SITE-SELECTIVE AND STEREOSPECIFIC FUNCTIONALIZATION OF ORGANOBORONATE COMPOUNDS

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Abstract: This dissertation presents three projects focusing on catalytic, site-selective and stereospecific functionalization of organoboronate compounds.

First, we have developed a Cu-catalyzed regioselective coupling of 1,2-bis(boronic esters). This transformation provided an effecient route to a range of enantiomerically enriched secondary boronic esters. Mechanistic studies indicated that a chelated cyclic boron "ate" complex may promote transmetallation to Cu catalyst.

We have also developed a Cu-catalyzed sterespecific cross-coupling of alkylboronic esters. Boron "ate" complexes derived from alkylboronic pinacol esters and *tert*-butyllithium underwent stereospecific transmetallation to copper cyanide. The so-formed organocopper species engaged alkynyl bromides, allyl halides, propargylic halides, *β*-haloenones, hydroxylamine esters, and acyl chlorides in coupling reactions.

Finally, we have developed non-directed site-selective activation of bis(boronic esters), followed by Cu-catalyzed cross-coupling. A bulky activator was shown to selectively activate the less hindered boronic ester, enabling it to undergo stereospecific cross-coupling to a variety of electrophiles. This steric-based site-selectivity offered a simple and efficient route to prepare propionate derivatives as well as other valuable difunctional molecules.

The appendix describes an ongoing study towards the synthesis of a novel analog of amphidinolide H. In an effort to elucidate the relationship between biological activity and structure of amphidinolide H, we designed a simplified analog that is likely to resemble amphidinolide H in shape. Development of its synthesis is currently underway. With an anticipated streamlined route to the analog, we expect to carry out rapid interrogation of its biological activity in collaboration with other research groups.

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To my parents

LIST OF ABBREVIATIONS

Å Angstrom

Ac acetyl

Ar aryl

BBN borabicyclo[3.3.1]nonane

Bn benzyl

Boc *tert*-butyloxycarbonyl

BOX bis(oxazoline)

cat catechol

COD cyclooctadiene

COE cyclooctene

conv. conversion

CPhos 2-dicyclohexylphosphino-2',6'-bis(*N*,*N*-dimethylamino)biphenyl

CuTC copper(I)-thiophene-2-carboxylate

Cy cyclohexyl

DART direct analysis in real time

dba dibenzylideneacetone

DBU 1,8-diazabicyclo-(5.4.0)undec-7-ene

DCE 1,2-dichloroethane

DCM dichloromethane

DFT density functional theory

DIBAL diisobutylaluminium hydride

DMAP 4-dimethylaminopyridine

DMF dimethylformamide

DMI 1,3-dimethyl-2-imidazolidinone

DMP Dess-Martin periodinane

DMSO dimethyl sulfoxide

dppm bis(diphenylphosphino)methane

dppf 1,1'-bis(diphenylphosphino)ferrocene

dr diastereomeric ratio

EDG electron donating group

ee enantiomeric excess

equiv. equivalent

er enantiomeric ratio

es enantiospecificity

Et ethyl

Et_2O diethyl ether

EtOAc ethyl acetate

EWG electron withdrawing group

GC gas chromatography

h hour(s)

HFIP 1,1,1,3,3,3-hexafluoro-isopropanol

HPLC high-performance liquid chromatography

HRMS high-resolution mass spectrometry

***i*-** iso

IR infrared spectroscopy

LDA lithium diisopropylamide

LiHMDS lithium bis(trimethylsilyl)amide

LiTMP lithium 2,2,6,6-tetramethylpiperidide

M molar concentration (1 mol/L)

***m*-** meta-

***m*CPBA** *meta*-chloroperoxybenzoic acid

MeCN acetonitrile

mida *N*-methyliminodiacetic acid

min minute(s)

mmol millimole(s)

mol mole(s)

MS molecular sieves

NA not available

nbd norbornadiene

NBS *N*-bromosuccinimide

***n*-BuLi** *n*-butyllithium

NCS *N*-chlorosuccinimide

ND not determined

neo neopentyl glycol

NHC *N*-hetereocyclic carbene

NMI neomenthylindenyl

NMR nuclear magnetic resonance

***o*-** ortho-

OAc acetoxy group

OMs methanesulfonate

OTf trifluoromethanesulfonate

OTs toluenesulfonate

***p*-** para-

PCC pyridinium chlorochromate

Ph phenyl

pin pinacol

PMB *para*-methoxy benzyl

PMP *para*-methoxy phenyl

PPTS pyridinium *p*-toluenesulfonate

Pr propyl

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

Rf retention factor

rt room temperature

RuPhos 2-dicyclohexylphosphino-2',6'-diisopropoxybiphenyl

Selectfluor 1-(chloromethyl)-4-fluoro-1,4-diazabicyclo-[2.2.2]octane-1,4-diium ditetrafluoroborate

SFC supercritical fluid chromatography

SPhos 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl

TASF tris(dimethylamino)sulfonium difluorotrimethylsilicate

TBAF tetra-*n*-butylammonium fluoride

TBDPS *tert*-butyldiphenylsilyl

TBS *tert*-butyldimethylsilyl

***t*-BuLi** *tert*-butyllithium

TEMPO 2,2,6,6-tetramethyl-1-piperidinyloxy

TFA trifluoroacetic acid

THF tetrahydrofuran

TIPS triisopropylsilyl

TLC thin-layer chromatography

TMEDA tetramethylethylenediamine

TMS trimethylsilyl

Tol tolyl

UV ultraviolet

XantPhos 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

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Chapter 1. Site-Selective Copper-Catalyzed Coupling of Alkyl Vicinal Bis(boronic Esters) to an Array of Electrophiles

1.1 Introduction

Catalytic enantioselective difunctionalization of unactivated α-olefins is an important problem in contemporary synthesis.[1] So far, elegant examples of catalytic enantioselective dihydroxylation (**1.2**),[2] cyclopropanation (**1.3**),[3] carboalumination (**1.4**),[4] epoxidation (**1.5**),[5] aziridination (**1.6**),[6] methylborylation (**1.7**),[7] diacetylation (**1.8**),[8] and aminoborylation (**1.9**)[9] have been demonstrated as effective functionalization strategies (Scheme 1.1a). Although these established enantioselective methods could deliver functionalized products in high efficiency, significant methodological gaps limit our ability to extend the range of enantiomerically enriched reaction products available from non-activated α-olefins **1.1**.

This chapter[10] will describe a strategy that addresses the following challenge: how to conduct catalytic enantioselective alkene diboration and then subject the vicinal bis(boronic ester)

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[1] For selected reviews on alkene difunctionalization, see: (a) Zhang, J. S.; Liu, L.; Chen, T.; Han, L. B. *Chem. Asian J.* **2018**, *13*, 2277–2291. (b) Derosa, J.; Apolinar, O.; Kang, T.; Tran, V. T.; Engle, K. M. *Chem. Sci.* **2020**, *11*, 4287–4296.

[2] Becker, H.; Sharpless, K.B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 448–451.

[3] Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270–10271.

[4] Negishi, E.; Tan, Z.; Liang, B.; Novak, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5782–5787.

[5] (a) Colladon, M.; Scarso, A.; Sgarbossa, P.; Michelin, R. A.; Strukul, G. *J. Am. Chem. Soc.* **2006**, *128*, 14006–14007. (b) Sawada, Y.; Matsumoto, K.; Katsuki, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 4559–4561.

[6] Subbarayan, V.; Ruppel, J. V.; Zhu, S.; Perman, J. A.; Zhang, X. P. *Chem. Commun.* **2009**, *28*, 4266–4268.

[7] Chen, B.; Cao, P.; Liao, Y.; Wang, M.; Liao, J. *Org. Lett.* **2018**, *20*, 1346–1349.

[8] Tian, B.; Chen, P.; Leng, X.; Liu, G. *Nat. Catal.* **2021**, *4*, 172–179.

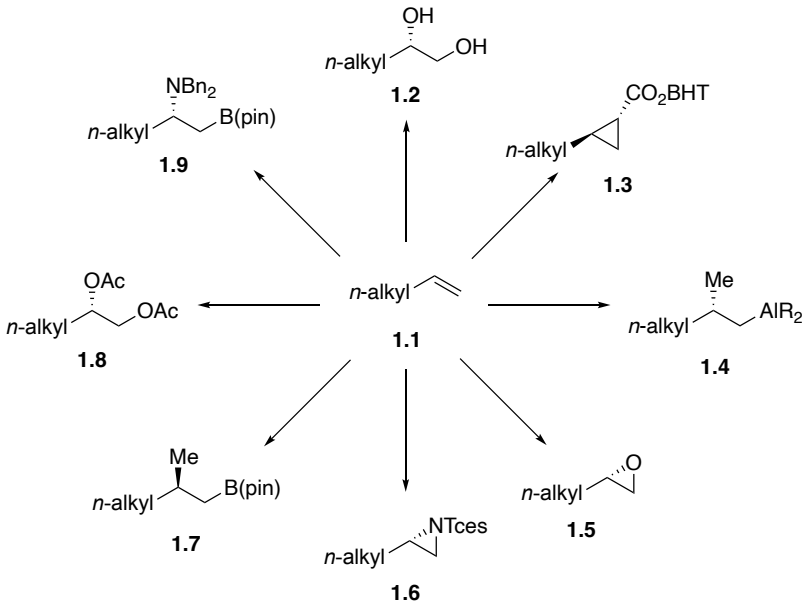
[9] Kato, K.; Hirano, K.; Miura, M. *Chem. Eur. J.* **2018**, *24,* 5775 –5778.

[10] Xu, N.; Kong, Z.; Wang, J. Z.; Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 17815–17823.

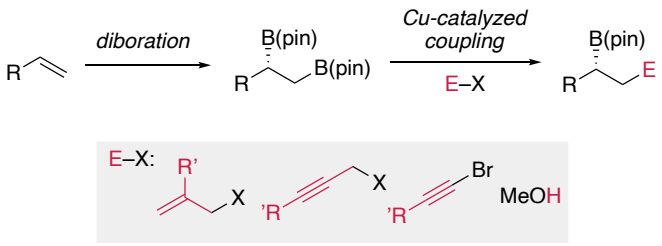
intermediate to subsequent Cu-catalyzed cross-coupling (Scheme 1.1b). This method operates under practical conditions with commercially available and inexpensive reagents, and it enables coupling between vicinal bis(boronic esters) and allyl, alkynyl, and propargyl electrophiles as well as a proton. Because the reactive substrates are vicinal bis(boronic esters), the cross-coupling also serves as an expedient new general procedure for the synthesis of enantiomerically enriched secondary boronic esters from α-olefins. Mechanistic experiments suggested that chelated five-membered cyclic "ate" complex may play a role in transmetallation.

Scheme 1.1. Catalytic Enantioselective Difunctinalization of Unactivated Terminal Alkenes

(a) Representative examples of catalytic enantioselective difunctionalization of unactivated α-olefins



(b) This work



1.2 Background

1.2.1 Synthesis of Enantiomerically Enriched 1,2-Bis(boronic Esters) by Alkene Diboration

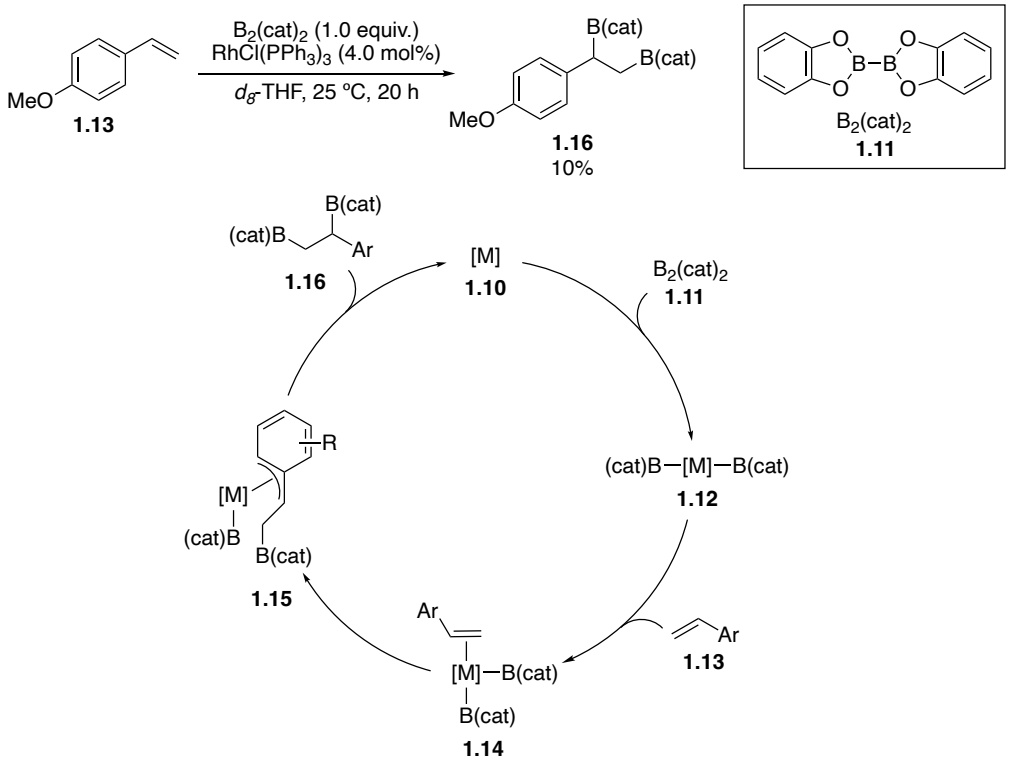
1.2.1.1 History of Catalytic Alkene Diboration

The earliest example of transition metal-catalyzed diboration of an alkene was reported by Baker, Marder and Westcott[11a] during their investigation of oxidation of Rh(I) complexes by bis(catecholato)diboron (Scheme 1.2).[12] Rh(III) complex **1.12** was generated through oxidative addition of $RhCl(PPh_3)_3$ (**1.10**) to $B_2(cat)_2$ (**1.11**). Then, alkene **1.13** coordinated to the complex and formed **1.14**, which then underwent migratory insertion to furnish intermediate **1.15**. Finally, reductive elimination of **1.15** delivered the diborated product **1.16** in 10% yield. Although the yield was low due to β-hydride elimination of intermediate **1.15**, the demonstration of reactivity inspired further studies of Rh(I) catalyzed alkene diboration.[11b,c]

[11] For selected reports on Rh-catalyzed alkene diboration, see: (a) Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1336–1338. (b) Dai, C.; Robins, E. G.; Scott, A. J.; Clegg, W.; Yufit, D. S.; Howard, J. A. K.; Marder, T. B. *Chem. Commun.* **1998**, 1983–1984. (c) Nguyen, P.; Coapes, R. B.; Woodward, A. D.; Taylor, N. J.; Burke, J. M.; Howard, J. A. K.; Marder, T. B. *J. Organomet. Chem.* **2002**, 652, 77–85.

[12] Nguyen, P.; Lesley, G.; Taylor, N. J.; Marder, T. B.; Pickett, N. L.; Clegg, W.; Elsegood, M. R. J.; Norman, N. C. *Inorg. Chem.* **1994**, *33*, 4623–4624.

Scheme 1.2. The First Example of Rh(I)-Catalyzed Terminal Alkene Diboration by Baker, Marder and Westcott



In 1995, Pt(0) complexes were shown to be capable of oxidative addition to not only $B_2(cat)_2$, but also bis(pinacolato)diboron, $B_2(pin)_2$.[13] In regards to reagent selection, $B_2(pin)_2$ is stable in the open atmosphere and can be purchased on kilogram scale (US$290/kg)[14] whereas $B_2(cat)_2$ is moisture sensitive and can only be purchased on gram scale (US$8/g).[15] Pt-catalyzed alkene diboration with $B_2(pin)_2$ was first demonstrated by Miyaura and coworkers in 1997 (Scheme

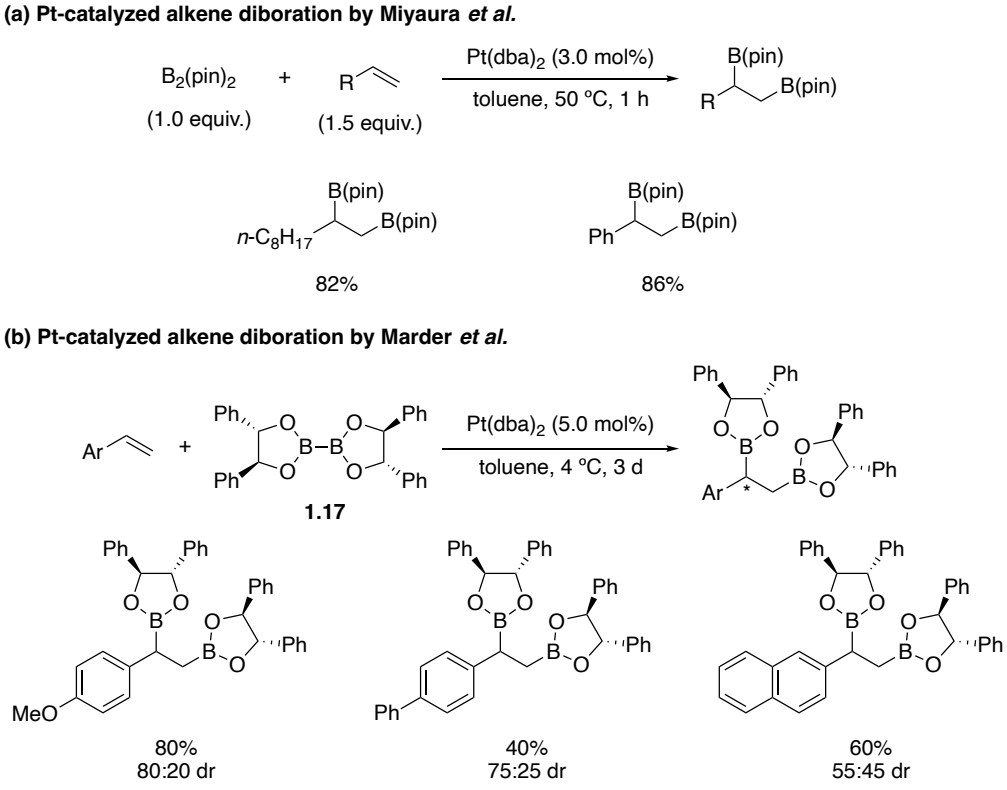
[13] For selected reports on oxidative addition of Pt(0) complexes to bis(pinacolato)diboron, see: (a) Iverson, C. N.; Smith, M. R. *J. Am. Chem. Soc.* **1995**, *117*, 4403–4404. (b) Lesley, G.; Nguyen, P.; Taylor, N. J.; Marder, T. B.; Scott, A. J.; Clegg, W.; Norman, N. C. *Organometallics*, **1996**, *15*, 5137–5154. (c) Clegg, W.; Lawlor, F. J.; Lesley, G.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Quayle, M. J.; Rice, C. R.; Scott, A. J.; Souza, F. E. S. *J. Organomet. Chem.* **1998**, *550*, 183–192.

[14] This price is from Oakwood Products, Inc. (www.oakwoodchemical.com) for orders of 10 kg. For smaller quantities, the price is $340 per kg.

[15] This price is from Oakwood Products, Inc. (www.oakwoodchemical.com) for orders of 25 g. For smaller quantities, the price is $20 per g.

1.3a).[16a] Both aliphatic and aromatic alkenes underwent Pt-catalyzed diboration smoothly, furnishing 1,2-bis(boronic pinacol esters) in up to 86% yield. In 1998, Marder and co-workers demonstrated moderate asymmetric induction with chiral diboron reagent **1.17** (Scheme 1.3b).[16b] Other than Rh(I) and Pt(0), Ag(I)–NHC complexes,[17] Pd(II)–NHC complexes[18] and Au(0) nanoparticles[19] were also reported to catalyze diboration of terminal alkenes.

Scheme 1.3. Early Examples of Pt-Catalyzed Diboration of Terminal Alkenes



[16] For selected reports on Pt-catalyzed alkene diboration, see: (a) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1997**, *7*, 689–690. (b) Marder, T. B.; Norman, N. C.; Rice, C. R. *Tetrahedron Lett.*, **1998**, *39*, 155–158. (c) Lillo, V.; Mata, J.; Ramirez, J.; Peris, E.; Fernandez, E. *Organometallics* **2006**, *25*, 5829–5831.

[17] Ramírez, J.; Corberán, R.; Sanaú, M.; Peris, E.; Fernandez, E. *Chem. Commun.* **2005**, *24*, 3056–3058.

[18] Lillo, V.; Mas-Marzá, E.; Segarra, A. M.; Carbó, J. J.; Bo, C.; Peris, E.; Fernandez, E. *Chem. Commun.* **2007**, *32*, 3380–3382.

[19] Ramírez, J.; Sanaú, M.; Fernández, E. *Angew. Chem., Int. Ed.* **2008**, *47*, 5194–5197.

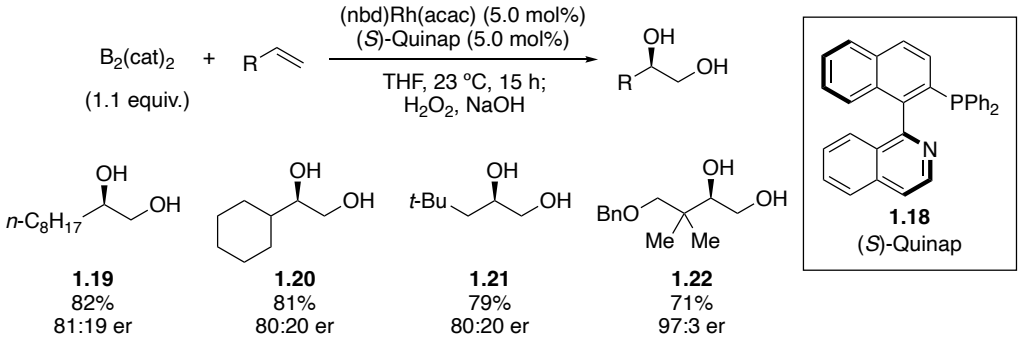
In 2003, Morken and co-workers demonstrated the first enantioselective alkene diboration (Scheme 1.4a).[20] It was found that this method is applicable to a range of aliphatic alkenes, including mono-substituted, 1,2-disubstituted and trisubstituted alkenes. The diborated products were oxidized to afford enantiomerically enriched diols. Aliphatic terminal alkenes (**1.19**–**1.21**) reacted with mediocre enantioselectivity (80:20 er), whereas those bearing sterically bulky substituents (**1.22**) reacted with enhanced enantioselectivity (97:3 er). In 2013, Nishiyama and co-workers reported a RhPhebox (**1.23**)-catalyzed diboration of terminal alkenes (Scheme 1.4b).[21] Remarkably, instead of $B_2(cat)_2$, the more affordable and bench stable $B_2(pin)_2$ was used as boron source. This method effectively functionalized sterically unencumbered terminal alkenes, affording 1,2-diols in up to 94% yield and 97:3 er.

[20] (a) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702–8703. (b) Miller, S. P.; Morgan, J. B.; Nepveux; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133. (c) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538–9544.

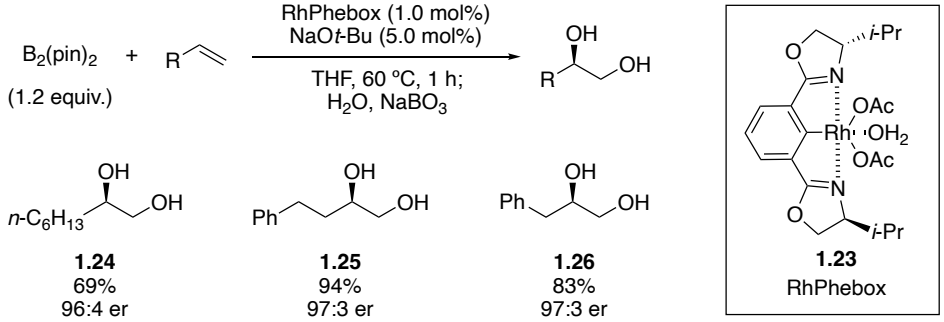
[21] Toribatake, K.; Nishiyama, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 11011–11015.

Scheme 1.4. Rh-Catalyzed Enantioselective Diboration of Terminal Alkenes

(a) Enantioselective alkene diboration by Morken *et al.*



(b) Enantioselective alkene diboration by Nishiyama *et al.*

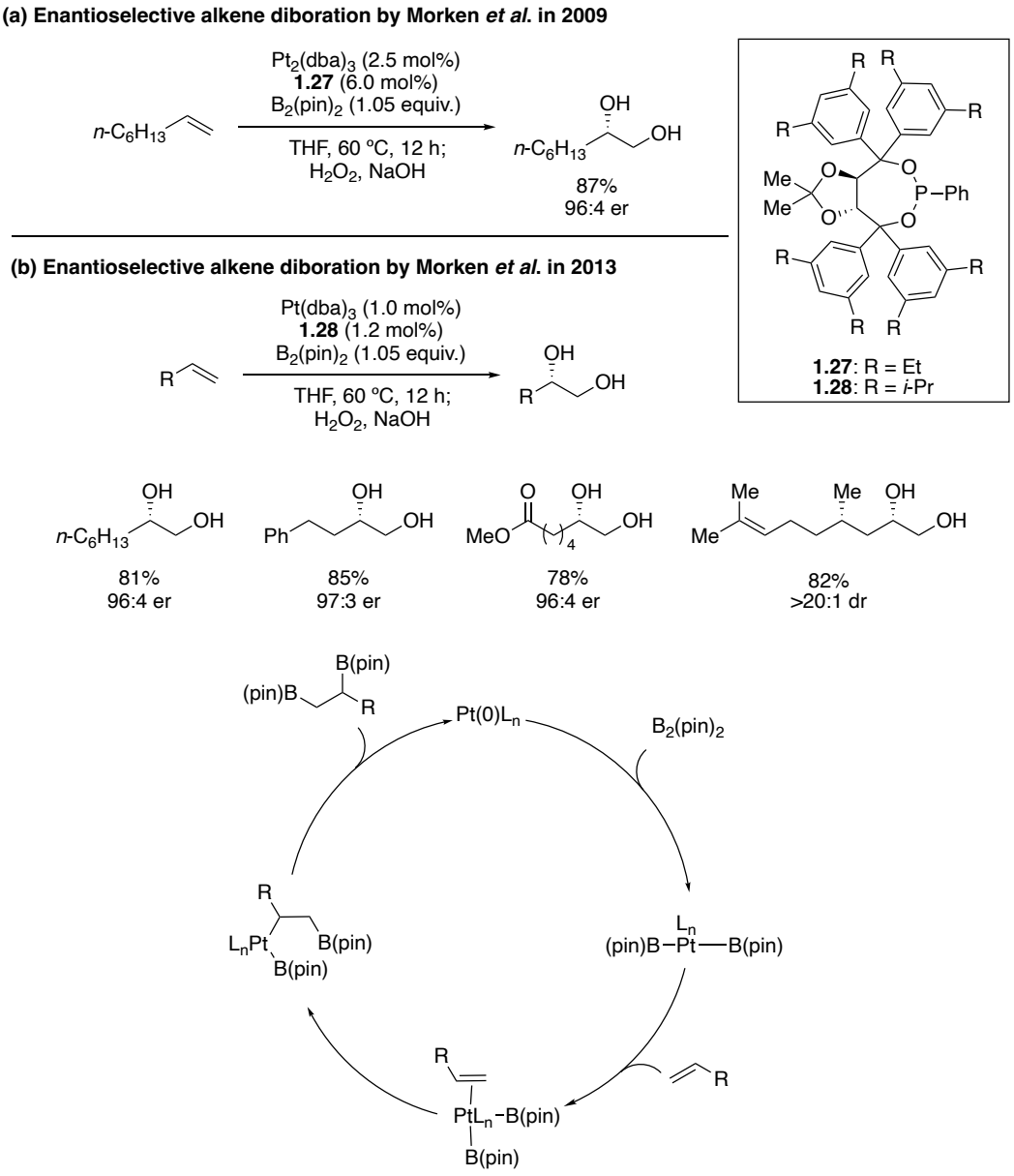


After their demonstration of Rh-catalyzed enantioselective diboration, the Morken group turned their attention to Pt catalysis. In 2009, they reported that $Pt_2(dba)_3$ complexed with a phosphonite ligand facilitated diboration of aliphatic terminal alkenes in high yields and excellent enantioselectivity (Scheme 1.5a).[22] In 2013, they demonstrated another diboration method with $Pt(dba)_3$ and phosphonite ligand. This report showed significant improvement in catalyst efficiency, with 80% less catalyst used compared to the previous method. The authors also demonstrated that this method may be used to incorporate carbonyl, nitrile and alkene functional groups. The results of detailed mechanism studies were provided in this report.[23]

[22] Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210–13211.

[23] Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222–11231.

Scheme 1.5. Pt-Catalyzed Enantioselective Diboration of Terminal Alkenes



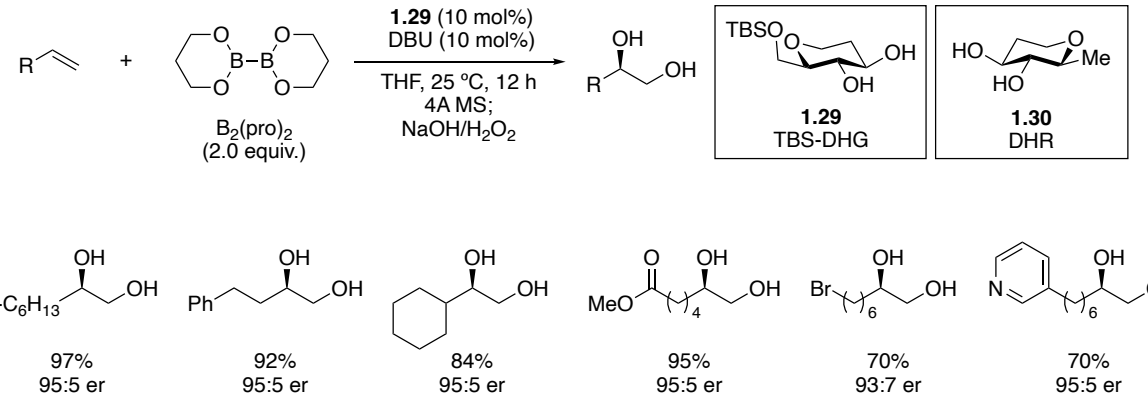
1.2.1.2 Carbohydrate-Catalyzed Terminal Alkene Diboration

In 2016, the Morken group reported a carbohydrate-catalyzed enantioselective diboration of alkenes.[24] Pseudoenantiomeric catalysts **1.29** and **1.30** can be easily derived from inexpensive and widely available D-glucal and L-rhamnal. Following oxidation, 1,2-diols were obtained in up to

[24] Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508–2511.

97% yield and 95:5 er. In 2018, the substrate scope was explored further and results of detailed mechanism studies were reported.[25] Functional groups that are incompatible with transition metal catalysis such as alkyl bromides and heterocycles were well-tolerated by carbohydrate catalysis.

Scheme 1.6. Carbohydrate-Catalyzed Enantioselective Diboration of Terminal Alkenes



1.2.2 Enantioselective Synthesis of 1,2-Bis(boronic Esters) by Other Pathways

As a synthetically useful building block, the 1,2-bis(boronic ester) has garnered interest from organic chemists over the years. Other than the well-studied alkene diboration, many other synthetic pathways towards enantiomerically enriched 1,2-bis(boronic esters) have been demonstrated.

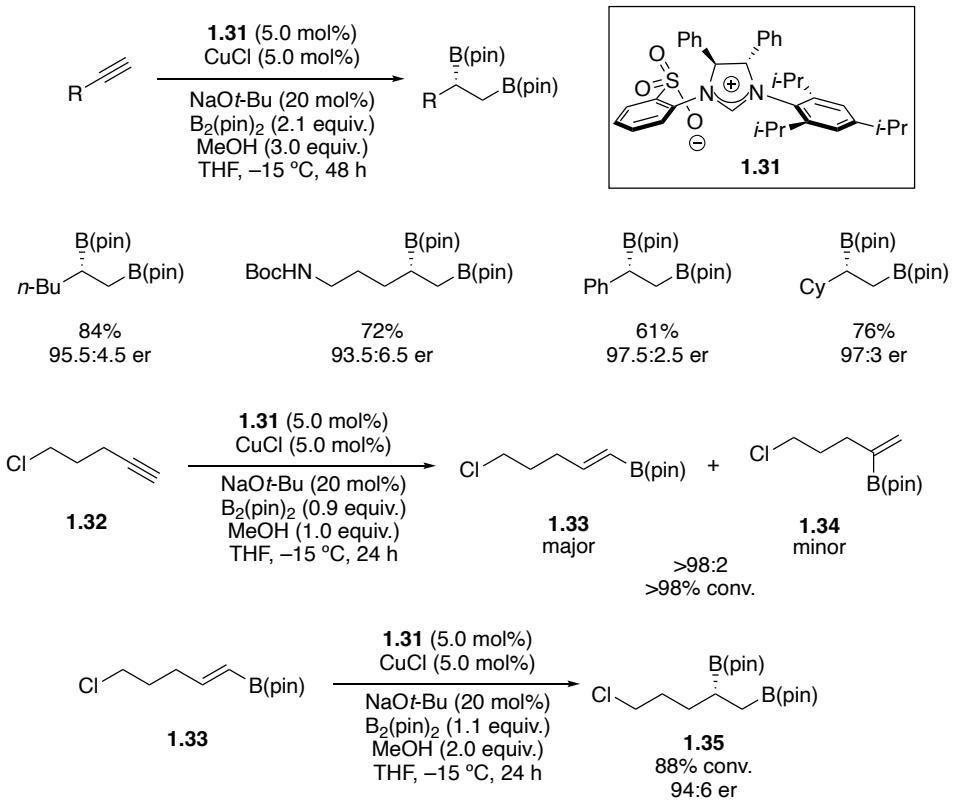
In 2009, the Hoveyda group reported one of the first enantioselective methods to furnish 1,2-bis(boronic pinacol esters) (Scheme 1.7).[26] This report involved a tandem site-selective NHC–Cu-catalyzed double protoboration of a range of unactivated terminal alkynes. Functional groups such as Boc-protected amine and alkyl chloride were well-tolerated. When alkyne **1.32** was

[25] Yan, L.; Meng, Y.; Haeffner, F.; Leon, R. M.; Crockett, M. P.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 3663–3673.

[26] Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235.

subjected to reaction conditions with 0.9 equivalent of $B_2(pin)_2$, alkenylboronic pinacol ester **1.33** was predominantly generated. Subjection of **1.33** to the same conditions with 1.1 equivalents of $B_2(pin)_2$ furnished 1,2-bis(boronic ester) **1.35** with excellent site-selectivity and 94:6 er. This result suggested that two protoborations occurred in tandem.

Scheme 1.7. Cu-Catalyzed Tandem Protoboration of Terminal Alkynes

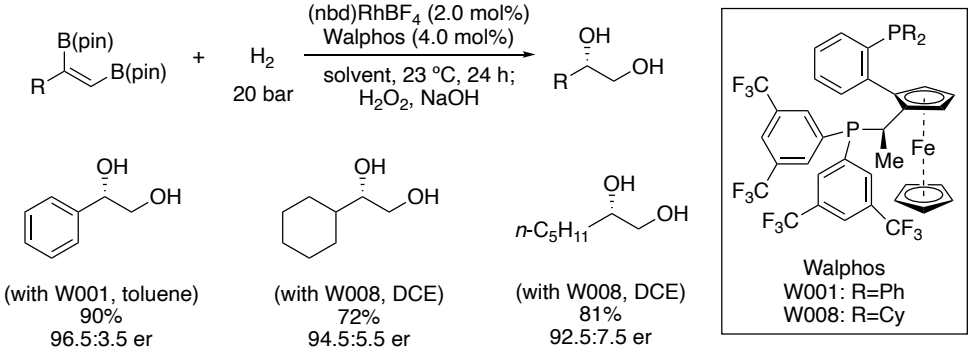


In 2004, the Morken group demonstrated Rh-catalyzed enantioselective hydrogenation of alkenyl bis(boronic esters) (Scheme 1.8). The authors developed reaction conditions for both aromatic and aliphatic alkenes.[27] This example provided a precedent for synthesis of

[27] Morgan, J. B.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 15338–15339.

1,2-bis(boronic esters) through enantioselective hydrogenation, and inspired future studies of this strategy.[28]

Scheme 1.8. Enantioselective Hydrogenation of Alkenyl Bis(boronic Esters)



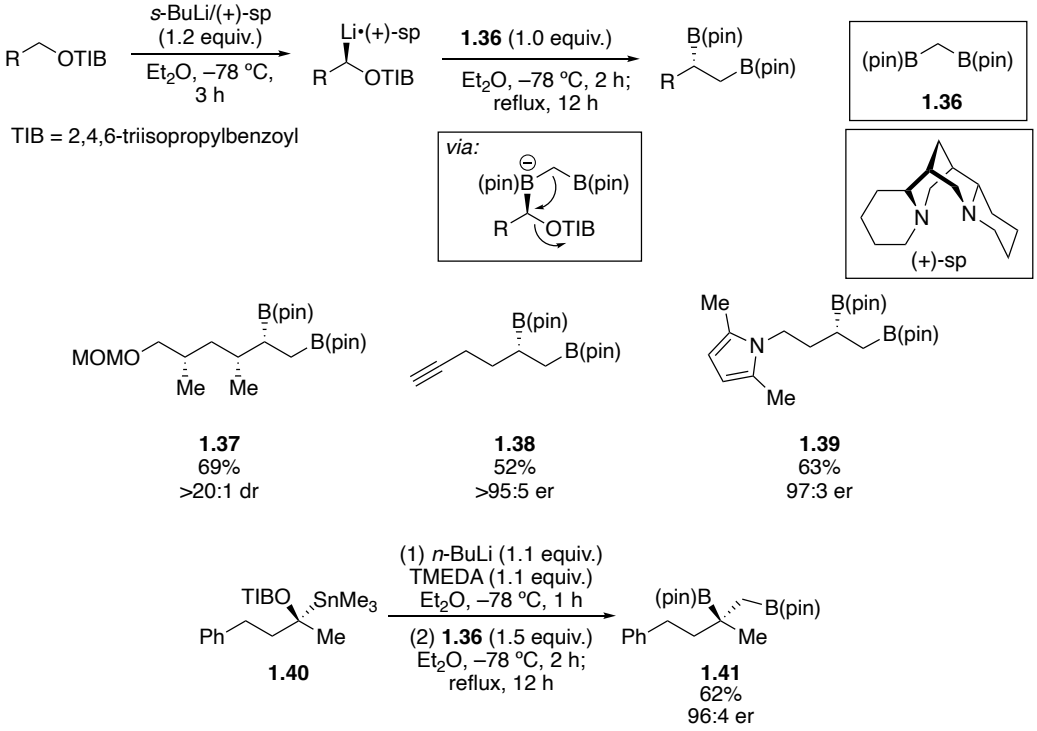
In 2017, Aggarwal and co-workers reported a route to enantiomerically enriched 1,2-bis(boronic esters) through homologation of diborylmethane **1.36** (Scheme 1.9).[29] Substrate **1.36** was treated with a sparteine-ligated enantiomerically enriched organolithium, generating a boron "ate" complex. This complex underwent facile 1,2-metallate shift to furnish a 1,2-bis(boronic ester). Notably, this method tolerated functional groups that typically hinder transition metal-catalyzed enantioselective alkene diboration, for example, sterically bulky R groups (**1.37**) and terminal alkynes (**1.38**).

When enantiomerically enriched organotin **1.40** was subjected to lithiation and homologation conditions, a sterically congested 1,2-bis(boronic ester) **1.41** was generated in 62% yield and 96:4 er. It is noteworthy that 1,2-bis(boronic esters) containing a enantiomerically enriched tertiary boronic ester (**1.41**) are challenging to synthesize by alkene diboration.

[28] For a report on Ir-catalyzed enantioselective hydrogenation of alkenyl bis(boronic esters), see: Paptchikhine, A.; Cheruku, P.; Engman, M.; Andersson, P. G. *Chem. Commun.* **2009**, *40*, 5996–5998.

[29] Blair, D. J.; Tanini, D.; Bateman, J. M.; Scott, H. K.; Myers, E. L.; Aggarwal, V. K. *Chem. Sci.* **2017**, *8*, 2898–2903.

Scheme 1.9. Stereospecific Homologation of Diborylmethane



1.2.3 Site-Selective Functionalization of 1,2-Bis(boronic Esters)[30]

1.2.3.1 Transition Metal-Catalyzed Suzuki-Miyaura Cross-Coupling with C(sp^2) Electrophiles

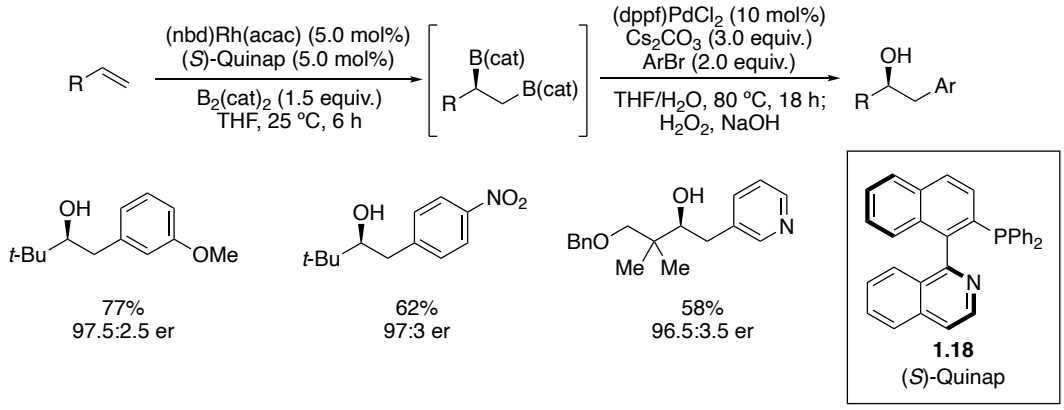
Among many examples of site-selective functionalization of 1,2-bis(boronic esters), Pd-catalyzed Suzuki-Miyaura cross-coupling is the most well-studied. In most cases, the less hindered primary boronic ester preferentially transmetallates to Pd(II) species. Many cases were reported where the transition metal-catalyzed cross-coupling proceeds in tandem with diboration. These examples demonstrated the versatility and practicality of diboration-functionalization sequence as an enantioselective alkene difunctionalization strategy.

[30] For a selected review on site-selective coupling of bis(boronic esters), see: Viso, A.; Fernández de la Pradilla, R.; Tortosa, M. *ACS Catal.* **2022**, *12*, 10603–10620.

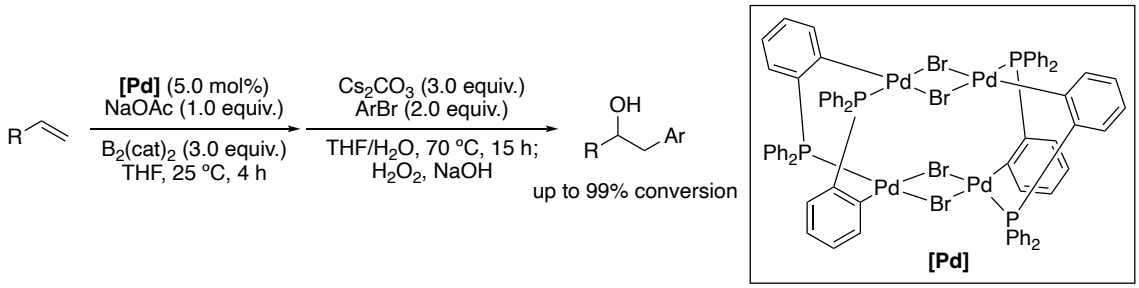
The first example of site-selective functionalization of 1,2-bis(boronic esters) was reported by Morken and co-workers in 2004 (Scheme 1.10a).[20b, 31] In this example, Suzuki-Miyaura cross-coupling proceeded after enantioselective diboration with $B_2(cat)_2$. The Pd-catalyzed coupling proceeded smoothly with both electron-rich and electron-deficient aryl electrophiles. Pyridine was also well-tolerated. In 2008, Fernandez and co-workers reported another tandem diboration/coupling sequence with $B_2(cat)_2$ as boron source (Scheme 1.10b).[32] In this sequence, a Pd complex catalyzed both steps.

Scheme 1.10. Tandem Diboration/Site-Selective Coupling with $B_2(cat)_2$ as Boron Source

(a) Site-selective coupling of 1,2-bis(boronic esters) by Morken *et al.*



(b) Site-selective coupling of 1,2-bis(boronic esters) by Fernandez *et al.*



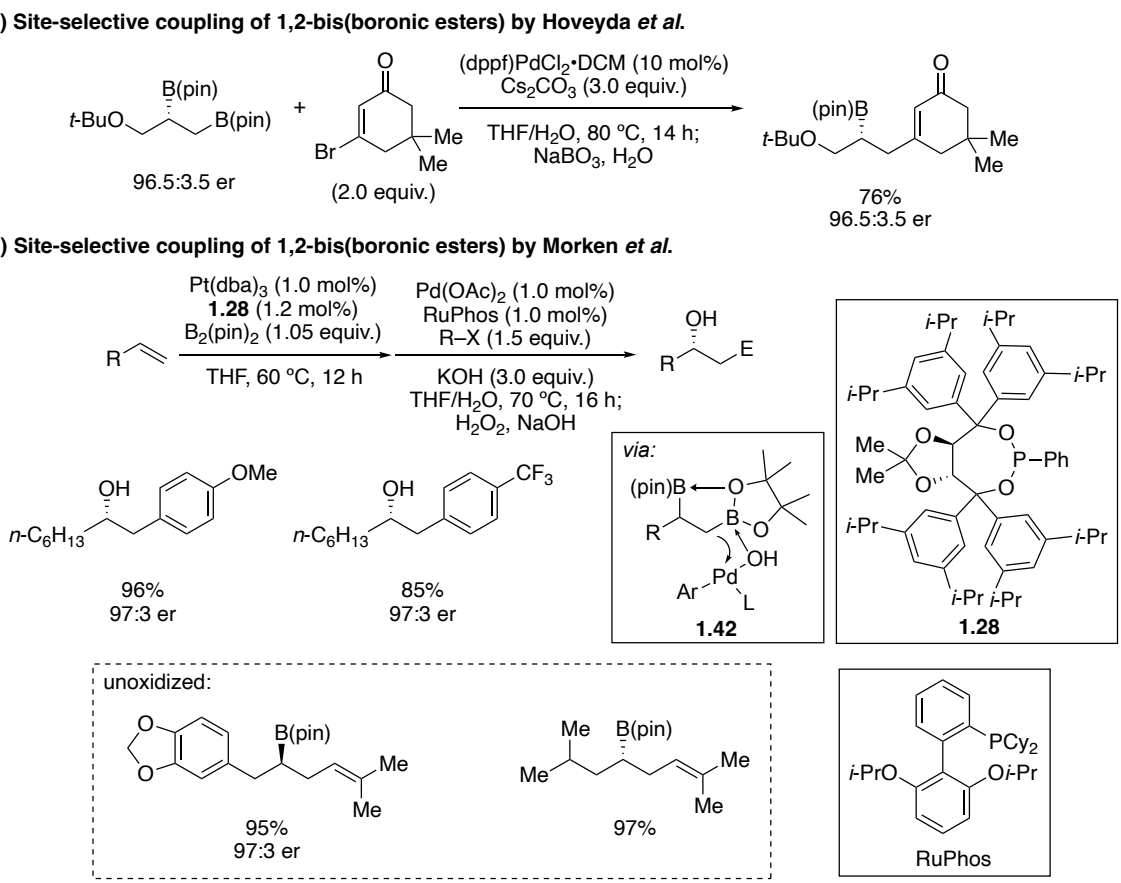
[31] For a report with similar protocol, see: Huang, M.; Hu, J.; Shi, S.; Friedrich, A.; Krebs, J.; Westcott, S. A.; Radius, U.; Marder, T. B. *Chem. Eur. J.* **2022**, *28*, e202200480.

[32] Penno, D.; Lillo, V.; Koshevoy, I. O.; Sanaú, M.; Ubeda, M. A.; Lahuerta, P.; Fernández, E. *Chem. Eur. J.* **2008**, *14*, 10648–10655.

Compared to catacol boronic esters and neopentylglycol boronic esters, boronic pinacol esters are bench and column stable, giving them higher synthetic value. In 2009, Hoveyda and co-workers reported the first example of Pd-catalyzed site-selective cross-coupling of a 1,2-bis(boronic pinacol ester) (Scheme 1.11a).[26] The regioselective coupling product was obtained in 76% yield and 96.5:3.5 er. In 2014, the Morken group reported tandem enantioselective diboration/site-selective cross-coupling sequence (Scheme 1.11b).[33a] It was proposed that the secondary boron atom may act as a Lewis acid to pinacol oxygen on the primary boronic ester (**1.42**), thereby enhancing the Lewis acidity of the primary boron atom and facilitating transmetallation. This Pd-catalyzed site-selective cross-coupling incorporated a range of aryl bromides and alkenyl chlorides as electrophiles. In this report, enantiomerically enriched, column-stable secondary alkylboronic pinacol esters were generated in up to 97% yield.

[33] For selected reports on enantioselective diboration/site-selective cross-coupling sequence, see: (a) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386–390. (b) Green, J. C.; Joannou, M. V.; Murray, S. A.; Zanghi, J. M.; Meek, S. J. *ACS Catal.* **2017**, *7*, 4441−4445. (c) Sun, S.-Z.; Talavera, L.; Spie., P.; Day, C. S.; Martin, R. *Angew. Chem., Int. Ed.* **2021**, *60*, 11740−11744.

Scheme 1.11. Site-Selective Coupling of 1,2-Bis(boronic Pinacol Esters)

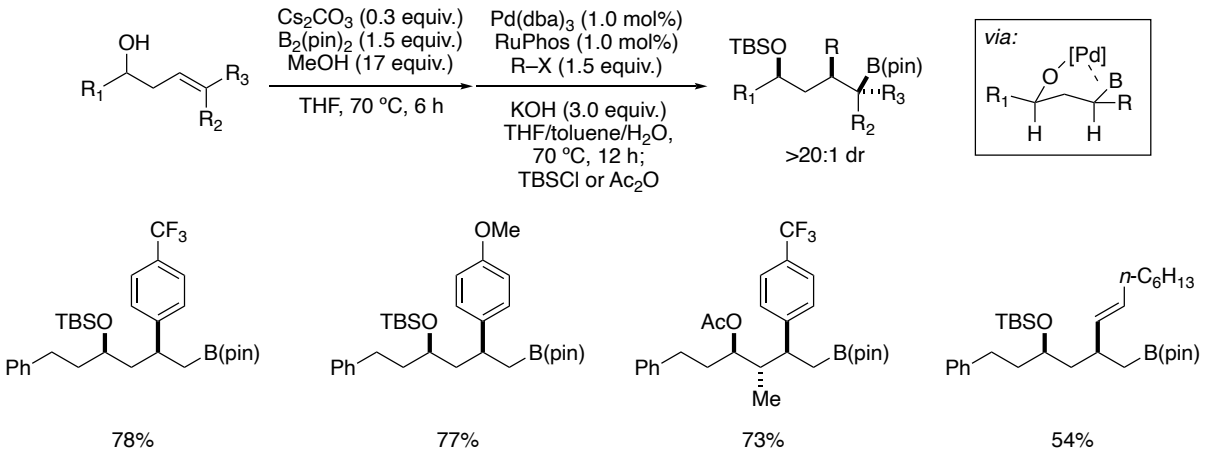


Later on, the same group disclosed a hydroxyl group-directed diastereoselective diboration/ Pd-catalyzed stereoretentive coupling sequence (Scheme 1.12).[34] The homoallylic alcohol directed Pd catalyst to site-selectively transmetallate to the secondary boronic ester, while the primary boronic ester remained unfunctionalized. This directed boronation/coupling sequence accounted for a regio- and stereoselective difunctionalization of homoallylic alcohols.[35]

[34] (a) Blaisdell, T. P.; Caya, T. C.; Zhang, L.; Sanz-Marco, A.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 9264–9267. (b) Blaisdell, T. P.; Morken, J. P. *J. Am. Chem. Soc.* **2015**, *137*, 8712–8715.

[35] For selected reports on hydroxyl group-directed coupling of alkylboronic esters, see: (a) Shi, Y.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 3455–3458. (b) Murray, S. A.; Liang, M. Z.; Meek, S. J. *J. Am. Chem. Soc.* **2017**, *139*, 14061–14064.

Scheme 1.12. Hydroxyl Group-Directed Coupling of 1,2-Bis(boronic Pinacol Esters)



1.2.3.2 Non-Catalyzed Site-Selective Functionalization

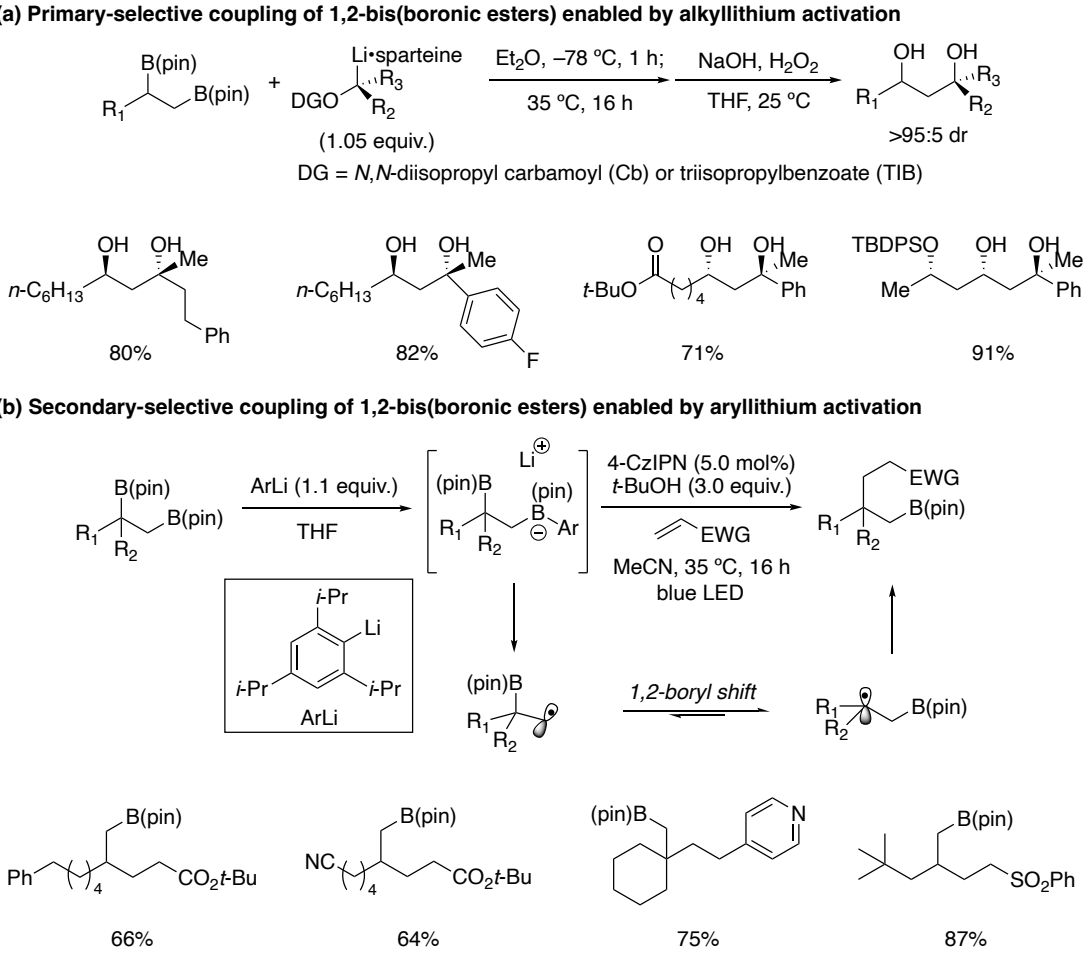
In 2016, Aggarwal and co-workers reported the first site-selective homologation of 1,2-bis(boronic esters) (Scheme 1.13a).[36] The less sterically hindered primary boronic ester reacted preferencially with the bulky tertiary alkyllithium, furnishing an enantiomerically enriched tertiary alcohol after homologation and oxidation. In 2019, the same group demonstrated a secondary-selective functionalization of 1,2-bis(boronic esters) through aryllithium activation (Scheme 1.13b).[37] Single electron transfer between the boron "ate" complex and a photocatalyst furnished a primary radical that underwent rapid 1,2-boryl shift to furnish the thermodynamically favored secondary radical. Then, the secondary radical was functionalized with a range of radical

[36] For selected reports on site-selective homologation of 1,2-bis(boronic esters), see: (a) Fawcett, A.; Nitsch, D.; Ali, M.; Bateman, J. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2016**, *55*, 14663–14667. (b) Fiorito, D.; Keskin, S.; Bateman, J. M.; George, M.; Noble, A.; Aggarwal, V. K. *J. Am. Chem. Soc*. **2022**, *144*, 7995−8001.

[37] Kaiser, D.; Noble, A.; Fasano, V.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2019**, *141*, 14104–14109.

acceptor. The Aggarwal group subsequently demonstrated several more examples of secondary-selective functionalization of 1,2-bis(boronic esters) enabled by the 1,2-boryl shift.[38]

Scheme 1.13. Site-Selective Functionalization of 1,2-Bis(boronic Esters) through Organolithium Activation



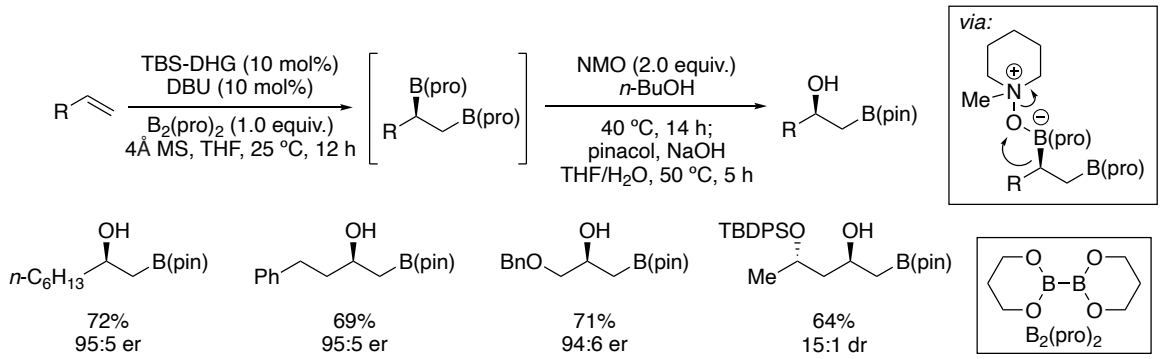
In 2019, Morken group reported the first site-selective oxidation of 1,2-bis(boronic esters) (Scheme 1.14).[39] It was proposed that 1,2-metallate shift is the rate-limiting step and coordination

[38] For selected reports on secondary-selective functionalization of 1,2-bis(boronic esters), see: (a) Wang, H.; Wu, J.; Noble, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2022**, *61*, e202202061. (b) Wang, H.; Han, W.; Noble, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2022**, *61*, e202207988. (c) Zou, X.-Z.; Ge, J.-F.; Yang, Y.-X.; Huang, Y.-F.; Gao, D.-W. *Org. Lett.* **2024**, *26*, 1595–1600

[39] Yan, L.; Morken, J. P. *Org. Lett.* **2019**, *21*, 3760–3763.

of the oxidant to boron is reversible, therefore the more substituted and electron-rich carbon migrated preferentially. Enantiomerically enriched β-hydroxyl boronic esters were obtained in up to 72% yield.

Scheme 1.14. Site-Selective Oxidation of 1,2-Bis(boronic Esters)



1.3 Development of Site-Selective Copper-Catalyzed Coupling of Alkyl Vicinal Bis(boronic Esters)

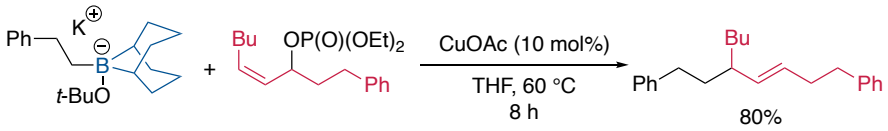
1.3.1 Inspiration of the Reaction

In order to obtain enantiomerically enriched secondary alkylboronic esters, it is a promising and versatile strategy to conduct enantioselective diboration of a terminal alkene and site-selectively functionalize the primary boronic ester. However, as described in Chapter 1.2, the majority of site-selective functionalization of 1,2-bis(boronic esters) are Pd-catalyzed couplings that can only incorporate C(sp^2) electrophiles. This significantly limits the reaction scope. To extend the range of enantiomerically enriched reaction products available from terminal alkenes by diboration, we considered other catalysts for site-selective reaction of vicinal bisboronate compounds with non-C(sp^2)-derived electrophiles.

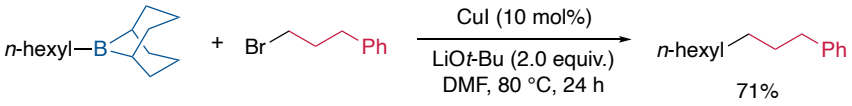
Copper catalysts have been demonstrated to enable coupling between primary alkyl 9-BBN and a range of electrophiles including but not limited to: allyl,[40] alkyl,[41] and amino[42] electrophiles (Scheme 1.15).[43] Inspired by the versatile reactivity of organocopper species, we decided to begin our investigation by employing copper salts as pre-catalysts for site-selective functionalization of 1,2-bis(boronic esters).

Scheme 1.15. Selected Examples of Cu-Catalyzed Functionalization of Alkyl Boronic Species

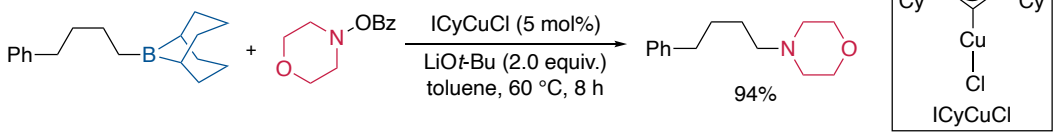
Allylation of alkyl 9-BBN by Sawamura *et al.*



Alkylation of alkyl 9-BBN by Liu *et al.*



Amination of alkyl 9-BBN by Lalic *et al.*



[40] Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895–2897.

[41] Yang, C.; Zhang, Z.; Liu, Y.; Liu, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 3904–3907.

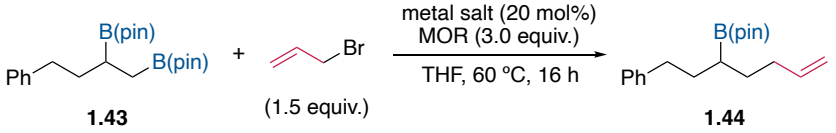
[42] Rucker, R. P.; Whittaker, A. M.; Dang, H.; Lalic, G. *J. Am. Chem. Soc.* **2012**, *134*, 6571–6574.

[43] For selected reviews on Cu-catalyzed coupling of organoboronate compounds, see: (a) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337–2364. (b) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113*, 6234–6458. (c) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400–5449. (d) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1470. (e) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632–2657.

1.3.2 Optimization of Reaction Conditions

Optimization of reaction conditions (Table 1.1) was conducted with vicinal bis(boronic ester) **1.43** and allyl bromide in the presence of 20 mol% of a metal salt and LiOMe at 60 ºC for 16 h. When CuBr was employed, allylation product **1.44** was isolated in 85% yield (entry 1) and as a single regioisomer. Encouraged by the high regioselecitvity and yield, we proceeded to investigate other Cu(I) salts as catalyst. Although the yield with CuI (entry 2) was inferior to that of CuBr, when CuCN was employed as the catalyst (entry 3), the reaction was enhanced, >95% conversion being achieved in 16 h. Reactions involving lower loadings of CuCN showed that diminished amounts of catalyst can still deliver the product, but yields were optimal with 20 mol% catalyst. Lower loading led to diminished yields (entries 4–7). Analysis of metal alkoxides revealed that although reactions with other alkoxides such as NaOMe (entry 8), KOMe (entry 9) and LiO*t*-Bu (entry 10) gave rise to adequate efficiency, LiOMe was the optimal metal alkoxide. Ligand screening revealed that NHC (entry 13) or phosphine-based ligands (entries 11, 12) were less effective. Employment of Ni(II), Co(II), Mn (II), and Fe(II) salts failed to provide any detectable amount of coupling product **1.44** (entries 14–17).

Table 1.1. Optimization of Cu-Catalyzed Coupling of Vicinal Bis(boronic Ester) with Allyl Bromide[a]



entry	metal salt	MOR	conv. (%)
1	CuBr	LiOMe	85
2	CuI	LiOMe	81
3	CuCN	LiOMe	>95
4	CuCN (10 mol%)	LiOMe	63
5	CuCN (5 mol%)	LiOMe	42
6	CuCN (2 mol%)	LiOMe	31
7	CuCN (1 mol%)	LiOMe	11
8	CuCN	NaOMe	50
9	CuCN	KOMe	53
10	CuCN	LiO*t*-Bu	63
11	CuCN/PPh_3	LiOMe	78
12	CuCN/PBu_3	LiOMe	65
13	CuCN/iMes	LiOMe	92
14	$NiCl_2$	LiOMe	<5
15	$CoCl_2$	LiOMe	<5
16	$MnCl_2$	LiOMe	<5
17	$FeCl_2$	LiOMe	<5

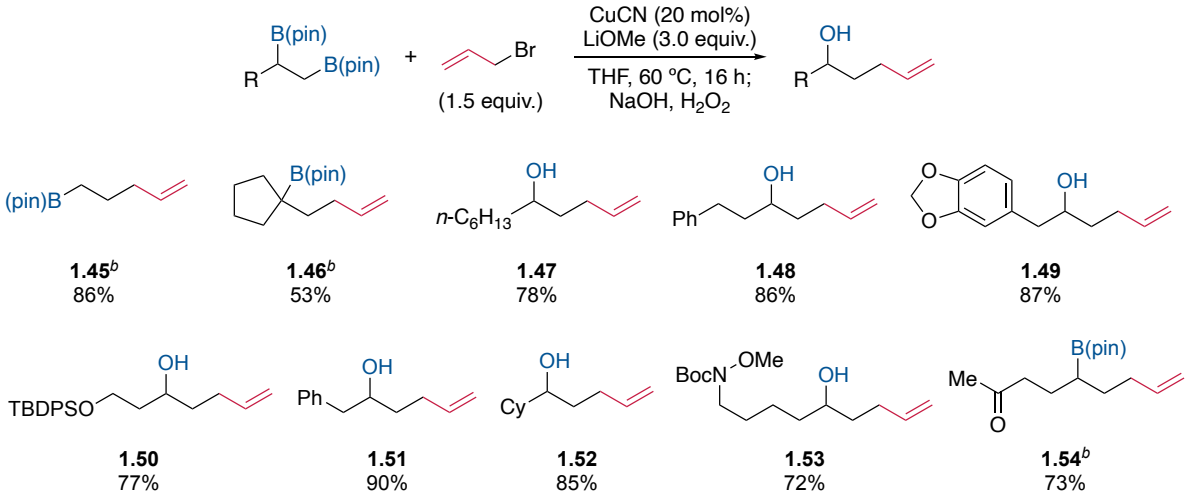
[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

1.3.3 Substrate Scope

With effective conditions in hand, we examined the substrate scope of the Cu-catalyzed coupling with allyl bromide (Scheme 1.16). It was found that the method is applicable to a range of terminal vicinal bis(boronic esters). Bis(boronic esters) derived from unactivated monosubstituted aliphatic alkenes (**1.47**, **1.48**, **1.51**, **1.52**), ethylene (**1.45**), 1,1-disubstuted alkenes (**1.46**), and those bearing aromatic rings (**1.49**), silyl ethers (**1.50**), or protected nitrogen-based

functional groups (**1.53**) were appropriate substrates for the cross-coupling and furnished allylation products in up to 90% yield.

Scheme 1.16. Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters) with Allyl Bromide[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). [b]Reactions were carried out without NaOH, H_2O_2.

Besides allyl bromide, coupling with functionalized allyl electrophiles proceeded smoothly, offering a concise route to a variety of useful building blocks (Scheme 1.17). Notably, we were able to incorporate alkenyl halides (**1.58**, **1.59**), allylic halides (**1.60**), allylic silanes (**1.61**), and other valuable functional groups.

It's worth mentioning that the Cu-catalyzed coupling preferentially occurs at the primary boronic ester. When enantiomerically enriched vicinal bis(boronic ester) **1.43** was employed, the corresponding enantiomerically enriched secondary boronic esters were obtained. Vinyl epoxide **1.63** proved to be an effective electrophile, allowing direct conversion to enantiomerically enriched boronic ester-containing allylic alcohol **1.64** with *E*/*Z* ratio of 3.2:1. Moreover, synthetically challenging chiral γ-boryl carbonyls (**1.65**), compounds containing dissonant oxidation patterns in

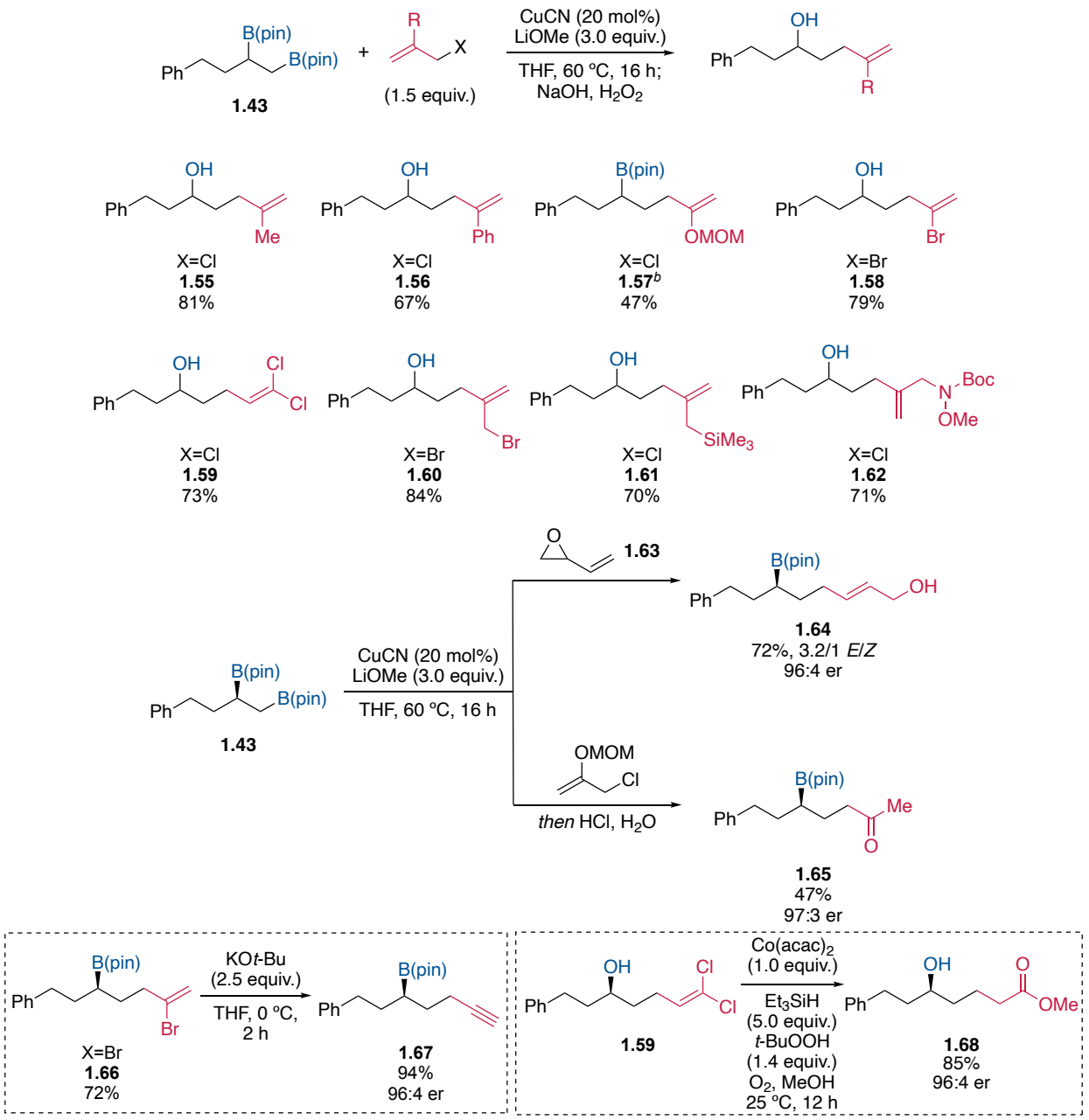
organic molecules,[44] were addressed by hydrolysis of an enol ether-containing allylation products. Simple transformation of products **1.66** [45] and **1.59** [46] afforded enantiomerically enriched compounds with remote terminal alkyne (**1.67**) and ester functional groups (**1.68**).

[44] (a) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147–155. (b) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239–258.

[45] Corey, E. J.; Yu, C. M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495–5496.

[46] Ma, X.; Herzon, S. B. *J. Org. Chem.* **2016**, *81*, 8673–8695.

Scheme 1.17. Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters) with Substituted Allyl Electrophiles[a]

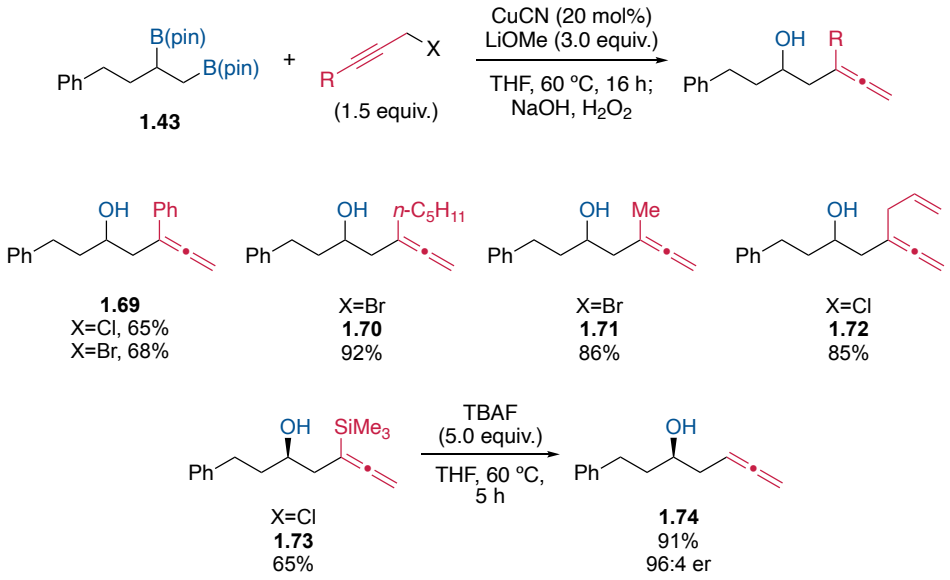


[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral SFC (±1%). [b]Reactions were carried out without NaOH, H_2O_2.

In addition to allylic halides, the Cu-catalyzed coupling of vicinal bis(boronic esters) can be extended to other electrophile classes. Substituted propargylic halides underwent S_N2' coupling with the primary organocopper species, furnishing disubstituted allenes in up to 92% yield

(Scheme 1.18). The trimethylsilyl group in allene **1.73** was readily removed upon treatment with TBAF. This sequence constitutes a route to enantiomerically enriched homoallenic alcohols (**1.74**).

Scheme 1.18. Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters) with Propargylic Halides[a]



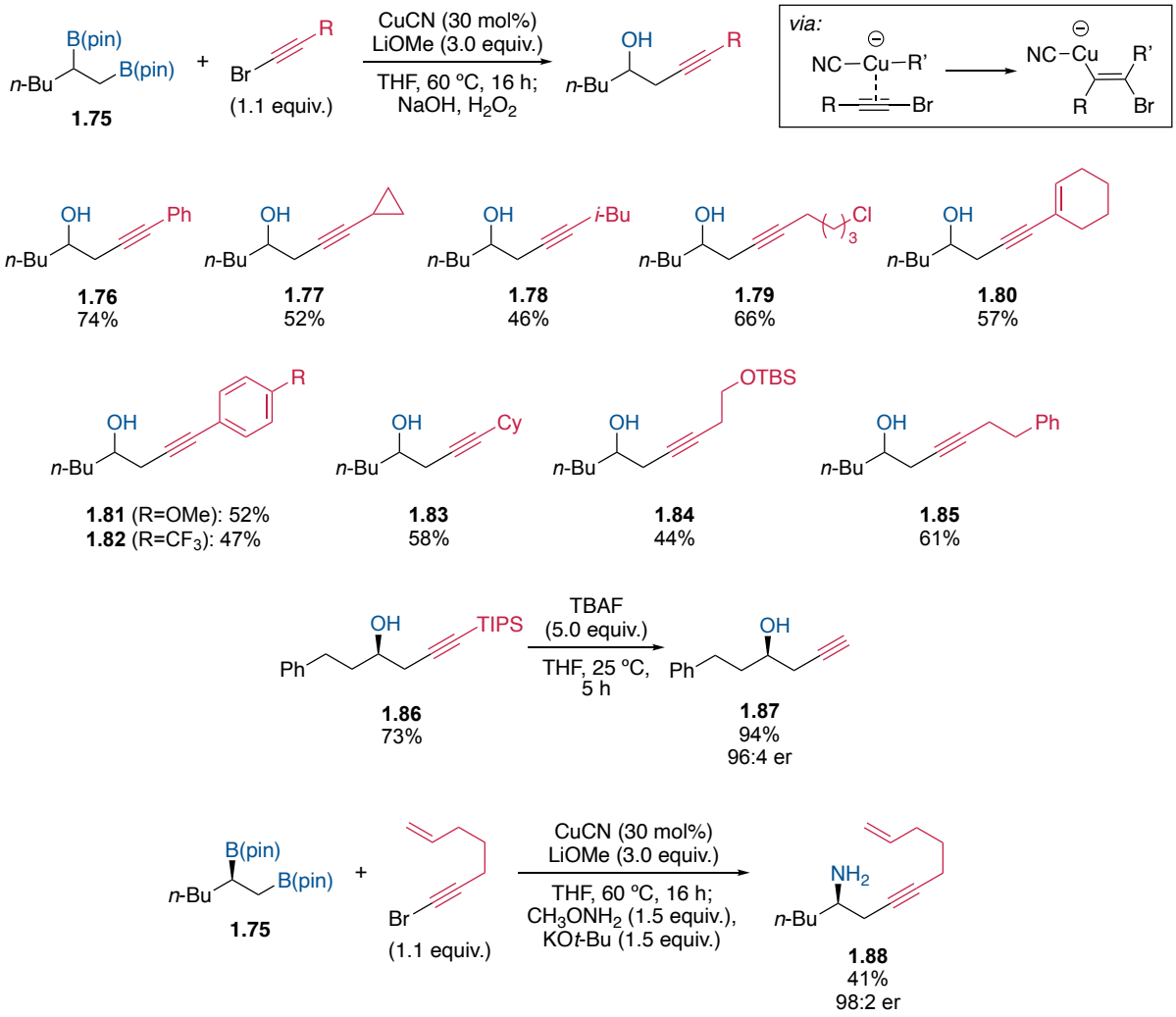
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral HPLC (±1%).

Alkynyl bromides also underwent coupling efficiently with vicinal bis(boronic esters) under the reaction conditions (Scheme 1.19), offering a route to a range of homopropargylic boronic esters that contain a halide, a silyl ether, an aryl, or an alkenyl group. It is likely that the coupling with alkynyl bromides occurs by carbocupration of alkyl bromide, followed by *β*-bromide elimination to afford the coupling product.[47] The enantiomerically enriched terminal alkyne **1.87** can be obtained easily by efficient desilylation of **1.86**. Moreover, the secondary boronic ester that remained after alkyne coupling can be stereospecifically modified. For example, stereospecific amination[48] offered access to homopropargylic amine **1.88** in 41% yield over two steps.

[47] Cahiez, G.; Gager, O.; Buendia, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1278–1281.

[48] Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett*. **2018**, *29*, 1749−1752.

Scheme 1.19. Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters) with Alkynyl Bromides[a]

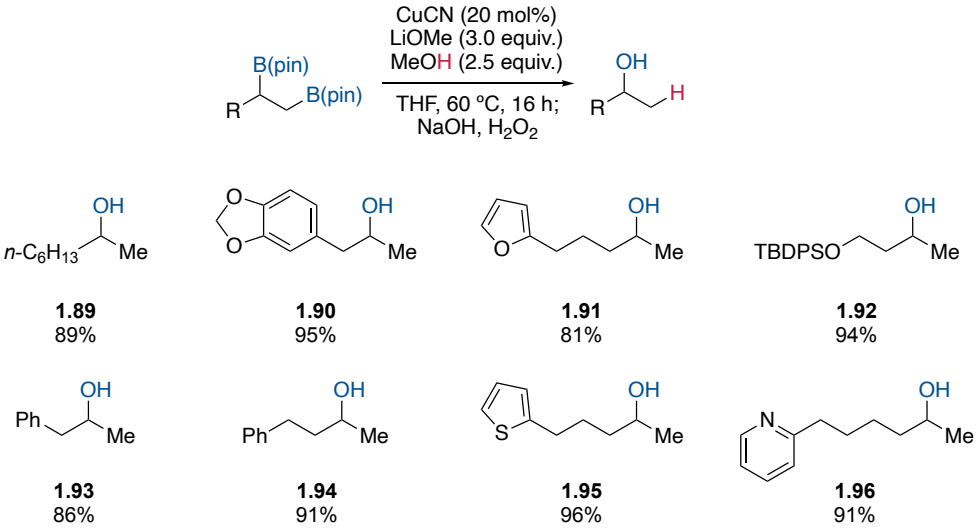


[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral SFC (±1%).

When electrophiles bearing aliphatic carbonyl groups, unprotected alcohols or amines, or nitrile functional groups were subjected to Cu-catalyzed coupling conditions, proto-deboroylation of the primary boronic ester occurred. This suggested that the organocopper intermediate is basic and can be protonated by acidic protons on these functional groups. Although the basicity of the organocopper species placed a limitation on the bis(boronic ester) scope, the proto-deborylation itself, following enantioselective diboration, provided an efficient equivalent to enantioselective

Markovnikov hydroboration of unactived terminal alkenes (Scheme 1.20).[49] Highly regio- and enantioselective syntheses of compounds **1.89**−**1.96** through hydroboration of monosubstituted α-olefins could be challenging with other methods. However, theses compounds were readily furnished by this diboration/Cu-catalyzed protonation sequence.

Scheme 1.20. Cu-Catalyzed Protonation of Vicinal Bis(boronic Esters)[a]



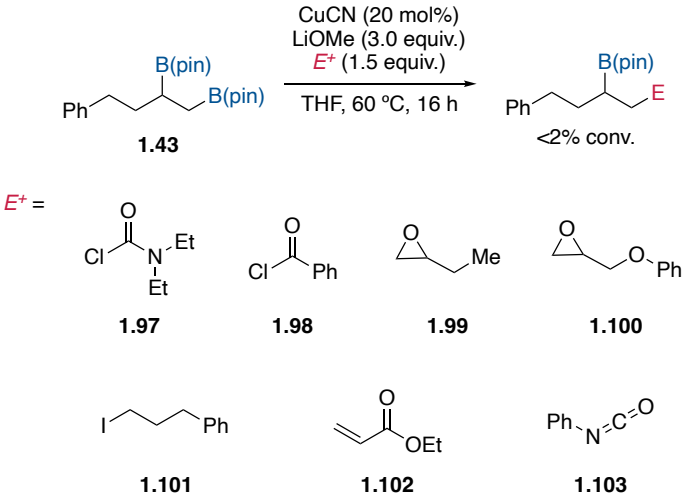
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%).

To expand the scope, we subjected a variety of electrophiles to catalytic coupling conditions (Scheme 1.21). Reactions with allyl, propargyl, alkynyl electrophiles as well as methanol (proton) were efficient. In contrast, when carbamoyl chlorides (**1.97**) or acyl chlorides (**1.98**) were used, the corresponding methyl esters (addition products of methoxide and electrophile) were generated (as judged by mass spectrometry). Most of **1.43** was recovered and no coupling product could be detected. With epoxide **1.99** as the electrophile, methoxide acted as nucleophile, adding to the

[49] For selected reports on enantioselective Markovnikov hydroboration of unactived terminal alkenes, see: (a) Smith, J. R.; Collins, B. S.; Hesse, M. J.; Graham, M. A.; Myers, E. L.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, *139*, 9148−9151. (b) Cai, Y.; Yang, X. T.; Zhang, S. Q.; Li, F.; Li, Y. Q.; Ruan, L. X.; Hong, X.; Shi, S. L. *Angew. Chem., Int. Ed.* **2018**, *57*, 1376−1380.

epoxide. When we replaced LiOMe with LiO*t*-Bu or LiO*i*-Pr, there was little difference to the outcome. We then investigated the reaction with glycol-derived epoxide (**1.100**) as electrophile. We reasoned that chelation between the Lewis acidic Cu and the two oxygen atoms might accelerate the coupling reaction. However, we did not detect any desired product (<2% by ^{1}H NMR analysis). Alkyl halides were similarly ineffective. When **1.101** was employed, a small amount of protonation product was generated along with >90% recovered starting material **1.43**. Reactions involving alkyl bromides, alkyl chlorides, and alkyl triflates were similarly inefficient. To access ester and amide moieties directly, Michael acceptors and isocyanates were used. In both instances, >90% of **1.43** was recovered and no desired product could be detected.

Scheme 1.21. Electrophiles that Afforded <2% Conversion in Cu-Catalyzed Coupling[a]



[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

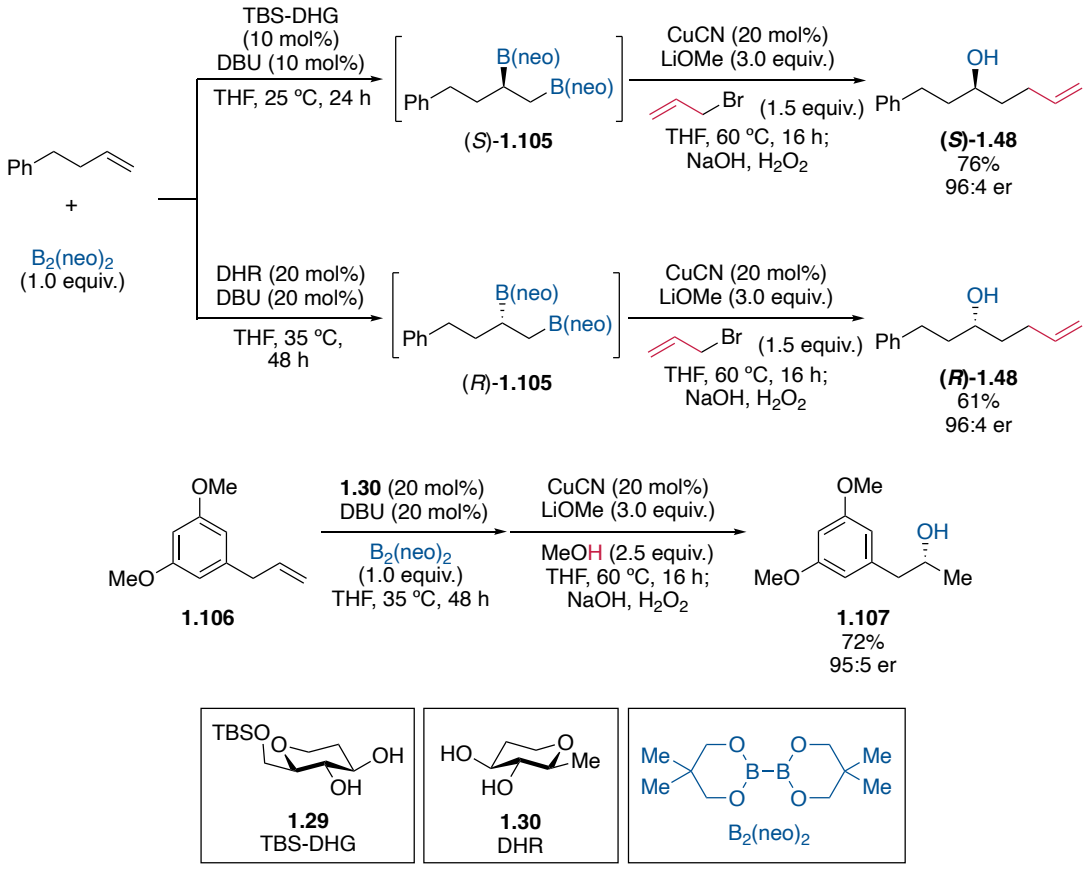
1.3.4 Utility of Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters)

1.3.4.1 Tandem Alkene Diboration/Cu-Catalyzed Site-Selective Functionalization

It is a testament to the robustness of the Cu-catalyzed site-selective reaction that it can be performed in tandem with enantioselective diboration of unactivated terminal alkenes. We examined further tandem sequences involving carbohydrate-catalyzed enantioselective diboration[24] (Scheme 1.22). When 4-phenyl-1-butene was subjected to diboration conditions with each of the pseudoenantiomeric TBS-DHG (**1.29**) and DHR (**1.30**) catalysts, 1,2-bis((neopentyl glycolato)boronic ester) **1.105** was generated. Without work-up or isolation, the mixtures were each directly subjected to Cu-catalyzed coupling conditions with allyl bromide. Either enantiomer of the chiral alcohol **1.48** could be obtained in 61–76% yield and 96:4 er. Notably, despite that the catalysts contain free alcohols, minimal protonation product was observed. This implies that allylation is faster than protonation of the organocopper species. Moreover, when α-olefin **1.106** was subjected to tandem diboration/Cu-catalyzed protonation/oxidation reaction sequence, alcohol **1.107** was obtained in 72% yield and 95:5 er. It is worth noting that **1.107** is an intermediate in syntheses of dihydroisocoumarin natural products.[50]

[50] For a selected report on asymmetric total syntheses of dihydroisocoumarins, see: (a) Markad, S. B.; Mane, B. B.; Waghmode, S. B. *Tetrahedron.* **2020**, *76*, 131524–131531. For a selected review on 3,4-dihydroisocoumarins, see: (b) Ortiz, A.; Castro, M.; Sansinenea, E. *Curr. Org. Synth.* **2019**, *16*, 112–129.

Scheme 1.22. Tandem Carbohydrate-Catalyzed Diboration/Cu-Catalyzed Coupling[a]



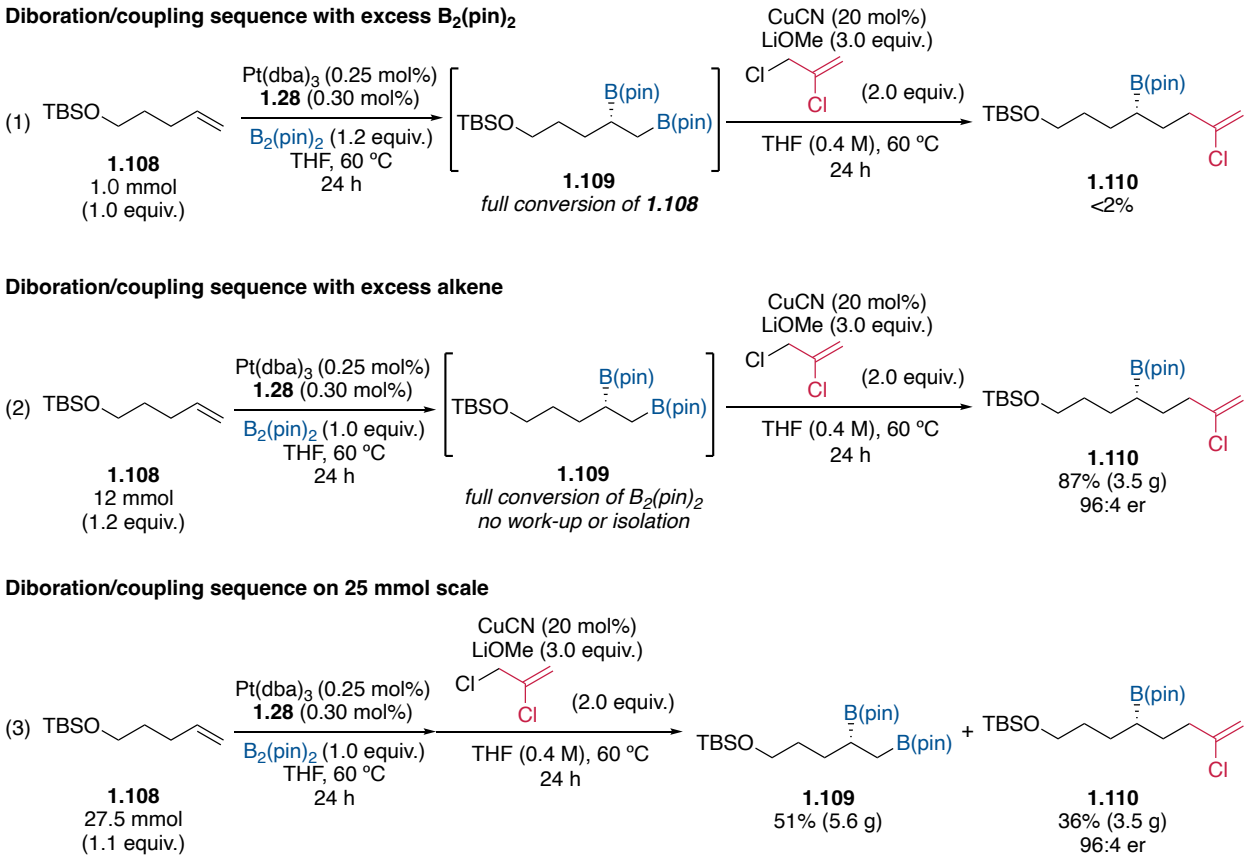
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral SFC (±1%).

Tandem diboration/Cu-catalyzed coupling can be carried out on multi-mmol scale (Scheme 1.23).[23] Pt-catalyzed enantioselective diboration could be accomplished with just 0.25 mol% loading. TLC analysis showed that after 24 h at 60 °C, $B_2(pin)_2$ was fully consumed (Scheme 1.23, equation 2). It is vital that $B_2(pin)_2$ is fully consumed before the next step, as excess $B_2(pin)_2$ was found to inhibit the catalytic coupling, leading to only trace amount of **1.110** (Scheme 1.23, equation 1). We suspect that alkoxide-activated $B_2(pin)_2$ transmetallated to Cu catalyst, forming

Cu–B(pin) species, thus hindering the transmetallation of bis(boronic ester) **1.109**.[51] After reaction of α-olefin **1.108** and $B_2(pin)_2$ reached full conversion, the reaction solution was diluted and subjected to Cu-catalyzed coupling condition. The single-flask transformation of α-olefin **1.108** to enantiomerically enriched secondary alkylboronic ester **1.110** proceeded efficiently (Scheme 1.23, equation 2). What is more, the unpurified mixture was remarkably clean, rendering product purification straightforward. Upon heating the coupling reaction at 60 ºC, the mixture congealed to a hard gel, presumably as a result of oligomerization of byproduct MeOB(pin). The latter issue did not lead to lower efficiency, but could complicate the stirring of the solution. The lack of sufficient stirring at 25 mmol scale might be the reason for the low conversion of **1.109** (Scheme 1.23, equation 3).

[51] For a selected review on Cu–boryl additions by transmetallation of $B_2(pin)_2$ to Cu catalyst, see: Hoveyda, A. H.; Koh, M. J.; Lee, K.; Lee, J. In *Organic Reactions*; Denmark, S. E., Hall, D., Eds.; Wiley, 2019; pp 959–1056.

Scheme 1.23. Gram-Scale Tandem Pt-Catalyzed Diboration/Cu-Catalyzed Coupling[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral SFC (±1%). Conversions of the substrates were determined by TLC analysis and analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

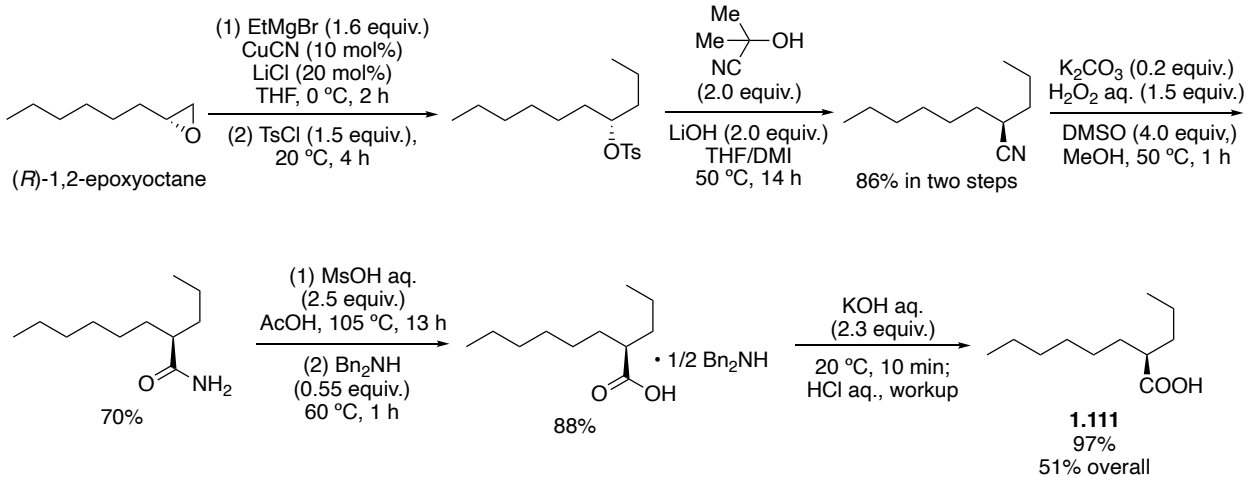
1.3.4.2 Synthesis of (R)-Arundic Acid

(*R*)-Arundic acid is an astrocyte activation inhibitor and has been shown effective in preventing neurological deficits and brain tissue damage following intracerebral hemorrhage, improving neuronal survival after acute stroke.[52] In 2005, Hasegawa and co-workers reported a gram-scale

[52] For selected reports on bioactivity of (*R*)-arundic acid, see: (a) Pettigrew, L. C.; Kasner, S. E.; Albers, G. W.; Gorman, M.; Grotta, J. C.; Sherman, D. G.; Funakoshi, Y.; Ishibashi, H. *J. Neurol. Sci.* **2006**, *251*, 50–56. (b) Cordeiro, J. L.; Neves, J. D.; Vizuete, A. F.; Aristimunha, D.; Pedroso, T. A.; Sanches, E. F.; Gonçalves, C. A.; Netto, C. A. *Neuroscience* **2020**, *440*, 97–112.

synthesis of (*R*)-arundic acid (**1.111**) (Scheme 1.24).[53] Their synthesis started with the addition of ethyl Grignard reagent to (*R*)-1,2-epoxyoctane. The resulting secondary alcohol was transformed into a tosylate by treatment with TsCl. Nucleophilic displacement of the tosylate with *in-situ* generated cyanide afforded (*R*)-2-propyloctanenitrile in 86% yield over two steps. The nitrile was converted into (*R*)-2-propyloctanamide, which was hydrolyzed to afford the corresponding carboxylic acid **1.111** in 51% overall yield.

Scheme 1.24. Synthesis of (*R*)-Arundic Acid by Hasegawa *et al*.

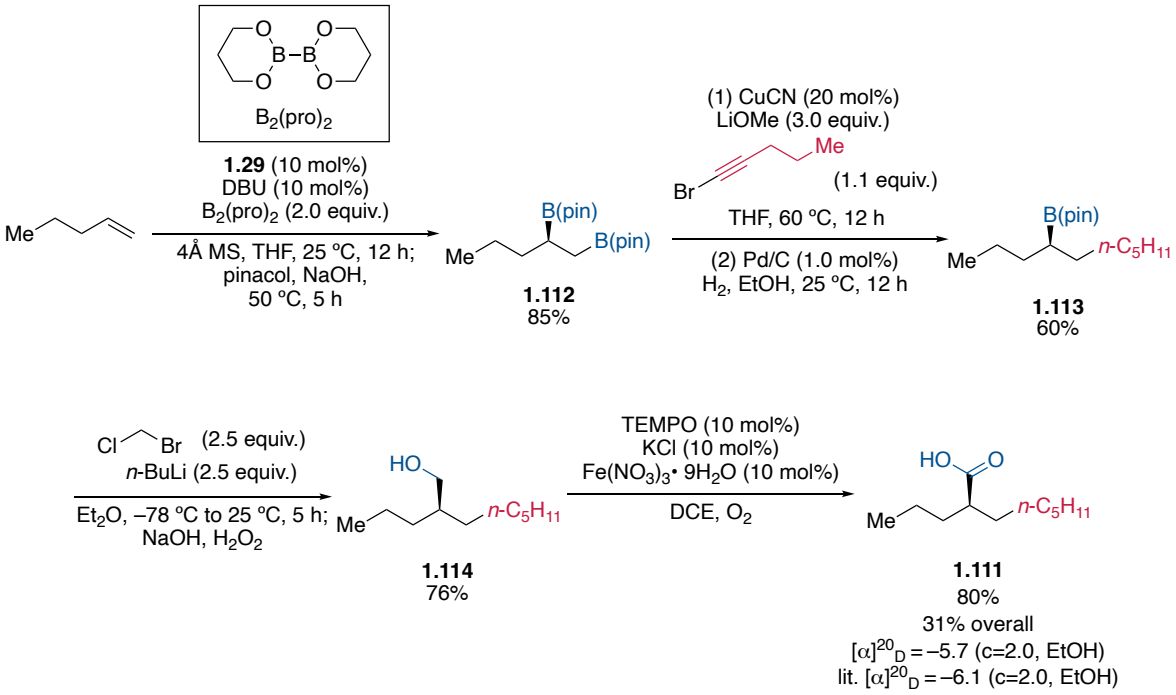


We employed diboration/Cu-catalyzed coupling strategy to the synthesis of (*R*)-arundic acid (Scheme 1.25). Enantioselective diboration of 1-pentene, followed by Cu-catalyzed coupling to 1-bromopentyne, and hydrogenation, provided a simple route to chiral secondary boronic ester **1.112**. The latter compound was easily converted into (*R*)-arundic acid by stereoretentive homologation of the secondary boronic ester followed by oxidation. Our synthesis afforded the carboxylic acid moiety through oxidation of **1.114**, avoiding the use of highly toxic acetone cyanohydrin. However, despite having the same number of steps, our route furnished a lower

[53] Hasegawa, T.; Kawanaka, Y.; Kasamatsu, E.; Ohta, C.; Nakabayashi, K.; Okamoto, M.; Hamano, M.; Takahashi, K.; Ohuchida, S.; Hamada, Y. *Org. Process Res. Dev.* **2005**, *9*, 774−781.

overall yield (31%) compared to Hasegawa's synthesis (51%). To improve the efficiency of our synthesis, it's crucial to develop: regioselective alkylation of 1,2-bis(boronic esters) that converts **1.112** into **1.113** in one step, and stereospecific acetylation of alkylboronic esters that directly converts **1.113** into **1.111**.

Scheme 1.25. Synthesis of (*R*)-Arundic Acid[a]



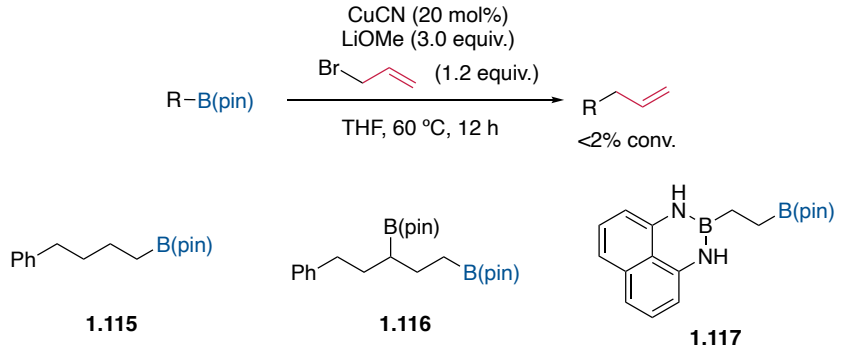
[a]Yields corresponded to isolated and purified products (±5%).

1.3.5 Mechanistic Investigations

In contrast to 1,2-bis(boronic esters), which undergo Cu-catalyzed coupling smoothly, a number of boronic esters proved to be ineffective (Scheme 1.26). Most notably, with primary boronic ester **1.115**, the desired allylation product was not detected and **1.115** was fully recovered. We proposed that the non-participating secondary boronic ester exerts an accelerating effect on the process. As shown in Scheme 1.16, the activating boronate group can be either primary (**1.45**), secondary, or tertiary (**1.46**) and still provide sufficient substrate activation. The lack of reactivity

exhibited by 1,3-bis(boronic ester) **1.116** indicted that the proposed activating effect requires precise positioning between the activating and reacting boronic esters. With a longer distance between the two boronic esters, reactivity was diminished. When the vicinal B(pin) was replaced by a B(dan) (**1.117**), a weaker Lewis acid, no desired product was observed. Therefore, Lewis acidity of the activating boron group appears to be crucial to reactivity.

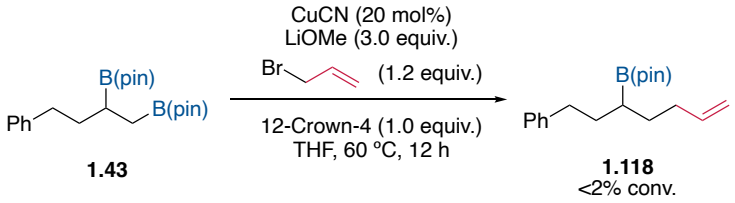
Scheme 1.26. Organoboronic Esters that Afforded <2% Conversion in Cu-Catalyzed Coupling[a]



[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

The addition of lithium cation scavenger[54] 12-Crown-4 lowered the efficiency, indicating that lithium cation is key to efficiency (Scheme 1.27).

Scheme 1.27. Cu-Catalyzed Coupling in the Presence of 12-Crown-4[a]

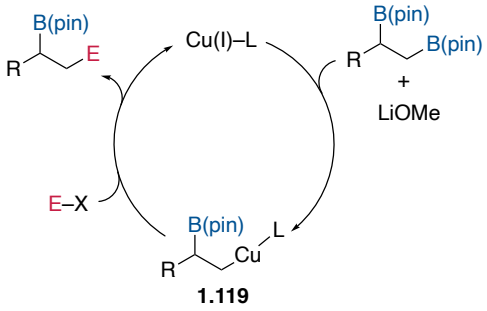


[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

[54] Hopkins, H. P., Jr.; Norman, A. B. *J. Phys. Chem.* **1980**, *84*, 309−314.

We proposed that transmetallation of organoboronic ester to copper is an essential elementary step. The observation that protodeborylation (see Scheme 1.20) proceeded efficiently without a redox-active electrophile implies that oxidation of Cu(I) is likely not required for transmetallation. It is therefore more likely that transmetallation of 1,2-bis(boronic ester) occurs directly with either CuCN, or a Cu(I) alkoxide,[55] or an alkoxy-derived cuprate,[56] to afford an intermediate such as **1.119**. Addition to the electrophile releases the catalyst and the coupling product (Scheme 1.28).

Scheme 1.28. Proposed Catalytic Cycle of Cu-Catalyzed Coupling of Vicinal Bis(boronic Esters)



To gain more insight regarding the nature of the transmetallation and the origin of the rate acceleration caused by the vicinal boronic ester, we performed a series of experiments (Scheme 1.29). First, we examined the stoichiometric reaction between vicinal bis(boronic ester) **1.43** and CuO*t*-Bu. Transformation of bis(boronic ester) **1.43** to alkene **1.120** and monoboronic esters **1.115** and **1.121** occurred slowly at 60 ºC, affording 44% conversion in 12 h (Scheme 1.29, equation 1).

---

[55] For selected reports on transmetallations between copper (I) alkoxides and aryl boronic esters, see: (a) Ohishi, T.; Nishiura, M.; Hou, Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 5792−5795. (b) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216−3218. For transmetallations between copper (I) alkoxides and alkenyl and alkylboronic esters, see: (c) Hoveyda, A. H.; Zhou, Y.; Shi, Y.; Brown, M. K.; Wu, H.; Torker, S. *Angew. Chem., Int. Ed.* **2020**, *59*, 21304–21359.

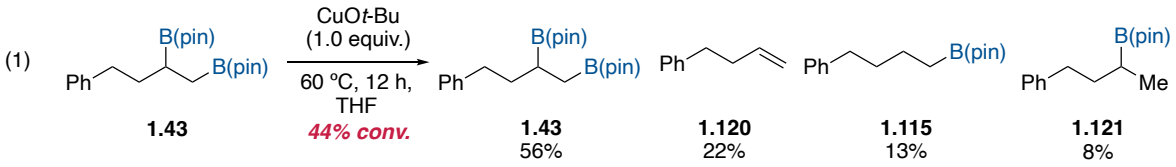
[56] (a) Aalten, H. L.; van Koten, G.; Grove, D. M.; Kuilman, T.; Piekstra, O. G.; Hulshof, L. A.; Sheldon, R. A. *Tetrahedron* **1989**, *45*, 5565−5578. (b) Konovalov, A. I.; Benet-Buchholz, J.; Martin, E.; Grushin, V. V. *Angew. Chem., Int. Ed.* **2013**, *52*, 11637−11641.

The reaction was accelerated when one equivalent of KOMe was present, affording full conversion in 12 h (Scheme 1.29, equation 2). The products of equations 1 and 2 are consistent with the intermediacy of an organocopper species **1.119**: alkene **1.120** would arise from *β*-boryl elimination;[57] monoboronic ester **1.121** would arise from protonation of the organocopper intermediate **1.119** (see Scheme 1.20). Although regioselective functionalization of secondary boronic ester was not observed under standard conditions, **1.115** likely arises from homolytic cleavage of Cu–C bond in **1.119**, followed by a 1,2-boryl shift.[37,38] Unlike the reaction of bis(boronic ester) **1.43**, treatment of primary monoboronic ester **1.115** with CuO*t*-Bu and KOMe did not result in any transformation (Scheme 1.29, equation 3), a finding that highlights the activating effect of a vicinal boronic ester.

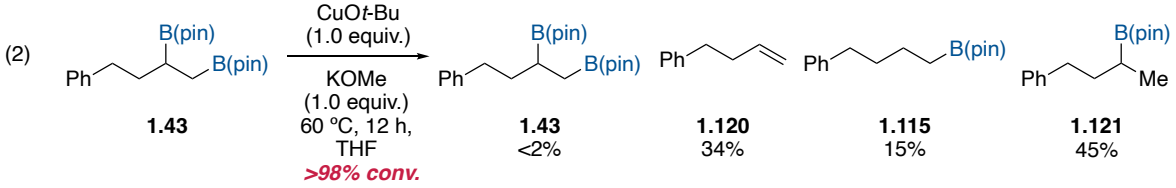
[57] Lam, K. C.; Lin, Z.; Marder, T. B. *Organometallics* **2007**, *26*, 3149−3156.

Scheme 1.29. Stoichiometric Reactions between Organoboronic Esters and CuO*t*-Bu[a]

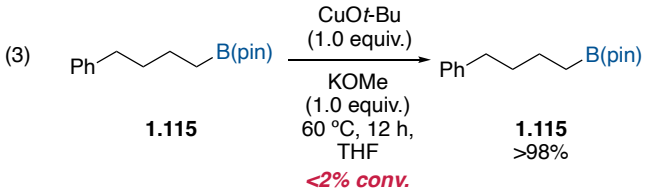
Transmetallation of 1,2-bis(boronic ester) to CuO*t*-Bu



Transmetallation of 1,2-bis(boronic ester) to CuO*t*-Bu in the presence of KOMe



Transmetallation of alkylboronic ester to CuO*t*-Bu in the presence of KOMe



[a]Reactions were carried out under argon atmosphere. Conversions of organoboronic esters were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

Our investigations suggested that substrate activation may involve a methoxide bridging between two boron atoms of **1.43**. To probe this, alkoxide complexation with several organoboron compounds was examined by ^{11}B NMR spectroscopy. Treatment of primary monoboronic ester **1.122** with 0.5 equivalent of KOMe resulted in partial conversion (48% conv.) of the starting material (35.0 ppm) to a species with an upfield-shifted resonance (8.8 ppm). The finding is consistent with the formation of the derived four-coordinate methoxide-derived boron "ate" complex (Scheme 1.30a). When bis(boronic ester) **1.43** was treated with one equivalent of methoxide (0.5 equivalent of methoxide relative to each boronic ester), we observed 84% conversion of three-coordinate boron species to a new upfield resonance (11.6 ppm), suggesting a bonding mode that involves both boron atoms (Scheme 1.30b). *Cis*-1,2-diborylcyclopentane **1.125**, a compound that is predisposed to internal chelation, was converted into a structure with upfield

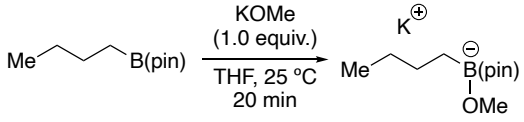
resonance (13.2 ppm) with 88% conversion (Scheme 1.30c). Gauge-including atomic orbital DFT calculations were carried out to predict the chemical shifts of complexes **1.123**, **1.124**, and **1.126**. The computational results are consistent with the experimental data.

Although oxygen-bridged bis(boronic esters) "ate" complexes have not been previously reported, there is an account of oxygen-bridged 1,2-phenylenediboronate anion (Scheme 1.30d).[58a] DFT calculations performed later revealed that the barrier for reaction of alkyl boron "ate" complex **1.128** (Scheme 1.30e) is nearly 10 kcal/mol higher than that for reaction of the cyclic chelate **1.127**. Part of the difference in energy barriers can be traced to the difference in the starting material strain. For the ground state of the cyclic chelate **1.127**, the B−C−C bond angles are more compressed relative to the unstrained acyclic compound **1.128**.

[58] For selected reports on oxygen-bridged organoboronate compounds, see: (a) Durka, K.; Luliński, S.; Serwatowski, J.; Woźniak, K. *Organometallics* **2014**, *33*, 1608–1616. (b) Biallas, M. J. *J. Am. Chem. Soc.* **1969**, *91*, 7290−7292.

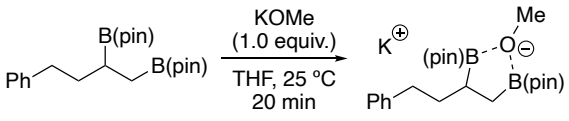
Scheme 1.30. Studies of Internally Chelated Boron "Ate" Complexes

(a) Treatment of primary alkylboronic ester with KOMe[a]



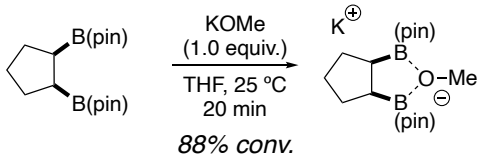
1.122 35.0 ppm — *48% conv.* — **1.123** 8.8 ppm

(b) Treatment of bis(boronic ester) with KOMe[a]



1.43 35.5 ppm — *84% conv.* — **1.124** 11.6 ppm

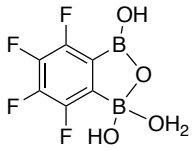
(c) Treatment of *cis*-1,2-diborylcyclopentane with KOMe[a]



88% conv.

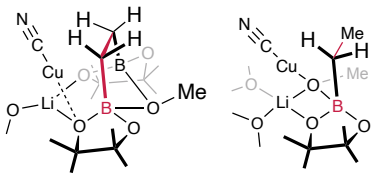
1.125 35.1 ppm — **1.126** 13.2 ppm

(d) Oxygen-bridged 1,2-phenylenediboronate anion



CCDC: 1002723

(e) Ground state structures of methoxide-activated vicinal bis(boronic ester) and EtB(pin)[b]



1.127 B–C–C=108.5° — **1.128** B–C–C=113.8°

[a]Reactions were carried out under argon atmosphere. Conversions of organoboronic esters were determined by analysis of ^{11}B NMR spectra of unpurified mixtures (±5%). [b]Ground state geometries were optimized with DFT methodology. The B3LYP-D3 functional and 6-311++G** basis sets were employed. Tetrahydrofuran solvation was modeled with the PCM model.

1.4 Conclusions

We have developed a method for Cu-catalyzed site-selective coupling of 1,2-bis(boronic esters) with allyl, alkynyl, propargyl electrophiles and a proton. The propensity of bis(boronic esters) to participate in coupling reactions offers new synthesis strategies for generation of strategically functionalized chiral organoboronic esters from aliphatic terminal alkene building blocks. We anticipate that these processes will be of considerable utility in preparation of bioactive molecules.

The robustness of the catalytic process enabled a large-scale single-flask reaction in tandem with α-olefin diboration.

Mechanistic studies have revealed the vital roles that vicinal boronic ester plays in this reaction, where the two boronic esters simultaneously chelate with an alkoxide. The unique reactivity of chelated "ate" complexes in transmetallation foreshadows the development of other metal-catalyzed couplings.

1.5 Acknowledgments

I thank Prof. James P. Morken for providing me the opportunity to study this project. I am also grateful for Dr. Ziyin Kong for her valuable contribution and her work on DFT analysis. I would like to thank Johnny Wang for his hard work, and Dr. Gabriel Lovinger for his contribution to DFT analysis. I appreciate the insightful discussions with all the other Morken group members.

This work was supported financially by the NIH (R35-GM1217140). We thank Boston College and the chemistry department for assistance.

1.6 Experimental Section

1.6.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), Varian Gemini-400 (400 MHz), Varian Inova-500 (500 MHz) spectrometer or a AVANCE NEO 500 MHz spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125

MHz), Varian Gemini-600 (150 MHz), Varian Gemini-400 (105 MHz), a Varian Inova-500 (125 MHz) or a AVANCE NEO 500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. ^{11}B NMR spectra were recorded on a Varian Gemini-500 (160 MHz), Varian Inova-500 (160 MHz) or a AVANCE NEO 500 (160 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry direct analysis in real time (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed with forced flow (flash chromatography) on silica gel (SiO_2, 230 × 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed with ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and potassium permanganate ($KMnO_4$) in water. Analytical chiral supercritical fluid chromatography (SFC) was performed either on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector or a Jasco SFC-4000 analytical SFC system with isopropanol as the modifier on CHIRALCEL OD-H, CHIRALCEL OJ-H, CHIRALPAK AD-H, CHIRALPAK AS-H or CHIRALCEL OD-RH from Chiral Technologies. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel OD-H column.

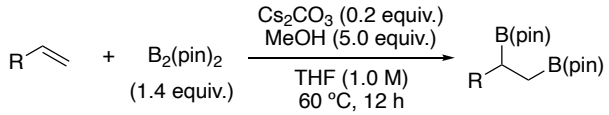
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon unless otherwise stated. Tetrahydrofuran (THF) was purified by Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. 3,3,3-trichloroprop-1-ene was purchased

from Combi Blocks and used without purification. Methanol, 1-bromo-2-butyne, 3-chloro-2-methylpropene, butadiene monoxide, 3-bromo-2-bromomethyl-1-propene, ethyl 2-(bromomethyl)acrylate, 2-methyl-2-vinyloxirane were purchased from Aldrich and used without purification. 1,4-dichloro-2-butyne, 2-(chloromethyl)-3,5-dioxahex-1-ene were purchased from TCI America and used without purification. Copper(I) cyanide and lithium methoxide were purchased from Oakwood Chemicals and used without purification. 2,3-dibormopropene was purchased from AK Scientific and used without purification. All other reagents were purchased from either Alfa Aesar or Acros and used without purification.

1.6.2 Experimental Procedures

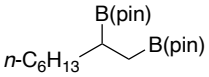
1.6.2.1 Procedures for Preparation of Boronic Substrates

General Procedure A: Preparation of racemic 1,2-bis(boronic pinacol esters)

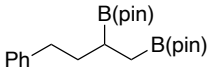


Racemic 1,2-bis(boronic pinacol esters) were prepared according to a modified literature procedure.[59] Cesium carbonate (0.20 equiv.) and bis(pinacolato)diboron (1.40 equiv.) were transferred into an oven-dried flask with a stir bar, under argon. THF (1.0 M) was added to dissolve the mixture. Subsequently, the alkene (1.0 equiv.) and MeOH (5.0 equiv.) were added, and the mixture was allowed to stir at 60 ºC overnight, after which it was filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel chromatography with EtOAc/hexanes.

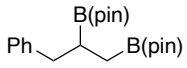
[59] Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyás, H.; Fernández, E. *Angew. Chem., Int. Ed.* **2011**, *50* (31), 7158–7161.



2,2'-(1-Hexyl-1,2-ethanediyl)bis[4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (1.129). This compound was prepared according to *General Procedure A* with 1-octene (1.6 g, 10 mmol), bis(pinacolato)diboron (3.6 g, 14 mmol), cesium carbonate (651 mg, 2.0 mmol), methanol (1.6 g, 50 mmol) and THF (10 mL). The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 80% (2.9 g, 8.0 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[60]

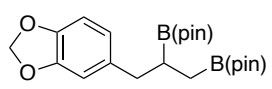


2,2'-[1-(2-Phenylethyl)-1,2-ethanediyl]bis[4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (1.43). This compound was prepared according to *General Procedure A* with but-3-enylbenzene (2.6 g, 20 mmol), bis(pinacolato)diboron (5.6 g, 22 mmol), cesium carbonate (1.3 g, 4.0 mmol), methanol (3.2 g, 100 mmol) and THF (20 mL). The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 64% (4.9 g, 12.8 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[60]

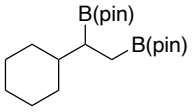


2,2'-[1-(Phenylmethyl)-1,2-ethanediyl]bis[4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (1.130). This compound was prepared according to *General Procedure A* with allylbenzene (1.2 g, 10 mmol), bis(pinacolato)diboron (3.6 g, 14 mmol), cesium carbonate (651 mg, 2.0 mmol), methanol (1.6 g, 50 mmol) and THF (10 mL). The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 82% (2.9 g, 8.2 mmol) of the product as colorless oil. All spectral data are in accordance with the literature. [60]

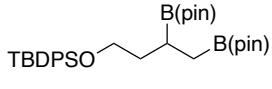
[60] Wang, X.-X.; Li, L.; Gong, T.-J.; Xiao, B.; Lu, X.; Fu, Y. *Org. Lett.* **2019**, *21*, 4298–4302.



2-[1-(1,3-Benzodioxol-5-ylmethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.131). This compound was prepared according to *General Procedure A* with 5-allyl-1,3-benzodioxole (811 mg, 5.0 mmol), bis(pinacolato)diboron (1.8 g, 7.0 mmol), cesium carbonate (326 mg, 1.0 mmol), methanol (801 mg, 25 mmol) and THF (5.0 mL). The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 88% (1.8 g, 4.4 mmol) of the product as colorless viscous gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 – 6.43 (m, 3H), 5.72 (s, 2H), 2.56 (dd, *J* = 13.5, 7.4 Hz, 1H), 2.36 (dd, *J* = 13.5, 7.3 Hz, 1H), 1.23 (tt, *J* = 13.8, 7.3, 1H), 1.19 – 0.89 (m, 24H), 0.65 (d, *J* = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 145.5, 136.4, 122.1, 109.8, 107.9, 100.9, 83.1, 39.4, 25.1. IR (neat) ν_{max} 2977 (m), 2925 (br), 1489 (m), 1441 (w), 1370 (s), 1314 (s), 1247 (s), 1142 (s), 1040 (m), 968 (w), 848 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{22}H_{35}B_2O_6$ 417.2614; Found 417.2627.

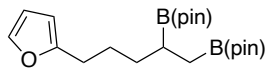


2,2'-(1-Cyclohexyl-1,2-ethanediyl)bis[4,4,5,5-tetramethyl-1,3,2-Dioxaborolane] (1.132). This compound was prepared according to *General Procedure A* with vinylcyclohexane (551 mg, 5.0 mmol), bis(pinacolato)diboron (1.8 g, 7.0 mmol), cesium carbonate (326 mg, 1.0 mmol), methanol (801 mg, 25 mmol) and THF (5.0 mL). The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 65% (3.2 g, 3.24 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[59]

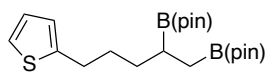


2,2'-[4-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1,2-butanediyl]bis[4,4,5,5-tetramethyl]-1,3,2-dioxaborolane (1.133). This compound was prepared according to *General Procedure A*. with but-3-enoxy-tert-butyl-diphenyl-silane (777 mg, 2.5 mmol), bis(pinacolato)diboron (635 mg, 2.5 mmol), cesium carbonate (123

mg, 0.38 mmol), methanol (401 mg, 12.5 mmol) and THF (2.5 mL). The colorless oil residue was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford 75% (1.06 g, 1.9 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[61]



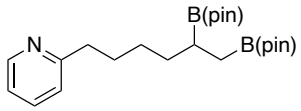
2-[4-(2-Furyl)-1-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]butyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.134). This compound was prepared according to *General Procedure A* with 2-pent-4-enylfuran (154 mg, 1.1 mmol), bis(pinacolato)diboron (402 mg, 1.6 mmol), cesium carbonate (181 mg, 0.23 mmol), methanol (182 mg, 5.7 mmol) and THF (1.0 mL). The colorless oil residue was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford 73% (313 mg, 0.8 mmol) of the product as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 2.0 Hz, 1H), 6.24 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.95 (dt, *J* = 3.1, 0.9 Hz, 1H), 2.59 (t, *J* = 7.7 Hz, 2H), 1.64 (m, 2H), 1.56 – 1.47 (m, 1H), 1.43 – 1.33 (m, 1H), 1.22 (m, 24H), 1.13 – 1.17 (m, 1H), 0.80 – 0.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9, 140.7, 110.2, 104.6, 83.1, 33.5, 28.4, 27.4, 25.3, 25.1, 24.9. IR (neat) ν_{max} 2977 (m), 2925 (m), 2854 (w), 2226 (w), 2039 (w), 1740 (w), 1378 (s), 1314 (s), 1271 (w), 1215 (w), 1142 (s), 968 (w), 848 (w), 691 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{21}H_{37}B_2O_5$ 391.2821; Found 391.2830.



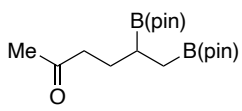
4,4,5,5-Tetramethyl-2-[1-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-4-(2-thienyl)butyl]-1,3,2-dioxaborolane (1.135). This compound was prepared according *General Procedure A* with 2-pent-4-enylthiophenen (609 mg, 4.0 mmol), bis(pinacolato)diboron (1.4 g, 5.6 mmol), cesium carbonate (261 mg, 0.8 mmol),

[61] Farre, A.; Soares, K.; Briggs, R. A.; Balanta, A.; Benoit, D. M.; Bonet, A. *Chem. Eur. J.* **2016**, *22*, 17552–17556.

methanol (641 mg, 20 mmol) and THF (4.0 mL). The yellow oil residue was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford 86% (1.4 g, 3.4 mmol) of the product as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07 (dd, *J* = 5.1, 0.9 Hz, 1H), 6.88 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.76 (dd, *J* = 3.3, 1.0 Hz, 1H), 2.86 – 2.76 (m, 2H), 1.75 – 1.64 (m, 2H), 1.54 (m, 1H), 1.41 (m, 1H), 1.22 (m, 24H), 1.13 – 1.17 (m, 1H), 0.80 – 0.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.2, 126.8, 124.0, 122.9, 83.1, 33.5, 31.3, 30.4, 25.19, 25.16.; IR (neat) ν_{max} 2977 (m), 2930 (br), 2032 (w), 1379 (s), 1314 (s), 1214 (w), 1143 (s), 1005 (w), 968 (w), 884 (w), 848 (w), 726 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{21}H_{37}B_2O_4S$ 407.2593; Found 407.2603.

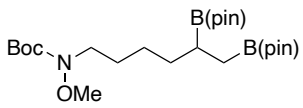


2-[5,6-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]pyridine (1.136). This compound was prepared according to *General Procedure A* with 2-hex-5-enylpyridine (645 mg, 4.0 mmol), bis(pinacolato)diboron (1.4 g, 5.6 mmol), cesium carbonate (261 mg, 0.80 mmol), methanol (641 mg, 20 mmol) and THF (4.0 mL). The colorless oil residue was purified by silica gel chromatography (10% EtOAc in hexanes with 2% triethylamine, stained in CAM) to afford 90% (1.5 g, 3.6 mmol) of the product as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 – 8.46 (m, 1H), 7.55 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.12 (d, *J* = 7.9 Hz, 1H), 7.06 (m, 1H), 2.81 – 2.68 (m, 2H), 1.73 – 1.65 (m, 2H), 1.52 – 1.44 (m, 1H), 1.35 (m, 3H), 1.25 – 1.17 (m, 24H), 1.10 (m, 1H), 0.77 – 0.85 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8, 149.1, 136.3, 122.8, 121.1, 83.0, 38.7, 33.9, 30.4, 28.8, 25.2. IR (neat) ν_{max} 2977 (m), 2925 (m), 2854 (w), 2226 (w), 2039 (w), 1740 (w), 1378 (s), 1314 (s), 1271 (w), 1215 (w), 1142 (s), 968 (w), 848 (w), 691 (w). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{23}H_{40}B_2NO_4$ 416.3138; Found 416.3153.

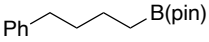


5,6-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-2-one (1.137). This compound was prepared according to *General Procedure A* with hex-5-

en-2-one (982 mg, 10 mmol), bis(pinacolato)diboron (3.6 g, 14 mmol), cesium carbonate (651 mg, 2.0 mmol), methanol (1.6 g, 50 mmol) and THF (10 mL). The colorless oil residue was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford 65% (2.3 g, 6.5 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[62]



***tert*-Butyl *N*-[5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-N-methoxy-carbamate (1.138).** This compound was prepared according to *General Procedure A* with *tert*-butyl *N*-hex-5-enyl-*N*-methoxy-carbamate (2.1 g, 9.0 mmol), bis(pinacolato)diboron (3.6 g, 14 mmol), cesium carbonate (440 mg, 1.4 mmol), methanol (1.5 g, 45 mmol) and THF (9.0 mL). The colorless oil residue was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford 67% (2.9 g, 6.0 mmol) of the product as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.38 – 3.34 (m, 2H), 1.59 – 1.53 (m, 3H), 1.48 – 1.43 (m, 9H), 1.33 – 1.27 (m, 4H), 1.20 (s, 24H), 0.84 – 0.74 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 83.1, 81.1, 62.6, 62.5, 49.6, 33.7, 28.6, 28.5, 27.6, 25.2, 25.1, 18.6. IR (neat) ν_{max} 2977 (br), 1704 (m), 1369 (s), 1313 (s), 1144 (s), 968 (w), 847 (w). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{24}H_{48}B_2NO_7$ 484.3611; Found 484.3628.

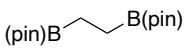


4,4,5,5-Tetramethyl-2-(4-phenylbutyl)-1,3,2-dioxaborolane (1.139). This compound was prepared according to the literature procedure[63] and all spectral data are in accordance with the literature.[64]

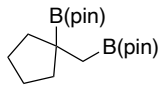
[62] Rzhevskiy, S. A.; Topchiy, M. A.; Lyssenko, K. A.; Philippova, A. N.; Belaya, M. A.; Ageshina, A. A.; Bermeshev, M. V.; Nechaev, M. S.; Asachenko, A. F. *J. Organomet. Chem.* **2020**, *912*, 121140.

[63] Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695–10700.

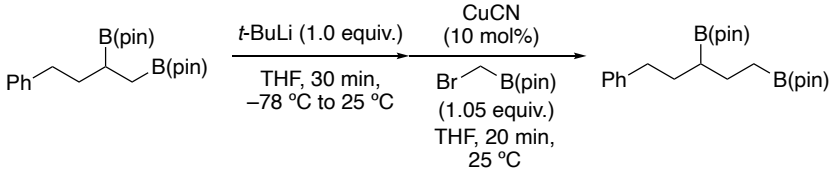
[64] Li, S.; Hu, C.; Cui, X.; Zhang, J.; Liu, L. L.; Wu, L. *Angew. Chem., Int. Ed.* **2021**, *60*, 26238–26245.



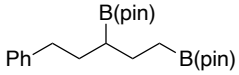
1,2-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethane (1.140). This compound was prepared according to the literature procedure with ethylene gas as the alkene feedstock and all spectral data are in accordance with the literature.[65]



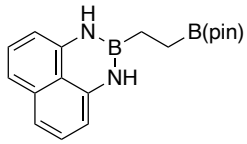
4,4,5,5-Tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (1.141). To a flame-dried Schlenk flask were added methylenecyclopentane (821.4 mg, 10 mmol) and sodium *t*-butoxide (672.7 mg, 7.0 mmol), after which the flask was evacuated and back-filled with nitrogen three times. Subsequently, anhydrous methanol (25 mL), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (3.6 g, 14.0 mmol) were added. The resulting suspension was allowed to stir at 70 ºC for 16 h, after which the mixture was filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure and the colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford 75% (2.5 g, 7.5 mmol) of the product as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84 – 1.77 (m, 2H), 1.67 – 1.49 (m, 4H), 1.29 – 1.25 (m, 2H), 1.23 (s, 12H), 1.21 (s, 12H), 0.89 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.73, 82.70, 37.6, 25.1, 24.8, 24.7.; IR (neat) ν_{max} 2974 (w), 2942 (w), 2866 (w), 1450 (w), 1358 (m), 1300 (m), 1272 (w), 1212 (w), 1192 (m), 1139 (s), 1109 (w), 968 (w), 882 (w), 846 (w), 671 (w), 578 (w). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{18}H_{35}B_2O_4$: 337.2716; Found 337.2721.



[65] Willems, S.; Toupalas, G.; Reisenbauer, J. C.; Morandi, B. *Chem. Commun.* **2021**, *57*, 3909–3912.



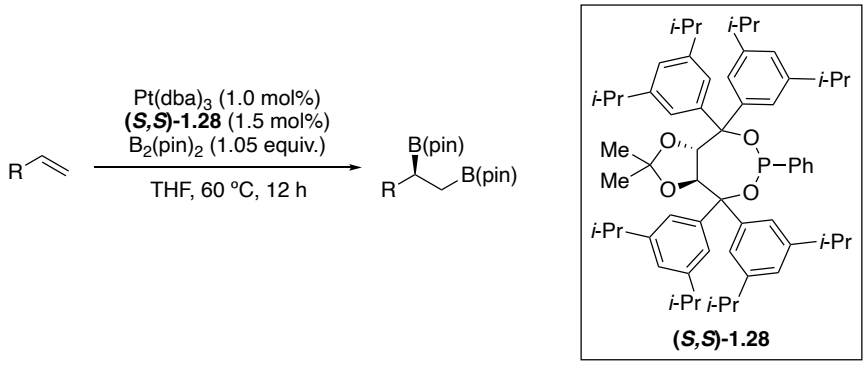
2,2'-(5-Phenylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.142). This compound was prepared according to the procedure above. To an oven-dried round-bottom flask with a magnetic stir bar in an Ar-filled glovebox was added 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **1.43** (1.9 g, 5.0 mmol), THF (12.5 mL), the flask was transferred out of glovebox. *t*-butyllithium (3.3 mL, 1.5 M, 5.0 mmol) was added dropwise to the solution under –78 ºC. The mixture was allowed to stir at –78 ºC for 5 min before allowed to warm to 25 ºC over 25 min. 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.16 g, 5.05 mmol) and copper cyanide (44.8 mg, 0.5 mmol) was added under inert atmosphere. The mixture was allowed to stir at 25 ºC for another 20 min. The colorless oil residue was purified by silica gel chromatography (4% EtOAc in hexanes, stained in CAM) to afford the product as colorless oil (1.86 g, 4.7 mmol, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 2H), 7.19 – 7.11 (m, 3H), 2.58 (qdd, J = 13.6, 10.1, 6.1 Hz, 2H), 1.78 – 1.62 (m, 2H), 1.59 – 1.49 (m, 2H), 1.25 – 1.21 (m, 24H), 1.02 (tt, J = 8.7, 6.1 Hz, 1H), 0.86 – 0.71 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.2, 128.4, 128.1, 125.4, 82.9, 35.5, 33.2, 25.2, 24.9, 24.82, 24.79 (overlapped).; IR (neat) ν_{max} 2974 (w), 2925 (w), 2857 (w), 1453 (w), 1368 (s), 1311 (s), 1269 (w), 1213 (w), 1140 (s), 1108 (w), 966 (m), 866 (w), 846 (m), 747 (w), 698 (m), 671 (w), 578 (w). All spectral data are in accordance with the literature.[36a]



2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine (1.143). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added $Pt(dba)_3$ (6.7 mg, 7.50 μmol), $B_2(pin)_2$ (66 mg, 0.26 mmol) and 2-vinyl-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine (48 mg, 0.25 mmol). The mixture was dissolved in anhydrous THF (0.25 mL) and was allowed to stir at 60 ºC for 16 h. The mixture was filtered

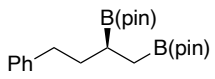
through a pad of silica gel and was directly used in the following step without purification. The reaction was performed according to *General Procedure G* with *2-(1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine* (0.25 mmol, 1.0 equiv., unpurified from previous step), methanol (9.6 mg, 0.30 mmol), copper cyanide (4.5 mg, 0.05 mmol), lithium methoxide (29 mg, 0.75 mmol) in THF (0.75 mL). The white solid mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained in CAM) to afford the product as colorless gel (70 mg, 0.22 mmol, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.1 – 7.1 (m, 2H), 7.0 (d, *J* = 8.3 Hz, 2H), 6.3 (d, *J* = 7.3 Hz, 2H), 5.9 (s, 2H), 1.3 (s, 12H), 1.0 – 0.9 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 127.7, 117.3, 105.4, 83.5, 25.1. IR(neat) ν_{max} 2925 (m), 1371 (m), 1142 (m), 1588 (w), 1315 (w), 1213 (w). HRMS (DART) for $C_{18}H_{24}B_2O_2N_2$ $(M+H)^+$ calculated: 323.20967, found 323.20982.

General Procedure B: Preparation of enantiomerically enriched 1,2-bis(boronic pinacol esters)

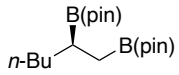


Enantiomerically enriched 1,2-bis(boronic pinacol esters) were prepared according to a literature procedure.[23] To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (1.0 mol%), **(*S,S*)-1.28** (1.5 mol%), and $B_2(pin)_2$ (1.05 equiv.). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added by syringe, and the mixture was allowed to stir at 80 ºC for 30 min. The flask was allowed to cool to room temperature and was charged with terminal alkene (1.0 equiv.). After purging once more with N_2,

the mixture was allowed to stir at 60 ºC overnight, after which it was filtered through a silica gel plug and concentrated under reduced pressure. The residue was purified by silica gel chromatography (5% EtOAc in hexanes) to afford the products.



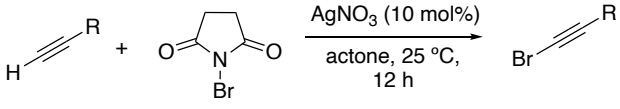
(S)-2,2'-(4-Phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S-1.43). This compound was prepared according to *General Procedure B* with but-3-enylbenzene (396.61 mg, 3.0 mmol), bis(pinacolato)diboron (761.8 mg, 3.15 mmol), $Pt(dba)_3$ (26.9 mg, 0.03 mmol), **(*S,S*)-1.28** (35.9 mg, 0.045 mmol) and THF (3 mL). The colorless oil residue was purified by silica gel chromatography (5% EtOAc in hexanes, stained in CAM) to afford 90% (1.0 g, 2.7 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[60] This compound was subjected to transformations without analysis of stereochemistry.



(S)-2,2'-(Hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.75). This compound was prepared according to *General Procedure B* with 1-hexene (252.27 mg, 3.0 mmol), bis(pinacolato)diboron (761.8 mg, 3.15 mmol), $Pt(dba)_3$ (26.94 mg, 0.03 mmol), **(*S,S*)-1.28** (35.9 mg, 0.045 mmol) and THF (3 mL). The colorless oil residue was purified by silica gel chromatography (5% EtOAc in hexanes, stained in CAM) to afford 77% (780 mg, 2.3 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[60] This compound was subjected to transformations without analysis of stereochemistry.

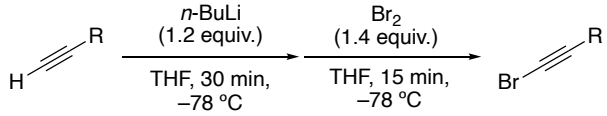
1.6.2.2 Procedures for Preparation of Alkynyl Bromides

General Procedure C: Preparation of alkynyl bromides

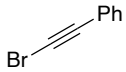


To the mixture of alkyne (1.0 equiv.), NBS (1.2 equiv.), and acetone (0.2 M), silver nitrate (0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvent was evaporated, and the residue was purified by silica gel chromatography in hexanes.

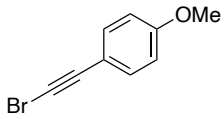
General Procedure D: Preparation of alkynyl bromides



n-BuLi (1.2 equiv.) was added dropwise to a stirring solution of the alkyne (1.0 equiv.) in THF (3.0 M) at −78 ºC. The solution was allowed to stir at −78 ºC for 30 min, then bromine (1.4 equiv.) was added dropwise. The mixture was allowed to stir for another 15 min, after which the reaction was quenched by addition of a saturated aqueous solution of $Na_2S_2O_3$ and then allowed to warm to 25 ºC. The mixture was washed with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated to afford the corresponding bromoalkyne, which was used without purification.



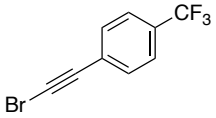
(Bromoethynyl)benzene (1.144). This compound was prepared according to *General Procedure D* with *n*-BuLi (2.5 M, 16 mL, 40 mmol), ethynylbenzene (4.0 g, 31 mmol), bromine (6.8 g, 43 mmol) and THF (10 mL) to give 87% (4.88 g, 27 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[66]



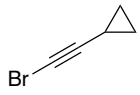
1-(Bromoethynyl)-4-methoxybenzene (1.145). This compound was prepared according to *General Procedure C* with 1-ethynyl-4-methoxy-benzene (1.3 g, 10 mmol), NBS (2.2 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg,

[66] Beltran, F.; Fabre, I.; Ciofini, I.; Miesch, L. *Org. Lett.* **2017**, *19*, 5042–5045.

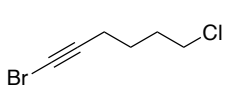
1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 90% (1.9 g, 9.0 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[66]



1-(Bromoethynyl)-4-(trifluoromethyl)benzene (1.146). This compound was prepared according to *General Procedure C* with 1-ethynyl-4-(trifluoromethyl)benzene (1.7 g, 10 mmol), NBS (2.2 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 56% (1.4 g, 5.6 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[67]



(Bromoethynyl)cyclopropane (1.147). This compound was prepared according to *General Procedure C* with ethynylcyclopropane (992 mg, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 45% (982 mg, 6.8 mmol) of the product as colorless, volatile liquid. All spectral data are in accordance with the literature.[68]

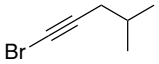


1-Bromo-6-chlorohex-1-yne (1.148). This compound was prepared according to *General Procedure C* with 6-chlorohex-1-yne (1.2 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 79% (1.54 g, 7.9 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[69]

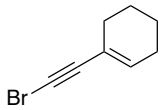
[67] Watanabe, K.; Mino, T.; Ishikawa, E.; Okano, M.; Ikematsu, T.; Yoshida, Y.; Sakamoto, M.; Sato, K.; Yoshida, K. *Eur. J. Org. Chem.* **2017**, *16*, 2359–2368.

[68] Li, C.; Pati, K.; Lin, G.; Sohel, S. Md. A.; Hung, H.; Liu, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 9891–9894.

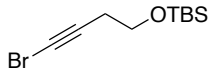
[69] Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006***, 71*, 5743–5747.



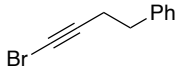
1-Bromo-4-methylpent-1-yne (1.149). This compound was prepared according to *General Procedure C* with 4-methylpent-1-yne (1.2 g, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 62% (1.5 g, 9.3 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[70]



(Bromoethynyl)cyclohex-1-ene (1.150). This compound was prepared according to *General Procedure C* with 4-methylpent-1-yne (1.2 g, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 67% (1.85 g, 10 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[71]



((4-Bromobut-3-yn-1-yl)oxy)(tert-butyl)dimethylsilane (1.151). This compound was prepared according to *General Procedure C* with (but-3-yn-1-yloxy)(tert-butyl)dimethylsilane (1.8 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 75% (1.98 g, 7.5 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[72]



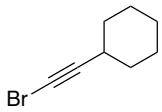
(4-Bromobut-3-yn-1-yl)benzene (1.152). This compound was prepared according to *General Procedure C* with but-3-ynylbenzene (1.3 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid

[70] Peng, B.; Huang, X.; Xie, L.; Maulide, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 8718–8721.

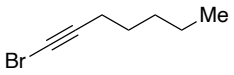
[71] Gao, Y.; Yang, C.; Bai, S.; Liu, X.; Wu, Q.; Wang, J.; Jiang, C.; Qi, X. *Chem.* **2020**, *6*, 675–688.

[72] Chen, A.; Yu, H.; Yan, J.; Huang, H. *Org. Lett.* **2020**, *22*, 755–759.

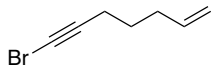
residue was purified by silica gel chromatography in hexanes to afford 86% (1.8 g, 8.6 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[73]



(Bromoethynyl)cyclohexane (1.153). This compound was prepared according to *General Procedure C* with ethynylcyclohexane (750 mg 6.9 mmol), NBS (1.5 g, 8.3 mmol), and acetone (50 mL), silver nitrate (118 mg, 0.069 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 35% (460 mg, 2.5 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[74]



1-Bromohept-1-yne (1.154). This compound was prepared according to *General Procedure C* with hept-1-yne (0.96 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 89% (1.56 g, 8.9 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[75]



7-Bromohept-1-en-6-yne (1.155). This compound was prepared according to *General Procedure C*, with hept-1-en-6-yne (2.10 g, 22.3 mmol), NBS (4.76 g, 26.8 mmol), and acetone (223 mL), silver nitrate (379 mg, 2.23 mmol). The colorless oil residue was purified by silica gel chromatography in pentane to afford the product as colorless oil (2.24 g, 12.9 mmol, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddt, J = 17.2, 10.2, 6.7 Hz, 1H), 5.04 (dt, J = 17.2, 1.7 Hz, 1H), 4.99 (dd, J = 10.2, 1.7 Hz, 1H), 2.22 (t, J = 7.1 Hz, 2H), 2.20 – 2.09 (m, 2H), 1.61 (dd, J = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 115.5, 80.2, 38.0, 32.8, 27.6, 19.2.

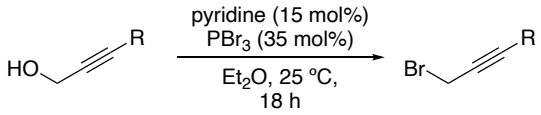
[73] Gauthier, R.; Mamone, M.; Paquin, J.-F. *Org. Lett.* **2020**, *21*, 9024–9027.

[74] Pan, R.; Shi, C.; Zhang, D.; Tian, Y.; Guo, S.; Yao, H.; Lin, A. *Org. Lett.* **2019**, *21*, 8915–8920.

[75] Barbu, E.; Tsibouklis, J. *Tetrahedron Lett.* **1996**, *37*, 5023-5026.

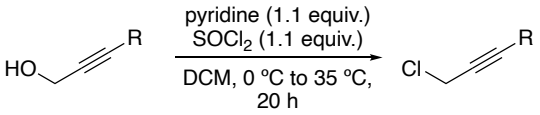
1.6.2.3 Procedure for Preparation of Propargyl Halides

General Procedure E: Preparation of propargyl bromides



To a stirring solution of propargyl alcohol (1.0 equiv.) and pyridine (0.15 equiv.) at 25 ºC in Et_2O was slowly added a solution of phosphorus tribromide (0.35 equiv.) in Et_2O (2.0 mL). The resulting solution was allowed to stir for 18 h at room temperature and was quenched by addition of a saturated aqueous solution of $NaHCO_3$ (80 mL). The mixture was washed with Et_2O (3 × 45 mL). Combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography in hexanes.

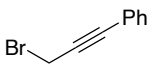
General Procedure F: Preparation of propargyl chlorides



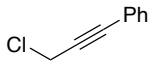
In a flame-dried flask was added propargyl alcohol (1.0 equiv.), anhydrous and degassed CH_2Cl_2 and pyridine (1.1 equiv.) under argon. After the addition of $SOCl_2$ (1.1 equiv.) at 0 ºC, the mixture was allowed to stir at 35 °C for 20 h. The solution was poured into water (20 mL) and the resulting mixture was washed with CH_2Cl_2 (3 × 15 mL). The organic layers were dried over anhydrous $MgSO_4$. After concentration under reduced pressure, the resulting residue was purified by silica gel chromatography in hexanes.

(3-Bromoprop-1-yn-1-yl) trimethylsilane (1.156). This compound was prepared according to *General Procedure E* without pyridine. With 3-trimethylsilylprop-2-yn-1-ol (1.7 g, 13 mmol), phosphorus tribromide (1.2 g, 4.5 mmol), and Et_2O (20 mL). The

colorless oil residue was purified by silica gel chromatography in hexanes to afford 68% (1.7 g, 8.9 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[76]

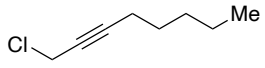


(3-Bromoprop-1-yn-1-yl)benzene (1.157). This compound was prepared according to *General Procedure E* with 3-phenylprop-2-yn-1-ol (661 mg, 5.0 mmol), pyridine (59 mg, 0.75 mmol), phosphorus tribromide (541 mg, 2.0 mmol), and Et_2O (20 mL). The brown oil residue was purified by silica gel chromatography in hexanes to afford 86% (846 mg, 4.3 mmol) of the product as yellow oil. All spectral data are in accordance with the literature.[77]



(3-Chloroprop-1-yn-1-yl)benzene (1.158). This compound was prepared according to *General Procedure F* with 3-phenylprop-2-yn-1-ol (3.9 g, 30 mmol), pyridine (2.6 g, 33 mmol), thionyl chloride (3.9 g, 33 mmol), and CH_2Cl_2 (20 mL). The yellow oil residue was purified by silica gel chromatography in hexanes to afford 84% (3.8 g, 25.2 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[78]

6-Chlorohex-1-en-4-yne (1.159). This compound was prepared according to *General Procedure F* with hex-5-en-2-yn-1-ol (385 mg, 4.0 mmol), pyridine (348 mg, 4.4 mmol), thionyl chloride (523 mg, 4.4 mmol), and CH_2Cl_2 (10 mL). The colorless oil residue was purified by silica gel chromatography in hexanes to afford 53% (243 mg, 2.1 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[79]



1-Chlorooct-2-yne (1.160). This compound was prepared according to *General Procedure F* with oct-2-yn-1-ol (505 mg, 4.0 mmol), pyridine (348

[76] Xin, T. T.; Lei, W.; Lv, Y.; Li, Z. *Eur. J. Org. Chem.* **2020***,* 4425–4428.

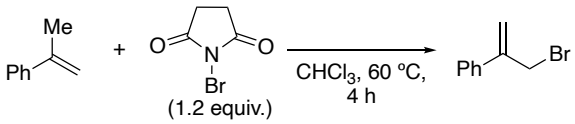
[77] Kleinbeck, F.; Toste, D. F. *J. Am. Chem. Soc.* **2009**, *131*, 9178–9179.

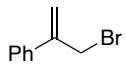
[78] Pereira, A. R.; Cabezas, J. A. *J. Org. Chem.* **2005**, *70*, 2594–2597.

[79] Bieber, L. W.; Silva, M. F. *Tetrahedron Lett.* **2007**, *48*, 7088–7090.

mg, 4.4 mmol), phosphorus tribromide (523 mg, 4.4 mmol), and CH_2Cl_2 (10 mL). The colorless oil residue was purified by silica gel chromatography in hexanes to afford 61% (354 mg, 2.45 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[78]

1.6.2.4 Procedure for Preparation of Allyl Bromides

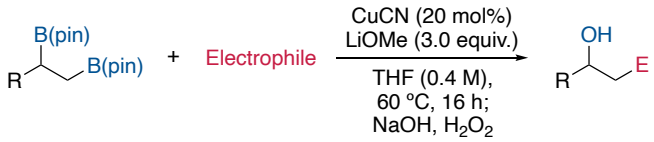




(3-Bromoprop-1-en-2-yl)benzene (1.161). This compound was prepared according to a procedure illustrated above. To a solution of isopropenylbenzene (1.2 g, 10 mmol, 1.0 equiv.) in 6.0 mL $CHCl_3$ was added NBS (2.1 g, 12 mmol, 1.2 equiv.). The mixture was heated to reflux and allowed to stir for 4 h. Then the mixture was concentrated and Et_2O was added. The formed precipitate was filtered off and then the mixture was concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography in hexanes to give 83% (1.6 g, 8.3 mmol) of the product as yellow oil. All spectral data are in accordance with the literature.[80]

1.6.2.5 Procedures for Cu-Catalyzed Cross-coupling

General Procedure G: Preparation from 1,2-bis(boronic esters)

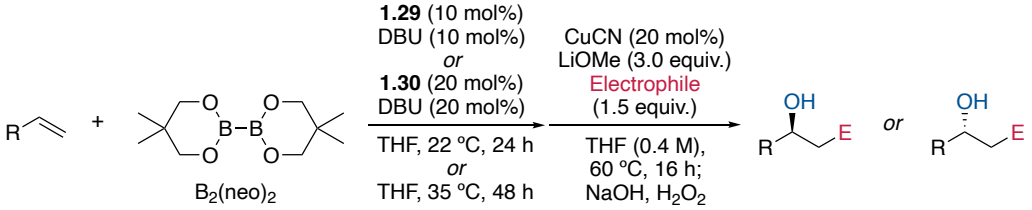


To an oved dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added copper cyanide (0.040 mmol, 0.20 equiv.), lithium methoxide (0.60 mmol, 3.0 equiv.), 1,2-bis(boronic ester) (0.20 mmol, 1.0 equiv.), electrophile (1.5–3.0 equiv.) and THF (0.50 mL). The

[80] Budai, B.; Leclair, A.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2019**, *58*, 10305–10309.

reaction vial was sealed with a polypropylene cap, taped and brought out of the glovebox. The mixture was allowed to stir at 60 ºC for 16 h, and was allowed to cool to room temperature, filtered through a silica gel plug, and concentrated under reduced pressure. The mixture was diluted with THF (1.5 mL), cooled to 0 ºC in an ice bath, and 3.0 M NaOH (1.0 mL) was added, followed by 30% H_2O_2 (1.0 mL) dropwise. The mixture was allowed to warm up to room temperature and was allowed to stir for 2 h. The mixture was cooled to 0 °C and a saturated aqueous solution of $Na_2S_2O_3$ (3.0 mL) was added dropwise. The mixture was allowed to warm to room temperature and the aqueous layer was washed with EtOAc (3 × 1 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure, and subsequently purified by silica gel chromatography to afford the desired products.

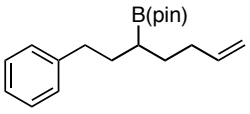
General Procedure H: Preparation from alkenes



To an oved dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added TBS-DHG catalyst **1.29** (0.02 mmol, 0.1 equiv.) or DHR catalyst **1.30** (0.04 mmol, 0.2 equiv.), bis(neopentyl glycolato)diboron (0.20 mmol, 1.0 equiv.), the alkene substrate (0.20 mmol, 1.0 equiv.) and THF (0.50 mL). DBU (0.02 mmol, 0.1 equiv.) or (0.04 mmol, 0.2 equiv.) was then added to the solution. The vial was sealed with a polypropylene cap, taped and brought out of the glovebox where it was allowed to stir at 22 ºC for 24 h (TBS-DHG) or 35 ºC for 48 h (DHR). The

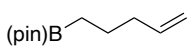
vial was brought back into the glovebox and copper cyanide (0.040 mmol, 0.20 equiv.), lithium methoxide (0.60 mmol, 3.0 equiv.), 1,2-bis(boronic ester) (0.20 mmol, 1.0 equiv.), electrophile (1.5–3.0 equiv.) were added. The vial was brought out of the glovebox where it was allowed to stir at 60 ºC for 16 h. The mixture was allowed to cool to room temperature, filtered through a silica gel plug, and concentrated under reduced pressure. The mixture was diluted with THF (1.5 mL), cooled to 0 ºC in an ice bath, then 3.0 M NaOH (1.0 mL) was added, followed by 30% H_2O_2 (1.0 mL) dropwise. The mixture was allowed to warm to room temperature and was allowed to stir for 2 h. The mixture was cooled to 0 °C and a saturated aqueous solution of $Na_2S_2O_3$ (3.0 mL) was added dropwise. The mixture was allowed to warm up to room temperature and the aqueous layer was washed with ethyl acetate (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure, and subsequently purified by silica gel chromatography to afford the desired products.

1.6.3 Characterization of Cu-Catalyzed Cross-Coupling Products and Analysis of Stereochemistry

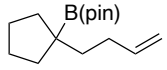


4,4,5,5-Tetramethyl-2-(1-phenylhept-6-en-3-yl)-1,3,2-dioxaborolane (1.44). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[4-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl]-1,3,2-dioxaborolane (77.3 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M), without oxidation after 16 h at 60 ºC. The colorless liquid mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes) to afford the product as colorless liquid (56 mg, 0.19 mmol, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 2H), 7.18 – 7.13 (m, 3H), 5.80 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 4.98 (dq, J = 17.1, 1.5 Hz, 1H), 4.91

(ddd, J = 10.1, 2.3, 1.1 Hz, 1H), 2.59 (qdd, J = 13.4, 10.3, 6.0 Hz, 2H), 2.13 – 1.97 (m, 2H), 1.74 (dddd, J = 13.0, 10.4, 8.8, 5.7 Hz, 1H), 1.65 (ddd, J = 13.1, 10.5, 6.5 Hz, 1H), 1.62 – 1.51 (m, 1H), 1.48 (ddd, J = 13.1, 9.5, 6.6 Hz, 1H), 1.25 (s, 12H), 1.07 (tt, J = 8.9, 6.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 139.1, 128.4, 128.2, 125.6, 114.3, 83.0, 35.6, 33.41, 33.40, 30.6, 24.89, 24.86. IR (neat) ν_{max} 2977 (m), 2924 (m), 1380 (s), 1371 (s), 1316 (s), 1264 (w), 1143 (s), 699 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{19}H_{30}BO_2$ 301.23397 ; Found 301.23334.

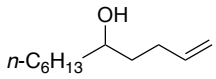


4,4,5,5-Tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane (1.45). This compound was prepared according to *General Procedure G* with 1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethane (56.4 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M), without oxidation after 16 h at 60 ºC. The colorless liquid mixture was purified by silica gel chromatography (1% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (33.7 mg, 0.17 mmol, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 4.99 (ddd, J = 17.1, 2.6, 1.1 Hz, 1H), 4.93 (ddt, J = 10.2, 2.3, 1.2 Hz, 1H), 2.11 – 1.99 (m, 2H), 1.58 – 1.46 (m, 2H), 1.24 (s, 13H), 0.79 (t, J = 7.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 114.4, 82.9, 36.4, 24.8, 23.4. IR (neat) ν_{max} 2958 (m), 2924 (m), 2855 (m), 1729 (m), 1463 (m), 1379 (w), 1273 (m), 1123 (w), 1073 (w) cm^{-1}. HRMS (DART) m/z: $[M-CH_2]^+$ Calcd for $C_{10}H_{20}BO_2$ 183.155635; Found 183.13650.

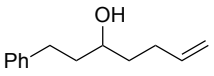


2-(1-(But-3-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.46). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol,

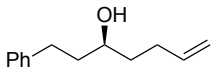
3.0 equiv.) in THF (0.50 mL, 0.4 M), without oxidation after 16 h at 60 ºC. The colorless liquid mixture was purified by silica gel chromatography (2% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (26.7 mg, 0.1 mmol, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.98 (ddt, *J* = 17.1, 2.2, 1.6 Hz, 1H), 4.89 (ddt, *J* = 10.2, 2.3, 1.2 Hz, 1H), 2.08 – 1.96 (m, 2H), 1.86 – 1.76 (m, 2H), 1.64 – 1.59 (m, 2H), 1.58 – 1.50 (m, 2H), 1.48 – 1.43 (m, 2H), 1.29 – 1.25 (m, 2H), 1.23 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.8, 113.7, 82.9, 38.2, 35.3, 32.3, 25.2, 24.7. IR (neat) ν_{max} 2974 (w), 2945 (w), 2865 (w), 1638 (w), 1452 (w), 1407 (s), 1341 (s), 1271 (m), 1140 (s), 993 (w), 966 (w), 905 (m), 854 (m), 671 (w), 579 (w), 446 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{15}H_{28}BO_2$: 251.2177; Found 251.2184.



Undec-1-en-5-ol (1.47). This compound was prepared according to *General Procedure G* with 2,2'-(octane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.2 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (2% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (26.6 mg, 0.16 mmol, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.05 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.97 (dd, *J* = 10.1, 1.8 Hz, 1H), 3.61 (dq, *J* = 8.4, 4.4, 3.9 Hz, 1H), 2.21 (td, *J* = 14.7, 6.4 Hz, 1H), 2.13 (h, *J* = 6.8 Hz, 1H), 1.61 – 1.39 (m, 7H), 1.31 – 1.26 (m, 6H), 0.88 (t, *J* = 6.4 Hz, 3H)., ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 114.8, 71.7, 37.7, 36.6, 32.0, 30.2, 29.5, 25.7, 22.8, 14.2.; IR (neat) ν_{max} 3352 (br), 3062 (w), 2878 (m), 2956 (w), 2936 (m), 2859 (w), 1661 (m), 1462 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{11}H_{22}O$ 170.1671; Found 170.1664.



1-Phenylhept-6-en-3-ol (1.48). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (78.2 mg, 0.20 mmol), allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) were added. The colorless liquid mixture was purified by silica gel chromatography (6% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (32.7 mg, 0.17 mmol, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (m, 2H), 7.27 – 7.17 (m, 3H), 5.86 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.07 (dd, *J* = 16.9, 1.5 Hz, 1H), 5.00 (dd, *J* = 10.2, 1.5 Hz, 1H), 3.68 (tt, *J* = 8.2, 4.5 Hz, 1H), 2.82 (m, 1H), 2.76 – 2.67 (m, 1H), 2.30 – 2.13 (m, 2H), 1.88 – 1.75 (m, 2H), 1.61 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.3, 138.7, 128.6 (2 overlapped signals), 126.1, 115.1, 71.1, 39.3, 36.7, 32.2, 30.2. IR (neat) ν_{max} 3343 (br), 3062 (w), 2975 (w), 2857 (w), 2158 (w), 1640 (m), 1153 (w), 1078 (w), 910 (m), 644 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{13}H_{19}O$ 191.1344; Found 191.1345.



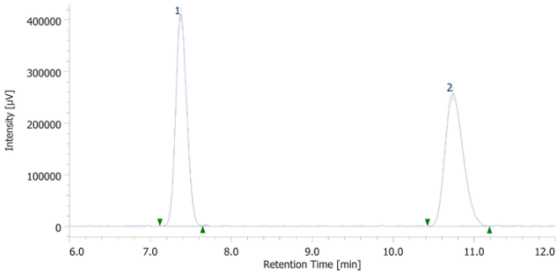
(*S*)-1-Phenylhept-6-en-3-ol (S-1.48). This compound was prepared according to *General Procedure H* with TBS-DHG catalyst (5.3 mg, 0.020 mmol, 0.10 equiv.), Bis(neopentyl glycolato)diboron (90.4 mg, 0.40 mmol, 2.00 equiv.), but-3-en-1-ylbenzene (26.4 mg, 0.20 mmol, 1.0 equiv.), DBU (3.1 mg, 0.02 mmol, 0.1 equiv.) and THF (0.50 mL). After the diboration, allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) were added. The pale-yellow liquid mixture was purified by silica gel chromatography (6% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (29.2 mg, 0.14 mmol, 72% yield, 96:4 e.r). $[\alpha]^{20}_{D}$: +12.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Method G* with racemic 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Absolute stereochemistry was assigned by analogy.

Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 40 °C, 200-400 nm)– analysis of 1-phenylhept-6-en-3-ol

Racemic Material



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
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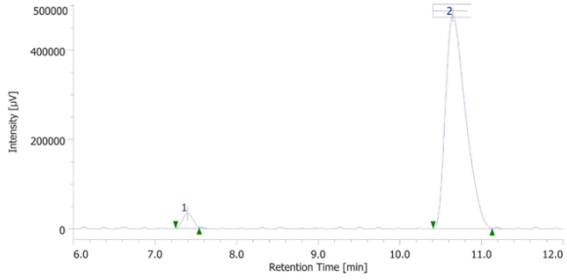
2	Unknown	11	10.737	4016408	256964	50.462	38.534

Standard Conditions



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
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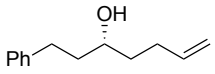


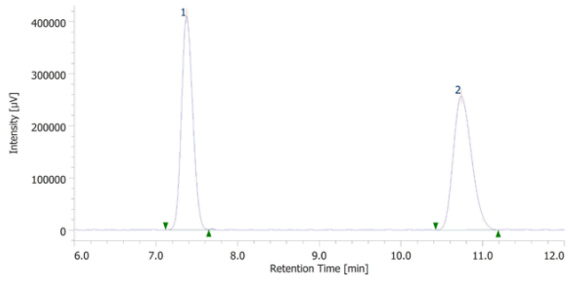
(*R*)-1-Phenylhept-6-en-3-ol (R-1.48). This compound was prepared according to *General Procedure H* with DHR catalyst (13.3 mg, 0.10 mmol, 0.10 equiv.), Bis(neopentyl glycolato)diboron (226 mg, 1.0 mmol, 2.00 equiv.), but-3-en-1-ylbenzene (66 mg, 0.50 mmol, 1.0 equiv.), DBU (15.2 mg, 0.10 mmol, 0.1 equiv.) and THF (1.25 mL). After the diboration, allyl bromide (90.8 mg, 0.75 mmol, 1.5 equiv.), copper cyanide (9.0 mg, 0.10 mmol, 0.20 equiv.), lithium methoxide 57 mg, 1.50 mmol, 3.0 equiv.) were added. The yellow liquid mixture was purified by silica gel chromatography (6% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (57.9 mg, 0.31 mmol, 61% yield, 4:96 er). $[\alpha]^{20}_{D}$: –11.7 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Method G* with racemic 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane).

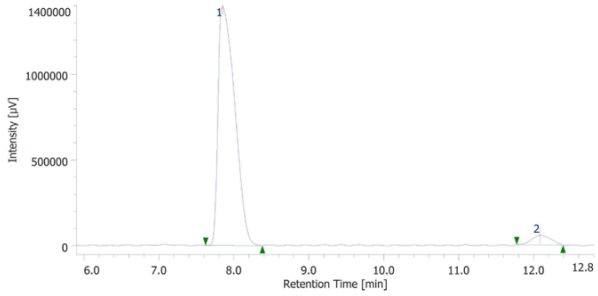
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 40 °C, 200-400 nm)– analysis of 1-phenylhept-6-en-3-ol

Racemic Material

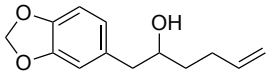


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	Unknown	11	7.373	3942801	409887	49.538	61.466
2	Unknown	11	10.737	4016408	256964	50.462	38.534

Standard Conditions

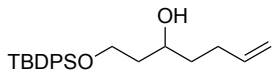


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	Unknown	11	7.850	21527920	1391757	95.554	96.130
2	Unknown	11	12.083	1001765	56030	4.446	3.870

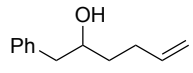


1-(Benzo[d][1,3]dioxol-5-yl)hex-5-en-2-ol (1.49). This compound was prepared according to *General Procedure G* with 2,2'-(3-(benzo[*d*][1,3]dioxol-5-yl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (83 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (39 mg, 0.18 mmol, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 – 6.57 (m, 3H), 5.94 (s, 2H), 5.85 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.06 (dd, *J* = 16.9, 1.7 Hz, 1H), 5.01 – 4.95 (m, 1H), 3.79 (tt, *J* = 8.5, 4.4 Hz, 1H), 2.75 (dd, *J* = 13.7,

4.4 Hz, 1H), 2.58 (dd, *J* = 13.7, 8.5 Hz, 1H), 2.36 – 2.10 (m, 2H), 1.73 – 1.51 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.9, 146.4, 138.6, 132.3, 122.5, 115.1, 109.9, 108.5, 101.1, 72.3, 43.9, 35.9, 30.3. IR (neat) ν_{max} 3390 (br), 2916 (w), 1640 (w), 1502 (s), 1354 (w), 1121 (m), 809 (m), 607 (w) cm^{-1}. HRMS (DART) m/z: $[M+H-H_2O]^+$ Calcd for $C_{13}H_{15}O_2$ 203.1061; Found 203.1066.

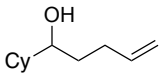


1-((*tert*-Butyldiphenylsilyl)oxy)hept-6-en-3-ol (1.50). This compound was prepared according to *General Procedure G* with (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-butyl)diphenylsilane (113 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (57 mg, 0.15 mmol, 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 – 7.69 (m, 4H), 7.46 – 7.40 (m, 6H), 5.87 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.06 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.98 (dd, *J* = 10.2, 1.1 Hz, 1H), 3.98 – 3.82 (m, 3H), 3.23 (s, 1H), 2.28 – 2.20 (m, 1H), 2.20 – 2.11 (m, 1H), 1.77 – 1.61 (m, 3H), 1.58 – 1.51 (m, 1H), 1.08 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.9, 135.81, 135.79, 133.3, 133.2, 130.09, 130.06, 128.0, 114.8, 71.4, 63.7, 38.6, 36.9, 30.1, 27.1, 19.3. IR (neat) ν_{max} 3377 (br), 3145 (w), 3057 (w), 2992 (w), 1530 (w), 1453 (m), 1087 (w), 978 (s), 701 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}O_2$ 368.2172; Found 368.2164.

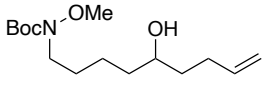


1-Phenylhex-5-en-2-ol (1.51). This compound was prepared according to *General Procedure G* with 2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (74.4 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.2 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel

chromatography (6% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (32 mg, 0.18 mmol, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.27 – 7.19 (m, 3H), 5.85 (dd, *J* = 17.1, 10.2, 6.7 Hz, 1H), 5.06 (dd, *J* = 17.1, 1.7 Hz, 1H), 4.99 (dd, *J* = 10.2, 1.7 Hz, 1H), 3.85 (m, 1H), 2.84 (dd, *J* = 13.5, 4.3 Hz, 1H), 2.67 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.33 – 2.24 (m, 1H), 2.18 (m, 1H), 1.66 – 1.58 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.7, 138.65, 129.7, 128.7, 126.7, 115.1, 72.4, 44.1, 36.1, 29.9. IR (neat) ν_{max} 3382 (br), 3062 (w), 2957 (w), 2852 (w), 1640 (m), 1321 (m), 1081 (w), 910 (m), 701 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}O$ 176.1201; Found 176.1204.

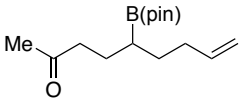


1-Cyclohexylpent-4-en-1-ol (1.52). This compound was prepared according to *General Procedure G* with 2,2'-(1-cyclohexylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (72.8 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (6% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (28 mg, 0.17 mmol, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 (ddt, *J* = 17.0, 10.2, 6.6 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.8 Hz, 1H), 4.97 (dd, *J* = 10.2, 1.8 Hz, 1H), 3.38 (ddd, *J* = 8.9, 5.4, 3.3 Hz, 1H), 2.29 – 2.07 (m, 2H), 1.85 – 1.57 (m, 4H), 1.42 – 1.06 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.1, 114.9, 75.9, 43.9, 33.5, 30.6, 29.9, 29.5, 28.0, 26.8, 26.6. IR (neat) ν_{max} 3345 (br), 3077 (w), 2924 (w), 2852 (w), 2208 (m), 1640 (w), 1282 (w), 1086 (m), 643 (w) cm^{-1}. HRMS (DART) m/z: $[M+H-H_2O]^+$ Calcd for $C_{11}H_{19}$ 151.1482; Found 151.1481.



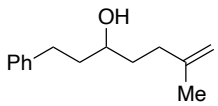
***tert*-Butyl (5-hydroxynon-8-en-1-yl)(methoxy)carbamate (1.53)**. This compound was prepared according to *General Procedure G* with *tert*-butyl (5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2 yl)hexyl)(methoxy)carbamate (96.6 mg, 0.20

mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (41.8 mg, 0.14 mmol, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.04 (dd, *J* = 16.9, 1.8 Hz, 1H), 4.96 (dd, *J* = 10.2, 1.8 Hz, 1H), 3.66 (s, 3H), 3.61 (tt, *J* = 8.3, 4.3 Hz, 1H), 3.43 (t, *J* = 7.2 Hz, 2H), 2.24 – 2.16 (m, 1H), 2.16 – 2.08 (m, 1H), 1.67 – 1.43 (m, 17H), 1.40 – 1.33 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 138.5, 114.7, 81.1, 71.1, 62.1, 48.71, 37.1, 36.4, 30.1, 28.3, 27.1, 22.6. IR (neat) ν_{max} 3447 (br), 3276 (w), 2934 (w), 2865 (w), 1701 (s), 1640 (m), 1392 (w), 1367 (m), 1073 (w), 909 (w), 737 (m) cm^{-1}.HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{15}H_{30}NO_4$ 288.2172; Found 288.2169.

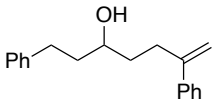


5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)non-8-en-2-one (1.54). This compound was prepared according to *General Procedure G* <u>without oxidation</u> with 5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-2-one (70.4 mg, 0.20 mmol, 1.0 equiv.), allyl bromide (36.3 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (39.4 mg, 0.15 mmol, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 4.99 (dd, *J* = 17.2, 1.8 Hz, 1H), 4.92 (dd, *J* = 10.2, 1.1 Hz, 1H), 2.43 (td, *J* = 7.6, 3.2 Hz, 2H), 2.12 (s, 3H), 2.06 (dq, *J* = 16.7, 7.1, 6.7 Hz, 2H), 1.75 – 1.63 (m, 2H), 1.55 – 1.48 (m, 1H), 1.46 – 1.39 (m, 1H), 1.24 – 1.19 (m, 12H), 1.01 – 0.93 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 209.5, 139.2, 114.7, 83.3, 43.5, 33.4, 30.7, 30.1, 25.4, 25.10, 25.09, 25.06. IR (neat) ν_{max} 3297 (w), 2962 (w), 2864 (w), 1700 (s), 1640 (m),

1364 (m), 1071 (w), 966 (w), 624 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{15}H_{27}BO_3$: 266.2053; Found 266.2056.

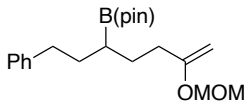


6-Methyl-1-phenylhept-6-en-3-ol (1.55). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 3-chloro-2-methylprop-1-ene (28 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (33 mg, 0.16 mmol, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.13 (m, 5H), 4.73 (m, 2H), 3.66 (tt, *J* = 7.7, 4.6 Hz, 1H), 2.75 (m, 2H), 2.23 – 2.02 (m, 2H), 1.90 – 1.76 (m, 2H), 1.74 (m, 3H), 1.68 – 1.56 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.1, 142.3, 128.6, 126.1 (2 overlapped signals), 110.4, 71.5, 39.3, 35.5, 34.2, 32.3, 22.7. IR (neat) ν_{max} 3359(br), 3060(m), 2859(s), 1650(m), 1495(w), 1450(w), 1088(m), 1030(m), 746(m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{21}O$ 205.1589; Found 205.1587.

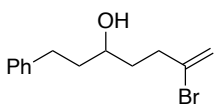


1,6-Diphenylhept-6-en-3-ol (1.56). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), (3-bromoprop-1-en-2-yl)benzene (59.1 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (35.4 mg, 0.13 mmol, 67% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (dt, *J* = 8.3, 1.2 Hz, 2H), 7.36 – 7.29 (m, 2H), 7.31 – 7.22 (m, 3H), 7.17 (d, *J* = 7.2 Hz, 3H), 5.27 (s, 1H), 5.08 (s, 1H), 3.67 (dddd, *J* = 7.9, 4.1 Hz, 1H), 2.76 (ddd, *J* = 14.9, 9.5, 5.9 Hz, 1H),

2.73 – 2.61 (m, 2H), 2.56 (ddd, *J* = 14.7, 9.5, 6.4 Hz, 1H), 1.82 – 1.71 (m, 2H), 1.69 – 1.57 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.5, 142.3, 141.2, 128.63 (overlapped), 128.57, 127.7, 126.3, 126.1, 112.8, 71.2, 39.3, 36.3, 32.3, 31.8. IR (neat) ν_{max} 3338 (br), 3079 (s), 2940 (m), 2880 (m), 1680 (w), 1495 (w), 1028 (w), 908 (m). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{19}H_{23}O$ 267.1740; Found 267.1743.

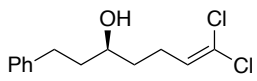


2-(6-(Methoxymethoxy)-1-phenylhept-6-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.57). This compound was prepared according to *General Procedure G* without oxidation with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 3-chloro-2-(methoxymethoxy)prop-1-ene (41 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (37 mg, 0.15 mmol, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 2H), 7.22 – 7.12 (m, 3H), 4.93 (s, 2H), 4.07 (d, *J* = 1.8 Hz, 1H), 3.97 (d, *J* = 1.8 Hz, 1H), 3.41 (s, 3H), 2.71 – 2.53 (m, 2H), 2.21 – 2.05 (m, 2H), 1.82 – 1.63 (m, 4H), 1.27 (s, 12H), 1.09 (tt, *J* = 8.8, 6.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2, 143.0, 128.4, 128.2, 125.6, 93.4, 83.9, 83.0, 56.1, 35.5, 34.4, 33.3, 28.8, 24.8. IR (neat) ν_{max} 2975 (w), 2923 (m), 2855 (w), 1630 (w), 1453 (m), 1379 (m), 1315 (w), 1261 (w), 1143 (s), 1096 (w), 1026 (s), 965 (w), 925 (w), 851 (w), 814 (w), 747 (w), 699 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{21}H_{34}BO_4$: 361.2545; Found 361.2553.



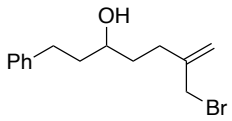
6-Bromo-1-phenylhept-6-en-3-ol (1.58). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 2,3-

dibromoprop-1-ene (60 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (43 mg, 0.16 mmol, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 2H), 7.25 – 7.15 (m, 3H), 5.60 (d, *J* = 1.5 Hz, 1H), 5.41 (d, *J* = 1.5 Hz, 1H), 3.67 (tt, *J* = 6.5, 3.4 Hz, 1H), 2.80 (ddd, *J* = 13.7, 9.2, 6.4 Hz, 1H), 2.75 – 2.47 (m, 3H), 1.89 – 1.75 (m, 3H), 1.68 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.0, 134.5, 128.7, 128.6, 126.0, 117.1, 70.5, 39.4, 37.9, 35.1, 32.2. IR (neat) ν_{max} 3343 (br), 2980 (w), 2931 (m), 2859 (w), 1630 (m), 1454 (m), 1373 (m), 1154 (m), 1058 (w), 951 (w), 885 (w), 746 (w), 700 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{13}H_{18}OBr$ 269.0463; Found 269.0459.

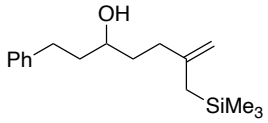


(*S*)-7,7-Dichloro-1-phenylhept-6-en-3-ol (1.59). This compound was prepared according to *General Procedure G* with (*S*)-2,2' (4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 3,3,3-trichloroprop-1-ene (44 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The pale-yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (41 mg, 0.16 mmol, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H), 7.25 – 7.18 (m, 3H), 5.88 (t, *J* = 7.5 Hz, 1H), 3.65 (tt, *J* = 8.3, 4.4 Hz, 1H), 2.80 (ddd, *J* = 13.7, 9.5, 6.0 Hz, 1H), 2.69 (ddd, *J* = 13.7, 9.4, 6.8 Hz, 1H), 2.41 – 2.21 (m, 2H), 1.89 – 1.70 (m, 2H), 1.68 – 1.51 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 129.4, 128.5, 128.4, 125.9, 120.3, 70.6, 39.1, 35.6, 32.0, 26.0. IR (neat) ν_{max} 3380(br), 2941(s), 2857(m), 1496(m), 1263(w), 999(w), 928(w), 735(m). HRMS (DART) m/z: $[M+H]^+$ Calcd for

$C_{13}H_{17}OCl_2$ 259.0571; Found 259.0580. This compound was subjected to transformations without analysis of stereochemistry.

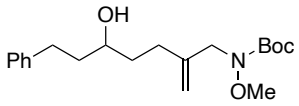


6-(Bromomethyl)-1-phenylhept-6-en-3-ol (1.60). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 3-bromo-2-(bromomethyl)prop-1-ene (65 mg, 0.30 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (48 mg, 0.17 mmol, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 5.19 (d, *J* = 1.4 Hz, 1H), 4.98 (d, *J* = 1.4 Hz, 1H), 3.98 (d, *J* = 1.4 Hz, 2H), 3.67 (tt, *J* = 8.2, 4.3 Hz, 1H), 2.87 – 2.76 (m, 1H), 2.70 (ddd, *J* = 14.0, 9.3, 6.8 Hz, 1H), 2.39 (ddd, *J* = 15.6, 10.2, 5.6 Hz, 1H), 2.28 (ddd, *J* = 15.6, 10.2, 6.1 Hz, 1H), 1.81 (m, 2H), 1.76 – 1.56 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4, 142.1, 128.7, 128.6, 126.1, 115.4, 71.1, 39.3, 37.1, 35.4, 32.2, 29.7. IR (neat) ν_{max} 3375(br), 2940(s), 2875(m), 1495(m), 1429(w), 1090(w), 887(w), 746(m). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{20}OBr$ 283.0688; Found 283.0692.

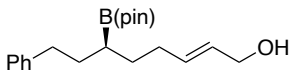


1-Phenyl-6-((trimethylsilyl)methyl)hept-6-en-3-ol (1.61). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), (2-(chloromethyl)allyl)trimethylsilane (98 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (29 mg, 0.14 mmol,

70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 2H), 7.24 – 7.14 (m, 3H), 4.63 (d, *J* = 1.4 Hz, 1H), 4.54 (d, *J* = 1.4 Hz, 1H), 3.66 (tt, *J* = 8.1, 4.4 Hz, 1H), 2.81 (ddd, *J* = 13.7, 9.5, 6.0 Hz, 1H), 2.69 (ddd, *J* = 13.7, 9.5, 6.8 Hz, 1H), 2.17 – 2.08 (m, 1H), 2.08 – 2.00 (m, 1H), 1.85 – 1.72 (m, 2H), 1.71 – 1.58 (m, 3H), 1.56 – 1.52 (m, 2H), 0.03 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.9, 142.4, 128.7, 128.6, 126.0, 107.5, 71.6, 39.4, 35.8, 34.7, 32.3, 27.0, -1.1. IR (neat) ν_{max} 3382 (br), 3062 (w), 2957 (w), 2852 (w), 1640 (m), 1453 (m), 1081 (w), 910 (m), 699 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{17}H_{29}OSi$ 277.1981; Found 277.1982.



***tert*-Butyl-(5-hydroxy-2-methylene-7-phenylheptanoyl)(methoxy)carbamate (1.62).** This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl (3-chloroprop-1-en-2-yl)(methoxy)carbamate (118 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (49 mg, 0.14 mmol, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (m, 2H), 7.23 – 7.14 (m, 3H), 4.95 (d, *J* = 1.6 Hz, 1H), 4.90 (d, *J* = 1.6 Hz, 1H), 4.02 (m, 2H), 3.64 (s, 3H), 2.79 (ddd, *J* = 13.8, 9.3, 6.2 Hz, 1H), 2.66 (ddd, *J* = 13.8, 9.3, 7.0 Hz, 1H), 2.20 (ddd, *J* = 15.2, 9.8, 5.5 Hz, 1H), 2.10 (ddd, *J* = 15.2, 9.8, 6.2 Hz, 1H), 1.80 – 1.72 (m, 2H), 1.71 – 1.59 (m, 2H), 1.48 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.3, 144.5, 142.3, 128.6, 128.5, 125.9, 112.6, 81.6, 71.1, 62.3, 53.8, 39.4, 35.7, 32.3, 29.7, 28.5. IR (neat) ν_{max} 3288 (w), 2960 (w), 2862 (w), 1701 (s), 1643 (m), 1360 (m), 1071 (w), 966 (w), 624 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{20}H_{32}O_4N$ 350.2326; Found 350.2334.



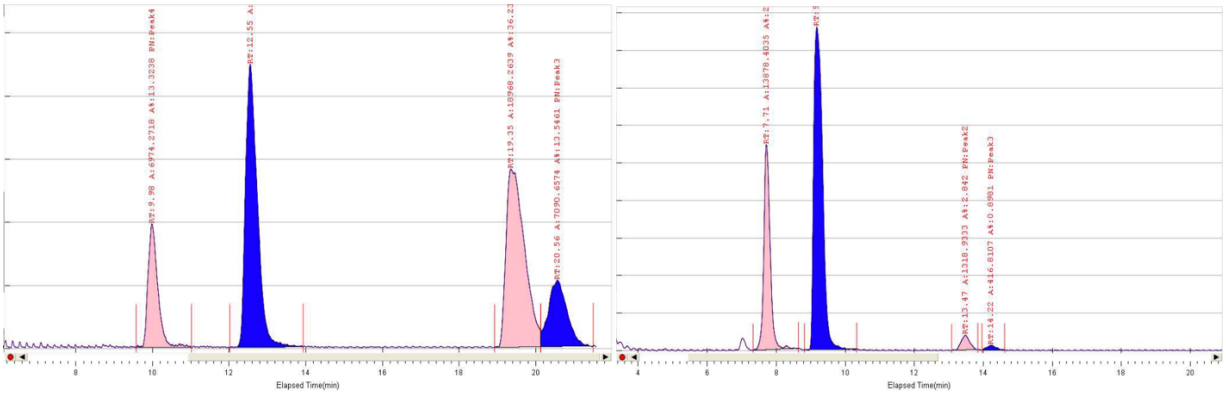
(*S*,*E*)-8-Phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-en-1-ol (1.64). This compound was prepared according to *General Procedure G* without oxidation with (*S*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.43** (77.2 mg, 0.20 mmol, 1.0 equiv.), 2-vinyloxirane (70.1 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (49 mg, 0.15 mmol, 74% yield, *E*/*Z* = 3.2:1 (integrated from ^{13}C and ^{1}H NMR), 96:4 er). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 2H), 7.23 – 7.12 (m, 3H), 5.76 – 5.47 (m, 2H), 4.25 – 4.01 (m, 2H), 2.69 – 2.50 (m, 2H), 2.14 – 2.01 (m, 2H), 1.81 – 1.71 (m, 1H), 1.71 – 1.61 (m, 1H), 1.61 – 1.53 (m, 1H), 1.52 – 1.45 (m, 1H), 1.32 – 1.23 (m, 12H), 1.08 (ddd, *J* = 9.0, 7.4, 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.93, 142.87 (minor), 133.4, 133.2 (minor), 129.0, 128.8 (minor), 128.38, 128.36 (minor), 128.24 (minor), 128.22, 125.60 (minor), 125.57, 83.2 (minor), 83.0, 63.8, 58.2 (minor), 35.6 (minor), 35.5, 33.7 (minor), 33.3, 31.7, 31.1 (minor), 30.6, 26.9 (minor), 24.90 (minor), 24.85, 24.84, 24.79 (minor). IR (neat) ν_{max} 3417 (br), 2977 (s), 2922 (m), 2886 (m), 1457 (w), 1387 (w), 1315 (w), 1233 (m), 967 (m), 737 (s), 586 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{20}H_{32}O_3B$ 331.2417; Found 331.2368. $[\alpha]^{20}_D$: +11.6 (c = +1.2, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

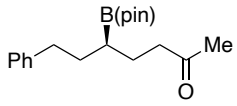
Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 8-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-en-1-ol

Racemic Compound Standard Conditions



Peak No	% Area	Area	RT (min)
1	13.3238	6974.2718	9.98
2	36.8929	19311.4636	12.55
3	36.2372	18968.2639	19.35
4	13.5461	7090.6574	20.56
Total:	100	52344.6567	

Peak No	% Area	Area	RT (min)
1	29.9046	13878.4035	7.71
2	66.3553	30794.8382	9.16
3	2.842	1318.9333	13.47
4	0.8981	416.8107	14.22
Total:	100	46408.9857	



(*R*)-7-Phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptan-2-one (1.65). This compound was prepared according to *General Procedure G* without oxidation with (*S*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.43** (77.2 mg, 0.20 mmol), 3-chloro-2-(methoxymethoxy)prop-1-ene (81.95 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.6 mmol, 3.0 equiv.) were added to a 2-dram vial, then THF (0.5 mL, 0.4 M) was added. The reaction vial was sealed with a polypropylene cap, taped and brought out of the glovebox where it was allowed to stir at 60 °C for 16 h. The mixture was allowed to cool to room temperature, filtered through a silica gel plug, and concentrated under reduced pressure. The mixture was diluted with THF (1.0 mL) and a saturated aqueous solution of NH_4Cl (1.0 mL), followed by addition of two drops (20 μL) of HCl (6.0 N). The mixture was allowed to stir at room temperature for 30 min, diluted with EtOAc (5.0 mL) and a saturated aqueous solution of $NaHCO_3$ (5.0 mL). The mixture was washed with EtOAc (3 × 5 mL) and the combined organics were dried over anhydrous Na_2SO_4.

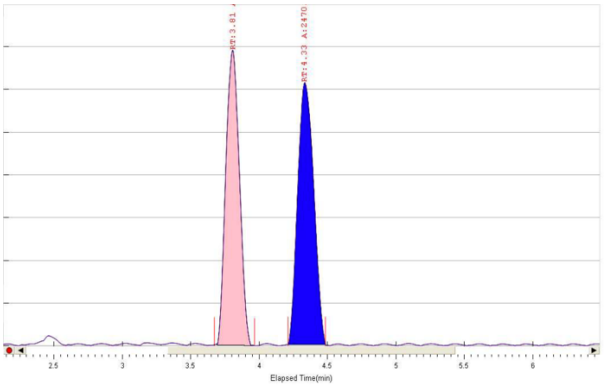
Filtration and concentration in vacuo furnished colorless oil, which was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (30.20 mg, 0.09 mmol, 47% yield, 97:3 er). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.17 (m, 3H), 2.61 (dd, J = 13.6, 6.0 Hz, 2H), 2.44 (dt, J = 7.6, 4.0 Hz, 2H), 2.13 (s, 3H), 1.72 (m, 2H), 1.67 – 1.60 (m, 2H), 1.27 (s, 12H), 1.03 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.2, 142.8, 128.4, 128.2, 125.6, 83.1, 43.3, 35.4, 33.2, 29.8, 25.1, 24.9. IR (neat) ν_{max} 2977 (m), 2926 (m), 2857 (w), 1716 (s), 1454 (w), 1380 (m), 1319 (m), 1143 (s), 967 (w), 772 (s), 700 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{19}H_{30}O_3B$ 317.2210; Found 317.1990. $[\alpha]^{20}_D$: +0.97 (c = 1.0, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 7-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptan-2-one.

Racemic Compound



Peak No	% Area	Area	RT (min)
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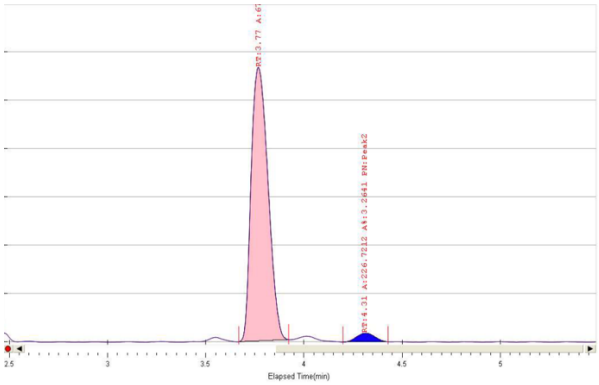
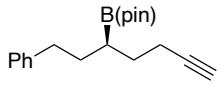
2	50.135	1108.5626	4.31
Total:	100	2211.1564	

Standard Conditions

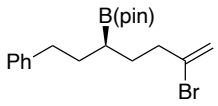


Peak No	% Area	Area	RT (min)
1	96.7359	6719.085	3.77
2	3.2641	226.7212	4.31
Total:	100	6945.8062	



(*R*)-2-(6-Bromo-1-phenylhept-6-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.67). This compound was prepared according to *General Procedure G* without oxidation with (*S*)-4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane **S-1.43** (115.9 mg, 0.30 mmol, 1.0 equiv.), 2,3-dibromoprop-1-ene (89.9 mg, 0.45 mmol, 1.5 equiv.), copper cyanide (8.1 mg, 0.090 mmol, 0.3 equiv.), lithium methoxide (34.2 mg, 0.90 mmol, 3.0 equiv.) in THF (0.75 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained in KMnO4) to afford the product as colorless liquid (78 mg, 0.21 mmol, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 2H), 7.23 – 7.16 (m, 3H), 5.55 (d, J = 1.5 Hz, 1H), 5.39 (d, J = 1.6 Hz, 1H), 2.63 (qdd, J = 13.5, 10.3, 6.0 Hz, 2H), 2.51 – 2.41 (m, 2H), 1.84 – 1.64 (m, 4H), 1.29 (s, 12H), 1.10 (tt, J = 8.6, 6.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.8, 134.9, 128.4, 128.3, 125.6, 116.3, 83.1, 40.9, 35.5, 33.2, 29.6, 24.9. IR (neat) ν_{max} 2977 (m), 2927 (m), 2858 (w), 1629 (w), 1379 (s), 1316 (s), 1214 (m), 1143 (s), 966 (m), 883 (m), 747 (w), 699 (m) cm^{-1}. HRMS

(DART) m/z: $[M+H]^+$ Calcd for $C_{19}H_{29}BO_2Br$ 379.1438; Found 379.1450. The title compound was subjected to transformations without analysis of stereochemistry.



(*S*)-4,4,5,5-Tetramethyl-2-(1-phenylhept-6-yn-3-yl)-1,3,2-dioxaborolane (1.66). The reaction was performed according to the literature procedure with (*R*)-2-(6-bromo-1-phenylhept-6-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1.66** (114 mg, 0.3 mmol, 1.0 equiv.), potassium *tert*-butoxide (37 mg, 0.33 mmol, 1.1 equiv.), toluene (5.4 mL) and THF (0.54 mL).[81] The pale-yellow liquid mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (58 mg, 0.28 mmol, 93% yield, 96:4 e.r). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.24 – 7.11 (m, 3H), 2.63– 2.71 (m, 2H), 2.32 – 2.14 (m, 2H), 1.95 (s, 1H), 1.81 – 1.63 (m, 4H), 1.27 (s, 12H), 1.21 (tt, J = 8.7, 6.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.8, 134.9, 128.4, 128.3, 125.6, 116.3, 83.1, 40.9, 35.4, 33.2, 29.5, 24.9.; IR (neat) ν_{max} 2977 (m), 2928 (m), 2859 (w), 1454 (m), 1380 (s), 1318 (s), 1234 (m), 1150 (s), 966 (w), 851 (w), 748 (w), 699 (m), 631 (w) cm^{-1}. HRMS (DART) m/z: $[M+NH_4]^+$ Calcd for $C_{19}H_{31}BO_2N$ 316.2446; Found 316.2442. $[\alpha]^{20}_D$: +30.4 (c = 1.6, $CHCl_3$, l = 50 mm).

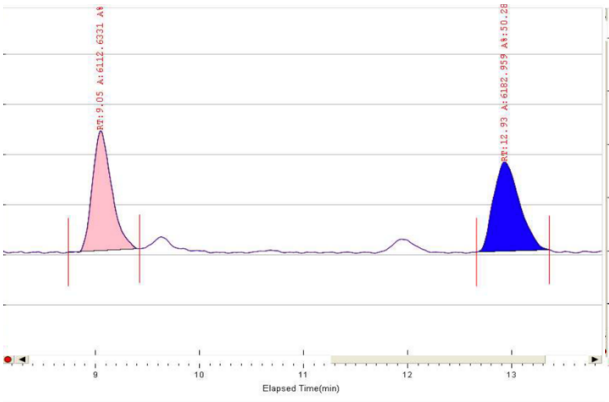
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

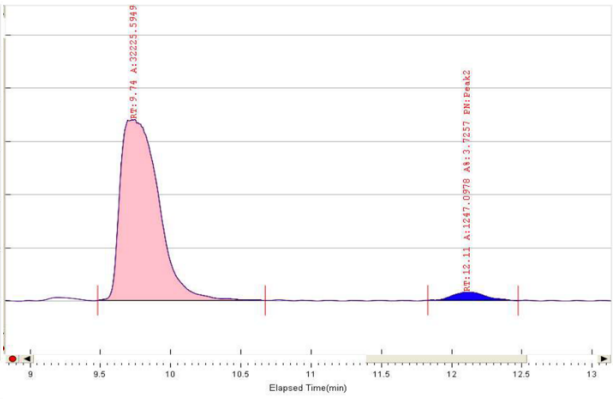
[81] Corey, E. J.; Yu, C. M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495–5496.

Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-phenylhept-6-yn-3-ol

Racemic Compound

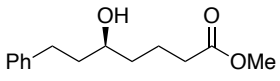


Standard Conditions



Peak No	% Area	Area	RT (min)
1	49.714	6112.6331	9.05
2	50.286	6182.959	12.93
Total:	100	12295.5921	

Peak No	% Area	Area	RT (min)
1	96.2743	32225.5949	9.74
2	3.7257	1247.0978	12.11
Total:	100	33472.6927	



Methyl (*S*)-5-hydroxy-7-phenylheptanoate (1.68). The reaction was performed according to the literature procedure[46] with (*S*)-7,7-dichloro-1-phenylhept-6-en-3-ol **1.59,** cobalt (II) acetylacetonate (97 mg, 0.38 mmol, 1.0 equiv.), triethylsilane (220 mg, 1.9 mmol, 5.0 equiv.), *tert*-butyl hydroperoxide solution (70% solution in H_2O) (46 mg, 0.53 mmol, 1.4 equiv.) in MeOH (4.0 mL, 0.1 M). The yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as yellow liquid (76 mg, 0.33 mmol, 86% yield, 96:4 e.r). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.21 – 7.16 (m, 3H), 3.66 (s, 3H), 3.61 (dq, *J* = 8.0, 4.1 Hz, 1H), 2.78 (ddd, *J* = 13.6, 9.6, 5.9 Hz, 1H), 2.66 (ddd, *J* = 13.6, 9.4, 6.8 Hz, 1H), 2.33 (td, *J* = 7.4, 1.7 Hz, 2H), 1.82 – 1.66 (m, 5H), 1.56 – 1.43 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 142.0, 128.4, 125.81, 125.78, 70.7, 51.6, 39.1, 36.8, 33.8, 32.0, 20.9. IR (neat) ν_{max} 3450 (br), 3010 (w), 2947 (w), 1730

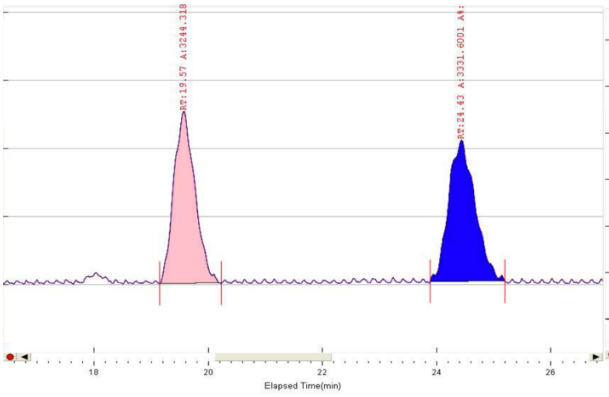
(m), 1493 (m), 1252 (m), 1149 (w), 913 (w), 698 (m). $[M+H]^+$ Calcd for $C_{14}H_{21}O_3$ 237.1491; Found 237.1480. $[\alpha]^{20}_D$: +71.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

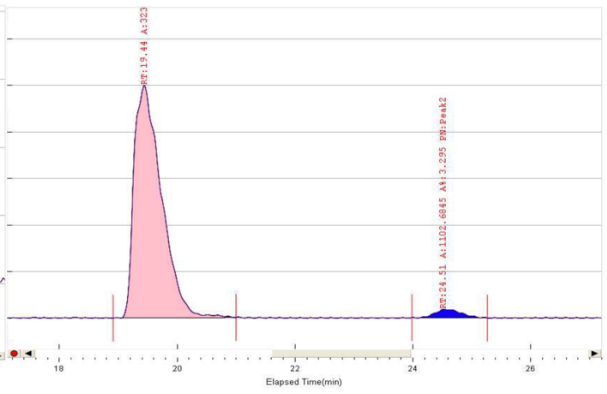
Chiral SFC (OD-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-phenylhept-6-yn-3-ol

Racemic Compound

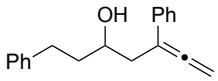


Peak No	% Area	Area	RT (min)
1	49.3364	3244.3183	19.57
2	50.6636	3331.6001	24.43
Total:	100	6575.9184	

Standard Conditions

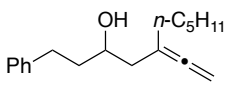


Peak No	% Area	Area	RT (min)
1	96.705	32362.2758	19.44
2	3.295	1102.6845	24.51
Total:	100	33464.9603	

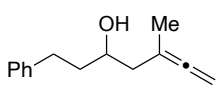


1,5-Diphenylhepta-5,6-dien-3-ol (1.69). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), (3-chloroprop-1-yn-1-yl)benzene (90.36 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M).

The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (36.8 mg, 0.13 mmol, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.33 (m, 4H), 7.28 – 7.20 (m, 4H), 5.23 – 5.10 (m, 2H), 3.95 (tt, *J* = 8.5, 4.6 Hz, 1H), 2.90 (ddd, *J* = 13.7, 8.9, 6.8 Hz, 1H), 2.80 – 2.67 (m, 2H), 2.60 (ddt, *J* = 14.7, 8.5, 2.8 Hz, 1H), 2.01 – 1.89 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.9, 142.3, 135.9, 128.73, 128.66, 128.61, 127.2, 126.2, 126.03, 102.4, 78.8, 69.7, 38.8, 38.4, 32.2. IR (neat) ν_{max} 3388 (br), 3026 (w), 2921 (s), 2886 (s), 1959 (w), 1734 (w), 1453 (m), 1053 (m), 741 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}O$ 265.1514; Found 265.1517.

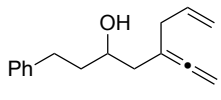


1-Phenyl-5-vinylidenedecan-3-ol (1.70). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 1-bromooct-2-yne (113.5 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (47.8 mg, 0.18 mmol, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.26 – 7.15 (m, 3H), 4.75 (m, 2H), 3.82 (tt, *J* = 5.3, 3.1 Hz, 1H), 2.95 – 2.62 (m, 2H), 2.24 – 2.07 (m, 2H), 2.01 (d, *J* = 3.1 Hz, 1H), 1.96 (m, 2H), 1.86 – 1.78 (m, 2H), 1.49 – 1.41 (m, 2H), 1.36 – 1.27 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.1, 142.4, 128.67, 128.58, 125.9, 100.7, 76.4, 69.3, 40.8, 38.8, 32.6, 32.3, 31.7, 27.3, 22.7, 14.3. IR (neat) ν_{max} 3724 (br), 3016 (w), 2835 (s), 2776 (s), 1959 (w), 1732 (w), 1451 (m), 988 (m), 649 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{18}H_{27}O$ 259.1984; Found 259.1980.



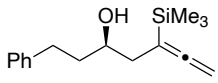
5-Methyl-1-phenylhepta-5,6-dien-3-ol (1.71). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-

diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 1-bromobut-2-yne (79.8 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (35.6 mg, 0.17 mmol, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.25 – 7.15 (m, 3H), 4.68 (dtq, *J* = 12.7, 6.3, 3.1 Hz, 2H), 3.88 – 3.76 (m, 1H), 2.90 – 2.79 (m, 1H), 2.76 – 2.65 (m, 1H), 2.20 – 2.06 (m, 2H), 1.93 (br, s, 1H), 1.88 – 1.77 (m, 2H), 1.71 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.4, 142.2, 128.42, 128.35, 125.8, 95.6, 74.7, 69.0, 41.9, 38.6, 32.1, 19.1. IR (neat) ν_{max} 3388 (br), 3026 (w), 2921 (s), 2886 (s), 1959 (w), 1734 (w), 1453 (m), 1053 (m), 741 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{19}O$ 203.1430; Found 203.1432.

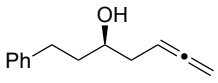


1-Phenyl-5-vinylideneoct-7-en-3-ol (1.72). This compound was prepared according to *General Procedure G* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.2 mg, 0.20 mmol, 1.0 equiv.), 6-chlorohex-1-en-4-yne (68.74 mg, 0.60 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (38.8 mg, 0.17 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.25 – 7.17 (m, 3H), 5.81 (ddt, *J* = 16.9, 10.1, 6.9 Hz, 1H), 5.15 – 5.02 (m, 2H), 4.78 (m, 2H), 3.82 (dddd, *J* = 8.8, 5.5, 3.3, 2.9 Hz, 1H), 2.89 – 2.78 (m, 1H), 2.79 – 2.65 (m, 3H), 2.24 – 2.07 (m, 2H), 1.94 (d, *J* = 3.3 Hz, 1H), 1.89 – 1.78 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.4, 142.4, 135.5, 128.7, 128.6, 126.0, 116.6, 99.1, 76.5, 69.3, 40.3, 38.8, 37.6, 32.3.

IR (neat) ν_{max} 3387 (br), 3122 (w), 3061 (s), 2740 (s), 1857 (w), 1732 (w), 1455 (m), 1163 (m), 667 (s) cm^{-1}. HRMS (DART) m/z: $[M+H-H_2O]^+$ Calcd for $C_{16}H_{19}$ 211.1513; Found 211.1509.



(*R*)-1-Phenyl-5-(trimethylsilyl)hepta-5,6-dien-3-ol (1.73). This compound was prepared according to *General Procedure G* with (*S*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.43** (77.2 mg, 0.20 mmol, 1.0 equiv.), (3-bromoprop-1-yn-1-yl)trimethylsilane (57.34 mg, 0.3 mmol, 1.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (31.3 mg, 0.13 mmol, 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.17 (m, 5H), 4.42 (m, 2H), 3.82 (tt, *J* = 6.9, 5.6 Hz, 1H), 2.90 – 2.79 (m, 1H), 2.70 (dt, *J* = 14.0, 8.6 Hz, 1H), 2.17 – 2.08 (m, 2H), 2.05 (d, *J* = 5.6 Hz, 1H), 1.82 (ddd, *J* = 8.6, 6.9, 1.7 Hz, 2H), 0.10 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 208.2, 142.4, 128.7, 128.6, 125.9, 92.2, 70.7, 69.6, 38.7, 37.2, 32.3, -1.5. IR (neat) ν_{max} 3388 (br), 3026 (w), 2921 (s), 2886 (s), 1959 (w), 1734 (w), 1453 (m), 1053 (m), 741 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{16}H_{25}OSi$ 261.1597; Found 261.1594. The compound was subjected to transformations without analysis of stereochemistry.



(*R*)-1-Phenylhepta-5,6-dien-3-ol (1.74). (*R*)-1-phenyl-5-(trimethylsilyl)hepta-5,6-dien-3-ol **1.73** (123 mg, 0.50 mmol, 1.0 equiv.) was treated with tetrabutylammonium fluoride (1.0 M in THF, 0.5 mL) and THF (1.0 mL, 0.5 M). The solution was allowed to stir at 25 ºC for 12 h. The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (79 mg, 0.45 mmol, 91% yield, 96:4 e.r). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.30 (m, 2H), 7.26 – 7.22 (m, 3H), 5.18 (tt, *J* = 6.9, 6.9 Hz, 1H), 4.74 (dt, *J* = 6.9, 2.9 Hz, 1H), 3.93 (tt, *J* =

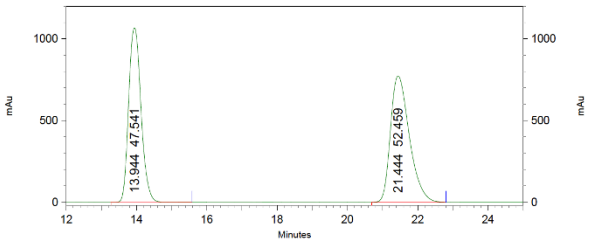
7.7, 4.9 Hz, 1H), 2.87 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.75 (dd, *J* = 13.7, 7.7 Hz, 1H), 2.27 (dddt, *J* = 13.2, 7.7, 6.9, 2.9, 1H), 2.20 (dddt, *J* = 13.2, 6.9, 4.9, 2.9, 1H), 1.81 – 1.78 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.6, 138.4, 129.5, 128.7, 126.6, 86.4, 75.1, 72.2, 43.3, 35.8. IR (neat) ν_{max} 3398 (w), 3061 (s), 3027 (s), 2918 (w), 1955, (w), 1729 (w), 1447 (w), 1056 (s) cm^{-1}. $[M+H]^+$ calc. for $C_{12}H_{15}O$ 175.1123; Found 175.1134. $[\alpha]^{20}_D$: +14.7 (c = +0.8, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

Chiral HPLC (OD-H, 5% IPA, 95% Hexanes, 0.8 mL/min, 254 nm) – analysis of 1-phenylhepta-5,6-dien-3-ol

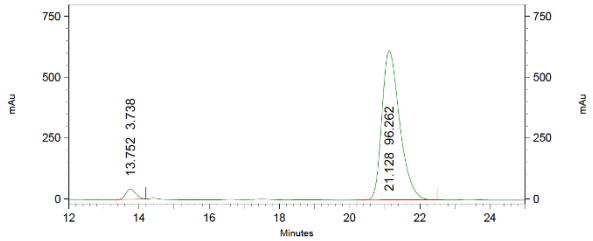
Racemic Material



6: 216 nm, 4 nm Results

Pk #	Retention Time	Area Percent
1	13.944	47.541
2	21.444	52.459
Totals		100.000

Standard Conditions



6: 216 nm, 4 nm Results

Pk #	Retention Time	Area Percent
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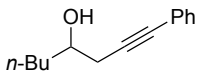
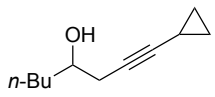
2	13.752	3.738
3	21.128	96.262
Totals		100.000

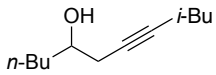


1-Phenyloct-1-yn-4-ol (1.76). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 2-bromoethynylbenzene (39.8 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The yellow

liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as pale-yellow liquid (30.2 mg, 0.15 mmol, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 2H), 7.34 – 7.23 (m, 3H), 3.83 (tdd, *J* = 12.6, 6.9, 4.8 Hz, 1H), 2.66 (dd, *J* = 16.7, 4.8 Hz, 1H), 2.62 – 2.51 (dd, *J* = 16.7, 6.9 Hz, 1H), 1.60 (m, 2H), 1.50 – 1.23 (m, 5H), 0.93 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.8, 128.5, 128.2, 123.6, 86.4, 83.3, 70.5, 36.3, 28.6, 28.1, 22.9, 14.3. IR (neat) ν_{max} 3383 (br), 2956 (m), 2930 (m), 2859 (w), 1599 (w), 1490 (m), 1442 (w), 1378 (w), 1124 (w), 1070 (w), 1027 (m), 755 (s), 691 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{19}O$ 203.1432; Found 203.1430.

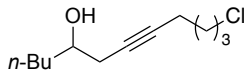


1-Cyclopropyloct-1-yn-4-ol (1.77). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 2-bromoethynylcyclopropane (31.9 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (17.2 mg, 0.10 mmol, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (m, 1H), 2.36 (dd, *J* = 16.5, 4.6 Hz, 1H), 2.23 (dd, *J* = 16.5, 7.0 Hz, 1H), 1.92 (s, 1H), 1.48 (m, 2H), 1.44 – 1.27 (m, 4H), 1.21 (m, 1H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.72 (m, 2H), 0.65 – 0.58 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 85.4, 70.7, 69.4, 35.2, 27.1, 27.0, 21.9, 13.3, 7.34, 7.32, -1.2. IR (neat) ν_{max} 3382 (br), 2931 (s), 2860 (m), 1456 (w), 1427 (w), 1379 (w), 1361 (w), 1267 (w),1217 (w), 1124 (w), 1041 (m), 885 (m), 812 (w), 739 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{11}H_{19}O$ 167.1433; Found 167.1430.



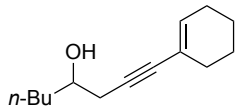
10-Methylundec-7-yn-5-ol (1.78). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-

1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 1-bromo-4-methyl-pent-1-yne (35.4 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (36.5 mg, 0.09 mmol, 46% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.72 – 3.65 (m, 1H), 2.40 (dd, *J* = 16.4, 4.7 Hz, 1H), 2.31 – 2.24 (m, 1H), 2.05 (dd, *J* = 6.5, 2.4 Hz, 2H), 1.92 (s, 1H), 1.77 (m, 1H), 1.55 – 1.49 (m, 2H), 1.43 – 1.26 (m, 4H), 0.95 (d, *J* = 6.5 Hz, 6H), 0.90 (t, *J* = 7.1 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 82.1, 76.9, 70.2, 35.9, 28.1, 27.9, 27.8, 27.7, 22.6, 21.9, 14.0. IR (neat) ν_{max} 3418 (br), 2957 (m), 2871 (w), 1465 (w), 1368 (w), 1264 (m), 908 (m), 733 (s), 704 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{12}H_{23}O$ 183.1745; Found 183.1743.

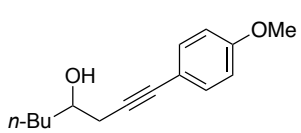


12-Chlorododec-7-yn-5-ol (1.79). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 1-bromo-6-chloro-hex-1-yne (43 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (28.4 mg, 0.13 mmol, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (tt, *J* = 6.6, 4.8 Hz, 1H), 3.56 (t, *J* = 6.6 Hz, 2H), 2.39 (dd, *J* = 16.3, 4.7 Hz, 1H), 2.32 – 2.20 (m, 3H), 1.88 (dt, *J* = 14.6, 6.6 Hz, 2H), 1.70 – 1.60 (m, 2H), 1.55 – 1.48 (m, 2H), 1.43 – 1.27 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.4, 77.2, 70.4, 44.8, 36.2, 31.8, 28.1, 27.9, 26.3, 22.9, 18.3, 14.3. IR (neat) ν_{max} 3382 (br), 2931 (s),

2861 (m), 1455 (m), 1379 (w), 1301 (w), 1266 (w), 1124 (w), 1080 (w), 1031 (m), 906 (w), 736 (m), 651 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{12}H_{22}OCl$ 217.1361; Found 217.1353.

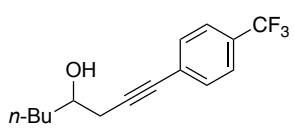


1-(Cyclohex-1-en-1-yl)oct-1-yn-4-ol (1.80). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 1-(2 bromoethynyl)cyclohexene (40.7 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as yellow liquid (38.4 mg, 0.11 mmol, 57% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.03 (m, 1H), 3.71 (tt, *J* = 6.5, 4.6 Hz, 1H), 2.52 (dd, *J* = 16.7, 4.7 Hz, 1H), 2.40 (dd, *J* = 16.7, 4.6 Hz, 1H), 2.14 – 2.04 (m, 4H), 1.65 – 1.50 (m, 6H), 1.45 – 1.27 (m, 5H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 134.4, 120.8, 85.2, 83.3, 70.4, 36.2, 29.7, 28.6, 28.1, 25.8, 22.9, 22.6, 21.8, 14.3. IR (neat) ν_{max} 3368 (br), 2930 (s), 2858 (m), 2194 (w), 2028 (w), 1717 (w), 1436 (w), 1347 (w), 1268 (w), 1125 (w), 1030 (w), 918 (w), 842 (w), 749 (w), 573 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{22}O$ 207.1743; Found 207.1749.

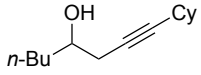


1-(4-Methoxyphenyl)oct-1-yn-4-ol (1.81). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 1-(2-bromoethynyl)-4-methoxy-benzene (46.4 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as yellow liquid (24 mg, 0.10 mmol, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.32 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H),

3.83 – 3.78 (m, 4H), 2.63 (dd, J = 16.7, 4.7 Hz, 1H), 2.52 (dd, J = 16.7, 6.8 Hz, 1H), 1.66 – 1.53 (m, 3H), 1.51 – 1.31 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 133.2, 115.8, 114.1, 84.8, 83.1, 70.5, 55.5, 36.3, 28.7, 28.1, 22.9, 14.3. IR (neat) ν_{max} 3383 (br), 2956 (w), 2831 (w), 2859 (w), 1607 (m), 1509 (s), 1465 (w), 1289 (m), 1246 (s),1173 (m), 1032 (m), 832 (m), 736 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{15}H_{21}O_2$ 233.1538; Found 233.1536.

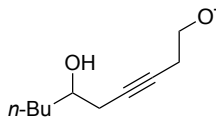


1-(4-(Trifluoromethyl)phenyl)oct-1-yn-4-ol (1.82). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 1-(2-bromoethynyl)-4-(trifluoromethyl)benzene (54.7 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.37 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as yellow liquid (26 mg, 0.09 mmol, 47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (m, 4H), 3.85 (ddd, J = 12.0, 6.6, 4.8 Hz, 1H), 2.67 (dd, J = 16.8, 4.8 Hz, 1H), 2.57 (dd, J = 16.8, 6.6 Hz, 1H), 1.60 (m, 3H), 1.48 – 1.32 (m, 4H), 0.98 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.9, 129.6 (q, $^2J_{C\text{-}F}$ = 33.2 Hz), 126.6, 125.1 (q, $^3J_{C\text{-}F}$ = 3.9 Hz), 123.9 (q, $^1J_{C\text{-}F}$ = 272.92 Hz), 89.2, 81.7, 70.0, 36.1, 28.3, 27.7, 22.6, 14.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.71.; IR (neat) ν_{max} 3383 (br), 2933 (w), 1616 (w), 1406 (w), 1324 (s), 1167 (m), 1128 (m), 1068 (m), 1018 (w), 842 (w), 739 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{15}H_{18}OF_3$ 271.1313; Found 271.1304.

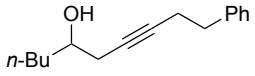


1-Cyclohexyloct-1-yn-4-ol (1.83). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 2-bromoethynylcyclohexane (41.1 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol,

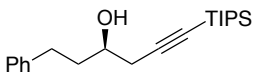
0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (41.7 mg, 0.11 mmol, 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.66 (tt, *J* = 11.3, 5.5 Hz, 1H), 2.39 (dd, *J* = 16.4, 11.3 Hz, 1H), 2.35 (m, 1H), 2.26 (dd, *J* = 16.4, 5.5, Hz, 1H), 1.95 (s, 1H), 1.77 (dt, *J* = 11.3, 5.5 Hz, 2H), 1.66 (m, 2H), 1.53 – 1.45 (m, 3H), 1.44 – 1.35 (m, 3H), 1.35 – 1.23 (m, 6H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 87.9, 76.2, 70.4, 36.1, 33.3, 29.4, 28.05, 28.01, 26.1, 25.1, 22.9, 14.3. IR (neat) ν_{max} 3383 (br), 2929 (s), 2854 (m), 1449 (m), 1265 (w), 1031 (w), 908 (w), 735 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{14}H_{24}O$ 209.1827; Found 209.1822.



10-((*tert*-Butyldimethylsilyl)oxy)dec-7-yn-5-ol (1.84). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 4-bromobut-3-ynoxy-tert-butyl-dimethyl-silane (35.4 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained in CAM) to afford the product as colorless liquid (25.3 mg, 0.09 mmol, 44% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.68 (m, 3H), 2.44 – 2.35 (m, 3H), 2.33 – 2.19 (m, 1H), 1.96 (s, 1H), 1.50 (ddd, *J* = 9.0, 6.9, 3.9 Hz, 2H), 1.45 – 1.21 (m, 4H), 0.92 – 0.85 (m, 12H), 0.05 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 80.3, 77.7, 70.4, 62.4, 36.2, 28.1, 28.0, 26.1, 23.4, 22.9, 18.6, 14.3, -5.0. IR (neat) ν_{max} 3358 (br), 2928 (w), 2605 (br), 2194 (w), 2054 (w), 1264 (m), 1103 (w), 909 (w), 838 (w), 731 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{16}H_{32}O_2Si$: 285.2244; Found 285.2248.

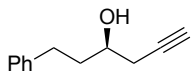


10-Phenyldec-7-yn-5-ol (1.85). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl]-1,3,2-dioxaborolane (67.6 mg, 0.20 mmol, 1.0 equiv.), 4-bromobut-3-ynylbenzene (46 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.4 mg, 0.060 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes) to afford the product as colorless liquid (27.9 mg, 0.12 mmol, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 3.62 (m, 1H), 2.81 (t, *J* = 7.4 Hz, 2H), 2.49 (t, *J* = 7.4, 2H), 2.37 (dd, *J* = 16.4, 4.6 Hz, 1H), 2.22 (dd, *J* = 16.4, 6.9 Hz, 1H), 1.77 (s, 1H), 1.50 – 1.41 (m, 2H), 1.39 – 1.23 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 128.7, 128.6, 126.5, 82.5, 77.4, 70.3, 36.1, 35.5, 28.1, 27.9, 22.9, 21.1, 14.3. IR (neat) ν_{max} 3383 (br), 3028 (w), 2929 (s), 2859 (m), 1496 (w), 1454 (m), 1379 (w), 1340 (w), 1265 (w), 1124 (w), 1077 (m), 1031 (m), 906 (w), 845 (w), 740 (s), 698 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{16}H_{23}O$ 231.1752; Found 231.1755.



(*R*)-1-Phenyl-6-(triisopropylsilyl)hex-5-yn-3-ol (1.86). This compound was prepared according to *General Procedure G* with (*S*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.43** (77.2 mg, 0.20 mmol, 1.0 equiv.), 2-bromoethynyl(triisopropyl)silane (57.5 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.37 mg, 0.06 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.6 mmol, 3.0 equiv.) in THF (0.5 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (7% EtOAc in hexanes) to afford the product as yellow liquid (48.0 mg, 0.15 mmol, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 3.83 – 3.74 (m, 1H), 2.83 (ddd, *J* = 14.9, 9.1, 6.2 Hz, 1H), 2.71 (ddd, *J* = 13.8, 9.2, 7.3 Hz, 1H), 2.53 (dd, *J* = 16.8, 5.1 Hz, 1H), 2.44 (dd, *J*

= 16.8, 6.5 Hz, 1H), 1.99 (s, 1H), 1.94 – 1.85 (m, 2H), 1.10 – 1.06 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1, 128.7, 128.6, 126.1, 104.7, 84.1, 69.5, 38.1, 32.2, 29.2, 18.9, 11.5. IR (neat) ν_{max} 3354 (br), 2941(s), 2864(s), 2172(m), 1463(m), 1030(m), 883(m), 699(m), 677(s), 664(s). HRMS(DART) for $C_{21}H_{35}OSi$ $(M+H)^+$ calculated 331.24572, found 331.24569. This compound was subjected to transformations without analysis of stereochemistry.



