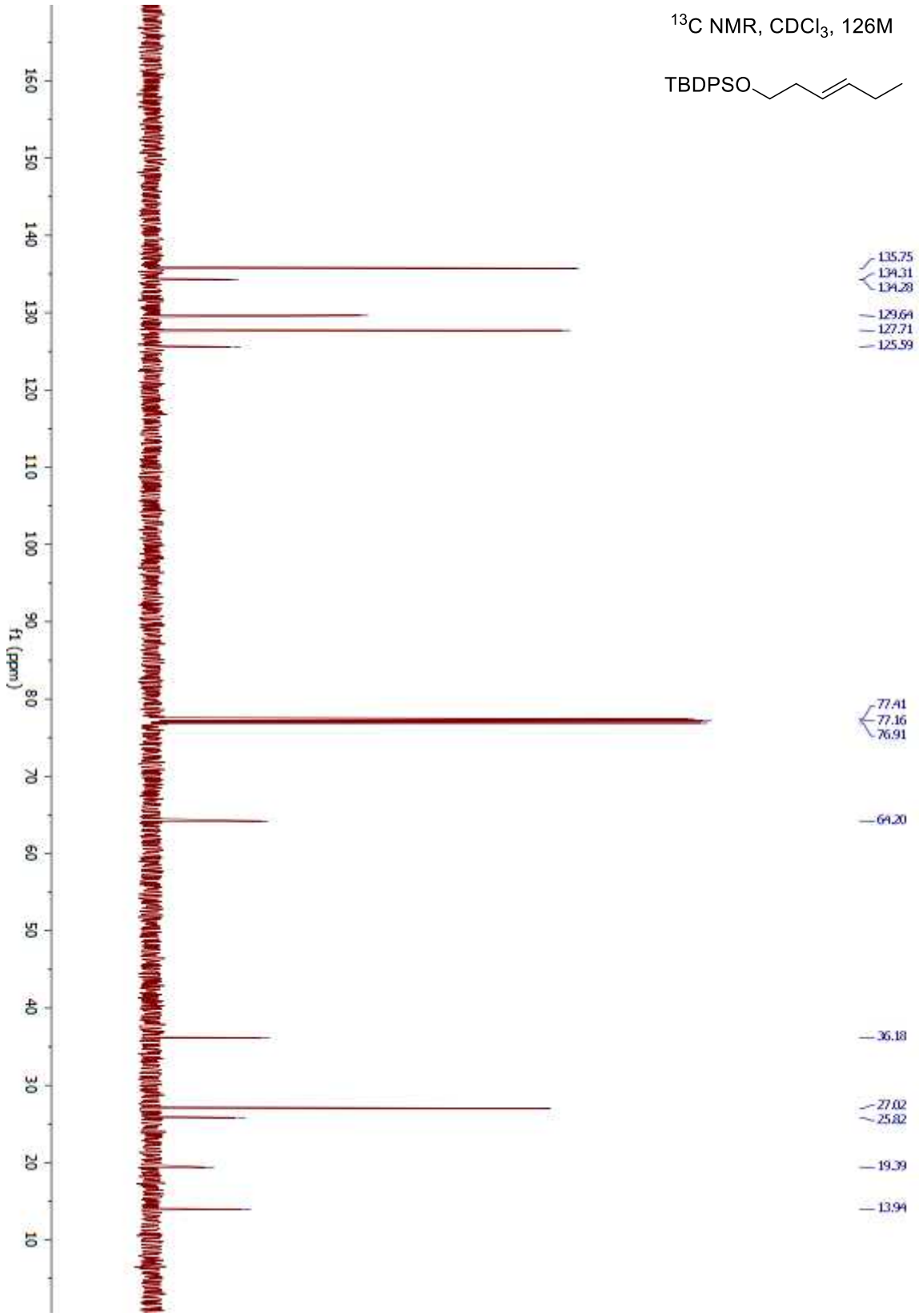

^{1}H NMR, $CDCl_3$, 600M
TBDPSO
4.43
6.66
1.00
2.08
2.38
2.34
10.91
f1 (ppm)

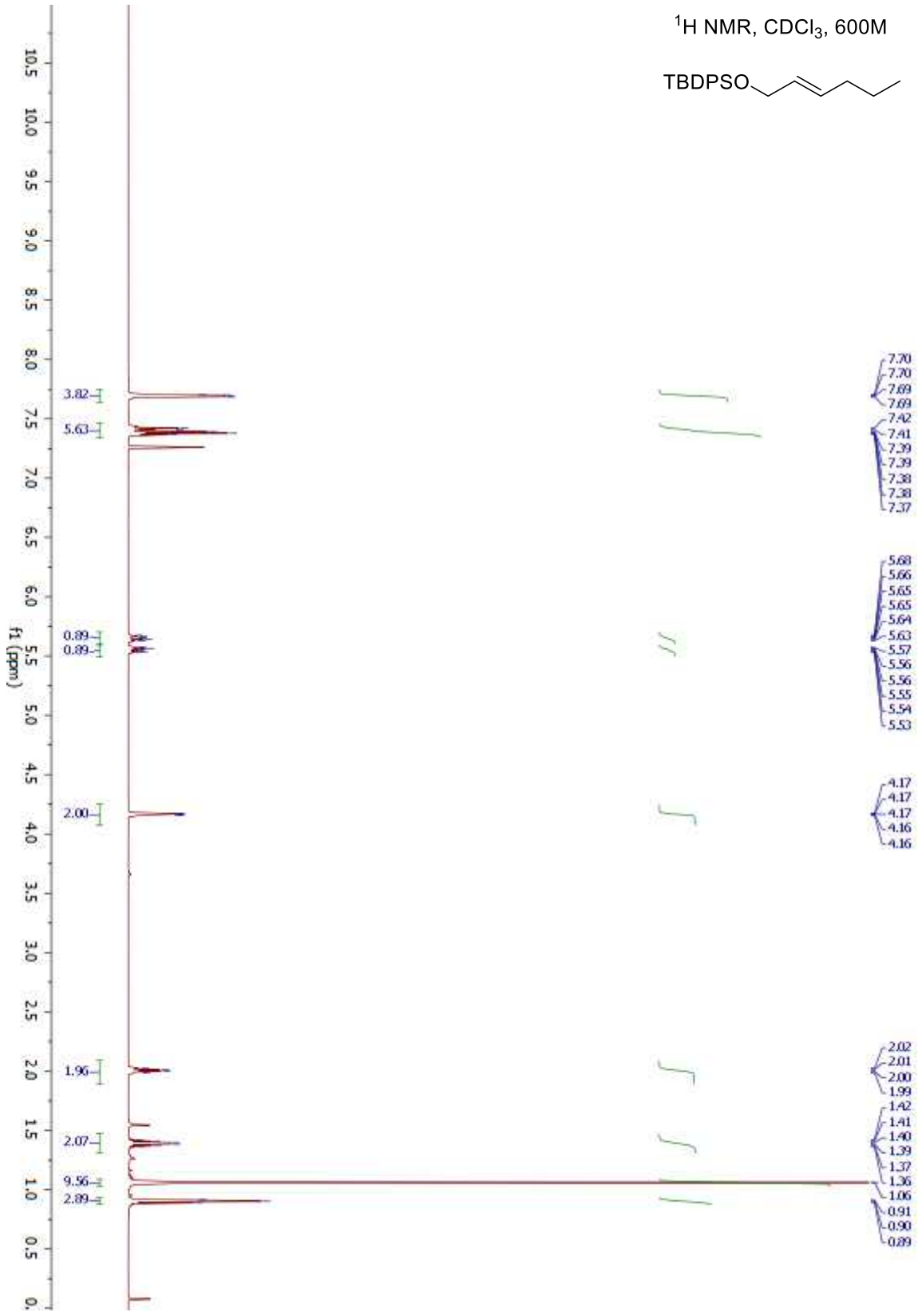

^{13}C NMR, $CDCl_3$, 126M
TBDPSO
135.74
135.58
134.13
129.69
127.74
116.49
63.66
37.36
27.00
19.39
f1 (ppm)

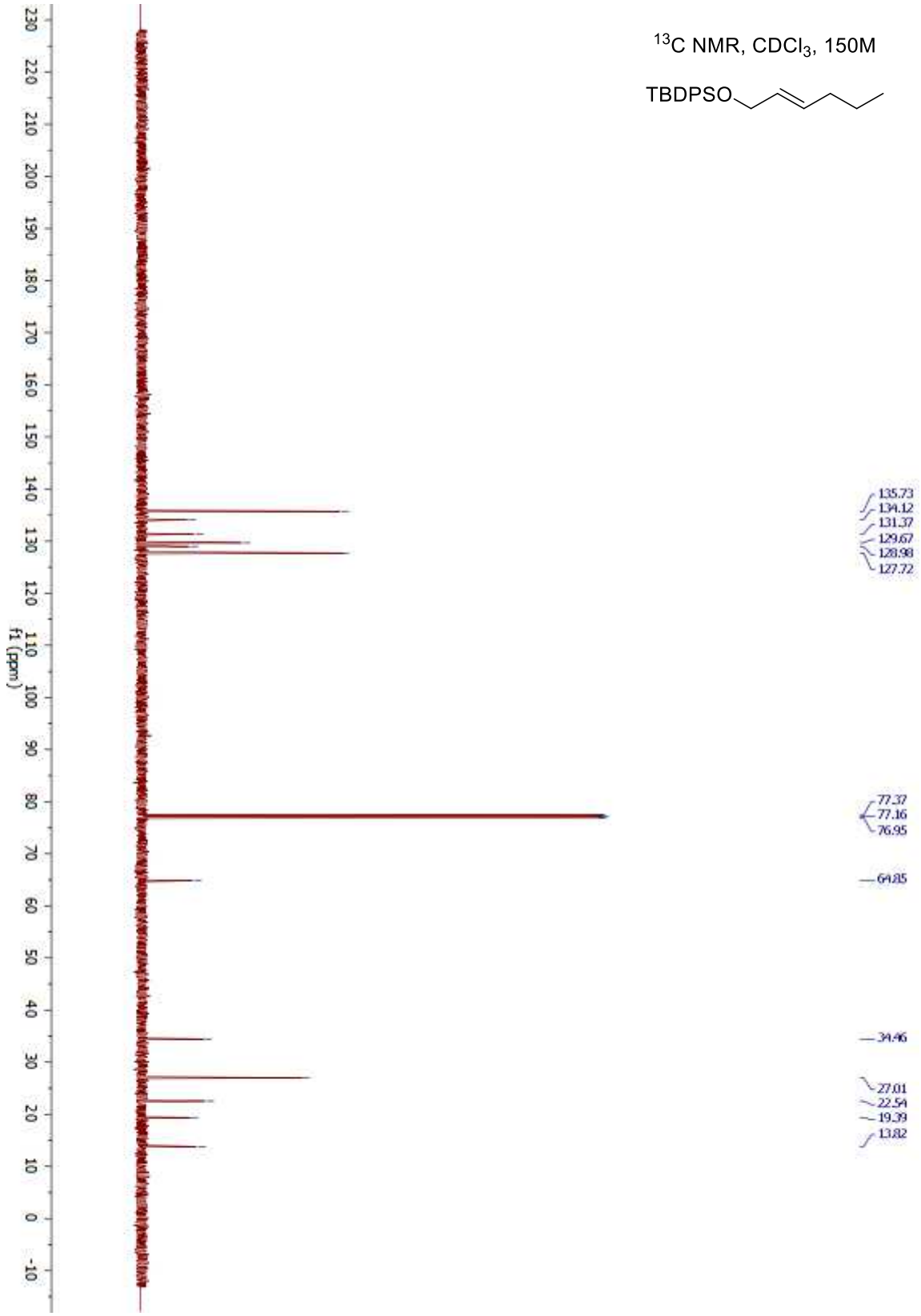

^{1}H NMR, $CDCl_3$, 500M
TBDPSO
f1 (ppm)
4.18
6.18
1.00
1.00
2.26
2.27
2.06
10.48
3.06

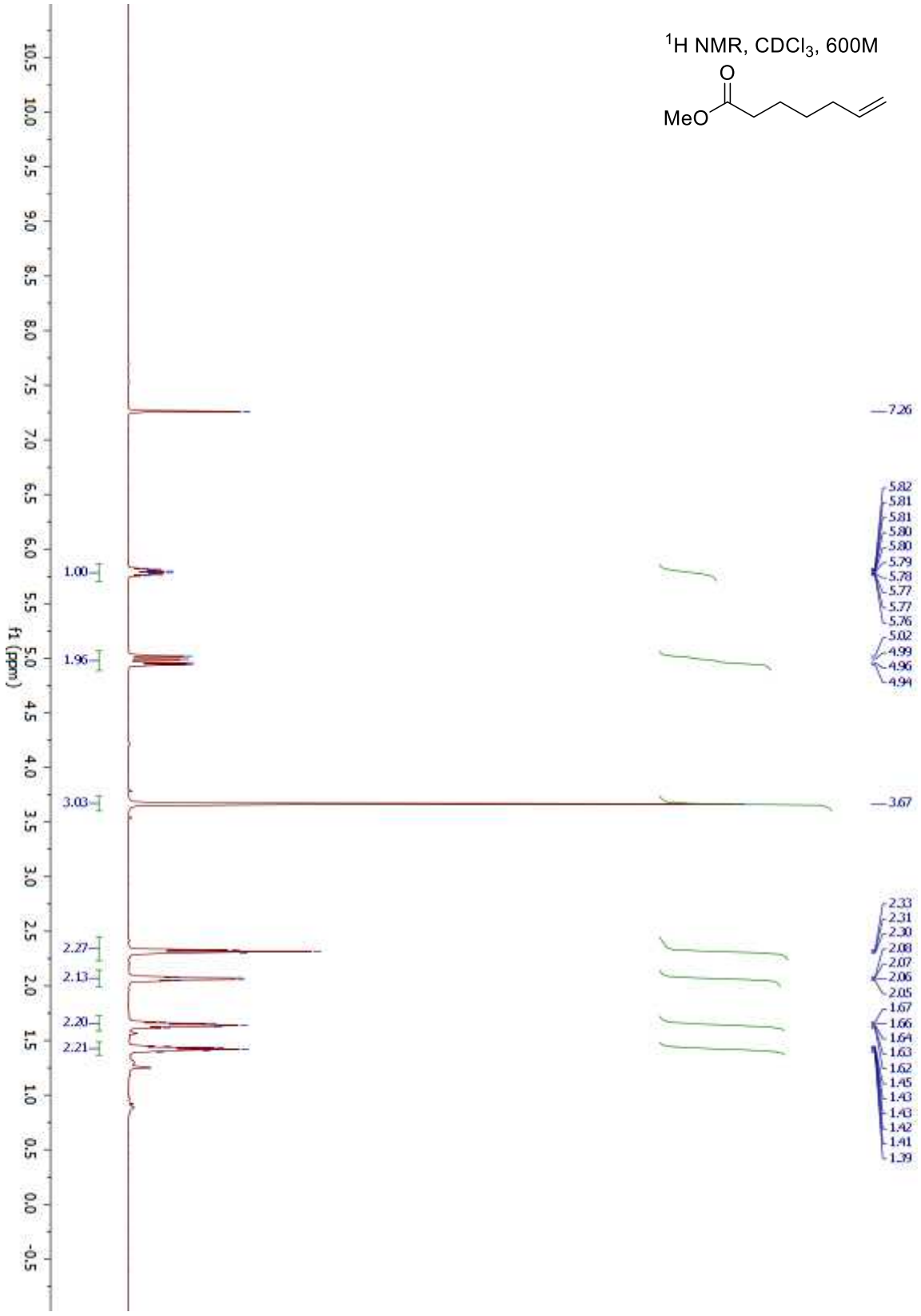

^{13}C NMR, $CDCl_3$, 126M
TBDPSO
135.75
134.20
133.68
129.66
127.73
125.12
77.41
77.36
77.16
76.91
63.93
30.91
27.01
20.73
19.36
14.47
f1 (ppm)

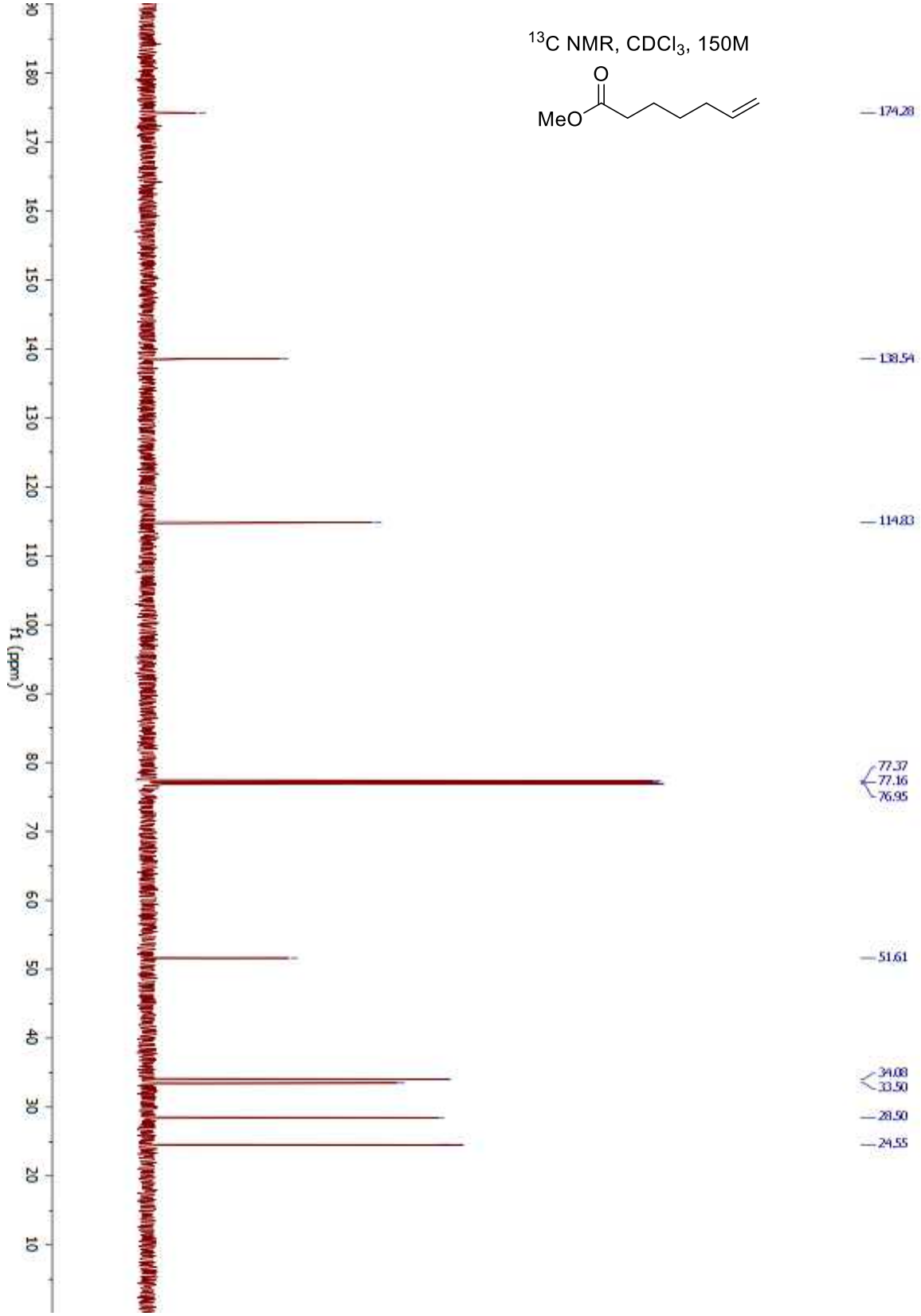

^{1}H NMR, $CDCl_3$, 500M
TBDPSO
f1 (ppm)
4.30
6.32
1.00
1.04
2.29
2.33
2.21
10.71
3.17

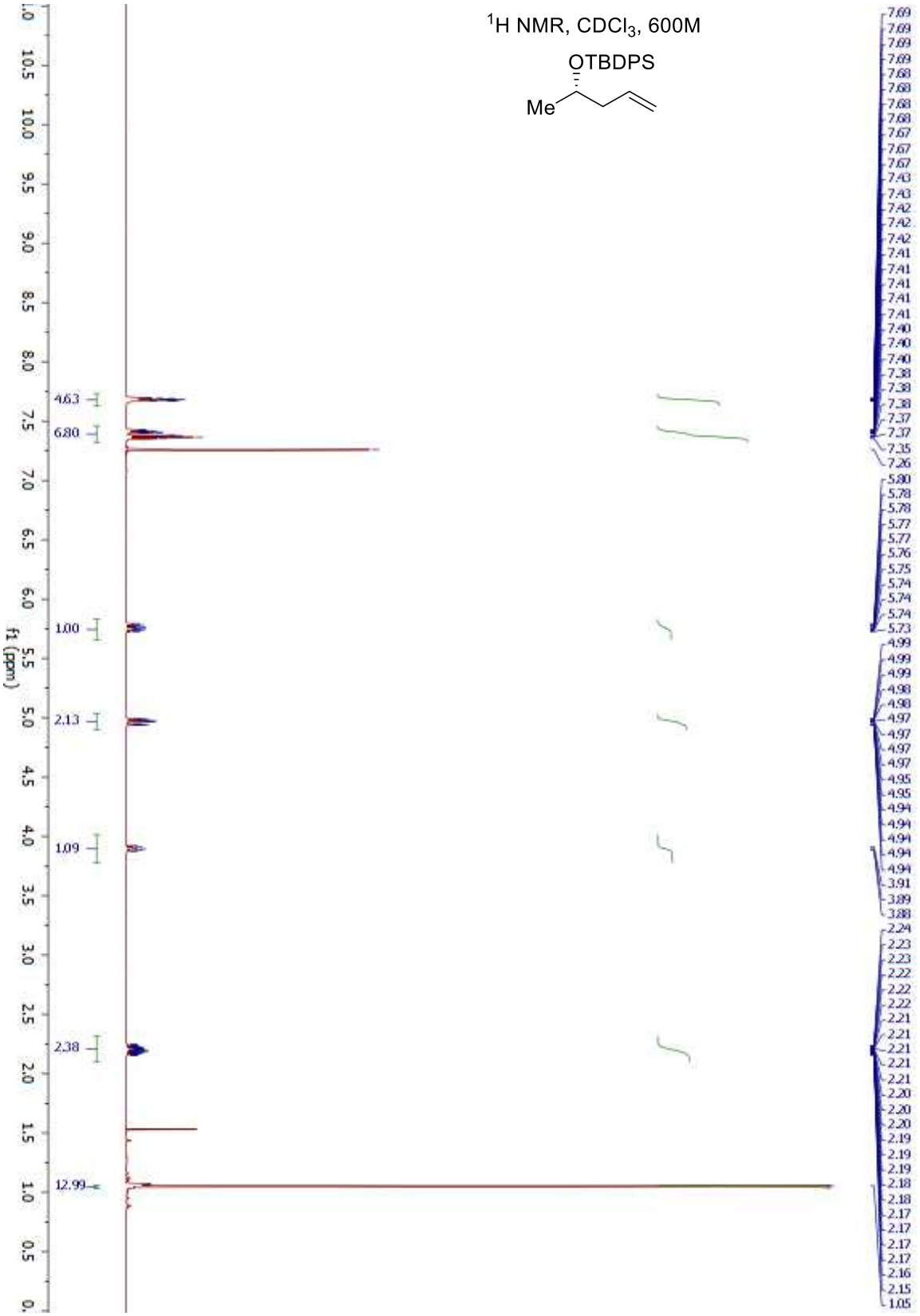

^{13}C NMR, $CDCl_3$, 126M
TBDPSO
135.75
134.31
134.28
129.64
127.71
125.59
77.41
77.16
76.91
64.20
36.18
27.02
25.82
19.39
13.94
f1 (ppm)

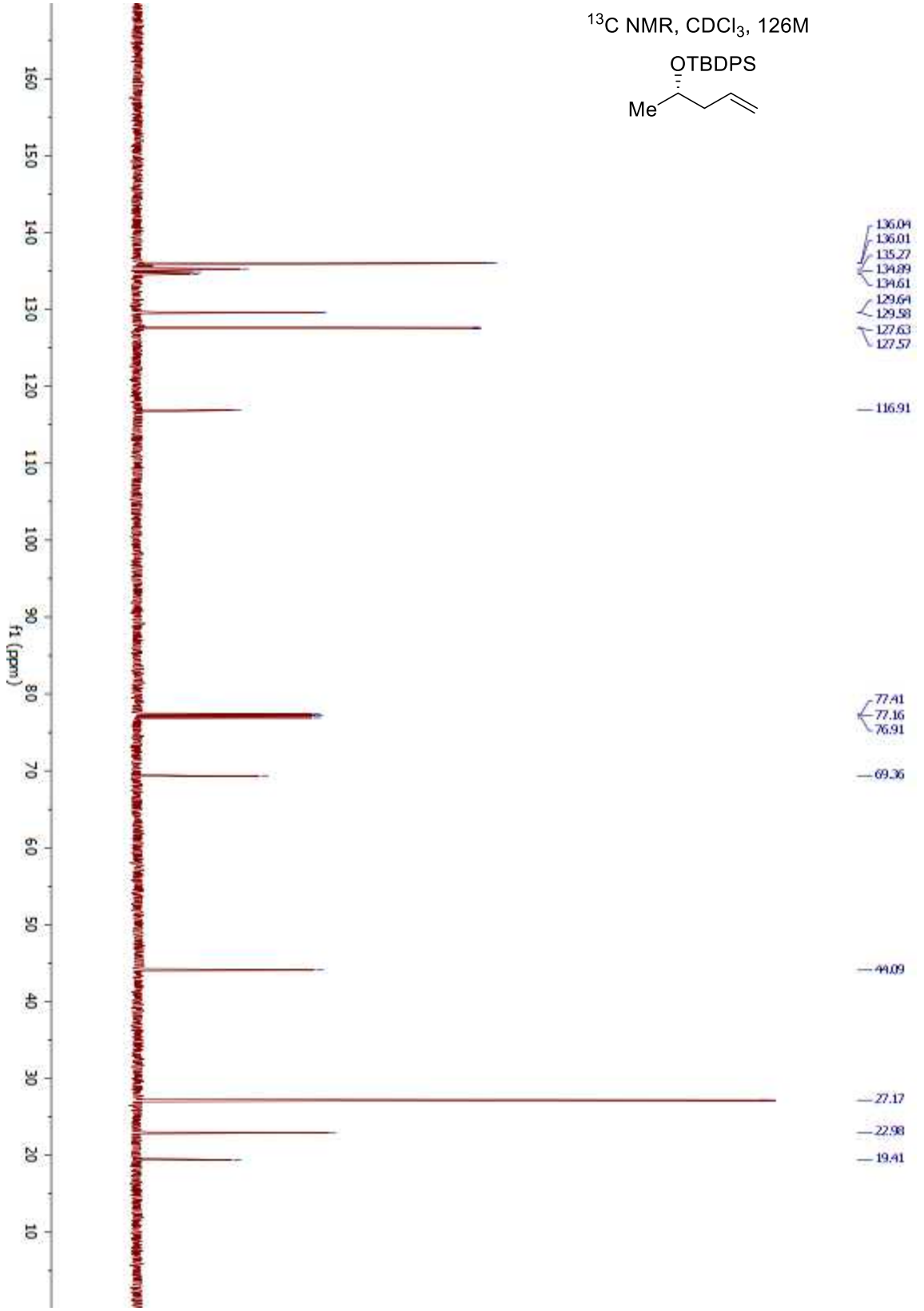

^{1}H NMR, $CDCl_3$, 600M
TBDPSO
f1 (ppm)
3.82
5.63
0.89
0.89
2.00
1.96
2.07
9.56
2.89
7.70
7.70
7.69
7.69
7.42
7.41
7.39
7.39
7.38
7.38
7.37
5.68
5.66
5.65
5.65
5.64
5.63
5.57
5.56
5.56
5.55
5.54
5.53
4.17
4.17
4.17
4.16
4.16
2.02
2.01
2.00
1.99
1.42
1.41
1.40
1.39
1.37
1.36
1.06
0.91
0.90
0.89

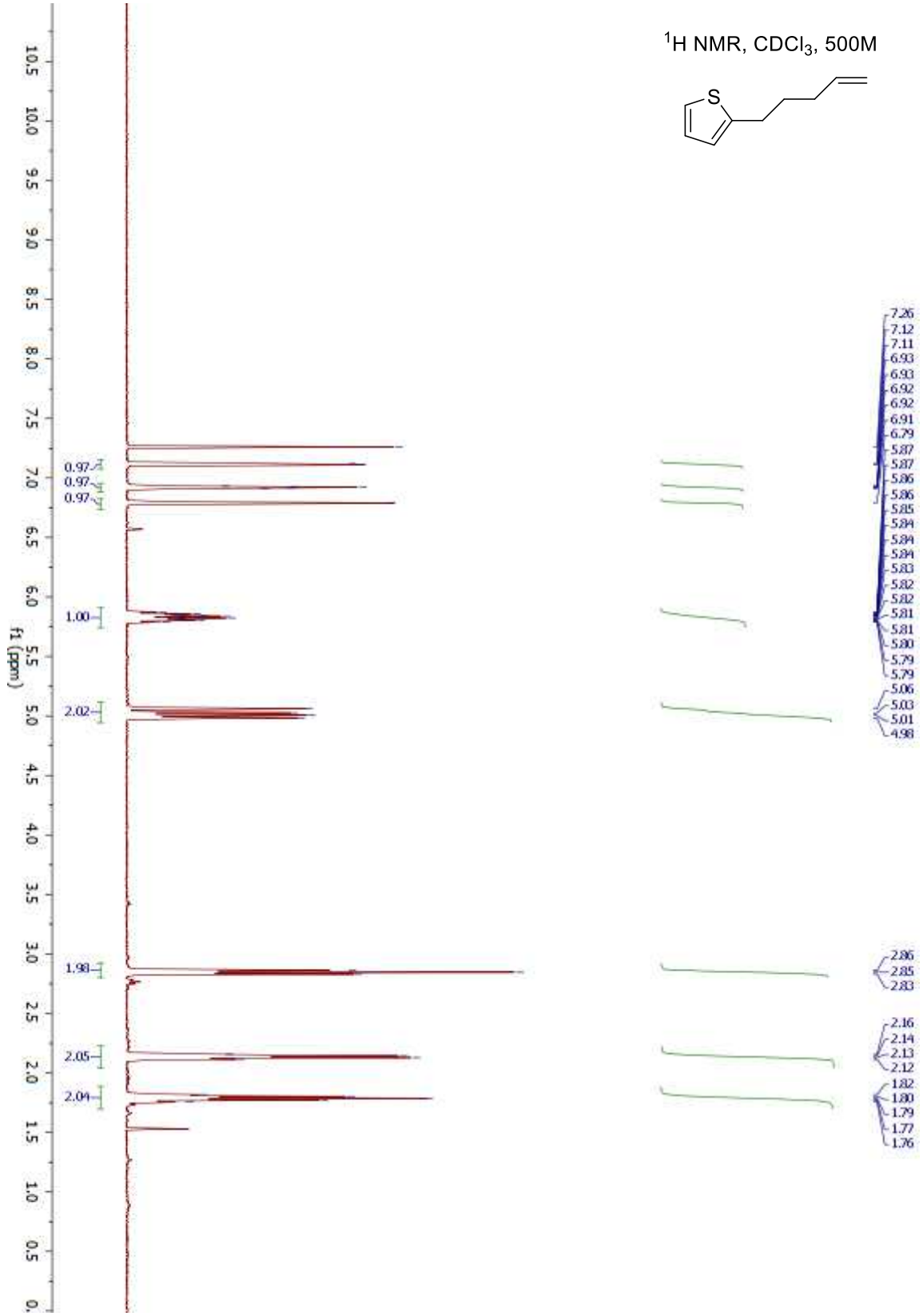

^{13}C NMR, $CDCl_3$, 150M
TBDPSO
135.73
134.12
131.37
129.67
128.98
127.72
77.37
77.16
76.95
64.85
34.46
27.01
22.54
19.39
13.82
f1 (ppm)


^{1}H NMR, $CDCl_3$, 600M
O
MeO
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
1.00
1.96
3.03
2.27
2.13
2.20
2.21
7.26
5.82
5.81
5.81
5.80
5.80
5.79
5.78
5.77
5.77
5.76
5.02
4.99
4.96
4.94
3.67
2.33
2.31
2.30
2.08
2.07
2.06
2.05
1.67
1.66
1.64
1.63
1.62
1.45
1.43
1.43
1.42
1.41
1.39


^{13}C NMR, $CDCl_3$, 150M
O
MeO
174.28
138.54
114.83
77.37
77.16
76.95
51.61
34.08
33.50
28.50
24.55
f1 (ppm)


^{1}H NMR, $CDCl_3$, 600M
OTBDPS
Me
f1 (ppm)
4.63
6.80
1.00
2.13
1.09
2.38
12.99


^{13}C NMR, $CDCl_3$, 126M
OTBDPS
Me
136.04
136.01
135.27
134.89
134.61
129.64
129.58
127.63
127.57
116.91
77.41
77.16
76.91
69.36
44.09
27.17
22.98
19.41
f1 (ppm)


^{1}H NMR, $CDCl_3$, 500M
S
f1 (ppm)
0.97
0.97
0.97
1.00
2.02
1.98
2.05
2.04
7.26
7.12
7.11
6.93
6.93
6.92
6.92
6.91
6.79
5.87
5.87
5.86
5.86
5.85
5.84
5.84
5.84
5.83
5.82
5.82
5.81
5.81
5.80
5.79
5.79
5.06
5.03
5.01
4.98
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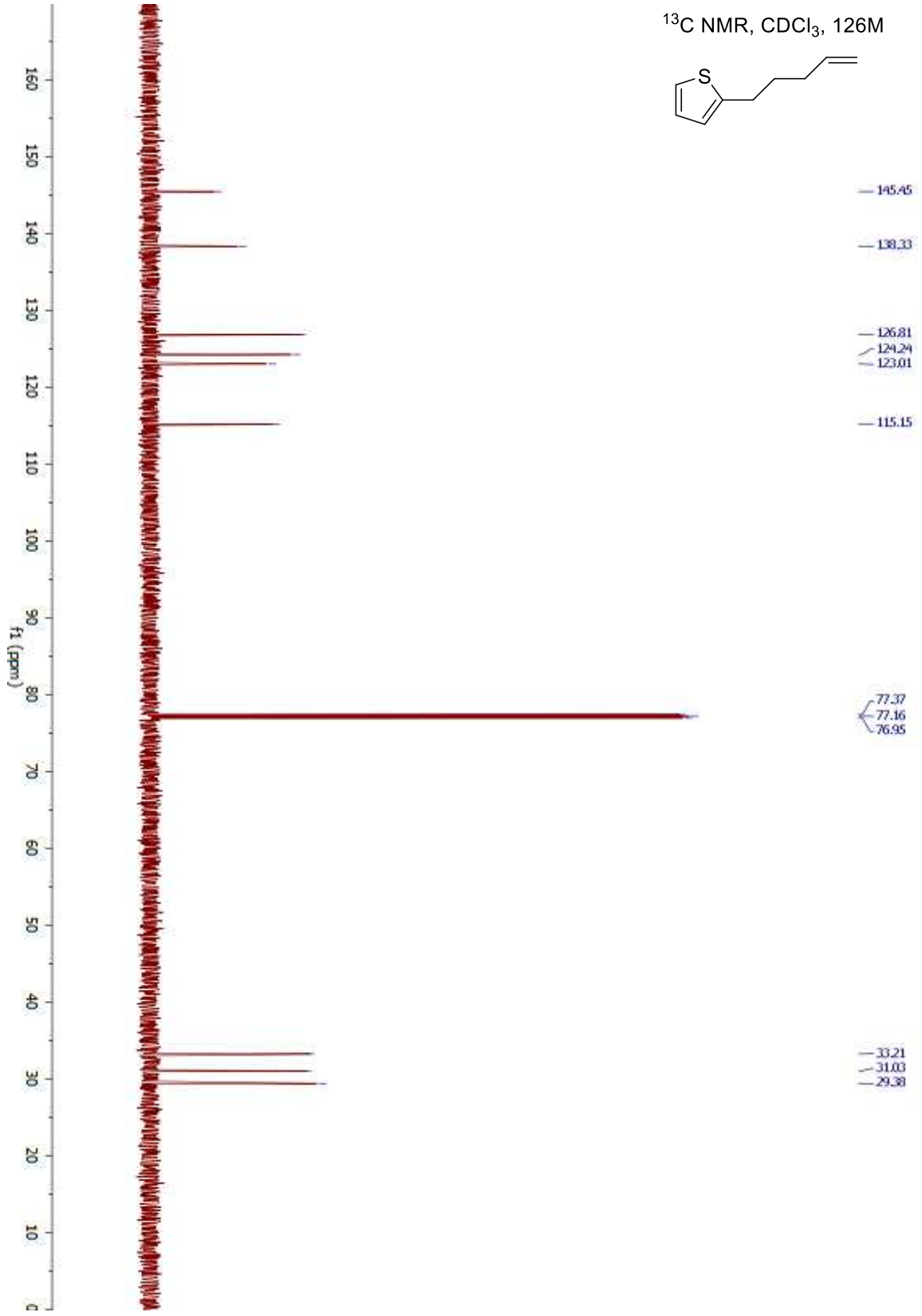
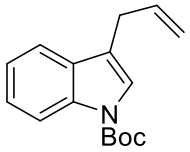
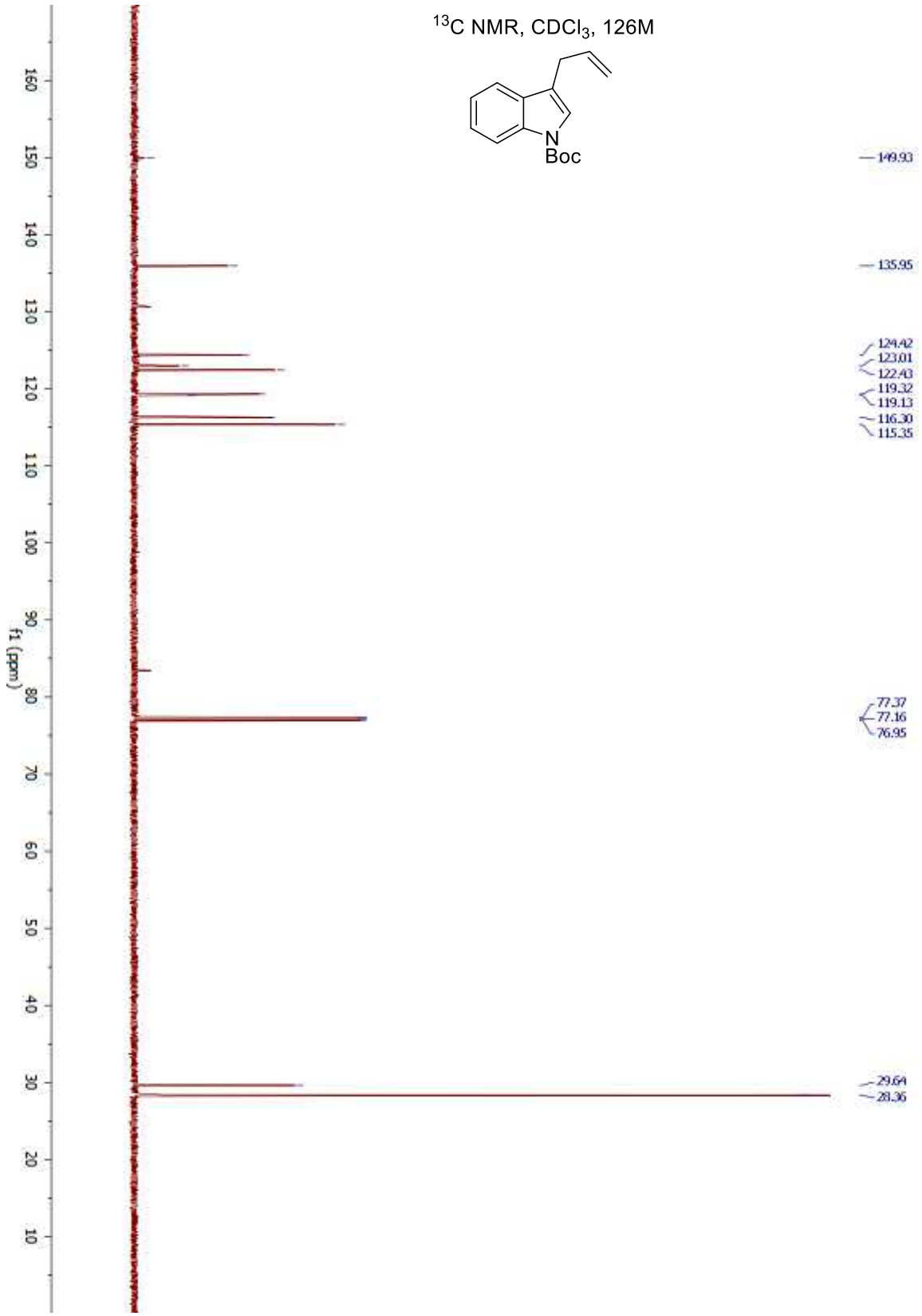
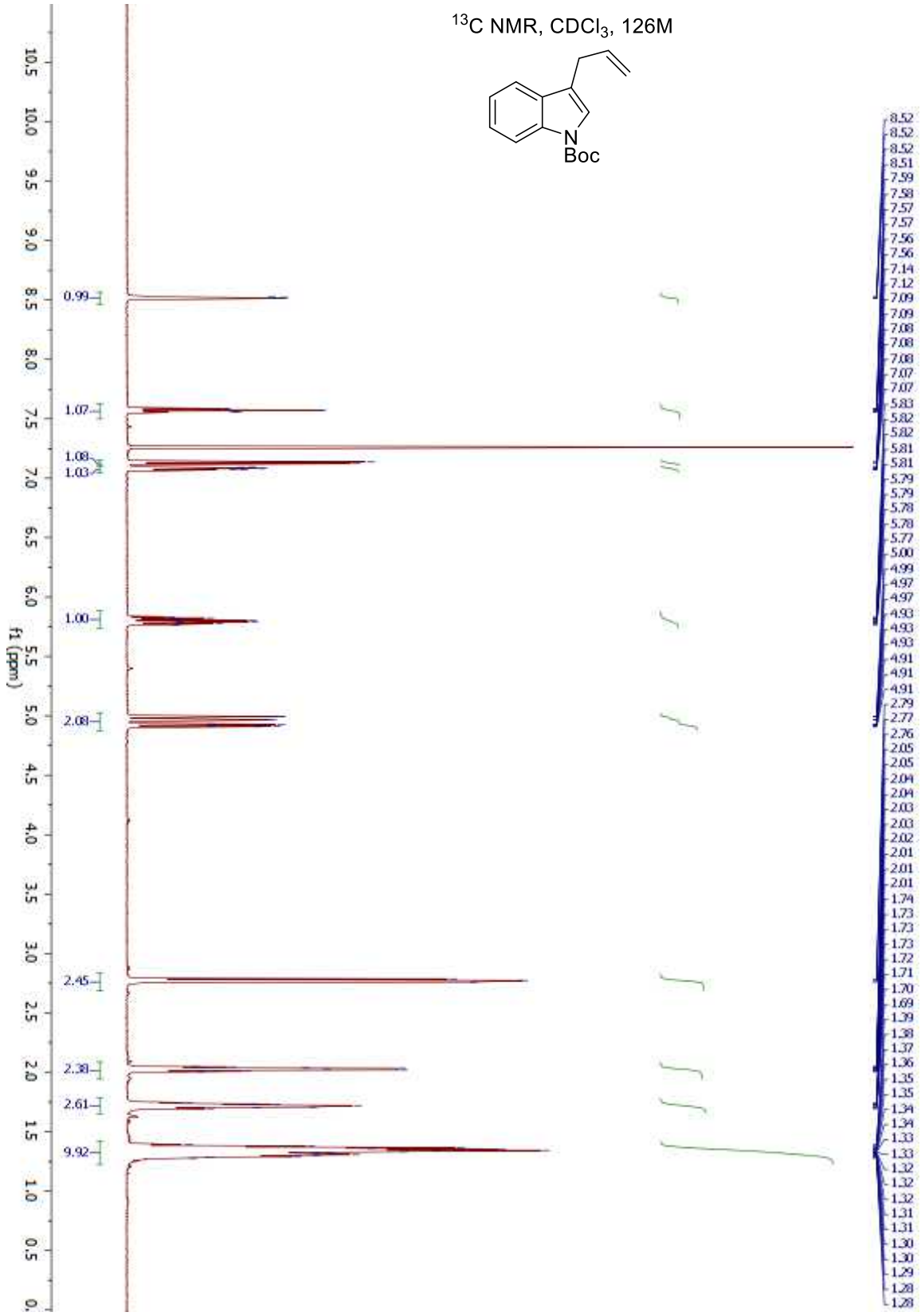
2.12
1.82
1.80
1.79
1.77
1.76

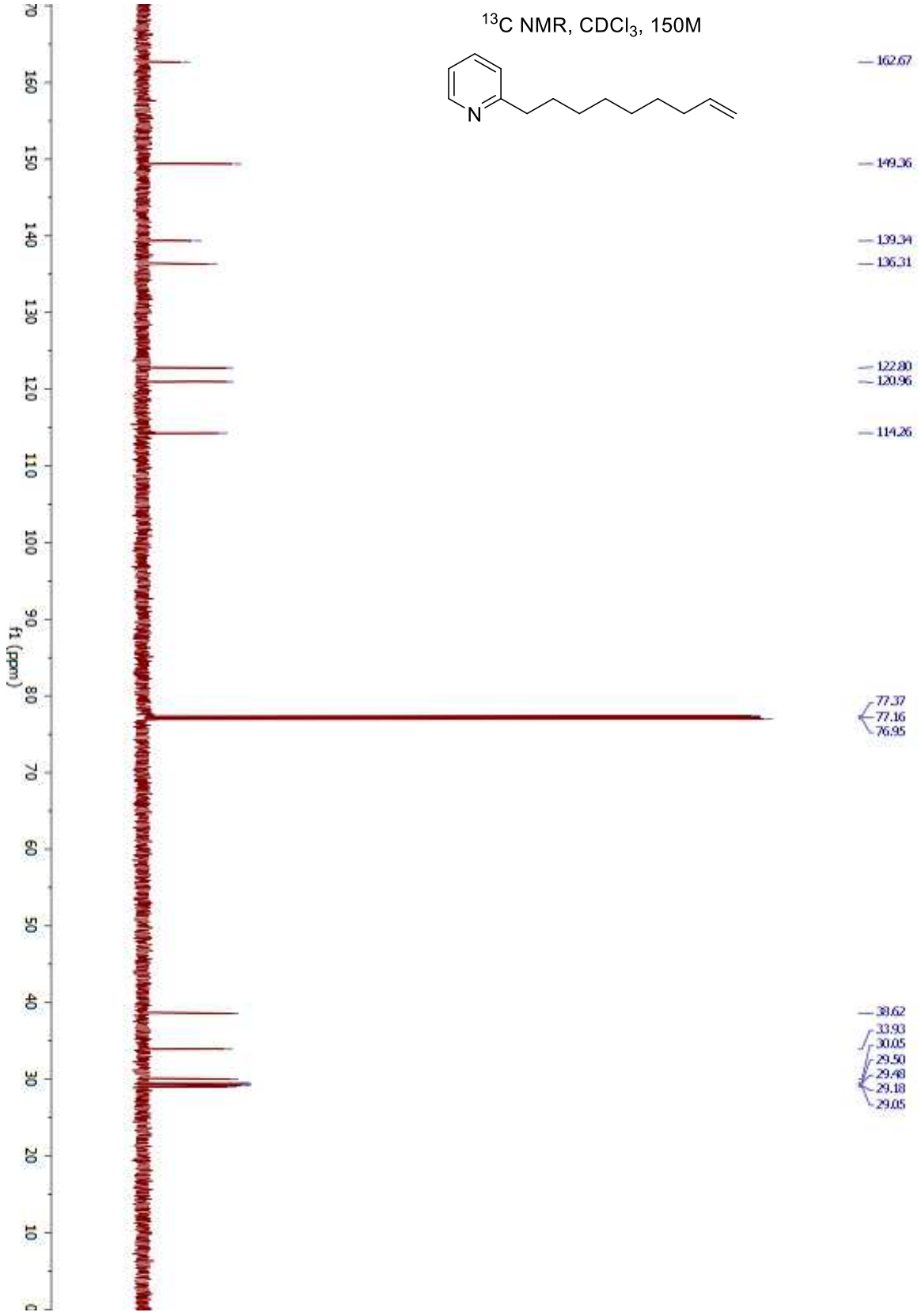

^{13}C NMR, $CDCl_3$, 126M
S
145.45
138.33
126.81
124.24
123.01
115.15
77.37
77.16
76.95
33.21
31.03
29.38
f1 (ppm)

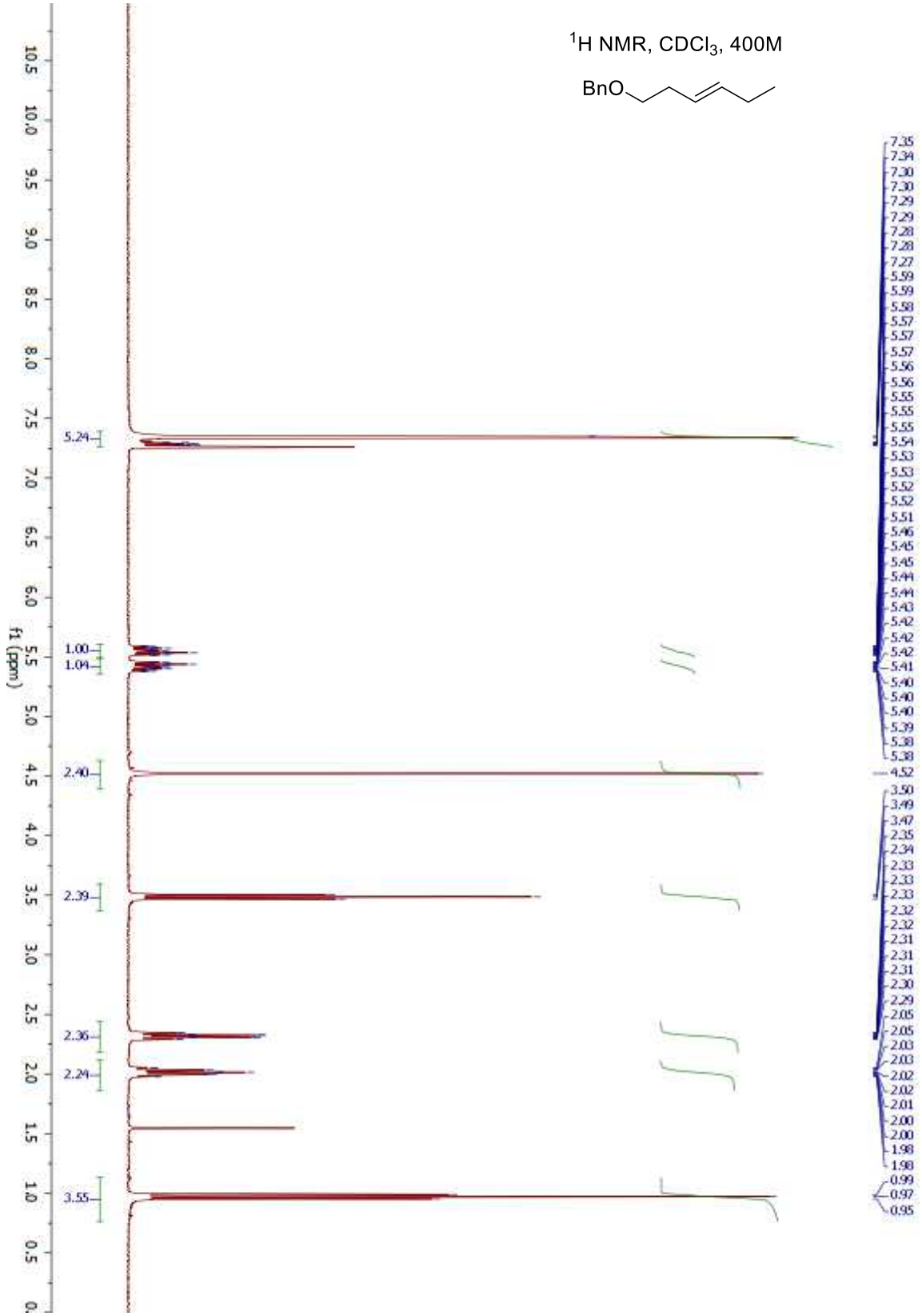
^{1}H NMR, $CDCl_3$, 500M

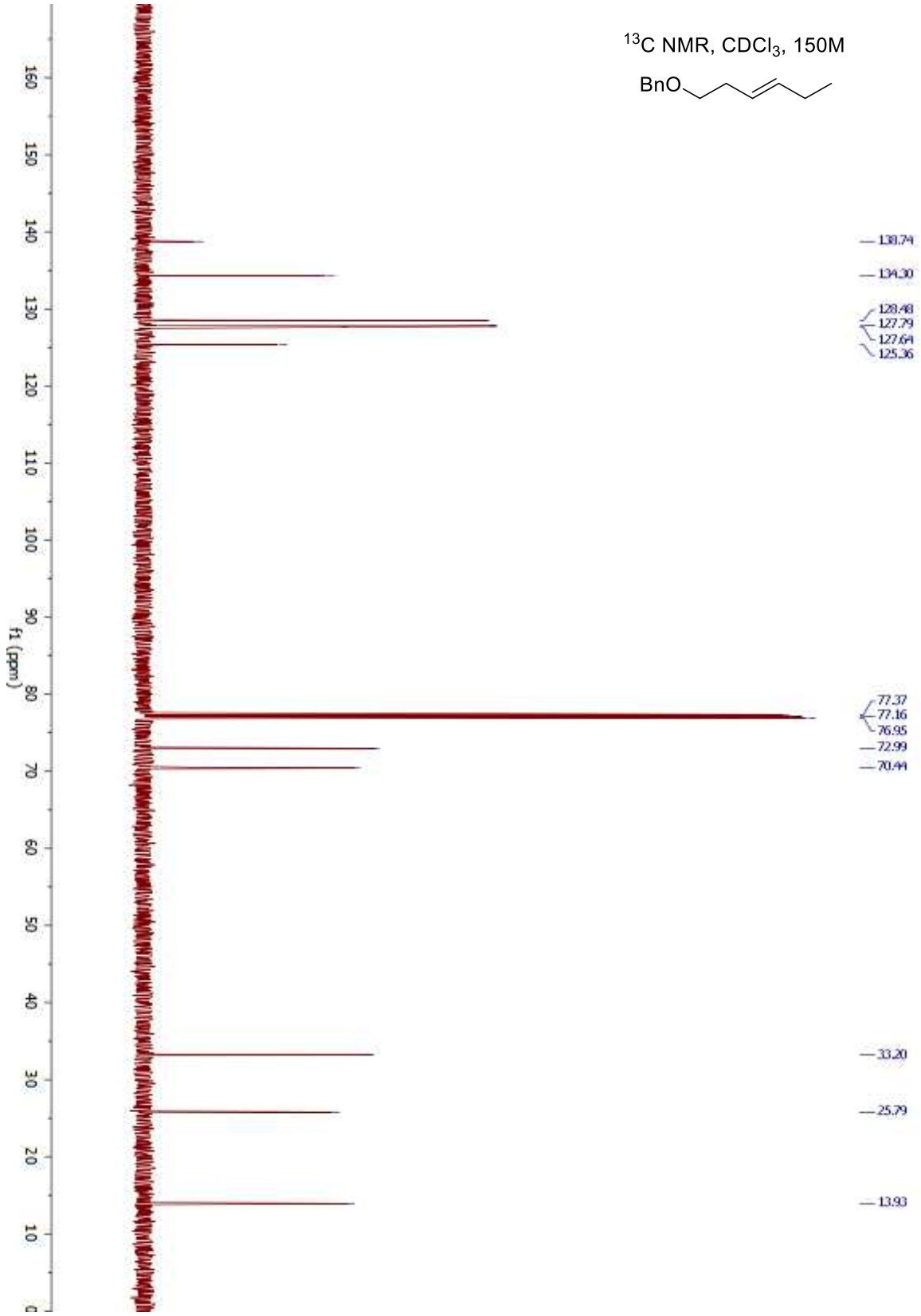


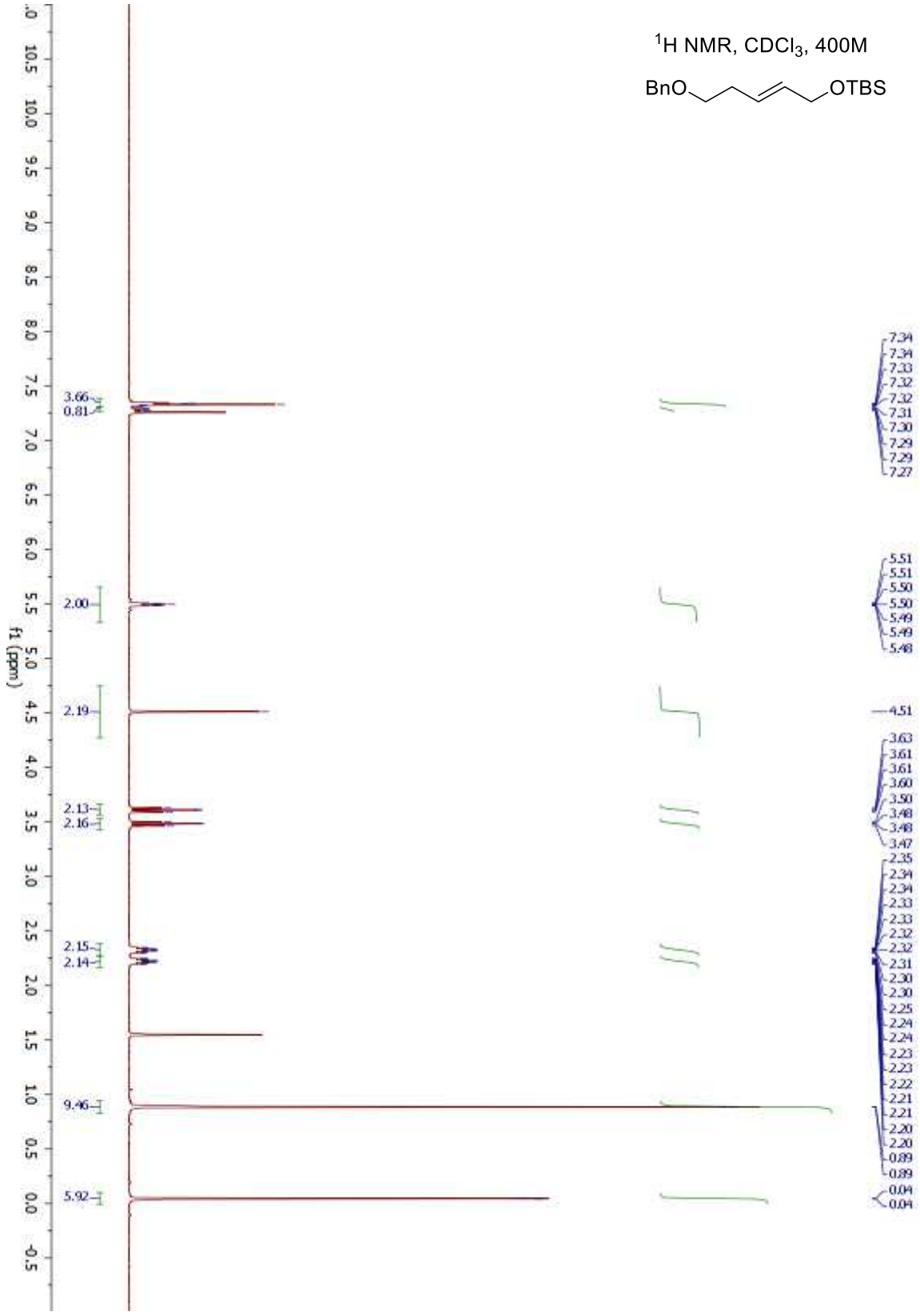

^{13}C NMR, $CDCl_3$, 126M
N
Boc
149.93
135.95
124.42
123.01
122.43
119.32
119.13
116.30
115.35
77.37
77.16
76.95
29.69
28.36
f1 (ppm)

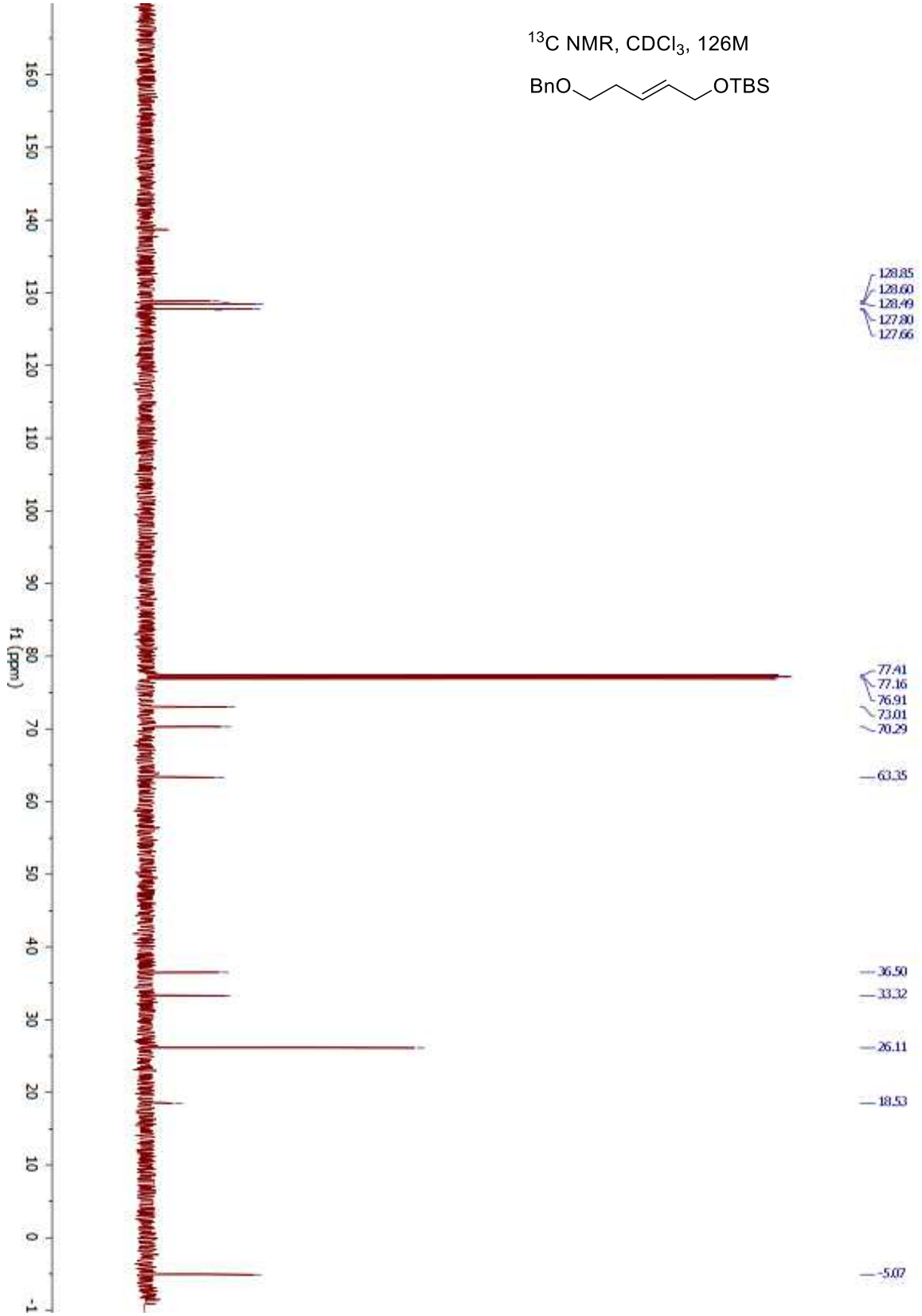

^{13}C NMR, $CDCl_3$, 126M
N
Boc
f1 (ppm)
0.99
1.07
1.08
1.03
1.00
2.08
2.45
2.38
2.61
9.92

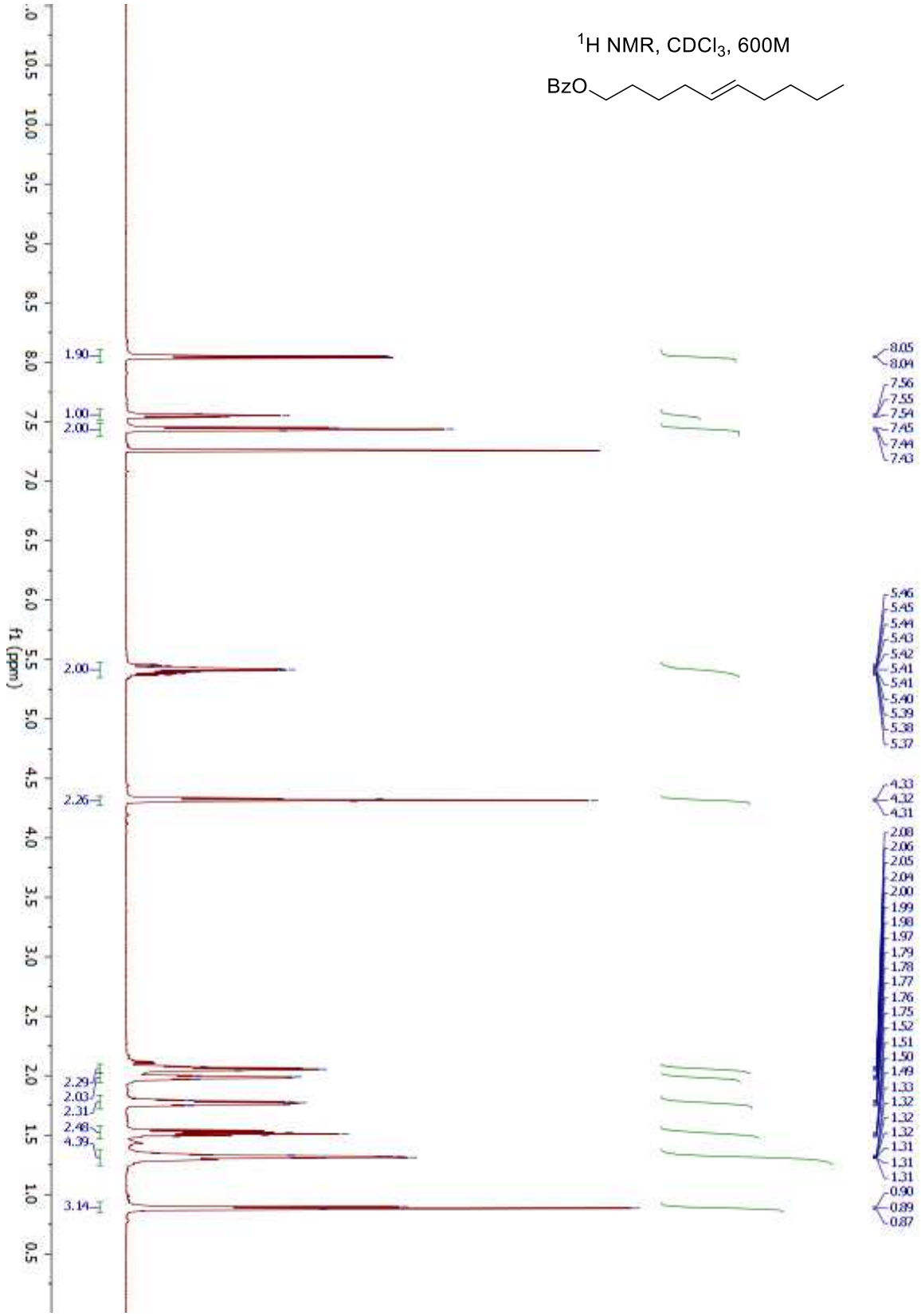

13C NMR, CDCl3, 150M
N
162.67
149.36
139.34
136.31
122.80
120.96
114.26
77.37
77.16
76.95
38.62
33.93
30.05
29.50
29.48
29.18
29.05
f1 (ppm)

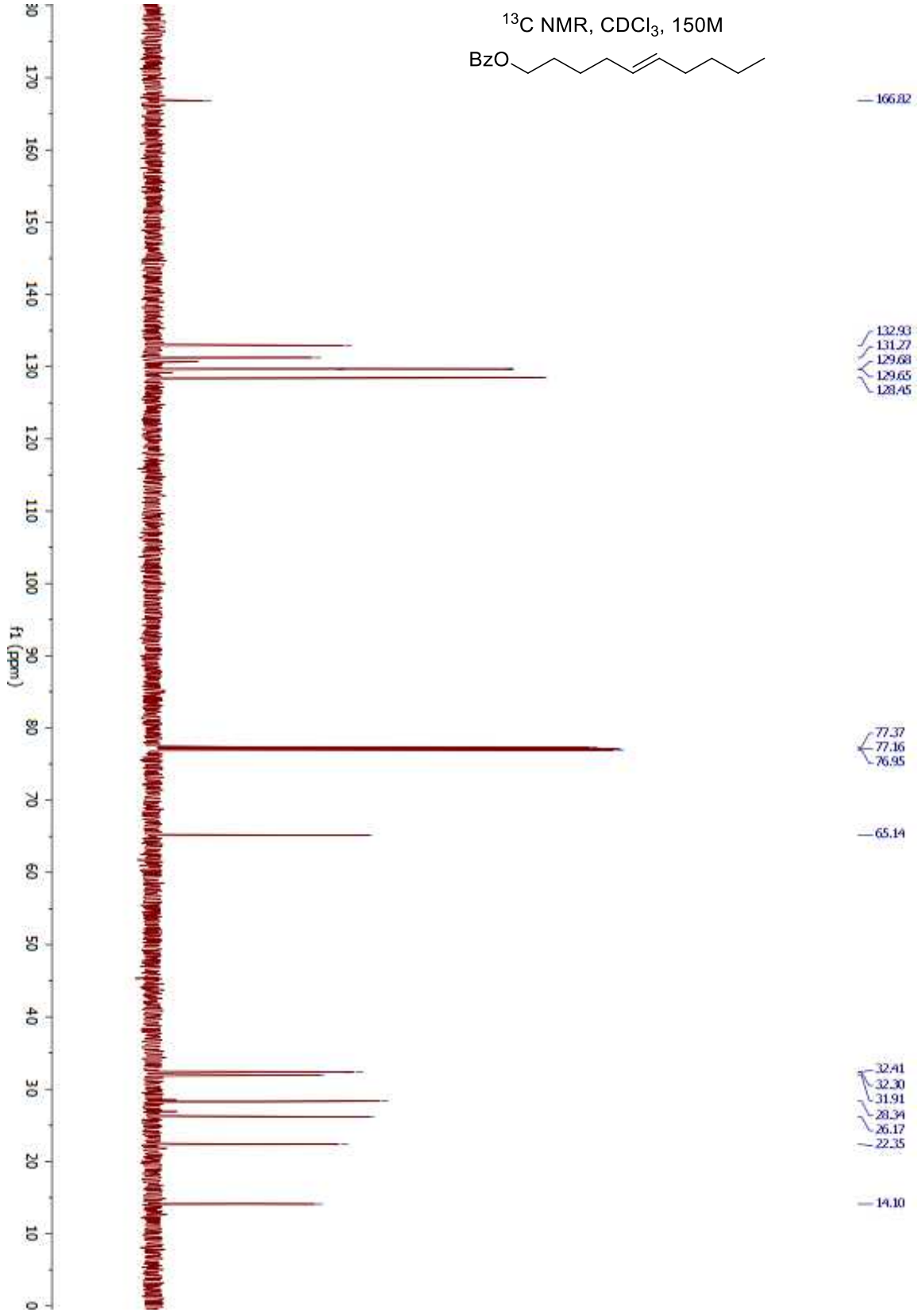

^{1}H NMR, $CDCl_3$, 400M
BnO
f1 (ppm)
5.24
1.00
1.04
2.40
2.39
2.36
2.24
3.55

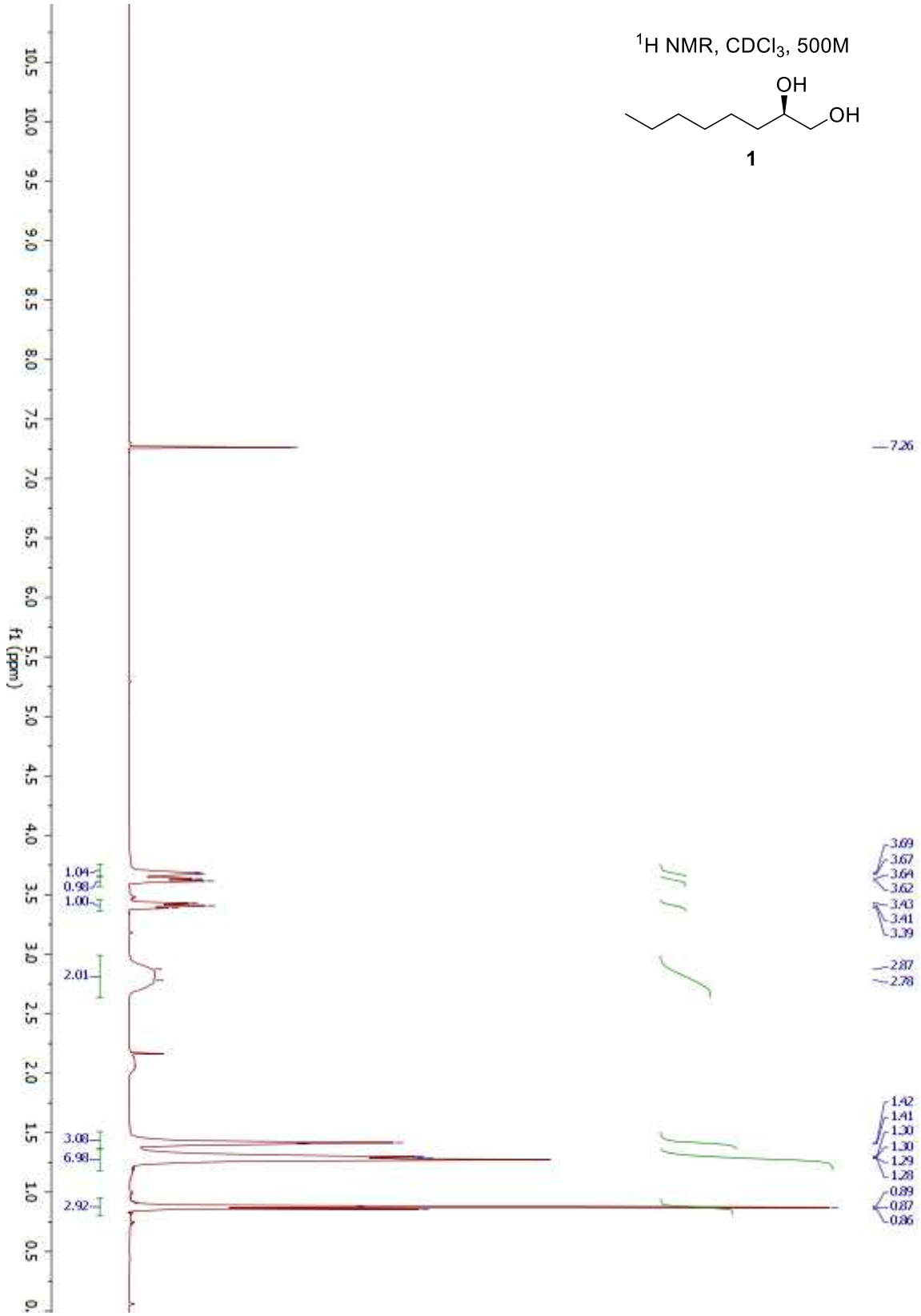

^{13}C NMR, $CDCl_3$, 150M
BnO
138.74
134.30
128.48
127.79
127.69
125.36
77.37
77.16
76.95
72.99
70.44
33.20
25.79
13.93
f1 (ppm)

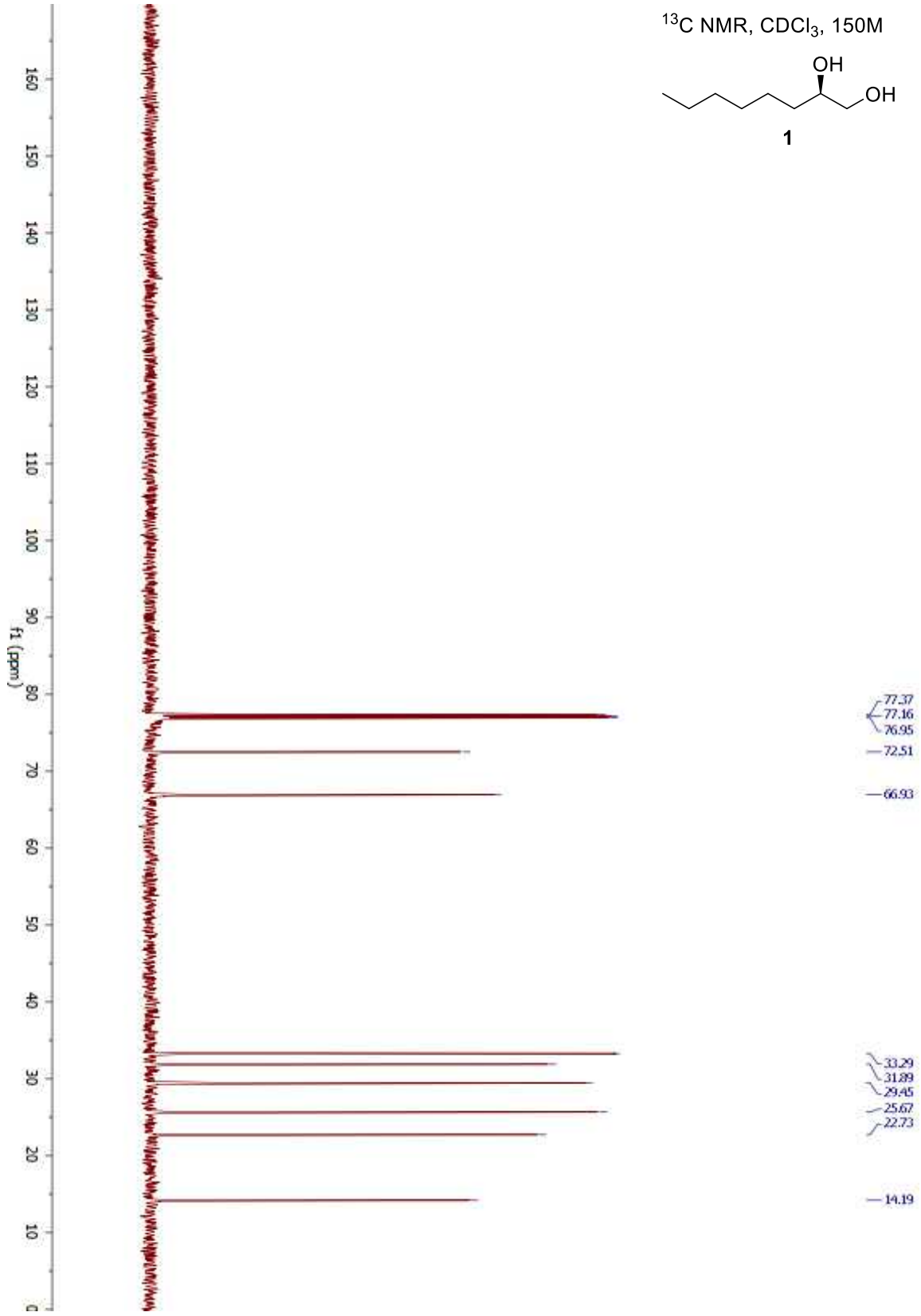

^{1}H NMR, $CDCl_3$, 400M
BnO
OTBS
f1 (ppm)
3.66
0.81
2.00
2.19
2.13
2.16
2.15
2.14
9.46
5.92
7.34
7.34
7.33
7.32
7.32
7.31
7.30
7.29
7.29
7.27
5.51
5.51
5.50
5.50
5.49
5.49
5.48
4.51
3.63
3.61
3.61
3.60
3.50
3.48
3.48
3.47
2.35
2.34
2.34
2.33
2.33
2.32
2.32
2.31
2.30
2.30
2.25
2.24
2.24
2.23
2.23
2.22
2.21
2.21
2.20
2.20
0.89
0.89
0.04
0.04


^{13}C NMR, $CDCl_3$, 126M
BnO
OTBS
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
128.85
128.60
128.49
127.80
127.66
77.41
77.16
76.91
73.01
70.29
63.35
36.50
33.32
26.11
18.53
-5.07

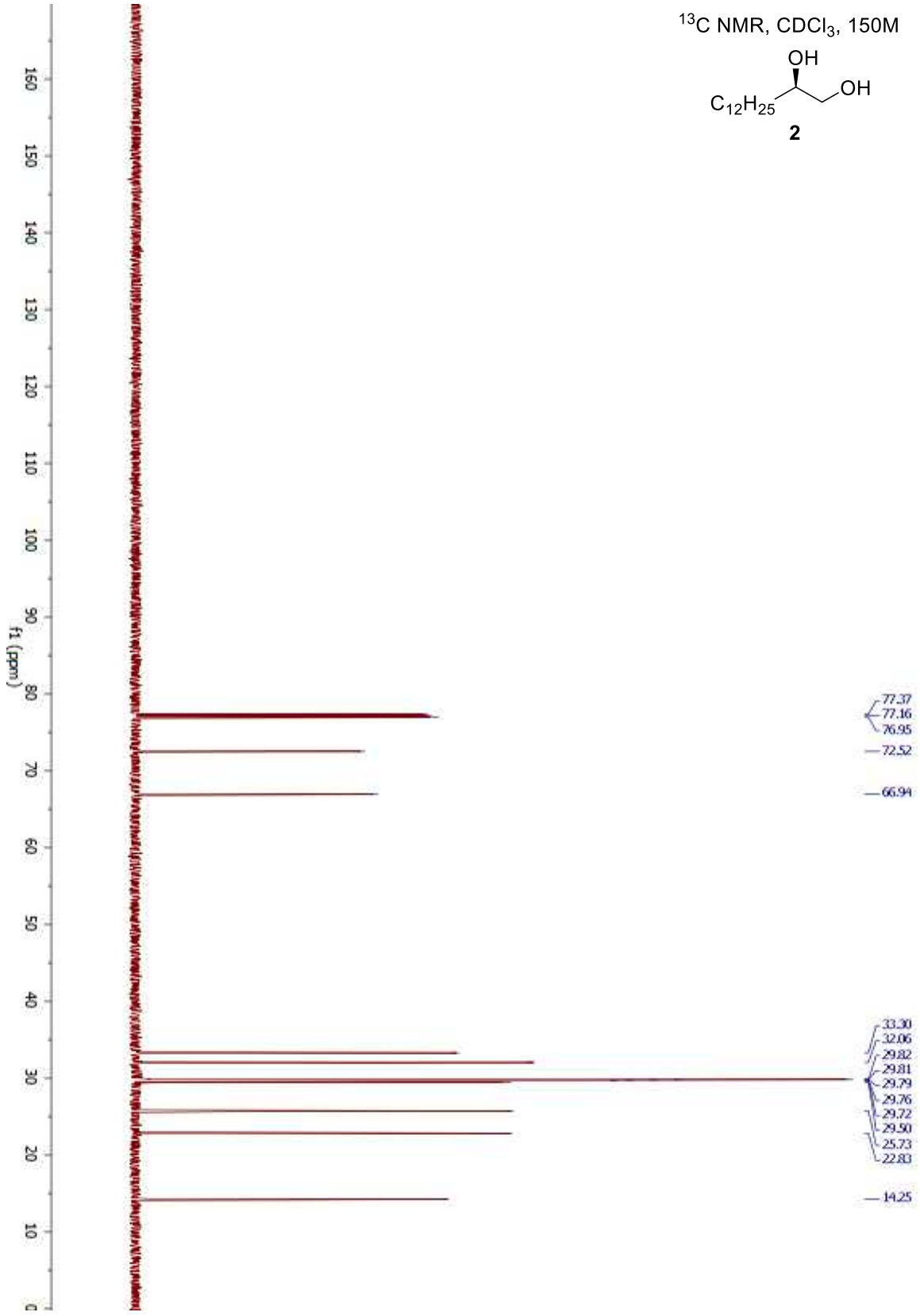

^{1}H NMR, $CDCl_3$, 600M
BzO
f1 (ppm)
1.90
1.00
2.00
2.00
2.26
2.29
2.03
2.31
2.48
4.39
3.14
8.05
8.04
7.56
7.55
7.54
7.45
7.44
7.43
5.46
5.45
5.44
5.43
5.42
5.41
5.41
5.40
5.39
5.38
5.37
4.33
4.32
4.31
2.08
2.06
2.05
2.04
2.00
1.99
1.98
1.97
1.79
1.78
1.77
1.76
1.75
1.52
1.51
1.50
1.49
1.33
1.32
1.32
1.32
1.31
1.31
1.31
0.90
0.89
0.87

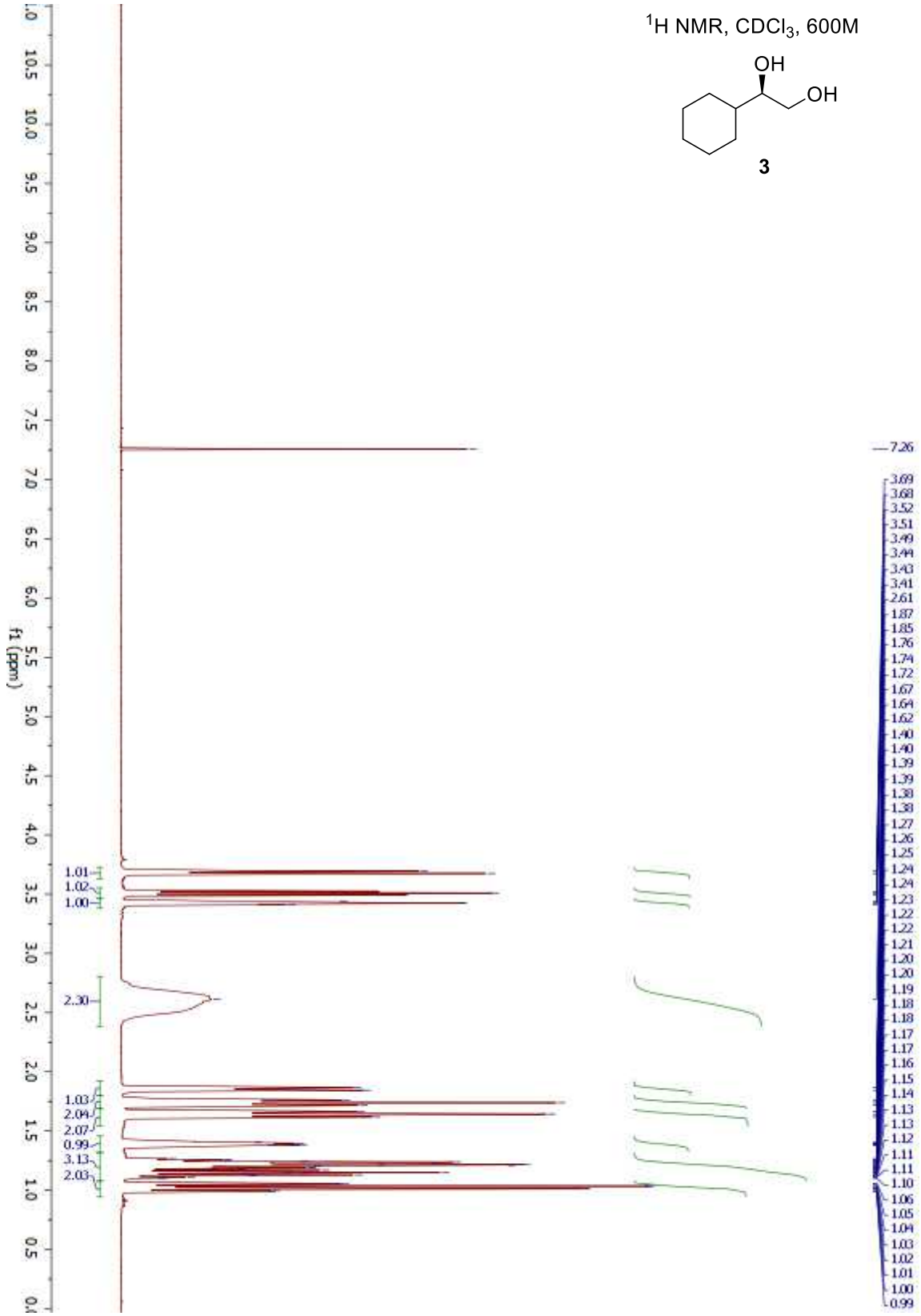

^{13}C NMR, $CDCl_3$, 150M
BzO
166.82
132.93
131.27
129.68
129.65
128.45
77.37
77.16
76.95
65.14
32.41
32.30
31.91
28.34
26.17
22.35
14.10
f1 (ppm)

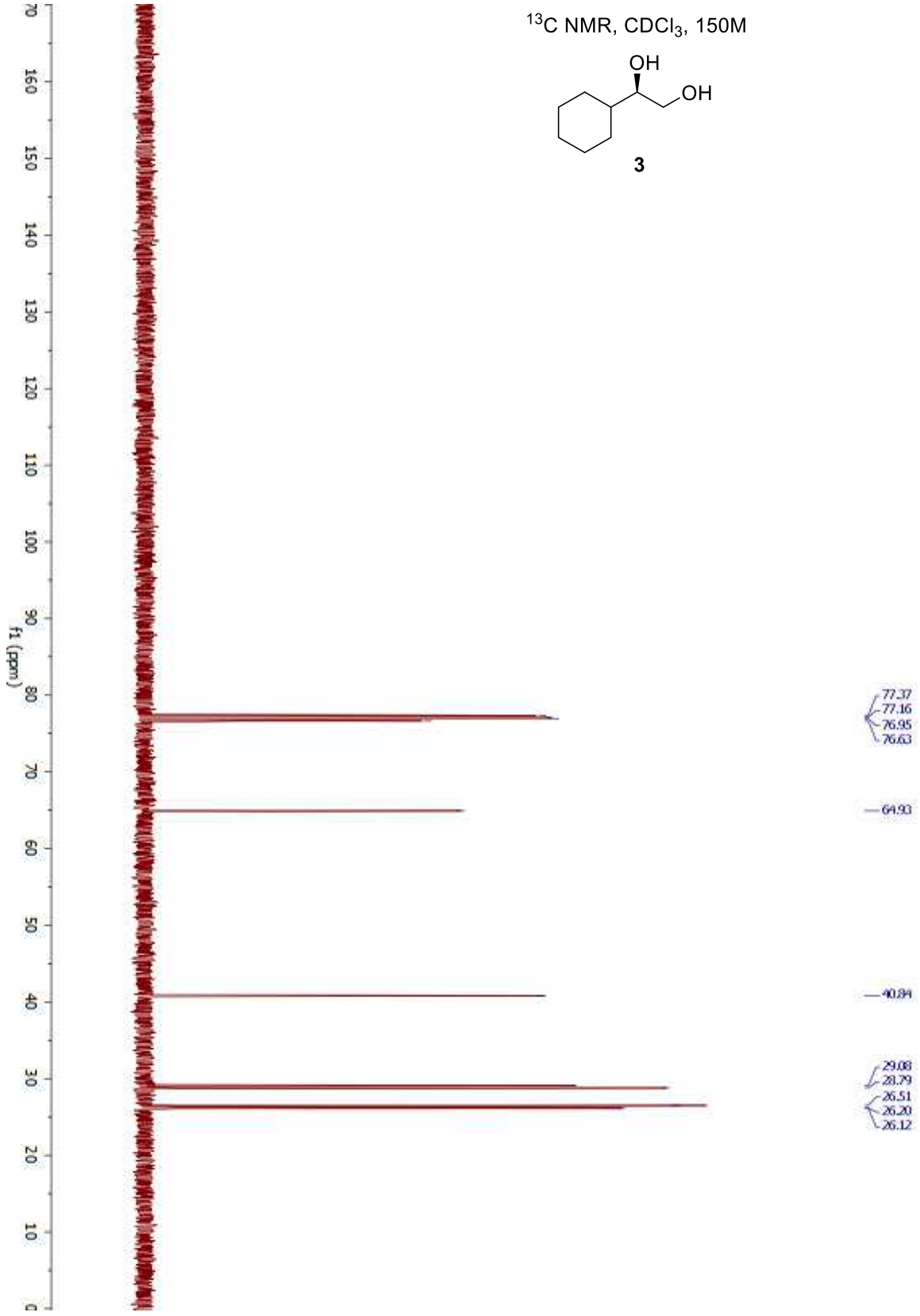

^{1}H NMR, $CDCl_3$, 500M
OH
OH
1
f1 (ppm)
7.26
3.69
3.67
3.64
3.62
3.43
3.41
3.39
2.87
2.78
1.42
1.41
1.30
1.30
1.29
1.28
0.89
0.87
0.86
1.04
0.98
1.00
2.01
3.08
6.98
2.92

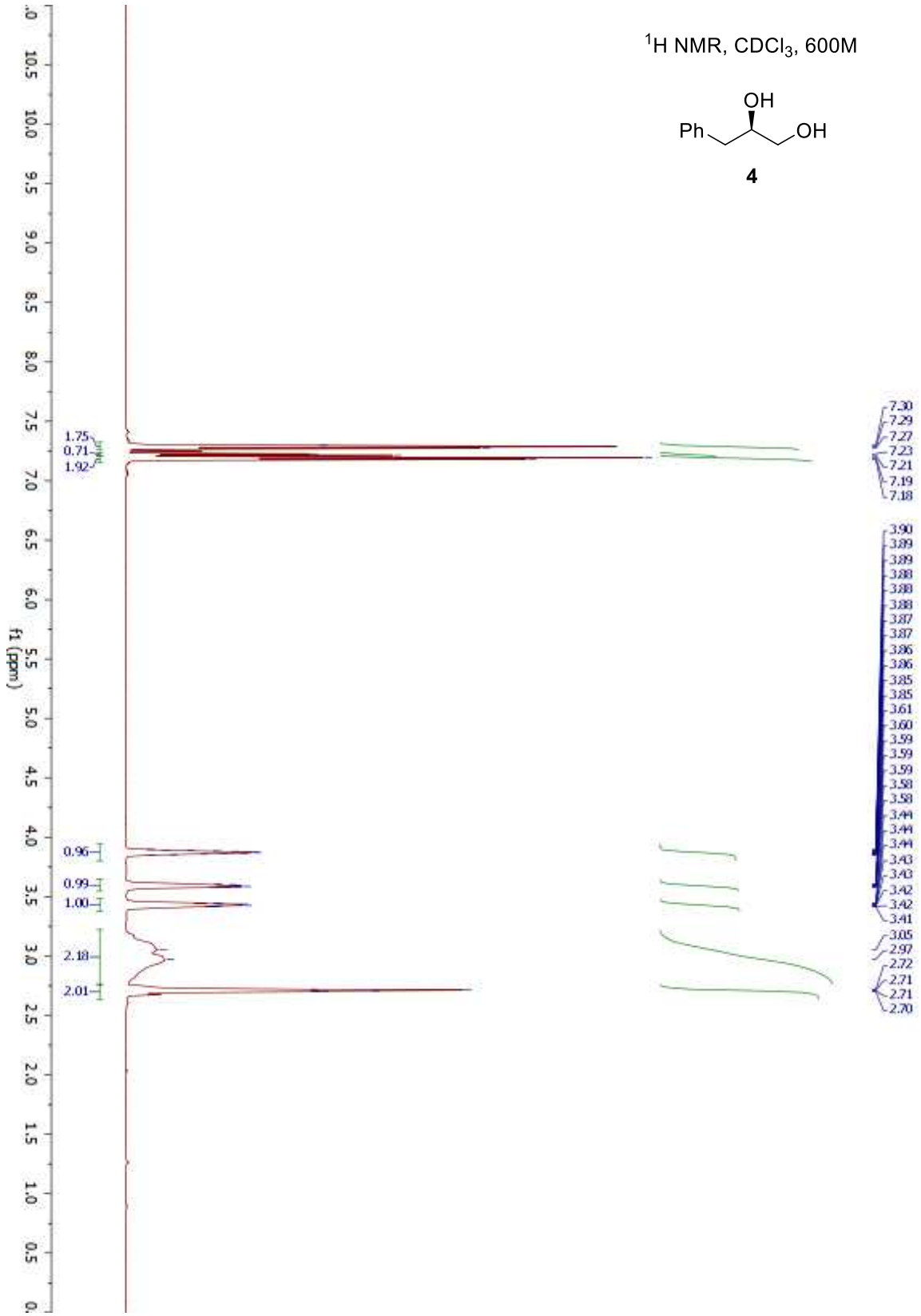

^{13}C NMR, $CDCl_3$, 150M
OH
OH
1
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
77.37
77.16
76.95
72.51
66.93
33.29
31.89
29.45
25.67
22.73
14.19


^{1}H NMR, $CDCl_3$, 500M
OH
OH
$C_{12}H_{25}$
2
f1 (ppm)
7.26
3.71
3.68
3.65
3.46
3.42
1.95
1.81
1.55
1.55
1.44
1.26
0.89
0.88
0.87
0.86
0.87
1.00
0.91
1.17
2.34
3.10
18.53
2.81


^{13}C NMR, $CDCl_3$, 150M
OH
OH
$C_{12}H_{25}$
2
f1 (ppm)
77.37
77.16
76.95
72.52
66.94
33.30
32.06
29.82
29.81
29.79
29.76
29.72
29.50
25.73
22.83
14.25


^{1}H NMR, $CDCl_3$, 600M
OH
OH
3
f1 (ppm)
7.26
1.01
1.02
1.00
2.30
1.03
2.04
2.07
0.99
3.13
2.03


^{13}C NMR, $CDCl_3$, 150M
OH
OH
3
f1 (ppm)
77.37
77.16
76.95
76.63
64.93
40.89
29.08
28.79
26.51
26.20
26.12


^{1}H NMR, $CDCl_3$, 600M
OH
Ph
OH
4
f1 (ppm)
1.75
0.71
1.92
0.96
0.99
1.00
2.18
2.01
7.30
7.29
7.27
7.23
7.21
7.19
7.18
3.90
3.89
3.89
3.88
3.88
3.88
3.87
3.87
3.86
3.86
3.85
3.85
3.61
3.60
3.59
3.59
3.59
3.58
3.58
3.44
3.44
3.44
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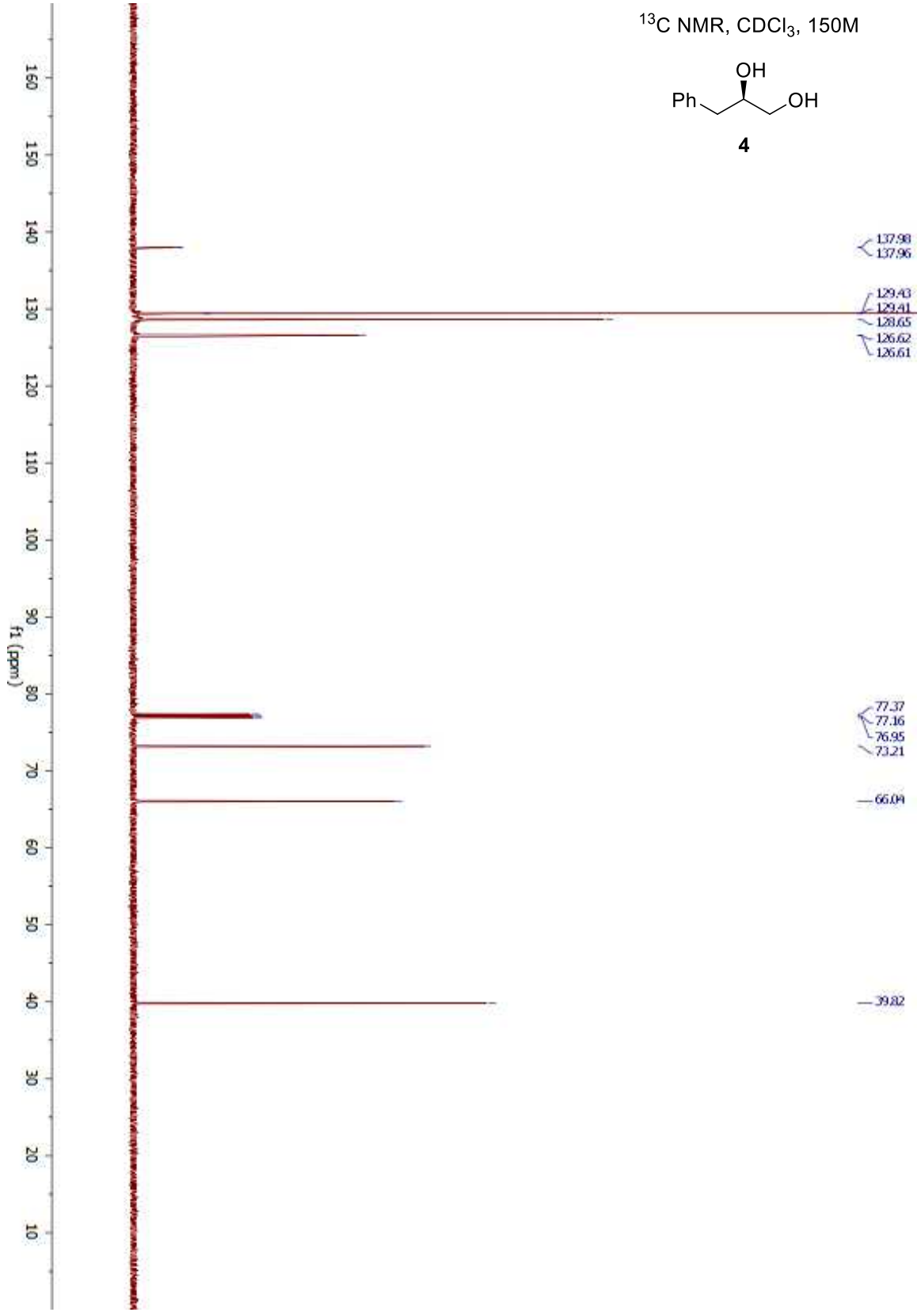
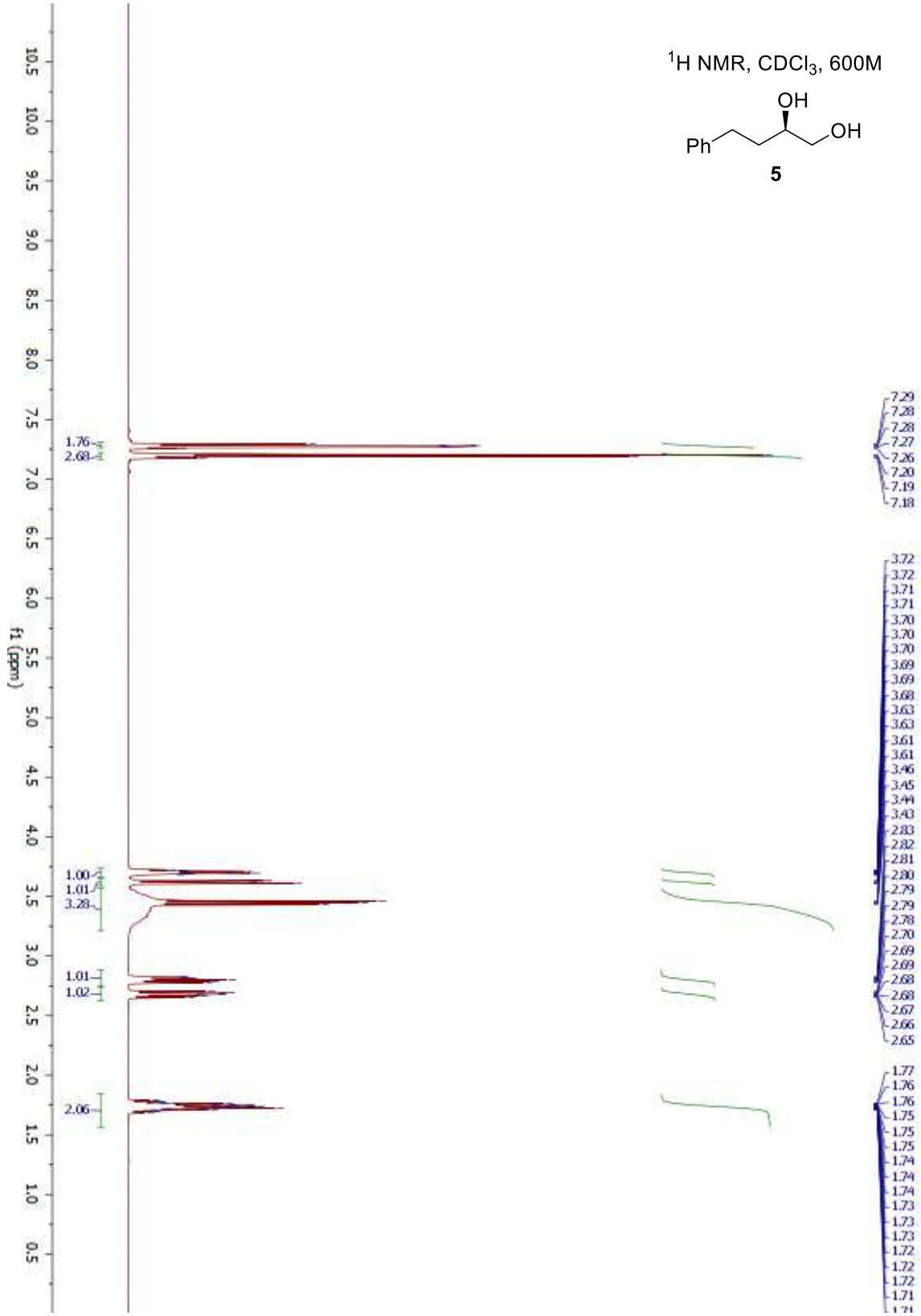
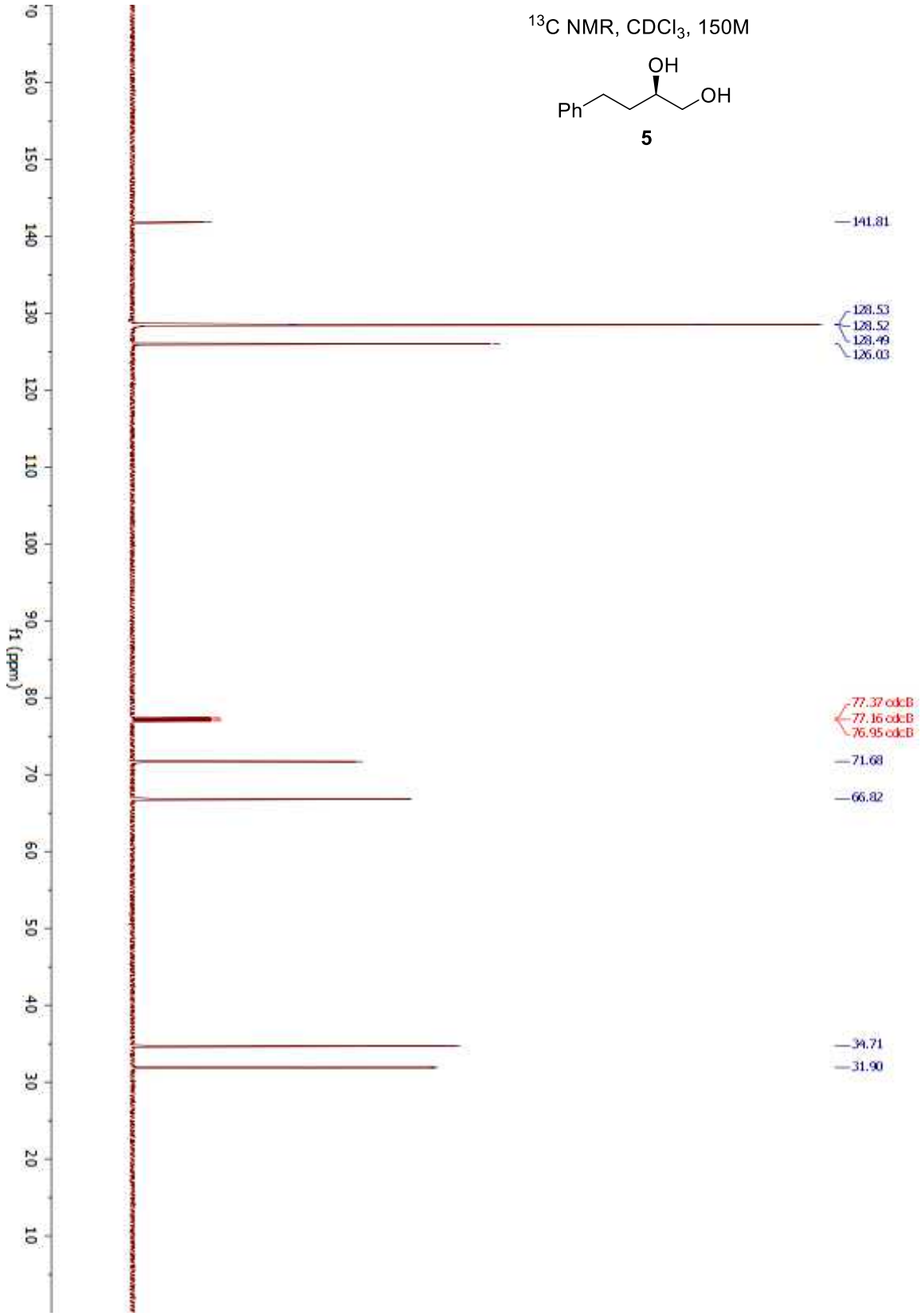
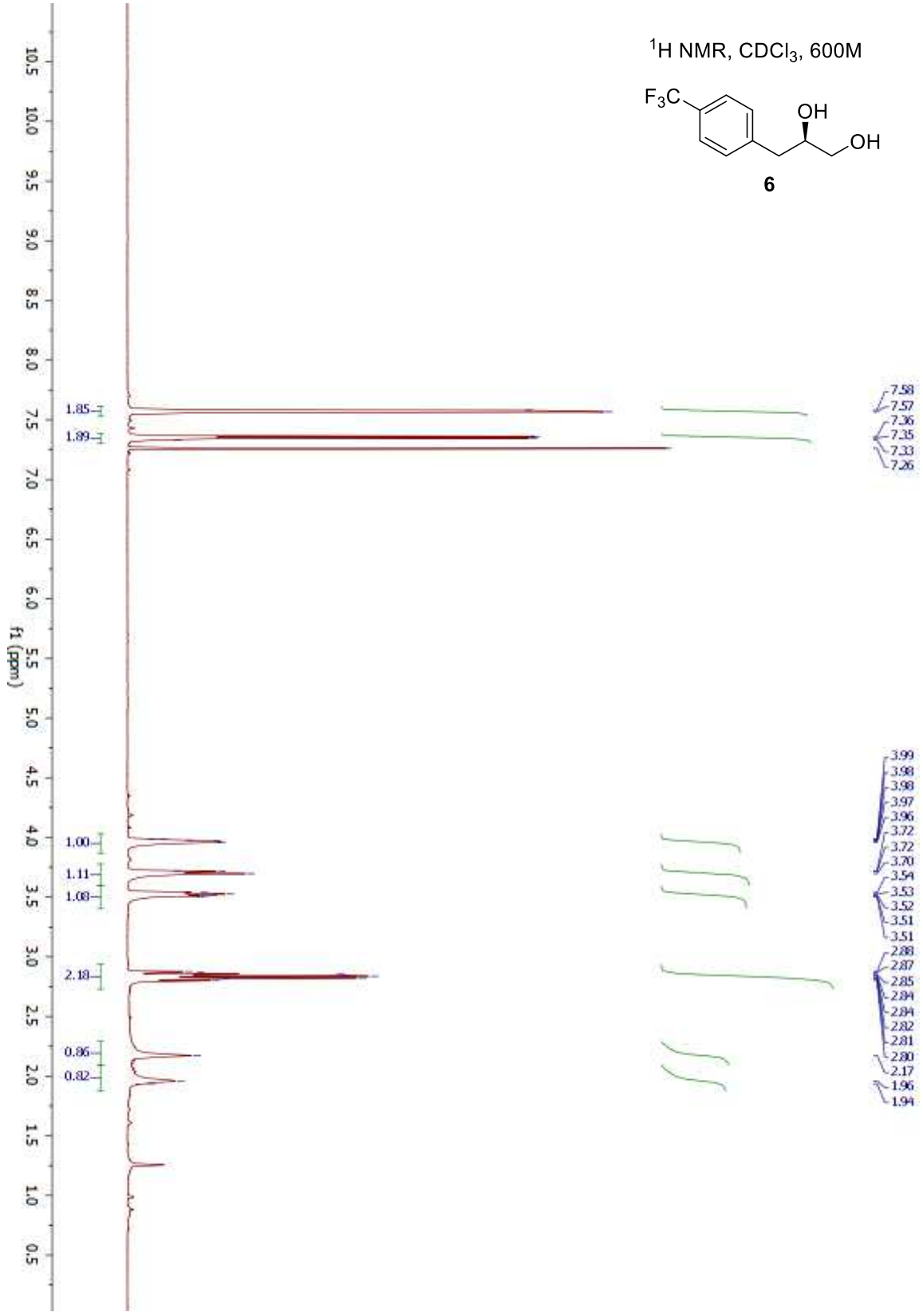
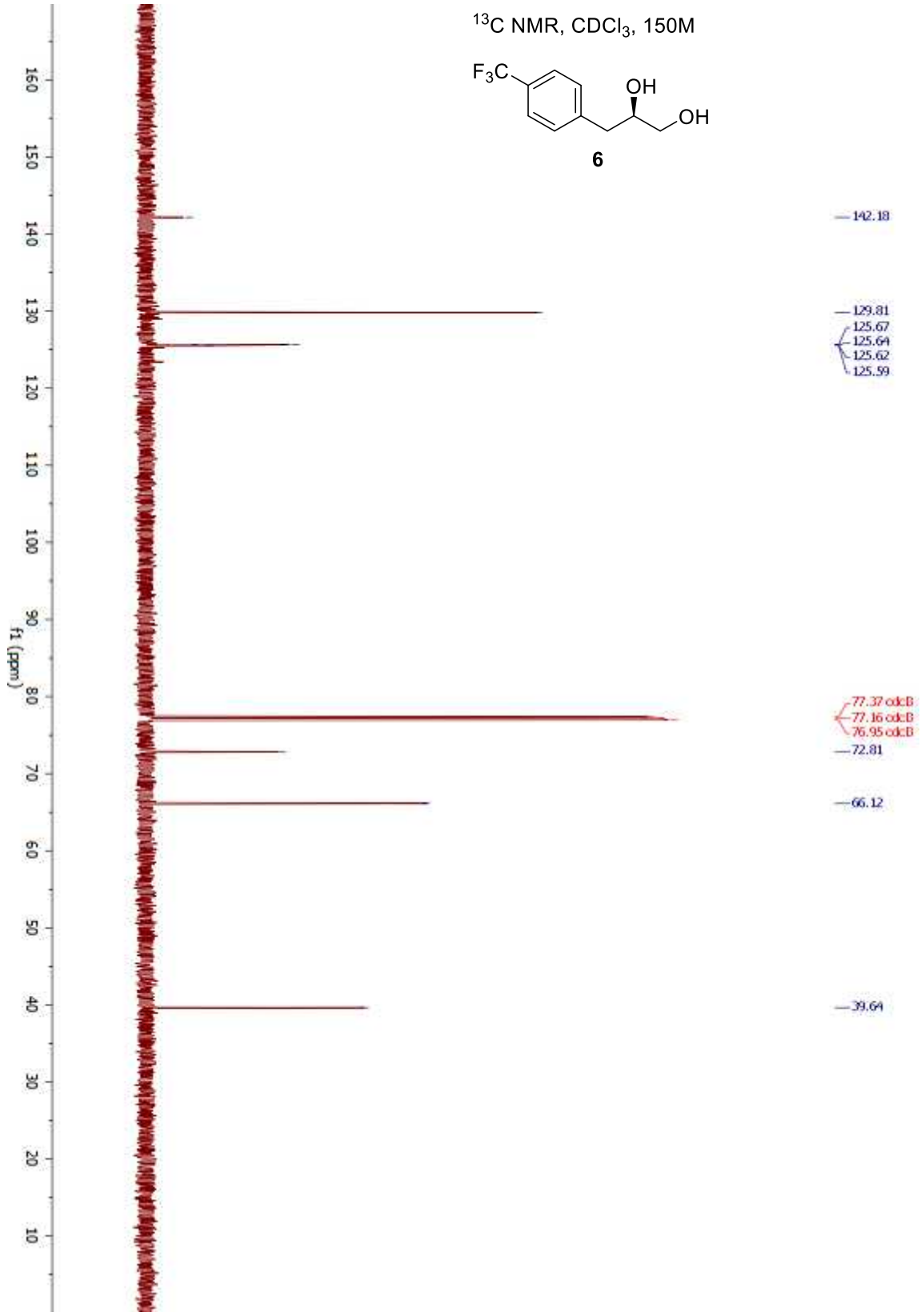
3.43
3.42
3.42
3.41
3.05
2.97
2.72
2.71
2.71
2.70