(*R*)-1-Phenylhex-5-yn-3-ol (1.87). To an oved dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added (*S*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.43** (77.2 mg, 0.20 mmol, 1.0 equiv.), 2-bromoethynyl(triisopropyl)silane (57.5 mg, 0.22 mmol, 1.1 equiv.), copper cyanide (5.37 mg, 0.06 mmol, 0.3 equiv.), lithium methoxide (22.8 mg, 0.6 mmol, 3.0 equiv.) in THF (0.5 mL, 0.4 M). The reaction vial was sealed with a polypropylene cap, taped and brought out of the glovebox where the mixture was allowed to stir at 60 ˚C for 16 h. The mixture was allowed to cool to room temperature, filtered through a silica gel plug, and concentrated under reduced pressure. The mixture was diluted with THF (1.5 mL), cooled to 0 ˚C in an ice bath, and was added 3.0 M NaOH (1.0 mL), followed by 30% H_2O_2 (1.0 mL) dropwise. The mixture was allowed to warm up to room temperature and was allowed to stir for 2 h. The mixture was cooled to 0 ˚C and a saturated aqueous solution of $Na_2S_2O_3$ (3.0 mL) was added dropwise. The mixture was allowed to warm up to room temperature and the aqueous layer was washed with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The mixture was then dissolved in THF (1.0 mL) under inert atmosphere and cooled to 0 ºC in an ice bath. Tetrabutylammonium fluoride solution (0.4 mL, 0.4 mmol, 2.0 equiv.) (1.0 M in THF) was added dropwise. The mixture was allowed to warm to room temperature and to stir for 2 h. The reaction was quenched by addition of water and washed with Et_2O (3 × 10 mL). The combined

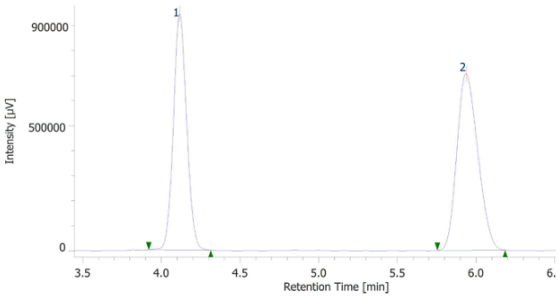
organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The colorless liquid was purified by silica gel chromatography (5% EtOAc in hexanes) to afford the product as colorless liquid (23.7 mg, 0.14 mmol, 68% yield, over three steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.3 – 7.3 (m, 2H), 7.2 – 7.2 (m, 3H), 3.8 (dddd, *J* = 6.7, 4.8 Hz, 1H), 2.9 – 2.8 (m, 1H), 2.7 (dt, *J* = 13.8, 8.1 Hz, 1H), 2.5 (ddd, *J* = 16.8, 4.8, 2.7 Hz, 1H), 2.4 (ddd, *J* = 16.8, 6.7, 2.7 Hz, 1H), 2.1 (t, *J* = 2.6 Hz, 1H), 2.0 (s, 1H), 1.9 – 1.8 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 128.58, 128.56, 126.1, 80.8, 71.1, 69.2, 37.9, 32.0, 27.6. IR(neat) ν_{max} 3556(br), 3386(br), 3295(m), 2930(m), 1079(m), 1053(m), 700(s), 641(m). HRMS (DART) for $C_{12}H_{15}O$ $(M+H)^+$ calculated: 175.11174, found: 175.11129. $[\alpha]^{20}_D$: +17.3 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OD-H, 8% IPA, 3 mL/min, 100 bar, 40 °C, 200-400 nm) – analysis of 1-phenylhept-6-yn-3-ol

Racemic Material



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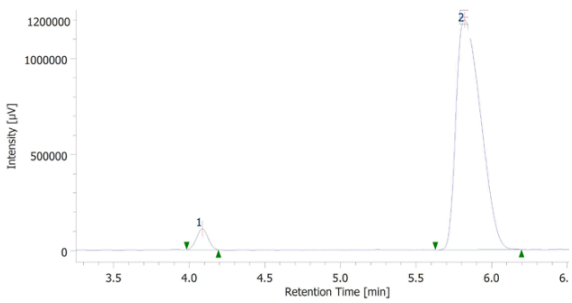
Standard Conditions



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
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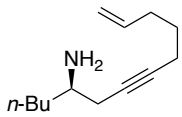


(*R*)-Tridec-12-en-7-yn-5-amine (1.88). To an oved dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added (*S*)-2,2'-(hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **S-1.75** (169 mg, 0.50 mmol, 1.0 equiv.), 7-bromohept-1-en-6-yne (95.2 mg, 0.55 mmol, 1.1 equiv.), copper cyanide (13.4 mg, 0.15 mmol, 0.3 equiv.), lithium methoxide (57.0 mg, 1.5 mmol, 3.0 equiv.) in THF (1.25 mL, 0.4 M). The reaction vial was sealed with a polypropylene cap, taped and brought out of the glovebox where it was allowed to stir at 60 ˚C for 16 h. The resulting mixture was allowed to cool to room temperature, filtered through a silica gel plug, and concentrated under reduced pressure. The yellow liquid residue was purified by silica gel chromatography (30% toluene in hexanes) to afford the product as yellow liquid (85.4 mg, 0.28 mmol, 56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.8 (ddt, *J* = 17.0, 10.1, 6.7 Hz, 1H), 5.0 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.0 (dd, *J* = 10.2, 1.8 Hz, 1H), 2.3 – 2.2 (m, 2H), 2.1 (tdd, *J* = 9.2, 5.1, 1.4 Hz, 4H), 1.6 (dd, *J* = 7.1 Hz, 2H), 1.5 – 1.4 (m, 2H), 1.3 – 1.3 (m, 4H), 1.2 (d, *J* = 2.3 Hz, 12H), 1.2 (p, *J* = 7.3 Hz, 1H), 0.9 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3, 115.0, 83.2, 80.0, 33.0, 31.2, 30.3, 28.5, 24.87, 24.88, 23.0, 20.3, 18.4, 14.2.

In an Ar-filled glovebox to a 2-dram vial equipped with magnetic stir bar was added potassium *tert*-butoxide (47.1 mg, 0.42 mmol, 1.5 equiv.). The vial was sealed with a septa cap and was removed from the glovebox. Toluene (0.3 mL) and methoxyamine (2.0 M in THF, 210 μL, 1.5 equiv.) were added. (*R*)-4,4,5,5-tetramethyl-2-(tridec-12-en-7-yn-5-yl)-1,3,2-dioxaborolane (85.4 mg, 0.28 mmol, 1.0 equiv.) was added as a solution in THF. The mixture was allowed to stir for 16 h at 80 °C, it was then diluted with ethyl acetate and water. The mixture was washed with EtOAc (3 × 5.0 mL), the organic layers were dried over Na_2SO_4, and concentrated under reduced pressure to afford the residue. The brown liquid residue was purified by silica gel chromatography

(Et_3N in DCM) to afford orange liquid (39.5 mg, 0.15 mmol, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.8 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.0 (dd, *J* = 16.8, 2.2 Hz, 1H), 5.0 (dd, *J* = 10.2, 2.2 Hz, 1H), 2.8 (tt, *J* = 7.0 Hz, 1H), 2.3 (ddd, *J* = 16.3, 4.8, 2.5 Hz, 1H), 2.2 – 2.1 (m, 5H), 1.6 (tt, *J* = 7.2 Hz, 2H), 1.4 (tq, *J* = 5.6, 3.0 Hz, 2H), 1.4 – 1.2 (m, 6H), 0.9 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 138.1, 115.1, 82.0, 77.7, 50.8, 36.9, 33.0, 28.6, 28.4, 28.3, 22.9, 18.3, 14.2. IR(neat) ν_{max} 2955(m), 2928(s), 2853(m), 1601(w), 1578(br), 1456(w), 1436(w), 992(w), 912(m), 821(br). HRMS (DART) for $C_{13}H_{24}N$ $(M+H)^+$ calculated: 194.19033, found: 194.18960. $[\alpha]^{20}_D$: +14.6 (c = 0.5, $CHCl_3$, *l* = 50 mm).

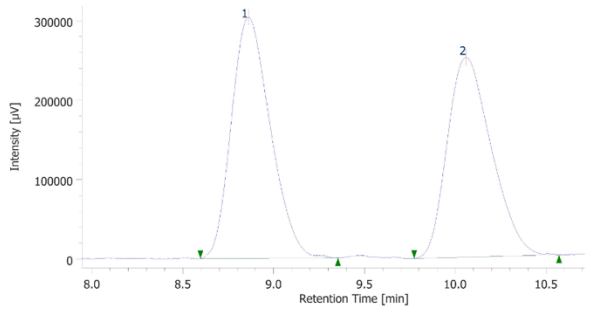
Analysis of Stereochemistry:

The title compound was treated with benzoyl chloride and triethyl amine to afford (*R*)-N-(tridec-12-en-7-yn-5-yl)benzamide (**1.162**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.8 – 7.7 (m, 2H), 7.5 – 7.5 (m, 1H), 7.5 – 7.4 (m, 2H), 6.2 (d, *J* = 8.9 Hz, 0.5 H), 5.8 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.0 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.0 (dd, *J* = 10.3, 2.0 Hz, 1H), 4.3 – 4.2 (m, 0.5 H), 2.6 (ddt, *J* = 16.6, 5.1, 2.4 Hz, 1H), 2.4 (ddt, *J* = 16.8, 4.4, 2.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 138.0, 135.1, 131.5, 128.7, 127.0, 115.3, 82.9, 76.1, 48.0, 33.7, 32.9, 28.4, 28.3, 24.6, 22.7, 18.3, 14.1. The amide was compared to the racemic amide prepared by the same synthetic route.

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OD-H, 6% IPA, 3 mL/min, 100 bar, 40 °C, 200-400 nm) – analysis of N-(tridec-12-en-7-yn-5-yl)benzamide

Racemic Material



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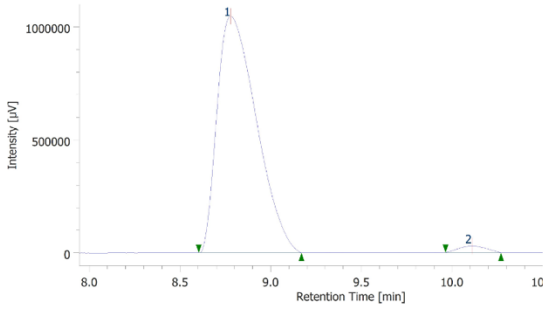
Standard Conditions



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
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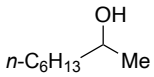
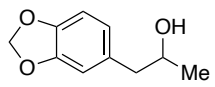
2	Unknown	11	10.110	318625	29956	1.984	2.783

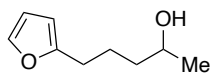


Octan-2-ol (1.89). This compound was prepared according to *General Procedure G* with 2,2'-(octane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.2 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (23.1 mg, 0.18 mmol, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 – 3.75 (m, 1H), 1.52 – 1.35 (m, 4H), 1.35 – 1.22 (m, 8H), 1.17 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 68.4, 39.6, 32.1, 29.6, 26.0, 23.7, 22.9, 14.3. IR (neat) ν_{max} 3346 (br), 2925 (s), 2855 (m), 1727 (w), 1460 (w), 1376 (w), 1115 (w), 940 (w), 743 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_8H_{18}O$ 130.1357; Found 130.1354.

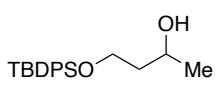


1-(Benzo[d][1,3]dioxol-5-yl)propan-2-ol (1.90). This compound was prepared according to *General Procedure G* with 2,2'-(3-(benzo[*d*][1,3]dioxol-5-yl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (83.2 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford

the product as colorless liquid (34.3 mg, 0.19 mmol, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 1.4 Hz, 1H), 6.65 (dd, *J* = 7.9, 1.4 Hz, 1H), 5.93 (s, 2H), 3.96 (ddq, *J* = 8.0, 6.3, 4.0 Hz, 1H), 2.71 (dd, *J* = 13.6, 4.0 Hz, 1H), 2.59 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.23 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 146.3, 132.3, 122.3, 109.8, 108.4, 101.1, 69.1, 45.5, 22.8. IR (neat) ν_{max} 3382 (br), 2969 (w), 2926 (w), 1489 (s), 1442 (m), 1371 (w), 1246 (s), 1181 (w), 1039 (s), 939 (m), 804 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}O_3$ 180.0779; Found 180.0781.

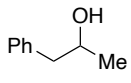


5-(Furan-2-yl)pentan-2-ol (1.91). This compound was prepared according to *General Procedure G* with 2,2'-(5-(furan-2-yl)pentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (78 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (25 mg, 0.16 mmol, 81% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, *J* = 1.6 Hz, 1H), 6.27 (dd, *J* = 3.2, 1.6 Hz, 1H), 5.99 (d, *J* = 3.2 Hz, 1H), 3.82 (tq, *J* = 12.9, 6.3 Hz, 1H), 2.65 (t, *J* = 7.5 Hz, 2H), 1.82 – 1.73 (m, 1H), 1.72 – 1.64 (m, 1H), 1.54 – 1.44 (m, 3H), 1.20 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1, 140.9, 110.2, 104.9, 68.0, 38.8, 28.0, 24.4, 23.7. IR (neat) ν_{max} 3382 (br), 2972 (br), 1507 (w), 1457 (w), 1373 (w), 1264 (m), 1146 (w), 1086 (w), 1008 (w), 731 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_9H_{14}O_2$ 155.1071; Found 155.1067.

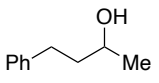


4-((*tert*-Butyldiphenylsilyl)oxy)butan-2-ol (1.92). This compound was prepared according to *General Procedure G* with (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(tert-butyl)diphenylsilane (109 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.),

lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (60.2 mg, 0.19 mmol, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.66 (m, 4H), 7.49 – 7.36 (m, 6H), 4.11 (ddq, *J* = 9.0, 6.2, 2.9 Hz, 1H), 3.93 – 3.80 (m, 2H), 1.75 (dddd, *J* = 14.3, 8.4, 5.0, 2.9 Hz, 1H), 1.64 (dddd, *J* = 14.3, 5.0, 4.1, 2.9 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.06 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.80, 135.78, 133.3, 133.2, 130.08, 130.06, 128.0, 127.9, 68.2, 63.7, 40.3, 27.0, 23.6, 19.3. IR (neat) ν_{max} 3382 (br), 2960 (w), 2931 (w), 2857 (w), 1472 (w), 1427 (m), 1110 (s), 1079 (s), 997 (w), 910 (w), 822 (m), 736 (m), 700 (s), 614 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{20}H_{29}O_2Si$ 329.1941; Found 329.1931.

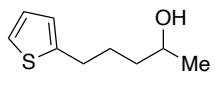


1-Phenylpropan-2-ol (1.93). This compound was prepared according to *General Procedure G* with 2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (74.42 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.8 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (23.4 mg, 0.17 mmol, 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.7 Hz, 2H), 7.22 (dd, *J* = 16.8, 7.7 Hz, 3H), 4.01 (tq, *J* = 13.0, 6.2 Hz, 1H), 2.78 (dd, *J* = 13.0, 6.2 Hz, 1H), 2.69 (dd, *J* = 13.0, 6.2 Hz, 1H), 1.24 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6, 129.6, 128.6, 126.6, 69.1, 45.9, 22.9. IR (neat) ν_{max} 3362 (br), 2936 (s), 2754 (w), 2460 (w), 1741 (w), 1273 (m), 1181 (w), 710 (m), 659 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_9H_{13}O$ 137.0887; Found 137.0879.

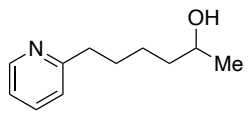


4-Phenylbutan-2-ol (1.94). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-(4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)-1,3,2-dioxaborolane (77.2 mg, 0.20 mmol, 1.0 equiv.), methanol

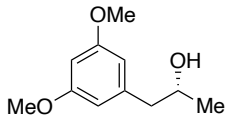
(16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (22.7 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (27.3 mg, 0.18 mmol, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.24 – 7.18 (m, 3H), 3.85 (tq, *J* =12.5, 6.2 Hz, 1H), 2.78 (ddd, *J* = 13.9, 9.4, 6.2 Hz, 1H), 2.69 (ddd, J = 13.9, 9.4, 6.2 Hz, 1H), 1.83 – 1.76 (m, 2H), 1.25 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1, 128.53, 128.52, 125.9, 67.7, 40.9, 32.2, 23.7. IR (neat) ν_{max} 3357 (br), 2930 (s), 1594 (s), 1477 (s), 1435 (s), 1129 (w), 1002 (w), 765 (m), 632 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{10}H_{14}O$ 150.1044; Found 150.1049.



5-(Thiophen-2-yl)pentan-2-ol (1.95). This compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(thiophen-2-yl)pentan-2-yl)-1,3,2-dioxaborolane (81 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (23 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid residue was purified by silica gel chromatography (10% EtOAc/hexanes) to afford the product as colorless liquid (32.7 mg, 0.19 mmol, 96% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.92 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.79 (dd, *J* = 3.4, 1.2 Hz, 1H), 3.83 (tq, *J* = 12.5, 6.2 Hz, 1H), 2.86 (t, *J* = 7.5 Hz, 2H), 1.90 – 1.69 (m, 2H), 1.56 – 1.47 (m, 4H), 1.20 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.5, 126.9, 124.4, 123.1, 68.1, 38.8, 30.0, 28.2, 23.8. IR (neat) ν_{max} 3356 (br), 2965 (m), 2932 (s), 2859 (w), 1457 (w), 1440 (w), 1373 (m), 1322 (w), 1127 (m), 1083 (w), 849 (w), 823 (w), 692 (s) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_9H_{15}OS$ 171.0836; Found 171.0838.



6-(Pyridin-3-yl)hexan-2-ol (1.96). This compound was prepared according to *General Procedure G* with 3-(5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)pyridine (83 mg, 0.20 mmol, 1.0 equiv.), methanol (16 mg, 0.50 mmol, 2.5 equiv.), copper cyanide (3.6 mg, 0.040 mmol, 0.20 equiv.), lithium methoxide (23 mg, 0.60 mmol, 3.0 equiv.) in THF (0.50 mL, 0.4 M). The colorless liquid mixture was purified by silica gel chromatography (20% EtOAc/hexanes) to afford the product as colorless liquid (32.5 mg, 0.18 mmol, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.2 Hz, 1H), 7.58 (td, *J* = 7.8, 1.8 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.09 (dd, *J* = 7.8, 4.2 Hz, 1H), 3.86 – 3.77 (m, 1H), 2.80 (t, *J* = 7.7 Hz, 2H), 1.82 – 1.69 (m, 2H), 1.55 – 1.36 (m, 4H), 1.17 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 149.2, 136.6, 123.0, 121.2, 68.0, 39.3, 38.3, 29.8, 25.6, 23.7. IR (neat) ν_{max} 3357 (br), 2930 (s), 1594 (s), 1477 (s), 1435 (s), 1129 (w), 1002 (w), 765 (m), 632 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{11}H_{18}NO$ 180.1382; Found 180.1379.



(*R*)-1-(3,5-Dimethoxyphenyl)propan-2-ol (1.107). This compound was prepared according to *General Procedure H* with DHR catalyst **1.30** (52.5 mg, 0.20 mmol, 0.20 equiv.), Bis(neopentyl glycolato)diboron **1.104** (226 mg, 1.0 mmol, 2.00 equiv.), 1-allyl-3,5-dimethoxy-benzene (178.2 mg, 1.0 mmol, 1.0 equiv.), DBU (30.5 mg, 0.20 mmol, 0.2 equiv.) and THF (1.25 mL). After the diboration, methanol (65 mg, 2.0 mmol, 2.0 equiv.), copper cyanide (19 mg, 0.20 mmol, 0.20 equiv.), lithium methoxide (114 mg, 3.0 mmol, 3.0 equiv.) in THF (2.5 mL, 0.4 M). The yellow liquid mixture was purified by silica gel chromatography (10% EtOAc in hexanes) to afford the product as yellow liquid (142 mg, 0.72 mmol, 72% yield, 95:5 er). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.37 – 6.32 (m, 3H), 4.03 – 3.97 (m, 1H), 3.77 (s, 6H), 2.72 (dd, *J* = 13.1, 4.9 Hz, 1H), 2.60 (dd, *J* = 13.4, 8.2, 1H), 1.63 (s, 1H), 1.24 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1, 141.0, 107.5, 98.6, 68.8, 55.4, 46.3, 22.9. IR (neat) ν_{max} 3387

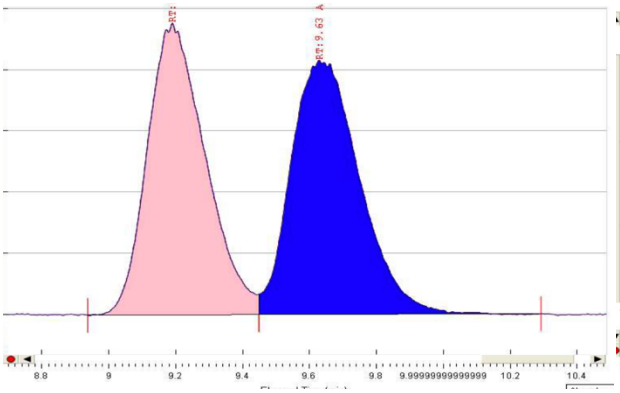
(br), 2964 (m), 2837 (m), 1459 (m), 1343 (w), 1322 (m), 1205 (w), 933 (m), 700 (w) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{11}H_{17}O_3$ 197.1092; Found 197.1101. $[\alpha]^{20}_D$: –46.3 (c = 0.7, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

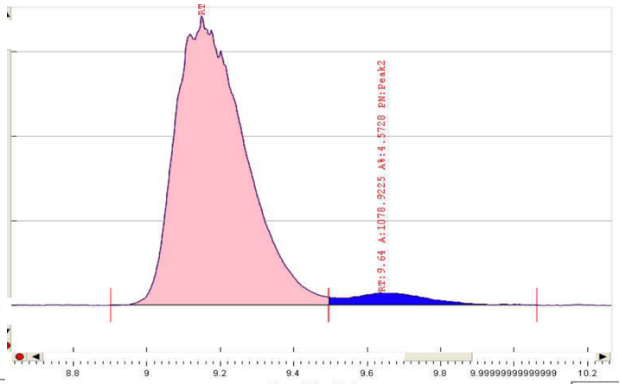
Chiral SFC (OD-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 220nm) – analysis of 1-phenylhept-6-yn-3-ol.

Racemic Compound



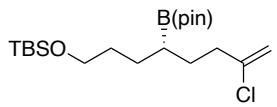
Peak No	% Area	Area	RT (min)
1	49.2484	11478.2236	9.19
2	50.7516	11828.5725	9.63
Total:	100	23306.7961	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.4272	22515.575	9.15
2	4.5728	1078.9225	9.64
Total:	100	23594.4975	

1.6.4 Procedure for Preparative Scale Diboration/Cu-Catalyzed Coupling

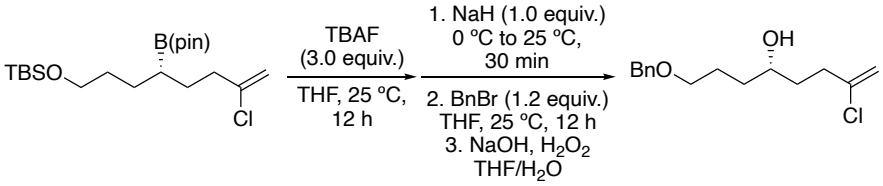


(*S*)-*tert*-Butyl((7-chloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)oxy)dimethylsilane (1.110). The reaction was performed according to the literature procedure.[23] $Pt(dba)_3$ (22.45 mg, 0.025 mmol), **1.28** (27.28

mg, 0.030 mmol), $B_2(pin)_2$ (2.54 g, 10 mmol), THF (10 mL, 1.0M) were added to a pressure vessel equipped with a stirrer bar in an Ar-filled glovebox. The vessel was removed from glovebox and the mixture was allowed to stir at 80 ºC for 30 min. Then, the vessel was put back in the glovebox and *tert*-butyldimethyl(pent-4-en-1-yloxy)silane (2.4 g, 12 mmol) was added. The reaction mixture was allowed to stir at 60 ºC for 24 h, then it was allowed to cool to room temperature and brought back into the glovebox. The copper-catalyzed cross-coupling was performed according to the *General Procedure G*. 2,3-dichloropropene (2.22 g, 2.0 equiv.), copper cyanide (179 mg, 0.2 equiv.), lithium methoxide (1.14 g, 3.0 equiv.), and additional 15 mL of THF were added so the concentration of bisboronate compound would be 0.4 M. The mixture was allowed to stir at 60 ºC for 12 h. The mixture was allowed to cool to room temperature, and concentrated under reduced pressure. The light-brown residue was purified by silica gel chromatography (5% EtOAc in hexanes) to afford the product as pale-yellow liquid (3.5 g, 8.7 mmol, 87% yield, 96:4 er). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.11 (d, J = 8.1 Hz, 2H), 3.59 (td, J = 6.5, 1.0 Hz, 2H), 2.40 – 2.27 (m, 2H), 1.73 – 1.61 (m, 2H), 1.57 – 1.35 (m, 4H), 1.24 (s, 12H), 1.03 – 0.97 (m, 1H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 111.7, 83.0, 63.4, 38.7, 32.3, 28.9, 27.1, 26.0, 24.81, 24.77, 18.4, -5.3. IR (neat) ν_{max} 2975 (w), 2949 (m), 2855 (w), 1632 (w), 1461 (w), 1386 (m), 1317 (m), 1253 (m), 1143 (s), 1099 (s), 966 (w), 876 (w), 834 (s), 774 (m) cm^{-1}. HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{20}H_{40}BClO_3Si$ 403.26; Found 403.26. $[\alpha]^{20}_D$: +0.4 (c = 1.0, $CHCl_3$, l = 50 mm).

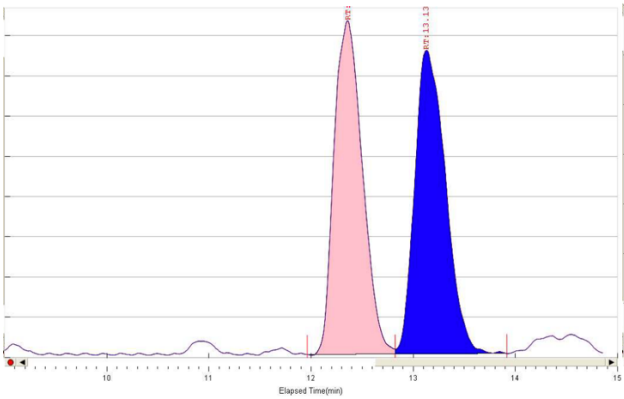
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described without **1.28**. Both enantiomerically enriched and racemic compounds were derivatized according to the following sequence. Absolute stereochemistry was assigned by analogy.



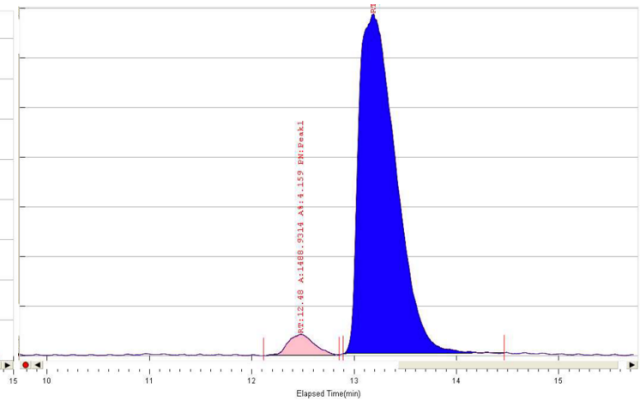
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(benzyloxy)-7-chlorooct-7-en-4-ol.

Racemic Compound



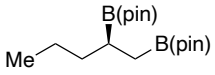
Peak No	% Area	Area	RT (min)
1	50.1848	16033.9338	12.36
2	49.8152	15915.8785	13.13
Total:	100	31949.8123	

Standard Conditions



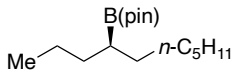
Peak No	% Area	Area	RT (min)
1	4.159	1488.9314	12.48
2	95.841	34311.6632	13.19
Total:	100	35800.5946	

1.6.5 Procedure for Synthesis of (*R*)-Arundic Acid



(*S*)-2,2'-(Pentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.111). This compound was prepared according to a modified *General Procedure H*. In the glovebox, an oven-dried 50 mL round bottom flask equipped with a magnetic stir bar was charged with TBS-DHG catalyst (79 mg, 0.30 mmol, 0.10 equiv.), propanediol diboron (1.02 g, 6.0 mmol, 2.0 equiv.), 4Å molecular sieves (200 mg), pent-1-ene (210.4 mg, 3.0 mmol,

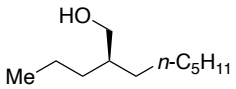
1.0 equiv.) and THF (6.0 mL). DBU (46 mg, 0.20 mmol, 0.10 equiv.) was then added to the solution. The vial was sealed with a rubber septum, removed from the glovebox. The mixture was allowed to stir at room temperature for 12 h. After completion, the reaction vial was charged with pinacol (2.1 g, 18 mmol, 6.0 equiv.) and 3.0 M aqueous solution of sodium hydroxide (0.5 mL, 0.50 equiv.), sealed with a rubber septum. The mixture was allowed to stir at 50 ºC for 5 h. The mixture was then diluted with EtOAc, filtered through a plug of silica gel and concentrated *in vacuo*. The pale-yellow oil residue was purified by silica gel chromatography (5% EtOAc in hexanes) to afford the product as colorless oil (829 mg, 2.6 mmol, 85% yield). All spectral data are in accordance with the literature.[82]



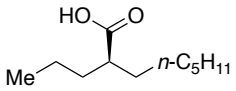
(*R*)-2-(Decan-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.112). The copper-catalyzed cross-coupling was performed according to the *General Procedure G* with (*S*)-2,2'-(pentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **1.111** (810 mg, 2.5 mmol, 1.0 equiv.), 1-bromopent-1-yne (404 mg, 2.75 mmol, 1.1 equiv.), copper cyanide (45 mg, 0.5 mmol, 0.20 equiv.), lithium methoxide (285 mg, 7.5 mmol, 3.0 equiv.) in THF (7.0 mL, 0.4 M). The mixture was diluted with Et_2O and passed through a silica gel pad and concentrated under reduced pressure. The residue was dissolved in EtOH (8.0 mL), Pd/C (10% w/w, 27 mg) was added to the mixture. The mixture was purged with H_2 for 10 min, and was allowed to stir under H_2 atmosphere for 12 h at room temperature. The yellow liquid mixture was diluted with Et_2O, passed through a silica gel pad and concentrated under reduced pressure. The yellow liquid residue was then purified by silica gel chromatography to afford the product as yellow liquid (400 mg, 1.5 mmol, 60% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 – 1.25 (m, 14H), 1.24 (s, 12H), 0.97 (tt, *J* = 8.7, 5.5 Hz, 1H), 0.91 – 0.85 (m, 6H). ^{13}C NMR (126 MHz,

[82] Xie, T.; Zheng, C.; Chen, K.; He, H.; Gao, S. *Angew. Chem., Int. Ed.* **2020**, *59*, 4360–4364.

$CDCl_3$) δ 82.7, 33.8, 31.8, 31.4, 29.6, 29.3, 24.8, 22.6, 22.4, 14.4, 14.1. IR (neat) ν_{max} 2954 (m), 2921 (s), 2853 (w), 1464 (w), 1386 (m), 1313 (m), 1250 (w), 1213 (w), 1144 (s), 967 (w), 862 (w). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{16}H_{34}BO_2$ 269.26; Found 269.27. $[\alpha]^{20}_D$: –1.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).



(*R*)-2-Propyloctan-1-ol (1.113). To a 50 mL round bottom flask was added (*R*)-2-(decan-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1.112** (380 mg, 1.4 mmol, 1.0 equiv.) and chlorobromomethane (458 mg, 3.5 mmol, 2.5 equiv.), sealed with a rubber septum and purged with nitrogen. Anhydrous Et_2O (0.15 M) was added and *n*-BuLi (1.42 mL, 3.5 mmol, 2.5 equiv.) was added dropwise at –78 °C. The solution was allowed to stir at –78 °C for 1 h and was allowed to warm to room temperature and to stir for 4 h. The mixture was cooled to 0 °C (ice/water) and charged with 3.0 M aqueous solution of sodium hydroxide (6.0 mL), followed by dropwise addition of 30% hydrogen peroxide (3.0 mL). The mixture was allowed to warm to room temperature and allowed to stir for another 2 h. The mixture was then cooled to 0 °C (ice/water) and a saturated aqueous solution of sodium thiosulfate (8.0 mL) was added dropwise over 5 min. The mixture was diluted with ethyl acetate. Aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 × 10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting yellow liquid residue was purified by silica gel chromatography to afford the product as pale-yellow liquid (186 mg, 1.1 mmol, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.53 (d, *J* = 5.6 Hz, 2H), 1.54 – 1.40 (m, 2H), 1.29 (dt, *J* = 16.2, 3.9 Hz, 13H), 0.94 – 0.85 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 65.7, 40.3, 33.3, 31.9, 30.9, 29.7, 26.8, 22.7, 20.0, 14.4, 14.1. IR (neat) ν_{max} 3317 (br), 2953 (m), 2921 (s), 2854 (m), 1464 (w), 1377 (w), 1040 (w), 736 (w). HRMS (DART) m/z: $[M+H-H_2O]^+$ Calcd for $C_{11}H_{23}$ 155.18; Found 155.18. $[\alpha]^{20}_D$: –0.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).



(*R*)-2-Propyloctanoic acid (1.114). To a Schlenk tube were added (*R*)-2-propyloctan-1-ol **1.113** (90 mg, 0.5 mmol, 1.0 equiv.), $Fe(NO_3)_3 \cdot 9H_2O$ (21.1 mg, 0.1 mmol), TEMPO (8.2 mg, 0.1 mmol), KCl (3.9 mg, 0.1 mmol), and DCE (4 mL). The mixture was purged with oxygen gas for 15 min and was allowed to stir at 25 ºC under the atmosphere of oxygen from a balloon for 12 h.[83] The reaction was quenched by addition of H_2O (5 mL) and was washed with Et_2O (3 × 10 mL). The organic layers were combined and dried with Na_2SO_4, and concentrated under reduced pressure. The yellow liquid residue was purified by silica gel chromatography to afford the product as yellow liquid (78 mg, 0.4 mmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.36 (tt, *J* = 8.7, 5.3 Hz, 1H), 1.68 – 1.58 (m, 2H), 1.52 – 1.42 (m, 2H), 1.40 – 1.23 (m, 10H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.9, 45.3, 34.3, 32.2, 31.6, 29.0, 27.3, 22.6, 20.5, 14.03, 13.97. IR (neat) ν_{max} 3012 (br), 2955 (m), 2925 (m), 2856 (w), 1702 (s), 1464 (w), 1240 (w), 1214 (w), 1111 (w), 942 (w). HRMS (DART) m/z: $[M+H]^+$ Calcd for $C_{11}H_{23}O_2$ 187.17; Found 187.17. $[\alpha]^{20}_D$: –5.7 (c = 2.0, EtOH, *l* = 50 mm). All spectral data are in accordance with previous reports.[84]

1.6.6 Procedure for Experiments with CuO*t*-Bu

1.6.6.1 Preparation for CuOt-Bu solution

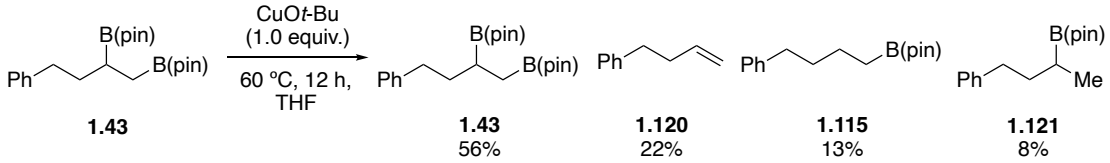
An oven-dried 2-dram vial was charged with CuI (0.2 mmol) under argon, the vial was sealed and placed in an ice-bath. A solution of NaO*t*-Bu (0.21 mmol) dissolved in THF (0.5 mL) was then injected dropwise and the mixture was allowed to stir for 30 min at 0 ºC. The resulting CuO*t*-Bu was used as solution in THF directly in the following transformations.

[83] Jiang, X.; Zhang, J.; Ma, S. *J. Am. Chem. Soc.* **2016**, *138*, 8344–8347.

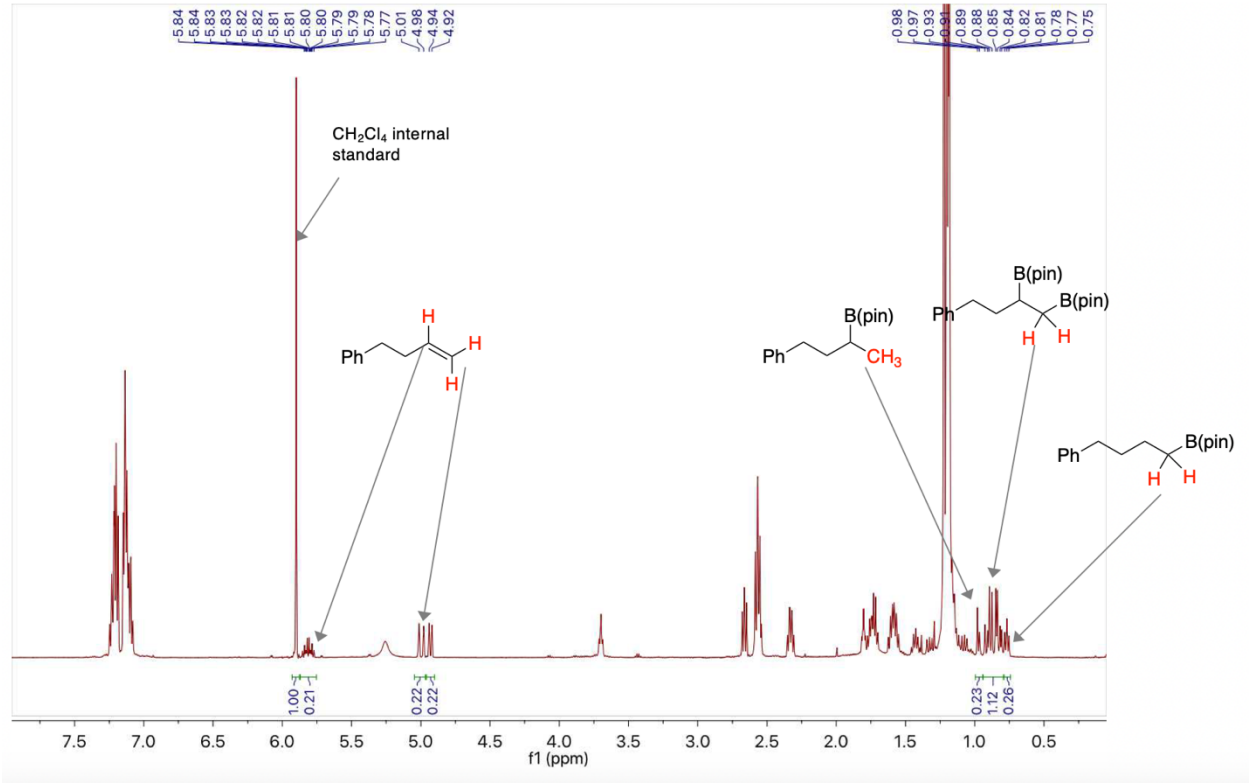
[84] Pelotier, B.; Holmes, T.; Piva, O. *Asymmetry*. **2005**, *16*, 1513–1520.

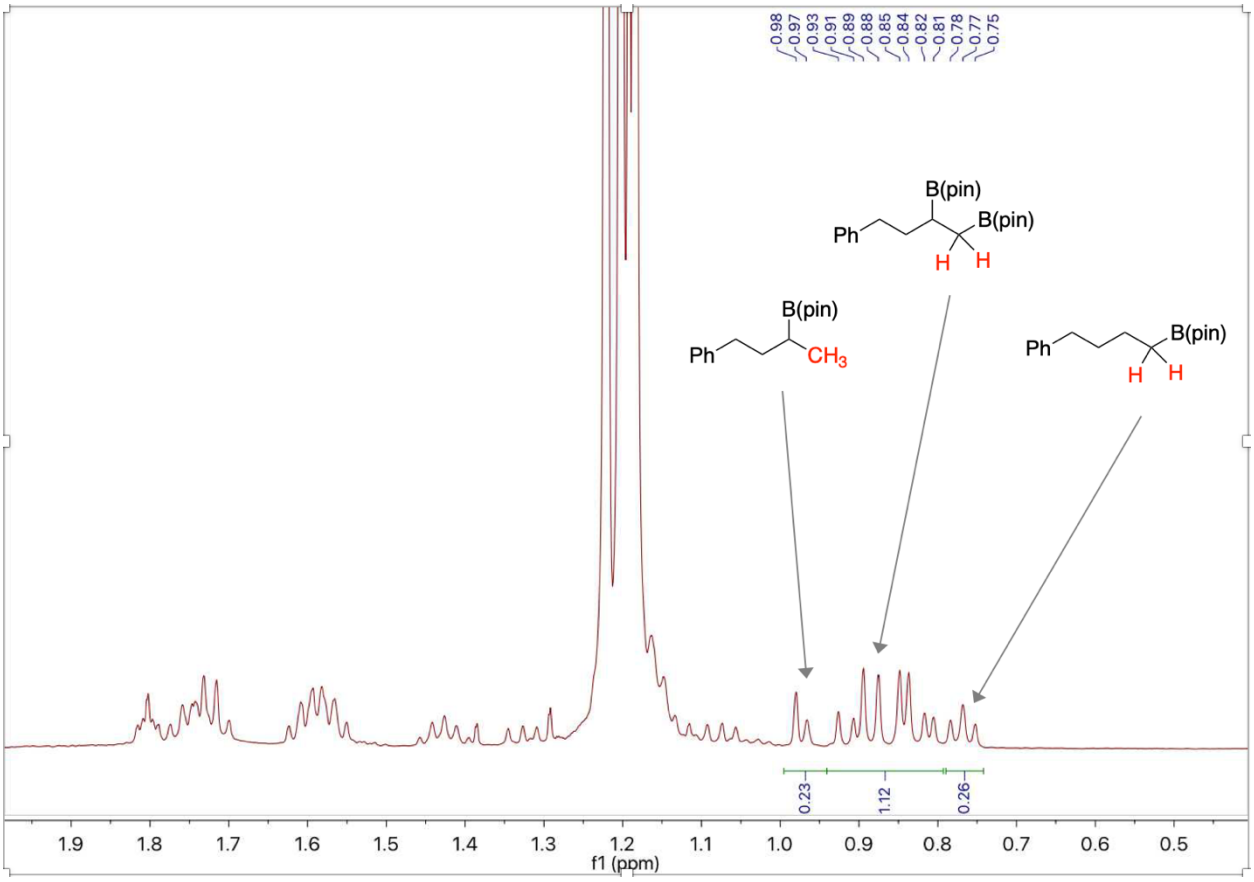
1.6.6.2 Experiment 1

An oven-dried 2-dram vial was charged with **1.43** (77.2 mg, 0.2 mmol), sealed and purgued with argon. CuO*t*-Bu (solution in THF) was transferred to the vial. The mixture was allowed to stir at 60 ºC for 12 h. It was then allowed to cool to room temperature, diluted with Et_2O, and filtered through a silica gel pad. The mixture was concentrated under reduced pressure, 1,1,2,2-tetrachloroethane (16.7 mg, 0.1 mmol) was added as internal standard. The mixture was dissolved in 0.5 mL $CDCl_3$ and was transferred to an NMR tube.



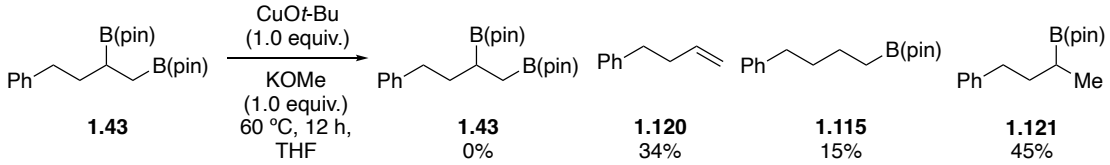
1.43 **1.43** 56% **1.120** 22% **1.115** 13% **1.121** 8%

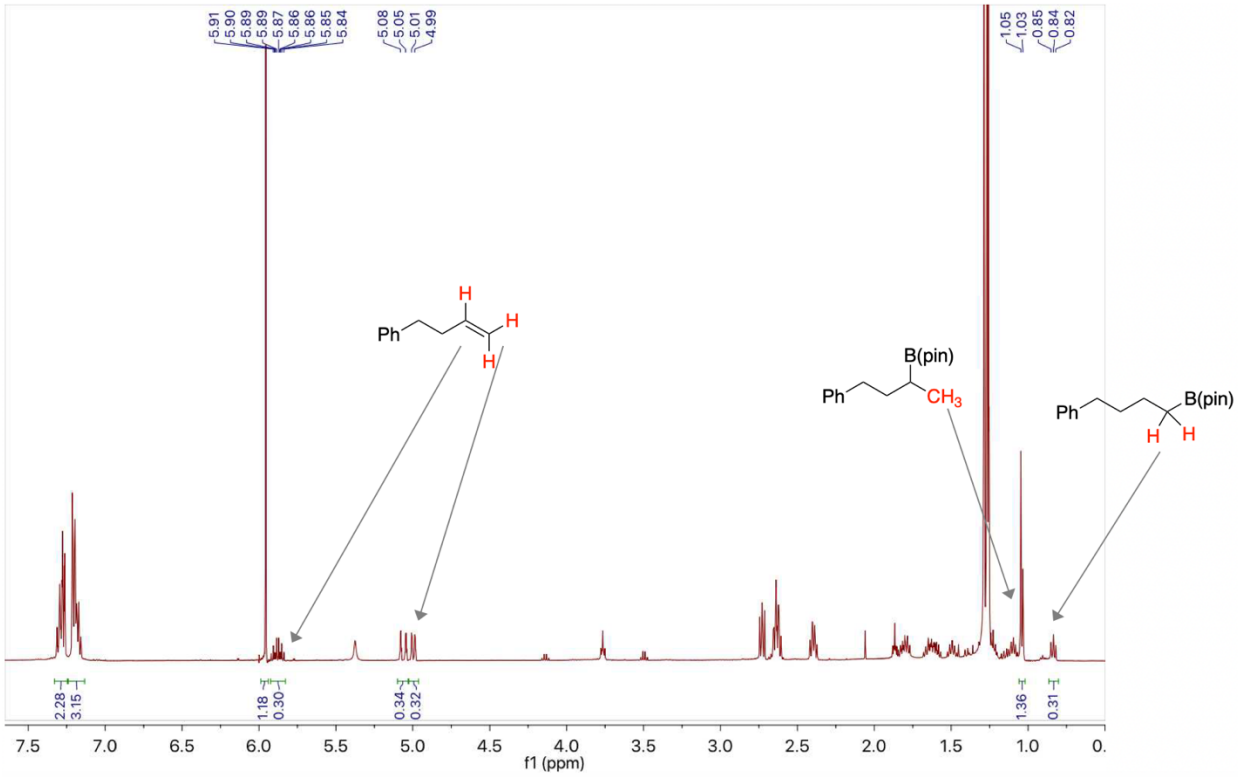

5.84
5.84
5.83
5.83
5.82
5.82
5.81
5.81
5.80
5.80
5.79
5.79
5.78
5.77
5.01
4.98
4.94
4.92
0.98
0.97
0.93
0.91
0.89
0.88
0.85
0.84
0.82
0.81
0.78
0.77
0.75
CH2Cl4 internal standard
Ph
H
H
H
Ph
B(pin)
CH3
Ph
B(pin)
B(pin)
H
H
Ph
B(pin)
H
H
1.00
0.21
0.22
0.22
0.23
1.12
0.26
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

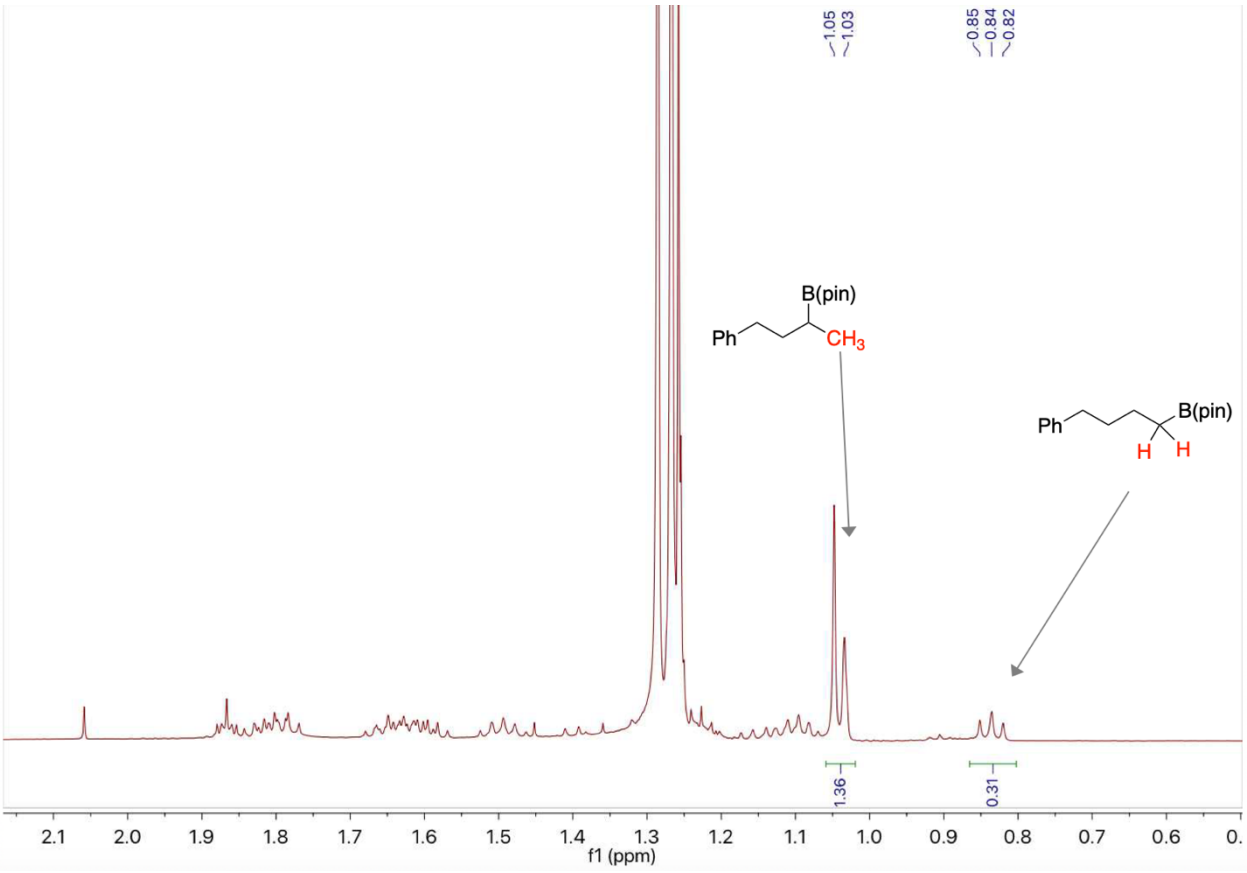

0.98
0.97
0.93
0.91
0.89
0.88
0.85
0.84
0.82
0.81
0.78
0.77
0.75
Ph
B(pin)
B(pin)
H
H
Ph
B(pin)
CH3
Ph
B(pin)
H
H
0.23
1.12
0.26
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
f1 (ppm)

1.6.6.3 Experiment 2

An oven-dried 2-dram vial was charged with **1.43** (77.2 mg, 0.2 mmol), KOMe (14.7 mg, 0.21 mmol), sealed and purgued with argon. CuO*t*-Bu (solution in THF) was transferred to the vial. The mixture was allowed to stir at 60 ºC for 12 h. It was then allowed to cool to room temperature, diluted with Et_2O, and filtered through a silica gel pad. The mixture was concentrated under reduced pressure, 1,1,2,2-tetrachloroethane (16.7 mg, 0.1 mmol) was added as internal standard. The mixture was dissolved in 0.5 mL $CDCl_3$ and was transferred to an NMR tube.

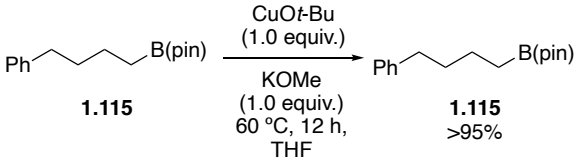


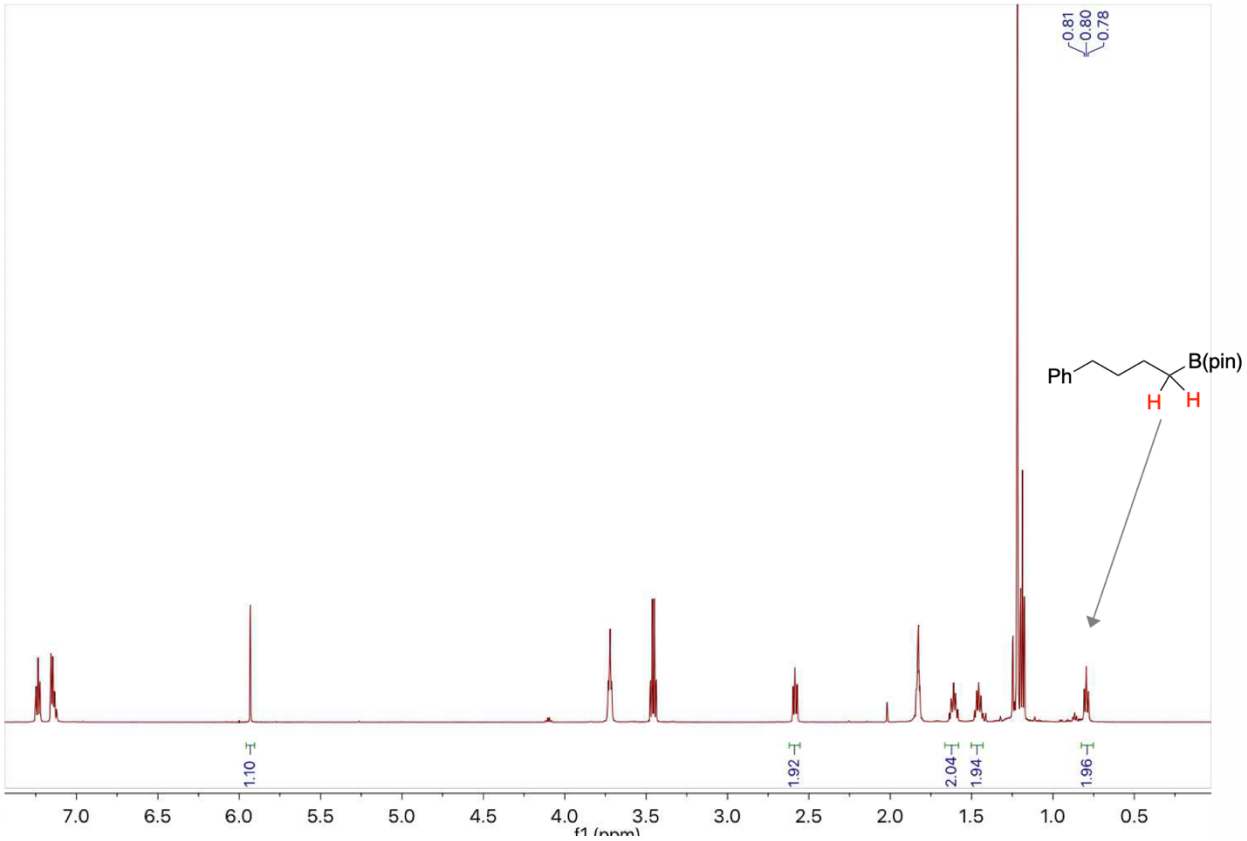




1.6.6.4 Experiment 3

An oven-dried 2-dram vial was charged with **1.15** (52.0 mg, 0.2 mmol), KOMe (14.7 mg, 0.21 mmol), sealed and purgued with argon. CuO*t*-Bu (solution in THF) was transferred to the vial. The mixture was allowed to stir at 60 ºC for 12 h. It was then allowed to cool to room temperature, diluted with Et_2O, and filtered through a silica gel pad. The mixture was concentrated under reduced pressure, 1,1,2,2-tetrachloroethane (16.7 mg, 0.1 mmol) was added as internal standard. The mixture was dissolved in 0.5 mL $CDCl_3$ and was transferred to an NMR tube.

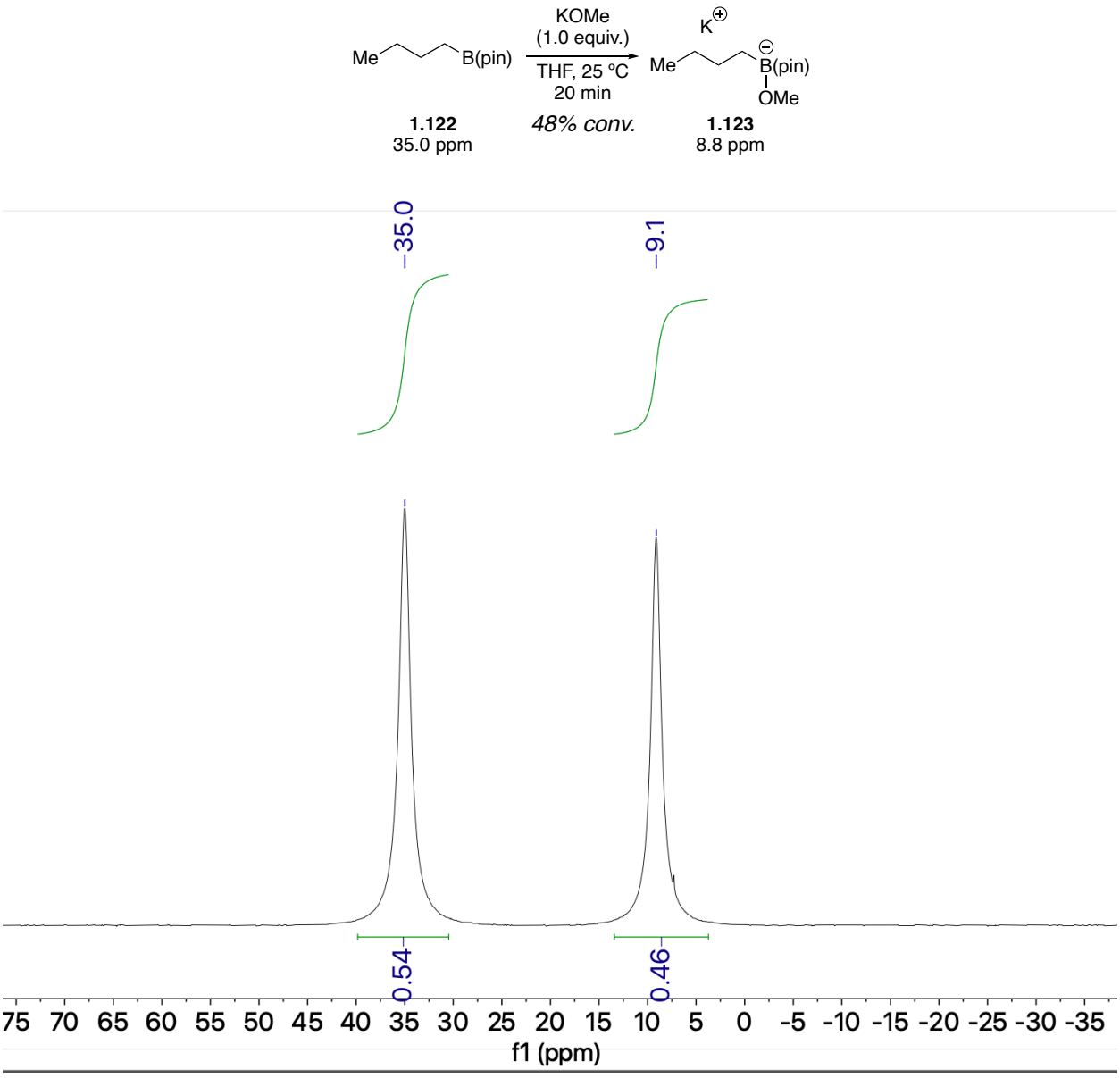




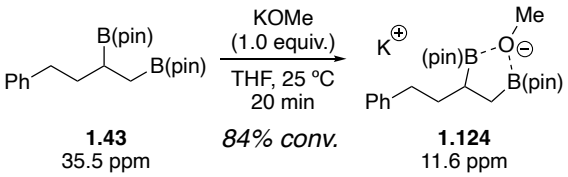
1.6.7 ^{11}B NMR Experiments

An oven-dried 2-dram vial was charged with the desired boronate compound (0.2 mmol), KOMe (0.2 mmol), THF (0.5 mL) under argon atmosphere. The mixture was allowed to stir at room temperature for 15 min and was directly transferred into the NMR tube in the glovebox.

1.6.7.1 Experiment 1



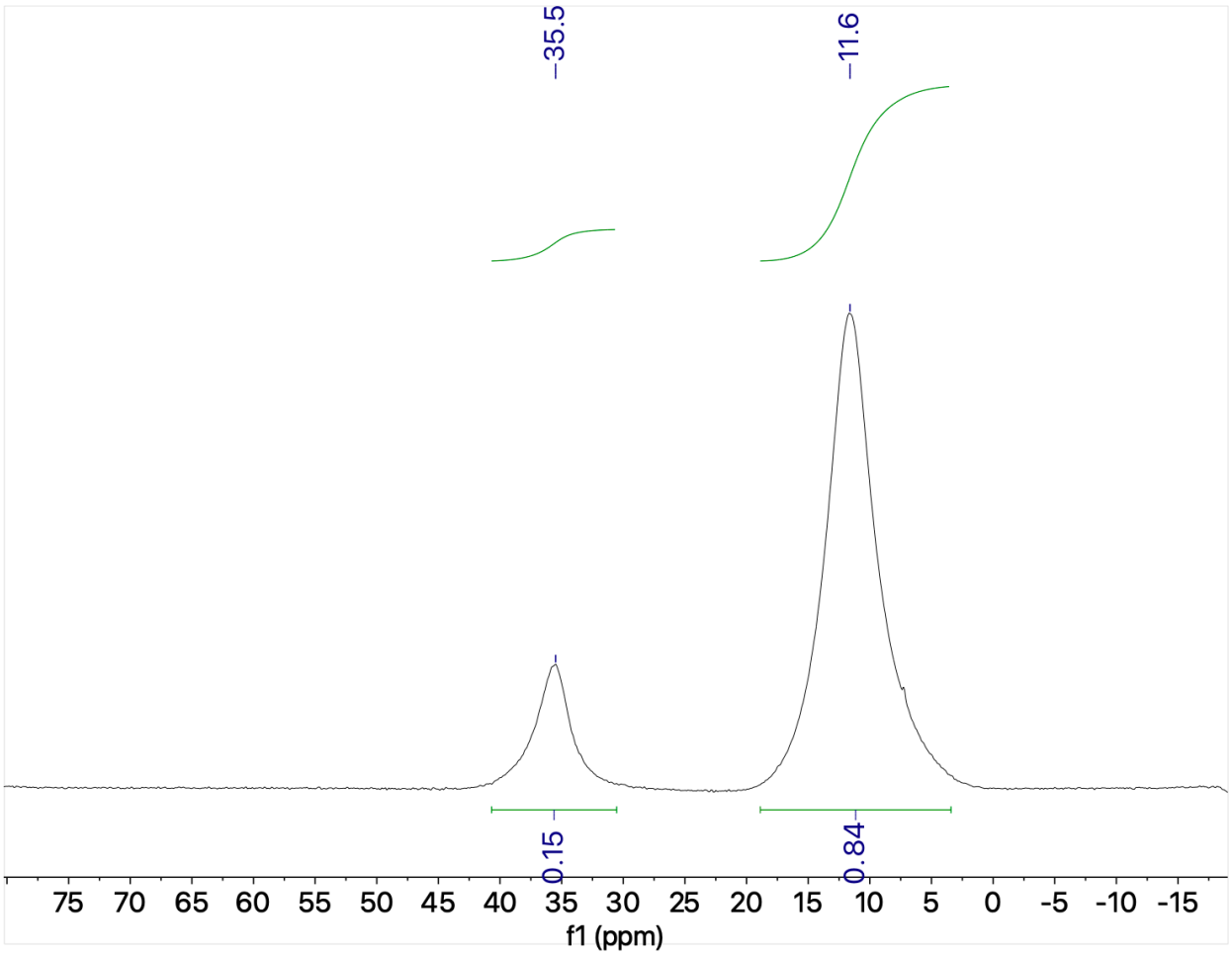
1.6.7.2 Experiment 2



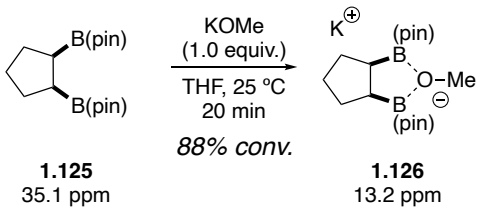
1.43
35.5 ppm

84% conv.

1.124
11.6 ppm

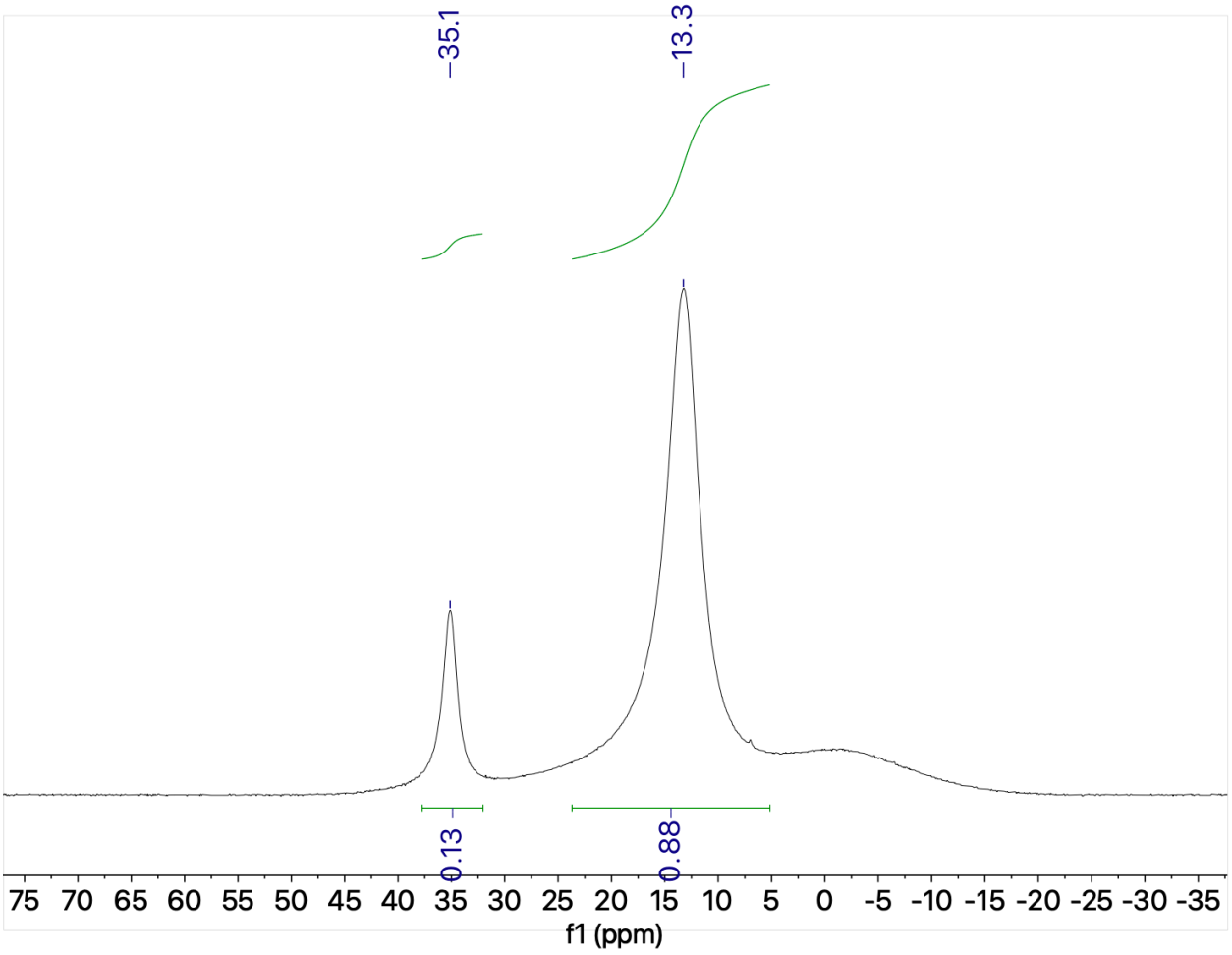


1.6.7.3 Experiment 3

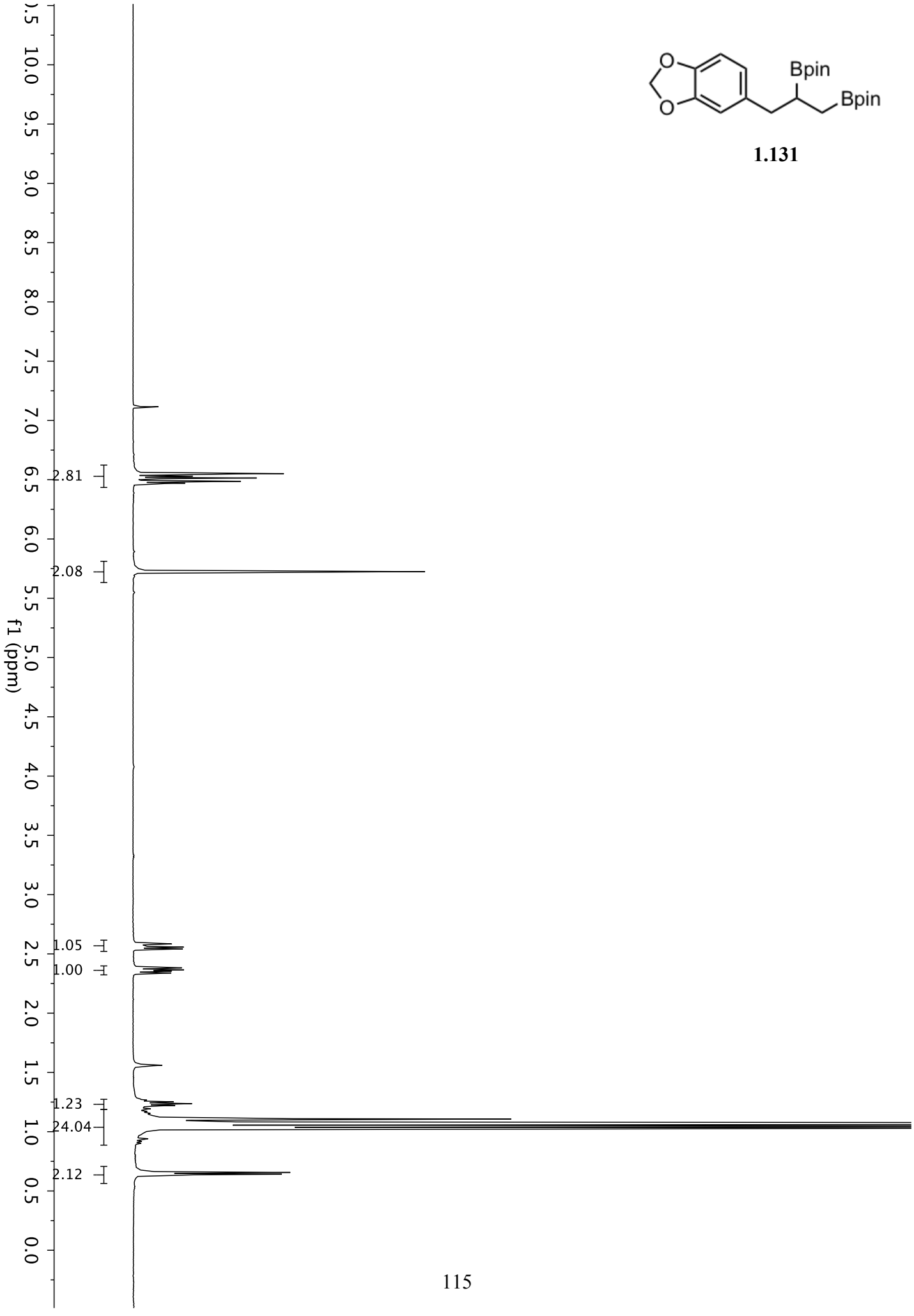


1.125
35.1 ppm

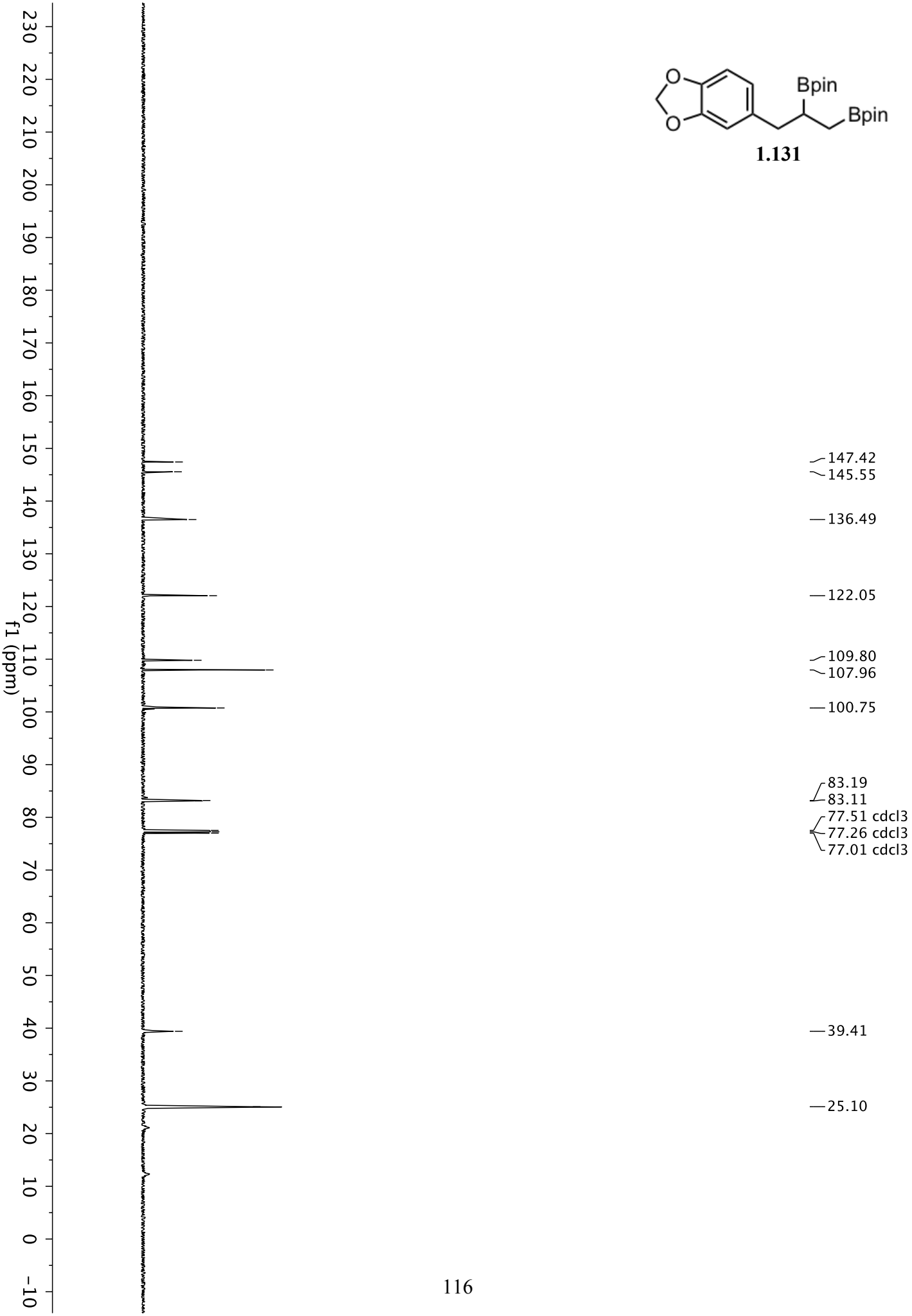
1.126
13.2 ppm

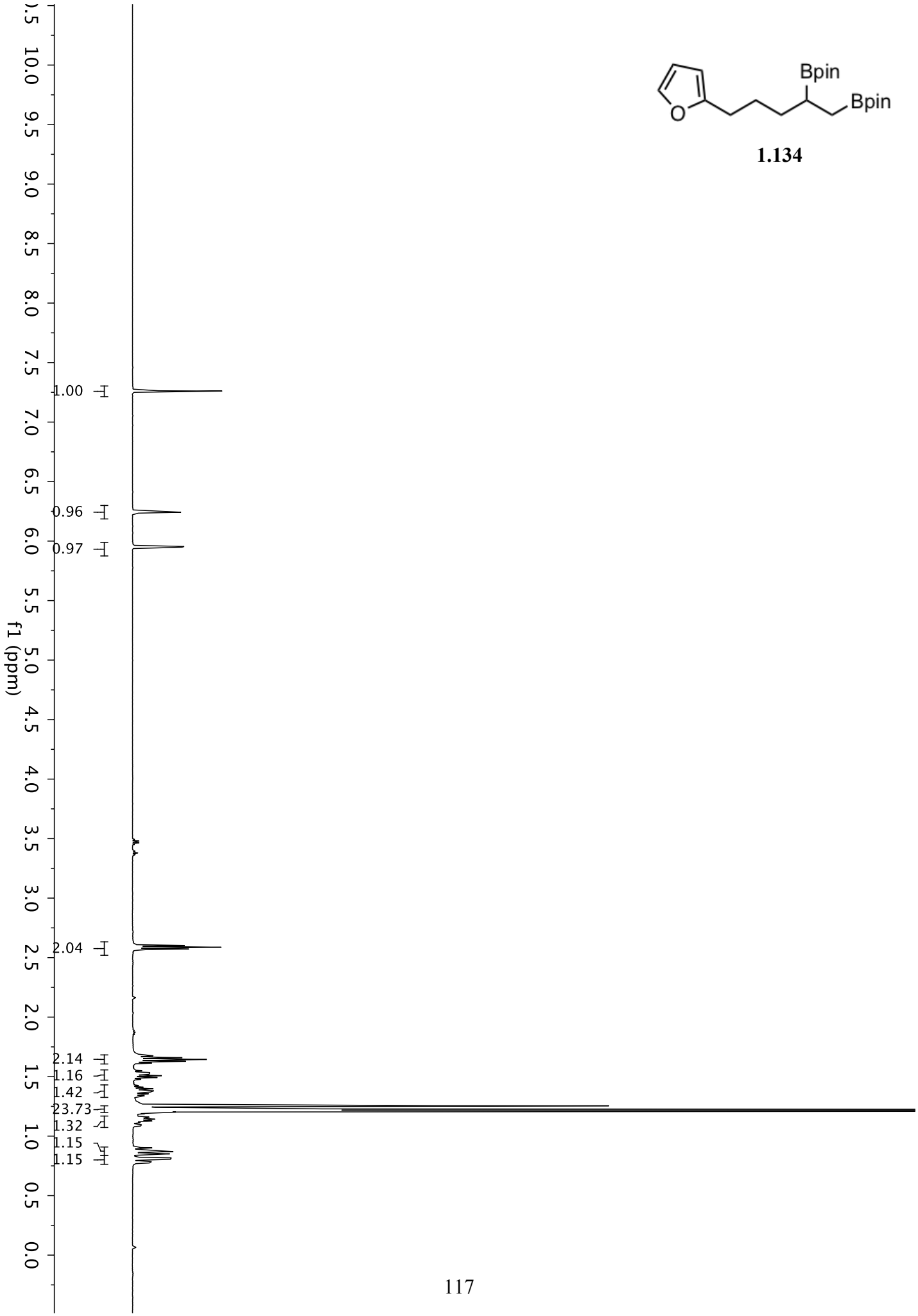


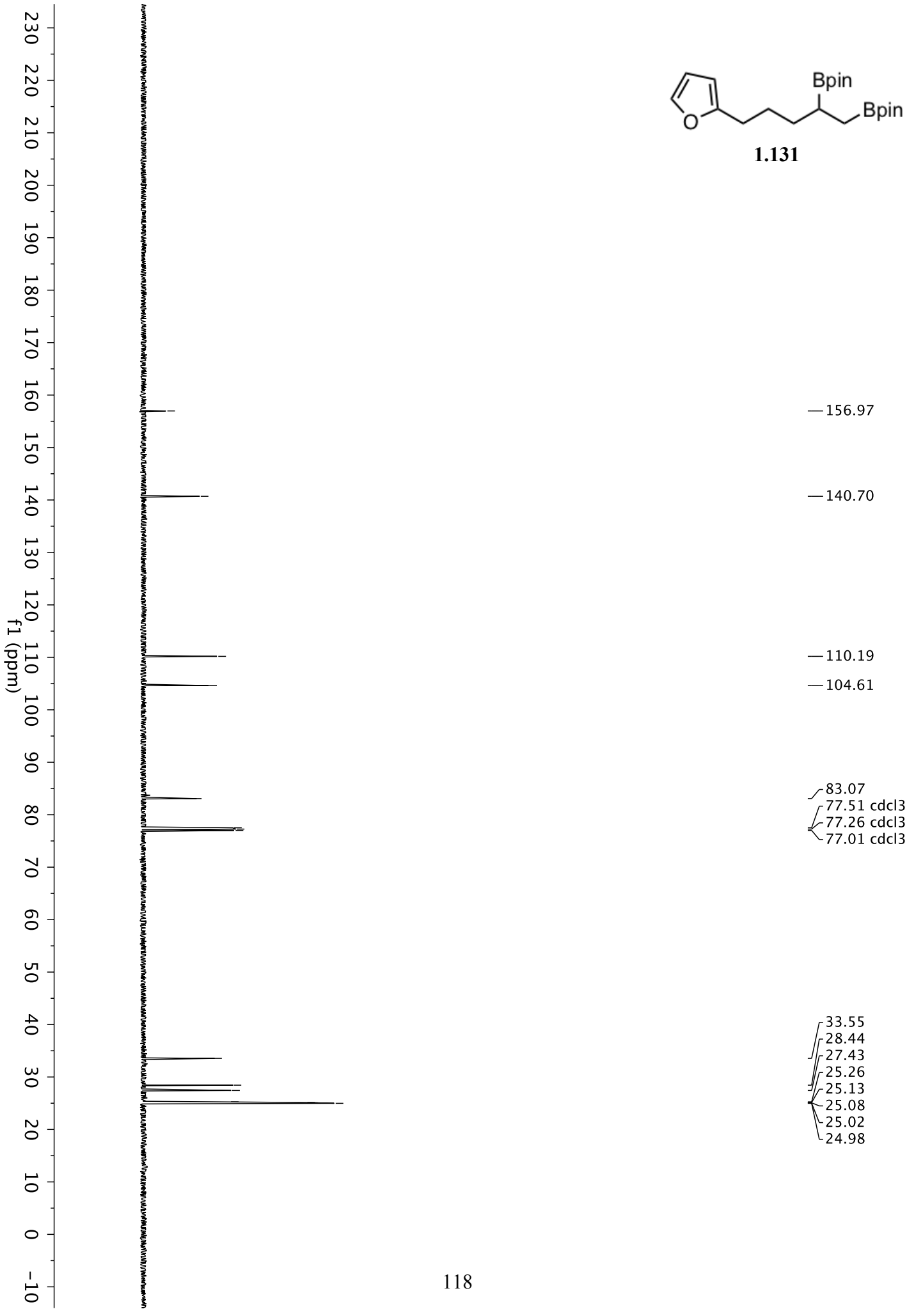
1.7 Spectra

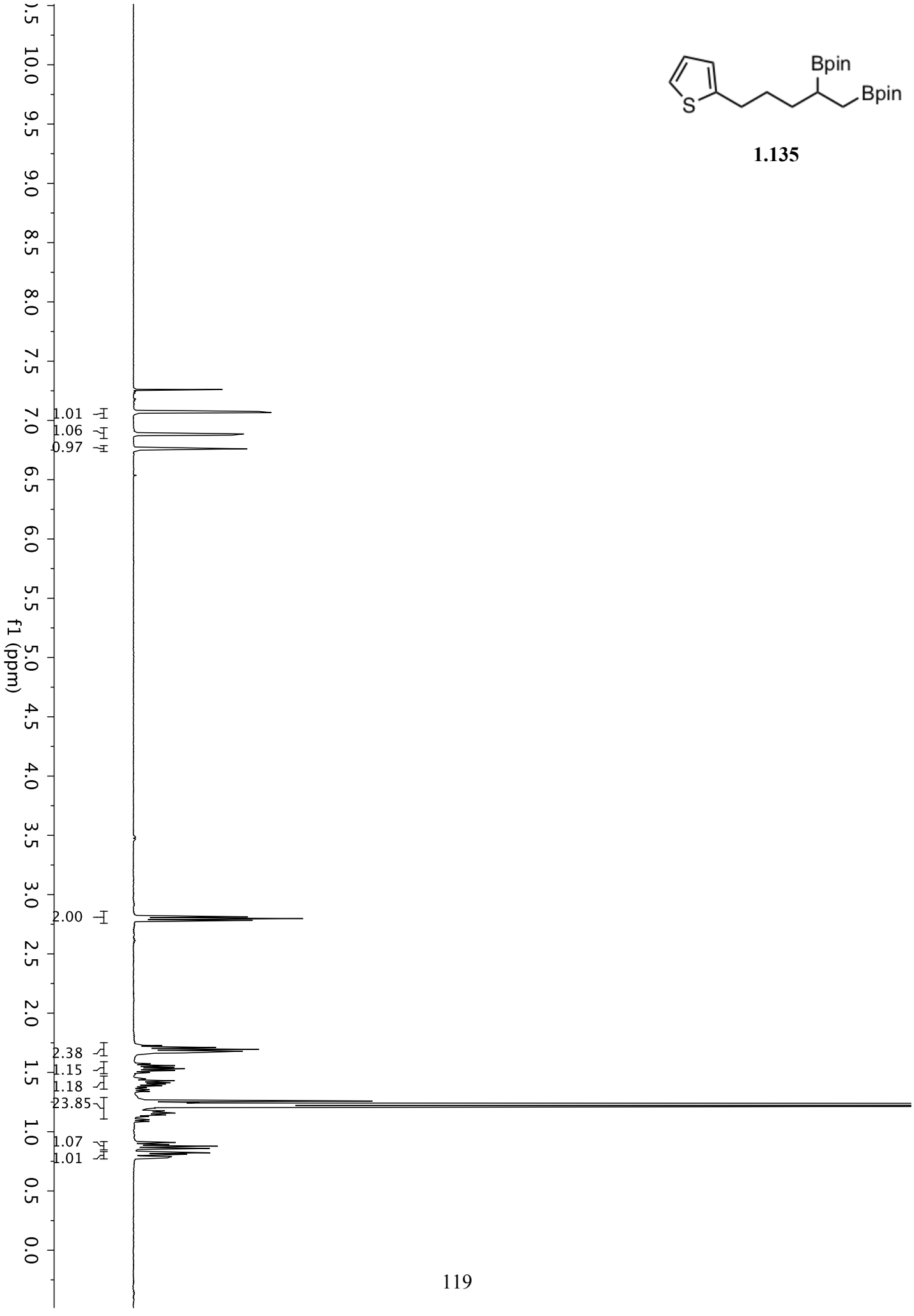


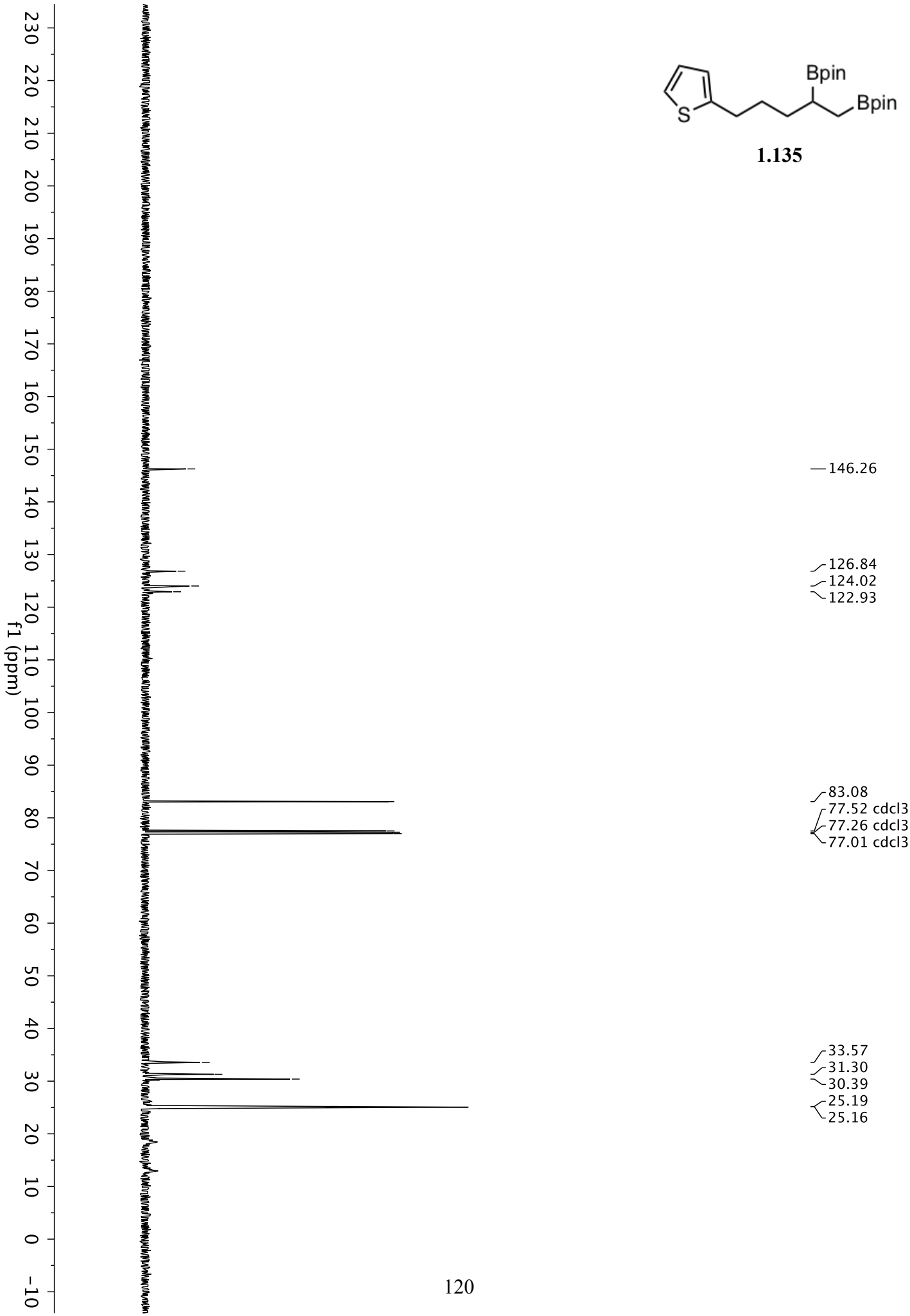
1.131

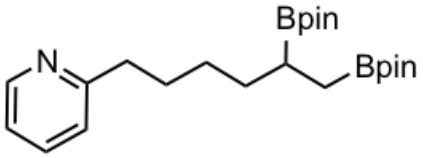

Bpin
Bpin
O
O
O
1.131
147.42
145.55
136.49
122.05
109.80
107.96
100.75
83.19
83.11
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
39.41
25.10
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Bpin
Bpin
O
1.134
f1 (ppm)
1.00
0.96
0.97
2.04
2.14
1.16
1.42
23.73
1.32
1.15
1.15

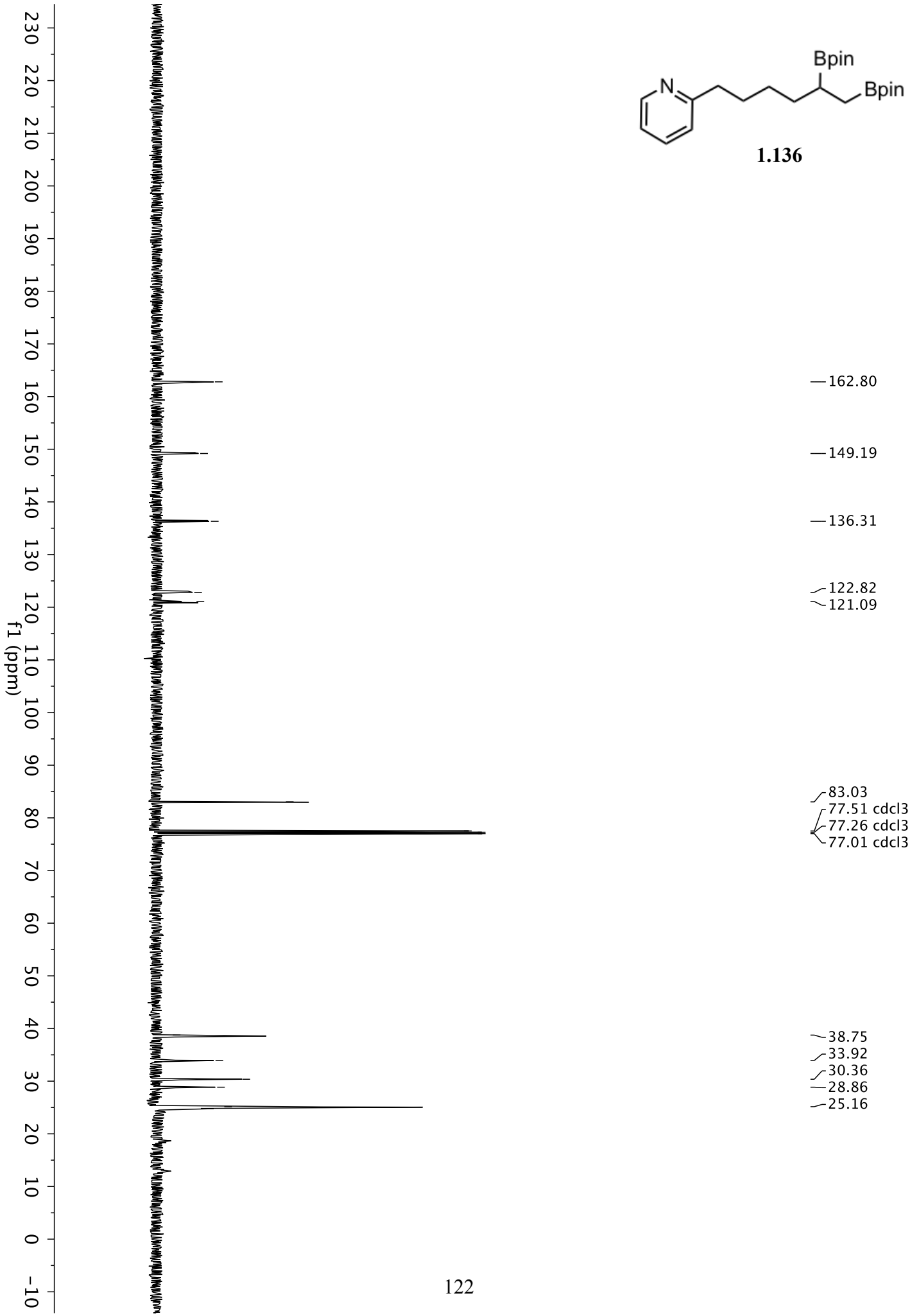

Bpin
Bpin
O
1.131
156.97
140.70
110.19
104.61
83.07
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
33.55
28.44
27.43
25.26
25.13
25.08
25.02
24.98
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

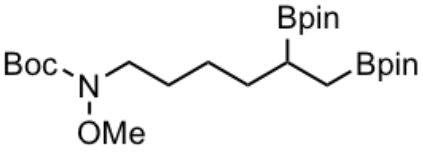

Bpin
Bpin
S
1.135
1.01
1.06
0.97
2.00
2.38
1.15
1.18
23.85
1.07
1.01
f1 (ppm)


Bpin
Bpin
S
1.135
146.26
126.84
124.02
122.93
83.08
77.52 cdcl3
77.26 cdcl3
77.01 cdcl3
33.57
31.30
30.39
25.19
25.16
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

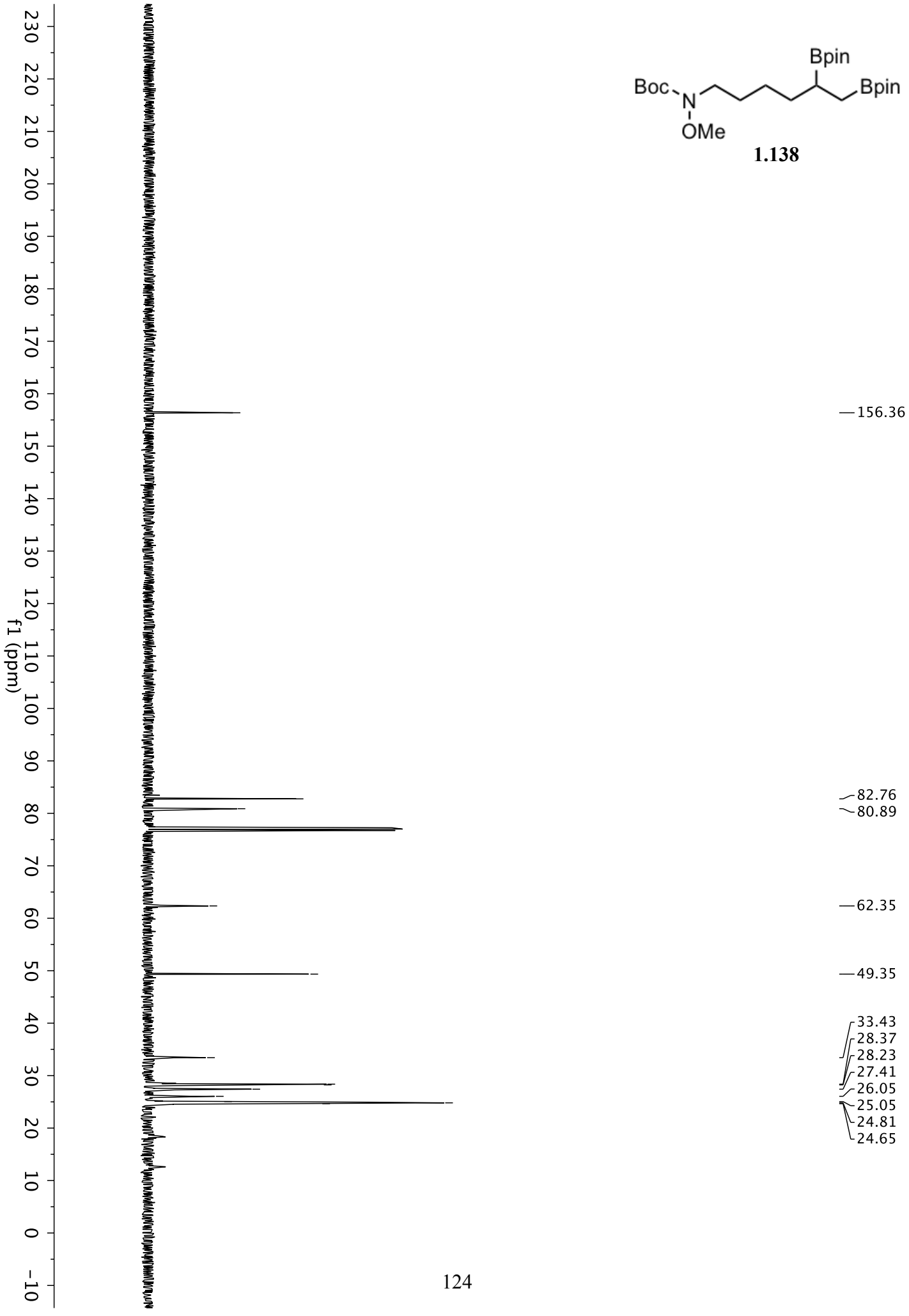


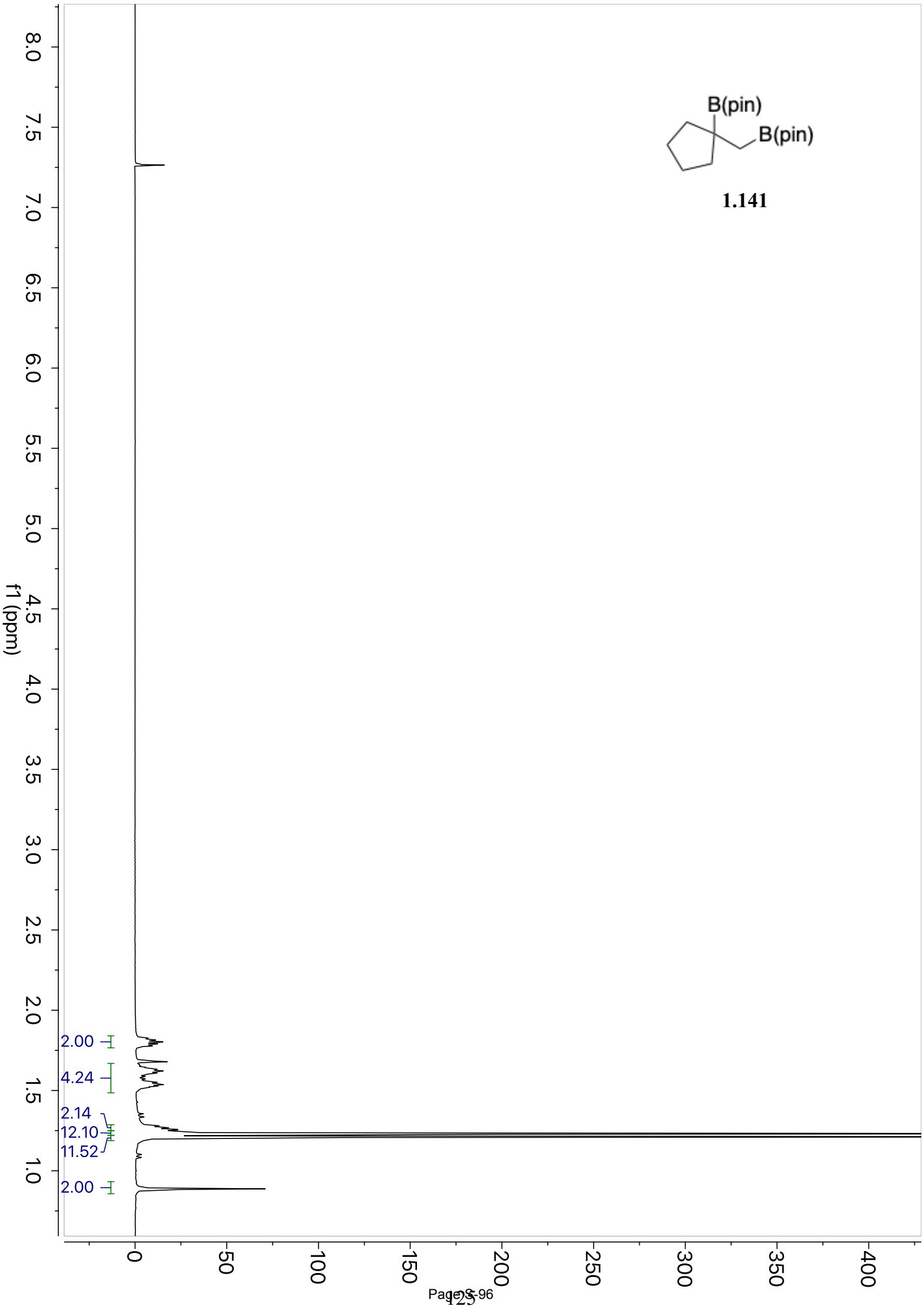
1.136

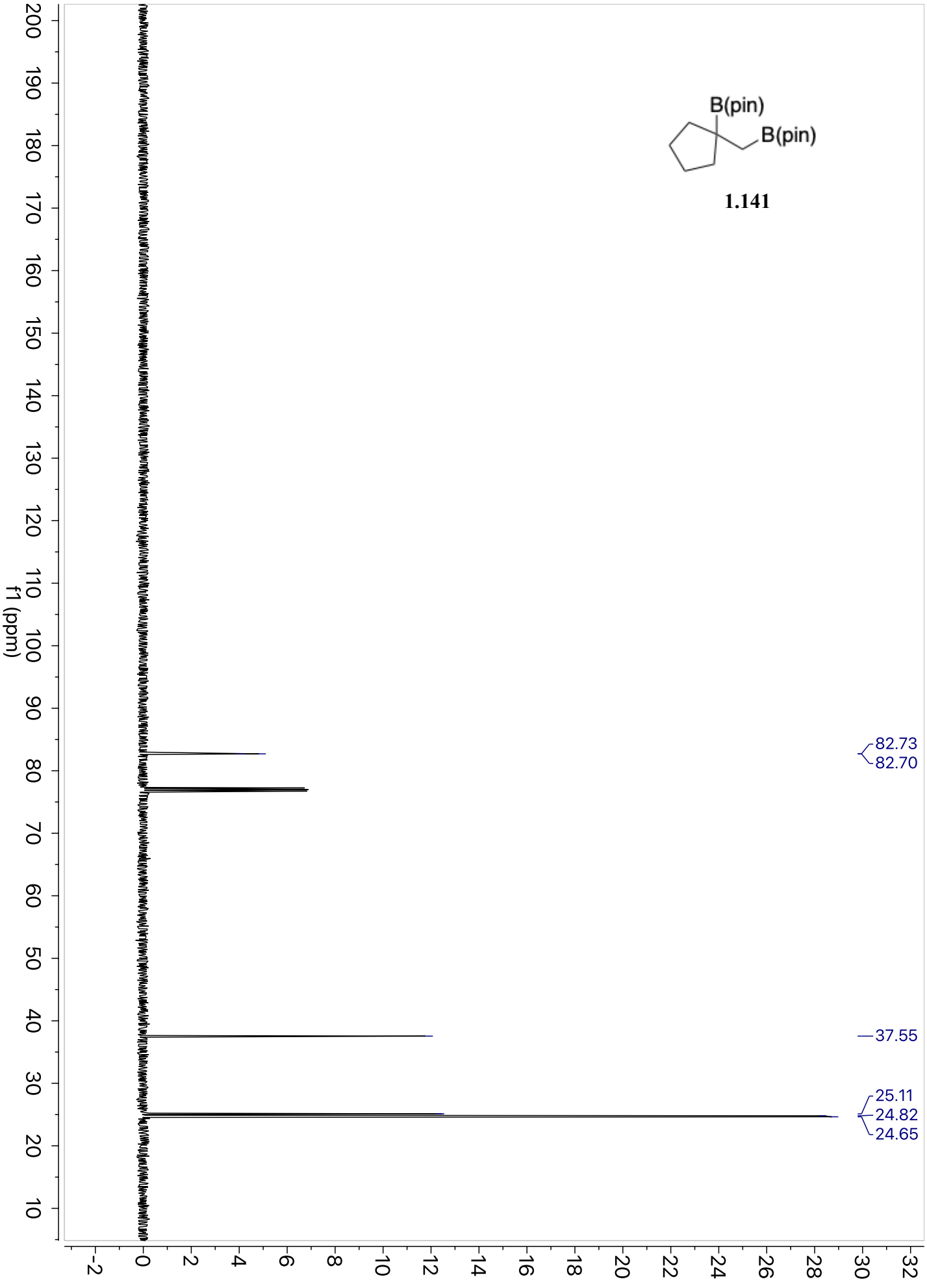

Bpin
N
Bpin
1.136
162.80
149.19
136.31
122.82
121.09
83.03
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
38.75
33.92
30.36
28.86
25.16
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

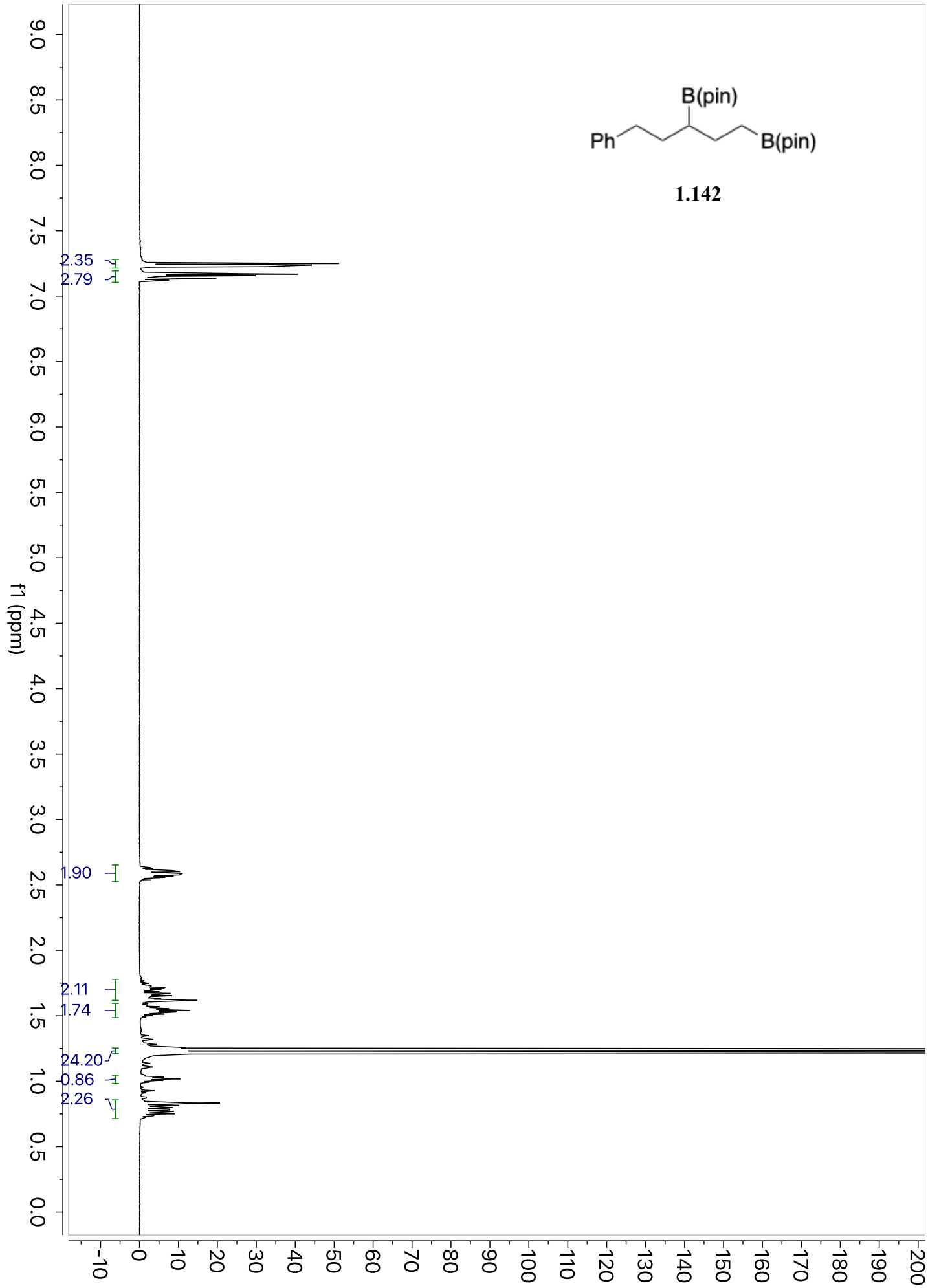


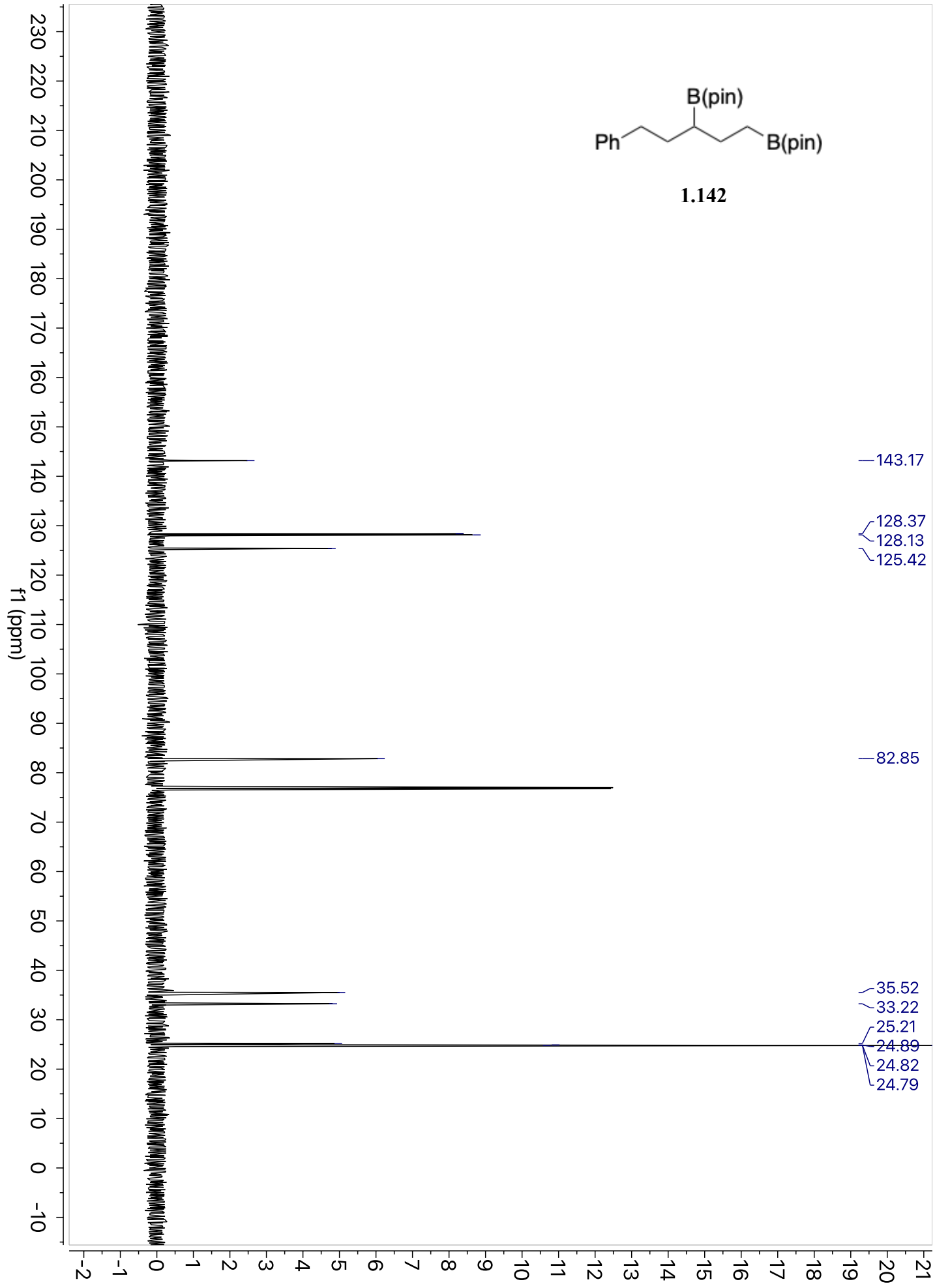
1.138

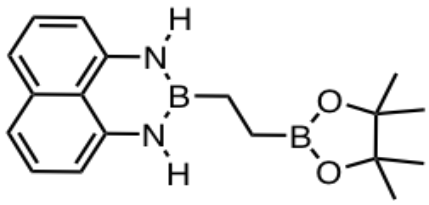

Bpin
Boc
N
Bpin
OMe
1.138
156.36
82.76
80.89
62.35
49.35
33.43
28.37
28.23
27.41
26.05
25.05
24.81
24.65
f1 (ppm)


B(pin)
B(pin)
1.141
f1 (ppm)
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
2.00
4.24
2.14
12.10
11.52
2.00
0
50
100
150
200
250
300
350
400

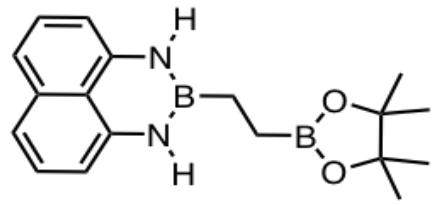

B(pin)
B(pin)
1.141
82.73
82.70
37.55
25.11
24.82
24.65
f1 (ppm)


B(pin)
Ph
B(pin)
1.142
2.35
2.79
1.90
2.11
1.74
24.20
0.86
2.26
f1 (ppm)

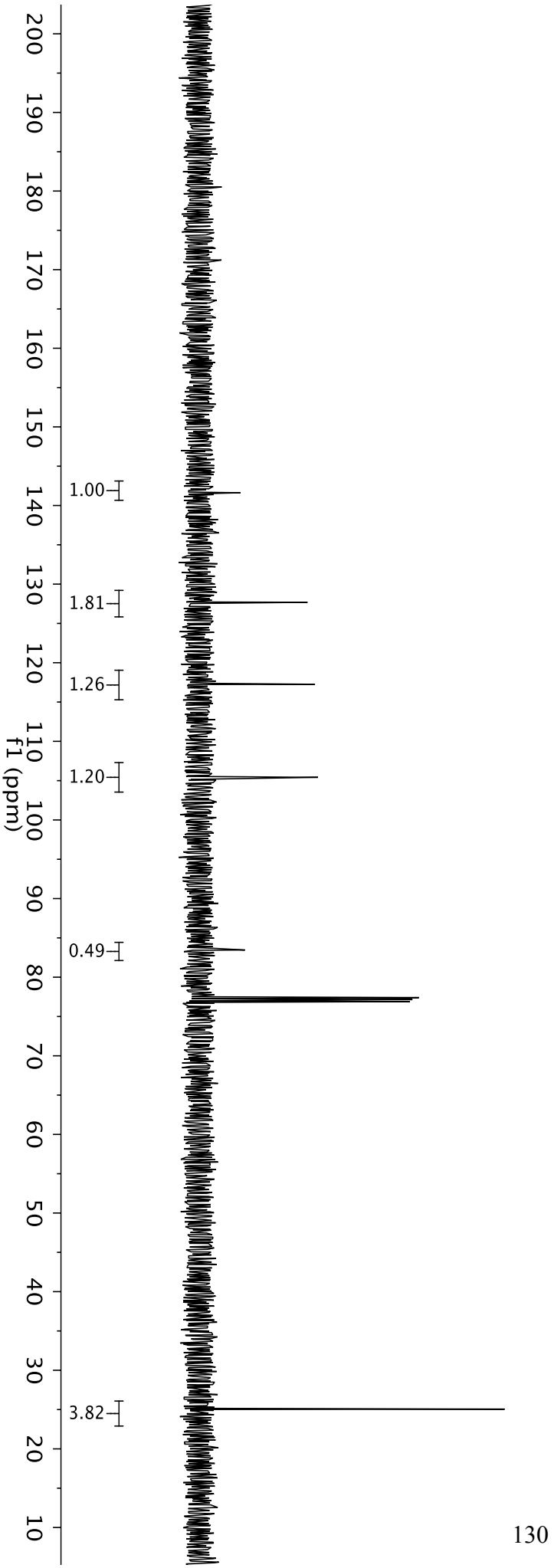

B(pin)
Ph
B(pin)
1.142
143.17
128.37
128.13
125.42
82.85
35.52
33.22
25.21
24.89
24.82
24.79
f1 (ppm)

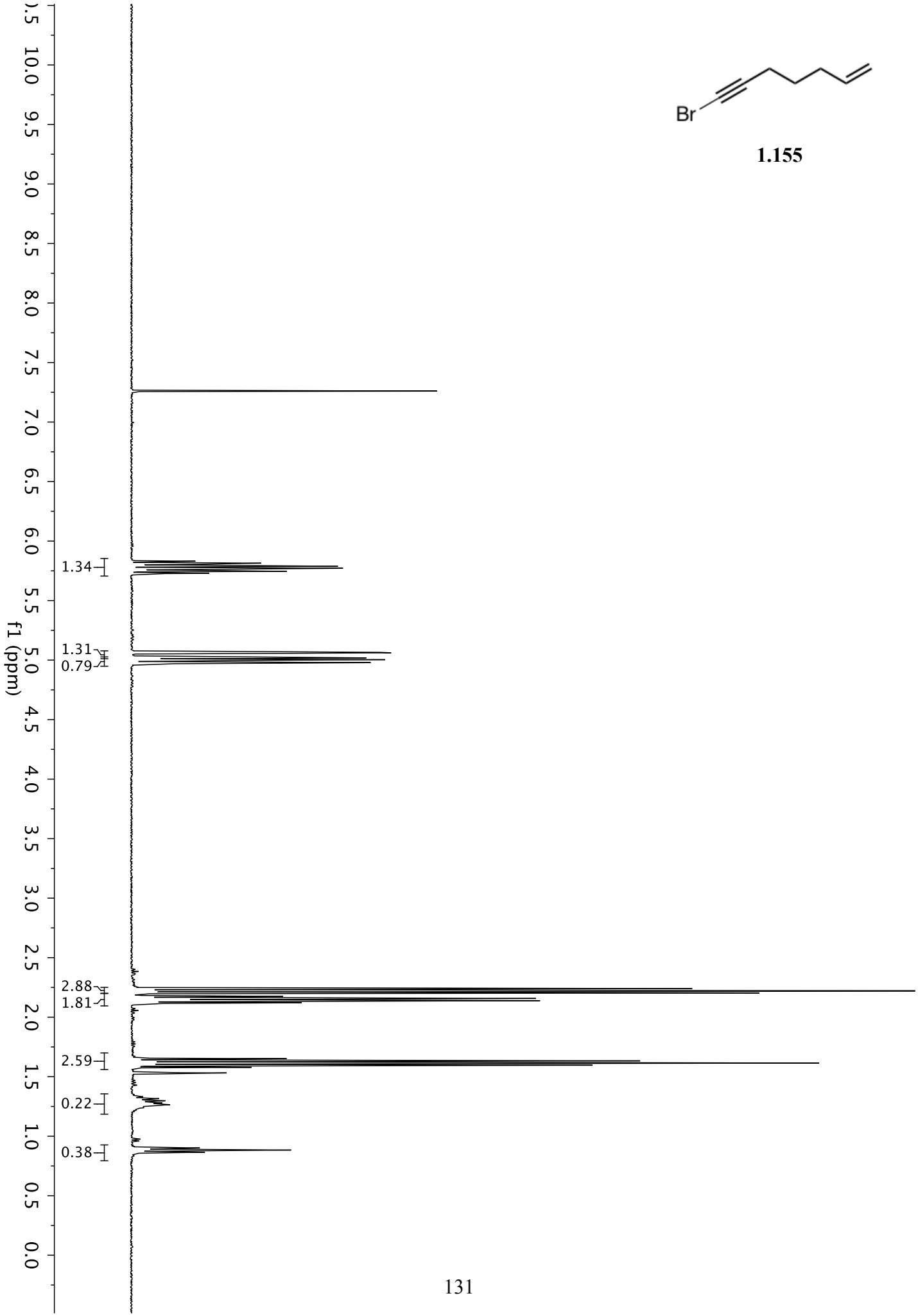


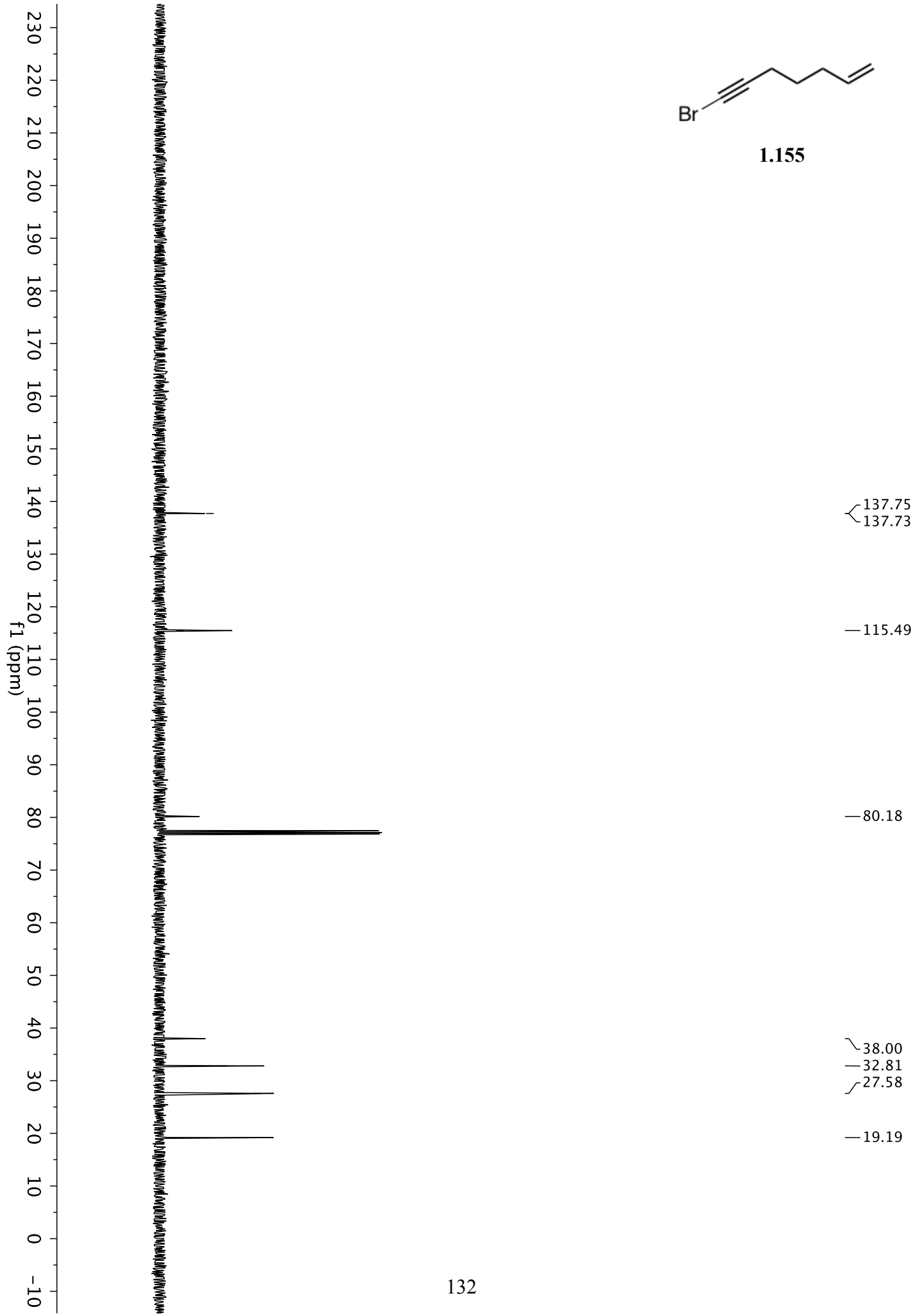
1.117

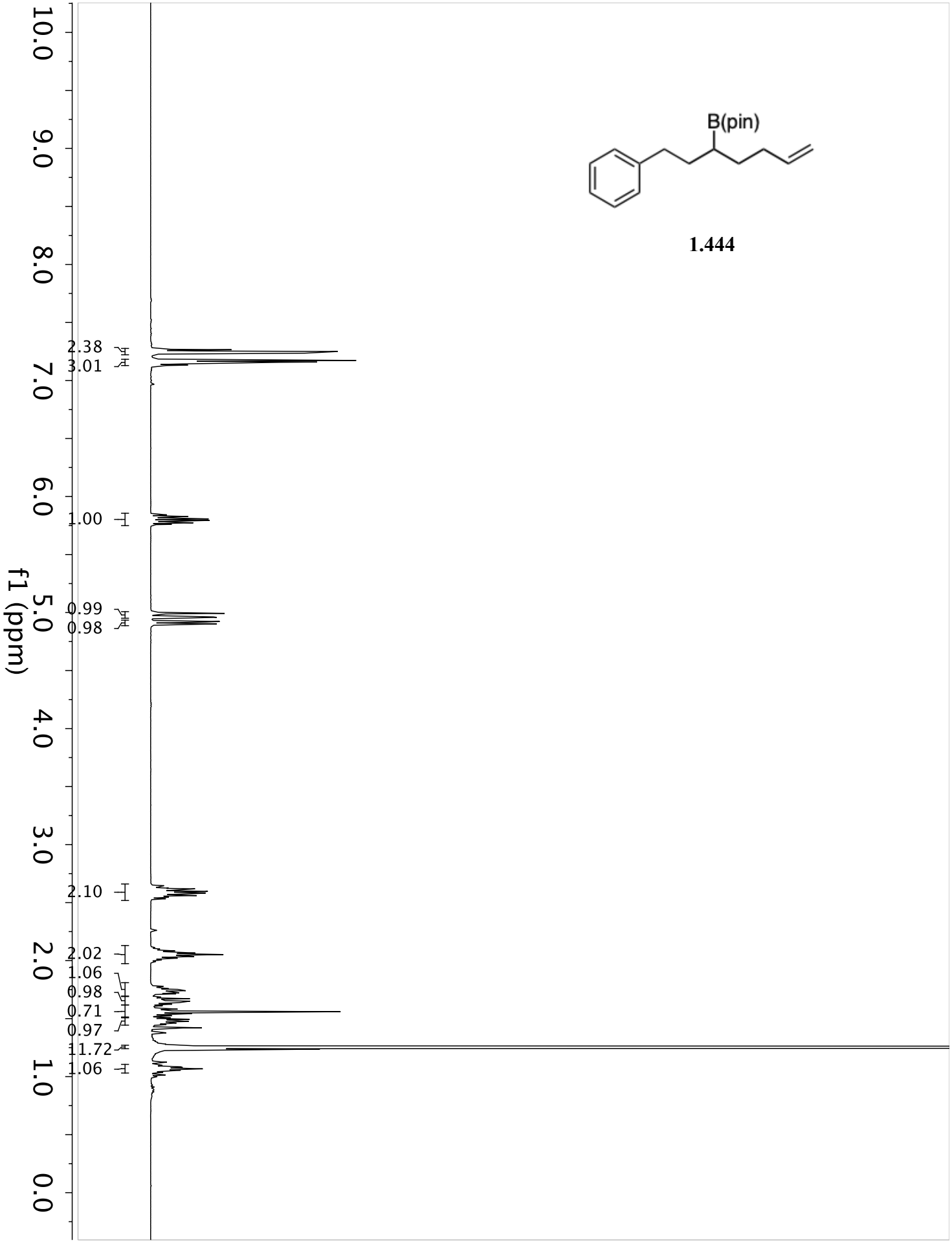


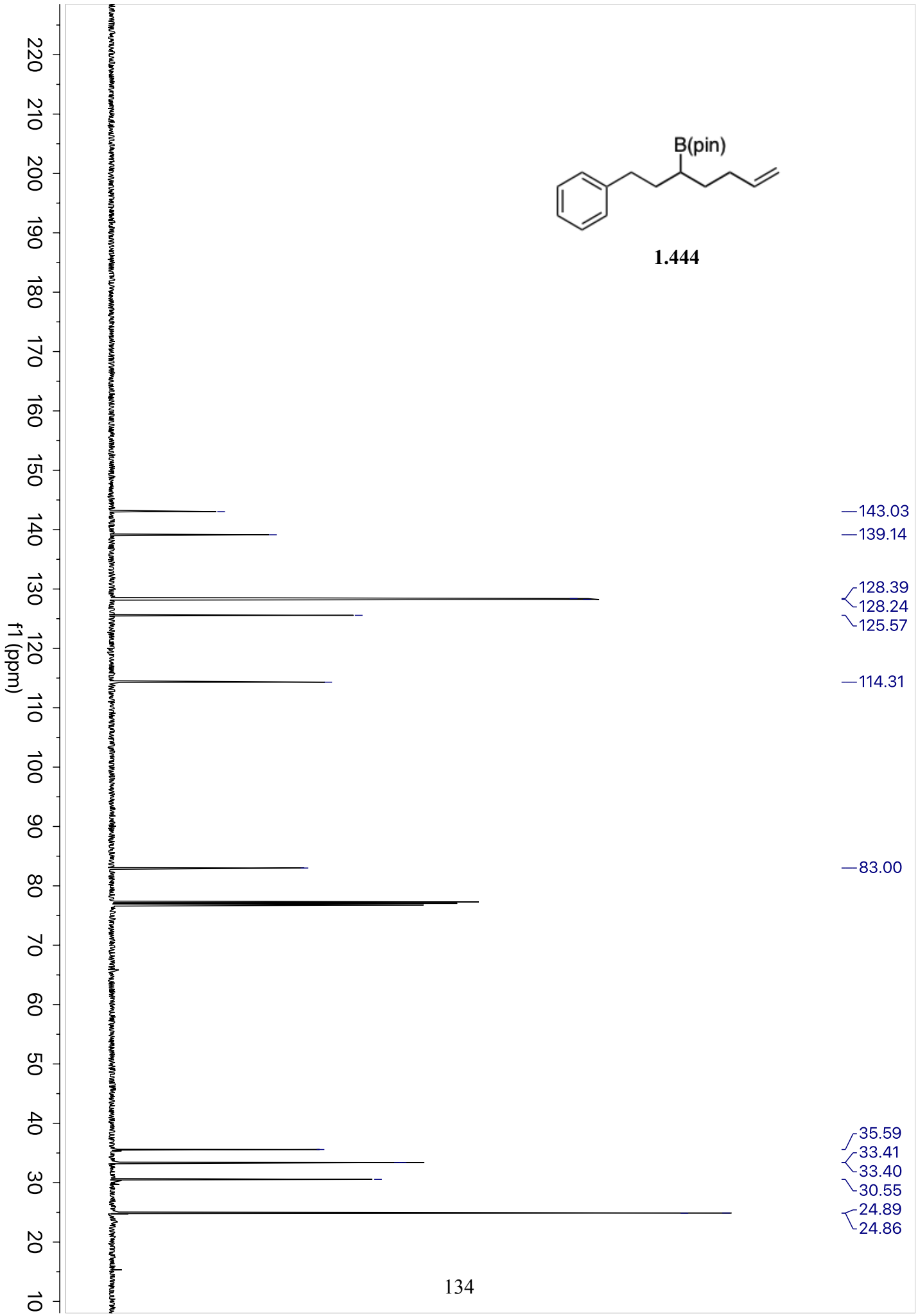
1.117

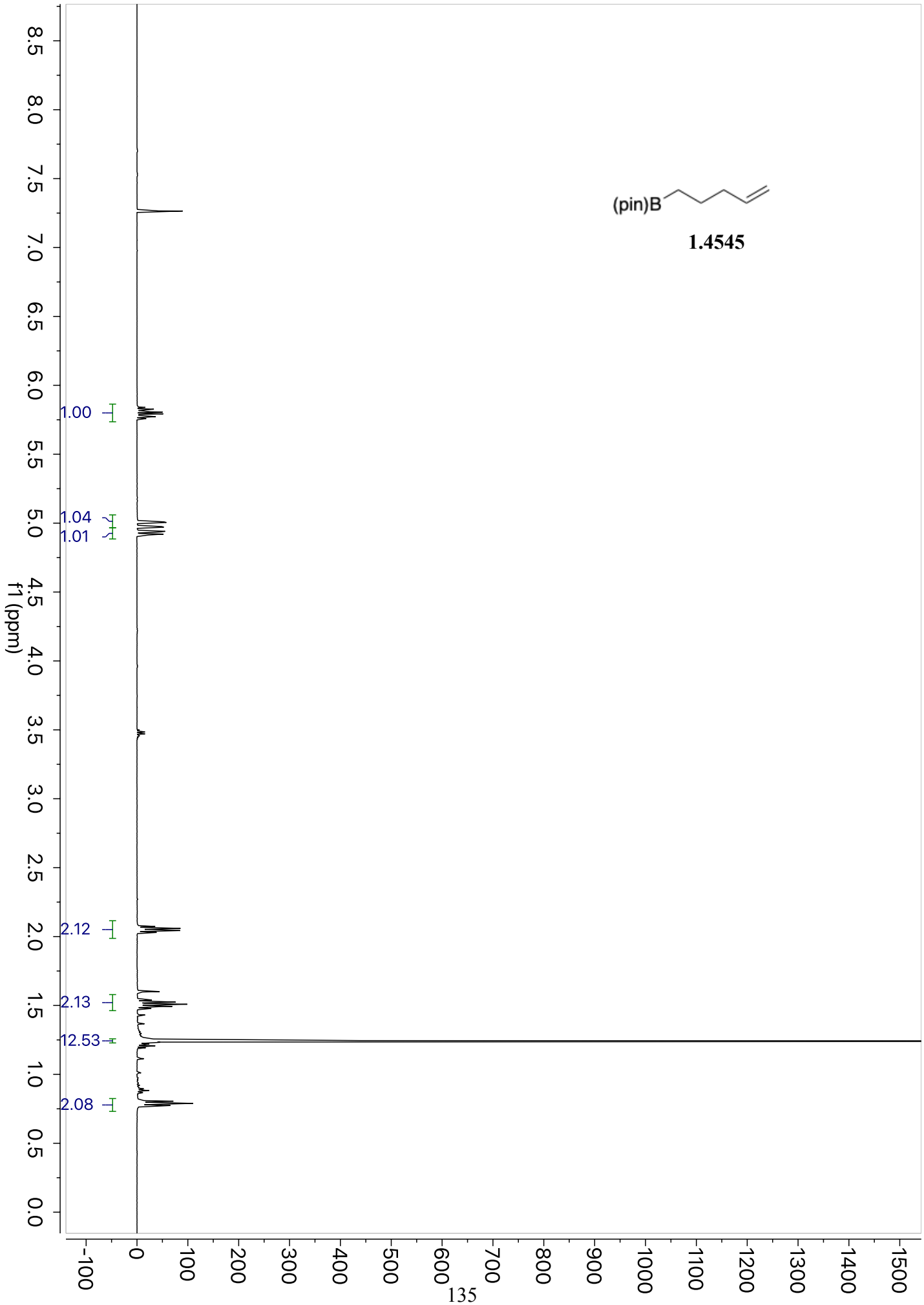

f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
1.00
1.81
1.26
1.20
0.49
3.82

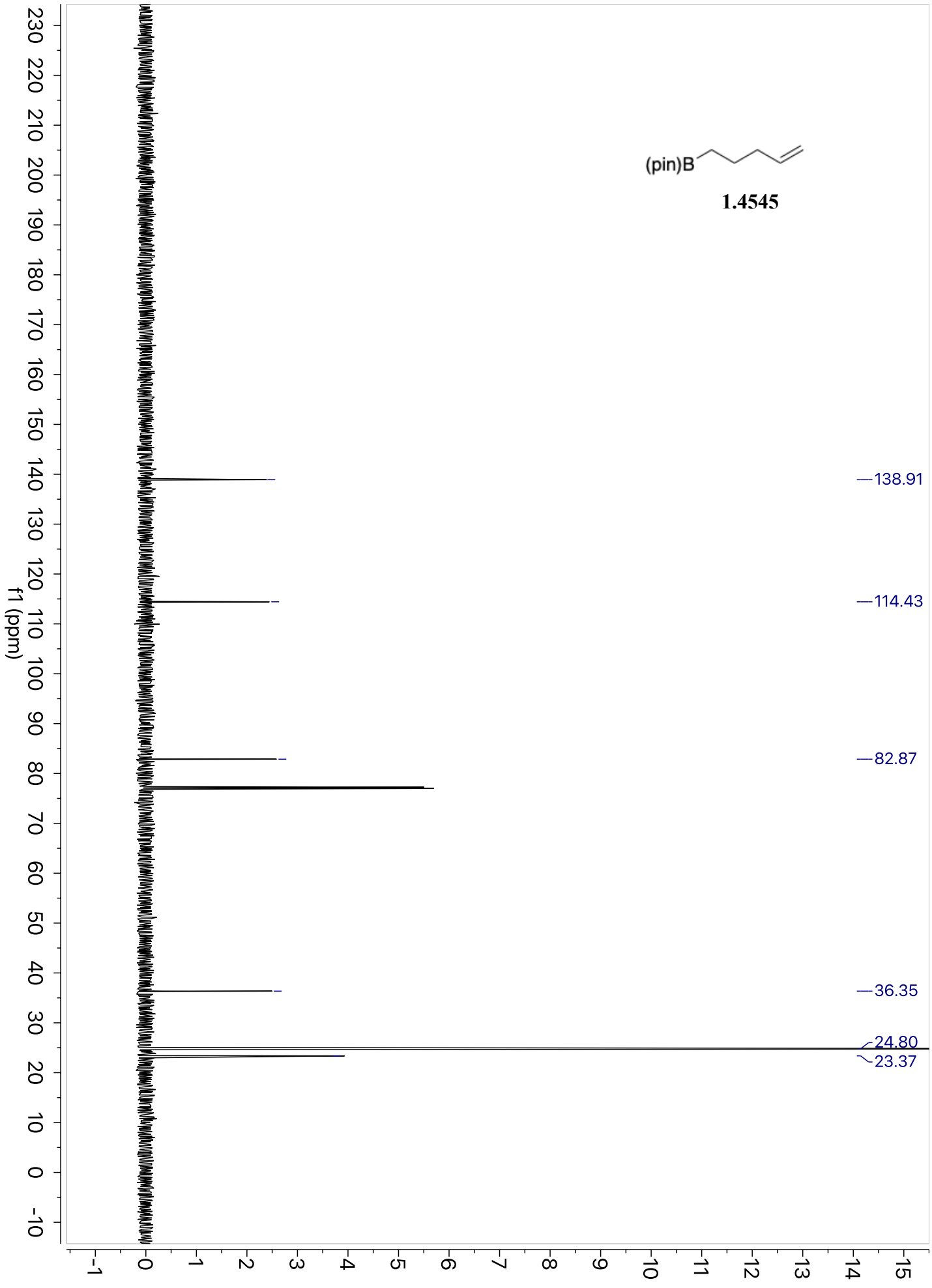

Br
1.155
1.34
1.31
0.79
2.88
1.81
2.59
0.22
0.38
f1 (ppm)

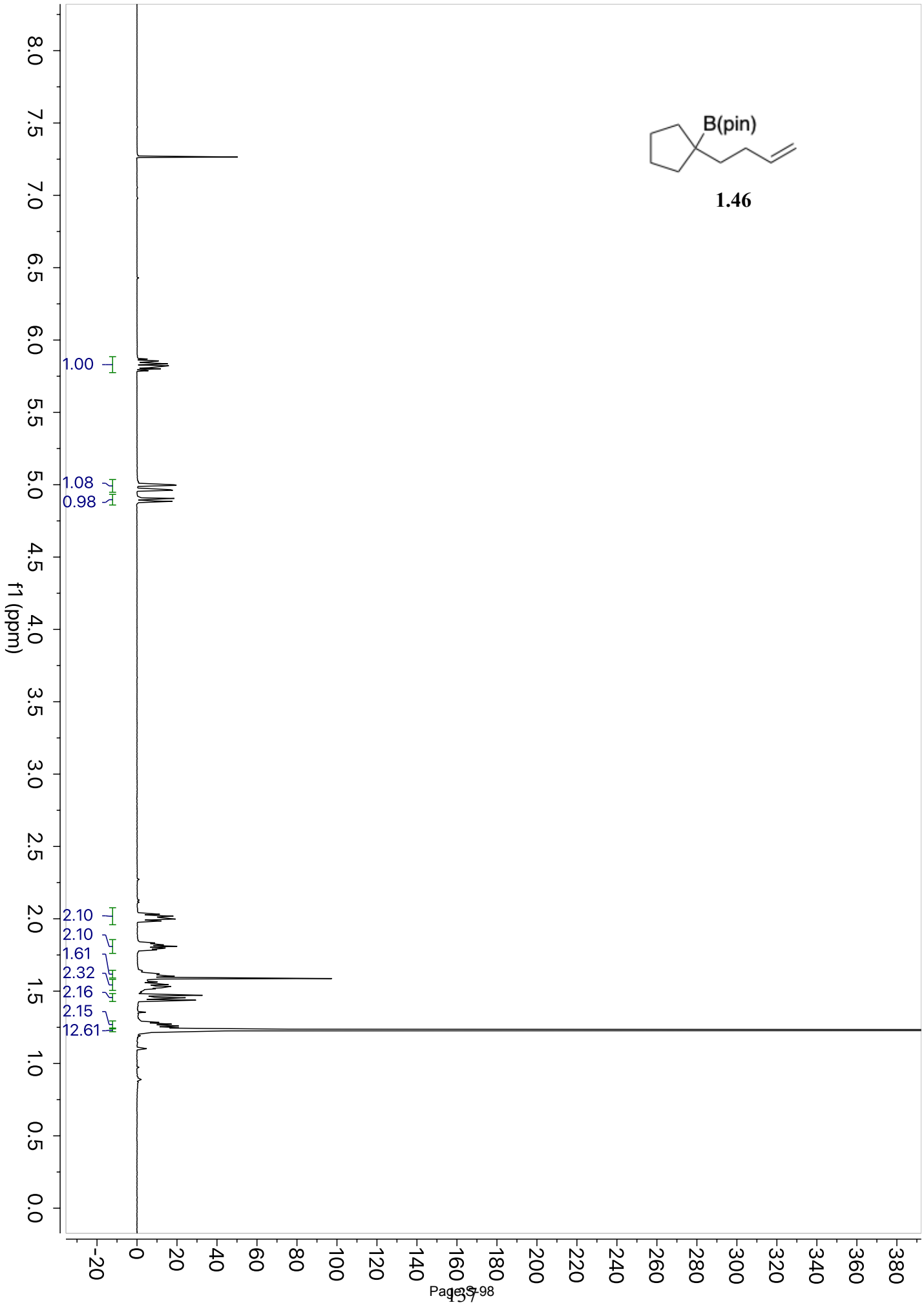

Br
1.155
137.75
137.73
115.49
80.18
38.00
32.81
27.58
19.19
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

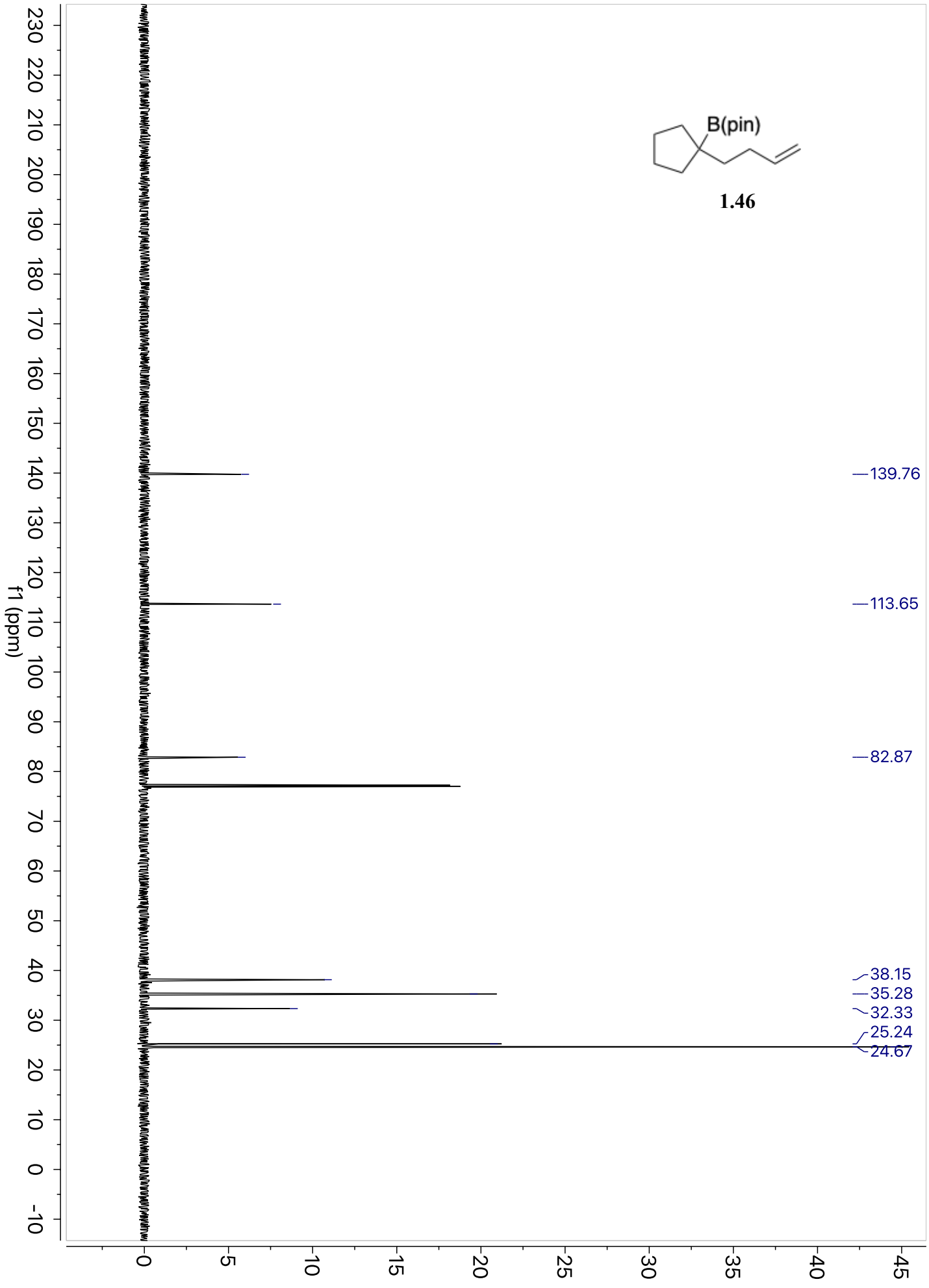

B(pin)
1.444
2.38
3.01
1.00
0.99
0.98
2.10
2.02
1.06
0.98
0.71
0.97
11.72
1.06
f1 (ppm)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

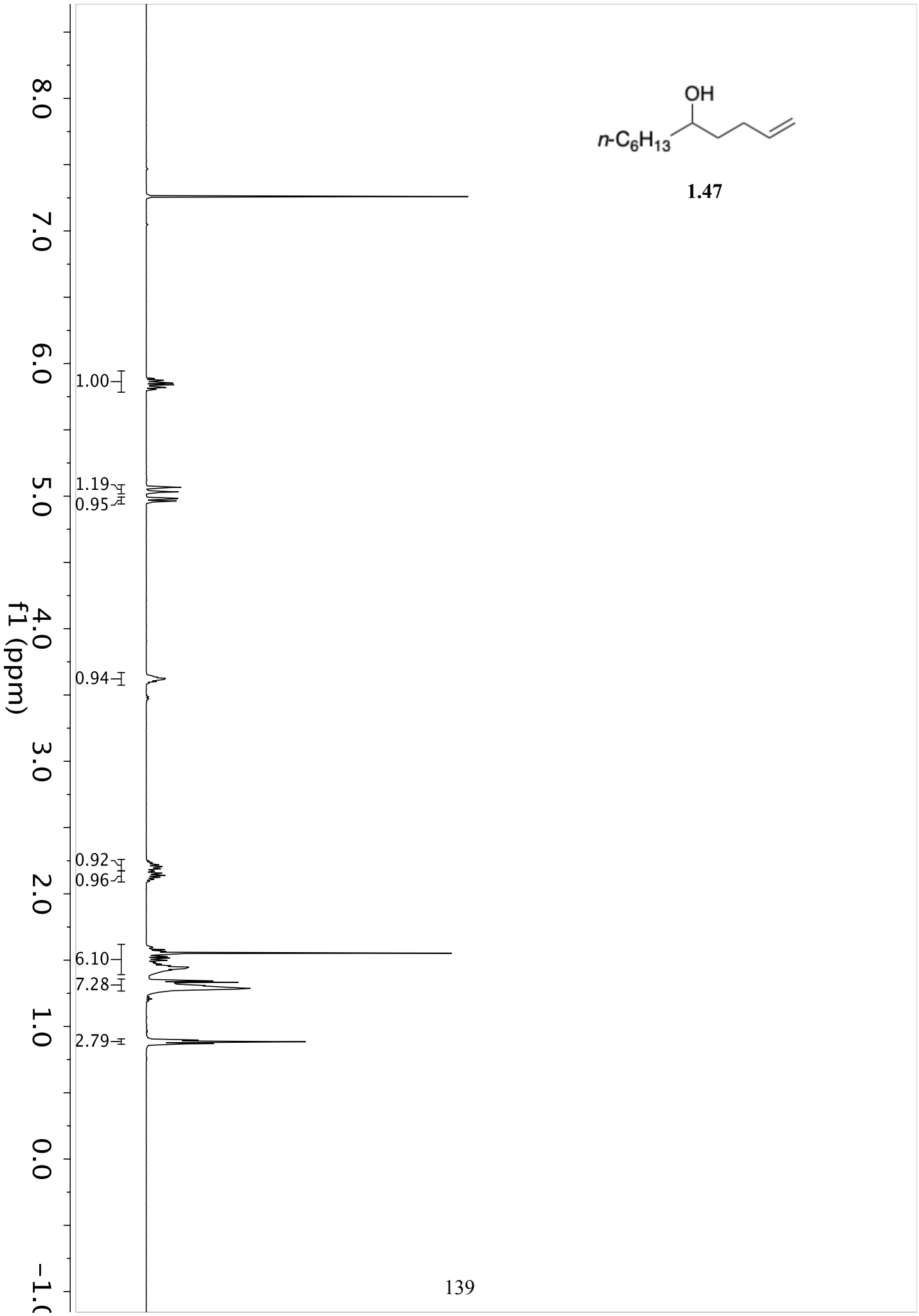

B(pin)
1.444
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
143.03
139.14
128.39
128.24
125.57
114.31
83.00
35.59
33.41
33.40
30.55
24.89
24.86

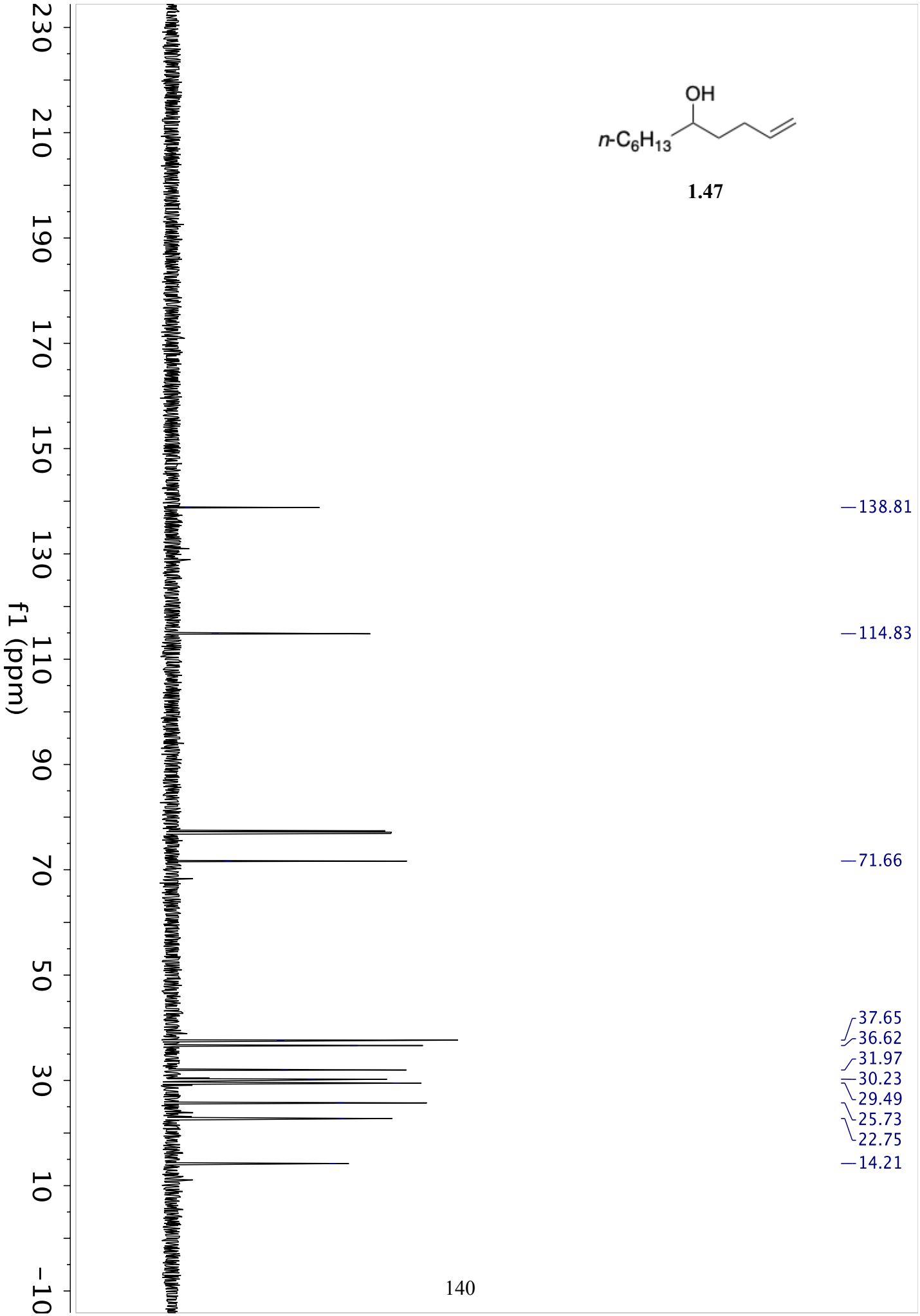

(pin)B
1.4545
1.00
1.04
1.01
2.12
2.13
12.53
2.08
f1 (ppm)

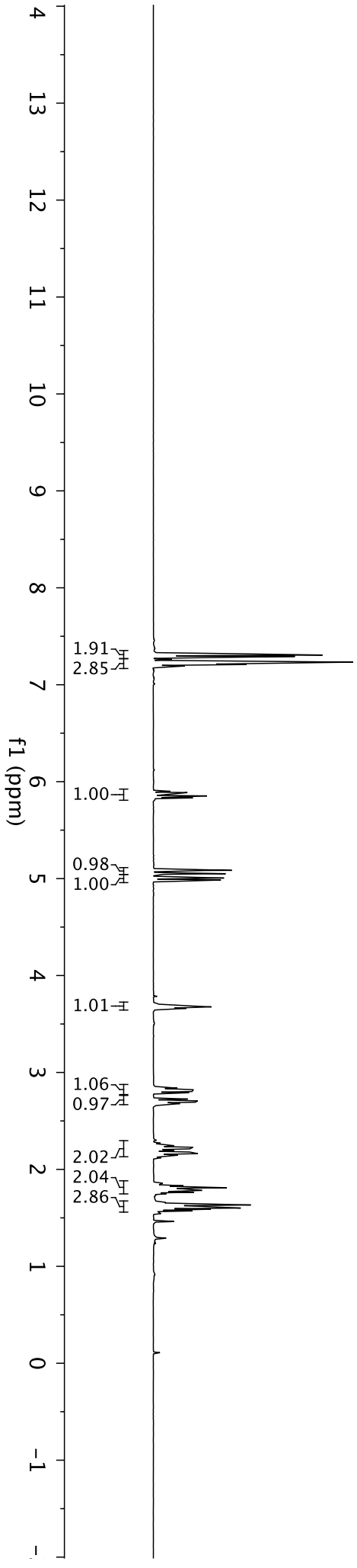

(pin)B
1.4545
138.91
114.43
82.87
36.35
24.80
23.37
f1 (ppm)

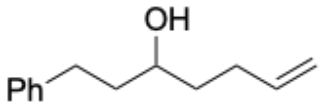

B(pin)
1.46
1.00
1.08
0.98
2.10
2.10
1.61
2.32
2.16
2.15
12.61
f1 (ppm)


B(pin)
1.46
139.76
113.65
82.87
38.15
35.28
32.33
25.24
24.67
f1 (ppm)

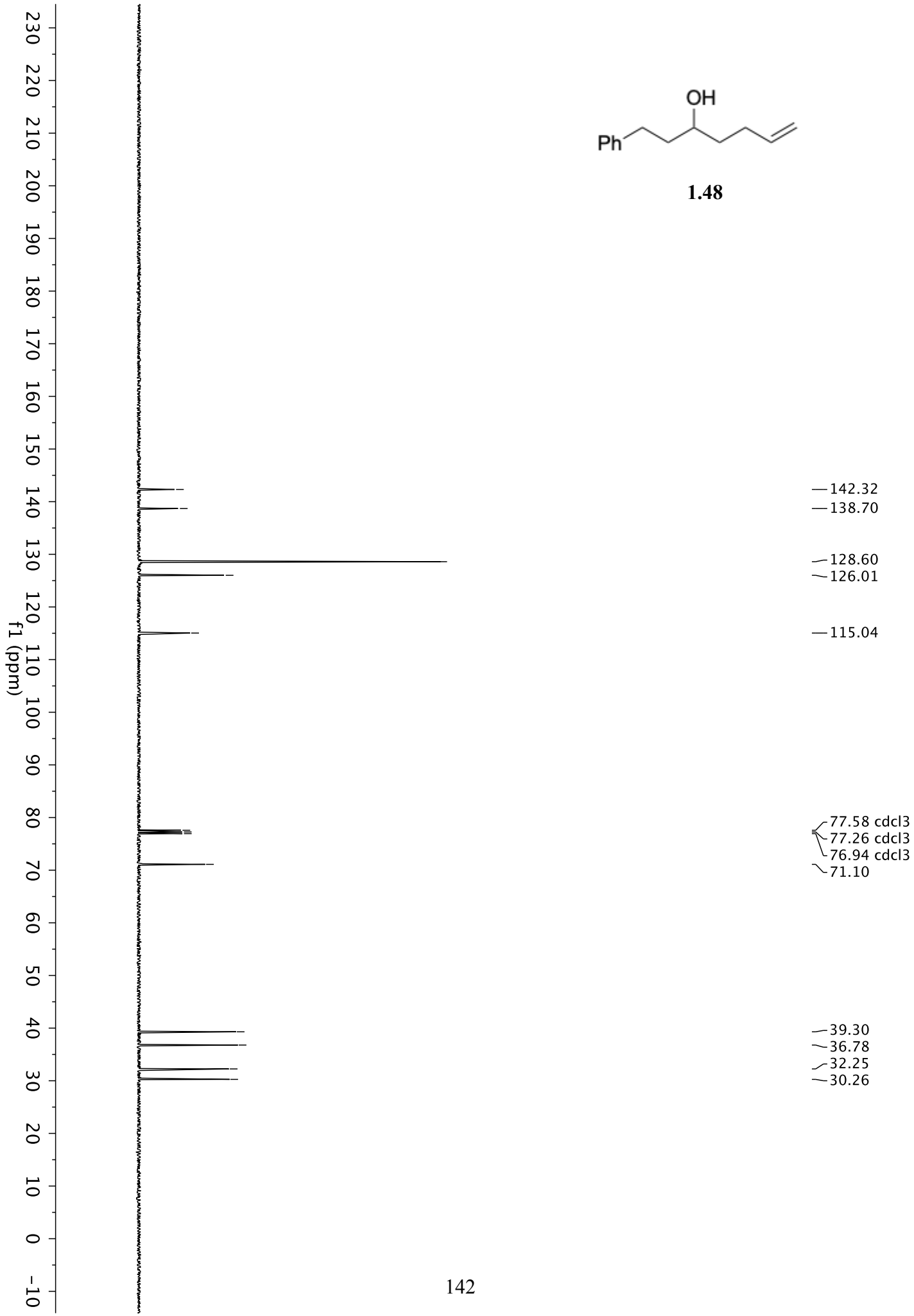

OH
n-C6H13
1.47
1.00
1.19
0.95
0.94
0.92
0.96
6.10
7.28
2.79
f1 (ppm)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


OH
n-C6H13
1.47
138.81
114.83
71.66
37.65
36.62
31.97
30.23
29.49
25.73
22.75
14.21
f1 (ppm)
230
210
190
170
150
130
110
90
70
50
30
10
-10

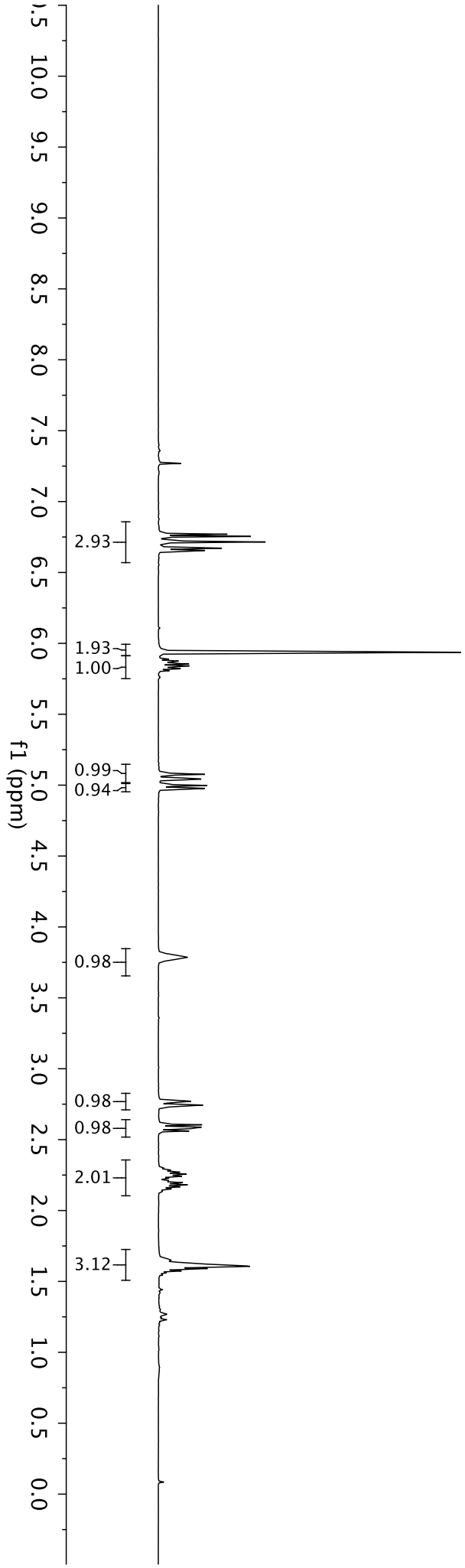


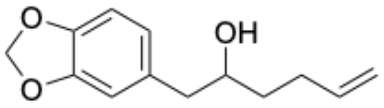


1.48

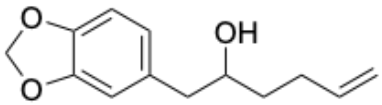

OH
Ph
142.32
138.70
128.60
126.01
115.04
77.58 cdcl3
77.26 cdcl3
76.94 cdcl3
71.10
39.30
36.78
32.25
30.26
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

1.48


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
f1 (ppm)
2.93
1.93
1.00
0.99
0.94
0.98
0.98
0.98
2.01
3.12

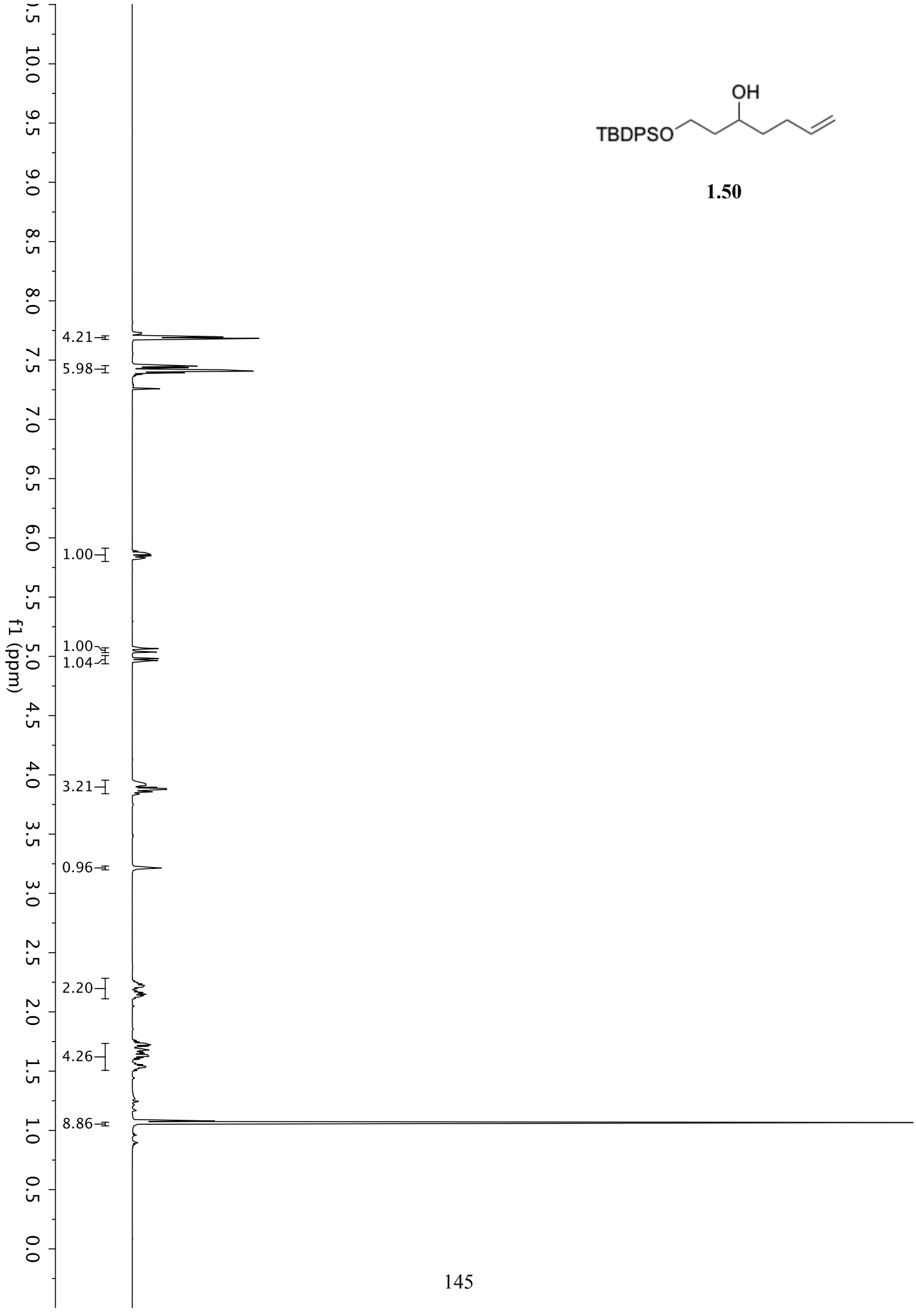

O
O
OH

1.49

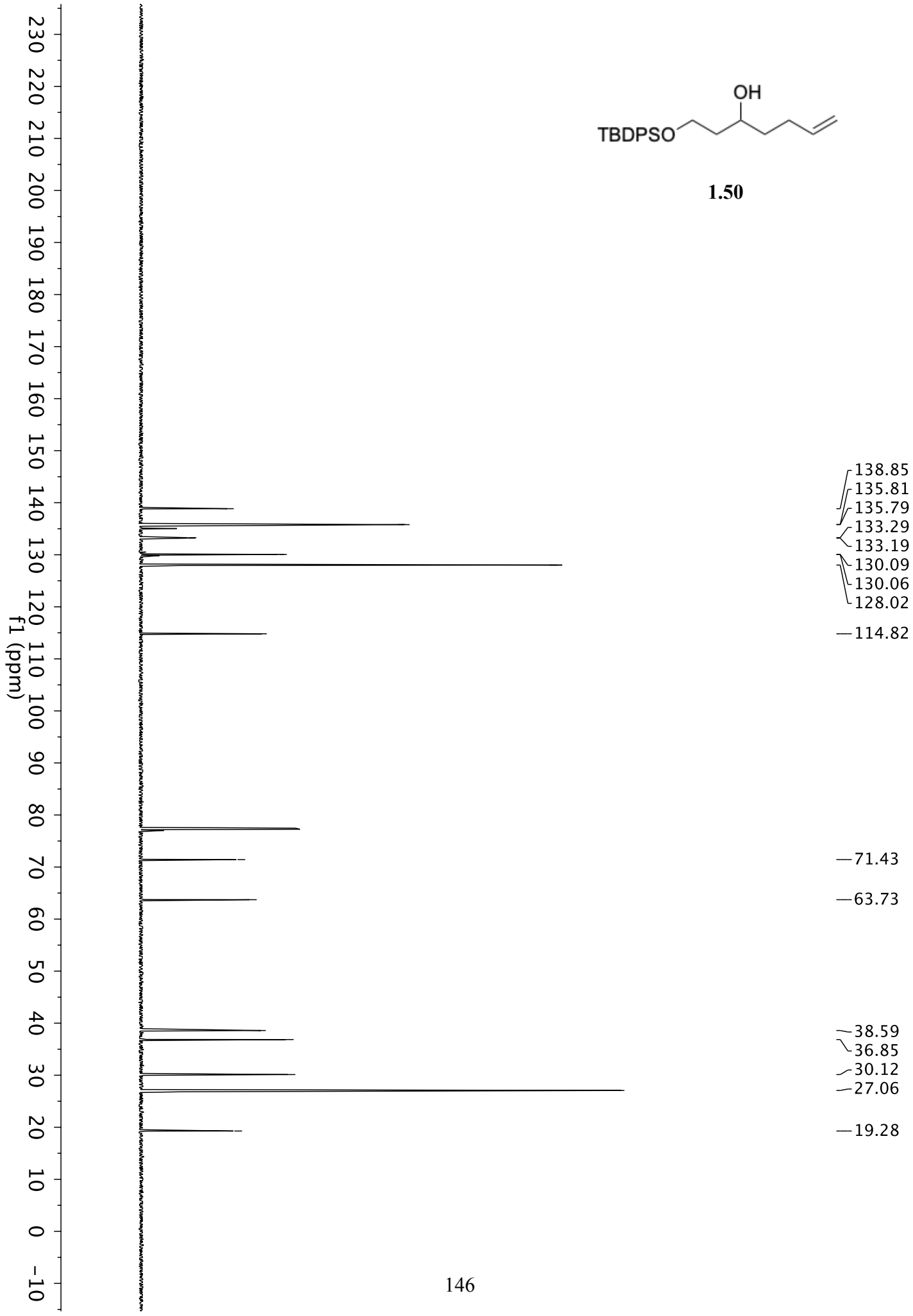

O
O
OH

1.49

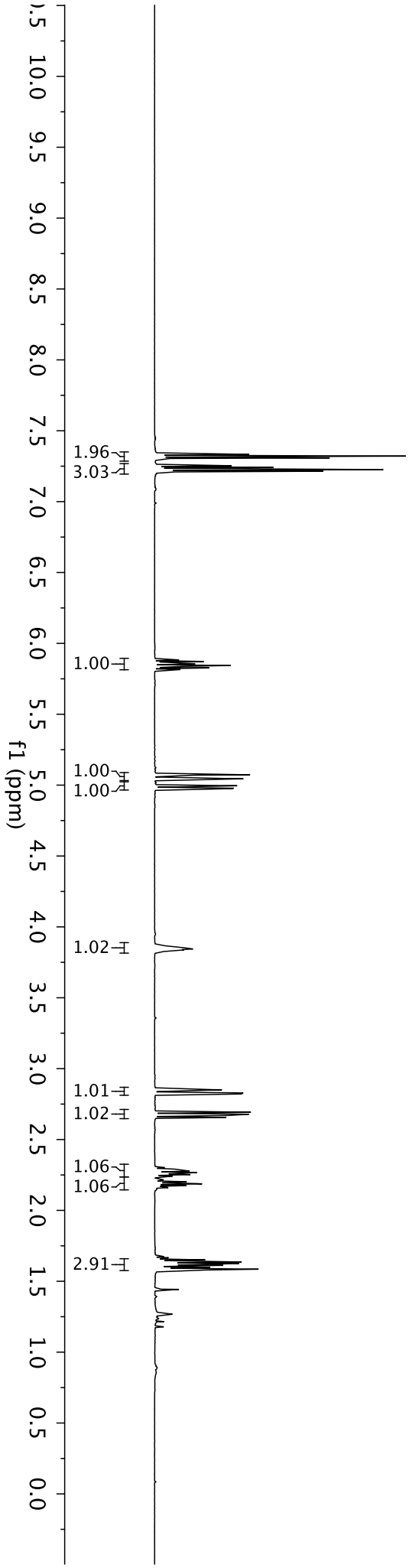
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
147.99
146.42
138.63
132.38
122.50
115.10
109.91
108.53
101.10
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
72.38
43.95
35.98
30.35

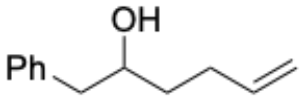


1.50

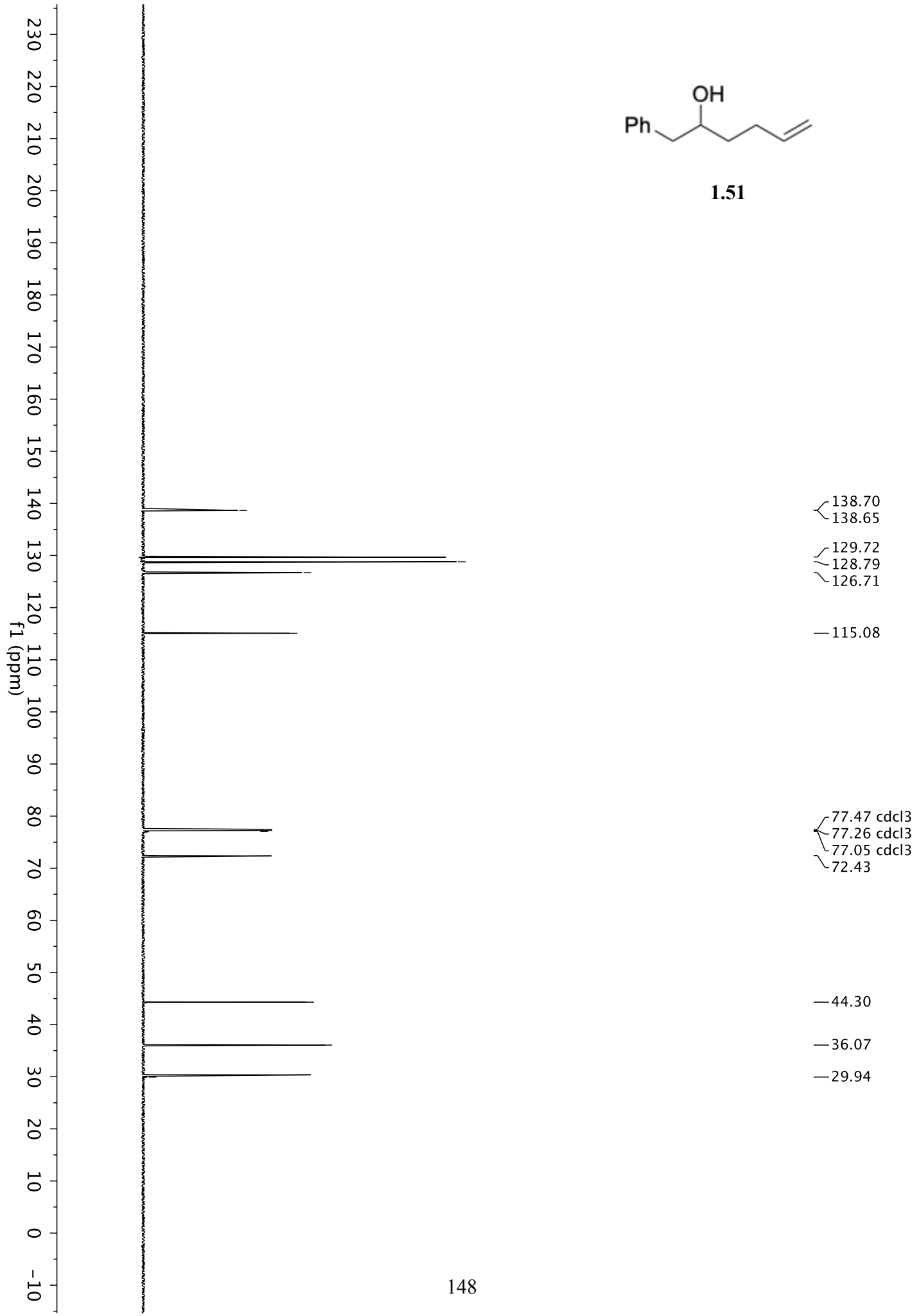

OH
TBDPSO
138.85
135.81
135.79
133.29
133.19
130.09
130.06
128.02
114.82
71.43
63.73
38.59
36.85
30.12
27.06
19.28
f1 (ppm)

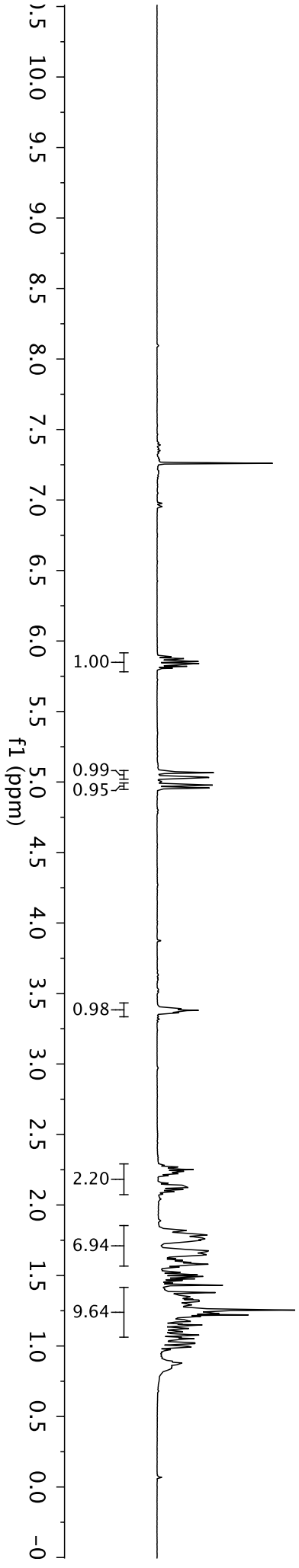
1.50

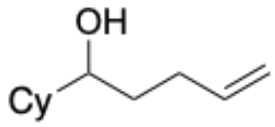




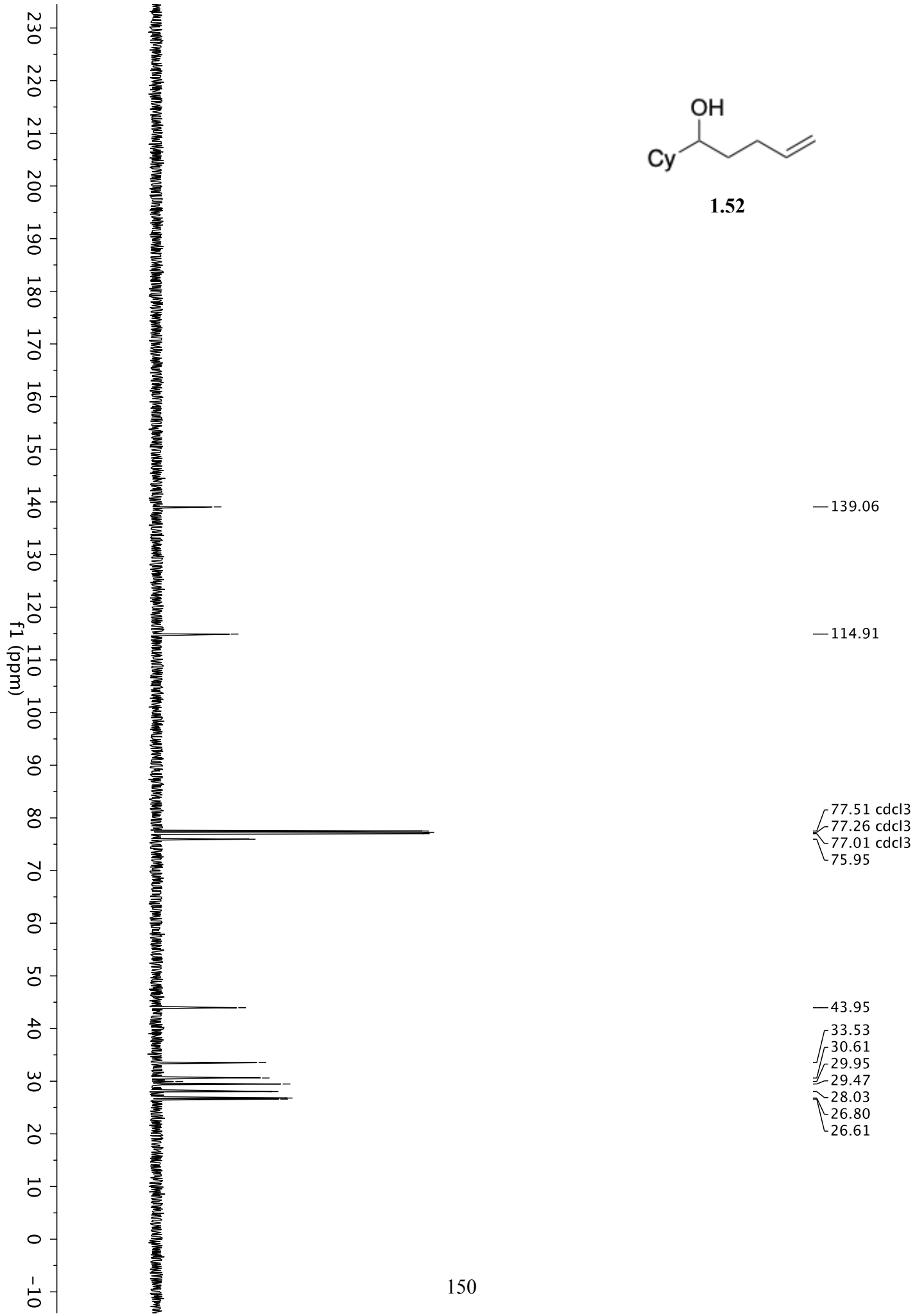
1.51

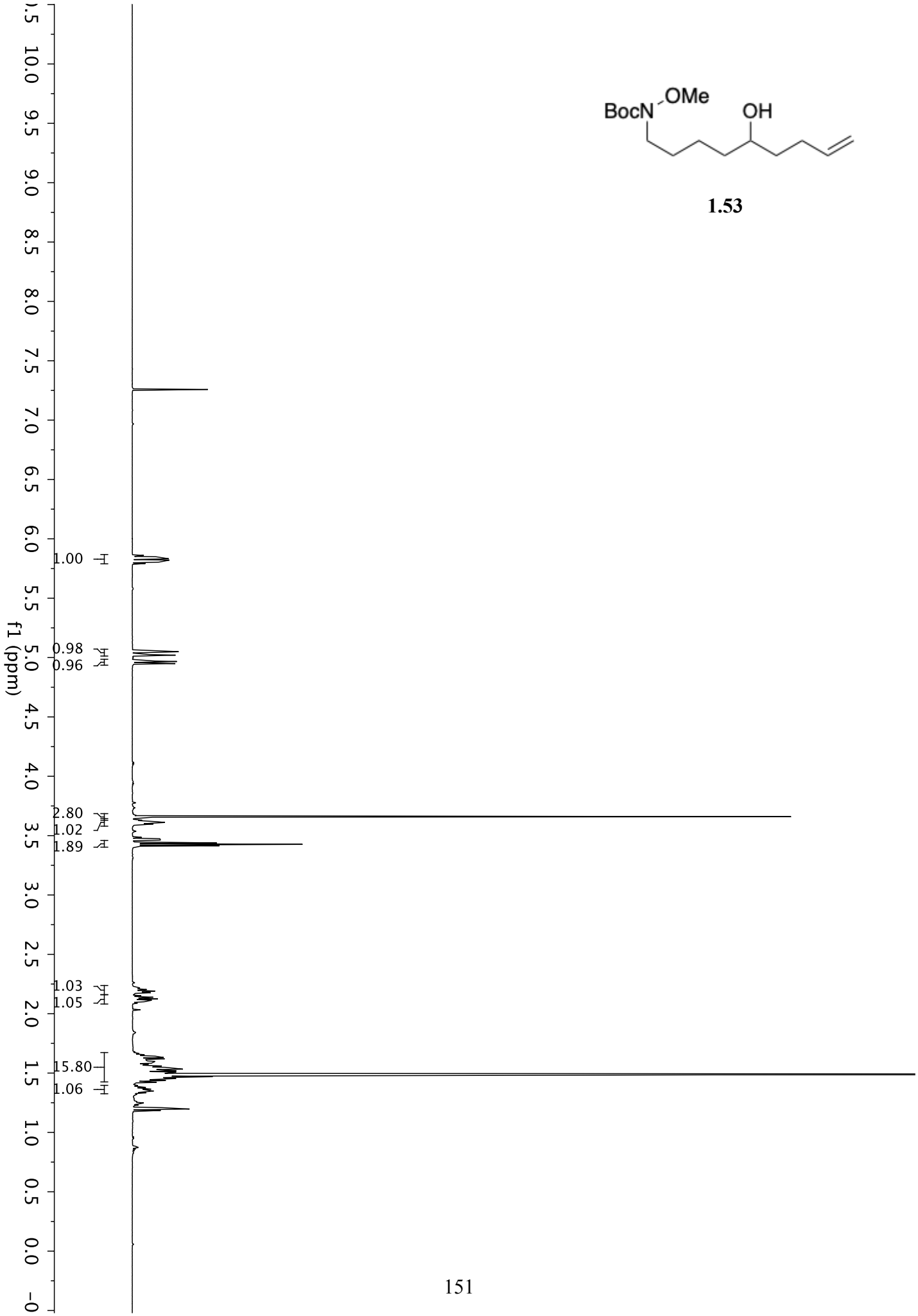

OH
Ph
1.51
138.70
138.65
129.72
128.79
126.71
115.08
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
72.43
44.30
36.07
29.94
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



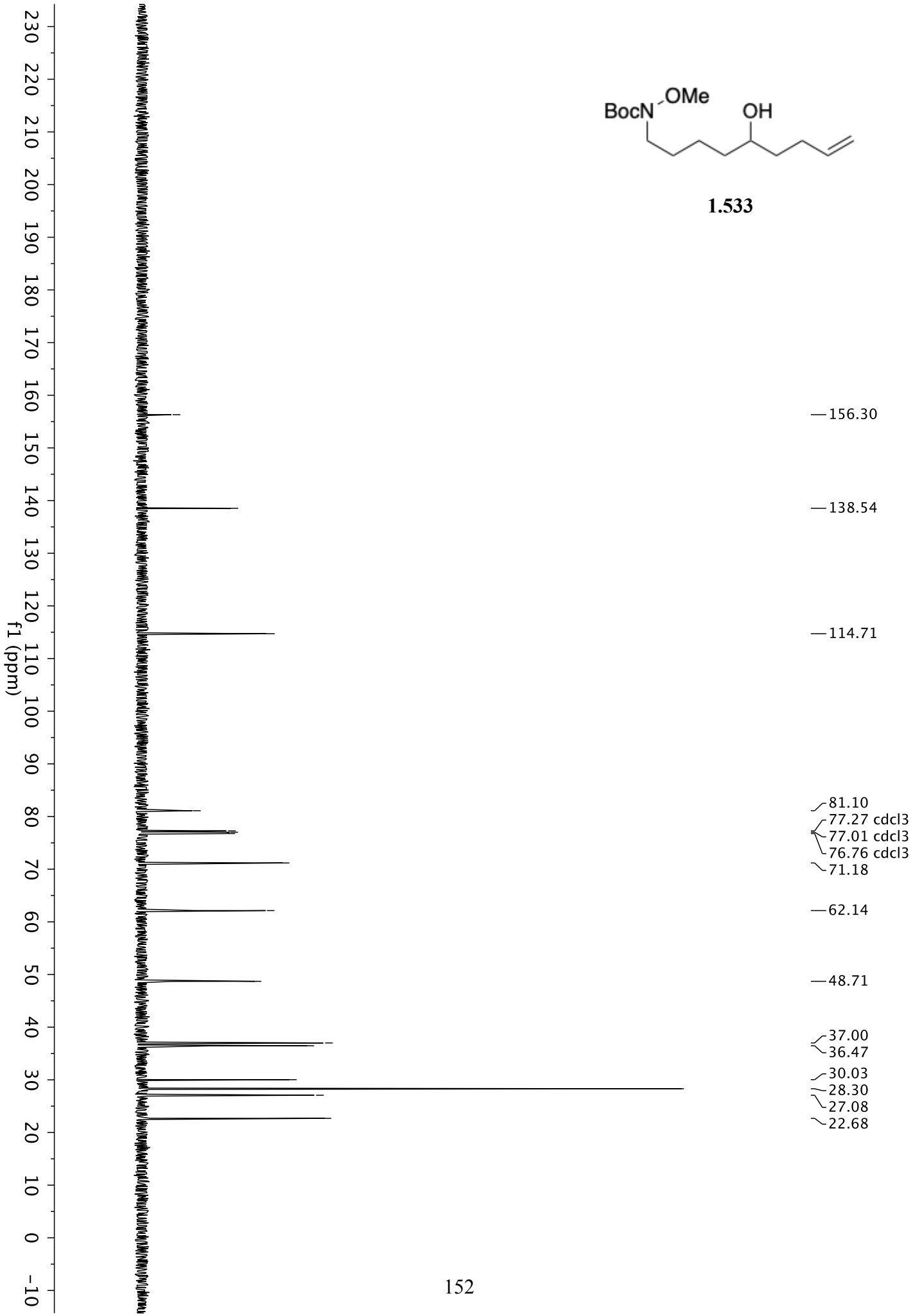


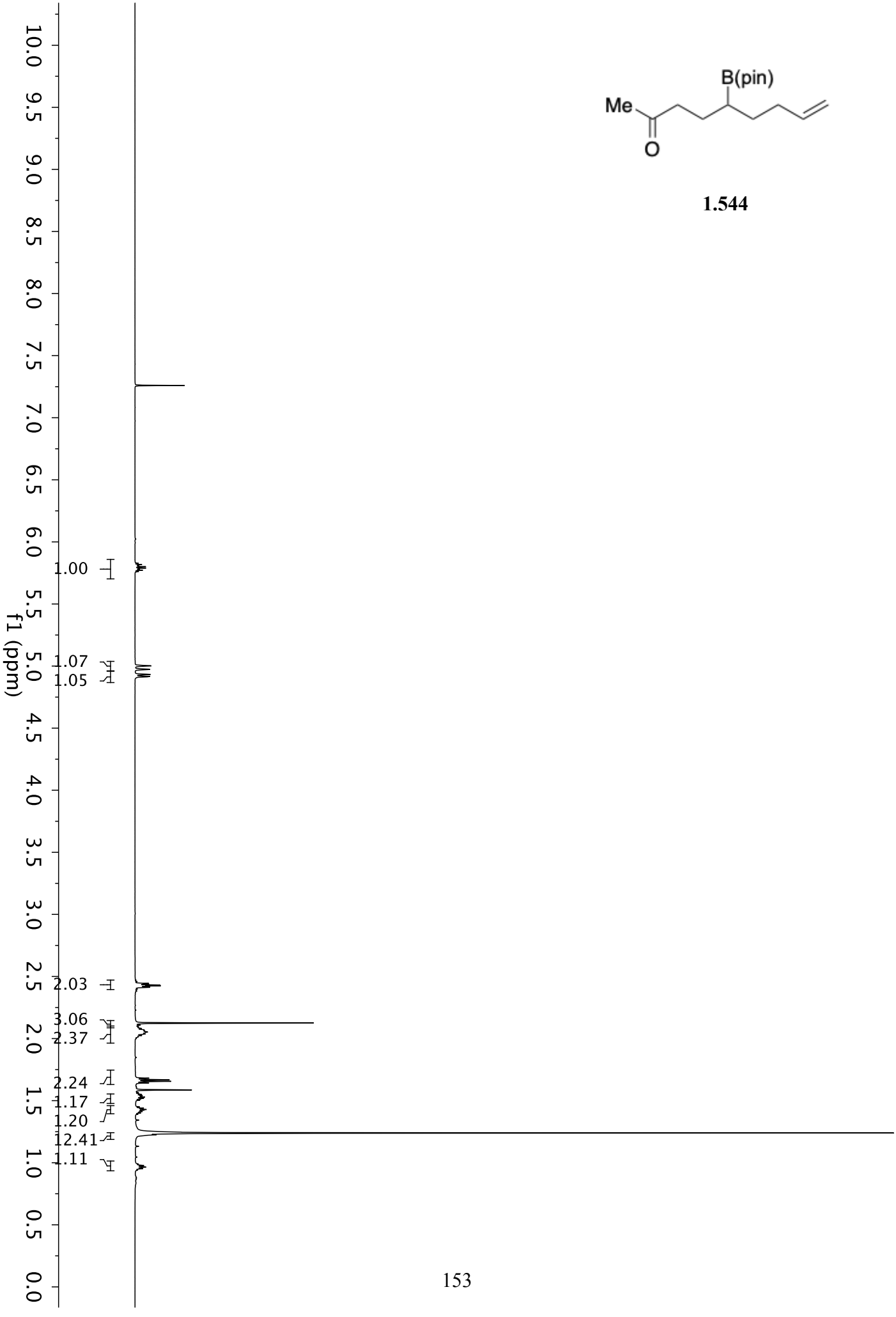
1.52

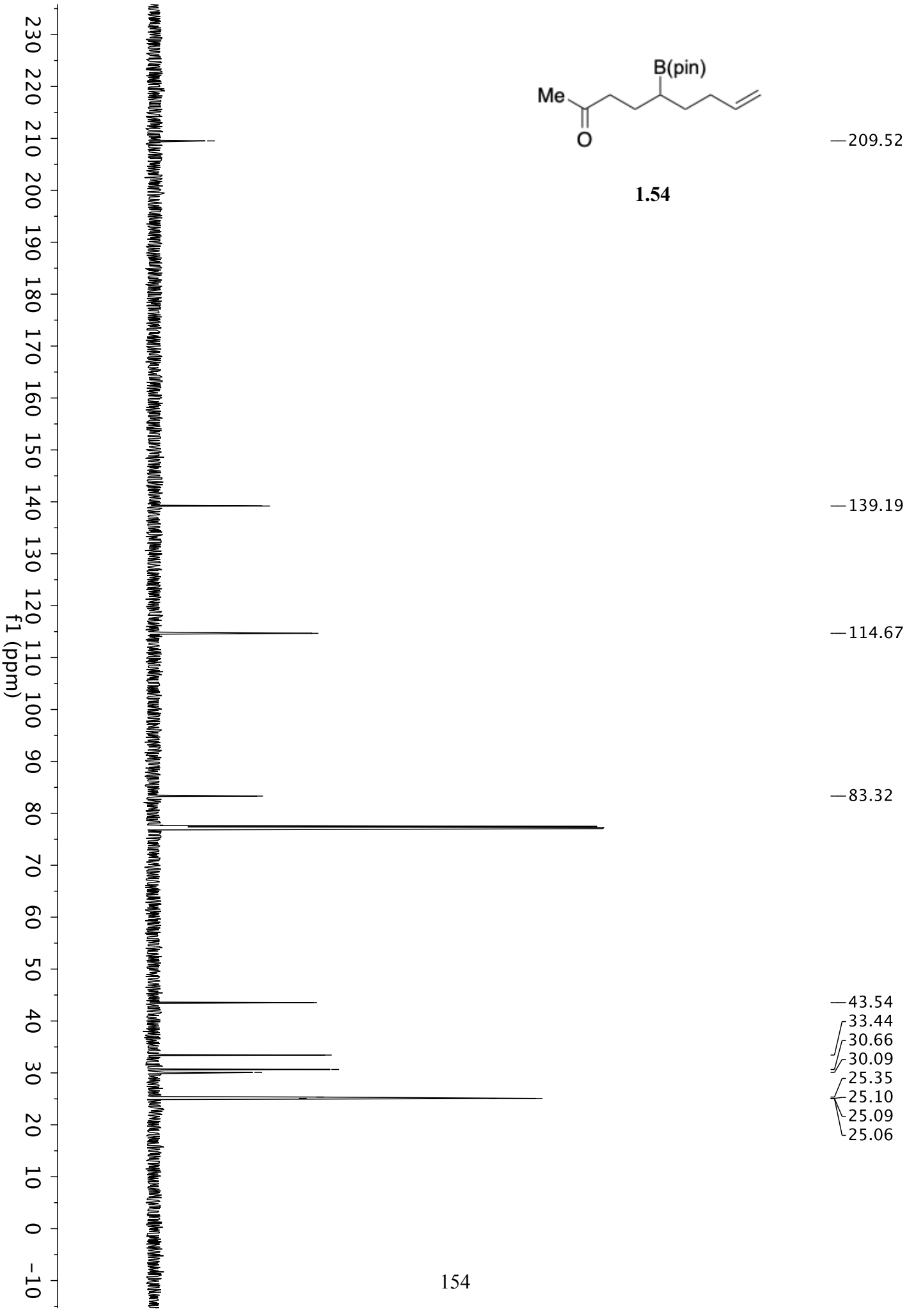

OH
Cy
1.52
139.06
114.91
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
75.95
43.95
33.53
30.61
29.95
29.47
28.03
26.80
26.61
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

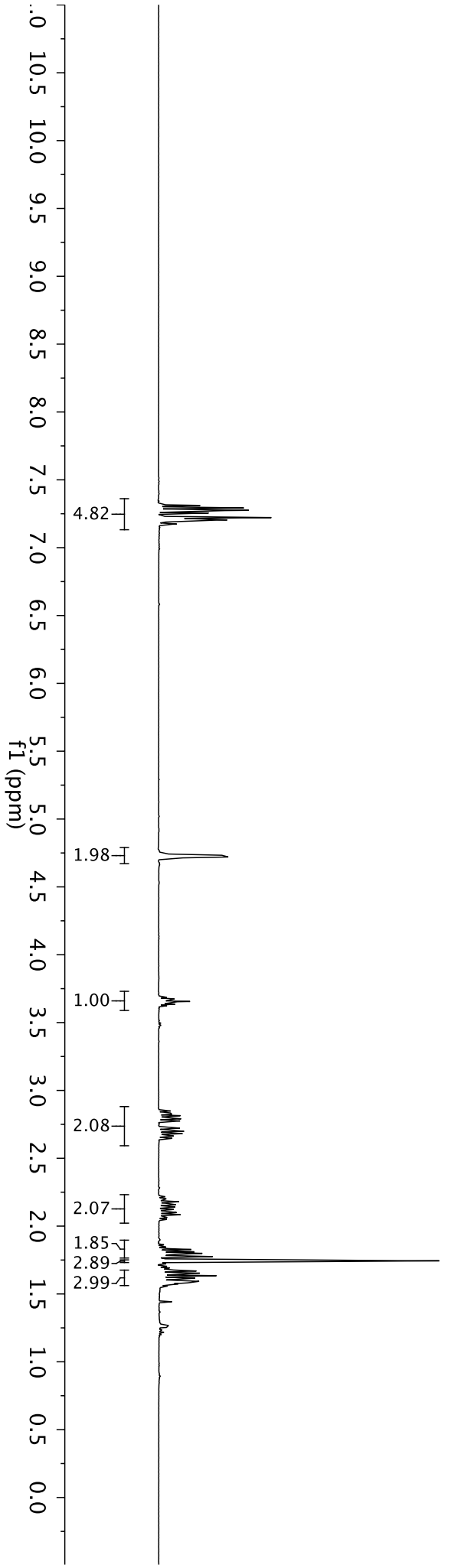


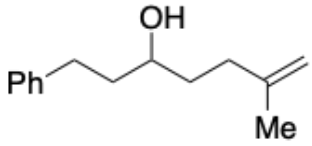
1.53


BocN
OMe
OH
1.533
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
156.30
138.54
114.71
81.10
77.27 cdcl3
77.01 cdcl3
76.76 cdcl3
71.18
62.14
48.71
37.00
36.47
30.03
28.30
27.08
22.68

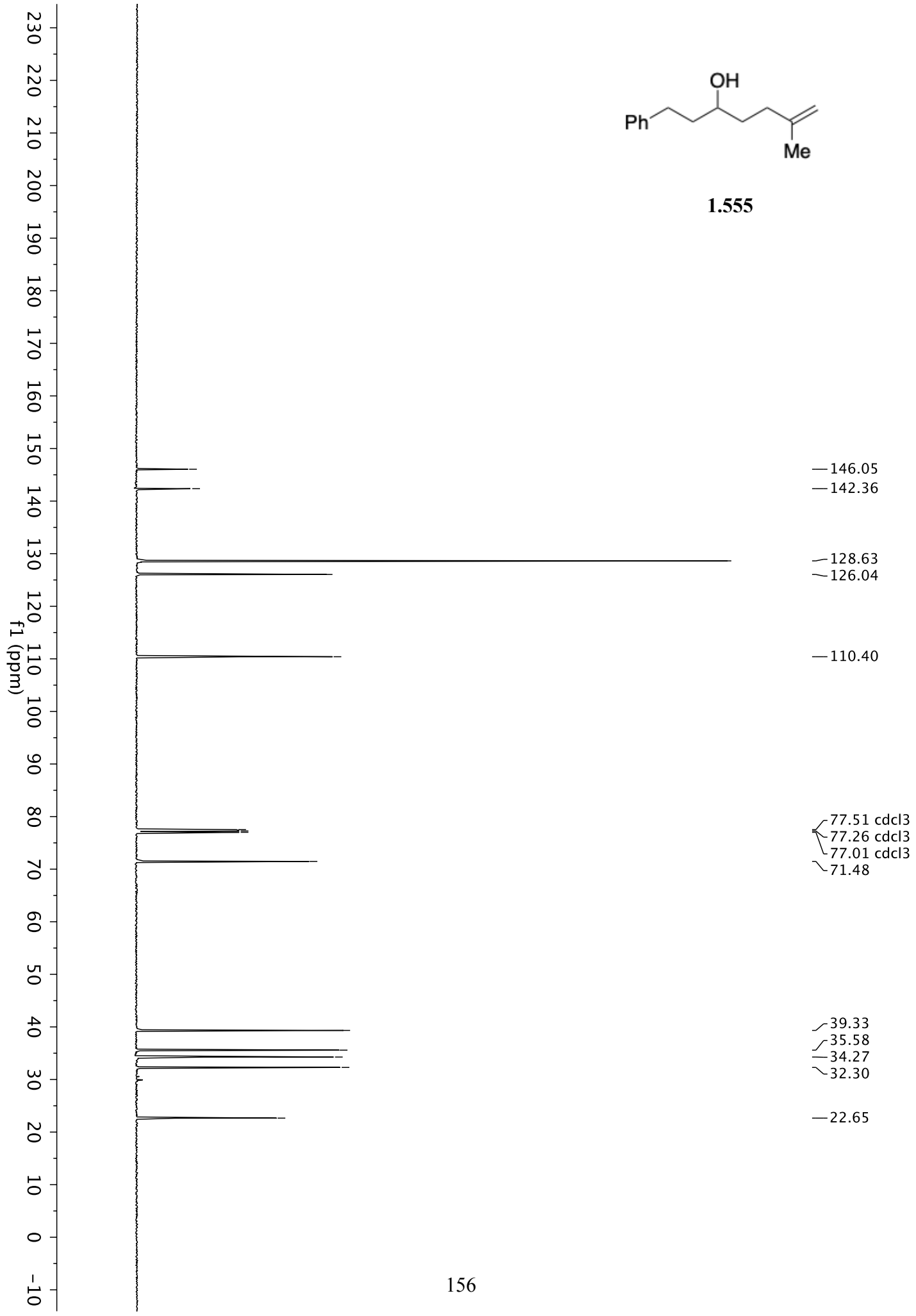

B(pin)
Me
O
1.544
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.00
1.07
1.05
2.03
3.06
2.37
2.24
1.17
1.20
12.41
1.11

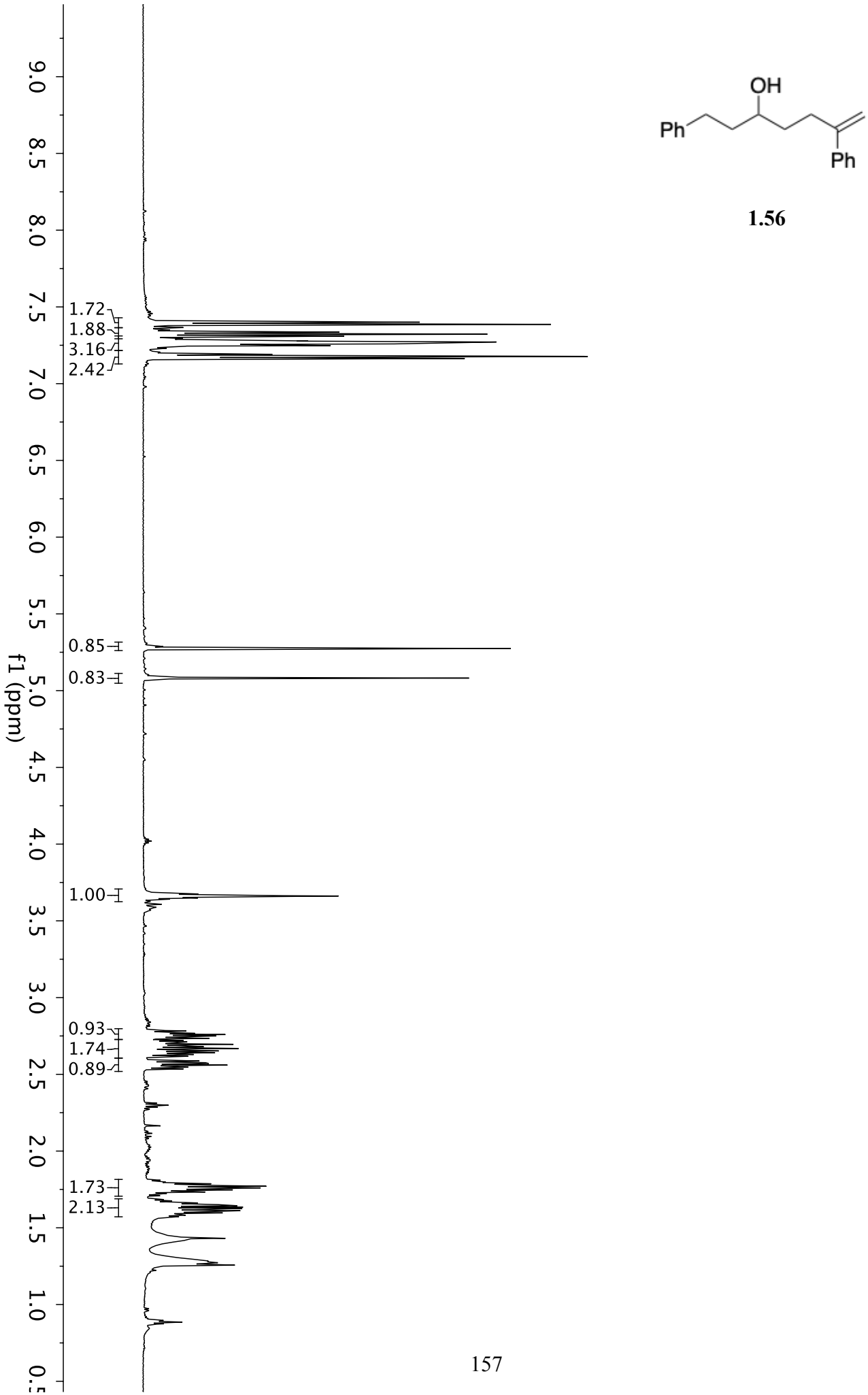

B(pin)
Me
O
1.54
209.52
139.19
114.67
83.32
43.54
33.44
30.66
30.09
25.35
25.10
25.09
25.06
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



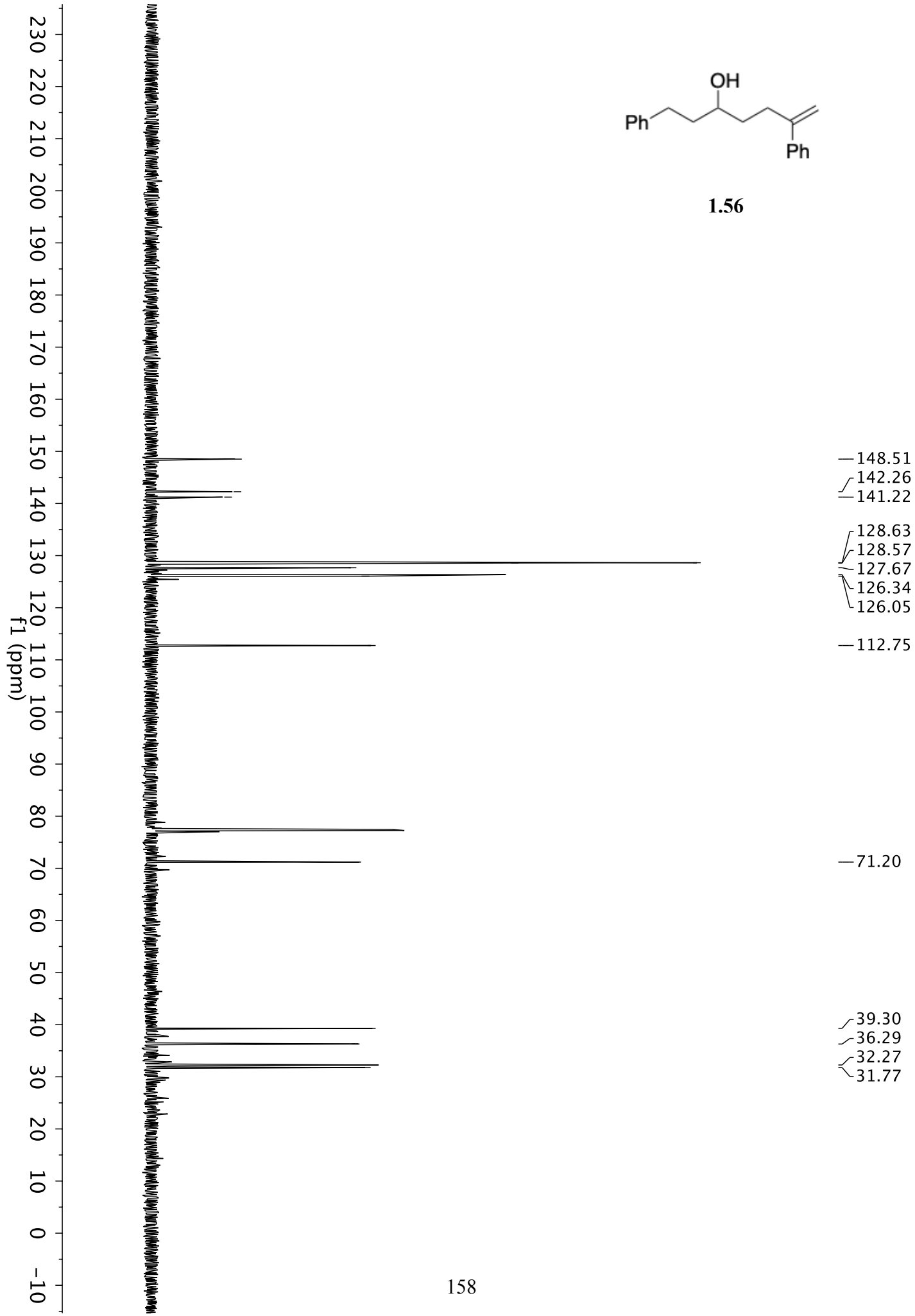


1.555

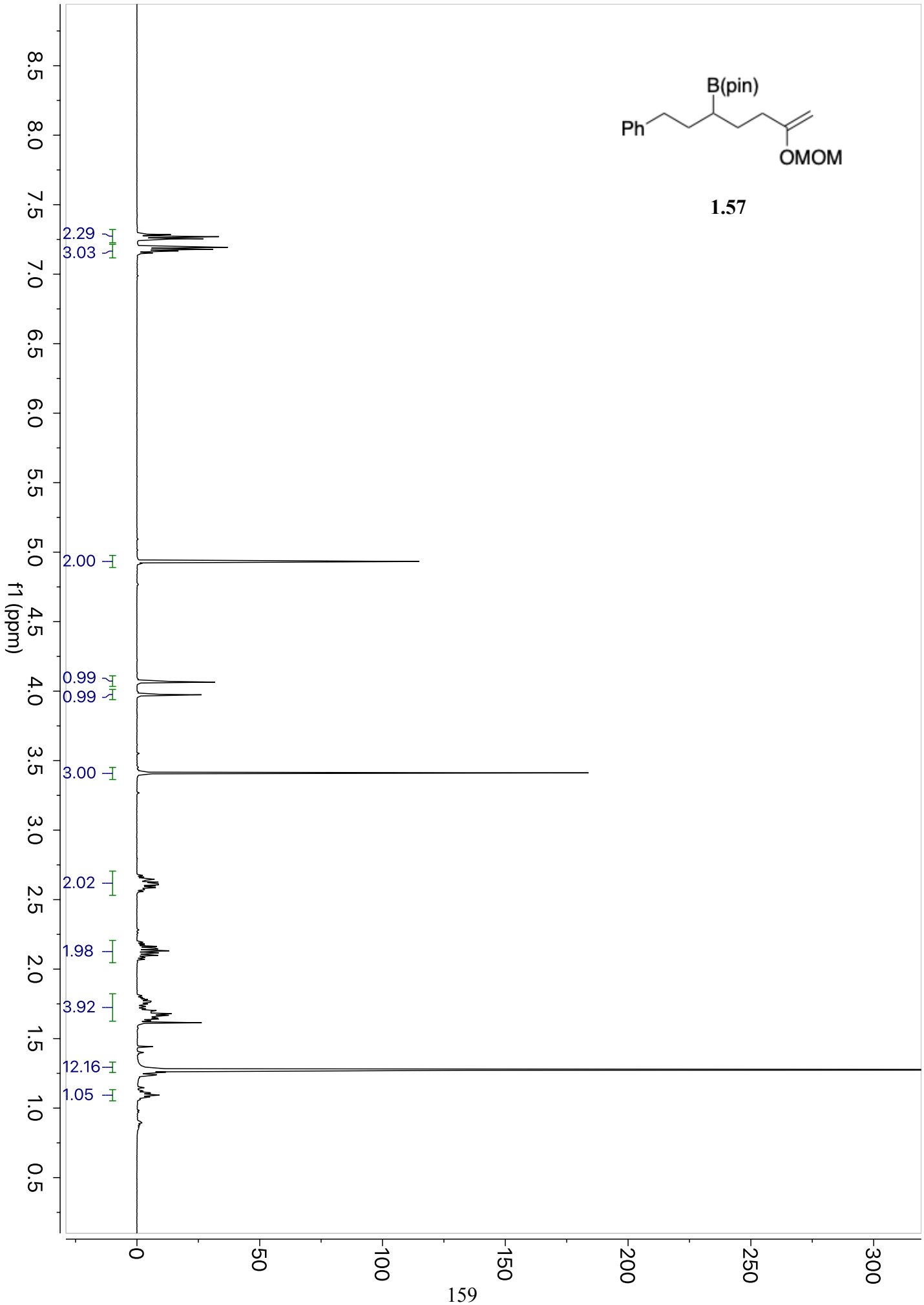

OH
Ph
Me
1.555
146.05
142.36
128.63
126.04
110.40
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
71.48
39.33
35.58
34.27
32.30
22.65
f1 (ppm)

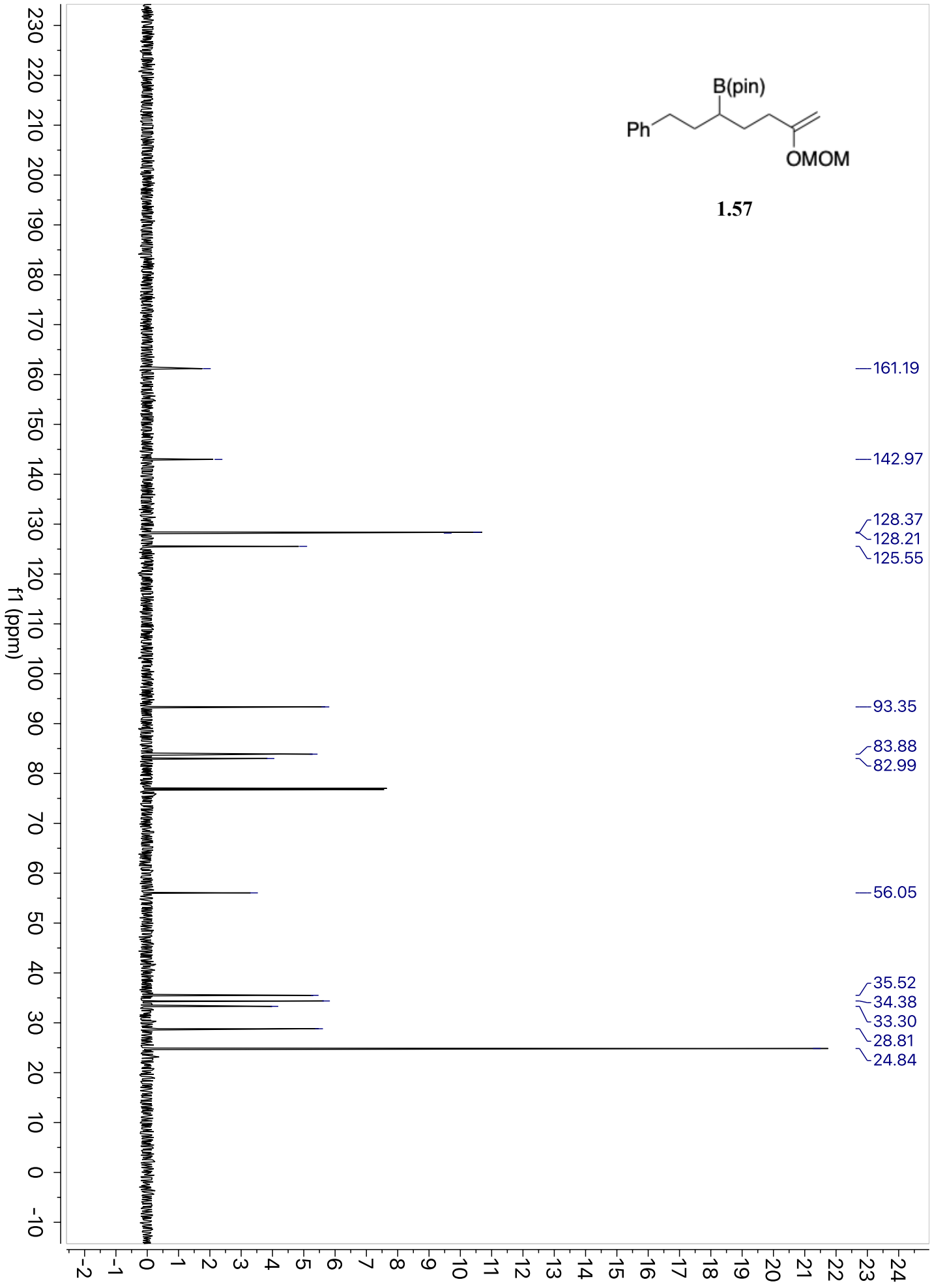

OH
Ph
Ph
1.72
1.88
3.16
2.42
0.85
0.83
1.00
0.93
1.74
0.89
1.73
2.13
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

1.56

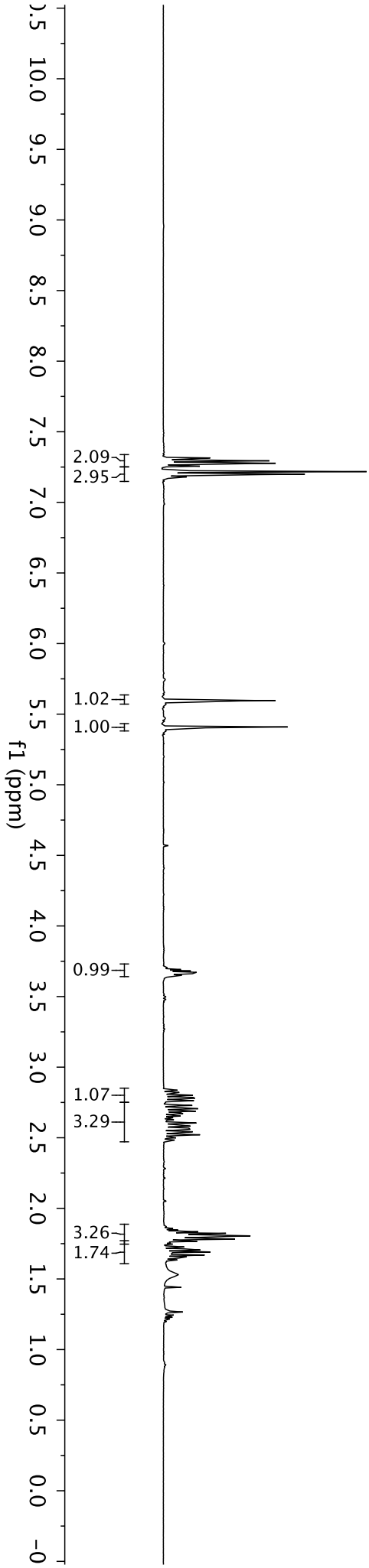

OH
Ph
Ph
148.51
142.26
141.22
128.63
128.57
127.67
126.34
126.05
112.75
71.20
39.30
36.29
32.27
31.77
f1 (ppm)

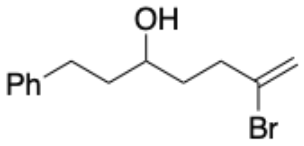
1.56


B(pin)
Ph
OMOM
1.57
2.29
3.03
2.00
0.99
0.99
3.00
2.02
1.98
3.92
12.16
1.05
f1 (ppm)