^{13}C NMR, $CDCl_3$, 150M
OH
Ph
OH
4
137.98
137.96
129.43
129.41
128.65
126.62
126.61
77.37
77.16
76.95
73.21
66.09
39.82
f1 (ppm)

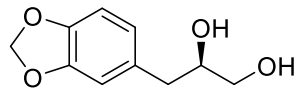

^{1}H NMR, $CDCl_3$, 600M
OH
OH
Ph
5
f1 (ppm)
1.76
2.68
1.00
1.01
3.28
1.01
1.02
2.06


^{13}C NMR, $CDCl_3$, 150M
OH
OH
Ph
5
141.81
128.53
128.52
128.49
126.03
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
71.68
66.82
34.71
31.90
f1 (ppm)

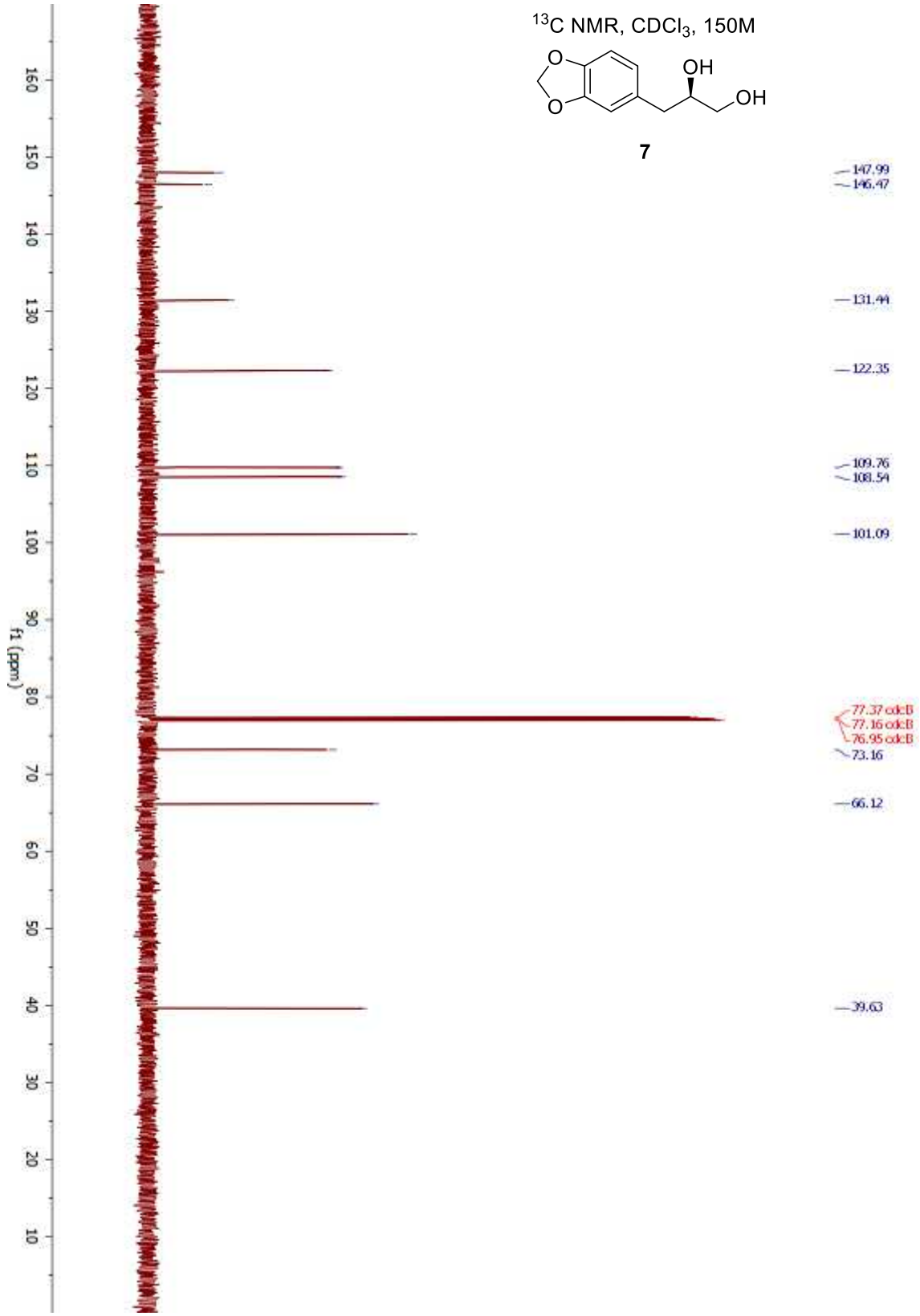

^{1}H NMR, $CDCl_3$, 600M
F_3C
OH
OH
6
f1 (ppm)
1.85
1.89
1.00
1.11
1.08
2.18
0.86
0.82
7.58
7.57
7.36
7.35
7.33
7.26
3.99
3.98
3.98
3.97
3.96
3.72
3.72
3.70
3.54
3.53
3.52
3.51
3.51
2.88
2.87
2.85
2.84
2.84
2.82
2.81
2.80
2.17
1.96
1.94

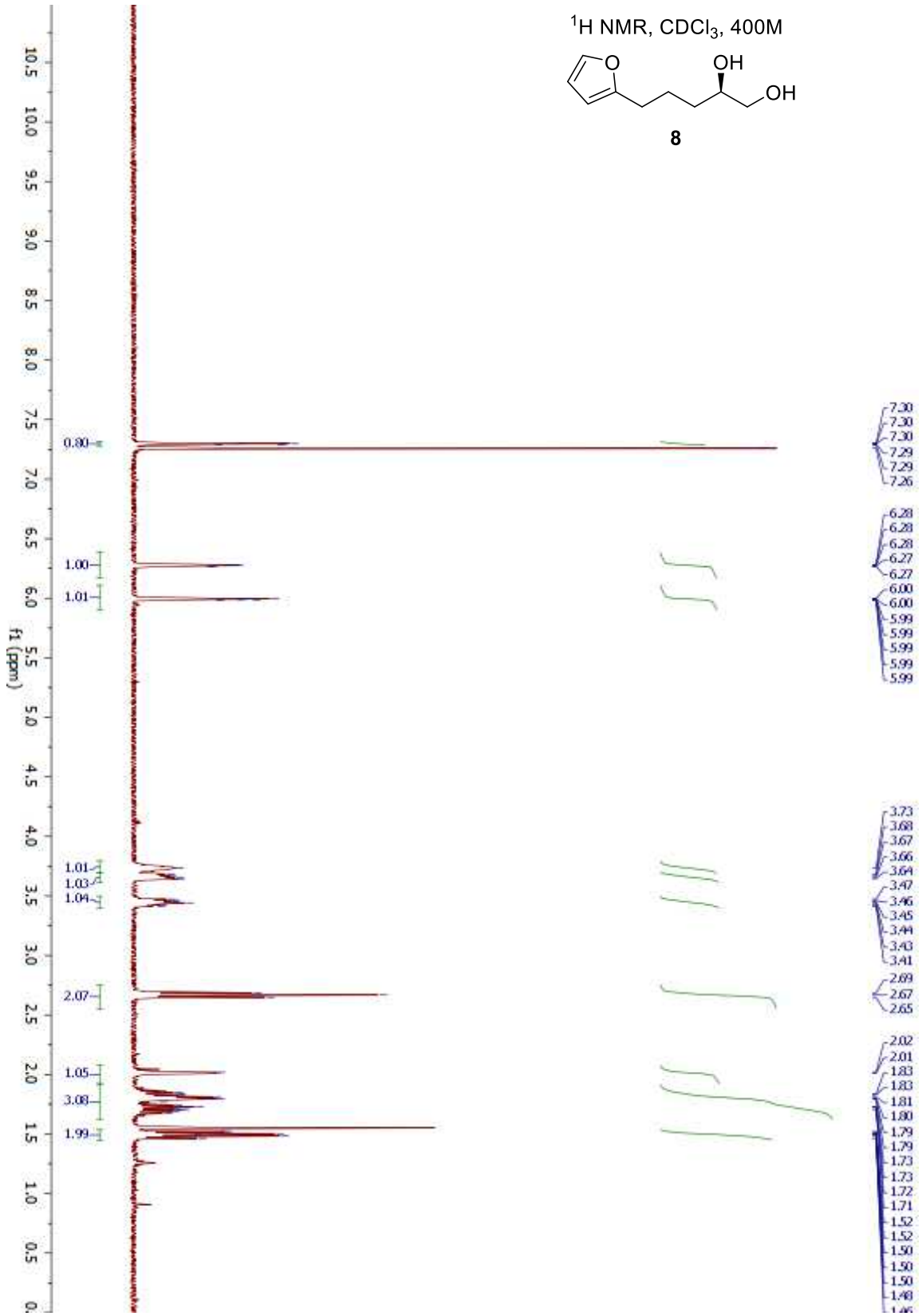

^{13}C NMR, $CDCl_3$, 150M
F_3C
OH
OH
6
142.18
129.81
125.67
125.64
125.62
125.59
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
72.81
66.12
39.64
f1 (ppm)

^{1}H NMR, $CDCl_3$, 600M



7


^{13}C NMR, CDCl$_3$, 150M
OH
OH
7
147.99
146.47
131.44
122.35
109.76
108.54
101.09
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
73.16
66.12
39.63
f1 (ppm)


^{1}H NMR, $CDCl_3$, 400M
O
OH
OH
8
f1 (ppm)
0.00
1.00
1.01
1.01
1.03
1.04
2.07
1.05
3.08
1.99
7.30
7.30
7.30
7.29
7.29
7.26
6.28
6.28
6.28
6.27
6.27
6.00
6.00
5.99
5.99
5.99
5.99
5.99
3.73
3.68
3.67
3.66
3.64
3.47
3.46
3.45
3.44
3.43
3.41
2.69
2.67
2.65
2.02
2.01
1.83
1.83
1.81
1.80
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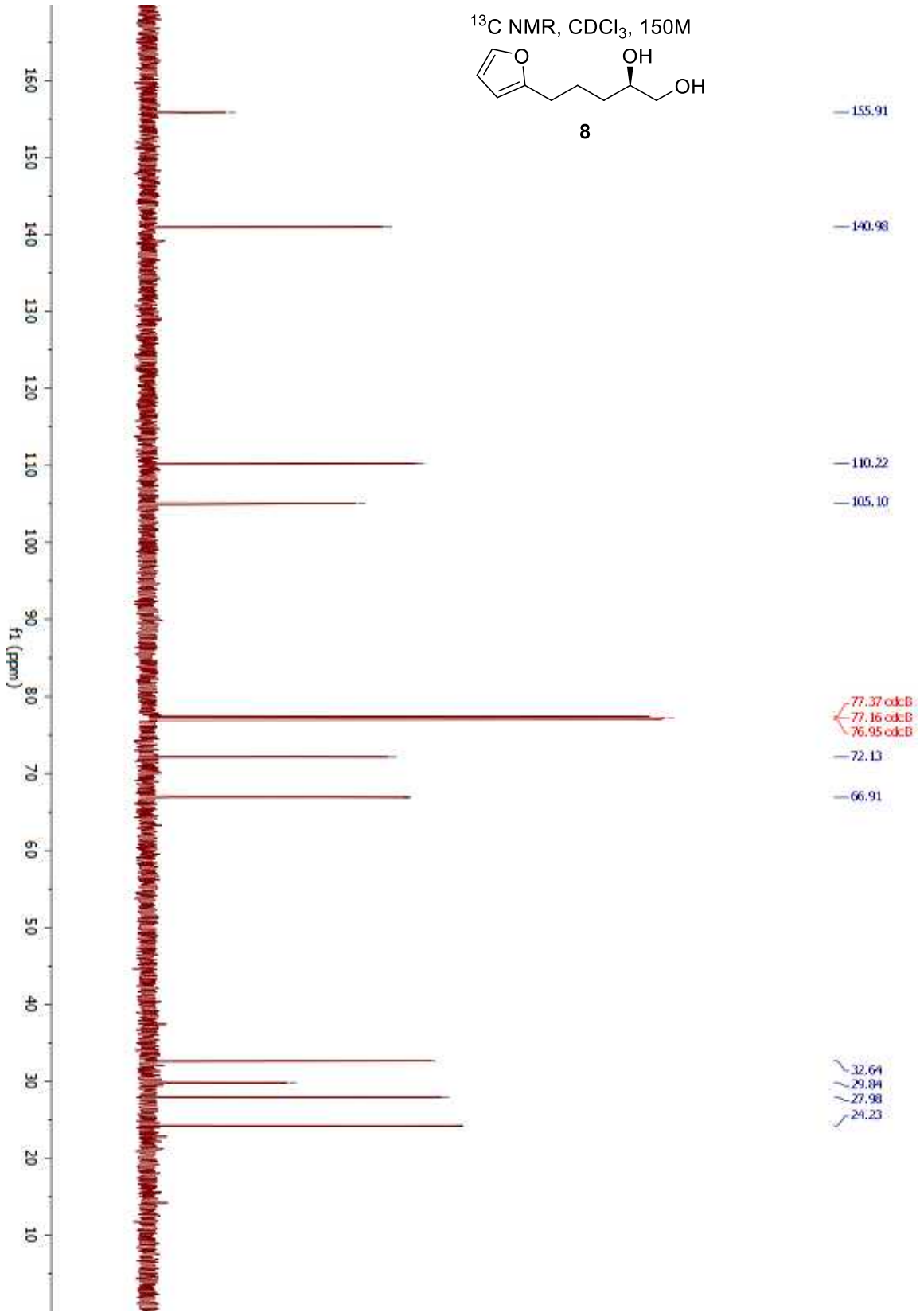
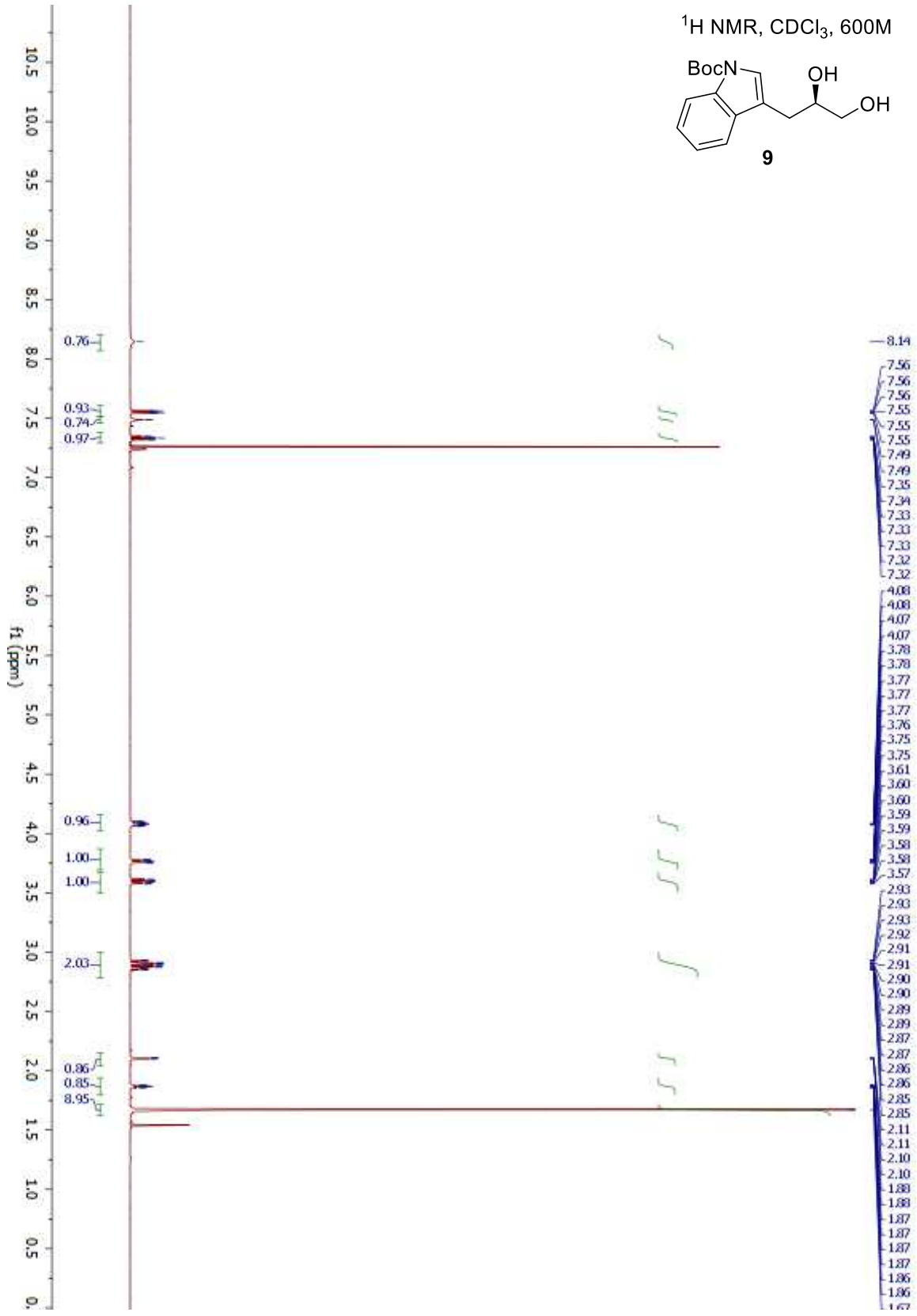
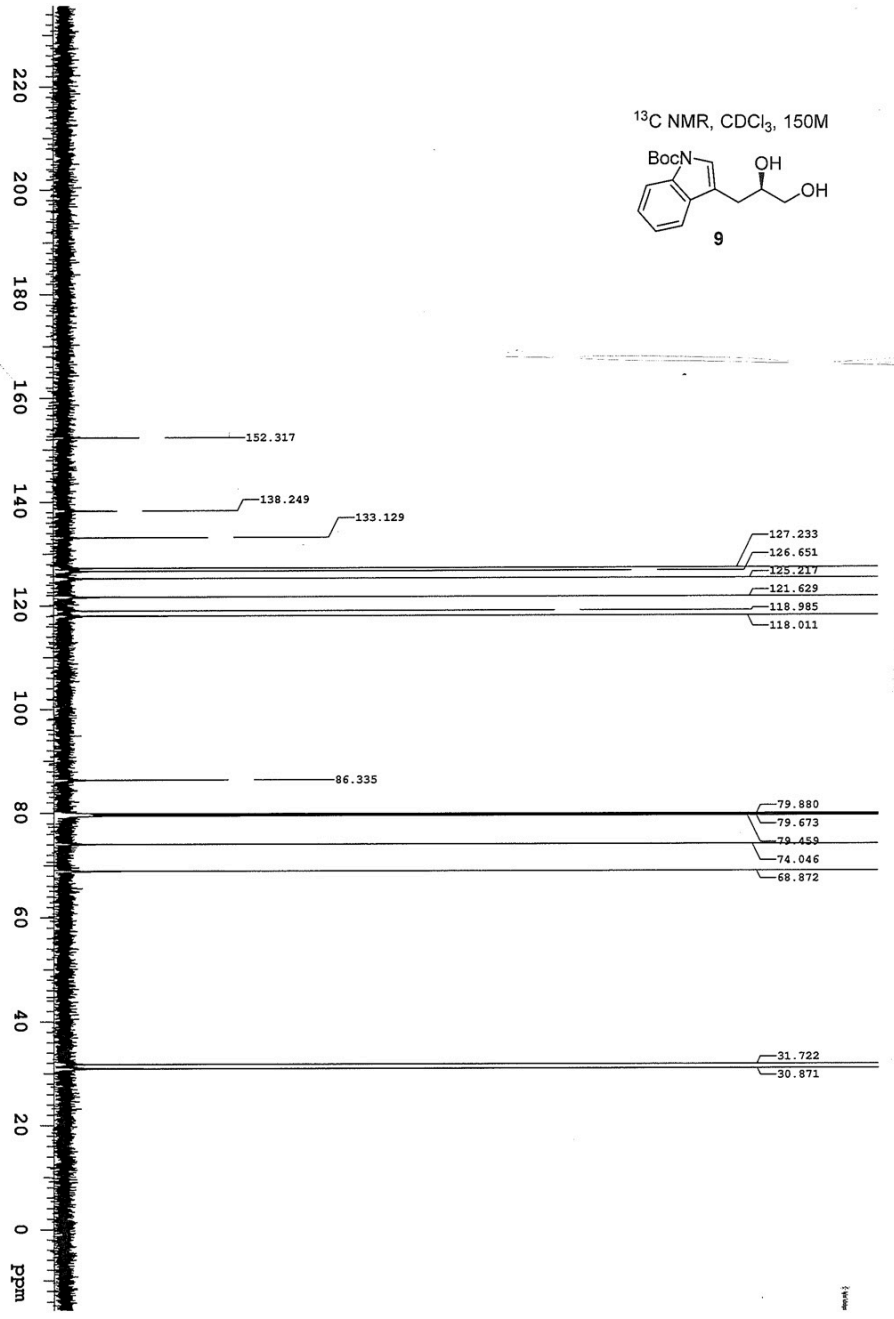
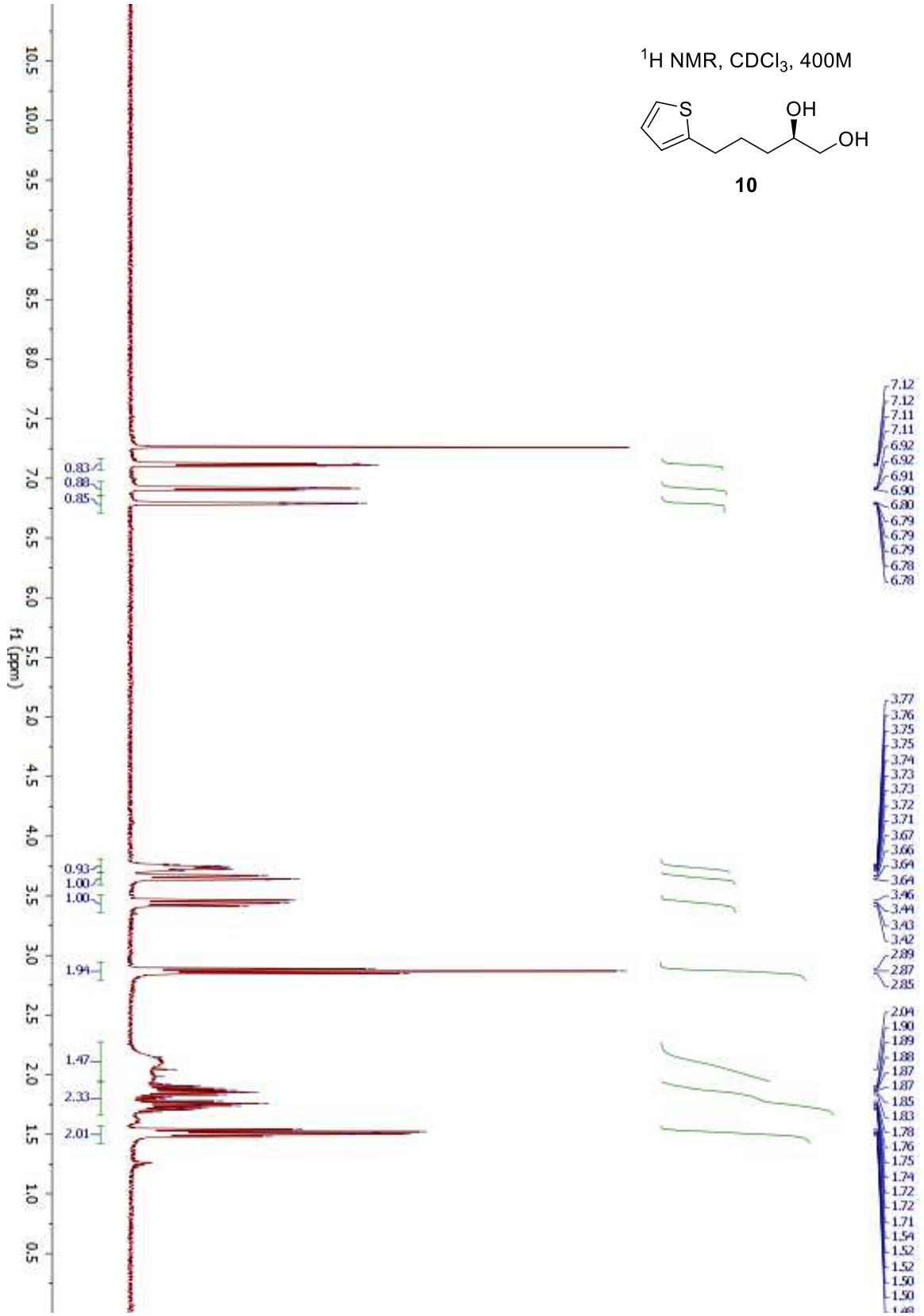
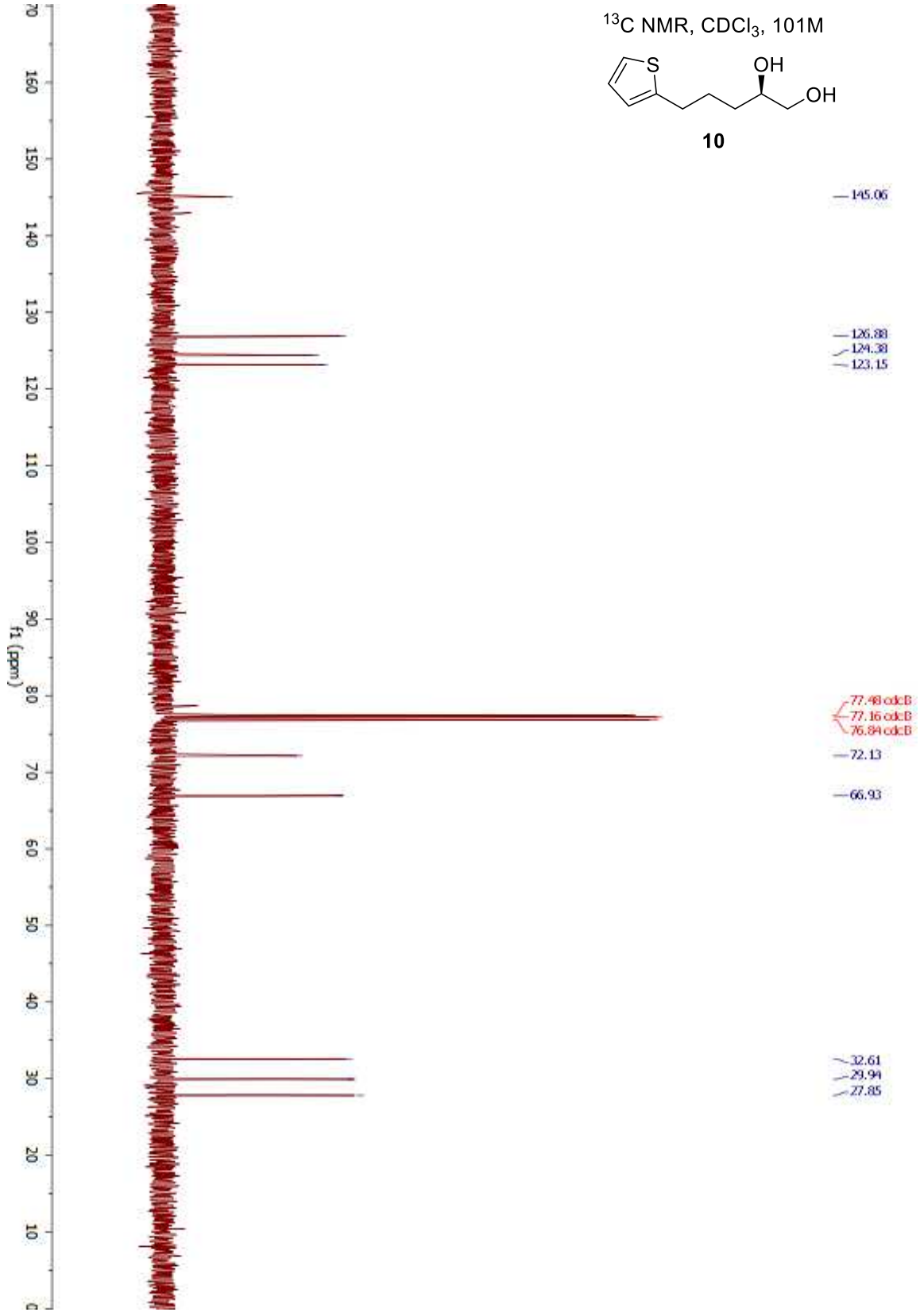
1.73
1.72
1.71
1.52
1.52
1.50
1.50
1.50
1.48

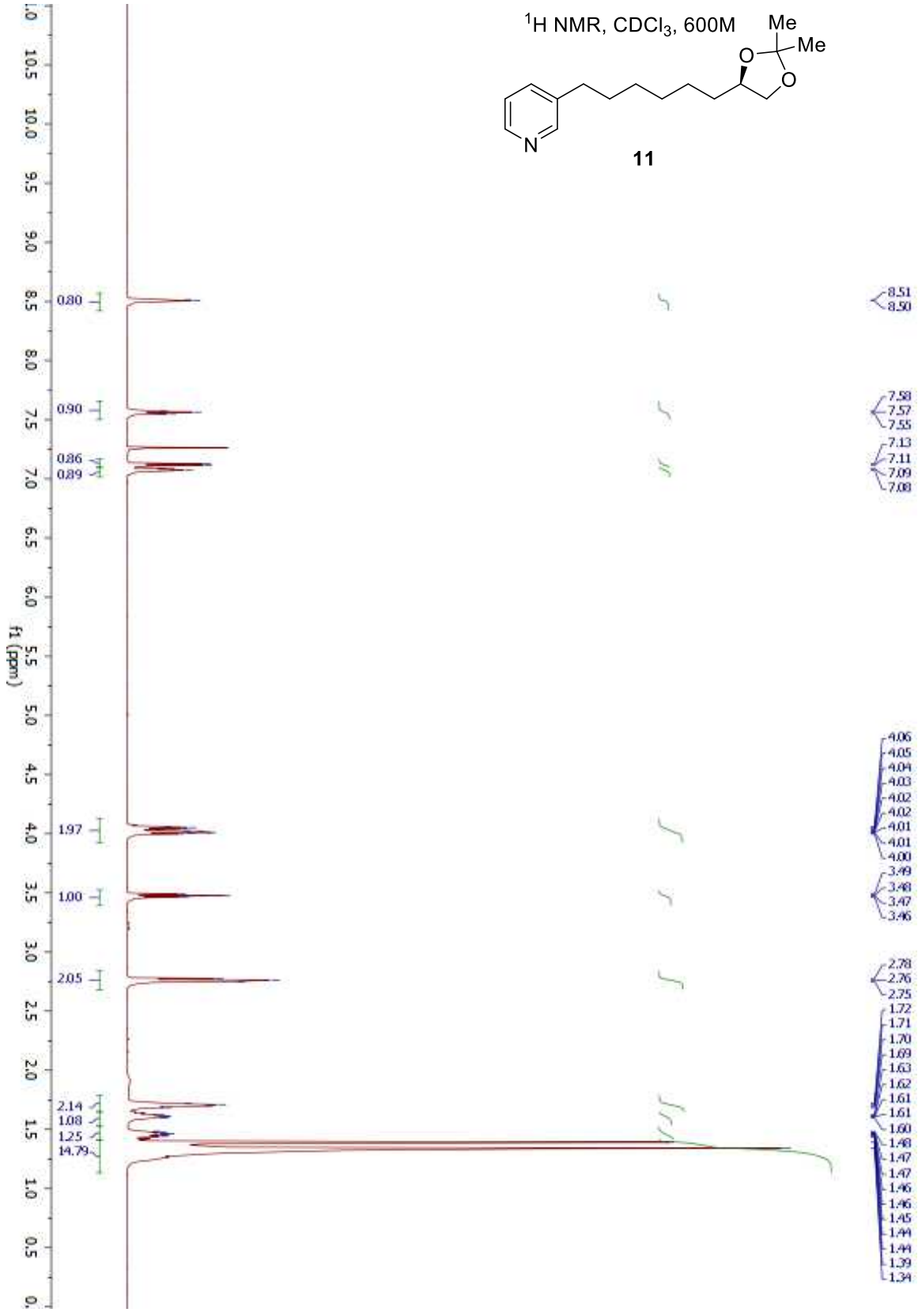

^{13}C NMR, $CDCl_3$, 150M
O
OH
OH
8
155.91
140.98
110.22
105.10
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
72.13
66.91
32.64
29.84
27.98
24.23
f1 (ppm)

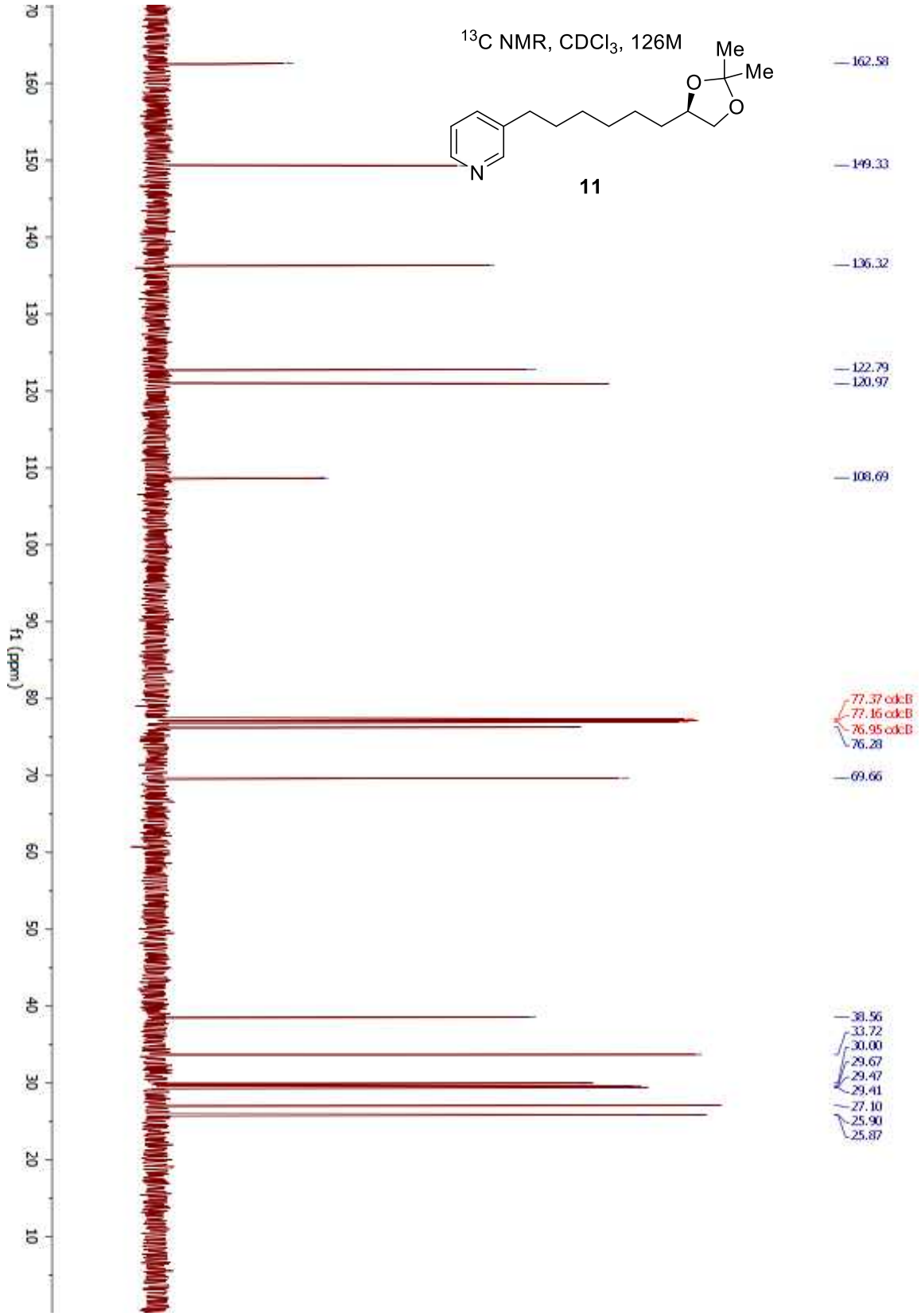

^{1}H NMR, $CDCl_3$, 600M
BocN
OH
OH
9
f1 (ppm)
0.76
0.93
0.74
0.97
0.96
1.00
1.00
2.03
0.86
0.85
8.95

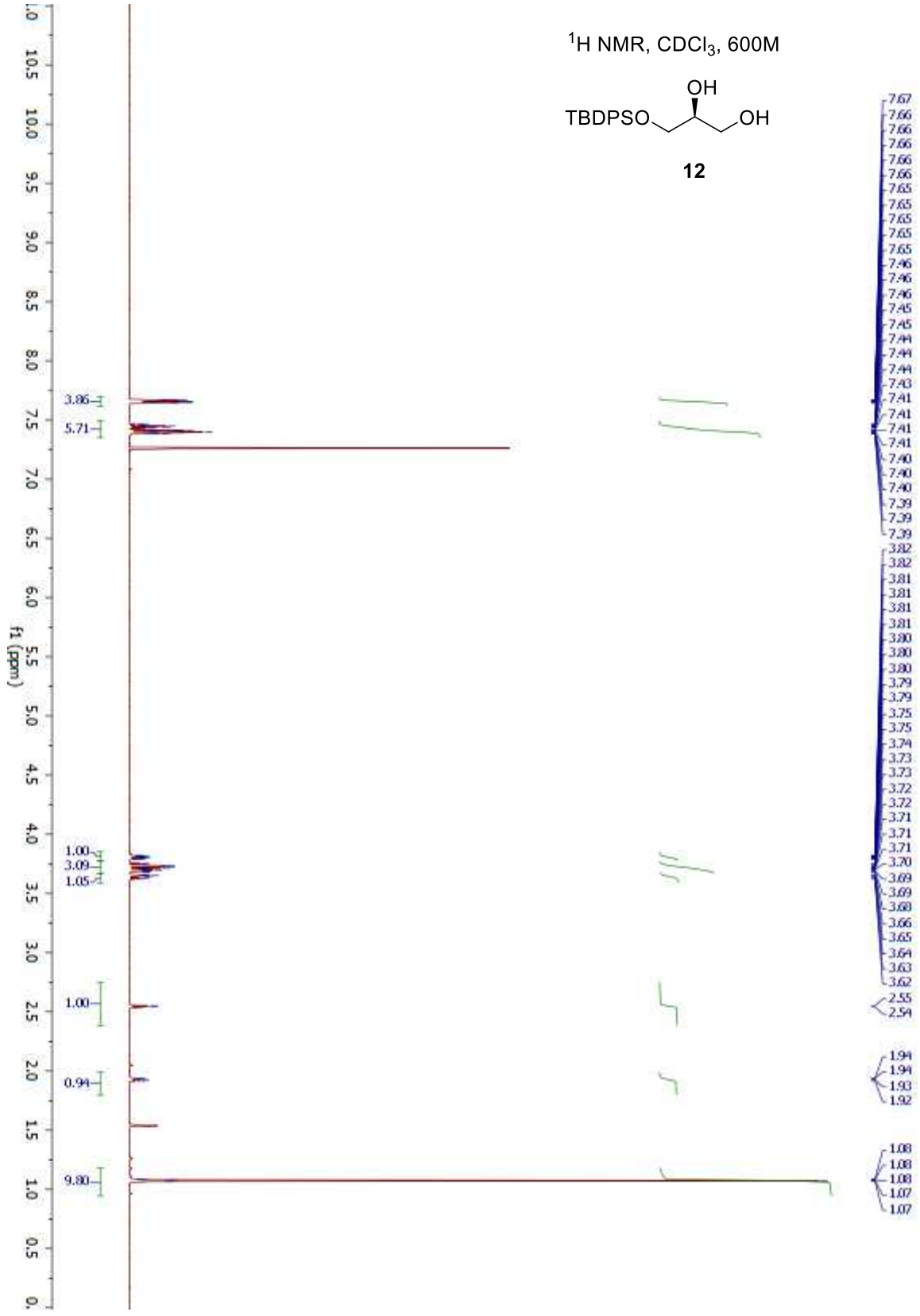

^{13}C NMR, $CDCl_3$, 150M
BocN
OH
OH
9
152.317
138.249
133.129
127.233
126.651
125.217
121.629
118.985
118.011
86.335
79.880
79.673
79.459
74.046
68.872
31.722
30.871
220
200
180
160
140
120
100
80
60
40
20
0
ppm

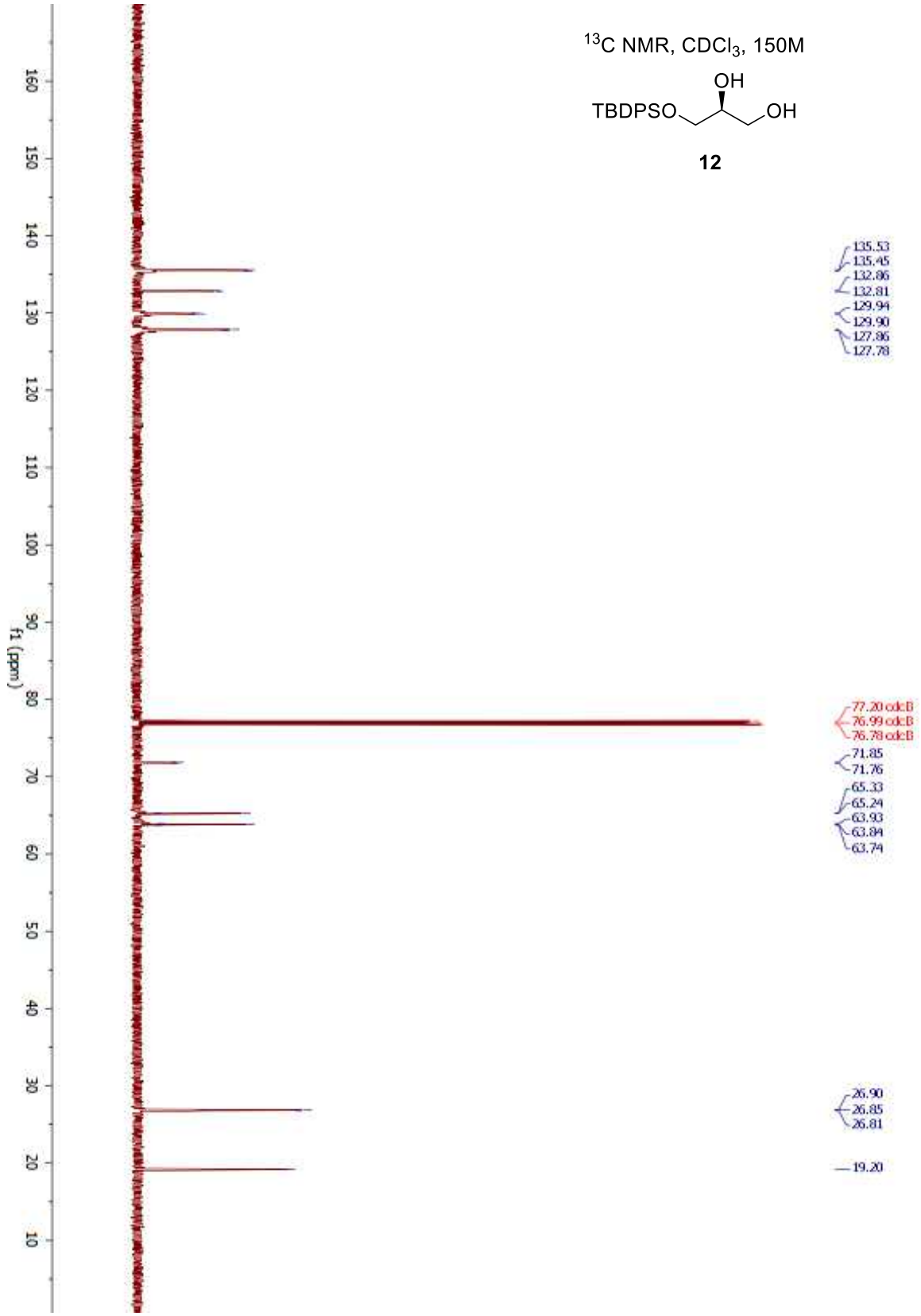

^{1}H NMR, $CDCl_3$, 400M
S
OH
OH
10
f1 (ppm)
0.83
0.88
0.85
0.93
1.00
1.00
1.94
1.47
2.33
2.01


^{13}C NMR, $CDCl_3$, 101M
S
OH
OH
10
145.06
126.88
124.38
123.15
77.48 cdcl3
77.16 cdcl3
76.84 cdcl3
72.13
66.93
32.61
29.94
27.85
f1 (ppm)

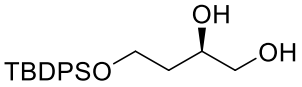

^{1}H NMR, $CDCl_3$, 600M
Me
Me
O
O
N
11
f1 (ppm)
0.80
0.90
0.86
0.89
1.97
1.00
2.05
2.14
1.08
1.25
14.79
8.51
8.50
7.58
7.57
7.55
7.13
7.11
7.09
7.08
4.06
4.05
4.04
4.03
4.02
4.02
4.01
4.01
4.00
3.49
3.48
3.47
3.46
2.78
2.76
2.75
1.72
1.71
1.70
1.69
1.63
1.62
1.61
1.61
1.60
1.48
1.47
1.47
1.46
1.46
1.45
1.44
1.44
1.39
1.34


^{13}C NMR, $CDCl_3$, 126M
Me
Me
O
O
O
N
11
162.58
149.33
136.32
122.79
120.97
108.69
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
76.28
69.66
38.56
33.72
30.00
29.67
29.47
29.41
27.10
25.90
25.87
f1 (ppm)

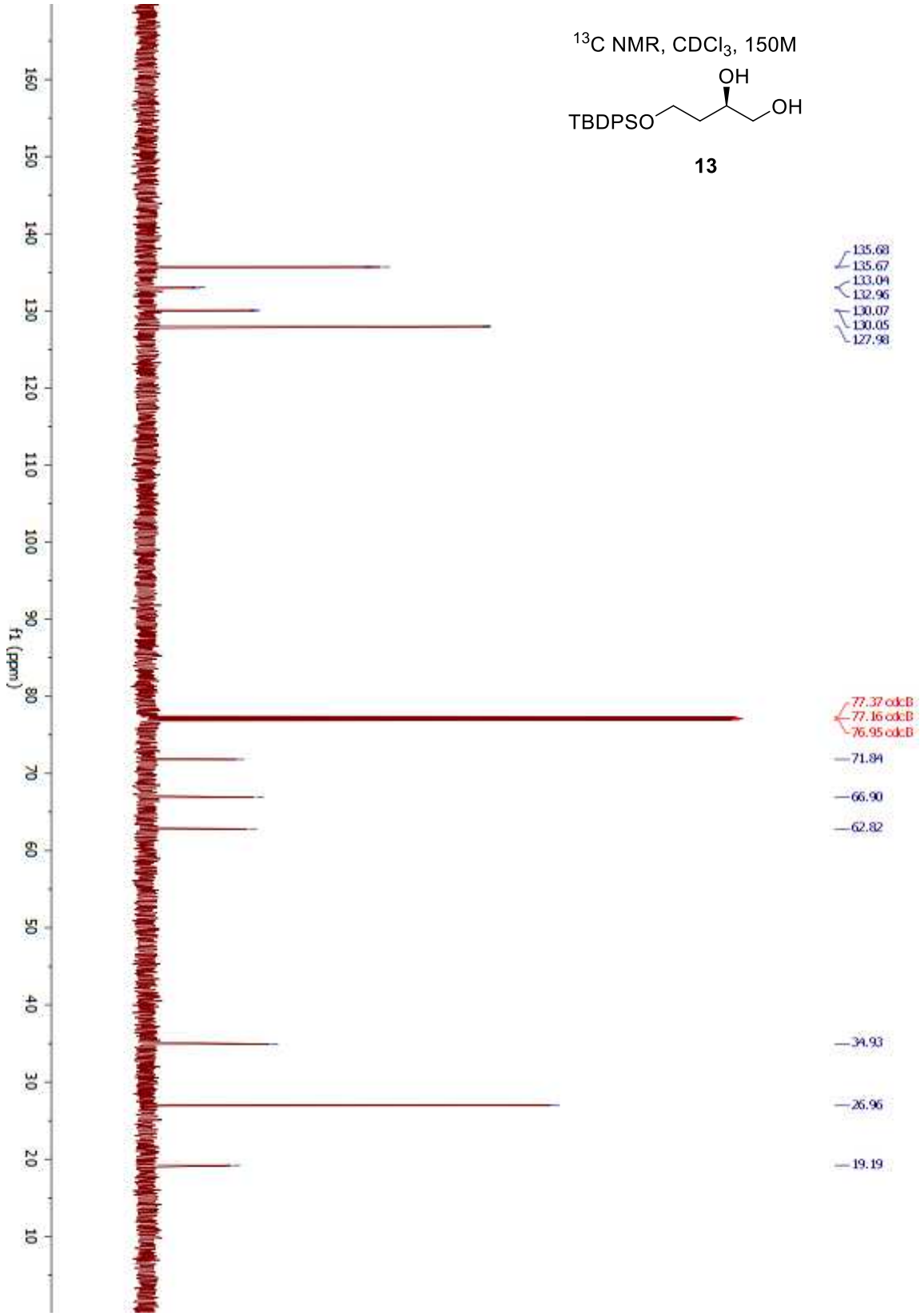

^{1}H NMR, $CDCl_3$, 600M
OH
TBDPSO
OH
12
f1 (ppm)
3.86
5.71
1.00
3.09
1.05
1.00
0.94
9.80

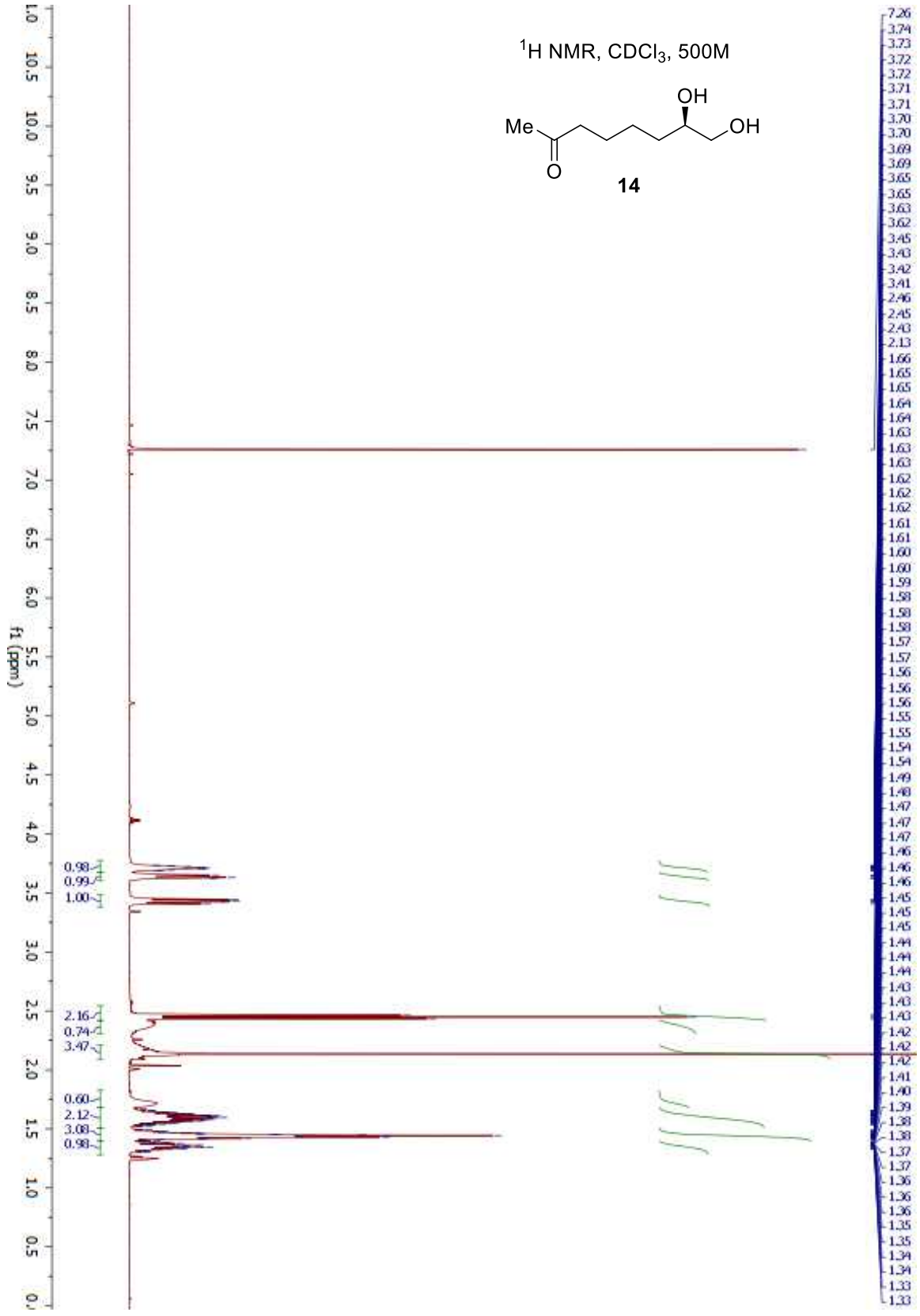

^{13}C NMR, $CDCl_3$, 150M
OH
TBDPSO
OH
12
135.53
135.45
132.86
132.81
129.94
129.90
127.86
127.78
77.20 cdcl3
76.99 cdcl3
76.78 cdcl3
71.85
71.76
65.33
65.24
63.93
63.84
63.74
26.90
26.85
26.81
19.20
f1 (ppm)

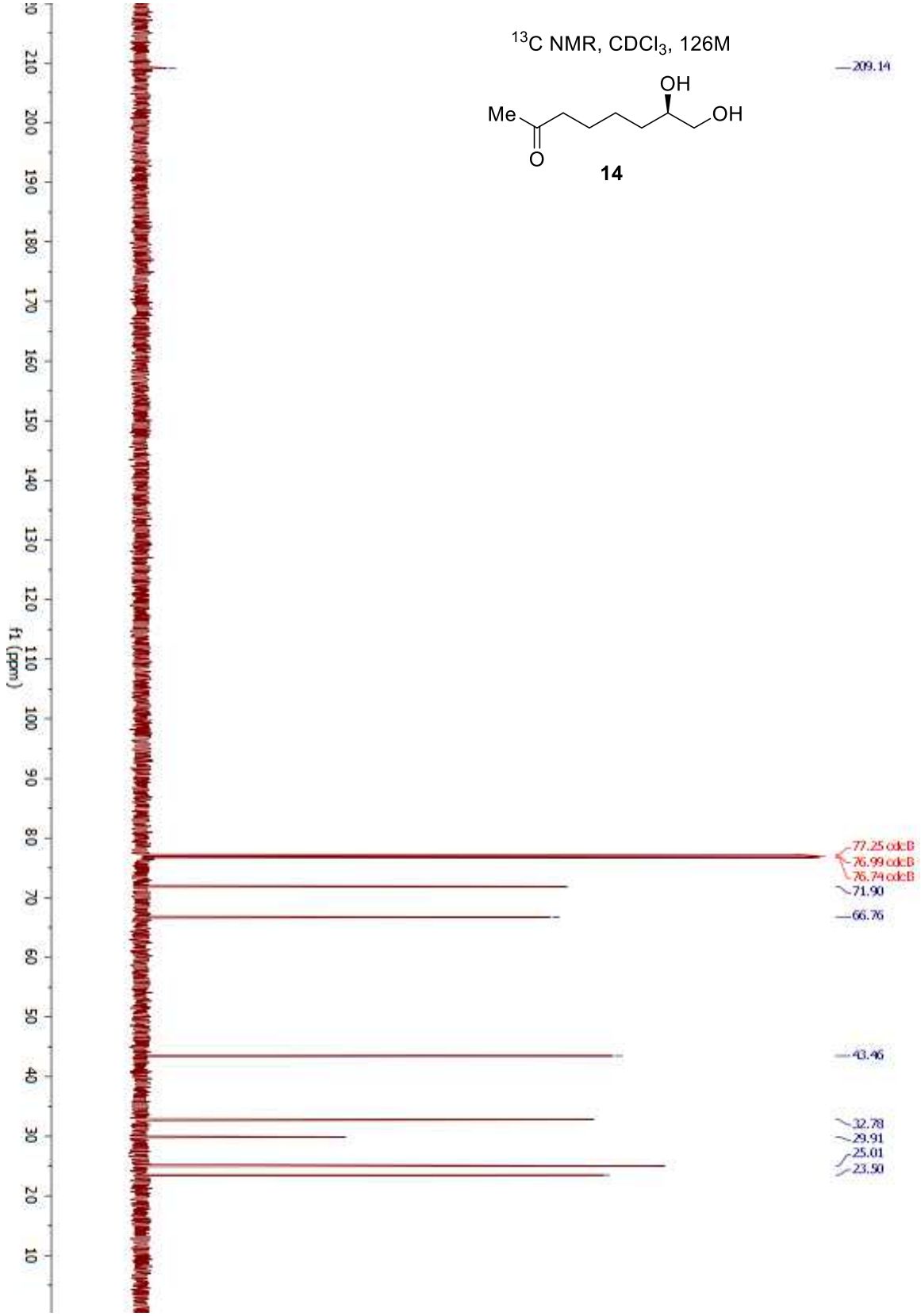
^{1}H NMR, $CDCl_3$, 600M



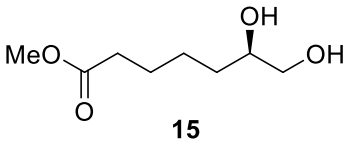
13


^{13}C NMR, $CDCl_3$, 150M
OH
TBDPSO
OH
13
135.68
135.67
133.04
132.96
130.07
130.05
127.98
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
71.84
66.90
62.82
34.93
26.96
19.19
f1 (ppm)


^{1}H NMR, $CDCl_3$, 500M
OH
Me
OH
O
14
f1 (ppm)
0.98
0.99
1.00
2.16
0.74
3.47
0.60
2.12
3.08
0.98


^{13}C NMR, $CDCl_3$, 126M
OH
Me
OH
O
14
209.14
77.25 cdcl3
76.99 cdcl3
76.74 cdcl3
71.90
66.76
43.46
32.78
29.91
25.01
23.50
f1 (ppm)

^{1}H NMR, $CDCl_3$, 600M



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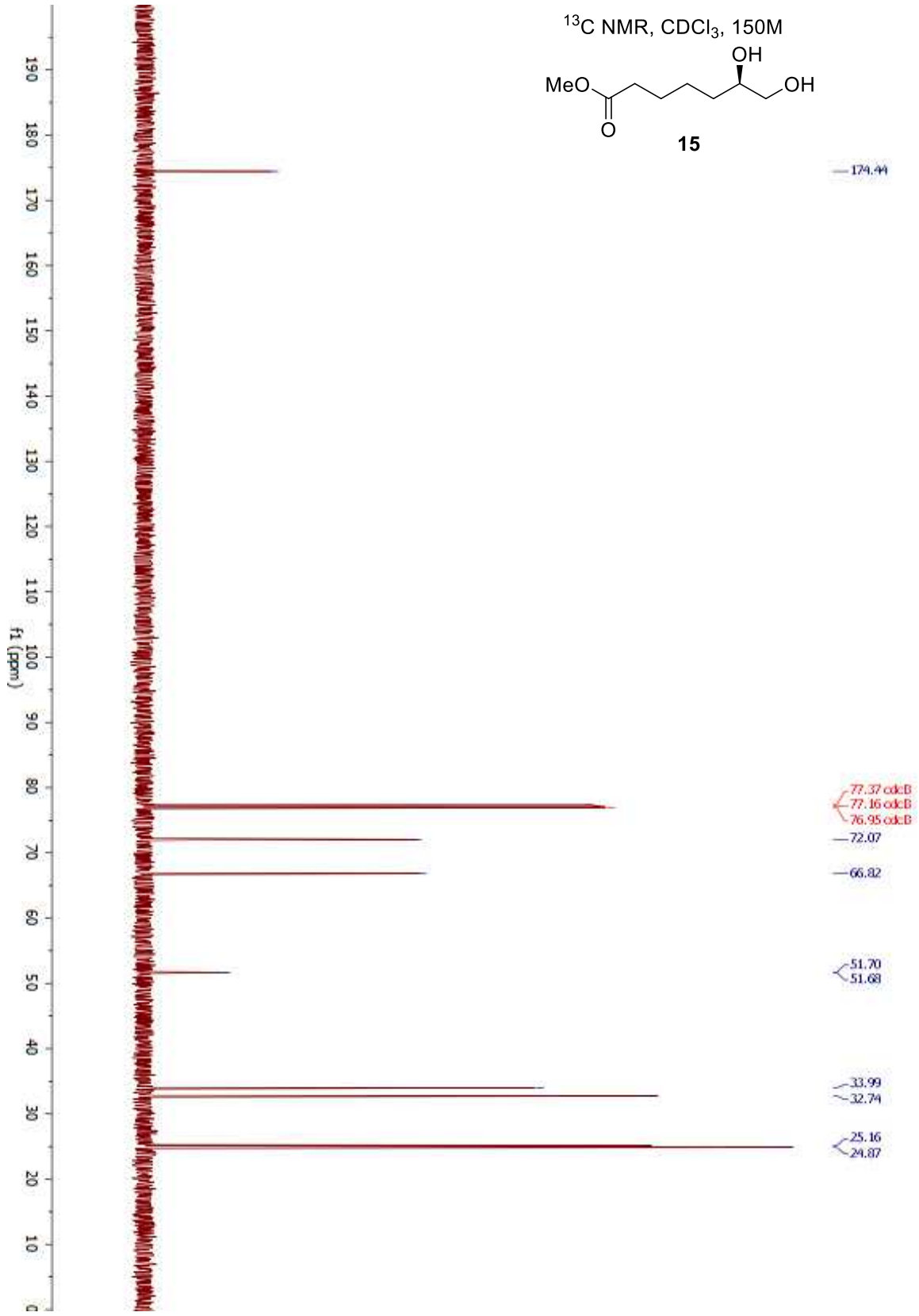
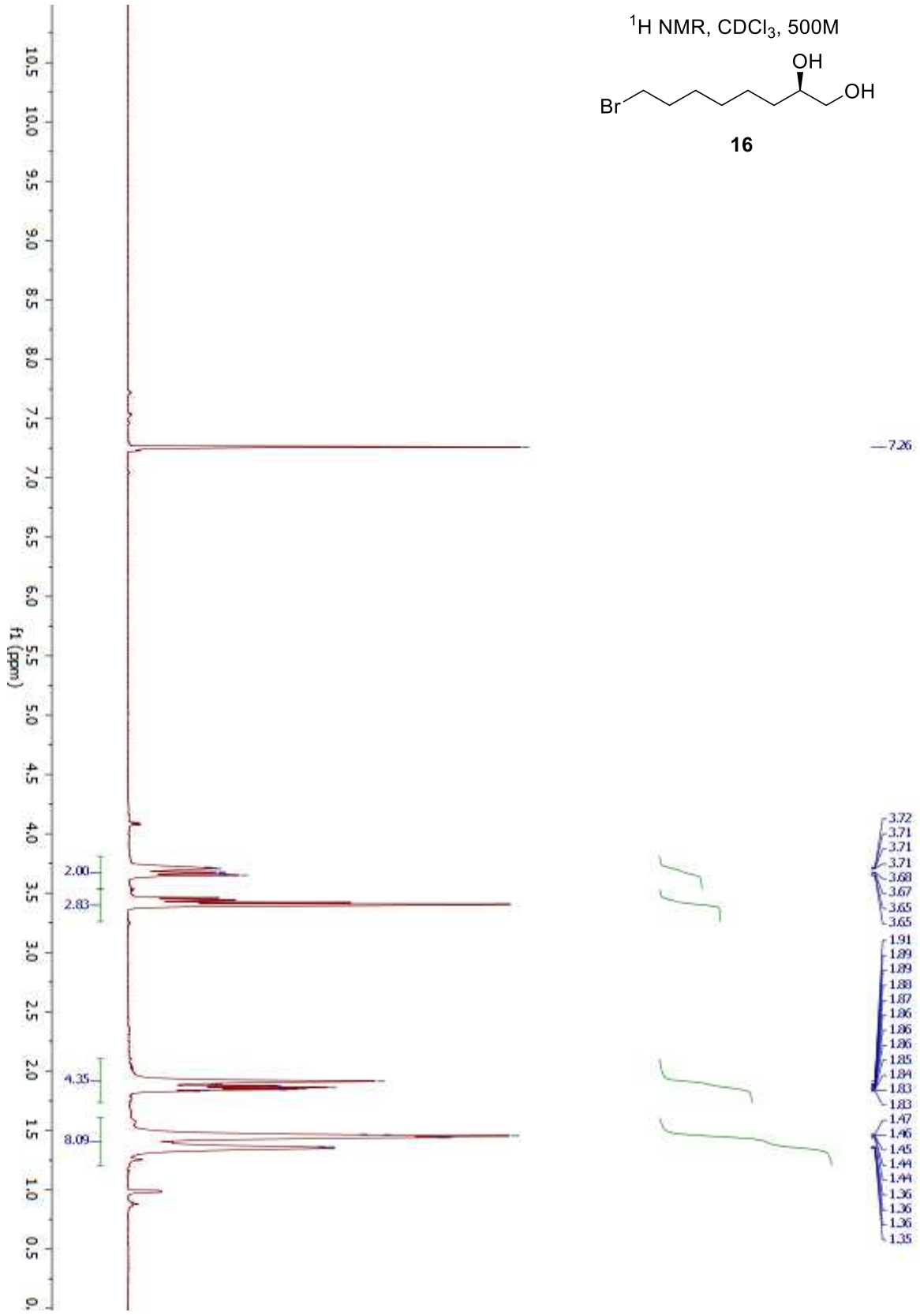
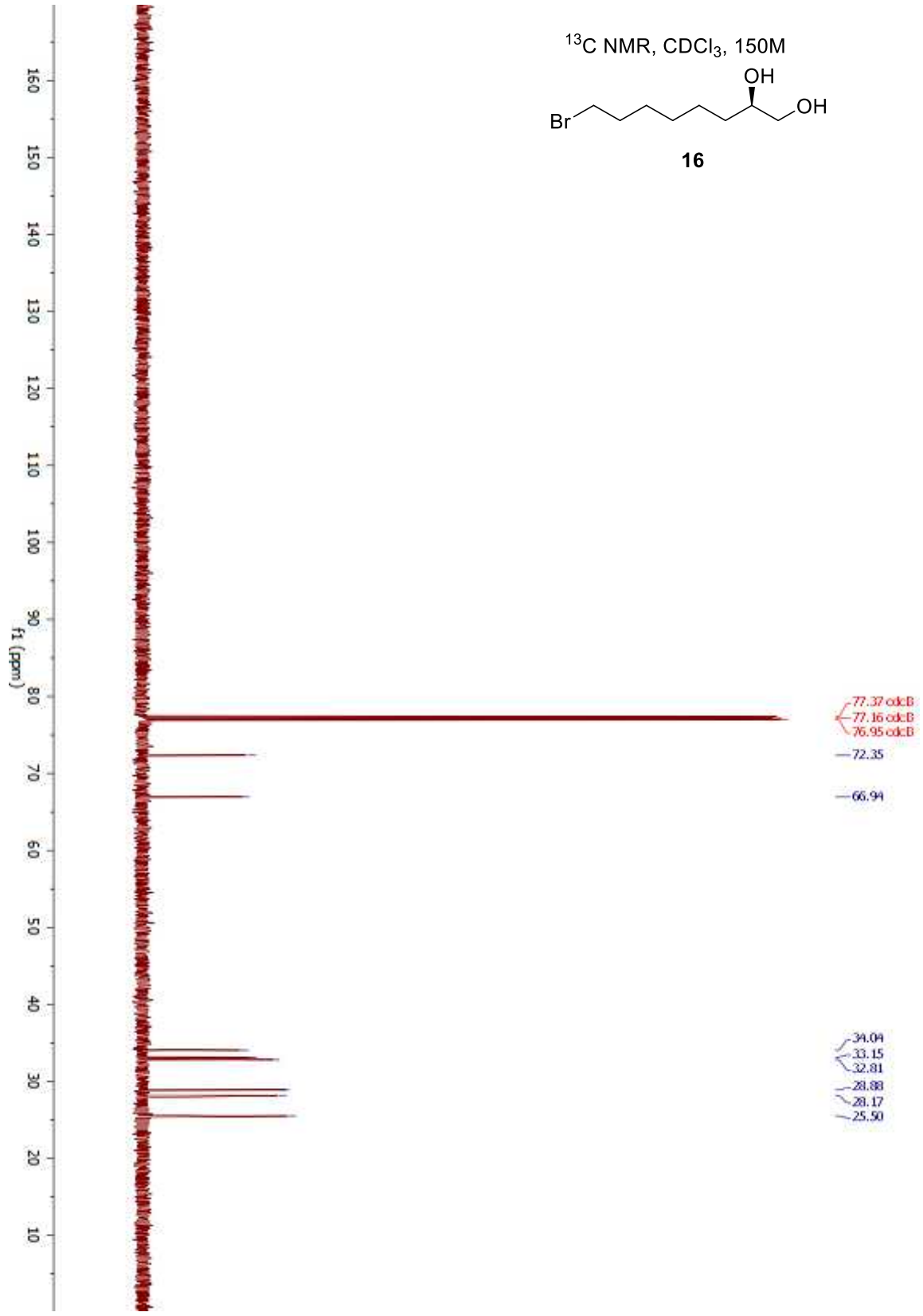
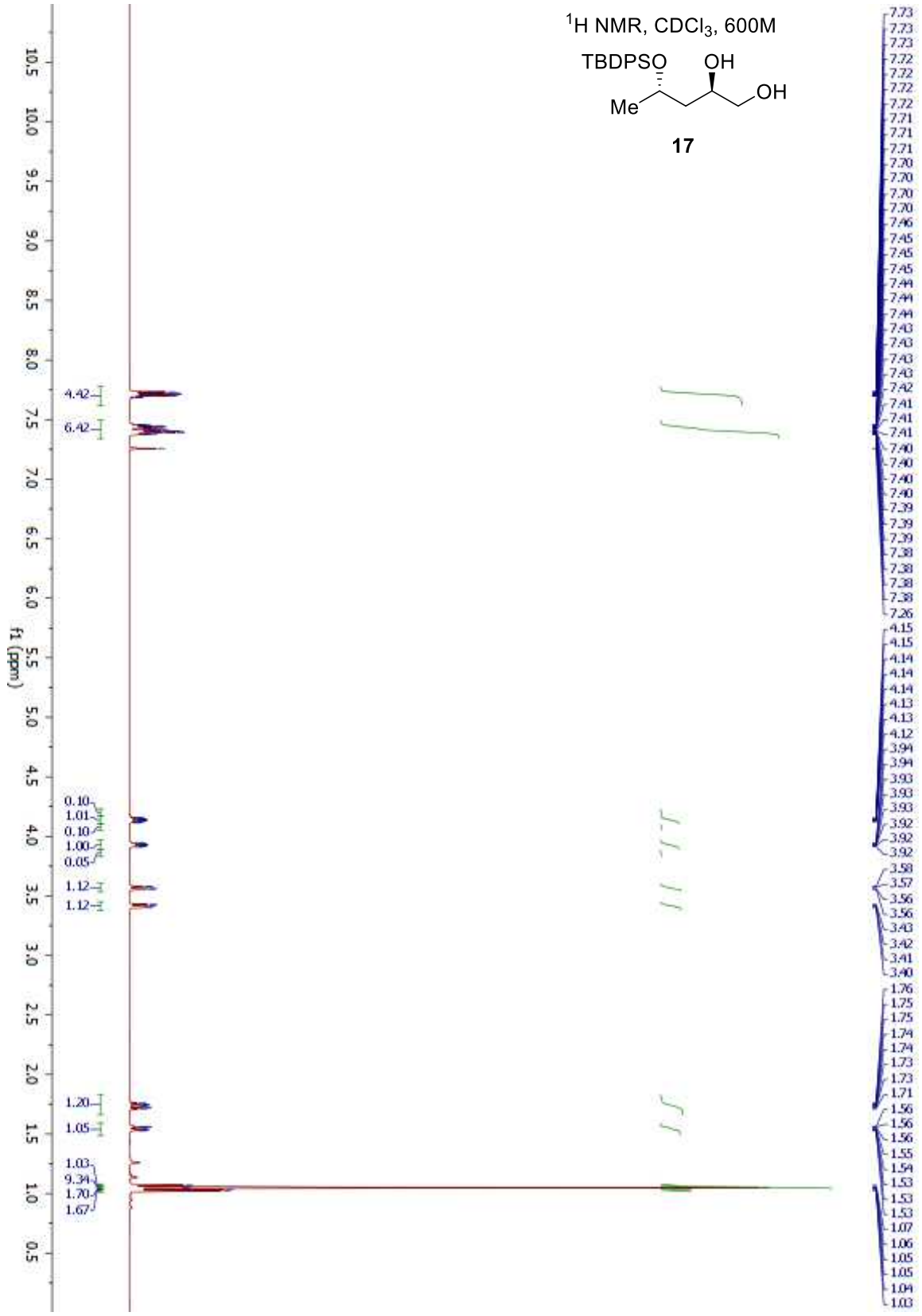
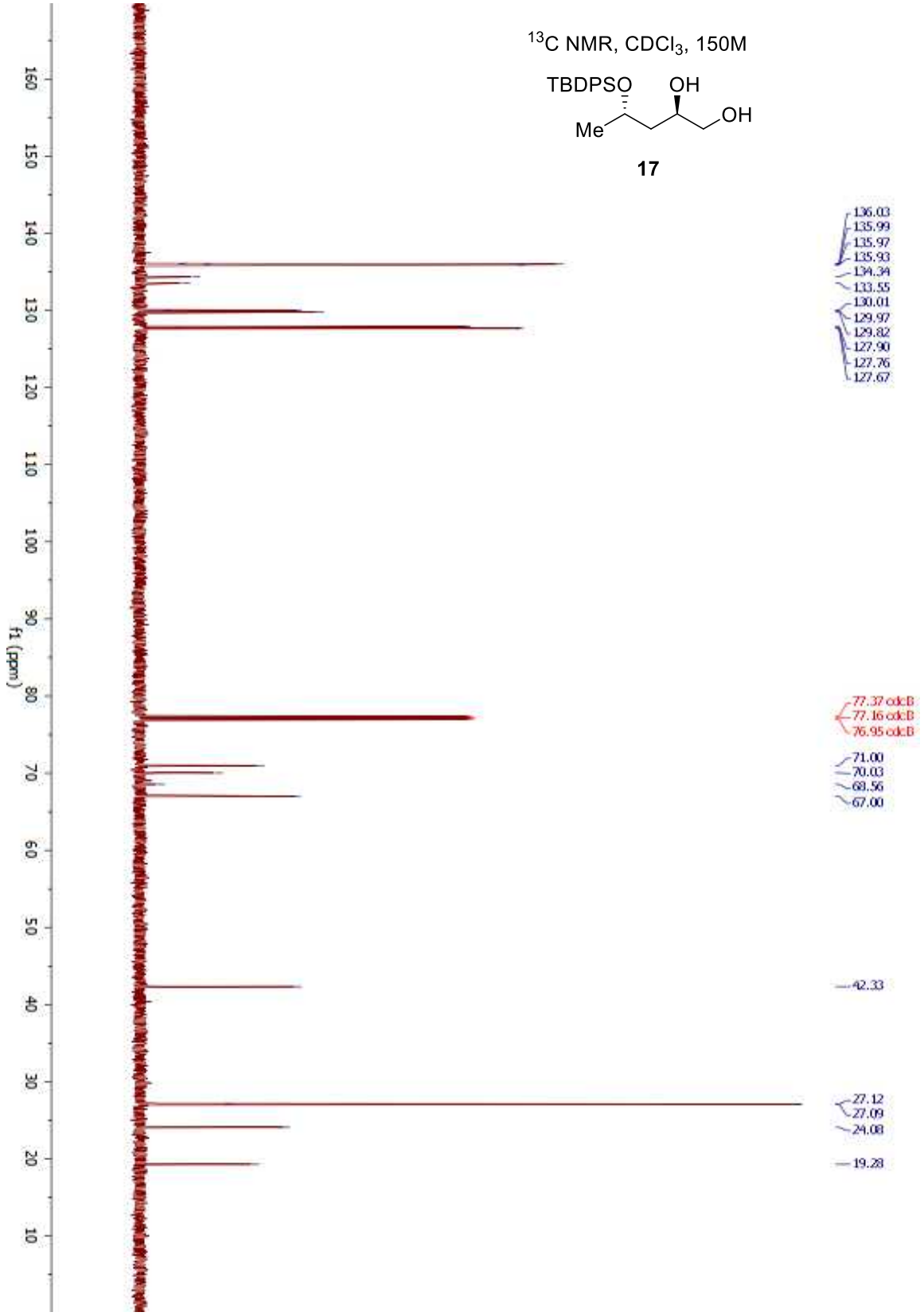
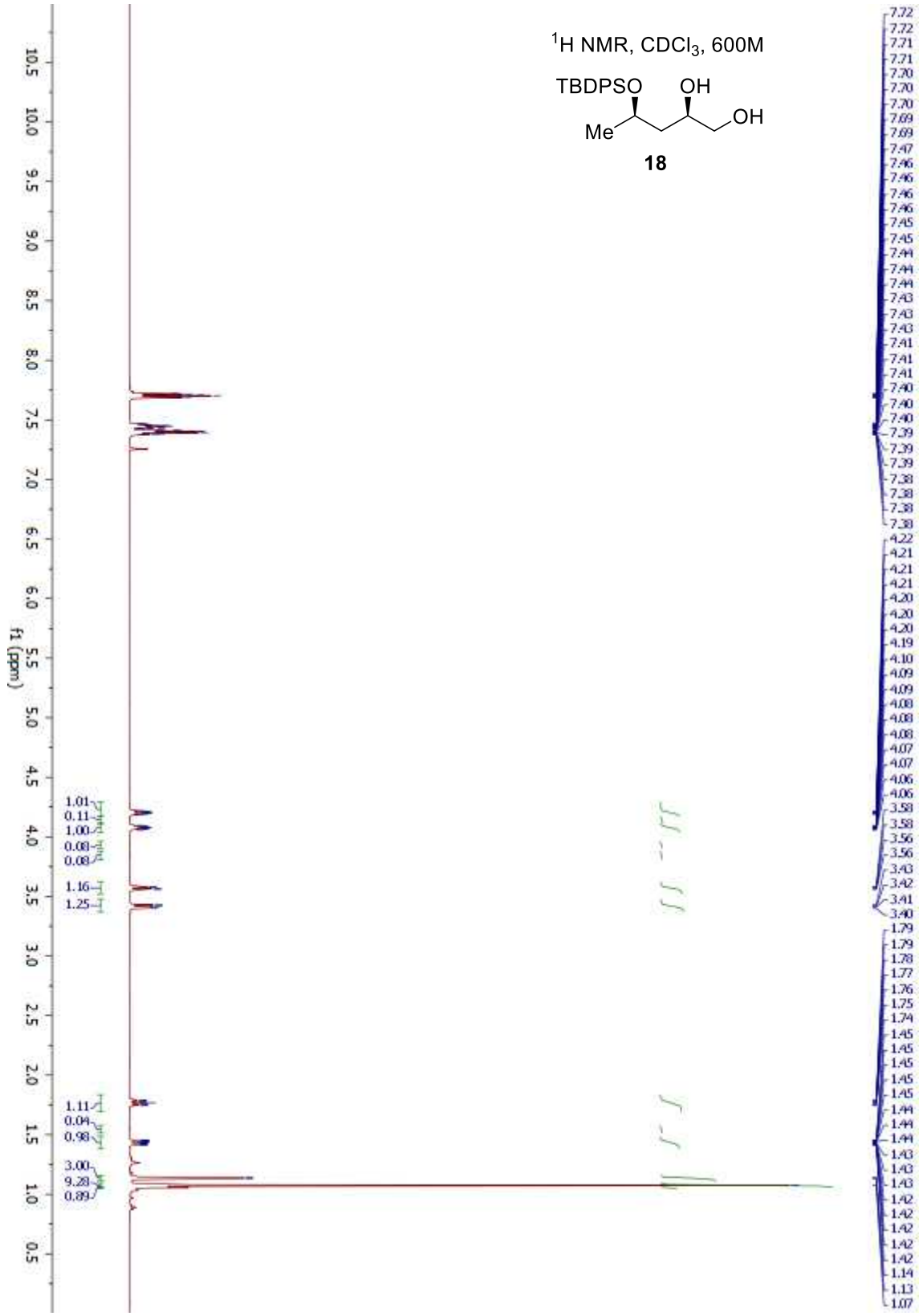

^{13}C NMR, $CDCl_3$, 150M
OH
MeO
OH
O
15
174.44
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
72.07
66.82
51.70
51.68
33.99
32.74
25.16
24.87
f1 (ppm)

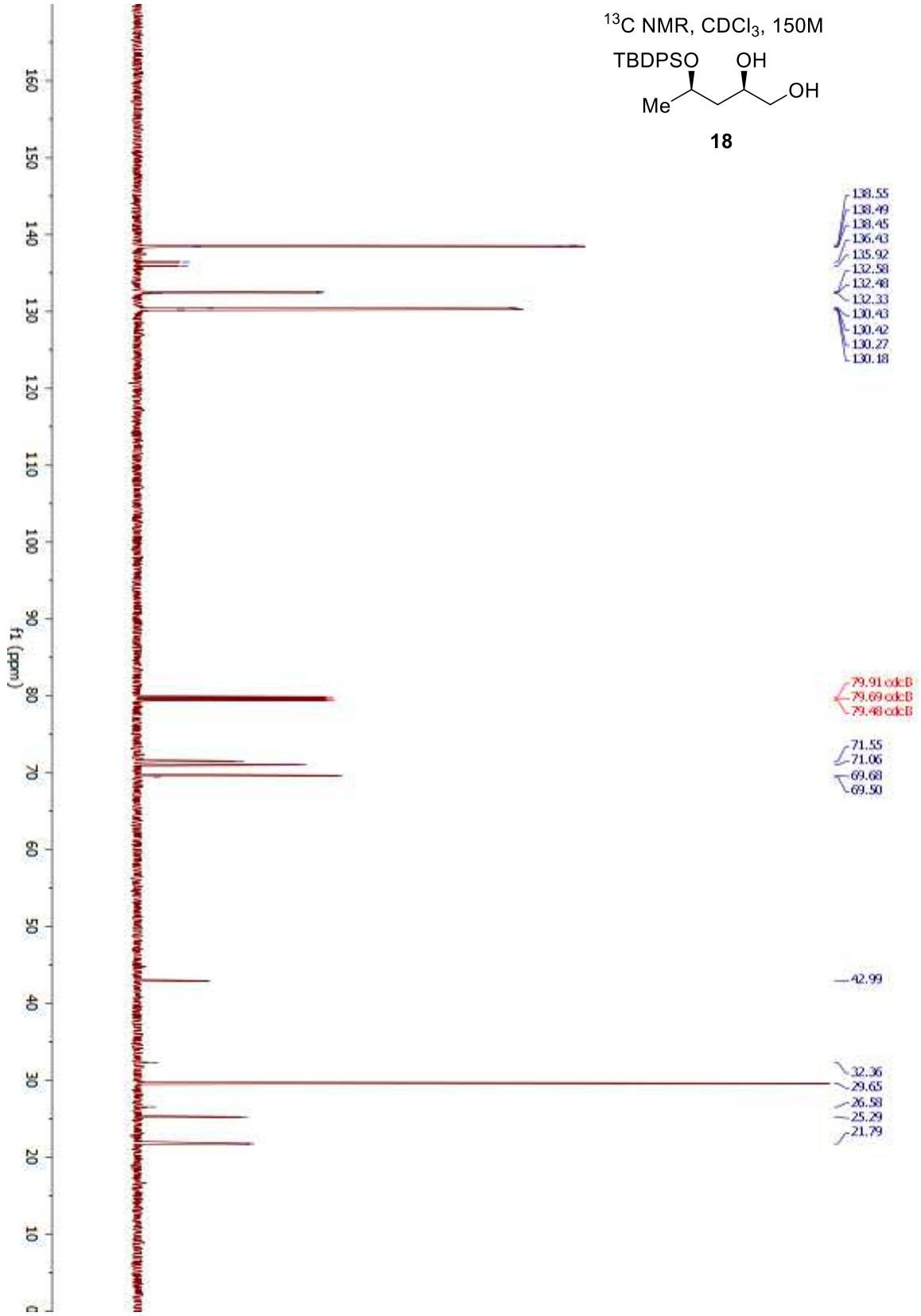

^{1}H NMR, $CDCl_3$, 500M
OH
OH
Br
16
7.26
3.72
3.71
3.71
3.71
3.68
3.67
3.65
3.65
1.91
1.89
1.89
1.88
1.87
1.86
1.86
1.86
1.85
1.84
1.83
1.83
1.47
1.46
1.45
1.44
1.44
1.36
1.36
1.36
1.35
2.00
2.83
4.35
8.09
f1 (ppm)

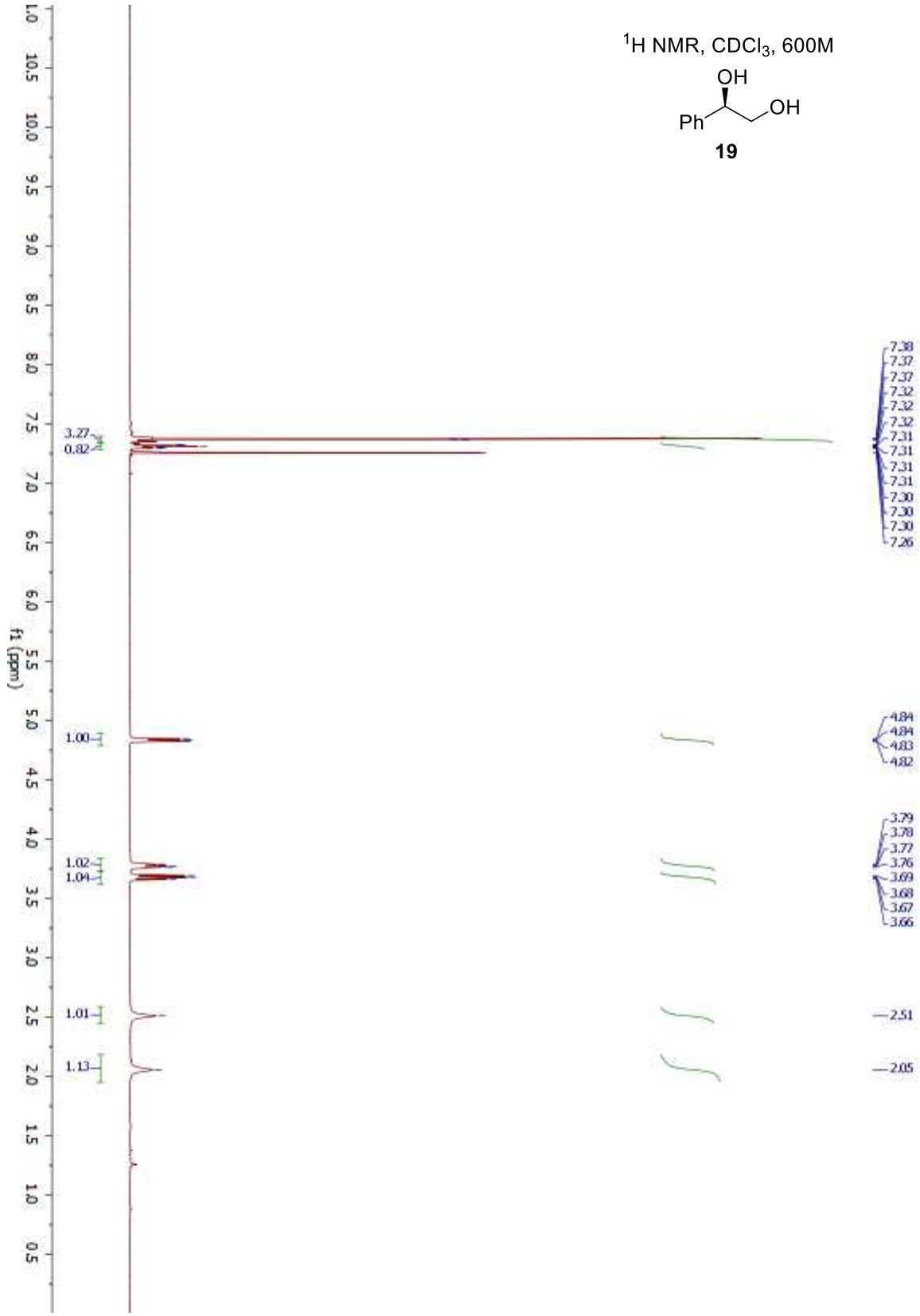

^{13}C NMR, $CDCl_3$, 150M
OH
Br
OH
16
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
72.35
66.94
34.09
33.15
32.81
28.88
28.17
25.50

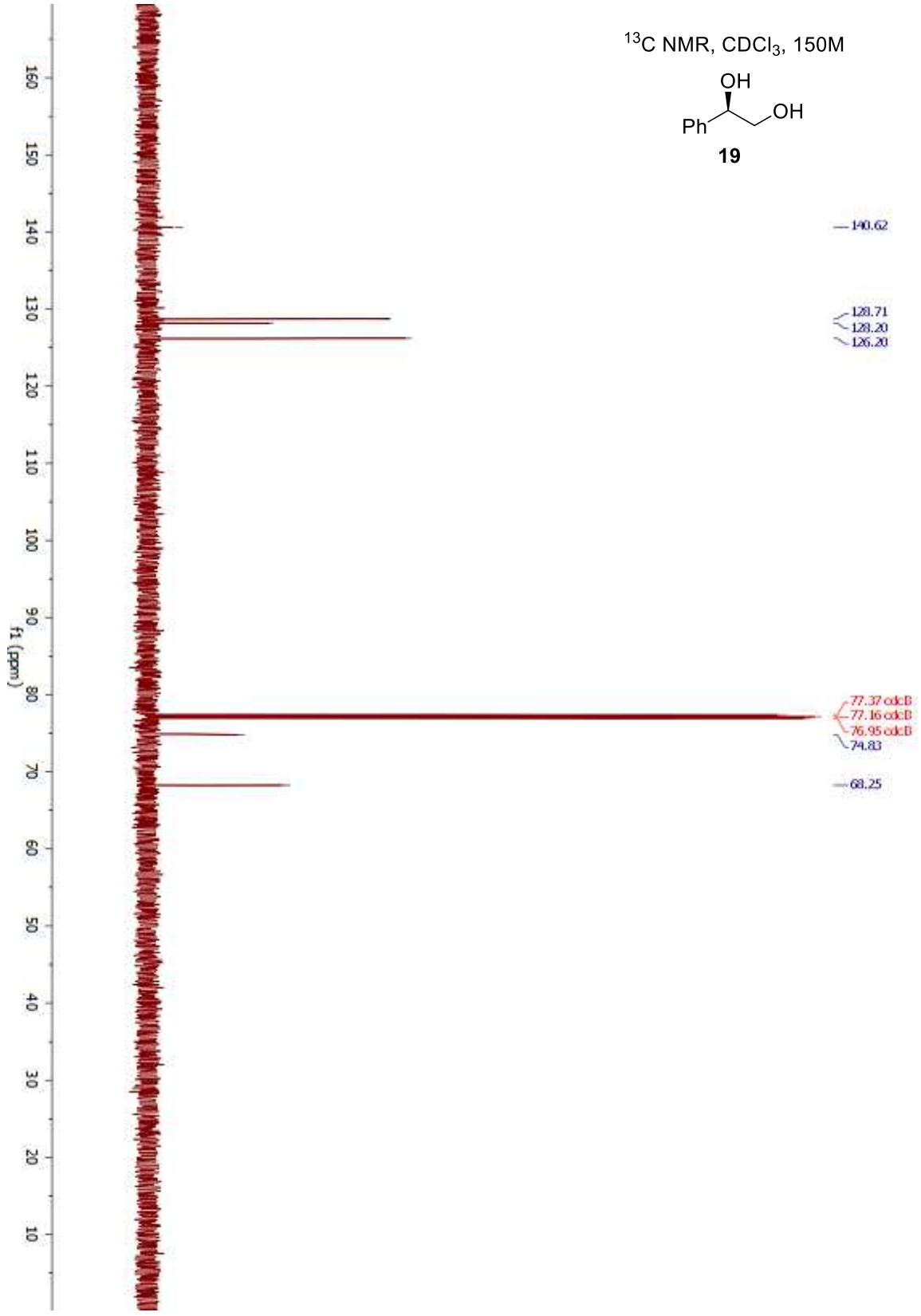

^{1}H NMR, $CDCl_3$, 600M
TBDPSO
OH
OH
Me
17
f1 (ppm)

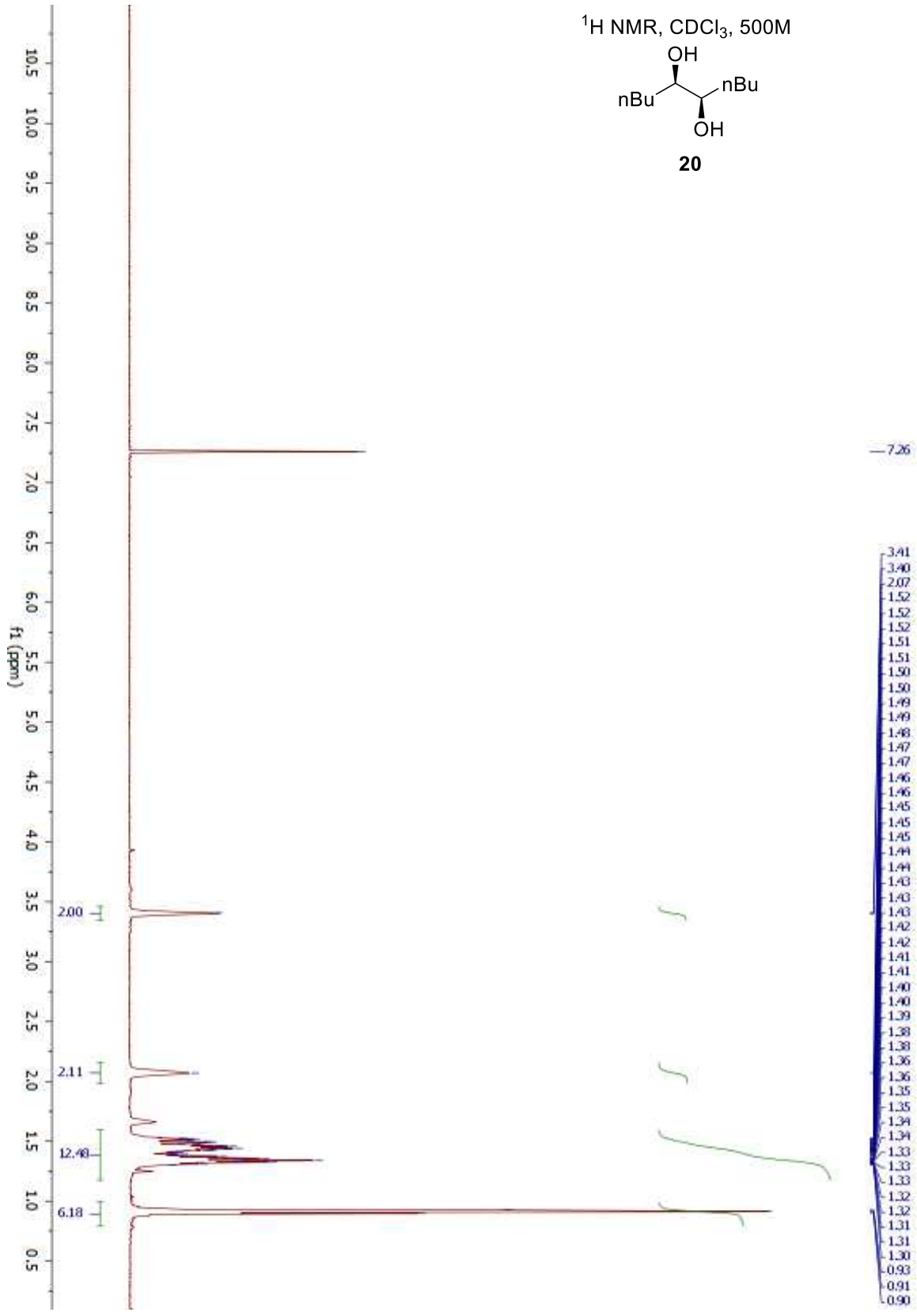

^{13}C NMR, $CDCl_3$, 150M
TBDPSO
OH
OH
Me
17
136.03
135.99
135.97
135.93
134.34
133.55
130.01
129.97
129.82
127.90
127.76
127.67
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
71.00
70.03
68.56
67.00
42.33
27.12
27.09
24.08
19.28
f1 (ppm)

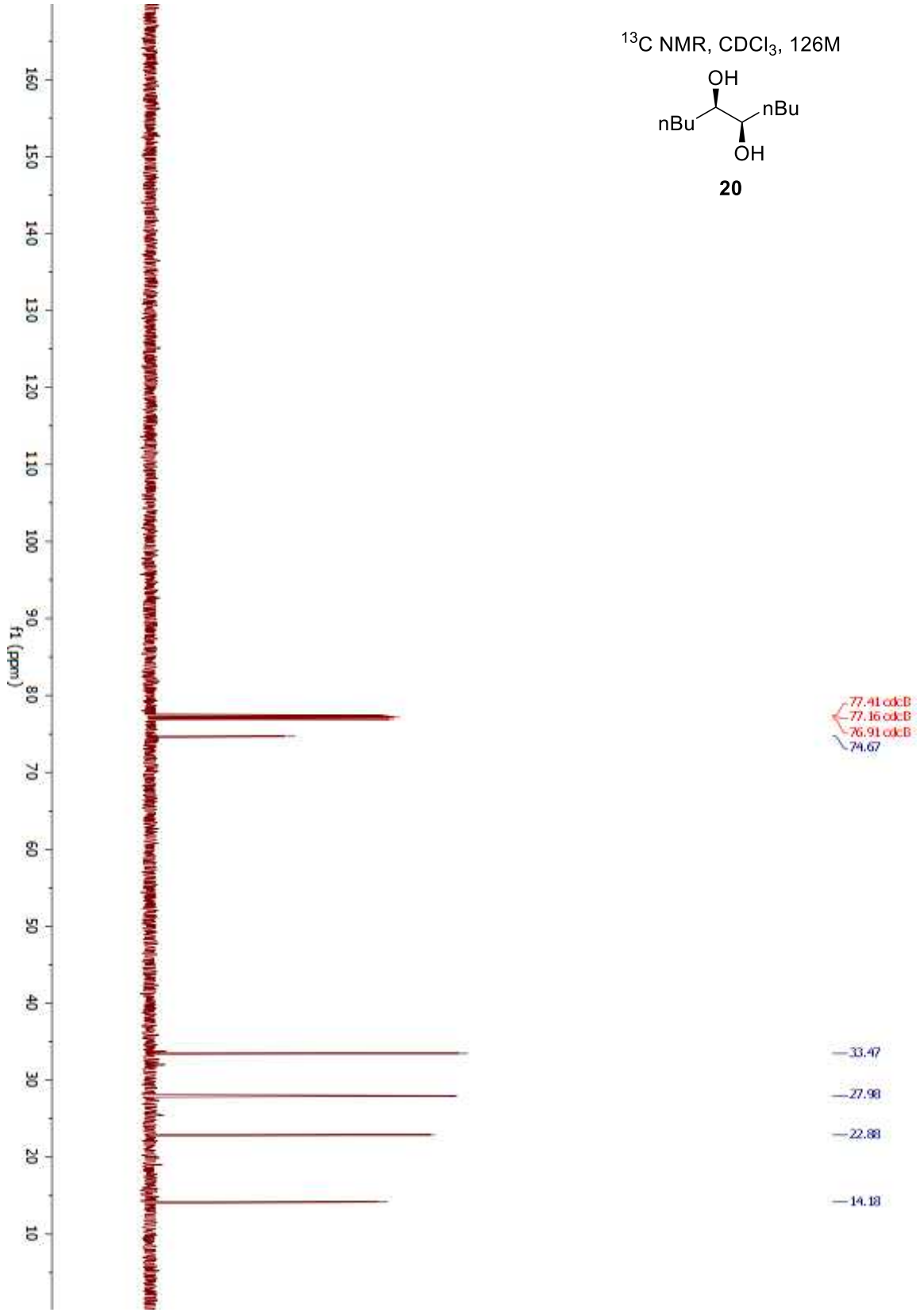

^{1}H NMR, $CDCl_3$, 600M
TBDPSO
OH
OH
Me
18
f1 (ppm)


^{13}C NMR, $CDCl_3$, 150M
TBDPSO
OH
OH
Me
18
138.55
138.49
138.45
136.43
135.92
132.58
132.48
132.33
130.43
130.42
130.27
130.18
79.91 cdcl3
79.69 cdcl3
79.48 cdcl3
71.55
71.06
69.68
69.50
42.99
32.36
29.65
26.58
25.29
21.79
f1 (ppm)

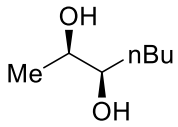

^{1}H NMR, $CDCl_3$, 600M
OH
Ph
OH
19
f1 (ppm)
3.27
0.82
1.00
1.02
1.04
1.01
1.13
7.38
7.37
7.37
7.32
7.32
7.32
7.31
7.31
7.31
7.31
7.30
7.30
7.30
7.26
4.84
4.84
4.83
4.82
3.79
3.78
3.77
3.76
3.69
3.68
3.67
3.66
2.51
2.05


^{13}C NMR, $CDCl_3$, 150M
OH
OH
Ph
19
140.62
128.71
128.20
126.20
77.37 odcb
77.16 odcb
76.95 odcb
74.83
68.25
f1 (ppm)

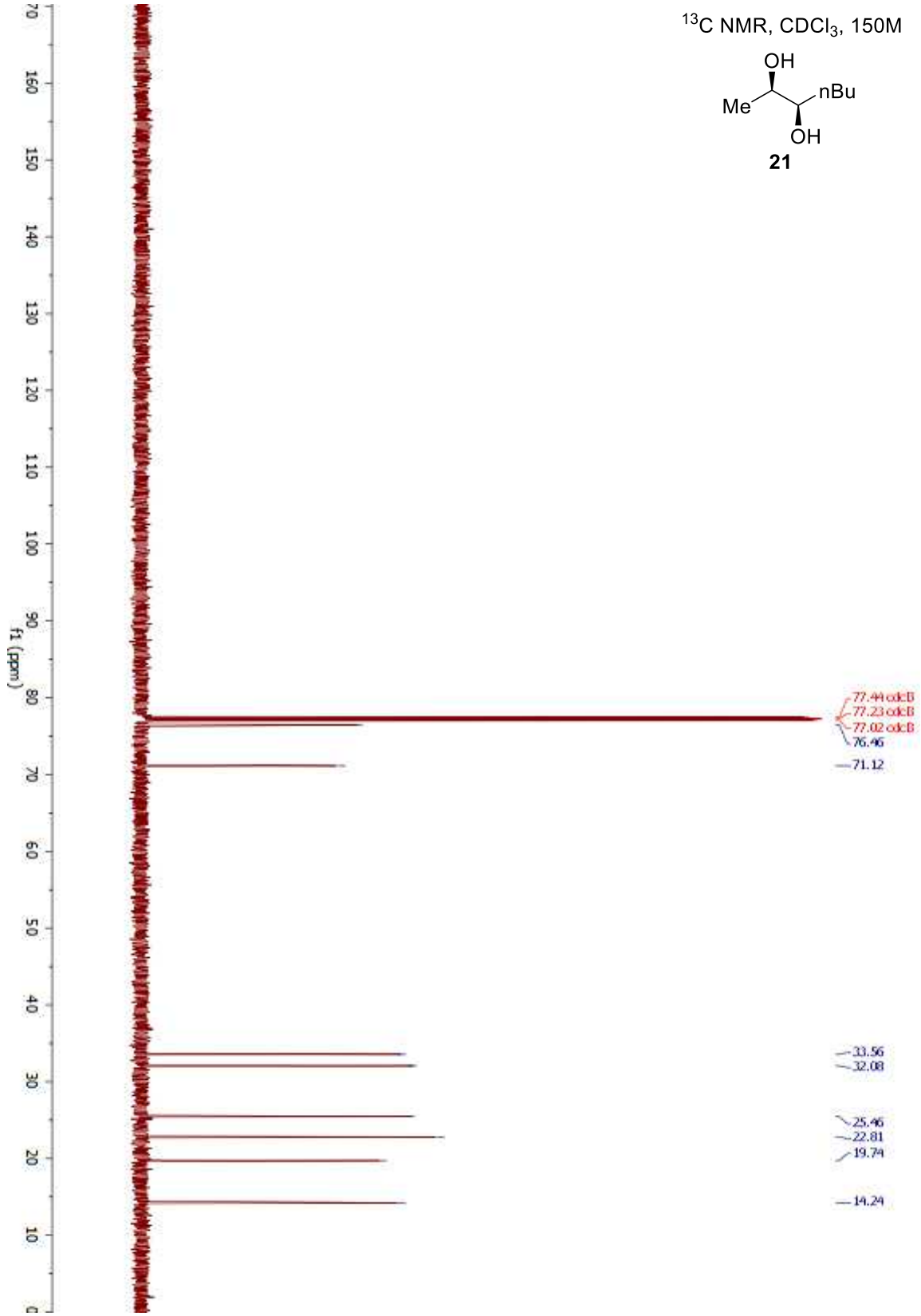

^{1}H NMR, $CDCl_3$, 500M
OH
nBu
nBu
OH
20
f1 (ppm)
2.00
2.11
12.48
6.18
7.26


^{13}C NMR, $CDCl_3$, 126M
OH
nBu
nBu
OH
20
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
74.67
33.47
27.98
22.88
14.18

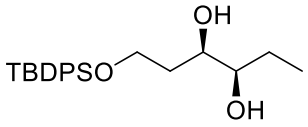
^{1}H NMR, $CDCl_3$, 600M



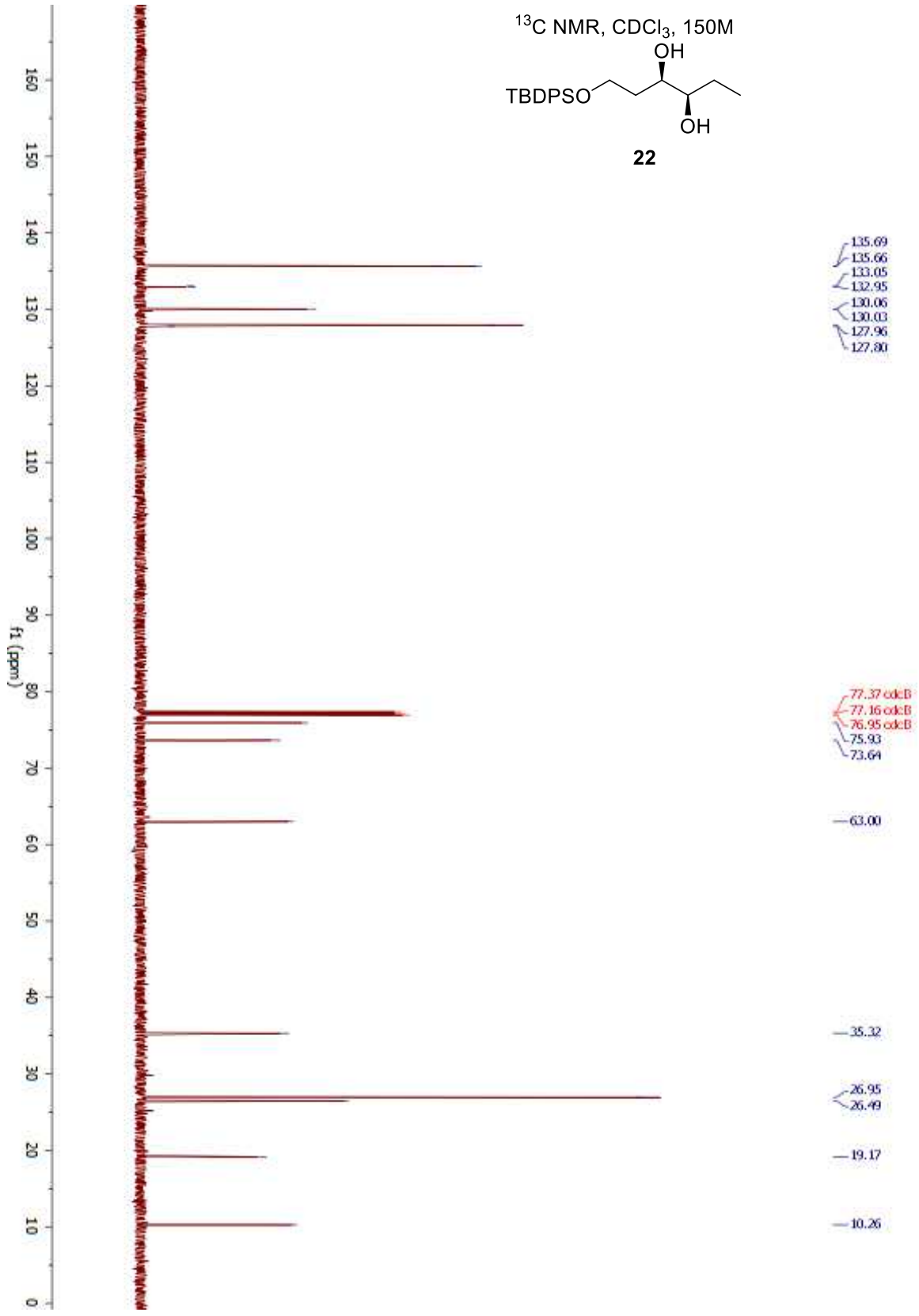
21

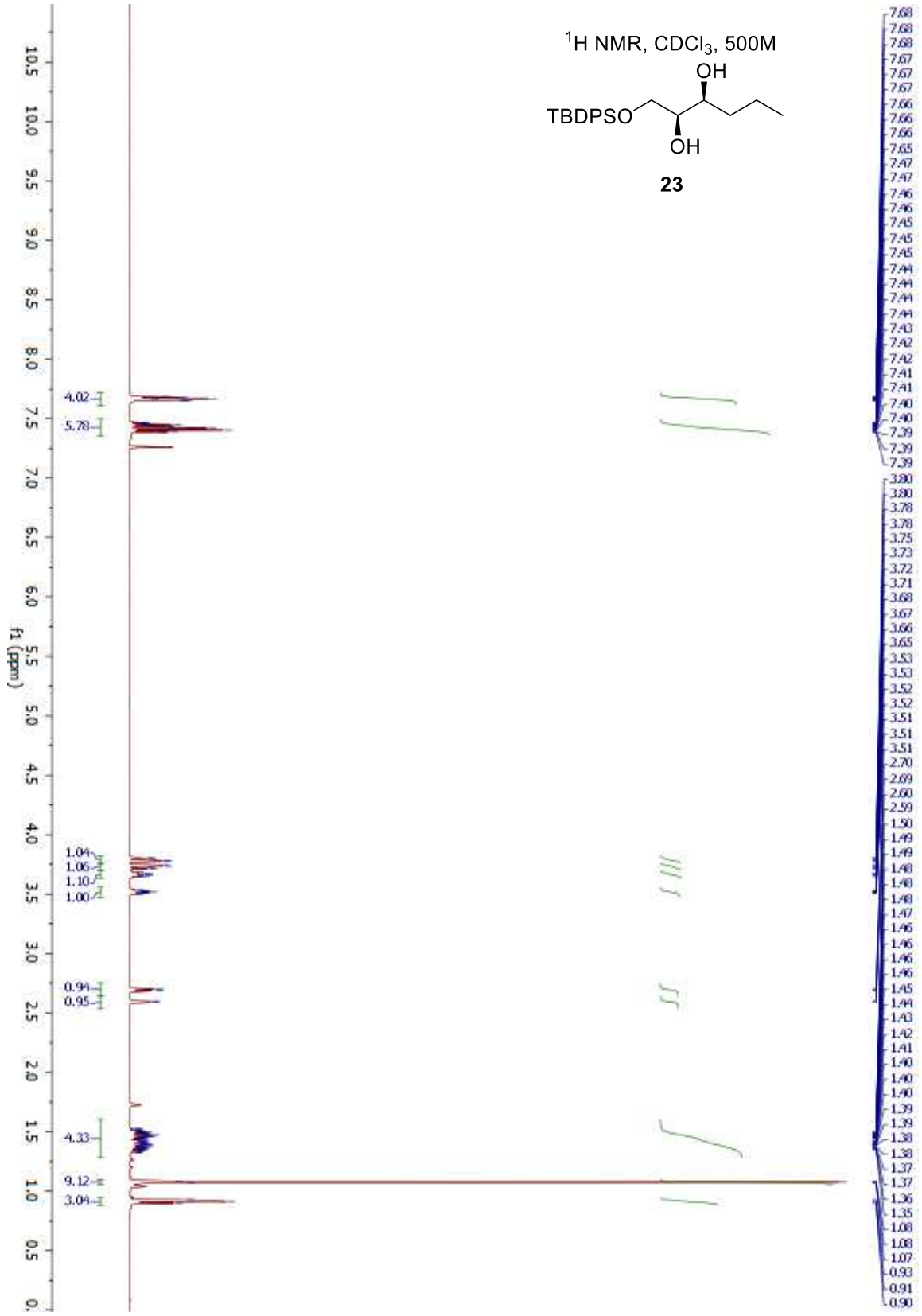

^{13}C NMR, $CDCl_3$, 150M
OH
Me
nBu
OH
21
f1 (ppm)
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
76.46
71.12
33.56
32.08
25.46
22.81
19.74
14.24

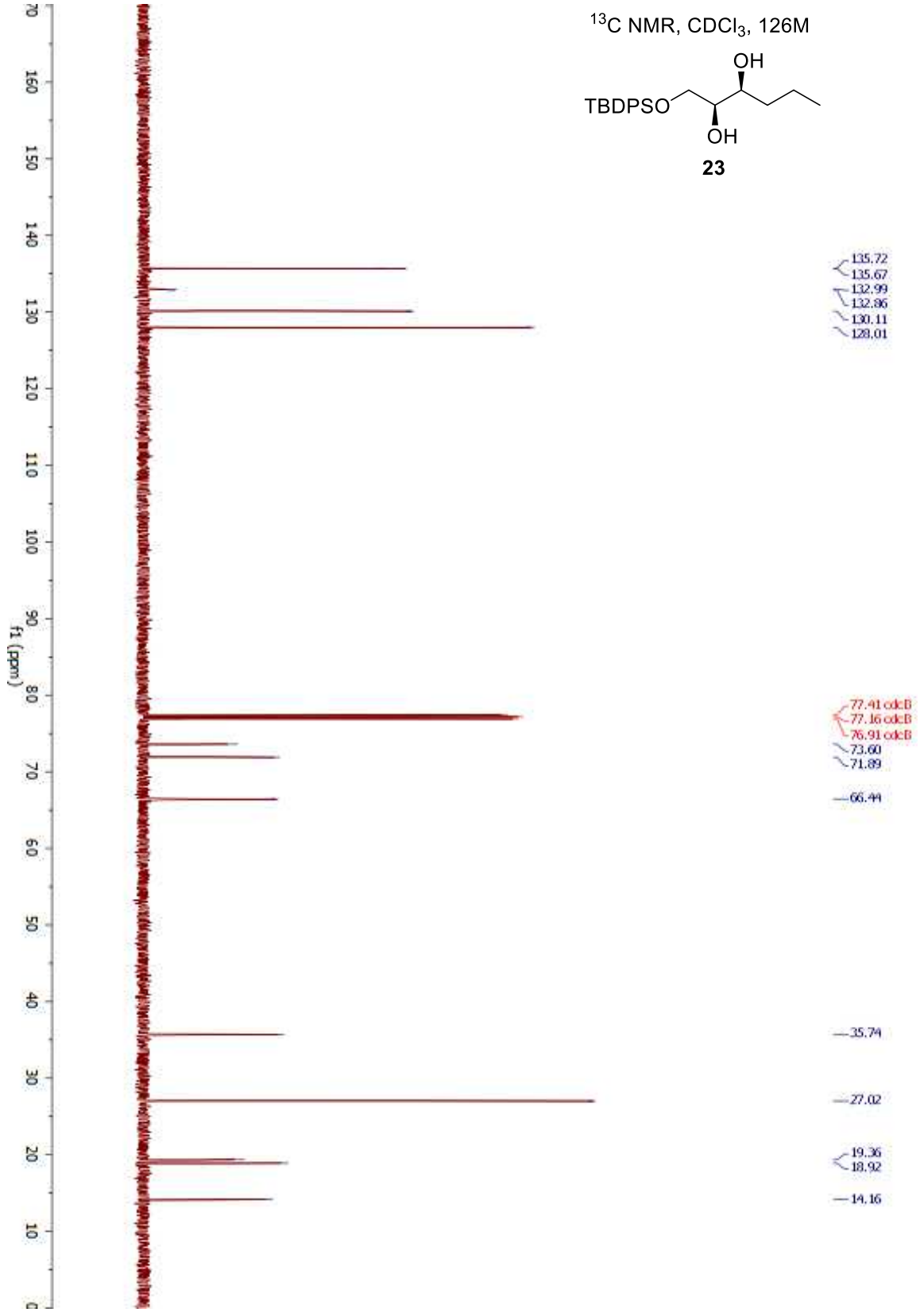
^{1}H NMR, $CDCl_3$, 600M



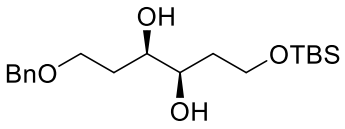
22


^{13}C NMR, $CDCl_3$, 150M
OH
TBDPSO
OH
22
135.69
135.66
133.05
132.95
130.06
130.03
127.96
127.80
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
75.93
73.64
63.00
35.32
26.95
26.49
19.17
10.26
f1 (ppm)

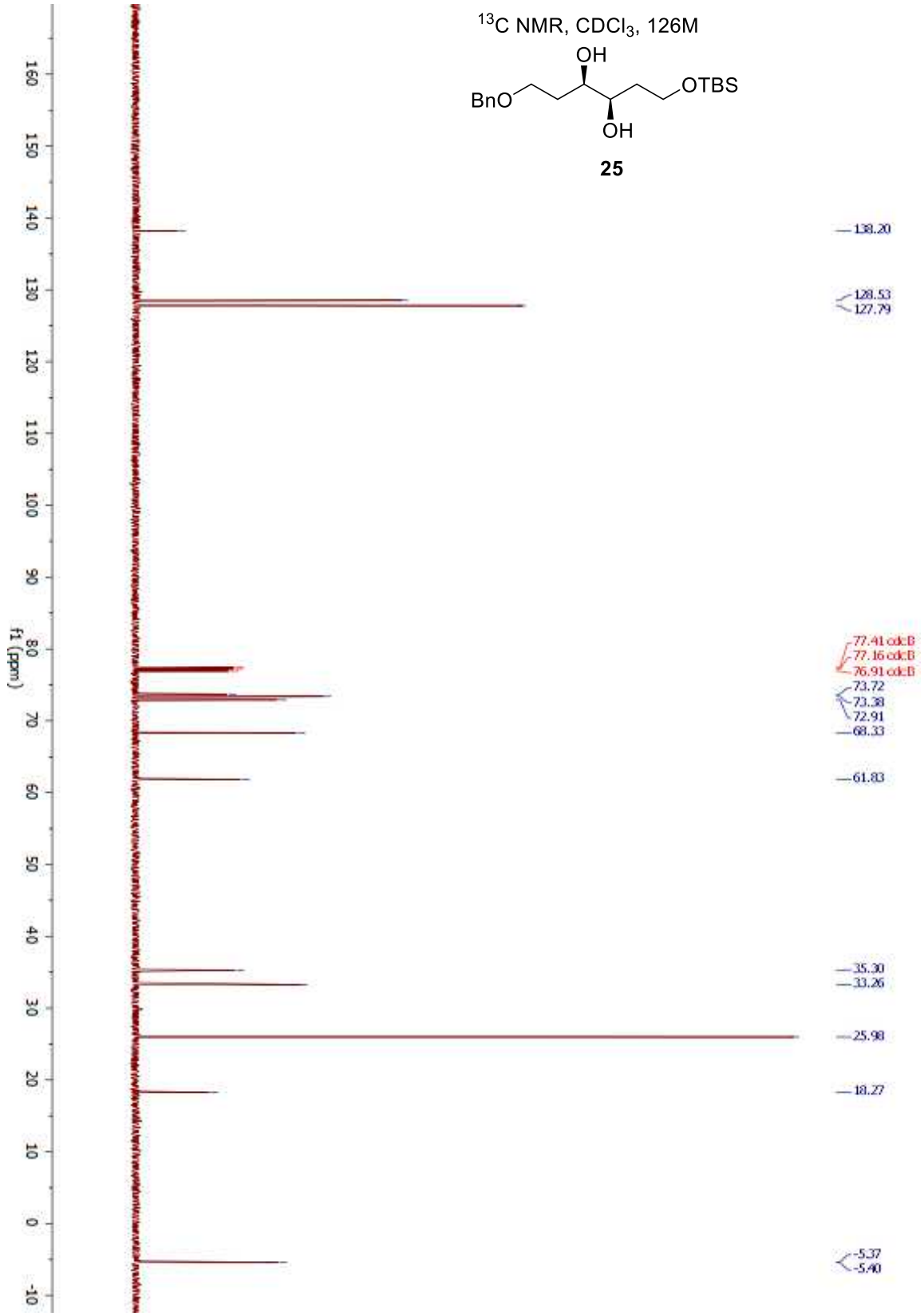

^{1}H NMR, $CDCl_3$, 500M
OH
TBDPSO
OH
23
f1 (ppm)
4.02
5.78
1.04
1.06
1.10
1.00
0.94
0.95
4.33
9.12
3.04

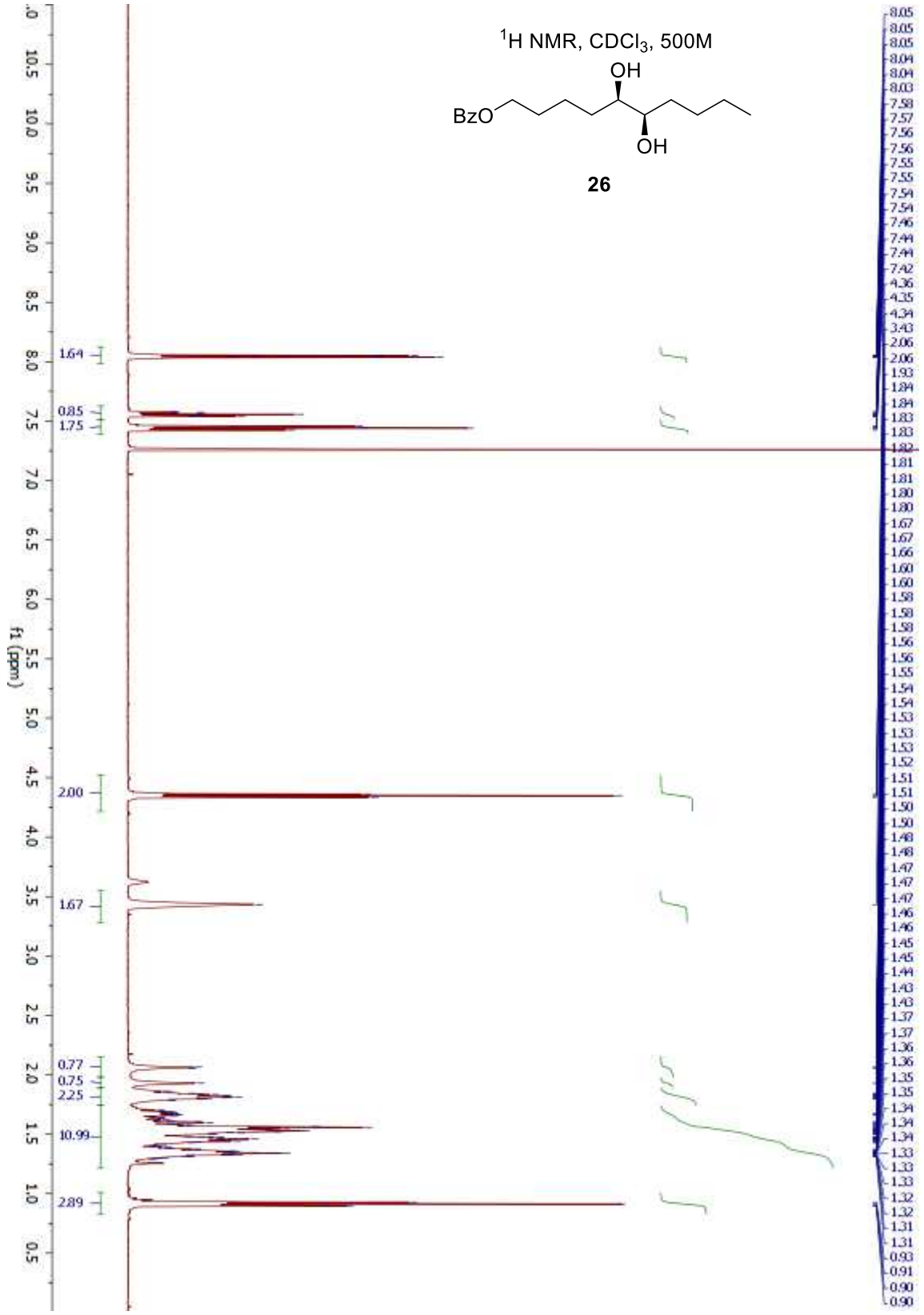

^{13}C NMR, $CDCl_3$, 126M
OH
TBDPSO
OH
23
135.72
135.67
132.99
132.86
130.11
128.01
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
73.60
71.89
66.44
35.74
27.02
19.36
18.92
14.16
f1 (ppm)

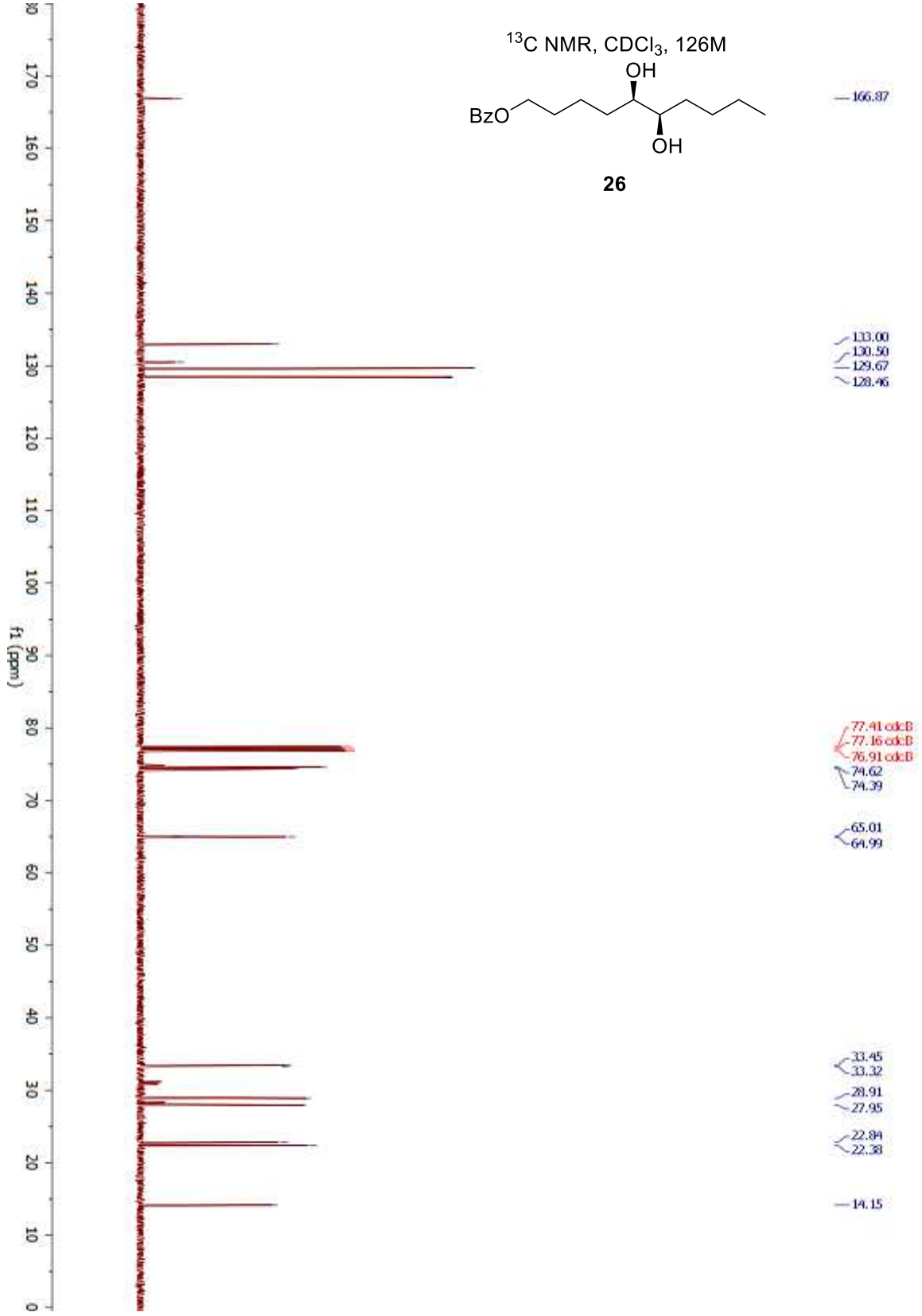
^{1}H NMR, $CDCl_3$, 400M

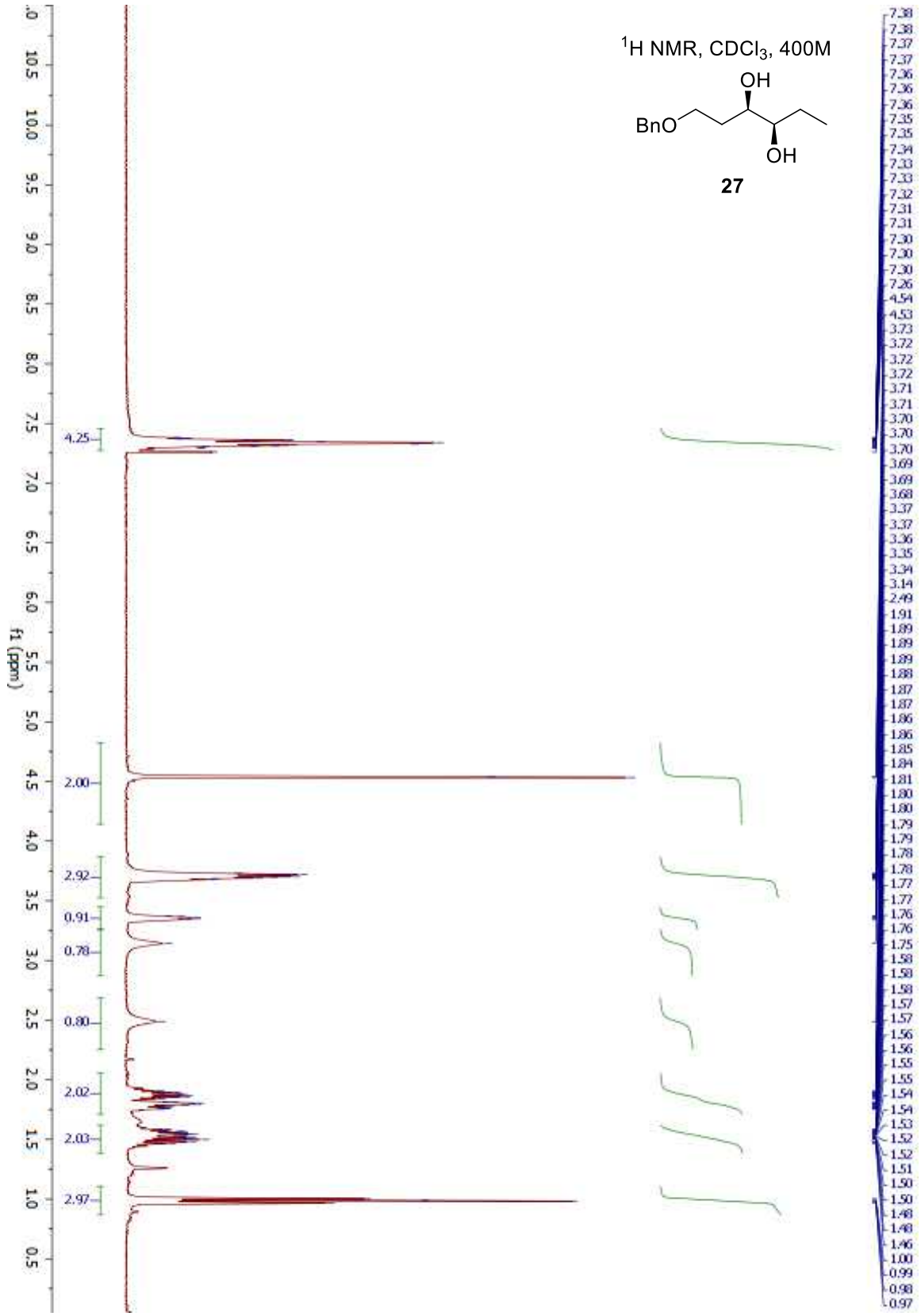


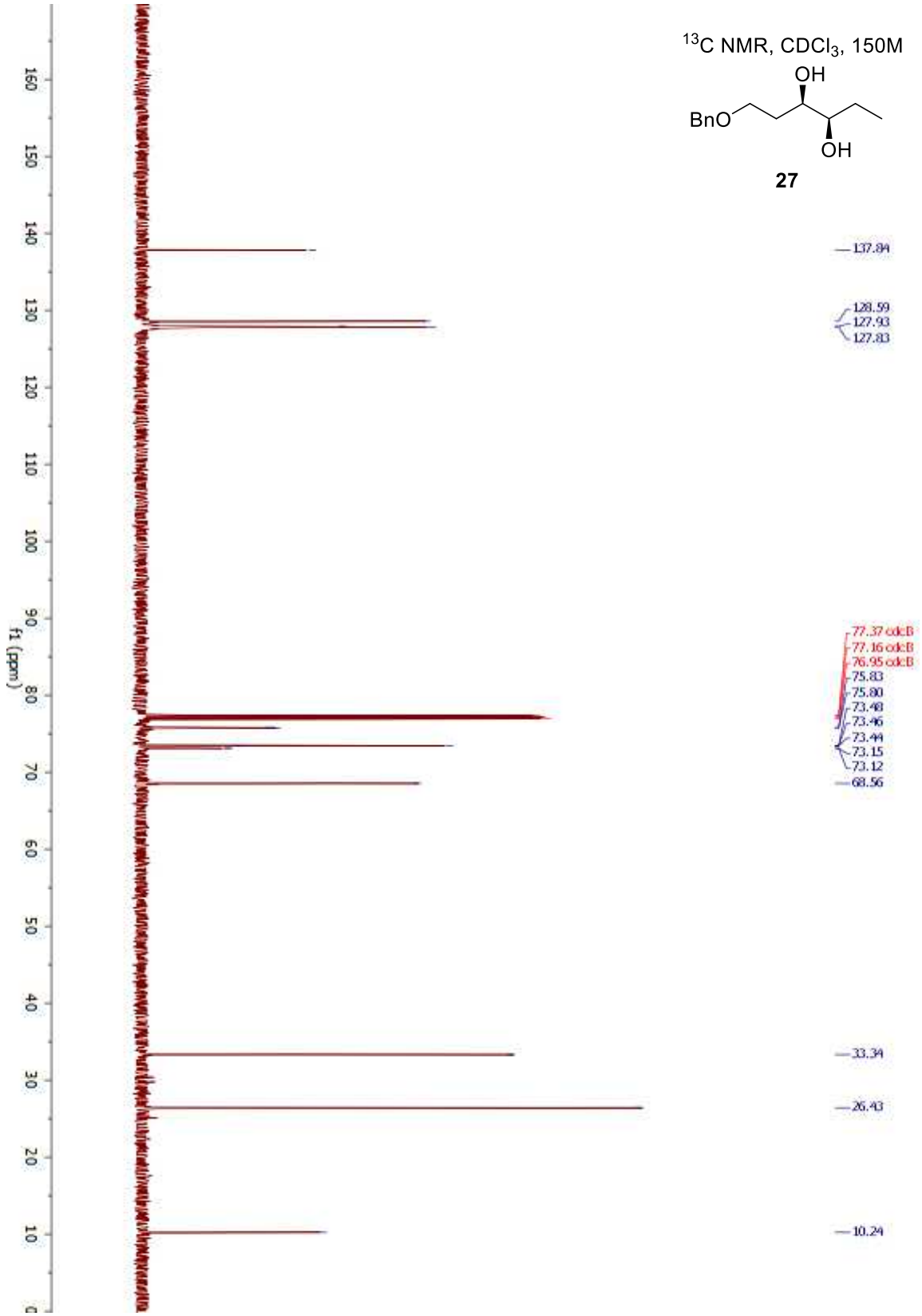
25

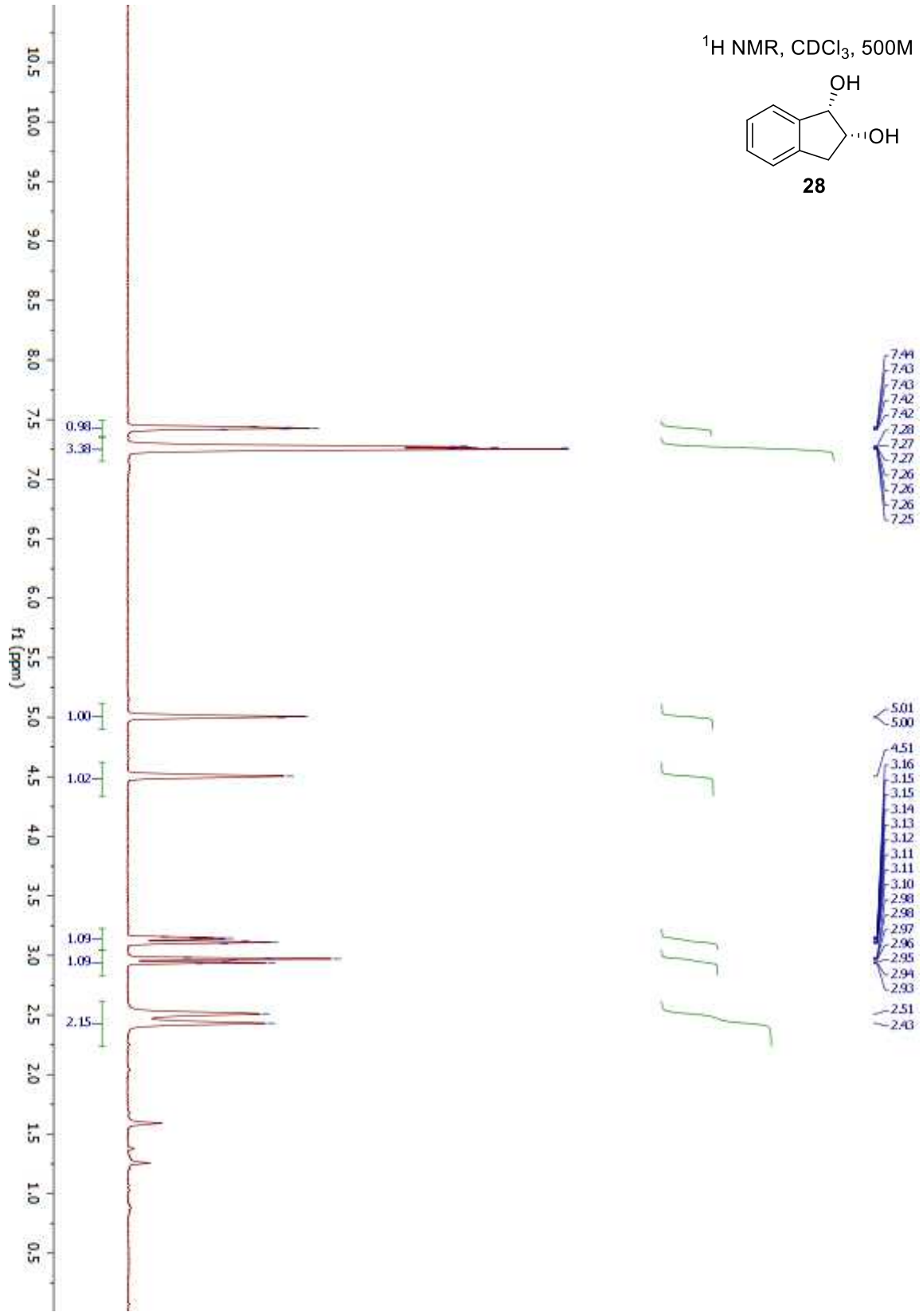

^{13}C NMR, $CDCl_3$, 126M
OH
BnO
OTBS
OH
25
138.20
128.53
127.79
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
73.72
73.38
72.91
68.33
61.83
35.30
33.26
25.98
18.27
-5.37
-5.40
f1 (ppm)


^{1}H NMR, $CDCl_3$, 500M
OH
BzO
OH
26
f1 (ppm)
1.64
0.85
1.75
2.00
1.67
0.77
0.75
2.25
10.99
2.89


13C NMR, CDCl3, 126M
OH
BzO
OH
26
166.87
133.00
130.50
129.67
128.46
77.41 cdcl3
77.16 cdcl3
76.91 cdcl3
74.62
74.39
65.01
64.99
33.45
33.32
28.91
27.95
22.84
22.38
14.15
f1 (ppm)


^{1}H NMR, $CDCl_3$, 400M
OH
BnO
OH
27
f1 (ppm)
4.25
2.00
2.92
0.91
0.78
0.80
2.02
2.03
2.97


^{13}C NMR, $CDCl_3$, 150M
OH
BnO
OH
27
137.84
128.59
127.93
127.83
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
75.83
75.80
73.48
73.46
73.44
73.15
73.12
68.56
33.34
26.43
10.24
f1 (ppm)


^{1}H NMR, $CDCl_3$, 500M
OH
OH
28
f1 (ppm)
0.98
3.38
1.00
1.02
1.09
1.09
2.15
7.44
7.43
7.43
7.42
7.42
7.28
7.27
7.27
7.26
7.26
7.26
7.25
5.01
5.00
4.51
3.16
3.15
3.15
3.14
3.13
3.12
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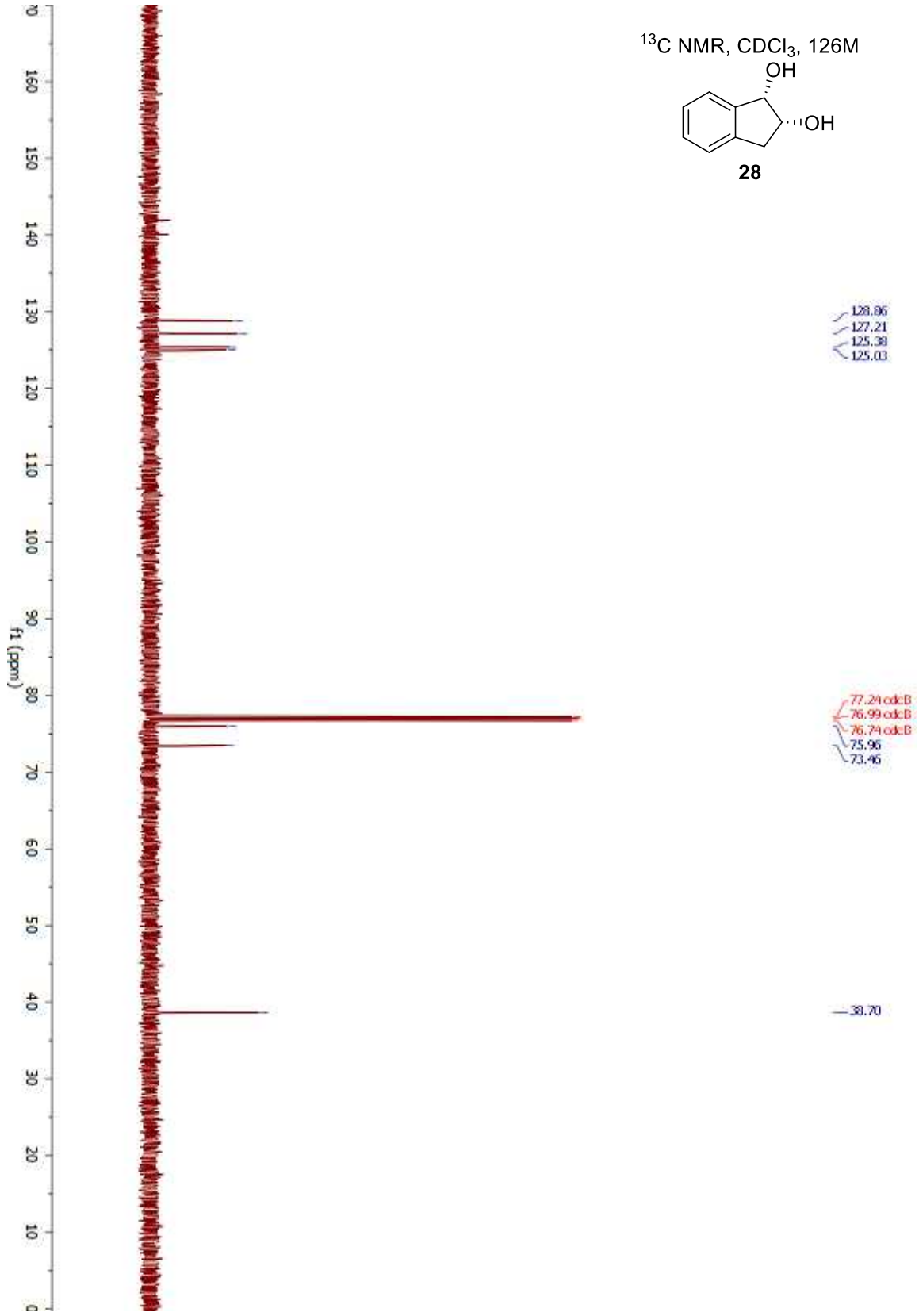
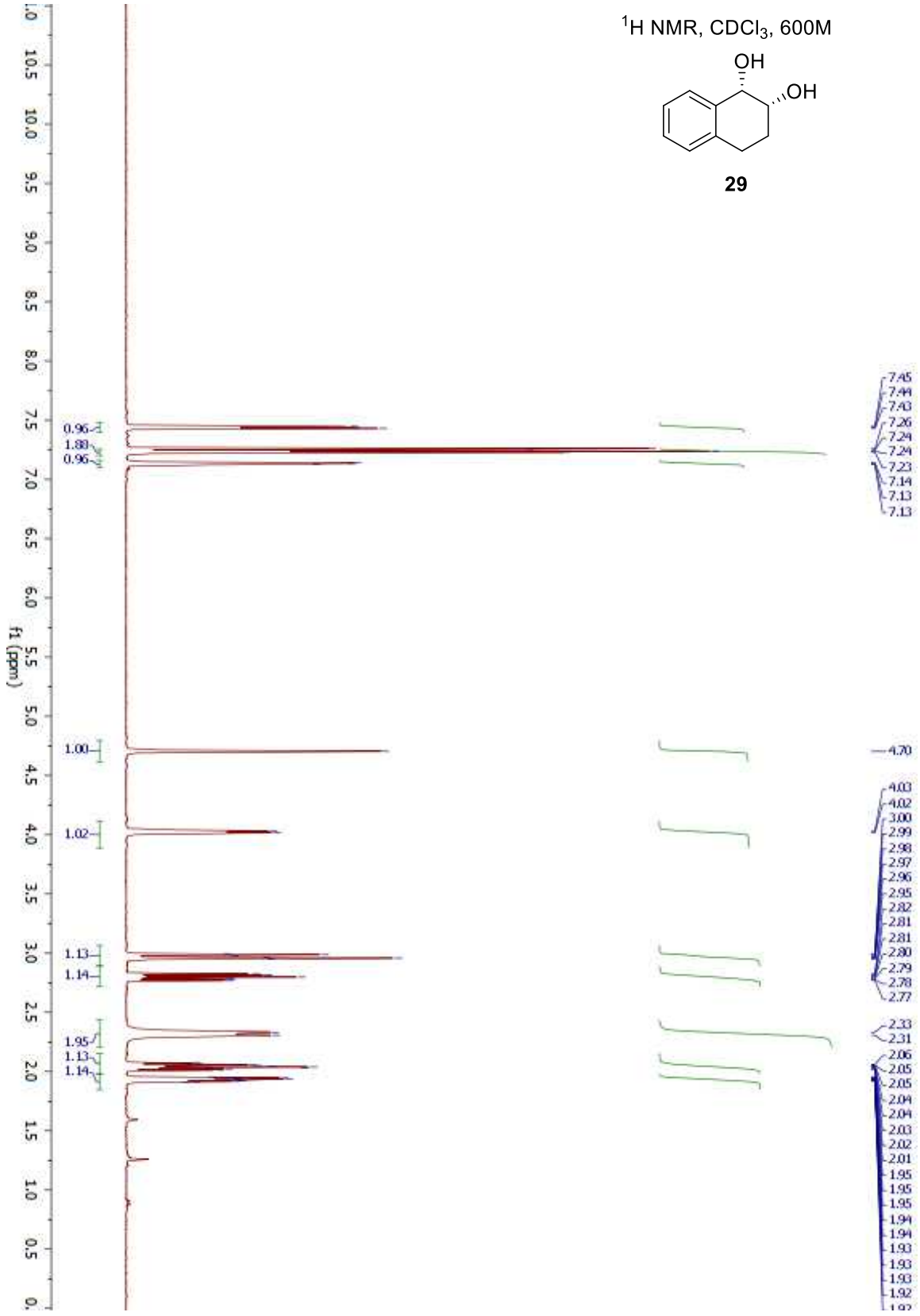
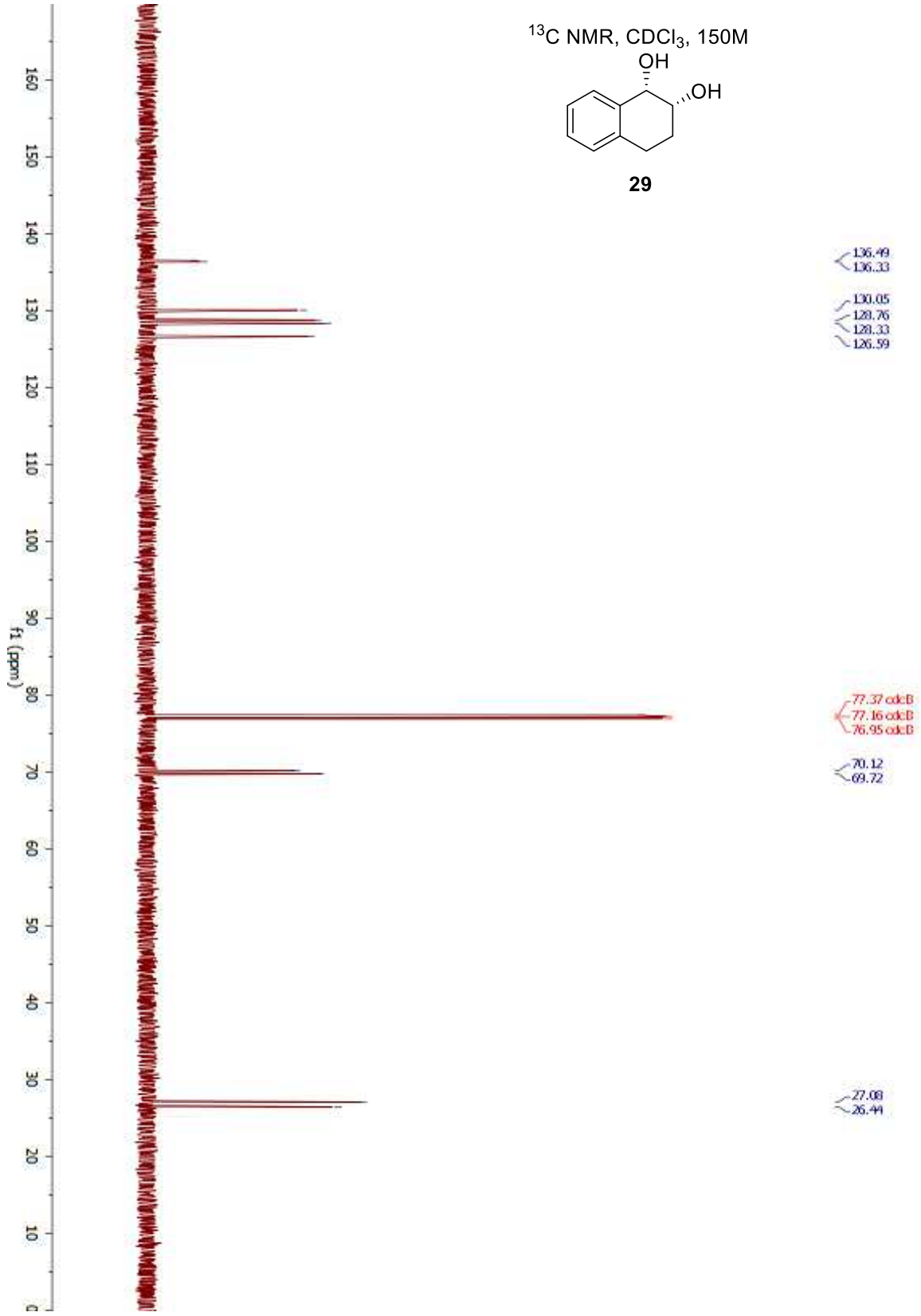
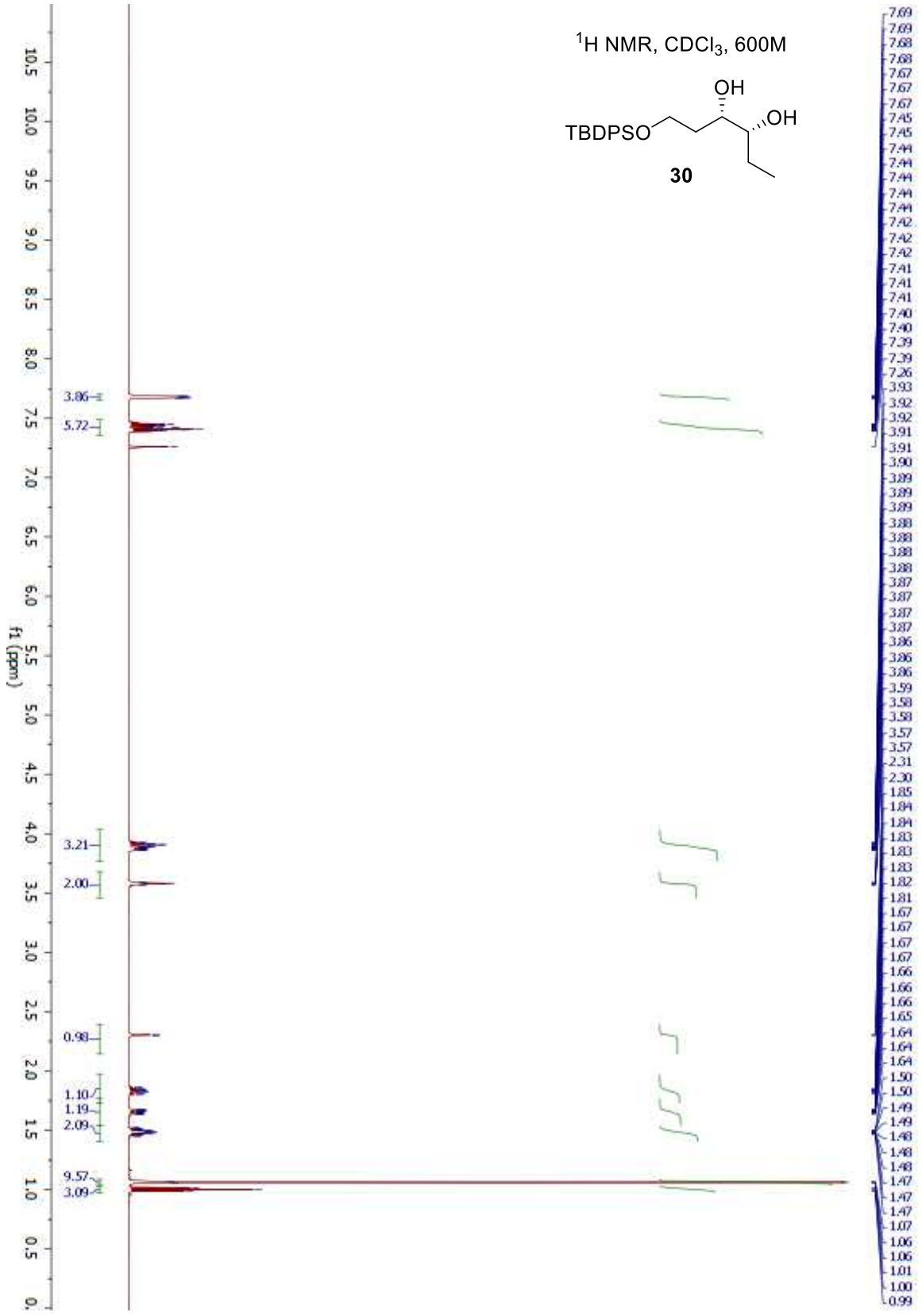
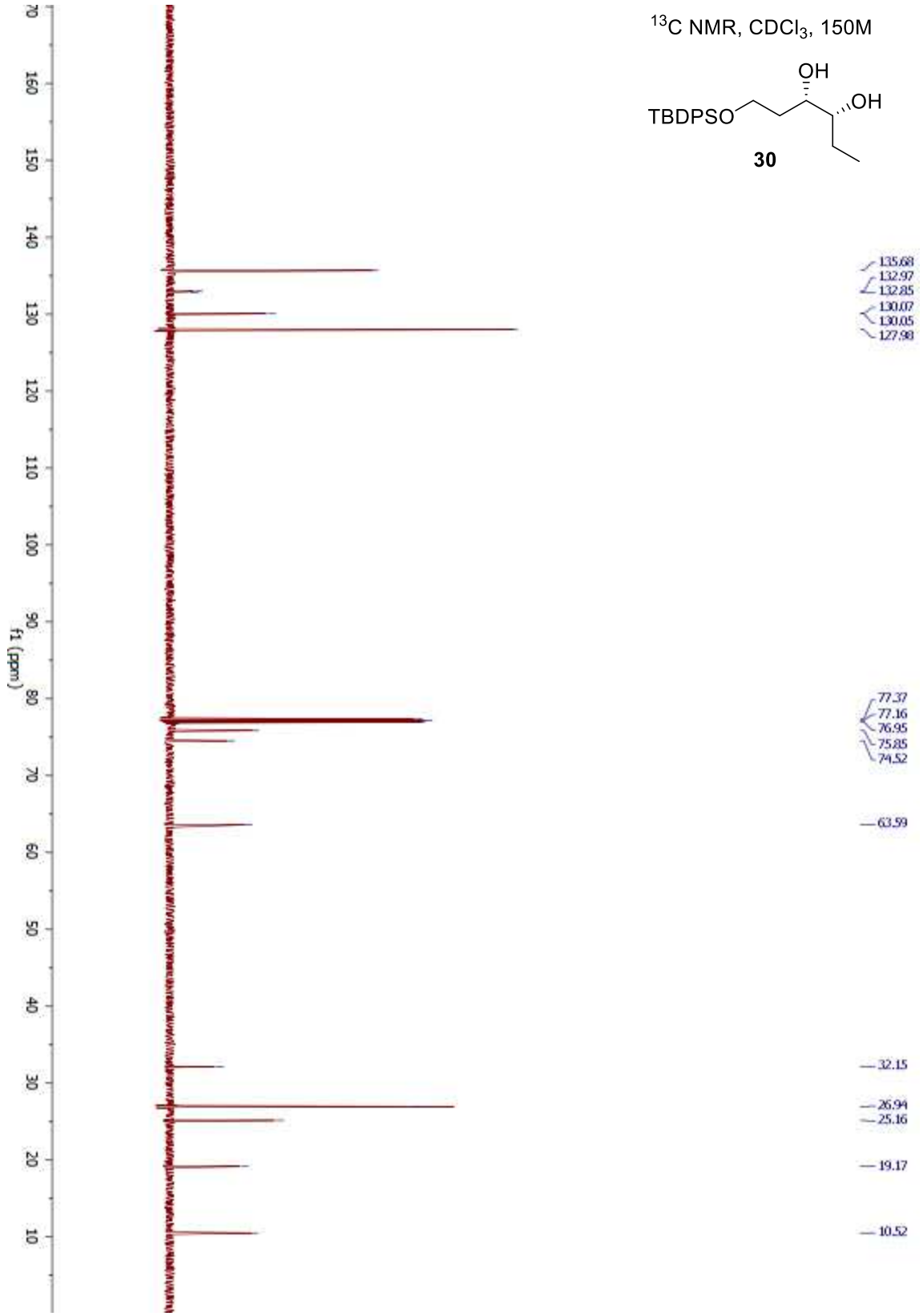
2.96
2.95
2.94
2.93
2.51
2.43


^{13}C NMR, $CDCl_3$, 126M
OH
OH
28
128.86
127.21
125.38
125.03
77.24 cdcl3
76.99 cdcl3
76.74 cdcl3
75.96
73.46
38.70
f1 (ppm)


^{1}H NMR, $CDCl_3$, 600M
OH
OH
29
f1 (ppm)
0.96
1.88
0.96
1.00
1.02
1.13
1.14
1.95
1.13
1.14
7.45
7.44
7.43
7.26
7.24
7.24
7.23
7.14
7.13
7.13
4.70
4.03
4.02
3.00
2.99
2.98
2.97
2.96
2.95
2.82
2.81
2.81
2.80
2.79
2.78
2.77
2.33
2.31
2.06
2.05
2.05
2.04
2.04
2.03
2.02
2.01
1.95
1.95
1.95
1.94
1.94
1.93
1.93
1.93
1.92

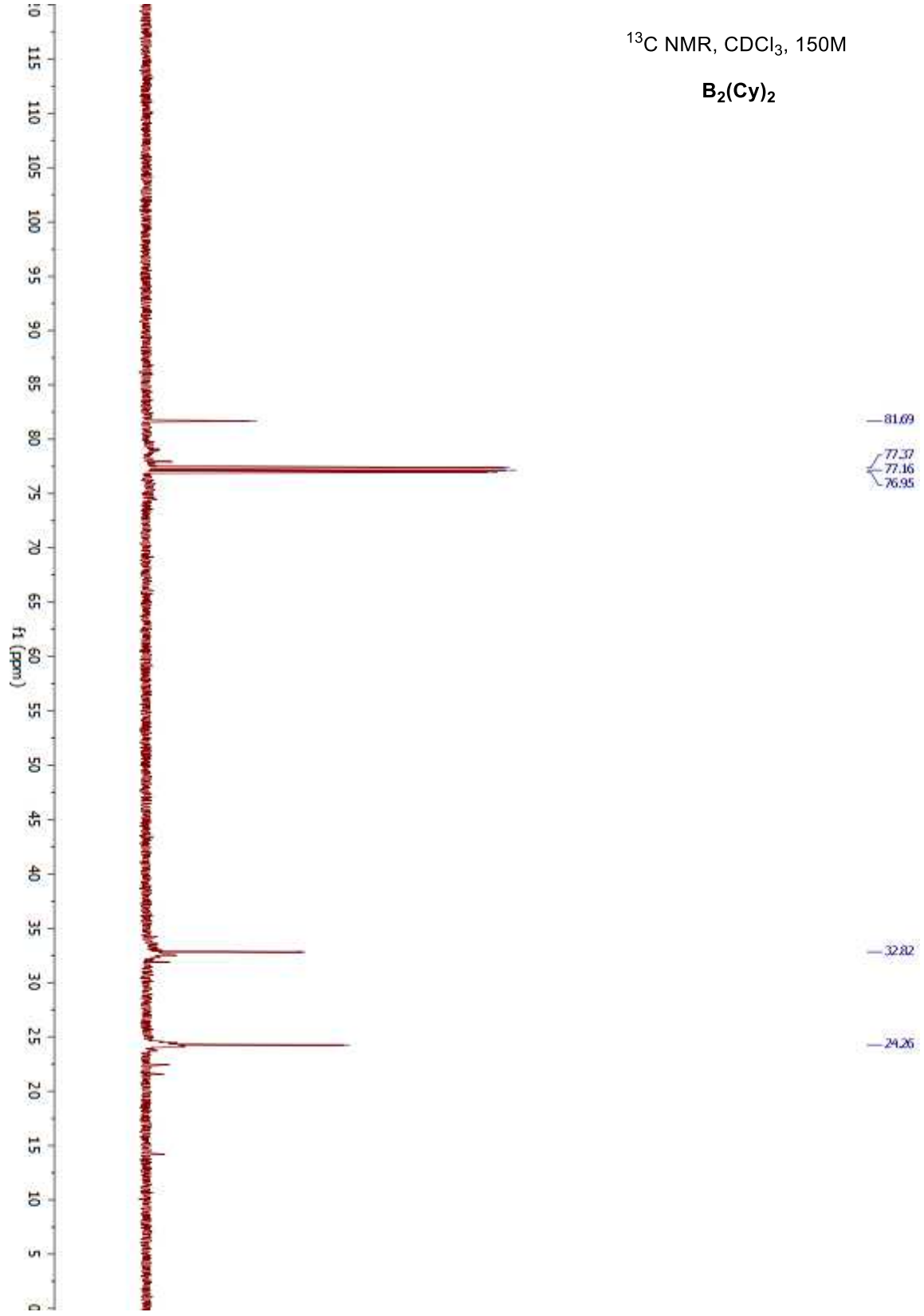

^{13}C NMR, $CDCl_3$, 150M
OH
OH
29
136.49
136.33
130.05
128.76
128.33
126.59
77.37 cdcl3
77.16 cdcl3
76.95 cdcl3
70.12
69.72
27.08
26.49
f1 (ppm)


^{1}H NMR, $CDCl_3$, 600M
OH
OH
TBDPSO
30
f1 (ppm)
3.86
5.72
3.21
2.00
0.98
1.10
1.19
2.09
9.57
3.09


^{13}C NMR, $CDCl_3$, 150M
OH
OH
TBDPSO
30
135.68
132.97
132.85
130.07
130.05
127.98
77.37
77.16
76.95
75.85
74.52
63.59
32.15
26.94
25.16
19.17
10.52
f1 (ppm)

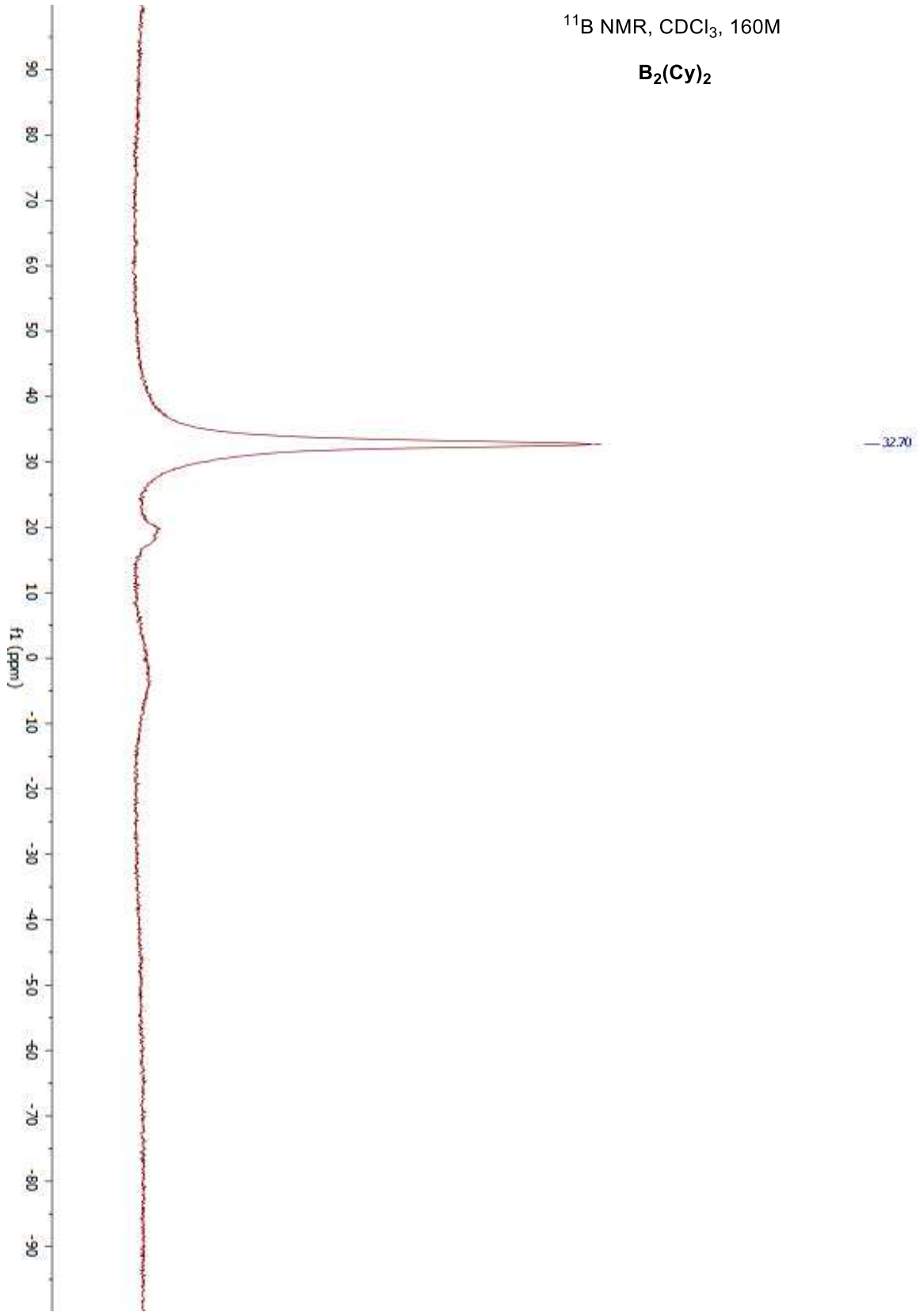
^{13}C NMR, $CDCl_3$, 150M

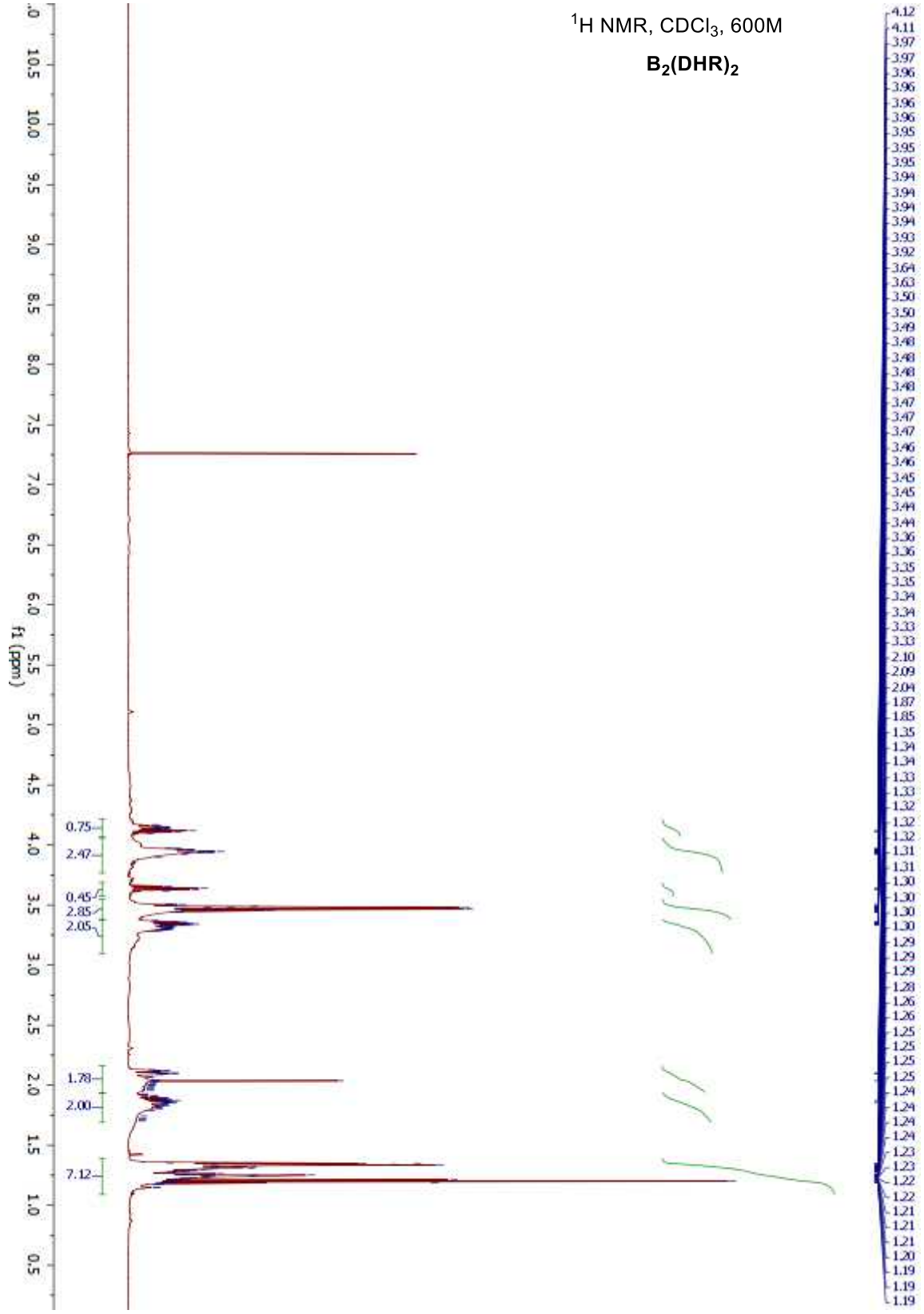
$B_2(Cy)_2$

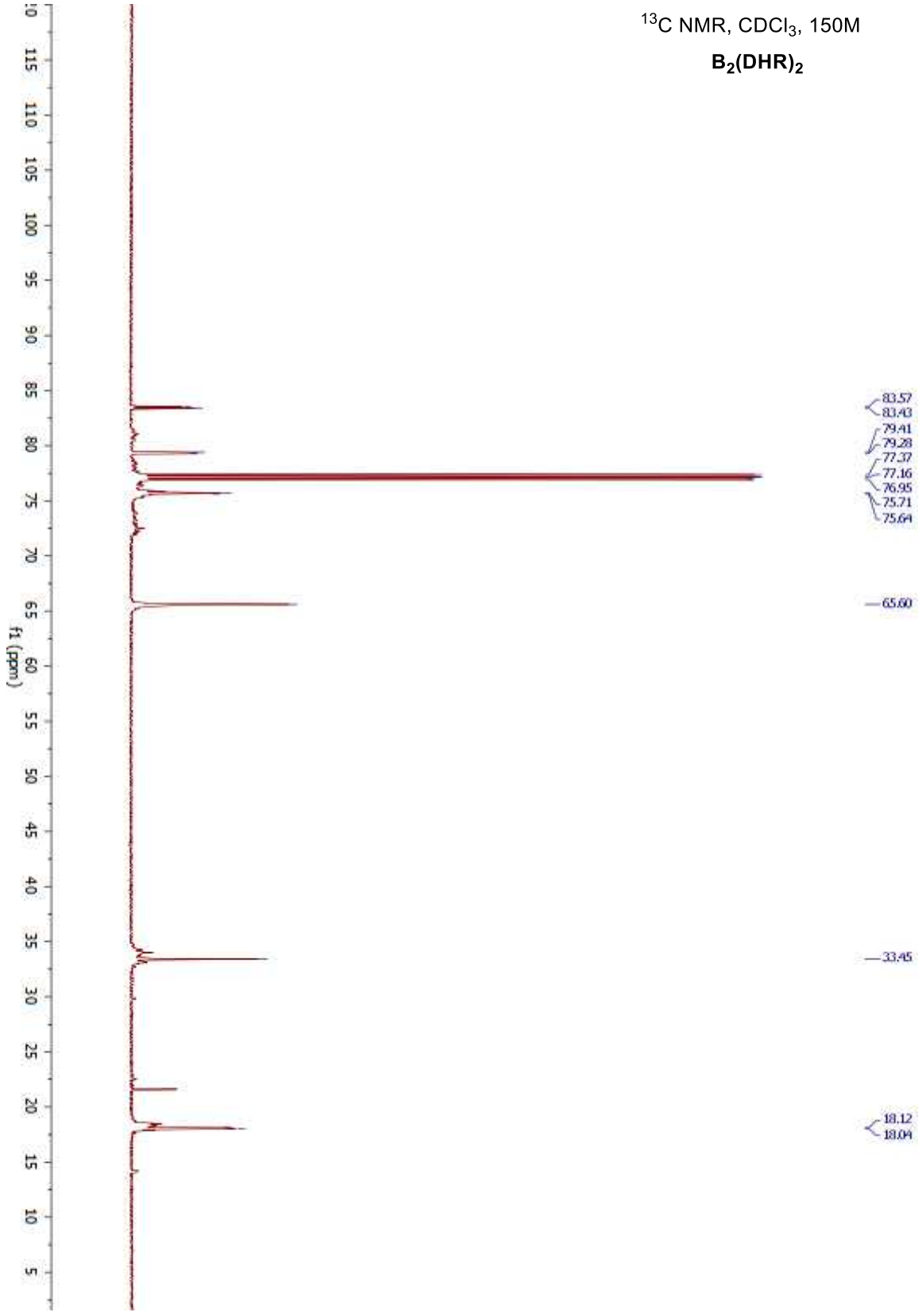


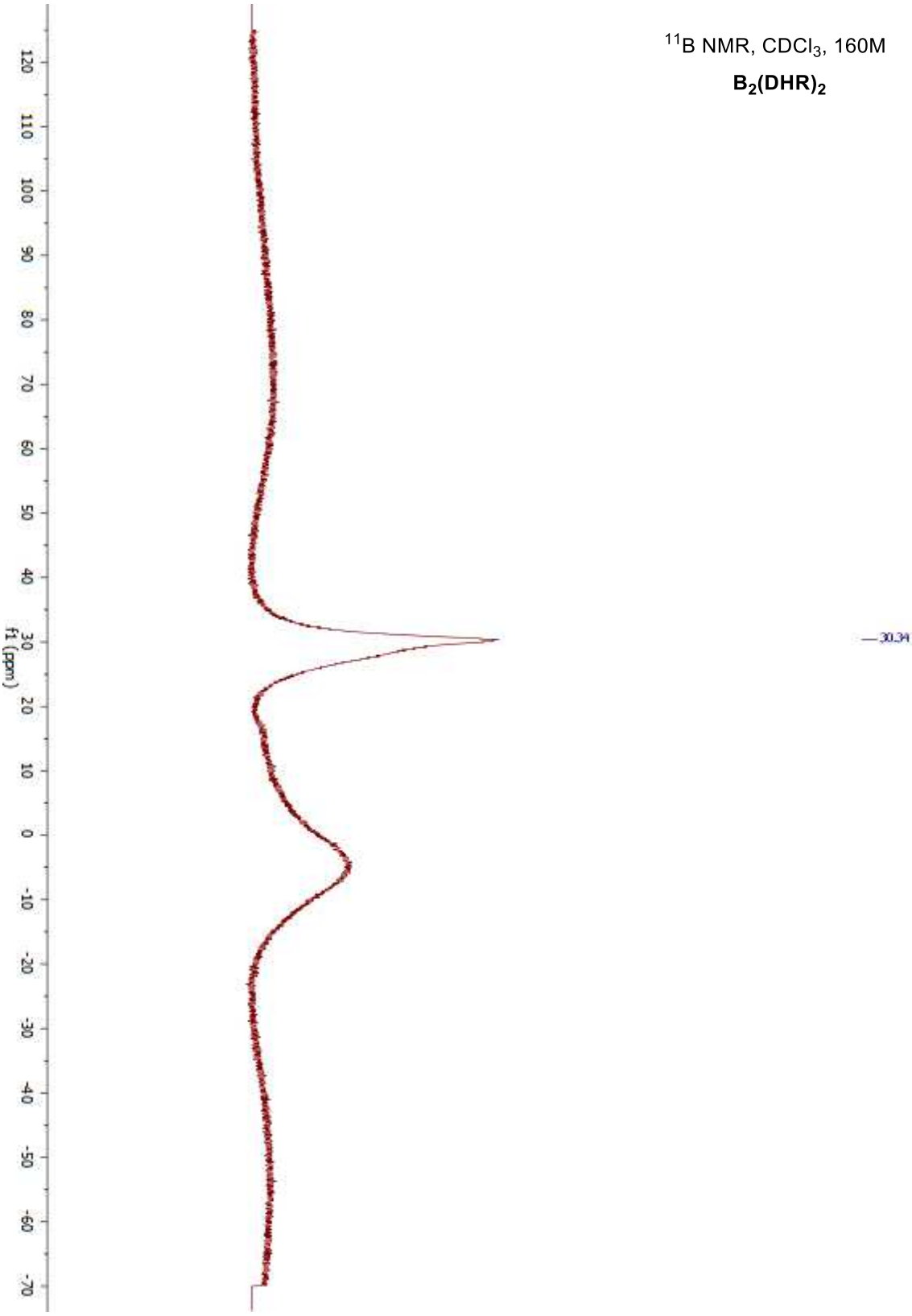
^{11}B NMR, $CDCl_3$, 160M

$B_2(Cy)_2$



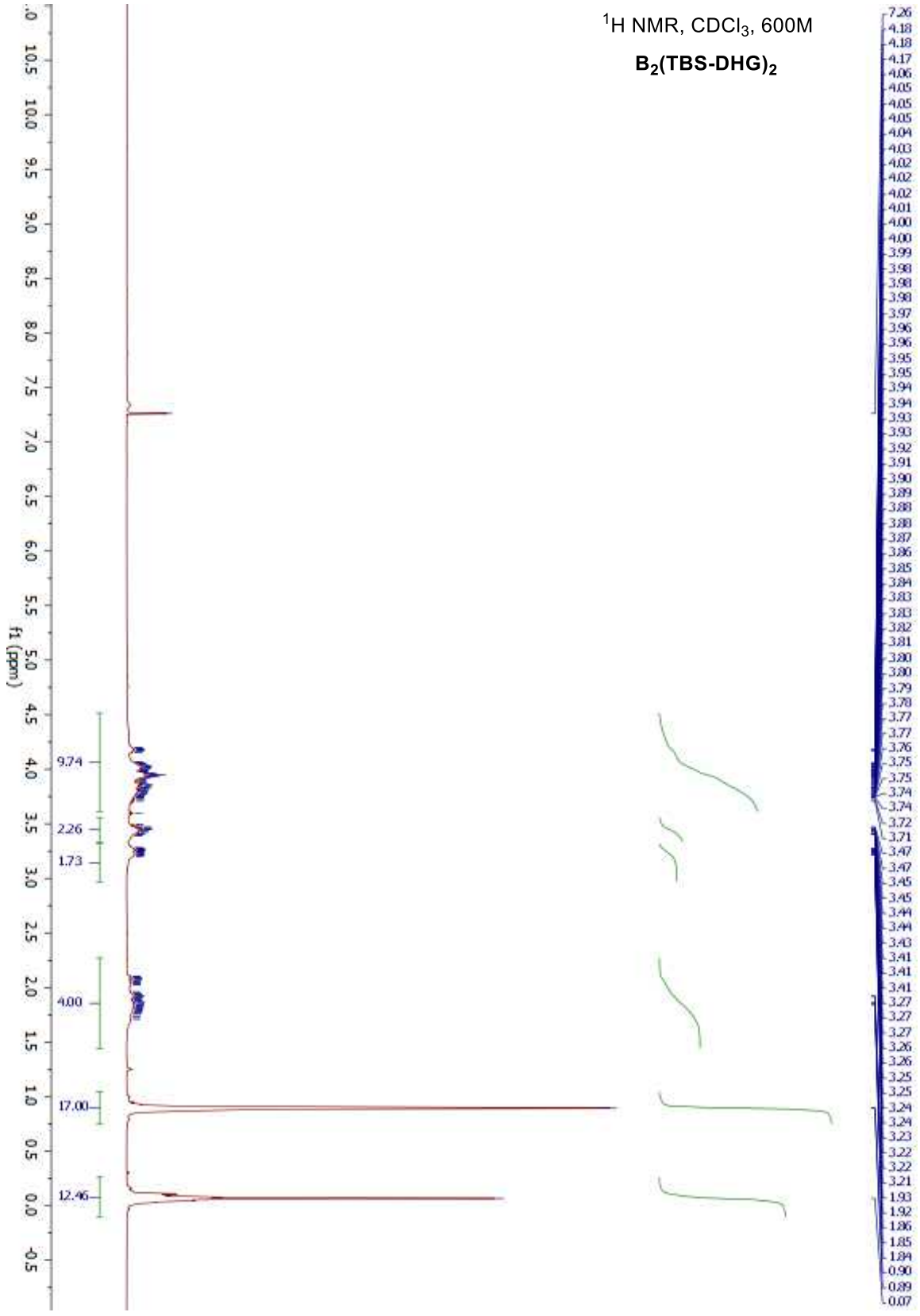

^{1}H NMR, $CDCl_3$, 600M
$B_2(DHR)_2$
f1 (ppm)
0.75
2.47
0.45
2.85
2.05
1.78
2.00
7.12

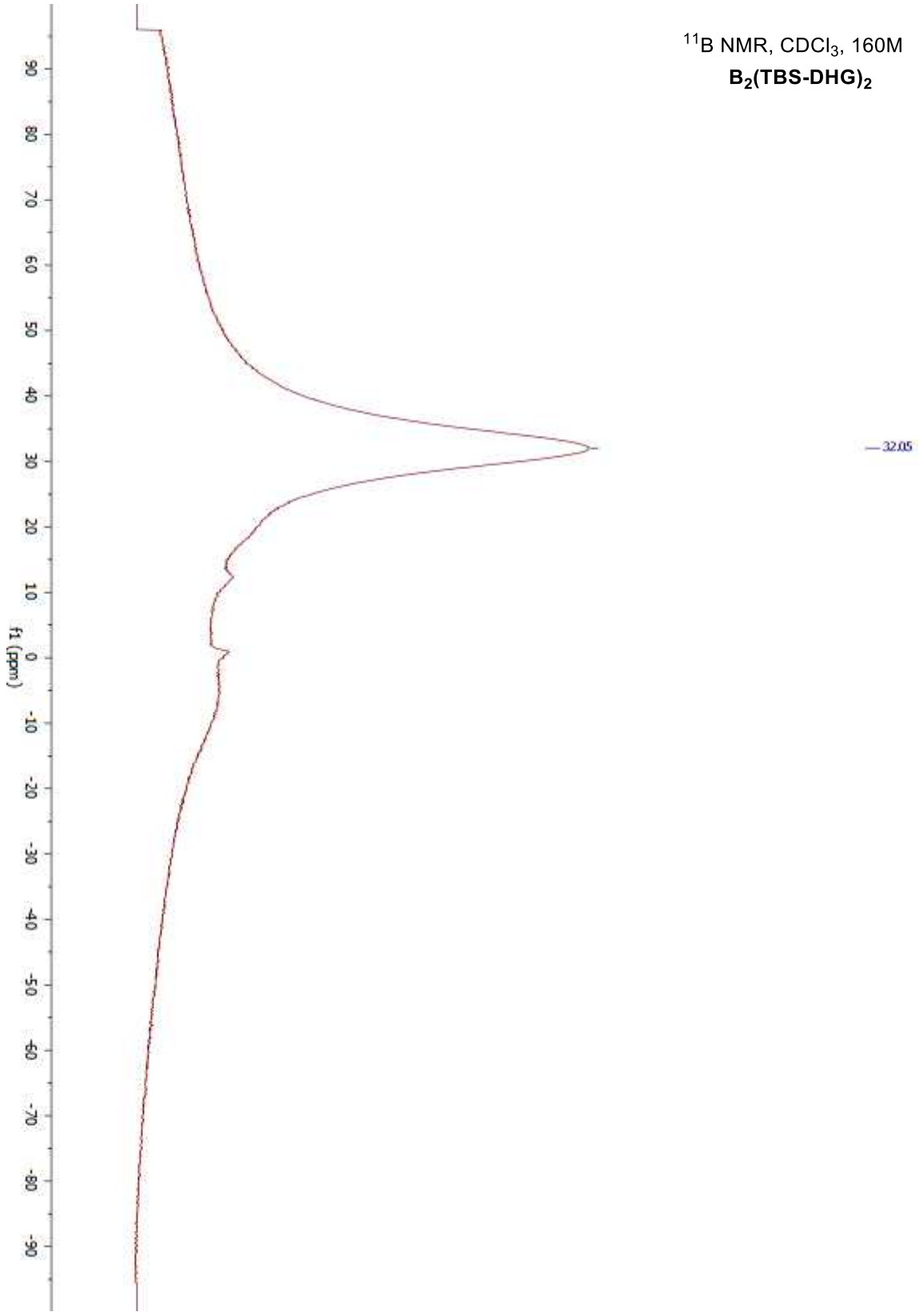

^{13}C NMR, $CDCl_3$, 150M
$B_2(DHR)_2$
83.57
83.43
79.41
79.28
77.37
77.16
76.95
75.71
75.64
65.60
33.45
18.12
18.04
f1 (ppm)



^{11}B NMR, $CDCl_3$, 160M

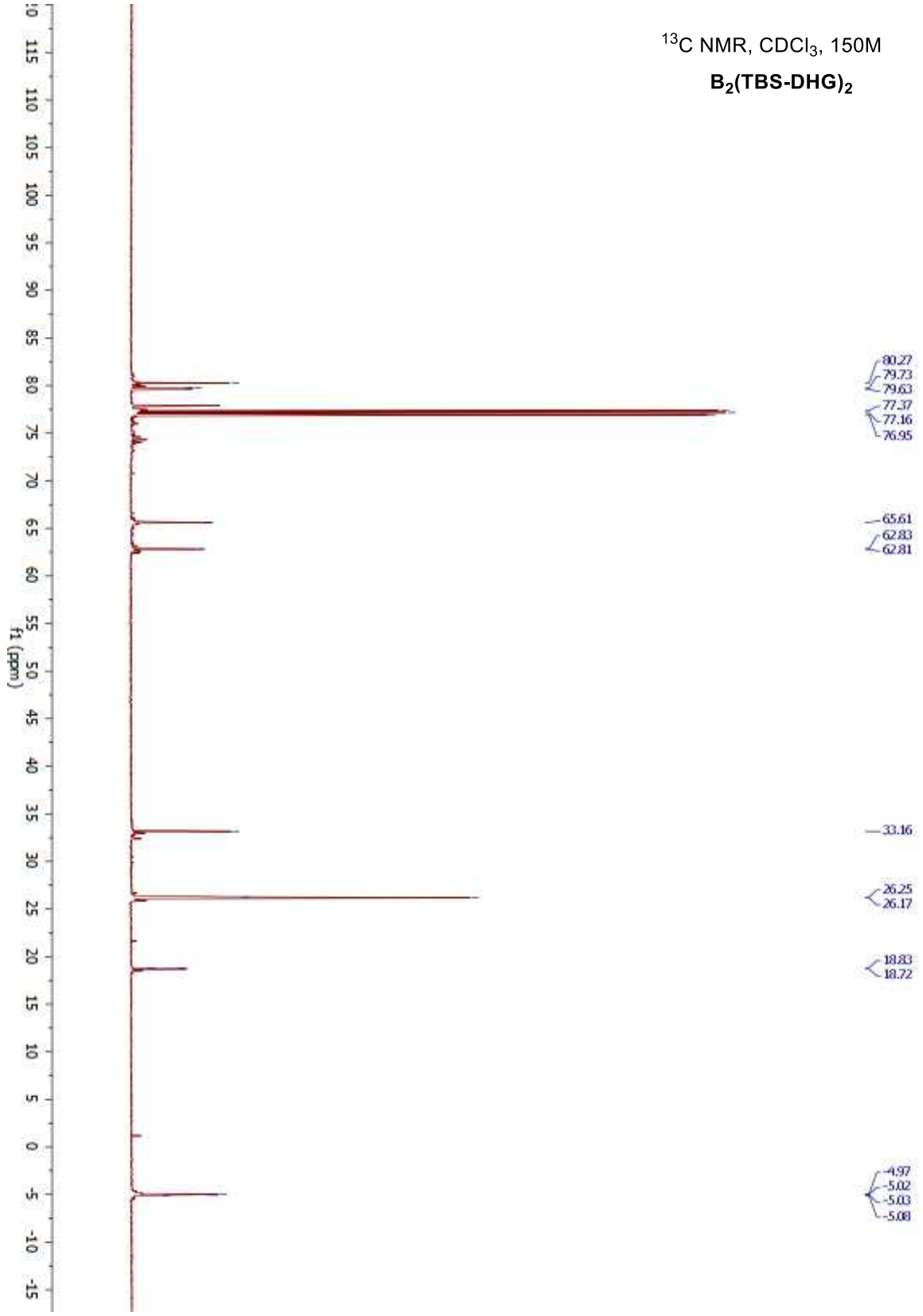
$B_2(DHR)_2$


^{1}H NMR, $CDCl_3$, 600M
B_2(TBS-DHG)$_2$
f1 (ppm)
9.74
2.26
1.73
4.00
17.00
12.46



^{11}B NMR, $CDCl_3$, 160M

B_2(TBS-DHG)$_2$


^{13}C NMR, $CDCl_3$, 150M
B_2(TBS-DHG)$_2$
80.27
79.73
79.63
77.37
77.16
76.95
65.61
62.83
62.81
33.16
26.25
26.17
18.83
18.72
-4.97
-5.02
-5.03
-5.08
f1 (ppm)

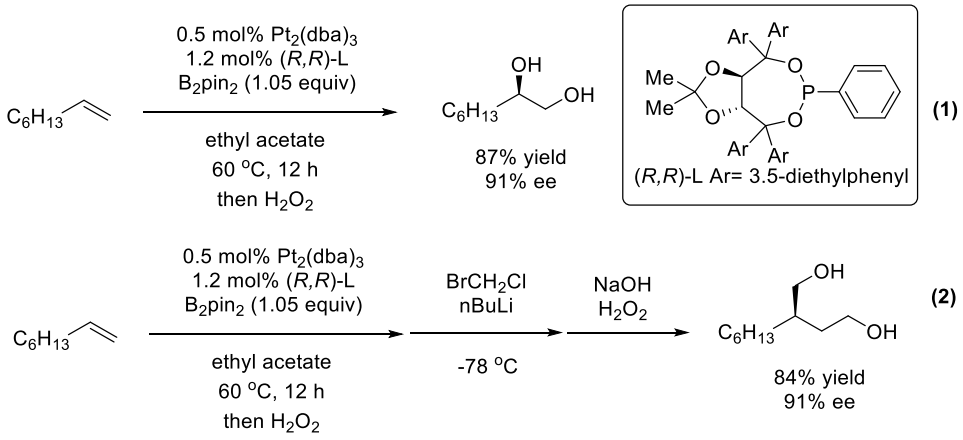
Chapter 3. Site –Selective Mono-Oxidation of 1,2-Bis(boronate)

3.1 Introduction

As stated in the first two chapters, the catalytic enantioselective diboration reaction is a valuable tool for transforming inexpensive and abundant alkenes into chiral products. The Morken group has reported several generations of efficient enantioselective alkene diboration reactions using chiral rhodium[70] and platinum[71] complexes. Most recently, carbohydrate catalyzed[72] enantioselective alkene diboration was introduced. In addition to these reports, the Nishiyama group also developed a Rh(phebox) catalyzed enantioselective alkene diboration process.[73] As shown in Scheme 3.1, the product of terminal alkene diboration, namely 1,2-bis(boronates) readily undergo stereo-retentive oxidation, furnishing enantio-enriched 1,2-diols in nearly quantitative yields (equation 1). Both of the boronic esters can also be homologated at the same time, furnishing enantio-enriched 1,4-diols after oxidation (equation 2).

[70] (a) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702. (b) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538.
[71] (a) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210. (b) Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222
[72] (a) Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508. (b) Yan, L.; Meng, Y.; Haeffner, F.; Leon, R. M.; Crockett, M. P.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 3663.
[73] Toribatake, K.; Nishiyama, H. *Angew. Chem. Int. Ed.* **2013**, *52,* 11011.

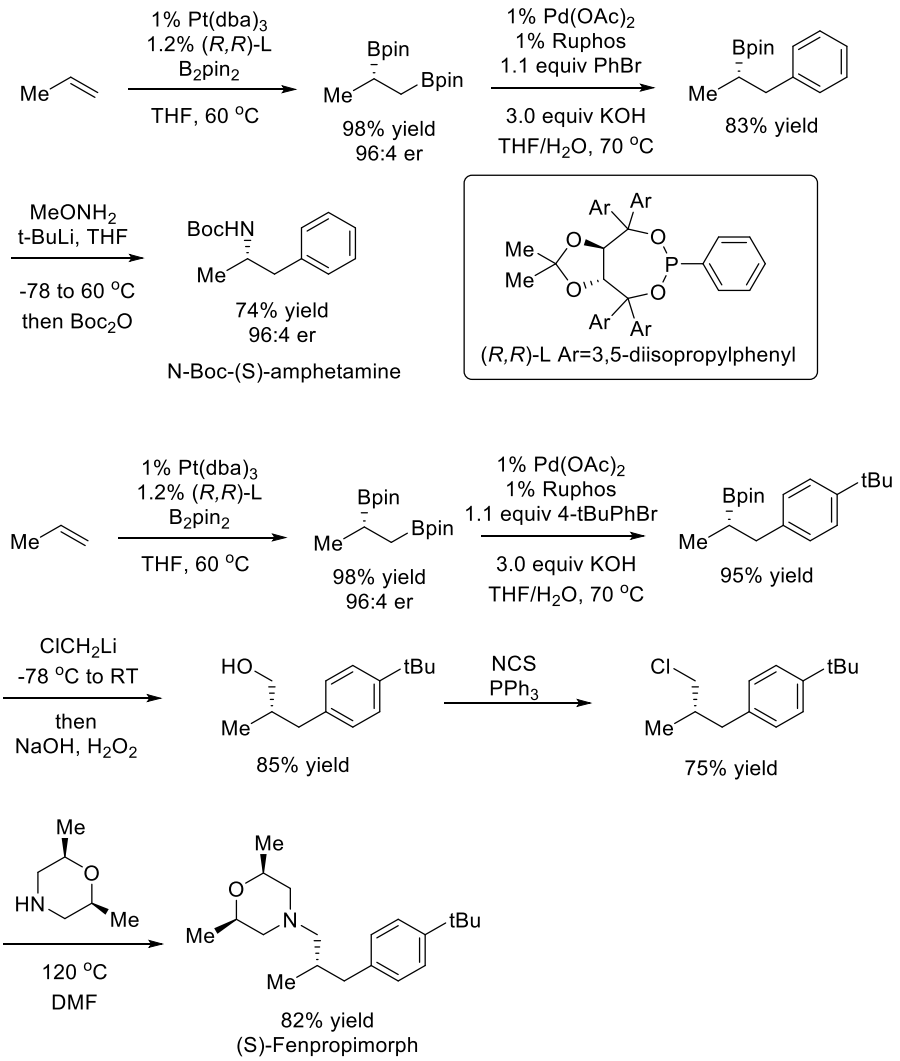
Scheme 3.1 Known transformations of 1,2-bis(boronates)



We envisioned that it would be particularly useful if site-selective monofunctionalization of 1,2-bis(boronates) can be achieved, as the remaining boronic ester can then be functionalized separately, such that the overall process will give rise to a broad array of useful structural motifs. Up untill now, there are only two reported methods concerned with site selective transformations of 1,2-bis(boronates). The first example was introduced by the Morken group in 2014,[74] in which the 1,2-bis(boronates) were reported to undergo site-selective Suzuki-Miyaura cross-coupling at the terminal boronic ester; the untouched secondary boronic ester was then further transformed to other functional groups such as alcohols and amines. This cascade diboration/cross-coupling/ functionalization sequence proved to be a powerful synthetic strategy for complex molecule synthesis, and a few pharmaceutically relevant compounds were made efficiently using this method (Scheme 3.2).

[74] Mlynarski, S. N.; Schuster, C. H. Morken, J. P. *Nature*, **2014**, *505*, 386

Scheme 3.2 Synthetic Application of Cascade Diboration/Cross-coupling/Functionalization

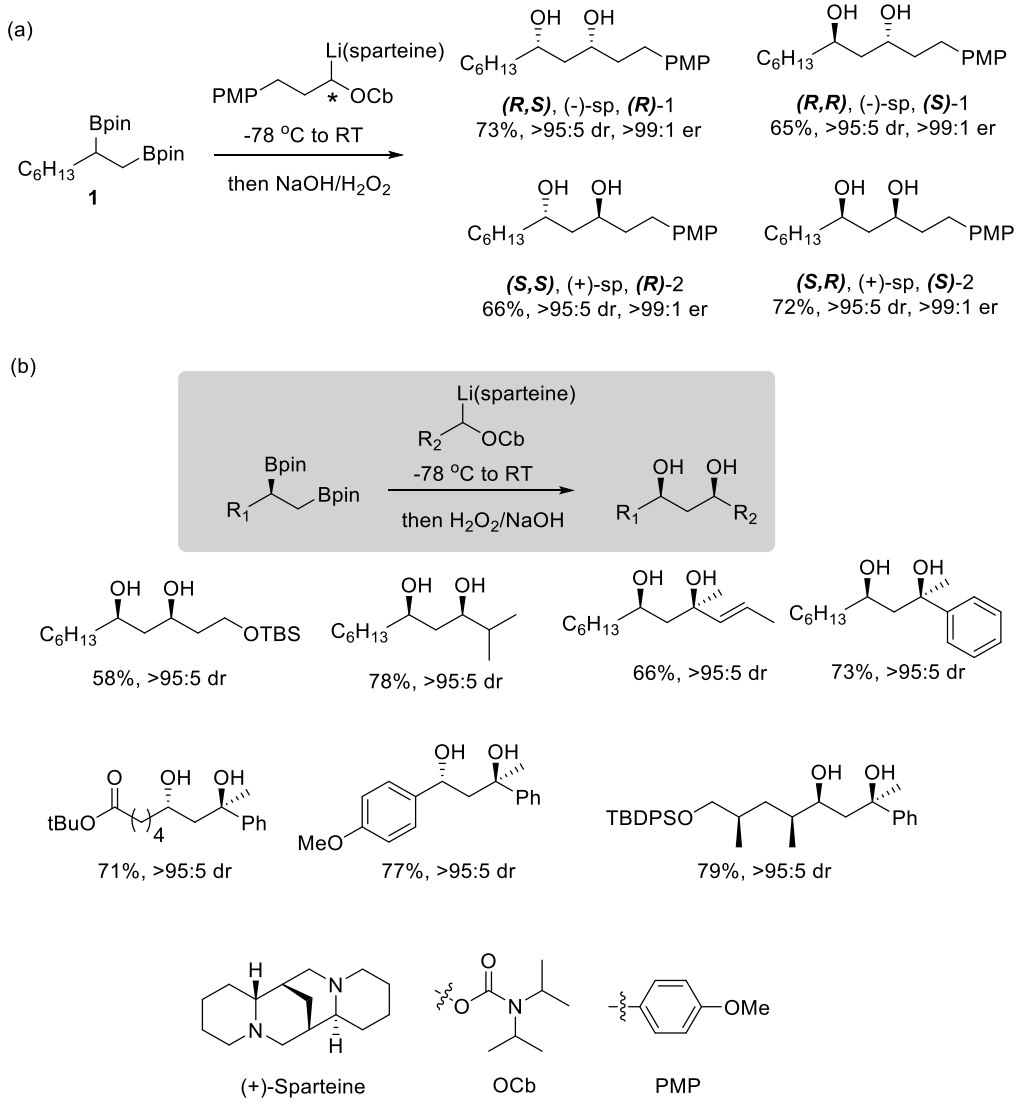


The second example of site-selective functionalization of 1,2-bis(boronates) was reported by Professor Aggarwal and coworkers in 2016. They achieved the regio- and stereoselective homologation of 1,2-bis(boronates) by using sparteine-ligated lithiated carbamates. Stereocontrolled 1,3-diols were efficiently prepared by this method.[75] As depicted in Scheme 3.3a, the lithiated carbamate can selective bind to the less hindered terminal boron of the 1,2-bis(boronates) to form a boron "ate" complex. Subsequent 1,2-

[75] Fawcett, A.; Nitsch, D.; Ali, M.; Bateman, J. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2016**, *55*, 14663.

boron shift afforded the 1,3-diol product in excellent diastereoselectivity after oxidation. Thus, the four diastereomers of the 1,3-diol products could be obtained separately by using different enantiomers of 1,2-bis(boronates) and either (-) or (+) – sparteine. Furthermore, this method has a broad substrate scope, tolerating a variety of different functional groups and pre-existing stereocenters (Scheme 3.3 (b)).

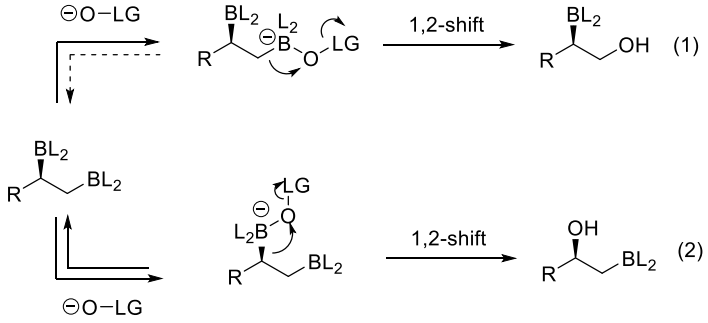
Scheme 3.3 Regio and Stereo-Selective Homologation of 1,2-bis(boronates)



Our strategy for selective functionalization of 1,2-bis(boronates) was to selectively oxidize one of the boronic ester in preference to the other one. As depicted in Scheme 3.4,

we believed that the regioselectivity in 1,2-bis(boronate) oxidation could come from either of the following manifolds. First, if the coordination of the oxidant to boron was sensitive to steric effects and the subsequent 1,2-boron shift was facile, then the sterically less hindered primary boronic ester will be preferentially oxidized (equation 1). Alternatively, if the 1,2-boron shift is the rate-limiting step and the coordination of the oxidant to boron is reversible, then the secondary boronic ester should be preferentially oxidized. This outcome is anticipated because the secondary carbon is more electron rich than the primary carbon, so it migrates faster in the 1,2-boron shift (equation 2).

Scheme 3.4 Proposed Mechanism for Regio-Selective Oxidation of 1,2-Bis(boronates)

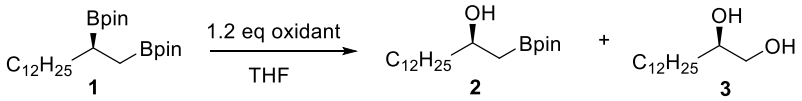


3.2 Reaction Optimization

To gain an understanding of regioselectivity in the the 1,2-bis(boronate) oxidation reaction, compound **1** was treated with 1.2 equivalents of potassium hydride and tert-butyl hydroperoxide. After 1 hour, the reaction was found to proceed to 65% conversion. The product of oxidation of the secondary boronic ester, compound **2,** was formed in 10% yield, together with 52% over-oxidized byproduct **3**. Selective oxidation of the primary boronic ester was not observed (Table 1, entry 1). Other oxidants were also tested in this selective oxidation reaction: m-chloroperbenzoic acid afforded over-oxidized byproduct exclusively (entry 2). Neutral peroxides such as di-tert-butyl peroxide and dibenzoyl

peroxide were unreactive (entry 3 and 4). Although pyridine N-oxide was unreactive towards 1,2-(bisboronate) oxidation (entry 5), the more electron rich trimethylamine N-oxide selectively oxidizes the secondary boronic ester to an alcohol group. In this case, the oxidation proceeded to 65% conversion, and 42% of mono-oxidized product was isolated, together with 23 % over oxidized byproduct (entry 6). Of note, trimethylamine N-oxide was known to be effective in organoborane oxidations before.[76]

Table 1. Survey of Oxidants in Selective Oxidation of 1,2-Bis(boronates)

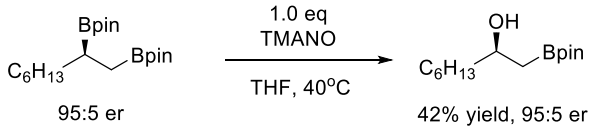


entry	oxidant	conversion[a]	yield of **2**[b]	yield of **3**[b]
1	KH/tBuOOH	65%	10%	52%
2	mCpBA	62%	n.r.	43%
3	Di-tert-butyl peroxide	<5%		
4	Benzoyl peroxide	<5%		
5	Pyridine N-oxide	<5%		
6	Trimethylamine N-oxide	65%	42%	23%

a. Conversion determined by ^{1}H NMR. 1,1,2,2-tetrachloroethane was used as reference
b. Yield determined after purification by silica gel chromatography.

Additionally, as depicted in Scheme 3.5, when an enantio-enriched 1,2-bis(boronate) was subjected to the selective oxidation reaction with trimethylamine N-oxide as oxidant, the product was formed with >95% enantiospecificity.

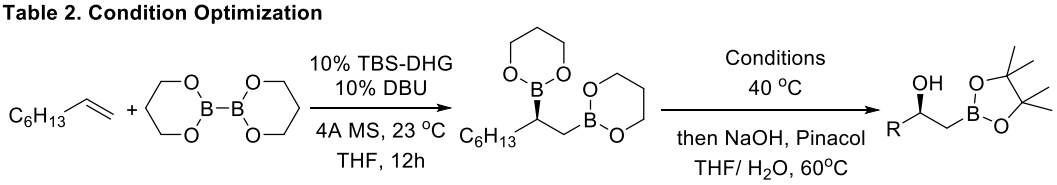
Scheme 3.5 Mono-oxidation of enantio-enriched 1,2-bisboronates



[76] Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51,* 1330.

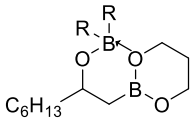
After observing regioselectivity in the initial experiment, we decided to develop a cascade diboration/mono-oxidation reaction sequence that employs easily accessed alkenes as starting materials. For the cascade diboration/mono-oxidation reaction, amine N-oxide oxidants were directly introduced to reaction mixtures obtained from carbohydrate-catalyzed diboration, and the crude mixture after the mono-oxidation step was further treated with pinacol to afford the chromatographically-stable pinacolato boronate products. Optimization data of the diboration/mono-oxidation cascade is shown in Table 2. To improve the conversion of the mono-oxidation reaction, additional trimethylamine N-oxide was added (1.5 equivalents). However, although the extent of the reaction did increase from 65% (Table 1, entry 6) to 72% (Table 2, entry 1), the isolated yield of mono-oxidation product remained the same, suggesting that increasing amounts of over-oxidation resulted. Other solvents such as DMF, chloroform and toluene all gave similar results (Table 2, entries 2, 3, 5). These results suggested that the mono-oxidation product is more prone to be oxidized by trimethylamine N-oxide than the 1,2-bis(boronate) starting material. We suspect this might be because of the intramolecular Lewis acid activation shown in Scheme 3.6. Therefore, we proposed that protic solvents that can interrupt the internal chelation could possibly prohibit the problematic over-oxidation. Indeed, when 1-butanol was used as solvent in the mono-oxidation reaction, the isolated yield became much more reflective of the reaction conversion (entry 5). Other amine N-oxides and reaction conditions were then examined with 1-butanol as reaction solvent (entries 6-9). Based on the optimization, the best reaction conditions were considered to be using 2.0 equivalents of N-methylmorpholine N-oxide (NMO) and 1-butanol as solvent. With these conditions, the product was formed in 70% isolated yield.