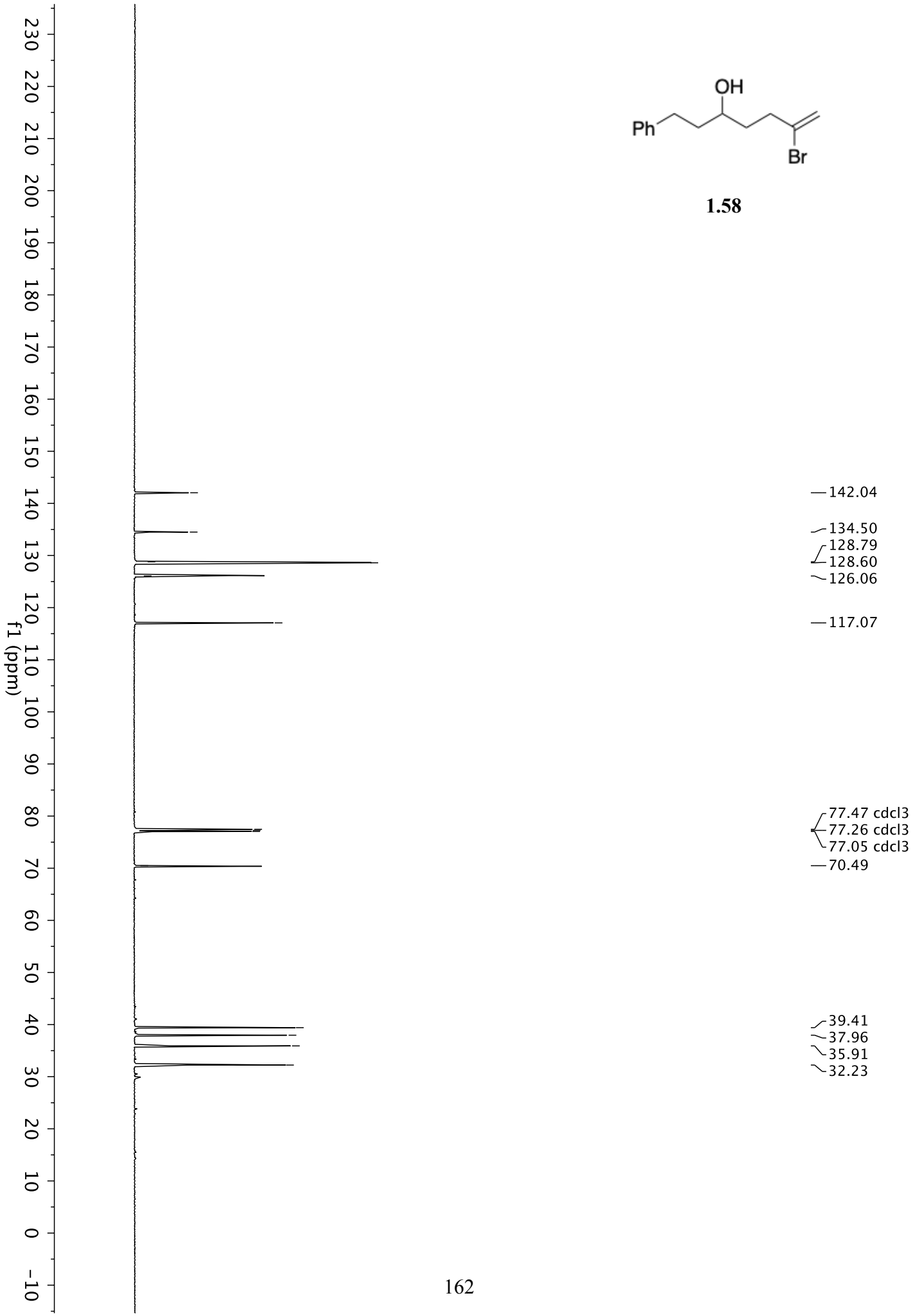

B(pin)
Ph
OMOM
161.19
142.97
128.37
128.21
125.55
93.35
83.88
82.99
56.05
35.52
34.38
33.30
28.81
24.84
f1 (ppm)

1.57

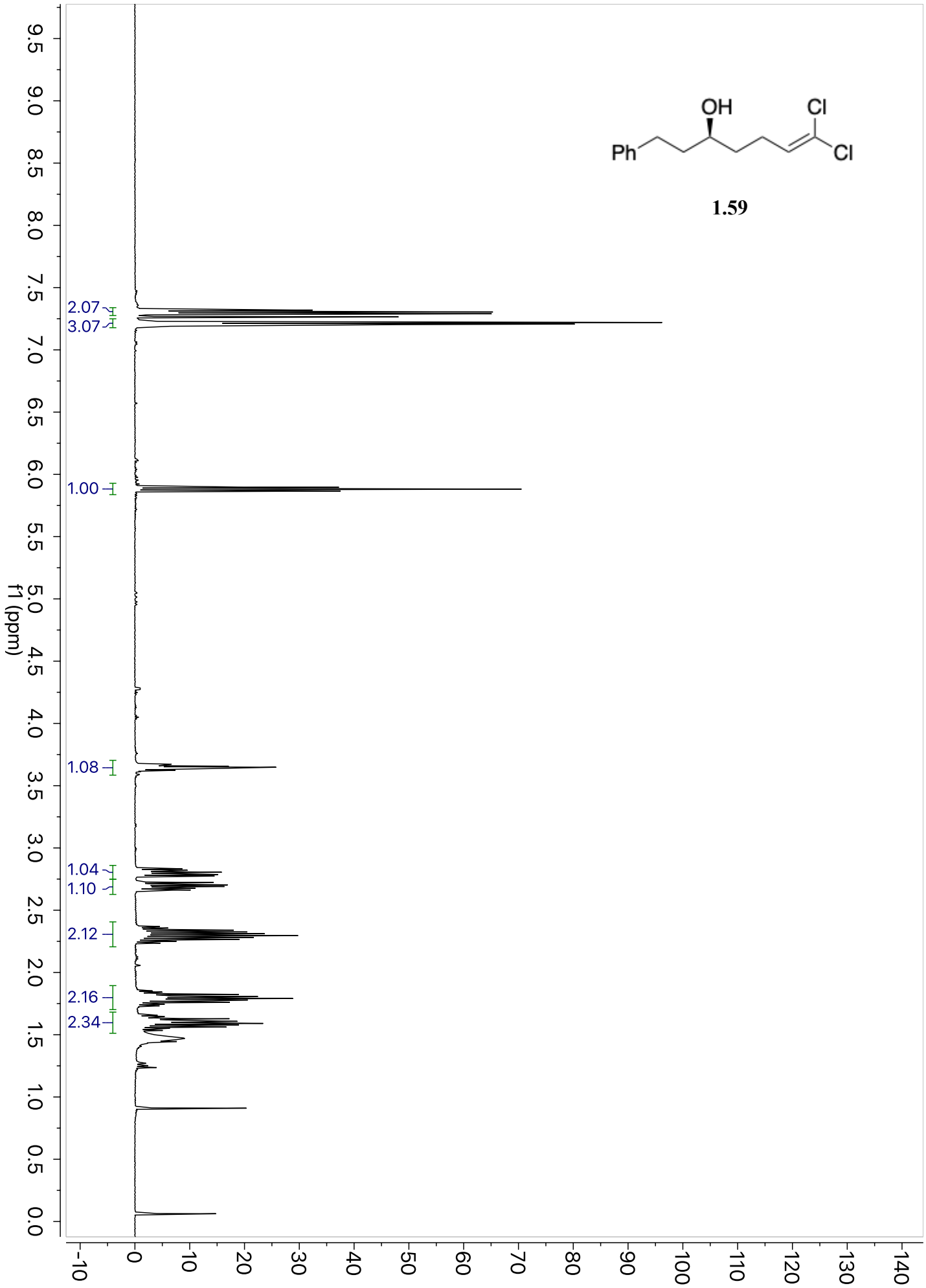




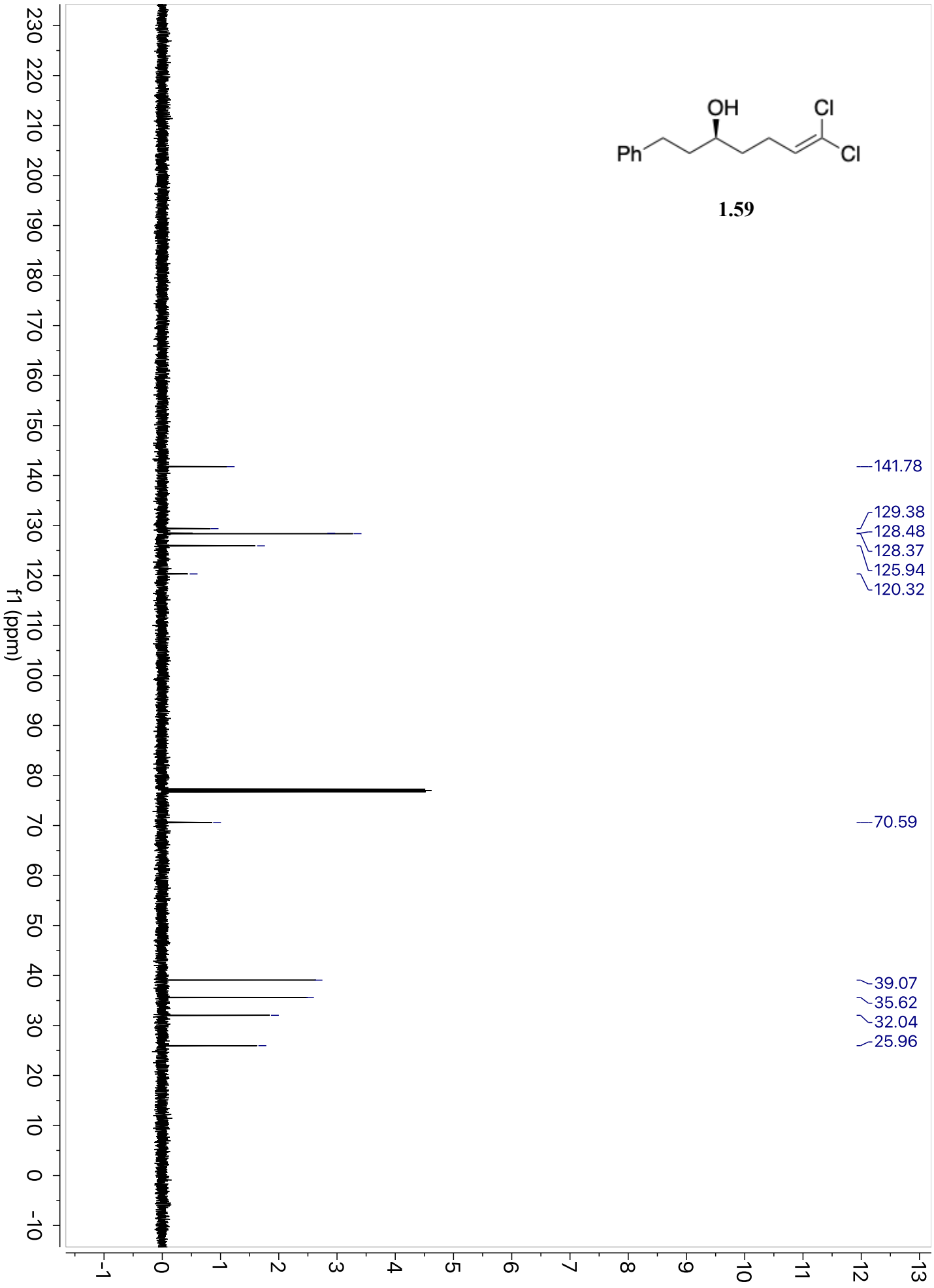
1.58

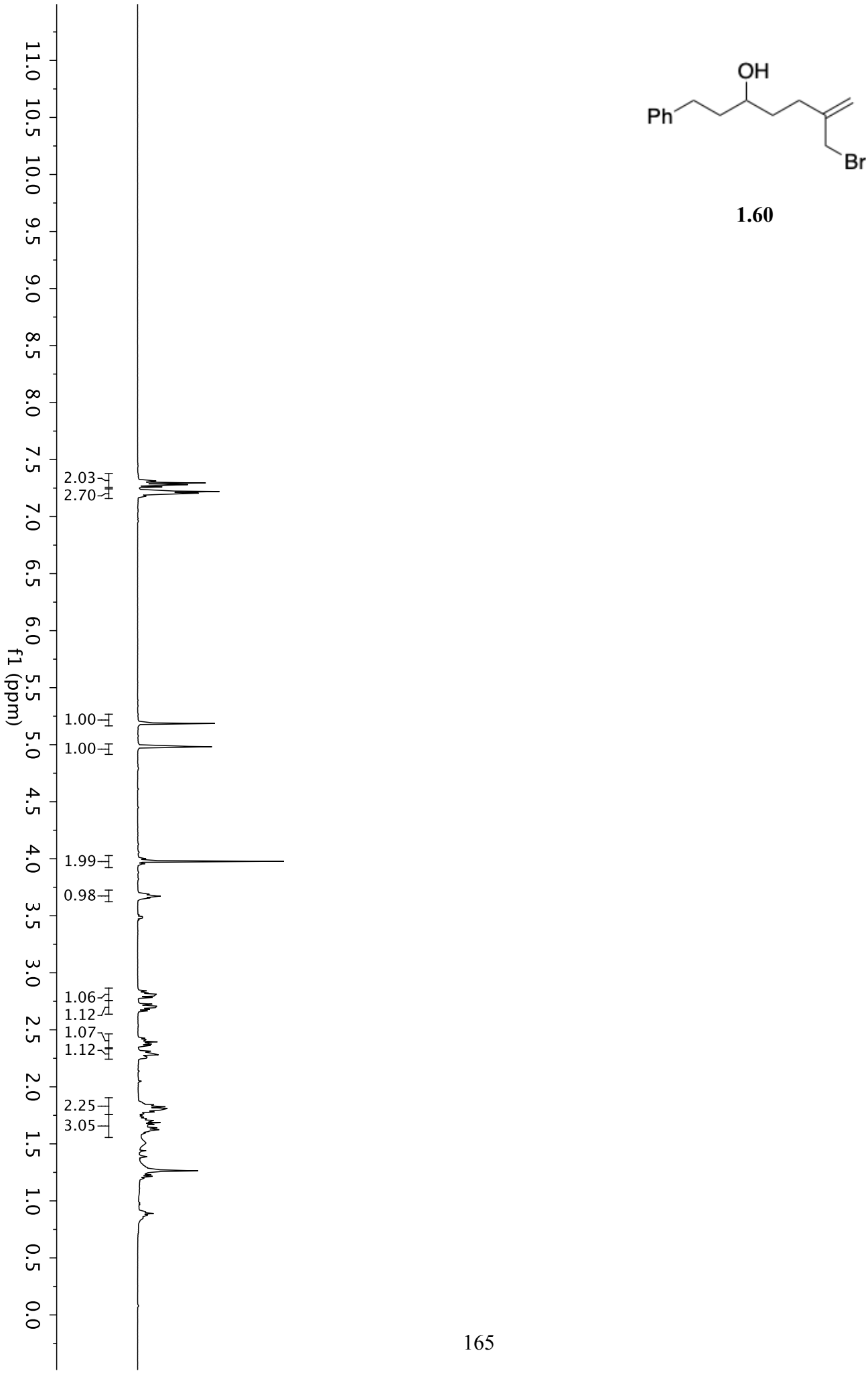

OH
Ph
Br
142.04
134.50
128.79
128.60
126.06
117.07
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
70.49
39.41
37.96
35.91
32.23
f1 (ppm)

1.58

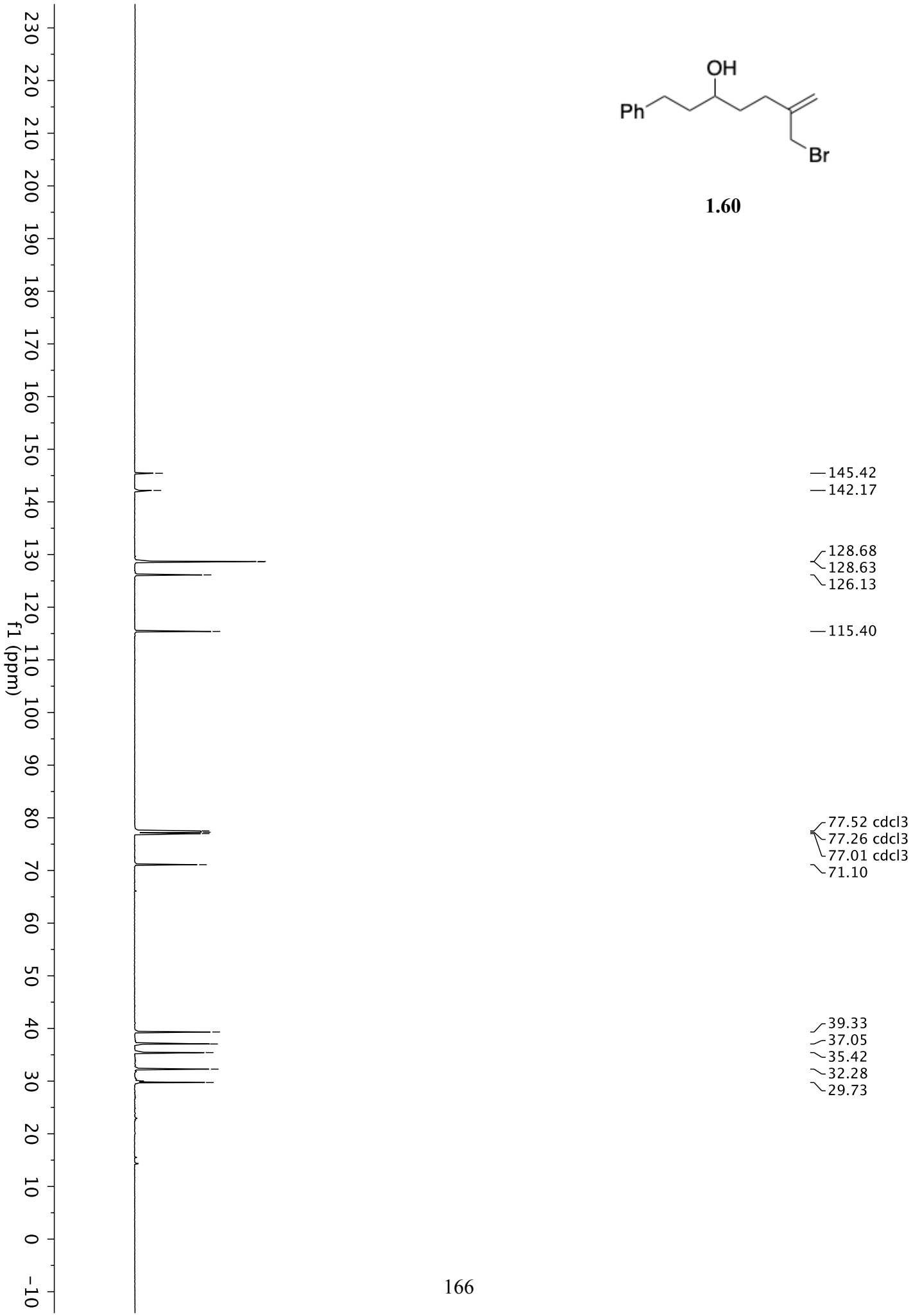


1.59

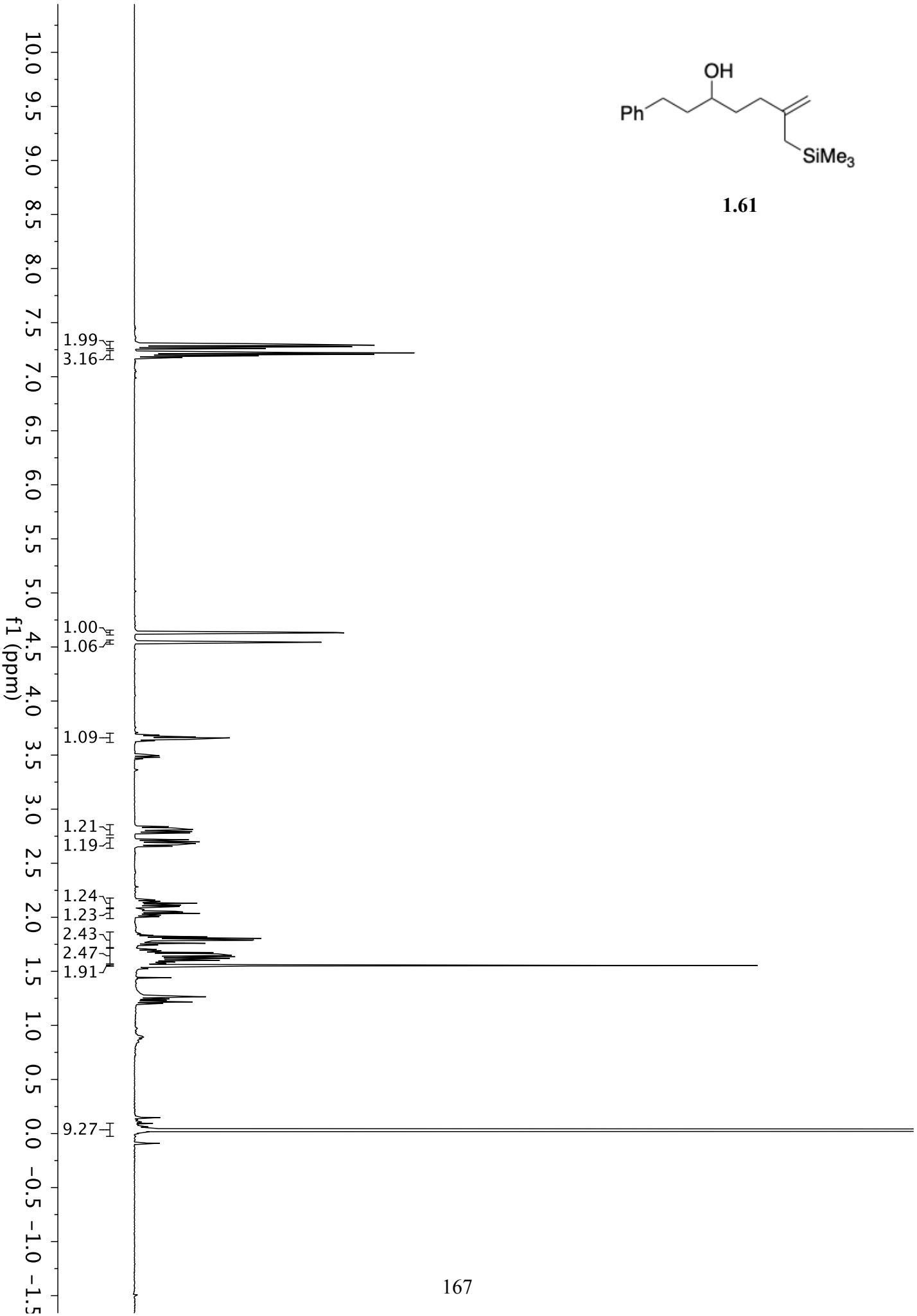

OH
Cl
Ph
Cl
1.59
141.78
129.38
128.48
128.37
125.94
120.32
70.59
39.07
35.62
32.04
25.96
f1 (ppm)

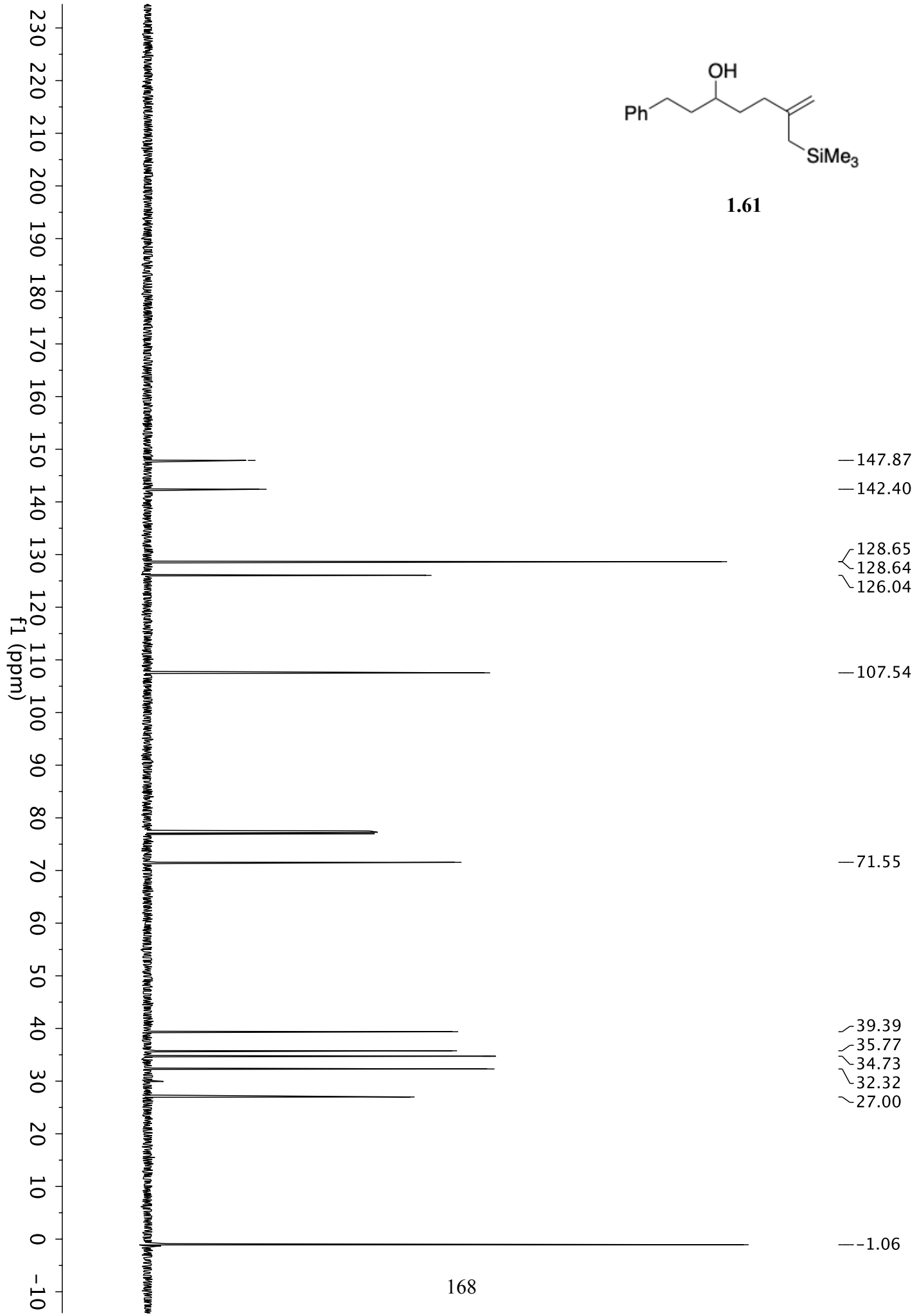

OH
Ph
Br
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
2.03
2.70
1.00
1.00
1.99
0.98
1.06
1.12
1.07
1.12
2.25
3.05

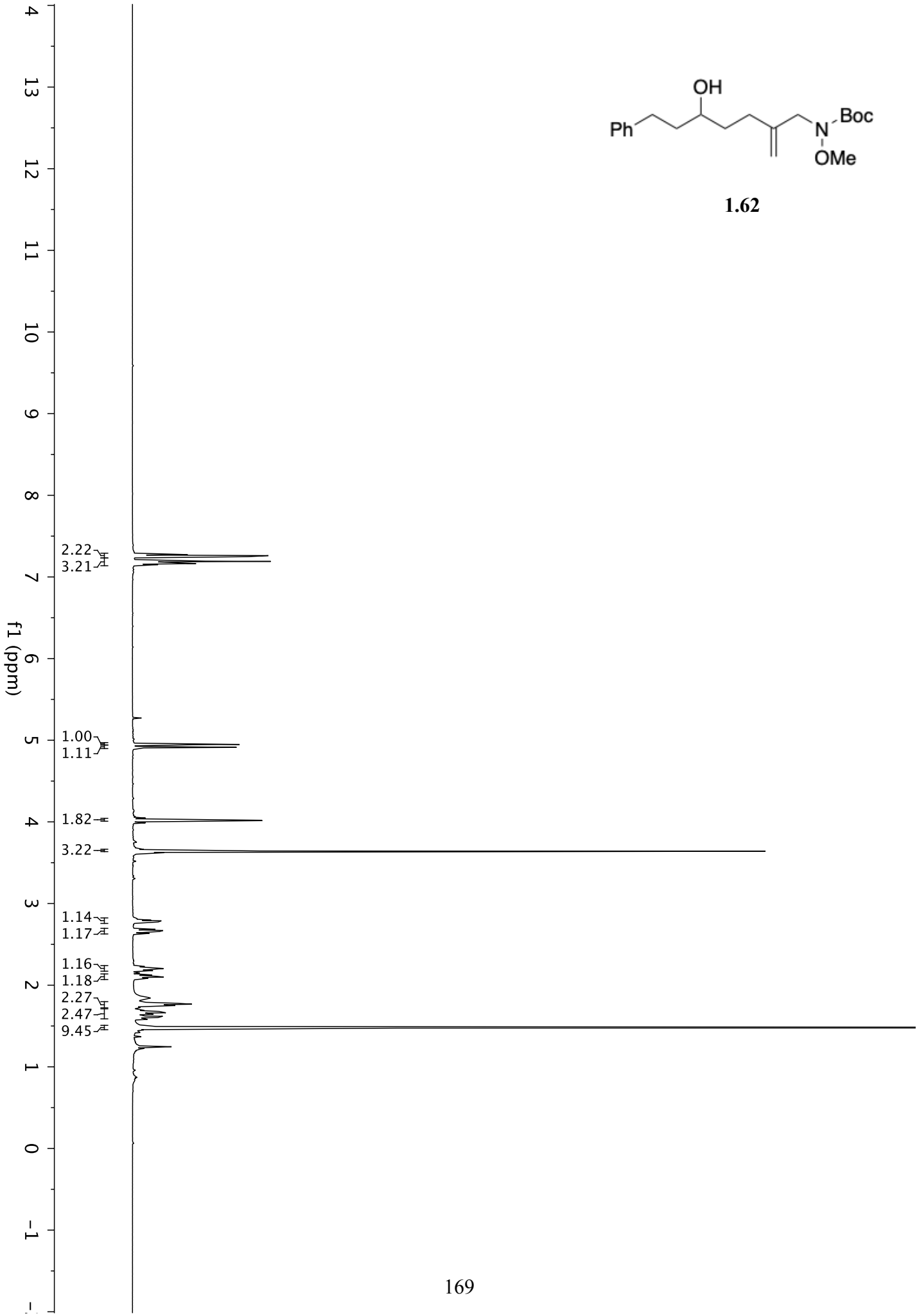
1.60


OH
Ph
Br
145.42
142.17
128.68
128.63
126.13
115.40
77.52 cdcl3
77.26 cdcl3
77.01 cdcl3
71.10
39.33
37.05
35.42
32.28
29.73
f1 (ppm)

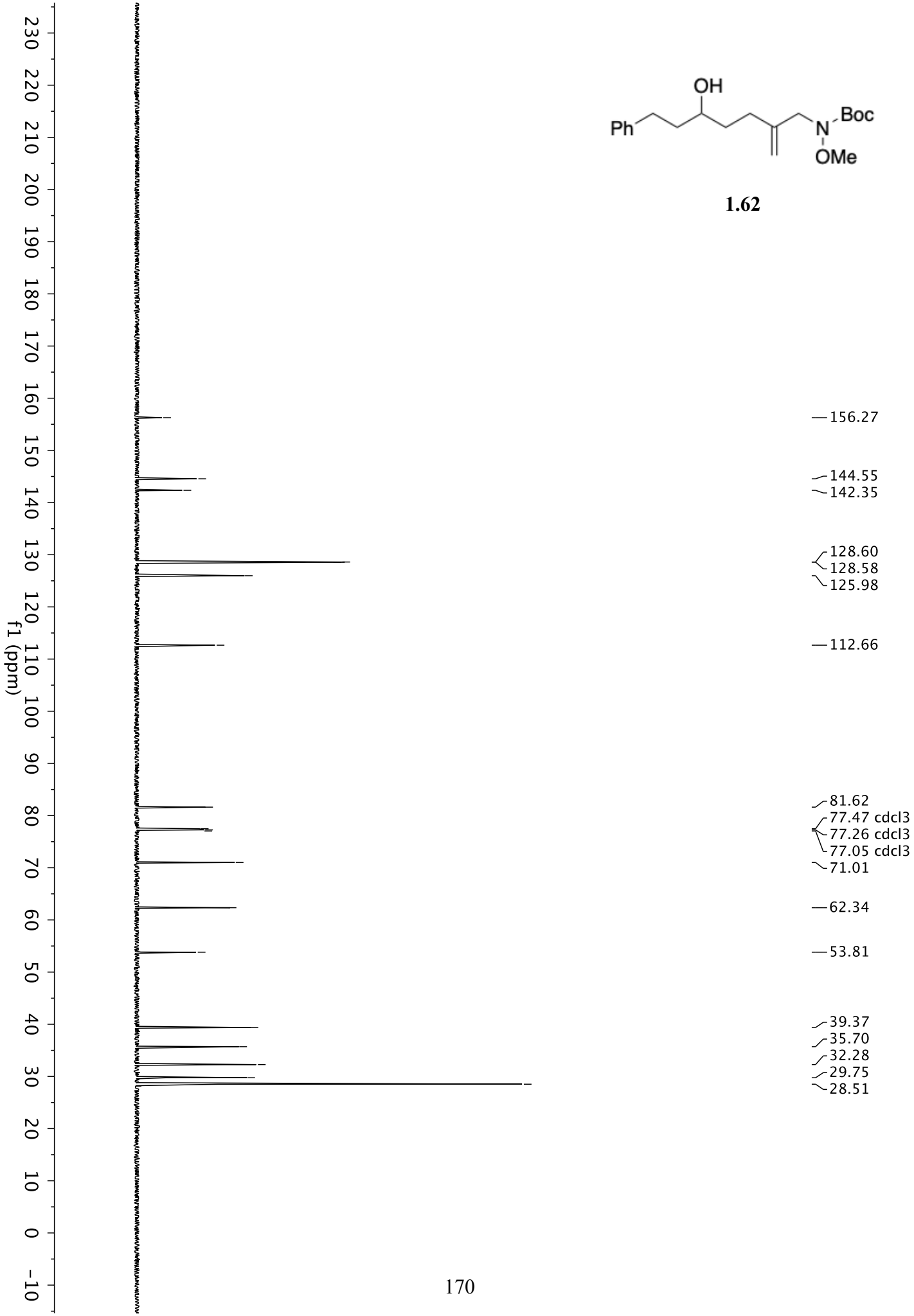
1.60

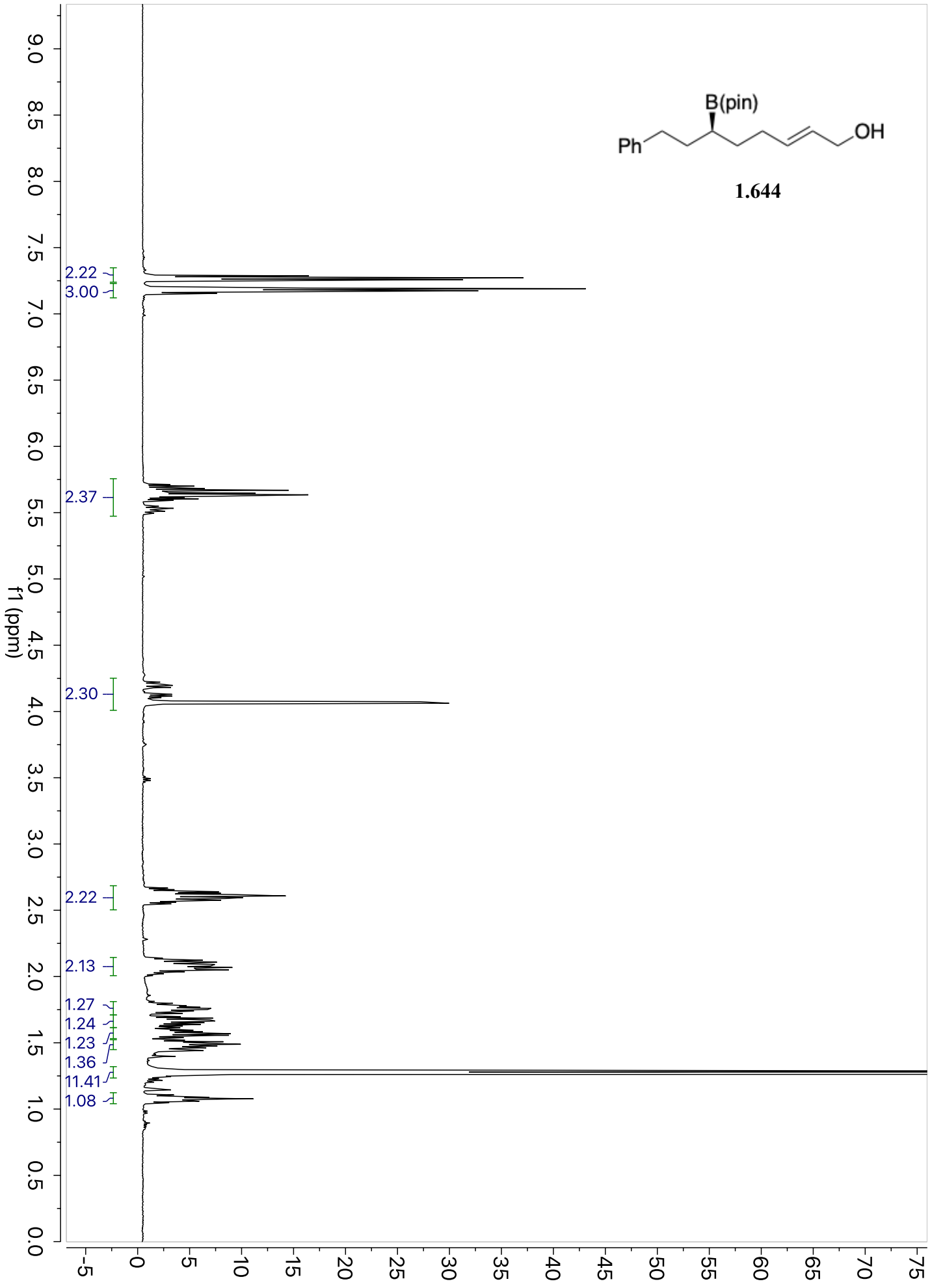

OH
Ph
SiMe3
1.61
1.99
3.16
1.00
1.06
1.09
1.21
1.19
1.24
1.23
2.43
2.47
1.91
9.27
f1 (ppm)

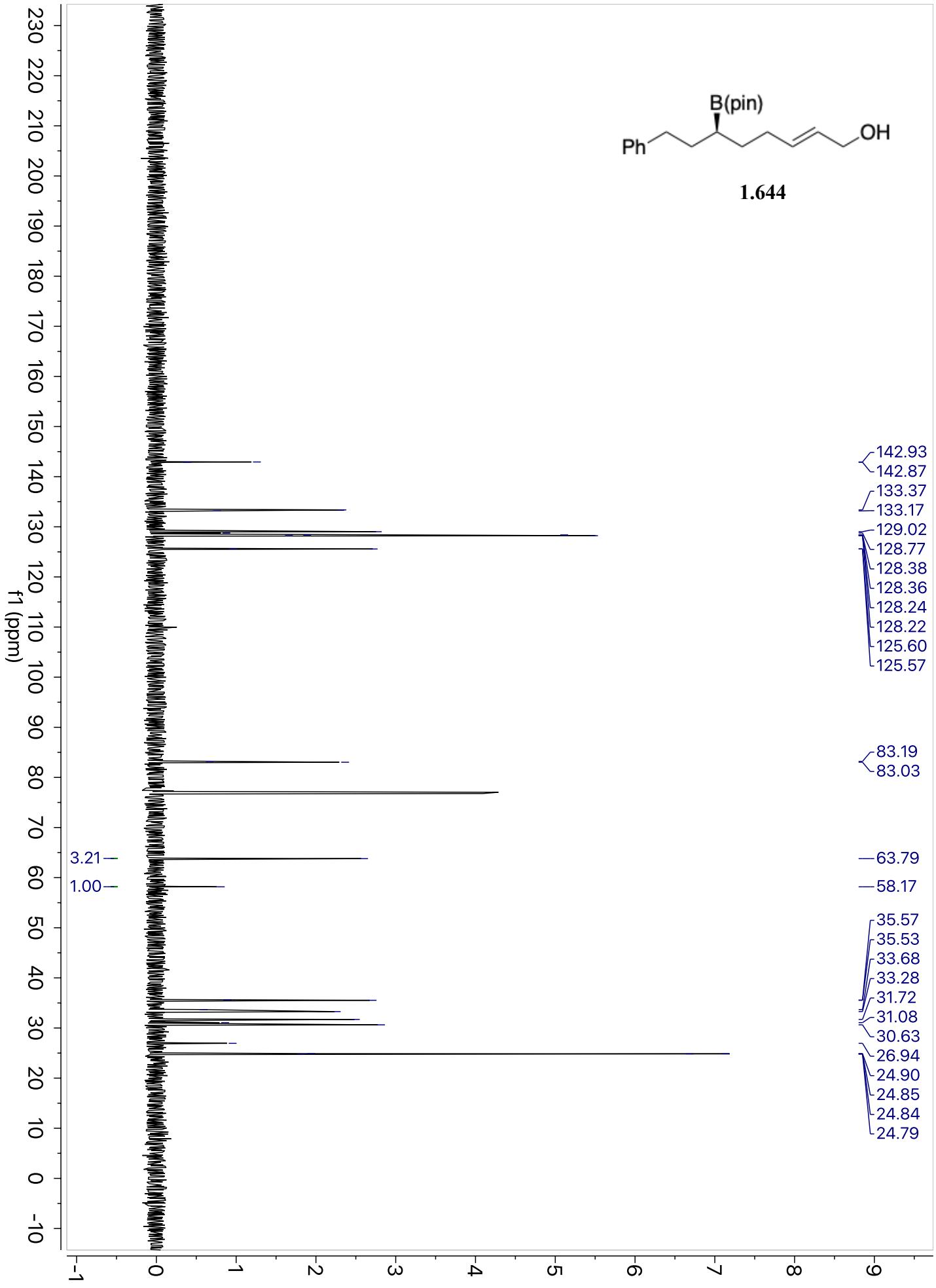

OH
Ph
SiMe3
1.61
147.87
142.40
128.65
128.64
126.04
107.54
71.55
39.39
35.77
34.73
32.32
27.00
-1.06
f1 (ppm)

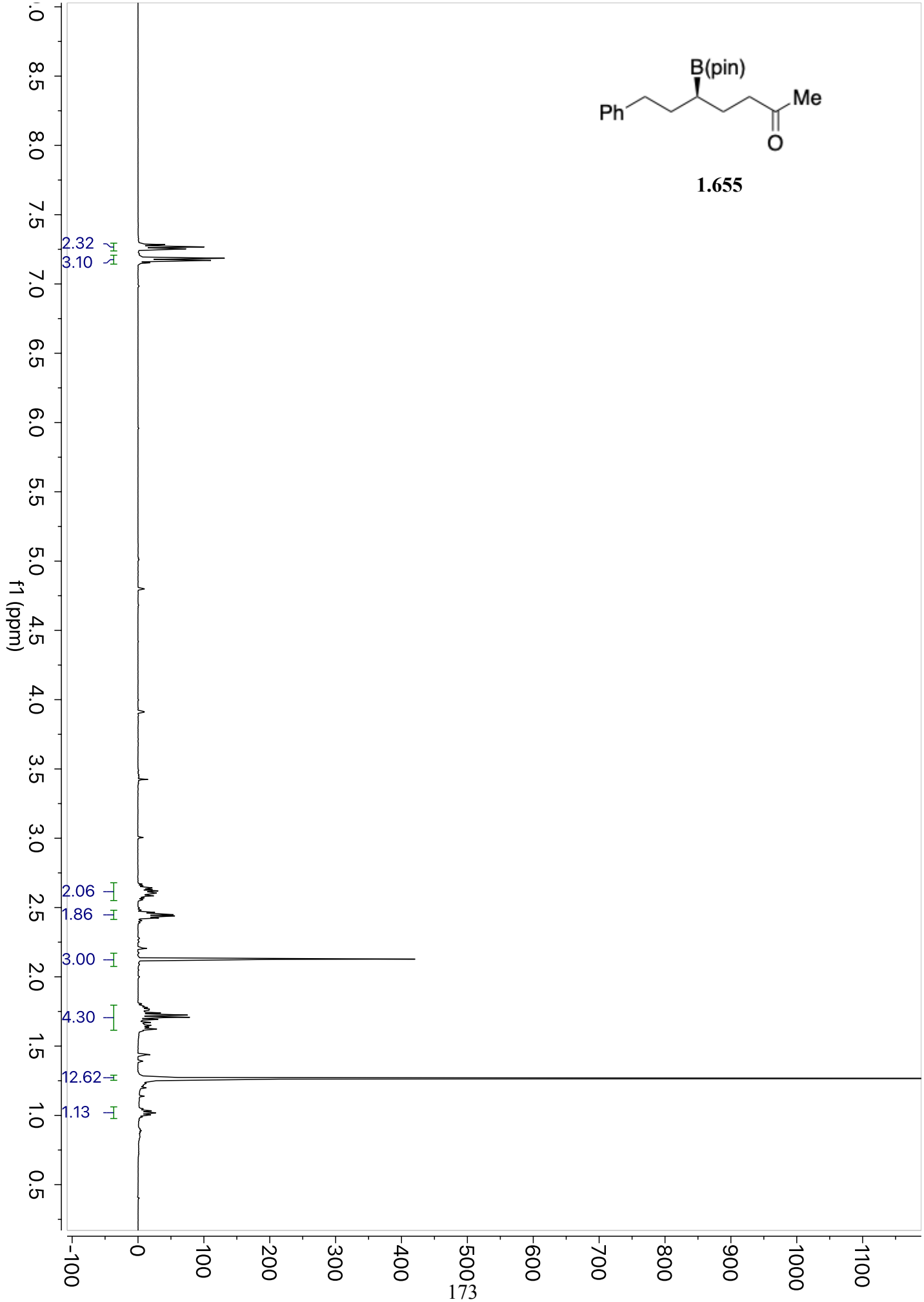

OH
Ph
N
Boc
OMe
2.22
3.21
1.00
1.11
1.82
3.22
1.14
1.17
1.16
1.18
2.27
2.47
9.45
f1 (ppm)

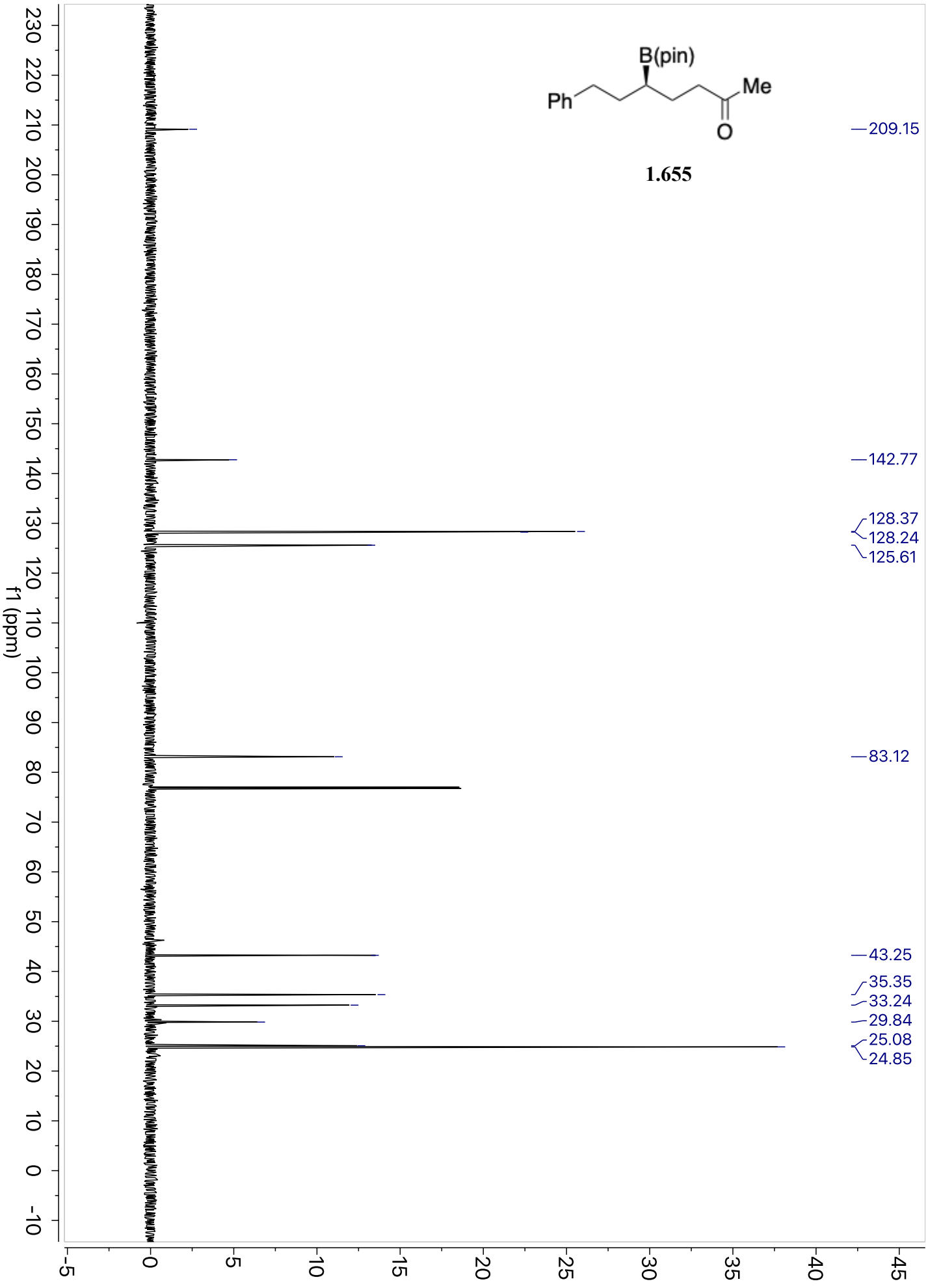
1.62

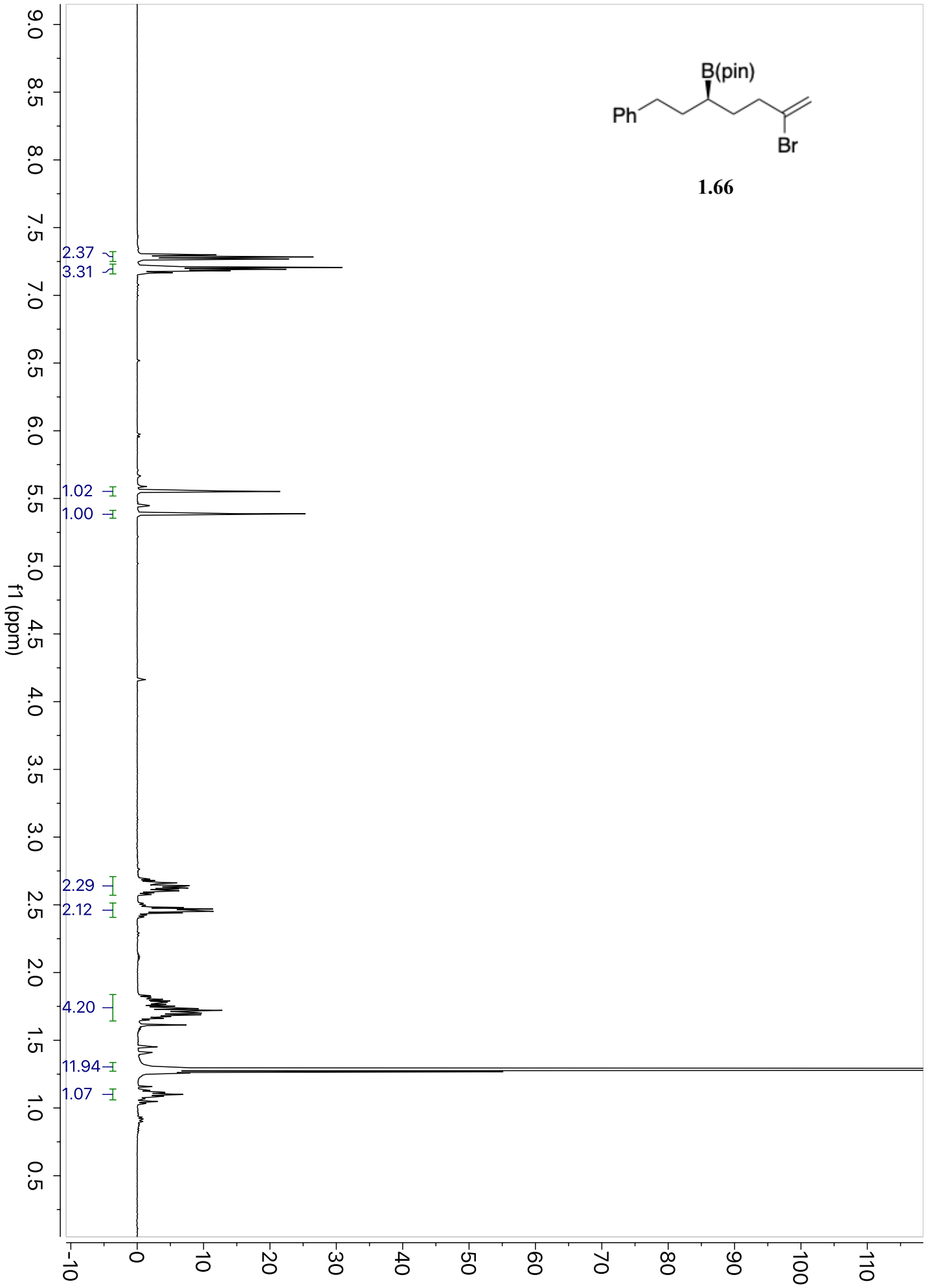

OH
Ph
N
Boc
OMe
1.62
156.27
144.55
142.35
128.60
128.58
125.98
112.66
81.62
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
71.01
62.34
53.81
39.37
35.70
32.28
29.75
28.51
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

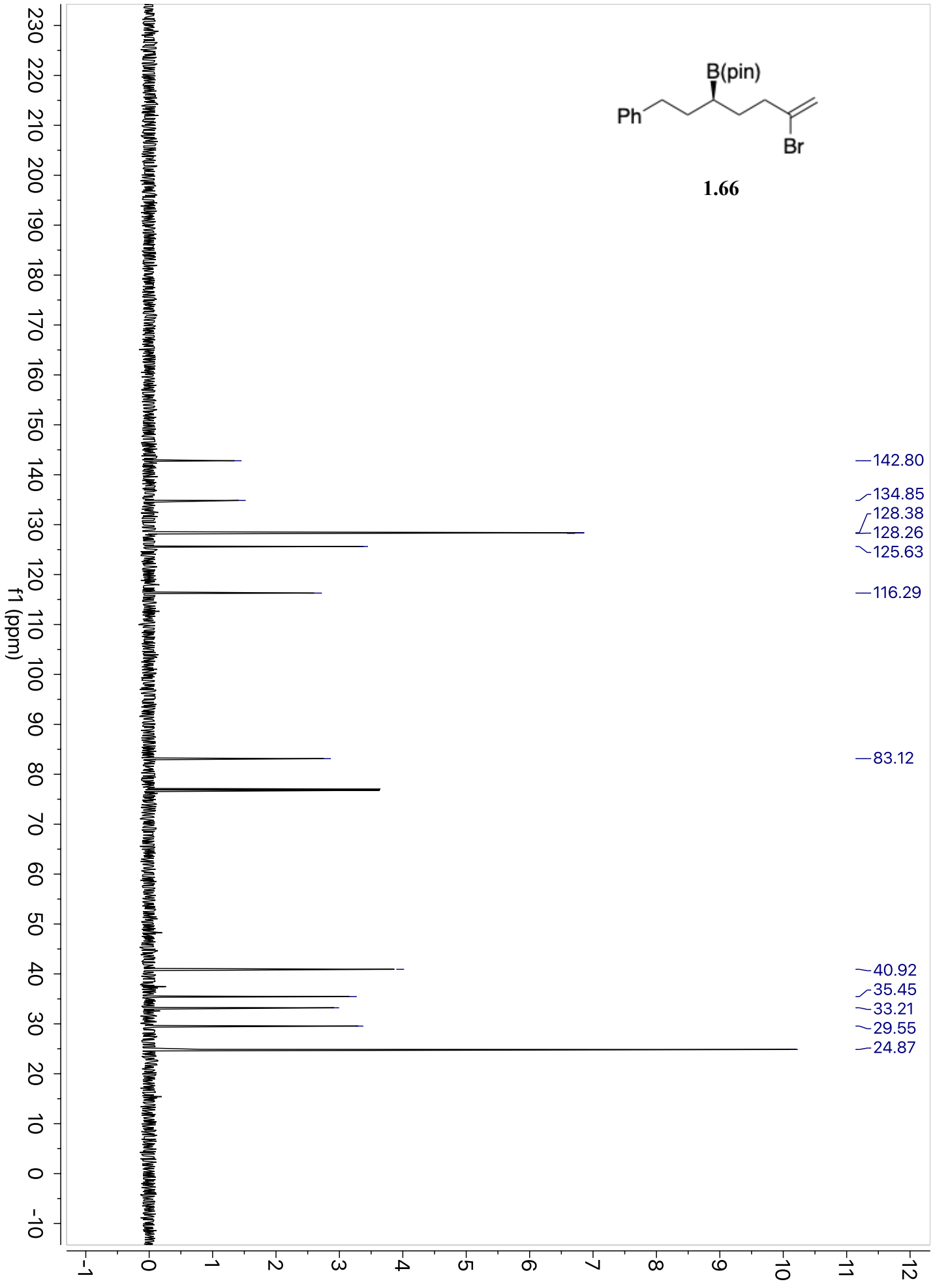

B(pin)
Ph
OH
1.644
2.22
3.00
2.37
2.30
2.22
2.13
1.27
1.24
1.23
1.36
11.41
1.08
f1 (ppm)

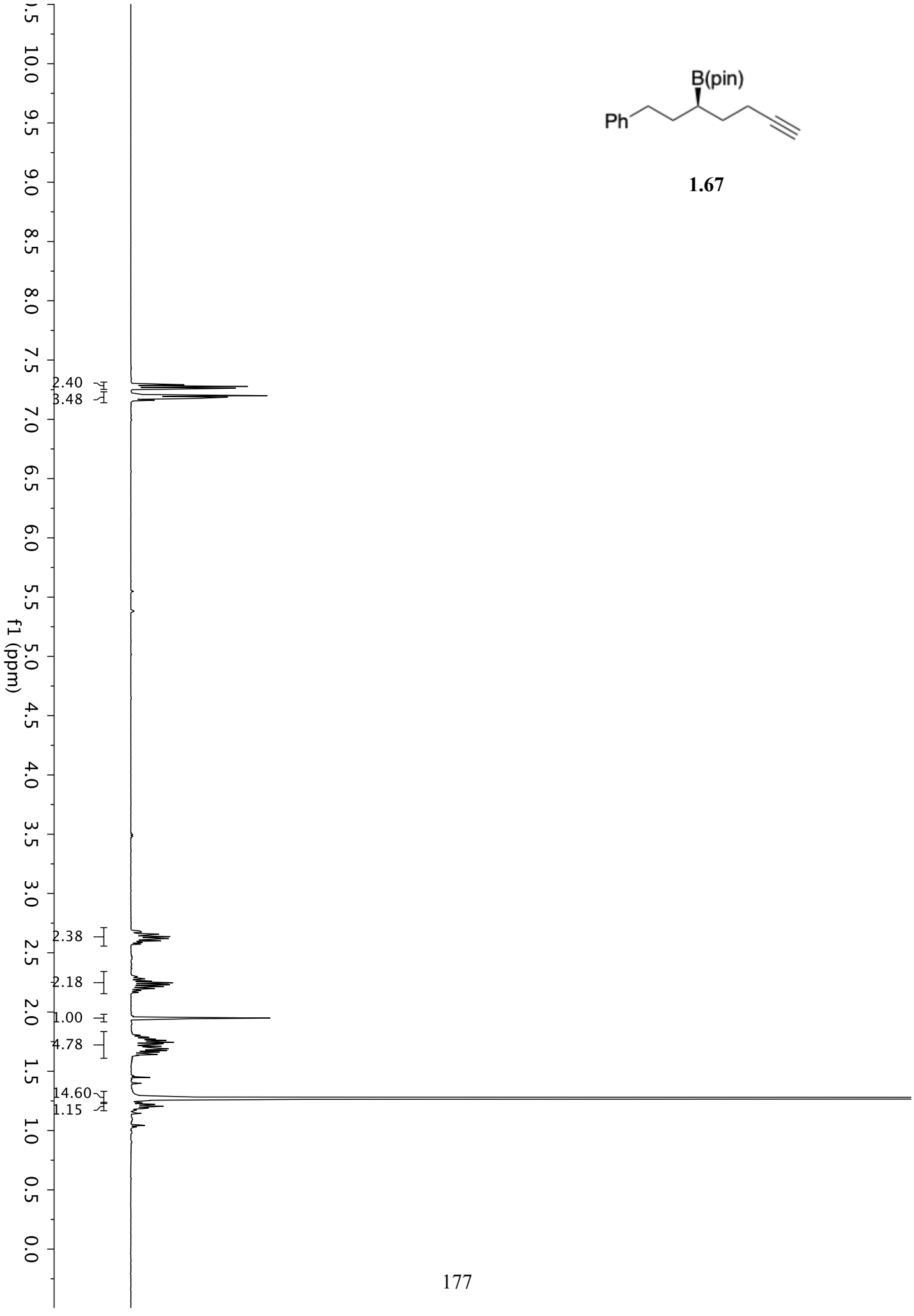

B(pin)
Ph
OH
1.644
142.93
142.87
133.37
133.17
129.02
128.77
128.38
128.36
128.24
128.22
125.60
125.57
83.19
83.03
63.79
58.17
35.57
35.53
33.68
33.28
31.72
31.08
30.63
26.94
24.90
24.85
24.84
24.79
3.21
1.00
f1 (ppm)

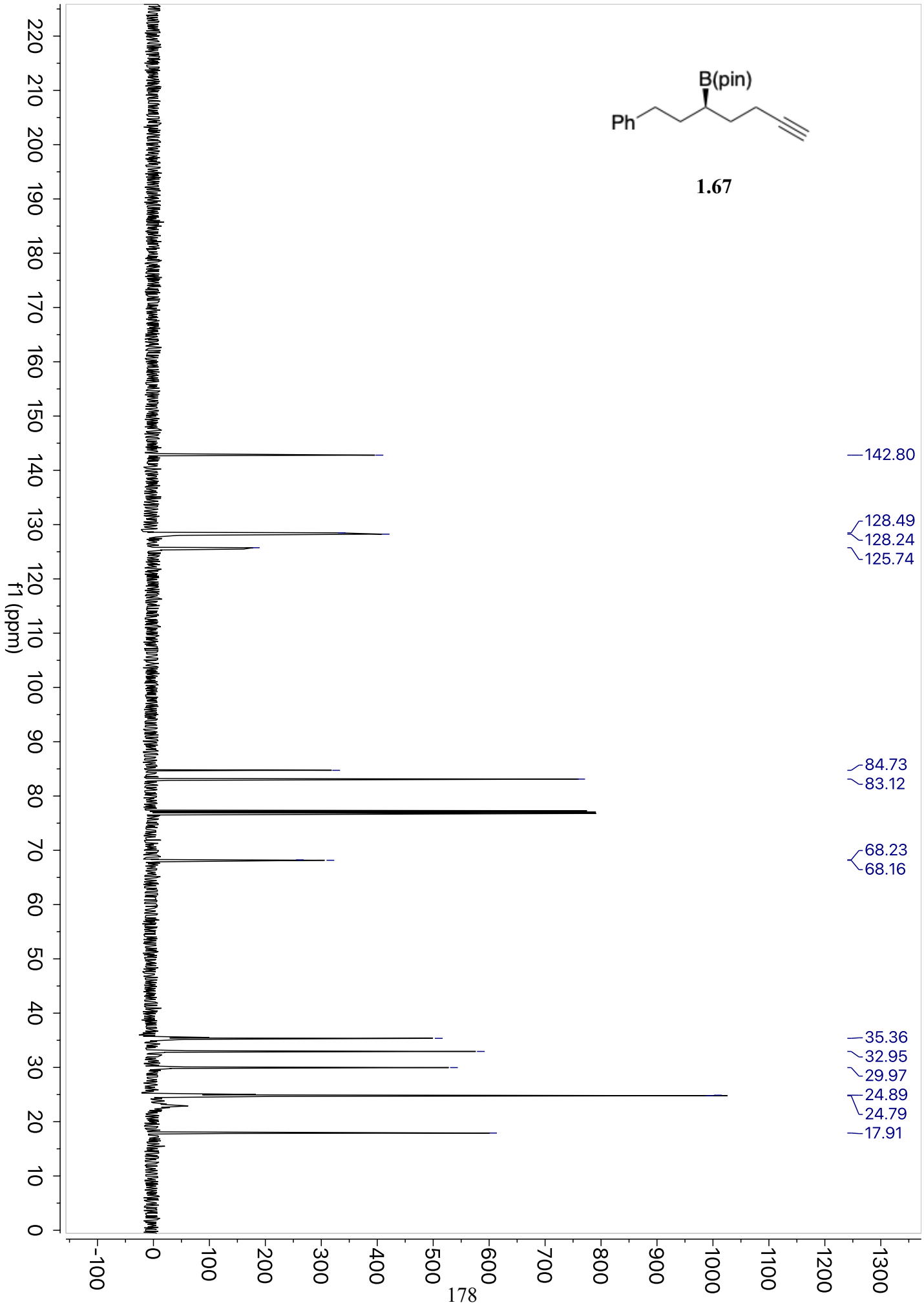

B(pin)
Ph
Me
O
1.655
2.32
3.10
2.06
1.86
3.00
4.30
12.62
1.13
f1 (ppm)

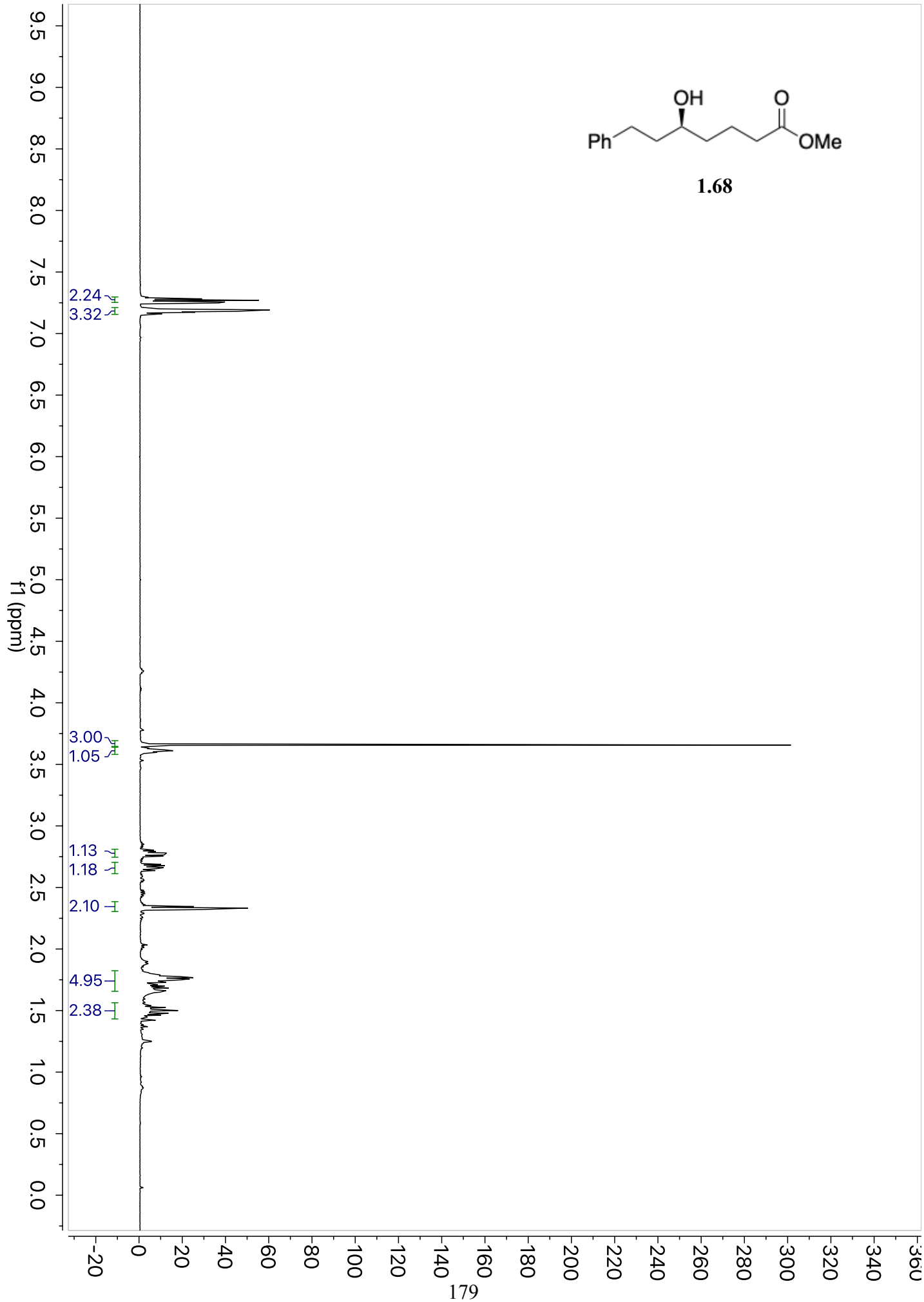

B(pin)
Ph
Me
O
1.655
209.15
142.77
128.37
128.24
125.61
83.12
43.25
35.35
33.24
29.84
25.08
24.85
f1 (ppm)


B(pin)
Ph
Br
1.66
2.37
3.31
1.02
1.00
2.29
2.12
4.20
11.94
1.07
f1 (ppm)

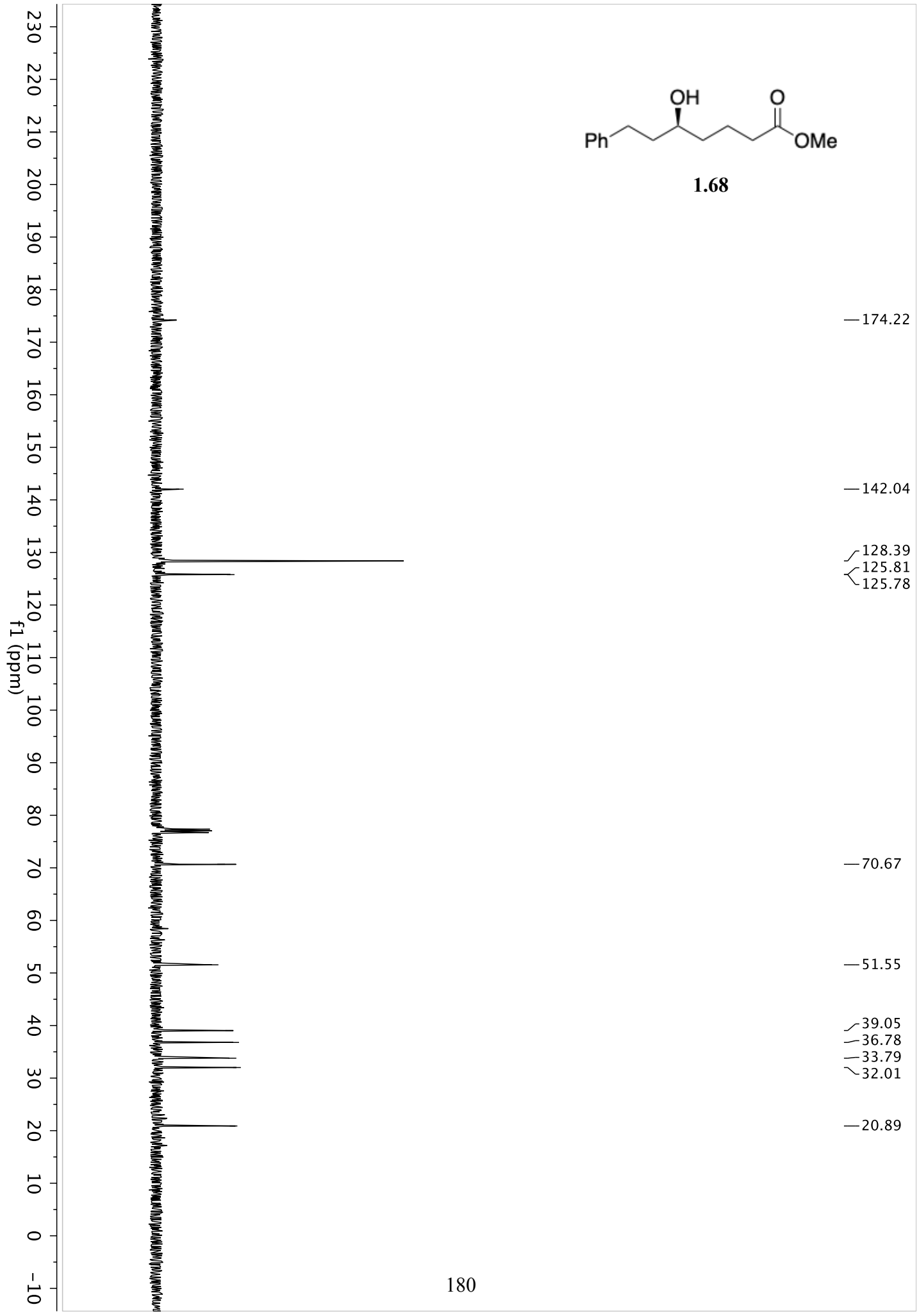

B(pin)
Ph
Br
1.66
142.80
134.85
128.38
128.26
125.63
116.29
83.12
40.92
35.45
33.21
29.55
24.87
f1 (ppm)

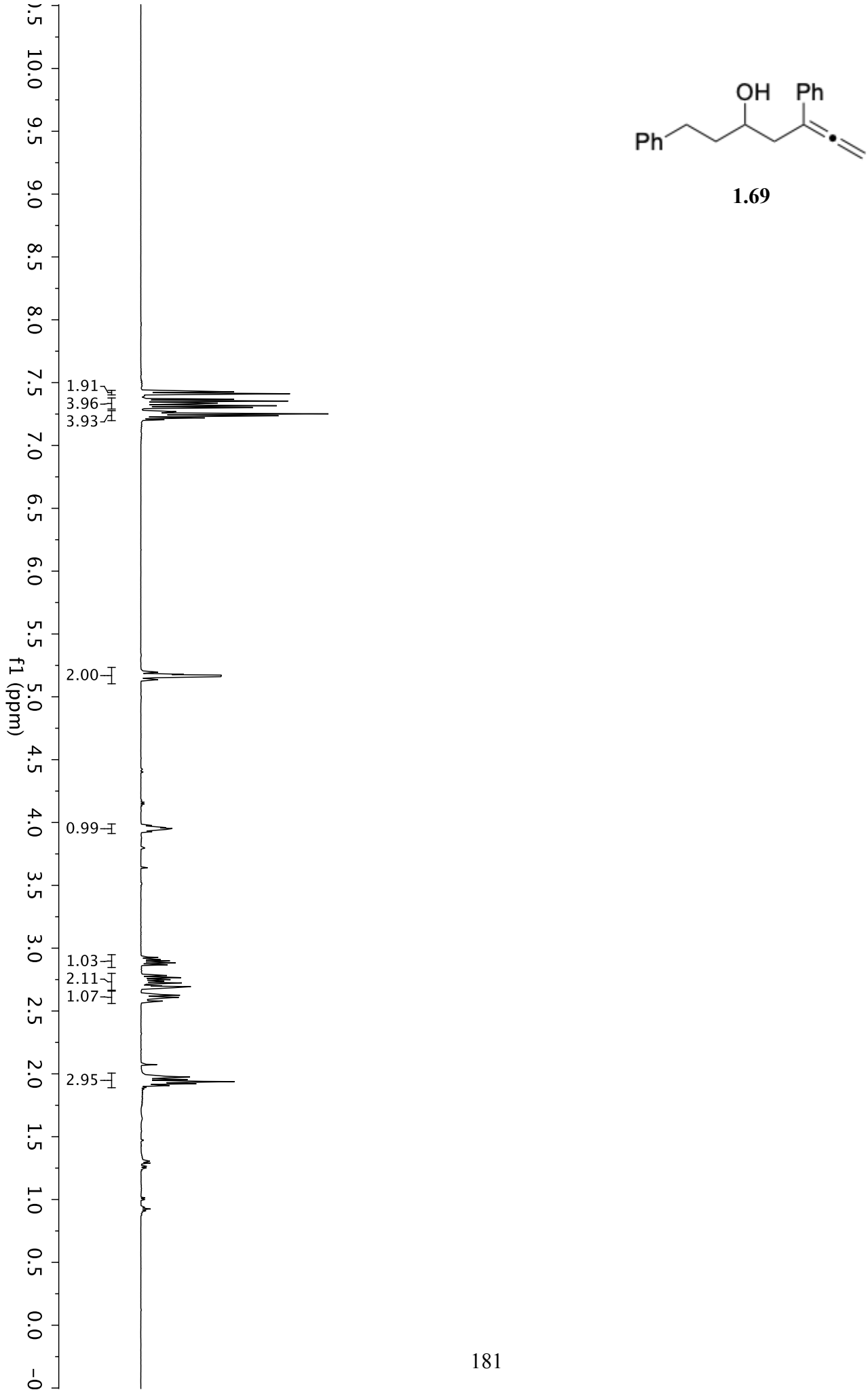

B(pin)
Ph
1.67
2.40
3.48
2.38
2.18
1.00
4.78
14.60
1.15
f1 (ppm)

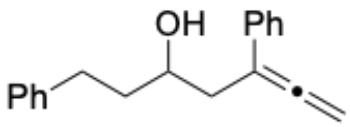

B(pin)
Ph
1.67
142.80
128.49
128.24
125.74
84.73
83.12
68.23
68.16
35.36
32.95
29.97
24.89
24.79
17.91
f1 (ppm)



1.68

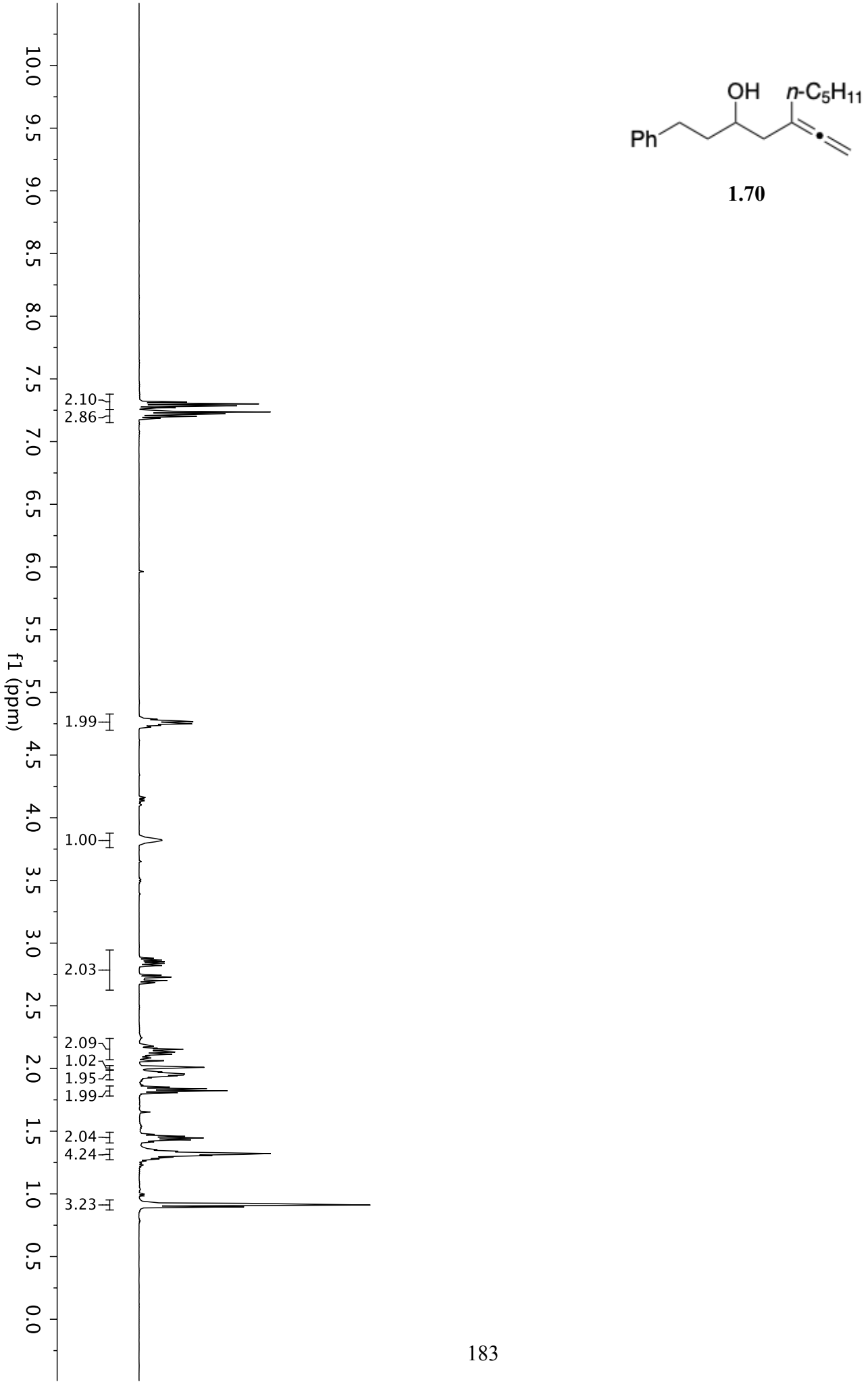

OH
O
Ph
OMe
1.68
174.22
142.04
128.39
125.81
125.78
70.67
51.55
39.05
36.78
33.79
32.01
20.89
f1 (ppm)


OH
Ph
Ph
1.69
1.91
3.96
3.93
2.00
0.99
1.03
2.11
1.07
2.95
f1 (ppm)

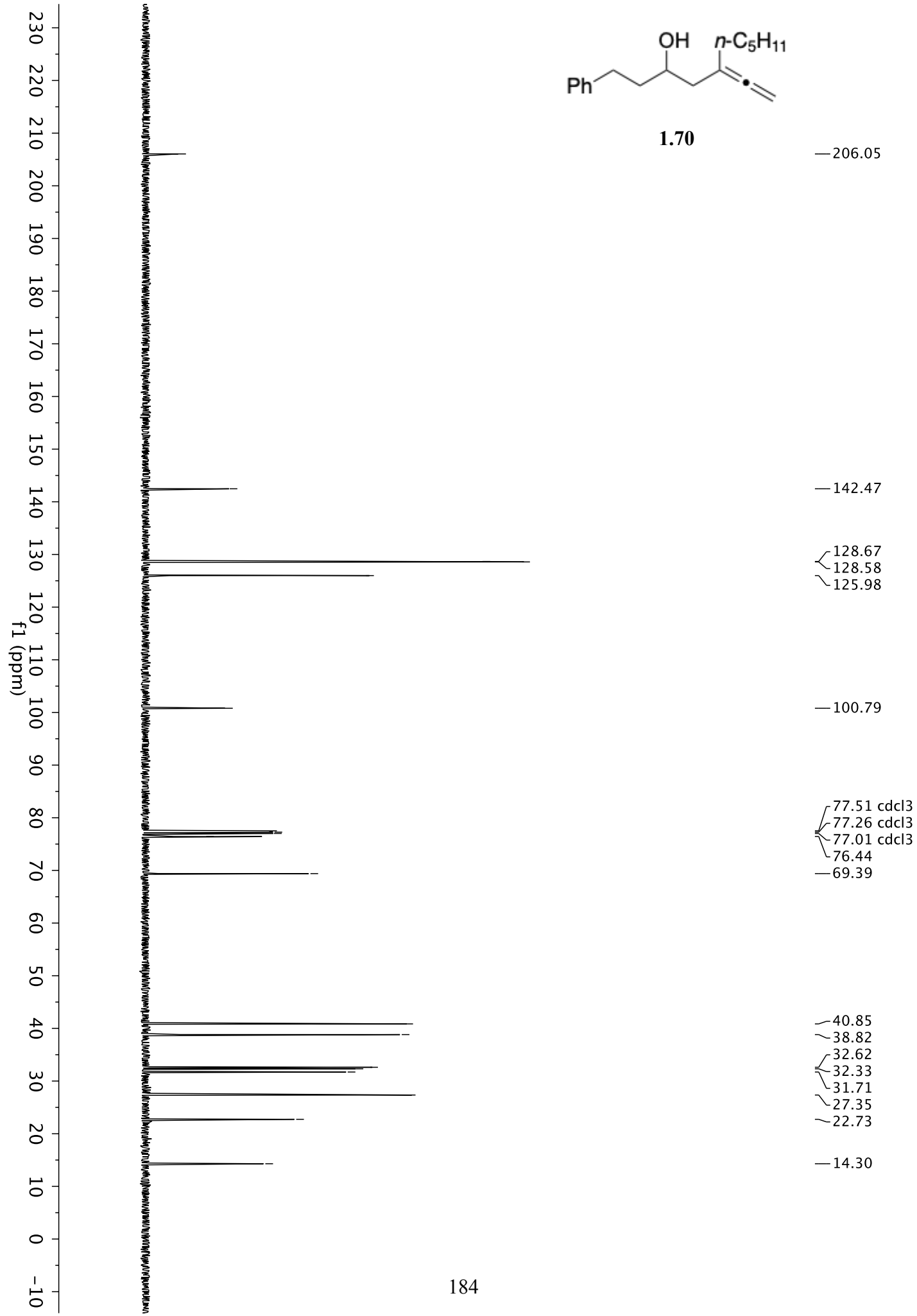

OH
Ph
Ph

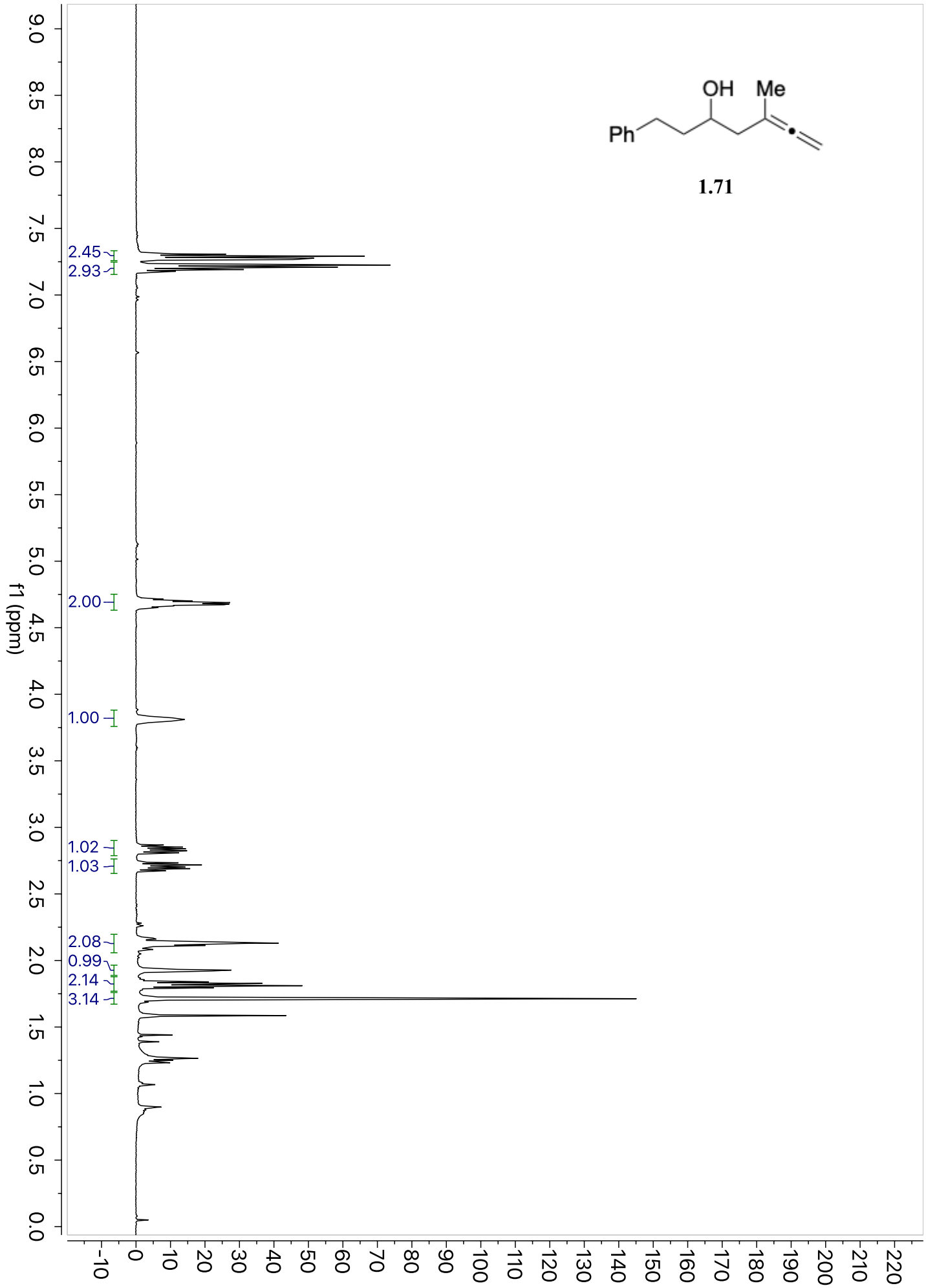
1.69

208.99
142.34
135.90
128.73
128.66
128.61
127.22
126.29
126.03
102.41
78.84
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
69.75
38.87
38.40
32.29
f1 (ppm)

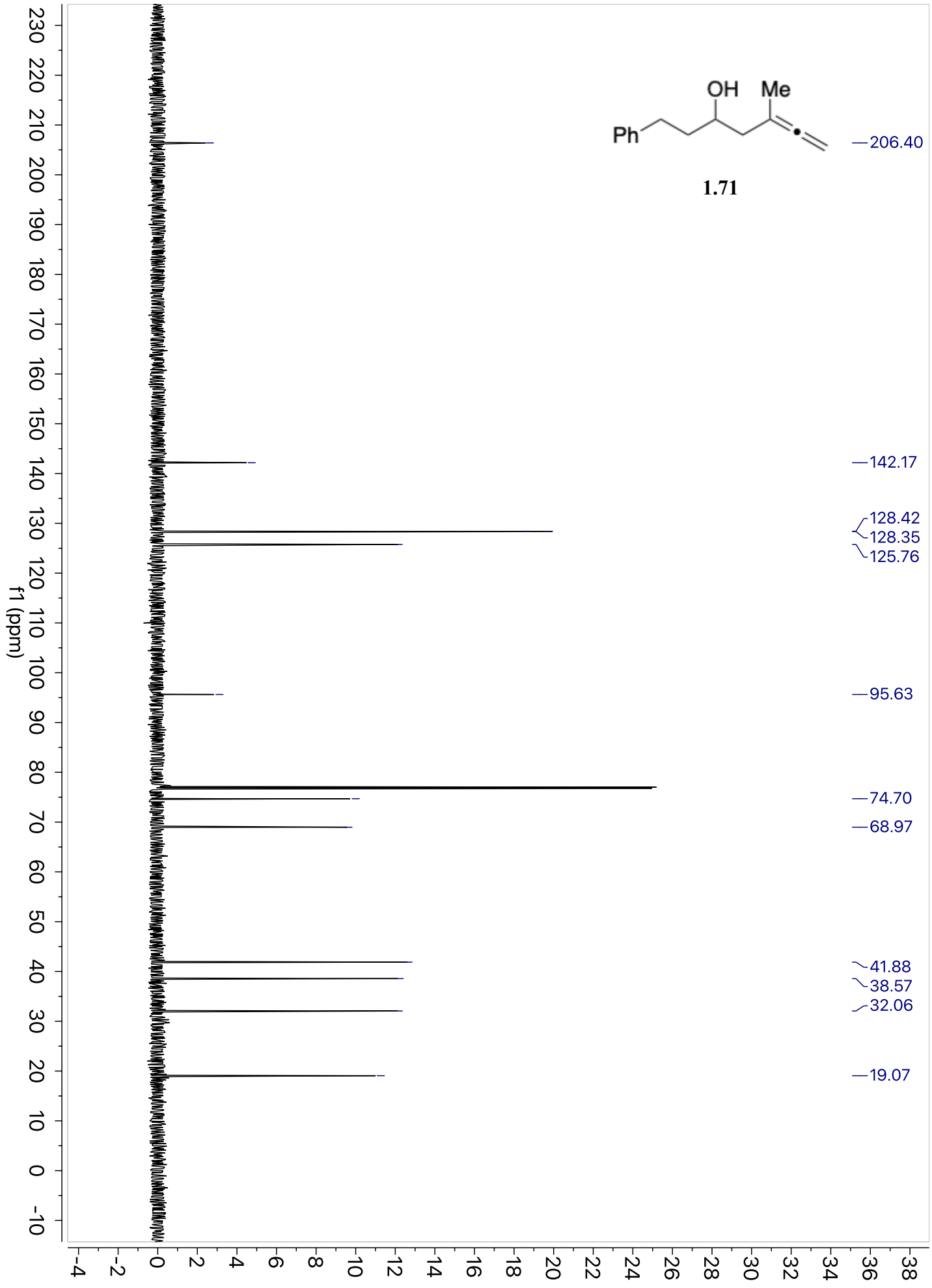

OH
n-C5H11
Ph
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
2.10
2.86
1.99
1.00
2.03
2.09
1.02
1.95
1.99
2.04
4.24
3.23

1.70

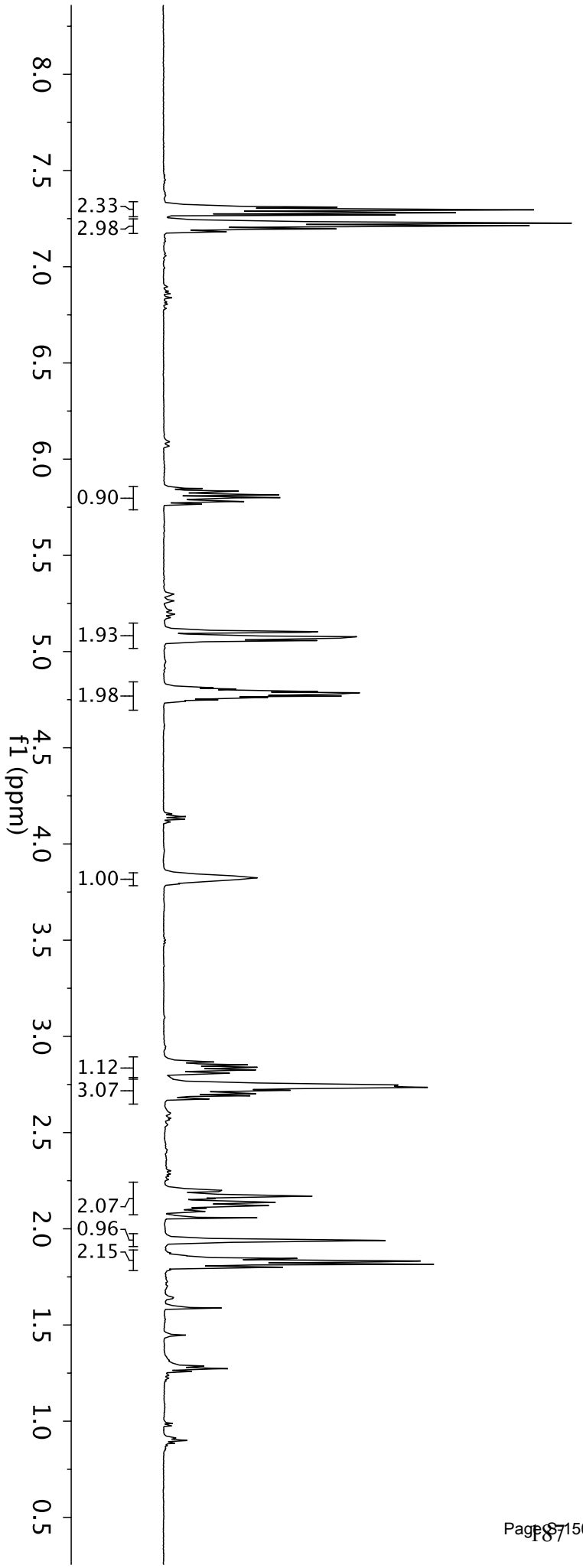

OH
n-C5H11
Ph
1.70
206.05
142.47
128.67
128.58
125.98
100.79
77.51 cdcl3
77.26 cdcl3
77.01 cdcl3
76.44
69.39
40.85
38.82
32.62
32.33
31.71
27.35
22.73
14.30
f1 (ppm)

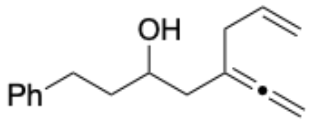


1.71

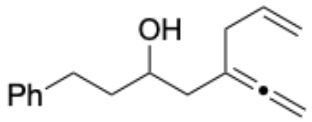

OH
Me
Ph
206.40
142.17
128.42
128.35
125.76
95.63
74.70
68.97
41.88
38.57
32.06
19.07
f1 (ppm)

1.71


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
f1 (ppm)
2.33
2.98
0.90
1.93
1.98
1.00
1.12
3.07
2.07
0.96
2.15

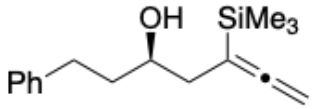

OH
Ph

1.72

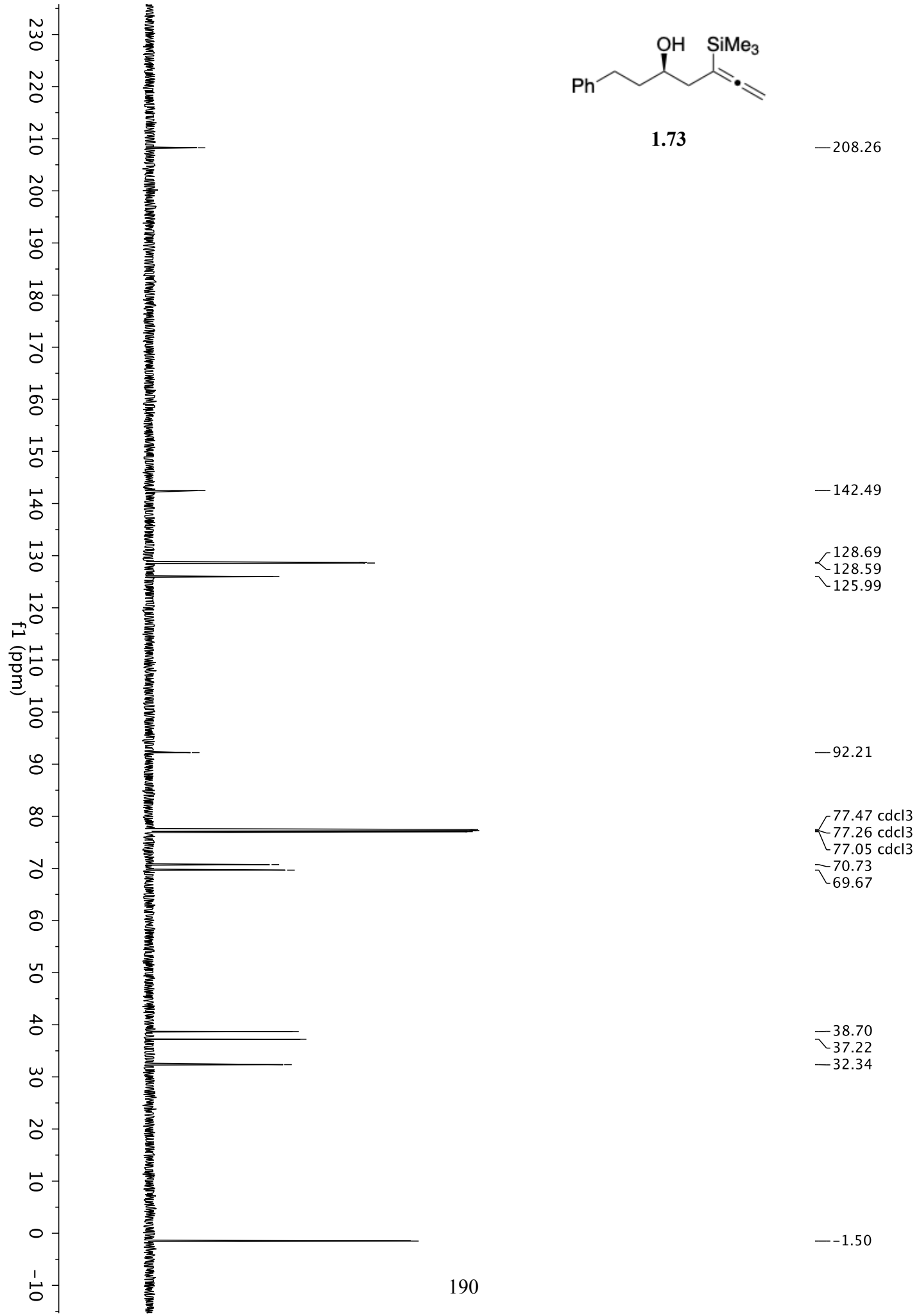

OH
Ph

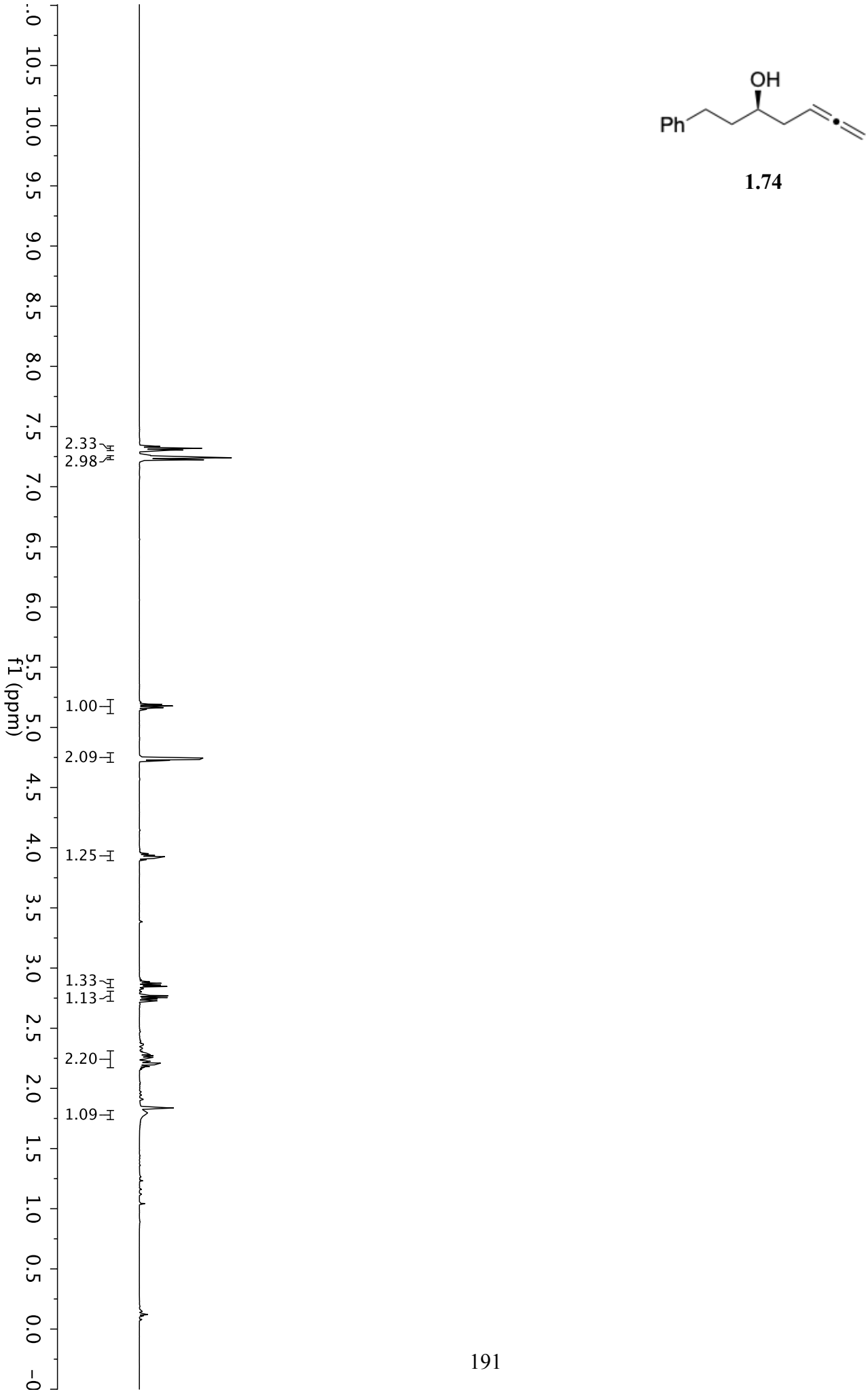
1.72

206.46
142.41
135.59
128.68
128.61
126.02
116.63
99.19
77.52 cdcl3
77.26 cdcl3
77.01 cdcl3
76.54
69.38
40.31
38.81
37.64
32.30
f1 (ppm)

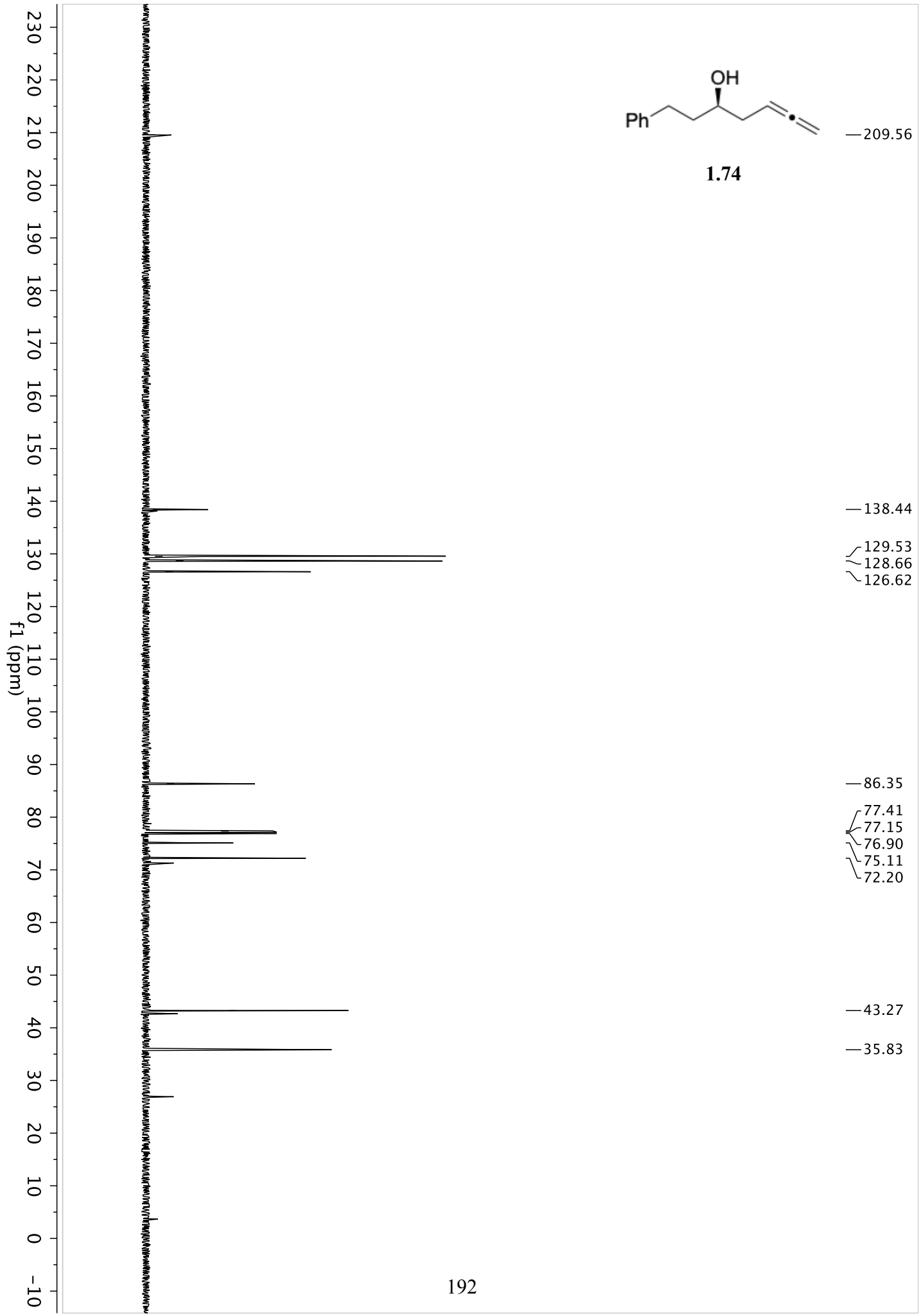


1.73

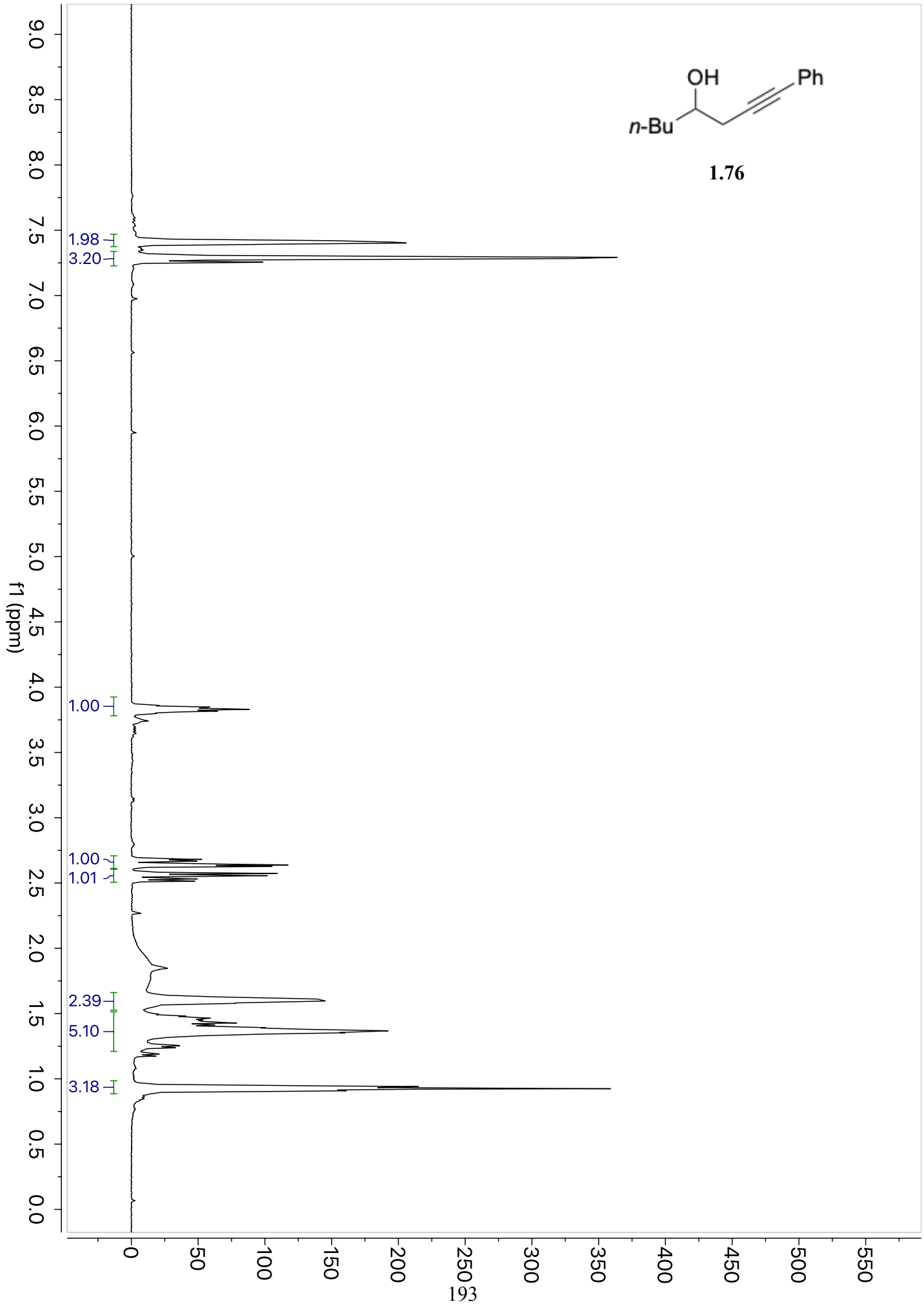

OH
SiMe3
Ph
1.73
208.26
142.49
128.69
128.59
125.99
92.21
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
70.73
69.67
38.70
37.22
32.34
-1.50
f1 (ppm)

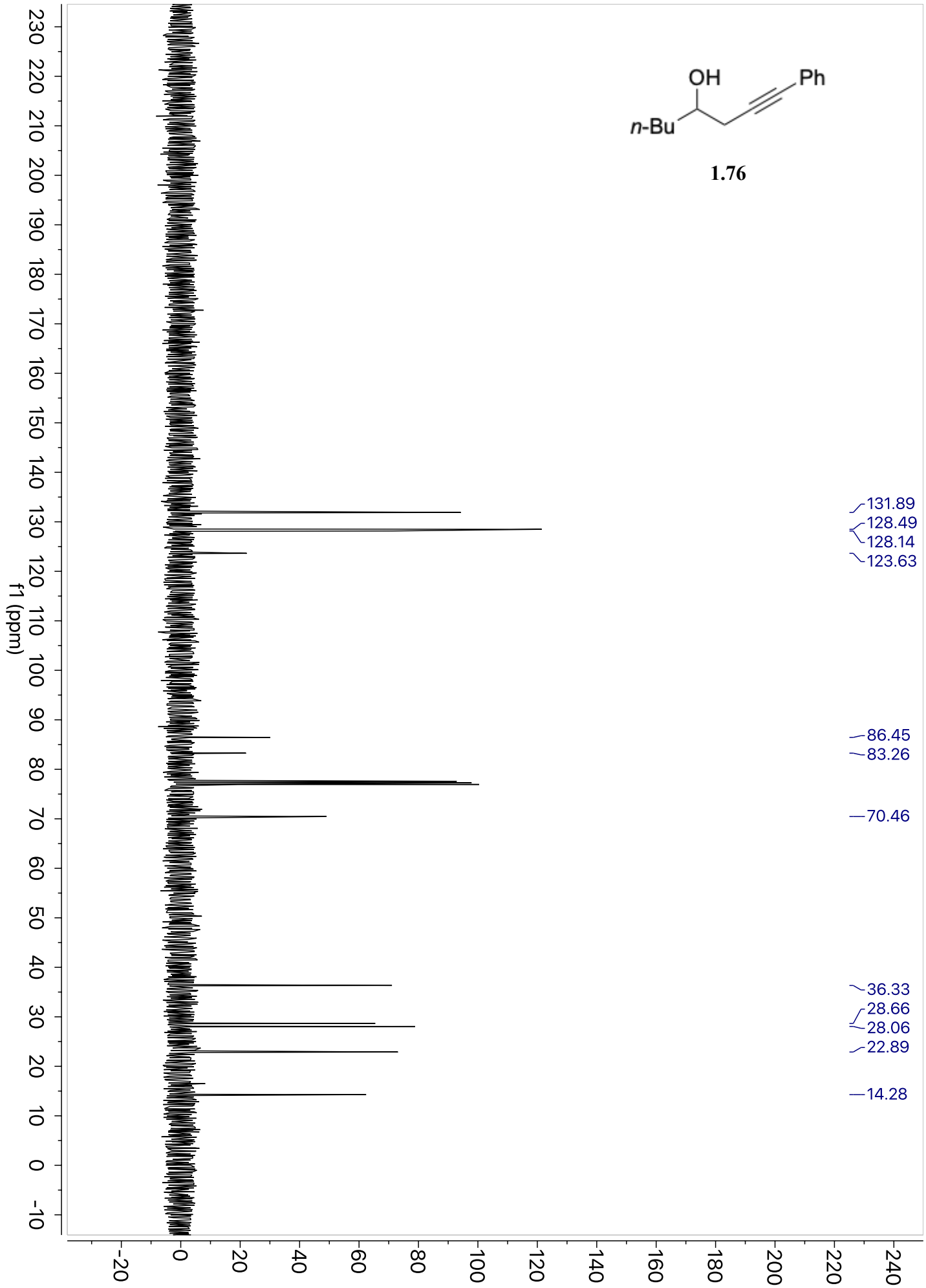


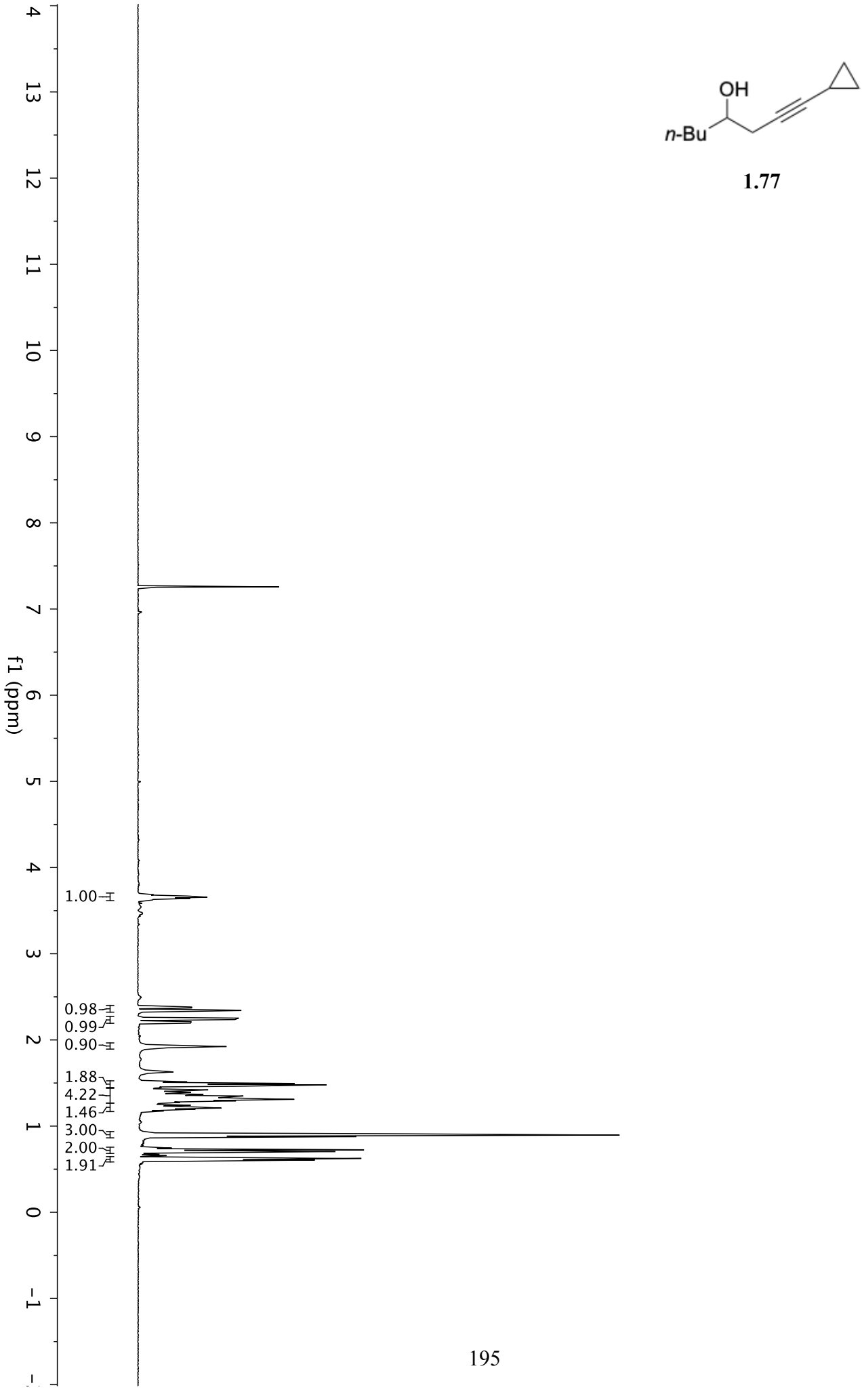
1.74


OH
Ph
209.56
138.44
129.53
128.66
126.62
86.35
77.41
77.15
76.90
75.11
72.20
43.27
35.83
f1 (ppm)

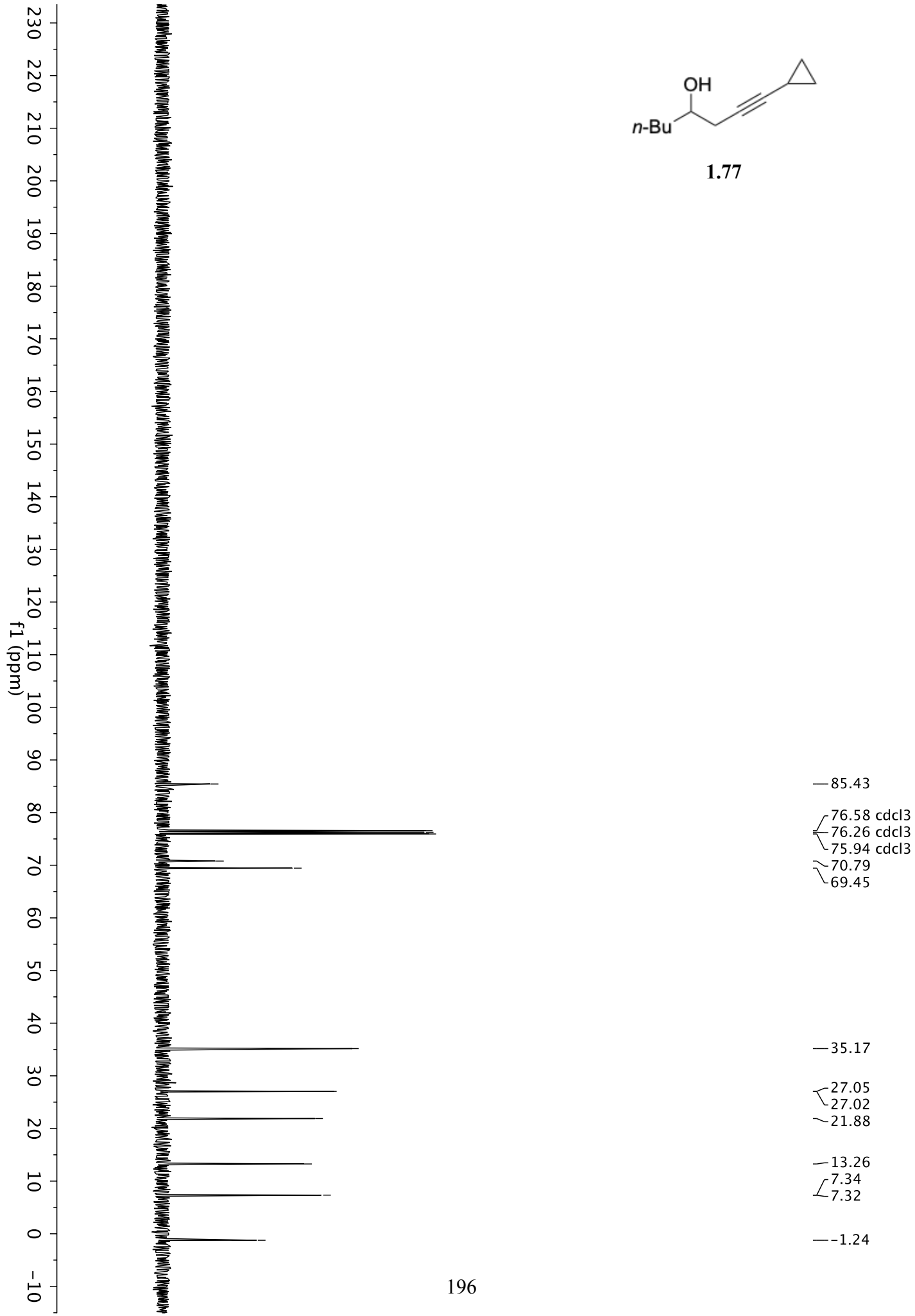
1.74

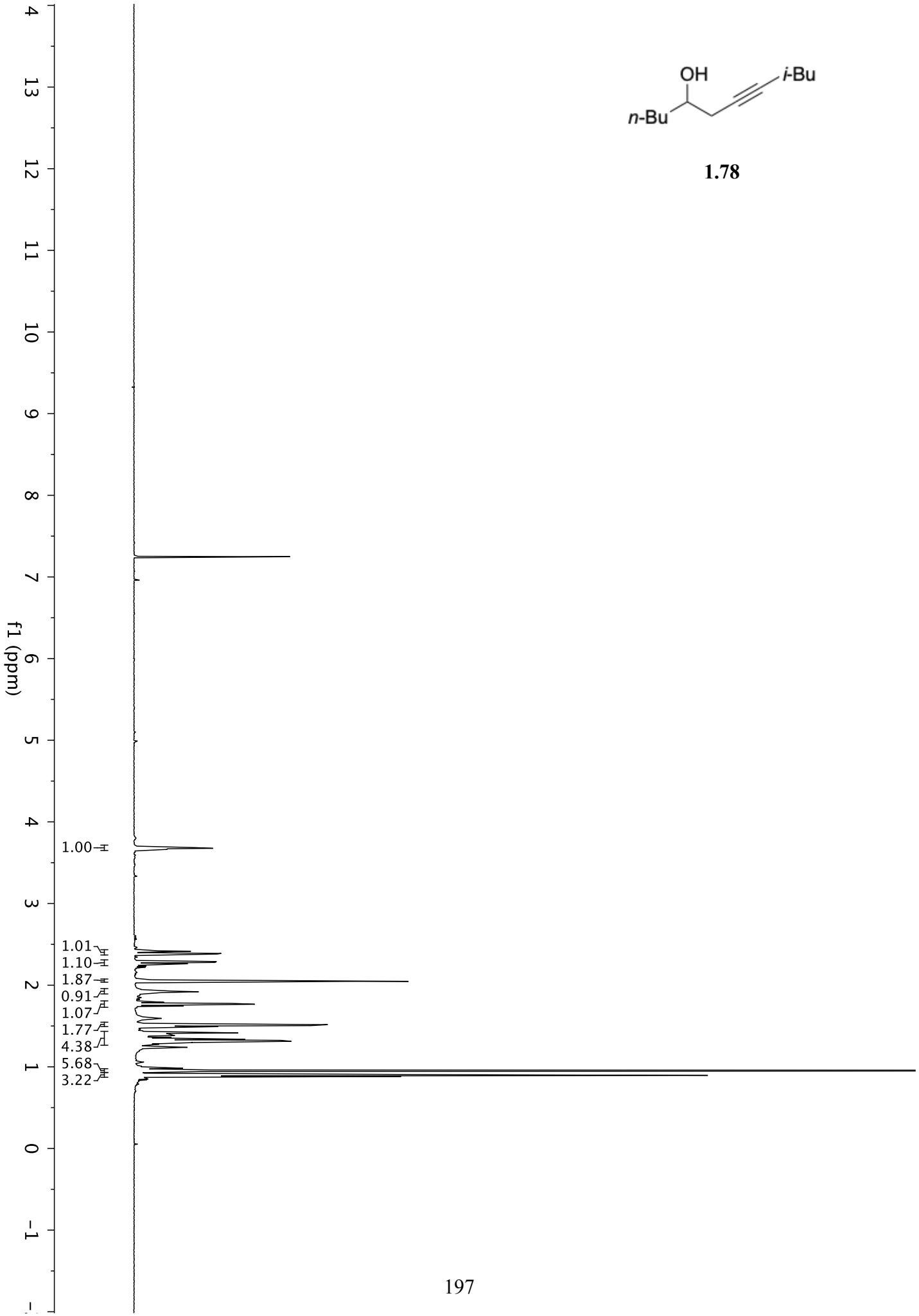

OH
Ph
n-Bu
1.76
1.98
3.20
1.00
1.00
1.01
2.39
5.10
3.18
f1 (ppm)

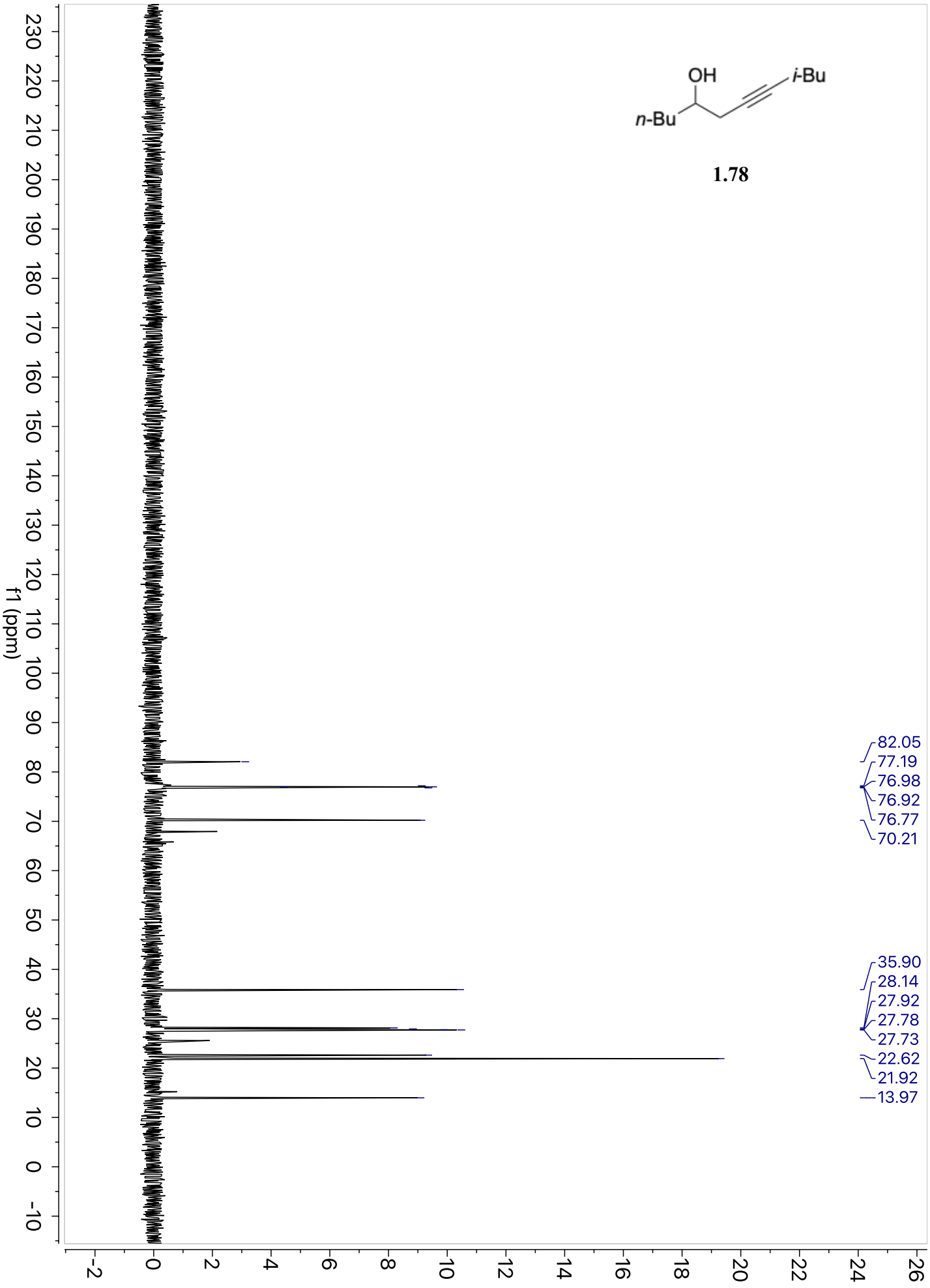

OH
Ph
n-Bu
1.76
131.89
128.49
128.14
123.63
86.45
83.26
70.46
36.33
28.66
28.06
22.89
14.28
f1 (ppm)



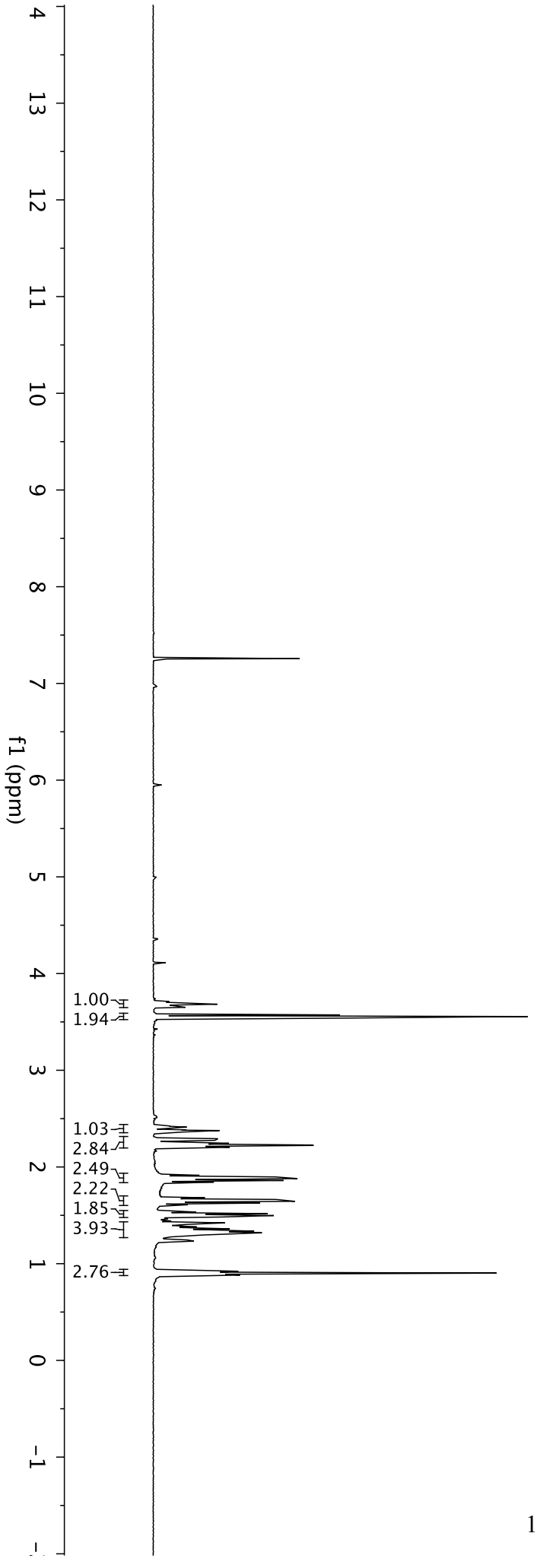
1.77

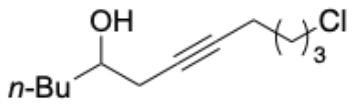

OH
n-Bu
1.77
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
85.43
76.58 cdcl3
76.26 cdcl3
75.94 cdcl3
70.79
69.45
35.17
27.05
27.02
21.88
13.26
7.34
7.32
-1.24


OH
i-Bu
n-Bu
1.78
f1 (ppm)
1.00
1.01
1.10
1.87
0.91
1.07
1.77
4.38
5.68
3.22

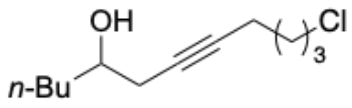

OH
i-Bu
n-Bu
82.05
77.19
76.98
76.92
76.77
70.21
35.90
28.14
27.92
27.78
27.73
22.62
21.92
13.97
f1 (ppm)

1.78



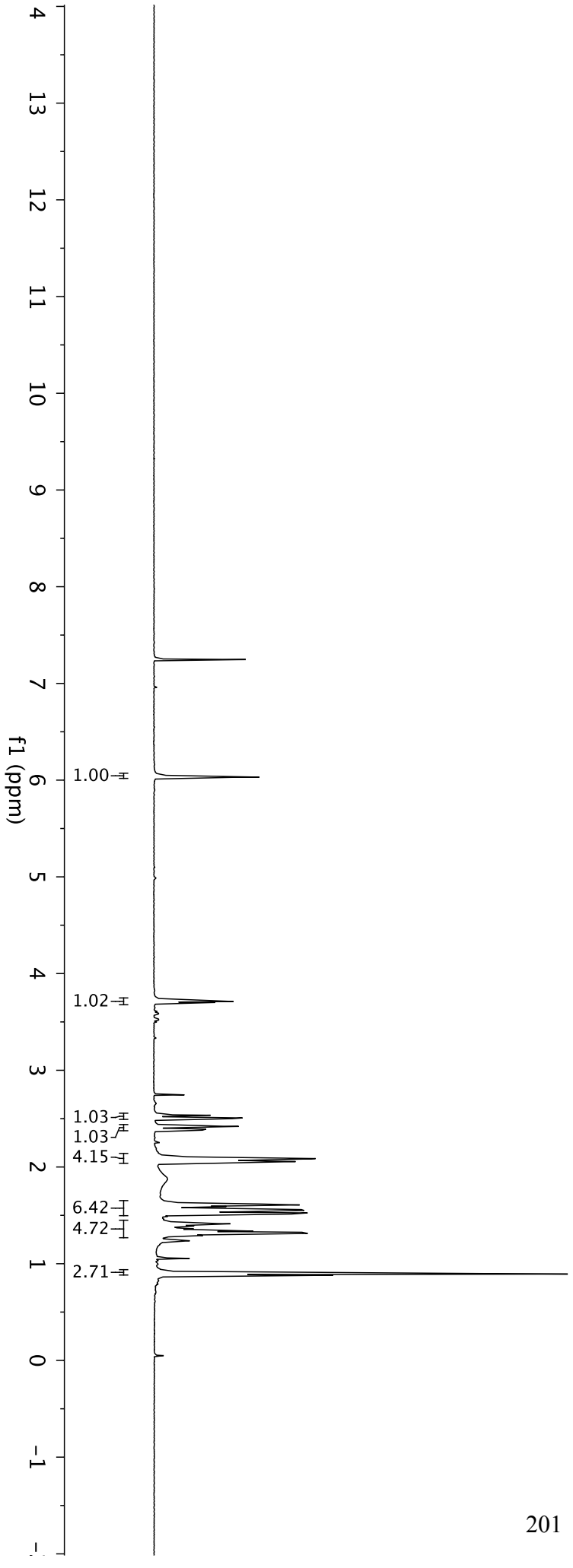


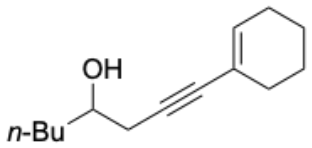
1.79


OH
Cl
3
n-Bu

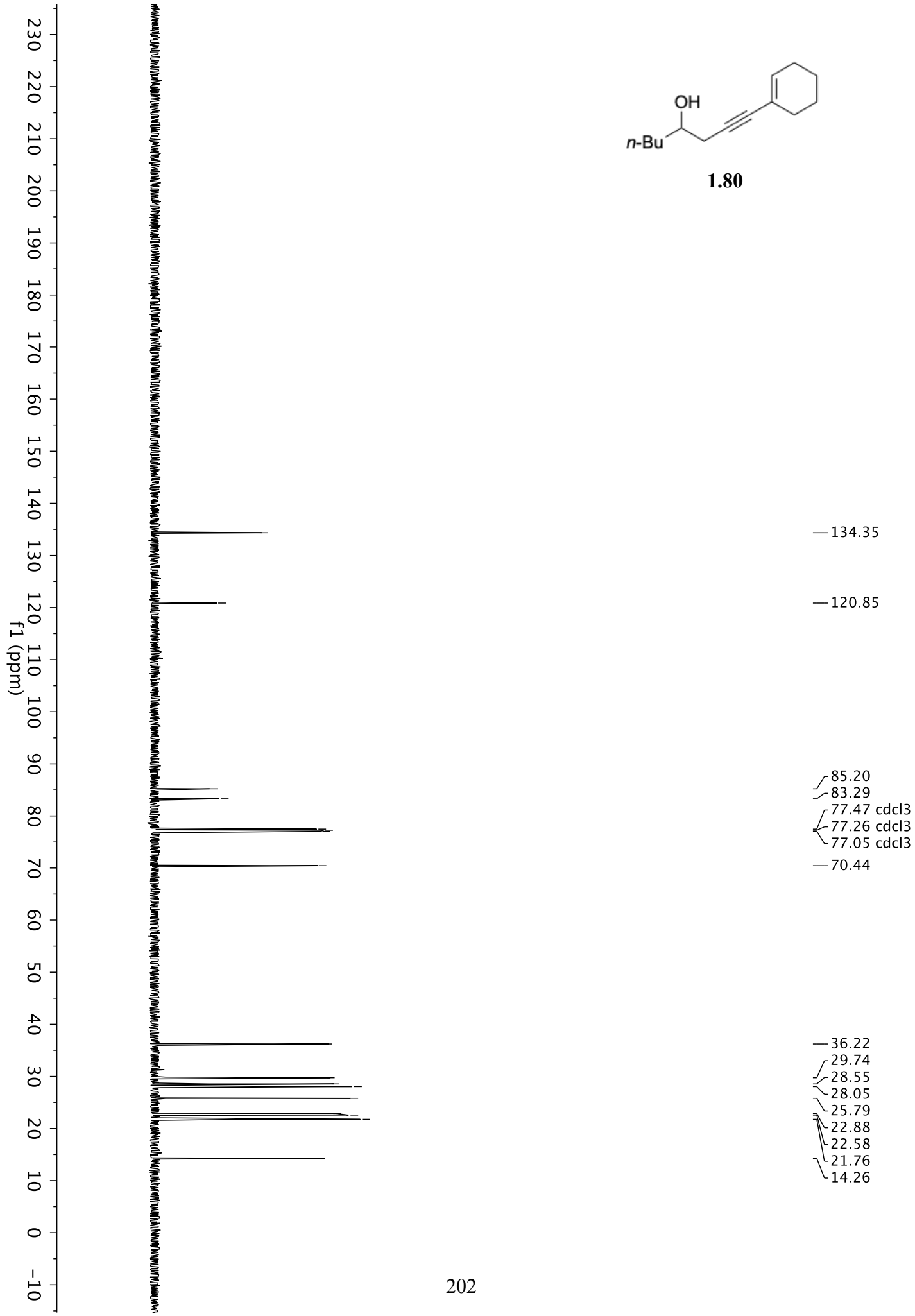
1.79

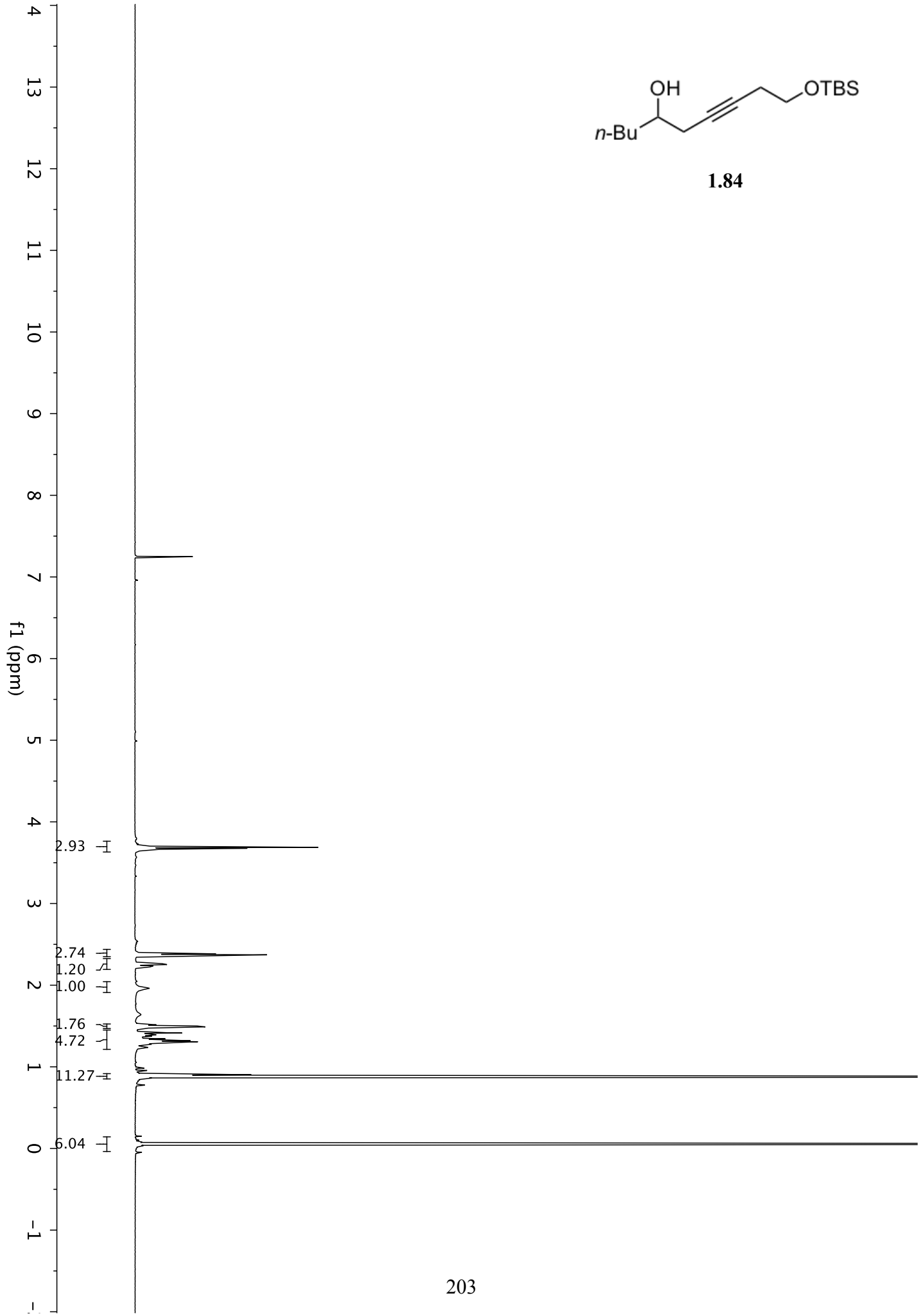
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
82.39
77.58 cdcl3
77.26 cdcl3
77.19
76.94 cdcl3
70.45
44.80
36.21
31.84
28.05
27.96
26.35
22.89
18.34
14.27

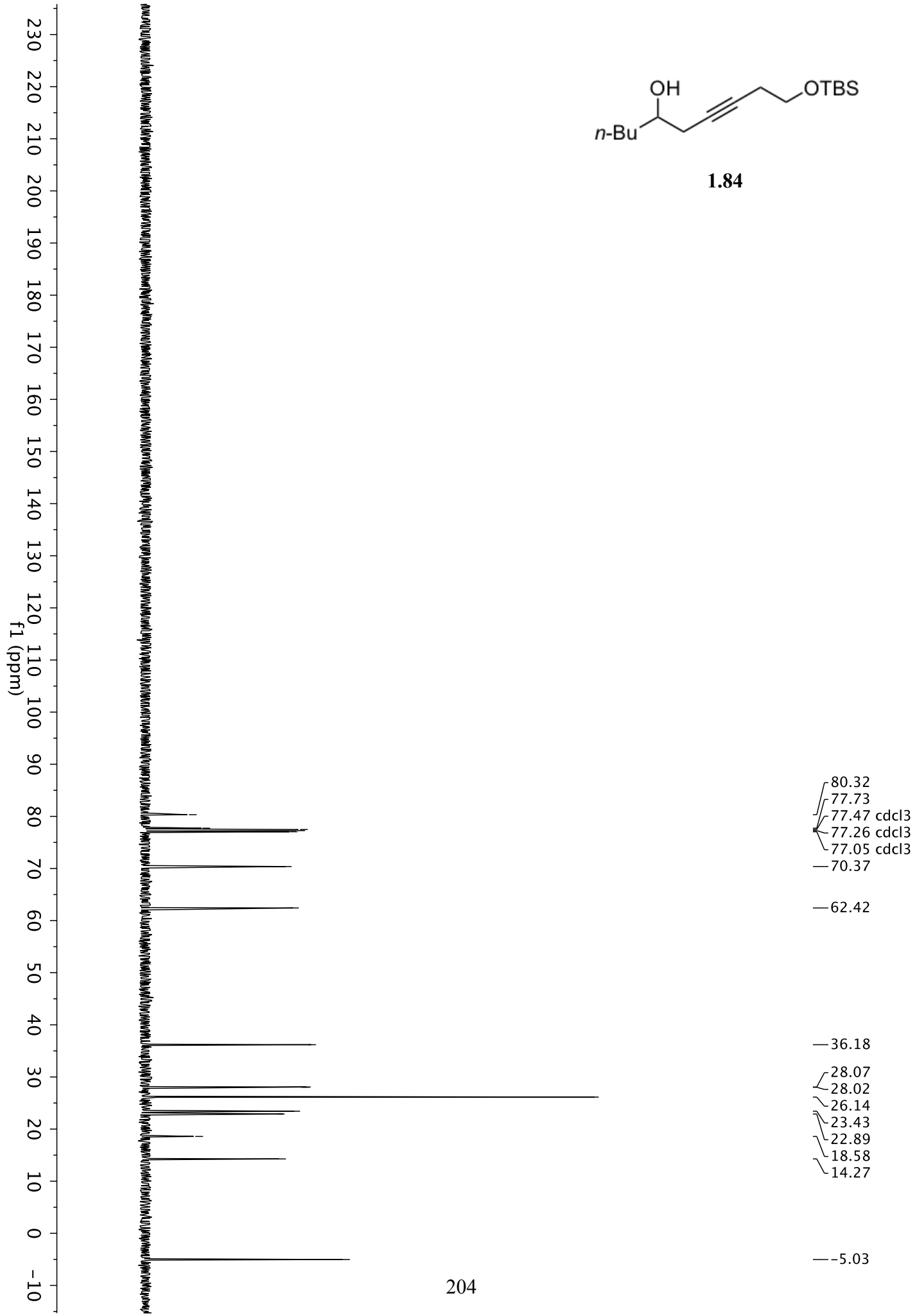


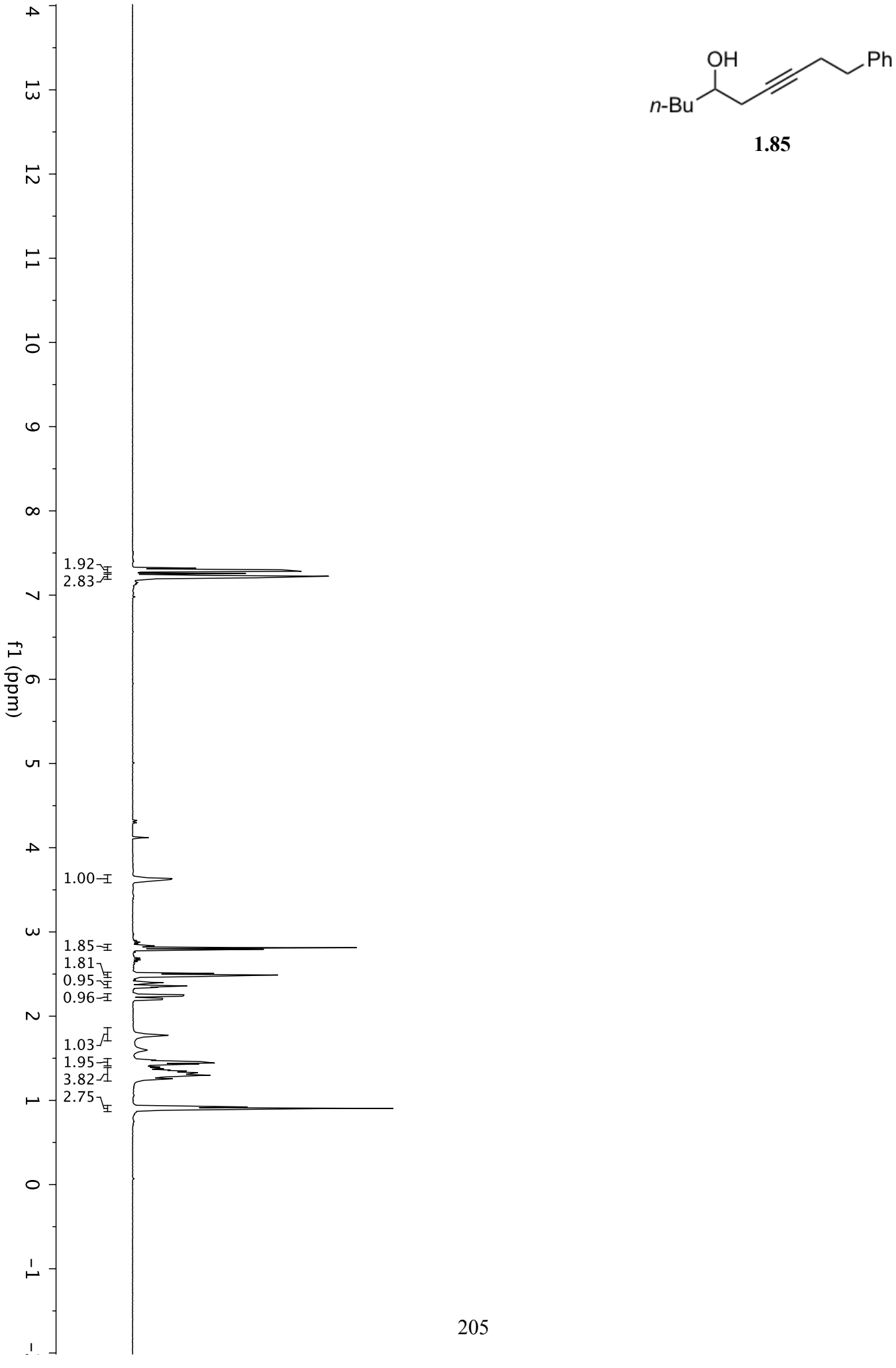


1.80

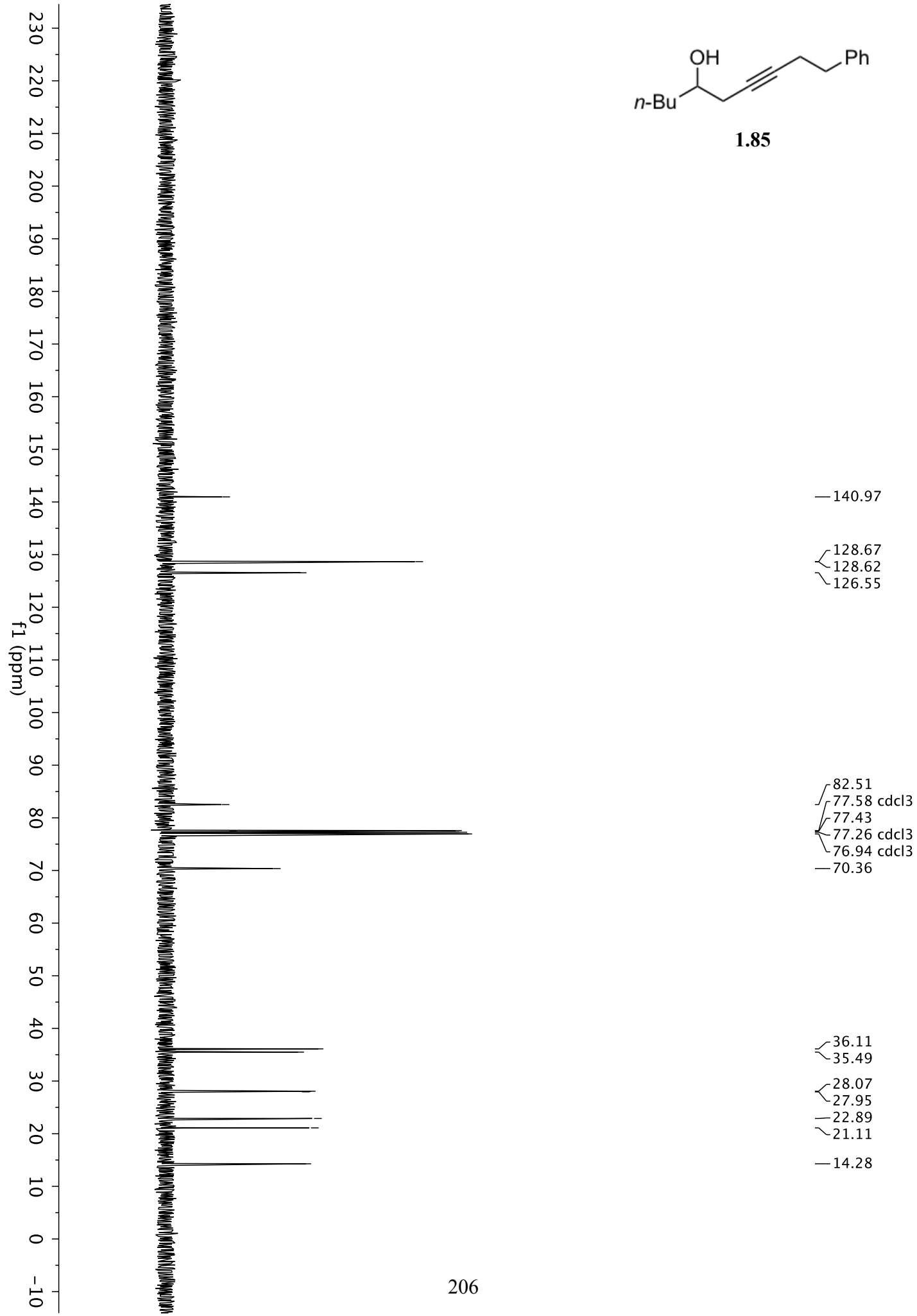

OH
n-Bu
1.80
134.35
120.85
85.20
83.29
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
70.44
36.22
29.74
28.55
28.05
25.79
22.88
22.58
21.76
14.26
f1 (ppm)

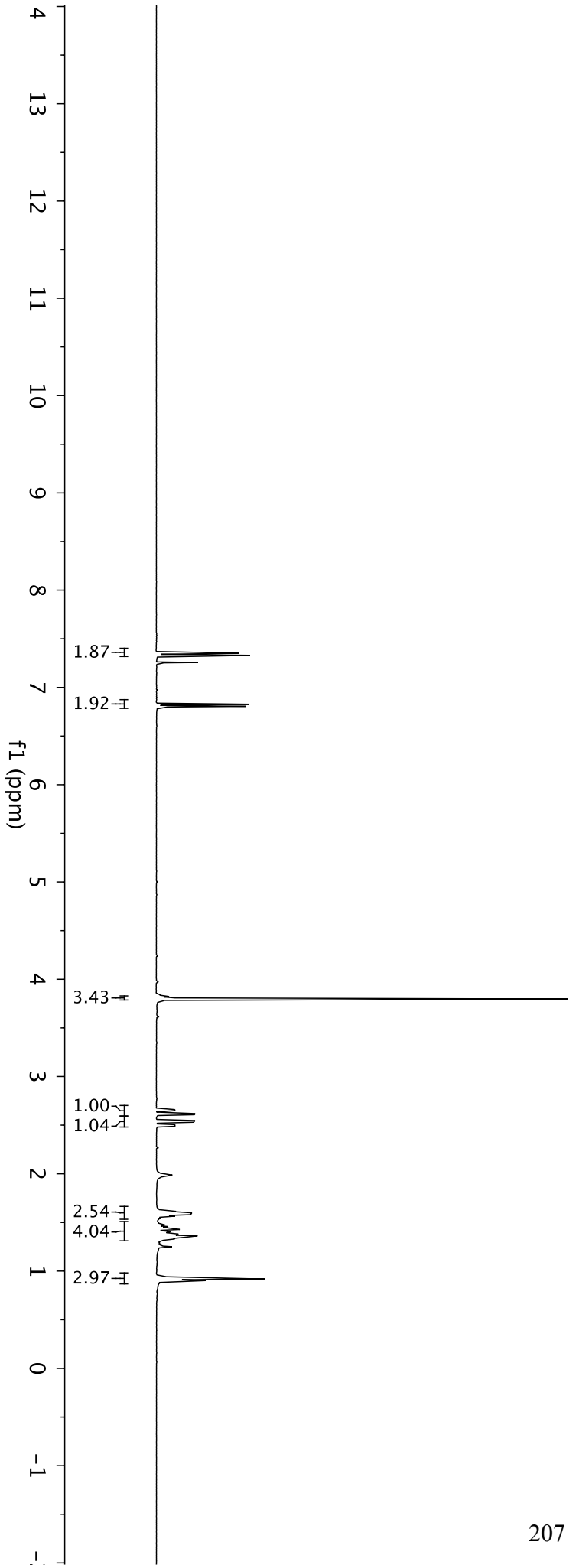

OH
OTBS
n-Bu
1.84
f1 (ppm)
2.93
2.74
1.20
1.00
1.76
4.72
11.27
6.04

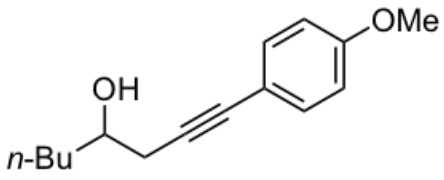

OH
OTBS
n-Bu
1.84
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
80.32
77.73
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
70.37
62.42
36.18
28.07
28.02
26.14
23.43
22.89
18.58
14.27
-5.03



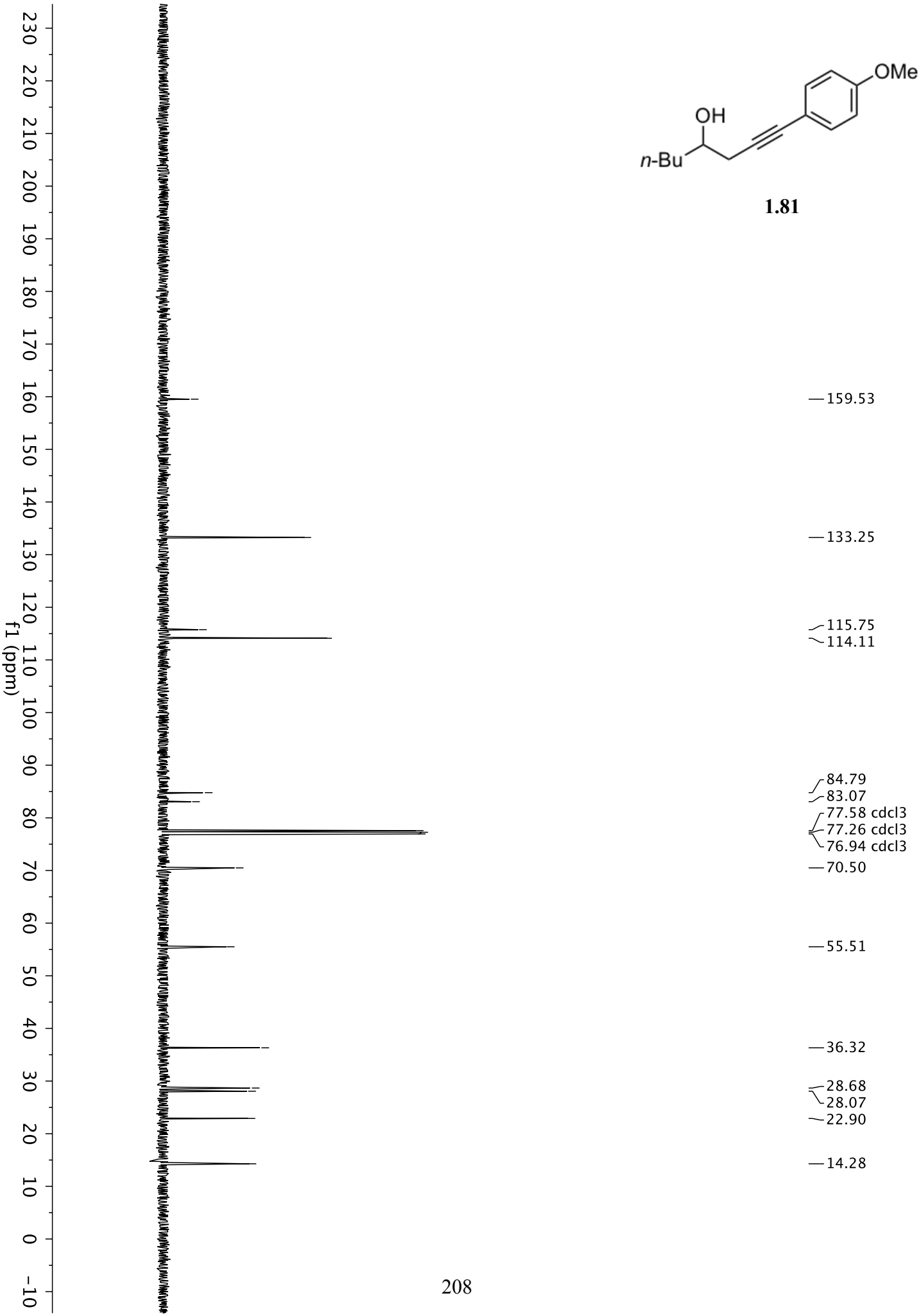
1.85

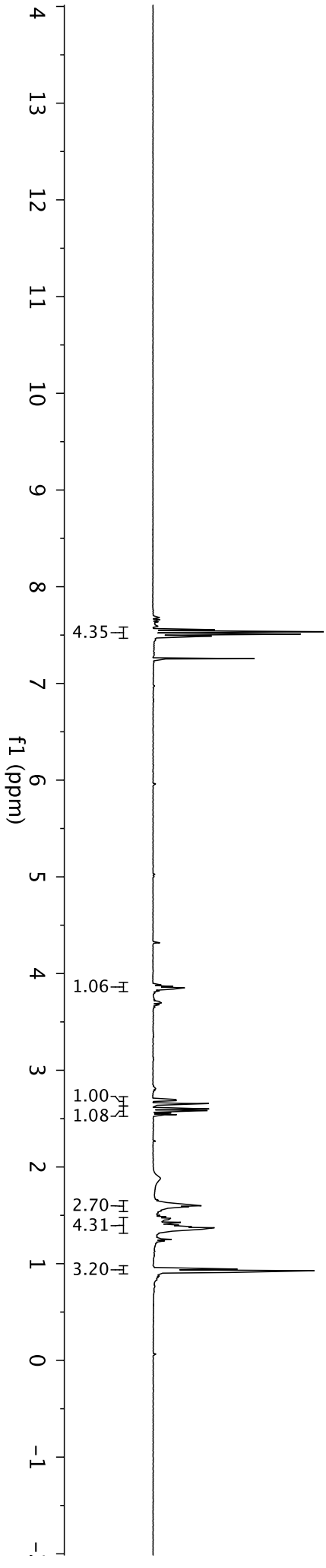

OH
Ph
n-Bu
1.85
140.97
128.67
128.62
126.55
82.51
77.58 cdcl3
77.43
77.26 cdcl3
76.94 cdcl3
70.36
36.11
35.49
28.07
27.95
22.89
21.11
14.28
f1 (ppm)

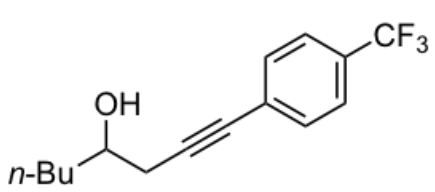




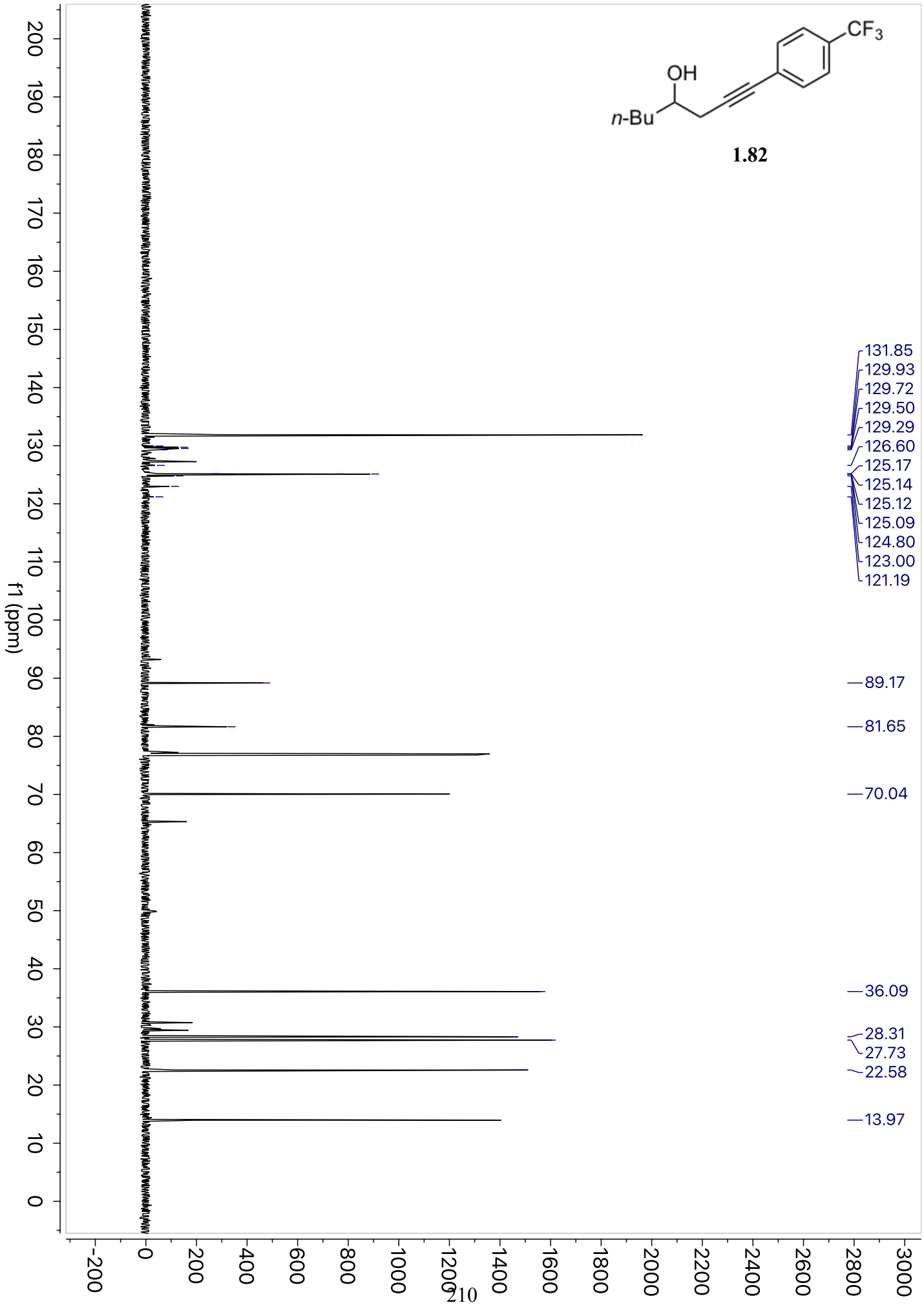
1.81

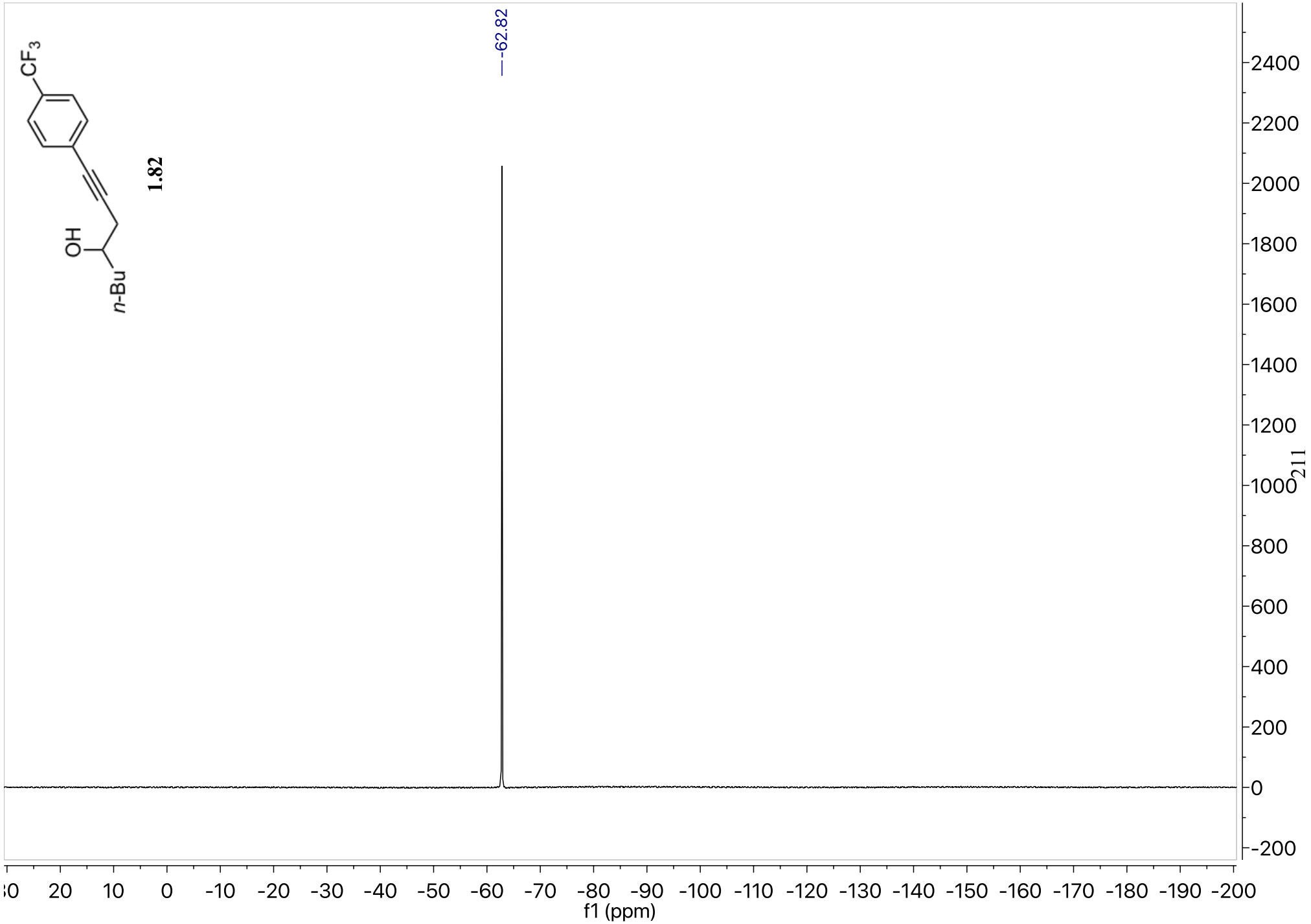

OMe
OH
n-Bu
1.81
159.53
133.25
115.75
114.11
84.79
83.07
77.58 cdcl3
77.26 cdcl3
76.94 cdcl3
70.50
55.51
36.32
28.68
28.07
22.90
14.28
f1 (ppm)

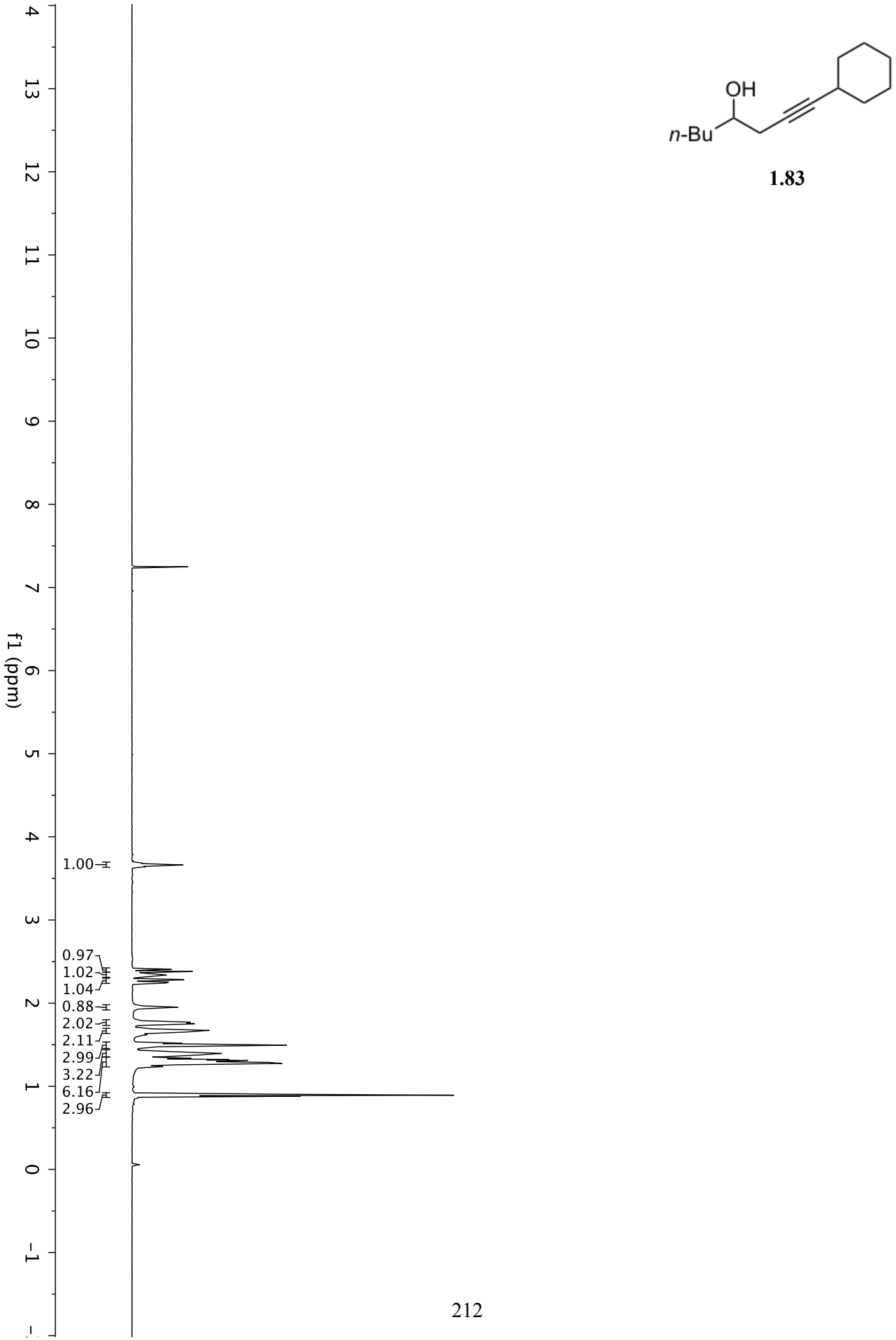




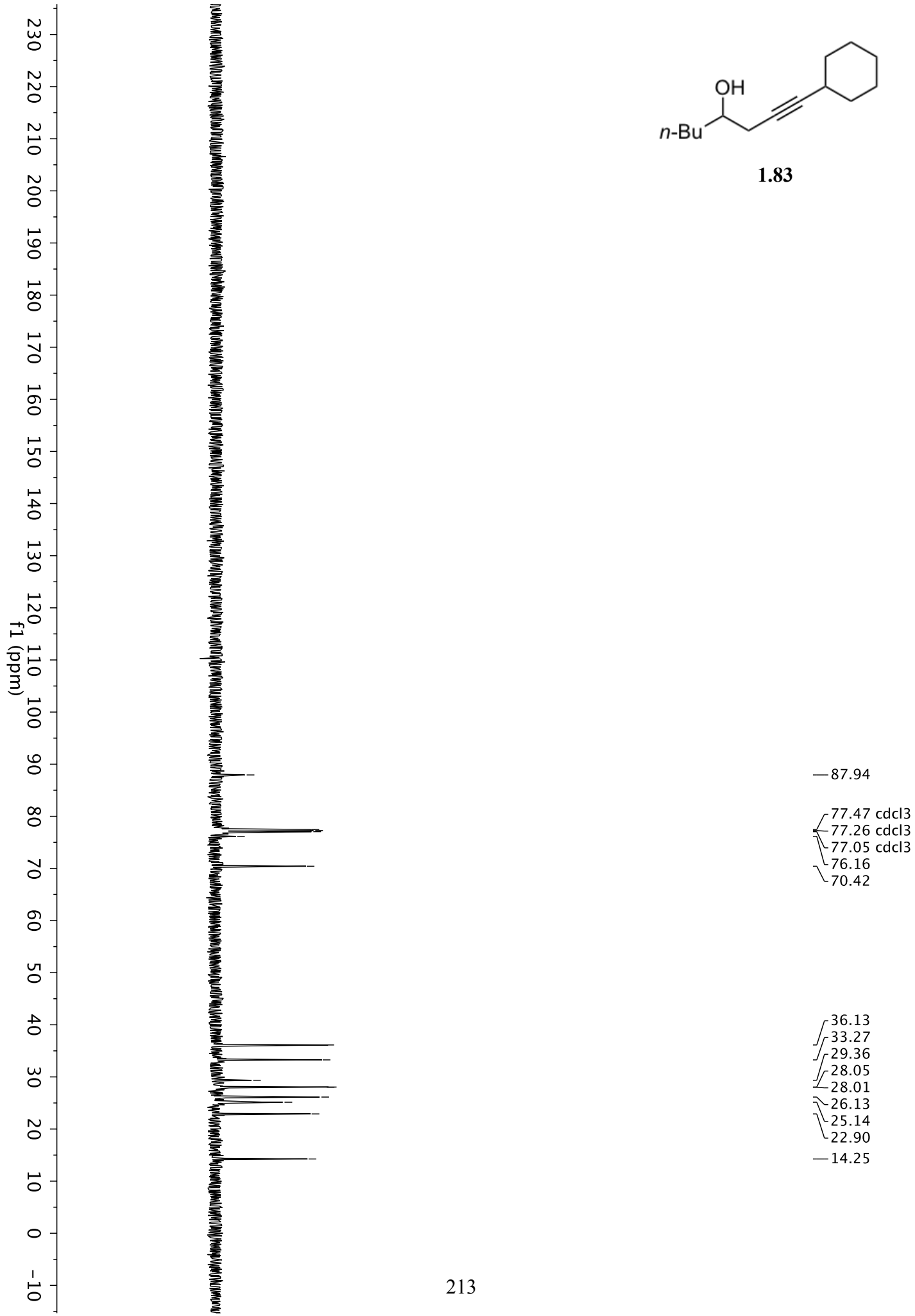
1.82

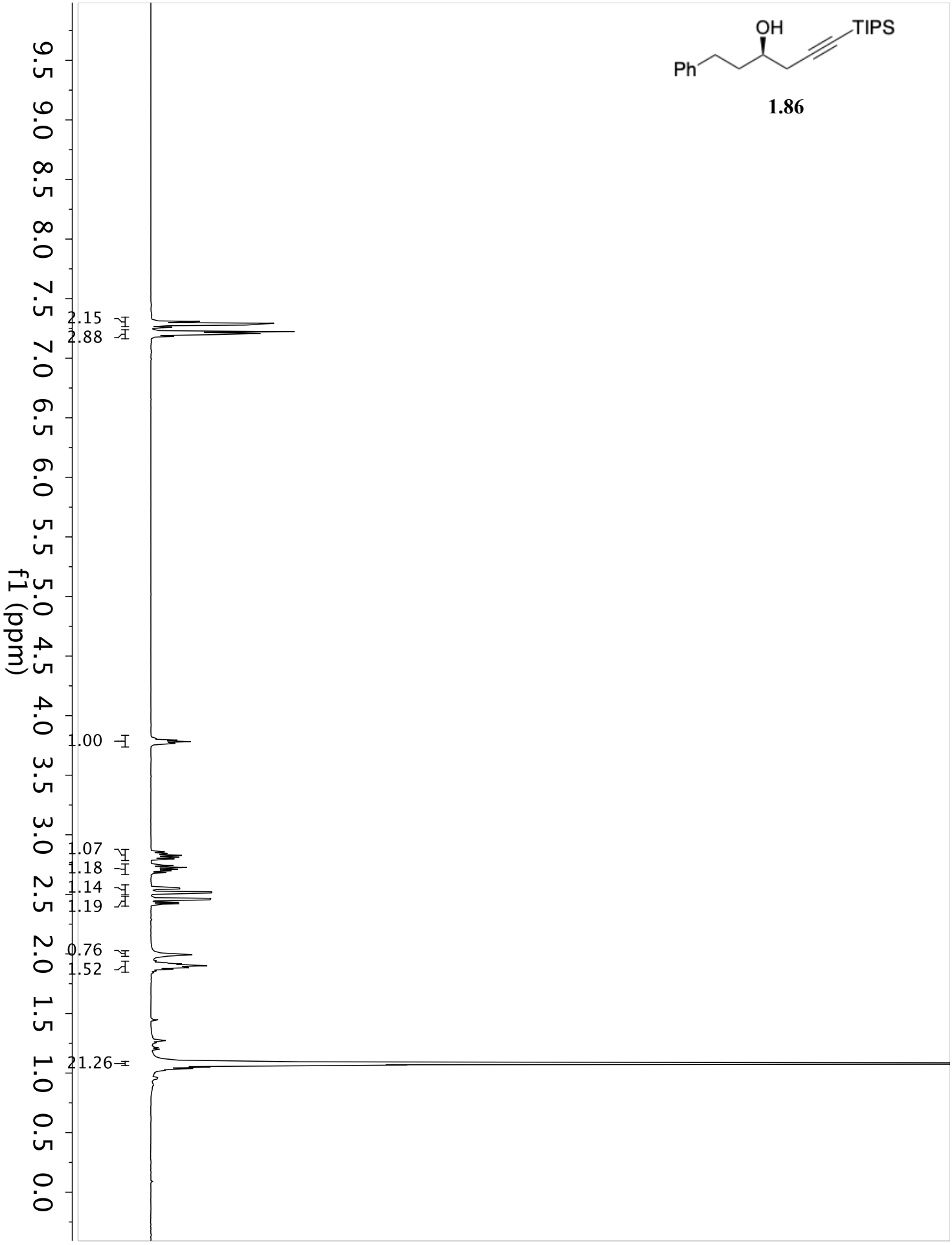

CF3
OH
n-Bu
1.82
131.85
129.93
129.72
129.50
129.29
126.60
125.17
125.14
125.12
125.09
124.80
123.00
121.19
89.17
81.65
70.04
36.09
28.31
27.73
22.58
13.97
f1 (ppm)

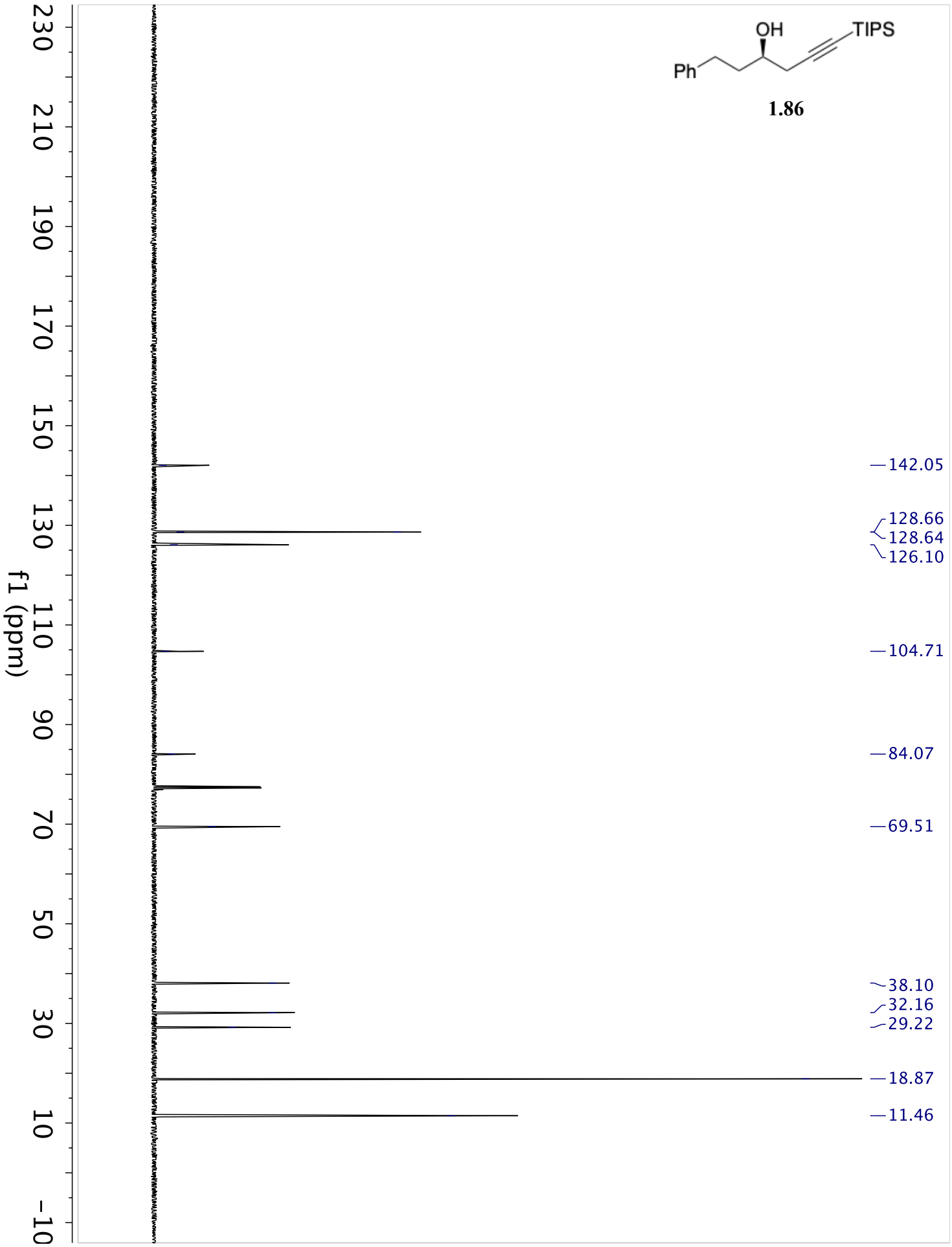

-62.82
CF3
OH
n-Bu
1.82
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
211
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

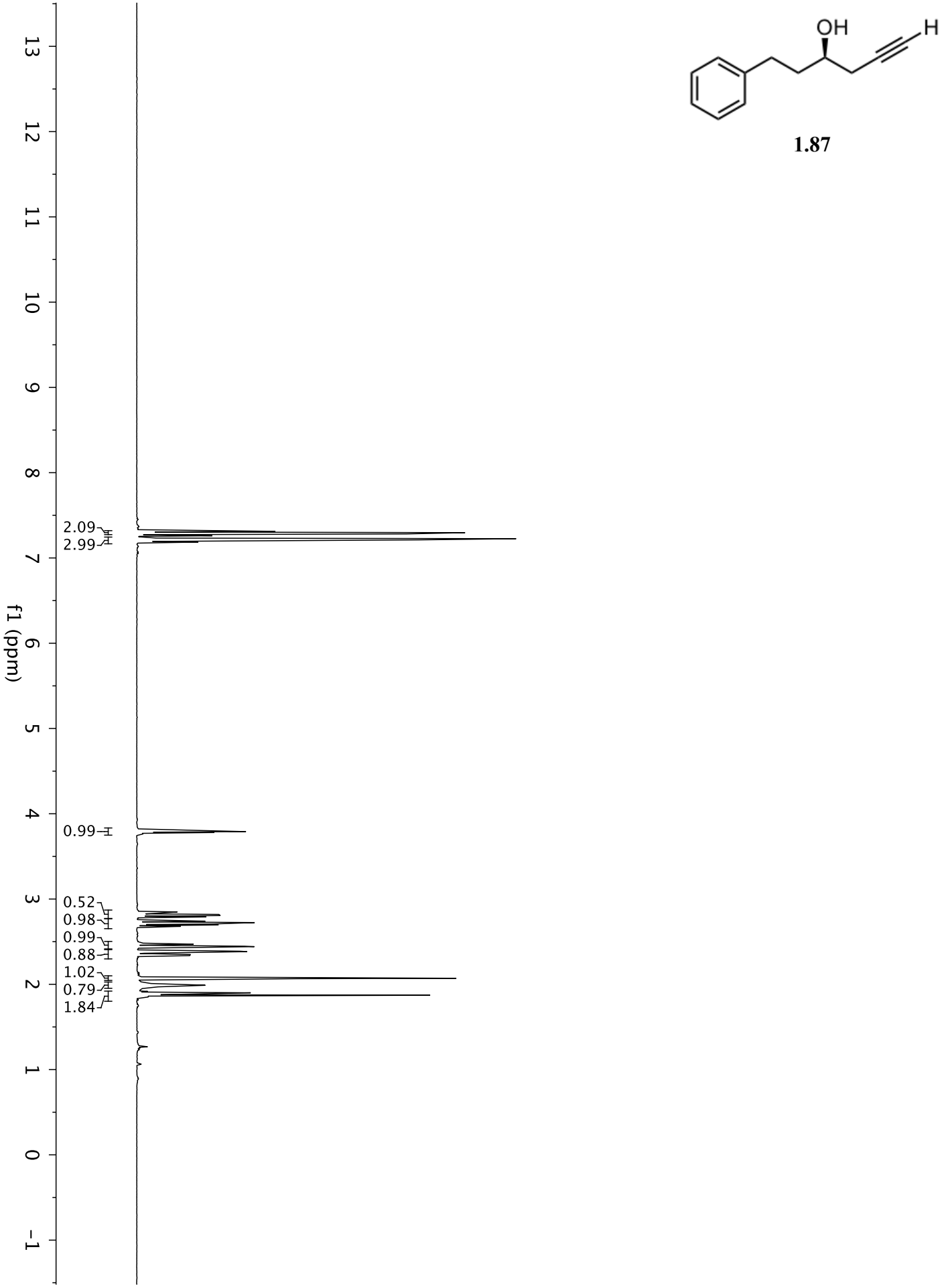


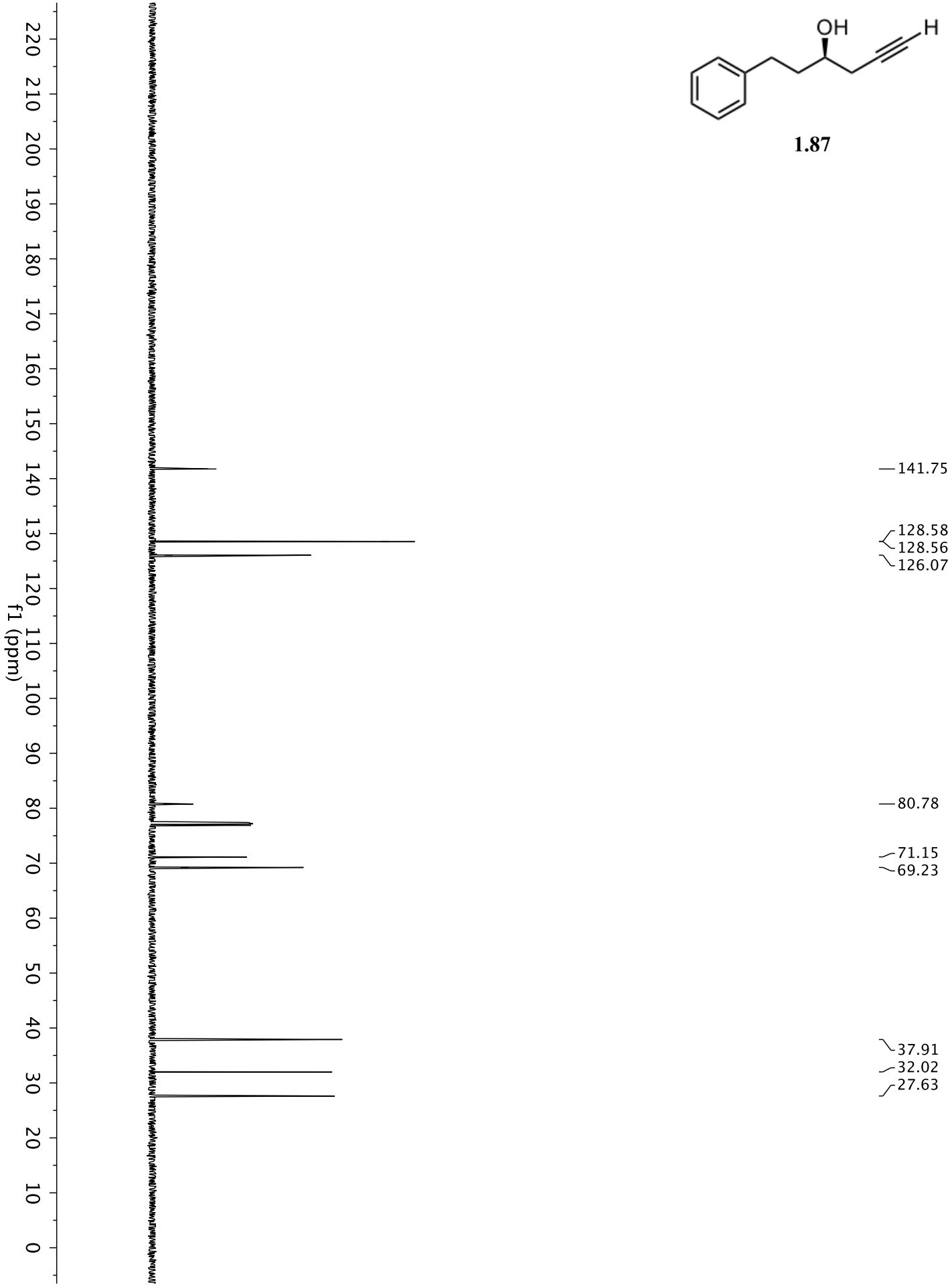
1.83

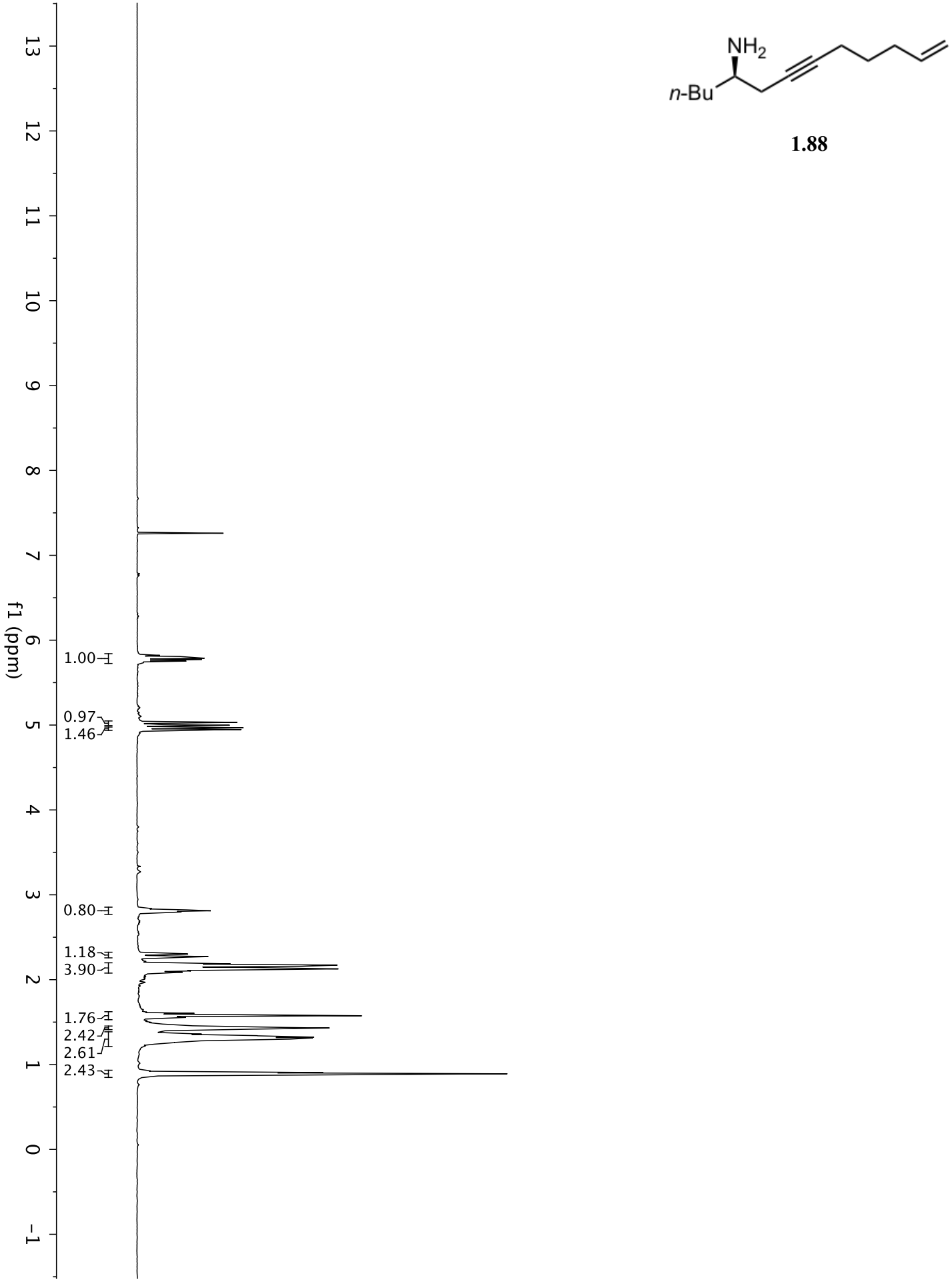

OH
n-Bu
1.83
87.94
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
76.16
70.42
36.13
33.27
29.36
28.05
28.01
26.13
25.14
22.90
14.25
f1 (ppm)


OH
TIPS
Ph
1.86
2.15
2.88
1.00
1.07
1.18
1.14
1.19
0.76
1.52
21.26
f1 (ppm)
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

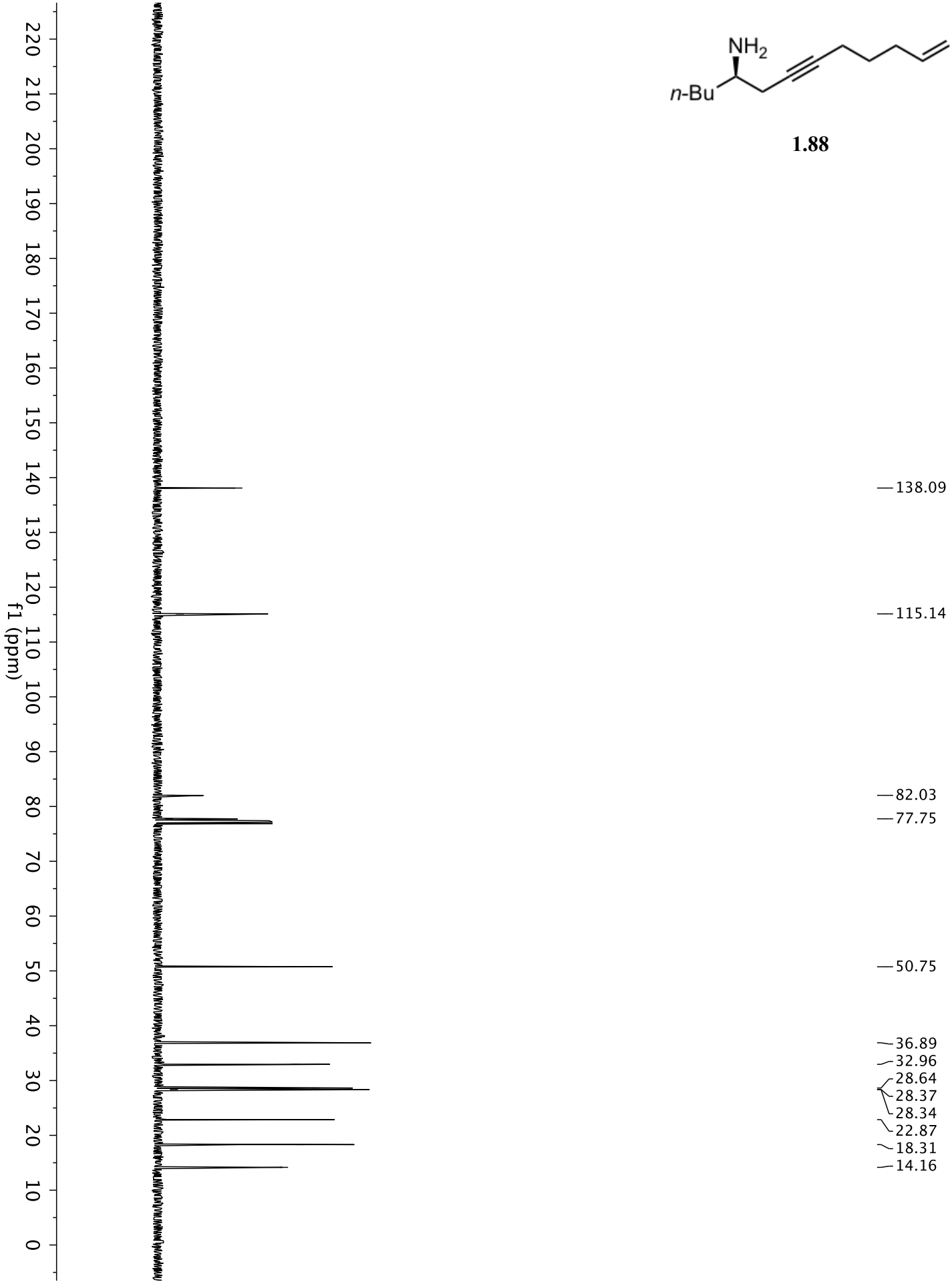

OH
TIPS
Ph
1.86
142.05
128.66
128.64
126.10
104.71
84.07
69.51
38.10
32.16
29.22
18.87
11.46
f1 (ppm)
230
210
190
170
150
130
110
90
70
50
30
10
-10


OH
H
1.87
f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
2.09
2.99
0.99
0.52
0.98
0.99
0.88
1.02
0.79
1.84

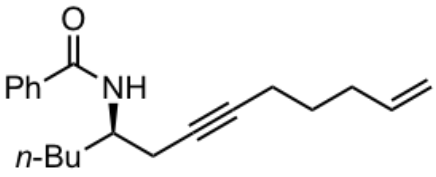

OH
H
1.87
141.75
128.58
128.56
126.07
80.78
71.15
69.23
37.91
32.02
27.63
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


NH2
n-Bu
f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
1.00
0.97
1.46
0.80
1.18
3.90
1.76
2.42
2.61
2.43

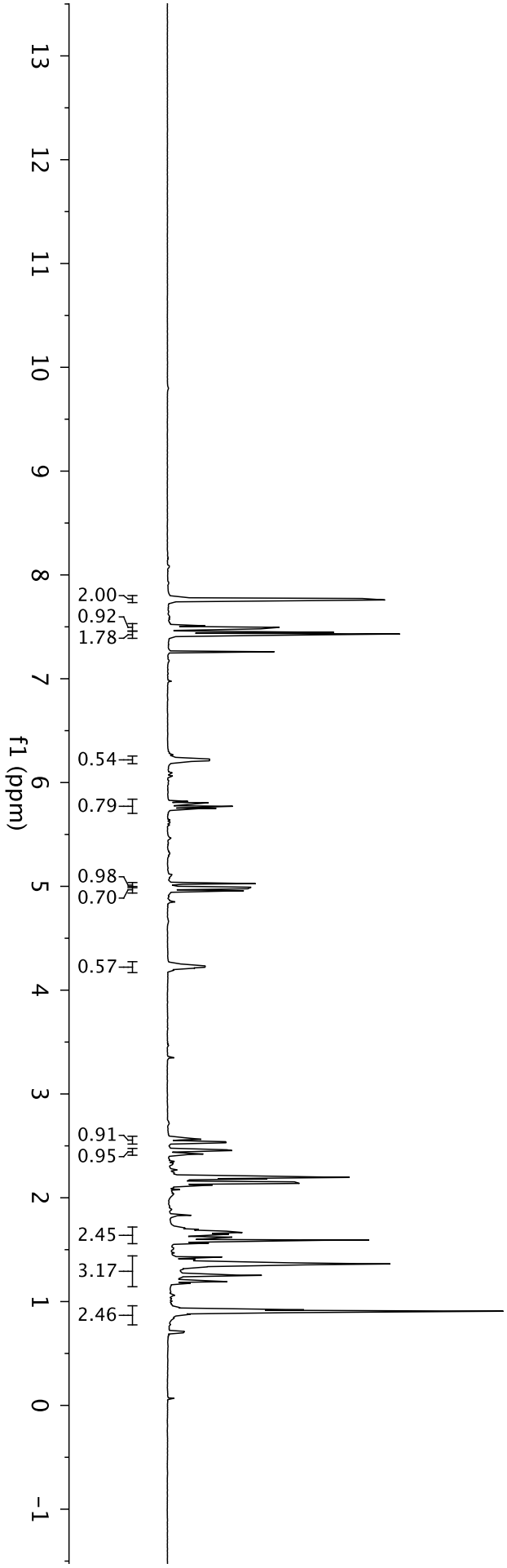
1.88

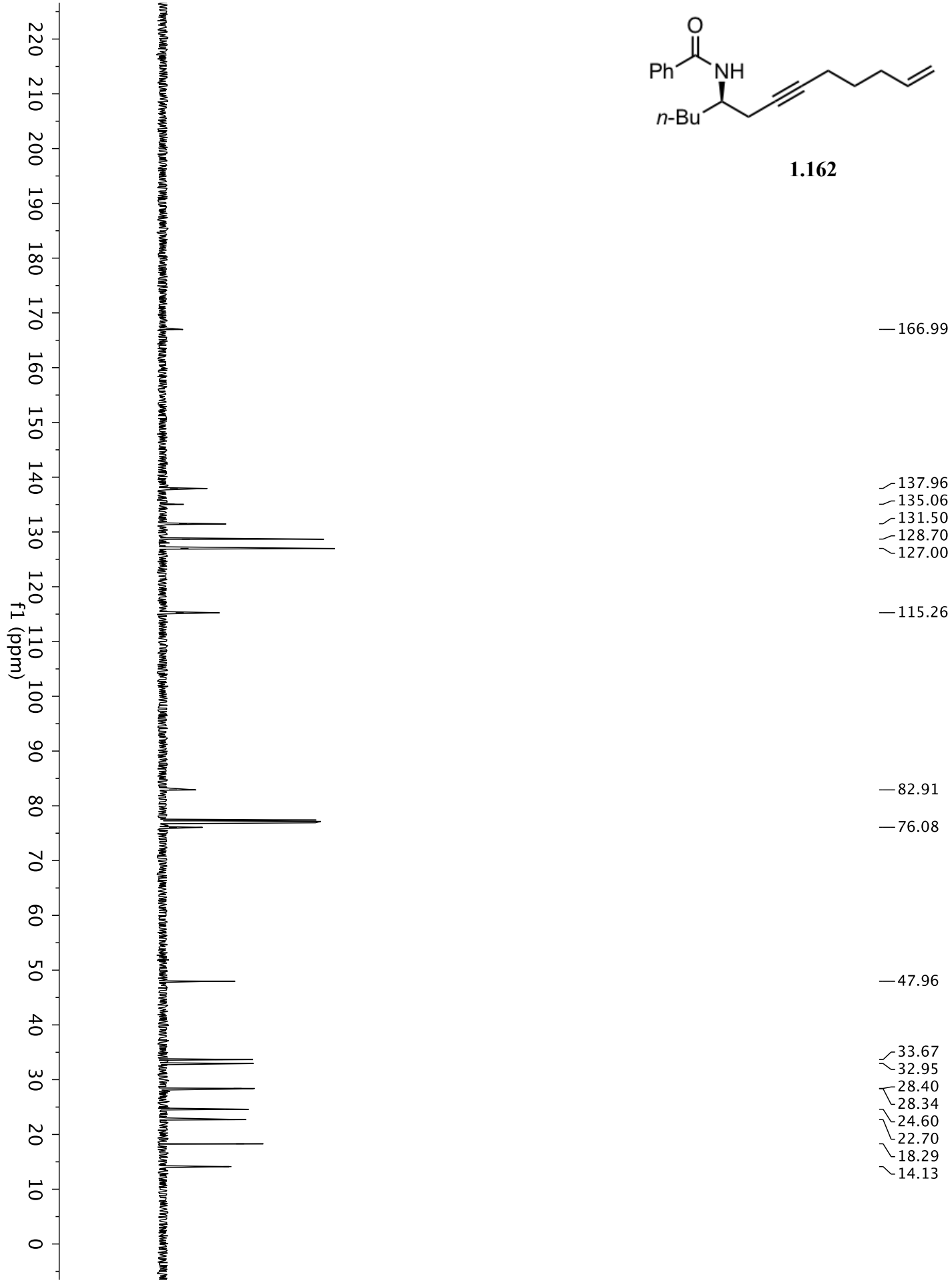

NH2
n-Bu
138.09
115.14
82.03
77.75
50.75
36.89
32.96
28.64
28.37
28.34
22.87
18.31
14.16
f1 (ppm)

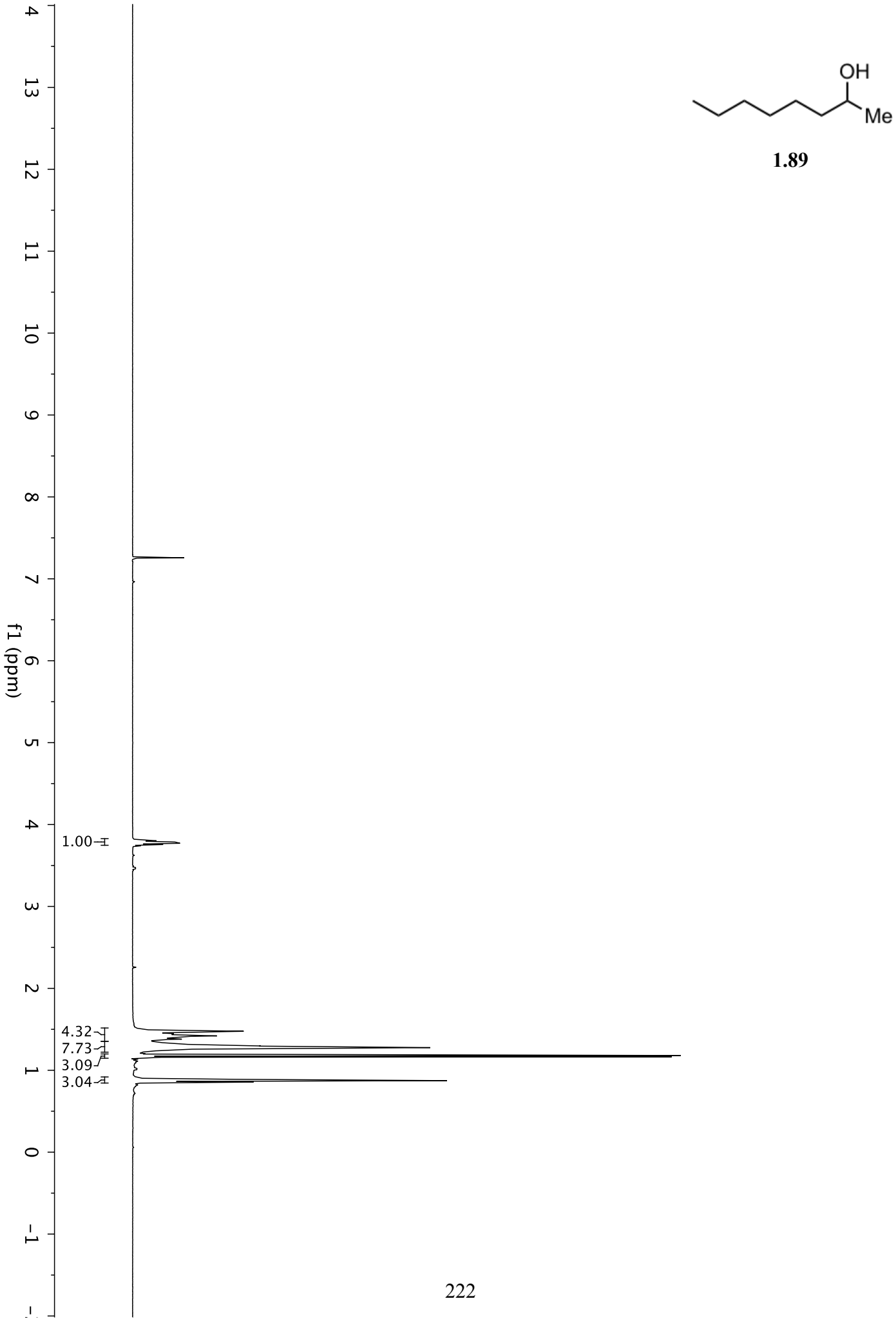
1.88


O
Ph
NH
n-Bu

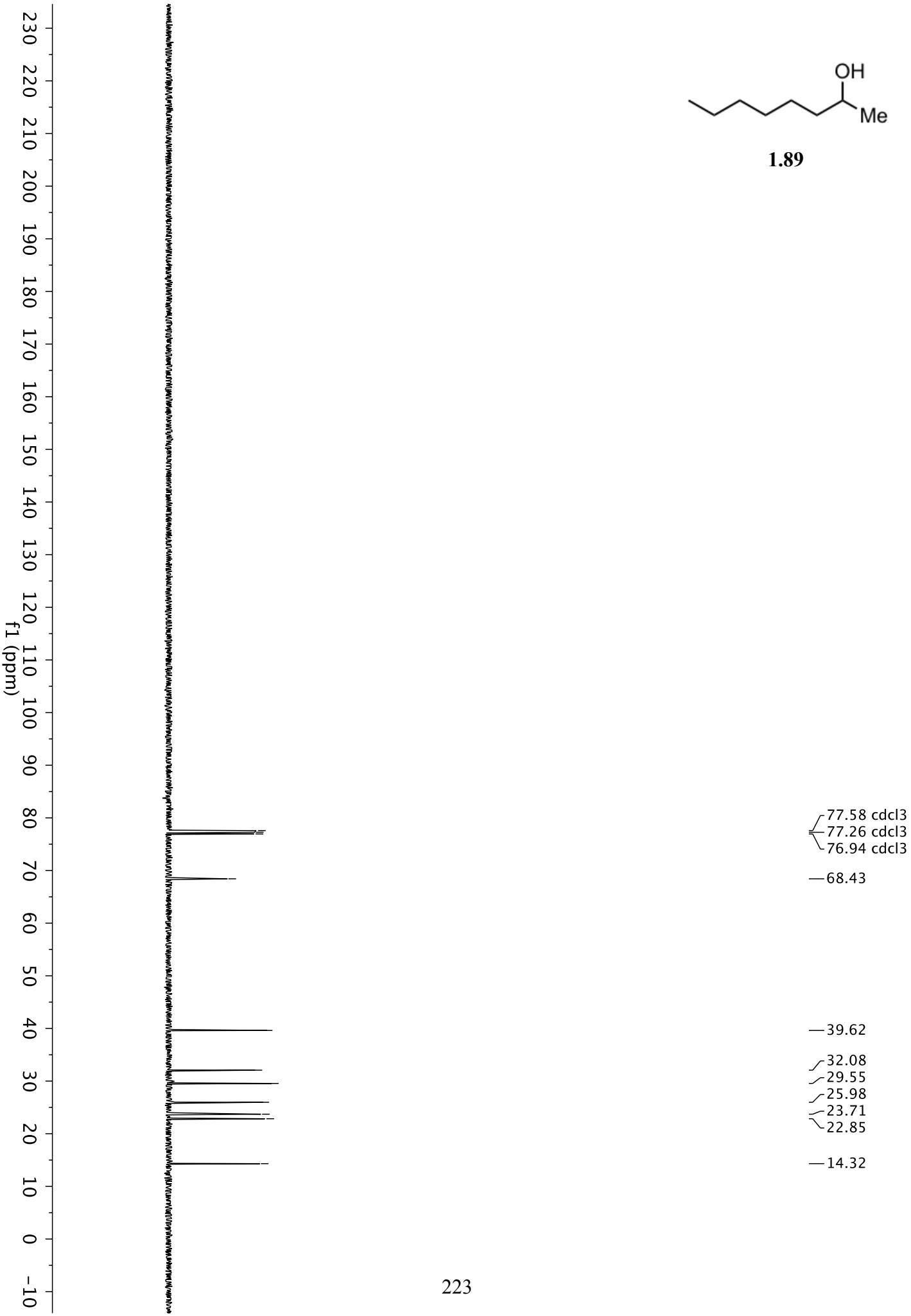
1.162

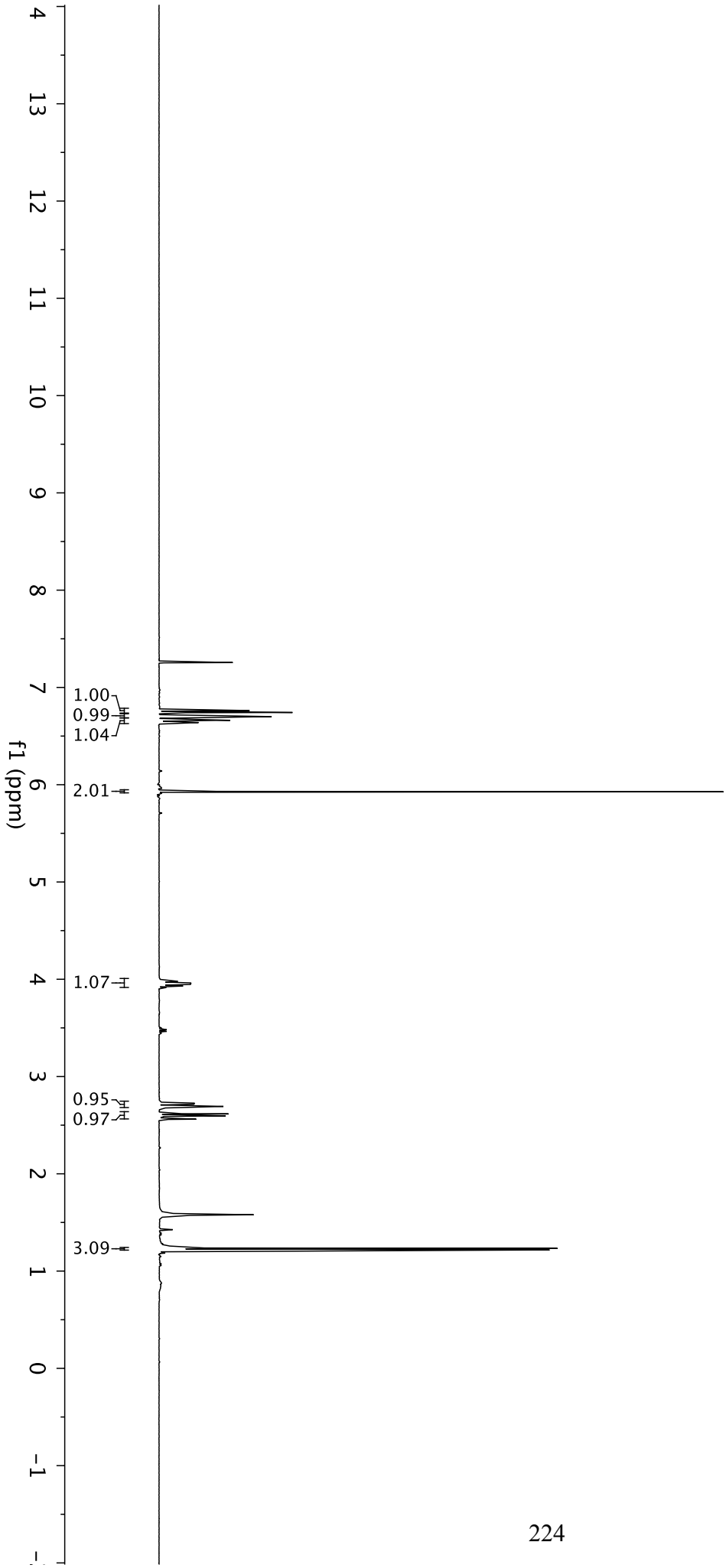

f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
2.00
0.92
1.78
0.54
0.79
0.98
0.70
0.57
0.91
0.95
2.45
3.17
2.46

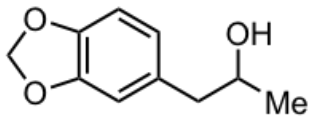

O
Ph
NH
n-Bu
1.162
166.99
137.96
135.06
131.50
128.70
127.00
115.26
82.91
76.08
47.96
33.67
32.95
28.40
28.34
24.60
22.70
18.29
14.13
f1 (ppm)



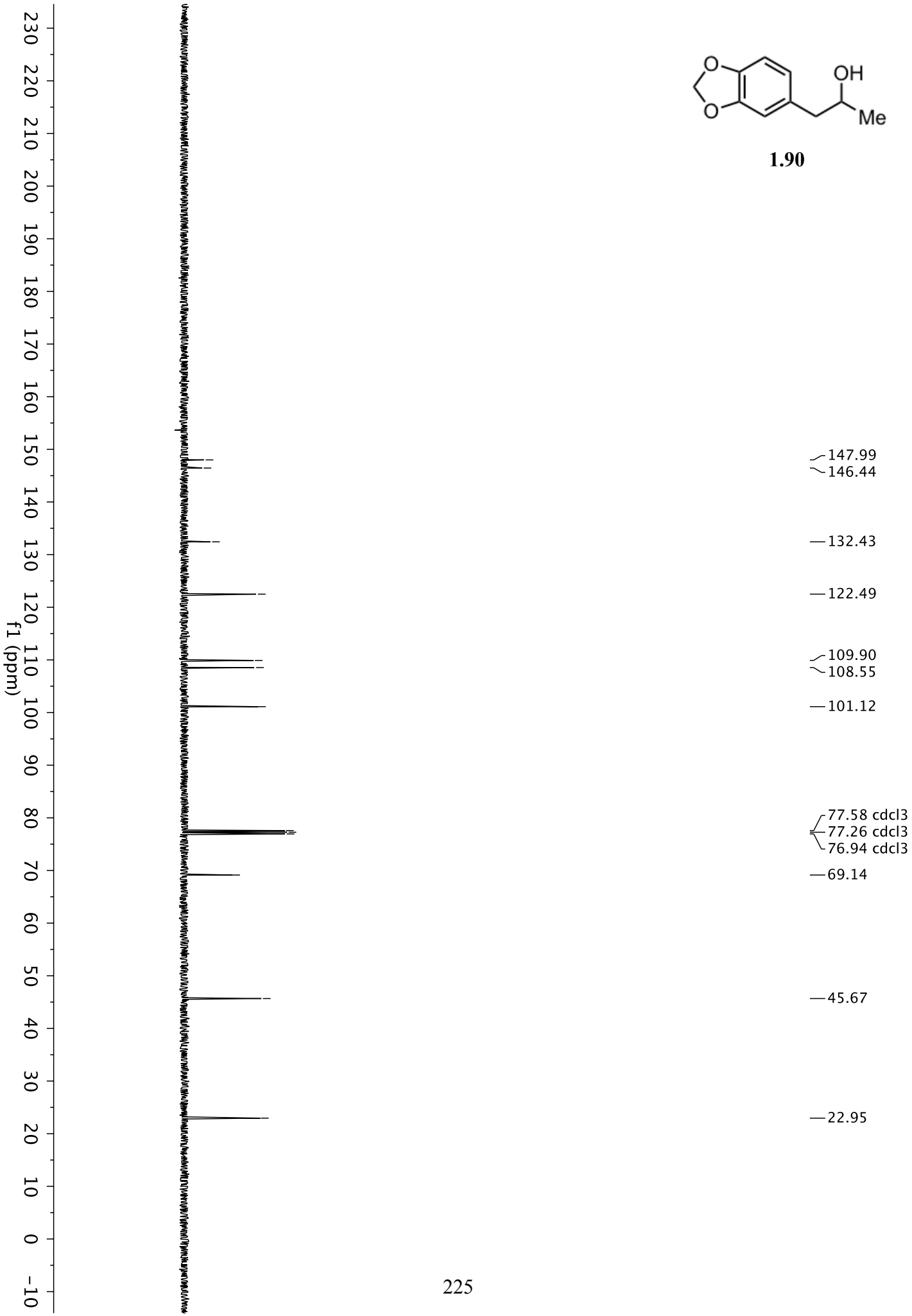
1.89


OH
Me
1.89
77.58 cdcl3
77.26 cdcl3
76.94 cdcl3
68.43
39.62
32.08
29.55
25.98
23.71
22.85
14.32
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

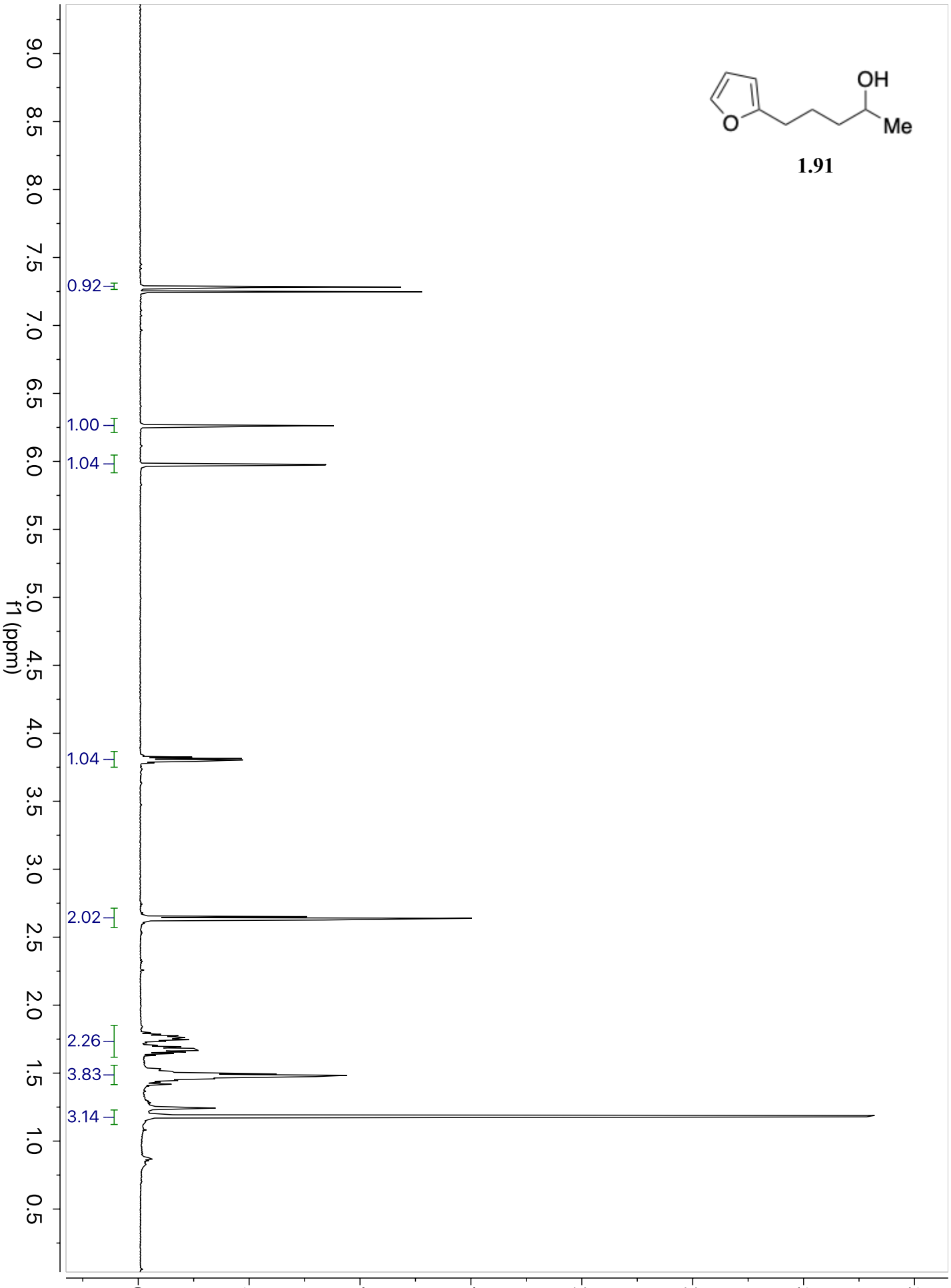


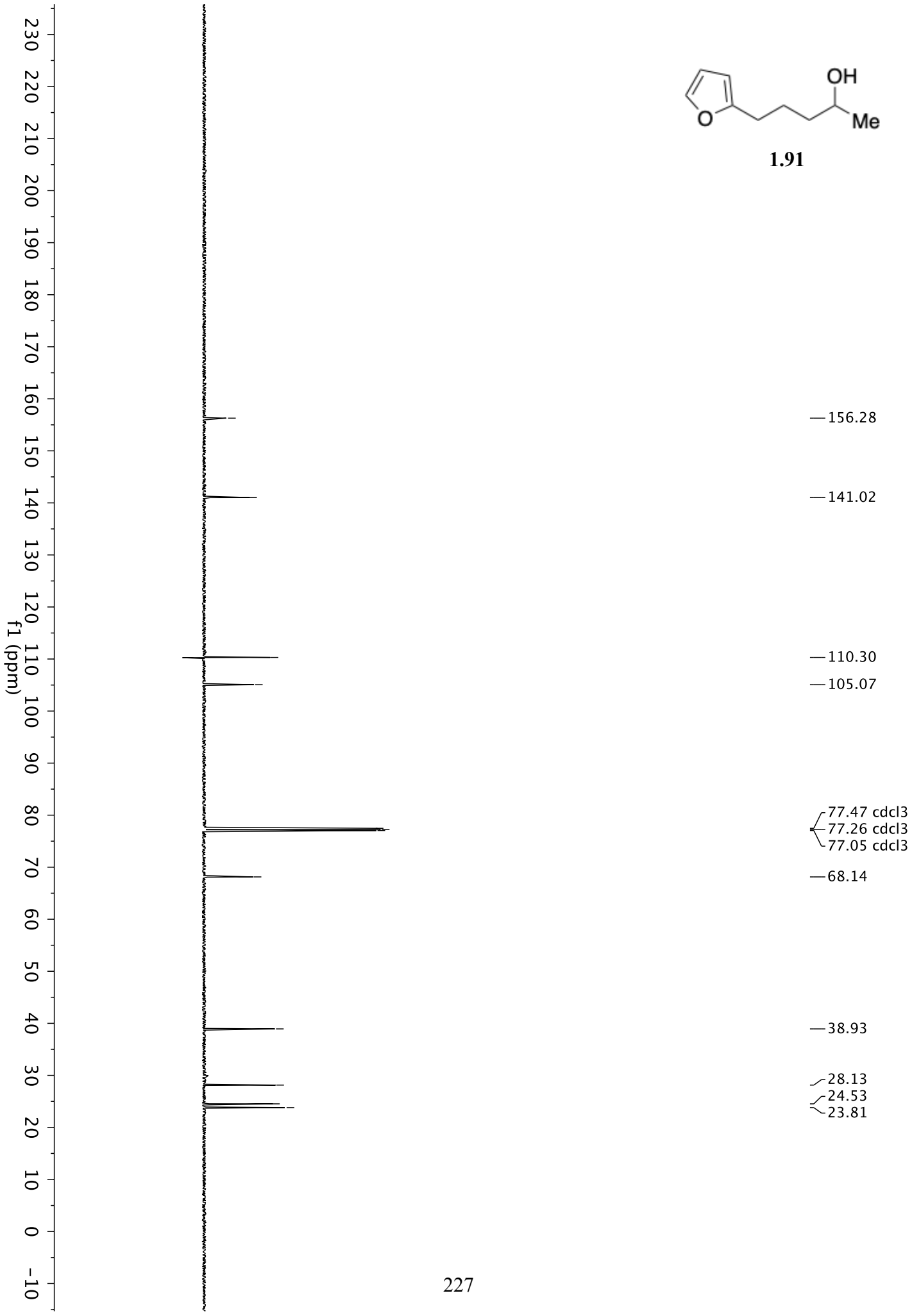


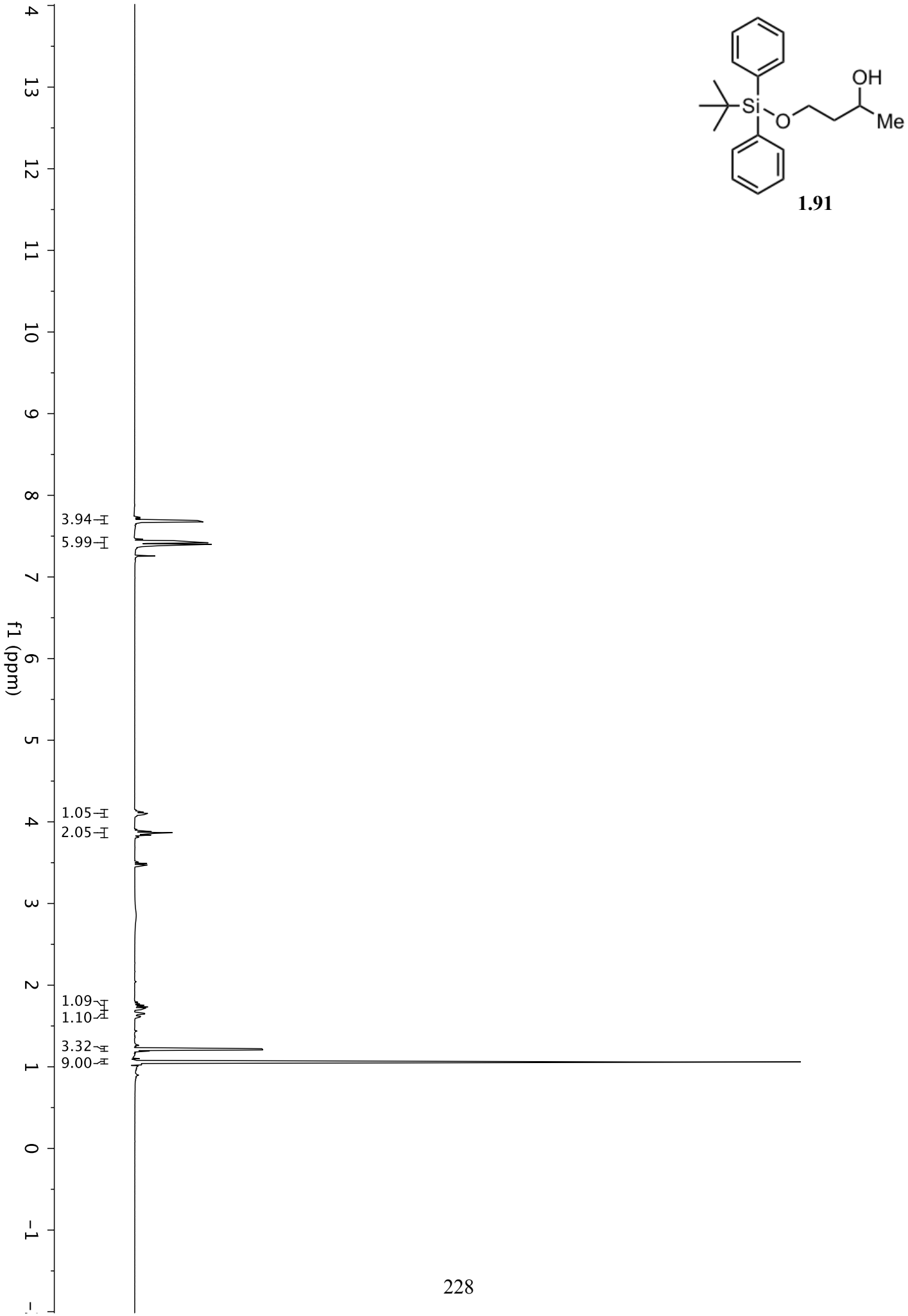
1.90


f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
147.99
146.44
132.43
122.49
109.90
108.55
101.12
77.58 cdcl3
77.26 cdcl3
76.94 cdcl3
69.14
45.67
22.95
O
O
OH
Me

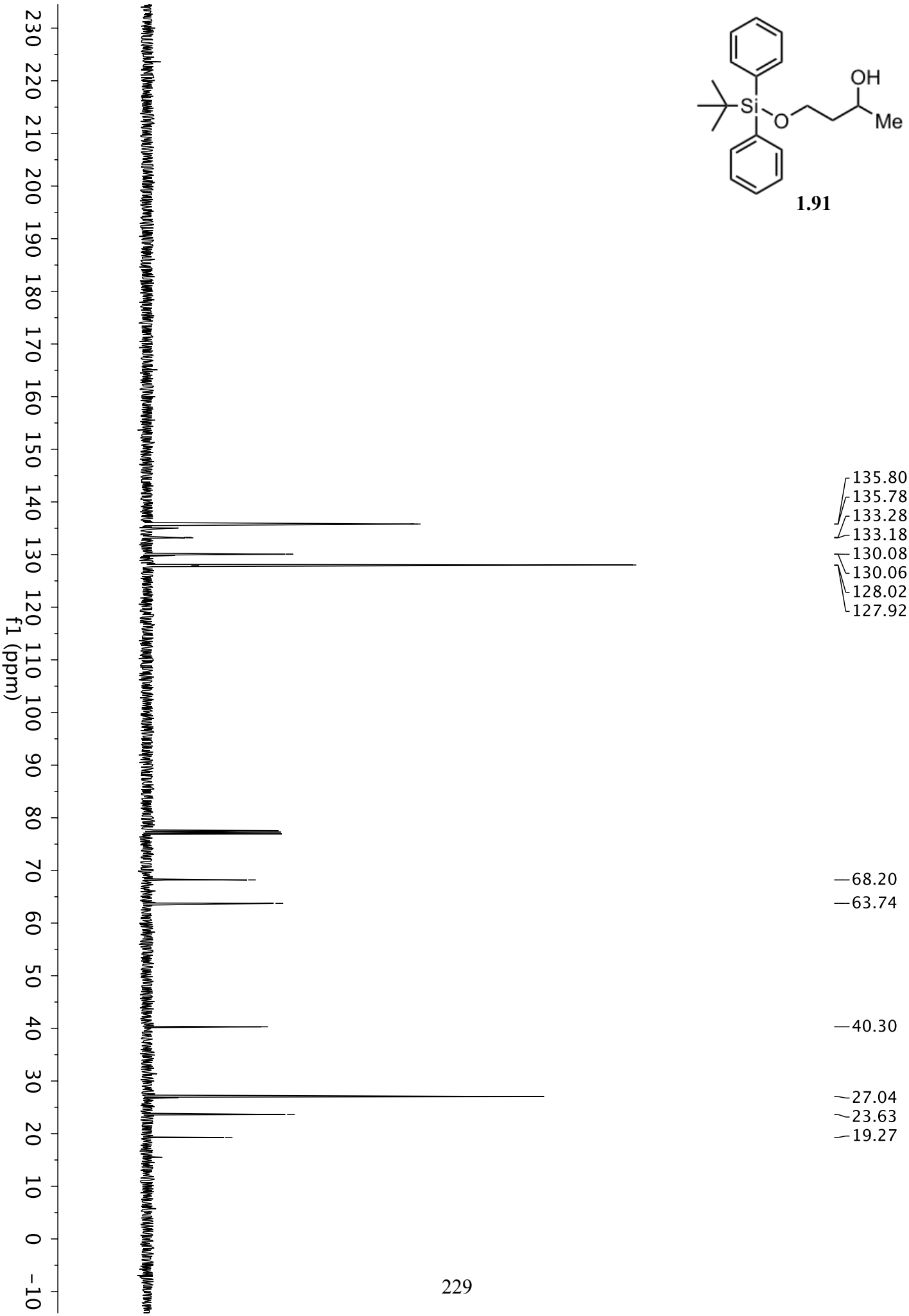
1.90

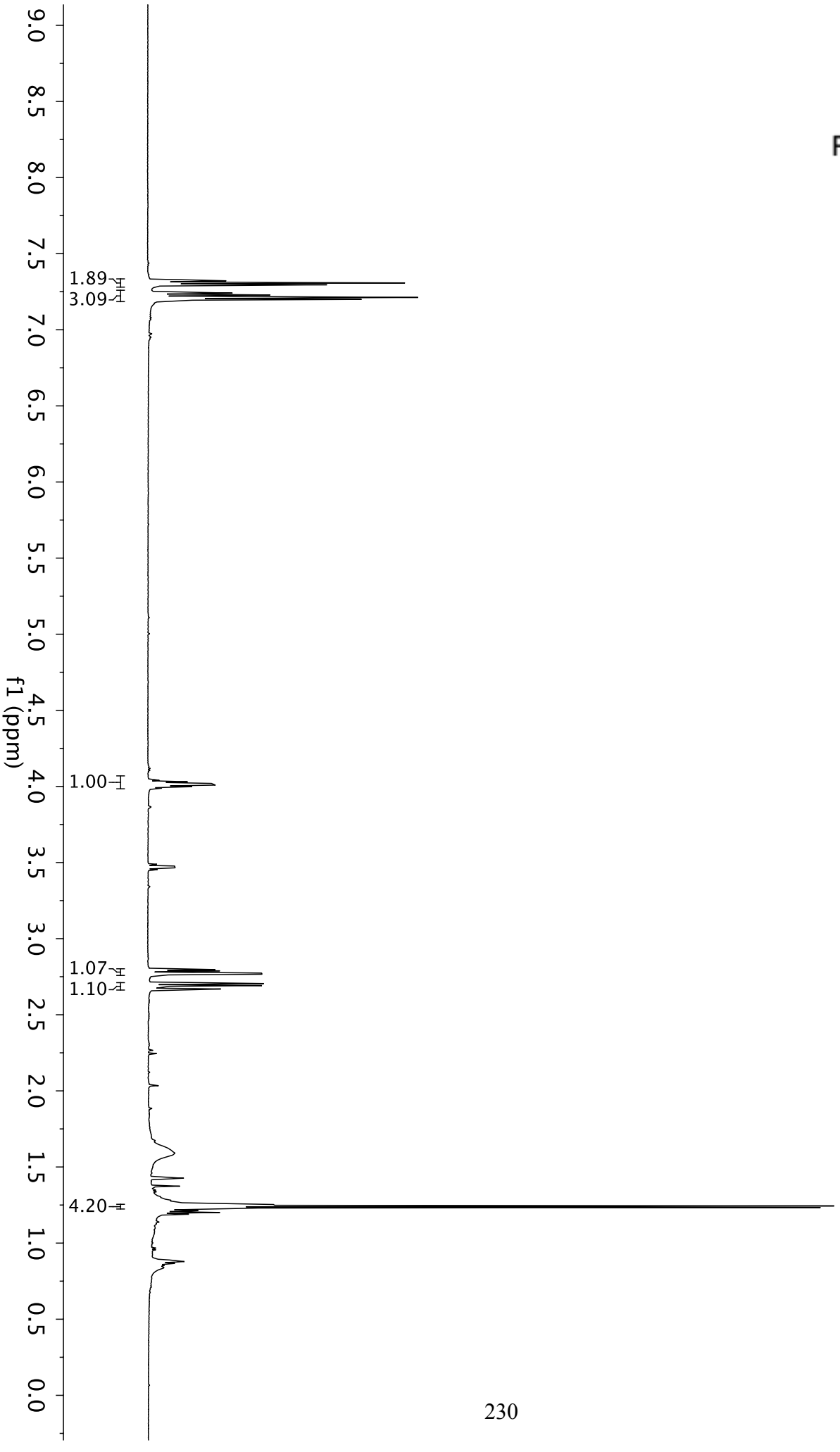

OH
O
Me
1.91
0.92
1.00
1.04
1.04
2.02
2.26
3.83
3.14
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
50
100
150
200
250
300
350

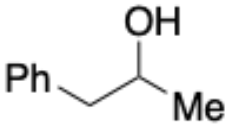

OH
O
Me
1.91
156.28
141.02
110.30
105.07
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
68.14
38.93
28.13
24.53
23.81
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



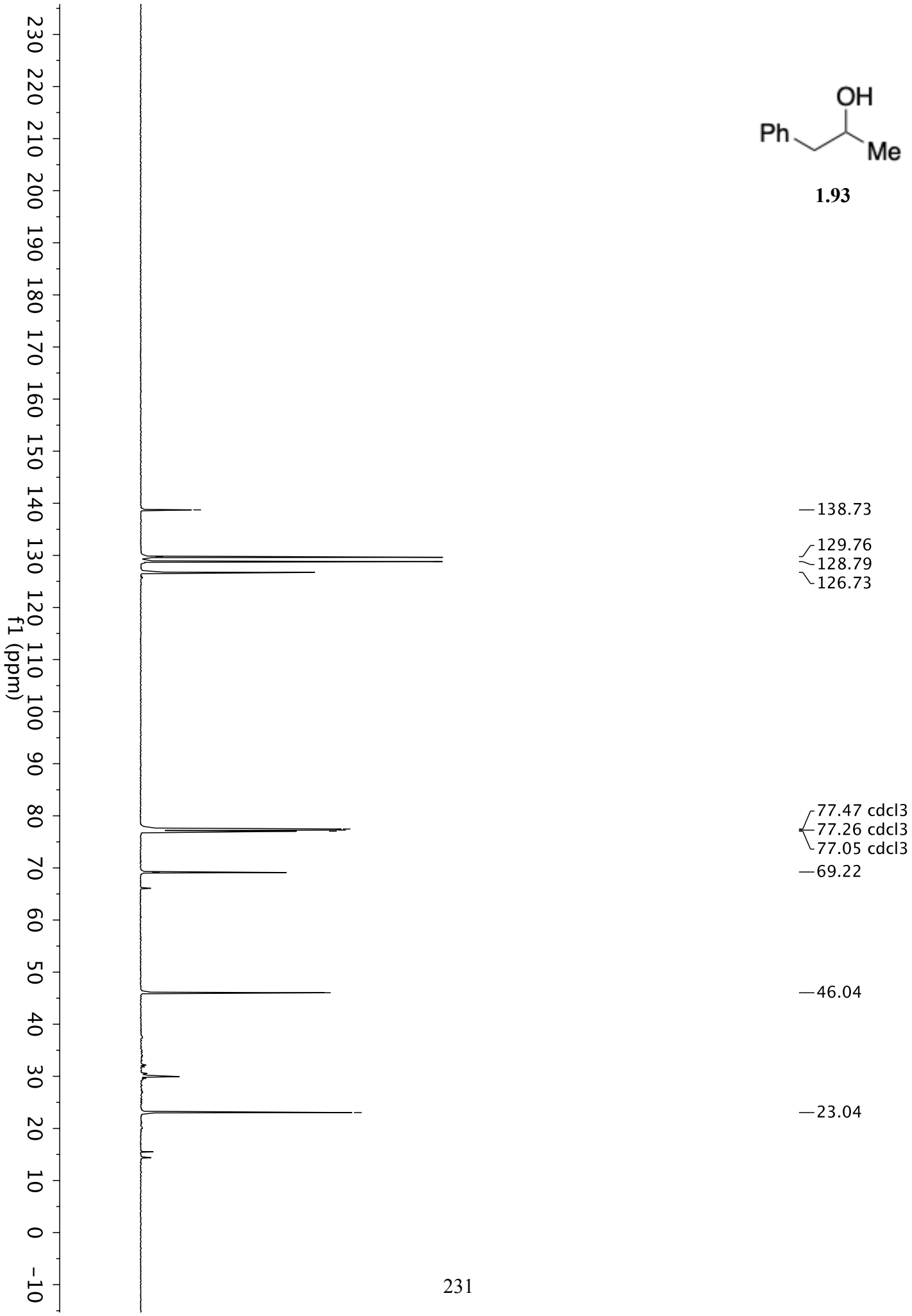
1.91

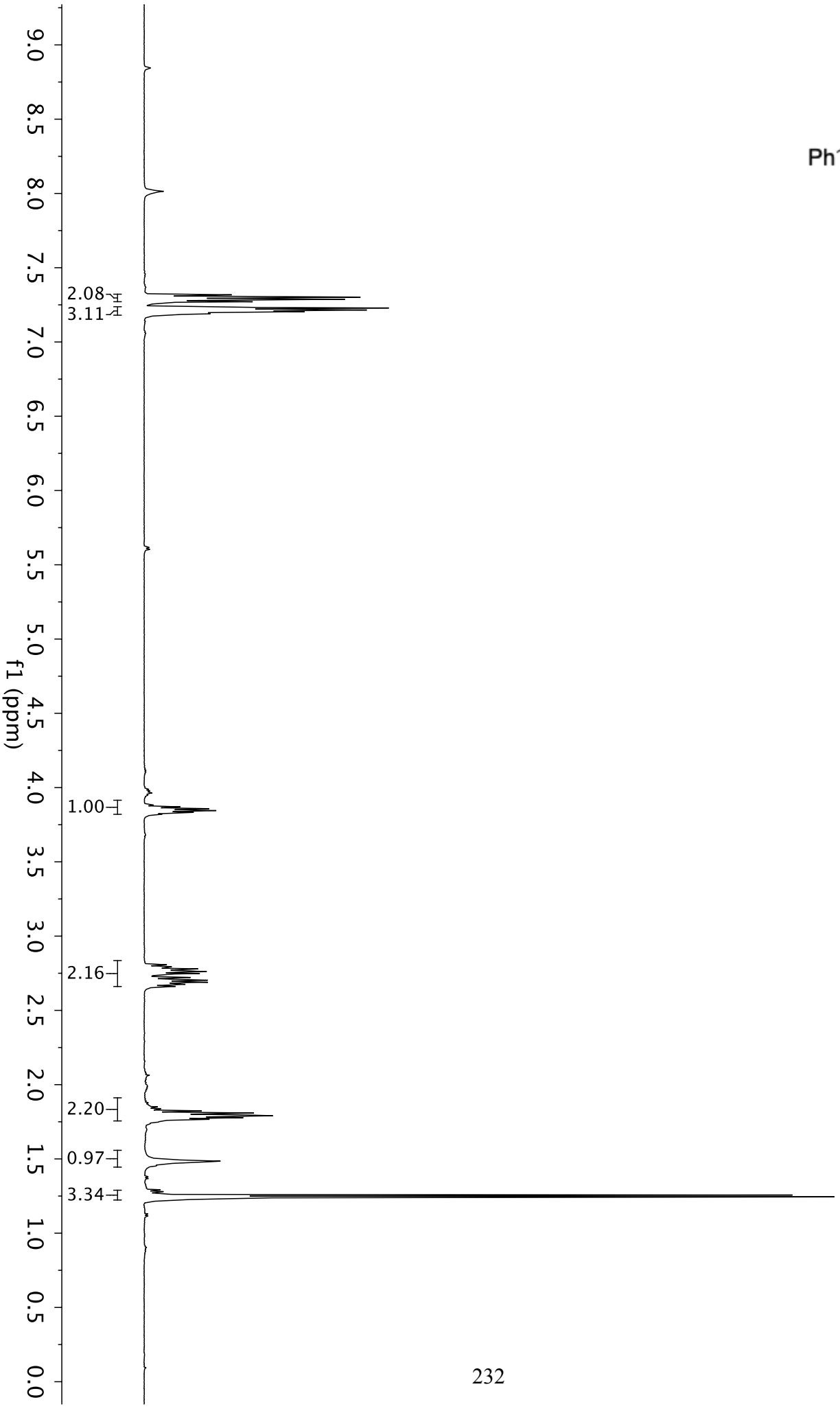

OH
Si
O
Me
1.91
135.80
135.78
133.28
133.18
130.08
130.06
128.02
127.92
68.20
63.74
40.30
27.04
23.63
19.27
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

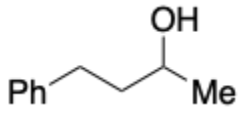

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1.89
3.09
1.00
1.07
1.10
4.20


OH
Ph
Me

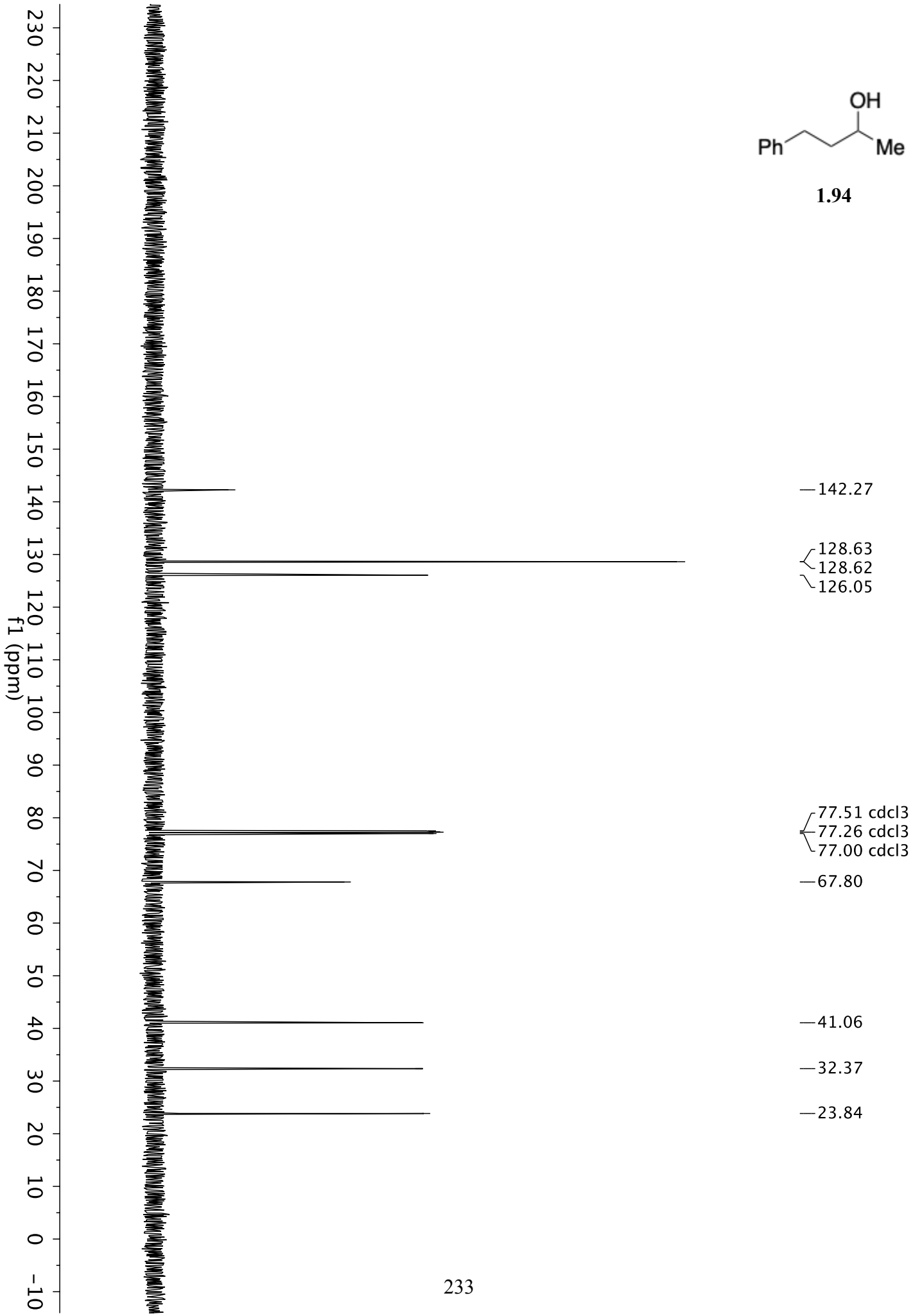
1.93

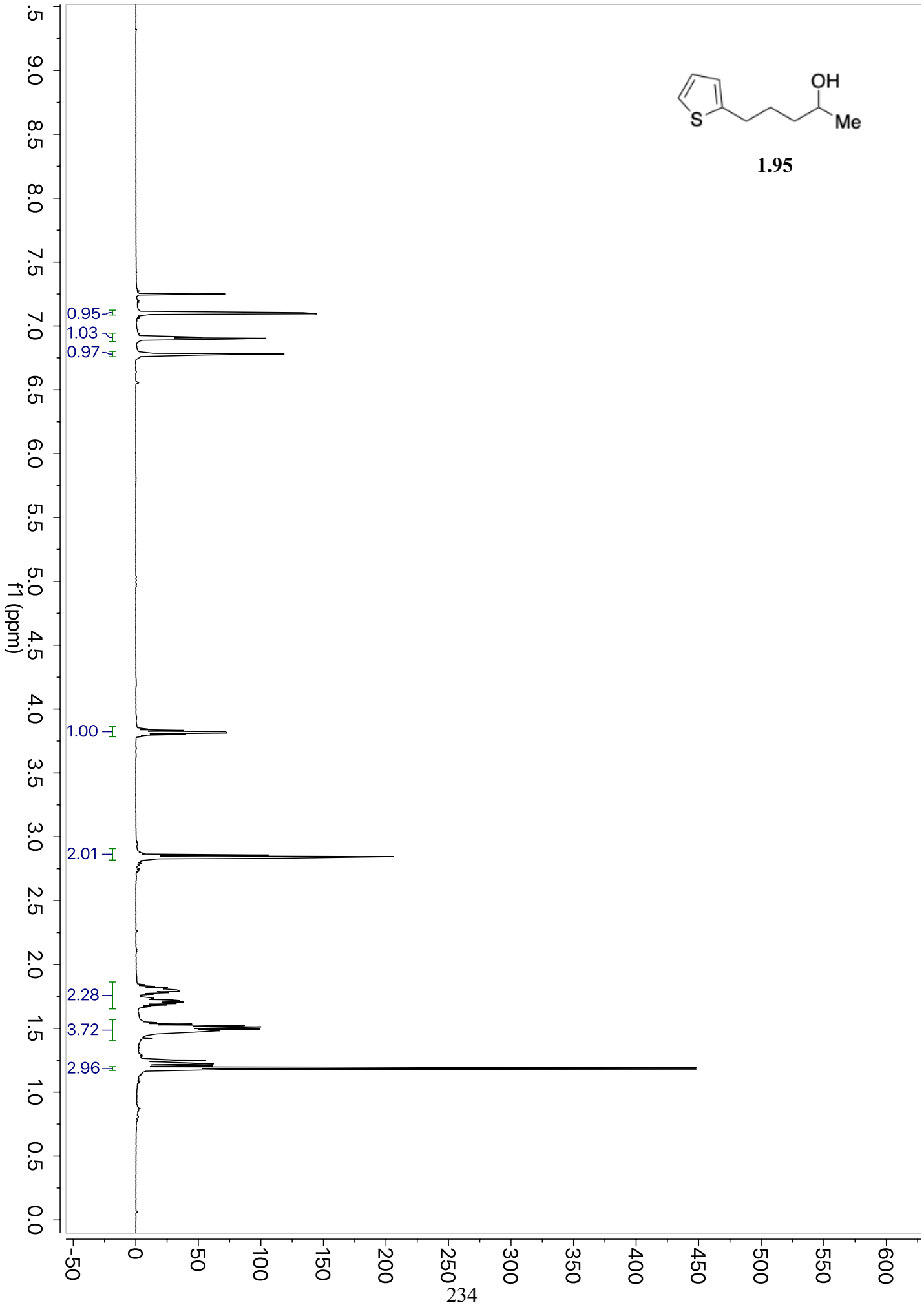

OH
Ph
Me
1.93
138.73
129.76
128.79
126.73
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
69.22
46.04
23.04
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

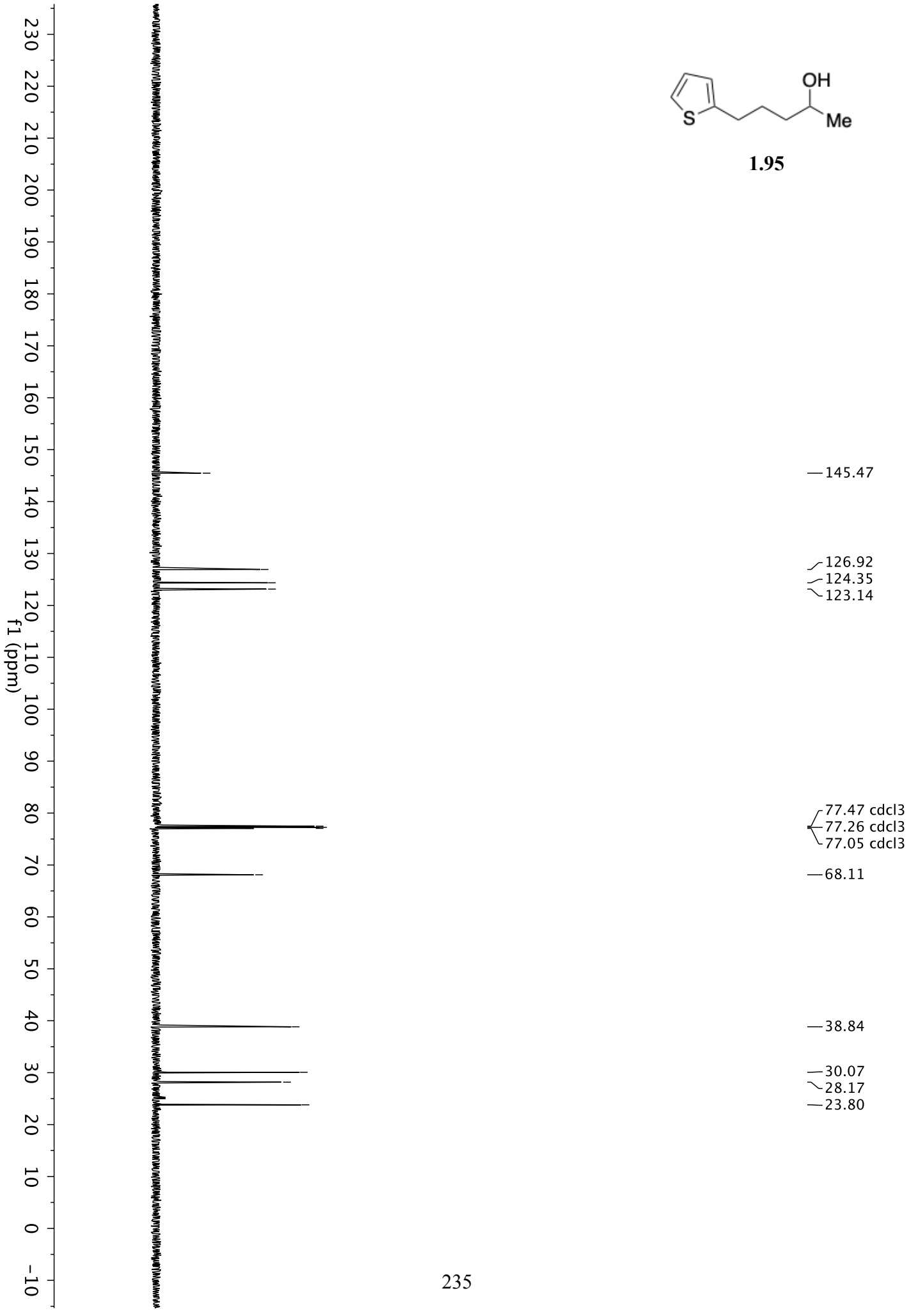

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
2.08
3.11
1.00
2.16
2.20
0.97
3.34

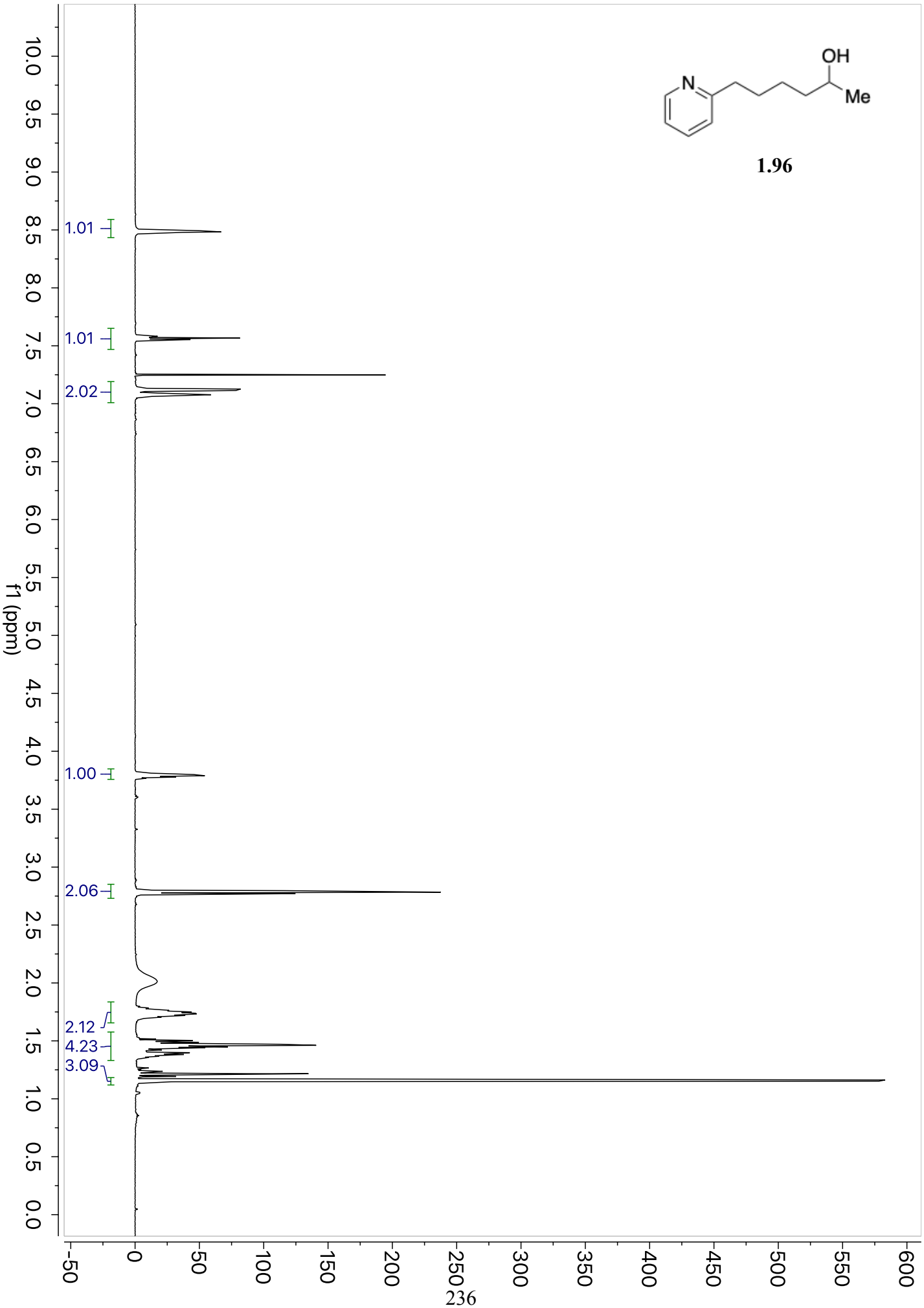

OH
Ph
Me

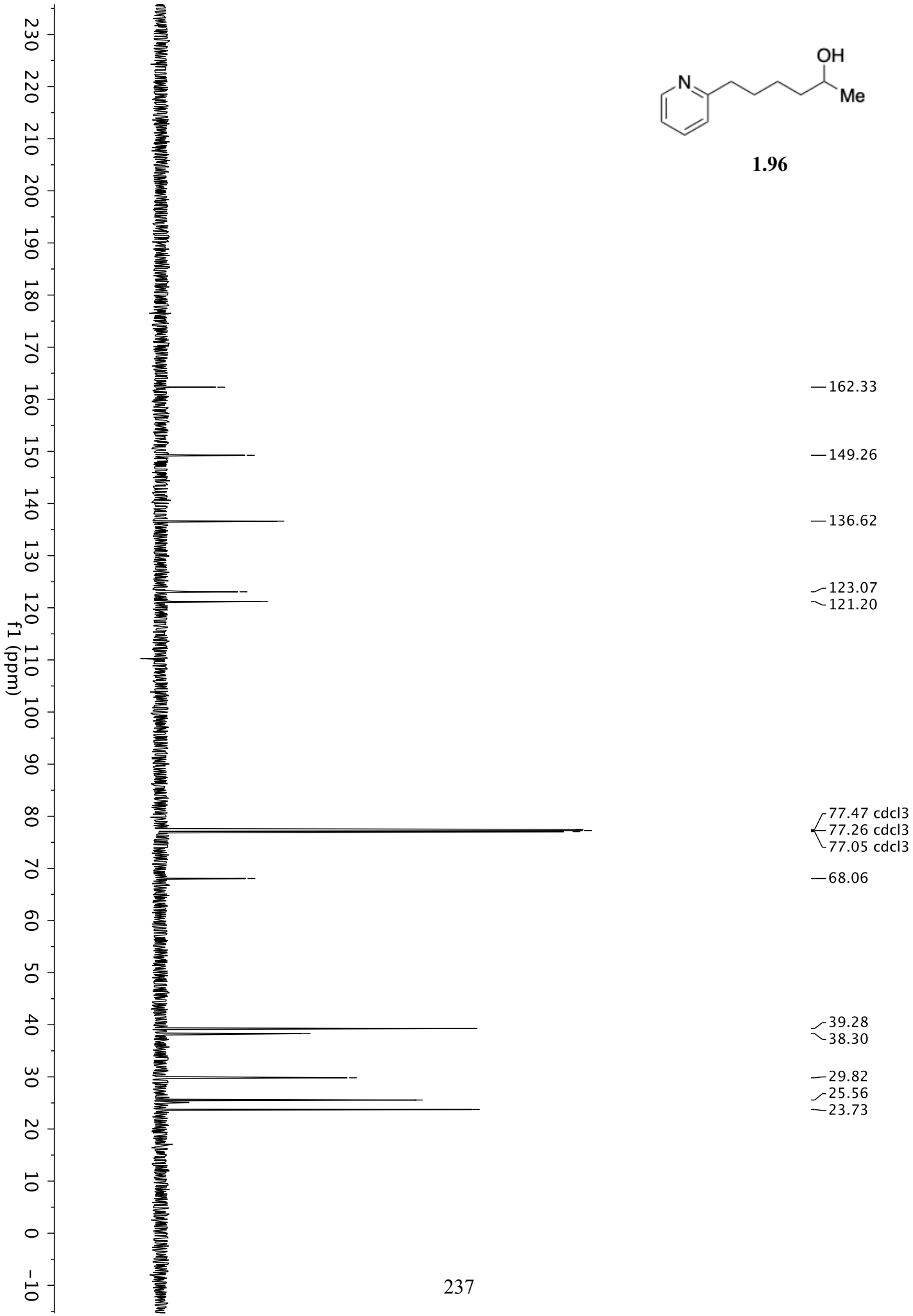
1.94

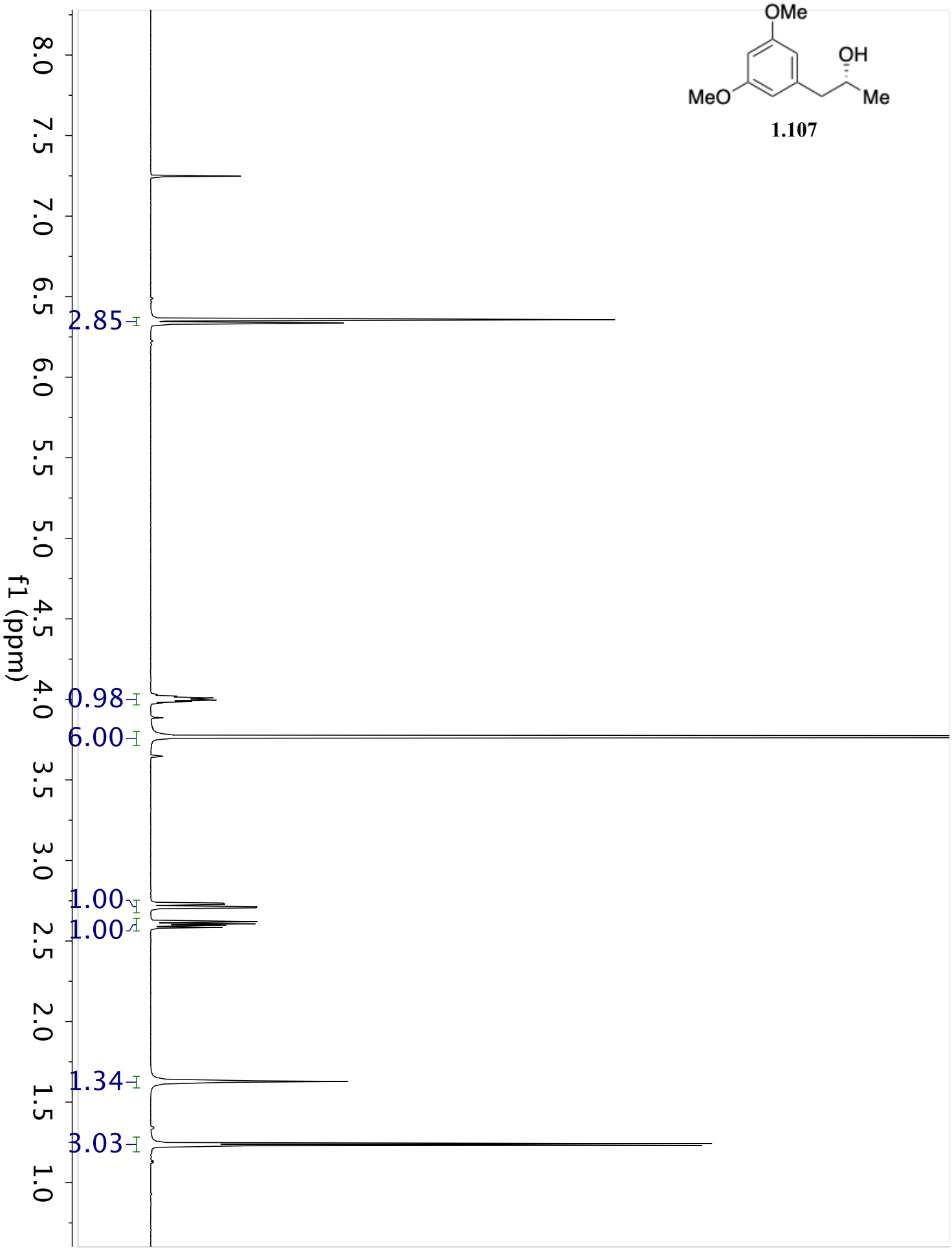

OH
Ph
Me
1.94
142.27
128.63
128.62
126.05
77.51 cdcl3
77.26 cdcl3
77.00 cdcl3
67.80
41.06
32.37
23.84
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

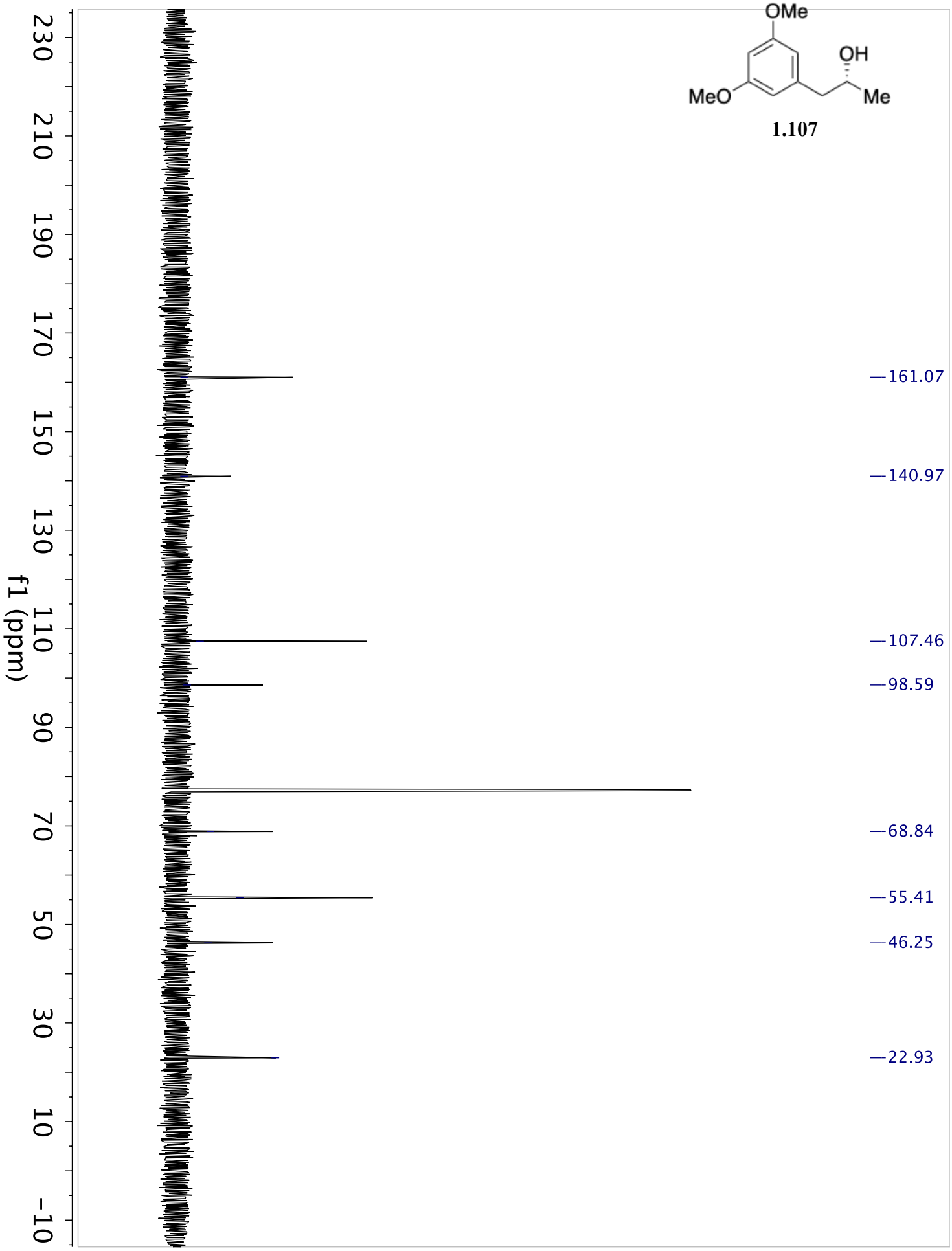

OH
S
Me
1.95
0.95
1.03
0.97
1.00
2.01
2.28
3.72
2.96
f1 (ppm)

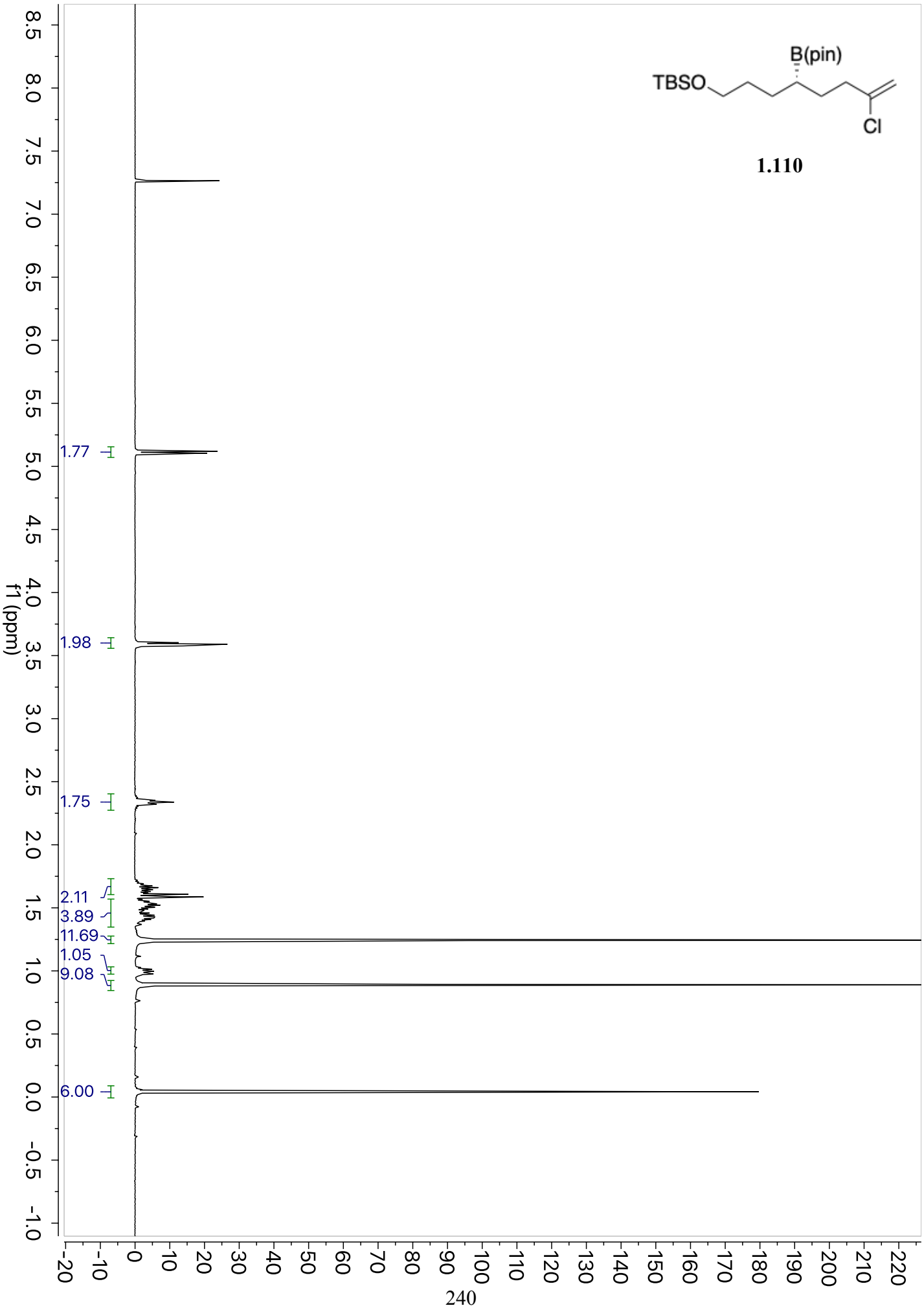

OH
S
Me
1.95
145.47
126.92
124.35
123.14
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
68.11
38.84
30.07
28.17
23.80
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

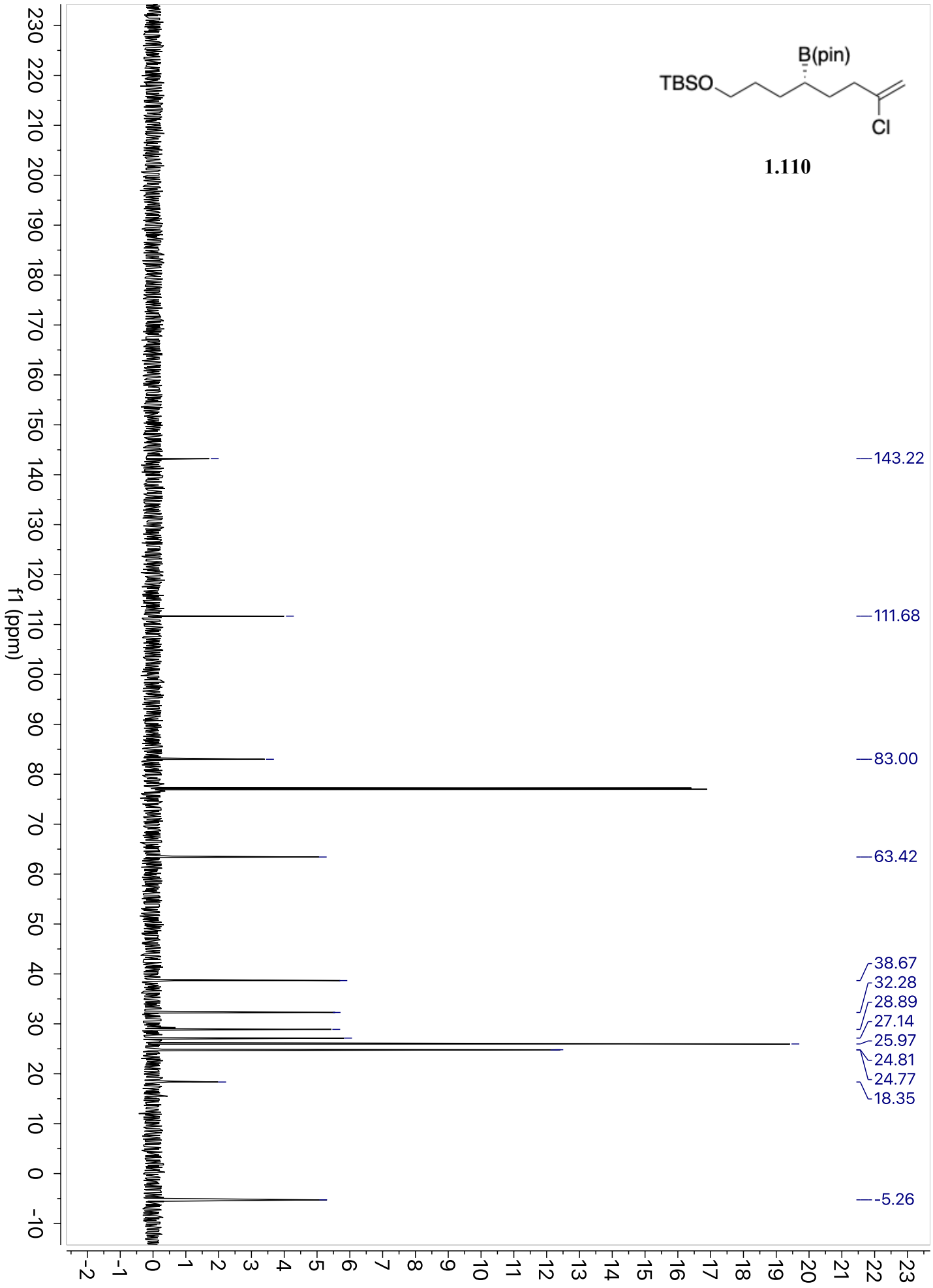

OH
N
Me
1.96
1.01
1.01
2.02
1.00
2.06
2.12
4.23
3.09
f1 (ppm)

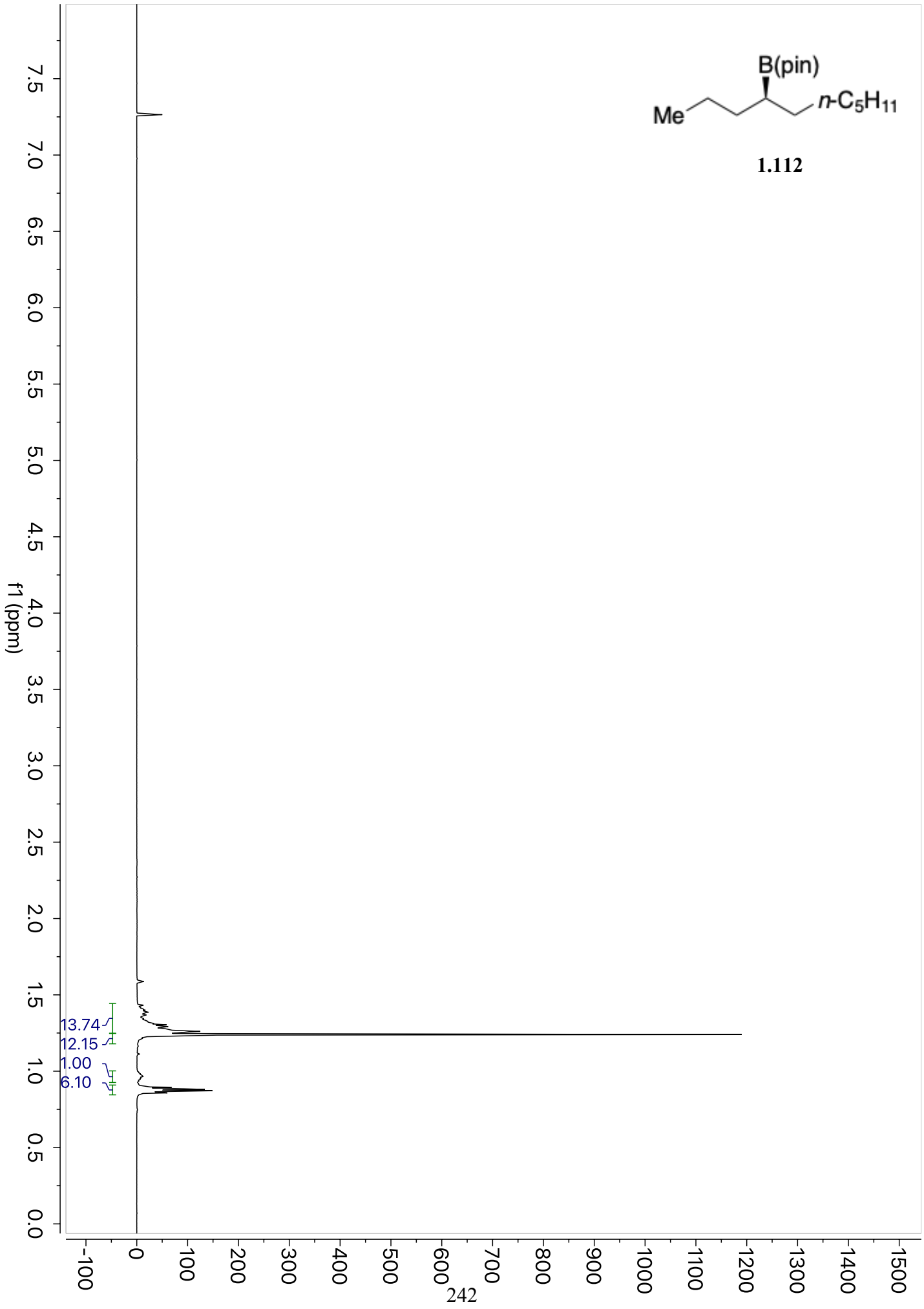

OH
N
Me
1.96
162.33
149.26
136.62
123.07
121.20
77.47 cdcl3
77.26 cdcl3
77.05 cdcl3
68.06
39.28
38.30
29.82
25.56
23.73
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

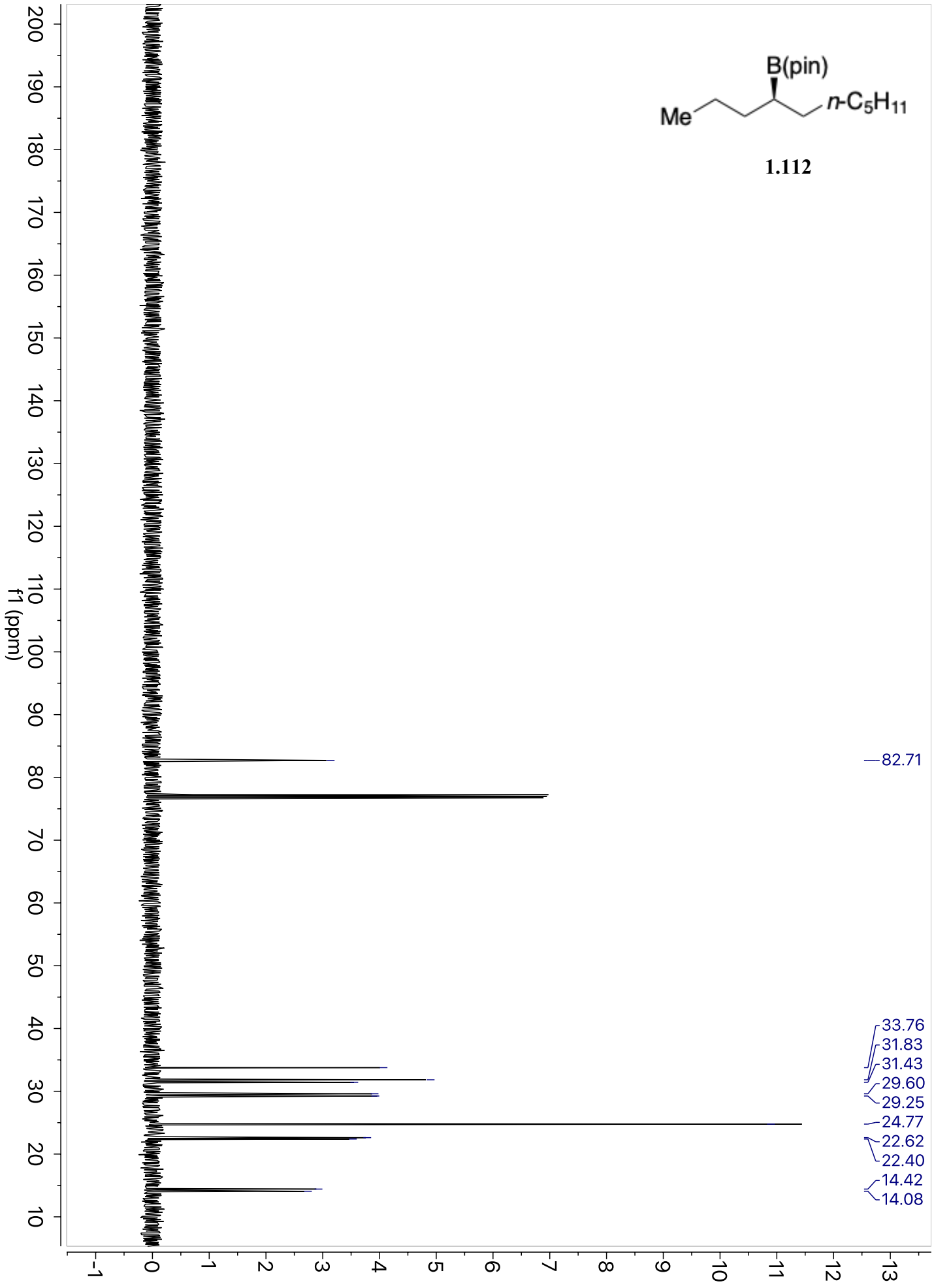

OMe
OH
MeO
Me
1.107
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
2.85
0.98
6.00
1.00
1.00
1.34
3.03

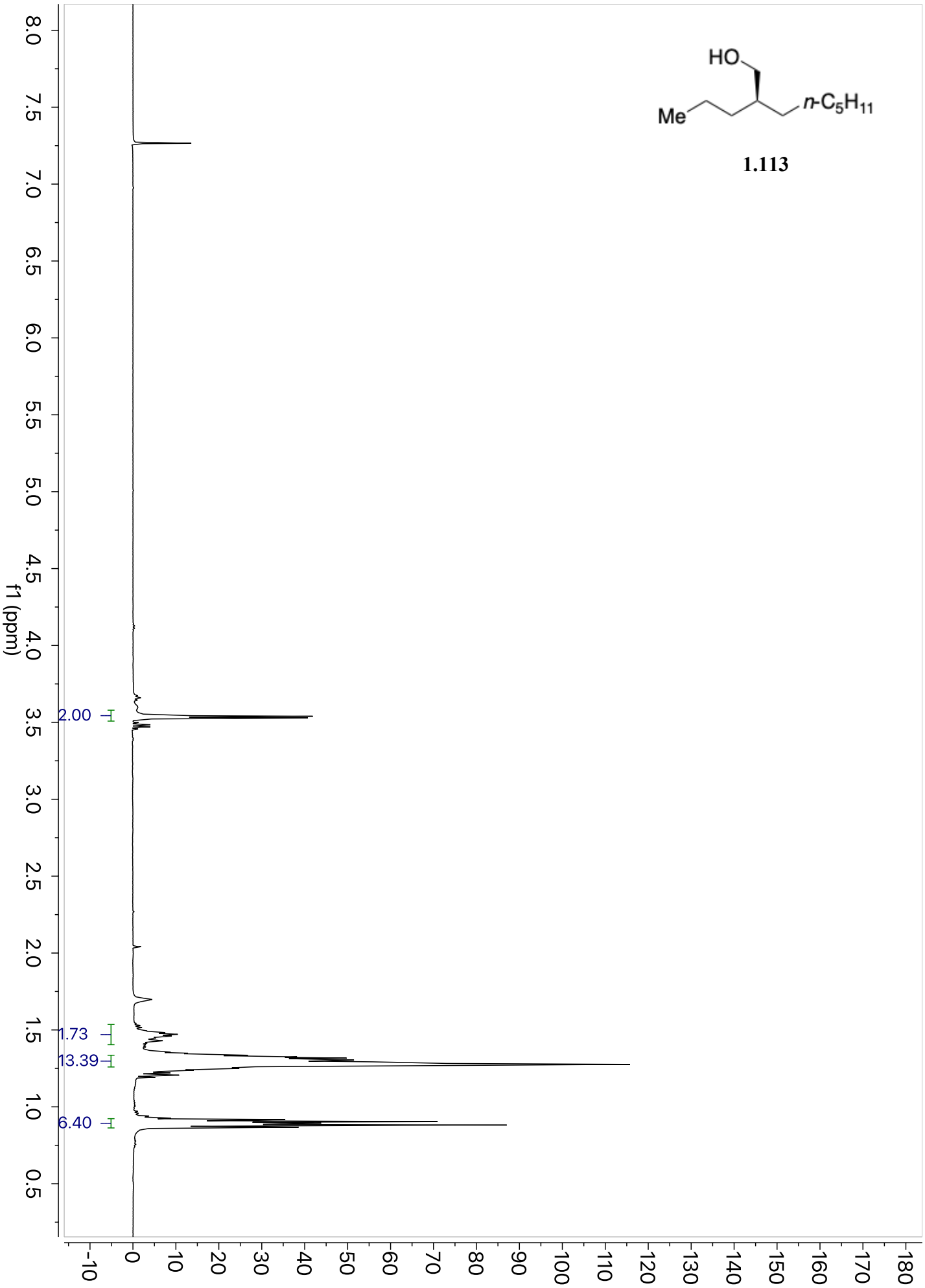

OMe
OH
MeO
Me
1.107
f1 (ppm)
230
210
190
170
150
130
110
90
70
50
30
10
-10
161.07
140.97
107.46
98.59
68.84
55.41
46.25
22.93

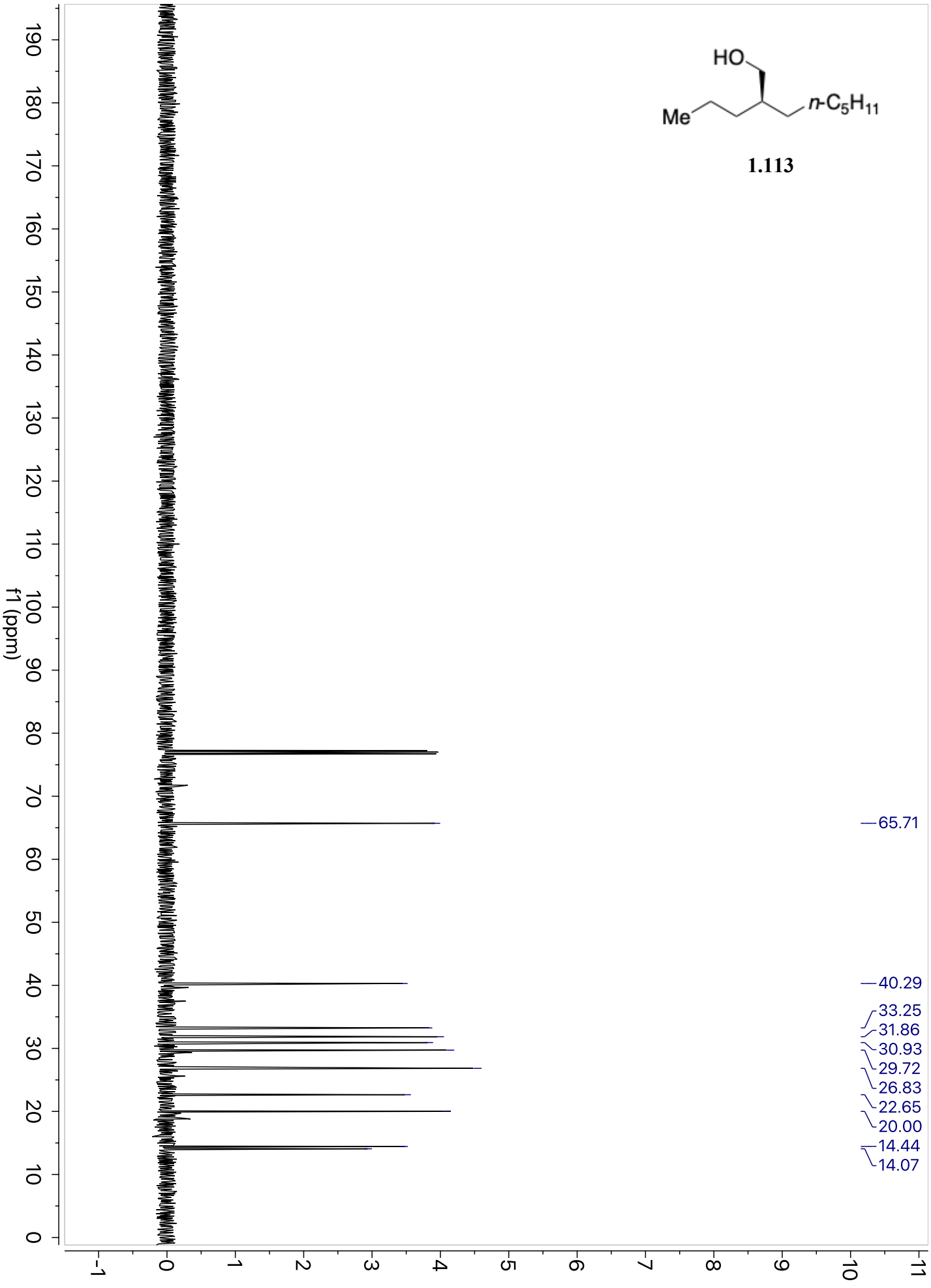

B(pin)
TBSO
Cl
1.110
1.77
1.98
1.75
2.11
3.89
11.69
1.05
9.08
6.00
f1 (ppm)


B(pin)
TBSO
Cl
1.110
f1 (ppm)
143.22
111.68
83.00
63.42
38.67
32.28
28.89
27.14
25.97
24.81
24.77
18.35
-5.26


B(pin)
Me
n-C5H11
1.112
13.74
12.15
1.00
6.10
f1 (ppm)


B(pin)
Me
n-C5H11
1.112
f1 (ppm)
82.71
33.76
31.83
31.43
29.60
29.25
24.77
22.62
22.40
14.42
14.08


HO
Me
n-C5H11
1.113
f1 (ppm)
2.00
1.73
13.39
6.40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n-C5H11
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40.29
33.25
31.86
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29.72
26.83
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20.00
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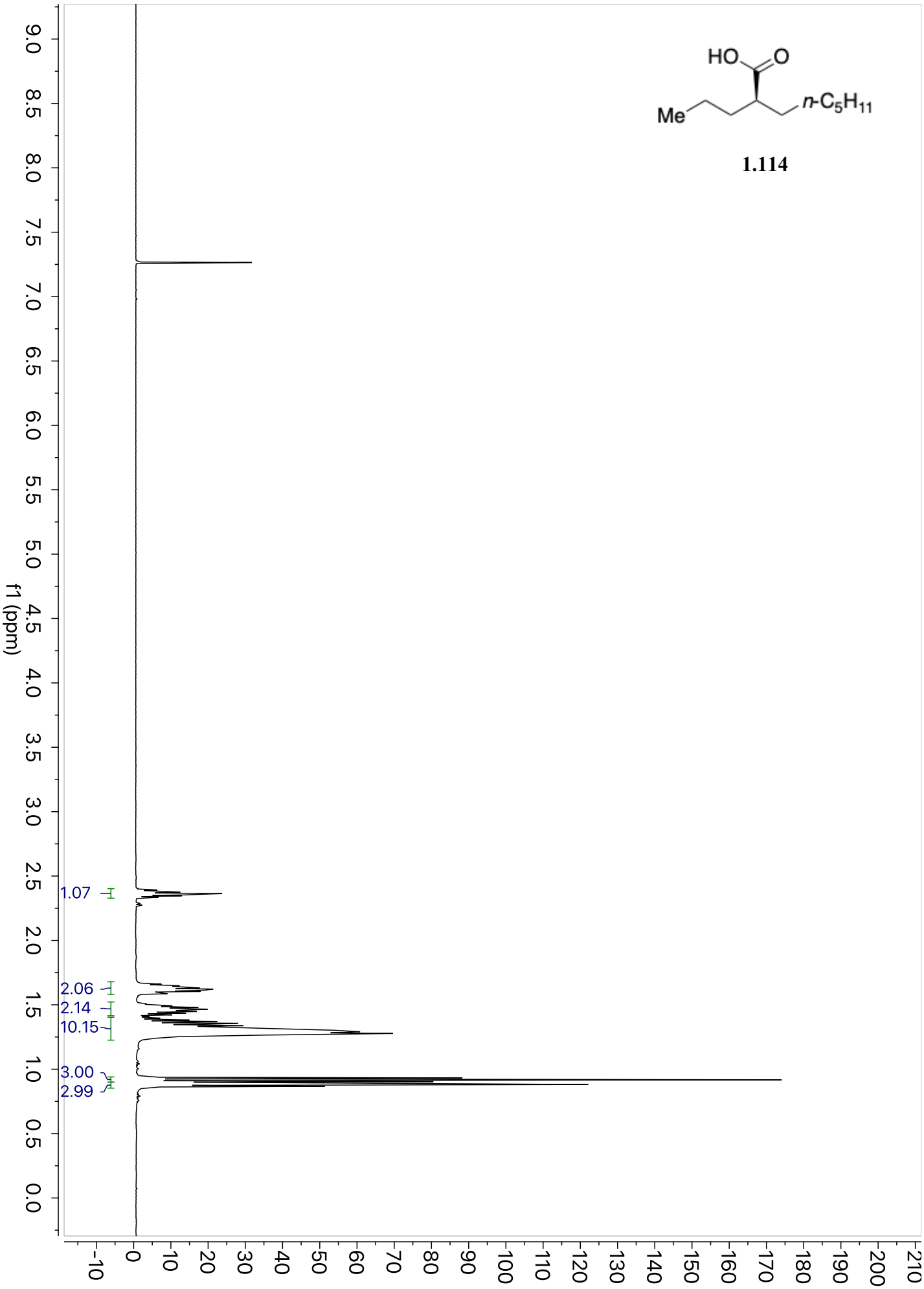
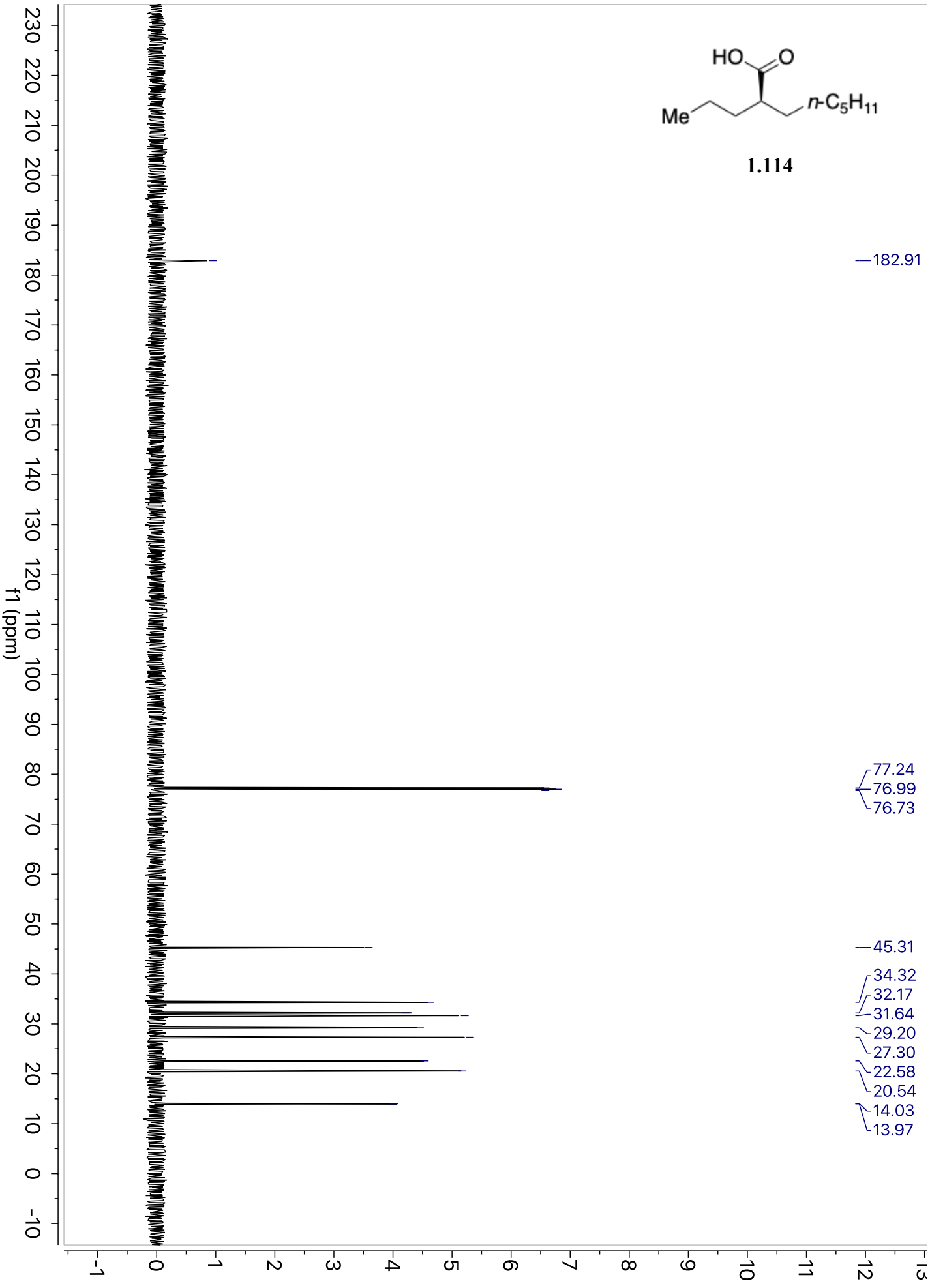
14.07
f1 (ppm)


HO
O
Me
n-C5H11
1.114
f1 (ppm)
1.07
2.06
2.14
10.15
3.00
2.99


HO
O
Me
n-C5H11
1.114
182.91
77.24
76.99
76.73
45.31
34.32
32.17
31.64
29.20
27.30
22.58
20.54
14.03
13.97
f1 (ppm)

Chapter 2. Copper-Catalyzed Stereospecific Transformations of Alkylboronic Esters

2.1 Introduction

Enantiomerically enriched secondary alkylboronic esters are valuable compounds in organic chemistry and can be readily obtained through various synthetic methods.[1] Numerous synthesis strategies have offered access to a diverse array of organic compounds by transformations of the boronic ester group. So far, oxidation,[2] amination,[3] homologation,[4] olefination,[5] and arylation[6] have been demonstrated to be efficient stereospecific transformations.

In many of these transformations, the boronic esters are activated by an activator (A) that is attached to a leaving group (X), forming a boron "ate" complex **2.1** (Scheme 2.1a).[7] **2.1** rapidly

[1] For selected reviews on enantioselective synthesis of alkylboronic esters, see: (a) Collins, B. S. L.; Wilson, C. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2017**, *56*, 11700−11733. (b) Hu, J.; Ferger, M.; Shi, Z.; Marder, T. *Chem. Soc. Rev.* **2021**, *50*, 13129−13188.

[2] (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 2544−2551. (b) Brown, H. C.; Snyder, C.; Subba Rao, B. C.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505−5510. (c) Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51*, 1330−1336.

[3] (a) Brown, H. C.; Kim, K. W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761−6764. (b) Edelstein, E.; Grote, A.; Palkowitz, M.; Morken, J. P. *Synlett.* **2018**, *29*, 1749−1752. (c) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449−16451. (d) Bagutski, V.; Elford, T. G.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 1080–1083. (e) Hupe, E.; Marek, I.; Knochel, P. *Org. Lett.* **2002**, *4*, 2861−2863. (f) Liu, X.; Zhu, Q.; Chen, D.; Wang, L.; Jin, L.; Liu, C. *Angew. Chem., Int. Ed.* **2020**, *59*, 2745−2749.

[4] (a) Sadhu, K. M.; Matteson, D. S. *Organometallics.* **1985**, *4*, 1687−1689. (b) Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 3760−3763.

[5] (a) Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652−3653. (b) Evans, D. A.; Crawford, T. C.; Thomas, R. C.; Walker, J. A. *J. Org. Chem.* **1976**, *41*, 3947−3953. (c) Armstrong, R. J.; Niwetmarin, W.; Aggarwal, V. K. *Org. Lett.* **2017**, *19*, 2762−2765. (d) Wang, Y.; Noble, A.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2016**, *55*, 4270–4274. For a selected review on Zweifel olefination, see: (e) Armstrong, R.; Aggarwal, V. K. *Synthesis.* **2017**, *49*, 3323−3336.

[6] (a) Bonet, A.; Odachowski, M.; Leonori, D.; Essafi, S.; Aggarwal, V. K. *Nature Chem.* **2014**, *6*, 584−589. (b) Odachowski, M.; Bonet, A.; Essafi, S.; Conti-Ramsden, P.; Harvey, J. N.; Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2016**, *138*, 9521−9532.

[7] For a selected review on 1,2-metallate shift of boron "ate" complex, see: Sandford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481−5494.

undergoes 1,2-metallate shift to furnish the desired product. The stereoretentive characteristic of the 1,2-metallate shift is pivotal to the synthetic utility of enantiomerically enriched boronic esters, as it enables the stereospecific formation of C–O, C–N and C–C bonds through this crucial step. Compared to stoichiometric transformations, catalytic stereospecific cross-coupling reactions of secondary alkylboronic esters are relatively scarce, with catalysts predominantly limited to palladium complexes.

In this field, Pd-catalyzed cross-coupling of benzylic, allylic, and cyclopropyl boronate compounds, or boronate compounds with directing groups, proved to be effective.[8] However, Pd-catalyzed stereospecific coupling of electronically isolated (unactivated) secondary alkylboronate compounds without directing groups has only been achieved by Biscoe and Sigman for trifluoroborates[9] and by Burke and colleagues for boronic acids.[10]

In this chapter,[11] we present a stereospecific Cu-catalyzed cross-coupling method that enables the functionalization of unactivated secondary boronic esters (Scheme 2.1b). This process appears to proceed by a facile transmetallation that provides a configurationally stable organocopper(I) species (**2.3**). The organocopper species effectively reacts with alkynyl bromides, allyl halides, propargyl halides, *β*-haloenones, hydroxylamine esters, and acyl chlorides. We anticipate that this method will prove valuable in broadening the application scope of such organoboronate compounds.

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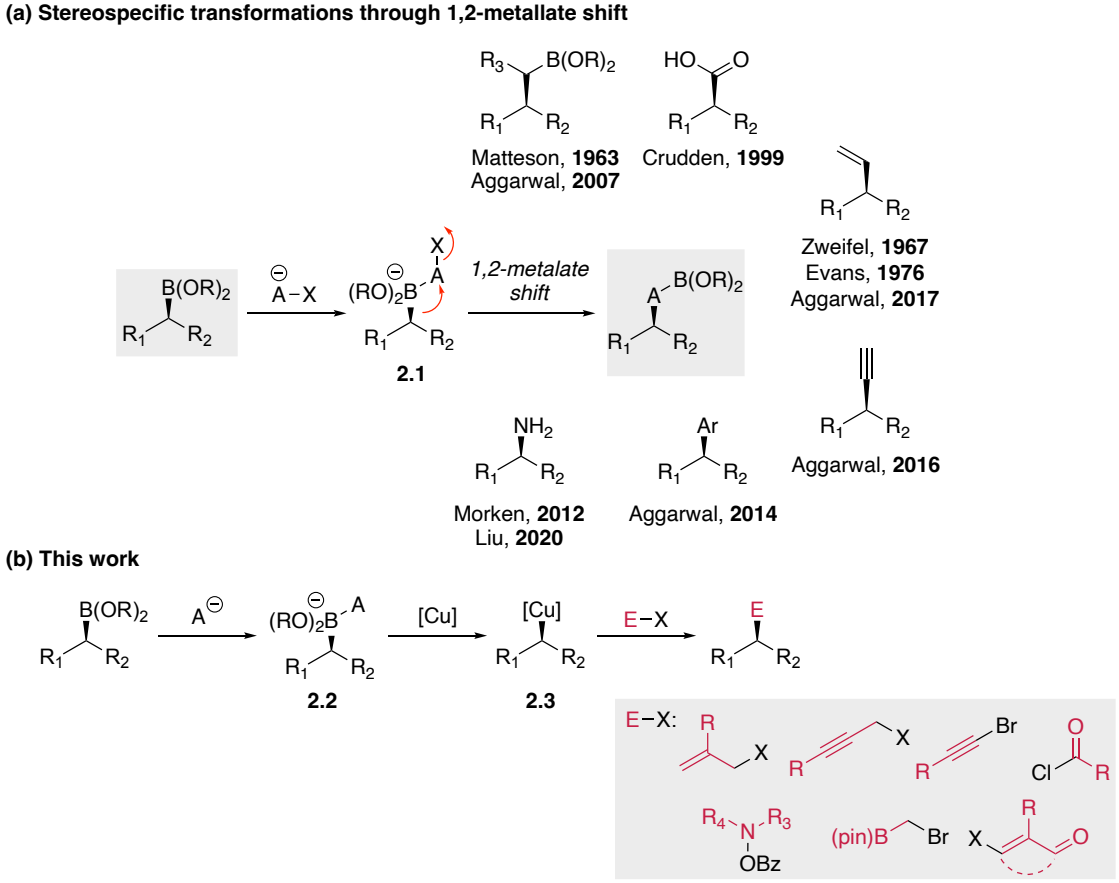
[8] For a selected review on Pd-catalyzed coupling of organoboronate compounds: Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *Chem. Rev.* **2015**, *115*, 9587−9652.

[9] (a) Li, L.; Zhao, S.; Joshi-Pangu, A.; Diane, M.; Biscoe, M. R. *J. Am. Chem. Soc.* **2014**, *136*, 14027−14030. (b) Zhao, S.; Gensch, T.; Murray, B.; Niemeyer, Z. L.; Sigman, M. S.; Biscoe, M. R. *Science* **2018**, *362*, 670−674. (c) Murray, B.; Zhao, S.; Aramini, J. M.; Wang, H.; Biscoe, M. R. *ACS Catal.* **2021**, *11*, 2504−2510.

[10] Lehmann, J. W.; Crouch, I. T.; Blair, D. J.; Trobe, M.; Wang, P.; Li, J.; Burke, M. D. *Nat. Commun.* **2019**, *10*, 1263–1272.

[11] Xu, N.; Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 11546–11552.

Scheme 2.1. Stereospecific Transformations of Unactivated Secondary Alkyl Boronic Compounds



2.2 Background

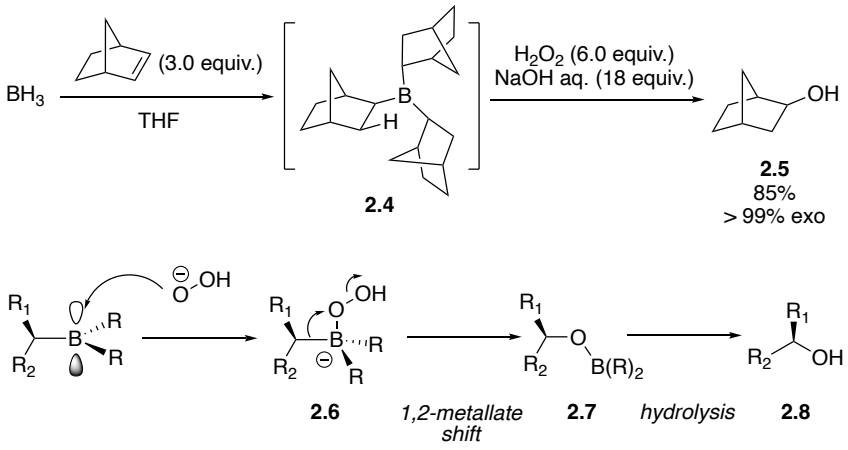
2.2.1 Selected Examples of Stereospecific Functionalization of Alkylboronic Esters

2.2.1.1 Oxidation

The first example of stereospecific transformation of organoboronic compounds was reported by Brown and Zweifel (Scheme 2.2).[2a] Trialkylborane **2.4** was generated by treating norbornene with BH_3 in THF. Upon subjecting **2.4** to an aqueous solution of hydrogen peroxide and base, exonorborneol (**2.5**) was exclusively obtained. This study also marked the first proposal of the mechanism of oxidation. Addition of the peroxide anion to the boron atom's vacant p-orbital led

to the formation of boron "ate" complex **2.6**. Subsequently, the boron "ate" complex underwent a 1,2-metallate shift to furnish intermediate **2.7**, The C–B bond was cleaved during 1,2-metallate shift, and a new C–O bond was formed in a stereospecific manner. Finally, hydrolysis cleaved the B–O bond, affording alcohol **2.8**.

Scheme 2.2. Stereoretentive Oxidation of Alkyl Boronic Compounds



2.2.1.2 Homologation

A one-carbon homologation was disclosed by Matteson and colleagues in 1985 (Scheme 2.3a).[4a] In this process, (chloromethyl)lithium was formed *in situ*, it then added to an enantiomerically enriched boronic ester **2.9**, forming the boron "ate" complex **2.10**. Swift 1,2-metallate shift of complex **2.10** furnished the homologated product **2.11** stereoretentively in 95% yield. In 2011, Aggarwal and co-workers reported a robust homologation method.[4b] Homologation of sterically congested tertiary boronic esters could be accomplished with dibromomethane and *n*-BuLi.

In 1999, the Crudden group demonstrated a route to access primary carboxylic acids or aldehydes through a homologation/oxidation sequence (Scheme 2.3b).[12] The use of (dichloromethyl)lithium as homologation reagent furnished chloro-substituted secondary boronic ester **2.13**, which afforded carboxylic acid **2.14** through oxidation/hydrolysis.

In 2007, Aggarwal and co-workers developed a process for homologation of boranes and boronic esters through the use of Hoppe-type lithiated carbamates (**2.16**) (Scheme 2.3c).[13a] Enantiomerically enriched lithiated carbamate **2.16** was formed by deprotonating carbamate **2.15** with *sec*-butyllithium in the presence of (+)-sparteine.[14] Upon addition of lithiated carbamate **2.16** to an enantiomerically enriched secondary boronic ester **2.17**, boron "ate" complex **2.18** was generated. 1,2-Metallate shift afforded the product (**2.20**) in 63% yield and >98:2 er, with stereoretention of both enantiomerically enriched stereogenic centers. Furthermore, the authors demonstrated syntheses of all four diastereomers of the product (**2.19**–**2.22**) through combinations of diastereomers **2.16a**, **2.16b** and enantiomers **2.17a**, **2.17b**.

[12] Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704–9710.

[13] For selected reports on homologation of alkylboronic esters through the use of lithiated carbamates, see: (a) Stymiest, J. L.; Dutheuil, G.; Mahmood, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 7491–7494. For other examples, see: (b) Larouche-Gauthier, R.; Fletcher, C. J.; Couto, I.; Aggarwal, V. K. *Chem. Commun.* **2011**, *47*, 12592. (c) Blair, D. J.; Fletcher, C. J.; Wheelhouse, K. M. P.; Aggarwal, V. K. *Angew. Chem., Int. Ed.*, **2014**, *53*, 5552–5555. (d) Blair, D. J.; Tanini, D.; Bateman, J. M.; Scott, H. K.; Myers, E. L.; Aggarwal, V. K. *Chem. Sci.* **2017**, *8*, 2898–2903.

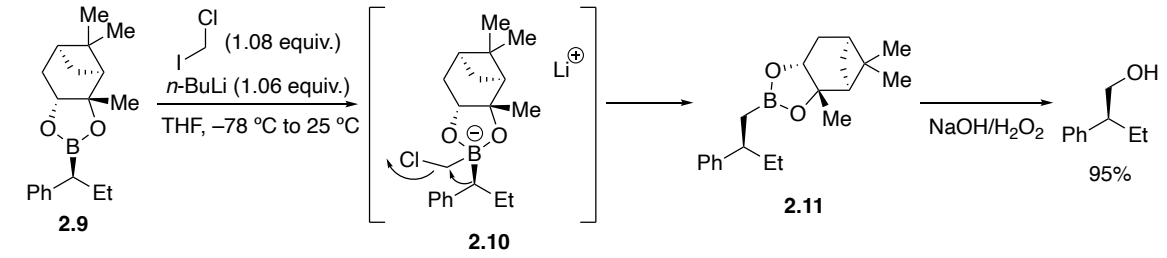
[14] Hoppe, D.; Hintze, F.; Tebben, P. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1422–1424.

The synthetic versatility of this method lies in its iterative applicability. Over the years, the Aggarwal group has demonstrated numerous examples of stereocontrolled synthesis of alkyl chains bearing contiguous stereogenic centers. This strategy has also been applied to syntheses of natural products.[15]

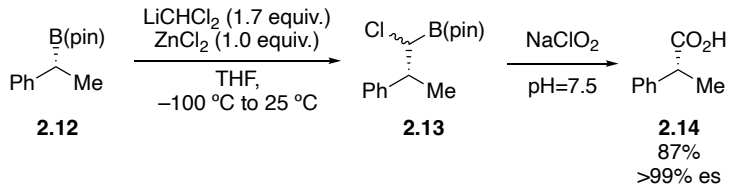
[15] For selected reports on iterative synthesis through homologation of alkyl(boronic esters), see: (a) Burns, M.; Essafi, S.; Bame, J. R.; Bull, S. P.; Webster, M. P.; Balieu, S.; Dale, J. W.; Butts, C. P.; Harvey J. N.; Aggarwal, V. K. *Nature*, **2014**, *513*, 183–188. (b) Balieu, S.; Hallett, G. E.; Burns, M.; Bootwicha, T.; Studley, J.; Aggarwal, V. K. *J. Am. Chem. Soc.*, **2015**, *137*, 4398–4403. (c) Millan, A.; Smith, J. R.; Chen, J. L. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.*, **2016**, *55*, 2498–2502. (d) Noble, A.; Roesner, S. Aggarwal, V. K. *Angew. Chem., Int. Ed.*, **2016**, *55*, 15920–15924. (e) Varela, A.; Garve, L. K. B.; Leonori, D.; Aggarwal, V. K. *Angew. Chem., Int. Ed.*, **2017**, *56*, 2127–2131. (f) Wu, J.; Lorenzo, P.; Zhong, S.; Ali, M.; Butts, C. P.; Myers, E. L.; Aggarwal, V. K. *Nature* **2017**, *547*, 436–440. (g) Bootwicha, T.; Feilner, J. M.; Myers, E. L.; Aggarwal, V. K. *Nat. Chem.* **2017**, *9*, 896–902. (h) Pradeilles, J. A.; Zhong, S.; Baglyas, M.; Tarczay, G.; Butts, C. P.; Myers, E. L.; Aggarwal, V. K. *Nat. Chem.* **2020**, *12*, 475–480. (i) Fiorito, D.; Keskin, S.; Bateman, J. M.; George, M.; Noble, A.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2022**, *144*, 7995–8001. (j) Aiken, S. G.; Bateman, J. M.; Liao, H.H.; Fawcett, A.; Bootwicha, T.; Vincetti, P.; Myers, E. L.; Noble, A.; Aggarwal, V. K. *Nat. Chem.* **2023**, *15*, 248–256. For a review, see: (k) Yeung, K., Mykura, R. C., Aggarwal, V. K., *Nat. Synth.*, **2022**, *1*, 117–126.

Scheme 2.3. Examples and Development of Matteson Homologation

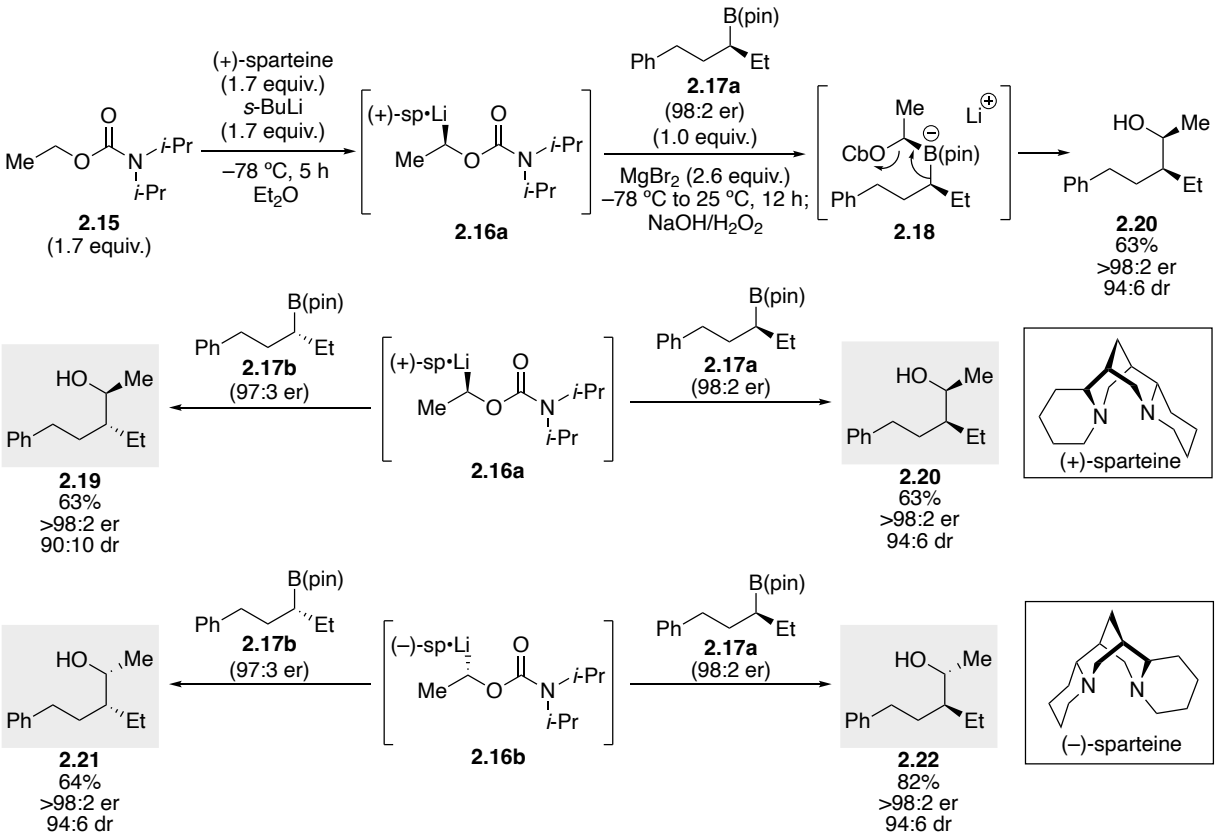
(a) Homologation of organoboronic esters by Matteson *et al.*



(b) Homolgation/oxidation sequence of organoboronic esters by Crudden *et al.*



(c) Homologation of organoboronic esters by Aggarwal *et al.*



2.2.1.3 Olefination

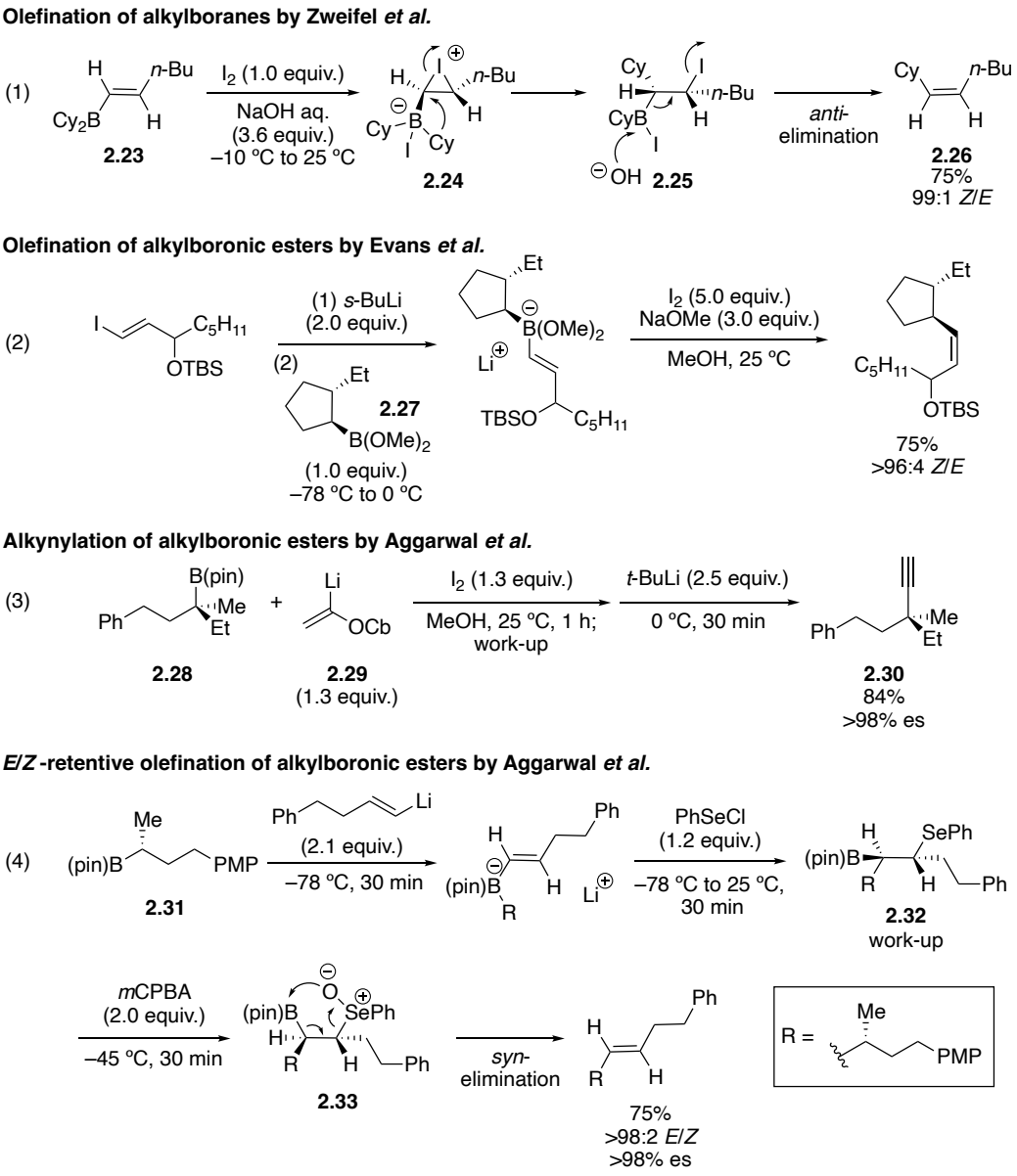
Zweifel and co-workers reported the first synthesis of alkene from an organoboron in 1967 (Scheme 2.4, equation 1).[5a] Upon addition of iodine to *E*-alkenylborane **2.23**, iodonium complex **2.24** was generated. Subsequent migration of an alkyl substituent of the borane led to the ring-opening of iodonium complex **2.24**, affording *β*-iodo-organoborane **2.25**. Hydroxide then facilitated the *anti*-elimination of boron and iodide to furnish *Z*-alkene **2.26**. In 1976, Evans and co-workers extended the olefination reaction to the coupling of an alkylboronic ester (**2.27**) with an alkenyllithium (generated from *E*-alkenyl iodide and *sec*-butyllithium) (Scheme 2.4, equation 2).[5b] *Z*-alkene was obtained in 75% yield with high level of retention of stereochemistry.

In 2016, Aggarwal and co-workers demonstrated a stereospecific alkynylation of alkylboronic esters (Scheme 2.4, equation 3).[5d] A boronic ester (**2.28**) was coupled with an alkenyllithium (**2.29**) substituted with a leaving group (OCb) through Zweifel olefination. The product then underwent base-facilitated 1,2-elimination to afford the alkynylation product **2.30** in 84% yield with high level of stereoretention.

In 2017, the Aggarwal group reported the first example of *E*/*Z*-retentive olefination (Scheme 2.4, equation 4).[16] Alkenyl boron "ate" complex was treated with PhSeCl to afford *β*-selenoboronic ester intermediate **2.32**. Subsequent oxidation of **2.32** by *m*CPBA generated the corresponding selenoxide **2.33**. The selenoxide then underwent facile *syn*-elimination of selenium oxide and boronic ester to furnish *E*-alkene in 75% yield, with >98% enantiospecificity and >98:2 *E*/*Z* ratio.

[16] Armstrong, R. J.; García-Ruiz, C.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed*. **2017**, *56*, 786–790.

Scheme 2.4. Examples and Development of Zweifel Olefination



2.2.1.4 Arylation

Aggarwal and co-workers reported a stereospecific sp^2–sp^3 coupling of secondary and tertiary boronic esters. Boron "ate" complex **2.35** was obtained when enantiomerically enriched secondary boronic ester **2.34** was treated with 2-furyllithium (Scheme 2.5, equation 1).[6] Analogous to the activation of alkenyl boron "ate" complex with iodide, activation of **2.35** with NBS furnished

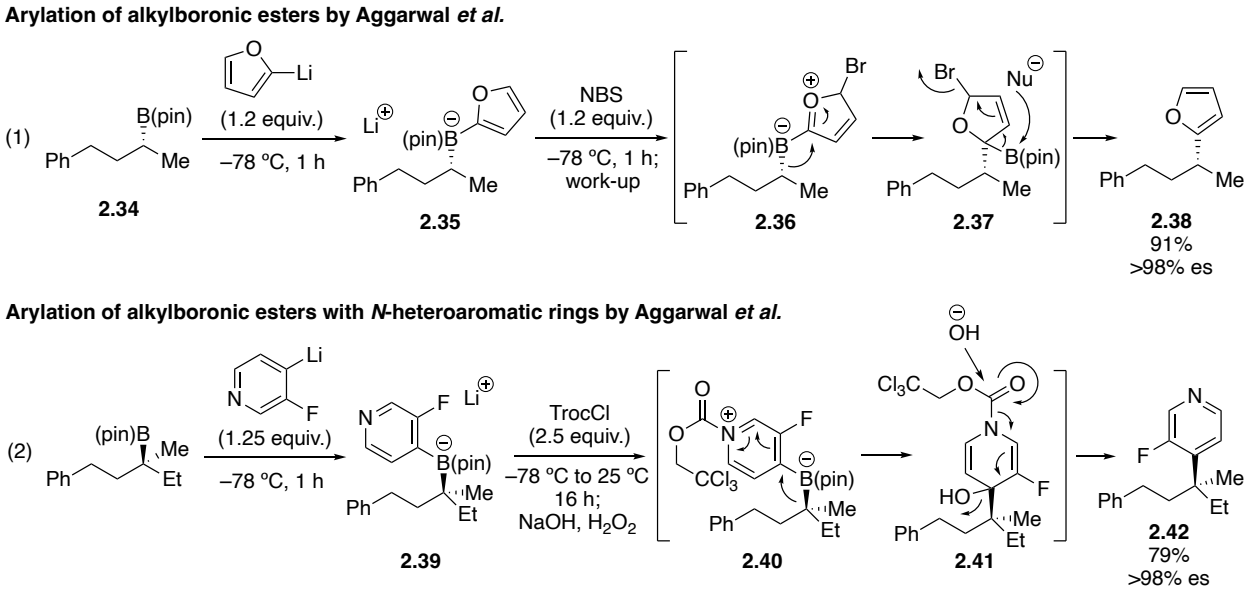
brominated complex **2.36**. Through 1,2-metallate shift, intermediate **2.37** was generated. Upon nucleophilic attack at the boron atom, intermediate **2.37** would re-aromatize with the elimination of bromide, affording the desired product **2.38** in 91% yield and >98% enantiospecificity. The coupling reaction can incorporate many electron-rich aromatic rings as the C(sp^2) component. In addition to 2-substituted furan, heterocycles such as 3-substituted furan, thiophene, benzofuran, and *N*-methylindole furnished respective coupling products in high yields and enantiospecificity. Phenyl rings substituted with electron-donating groups such as OMe and NMe_2 also underwent coupling reaction efficiently. Subsequently, the Aggarwal group developed strategies to incorporate electron-deficient 2-CF_3-furans as the aromatic component by radical addition of the trifluoromethyl group.[17]

The Aggarwal group extended the scope of this coupling reaction to *N*-heteroaromatic rings (Scheme 2.5, equation 2).[18] Lithiation of an *N*-heterocycle and addition to an enantiomerically enriched boronic ester afforded a boron "ate" complex (**2.39**). Treatment of **2.39** with TrocCl resulted in acylation of the nitrogen heterocycle and triggered 1,2-migration. Oxidative workup afforded the coupling product **2.42** in 79% yield and high enantiospecificity. The aromatic component's scope extends to pyridines with various substitutions, as well as quinolines and isoquinolines.

[17] Wang, Y.; Noble, A.; Sandford, C.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2017**, *56*, 1810–1814.

[18] Llaveria, J.; Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2015**, *137*, 10958–10961.

Scheme 2.5. Arylation of Alkylboronic Esters



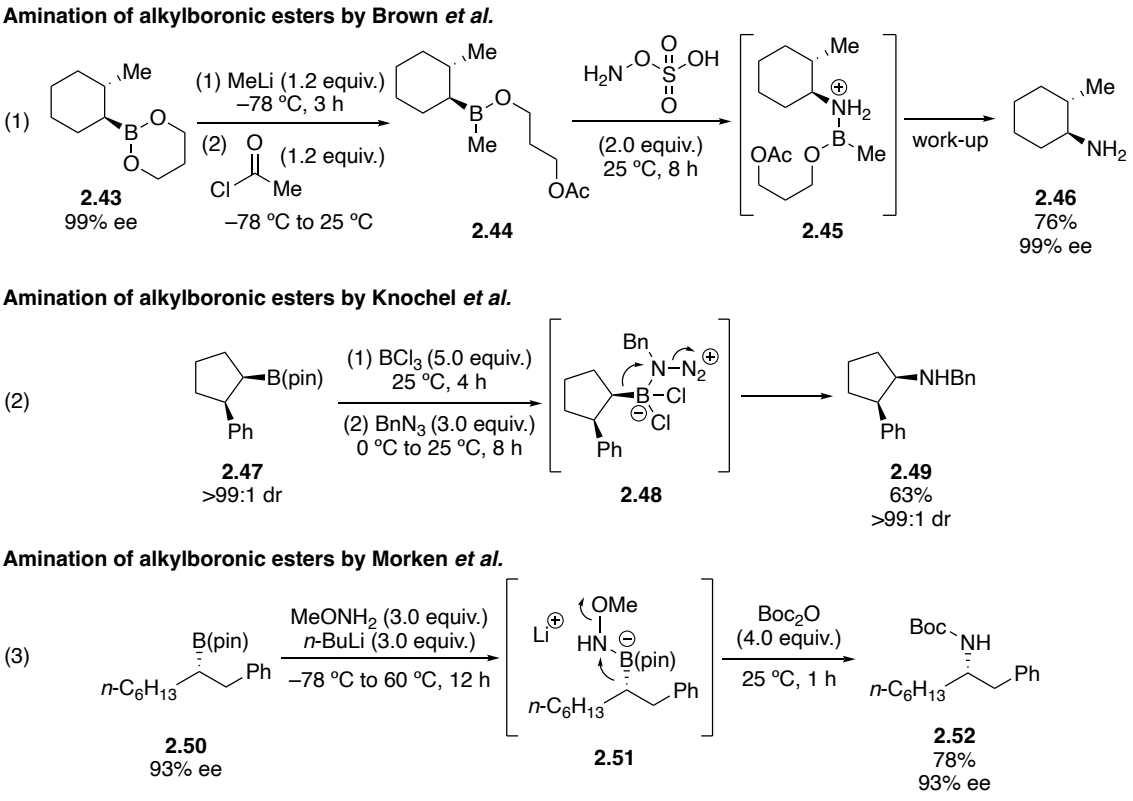
2.2.1.5 Amination

The first example of stereoretentive amination of boronic esters was reported by Brown and co-workers in 1986 (Scheme 2.6, equation 1).[3a] Enantiomerically enriched secondary propanediol-derived boronic ester **2.43** was activated by methyllithium to furnish **2.44**, which is more electrophilic compared to **2.43**. **2.44** was then treated with hydroxylamine-*O*-sulfonic acid. A C–N bond (**2.45**) was formed through 1,2-metallate shift. Finally, primary amine **2.46** was obtained in 76% yield and >98% enantiospecificity. In 2002, Knochel and co-workers reported a stereoretentive amination of a secondary boronic pinacol ester (**2.47**) (Scheme 2.6, equation 2).[3e] In this case, BCl_3 was employed to activate the boronic ester,[19] subsequent reaction with benzyl azide furnished "ate" complex **2.48**. Upon 1,2-metallate shift, benzyl-substituted amine **2.49** was obtained in 63% yield and >98% enantiospecificity.

[19] Chavant, P. Y.; Lhermitte, F.; Vaultier, M. *Synlett.* **1993**, 519–521.

In 2012, Morken and co-workers reported stereoretentive amination of secondary and tertiary boronic esters (Scheme 2.6, equation 3).[3c] Instead of activating the boronic ester to enhance its electrophilicity, the authors employed a strong nucleophile as the amination reagent. Addition of lithiated methoxyamine (MeONHLi) to boronic ester **2.50** proceeded smoothly, generating boron "ate" complex **2.51**. Subsequent 1,2-metallate shift and Boc protection afforded amination product **2.52** in 78% yield and full stereoretention. Notably, this method applies to not only primary and secondary alkylboronic esters, but also arylboronic esters.

Scheme 2.6. Amination of Alkylboronic esters



2.2.1.6 S_E2_{inv} reactions

In 1976, Brown and co-workers demonstrated that alkylboranes, activated by an alkoxide, can been iodinated with predominantly inversion of configuration (Scheme 2.7a).[20] It was proposed that the electron-rich C–B bond of the activated organoborane acts as nucleophile in reaction with iodine.

In 2011, the Aggarwal group reported that secondary boronic pinacol esters can be converted into reactive nucleophiles by the addition of aryllithium. The boron "ate" complexes (**2.53**) are configurationally stable and capable of reacting with a range of electrophiles, affording the products with inversion of stereochemistry (Scheme 2.7b).[21] With appropriate electrophiles, iodination (**2.54**), bromination (**2.55**), chlorination (**2.56**), and fluorination (**2.57**) were effective. Eschenmoser's salt and DBAD were also suitable electrophiles, affording the corresponding amines (**2.58**) and azo-products (**2.59**) with high enantiospecificity. Furthermore, reaction with tropylium tetrafluoroborate furnished **2.60** in 62% yield and complete stereoinversion. As a complementary approach to the stereoretentive oxidation of alkylboronic esters with peroxides,[2b] this study demonstrated a stereoinvertive oxidation with 2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate as an electrophilic oxidant. Secondary alcohol **2.61** was obtained in 64% yield and 70% enantiospecificity with inversion of stereochemistry.

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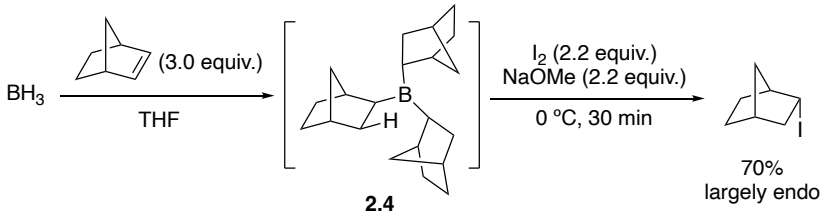
[20] (a) Brown, H. C.; De Lue, N. R.; Kabalka, G. W.; Hedgecock, H. C., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 1290–1291. (b) Bergbreiter, D. E.; Rainville, D. P. *J. Organomet. Chem*. **1976**, *121*, 19–23. (c) Kabalka, G. W.; Gooch, E. E., III. *J. Org. Chem.* **1980**, *45*, 3578–3580. (d) Hall, L. D.; Neeser, J. -R. *Can. J. Chem.* **1982**, *60*, 2082–2086. (e) Brown, H. C.; Lane, C. F.; De Lue, N. R. *Tetrahedron*. **1988**, *44*, 2773–2784.

[21] (a) Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133*, 16794–16797. (b) Mohiti, M.; Rampalakos, C.; Feeney, K.; Leonori, D.; Aggarwal, V. K. *Chem. Sci.* **2014**, *5*, 602–607. (c) Sandford, S.; Rasappan, R.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2015**, *137*, 10100−10103.

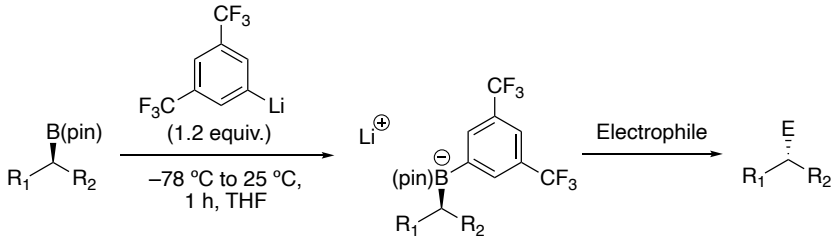
Scheme 2.7. Transformations of Alkylboronic Compounds through S_E2 Reactions

(a) Stereoinvertive iodonation of alkylboranes by Brown *et al.*

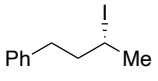
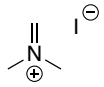
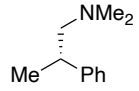
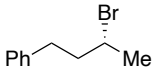
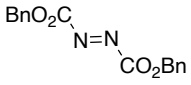
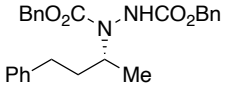
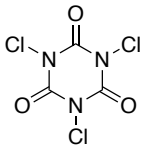
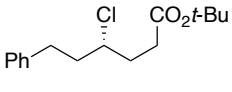
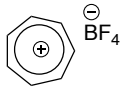
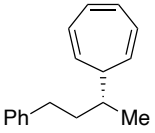
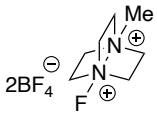
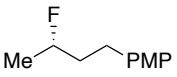
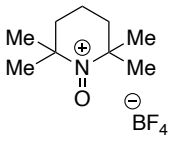
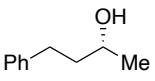


2.4

(b) Stereoinvertive transformations of alkylboronic esters by Aggarwal *et al.*



2.53

Electrophile	Product	Electrophile	Product
NIS	 **2.54**, 85% 99% es		 **2.58**, 64% 94% es
NBS	 **2.55**, 85% 100% es	 (DBAD)	 **2.59**, 66% 92% es
 (TCCA)	 **2.56**, 84% 100% es		 **2.60**, 62% 100% es
	 **2.57**, 83% 100% es		 **2.61**, 64% 70% es

2.2.2 Transition Metal-Catalyzed Stereospecific Functionalization of Alkylboronic Esters

The first example of stereospecific Suzuki-Miyaura cross-coupling of alkylboronic esters was demonstrated by Crudden and co-workers in 2009 (Scheme 2.8a).[22] With commercially available $Pd_2(dba)_3/PPh_3$ as catalyst, methyl-substituted benzylic boronic esters underwent cross-coupling with aryl iodides in a stereoretentive manner. Both electron rich (**2.63**) and electron poor (**2.62**) aryl iodides afforded moderate yields and excellent enantiospecificity. Aryl chlorides are orthogonal to this Pd-catalyzed coupling reaction (**2.64**). Later on, the group developed further the Pd-catalyzed cross-coupling reaction to enable the coupling of dibenzylic neopentyl glycol boronic esters.[23]

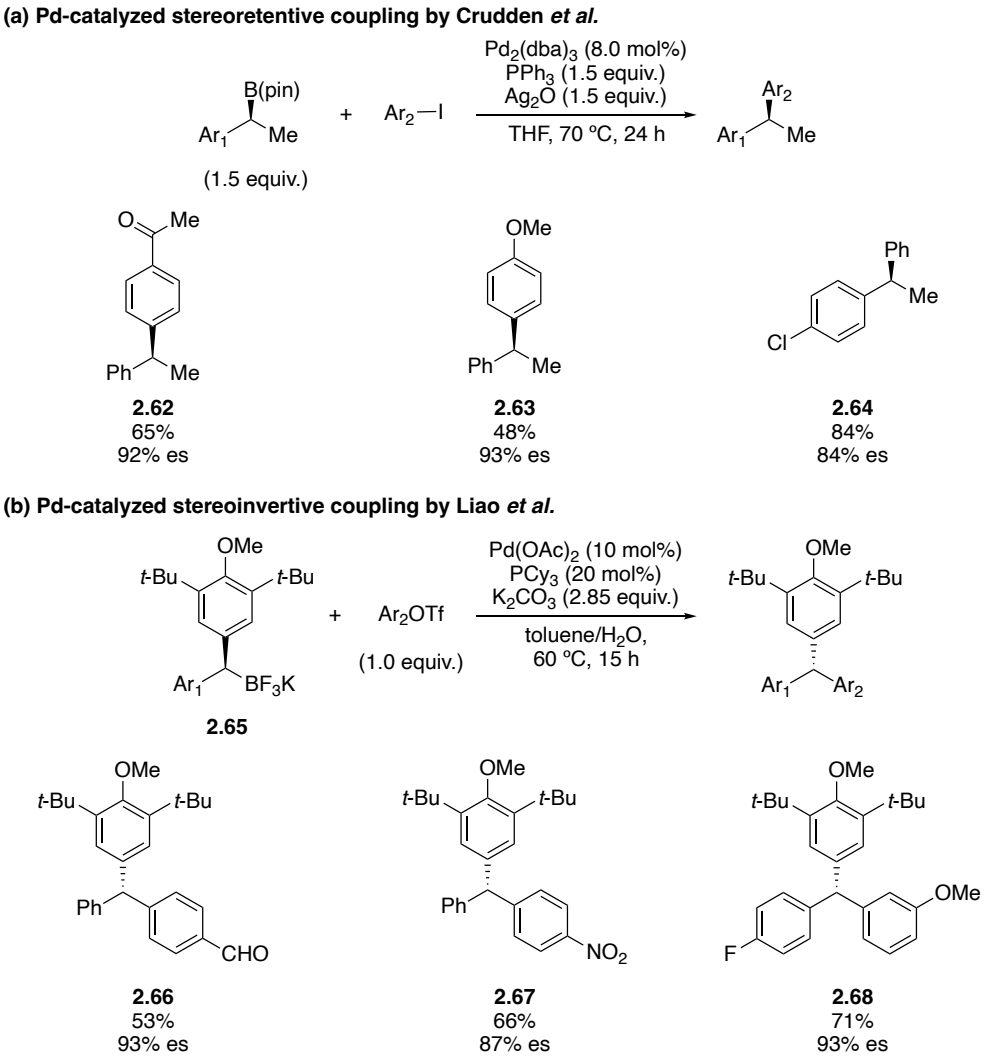
Liao and co-workers reported that although dibenzylic boronic esters underwent Pd-catalyzed cross-coupling with retention of stereochemistry, the corresponding trifluoroborates underwent the coupling with inversion of stereochemistry (Scheme 2.8b).[24] In their study, electron-rich dibenzylic trifluoroborate **2.65** coupled with aryl triflates in a stereoinvertive manner. Both electron rich (**2.68**) and electron deficient (**2.66**, **2.67**) aryl triflates proved to be effective.

[22] Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024–5025.

[23] Matthew, D. C.; Glasspole, B. W.; Eisenberger P.; Crudden, C. M. *J. Am. Chem. Soc.*, **2014**, *136*, 5828–5831.

[24] Lou, Y.; Cao, P.; Jia, T.; Zhang, Y.; Wang M.; Liao, J. *Angew. Chem., Int. Ed.*, **2015**, *54*, 12134–12138.

Scheme 2.8. Pd-Catalyzed Cross-Coupling of Benzylic Boronate Compounds



The first example of enantiospecific Suzuki-Miyaura coupling of unactivated alkylboronate compounds was reported by Biscoe and co-workers in 2014 (Scheme 2.9, equation 1).[25] Stereoinvertive cross-coupling of enantiomerically enriched secondary alkyltrifluoroborate **2.69** with chlorobenzene afforded **2.71** in 93% yield and 98% enantiospecificity. The bulky, electron-rich P(*t*-Bu)$_3$ ligand is crucial in suppressing *β*-hydride elimination and subsequent isomerization. In 2018, in collaboration with the Sigman group, Biscoe reported an

[25] Li, L.; Zhao, S.; Joshi-Pangu, A.; Diane, M.; Biscoe, M. R. *J. Am. Chem. Soc.* **2014**, *136*, 14027–14030.

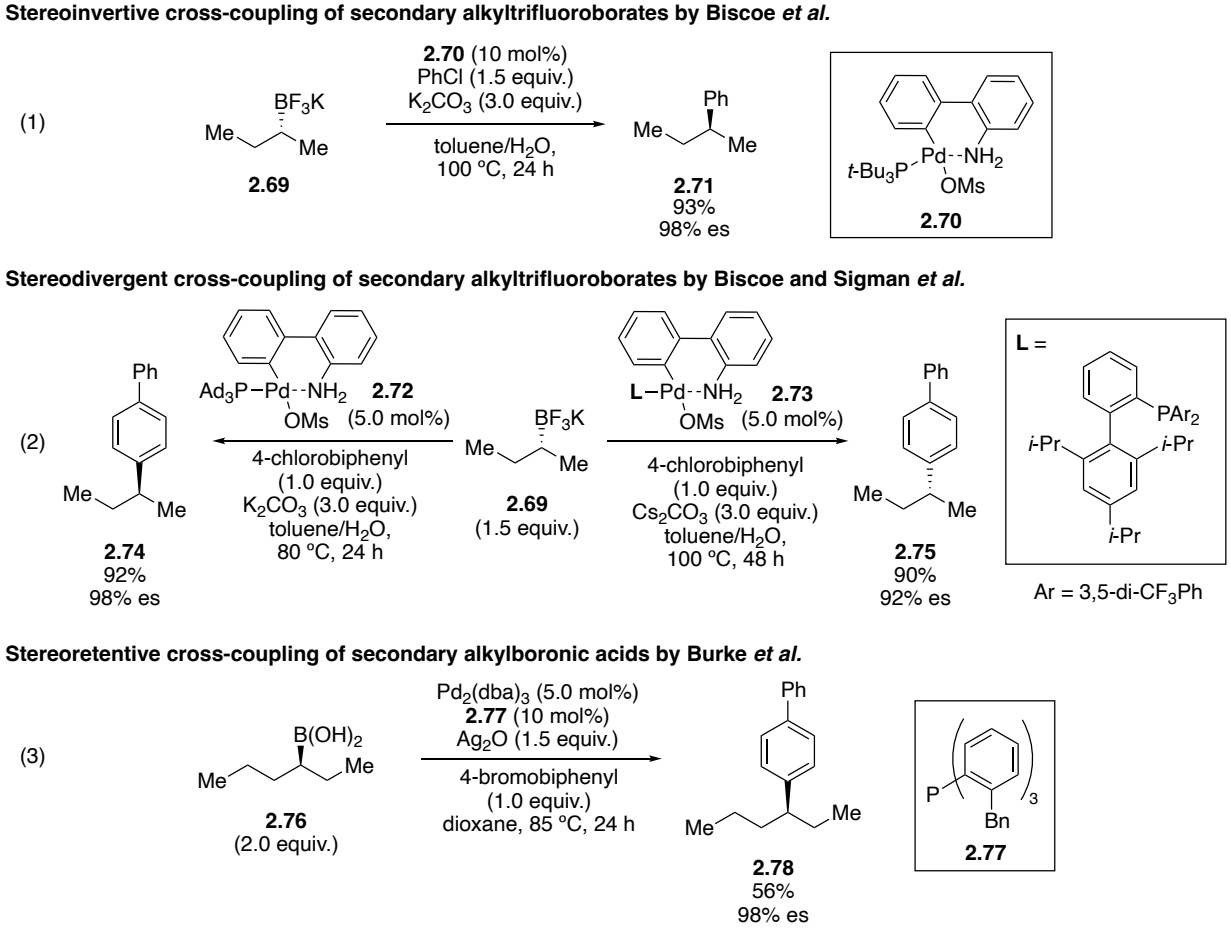
enantiodivergent Suzuki-Miyaura coupling method (Scheme 2.9, equation 2). The use of bulky, electron-rich tris(1-adamantyl)phosphine (PAd_3) in catalyst **2.72** resulted in a significant preference for the stereoinvertive outcome, furnishing product **2.74** in 92% yield and 98% enantiospecificity. Conversely, the use of catalyst **2.73** facilitated the stereoretentive outcome. The authors concluded that strongly π-accepting ligands preferentially promote the stereoretentive pathway, whereas strongly σ-donating ligands preferentially promote the stereoinvertive pathway.[26] Computational outcome suggested that the strong σ-donation from ligands such as PAd_3 may stabilize a two-coordinate, cationic palladium complex and promote stereoinvertive pathway. On the other hand, the stereoretentive pathway is enhanced by π-back bonding, which may stabilize the coordination of a π-donor ligand (presumably OH^-) to Pd.

In 2019, Burke and co-workers reported an example of stereoretentive coupling of unactived secondary boronic acids (Scheme 2.9, equation 3). With commercially available $Pd_2(dba)_3$/P(2-Bn-Ph)$_3$ as catalyst, unactivated secondary boronic acid (**2.76**) underwent coupling with an aryl bromide, affording the desired product in 56% yield and 98% enantiospecificity.[27] The authors reasoned that ligand P(2-Bn-Ph)$_3$ selectively shields the axial positions by projecting steric bulk above and below the Pd(II) square plane. The axial shielding effectively inhibited stereoinvertive transmetallation. As a result, high level of stereoretention was achieved.

[26] Zhao, S.; Gensch, T.; Murray, B.; Niemeyer, Z. L.; Sigman, M. S.; Biscoe, M. R. *Science* **2018**, *362*, 670–674.

[27] Lehmann, J. W.; Crouch, I. T.; Blair, D. J.; Trobe, M.; Wang, P.; Li, J.; Burke, M. D. *Nat. Commun.* **2019**, *10*, 1263–1271.

Scheme 2.9. Pd-Catalyzed Cross-Coupling of Unactivated Alkylboronate Compounds



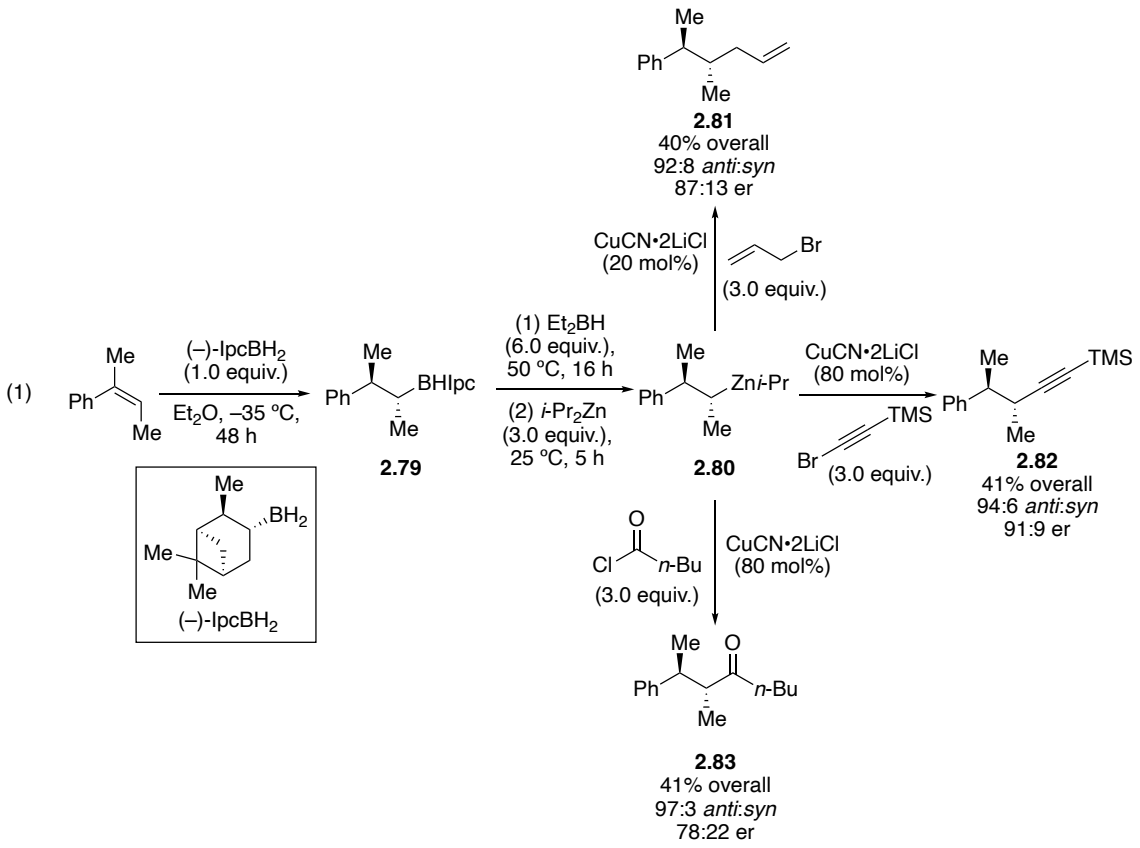
In 1998, Knochel and co-workers reported the first example of a stereospecific transformation from alkylborane **2.79** to the corresponding configurationally stable organozinc species **2.80** (Scheme 2.10, equation 1).[28] With 40–80 mol% CuCN•2LiCl, organozinc **2.80** underwent stereoretentive coupling with allylic halides (affording **2.81**), 1-bromoalkynes (affording **2.82**), and acid chlorides (affording **2.83**). Coupling products were afforded in up to 41% overall yield and 91:9 er.

[28] For selected reports on Cu-catalyzed coupling of organoboranes through the intermediacy of organozinc reagents, see: (a) Boudier, A.; Flachsmann, F.; Knochel, P. *Synlett* **1998**, *12*, 1438–1440. For diastereoselective examples, see: (b) Darcel, C.; Flachsmann, F.; Knochel, P. *Chem. Commun.* **1998**, *2*, 205–206. (c) Hupe, E.; Calaza, M. I.; Knochel, P. *J. Organomet. Chem.* **2003**, *680,* 136–142. (d) Hupe, E.; Calaza, M. I.; Knochel, P. *Chem. Eur. J.* **2003**, *9*, 2789–2796.

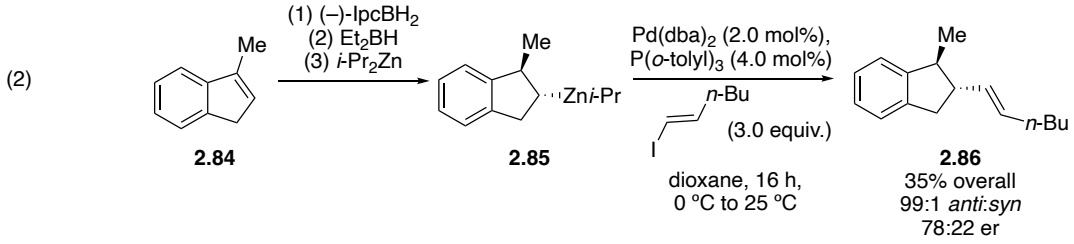
Subsequently, the Knochel group reported a Pd-catalyzed Negishi cross-coupling of enantiomerically enriched dialkylzinc species (**2.85**) with alkenyl iodides. The product (**2.86**) was obtained in 35% overall yield, 99:1 dr and 78:22 er (Scheme 2.10, equation 2). In a separate report, the authors showed that acid chlorides are also suitable electrophiles for stereospecific Negishi cross-coupling of dialkylzinc species.[29]

[29] For selected reports on Pd-catalyzed coupling of organoboranes through the intermediacy of organozinc reagents, see: (a) Boudier, A.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 687–690. See also: (b) Boudier, A.; Darcel, C.; Flachsmann, F.; Micouin, L.; Oestreich, M.; Knochel, *Chem. Eur. J.* **2000**, *6*, 2748–2761. (c) Thaler, T.; Haag, B.; Gavryushin, A.; Schober, K.; Hartmann, E.; Gschwind, R. M.; Zipse, H.; Mayer, P.; Knochel, P. *Nat. Chem.* **2010**, *2*, 125–130. (d) Thaler, T.; Guo, L.; Mayer, P.; Knochel, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 2174–2177.

Scheme 2.10. Transformation of Alkyl Boranes to Configurationally Stable Organozinc Species



Pd-catalyzed stereospecific cross-coupling of organozinc species



2.3 Development of Copper-Catalyzed Stereospecific Transformations of Alkylboronic Esters

2.3.1 Inspiration of the Reaction

So far, Pd-catalyzed stereospecific coupling of unactivated secondary acyclic alkylboron compounds has only been achieved by Biscoe and Sigman[25,26] for trifluoroborates and Burke[27] for boronic acids. Despite the high efficiency and enantiospecificity of these processes, their couplig partners are limited to C(sp^2) electrophiles. Compared to Pd catalysts, Cu catalysts exhibit reactivity with a broad scope of electrophiles.[30] Knochel and co-workers reported Cu-catalyzed coupling of organoboranes through the intermediacy of organozinc species.[28] However, to the extent of our knowledge, Cu-catalyzed cross-coupling with secondary alkylboronic esters is yet to be developed.

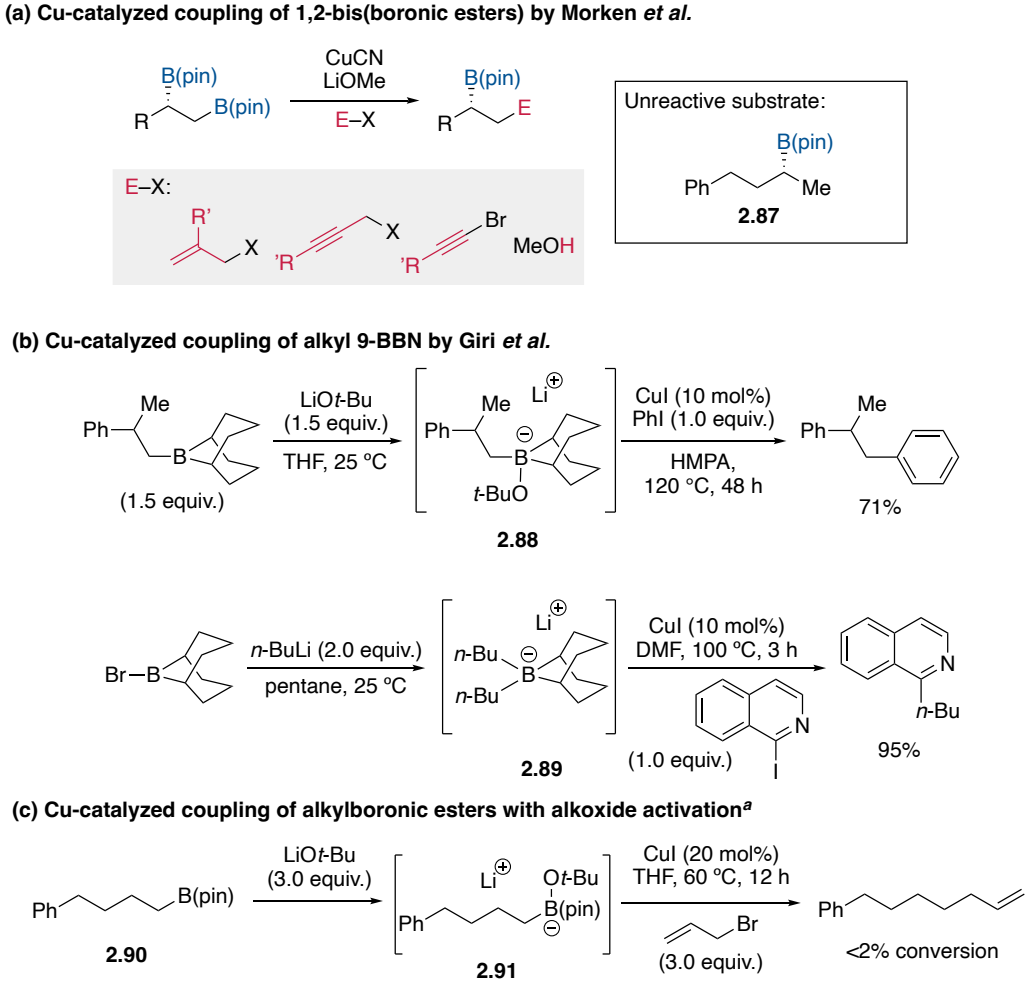
In Chapter 1, we described a copper-catalyzed site-selective cross-coupling of 1,2-bis(boronic esters) activated by methoxide (Scheme 2.11a).[31] The reactivity is dependent on the vicinal positioning of the boronic esters. We observed that secondary boronic esters (**2.87**) were unreactive under coupling conditions. When considering incorporation of unactivated secondary boronic esters in copper-catalyzed couplings, alternative activation methods become necessary. In 2016, Giri and co-workers demonstrated that both alkoxide-activated alkyl 9-BBN reagent (**2.88**) and 9-BBN-derived tetraalkylborate (**2.89**) underwent transmetallation to copper(I) iodide and subsequent cross-coupling with aryl iodides (Scheme 2.11b). However, when we treated alkylboronic ester **2.90** with alkoxide base, the so-formed four-coordinated boron "ate" complex

[30] For selected reviews on Cu-catalyzed cross-coupling reactions, see: (a) Thapa, S.; Shrestha, B.; Gurung, S. K.; Giri, R. *Org. Biomol. Chem.* **2015**, *13*, 4816−4827. (b) Evano, G.; Blanchard, N. *Copper-Mediated Cross-Coupling Reactions*; John Wiley & Sons: Hoboken, NJ, 2014.

[31] Xu, N.; Kong, Z.; Wang, J. Z.; Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 17815–17823.

2.91 did not undergo transmetallation to copper(I) iodide. Alkylboronic ester **2.90** was fully recovered after the reaction (Scheme 2.11c).

Scheme 2.11. Cu-Catalyzed Reactions of Boronic Compounds



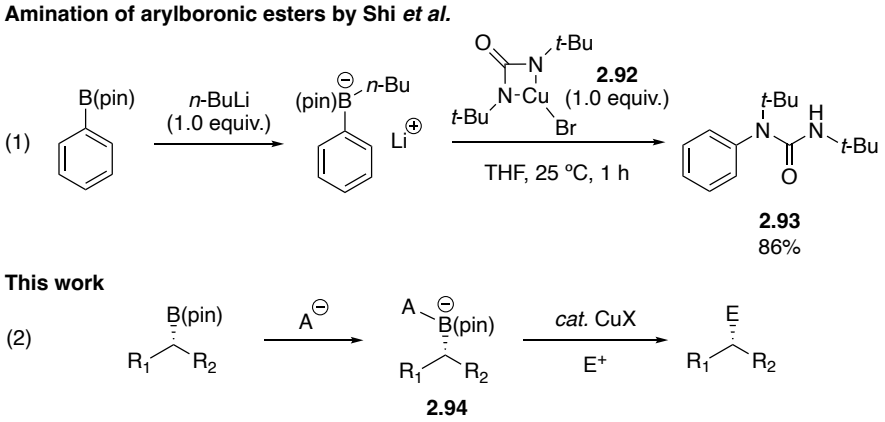
[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

In 2021, Shi and colleagues reported that a boron "ate" complex (aryl boronic ester activated by *n*-BuLi) coupled with Cu(III) complex **2.92** through transmetallation-reduction mechanism, furnishing amination product **2.93** in 86% yield (Scheme 2.12, equation 1).[32] We considered that

[32] (a) Li, J.; Wang, X.; Wang, Z.; Shi, Y. *Org. Lett.* **2021**, *23*, 8958–8962.

a Lewis basic activator capable of irreversibly forming the activated species **2.94** might effectively enable transmetallation (Scheme 2.12, equation 2).

Scheme 2.12. Transmetallation of Irreversibly Formed Boron "Ate" Complex to Cu-Complexes



As a strong Lewis base, alkyllithium has been employed to activate primary alkylboronic esters, arylboronic esters, and alkenylboronic esters, enabling transmetallation to Pd,[33] Ni,[34] Fe,[35] Zn,[36] Co[37] catalysts (Scheme 2.13). As far as we are aware, alkyllithium activation of secondary alkylboronic esters has heretofore remained undeveloped.

[33] Zou, G.; Falck, J. R. *Tetrahedron Lett.* **2001**, *42*, 5817–5819.

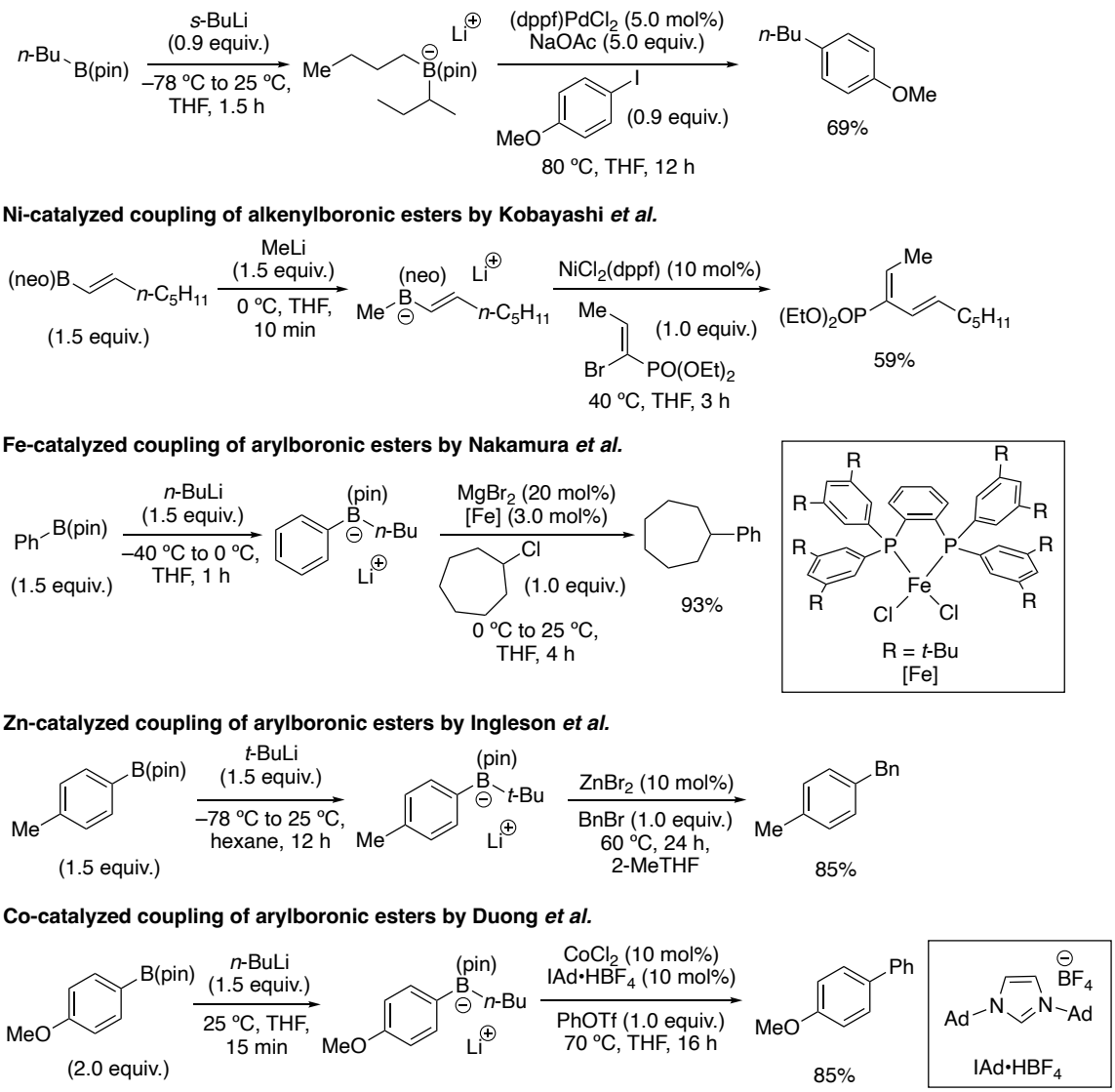
[34] (a) Kobayashi, Y.; William, A. D. *Org. Lett.* **2002**, *4*, 4241–4244. See also: (b)Kobayashi, Y.; Nakayama, Y.; Mizojiri, R. *Tetrahedron.* **1998**, *54*, 1053–1062.

[35] (a) Hatakeyama, T.; Hashimoto, T.; Kondo, Y.; Fujiwara, Y.; Seike, H.; Takaya, H.; Tamada, Y.; Ono, T.; Nakamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 10674–10676. See also: (b) Hashimoto, T.; Hatakeyama, T.; Nakamura, M. *J. Org. Chem.* **2012**, *77*, 1168–1173. (c) Hatakeyama, T.; Hashimoto, T.; Kathriarachchi, K. K. A. D. S.; Zenmyo, T.; Seike, H.; Nakamura, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 8834−8837. (d) Messinis, A. M.; Luckham, S. L. J.; Wells, P. P.; Gianolio, D.; Gibson, E. K.; O'Brien, H. M.; Sparkes, H. A.; Davis, S. A.; Callison, J.; Elorriaga, D.; Hernandez-Fajardo, O.; Bedford, R. B. *Nat. Catal.* **2018**, *2*, 123–133.

[36] (a) Procter, R. J.; Dunsford, J. J.; Rushworth, P. J.; Hulcoop, B. G.; Layfield, R. A.; Ingleson, M. J. *Chem. Eur. J.* **2017**, *23*, 15889–15893. See also: (b) Huang, W.; Hu, M.; Wan, X.; Shen, Q. *Nat. Commun*. **2019**, *10*, 2963–2971.

[37] (a) Duong, H. A.; Yeow, Z.-H.; Tiong, Y.-L. *J. Org. Chem.* **2019**, *84*, 12686–12691. See also: (b) Huang, W.; Wan, X.; Shen, Q. *Org. Lett.* **2020**, *22*, 4327−4332. (c) Asghar, S.; Tailor, S. B.; Elorriaga, D.; Bedford, R. B. *Angew. Chem., Int. Ed.* **2017**, *56*, 16367–16370.

Scheme 2.13. Representative Examples of Catalytic Coupling Reactions Enabled by Alkyllithium Activation



2.3.2 Optimization of Reaction Conditions

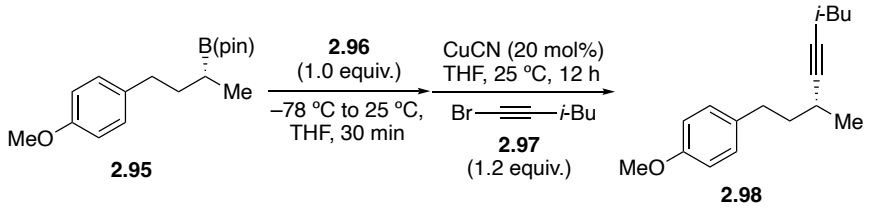
We examined alkyllithium, alkyl Grignard reagents and metal amide reagents as convenient and inexpensive activators for Cu-catalyzed stereospecific coupling of secondary alkylboronic esters. In these experiments, enantiomerically enriched secondary alkylboronic ester **2.95** was treated with slow addition of the activator in THF at –78 ºC (Table 2.1). In all cases except entries

8 and 10, ^{11}B NMR indicated >95% conversion to the corresponding four-coordinate "ate" complex. The "ate" complex was subsequently subjected to a Cu-catalyzed cross-coupling reaction with alkynyl bromide **2.97**.[38] The initial survey revealed CuCN to be an effective catalyst for the reaction of the *t*-BuLi-activated complex at ambient temperature, delivering the stereoretentive coupling product **2.98** in 90% yield and >98% enantiospecificity. When CuCl (entry 2) and CuBr (entry 3) were used instead of CuCN, both conversion and enantiospecificity were diminished. *t*-BuLi proved to be a superior activator (entry 1), relative to *s*-BuLi (entry 4), which delivered the product in 29% yield and >98% enantiospecificity. Reactions that employed *n*-BuLi (entry 5), PhLi (entry 6), $LiNEt_2$ (entry 7), and LiTMP (entry 9) as activators[39] afforded full conversion of the "ate" complex. However, these reactions furnished only trace amounts of cross-coupling product **2.98** and instead returned >95% of the alkylboronic ester substrate (**2.95**). We observed with mass spectrometry that the reactions with PhLi and *n*-BuLi activation furnished the product of the activator coupled to alkynyl bromide (**2.97**). LiHMDS (entry 8) and *t*-BuMgBr (entry 10) afforded low conversion of **2.95** to four-coordinate boron "ate" complex (<50% by ^{11}B NMR analysis). Both entries furnished no desired product (**2.98**). We consider that the successful reaction with *t*-BuLi as activator is due to it being electron rich yet encumbered enough that it does not undergo transmetallation itself.

[38] For selected reports on Cu-catalyzed coupling reaction with alkynyl halides: (a) Cahiez, G.; Gager, O.; Buenida, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1278−1281. (b) Cornelissen, L.; Lefrancq, M.; Riant, O. *Org. Lett.* **2014**, *16*, 3024−3027. (c) Wang, S.; Wang, M.; Wang, L.; Wang, B.; Li, P.; Yang, J. *Tetrahedron* **2011**, *67*, 4800−4806.

[39] For selected reports on Fe-catalyzed cross-coupling of aryl boronic esters with lithium amides as activators, see: (a) Crockett, M. P.; Wong, A. S.; Li, B.; Byers, J. A. *Angew. Chem., Int. Ed.* **2020**, *59*, 5392−5397. (b) Crockett, M. P.; Tyrol, C. C.; Wong, A. S.; Li, B.; Byers, J. A. *Org. Lett.* **2018**, *20*, 5233–5237. (c) Tyrol, C. C.; Yone, N. S.; Gallin, C. F.; Byers, J. A. *Chem.Commun.*, **2020**, *56*, 14661–14664.

Table 2.1. Effect of Activator on Cu-Catalyzed Coupling of Secondary Alkylboronic Esters[a]



entry	**2.96**	yield (%)	es (%)
1	*t*-BuLi	90	>98
2	*t*-BuLi (CuCl catalyst)	45	82
3	*t*-BuLi (CuBr catalyst)	41	75
4	*s*-BuLi	29	>98
5	*n*-BuLi	<5	na
6	PhLi	<5	na
7	$LiNEt_2$	<5	na
8	LiHMDS	<5	na
9	LiTMP	<5	na
10	*t*-BuMgBr	<5	na

[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%).

2.3.3 Substrate Scope

With conditions for efficient Cu-catalyzed cross-coupling of alkylboronic esters in hand, we surveyed a selection of alkynyl bromides in the reaction (Scheme 2.14). In addition to **2.96**, couplings with other alkynyl electrophiles were also found to afford enantiomerically enriched alkynes with up to 91% yield (**2.98**–**2.103**). Although unprotected bromoacetylene was incompatible with this reaction, the silyl-protected bromoacetylene was a suitable substrate and delivered the coupling product **2.103** in 81% yield and >98% enantiospecificity. Moreover, a single-step removal of the TMS group was accomplished by treatment with TBAF and effectively furnished the terminal alkyne **2.104**.

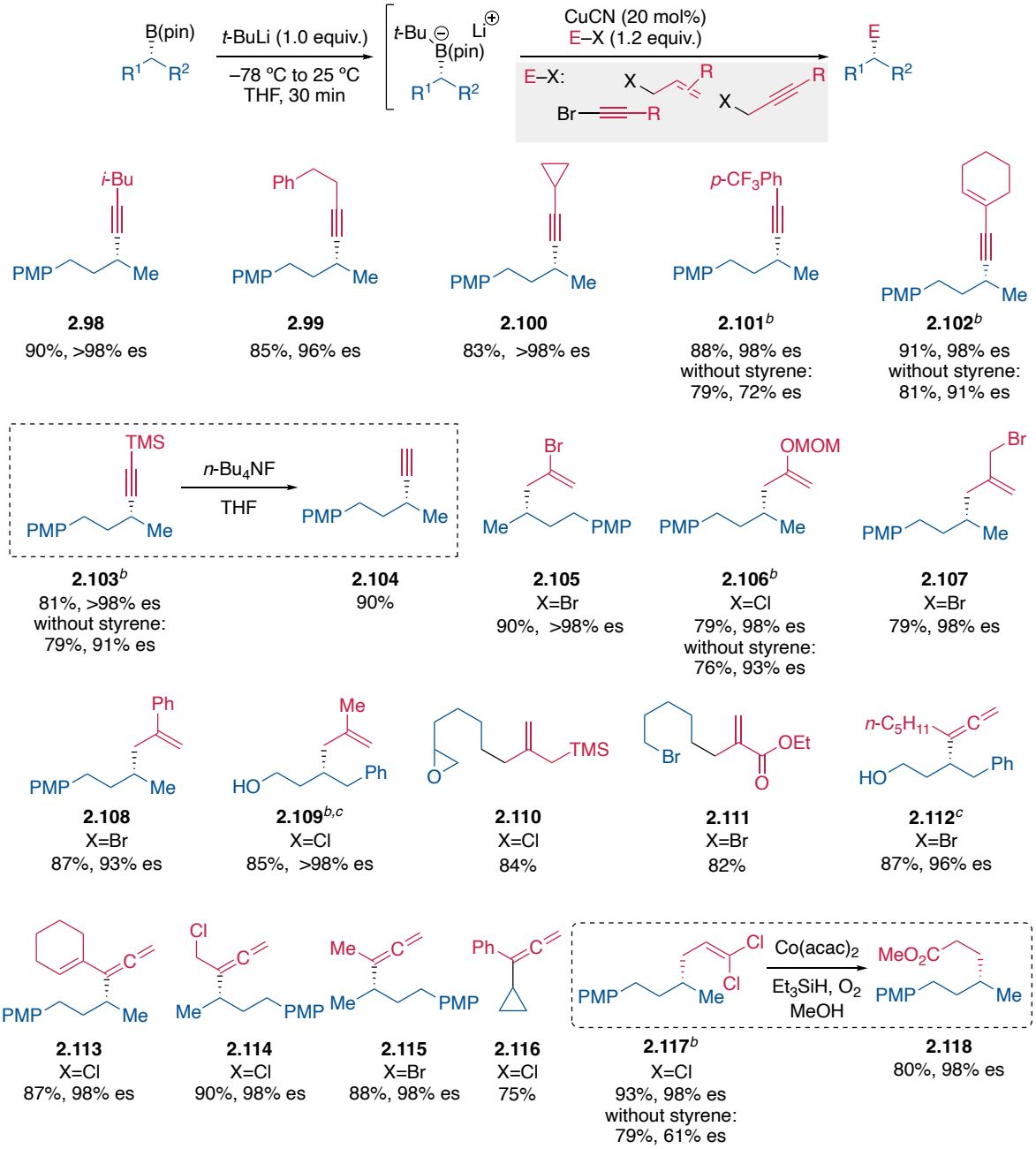
In addition to alkynyl bromides, the Cu-catalyzed coupling of boronic esters can be extended to allylic halides as shown in compounds **2.105**−**2.111**.[40] A wide selection of strategically functionalized substrates participated in thie reaction efficiently, furnishing products with alkenyl bromide (**2.105**), enol ether (**2.106**), allylic bromide (**2.107**), allyl silane (**2.110**), α,β-unsaturated ester (**2.111**), and geminal dichloroalkene (**2.117**) functional groups. Notably, the geminal dichloroalkene **2.117** was transformed to aliphatic ester **2.118** by Co-mediated oxidative hydrogen atom transfer.[41] Propargylic electrophiles also underwent coupling smoothly, offering an efficient route to enantiomerically enriched products containing 1,1-disubstituted allene (**2.112**−**2.116**).

Although *t*-BuLi activation might appear to pose a functional group compatibility challenge, due to the irreversible nature of boron "ate" complex formation, boronic ester substrates bearing epoxides (**2.110**), primary alkyl bromides (**2.111**), and silyl ethers (**2.109**, **2.112**) were tolerated in the reaction.

[40] For selected reviews on Cu-catalyzed allylic substitution, see: (a) Shintani, R. *Synthesis* **2016**, *48*, 1087−1100. (b) Zhou, F.; Cai, Q. *Beilstein J. Org. Chem.* **2015**, *11*, 2600−2615.

[41] Ma, X.; Herzon, S. B. *J. Org. Chem.* **2016**, *81*, 8673−8695.

Scheme 2.14. Copper-Catalyzed Coupling of Organoboronic Esters with Alkynyl, Allyl, and Propargyl Electrophiles[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%). [b]50 mol % Styrene was added. [c]Reactions were carried out at 60 °C. The substrates are the corresponding TBS ether, the TBS group was removed by treatment with TBAF solution after the reaction.

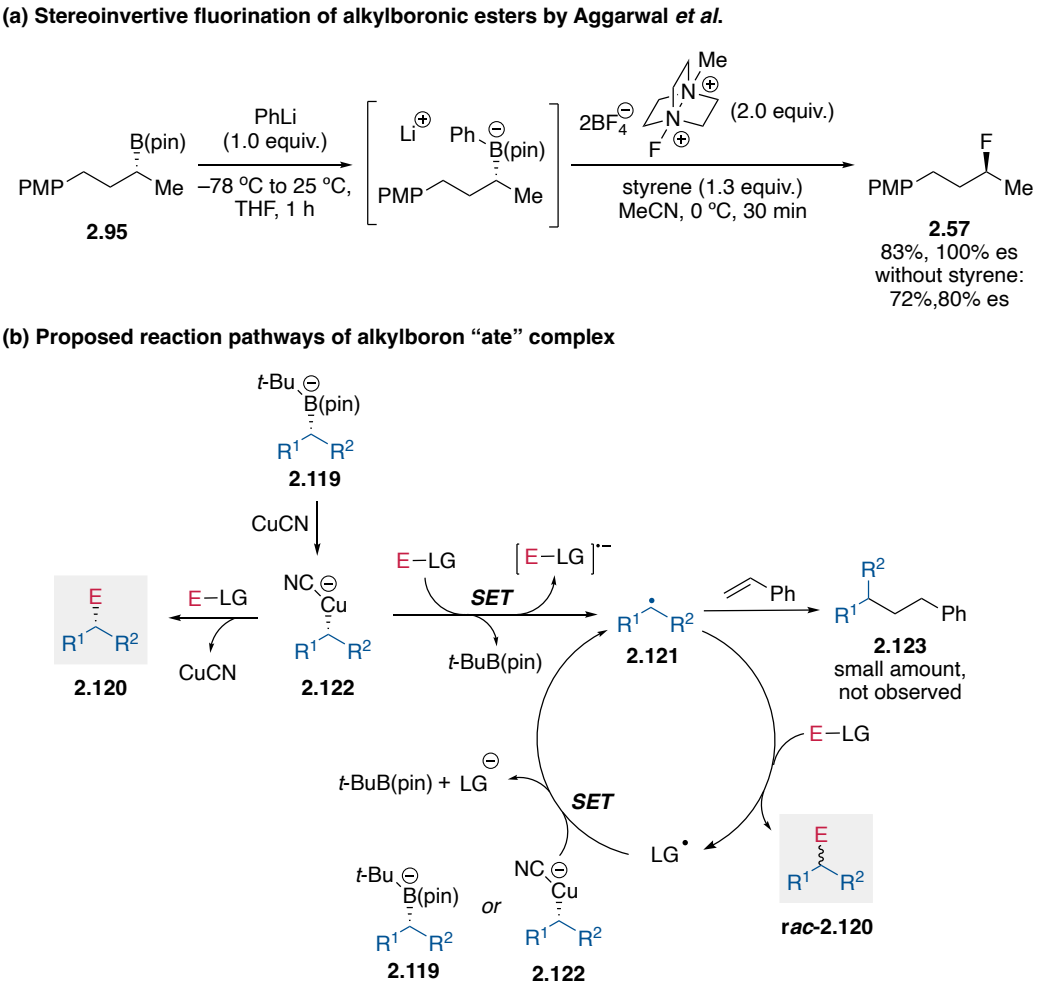
So far, we observed that for coupling reactions with some electrophiles (**2.101**, **2.102**, **2.103**, **2.106**, **2.117**), enantiospecificity was low, thereby suggesting a competing radical-based C−C

coupling pathway. Drawing inspiration from a report by Aggarwal and coworkers (Scheme 2.15a),[21c] we discovered that the inclusion of styrene restored stereospecificity to high levels. Notably, the presence of styrene improved the yields of the coupling reactions. Similar findings were reported by the Aggarwal group in their study.[21c]

We proposed that styrene acts as a scavenger, trapping propagating radical species (Scheme 2.15b). It is likely that boron "ate" complex **2.119** transmetallates to CuCN stereoretentively to furnish a configurationally stable cyano alkyl cuprate **2.122**. The cuprate (**2.122**) then reacts with electrophile to furnish stereoretentive product **2.120** and regenerates CuCN. It is plausible that the cuprate (**2.122**) may undergo single electron transfer (SET) with certain electrophiles and afford radical species **2.121**. It then reacts with the electrophile and furnishes racemic coupling product ***rac*-2.120**. The leaving group (LG) radical can undergo single electron transfer with either **2.119** or **2.122** to regenerate radical **2.121**. The radical propagation cycle could be inhibited by styrene, which traps nucleophilic alkyl radical **2.121**. The radical trapping product **2.123** was not detected by analysis of ^{1}H NMR spectra. The absence of detectable amount of **2.123** is in line with the observation that the yield of **2.120** was not diminished by the addition of radical scavenger. It is likely that only a very small amount of radical **2.121** needs to be intercepted in order to inhibit propagation.[42]

[42] For single electron transfer processes in Cu-catalyzed reactions, see: (a) Goj, L. A.; Blue, E. D.; Delp, S. A.; Gunnoe, T. B.; Cundari, T. R.; Petersen, J. L. *Organometallics* **2006**, *25*, 4097−4104. (b) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464−3484. (c) Ashby, E. C.; Coleman, D. *J. Org. Chem.* **1987**, *52*, 4554−4565. For reactions between alkyl radicals and styrene, see: (d) Moad, G.; Rizzardo, E.; Solomon, D. H. *Macromolecules* **1982**, *15*, 909−914.

Scheme 2.15. Reaction Pathways of Alkylboron "Ate" Complex

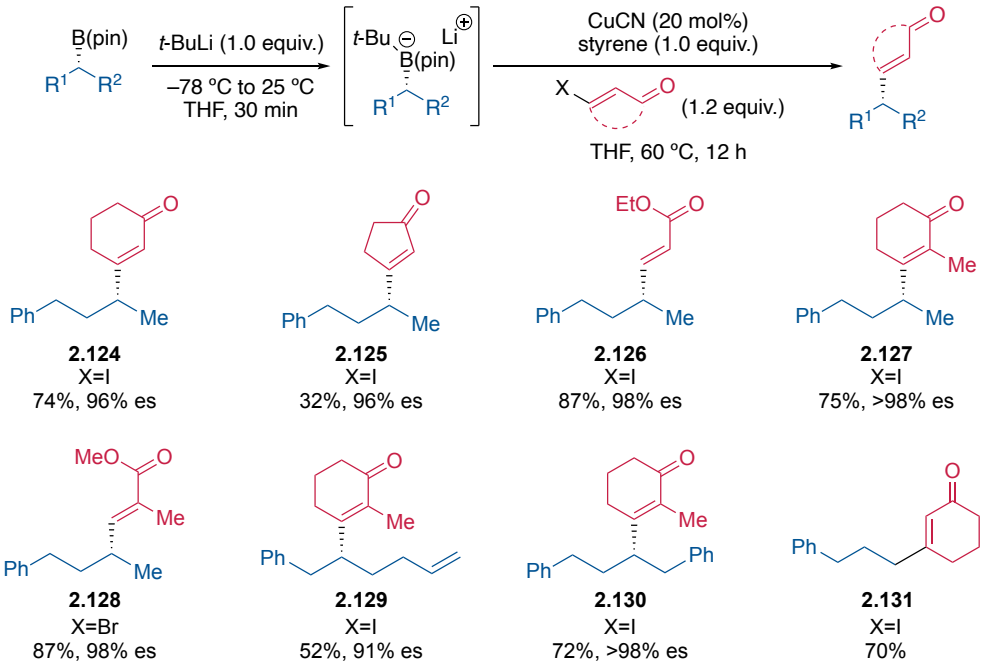


Because of the breadth of reactivity available in copper-catalyzed coupling reactions, a number of other processes were probed as useful stereospecific transformations of organoboronate compounds. Catalytic coupling to *β*-haloenones[43] proceeded effectively and with high levels of enantiospecificity in the presence of styrene (Scheme 2.16). In the absence of styrene, the coupling reactions with *β*-haloenones were efficient, but occurred with significant erosion of enantiomeric

[43] (a) Piers, E.; Nagakura, I. *J. Org. Chem.* **1975**, *40*, 2694−2696. (b) Dieter, R. K.; Silks, L. A.; Fishpaugh, J. R.; Kastner, M. E. *J. Am. Chem. Soc.* **1985**, *107*, 4679−4692. (c) Kremsmair, A.; Skotnitzki, J.; Knochel, P. *Chem. Eur. J.* **2020**, *26*, 11971−11973.

purity. A variety of di-, tri-, and tetrasubstituted β-haloenones, both cyclic and acyclic, participated in the reaction with up to >98% enantiospecificity.

Scheme 2.16. Copper-Catalyzed Coupling of Organoboronic Esters with β-Haloenones[a]



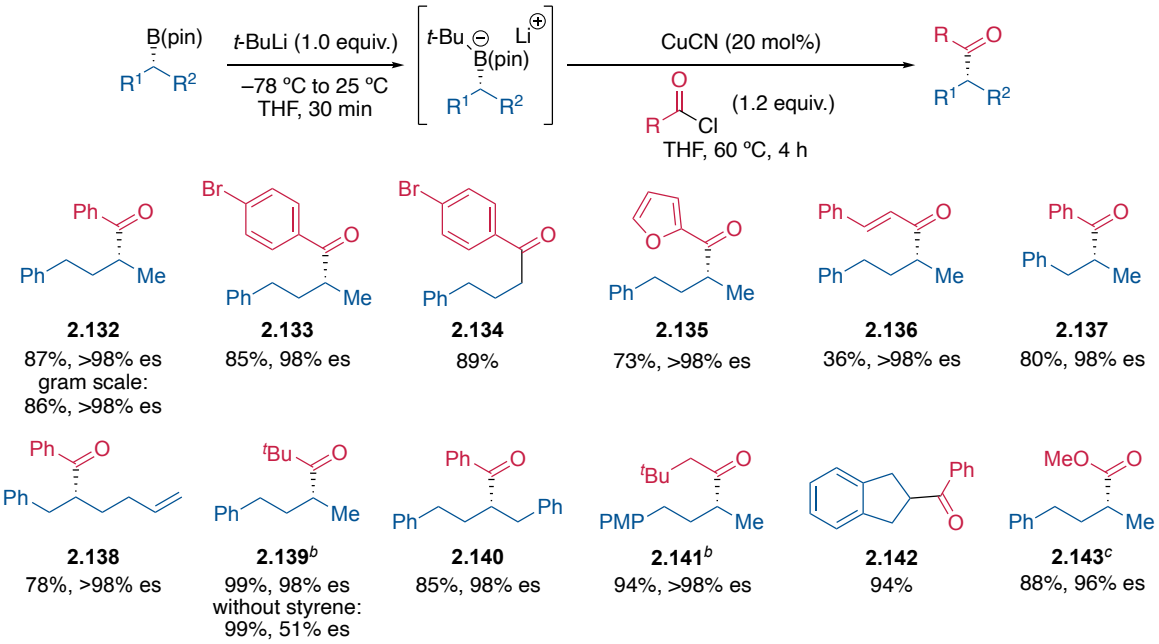
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%).

The use of acyl chlorides[44] as electrophiles in the copper-catalyzed coupling reaction also provided satisfactory results (Scheme 2.17). Our survey indicated that a number of acyl chlorides participated in this reaction. The coupling also occurred with an α,β-unsaturated acid chloride in 36% yield and >98% enantiospecificity (**2.136**). Methyl chloroformate underwent the coupling reaction, offering a direct pathway for converting the alkylboronic ester into the corresponding homologous carboxylic ester. **2.143** was obtained in 88% yield and 96% enantiospecificity. When

[44] For review, see: Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177−4236.

conducted on gram-scale, the coupling reaction (**2.132**) afforded similar result with small scale reaction, without significantly diminished yield or enantiospecificity.

Scheme 2.17. Copper-Catalyzed Coupling of Organoboronic Esters with Acyl Chlorides[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%). [b]Reactions were carried out in the presence of 50 mol% styrene. [c]Reactions were carried out in the presence of 300 mol% styrene.

Although many research groups have demonstrated efficient, stereoretentive, direct amination of secondary boronate compounds, these processes are limited to the synthesis of primary amine compounds.[3] Non-catalytic stereospecific amination to afford secondary amines is feasible, albeit it calls for the transformation of the boronic ester into the dihaloborane.[3d,e] Through organophosphorous catalysis, the stereospecific amination of boronic acids with nitroarenes offers a route to secondary anilines.[45] Only oxidative Chan-Lam couplings have proven effective for

[45] Nykaza, T. V.; Cooper, J. C.; Li, G.; Mahieu, N.; Ramirez, A.; Luzung, M. R.; Radosevich, A. T. *J. Am. Chem. Soc.* **2018**, *140*, 15200−15205.

direct amination of boronic esters to directly furnish secondary and tertiary alkyl amines. However, the oxidative Chan-Lam coupling reactions occur with stereoablation, presumably by way of radical intermediates.[46] As an alternative to these processes, we considered employing hydroxylamine esters as electrophiles in the copper-catalyzed coupling of alkylboronic esters.[47] Indeed, direct and stereospecific amination of a number of organoboronic esters was found to be efficient (Scheme 2.18). It is worth noting that three equivalents of CsF was found to enhance reaction efficiency, presumably by lithium-cesium ion exchange to furnish a more reactive "ate" complex with Cs as the cation.[48] We also observed that hydroxylamine esters are relatively potent oxidants, potentially oxidizing Cu(I) catalyst to inactive Cu(II) species, rendering the reaction inefficient. Addition of 40 mol% of PPh_3 was effective in preventing such oxidation in challenging reactions.[47h,49] Both cyclic and acyclic boronic esters underwent efficient stereoretentive amination, and a wide variety of secondary and tertiary amines were directly obtained as the products.

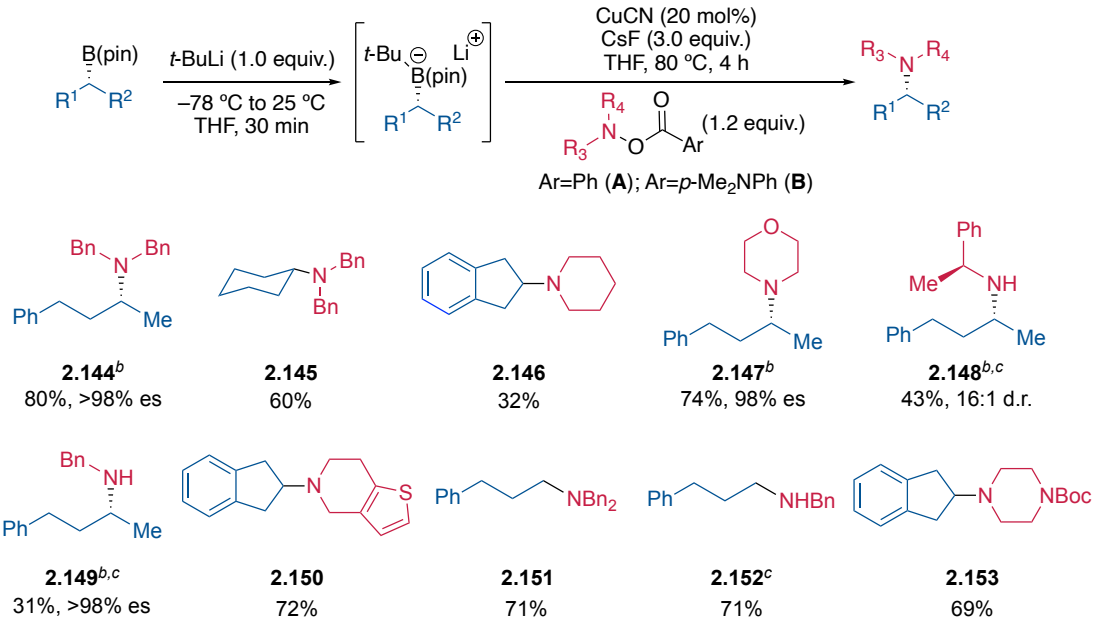
[46] (a) Mori-Quiroz, L. M.; Shimkin, K. W.; Rezazadeh, S.; Kozlowski, R. A.; Watson, D. A. *Chem. Eur. J.* **2016**, *22*, 15654−15658. (b) Racine, E.; Monnier, F.; Vors, J.-P.; Taillefer, M. *Chem. Commun.* **2013**, *49*, 7412−7414. (c) Grayson, J. D.; Dennis, F. M.; Robertson, C. C.; Partridge, B. M. *J. Org. Chem.* **2021**, *86*, 9883−9887.

[47] For selected reports on Cu-catalyzed reactions with hydroxylamine esters as electrophile, see: (a) Berman, A. M.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 5680−5681. (b) Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2007**, *9*, 1521−1524. (c) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3642−3645. (d) Rucker, R. P.; Whittaker, A. M.; Dang, H.; Lalic, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 3953−3956. (e) Rucker, R. P.; Whittaker, A. M.; Dang, H.; Lalic, G. *J. Am. Chem. Soc.* **2012**, *134*, 6571−6574. For selected reviews, see: (f) Yan, X.; Yang, X.; Xi, C. *Catal. Sci. Technol.* **2014**, *4*, 4169−4177. (g) Dong, X.; Liu, Q.; Dong, Y.; Liu, H. *Chem. Eur. J.* **2017**, *23*, 2481−2511. (h) Liu, R. Y.; Buchwald, S. L. *Acc. Chem. Res.* **2020**, *53*, 1229−1243. (i) Hirano, K.; Miura, M. *J. Am. Chem. Soc.* **2022**, *144*, 648−661.

[48] (a) Meng, Y.; Kong, Z.; Morken, J. P. *Angew. Chem., Int. Ed.* **2020**, *59*, 8456−8459. (b) Loupy, A.; Tchoubar, B. *Salt Effects in Organic and Organometallic Chemistry*; VCH: Weinheim, 1992; p 1−6.

[49] Ichikawa, S.; Zhu, S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2018**, *57*, 8714−8718.

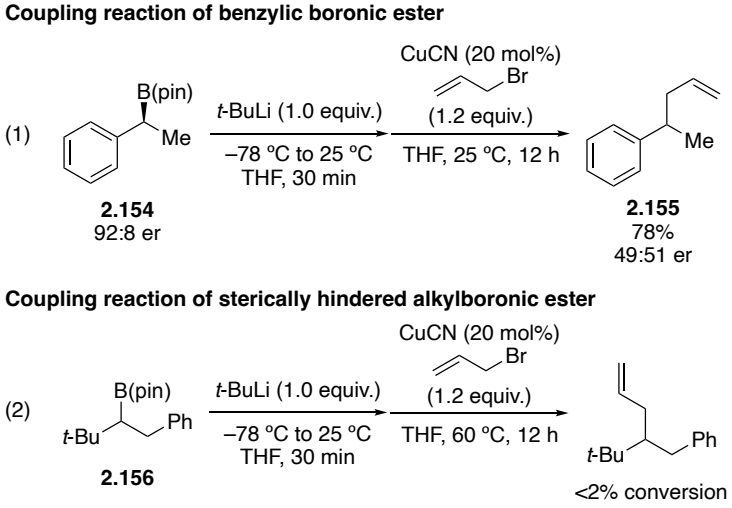
Scheme 2.18. Copper-Catalyzed Coupling of Organoboronic Esters with Hydroxylamine Esters[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%). Reactions were carried out with reagent **A** (Ar=Ph) as electrophile unless noted otherwise. [b]Reactions were carried out in the presence of 50 mol% styrene. [c]Reactions were carried out with reagent **B** (Ar=*p*-Me_2NPh) as electrophile, in the presence of 40 mol% triphenylphosphine.

It is worth noting that benzylic boronic ester (**2.154**) underwent copper-catalyzed coupling reaction to furnish the allylation product **2.155** in 78% yield, albeit in a racemic fashion (Scheme 2.19, equation 1). Sterically hindering groups such as *tert*-butyl group α to the boronic ester (**2.156**) completely inhibited the reaction (Scheme 2.19, equation 2).

Scheme 2.19. Functional Group Compatibility of Cu-Catalyzed Coupling Reaction[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios were determined by analysis of chiral SFC (±1%). Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

2.3.4 Utility of Copper-Catalyzed Stereospecific Transformations of Alkylboronic Esters

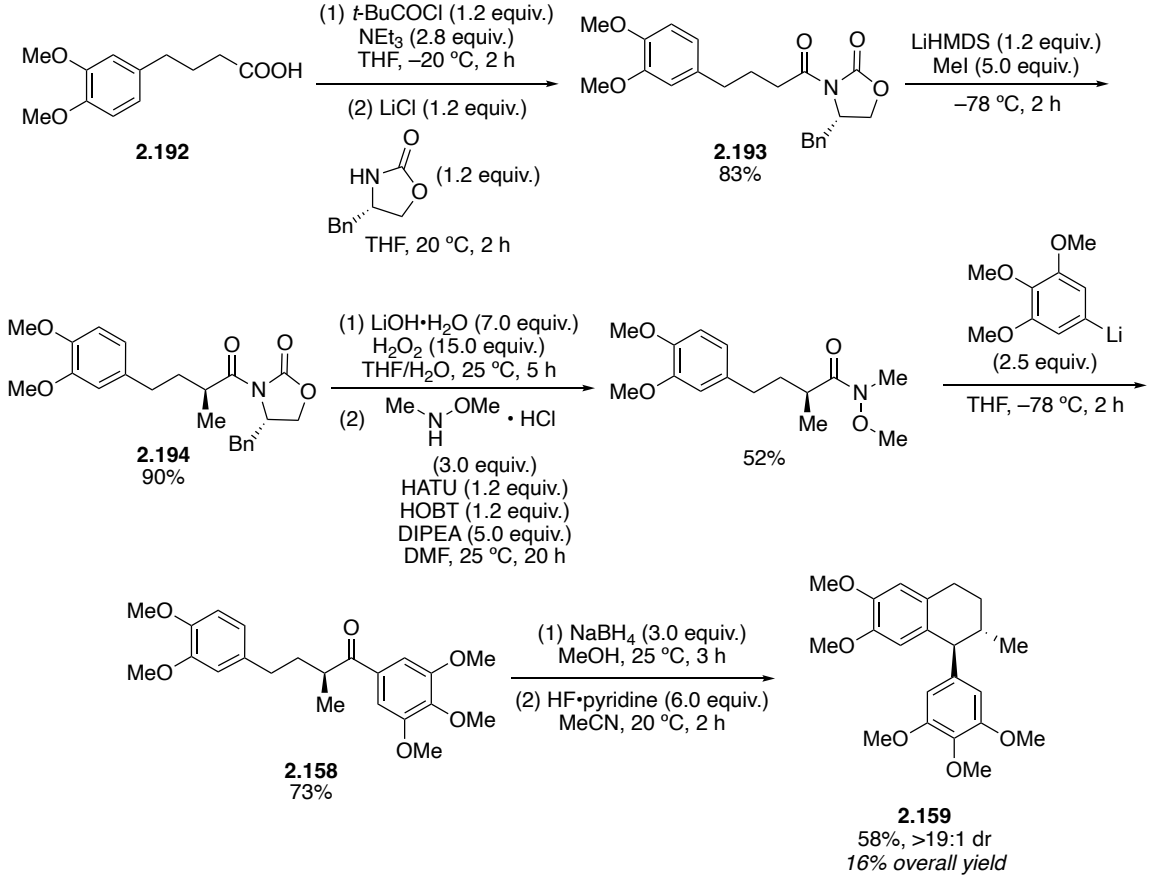
With an effective strategy for stereospecific transformation of chiral secondary boronic esters, we employed the Cu-catalyzed coupling on highly oxygenated substrates. In 2018, Xie and co-workers reported the enantioselective synthesis of the anti-HIV compound **2.159**,[50] a derivative of natural product Galbulin.[51] The strategy involved diastereoselective methylation of an Evans *N*-oxazolidinone **2.193** (Scheme 2.20). Starting from 4-(3,4-dimethoxyphenyl)butanoic acid (**2.192**), **2.193** was obtained in 83% yield over two steps. Deprotonation of **2.193** followed by methylation afforded **2.194** in 90% yield. **2.194** was then transformed to a Weinreb amide, which was then treated with (3,4,5-trimethoxyphenyl)lithium to furnish ketone **2.158** in 73% yield.

[50] Liu, X.; Chen, P.; Li, X.; Ba, M.; Jiao, X.; Guo, Y.; Xie, P. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 1699−1703.

[51] For isolation of Galbulin, see: (a) Hughes, G.; Ritchie, E. *Aust. J. Chem.* **1954**, *7*, 104−112. For synthesis of (+)-Galbulin, see: (b) Clausen, F.; Studer, A. *Org. Lett.* **2020**, *22*, 6780–6783.

Finally, reduction of ketone **2.158** and subsequent intramolecular aromatic substitution furnished **2.159** in 16% overall yield.

Scheme 2.20. Synthesis of Bioactive Galbulin Derivative **2.159** by Xie *et al.*

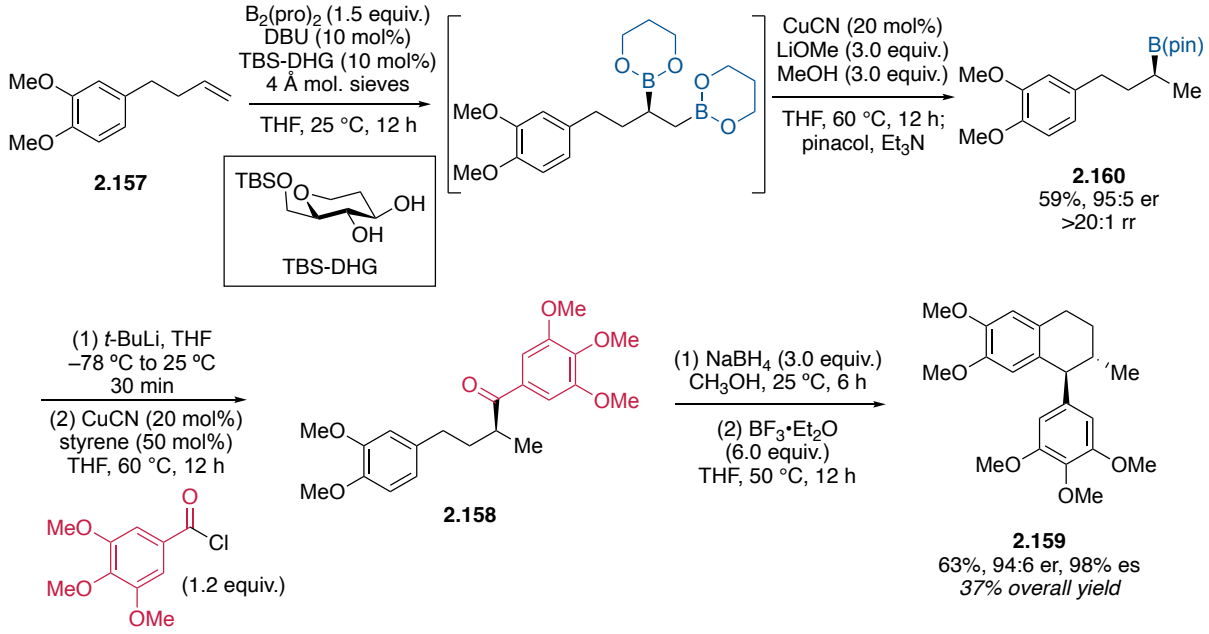


We conducted carbohydrate-catalyzed enantioselective diboration of the terminal alkene **2.157**,[52] followed by Cu-catalyzed regioselective protodeboration.[31] Enantiomercially enriched secondary boronic ester **2.160** was obtained in 59% yield, 95:5 er and >20:1 rr. The Cu-catalyzed coupling with acyl chloride proceeded smoothly to afford ketone **2.158**. Then, we conducted ketone reduction and intramolecular aromatic substitution. The reactions in this three-step sequence were efficient enough that isolation and purification of intermediate **2.158** were not

[52] Yan, L.; Meng, Y.; Haeffner, F.; Leon, R. M.; Crockett, M. P.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 3663−3673.

required. **2.159** was isolated in 37% overall yield and 98% enantiospecificity. Compared to the previous synthesis by Xie and co-workers, our strategy does not require an auxiliary and thereby offers a shorter route with higher overall yield.

Scheme 2.21. Application of Cu-Catalyzed Coupling to the Synthesis of Galbulin Derivative **2.159**[a]



[a]Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios and enantiospecificity (es) values were determined by analysis of chiral SFC (±1%). Regioisomeric ratios were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

2.4 Conclusions

We have developed a stereospecific copper-catalyzed coupling of organoboronic esters with a wide selection of electrophiles, delivering products with synthetically useful moieties. Through this method, C(sp^3)–B bonds can be transformed to C(sp^3)–C(sp^3), C(sp^3)–C(sp^2), C(sp^3)–C(sp), C(sp^3)–N bonds in a stereoretentive fashion. The coupling reactions require only commercially available and inexpensive activator and catalyst, and they occur with an operationally simple

procedure and often with good efficiency. This process may extend the application scope of the array of synthetic methods that produce unactivated chiral alkylboronic esters.

2.5 Acknowledgments

I thank Prof. James P. Morken for providing me the opportunity to start and study this project. I deeply appreciate Hao Liang for his valuable contribution to this project. I am also grateful for the discussions with all the other Morken group members.

This work was supported financially by the NIH (R35-GM1217140). We thank Boston College and the chemistry department for assistance.

2.6 Experimental Section

2.6.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (126 MHz), Varian Gemini-600 (151 MHz) or a Varian Inova-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer.^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as

follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed with 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 aluminum-backed plates from Silicycle. Visualization was performed with ultraviolet light (254 nm), or potassium permanganate stain ($KMnO_4$, sodium carbonate, and water), or CAM stain (ammonium molybdate tetrahydrate, cerium ammonium sulfate dehydrate, sulfuric acid).

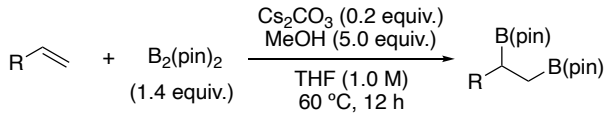
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector, or Jasco AS-4350 SFC Autosampler with Jasco CO-4065 Column Oven and Jasco MD-4017 Photo Diode Array Detector with isopropanol or methanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified by Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. All other reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without purification.

2.6.2 Experimental Procedures

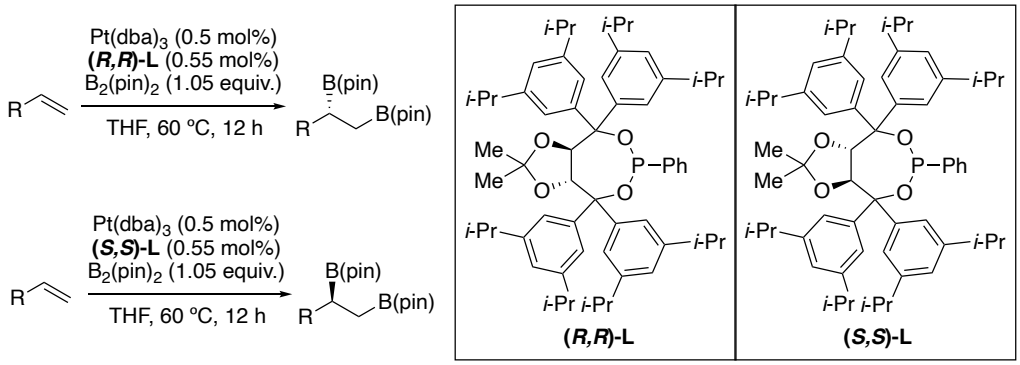
2.6.2.1 Procedures for Preparation of Boronic Substrates

General Procedure A: Preparation of racemic 1,2-bis(boronic pinacol esters)



Racemic 1,2-bis(boronic pinacol esters) were prepared according to a modified literature procedure.[53] Cesium carbonate (0.20 equiv.) and bis(pinacolato)diboron (1.40 equiv.) were transferred into an oven-dried flask with a stir bar, under argon. THF (1.0 M) was added to dissolve the mixture. Subsequently, the alkene (1.0 equiv.) and MeOH (5.0 equiv.) were added, and the mixture was allowed to stir at 60 ºC overnight, after which it was filtered through a plug of silica gel. The mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography.

General Procedure B: Preparation of enantiomerically enriched 1,2-bis(boronic pinacol esters)

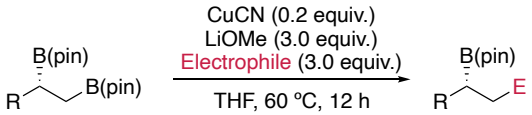


Enantiomerically enriched 1,2-bis(boronic pinacol esters) were prepared according to a literature procedure.[54] To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (0.5 mol%), (*R,R*)-L or (*S,S*)-L (0.55 mol%), and $B_2(pin)_2$ (1.05 equiv.). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added

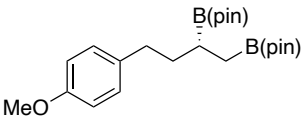
[53] Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyás, H.; Fernández, E. *Angew. Chem., Int. Ed.* **2011**, *50*, 7158–7161.
[54] Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222–11231.

by syringe, and the mixture was allowed to stir at 80 °C for 30 min. The flask was then allowed to cool to room temperature and was charged with terminal alkene (1.0 equiv.). After purging once more with N_2, the mixture was allowed to stir at 60 ºC overnight. It was then filtered through a silica gel plug and concentrated under reduced pressure. The residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the products.

General Procedure C: Preparation of secondary boronic pinacol esters

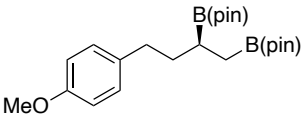


Secondary boronic pinacol esters were prepared according to a literature procedure.[31] To an oven-dried round-bottom flask equipped with a magnetic stir bar in an Ar-filled glovebox was added copper cyanide (0.20 equiv.), lithium methoxide (3.0 equiv.), 1,2-bis(boronic ester) (1.0 equiv.), electrophile (3.0 equiv.) and THF (0.4 M). The reaction flask was sealed with a polypropylene cap, taped and brought out of the glovebox. The mixture was allowed to stir at 60 °C for 16 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether, filtered through a silica gel plug, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (5% ethyl acetate in hexanes).

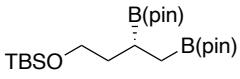


(*R*)-2,2'-(4-(4-Methoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.161). The title compound was prepared according to *General Procedure B* with 1-(but-3-en-1-yl)-4-methoxybenzene (1.6 g, 10.0 mmol), $B_2(pin)_2$ (2.7 g, 10.5 mmol), $Pt(dba)_3$ (44.9 mg, 0.05 mmol), (*R,R*)-**L** (50.01 mg, 0.055 mmol) in THF. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.5 g, 8.4 mmol, 84% yield) as pale-yellow oil. All

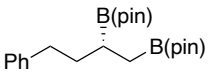
spectral data are in accordance with the literature.[13d] The title compound was subjected to transformations without analysis of stereochemistry.



(*S*)-2,2'-(4-(4-Methoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S-2.161). The title compound was prepared according to *General Procedure B* with 1-(but-3-en-1-yl)-4-methoxybenzene (1.6 g, 10.0 mmol), $B_2(pin)_2$ (2.7 g, 10.5 mmol), $Pt(dba)_3$ (44.9 mg, 0.05 mmol), (*S,S*)-**L** (50.01 mg, 0.055 mmol) in THF. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.7 g, 8.9 mmol, 89% yield) as pale-yellow oil. All spectral data are in accordance with the literature.[13d] The title compound was subjected to transformations without analysis of stereochemistry.



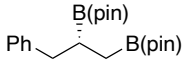
(*R*)-(3,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-butyl)dimethylsilane (2.162). The title compound was prepared according to *General Procedure B* with (but-3-en-1-yloxy)(*tert*-butyl)dimethylsilane (1.5 g, 8.0 mmol), $B_2(pin)_2$ (2.1 g, 8.4 mmol), $Pt(dba)_3$ (35.9 mg, 0.040 mmol), (*R,R*)-**L** (40.0 mg, 0.044 mmol) in THF. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.2 g, 7.3 mmol, 90% yield) as colorless oil. All spectral data are in accordance with the literature.[55] The title compound was subjected to transformations without analysis of stereochemistry.



(*R*)-2,2'-(4-Phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.163). The title compound was prepared according to *General Procedure B* with pent-4-enylbenzene (2.9 g, 20.0 mmol), $B_2(pin)_2$ (5.3 g, 21.0 mmol), $Pt(dba)_3$

[55] Blaisdell, T. P.; Morken, J. P. *J. Am. Chem. Soc.* **2015**, *137*, 8712–8715.

(44.9 mg, 0.050 mmol), (*R,R*)-**L** (54.6 mg, 0.060 mmol) in THF. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (7.7 g, 19.9 mmol, 99% yield) as yellow oil. All spectral data are in accordance with the literature.[15c] The title compound was subjected to transformations without analysis of stereochemistry.



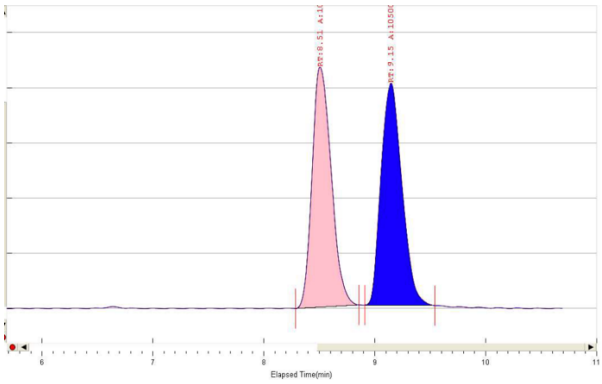
***(R)*-2,2'-(3-Phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.164).** The title compound was prepared according to *General Procedure B* with prop-3-enylbenzene (590.9 mg, 5.0 mmol), $B_2(pin)_2$ (1.3 g, 5.25 mmol), $Pt(dba)_3$ (22.4 mg, 0.025 mmol), (*R,R*)-**L** (27.3 mg, 0.030 mmol) in THF. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (1.7 g, 4.5 mmol, 90% yield) as colorless oil. All spectral data are in accordance with the literature.[3b]

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

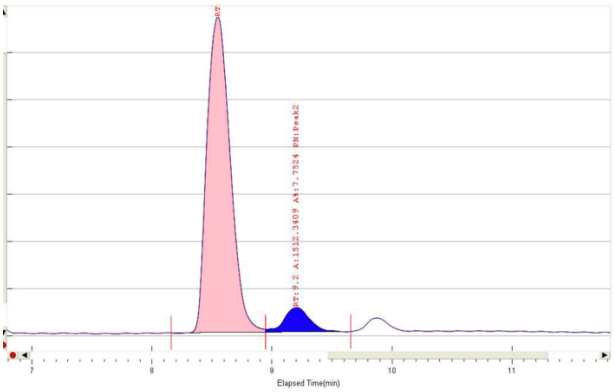
Chiral SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 3-phenylpropane-1,2-diol

Racemic compound

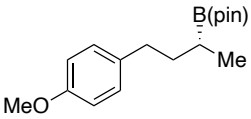


Peak No	% Area	Area	RT (min)
1	49.5065	14642.1097	7.93
2	50.4935	14934.0008	8.39
Total:	100	29576.1105	

Standard conditions



Peak No	% Area	Area	RT (min)
1	4.2255	324.0127	7.92
2	95.7745	7344.0845	8.4
Total:	100	7668.0972	



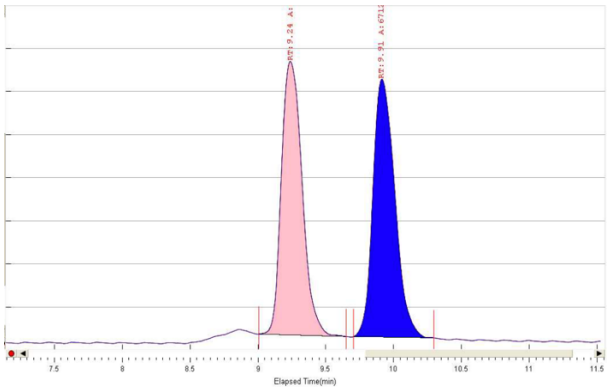
(*R*)-2-(4-(4-Methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.95). The title compound was prepared according to *General Procedure C* with (*R*)-2,2'-(4-(4-methoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) **(2.161)** (3.3 g, 8.0 mmol), methanol (as electrophile) (769 mg, 24.0 mmol), copper (I) cyanide (143.3 mg, 1.6 mmol), lithium methoxide (911.3 mg, 24.0 mmol). The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (2.1 g, 7.2 mmol, 91% yield) as colorless oil. All spectral data are in accordance with the literature.[21a]

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

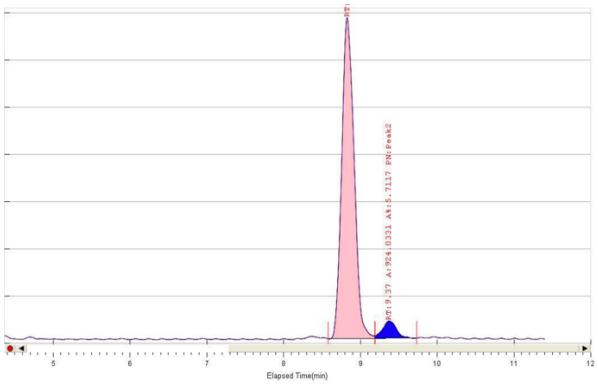
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 4-(4-methoxyphenyl)butan-2-ol

Racemic compound



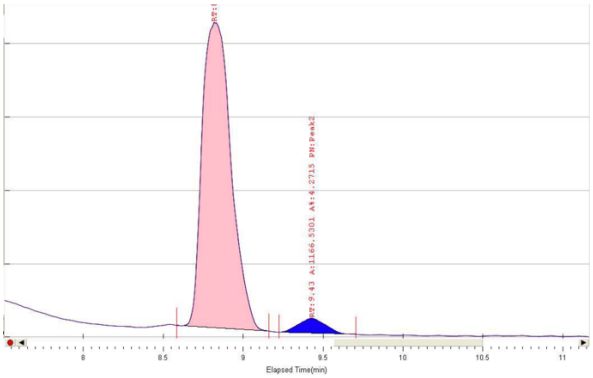
Peak No	% Area	Area	RT (min)
1	50.1065	6741.1192	9.24
2	49.8935	6712.4692	9.91
Total:	100	13453.5884	

Standard Conditions (first run)

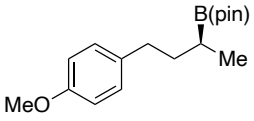


Peak No	% Area	Area	RT (min)
1	94.2883	15253.9114	8.83
2	5.7117	924.0331	9.37
Total:	100	16177.9445	

Standard Conditions (second run)



Peak No	% Area	Area	RT (min)
1	95.7285	26143.119	8.82
2	4.2715	1166.5301	9.43
Total:	100	27309.6491	



(*S*)-2-(4-(4-Methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S-2.95). The title compound was prepared according to *General Procedure C* with (*S*)-2,2'-(4-(4-methoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-

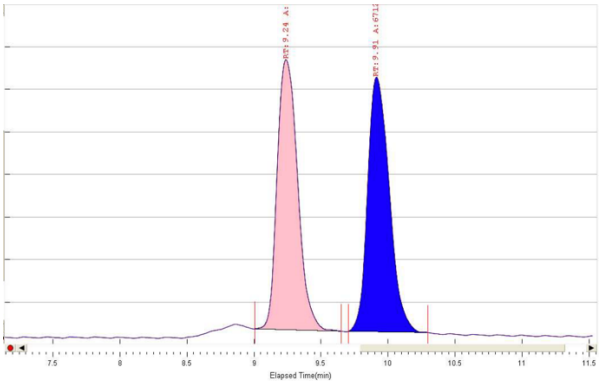
1,3,2-dioxaborolane) **(S-2.161)** (3.3 g, 8.0 mmol), methanol (as electrophile) (769 mg, 24.0 mmol), copper (I) cynanide (143.3 mg, 1.6 mmol), lithium methoxide (911.3 mg, 24.0 mmol). The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (2.2 g, 7.6 mmol, 94% yield) as colorless oil. All spectral data are in accordance with the literature.[21a]

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

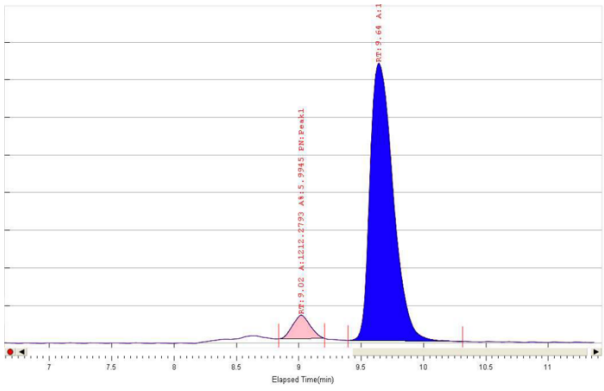
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 4-(4-methoxyphenyl)butan-2-ol

Racemic Compound



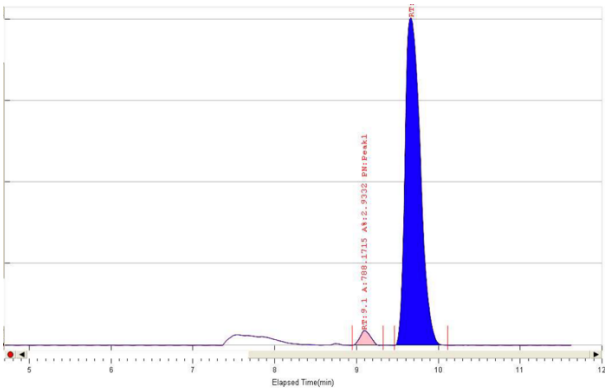
Peak No	% Area	Area	RT (min)
1	50.1065	6741.1192	9.24
2	49.8935	6712.4692	9.91
Total:	100	13453.5884	

Standard Conditions (first run)

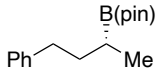


Peak No	% Area	Area	RT (min)
1	5.9945	1212.2793	9.02
2	94.0055	19011.0619	9.64
Total:	100	20223.3412	

Standard Conditions (second run)



Peak No	% Area	Area	RT (min)
1	2.9332	788.1715	9.1
2	97.0668	26082.5432	9.67
Total:	100	26870.7147	



(*R*)-4,4,5,5-Tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (2.34).

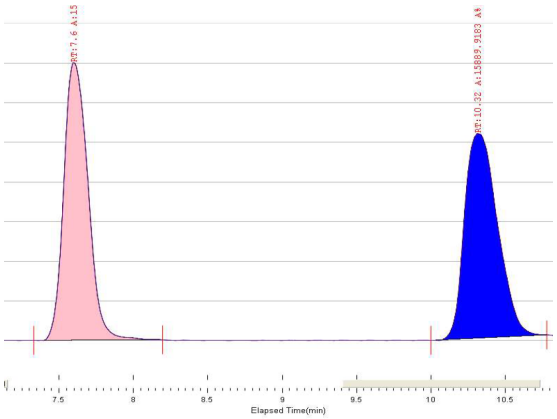
The title compound was prepared according to *General Procedure C* with (*R*)-2,2'-(4-(4-phenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2.162**) (7.7 g, 20.0 mmol), methanol (as electrophile) (3.2 g, 24.0 mmol), copper (I) cyanide (358.3 g, 4.0 mmol), lithium methoxide (2.3 g, 60.0 mmol). The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.7 g, 14.2 mmol, 71% yield) as colorless oil. All spectral data are in accordance with the literature.[21a]

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

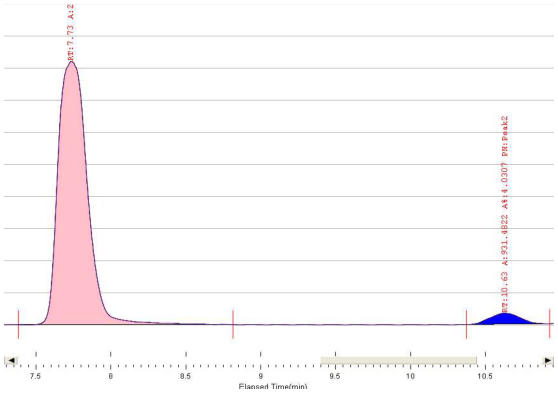
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 4-phenylbutan-2-ol

Racemic compound

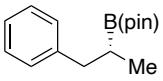


Peak No	% Area	Area	RT (min)
1	49.9226	15840.7992	7.6
2	50.0774	15889.9183	10.32
Total:	100	31730.7175	

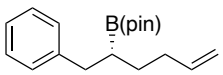
Standard conditions



Peak No	% Area	Area	RT (min)
1	95.9693	22178.3617	7.73
2	4.0307	931.4822	10.63
Total:	100	23109.8439	



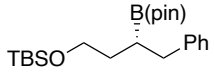
(*R*)-4,4,5,5-Tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane (2.164). The title compound was prepared according to *General Procedure C* with (*R*)-2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2.163**) (744.3 mg, 2.0 mmol, 96:4 er), methanol (as electrophile) (320 mg, 2.4 mmol), copper (I) cyanide (35.8 g, 0.4 mmol), lithium methoxide (228 mg, 6.0 mmol). The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (236.5 mg, 0.96 mmol, 48% yield) as colorless oil. All spectral data are in accordance with the literature.[56]



(*R*)-4,4,5,5-Tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane (2.165). The title compound was prepared according to *General Procedure C* with (*R*)-2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2.163**)

[56] Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415.

(372.1 mg, 1.0 mmol, 96:4 er), allyl bromide (241.9 mg, 2.0 mmol), copper (I) cynanide (17.9 g, 0.2 mmol), lithium methoxide (113.9 mg, 3.0 mmol). The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (189.3 mg, 0.66 mmol, 66% yield) as colorless oil. All spectral data are in accordance with the literature.[57]



(*R*)-*tert*-Butyldimethyl(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane) (2.166). The title compound was prepared according to a literature procedure[58] with (*R*)-(3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-butyl)dimethylsilane (**2.162**) (3.0 g, 6.81 mmol), phenyl bromide (1.6 g, 10.22 mmol), potassium hydride (1.2 g, 20.44 mmol), palladium (II) acetate (15.0 mg, 0.068 mmol), Ruphos (31.8 mg, 0.068 mmol) in THF (50 mL): H_2O (5 mL). The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (1.8 g, 4.6 mmol, 68% yield) as colorless oil. All spectral data are in accordance with the literature.[13d]

Analysis of Stereochemistry:

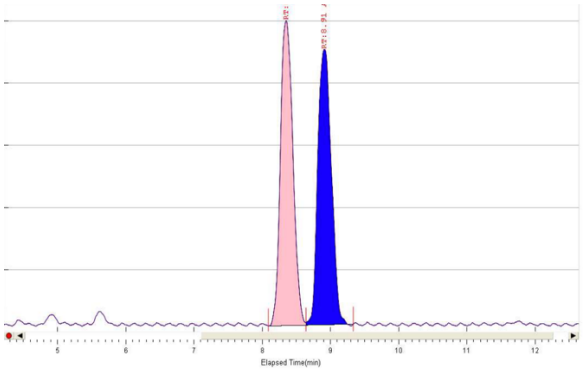
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 4-((tert-butyldimethylsilyl)oxy)-1-phenylbutan-2-ol

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

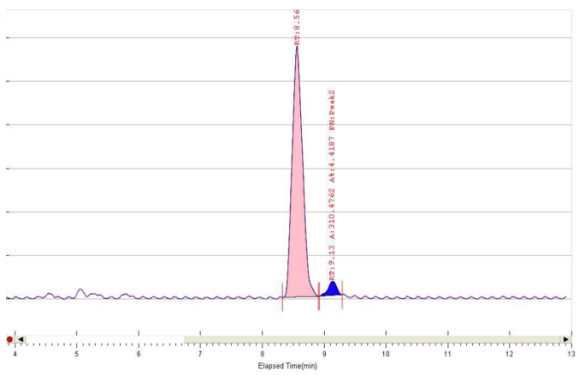
[58] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386–390.

Racemic Compound

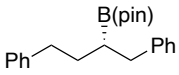


Peak No	% Area	Area	RT (min)
1	50.4919	6236.6438	8.35
2	49.5081	6115.1239	8.91
Total:	100	12351.7677	

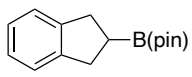
Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.5813	6715.9878	8.56
2	4.4187	310.4762	9.13
Total:	100	7026.464	



***(S)*-2-(1,4-Diphenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.167).** The title compound was prepared according to a literature procedure[58] with (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**2.162**) (772.3 mg, 2.0 mmol, 96:4 er), phenyl bromide (471.0 mg, 3.0 mmol), potassium hydride (336.6 mg, 6.0 mmol), palladium (II) acetate (4.5 mg, 0.020 mmol), Ruphos (9.3 mg, 0.020 mmol) in THF (5 mL): H_2O (0.5 mL). The light brown oil mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (595 mg, 1.8 mmol, 88% yield) as colorless oil. All spectral data are in accordance with the literature.[59]

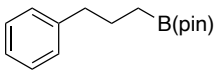


2-(2,3-Dihydro-1*H*-inden-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.168). The title compound was prepared according to a literature procedure[60]

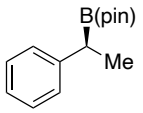
[59] Tao, Z.; Robb, K. A.; Panger, J. L.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140* (46), 15621–15625.

[60] Liu, Y.; Zhou, Y.; Wang, H.; Qu, J. *RSC Adv.* **2015**, *5*, 73705–73713.

on a 5.0 mmol scale to afford the title compound (849 mg, 3.5 mmol, 70% yield) as colorless oil. All spectral data are in accordance with the literature.[60]



4,4,5,5-Tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (2.169). The title compound was prepared according to a literature procedure[61] on a 20.0 mmol scale to afford the title compound (4.9 g, 20.0 mmol, 99% yield) as colorless oil. All spectral data are in accordance with the literature.[61]



(*S*)-4,4,5,5-Tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane (2.154). The title compound was prepared according to a literature[62] procedure on a 2.0 mmol scale to afford the title compound (368.3 mg, 1.6 mmol, 79% yield) as colorless oil. All spectral data are in accordance with the literature.[62]

Analysis of Stereochemistry:

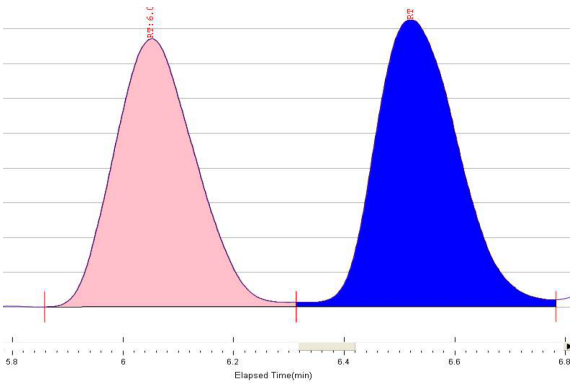
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared with racemic ligand according to the literature procedure[17]. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

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

[61] Bismuto, A.; Cowley, M. J.; Thomas, S. P. *ACS Catal.* **2018**, *8*, 2001–2005.