Table 2. Condition Optimization



entry	oxidant	equivalents	slovent	conversion	yield
1	trimethylamine N-oxide	1.5	THF	72%	41%
2	trimethylamine N-oxide	1.5	DMF	80%	36%
3	trimethylamine N-oxide	1.5	chloroform	68%	40%
4	trimethylamine N-oxide	1.5	toluene	67%	32%
5	trimethylamine N-oxide	1.5	1-butanol	65%	44%
6	tributylamine N-Oxide	1.5	1-butanol	49%	42%
7	tributylamine N-Oxide	2.0	1-butanol	82%	64%
8	N-methyl morphline N-oxide	1.5	1-butanol	54%	46%
9	N-methyl morphline N-oxide	2.0	1-butanol	92%	70%

Scheme 3.6 Proposed Model for Intramolecular Lewis Acid Activation

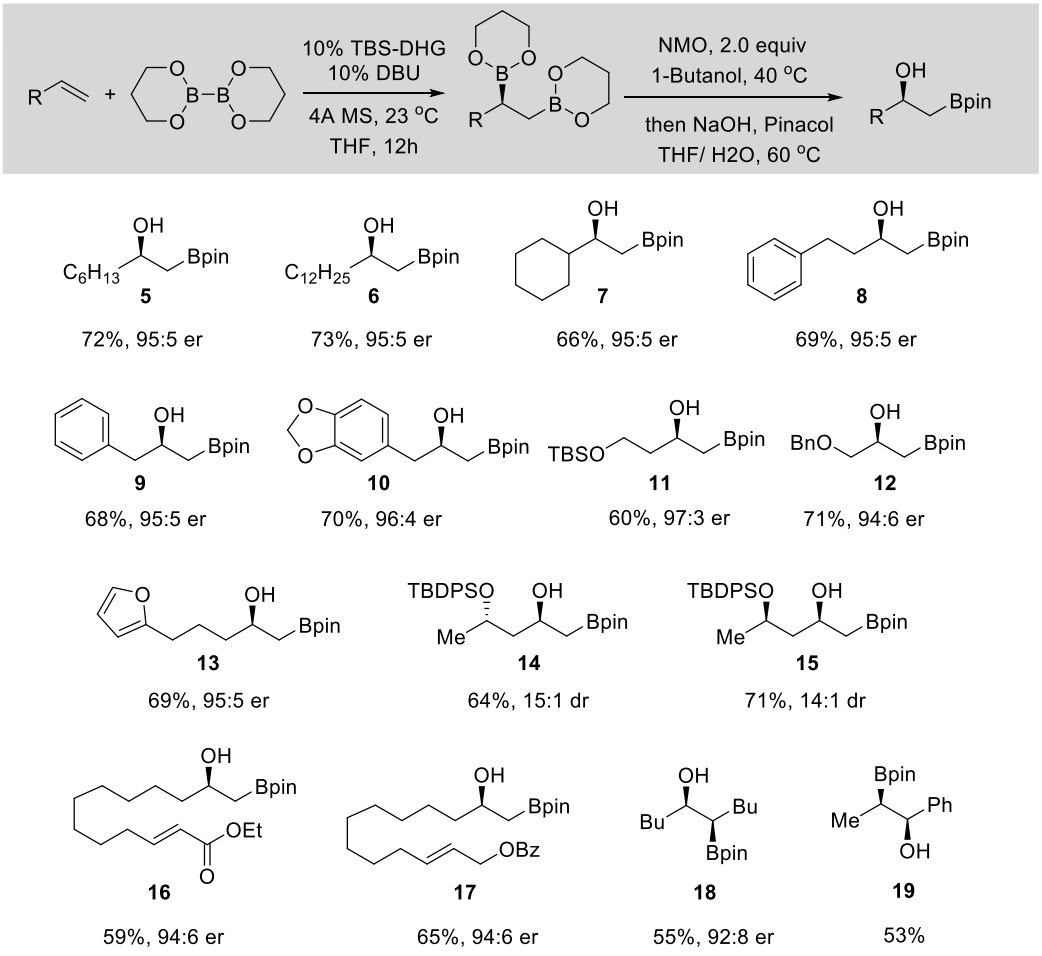


3.3 Substrate Scope

With the optimized reaction conditions in hand, various types of alkenes were examined in the tandem carbohydrate-catalyzed enantioselective diboration/mono-oxidation reaction sequence. As shown in Scheme 3.7, aliphatic alkenes underwent the cascade reaction smoothly. Products **5-8** were formed in good yields and high enantioselectvities. Allyl benzene and its derivatives also worked efficiently in the cascade reaction (compounds **9** and **10**). Functional groups such as protected alcohols and furan were well tolerated in the reaction (compounds **11**, **12**, **13**). With respect to synthetic utility, alkenes bearing adjacent stereogenic centers were tested. They performed well in the cascade diboration/mono-oxidation reaction sequence. Products **14** and **15** were formed in good yields and good diastereoselectivities, with the

stereochemistry completely controlled by the catalyst. As shown with compounds **16** and **17**, terminal alkenes can selectively undergo carbohydrate catalyzed diboration reaction in presense of internal alkenes. Subsequent mono-oxidation afforded products in good yield and enantioselectivity. Additionally, internal alkenes also underwent the cascade diboration/mono-oxidation smoothly. The symmetrical alkene substrate 5-*trans*-decene afforded the mono-oxidized product **18** in acceptable yield. When asymmetric alkene substrate such as *trans* β-methyl styrene was subjected to the mono-oxidation reaction, the benzylic carbon migrates in preference to a secondary alkyl group (compound **19**).

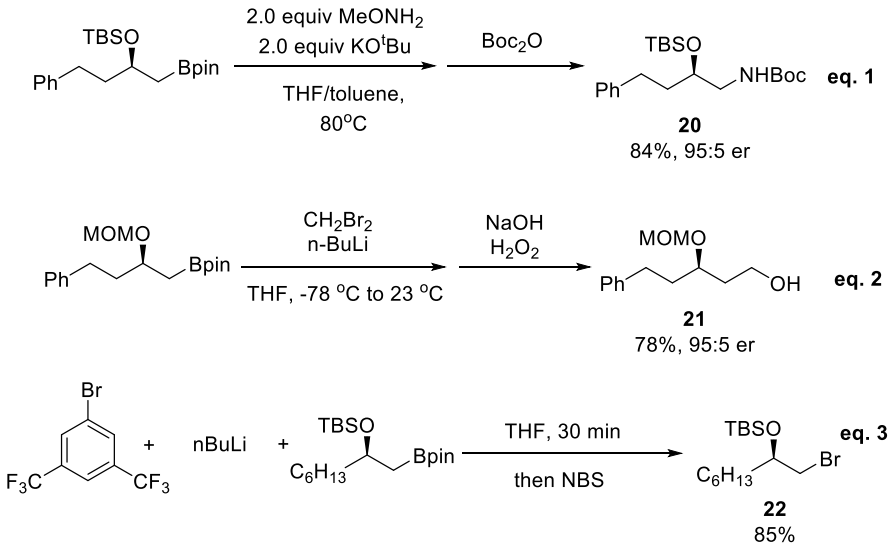
Scheme 3.7 Substrate Scope



3.4 Product Transformations

In order to demonstrate the synthetic utility of the diboration/mono-oxidation cascade reaction, the cascade reaction product was protected with either a silyl ether or a methoxymethyl ether. The primary boronic ester was then subjected to various chemical transformations. As depicted in Scheme 3.8, the primary boronic ester can be transformed to a Boc-protected amine by employing the method developed from the Morken group[77] (equation 1). Of note, this transformation could be useful in the synthesis of 1,2-amino alcohols. Additionally, the boronic ester can undergo homologation when treated with $ClCH_2Li$ under reaction conditions developed by Professor Matteson and coworkers (equation 2).[78] Lastly, the primary boronic ester was successfully transformed to the bromide by employing the method developed in Aggarwal Lab.[79] (equation 3)

Scheme 3.8. Product Functionalization



[77] (a) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449. (b) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett.* **2018.** *29*. 1749.
[78] Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 74
[79] Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133*, 16794.

3.5 Conclusion

In conclusion, we have developed a regioselective mono-oxidation of 1,2-bis(boronate) which are easily accessed from carbohydrate catalyzed enantioselective diboration of terminal alkenes. The β-hydroxy boronic ester obtained from cascade alkene diboration/mono-oxidation can be transformed into chiral materials bearing other functional groups.

3.6 Experimental Section

3.6.1 General Information

^{1}H NMR spectra were recorded on Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz) or Varian Gemini 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: integration, chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz) or a Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl3: 77.23 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (160 MHz). Chemical shifts are reported in ppm with an external standard ($BF_3 \cdot Et_2O$: 0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm-1) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass

Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol, or potassium permanganate.

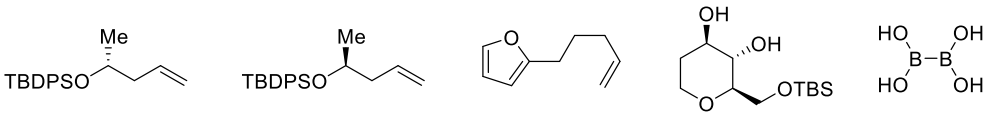
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier. Analytical chiral gas-liquid chromatography (GLC) was performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β -Dex 120 column with helium as the carrier gas.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et2O), dichloromethane (CH_2Cl_2) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Tetrahydroxydiboron was purchased from Frontier Scientific. It was recrystallized by water before use. D-glucal triacetate was purchased from Alfa Aesar. Activated 4Å Molecular Seives was bought from Sigma-Aldrich. 4-Methylmorpholine N-oxide was purchased from Oakwood Chemicals. Anhydrous 1-butanol was purchased from Sigma-Aldrich. All other reagents were purchased either from Aldrich, Alfa Aesar, Acros, Oakwood Chemicals, Combi Blocks, or TCI and were used without further purification.

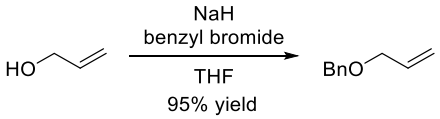
3.6.2 Synthesis of Alkenes, Catalysts and Diborons.

A. Synthesis of some alkenes, diboron, and catalyst.

Compounds shown in the following scheme were prepared according to literature procedures. Spectral data were in accordance with the literature report[80].

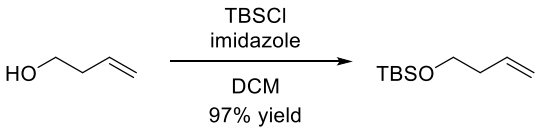


B. Synthesis of ((allyloxy)methyl)benzene



((Allyloxy)methyl)benzene was prepared according to literature procedure. Spectral data were in accordance with literature report[81].

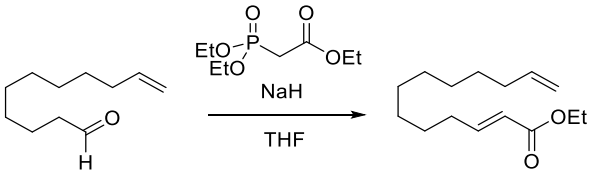
C. Synthesis of (but-3-en-1-yloxy)(tert-butyl)dimethylsilane.



(But-3-en-1-yloxy)(tert-butyl)dimethylsilane was prepared according to literature procedure. Spectral data were in accordance with literature report[82].

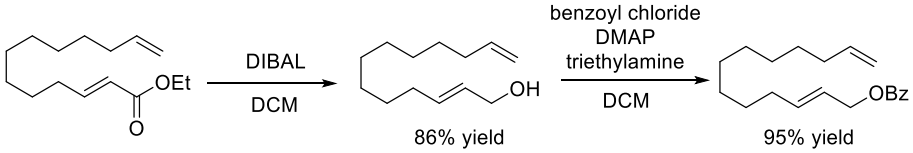
D. Synthesis of ethyl (E)-trideca-2,12-dienoate.

[80] Yan, L.; Meng, Y.; Haeffner, F.; Leon, R. M.; Crockett, M. P. Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 3633
[81] Pollex, A.; Hiersemann, M. *Organic Lett.* **2005**, *7*, 5705.
[82] Paterson, I.; Haslett, G. W. *Organic Lett.* **2013**, *15*, 1338



(E)-Trideca-2,12-dienoate was prepared according to literature procedure. Spectral data were in accordance with literature report[83].

E. Synthesis of (E)-trideca-2,12-dien-1-yl benzoate.

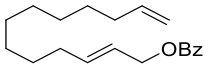


To a flame-dried 50 ml round bottom flask charged with (E)-trideca-2,12-dienoate (357.6 mg, 1.5 mmol, 1.0 equiv) was added THF (10 ml) under nitrogen atmosphere. The flask was cooled to 0 ^{o}C by ice bath, DIBAL (0.54 ml, 3.0 mmol, 2.0 equiv) was added dropwise. The reaction was allowed to stir at 0 ^{o}C for 1 hour. The reaction was then carefully quenched by adding 0.55 ml of 3M NaOH. The mixture was then transferred to a 100 ml Erlenmeyer flask. MgSO4 was then added. After 20 minutes, the mixture was filtered through celite. The filtrate was condensed. The crude product was used in the next step without further purification.

To a 50 ml round bottom flask charged with crude (E)-trideca-2,12-dien-1-ol (1.5 mmol, 1.0 equiv) was added CH_2Cl_2 (10 ml), DMAP (18.3 mg, 0.15 mmol, 0.1 equiv), triethylamine (0.42 ml, 3.0 mmol, 2.0 equiv). Benzoyl chloride (0.35 ml, 3.0 mmol, 2.0 equiv) was then added. The reaction was allowed to stir at room temperature for 14 hours. Upon the completion of the reaction, volatiles were removed by rotovap to afford the

[83] Concellon, J. M.; Rodriguez-Solla, H.; Diaz, P.; Llavona, R. *J. Org. Chem.* **2007**, *72*, 4396.

crude product, which was purified through silica gel column (5% ethyl acetate in hexane) to afford the product as clear oil (273 mg, 61% yield).



(E)-trideca-2,12-dien-1-yl benzoate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 5.95 – 5.75 (m, 2H), 5.74 – 5.63 (m, 1H), 5.06 – 4.90 (m, 2H), 4.82 – 4.71 (m, 2H), 2.06 (m, *J* = 21.4, 4H), 1.38 (dq, *J* = 13.1, 6.7 Hz, 4H), 1.28 (s, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 139.4, 136.9, 133.0, 130.7, 129.8, 128.5, 124.0, 114.3, 66.0, 34.0, 32.5, 29.6, 29.6, 29.4, 29.3, 29.1, 29.1. HRMS-(DART+) for $C_{20}H_{29}BO_2$ $[M+H]^+$: calculated: 301.2161, found: 301.2151. IR (neat): 2975.8 (w), 2923.0 (s), 2851.9 (m), 1719.0 (s), 1653.0 (m), 1462.4 (s), 1365.7 (m), 1306.5 (s), 1177.0 (s), 1042.9 (m), 978.2 (m), 907.8 (m).

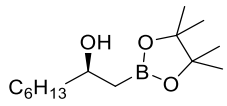
3.6.3 General Procedure for Diboration/Mono-oxidation

In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (5.87 mg, 0.03 mmol, 0.1 equiv), propanediol diboron (76.5 mg, 0. 45 mmol, 1.5 equiv), 4A molecular sieves (40 mg), the alkene substrate (0.30 mmol, 1.0 equiv) and THF (0.30 mL). DBU (4.5 mg, 0.03 mmol, 0.1 equiv) was then added to the solution. The vial was sealed with a Teflon septum, and removed from the glove box. The reaction mixture was allowed to stir at room temperature for 12 hours. The reaction mixture was filtered through a plug of silica gel (1 centimeter in diameter, 5 centimeter in length) with 30% ethyl acetate in hexane as eluent. The filtrate was transferred to a 2-dram vial and concentrated by rotavap. To the 2-dram vial charged with 1,2-bis(boronate) product was added 1-butanol (0.6 ml) and 4-methyl morpholine N-

oxide (70.29 mg, 0.6 mmol, 2.0 equiv) in the glovebox. The vial was sealed with a Teflon cap and removed from the box. The reaction was allowed to stir at 40 ^{o}C for 14 hours. Upon the completion of the reaction, 1-butanol was removed by rotovap. The residue was treated with THF (2 ml), water (0.2 ml), sodium hydroxide (2.4 mg, 0.06 mmol, 0.2 equiv), and pinacol (71 mg, 0.6 mmol, 2.0 equiv). The mixture was allowed to stir at 50 ^{o}C for 5 hours. The mixture was then filtered through a plug of silica gel (1 centimeter in diameter, 5 centimeter in length) with diethyl ether as eluent. The filtrate was concentrated by rotovap to afford the crude product.

3.6.4 Full Characterization and Proof of Stereochemistry

Note: ^{11}B NMR spectra were recorded on a Varian Gemini-500 (160 MHz). Chemical shifts for all the compounds are 34 ppm. Standard ($BF_3 \cdot Et_2O$: 0 ppm).



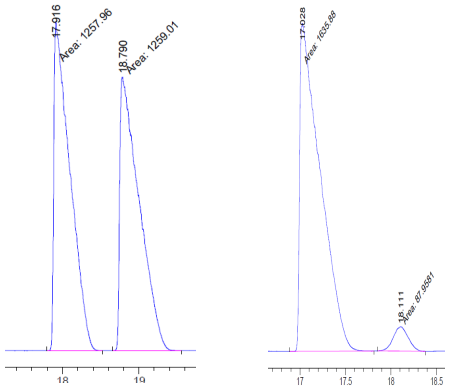
(S)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-ol (5). The diboration/mono oxidation cascade was performed according to the general procedure with 1-octene (33.7 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (55.0 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.83 (p, 1H *J*=3.6 Hz), 2.24 (s, 1H), 1.53 – 1.44 (m, 1H), 1.44 – 1.36 (m, 2H), 1.32 – 1.22 (m, 19H), 1.13 (dd, *J* = 16.1, 4.7 Hz, 1H), 1.02 (dd, *J* = 16.0, 8.1 Hz, 1H), 0.86 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 83.5, 69.3, 39.8, 32.0, 29.5, 26.0, 25.0, 22.8, 14.3. HRMS-(DART+) for $C_{14}H_{28}BO_2$ $[M+H-H_2O]^+$: calculated: 239.2182, found: 239.2186. IR (neat): 2924.9 (w), 2923.9 (s), 2853.9 (m),

1369.3 (s), 1315.0 (s), 1142.9 (s), 966.2 (m), 846.7 (m). $[\alpha]_D^{20}$= -2.86 (c=1.328, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with ruthenium trichloride and sodium periodiate[84].

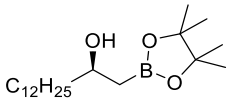
Chiral GLC (β-dex, Supelco, 100 °C 30 min, 20 psi)- analysis of the acetonide of octane-1,2-diol.



Racemic Enriched

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	17.028	MM	0.2614	1635.88281	104.29852	94.89755
2	18.111	MM	0.1889	87.95814	7.76046	5.10245

[84] Shing, T. K. M.; Tam, E. K. W.; Tai, V. W. F.; Chung, I. H. F.; Jiang, Q. *Chem. Eur. J.* **1996**, *2*, 50.



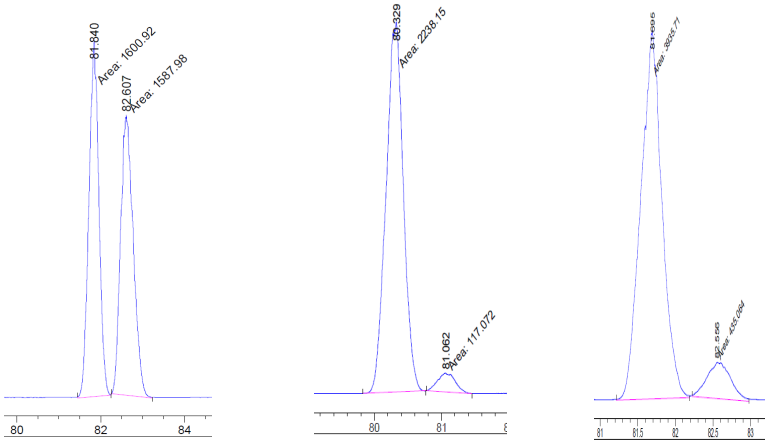
(S)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetradecan-2-ol (6). The diboration-mono oxidation cascade was performed according to the general procedure with 1-tetradecene (58.9 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (74.5 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.83 (p, 1H, *J*=3.6 Hz), 2.24 (s, 1H), 1.53 – 1.44 (m, 1H), 1.44 – 1.35 (m, 2H), 1.25 (s, 31H), 1.13 (dd, *J* = 16.0, 4.7 Hz, 1H), 1.01 (dd, *J* = 15.9, 8.1 Hz, 1H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 83.5, 69.4, 39.8, 32.1, 30.5, 29.89, 29.85, 29.83, 29.6, 26.1, 25.0, 22.9, 14.3. HRMS-(DART+) for $C_{20}H_{42}BO_3$ $[M+H]^+$: calculated: 341.3222, found: 341.3220. IR (neat): 2974.6 (w), 2919.9 (s), 2850.6 (m), 1369.8 (s), 1315.6 (s), 1164.1 (s), 967.0 (m), 846.9 (m). $[\alpha]_D^{20}$= -2.80 (c=1.22, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of tetradecane-1,2-diol prepared from dihydroxylation of 1-tetradecene with ruthenium trichloride and sodium periodiate.[15] The absolute stereochemistry was assigned by analogy. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-tetradecene utilizing AD-mix-β[85].

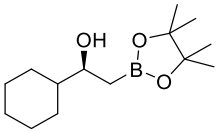
[85] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.

Chiral GLC (β-dex, Supelco, 120 °C 15min, then 0.5°C /min to 180 °C, 20 psi)- analysis of the acetonide of tetradecane-1,2-diol.



Racemic Enriched Authentic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	80.329	MM	0.2978	2238.15308	125.27486	95.02927
2	81.062	MM	0.3038	117.07190	6.42210	4.97073



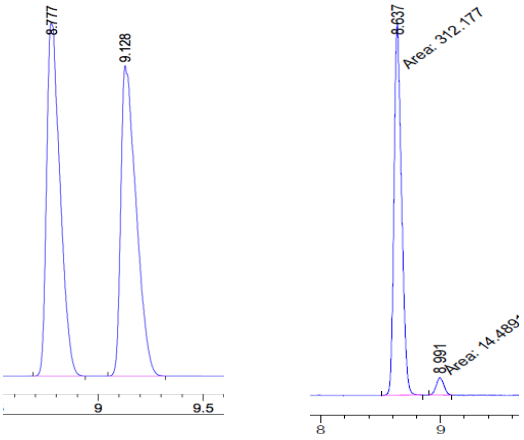
(S)-1-cyclohexyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethan-1-ol (7). The diboration-mono oxidation cascade was performed according to the general procedure with vinylcyclohexane (33.1 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (50.3 mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.68 – 3.51 (m, 1H), 1.87 (d, J = 12.6 Hz, 1H), 1.77 – 1.68 (m, 2H), 1.64 (d, J = 11.8 Hz, 2H), 1.32 – 1.19 (m, 15H), 1.15 – 1.05 (m, 2H), 1.04 – 0.89 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 86.0, 75.9, 48.0, 31.6, 31.1,

29.2, 29.0, 28.8, 27.4, 27.4. HRMS-(DART+) for $C_{14}H_{28}BO_3$ $[M+H]^+$: calculated: 255.2132, found: 255.2138. IR (neat): 2974.8 (w), 2919.9 (s), 2889.3 (m), 1368.3 (s), 1313.7 (s), 1163.8 (s), 966.6 (m), 846.3 (m). $[\alpha]_D^{20}$= -8.68 (c=1.982, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

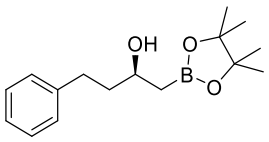
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from dihydroxylation of vinylcyclohexane with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral GLC (β-dex, Supelco, 130 °C 20 min)- analysis of the acetonide of 1-cyclohexylethane-1,2-diol



Racemic Enriched

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	8.637	MM	0.0728	312.17676	71.49557	95.56456
2	8.991	MM	0.0726	14.48905	3.32531	4.43544

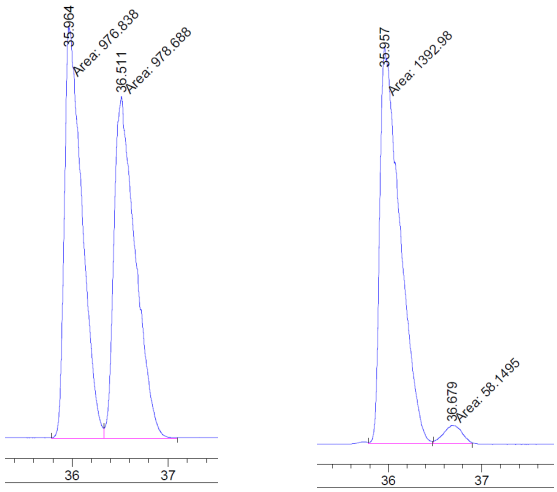


(S)-4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-ol (8). The diboration-mono oxidation cascade was performed according to the general procedure with 4-phenyl-1-butene (39.7 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (57.2 mg, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 3.89 (tt, *J* = 8.2, 4.6 Hz, 1H), 2.79 (ddd, *J* = 13.7, 10.0, 5.6 Hz, 1H), 2.67 (ddd, *J* = 13.7, 9.7, 6.6 Hz, 1H), 1.90 – 1.71 (m, 2H), 1.26 (s, 12H), 1.18 (dd, *J* = 16.1, 4.8 Hz, 1H), 1.08 (dd, *J* = 16.1, 8.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 128.6, 128.5, 125.9, 83.6, 68.7, 41.4, 32.5, 25.0, 25.0. HRMS-(DART+) for $C_{16}H_{26}BO_3$ $[M+H]^+$: calculated: 277.1970, found: 277.1970. IR (neat): 2975.0 (m), 2926.5 (m), 1369.3 (s), 1316.6 (s), 1141.8 (s), 966.3 (m), 846.1 (m), 698.7 (m). $[\alpha]_D^{20}$= +6.96 (c=1.15, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

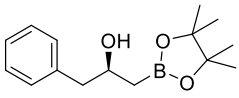
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was treated with 2,2-dimethoxypropane and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 4-phenylbutane-1,2-diol prepared from dihydroxylation of 4-phenyl-1-butene with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral GLC (β-dex, Supelco, 120 °C 5min, then 0.5 °C /min to 140 °C, 20 psi)- analysis of the acetonide of 4-phenylbutane-1,2-diol.



Racemic Enriched

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	35.228	MM	0.2604	2155.20508	137.93863	96.27333
2	35.995	MM	0.2186	83.42645	6.36162	3.72667



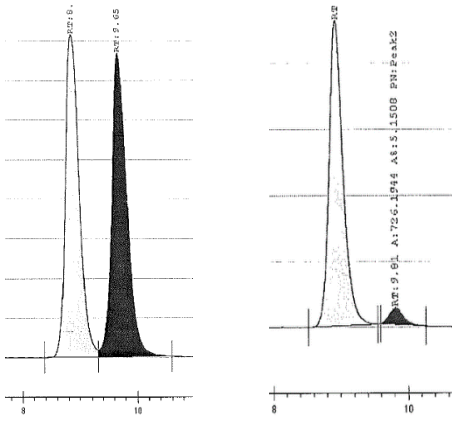
(S)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-ol (9). The diboration-mono oxidation cascade was performed according to the general procedure with allylbenzene (35.5 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (53.5 mg, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.18 (m, 3H), 4.09 (p, *J* = 6.4 Hz, 1H), 2.78 (d, *J* = 6.3 Hz, 2H), 2.30 (s, 1H), 1.26 (s, 12H), 1.13 (qd, *J* = 16.0, 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.1, 129.7, 128.6, 126.5, 83.6, 70.4,

46.1, 25.1, 25.0. HRMS-(DART+) for $C_{16}H_{26}BO_4$ $[M+H]^+$: calculated: 263.1819, found: 263.1824. IR (neat): 2974.8 (w), 2926.9 (w), 1367.8 (s), 1316.6 (s), 1141.5 (s), 966.8 (m), 846.4 (m), 699.3 (m). $[\alpha]_D^{20}$= +4.35 (c=1.15, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

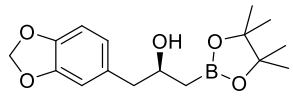
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was compared to the racemic 3-phenylpropane-1,2-diol prepared from dihydroxylation of allylbenzene with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral SFC (Chiracel OJ-H, 4% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-phenylpropane-1,2-diol.



Racemic Enriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.8492	13372.3692	8.93	927.252	0.0068
2	5.1508	726.1944	9.81	50.3872	0.0074
Total:	100	14098.5636			

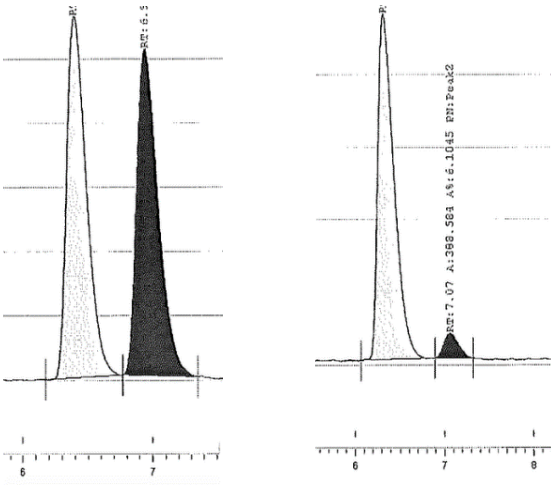


(S)-1-(benzo[d][1,3]dioxol-5-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-ol (10). The diboration-mono oxidation cascade was performed according to the general procedure with safrole (48.7 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (64.3 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 – 6.69 (m, 2H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.91 (s, 2H), 4.03 (t, *J* = 7.1, 6.3 Hz, 1H), 2.74 – 2.63 (m, 2H), 2.28 (s, 1H), 1.25 (s, 12H), 1.11 (qd, *J* = 16.0, 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8, 146.2, 132.9, 122.5, 110.1, 108.4, 101.0, 83.6, 70.5, 45.8, 25.1, 25.0. HRMS-(DART+) for $C_{16}H_{22}BO_4$ $[M+H-H2O]^+$: calculated: 289.1611, found: 289.1619. IR (neat): 2975.9 (s), 2926.3 (m), 1502.2 (s), 1488.4 (s), 1369.8 (m), 1319.6 (s), 1212.2 (s), 1038.5 (m). $[\alpha]_D^{20}$= +2.62 (c=1.3, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

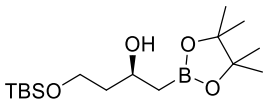
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was compared to the racemic 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol prepared from dihydroxylation of safrole with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral SFC (Chiracel ODR-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-(benzo[d][1,3]dioxol-5-yl)propane-1,2-diol.



Racemic Enriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.8955	5976.94	6.31	475.5711	0.0084
2	6.1045	388.584	7.07	33.6678	0.0094
Total:	100	6365.524			

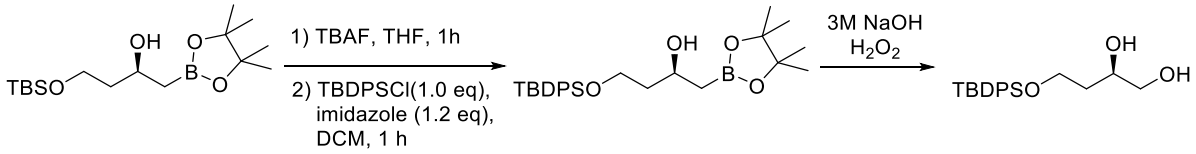


(S)-4-((tert-butyldimethylsilyl)oxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-ol (11). The diboration-mono oxidation cascade was performed according to the general procedure with (but-3-en-1-yloxy)(tert-butyl)dimethylsilane (55.9 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (59.5 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.15 – 4.01 (m, 1H), 3.91 – 3.72 (m, 2H), 3.24 (s, 1H), 1.78 – 1.60 (m, 2H), 1.24 (d, J = 2.0 Hz, 12H), 1.11 (dd, J = 6.8, 3.9 Hz, 2H), 0.88 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 83.4, 68.9, 62.4, 41.1, 26.1, 25.1, 25.0, 18.4, -5.23, -5.25. HRMS-(DART+) for $C_{16}H_{36}BO_4Si$ $[M+H]^+$: calculated: 331.2470, found: 331.2467. IR

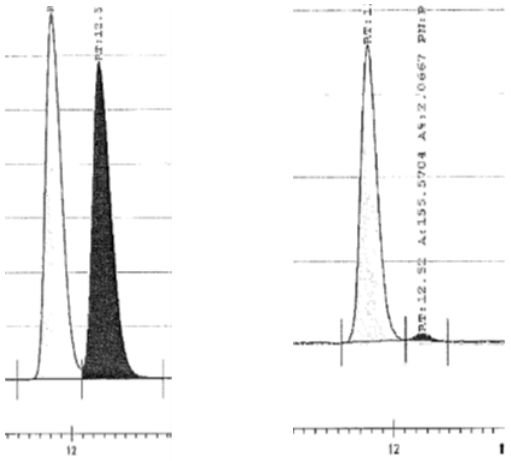
(neat): 2975.2 (w), 2950.0 (m), 2926.6 (s), 2854.3 (m), 1470.0 (m), 1369.5 (s), 1316.8 (s), 1142.9 (s), 882.5 (s), 833.7 (s). $[\alpha]_D^{20}$= -3.02 (c=1.325, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The product was transformed to (R)-4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol by the reaction sequence shown in the following scheme. The 1,2-diol was compared to the racemic 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol prepared from dihydroxylation of (but-3-en-1-yloxy)(tert-butyl)diphenylsilane with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

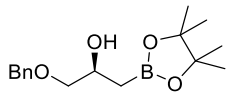


Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-((tert-butyldiphenylsilyl)oxy)butane-1,2-diol.



Racemic Enriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	97.9333	7371.9665	11.54	353.533	0.0092
2	2.0667	155.5704	12.52	8.819	0.01
Total:	100	7527.5369			

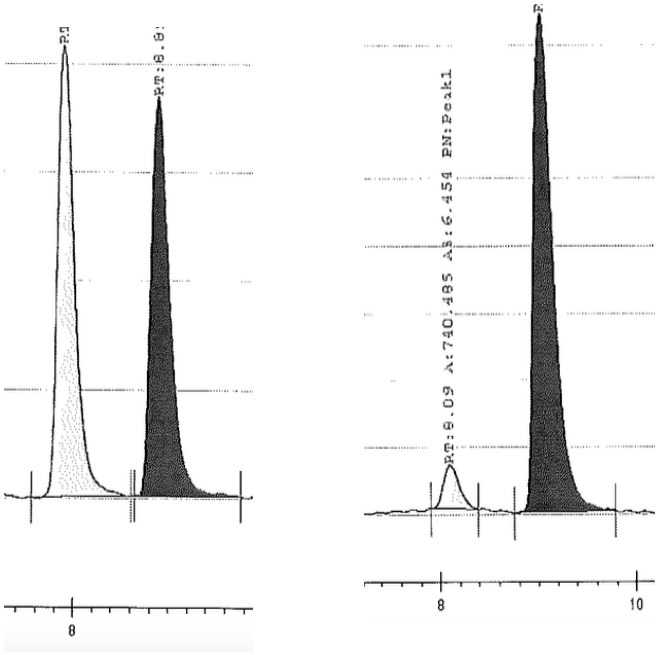


(S)-1-(benzyloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-ol (12). The diboration-mono oxidation cascade was performed according to the general procedure with ((allyloxy)methyl)benzene (44.5 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (62.2 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 4H), 7.30 – 7.25 (m, 1H), 4.56 (s, 2H), 4.09 (qd, *J* = 7.0, 3.3 Hz, 1H), 3.48 (dd, *J* = 9.4, 3.4 Hz, 1H), 3.35 (dd, *J* = 9.5, 7.3 Hz, 1H), 1.23 (s, 12H), 1.15 – 1.01 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.4, 128.6, 127.9, 127.8, 83.5, 75.9, 73.3, 68.2, 25.1, 24.98, 24.95. HRMS-(DART+) for $C_{16}H_{26}BO_4$ $[M+H]^+$: calculated: 293.1924, found: 293.1934. IR (neat): 2974.4 (w), 2924.5 (w), 2856.6 (w), 1368.3 (s), 1316.3 (s), 1142.5 (s), 1104.85 (s), 736.0 (m), 697.4 (m). $[\alpha]_D^{20}$= +3.09 (c=1.23, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

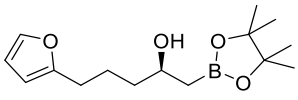
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was compared to the racemic 3-(benzyloxy)propane-1,2-diol prepared from dihydroxylation of ((allyloxy)methyl)benzene with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral SFC (Chiral OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-(benzyloxy)propane-1,2-diol



Racemic Enriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	6.454	740.485	8.09	65.3947	0.0086
2	93.546	10732.7926	9.03	743.6623	0.0096
Total:	100	11473.2776			



(S)-5-(furan-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-ol (13).

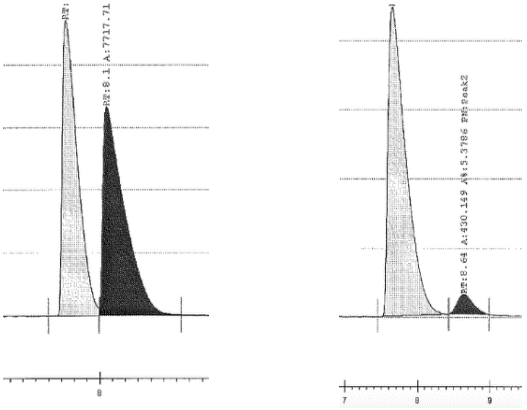
The diboration-mono oxidation cascade was performed according to the general procedure with 2-(pent-4-en-1-yl) furan (40.9 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (58.0 mg, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 1H), 6.26 (s, 1H), 5.98 (s, 1H), 3.87 (s, 1H), 2.64 (t, J = 7.5 Hz, 2H), 2.27 (s, 1H), 1.86 – 1.74 (m, 1H), 1.68 (dp, J = 20.3, 6.8 Hz, 1H), 1.59 – 1.43 (m, 2H), 1.24 (s, 12H), 1.14 (dd, J = 16.2, 5.0

Hz, 1H), 1.03 (dd, *J* = 16.0, 8.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5, 140.9, 110.2, 104.9, 83.6, 69.1, 39.1, 28.1, 25.02, 25.00, 24.6. HRMS-(DART+) for $C_{15}H_{24}BO_3$ $[M+H-H2O]^+$: calculated: 263.1813, found: 263.1818. IR (neat): 2975.2 (m), 2927.9 (m), 1369.2 (s), 1317.0 (s), 1141.8 (s), 883.7 (m), 846.7 (m), 726.8 (m). $[\alpha]_D^{20}$= +1.20 (c=1.01, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

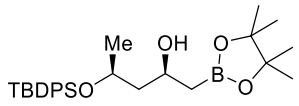
The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was compared to the racemic 5-(furan-2-yl)pentane-1,2-diol prepared from dihydroxylation of 2-(pent-4-en-1-yl) furan with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral SFC (Chiracel ODR-H, 5% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 5-(furan-2-yl)pentane-1,2-diol.



Racemic Enriched

Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.6214	7567.2424	7.64	446.8813	0.0087
2	5.3786	430.149	8.64	28.7569	0.0098
Total:	100	7997.3914			

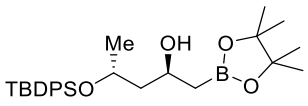


(2S,4S)-4-((tert-butyldiphenylsilyl)oxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-ol (14). The diboration-mono oxidation cascade was performed according to the general procedure with (S)-tert-butyl (pent-4-en-2-yloxy) diphenylsilane (97.4 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (90.0 mg, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.66 (m, 4H), 7.47 – 7.31 (m, 6H), 4.10 (h, *J* = 6.0 Hz, 1H), 4.02 (s, 1H), 2.80 (d, *J* = 3.8 Hz, 1H), 1.80 (ddd, *J* = 13.8, 9.0, 7.1 Hz, 1H), 1.55 (ddd, *J* = 13.9, 5.9, 3.6 Hz, 1H), 1.24 (s, 12H), 1.08 – 1.00 (m, 14H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.08, 136.07, 134.9, 134.2, 129.8, 129.7, 127.8, 127.6, 83.5, 69.5, 67.7, 48.9, 27.2, 25.0, 25.0, 23.9, 19.4. HRMS-(DART+) for $C_{27}H_{42}BO_4Si$ $[M+H]^+$: calculated: 469.2940, found:469.2950. IR (neat): 2971.2 (m), 2928.1 (m), 2854.6 (w) 1370.6 (s), 1318.5 (s), 1141.4 (s), 1107.7 (s), 701.5 (s), 505.6 (s). $[\alpha]_D^{20}$= +3.18 (c=1.26, $CHCl_3$, l=50 mm).

Proof of stereochemistry:

The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The relative configuration was assigned by comparison of the ^{13}C NMR and ^{1}H NMR spectrum with literature report of (2R,4S)-4-((tert-butyldiphenylsilyl)oxy)pentane-1,2-diol[86].

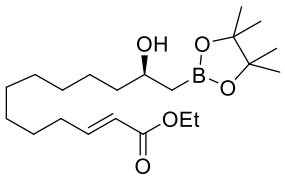
[86] Kumar, P.; Gupta, P.; Vasudeva Naida, S. *Chem. Eur. J.* **2006**, *12*, 1397.



(2S,4R)-4-((tert-butyldiphenylsilyl)oxy)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-ol (15). The diboration-mono oxidation cascade was performed according to the general procedure with (R)-tert-butyl (pent-4-en-2-yloxy) diphenylsilane (97.4 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (99.8 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (td, *J* = 8.1, 1.4 Hz, 4H), 7.47 – 7.33 (m, 6H), 4.22 (dtd, *J* = 9.4, 6.8, 2.5 Hz, 1H), 4.18 – 4.10 (m, 1H), 1.71 (ddd, *J* = 13.9, 9.7, 4.0 Hz, 1H), 1.57 (ddd, *J* = 14.2, 5.7, 2.5 Hz, 1H), 1.24 (d, *J* = 4.8 Hz, 12H), 1.10 – 1.03 (m, 15H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.2, 136.1, 135.0, 134.5, 133.9, 129.9, 129.8, 127.8, 127.7, 83.4, 68.8, 66.0, 47.4, 27.2, 25.1, 25.0, 23.1, 19.4. HRMS-(DART+) for $C_{27}H_{42}BO_4Si$ $[M+H]^+$: calculated: 469.2940, found:469.2931. IR (neat): 2972.1 (m), 2928.5 (m), 2854.8 (w), 1426.0 (w), 1370.8 (s), 1318.9 (s), 1141.8 (s), 1108.1 (s), 686.9 (s), 504.8 (s). $[\alpha]_D^{20}$= +3.18 (c=1.26, $CHCl_3$, l=50 mm).

Proof of stereochemistry:

The product was treated with 3M sodium hydroxide (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The relative configuration was assigned by comparison of the ^{13}C NMR and ^{1}H NMR spectrum with literature report of (2R,4R)-4-((tert-butyldiphenylsilyl)oxy)pentane-1,2-diol[17].

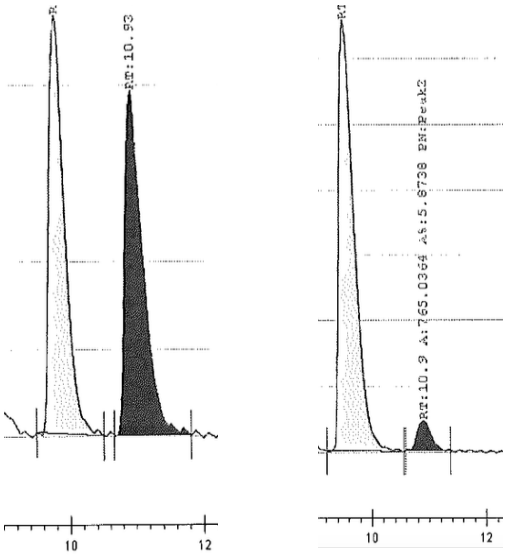


Ethyl (S,E)-12-hydroxy-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tridec-2-enoate (16). The diboration-mono oxidation cascade was performed according to the general procedure with ethyl (E)-trideca-2,12-dienoate (71.5 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (67.7 mg, 59% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.94 (dt, *J* = 14.9, 6.9 Hz, 1H), 5.79 (d, *J* = 15.6 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 1H), 2.24 (s, 1H), 2.17 (q, *J* = 7.2 Hz, 2H), 1.53 – 1.35 (m, 6H), 1.30 – 1.25 (m, 11H), 1.25 (s, 12H), 1.12 (dd, *J* = 16.0, 4.6 Hz, 1H), 1.01 (dd, *J* = 16.0, 8.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 150.0, 121.4, 83.5, 69.3, 60.3, 39.7, 32.4, 29.8, 29.7, 29.5, 29.3, 28.2, 26.0, 25.1, 25.0, 14.5. HRMS-(DART+) for $C_{21}H_{40}BO_5$ $[M+H]^+$: calculated: 383.2963, found: 383.2964. IR (neat): 2975.5 (w), 2923.4 (m), 2852.2 (w), 1718.1 (s), 1652.40 (m), 1367.9 (s), 1314.1 (s), 1267.6 (s), 1141.4 (s). $[\alpha]_D^{20}$= -1.60 (c=1.125, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The product was treated with pH=7.00 buffer (1 ml), hydrogen peroxide (0.5 ml) to afford corresponding 1,2-diol. The 1,2-diol was compared to the racemic ethyl (E)-12,13-dihydroxytridec-2-enoate prepared from dihydroxylation of ethyl (E)-trideca-2,12-dienoate with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

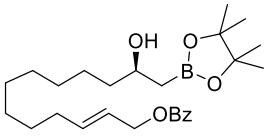
Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of ethyl (E)-12,13-dihydroxytridec-2-enoate



Racemic Enriched

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.1262	12259.5717	9.5	655.7848	0.0099
2	5.8738	765.0364	10.9	45.1807	0.0114
Total:	100	13024.6081			



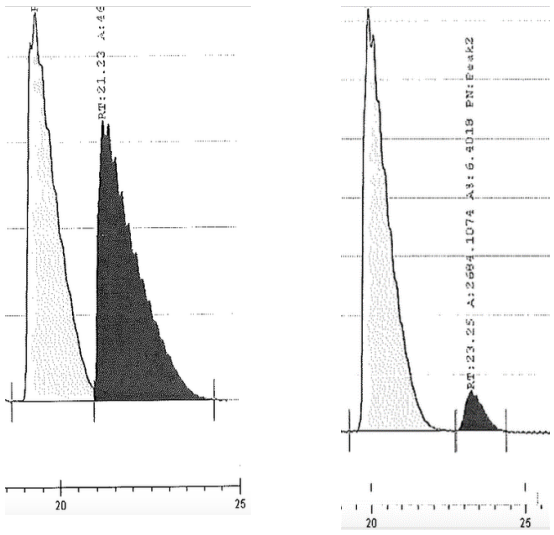
(S,E)-12-hydroxy-13-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tridec-2-en-1-yl benzoate (17). The diboration-mono oxidation cascade was performed according to the general procedure with (E)-trideca-2,12-dien-1-yl benzoate (90.2 mg, 0.3 mmol). The crude product was purified by silica gel column (25% to 35% ethyl acetate in hexane) to afford the product as clear oil (86.7 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.1 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.85 (dt, *J* = 13.5, 6.7 Hz, 1H), 5.67 (dt, *J* = 15.3, 6.4 Hz, 1H), 4.76 (d, *J* = 6.1 Hz, 2H), 3.84 (tt, *J* = 7.8, 4.3

Hz, 1H), 2.25 (s, 1H), 2.07 (q, *J* = 7.0 Hz, 2H), 1.58 – 1.33 (m, 6H), 1.30 – 1.26 (m, 8H), 1.25 (s, 12H), 1.13 (dd, *J* = 16.0, 4.8 Hz, 1H), 1.02 (dd, *J* = 16.0, 8.1 Hz, 1H). 13C NMR (151 MHz, $CDCl_3$) δ 166.6, 137.0, 133.0, 130.6, 129.8, 128.5, 124.0, 83.5, 69.4, 66.0, 39.8, 32.5, 29.8, 29.7, 29.6, 29.4, 29.1, 26.1, 25.1, 25.0. HRMS-(DART+) for $C_{26}H_{42}BO_5$ $[M+H]^+$: calculated:445.3125, found:445.3138. IR (neat): 2974.4 (w), 2922.7 (s), 2851.2 (m), 1717.5 (s), 1450.2 (w), 1369.7 (m), 1313.3 (m), 1267.9 (s), 1164.6 (m), 1142.7 (m), 711.2 (s). $[\alpha]_D^{20}$= -2.00 (c=1.125, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

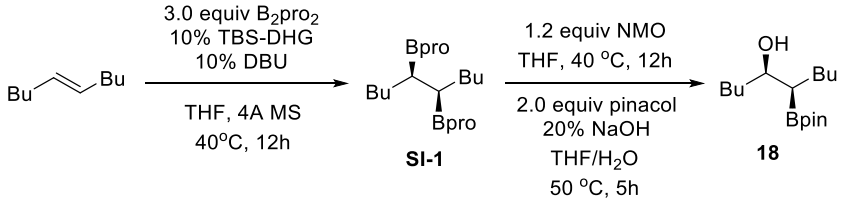
The product was treated with pH=7.00 buffer (1 ml) and hydrogen peroxide (0.5 ml) to afford the corresponding 1,2-diol. The 1,2-diol was compared to the racemic (E)-12,13-dihydroxytridec-2-en-1-yl benzoate prepared from dihydroxylation of (E)-trideca-2,12-dien-1-yl benzoate with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral SFC (Chiracel OD-H, 8% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (E)-12,13-dihydroxytridec-2-en-1-yl



Racemic Enriched

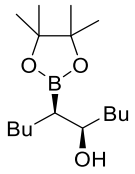
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.5982	39243.0059	19.96	715.8566	0.0185
2	6.4018	2684.1074	23.25	67.553	0.0215
Total:	100	41927.1133			



In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with TBS-DHG catalyst (5.87 mg, 0.03 mmol, 0.1 equiv), propanediol diboron (76.5 mg, 0. 45 mmol, 1.5 equiv), 4A molecular sieves (40 mg), the trans 5-decene (42.1 mg, 0.30 mmol, 1.0 equiv) and THF (0.30 mL). DBU (4.5 mg, 0.03 mmol, 0.1 equiv) was then added to the solution. The vial was sealed with a Teflon septum, removed from the glove box. The reaction mixture was allowed to stir at 40 ^{o}C for 12 hours. The reaction mixture was filtered through a pipet of silica gel with 25% ethyl acetate in hexane in order to get rid of the 4A molecular sieves and excess diboron starting material. The filtrate was condensed to crude product.

In the glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with crude product SI-1 (56.9 mg. 0.2 mmol, 1.0 equiv), THF (0.4 ml), 4-methyl morpholine N-oxide (28.1 mg, 0.24 mmol, 1.2 equiv). The vial was sealed with a cap and removed from the glovebox. The vial was heated to 40 ^{o}C for 12h. Upon the completion of the reaction, 1-butanol was removed by rotavap. The crude product was then treated

with pinacol (70.9 mg, 0.60 mmol, 2.0 equiv), NaOH (1.6 mg, 0.04 mmol, 0.2 equiv), THF (2 ml) and H_2O (0.2 ml). The mixture was allowed to stir at 50 ^oC for 5 hours. The mixture was then filtered through a pipet of silica gel with diethyl ether. The filtrate was condensed. The crude product was purified by silica gel column (10% ethyl acetate in hexane) to afford product (5R,6R)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)decan-5-ol as clear oil (31.3 mg, 55% yield). The mixture was then filtered through a pipet of silica gel with ether. The solvent was removed by rotavap. The crude product was purified by silica gel column (2-5% ethyl acetate in hexane) to afford product SI-1 (71.0 mg, 60% yield).



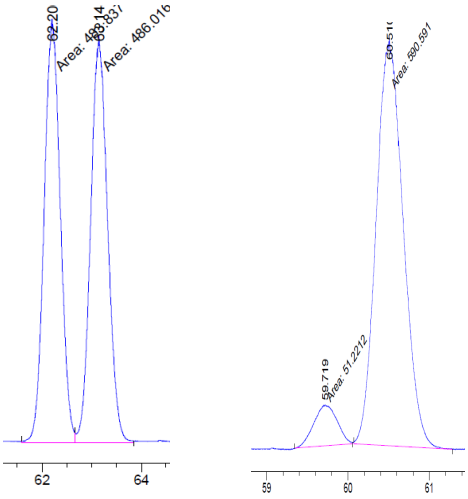
(5R,6R)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)decan-5-ol (18). ^1H NMR (600 MHz, $CDCl_3$) δ 3.58 (tt, *J* = 8.2, 4.1 Hz, 1H), 2.05 (d, *J* = 8.0 Hz, 1H), 1.58 – 1.37 (m, 6H), 1.36 – 1.20 (m, 16H), 1.14 (dt, *J* = 10.6, 5.7 Hz, 1H), 0.98 – 0.80 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 83.5, 74.0, 37.8, 31.7, 28.5, 25.1, 25.1, 24.9, 23.2, 22.9, 14.3, 14.2. HRMS-(DART+) for $C_{26}H_{42}BO_5$ $[M+H-H2O]^+$: calculated: 267.2490, found: 267.2490. IR (neat): 2953.4 (m), 2923.9 (m), 2856.2 (m), 1464.54 (w), 1371.3 (s), 1314.8 (s), 1142.7 (s), 966.6 (m), 853.4 (m). $[\alpha]_D^{20}$= +5.31 (c=1.28, $CHCl_3$, l=50 mm).

Analysis of Stereochemistry:

The product was treated with 3M sodium hydroxide (1 ml), hydrogen peroxide (0.5 ml) to afford corresponding 1,2-diol. The 1,2-diol was treated with 2,2-dimethoxypropane

and catalytic toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of decane-5,6-diol prepared from dihydroxylation of trans-5-decene with ruthenium trichloride and sodium periodiate[15]. The absolute stereochemistry was assigned by analogy[16].

Chiral GLC (β-dex, Supelco, 70 °C 15min, 0.25 °C/min to 90 °C 20 psi)- analysis of the acetonide of decane-5,6-diol.



Racemic Enriched

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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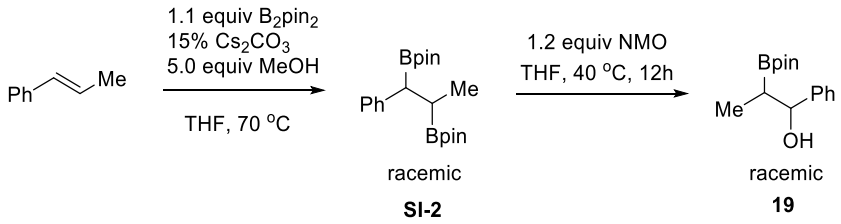
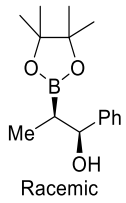
2	60.510	MM	0.3821	590.59149	25.76274	92.01929



In the glove box, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with Cs_2CO_3 (14.7 mg, 0.045 mmol, 0.15 equiv), Bis(pinacolato)diboron (83.8 mg, 0. 33 mmol, 1.1 equiv), THF (0.30 mL), and b-methyl styrene (35.5 mg, 0.30 mmol, 1.0 equiv). The vial was sealed with a Teflon septum, and removed from the glove box. The nitrogen outlet was introduced, anhydrous methanol (0.06 ml, 1.50 mmol, 5.0 equiv) were added to the reaction. The reaction was then allowed to stir at 70 ^{o}C for 14h. Upon the completion of the reaction, solvents were removed by rotavap. The crude product was purified on silica gel column (5% ethyl acetate in hexane) to afford the product SI-2 (50.2 mg, 45% yield). Spectral was in accordance with literature report[87].

In the glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with SI-2 (74.4 mg. 0.2 mmol, 1.0 equiv), THF (0.4 ml), 4-methyl morpholine N-oxide (28.1 mg, 0.24 mmol, 1.2 equiv). The vial was sealed with a cap and removed from the glovebox. The vial was heated to 40 ^{o}C for 12h. Upon the completion of the reaction, solvent was removed by rotavap. The crude product was purified by silica gel column (10% ethyl acetate in hexane) to afford product (1R,2R)-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-ol as clear oil (27.8 mg, 53% yield)

[87] Morgan, J. B. Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702.

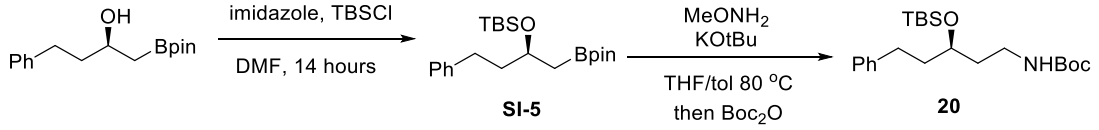


Racemic

(1R,2R)-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-2-ol (19). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 4H), 7.26 – 7.21 (m, 1H), 4.60 (dd, *J* = 7.9, 4.6 Hz, 1H), 2.77 (d, *J* = 4.6 Hz, 1H), 1.55 (p, *J* = 7.6 Hz, 1H), 1.25 (s, 12H), 0.88 (d, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.57, 128.35, 127.46, 126.54, 83.65, 77.68, 24.96, 24.84, 12.59. HRMS-(DART+) for $C_{15}H_{22}BO_2$ $[M+H-H2O]^+$: calculated: 245.1707, found: 245.1709. IR (neat): 2974.2 (m), 2928.4 (w), 2873.3 (w), 1445.0 (m), 1378.8 (s), 1317.5 (s), 1165.4 (s), 700.4 (s).

3.6.5 Transformations and Corresponding Characterization

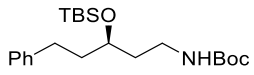
A. Amination



A 20 ml scintillation vial with stir bar was charged with mono-oxidation product (S)-4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-ol (82.9 mg, 0.3 mmol). Imidazole (30.6 mg, 0.45 mmol, 1.5 equiv), DMF (0.6 ml), and TBSCl (90.4 mg, 0.6 mmol, 2.0 equiv) were successively added to the vial. The reaction was allowed to stir at room temperature for 14 hours. Upon the completion of the reaction, volatiles were removed by rotavap. The residue was then filtered through a plug of silica gel (1

centimeter in diameter, 5 centimeter in length) with 5% ethyl acetate in hexane as eluent. Solvents were removed by rotavap. The crude SI-5 was used without further purification.

To a oven-dried 4-dram vial with stir bar was added crude SI-5 in toluene (1.5 ml) and potassium tert-butoxide (67.3 mg, 0.6 mmol. 2.0 equiv) in the glovebox. The vial was sealed with a teflon septa and removed from the glovebox. A nitrogen inlet was introduced, methoxy amine in THF (0.33 ml, 0.6 mmol, 2.0 equiv, 1.82 M prepared according to reported literature) was added to the vial. The vial was then sealed with electric tape. The reaction was allowed to stir at 60 ^{o}C for 14 hours. Upon the completion of the reaction, the flask was cooled down to room temperature, Boc_2O in THF (0.3 ml, 2.0 M, 0.6 mmol) was then added. The reaction was allowed to stir at room temperature for another 60 minutes. Water was added to the reaction. The mixture was transferred to a sep funnel. Layers were separated. The aqueous layer was extracted three times by ethyl acetate. The organic layers are combined, dried over sodium sulfate and filtered to afford the crude product. The crude product was purified through silica gel column by 5% to 20% ethyl acetate in hexane. The product tert-butyl (R)-(3-(methoxymethoxy)-5-phenylpentyl)carbamate was obtained clear oil (96.7 mg, 85%).



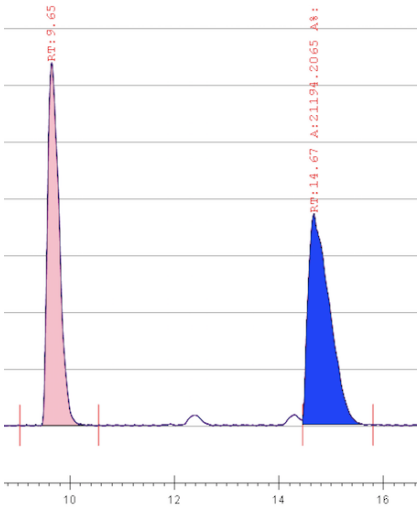
tert-butyl (R)-(3-(methoxymethoxy)-5-phenylpentyl)carbamate) (20). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 7.20 – 7.15 (m, 3H), 4.74 (s, 1H), 3.81 (s, 1H), 3.35 – 3.20 (m, 1H), 3.13 (dt, *J* = 13.1, 6.1 Hz, 1H), 2.77 – 2.53 (m, 2H), 1.45 (s, 9H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 142.3, 128.6, 128.5, 126.0, 79.3, 71.3, 46.0, 37.1, 31.7, 28.6, 26.1, 18.3, -4.34, -4.35. HRMS-(DART+) for $C_{21}H_{38}NO_3Si$

$[M+H]^+$: calculated: 380.2616, found:380.2606. IR neat: 2982.0 (w), 2923.4 (w), 1768.0 (s), 1719.6 (w), 1376.1 (m), 1284.9 (s), 1148.0 (s), 1089.6 (m), 1028.5 (s), 1009.4 (m). $[\alpha]_D^{20}$= -3.56 (c=0.73, $CHCl_3$, l=50 mm).

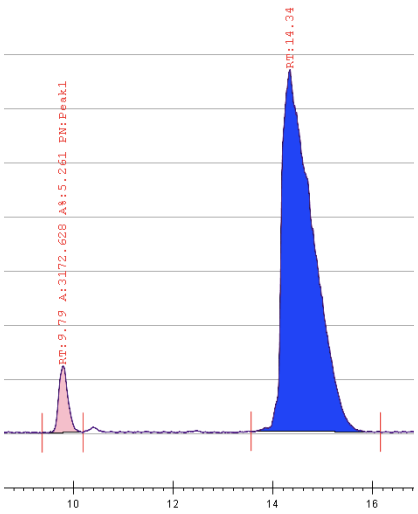
Analysis of Stereochemistry:

The product was compared to the racemic tert-butyl 3-(methoxymethoxy)-5-phenylpentyl carbamate prepared by procedure shown in the following Scheme.

Chiral SFC (Chiracel OD-H, 2% isopropanol, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (R)-(3-(methoxymethoxy)-5-phenylpentyl)carbamate)



Racemic



Enriched

Reporting Information

	Peak Name	Peak Number	Peak Concentration	Area Percent	Area	Area Sum	Retention Time	Start Time	Stop Time
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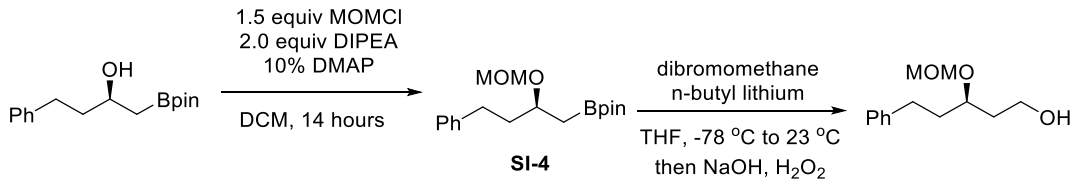
	Peak2	2	0	94.739	57131.749	60304.377	14.34 min	13.5575 min	16.1498 min

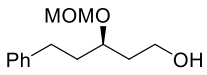
B. Homologation



A 20 ml scintillation vial with stir bar was charged with mono-oxidation product (S)-4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-ol (82.9 mg, 0.3 mmol). 4-Dimethylaminopyridine (3.6 mg, 0.03 mmol), DCM (1.5 ml), N, N-diisopropylethylamine (0.1 ml, 0.6 mmol), MOMCl (35.2 μl, 0.45 mmol) were successively added to the vial. The reaction was allowed to stir at room temperature for 14 hours. Upon the completion of the reaction, volatiles were removed by rotavap. The residue was then filtered through a plug of silica gel (1 centimeter in diameter, 5 centimeter in length) with 25% ethyl acetate in hexane as eluent. Solvents were removed by rotavap. The crude SI-4 was used without further purification.

To an oven-dried 2-dram vial with stir bar was added SI-4 in THF (1 ml) and dibromomethane (260.7 mg, 1.5 mmol, 5.0 equiv) in glovebox. The vial was sealed with a Teflon septa and removed from the glovebox. A nitrogen inlet was then introduced. The vial was cooled down to -78 ^{o}C by dry ice/acetone bath. n-BuLi (0.6 ml, 2.5 M in hexane, 5.0 equiv) was added dropwise. The reaction was allowed to slowly warm up to room temperature and stir for 14 hours. Upon the completion of the reaction, PH=7.0 buffer (1 ml) was added to the vial. The vial was then cooled down to 0 ^{o}C, hydrogen peroxide (0.5 ml) was added to the vial in drop. The reaction was allowed to stir at room temperature for 3 hours. Sodium thiosulfate was then added. The mixture was transformed to a sep funnel. The layers were separated. The aqueous layer was extracted with ethyl acetate for

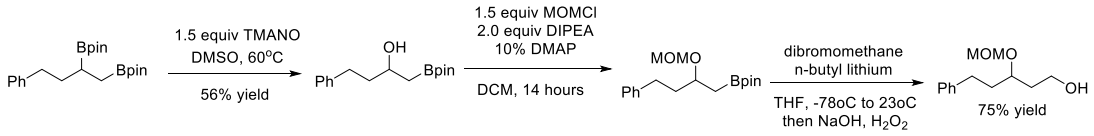
3 times. The organic layers were combined, dried over sodium sulfate, filtered and evaporated down to crude product. The crude product was purified through silica gel column (25% ethyl acetate in hexane) to afford the product (R)-3-(methoxymethoxy)-5-phenylpentan-1-ol as clear oil (52.5 mg, 78% yield).



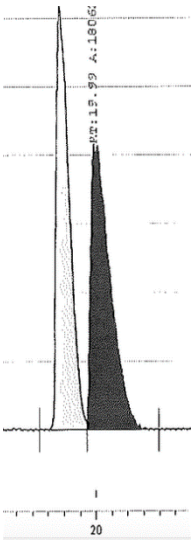
(R)-3-(methoxymethoxy)-5-phenylpentan-1-ol (21). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70 (d, J = 2.5 Hz, 2H), 3.83 (d, J = 1.9 Hz, 2H), 3.78 – 3.69 (m, 1H), 3.43 (s, 3H), 2.68 (tq, J = 19.7, 6.9, 6.1 Hz, 2H), 2.03 – 1.67 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1, 128.6, 128.5, 126.1, 96.4, 76.4, 60.0, 56.1, 37.0, 36.7, 31.8. HRMS-(DART+) for $C_{12}H_{17}O_2$ $[M+H-H2O]^+$: calculated: 193.1223, found: 193.1215. IR (neat): 2930.6 (m), 2885.1 (m), 2856.2 (m), 1452.8 (m), 1368.7 (m), 1146.5 (s), 1099.1 (s), 1029.6 (s), 699.1 (s). $[\alpha]_D^{20}$= -32.2 (c=0.85, $CHCl_3$, l=50 mm).

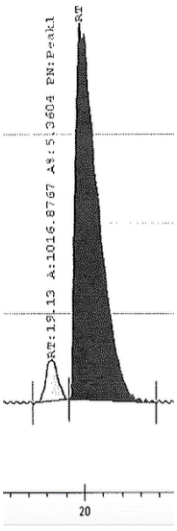
Analysis of Stereochemistry:

The product was compared to the racemic 3-(methoxymethoxy)-5-phenylpentan-1-ol prepared by procedure shown in the following Scheme.



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





Racemic Enriched

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
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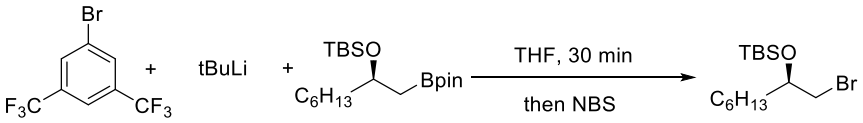
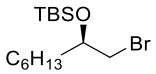
2	94.6396	17953.2903	19.89	419.8486	0.0199
Total:	100	18970.167			

C. Bromination

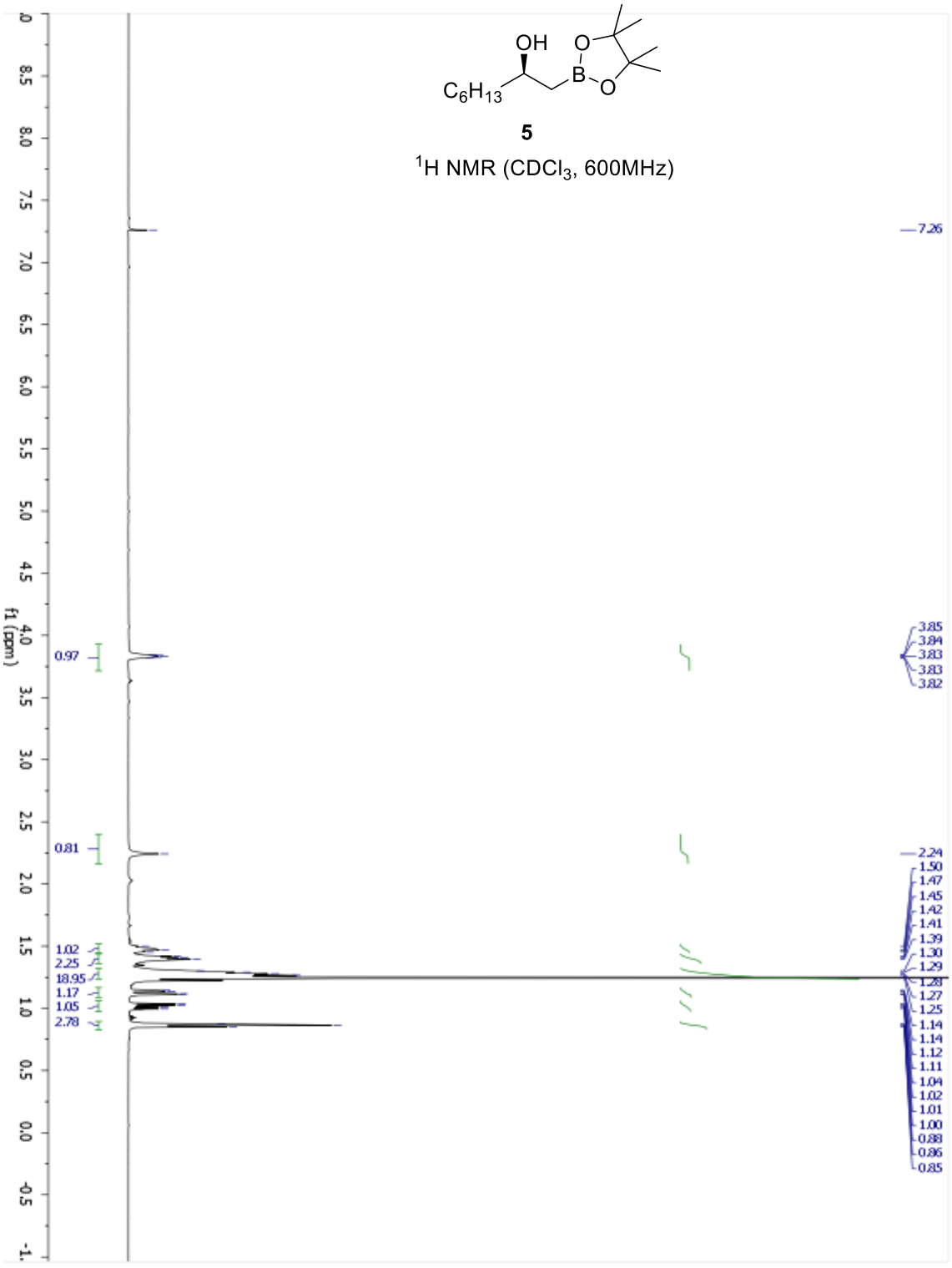


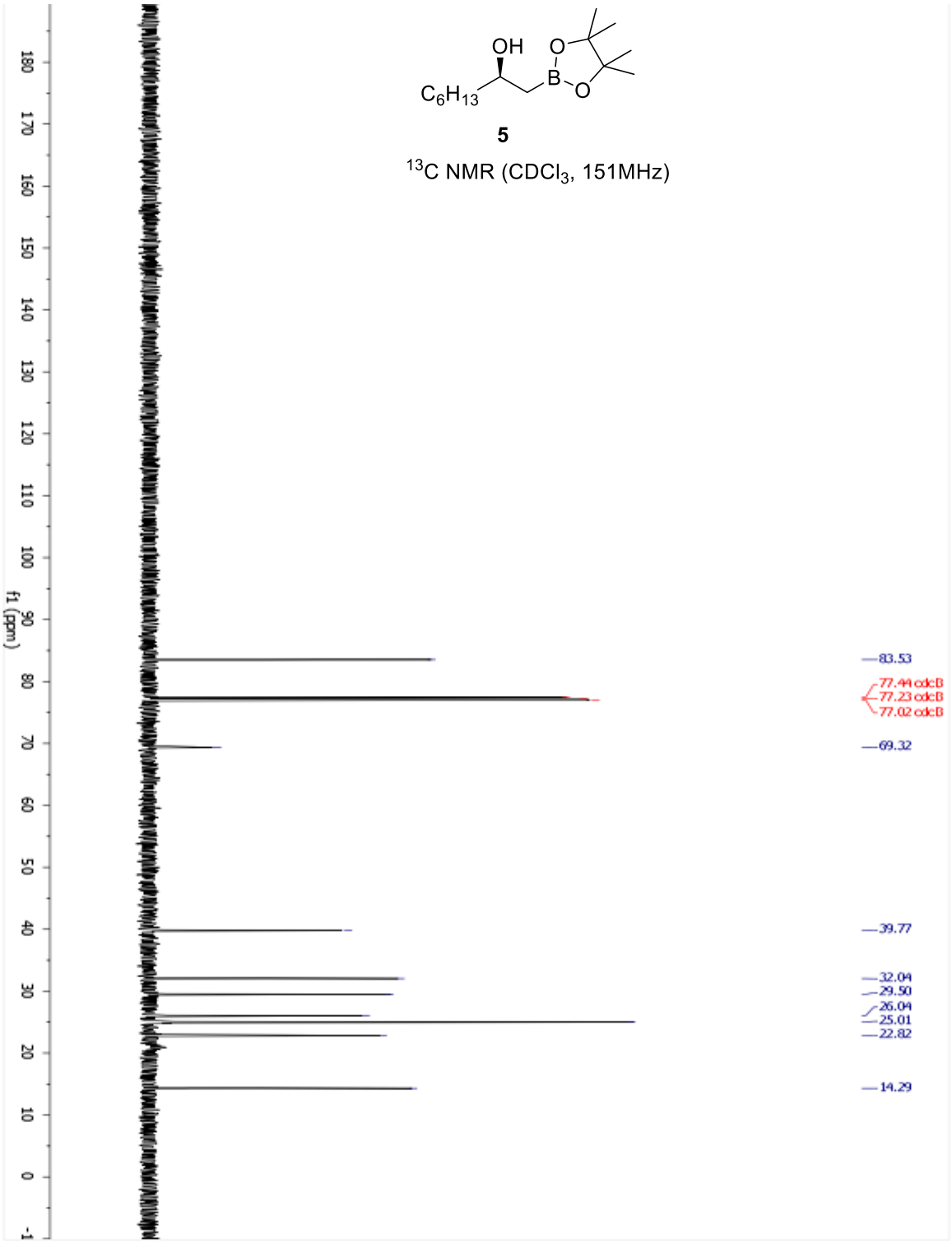
To an oven-dried 2-dram vial with stir bar was added the 1-bromo-3,5-bis(trifluoromethyl)benzene (96.7 mg, 0.33 mmol) and THF (0.5 ml) in glovebox. The vial was sealed with a Teflon septa and removed from the glovebox. The nitrogen inlet was introduced. The vial was cooled down to -78 ^{o}C by acetone/dry ice bath. tert-Butyl lithium (0.39 ml, 1.7 M in pentane, 0.66 mmol) was then added in drop. The reaction was allowed to stir at -78 ^{o}C for 15 minutes, the boronic ester substrate (S)-tert-butyldimethyl((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-yl)oxy)silane (111.1 mg, 0.3 mmol) in THF (1 ml) was then added to the reaction. The reaction was allowed to warm up to room temperature and stir at room temperature for 15 minutes. The reaction was brought back to the glovebox, NBS (64.1 mg, 0.36 mmol) was added in one portion. The vial was sealed with a cap and removed from the glovebox. The reaction was allowed to stir at room temperature for 1 hour. Upon the completion of the reaction, the mixture was filtered through a pipet of silica gel with diethyl ether. Solvents were then removed by rotavap. The crude product was purified by silica gel column (5% DCM in hexane) to afford the product (R)-((1-bromooctan-2-yl)oxy)(tert-butyl)dimethylsilane as a clear oil (82.5 mg, 85% yield).



(R)-((1-bromooctan-2-yl)oxy)(tert-butyl)dimethylsilane (21). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (p, J = 5.3 Hz, 1H), 3.32 (d, J = 5.2 Hz, 2H), 1.68 – 1.59 (m, 1H), 1.58 –

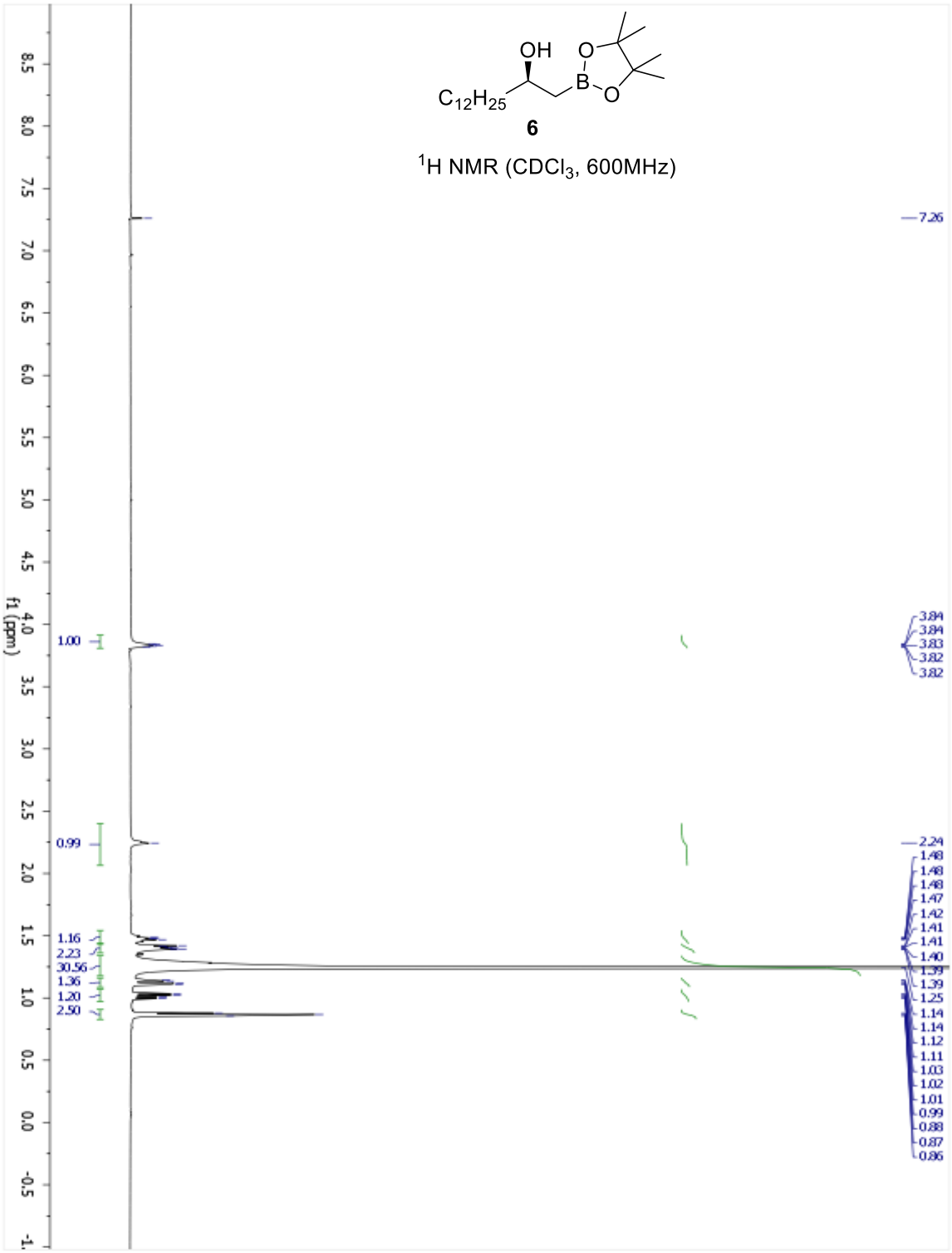
1.48 (m, 1H), 1.39 – 1.21 (m, 8H), 0.90 (s, 12H), 0.08 (d, J = 11.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 72.2, 38.2, 35.8, 32.0, 29.5, 26.0, 25.0, 22.8, 18.3, 14.3, -4.2, -4.4. HRMS-(DART+) for $C_{14}H_{32}OSiBr$ $[M+H]^+$: calculated: 323.1400, found: 323.1390. IR neat: 2952.5 (m), 2925.1 (s), 2853.9 (m), 1461.6 (w), 1253.1 (m), 1087.9 (m), 834.5 (s), 773.9 (s). $[\alpha]_D^{20}$= +6.15 (c=1.27, $CHCl_3$, l=50 mm).

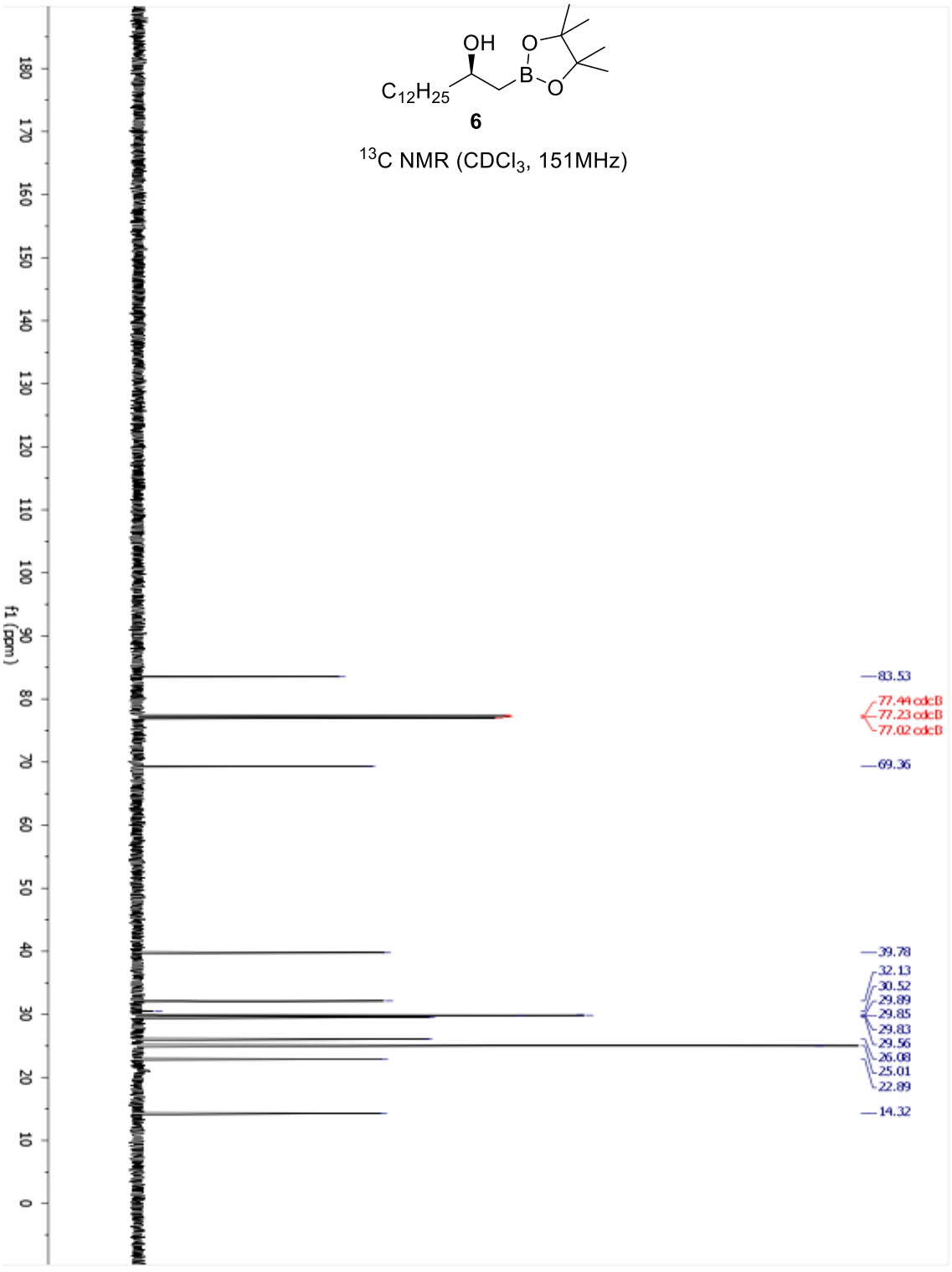

OH
O
B
O
C6H13
5
1H NMR (CDCl3, 600MHz)
7.26
3.85
3.84
3.83
3.83
3.82
2.24
1.50
1.47
1.45
1.42
1.41
1.39
1.30
1.29
1.28
1.27
1.25
1.14
1.14
1.12
1.11
1.04
1.02
1.01
1.00
0.88
0.86
0.85
0.97
0.81
1.02
2.25
18.95
1.17
1.05
2.78
f1 (ppm)

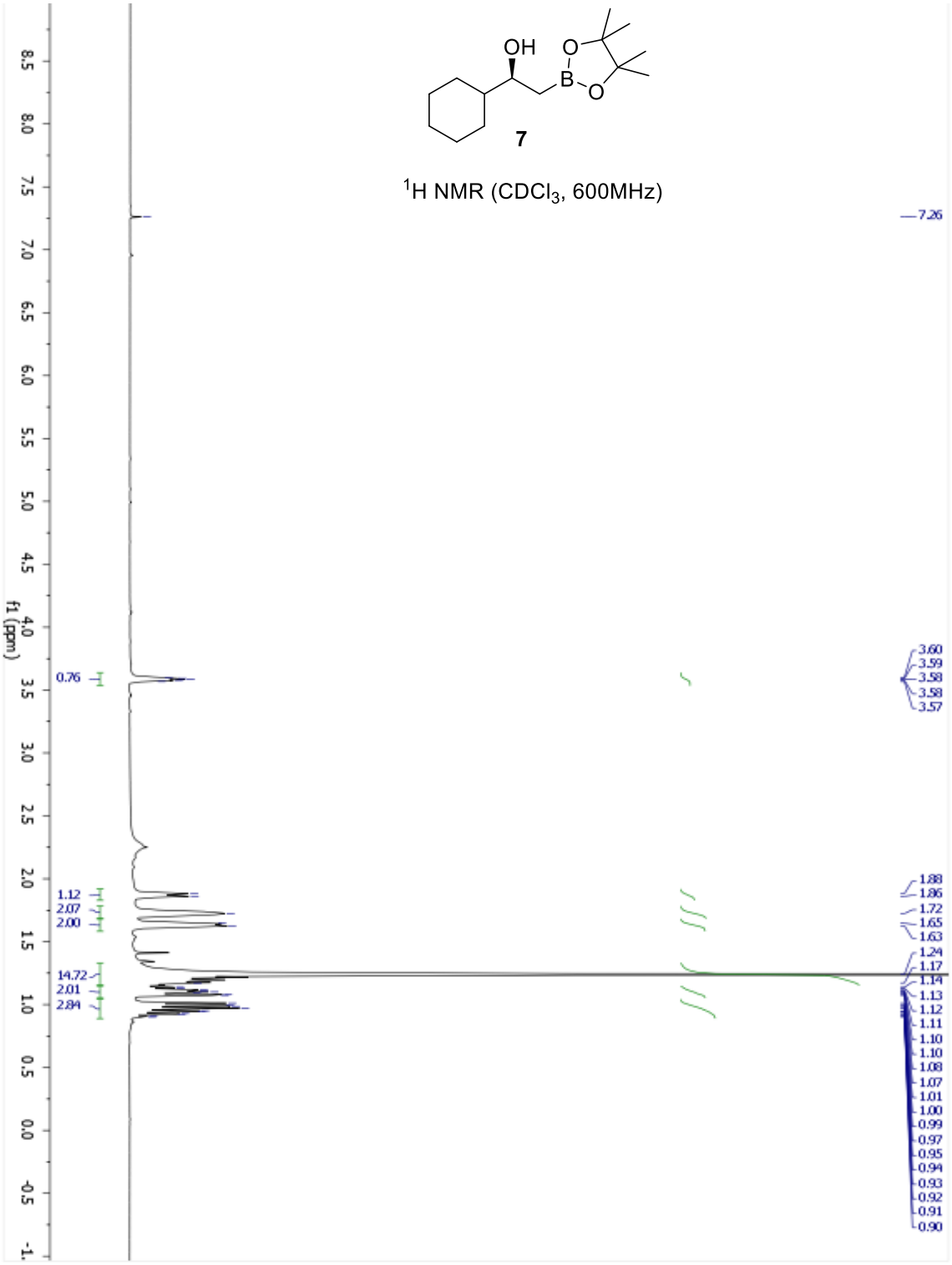


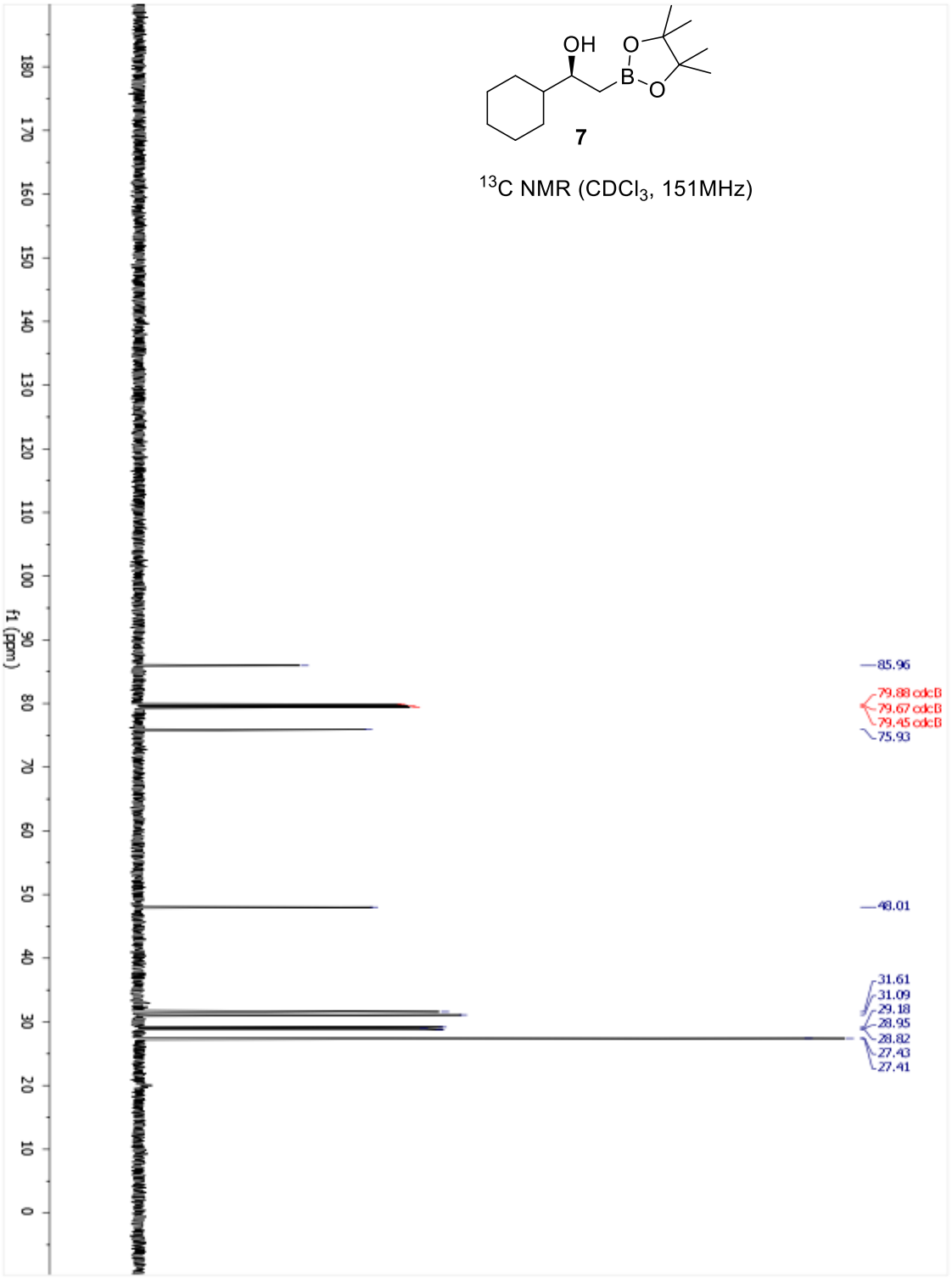
5

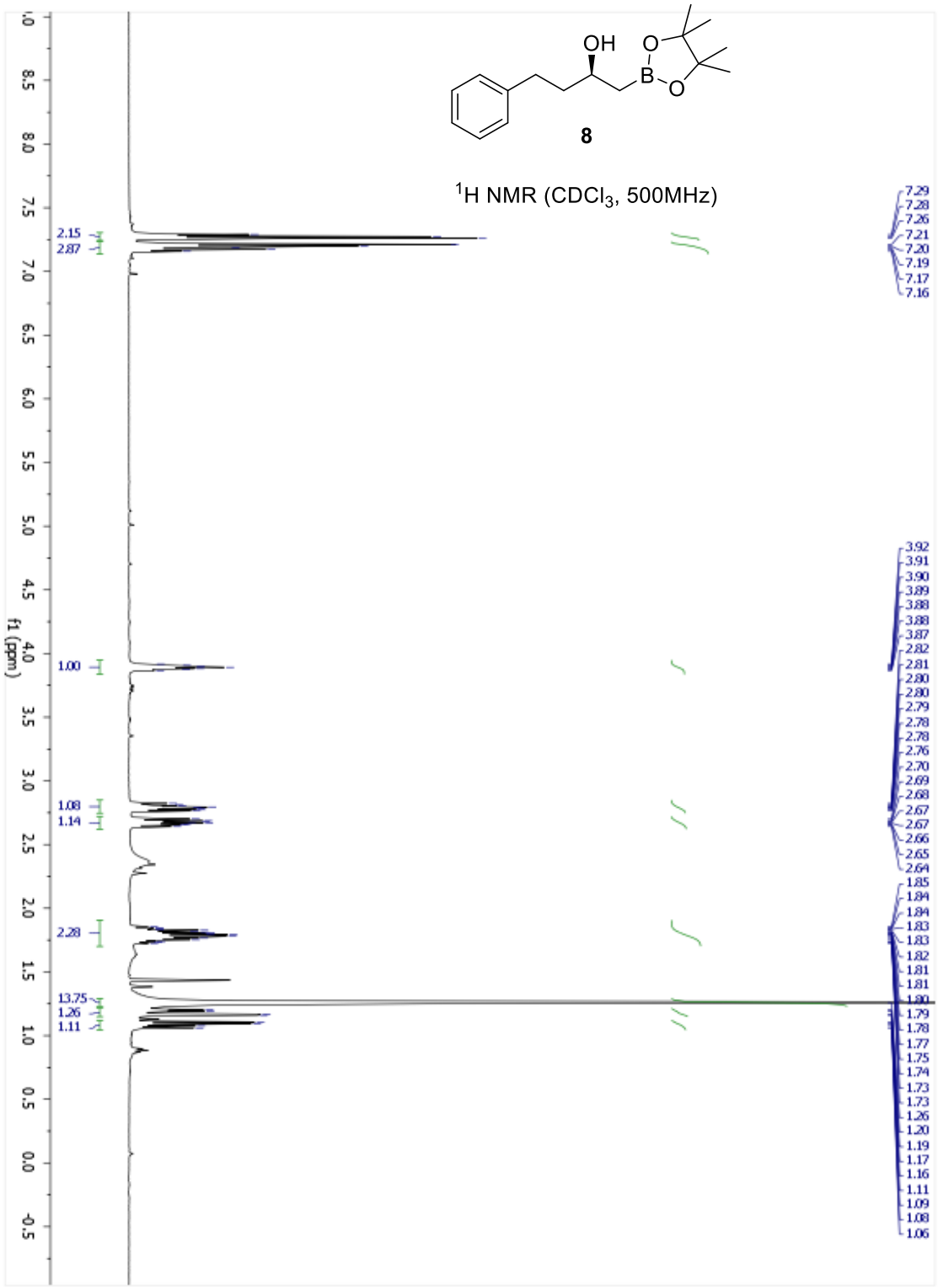
^{13}C NMR ($CDCl_3$, 151MHz)

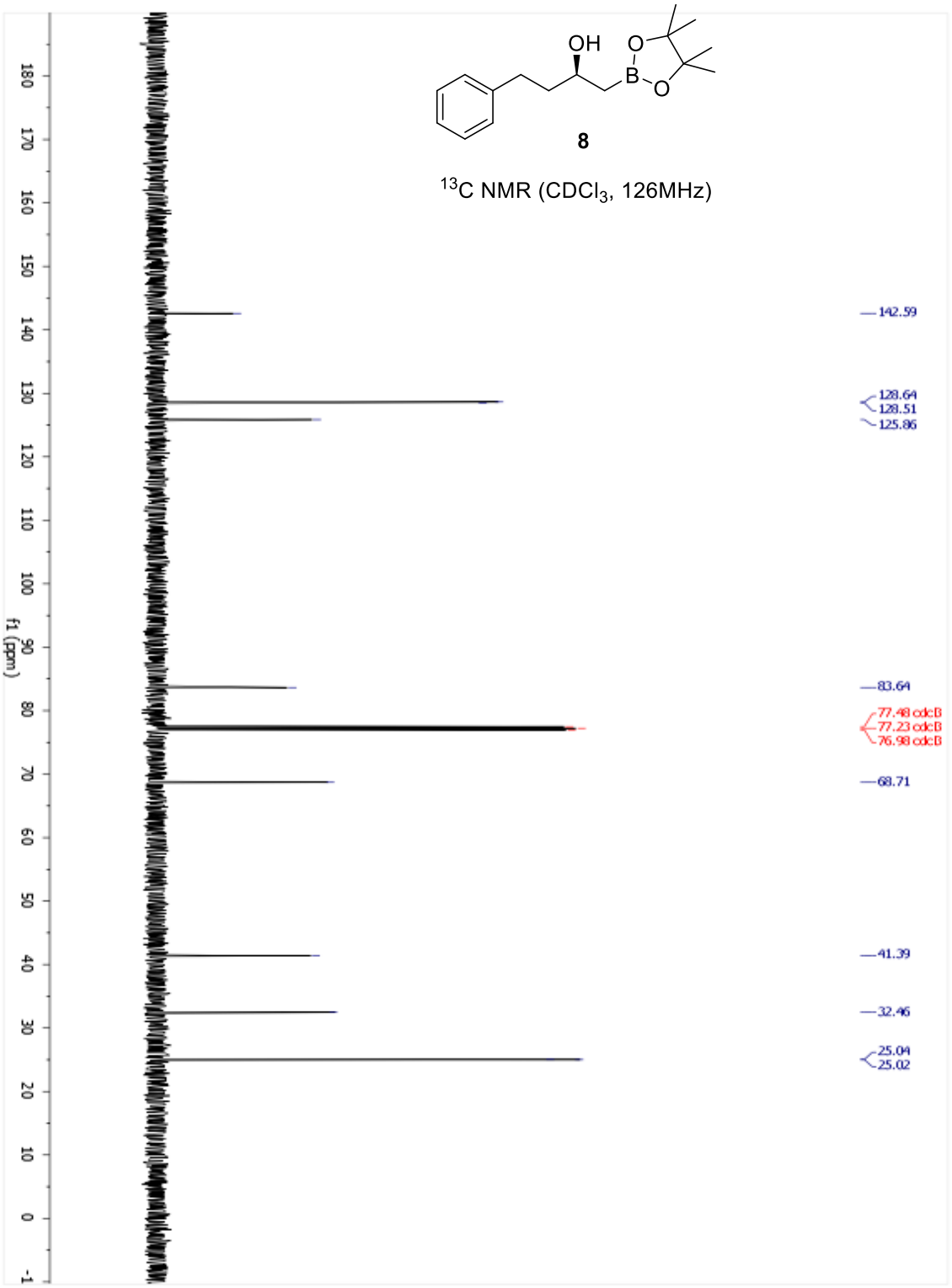

OH
O
B
O
$C_{12}H_{25}$
6
^{1}H NMR ($CDCl_3$, 600MHz)
f1 (ppm)
7.26
3.84
3.84
3.83
3.82
3.82
2.24
1.48
1.48
1.48
1.47
1.42
1.41
1.41
1.40
1.39
1.39
1.25
1.14
1.14
1.12
1.11
1.03
1.02
1.01
0.99
0.88
0.87
0.86
1.00
0.99
1.16
2.23
30.56
1.36
1.20
2.50

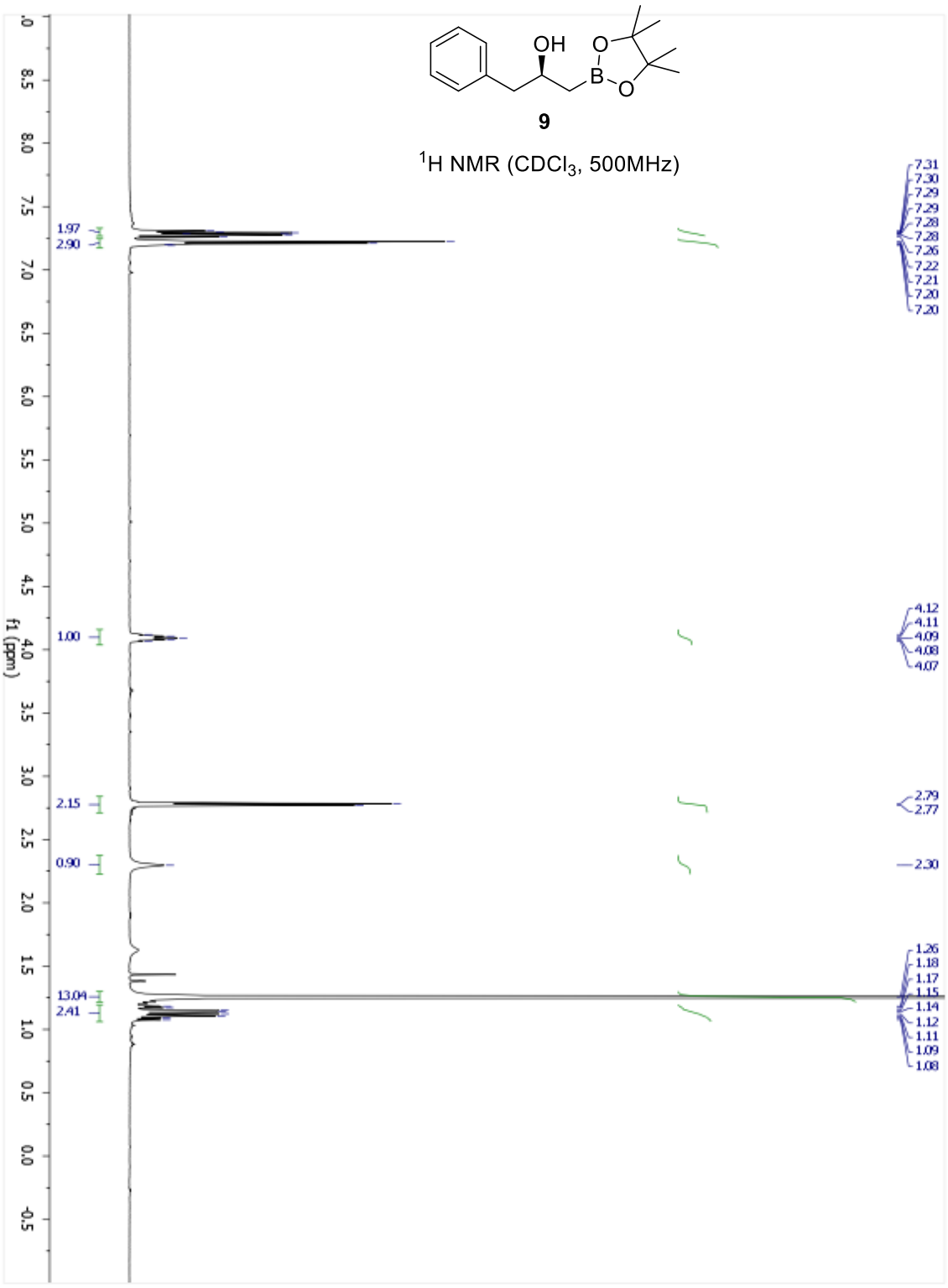

OH
O
B
O
$C_{12}H_{25}$
6
^{13}C NMR ($CDCl_3$, 151MHz)
f1 (ppm)
83.53
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
69.36
39.78
32.13
30.52
29.89
29.85
29.83
29.56
26.08
25.01
22.89
14.32

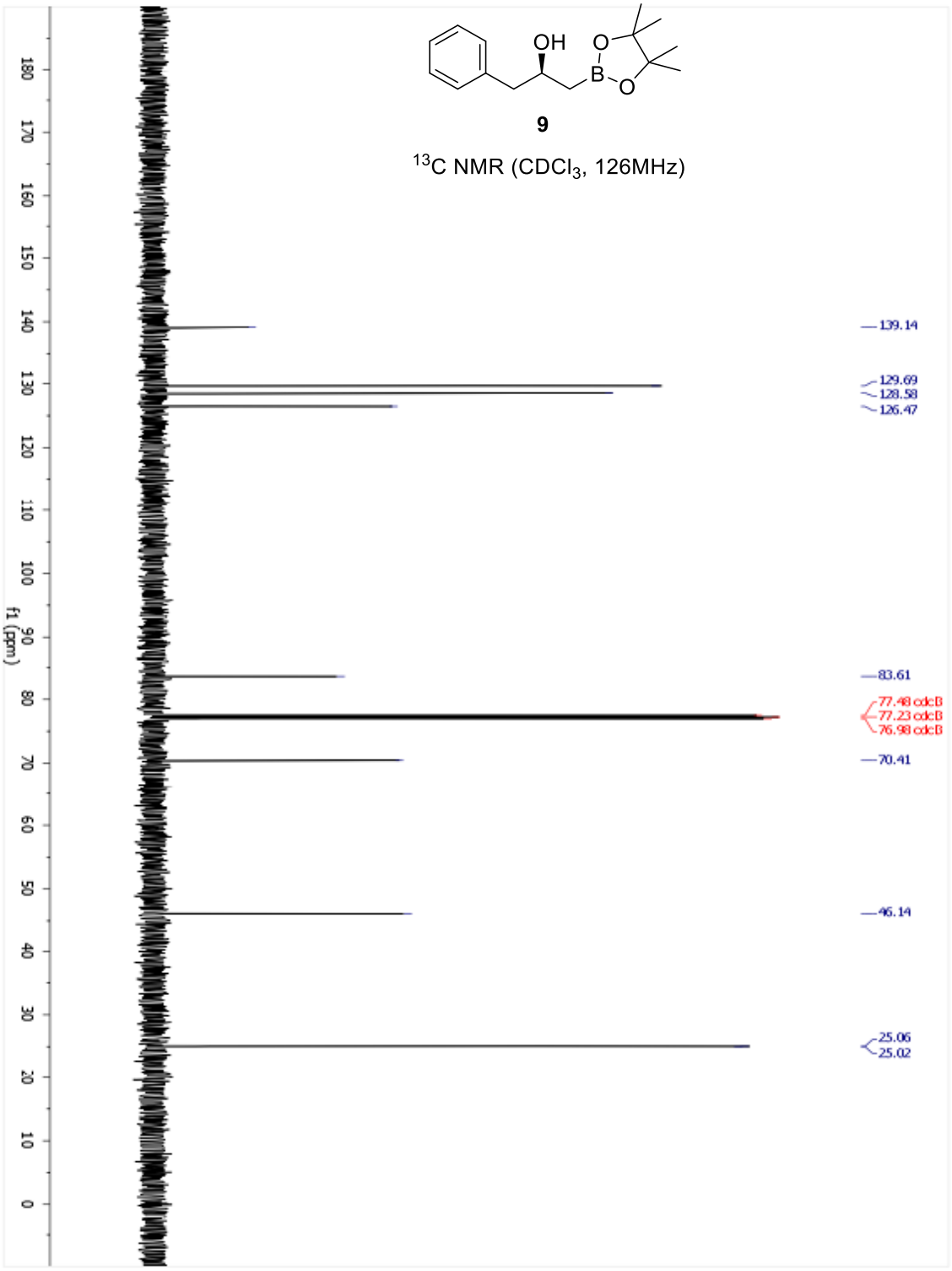

OH
O
B
O
7
1H NMR (CDCl3, 600MHz)
f1 (ppm)
7.26
3.60
3.59
3.58
3.58
3.57
1.88
1.86
1.72
1.65
1.63
1.24
1.17
1.14
1.13
1.12
1.11
1.10
1.10
1.08
1.07
1.01
1.00
0.99
0.97
0.95
0.94
0.93
0.92
0.91
0.90
0.76
1.12
2.07
2.00
14.72
2.01
2.89