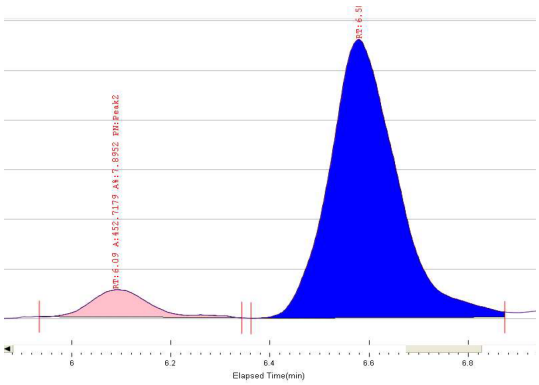
[62] Noh, D.; Chea, H.; Ju, J.; Yun, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6062–6064.

Racemic compound

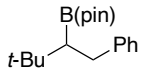


Peak No	% Area	Area	RT (min)
1	47.8008	7860.6037	6.05
2	52.1992	8583.8818	6.52
Total:	100	16444.4855	

Standard conditions

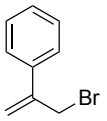


Peak No	% Area	Area	RT (min)
1	7.8952	452.7179	6.09
2	92.1048	5281.3665	6.58
Total:	100	5734.0844	



2-(3,3-Dimethyl-1-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.156). The title compound was prepared according to a literature procedure[57] on a 2.0 mmol scale to afford the title compound (468.8 mg, 1.6 mmol, 81% yield) as colorless oil. All spectral data are in accordance with the literature.[57]

2.6.2.2 Procedures for Preparation of Electrophiles

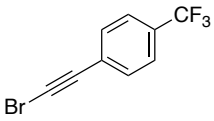


(3-Bromoprop-1-en-2-yl)benzene (2.170). To a solution of isopropenylbenzene (1.2 g, 10 mmol, 1.0 equiv.) in 6.0 mL $CHCl_3$ was added NBS (2.1 g, 12 mmol, 1.2 equiv.). The mixture was heated to reflux and allowed to stir for 4 h. Then the mixture was concentrated and Et_2O was added. The formed precipitate was filtered off and then the mixture was concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography in hexanes to afford 83% (1.6 g, 8.3 mmol) of the product as yellow oil. All spectral data are in accordance with the literature.[63]

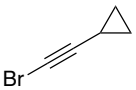
[63] Donohoe, T. J.; Fishlock, L. P.; Procopiou, P. A. *Org. Lett.* **2008**, *10*, 285–288.

General Procedure D: Preparation of alkynyl bromides

To the mixture of alkyne (1.0 equiv.), NBS (1.2 equiv.), and acetone (0.2 M), silver nitrate (0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography in hexanes.



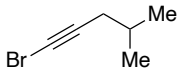
1-(Bromoethynyl)-4-(trifluoromethyl)benzene (2.171). The title compound was prepared according to the *General Procedure D*, with 1-ethynyl-4-(trifluoromethyl)benzene (1.7 g, 10 mmol), NBS (2.2 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 56% (1.4 g, 5.6 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[64]



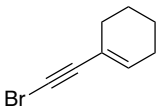
(Bromoethynyl)cyclopropane (2.172). The title compound was prepared according to *General Procedure D*, with ethynylcyclopropane (992 mg, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 45% (982 mg, 6.8 mmol) of the product as colorless, volatile liquid. All spectral data are in accordance with the literature.[65]

[64] Watanabe, K.; Mino, T.; Ishikawa, E.; Okano, M.; Ikematsu, T.; Yoshida, Y.; Sakamoto, M.; Sato, K.; Yoshida, K. *Eur. J. Org. Chem.* **2017**, *16*, 2359–2368.

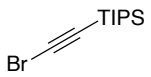
[65] Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743–5747.



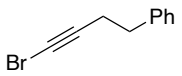
1-Bromo-4-methylpent-1-yne (2.173). The title compound was prepared according to *General Procedure D*, with 4-methylpent-1-yne (1.2 g, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 62% (1.5 g, 9.3 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[66]



(Bromoethynyl)cyclohex-1-ene (2.174). The title compound was prepared according to *General Procedure D*, with 4-methylpent-1-yne (1.2 g, 15 mmol), NBS (3.2 g, 18 mmol), acetone (100 mL), and silver nitrate (255 mg, 1.5 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 67% (1.85 g, 10 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[67]



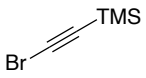
(Bromoethynyl)triisopropylsilane (2.175). The title compound was prepared according to *General Procedure D*, with ethynyl(triisopropyl)silane (1.8 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless oil residue was purified by silica gel chromatography in hexanes to afford 89% (2.3g, 8.9 mmol) of the product as colorless oil. All spectral data are in accordance with the literature.[68]



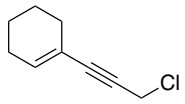
(4-Bromobut-3-yn-1-yl)benzene (2.176). The title compound was prepared according to *General Procedure D*, with but-3-ynylbenzene (1.3 g, 10 mmol), NBS (2.1 g, 12 mmol), acetone (100 mL), and silver nitrate (170 mg, 1.0 mmol). The colorless

[66] Peng, B.; Huang, X.; Xie, L.-G.; Maulide, N. *Angew. Chem., Int. Ed.* **2014**, *53*, 8718–8721.
[67] Gao, Y.; Yang, C.; Bai, S.; Liu, X.; Wu, Q.; Wang, J.; Jiang, C.; Qi, X. *Chem.* **2020**, *6*, 675–688.
[68] Chen, A.; Yu, H.; Yan, J.; Huang, H. *Org. Lett.* **2020**, *22*, 755–759.

liquid residue was purified by silica gel chromatography in hexanes to afford 86% (1.8 g, 8.6 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[69]



(Bromoethynyl)trimethylsilane (2.177). The title compound was prepared according to *General Procedure D*, with ethynyl(trimethyl)silane (2.0 g, 20 mmol), NBS (4.3 g, 24 mmol), acetone (100 mL), and silver nitrate (340 mg, 2.0 mmol). The colorless liquid residue was purified by silica gel chromatography in hexanes to afford 59% (2.1 g, 11.8 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[70]



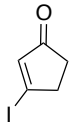
1-(3-Chloroprop-1-yn-1-yl)cyclohex-1-ene (2.178). To a solution of 1-ethynylcyclohexene (1.1 g, 10.0 mmol) in anhydrous THF (10 mL), *n*-butyllithium (2.5 M, 4.4 mL) was dropwise added over 10 min at –78 ºC under nitrogen atmosphere. The mixture was allowed to warm to 0 ºC and it was allowed to stir for 1 h, at which point the mixture was cooled to –78 ºC again and paraformaldehyde (360.3 mg, 12.0 mmol) was added. It was allowed to warm to room temperature and to stir for 12 h. The reaction was quenched by a saturated aqueous solution of NH_4Cl (30 mL). The mixture was washed with diethyl ether (3 × 30 mL), the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give 3-(cyclohex-1-en-1-yl)prop-2-yn-1-ol, which was used in the next step without purification.

To a solution of 3-(cyclohex-1-en-1-yl)prop-2-yn-1-ol in carbon tetrachloride (14 mL) was added triphenylphosphine (3.41 g, 13.0 mmol). The mixture was heated to reflux for 2 h. After being allowed to cool to room temperature, hexanes were added and triphenylphosphine oxide was

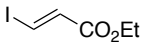
[69] Gauthier, R.; Mamone, M.; Paquin, J.-F. *Org. Lett.* **2019**, *21*, 9024–9027.

[70] Fox, M. A.; Cameron, A. M.; Low, P. J.; Paterson, M. A. J.; Batsanov, A. S.; Goeta, A. E.; Rankin, D. W. H.; Robertson, H. E.; Schirlin, J. T. *Dalton Trans.* **2006**, *29*, 3544–3560.

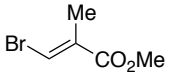
precipitated. Solvents were removed under reduced pressure and the yellow liquid residue was purified by silica gel chromatography (100% hexanes) to afford the title compound (1.0 g, 6.5 mmol, 65% yield) as clear liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.21 – 6.11 (m, 1H), 4.28 (s, 2H), 2.17 – 2.03 (m, 4H), 1.67 – 1.52 (m, 4H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.7, 120.0, 88.4, 81.2, 31.6, 29.0, 25.8, 22.3, 21.5.; IR: ν_{max} 2928 (s), 2857 (m), 2225 (w), 1434 (w), 1258 (s), 919 (w), 690 (m) cm^{-1}.; HRMS (DART) for $C_9H_{12}Cl$ $[M+H]^+$: calculated: 155.0622, found: 155.0626.



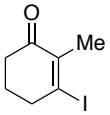
3-Iodocyclopent-2-en-1-one (2.179). The title compound was prepared according to a literature procedure[43c] on 10.0 mmol scale to afford the title compound (1.2 g, 5.5 mmol, 55% yield) as yellow oil. All spectral data are in accordance with the literature.[43c]



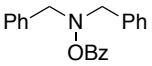
Ethyl (*E*)-3-iodoacrylate (2.180). The title compound was prepared according to a literature procedure[43c] on 18.0 mmol scale to afford the title compound (3.4 g, 15.2 mmol, 84% yield, *E*/*Z* = 20:1) as yellow oil. All spectral data are in accordance with the literature.[43c]

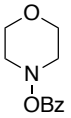


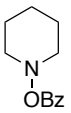
Methyl (*E*)-3-bromo-2-methylacrylate (2.181). The title compound was prepared according to a literature procedure[43c] on 50.0 mmol scale to afford the title compound (7.7 g, 43.3 mmol, 86% yield, *E*/*Z* >20:1) as yellow oil. All spectral data are in accordance with the literature.[43c]

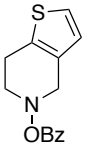


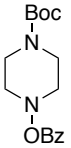
3-Iodo-2-methylcyclohex-2-en-1-one (2.182). The title compound was prepared according to a literature procedure[43c] on 10.0 mmol scale to afford the title compound (1.2 g, 5.1 mmol, 51% yield) as yellow solid. All spectral data are in accordance with the literature.[43c]

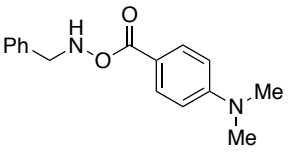
 ***O*-Menzoyl-*N*,*N*-dibenzylhydroxylamine (2.183).** The title compound was prepared according to a literature procedure[71] on 25.0 mmol scale to afford the title compound (6.2 g, 19.6 mmol, 78% yield) as white solid. All spectral data are in accordance with the literature.[71]

 **Morpholino benzoate (2.184).** The title compound was prepared according to a literature procedure[71] on 3.0 mmol scale to afford the title compound (381.2 mg, 1.8 mmol, 61% yield) as white solid. All spectral data are in accordance with the literature.[71]

 **Piperidin-1-yl benzoate (2.185).** The title compound was prepared according to a literature procedure[71] on 25.0 mmol scale to afford the title compound (1.7 g, 8.2 mmol, 33% yield) as white solid. All spectral data are in accordance with the literature.[71]

 **6,7-Dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl benzoate (2.186).** The title compound was prepared according to a literature procedure[71] on 5.0 mmol scale to afford the title compound (578.4 mg, 2.2 mmol, 45% yield) as white solid. All spectral data are in accordance with the literature.[72]

 ***tert*-Butyl 4-(benzoyloxy)piperazine-1-carboxylate (2.187).** The title compound was prepared according to a literature procedure[71] on 5.0 mmol scale to afford the title compound (1.1 g, 1.4 mmol, 72% yield) as white solid. All spectral data are in accordance with the literature.[47d]

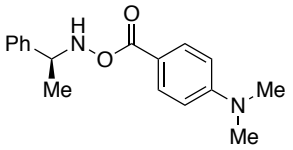
 **4-(((Benzylamino)oxy)carbonyl)-*N*,*N*-dimethylaniline (2.188).** The title compound was prepared according to a literature procedure[73] on 7.0

[71] Banerjee, A.; Yamamoto, H. *Chem. Sci.* **2019**, *10*, 2124–2129.

[72] Graßl, S.; Chen, Y.-H.; Hamze, C.; Tüllmann, C. P.; Knochel, P. *Org. Lett.* **2019**, *21*, 494–497.

[73] Niu, D.; Buchwald, S. L. *J. Am. Chem. Soc.* **2015**, *137* (30), 9716–9721.

mmol scale to afford the title compound (1.7 g, 6.2 mmol, 89% yield) as white solid. All spectral data are in accordance with the literature.[73]



(*S*)-*N*,*N*-Dimethyl-4-((((1-phenylethyl)amino)oxy)carbonyl)aniline. (2.189) The title compound was prepared according to a literature procedure[73] on 10.0 mmol scale to afford the title compound (419 mg, 1.4 mmol, 14% yield) as white solid. All spectral data are in accordance with the literature.[73]

2.6.2.3 Procedures for Cu-Catalyzed Cross-Couplings

General Procedure E: Coupling with ß-haloenone

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and was allowed to stir for 30 min. The reaction vial was transferred into glovebox again, styrene (20.8 mg, 1.0 equiv., for enantiomerically enriched substrates only), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and enone (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The mixture was allowed to stir at 60 ºC for 12 h. The mixture was diluted with diethyl ether and was filtered through a silica gel plug. Solvents were removed under reduced pressure. The residue was purified by silica gel chromatography (10–20% diethyl ether in hexanes, visualized by UV light) to furnish the desired product.

General Procedure F: Coupling with tertiary hydroxylamine esters

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and allowed to stir for 30 min. The reaction vial was then transferred into the glovebox, and styrene (10.4 mg, 0.5 equiv., for enantiomerically enriched substrates only), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%), cesium fluoride (91.1 mg, 0.6 mmol, 3.0 equiv.) and amination reagent (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from the glovebox. The mixture was allowed to stir at 80 ºC for 4 h. Subsequently, the mixture was diluted with diethyl ether, filtered through a silica gel plug with diethyl ether/triethyl amine (10/1) as eluent, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexanes/diethyl ether/triethyl amine, 100/5/1, visualized by UV light) to furnish the desired product.

General Procedure G: Coupling with secondary hydroxylamine esters

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was cooled to –78 ºC and *tert*-butyl lithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and allowed to stir for 30 min. The reaction vial was transferred into the glovebox, and styrene (10.4 mg, 0.5 equiv., for enantiomerically enriched substrates only), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%), triphenylphosphine (21.0 mg, 0.4 mmol, 40 mol%) cesium fluoride (91.1 mg, 0.6 mmol, 3.0 equiv.)

and amination reagent (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from the glovebox. The mixture was allowed to stir at 80 ºC for 4 h. The mixture was diluted with diethyl ether, passed through a silica gel plug with diethyl ether/triethyl amine (5/1 *v/v*) as eluent, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexanes/diethyl ether/triethyl amine, 100/20/1, visualized by UV light) to furnish the desired product.

General Procedure H: Coupling with acyl chlorides

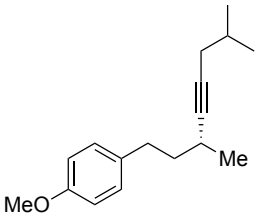
In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and allowed to stir for 30 min. The reaction vial was then transferred into the glovebox, and styrene (0.5–3.0 equiv., for certain substrates), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and acryl chloride (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from the glovebox. The mixture was allowed to stir at 60 ºC for 4 h. The mixture was subsequently diluted with diethyl ether, filtered through a silica gel plug, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (10–20% diethyl ether in hexanes, visualized by UV light) to furnish the desired product.

General Procedure I: Coupling with alkynyl bormides, allyl halides and propargyl halides

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was then cooled to

–78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and allowed to stir for 30 min. The reaction vial was transferred into the glovebox, styrene (0.5 equiv., for certain substrates, must be added before electrophile), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and electrophile (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from the glovebox. The mixture was allowed to stir for 12 h at 25 ºC or 60 ºC. The mixture was diluted with diethyl ether, filtered through a silica gel plug, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (5% diethyl ether in hexanes, stained in $KMnO_4$) to furnish the desired product.

2.6.3 Characterization of Cu-Catalyzed Cross-Coupling Products and Analysis of Stereochemistry



(*R*)-1-(3,7-Dimethyloct-4-yn-1-yl)-4-methoxybenzene (2.98). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 94:6 er), 1-bromo-4-methyl-pent-1-yne (38.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (44.0 mg, 0.18mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 – 7.07 (m, 2H), 6.88 – 6.80 (m, 2H), 3.80 (s, 3H), 2.86 – 2.76 (ddd, *J* = 14.5, 8.7, 6.1 Hz, 1H), 2.66 (ddd, *J* = 13.8, 9.3, 7.0 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.10 (dd, *J* = 6.5, 2.3 Hz, 2H), 1.86 – 1.76 (m, 1H), 1.71 – 1.63 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 6H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 134.6, 129.5, 113.9, 85.5, 79.9, 77.4, 77.2, 76.9, 55.4, 39.6, 33.0, 28.5, 28.2, 25.6, 22.1, 21.7.; IR: ν_{max}

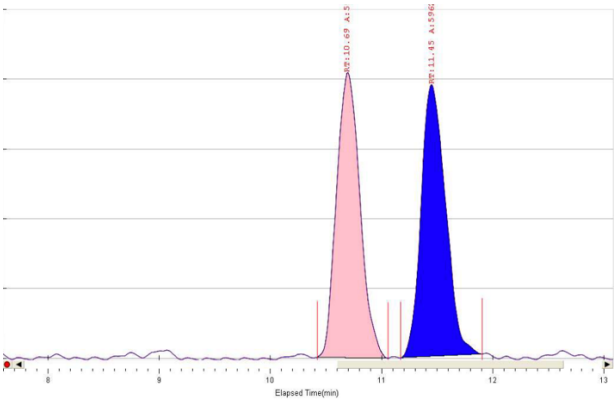
2956 (m), 1611 (w), 1511 (s), 1462 (w), 1245 (s), 1176 (w), 1038 (m), 822 (w) cm^{-1}.; HRMS (DART) for $C_{17}H_{25}O$ $[M+H]^+$: calculated: 245.1900, found: 245.1898.; $[\alpha]_D^{20}$: –49.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

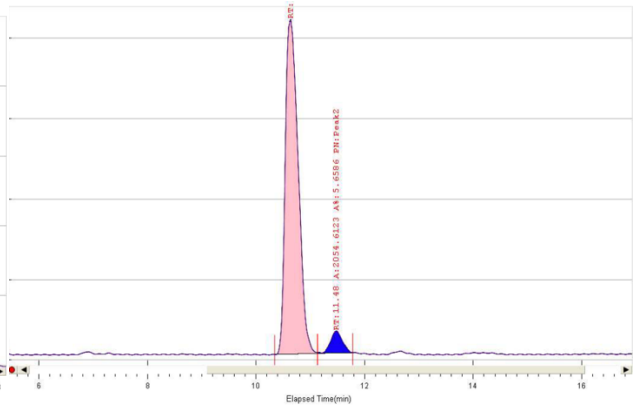
Chiral SFC (Chiralcel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(3,7-dimethyloct-4-yn-1-yl)-4-methoxybenzene

Racemic Compound

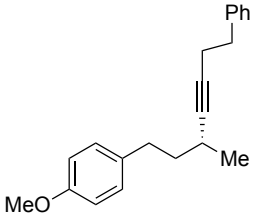


Peak No	% Area	Area	RT (min)
1	50.0557	5975.9703	10.69
2	49.9443	5962.6733	11.45
Total:	100	11938.6436	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.9176	13884.5523	10.61
2	6.0824	899.2017	11.45
Total:	100	14783.754	



(*R*)-1-Methoxy-4-(3-methyl-7-phenylhept-4-yn-1-yl)benzene (2.99). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), (4-bromobut-3-yn-1-yl)benzene (50.2 mg, 0.24 mmol), copper

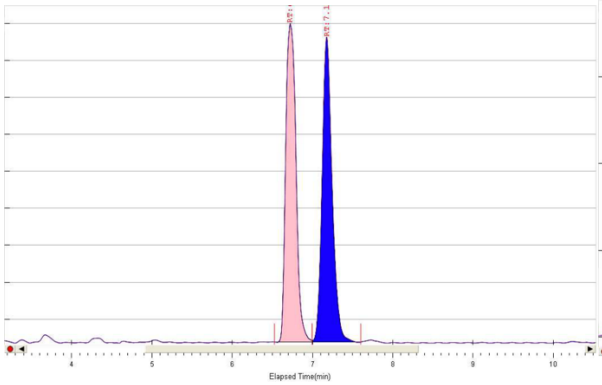
cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (50.1 mg, 0.17 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H), 7.27 – 7.20 (m, 3H), 7.12 – 7.07 (m, 2H), 6.86 – 6.80 (m, 2H), 3.80 (s, 3H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.71 (ddd, *J* = 14.4, 8.7, 6.1 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.51 (td, *J* = 7.5, 2.2 Hz, 2H), 2.42 – 2.32 (m, 1H), 1.71 – 1.59 (m, 2H), 1.15 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 141.1, 134.5, 129.5, 128.7, 128.4, 126.3, 113.8, 85.4, 80.3, 77.4, 77.2, 76.9, 55.4, 39.3, 35.8, 32.9, 25.5, 21.6, 21.1.; IR: ν_{max} 2926 (m), 1610 (w), 1510 (s), 1453 (m), 1244 (s), 1176 (w), 1036 (m), 826 (w), 747 (w), 698 (s) cm^{-1}.; HRMS (DART) for $C_{21}H_{25}O$ $[M+H]^+$: calculated: 293.1900, found: 293.1900.; $[\alpha]_D^{20}$: –64.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

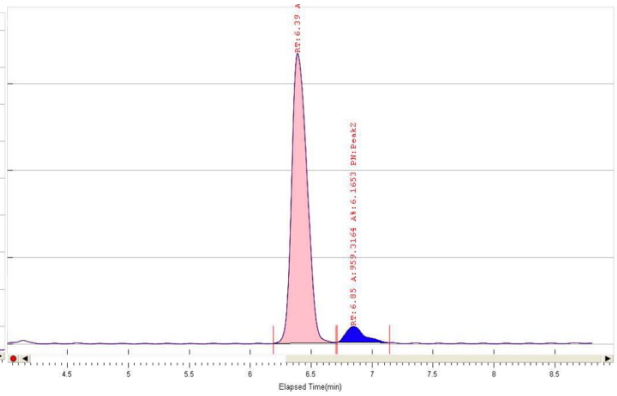
Chiral SFC (Chiralcel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-methoxy-4-(3-methyl-7-phenylhept-4-yn-1-yl)benzene

Racemic Compound

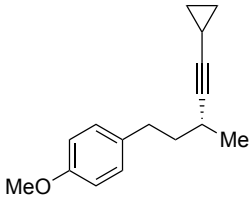


Peak No	% Area	Area	RT (min)
1	51.6977	15278.1742	6.72
2	48.3023	14274.7511	7.18
Total:	100	29552.9253	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.8347	14600.5819	6.39
2	6.1653	959.3164	6.85
Total:	100	15559.8983	



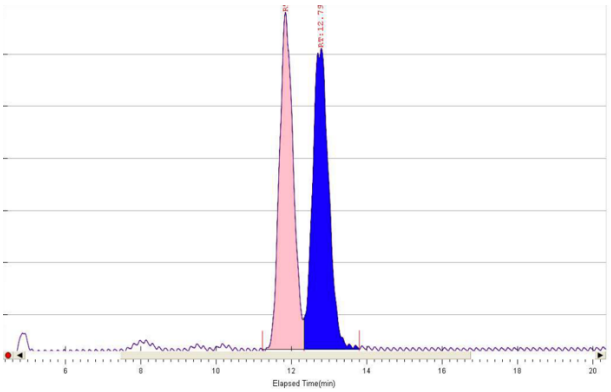
(*R*)-1-(5-Cyclopropyl-3-methylpent-4-yn-1-yl)-4-methoxybenzene (2.100). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), 2-bromoethynylcyclopropane (34.8 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (37.9 mg, 0.17 mmol, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.09 (m, 2H), 6.86 – 6.78 (m, 2H), 3.79 (s, 3H), 2.77 – 2.68 (m, 1H), 2.66 – 2.57 (m, 1H), 2.41 – 2.32 (m, 1H), 1.69 – 1.58 (m, 2H), 1.28 – 1.19 (m, 1H), 1.14 (d, *J* = 6.9 Hz, 3H), 0.77 – 0.69 (m, 2H), 0.65 – 0.59 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 134.5, 129.5, 113.9, 84.1, 79.9, 77.4, 77.2, 76.9, 55.4, 39.4, 32.9, 25.5, 21.6, 8.4, 8.3, -0.3.; IR: ν_{max} 2928 (w), 1610 (w), 1511 (s), 1454 (w), 1244 (s), 1176 (w), 1037 (m), 827 (w) cm^{-1}.; HRMS (DART) for $C_{16}H_{21}O$ $[M+H]^+$: calculated: 229.1587, found: 229.1587.; $[\alpha]_D^{20}$: –54.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

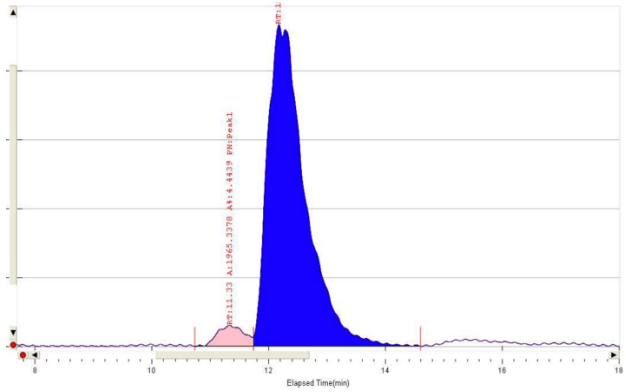
Chiral SFC (Chiralcel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(5-cyclopropyl-3-methylpent-4-yn-1-yl)-4-methoxybenzene

Racemic Compound

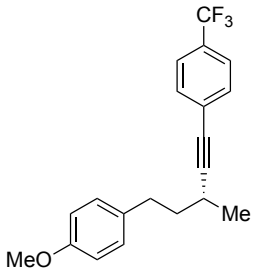


Peak No	% Area	Area	RT (min)
1	49.9655	8270.4383	11.77
2	50.0345	8281.8701	12.78
Total:	100	16552.3084	

Standard Condition



Peak No	% Area	Area	RT (min)
1	4.4439	1965.3378	11.33
2	95.5561	42259.8379	12.17
Total:	100	44225.1757	



(*R*)-1-Methoxy-4-(3-methyl-5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl)benzene (2.101). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), styrene (10.4 mg, 0.10 mmol), 1-(2-bromoethynyl)-4-(trifluoromethyl)benzene (59.8 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was

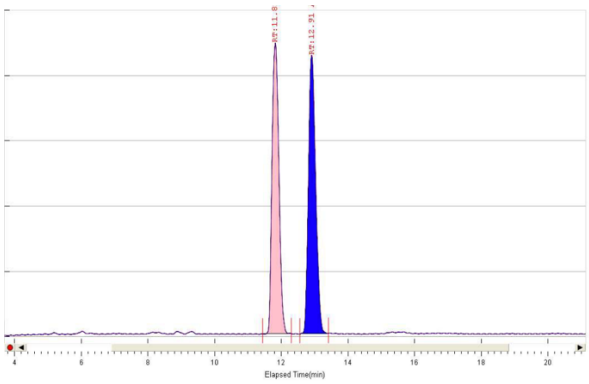
purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as pale-yellow oil (58.6 mg, 0.17 mmol, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H)7.20 – 7.14 (m, 2H), 6.89 – 6.83 (m, 2H), 3.81 (s, 3H), 2.88 – 2.80 (m, 1H), 2.79 – 2.73 (m, 1H), 2.73 – 2.64 (m, 1H), 1.92 – 1.77 (m, 2H), 1.31 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 134.0, 131.9, 129.5, 129.4 (q, $^{2}J_{C\text{-}F}$ = 32.9 Hz), 128.0, 125.2 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 125.0 (q, $^{1}J_{C\text{-}F}$ = 272.92 Hz), 114.0, 97.3, 80.4, 55.4, 38.9, 32.9, 26.1, 21.0. ^{19}F NMR (470 MHz, cdcl$_3$) δ -62.71.; IR: ν_{max} 2931 (w), 1612 (w), 1511 (m), 1321 (s), 1245 (m), 1165 (m), 1125 (s), 1066 (m), 1037 (w), 841 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{20}OF_3$.; $[M+H]^+$: calculated: 333.1461, found: 333.1461.; $[\alpha]_D^{20}$: –83.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

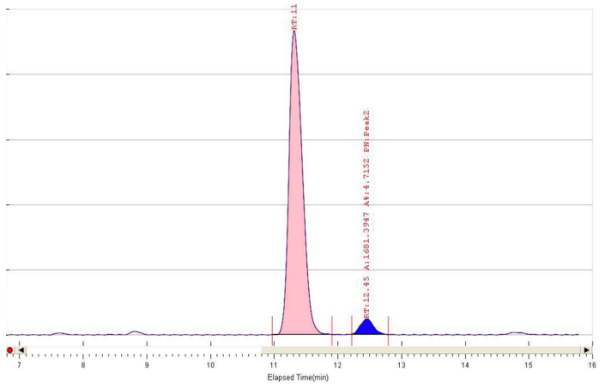
Chiral SFC (Chiralcel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-methoxy-4-(3-methyl-5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl)benzene

Racemic Compound

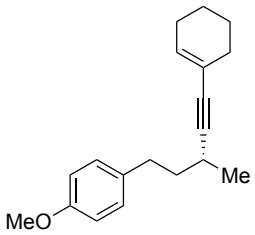


Peak No	% Area	Area	RT (min)
1	49.5471	31774.19	11.82
2	50.4529	32355.0755	12.91
Total:	100	64129.2655	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.2848	33977.8947	11.32
2	4.7152	1681.3947	12.45
Total:	100	35659.2894	



(*R*)-1-(5-(Cyclohex-1-en-1-yl)-3-methylpent-4-yn-1-yl)-4-methoxybenzene (2.102). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), styrene (10.4 mg, 0.10 mmol), 1-(2-bromoethynyl)cyclohexene (44.41 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (49.0 mg, 0.18 mmol, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 – 7.11 (m, 2H), 6.85 – 6.81 (m, 2H), 6.05 (tt, *J* = 3.9, 1.7 Hz, 1H), 3.79 (s, 3H), 2.77 (ddd, *J* = 14.4, 9.0, 5.7 Hz, 1H), 2.67 (ddd, *J* = 13.8, 9.1, 7.3 Hz, 1H), 2.58 – 2.50 (m, 1H), 2.17 – 2.12 (m, 2H), 2.11 – 2.05 (m, 2H), 1.75 – 1.68 (m, 2H), 1.67 – 1.62 (m, 2H), 1.61 – 1.53 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.8, 134.4, 133.3, 129.5, 121.1, 113.8, 91.5, 83.2, 77.4, 77.2, 76.9, 55.4, 39.3, 32.9, 29.9, 26.0, 25.7, 22.6, 21.7, 21.4.; IR: ν_{max} 2927 (m), 2855 (w), 1610 (w), 1510 (s), 1452 (w),

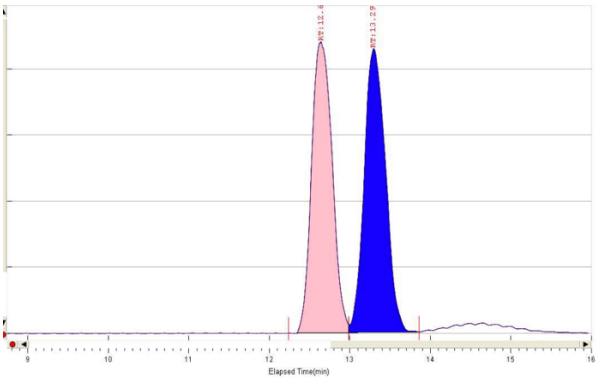
1244 (s), 1176 (w), 1037 (w), 824 (w) cm^{-1}. HRMS (DART) for $C_{19}H_{25}O$ $[M+H]^+$: calculated: 269.1900, found: 269.1903.; $[\alpha]_D^{20}$: –63.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

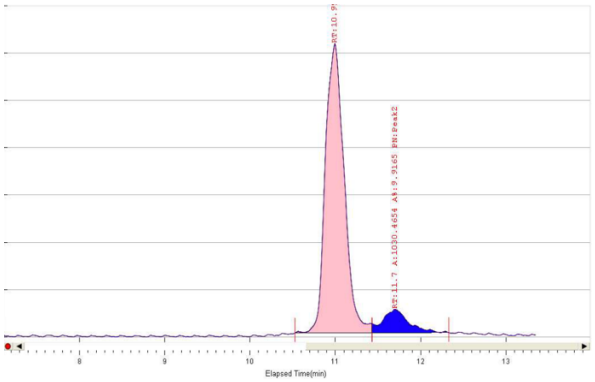
Chiral SFC (Chiralcel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(5-(cyclohex-1-en-1-yl)-3-methylpent-4-yn-1-yl)-4-methoxybenzene

Racemic Compound

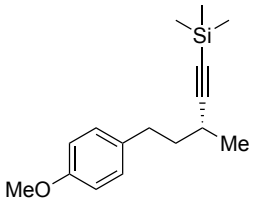


Peak No	% Area	Area	RT (min)
1	49.6234	39105.9159	12.64
2	50.3766	39699.4974	13.29
Total:	100	78805.4133	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.9571	47608.9616	12.67
2	5.0429	2528.3907	13.34
Total:	100	50137.3523	



(*R*)-(5-(4-Methoxyphenyl)-3-methylpent-1-yn-1-yl)trimethylsilane (2.103). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 94:6 er), styrene (10.4 mg, 0.10 mmol), 2-bromoethynyl(trimethyl)silane (42.5 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The

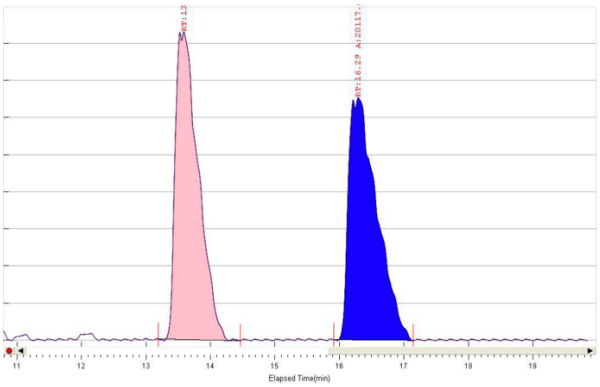
mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (43.0 mg, 0.16 mmol, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 – 7.07 (m, 2H), 6.86 – 6.80 (m, 2H), 3.79 (s, 3H), 2.75 (ddd, *J* = 14.4, 9.1, 5.6 Hz, 1H), 2.66 (ddd, *J* = 13.8, 9.1, 7.3 Hz, 1H), 2.48 – 2.39 (m, 1H), 1.77 – 1.62 (m, 2H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.18 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 134.3, 129.5, 113.9, 111.8, 84.8, 77.4, 77.2, 76.9, 55.4, 39.0, 32.8, 26.4, 21.1, 0.4. IR: ν_{max} 2957 (w), 2158 (w), 1611 (w), 1511 (s), 1462 (w), 1246 (s), 1176 (w), 1038 (w), 841 (s), 759 (w) cm^{-1}.; HRMS (DART) for $C_{16}H_{25}OSi$ $[M+H]^+$: calculated: 261.1669, found: 261.1666.; $[\alpha]_D^{20}$: –43.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

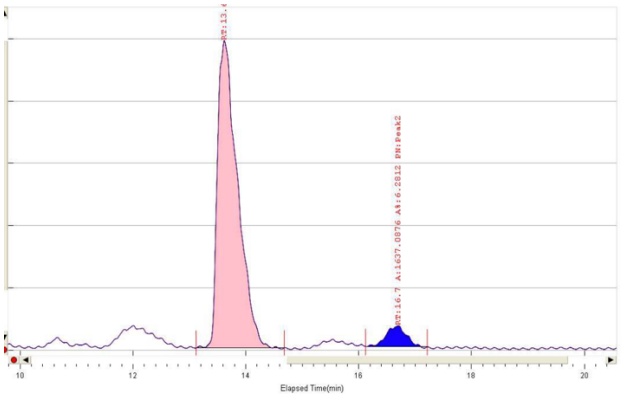
Chiral SFC (Chiralcel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of (5-(4-methoxyphenyl)-3-methylpent-1-yn-1-yl)trimethylsilane.

Racemic Compound

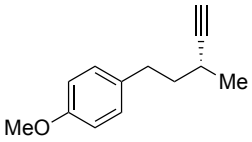


Peak No	% Area	Area	RT (min)
1	50.6665	20660.9689	13.59
2	49.3335	20117.4237	16.29
Total:	100	40778.3926	

Standard Conditions



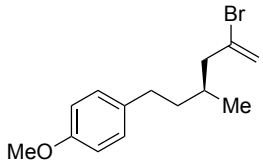
Peak No	% Area	Area	RT (min)
1	93.7188	24426.0733	13.62
2	6.2812	1637.0876	16.7
Total:	100	26063.1609	



(*R*)-1-Methoxy-4-(3-methylpent-4-yn-1-yl)benzene (2.104). To a 2-dram vial equipped with a magnetic stir bar was added *(R)*-(5-(4-methoxyphenyl)-3-methylpent-1-yn-1-yl)trimethylsilane **(2.103)** (68.9 mg, 0.20 mmol, 95:5 er) and tetrabutylammonium fluoride (1.0 M in THF, 0.5 mL, 0.50 mmol). The solution was quenched by addition of 1.0 mL of water, washed with Et_2O, and concentrated under reduced pressure. The pale-yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (34.1 mg, 0.18 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.08 (m, 2H), 6.88 – 6.80 (m, 2H), 3.80 (s, 3H), 2.78 (ddd, J = 14.5, 9.2, 5.5 Hz, 1H), 2.67 (ddd, J = 13.8, 9.2, 7.2 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.11 (d, J = 2.4 Hz, 1H), 1.80 – 1.66 (m, 2H), 1.21 (d, J = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 134.1, 129.5, 113.9, 88.9, 77.4, 77.2, 76.9, 68.8, 55.4, 38.8, 32.7, 25.2, 21.1.; IR: ν_{max} 3294 (w), 2931 (w), 1610 (w), 1511 (s), 1454 (w), 1243 (s), 1177 (w), 1036 (m), 825 (w), 631 (w), 524 (w) cm^{-1}.; HRMS (DART) for $C_{13}H_{17}O$ $[M+H]^+$: calculated: 189.1274, found: 189.1283.; $[\alpha]_D^{20}$: –52.8 (c = 1.0, $CHCl_3$, l = 50 mm)

Proof of Absolute Stereochemistry:

Literature characterization of (*R*)-1-methoxy-4-(3-methylpent-4-yn-1-yl)benzene: $[\alpha]_D^{23} := -50$ (c = 1.0, $CHCl_3$), 96:4 er.[5d]



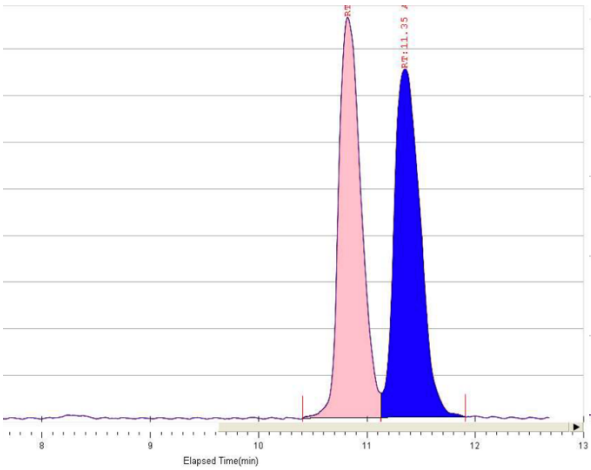
(*S*)-1-(5-Bromo-3-methylhex-5-en-1-yl)-4-methoxybenzene (2.105). The title compound was prepared according to *General Procedure I* with (*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 94:6 er), 2,3-dibromoprop-1-ene (48.0mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as pale-yellow oil (51 mg, 0.18 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.08 (m, 2H), 6.85 – 6.81 (m, 2H), 5.55 (d, *J* = 1.2 Hz, 1H), 5.43 (d, *J* = 1.3 Hz, 1H), 3.79 (s, 3H), 2.68 – 2.60 (m, 1H), 2.58 – 2.50 (m, 1H), 2.46 (dd, *J* = 14.3, 6.2, 1H), 2.24 (dd, *J* = 14.3, 6.2, 1H), 1.95 – 1.85 (m, 1H), 1.70 – 1.61 (m, 1H), 1.47 – 1.38 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 134.8, 133.9, 129.3, 117.8, 113.9, 77.4, 77.2, 76.9, 55.4, 48.9, 38.3, 32.5, 31.0, 18.9.; IR: ν_{max} 2927 (w), 1627 (w), 1510 (s), 1461 (w), 1244 (s), 1177 (m), 1037 (m), 855 (w), 822 (w) cm^{-1}.; HRMS (DART) for $C_{14}H_{20}BrO$ $[M+H]^+$: calculated: 283.0692, found: 283.0696.; $[\alpha]_D^{20}$: –12.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

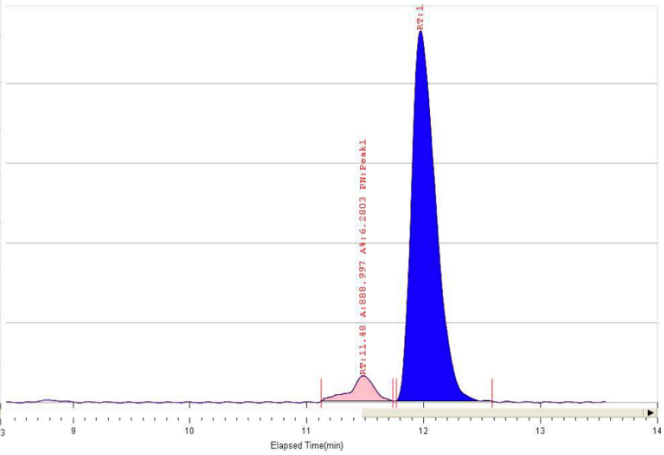
Chiral SFC (Chiralcel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(5-bromo-3-methylhex-5-en-1-yl)-4-methoxybenzene

Racemic Compound

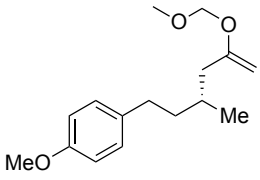


Peak No	% Area	Area	RT (min)
1	49.8277	12348.1181	10.82
2	50.1723	12433.4948	11.35
Total:	100	24781.6129	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	6.2803	888.997	11.48
2	93.7197	13266.4218	11.97
Total:	100	14155.4188	



(*R*)-1-Methoxy-4-(5-(methoxymethoxy)-3-methylhex-5-en-1-yl)benzene (2.106). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), 3-chloro-2-(methoxymethoxy)prop-1-ene (32.8 mg, 0.24 mmol), Styrene (10.4 mg, 0.10 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as pale-yellow oil (41.8 mg, 0.16 mmol, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 – 7.08 (m, 2H), 6.85 – 6.80 (m, 2H), 4.92 (d, *J* = 6.0 Hz, 1H), 4.94 (d, *J* = 6.0 Hz, 1H), 4.13 (d, *J* = 1.8 Hz, 1H), 3.97 (d, *J* = 1.7 Hz, 1H), 3.40 (s, 3H), 2.64 (ddd, *J* = 13.7, 10.6, 5.5 Hz, 1H), 2.53 (ddd, *J* = 13.7, 10.4, 6.0 Hz,

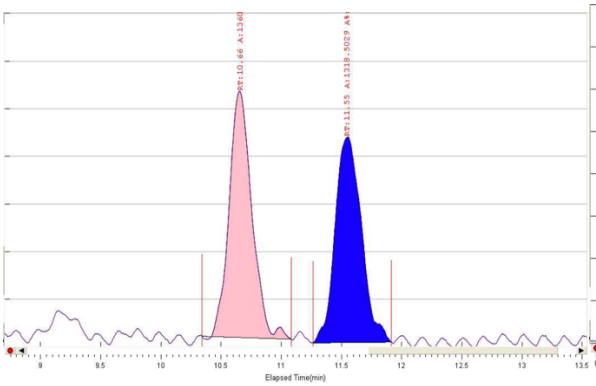
1H), 2.17 (dd, J = 13.8, 6.3 Hz, 1H), 1.94 (dd, J = 13.8, 7.9 Hz, 1H), 1.85 – 1.74 (m, 1H), 1.72 – 1.62 (m, 1H), 1.46 – 1.38 (m, 1H), 0.97 (d, J = 6.7 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 157.7, 135.1, 129.3, 113.8, 93.6, 85.5, 77.4, 77.2, 76.9, 56.2, 55.4, 42.8, 38.9, 32.6, 30.6, 19.4.; IR: ν_{max} 2929 (w), 1611 (w), 1510 (s), 1462 (w), 1244 (s), 1152 (m), 1097 (w), 1018 (s), 926 (w), 820 (m) cm^{-1}.; HRMS (DART) for $C_{16}H_{25}O_3$ $[M+H]^+$: calculated: 265.1798, found: 265.1804.; $[\alpha]_D^{20}$: +6.8 (c = 1.0, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

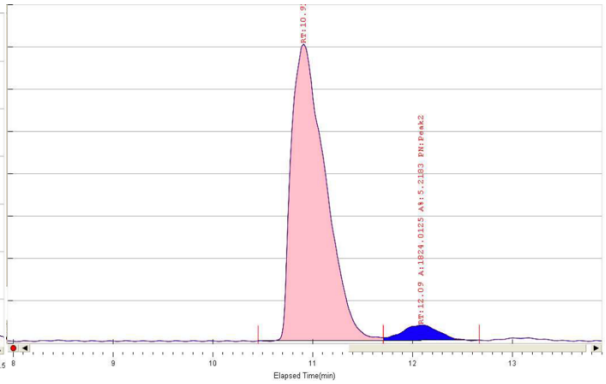
Chiral SFC (Chiralcel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-methoxy-4-(5-(methoxymethoxy)-3-methylhex-5-en-1-yl)benzene

Racemic Compound

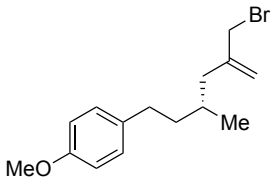


Peak No	% Area	Area	RT (min)
1	50.783	1360.455	10.66
2	49.217	1318.5029	11.55
Total:	100	2678.9579	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.7817	33129.879	10.91
2	5.2183	1824.0125	12.09
Total:	100	34953.8915	



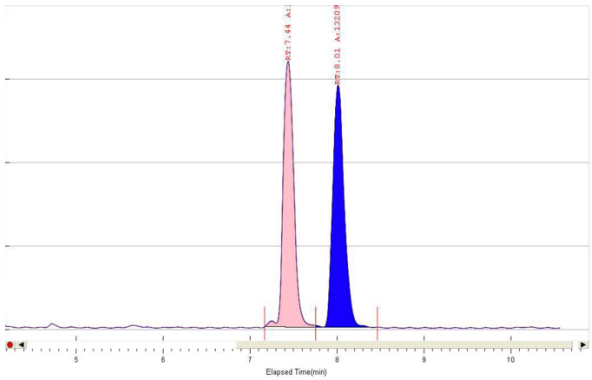
(*R*)-1-(5-(Bromomethyl)-3-methylhex-5-en-1-yl)-4-methoxybenzene (2.107). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), 3-bromo-2-(bromomethyl)prop-1-ene (51.3 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as pale-yellow oil (47.3 mg, 0.16 mmol, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.06 (m, 2H), 6.87 – 6.79 (m, 2H), 5.21 (s, 1H), 4.97 – 4.90 (m, 1H), 3.95 – 3.88 (m, 2H), 3.79 (s, 3H), 2.65 (ddd, *J* = 13.5, 9.8, 5.7 Hz, 1H), 2.55 (ddd, *J* = 13.6, 10.0, 5.9 Hz, 1H), 2.33 (dd, *J* = 14.4, 6.1, 1H), 2.03 (dd, *J* = 14.4, 8.1, 1H), 1.71 – 1.58 (m, 2H), 1.48 – 1.38 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 144.3, 134.8, 129.3, 116.7, 113.9, 77.4, 77.2, 76.9, 55.4, 41.2, 38.9, 36.8, 32.5, 30.2, 19.6.; IR: ν_{max} 2925 (w), 1610 (w), 1510 (s), 1461 (w), 1244 (s), 1176 (w), 1037 (m), 910 (w), 824 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{22}BrO$ $[M+H]^+$: calculated: 297.0849, found: 297.0857.; $[\alpha]_D^{20}$: +6.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

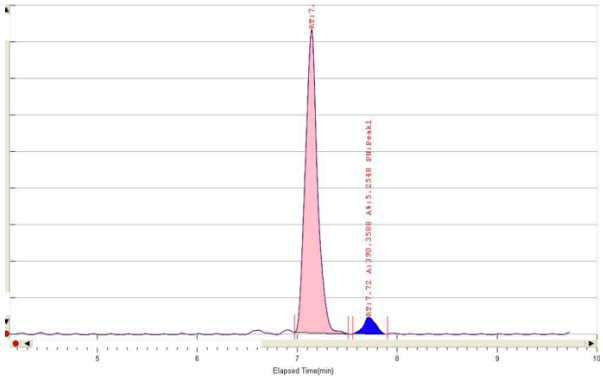
Chiral SFC (Chiralcel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(5-(bromomethyl)-3-methylhex-5-en-1-yl)-4-methoxybenzene

Racemic Compound

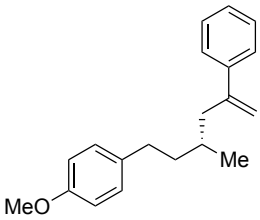


Peak No	% Area	Area	RT (min)
1	50.5134	13483.3109	7.44
2	49.4866	13209.2511	8.01
Total:	100	26692.562	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.7452	7038.2224	7.15
2	5.2548	390.3588	7.72
Total:	100	7428.5812	



(*R*)-1-Methoxy-4-(3-methyl-5-phenylhex-5-en-1-yl)benzene (2.108). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), 1-(bromomethyl)vinylbenzene (47.3 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as yellow oil (53.5 mg, 0.19 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H), 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 1H), 7.11 – 7.00 (m, 2H), 6.89 – 6.80 (d, *J* = 8.6 Hz, 2H), 5.30 (d, *J* = 1.8 Hz, 1H), 5.07 (d, *J* = 1.5 Hz, 1H), 3.81 (s, 3H), 2.69 – 2.59 (m, 2H), 2.52 (ddd, *J* = 13.8, 10.4, 5.8 Hz, 1H), 2.34 (ddd, *J* = 13.9, 8.1, 1.0 Hz, 1H), 1.73 – 1.57 (m, 2H), 1.51 – 1.40 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 147.7, 141.5, 135.0, 129.3, 128.3, 127.3, 126.4, 113.9, 113.8, 77.4, 77.2, 76.9, 55.4, 43.4, 38.9, 32.5, 30.9, 19.6.; IR: ν_{max} 2923 (w), 1611 (w), 1510 (s), 1456 (w), 1244 (s), 1176 (w), 1037 (m), 895 (w), 822 (w),

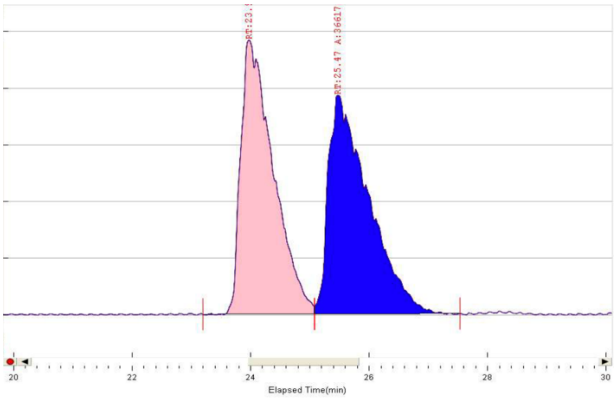
778 (m), 704 (m) cm^{-1}.; HRMS (DART) for $C_{20}H_{25}O$ $[M+H]^+$: calculated: 281.1900, found: 281.1893.; $[\alpha]_D^{20}$: +40.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

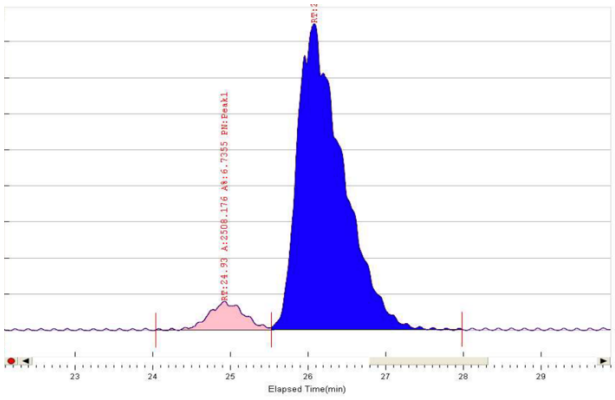
Chiral SFC (Chiralcel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of methyl-6-(4-methoxyphenyl)-4-methylhexanoate

Racemic Compounds

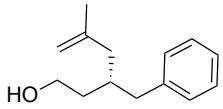


Peak No	% Area	Area	RT (min)
1	50.1623	36855.6729	23.97
2	49.8377	36617.1897	25.47
Total:	100	73472.8626	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	6.7355	2508.176	24.93
2	93.2645	34730.0142	26.08
Total:	100	37238.1902	



(*R*)-3-Benzyl-5-methylhex-5-en-1-ol (2.109). The title compound was prepared according to *General Procedure I* with (*R*)-*tert*-butyldimethyl(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane (78.1 mg, 0.20 mmol, 96:4 er), styrene (10.4 mg, 0.10 mmol), 3-chloro-2-methyl-prop-1-ene (21.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 60 ºC overnight, filtered through

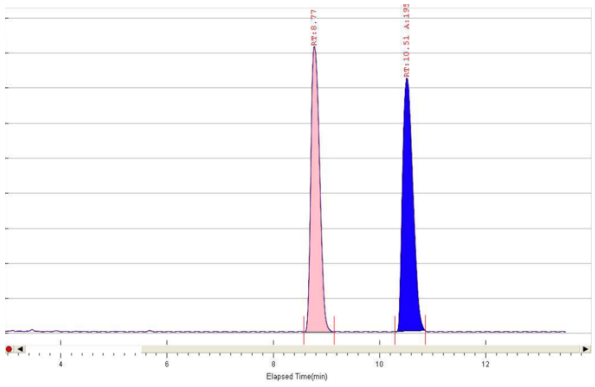
a silica gel plug and concentrated under reduced pressure. The mixture was put on vaccum for 2 h before being treated with tetrabutylammonium fluoride (1.0 M, 0.50 mmol, 0.5 mL) and allowed to stir at 25 ºC overnight. The solution was quenched by addition of 1.0 mL of water, washed with Et_2O, the organic layers were concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the product as yellow oil (53.5 mg, 0.19 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.20 – 7.09 (m, 3H), 4.78 (s, 1H), 4.72 (s, 1H), 3.70 – 3.56 (m, 2H), 2.61 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.49 (dd, *J* = 13.6, 5.7 Hz, 1H), 2.04 – 1.92 (m, 3H), 1.68 (s, 3H), 1.55 – 1.48 (m, 2H), 1.10 (br, 1H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.4, 141.1, 129.3, 128.4, 126.0, 112.3, 77.4, 77.2, 76.9, 61.1, 43.2, 40.9, 36.6, 34.5, 22.4.; IR: ν_{max} 3343 (br), 2923 (s), 1646 (w), 1494 (m), 1246 (w), 1052 (m), 887 (m), 742 (m), 699 (s) cm^{-1}.; HRMS (DART) for $C_{14}H_{21}O$ $[M+H]^+$: calculated: 205.1587, found: 205.1583.; $[\alpha]_D^{20}$: +7.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic *tert*-butyldimethyl(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane. Absolute stereochemistry was assigned by analogy.

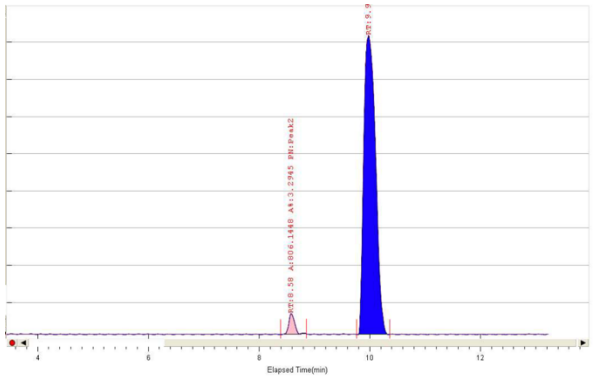
Chiral SFC (Chiralcel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 3-benzyl-5-methylhex-5-en-1-ol

Racemic Compound

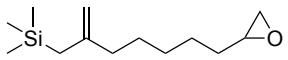


Peak No	% Area	Area	RT (min)
1	48.7712	18600.022	8.77
2	51.2288	19537.3235	10.51
Total:	100	38137.3455	

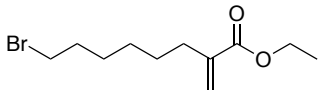
Standard Conditions



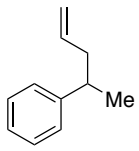
Peak No	% Area	Area	RT (min)
1	3.2945	806.1448	8.58
2	96.7055	23663.5699	9.98
Total:	100	24469.7147	



Trimethyl(2-methylene-7-(oxiran-2-yl)heptyl)silane (2.110). The title compound was prepared according to *General Procedure I* with 4,4,5,5-tetramethyl-2-[4-(oxiran-2-yl)butyl]-1,3,2-dioxaborolane (45.2 mg, 0.20 mmol), 2-(chloromethyl)allyl-trimethyl-silane (39.1 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (38.2 mg, 0.17 mmol, 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.60 – 4.54 (m, 1H), 4.52 – 4.46 (m, 1H), 2.93 – 2.87 (m, 1H), 2.74 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.46 (dd, *J* = 5.1, 2.8 Hz, 1H), 1.99 – 1.87 (m, 2H), 1.56 – 1.50 (m, 4H), 1.49 – 1.40 (m, 4H), 1.38 – 1.31 (m, 2H), 0.01 (s, 9H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.8, 106.9, 77.4, 77.2, 76.9, 52.5, 47.3, 38.2, 32.6, 29.3, 27.9, 26.9, 26.0, -1.2.; IR: ν_{max} 2929 (w), 2855 (w), 1631 (w), 1410 (w), 1246 (m), 1155 (w), 838 (s), 693 (w) cm^{-1}.; HRMS (DART) for $C_{13}H_{27}OSi$ $[M+H]^+$: calculated: 227.1826, found: 227.1814.



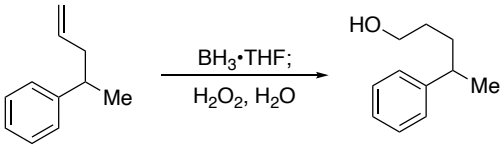
Ethyl 8-bromo-2-methyleneoctanoate (2.111). The title compound was prepared according to *General Procedure I* with 2-(5-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (55.4 mg, 0.20 mmol), ethyl 2-(bromomethyl)acrylate (46.3 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (43.6 mg, 0.16 mmol, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 – 6.07 (m, 1H), 5.50 (q, *J* = 1.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.33 – 2.24 (m, 2H), 1.91 – 1.80 (m, 2H), 1.53 – 1.40 (m, 4H), 1.39 – 1.31 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 140.9, 124.3, 60.5, 33.9, 32.7, 31.7, 28.3, 28.2, 27.9, 14.2.; IR: ν_{max} 2930 (m), 2857 (w), 1715 (s), 1639 (w), 1461 (w), 1368 (w), 1303 (w), 1177 (m), 1027 (w), 943 (w) cm^{-1}. HRMS (DART) for $C_{11}H_{20}BrO_2$ $[M+H]^+$: calculated: 263.0641, found: 263.0653.



Pent-4-en-2-ylbenzene (2.155). The title compound was prepared according to *General Procedure I* with (*S*)-4,4,5,5-tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane (0.20 mmol, 92:8 er), allyl bromide (0.24 mmol), copper cyanide (0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as colorless oil (22.7 mg, 0.16 mmol, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.25 – 7.17 (m, 3H), 5.74 (dddd, *J* = 16.8, 10.1, 7.6, 6.5 Hz, 1H), 5.02 (ddt, *J* = 17.1, 2.2, 1.5 Hz, 1H), 4.98 (ddt, *J* = 10.1, 2.1, 1.1 Hz, 1H), 2.81 (h, *J* = 7.0 Hz, 1H), 2.41 (dtt, *J* = 13.6, 6.7, 1.4 Hz, 1H), 2.31 (dtt, *J* = 13.9, 7.5, 1.2 Hz, 1H), 1.28 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 137.2,

128.3, 127.0, 125.9, 115.9, 42.7, 39.8, 21.5.; IR: ν_{max} 3005 (w), 2988 (w), 1592 (m), 1546 (m), 1475 (m), 1421 (m), 1362 (m), 971 (m), 915 (m).

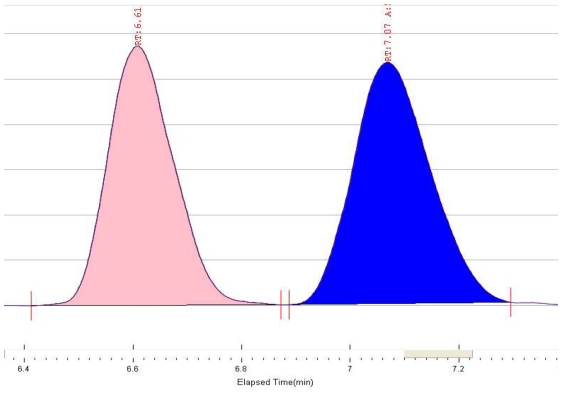
Analysis of Stereochemistry:



Racemic compound was prepared according to the procedure described above with racemic 4,4,5,5-tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

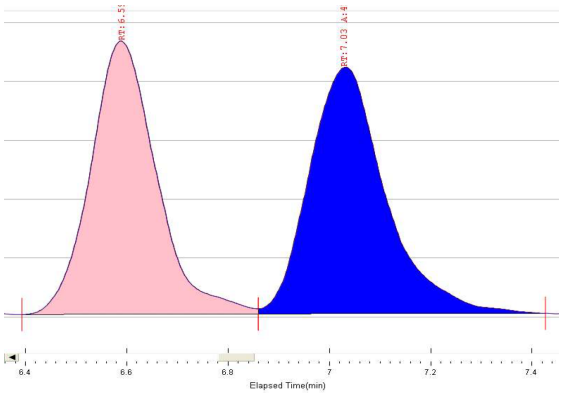
Chiral SFC (Chiralcel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 4-phenylpentan-1-ol

Racemic Compound

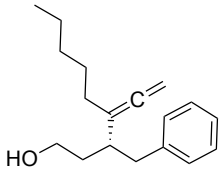


Peak No	% Area	Area	RT (min)
1	47.7534	4818.5698	6.61
2	52.2466	5271.9631	7.07
Total:	100	10090.5329	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	49.0119	4189.3744	6.59
2	50.9881	4358.3012	7.03
Total:	100	8547.6756	



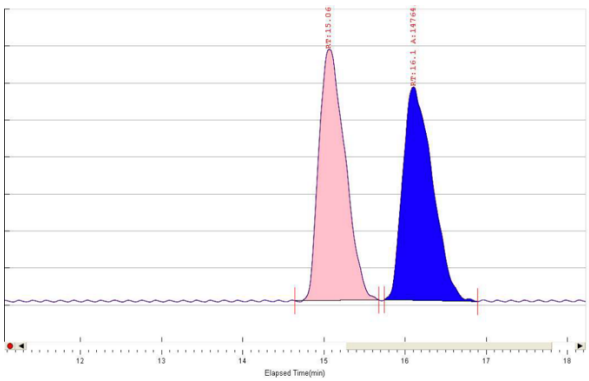
(*R*)-3-Benzyl-4-vinylidenenonan-1-ol (2.112). The title compound was prepared according to *General Procedure I* with (*R*)-*tert*-butyldimethyl(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane (78.1 mg, 0.20 mmol, 96:4 er), 1-bromooct-2-yne (45.4 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 60 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The mixture was put on vaccum for 2 h before being treated with tetrabutylammonium fluoride (1.0 M, 0.50 mmol, 0.5 mL) and was allowed to stir at 25 ºC overnight. The solution was quenched by addition of 1.0 mL of water, washed with Et_2O, the organic layers were concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the product as yellow oil (47.9 mg, 0.17 mmol, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 2H), 7.23 – 7.07 (m, 3H), 4.73 – 4.62 (m, 2H), 3.72 – 3.64 (m, 1H), 3.64 – 3.56 (m, 1H), 2.79 (dd, *J* = 13.5, 7.1 Hz, 1H), 2.62 (dd, *J* = 13.5, 7.4 Hz, 1H), 2.36 – 2.24 (m, 1H), 1.93 – 1.79 (m, 2H), 1.74 – 1.64 (m, 2H), 1.42 – 1.34 (m, 2H), 1.32 – 1.25 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.7, 140.7, 129.3, 128.2, 126.0, 106.1, 77.4, 77.2, 77.1, 76.9, 61.4, 41.02, 40.97, 36.2, 31.7, 30.7, 27.3, 22.7, 14.2.; IR: ν_{max} 3351 (br), 2926 (s), 2854 (m), 1951 (w), 1453 (m), 1049 (m), 844 (m), 750 (w), 699 (m) cm^{-1}.; HRMS (DART) for $C_{18}H_{27}O$ $[M+H]^+$: calculated: 259.2056, found: 259.2048.; $[\alpha]_D^{20}$: +36.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic *tert*-butyldimethyl(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane. Absolute stereochemistry was assigned by analogy.

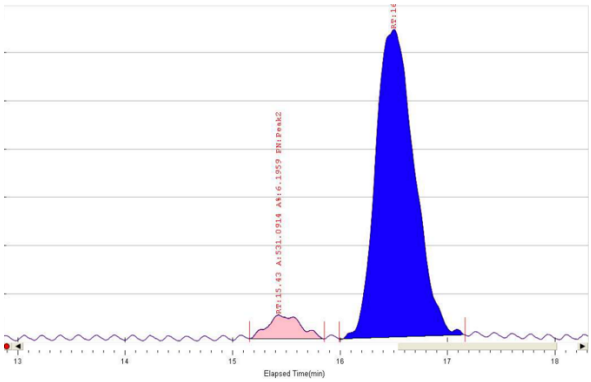
Chiral SFC (Chiralcel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 3-benzyl-4-vinylidenenonan-1-ol

Racemic Compound

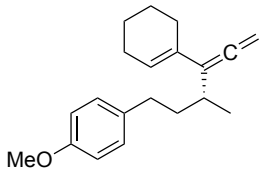


Peak No	% Area	Area	RT (min)
1	50.7973	15242.9709	15.06
2	49.2027	14764.4548	16.1
Total:	100	30007.4257	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	5.786	493.8051	15.43
2	94.214	8040.6155	16.5
Total:	100	8534.4206	



(*R*)-1-(4-(Cyclohex-1-en-1-yl)-3-methylhexa-4,5-dien-1-yl)-4-methoxybenzene (2.113). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), 1-(3-chloroprop-1-ynyl)cyclohexene (37.1 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as yellow oil (52.0 mg, 0.17 mmol, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 – 7.04 (m, 2H), 6.87 – 6.80 (m, 2H), 5.70 – 5.60 (m, 1H), 4.97 (d, *J* = 1.5 Hz, 2H), 3.79 (s, 3H), 2.56 (t, *J* = 8.0 Hz, 2H), 2.45 – 2.37 (m, 1H), 2.17 – 2.06 (m, 4H), 1.85 – 1.76 (m, 1H), 1.66 (dd, *J* = 5.9, 2.4 Hz, 2H), 1.62 – 1.57 (m, 3H), 1.10 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 207.8, 157.7, 135.1, 131.5, 129.4, 122.2, 113.8, 112.9, 79.2, 77.4, 77.2, 76.9, 55.4, 38.5, 33.0, 30.7, 27.9, 26.1, 23.2, 22.6, 20.7.; IR: ν_{max} 2930 (m), 2855 (w), 1691 (m), 1610 (w),

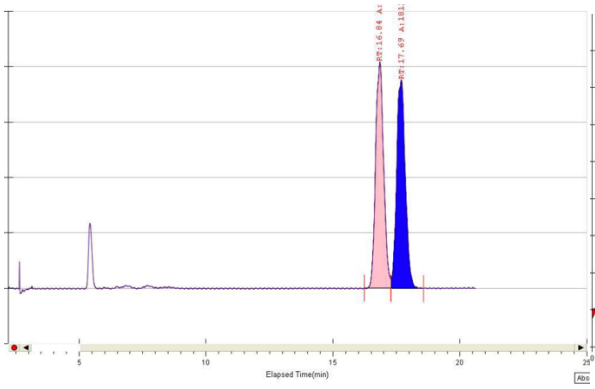
1510 (s), 1455 (w), 1244 (s), 1176 (w), 1035 (w), 826 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{25}O$ $[M+H]^+$: calculated: 281.1900, found: 281.1899.; $[\alpha]_D^{20}$: +1.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

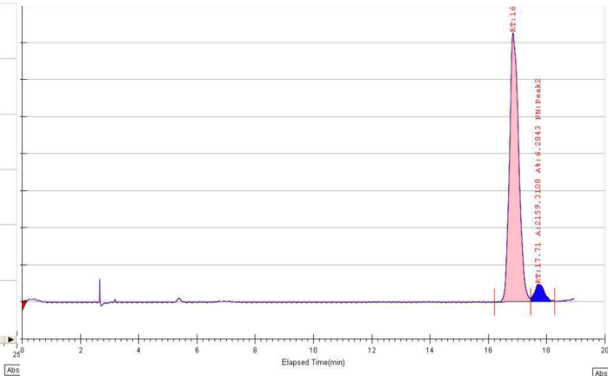
Chiral SFC (Chiralcel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(4-(cyclohex-1-en-1-yl)-3-methylhexa-4,5-dien-1-yl)-4-methoxybenzene

Racemic Compound

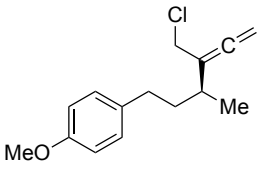


Peak No	% Area	Area	RT (min)
1	49.9378	18072.3727	16.84
2	50.0622	18117.4231	17.69
Total:	100	36189.7958	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.7157	32201.0688	16.84
2	6.2843	2159.3108	17.71
Total:	100	34360.3796	



(*S*)-1-(4-(Chloromethyl)-3-methylhexa-4,5-dien-1-yl)-4-methoxybenzene (2.114). The title compound was prepared according to *General Procedure I* with (*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 97:3 er), 1,4-dichlorobut-2-yne (29.5 mg,

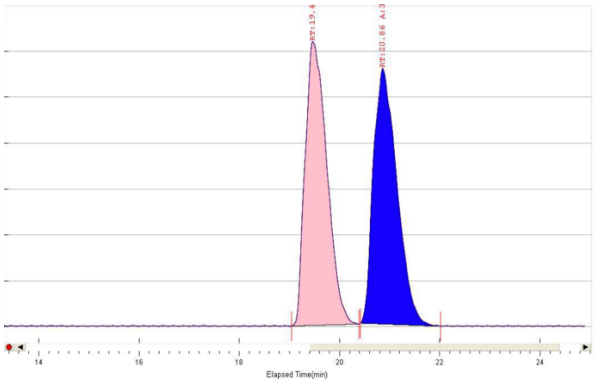
0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as yellow oil (45.0 mg, 0.18 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 – 7.05 (m, 2H), 7.88 – 7.78 (m, 2H), 4.91 (s, 2H), 4.15 (s, 2H), 3.80 (s, 3H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.35 – 2.25 (m, 1H), 1.88 – 1.74 (m, 1H), 1.68 – 1.53 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.9, 157.8, 134.7, 129.4, 113.9, 106.1, 78.1, 77.4, 77.2, 76.9, 55.4, 46.1, 37.6, 33.0, 32.6, 19.8.; IR: ν_{max} 2929 (w), 1949 (w), 1610 (w), 1510 (s), 1455 (w), 1243 (s), 1176 (m), 1037 (m), 851 (w), 822 (w), 711 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{20}OCl$ $[M+H]^+$: calculated: 251.1197, found: 251.1200.; $[\alpha]_D^{20}$: +21.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

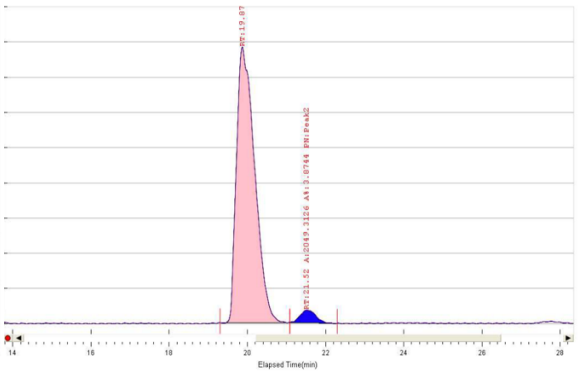
Chiral SFC (Chiralcel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(4-(chloromethyl)-3-methylhexa-4,5-dien-1-yl)-4-methoxybenzene

Racemic Compound

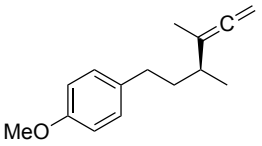


Peak No	% Area	Area	RT (min)
1	50.4529	37237.0995	19.46
2	49.5471	36568.5123	20.86
Total:	100	73805.6118	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.1256	50844.937	19.87
2	3.8744	2049.3126	21.52
Total:	100	52894.2496	



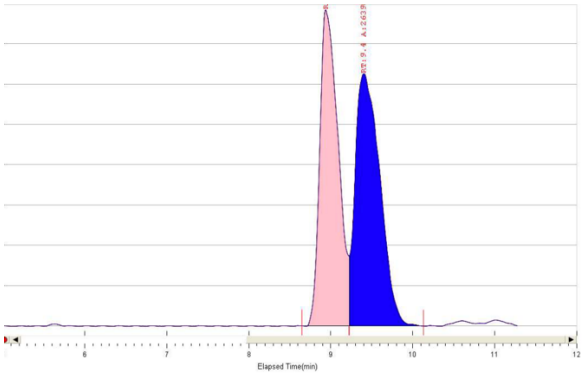
(*S*)-1-(3,4-Dimethylhexa-4,5-dien-1-yl)-4-methoxybenzene (2.115). The title compound was prepared according to *General Procedure I* with (*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 97:3 er), 1-bromobut-2-yne (31.9 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as yellow oil (37.6 mg, 0.17 mmol, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 – 7.07 (m, 2H), 6.90 – 6.77 (m, 2H), 4.70 – 4.60 (m, 2H), 3.80 (s, 3H), 2.62 – 2.48 (m, 2H), 2.09 – 2.00 (m, 1H), 1.79 – 1.71 (m, 1H), 1.69 (t, J = 3.1 Hz, 3H), 1.62 – 1.52 (m, 1H), 1.07 (d, J = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.9, 157.8, 135.0, 129.4, 113.8, 102.6, 77.4, 77.2, 76.9, 74.5, 55.4, 37.3, 36.7, 32.8, 19.5, 16.5.; IR: ν_{max} 2927 (w), 1955 (w), 1610 (w), 1510 (s), 1455 (w), 1244 (s), 1176 (w), 1038 (m), 842(m) cm^{-1}.; HRMS (DART) for $C_{15}H_{21}O$ $[M+H]^+$: calculated: 217.1587, found: 217.1582.; $[\alpha]_D^{20}$: +19.0 (c = 1.0, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

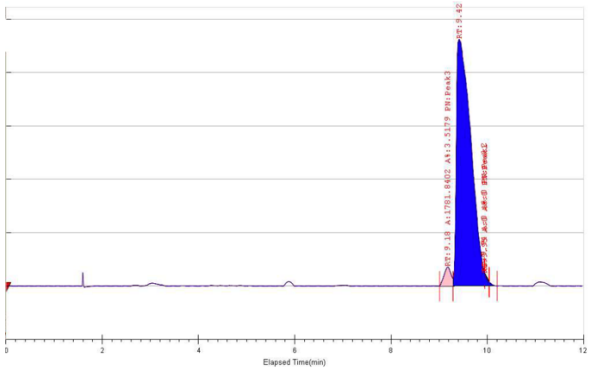
Chiral SFC (Chiralcel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-(4-(chloromethyl)-3-methylhexa-4,5-dien-1-yl)-4-methoxybenzene.

Racemic Compound

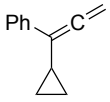


Peak No	% Area	Area	RT (min)
1	47.9648	24326.2651	8.94
2	52.0352	26390.623	9.4
Total:	100	50716.8881	

Standard Conditions

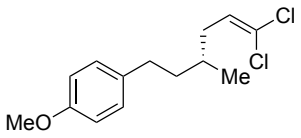


Peak No	% Area	Area	RT (min)
1	3.5179	1781.8402	9.18
2	96.4821	48868.5229	9.42
3	0	0	9.94
4	0	0	9.95
Total:	100	50650.3631	

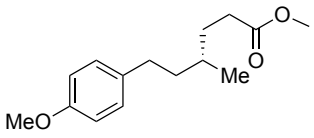


(1-Cyclopropylpropa-1,2-dien-1-yl)benzene (2.116). The title compound was prepared according to *General Procedure I* with 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (33.6 mg, 0.20 mmol), 3-chloroprop-1-ynylbenzene (36.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (100% hexanes) to afford the product as colorless oil (23.4 mg, 0.15 mmol, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 7.8 Hz, 2H), 7.37 (t, *J* =

7.7 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 5.18 – 5.05 (m, 2H), 1.63 – 1.55 (m, 1H), 0.93 – 0.87 (m, 2H), 0.62 – 0.55 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.0, 136.9, 128.4, 126.9, 126.3, 108.4, 79.4, 77.4, 77.2, 76.9, 10.5, 7.0.; IR: ν_{max} 3004 (w), 1726 (s), 1597 (w), 1383 (m), 1225 (m), 1033 (w), 991 (m), 760 (w), 704 (m) cm^{-1}.; HRMS (DART) for $C_{12}H_{13}$ $[M+H]^+$: calculated: 157.1012, found: 157.1021.



(*R*)-1-(6,6-Dichloro-3-methylhex-5-en-1-yl)-4-methoxybenzene (2.117). The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 94:6 er), styrene (10.4 mg, 0.10 mmol), 3,3-trichloroprop-1-ene (51.3 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The pale-yellow oil residue was purified by silica gel chromatography (0–2% ethyl acetate in hexanes) to afford the product as pale-yellow oil (51.2 mg, 0.19 mmol, 93% yield). Analysis of stereochemistry was performed after further transformation. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.06 (m, 2H), 6.86 – 6.82 (m, 2H), 5.87 (t, *J* = 7.5 Hz, 1H), 3.80 (s, 3H), 2.62 (ddd, *J* = 13.8, 9.7, 5.8 Hz, 1H), 2.54 (ddd, *J* = 13.9, 10.1, 6.0 Hz, 1H), 2.22 (ddd, *J* = 14.7, 7.4, 5.5 Hz, 1H), 2.09 (dt, *J* = 14.8, 7.4 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.52 – 1.42 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 134.6, 129.3, 128.8, 120.4, 113.9, 77.4, 77.2, 76.9, 55.4, 38.6, 36.8, 32.6, 32.4, 19.6.; IR: ν_{max} 2928 (w), 1612 (w), 1510 (s), 1461 (w), 1244 (s), 1176 (m), 1037 (m), 822 (m) cm^{-1}. HRMS (DART) for $C_{14}H_{19}Cl_2O$ $[M+H]^+$: calculated: 273.0808, found: 273.0807.; $[\alpha]_D^{20}$: –1.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).



Methyl (*R*)-6-(4-methoxyphenyl)-4-methylhexanoate (2.118). The title coumpound was prepared according to a literature procedure.[74] To a 2-dram vial charged with a magnetic stir bar and (*R*)-1-(6,6-dichloro-3-methylhex-5-en-1-yl)-4-methoxybenzene **(2.117)** (54.6 mg, 0.20 mmol) was added bis[(Z)-1-methyl-3-oxo-but-1-enoxy]cobalt (51.4 mg, 0.20 mmol) . The flask was sealed with rubber septa and purged with O_2 for 20 min. Then, MeOH (1.1 mL), triethylsilane (116.3 mg, 1.0 mmol, 159.7 μL) and *tert*-butyl hydroperoxide (0.3 mmol, 49.4 μL) were added to the reaction under O_2 atmosphere. The solution was allowed to stir at 25 ºC for 12 h. Upon completion, the mixture was diluted with Et_2O, passed through a pad of silica gel, and concentrated under reduced pressure. The brown oil residue was purified by silica gel chromatography (0–10% EtOAc/hexanes) to afford the product as pale-yellow oil (40.0 mg, 0.16 mmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 – 7.07 (m, 2H), 6.85 – 6.79, (m, 2H), 3.79 (s, 3H), 3.67 (s, 3H), 2.61 (ddd, *J* = 13.4, 10.1, 5.2 Hz, 1H), 2.53 (ddd, *J* = 13.6, 9.7, 6.1 Hz, 1H), 2.40 – 2.25 (m, 2H), 1.78 – 1.69 (m, 1H), 1.66 – 1.57 (m, 1H), 1.55 – 1.39 (m, 3H), 0.95 (d, *J* = 5.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 157.7, 134.8, 129.3, 129.2, 113.8, 77.4, 77.2, 76.9, 55.3, 51.6, 38.9, 32.4, 32.1, 31.88, 31.86, 19.3.; IR: ν_{max} 2927 (m), 2854 (w), 1737 (s), 1611 (w), 1511 (s), 1457 (w), 1245 (s), 1175 (m), 1037 (w), 824 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{23}O_3$ $[M+H]^+$: calculated: 251.1642, found: 251.1653.; $[\alpha]_D^{20}$: +6.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).

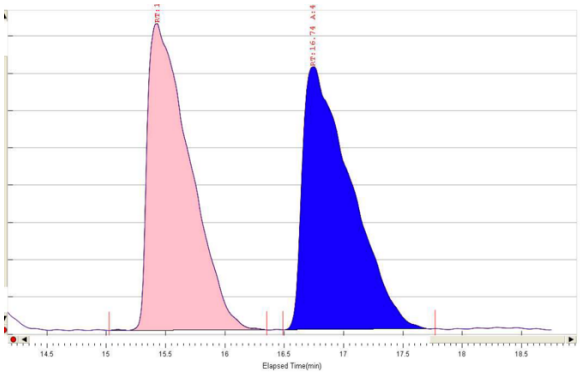
[74] Ma, X.; Herzon, S. B. *J. Org. Chem.* **2016**, *81*, 8673–8695.

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 1-(6,6-dichloro-3-methylhex-5-en-1-yl)-4-methoxybenzene. Absolute stereochemistry was assigned by analogy.

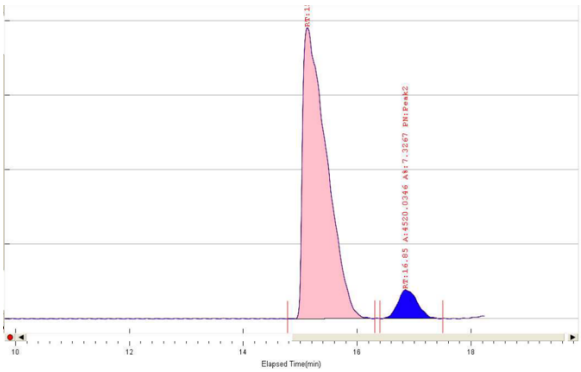
Chiral SFC (Chiralcel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of methyl-6-(4-methoxyphenyl)-4-methylhexanoate

Racemic Compound

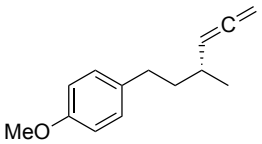


Peak No	% Area	Area	RT (min)
1	50.2832	40574.2947	15.43
2	49.7168	40117.1974	16.74
Total:	100	80691.4921	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	92.6733	57172.7761	15.13
2	7.3267	4520.0346	16.85
Total:	100	61692.8107	



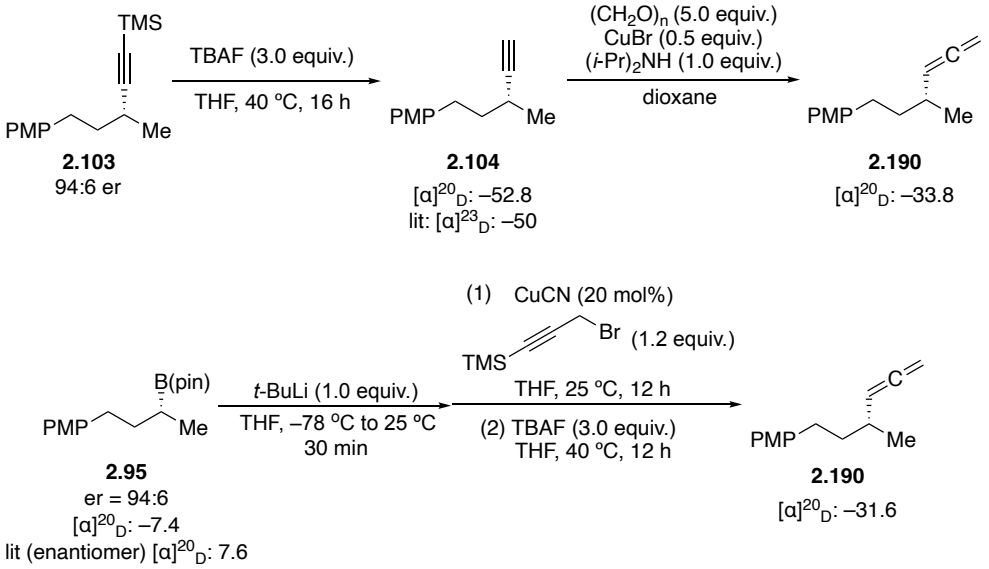
(*R*)-1-Methoxy-4-(3-methylhexa-4,5-dien-1-yl)benzene (2.190). The title compound was prepared according to two routes:

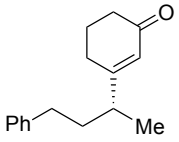
Route 1: (*R*)-1-methoxy-4-(3-methylpent-4-yn-1-yl)benzene (160 mg, 0.85 mmol, 94:6 er) was dissolved in 10 mL anhydrous 1,4-dioxane. To the solution was added copper(I) bromide (61.0 mg, 0.42 mmol), paraformaldehyde (127.6 mg, 4.25 mmol), and diisopropylamine (86.0 mg, 0.85 mmol). The resulting orange solution was heated to reflux and was allowed to stir for 16 h. The mixture was filtered through a thick silica gel pad, diluted with Et_2O, and concentrated under

reduced pressure. The dark brown oil residue was purified by silica gel chromatography (100% hexanes) to afford the product as colorless oil (106 mg, 0.52 mmol, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.05 (m, 2H), 6.91 – 6.80 (m, 2H), 5.12 (q, *J* = 6.7 Hz, 1H), 4.75 (d, *J* = 2.7 Hz, 1H), 4.74 (d, *J* = 2.7 Hz, 1H), 3.81 (s, 3H), 2.69 – 2.56 (m, 2H), 2.26 – 2.15 (m, 1H), 1.73 – 1.57 (m, 2H), 1.08 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.8, 157.8, 134.8, 129.4, 113.8, 95.9, 77.4, 77.2, 76.9, 75.7, 55.4, 39.2, 32.8, 32.5, 20.6.; IR: ν_{max} 2925 (w), 1951 (w), 1611 (w), 1510 (s), 1456 (w), 1244 (s), 1176 (m), 1037 (m), 825 (m) cm^{-1}.; HRMS (DART) for $C_{14}H_{19}O$ $[M+H]^+$: calculated: 203.1430, found: 203.1422.; $[\alpha]_D^{20}$: –33.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Route 2: The title compound was prepared according to *General Procedure I* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (87.1 mg, 0.30 mmol, 94:6 er), 3-bromoprop-1-ynyl(trimethyl)silane (68.8 mg, 0.36 mmol), copper cyanide (5.4 mg, 0.06 mmol). The mixture was allowed to stir at 25 ºC overnight, filtered through a silica gel plug and concentrated under reduced pressure. The mixture was put on vaccum for 2 h before being treated with tetrabutylammonium fluoride (1.0 M, 0.9 mmol, 0.9 mL) and was allowed to stir at 40 ºC overnight. The reaction was quenched by addition of 1.0 mL of water, washed with Et_2O, and organic layers were concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (100% hexanes) to afford the product as colorless oil (52.0 mg, 0.26 mmol, 85% yield). $[\alpha]_D^{20}$: –31.6 (c = 1.0, $CHCl_3$, *l* = 50 mm). All other spectural data match data acquired in route 1.

Proof of Stereoretention in SN2' Reactions:





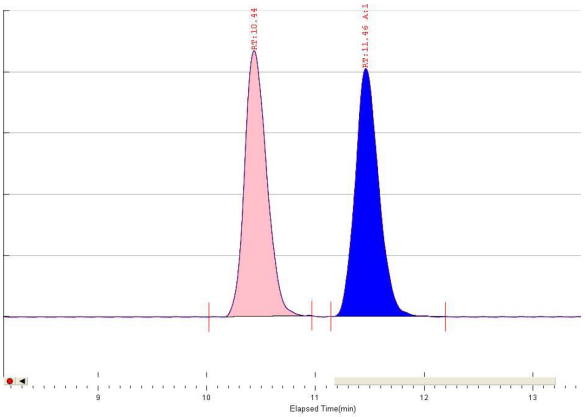
(*R*)-3-(4-Phenylbutan-2-yl)cyclohex-2-en-1-one (2.124). The title compound was prepared according to *General Procedure E* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.8 mg, 0.20 mmol, 96:4 er). The brown oil residue was purified by silica gel chromatography to afford the product as pale-yellow oil (33.6 mg, 0.15 mmol, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.21 – 7.17 (m, 1H), 7.17 – 7.13 (m, 2H), 5.91 (d, *J* = 2.0 Hz, 1H), 2.62 – 2.51 (m, 2H), 2.40 – 2.36 (m, 2H), 2.34 (q, *J* = 6.9 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.04 – 1.92 (m, 2H), 1.87 – 1.78 (m, 1H), 1.76 – 1.66 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.1, 170.4, 141.7, 128.4, 128.3, 125.9, 125.4, 41.2, 37.7, 36.3, 33.6, 26.9, 22.9, 18.9. IR ν_{max} 2931 (w), 2866 (w), 1667 (s), 1620 (m), 1453 (w), 1253 (m), 1191 (w), 888 (m), 748 (m), 700 (m). HRMS (DART) for $C_{16}H_{21}O[M+H]^+$: calculated: 229.1587, found: 229.1583. $[\alpha]_D^{20}$: –12.5 (c = 0.93, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

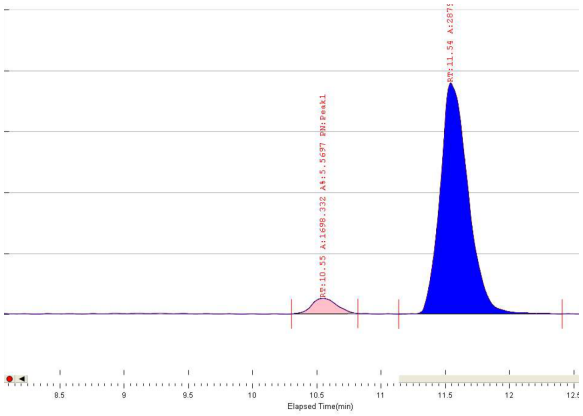
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 3-(4-phenylbutan-2-yl)cyclohex-2-en-1-one

Racemic compound

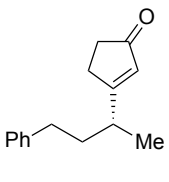


Peak No	% Area	Area	RT (min)
1	50.1181	12284.5639	10.44
2	49.8819	12226.6644	11.46
Total:	100	24511.2283	

Standard conditions



Peak No	% Area	Area	RT (min)
1	5.5697	1698.332	10.55
2	94.4303	28794.1964	11.54
Total:	100	30492.5284	



(*R*)-3-(4-Phenylbutan-2-yl)cyclopent-2-en-1-one (2.125). The title compound was prepared according to *General Procedure E* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.8 mg, 0.20 mmol, 96:4 er). The yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow oil (13.2 mg, 0.06 mmol, 32% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.13 (m, 3H), 5.98 (d, *J* = 2.0 Hz, 1H), 2.67 – 2.55 (m, 5H), 2.45 – 2.35 (m, 2H), 1.91 (ddt, *J* = 13.6, 9.3, 6.8 Hz, 1H), 1.78 (ddt, *J* = 13.4, 9.3, 6.7 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126

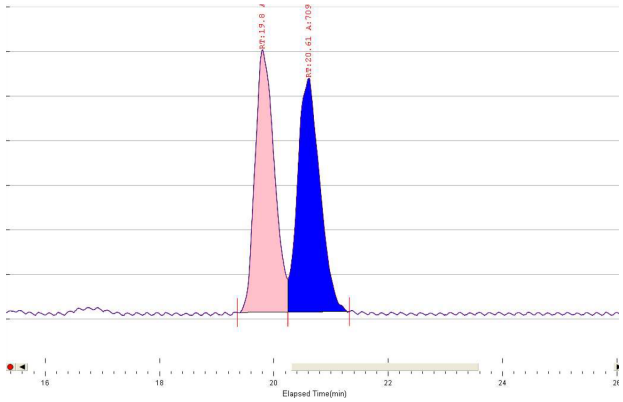
MHz, $CDCl_3$) δ 210.1, 187.0, 141.5, 129.1, 128.5, 128.3, 126.0, 36.9, 36.6, 35.1, 33.4, 29.0, 18.9. IR ν_{max} 3016 (w), 2970 (w), 1739 (s), 1435 (w), 1366 (s), 1229 (s), 528 (m). HRMS (DART) for $C_{15}H_{19}O$ $[M+H]^+$: calculated: 215.1430, found: 215.1428. $[\alpha]_D^{20}$: –24.3 (c = 0.37, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

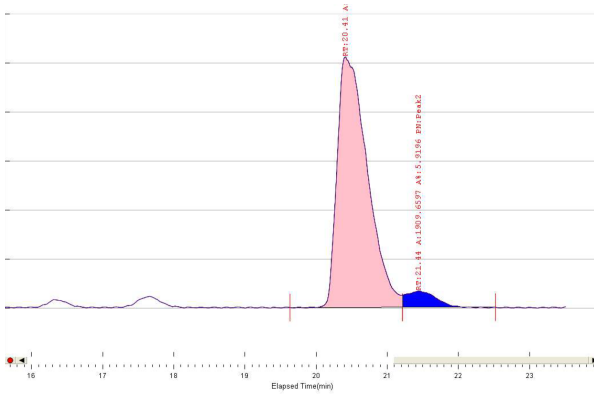
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 3-(4-phenylbutan-2-yl)cyclopent-2-en-1-one

Racemic compound

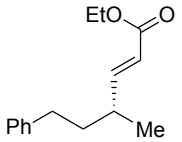


Peak No	% Area	Area	RT (min)
1	49.4099	6929.3981	19.8
2	50.5901	7094.9221	20.61
Total:	100	14024.3202	

Standard conditions



Peak No	% Area	Area	RT (min)
1	94.0804	30350.3973	20.41
2	5.9196	1909.6597	21.44
Total:	100	32260.057	



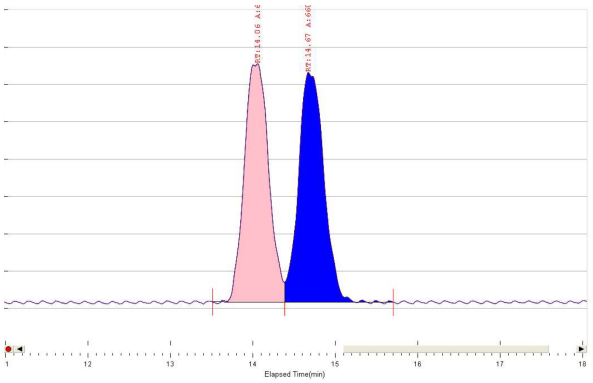
Ethyl (*R*,*E*)-4-methyl-6-phenylhex-2-enoate (2.126). The title compound was prepared according to *General Procedure E* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.8 mg, 0.20 mmol, 96:4 er). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (40.6 mg, 0.17 mmol, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.22 – 7.13 (m, 3H), 6.90 (dd, *J* = 15.7, 8.0 Hz, 1H), 5.81 (dd, *J* = 15.7, 1.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 2.70 – 2.51 (m, 2H), 2.44 – 2.25 (m, 1H), 1.80 – 1.64 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 6.7 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8, 154.0, 142.0, 128.4, 128.3, 125.8, 120.1, 60.2, 37.7, 36.0, 33.4, 19.5, 14.3.; IR: ν_{max} 3016 (w), 2970 (m), 2945 (w), 1739 (s), 1652 (w), 1435 (m), 1366 (s), 1229 (s), 1217 (s), 1092 (w), 900 (w), 539 (m). HRMS (DART) for $C_{15}H_{21}O_2$ $[M+H]^+$ calculated: 233.1536, found: 233.1540. $[\alpha]_D^{20}$: –38.0 (c = 1.10, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

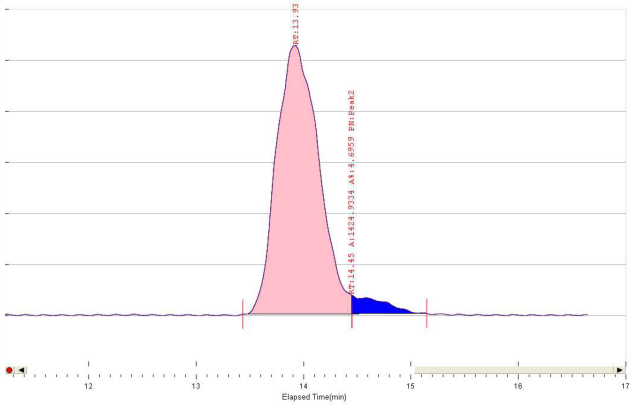
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis of ethyl (R,E)-4-methyl-6-phenylhex-2-enoate

Racemic compound



Peak No	% Area	Area	RT (min)
1	50.0333	6613.5429	14.06
2	49.9667	6604.7469	14.67
Total:	100	13218.2898	

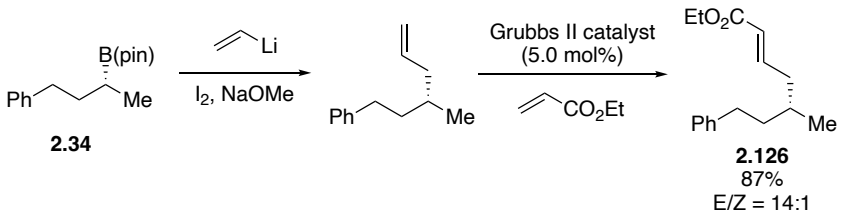
Standard conditions



Peak No	% Area	Area	RT (min)
1	95.3041	28919.5114	13.93
2	4.6959	1424.9334	14.45
Total:	100	30344.4448	

Analysis of Absolute Configuration

Absolute configuration of product was confirmed by comparing SFC retention time of major isomer with compound obtained from other methods.



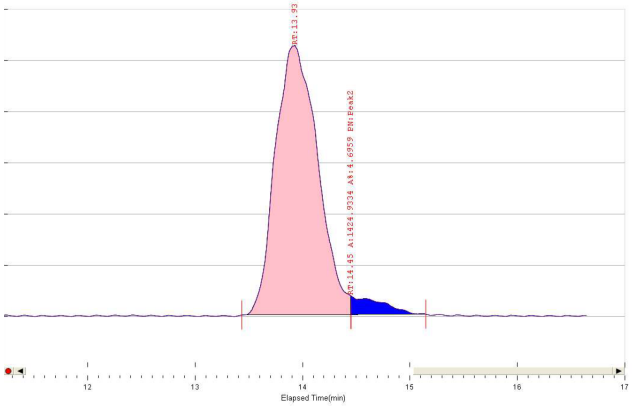
In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkylboronic ester (104.1 mg, 0.4 mmol) and anhydrous tetrahydrofuran (1.0 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was cooled to –78 ºC and vinyl lithium (0.8 mL, 1.5 equiv., 0.75 M solution in THF) was added dropwise by a syringe, and was then allow to warm to room temperature and to stir for

30 min. The mixture was cooled to –78 ºC again and a solution of iodine (253.8 mg in 1.0 mL tetrahydrofuran, 1.0 mmol, 2.5 equiv.) was added dropwise by syringe. The mixture was allowed to stir at –78 ºC for 1 h, then sodium methoxide (54.0 mg, 1.6 mmol, 1.5 equiv.) dissolved in methanol (1.0 mL) and added dropwise. The mixture was warmed to room temperature and allowed to stir for 12 h. After that, the reaction was quenched by addition of a saturated aqueous solution of Na_2SO_3 and was washed with diethyl ether. The organic layers were combined, dried over Na_2SO_4 and concentrated under reduced pressure. The brown oil residue was purified by silica gel chromatography (hexanes, visualized by UV light) to furnish the desired product as colorless oil (33.1 mg, 0.21 mmol, 52% yield)

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added alkene (33.1 mg, 0.21 mmol, 1.0 equiv.), ethyl prop-2-enoate (51.7 mg, 0.52 mmol, 2.5 equiv.), Grubbs-II catalyst (8.8 mg, 0.01 mmol, 5.0 mol%) and dichloromethane (1.0 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was allowed to stir at 40 ºC for 12 h. After that, the mixture was passed through a short silica gel plug and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography (0–10% diethyl ether in hexanes, visualized by UV light) to furnish the desired product (**2.126**) as colorless oil (40.8 mg, 0.18 mmol, 87% yield, 14:1 *E*/*Z*).

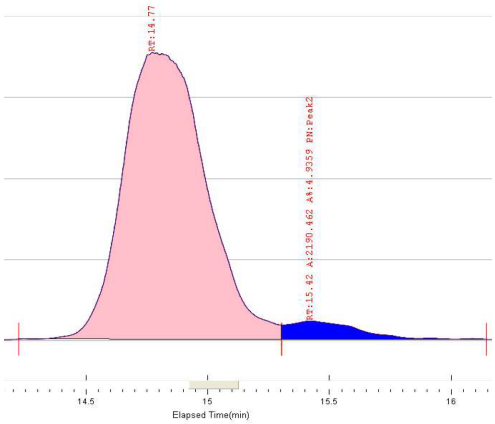
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis of ethyl (R,E)-4-methyl-6-phenylhex-2-enoate

From this method

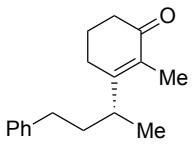


Peak No	% Area	Area	RT (min)
1	95.3041	28919.5114	13.93
2	4.6959	1424.9334	14.45
Total:	100	30344.4448	

From known method



Peak No	% Area	Area	RT (min)
1	95.0641	42187.4096	14.77
2	4.9359	2190.462	15.42
Total:	100	44377.8716	



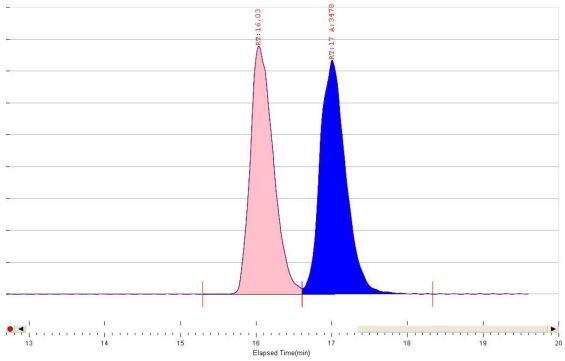
(*R*)-2-Methyl-3-(4-phenylbutan-2-yl)cyclohex-2-en-1-one (2.127). The title compound was prepared according to *General Procedure E* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.84 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (36.5 mg, 0.15 mmol, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.21 – 7.17 (m, 1H), 7.17 – 7.13 (m, 2H), 5.91 (s, 1H), 2.62 – 2.51 (m, 2H), 2.40 – 2.36 (m, 2H), 2.34 (q, J = 6.9 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.04 – 1.92 (m, 2H), 1.87 – 1.78 (m, 1H), 1.76 – 1.66 (m, 1H), 1.13 (d, J = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.6, 162.2, 141.8, 130.8, 128.4, 128.3, 125.9, 38.1, 36.6, 36.2, 34.0, 24.8, 22.7, 18.2, 10.4.; IR: ν_{max} 3016 (w), 2969 (m), 2942 (w), 1739 (s), 1662 (m), 1454 (m), 1366 (s), 1229 (s), 1217 (s), 699 (w), 540 (m).; HRMS (DART) for $C_{17}H_{23}O$ $[M+H]^+$ calculated: 243.1743, found 243.1744.; $[\alpha]_D^{20}$: +11.4 (c = 1.00, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

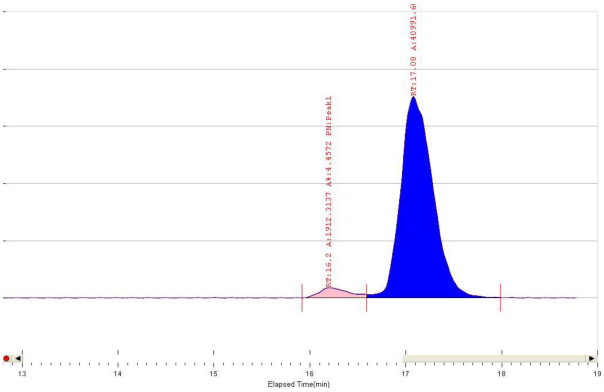
Chiral SFC (Chiracel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis for 2-methyl-3-(4-phenylbutan-2-yl)cyclohex-2-en-1-one

Racemic compound

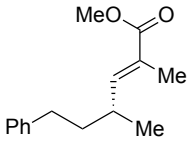


Peak No	% Area	Area	RT (min)
1	48.905	33291.8376	16.03
2	51.095	34782.6994	17
Total:	100	68074.537	

Standard conditions



Peak No	% Area	Area	RT (min)
1	4.4572	1912.3137	16.2
2	95.5428	40991.6063	17.08
Total:	100	42903.92	



Methyl (*R*,*E*)-2,4-dimethyl-6-phenylhex-2-enoate (2.128). The title compound was prepared according to *General Procedure E* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.84 mg, 0.20 mmol, 96:4 er). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (40.8 mg, 0.17 mmol, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.22 – 7.12 (m, 3H), 6.62 (dq, *J* = 10.1, 1.5 Hz, 1H), 3.76 (s, 3H), 2.72 – 2.44 (m, 3H), 1.82 (d, *J* = 1.5 Hz, 3H), 1.79 – 1.71 (m, 1H), 1.70 – 1.62 (m, 1H), 1.05 (d, *J* = 6.7 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8,

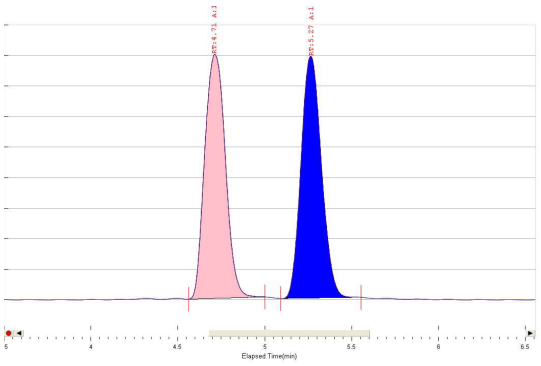
147.8, 142.1, 128.33, 128.32, 126.6, 125.8, 51.7, 38.5, 33.7, 32.8, 20.0, 12.6.; IR: ν_{max} 3016 (w), 2970 (m), 2947 (w), 1739 (s), 1435 (m), 1366 (s), 1229 (s), 1217 (s), 1092 (w), 900 (w), 539 (m).; HRMS (DART) for $C_{15}H_{21}O_2$ $[M+H]^+$ calculated: 233.1536, found 233.1537.; $[\alpha]_D^{20}$: –25.3 (c = 1.24, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

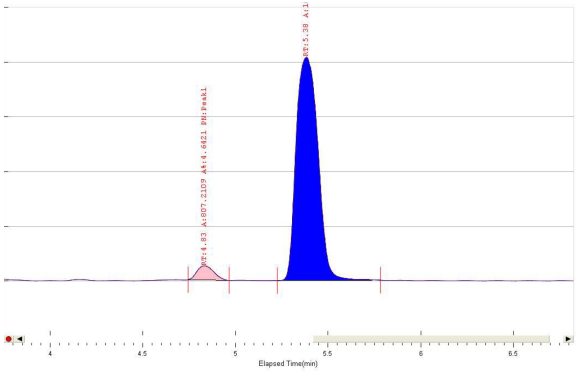
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis of methyl (R,E)-2,4-dimethyl-6-phenylhex-2-enoate

Racemic compound

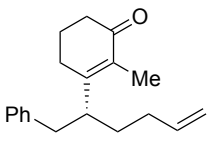


Peak No	% Area	Area	RT (min)
1	50.5848	13189.7446	4.71
2	49.4152	12884.7914	5.27
Total:	100	26074.536	

Standard conditions



Peak No	% Area	Area	RT (min)
1	4.6421	807.2109	4.83
2	95.3579	16581.5276	5.38
Total:	100	17388.7385	



(*R*)-2-Methyl-3-(1-phenylhex-5-en-2-yl)cyclohex-2-en-1-one (2.129). The title compound was prepared according to *General Procedure E* with (*R*)-4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane (57.24 mg, 0.20 mmol, 96:4

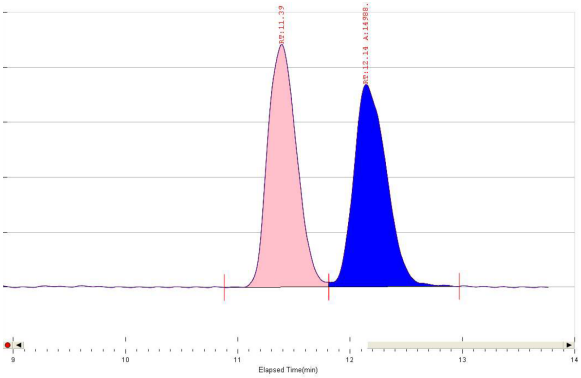
er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (27.9 mg, 0.10 mmol, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 2H), 7.20 – 7.13 (m, 1H), 7.13 – 7.06 (m, 2H), 5.75 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.00 – 4.93 (m, 2H), 3.11 (tt, *J* = 9.1, 5.9 Hz, 1H), 2.79 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.66 (dd, *J* = 13.6, 8.7 Hz, 1H), 2.36 (t, *J* = 6.7 Hz, 2H), 2.33 – 2.18 (m, 1H), 2.09 – 1.82 (m, 3H), 1.67 – 1.57 (m, 2H), 1.57 (t, *J* = 1.7 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 159.4, 139.6, 138.0, 132.7, 128.7, 128.3, 126.2, 115.0, 44.3, 39.6, 38.1, 31.9, 31.7, 25.1, 22.5, 10.6.; IR: ν_{max} 3016 (w), 2970 (m), 2945 (w), 1739 (s), 1663 (w), 1435 (m), 1366 (s), 1229 (s), 1217 (s), 907 (w), 539 (m).; HRMS (DART) for $C_{19}H_{25}O$ $[M+H]^+$ calculated: 269.1900, found: 269.1909.; $[\alpha]_D^{20}$: –34.7 (c = 0.83 $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

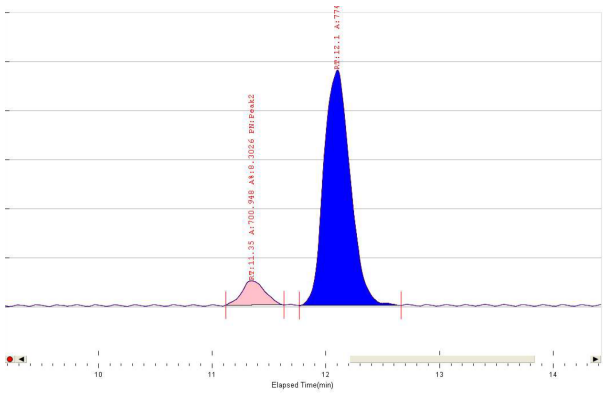
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis of 4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane

Racemic compound

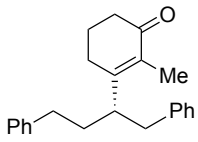


Peak No	% Area	Area	RT (min)
1	51.3994	15851.1388	11.39
2	48.6006	14988.0051	12.14
Total:	100	30839.1439	

Standard conditions



Peak No	% Area	Area	RT (min)
1	8.3026	700.948	11.35
2	91.6974	7741.5956	12.1
Total:	100	8442.5436	



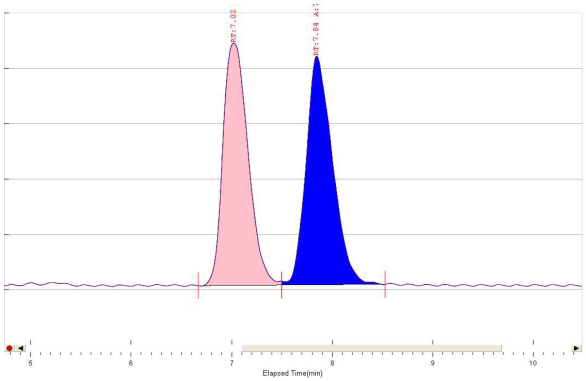
(*S*)-3-(1,4-Diphenylbutan-2-yl)-2-methylcyclohex-2-en-1-one (2.130). The title compound was prepared according to *General Procedure E* with (*S*)-2-(1,4-diphenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.26 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (45.8 mg, 0.14 mmol, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 4H), 7.22 – 7.16 (m, 2H), 7.15 – 7.07 (m, 4H), 3.20 – 3.07 (m, 1H), 2.83 (dd, J = 13.6, 6.4 Hz, 1H), 2.70 (dd, J = 13.6, 8.7 Hz, 1H), 2.61 – 2.48 (m, 2H), 2.42 – 2.25 (m, 4H), 2.01 – 1.77 (m, 4H), 1.53 (s, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.3, 159.3, 141.6, 139.5, 132.8, 128.8, 128.4, 128.32, 128.31, 128.26, 126.3, 126.0, 44.5, 39.7, 38.1, 34.3, 33.9, 25.2, 22.6, 10.6.; IR: ν_{max} 3025 (w), 2970 (m), 2944 (w), 1739 (s), 1661 (m), 1454 (m), 1366 (s), 1229 (s), 1217 (s), 1092 (w), 900 (w), 700 (w), 539 (m).; HRMS (DART) for $C_{23}H_{27}O$ $[M+H]^+$ calculated: 319.2056, found: 319.2055.; $[\alpha]_D^{20}$: +33.0 (c = 1.34, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(1,4-diphenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

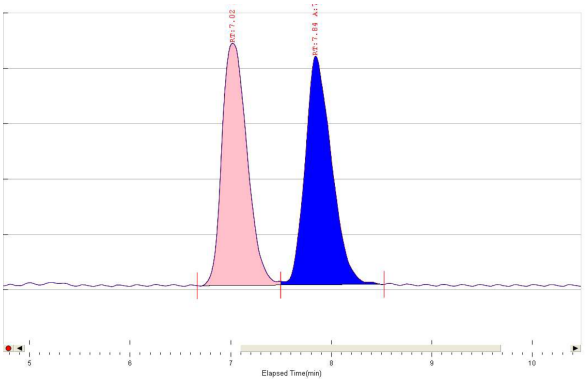
Chiral SFC (Chiracel AS-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)–analysis of 3-(1,4-diphenylbutan-2-yl)-2-methylcyclohex-2-en-1-one

Racemic compound

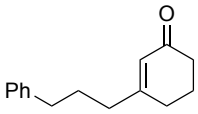


Peak No	% Area	Area	RT (min)
1	50.1404	7602.1665	7.02
2	49.8596	7559.5999	7.84
Total:	100	15161.7664	

Standard conditions

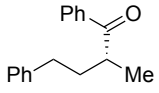


Peak No	% Area	Area	RT (min)
1	4.1279	1266.9635	7.55
2	95.8721	29425.6167	8.36
Total:	100	30692.5802	



3-(3-Phenylpropyl)cyclohex-2-en-1-one (2.131). The title compound was prepared according to *General Procedure E* with 4,4,5,5-tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (29.9 mg, 0.14 mmol, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.23 – 7.10 (m, 3H), 5.90 (s, 1H), 2.64 (t, J = 7.6 Hz, 2H), 2.40 – 2.33 (m, 2H), 2.30 – 2.21 (m, 4H), 1.98 (p, J = 6.2 Hz, 2H), 1.85 (p, J = 7.6 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.8, 166.0, 141.5, 128.42, 128.4, 126.0, 125.9, 37.45, 37.36, 35.3, 29.7, 28.5, 22.7.; IR: ν_{max} 3016 (w), 2970 (m), 2944 (w), 1739 (s), 1667 (m),

1624 (w), 1435 (m), 1366 (s), 1229 (s), 1217 (s), 889 (w), 700 (w), 540 (m).; HRMS (DART) for $C_{15}H_{19}O$ $[M+H]^+$ calculated: 215.1430, found: 215.1440.



(*R*)-2-Methyl-1,4-diphenylbutan-1-one. (2.132) The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (41.5 mg, 0.17 mmol, 87% yield).

Gram-scale synthesis:

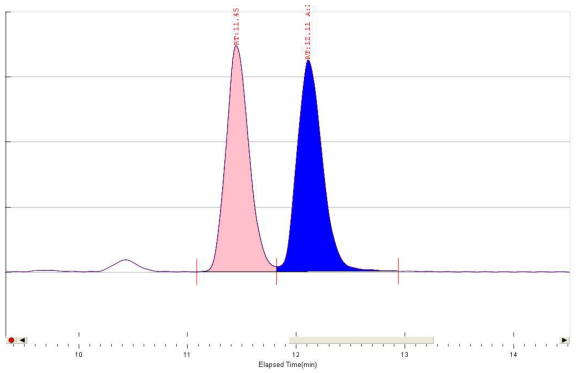
The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (1.50 g, 5.77 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (1.18 g, 4.96 mmol, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.59 – 7.52 (m, 1H), 7.48 – 7.41 (m, 2H), 7.33 – 7.25 (m, 2H), 7.24 – 7.13 (m, 3H), 3.49 (h, 1H), 2.73 – 2.58 (m, 2H), 2.19 (ddt, J = 13.7, 8.7, 7.0 Hz, 1H), 1.77 (ddt, J = 13.6, 8.6, 6.7 Hz, 1H), 1.25 (d, J = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.1, 141.8, 136.6, 132.9, 128.6, 128.5, 128.4, 128.3, 125.9, 39.7, 35.2, 33.5, 17.3.; IR: ν_{max} 3061 (w), 3026 (w), 2932 (w), 1681 (s), 1596 (m), 1496 (m), 1226 (m), 974 (m), 748 (s).; HRMS (DART) for $C_{23}H_{23}O$ $[M+H]^+$ calculated: 315.1743, found: 315.1739. $[\alpha]_D^{20}$: – 34.6 (c = 1.44, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

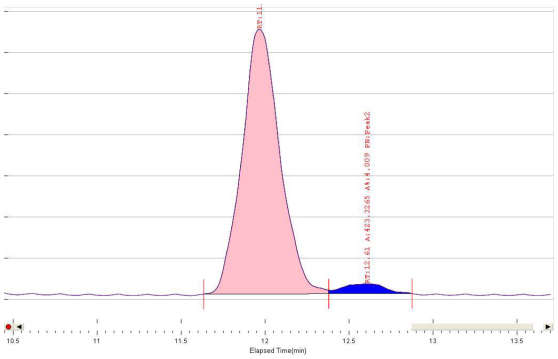
Chiral SFC (Chiracel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 2-methyl-1,4-diphenylbutan-1-one

Racemic compound



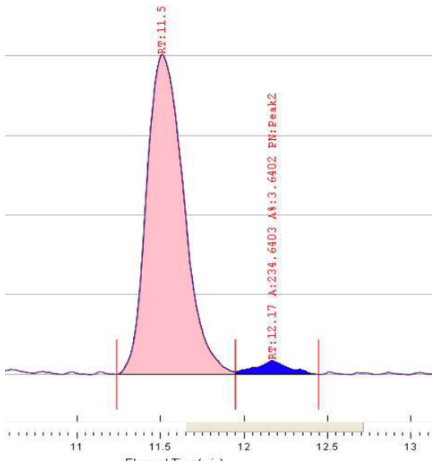
Peak No	% Area	Area	RT (min)
1	49.5211	25794.5712	11.45
2	50.4789	26293.5032	12.11
Total:	100	52088.0744	

Standard conditions

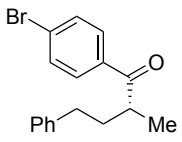


Peak No	% Area	Area	RT (min)
1	95.991	10136.1334	11.97
2	4.009	423.3265	12.61
Total:	100	10559.4599	

Gram-scale reaction



Peak No	% Area	Area	RT (min)
1	96.3598	6211.1523	11.51
2	3.6402	234.6403	12.17
Total:	100	6445.7926	



(*R*)-1-(4-Bromophenyl)-2-methyl-4-phenylbutan-1-one (2.133). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The yellow oil residue

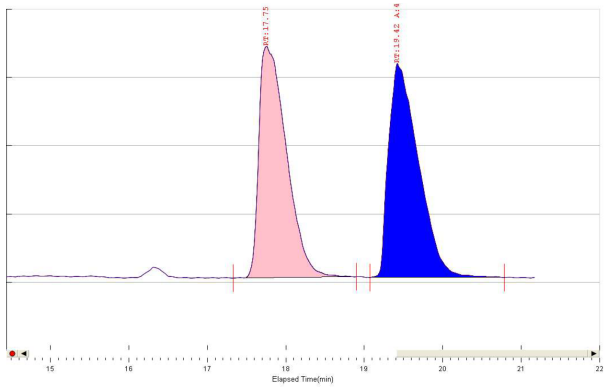
was purified by silica gel chromatography to afford the product as colorless oil (54.1 mg, 0.17 mmol, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.59 – 7.53 (m, 2H), 7.31 – 7.24 (m, 2H), 7.23 – 7.19 (m, 1H), 7.17 – 7.12 (m, 2H), 3.38 (h, J = 6.8 Hz, 1H), 2.68 – 2.60 (m, 2H), 2.20 – 2.08 (m, 1H), 1.77 – 1.70 (m, 1H), 1.22 (d, J = 6.9 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.9, 141.5, 135.2, 131.9, 129.8, 128.5, 128.4, 128.0, 126.0, 39.6, 35.1, 33.4, 17.1.; IR: ν_{max} 3026 (w), 2930 (w), 2360 (m), 2341 (m), 1683 (s), 1584 (s), 1496 (w), 1455 (m), 1396 (m), 1375 (w), 1071 (m), 1010 (s), 975 (s).; HRMS (DART) for $C_{17}H_{18}OBr$ $[M+H]^+$ calculated: 317.0536, found: 317.0534.; $[\alpha]_D^{20}$: –36.0 (c = 1.16, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

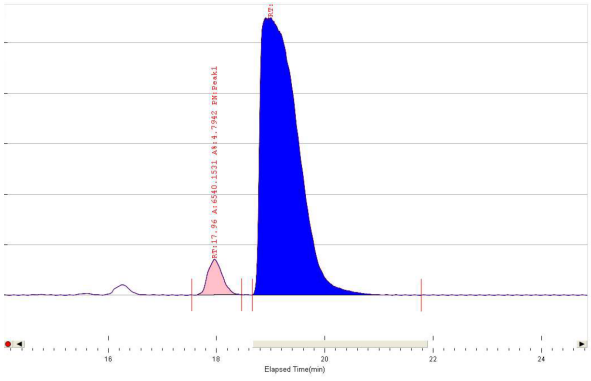
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 1-(4-bromophenyl)-2-methyl-4-phenylbutan-1-one

Racemic compound

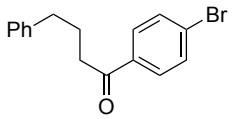


Peak No	% Area	Area	RT (min)
1	49.8791	41297.061	17.75
2	50.1209	41497.3034	19.42
Total:	100	82794.3644	

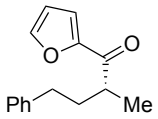
Standard conditions



Peak No	% Area	Area	RT (min)
1	4.7942	6540.1531	17.96
2	95.2058	129877.5742	19
Total:	100	136417.7273	



1-(4-Bromophenyl)-4-phenylbutan-1-one (2.134). The title compound was prepared according to *Method G* with 4,4,5,5-tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow solid (54.0 mg, 0.18 mmol, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.61 – 7.55 (m, 2H), 7.33 – 7.26 (m, 2H), 7.23 – 7.17 (m, 3H), 2.93 (t, *J* = 7.3 Hz, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.08 (p, *J* = 7.4 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.0, 141.5, 135.7, 131.9, 129.6, 128.5, 128.4, 128.1, 126.0, 37.6, 35.1, 25.6.; IR: ν_{max} 3206 (w), 2931 (w), 2229 (m), 1737 (m), 1686 (s), 1585 (s), 1496 (m), 1397 (m), 1225 (m), 1070 (m), 1010 (m), 812 (w), 747 (m), 700 (m).; HRMS (DART) for $C_{16}H_{16}OBr$ $[M+H]^+$ calculated: 303.0379, found: 303.0392.



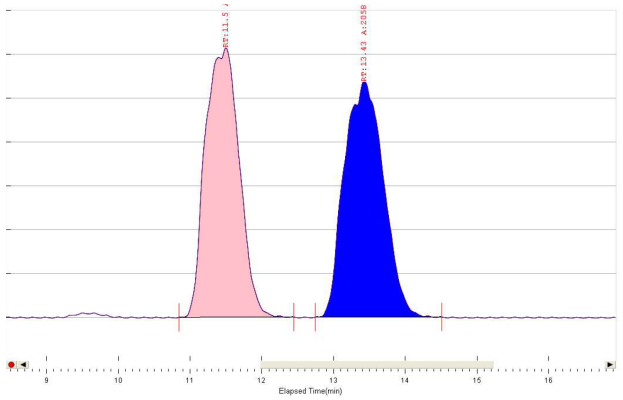
(*R*)-1-(Furan-2-yl)-2-methyl-4-phenylbutan-1-one (2.135). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (33.5 mg, 0.15 mmol, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 1H), 7.31 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 7.10 (d, *J* = 3.5 Hz, 1H), 6.52 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.26 (h, *J* = 6.9 Hz, 1H), 2.64 (t, *J* = 7.9 Hz, 2H), 2.21 – 2.11 (m, 1H), 1.83 – 1.72 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.1, 152.4, 146.4, 141.7, 128.42, 128.35, 125.9, 117.3, 112.1, 40.9, 35.0, 33.5, 17.1.; IR: ν_{max} 3026 (w), 2930 (w), 2360 (m), 2341 (w), 1671 (s), 1565 (m), 1467 (s), 1395 (m), 1258 (m), 1015 (m), 700 (m), 594 (m).; HRM (DART) for $C_{15}H_{17}O$ $[M+H]^+$ calculated: 229.1223, found: 229.1223.; $[\alpha]_D^{20}$: –28.1 (c = 0.87, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

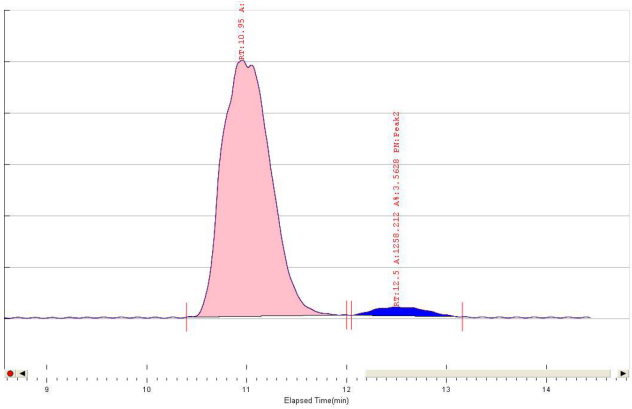
Chiral SFC (Chiracel AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm))– analysis of 1-(furan-2-yl)-2-methyl-4-phenylbutan-1-one

Racemic compound

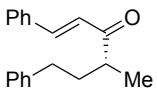


Peak No	% Area	Area	RT (min)
1	49.7133	20351.3532	11.5
2	50.2867	20586.0957	13.43
Total:	100	40937.4489	

Standard conditions



Peak No	% Area	Area	RT (min)
1	96.4372	34057.2405	10.95
2	3.5628	1258.212	12.5
Total:	100	35315.4525	



(*R*,*E*)-4-Methyl-1,6-diphenylhex-1-en-3-one (2.136). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (19.1 mg, 0.072 mmol, 36% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 3H), 7.43 – 7.37 (m, 3H), 7.33 – 7.28 (m, 2H), 7.25 – 7.16 (m, 3H), 6.78 (d, *J* = 16.1 Hz, 1H), 2.89 (h, *J* = 6.9 Hz, 1H), 2.66 (t, *J* = 7.8 Hz, 2H), 2.19 – 2.06 (m, 1H), 1.80 – 1.70 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ

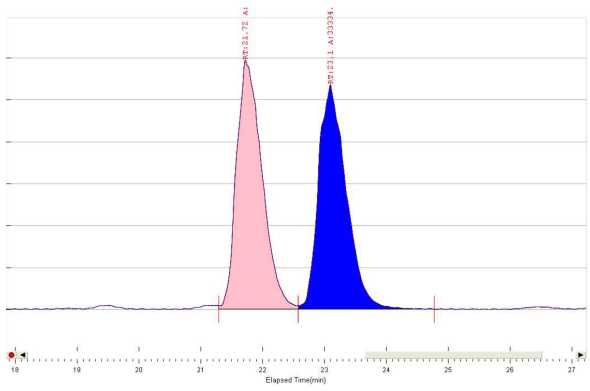
203.5, 142.6, 141.8, 134.6, 130.4, 128.9, 128.5, 128.4, 128.3, 125.9, 125.0, 43.6, 34.8, 33.4, 16.7.; IR: ν_{max} 3060 (w), 3026 (w), 2929 (w), 2859 (w), 1739 (m), 1686 (s), 1609 (s), 1495 (m), 1374 (m), 1228 (s), 1056 (m), 979 (m), 760 (m).; HRMS (DART) for $C_{19}H_{21}O$ $[M+H]^+$ calculated: 265.1587, found: 265.1584.; $[\alpha]_D^{20}$: –54.7 (c = 0.15, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

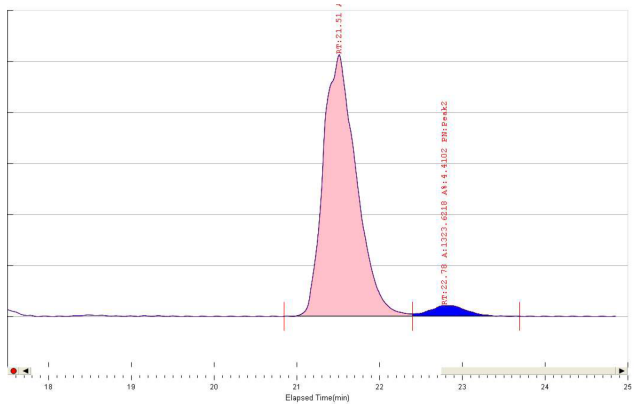
Chiral SFC (Chiracel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of (R,E)-4-methyl-1,6-diphenylhex-1-en-3-one

Racemic compound

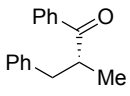


Peak No	% Area	Area	RT (min)
1	50.5715	34105.8711	21.72
2	49.4285	33334.963	23.1
Total:	100	67440.8341	

Standard conditions



Peak No	% Area	Area	RT (min)
1	95.5898	28688.8532	21.51
2	4.4102	1323.6218	22.78
Total:	100	30012.475	



(*R*)-2-Methyl-1,3-diphenylpropan-1-one (2.137). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel

chromatography to afford the product as colorless oil (36.1 mg, 0.16 mmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.89 (m, 2H), 7.59 – 7.49 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.23 (m, 2H), 7.23 – 7.16 (m, 3H), 3.75 (h, *J* = 6.9 Hz, 1H), 3.17 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.69 (dd, *J* = 13.7, 7.8 Hz, 1H), 1.20 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.8, 140.0, 136.5, 132.9, 129.1, 128.6, 128.4, 128.3, 126.2, 42.8, 39.4, 17.4.; IR: ν_{max} 2360 (m), 1683 (s), 1448 (w), 973 (m), 699 (s). HRMS (DART) for $C_{16}H_{17}O$ $[M+H]^+$ calculated: 225.1274, found: 225.1275.; $[\alpha]_D^{20}$: –66.7 (c = 0.93, $CHCl_3$, *l* = 50 mm).

Proof of Absolute Stereochemistry:

Literature characterization of (*R*)-2-methyl-1,3-diphenylpropan-1-one (99% ee): $[\alpha]_D^{26}$: –70.0 (c = 0.1, $CHCl_3$).[75]

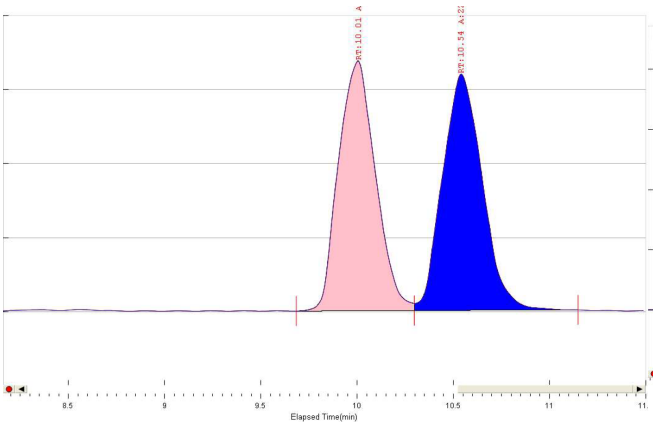
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 4,4,5,5-tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

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

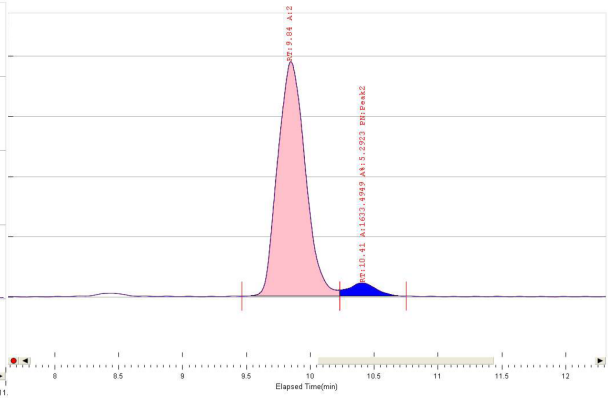
[75] Peters, B. B. C.; Jongcharoenkamol, J.; Krajangsri, S.; Andersson, P. G. *Org. Lett.* **2021**, *23*, 242–246.

Racemic compound

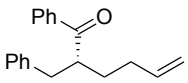


Peak No	% Area	Area	RT (min)
1	49.5748	22531.9384	10.01
2	50.4252	22918.4403	10.54
Total:	100	45450.3787	

Standard conditions



Peak No	% Area	Area	RT (min)
1	94.7077	29232.2977	9.84
2	5.2923	1633.4949	10.41
Total:	100	30865.7926	



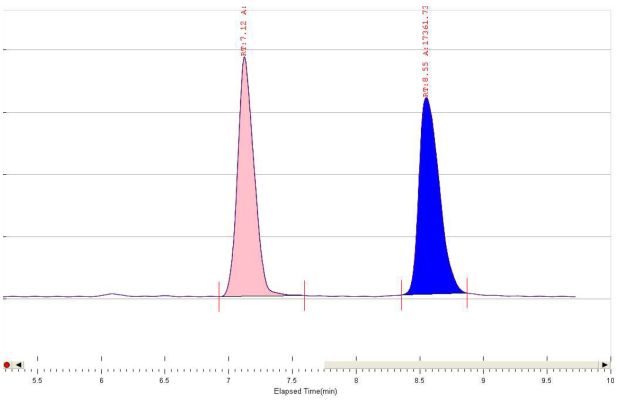
(*R*)-2-Benzyl-1-phenylhex-5-en-1-one (2.138). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane (57.2 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (41.5 mg, 0.15 mmol, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 – 7.84 (m, 2H), 7.57 – 7.51 (m, 1H), 7.45 – 7.38 (m, 2H), 7.27 – 7.20 (m, 2H), 7.19 – 7.13 (m, 3H), 5.74 (ddt, *J* = 17.1, 10.6, 6.6 Hz, 1H), 4.97 – 4.91 (m, 2H), 3.86 – 3.73 (m, 1H), 3.11 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.79 (dd, *J* = 13.7, 6.6 Hz, 1H), 2.16 – 2.06 (m, 1H), 2.06 – 1.89 (m, 2H), 1.74 – 1.61 (m, 1H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.8, 139.7, 137.9, 137.4, 132.9, 129.0, 128.6, 128.4, 128.18, 128.17, 126.2, 115.3, 47.4, 38.3, 31.4, 31.2.; IR: ν_{max} 2925 (w), 2360 (m), 1680 (s), 1597 (w), 1448 (m), 1001 (w), 914 (m), 699 (m), 668 (w).; HRMS (DART) for $C_{19}H_{21}O$ $[M+H]^+$ calculated: 265.1587, found: 265.1598.; $[\alpha]_D^{20}$: –47.4 (c = 0.93, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 4,4,5,5-tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

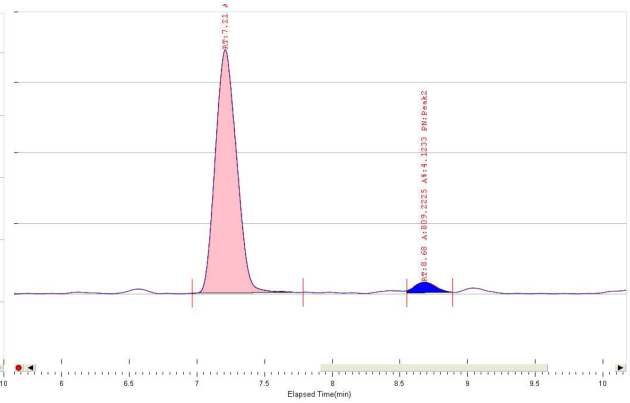
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 2-benzyl-1-phenylhex-5-en-1-one

Racemic compound

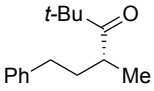


Peak No	% Area	Area	RT (min)
1	49.838	17249.625	7.12
2	50.162	17361.7326	8.55
Total:	100	34611.3576	

Standard conditions



Peak No	% Area	Area	RT (min)
1	96.1595	33956.1654	7.18
2	3.8405	1356.1686	8.68
Total:	100	35312.334	



(*R*)-2,2,4-Trimethyl-6-phenylhexan-3-one (2.139). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er) and styrene (10.4 mg, 50 mol%). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (43.2 mg, 0.20 mmol, 99% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.21 – 7.14 (m, 3H), 3.04 (h, *J* = 6.8 Hz, 1H), 2.60 (ddd, *J* = 13.7, 10.4, 5.2 Hz, 1H), 2.49 (ddd, *J* = 13.6, 10.4, 6.3 Hz, 1H), 1.93 (ddt, *J* = 13.3, 10.4, 6.5 Hz, 1H), 1.64 (dddd, *J* = 13.6, 10.4, 6.9, 5.3 Hz, 1H), 1.13 (s, 9H), 1.10 (d, *J* = 6.7 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 219.4, 141.9, 128.34,

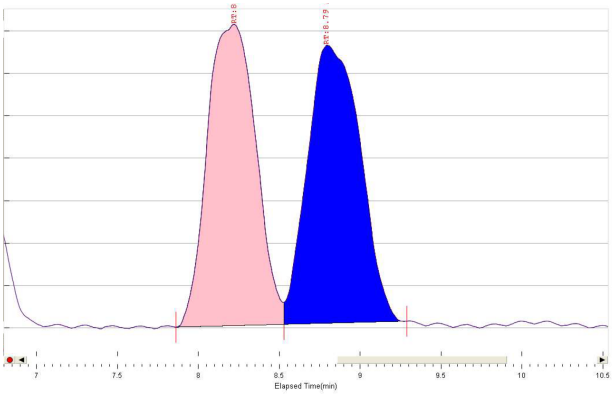
128.28, 125.9, 44.6, 39.1, 35.8, 33.7, 26.2, 18.2.; IR ν_{max} 2969 (m), 2359 (m), 2342 (w), 1702 (s), 1456 (w), 1367 (w), 1052 (w), 991 (w), 699 (m), 555 (w).; HRMS (DART) for $C_{15}H_{23}O$ $[M+H]^+$ calculated: 219.1745, found: 219.1743.; $[\alpha]_D^{20}$: –23.1 (c = 0.92, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

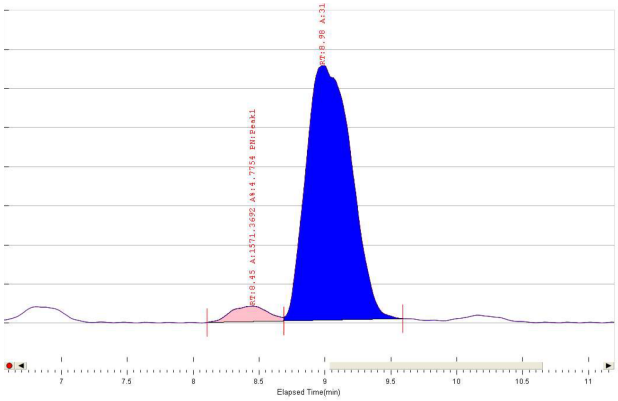
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 2,2,4-trimethyl-6-phenylhexan-3-one

Racemic compound

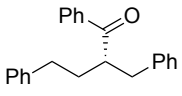


Peak No	% Area	Area	RT (min)
1	49.8299	7414.3253	8.22
2	50.1701	7464.9589	8.79
Total:	100	14879.2842	

Standard conditions



Peak No	% Area	Area	RT (min)
1	4.7754	1571.3692	8.45
2	95.2246	31334.2721	8.98
Total:	100	32905.6413	



(*S*)-2-Benzyl-1,4-diphenylbutan-1-one (2.140). The title compound was prepared according to *Method G* with (*S*)-2-(1,4-diphenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (53.2 mg, 0.17 mmol,

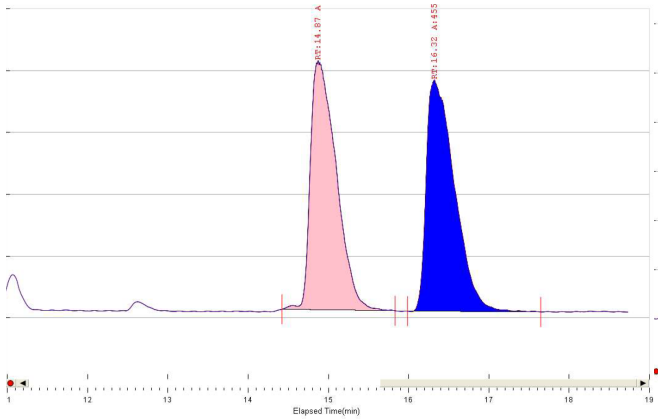
85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.75 (m, 2H), 7.56 – 7.49 (m, 1H), 7.43 – 7.36 (m, 2H), 7.29 – 7.20 (m, 4H), 7.22 – 7.12 (m, 4H), 7.11 – 7.05 (m, 2H), 3.75 (qd, *J* = 7.4, 5.5 Hz, 1H), 3.14 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.83 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.66 (ddd, *J* = 13.8, 9.7, 6.0 Hz, 1H), 2.55 (ddd, *J* = 13.8, 9.5, 6.2 Hz, 1H), 2.16 (dddd, *J* = 13.7, 9.6, 7.7, 6.0 Hz, 1H), 1.87 (dddd, *J* = 13.7, 9.4, 6.2, 5.3 Hz, 1H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.5, 141.5, 139.6, 137.3, 132.9, 129.0, 128.6, 128.5, 128.39, 128.37, 128.2, 126.2, 126.0, 47.4, 38.2, 33.6, 33.4.; IR: ν_{max} 3026 (w), 2925 (w), 2359 (m), 1679 (s), 1597 (w), 1495 (m), 1448 (m), 1372 (w), 1220 (s), 1179 (w), 1029 (w), 772 (s), 698 (s).; HRMS (DART) for $C_{23}H_{23}O$ $[M+H]^+$ calculated: 315.1743, found: 315.1739.; $[\alpha]_D^{20}$: +21.1 (c = 1.05, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(1,4-diphenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

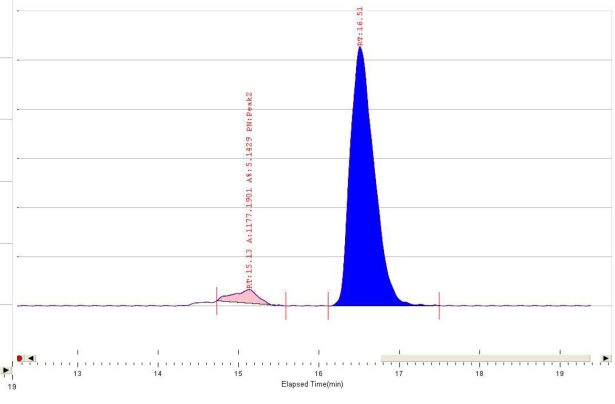
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 2-benzyl-1,4-diphenylbutan-1-one

Racemic compound

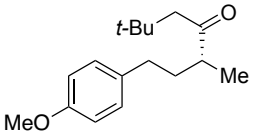


Peak No	% Area	Area	RT (min)
1	49.7037	45054.6656	14.87
2	50.2963	45591.7503	16.32
Total:	100	90646.4159	

Standard conditions



Peak No	% Area	Area	RT (min)
1	5.1429	1177.1901	15.13
2	94.8571	21712.3109	16.51
Total:	100	22889.501	



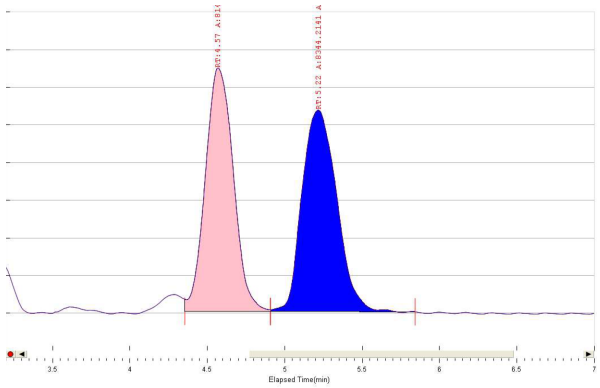
(*R*)-1-(4-Methoxyphenyl)-3,6,6-trimethylheptan-4-one (2.141). The title compound was prepared according to *Method G* with (*R*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (58.0 mg, 0.20 mmol, 96:4 er), The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (49.4 mg, 0.19 mmol, 94% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 – 7.03 (m, 2H), 6.88 – 6.77 (m, 2H), 3.78 (s, 3H), 2.58 – 2.45 (m, 3H), 2.34 (d, J = 15.6 Hz, 1H), 2.29 (d, J = 15.5 Hz, 1H), 2.01 – 1.88 (m, 1H), 1.61 – 1.50 (m, 1H), 1.08 (d, J = 7.0 Hz, 3H), 1.01 (s, 9H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 214.1, 157.8, 133.9, 129.2, 113.8, 55.2, 53.5, 46.8, 34.6, 32.5, 30.9, 29.7, 16.1.; IR: ν_{max} 2953 (m), 2359 (m), 2341 (w), 1712 (s), 1612 (w), 1513 (s), 1458 (w), 1363 (w), 1246 (s), 1038 (m), 823 (w).; HRMS (DART) for $C_{17}H_{27}O_2$ $[M+H]^+$ calculated: 263.2000, found: 263.2006.; $[\alpha]_D^{20}$: –20.7 (c = 0.91, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

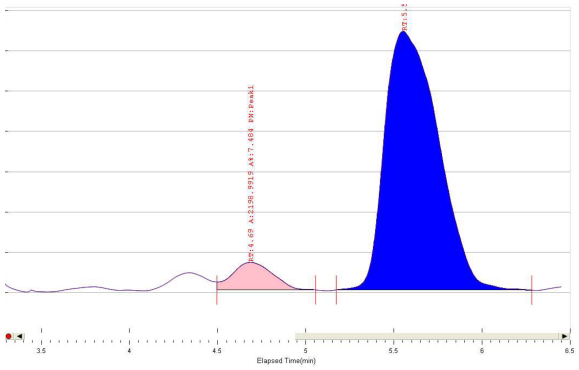
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 1-(4-methoxyphenyl)-3,6,6-trimethylheptan-4-one

Racemic compound

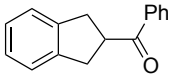


Peak No	% Area	Area	RT (min)
1	49.4057	8148.1809	4.57
2	50.5943	8344.2141	5.22
Total:	100	16492.395	

Standard conditions

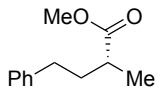


Peak No	% Area	Area	RT (min)
1	4.2571	183.1303	4.88
2	95.7429	4118.6451	5.6
Total:	100	4301.7754	



(2,3-Dihydro-1*H*-inden-2-yl)(phenyl)methanone (2.142). The title compound was prepared according to *Method G* with 2-(2,3-dihydro-1*H*-inden-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (48.8 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as white solid (44.5 mg, 0.19 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.65 – 7.58 (m, 1H), 7.56 – 7.49 (m, 2H), 7.27 – 7.22 (m, 2H), 7.22 – 7.17 (m, 2H), 4.33 (tt, *J* = 9.0, 7.7 Hz, 1H), 3.42 (dd, *J* = 15.8, 7.7 Hz, 2H), 3.30 (dd, *J* = 15.8, 8.9 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.9, 141.6, 136.4, 133.1, 128.7, 128.6, 126.6, 124.4, 46.3, 36.3.; IR: ν_{max} 3067 (w), 3024 (w), 2940 (w), 2849 (w), 1769 (m), 1681

(s), 1596 (m), 1484 (m), 1447 (m), 1359 (m), 1229 (s), 1181 (w), 1025 (m), 708 (s), 663 (m). HRMS (DART) for $C_{16}H_{15}O$ $[M+H]^+$ calculated: 223.1117, found: 223.1123.



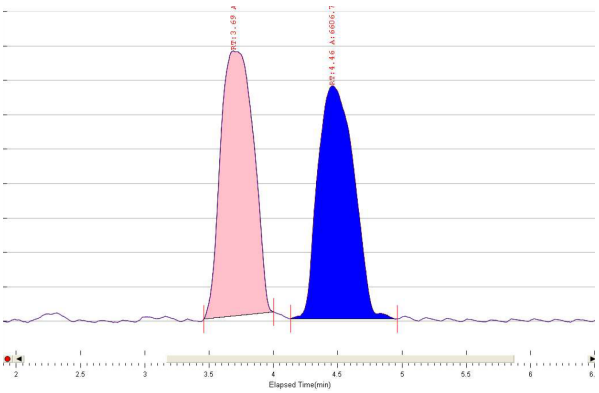
Methyl (*R*)-2-methyl-4-phenylbutanoate (2.143). The title compound was prepared according to *Method G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er) and styrene (62.4 mg, 300 mol%). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (33.7 mg, 0.17 mmol, 88% yield). ^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 3.69 (s, 3H), 2.63 (t, J = 8.0 Hz, 2H), 2.54 – 2.45 (m, 1H), 2.08 – 1.98 (m, 1H), 1.79 – 1.69 (m, 1H), 1.21 (d, J = 7.0 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 177.0, 141.6, 128.40, 128.36, 125.9, 51.5, 38.9, 35.4, 33.5, 17.1.; IR: ν_{max} 3027 (w), 2970 (w), 2949 (w), 2359 (w), 1736 (s), 1496 (m), 1455 (m), 1365 (m), 1229 (s), 1204 (m), 1162 (m), 1054 (w), 745 (w).; HRMS (DART) for $C_{12}H_{17}O_2$ $[M+H]^+$ calculated: 193.1223, found: 193.1224.; $[\alpha]_D^{20}$: –24.1 (c = 1.12, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

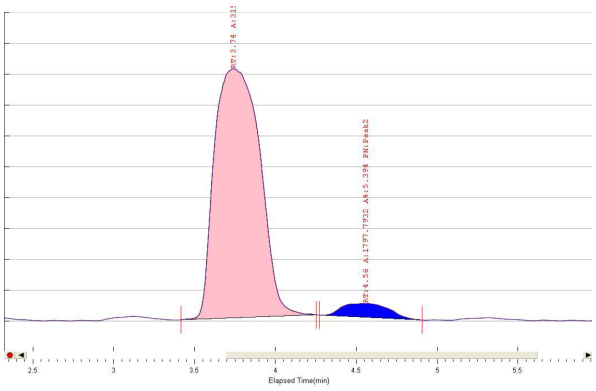
Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of methyl 2-methyl-4-phenylbutanoate

Racemic compound

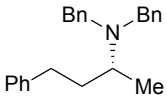


Peak No	% Area	Area	RT (min)
1	50.964	6866.5415	3.69
2	49.036	6606.7791	4.46
Total:	100	13473.3206	

Standard conditions



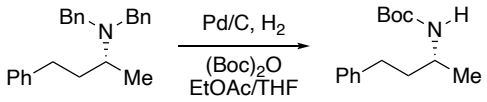
Peak No	% Area	Area	RT (min)
1	94.606	31531.9491	3.74
2	5.394	1797.7932	4.56
Total:	100	33329.7423	



(*R*)-*N*,*N*-Dibenzyl-4-phenylbutan-2-amine (2.144). The title compound was prepared according to *General Procedure F* with (*R*)-2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51.8 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (53.0 mg, 0.16 mmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 4H), 7.37 – 7.29 (m, 4H), 7.28 – 7.21 (m, 4H), 7.19 – 7.14 (m, 1H), 7.12 – 7.07 (m, 2H), 3.77 (d, J = 13.7 Hz, 2H), 3.47 (d, J = 13.8 Hz, 2H), 2.94 – 2.75 (m, 2H), 2.58 – 2.47 (m, 1H), 2.01 – 1.87 (m, 1H), 1.63 – 1.54 (m, 1H), 1.08 (d, J = 6.6 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 140.7, 128.8, 128.4, 128.3, 128.2, 126.7, 125.5, 53.4, 52.4, 36.1, 33.4, 13.4.; IR: ν_{max} 3084 (w), 2959 (m), 2829 (w), 2360 (m), 1770 (s), 1494 (m), 1375 (m), 1246 (s), 1151 (w), 1062 (w), 697 (s).; HRMS (DART) for $C_{24}H_{28}N$ $[M+H]^+$ calculated: 330.2216, found: 330.2225.; $[\alpha]_D^{20}$: +23.5 (c = 1.99, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Amines are converted into corresponding Boc protected amides for SFC analysis.

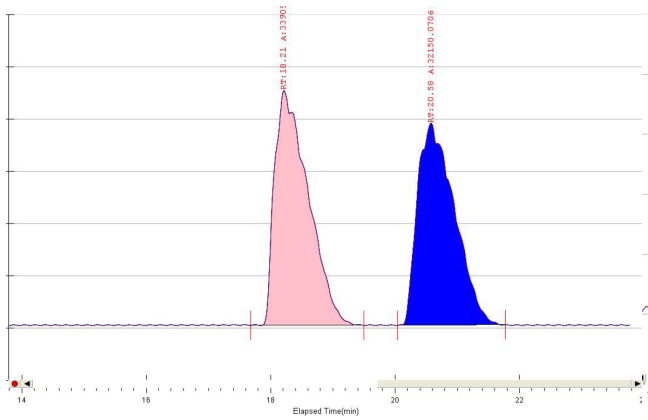


2.144

To an oven-dried 2-necked flask equipped with a magnetic stir bar was added amine (53.0 mg, 0.16 mmol, 1.0 equiv.), ethyl acetate (1.0 mL) and Boc_2O (0.8 mL, 1.0 M solution in THF, 5.0 equiv.). Then Pd/C (10 mg, 10% wt.) was added. The flask was equipped with a hydrogen balloon and connected to a vacuum pump. The flask was evacuated and backfilled with hydrogen gas. The procedure was repeated for three times. Then the mixture was allowed to stir for 24 h at room temperature. The mixture was passed through a silica gel plug and concentrated. The colorless oil residue was purified by preparative TLC (hexanes/diethyl ether/triethyl amine, 100/20/1, visualized by UV light) to furnish the desired product as white solid for SFC analysis. Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

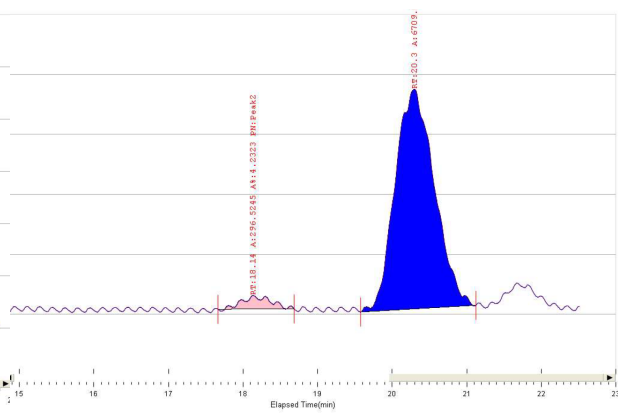
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of tert-butyl (R)-(4-phenylbutan-2-yl)carbamate

Racemic compound



Peak No	% Area	Area	RT (min)
1	51.3314	33909.1276	18.21
2	48.6686	32150.0706	20.58
Total:	100	66059.1982	

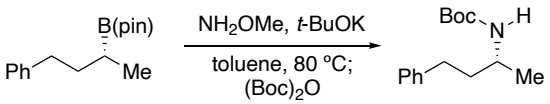
Standard conditions



Peak No	% Area	Area	RT (min)
1	3.8299	1500.4543	18.75
2	96.1701	37677.061	20.76
Total:	100	39177.5153	

Analysis of Absolute Configuration

Absolute configuration of product was confirmed by comparing SFC retention time of major isomer. Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.



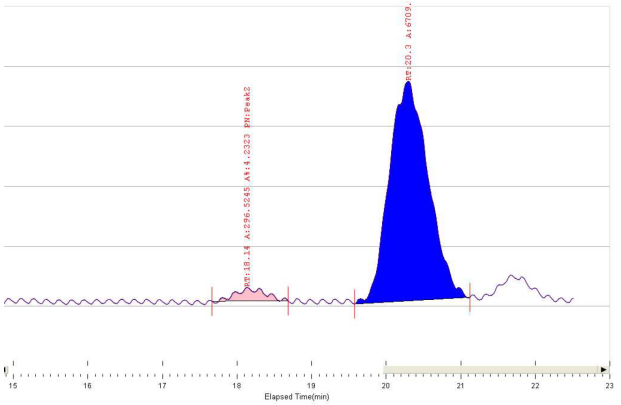
2.34

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.2 mmol, 1.0 equiv.), methoxy amine (0.3 mmol, 0.75 mL, 4.0 M solution in toluene, 1.5 equiv.), and potassium *tert*-butoxide (33.7 mg, 0.3 mmol, 1.5 equiv.). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was allowed to stir at 80 ºC for 2 h. The mixture was then allowed to cool to room temperature before Boc_2O (5.0 equiv.) and a saturated aquaeous solution of $NaHCO_3$ were added. After being allowed to stir under N_2 at

80 °C for 5 h, the mixture was allowed to cool to room temperature, water was added. The mixture was washed three times with ethyl acetate. The organic layers were combined and concentrated under reduced temperature. The colorless oil residue was purified by silica gel chromatography (hexanes/diethyl ether/triethyl amine, 100/20/1, visualized by UV light) to furnish the desired product as white solid (47.9 mg, 0.19 mmol, 96% yield).

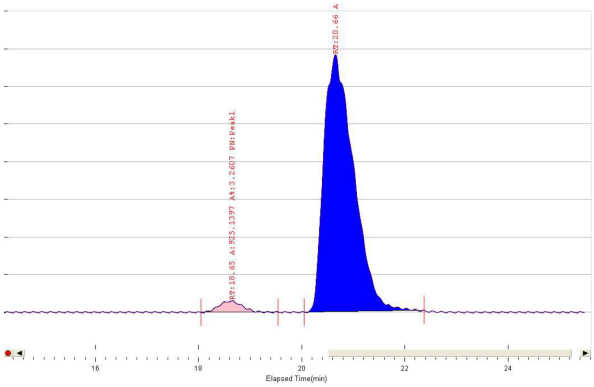
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of tert-butyl-(4-phenylbutan-2-yl)carbamate

From this method



Peak No	% Area	Area	RT (min)
1	3.8299	1500.4543	18.75
2	96.1701	37677.061	20.76
Total:	100	39177.5153	

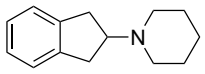
From known method



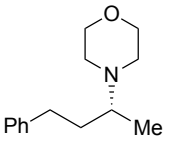
Peak No	% Area	Area	RT (min)
1	3.2607	925.1397	18.65
2	96.7393	27447.1478	20.66
Total:	100	28372.2875	

***N,N*-Dibenzylcyclohexanamine (2.145).** The title compound was prepared according to *General Procedure F* with cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (42.0 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (34.0 mg, 0.12 mmol, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 4H), 7.33 – 7.26 (m, 4H), 7.25 – 7.18 (m, 2H), 3.65 (s, 4H), 2.50 (tt, J = 11.7, 3.4 Hz, 1H), 1.95 – 1.86 (m, 2H), 1.82 – 1.74 (m, 2H), 1.40 – 1.28 (m, 2H), 1.21 – 1.07 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.3, 128.4, 128.1, 126.5, 57.7, 53.8, 28.6, 26.5, 26.2.; IR: ν_{max} 3026 (w),

2926 (s), 2852 (m), 2797 (w), 1493 (s), 1451 (s), 1361 (w), 1262 (w), 1129 (m), 1027 (m), 963 (w), 891 (w), 733 (s), 697 (s).; HRMS (DART) for $C_{20}H_{26}N$ $[M+H]^+$ calculated: 280.2060, found 280.2058.



1-(2,3-Dihydro-1*H*-inden-2-yl)piperidine (2.146). The title compound was prepared according to *General Procedure F* with 2-(2,3-dihydro-1*H*-inden-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (48.8 mg, 0.20 mmol). The yellow solid residue was purified by silica gel chromatography to afford the product as yellow solid (12.8 mg, 0.064 mmol, 32% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 – 7.16 (m, 2H), 7.15 – 7.10 (m, 2H), 3.23 – 3.11 (m, 1H), 3.07 (dd, *J* = 15.3, 7.1 Hz, 2H), 2.91 (dd, *J* = 15.0, 8.7 Hz, 2H), 2.49 (s, 4H), 1.64 (p, *J* = 5.7 Hz, 4H), 1.53 – 1.43 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 126.3, 124.3, 67.5, 52.7, 37.1, 26.0, 24.4.; IR ν_{max} 2954 (s), 2935 (s), 2853 (m), 2758 (w), 1770 (s), 1376 (m), 1241 (s), 1129 (m), 1058 (m), 743 (m).; HRMS (DART) for $C_{14}H_{20}N[M+H]^+$ 202.1590, found 202.1585.



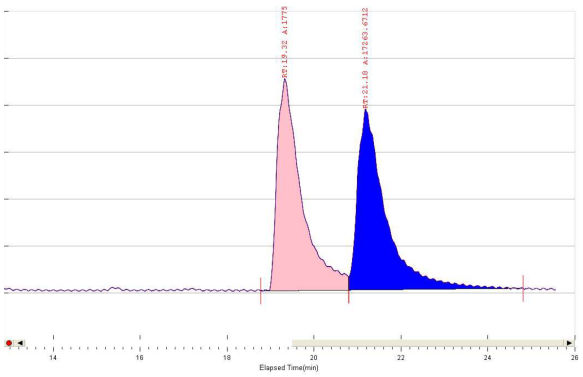
(*R*)-4-(4-Phenylbutan-2-yl)morpholine (2.147). The title compound was prepared according to *General Procedure F* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (32.5 mg, 0.15 mmol, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 2H), 7.22 – 7.15 (m, 3H), 3.80 – 3.67 (m, 4H), 2.74 – 2.62 (m, 2H), 2.60 – 2.51 (m, 3H), 2.50 – 2.42 (m, 2H), 1.86 (ddt, *J* = 13.5, 9.6, 6.2 Hz, 1H), 1.58 (ddt, *J* = 13.7, 9.5, 6.9 Hz, 1H), 1.02 (d, *J* = 6.6 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 128.4, 128.3, 125.7, 67.5, 58.4, 48.7, 35.2, 32.8, 13.9.; IR: ν_{max} 2958 (s), 2852 (m), 2811 (w), 2360 (s), 2341 (m), 1739 (s), 1453 (m), 1375 (s), 1229 (s), 1118 (s), 750 (m), 699 (s), 569 (s).; HRMS (DART) for $C_{14}H_{22}NO[M+H]^+$ calculated: 220.1696, found: 220.1703.; $[\alpha]_D^{20}$: –9.9 (c = 0.63, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

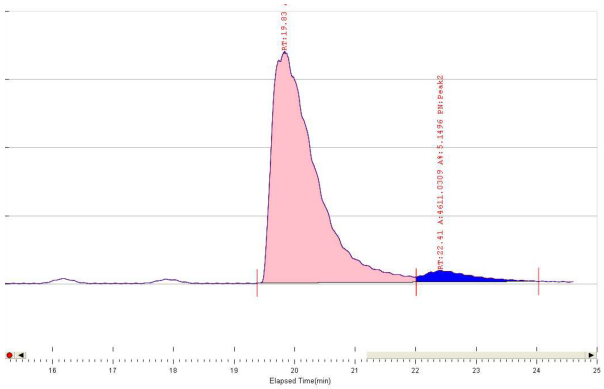
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of 4-(4-phenylbutan-2-yl)morpholine

Racemic compound

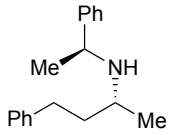


Peak No	% Area	Area	RT (min)
1	50.7036	17756.4908	19.32
2	49.2964	17263.6712	21.18
Total:	100	35020.162	

Standard conditions

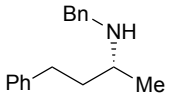


Peak No	% Area	Area	RT (min)
1	94.8504	84930.1376	19.83
2	5.1496	4611.0309	22.41
Total:	100	89541.1685	



(*R*)-4-Phenyl-*N*-((*S*)-1-phenylethyl)butan-2-amine (2.148). The title compound was prepared according to *General Procedure G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The pale-yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (21.6 mg, 0.086 mmol, 43% yield, 16:1 *d.r.*). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 5H), 7.27 – 7.21 (m, 3H), 7.18 – 7.13 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 2H), 3.92 (q, *J* = 6.6 Hz, 1H), 2.66 (ddd, *J* = 13.6, 10.3, 5.8 Hz, 1H), 2.52 (ddt, *J* = 29.4, 12.5, 6.1 Hz, 2H), 1.74 – 1.55 (m, 2H), 1.35 (dd, *J* = 6.6, 1.0 Hz, 3H), 1.07 (dd, *J* = 6.3, 1.0 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.0,

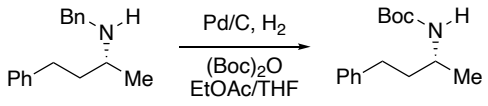
142.6, 128.4, 128.3, 128.2, 126.8, 126.6, 125.6, 55.0, 49.6, 39.9, 32.4, 25.1, 20.2.; IR: ν_{max} 3025 (w), 2959 (s), 2923 (m), 2862 (m), 2360 (s), 2342 (m), 1740 (s), 1494 (s), 1452 (s), 1371 (s), 1229 (s), 1217 (m), 762 (m), 699 (s), 553 (s).; HRMS (DART) for $C_{18}H_{24}N$ $[M+H]^+$ calculated: 254.1903, found: 254.1902.; $[\alpha]_D^{20}$: –24.5 (c = 0.73, $CHCl_3$, *l* = 50 mm).



(*R*)-*N*-Benzyl-4-phenylbutan-2-amine (2.149). The title compound was prepared according to *General Procedure G* with (*R*)-4,4,5,5-tetramethyl-2-(4-phenylbutan-2-yl)-1,3,2-dioxaborolane (52.0 mg, 0.20 mmol, 96:4 er). The pale-yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow oil (14.8 mg, 0.062 mmol, 31% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.30 (m, 4H), 7.31 – 7.24 (m, 2H), 7.24 – 7.15 (m, 4H), 3.83 (d, *J* = 13.0 Hz, 1H), 3.75 (d, *J* = 13.0 Hz, 1H), 2.81 – 2.71 (m, 1H), 2.70 – 2.56 (m, 2H), 2.17 (s, 1H), 1.86 – 1.76 (m, 1H), 1.74 – 1.63 (m, 1H), 1.15 (d, *J* = 6.3 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 128.402, 128.403, 128.35, 128.3, 128.2, 126.9, 125.7, 52.0, 51.3, 38.7, 32.3, 20.3.; IR: ν_{max} 3025 (w), 2995 (w), 2956 (w), 2360 (m), 2342 (w), 1770 (s), 1495 (w), 1374 (w), 1246 (s), 1057 (m), 698 (m).; HRMS (DART) for $C_{26}H_{30}N$ $[M+H]^+$ calculated: 240.1747, found: 240.1753.; $[\alpha]_D^{20}$: –7.8 (c = 0.49, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Amines are converted into corresponding Boc-protected amides for SFC analysis according to the hydrogenation/protection procedure described above.

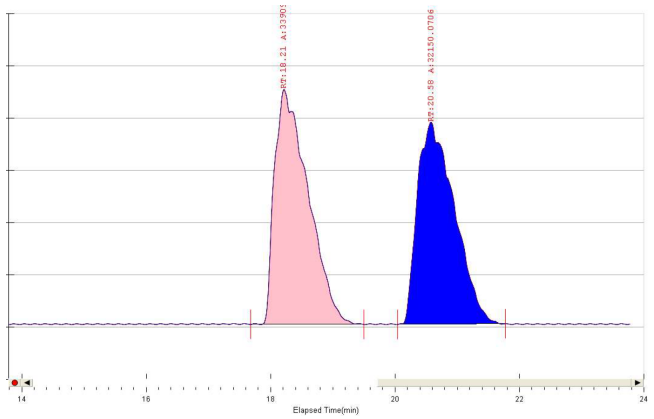


2.149

Racemic compound was prepared according to the procedure described above with racemic 2-(4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Absolute stereochemistry was assigned by analogy.

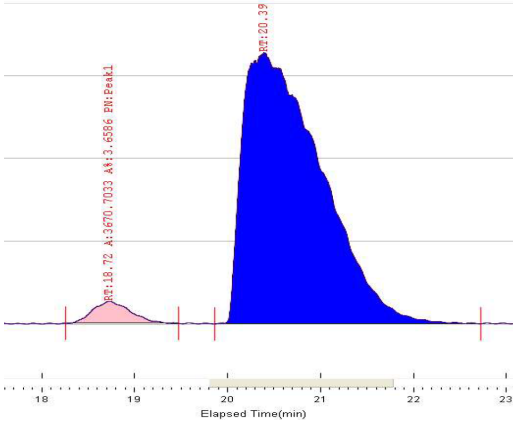
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm)– analysis of tert-butyl-(4-phenylbutan-2-yl)carbamate

Racemic compound

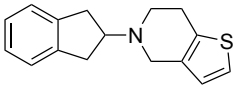


Peak No	% Area	Area	RT (min)
1	51.3314	33909.1276	18.21
2	48.6686	32150.0706	20.58
Total:	100	66059.1982	

Standard conditions

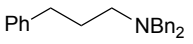


Peak No	% Area	Area	RT (min)
1	3.6586	3670.7033	18.72
2	96.3414	96660.2353	20.39
Total:	100	100330.9386	

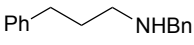


5-(2,3-Dihydro-1*H*-inden-2-yl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine (2.150). The title compound was prepared according to *General Procedure F* with 2-(2,3-dihydro-1*H*-inden-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (48.8 mg, 0.20 mmol). The pale-yellow solid residue was purified by silica gel chromatography to afford the product as white solid (37.0 mg, 0.14 mmol, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 2H), 7.21 – 7.14 (m, 2H), 7.10 (d, J = 5.1 Hz, 1H), 6.76 (d, J = 5.1 Hz, 1H), 3.70 (s, 2H), 3.52 – 3.40 (m, 1H), 3.19 (dd, J = 15.2, 7.5 Hz, 2H), 3.03 (dd, J = 15.1, 8.9 Hz, 2H), 2.99 – 2.93 (m, 2H), 2.93 – 2.89 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 133.7, 133.4, 126.5, 125.3, 124.4, 122.8, 66.2, 51.6, 48.9, 37.5, 25.6.; IR: ν_{max} 3305 (w), 2964 (w), 1592 (w), 1474 (w), 1363

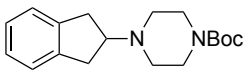
(w), 1275 (s), 1261 (s), 971 (w), 764 (s), 750 (s), 724 (w).; HRMS (DART) for $C_{16}H_{18}NS$ $[M+H]^+$ calculated: 256.1155, found: 256.1158.



***N*,*N*-Dibenzyl-3-phenylpropan-1-amine (2.151).** The title compound was prepared according to *General Procedure F* with 4,4,5,5-tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (45.4 mg, 0.14 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 4H), 7.40 – 7.34 (m, 4H), 7.32 – 7.24 (m, 4H), 7.23 – 7.18 (m, 1H), 7.17 – 7.12 (m, 2H), 3.63 (s, 4H), 2.68 – 2.61 (m, 2H), 2.55 (t, J = 7.0 Hz, 2H), 1.93 – 1.85 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 139.9, 128.9, 128.4, 128.3, 128.2, 126.8, 125.6, 58.4, 53.0, 33.6, 29.1.; IR: ν_{max} 3061 (w), 3025 (m), 2940 (m), 2794 (m), 2361 (w), 1739 (w), 1602 (w), 1494 (s), 1452 (s), 1366 (m), 1126 (m), 1028 (m), 742 (s).; HRMS (DART) for $C_{23}H_{26}N$ $[M+H]^+$ calculated: 316.2060, found: 316.2047.

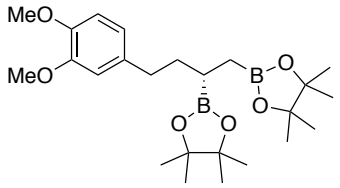


***N*-Benzyl-3-phenylpropan-1-amine (2.152).** The title compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (49.2 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (31.9 mg, 0.14 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 4H), 7.32 – 7.25 (m, 3H), 7.24 – 7.17 (m, 3H), 3.80 (s, 2H), 2.70 (q, J = 7.6, 7.0 Hz, 4H), 1.94 – 1.80 (m, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 140.5, 128.4, 128.3, 128.1, 126.9, 125.8, 54.0, 48.9, 33.7, 31.7.; IR: ν_{max} 3061 (w), 3025 (m), 2927 (m), 2856 (m), 2360 (m), 1739 (s), 1602 (m), 1495 (s), 1453 (s), 1365 (m), 1217 (w), 1119 (m), 1028 (m), 908 (w), 736 (s), 569 (w).; HRMS (DART) for $C_{16}H_{20}N$ $[M+H]^+$ calculated: 226.1590, found: 226.1953.

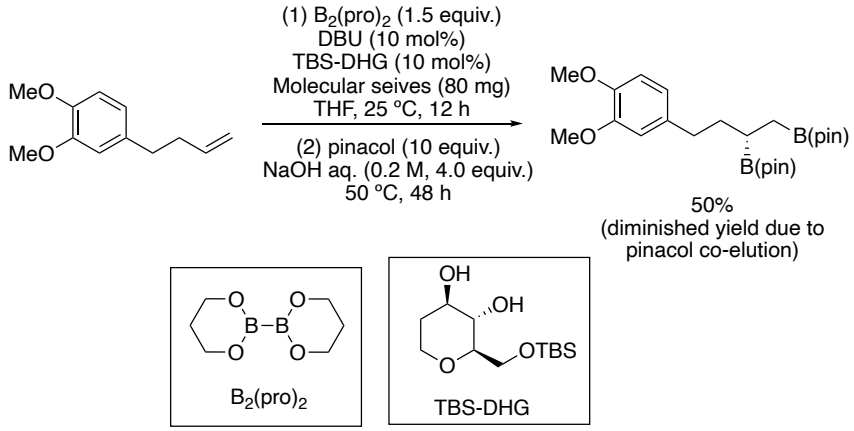


***tert*-Butyl 4-(2,3-dihydro-1*H*-inden-2-yl)piperazine-1-carboxylate. (2.153)** The title compound was prepared according to *General Procedure F* with 2-(2,3-dihydro-1*H*-inden-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (48.8 mg, 0.20 mmol). The white solid residue was purified by silica gel chromatography to afford the product as white solid (41.7 mg, 0.14 mmol, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 2H), 7.16 – 7.10 (m, 2H), 3.52 – 3.43 (m, 4H), 3.25 – 3.14 (m, 1H), 3.07 (dd, *J* = 15.2, 7.4 Hz, 2H), 2.89 (dd, *J* = 15.1, 8.6 Hz, 2H), 2.52 – 2.43 (m, 4H), 1.46 (s, 9H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 141.4, 126.5, 124.4, 79.6, 66.8, 51.2, 37.0, 28.4.; IR: ν_{max} 2995 (w), 2933 (m), 2806 (w), 2360 (w), 1770 (m), 1692 (s), 1417 (s), 1318 (m), 1247 (s), 1168 (s), 1121 (s), 1012 (m), 881 (m), 741 (m), 668 (w).; HRMS (DART) for $C_{18}H_{27}N_2O_2$ $[M+H]^+$ calculated: 303.2067, found: 303.2071.

2.6.4 Procedure for Synthesis of Galbulin Derivative



(*S*)-2,2'-(4-(3,4-Dimethoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.191). The title compound was isolated in order to determine the er of **2.160**.



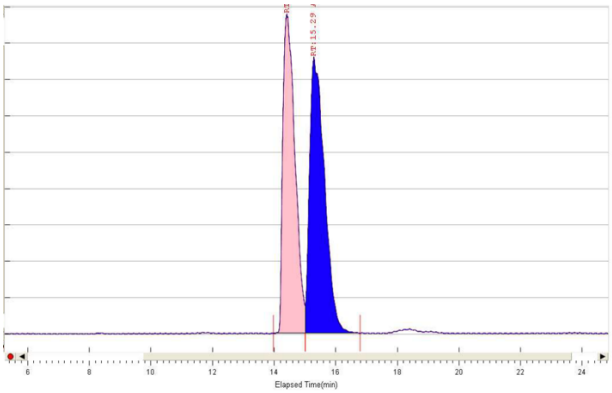
The title compound was prepared according to modified literature procedure.[52] To an oven-dried round bottom flask was charged with 4-but-3-enyl-1,2-dimethoxy-benzene (96.1 mg, 0.5 mmol), 2,2'-bi(1,3,2-dioxaborinane) (127.3 mg, 0.75 mmol), TBS-DHG (13.1 mg, 0.05 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (7.6 mg, 0.05 mmol), dissolved in THF (1.0 M) in glovebox. The mixture was allowed to stir at 25 ºC for 12 h. Then, the solution was opened to air, pinacol (5 mmol), 0.2 M NaOH aqueous solution (4 mL) was added, the mixture was diluted with 5 mL THF, and was allowed to stir at 50 ºC for 48 h. The mixture was allowed to cool to room temperature, Et_2O (10 ml) and water (10 ml) was added. The phases were separated and the mixture was washed with Et_2O (3 × 10 ml). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. The yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow oil (102 mg, 0.25 mmol, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (d, *J* = 8.2 Hz, 1H), 6.72-6.71 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.56 (dd, *J* = 9.2, 7.1 Hz, 2H), 1.82 – 1.72 (m, 1H), 1.66 – 1.57 (m, 1H), 1.27-1.25 (m, 1H), 1.25 (s, 12H), 1.23 (s, 12H), 0.94 (dd, *J* = 15.8, 9.5 Hz, 2H), 0.87 (dd, *J* = 15.8, 5.8 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 146.9, 136.0, 120.1, 111.9, 111.2, 82.9, 55.9, 55.7, 36.0, 34.9, 24.90, 24.88, 24.79, 24.77.; IR: ν_{max} 2974 (m), 2927 (w), 1589 (m), 1514 (w), 1463 (w), 1369 (s), 1313 (s), 1260 (w), 1235 (w), 1141 (s), 1031 (w), 967 (w), 845 (w) cm^{-1}.; HRMS (DART) for $C_{24}H_{41}B_2O_6$ $[M+H]^+$: calculated: 447.3084, found: 447.3084.; $[\alpha]_D^{20}$: +6.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the General Procedure for the Preparation of racemic 1,2-bis(boronic pinacol esters). Absolute stereochemistry was assigned by analogy.

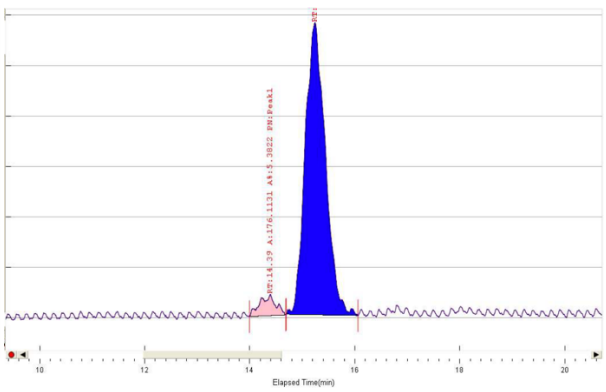
Chiral SFC (Chiralcel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 2,2'-(4-(3,4-dimethoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

Racemic Compound

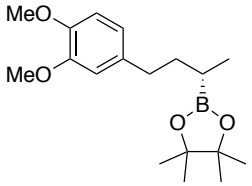


Peak No	% Area	Area	RT (min)
1	48.3691	47905.173	14.41
2	51.6309	51135.671	15.29
Total:	100	99040.844	

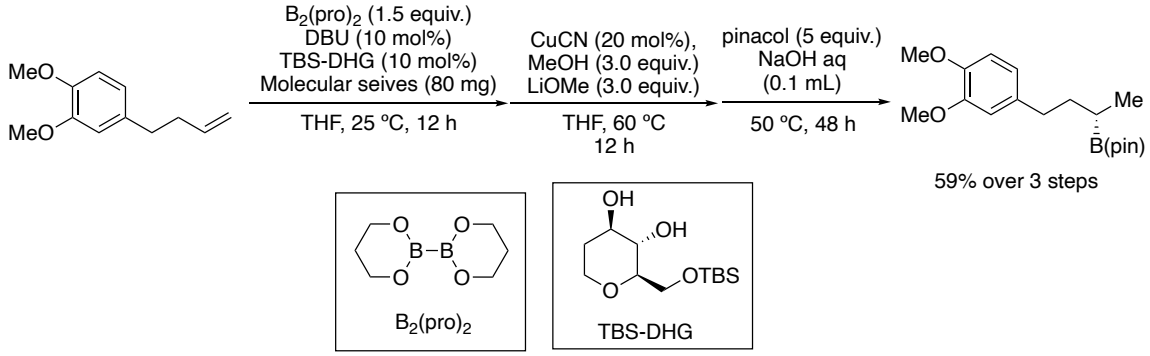
Enantioselective Conditions



Peak No	% Area	Area	RT (min)
1	5.369	174.2699	14.39
2	94.631	3071.5923	15.24
Total:	100	3245.8622	



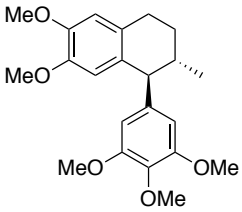
(*S*)-2-(4-(3,4-Dimethoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.160) The title compound was prepared in three consecutive steps without purification in between.



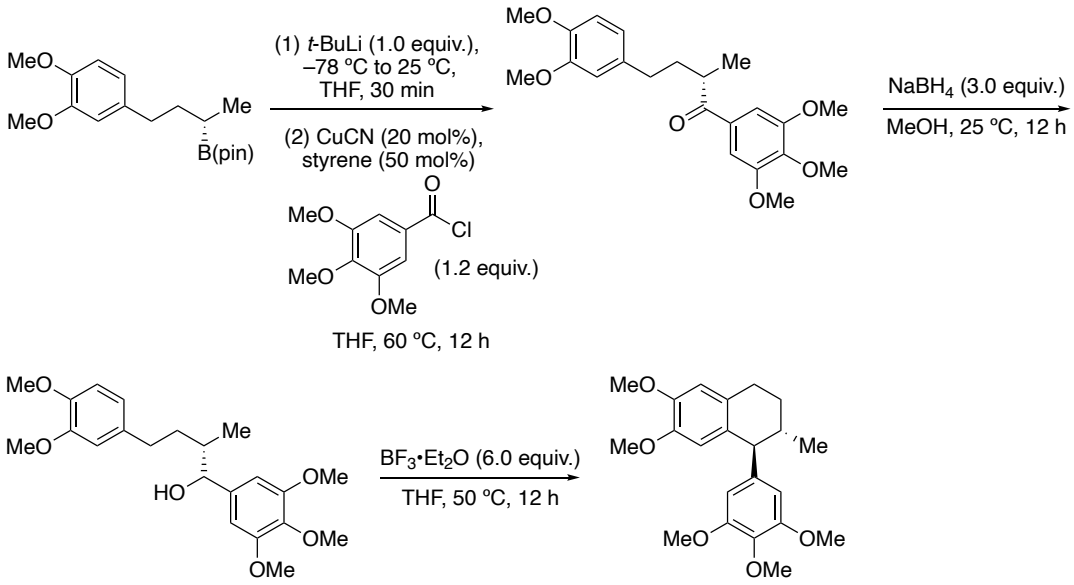
To an oven-dried round bottom flask was charged 4-but-3-enyl-1,2-dimethoxy-benzene (96.1 mg, 0.5 mmol), 2,2'-bi(1,3,2-dioxaborinane) (127.3 mg, 0.75 mmol), TBS-DHG (13.1 mg, 0.05 mmol), 1,8-Diazabicyclo[5.4.0]undec-7-ene (7.6 mg, 0.05 mmol), dissolved in THF (1.0 M) in glovebox. The mixture was allowed to stir at 25 ºC for 12 h.

The mixture was diluted with 0.5 mL anhydrous THF in glovebox, CuCN (9.0 mg, 0.1 mmol), LiOMe (57.0 mg, 1.5 mmol) and MeOH (48.1 mg, 1.5 mmol) were added. The mixture was allowed to stir at 60 ºC for 12 h. Then, the mixture was filtered through a short silica plug and was concentrated under reduced pressure.

Pinacol (295 mg, 2.5 mmol), 3.0 M NaOH aqueous solution (0.1 mL) were added under air, the mixture was diluted with 5 mL THF, and was allowed to stir at 50 ºC for 48 h. The mixture was allowed to cool to ambient temperature, Et_2O (10 ml) and water (10 ml) was added. The phases were separated and the mixture was washed with Et_2O (3 × 10 ml). The combined organic layers were dried over $MgSO_4$ and the solvents were removed *in vacuo*. The colorless oil residue was purified by silica gel chromatography to afford the title compound (160.1 mg, 0.29 mmol, 59% yield over three steps) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 – 6.75 (m, 1H), 6.74 – 6.70 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 2.58-2.55 (m, 2H), 1.83 – 1.72 (m, 1H), 1.63 – 1.52 (m, 1H), 1.25 (s, 12H), 1.11 – 1.04 (m, 1H), 1.02 (d, J = 6.2, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 147.0, 135.8, 120.2, 111.8, 111.2, 82.9, 55.9, 55.8, 35.4, 34.9, 24.8, 24.7, 15.4.; IR: ν_{max} 2973 (w), 2930 (w), 1589 (s), 1514 (m), 1369 (m), 1314 (s), 1260 (s), 1235 (s), 1142 (s), 1030 (m), 966 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{30}BO_4$ $[M+H]^+$: calculated: 321.2237, found: 321.2244.; $[\alpha]_D^{20}$: +7.2 (c = 1.0, $CHCl_3$, l = 50 mm).



(1*S*,2*S*)-6,7-Dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydronaphthalene (2.159). The title compound was prepared according to the following sequence:



In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added (*S*)-2-(4-(3,4-dimethoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (174 mg, 0.54 mmol) and anhydrous tetrahydrofuran (1.0 mL). The vial was sealed with a septum cap and removed from the glovebox. Outside the glovebox, the mixture was cooled to –78 ºC and *tert*-butyllithium (0.54 mmol, solution in pentane) was added dropwise by a syringe. The mixture was then allowed to warm to room temperature and to stir for 30 min. The reaction vial was then transferred into the glovebox, and styrene (28.3 mg, 0.27 mmol), copper cyanide (34.8 mg, 0.1 mmol) and 3,4,5-trimethoxybenzoyl chloride (150.4 mg, 0.65 mmol) were added. The vial was sealed with septum cap and removed from the glovebox. The mixture was then allowed to stir at 60 ºC for 12 h. The mixture was subsequently diluted with diethyl ether and was filtered through a silica gel plug. The solvents were removed under reduced pressure. The pale-yellow oil residue was subjected to the next step without purification.

The mixture was dissolved in 10 mL MeOH, $NaBH_4$ (61.6 mg, 1.63 mmol) was added slowly. The mixture was allowed to stir at room temperature for 12 h. 10 mL H_2O and 10 mL diethyl ether were added to the mixture. The mixture was washed with Et_2O (3 × 10 ml). The combined organic

layers were dried over $MgSO_4$, and was concentrated *in vacuo*. The pale-yellow oil residue was subjected to the next step without purification.

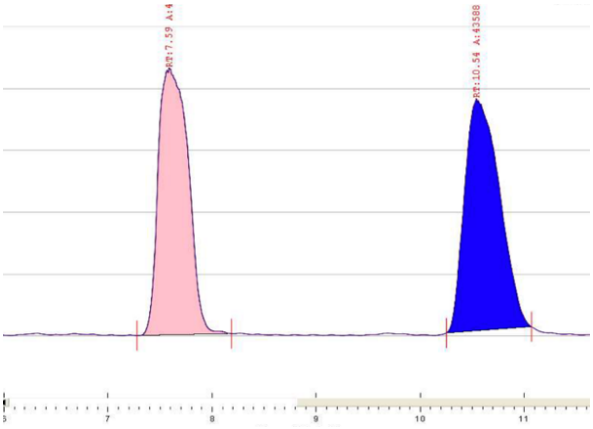
The mixture was dissolved in 10 ml THF and $BF_3 \cdot Et_2O$ (1.08 mmol, 0.11 mL) was added. The mixture was allowed to stir at 50 ºC. An additional 1.08 mmol $BF_3 \cdot Et_2O$ (0.11 mL) was added after 1 h and again after 2 h. The mixture was allowed to stir at 50 ºC for 6 h. 10 mL H_2O and 10 mL diethyl ether was added were added to the mixture, the phases were separated and the mixture washed with Et_2O (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, and was concentrated *in vacuo*. The colorless oil residue was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the title compound (128 mg, 0.34 mmol, 63% yield over three steps) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1H), 6.30 (s, 2H), 6.25 (s, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.78 (s, 6H), 3.61 (s, 3H), 3.44 (d, J = 8.9 Hz, 1H), 2.95 – 2.85 (m, 1H), 2.77 (dt, J = 16.4, 4.6 Hz, 1H), 1.97 – 1.83 (m, 2H), 1.58 – 1.47 (m, 1H), 0.94 (d, J = 6.5 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 147.2, 146.9, 142.1, 136.2, 131.3, 129.1, 113.1, 111.0, 106.3, 77.3, 77.1, 76.8, 60.9, 56.1, 55.9, 55.7, 54.2, 37.3, 30.6, 28.7, 20.6.; IR: ν_{max} 2926 (m), 2841 (w), 1586 (m), 1511 (s), 1457 (m), 1419 (w), 1326 (w), 1228 (m), 1209 (s), 1125 (s), 1009 (w), 865 (w), 764 (w) cm^{-1}.; HRMS (DART) for $C_{22}H_{29}O_5$ $[M+H]^+$: calculated: 373.2009, found: 373.2026.; $[\alpha]_D^{20}$: –8.9 (c = 1.0, $CHCl_3$, l = 50 mm). All spectral data are in accordance with the literature.[50]

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure above with racemic 2,2'-(4-(3,4-dimethoxyphenyl)butane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Absolute stereochemistry was assigned by analogy.