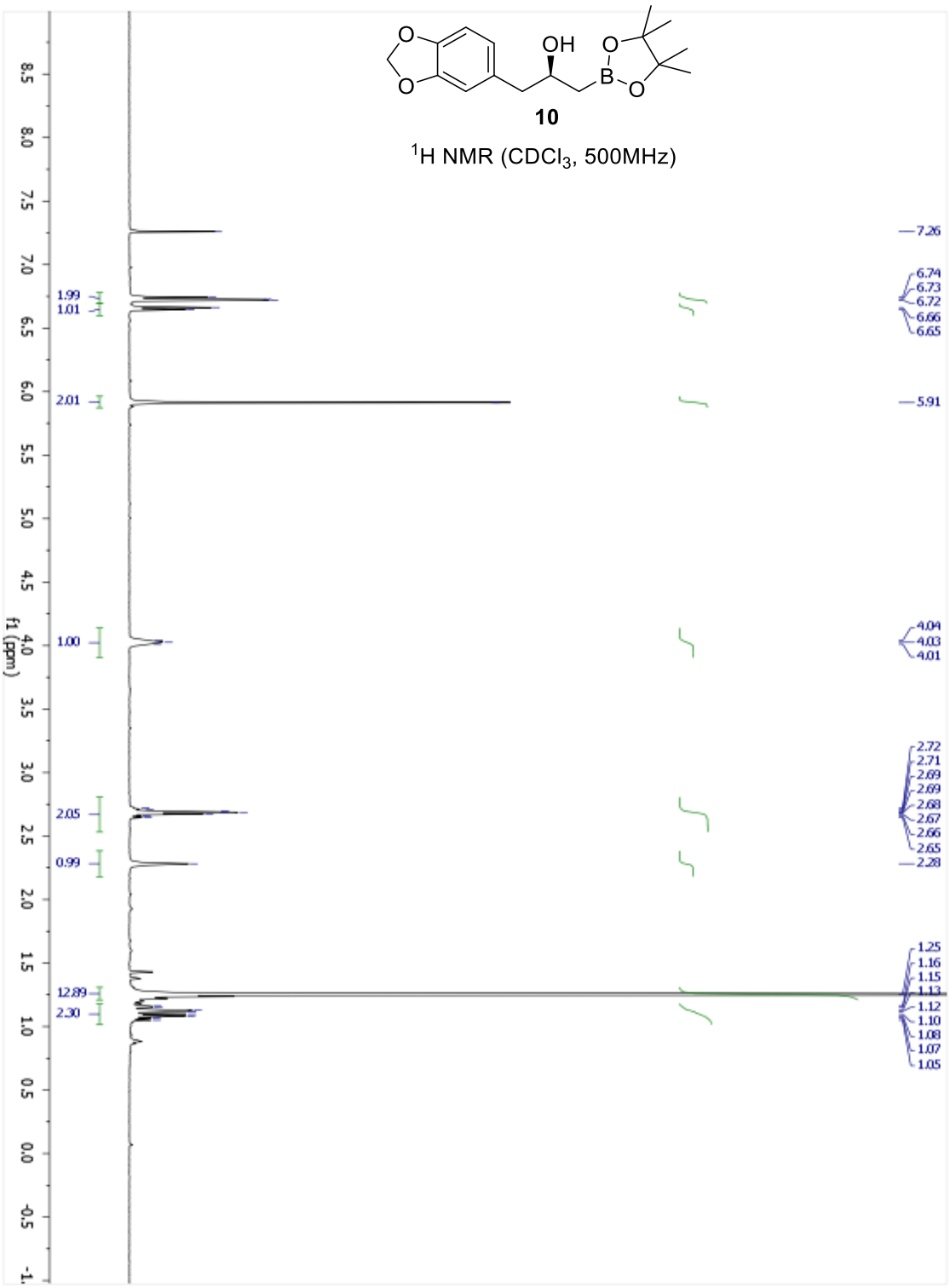

OH
O
B
O
7
^{13}C NMR ($CDCl_3$, 151MHz)
f1 (ppm)
85.96
79.88 cdcl3
79.67 cdcl3
79.45 cdcl3
75.93
48.01
31.61
31.09
29.18
28.95
28.82
27.43
27.41

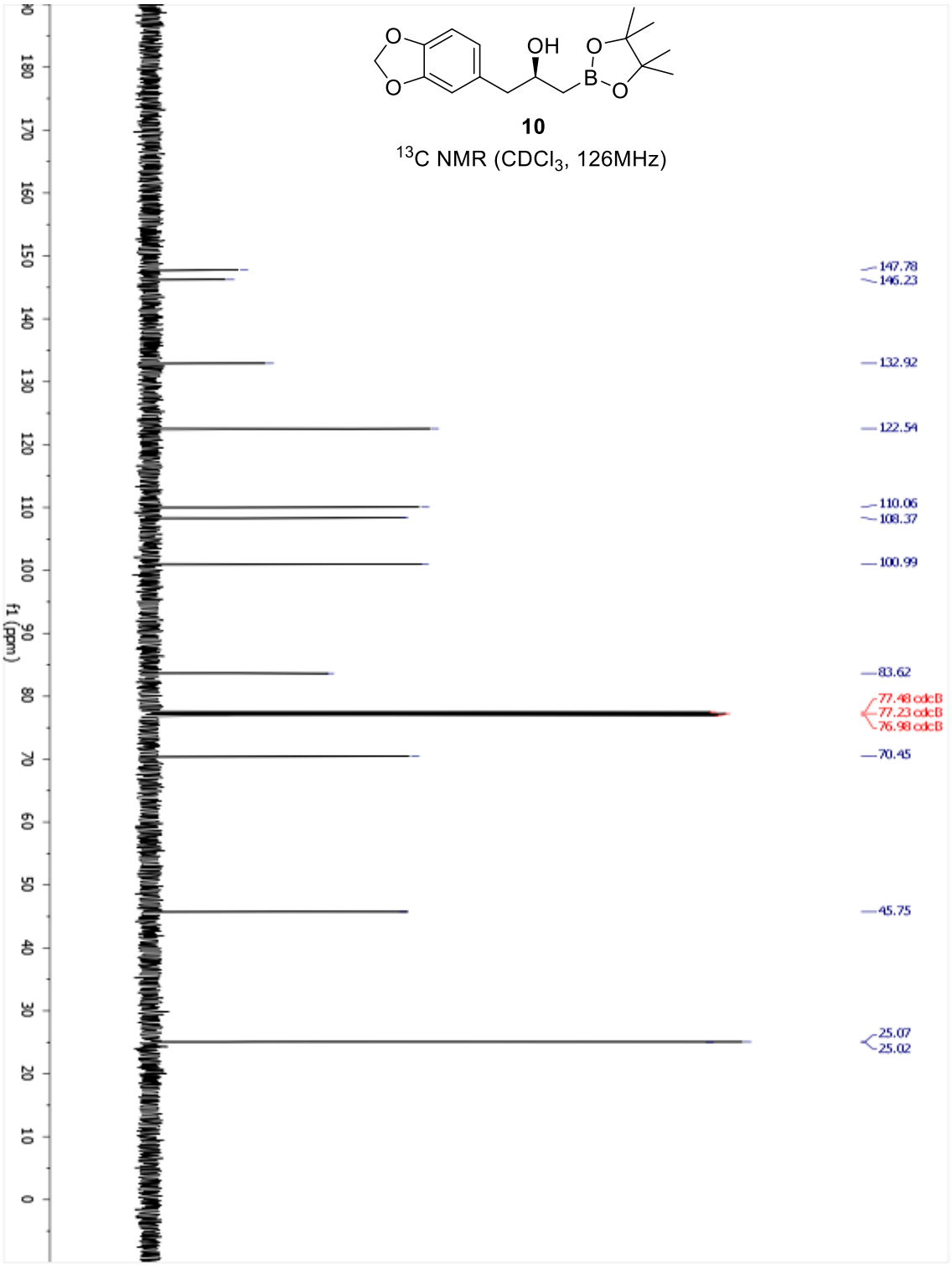

OH
O
B
O
8
1H NMR (CDCl3, 500MHz)
f1 (ppm)
2.15
2.87
1.00
1.08
1.14
2.28
13.75
1.26
1.11
7.29
7.28
7.26
7.21
7.20
7.19
7.17
7.16
3.92
3.91
3.90
3.89
3.88
3.88
3.87
2.82
2.81
2.80
2.80
2.79
2.78
2.78
2.76
2.70
2.69
2.68
2.67
2.67
2.66
2.65
2.64
1.85
1.84
1.84
1.83
1.83
1.82
1.81
1.81
1.80
1.79
1.78
1.77
1.75
1.74
1.73
1.73
1.26
1.20
1.19
1.17
1.16
1.11
1.09
1.08
1.06


OH
O
B
O
8
13C NMR (CDCl3, 126MHz)
142.59
128.64
128.51
125.86
83.64
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
68.71
41.39
32.46
25.04
25.02
f1 (ppm)


OH
O
B
O
9
1H NMR (CDCl3, 500MHz)
f1 (ppm)
1.97
2.90
1.00
2.15
0.90
13.04
2.41
7.31
7.30
7.29
7.29
7.28
7.28
7.26
7.22
7.21
7.20
7.20
4.12
4.11
4.09
4.08
4.07
2.79
2.77
2.30
1.26
1.18
1.17
1.15
1.14
1.12
1.11
1.09
1.08

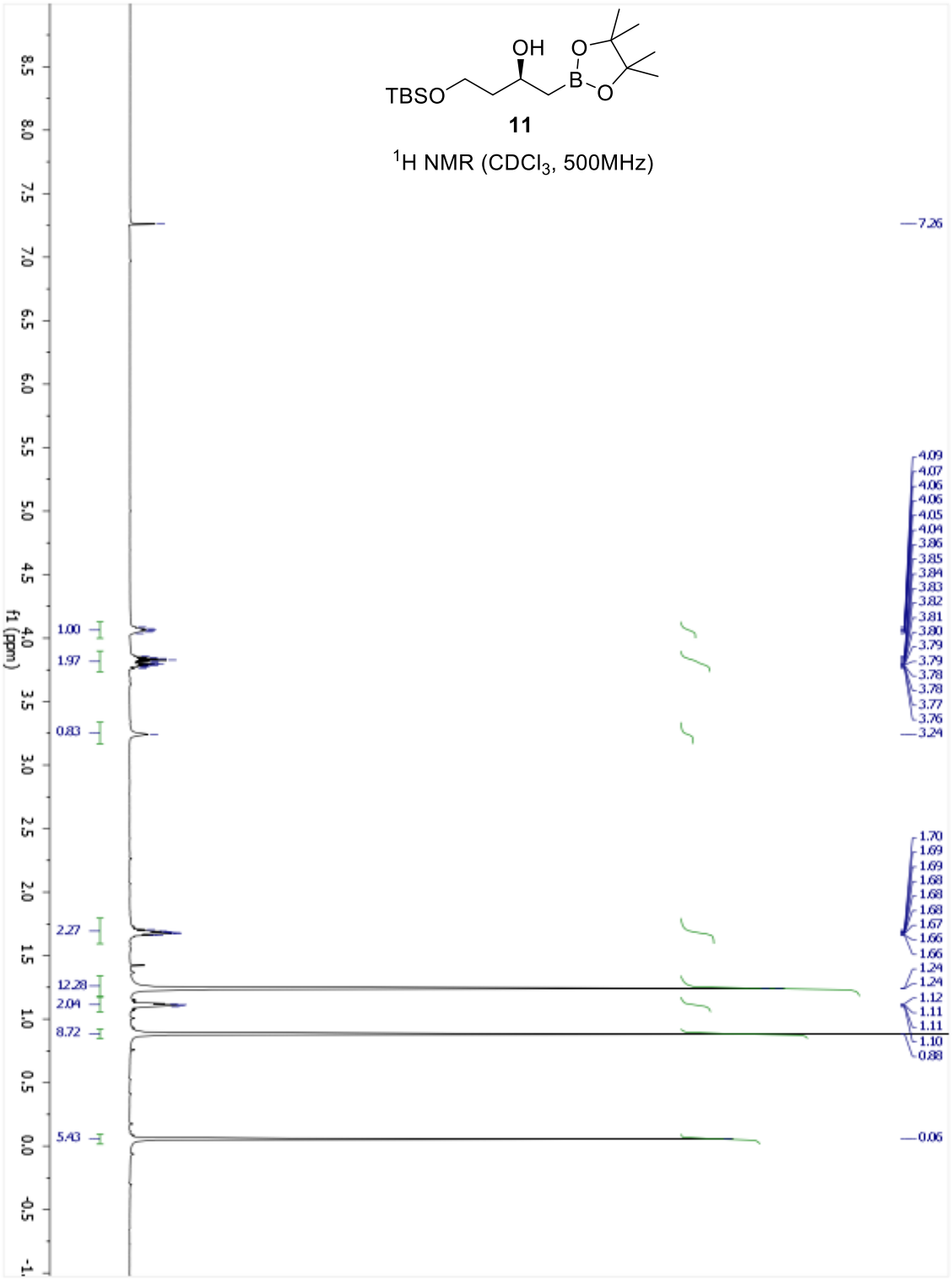

OH
O
B
O
9
13C NMR (CDCl3, 126MHz)
f1 (ppm)
139.14
129.69
128.58
126.47
83.61
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
70.41
46.14
25.06
25.02

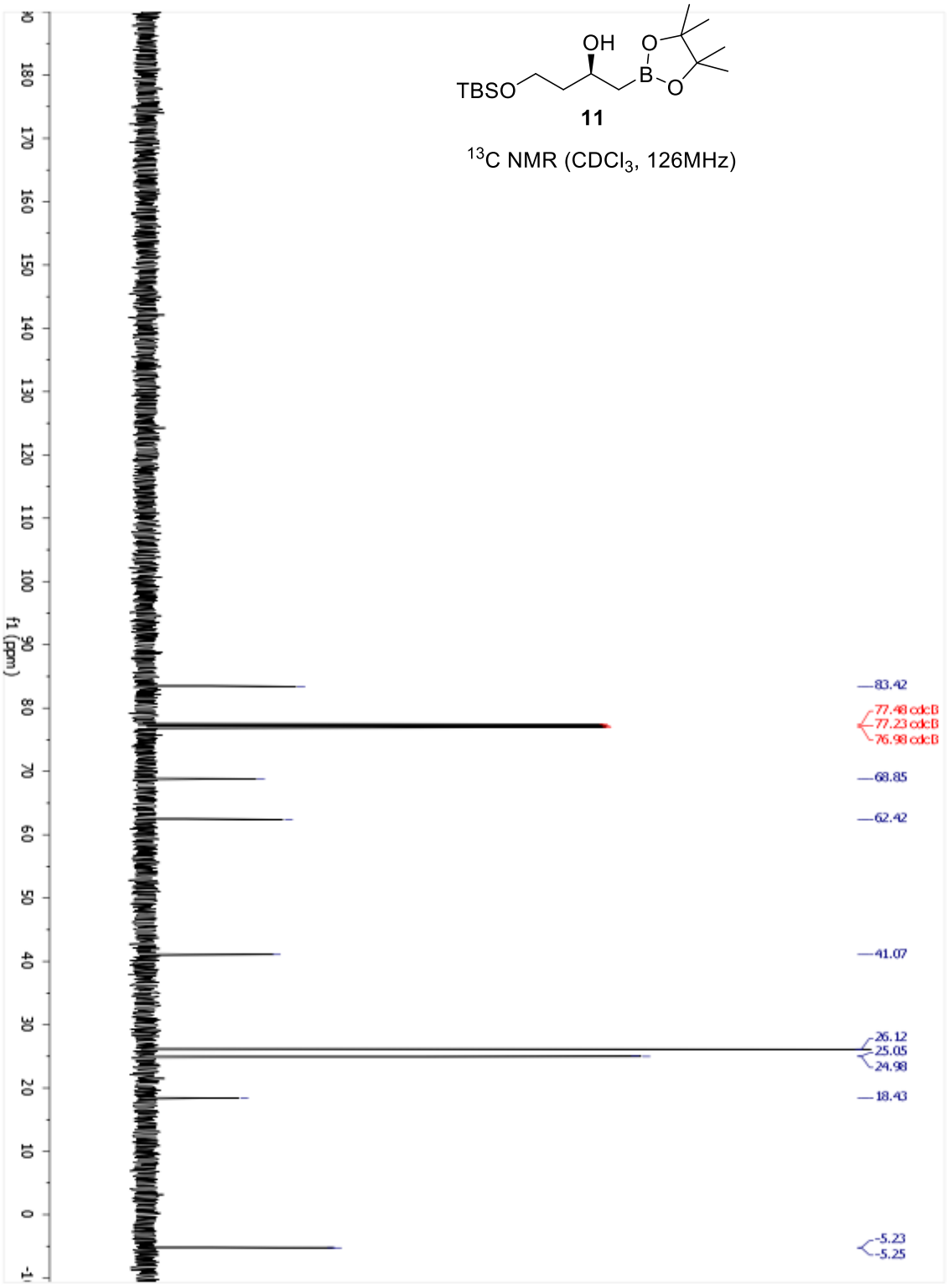

O
O
OH
O
B
O
10
1H NMR (CDCl3, 500MHz)
f1 (ppm)
1.99
1.01
2.01
1.00
2.05
0.99
12.89
2.30
7.26
6.74
6.73
6.72
6.66
6.65
5.91
4.04
4.03
4.01
2.72
2.71
2.69
2.69
2.68
2.67
2.66
2.65
2.28
1.25
1.16
1.15
1.13
1.12
1.10
1.08
1.07
1.05

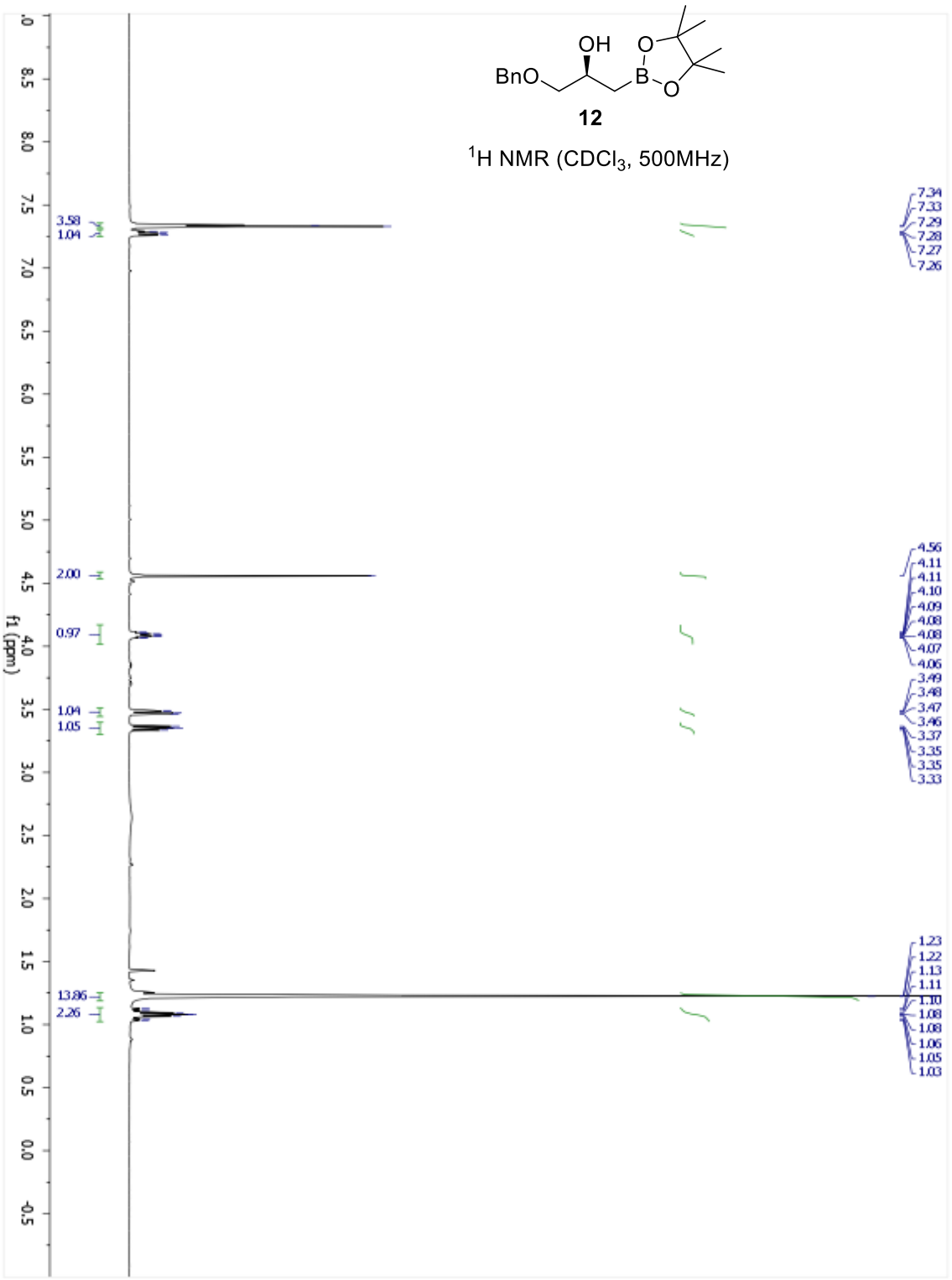


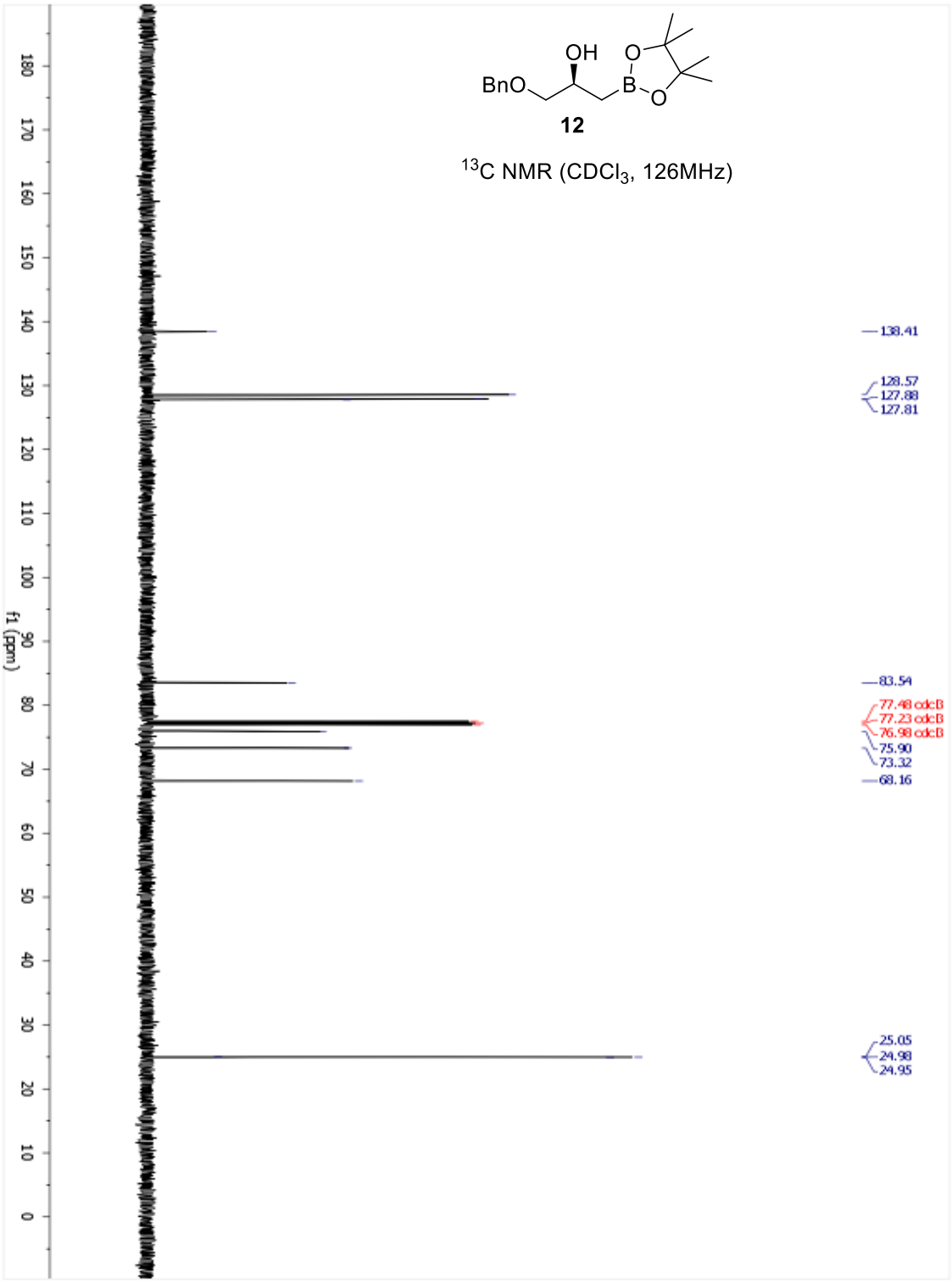
10

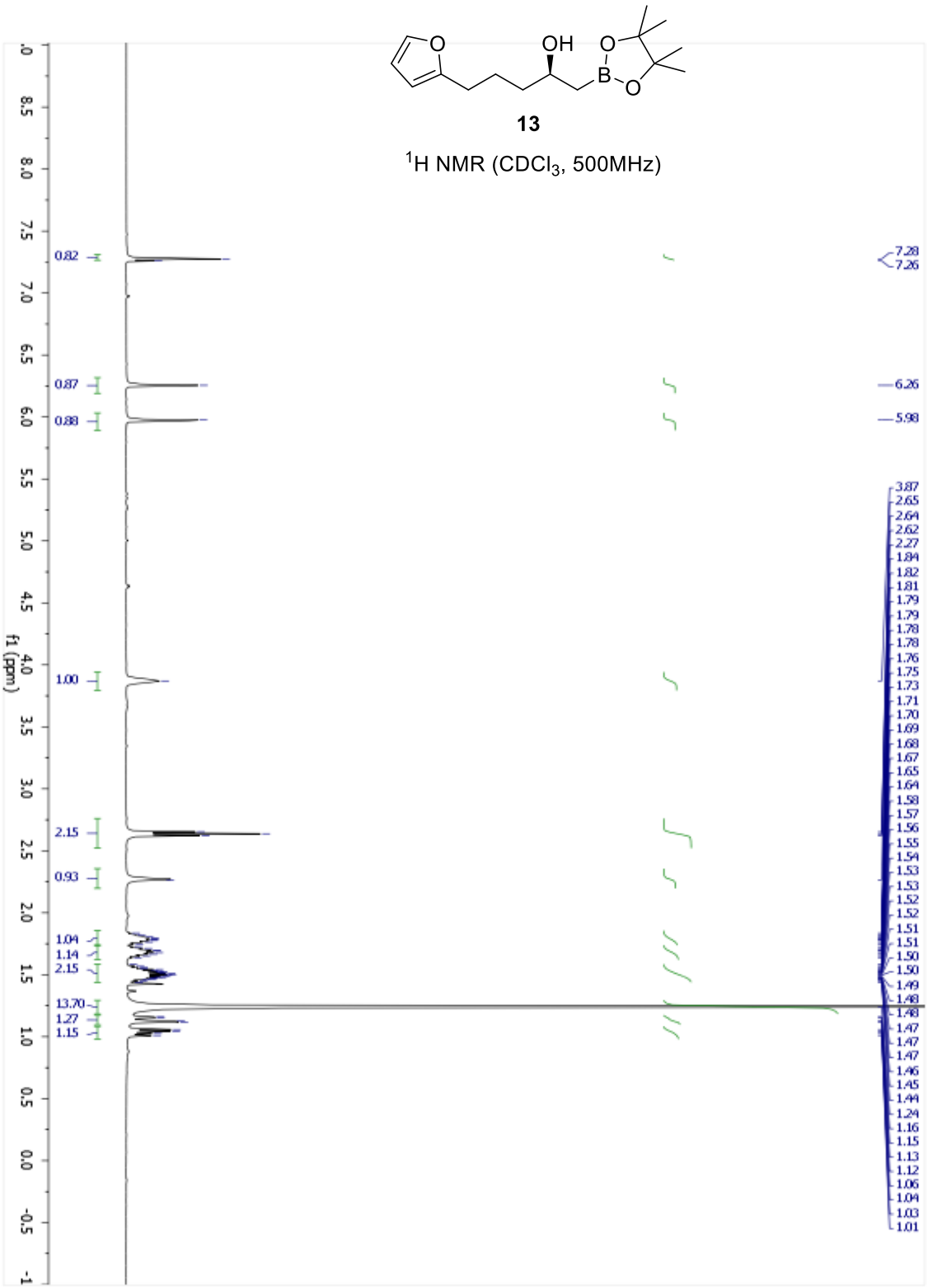
^{13}C NMR ($CDCl_3$, 126MHz)

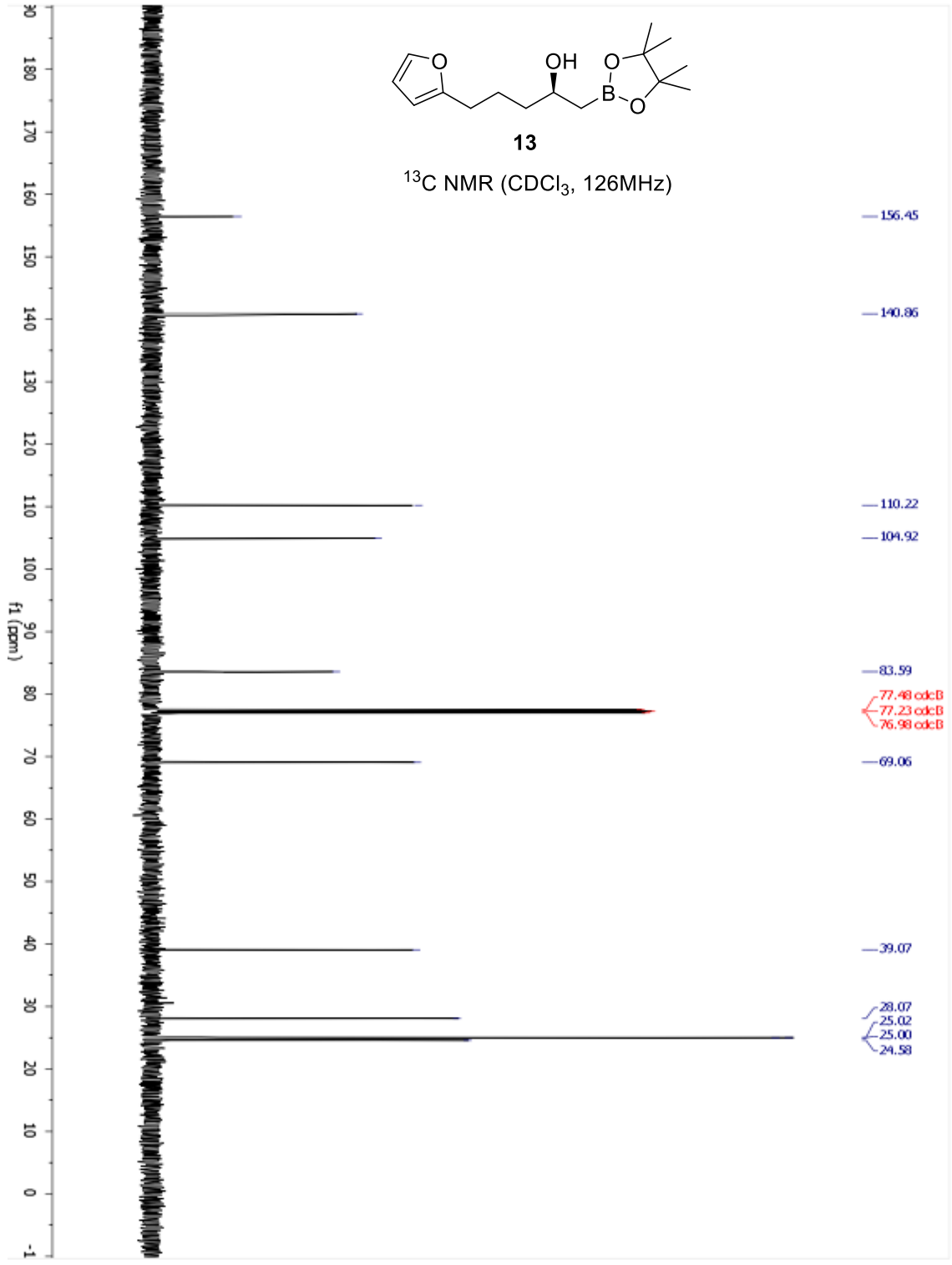

OH
O
B
O
TBSO
11
1H NMR (CDCl3, 500MHz)
f1 (ppm)
7.26
4.09
4.07
4.06
4.06
4.05
4.04
3.86
3.85
3.84
3.83
3.82
3.81
3.80
3.79
3.79
3.78
3.78
3.77
3.76
3.24
1.70
1.69
1.69
1.68
1.68
1.68
1.67
1.66
1.66
1.24
1.24
1.12
1.11
1.11
1.10
0.88
0.06
1.00
1.97
0.83
2.27
12.28
2.04
8.72
5.43

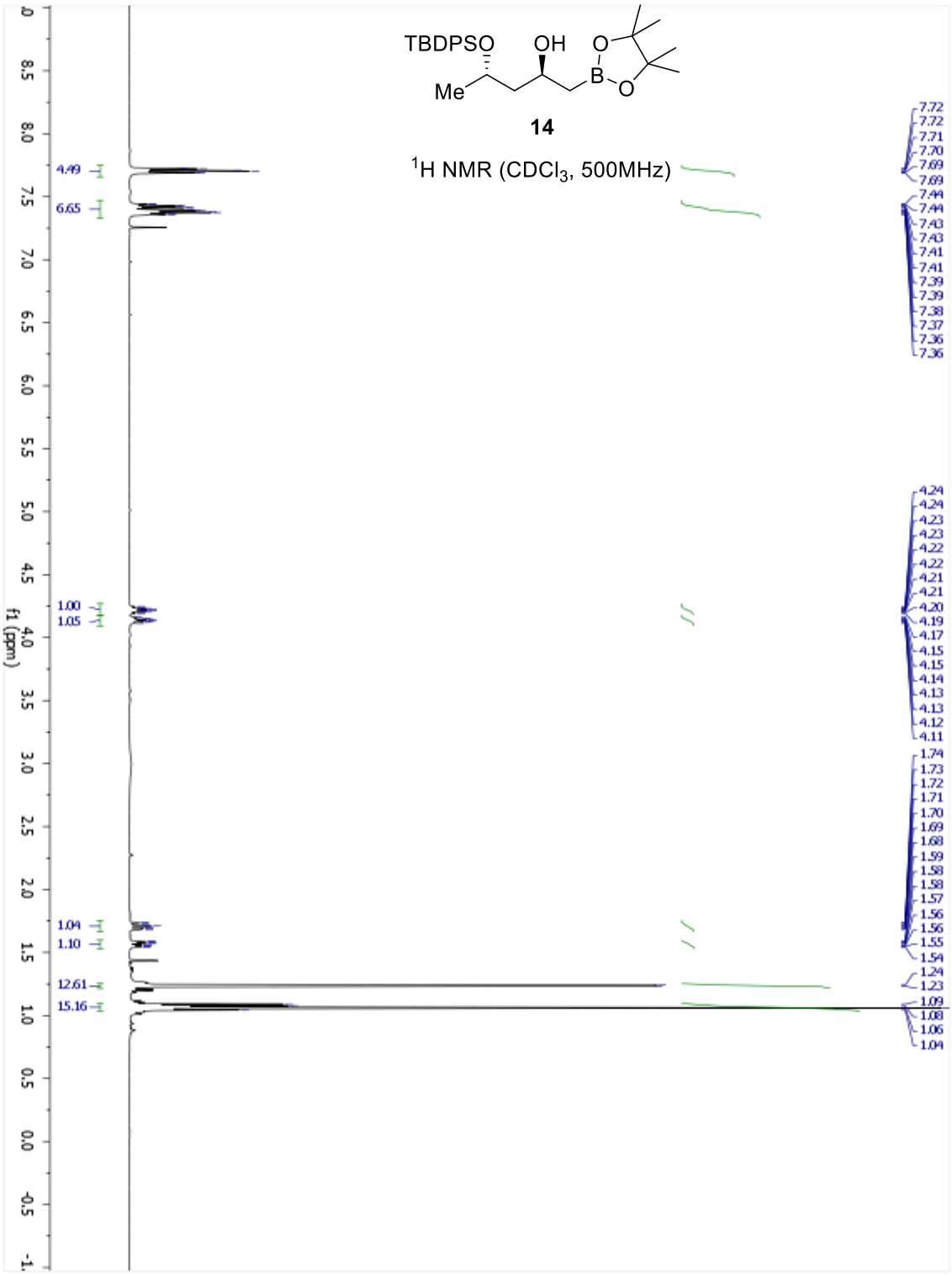

OH
O
B
O
TBSO
11
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
83.42
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
68.85
62.42
41.07
26.12
25.05
24.98
18.43
-5.23
-5.25

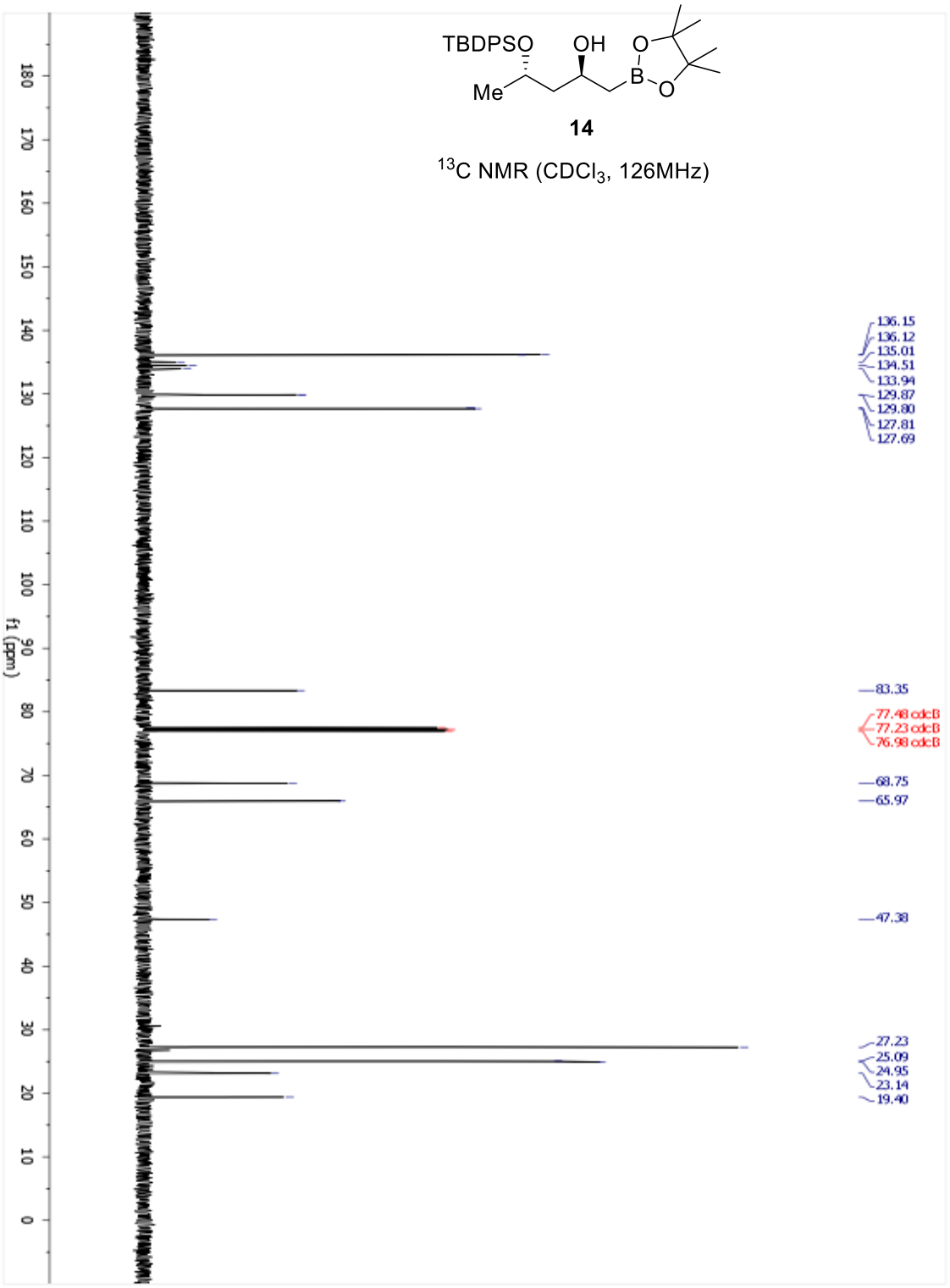

OH
O
BnO
B
O
12
1H NMR (CDCl3, 500MHz)
f1 (ppm)
3.58
1.04
2.00
0.97
1.04
1.05
13.86
2.26
7.34
7.33
7.29
7.28
7.27
7.26
4.56
4.11
4.11
4.10
4.09
4.08
4.08
4.07
4.06
3.49
3.48
3.47
3.46
3.37
3.35
3.35
3.33
1.23
1.22
1.13
1.11
1.10
1.08
1.08
1.06
1.05
1.03

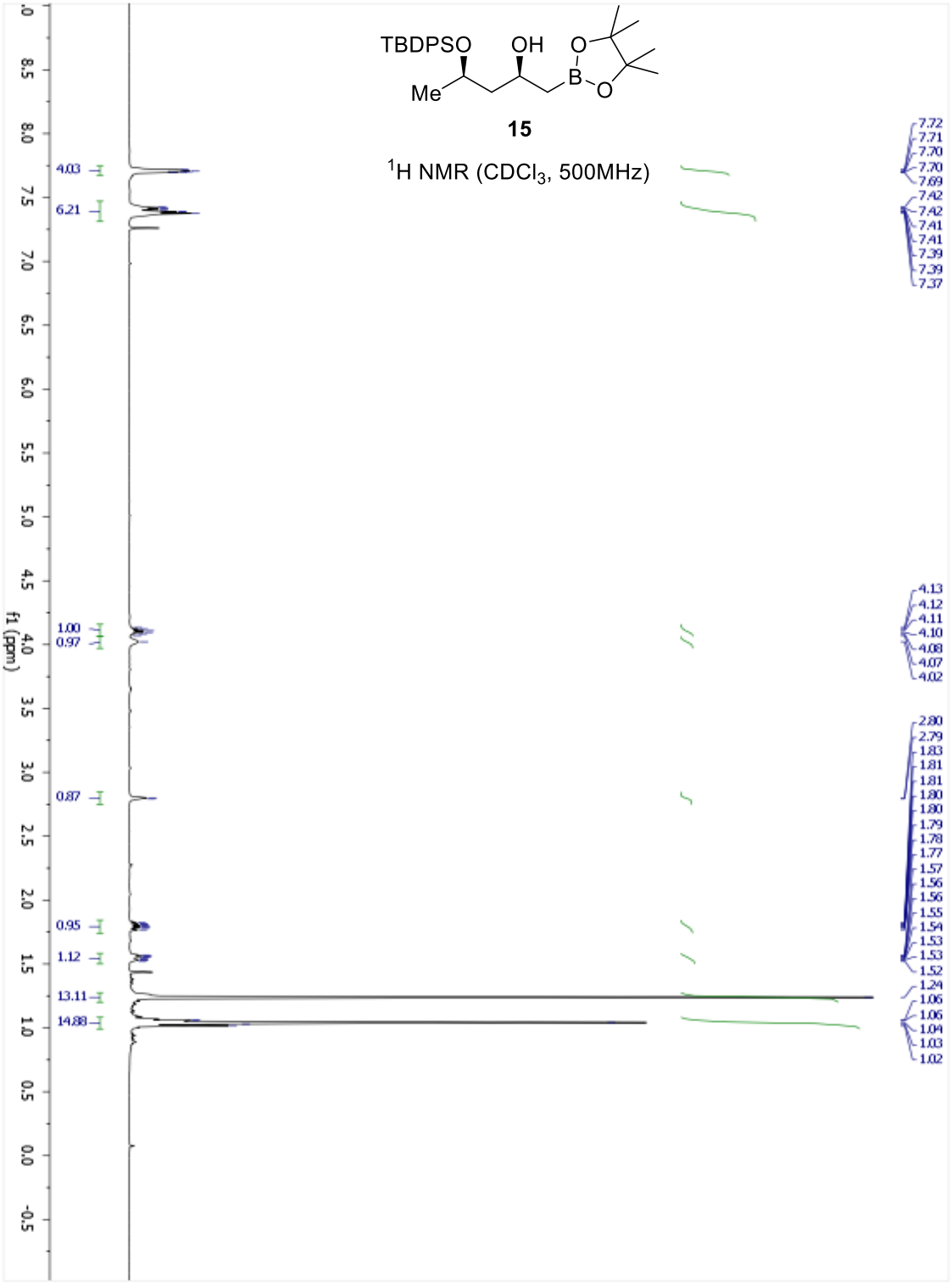

OH
O
BnO
B
O
12
^{13}C NMR ($CDCl_3$, 126MHz)
138.41
128.57
127.88
127.81
83.54
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
75.90
73.32
68.16
25.05
24.98
24.95
f1 (ppm)

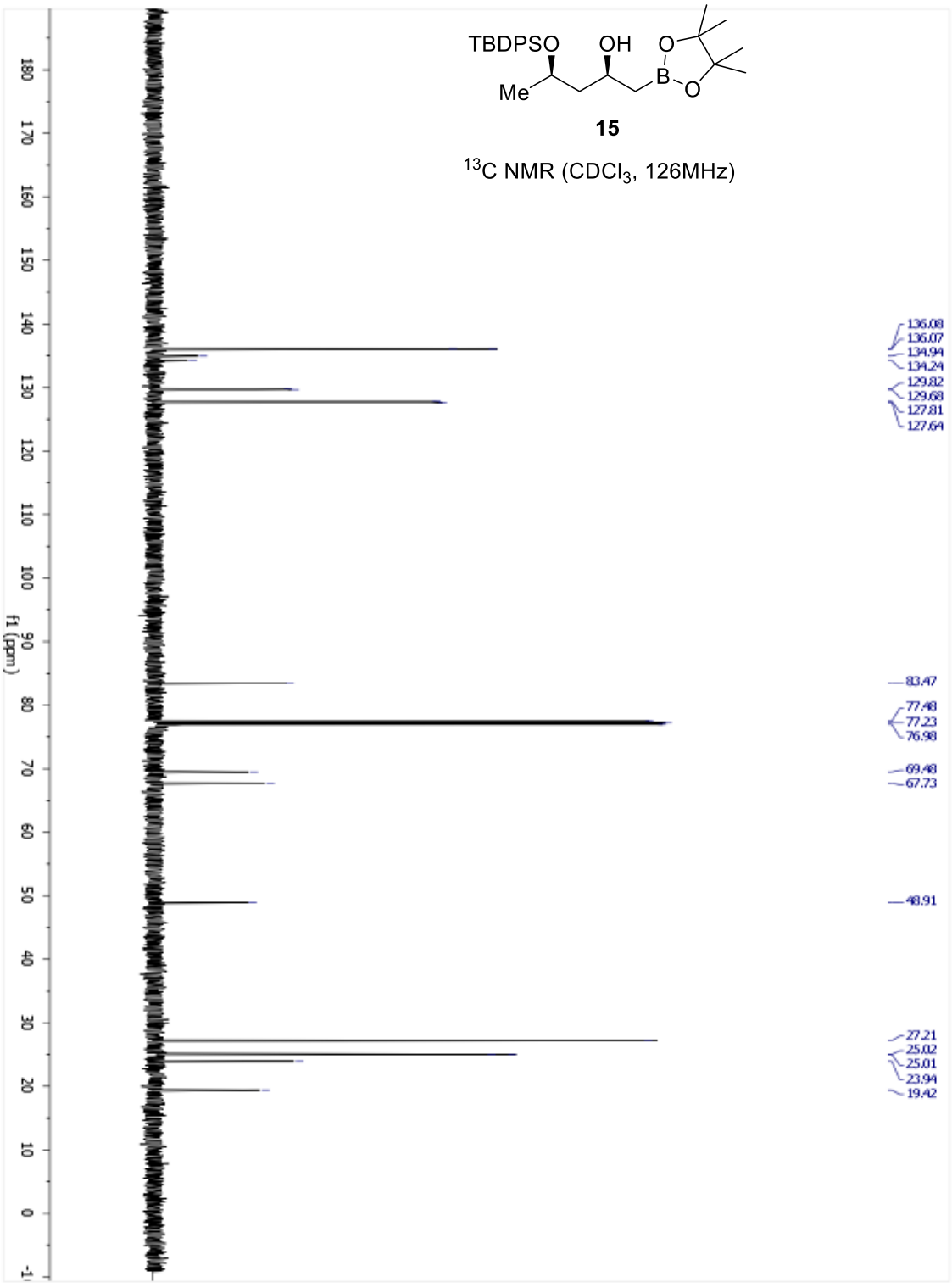

O
OH
O
B
O
13
1H NMR (CDCl3, 500MHz)
f1 (ppm)
0.82
0.87
0.88
1.00
2.15
0.93
1.04
1.14
2.15
13.70
1.27
1.15
7.28
7.26
6.26
5.98
3.87
2.65
2.64
2.62
2.27
1.84
1.82
1.81
1.79
1.79
1.78
1.78
1.76
1.75
1.73
1.71
1.70
1.69
1.68
1.67
1.65
1.64
1.58
1.57
1.56
1.55
1.54
1.53
1.53
1.52
1.52
1.51
1.51
1.50
1.50
1.49
1.48
1.48
1.47
1.47
1.47
1.46
1.45
1.44
1.24
1.16
1.15
1.13
1.12
1.06
1.04
1.03
1.01

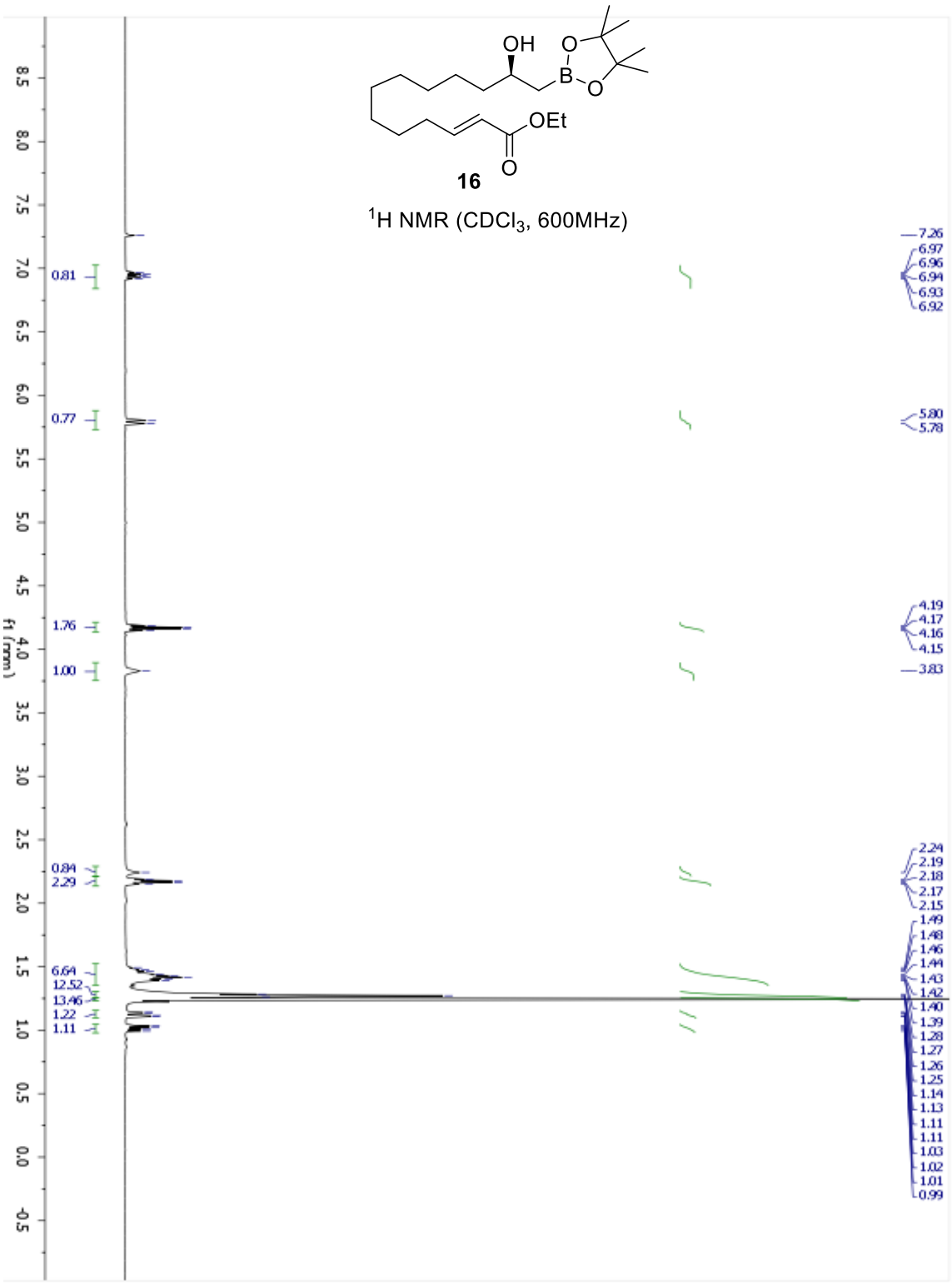

O
OH
O
B
O
13
13C NMR (CDCl3, 126MHz)
156.45
140.86
110.22
104.92
83.59
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
69.06
39.07
28.07
25.02
25.00
24.58
f1 (ppm)

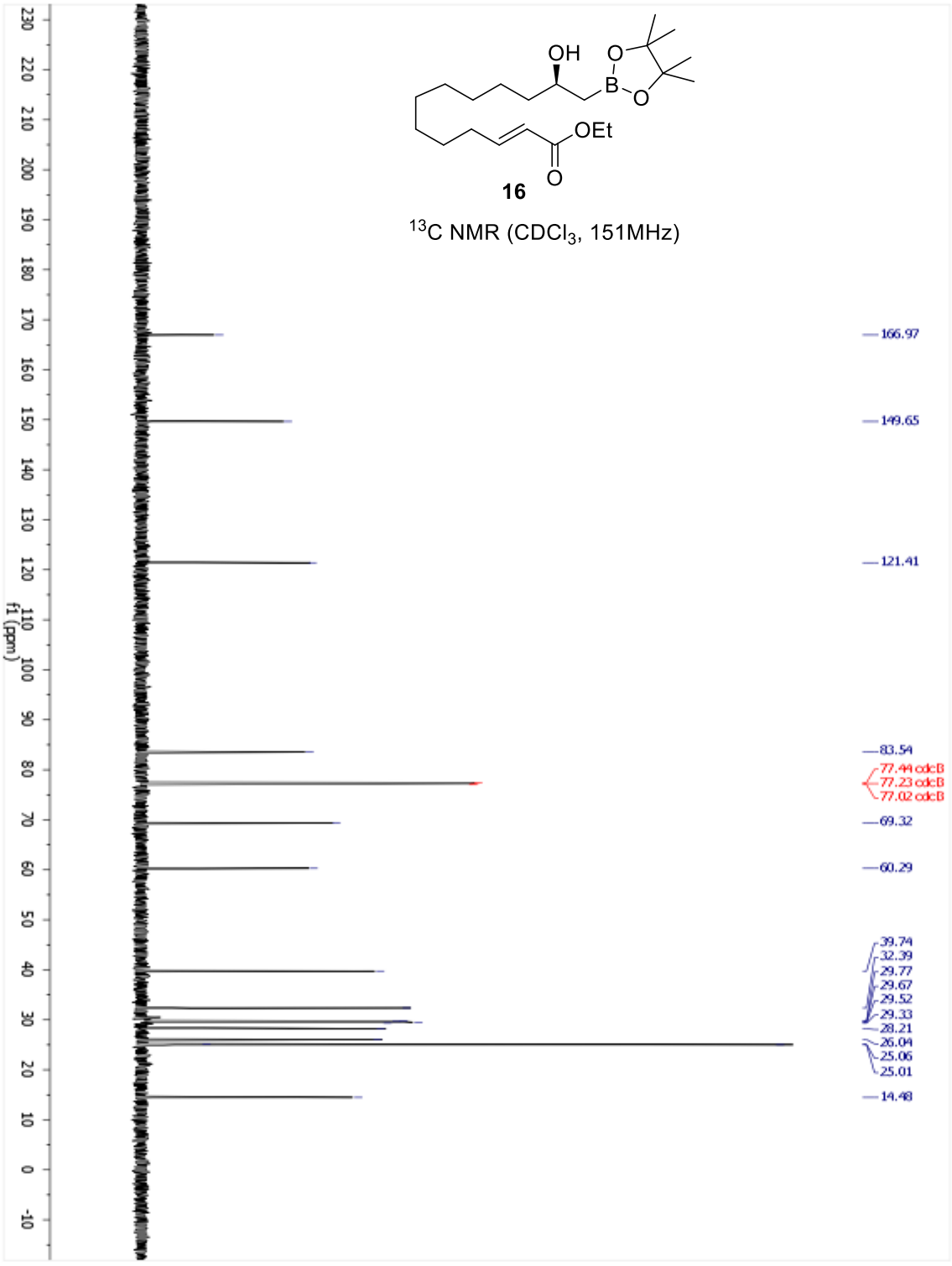

TBDPSO
OH
O
B
O
Me
14
^{1}H NMR ($CDCl_3$, 500MHz)
f1 (ppm)


TBDPSO
OH
O
B
O
Me
14
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
136.15
136.12
135.01
134.51
133.94
129.87
129.80
127.81
127.69
83.35
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
68.75
65.97
47.38
27.23
25.09
24.95
23.14
19.40


TBDPSO
OH
O
B
O
Me
15
1H NMR (CDCl3, 500MHz)
f1 (ppm)
4.03
6.21
1.00
0.97
0.87
0.95
1.12
13.11
14.88
7.72
7.71
7.70
7.70
7.69
7.42
7.42
7.41
7.41
7.39
7.39
7.37
4.13
4.12
4.11
4.10
4.08
4.07
4.02
2.80
2.79
1.83
1.81
1.81
1.80
1.80
1.79
1.78
1.77
1.57
1.56
1.56
1.55
1.54
1.53
1.53
1.52
1.24
1.06
1.06
1.04
1.03
1.02

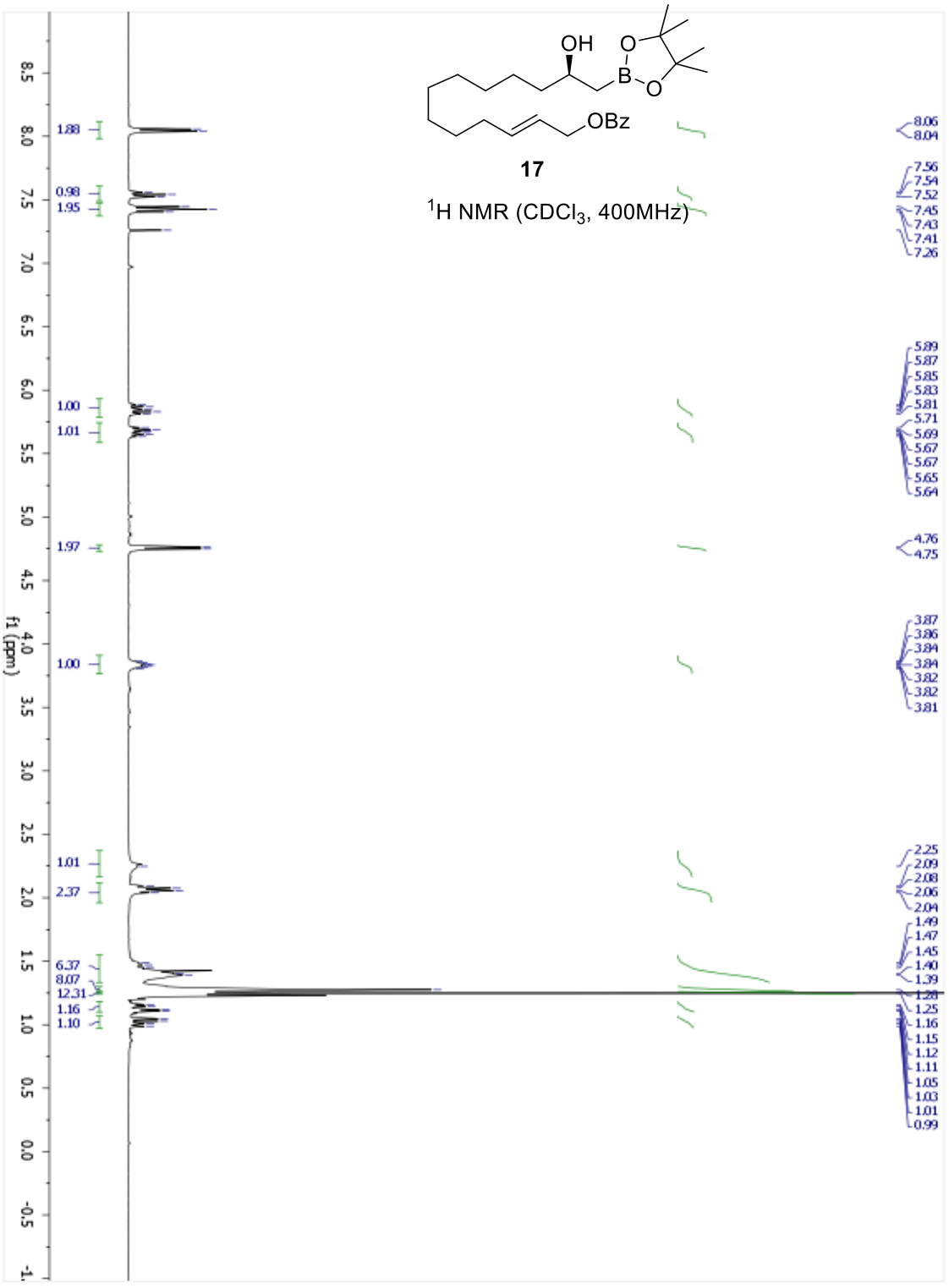

TBDPSO
OH
O
B
O
Me
O
15
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
136.08
136.07
134.94
134.24
129.82
129.68
127.81
127.64
83.47
77.48
77.23
76.98
69.48
67.73
48.91
27.21
25.02
25.01
23.94
19.42

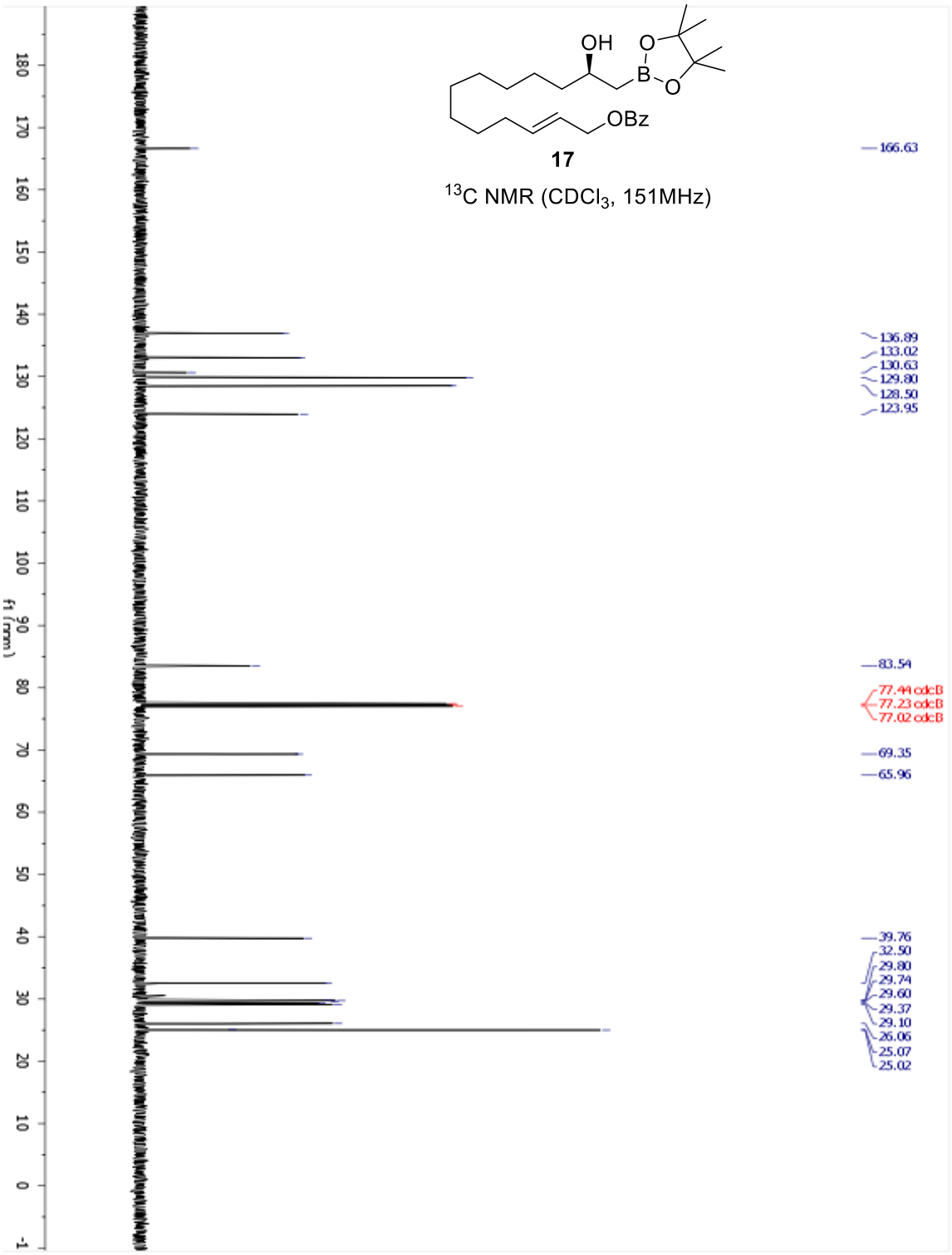

OH
O
B
O
OEt
O
16
1H NMR (CDCl3, 600MHz)
f1 (ppm)
0.81
0.77
1.76
1.00
0.89
2.29
6.69
12.52
13.46
1.22
1.11
7.26
6.97
6.96
6.94
6.93
6.92
5.80
5.78
4.19
4.17
4.16
4.15
3.83
2.24
2.19
2.18
2.17
2.15
1.49
1.48
1.46
1.44
1.43
1.42
1.40
1.39
1.28
1.27
1.26
1.25
1.14
1.13
1.11
1.11
1.03
1.02
1.01
0.99



16

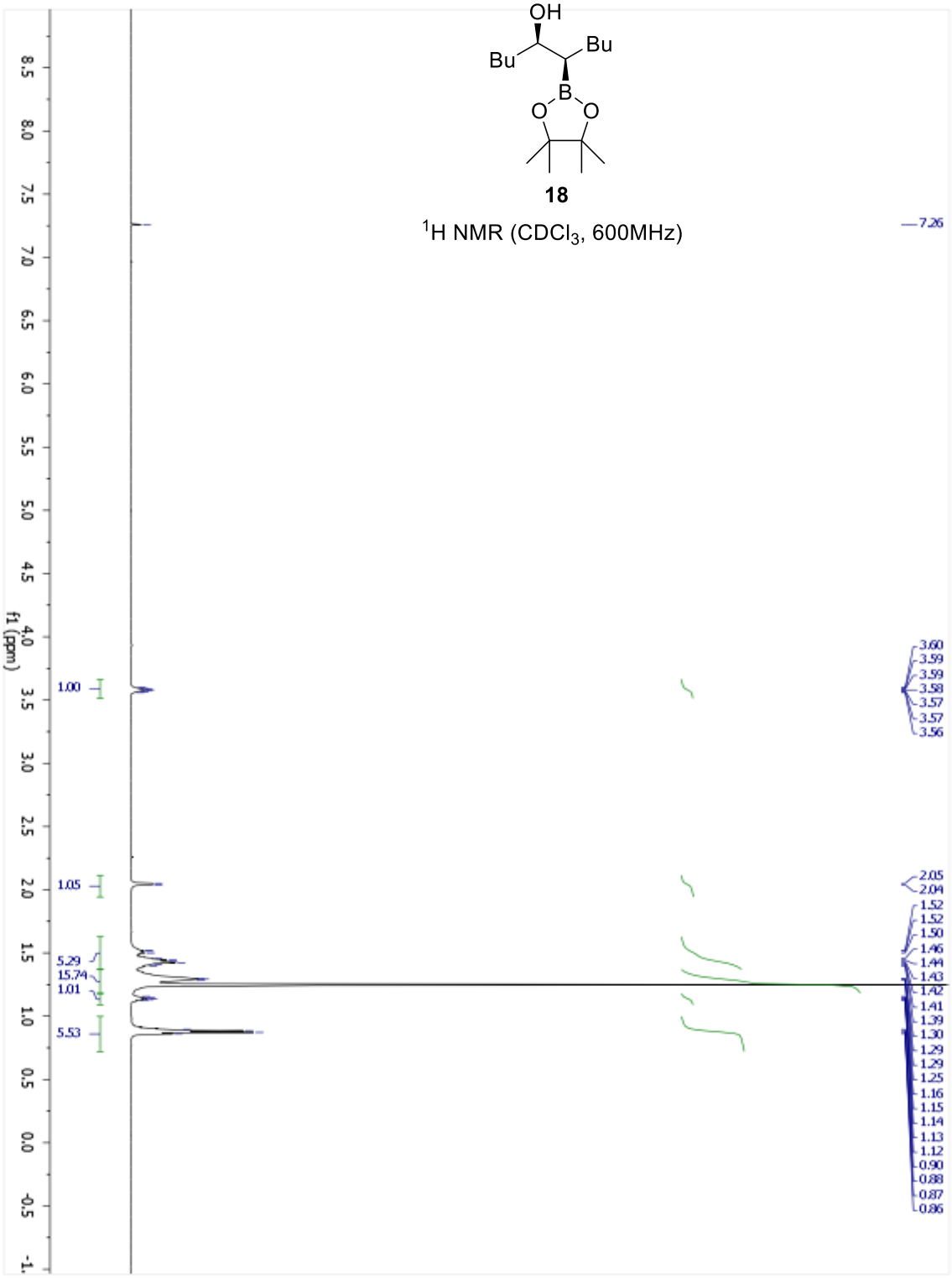
^{13}C NMR ($CDCl_3$, 151MHz)

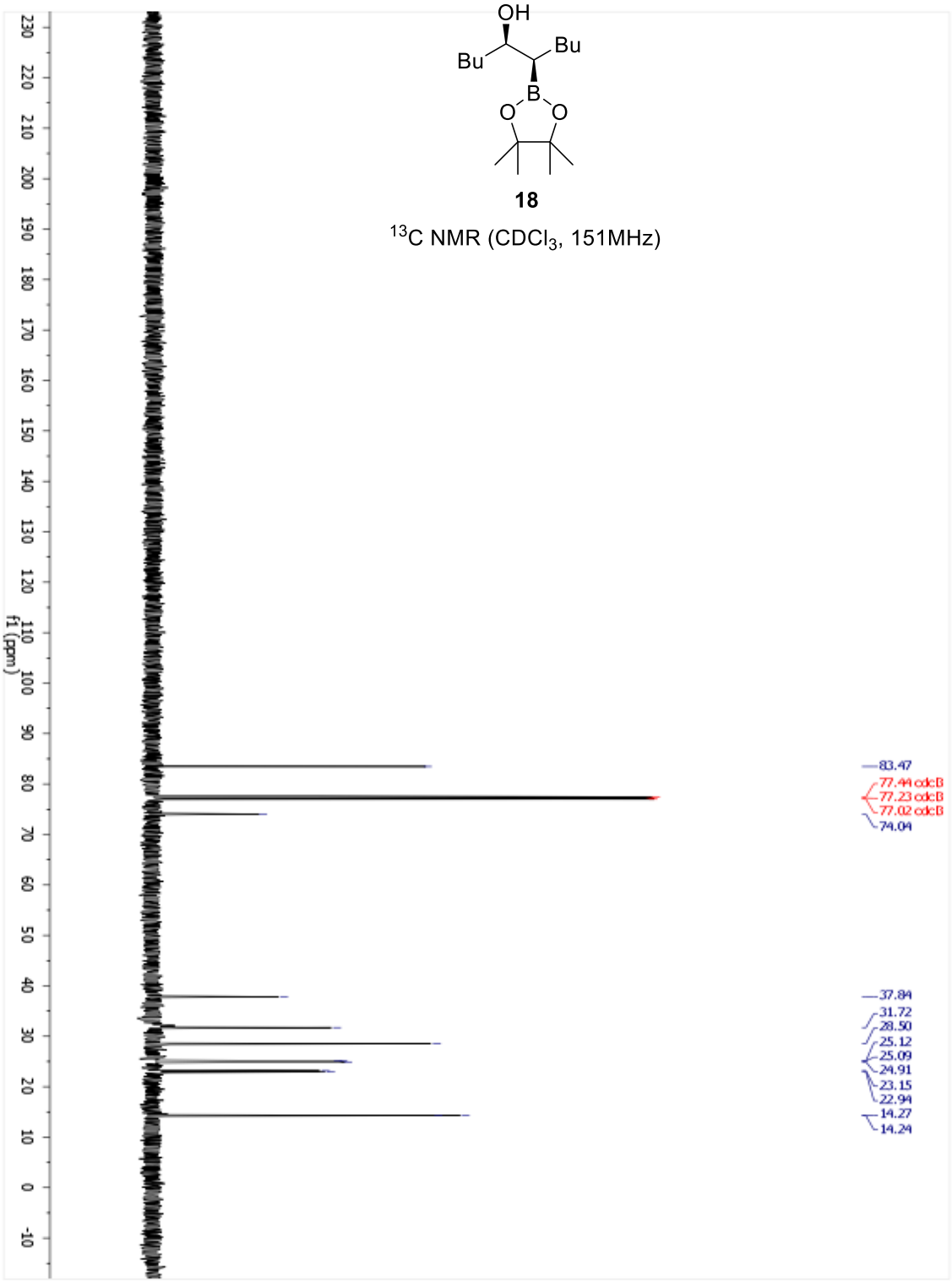

OH
O
B
O
OBz
17
^{1}H NMR ($CDCl_3$, 400MHz)
f1 (ppm)



17

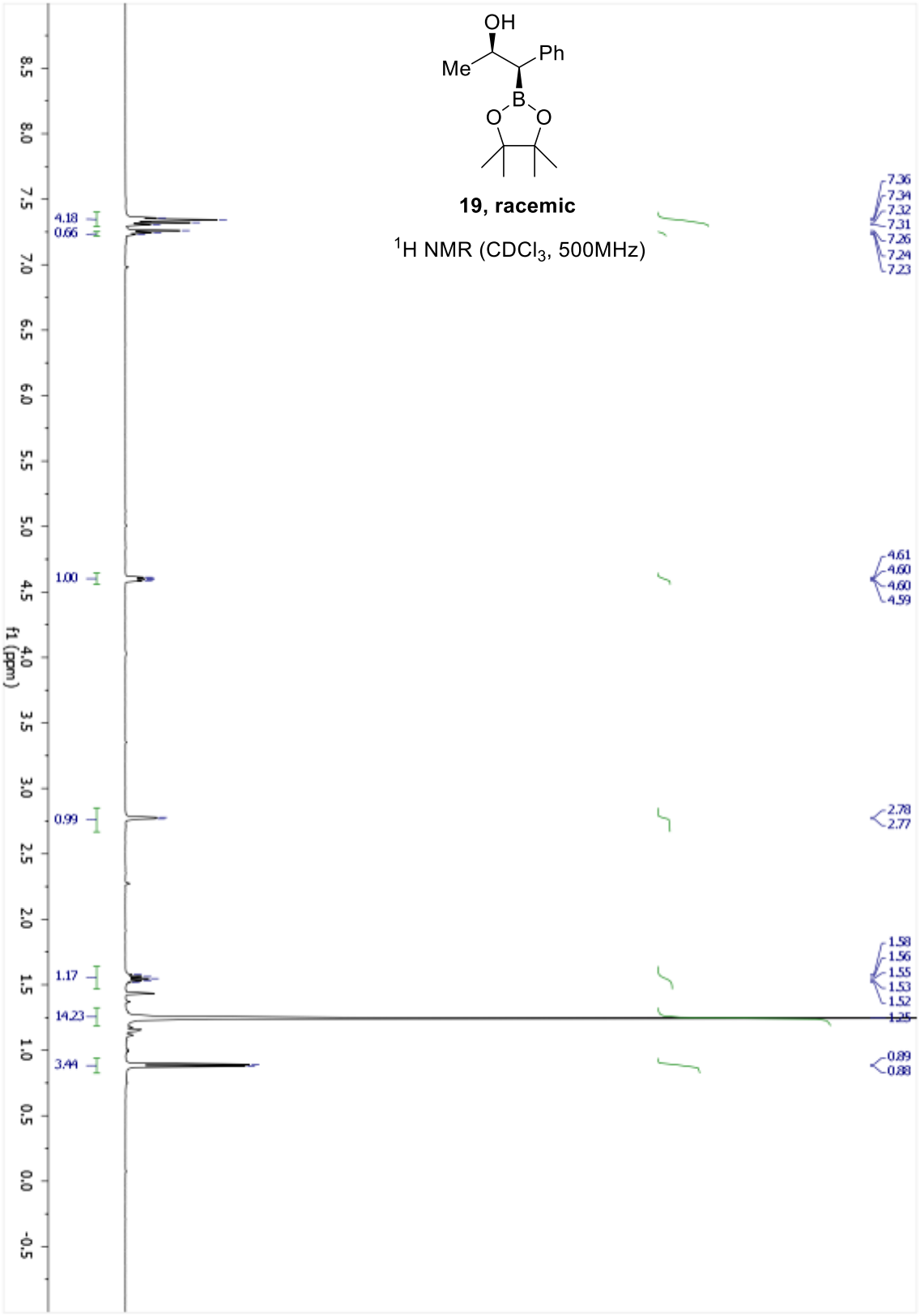
^{13}C NMR ($CDCl_3$, 151MHz)

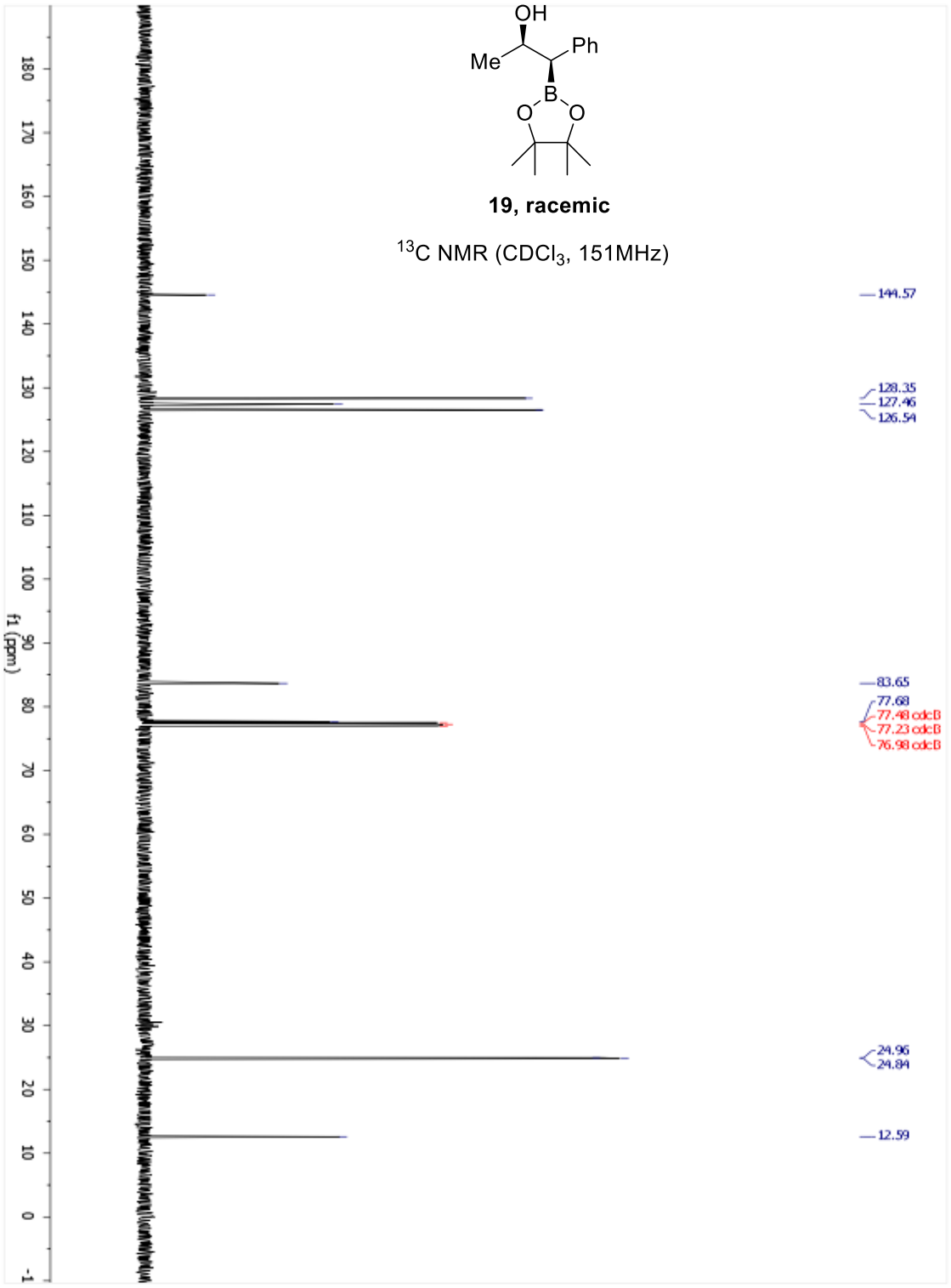

OH
Bu
Bu
B
O
O
18
1H NMR (CDCl3, 600MHz)
7.26
3.60
3.59
3.59
3.58
3.57
3.57
3.56
2.05
2.04
1.52
1.52
1.50
1.46
1.44
1.43
1.42
1.41
1.39
1.30
1.29
1.29
1.25
1.16
1.15
1.14
1.13
1.12
0.90
0.88
0.87
0.86
1.00
1.05
5.29
15.74
1.01
5.53
f1 (ppm)

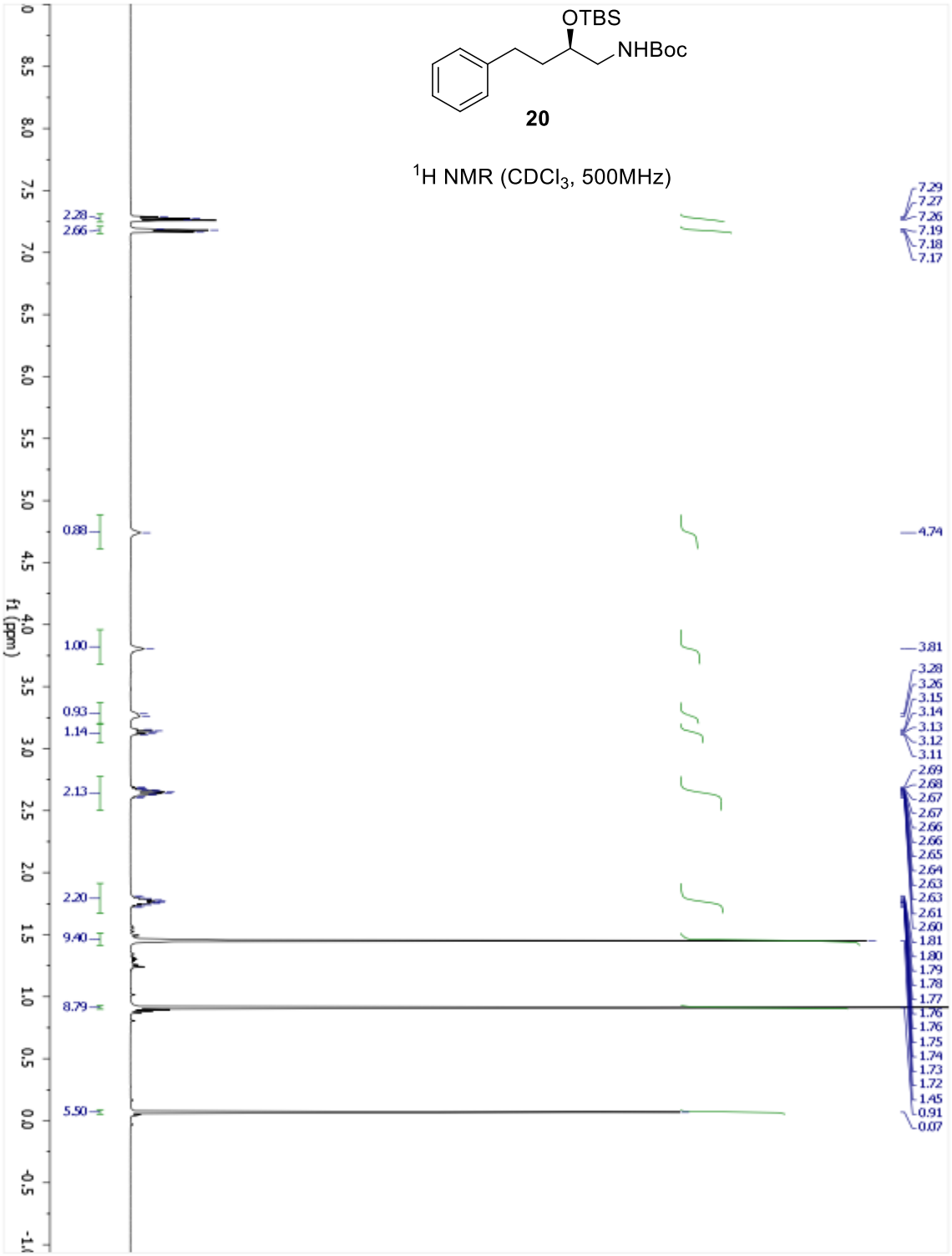


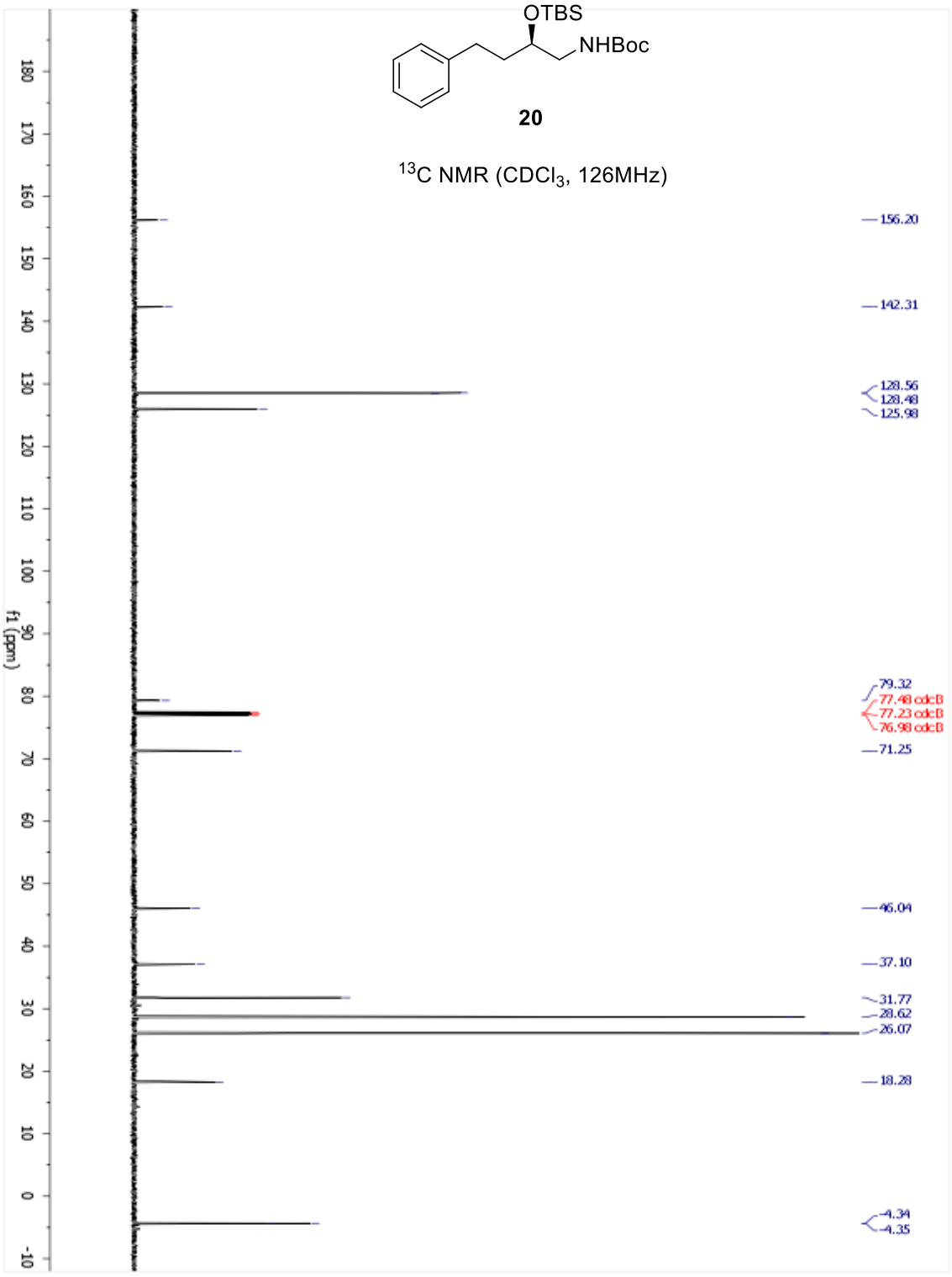
18

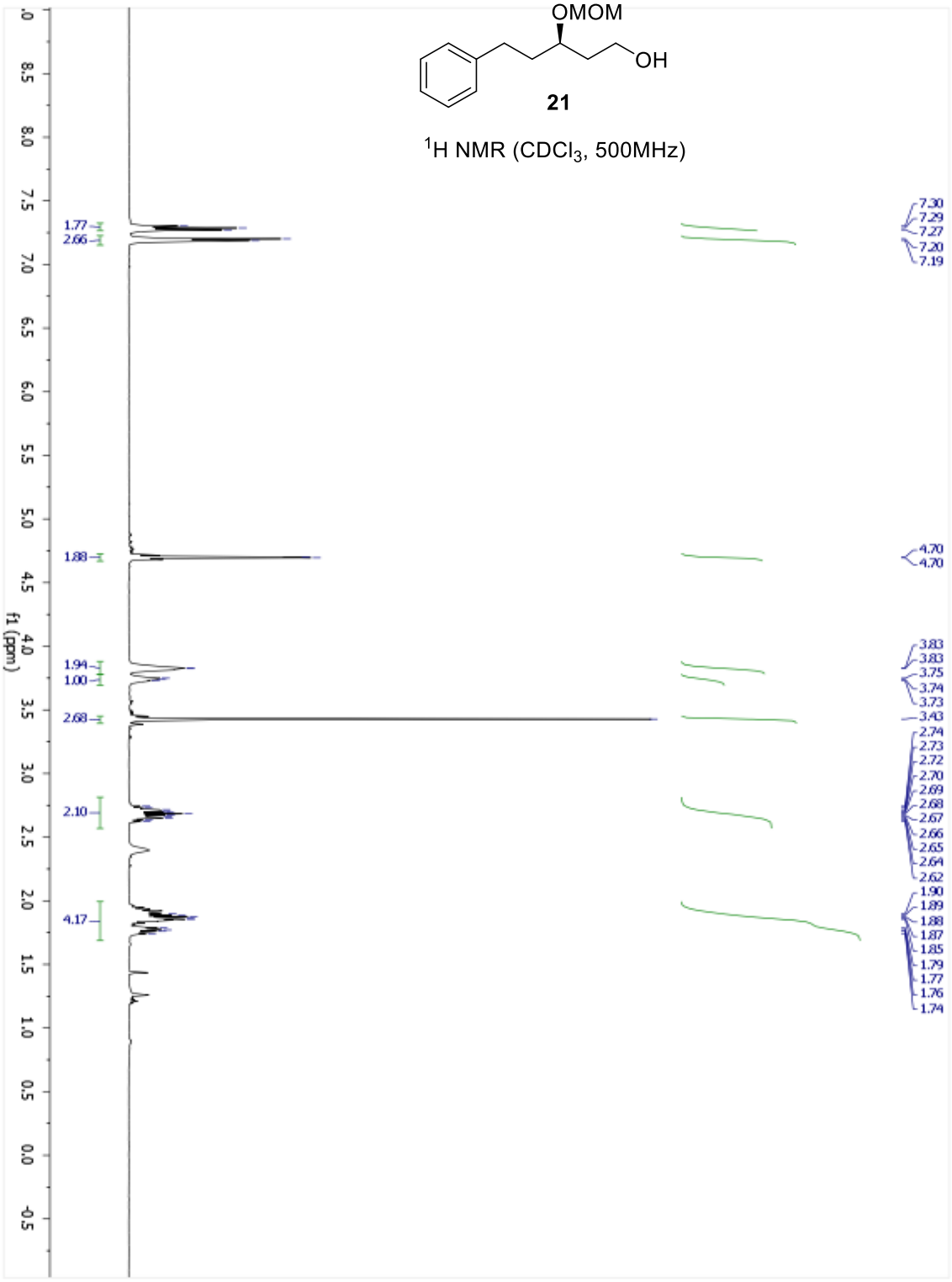
^{13}C NMR ($CDCl_3$, 151MHz)

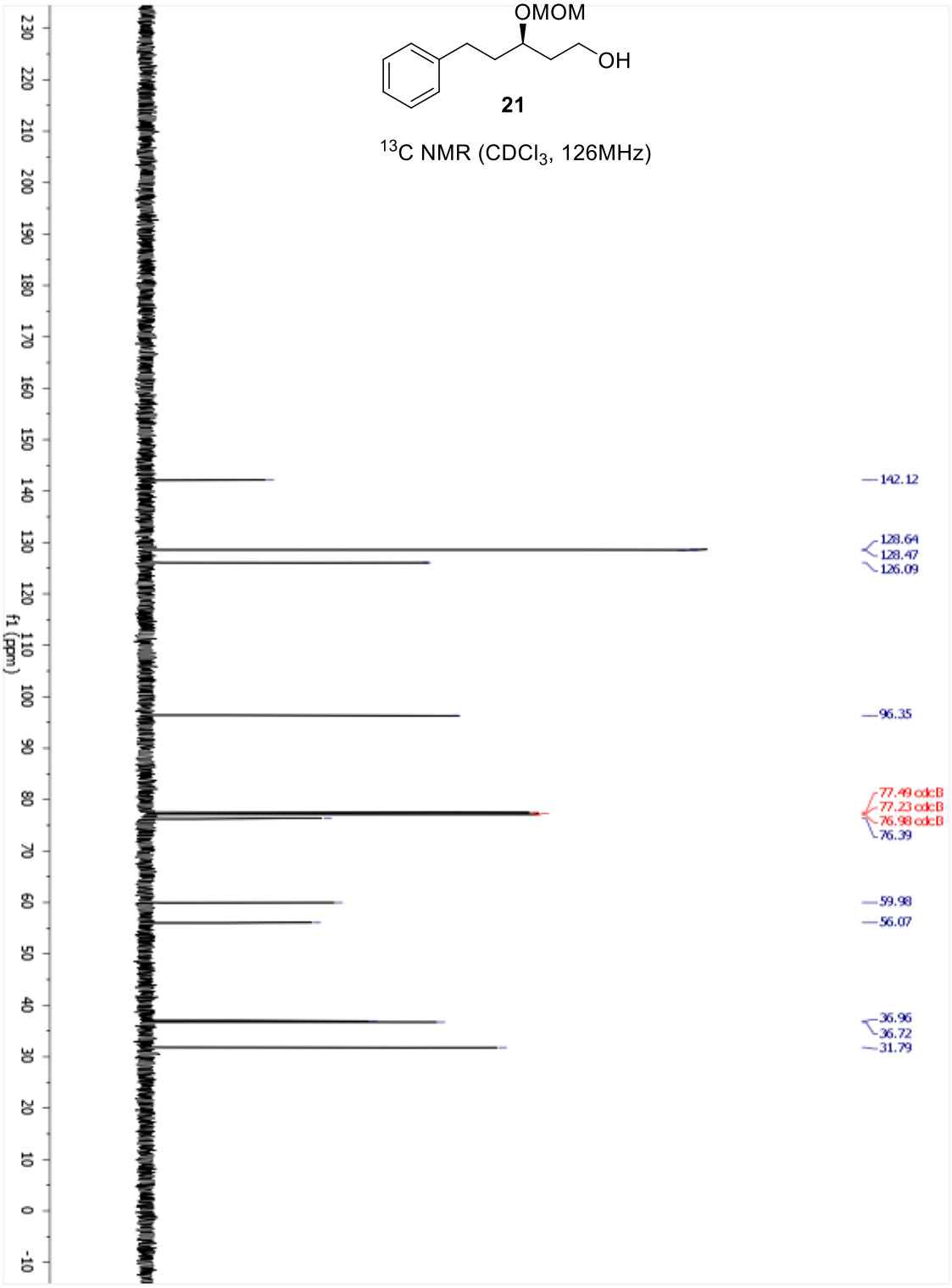

OH
Me
Ph
B
O
O
19, racemic
1H NMR (CDCl3, 500MHz)
f1 (ppm)
4.18
0.66
1.00
0.99
1.17
14.23
3.44
7.36
7.34
7.32
7.31
7.26
7.24
7.23
4.61
4.60
4.60
4.59
2.78
2.77
1.58
1.56
1.55
1.53
1.52
1.25
0.89
0.88

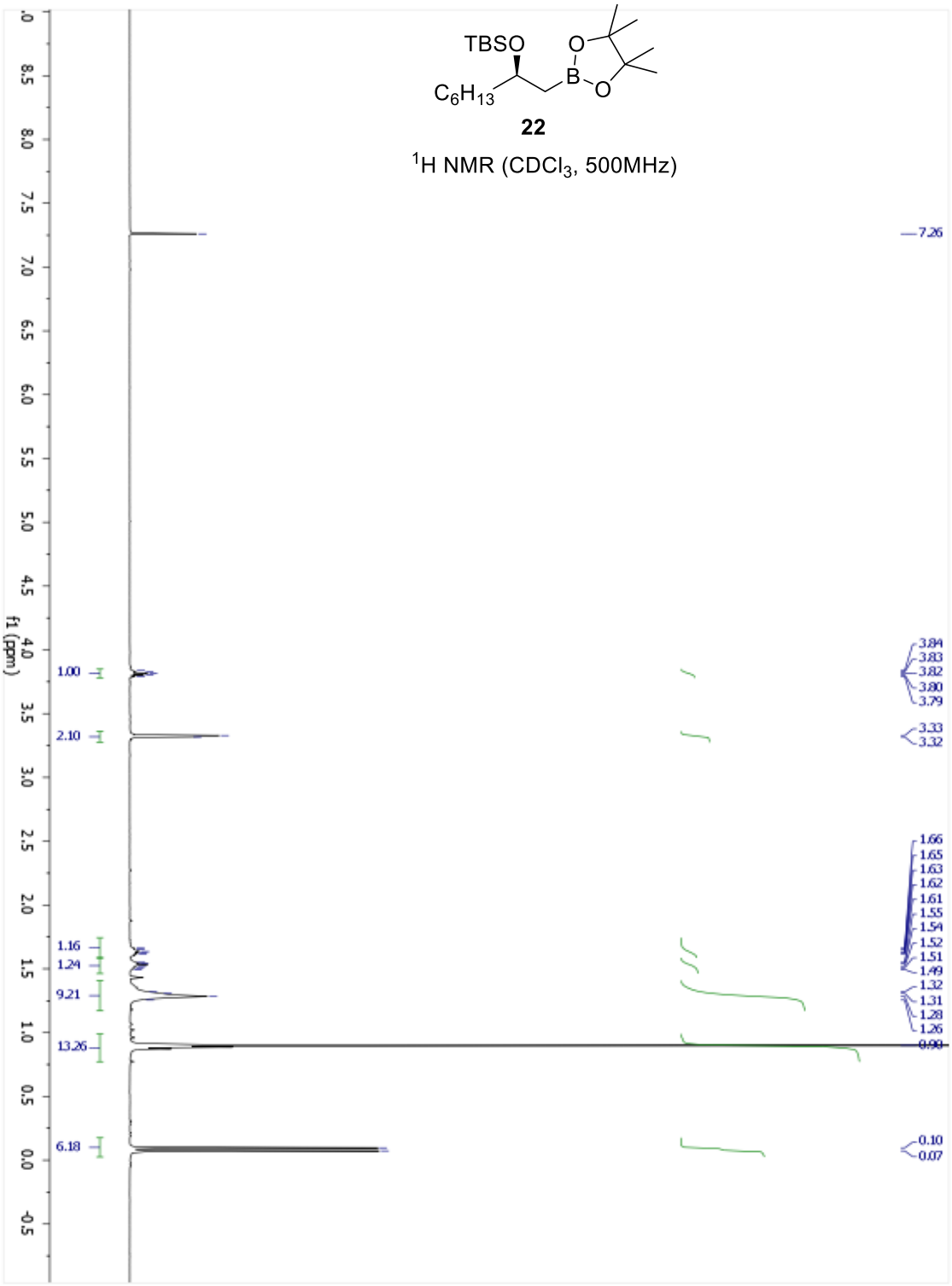

OH
Me
Ph
B
O
O
19, racemic
13C NMR (CDCl3, 151MHz)
144.57
128.35
127.46
126.54
83.65
77.68
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
24.96
24.84
12.59
f1 (ppm)

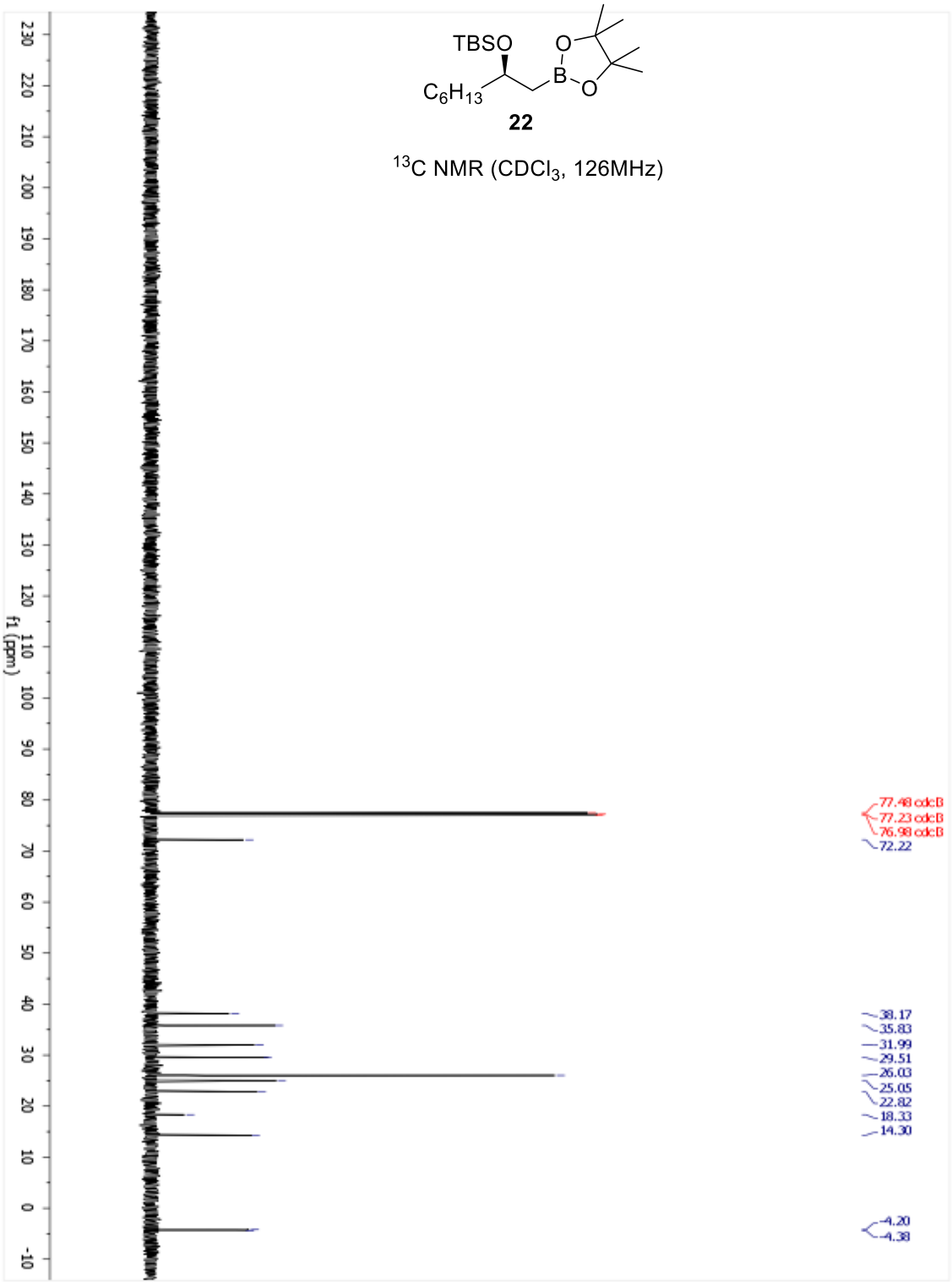

OTBS
NHBoc
20
1H NMR (CDCl3, 500MHz)
f1 (ppm)

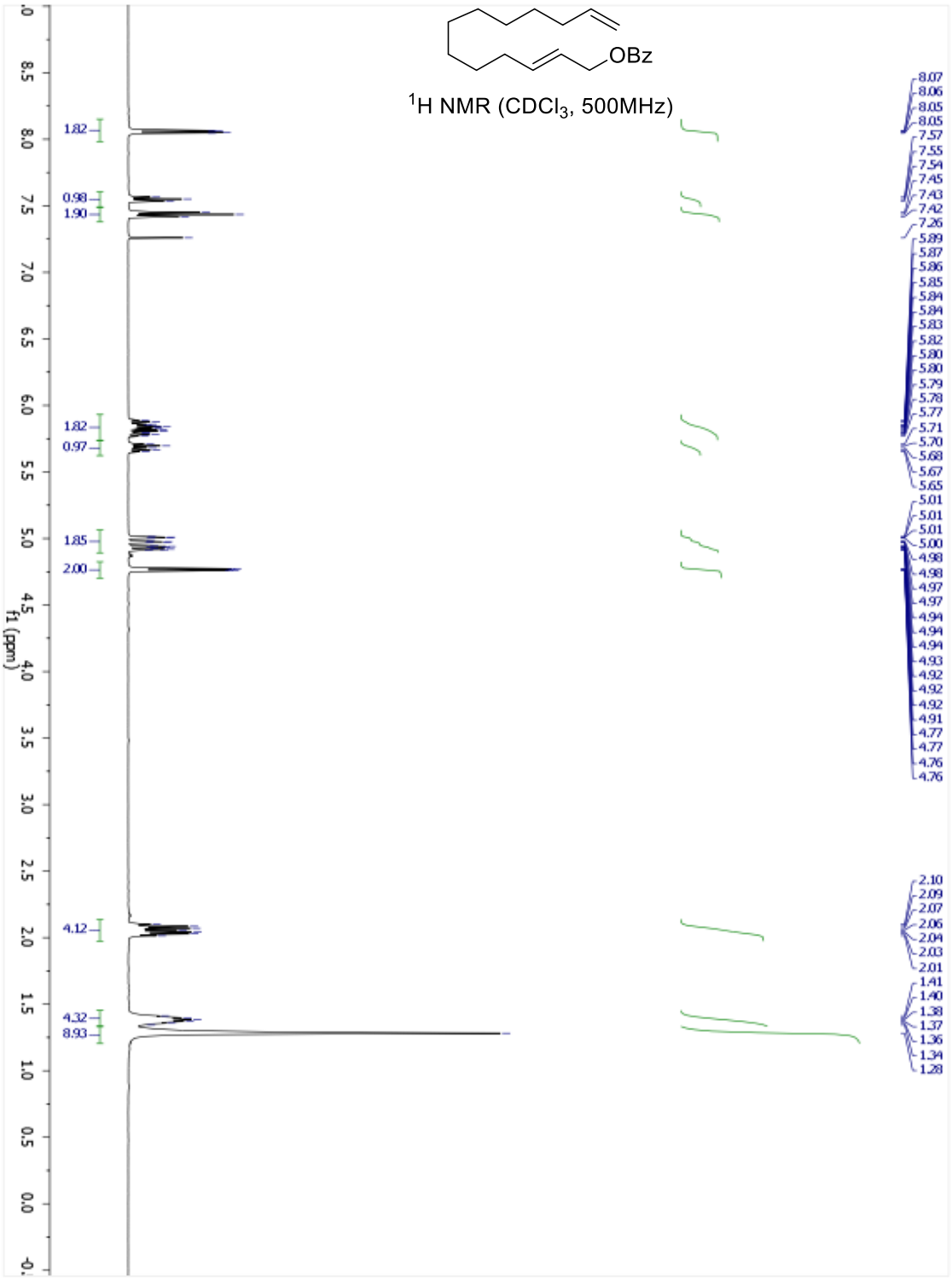

OTBS
NHBoc
20
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
156.20
142.31
128.56
128.48
125.98
79.32
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
71.25
46.04
37.10
31.77
28.62
26.07
18.28
-4.34
-4.35

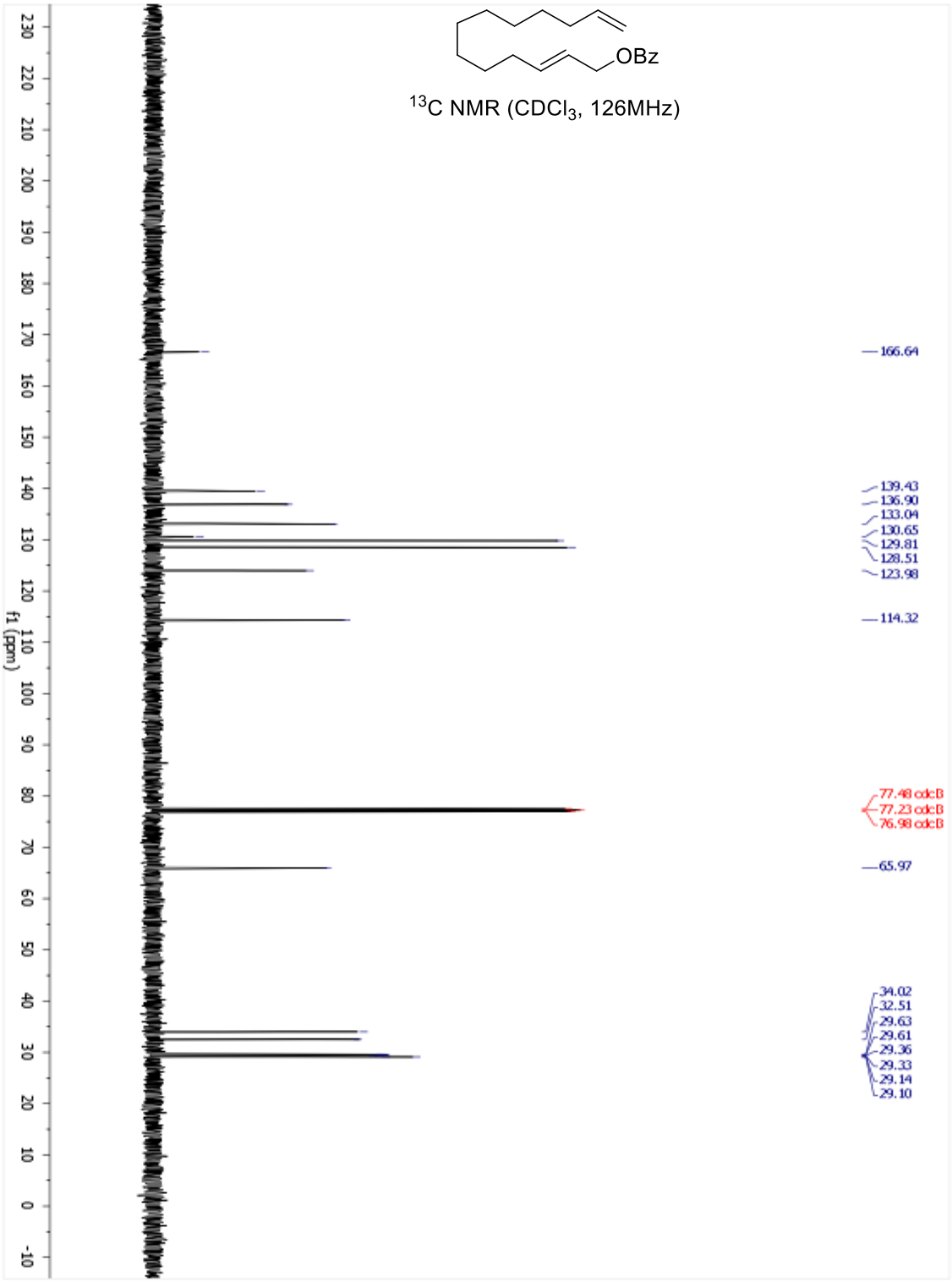

OMOM
OH
21
^{1}H NMR ($CDCl_3$, 500MHz)
f1 (ppm)
1.77
2.66
1.88
1.94
1.00
2.68
2.10
4.17
7.30
7.29
7.27
7.20
7.19
4.70
4.70
3.83
3.83
3.75
3.74
3.73
3.43
2.74
2.73
2.72
2.70
2.69
2.68
2.67
2.66
2.65
2.64
2.62
1.90
1.89
1.88
1.87
1.85
1.79
1.77
1.76
1.74


OMOM
OH
21
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
142.12
128.64
128.47
126.09
96.35
77.49 cdcl3
77.23 cdcl3
76.98 cdcl3
76.39
59.98
56.07
36.96
36.72
31.79


TBSO
O
B
O
C6H13
22
1H NMR (CDCl3, 500MHz)
f1 (ppm)
7.26
3.84
3.83
3.82
3.80
3.79
3.33
3.32
1.66
1.65
1.63
1.62
1.61
1.55
1.54
1.52
1.51
1.49
1.32
1.31
1.28
1.26
0.10
0.07
1.00
2.10
1.16
1.24
9.21
13.26
6.18


TBSO
O
B
O
C6H13
22
13C NMR (CDCl3, 126MHz)
f1 (ppm)
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
72.22
38.17
35.83
31.99
29.51
26.03
25.05
22.82
18.33
14.30
-4.20
-4.38


OBz
^{1}H NMR ($CDCl_3$, 500MHz)
f1 (ppm)


OBz
^{13}C NMR ($CDCl_3$, 126MHz)
f1 (ppm)
166.64
139.43
136.90
133.04
130.65
129.81
128.51
123.98
114.32
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
65.97
34.02
32.51
29.63
29.61
29.36
29.33
29.14
29.10

Chapter 4. Synthetic Studies towards Amphidinolide C and F

4.1 Introduction

One important goal for synthetic methods developments is to apply the method in bioactive molecule synthesis. After developing the carbohydrate-catalyzed enantioselective alkene diboration, as well as new functionalizations of the 1,2-bis(boronates), efforts have been spent on synthetic studies towards potent natural products: amphidinolide C and F. It will be disclosed in this chapter that the carbohydrate-catalyzed enantioselective alkene diboration reaction proved to be efficient in both early stage starting material preparation, and also late stage functionalization of complex structure scaffolds.

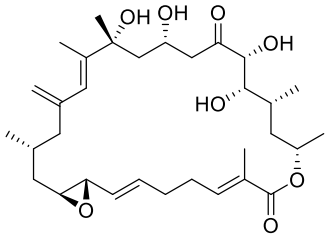
4.2 Amphidinolides

The Kobayashi group has been working on the isolation and structure elucidation of the amphidinolide family of natural products since the 1980's. All the amphidinolides were isolated from the marine dinoflagellates *Amphidinium sp*. Marine dinoflagellates are a group of unicellular eukaryotes that produce many marine toxins, and they are very important sources of bioactive natural products. Until now, the Kobayashi group has isolated 45 macrolides from *Amphidinium sp.*[88] Some of the isolated amphidinolides have very impressive cytotoxicity against both murine lymphoma cells and human epidermoid carcinoma cells. Toxic members of amphidinolides are listed in Scheme 4.1. Interestingly, cytotoxic members amphidinolides B, D, G, H have a very similar macrolide ring

[88] Reviews on Amphidinolides: (a) Kobayashi, J.; Ishibashi, M. *Chem. Rev.* **1993**, *93*, 1753. (b) Kobayashi, J.; Ishibashi, M. *Heterocycles.* **1997**, *44*, 543. (c) Kobayashi, J.; Tsuda, M.; Ishibashi, M. *Pure. Appl. Chem.* **1999**, *71*, 1123. (d) Kobayashi, J.; Shimbo, K.; Kubota, T.; Tsuda, M. *Pure. Appl. Chem.* **2003**, *75*, 337. (e) Kobayashi, J.; Tsuda, M. *Nat. Prod. Rep.* **2004**, *21*, 77. (f) Kobayashi, J.; Kubota, T. *J. Nat. Prod.* **2007**, *70*, 451. (g) Kobayashi, J. *J. Antibiot.* **2008**, *61*, 271.

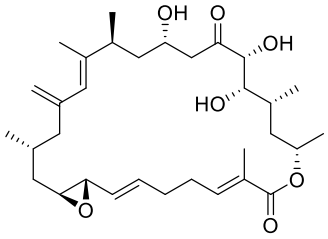
scaffold, while the structure of amphidinolide C is quite distinctive, and notably, it is the only active member of the family that does not have an epoxide.

Scheme 4.1 Summary of potent natural producs of Amphidinolides family



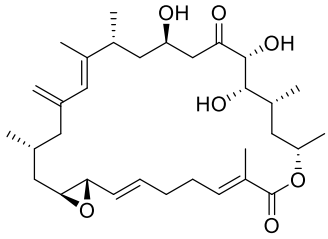
Amphidinolide B_1

L1210: 0.0014
KB: 0.0042
Total Synthesis:
Rich G. Carter (2008, 2013)
Alois Furstner (2009)
Shigeru Nishiyama (2012)



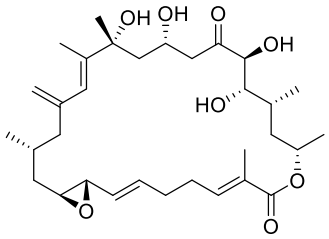
Amphidinolide B_4

L1210: 0.0012
KB: 0.001
Total Synthesis:
Alois Furstner (2009)
Shigeru Nishiyama (2012)



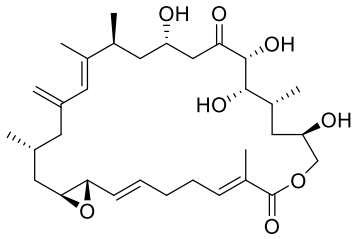
Amphidinolide B_5

L1210: 0.0014
KB: 0.004



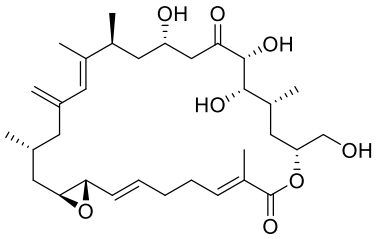
Amphidinolide D

L1210: 0.019
KB: 0.08



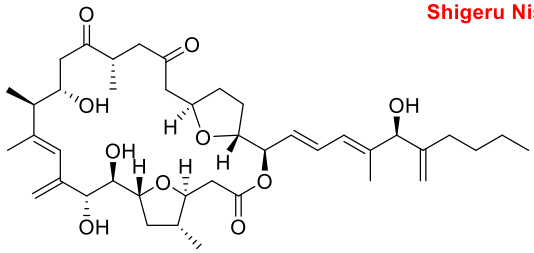
Amphidinolide G

L1210: 0.0054
KB: 0.0059
Total Synthesis:
Alois Furstner (2009)
Shigeru Nishiyama (2012)



Amphidinolide H

L1210: 0.00048
KB: 0.0005
Total Synthesis:
Alois Furstner (2009)
Shigeru Nishiyama (2012)



Amphidinolide C

L1210: 0.0058
KB: 0.0046
Total Synthesis:
Rich G. Carter (2013)
Alois Furstner (2015)

L1210: Cytotoxicity (IC_{50}, □g/ml) towards murine lymphoma cells.
KB: Cytotoxicity (IC_{50}, □g/ml) towards human epidermoid carcinoma cells

Due to the unique structure motifs and potent cytotoxicity, the amphidinolides listed above have been attractive targets for synthetic chemists. Amphidinolide B, C, G, H have

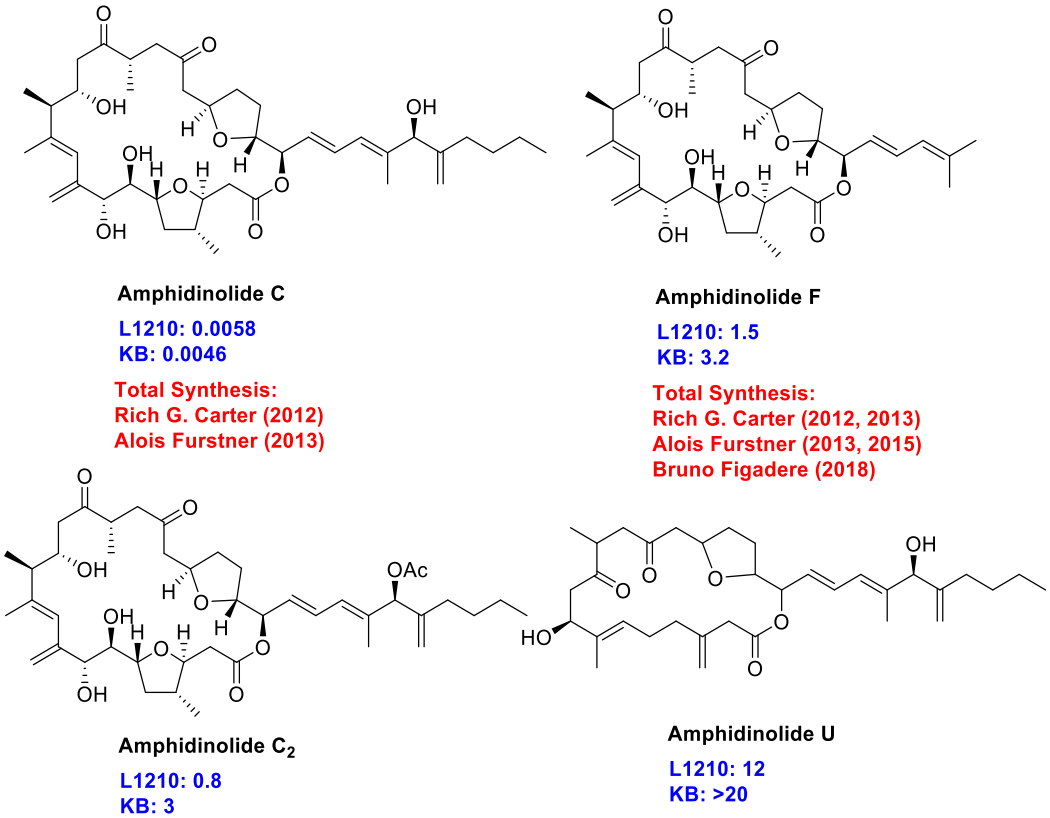
already been synthesized. Professor Alois Fürstner's[89], Professor Rich. G. Carter's[90] and Professor Nishiyama's[91] research groups pioneered the total synthesis studies of amphidinolides.

Amphidinolide C was chosen as our target for demonstrating the synthetic utility of the carbohydrate-catalyzed enantioselective alkene diboration, as well as other synthetic methods that have been recently developed by the Morken group. Amphidinolide C is a quite potent member (IC_{50}(L2120)=0.0058 μg/ml, IC_{50}(KB)=0.0046 μg/ml) from the amphidinolides family. The free secondary alcohol in the side chain proved to be crucial for the impressive cytotoxicity, as the acetate protected amphidinolide C, natural product amphidinolide C_2, shows diminished potency (IC_{50}(L2120)=0.8 μg/ml, IC_{50}(KB)=3 μg/ml) (Scheme 4.2). Additionally, there are two members of amphidinolide family that are structurally very similar to amphidinolide C, namely amphidinolide F and amphidinolide U. Amphidinolide F has an identical macrolactone ring as amphidinolide C and a simplified side chain, while amphidinolide U has an identical side chain as amphidinolide C but has a simplified macrolactone ring. Interestingly, both amphidinolide F (IC_{50}(L2120)=1.5 μg/ml, IC_{50}(KB)=3.2 μg/ml) and amphidinolide U (IC_{50}(L2120)=12 μg/ml, IC_{50}(KB)>20 μg/ml) have much diminished cytotoxicity. Of note, due to the structural similarity to amphidinolide C, amphdinolide F has also been synthesized by

[89] **Amphidinolide B, G, H**: Furstner, A.; Bouchez, L. C.; Morency, L.; Funel, J.; Liepins, V.; Poree, F.; Gilmour, R.; Laurich, D.; Beaufils, F.; Tamiya, M. *Chem. Eur. J.* **2009**, *15*, 3983**. Amphidinolide G, H:** Furstner, A.; Bouchez, L. C.; Funel, J.; Liepins, V.; Poree, F.; Gilmour, R.; Beaufils F.; Laurich, D.; Tamiya, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 9265. **Amphidinolide C**: Valot, G.; Maihol, D.; Regens, C. S.; O'Malley, D. P.; Godineau, E.; Takikawa, H.; Philipps, P.; Furstner, A. *Chem. Eur. J.* **2015**, *21*, 2398.
[90] **Amphidinolide B:** (a) Lu, L.; Zhang, W.; Carter, R. G. *J. Am. Chem. Soc.* **2008**, *130*, 7253. (b) Lu, L.; Zhang, W.; Nam, S.; Horne, D. A.; Jove, R.; Carter, R. G. *J. Org. Chem.* **2013**, *78*, 2213. **Amphidinolide C:** Mahapatra, S.; Carter, R. G. *J. Am. Chem. Soc.* **2013**, *135*, 10792.
[91] **Amphidinolide B, G, H:** Hara, A.; Morimoto, R.; Iwasaki, Y.; Saitoh, T.; Ishikawa, Y.; Nishiyama, S. *Angew. Chem. Int. Ed.* **2012**, *51*, 9877.

several groups.[92] We believed that developing an efficient synthetic route to amphidinolide C may be helpful for further biological study and natural product derivatization.

Scheme 4.2 Comparison of Amphidinolide C, F, and U



[92] (a) Mahapatra, S.; Carter, R. G. *Angew. Chem. Int. Ed.* **2012**, *51*, 7948. (b) Mahapatra, S.; Carter, R. G. *J. Am. Chem. Soc.* **2013**, *135*, 10792. (c) Valot, G.; Regens, C. S.; O'Malley, D. P.; Godineau, E.; Takikawa, H.; Furstner, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 9534. (d) Valot, G.; Maihol, D.; Regens, C. S.; O'Malley, D. P.; Godineau, E.; Takikawa, H.; Philipps, P.; Furstner, A. *Chem. Eur. J.* **2015**, *21*, 2398. (e) Ferrie, L.; Fenneteau, J.; Figadere, B. *Org. Lett.* **2018**, *20*, 3192.

4.3 Previous Total Syntheses of Amphidinolide C and F.

Amphidinolide C was isolated in 1988,[93] and amphidinolide F was isolated in 1991.[94] As introduced before, both of these structures were isolated from marine dinoflagellates *Amphidinium sp*. Since then, a number of synthetic chemists have pursued the total synthesis of both natural products. Although there are many fragment syntheses reported in the literature,[95] only two total synthesis have been accomplished for Amphidinolide C[2,3] and three total syntheses have been reported for amphidinolide F.[5] Total syntheses of amphidinolide C from Professor Rich G. Carter's group and Professor Alois Fürstner's group, and total synthesis of amphidinolide F from Professor Bruno Figadère's group will be discussed.

4.3.1 Total Synthesis of Amphidinolide C by Prof. Rich. G. Carter

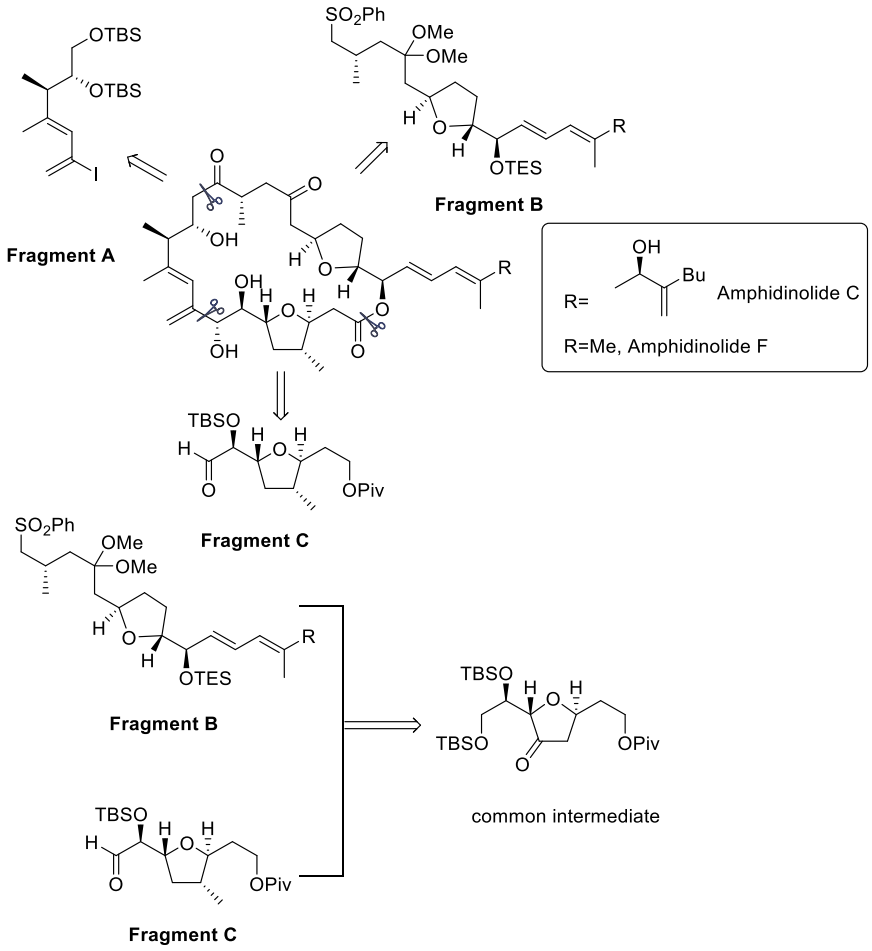
Professor Rich G. Carter and coworkers reported the first total synthesis of natural product amphidinolide F in 2012. Three years later, the group accomplished the total synthesis of both amphidinolide C and F with slightly revised routes, and this is the first time amphidinolide C was successfully synthesized in the laboratory. As both of the

[93] Kobayashi, J.; Ishibashi, M.; Walchli, M. R. Nakamura, H.; Hirata, Y.; Sasaki, T.; Ohizumi, Y. *J. Am. Chem. Soc.* **1988**, *110*, 490.
[94] Kobayashi, J.; Tsuda, M.; Ishibashi, M.; Shigemori, H.; Yamasu, T.; Hirota, H.; Sasaki, T. *J. Antibiot.* **1991**, *44*, 1259.
[95] (a) Shotwell, J. B.; Roush, W. R. *Org. Lett.* **2004**, *6*, 3865−3868. (b) Mohapatra, D. K.; Rahaman, M.; Chorghade, S.; Gurjar, M. K. *Synlett.* **2007**, *18*, 567−570. (c) Bates, R. H.; Shotwell, J. B.; Roush, W. R. *Org. Lett.* **2008**, *10*, 4343−4346. (d) Armstrong, A.; Pyrkotis, C. *Tetrahedron Lett.* **2009**, *50*, 3325−3328. (e) Mohapatra, D. K.; Dasari, P.; Rahaman, H.; Pal, R. *Tetrahedron Lett.* **2009**, *50*, 6276−6279. (f) Paudyal, M. P.; Rath, N. P.; Spilling, C. D. *Org. Lett.* **2010**, *12*, 2954−2957. (g) Ferrié, L.; Figadère, B. *Org. Lett.* **2010**, *12*, 4976−4979. (h) Roy, S.; Spilling, C. D. *Org. Lett.* **2010**, *12*, 5326−5329. (h) Morra, N. A.; Pagenkopf, B. L. *Org. Lett.* **2011**, *13*, 572−575. (i) Wu, D.; Forsyth, C. J. *Org. Lett.* **2013**, *15*, 1178−1181. (j) Clark, J. S.; Yang, G.; Osnowski, A. P. *Org. Lett.* **2013**, *15*, 1460−1463. (k) Clark, J. S.; Yang, G.; Osnowski, A. P. *Org. Lett.* **2013**, *15*, 1464−1467. (l) Morra, N. A.; Pagenkopf, B. L. *Tetrahedron.* **2013**, *69*, 8632−8644. (m) Morra, N. A.; Pagenkopf, B. L. *Eur. J. Org. Chem.* **2013**, 756−760.

natural products were synthesized from an identical route, except for the side chain, only the synthesis of amphidinolide C will be discussed.

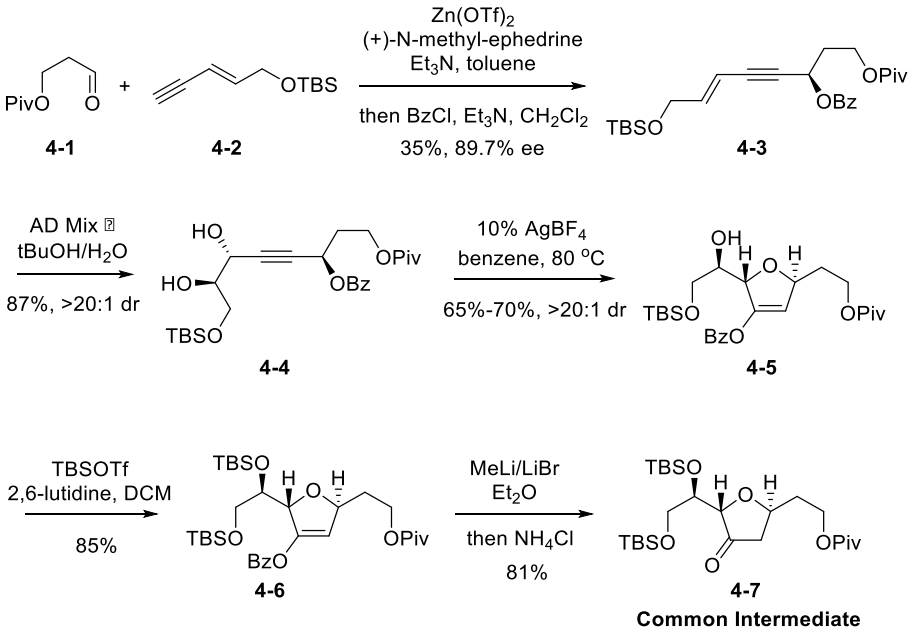
Retrosynthetic analysis from Professor Carter's group is depicted in Scheme 4.3. The target molecule Amphidinolide C was divided into three fragments, namely fragment A, B and C. Fragment A and C were first coupled together via lithium-halogen exchange and subsequent nucleophilic addition. Fragment B was then attached by S_N2 displacement mediated by alkyl sulfonate. Lastly, macrolactonization and global deprotection were supposed to accomplish the total synthesis of amphidinolide C. Of note, both fragment B and C can be obtained from one common intermediate.

Scheme 4.3 Retrosynthetic Analysis



Synthesis of common intermediate is depicted in Scheme 4.4: Compound **4-3** was prepared from known aldehyde **4-1** and enyne **4-2** through Carreira's asymmetric alkynylation[96] followed by in situ benzoate protection. Subsequent Sharpless asymmetric dihydroxylation afforded the cyclization precursor **4-4** in good yield and diastereoselectivity. Silver-catalyzed cyclization went smoothly with **4-4**, affording the desired cyclization product **4-5** in good yield. After standard TBS protection and enol ether hydrolysis, the common intermediate **4-7** was obtained efficiently.

Scheme 4.4 Synthesis of Common Intermediate

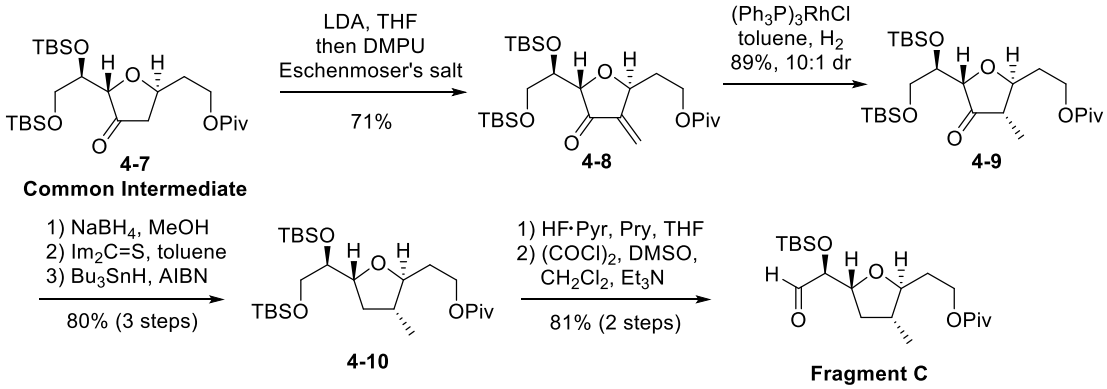


With common intermediate **4-7** in hand, the team commenced to the synthesis of fragment B and C. The synthetic route to fragment B is shown in Scheme 4.5. Standard methylenation followed by stereoselective hydrogenation catalyzed by Wilkinson catalyst afforded compound **4-9** in 89% yield and 10:1 dr. Of note, direct alkylation of **4-7** gave the wrong diastereomer. Next, **4-9** was subjected to a three-step Barton-McCombie

[96] Boyall, D.; Lopez, F.; Sasaki, H.; Frantz, D.; Carreira, E. M. *Org. Lett.* **2001**, *2*, 4233.

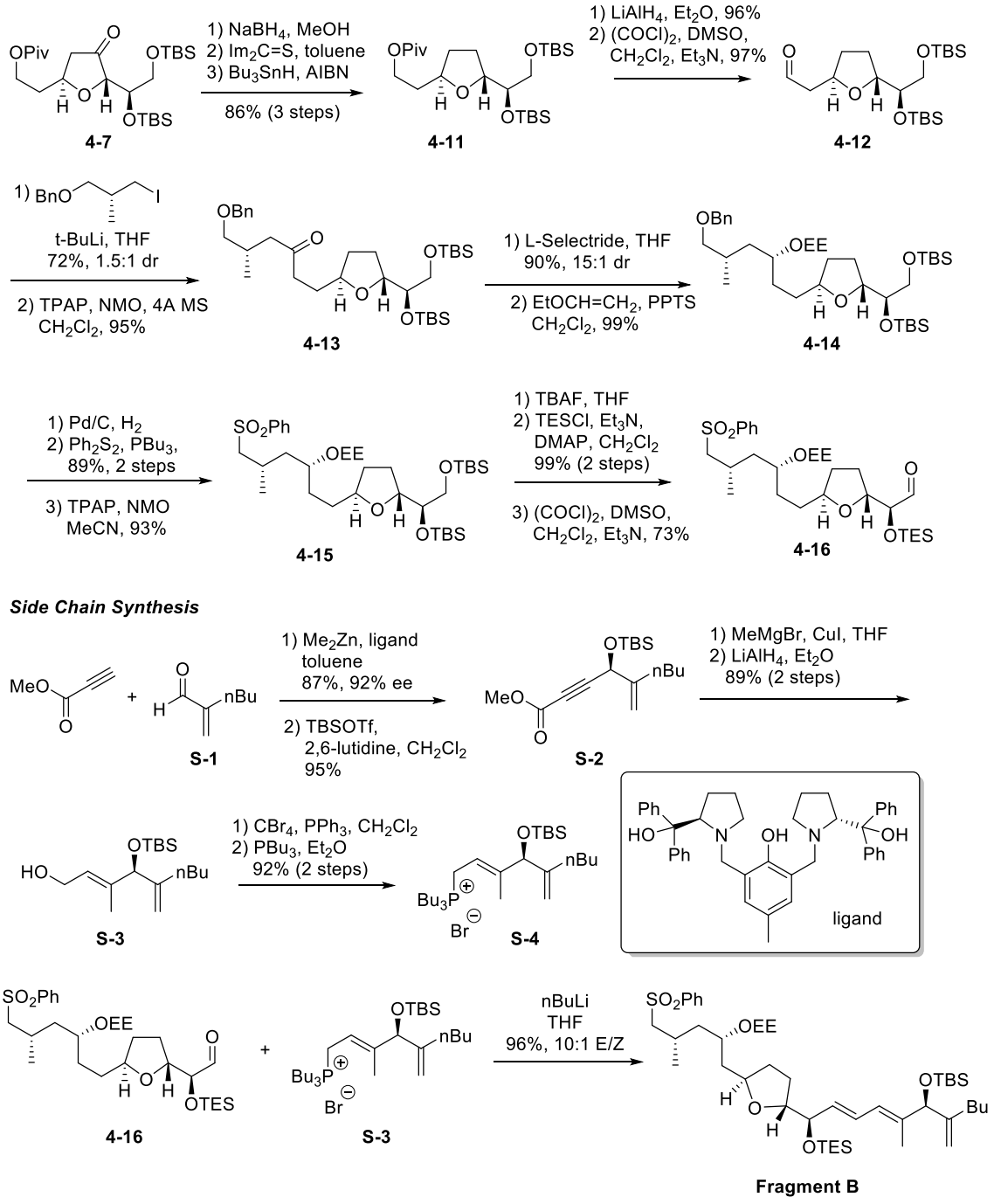
deoxygenation process to afford compound **4-10**. After regioselective TBS deprotection of the primary alcohol followed by Swern oxidation, fragment C was prepared.

Scheme 4.5 Synthesis of Fragment C



Fragment B is the largest fragment among the three fragments and it is the most challenging fragment to make. A series of synthetic routes were explored by the authors. The ultimate route is discussed in Scheme 4.6. Starting from the common intermediate **4-7**, the three-step Barton-McCombie deoxygenation afforded compound **4-11** in good yield. After pivolate deprotection and Swern oxidation, the aldehyde **4-12** was then coupled with an organolithium reagent derived from corresponding alkyl iodide. The diastereomeric mixture of alcohols from nucleophilic addition was then oxidized to a ketone **4-13**. After L-selectride reduction and protection of the free alcohol with ethoxyvinyl ether, compound **4-14** was obtained in nearly quantitative yield and 15:1 dr. The benzyl protected primary hydroxyl group was then converted to corresponding sulfonate efficiently. The two TBS protecting groups in compound **4-15** were replaced with TES protecting groups because they are easier to remove at the late stage. Finally, the primary TES protected alcohol was directly oxidized to an aldehyde by Swern oxidation to afford aldehyde **4-16**.

Scheme 4.6 Synthesis of Fragment B



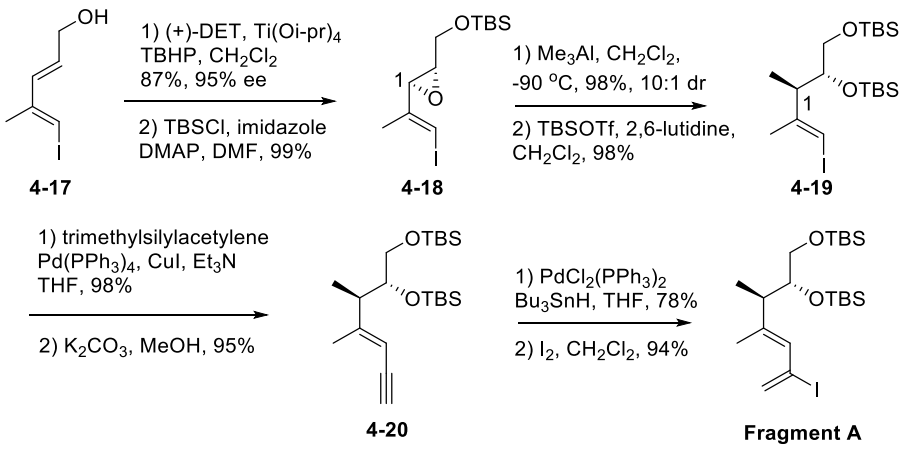
After synthesizing compound **4-16**, the group started working on the synthesis of the side chain of amphidinolide C. This side chain is quite complex and needed several steps to prepare. As shown in Scheme 4.6 *side chain preparation*, commercially available

propynoic acid methyl ester underwent Trost asymmetric alkynylation[97] with known aldehyde **S-1** to afford compound **S-2** after TBS protection. Methyl cuprate conjugate addition to the alkynoate **S-2** followed by lithium aluminum hydride reduction generated the desired allylic alcohol **S-3** favoring the E alkene geometry. The primary alcohol was transformed to a tributylphosphonium salt **S-4** through standard conditions. Lastly, the side chain **S-4** was successfully attached to compound **4-16** though Tamura/Vedejs olefination,[98] generating fragment B in nearly quantitative yield and 10:1 E:Z selectivity.

The synthesis of fragment A is more straightforward. As depicted in Scheme 4.7, known dienyl iodide **4-17** was subjected to Sharpless asymmetric epoxidation, followed by TBS protection to produce compound **4-18**. Epoxide opening with trimethylaluminum occured selectively at carbon **1**, followed by TBS protection to generate compound **4-19**. The alkenyl iodide **4-19** then underwent Sonogashira coupling with trimethylsilylacetylene. After TMS deprotection, enyne product **4-20** was formed in good yields. Enyne **4-20** was then subjected to palladium catalyzed hydrostannylation followed by iodination to afford the desired fragment A.

[97] Trost, B. M.; Weiss, A. H.; Wangelin, A. K.-V. *J. Am. Chem. Soc.* **2006**, *128*, 8.
[98] (a) Tamura, R.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* **1998**, *53*, 2723−2728. (b) Wang, Y.; Panagabko, C.; Atkinson, *J. Bioorg. Med. Chem.* **2010**, *18*, 777−786. (c) Vedejs, E.; Marth, C. F.; Ruggeri, R. *J. Am. Chem. Soc.* **1998**, *110*, 3940−3948.

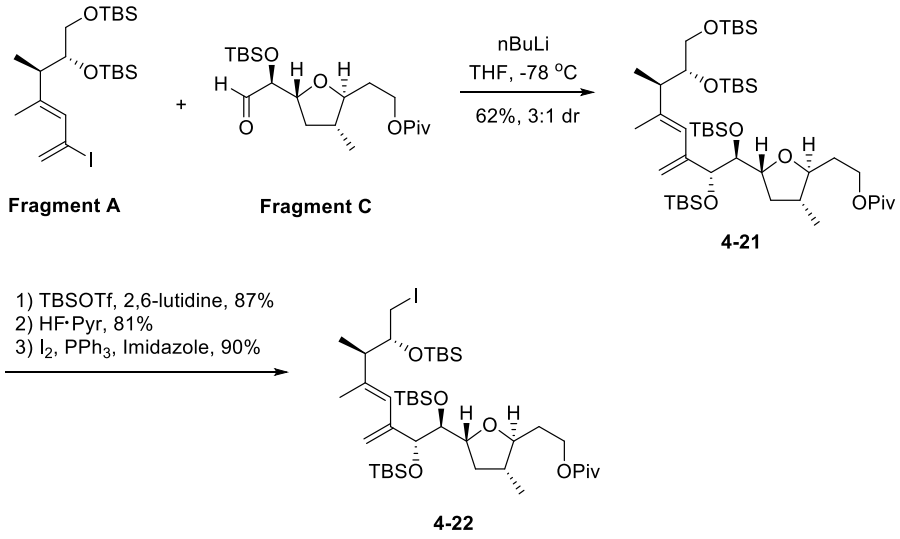
Scheme 4.7 Synthesis of Fragment A



4-17 **4-18** **4-19** **4-20** **Fragment A**

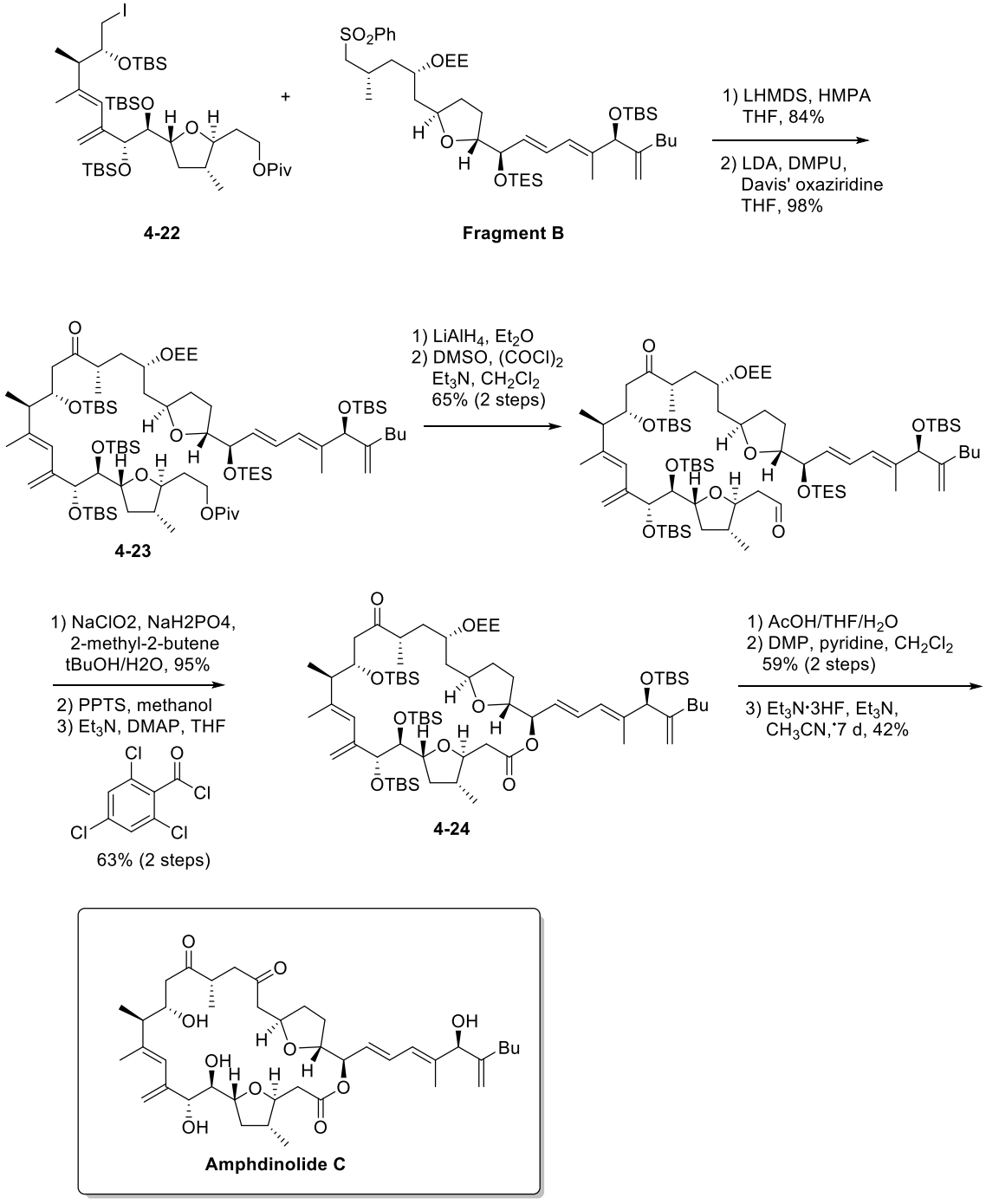
With three fragments in hand, the researchers started to work on the final assembly of the target molecule. As depicted in Scheme 4.8, fragment A and fragment C were annealed together through lithium halogen exchange and subsequent nucleophilic addition into the aldehyde. The reaction afforded the allylic alcohol product in 62% yield, 3:1 dr. The desired diastereomer **4-21** is favored. Then, the primary TBS protected alcohol was selectively deprotected and transformed to the iodide **4-22** through standard conditions.

Scheme 4.8 Assemble of Fragment A and Fragment C



Fragment A **Fragment C** **4-21** **4-22**

Scheme 4.9 Total Synthesis of Amphidinolide C



As depicted in Scheme 4.9, compound **4-22** was then coupled with fragment B through deprotonation-alkylation. This step afforded the adduct in 84% yield. Subsequent

oxidative desulfurization proceeded smoothly by using LDA, DMPU, and Davis oxaziridine, affording compound **4-23** in excellent yield. After adjusting the oxidation state and subsequent Yamaguchi lactonization, macrolactide **4-24** was successfully produced. Finally, the total synthesis of amphidinolide C was accomplished after deprotection-oxidation-global deprotection sequence.

In summary, Professor Rich Carter and his coworker Subham Mahapatra accomplished the first total synthesis of amphidinolide C in a 34 (longest linear) steps sequence (62 total steps). Highlights of their synthesis are: They used one common intermediate to access both of the *trans*-substituted THF rings in the macrocyclic core of the target molecule. A silver-catalyzed stereoselective cyclization of propargyl benzoate/diol was applied to construct the *trans*-fused THF ring in the common intermediate. Sulfone alkylation/oxidative desulfurization was utilized to connect two major fragments efficiently.

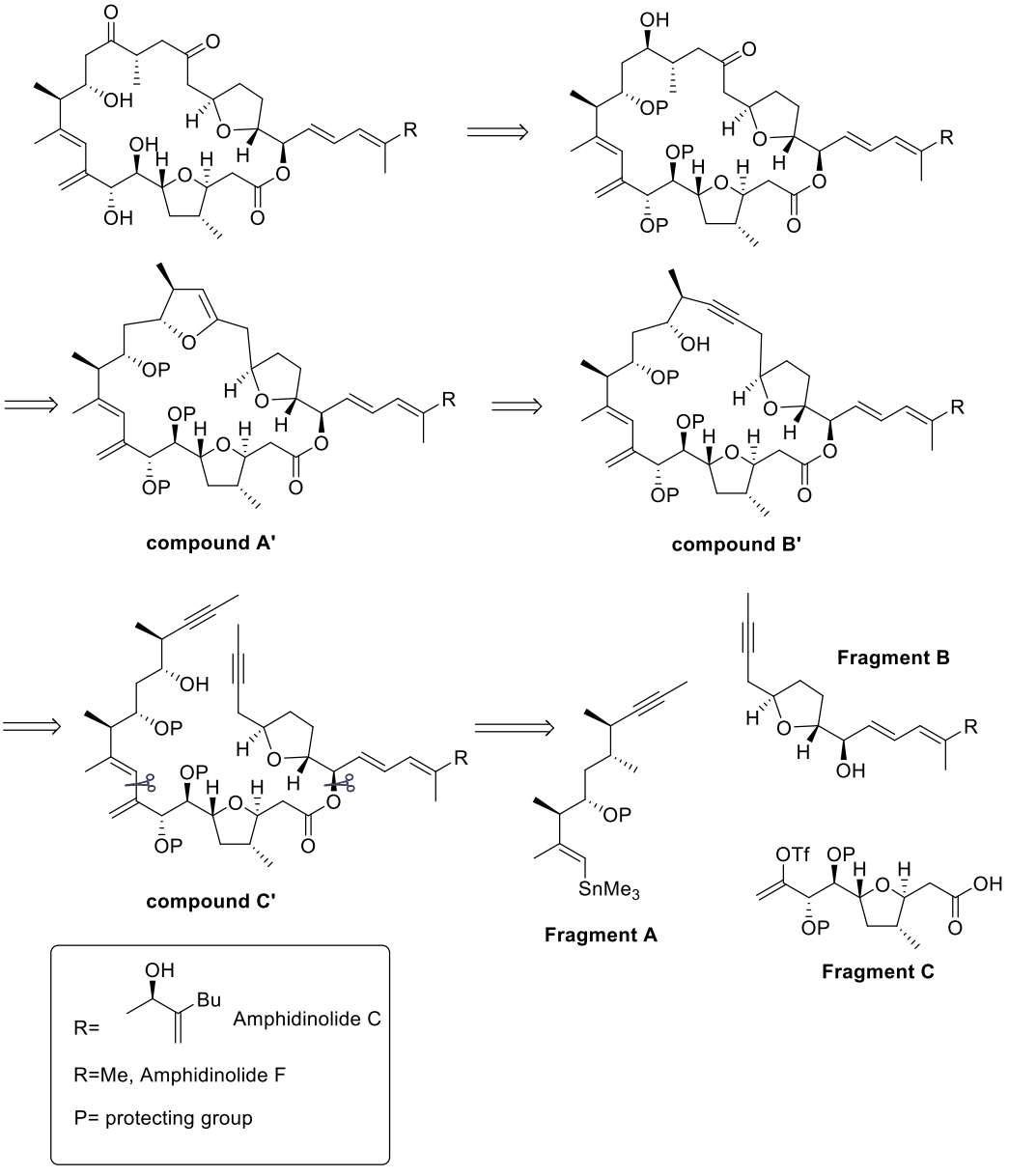
4.3.2 Total Synthesis of Amphidinolide C by Prof. Alois Fürstner

Shortly after Professor Rich Carter reported the first total synthesis of amphidinolide F in 2012, Professor Alois Fürstner and coworkers also finished the total synthesis of amphidinolide F. The group further refined their synthetic route and reported the total synthesis of both amphidinolide C and amphidinolide F in 2015. As amphidinolide C and F were synthesized with identical route except for the side chain, only total synthesis route towards amphidinolide C will be discussed.

The retrosynthetic analysis from Professor Fürstner's group is depicted in Scheme 4.10. A distinctive synthetic route was proposed by these researchers for constructing the

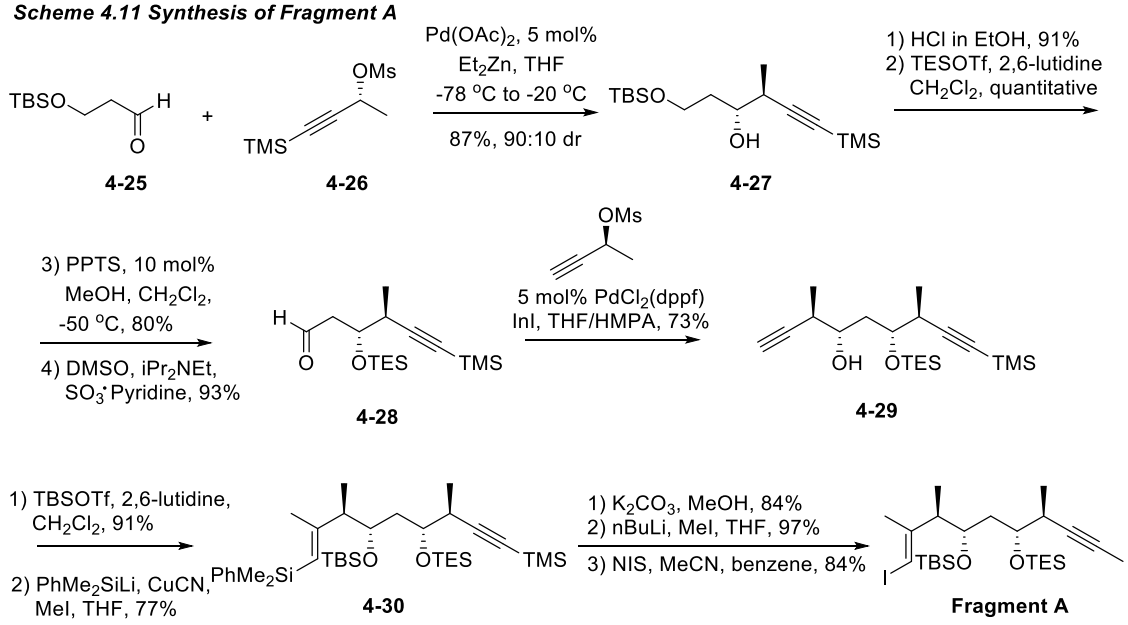
target molecule amphidinolide C. The 1,4-diketone motif in amphidinolide C was proposed to come from hydrolysis of a dihydrofuran (compound **A'**). Compound **A'** was product of the intramolecular alkyne hydration of compound **B'**. Alkyne ring closing metathesis (RCM) was proposed to achieve the macrocyclic ring closure. The RCM precursor, advanced synthetic intermediate compound **C'**, was then further divided into fragments A, B and C.

Scheme 4.10 Retrosynthetic Analysis



As shown in Scheme 4.11, fragment A was prepared from known aldehyde **4-25** and mesylate **4-26**. The anti-selective propargylation reaction developed by Marshal and coworkers successfully afforded product **4-27** in 87% yield, 90:10 dr.[99] After a standard protection and oxidation sequence, compound **4-27** was transformed to aldehyde **4-28**. Another palladium-catalyzed anti-propargylation was then employed to synthesize compound **4-29**. After TBS protection of the free secondary hydroxyl in **4-29**, the terminal alkyne was subjected to a silylcupration reaction, followed by methyl iodide quench, to synthesize compound **4-30**. Subsequent TMS deprotection followed by alkyne methylation and iodine-silicon exchange successfully afforded fragment A in good yield.

Scheme 4.11 Synthesis of Fragment A



As depicted in Scheme 4.12, fragment B was prepared efficiently from known enantiopure epoxide **4-31**.[100] Site-selective epoxide opening by acetylide afforded

[99] Marshall, J. A. *J. Org. Chem.* **2007**, *72*, 8153

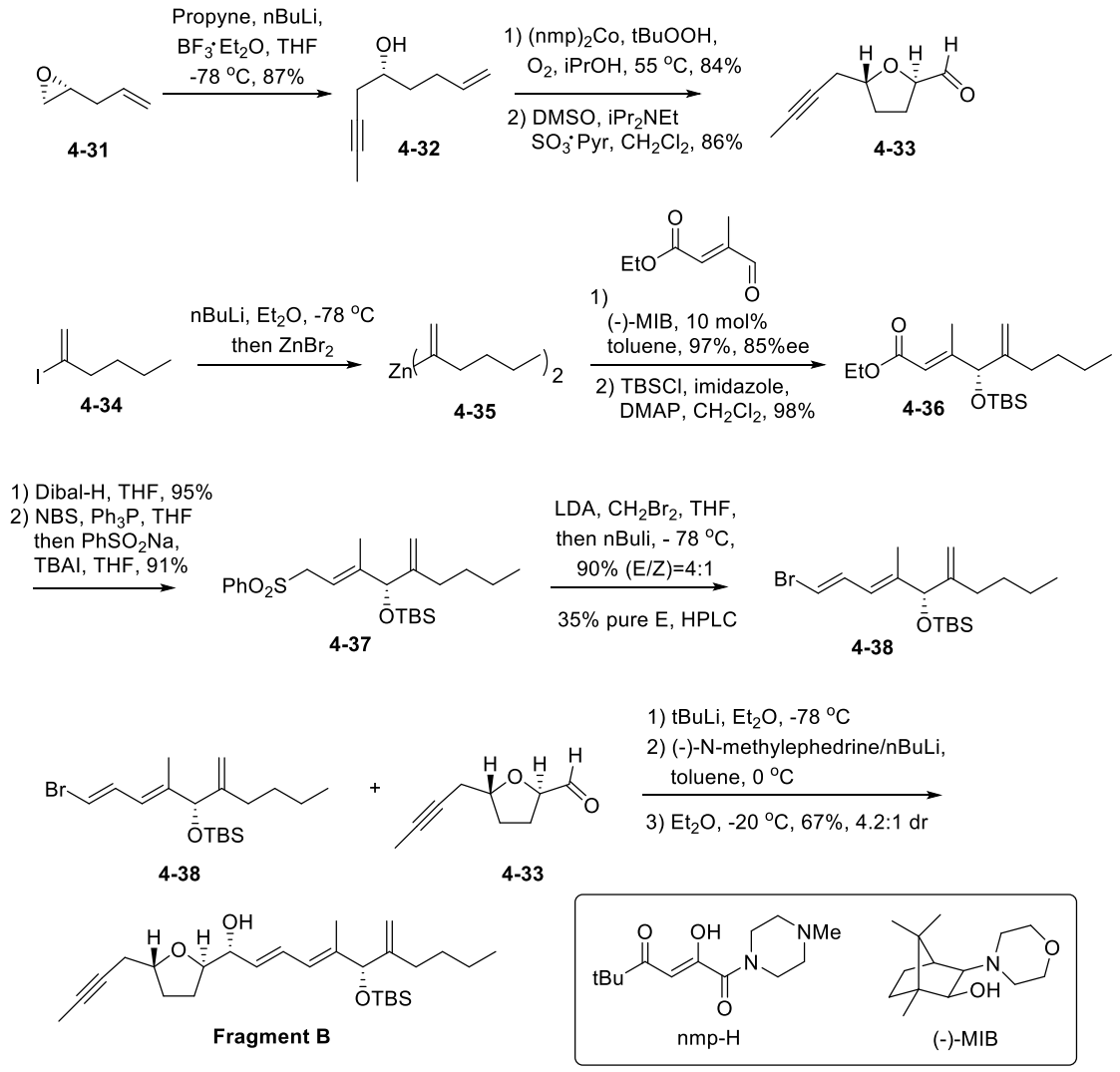
[100] Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science*, **1997**, *277*, 936.

compound **4-32** in 87% yield. Subsequent Mukaiyama cyclization catalyzed by cobalt complex successfully produced the trans-THF ring in good yield and excellent diastereoselectivity.[101] Of note, the Mukaiyama cyclization proved to be chemoselective, only reacting with the alkene in presence of the alkyne moiety. After standard Parikh-Doering oxidation, aldehyde **4-33** was readily obtained.

The side chain of amphidinolide C is rather complex, so it took a few steps to synthesize. Starting from the known alkenyl iodide **4-34**, the zinc reagent **4-35** was prepared from lithium-halogen exchange/zinc transmetallation. The zinc reagent **4-35** was then allowed to add to the commercially available aldehyde enantioselctively, with (-)-MIB as ligand. Standard TBS protection afforded compound **4-36** in good yield and enantioselectivity. The ester group in **4-36** was transformed to the sulfone **4-37** through reduction, bromination and S_N2 displacement. Sulfone **4-37** was then allowed to react with *in-situ* generated carbenoid from LDA and dibromomethane. The dienyl bromide **4-38** was formed as E/Z=4:1 mixture. The desired (E,E) isomer was isolated from the (Z,E) isomer through preparative HPLC in 35% yield. Next, the careful temperature-controlled lithium-halogen exchange of the bromide **4-38** followed by zinc transmetallation, generated the desired zinc reagent, which added to the aldehyde **4-33** diastereoselectively by using (-)-MIB as a ligand. Fragment B was prepared in 67% yield, 4.2:1 dr.

[101] a) Inoki, S.; Mukaiyama, T.; *Chem. Lett.* **1990**. 67. b) Menendez Perez, B.; Schuch, D.; Hartung, *J. Org. Biomol. Chem.* **2008**, *6*, 3532.

Scheme 4.12 Synthesis Of Fragment B

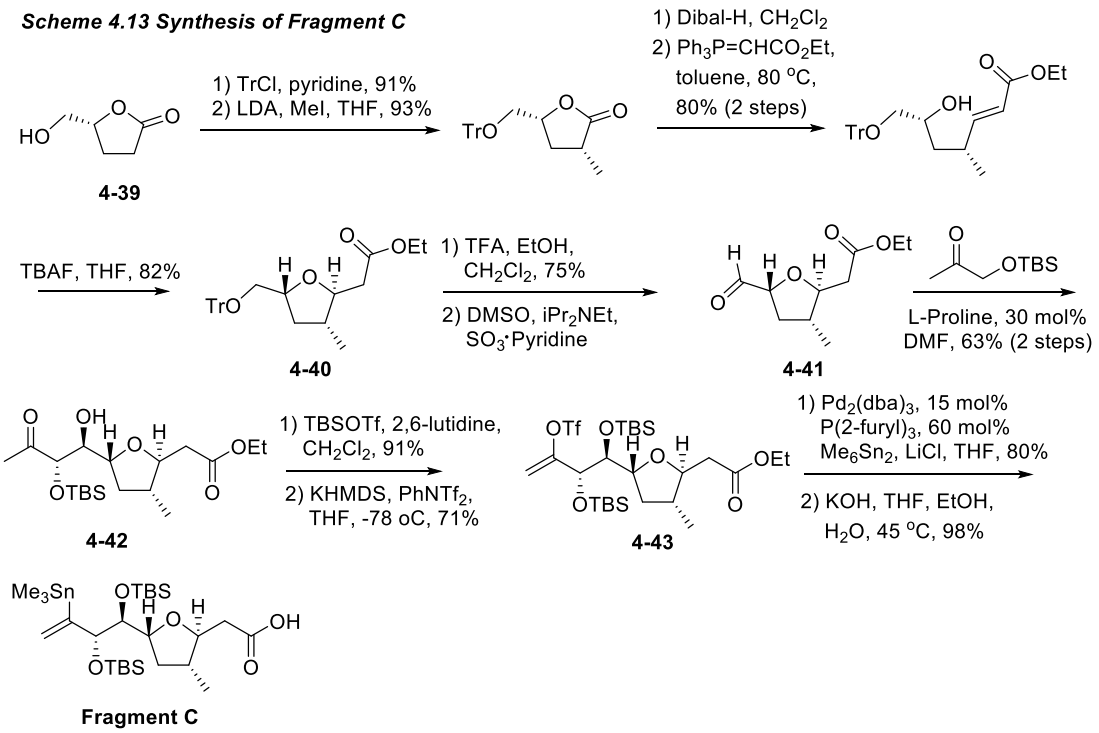


For the synthesis of fragment C, the authors adopted a known procedure to prepare compound **4-40** from commercially available lactone **4-39**.[102] The key step of the 5-step synthesis is the TBAF-mediated oxa-Michael addition to form the trans-configured THF ring. Next, compound **4-40** was oxidized to an aldehyde by Parikh-Doering oxidation. Aldehyde **4-41** was then subjected to a proline-catalyzed aldol reaction with TBS-

[102] a) Nishida, Y. K.; Konno, M.; Fukushima, Y.; Ohrui, H.; Meguro, H. *Agric. Biol. Chem.* **1986**, *50*, 191. b) Shiro, Y.; Kato, K.; Fujii, M.; Ida, Y.; Akita, H. *Tetrahedron,* **2006**, *62*, 8687.

protected acetol to furnish the anti-adol product **4-42**.[103] After TBS-protection and regio-selective deprotonation/triflation, alkenyl triflate **4-43** was successfully prepared. Subsequent palladium catalyzed stannylation and saponification of the ester completed the preparation of fragment C in good yields.

Scheme 4.13 Synthesis of Fragment C

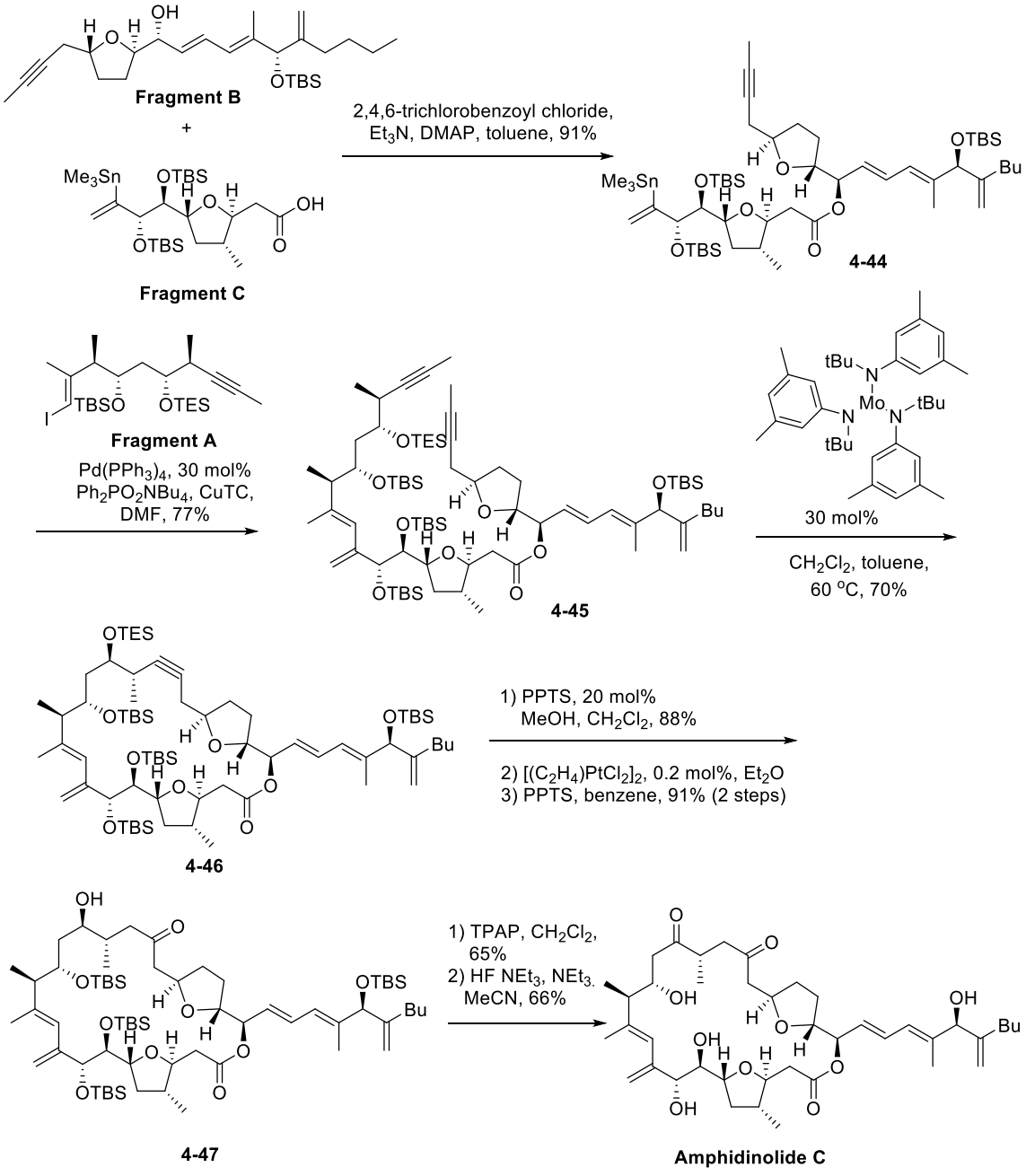


After successfully synthesizing fragments A, B and C, it was time to assemble them. As shown in Scheme 4.14, fragment B and and fragment C were first annealed together by Yamaguchi lactonization. Fragment A was then joined through Stille coupling. Next, the advanced intermediate **4-45** was subjected to molybdenum-catalyzed ring-closing alkyne metathesis. Excitingly, macrolide **4-46** was formed in 70% yield. Subsequent alkyne hydration/2-hydrofuran hydrolysis catalyzed by Zeise's dimer worked very well.

[103] a) Notz, W.; List, B. *J. Am. Chem. Soc.* **2000**, *122*, 7386. b) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471.

Compound **4-47** was obtained in nearly quantitative yield. Then, after adjusting the oxidation state and global deprotection, target molecule amphidinolide C was synthesized.

Scheme 4.14 Fragments Coupling to Amphidinolide C



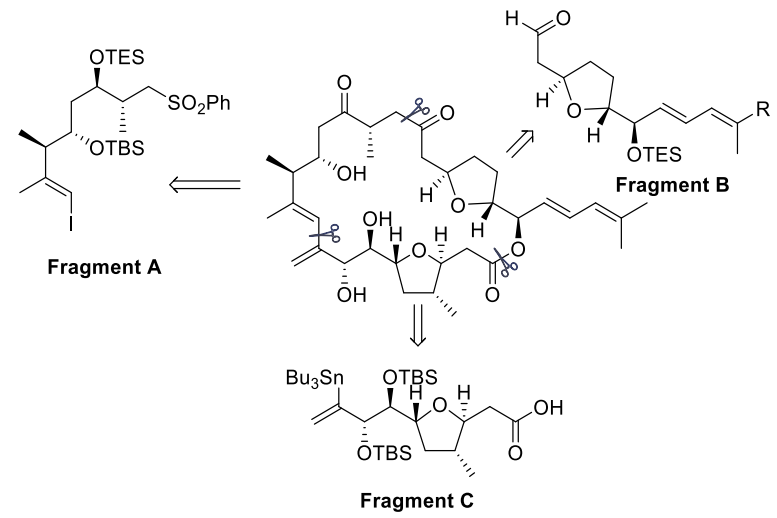
In conclusion, Professor Alois Fürstner's group synthesized the natural product amphidinolide C in 21 longest linear steps (39 total steps). Their synthetic approach

proved to be robust. Several advanced synthetic intermediates were prepared in gram scale. The key steps of Fürstner's synthesis are the Marshall *anti* propargylation, a cobalt-catalyzed Mukaiyama *trans* cyclization, and a molybdenum-catalyzed ring-closing alkyne metathesis and alkyne hydration/hydrolysis. Of note, this was the first example of an alkyne ring-closing metathesis reaction used at the late stage of a complex natural product synthesis.

4.3.3 Total Synthesis of Amphidinolide F by Prof. Bruno Figadère

Most recently, Professor Bruno Figadère and coworkers accomplished the total synthesis of amphidinolide F in 2018. Their retrosynthetic analysis is presented in Scheme 4.15. Target molecule amphidinolide F was divided into three fragments: fragments A, B and C. Similar to Professor Alois Fürstner's approach, Stille coupling was proposed to bring fragment A and fragment C together. Similar to Professor Rich G. Carter's synthetic route, the sulfone alkylation/desulfonation was proposed to anneal fragment A and fragment B. However, Professor Rich G. Carter and coworkers used alkyl iodide as electrophile, while Professor Bruno Figadère and coworkers proposed to use an aldehyde as the electrophile instead.

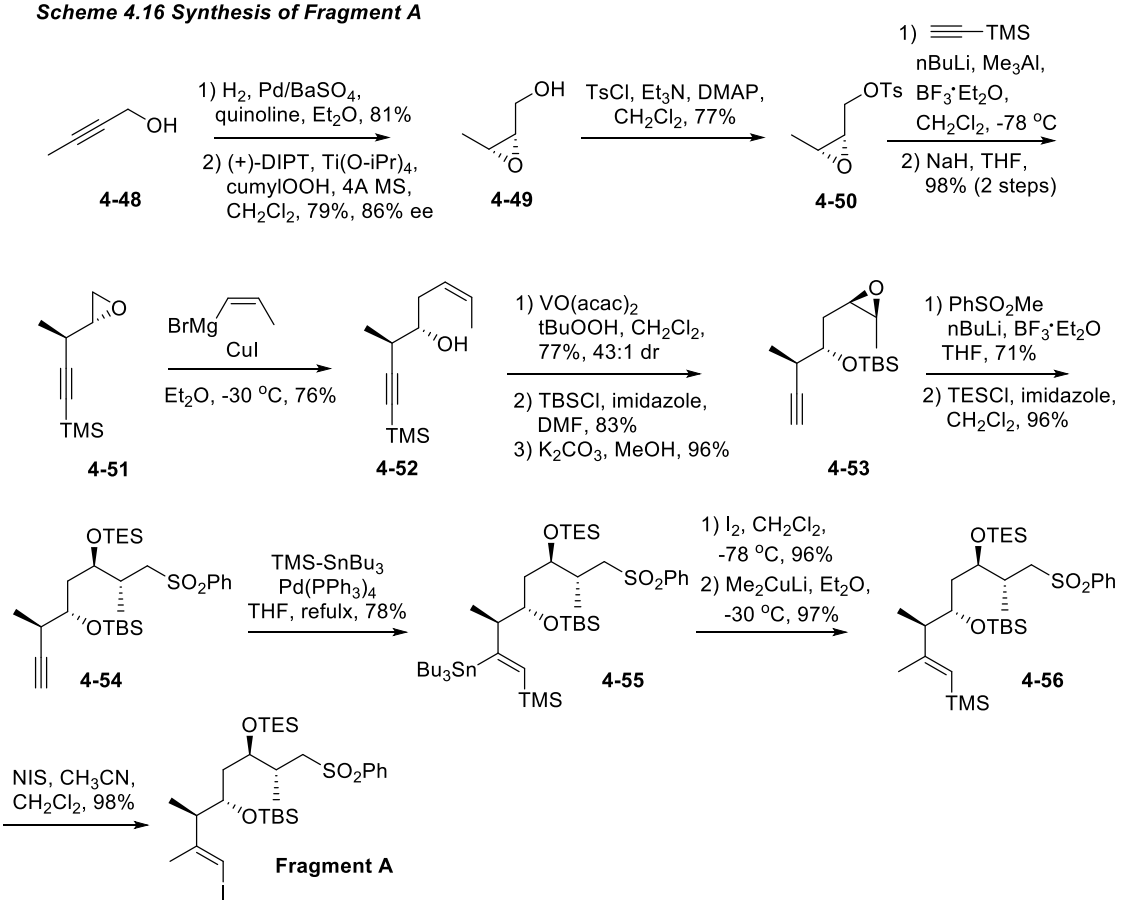
Scheme 4.15 Retrosynthetic Analysis



Synthesis of fragment A was achieved through a series of epoxide forming/opening reactions from commercially available propargyl alcohol **4-48**. Standard Lindlar reduction followed by Sharpless asymmetric epoxidation afforded epoxide **4-49** in good yield and decent enantioselectivity. The free primary hydroxyl group was then allowed to undergo tosylation to obtain compound **4-50**. Next, the epoxide was opened at the less hindered and more electron-deficient side by lithium acetylide. The formed secondary alcohol was deprotonated with sodium hydride and then used to displace the tosylate to form epoxide **4-51**. Another site-selective epoxide opening by *cis*-propenyl magnesium bromide converted **4-51** to enantio-enriched secondary alcohol **4-52** in 76% yield. Subsequent hydroxyl-directed epoxidation followed by TBS protection and TMS deprotection afforded epoxide **4-53** in good yields and great dr (43:1 dr). Epoxide **4-53** was opened at the less hindered side by lithiated methylphenylsulfone. After TES protection, compound **4-54** was synthesized in good yield.

From alkyne **4-54**, various approaches were explored to acess fragment A. The known four-step sequence shown in Scheme 4.16 turned out to work the best for the authors.[104] The alkyne **4-54** was first subjected to a palladium-mediated regio- and stereoselective silyl-stannylation. The tributyltin group in compound **4-55** was first transformed into an iodide. The alkenyl iodide was then substituted by dimethylcuprate to access compound **4-56**. Compound **4-56** was finally transformed to fragment A by iodinlysis of the alkenyl TMS group with NIS.

Scheme 4.16 Synthesis of Fragment A

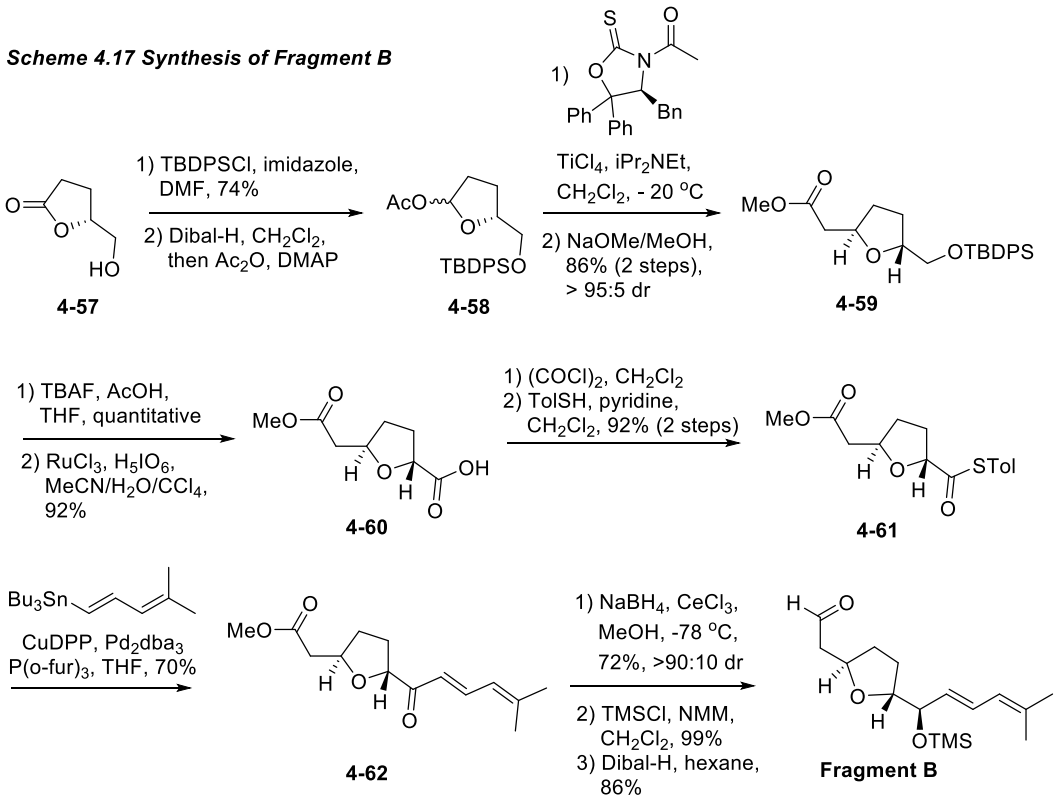


[104] (a) Belen Cid, M.; Pattenden, G. Synlett. 1998, 540. (b) Williams, D. R.; Walsh, M. J.; Miller, N. A. *J. Am. Chem. Soc.* **2009**, *131*, 9038.

Fragment B was synthesized from commercially available lactone **4-57**. First, acetal **4-58** was prepared in good yield through standard transformations such as protection, reduction, and acylation. The challenging *trans*-THF motif was formed through diastereoselective glycosylation of compound **4-58** with bulky oxazolidinethione titanium enolate.[105] Compound **4-59** was isolated in good yield and almost one diastereomer after methanolysis of the auxiliary. Of note, this titanium mediated enolate glycosidation reaction was previously developed by the same group. Furthermore, after deprotection/oxidation, product **4-60** was obtained. Compound **4-60** was further transformed into thioester **4-61**. Chemoselective Liebeskind-Srogl cross-coupling with dienyl tributyltin reagent allowed the installation of the amphidinolide F side chain.[106] Gratifyingly, product **4-62** was afforded in acceptable yield. After Luche reduction of the enone, TMS protection and ester reduction to an aldehyde, fragment B was obtained in overall excellent yield with 90:10 dr.

[105] (a) Jalce, G.; Seck, M.; Franck, X.; Hocquemiller, R.; Figadere, B. *J. Org. Chem.* **2004**, *69*, 3240. (b) Jalce, G.; Franck, X.; Seon-Meniel, B.; Hocquemiller, R. Figadere, B. *Tetrahedron Lett.* **2006**, *47*, 5905. (c) Jalce, G. Franck, X.; Figadere, B. *Eur. J. Org. Chem.* **2009**, 378.
[106] (a) Wittenberg, R.; Srogl, J.; Egi, M.; Liebeskind, L. S. *Org. Lett.* **2003**, *5*, 3033. (b) Li, H.; Yang, H.; Liebeskind, L. S. *Org. Lett.* **2008**, *10*, 4375.

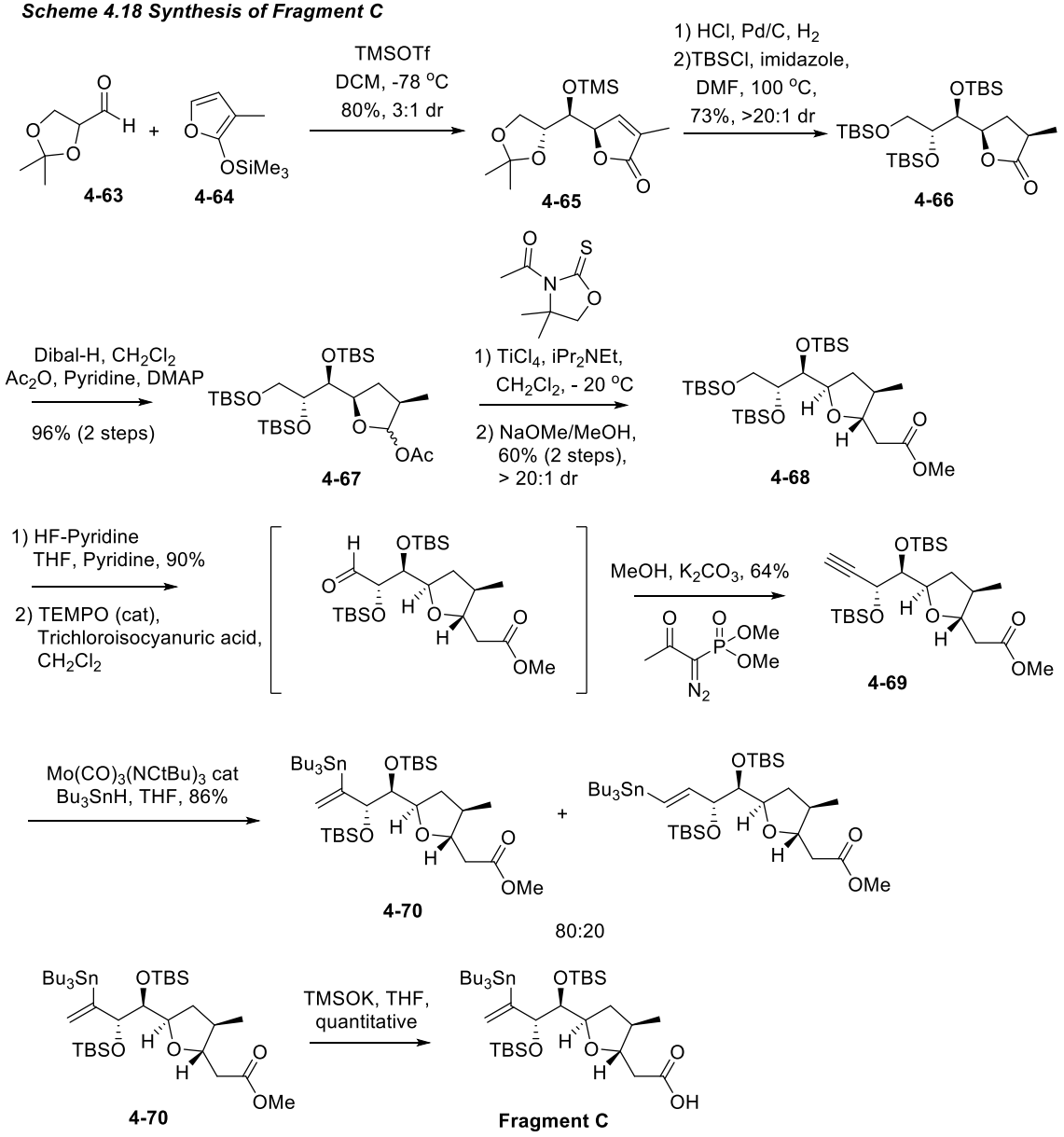
Scheme 4.17 Synthesis of Fragment B



For preparation of the last fragment (fragment C), Bruno Figadere and coworkers used the same route they studied eight years before. As depicted in Scheme 4.18, starting from easily prepared aldehyde **4-63** and 2-methyl-silyloxyfuran **4-64**, a TMSOTf-induced diastereoselective aldol reaction afforded compound **4-65** and its diastereomer in 3:1 dr, combined 80% yield. Subsequent substrate controlled diastereoselective alkene reduction generated compound **4-66** as a single diastereomer. The lactone in compound **4-66** was then reduced to acetal **4-67** in nearly quantitative yield. Compound **4-67** was then subjected to titanium mediated diastereoselective enolate glycosidation to synthesize methyl ester **4-68** in 60% yield after auxiliary hydrolysis. After selective deprotection of primary alcohol and subsequent TEMPO oxidation, the intermediate aldehyde was directly subjected to Bestmann-Ohira alkynylation without further purification. The alkyne **4-69** was prepared in decent yield. Compound **4-69** was allowed to undergo

regioselective hydrostannylation reaction catalyzed by Molybdic complex $Mo(CO)_3(NCtBu)_3$. Desired regio-isomer **4-70** was favored with 4:1 regio-selectivity.[107] Finally, after methyl ester hydrolysis, fragment C was prepared.

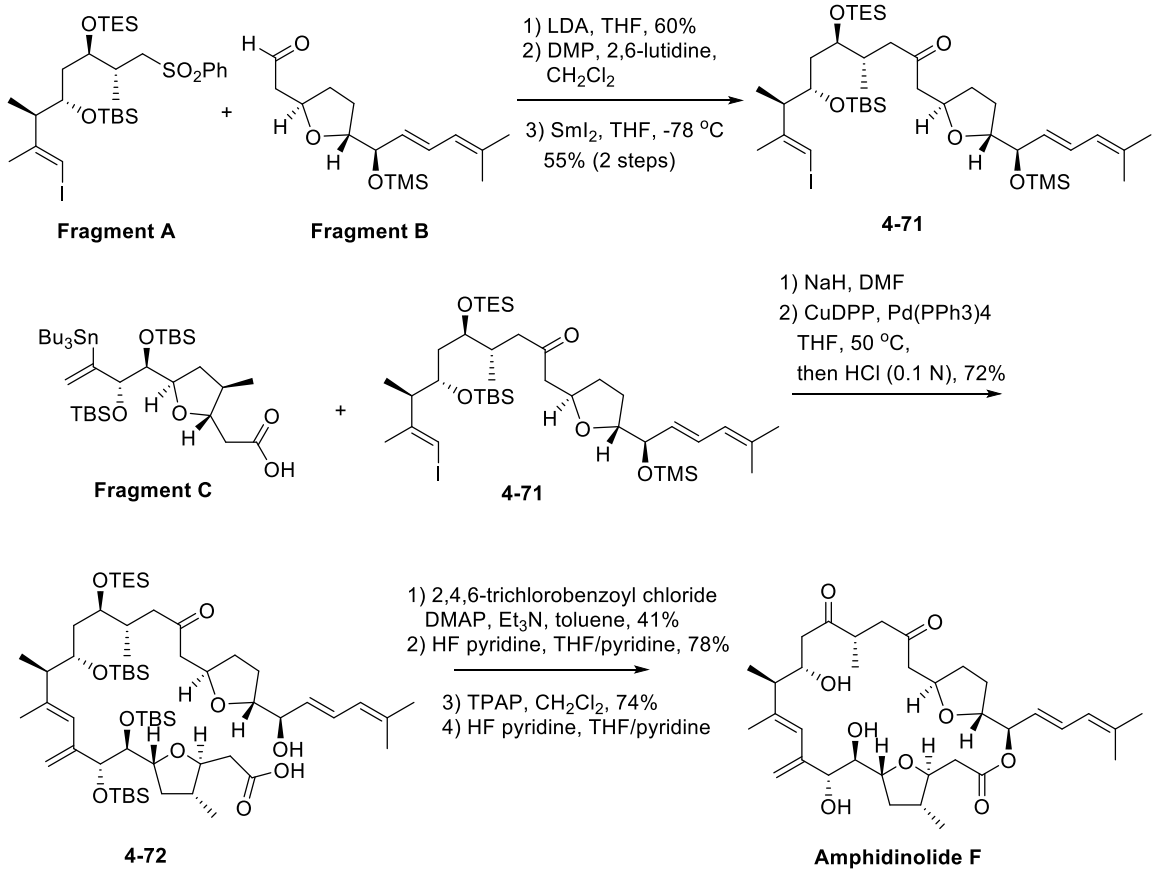
Scheme 4.18 Synthesis of Fragment C



[107] (a) Albers, M. O.; Coville, N. J.; Ashworth, T. V.; Singleton, E.; Swanepoel, H. E. *J. Organomet. Chem.* **1980**, *199*, 55.

Final assembly of fragments A, B and C was depicted in Scheme 4.19. First, fragment A and B were connected together through sulfone alkylation/desulfonylation to afford compound **4-71**. The advanced intermediate **4-71** was then allowed to undergo Stille cross-coupling with fragment C. Product **4-72** was synthesized in good yield. Subsequent Yamaguchi lactonization followed by oxidation state adjustments and global deprotection successfully afforded target molecule amphidinolide F in good yield.

Scheme 4.19 Total Synthesis of Amphidinolide F



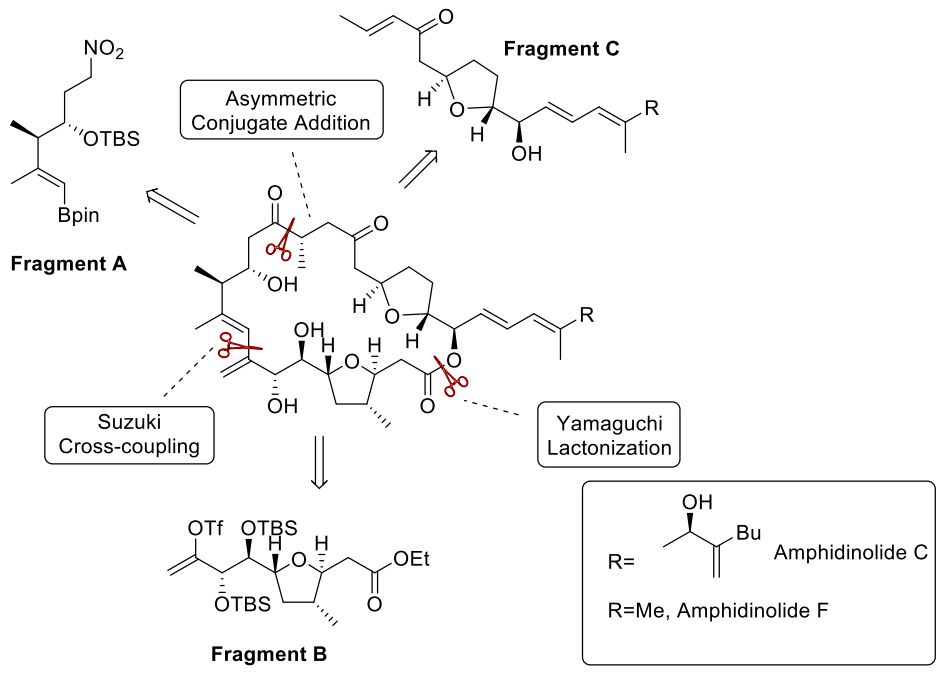
In summary, Professor Bruno Figadère and coworkers accomplished the total synthesis of amphidinolide F in a longest linear sequence of 23 steps and 47 total steps. The key steps of their synthesis are constructing both trans-THF rings using enolate

glycosylation reaction mediated by titanium, and installing the dienyl side chain via Liebeskind-Srogl coupling.

4.4 Retrosynthetic Analysis

After discussing all of the previous synthesis, the rest of the chapter will focus on discussing the synthetic approaches that we adopted. As depicted in Scheme 4.20, we divided the target molecules amphidinolide C and amphidinolide F into three fragments, namely fragment A, fragment B and fragment C. Suzuki cross-coupling was proposed to attach fragment A and fragment B. Fragment C was then joined by asymmetric conjugate addition. Lastly, Yamaguchi cyclization was proposed to effect the late stage intramolecular lactonization reaction to finish up the total synthesis.

Scheme 4.20 Retrosynthetic Analysis

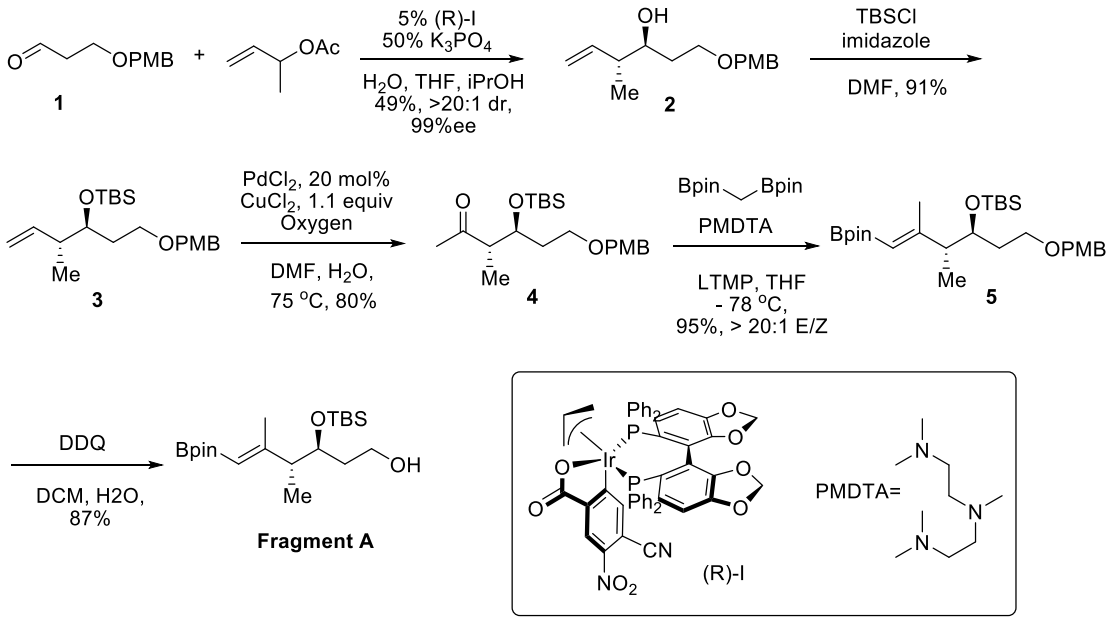


4.5 Fragments Synthesis

4.5.1 Synthesis of Fragment A

The synthetic route to fragment A is shown in Scheme 4.21. Starting from known aldehyde **1**, iridium catalyzed asymmetric crotylation reaction developed by Professor Krische's group successfully generated *anti* product **2** in useful yield and perfect stereoselectivity (>20:1 dr, 99% ee).[108] After standard TBS protection and Wacker oxidation, compound **4** was synthesized efficiently. The next step is a E-selective boron Wittig reaction of ketones recently developed in the Morken group,[109] affording the trisubstituted alkenyl boronic ester **5** as pure E isomer in almost quantitative yield. Finally, to our delight, the boronic ester in compound **5** survived the PMB group deprotection, and fragment A was successfully prepared.

Scheme 4.21 Synthesis of Fragment A



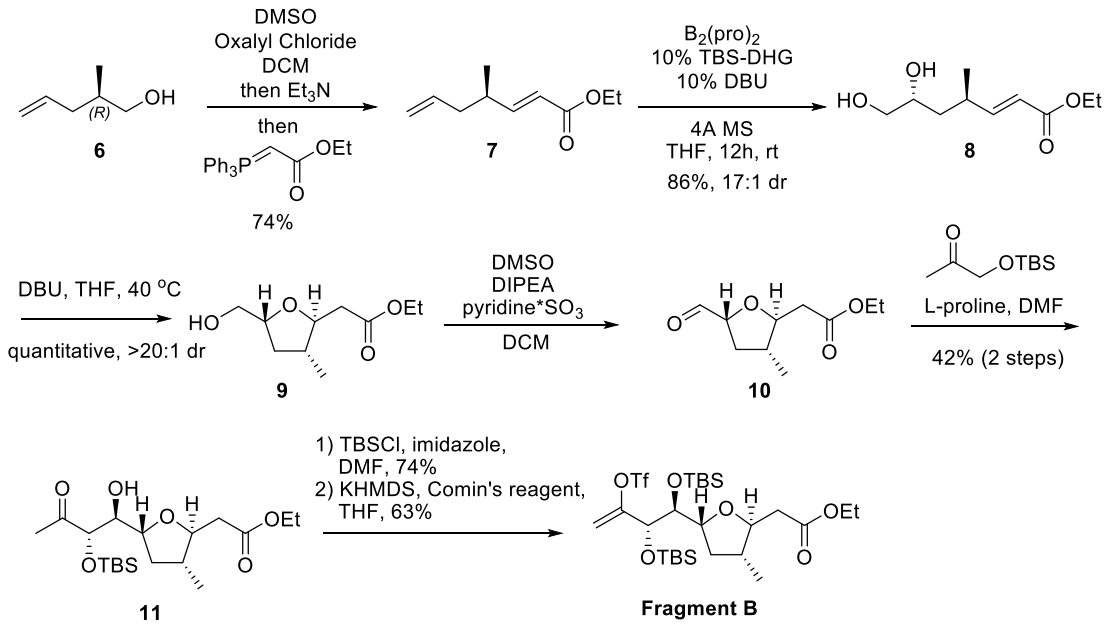
[108] (a) Kim, I. S.; Han, S. B.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 2514. (b) Gao, X.; Townsend, I. A.; Krische, M. J. *J. Org. Chem.* **2011**, *76*, 2350.
[109] Namirembe, S.; Gao, C.; Wexler, R. P. *Org. Lett.* **2019**, *21*, 4392.

4.5.2 Synthesis of Fragment B

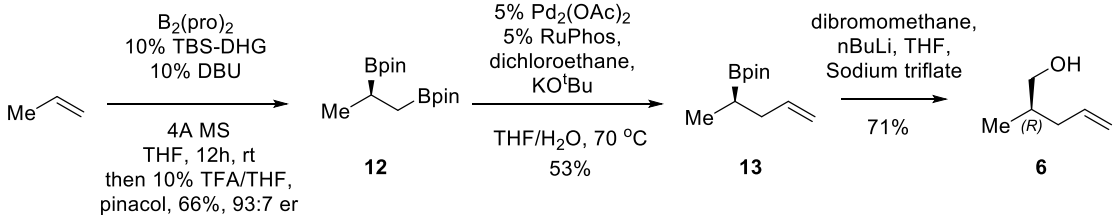
Synthesis of fragment B is depicted in Scheme 4.22. We started from known chiral alcohol (*R*)-2-methylpent-4-en-1-ol 6. One-pot Swern oxidation-Wittig cascade reaction generated enone **7** in 74% yield. Enone **7** was then converted to diol **8** smoothly through a carbohydrate-catalyzed enantioselective alkene diboration/oxidation reaction sequence. Of note, the terminal alkene in compound **7** was selectively diborated under the carbohydrate-catalyzed alkene diboration reaction conditions, while the enone double bond stayed untouched. Next, the first THF ring in the target molecule was synthesized through DBU promoted oxo-Michael addition of diol **8**. Of note, the cyclization product compound **9** was prepared as a single diastereomer, in excellent yield. Additionally, only the secondary alcohol underwent oxo-Michael addition under the reaction conditions, the six-membered ring byproduct was not observed. The primary alcohol in compound **9** was then oxidized to aldehyde **10** through Parikh-Doering oxidation. Due to compound stability, aldehyde **10** was directly subjected to the proline-catalyzed aldol reaction with TBS protected acetol. Advanced intermediate **11** was prepared in useful yield through this two-step sequence (42%). After standard TBS protection, ketone **11** was converted to a triflate through selective deprotonation followed by trap with Comins' reagent. Thus, fragment B was synthesized efficiently. Furthermore, synthesis of starting material **6** is worth a comment. Initially, we used route I to prepare chiral alcohol **6**. Thus, the feedstock chemical propene can undergo carbohydrate catalyzed alkene diboration reaction smoothly, generating product **12** after pinacol swap in 65% yield, 93:7 er. Compound **12** was then subjected to selective Suzuki cross-coupling with in situ generated vinyl chloride. Enantio-enriched boronic ester **13** was formed in moderate yield

(55%). After standard Zweifel homologation/oxidation reaction sequence, compound **6** was prepared. However, due to the challenges in scale up of in the Suzuki cross-coupling step, we finally decided to use the literature reported route[110] (route II) starting from Evans' chiral auxiliary so as to achieve the large scale material preparation.

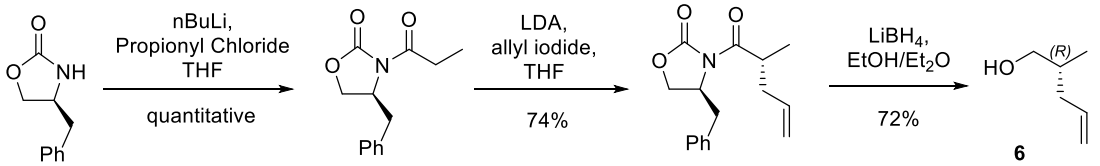
Scheme 4.22 Synthesis of Fragment B



Route I



Route II



[110] Speltz, T. E.; Fanning, S. W.; Mayne, C. G.; Fowler, C.; Tajkhorshid, E.; Greene, G. L.; Moore, T. W. *Angew. Chem. Int. Ed.* **2016**, *55*, 4532.

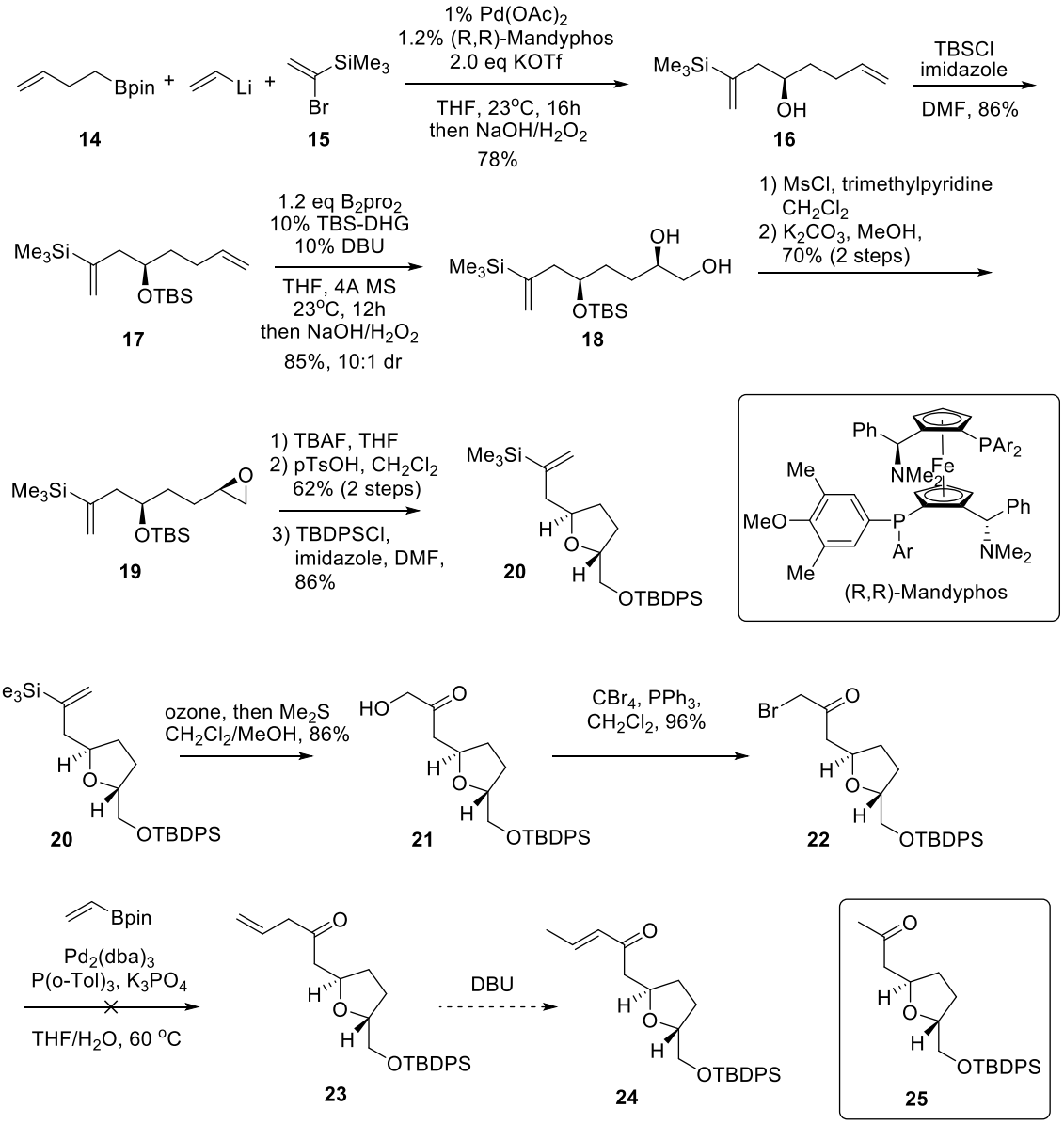
4.5.3 Synthetic Studies toward Fragment C

As depicted in Scheme 4.23, for the synthesis of fragment C, we started from a simple alkyl boronic acid pinacol ester **14**, vinyl lithium, and alkenyl bromide **15**. First, the three-component conjunctive cross-coupling developed by the Morken group was utilized to synthesize enantio-enriched secondary alcohol **16**.[111] After standard TBS protection, compound **17** was subjected to the carbohydrate-catalyzed alkene diboration/oxidation reaction. Diol product **18** was afforded in good yield and acceptable diastereoselectivity (10:1 dr). Of note, the terminal alkene in compound **17** underwent the carbohydrate-catalyzed diboration reaction selectively, while the alkenyl silane stayed intact. Diol **18** was then converted to epoxide **19** through standard reaction conditions. Next, the TBS protecting group in compound **19** was deprotected by TBAF, and subsequent acid promoted intramolecular epoxide opening by secondary hydroxyl group successfully afforded the second THF ring of the target molecule. Following TBDPS protection of the generated primary alcohol, compound **20** was synthesized. From compound **20**, our goal was to convert the alkenyl silane functional group to an enone such as compound **24**. In order to achieve this goal, compound **20** was firstly transformed to compound **21** through ozonolysis.[112] The hydroxyl group in compound **21** was then brominated. The bromination product **22** was subjected to Suzuki cross coupling with vinyl boronic acid pinacol ester. Our plan was to synthesize compound **23** which can be further subjected to DBU promoted isomerization to form the desired enone product **24**. Unfortunately, the designed Suzuki cross-coupling did not afford any product under various reaction

[111] (a) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science*, **2016**, *351*, 70. (b) Edelstein, E. K.; Namirembe, S.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 5027.
[112] Buechi, G.; Wuest, H. *J. Am. Chem. Soc.* **1978**, *100*, 294.

conditions. Only debrominated byproduct **25** was observed. As a consequence, we are now working on designing new synthetic route towards the synthesis of fragment C.

Scheme 4.23 Snythetic Study toward Fragment C



4.5.4 Coupling of Fragment A and Fragment B

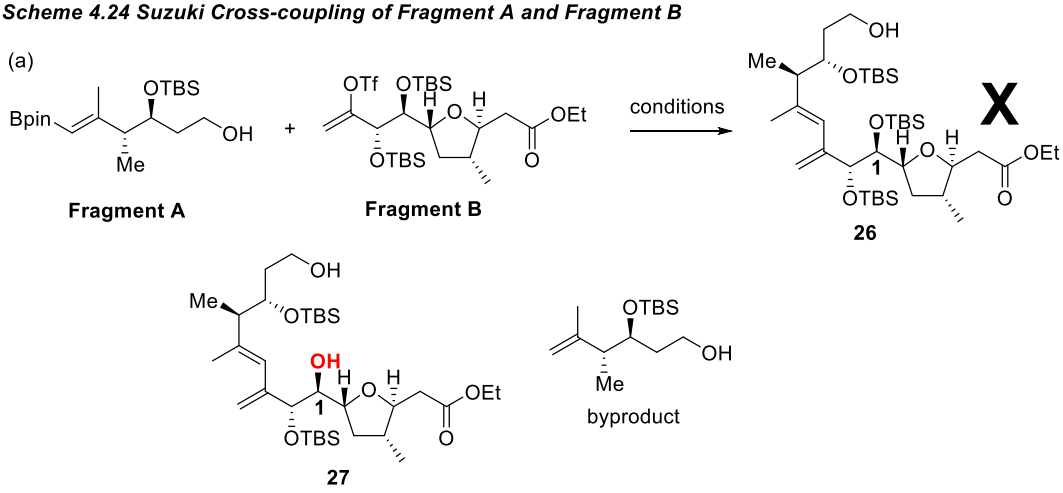
While the synthesis of Fragment C is still under development, we decided to study the Suzuki cross-coupling between fragment A and fragment B. As depicted in Scheme 4.24,

initially, with 20% $Pd(PPh_3)_2Cl_2$ as catalyst, potassium phosphate as base, and THF as solvent, fragment B did undergo Suzuki cross-coupling reaction with fragment A in full conversion when 2.5 equivalents of fragment A was employed (entry 1). However, the isolated product is not the tri-TBS protected compound **26**, Instead, one of the TBS protecting group was removed during the cross-coupling. After careful NMR analysis, we believe that the isolated compound could be deprotected product **27**. Since it is not appealing to use a large access amount of fragment A in the coupling step, we explored other reaction conditions that employ smaller amounts of fragment A. As shown in entry 2, unfortunately, when a smaller amount of fragment A was applied to the cross-coupling reaction (1.2 equiv instead of 2.5 equiv), only about 20% of fragment B was cross-coupled. The rest of the fragment A underwent proto-deborylation. When 20% $Pd(OAc)_2$ and 20% Ruphos were involved as catalyst, no conversion of fragment B was observed; all of fragment A was decomposed by proto-deborylation (entry 3). These results suggested that the proto-deborylation of fragment A might be faster than the oxidative addition of fragment B and subsequent transmetallation of fragment A. Thus, in order to slow down the proto-deborylation of fragment A, Suzuki cross-coupling reaction conditions that do not involved water were tested. As depicted Scheme 4.24 (b), according to Professor J. R. Falck's report,[113] when the alkyl boronic ester was treated with tert-butyllithium to form the ate complex, the ate complex underwent Suzuki cross-coupling smoothly with alkenyl halides and triflates under anhydrous reaction condition (equation 1). Unfortunately, when we attempted these reaction conditions, no product was observed. Instead, only unreacted starting material was recovered. As a consequence, this Suzuki cross-coupling reaction is now the subject of further optimization.

[113] Zou, G. Falck, J. R. *Tetrahedron Letters*. **2001**, *42*, 5817.

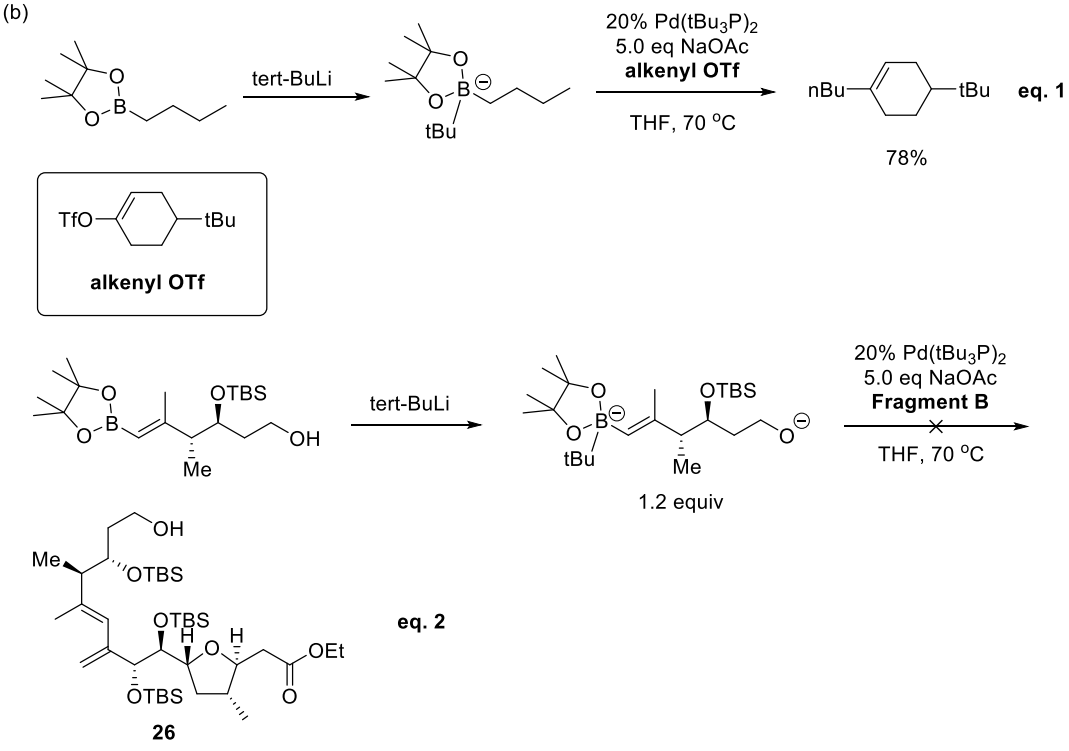
Scheme 4.24 Suzuki Cross-coupling of Fragment A and Fragment B

(a)



entry	A:B ratio	catalyst	base	solvent	temperature/ ^{o}C	conversion of Fragment B
1	2.5:1	20% $Pd(PPh_3)_2Cl_2$	K_3PO_4	THF/H2O	60 ^{o}C	Full conversion (41% isolation yield)
2	1.2:1	20% $Pd(PPh_3)_2Cl_2$	K_3PO_4	THF/H2O	60 ^{o}C	20% conversion
3	1.2:1	20% $Pd(OAc)_2$/RuPhos	K_3PO_4	THF/H2O	60 ^{o}C	no conversion

(b)



4.6 Conclusions

Reaction methodologies recently developed in the Morken group such as the carbohydrate-catalyzed enantioselective alkene diboration, conjunctive cross-coupling, and E-selective ketone boron Wittig reaction were successfully used in the synthetic studies towards potent natural products amphidinolide C and F. Of note, the carbohydrate-catalyzed alkene diboration reaction proved to be a powerful transformation that can be used both in early stage synthetic material preparation (propene diboration) and late stage selective functionalization of multiple carbon-carbon double bond containing substrates.