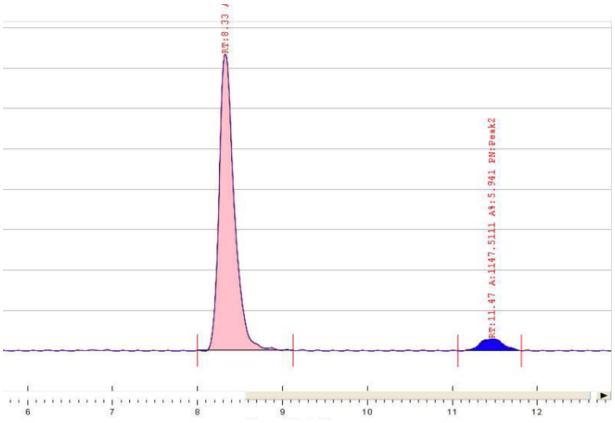
Chiral SFC (Chiralcel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydronaphthalene

Racemic Compound



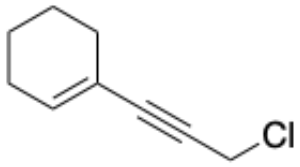
Peak No	% Area	Area	RT (min)
1	49.5279	42773.3787	7.59
2	50.4721	43588.8514	10.54
Total:	100	86362.2301	

Standard Conditions



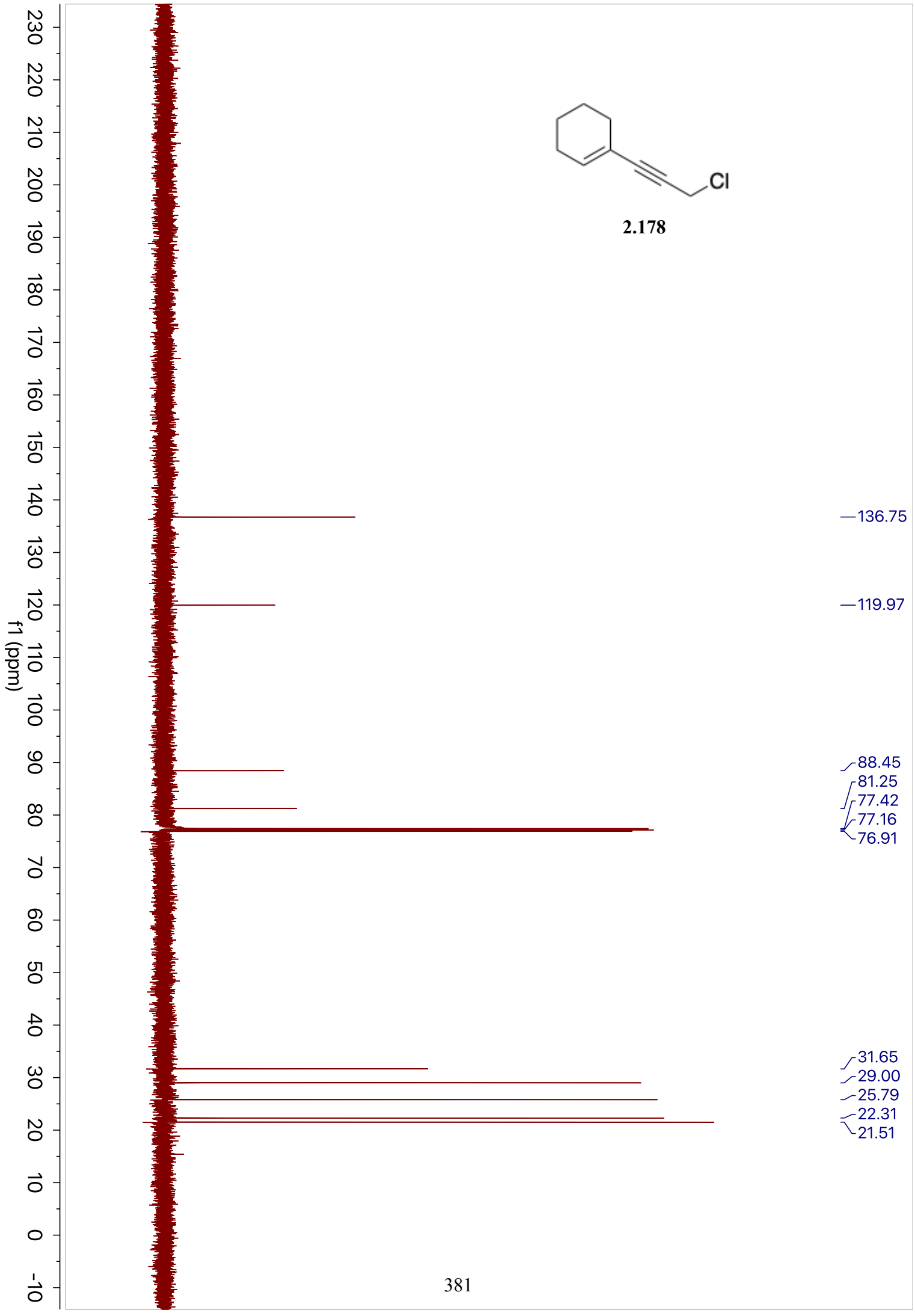
Peak No	% Area	Area	RT (min)
1	94.059	18167.7447	8.33
2	5.941	1147.5111	11.47
Total:	100	19315.2558	

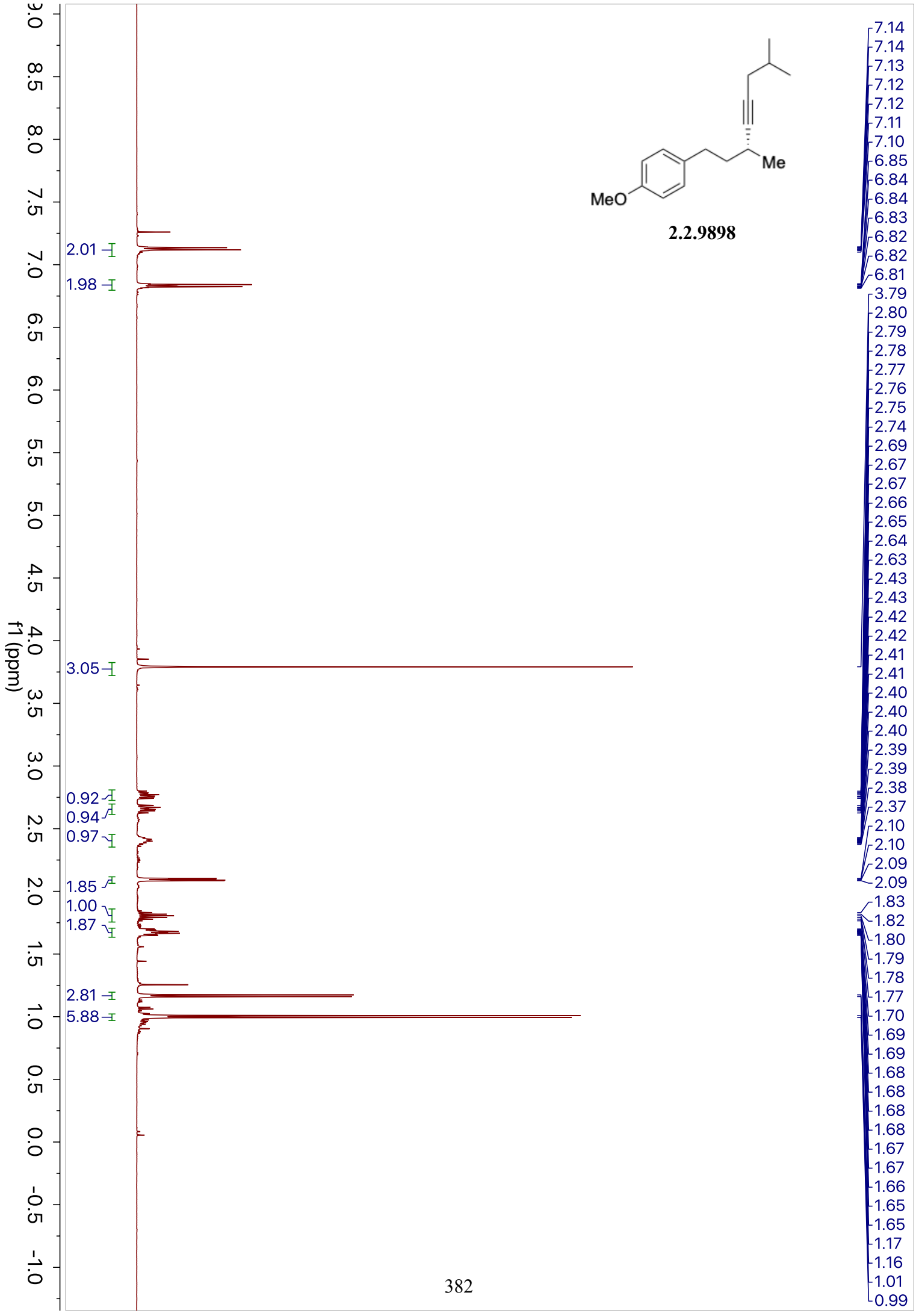
2.7 Spectra

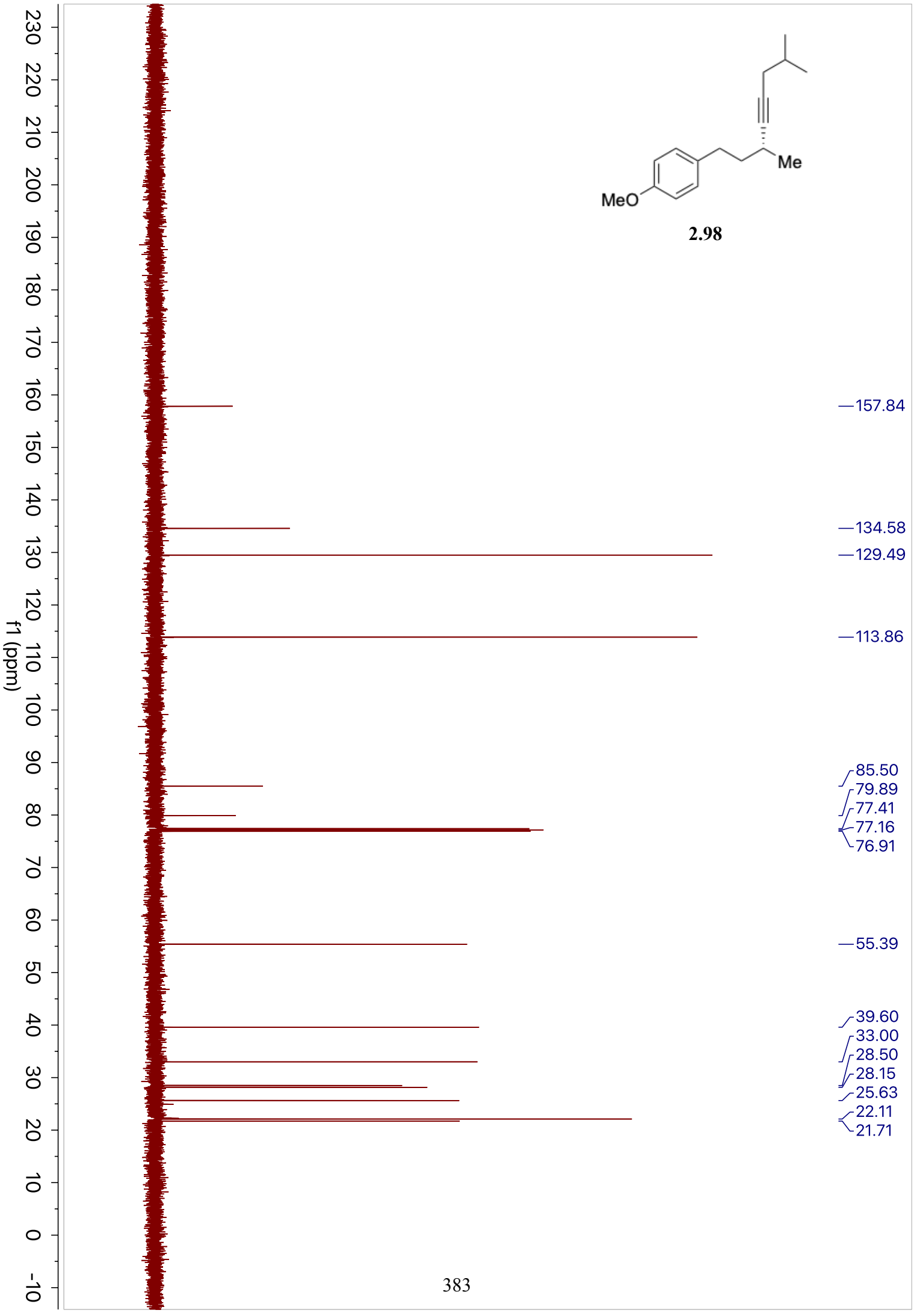

Cl

2.178

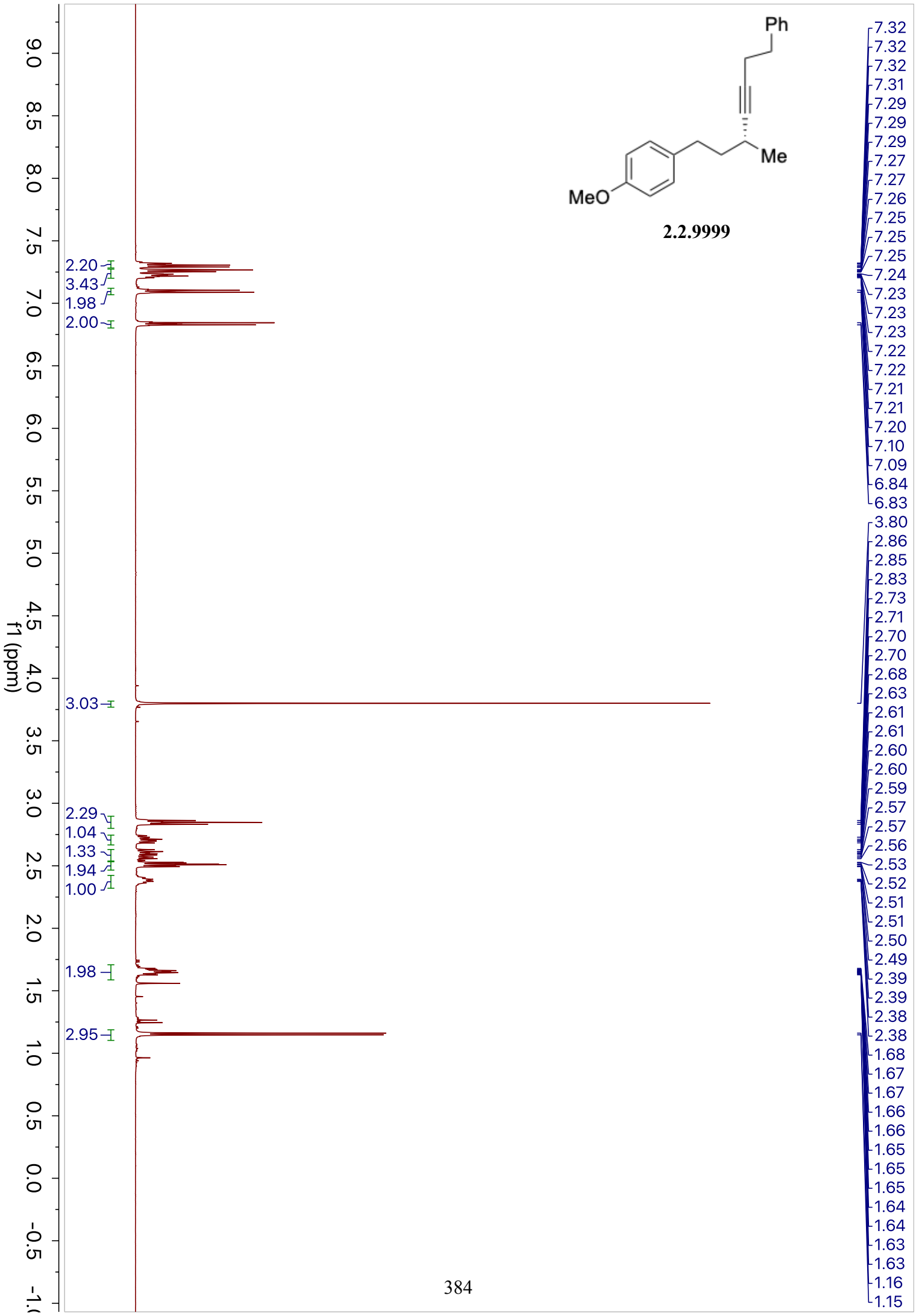
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
2.04
4.18
4.34
6.17
6.16
6.16
4.28
2.13
2.13
2.12
2.12
2.11
2.11
2.10
2.10
2.09
2.09
2.08
1.65
1.64
1.63
1.63
1.62
1.62
1.61
1.60
1.60
1.59
1.59
1.59
1.58
1.58
1.57
1.57

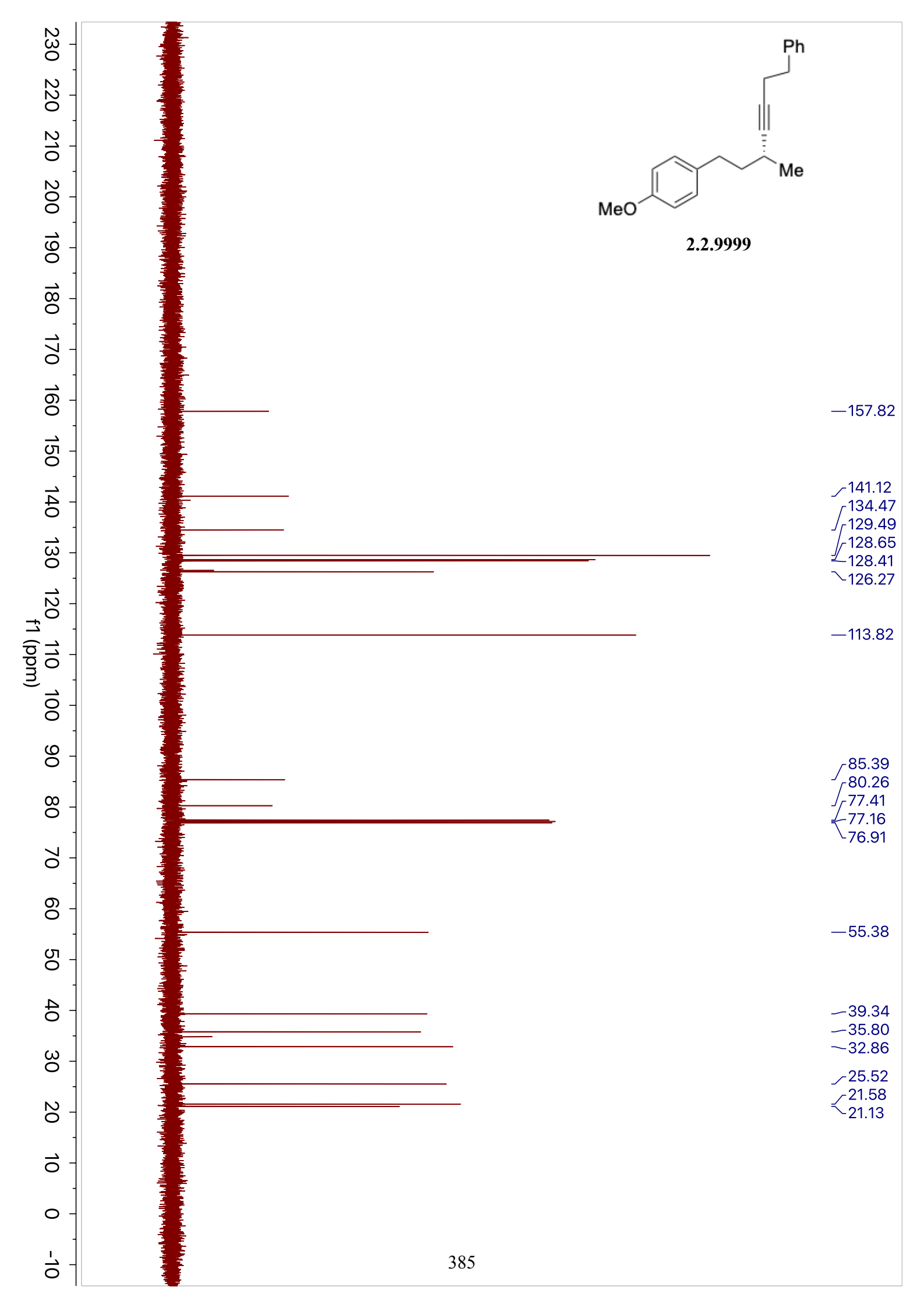

Cl
2.178
136.75
119.97
88.45
81.25
77.42
77.16
76.91
31.65
29.00
25.79
22.31
21.51
f1 (ppm)

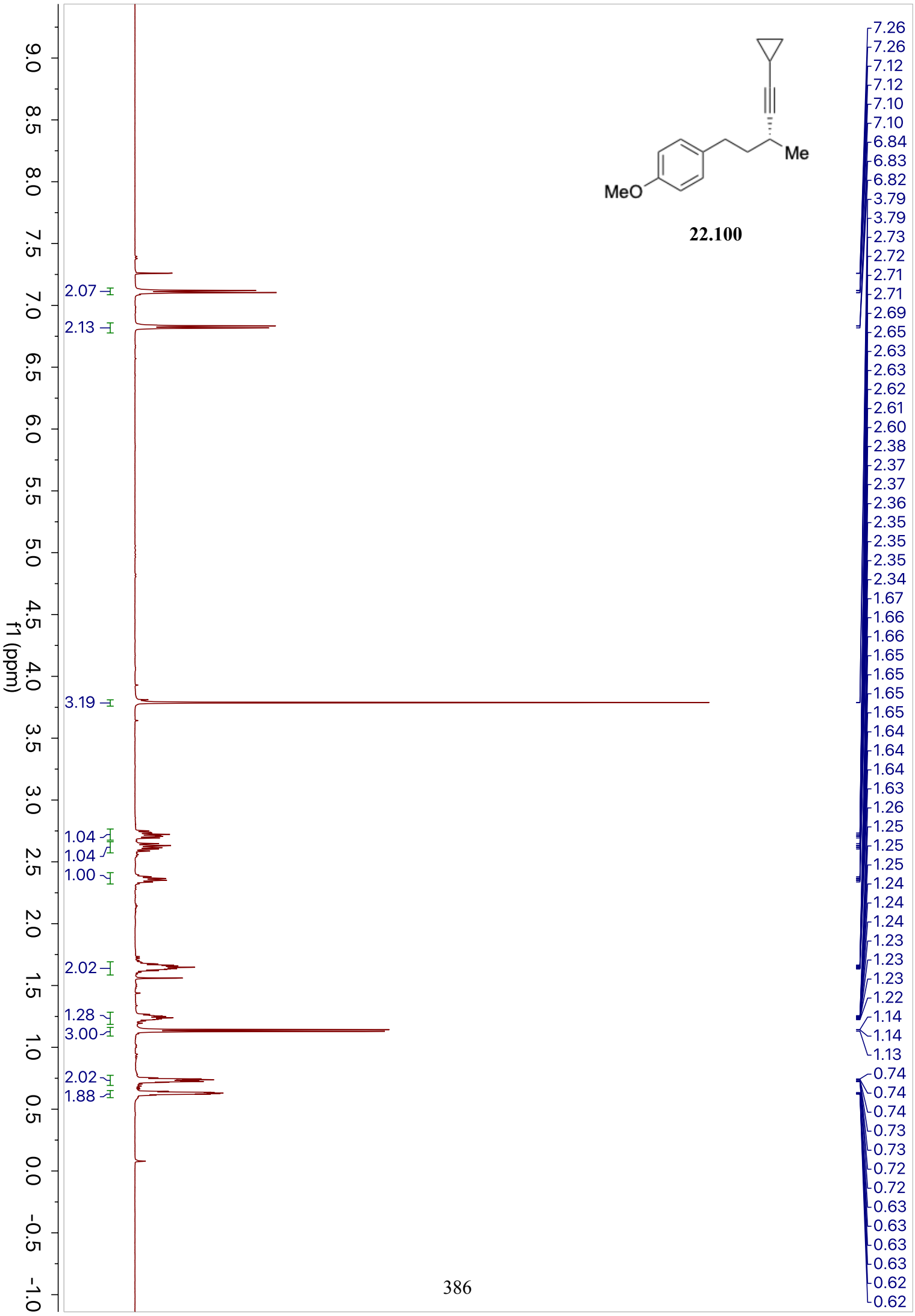

MeO
Me
2.2.9898
f1 (ppm)
2.01
1.98
3.05
0.92
0.94
0.97
1.85
1.00
1.87
2.81
5.88

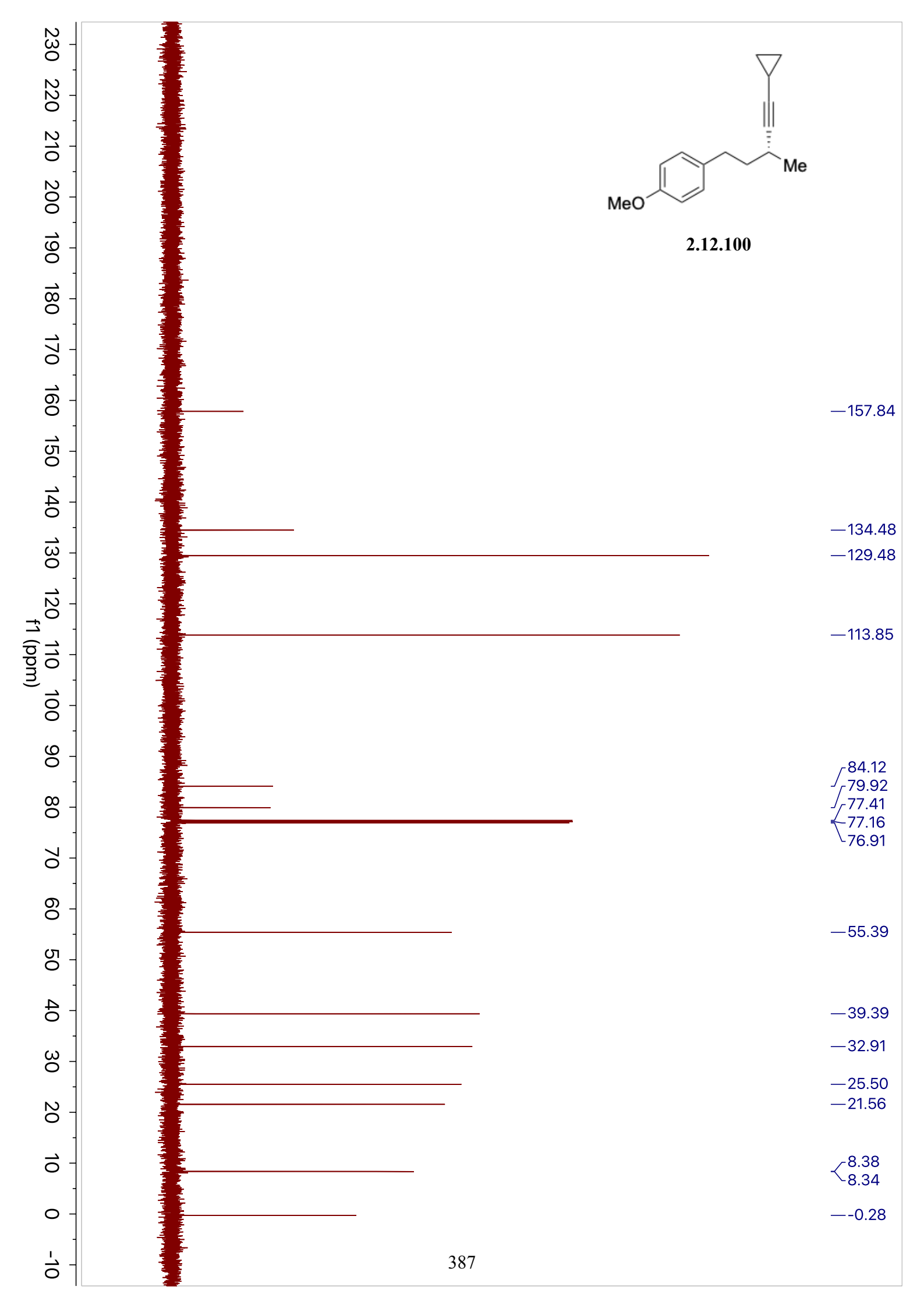

f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.84
134.58
129.49
113.86
85.50
79.89
77.41
77.16
76.91
55.39
39.60
33.00
28.50
28.15
25.63
22.11
21.71
MeO
Me

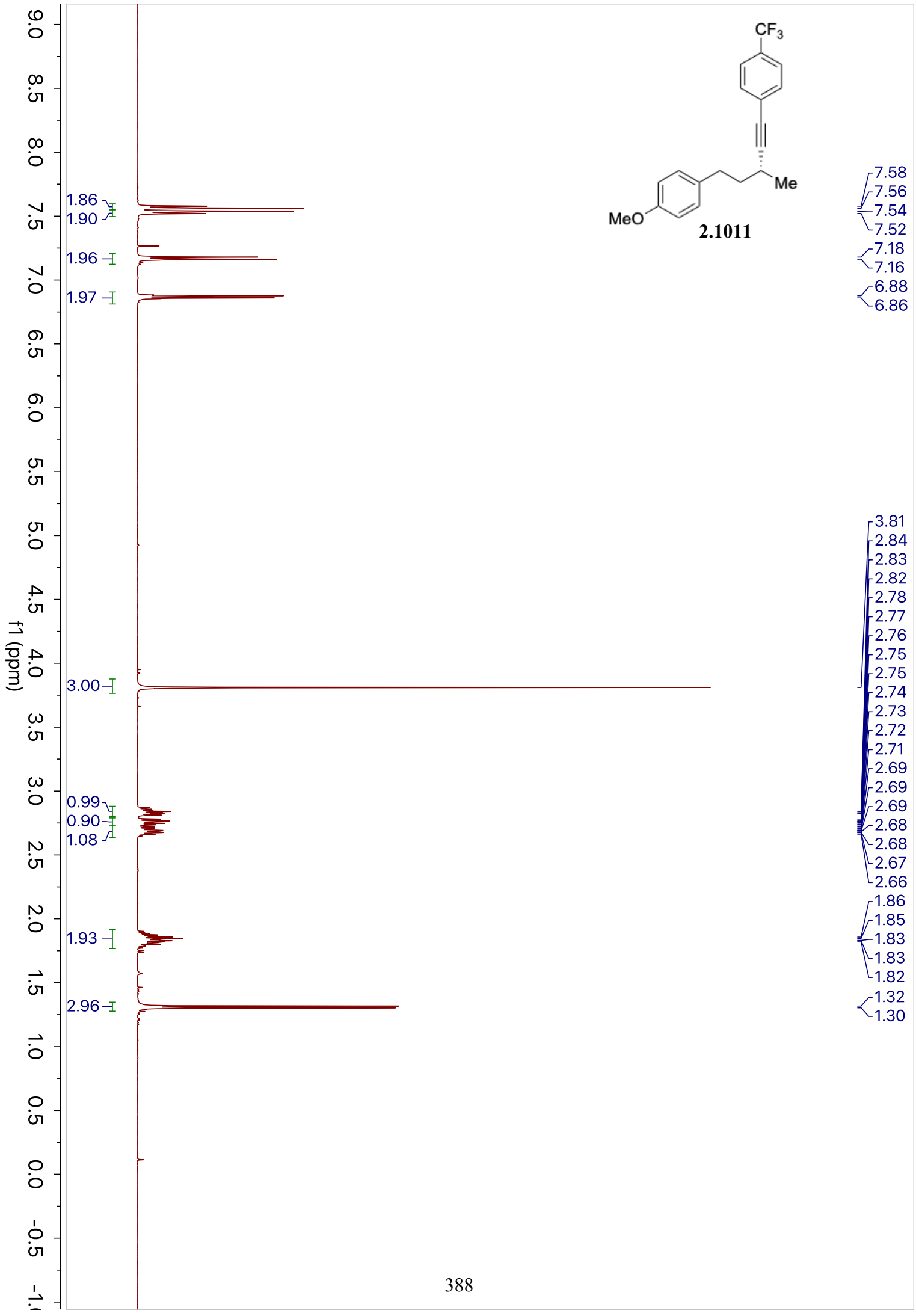
2.98

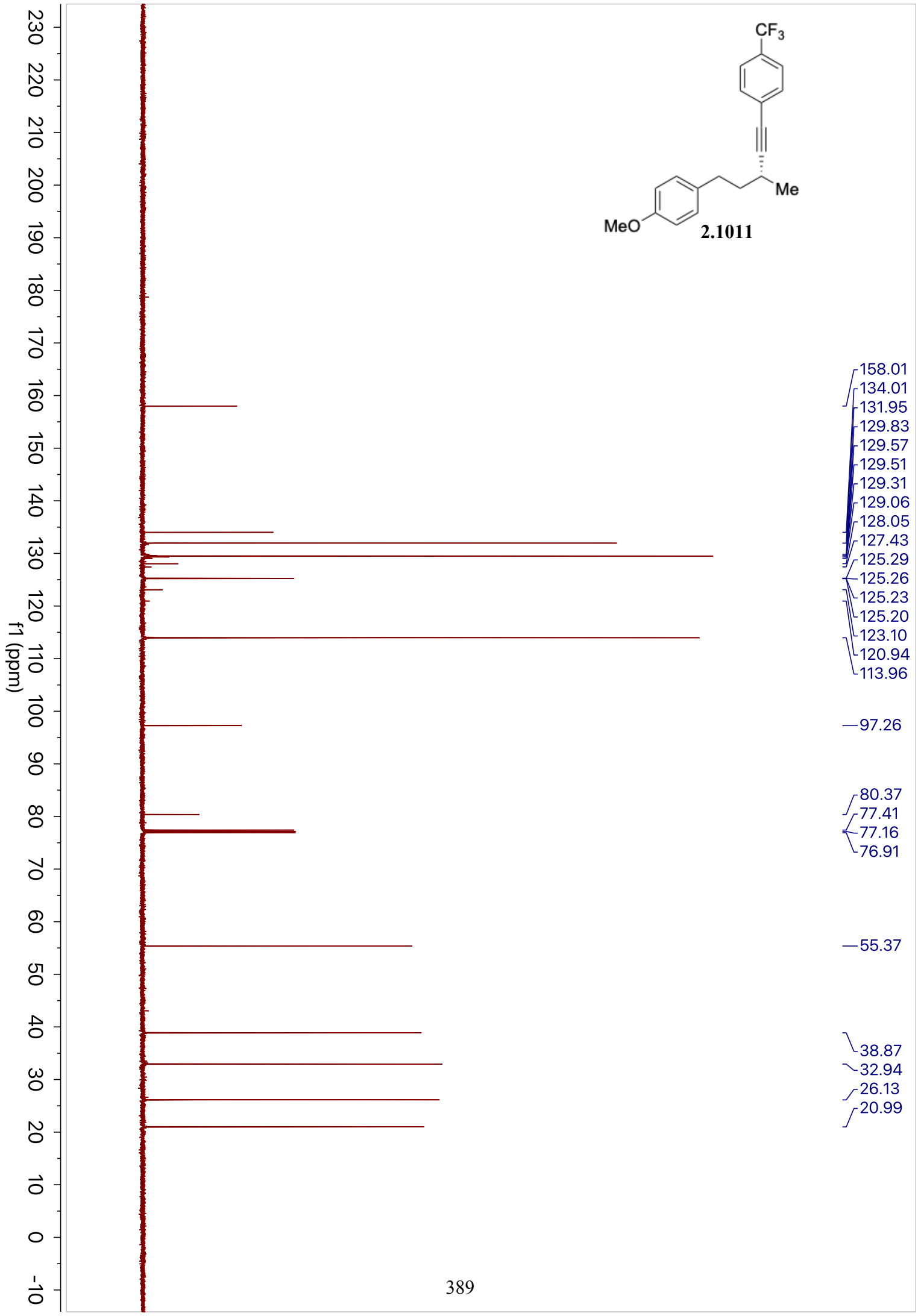

Ph
Me
MeO
2.2.9999
f1 (ppm)
2.20
3.43
1.98
2.00
3.03
2.29
1.04
1.33
1.94
1.00
1.98
2.95

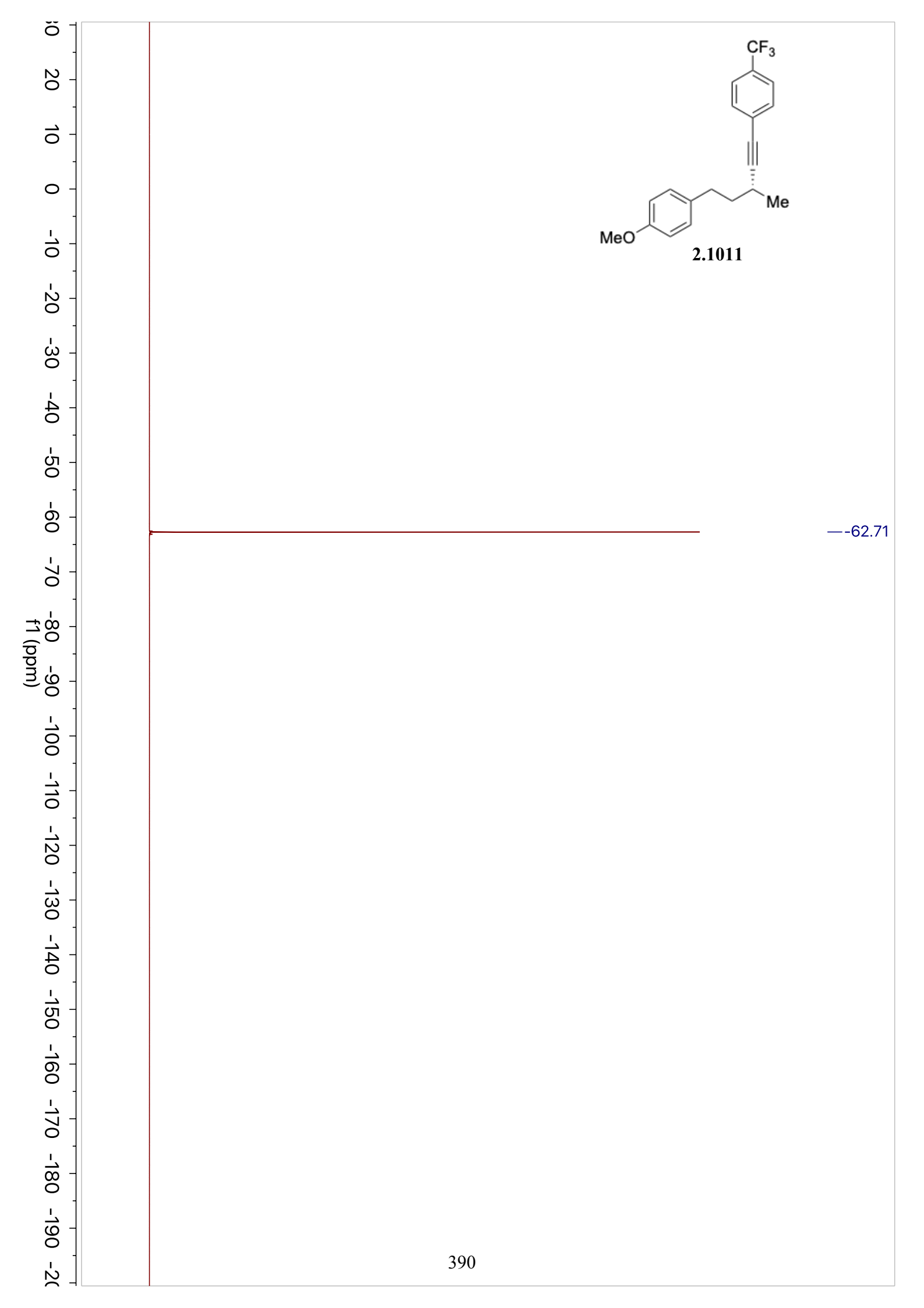

Ph
Me
MeO
2.2.9999
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.82
141.12
134.47
129.49
128.65
128.41
126.27
113.82
85.39
80.26
77.41
77.16
76.91
55.38
39.34
35.80
32.86
25.52
21.58
21.13

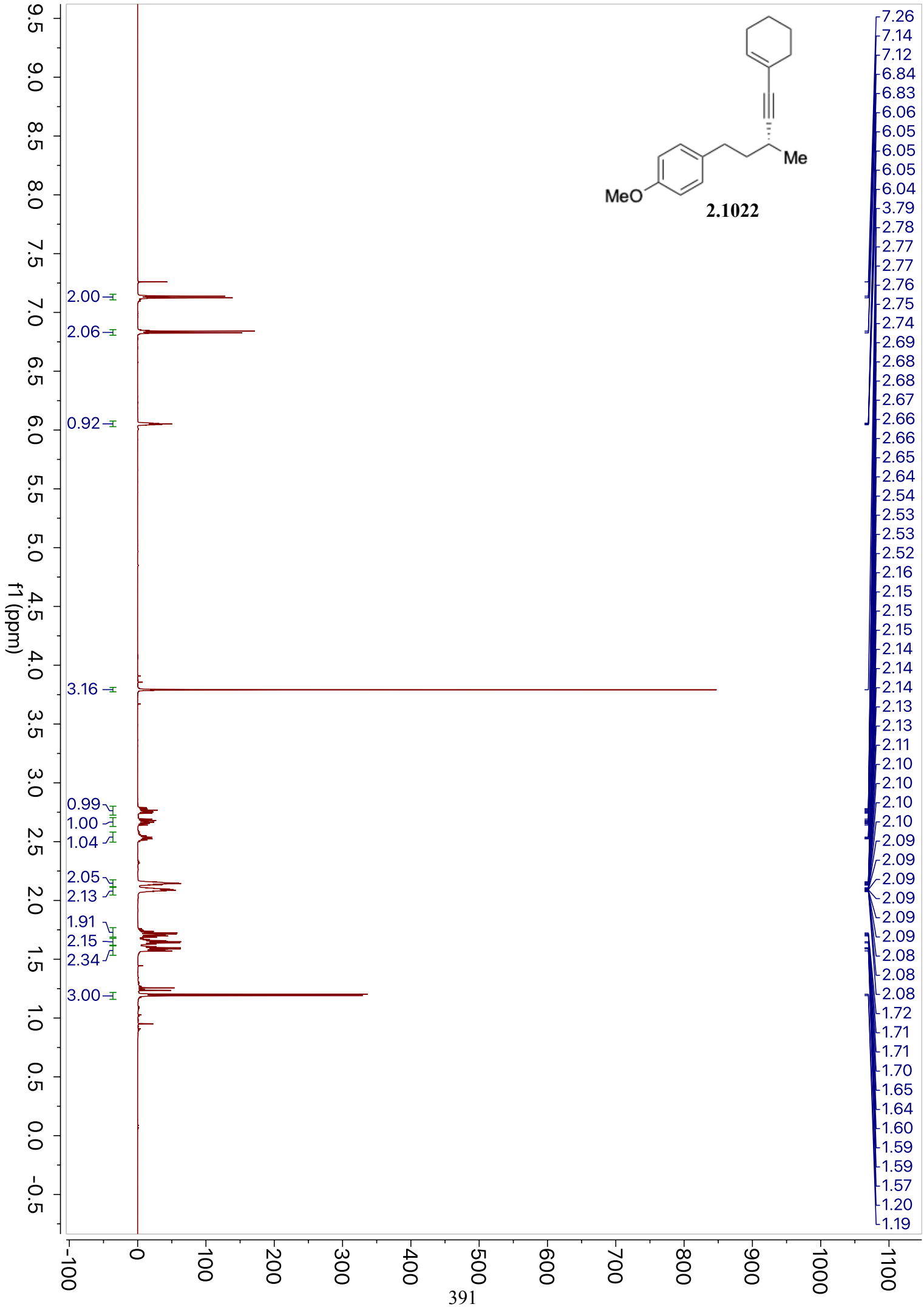

MeO
Me
22.100
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.07
2.13
3.19
1.04
1.04
1.00
2.02
1.28
3.00
2.02
1.88
7.26
7.26
7.12
7.12
7.10
7.10
6.84
6.83
6.82
3.79
3.79
2.73
2.72
2.71
2.71
2.69
2.65
2.63
2.63
2.62
2.61
2.60
2.38
2.37
2.37
2.36
2.35
2.35
2.35
2.34
1.67
1.66
1.66
1.65
1.65
1.65
1.65
1.64
1.64
1.64
1.63
1.26
1.25
1.25
1.25
1.24
1.24
1.24
1.23
1.23
1.23
1.22
1.14
1.14
1.13
0.74
0.74
0.74
0.73
0.73
0.72
0.72
0.63
0.63
0.63
0.63
0.62
0.62

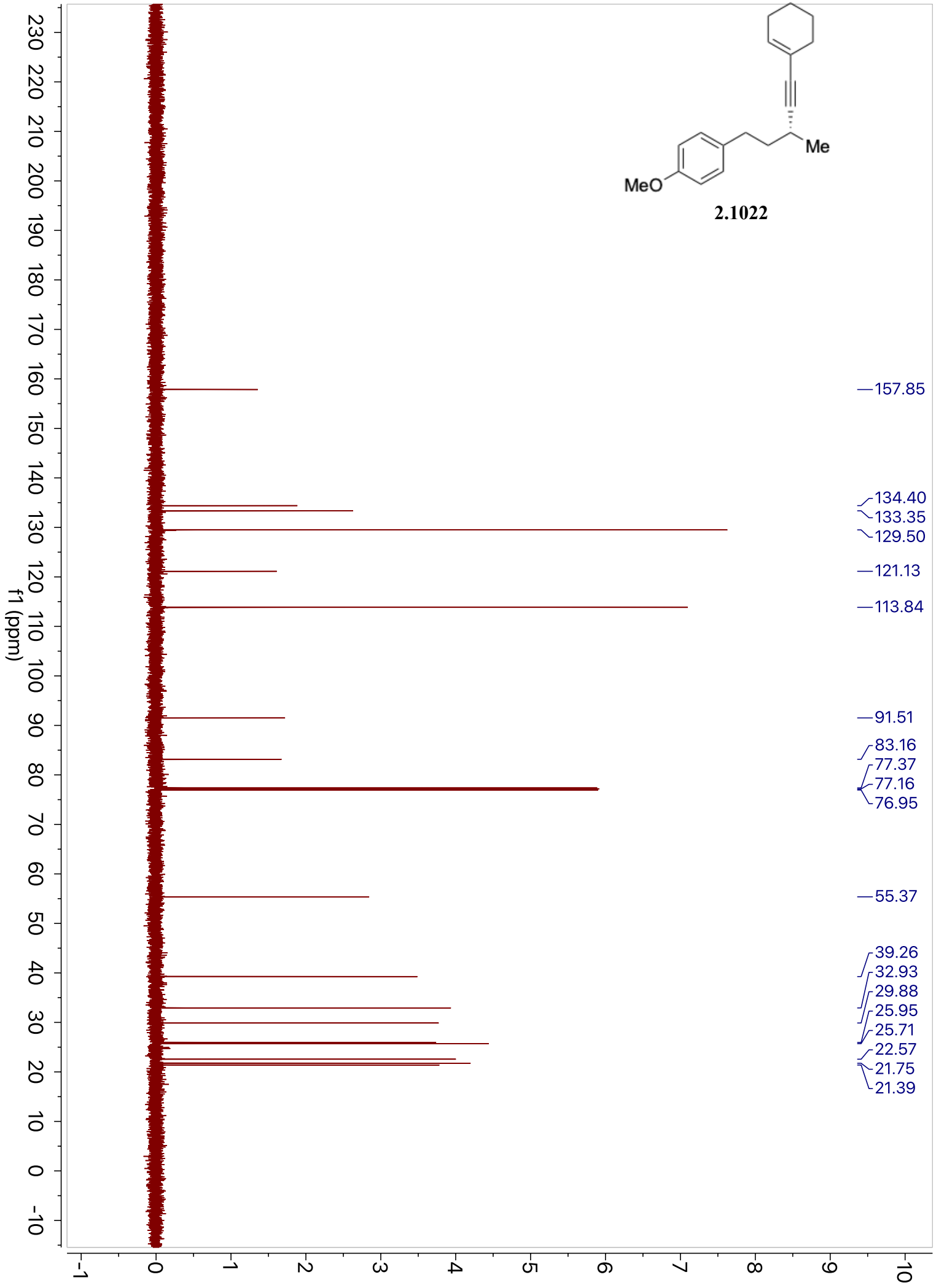

MeO
Me
2.12.100
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.84
134.48
129.48
113.85
84.12
79.92
77.41
77.16
76.91
55.39
39.39
32.91
25.50
21.56
8.38
8.34
-0.28

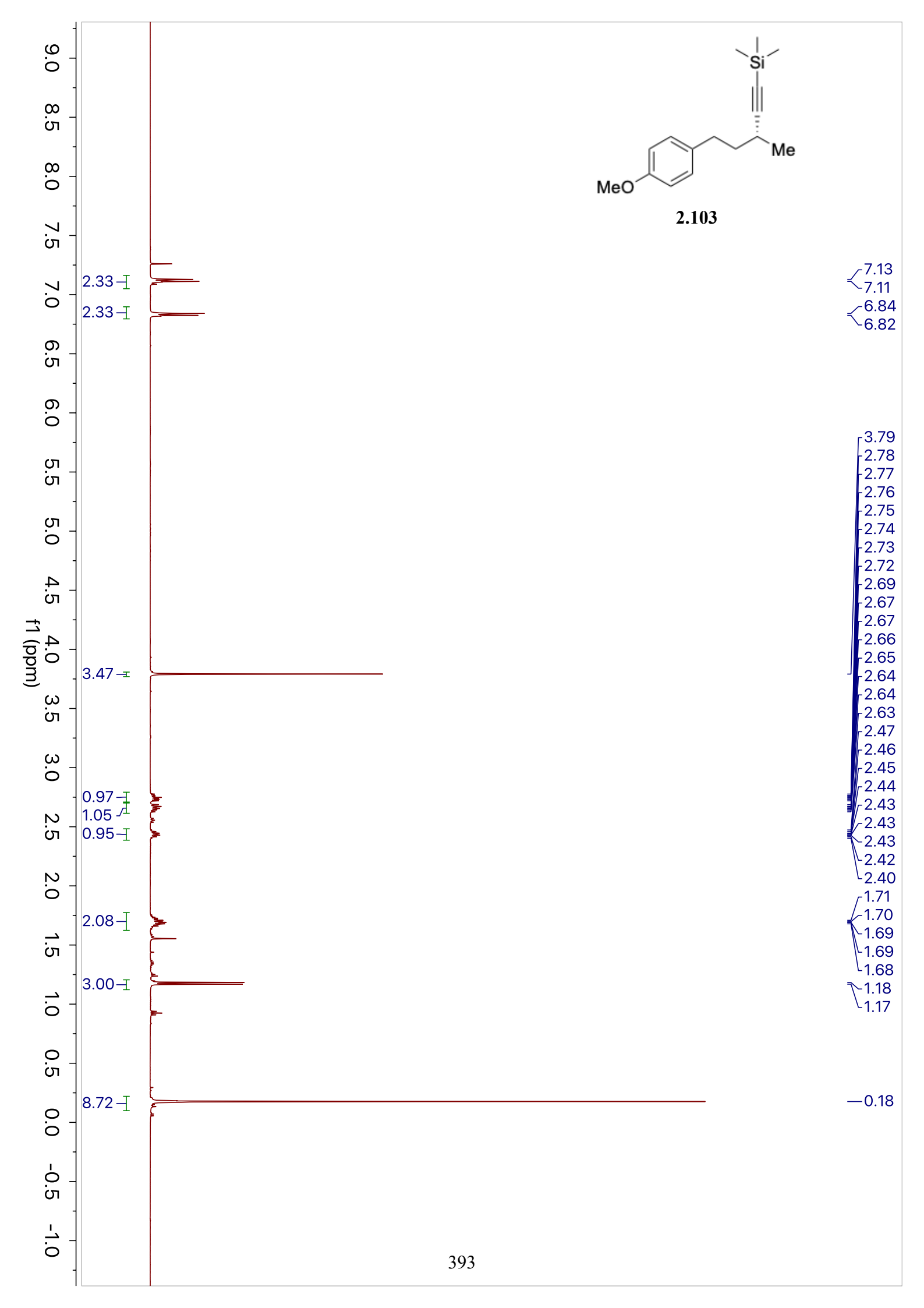

CF3
Me
MeO
2.1011
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.86
1.90
1.96
1.97
3.00
0.99
0.90
1.08
1.93
2.96
7.58
7.56
7.54
7.52
7.18
7.16
6.88
6.86
3.81
2.84
2.83
2.82
2.78
2.77
2.76
2.75
2.75
2.74
2.73
2.72
2.71
2.69
2.69
2.69
2.68
2.68
2.67
2.66
1.86
1.85
1.83
1.83
1.82
1.32
1.30

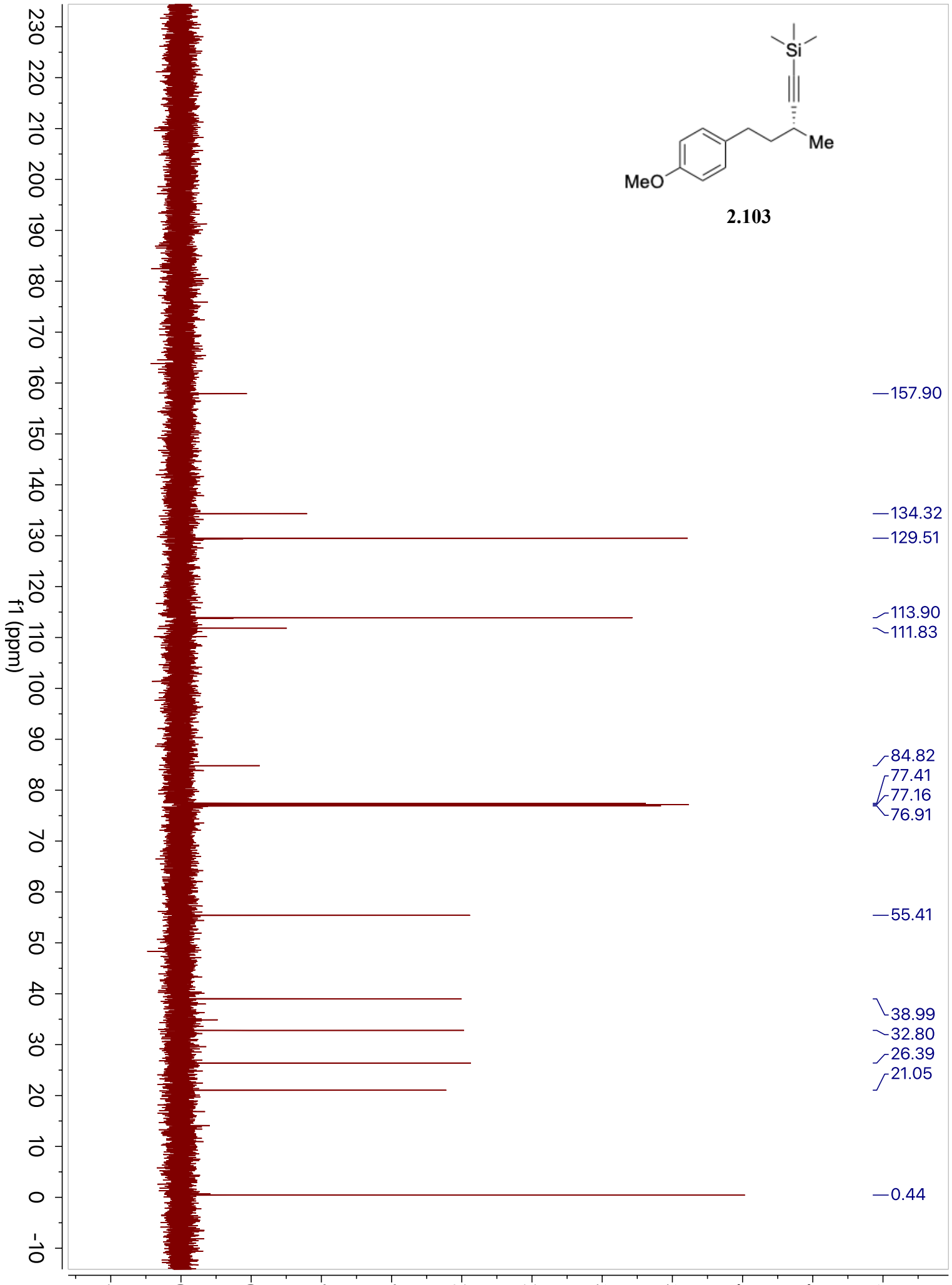

CF3
Me
MeO
2.1011
158.01
134.01
131.95
129.83
129.57
129.51
129.31
129.06
128.05
127.43
125.29
125.26
125.23
125.20
123.10
120.94
113.96
97.26
80.37
77.41
77.16
76.91
55.37
38.87
32.94
26.13
20.99
f1 (ppm)

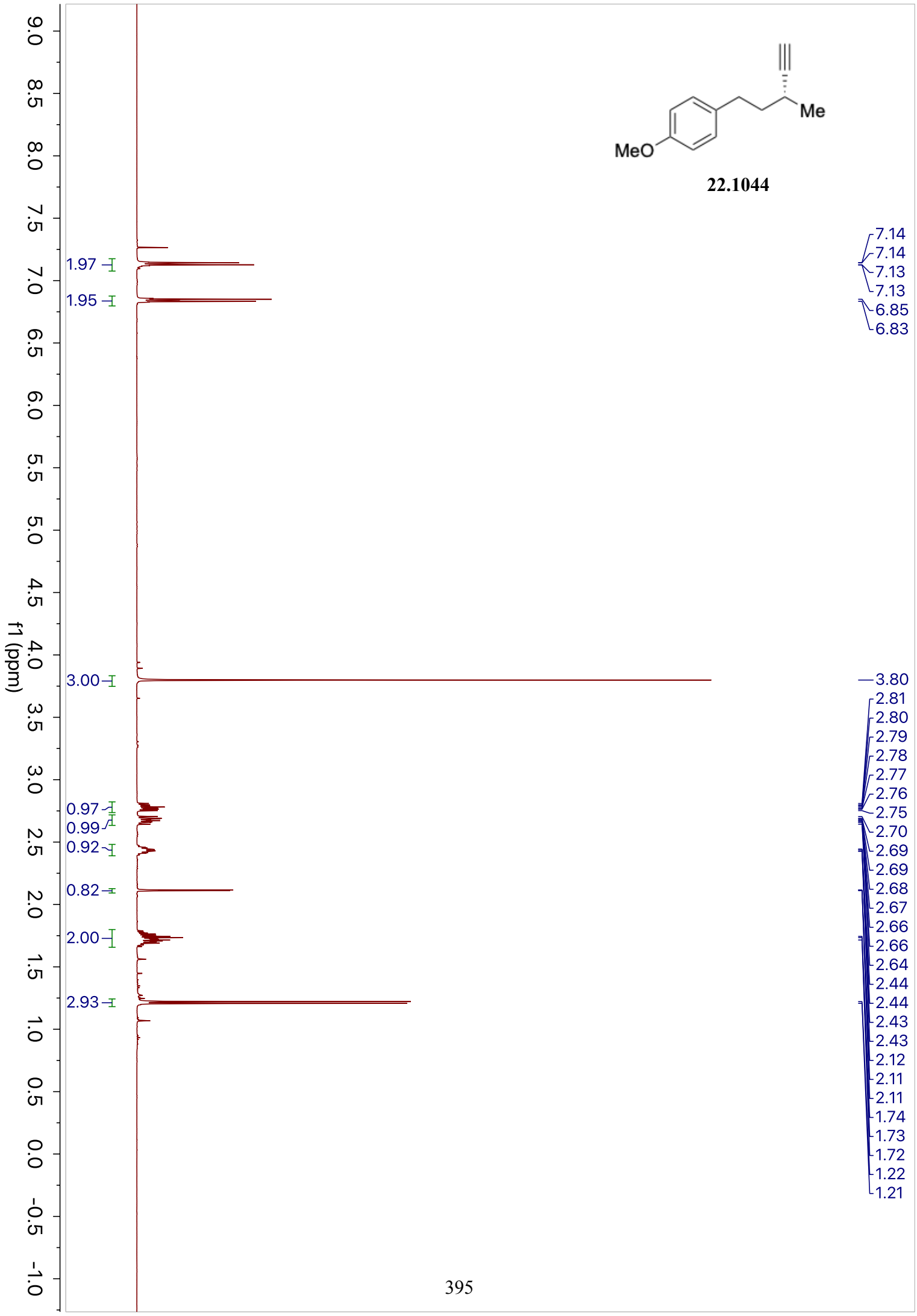

CF3
Me
MeO
2.1011
-62.71
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20

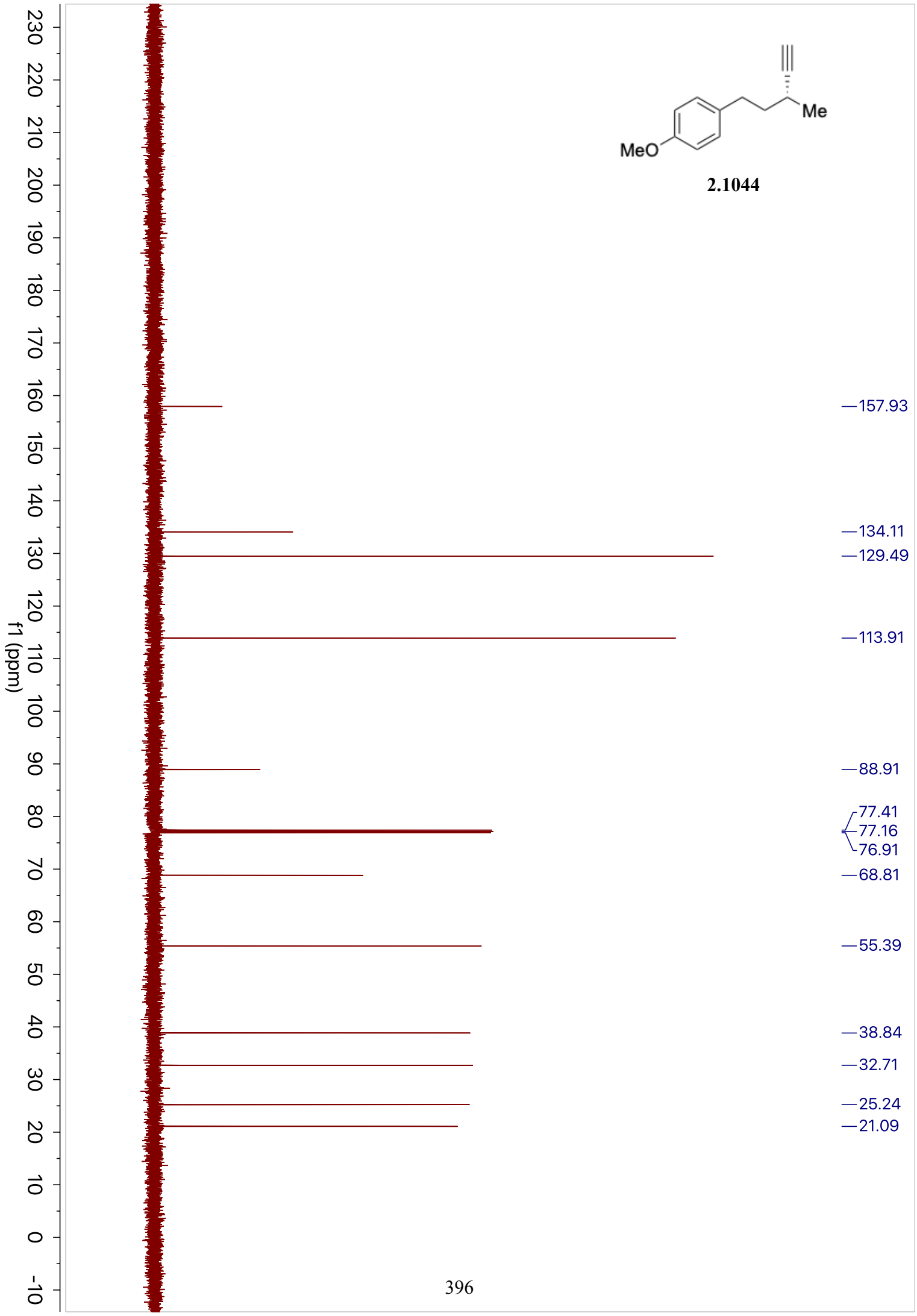

MeO
Me
2.1022
2.00
2.06
0.92
3.16
0.99
1.00
1.04
2.05
2.13
1.91
2.15
2.34
3.00
f1 (ppm)

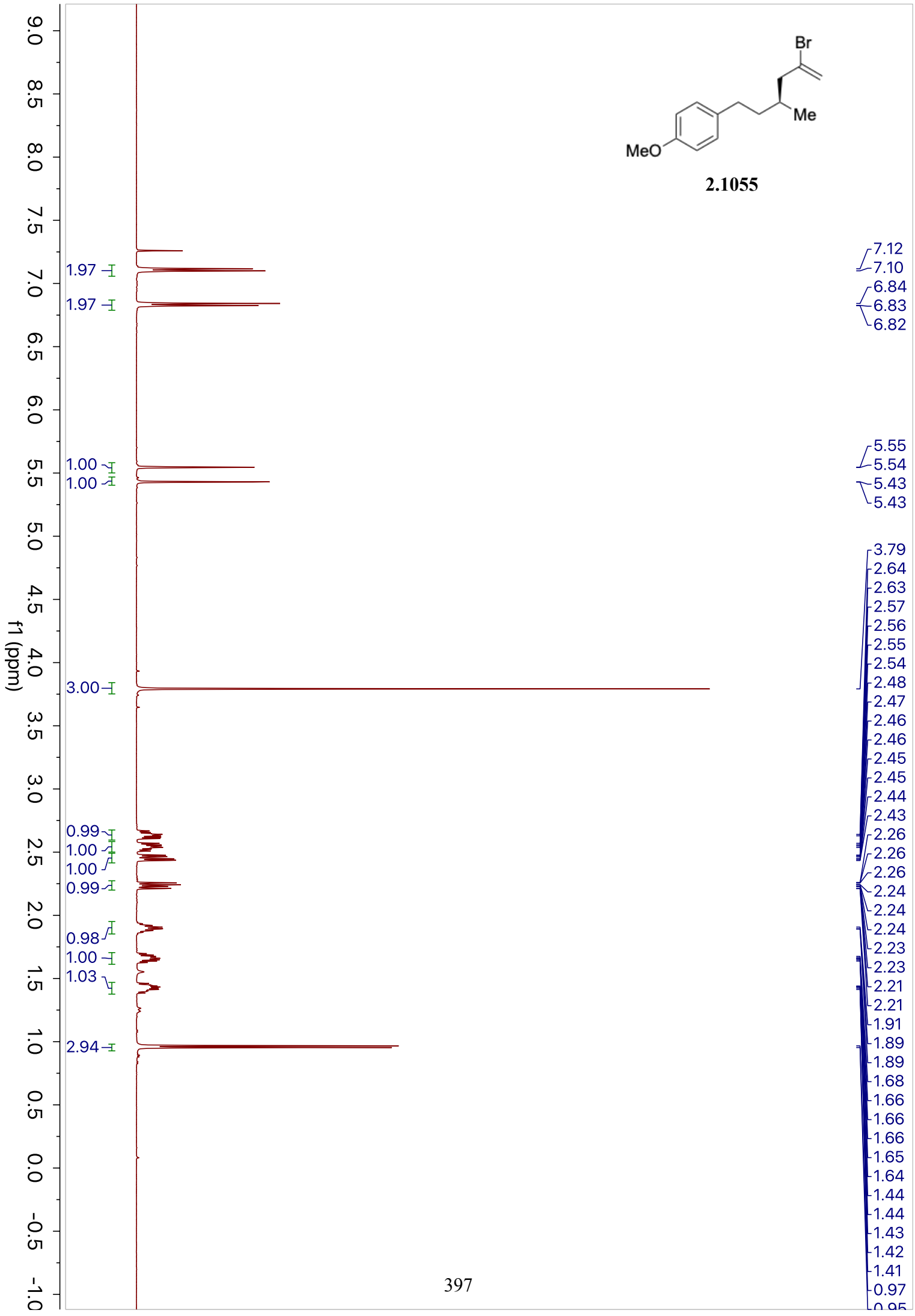

MeO
Me
2.1022
157.85
134.40
133.35
129.50
121.13
113.84
91.51
83.16
77.37
77.16
76.95
55.37
39.26
32.93
29.88
25.95
25.71
22.57
21.75
21.39
f1 (ppm)

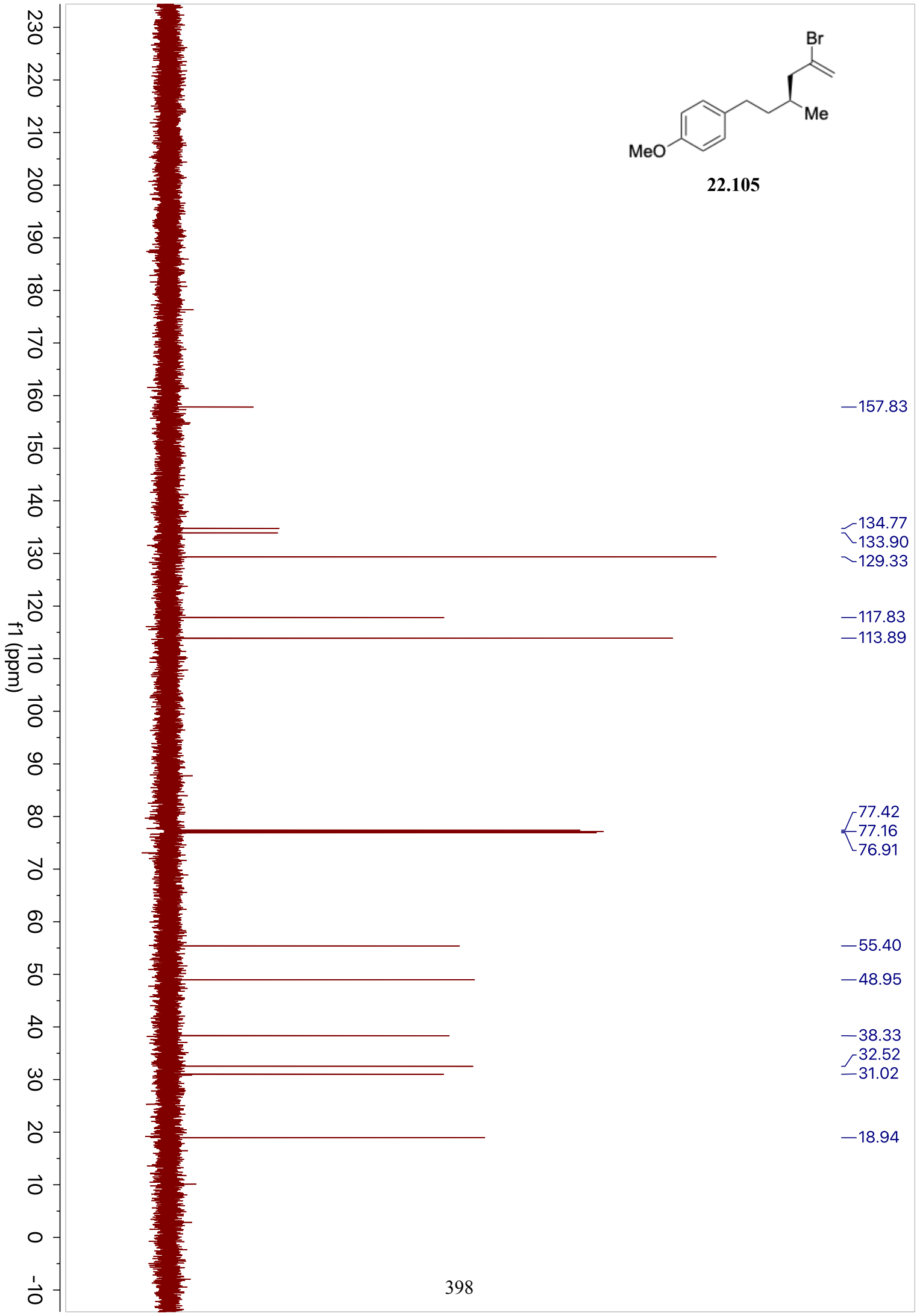

Si
Me
MeO
2.103
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.33
2.33
3.47
0.97
1.05
0.95
2.08
3.00
8.72
7.13
7.11
6.84
6.82
3.79
2.78
2.77
2.76
2.75
2.74
2.73
2.72
2.69
2.67
2.67
2.66
2.65
2.64
2.64
2.63
2.47
2.46
2.45
2.44
2.43
2.43
2.43
2.42
2.40
1.71
1.70
1.69
1.69
1.68
1.18
1.17
0.18

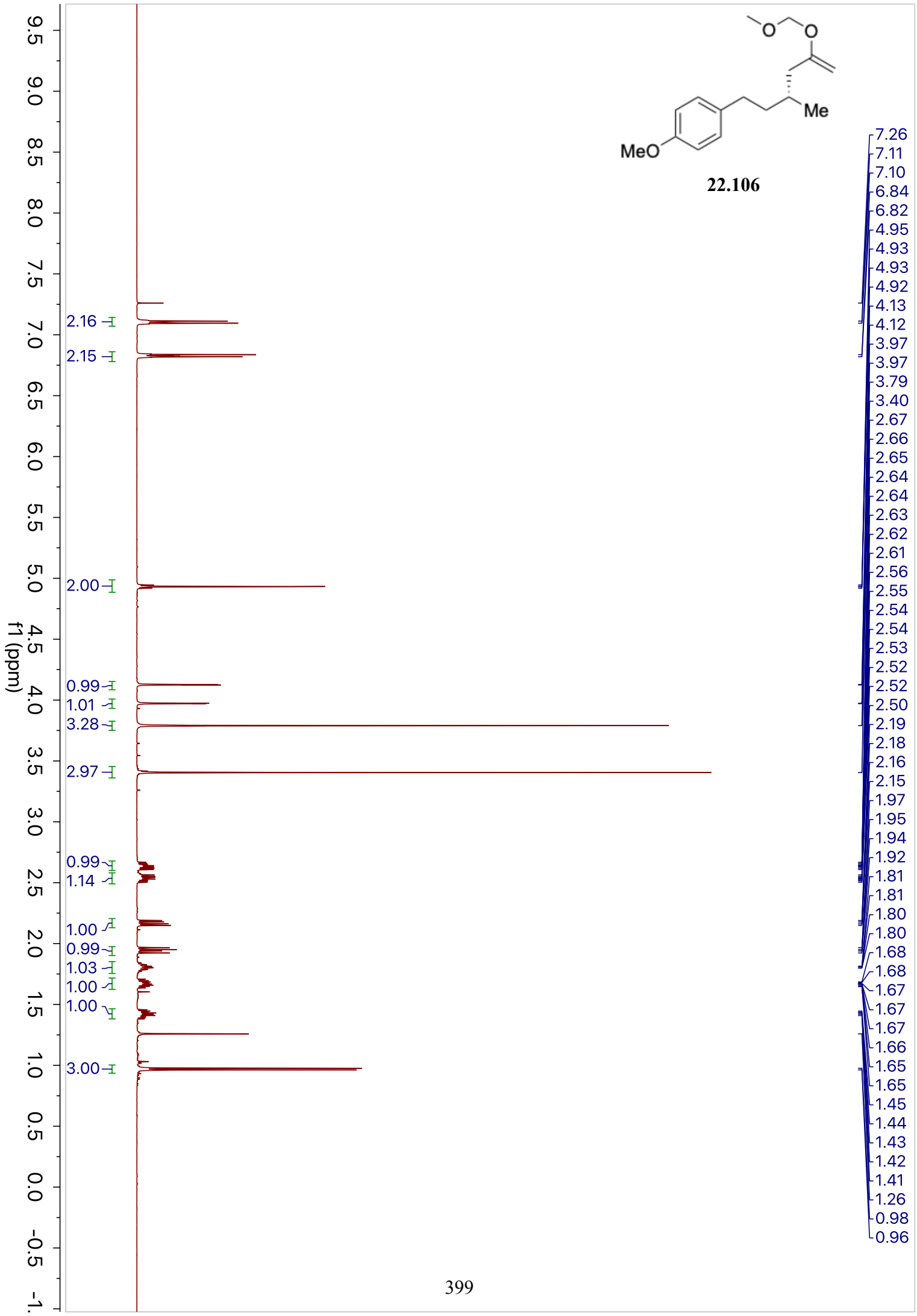

Si
Me
MeO
2.103
157.90
134.32
129.51
113.90
111.83
84.82
77.41
77.16
76.91
55.41
38.99
32.80
26.39
21.05
0.44
f1 (ppm)

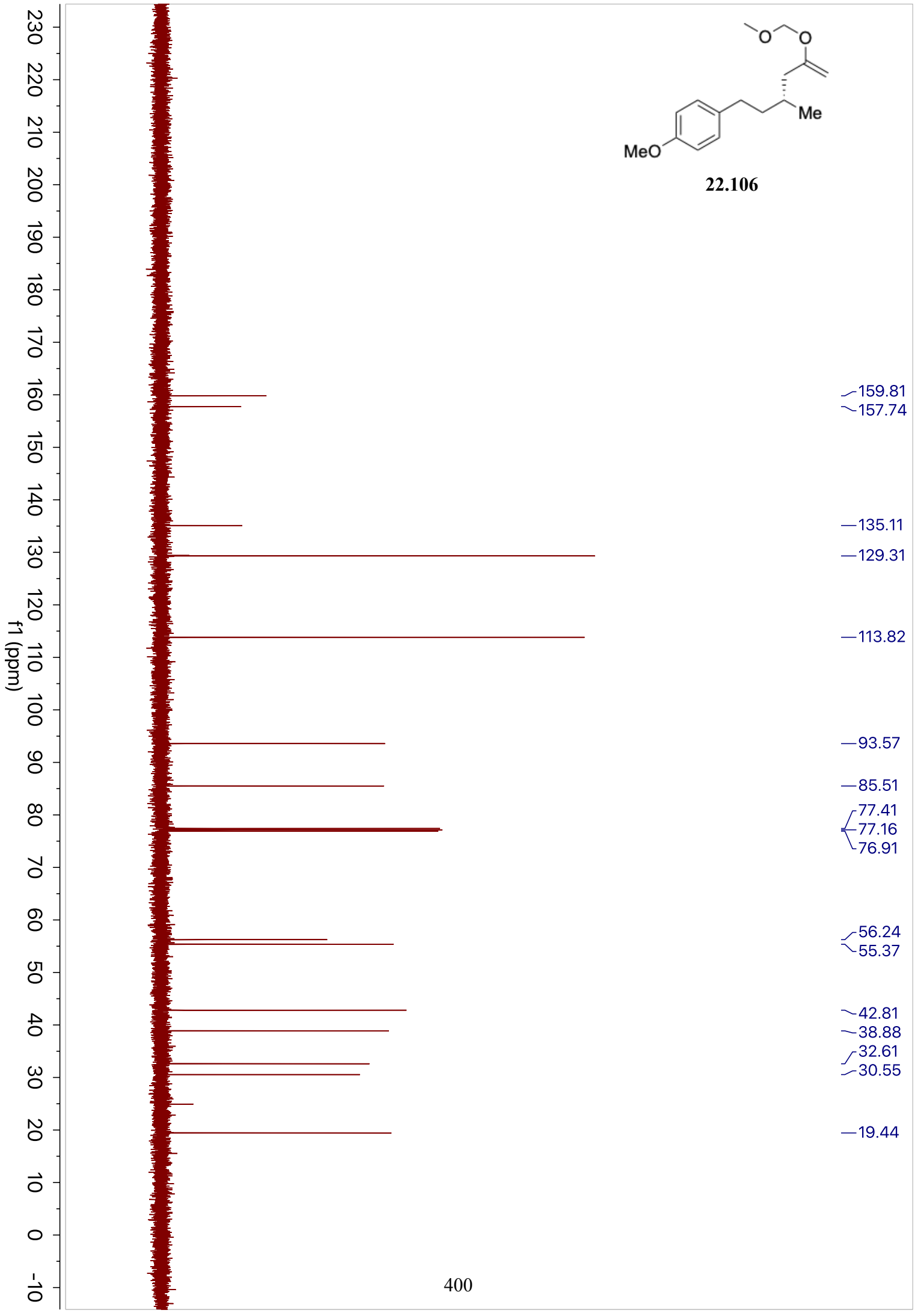

MeO
Me
22.1044
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.97
1.95
3.00
0.97
0.99
0.92
0.82
2.00
2.93
7.14
7.14
7.13
7.13
6.85
6.83
3.80
2.81
2.80
2.79
2.78
2.77
2.76
2.75
2.70
2.69
2.69
2.68
2.67
2.66
2.66
2.64
2.44
2.44
2.43
2.43
2.12
2.11
2.11
1.74
1.73
1.72
1.22
1.21

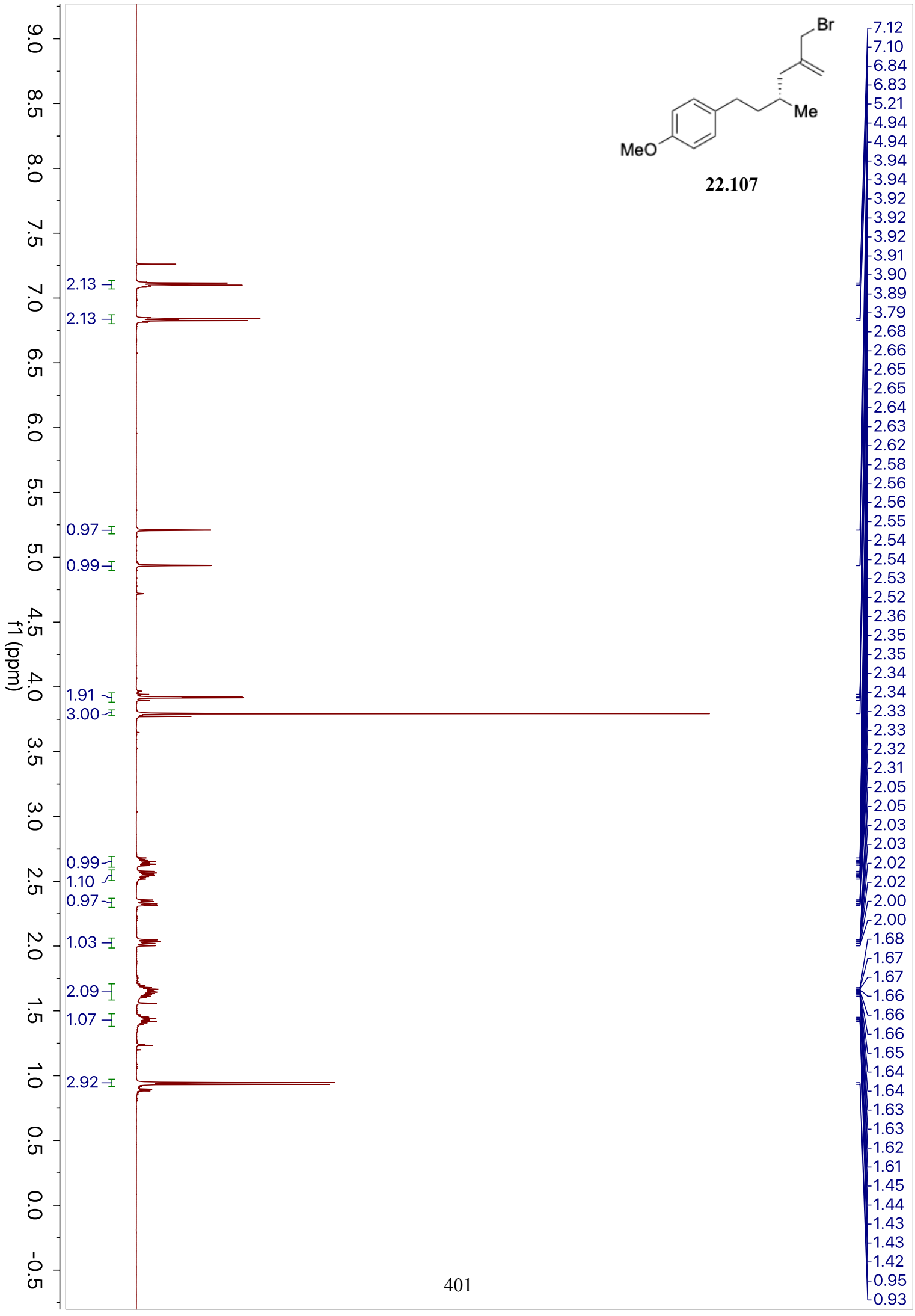

MeO
Me
2.1044
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.93
134.11
129.49
113.91
88.91
77.41
77.16
76.91
68.81
55.39
38.84
32.71
25.24
21.09

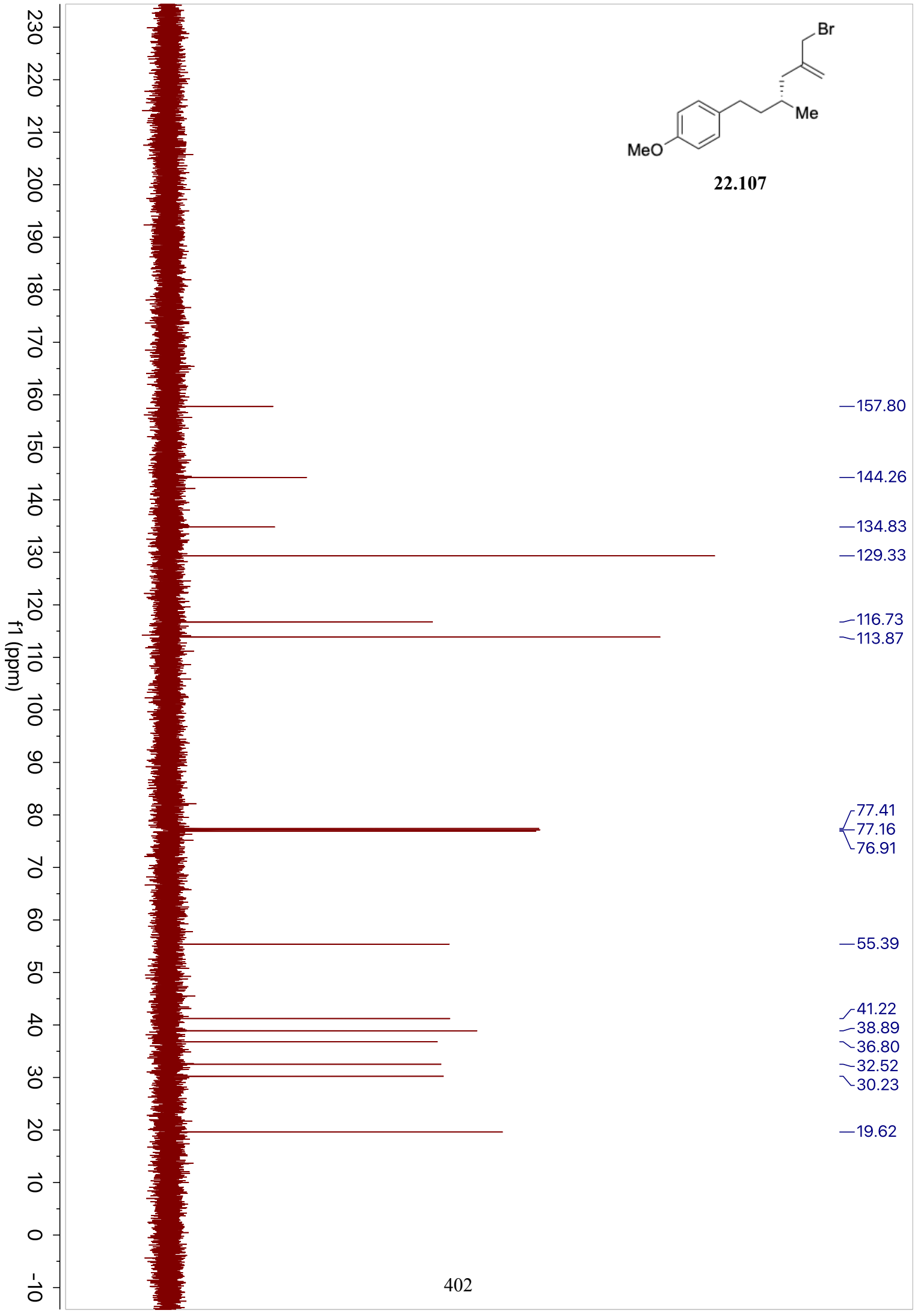

Br
Me
MeO
2.1055
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.97
1.97
1.00
1.00
3.00
0.99
1.00
1.00
0.99
0.98
1.00
1.03
2.94
7.12
7.10
6.84
6.83
6.82
5.55
5.54
5.43
5.43
3.79
2.64
2.63
2.57
2.56
2.55
2.54
2.48
2.47
2.46
2.46
2.45
2.45
2.44
2.43
2.26
2.26
2.26
2.24
2.24
2.24
2.23
2.23
2.21
2.21
1.91
1.89
1.89
1.68
1.66
1.66
1.66
1.65
1.64
1.44
1.44
1.43
1.42
1.41
0.97

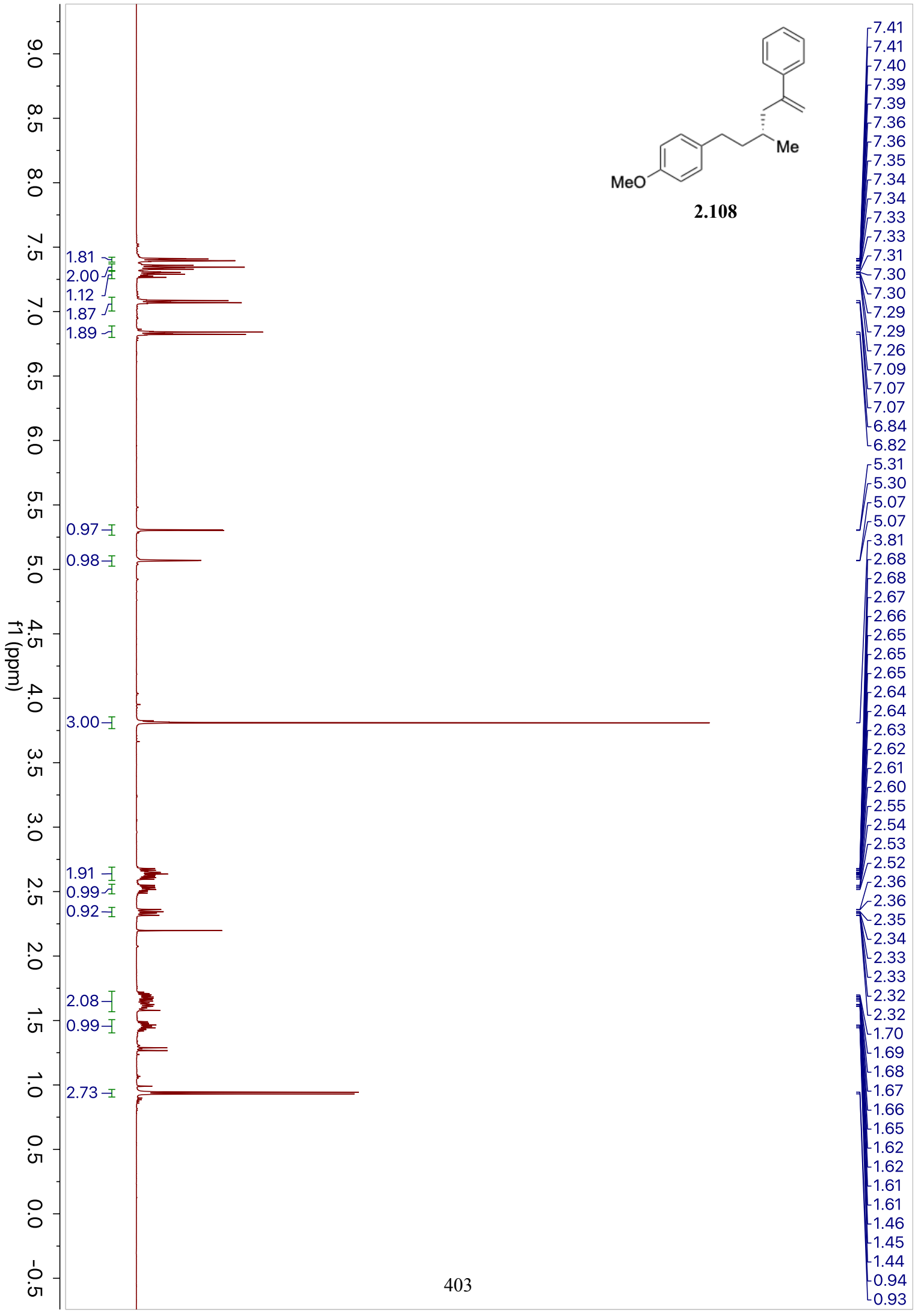

Br
Me
MeO
22.105
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.83
134.77
133.90
129.33
117.83
113.89
77.42
77.16
76.91
55.40
48.95
38.33
32.52
31.02
18.94

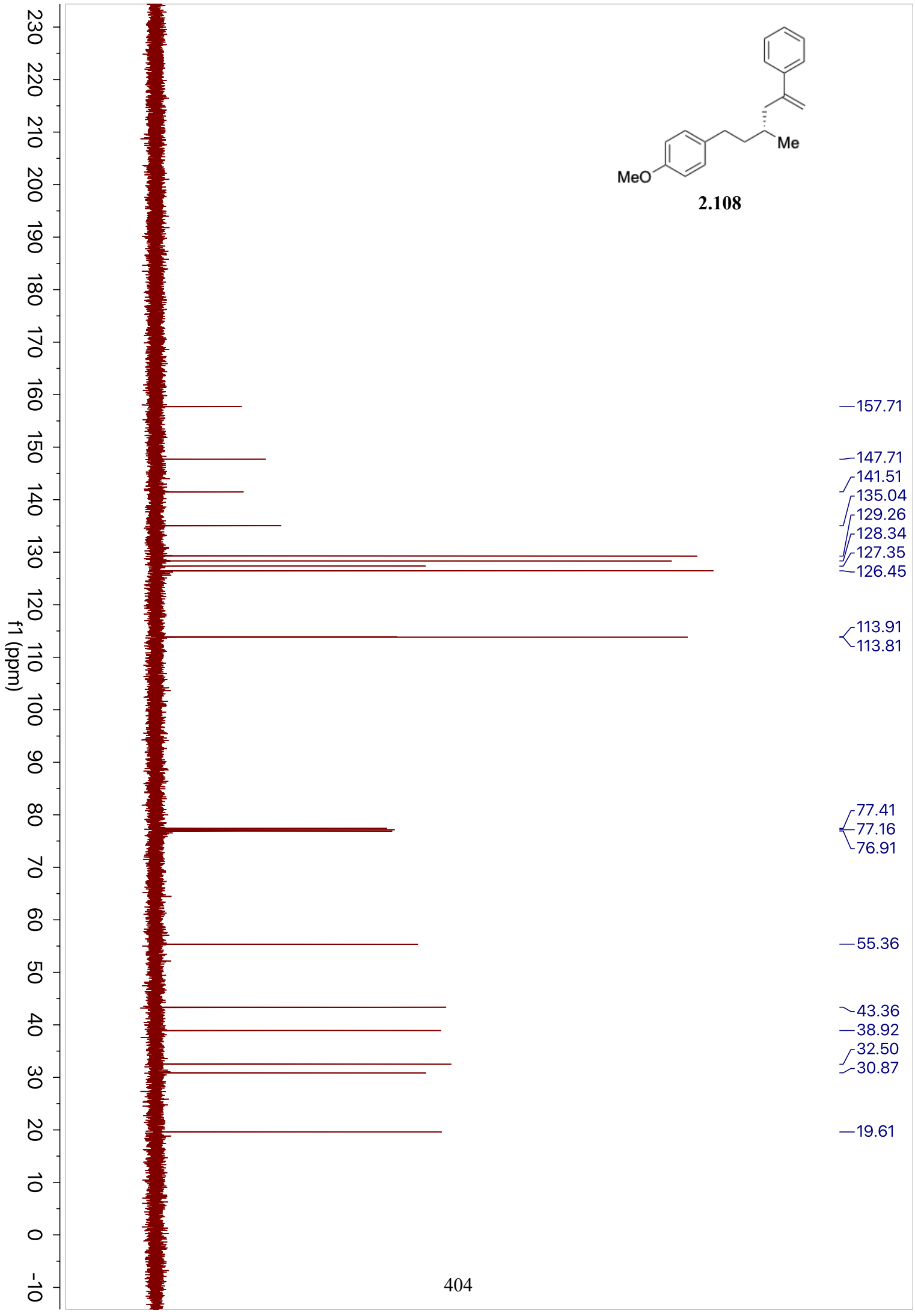

O
O
Me
MeO
22.106
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
2.16
2.15
2.00
0.99
1.01
3.28
2.97
0.99
1.14
1.00
0.99
1.03
1.00
1.00
3.00
7.26
7.11
7.10
6.84
6.82
4.95
4.93
4.93
4.92
4.13
4.12
3.97
3.97
3.79
3.40
2.67
2.66
2.65
2.64
2.64
2.63
2.62
2.61
2.56
2.55
2.54
2.54
2.53
2.52
2.52
2.50
2.19
2.18
2.16
2.15
1.97
1.95
1.94
1.92
1.81
1.81
1.80
1.80
1.68
1.68
1.67
1.67
1.67
1.66
1.65
1.65
1.45
1.44
1.43
1.42
1.41
1.26
0.98
0.96

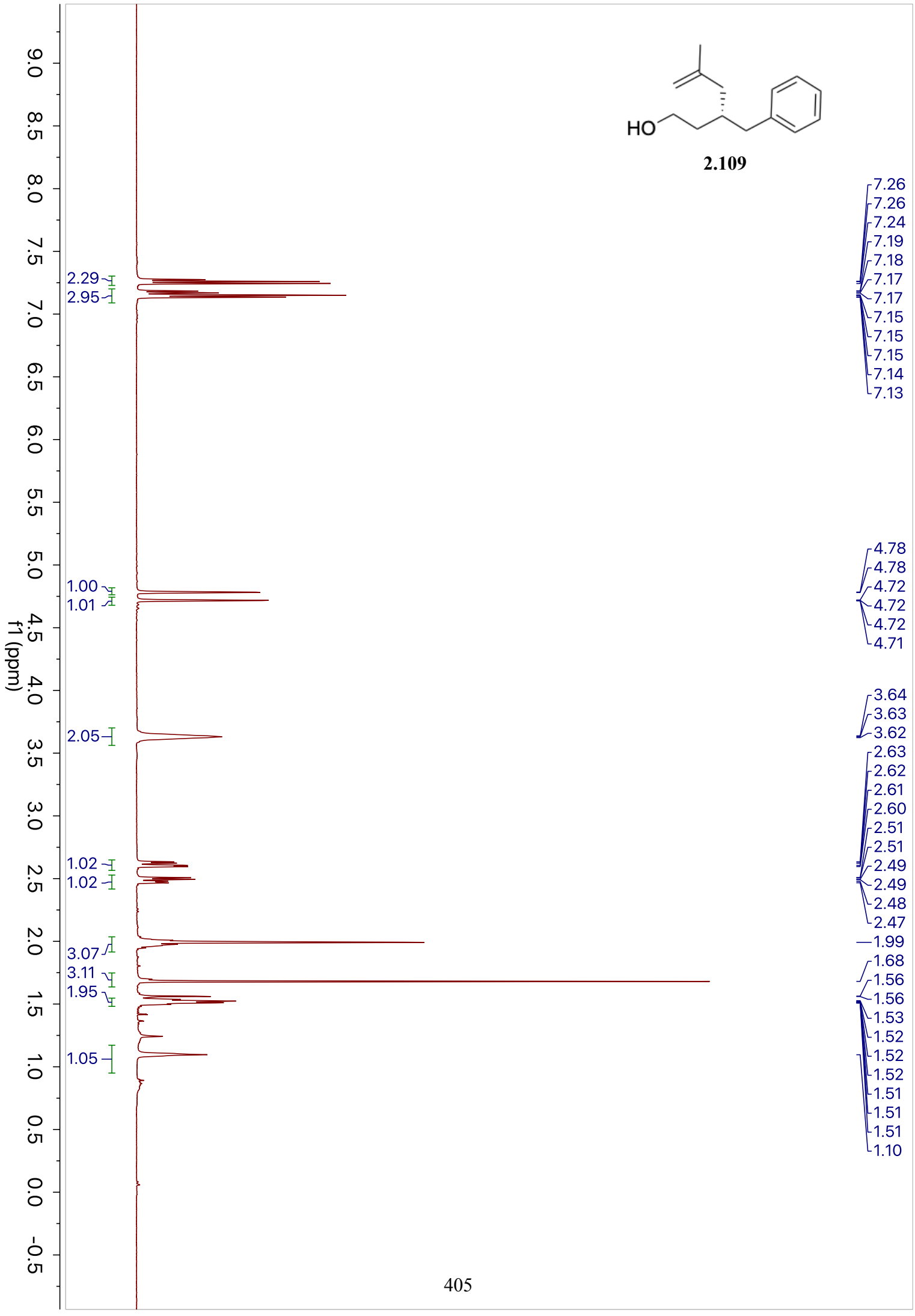

O
O
Me
MeO
22.106
159.81
157.74
135.11
129.31
113.82
93.57
85.51
77.41
77.16
76.91
56.24
55.37
42.81
38.88
32.61
30.55
19.44
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

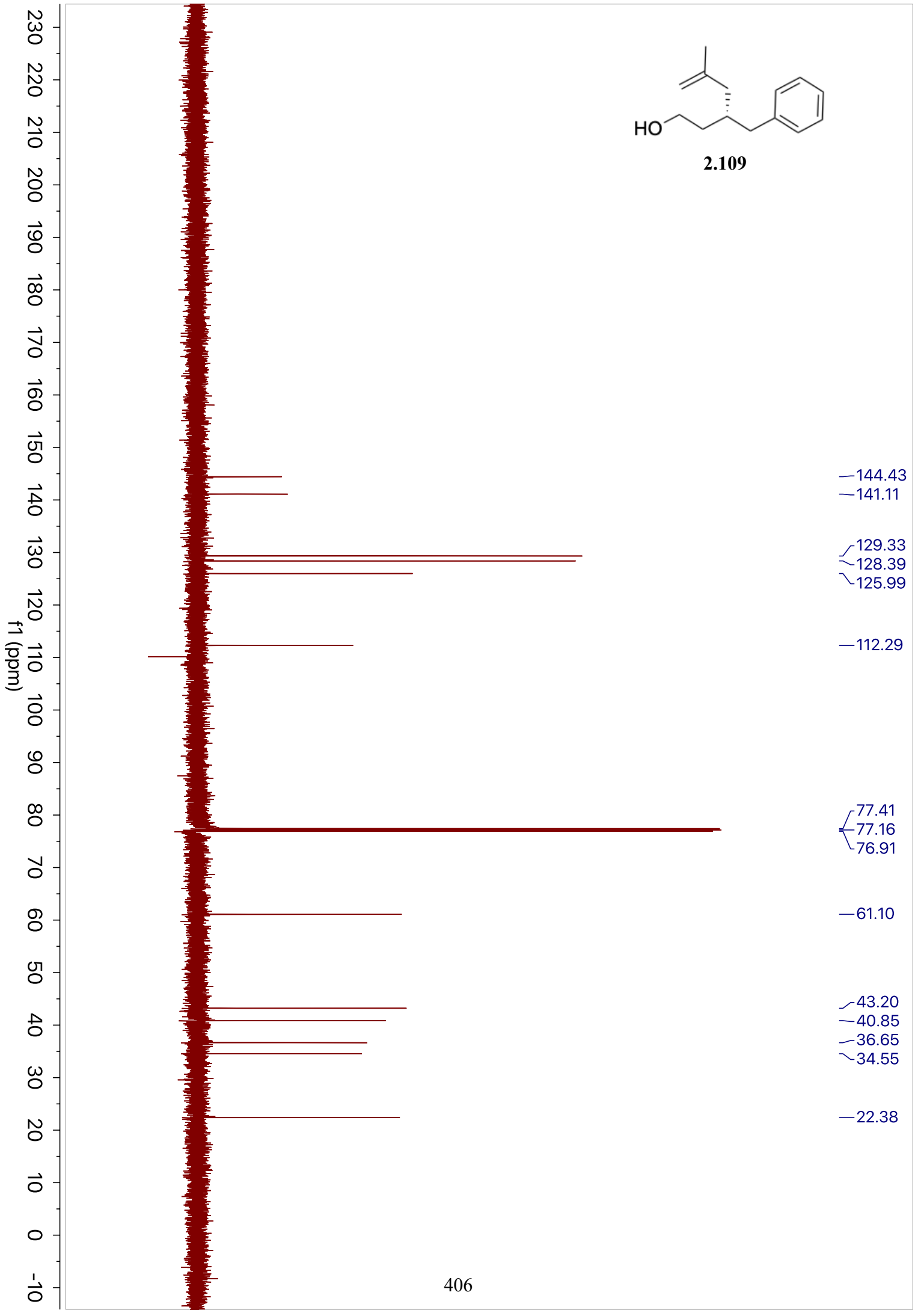

Br
Me
MeO
22.107
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.13
2.13
0.97
0.99
1.91
3.00
0.99
1.10
0.97
1.03
2.09
1.07
2.92
7.12
7.10
6.84
6.83
5.21
4.94
4.94
3.94
3.94
3.92
3.92
3.92
3.91
3.90
3.89
3.79
2.68
2.66
2.65
2.65
2.64
2.63
2.62
2.58
2.56
2.56
2.55
2.54
2.54
2.53
2.52
2.36
2.35
2.35
2.34
2.34
2.33
2.33
2.32
2.31
2.05
2.05
2.03
2.03
2.02
2.02
2.00
2.00
1.68
1.67
1.67
1.66
1.66
1.66
1.65
1.64
1.64
1.63
1.63
1.62
1.61
1.45
1.44
1.43
1.43
1.42
0.95
0.93

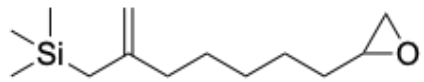

Br
Me
MeO
22.107
157.80
144.26
134.83
129.33
116.73
113.87
77.41
77.16
76.91
55.39
41.22
38.89
36.80
32.52
30.23
19.62
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


MeO
Me
2.108
f1 (ppm)
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
1.81
2.00
1.12
1.87
1.89
0.97
0.98
3.00
1.91
0.99
0.92
2.08
0.99
2.73
7.41
7.41
7.40
7.39
7.39
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.31
7.30
7.30
7.29
7.29
7.26
7.09
7.07
7.07
6.84
6.82
5.31
5.30
5.07
5.07
3.81
2.68
2.68
2.67
2.66
2.65
2.65
2.65
2.64
2.64
2.63
2.62
2.61
2.60
2.55
2.54
2.53
2.52
2.36
2.36
2.35
2.34
2.33
2.33
2.32
2.32
1.70
1.69
1.68
1.67
1.66
1.65
1.62
1.62
1.61
1.61
1.46
1.45
1.44
0.94
0.93

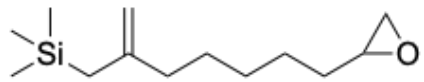

Me
MeO
2.108
157.71
147.71
141.51
135.04
129.26
128.34
127.35
126.45
113.91
113.81
77.41
77.16
76.91
55.36
43.36
38.92
32.50
30.87
19.61
f1 (ppm)


HO
2.109
f1 (ppm)
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
2.29
2.95
1.00
1.01
2.05
1.02
1.02
3.07
3.11
1.95
1.05
7.26
7.26
7.24
7.19
7.18
7.17
7.17
7.15
7.15
7.15
7.14
7.13
4.78
4.78
4.72
4.72
4.72
4.71
3.64
3.63
3.62
2.63
2.62
2.61
2.60
2.51
2.51
2.49
2.49
2.48
2.47
1.99
1.68
1.56
1.56
1.53
1.52
1.52
1.52
1.51
1.51
1.51
1.10


HO
2.109
144.43
141.11
129.33
128.39
125.99
112.29
77.41
77.16
76.91
61.10
43.20
40.85
36.65
34.55
22.38
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

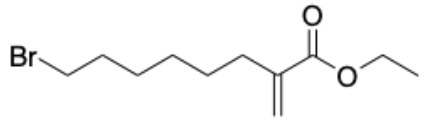


2.110

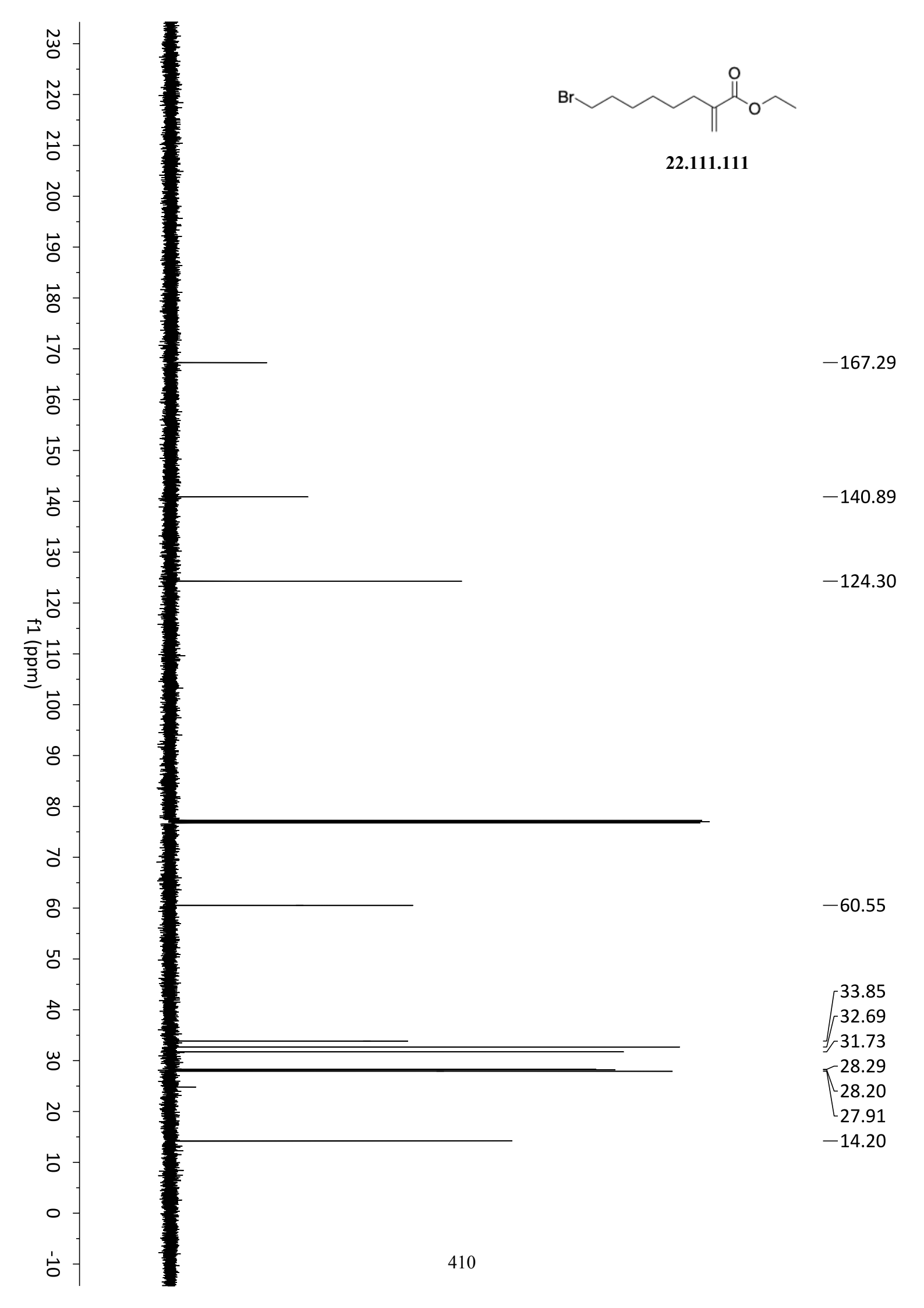

Si
O

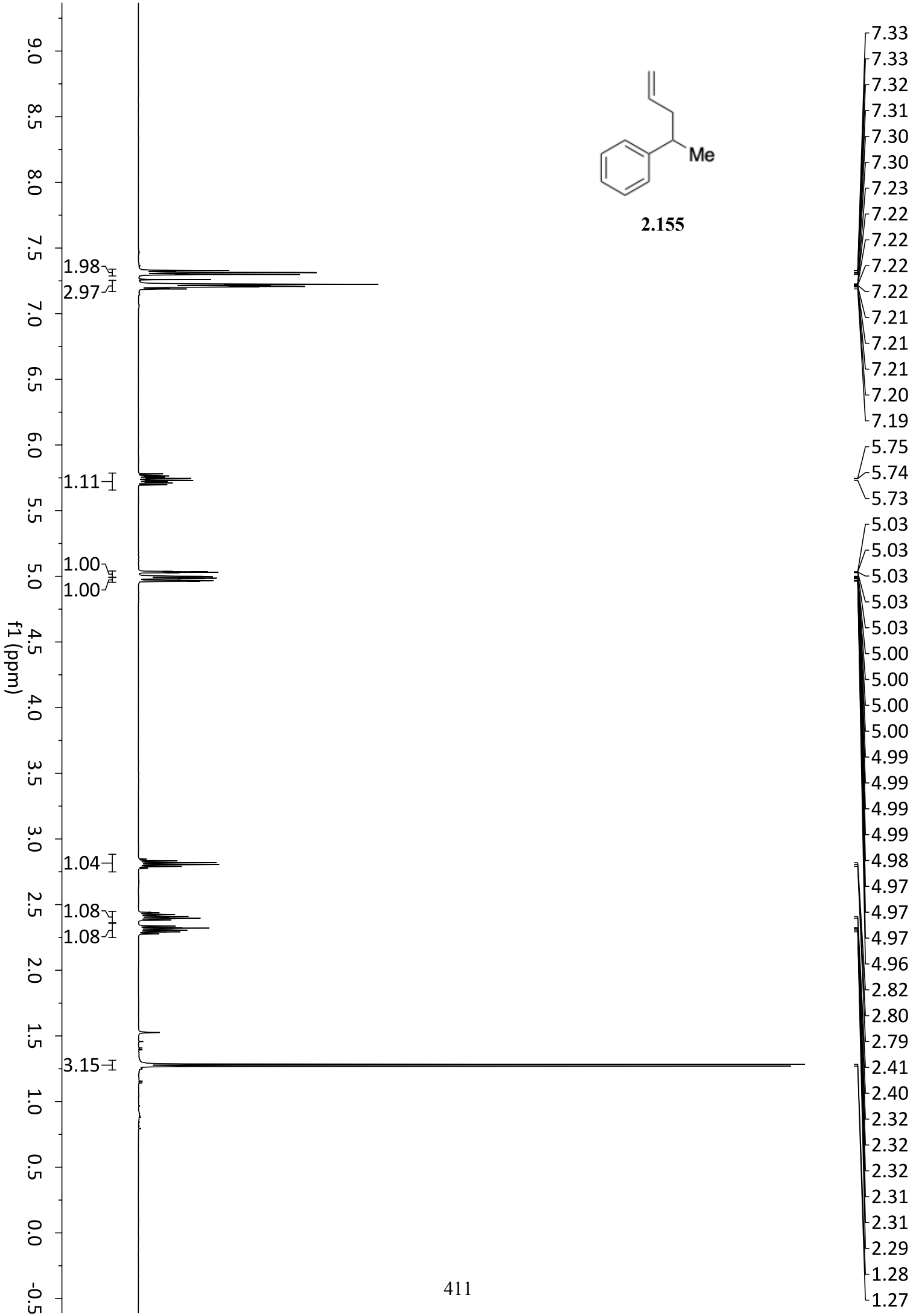
2.110

f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
147.81
106.92
77.37
77.16
76.95
52.50
47.27
38.22
32.61
29.33
27.85
26.90
26.04
-1.16



22.111.111


Br
O
O
22.111.111
167.29
140.89
124.30
60.55
33.85
32.69
31.73
28.29
28.20
27.91
14.20
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Me
2.155
1.98
2.97
1.11
1.00
1.00
1.04
1.08
1.08
3.15
f1 (ppm)
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
7.33
7.33
7.32
7.31
7.30
7.30
7.23
7.22
7.22
7.22
7.22
7.21
7.21
7.21
7.20
7.19
5.75
5.74
5.73
5.03
5.03
5.03
5.03
5.03
5.00
5.00
5.00
5.00
4.99
4.99
4.99
4.99
4.98
4.97
4.97
4.97
4.96
2.82
2.80
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2.40
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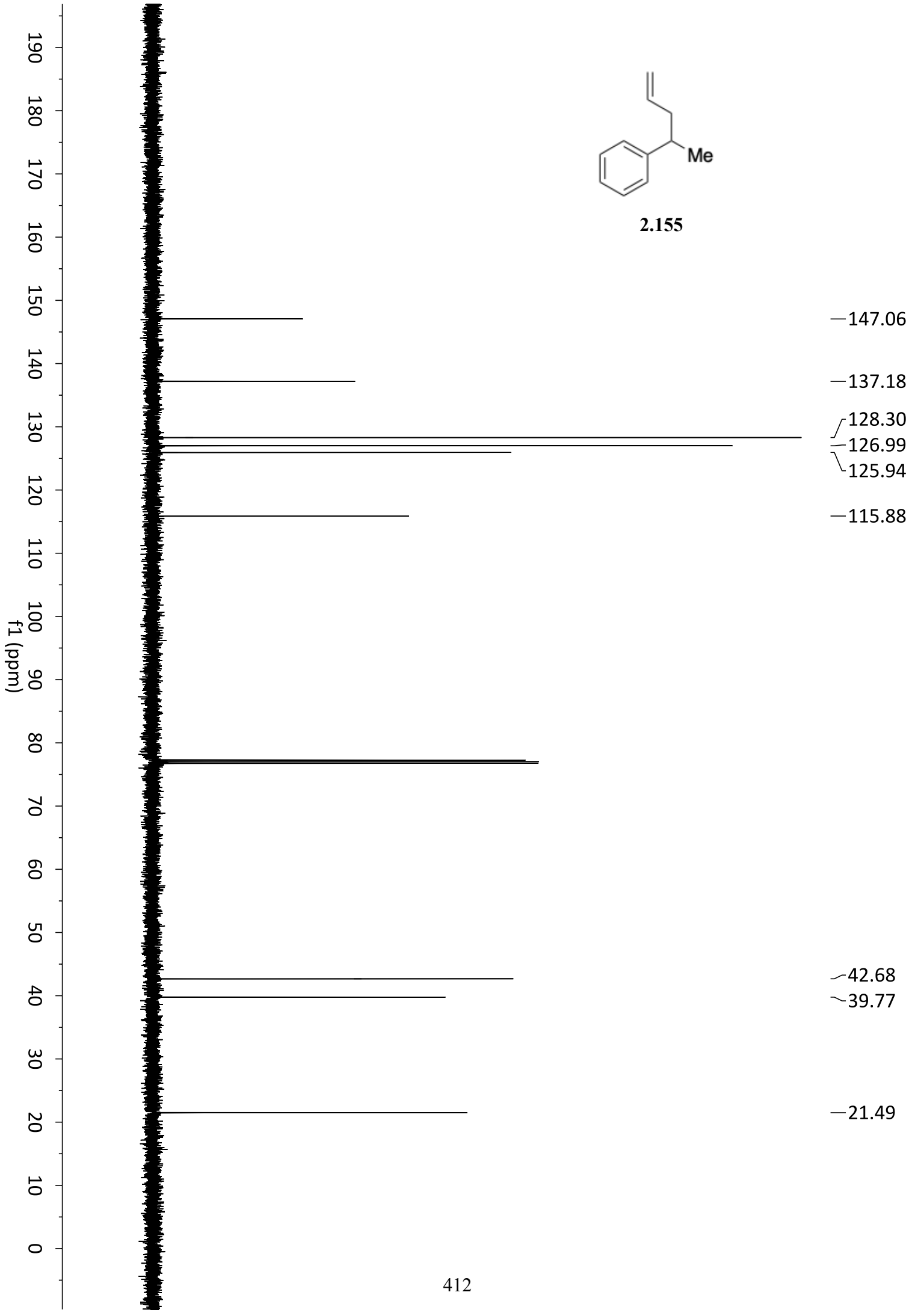
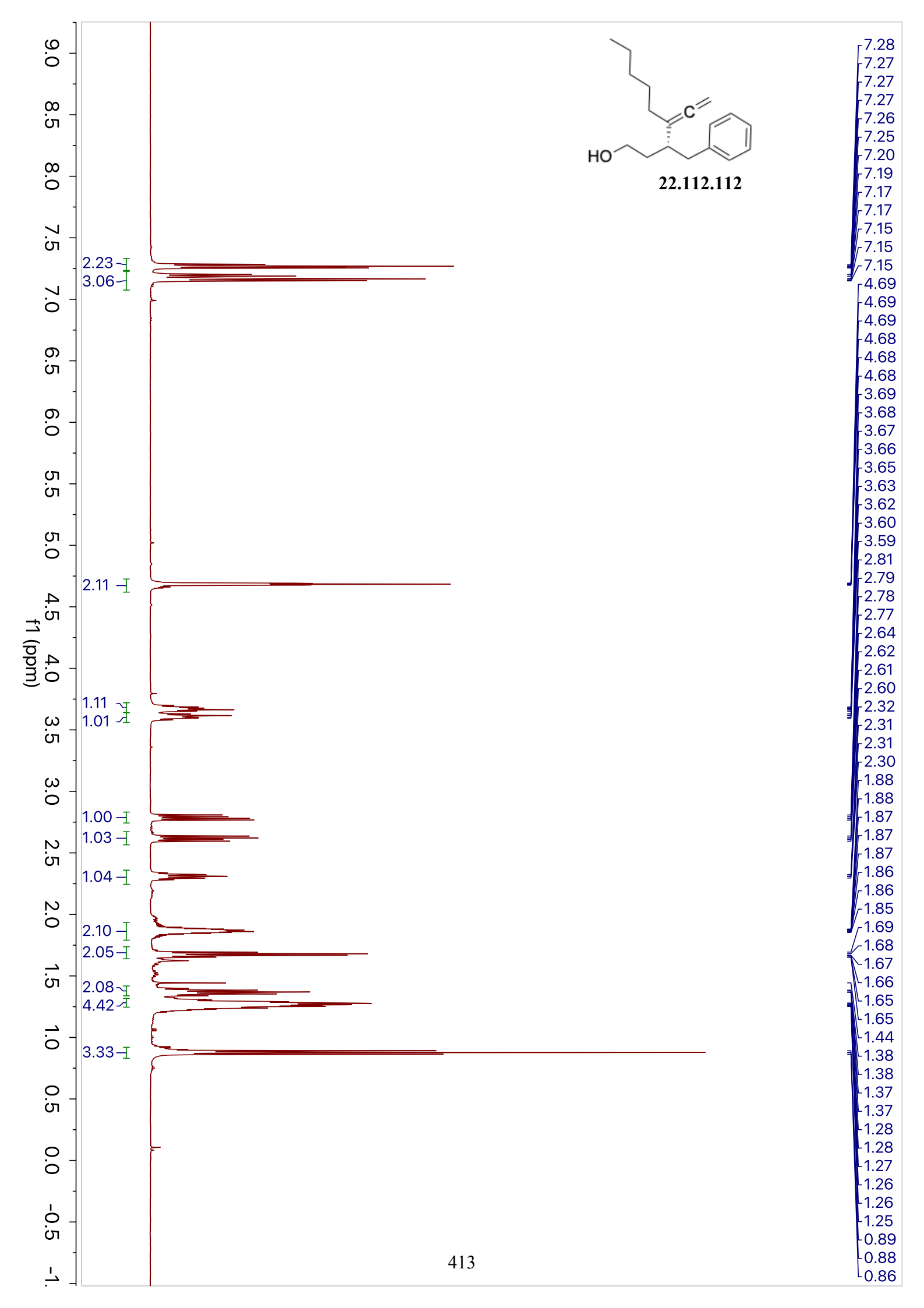
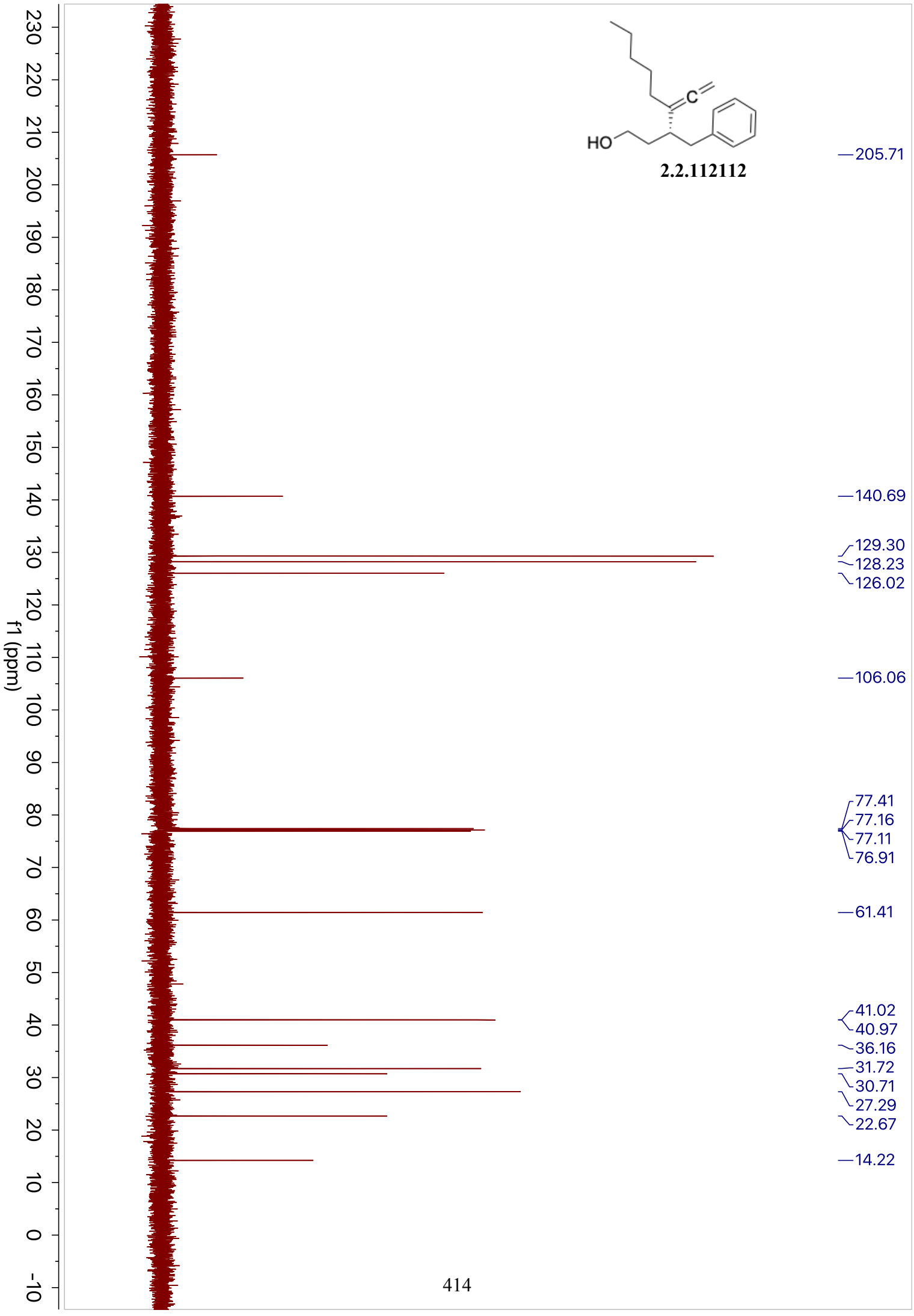
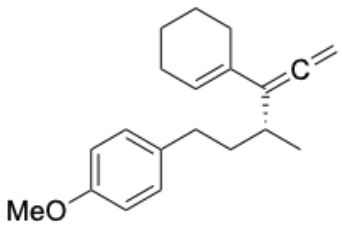
2.32
2.32
2.31
2.31
2.29
1.28
1.27

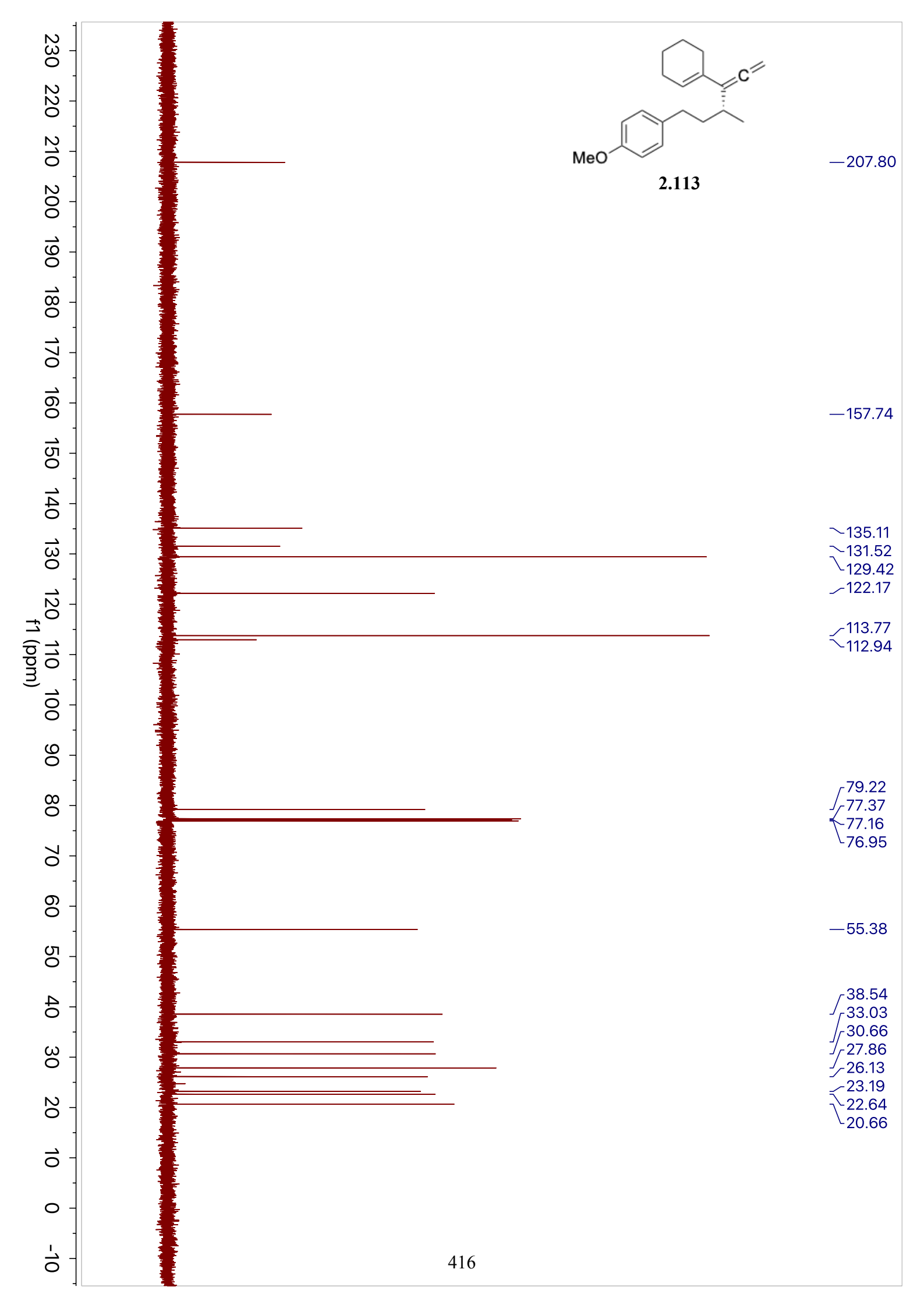

Me
2.155
147.06
137.18
128.30
126.99
125.94
115.88
42.68
39.77
21.49
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

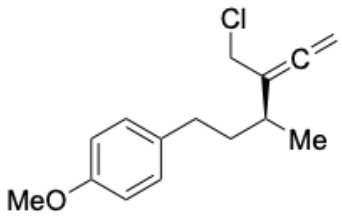

22.112.112
HO
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.23
3.06
2.11
1.11
1.01
1.00
1.03
1.04
2.10
2.05
2.08
4.42
3.33
7.28
7.27
7.27
7.27
7.26
7.25
7.20
7.19
7.17
7.17
7.15
7.15
7.15
4.69
4.69
4.69
4.68
4.68
4.68
3.69
3.68
3.67
3.66
3.65
3.63
3.62
3.60
3.59
2.81
2.79
2.78
2.77
2.64
2.62
2.61
2.60
2.32
2.31
2.31
2.30
1.88
1.88
1.87
1.87
1.87
1.86
1.86
1.85
1.69
1.68
1.67
1.66
1.65
1.65
1.44
1.38
1.38
1.37
1.37
1.28
1.28
1.27
1.26
1.26
1.25
0.89
0.88
0.86


HO
2.2.112112
205.71
140.69
129.30
128.23
126.02
106.06
77.41
77.16
77.11
76.91
61.41
41.02
40.97
36.16
31.72
30.71
27.29
22.67
14.22
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



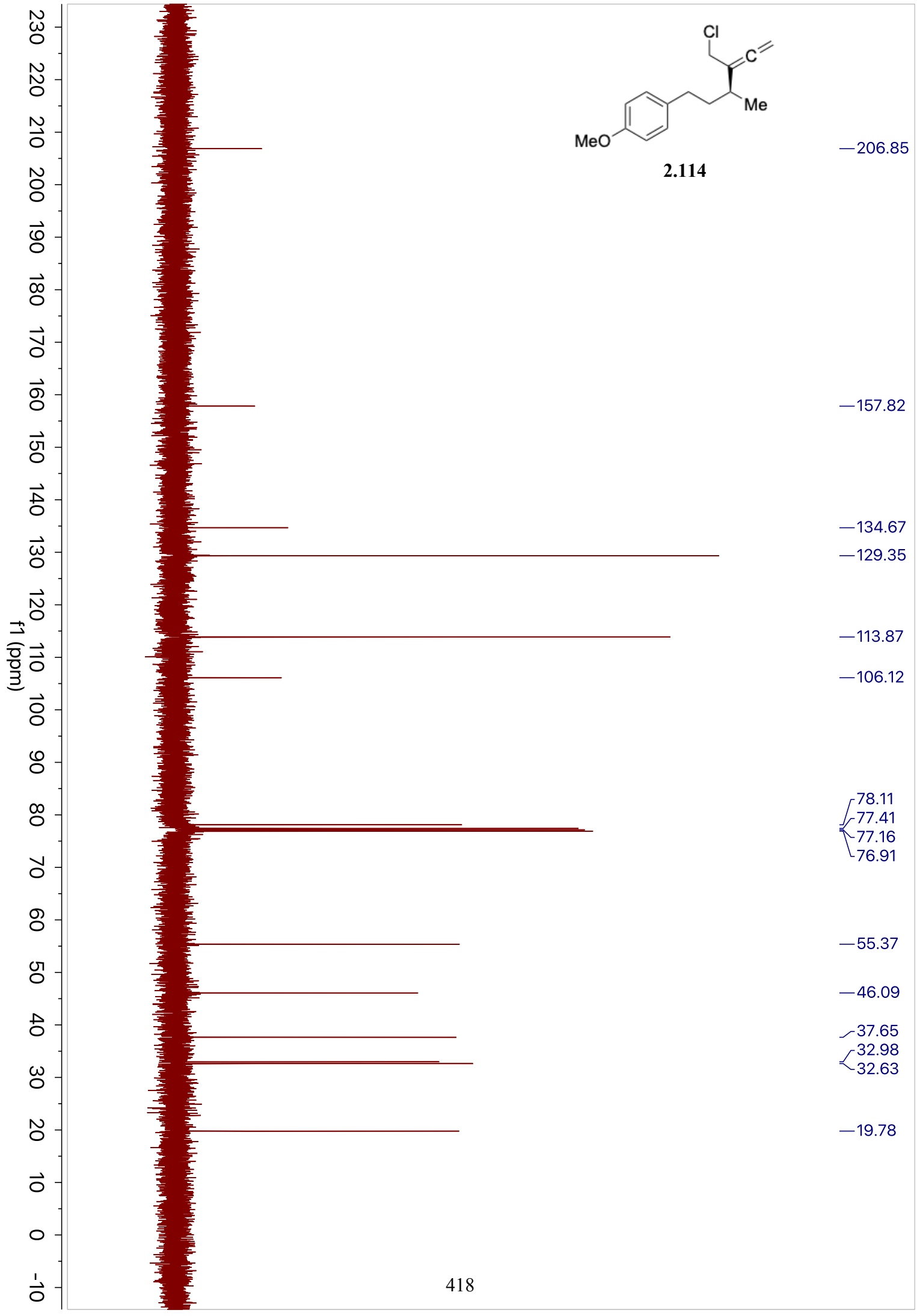
2.113

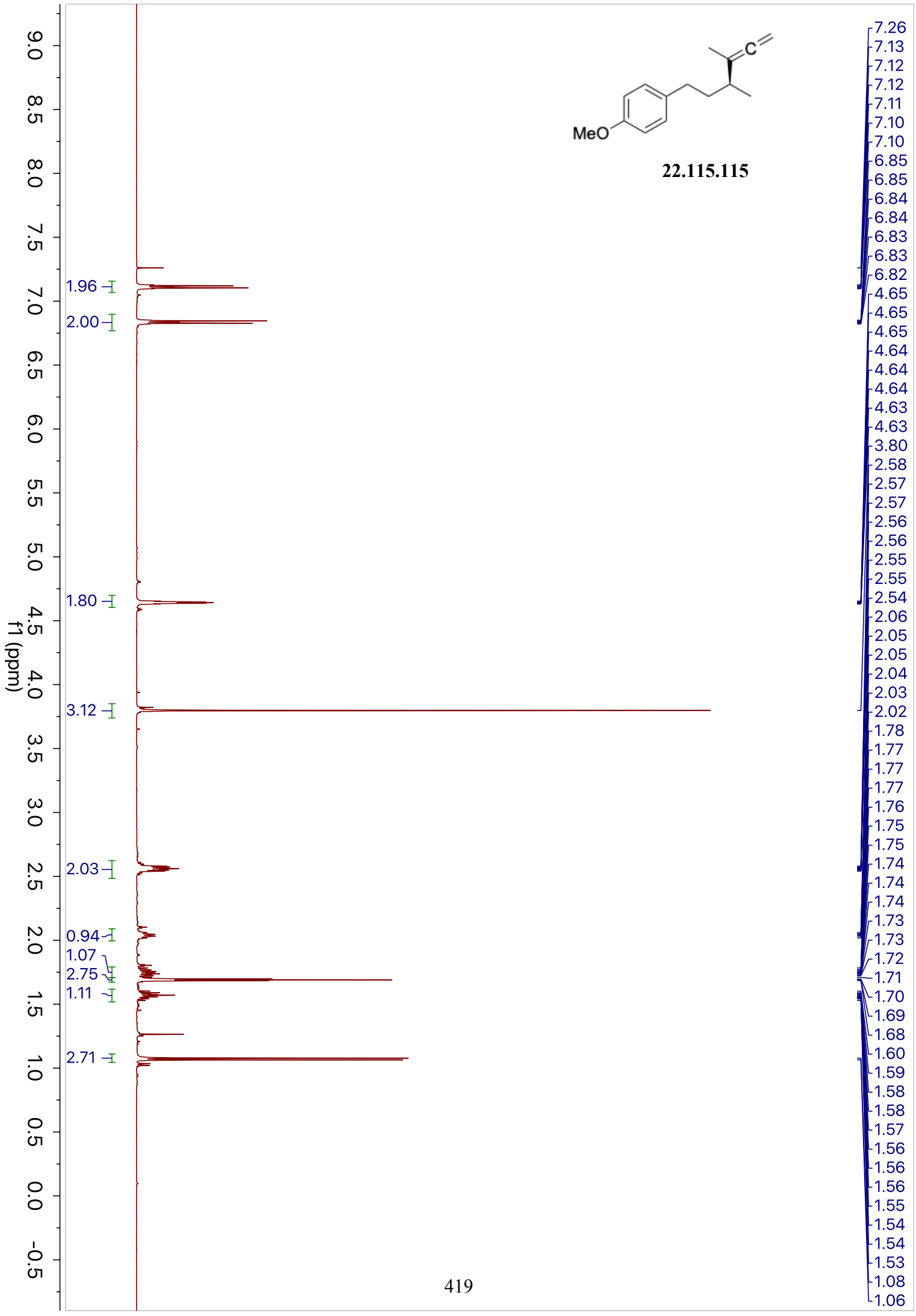

MeO
2.113
207.80
157.74
135.11
131.52
129.42
122.17
113.77
112.94
79.22
77.37
77.16
76.95
55.38
38.54
33.03
30.66
27.86
26.13
23.19
22.64
20.66
f1 (ppm)

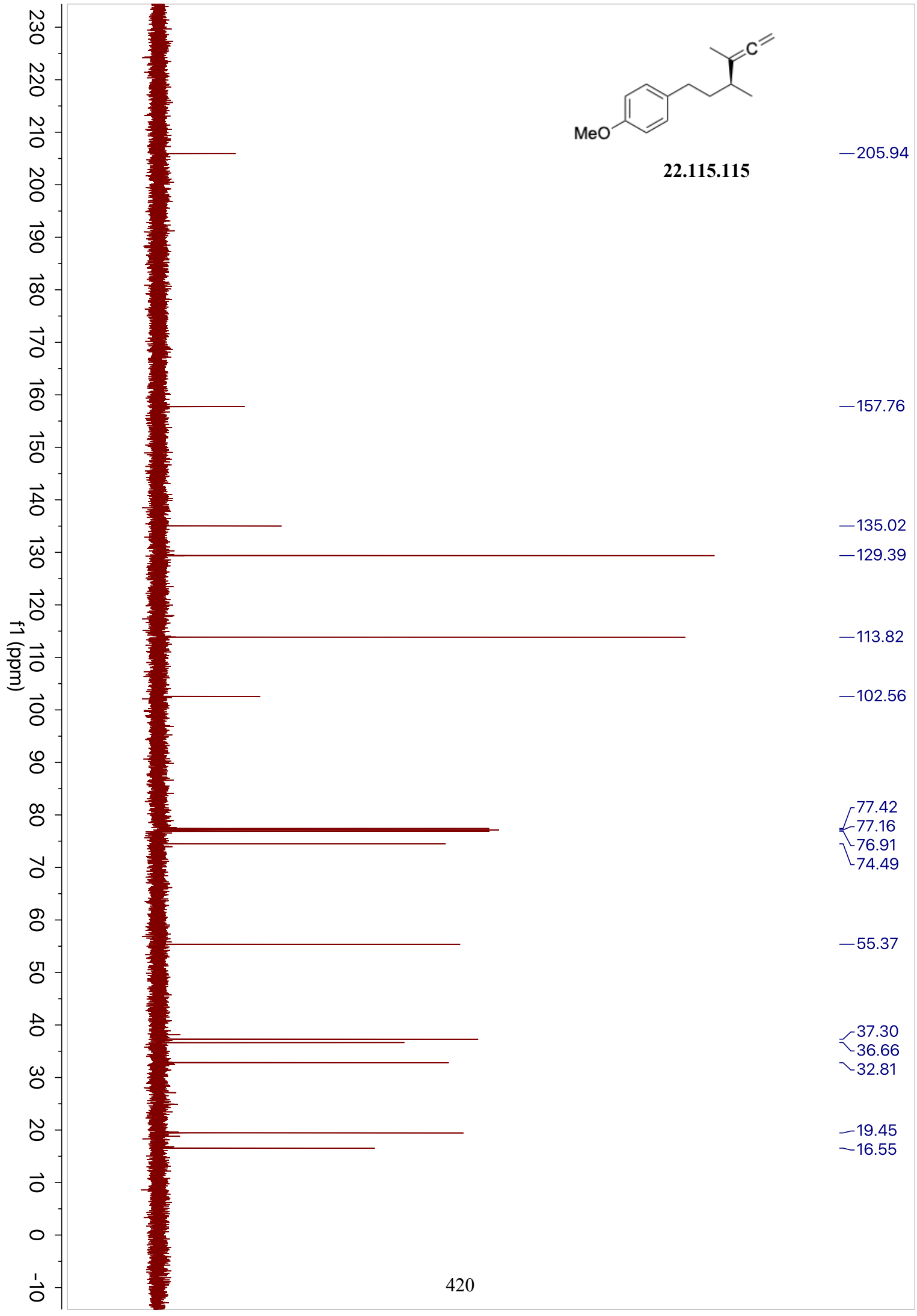

Cl
C
Me
MeO

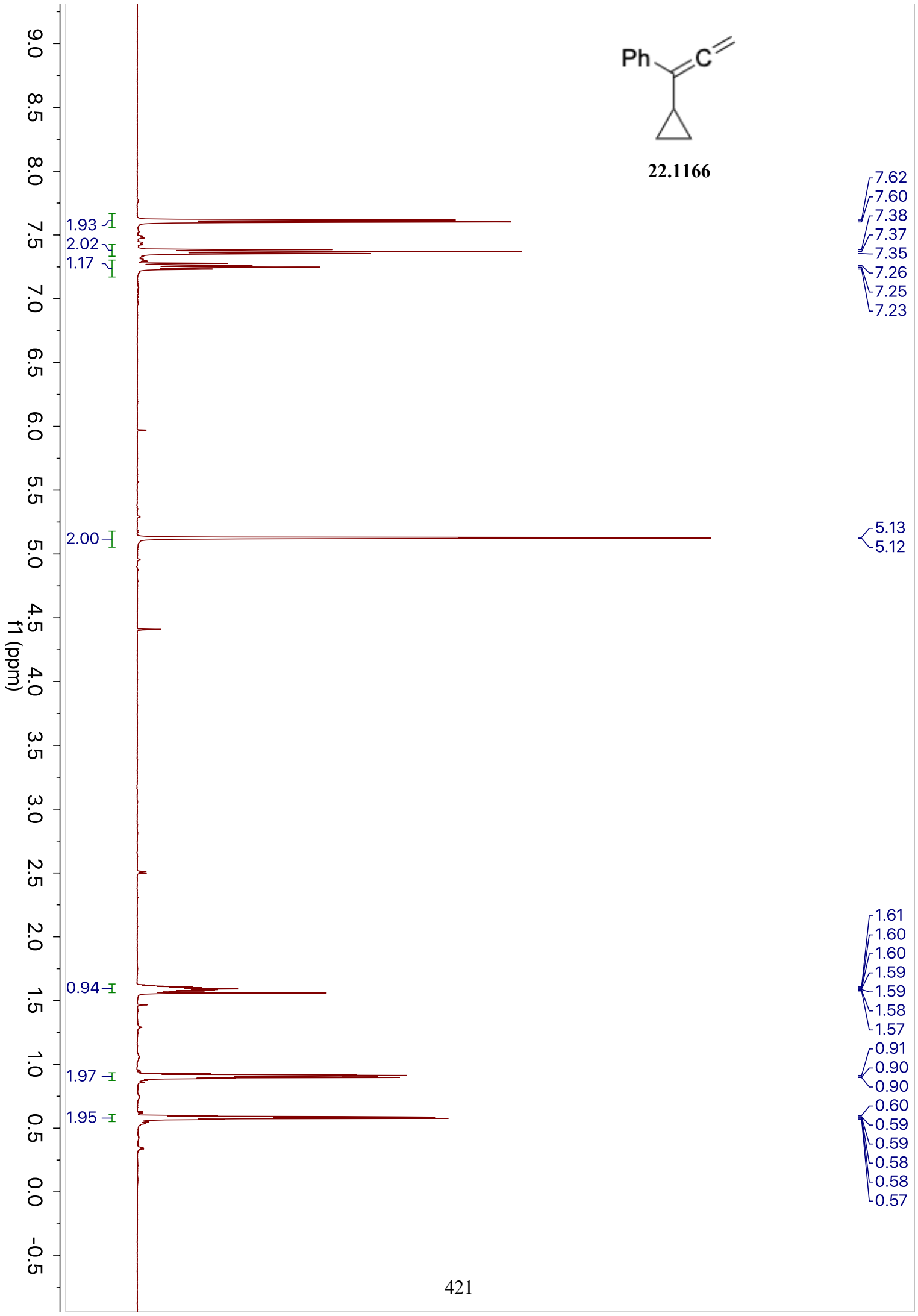
22.114

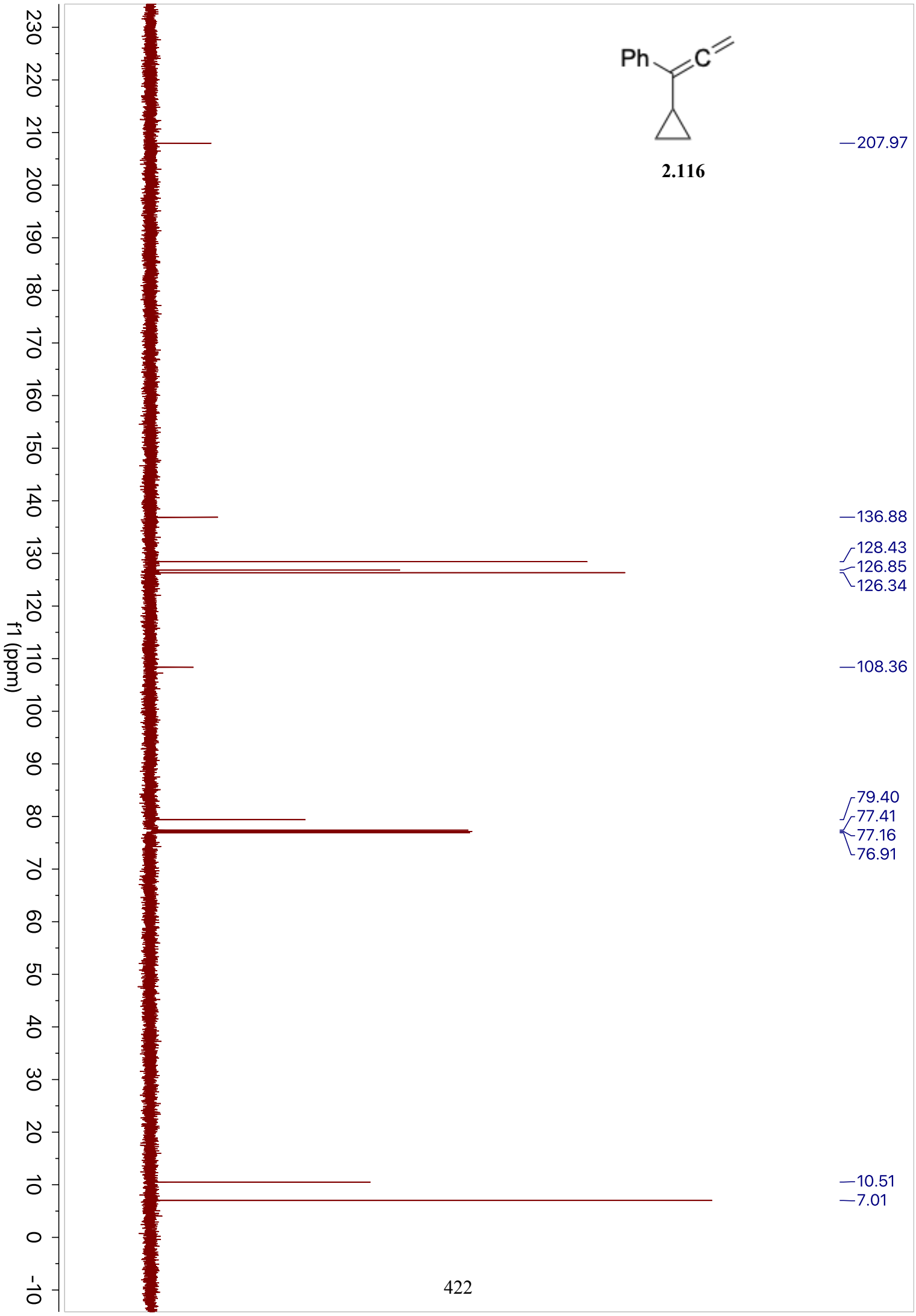
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.19
2.09
1.88
1.90
3.18
2.16
1.16
1.09
1.34
3.00
7.12
7.11
6.85
6.83
4.91
4.15
3.80
2.61
2.59
2.57
2.31
2.30
1.82
1.82
1.81
1.81
1.79
1.63
1.61
1.61
1.61
1.60
1.14
1.13


Cl
C
Me
MeO
2.114
206.85
157.82
134.67
129.35
113.87
106.12
78.11
77.41
77.16
76.91
55.37
46.09
37.65
32.98
32.63
19.78
f1 (ppm)

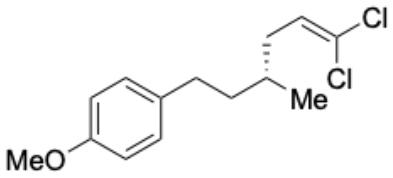

MeO
22.115.115
1.96
2.00
1.80
3.12
2.03
0.94
1.07
2.75
1.11
2.71
f1 (ppm)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
7.26 7.13 7.12 7.12 7.11 7.10 7.10 6.85 6.85 6.84 6.84 6.83 6.83 6.82 4.65 4.65 4.65 4.64 4.64 4.64 4.63 4.63 3.80 2.58 2.57 2.57 2.56 2.56 2.55 2.55 2.54 2.06 2.05 2.05 2.04 2.03 2.02 1.78 1.77 1.77 1.77 1.76 1.75 1.75 1.74 1.74 1.74 1.73 1.73 1.72 1.71 1.70 1.69 1.68 1.60 1.59 1.58 1.58 1.57 1.56 1.56 1.56 1.55 1.54 1.54 1.53 1.08 1.06


MeO
22.115.115
205.94
157.76
135.02
129.39
113.82
102.56
77.42
77.16
76.91
74.49
55.37
37.30
36.66
32.81
19.45
16.55
f1 (ppm)


Ph
C
22.1166
7.62
7.60
7.38
7.37
7.35
7.26
7.25
7.23
5.13
5.12
1.61
1.60
1.60
1.59
1.59
1.58
1.57
0.91
0.90
0.90
0.60
0.59
0.59
0.58
0.58
0.57
1.93
2.02
1.17
2.00
0.94
1.97
1.95
f1 (ppm)
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

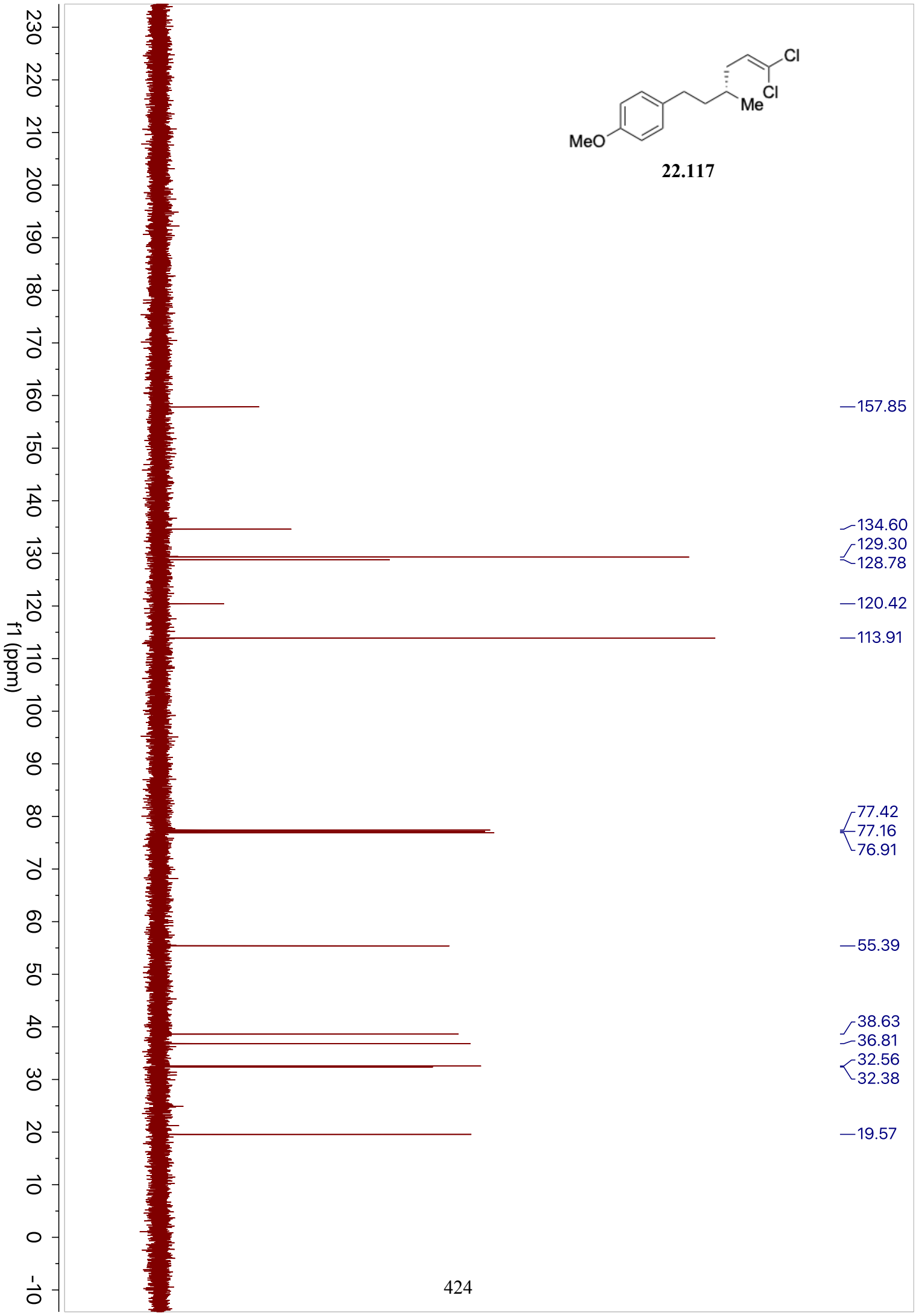

Ph
C
207.97
136.88
128.43
126.85
126.34
108.36
79.40
77.41
77.16
76.91
10.51
7.01
f1 (ppm)

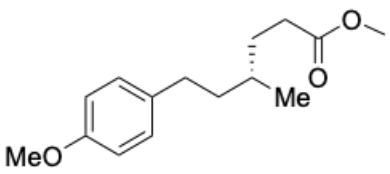
2.116


Cl
Cl
Me
MeO

22.117

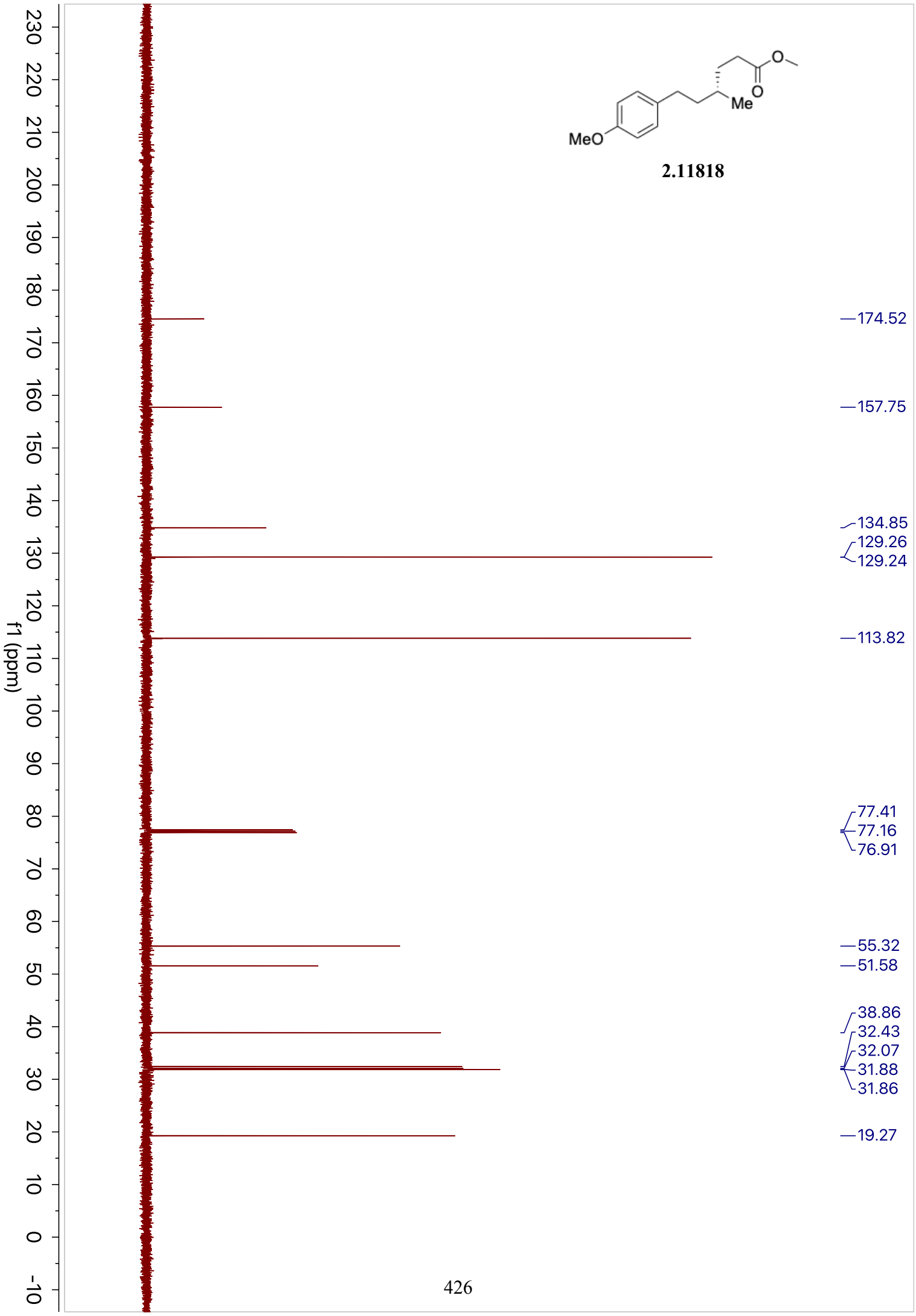
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.98
1.96
0.93
3.00
0.94
1.00
0.96
0.97
2.13
1.04
2.91
7.11
7.10
6.85
6.83
5.88
5.87
5.85
3.80
2.65
2.64
2.63
2.62
2.62
2.61
2.60
2.59
2.57
2.56
2.55
2.54
2.54
2.53
2.52
2.51
2.25
2.24
2.24
2.23
2.22
2.21
2.21
2.20
2.12
2.11
2.09
2.08
2.06
1.64
1.64
1.63
1.62
1.61
1.61
1.60
1.49
1.48
1.48
1.47
1.47
1.46
1.45
1.26
0.98
0.97

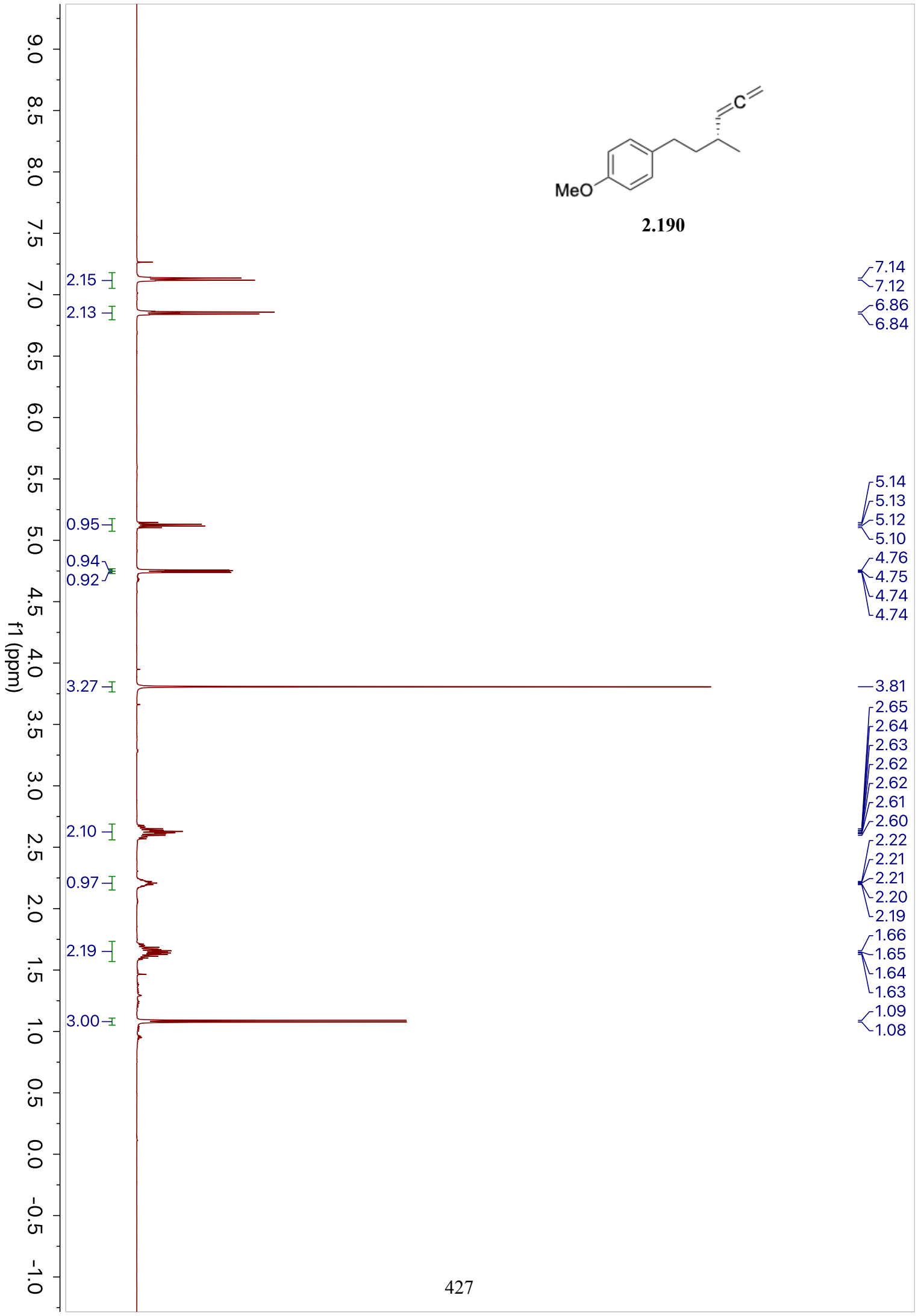

Cl
Cl
Me
MeO
22.117
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
157.85
134.60
129.30
128.78
120.42
113.91
77.42
77.16
76.91
55.39
38.63
36.81
32.56
32.38
19.57

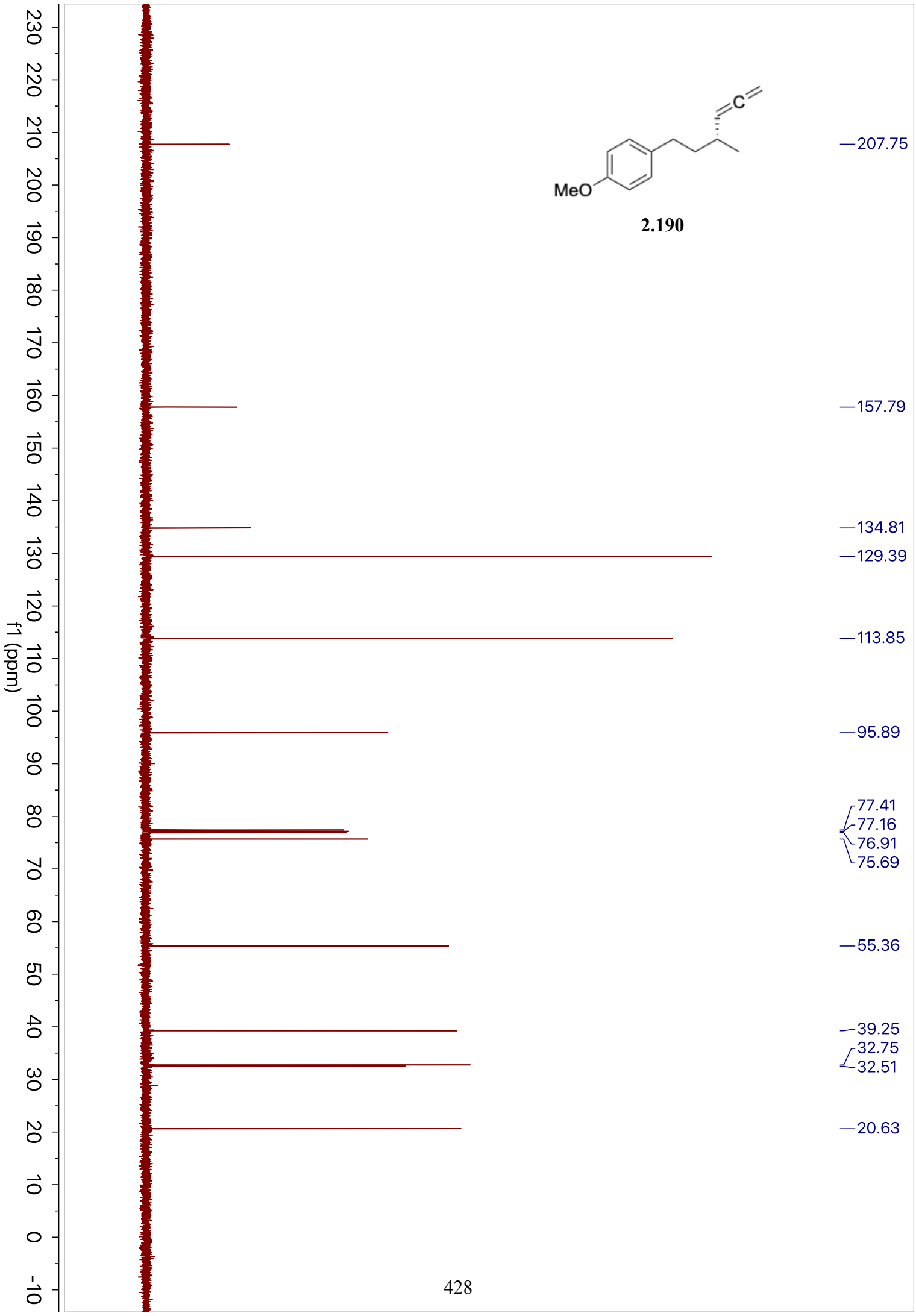

O
O
Me
MeO

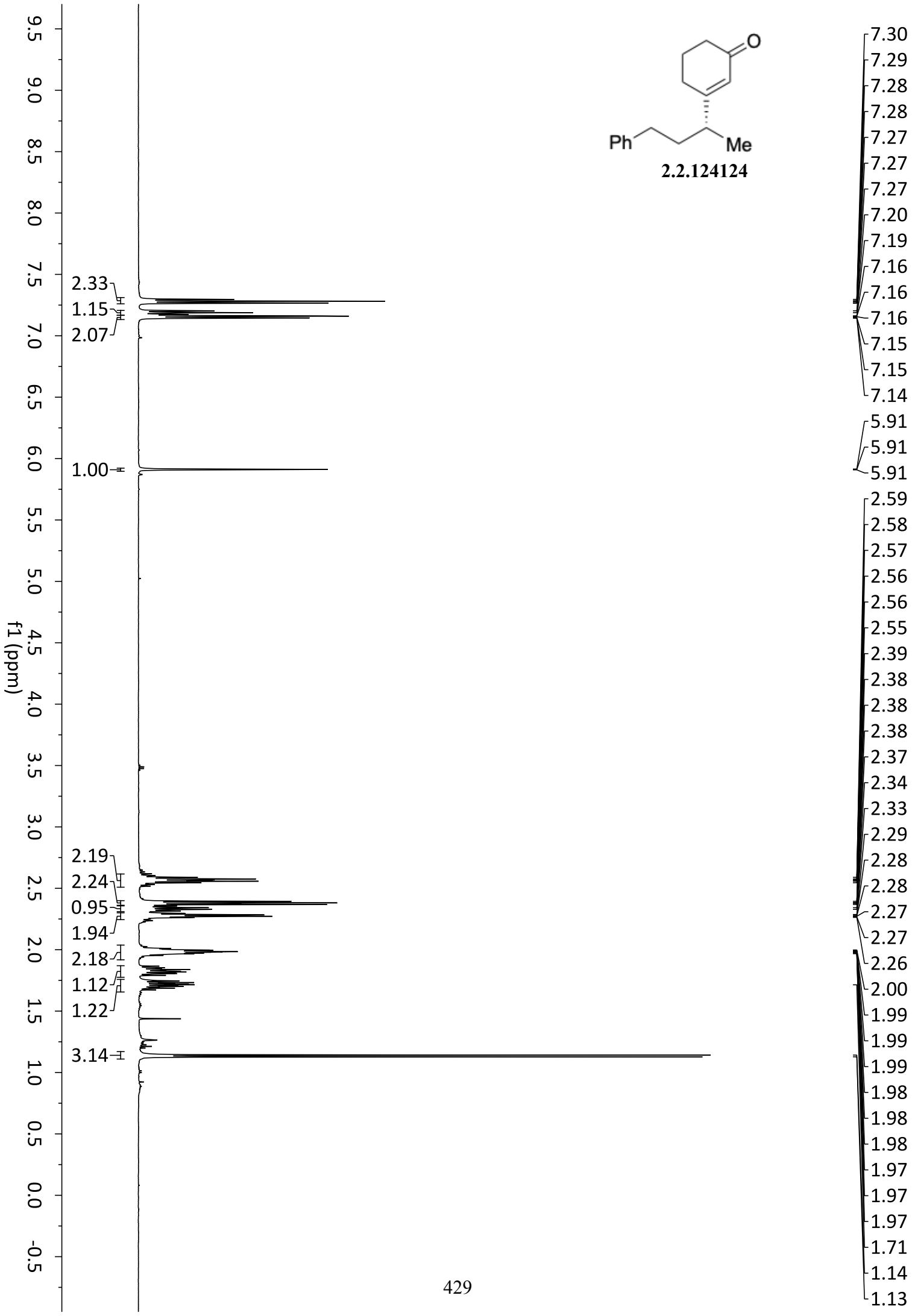
22.118

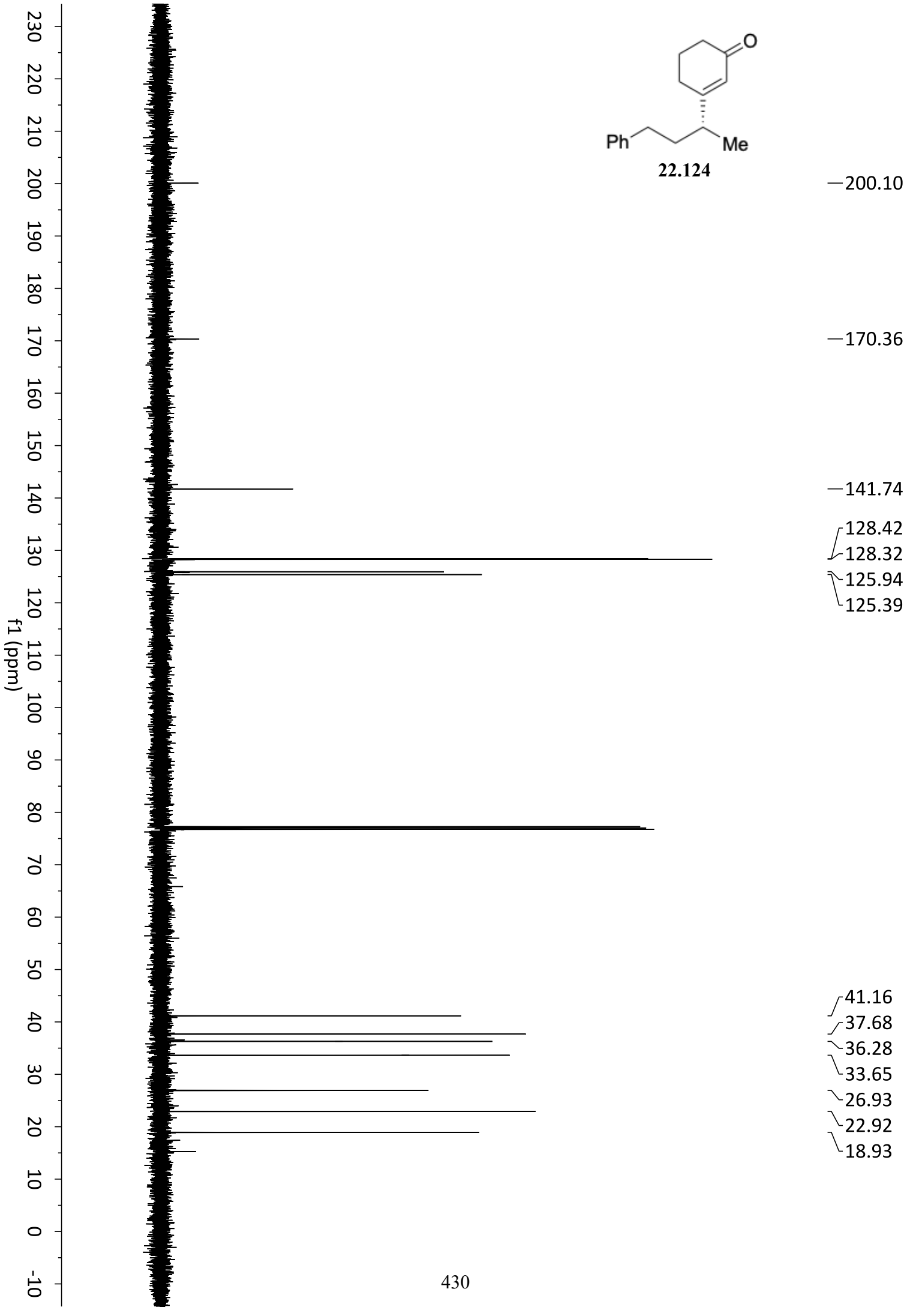
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
1.99
1.99
3.01
3.00
0.96
1.01
2.01
1.05
1.09
3.12
3.05
7.11
7.09
6.84
6.82
3.79
3.67
2.64
2.63
2.62
2.61
2.61
2.60
2.59
2.58
2.56
2.55
2.54
2.53
2.53
2.52
2.51
2.50
2.36
2.35
2.34
2.33
2.31
2.31
2.30
1.75
1.75
1.73
1.73
1.73
1.62
1.62
1.60
1.60
1.50
1.49
1.48
1.48
1.47
1.47
1.47
1.46
1.45
0.95

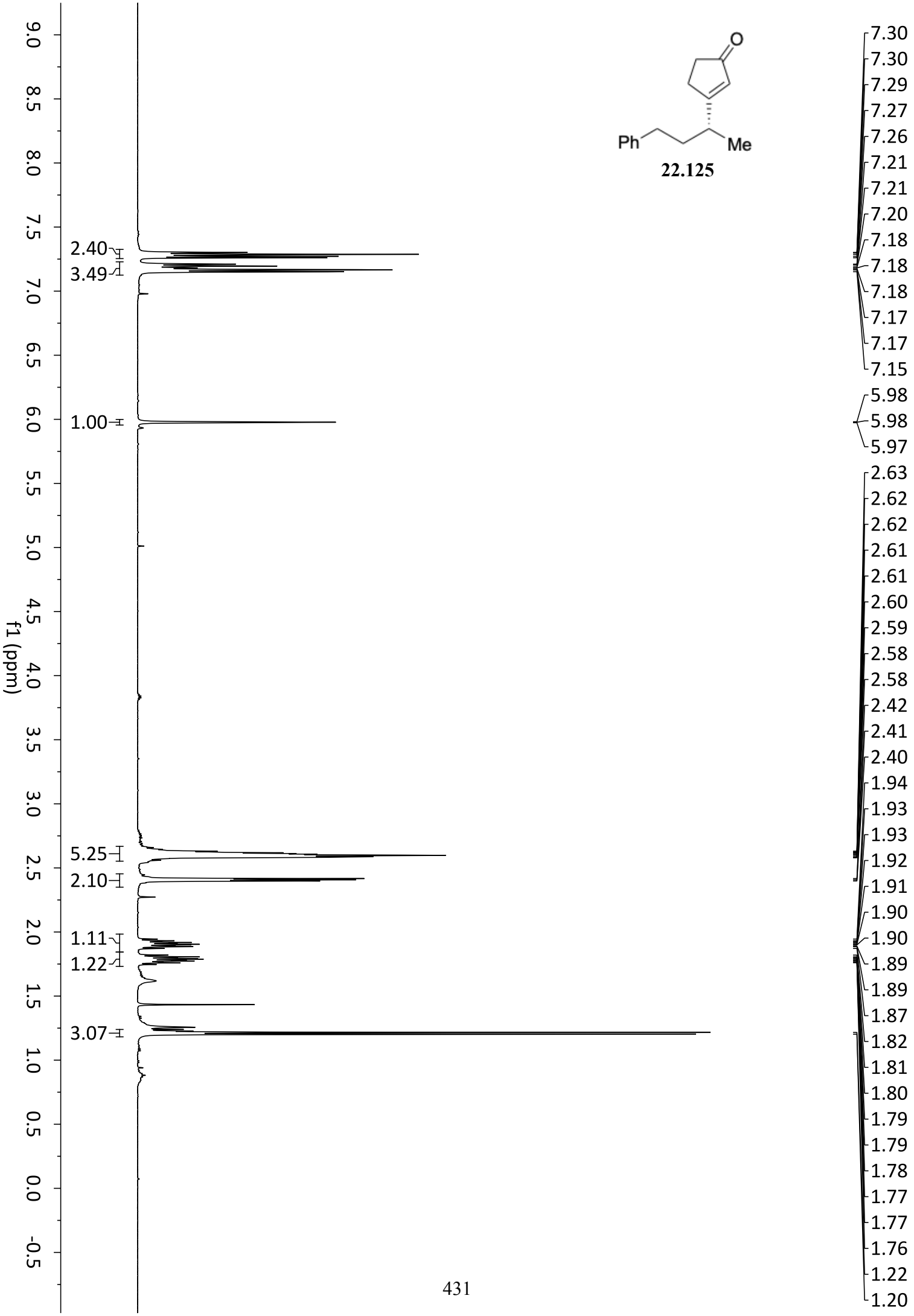

MeO
Me
O
O
2.11818
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
174.52
157.75
134.85
129.26
129.24
113.82
77.41
77.16
76.91
55.32
51.58
38.86
32.43
32.07
31.88
31.86
19.27

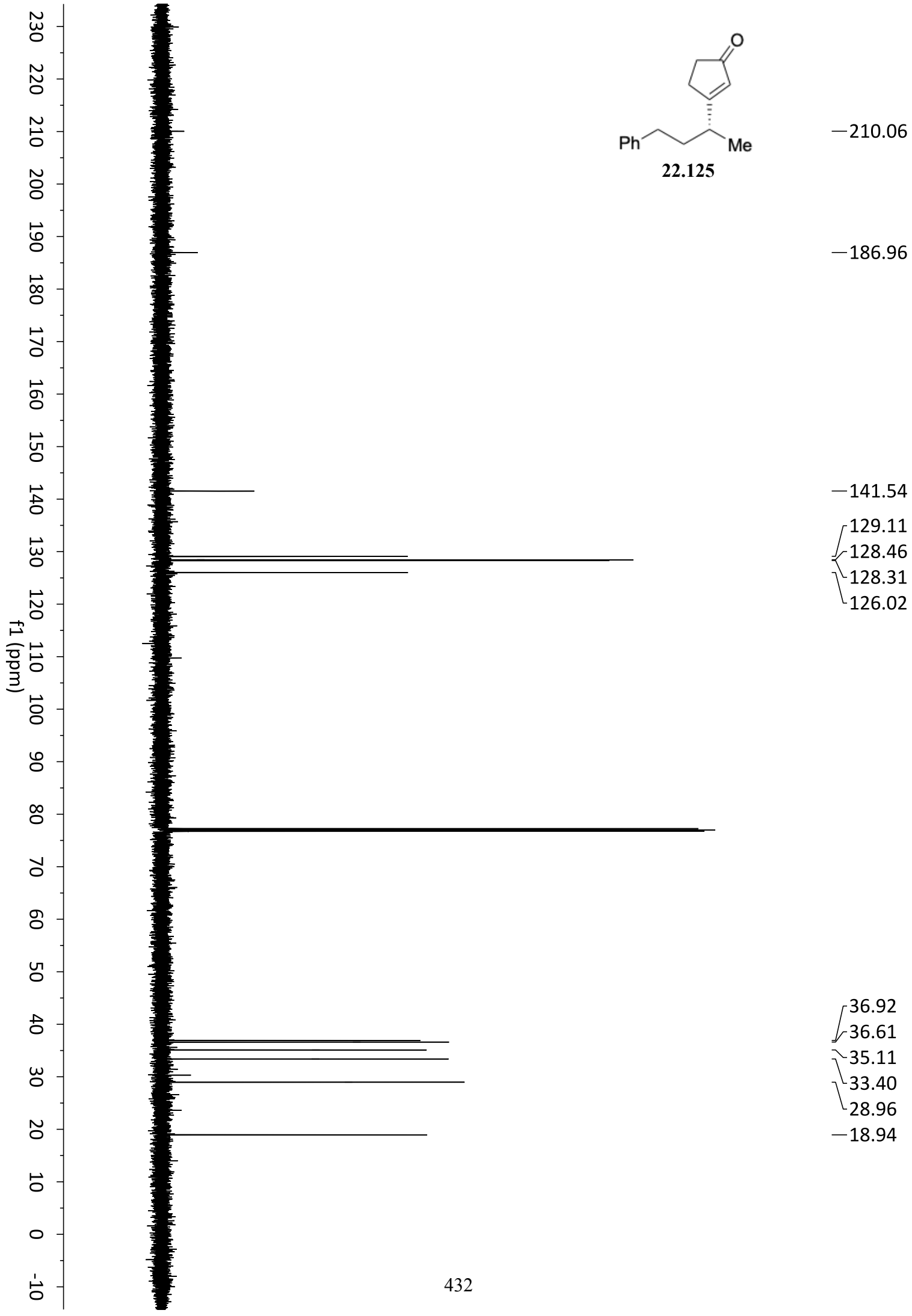

MeO
C
2.190
2.15
2.13
0.95
0.94
0.92
3.27
2.10
0.97
2.19
3.00
7.14
7.12
6.86
6.84
5.14
5.13
5.12
5.10
4.76
4.75
4.74
4.74
3.81
2.65
2.64
2.63
2.62
2.62
2.61
2.60
2.22
2.21
2.21
2.20
2.19
1.66
1.65
1.64
1.63
1.09
1.08
f1 (ppm)

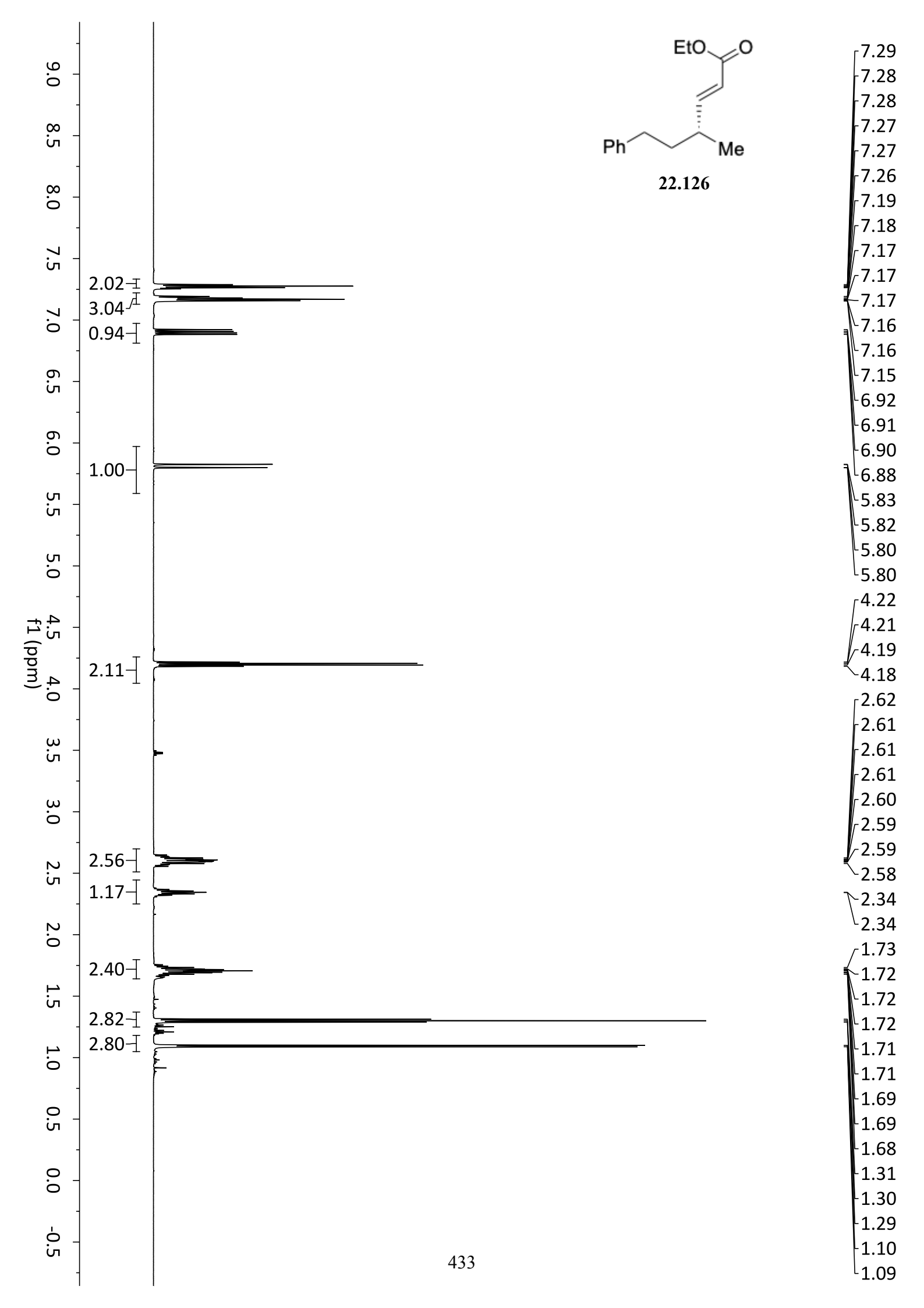

MeO
C
2.190
207.75
157.79
134.81
129.39
113.85
95.89
77.41
77.16
76.91
75.69
55.36
39.25
32.75
32.51
20.63
f1 (ppm)

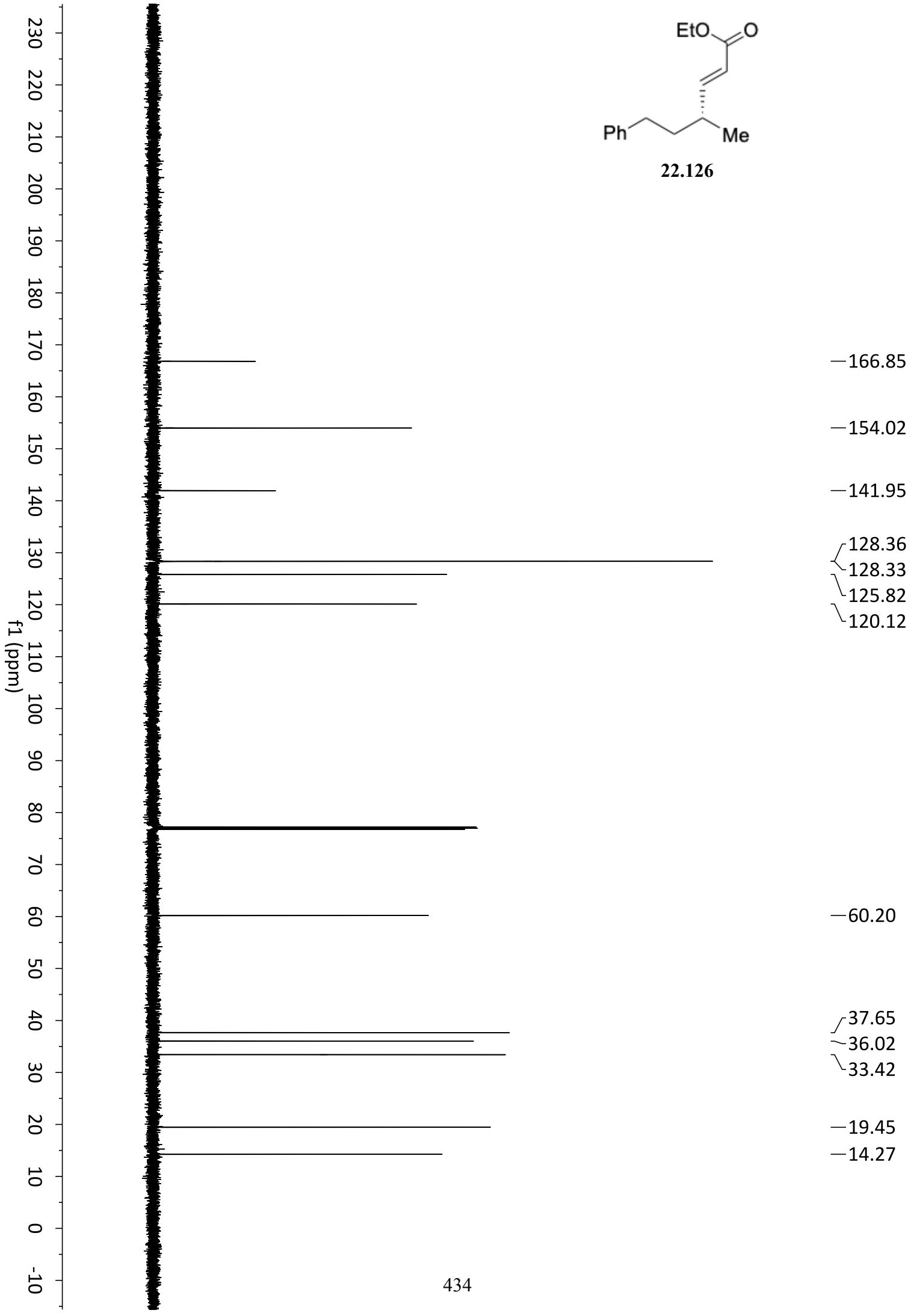

O
Ph
Me
2.2.124124
2.33
1.15
2.07
1.00
2.19
2.24
0.95
1.94
2.18
1.12
1.22
3.14
f1 (ppm)
7.30
7.29
7.28
7.28
7.27
7.27
7.27
7.20
7.19
7.16
7.16
7.16
7.15
7.15
7.14
5.91
5.91
5.91
2.59
2.58
2.57
2.56
2.56
2.55
2.39
2.38
2.38
2.38
2.37
2.34
2.33
2.29
2.28
2.28
2.27
2.27
2.26
2.00
1.99
1.99
1.99
1.98
1.98
1.98
1.97
1.97
1.97
1.71
1.14
1.13

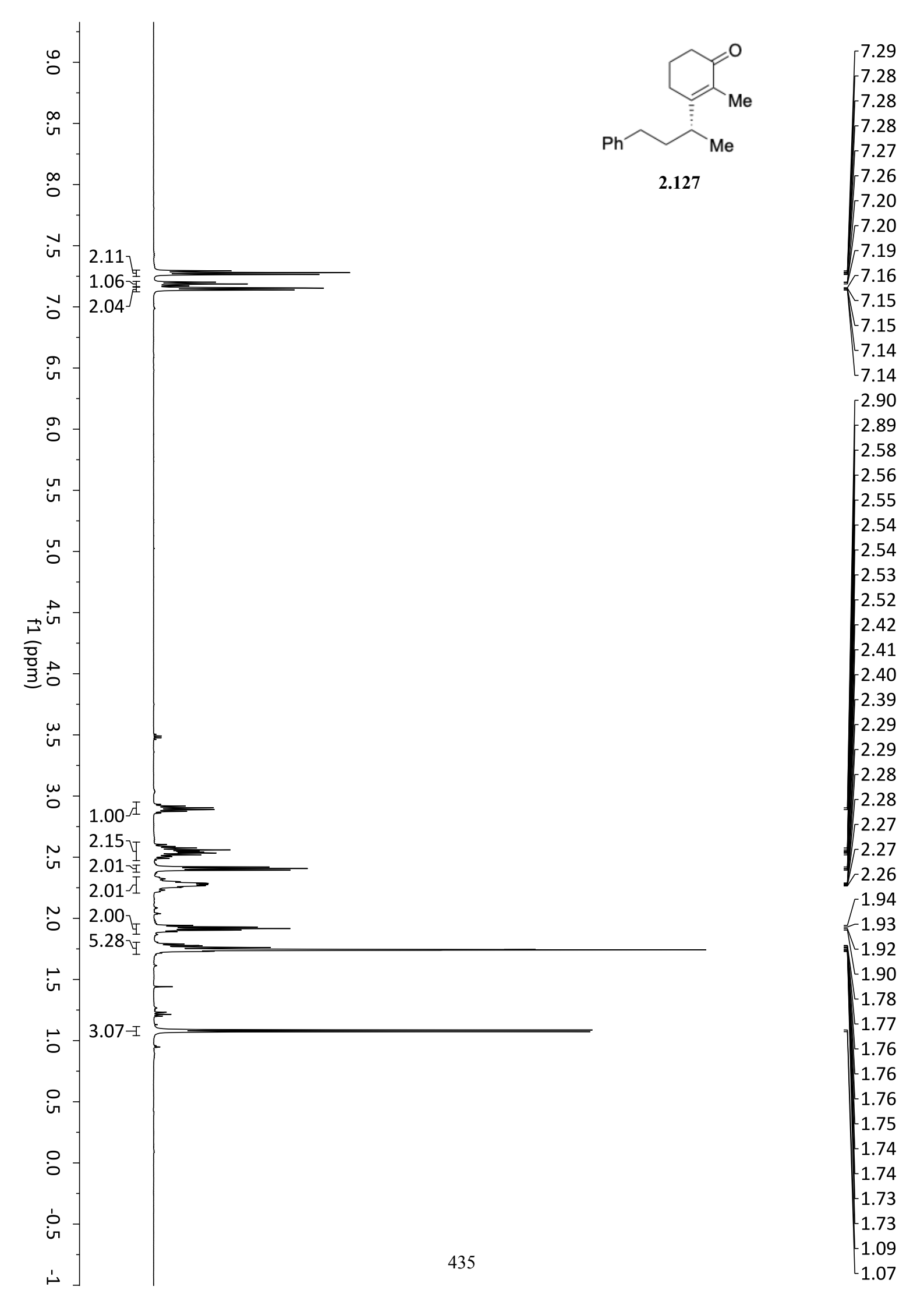

O
Ph
Me
22.124
200.10
170.36
141.74
128.42
128.32
125.94
125.39
41.16
37.68
36.28
33.65
26.93
22.92
18.93
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

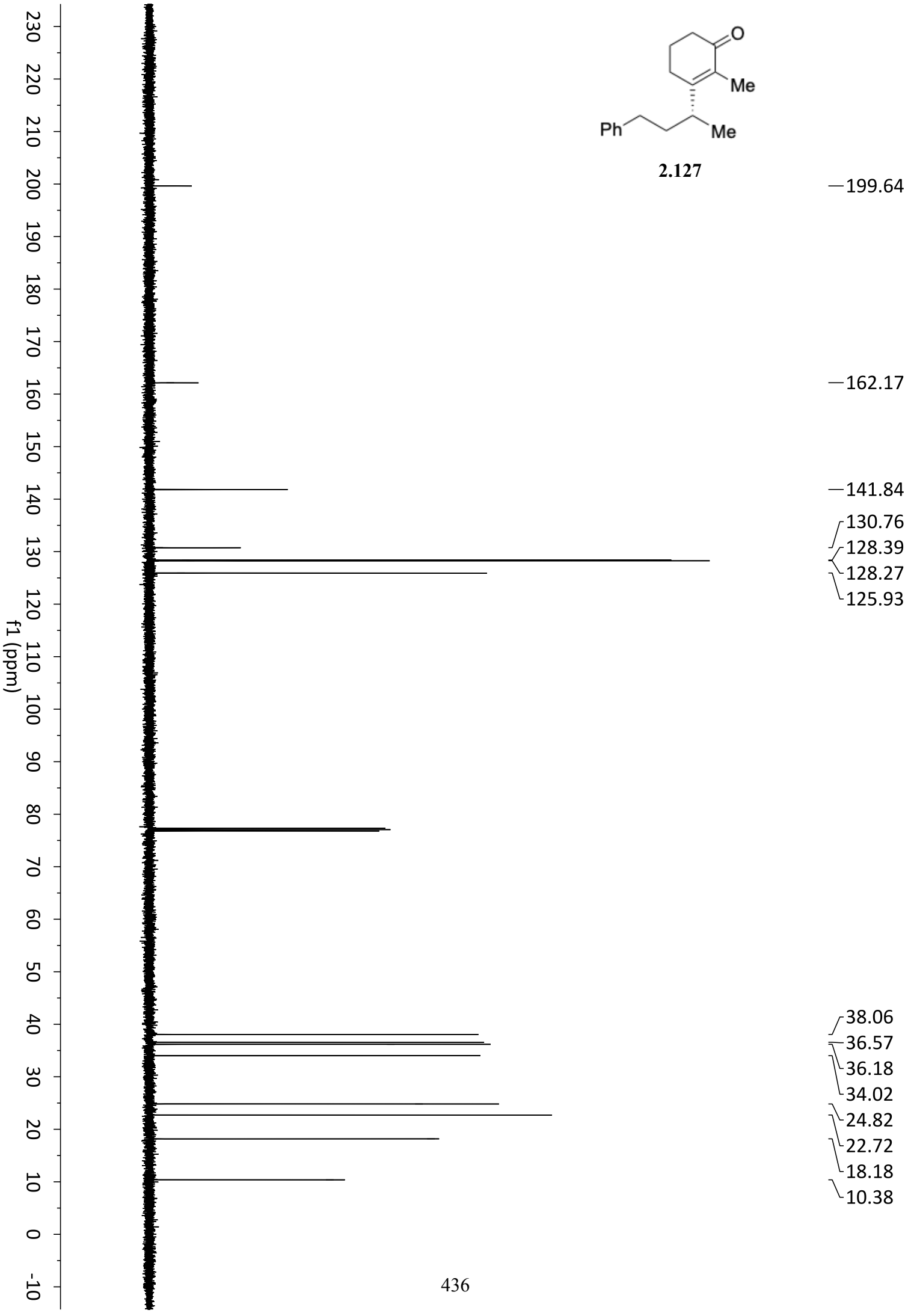

O
Ph
Me
22.125
2.40
3.49
1.00
5.25
2.10
1.11
1.22
3.07
f1 (ppm)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
7.30 7.30 7.29 7.27 7.26 7.21 7.21 7.20 7.18 7.18 7.18 7.17 7.17 7.15
5.98 5.98 5.97
2.63 2.62 2.62 2.61 2.61 2.60 2.59 2.58 2.58 2.42 2.41 2.40 1.94 1.93 1.93 1.92 1.91 1.90 1.90 1.89 1.89 1.87 1.82 1.81 1.80 1.79 1.79 1.78 1.77 1.77 1.76 1.22 1.20

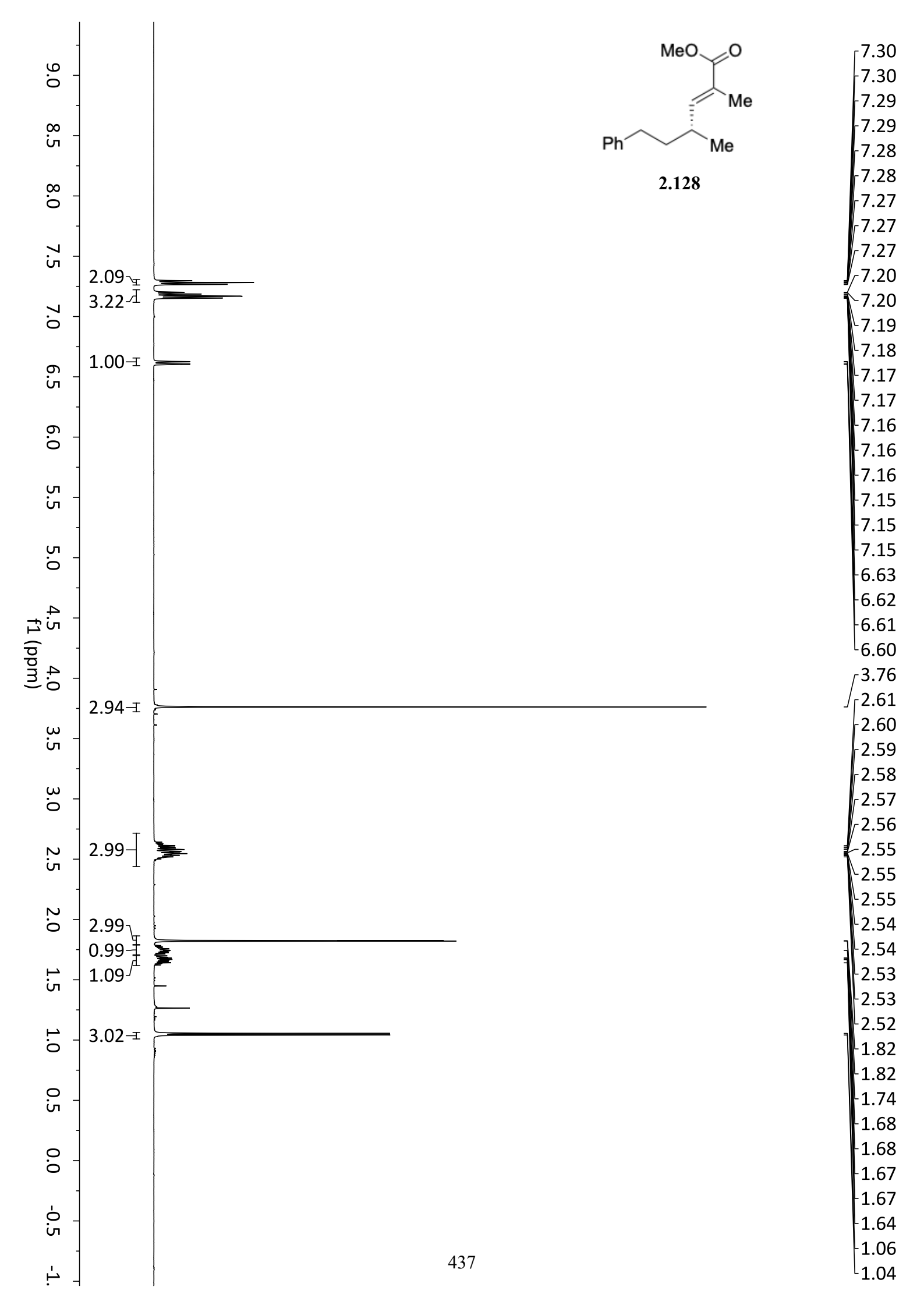

O
Ph
Me
22.125
210.06
186.96
141.54
129.11
128.46
128.31
126.02
36.92
36.61
35.11
33.40
28.96
18.94
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

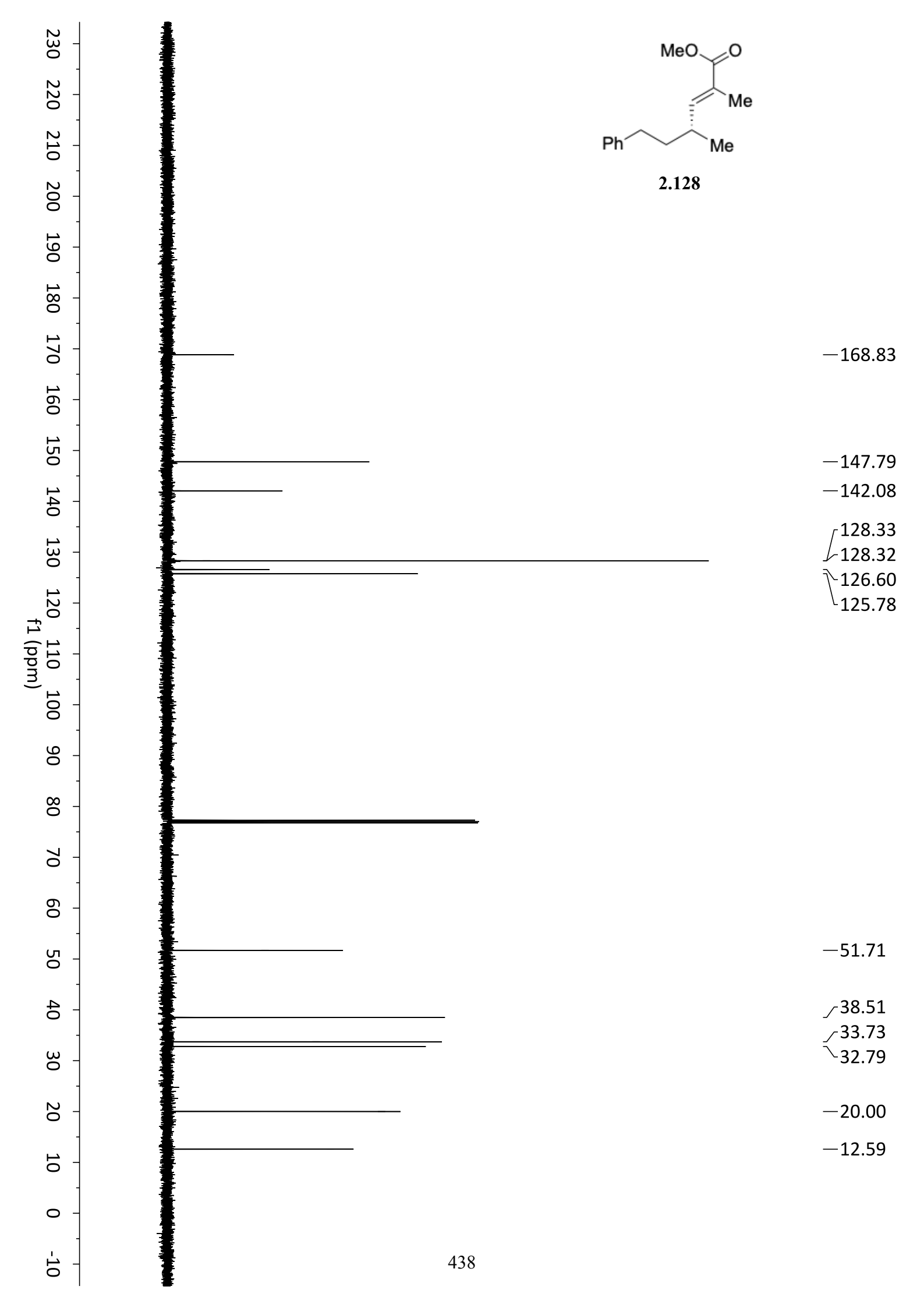

EtO
O
Ph
Me
22.126
f1 (ppm)
2.02
3.04
0.94
1.00
2.11
2.56
1.17
2.40
2.82
2.80
7.29
7.28
7.28
7.27
7.27
7.26
7.19
7.18
7.17
7.17
7.17
7.16
7.16
7.15
6.92
6.91
6.90
6.88
5.83
5.82
5.80
5.80
4.22
4.21
4.19
4.18
2.62
2.61
2.61
2.61
2.60
2.59
2.59
2.58
2.34
2.34
1.73
1.72
1.72
1.72
1.71
1.71
1.69
1.69
1.68
1.31
1.30
1.29
1.10
1.09

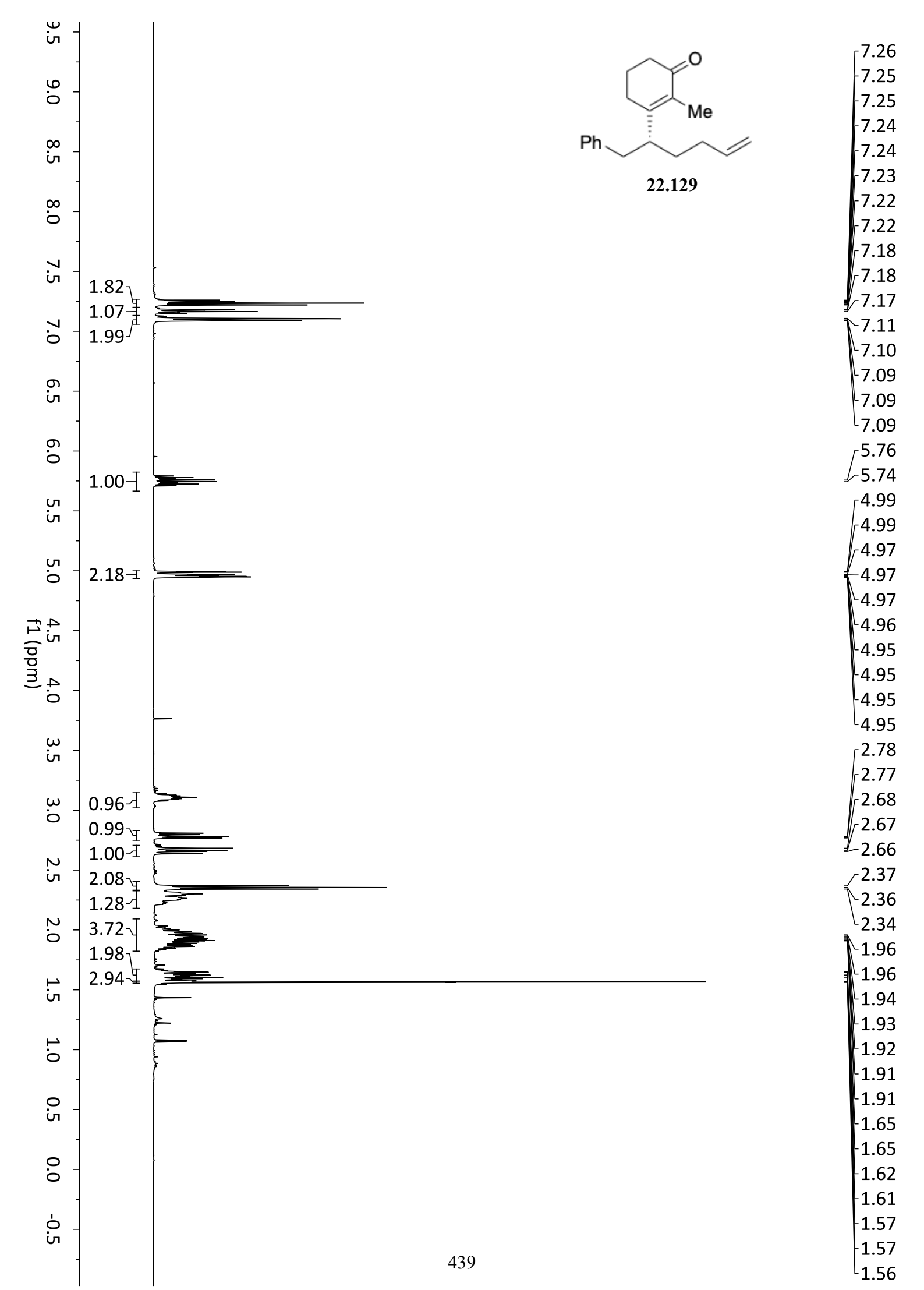

EtO
O
Ph
Me
22.126
166.85
154.02
141.95
128.36
128.33
125.82
120.12
60.20
37.65
36.02
33.42
19.45
14.27
f1 (ppm)

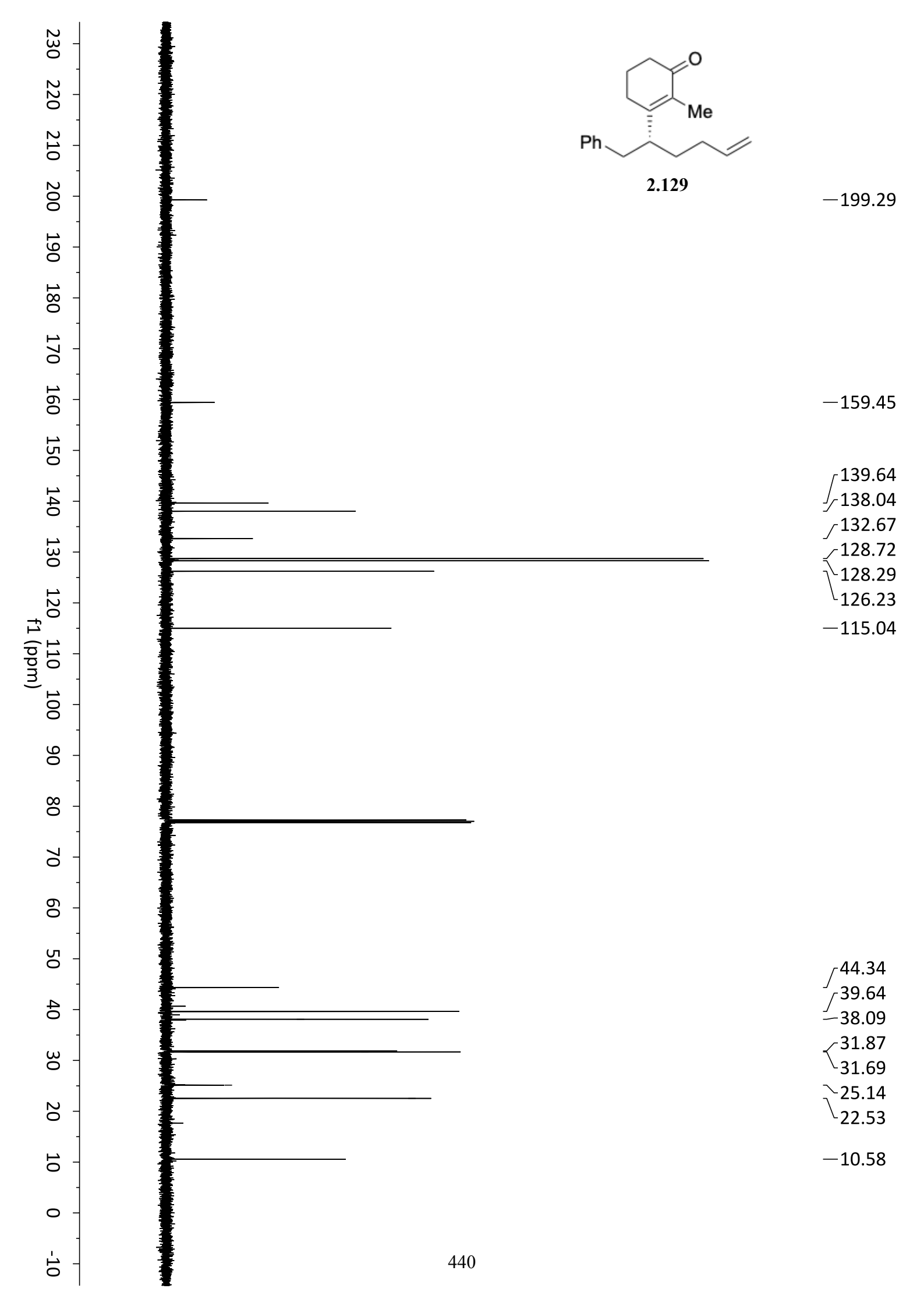

O
Me
Ph
Me
2.127
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
2.11
1.06
2.04
1.00
2.15
2.01
2.01
2.00
5.28
3.07
7.29
7.28
7.28
7.28
7.27
7.26
7.20
7.20
7.19
7.16
7.15
7.15
7.14
7.14
2.90
2.89
2.58
2.56
2.55
2.54
2.54
2.53
2.52
2.42
2.41
2.40
2.39
2.29
2.29
2.28
2.28
2.27
2.27
2.26
1.94
1.93
1.92
1.90
1.78
1.77
1.76
1.76
1.76
1.75
1.74
1.74
1.73
1.73
1.09
1.07

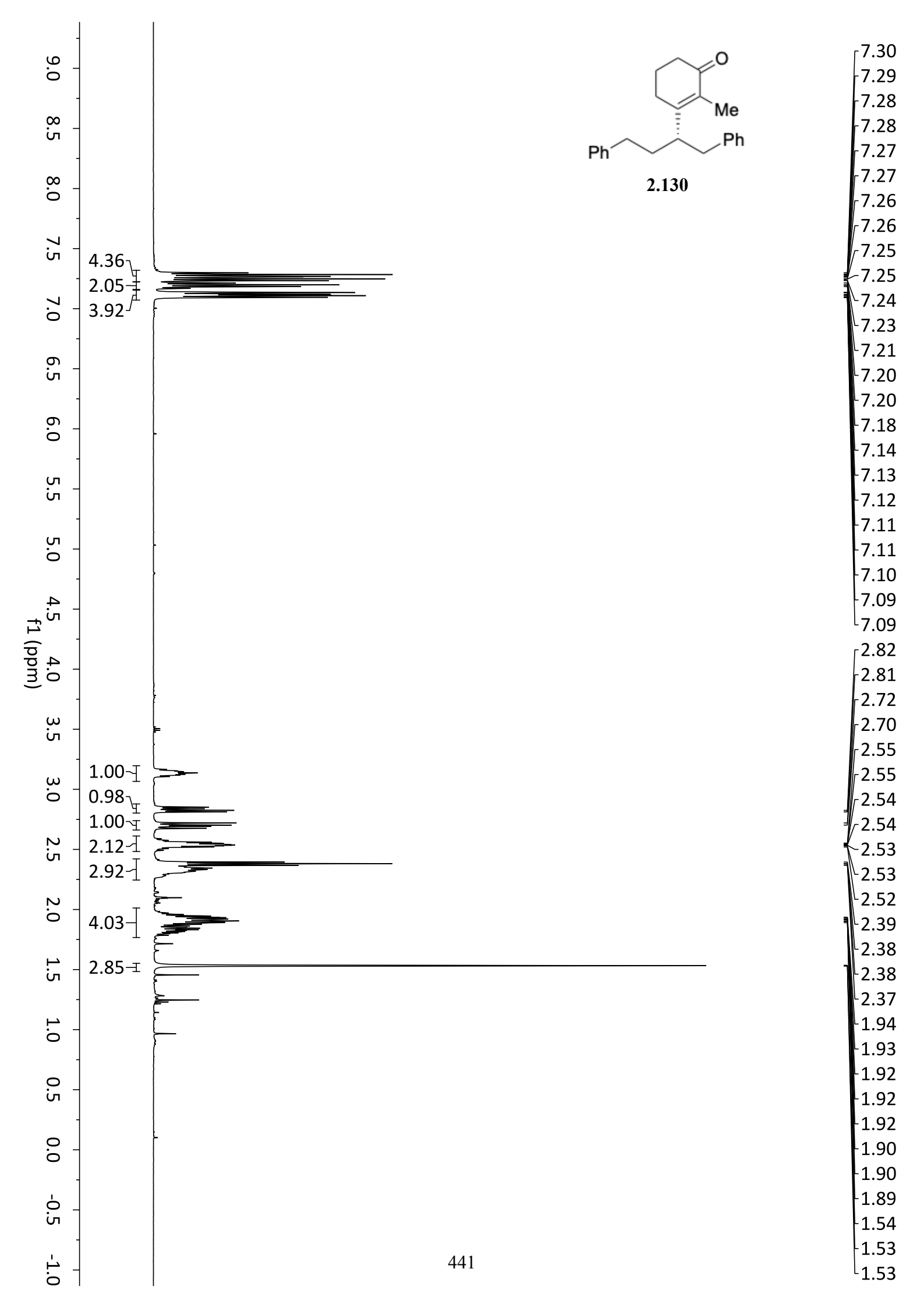

O
Me
Ph
Me
2.127
199.64
162.17
141.84
130.76
128.39
128.27
125.93
38.06
36.57
36.18
34.02
24.82
22.72
18.18
10.38
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

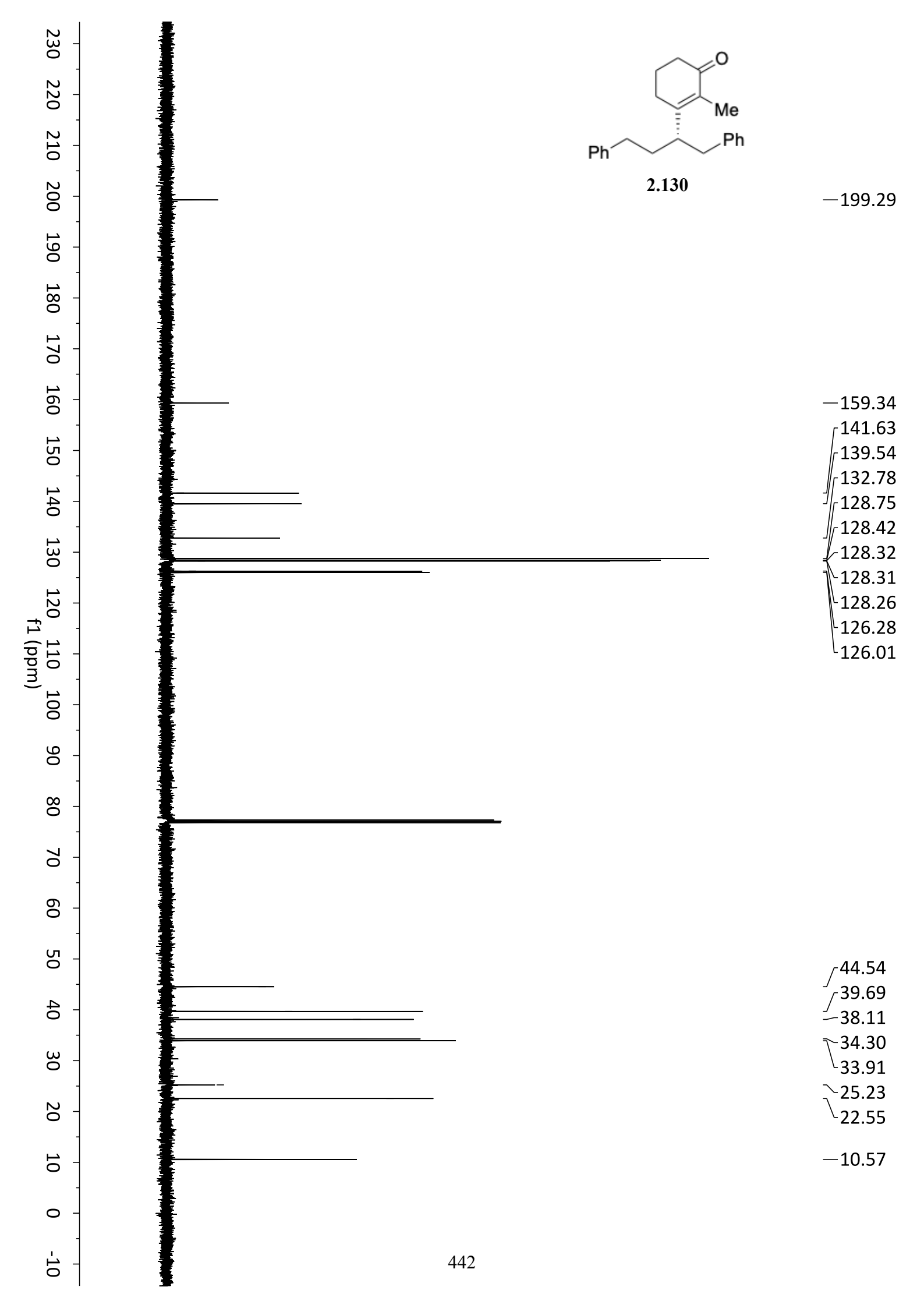

MeO
O
Me
Ph
Me
2.128
f1 (ppm)
2.09
3.22
1.00
2.94
2.99
2.99
0.99
1.09
3.02
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.27
7.20
7.20
7.19
7.18
7.17
7.17
7.16
7.16
7.16
7.15
7.15
7.15
6.63
6.62
6.61
6.60
3.76
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.55
2.55
2.54
2.54
2.53
2.53
2.52
1.82
1.82
1.74
1.68
1.68
1.67
1.67
1.64
1.06
1.04

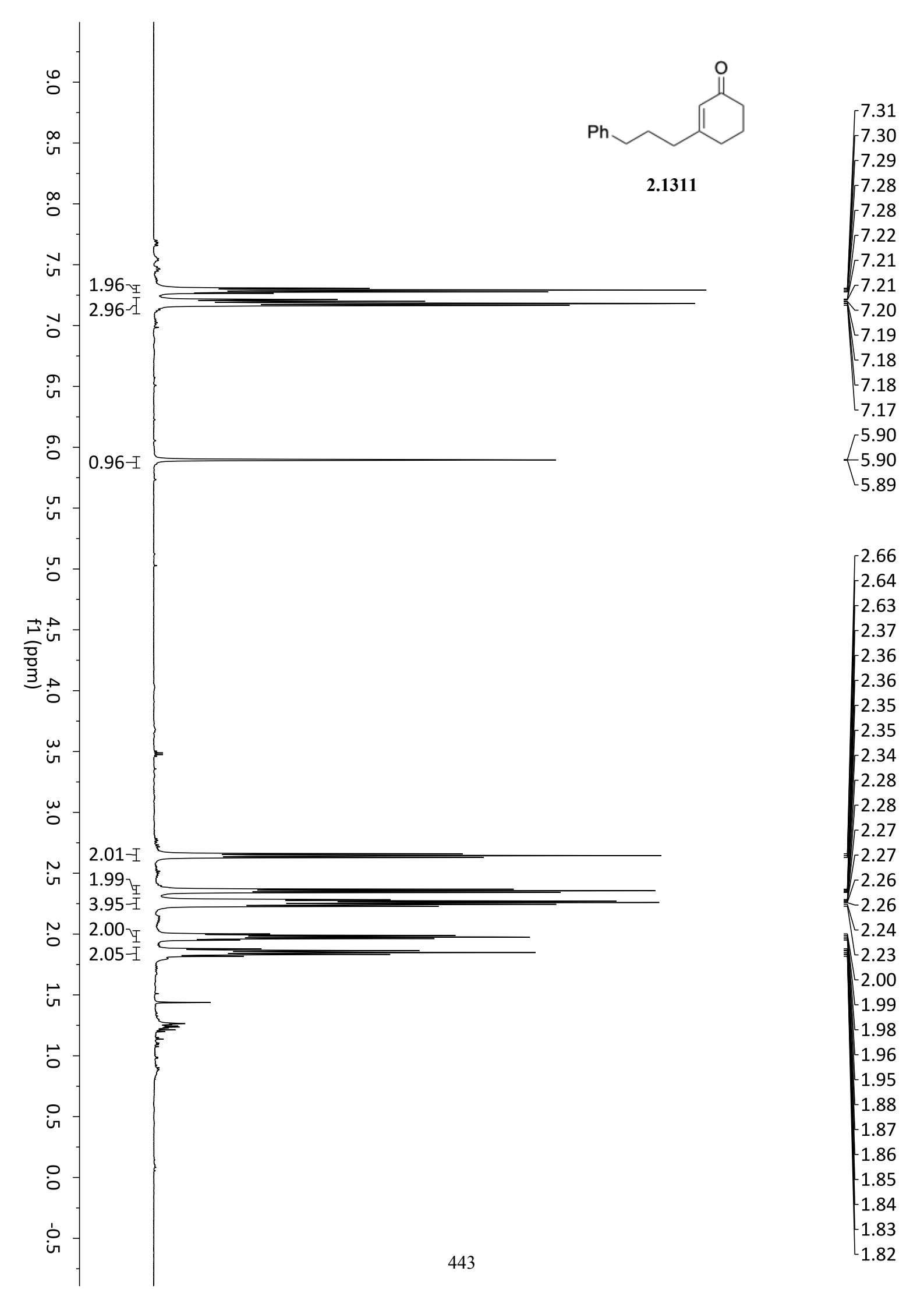

MeO
O
Me
Ph
Me
2.128
168.83
147.79
142.08
128.33
128.32
126.60
125.78
51.71
38.51
33.73
32.79
20.00
12.59
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


O
Me
Ph
22.129
f1 (ppm)
1.82
1.07
1.99
1.00
2.18
0.96
0.99
1.00
2.08
1.28
3.72
1.98
2.94
7.26
7.25
7.25
7.24
7.24
7.23
7.22
7.22
7.18
7.18
7.17
7.11
7.10
7.09
7.09
7.09
5.76
5.74
4.99
4.99
4.97
4.97
4.97
4.96
4.95
4.95
4.95
4.95
2.78
2.77
2.68
2.67
2.66
2.37
2.36
2.34
1.96
1.96
1.94
1.93
1.92
1.91
1.91
1.65
1.65
1.62
1.61
1.57
1.57
1.56


O
Me
Ph
2.129
199.29
159.45
139.64
138.04
132.67
128.72
128.29
126.23
115.04
44.34
39.64
38.09
31.87
31.69
25.14
22.53
10.58
f1 (ppm)


O
Me
Ph
Ph
2.130
4.36
2.05
3.92
1.00
0.98
1.00
2.12
2.92
4.03
2.85
f1 (ppm)
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
-1.0
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.26
7.25
7.25
7.24
7.23
7.21
7.20
7.20
7.18
7.14
7.13
7.12
7.11
7.11
7.10
7.09
7.09
2.82
2.81
2.72
2.70
2.55
2.55
2.54
2.54
2.53
2.53
2.52
2.39
2.38
2.38
2.37
1.94
1.93
1.92
1.92
1.92
1.90
1.90
1.89
1.54
1.53
1.53


O
Me
Ph
Ph
2.130
199.29
159.34
141.63
139.54
132.78
128.75
128.42
128.32
128.31
128.26
126.28
126.01
44.54
39.69
38.11
34.30
33.91
25.23
22.55
10.57
f1 (ppm)


O
Ph
2.1311
1.96
2.96
0.96
2.01
1.99
3.95
2.00
2.05
f1 (ppm)
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
7.31
7.30
7.29
7.28
7.28
7.22
7.21
7.21
7.20
7.19
7.18
7.18
7.17
5.90
5.90
5.89
2.66
2.64
2.63
2.37
2.36
2.36
2.35
2.35
2.34
2.28
2.28
2.27
2.27
2.26
2.26
2.24
2.23
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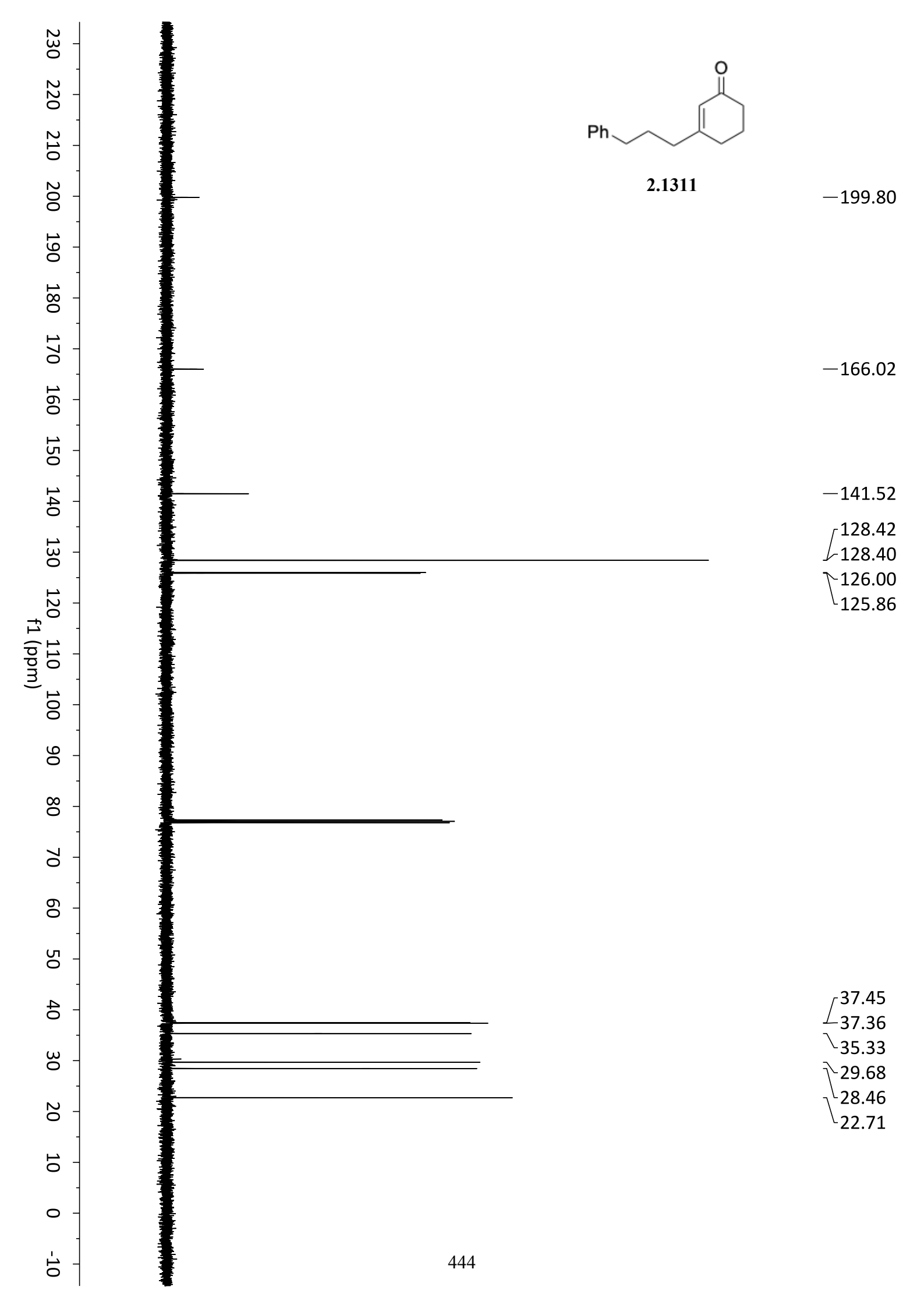
1.98
1.96
1.95
1.88
1.87
1.86
1.85
1.84
1.83
1.82


O
Ph
2.1311
199.80
166.02
141.52
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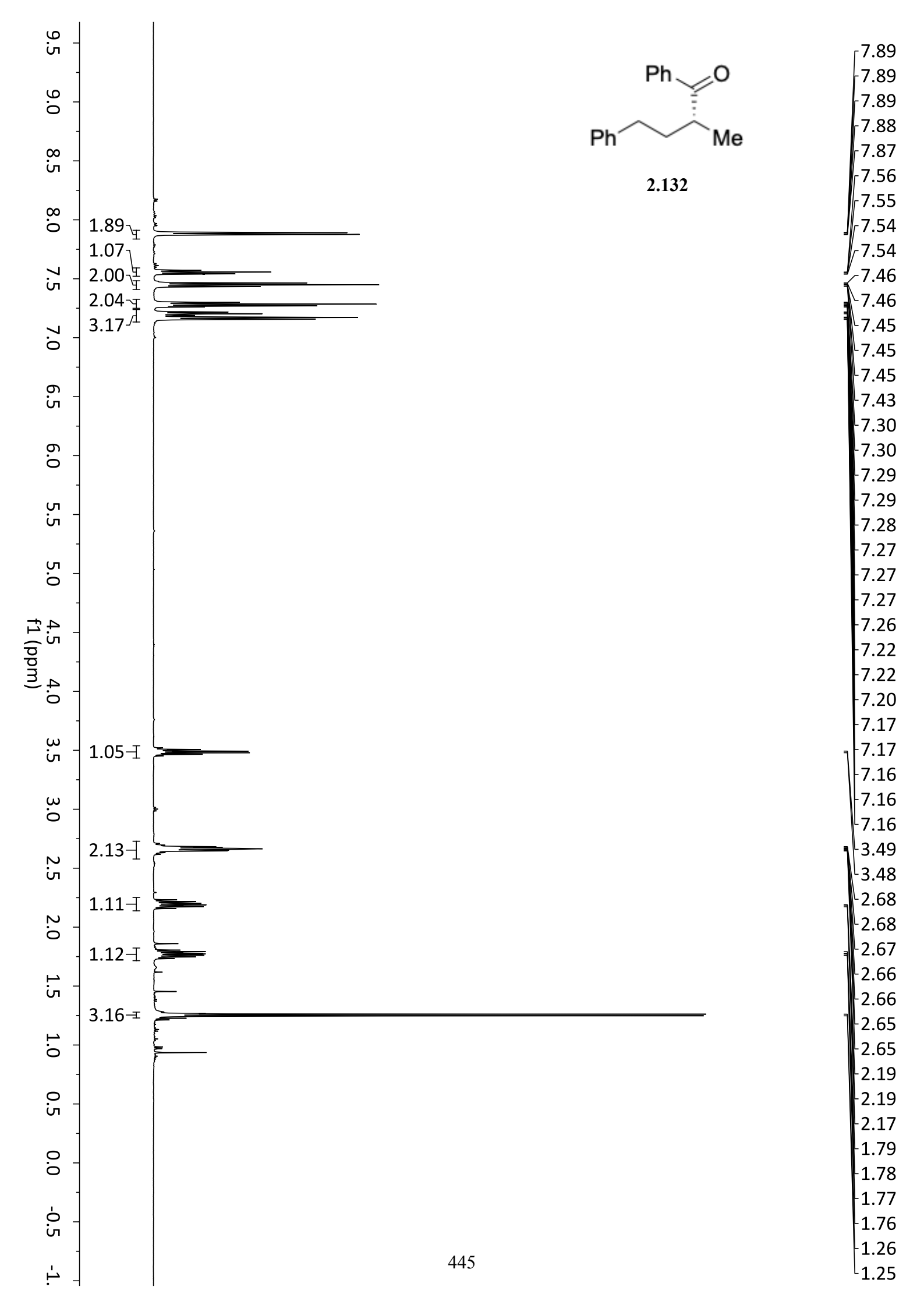
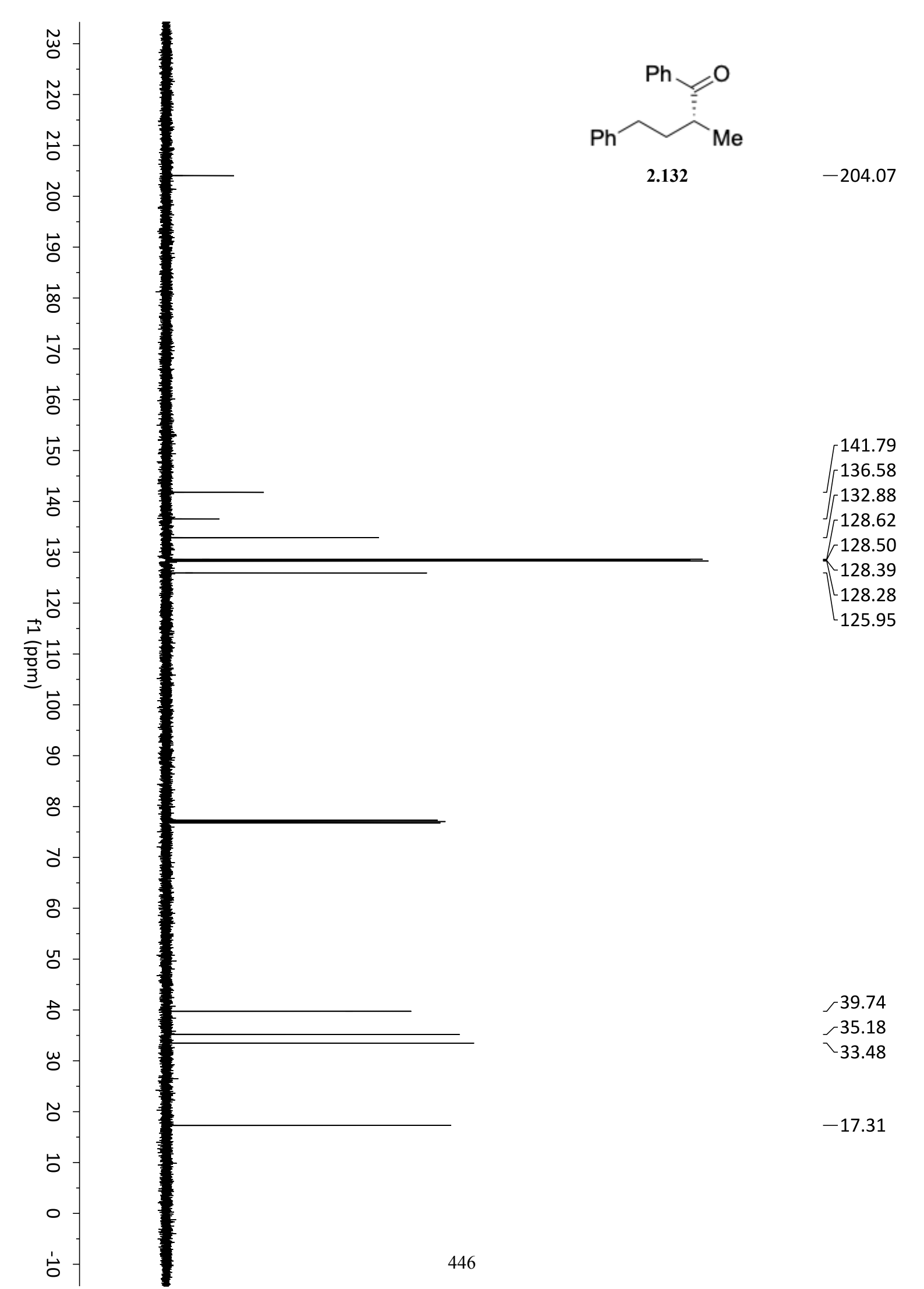
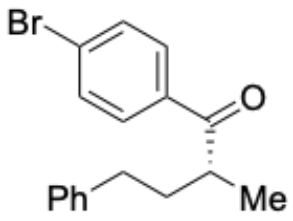
128.40
126.00
125.86
37.45
37.36
35.33
29.68
28.46
22.71
f1 (ppm)


Ph
O
Ph
Me
2.132
1.89
1.07
2.00
2.04
3.17
1.05
2.13
1.11
1.12
3.16
f1 (ppm)
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.
7.89 7.89 7.89 7.88 7.87 7.56 7.55 7.54 7.54 7.46 7.46 7.45 7.45 7.45 7.43 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.27 7.26 7.22 7.22 7.20 7.17 7.17 7.16 7.16 7.16 3.49 3.48 2.68 2.68 2.67 2.66 2.66 2.65 2.65 2.19 2.19 2.17 1.79 1.78 1.77 1.76 1.26 1.25


Ph
O
Ph
Me
2.132
204.07
141.79
136.58
132.88
128.62
128.50
128.39
128.28
125.95
39.74
35.18
33.48
17.31
f1 (ppm)



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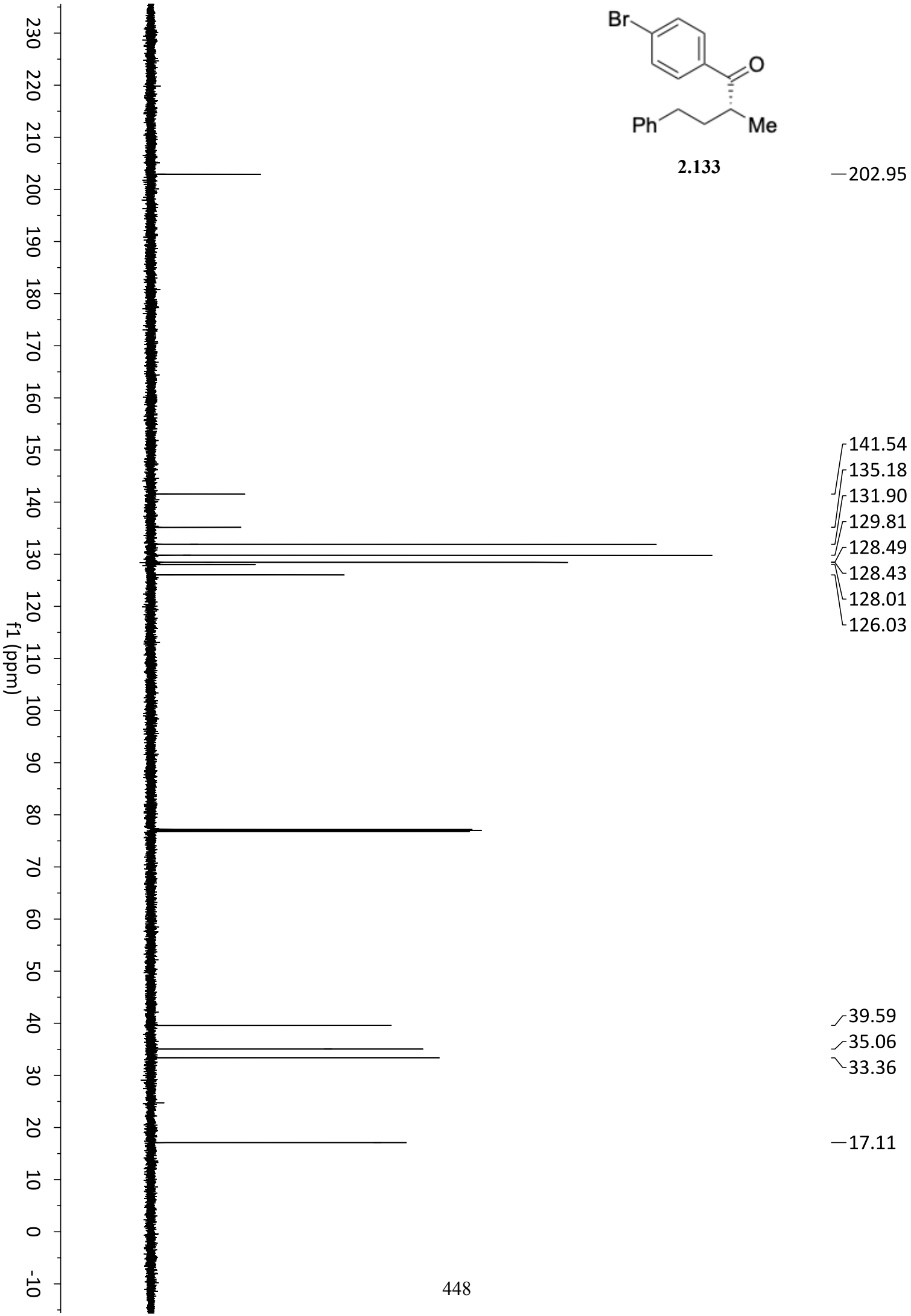
Br
O
Ph
Me
2.133
202.95
141.54
135.18
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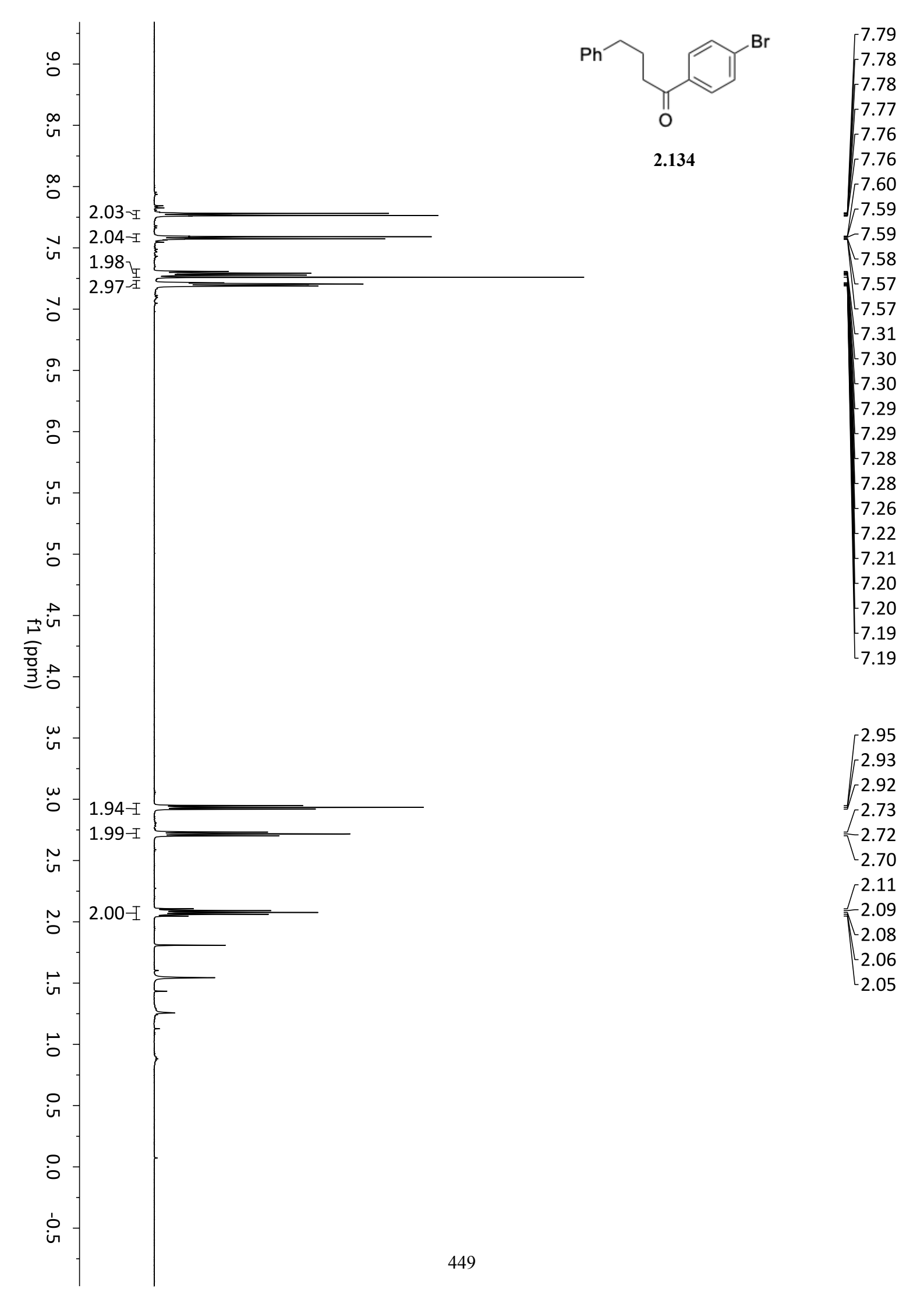
129.81
128.49
128.43
128.01
126.03
39.59
35.06
33.36
17.11
f1 (ppm)