4.7 Experimental Section

4.7.1 General Information

^{1}H NMR spectra were recorded on Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz) or Varian Gemini 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: integration, chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz) or a Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl3: 77.23 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (160 MHz). Chemical shifts are reported in ppm with an external standard ($BF_3 \cdot Et_2O$: 0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are

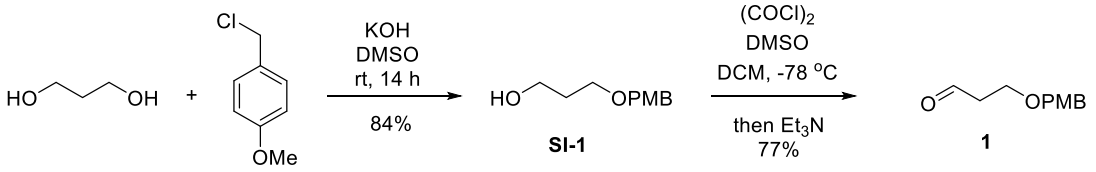
reported in wavenumbers (cm-1) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol, or potassium permanganate.

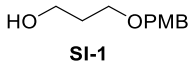
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier. Analytical chiral gas-liquid chromatography (GLC) was performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β -Dex 120 column with helium as the carrier gas.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Tetrahydroxydiboron was purchased from Frontier Scientific. It was recrystallized by water before use. D-glucal triacetate was purchased from Alfa Aesar. Activated 4Å Molecular Seives was bought from Sigma-Aldrich. (*R*)-Krische iridium complex was purchased from Strem. All other

reagents were purchased either from Aldrich, Alfa Aesar, Acros, Oakwood Chemicals, Combi Blocks, or TCI and were used without further purification.

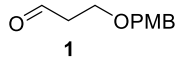
4.7.2 Synthesis of Fragment A





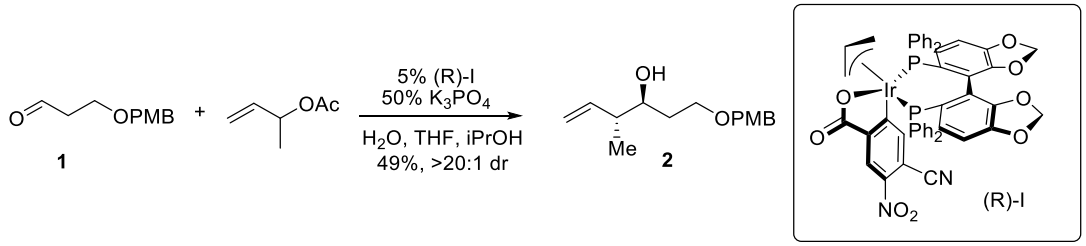
3-((4-methoxybenzyl)oxy)propan-1-ol (SI-1). To a flame-dried 100 ml 2-neck round bottom flask with magnetic stir bar was added potassium hydroxide (1.12 g, 20.00 mmol). The flask was then purged with nitrogen. DMSO (20 mL) and propane-1,3-diol (1.52 g, 20.00 mmol, 1.45 mL) were added to the flask. The mixture was allowed to stir at room temperature for 1 hour. 1-(chloromethyl)-4-methoxy-benzene (1.57 g, 10 mmol, 1.36 mL) was then injected to the reaction mixture. The reaction mixture was allowed to stir at room temperature for 14 hours. Upon completion of the reaction, water (20 ml) was added. The mixture was then transfered to a sep funnel. Layers were separated. The aqueous layer was extracted by ethyl acetate for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product product. The crude product was purified through silica gel column using 1:1 hexane to ethyl acetate as eluent. The product was obtained as clear oil (1.64 g, 8.36 mmol, 83.57% yield). Spectral data are in accordance with literature report[114].

[114] Kretschmer, M.; Menche, D. *Org. Lett.* **2012**, *14*, 382.

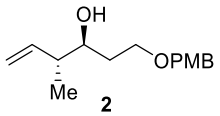


1

3-((4-methoxybenzyl)oxy)propanal (1). To a flame-dried 100 ml round-bottomed flask with stir bar was added DMSO (2.47 g, 31.55 mmol, 2.24 mL) and DCM (20 mL) under nitrogen. The mixture was cooled to −78 °C, followed by the dropwise addition of oxalyl chloride (1.84 g, 14.46 mmol, 1.26 mL). The reaction was then allowed to stir at -78 °C for 30 min. Alcohol **SI-1** 3-((4-methoxybenzyl)oxy)propan-1-ol (1.29 g, 6.57 mmol) in CH_2Cl_2 (8 mL) was added and the reaction was allowed to stirr for additional 1.5 h at −78 °C . Triethylamine (4.86 g, 47.99 mmol, 6.69 mL) was then added and the reaction mixture was allowed to warm to rt. Water (20 ml) was added to the reaction mixture. The mixture was then transferred to a sep funnel. Layers were separated. The aqueous layer was extracted with CH_2Cl_2 for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 30% ethyl acetate in hexane as eluent. Product was afforded as clear oil (980 mg, 5.05 mmol, 76.76% yield). Spectral data are in accordance with literature report[115]. HRMS-(DART+) for $C_{11}H_{13}O_3$ $[M+H]^+$: calculated: 193.0859, found: 193.0863.

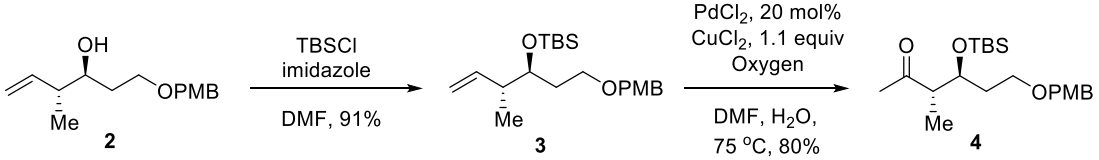


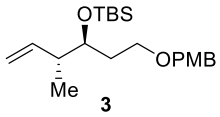
[115] Hayashi, Y.; Yamaguchi, H.; Toyoshima, M.; Okado, K.; Toyo, T.; Shoji, M. *Chem. Eur. J.* **2016**, *16*, 10150.



2

(3S,4R)-1-((4-methoxybenzyl)oxy)-4-methylhex-5-en-3-ol (2). Compound 2 was prepared according to literature report with slight modification[116]. An oven-dried 4-dram vial with magnetic stir bar was charged with 3-(4- methoxybenzyloxy)propanal **1** (388.5 mg, 2.0 mmol), (R)-I (51.70 mg, 0.0025 mmol, 2.5 mol%), K_3PO_4 (212.3 mg, 1.0 mmol), THF (1.0 mL, 2.0 M) in the glovebox. The vial was sealed with a teflon septa and removed from the glovebox. A nitrogen inlet was introduced. Degassed isopropanol (0.31 mL, 4.0 mmol) and H_2O (0.18 mL, 1.0 mmol) was then added to the reaction. Finally, but-3-en-2-yl acetate (0.51 mL, 4.0 mmol) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vial was placed in an oil bath at 60 ^oC and was allowed to stir for 48 h. The reaction mixture was concentrated in vacuo. Purification of the residue by silica gel column (ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **2** (245.3 mg) as a colorless oil in 49% yield (>20:1 dr). Spectral data are in accordance with literature report[27]. HRMS-(DART+) for $C_{15}H_{23}O_3$ $[M+H]^+$: calculated: 251.1642, found: 251.1645.

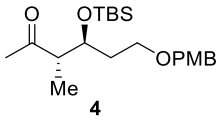




3

[116] Gao, X.; Townsend, I. A. Krische, M. J. *J. Org. Chem.* **2011**, *76*, 2350.

tert-butyl(((3S,4R)-1-((4-methoxybenzyl)oxy)-4-methylhex-5-en-3yl)oxy)dimethylsilane (3). To a 20 ml scintillation vial with magnetic stir bar and compound **2** (210 mg, 838.88 umol) was added DMF (1.5 mL) and imidazole (114.22 mg, 1.68 mmol). The mixture was allowed to stir for 2 minutes. TBSCl (221.26 mg, 1.47 mmol) was then added. The reaction was allowed to stir at room temperature for 14 hours. Upon the completion of the reaction, water (5 ml) was added. The mixture was transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by hexane for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified by silica gel column with 2% ethyl acetate in hexane as eluent. The product was afforded as clear oil (276 mg, 757.01 umol, 90.24% yield). Spectral data are in accordance with literature report.[117] HRMS-(DART+) for $C_{21}H_{35}O_3Si$ $[M+H]^+$: calculated: 363.2350, found: 363.2345.

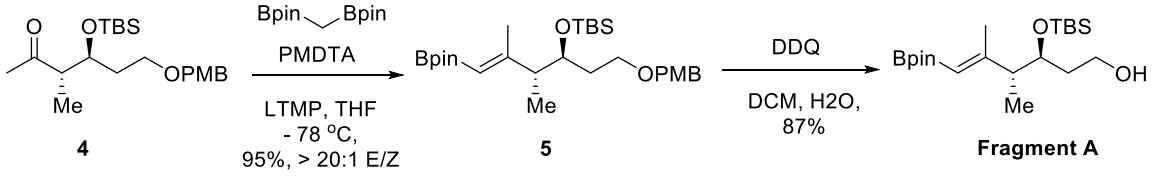


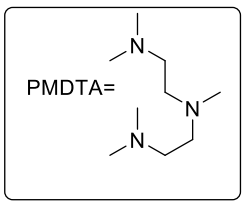
4

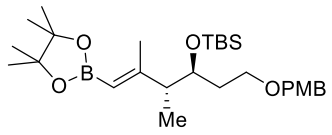
(3S,4S)-4-((tert-butyldimethylsilyl)oxy)-6-((4-methoxybenzyl)oxy)-3-methylhexan-2-one (4). To an oven-dried 4-dram vial with stir bar was added palladium chloride (12.94 mg, 72.96 umol), Copper (I) Chloride (39.73 mg, 401.27 umol) in the glove box. The vial was sealed with a teflon septa and removed from the glovebox. DMF (2.5 mL) and water (2 ml) was then added to the vial. The vial was purged with oxygen ballon. The mixture was allowed to stir under oxygen for 2 hours at room temperature. Compound **3**(133 mg,

[117] Eggen, M.; Mossman, C. J.; Buck, S. B.; Nair, S. K.; Bhat, L.; Ali, S. M.; Reiff, E. A.; Boge, T. C.; Georg, G. L. *J. Org. Chem.* **2000**. *65*. 7792.

364.79 umol) in DMF (2.5 ml) was then injected. The reaction was heated up to 75 ^{o}C and stir at 75 ^{o}C for 14 hours. Upon the completion of the reaction, water (5 ml) and hexane (5 ml) were added. The mixture was transfered to a sep funnel. The layers were separated. The aqueous layer was extracted by hexane (2 times) and ethyl acetate (2 times). The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 5% to 10% ethyl acetate in hexane as eluent. The prodcut was afforded as clear oil (110 mg, 289.02 umol, 79.23% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 8.1 Hz, 2H), 4.51 – 4.38 (m, 2H), 4.14 (q, J = 5.8 Hz, 1H), 3.83 (s, 3H), 3.54 (t, J = 6.4 Hz, 2H), 2.74 (p, J = 6.8 Hz, 1H), 2.17 (s, 3H), 1.78 (dq, J = 12.8, 6.3 Hz, 1H), 1.69 (td, J = 13.9, 12.9, 7.0 Hz, 1H), 1.06 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.06 (d, J = 9.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.6, 159.3, 130.8, 129.4, 114.0, 72.8, 71.1, 66.1, 55.5, 52.7, 33.8, 30.5, 26.0, 18.2, 12.0, -4.5, -4.6. HRMS-(DART+) for $C_{21}H_{40}NO_4Si$ $[M+NH_4]^+$: calculated: 398.2721, found:398.2719. IR (neat): 2951.0 (m), 2927.0 (m), 2853.8 (m), 1713.3 (s), 1512.0 (m), 1358.8 (w), 1247.3 (s), 1098.9 (s), 1037.6 (s), 834.2 (s). $[\alpha]_D^{20}$= +30.217 (c=0.9, $CHCl_3$, l=50 mm).



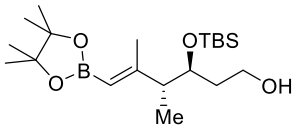




5

tert-butyl(((3S,4R,E)-1-((4-methoxybenzyl)oxy)-4,5-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-3-yl)oxy)dimethylsilane (5). To a flame-dried 25 ml round bottom flask with magnetic stir bar was added (2,2,6,6-tetramethyl-1-piperidyl)lithium (131.49 mg, 893.34 umol), PMDTA (38.70 mg, 223.34 umol) and THF (2.0 ml) in the glovebox. The flask was sealed with a rubber septa and removed from the glovebox. A nitrogen inlet was introduced. The flask was cooled down to 0 ^{o}C. methylene bisboronic acid pinacol ester (239.38 mg, 893.34 umol) in THF (1.0 ml) was then added. The mixture was allowed to stir at 0 ^{o}C for 5 minutes and then cool down to -78 oC. Compound **4** (170 mg, 446.67 umol) in THF (2.0 ml) was added last. The reaction was allowed to stir at -78 ^{o}C for 8 hours and then warm up to room temperature. Upon the completion of the reaction, solvent was removed in vacuo. The residue was purified through silica gel column with 2% ethyl acetate in hexane as eluent. The product was afforded as clear oil (214.1 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.15 (s, 1H), 4.51 – 4.29 (m, 2H), 3.99 – 3.88 (m, 1H), 3.80 (s, 3H), 3.55 – 3.41 (m, 2H), 2.34 (p, J = 7.8, 7.2 Hz, 1H), 1.99 (s, 3H), 1.79 – 1.59 (m, 2H), 1.26 (s, 12H), 1.01 (d, J = 6.9 Hz, 3H), 0.87 (s, 9H), 0.03 (d, J = 6.1 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 159.3, 131.0, 129.4, 113.9, 82.8, 72.71, 71.65, 67.3, 55.5, 50.1, 32.7, 26.1, 25.1, 25.0, 22.6, 21.0, 18.3, 14.3, 13.4, -4.3, -4.4. ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.25. HRMS-(DART+) for $C_{28}H_{50}BO_5Si$ $[M+H]^+$: calculated: 505.3515, found:505.3525. IR (neat): 2952.9 (m), 2926.4 (m), 2853.5 (m), 1634.2 (m), 1511.9 (m),

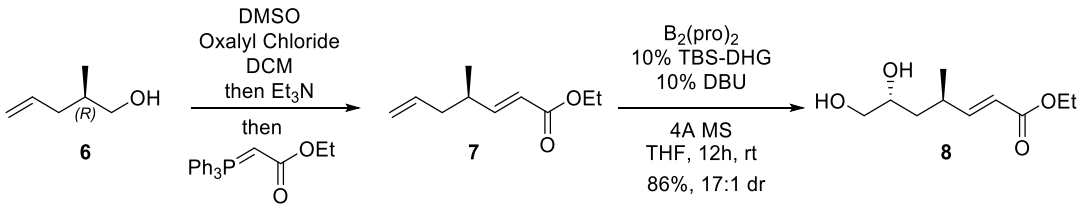
1360.7 (w), 1318.9 (s), 1247.0 (s), 1144.1 (s), 1100.6 (m), 834. 4(s). $[\alpha]_D^{20}$= +9.332 (c=1.05, $CHCl_3$, l=50 mm).

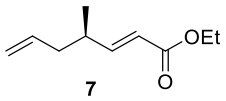


Fragment A

(3S,4R,E)-3-((tert-butyldimethylsilyl)oxy)-4,5-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-ol(Fragment A). To a 20 ml scintillation vial with stir bar and compound **5** (142 mg, 281.42 umol), was added CH_2Cl_2(1.8 ml) and water (0.2 ml). The mixture was allowed to stir for 2 minutes at room temperature. DDQ (70.27 mg, 309.56 umol) was then added. The reaction was allowed to stir at room temperature for 3 hours. Upon the completion of the reaction, water (3 ml) was added. The mixture was transferred to a sep funnel. Layers were separated. The aqueous layer was extracted by CH_2Cl_2 for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 10% ethyl acetate in hexane as eluent. The product was afforded as clear oil (94.1 mg, 87%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.18 (s, 1H), 3.98 (ddd, J = 7.1, 5.5, 4.2 Hz, 1H), 3.72 (dtt, J = 15.5, 9.9, 5.1 Hz, 2H), 2.42 (p, J = 6.6 Hz, 1H), 2.00 (s, 3H), 1.75 – 1.57 (m, 2H), 1.26 (s, 12H), 1.01 (d, J = 7.0 Hz, 3H), 0.89 (s, 9H), 0.08 (d, J = 14.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8, 82.9, 73.6, 60.8, 49.5, 34.2, 26.1, 25.1, 25.1, 21.2, 18.2, 13.2, -4.2, -4.4. HRMS-(DART+) for $C_{11}H_{41}BO_4$ $[M+H]^+$: calculated: 385.2920, found:385.2937. IR (neat): 2953.1 (m), 2927.2 (m), 2854.3 (w), 1634.4 (m), 1369.2 (s), 1320.0 (s), 1254.3 (s), 1101.8 (m), 1049.0 (m), 835. 0(s), 773.4(m). $[\alpha]_D^{20}$= +5.774 (c=1.05, $CHCl_3$, l=50 mm).

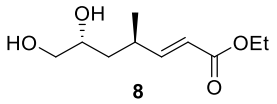
4.7.3 Synthesis of Fragment B





ethyl (R,E)-4-methylhepta-2,6-dienoate (7). To a flame-dried 50 ml 2-neck round bottom flask with stir bar was added DMSO (312.03 mg, 3.99 mmol, 283.66 uL) and CH_2Cl_2 (5 ml) under nitrogen. The flask was cooled down to -78 ^oC. Oxalyl dichloride (380.19 mg, 3.00 mmol, 260.40 uL) was then added in drop. The mixture was allowed to stir at -78 ^oC for 30 minutes. (2R)-2-methylpent-4-en-1-ol **5** (200 mg, 2.00 mmol) in CH_2Cl_2 (10 ml) was added. The reaction was then allowed to stir at -78 ^oC for additional 1.5 hour. Triethylamine (808.24 mg, 7.99 mmol, 1.11 mL) was added. The reaction was then allowed to warm up to room temperature. Lastly, Wittig reagent (Carbethoxymethylene) triphenylphosphorane (2.09 g, 5.99 mmol) was added to the reaction, and the reaction mixture was stirring at room temperature for another 16 hours. Upon the completion of the reaction, water was added (20 ml). The mixture was transferred to a sep funnel. Layers were separated. The aqueous layer was extracted by CH_2Cl_2 for 3 times. Organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 2% to 5% diethyl ether in pentane as eluent. The product was afforded as clear oil (246 mg, 1.46 mmol, 73.23% yield). Spectral data are in accordance with

literature report[118]. HRMS-(DART+) for $C_{10}H_{17}O_2$ $[M+H]^+$: calculated: 169.1223, found: 169.1212.

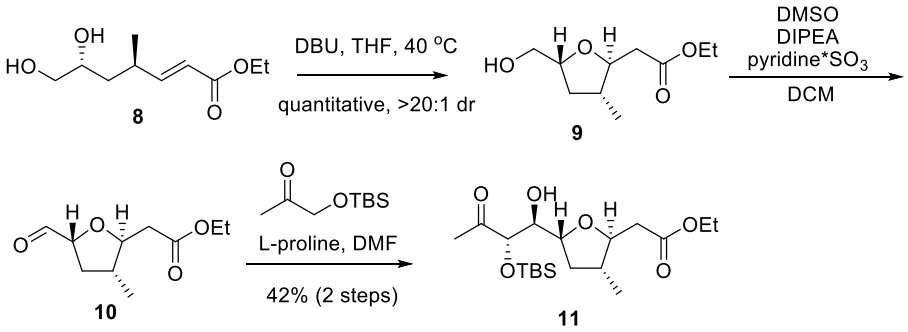


8

ethyl (4R,6R,E)-6,7-dihydroxy-4-methylhept-2-enoate (8). To an oven-dried 2-dram vial with stir bar in the glovebox, was added TBS-DHG (37.75 mg, 143.85 umol), B_2pro_2 (415.18 mg, 2.45 mmol), 4Å molecular sieves (200 mg) , THF (1.5 ml), enone **7** (242 mg, 1.44 mmol) and DBU (21.90 mg, 143.85 umol) . The vial was sealed with a teflon cap and removed from the glovebox. The reaction was allowed to stir at 30 ^oC for 12 hours. Upon the completion of the reaction, pH= 7 phosphate buffer (1.5 ml) was added. The vial was then cooled down to 0 ^oC by ice bath. 30% H_2O_2 was then added in drop. The reaction was allowed to stir at room temperature for 3 more hours. The mixture was transferred to a sep funnel. Saturated thiosulfate was added. Layers were separated. The aqueous layer was extracted by ethyl acetate for 5 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 70% ethyl acetate in hexane as eluent. The product was afforded as clear oil (250.2 mg, 96.24% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 6.92 (dd, J = 15.7, 7.7 Hz, 1H), 5.81 (d, J = 15.7 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.78 (tt, J = 7.6, 4.6 Hz, 1H), 3.65 (dd, J = 11.0, 2.9 Hz, 1H), 3.43 (dd, J = 11.0, 7.5 Hz, 1H), 2.64 – 2.49 (m, 1H), 1.60 (ddd, J = 15.0, 8.6, 6.6 Hz, 1H), 1.42 – 1.35 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.09 (d, J = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.1, 154.2, 120.0, 70.1, 67.0, 60.5, 39.2, 33.2, 19.2, 14.5. HRMS-(DART+) for $C_{10}H_{19}O_4$

[118] Sakamoto, K.; Hakamata, A.; Tsuda, M.; Fuwa, H. *Angew. Chem. Int. Ed.* **2018**, *57*, 3801.

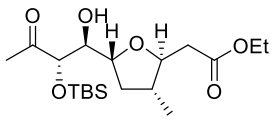
$[M+H]^+$: calculated: 203.1278, found:203.1274. IR (neat): 3384.1 (br), 2956.9 (m), 2928.8 (m), 2870.6 (w), 1714.0 (s), 1699.6 (s), 1648.7 (m), 1279.2 (s), 1036.9 (s), 834.8(w). $[\alpha]_D^{20}$= -18.997 (c=1.0, $CHCl_3$, l=50 mm).



To a 20 ml scintillation vial with stir bar and compound **8** (260 mg, 1.29 mmol) was added THF (2 mL), and DBU (391.42 mg, 2.57 mmol). The mixture was allowed to stir at 40 °C for 14 hours. Upon the completion of the reaction, water (5 ml) was added. The mixture was transferred to a sep funnel. Layers were separated. The aqueous layer was extracted by ethyl acetate for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product **9**. The crude product was taken to the next step without for the purification.

To a 20 ml scintillation vial with stir bar and crude product **9** (105 mg, 519.17 umol) was added CH_2Cl_2 (1.5 ml), dimethyl sulfide (161.28 mg, 2.60 mmol, 190.86 uL) and diisopropylethylamine (469.68 mg, 3.63 mmol, 632.99 uL). The mixture was allowed to stir at room temperature for 10 minutes. Pyridine sulfur trioxide (247.90 mg, 1.56 mmol) was then added. The reaction was allowed to stir at room temperature for another 3 hours. Upon the completion of the reaction, water (3 ml) was added. The mixture was transferred to a sep funnel. The layers were separated. The aqueous layer was extracted

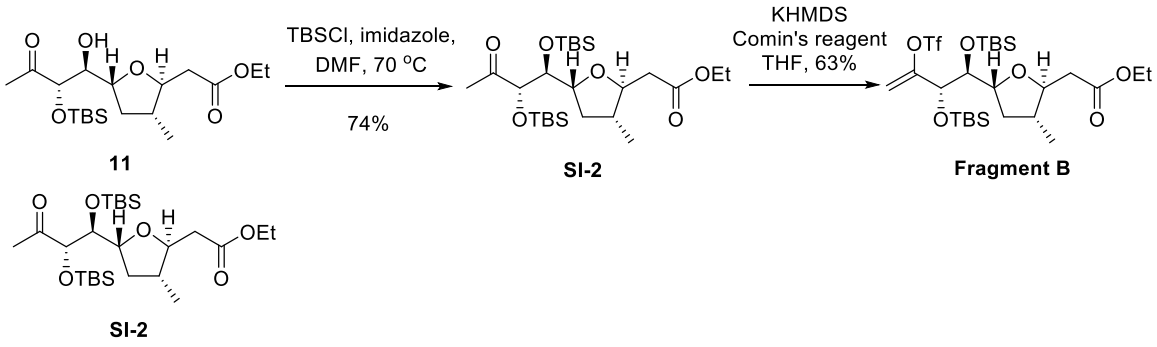
by CH_2Cl_2 for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product **10**. The crude product **10** was taken to the next step without further purification.



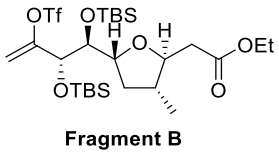
11

Ethyl 2-((2S,3R,5R)-5-((1S,2S)-2-((tert-butyldimethylsilyl)oxy)-1-hydroxy-3-oxobutyl)-3-methyltetrahydrofuran-2-yl)acetate (11). To a 20 ml scintillation vial with stir bar and crude aldehyde **10** (103.92 mg, 0.519 mmol) was added DMF (1.5 mL) , 1-[tert-butyl(dimethyl)silyl]oxypropan-2-one (488.74 mg, 2.60 mmol) and L-proline (59.75 mg, 519.00 umol) . The reaction was allowed to stir at room temperature for 24 hours. Upon the completion of the reaction, water (5 ml) was added. The mixture was transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by ethyl acetate for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude. The crude product was purified through silica gel column with 25% ethyl aceate in heaxane as eluent. The product was afforded as clear oil (84 mg, 216.18 umol, 41.65% yield). Spectral data are in accordance with literature report[119]. HRMS-(DART+) for $C_{19}H_{37}O_6Si$ $[M+H]^+$: calculated: 389.2354, found: 389.2361.

[119] Valot, G.; Maihol, D.; Regens, C. S.; O'Malley, D. P.; Godineau, E.; Takikawa, H.; Philipps, P.; Furstner, A. *Chem. Eur. J.* **2015**, *21*, 2398



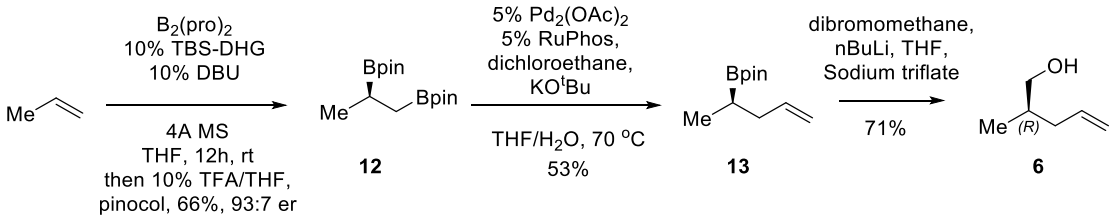
ethyl 2-((2S,3R,5R)-5-((5S,6S)-6-acetyl-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecan-5-yl)-3-methyltetrahydrofuran-2-yl)acetate (SI-2). To a 2-dram vial with compound **11** (136.1 mg, 350.26 umol) and stir bar was added imidazole (71.54 mg, 1.05 mmol) and DMF (0.5 mL). TBSCl (131.98 mg, 875.65 umol, 162.94 uL) was then added. The vial was sealed with a cap and heated to 70 ^{o}C. The reaction was allowed to stir at 70 ^{o}C for 14 hours. Upon the completion of the reaction, water (5 ml) and hexane (5 ml) were added. The mixture was then transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by hexane for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel colomn using 2% ethyl acetate in hexane as eluent. The product was afforded as clear oil (130 mg, 258.54 umol, 73.81% yield). Spectral data are in accordance with literature report[30]. HRMS-(DART+) for $C_{19}H_{37}O_6Si$ $[M+H]^+$: calculated: 503.3187, found: 503.3205.

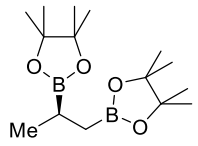


ethyl 2-((2S,3R,5R)-3-methyl-5-((5S,6S)-2,2,3,3,8,8,9,9-octamethyl-6-(1-(((trifluoromethyl)sulfonyl)oxy)vinyl)-4,7-dioxa-3,8-disiladecan-5-

yl)tetrahydrofuran-2-yl)acetate (fragment B). To an oven-dried 2- dram vial with stir bar was added compound **SI-2** (50.3 mg, 0.1 mmol) in THF (0.8 ml). The vial was then sealed with a teflon septa and removed from the glovebox. A nitrogen inlet was introduced. The vial was cooled down to -78 ^{o}C. Potassium bis(trimethylsilyl)amide (21.94 mg, 110.00 umol) in THF (0.5 ml) was then added in drop. The mixture was allowed to stir at -78 ^{o}C for 1 hour. Comins reagent (98.17 mg, 250.00 umol) in THF (0.5 ml) was then added. The reaction was allowed to stir at -78 ^{o}C for additional 3 hours. Upon completion of the reaction, saturated ammonium chloride aqueous solution (1.5 ml) was added at -78 ^{o}C. The mixture was then allowed to warm to room temperature. The mixture was transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by diethyl ether for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified by silica gel column with 1% to 5% diethyl ether in hexane as eluent. The product was afforded as clear oil (40.0 mg, 63% yield). Spectral data are in accordance with literature report[30]. HRMS-(DART+) for $C_{26}H_{50}O_8F_3Si_2S$ $[M+H]^+$: calculated: 635.2712. found: 635.2698.

Route I





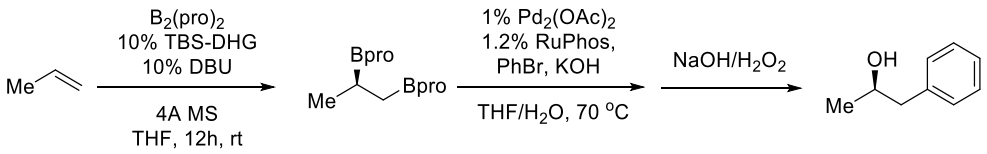
12

(R)-2,2'-(propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (12). To an oven-dried 2-dram vial with stir bar was added TBS-DHG (26.24 mg, 100.00 umol), B_2pro_2 (169.78 mg, 1.00 mmol), 4Å molecular seives, THF (1 mL) , and DBU (15.22 mg, 100.00 umol) in the glovebox. The vial was sealed with a teflon septa and removed from the box. A propene ballon inlet was introduced to the vial. The vial was cooled down to -78 ^oC. Propene was bubbled through the reaction mixture and condensed into the reaction mixture. After about 1 ml of propene was condensed, the reaction mixture was allowed to warm up to room temperature. The reaction was stirring at room temperature for 14 hous. Upon the completion of the reaction, the mixture was filtered through celite with diethyl ether as eluent. The filtrate was condensed to crude product.

To an oven dried 2-dram vial with stir bar was added crude product in THF (1 ml), pinacol (472.68 mg, 4.00 mmol) and 0.1 ml TFA. The vial was sealed with a cap and removed from the glovebox. The vial was allowed to stir at 60 ^oC for 12 hours. Upon the completion of the reaction, volatiles were removed in vacuo. The residue was purified through silica gel column with 1% to 3% ethyl acetate in hexane as eluent. The product was afforded as clear oil (195.4 mg. 66%). Spectral data are in accordance with literature report[120].

[120] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature*, **2014**, *505*, 386.

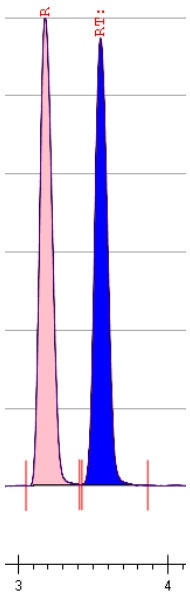
Analysis of Stereochemistry



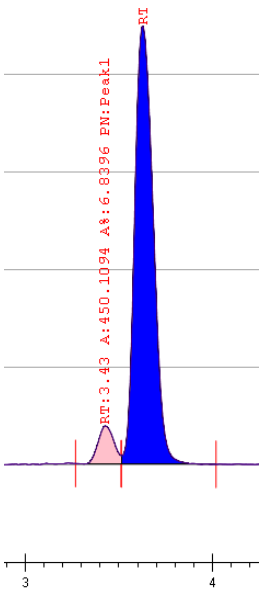
To an oven-dried 2-dram vial was added palladium acetate (2.25 mg, 0.01 mmol), Ruphos (5.60 mg, 0.012 mmol) in the dry box. The crude product from the propene diboration step (1.0 mmol) was transferred to the vial by tetrahydrofuran (1ml). Bromobenzene (235.52 mg, 1.5 mmol) and potassium hydroxide (168.33 mg, 3.0 mmol) was then added. The vial was sealed with Teflon septa and removed from the dry box. The nitrogen inlet was applied. Deionized water degassed by nitrogen for 30 min (0.2 ml) was then added. The reaction was allowed to stir at 70 ^{o}C for 14h. The reaction was then cooled down to room temperature. The reaction mixture was then cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (1 mL), followed by dropwise addition of 30% hydrogen peroxide (0.5 mL). The reaction was gradually warmed to room temperature and stirred for another 4 hours. The flask was then cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was added to the reaction dropwise over 5 minutes. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was further extracted with ethyl acetate (3 x 10 mL), and the combined organics were dried over Na2SO4, filtered, and concentrated by rotary evaporation to afford crude reaction mixture. The crude mixture was then purified through silica gel column (25% ethyl acetate in hexane) to afford the (*R*)-1-phenylethan-1-ol product as clear oil (61.0 mg, 44% yield). The spectral data are in accordance with commercialized product.

The product was compared to the racemic 1-phenylethan-1-ol (commercial). The absolute stereochemistry was assigned by analogy.

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



Racemic



Enriched

Reporting Information

Peak Name	Peak Number	Peak Concentration	Area Percent	Area	Area Sum	Retention Time
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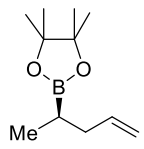
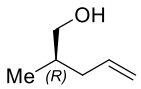
Peak2	2	0	93.1604	6130.833	6580.9424	3.63 min



13

(R)-4,4,5,5-tetramethyl-2-(pent-4-en-2-yl)-1,3,2-dioxaborolane (13). To an oven-dried 2-dram vial with stir bar was added palladium acetate (3.30 mg, 14.70 umol), Ruphos (8.23 mg, 17.63 umol), and THF (0.5 ml) in the glovebox. The mixture was allowed to stir in the glovebox at room temperature for 15 minutes. To an oven-dried 4-dram vial with stir bar was added potassium tert-butoxide (296.81 mg, 2.65 mmol) and compound **12** (87 mg, 293.90 umol) in THF (1.0 ml). The pre-complexed palladium acetate and Ruphos solution was then added. The 4-dram vial was sealed with a teflon septa and removed from the glovebox. 1,2-Dichloroethane (174.51 mg, 1.76 mmol, 138.50 uL) was added outside the glovebox, followed by degassed water (0.2 ml). The reaction was then allowed to stir at 70 ^{o}C for 14 hours. Upon completion of the reaction, water (5 ml) was added. The mixture was then transferred to a sep funnel. Layers were separated. The aqueous layer was extracted by diethyl ether for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 1% to 2% diethyl ether in pentane as eluent. The product was afforded as yellow oil (31 mg, 53%). Spectral data are in accordance with literature report[121]. HRMS-(DART+) for $C_{11}H_{22}BO_2$ $[M+H]^+$: calculated: 197.1707. found: 197.1717.

[121] Han, J. T.; Jang, W. J.; Kim, N.; Yun, J. *J. Am. Chem. Soc.* **2016**, *138*, 15146.

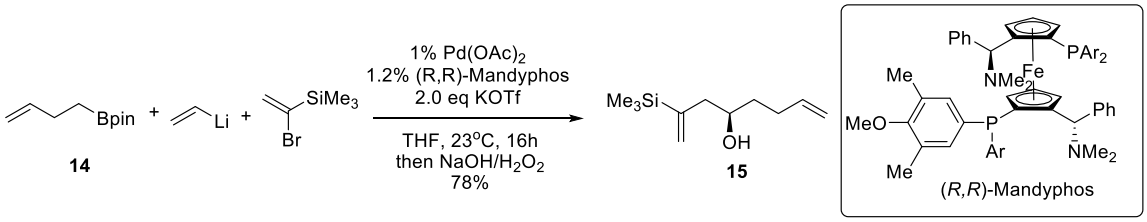


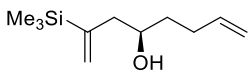
6

(R)-2-methylpent-4-en-1-ol (6). To an oven-dried two dram vial with stir bar was added compound 13 (30.0 mg, 0.153 mmol) in THF (1.0 ml), dibromomethane (265.95 mg, 1.53 mmol, 122.56 uL) and sodium trifluoromethanesulfonate (52.65 mg, 305.98 umol) in the glovebox. The vial was sealed with a teflon septa and removed from the glovebox. A nitrogen inlet was introduced. The vial was cooled down to -78 ^{o}C. n-Butyllithium (0.61 ml, 2.5 M in hexane, 1.53 mmol) was then added in drop. The reaction was allowed to stir at -78 ^{o}C for 1 hour. The reaction was then allowed to slowly warm up to room temperature. Upon completion of the reaction, 3M sodium hydroxide (1 ml) was added. The reaction was cooled down to 0 ^{o}C. 30% aqueous H_2O_2 was then added in drop. The reaction was further stiring at room temperature for 3 hours, the reaction was cooled down to 0 ^{o}C, and saturated thiosulfate aqueous solution (2 ml) was added. After that, the mixture was transferred to a sep funnel, The layers were separated. The aqueous layer was extracted by diethyl ether for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 25% diethyl ether in pentane as eluent. The product was afforded as clear oil (23.0 mg, 71%). Spectral data are in accordance with literature report[122].

[122] Speltz, T. E.; Fanning, S. W.; Mayne, C. G.; Fowler, C.; Tajkhorshid, E.; Greene, G. L.; Moore, T. W. *Angew. Chem. Int. Ed.* **2016**, *55*, 4252.

4.7.4 Synthetic Study towards Fragment C

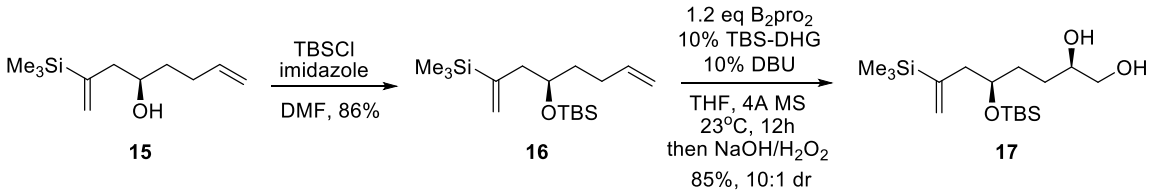


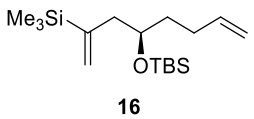


15

(R)-2-(trimethylsilyl)octa-1,7-dien-4-ol (15). To an oven-dried 20 ml scintillation vial with stir bar was added reagent **14** (502 mg, 2.76 mmol) and 3.0 ml of THF. The vial was sealed with a rubber septa and removed from the glovebox. A nitrogen inlet was introduced. The vial was cooled down to 0 ^{o}C followed by dropwise addition of vinyllithium (1.63 M, 1.69 mL). The vial was allowed to warm up to room temperature and stir at room temperature for additional 15 minutes. The vial was then brought back to the glovebox. To another oven dried 2-dram vial with stir bar was added Palladium (II) acetate (12.38 mg, 55.14 umol), (*R,R*)-Mandyphos (69.69 mg, 66.17 umol) and THF (2 ml). The mixture was allowed to stir at room temperature in the glovebox for 15 minutes. To the 20 ml scintillation vial just brought into the glovebox was added potassium trifluoromethanesulfonate (622.59 mg, 3.31 mmol), 1-bromovinyl(trimethyl)silane (593.28 mg, 3.31 mmol) and THF (6 ml). The $Pd(OAc)_2$ and Mandyphos solution was then added. The vial was sealed with a rubber septa and removed from the glovebox. The vial was allowed to stir at 40 ^{o}C for 16 hours. Upon the completion of the reaction, the mixture was transferred to a 100 ml round bottom flask. THF (10 ml) and 3M sodium hydroxide (15 ml) was then added. The flask was then cooled down to 0 ^{o}C. 30% H_2O_2 (8

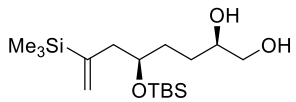
ml) aqueous solution was added in drop. The mixture was allowed to stir at room temperature for 4 hours. Upon the completion of the oxidation, the flask was cooled down to 0 ^{o}C, sodium thiosulfate (15 ml) was added in drop. The mixture was then transferred to a sep funnel. They layers were separated. The aqueous layer was extracted by ethyl acetate for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 25% ethyl acetate in hexane as eluent. The product was afforded as clear oil (427.1 mg, 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.83 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 5.67 (s, 1H), 5.50 (d, J = 3.0 Hz, 1H), 5.10 – 4.92 (m, 2H), 3.77 – 3.55 (m, 1H), 2.44 (dd, J = 13.4, 3.3 Hz, 1H), 2.23 (dq, J = 15.0, 7.9, 7.4 Hz, 1H), 2.15 (td, J = 13.5, 8.7 Hz, 2H), 1.74 (s, 1H), 1.57 (q, J = 8.0 Hz, 2H), 0.10 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.6, 138.70, 138.69, 128.1, 114.9, 69.2, 45.1, 36.4, 30.3, -1.14, -1.15. HRMS-(DART+) for $C_{11}H_{23}OSi$ $[M+H]^{+}$: calculated: 199.1513, found:199.1508. IR (neat): 2951.6 (w), 2925.6 (w), 2854.0 (w), 1246.9 (m), 927.3 (m), 909.0 (m), 832.4(s), 772.9 (m), 756.5 (m). $[\alpha]_D^{20}$= +5.599 (c=1.0, $CHCl_3$, l=50 mm).





(R)-tert-butyldimethyl((2-(trimethylsilyl)octa-1,7-dien-4-yl)oxy)silane (16). To a 20 ml scintillation vial with stir bar and compound **15** (77 mg, 388.15 umol) was added

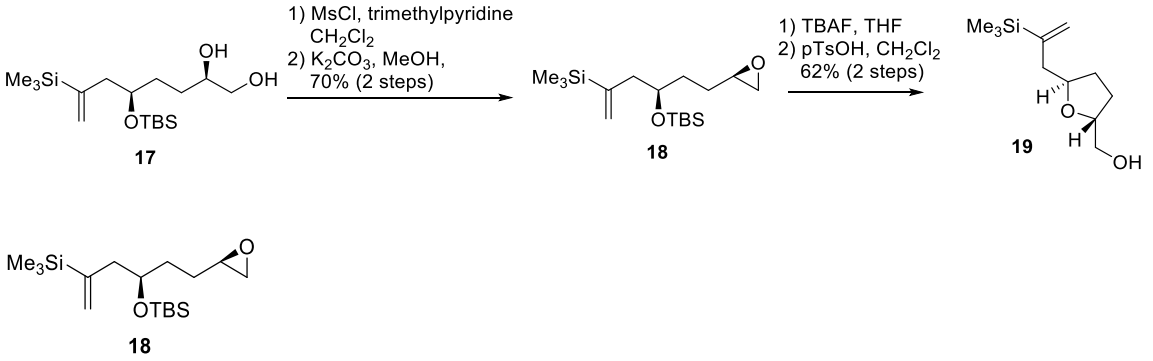
imidazole (66.06 mg, 970.38 umol) and DMF (1 mL). The mixture was allowed to stir at room temperature for 5 minutes. TBSCL (117.00 mg, 776.30 umol) was then added. The reaction was allowed to stir at room temperature for 16 hours. Upon the completion of the reaction, water (3 ml) was added. The mixture was then transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by hexane for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 1% to 2% ethyl acetate in hexane as eluent. The product was afforded as clear oil (104 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (ddt, J = 13.3, 10.2, 6.6 Hz, 1H), 5.60 (s, 1H), 5.41 (d, J = 2.8 Hz, 1H), 4.96 (dd, J = 33.2, 13.9 Hz, 2H), 3.87 – 3.74 (m, 2H), 2.40 (dd, J = 13.6, 5.2 Hz, 1H), 2.24 (dd, J = 13.6, 8.4 Hz, 1H), 2.20 – 2.11 (m, 1H), 2.04 (dq, J = 14.6, 6.3 Hz, 1H), 1.61 – 1.49 (m, 1H), 1.41 (dtd, J = 13.5, 7.8, 6.7, 2.9 Hz, 1H), 0.89 (s, 9H), 0.09 (s, 9H), 0.06 (d, J = 2.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 139.2, 127.7, 114.4, 71.2, 44.9, 36.0, 29.8, 26.2, 18.4, -1.0, -3.8, -4.2. HRMS-(DART+) for $C_{17}H_{37}OSi_2$ $[M+H]^+$: calculated: 313.2378, found:313.2376. IR (neat): 2951.9 (m), 2926.7 (m), 2854.7 (w), 1248.1 (m), 1090.1 (m), 929.0 (w), 834.1 (s), 772.6 (m), 756.8 (w). $[\alpha]_D^{20}$= +11.816 (c=1.1, $CHCl_3$, l=50 mm).



17

(2R,5R)-5-((tert-butyldimethylsilyl)oxy)-7-(trimethylsilyl)oct-7-ene-1,2-diol (17). To an oven-dried two dram flask with stir bar was added TBS-DHG (5.25 mg, 20.00 umol), B_2pro_2 (67.91 mg, 400.00 umol), and 4Å molecula seives (30 mg). THF (0.2 ml),

compound **16** (62.53 mg, 0.2 mmol) and DBU (3.04 mg, 20.00 umol) was then added. The vial was sealed with teflon cap and removed from the glovebox. The reaction was allowed to stir at 30 ^{o}C for 12 hours. Upon the completion of the reaction, THF (0.2 ml), 3M sodium hydroxide (0.6 ml) were added. The vial was cooled down 0 ^{o}C, 30% aqueous H_2O_2 was added in drop. The reaction was allowed to stir at room temperature for additional three hours. Upon the completion of the oxidation, saturated sodium thiosultate (1 ml) was added in drop. The reaction was then transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by ethyl acetate for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude. The crude product was purified through silica gel column with 30% to 40 % ethyl acetate as eluent. The product was afforded as clear oil (58.9 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.61 (s, 1H), 5.40 (d, J = 2.9 Hz, 1H), 3.87 – 3.80 (m, 1H), 3.68 (tt, J = 7.5, 4.2 Hz, 1H), 3.62 (dd, J = 11.0, 3.1 Hz, 1H), 3.43 (dd, J = 11.0, 7.7 Hz, 1H), 2.41 (dd, J = 13.6, 5.1 Hz, 1H), 2.25 (dd, J = 13.7, 8.7 Hz, 1H), 1.61 – 1.52 (m, 2H), 1.52 – 1.44 (m, 2H), 0.89 (s, 9H), 0.09 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (151 MHz, Chloroform-d) δ 148.7, 127.7, 72.5, 71.4, 67.0, 44.6, 31.9, 28.6, 26.1, 18.3, -1.0, -3.9, -4.2. HRMS-(DART+) for $C_{17}H_{39}O_3Si_2$ $[M+H]^+$: calculated: 347.2432, found: 347.2426. IR (neat): 2950.0 (w), 2925.7 (w), 2853.9 (w), 1246.8 (m), 1054.8 (m), 831.1 (s), 772.0 (s), 756.8 (m). $[\alpha]_D^{20}$= +8.119 (c=1.0, $CHCl_3$, l=50 mm).

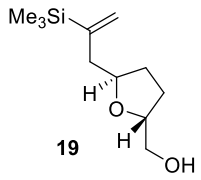


18

tert-butyldimethyl(((R)-1-((R)-oxiran-2-yl)-5-(trimethylsilyl)hex-5-en-3-yl)oxy)silane (18). To a 20 ml scintillation vial with stir bar and compound **17** (160 mg, 461.56 umol) was added CH_2Cl_2 (3 ml) and 2,4,6-trimethylpyridine (559.32 mg, 4.62 mmol, 610.61 uL). The vial was cooled down to 0 ^oC. Methanesulfonyl chloride (58.16 mg, 507.72 umol, 39.30 uL) was then added. The vial was allowed to stir at 0 ^oC for 2 hour. Upon the completion of the reaction, water (5 ml) was added. The mixture was transferred to a sep funnel. The aqueous layer was extracted by CH_2Cl_2 for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was taken to the next step without further purification.

To a 20 ml scintillation vial with stir bar and crude product from the last step (195.81 mg, 461.00 umol) was added methanol (5 mL). The mixture was allowed to stir for 5 minutes and potassium carbonate (223.00 mg, 1.61 mmol, 97.38 uL) was added. The mixture was stirring for another 1 hour at room temperature. Upon the completion of the reaction, water (5 ml) was added. The mixture was transferred to a sep funnel. The layers were separated. The aqueous layer was extracted by diethyl ether for 3 times. The organic layers were combined, dried over sodium sulfate, filtered and condensed to crude product. The crude product was purified through silica gel column with 5% to 10% ethyl acetate

in hexane as eluent. The product was afforded as clear oil. (106.1 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.61 (s, 1H), 5.41 (d, J = 2.4 Hz, 1H), 3.91 – 3.79 (m, 1H), 2.90 (s, 1H), 2.73 (t, J = 4.2 Hz, 1H), 2.48 – 2.43 (m, 1H), 2.40 (dd, J = 13.5, 4.9 Hz, 1H), 2.22 (dd, J = 13.6, 8.5 Hz, 1H), 1.73 – 1.64 (m, 1H), 1.64 – 1.39 (m, 3H), 0.88 (s, 9H), 0.09 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 127.8, 71.0, 52.6, 47.4, 44.8, 32.3, 28.2, 26.1, 18.3, -1.0, -3.8, -4.3. HRMS-(DART+) for $C_{17}H_{37}O_2Si_2$ $[M+H]^+$: calculated: 329.2327, found: 329.2324. IR (neat): 2951.3 (w), 2925.6 (w), 2853.9 (w), 1246.8 (m), 1093.1 (m), 1054.9 (m), 833.6 (s), 773.0 (m), 757.7 (m). $[\alpha]_D^{20}$= +12.598 (c=1.0, $CHCl_3$, l=50 mm).



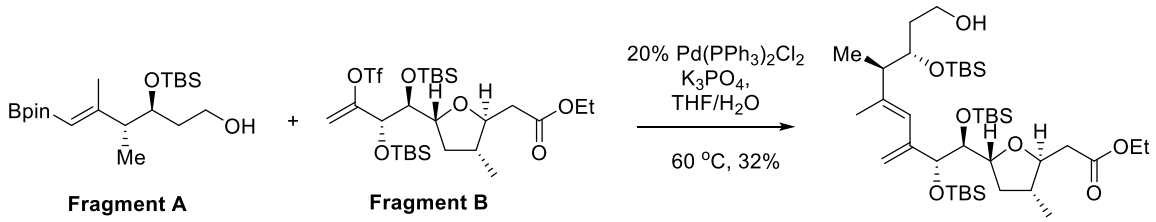
19

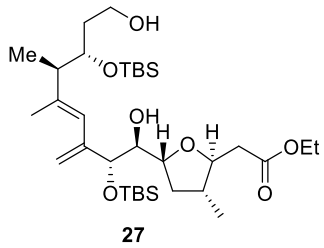
((2R,5R)-5-(2-(trimethylsilyl)allyl)tetrahydrofuran-2-yl)methanol (19). To a 20 ml scintillation vial with stir bar and compound **18** (71 mg, 216.04 umol) was added THF (1 ml). TBAF (1 M, 324.07 uL) was then added. The mixture was allowed to stir at room temperature for 14 hours. Upon the completion of the reaction, volatiles were removed in vacuo. The residue the filtered through silica gel plug with diethyl ether as eluent. The solvents was then removed in vacuo to afford the crude product. The crude product was taken to next step without further purification.

To a 20 ml scintillation vial with stir bar and the crude product from the last step (46.31 mg, 0.216 mmol) was added CH_2Cl_2 (1 ml) and (1S)-(+)-10-Camphorsulfonic acid (55.19 mg, 237.60 umol). The mixture was allowed to stir at room temperature for 2 hours. Upon the completion of the reaction, volatiles were removed in vacuo. The residue

was purified through silica gel column with 10% to 25% ethyl acetate in hexane as eluent. The product was afforded as clear oil (28.7 mg, 62% over 2 steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.63 (s, 1H), 5.40 (d, J = 2.9 Hz, 1H), 4.08 – 4.02 (m, 1H), 4.00 (ddd, J = 10.3, 7.1, 3.6 Hz, 1H), 3.69 (dd, J = 11.4, 3.3 Hz, 1H), 3.48 (dd, J = 11.4, 5.6 Hz, 1H), 2.52 (dd, J = 14.2, 6.3 Hz, 1H), 2.24 (dd, J = 14.2, 7.2 Hz, 1H), 1.99 – 1.92 (m, 1H), 1.92 – 1.85 (m, 1H), 1.77 – 1.68 (m, 1H), 1.56 – 1.47 (m, 1H), 0.09 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.2, 126.5, 79.6, 79.1, 65.4, 42.8, 31.5, 27.1, -1.2. HRMS-(DART+) for $C_{11}H_{23}O_2Si$ $[M+H]^+$: calculated: 215.1462, found:215.1450. IR (neat): 3427.5 (br), 2950.6 (m), 2870.5 (w), 1246.0 (m), 1047.8 (m), 927.6(w), 835.2 (s), 756.6 (m), 718.5 (w). $[\alpha]_D^{20}$= +8.779 (c=1.28, $CHCl_3$, l=50 mm).

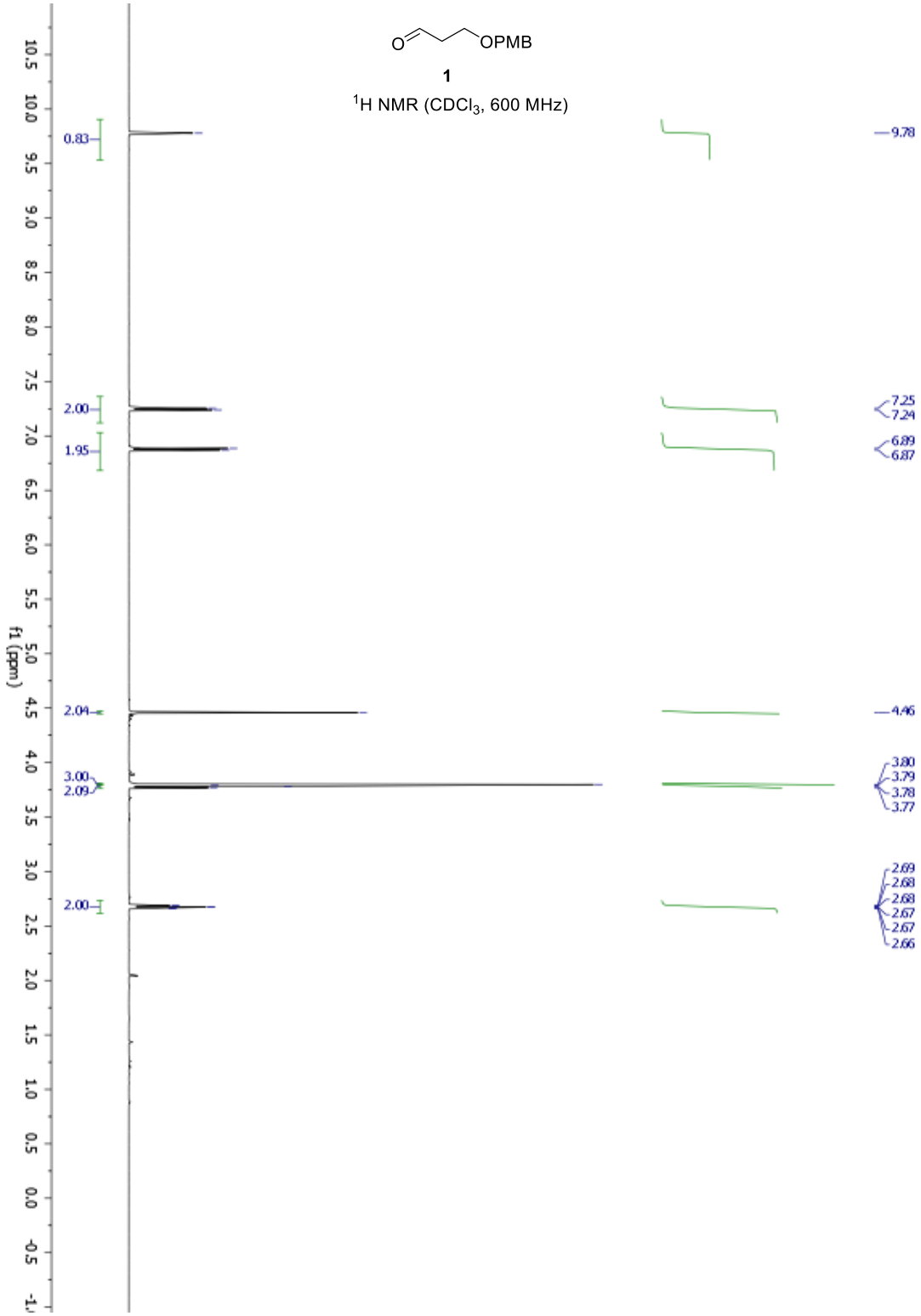
4.7.5 Cross Coupling of Fragment A and Fragment B

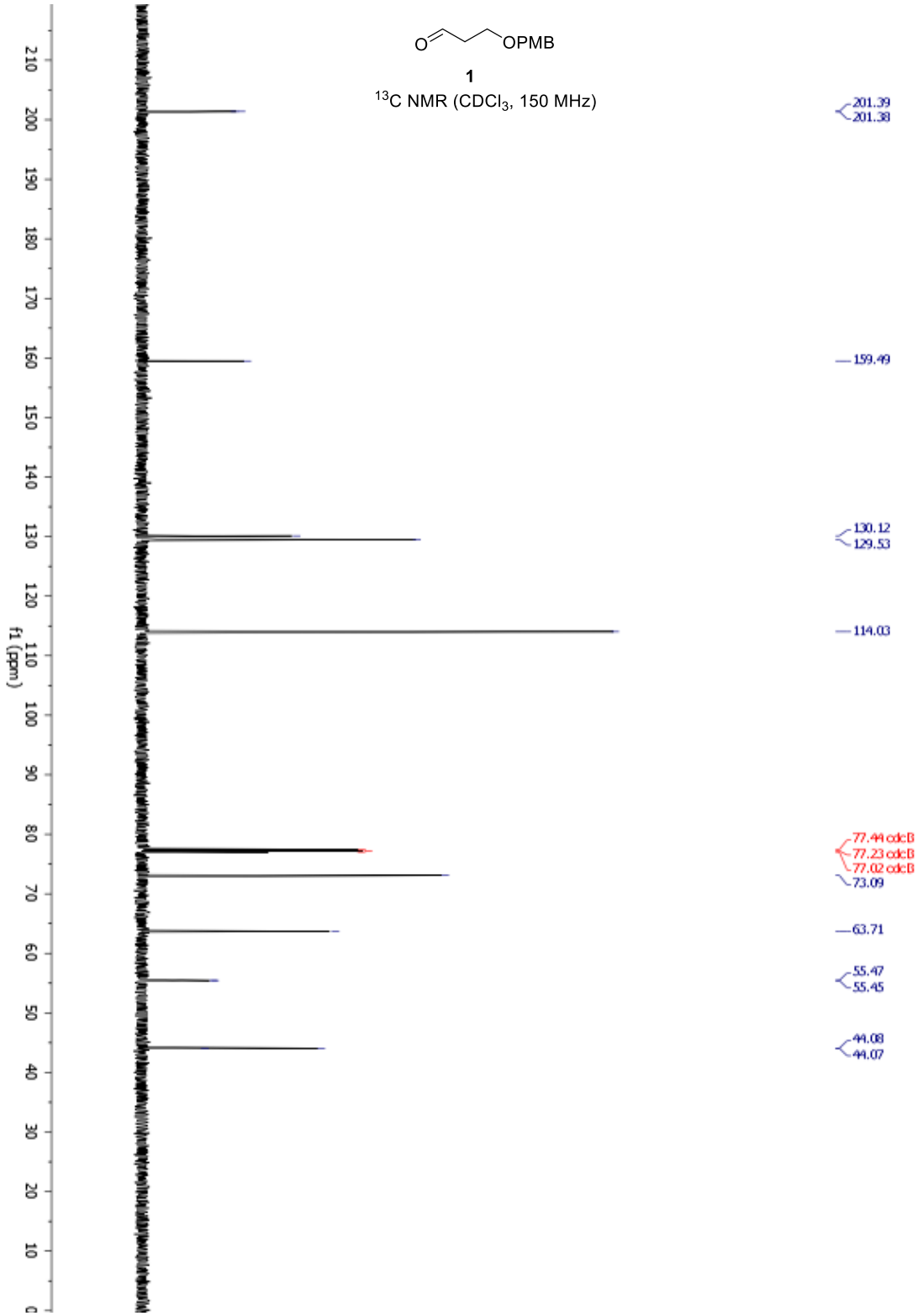


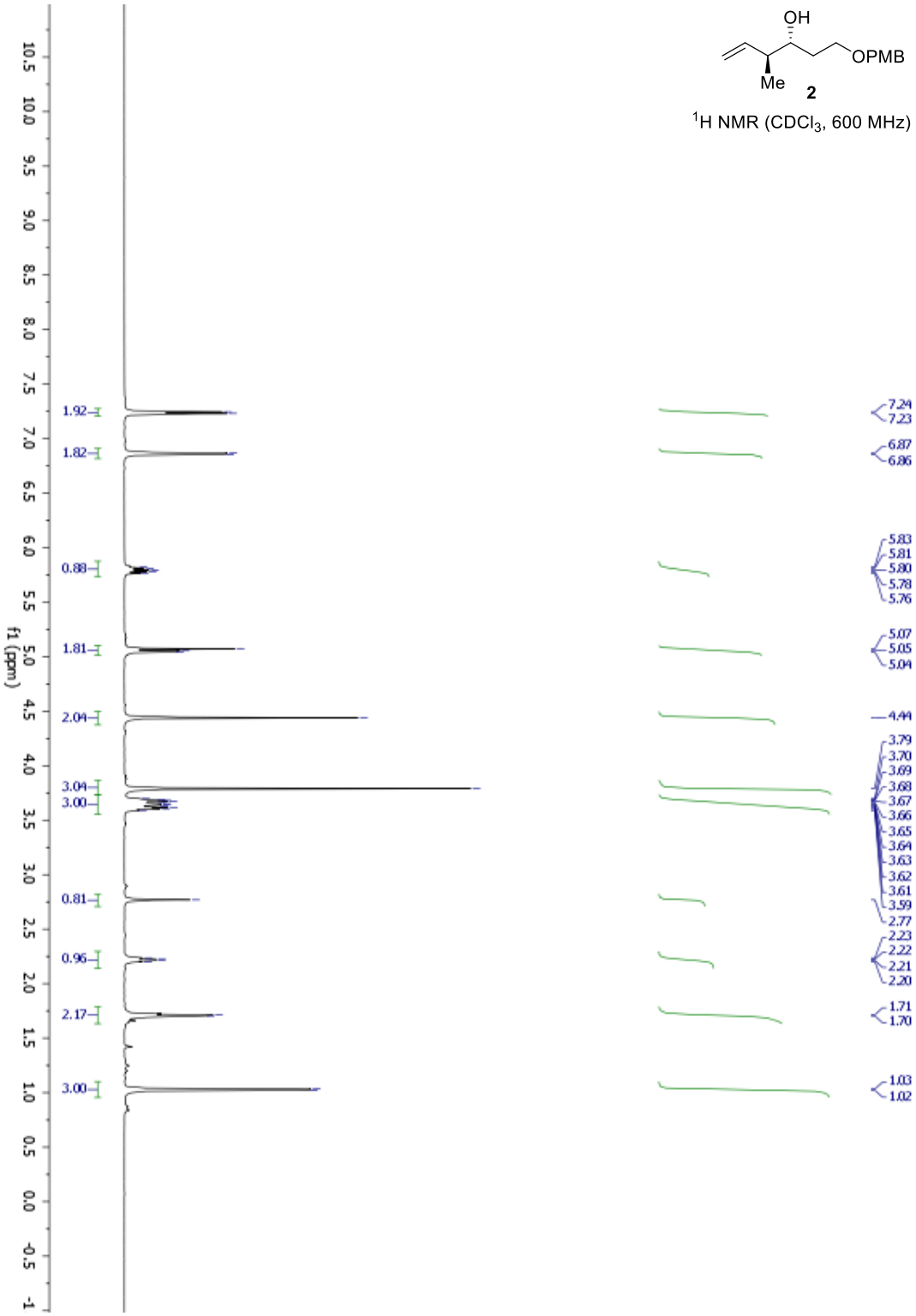


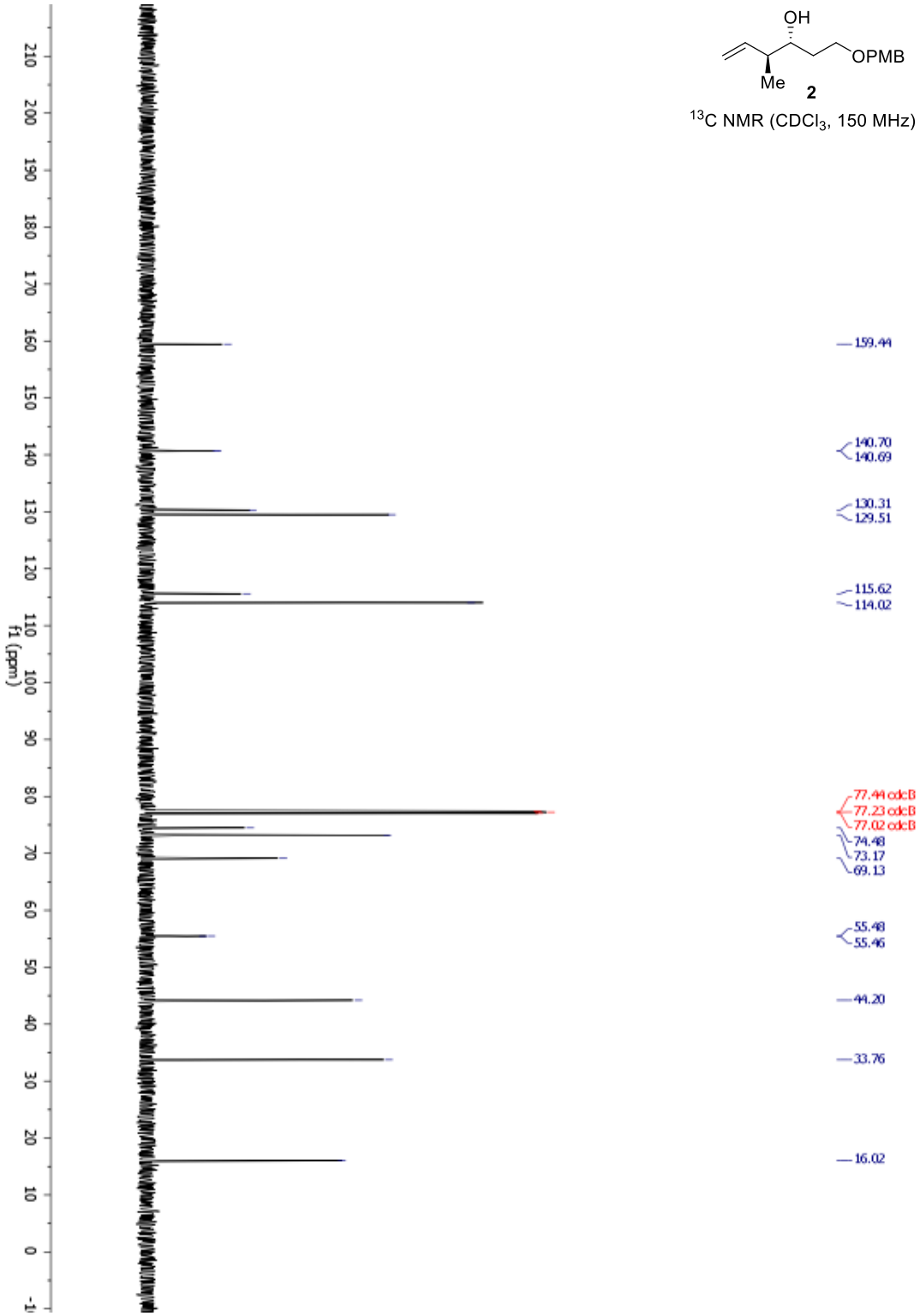
ethyl 2-((2S,3R,5R)-5-((5S,6R,10R,11S,E)-6-((tert-butyldimethylsilyl)oxy)-11-(2-hydroxyethyl)-2,2,3,3,9,10,13,13,14,14-decamethyl-7-methylene-4,12-dioxa-3,13-disilapentadec-8-en-5-yl)-3-methyltetrahydrofuran-2-yl)acetate (27). To an oven-

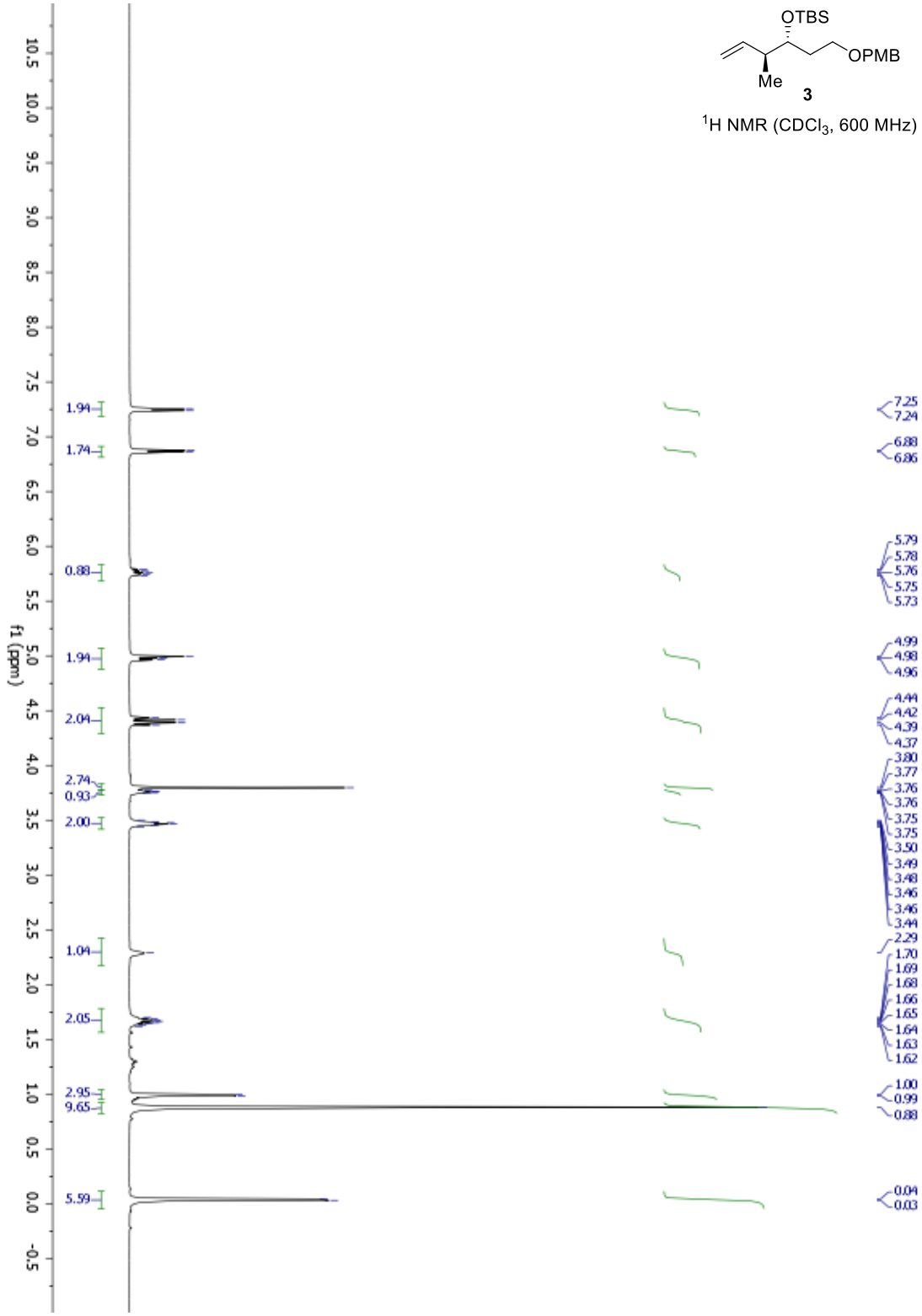
dried 2-dram vial with stir bar was added dichloropalladium triphenylphosphane (6.64 mg, 9.46 umol) and potassium triphosphate (100.30 mg, 472.52 umol) in the glovebox. **Fragment B** (30 mg, 47.25 umol) in THF (1.0 ml) and **Fragment A** (45.41 mg, 118.13 umol) in THF (1.0 ml) were also added in the glovebox. The vial was sealed with a teflon septa and removed from the glovebox. A nitrogen inlet was introduced. Degassed water (0.2 ml) was then added. The reaction was allowed to stir at 60 ^{o}C for 16 hours. Upon the completion of the reaction, the reaction mixture was filtered through a plug of silica gel with diethyl ether as eluent. Volatiles were then removed in vacuo. The residue was purified through silica gel column with 2% to 15% ethyl acetate in hexane as eluent. The product was afforded as clear oil (11 mg, 41%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.25 (s, 1H), 4.98 (s, 1H), 4.34 – 4.09 (m, 3H), 4.06 – 3.95 (m, 2H), 3.86 (q, J = 7.9 Hz, 1H), 3.70 (d, J = 5.0 Hz, 2H), 3.26 (t, J = 7.3 Hz, 1H), 2.55 – 2.44 (m, 2H), 2.44 – 2.35 (m, 1H), 2.14 (d, J = 7.4 Hz, 1H), 2.08 (s, 1H), 2.03 (dd, J = 12.0, 6.2 Hz, 1H), 1.96 (s, 1H), 1.82 (s, 3H), 1.33 – 1.19 (m, 6H), 1.14 – 0.98 (m, 6H), 0.91 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 146.1, 141.5, 123.1, 115.9, 82.1, 78.2, 74.6, 73.1, 60.8, 60.7, 48.4, 40.3, 39.9, 37.6, 34.8, 30.6, 26.1, 26.0, 25.1, 18.4, 18.3, 18.2, 16.6, 14.5, 13.0, -4.2, -4.36, -4.41, -4.9. HRMS-(DART+) for $C_{33}H_{65}O_7Si_2$ $[M+H]^+$: calculated:629.4259, found: 629.4249.

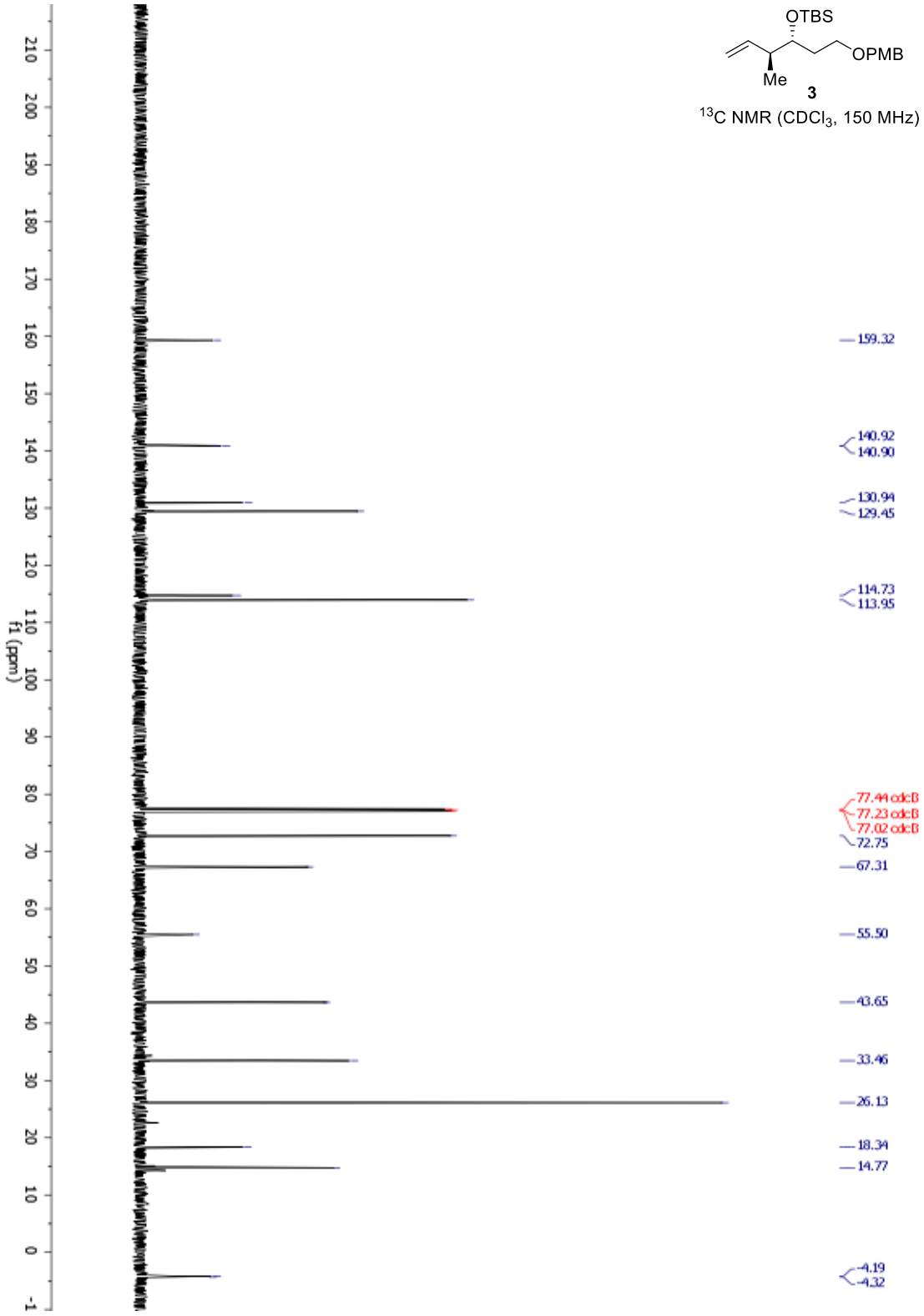

O
OPMB
1
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
0.83
2.00
1.95
2.04
3.00
2.09
2.00
9.78
7.25
7.24
6.89
6.87
4.46
3.80
3.79
3.78
3.77
2.69
2.68
2.68
2.67
2.67
2.66

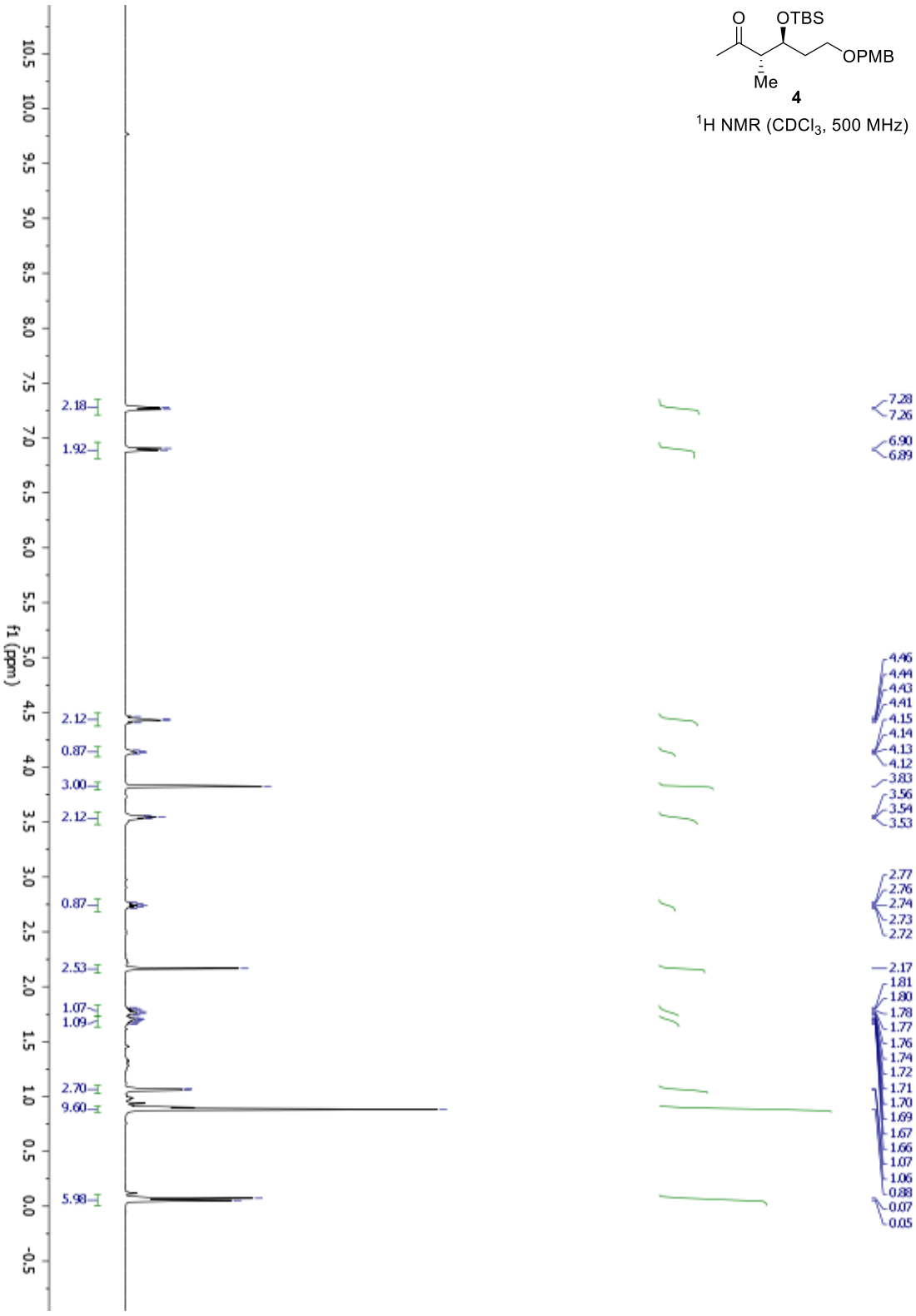

O
OPMB
1
13C NMR (CDCl3, 150 MHz)
201.39
201.38
159.49
130.12
129.53
114.03
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
73.09
63.71
55.47
55.45
44.08
44.07
f1 (ppm)

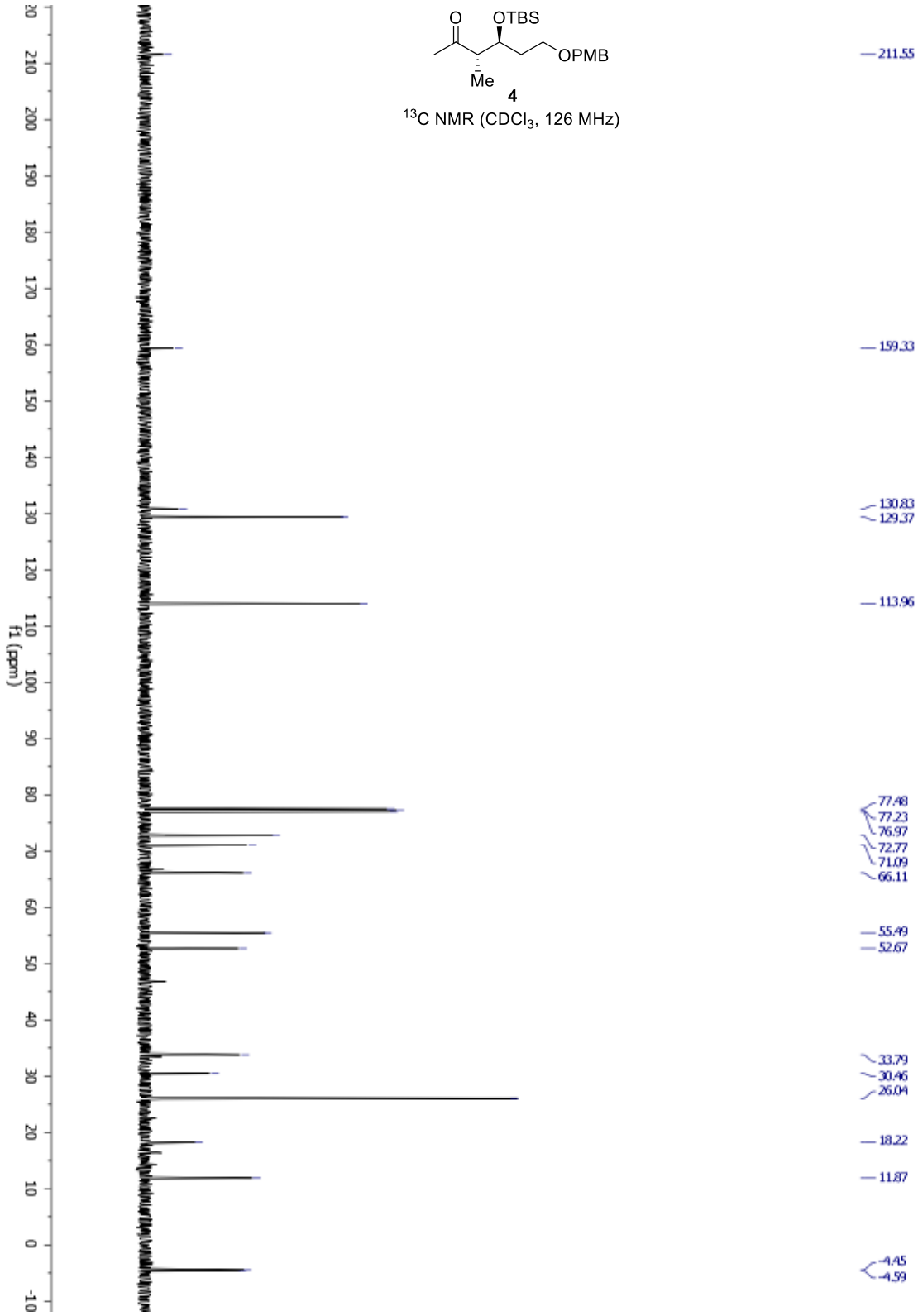

OH
OPMB
Me
2
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
1.92
1.82
0.88
1.81
2.04
3.04
3.00
0.81
0.96
2.17
3.00
7.24
7.23
6.87
6.86
5.83
5.81
5.80
5.78
5.76
5.07
5.05
5.04
4.44
3.79
3.70
3.69
3.68
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.59
2.77
2.23
2.22
2.21
2.20
1.71
1.70
1.03
1.02

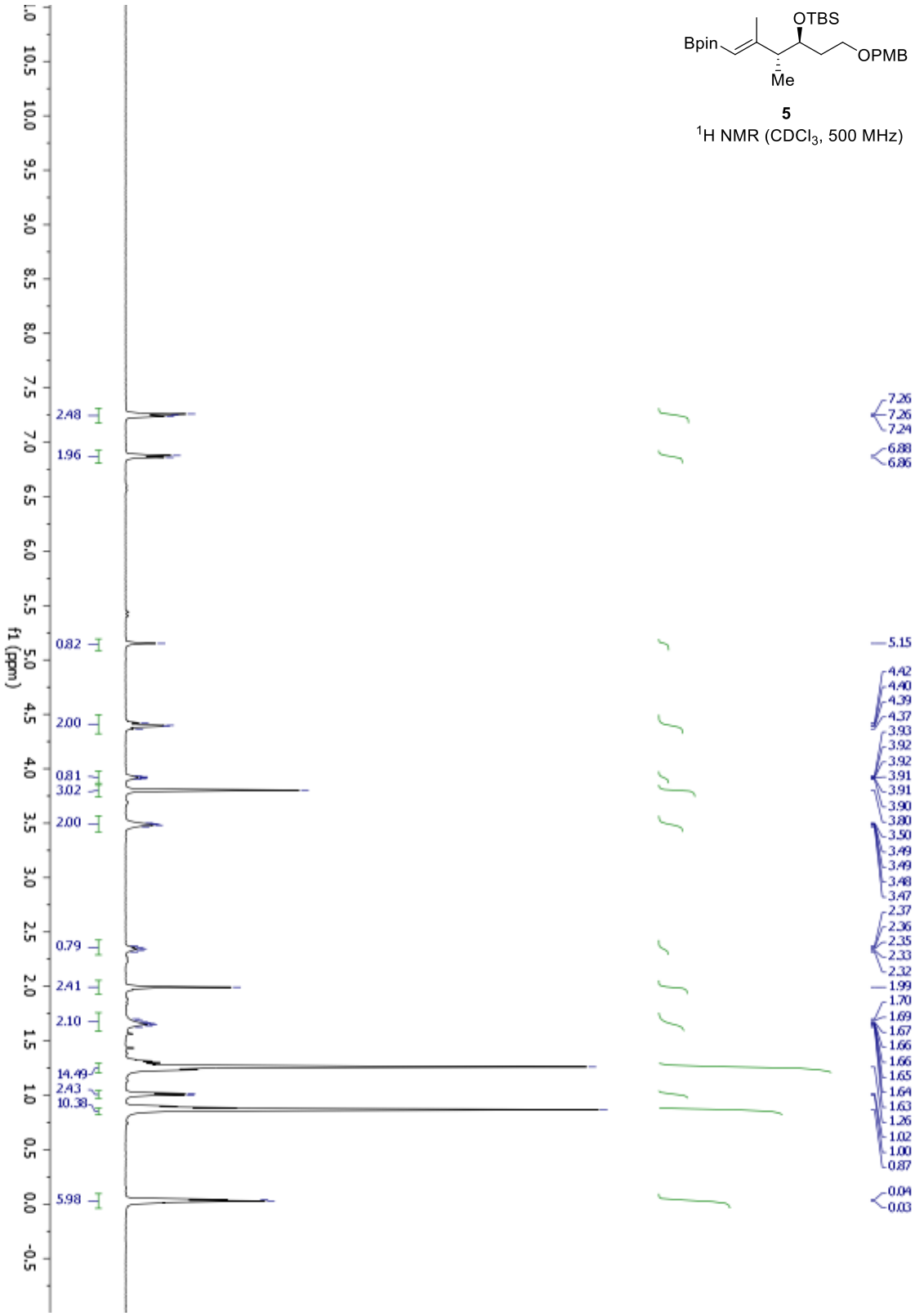

OH
OPMB
Me
2
13C NMR (CDCl3, 150 MHz)
f1 (ppm)
159.44
140.70
140.69
130.31
129.51
115.62
114.02
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
74.48
73.17
69.13
55.48
55.46
44.20
33.76
16.02

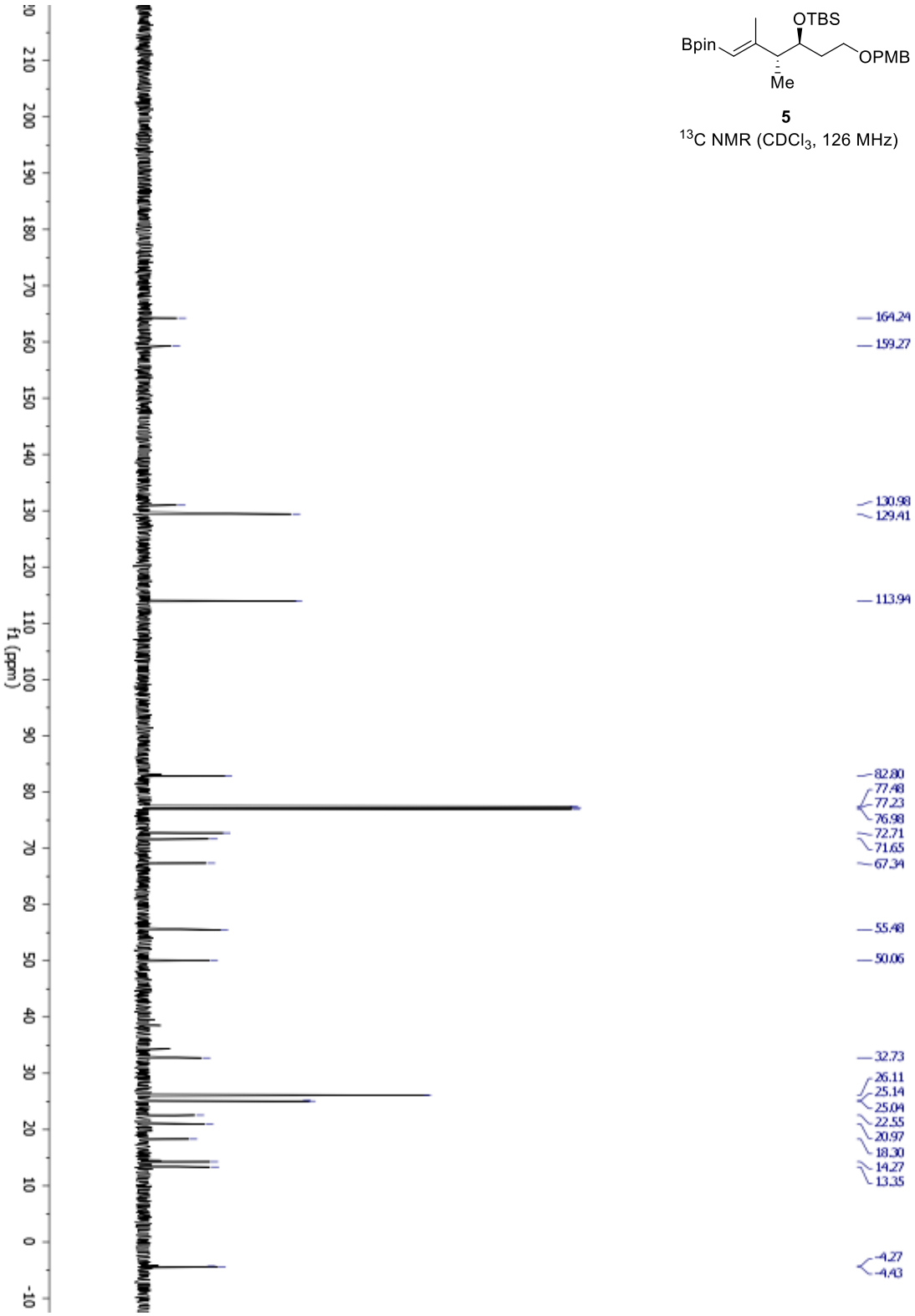

OTBS
OPMB
Me
3
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
1.94
1.74
0.88
1.94
2.04
2.74
0.93
2.00
1.04
2.05
2.95
9.65
5.59
7.25
7.24
6.88
6.86
5.79
5.78
5.76
5.75
5.73
4.99
4.98
4.96
4.44
4.42
4.39
4.37
3.80
3.77
3.76
3.76
3.75
3.75
3.50
3.49
3.48
3.46
3.46
3.44
2.29
1.70
1.69
1.68
1.66
1.65
1.64
1.63
1.62
1.00
0.99
0.88
0.04
0.03

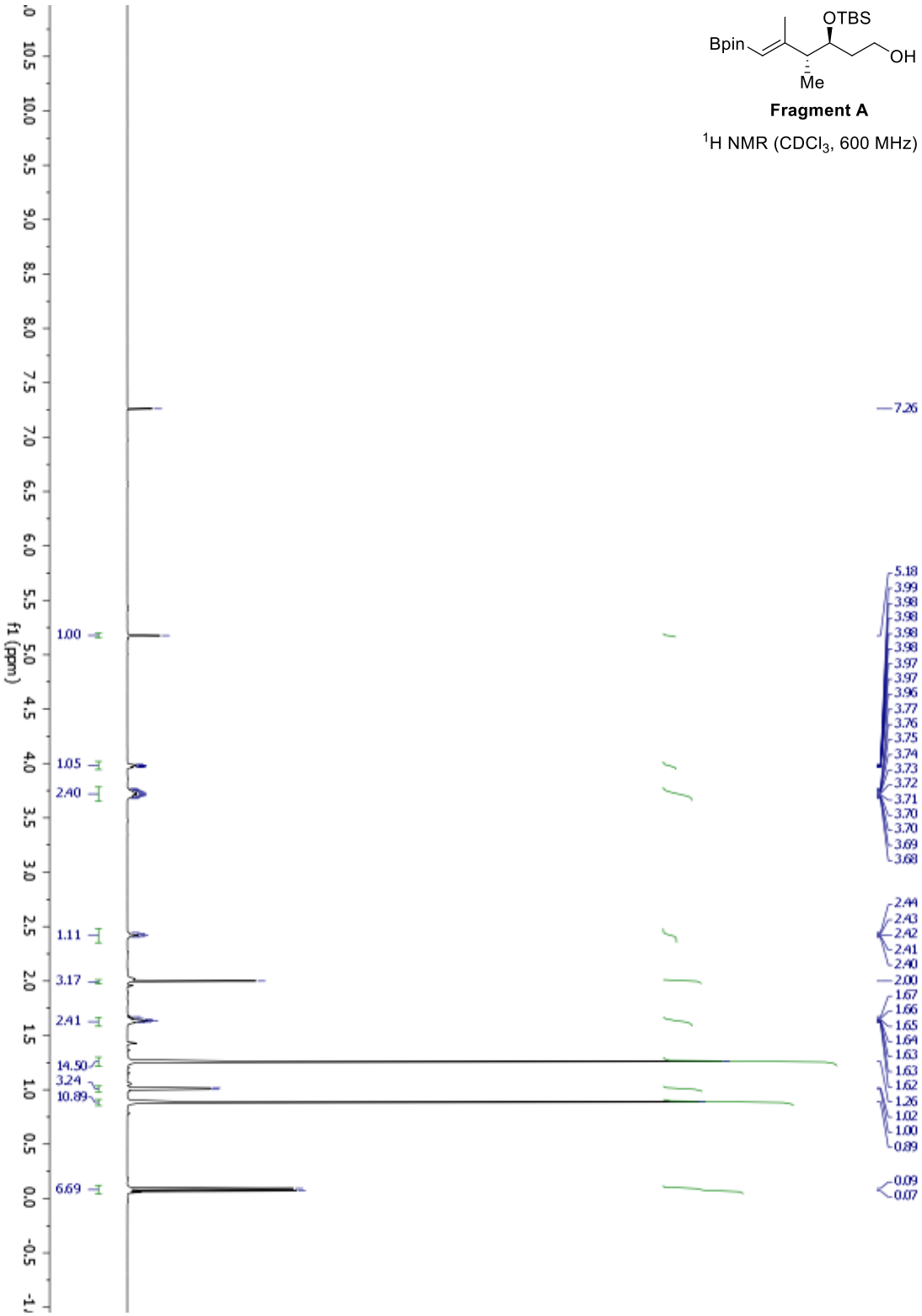

OTBS
OPMB
Me
3
^{13}C NMR ($CDCl_3$, 150 MHz)
f1 (ppm)
159.32
140.92
140.90
130.94
129.45
114.73
113.95
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
72.75
67.31
55.50
43.65
33.46
26.13
18.34
14.77
-4.19
-4.32

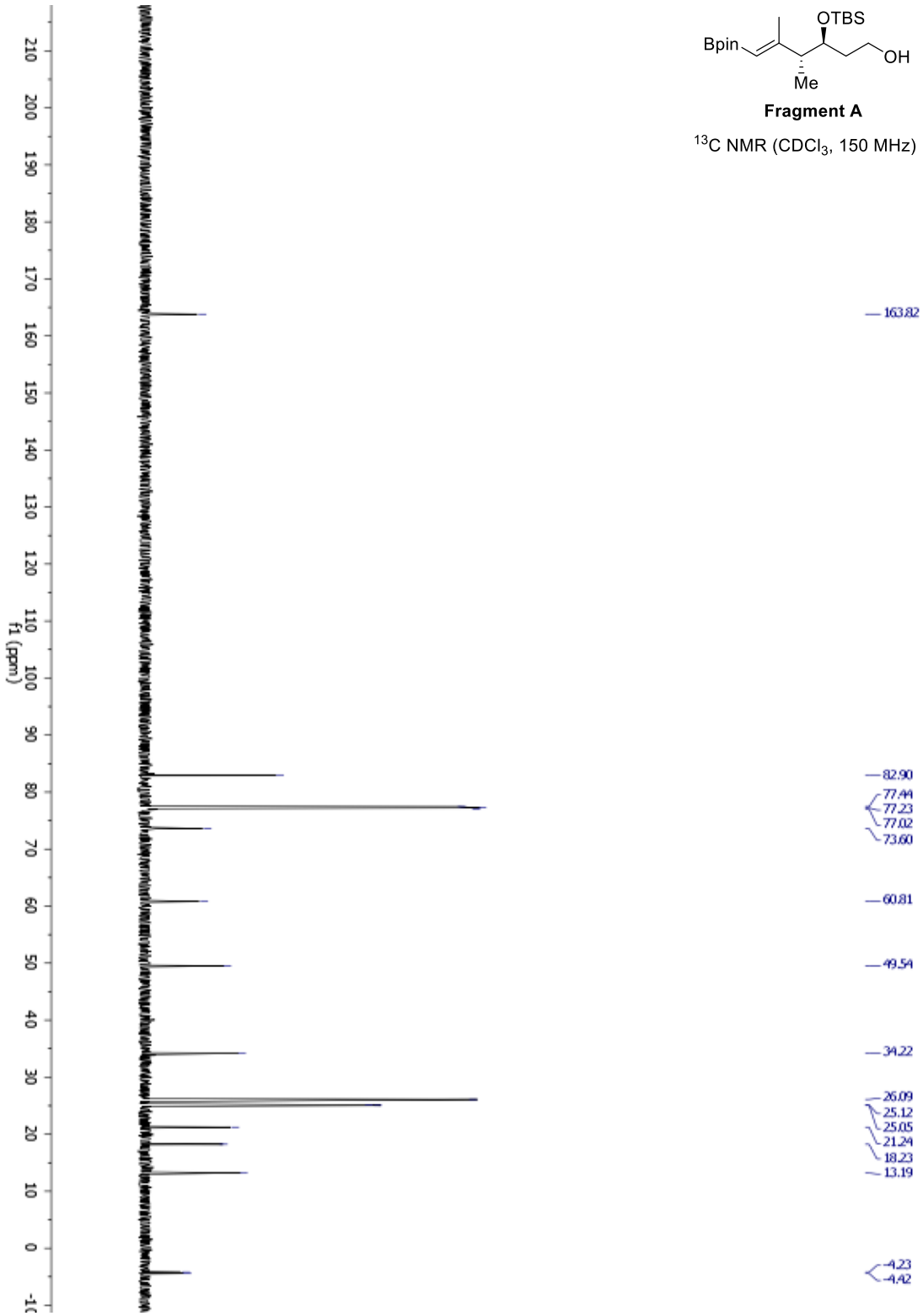

O
OTBS
OPMB
Me
4
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)
2.18
1.92
2.12
0.87
3.00
2.12
0.87
2.53
1.07
1.09
2.70
9.60
5.98
7.28
7.26
6.90
6.89
4.46
4.44
4.43
4.41
4.15
4.14
4.13
4.12
3.83
3.56
3.54
3.53
2.77
2.76
2.74
2.73
2.72
2.17
1.81
1.80
1.78
1.77
1.76
1.74
1.72
1.71
1.70
1.69
1.67
1.66
1.07
1.06
0.88
0.07
0.05

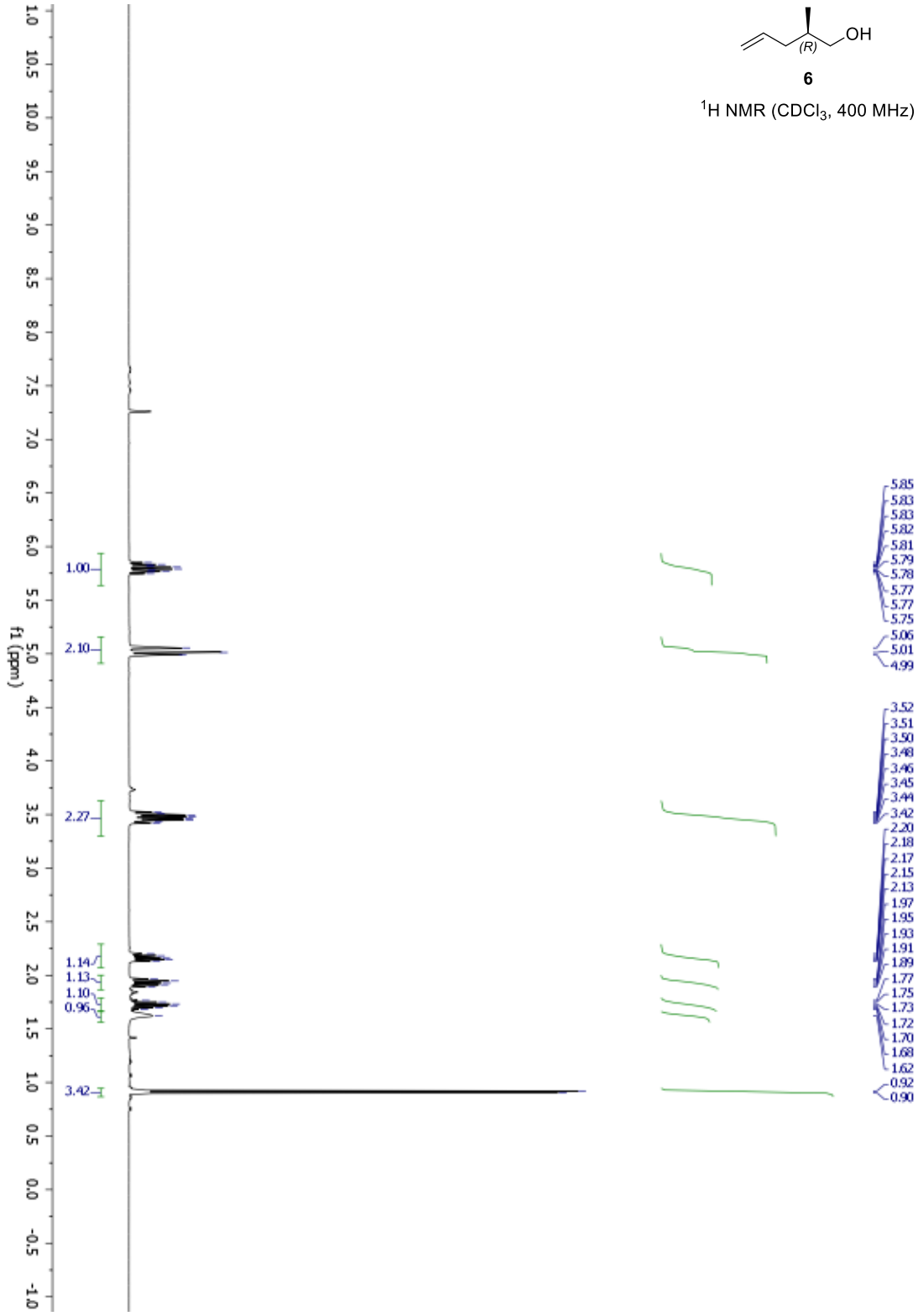

O
OTBS
OPMB
Me
4
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)
211.55
159.33
130.83
129.37
113.96
77.48
77.23
76.97
72.77
71.09
66.11
55.49
52.67
33.79
30.46
26.04
18.22
11.87
-4.45
-4.59

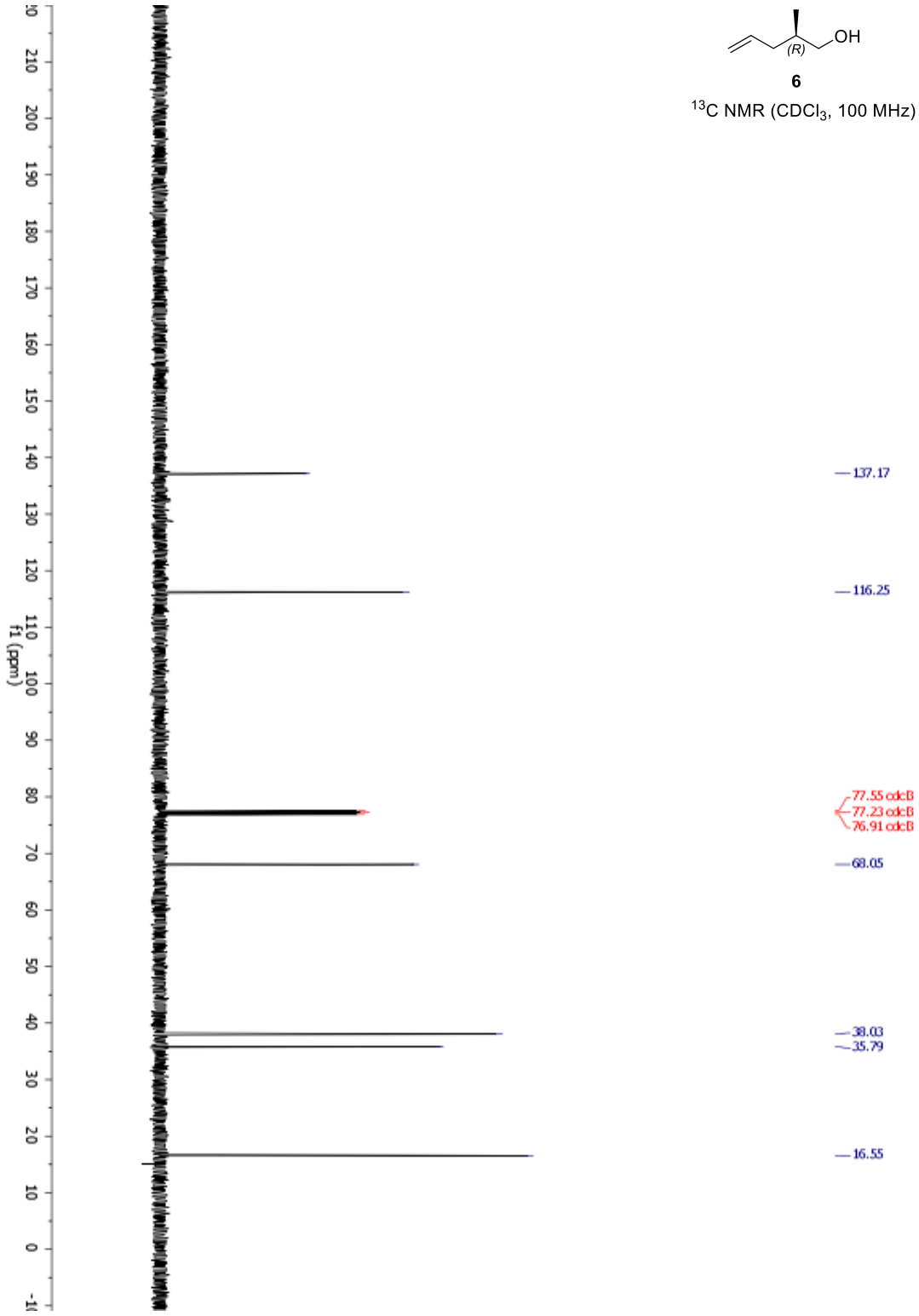

OTBS
Bpin
OPMB
Me
5
1H NMR (CDCl3, 500 MHz)
f1 (ppm)
2.48
1.96
0.82
2.00
0.81
3.02
2.00
0.79
2.41
2.10
14.49
2.43
10.38
5.98
7.26
7.26
7.24
6.88
6.86
5.15
4.42
4.40
4.39
4.37
3.93
3.92
3.92
3.91
3.91
3.90
3.80
3.50
3.49
3.49
3.48
3.47
2.37
2.36
2.35
2.33
2.32
1.99
1.70
1.69
1.67
1.66
1.66
1.65
1.64
1.63
1.26
1.02
1.00
0.87
0.04
0.03

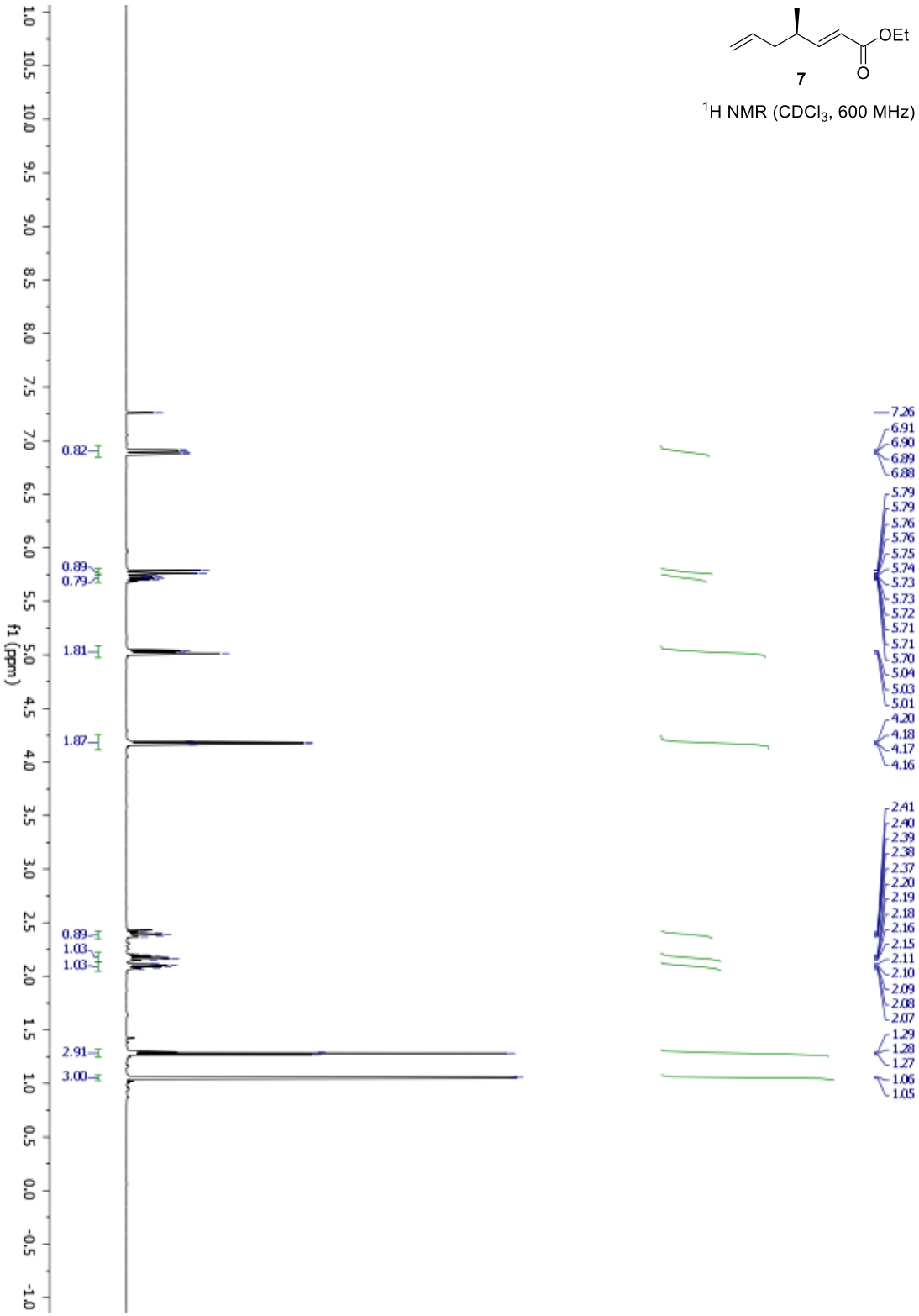

OTBS
Bpin
OPMB
Me
5
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)
164.24
159.27
130.98
129.41
113.94
82.80
77.48
77.23
76.98
72.71
71.65
67.34
55.48
50.06
32.73
26.11
25.14
25.04
22.55
20.97
18.30
14.27
13.35
-4.27
-4.43

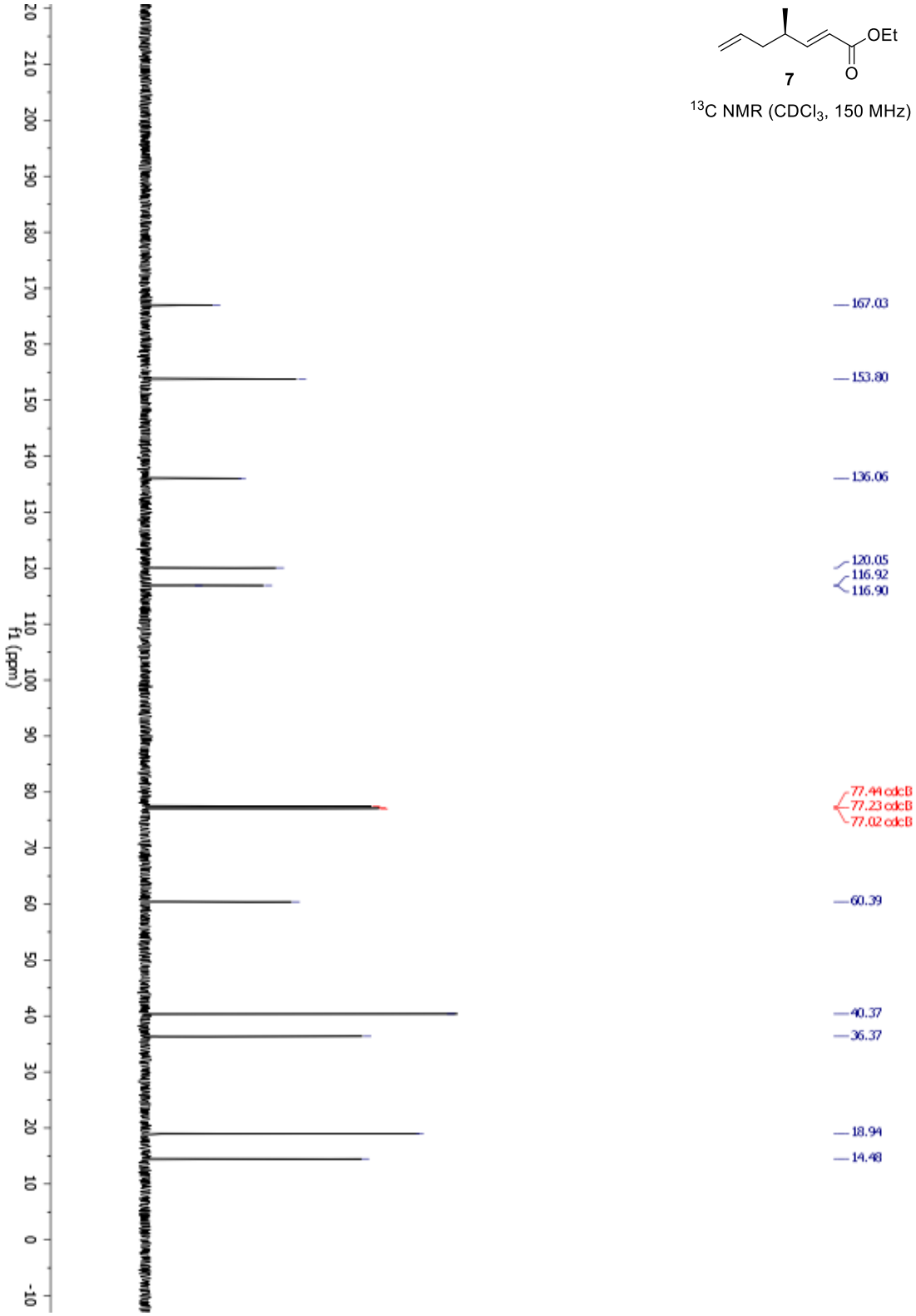

OTBS
Bpin
OH
Me
Fragment A
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
7.26
5.18
3.99
3.98
3.98
3.98
3.98
3.98
3.97
3.97
3.96
3.77
3.76
3.75
3.74
3.73
3.72
3.71
3.70
3.70
3.69
3.68
2.44
2.43
2.42
2.41
2.40
2.00
1.67
1.66
1.65
1.64
1.63
1.63
1.62
1.26
1.02
1.00
0.89
0.09
0.07
1.00
1.05
2.40
1.11
3.17
2.41
14.50
3.24
10.89
6.69

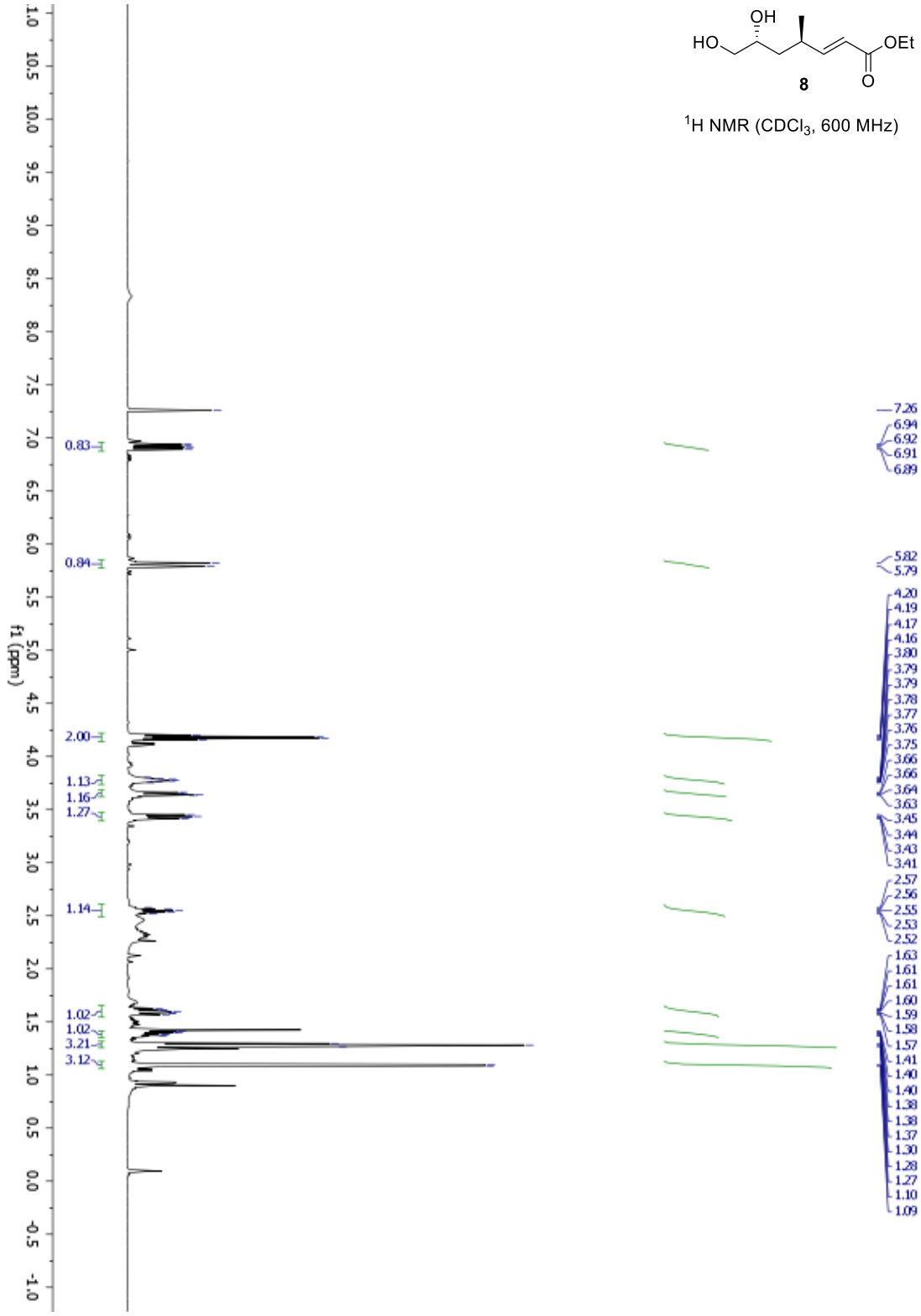

OTBS
Bpin
OH
Me
Fragment A
^{13}C NMR ($CDCl_3$, 150 MHz)
f1 (ppm)
163.82
82.90
77.44
77.23
77.02
73.60
60.81
49.54
34.22
26.09
25.12
25.05
21.24
18.23
13.19
-4.23
-4.42

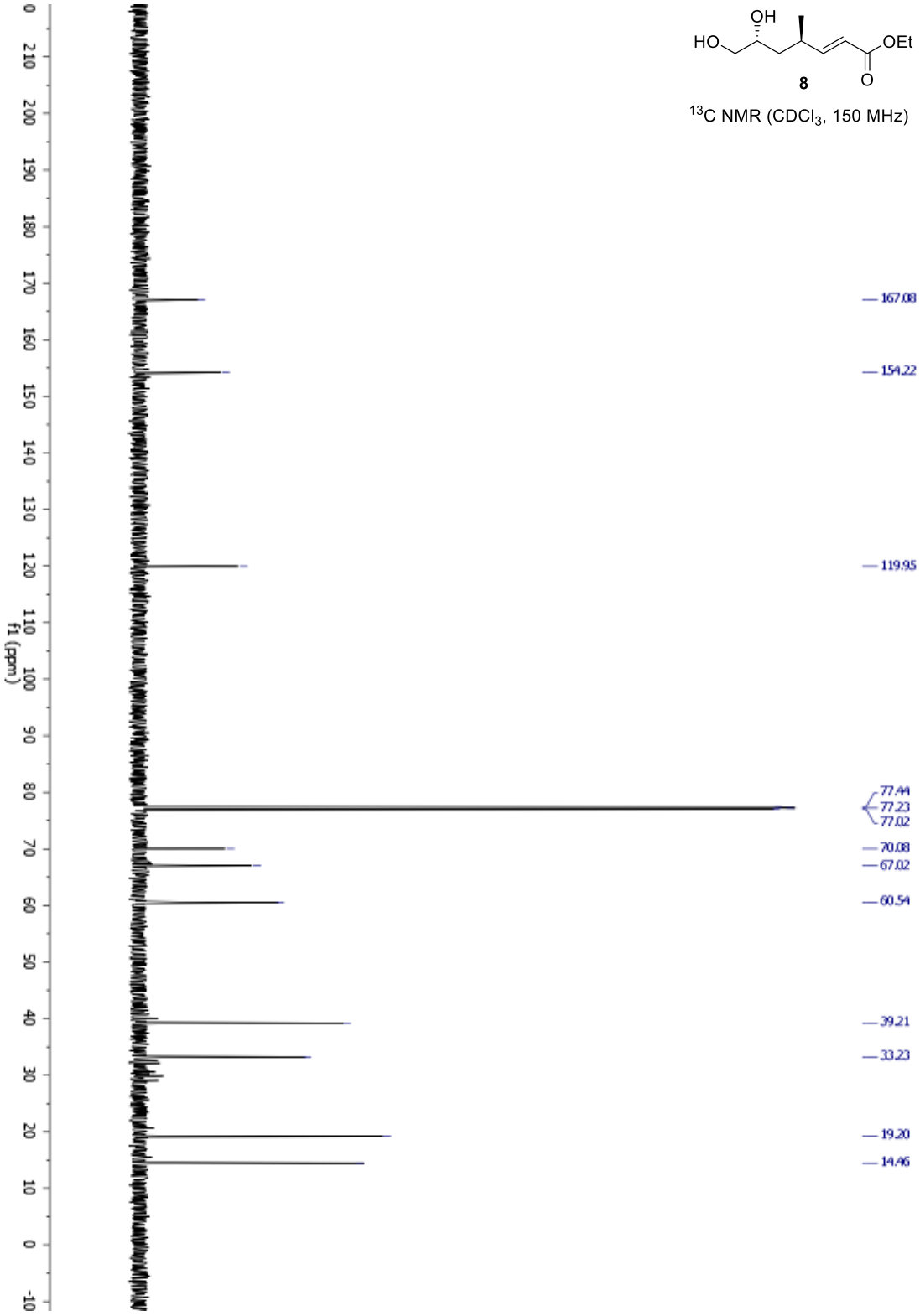

OH
(R)
6
^{1}H NMR ($CDCl_3$, 400 MHz)
f1 (ppm)
1.00
2.10
2.27
1.14
1.13
1.10
0.96
3.42
5.85
5.83
5.83
5.82
5.81
5.79
5.78
5.77
5.77
5.75
5.06
5.01
4.99
3.52
3.51
3.50
3.48
3.46
3.45
3.44
3.42
2.20
2.18
2.17
2.15
2.13
1.97
1.95
1.93
1.91
1.89
1.77
1.75
1.73
1.72
1.70
1.68
1.62
0.92
0.90

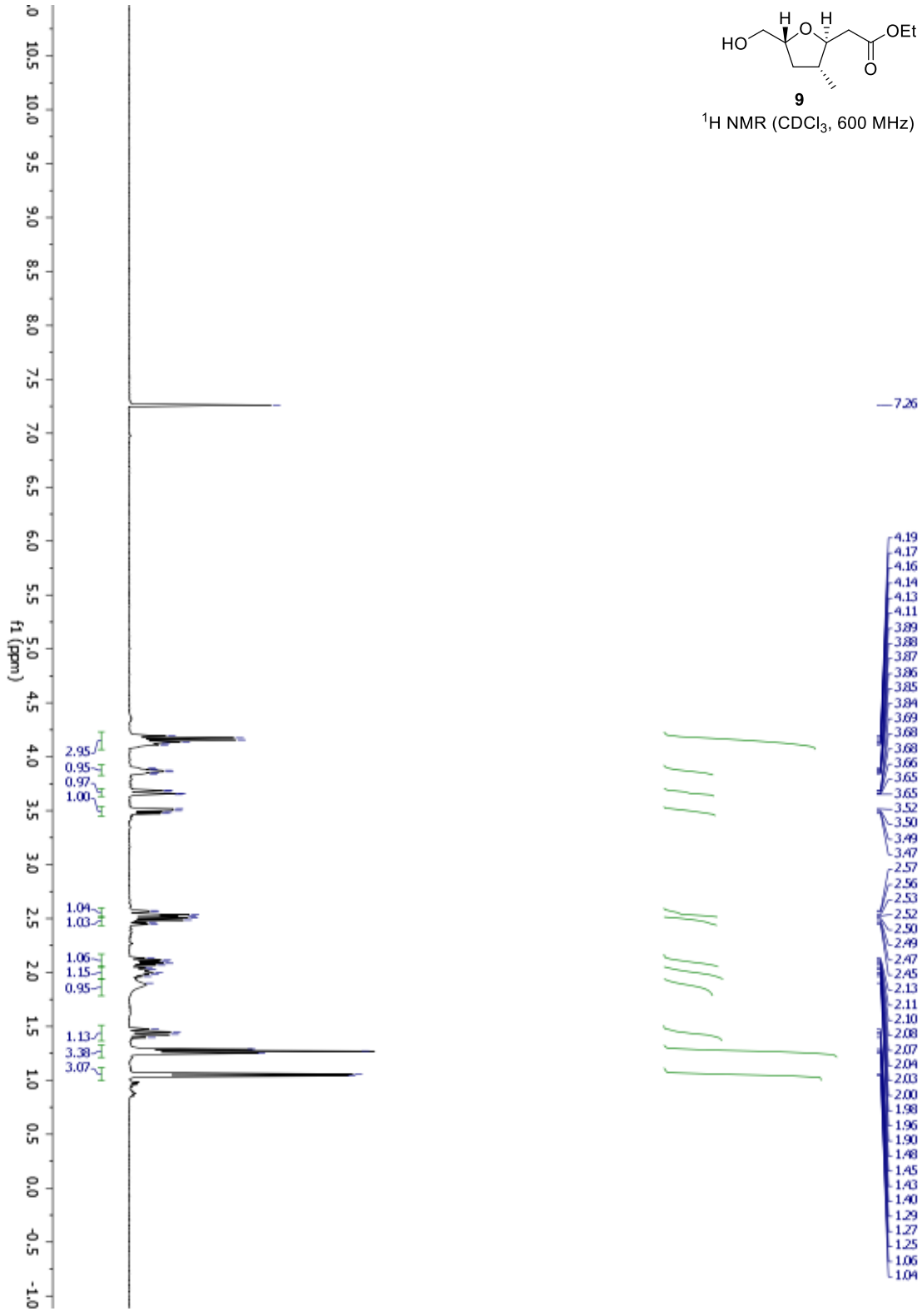

OH
(R)
6
^{13}C NMR ($CDCl_3$, 100 MHz)
137.17
116.25
77.55 cdcl3
77.23 cdcl3
76.91 cdcl3
68.05
38.03
35.79
16.55
f1 (ppm)

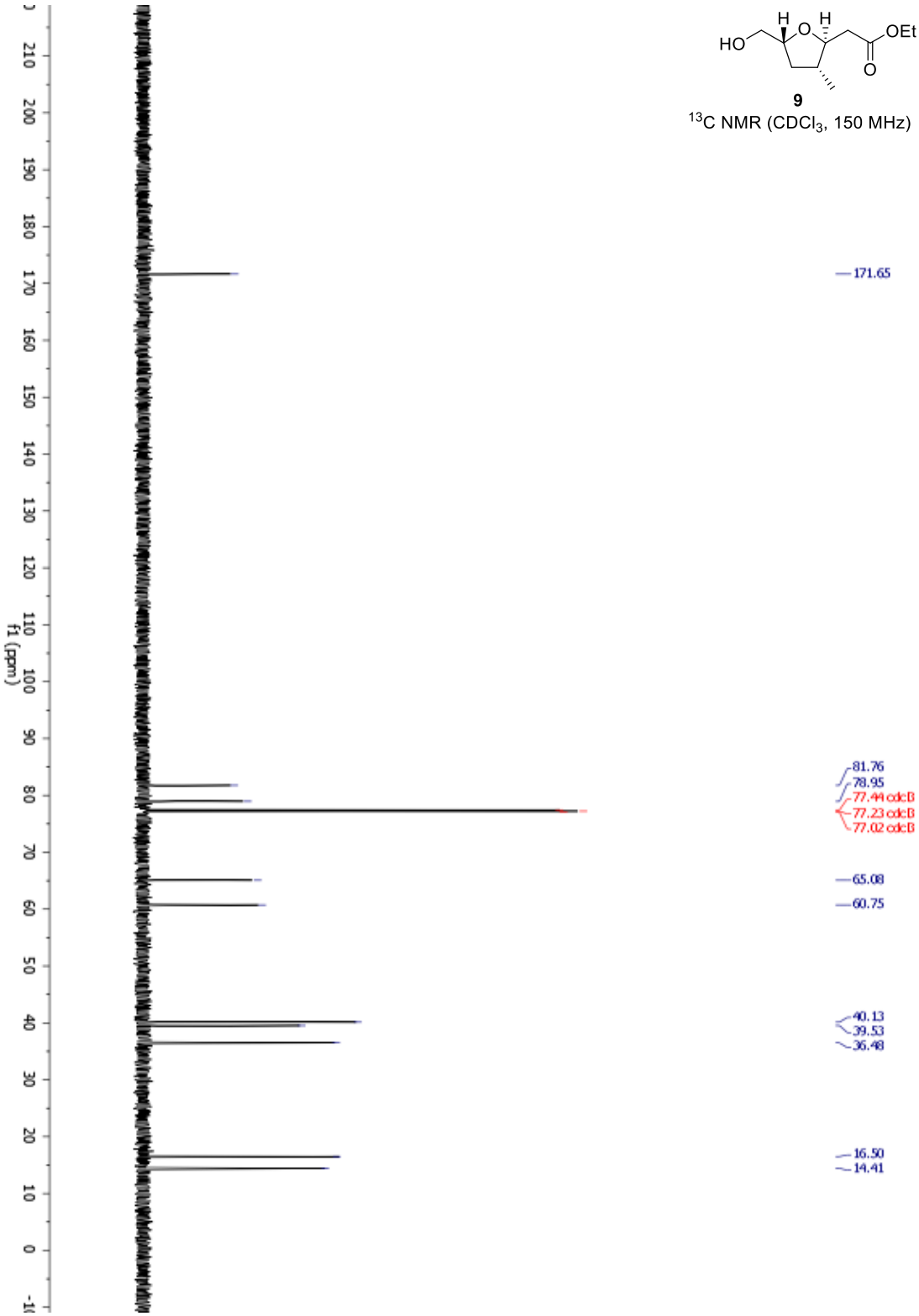

OEt
O
7
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
0.82
0.89
0.79
1.81
1.87
0.89
1.03
1.03
2.91
3.00
7.26
6.91
6.90
6.89
6.88
5.79
5.79
5.76
5.76
5.75
5.74
5.73
5.73
5.72
5.71
5.71
5.70
5.04
5.03
5.01
4.20
4.18
4.17
4.16
2.41
2.40
2.39
2.38
2.37
2.20
2.19
2.18
2.16
2.15
2.11
2.10
2.09
2.08
2.07
1.29
1.28
1.27
1.06
1.05

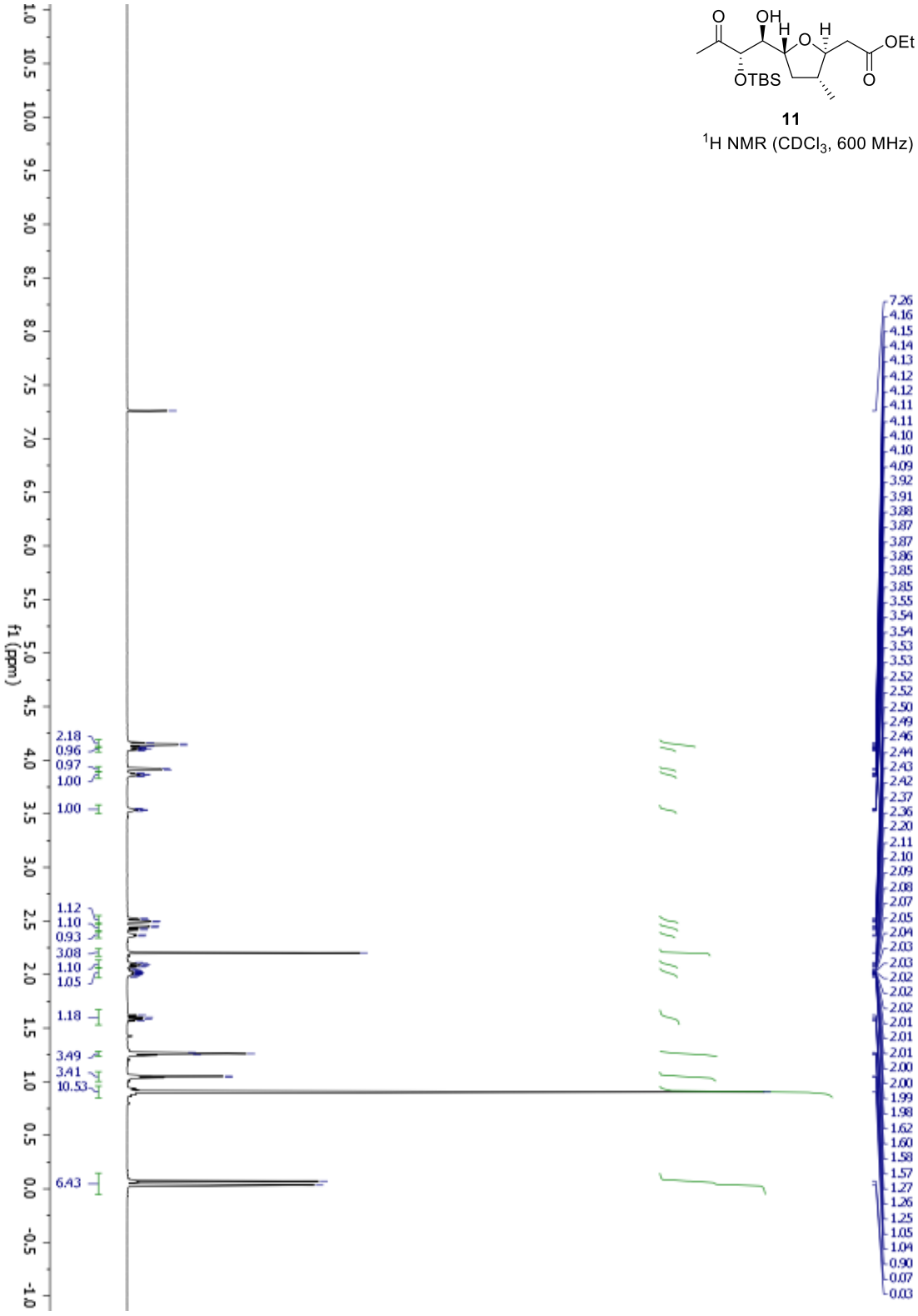

OEt
O
7
^{13}C NMR ($CDCl_3$, 150 MHz)
167.03
153.80
136.06
120.05
116.92
116.90
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
60.39
40.37
36.37
18.94
14.48
f1 (ppm)

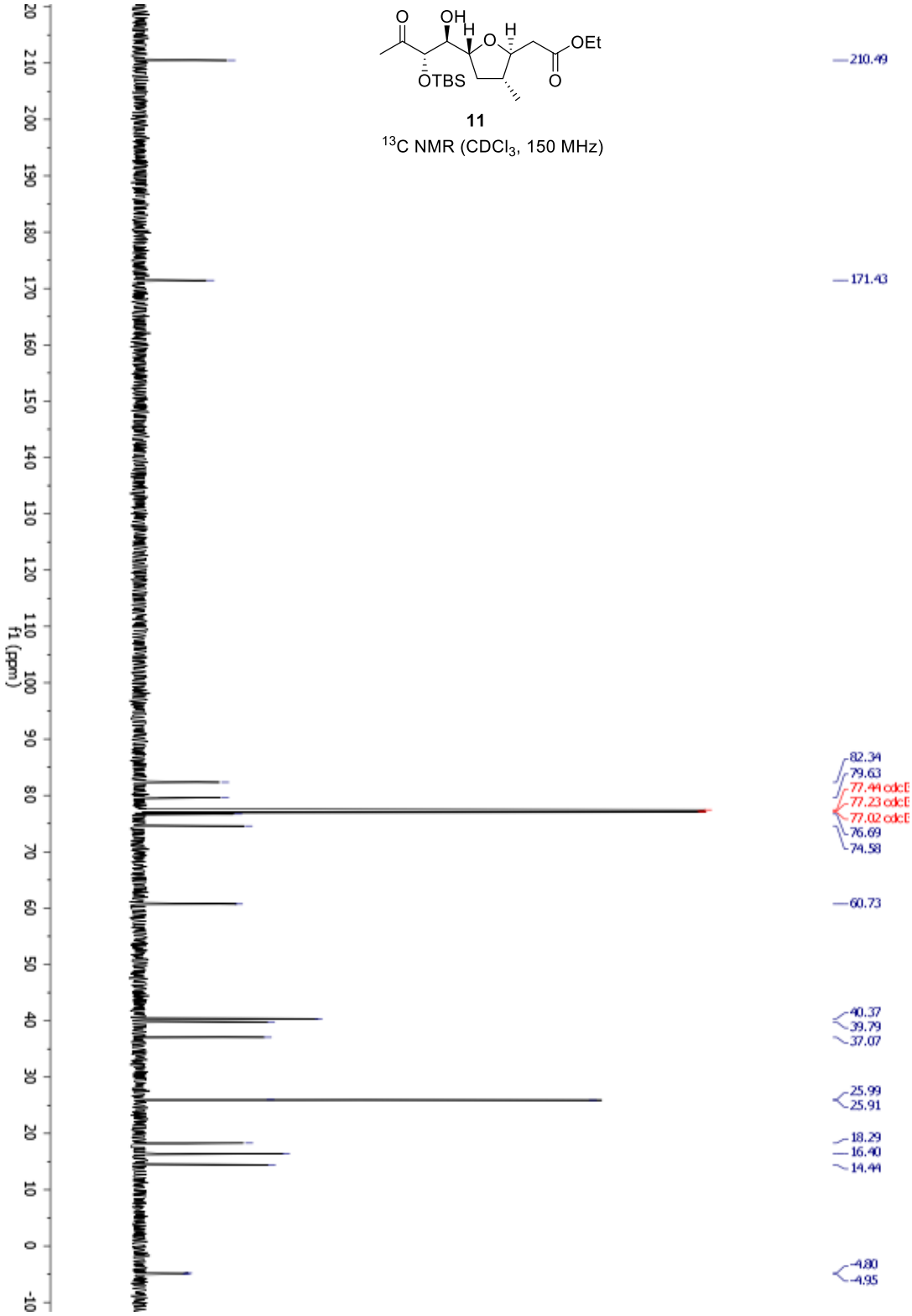

OH
HO
OEt
O
8
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)
0.83
0.84
2.00
1.13
1.16
1.27
1.14
1.02
1.02
3.21
3.12
7.26
6.94
6.92
6.91
6.89
5.82
5.79
4.20
4.19
4.17
4.16
3.80
3.79
3.79
3.78
3.77
3.76
3.75
3.66
3.66
3.64
3.63
3.45
3.44
3.43
3.41
2.57
2.56
2.55
2.53
2.52
1.63
1.61
1.61
1.60
1.59
1.58
1.57
1.41
1.40
1.40
1.38
1.38
1.37
1.30
1.28
1.27
1.10
1.09

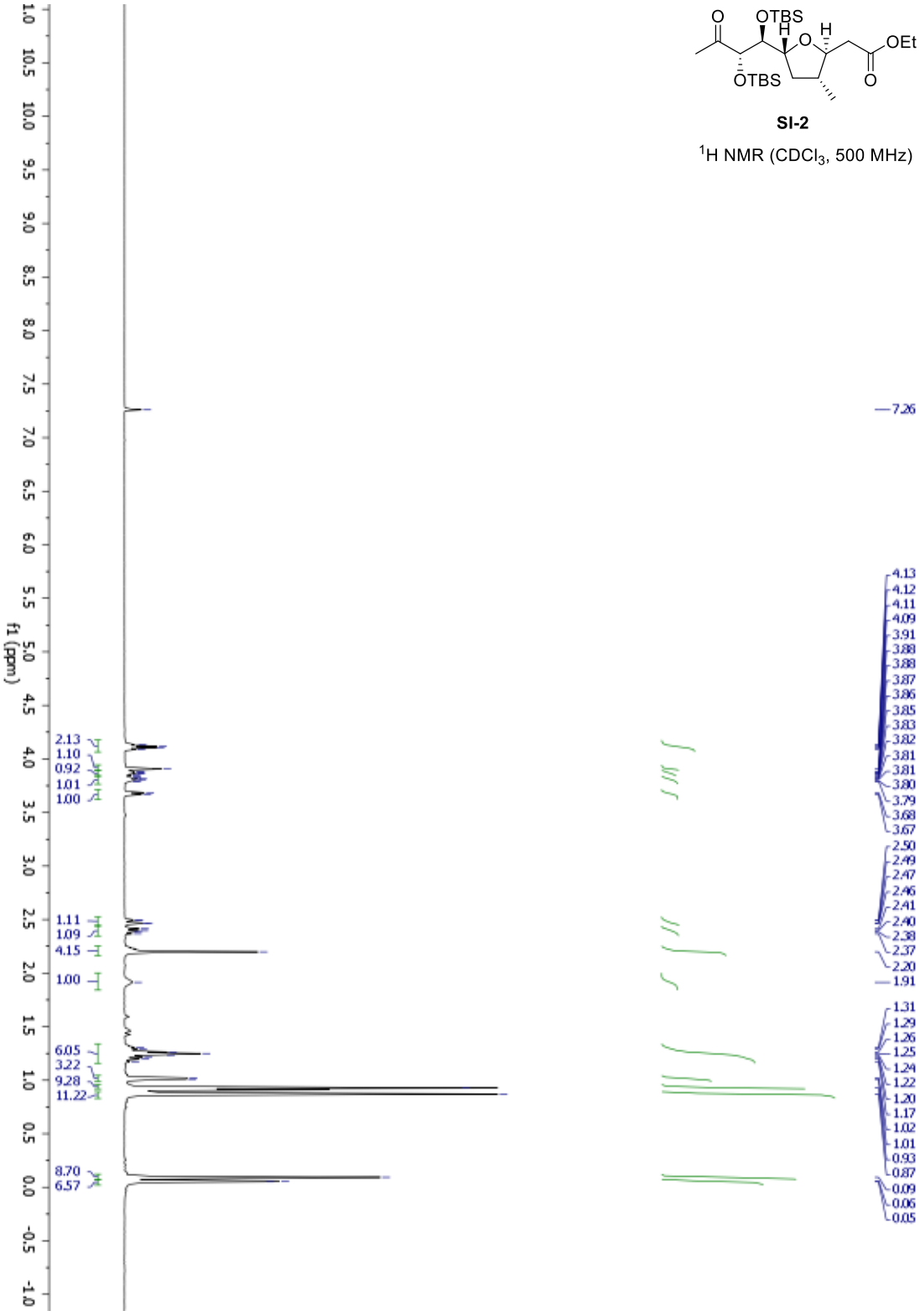

OH
HO
OEt
O
8
^{13}C NMR ($CDCl_3$, 150 MHz)
167.08
154.22
119.95
77.44
77.23
77.02
70.08
67.02
60.54
39.21
33.23
19.20
14.46
f1 (ppm)


HO
H
O
H
OEt
O
9
1H NMR (CDCl3, 600 MHz)
f1 (ppm)
7.26
2.95
0.95
0.97
1.00
1.04
1.03
1.06
1.15
0.95
1.13
3.38
3.07


HO
H
O
H
OEt
O
9
13C NMR (CDCl3, 150 MHz)
f1 (ppm)
171.65
81.76
78.95
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
65.08
60.75
40.13
39.53
36.48
16.50
14.41

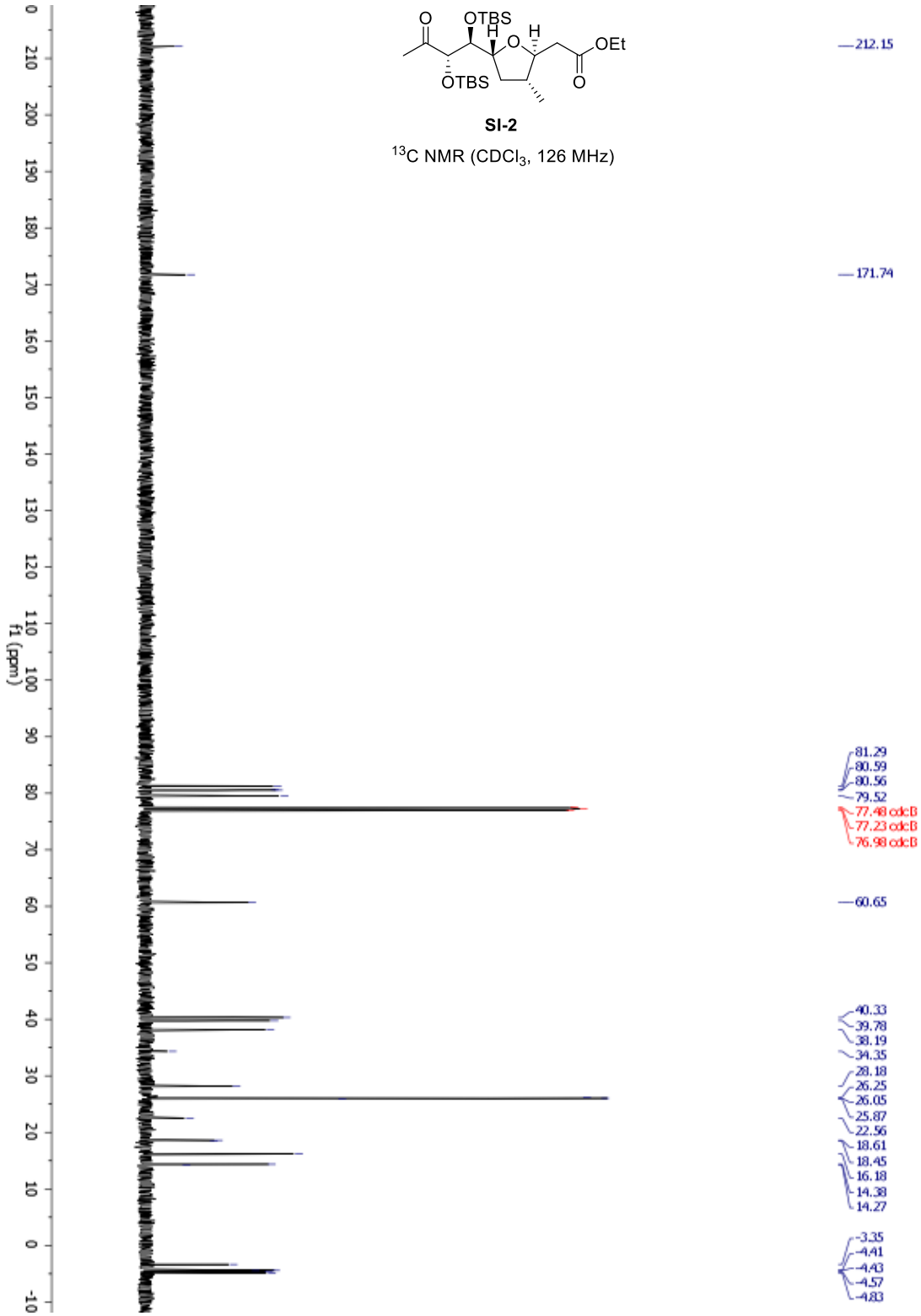

O
OH
H
O
H
OEt
OTBS
O
11
1H NMR (CDCl3, 600 MHz)
f1 (ppm)
2.18
0.96
0.97
1.00
1.00
1.12
1.10
0.93
3.08
1.10
1.05
1.18
3.49
3.41
10.53
6.43

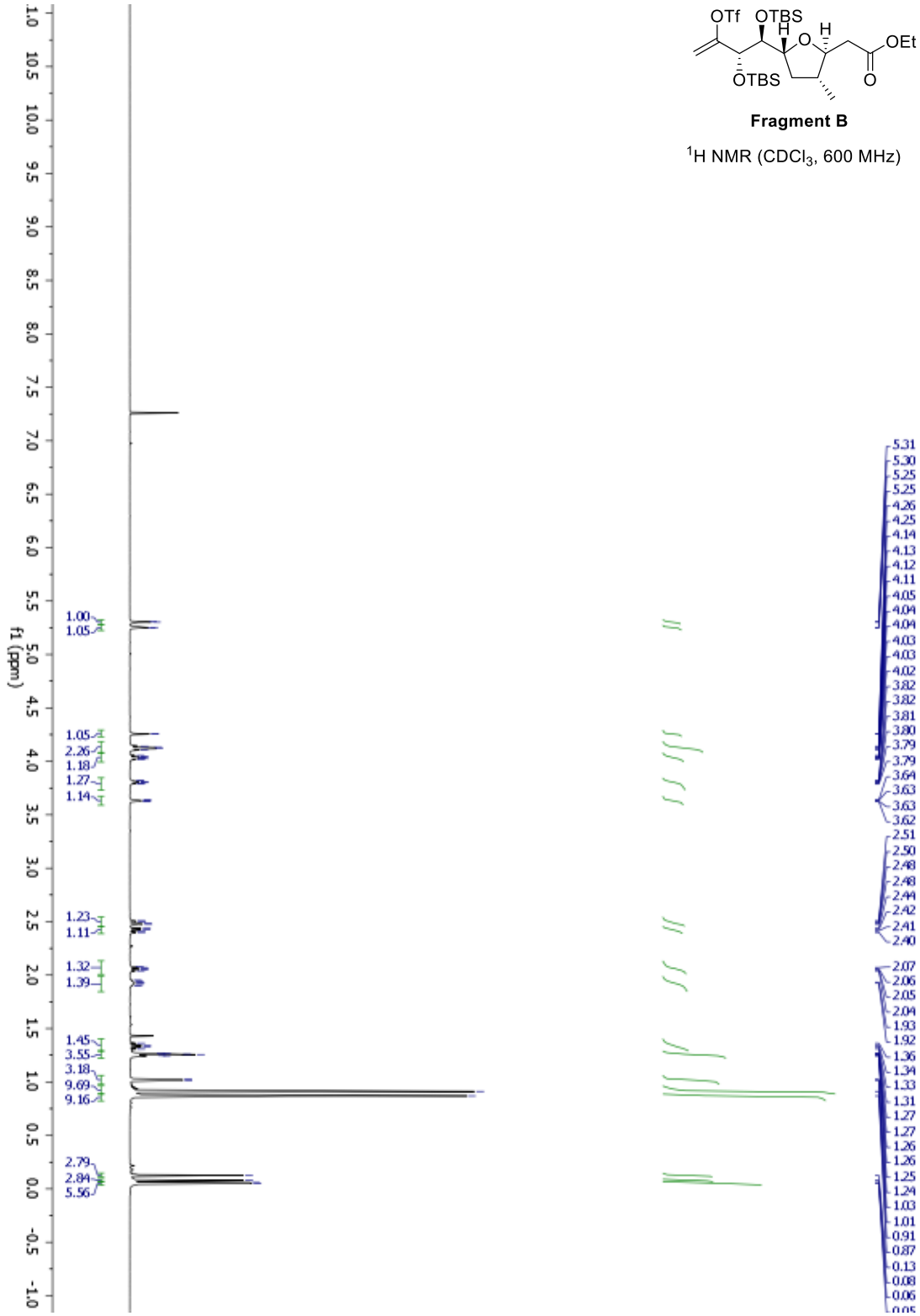

O
OH
H
O
H
OEt
OTBS
O
11
^{13}C NMR ($CDCl_3$, 150 MHz)
210.49
171.43
82.34
79.63
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
76.69
74.58
60.73
40.37
39.79
37.07
25.99
25.91
18.29
16.40
14.44
-4.80
-4.95
f1 (ppm)

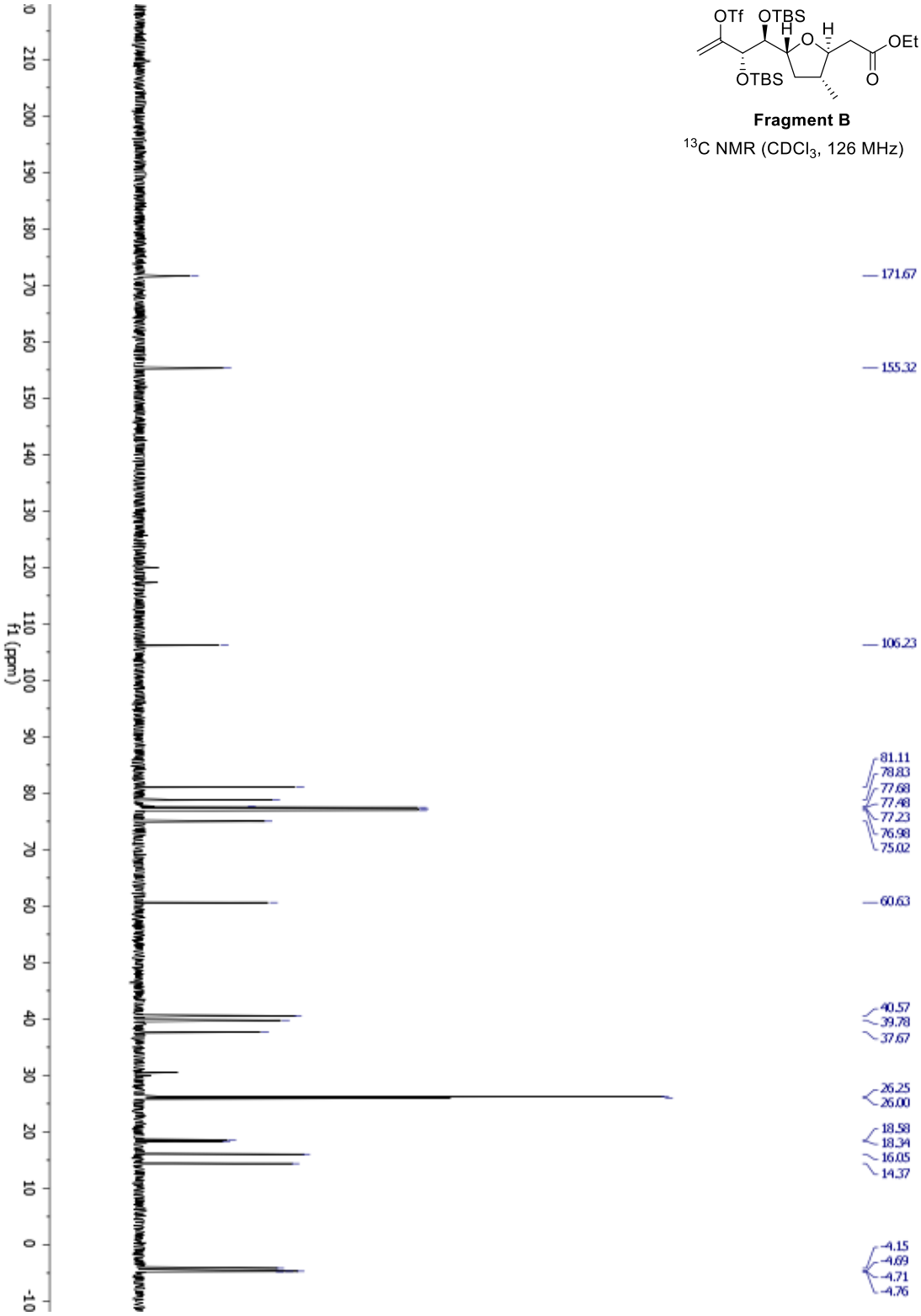


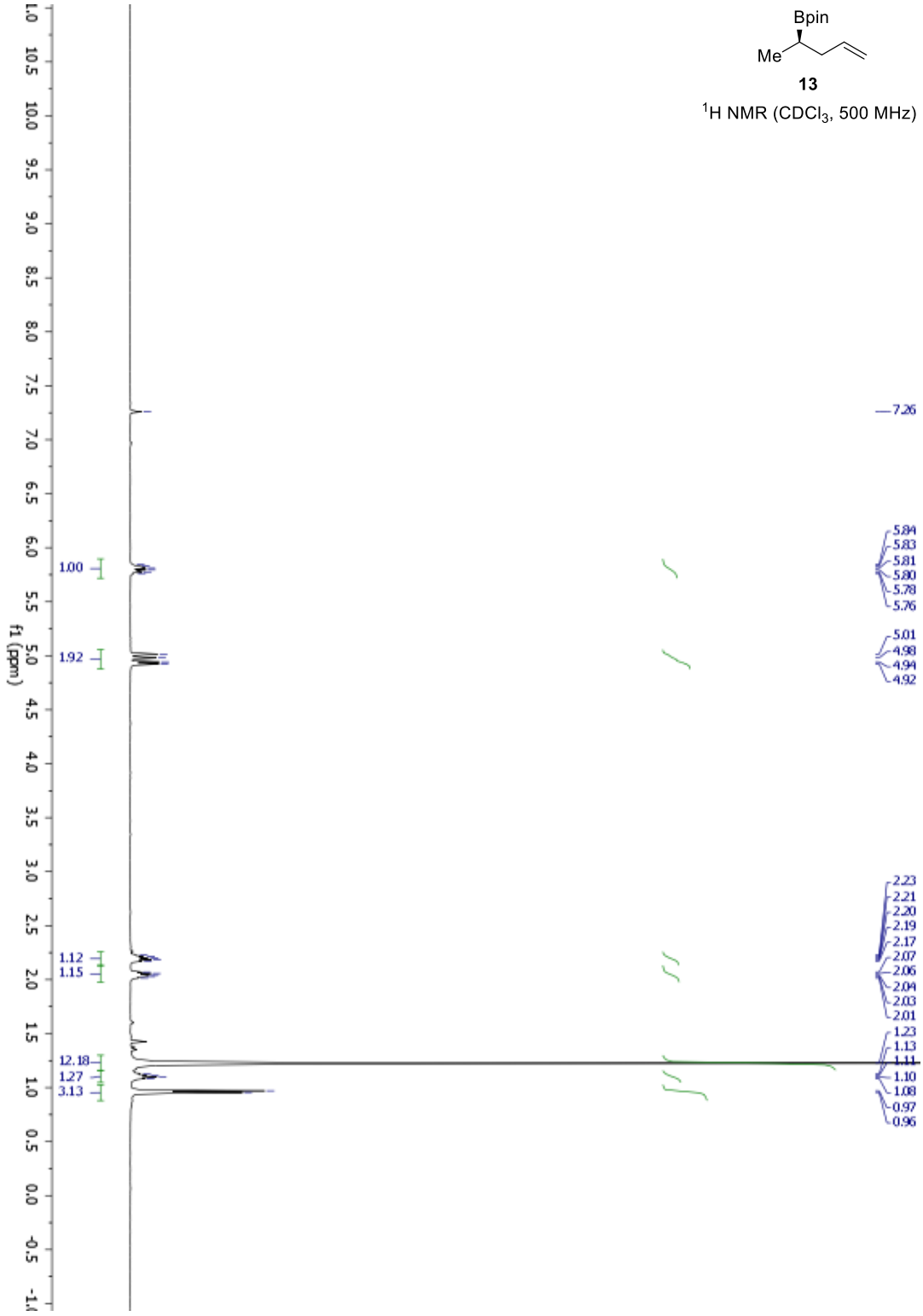
SI-2

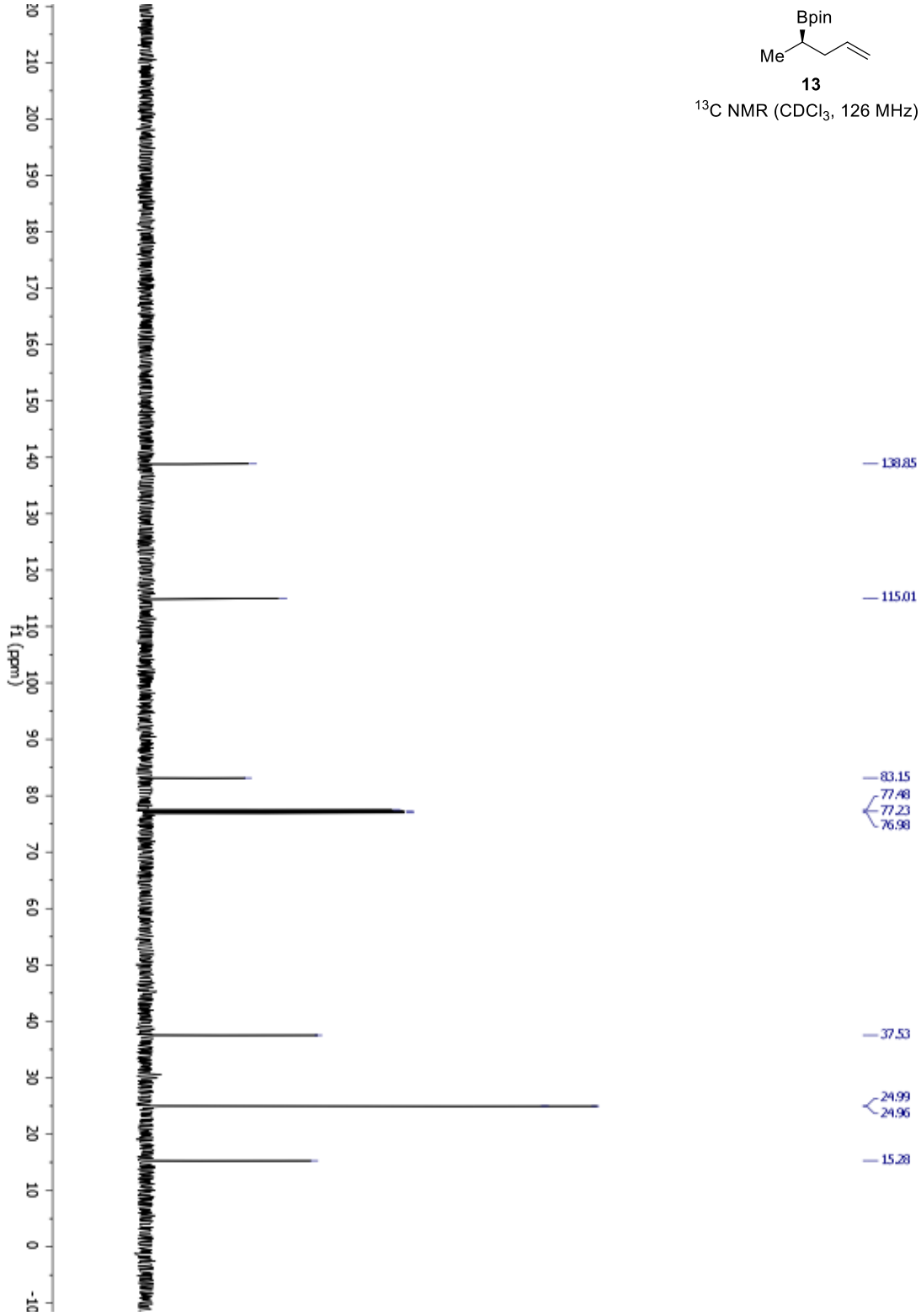
^{1}H NMR ($CDCl_3$, 500 MHz)

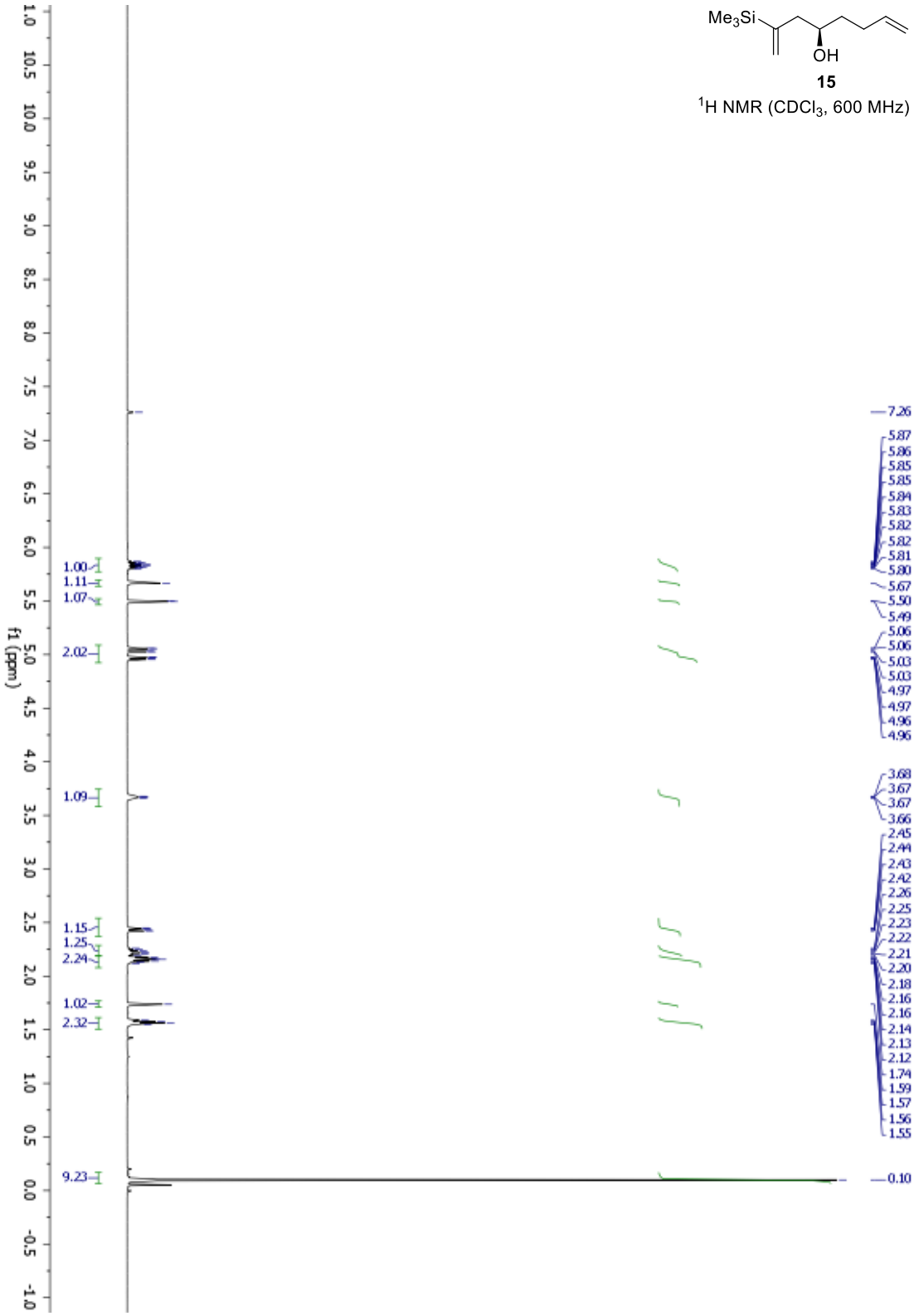

O
OTBS
H
H
O
OEt
OTBS
O
SI-2
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)
212.15
171.74
81.29
80.59
80.56
79.52
77.48 cdcl3
77.23 cdcl3
76.98 cdcl3
60.65
40.33
39.78
38.19
34.35
28.18
26.25
26.05
25.87
22.56
18.61
18.45
16.18
14.38
14.27
-3.35
-4.41
-4.43
-4.57
-4.83

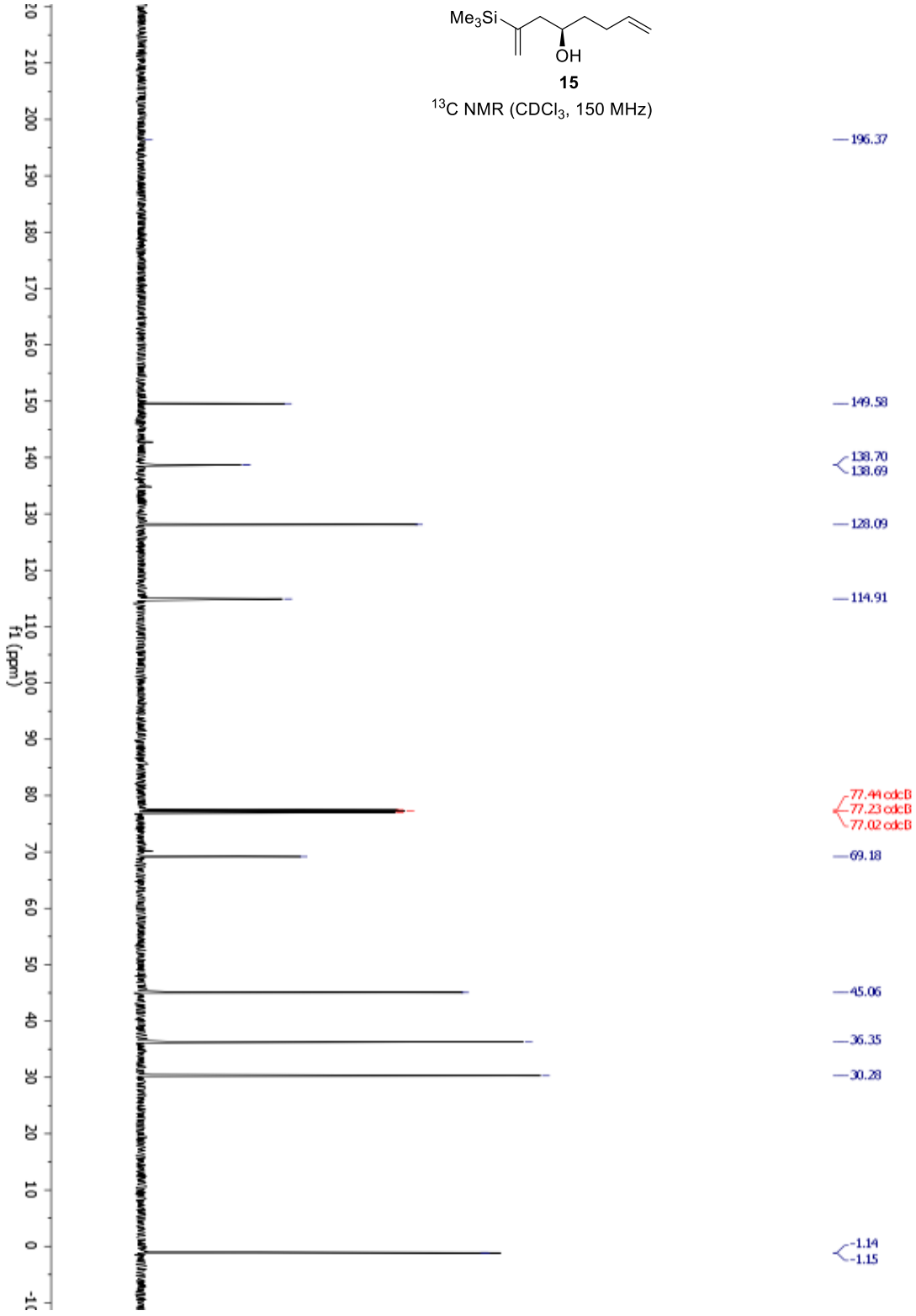

OTf
OTBS
H
O
H
OEt
OTBS
O
Fragment B
^{1}H NMR ($CDCl_3$, 600 MHz)
f1 (ppm)

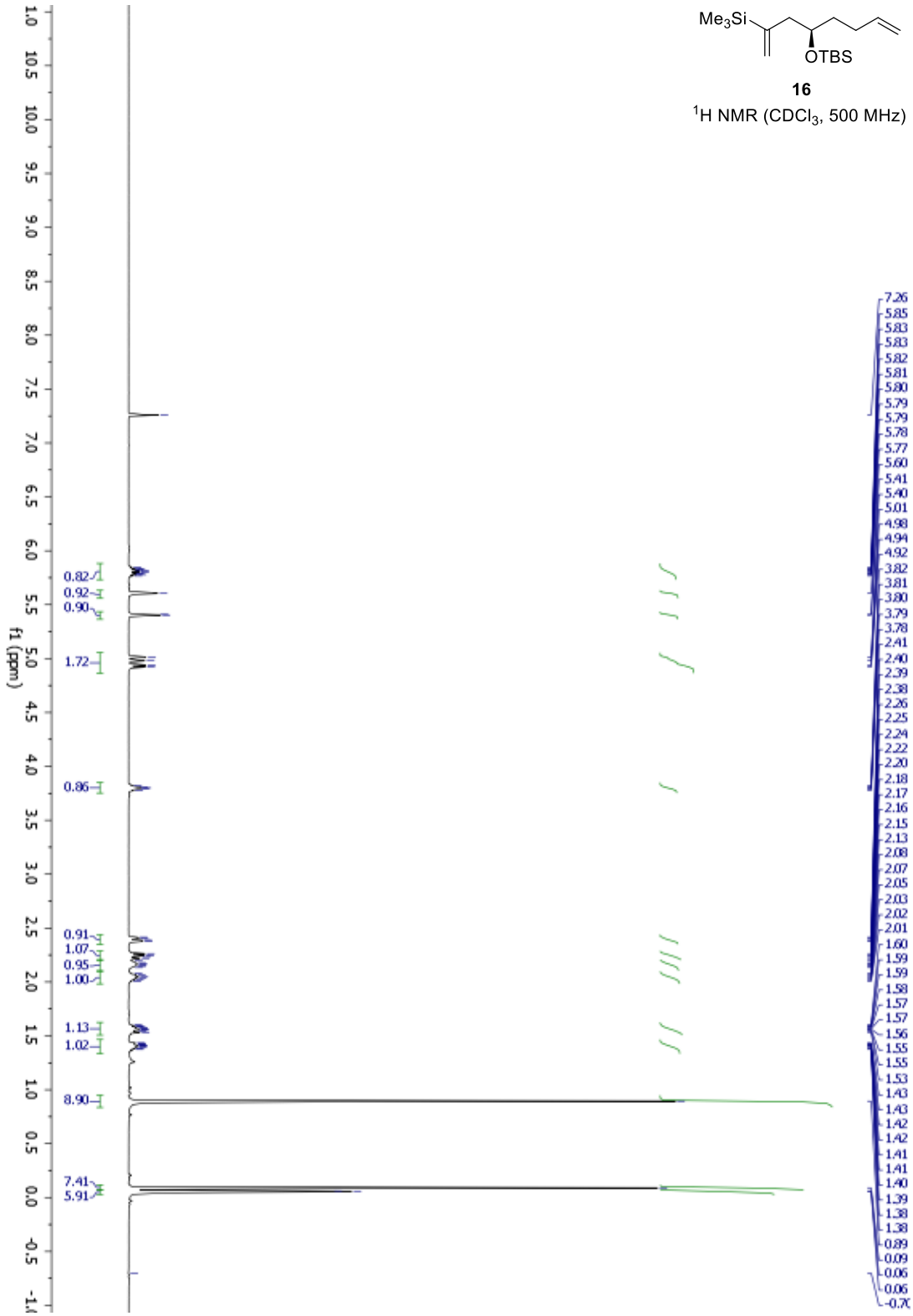

OTf
OTBS
H
O
H
OEt
OTBS
O
Fragment B
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)
171.67
155.32
106.23
81.11
78.83
77.68
77.48
77.23
76.98
75.02
60.63
40.57
39.78
37.67
26.25
26.00
18.58
18.34
16.05
14.37
-4.15
-4.69
-4.71
-4.76

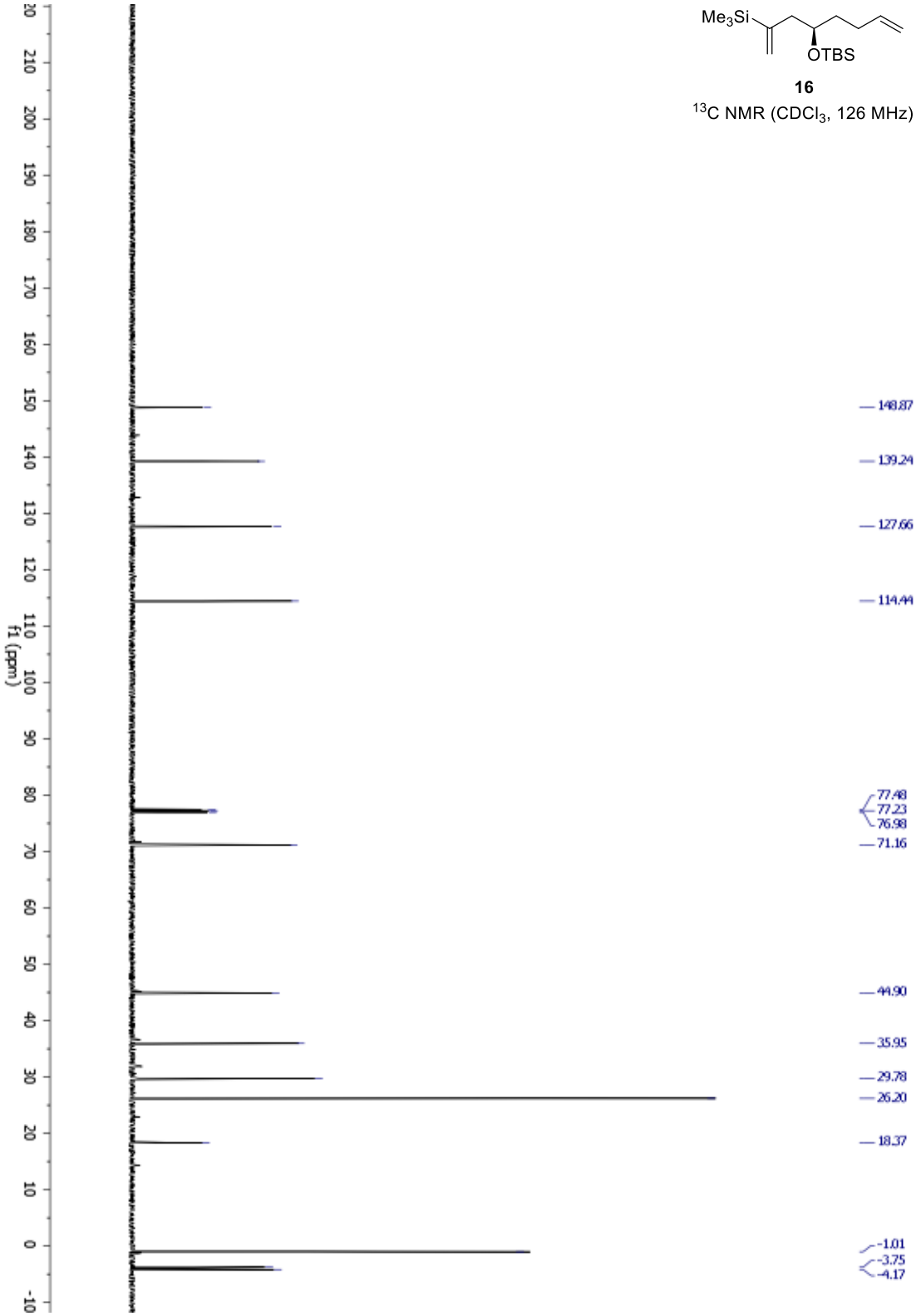

Bpin
Me
13
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)
7.26
5.84
5.83
5.81
5.80
5.78
5.76
5.01
4.98
4.94
4.92
2.23
2.21
2.20
2.19
2.17
2.07
2.06
2.04
2.03
2.01
1.23
1.13
1.11
1.10
1.08
0.97
0.96
1.00
1.92
1.12
1.15
12.18
1.27
3.13

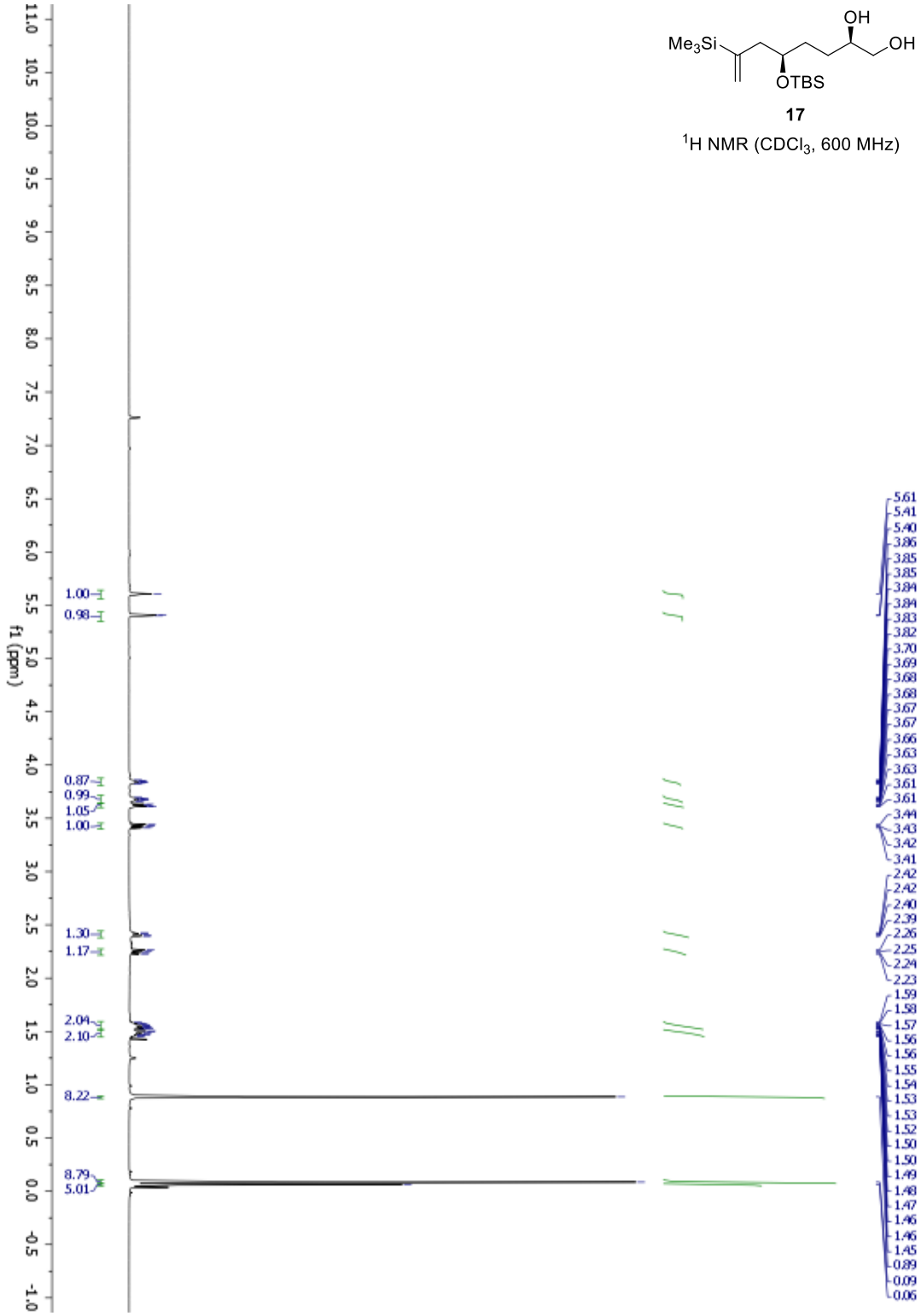

Bpin
Me
13
^{13}C NMR ($CDCl_3$, 126 MHz)
f1 (ppm)
138.85
115.01
83.15
77.48
77.23
76.98
37.53
24.99
24.96
15.28

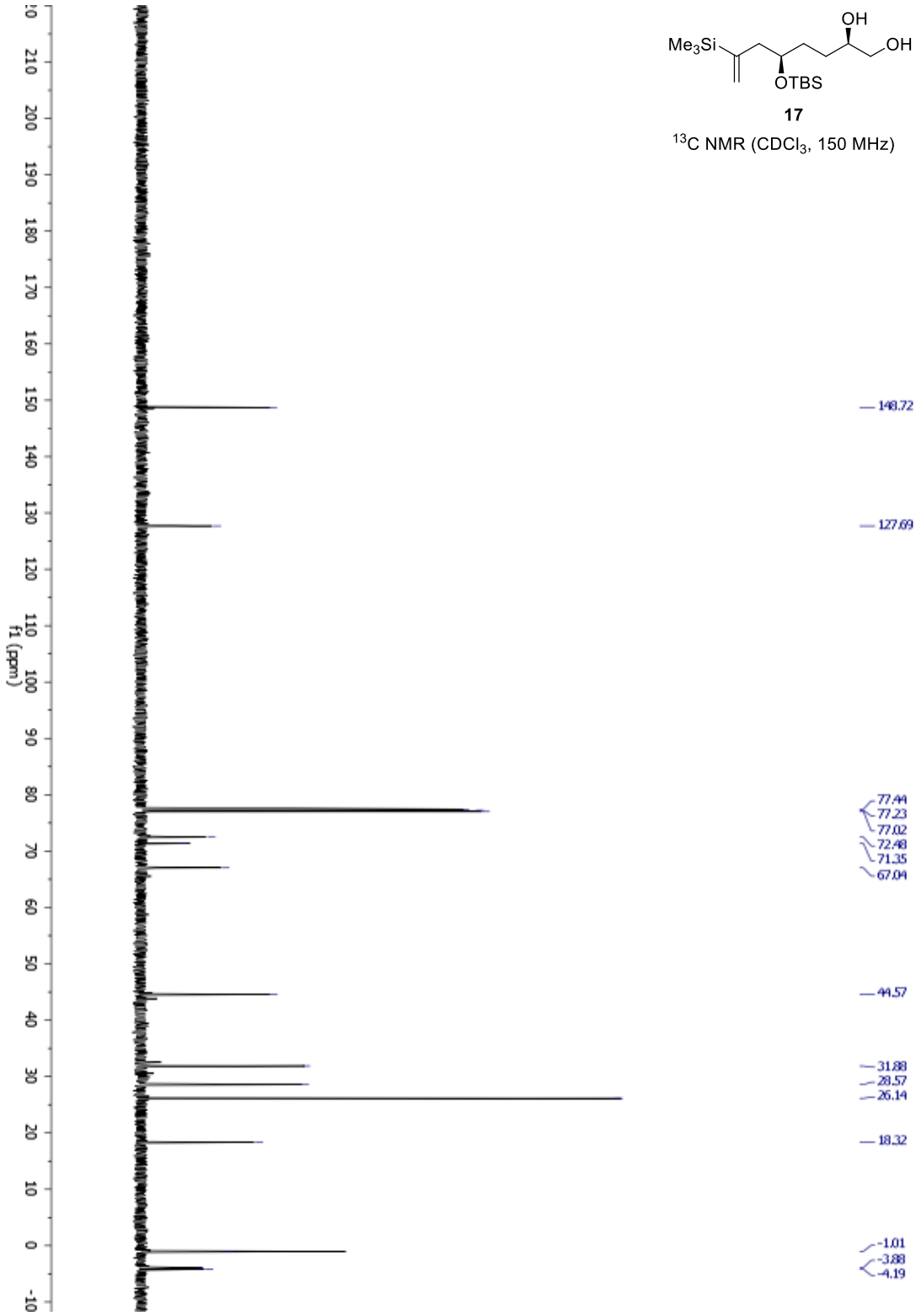

Me3Si
OH
15
1H NMR (CDCl3, 600 MHz)
f1 (ppm)
1.00
1.11
1.07
2.02
1.09
1.15
1.25
2.24
1.02
2.32
9.23
7.26
0.10

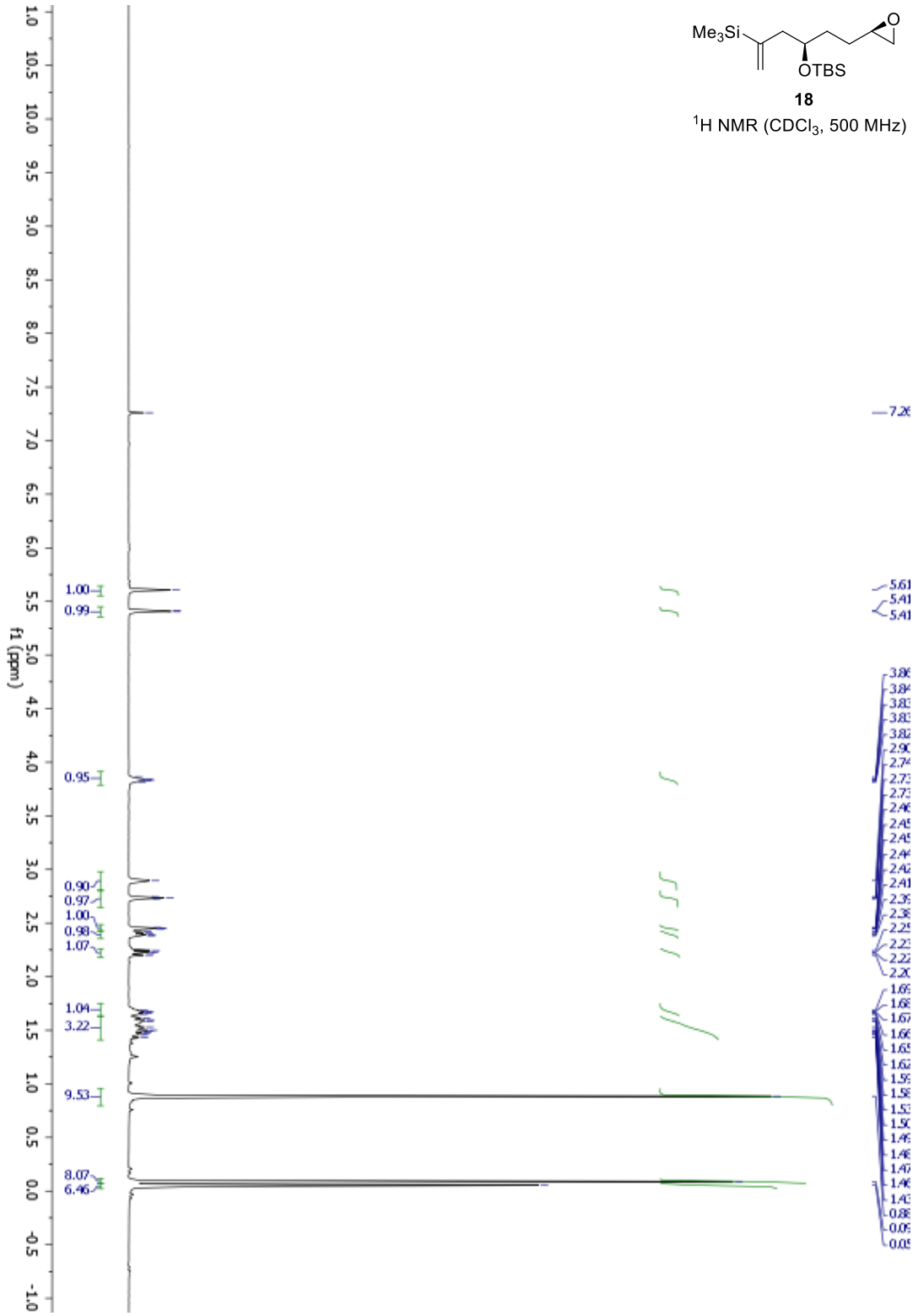

Me3Si
OH
15
13C NMR (CDCl3, 150 MHz)
196.37
149.58
138.70
138.69
128.09
114.91
77.44 cdcl3
77.23 cdcl3
77.02 cdcl3
69.18
45.06
36.35
30.28
-1.14
-1.15
f1 (ppm)

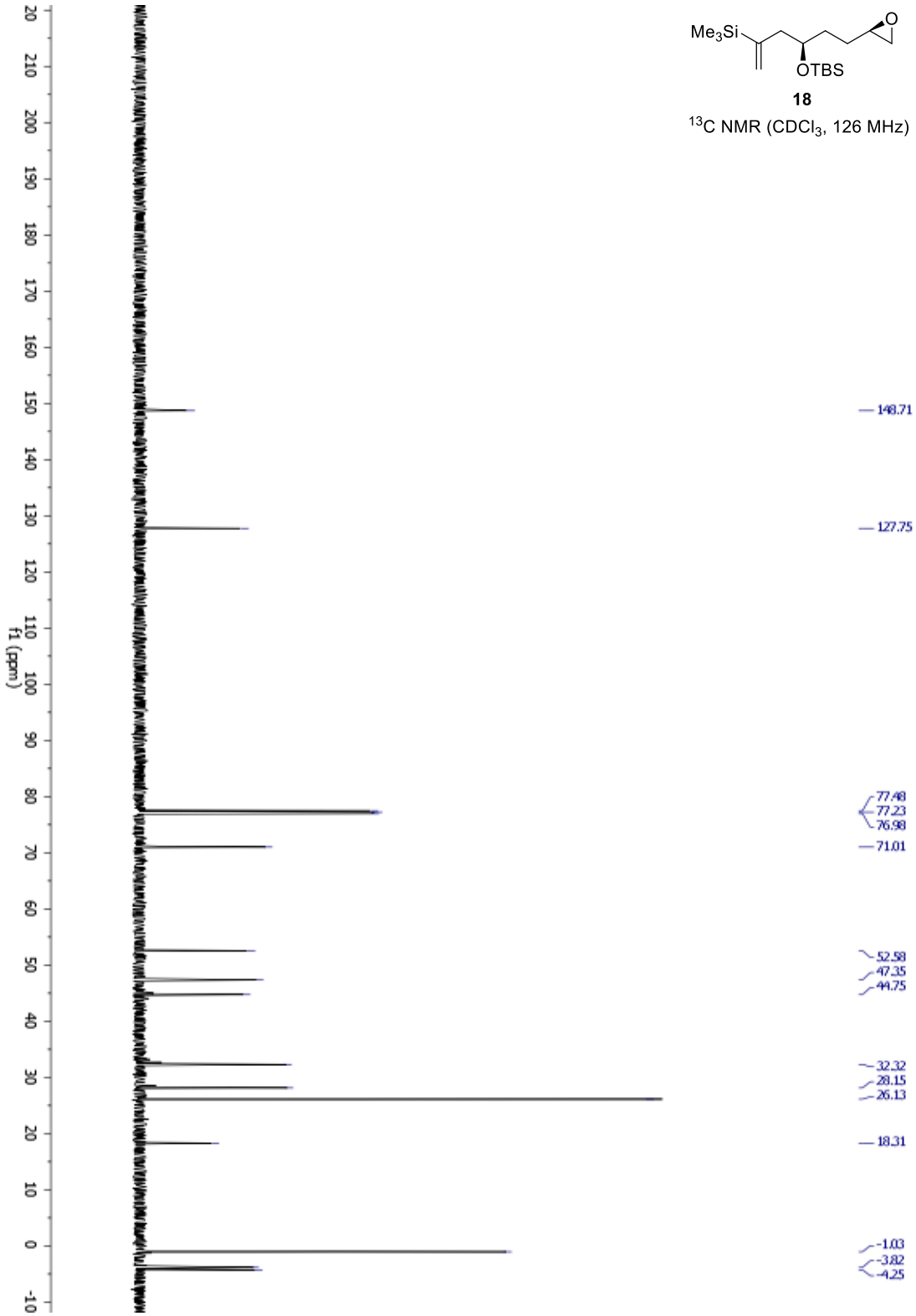

Me3Si
OTBS
16
1H NMR (CDCl3, 500 MHz)
f1 (ppm)
0.82
0.92
0.90
1.72
0.86
0.91
1.07
0.95
1.00
1.13
1.02
8.90
7.41
5.91

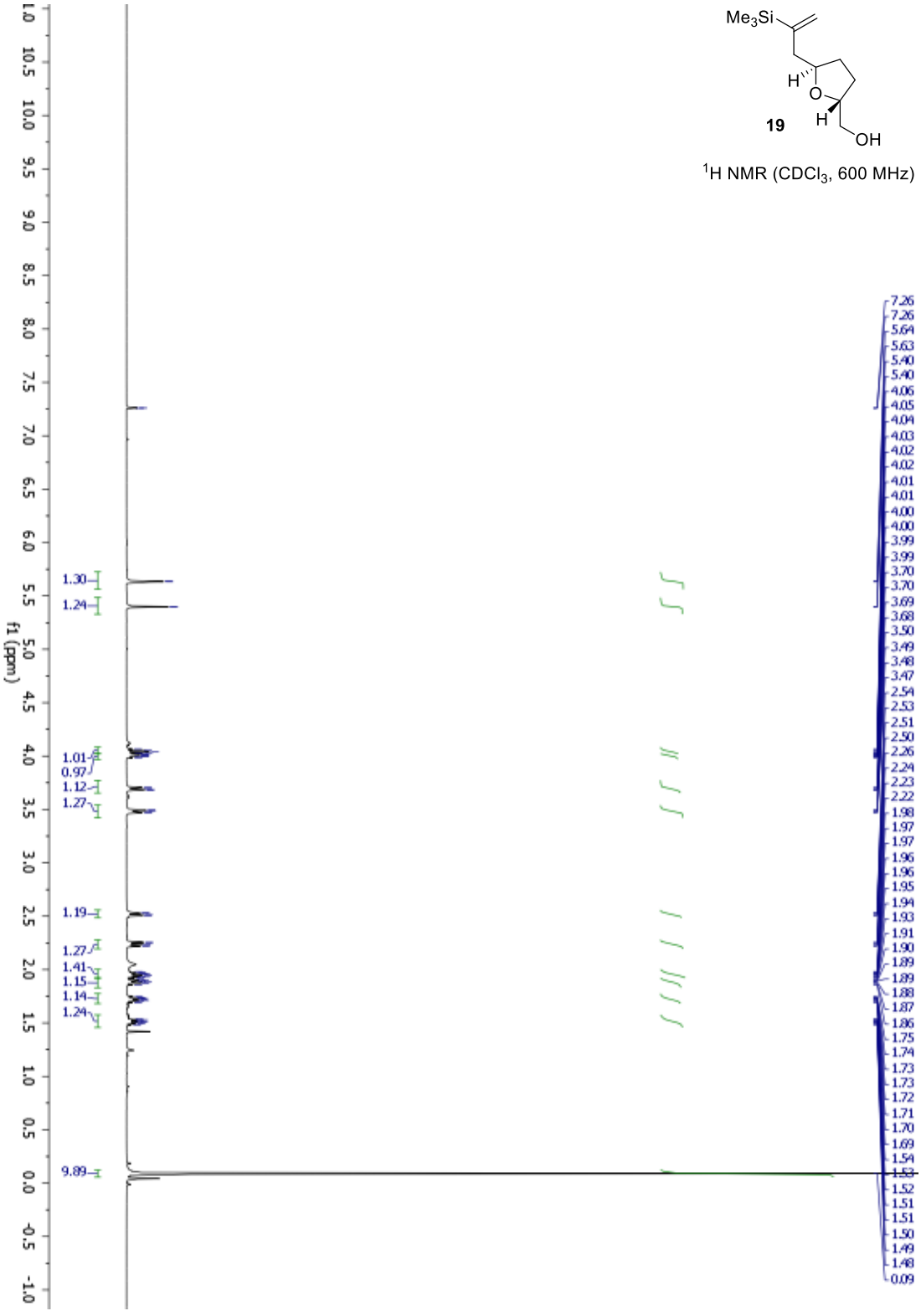

Me3Si
OTBS
16
13C NMR (CDCl3, 126 MHz)
f1 (ppm)
148.87
139.24
127.66
114.44
77.48
77.23
76.98
71.16
44.90
35.95
29.78
26.20
18.37
-1.01
-3.75
-4.17

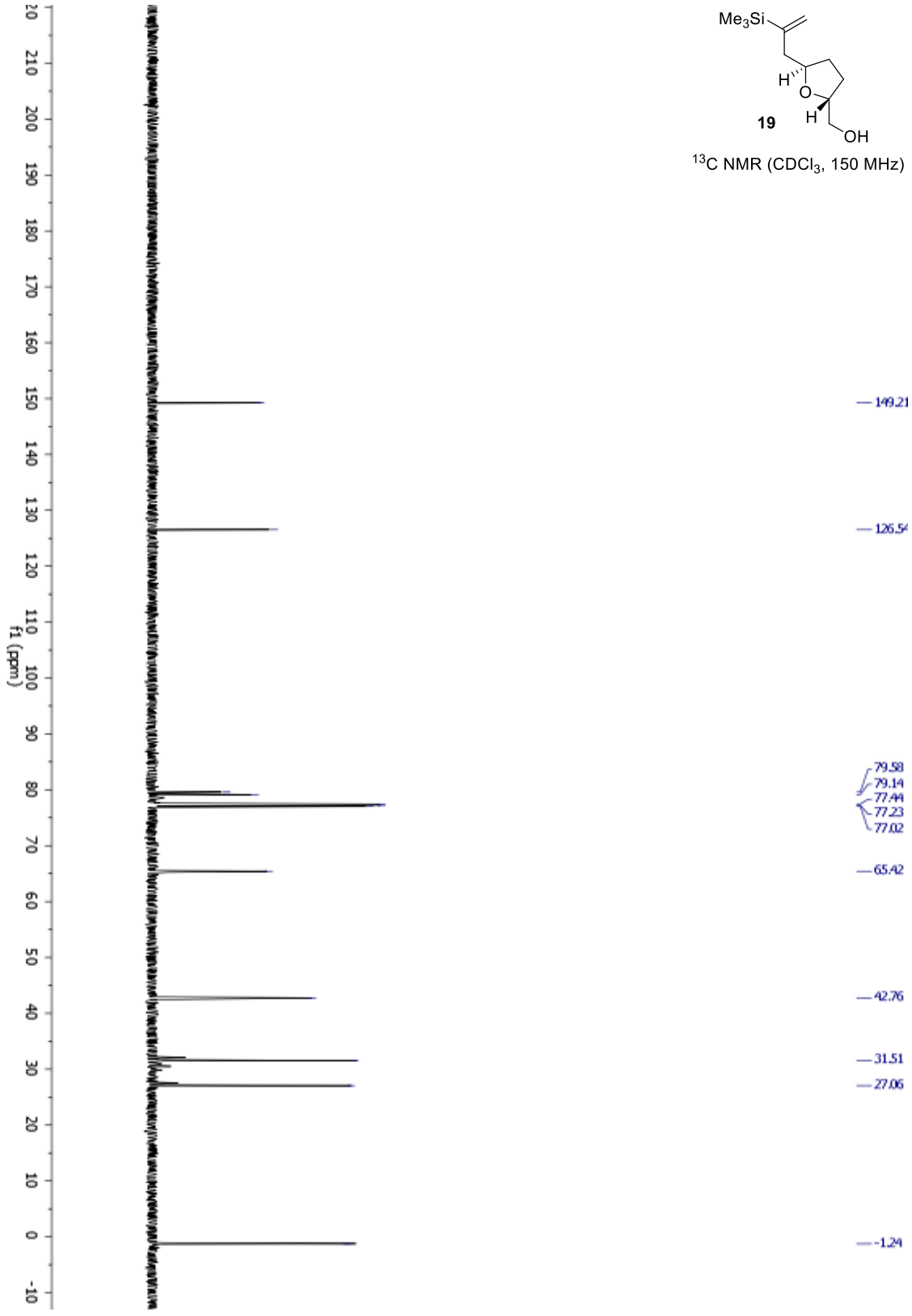

Me3Si
OH
OH
OTBS
17
1H NMR (CDCl3, 600 MHz)
f1 (ppm)

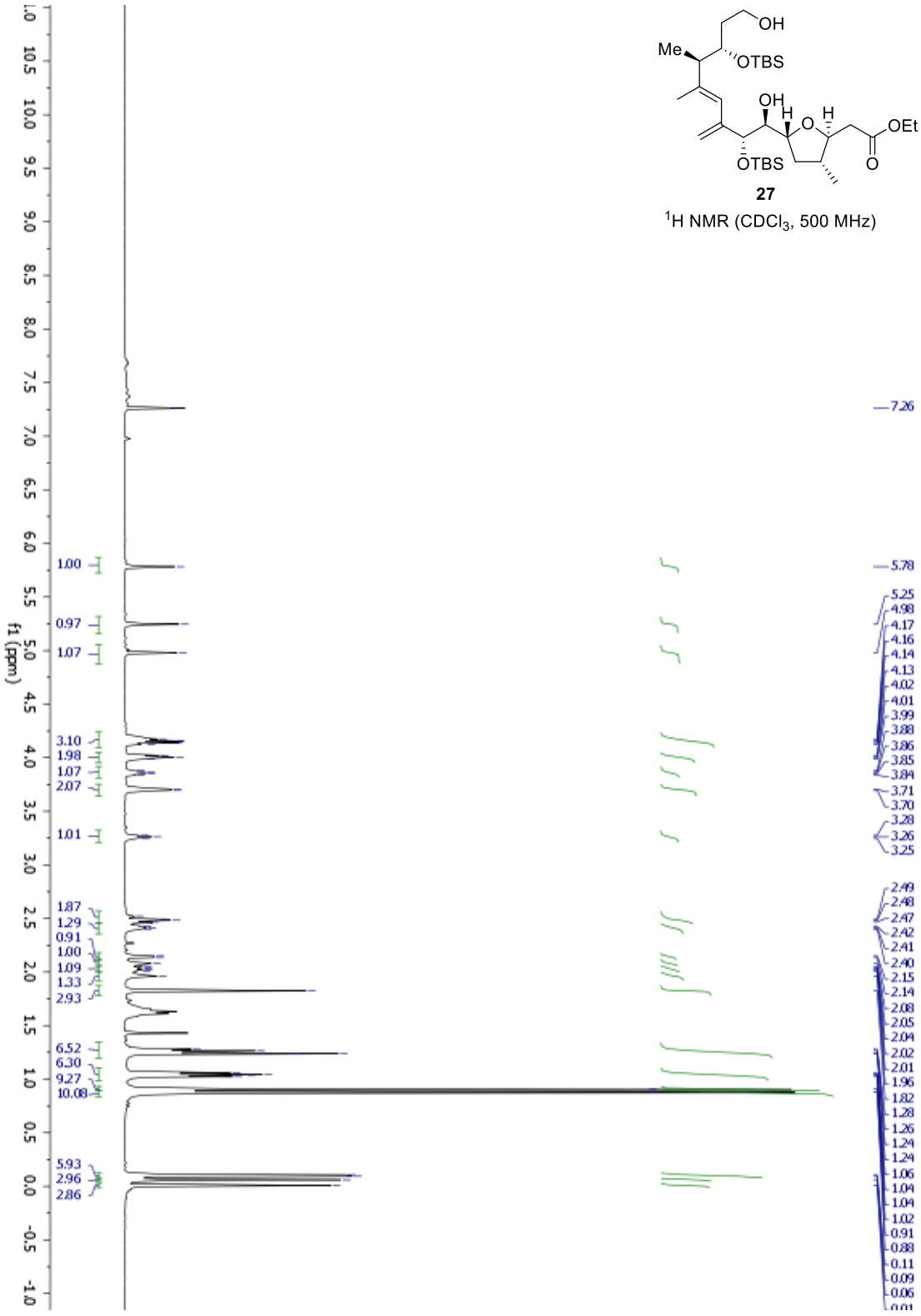

Me3Si
OH
OH
OTBS
17
13C NMR (CDCl3, 150 MHz)
f1 (ppm)
148.72
127.69
77.44
77.23
77.02
72.48
71.35
67.04
44.57
31.88
28.57
26.14
18.32
-1.01
-3.88
-4.19

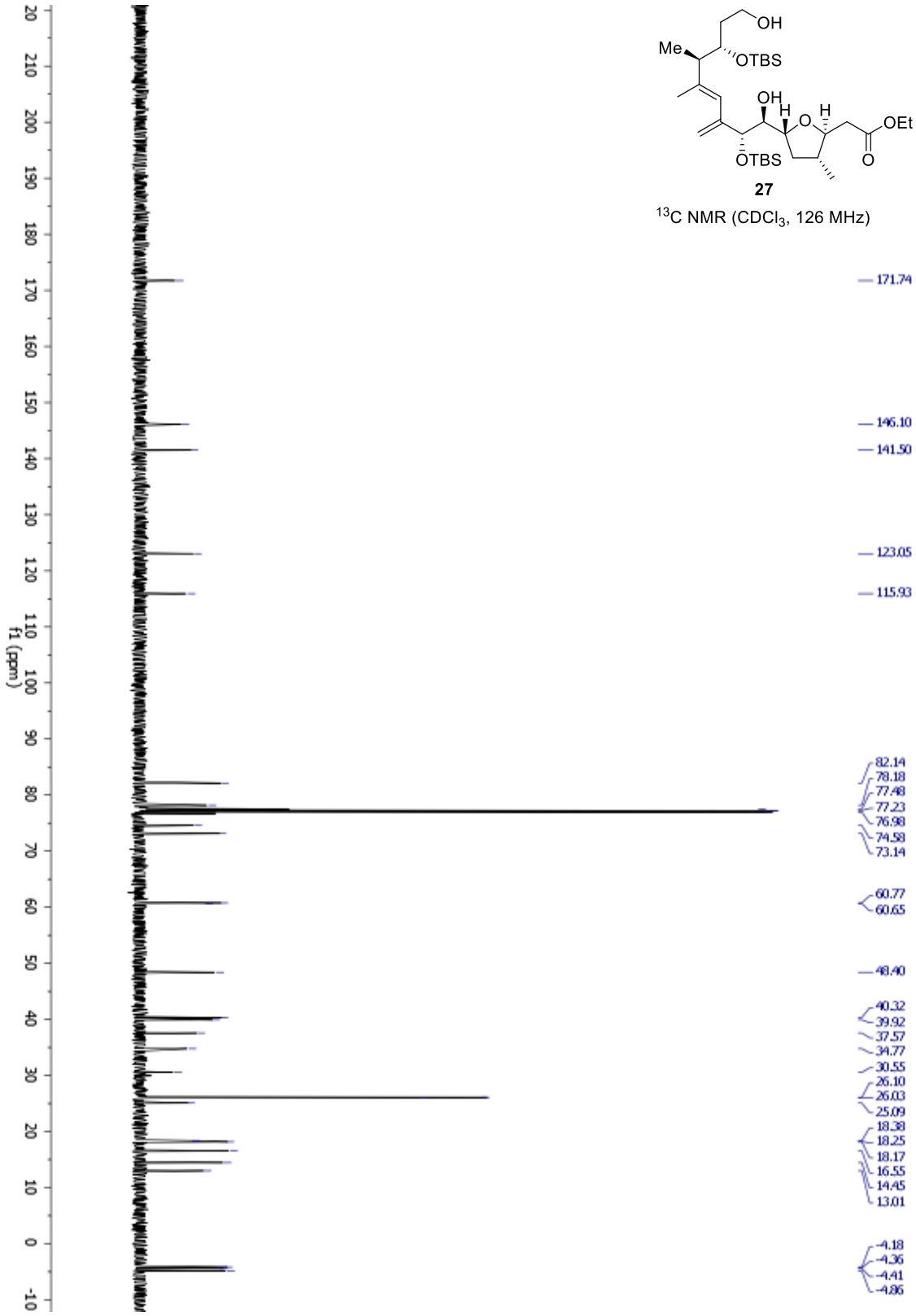

Me3Si
OTBS
O
18
1H NMR (CDCl3, 500 MHz)
f1 (ppm)
1.00
0.99
0.95
0.90
0.97
1.00
0.98
1.07
1.04
3.22
9.53
8.07
6.46


Me3Si
O
OTBS
18
13C NMR (CDCl3, 126 MHz)
f1 (ppm)
148.71
127.75
77.48
77.23
76.98
71.01
52.58
47.35
44.75
32.32
28.15
26.13
18.31
-1.03
-3.82
-4.25


Me3Si
H
O
H
OH
19
1H NMR (CDCl3, 600 MHz)
f1 (ppm)
1.30
1.24
1.01
0.97
1.12
1.27
1.19
1.27
1.41
1.15
1.14
1.24
9.89


Me3Si
H
O
H
OH
19
13C NMR (CDCl3, 150 MHz)
149.21
126.54
79.58
79.14
77.44
77.23
77.02
65.42
42.76
31.51
27.06
-1.24
f1 (ppm)


OH
Me
OTBS
OH
H
O
H
OEt
OTBS
O
27
^{1}H NMR ($CDCl_3$, 500 MHz)
f1 (ppm)
7.26
5.78
1.00
0.97
1.07
3.10
1.98
1.07
2.07
1.01
1.87
1.29
0.91
1.00
1.09
1.33
2.93
6.52
6.30
9.27
10.08
5.93
2.96
2.86


OH
Me
OTBS
OH
H
O
H
OEt
OTBS
O
27
13C NMR (CDCl3, 126 MHz)
171.74
146.10
141.50
123.05
115.93
82.14
78.18
77.48
77.23
76.98
74.58
73.14
60.77
60.65
48.40
40.32
39.92
37.57
34.77
30.55
26.10
26.03
25.09
18.38
18.25
18.17
16.55
14.45
13.01
-4.18
-4.36
-4.41
-4.86
f1 (ppm)