Ph
Br
O
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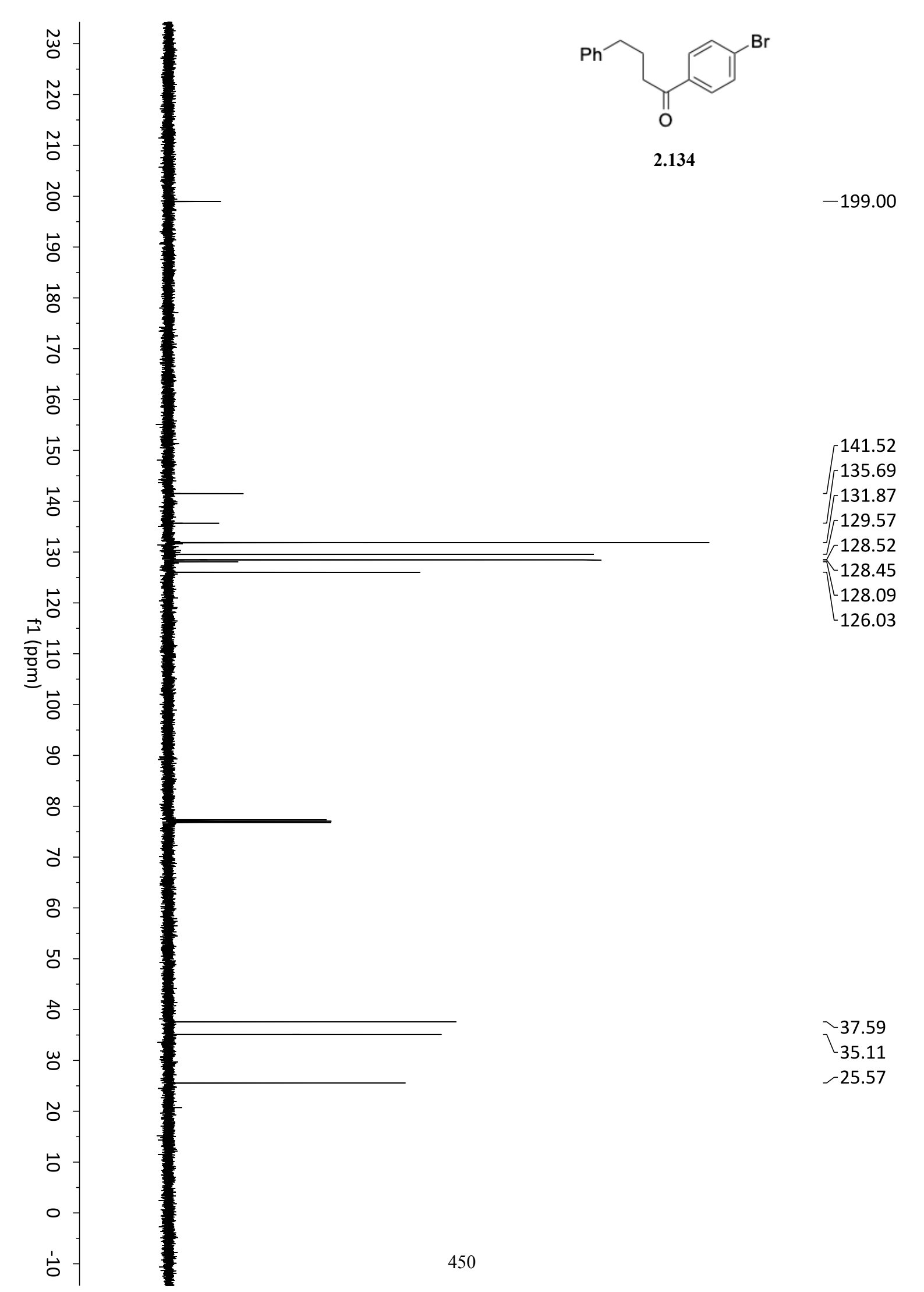
2.03
2.04
1.98
2.97
1.94
1.99
2.00
7.79
7.78
7.78
7.77
7.76
7.76
7.60
7.59
7.59
7.58
7.57
7.57
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.26
7.22
7.21
7.20
7.20
7.19
7.19
2.95
2.93
2.92
2.73
2.72
2.70
2.11
2.09
2.08
2.06
2.05
f1 (ppm)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Br
O
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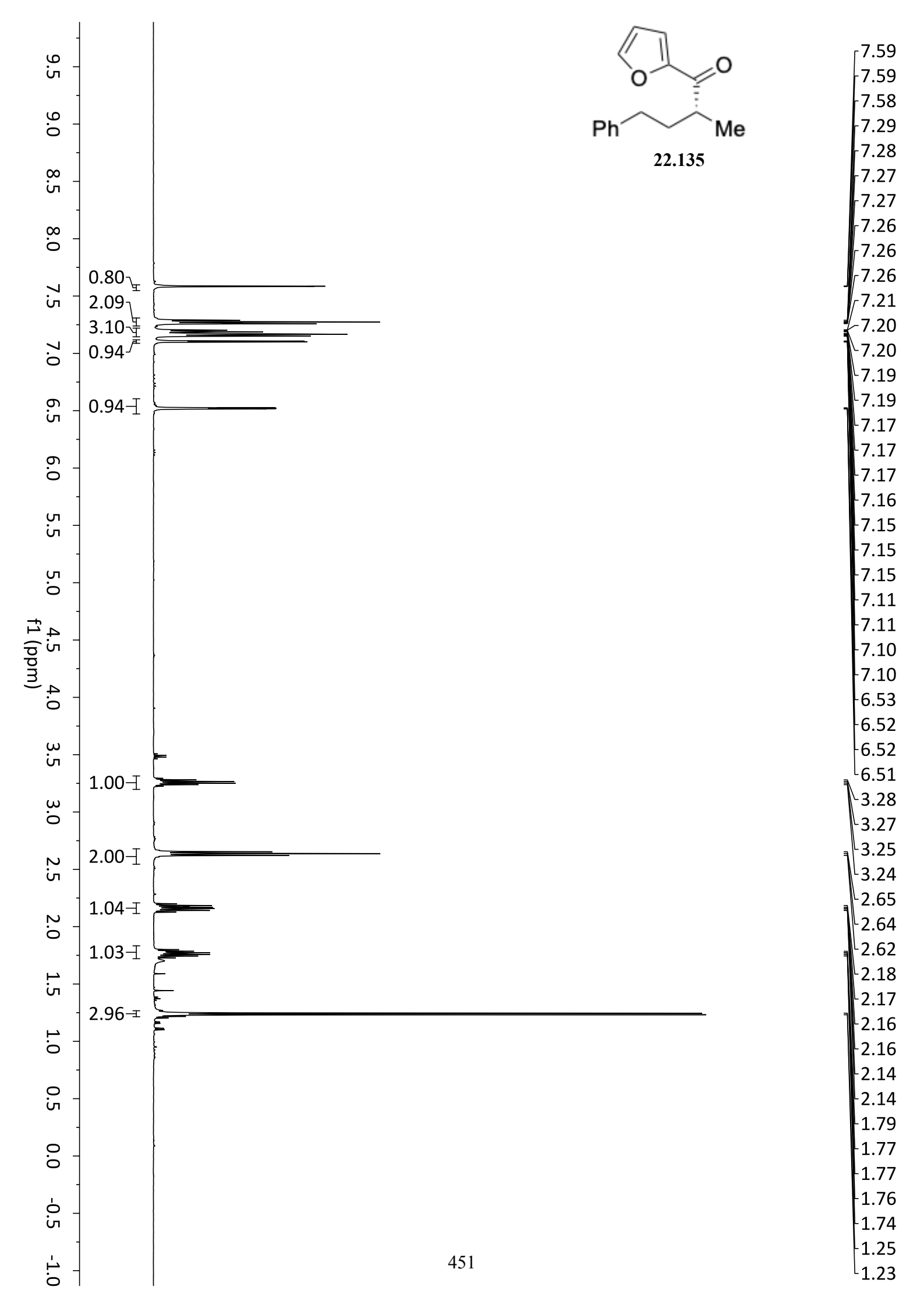
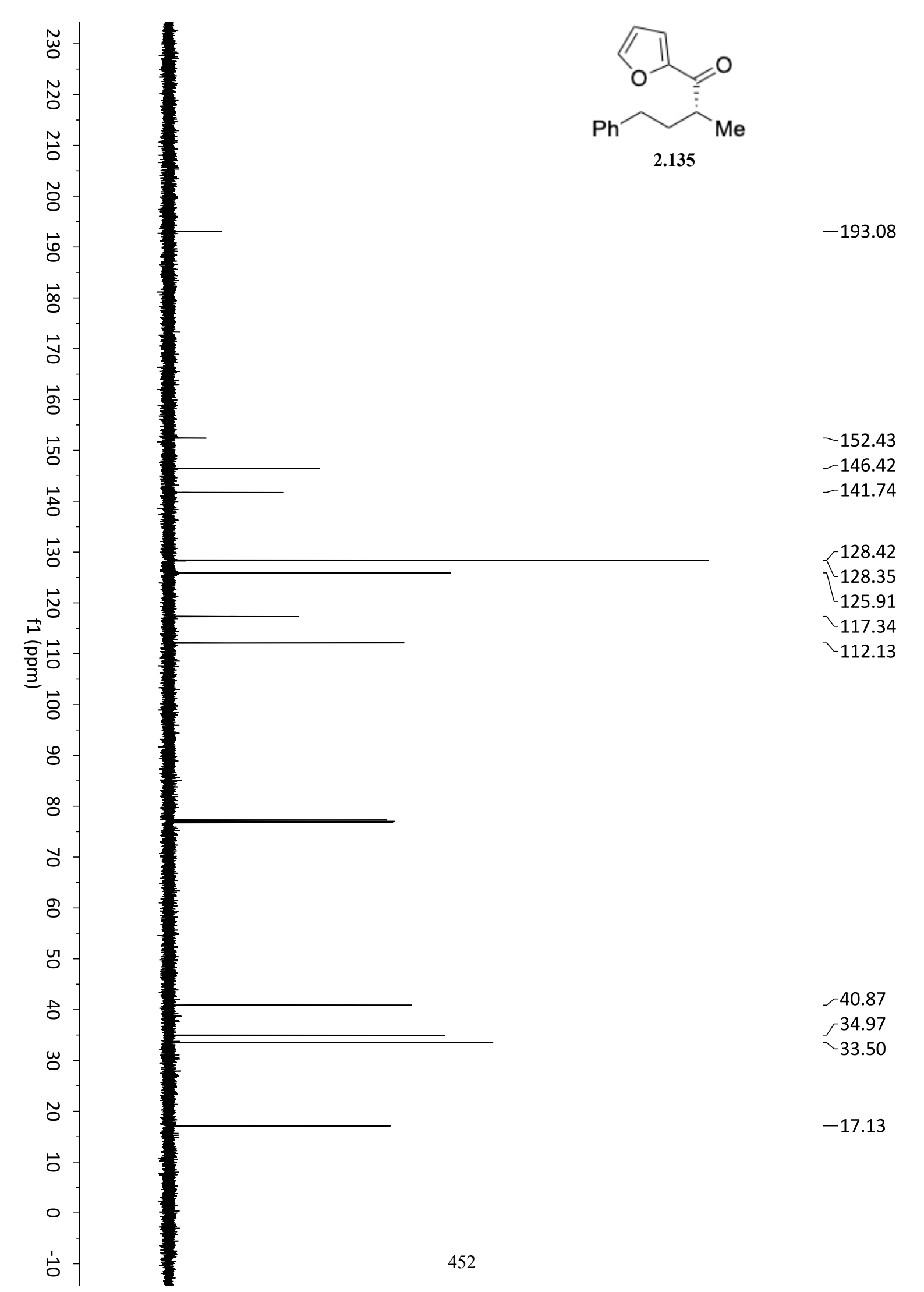
141.52
135.69
131.87
129.57
128.52
128.45
128.09
126.03
37.59
35.11
25.57
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


22.135
Ph
Me
O
O
0.80
2.09
3.10
0.94
0.94
1.00
2.00
1.04
1.03
2.96
f1 (ppm)
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 -1.0
7.59 7.59 7.58 7.29 7.28 7.27 7.27 7.26 7.26 7.26 7.21 7.20 7.20 7.19 7.19 7.17 7.17 7.17 7.16 7.15 7.15 7.15 7.11 7.11 7.10 7.10 6.53 6.52 6.52 6.51 3.28 3.27 3.25 3.24 2.65 2.64 2.62 2.18 2.17 2.16 2.16 2.14 2.14 1.79 1.77 1.77 1.76 1.74 1.25 1.23


O
O
Ph
Me
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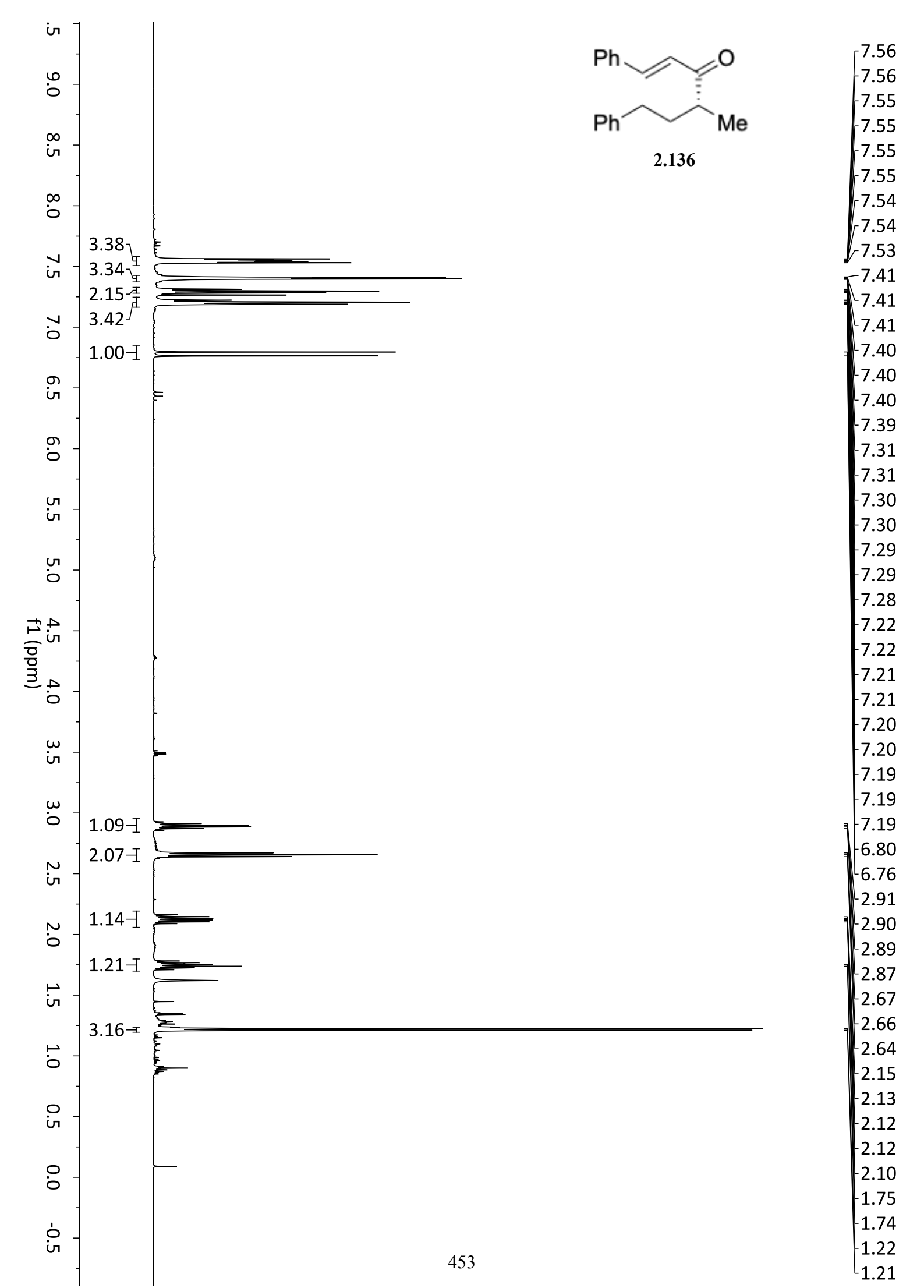
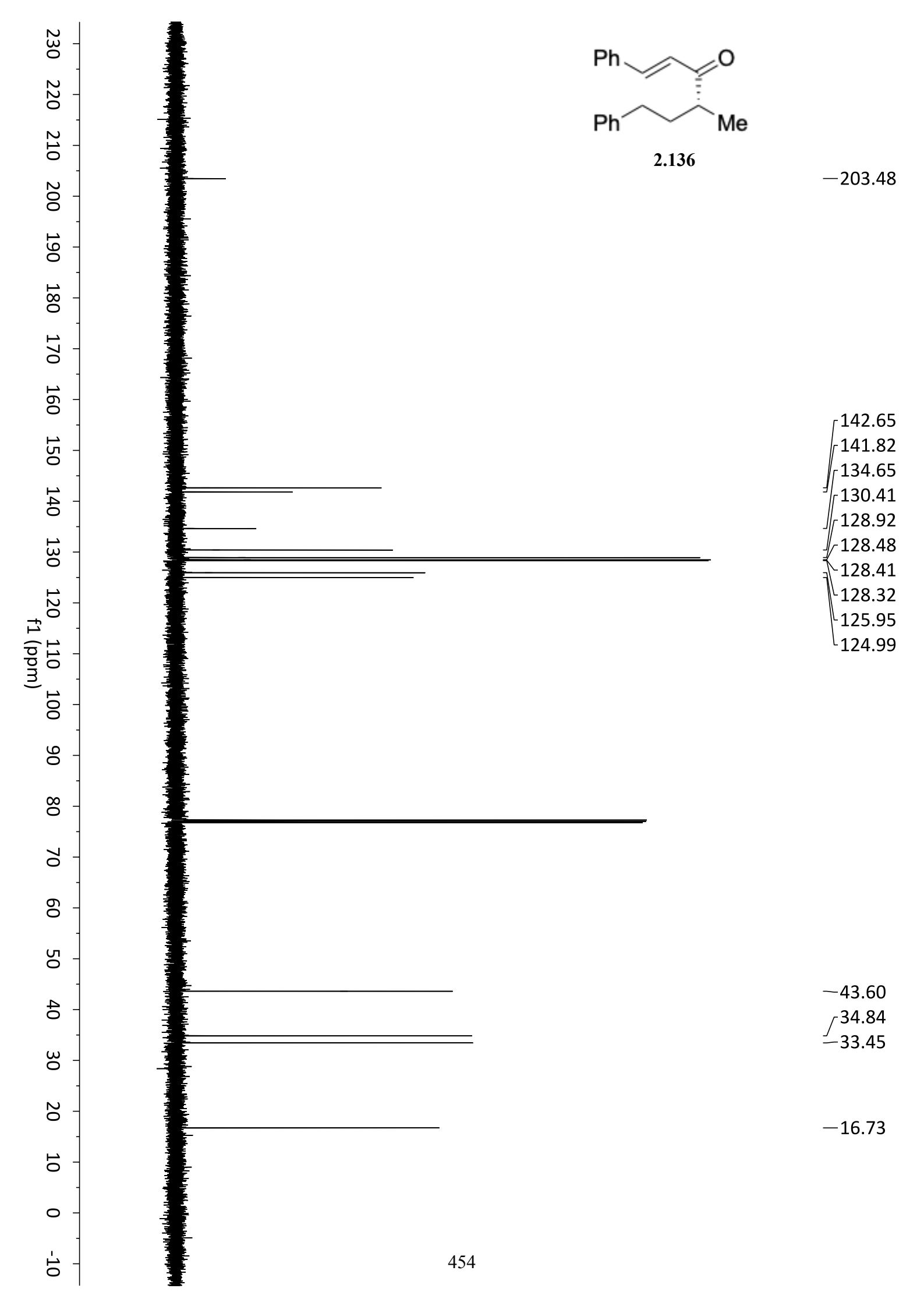
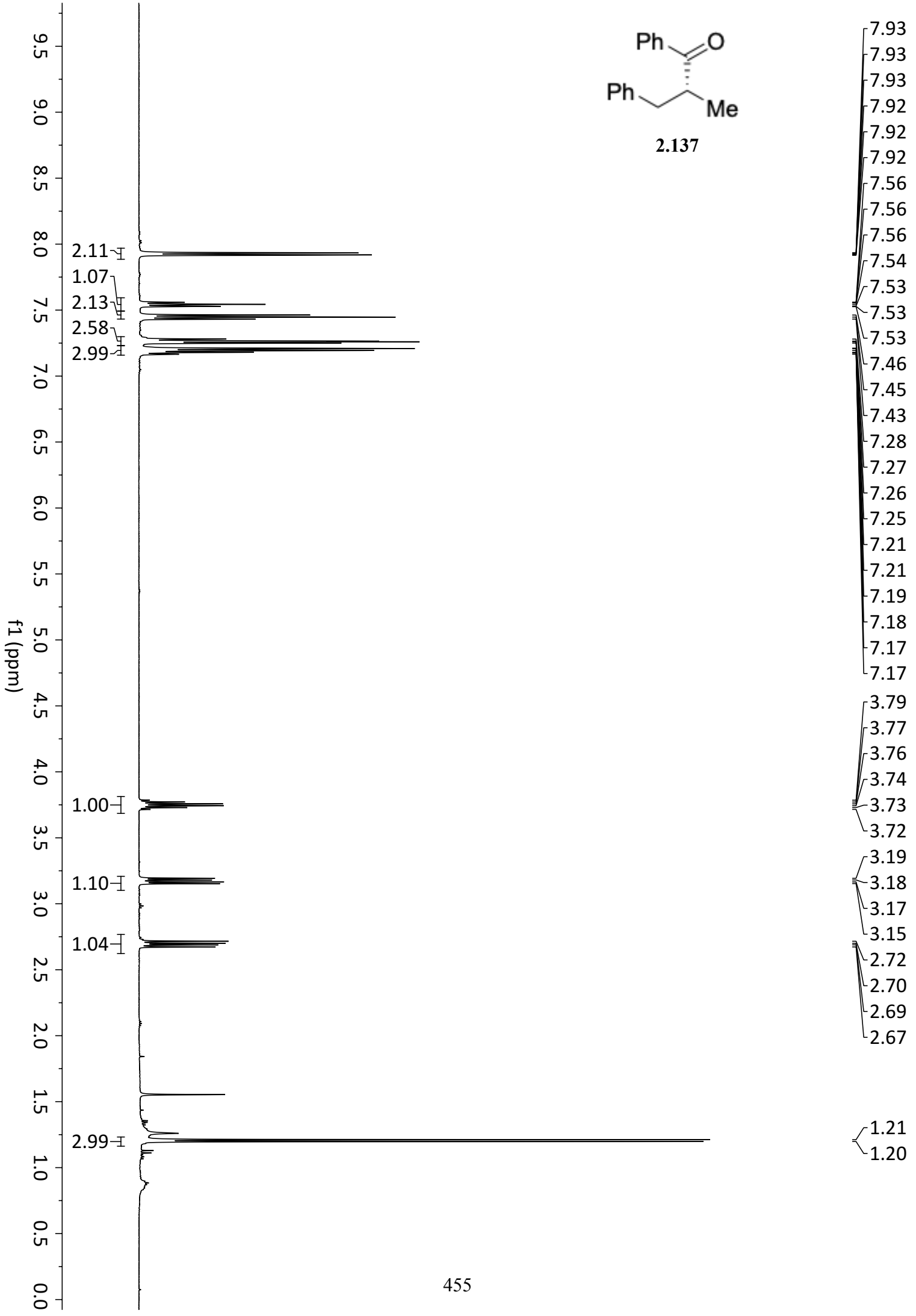
193.08
152.43
146.42
141.74
128.42
128.35
125.91
117.34
112.13
40.87
34.97
33.50
17.13
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
O
Ph
Me
2.136
3.38
3.34
2.15
3.42
1.00
1.09
2.07
1.14
1.21
3.16
f1 (ppm)
7.56
7.56
7.55
7.55
7.55
7.55
7.54
7.54
7.53
7.41
7.41
7.41
7.40
7.40
7.40
7.39
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.19
6.80
6.76
2.91
2.90
2.89
2.87
2.67
2.66
2.64
2.15
2.13
2.12
2.12
2.10
1.75
1.74
1.22
1.21


Ph
O
Ph
Me
2.136
203.48
142.65
141.82
134.65
130.41
128.92
128.48
128.41
128.32
125.95
124.99
43.60
34.84
33.45
16.73
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


Ph
O
Ph
Me
2.137
2.11
1.07
2.13
2.58
2.99
1.00
1.10
1.04
2.99
7.93
7.93
7.93
7.92
7.92
7.92
7.56
7.56
7.56
7.54
7.53
7.53
7.53
7.46
7.45
7.43
7.28
7.27
7.26
7.25
7.21
7.21
7.19
7.18
7.17
7.17
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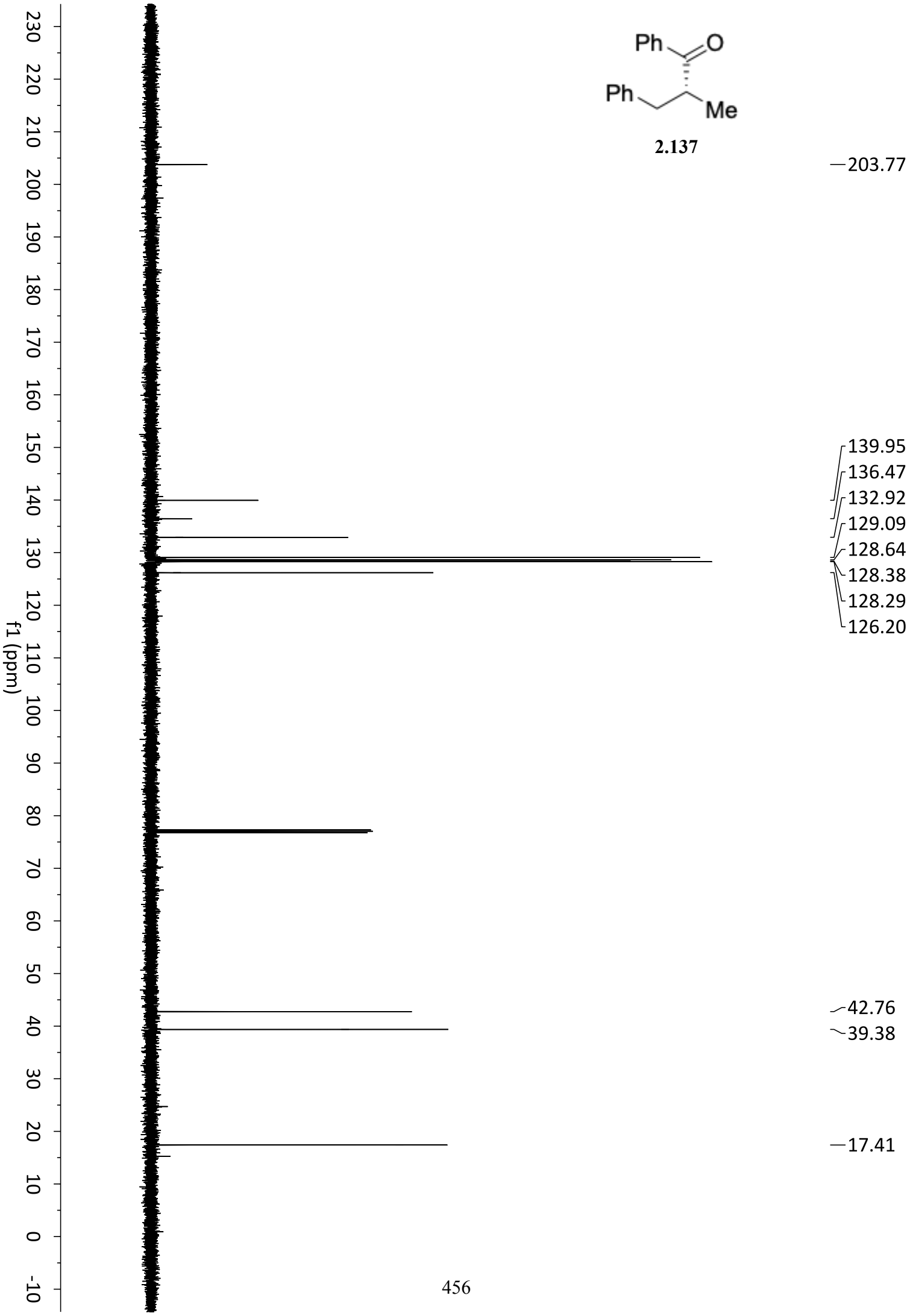
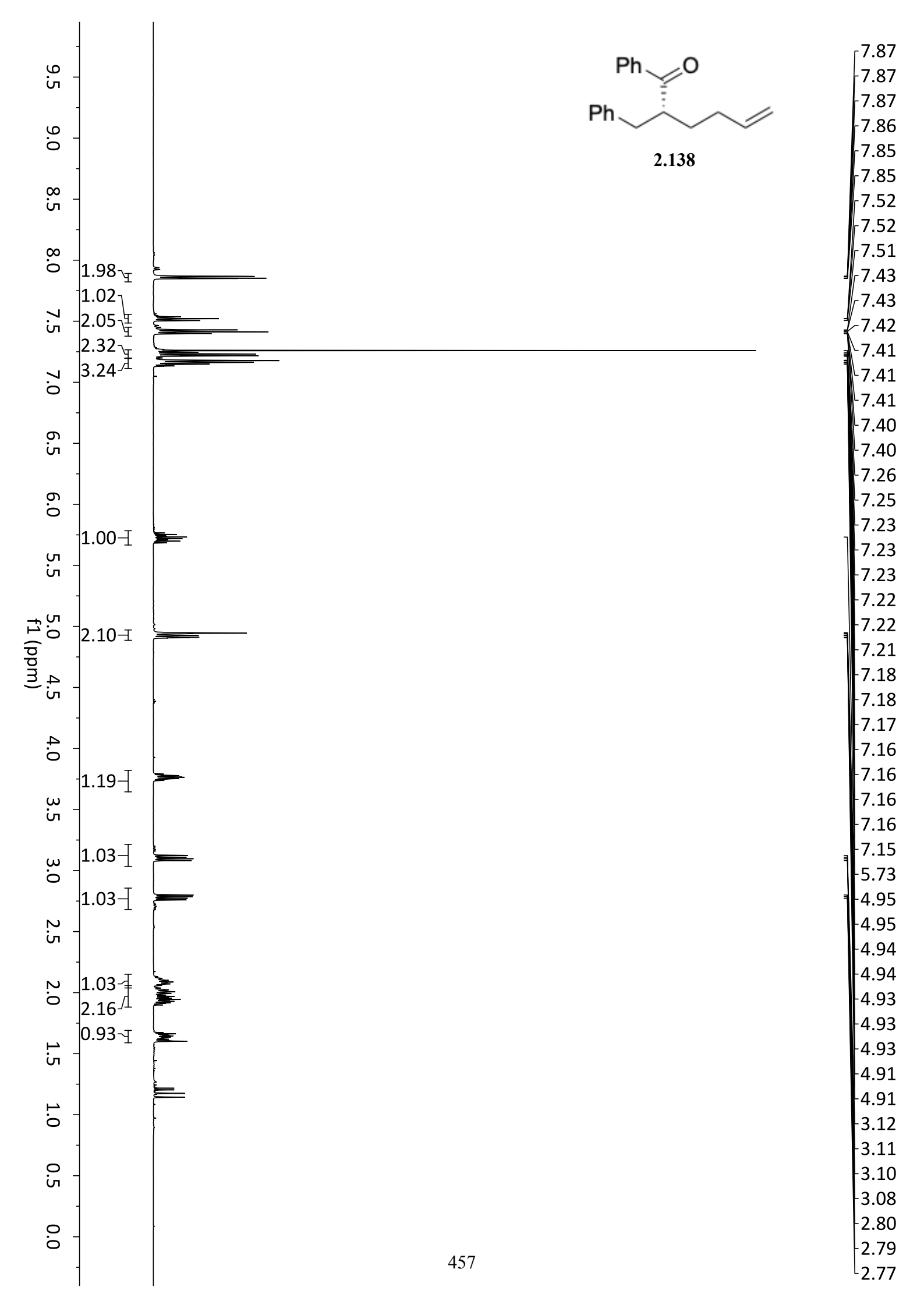
3.77
3.76
3.74
3.73
3.72
3.19
3.18
3.17
3.15
2.72
2.70
2.69
2.67
1.21
1.20
f1 (ppm)


Ph
O
Ph
Me
2.137
203.77
139.95
136.47
132.92
129.09
128.64
128.38
128.29
126.20
42.76
39.38
17.41
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
O
Ph
2.138
f1 (ppm)
1.98
1.02
2.05
2.32
3.24
1.00
2.10
1.19
1.03
1.03
1.03
2.16
0.93
7.87
7.87
7.87
7.86
7.85
7.85
7.52
7.52
7.51
7.43
7.43
7.42
7.41
7.41
7.41
7.40
7.40
7.26
7.25
7.23
7.23
7.23
7.22
7.22
7.21
7.18
7.18
7.17
7.16
7.16
7.16
7.16
7.15
5.73
4.95
4.95
4.94
4.94
4.93
4.93
4.93
4.91
4.91
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3.11
3.10
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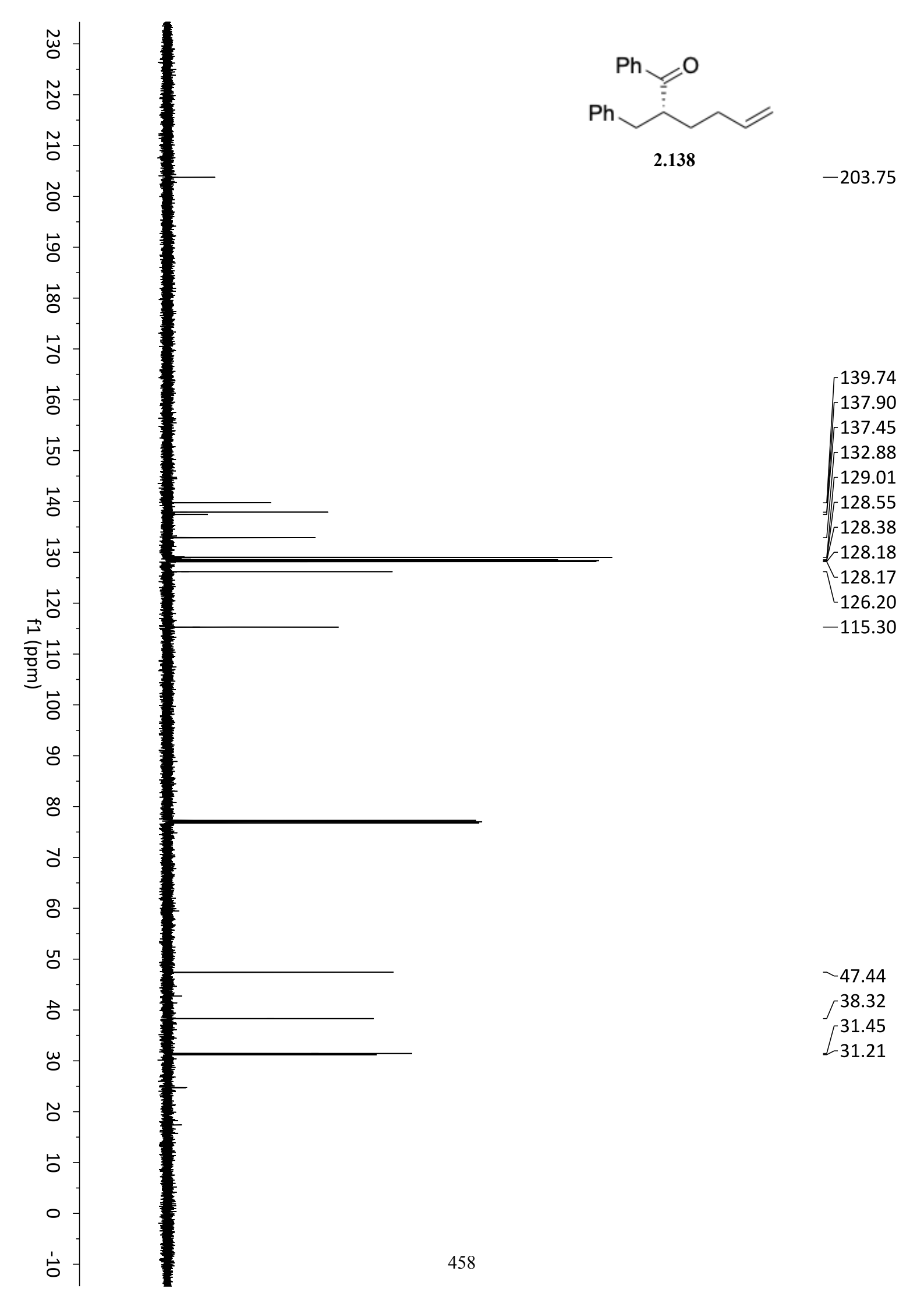
2.79
2.77


Ph
O
Ph
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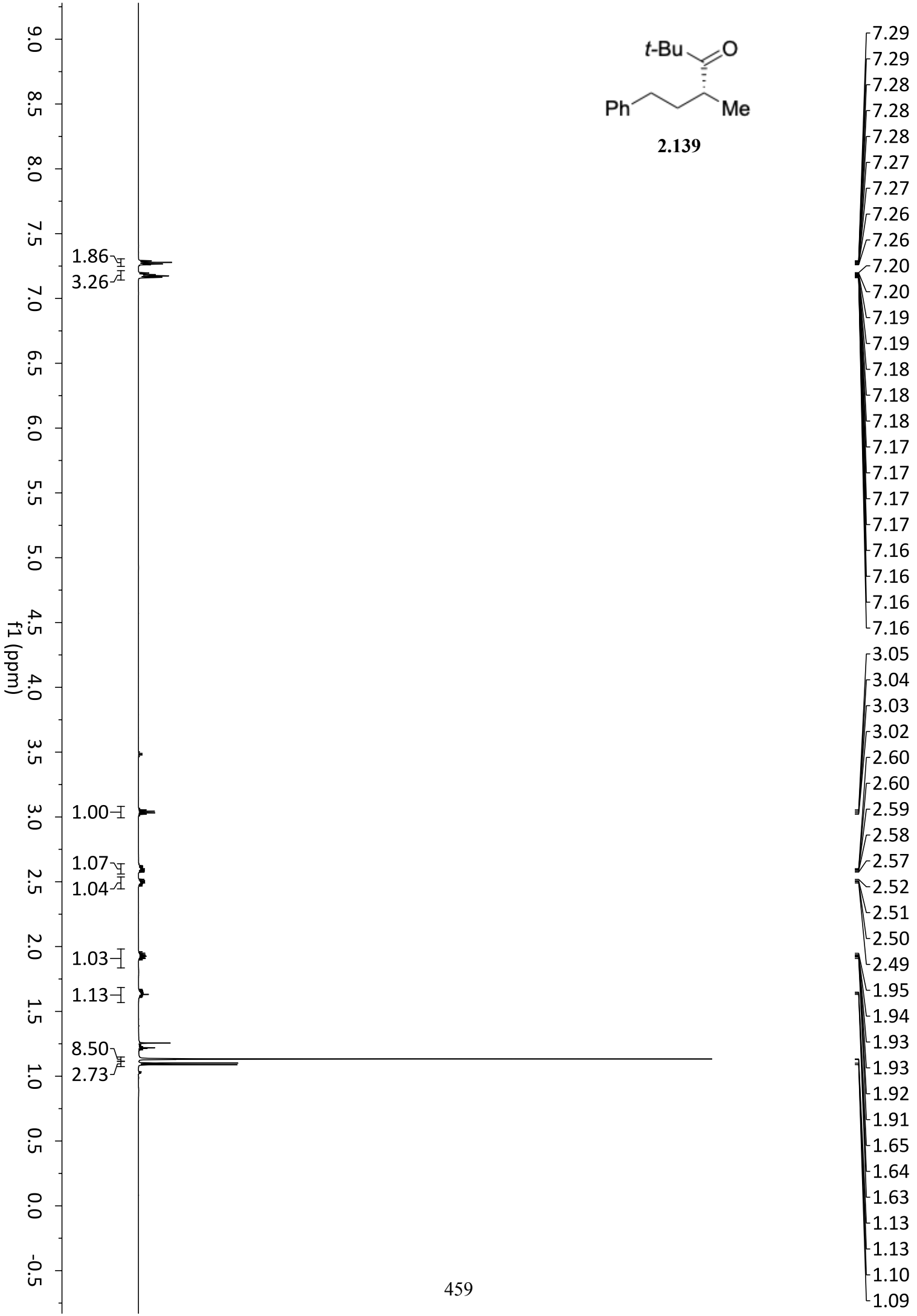
129.01
128.55
128.38
128.18
128.17
126.20
115.30
47.44
38.32
31.45
31.21
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


t-Bu
O
Ph
Me
2.139
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1.07
1.04
1.03
1.13
8.50
2.73
f1 (ppm)
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
7.29
7.29
7.28
7.28
7.28
7.27
7.27
7.26
7.26
7.20
7.20
7.19
7.19
7.18
7.18
7.18
7.17
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7.17
7.17
7.16
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7.16
7.16
3.05
3.04
3.03
3.02
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1.63
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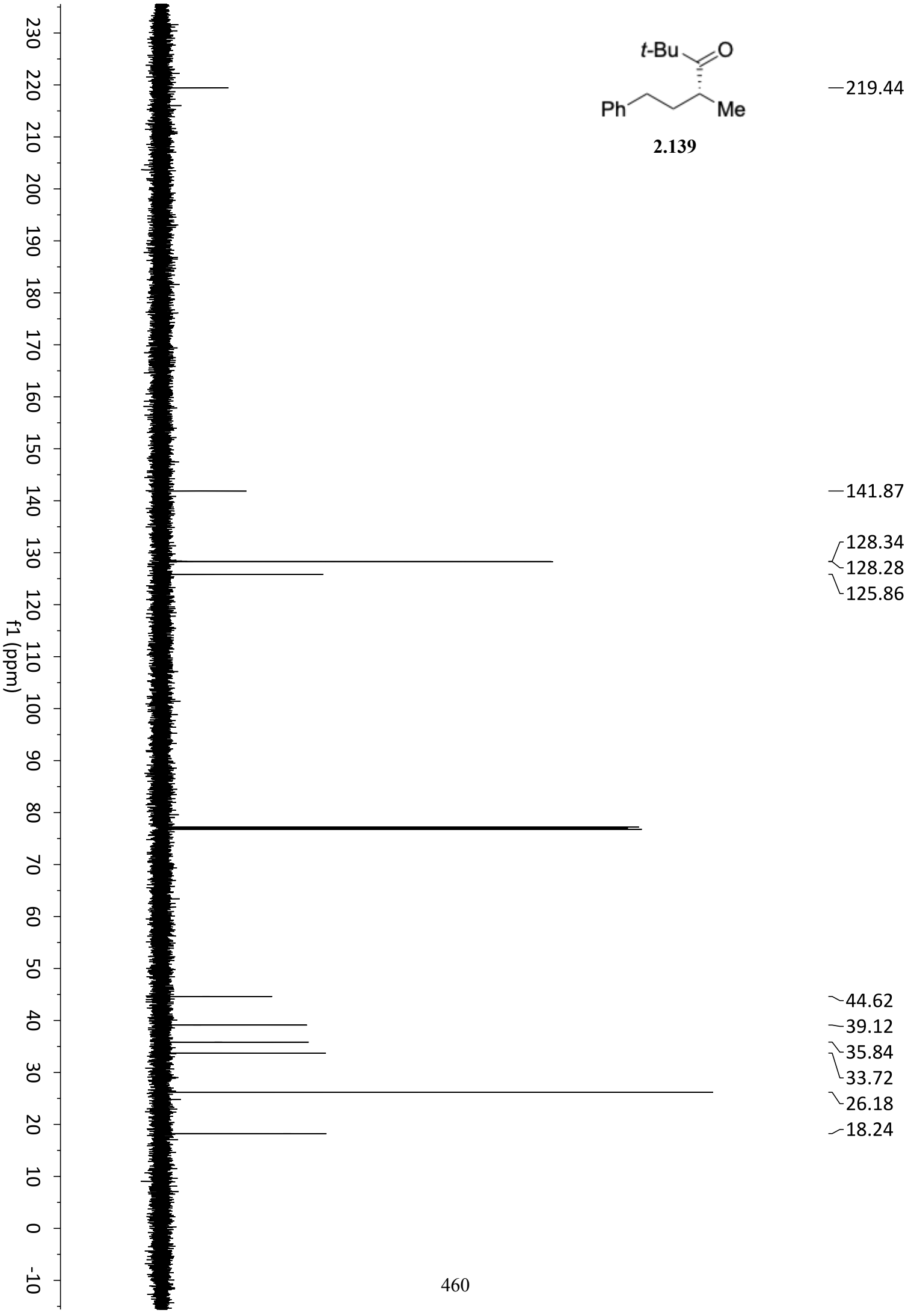
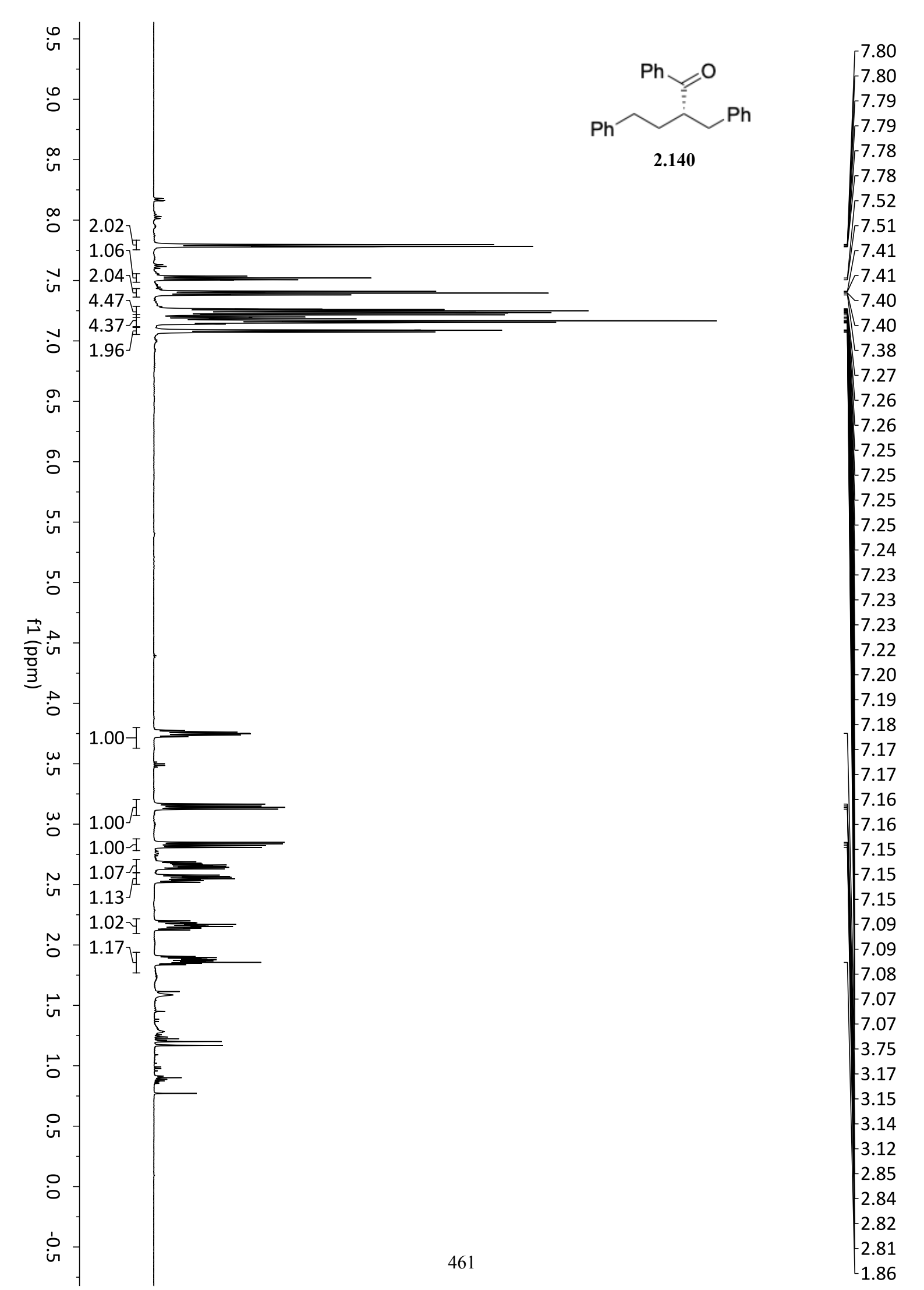
1.13
1.10
1.09


t-Bu
O
Ph
Me
2.139
219.44
141.87
128.34
128.28
125.86
44.62
39.12
35.84
33.72
26.18
18.24
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
O
Ph
Ph
2.140
2.02
1.06
2.04
4.47
4.37
1.96
1.00
1.00
1.00
1.07
1.13
1.02
1.17
f1 (ppm)
7.80
7.80
7.79
7.79
7.78
7.78
7.52
7.51
7.41
7.41
7.40
7.40
7.38
7.27
7.26
7.26
7.25
7.25
7.25
7.25
7.24
7.23
7.23
7.23
7.22
7.20
7.19
7.18
7.17
7.17
7.16
7.16
7.15
7.15
7.15
7.09
7.09
7.08
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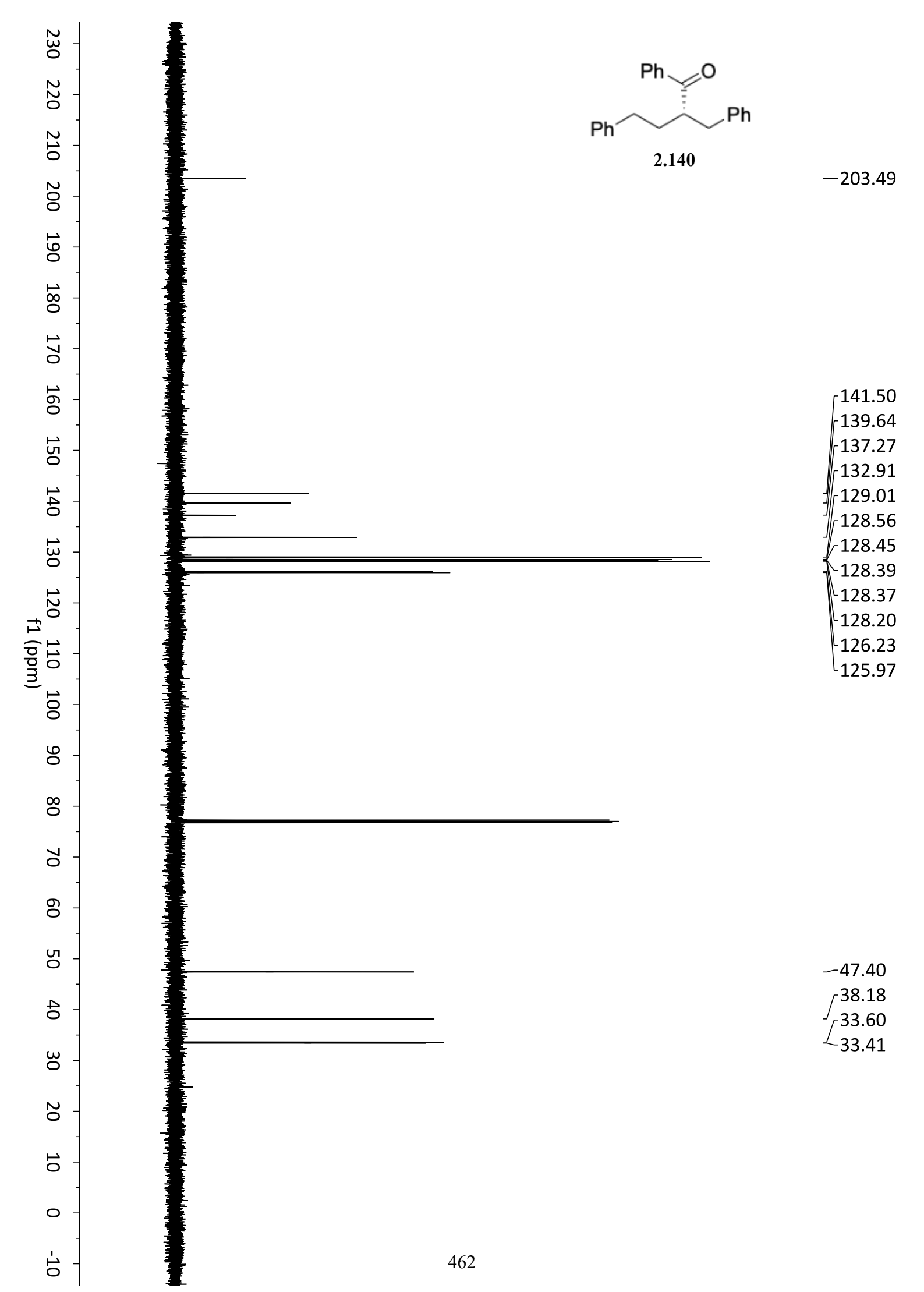
2.81
1.86


Ph
O
Ph
Ph
2.140
203.49
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139.64
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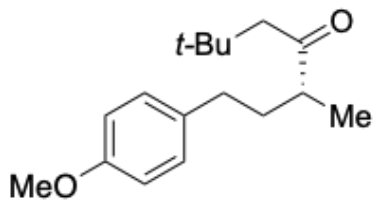
132.91
129.01
128.56
128.45
128.39
128.37
128.20
126.23
125.97
47.40
38.18
33.60
33.41
f1 (ppm)


t-Bu
O
Me
MeO

22.141

f1 (ppm)
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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
1.91
1.95
2.88
3.05
0.94
1.00
1.00
1.15
2.83
8.68
7.26
7.09
7.09
7.08
7.07
6.83
6.83
6.82
6.82
3.78
2.54
2.53
2.52
2.52
2.51
2.51
2.50
2.50
2.48
2.47
2.35
2.33
2.30
2.27
1.97
1.96
1.95
1.95
1.94
1.94
1.93
1.92
1.92
1.91
1.58
1.58
1.57
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1.53
1.08
1.07
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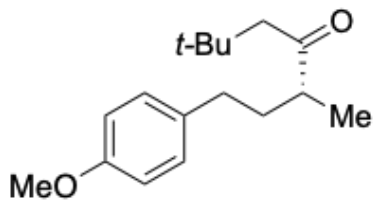
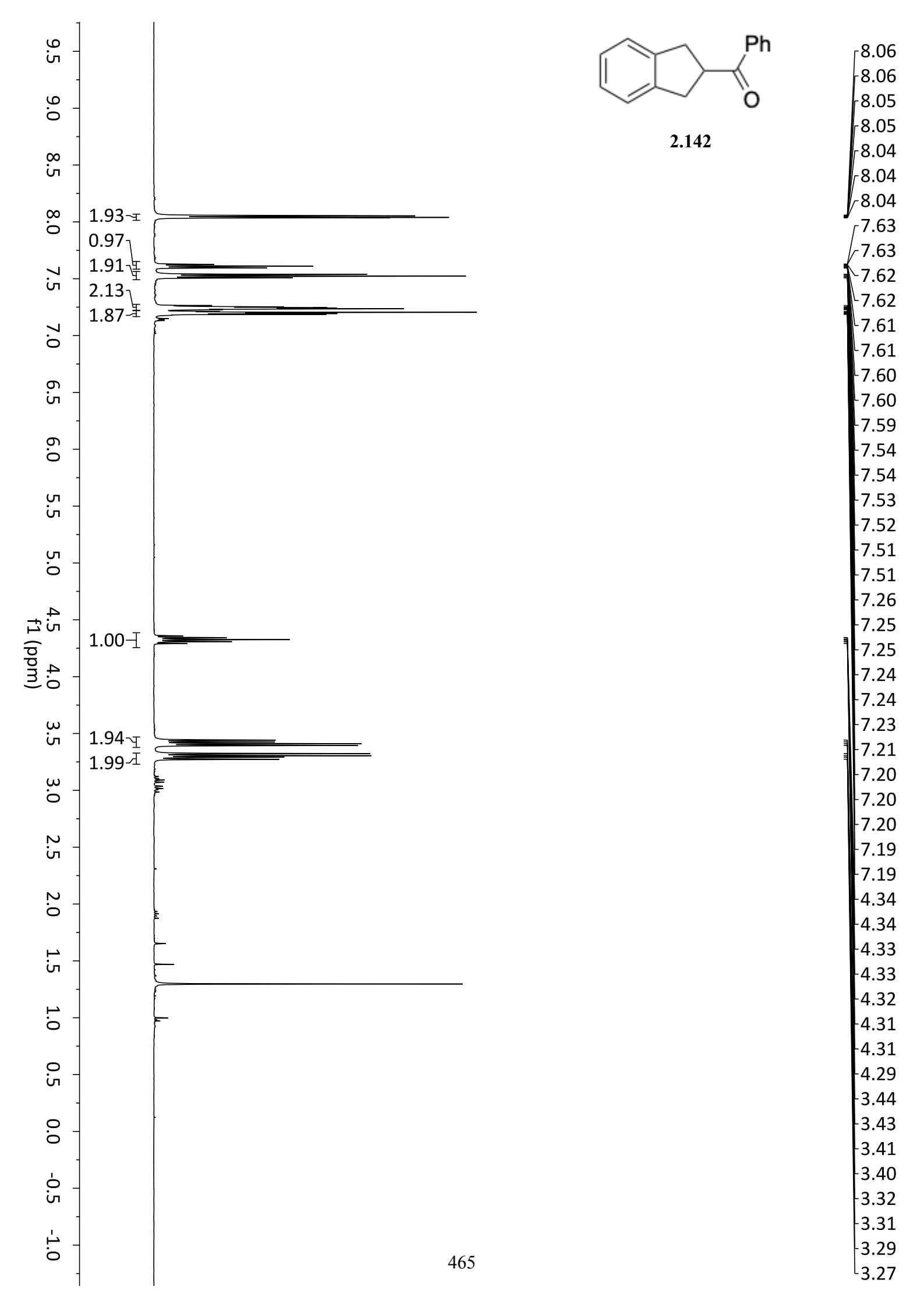
1.01
1.00



2.141

214.11
157.82
133.90
129.21
113.79
55.23
53.46
46.83
34.57
32.52
30.89
29.71
16.09

f1 (ppm)


Ph
O
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1.93
0.97
1.91
2.13
1.87
1.00
1.94
1.99
f1 (ppm)
8.06
8.06
8.05
8.05
8.04
8.04
8.04
7.63
7.63
7.62
7.62
7.61
7.61
7.60
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7.53
7.52
7.51
7.51
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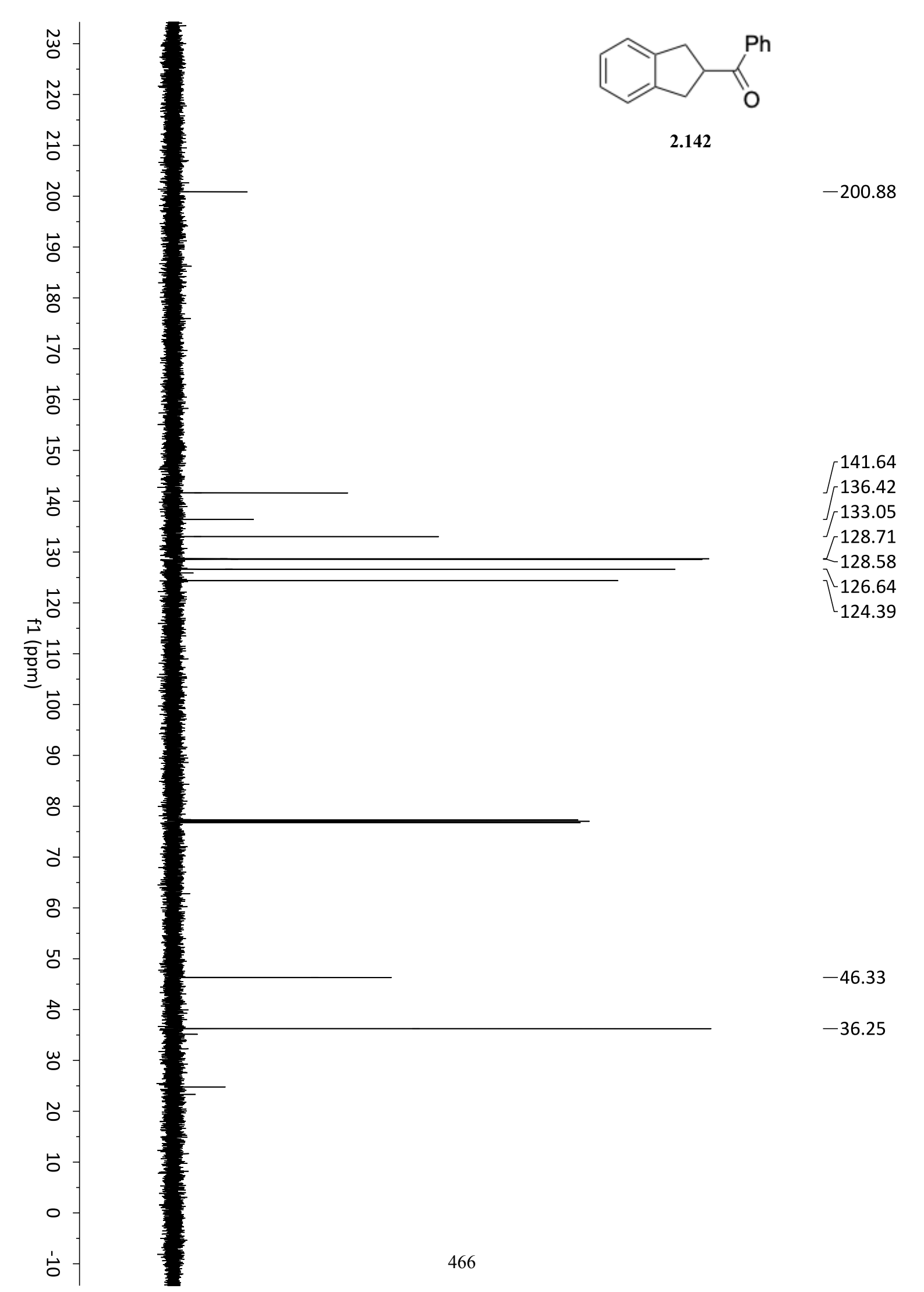
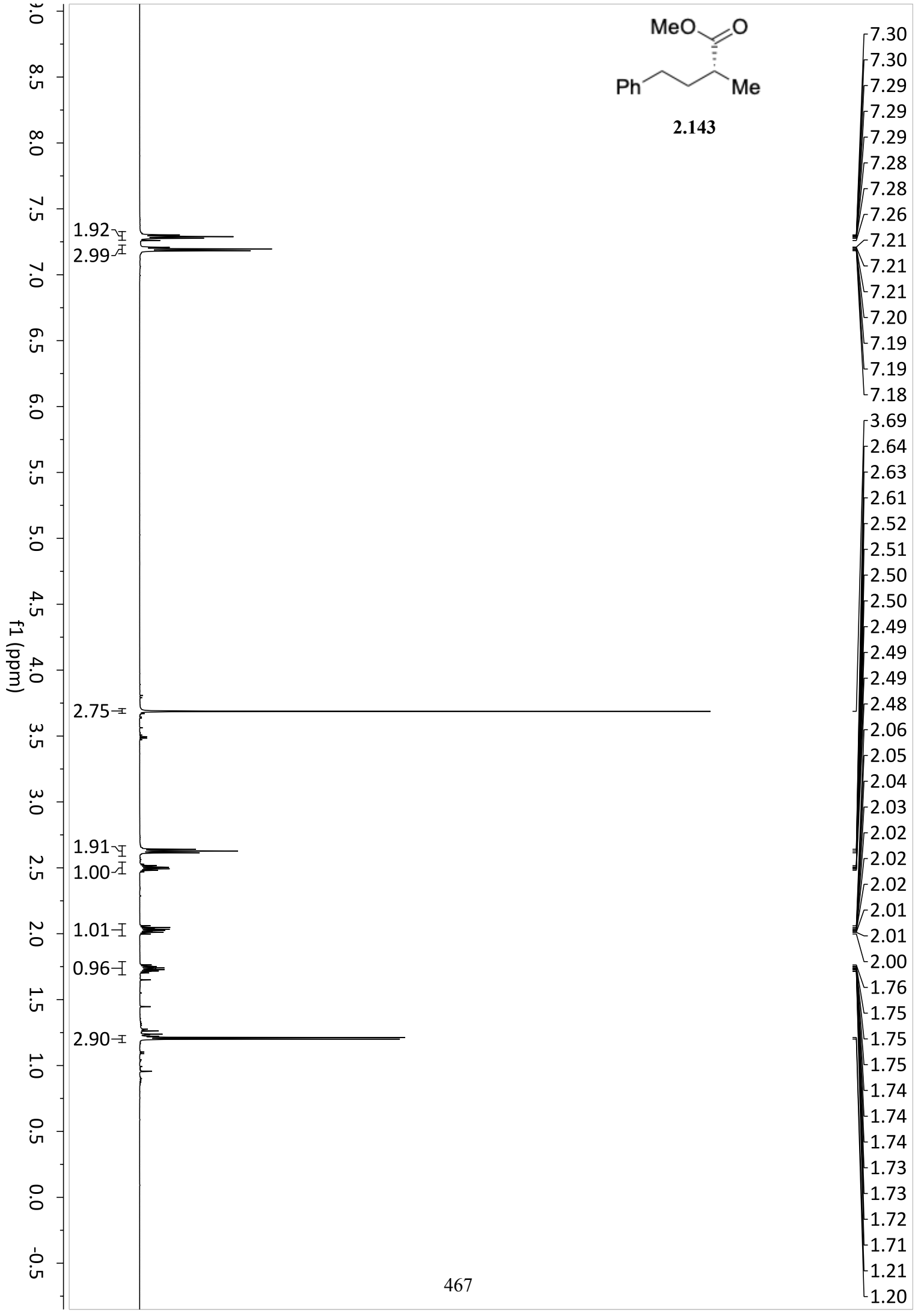
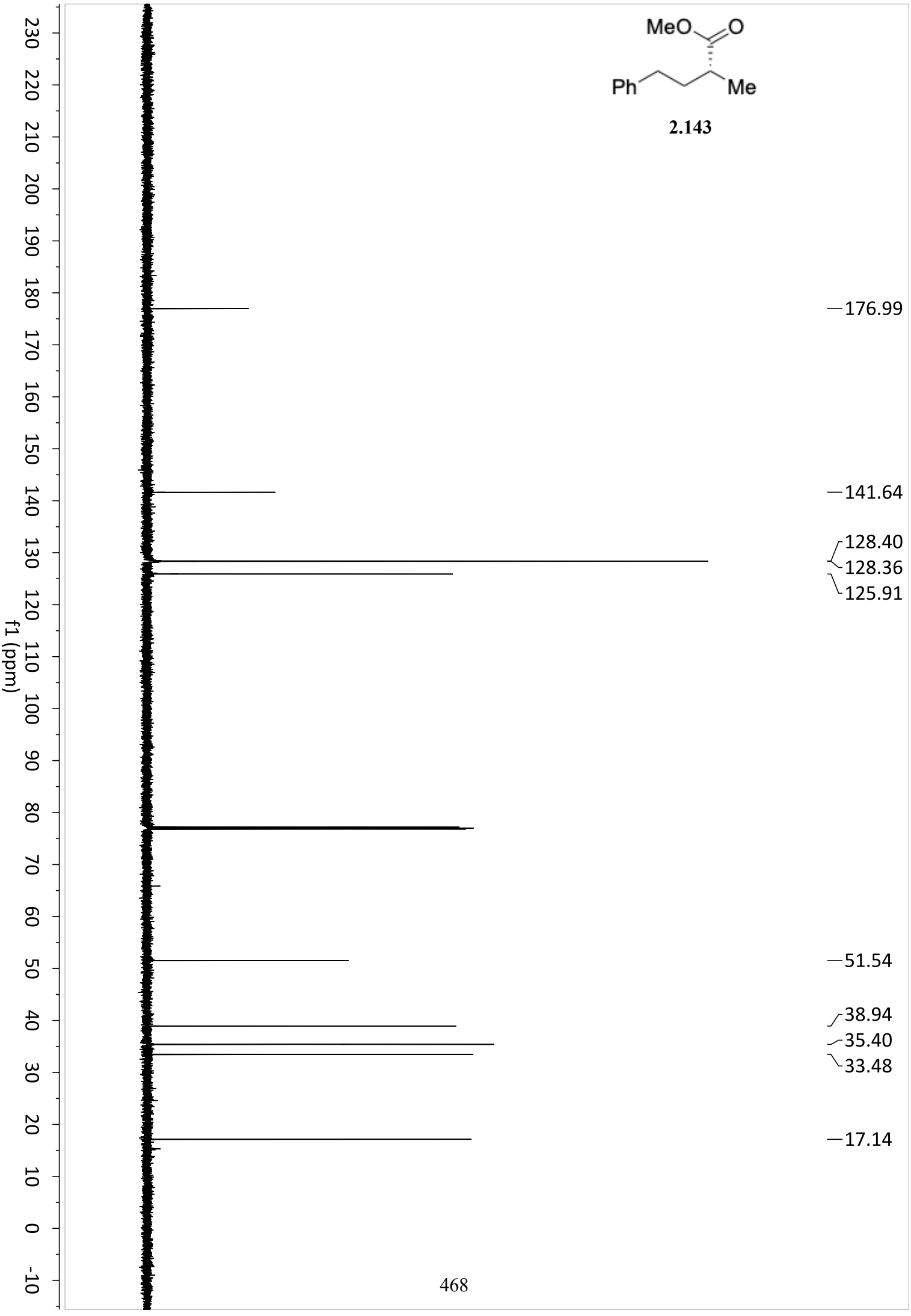
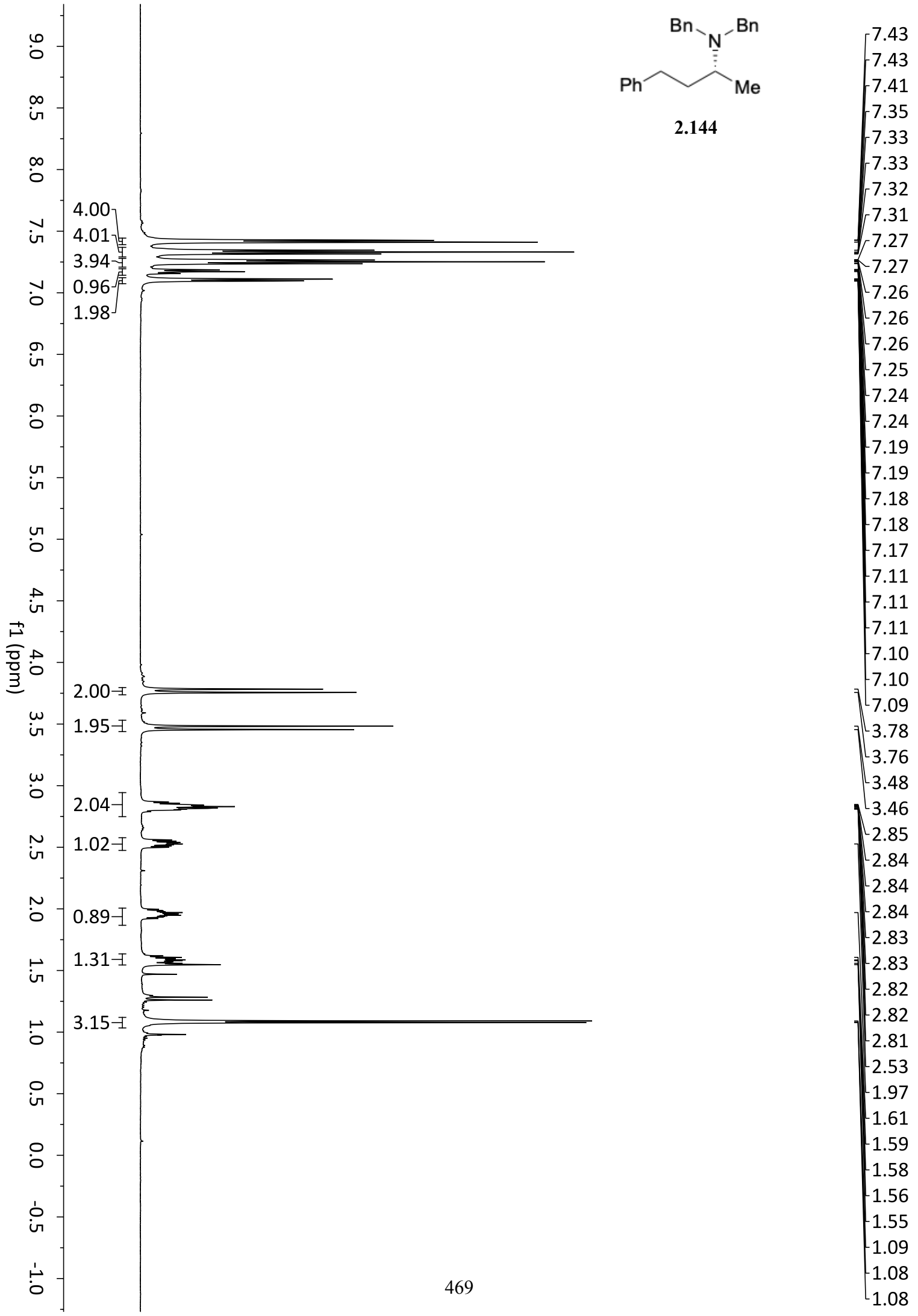
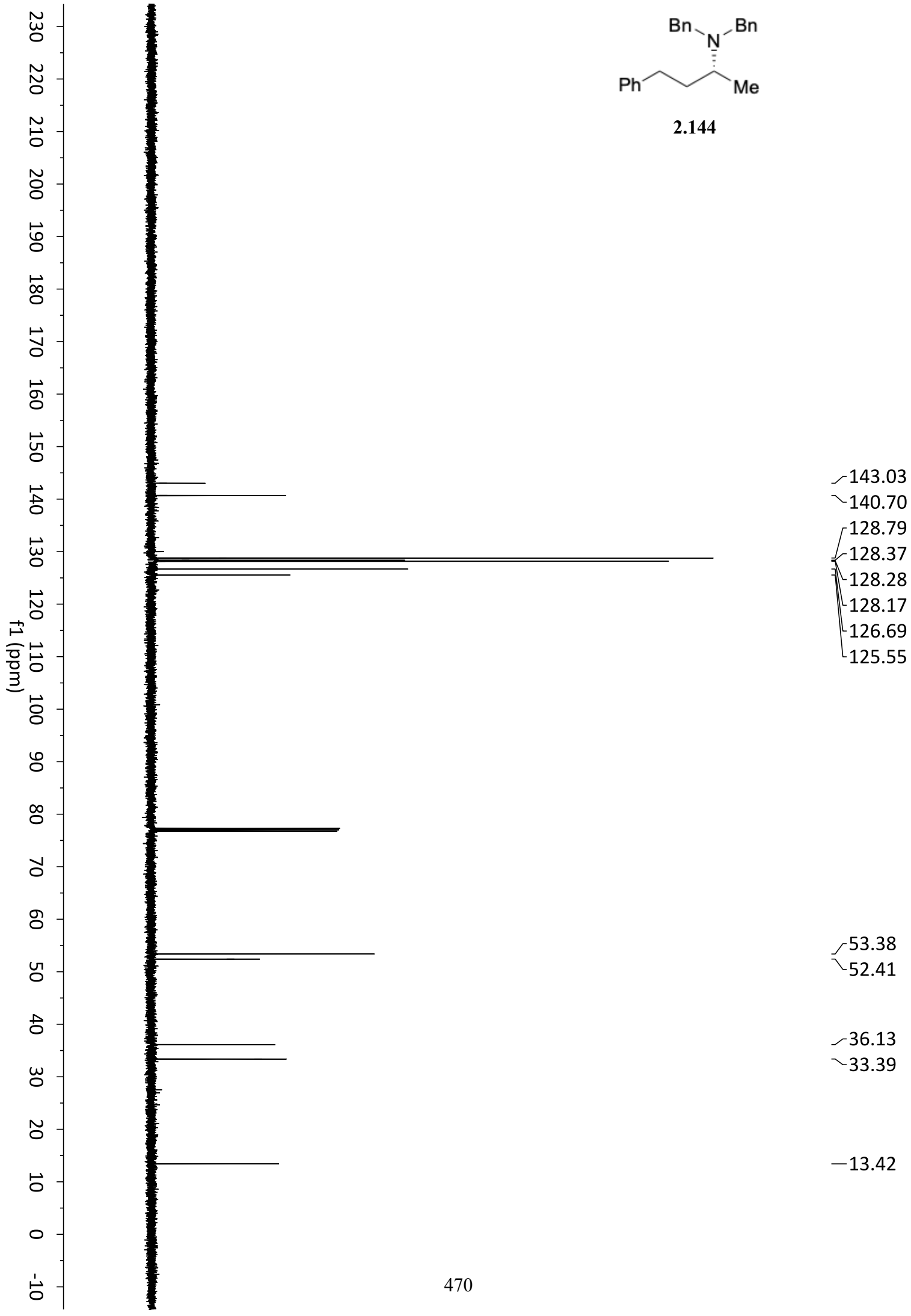
7.25
7.25
7.24
7.24
7.23
7.21
7.20
7.20
7.20
7.19
7.19
4.34
4.34
4.33
4.33
4.32
4.31
4.31
4.29
3.44
3.43
3.41
3.40
3.32
3.31
3.29
3.27


Ph
O
2.142
200.88
141.64
136.42
133.05
128.71
128.58
126.64
124.39
46.33
36.25
f1 (ppm)


MeO
O
Ph
Me
2.143
1.92
2.99
2.75
1.91
1.00
1.01
0.96
2.90
f1 (ppm)
7.30
7.30
7.29
7.29
7.29
7.28
7.28
7.26
7.21
7.21
7.21
7.20
7.19
7.19
7.18
3.69
2.64
2.63
2.61
2.52
2.51
2.50
2.50
2.49
2.49
2.49
2.48
2.06
2.05
2.04
2.03
2.02
2.02
2.02
2.01
2.01
2.00
1.76
1.75
1.75
1.75
1.74
1.74
1.74
1.73
1.73
1.72
1.71
1.21
1.20


MeO
O
Ph
Me
2.143
176.99
141.64
128.40
128.36
125.91
51.54
38.94
35.40
33.48
17.14
f1 (ppm)


Bn
N
Bn
Ph
Me
2.144
4.00
4.01
3.94
0.96
1.98
2.00
1.95
2.04
1.02
0.89
1.31
3.15
f1 (ppm)
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
-1.0
7.43
7.43
7.41
7.35
7.33
7.33
7.32
7.31
7.27
7.27
7.26
7.26
7.26
7.25
7.24
7.24
7.19
7.19
7.18
7.18
7.17
7.11
7.11
7.11
7.10
7.10
7.09
3.78
3.76
3.48
3.46
2.85
2.84
2.84
2.84
2.83
2.83
2.82
2.82
2.81
2.53
1.97
1.61
1.59
1.58
1.56
1.55
1.09
1.08
1.08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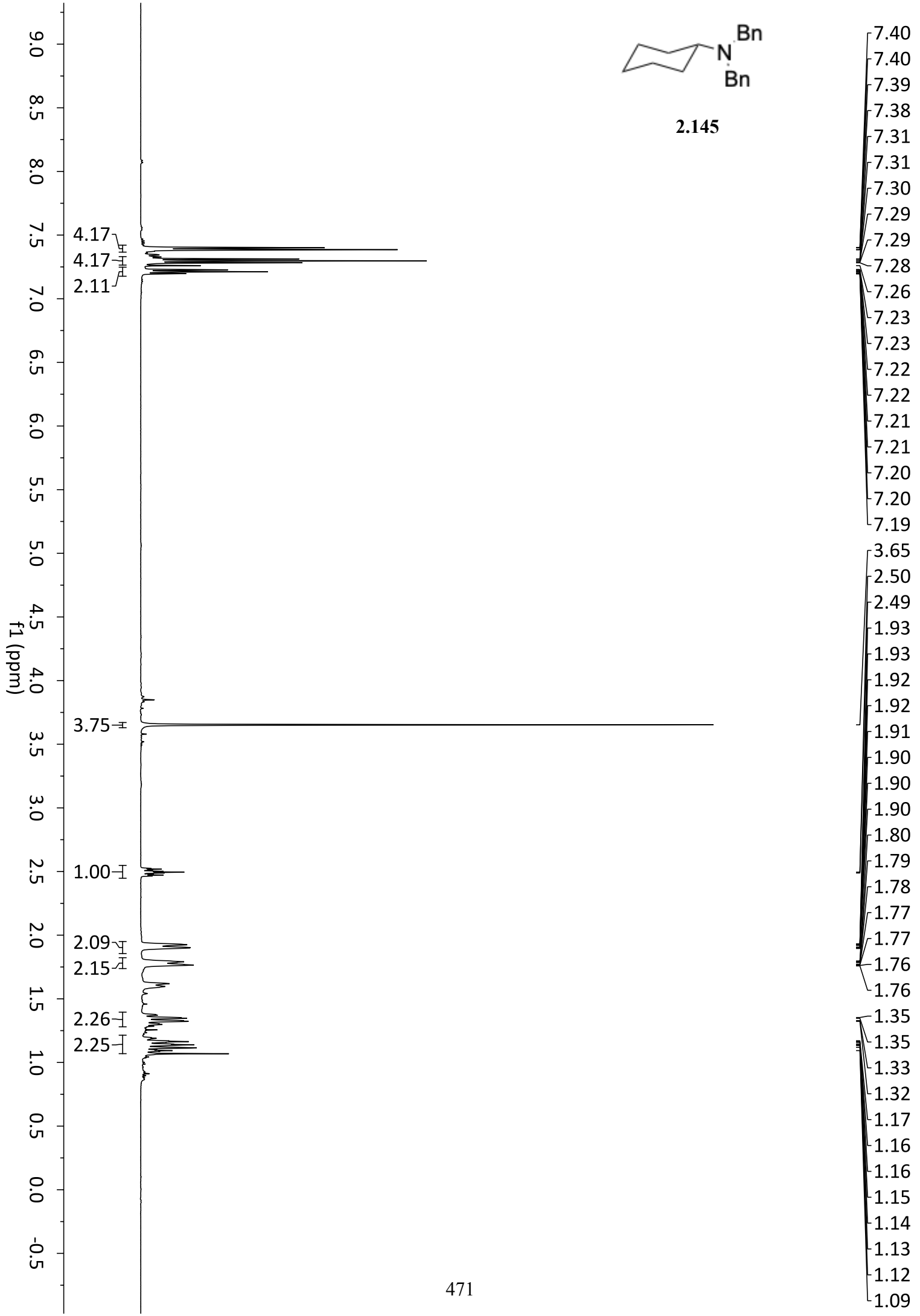
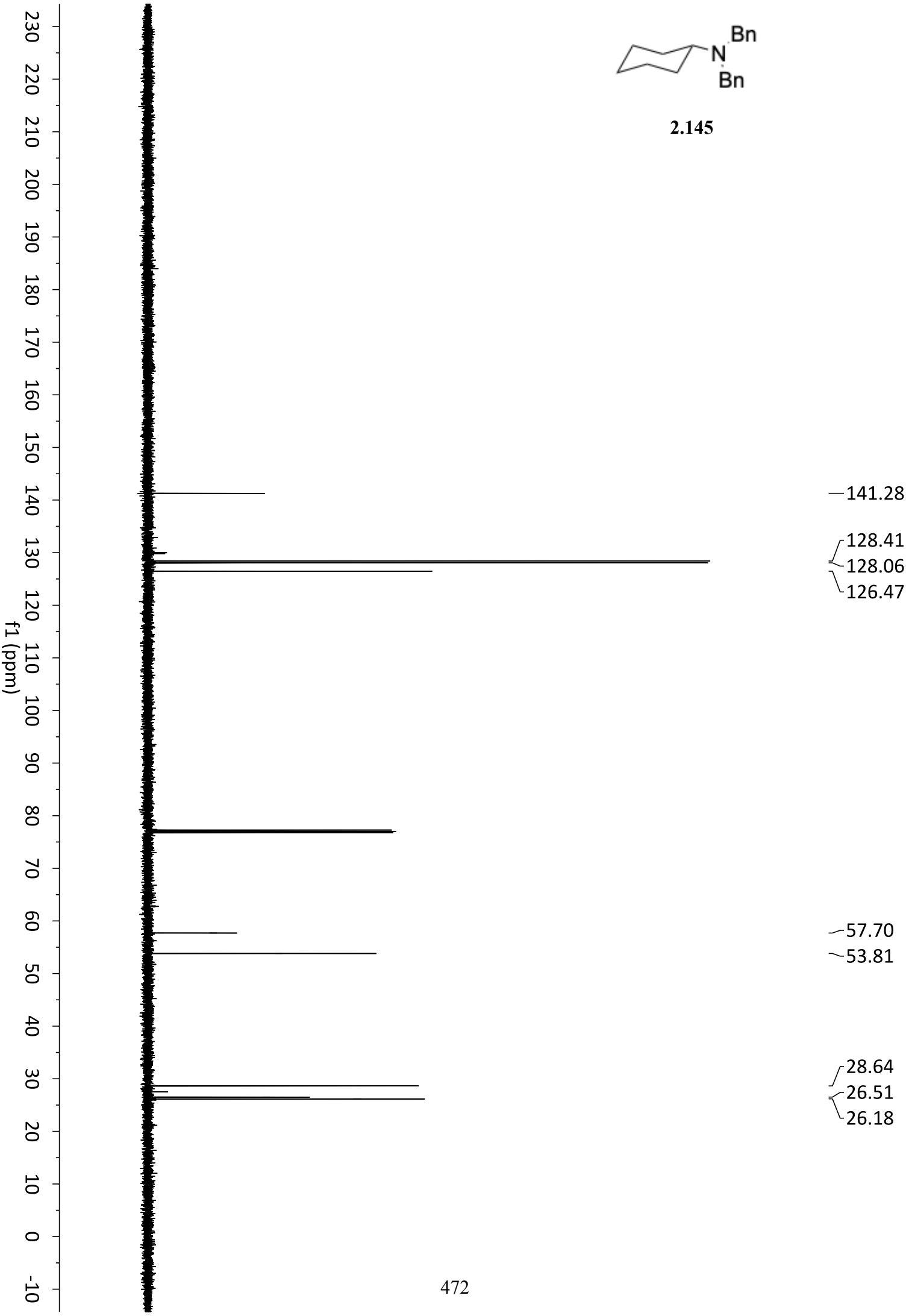
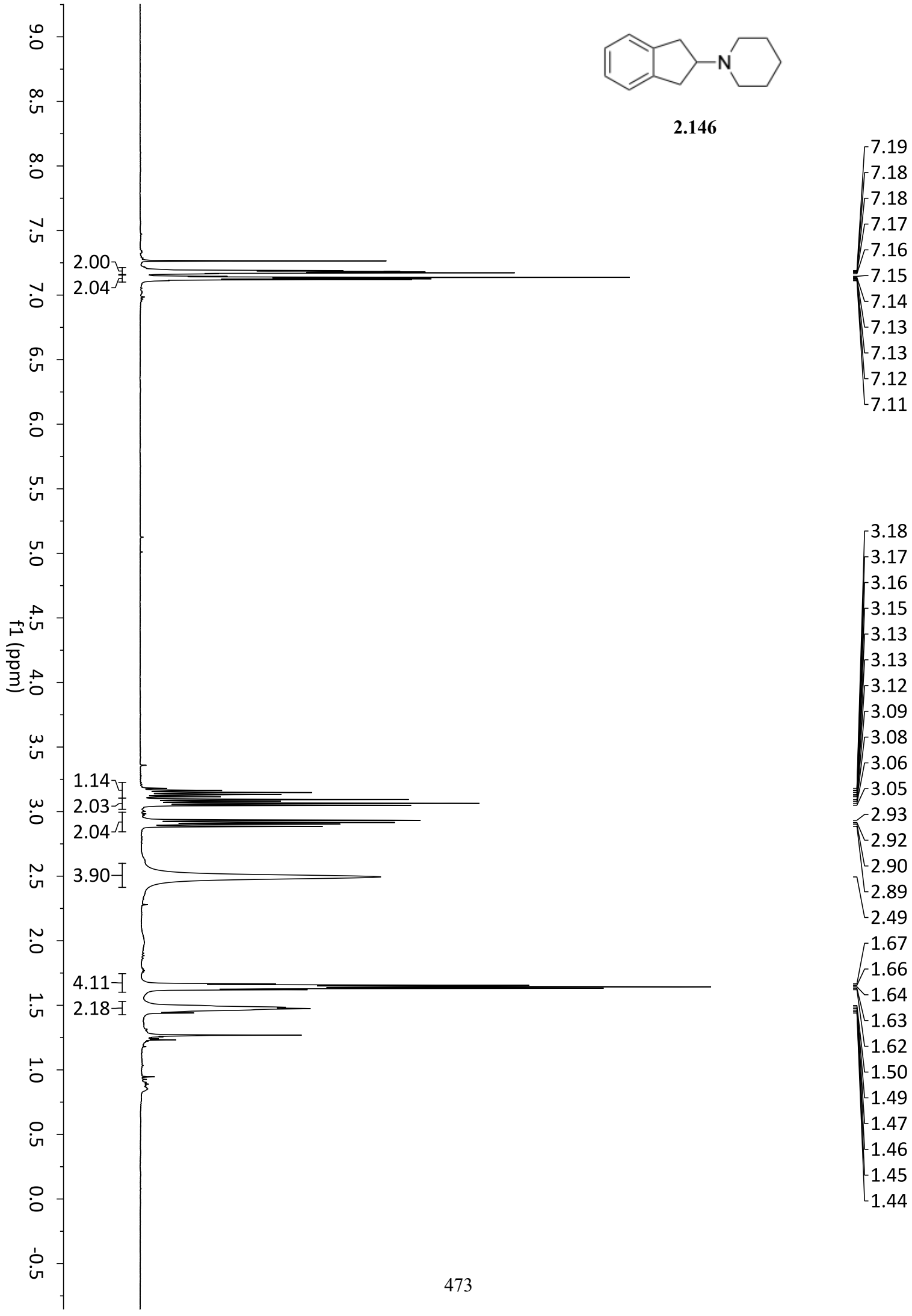
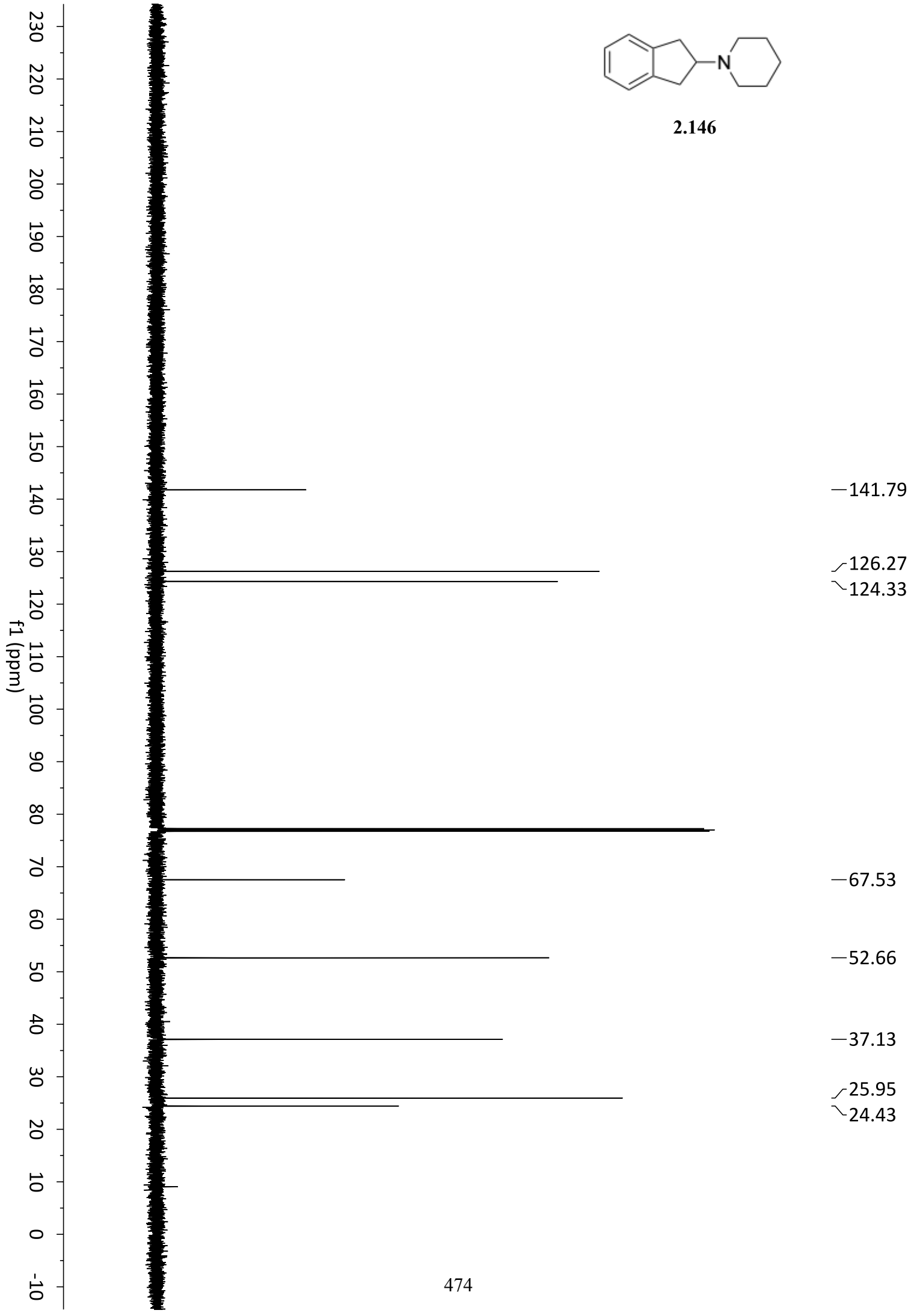
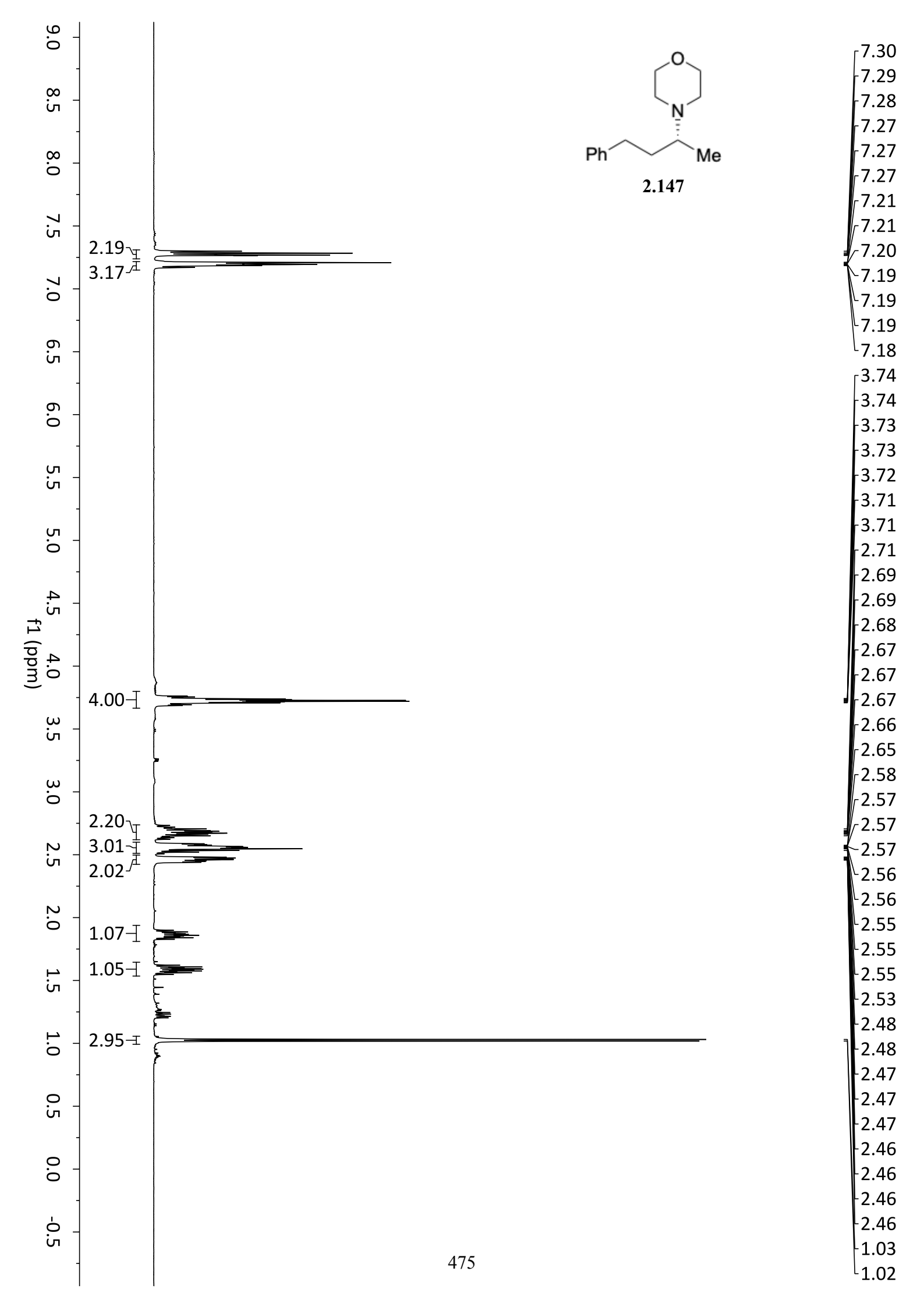
N
Bn
Ph
Me
2.144
143.03
140.70
128.79
128.37
128.28
128.17
126.69
125.55
53.38
52.41
36.13
33.39
13.42
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

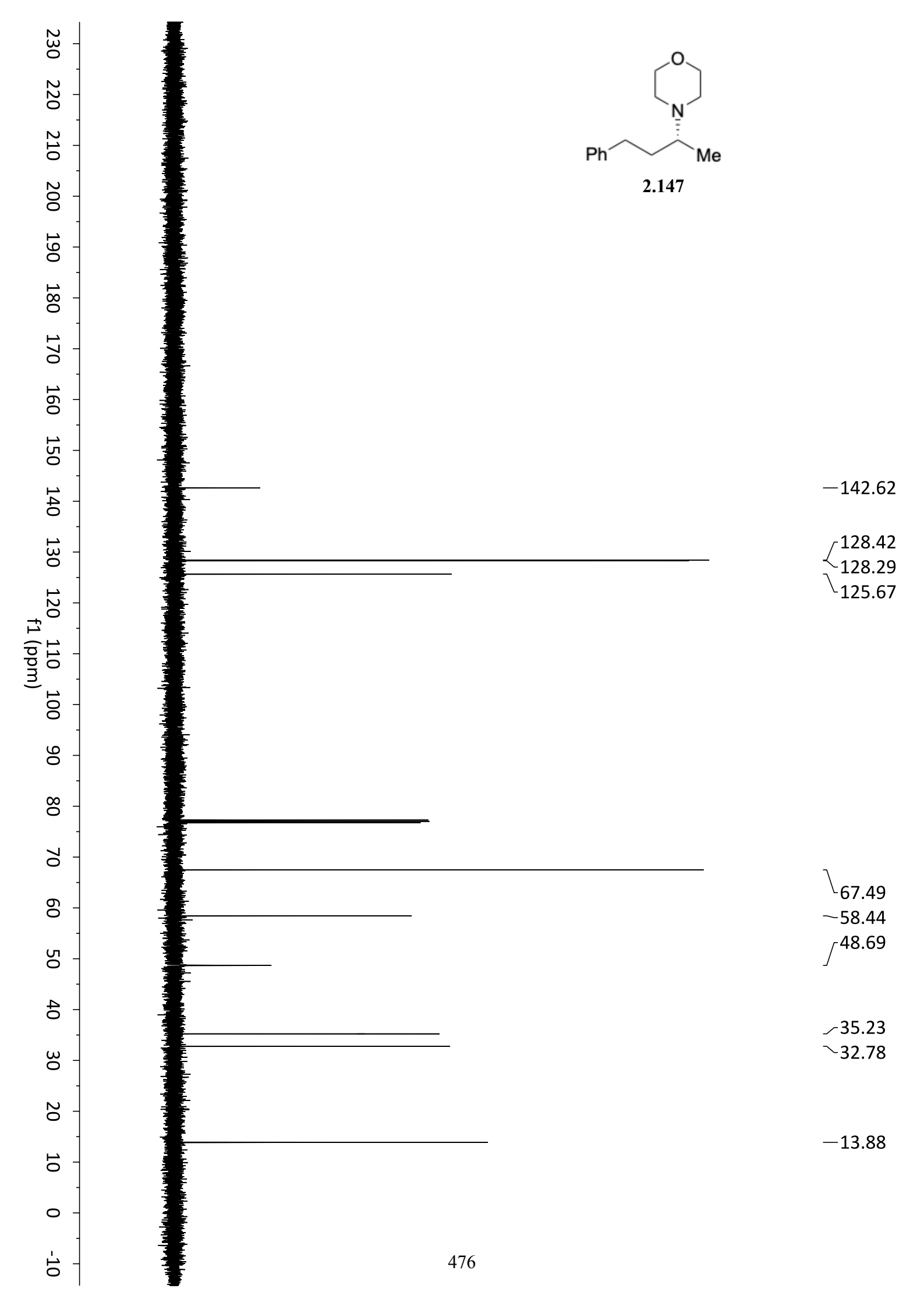

Bn
N
Bn
2.145
f1 (ppm)
4.17
4.17
2.11
3.75
1.00
2.09
2.15
2.26
2.25
7.40
7.40
7.39
7.38
7.31
7.31
7.30
7.29
7.29
7.28
7.26
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.20
7.19
3.65
2.50
2.49
1.93
1.93
1.92
1.92
1.91
1.90
1.90
1.90
1.80
1.79
1.78
1.77
1.77
1.76
1.76
1.35
1.35
1.33
1.32
1.17
1.16
1.16
1.15
1.14
1.13
1.12
1.09

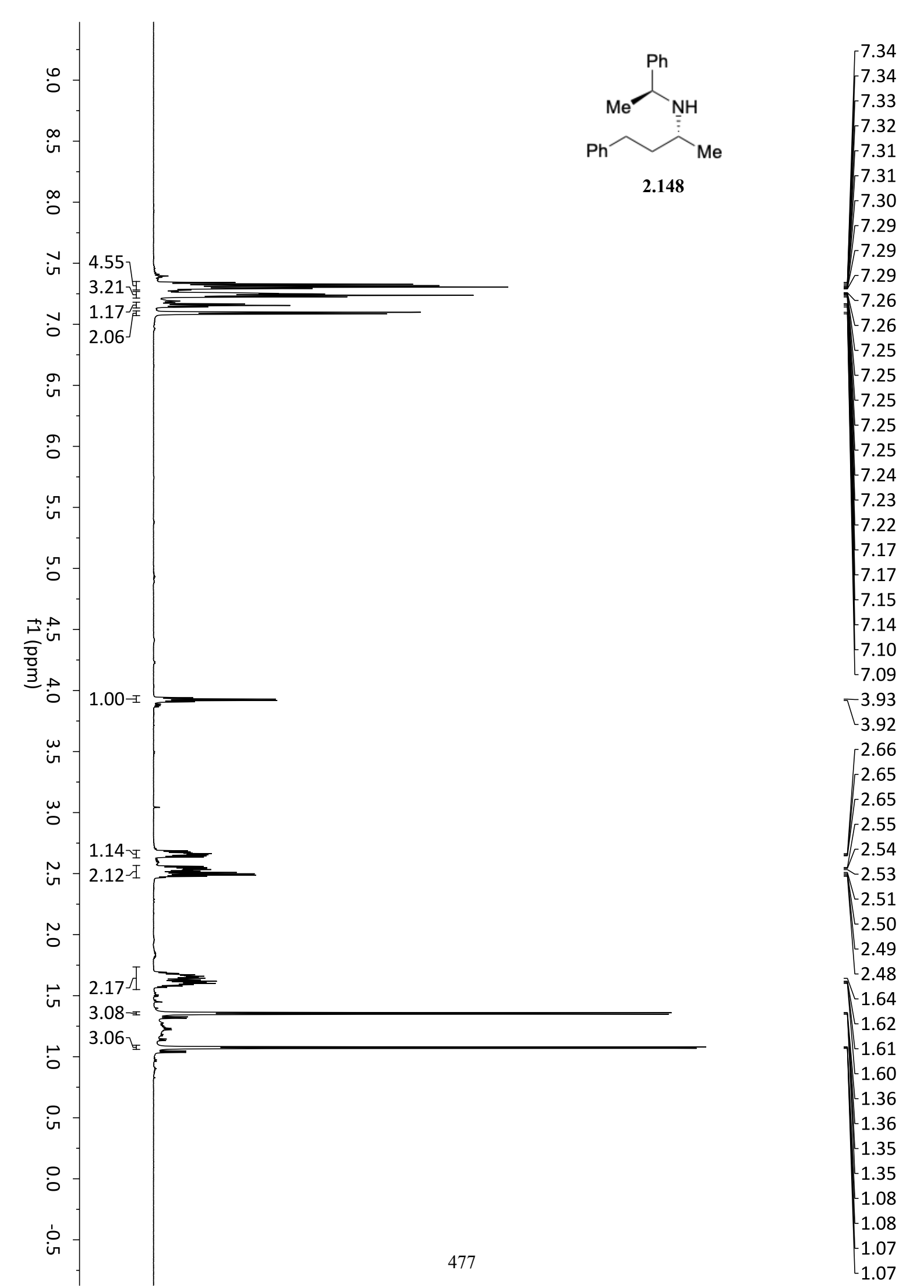

Bn
N
Bn
2.145
141.28
128.41
128.06
126.47
57.70
53.81
28.64
26.51
26.18
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

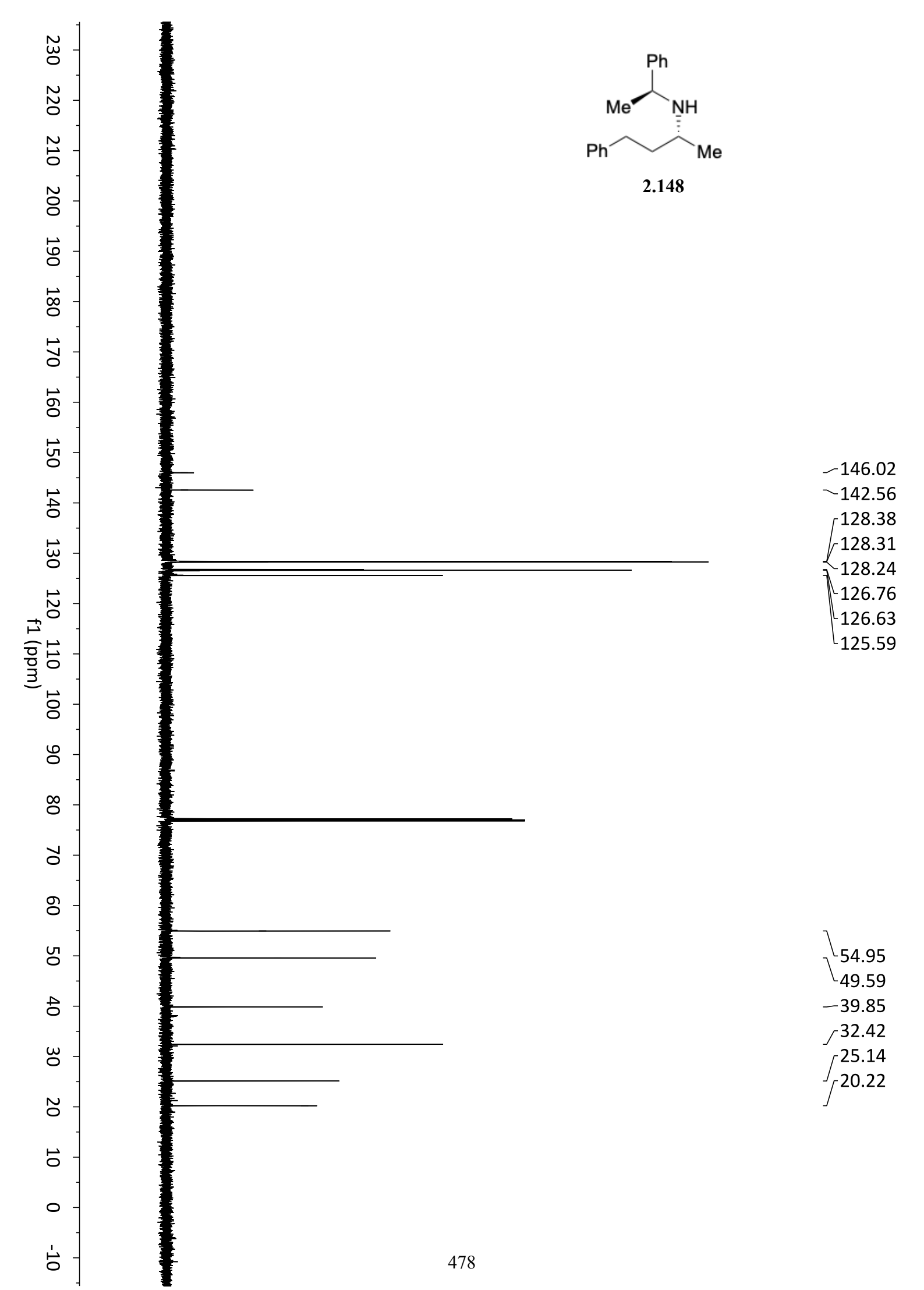

N
2.146
7.19
7.18
7.18
7.17
7.16
7.15
7.14
7.13
7.13
7.12
7.11
3.18
3.17
3.16
3.15
3.13
3.13
3.12
3.09
3.08
3.06
3.05
2.93
2.92
2.90
2.89
2.49
1.67
1.66
1.64
1.63
1.62
1.50
1.49
1.47
1.46
1.45
1.44
2.00
2.04
1.14
2.03
2.04
3.90
4.11
2.18
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

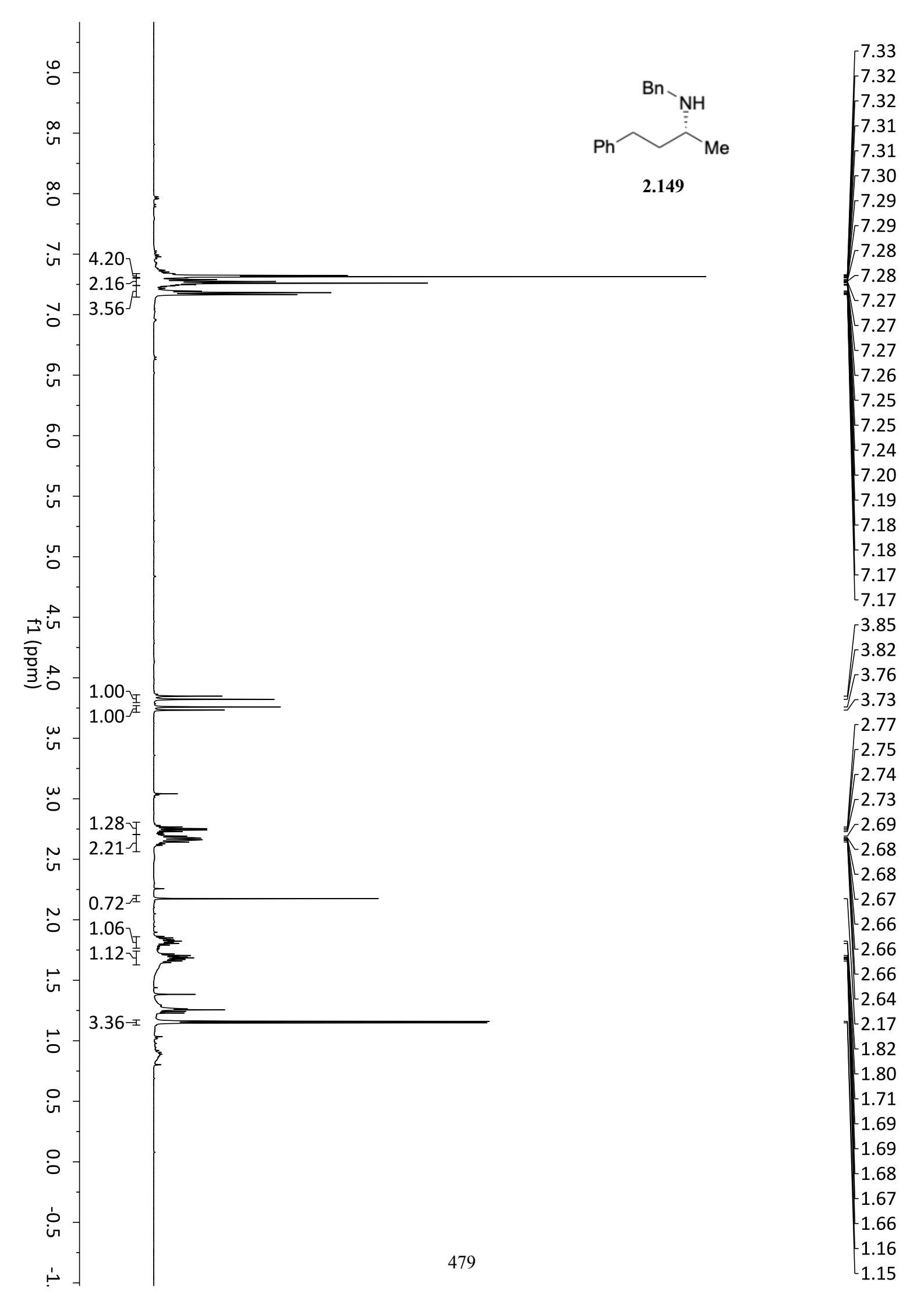

N
2.146
141.79
126.27
124.33
67.53
52.66
37.13
25.95
24.43
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

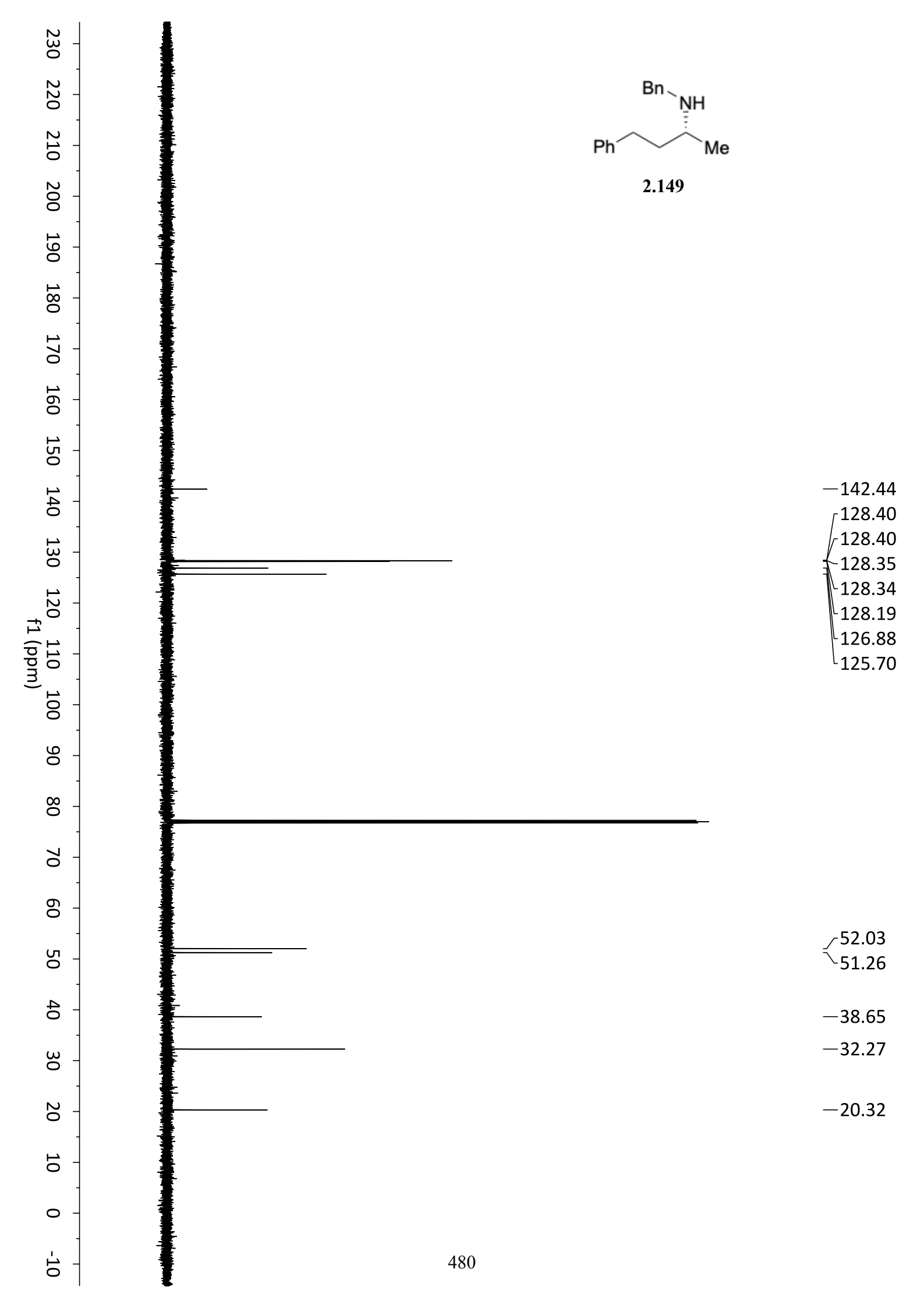

O
N
Ph
Me
2.147
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.19
3.17
4.00
2.20
3.01
2.02
1.07
1.05
2.95
7.30
7.29
7.28
7.27
7.27
7.27
7.21
7.21
7.20
7.19
7.19
7.19
7.18
3.74
3.74
3.73
3.73
3.72
3.71
3.71
2.71
2.69
2.69
2.68
2.67
2.67
2.67
2.66
2.65
2.58
2.57
2.57
2.57
2.56
2.56
2.55
2.55
2.55
2.53
2.48
2.48
2.47
2.47
2.47
2.46
2.46
2.46
2.46
2.46
1.03
1.02

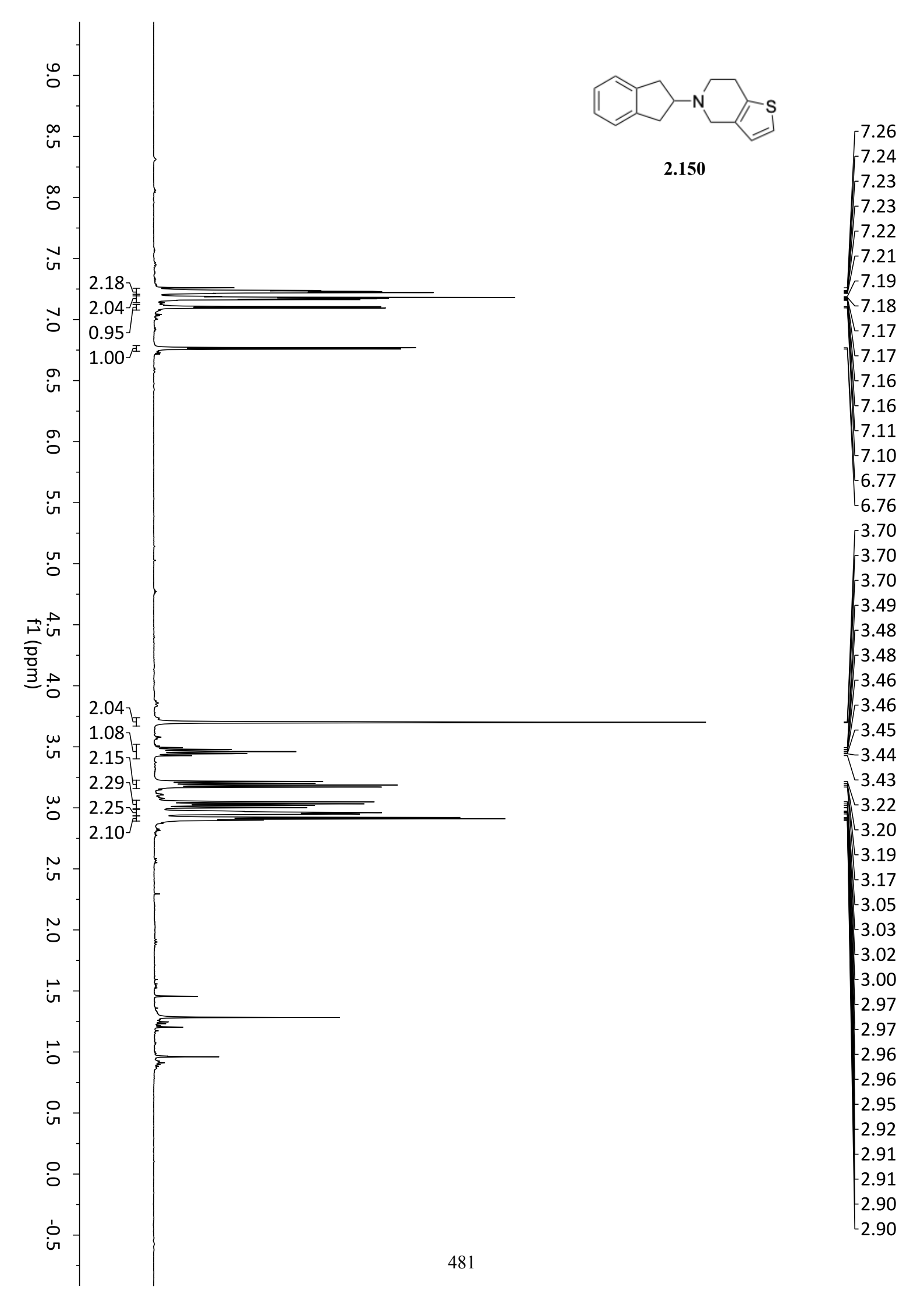

O
N
Ph
Me
2.147
142.62
128.42
128.29
125.67
67.49
58.44
48.69
35.23
32.78
13.88
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
Me
NH
Ph
Me
2.148
f1 (ppm)
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
4.55
3.21
1.17
2.06
1.00
1.14
2.12
2.17
3.08
3.06
7.34
7.34
7.33
7.32
7.31
7.31
7.30
7.29
7.29
7.29
7.26
7.26
7.25
7.25
7.25
7.25
7.25
7.24
7.23
7.22
7.17
7.17
7.15
7.14
7.10
7.09
3.93
3.92
2.66
2.65
2.65
2.55
2.54
2.53
2.51
2.50
2.49
2.48
1.64
1.62
1.61
1.60
1.36
1.36
1.35
1.35
1.08
1.08
1.07
1.07


Ph
Me
NH
Ph
Me
2.148
146.02
142.56
128.38
128.31
128.24
126.76
126.63
125.59
54.95
49.59
39.85
32.42
25.14
20.22
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Bn
NH
Ph
Me
2.149
4.20
2.16
3.56
1.00
1.00
1.28
2.21
0.72
1.06
1.12
3.36
f1 (ppm)
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.
7.33
7.32
7.32
7.31
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.27
7.26
7.25
7.25
7.24
7.20
7.19
7.18
7.18
7.17
7.17
3.85
3.82
3.76
3.73
2.77
2.75
2.74
2.73
2.69
2.68
2.68
2.67
2.66
2.66
2.66
2.64
2.17
1.82
1.80
1.71
1.69
1.69
1.68
1.67
1.66
1.16
1.15


Bn
NH
Ph
Me
2.149
142.44
128.40
128.40
128.35
128.34
128.19
126.88
125.70
52.03
51.26
38.65
32.27
20.32
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


N
S
2.150
2.18
2.04
0.95
1.00
2.04
1.08
2.15
2.29
2.25
2.10
f1 (ppm)
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
7.26
7.24
7.23
7.23
7.22
7.21
7.19
7.18
7.17
7.17
7.16
7.16
7.11
7.10
6.77
6.76
3.70
3.70
3.70
3.49
3.48
3.48
3.46
3.46
3.45
3.44
3.43
3.22
3.20
3.19
3.17
3.05
3.03
3.02
3.00
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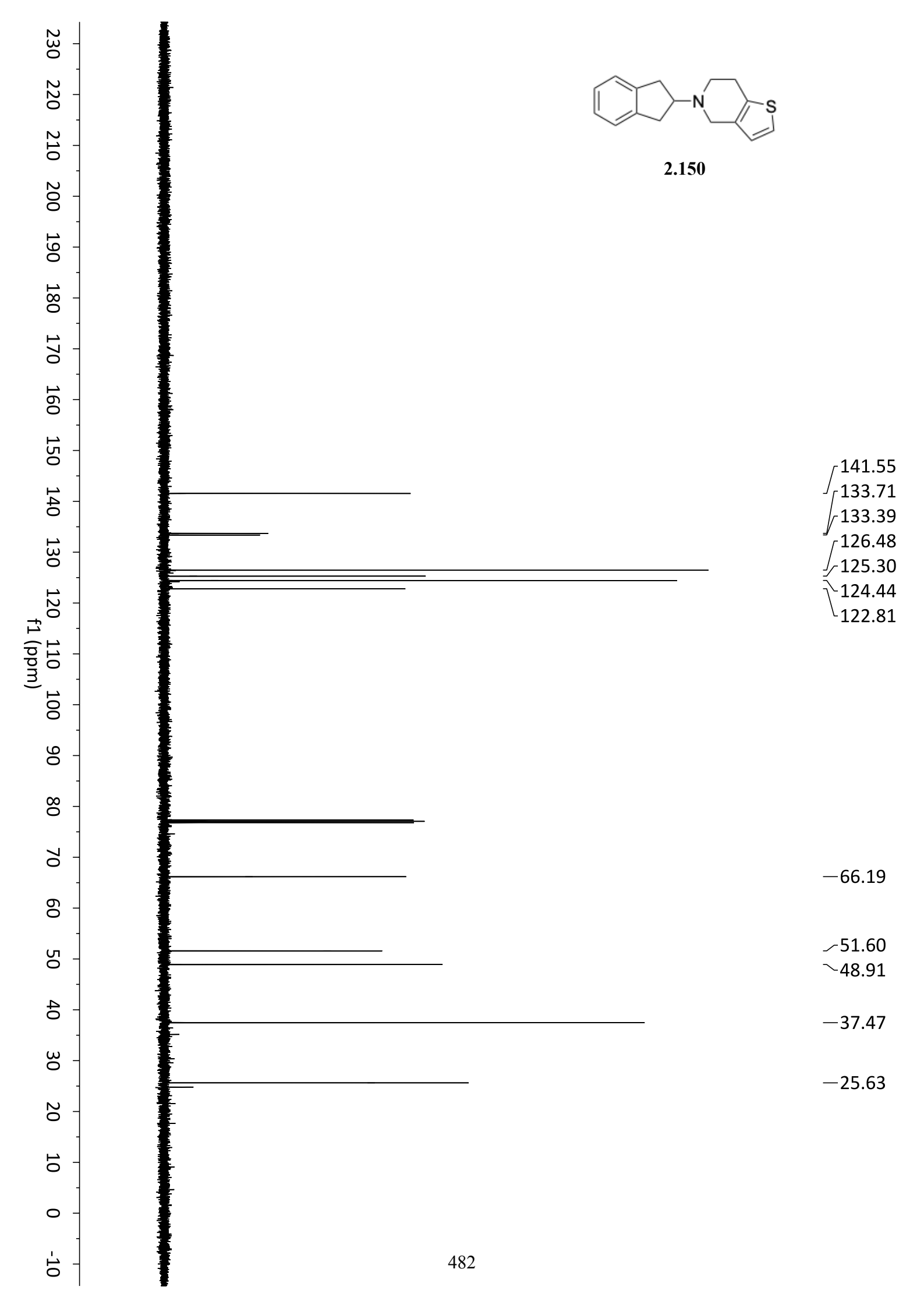
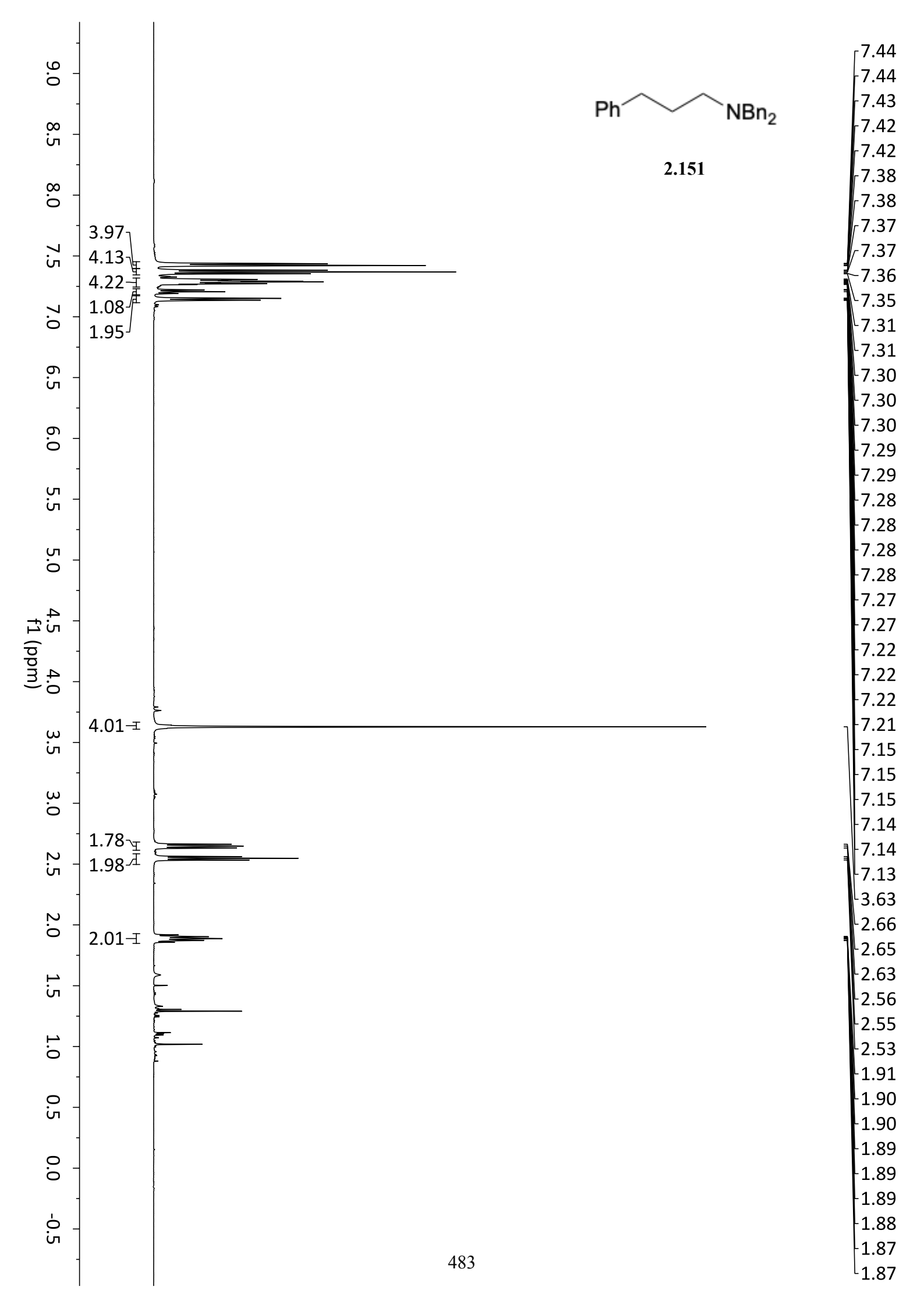
2.97
2.96
2.96
2.95
2.92
2.91
2.91
2.90
2.90


N
S
2.150
141.55
133.71
133.39
126.48
125.30
124.44
122.81
66.19
51.60
48.91
37.47
25.63
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
NBn2
2.151
3.97
4.13
4.22
1.08
1.95
4.01
1.78
1.98
2.01
f1 (ppm)
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
7.44
7.44
7.43
7.42
7.42
7.38
7.38
7.37
7.37
7.36
7.35
7.31
7.31
7.30
7.30
7.30
7.29
7.29
7.28
7.28
7.28
7.28
7.28
7.27
7.27
7.22
7.22
7.22
7.21
7.15
7.15
7.15
7.14
7.14
7.13
3.63
2.66
2.65
2.63
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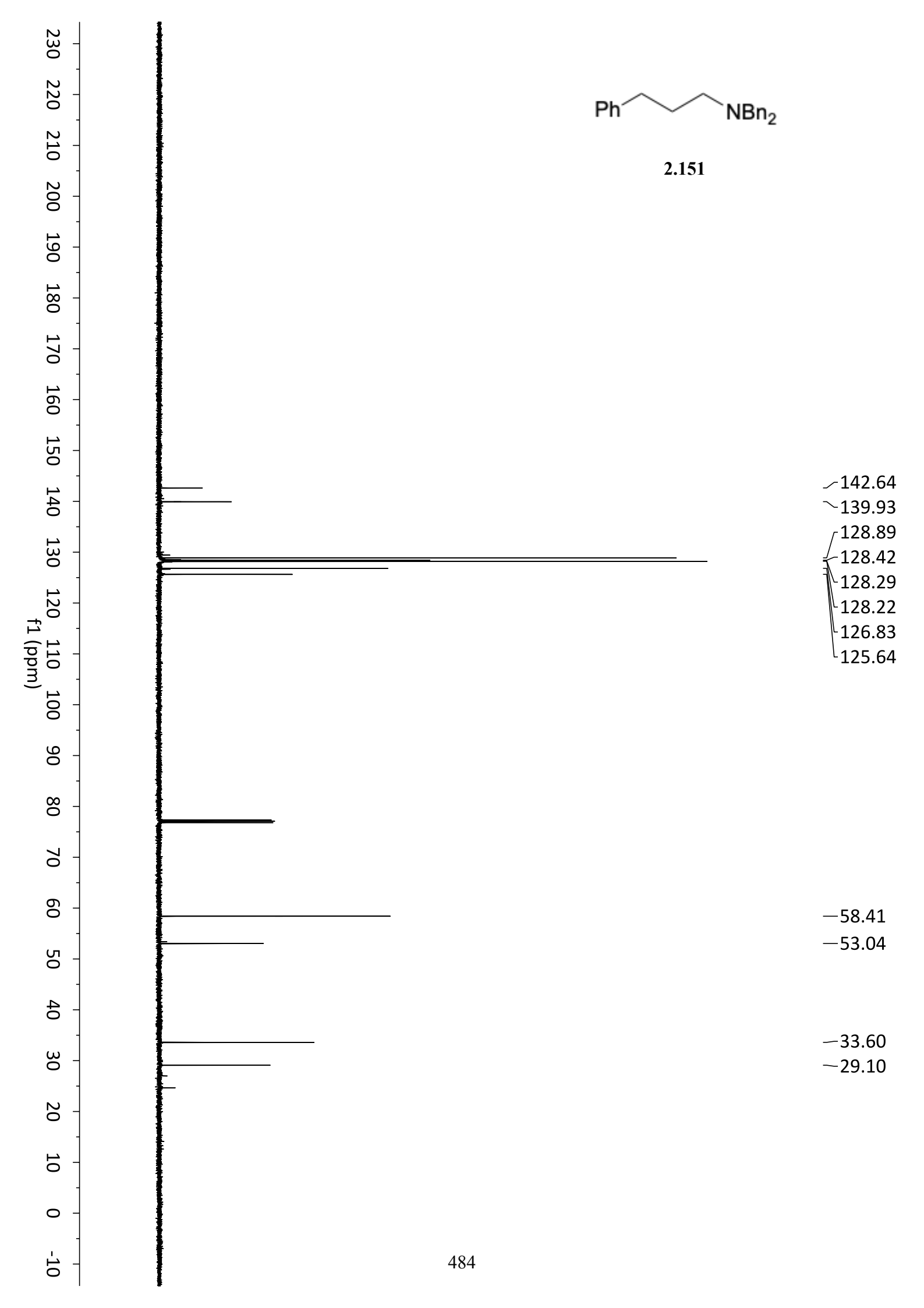
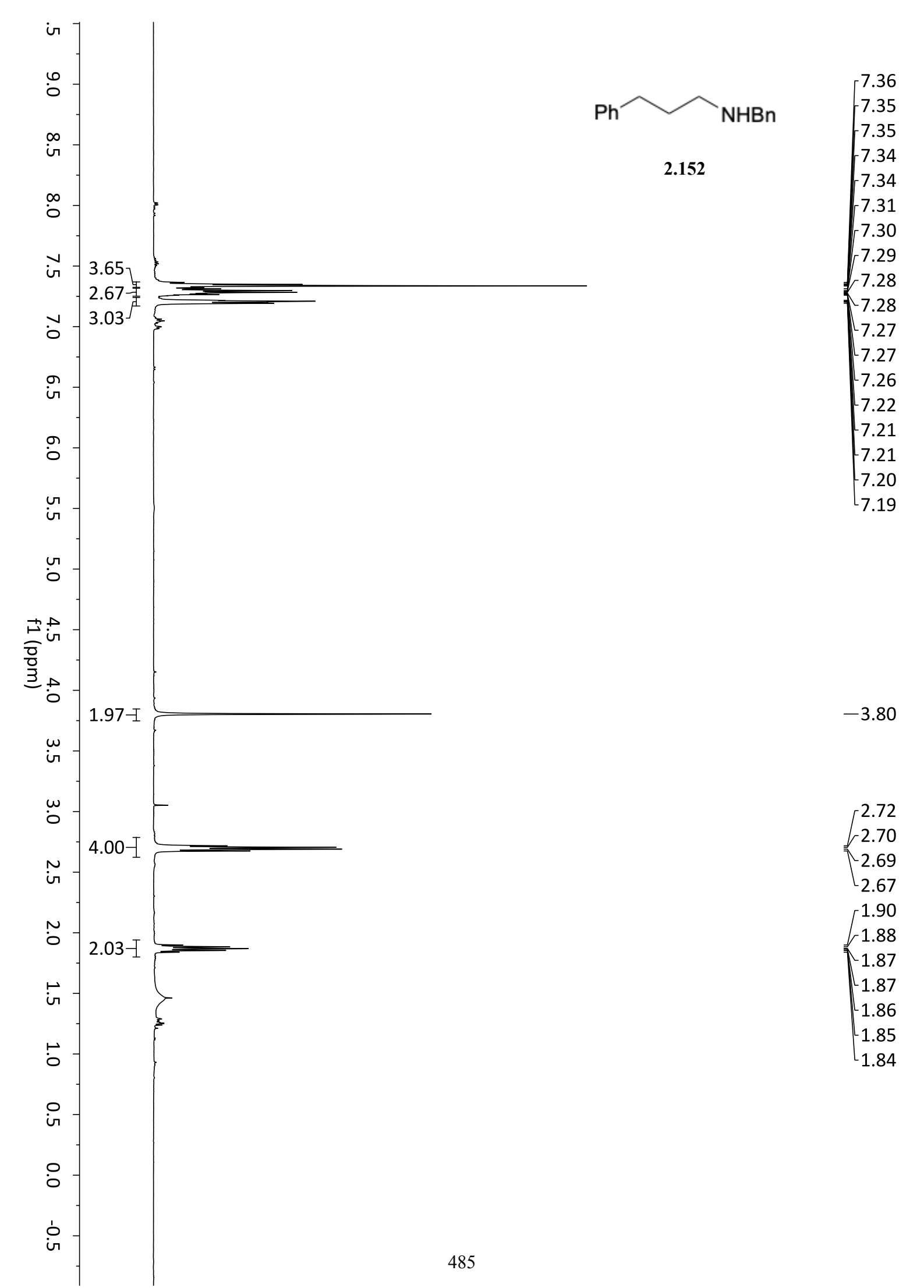
1.89
1.89
1.89
1.88
1.87
1.87


Ph
NBn2
2.151
142.64
139.93
128.89
128.42
128.29
128.22
126.83
125.64
58.41
53.04
33.60
29.10
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Ph
NHBn
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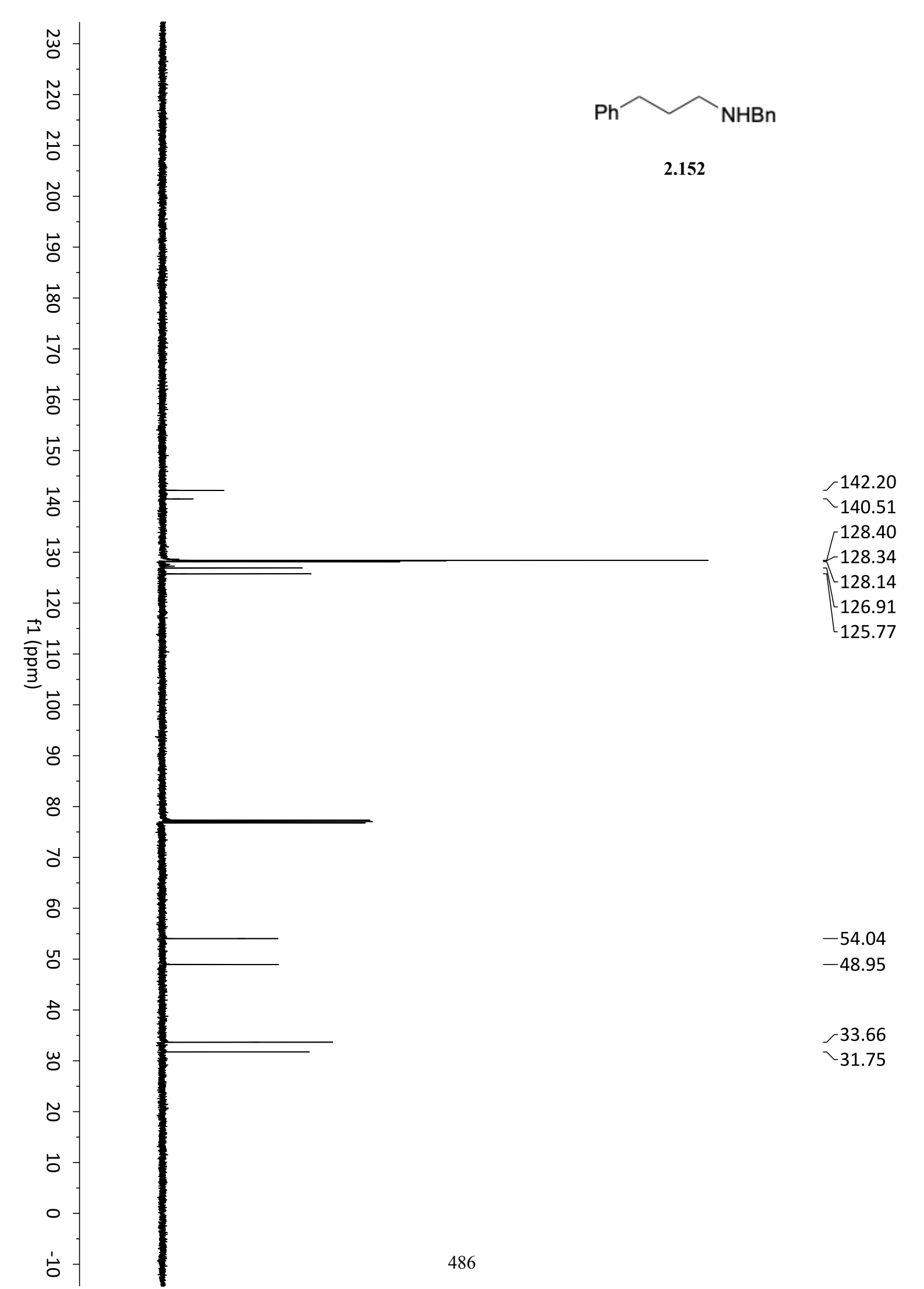
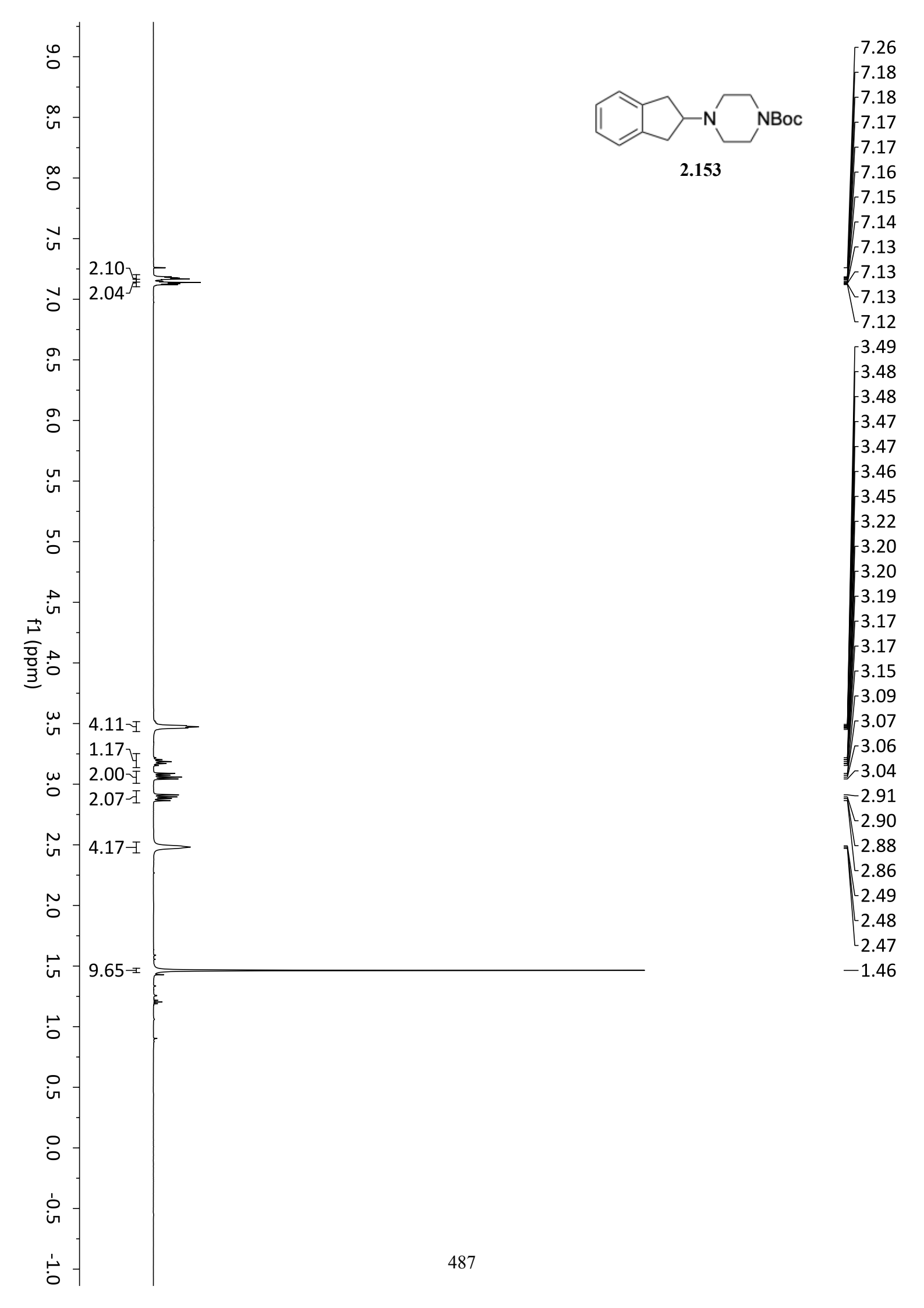
7.36
7.35
7.35
7.34
7.34
7.31
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.22
7.21
7.21
7.20
7.19
3.80
2.72
2.70
2.69
2.67
1.90
1.88
1.87
1.87
1.86
1.85
1.84
3.65
2.67
3.03
1.97
4.00
2.03
f1 (ppm)


Ph
NHBn
2.152
142.20
140.51
128.40
128.34
128.14
126.91
125.77
54.04
48.95
33.66
31.75
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10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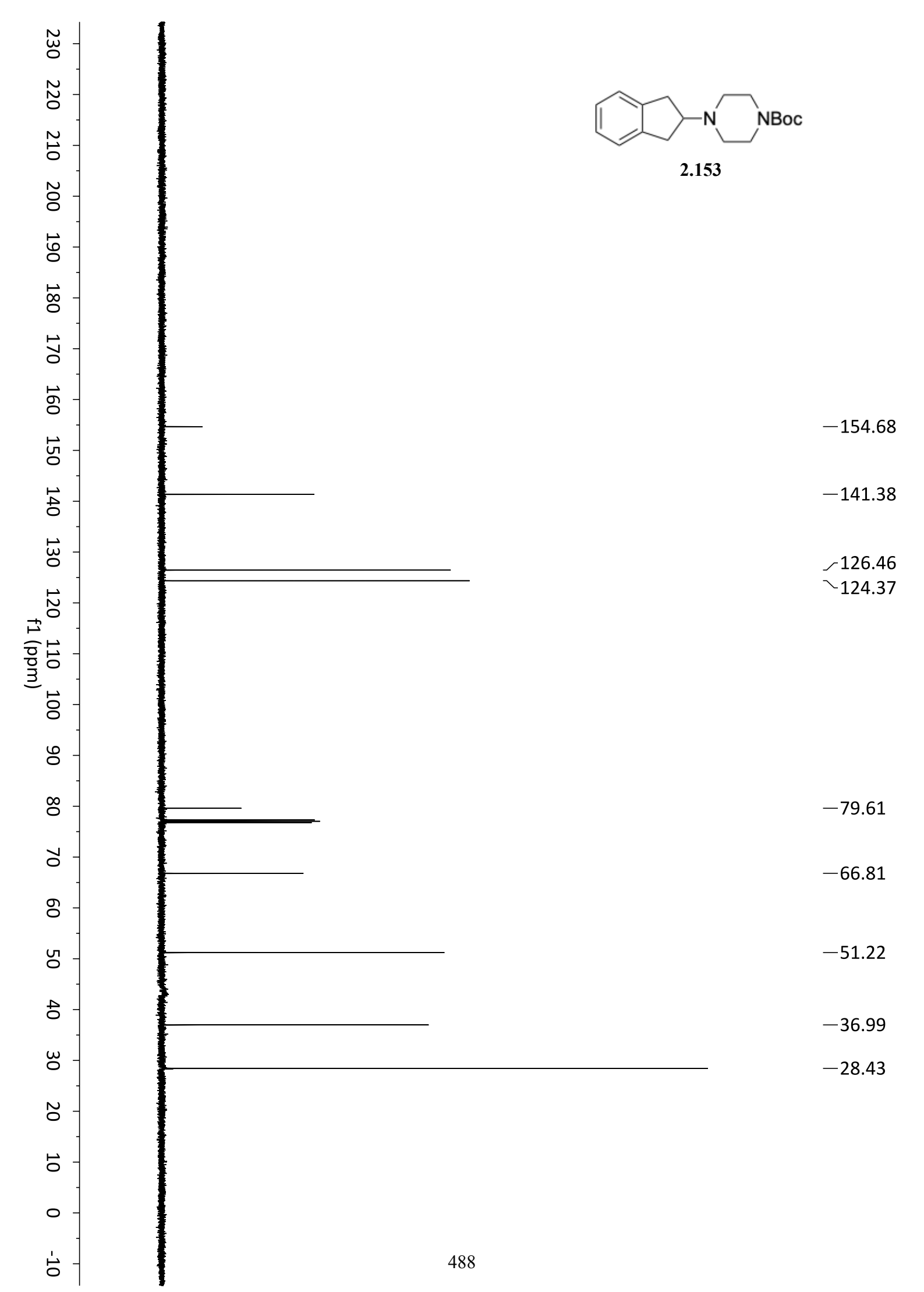
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
2.10
2.04
4.11
1.17
2.00
2.07
4.17
9.65
N
NBoc
2.153
7.26
7.18
7.18
7.17
7.17
7.16
7.15
7.14
7.13
7.13
7.13
7.13
7.12
3.49
3.48
3.48
3.47
3.47
3.46
3.45
3.22
3.20
3.20
3.19
3.17
3.17
3.15
3.09
3.07
3.06
3.04
2.91
2.90
2.88
2.86
2.49
2.48
2.47
1.46


N
NBoc
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154.68
141.38
126.46
124.37
79.61
66.81
51.22
36.99
28.43
f1 (ppm)
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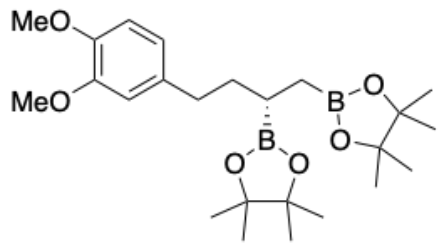
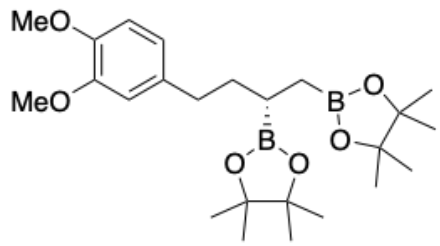
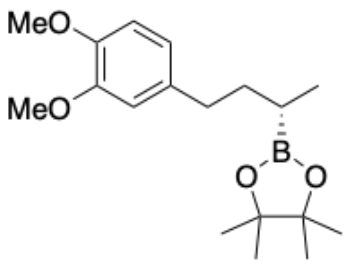


2.191

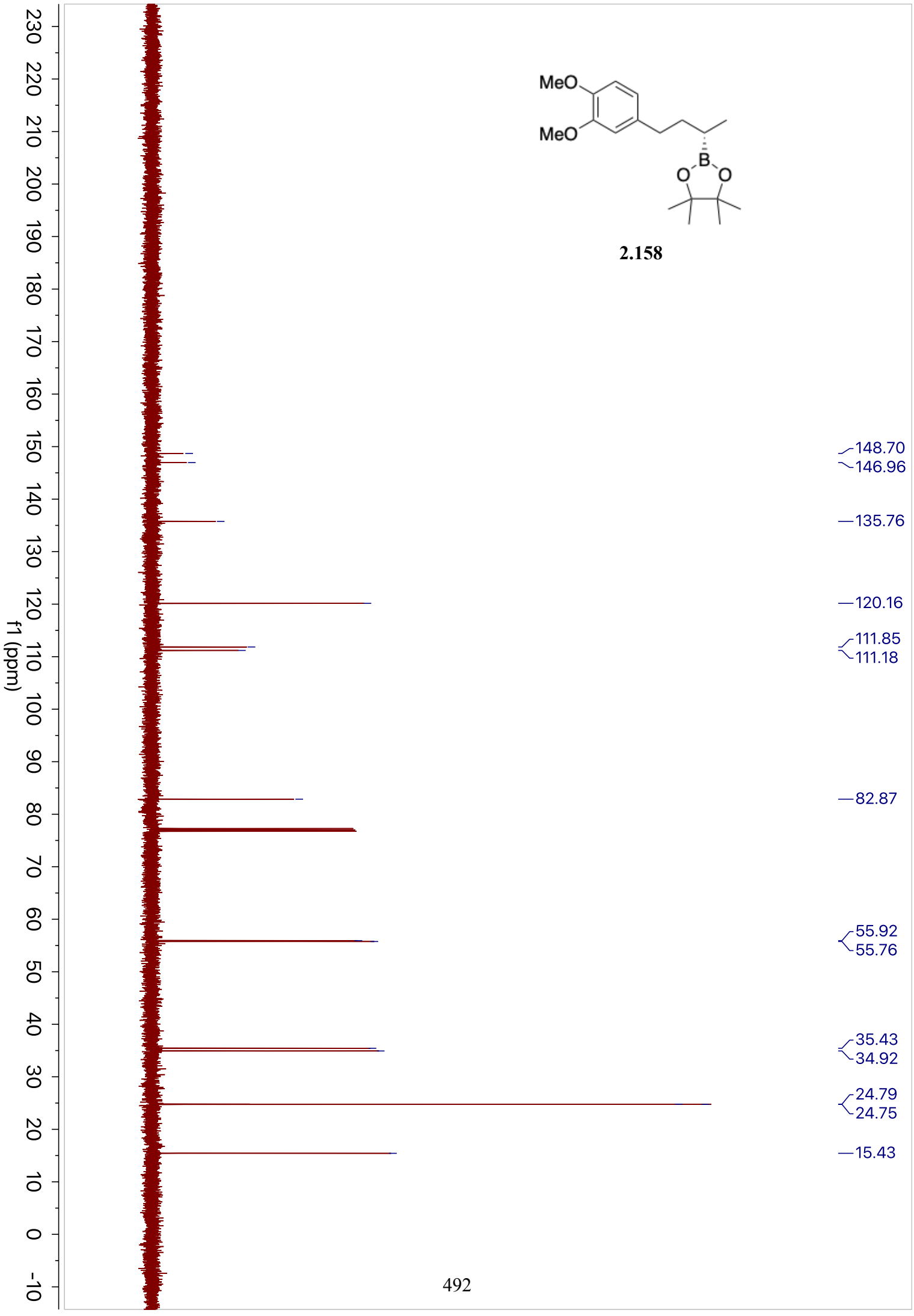

MeO
MeO
B
O
O
B
O
O

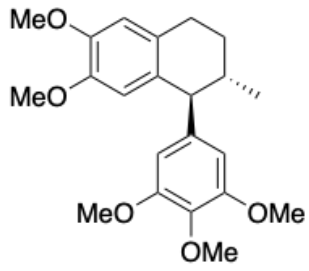
2.191

f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
148.67
146.90
136.00
120.14
111.88
111.19
82.85
55.93
55.74
36.04
34.88
24.90
24.88
24.79
24.77

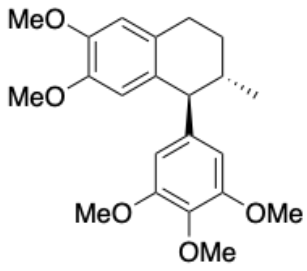


2.158


MeO
MeO
B
O
O
2.158
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
148.70
146.96
135.76
120.16
111.85
111.18
82.87
55.92
55.76
35.43
34.92
24.79
24.75
15.43



2.160


MeO
MeO
MeO
OMe
OMe

2.160

f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
152.89
147.18
146.94
142.09
136.25
131.34
129.08
113.14
111.02
106.32
77.33
77.08
76.82
60.85
56.12
55.93
55.74
54.20
37.27
30.58
28.68
20.57

Chapter 3. Site-Selective Activation and Stereospecific Functionalization of Bis(boronic Esters) Derived from 2-Alkenes: Construction of Propionates and Other 1,2-Difunctional Motifs

3.1 Introduction

Propionate-derived natural products are an important class of compounds that often exhibit potent biological activities.[1] Discodermolide[2] and erythronolide A[3] are archetypal polypropionates that have spurred the development of catalytic enantioselective methods for assembling motifs featuring a methyl-containing stereogenic center adjacent to an oxidized carbon center. Aldol addition and crotylation reactions (Scheme 3.1a) have been the primary methods for catalytic propionate synthesis, but several other approaches have also been devised to address propionate fragments.[4] In relation to these processes, a complementary method may arise from site-selective and enantioselective alkene difunctionalization (Scheme 3.1b).[5] This proposed method, specifically for propionate construction, would operate through the use of 2-alkene feedstocks. Notably, 2-alkenes can be easily prepared from inexpensive α-olefin precursors by scalable and

[1] Liu, Z.; Liu, H.; Zhang, W. *Marine Drugs* **2020**, *18*, 569

[2] (a) Gunasekera, S. P.; Gunasekera, M.; Longley, R. E.; Schulte, G. K. *J. Org. Chem.* **1990**, *55*, 4912–4915. For a selected review, see: (b) Paterson, I.; Florence, G. J. *Eur. J. Org. Chem.* **2003**, *12*, 2193–2208.

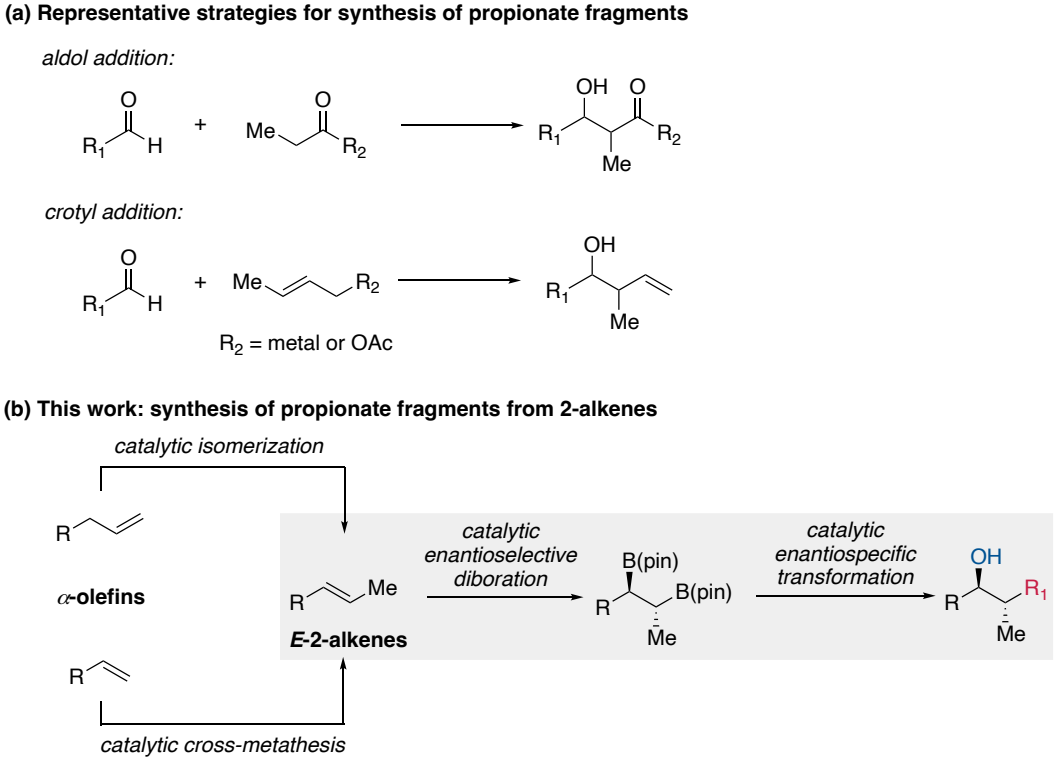
[3] (a) McGuire, J. M.; Bunch, R. L.; Anderson, R. C.; Boaz, H. E.; Flynn, E. H.; Powell, H. M.; Smith, J. W. *Antibiotics and Chemotherapy* **1952**, *2*, 281–283. For a selected review, see: (b) Mulzer, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1452–1454.

[4] For selected reviews on polypropionate synthesis, see: (a) Turks, M.; Laclef, S.; Vogel, P. In *Stereoselective Synthesis of Drugs and Natural Products*; Andrushko, V., Andrushko, N., Eds.; Wiley, 2013; pp 1–48. (b) Li, J.; Menche, D. *Synthesis* **2009**, *14*, 2293–2315.

[5] For selected reviews on enantioselective alkene difunctionalization, see: (a) Giofrè, S.; Molteni, L.; Beccalli, E. M. *Eur. J. Org. Chem.* **2023**, *26*, e202200976. (b) Bahamonde, A. *Trends in Chemistry* **2021**, *3*, 863–876.

stereoselective isomerization[6] or by stereoretentive, chain-extending catalytic cross-metathesis.[7] In this report, we describe a strategy for regio- and enantioselective difunctionalization of 2-alkenes and demonstrate its efficacy in constructing propionate derivatives as well as other valuable difunctional molecules.

Scheme 3.1. Strategies for Propionate Fragment Synthesis



3.2 Background

Despite the considerable attention devoted to enantioselective alkene transformations, there are significant methodological gaps that limit our ability to efficiently and selectively transform

[6] (a) Larsen, C. R.; Erdogan, G.; Grotjahn, D. B. *J. Am. Chem. Soc.* **2014**, *136*, 1226–1229. (b) Wang, Y.; Qin, C.; Jia, X.; Leng, X.; Huang, Z. *Angew. Chem., Int. Ed.* **2017**, *56*, 1614–1618. (c) Paulson, E. R.; Moore, C. E.; Rheingold, A. L.; Pullman, D. P.; Sindewald, R. W.; Cooksy, A. L.; Grotjahn, D. B. *ACS Catal.* **2019**, *9*, 7217–7231.

[7] (a) Xu, C.; Shen, X.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2017**, *139*, 10919–10928. (b) Ahmed, T. S.; Grubbs, R. H. *J. Am. Chem. Soc.* **2017**, *139*, 1532–1537.

these building blocks. For instance, even though selective *symmetric* catalytic difunctionalization of *E*-alkenes can be achieved (Scheme 3.2a), it is largely restricted to dihydroxylation,[8] dihalogenation,[9] diacetylation[10] and group transfer reactions (epoxidation, aziridination, cyclopropanation).[11] A more challenging task is the *non-symmetric* difunctionalization of disubstituted alkenes (Scheme 3.2b). A selective reaction outcome requires not only facial selectivity in the addition step but also regiocontrolled addition of different groups to each termini of the olefin. To accomplish regioselective non-symmetric difunctionalization of alkenes, a bias between the two alkene termini is required. This requirement is often met by employing alkenes bearing electronically differentiated substituents (such as styrenes, enones, enynes, etc.) or by incorporating a directing group in one alkene appendage.[12]

[8] For selected reviews on enantioselective dihydroxylation and diamination, see: (a) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547. (b) Bataille, C. J. R.; Donohoe, T. J. *Chem. Soc. Rev.* **2011**, *40*, 114–128. (c) Tao, Z.-L.; Denmark, S. E. *Synthesis* **2021**, *53*, 3951–3962.

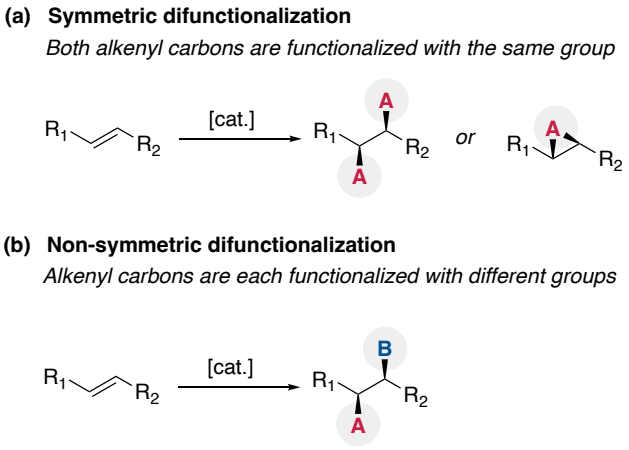
[9] (a) Cresswell, A. J.; Eey, S. T. -C.; Denmark, S. E. *Angew. Chem., Int. Ed.* **2015**, *54*, 15642–15682. (b) Denmark, S. E.; Kuester, W. E.; Burk, M. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 10938–10953.

[10] Tian, B.; Chen, P.; Leng, X.; Liu, G. *Nat. Catal.* **2021**, *4*, 172–179.

[11] For selected reviews on enantioselective group transfer reactions, see: (a) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977–1050. (b) Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Synthesis* **2014**, *46*, 979–1029. (c) Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603–1662. (d) Rose, E.; Andrioletti, B.; Zrig, S.; Quelquejeu-Ethève, M. *Chem. Soc. Rev.* **2005**, *34*, 573. (e) Pellissier, H. *Adv. Synth. Catal.* **2014**, *356*, 1899–1935. (f) Zhu, Y.; Wang, Q.; Cornwall, R. G.; Shi, Y. *Chem. Rev.* **2014**, *114*, 8199–8256.

[12] For selected reviews on catalytic enantioselective dicarbofunctionalization of alkenes, see: (a) Kang, T.; Apolinar, O.; Engle, K. M. *Synthesis* **2023**, *56*, 1–15. (b) Dong, Z.; Song, L.; Chen, L. *ChemCatChem* **2023**, *15*, e202300803.

Scheme 3.2. Catalytic Enantioselective Difunctionalization of *trans*-Alkenes



3.2.1 Enantioselective Symmetric Catalytic Difunctionalization of Unactived *E*-Alkenes

3.2.1.1 Dihydroxylation

In 1980, Sharpless and Hentges reported the first example to induce enantioselectivity in the osmylation with chiral cinchona alkaloids (**3.1**) as ligands.[13a] When (*E*)-hex-3-ene was used as substrate, stoichiometric OsO_4 and **3.1** afforded diol **3.2** in 69% yield and 75:25 er (Scheme 3.3, equation 1). Due to the high toxicity of osmium, the Sharpless group established a catalytic dihydroxylation with OsO_4 as catalyst (0.4 mol%) and cinchona alkaloid (**3.3**) as ligand.[14] Although this method afforded high enantioselectivity with aromatic alkenes, when an aliphatic *E*-alkene such as (*E*)-hex-3-ene was used, the product was afforded in 20% yield and 60:40 er (Scheme 3.3, equation 2). In 1992, Sharpless and co-workers developed the use of $K_2OsO_2(OH)_4$ as a nonvolatile osmium source in combination of $K_3Fe(CN)_6$ as cooxidant.[15] The chemical

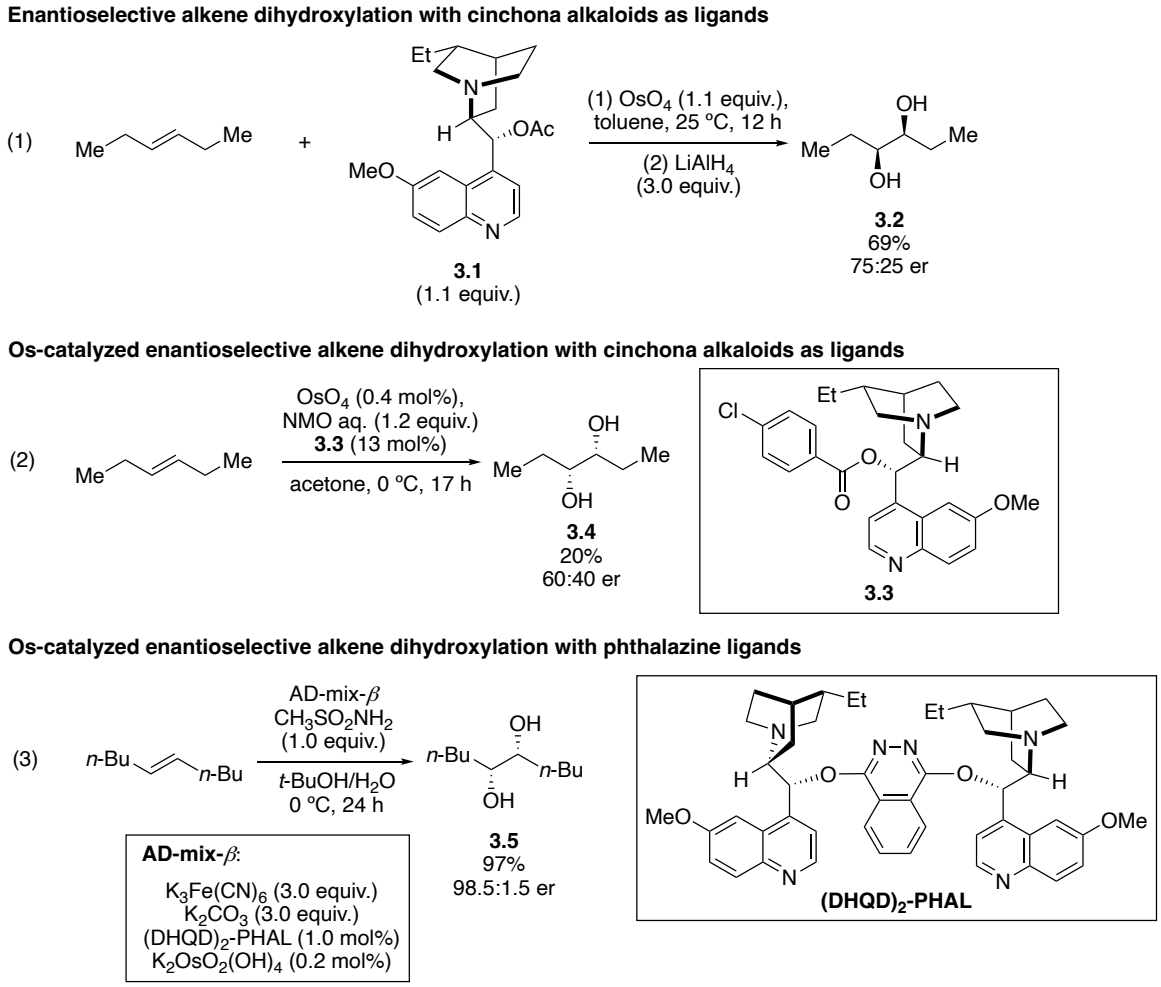
[13] (a) Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263–4265. For a selected review on Sharpless dihydroxylation, see: (b) Deubel, D. V.; Frenking, G. *Acc. Chem. Res.* **2003**, *36*, 645–651.

[14] Jacobsen, E. N.; Marko, Istvan.; Mungall, W. S.; Schroeder, Georg.; Sharpless, K. Barry. *J. Am. Chem. Soc.* **1988**, *110*, 1968–1970.

[15] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M. *J. Org. Chem.* **1992**, *57*, 2768–2771.

stability of these compounds allowed the group to formulate a mixture for enantioselective dihydroxylation: AD-mix. The use of phthalazine (PHAL) ligands significantly improved the efficiency and enantioselectivity of Os-catalyzed dihydroxylation. When aliphatic (*E*)-dec-5-ene was subjected to the catalytic conditions, diol **3.5** was obtained in 97% yield and 98.5:1.5 er (Scheme 3.3, equation 3).

Scheme 3.3. Os-Catalyzed Enantioselective Dihydroxylation of Aliphatic *E*-Alkenes



Ruthenium complexes,[16] manganese complexes,[17] palladium complexes,[18] phase-transfer catalysts,[19] and hypervalent iodine (III)[20] have also been reported to catalyze enantioselective alkene dihydroxylation.[8b] However, in these catalytic reactions, the substrates are limited to alkenes functionalized with an auxiliary, 1-alkenes, aromatic alkenes, and enones.

In 2008, Que and co-workers reported the first Fe-catalyzed enantioselective dihydroxylation of unactivated aliphatic *E*-alkenes such as (*E*)-2-heptene (Scheme 3.4, equation 1).[21] The use of bipyrrolidine ligand enhanced the catalyst TON and enantioselectivity. Vicinal diol **3.6** was obtained in quantitative yield and 98.5:1.5 er. Later on, Che and co-workers broadened the substrate scope of this transformation to include not only aliphatic *E*-alkenes but also 1-alkenes, aromatic alkenes, and enones (Scheme 3.4, equation 2).[22] Dihydroxylation of (*E*)-2-octene afforded **3.7** in 48% yield and 99:1 er.

[16] Neisius, N. M.; Plietker, B. *J. Org. Chem.* **2008***, 73*, 3218–3227.

[17] De Boer, J. W.; Browne, W. R.; Harutyunyan, S. R.; Bini, L.; Tiemersma-Wegman, T. D.; Alsters, P. L.; Hage, R.; Feringa, B. L. *Chem. Commun.* **2008**, *32*, 3747.

[18] (a) Zhang, Y.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3076–3077. (b) Tian, B.; Chen, P.; Leng, X.; Liu, G. *Nat. Catal.* **2021**, *4*, 172–179.

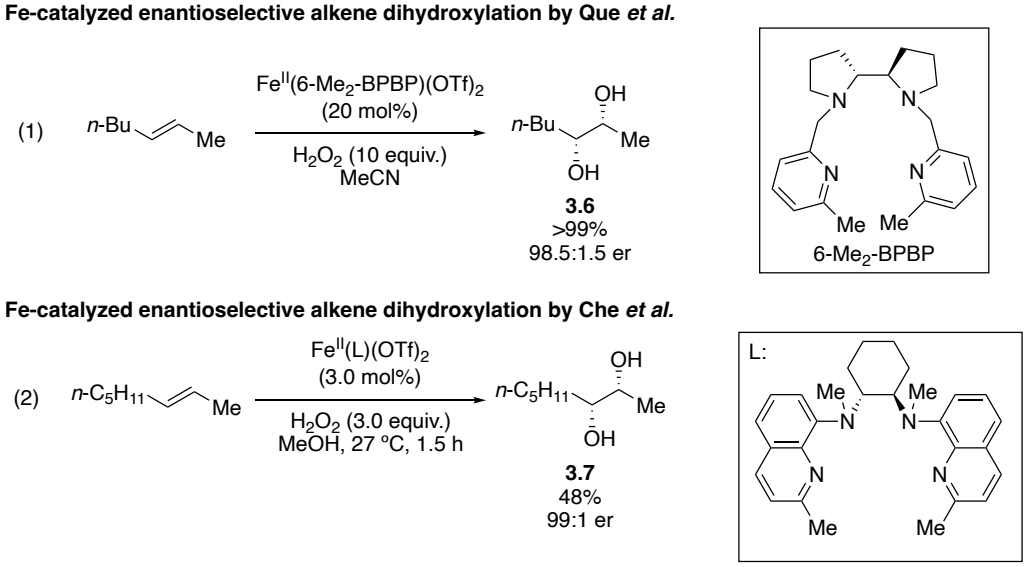
[19] Bhunnoo, R. A.; Hu, Y.; Lainé, D. I.; Brown, R. C. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3479–3480.

[20] (a) Fujita, M.; Wakita, M.; Sugimura, T. *Chem. Commun.* **2011**, *47*, 3983–3985. (b) Haubenreisser, S.; Wöste, T. H.; Martínez, C.; Ishihara, K.; Muñiz, K. *Angew. Chem., Int. Ed.* **2016**, *55*, 413–417.

[21] Suzuki, K.; Oldenburg, P. D.; Que, L. Jr. *Angew. Chem., Int. Ed.* **2008**, *47*, 1887–1889.

[22] Zang, C.; Liu, Y.; Xu, Z.; Tse, C.; Guan, X.; Wei, J.; Huang, J.; Che, C. *Angew. Chem., Int. Ed.* **2016**, *55*, 10253–10257.

Scheme 3.4. Fe-Catalyzed Enantioselective Dihydroxylation of Unactivated Aliphatic *E*-Alkenes

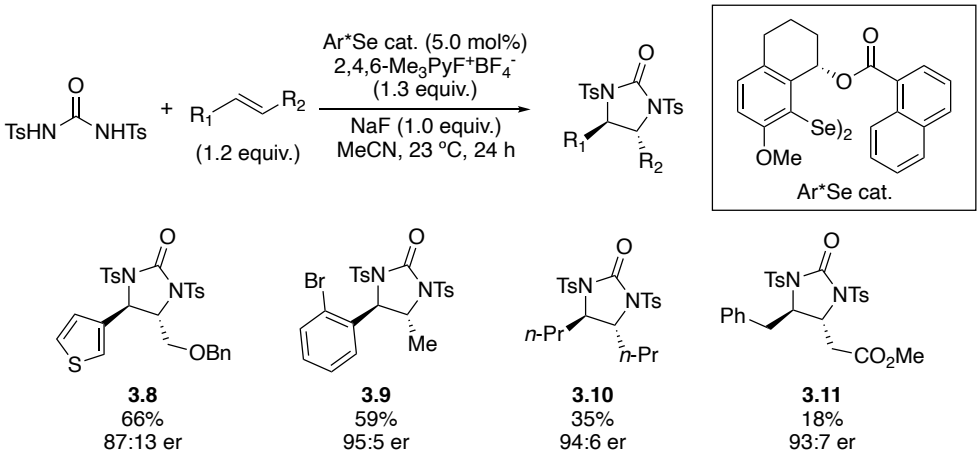


3.2.1.2 Diamination

Although a variety of enantioselective alkene diamination reactions have been developed,[8c] most methods require electronic or steric bias between the two alkene termini. In 2019, Denmark and co-workers reported a Se-catalyzed enantioselective, *syn*-diamination of *E*-alkenes (Scheme 3.5).[23] Aryl-alkyl olefins afforded the best results (**3.8**, **3.9**). The author's preliminary examination of dialkyl olefins (**3.10**, **3.11**) showed promise for further method development. *Syn*-addition products were obtained exclusively. Despite the diminished yield, high levels of enantioselectivity (up to 94:6 er) were achieved.

[23] Tao, Z.; Gilbert, B. B.; Denmark, S. E. *J. Am. Chem. Soc.* **2019**, *141*, 19161–19170.

Scheme 3.5. Se-Catalyzed Enantioselective Diamination of *E*-Alkenes



3.2.1.3 Dihalogenation

In 2011, Nicolau and co-workers reported an enantioselective dichlorination of *trans*-cinnamyl alcohol, with $(DHQ)_2PHAL$ as the catalyst (Scheme 3.6a).[24 a] The benzylic chloronium intermediate (**3.12**) underwent a regioselective nucleophilic attack by a chloride anion. It is likely that the hydroxyl moiety forms hydrogen bond with the catalyst, rigidifying the substrate-ligand complex and potentially enhancing enantioselectivity.

The first example of enantioselective dihalogenation of alkenes without electronic bias between the two alkene termini was reported by Burns and co-workers in 2015 (Scheme 3.6b).[25] Allylic alcohols were used as substrates, as the alcohol moiety invoked a ligand- and substrate-bound titanium complex **3.14**, which governed the regio- and enantioselectivity. The

[24] (a) Nicolaou, K. C.; Simmons, N. L.; Ying, Y.; Heretsch, P. M.; Chen, J. S. *J. Am. Chem. Soc.* **2011**, *133*, 8134–8137. For similar dihalogenation reactions, see also: (b) Hu, D. X.; Shibuya, G. M.; Burns, N. Z. *J. Am. Chem. Soc.* **2013**, *135*, 12960–12963. (c) Landry, M. L.; Hu, D. X.; McKenna, G. M.; Burns, N. Z. *J. Am. Chem. Soc.* **2016**, *138*, 5150–5158. (d) Soltanzadeh, B.; Jaganathan, A.; Yi, Y.; Yi, H.; Staples, R. J.; Borhan, B. *J. Am. Chem. Soc.* **2017**, *139*, 2132–2135. (e) Wedek, V.; Van Lommel, R.; Daniliuc, C. G.; De Proft, F.; Hennecke, U. *Angew Chem Int Ed* **2019**, *58*, 9239–9243.

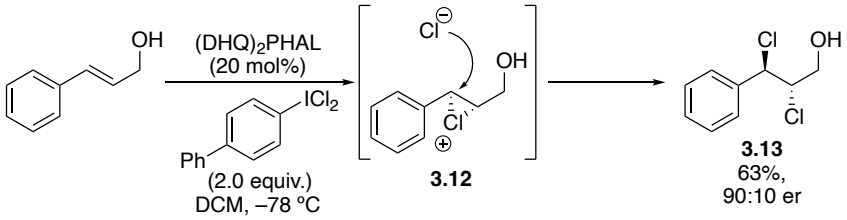
[25] Hu, D. X.; Seidl, F. J.; Bucher, C.; Burns, N. Z. *J. Am. Chem. Soc.* **2015**, *137*, 3795–3798.

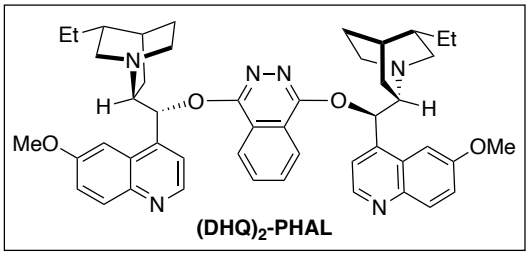
authors demonstrated effective dihalogenation of 1,1-disubstituted alkenes (**3.15**), 1,2,2-trisubstituted alkenes (**3.16**), and 1,2-disubstituted *Z*-alkenes (**3.17**), affording the desired products in up to 94% yield and 95:5 er. In 2019, Denmark and co-workers reported an organoselenium-catalyzed enantioselective *syn*-dichlorination of alkenes (Scheme 3.6c).[26] Aliphatic *E*-alkene **3.18** underwent the dichloronation to afford vicinal *syn*-dichloride **3.19** in 71% yield and 76:24 er.

[26] Gilbert, B. B.; Eey, S. T.-C.; Ryabchuk, P.; Garry, O.; Denmark, S. E. *Tetrahedron* **2019**, *75*, 4086–4098.

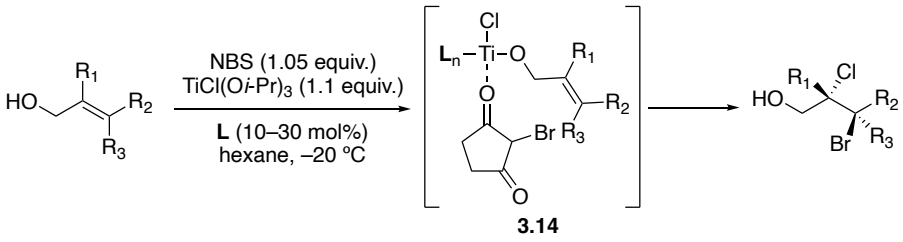
Scheme 3.6. Enantioselective Dihalogenation of Alkenes

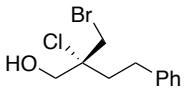
(a) Enantioselective dichlorination by Nicolau *et al.*



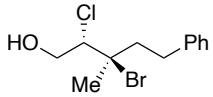


(b) Enantioselective dihalogenation by Burns *et al.*

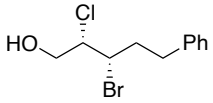




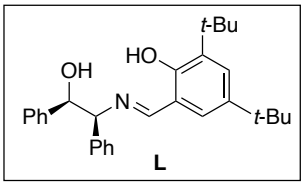
3.15
88%
95:5 er



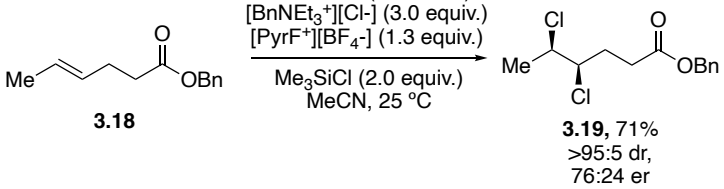
3.16
94%
95:5 er

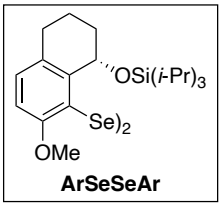


3.17
92%
95.5:4.5 er



(c) Enantioselective dichlorination by Denmark *et al.*





3.2.1.4 Diboration

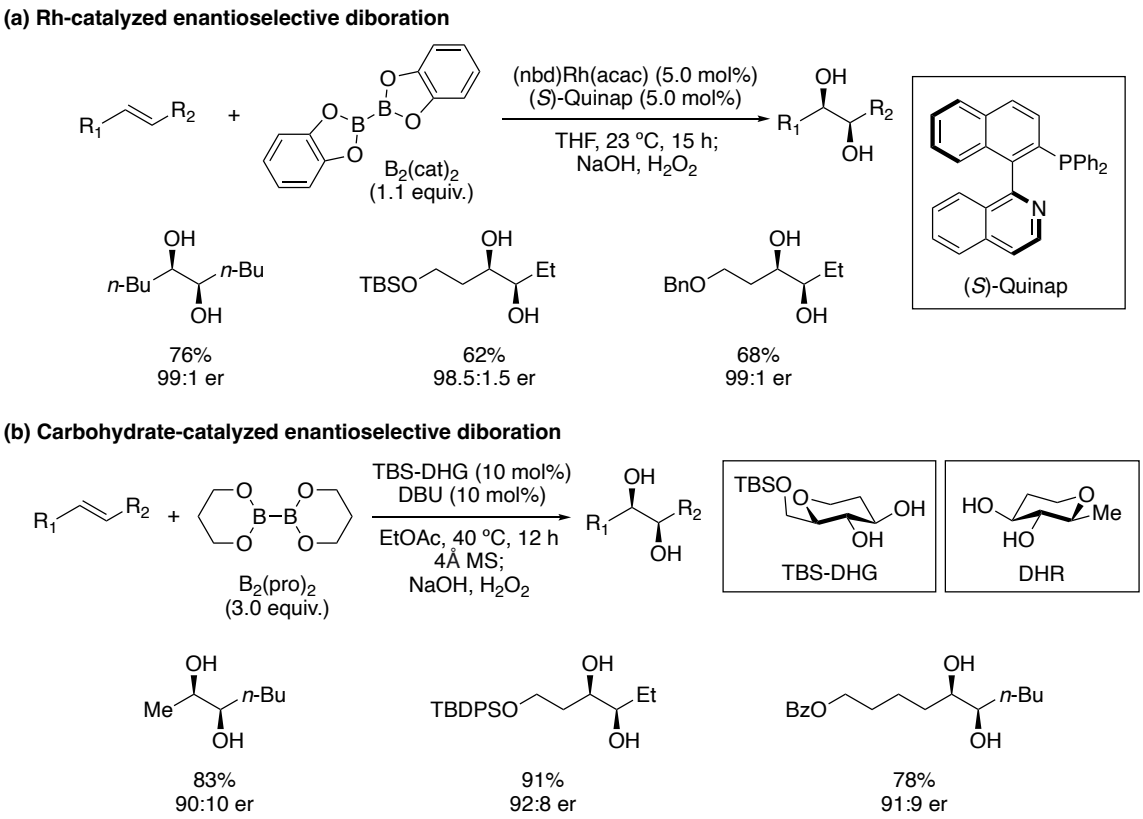
As described in Chapter 1.2.1.1, Morken and co-workers developed an enantioselective alkene diboration with Rh(I)–Quinap catalyst (Scheme 3.7a).[27] This method effectively enabled the enantioselective diboration of a broad range of unactivated aliphatic alkenes, including 1,2-disubstituted *E*-alkenes. Furthermore, the authors demonstrated that the catalyst loading can be reduced to 0.5 mol% in gram-scale reactions. The bis(boronic esters) were oxidized to afford enantiomerically enriched vicinal diols, rendering this method an alternative to Sharpless dihydroxylation.

In 2016, the Morken group reported an enantioselective diboration catalyzed by carbohydrates.[28] The catalysts, 6-*tert*-butyldimethylsilyl-1,2-dihydroglucal (TBS-DHG) and dihydrorhamnal (DHR), are derived from commercially available D-glucal and L-rhamnal. Unactivated aliphatic *E*-alkenes underwent carbohydrate-catalyzed diboration and oxidation efficiently, affording enatiomerically enriched diols in up to 91% yield and 92:8 er (Scheme 3.7b). It is worth noting that, thus far, only oxidation and Matteson homologation have been demonstrated as transformations of the diboration products.

[27] (a) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702–8703. (b) Miller, S. P.; Morgan, J. B.; Nepveux; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133. (c) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538–9544.

[28] (a) Fang, L.; Yan, L.; Haeffner, F.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, *138*, 2508–2511. See also: (b) Yan, L.; Meng, Y.; Haeffner, F.; Leon, R. M.; Crockett, M. P.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 3663–3673.

Scheme 3.7. Enantioselective Diboration of Unactivated *E*-Alkenes



3.2.1.5 Directed Diarylation

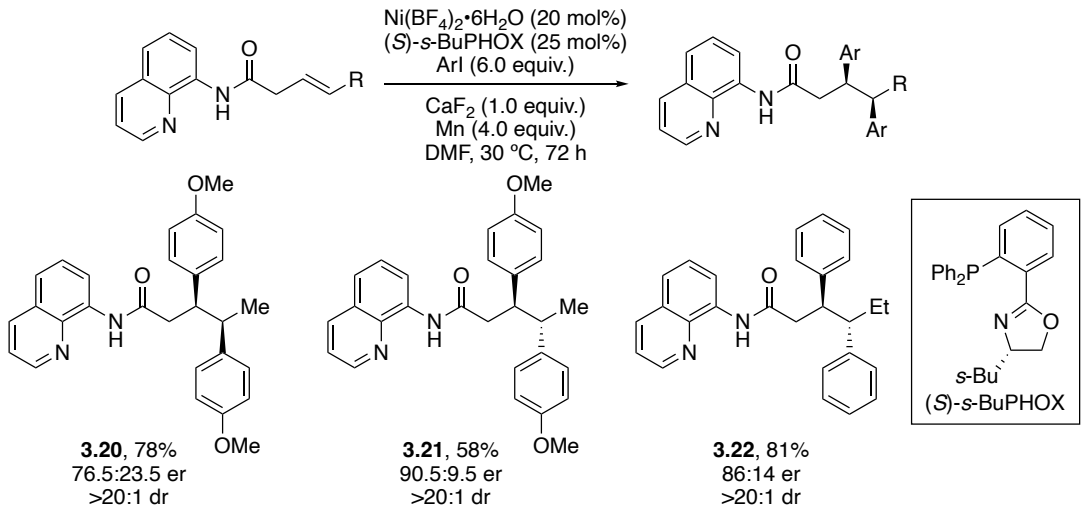
Recently, the Song and Chen groups reported a 1,2-homodiarylation of aliphatic alkenes facilitated by an amide-linked aminoquinoline (AQ) directing group (Scheme 3.8).[29] Although a catalytic cycle was not proposed, high *syn*-diastereoselectivity (>20:1 dr) and up to 90.5:9.5 er were achieved with 1,2-disubstituted aliphatic alkene substrates. This observation indicated that migratory insertion of aryl-Ni species is likely the enantio-determining step.[30] Notably, the stereochemistry of the alkene played a crucial role in enantioselectivity. The diarylation of

[29] Dong, Z.; Tang, Q.; Xu, C.; Chen, L.; Ji, H.; Zhou, S.; Song, L.; Chen, L. *Angew. Chem., Int. Ed.* **2023**, *62*, e202218286.

[30] For selected reports on likely mechanism of directed Ni-catalyzed alkene difunctionalization, see: (a) Kang, T.; Kim, N.; Cheng, P. T.; Zhang, H.; Foo, K.; Engle, K. M. *J. Am. Chem. Soc.* **2021**, *143*, 13962–13970. (b) Kang, T.; González, J. M.; Li, Z.-Q.; Foo, K.; Cheng, P. T. W.; Engle, K. M. *ACS Catal.* **2022**, *12*, 3890–3896. (c) Li, Z.-Q.; Cao, Y.; Kang, T.; Engle, K. M. *J. Am. Chem. Soc.* **2022**, *144*, 7189–7197.

E-alkene (**3.20**) proceeded with lower enantioselectivity compared to the corresponding *Z*-alkene (**3.21**). Enantiomerically enriched alkanes bearing two contiguous benzylic stereogenic centers were generated in up to 81% yield.

Scheme 3.8. Directed Enantioselective Diarylation of Aliphatic Alkenes



3.2.2 Enantioselective Non-Symmetric Catalytic Difunctionalization of Unactived Alkenes

3.2.2.1 Aminohydroxylation

Sharpless and co-workers reported the first example of catalytic *syn*-aminohydroxylation of *E*-alkenes in 1976.[31] When (*E*)-5-decene was treated with catalytic OsO_4, with ChloramineT trihydrate (**3.23**) as the amine source, *syn*-aminohydroxylation product **3.24** was furnished in 62% yield (Scheme 3.9, equation 1). The Sharpless group reported an enantioselective catalytic aminohydroxylation in 1996.[32] Chiral cinchona alkaloid-derived ligand $(DHQ)_2$-PHAL proved to be effective in Os-catalyzed aminohydroxylation (Scheme 3.9, equation 2). Only electronically

[31] Sharpless, K. B.; Chong, A. O.; Oshima, K. *J. Org. Chem.* **1976**, *41*, 177–179.

[32] (a) Li, G.; Chang, H.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451–454. See also: (b) Bruncko, M.; Schlingloff, G.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1483–1486.

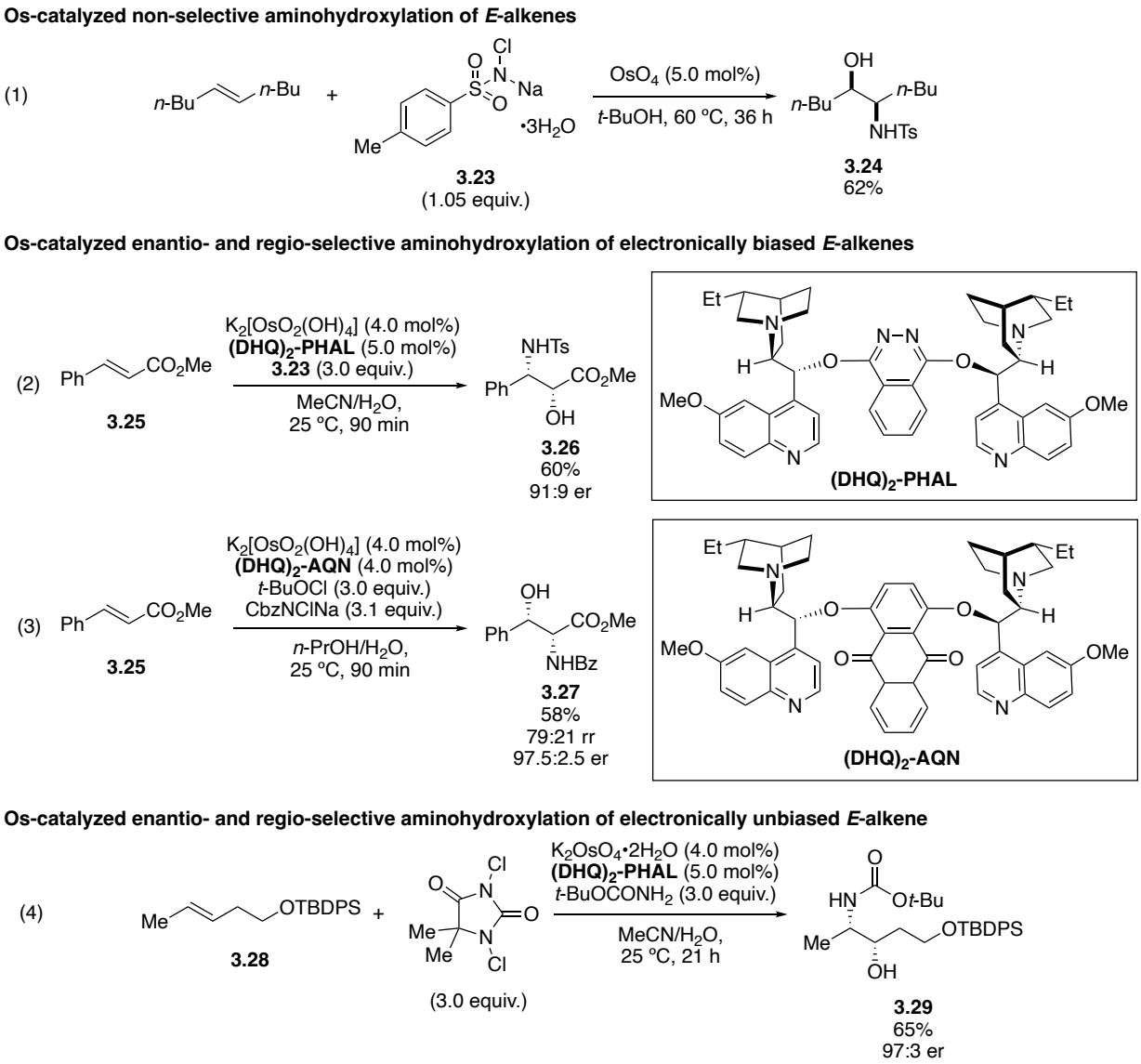
biased alkenes such as methyl cinnamate (**3.25**) were used as substrates. Enantiomerically enriched vicinal amino alcohol **3.26** was furnished in 60% yield and 91:9 er. In 2013, the Sharpless group reported that the other regioisomer (**3.27**) of the amino alcohol was obtained in 58% yield and 97.5:2.5 er through the use of a modified cinchona alkaloid ligand $(DHQ)_2$-AQN (Scheme 3.9, equation 3).[33] Overall, Os-catalyzed enantioselective aminohydroxylation serves as a powerful tool for synthesis of unnatural amino acids.

In 2013, Das and co-workers reported a regio- and enantioselective aminohydroxylation of an unactivated aliphatic *E*-alkene (**3.28**) in syntheses of crucigasterins (Scheme 3.9, equation 4).[34] Vicinal amino alcohol **3.29** was obtained in 69% yield and 97:3 er. It is likely that the regioselectivity stemmed from steric difference between the methyl group and the alkyl chain.

[33] Tao, B.; Schlingloff, G.; Sharpless, K. B. *Tetrahedron Lett.* **1998**, *39*, 2507–2510.

[34] Kumar, J. N.; Das, B. *Tetrahedron Lett.* **2013**, *54*, 3865–3867.

Scheme 3.9. Enantioselective Aminohydroxylation of *E*-Alkenes



3.2.2.2 Carboamination

Despite considerable effort devoted to enantioselective carboamination of alkenes over the years, most methods only apply to alkenes with directing groups, or with electronic bias between the alkene termini.[35] Undirected enantioselective carboamination of electronically unbiased

[35] For review, see: Hirano, K.; Miura, M. *J. Am. Chem. Soc.* **2022**, *144*, 648–661.

aliphatic alkenes remains a challenge, with the only known examples being of strained cyclic alkenes. In 2019, Zhang and co-workers reported a three-component Cu-catalyzed carboamination of cyclopropenes (Scheme 3.10, equation 1).[36] The authors described a carbocupration of olefins with organocopper species. The resulting cyclopropylcopper species was treated with hydroxylamine ester **3.30**[37] to furnish carboamination product **3.31** in 61%, 89:11 dr, and 84:16 er.

In 2021, Cramer and co-workers demonstrated a Co-catalyzed carboamination of [2.2.1]-bridged bicyclic alkenes through C–H activation of **3.32** (Scheme 3.10, equation 2).[38] Oxygen-bridged bicyclic alkene **3.33** underwent carboamination smoothly, generating highly functionalized [2.2.1]-bridged bicycle **3.34** in 96% yield and 93:7 er.

In the same year, Ellman and co-workers reported a Rh-catalyzed carboamination of [2.2.1]-bridged bicyclic alkenes through C–H activation of **3.35** (Scheme 3.10, equation 3).[39] Carbon-bridged bicylic alkene **3.36** underwent enantioselective migratory insertion, nitrene insertion by **3.37**, and protodemetallation to furnish the carboaminated bridged bicyclic alkane **3.38** in 59% yield and 90:10 er.

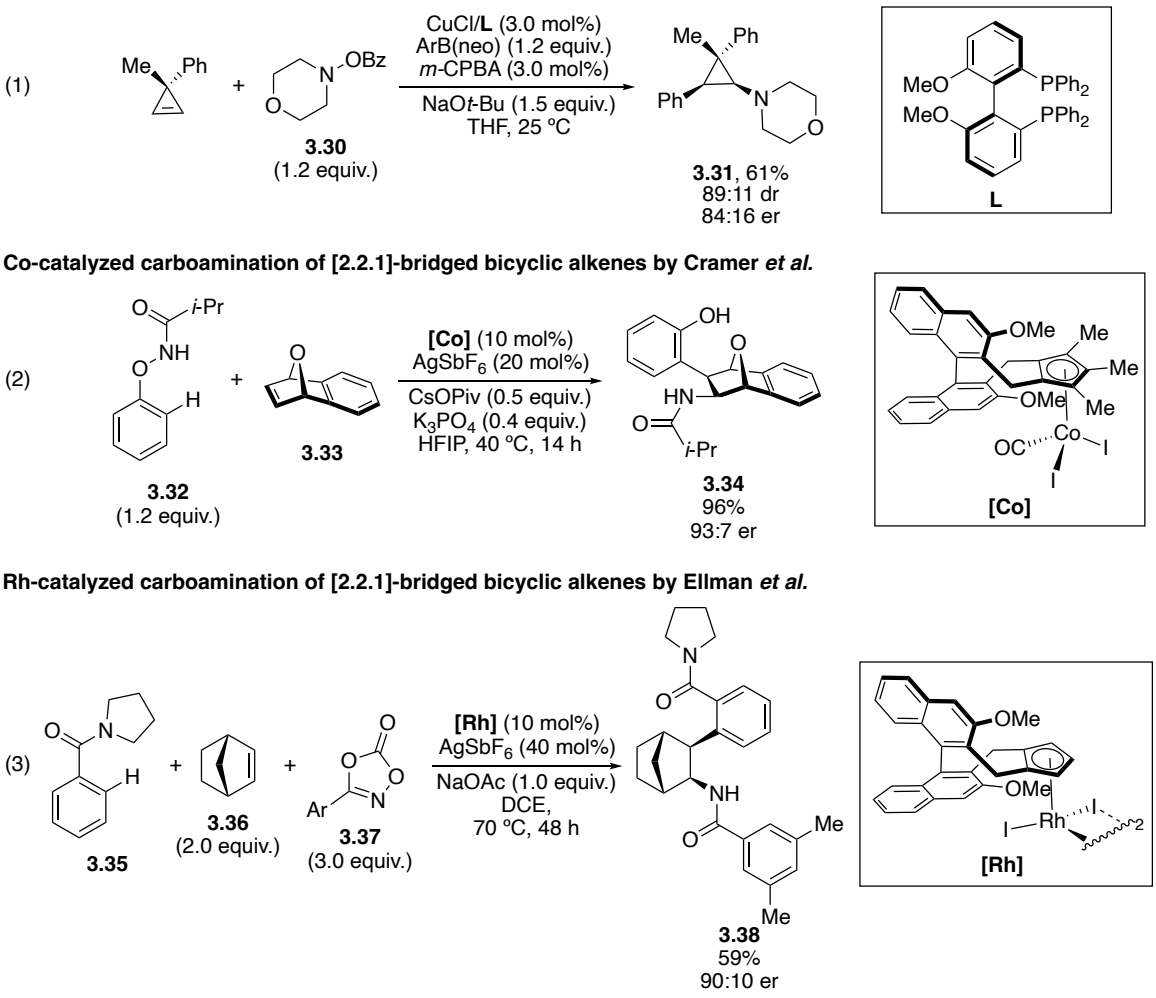
[36] Li, Z.; Zhang, M.; Zhang, Y.; Liu, S.; Zhao, J.; Zhang, Q. *Org. Lett.* **2019**, *21*, 5432–5437.

[37] Parra, A.; Amenós, L.; Guisán-Ceinos, M.; López, A.; García Ruano, J. L.; Tortosa, M. *J. Am. Chem. Soc.* **2014**, *136*, 15833−15836.

[38] Ozols, K.; Onodera, S.; Woźniak, Ł.; Cramer, N. *Angew Chem Int Ed* **2021**, *60*, 655–659.

[39] Brandes, D. S.; Sirvent, A.; Mercado, B. Q.; Ellman, J. A. *Org. Lett.* **2021**, *23*, 2836–2840.

Scheme 3.10. Enantioselective Carboamination of Strained Cyclic Alkenes



3.2.2.3 Carbozincation

A versatile method for the enantioselective non-symmetric difunctionalization of alkenes is carbozincation. The configurationally stable organozinc species can effectively transmetallate to Cu or Pd catalysts and cross-couple with a wide variety of electrophiles. However, successful examples are limited to strained and reactive cyclopropenes. In 2000, Nakamura and co-workers reported a Fe-catalyzed enantioselective carbozincation of cyclopropene **3.39** with dialkylzinc

reagents such as Et_2Zn (Scheme 3.11a).[40] The cyclopropyl zinc species was protonated by NH_4Cl during workup. Enantiomerically enriched cyclopropane **3.40** was afforded in 88% yield and 94.5:5.5 er.

In 2011, the Lautens group reported a Pd-catalyzed enantioselective carbozincation of cyclopropene **3.41** (Scheme 3.11b). The enantiomerically enriched organozinc species **3.42** was transmetallated to stoichiometric CuCN•LiCl and coupled with acyl chlorides. Acylation product **3.43** was obtained in 75% yield and 96.5:3.5 er.[41]

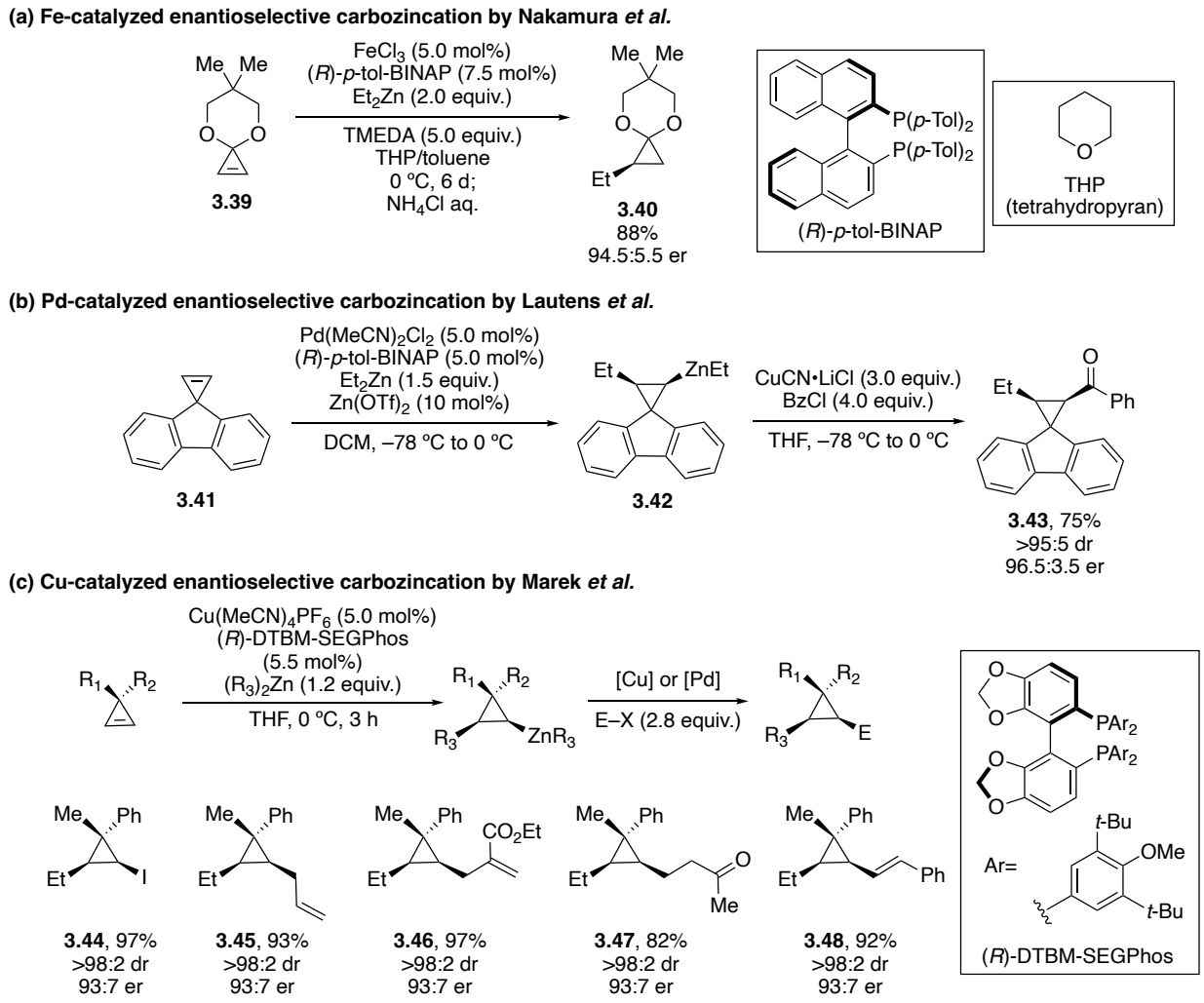
In 2015, the Marek group demonstrated a Cu-catalyzed example (Scheme 3.11c).[42] Addition of I_2 to the cyclopropylzinc species delivered a cyclopropyl iodide (**3.44**) in 97% yield and 93:7 er. The cyclopropylzinc species could also transmetallate to copper catalyst and undergo allylation and 1,4-addition reactions, furnishing the products **3.45**–**3.47** in 82–97% yield and 93:7 er. Pd-Catalyzed Negishi cross-coupling with alkenyl bromides also proceeded smoothly, the product **3.48** was obtained in 92% yield and 93:7 er.

[40] Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 978–979.

[41] Krämer, K.; Leong, P.; Lautens, M. *Org. Lett.* **2011**, *13*, 819–821.

[42] Müller, D. S.; Marek, I. *J. Am. Chem. Soc.* **2015**, *137*, 15414–15417.

Scheme 3.11. Enantioselective Carbozincation of Cyclopropyl Alkenes



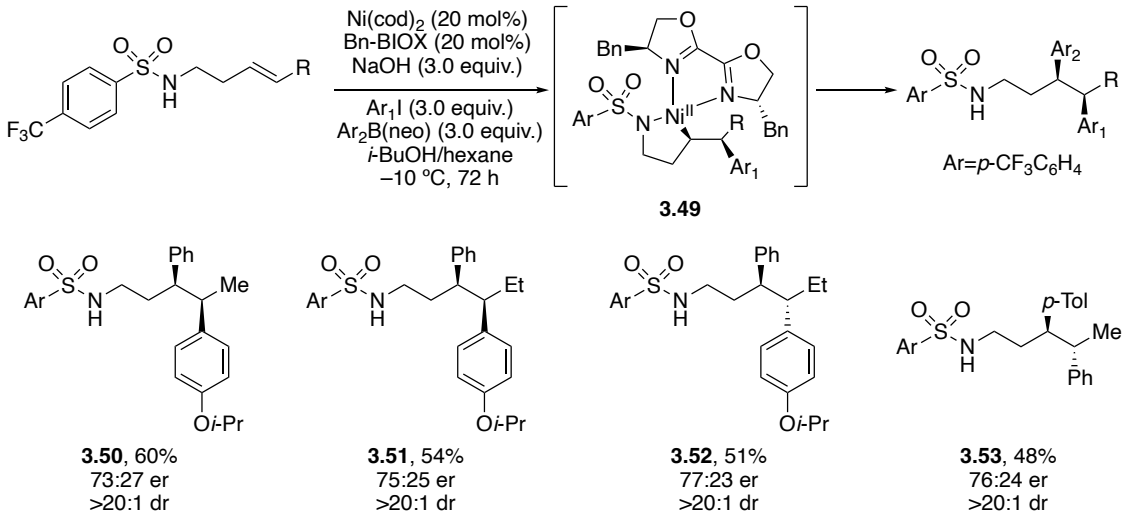
3.2.2.4 Directed Dicarbofunctionalization

A variety of catalytic strategies have been explored for enantioselective dicarbofunctionalization of alkenes.[12, 43] However, three-component difunctionalization of electronically unbiased 1,2-disubstituted alkenes remains a challenge. In 2022, the Engle and the Liu groups reported a Ni-catalyzed three-component dicarbofunctionalization of aliphatic *E*-

[43] For a selected review on Cu-catalyzed enantioselective dicarbofunctionalization of terminal alkenes, see: Li, Z.-L.; Fang, G.-C.; Gu, Q.-S.; Liu, X.-Y.; *Chem. Soc. Rev.* **2020**, *49*, 32–48.

alkenes with sulfonamide directing groups (Scheme 3.12).[44] In this report, a broad range of alkenes were functionalized with aryl iodides and arylboronic esters. The authors proposed that aryl–Ni(II) migratory insertion (intermediate **3.49**) is the enantio- and regio-determining step. Terminal alkenes, *E*-alkenes (**3.50**, **3.51**) and *Z*-alkenes (**3.52**, **3.53**) underwent this transformation smoothly. However, the yield and enantioselectivity of 1,2-disubstituted alkenes were significantly diminished compared to that of 1-alkenes. The difunctionalized products (**3.50**–**3.53**) were obtained in 48–60% yield, and 73:27–77:23 er.

Scheme 3.12. Directed Enantioselective Dicarbofunctionalization of Electronically Unbiased Alkenes



[44] Apolinar, O.; Kang, T.; Alturaifi, T. M.; Bedekar, P. G.; Rubel, C. Z.; Derosa, J.; Sanchez, B. B.; Wong, Q. N.; Sturgell, E. J.; Chen, J. S.; Wisniewski, S. R.; Liu, P.; Engle, K. M. *J. Am. Chem. Soc.* **2022**, *144*, 19337–19343.

3.3 Development of Site-Selective and Stereospecific Functionalization of Bis(boronic Esters) Derived from 2-Alkenes

3.3.1 Inspiration of the Reaction

Efforts in our laboratory and others have examined alkene difunctionalization by diboration-based strategies. In several examples, terminal alkenes underwent catalytic enantioselective diboration, followed by Pd- or Cu-catalyzed cross-coupling (Scheme 3.13, equation 1).[45] Site-selectivity in this sequence arises by steric effects that operate during the transmetallation: the primary carbon undergoes faster transfer to the catalytic metal center and is thereby selectively functionalized.

The use of diboration/cross-coupling strategy for the difunctionalization of internal alkenes faces significant challenges: first, stereospecific cross-coupling of secondary alkylboronic esters is more challenging than reactions of primary boronic esters; second, with two secondary boronic esters, site-selectivity becomes inherently more difficult.

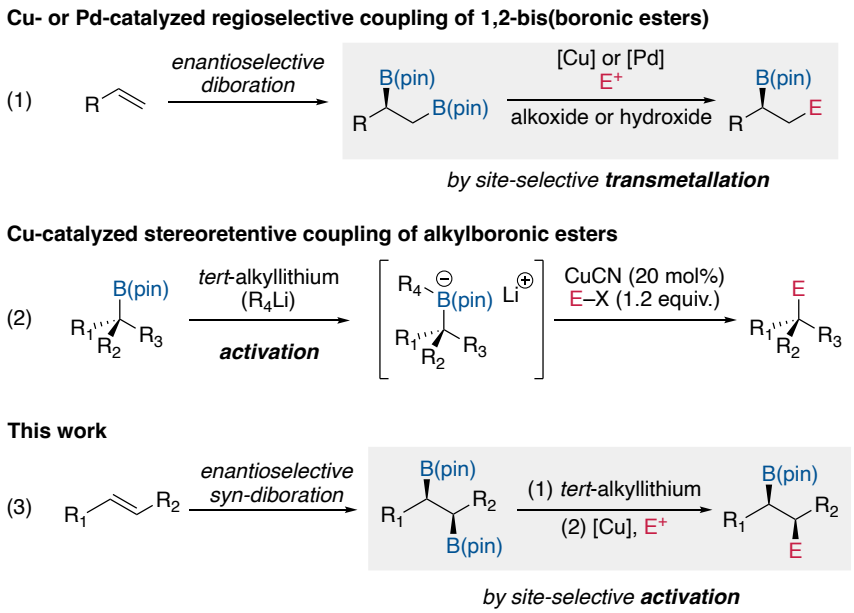
With respect to the first challenge, our group recently demonstrated that addition of sterically encumbered tertiary organolithium reagents to organoboronic esters enables stereospecific transmetallation of both secondary and tertiary carbons to Cu catalyst (Scheme 3.13, equation 2).[46] The organocopper species can undergo efficient cross-coupling with a variety of electrophiles. We

[45] For selected reports on diboration/coupling sequence, see: (a) Miller, S. P.; Morgan, J. B.; Nepveux; Morken, J. P. *Org. Lett.* **2004**, *6*, 131–133. (b) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386–390. (c) Willems, S.; Toupalas, G.; Reisenbauer, J. C.; Morandi, B. *Chem. Commun.* **2021**, *57*, 3909–3912. (d) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 18234–18235. (e) Xu, N.; Kong, Z.; Wang, J. Z.; Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 17815–17823.

[46] (a) Xu, N.; Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 11546–11552. (b) Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 20755–20760.

considered if this activation mode could apply to vicinal bis(boronic esters). We also wondered whether the size of the tertiary alkyl activator allows effective discrimination of the boronic esters based on the steric environment (Scheme 3.13, equation 3).[47]

Scheme 3.13. Enantioselective Difunctionalization of Alkenes



In order to study the site-selectivity in the addition of *tert*-butyllithium to vicinal bis(boronic esters), as well as to learn about the stability of the derived "ate" complexes, we prepared isotopically labelled substrate **3.54**, subjected it to activation by *t*-BuLi, and followed the process by both ^{13}C and ^{11}B NMR analysis (Scheme 3.14a). Notably, previous experiments in our group showed that the chemical shifts of carbon nuclei are sensitive to the coordination number of *β*-

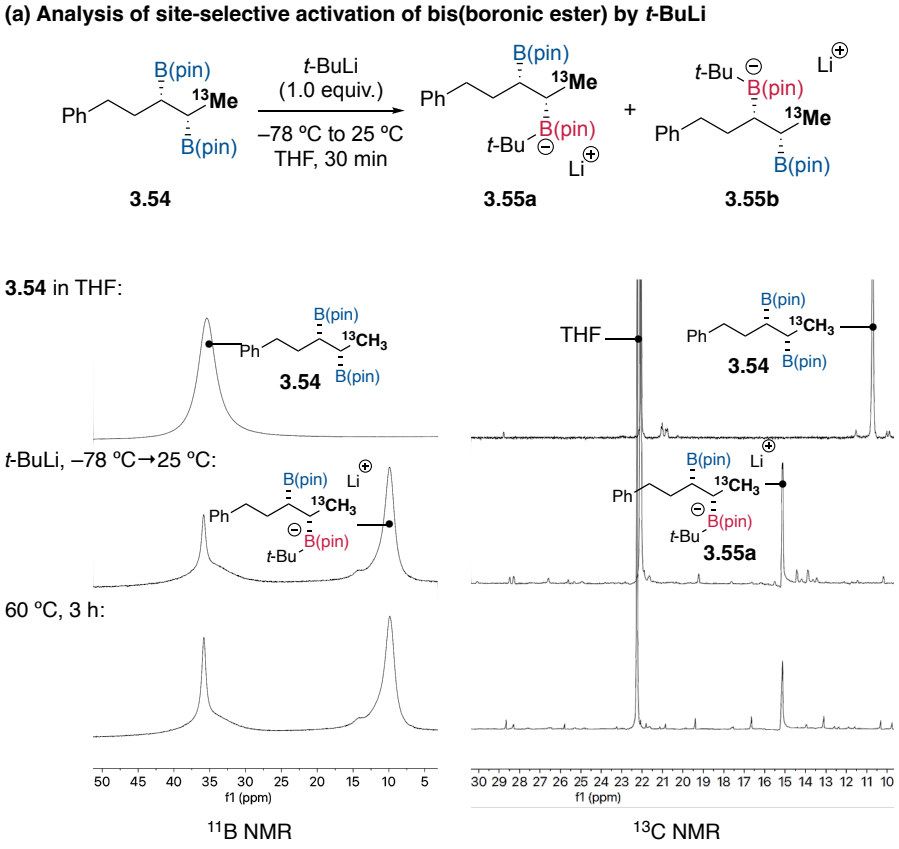
[47] For selected reports on site-selective activation of primary organoboronic esters by bulky alkyllithium, see: (a) Fawcett, A.; Nitsch, D.; Ali, M.; Bateman, J. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2016**, *55*, 14663–14667. (b) Aiken, S. G.; Bateman, J. M.; Liao, H.-H.; Fawcett, A.; Bootwicha, T.; Vincetti, P.; Myers, E. L.; Noble, A.; Aggarwal, V. K. *Nat. Chem.* **2023**, *15*, 248–256. For site-selective activation of primary organoboronic esters by bulky aryllithium, see: (c) Kaiser, D.; Noble, A.; Fasano, V.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2019**, *141*, 14104–14109. (d) Wang, H.; Han, W.; Noble, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2022**, e202207988. (e) Wang, H.; Wu, J.; Noble, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2022**, *61,* e202202061.

boronic groups,[48] with shifts (Δδ) of 1–6 ppm occurring upon conversion of boronic esters to four-coordinate boron "ate" complexes. In line with these observations, when **3.54** was treated with *tert*-butyllithium at –78 ºC in THF and was allowed to warm to 25 ºC, the ^{13}C resonance corresponding to **3.54** was replaced with a single new major species assigned to complex **3.55a**. Addition of drops of DMSO to the solutions resulted in clearer signals on the spectra. The ^{11}B NMR indicated that 55% of the boron centers were four-coordinate (δ 10 ppm). Integration of the ^{13}C signal for **3.55a** relative to minor species led to the conclusion that "ate" complex formation occurs with ≥9:1 site-selectivity. Allowing the mixture containing complex **3.55a** to stir at 60 ºC for 3 h did not lead to a substantial change in the NMR spectra, suggesting that not only is the "ate" complex formed selectively, but it is also not subject to significant decomposition or equilibration over the time course of a typical reaction.

We then investigated whether site-selective "ate" complex formation leads to site-selective coupling reactions. We prepared enantiomerically enriched substrate **3.56**, subjected it to activation by *t*-BuLi at –78 ºC, and then employed the "ate" complex in Cu-catalyzed coupling (Scheme 3.14b). Consistent with our previous analysis by NMR, the coupling product **3.57** was obtained with >98% enantiospecificity, in 7:1 regioselectivity and 72% isolated yield.

[48] For ^{13}C NMR analysis of "ate" complex formation: Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 9976–9981.

Scheme 3.14. Site-Selective "Ate" Complex Formation and Cross-Coupling[a]



[a]Reactions were carried out under argon atmosphere. [b]Yields corresponded to isolated and purified products (±5%). Enantiomeric specificity (es) values and enantiomeric ratios (er) were determined by analysis of chiral SFC (±1%). Regioisomeric ratios (rr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

3.3.2 Substrate Scope

With experiments suggesting that activation and coupling of vicinal bis(boronic esters) could be accomplished with site-selectivity, several bis(boronic esters) were examined in subsequent

copper-catalyzed cross-coupling reactions (Scheme 3.15a).[49] With 2,3-dichloropropene as an electrophile, a variety of 2,3-bis(boronic esters) were studied and product regioisomer ratios ranged from 6:1 to 10:1 by ^{1}H NMR analysis of unpurified mixtures. For most substrates, the regioisomers were easily separable during purification. In addition to aliphatic substrates that are devoid of any directing functionality (**3.59**), TBS-protected alcohol (**3.60**) and arene-containing (**3.61**) substrates were also effective. It is worth noting that discrimination between a methyl and an ethyl group was possible. Coupling reaction furnished allylation product **3.62** (8:1 rr on ^{1}H NMR of unpurified mixture) from the *syn*-diboration product of (*E*)-2-pentene. Additionally, the substrate derived from the diboration of (*Z*)-2-octene provided convenient access to the other diastereoisomer (**3.68**). However, we observed erosion in stereospecificity in this reaction (7:1 dr), and addition of styrene[46a] made little difference to the diminished stereospecificity. This outcome might be attributed to a transient *anti*-boratirane ion intermediate **3.68a** (Scheme 3.15b). Through an anionic intermediate, **3.68a** could epimerize to the more thermodynamically stable *syn*-boratirane ion intermediate **3.68b**.[50]

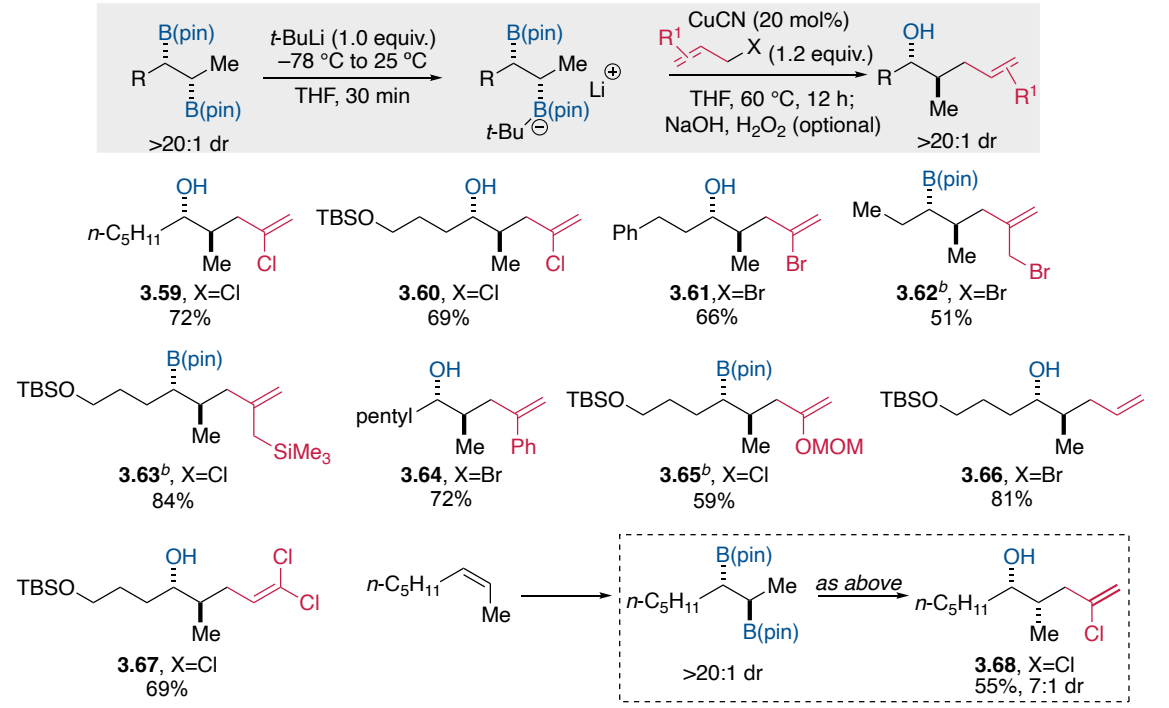
Furthermore, besides dichloropropene, other allylic electrophiles engaged in the reaction and delivered useful homoallylic alcohols bearing a range of functional groups, including allyl bromide (**3.62**), allyl silane (**3.63**), geminal dichloroalkene (**3.67**), and enol ether (**3.65**).

[49] For selected reports on stereospecific coupling of alkylcopper reagents, see: (a) Moriya, K.; Simon, M.; Mose, R.; Karaghiosoff, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2015**, *54*, 10963–10967. (b) Morozova, V.; Skotnitzki, J.; Moriya, K.; Karaghiosoff, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2018**, *57*, 5516–5519. For review, see: (c) Skotnitzki, J.; Kremsmair, A.; Knochel, P. *Synthesis.* **2020**, *52*, 189–196.

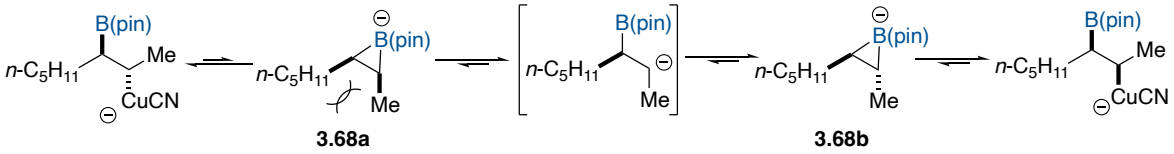
[50] Tao, Z.; Robb, K. A.; Panger, J. L.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 15621–15625.

Scheme 3.15. Site-Selective Coupling with Allyl Electrophiles[a]

(a) Site-selective coupling with allyl electrophiles



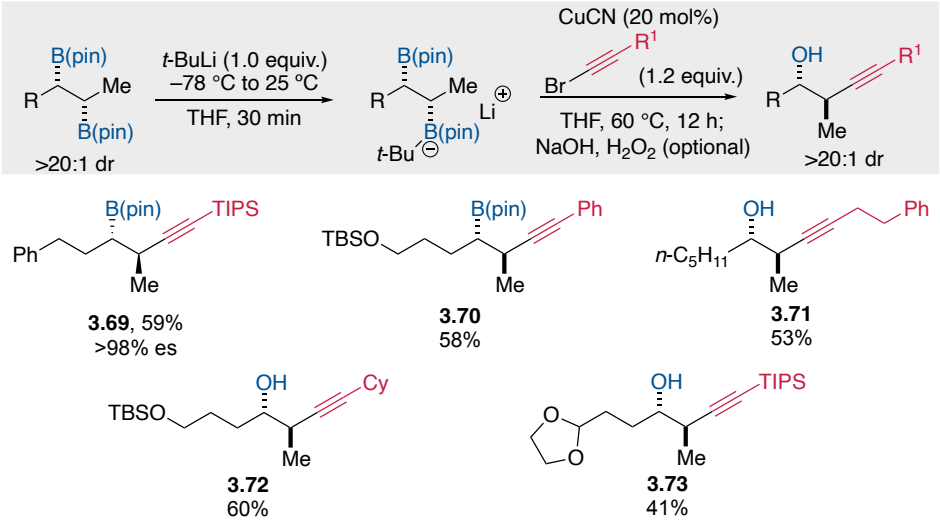
(b) Proposed mechanism for diminished stereospecificity of 3.68



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Enantiomeric specificity (es) values and enantiomeric ratios (er) were determined by analysis of chiral SFC (±1%). Diastereomeric ratios (dr) and regioisomeric ratios (rr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). [b]Reactions were carried out in the presence of 50 mol% styrene.

Other classes of electrophiles also participated in the reaction, including alkynyl bromides (**3.69**–**3.73**) (Scheme 3.16). Although regioselective alkynylation of bis(boronic esters) was demonstrated in our previous work,[45e] the substrate was limited to 1,2-bis(boronic ester) and only the primary boronic ester was reactive. With this method, the secondary boronic esters neighboring the methyl groups were selectively activated and coupled to a variety of alkynyl bromides.

Scheme 3.16. Site-Selective Coupling with Alkynyl Electrophiles[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%).

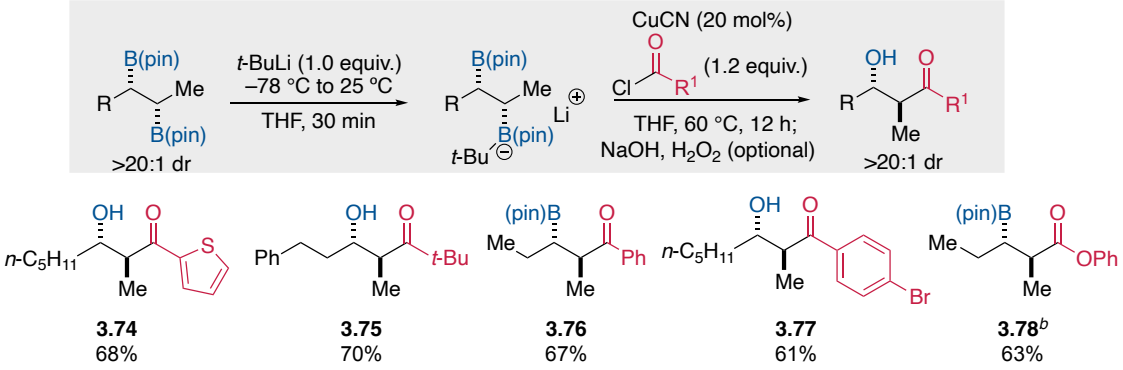
Particularly noteworthy is the ability of acyl chlorides to afford β-boryl ketones and esters (**3.74**–**3.78**) with high stereospecificity (Scheme 3.17). These compounds could potentially be synthesized through Cu-[51] or NHC-catalyzed[52] enantioselective conjugate addition of boronic esters to α,β-unsaturated carbonyl compounds. In conjugate addition reactions, achieving high diastereoselectivity for *anti*-methyl-substituted products proved to be challenging for many substrates. Our method provides an alternative route where high diastereomeric ratios can be achieved with a broad range of functional groups.

[51] For selected reports on Cu-catalyzed boronate conjugate addition, see: (a) Chen, I.-H.; Yin, L.; Itano, W.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 11664–11665. (b) Xie, J.-B.; Lin, S.; Qiao, S.; Li, G. *Org. Lett.* **2016**, *18*, 3926–3929. (c) Lee, J.-E.; Yun, J. *Angew. Chem., Int. Ed.* **2008**, *120*, 151–153. (d) Lillo, V.; Prieto, A.; Bonet, A.; Díaz-Requejo, M. M.; Ramírez, J.; Pérez, P. J.; Fernández, E. *Organometallics* **2009**, *28*, 659–662. (e) Kobayashi, S.; Xu, P.; Endo, T.; Ueno, M.; Kitanosono, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 12763–12766. (f) O'Brien, J. M.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630–10633.

[52] For selected reports on NHC-catalyzed boronate conjugate addition, see: (a) Lee, K.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253–7255. (b) Wu, H.; Radomkit, S.; O'Brien, J. M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 8277–8285.

Upon oxidation of boronic esters, *β*-hydroxy ketones and esters, which are obtainable from *anti*-aldol reactions,[53] could be furnished. *Anti*-aldol reactions depend on catalysts and the innate reactivity of substrates to achieve high enantio- or diastereoselectivity, whereas the selectivities of this method are dictated by the er and dr of bis(boronic esters).

Scheme 3.17. Site-Selective Coupling with Acyl Chlorides[a]



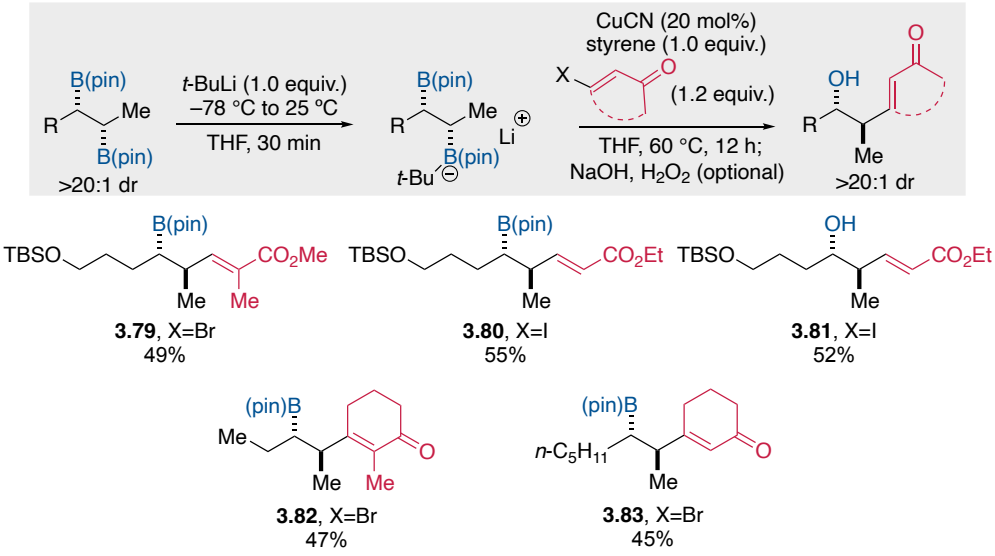
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). [b]Reactions were carried out in the presence of 300 mol% styrene.

β-Haloenones and enoates were effective electrophiles in the Cu-catalyzed coupling (Scheme 3.18). The oxidized products (**3.81**) of some examples could potentially be synthesized by vinylogous aldol reaction, an enantioselective transformation that has been extensively studied.[54] Our method presents an alternative route to access such moieties though the use of 2-alkenes.

[53] For selected reviews on enantioselective aldol reaction, see: (a) Trost, B. M.; Brindle, C. S. *Chem. Soc. Rev.* **2010**, *39*, 1600. (b) Yamashita, Y.; Yasukawa, T.; Yoo, W.-J.; Kitanosono, T.; Kobayashi, S. *Chem. Soc. Rev.* **2018**, *47*, 4388–4480.

[54] For selected reviews on vinylogous aldol reaction, see: (a) Casiraghi, G.; Zanardi, F.; Appendino, G.; Rassu, G. *Chem. Rev.* **2000**, *100*, 1929–1972. (b) Kalesse, M.; Cordes, M.; Symkenberg, G.; Lu, H. *Nat. Prod. Rep.* **2014**, *31*, 563–594. (c) Hosokawa, S. *Acc. Chem. Res.* **2018**, *51*, 1301–1314.

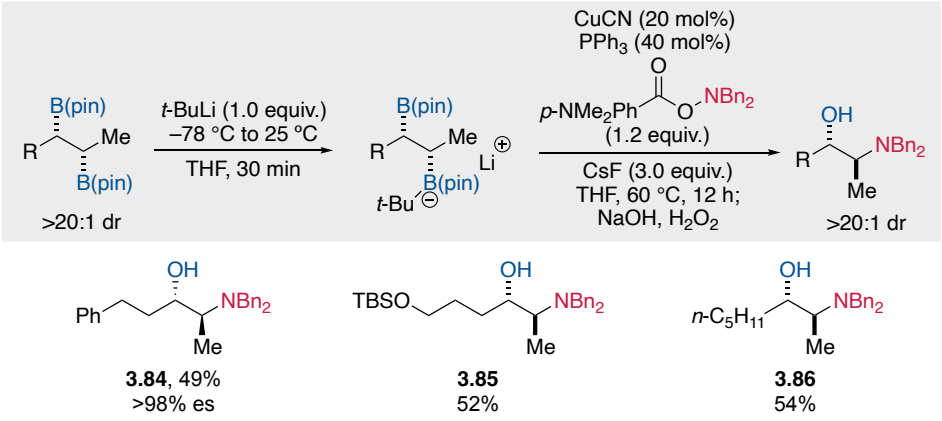
Scheme 3.18. Site-Selective Coupling with β-Haloenones and Enoates[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

Furthermore, amine electrophiles also participated in the reaction, offering a convenient route to a variety of amino alcohols (**3.84**–**3.86**) in 49%–54% yield (Scheme 3.19).

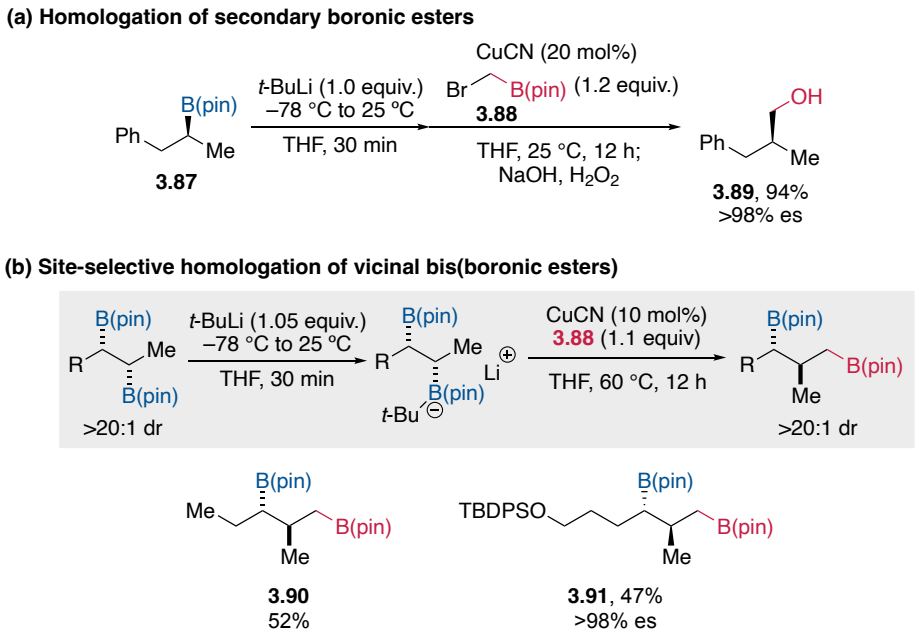
Scheme 3.19. Site-Selective Coupling with Hydroxylamine Esters[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%).

When (bromomethyl)boronic ester (**3.88**) was applied as electrophile in Cu-catalyzed coupling of a secondary boronic ester, a stereoretentive one-carbon homologation product (**3.89**) was obtained in 94% yield (Scheme 3.20a). Site-selective activation followed by catalytic coupling with **3.88** led to stereoretentive homologation of the less-hindered boronic ester (Scheme 3.20b). 1,3-Bis(boronic esters)[55] (**3.90**, **3.91**) were obtained in 47–52% yield.

Scheme 3.20. Site-Selective Coupling with (Bromomethyl)boronic Ester[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%).

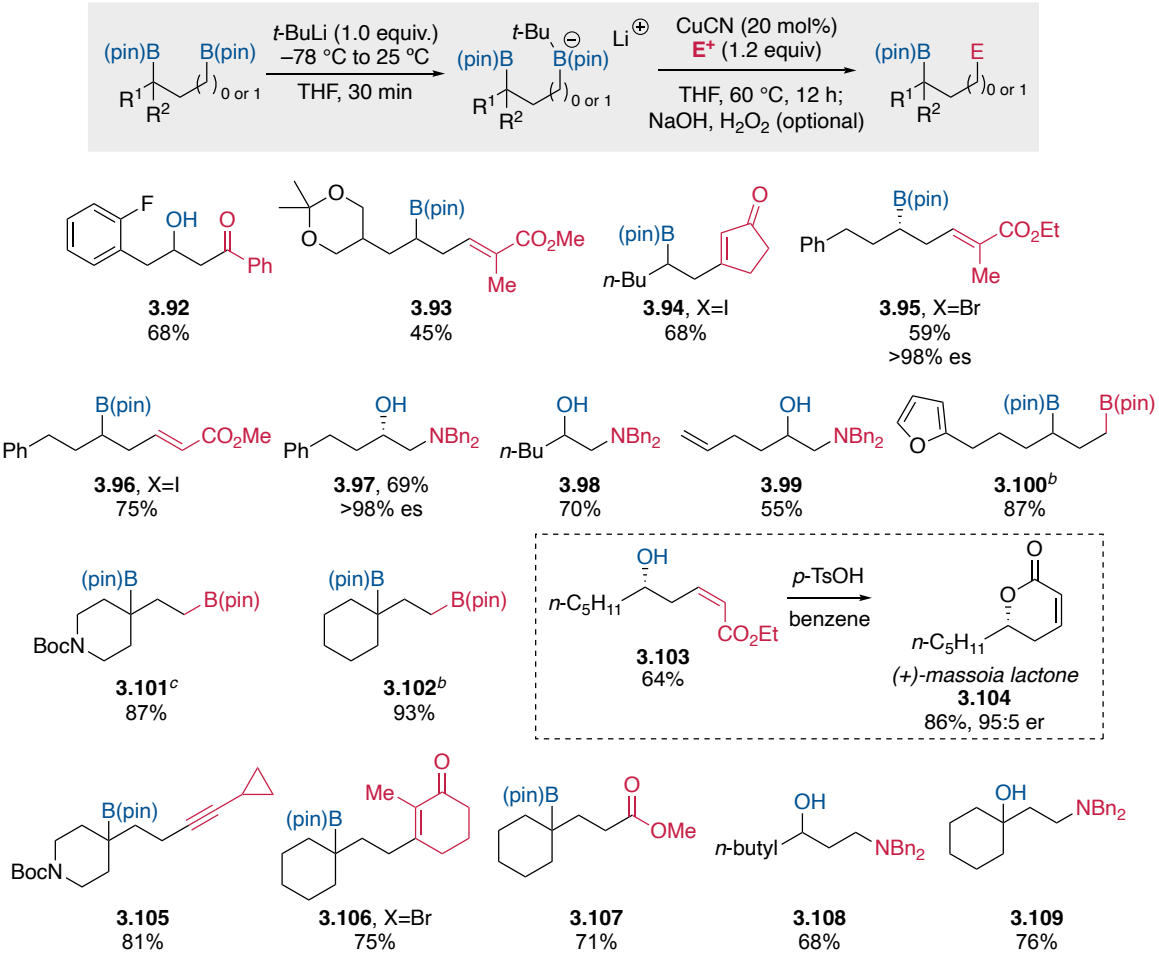
We anticipate that when the two boronic esters exhibit a significant difference in their local environment, site-selective activation becomes more straightforward. Upon subjecting the diboration products of monosubstituted terminal alkenes to selective activation and coupling, we

[55] For selected reports on synthesis of 1,3-bis(boronic esters), see: (a) You, C.; Studer, A. *Angew. Chem., Int. Ed.* **2020**, *59*, 17245–17249. (b) Blair, D. J.; Tanini, D.; Bateman, J. M.; Scott, H. K.; Myers, E. L.; Aggarwal, V. K. *Chem. Sci.* **2017**, *8*, 2898–2903. (c) Li, S.; Hu, C.; Cui, X.; Zhang, J.; Liu, L. L.; Wu, L. *Angew. Chem., Int. Ed.* **2021**, *60*, 26238–26245.

obtained products **3.92**–**3.100** in good yields, from acyl, enone, amine, and bromomethylboronate electrophiles (Scheme 3.21). Diboration of 1,1-disubstituted alkenes followed by the coupling process furnished 1,3-bis(boronic esters) bearing tertiary boronic esters (**3.101**, **3.102**). The Cu-catalyzed coupling with enoates demonstrated stereospecificity with respect to the electrophile, as demonstrated by the coupling of a (*Z*)-*β*-bromoenoate. The coupling afforded **3.103**, a compound that readily converted into massoia lactone (**3.104**) in 86% yield.

With reactions of **3.88** giving ready access to 1,3-bis(boronic esters), these compounds were examined as substrates for site-selective activation/coupling. It is worth noting that with methoxide activation, catalytic coupling of such 1,3-bis(boronic esters) is ineffective for all electrophile classes. However, with *t*-BuLi activation, these substrates were found to react with good efficiency and site-selectivity (**3.105**–**3.109**).

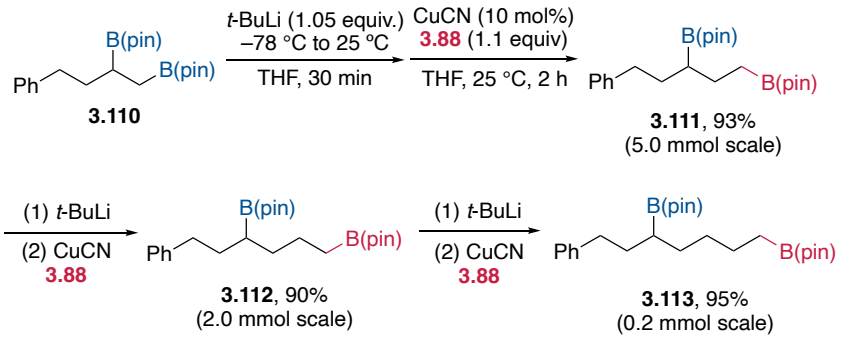
Scheme 3.21. Primary-Selective Coupling of 1,2- and 1,3-Bis(boronic Esters)[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios (er) and enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%). [b]Reactions were carried out at 25 ºC for 2 h. [c]Reaction were carried out at 25 ºC for 12 h.

Encouraged by this observation, sequential homologations were examined and found to provide a facile route to 1,3- (**3.111**) 1,4- (**3.112**) and 1,5-bis(boronic esters) (**3.113**) from the 1,2-bis(boronic ester) precursor (**3.110**) (Scheme 3.22).

Scheme 3.22. Sequential Homologation of Bis(boronic Esters)[a]

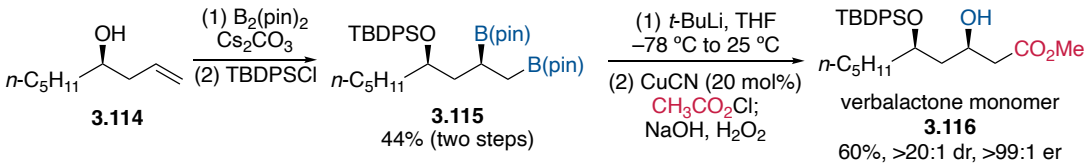


[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%).

3.3.3 Utility of Site-Selective Activation

We explored connecting the directed diboration process to site-selective coupling (Scheme 3.23).[56] Through directed diboration, homoallylic alcohol **3.114** was transformed to bis(boronic ester) **3.115**, which is an excellent substrate for site-selective activation. Cu-catalyzed cross-coupling with chloromethyl formate furnished the enantiomerically enriched verbalactone monomer (**3.116**) in 60% yield.

Scheme 3.23. Synthesis of Verbalactone Monomer[a]



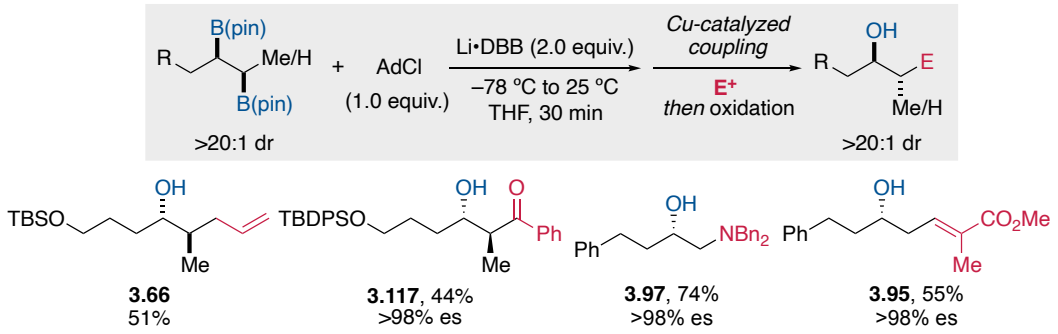
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios (er) were determined by analysis of chiral SFC (±1%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

With an understanding of the efficacy of activation-based selective coupling reactions, we examined the practical aspects of this process. We found that *tert*-butyllithium could be substituted

[56] Blaisdell, T. P.; Morken, J. P. *J. Am. Chem. Soc.* **2015**, *137*, 8712–8715.

with non-pyrophoric lithium-biphenylide (Li•DBB) and adamantyl chloride as the activator for the process (Scheme 3.24).[46b] This activation was conducted at –78 ºC by adding a pre-mixed solution of lithium metal and 4,4'-di-tert-butylbiphenyl (DBB) to a mixture of adamantyl chloride and bisboronate substrate. AdLi was generated *in situ* and activated bis(boronic esters) site-selectively. Subsequent Cu-catalyzed coupling reactions furnished **3.66**, **3.117**, **3.97**, **3.95** in up to 74% yield. For primary-selective coupling of 1,2- or 1,3-bis(boronic esters), activation by AdLi afforded comparable yields to *t*-BuLi activation (**3.97**, **3.95**). Slightly diminished yields were afforded by internal vincinal bis(boronic esters) (**3.66**, **3.117**), possibly due to the steric hindrance of the substrates. All examples exhibited excellent stereospecificity.

Scheme 3.24. Site-Selective Activation of Bis(boronic Esters) Enabled by AdLi[a]

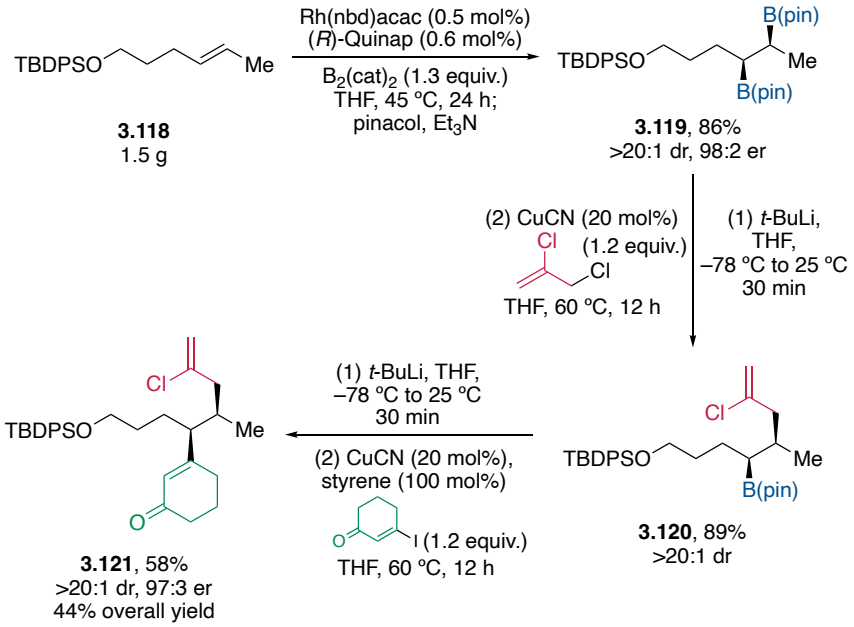


[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified major regioisomer of the products (±5%). Enantiomeric specificity (es) values were determined by analysis of chiral SFC (±1%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

We conducted an enantioselective difunctionalization of unactivated alkene **3.118** on gram-scale (Scheme 3.25). In this process, Rh-catalyzed enantioselective diboration[57] converted **3.118** to **3.119** in 86% yield and 98:2 er. Subsequent activation/coupling sequence delivered difuctionalized alkane **3.121** in 44% overall yield and 97:3 er.

[57] Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702–8703.

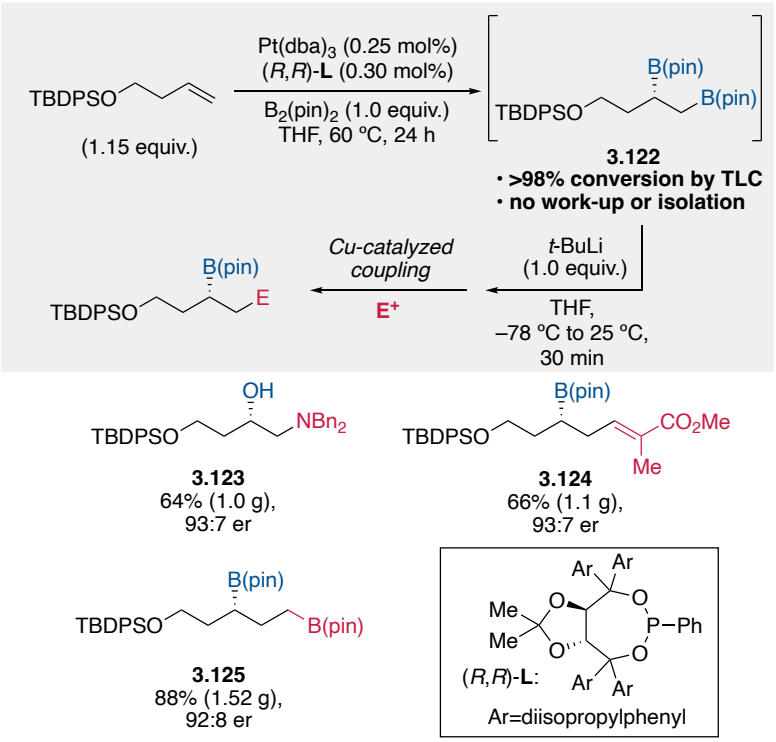
Scheme 3.25. Enantioselective Difunctionalization of Unactivated *E*-Alkene through Diboration/Coupling Sequence[a]



[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Enantiomeric ratios (er) were determined by analysis of chiral SFC (±1%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of purified products (±2%).

Finally, we considered the potential of an enantioselective Pt-catalyzed diboration/coupling sequence that transforms terminal alkenes into targets that were previously inaccessible through single-flask reactions (Scheme 3.26). The diboration/coupling sequence proved effective on gram-scale, affording enantiomerically enriched products including 1,2-aminoalcohol (**3.123**), boroyl enoate (**3.124**), and 1,3-bis(boronic ester) (**3.125**).

Scheme 3.26. Enantioselective Difunctionalizaiton of Unactivated Terminal Alkene through Diboration/Coupling Sequence[a]



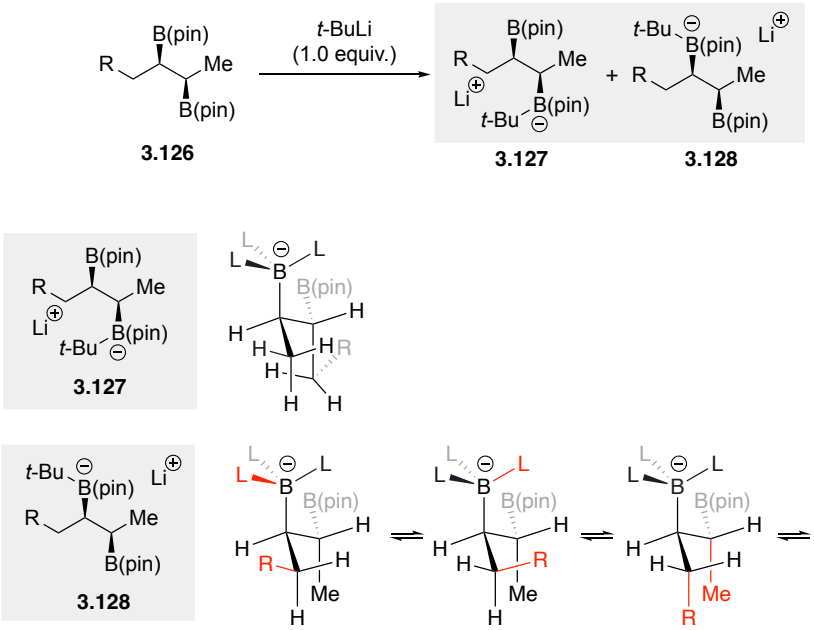
[a]Reactions were carried out under argon atmosphere. Yields corresponded to isolated and purified products (±5%). Conversions of bis(pinacolato)diboron were determined by analysis of TLC and analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).Enantiomeric ratios (er) were determined by analysis of chiral SFC (±1%).

3.3.4 Origin of Site-Selectivity

As depicted in Scheme 3.15, coupling reactions with internal vicinal bis(boronic esters) proceeded with good regioselectivity, even enabling discrimination between a methyl and an ethyl group (**3.62**). We analyzed the origin of site-selectivity when one equivalent of *t*-BuLi is added to a methyl-substituted bisboronic ester such as **3.126** (Scheme 3.27). Through conformational analysis, it could be observed that complex **3.128** possesses an additional *syn*-pentane interaction compared to complex **3.127**. Moreove, this *syn*-pentane interaction cannot be alleviated by bond rotation. Although the selectivities for formation of **3.127** over **3.128** cannot be strictly attributed

to thermodynamic control, it is possible that the energy gap between the products (**3.127** and **3.128**) reflects a disparity in the energy levels of the transition states involved in "ate" complex formation.

Scheme 3.27. Conformational Analysis of Regioisomeric "Ate" Complexes

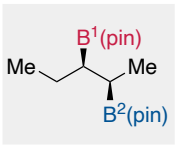


To gain a comprehensive understanding of the likely conformation of internal bis(boronic esters) in the transition state of *t*-BuLi addition, we explored the low-energy conformers of **3.129**, the *syn*-diboration product of (*E*)-2-pentene. Ground state energies of nine conformers of **3.129** (designated as **3.129-1** to **3.129-9**) were calculated by DFT analysis (Scheme 3.28a). Upon visualizing the lowest energy conformer, **3.129-8**, from two different perspectives (Scheme 3.28b), it became evident that the boronic ester (B^1(pin)) adjacent to the ethyl group is more hindered than the boronic ester (B^2(pin)) neighboring the methyl group.

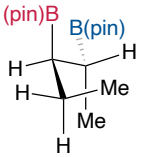
We propose that the variation in steric hindrance within the lowest energy conformer **3.129-8** may contribute to the site-selectivity observed in the formation of the "ate" complex formation with *t*-BuLi.

Scheme 3.28. Conformation Analysis of Bis(boronic Ester) **3.129**[a]

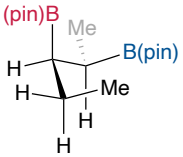
(a) Ground state energies of conformers of 3.129



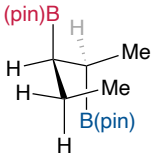
3.129



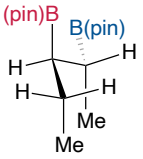
3.129-1
1.03 kcal/mol



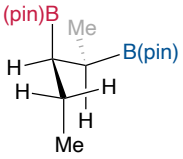
3.129-2
2.72 kcal/mol



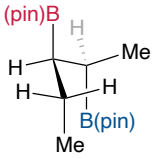
3.129-3
5.11 kcal/mol



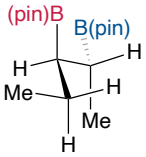
3.129-4
3.03 kcal/mol



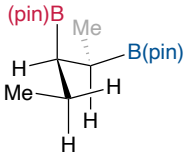
3.129-5
0.55 kcal/mol



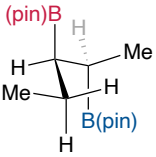
3.129-6
3.64 kcal/mol



3.129-7
0.73 kcal/mol

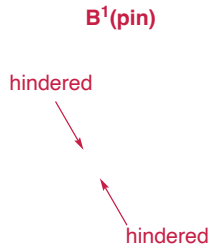


3.129-8
0 kcal/mol

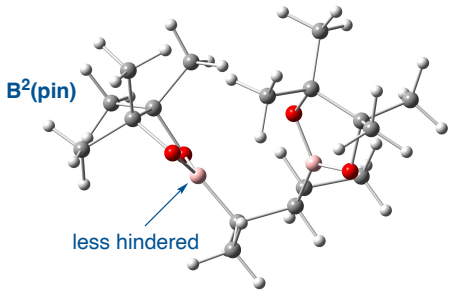


3.129-9
2.75 kcal/mol

(b) Visualization of the lowest energy conformer 3.129-8



3.129-8



3.129-8

[a]Ground state geometries were optimized with DFT methodology. The B3LYP(GD3BJ) functional and 6-31G* basis sets were employed. Tetrahydrofuran solvation was modeled with the PCM model.

3.4 Conclusions

In summary, steric-based regioselective activation of bis(boronic esters), followed by Cu-catalyzed stereospecific cross-coupling, can be implemented with a broad array of electrophiles. This approach offers straightforward routes to 1,2-difunctionalized compounds. By selective,

independent, and enantiospecific functionalization of each boronic ester, this method facilitates the enantioselective difunctionalization of unactivated alkenes.

3.5 Acknowledgments

I thank Prof. James P. Morken for providing me the opportunity to start and study this project. I deeply appreciate John Holmgren for his contribution to this project. I am also grateful for the discussions with all the other Morken group members.

This work was supported financially by the NIH (R35-GM1217140). We thank Boston College and the chemistry department for assistance.

3.6 Experimental Section

3.6.1 General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian/Agilent VNMRS DD1 system at 14.1 T (600 MHz) with a 5 mm PFG AutoX DB probe at 25 ºC, with the VJ 4.2 software, or a Varian/Agilent VNMRS DD1 system at 11.7 T (500 MHz) with a 5 mm PFG OneNMR probe at 25 ºC, with the VJ 4.2 software. COSY spectra were recorded on a Bruker AVANCE NEO system at 11.7 T (500 MHz) with a 5 mm X-nuclei optimized double resonance BBFO (He) CryoProbe and sample case, with Topspin 4.1. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz).

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).

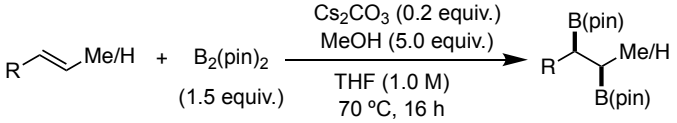
High- resolution mass spectrometry direct analysis in real time (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed with forced flow (flash chromatography) on silica gel (SiO_2, 230 × 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed with ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and potassium permanganate ($KMnO_4$) in water. Analytical chiral supercritical fluid chromatography (SFC) was performed either on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier on CHIRALCEL OD-H, CHIRALCEL OJ-H, CHIRALPAK AD-H, CHIRALPAK AS-H or CHIRALCEL OD-RH from Chiral Technologies. HPLC measurements were carried out on a Shimadzu HPLC system with Chiralcel AS-H column.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified by Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. All other reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without purification.

3.6.2 Experimental Procedures

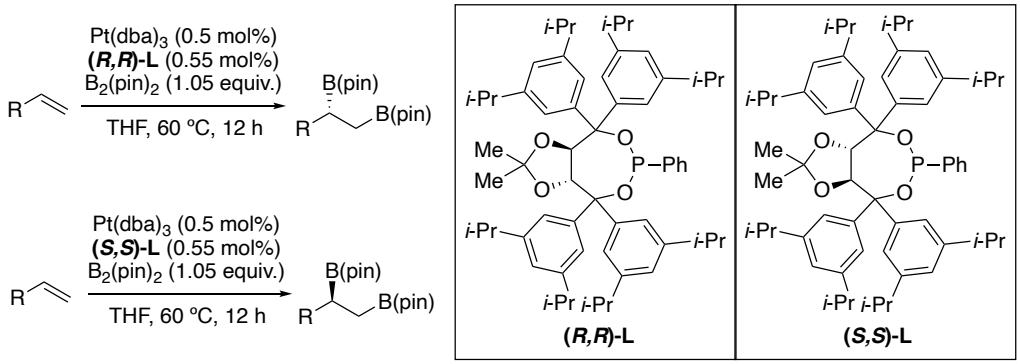
3.6.2.1 Preparation of Substrates

General Procedure A: Preparation of racemic 1,2-bis(boronic pinacol esters)



Racemic 1,2-bis(boronic pinacol esters) were prepared according to a modified literature procedure.[58] Cesium carbonate (0.20 equiv.) and bis(pinacolato)diboron (1.40 equiv.) were transferred into an oven-dried flask with a stir bar under argon. THF (1.0 M) was added to dissolve the mixture. Subsequently, the alkene (1.0 equiv.) and MeOH (5.0 equiv.) were added, and the mixture was allowed to stir at 60 ºC overnight, after which the mixture was filtered through a plug of silica gel. The mixture was concentrated under reduced pressure and the resulting mixture was purified by silica gel chromatography with EtOAc/hexanes. Of note, for disubstituted alkenes, it is crucial for the reaction to be run under inert atmosphere and at 1.0 M concentration in order to achieve high yield.

General Procedure B: Preparation of enantiomerically enriched 1,2-bis(boronic pinacol esters)



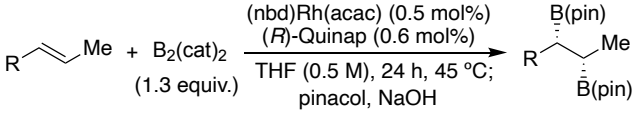
Enantiomerically enriched 1,2-bis(boronic pinacol esters) were prepared according to a literature procedure.[59] To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (0.5 mol%), (*R,R*)-L or (*S,S*)-L (0.55 mol%), and $B_2(pin)_2$ (1.05 equiv.). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added by syringe, and the mixture was allowed to stir at 80 °C for 30 min. The flask was then allowed to

[58] Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyás, H.; Fernández, E. *Angew. Chem., Int. Ed.* **2011**, *50* (31), 7158–7161.

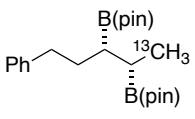
[59] Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222–11231.

cool to room temperature and was charged with terminal alkene (1.0 equiv.). After purging once more with N_2, the mixture was allowed to stir at 60 ºC overnight. The mixture was filtered through a silica gel plug and concentrated under reduced pressure. The mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product.

General Procedure C: Preparation of enantiomerically enriched bis(boronic pinacol esters)

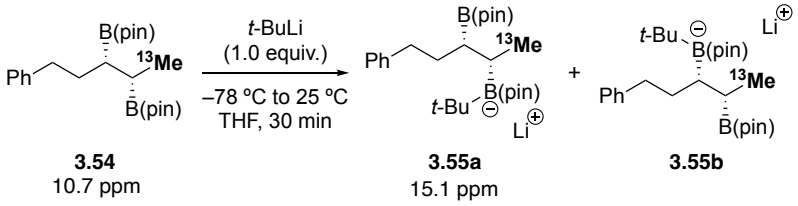


Enantiomerically enriched bis(boronic pinacol esters) were prepared according to a modified literature procedure.[27a] An oven-dried flask equipped with a stir bar was charged with (bicyclo[2.2.1]hepta-2,5-diene)-(2,4-pentanedionato)-rhodium(I) (0.5 mol%), (*R*)-Quinap (0.6 mol%), and THF (0.5 M to alkene) under an atmosphere of argon in a glovebox. The resulting yellow solution was allowed to stir for 5 min. Then, bis(catecholato)diboron (1.3 equiv.) was added to the solution under argon. The solution turned immediately from yellow to dark brown/red. The solution was allowed to stir for another 5 min. Then, alkene (1.0 equiv.) was added under argon. The flask was sealed and removed from the glovebox, and the solution was allowed to stir for 24 h at 45 ºC. The solution was allowed to cool to room temperature, pinacol (4.0 equiv.) and an aqueous solution of NaOH (0.1 equiv., 0.2 M) were added. The mixture was allowed to stir for 8 h at 60 ºC. The reaction was quenched by addition of water, washed with diethyl ether, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (3–5% diethyl ether in hexanes) to afford the products.



2,2'-((2*S*,3*S*)&(2*R*,3*R*)-5-Phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.54). The title compound was prepared according to

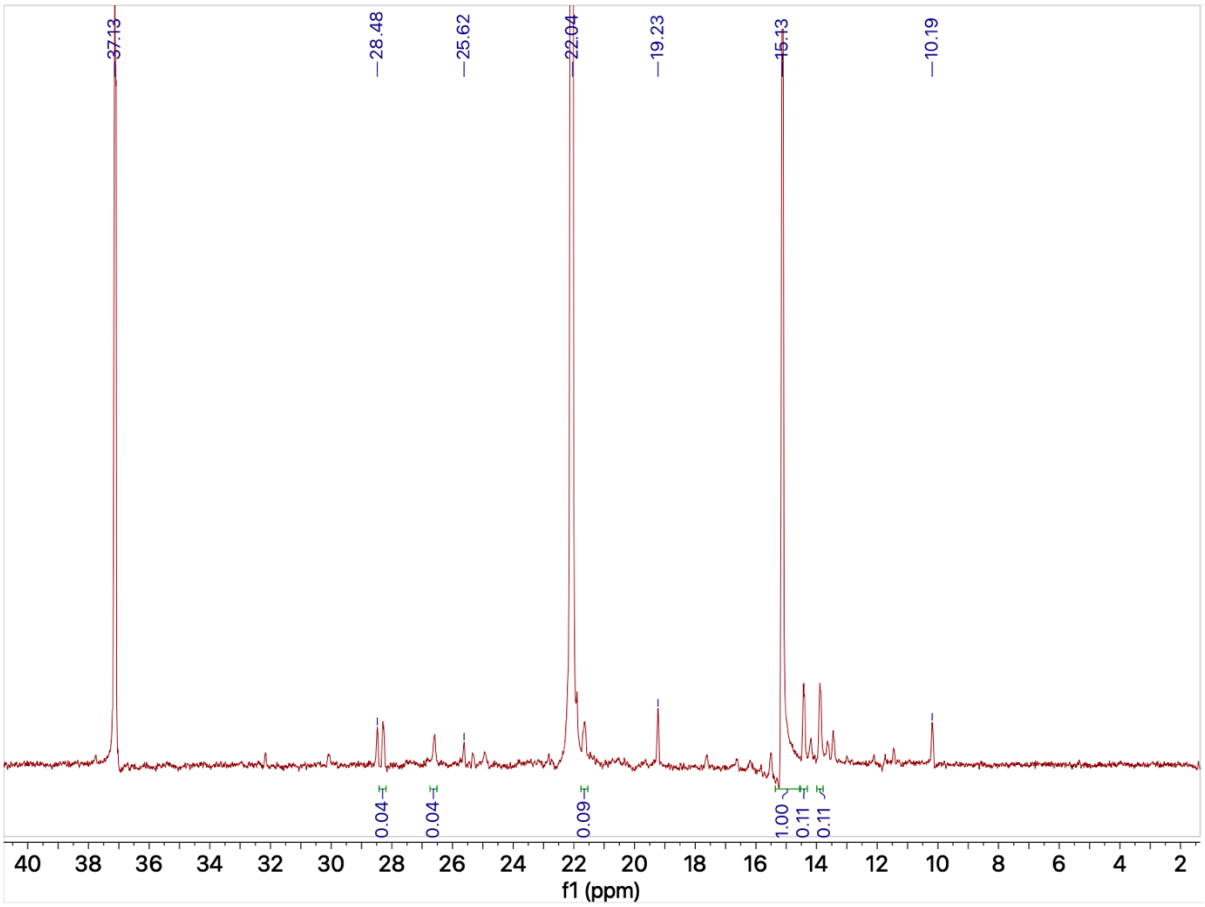
General Procedure A with ^{13}C labelled (*E*)-pent-3-en-1-ylbenzene (391.3 mg, 2.7 mmol), $B_2(pin)_2$ (1.0 g, 4.0 mmol), Cs_2CO_3 (174.4 mg, 0.54 mmol), methanol (428.7 mg, 13.4 mmol) in THF. The resulting colorless oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (1.07 g, 2.8 mmol, 70% yield) as colorless oil. ^{13}C labelled (*E*)-pent-3-en-1-ylbenzene was synthesized according to literature procedure[60] with $^{13}CH_3I$. ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 2.66 (ddd, *J* = 13.4, 10.9, 5.1 Hz, 1H), 2.55 (ddd, *J* = 13.4, 10.9, 6.0 Hz, 1H), 1.88 – 1.78 (m, 1H), 1.74 – 1.65 (m, 1H), 1.27 (s, 12H, overlapped with m, 1H), 1.24 (d, *J* = 3.9 Hz, 12H), 1.20 – 1.15 (m, 1H), 1.00 (dd, *J* = 125.7, 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 128.4, 128.1, 125.4, 82.9, 82.8, 35.7, 31.7 (d, *J* = 3.3 Hz), 25.1, 25.0, 24.8, 24.7, 14.3. IR: ν_{max} 2975 (m), 2864 (w), 1455 (w), 1369 (s), 1311 (s), 1214 (w), 1110 (s), 967 (w), 862 (w), 747 (w), 699 (w) cm^{-1}.; HRMS (DART) for $C_{22}{}^{13}CH_{39}B_2O_4$; $[M+H]^+$: calculated: 402.3063, found: 402.3068.



In a glovebox under argon atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added **3.54** (80.0 mg, 0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (0.2 mmol, solution in heptane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min, to warm to room temperature and to

[60] Doi, H.; Ban, I.; Nonoyama, A.; Sumi, K.; Kuang, C.; Hosoya, T.; Tsukada, H.; Suzuki, M. *Chem. Eur. J.* **2009**, *15*, 4165–4171

stir for 25 min. DMSO (20 μL) was added before the mixture was directly transferred to NMR tube.



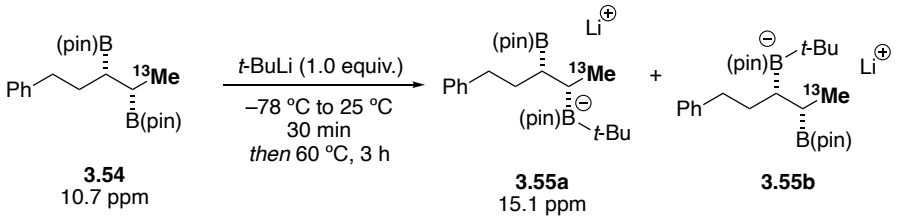
t-BuLi was added as solution in heptane. Therefore, heptane was in the mixture.

Heptane ^{13}C NMR shifts (in THF): δ 28.48, 25.62, 19.23, 10.19.

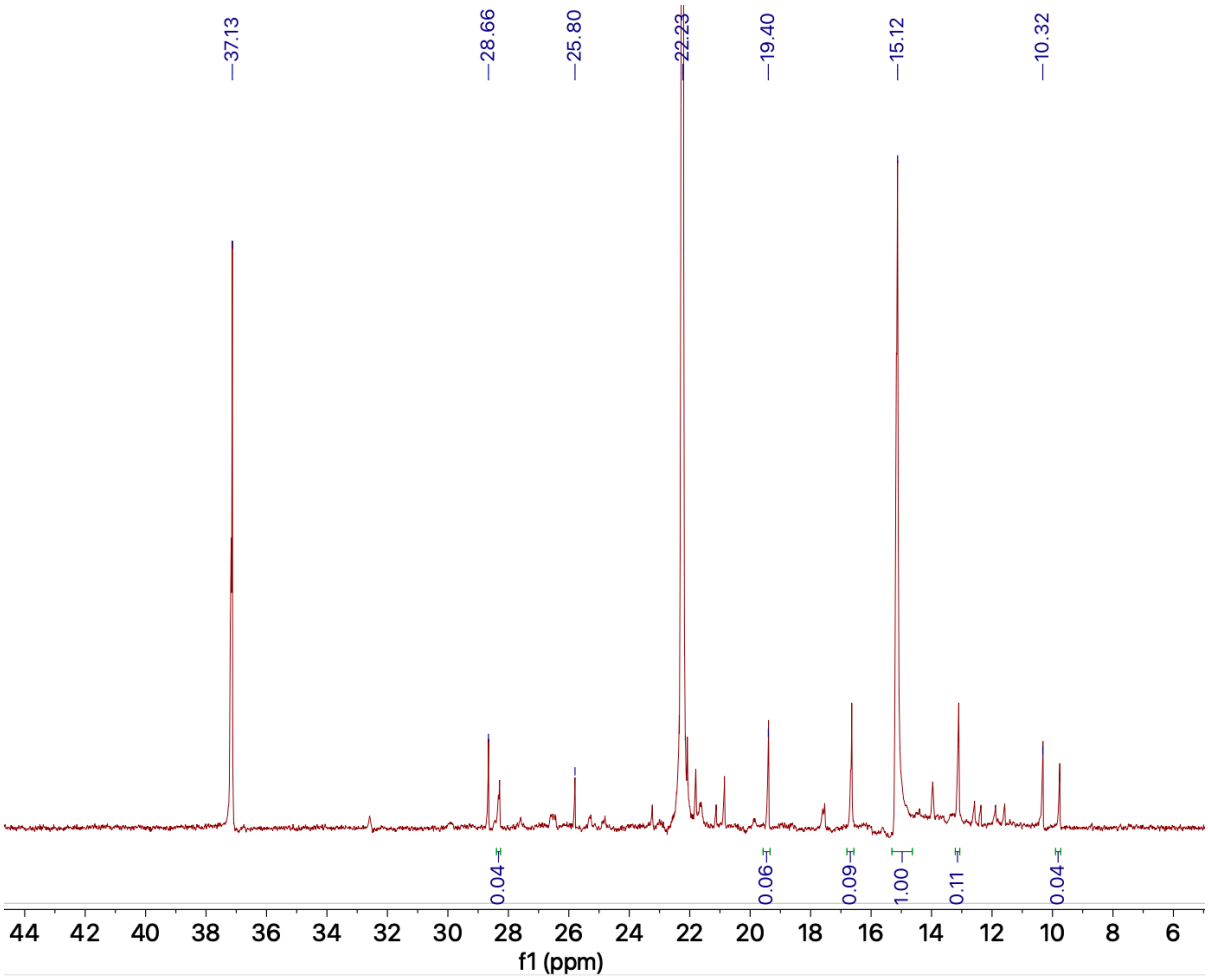
THF ^{13}C NMR shifts: δ 63.89, 22.04.

DMSO ^{13}C NMR shifts: δ 37.13.

Due to the difficulty in synthesizing **3.55b** exclusively, the chemical shift of the labelled carbon in **3.55b** is unknown. We then integrated every minor peak in the spectrum. The ratio of any minor peak to **3.55a** is lower than 1:9.



In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added **3.54** (80.0 mg, 0.2 mmol) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (0.2 mmol, solution in heptane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min, to warm to room temperature and to stir for 25 min. The mixture was then allowed to stir at 60 ºC for 3 h. DMSO (20 μL) was added before the mixture was directly transferred to NMR tube.

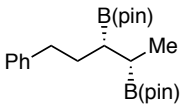


Heptane ^{13}C NMR shifts (in THF): δ 28.66, 25.80, 19.40, 10.32.

THF ^{13}C NMR shifts: δ 64.06, 22.23.

DMSO ^{13}C NMR shifts: δ 37.13.

The ratio of any minor peak to **3.55a** is lower than 1:9.



2,2'-((2*S*,3*S*)-5-Phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.56). The title compound was prepared according to *General Procedure C* with (*E*)-pent-3-en-1-ylbenzene (2.24 g, 15.3 mmol), $B_2(cat)_2$ (4.01 g, 16.7 mmol), (nbd)Rh(acac) (25.53 mg, 0.076 mmol), (*R*)-Quinap (33.66 mg, 0.076 mmol) in THF. The resulting

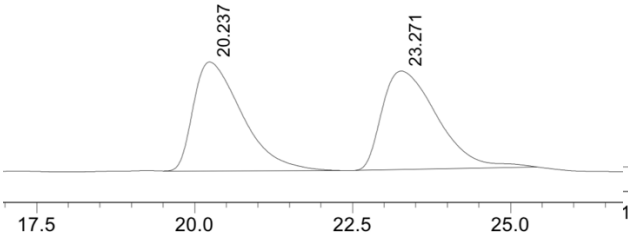
brown oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.51 g, 8.8 mmol, 58% yield) as pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 7.22 – 7.13 (m, 3H), 2.66 (ddd, *J* = 13.4, 11.1, 5.1 Hz, 1H), 2.54 (ddd, *J* = 13.4, 10.9, 6.0 Hz, 1H), 1.87 – 1.78 (m, 1H), 1.74 – 1.64 (m, 1H), 1.30 – 1.25 (m, 13H), 1.23 (d, *J* = 3.8 Hz, 12H), 1.20 – 1.13 (m, 1H), 1.00 (d, *J* = 7.5 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 128.4, 128.1, 125.4, 82.84, 82.76, 35.7, 31.7, 25.1, 25.0, 24.8, 24.7, 14.3.; IR: ν_{max} 2975 (m), 2864 (w), 1455 (w), 1369 (s), 1311 (s), 1214 (w), 1110 (s), 967 (w), 862 (w), 747 (w), 699 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{39}B_2O_4$; $[M+H]^+$: calculated: 401.3029, found: 401.3045. $[\alpha]_D^{20}$: –12.5 (c = 0.75, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral HPLC. Racemic compound was prepared according to the *General Procedure A*. Material was oxidized with NaOH and H_2O_2 and used for HPLC without purification. Absolute stereochemistry was assigned by analogy.

Chiral HPLC (AS-H, 2% IPA, 98% Hexanes, 1.0 mL/min, 40 ºC, 209 nm) – analysis of 5-phenylpentane-2,3-diol.

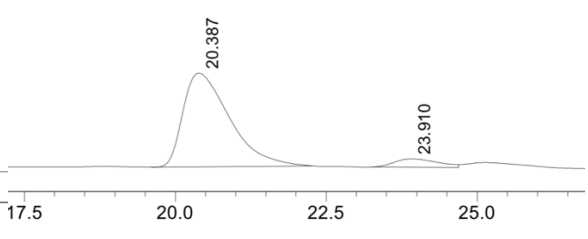
Racemic Compound



PDA Ch1 209nm

Peak#	Ret. Time	Area%
1	20.237	49.392
2	23.271	50.608
Total		100.000

Standard Conditions



PDA Ch1 209nm

Peak#	Ret. Time	Area%
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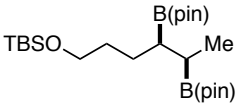
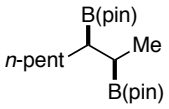
2	23.910	7.875
Total		100.000

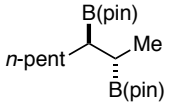


(((4*S*,5*S*)&(4*R*,5*R*)-4,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (3.130). The title compound was prepared according to *General Procedure A* with (*E*)-hex-4-en-1-ol (1.50 g, 15.0 mmol), $B_2(pin)_2$ (5.71 g, 22.5 mmol), Cs_2CO_3 (0.98g, 3.0 mmol), methanol (2.40 g, 75.0 mmol) in THF. The reaction was allowed to cool to room temperature and concentrated *in vacuo* (ensuring that all methanol has been removed from the residue). To the residue was added dichloromethane (23 mL) and imidazole (9.19 g, 135 mmol, 9.0 equiv.). The mixture was cooled to 0 ºC and TBSCl (6.78 g, 45 mmol, 3.0 equiv.) was added. It was then allowed to warm to room temperature and to stir overnight. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (15 mL). The layers were allowed to separate and the aqueous layer was washed with dichloromethane (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The pale-yellow oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (6.42 g, 13.5 mmol, 91% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 – 3.55 (m, 2H), 1.61 – 1.42 (m, 3H), 1.41 – 1.33 (m, 1H), 1.22 (s, 24H), 1.19 – 1.13 (m, 1H), 1.10 – 1.02 (m, 1H), 0.95 (d, J = 7.5 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126

MHz, $CDCl_3$) δ 82.7, 82.7, 63.8, 32.6, 26.0, 25.5, 25.0, 24.9, 24.7, 24.6, 18.3, 14.3, -5.2.; IR: ν_{max} 2974 (w), 2927 (w), 2854 (w), 1461 (w), 1369 (s), 1308 (s), 1253 (m), 1214 (m), 1140 (s), 1095 (s), 967 (m), 833 (s), 773 (s), 668 (w), 578 (w) cm^{-1}.; HRMS (DART) for $C_{24}H_{51}B_2O_5Si$; $[M+H]^+$: calculated: 469.3686, found: 469.3686.

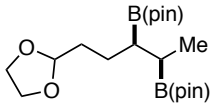


2,2'-((2*S*,3*S*)&(2*R*,3*R*)-Octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.131). The title compound was prepared according to *General Procedure A* with (*E*)-oct-2-ene (1.68 g, 15.0 mmol), $B_2(pin)_2$ (5.71 g, 22.5 mmol), Cs_2CO_3 (0.98 g, 3.0 mmol), methanol (2.40 g, 75.0 mmol) in THF. The resulting colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (4.09 g, 11.1 mmol, 74% yield) as colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.53 – 1.44 (m, 1H), 1.36 – 1.26 (m, 7H), 1.24 – 1.20 (m, 24H), 1.18 – 1.13 (m, 1H), 1.09 – 1.02 (m, 1H), 0.96 (d, *J* = 7.5 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.7, 32.2, 29.3, 28.9, 25.0, 24.9, 24.7, 24.6, 22.6, 14.3, 14.0.; IR: ν_{max} 2974 (w), 2924 (w), 2855 (w), 1459 (w), 1368 (s), 1307 (s), 1214 (m), 1140 (s), 967 (m), 859 (m), 725 (w), 669 (w), 578 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{41}B_2O_4$; $[M+H]^+$: calculated: 367.3186, found: 367.3191.

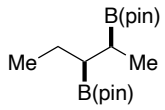


2,2'-((2*R*,3*S*)&(2*S*,3*R*)-Octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.132). The title compound was prepared according to *General Procedure A* with (*Z*)-oct-2-ene (112 mg, 1.0 mmol), $B_2(pin)_2$ (381 mg, 1.50 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), methanol (160 mg, 5.0 mmol) in THF. The resulting colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (366 mg, 0.8 mmol, 78% yield) as colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.53 – 1.44 (m, 1H), 1.34 – 1.25 (m, 7H), 1.23 (s, 24H), 1.18 – 1.09 (m, 2H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.69, 82.68, 32.1, 30.4, 29.1, 25.0, 24.8, 22.6, 14.0

(overlapped).; IR: ν_{max} 2974 (w), 2924 (w), 2855 (w), 1459 (w), 1368 (s), 1307 (s), 1214 (m), 1140 (s), 967 (m), 859 (m), 725 (w), 669 (w), 578 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{41}B_2O_4$; $[M+H]^+$: calculated: 367.3186, found: 367.3200.

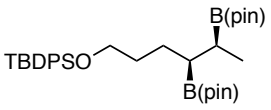


2,2'-((2*S*,3*S*)&(2*R*,3*R*)-5-(1,3-Dioxolan-2-yl)pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.133). The title compound was prepared according to *General Procedure A* with (*E*)-2-(pent-3-en-1-yl)-1,3-dioxolane (550 mg, 3.9 mmol), $B_2(pin)_2$ (1.28 g, 5.0 mmol), Cs_2CO_3 (189 mg, 0.58 mmol), methanol (620 mg, 19.3 mmol) in THF. The resulting colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (922 mg, 2.3 mmol, 60% yield) as colorless gel. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.84 – 4.81 (m, 1H), 3.95 – 3.91 (m, 2H), 3.83 – 3.78 (m, 2H), 1.73 – 1.66 (m, 1H), 1.62 – 1.53 (m, 2H), 1.51 – 1.45 (m, 1H), 1.21 (d, J = 2.5 Hz, 24H), 1.19 – 1.13 (m, 1H), 1.12 – 1.05 (m, 1H), 0.95 (d, J = 7.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 105.0, 82.81, 82.75, 64.69, 64.67, 33.4, 25.0, 24.9, 24.7, 24.6, 23.8, 14.2.; IR: ν_{max} 2974 (m), 2870 (w), 1457 (w), 1370 (s), 1311 (s), 1214 (m), 1141 (s), 1038 (w), 967 (m), 840 (w), 670 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{39}B_2O_6$; $[M+H]^+$: calculated: 397.2927, found: 397.2941.



2,2'-((2*S*,3*S*)&(2*R*,3*R*)-Pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.129). The title compound was prepared according to *General Procedure A* with (*E*)-pent-2-ene (701 mg, 10.0 mmol), $B_2(pin)_2$ (3.56 g, 14.0 mmol), Cs_2CO_3 (652 mg, 2.0 mmol), methanol (1.60 g, 50.0 mmol) in THF. The resulting colorless oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (2.79 g, 8.6 mmol, 86% yield) as colorless oil. All spectral data are in accordance with the literature.[61]

[61] Huang, M.; Hu, J.; Shi, S.; Friedrich, A.; Krebs, J.; Westcott, S. A.; Radius, U.; Marder, T. B. *Chem. Eur. J.* **2022**, *28*, e2022004.



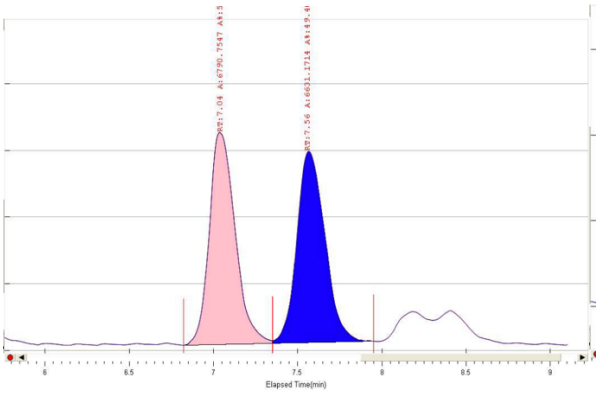
(((4*S*,5*S*)-4,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)diphenylsilane (**3.119**). The title compound was prepared according to *General Procedure C* with (*E*)-*tert*-butyl(hex-4-en-1-yloxy)diphenylsilane (1.5 g, 4.4 mmol), $B_2(cat)_2$ (1.37 g, 5.8 mmol), (nbd)Rh(acac) (6.52 mg, 0.022 mmol), (*R*)-Quinap (11.68 mg, 0.027 mmol) in THF. The resulting brown oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (2.26 g, 3.8 mmol, 86% yield) as pale-yellow viscous gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.65 (m, 4H), 7.43 – 7.34 (m, 6H), 3.66 (t, *J* = 6.0 Hz, 2H), 1.69 – 1.52 (m, 3H), 1.47 – 1.40 (m, 1H), 1.22 (s, 24H), 1.20 – 1.15 (m, 1H), 1.11 – 1.02 (m, 10H), 0.97 (d, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 134.32, 134.30, 129.4, 127.5, 82.74, 82.71, 64.6, 32.4, 26.9, 25.6, 25.01, 24.95, 24.7, 24.6, 19.2, 14.3.; IR: ν_{max} 2974 (w), 2928 (w), 2856 (w), 1460 (w), 1369 (s), 1310 (s), 1215 (w), 1141 (s), 1109 (s), 968 (w), 860 (w), 822 (w), 701 (s), 613 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{34}H_{55}B_2O_5Si$; $[M+H]^+$: calculated: 593.3999, found: 593.4016. $[\alpha]_D^{20}$: –6.9 (c = 1.0, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Procedure A*. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

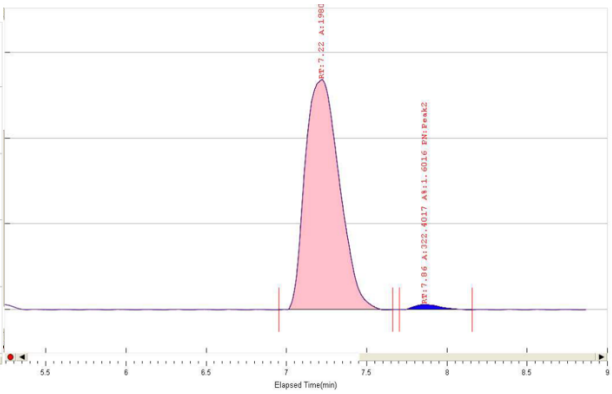
Chiral SFC (OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 6-((tert-butyldiphenylsilyl)oxy)hexane-2,3-diol.

Racemic Compound



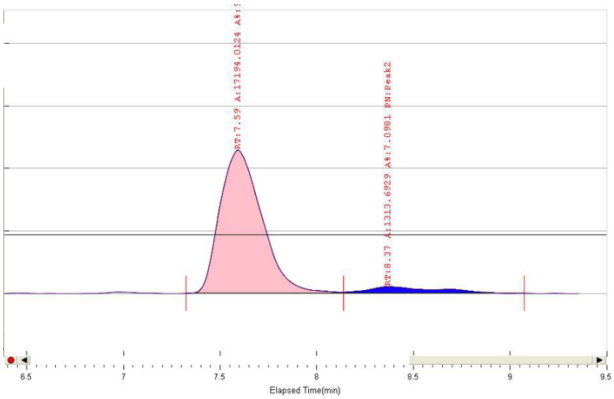
Peak No	% Area	Area	RT (min)
1	48.9831	28105.5517	6.9
2	51.0169	29272.5466	7.57
Total:	100	57378.0083	

Standard Conditions (first run)

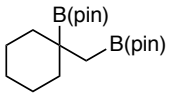


Peak No	% Area	Area	RT (min)
1	98.3984	19807.291	7.22
2	1.6016	322.4017	7.86
Total:	100	20129.6927	

Standard Conditions (second run)

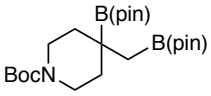


Peak No	% Area	Area	RT (min)
1	92.9019	17194.0124	7.59
2	7.0981	1313.6929	8.37
Total:	100	18507.7053	

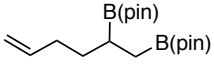


4,4,5,5-Tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)methyl)-1,3,2-dioxaborolane (**3.134**). The title compound was prepared according to *General Procedure A* with methylenecyclohexane (1.0 g, 10.4 mmol), $B_2(pin)_2$ (3.96 g, 15.6 mmol), Cs_2CO_3 (677 mg, 2.08 mmol), methanol (1.67 g, 52.0 mmol) in THF. The resulting white solid was purified by silica gel chromatography (5% ethyl acetate in hexanes)

to afford the title compound (2.16 g, 6.1 mmol, 59% yield) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90 – 1.83 (m, 2H), 1.66 – 1.55 (m, 4H), 1.42 – 1.34 (m, 2H), 1.24 (s, 12H), 1.23 (s, 12H), 0.88 (td, *J* = 12.7, 3.2 Hz, 2H), 0.75 – 0.69 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.8, 82.7, 34.9, 26.8, 25.4, 24.9, 24.8.; IR: ν_{max} 2974 (w), 2920 (w), 2849 (w), 1448 (w), 1354 (m), 1302 (m), 1271 (m), 1184 (s), 970 (w), 849 (w), 711 (w), 670 (w) cm^{-1}.; HRMS (DART) for $C_{19}H_{37}B_2O_4$; $[M+H]^+$: calculated: 351.2873, found: 351.2886.

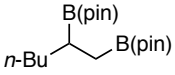


***tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)piperidine-1-carboxylate** (**3.135**). The title compound was prepared according to *General Procedure A* with *tert*-butyl 4-methylenepiperidine-1-carboxylate (1.97 g, 10.0 mmol), $B_2(pin)_2$ (3.81 g, 15.0 mmol), Cs_2CO_3 (652 mg, 2.0 mmol), methanol (1.60 g, 50.0 mmol) in THF. The resulting white solid was purified by silica gel chromatography (10–20% ethyl acetate in hexanes) to afford the title compound (3.1 g, 6.9 mmol, 69% yield) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (d, *J* = 13.5 Hz, 2H), 2.92 – 2.83 (m, 2H), 1.84 (d, *J* = 13.0 Hz, 2H), 1.44 (s, 9H), 1.25 (s, 12H), 1.22 (s, 12H), 1.20 – 1.14 (m, 2H), 0.83 (s, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 83.1, 82.9, 78.8, 42.8, 36.1, 28.5, 24.8.; IR: ν_{max} 2974 (w), 2925 (w), 1690 (s), 1444 (m), 1363 (s), 1307 (m), 1226 (m), 1140 (s), 973 (w), 862 (w), 846 (w), 701 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{44}B_2NO_6$; $[M+H]^+$: calculated: 452.3349, found: 452.3366.

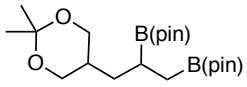


2,2'-(Hex-5-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.136**). The title compound was prepared according to a modified *General Procedure B* with $B_2(pin)_2$ (2.54 g, 10.0 mmol, 1.0 equiv.), hexa-1,5-diene (4.93 g, 60.0 mmol, 6.0 equiv.), $Pt(dba)_3$ (89.8 mg, 0.10 mmol, 1 mol%) in THF (30 mL), the mixture was heated at 50 ºC for 12 h. The resulting brown oil was purified by silica gel chromatography (3–5% ethyl acetate in hexanes) to

afford the title compound (3.1 g, 9.3 mmol, 93% yield) as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.98 (d, *J* = 17.1Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 2.06 (q, *J* = 7.3 Hz, 2H), 1.62 – 1.52 (m, 1H), 1.47 – 1.33 (m, 1H), 1.23 (d, *J* = 3.2 Hz, 24H), 1.19 – 1.08 (m, 1H), 0.93 – 0.77 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.4, 114.0, 82.82, 82.79, 33.12, 33.08, 24.9, 24.83, 24.77, 24.7.; IR: ν_{max} 2975 (w), 2924 (w), 1662 (w), 1368 (s), 1310 (s), 1213 (w), 1140 (s), 966 (m), 906 (w), 845 (w), 670 (w), 578 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{35}B_2O_4$; $[M+H]^+$: calculated: 337.2716, found: 337.2723.

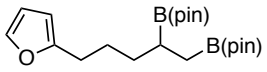


2,2'-(Hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.137**). The title compound was prepared according to *General Procedure A* with hex-1-ene (1.26 g, 15.0 mmol), $B_2(pin)_2$ (5.33 g, 21.0 mmol), Cs_2CO_3 (977 mg, 3.0 mmol), methanol (2.40 g, 75.0 mmol) in THF. The resulting colorless oil was purified by silica gel chromatography 3–5% diethyl ether in hexanes) to afford the title compound (3.9 g, 11.5 mmol, 77% yield) as colorless oil. All spectral data are in accordance with the literature.[61]

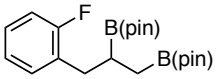


2,2'-(3-(2,2-Dimethyl-1,3-dioxan-5-yl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.138**). The title compound was prepared according to *General Procedure A* with 5-allyl-2,2-dimethyl-1,3-dioxane (1.81 g, 11.6 mmol), $B_2(pin)_2$ (3.53 g, 14.0 mmol), Cs_2CO_3 (566 mg, 1.74 mmol), methanol (1.86 g, 57.9 mmol) in THF. The resulting colorless oil was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the title compound (3.22 g, 7.9 mmol, 68% yield) as colorless gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 – 3.79 (m, 2H), 3.58 – 3.49 (m, 2H), 1.99 – 1.89 (m, 1H), 1.41 (s, 3H), 1.38 (s, 3H), 1.35 – 1.27 (m, 1H), 1.22 (s, 24H), 1.17 – 1.06 (m, 2H), 0.87 – 0.77 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 97.6, 83.0, 82.9, 65.3, 65.1, 33.0, 32.2, 28.2, 24.9, 24.82, 24.78, 24.7, 19.8.; IR: ν_{max} 2975 (w), 2926 (w), 2852 (w), 1452 (m), 1368 (m), 1258 (w), 1139 (s), 1069 (w),

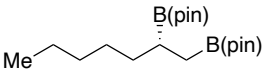
1035 (w), 966 (m), 833 (w), 671 (w), 578 (w) cm^{-1}.; HRMS (DART) for $C_{21}H_{41}B_2O_6$; $[M+H]^+$: calculated: 411.3084, found: 411.3090.



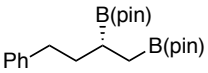
2,2'-(5-(Furan-2-yl)pentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.139**). The title compound was prepared according to *General Procedure A* with 2-pent-4-enylfuran (1.36 g, 10.0 mmol), $B_2(pin)_2$ (3.30 g, 13.0 mmol), Cs_2CO_3 (489 mg, 1.50 mmol), methanol (1.60 g, 50.0 mmol) in THF. The resulting colorless oil was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the title compound (2.35 g, 6.0 mmol, 60% yield) as colorless oil. All spectral data are in accordance with the literature.[45e]



2,2'-(3-(2-Fluorophenyl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.140**). The title compound was prepared according to *General Procedure A* with 1-allyl-2-fluoro-benzene (1.36 g, 10.0 mmol), $B_2(pin)_2$ (3.30 g, 13.0 mmol), Cs_2CO_3 (489 mg, 1.50 mmol), methanol (1.60 g, 50.0 mmol) in THF. The resulting colorless gel was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the title compound (2.52 g, 6.4 mmol, 64% yield) as colorless gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 1H), 7.14 – 7.08 (m, 1H), 7.03 – 6.92 (m, 2H), 2.83 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.65 (dd, *J* = 13.7, 8.6 Hz, 1H), 1.49 (p, *J* = 7.8 Hz, 1H), 1.22 (s, 12H), 1.19 (d, *J* = 9.8 Hz, 12H), 0.87 – 0.80 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.3 (d, *J* = 244.9 Hz), 131.3 (d, *J* = 5.0 Hz), 129.2 (d, *J* = 16.1 Hz), 127.1 (d, *J* = 8.1 Hz), 123.5 (d, *J* = 3.5 Hz), 114.9 (d, *J* = 22.7 Hz), 83.0, 82.9, 32.1 (d, *J* = 1.9 Hz), 24.9, 24.82, 24.78, 24.76. ^{19}F NMR (470 MHz, $CDCl_3$) δ -117.6. IR: ν_{max} 2975 (m), 2927 (w), 1499 (m), 1369 (s), 1314 (s), 1227 (w), 1141 (s), 1105 (w), 967 (w), 846 (w), 755 (m) cm^{-1}.; HRMS (DART) for $C_{21}H_{34}B_2O_4F$; $[M+H]^+$: calculated: 391.2622, found: 391.2631.



(*R*)-2,2'-(Heptane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.141). The title compound was prepared according to *General Procedure B* with hept-1-ene (687 mg, 7.00 mmol), $B_2(pin)_2$ (1.87 g, 7.35 mmol), $Pt(dba)_3$ (31.4 mg, 35.0 μmol), (*R,R*)-L (30.7 mg, 38.5 μmol) in THF. The resulting yellow oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound (3.0 g, 5.6 mmol, 81% yield) as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 – 1.24 (m, 8H), 1.23 (s, 12H), 1.22 (s, 12H), 1.15 – 1.07 (m, 1H), 0.89 – 0.83 (m, 4H), 0.79 (dd, *J* = 15.8, 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.8, 82.7, 33.8, 32.1, 28.5, 24.9, 24.83, 24.77, 24.7, 22.6, 14.1. IR ν_{max} 2978 (w), 2359 (w), 2237 (w), 2216 (w), 2163 (m), 2148 (w), 1370 (w), 1312 (w), 1143 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{38}B_2O_4$ $[M+H]^+$ calculated: 353.3034, found: 353.3042. $[\alpha]_D^{20}$: -1.0 (c = 1.00 CHCl3, *l* = 50 mm). The compound was subjected to transformation without determination of er All spectral data are in accordance with the literature.[62]



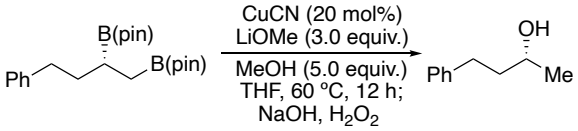
(*R*)-2,2'-(4-Phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.142). The title compound was prepared according to *General Procedure B* with phenylbut-1-ene (2.64 g, 20.0 mmol), $B_2(pin)_2$ (5.59 g, 22.0 mmol), $Pt(dba)_3$ (44.9 mg, 0.05 mmol), (*R,R*)-L (54.6 g, 0.06 mmol) in THF. The resulting yellow oil was purified by silica gel chromatography (5–10% ethyl acetate in hexanes) to afford the title compound (5.68 g, 14.8 mmol, 74% yield) as yellow oil. All spectral data are in accordance with the literature.[63] $[\alpha]_D^{20}$: − 6.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

[62] Sun, S.; Talavera, L.; Spieß, P.; Day, C. S.; Martin, R. *Angew. Chem., Int. Ed.* **2021**, *60*, 11740–11744.

[63] Wang, X.; Li, L.; Gong, T.; Xiao, B.; Lu, X.; Fu, Y. *Org. Lett.* **2019,** *21*, 4298–4302.

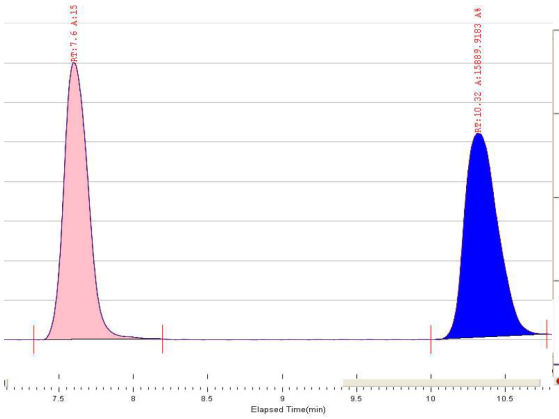
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to General Procedure A. Absolute stereochemistry was assigned by analogy. The title compound was derivatized and used for SFC without purification.



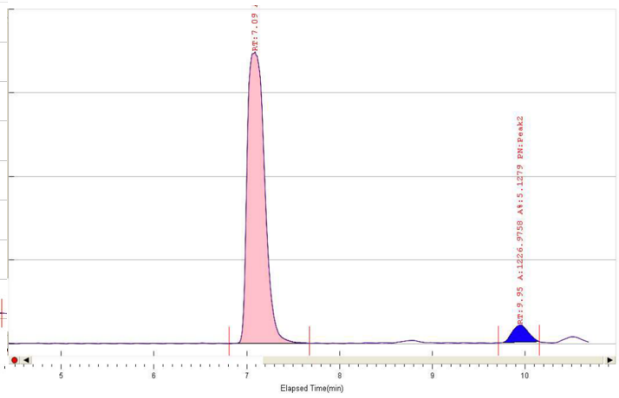
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 4-phenylbutan-2-ol.

Racemic compound

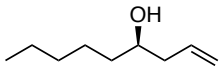


Peak No	% Area	Area	RT (min)
1	49.9226	15840.7992	7.6
2	50.0774	15889.9183	10.32
Total:	100	31730.7175	

Standard conditions

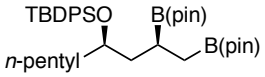


Peak No	% Area	Area	RT (min)
1	94.8721	22700.5856	7.09
2	5.1279	1226.9758	9.95
Total:	100	23927.5614	



(*R*)-Non-1-en-4-ol (3.114). To a slurry of CuI (303 mg, 1.6 mmol) in THF (50 mL) was added vinyl magnesium chloride (1.0 M in THF, 13.6 mL, 13.6 mmol) carefully dropwise by syringe at –78 ºC. The resulting mixture was allowed to stir for 15 min and (2*R*)-2-pentyloxirane (0.91 g, 8.0 mmol) was added. The yellow solution was allowed to stir for 30 min. The cooling bath was replaced with an acetonitrile/dry ice bath and the mixture was allowed to stir

at –40 ºC for 1 h. The black mixture was then allowed to stir for 1 h at 0 ºC before it was quenched by addition of a saturated aqueous solution of NH_4Cl (50 mL). The organic phase was separated, and the aqueous layer was washed with Et_2O (2 x 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under vaccum, the resulting colorless oil was purified by silica gel chromatography to afford the title compound (0.66 g, 4.6 mmol, 58% yield) as colorless oil. All spectral data are in accordance with the literature.[64]

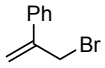


(((2*S*,4*R*)-1,2-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nonan-4-yl)oxy)(*tert*-butyl)diphenylsilane (3.115). To an oven-dried 50 mL round bottom flask with magnetic stir bar was added $B_2(pin)_2$ (509 mg, 2.0 mmol), Cs_2CO_3 (97.8 mg, 0.3 mmol) and THF (2 mL). (*R*)-non-1-en-4-ol (142 mg, 1.0 mmol) and methanol (0.69 mL, 17 mmol) were added sequentially to the reaction flask. The flask was sealed with a rubber septum and electrical tape. The mixture was allowed to stir for 6 h. It was then allowed to cool to room temperature and concentrated *in vacuo* (ensuring that all methanol has been removed from the residue). To the residue was added dichloromethane (4 mL) and imidazole (613 mg, 9.0 mmol). The mixture was cooled to 0 ºC and a solution of TBDPSCl (825 mg, 3.0 mmol) in toluene (5 mL) was added. It was then, allowed to warm to room temperature, and to stir overnight. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (15 mL). The layers were allowed to separate and the aqueous layer was washed with dichloromethane (3 x 30 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The colorless oil was purified by silica gel chromatography to afford the title compound (280 mg, 0.44 mmol, 44% yield) as colorless viscous gel. The material was used without analysis of stereochemistry. ^1H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 4H), 7.42 – 7.31 (m, 6H), 3.87 –

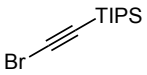
[64] Moslin, R. M.; Jamison, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 15106–15107.

3.80 (m, 1H), 1.72 (ddd, J = 13.3, 8.7, 6.1 Hz, 1H), 1.51 (dt, J = 13.3, 7.3 Hz, 1H), 1.41 – 1.32 (m, 2H), 1.27 – 1.16 (m, 18H), 1.13 (s, 12H), 1.04 (s, 9H+1H), 0.80 (t, J = 7.2 Hz, 3H), 0.74 (d, J = 7.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 135.9, 135.2, 134.9, 129.2, 129.1, 127.3, 127.2, 82.7, 82.6, 72.1, 40.3, 36.1, 31.9, 27.2, 24.9, 24.8, 24.7, 23.8, 22.6, 19.5, 14.0. IR: ν_{max} 3087 (w), 2927 (m), 2855 (w), 1465 (w), 1369 (s), 1312 (s), 1213 (w), 1140 (s), 1108 (s), 1054 (m), 967 (w), 821 (w), 701 (s), 610 (w), 508 (m) cm^{-1}.; HRMS (DART) for $C_{31}H_{61}B_2O_5Si$; $[M+H]^+$: calculated: 635.4469, found: 635.4481. $[\alpha]_D^{20}$: +1.2 (c = 1.0, $CHCl_3$, l = 50 mm).

3.6.2.2 Preparation of Electrophiles



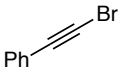
(3-Bromoprop-1-en-2-yl)benzene (**3.142**). To a solution of isopropenylbenzene (1.2 g, 10 mmol, 1.0 equiv.) in 6.0 mL $CHCl_3$ was added NBS (2.1 g, 12 mmol, 1.2 equiv.). The mixture was heated to reflux and allowed to stir for 4 h. Then the mixture was concentrated and Et_2O was added. The formed precipitate was filtered off and then the mixture was concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography in hexanes to give 83% (1.6 g, 8.3 mmol) of the product as yellow oil. All spectral data are in accordance with the literature.[65]



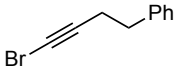
(Bromoethynyl)triisopropylsilane (**3.143**). To the mixture of ethynyl(triisopropyl)silane (1.8 g, 10 mmol, 1.0 equiv.), NBS (2.1 g, 12 mmol, 1.2 equiv.), and acetone (0.2 M), silver nitrate (170 mg, 1.0 mmol, 0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvents were evaporated and the colorless liquid was purified by silica gel

[65] Donohoe, T. J.; Fishlock, L. P.; Procopiou, P. A. *Org. Lett.* **2008**, *10*, 285–288.

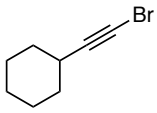
chromatography in hexanes to afford 89% (2.3 g, 8.9 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[66]



(Bromoethynyl)benzene (**3.144**). To the mixture of ethynylbenzene (2.0 g, 20 mmol, 1.0 equiv.), NBS (4.3 g, 24 mmol, 1.2 equiv.), and acetone (0.2 M), silver nitrate (340 mg, 2.0 mmol, 0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvents were evaporated and the yellow liquid was purified by silica gel chromatography in hexanes to afford 73% (2.6 g, 14.6 mmol) of the product as yellow liquid. All spectral data are in accordance with the literature.[67]



(4-Bromobut-3-yn-1-yl)benzene (**3.145**). To the mixture of but-3-ynylbenzene (1.3 g, 10 mmol, 1.0 equiv.), NBS (2.1 g, 12 mmol, 1.2 equiv.), and acetone (0.2 M), silver nitrate (170 mg, 1.0 mmol, 0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvents were evaporated and the colorless liquid residue was purified by silica gel chromatography in hexanes to afford 86% (1.8 g, 8.6 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[68]



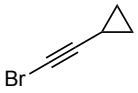
(Bromoethynyl)cyclohexane (**3.146**). To the mixture of ethynylcyclohexane (750 mg, 6.9 mmol, 1.0 equiv.), NBS (1.5 g, 8.3 mmol, 1.2 equiv.), and acetone (0.2 M), silver nitrate (118 mg, 0.69 mmol, 0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvents were

[66] Chen, A.; Yu, H.; Yan, J.; Huang, H. *Org. Lett.* **2020**, *22*, 755–759.

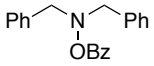
[67] Beltran, L.; Fabre, I.; Ciofini,I.; Miesch, L. *Org. Lett.* **2017***, 19*, 5042–5045.

[68] Gauthier, R.; Mamone, M.; Paquin, J. F. *Org. Lett.* **2019**, *21*, 9024–9027.

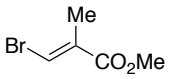
evaporated and the colorless liquid residue was purified by silica gel chromatography in hexanes to afford 35% (460 mg, 2.5 mmol) of the product as colorless liquid. All spectral data are in accordance with the literature.[69]



(Bromoethynyl)cyclopropane (**3.147**). To the mixture of ethynylcyclopropane (992 mg, 15 mmol, 1.0 equiv.), NBS (3.2 g, 18 mmol, 1.2 equiv.), and acetone (0.2 M), silver nitrate (255 mg, 1.5 mmol, 0.10 equiv.) was added and the mixture was allowed to stir at room temperature overnight open to air. After completion of the reaction, the solvents were evaporated and the colorless liquid residue was purified by silica gel chromatography in hexanes to afford 45% (982 mg, 6.8 mmol) of the product as colorless, volatile liquid. All spectral data are in accordance with the literature.[70]



***O*-Benzoyl-*N*,*N*-dibenzylhydroxylamine** (**3.148**). The title compound was prepared according to a literature procedure[71] on a 25.0 mmol scale to afford the title compound (6.2 g, 19.5 mmol, 78% yield) as white solid. All spectral data are in accordance with the literature mentioned above.



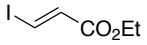
Methyl (*E*)-3-bromo-2-methylacrylate (**3.149**). The title compound was prepared according to a literature procedure[72] on 50.0 mmol scale to afford the title compound (7.7 g, 43.3 mmol, 86% yield, E/Z > 20:1) as yellow oil. All spectral data are in accordance with the literature.

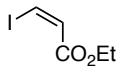
[69] Pan, R.; Shi, C.; Zhang, D.; Tian, Y.; Guo, S.; Yao, H.; and Lin, A. *Org. Lett.* **2019***, 21*, 8915–8920.

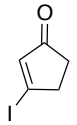
[70] Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743–5747.

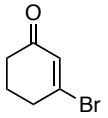
[71] Banerjee, A.; Yamamoto, H. *Chem. Sci.* **2019**, *10*, 2124–2129.

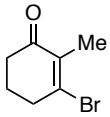
[72] Kremsmair, A.; Skotnitzki, J.; Knochel, P. *Chem. Eur. J.* **2020**, *26*, 11971–11973.

 **Ethyl (*E*)-3-iodoacrylate** (**3.150**). The title compound was prepared according to a literature procedure[72] on 18.0 mmol scale to afford the title compound (3.4 g, 15.1 mmol, 84% yield, E/Z = 20 :1) as yellow oil. All spectral data are in accordance with the literature mentioned above.

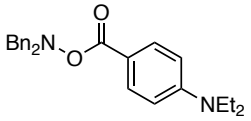
 **Ethyl (*Z*)-3-iodoacrylate** (**3.151**). The title compound was prepared according to a literature procedure[72] on 20.0 mmol scale to afford the title compound (4.2 g, 18.4 mmol, 92% yield, E/Z = 20 :1) as yellow oil. All spectral data are in accordance with the literature mentioned above.

 **3-Iodocyclopent-2-en-1-one** (**3.152**). The title compound was prepared according to a literature procedure[72] on a 10.0 mmol scale to afford the title compound (1.2 g, 5.5 mmol, 55% yield) as yellow oil. All spectral data are in accordance with the literature mentioned above.

 **3-Bromocyclohex-2-en-1-one** (**3.153**). The title compound was prepared according to a literature procedure[72] on a 15.0 mmol scale to afford the title compound (1.1 g, 6.3 mmol, 42% yield) as yellow oil. All spectral data are in accordance with the literature mentioned above.

 **3-Bromocyclohex-2-en-1-one** (**3.154**). Bromine (1.7 g, 10.6 mmol) was added dropwise to a solution of triphenylphosphine (2.8 g, 10.6 mmol) in dichloromethane (50 mL). To this solution was added 2-methylcyclohexane-1,3-dione (1.3 g, 10.0 mmol) and triethylamine (1.1 g, 10.6 mmol). The mixture was allowed to stir for 3 h, then the solvents were evaporated under reduced pressure. The resulting yellow oil residue was purified by silica gel

chromatography to afford the title compound (1.3 g, 6.8 mmol, 68%) as pale-yellow oil. All spectral data are in accordance with the literature.[73]



4-(((Dibenzylamino)oxy)carbonyl)-*N*,*N*-diethylaniline. (**3.155**) An oven-dried round bottom flask was charged with 4-(diethylamino)benzoic acid (2.1 g, 12.0 mmol) and CH_2Cl_2 (0.3 M). The flask was placed in an ice bath, and 1,1'-carbonyldiimidazole (2.0 g, 12.0 mmol) was added. The mixture was allowed to stir at this temperature for 30 min, and *N*,*N*-dibenzylhydroxylamine (2.1 g, 10.0 mmol) was added. The ice-bath was removed, and the mixture was allowed to stir at room temperature for 2 h. The resulting mixture was passed through a pad of Celite and concentrated. The brown solid residue was purified by silica gel chromatography to give the title compound (3.5 g, 8.9 mmol, 89%) as pale-yellow solid. All spectral data are in accordance with the literature.[74]

3.6.2.3 Copper-catalyzed site-selective cross-coupling

General Procedure D: Site-selective coupling with allyl halides, alkynyl bromides, acyl chlorides and halide substituted enones.

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added bis(boronic ester) (0.2 mmol, 1.0 equiv.) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to warm to room temperature and to stir for 25 min. The reaction vial was transferred into glovebox

[73] Vadalà, A.; Finzi, P. V.; Zanoni, G.; Vidari, G. *Eur. J. Org. Chem.* **2003**, *4*, 642–648.

[74] Xu, -X.; Q.-F.; Zhang, X.; You, S.-L. *Org. Lett.* **2019**, *21*, 5357–5362.

again, styrene (0 equiv. to 3.0 equiv., added before electrophile), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and electrophile (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The reaction and was allowed to stir at 60 ºC for 12 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug. Solvents were removed under reduced pressure. The residue was purified by silica gel chromatography to furnish the desired product.

General Procedure E: Site-selective homologation

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added bis(boronic ester) (1.0 equiv.) and anhydrous tetrahydrofuran (0.4 M). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (1.05 equiv., solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to stir at room temperature for 25 min. The reaction vial was transferred into glovebox again, copper cyanide (10 mol%) and 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.1 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The mixture was allowed to stir at 25 ºC for 2 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug. Solvents were removed under reduced pressure. The residue was purified by silica gel chromatography to furnish the desired product.

General Procedure F: Site-selective amination of secondary boronic esters

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added bis(boronic ester) (0.2 mmol, 1.0 equiv.) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was

subsquently cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and and then allowed to stir at room temperature for 25 min. The reaction vial was transferred into glovebox again, triphenylphosphine (21 mg, 0.08 mmol, 40 mol%), cesium fluoride (91 mg, 0.6 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and (dibenzylamino) benzoate (76 mg, 0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The mixture was heated to 60 ºC and was allowed to stir for 12 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug. Solvents were removed under reduced pressure. The residue was oxidized with $NaOH/H_2O_2$ and purified by silica gel chromatography to furnish the desired oxidized product.

General Procedure G: Site-selective amination of primary boronic esters

In a glovebox under Ar atmosphere, to an oven-dried 2-dram vial equipped with a magnetic stir bar was added bis(boronic ester) (0.2 mmol, 1.0 equiv.) and anhydrous tetrahydrofuran (0.5 mL). The vial was sealed with a septum cap and removed from the glovebox. The mixture was subsquently cooled to –78 ºC and *tert*-butyllithium (1.0 equiv., solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to stir at room temperature for 25 min. The reaction vial was transferred into glovebox again, cesium fluoride (91 mg, 0.6 mmol, 3.0 equiv.), copper cyanide (3.6 mg, 0.04 mmol, 20 mol%) and (dibenzylamino)4-(diethylamino)benzoate (93 mg, 0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The mixture was heated to 60 ºC and was allowed to stir for 12 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug with diethyl ether as eluent. Solvents were removed under reduced pressure. The

residue was oxidized with $NaOH/H_2O_2$ and purified by silica gel chromatography to furnish the desired oxidized product.

General Procedure H: AdLi-activated site-selective Cu-catalyzed coupling

In a glovebox under Ar atmosphere, to an oven-dried vial was added lithium (2.0 mmol, 10.0 equiv.) and 4,4′-di-tert-butylbiphenylide (0.4 mmol, 2.0 equiv.), 0.7 mL anhydrous THF was added, the solution turned dark blue instantly. (Note: scraping on the lithium beads to expose fresh, unoxidized lithium helps speeding up the process) This solution (referred to as Li•DBB solution) was allowed to stir at room temperature for 2.5 h.

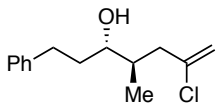
In a glovebox under Ar atmosphere, to another flame-dried vial was added bis(boronic ester) (0.2 mmol, 1.0 equiv.), adamantyl chloride (0.22 mmol, 1.1 equiv.), diluted with 0.5 mL THF. Li•DBB solution (0.7 mL) was added dropwise to this solution at –78 ºC, additional 0.5 mL THF was used to rinse the Li•DBB vial and was also added dropwise at –78 ºC. Upon addition of Li•DBB, the solution slowly turned red. The solution was allowed to stir at –78 ºC for 5 min, and then allowed to warm to room temperature and to stir for 25 min. The red color of the solution became paler in this process.

The reaction vial was transferred into glovebox again, copper cyanide (0.04 mmol, 20 mol%), cesium fluoride (0 or 3.0 equiv.), styrene (0 or 1.0 equiv.), electrophile (0.24 mmol, 1.2 equiv.) were added. The vial was sealed with septum cap and removed from glovebox. The mixture was heated to 60 ºC and was allowed to stir for 12 h, and then diluted with diethyl ether and passed through a silica gel plug. Solvents were removed under reduced pressure. The residue was oxidized and purified by silica gel chromatography to furnish the desired oxidized product.

NaOH/H_2O_2 oxidation: The mixture (0.2 mmol) was diluted with THF (1.5 mL), cooled to 0 ºC in an ice bath, then 3.0 M NaOH (1.0 mL) was added, followed by a 30% aqueous solution of H_2O_2 (1.0 mL). The mixture was allowed to warm to room temperature and was allowed to stir for 2 h. The mixture was cooled to 0 ºC and a saturated aqueous solution of $Na_2S_2O_3$ (3.0 mL) was added dropwise. The mixture was allowed to warm up to room temperature and the aqueous layer was washed with ethyl acetate (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was subsequently purified by silica gel chromatography to afford the oxidized product.

$NaBO_3$•H_2O oxidation: The mixture (0.2 mmol) was combined with sodium perborate monohydrate (100 mg, 5.0 equiv.), THF (1.0 mL), and water (1.0 mL). The mixture was allowed to vigorously stir for 12 h at 25 ºC. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (1.5 mL), and the aqueous layer was washed three times with diethyl ether, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the oxidized product.

3.6.3 Characterization of Site-Selective Cross-coupling Products and Analysis of Stereochemistry



(3*S*,4*R*)-6-Chloro-4-methyl-1-phenylhept-6-en-3-ol (**3.57**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)-5-phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (80.0 mg, 0.20 mmol, 92:8 er), 2,3-dichloroprop-1-ene (26.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The colorless oil residue was oxidized according to NaOH/H_2O_2 protocol and was purified by silica gel chromatography to afford the product as colorless oil (34.4 mg, 0.14 mmol, 72% yield). ^{1}H

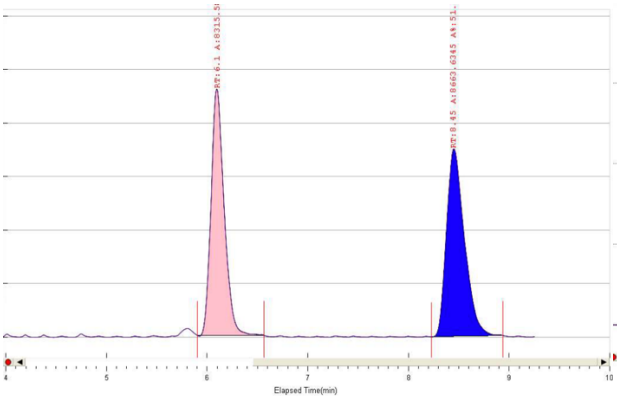
NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 3H), 5.19 (s, 1H), 5.12 (s, 1H), 3.54 (ddd, *J* = 8.7, 5.0, 3.4 Hz, 1H), 2.86 (ddd, *J* = 13.7, 9.7, 5.5 Hz, 1H), 2.68 (ddd, *J* = 13.7, 9.5, 6.8 Hz, 1H), 2.57 (dd, *J* = 14.1, 4.3 Hz, 1H), 2.15 (dd, *J* = 14.1, 9.7 Hz, 1H), 2.03 – 1.94 (m, 1H), 1.87 – 1.70 (m, 2H), 1.45 (d, *J* = 7.0 Hz, 1H), 0.93 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 141.8, 128.45, 128.42, 125.9, 113.6, 74.7, 41.6, 36.6, 35.6, 32.4, 15.0.; IR: ν_{max} 3394 (br), 3024 (w), 2927 (s), 2858 (w), 1633 (m), 1495 (w), 1453 (m), 1154 (w), 1038 (w), 881 (m), 747 (m), 699 (s), 644 (w) cm^{-1}.; HRMS (DART) for $C_{14}H_{23}NOCl$; $[M+NH_4]^+$: calculated: 256.1463, found: 256.1469. $[\alpha]_D^{20}$: –12.2 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

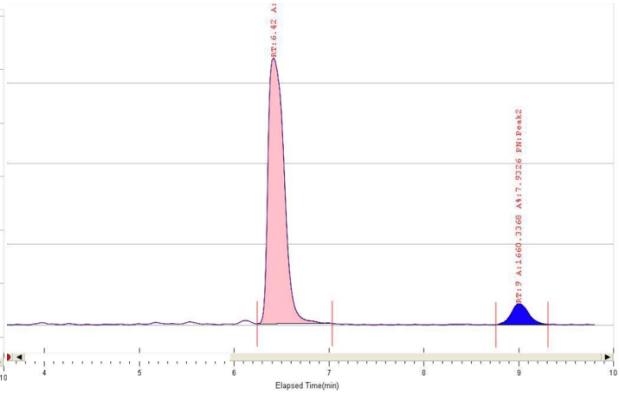
Chiral SFC (OD-H, 8% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 6-chloro-4-methyl-1-phenylhept-6-en-3-ol.

Racemic Compound

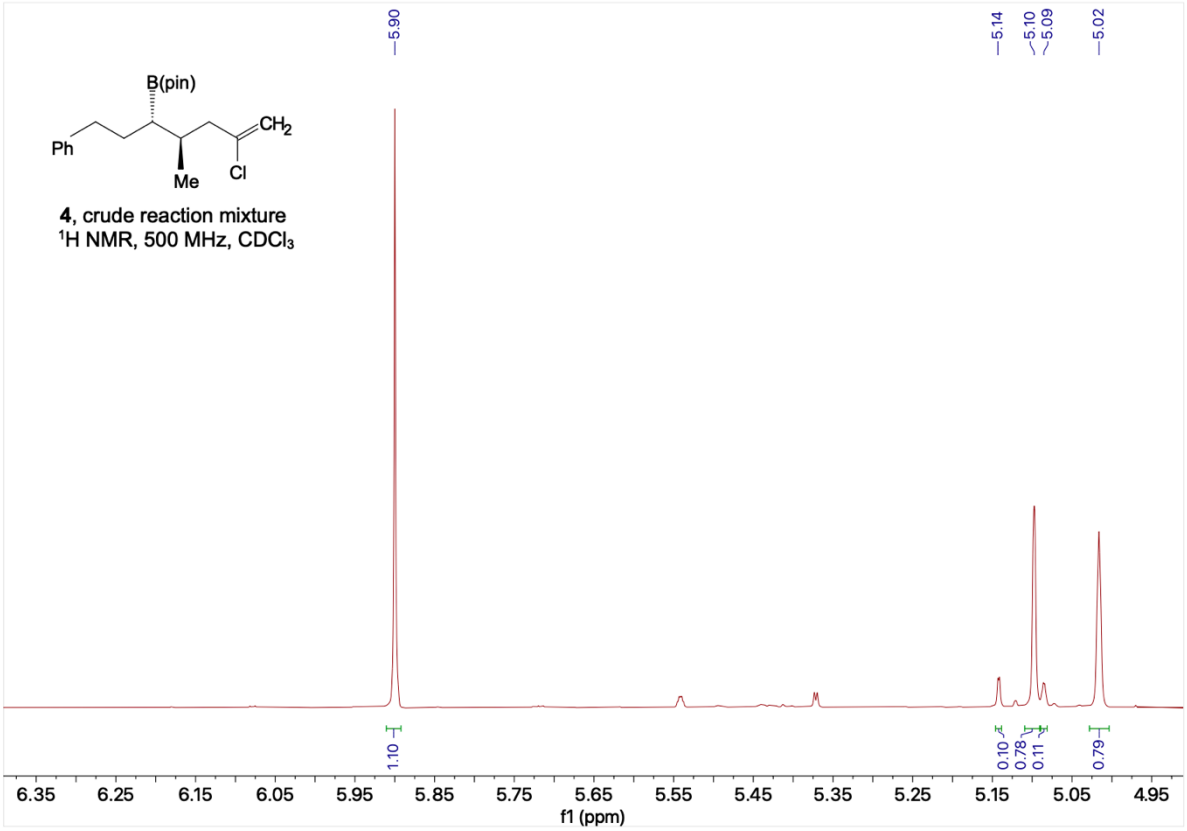


Peak No	% Area	Area	RT (min)
1	48.9751	8315.5839	6.1
2	51.0249	8663.6345	8.45
Total:	100	16979.2184	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	92.0674	19270.2353	6.42
2	7.9326	1660.3368	9
Total:	100	20930.5721	

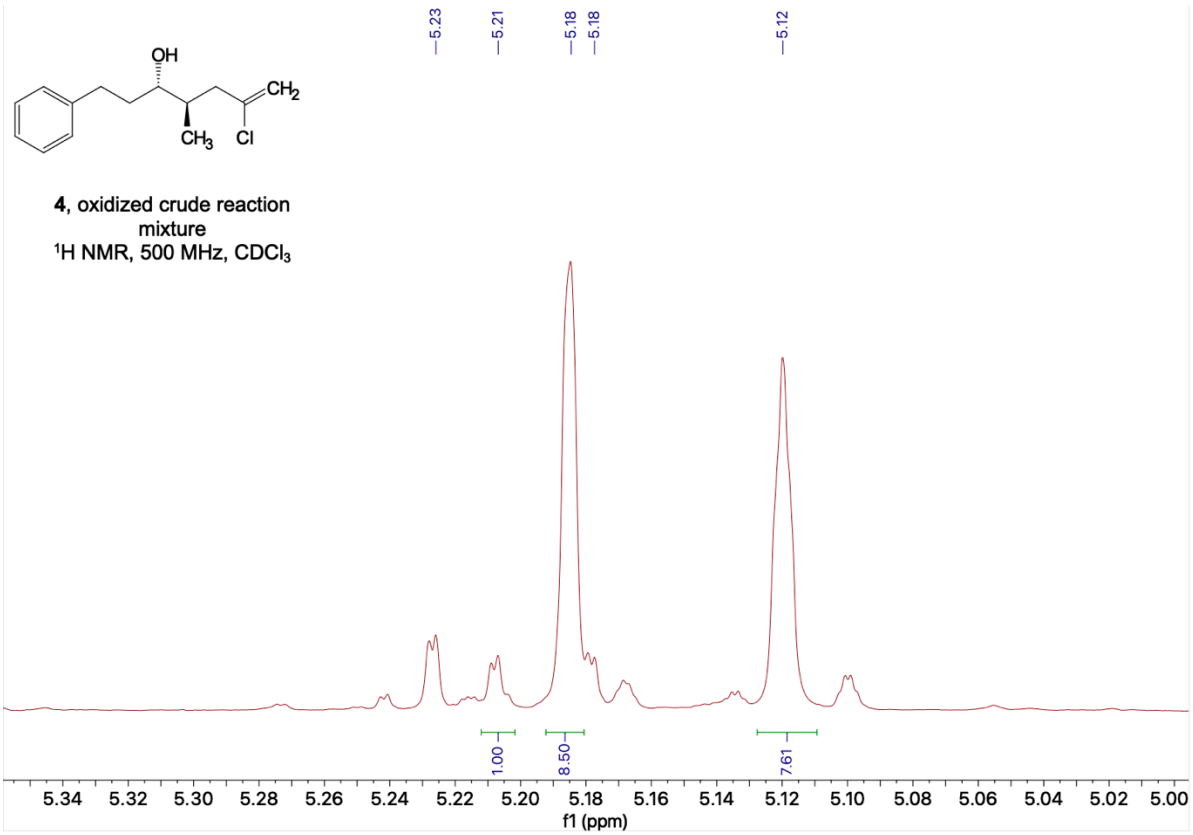


^{1}H NMR spectrum was taken upon the completion of the reaction.

1,1,2,2-tetrachloroethane (18.2 mg) as internal standard: δ 5.90

Major regioisomer: δ 5.02, 5.10.

Minor regioisomer: δ 5.09, 5.14

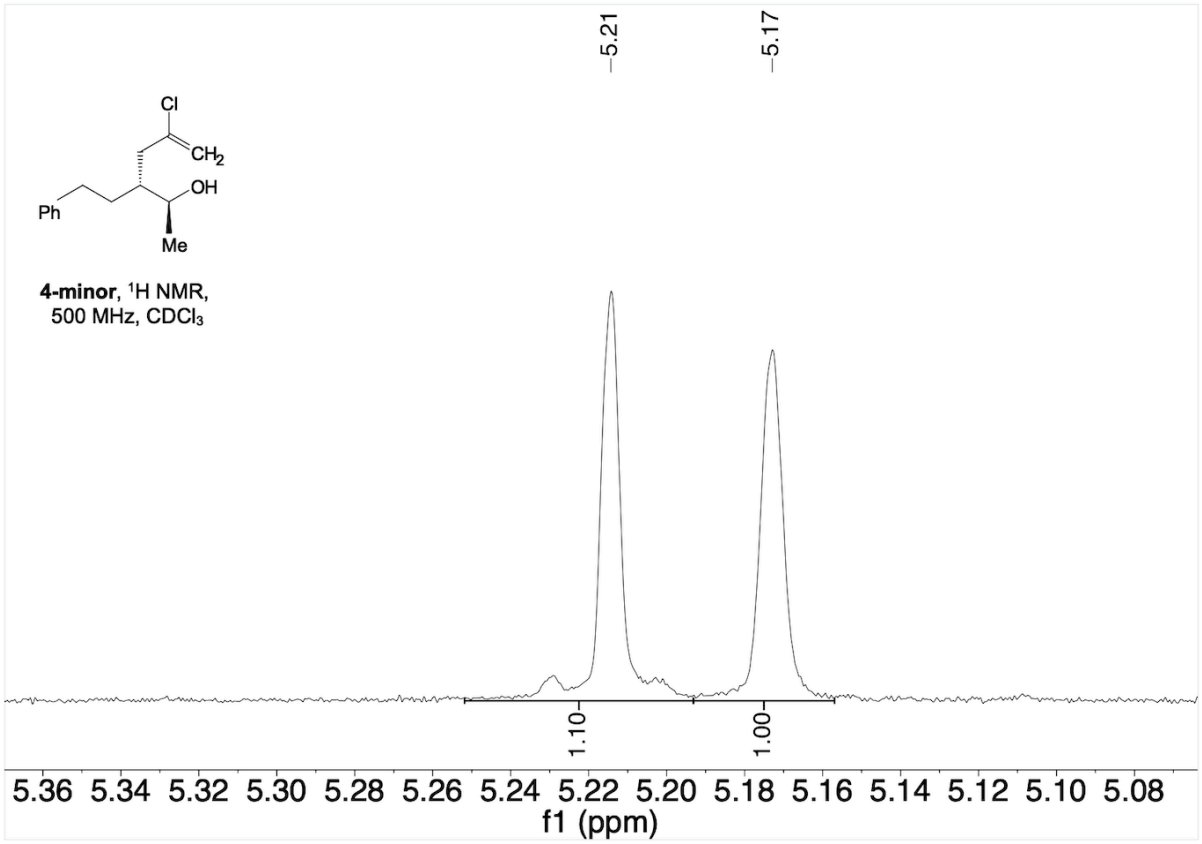


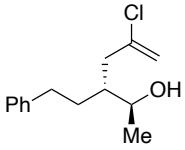
^{1}H NMR spectrum was taken after oxidation of the mixture.

Major regioisomer: δ 5.12, 5.185.

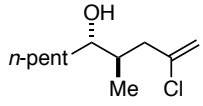
Minor regioisomer: δ 5.21, 5.17

Electrophile leftover: δ 5.23



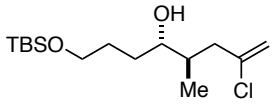


(2*S*,3*R*)&(*2R,3S*)-5-Chloro-3-phenethylhex-5-en-2-ol (**3.58**). A very small amount of the title compound was isolated as colorless oil and ^{1}H NMR spectra was acquired for the purpose of regioisomeric ratio analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.20 – 7.17 (m, 3H), 5.21 (s, 1H), 5.17 (s, 1H), 4.02 – 3.94 (m, 1H), 2.75 – 2.61 (m, 2H), 2.49 (dd, *J* = 14.5, 5.6 Hz, 1H), 2.37 (dd, *J* = 14.5, 8.0 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.69 – 1.53 (m, 4H).

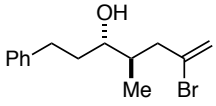


(4*R*,5*S*)&(4*S*,5*R*)-2-Chloro-4-methyldec-1-en-5-ol (**3.59**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), 2,3-dichloroprop-1-ene (26.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The yellow oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel

chromatography to afford the product as pale-yellow oil (29.4 mg, 0.14 mmol, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19 (s, 1H), 5.14 (s, 1H), 3.49 (dtd, *J* = 8.4, 3.4, 1.5 Hz, 1H), 2.58 (dd, *J* = 14.1, 4.2 Hz, 1H), 2.13 (dd, *J* = 14.2, 9.9Hz, 1H), 1.94 (dddd, *J* = 11.3, 9.6, 4.7, 3.2 Hz, 1H), 1.53 – 1.39 (m, 4H), 1.36 – 1.27 (m, 5H), 0.95 – 0.85 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 113.4, 75.4, 41.5, 36.3, 33.9, 31.9, 25.6, 22.6, 15.1, 14.0.; IR: ν_{max} 3498 (br), 2923 (s), 2853 (w), 1633 (w), 1461 (w), 1377 (m), 1304 (m), 1234 (w), 1142 (m), 970 (w), 881 (w) cm^{-1}.; HRMS (DART) for $C_{11}H_{22}OCl$; $[M+H]^+$: calculated: 205.1354, found: 205.1360.



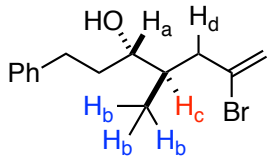
(4*S*,5*R*)&(4*R*,5*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-7-chloro-5-methyloct-7-en-4-ol (**3.60**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), 2,3-dichloroprop-1-ene (26.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The yellow oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (46.5 mg, 0.15 mmol, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.18 (s, 1H), 5.13 (s, 1H), 3.74 – 3.62 (m, 2H), 3.47 (ddd, *J* = 8.9, 5.4, 2.1 Hz, 1H), 2.63 (dd, *J* = 14.2, 4.1 Hz, 1H), 2.12 (dd, *J* = 14.2, 9.9 Hz, 1H), 2.00 – 1.88 (m, 1H), 1.75 – 1.61 (m, 3H), 1.55 – 1.43 (m, 1H), 0.90 (m, 12H, (*t*-Bu 9H, Me 3H)), 0.07 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 113.3, 74.8, 63.5, 41.8, 36.4, 31.4, 29.2, 25.9, 18.3, 15.1, -5.4.; IR: ν_{max} 3403 (br), 2926 (m), 2855 (w), 1633 (w), 1461 (w), 1253 (m), 1096 (s), 938 (w), 834 (s), 775 (s), 661 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{32}O_2SiCl$; $[M+H]^+$: calculated: 307.1855, found: 307.1855.

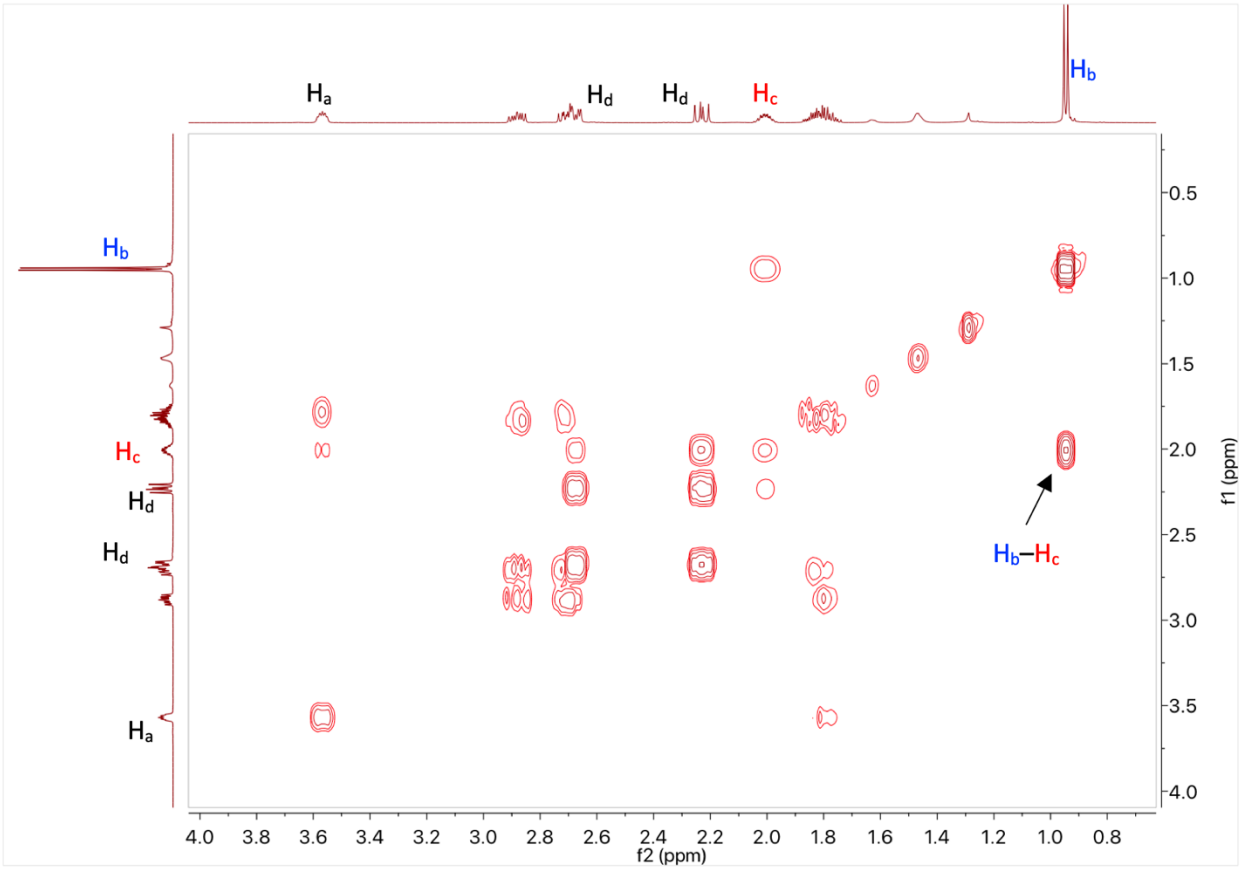


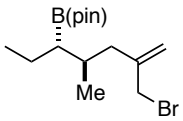
(3*S*,4*R*)&(3*R*,4*S*)-6-Bromo-4-methyl-1-phenylhept-6-en-3-ol (**3.61**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-5-phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (80.03

mg, 0.20 mmol), 2,3-dibromoprop-1-ene (48.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (37.4 mg, 0.13 mmol, 66% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 2H), 7.25 – 7.18 (m, 3H), 5.56 (s, 1H), 5.43 (s, 1H), 3.59 – 3.52 (m, 1H), 2.86 (ddd, *J* = 14.7, 9.6, 5.6 Hz, 1H), 2.74 – 2.62 (m, 2H), 2.21 (dd, *J* = 14.2, 9.7 Hz, 1H), 2.04 – 1.94 (m, 1H), 1.88 – 1.71 (m, 2H), 1.50 (s, 1H), 0.93 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 133.7, 128.5, 128.4, 125.9, 118.1, 74.6, 43.7, 37.1, 35.7, 32.4, 15.0.; IR: ν_{max} 3396 (br), 2927 (m), 1628 (m), 1494 (w), 1453 (m), 1150 (w), 1040 (w), 886 (m), 747 (w), 699 (s), 558 (w) cm^{-1}.; HRMS (DART) for $C_{14}H_{23}NOBr$; $[M+H]^+$: calculated: 300.0958, found: 300.0965.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)

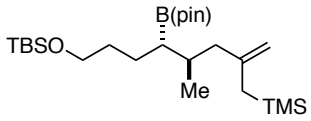




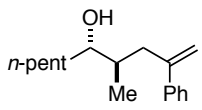


2-((3*S*,4*R*)&(3*R*,4*S*)-6-(Bromomethyl)-4-methylhept-6-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3.62**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (64.81 mg, 0.20 mmol), 3-bromo-2-(bromomethyl)prop-1-ene (51.3 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (33.8 mg, 0.10 mmol, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.18 (s, 1H), 4.92 (s, 1H), 3.98 – 3.90 (m, 2H), 2.41 (dd, *J*

= 14.1, 4.4 Hz, 1H), 1.89 (dd, *J* = 14.0, 10.2 Hz, 1H), 1.82 – 1.72 (m, 1H), 1.48 – 1.39 (m, 2H), 1.25 (d, *J* = 5.2 Hz, 12H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.86 – 0.81 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.7, 116.6, 82.9, 39.9, 36.6, 32.0, 25.0, 24.8, 20.9, 18.4, 14.0. IR: ν_{max} 2927 (w), 2869 (w), 1459 (w), 1378 (m), 1311 (m), 1264 (w), 1208 (w), 1142 (s), 968 (w), 907 (w), 851 (w); HRMS (DART) for $C_{15}H_{29}BO_2Br$; $[M+H]^+$: calculated: 331.1439, found: 331.1455.

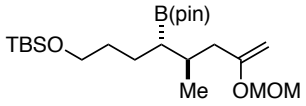


***tert*-Butyldimethyl(((4*S*,5*R*)&(4*R*,5*S*)-5-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-7-((trimethylsilyl)methyl)oct-7-en-1-yl)oxy)silane** (**3.63**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), 2-(chloromethyl)allyl-trimethyl-silane (39.1 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (60.1 mg, 0.17 mmol, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.58 – 4.49 (m, 2H), 3.59 (t, *J* = 6.4 Hz, 2H), 2.10 (dd, *J* = 13.5, 4.4 Hz, 1H), 1.85 – 1.76 (m, 1H), 1.71 (dd, *J* = 13.2, 10.5 Hz, 1H), 1.59 – 1.35 (m, 6H), 1.24 (d, *J* = 3.9 Hz, 12H), 0.96 – 0.91 (m, 1H), 0.89 (s, 9H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.04 (s, 6H), 0.01 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 108.4, 82.8, 63.6, 44.5, 33.0, 32.4, 26.1, 26.0, 25.0, 24.7, 24.1, 18.6, 18.3, -1.3, -5.2.; IR: ν_{max} 2926 (w), 2854 (w), 1378 (w), 1312 (w), 1247 (m), 1143 (m), 1097 (m), 833 (s), 772 (s), 694 (w) cm^{-1}.; HRMS (DART) for $C_{25}H_{54}BO_3Si_2$; $[M+H]^+$: calculated: 469.3699, found: 469.3697.

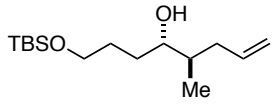


(4*R*,5*S*)&(4*S*,5*R*)-4-Methyl-2-phenyldec-1-en-5-ol (**3.64**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), (3-bromoprop-1-en-2-yl)benzene (59.1 mg, 0.3 mmol), copper cyanide (3.6 mg, 0.040 mmol), The

colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (35.4 mg, 0.14 mmol, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 1H), 5.28 (s, 1H), 5.07 (s, 1H), 3.48 – 3.41 (m, 1H), 2.89 (dd, *J* = 13.9, 4.5, 1.3 Hz, 1H), 2.19 (dd, *J* = 14.1, 9.8, 0.9 Hz, 1H), 1.66 – 1.57 (m, 1H), 1.53 – 1.18 (m, 8H), 0.91 – 0.88 (m, 3H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.5, 141.1, 128.3, 127.3, 126.3, 114.0, 75.9, 38.2, 37.0, 33.6, 31.9, 25.7, 22.7, 15.3, 14.1.; IR: ν_{max} 3382 (br), 2953 (m), 2925 (s), 2855 (m), 1625 (w), 1456 (m), 1376 (w), 1026 (w), 894 (m), 777 (s), 704 (s), 518 (w) cm^{-1}.; HRMS (DART) for $C_{17}H_{27}O$; $[M+H]^+$: calculated: 247.2056, found: 247.2054.

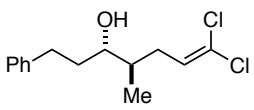


(7*R*,8*S*)&(7*S*,8*R*)-7,13,13,14,14-Pentamethyl-5-methylene-8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,4,12-trioxa-13-silapentadecane (**3.65**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), 3-chloro-2-(methoxymethoxy)prop-1-ene (32.8 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The pale-yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow oil (52 mg, 0.12 mmol, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.95 – 4.90 (m, 2H), 4.09 (s, 1H), 3.95 (s, 1H), 3.59 (t, *J* = 6.4 Hz, 3H), 3.41 (s, 3H), 2.27 (dd, *J* = 13.5, 4.4 Hz, 1H), 1.98 – 1.90 (m, 1H), 1.84 (dd, *J* = 13.5, 9.8 Hz, 1H), 1.60 – 1.35 (m, 4H), 1.24 (s, 12H), 0.97 – 0.93 (m, 1H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2, 93.3, 85.1, 82.8, 63.6, 56.0, 41.2, 33.0, 32.2, 26.0, 24.9, 24.8, 23.9, 18.4, 18.3, -5.2.; IR: ν_{max} 2926 (w), 1461 (w), 1378 (m), 1312 (m), 1253 (m), 1213 (w), 1143 (s), 1093 (s), 1018 (m), 970 (w), 833 (s), 774 (s), 663 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{48}BO_5Si$; $[M+H]^+$: calculated: 443.3359, found: 443.3375.



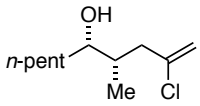
(4*S*,5*R*)&(4*R*,5*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-5-methyloct-7-en-4-ol (**3.66**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane. (93.67 mg, 0.20 mmol), 3-bromoprop-1-ene (29.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (44.3 mg, 0.16 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 – 5.75 (m, 1H), 5.07 – 4.95 (m, 2H), 3.73 – 3.61 (m, 2H), 3.43 (ddd, *J* = 8.7, 6.0, 2.2 Hz, 1H), 2.62 (s, 1H), 2.33 – 2.24 (m, 1H), 1.97 – 1.86 (m, 1H), 1.71 – 1.54 (m, 4H), 1.49 – 1.36 (m, 1H), 0.90 (s, 9H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.07 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.7, 115.7, 75.0, 63.5, 38.6, 37.1, 30.9, 29.2, 25.9, 18.3, 15.3, -5.4.; IR: ν_{max} 3367 (br), 2926 (w), 1639 (w), 1461 (w), 1386 (w), 1253 (w), 1095 (m), 991 (w), 908 (w), 832 (s), 773 (s), 661 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{33}SiO_2$; $[M+H]^+$: calculated: 273.2244, found: 273.2246.

<u>*With AdLi activation:*</u> The title compound was prepared according to *General Procedure E* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), and allyl bromide (29.03 mg, 0.24 mmol) as electrophile. The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (28.7 mg, 0.11 mmol, 53% yield).

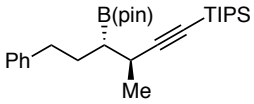


(3*S*,4*R*)&(3*R*,4*S*)-7,7-Dichloro-4-methyl-1-phenylhept-6-en-3-ol (**3.67**). The title compound was prepared according to *General Procedure A* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-5-phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (80.03 mg, 0.20 mmol), 3,3,3-trichloroprop-1-ene (34.9 mg, 0.24 mmol), copper cyanide (3.6 mg,

0.04 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (38.0 mg, 0.14 mmol, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 5.89 (t, *J* = 7.6 Hz, 1H), 3.54 – 3.44 (m, 1H), 2.86 (ddd, *J* = 13.6, 9.9, 5.3 Hz, 1H), 2.68 (ddd, *J* = 13.6, 9.7, 6.7 Hz, 1H), 2.37 (ddd, *J* = 14.6, 7.2, 4.7 Hz, 1H), 2.12 (dt, *J* = 14.6, 8.3 Hz, 1H), 1.90 – 1.80 (m, 1H), 1.78 – 1.68 (m, 2H), 1.47 (s, 1H), 0.94 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.9, 128.6, 128.5, 128.4, 125.9, 120.5, 74.8, 38.7, 35.7, 32.33, 32.30, 15.7.; IR: ν_{max} 3401 (br), 3024 (w), 2924 (m), 1618 (w), 1453 (m), 1380 (w), 1030 (w), 918 (s), 853 (m), 747 (m), 699 (s) cm^{-1}.; HRMS (DART) for $C_{14}H_{22}NOCl_2$; $[M+NH_4]^+$: calculated: 290.1073, found: 290.1081.



(4*S*,5*S*)&(4*R*,5*R*)-2-Chloro-4-methyldec-1-en-5-ol (**3.68**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*R*,3*S*)&(2*R*,3*S*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), 2,3-dichloroprop-1-ene (26.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as pale-yellow oil (20.6 mg, 0.11 mmol, 55% yield, 7:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20 (s, 1H), 5.19 (s, minor), 5.17 (s, 1H), 5.14 (s, minor) 3.61 – 3.53 (m, 1H), 3.49 (m, minor), 2.49 (dd, *J* = 14.1, 6.3, 1H), 2.58 (dd, *J* = 14.1, 4.2 Hz, minor), 2.25 (dd, *J* = 14.1, 8.3 Hz, 1H), 2.13 (dd, *J* = 14.2, 9.9 Hz, minor), 1.99 – 1.89 (m, 1H, overlap), 1.54 – 1.40 (m, 3H, overlap), 1.36 – 1.29 (m, 6H, overlap), 0.94 – 0.86 (m, 6H, overlap). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 113.6, 113.5 (minor), 75.4 (minor), 73.7, 43.3, 41.5 (minor), 36.3, 35.5, 34.8, 33.9 (minor), 31.8, 25.9, 25.6 (minor), 22.6, 15.1 (minor), 14.0, 12.2.; IR: ν_{max} 3498 (br), 2923 (s), 2853 (w), 1633 (w), 1461 (w), 1377 (m), 1304 (m), 1234 (w), 1142 (m), 970 (w), 881 (w) cm^{-1}.; HRMS (DART) for $C_{11}H_{22}ONCl$; $[M+NH_4]^+$: calculated: 222.1619, found: 222.1613.



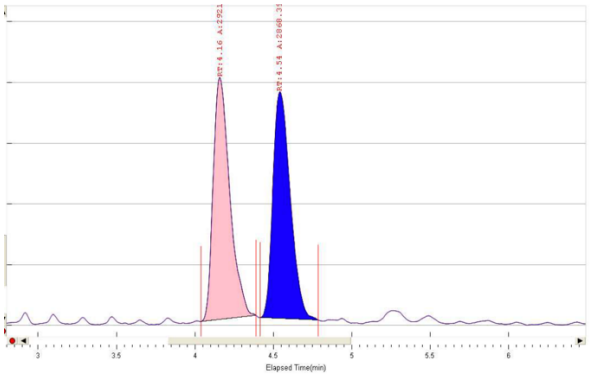
Triisopropyl((3*S*,4*S*)-3-methyl-6-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-1-yn-1-yl)silane (**3.69**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)-5-phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (80.03 mg, 0.20 mmol, 92:8 er), 2-bromoethynyl(triisopropyl)silane (62.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (20.8 mg, 0.20 mmol). The pale-yellow oil residue was purified by silica gel chromatography to afford the product as yellow oil (50.1 mg, 0.11 mmol, 55% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 2.76 (qd, *J* = 7.0, 5.3 Hz, 1H), 2.71 – 2.57 (m, 2H), 1.87 (q, *J* = 8.0 Hz, 2H), 1.26 (d, *J* = 2.2 Hz, 12H), 1.24 – 1.19 (m, 4H), 1.12 – 1.01 (m, 21H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.0, 128.4, 128.2, 125.5, 113.5, 83.1, 79.7, 35.6, 30.6, 27.9, 25.0, 24.7, 20.0, 18.7, 11.3.; IR: ν_{max} 2938 (s), 2862 (s), 2160 (w), 1461 (w), 1379 (s), 1319 (s), 1261 (w), 1213 (w), 1143 (s), 995 (w), 967 (w), 882 (m), 698 (m), 675 (m) cm^{-1}.; HRMS (DART) for $C_{28}H_{48}BO_2Si$; $[M+H]^+$: calculated: 455.3511, found: 455.3528. $[\alpha]_D^{20}$: –5.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

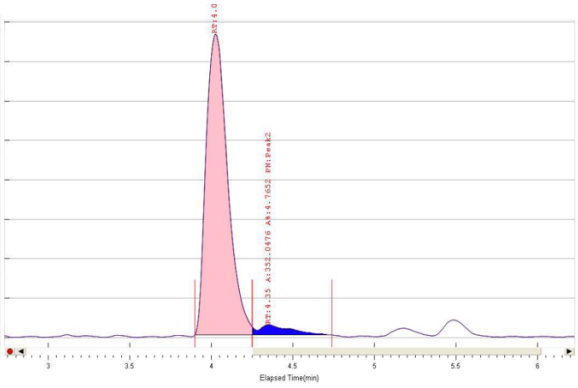
Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 4-methyl-1-phenyl-6-(triisopropylsilyl)hex-5-yn-3-ol.

Racemic Compound

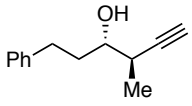


Peak No	% Area	Area	RT (min)
1	50.4592	2921.5673	4.16
2	49.5408	2868.3926	4.54
Total:	100	5789.9599	

Standard Conditions

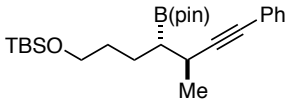


Peak No	% Area	Area	RT (min)
1	95.2348	7035.7915	4.02
2	4.7652	352.0476	4.35
Total:	100	7387.8391	

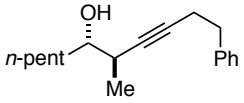


(3*S*,4*R*)-4-Methyl-1-phenylhex-5-yn-3-ol (**3.156**). Triisopropyl((3*S*,4*S*)-3-methyl-6-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-1-yn-1-yl)silane (90.87 mg, 0.20 mmol) was oxidized with $NaOH/H_2O_2$. After work-up, the colorless oil residue was diluted with 0.4 mL THF, treated with TBAF (0.6 mL, 1.0 M in THF, 0.6 mmol), and was allowed to stir at 25 ºC for 12 h. The mixture was washed three times with Et_2O, the organic layers were combined and concentrated under reduced pressure. The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (30 mg, 0.16 mmol, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.26 – 7.17 (m, 3H), 3.55 – 3.43 (m, 1H), 2.85 (dt, *J* = 14.6, 7.5 Hz, 1H), 2.72 (dt, *J* = 13.8, 8.1 Hz, 1H), 2.65 – 2.54 (m, 1H), 2.15 (d, *J* = 2.5 Hz, 1H), 1.94 – 1.85 (m, 2H), 1.80 (s, 1H), 1.24 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.9, 128.44, 128.40, 125.9, 85.0, 73.4, 71.2, 36.8, 33.1, 32.0, 17.4. IR: ν_{max} 3428 (br), 3300 (w), 2926 (s), 2855 (w), 1495 (w), 1453 (w), 1373 (w), 1310 (w), 1142 (w), 1044 (w), 748 (w), 699 (s), 637 (m) cm^{-1}.; HRMS (DART) for $C_{13}H_{17}O$; $[M+H]^+$: calculated: 189.1274, found: 189.1274. $[\alpha]_D^{20}$: +4.5 (c = 1.0, $CHCl_3$, *l* = 50 mm).

All spectra match literature,[75] except for the ^{13}C peak at 84.98 ppm was recorded in literature as 87.9 ppm. We suspect that it was a typo in previous literature.



***tert*-Butyldimethyl(((4*S*,5*S*)&(4*R*,5*R*)-5-methyl-7-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-yn-1-yl)oxy)silane (3.70).** The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), 2-bromoethynylbenzene (43.5 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (20.8 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (51.4 mg, 0.12 mmol, 58% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.27 – 7.21 (m, 3H), 3.61 (t, J = 5.8 Hz, 2H), 2.80 – 2.73 (m, 1H), 1.65 – 1.47 (m, 4H), 1.28 (d, J = 6.9, 3H), 1.23 (s, 12H), 1.17 – 1.11 (m, 1H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.5, 128.0, 127.2, 124.3, 94.9, 83.1, 80.7, 63.4, 32.5, 27.9, 26.0, 25.4, 24.9, 24.8, 20.2, 18.3, -5.2.; IR: ν_{max} 2927 (m), 2854 (w), 1489 (w), 1379 (m), 1319 (m), 1252 (m), 1143 (s), 1097 (s), 969 (w), 834 (s), 774 (m), 755 (m), 691 (w) cm^{-1}.; HRMS (DART) for $C_{26}H_{44}BO_3Si$; $[M+H]^+$: calculated: 443.3147, found: 443.3156.

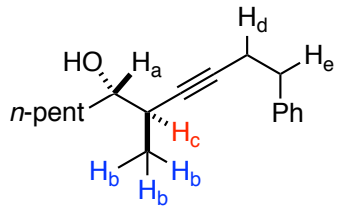


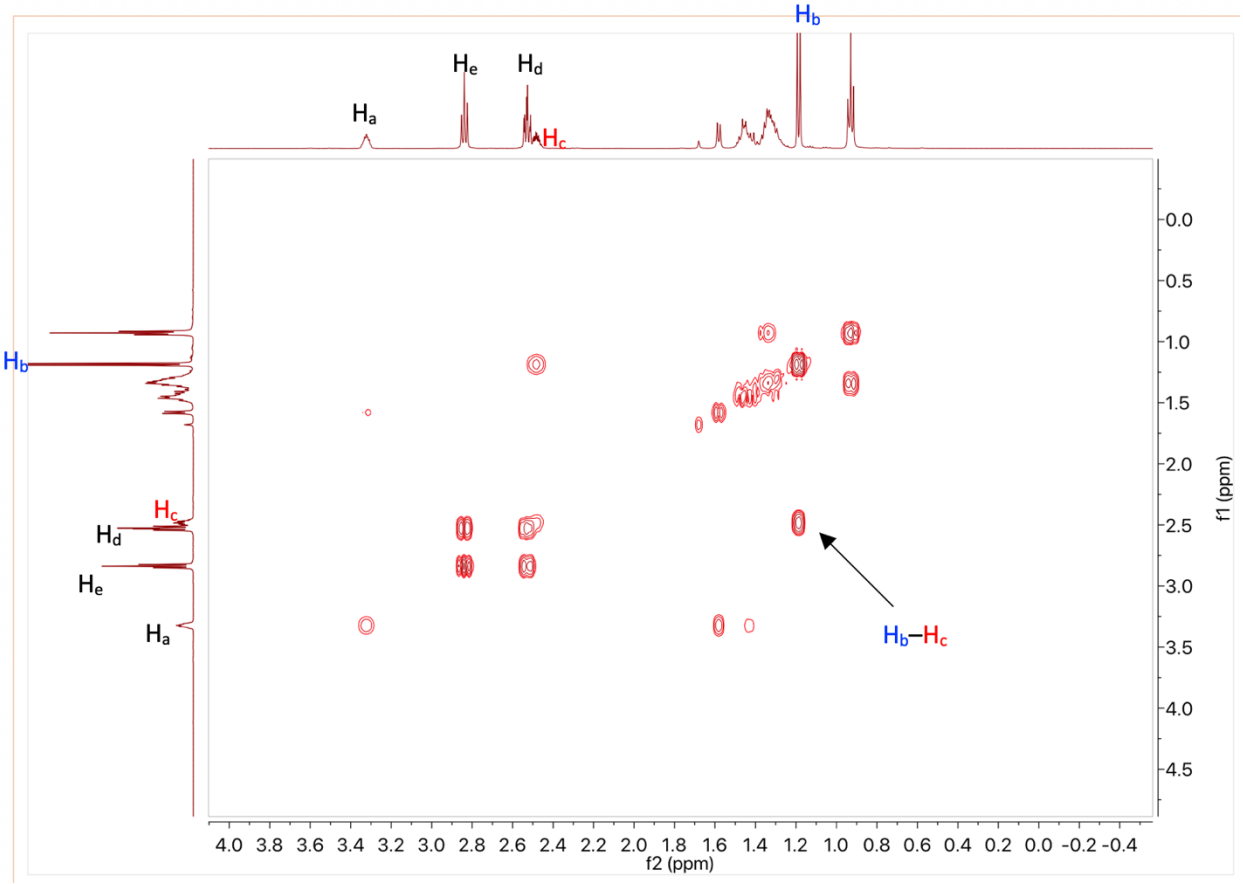
(5*R*,6*S*)&(5*S*,6*R*)-5-Methyl-1-phenylundec-3-yn-6-ol (3.71). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), 4-bromobut-3-ynylbenzene (50.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (20.8 mg, 0.20 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as pale-yellow oil

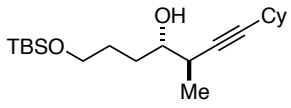
[75] Marshall, J. A.; Chobanian, H. R.; Yanik, M. M. *Org. Lett.* **2001**, *3*, 3369–3372.

(27.6 mg, 0.11 mmol, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.24 – 7.19 (m, 3H), 3.31 – 3.26 (m, 1H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.49 (td, *J* = 7.3, 2.1 Hz, 2H), 2.47 – 2.41 (m, 1H), 1.53 (br, 1H), 1.47 – 1.35 (m, 3H), 1.33 – 1.23 (m, 5H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.7, 128.4, 128.3, 126.3, 82.5, 81.6, 74.5, 35.3, 35.2, 33.2, 31.8, 25.4, 22.6, 20.8, 18.0, 14.0.; IR: ν_{max} 3431 (br), 2928 (s), 2855 (m), 1495 (w), 1453 (m), 1375 (w), 1075 (w), 1012 (w), 745 (w), 698 (s) cm^{-1}.; HRMS (DART) for $C_{18}H_{27}O$; $[M+H]^+$: calculated: 259.2056, found: 259.2059.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)

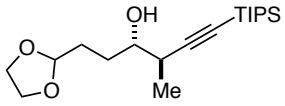




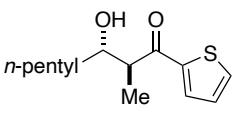


(3*R*,4*S*)&(3*S*,4*R*)-7-((*tert*-Butyldimethylsilyl)oxy)-1-cyclohexyl-3-methylhept-1-yn-4-ol (**3.72**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), 2-bromoethynylcyclohexane (44.9 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (20.8 mg, 0.20 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (40.4 mg, 0.12

mmol, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (td, *J* = 6.0, 1.5 Hz, 2H), 3.44 – 3.35 (m, 1H), 2.53 (qdd, *J* = 6.9, 4.6, 2.0 Hz, 1H), 2.39 – 2.33 (m, 1H), 1.82 – 1.73 (m, 2H), 1.72 – 1.61 (m, 5H), 1.54 – 1.36 (m, 4H), 1.35 – 1.25 (m, 3H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 87.7, 80.5, 74.3, 63.2, 33.2, 33.1, 31.7, 29.2, 29.0, 25.92, 25.90, 24.8, 18.3, 17.7, -5.3.; IR: ν_{max} 3446 (br), 2926 (s), 2852 (m), 1447 (w), 1387 (w), 1253 (w), 1095 (m), 1005 (w), 833 (s), 774 (m), 661 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{39}SiO_2$; $[M+H]^+$: calculated: 339.2714, found: 339.2710.

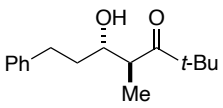


(3*S*,4*R*)&(3*R*,4*S*)-1-(1,3-Dioxolan-2-yl)-4-methyl-6-(triisopropylsilyl)hex-5-yn-3-ol (**3.73**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-5-(1,3-dioxolan-2-yl)pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (79.23 mg, 0.20 mmol), 2-bromoethynyl(triisopropyl)silane (62.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (20.8 mg, 0.20 mmol). The colorless oil residue was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (31.4 mg, 0.092 mmol, 46% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.90 (t, *J* = 4.4 Hz, 1H), 4.00 – 3.94 (m, 2H), 3.88 – 3.83 (m, 2H), 3.47 (ddt, *J* = 8.8, 6.5, 4.0 Hz, 1H), 2.60 (qd, *J* = 7.0, 4.6 Hz, 1H), 2.12 (d, *J* = 6.6 Hz, 1H), 1.91 – 1.84 (m, 1H), 1.83 – 1.70 (m, 2H), 1.69 – 1.61 (m, 1H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.09 – 1.01 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 109.4, 104.4, 83.3, 74.0, 64.91, 64.87, 34.4, 30.2, 29.1, 18.6, 17.4, 11.2.; IR: ν_{max} 3493 (br), 2939 (s), 2862 (s), 2159 (w), 1462 (w), 1382 (w), 1142 (w), 1037 (w), 995 (w), 882 (m), 675 (m) cm^{-1}.; HRMS (DART) for $C_{19}H_{37}SiO_3$; $[M+H]^+$: calculated: 341.2507, found: 341.2511.

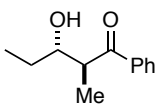


(2*S*,3*S*)&(2*R*,3*R*)-3-Hydroxy-2-methyl-1-(thiophen-2-yl)octan-1-one (**3.74**). The title compound was prepared according to *General Procedure D*

with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.2 mg, 0.20 mmol), thiophene-2-carbonyl chloride (35.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The pale-yellow oil residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (48.1 mg, 0.13 mmol, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 3.8, 1.1 Hz, 1H), 7.68 (dd, J = 5.0, 1.1 Hz, 1H), 7.15 (dd, J = 4.9, 3.8 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.37 (qd, J = 7.2, 5.8 Hz, 1H), 2.79 (s, 1H), 1.58 – 1.48 (m, 2H), 1.41 – 1.23 (m, 9H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 144.2, 134.4, 132.4, 128.3, 74.1, 47.6, 35.1, 31.7, 25.5, 22.6, 15.9, 14.0. IR(neat) ν_{max} 3454 (br), 2919 (s), 2852 (m), 2166 (w), 1961 (w), 1519 (w), 1415 (m), 1210 (w), 721 (m). HRMS (DART) $[M+H]^+$ calcd. for $C_{13}H_{21}O_2S$ 241.1262, found 241.1262.

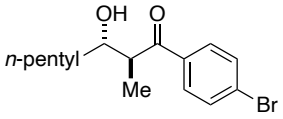


(4*R*,5*R*)&(4*S*,5*S*)-5-Hydroxy-2,2,4-trimethyldecan-3-one (**3.75**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.2 mg, 0.20 mmol), 2,2-dimethylpropanoyl chloride (28.9 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The white solid mixture was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (42.9 mg, 0.14 mmol, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 – 3.59 (m, 1H), 3.05 (p, *J* = 7.0 Hz, 1H), 2.65 (d, *J* = 6.5 Hz, 1H), 1.39 – 1.21 (m, 8H), 1.16 (s, 9H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 222.1, 142.0, 128.5, 128.4, 125.8, 74.2, 45.0, 44.9, 37.3, 32.2, 26.2, 16.3. IR(neat) ν_{max} 2970 (w), 2362 (w), 1737 (s), 1435 (w), 1365 (m), 1229 (m), 1217 (m). HRMS (DART) $[M+H]^+$ calcd. for $C_{13}H_{27}O_2$ 215.2011, found 215.1997.



(2*S*,3*S*)&(2*R*,3*R*)-3-Hydroxy-2-methyl-1-phenylpentan-1-one (**3.76**). The title compound was prepared according to modified *General Procedure D* with 2,2'-

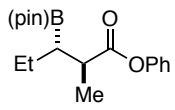
((2*R*,3*R*)&(2*S*,3*S*)-pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (64.81 mg, 0.2 mmol), benzoyl chloride (50.6 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The colorless oil residue was oxidized according to $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (34.2 mg, 0.12 mmol, 59% yield). Note: a small amount of retro-aldol product was observed after oxidation. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.94 (m, 2H), 7.62 – 7.55 (m, 1H), 7.54 – 7.44 (m, 2H), 3.85 – 3.74 (m, 1H), 3.58 (p, *J* = 6.8 Hz, 1H), 2.89 (d, *J* = 6.7 Hz, 1H), 1.65 – 1.60 (m, 1H), 1.57 – 1.46 (m, 1H), 1.26 (d, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.8, 136.7, 133.3, 128.7, 128.4, 75.4, 45.3, 27.7, 15.5, 10.2. IR: ν_{max} 3452 (br), 2963 (w), 2934 (w), 2875 (w), 1676 (s), 1595 (w), 1448 (m), 1374 (w), 1286 (m), 1208 (m), 1119 (w), 965 (s), 702 (s) cm^{-1}.; HRMS (DART) for $C_{12}H_{17}O_2$; $[M+H]^+$: calculated: 193.1223, found: 193.1224. All spectra match literature.[76]



(2*R*,3*R*)&(2*S*,3*S*)-1-(4-Bromophenyl)-3-hydroxy-2-methyloctan-1-one (**3.77**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.2 mg, 0.20 mmol), 4-bromobenzoyl chloride (52.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The pale-yellow oil residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless gel (38.1 mg, 0.12 mmol, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.2, 1.6 Hz, 2H), 7.65 – 7.57 (m, 2H), 3.86 (ddd, *J* = 9.3, 6.4, 2.8 Hz, 1H), 3.48 (p, *J* = 7.1 Hz, 1H), 2.73 (s, 1H), 1.59 – 1.25 (m, 9H), 1.23 (d, *J* = 7.2 Hz, 3H), 0.93 – 0.84 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.6, 135.4, 132.0, 129.9, 128.6, 73.9, 45.9, 34.7, 31.8, 25.4, 22.6, 15.3, 14.0. IR(neat) ν_{max} 3461 (br), 2928 (s),

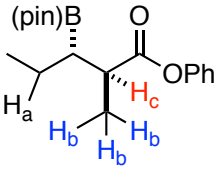
[76] Kirsch, S. F.; Liébert, C. *Eur. J. Org. Chem.* **2007**, *22*, 3711–3717.

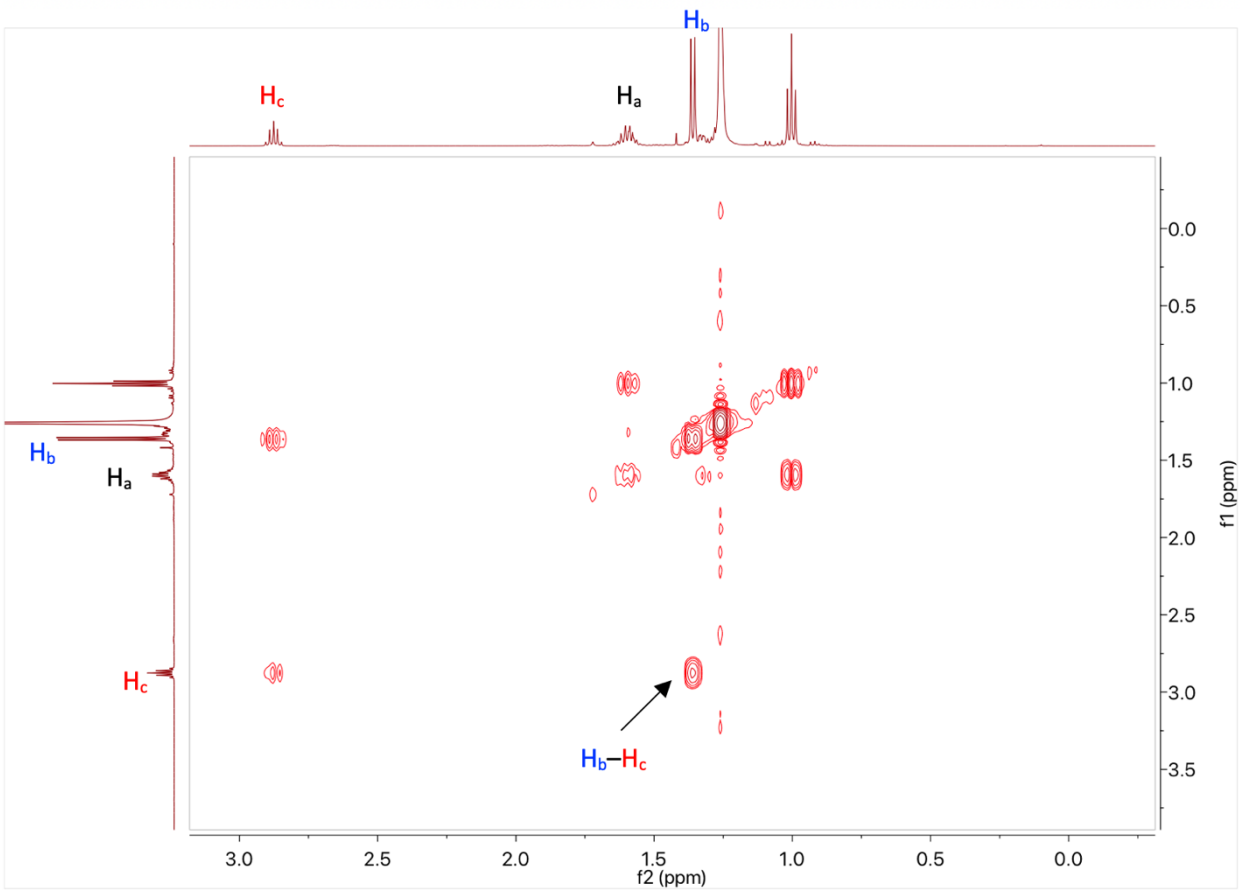
2857 (m), 1719 (w), 1681 (s), 1585 (s), 1397 (m), 1231 (m), 1071 (s), 971 (m). HRMS (DART) $[M+H]^+$ calcd. for $C_{15}H_{22}BrO_2$ 313.0803, found 313.0792.

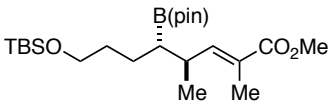


Phenyl (2*S*,3*S*)&(2*R*,3*R*)-2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (**3.78**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (648 mg, 2.0 mmol), phenyl carbonochloridate (375.8 mg, 2.4 mmol), copper cyanide (35.8 mg, 0.4 mmol), styrene (625 mg, 6.0 mmol) was added. The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (399 mg, 1.3 mmol, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.23 – 7.19 (m, 1H), 7.11 – 7.07 (m, 2H), 2.85 (p, *J* = 7.2 Hz, 1H), 1.64 – 1.53 (m, 2H), 1.34 (d, *J* = 7.2 Hz, 3H), 1.31 – 1.26 (m, 1H), 1.24 (d, *J* = 2.6 Hz, 12H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 151.0, 129.2, 125.5, 121.6, 83.2, 40.5, 24.9, 24.8, 21.2, 16.0, 13.4. IR: ν_{max} 2973 (w), 2872 (w), 1753 (m), 1492 (w), 1457 (w), 1379 (m), 1315 (m), 1266 (w), 1197 (m), 1142 (s), 968 (w), 853 (w), 690(w) cm^{-1}.; HRMS (DART) for $C_{18}H_{28}BO_4$; $[M+H]^+$: calculated: 319.2075, found: 319.2085.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)

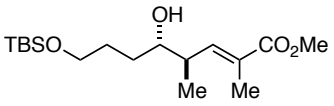






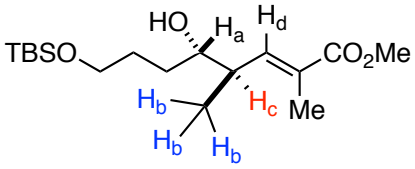
Methyl (4*S*,5*S*,*E*)&(4*R*,5*R*,*E*)-8-((*tert*-butyldimethylsilyl)oxy)-2,4-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-enoate (**3.79**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (43.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as pale-yellow

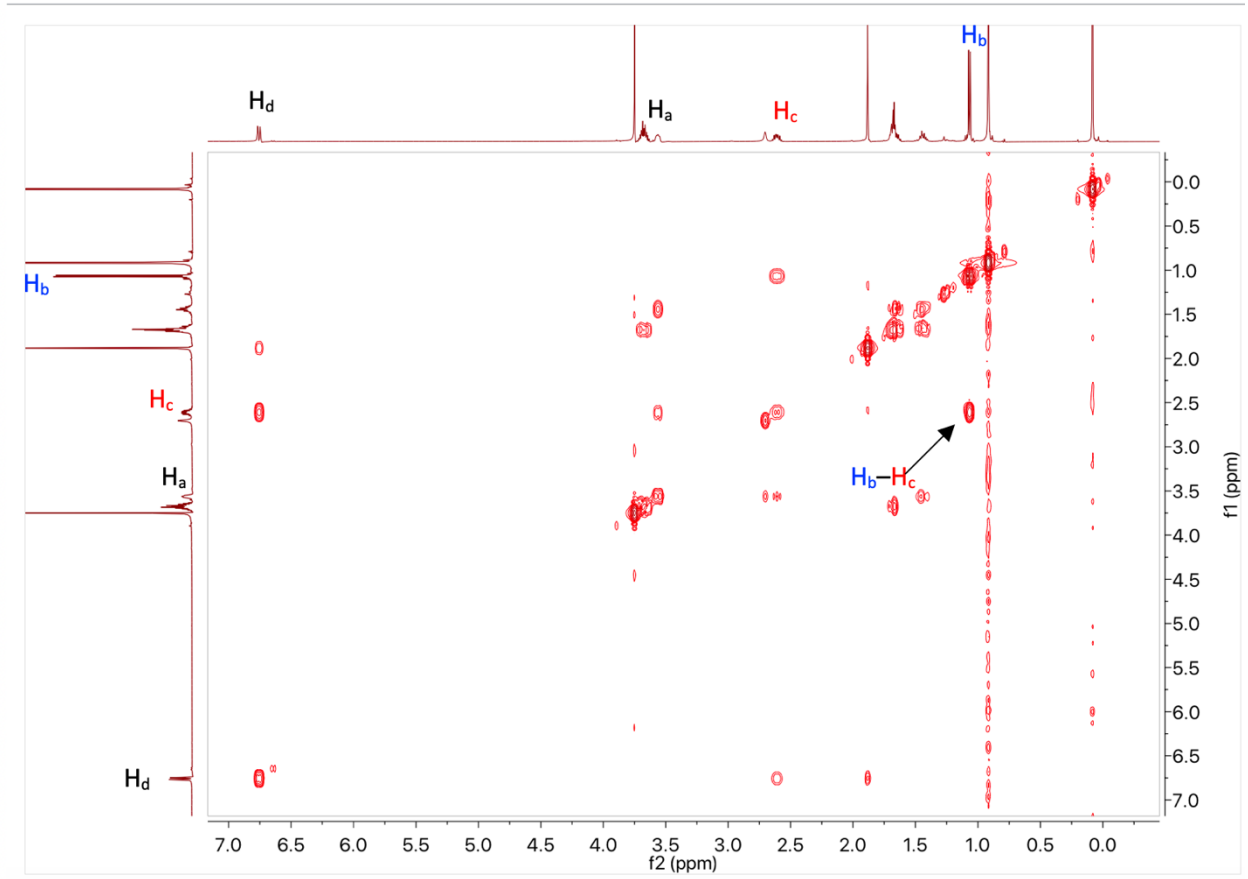
oil (43.5 mg, 0.10 mmol, 49% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (d, *J* = 10.6 Hz, 1H), 3.70 (s, 3H), 3.57 (t, *J* = 6.1 Hz, 2H), 2.66 – 2.56 (m, 1H), 1.84 (s, 3H), 1.57 – 1.49 (m, 1H), 1.49 – 1.35 (m, 3H), 1.20 (d, *J* = 3.9 Hz, 12H), 1.02 (d, *J* = 6.8 Hz, 3H), 1.01 – 0.97 (m, 1H), 0.87 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 147.7, 125.8, 83.1, 63.3, 51.6, 34.9, 32.6, 25.9, 25.4, 24.9, 24.7, 19.3, 18.3, 12.5, -5.27, -5.28.; IR: ν_{max} 2927 (m), 2855 (w), 1713 (s), 1647 (w), 1460 (w), 1379 (m), 1317 (m), 1252 (s), 1203 (w), 1142 (s), 1096 (s), 1040 (w), 970 (w), 834 (s), 774 (m), 668 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{46}BSiO_5$; $[M+H]^+$: calculated: 441.3202, found: 441.3217.

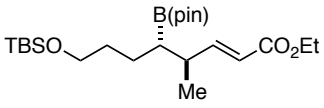


Methyl (4*R*,5*S*,*E*)&(4*S*,5*R*,*E*)-8-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-2,4-dimethyloct-2-enoate (**3.157**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol) methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (43.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was oxidized with $NaBO_3/H_2O$ protocol and purified by silica gel chromatography to afford the product as colorless oil (32.3 mg, 0.10 mmol, 49% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (d, *J* = 10.2 Hz, 1H), 3.73 (s, 3H), 3.70 – 3.60 (m, 2H), 3.57 – 3.51 (m, 1H), 2.59 (dqd, *J* = 10.1, 6.8, 5.1 Hz, 1H), 1.86 (d, *J* = 1.5 Hz, 3H), 1.69 – 1.58 (m, 3H), 1.46 – 1.37 (m, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 144.1, 128.0, 74.8, 63.4, 51.7, 39.3, 31.9, 29.1, 25.9, 18.3, 16.2, 12.7, -5.41, -5.42.; IR: ν_{max} 3453 (br), 2926 (w), 2855 (w), 1713 (m), 1647 (w), 1435 (w), 1386 (w), 1251 (m), 1093 (s), 1003 (w), 834 (s), 775 (m) cm^{-1}.; HRMS (DART) for $C_{17}H_{35}SiO_4$; $[M+H]^+$: calculated: 331.2299, found: 331.2303.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)

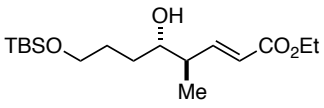




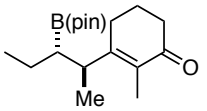


Ethyl (4*S*,5*S*,*E*)&(4*R*,5*R*,*E*)-8-((*tert*-Butyldimethylsilyl)oxy)-4-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-enoate (**3.80**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol) ethyl (*E*)-3-iodoprop-2-enoate (54.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as yellow oil (48.7 mg, 0.11 mmol,

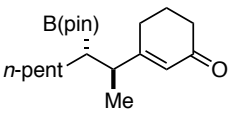
55% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (dd, *J* = 15.6, 8.2 Hz, 1H), 5.76 (d, *J* = 15.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.58 (t, *J* = 6.2 Hz, 2H), 2.50 – 2.40 (m, 1H), 1.58 – 1.52 (m, 1H), 1.49 – 1.36 (m, 3H), 1.27 (t, *J* = 7.2, 3H), 1.23 (s, 12H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.05 – 0.99 (m, 1H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 154.2, 119.9, 83.1, 63.3, 60.0, 38.1, 32.5, 26.0, 24.93, 24.87, 24.8, 18.6, 18.3, 14.3, -5.3.; IR: ν_{max} 2975 (w), 2927 (s), 2855 (w), 1719 (m), 1649 (w), 1461 (w), 1379 (m), 1318 (m), 1254 (m), 1212(w), 1141 (s), 1096 (s), 1040 (w), 970 (w), 834 (s), 774 (m), 668 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{46}BSiO_5$; $[M+H]^+$: calculated: 441.3202, found: 441.3216.



Methyl (4*R*,5*S*,*E*)& (4*S*,5*R*,*E*)-8-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-2,4-dimethyloct-2-enoate (**3.81**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), ethyl (*E*)-3-iodoprop-2-enoate (54.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (34.6 mg, 0.10 mmol, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 15.8, 8.0 Hz, 1H), 5.84 (dd, *J* = 15.7, 1.1 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.71 – 3.61 (m, 2H), 3.57 (ddd, *J* = 9.0, 4.9, 2.4 Hz, 1H), 2.42 (dddd, *J* = 8.1, 6.5, 5.0, 1.3 Hz, 1H), 1.70 – 1.58 (m, 3H), 1.48 – 1.39 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 150.8, 121.8, 74.4, 63.4, 60.2, 42.6, 31.8, 29.2, 25.9, 18.3, 15.5, 14.2, -5.4.; IR: ν_{max} 3446 (br), 2926 (w), 2855 (w), 1718 (m), 1650 (w), 1462 (w), 1368 (w), 1253 (m), 1178 (w), 1094 (m), 1039 (w), 987 (w), 834 (s), 775 (m) cm^{-1}.; HRMS (DART) for $C_{17}H_{35}SiO_4$; $[M+H]^+$: calculated: 331.2299, found: 331.2311.

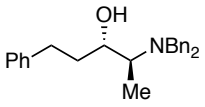


2-Methyl-3-((2*S*,3*S*)&(2*R*,3*R*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl)cyclohex-2-en-1-one (**3.82**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (64.81 mg, 0.20 mmol), 3-bromo-2-methyl-cyclohex-2-en-1-one (45.4 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless gel (28.5 mg, 0.094 mmol, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87 (dq, *J* = 11.0, 6.8 Hz, 1H), 2.43 – 2.22 (m, 4H), 1.99 – 1.90 (m, 1H), 1.89 – 1.83 (m, 1H), 1.81 (s, 3H), 1.68 – 1.59 (m, 1H), 1.42 – 1.31 (m, 1H), 1.15 (d, *J* = 2.7 Hz, 12H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.00 (td, *J* = 11.2, 4.3 Hz, 1H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.9, 163.7, 129.6, 83.1, 38.5, 38.1, 25.4, 25.1, 24.7, 22.7, 22.3, 17.1, 13.7, 10.5.; IR: ν_{max} 2928 (w), 2869 (w), 1663 (s), 1613 (w), 1455 (w), 1377 (m), 1316 (m), 1187 (w), 1142 (m), 966 (w), 861 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{32}BO_3$; $[M+H]^+$: calculated: 307.2439, found: 307.2445.



3-((2*S*,3*S*)&(2*R*,3*R*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-yl)cyclohex-2-en-1-one (**3.83**). The title compound was prepared according to *General Procedure D* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), 3-bromocyclohex-2-en-1-one (42.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (30.0 mg, 0.090 mmol, 45% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (s, 1H), 2.42 – 2.26 (m, 5H), 2.00 – 1.92 (m, 2H), 1.41 – 1.27 (m, 6H), 1.24 – 1.20 (m, 2H), 1.19 (d, *J* = 3.4 Hz, 12H), 1.14 – 1.05 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.2, 171.7, 125.1, 83.1, 42.9, 37.7, 32.1, 29.0, 28.2, 27.4, 25.0, 24.9, 22.9, 22.5, 17.5, 14.0.; IR: ν_{max} 2927 (m), 2866 (w),

1670 (s), 1617 (w), 1456 (w), 1378 (m), 1321 (m), 1252 (w), 1142 (s), 965 (w), 889 (w), 850 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{36}BO_3$; $[M+H]^+$: calculated: 335.2752, found: 335.2757.



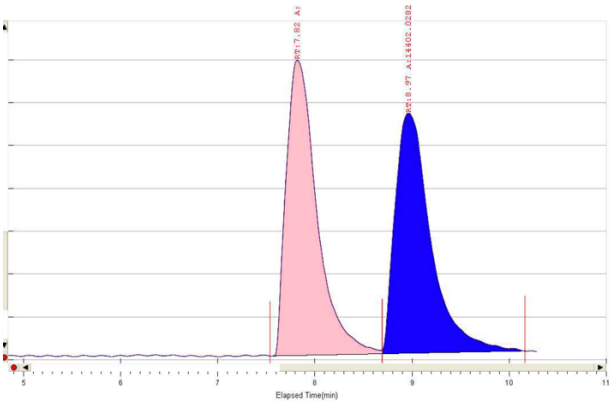
(3*S*,4*S*)-4-(Dibenzylamino)-1-phenylpentan-3-ol (**3.84**). The title compound was prepared according to *General Procedure F* with 2,2'-((2*S*,3*S*)-5-phenylpentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (80.03 mg, 0.20 mmol, 92:8 er), (dibenzylamino) benzoate (76.2 mg, 0.24 mmol), cesium fluoride (91.1 mg, 0.6 mmol), triphenyl phosphine (21.0 mg, 0.8 mmol), copper cyanide (3.6 mg, 0.04 mmol). The yellow solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (34.9 mg, 0.10 mmol, 49% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 12H), 7.23 – 7.17 (m, 3H), 4.55 (s, 1H), 3.85 (d, *J* = 13.2 Hz, 2H), 3.53 (td, *J* = 9.2, 2.4 Hz, 1H), 3.33 (d, *J* = 13.3 Hz, 2H), 2.87 (ddd, *J* = 13.8, 10.7, 5.0 Hz, 1H), 2.72 – 2.58 (m, 2H), 1.85 – 1.74 (m, 1H), 1.54 – 1.42 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 138.9, 129.0, 128.5, 128.4, 128.3, 127.3, 125.6, 70.2, 58.4, 53.3, 35.9, 32.1, 8.0.; IR: ν_{max} 3406 (br), 3024 (w), 2928 (w), 2843 (w), 1601 (w), 1493 (w), 1452 (w), 1379 (w), 1303 (w), 1143 (w), 1059 (w), 1028 (w), 747 (m), 698 (s), 506 (w) cm^{-1}.; HRMS (DART) for $C_{25}H_{30}NO$; $[M+H]^+$: calculated: 360.2322, found: 360.2326. $[\alpha]_D^{20}$: +31.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

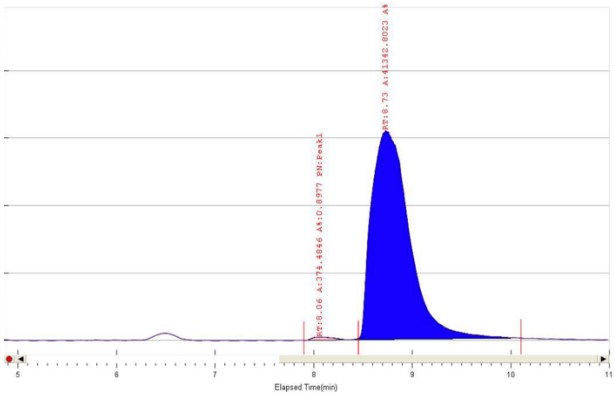
Chiral SFC (AD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 4-(dibenzylamino)-1-phenylpentan-3-ol

Racemic Compound



Peak No	% Area	Area	RT (min)
1	51.3099	15176.9272	7.82
2	48.6901	14402.0282	8.97
Total:	100	29578.9554	

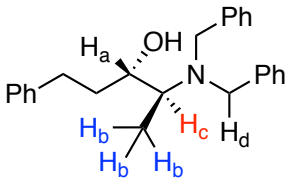
Standard Conditions

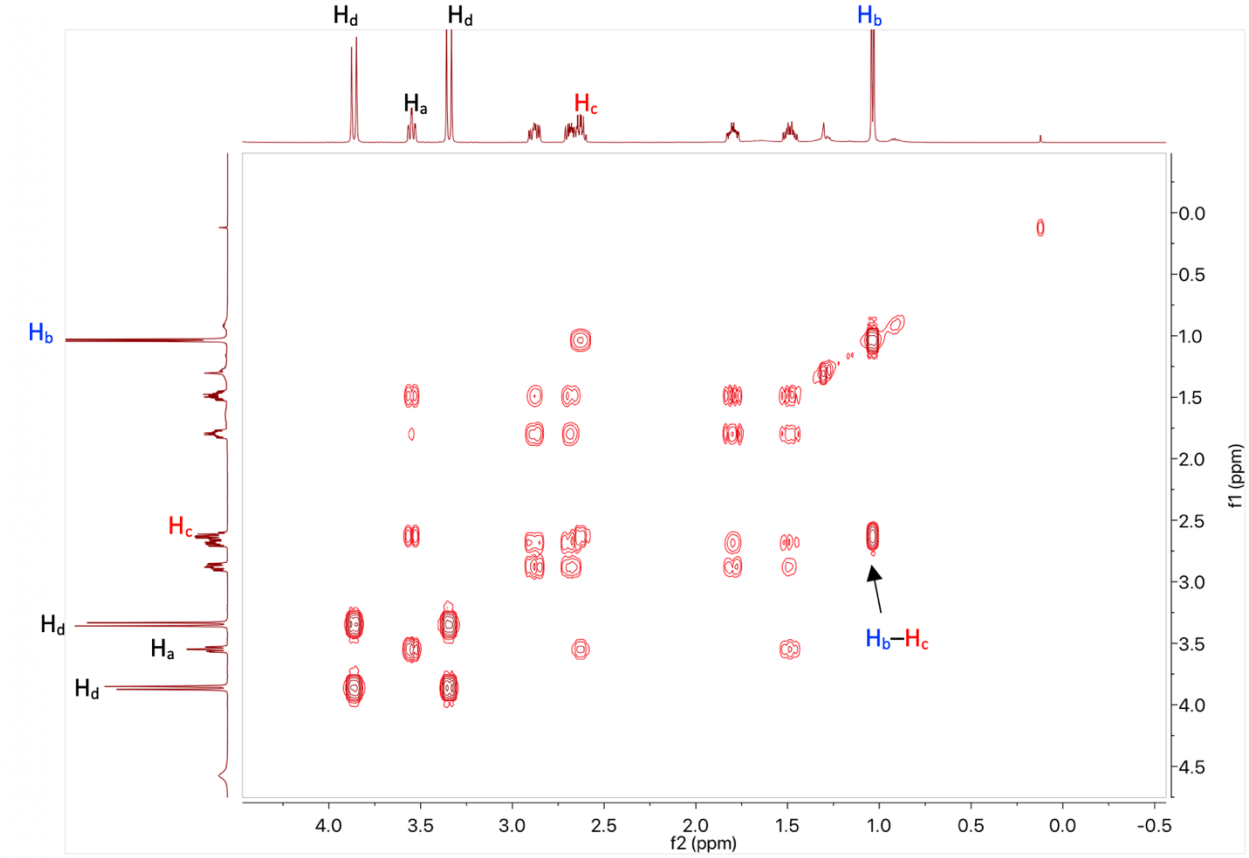


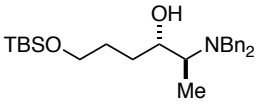
Peak No	% Area	Area	RT (min)
1	0.8977	374.4846	8.06
2	99.1023	41342.8023	8.73
Total:	100	41717.2869	

It is noteworthy that isolated product has a much higher optical purity than starting material (confirmed over several runs of chiral SFC). We suspect that this amino alcohol formed a dimer due to hydrogen bonding, thus the enantiomers were separable by silica gel chromatography.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)

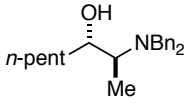




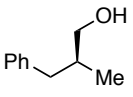


(2*S*,3*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-(dibenzylamino)hexan-3-ol (**3.85**). The title compound was prepared according to *General Procedure F* with (((4*S*,5*S*)&(4*R*,5*R*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)dimethylsilane (93.67 mg, 0.20 mmol), (dibenzylamino) benzoate (76.2 mg, 0.24 mmol), cesium fluoride (91.1 mg, 0.6 mmol), triphenyl phosphine (21.0 mg, 0.8 mmol), copper cyanide (3.6 mg, 0.04 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (44.2 mg, 0.10

mmol, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 10H), 4.43 (s, 1H), 3.84 (d, *J* = 13.3 Hz, 2H), 3.67 – 3.55 (m, 2H), 3.49 (td, *J* = 9.1, 2.3 Hz, 1H), 3.32 (d, *J* = 13.3 Hz, 2H), 2.57 (dq, *J* = 9.5, 6.7 Hz, 1H), 1.74 – 1.52 (m, 4H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.0, 129.0, 128.5, 127.2, 70.5, 63.1, 58.5, 53.3, 29.9, 28.9, 26.0, 18.3, 8.1, -5.3.; IR: ν_{max} 3414 (br), 2925 (w), 2852 (w), 1452 (w), 1410 (w), 1381 (w), 1251 (w), 1094 (m), 984 (w), 937 (w), 833 (s), 774 (m), 747 (m), 698 (s), 507 (w) cm^{-1}.; HRMS (DART) for $C_{26}H_{42}NO_2Si$; $[M+H]^+$: calculated: 428.2979, found: 428.2984.



(2*S*,3*S*)&(2*R*,3*R*)-2-(Dibenzylamino)octan-3-ol (**3.86**). The title compound was prepared according to *General Procedure F* with 2,2'-((2*S*,3*S*)&(2*R*,3*R*)-octane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.23 mg, 0.20 mmol), (dibenzylamino) benzoate (76.2 mg, 0.24 mmol), cesium fluoride (91.1 mg, 0.6 mmol), triphenyl phosphine (21.0 mg, 0.8 mmol), copper cyanide (3.6 mg, 0.04 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (35.3 mg, 0.11 mmol, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.20 (m, 10H), 4.49 (s, 1H), 3.84 (d, *J* = 13.3 Hz, 2H), 3.47 (td, *J* = 9.2, 2.3 Hz, 1H), 3.32 (d, *J* = 13.3 Hz, 2H), 2.55 (dq, *J* = 9.4, 6.6 Hz, 1H), 1.57 – 1.41 (m, 2H), 1.41 – 1.19 (m, 5H), 1.19 – 1.06 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 129.0, 128.5, 127.2, 70.8, 58.5, 53.3, 33.8, 32.1, 25.6, 22.7, 14.0, 8.1.; IR: ν_{max} 3401 (br), 2927 (m), 2853 (w), 1494 (w), 1452 (m), 1411 (w), 1377 (w), 1303 (w), 1142 (w), 1056 (w), 748 (s), 698 (s), 506 (w) cm^{-1}.; HRMS (DART) for $C_{22}H_{32}NO$; $[M+H]^+$: calculated: 326.2478, found: 326.2477.



(*S*)-2-Methyl-3-phenylpropan-1-ol (**3.89**). The title compound was prepared according to modified *General Procedure E* with (*S*)-4,4,5,5-tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane (61.1 mg, 0.25 mmol, 92:8 er). The colorless oil residue was oxidized with $NaOH/H_2O_2$, and purified by silica gel chromatography to afford the product as colorless oil (35.2 mg, 0.19 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.25 (m, 2H), 7.24 – 7.14 (m, 3H), 3.58 – 3.46 (m, 2H), 2.77 (dd, *J* = 13.5, 6.3 Hz, 1H), 2.44 (dd, *J* = 13.4, 8.1 Hz, 1H), 2.05 – 1.90 (m, *J* = 6.0 Hz, 1H), 1.40 (s, 1H), 0.93 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6, 129.1, 128.3, 125.9, 67.7, 39.7, 37.8, 16.5.; IR: ν_{max}. 3361 (br), 2955 (m), 2920 (s), 2870 (w), 1453 (m), 1377 (w), 1141 (w), 1031 (s), 985 (w), 738 (s), 699 (s); HRMS (DART) for $C_{10}H_{15}O$; $[M+H]^+$: calculated: 151.1117, found: 151.1116. $[\alpha]_D^{20}$: –6.2 (c = 1.0, $CHCl_3$, *l* = 50 mm). All spectra match literature.[77]

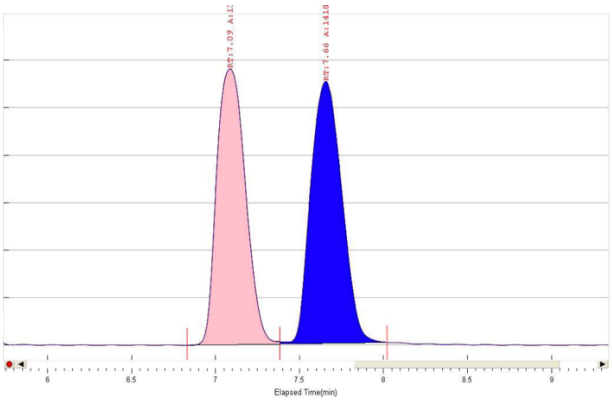
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 2-methyl-3-phenylpropan-1-ol

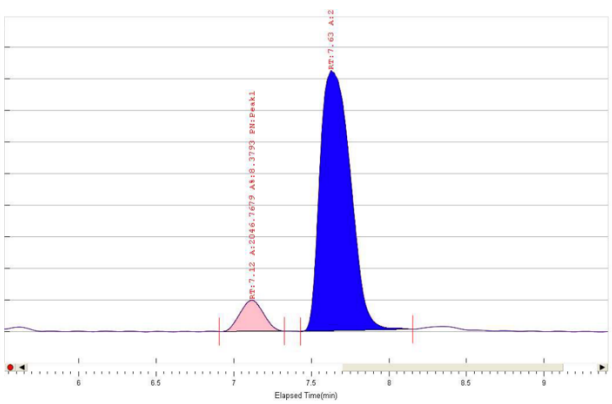
[77] Fronza, G.; Fuganti, C.; Serra, S. *Eur. J. Org. Chem.* **2009**, *35*, 6160–6171.

Racemic Compound



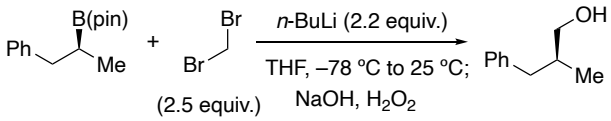
Peak No	% Area	Area	RT (min)
1	49.3459	13814.0524	7.09
2	50.6541	14180.263	7.66
Total:	100	27994.3154	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.3793	2046.7679	7.12
2	91.6207	22379.5686	7.63
Total:	100	24426.3365	

Proof of Absolute Stereochemistry:

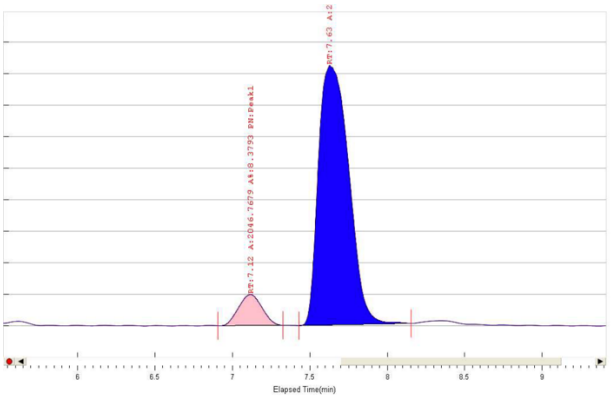


Matteson homologation was carried out according to a literature procedure.[78] To a stirring solution of the (*S*)-4,4,5,5-tetramethyl-2-(1-phenylpropan-2-yl)-1,3,2-dioxaborolane (56.1 mg, 0.23 mmol) and dibromomethane (99.05 mg, 0.57 mmol) in anhydrous THF (0.1 M) at –78 ºC, *n*-BuLi (1.6 M in hexanes, 0.66 mmol) was added dropwise. The resulting mixture was allowed to stir for 10 min at –78 ºC, and was allowed to warm to room temperature and to stir for 2 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl slowly, and the mixture was washed with EtOAc (10 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The colorless oil residue was oxidized with $NaOH/H_2O_2$, and

[78] Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 3760–3763.

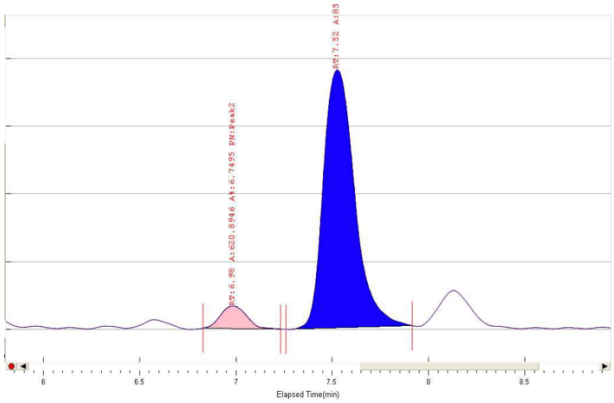
purified by silica gel chromatography to afford the product (28.3 mg, 0.19 mmol, 82% yield) as colorless oil.

This Method

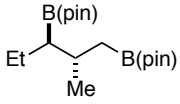


Peak No	% Area	Area	RT (min)
1	8.3793	2046.7679	7.12
2	91.6207	22379.5686	7.63
Total:	100	24426.3365	

Matteson Homologation

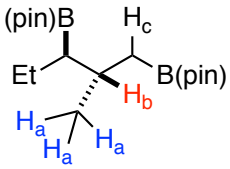


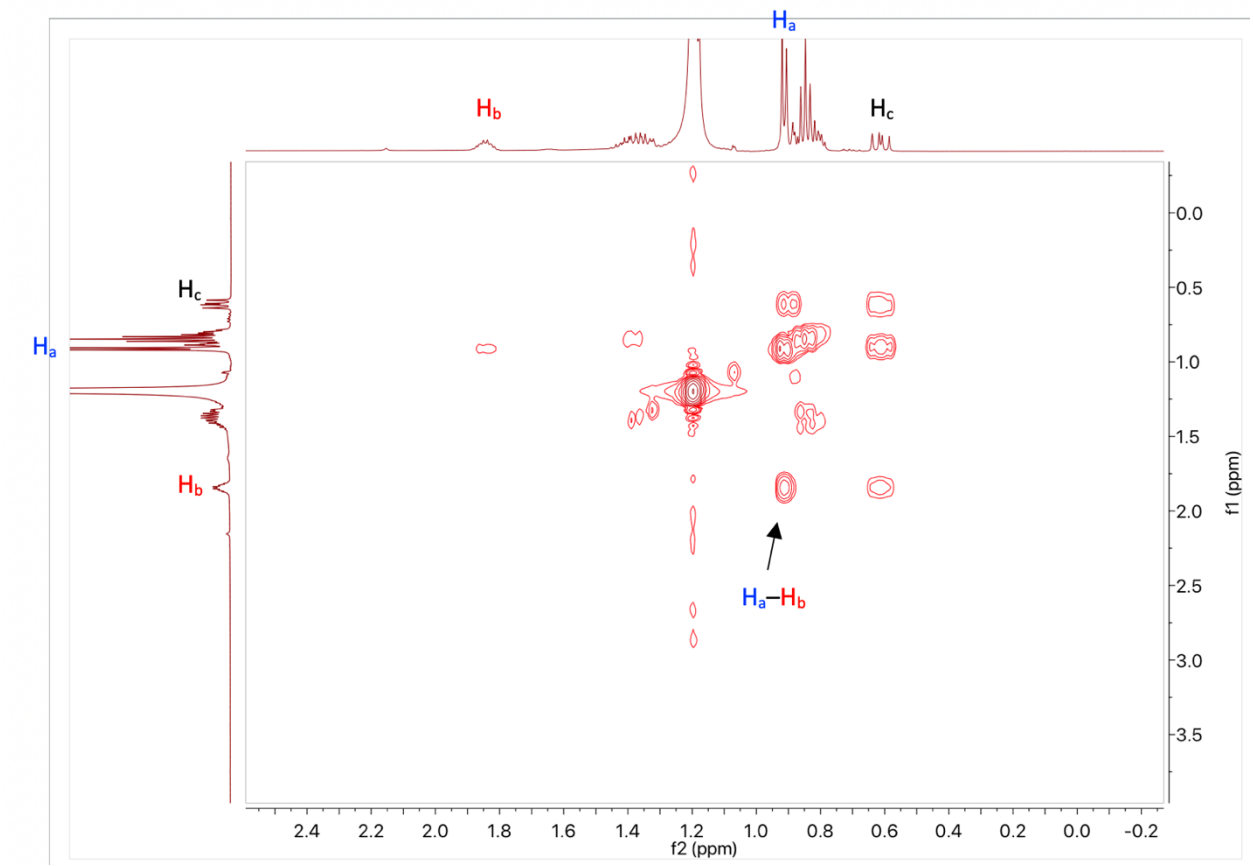
Peak No	% Area	Area	RT (min)
1	6.7495	620.8946	6.98
2	93.2505	8578.2378	7.52
Total:	100	9199.1324	

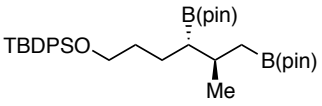


2,2'-((2*S*,3*R*)&(2*R*,3*S*)-2-Methylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.90). The title compound was prepared according to modified *General Procedure E* with 2,2'-((2*R*,3*R*)&(2*S*,3*S*)-pentane-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (64.81 mg, 0.2 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (46.4 mg, 0.21 mmol), copper cyanide (1.8 mg, 0.02 mmol). The mixture was allowed to stir at 60 ºC for 12 h. The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (35.4 mg, 0.10 mmol, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.92 – 1.84 (m, 1H), 1.48 – 1.33 (m, 2H), 1.23 (s, 24H), 0.94 (d, J = 6.8 Hz, 3H), 0.92 – 0.80 (m, 5H), 0.69 – 0.61 (m, 1H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.67, 82.65, 30.9, 25.0, 24.9, 24.8, 24.7, 21.8, 21.7, 14.1.; IR: ν_{max} 2975 (m), 2870 (w), 1459 (w), 1369 (s), 1309 (s), 1267 (w), 1212 (w), 1143 (s), 969 (w), 849 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{37}B_2O_4$; $[M+H]^+$: calculated: 339.2873, found: 339.2875.

Regioisomeric analysis: (COSY NMR, full spectra included in Spectral Data)







***tert*-Butyl(((4*S*,5*R*)-5-methyl-4,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)diphenylsilane** (**3.91**). The title compound was prepared according to modified *General Procedure E* with (((4*S*,5*S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)diphenylsilane (178 mg, 0.3 mmol, 93:7 er), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (69.6 mg, 0.32 mmol), copper cyanide (2.7 mg, 0.03 mmol). The mixture was allowed to stir at 60 ºC for 12 h. The colorless oil residue was purified by silica gel chromatography to afford the product as

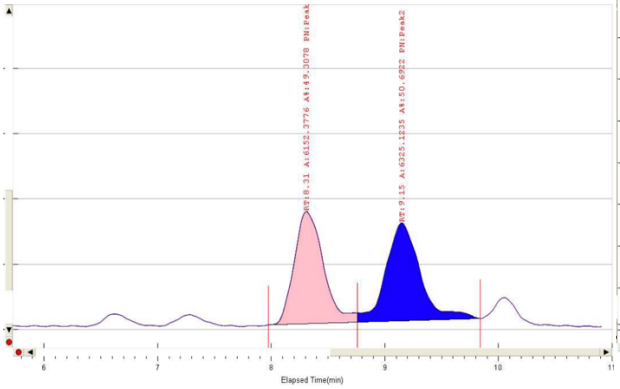
colorless oil (86.3 mg, 0.14 mmol, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 4H), 7.42 – 7.36 (m, 6H), 3.65 (t, *J* = 6.4 Hz, 2H), 1.94 – 1.83 (m, 1H), 1.65 – 1.40 (m, 4H), 1.24 (dd, *J* = 7.6, 3.2 Hz, 24H), 1.05 (s, 9H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.95 – 0.85 (m, 2H), 0.67 (dd, *J* = 15.5, 11.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 134.29, 134.27, 129.4, 127.5, 82.7, 64.4, 32.7, 31.0, 26.9, 25.0 (overlapped), 24.9, 24.8, 24.7, 21.8, 19.2.; IR: ν_{max} 2928 (m), 2856 (w), 1462 (w), 1369 (s), 1214 (w), 1142 (s), 1109 (w), 969 (w), 822 (w), 740 (w), 702 (m), 613 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{35}H_{57}B_2O_5Si$; $[M+H]^+$: calculated:607.4156, found: 607.4165. $[\alpha]_D^{20}$: +1.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

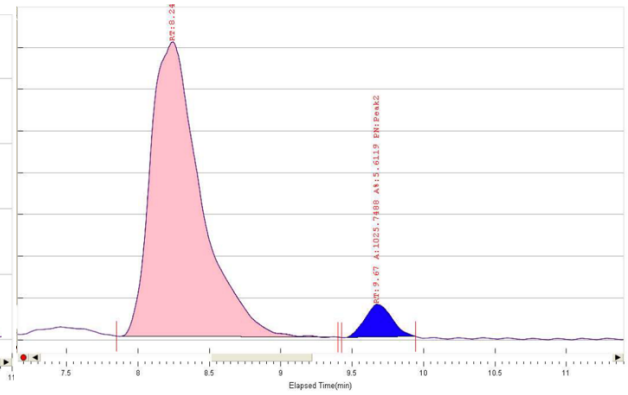
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Material was oxidized with NaOH and H_2O_2 and used for SFC without purification. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 6-((tert-butyldiphenylsilyl)oxy)-2-methylhexane-1,3-diol

Racemic Compound

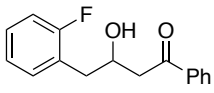


Standard Conditions



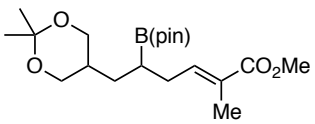
Peak No	% Area	Area	RT (min)
1	49.3078	6152.3776	8.31
2	50.6922	6325.1235	9.15
Total:	100	12477.5011	

Peak No	% Area	Area	RT (min)
1	94.3881	17252.3767	8.24
2	5.6119	1025.7488	9.67
Total:	100	18278.1255	

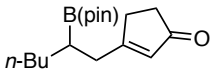


4-(2-Fluorophenyl)-3-hydroxy-1-phenylbutan-1-one (**3.92**). The title compound was prepared according to *General Procedure D* with 2,2'-(3-(2-fluorophenyl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (78.0 mg, 0.20 mmol), benzoyl chloride (33.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (10.4 mg, 0.1 mmol). The colorless oil residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as white solid (35.0 mg, 0.13 mmol, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.60 – 7.54 (m, 1H), 7.48 – 7.42 (m, 2H), 7.31 (td, *J* = 7.6, 1.8 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.10 (td, *J* = 7.5, 1.3 Hz, 1H), 7.05 (ddd, *J* = 9.7, 8.2, 1.2 Hz, 1H), 4.55 – 4.48 (m, 1H), 3.36 (s, 1H), 3.19 (dd, *J* = 17.7, 2.9 Hz, 1H), 3.10 (dd, *J* = 17.7, 8.7 Hz, 1H), 3.02 – 2.90 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.6, 162.3, 160.3, 136.7, 133.6, 132.0 (d, *J* = 4.5 Hz), 128.7, 128.4 (d, *J* = 8.0 Hz), 128.1, 125.0 (d, *J* = 15.5 Hz), 124.1 (d, *J* = 3.5 Hz), 115.4 (d, *J* = 22.4 Hz), 67.9, 44.1, 35.8. ^{19}F NMR (470 MHz, CDCl3) δ -117.65 – -117.72 (m). IR(neat) ν_{max} 3461 (br), 2925 (w), 1737 (w), 1679 (s), 1597 (w), 1581 (w), 1492 (m),

1229 (s), 1211 (m), 1104 (w). HRMS (DART) $[M+H]^+$ calcd. for $C_{16}H_{16}FO_2$ 259.1134, found 259.1133.

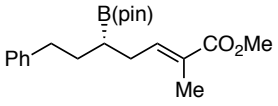


Methyl (*E*)-6-(2,2-dimethyl-1,3-dioxan-5-yl)-2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-2-enoate (**3.93**). The title compound was prepared according to *General Procedure D* with 2,2'-(3-(2,2-dimethyl-1,3-dioxan-5-yl)propane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (82.03 mg, 0.20 mmol), methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (43.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (34.3 mg, 0.090 mmol, 45% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72 (td, *J* = 7.5, 1.5 Hz, 1H), 3.89 – 3.80 (m, 2H), 3.71 (s, 3H), 3.59 – 3.49 (m, 2H), 2.30 – 2.20 (m, 2H), 1.94 – 1.85 (m, 1H), 1.83 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.37 – 1.27 (m, 2H), 1.22 (s, 12H), 1.16 – 1.09 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 141.6, 128.0, 97.7, 83.4, 65.1, 64.9, 51.6, 33.4, 30.4, 29.9, 27.8, 24.8, 24.7, 20.1, 12.5.; IR: ν_{max} 2976 (w), 2928 (w), 2851 (w), 1713 (m), 1369 (m), 1316 (m), 1257 (m), 1195 (m), 1140 (s), 1069 (w), 967 (w), 832 (w), 747 (w), 519 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{36}BO_6$; $[M+H]^+$: calculated: 383.2600, found: 383.2605.

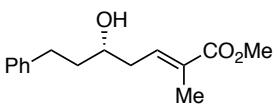


3-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)cyclopent-2-en-1-one (**3.94**). The title compound was prepared according to *General Procedure D* with 2,2'-(hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (67.62 mg, 0.20 mmol), 3-iodocyclopent-2-en-1-one (50.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (40.0 mg, 0.13 mmol, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$)

δ 5.93 (s, 1H), 2.59 – 2.54 (m, 2H), 2.51 (dd, *J* = 15.9, 9.1 Hz, 1H), 2.41 (dd, *J* = 15.8, 6.5 Hz, 1H), 2.36 (t, *J* = 4.8 Hz, 2H), 1.48 – 1.40 (m, 1H), 1.39 – 1.33 (m, 1H), 1.31 – 1.24 (m, 5H), 1.19 (d, *J* = 2.5 Hz, 12H), 0.86 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.2, 183.6, 129.7, 83.3, 35.3, 35.1, 31.6, 31.1, 30.9, 24.8, 24.7, 22.8, 14.0.; IR: ν_{max} 2922 (m), 2856 (w), 1708 (s), 1674 (w), 1614 (w), 1438 (w), 1380 (m), 1321 (m), 1238 (w), 1142 (m), 966 (w), 848 (w) cm^{-1}.; HRMS (DART) for $C_{17}H_{30}BO_3$; $[M+H]^+$: calculated: 293.2283, found: 293.2285.



Methyl (*S*,*E*)-2-methyl-7-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enoate (**3.95**). The title compound was prepared according to *General Procedure D* with (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20 mmol, 95:5 er), methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (43.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as yellow oil (42.0 mg, 0.12 mmol, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.20 – 7.15 (m, 3H), 6.78 (td, *J* = 7.6, 1.6 Hz, 1H), 3.72 (s, 3H), 2.72 – 2.55 (m, 2H), 2.37 – 2.24 (m, 2H), 1.85 (s, 3H), 1.83 – 1.75 (m, 1H), 1.74 – 1.65 (m, 1H), 1.28 – 1.18 (m, 13H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 142.6, 142.4, 128.4, 128.3, 127.6, 125.7, 83.3, 51.6, 35.4, 33.1, 30.1, 24.81, 24.76, 12.5.; IR: ν_{max} 2975 (w), 2923 (w), 2854 (w), 1713 (s), 1648 (w), 1434 (w), 1379 (m), 1319 (m), 1261 (m), 1142 (s), 1115 (w), 966 (w), 848 (s), 747 (m), 699 (w) cm^{-1}.; HRMS (DART) for $C_{21}H_{32}BO_4$; $[M+H]^+$: calculated: 359.2388, found: 359.2404. $[\alpha]_D^{20}$: –7.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).



Methyl (*S*, *E*)-5-hydroxy-2-methyl-7-phenylhept-2-enoate (**3.158**). The title compound was prepared according to *General Procedure D* with (*R*)-

2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20 mmol, 95:5 er) methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (43.0 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (30.1 mg, 0.12 mmol, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 6.82 (td, *J* = 7.5, 1.5 Hz, 1H), 3.80 (p, *J* = 6.2 Hz, 1H), 3.74 (s, 3H), 2.86 – 2.78 (m, 1H), 2.74 – 2.66 (m, 1H), 2.39 (t, *J* = 6.8 Hz, 2H), 1.87 (s, 3H), 1.86 – 1.80 (m, 2H), 1.70 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 141.7, 137.9, 129.9, 128.5, 128.4, 125.9, 70.4, 51.8, 38.7, 36.9, 32.0, 12.7.; IR: ν_{max} 3437 (br), 2924 (m), 2856 (w), 1711 (s), 1647 (w), 1435 (w), 1261 (m), 1124 (w), 1087 (w), 746 (w), 700 (w) cm^{-1}.; HRMS (DART) for $C_{15}H_{21}O_3$; $[M+H]^+$: calculated: 249.1485, found: 249.1486. $[\alpha]_D^{20}$: –8.1 (c = 1.0, $CHCl_3$, *l* = 50 mm).

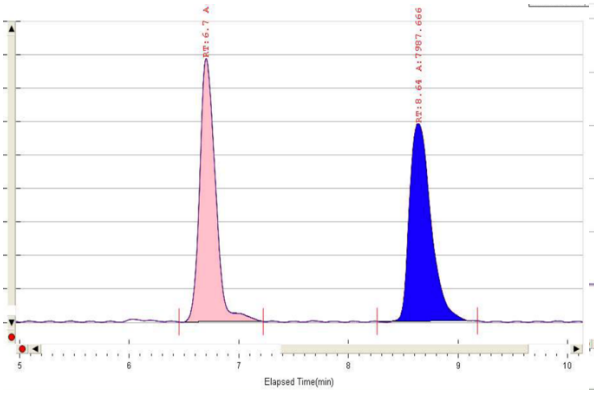
<u>*With AdLi activation:*</u> The title compound was prepared according to *General Procedure E* with (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20 mmol, 95:5 er), styrene (20.83 mg, 0.20 mmol), methyl (*E*)-3-bromo-2-methyl-prop-2-enoate (42.96 mg, 0.24 mmol). The white solid mixture was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (27.1 mg, 0.11 mmol, 55% yield).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

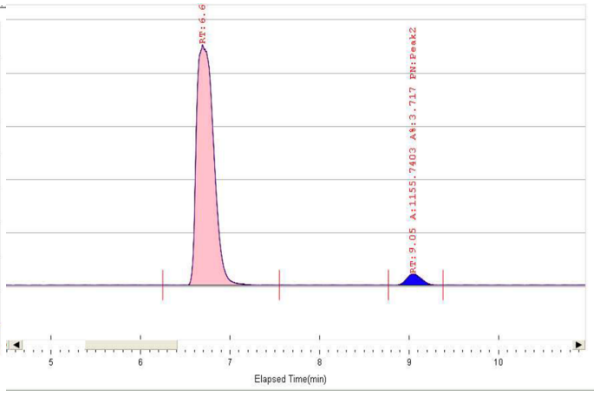
Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of methyl (E)-5-hydroxy-2-methyl-7-phenylhept-2-enoate.

Racemic Compound



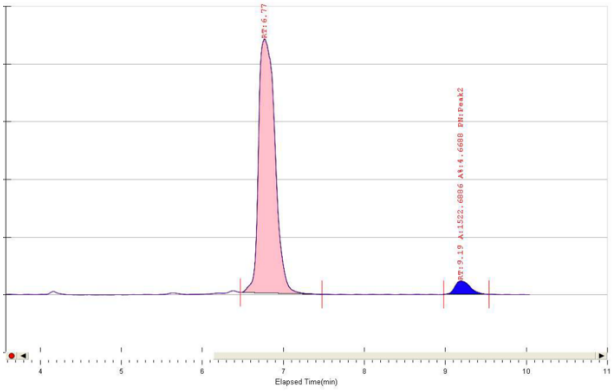
Peak No	% Area	Area	RT (min)
1	49.5543	7846.5114	6.7
2	50.4457	7987.666	8.64
Total:	100	15834.1774	

Standard Conditions

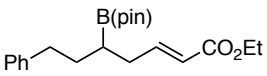


Peak No	% Area	Area	RT (min)
1	96.283	29937.4989	6.69
2	3.717	1155.7403	9.05
Total:	100	31093.2392	

Conditions with AdLi activation

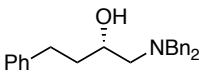


Peak No	% Area	Area	RT (min)
1	95.3312	31091.584	6.77
2	4.6688	1522.6886	9.19
Total:	100	32614.2726	



Ethyl (*E*)-7-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enoate (**3.96**). The title compound was prepared according to *General Procedure D* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20

mmol), ethyl (*E*)-3-iodoprop-2-enoate (54.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (53.5 mg, 0.15 mmol, 75% yield). No *Z*-isomer was observed. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.21 – 7.15 (m, 3H), 6.96 (dt, *J* = 15.6, 7.2 Hz, 1H), 5.83 (d, *J* = 15.7 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.70 – 2.56 (m, 2H), 2.41 – 2.26 (m, 2H), 1.82 – 1.74 (m, 1H), 1.73 – 1.63 (m, 1H), 1.30 – 1.24 (m, 16H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 148.9, 142.5, 128.4, 128.3, 125.7, 121.8, 83.3, 60.0, 35.3, 33.7, 32.9, 24.8, 14.3.; IR: ν_{max} 2976 (w), 2924 (w), 1717 (s), 1651 (w), 1379 (m), 1316 (m), 1265 (m), 1141 (s), 1043 (w), 967 (w), 848 (w), 748 (w), 699 (s) cm^{-1}.; HRMS (DART) for $C_{21}H_{32}BO_4$; $[M+H]^+$: calculated: 359.2388, found: 359.2398.



(*S*)-1-(Dibenzylamino)-4-phenylbutan-2-ol (**3.97**). The title compound was prepared according to *General Procedure G* with (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20 mmol, 95:5 er), (dibenzylamino) 4-(diethylamino)benzoate (93.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), cesium fluoride (91.1 mg, 0.6 mmol). The yellow solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (48.3 mg, 0.14 mmol, 69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 12H), 7.25 – 7.16 (m, 3H), 3.87 (d, *J* = 13.4 Hz, 2H), 3.80 – 3.70 (m, 1H), 3.41 (d, *J* = 13.4 Hz, 2H), 3.35 (s, 1H), 3.26 (s, 1H), 2.81 (ddd, *J* = 14.9, 9.5, 6.0 Hz, 1H), 2.66 (ddd, *J* = 13.8, 9.3, 7.0 Hz, 1H), 2.56 – 2.42 (m, 2H), 1.73 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 138.5, 129.1, 128.5, 128.4, 128.3, 127.3, 125.7, 66.3, 59.7, 58.5, 36.4, 31.9.; IR: ν_{max} 3431 (br), 3023 (w), 2930 (w), 2802 (w), 1601 (w), 1493 (w), 1452 (w), 1371 (w), 1247 (w), 1126 (w), 1073 (w), 1027 (w), 746 (m), 697 (s), 473

(w) cm^{-1}.; HRMS (DART) for $C_{24}H_{28}NO$; $[M+H]^+$: calculated: 346.2165, found: 346.2170. $[\alpha]_D^{20}$: +50.1 (c = 1.0, $CHCl_3$, *l* = 50 mm).

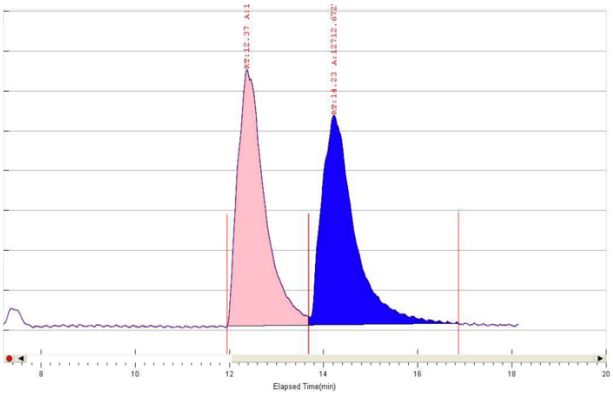
With AdLi activation: The title compound was prepared according to *General Procedure E* with (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.23 mg, 0.20 mmol, 95:5 er), cesium fluoride (91.14 mg, 0.60 mmol), (dibenzylamino) 4-(diethylamino)benzoate (93.24 mg, 0.24 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (51 mg, 0.15 mmol, 74% yield).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

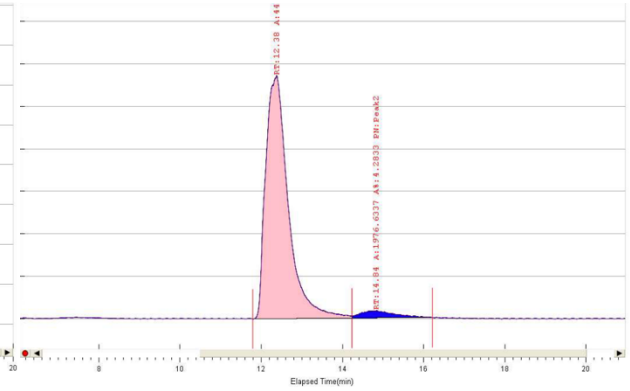
Chiral SFC (AD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 1-(dibenzylamino)-4-phenylbutan-2-ol.

Racemic Compound



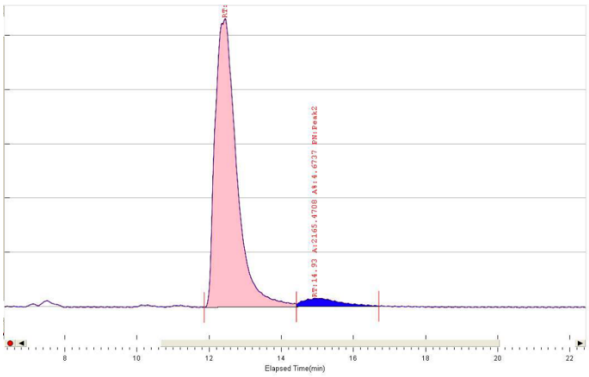
Peak No	% Area	Area	RT (min)
1	50.3517	12892.7841	12.37
2	49.6483	12712.6727	14.23
Total:	100	25605.4568	

Standard Conditions

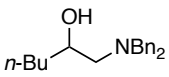


Peak No	% Area	Area	RT (min)
1	95.7167	44171.1221	12.38
2	4.2833	1976.6337	14.84
Total:	100	46147.7558	

Conditions with AdLi activation

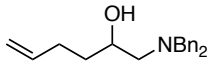


Peak No	% Area	Area	RT (min)
1	95.3263	44167.5311	12.44
2	4.6737	2165.4708	14.93
Total:	100	46333.0019	

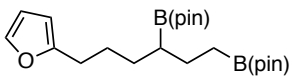


1-(Dibenzylamino)hexan-2-ol (**3.98**). The title compound was prepared according to *General Procedure G* with 2,2'-(hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (67.62 mg, 0.20 mmol), (dibenzylamino) 4-(diethylamino)benzoate (93.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), cesium fluoride (91.1 mg, 0.6 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (41.5 mg, 0.14 mmol, 70% yield). ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.42 – 7.22 (m, 10H), 3.87 (d, *J* = 13.4 Hz, 2H), 3.71 (qd, *J* = 7.0, 4.5 Hz, 1H), 3.40 (d, *J* = 13.4 Hz, 2H), 2.44 (d, *J* = 7.1 Hz, 2H), 1.46 – 1.26 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 129.0, 128.4, 127.2, 67.0, 59.9, 58.4, 34.5, 27.8, 22.8, 14.0.; IR: ν_{max} 3437 (br), 3059 (w), 2927 (m), 2855 (w), 1601 (w), 1493 (w), 1452 (m), 1371 (w), 1120 (w), 1075 (w), 975 (w), 746 (m), 698 (s), 473 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{28}NO$; $[M+H]^+$: calculated: 298.2165, found: 298.2181.

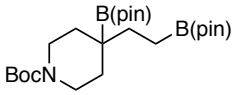


1-(Dibenzylamino)hex-5-en-2-ol (**3.99**). The title compound was prepared according to *General Procedure G* with 2,2'-(hex-5-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (67.22 mg, 0.20 mmol), (dibenzylamino) 4-(diethylamino)benzoate (93.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), cesium fluoride (91.1 mg, 0.6 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as pale-yellow oil (32.4 mg, 0.11 mmol, 55% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 10H), 5.81 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 5.02 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.95 (dd, *J* = 10.2, 1.8 Hz, 1H), 3.87 (d, *J* = 13.5 Hz, 2H), 3.73 (tt, *J* = 7.7, 5.0 Hz, 1H), 3.40 (d, *J* = 13.4 Hz, 2H), 3.31 (s, 1H), 2.48 – 2.44 (m, 2H), 2.25 – 2.16 (m, 1H), 2.15 – 2.04 (m, 1H), 1.51 – 1.36 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.50, 138.46, 129.0, 128.4, 127.3, 114.6, 66.4, 59.7, 58.4, 33.9, 29.9.; IR: ν_{max} 3449 (br), 3025 (w), 2931 (m), 2832 (w), 1639 (w), 1493 (w), 1451 (w), 1371 (w), 1120 (w), 1075 (w), 1027 (w), 910 (w), 746 (m), 698 (s) cm^{-1}.; HRMS (DART) for $C_{20}H_{26}NO$; $[M+H]^+$: calculated: 296.2009, found: 296.2001.



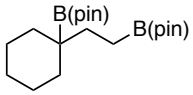
2,2'-(6-(Furan-2-yl)hexane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.100**). The title compound was prepared according to *General Procedure E* with 2,2'-(5-(furan-2-yl)pentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-

dioxaborolane) (1.17 g, 3.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (695.8 mg, 3.2 mmol), copper cyanide (26.9 mg, 0.3 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (1.05 g, 2.6 mmol, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.21 (m, 1H), 6.22 – 6.19 (m, 1H), 5.91 (d, *J* = 3.1 Hz, 1H), 2.55 (t, *J* = 7.6 Hz, 2H), 1.66 – 1.32 (m, 6H), 1.19 (s, 24H), 0.94 (tt, *J* = 8.7, 6.1 Hz, 1H), 0.81 – 0.67 (m, 2H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.5, 140.4, 109.9, 104.4, 82.75, 82.72, 30.7, 28.2, 27.4, 25.3, 24.80, 24.76.; IR: ν_{max} 2975 (w), 2926 (w), 2858 (w), 1459 (w), 1369 (m), 1312 (m), 1213 (w), 1142 (s), 1005 (w), 967 (w), 847 (w), 726 (w) cm^{-1}.; HRMS (DART) for $C_{22}H_{39}B_2O_5$; $[M+H]^+$: calculated: 405.2978, found: 405.2994.

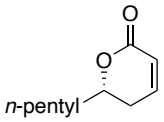


***tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate** (**3.101**). The title compound was prepared according to *General Procedure E* with *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)piperidine-1-carboxylate (902.4 mg, 2.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (486.0 mg, 2.2 mmol), copper cyanide (17.9 mg, 0.2 mmol) . The mixture was allowed to stir at 25 ºC for 12 h instead of 2 h due to the poor solubility of this "ate" complex in THF. By the time the reaction was complete, the reaction solution was clear and homogenous. The white solid mixture was purified by silica gel chromatography to afford the product as white solid (810 mg, 1.7 mmol, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (d, *J* = 13.7, 3.6 Hz, 2H), 2.74 (td, *J* = 13.0, 2.7 Hz, 2H), 1.83 (d, *J* = 13.6 Hz, 2H), 1.44 (s, 9H), 1.43 – 1.34 (m, 1H), 1.23 (d, *J* = 3.1, 1.0 Hz, 24H), 1.06 (td, *J* = 12.8, 4.2 Hz, 2H), 0.74 – 0.67 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 83.2, 82.9, 78.9, 43.2, 33.9, 33.8, 28.5, 24.9, 24.8.; IR: ν_{max} 2974 (w), 2927 (w), 1691 (s), 1420 (w), 1364 (s), 1306 (w), 1227 (w), 1142 (s), 967

(w), 850 (w) cm^{-1}.; HRMS (DART) for $C_{24}H_{46}B_2NO_6$; $[M+H]^+$: calculated: 466.3506, found: 466.3507.



4,4,5,5-Tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxaborolane (**3.102**). The title compound was prepared according to *General Procedure E* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)methyl)-1,3,2-dioxaborolane (1.40 g, 4.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.97 g, 4.4 mmol), copper cyanide (35.8 mg, 0.4 mmol) The white solid mixture was purified by silica gel chromatography to afford the product as white solid (1.36 g, 3.7 mmol, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.85 (d, J = 12.7 Hz, 2H), 1.64 – 1.52 (m, 3H), 1.38 – 1.31 (m, 2H), 1.26 – 1.16 (m, 26H), 1.12 – 1.02 (m, 1H), 0.85 (td, J = 12.5, 3.3 Hz, 2H), 0.73 – 0.65 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 82.8, 82.7, 34.9, 34.5, 26.8, 25.3, 24.9, 24.7.; IR: ν_{max} 2975 (w), 2921 (w), 2848 (w), 1451 (w), 1369 (s), 1300 (m), 1231 (w), 1212 (w), 1142 (s), 968 (w), 883 (w), 847 (w) cm^{-1}.; HRMS (DART) for $C_{20}H_{39}B_2O_4$; $[M+H]^+$: calculated: 365.3029, found: 365.3038.



(*S*)-6-Pentyl-5,6-dihydro-2*H*-pyran-2-one (**3.104**). To a flame dried 2 dram vial charged with stir bar in the glovebox was added (*R*)-2,2'-(heptane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (141 mg, 0.4 mmol, 1.0 equiv.) and anhydrous THF (1.2 mL). The vial was fitted with a septum cap, sealed, and removed from the glovebox. The solution was cooled to –78 °C (dry ice/acetone bath) and *tert*-butyllithium (0.25 mL, 1.58 M, 1.0 equiv.) was added dropwise. The solution was allowed to stir at –78 °C for 5 min, then was allowed to warm to room temperature and stir for 30 min. The vial was returned to the glovebox and copper (I) cyanide (7.2 mg, 80 mmol, 0.2 equiv.), styrene (42 mg, 0.4 mmol, 1.0 equiv.), and ethyl (*Z*)-3-

iodoacrylate (180.8 mg, 0.8 mmol, 2.0 equiv.) were added. The vial was sealed with a polypropylene cap, removed from the glovebox, and heated to 60 °C. The solution was allowed to stir for 20 h. The solution was then allowed to cool to room temperature, diluted with ether, and filtered through a silica gel plug. The filtrate was concentrated to give a brown oil. The residue was oxidized with $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford a mixture of **3.103** and a small amount of **3.104** as colorless oil (53 mg, 0.26 mmol, 64%).

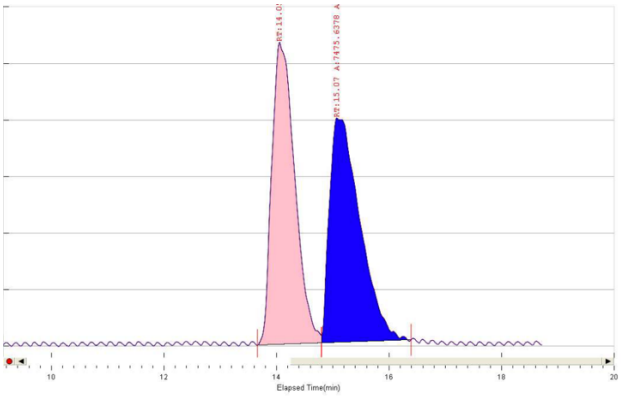
To a flame-dried 2-dram vial charged with stir bar open to air was added the mixture of **3.103** and **3.104** (42.9 mg, 0.2 mmol, 1.0 equiv.) and anhydrous benzene (1.0 mL). *p*-toluenesulfonic acid monohydrate (3.8 mg, 20 mmol, 0.1 equiv.) was added. The vial was sealed with a polypropylene cap, heated to 60 °C, and was allowed to stir for 10 h. The solution was allowed to cool to room temperature, and the reaction was quenched by addition of a saturated aqueous solution of sodium bicarbonate (1.0 mL). The layers were separated, and the aqueous layer was washed with EtOAc (1.0 mL x 2). The combined organic layers were filtered through a plug of silica gel and concentrated to give yellow oil. The mixture was purified by silica gel chromatography (0% to 10% EtOAc in hexanes) to afford the product as colorless oil (28.5 mg, 0.17 mmol, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 – 6.84 (m, 1H), 6.01 (ddd, J = 9.7, 2.4, 1.3 Hz, 1H), 4.41 (ddt, J = 10.3, 7.4, 5.2 Hz, 1H), 2.35 – 2.30 (m, 2H), 1.79 (dddd, J = 13.7, 10.3, 7.4, 5.0 Hz, 1H), 1.63 (ddt, J = 13.8, 10.6, 5.4 Hz, 1H), 1.57 – 1.46 (m, 1H), 1.45 – 1.36 (m, 1H), 1.35 – 1.26 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 145.0, 121.4, 78.0, 34.8, 31.5, 29.4, 24.5, 22.5, 13.9.; IR(neat) ν_{max} 2929 (m), 2858 (w), 2361 (w), 1726 (s), 1379 (w), 1251 (m), 1232 (w). HRMS (DART) $[M+H]^+$ calcd. for $C_{10}H_{16}O_2$: 169.1223, found: 169.1226. $[\alpha]_D^{20}$: +137.63° (c = 1.0, CH_2Cl_2, l = 50 mm)

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described with racemic starting material. Absolute stereochemistry was assigned by analogy.

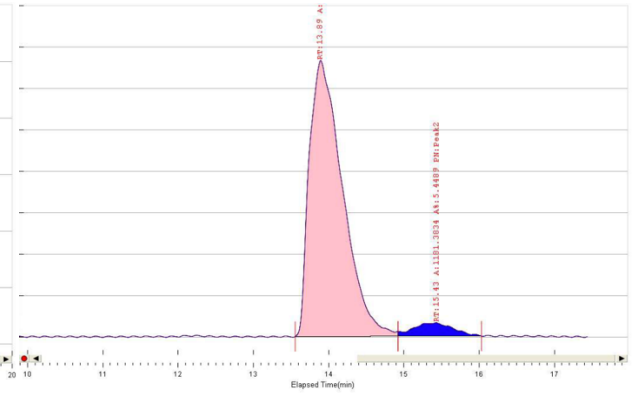
Chiral SFC (OD-H, 1% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 6-pentyl-5,6-dihydro-2H-pyran-2-one.

Racemic Compound

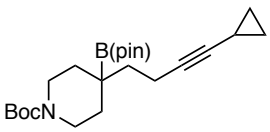


Peak No	% Area	Area	RT (min)
1	50.3255	7573.6078	14.05
2	49.6745	7475.6378	15.07
Total:	100	15049.2456	

Standard Conditions

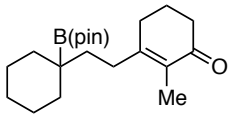


Peak No	% Area	Area	RT (min)
1	94.5511	20499.5886	13.89
2	5.4489	1181.3834	15.43
Total:	100	21680.972	

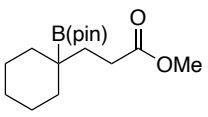


***tert*-Butyl 4-(4-cyclopropylbut-3-yn-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate** (**3.105**). The title compound was prepared according to *General Procedure D* with *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate (93.05 mg, 0.20 mmol), 2-bromoethynylcyclopropane (34.8 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (69.0 mg, 0.17 mmol,

86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 2H), 2.73 (t, *J* = 12.8 Hz, 2H), 2.13 – 2.03 (m, 2H), 1.80 (d, *J* = 12.8 Hz, 3H), 1.59 – 1.46 (m, 2H), 1.44 (s, 9H), 1.23 (s, 12H), 1.22 – 1.12 (m, 1H), 1.09 (td, *J* = 12.8, 4.3 Hz, 2H), 0.73 – 0.62 (m, 2H), 0.59 (ddd, *J* = 7.0, 4.9, 3.8 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 83.4, 82.9, 79.1, 75.9, 39.7, 33.9, 28.4, 24.9, 15.0, 7.9, -0.5.; IR: ν_{max} 2973 (w), 2926 (w), 1691 (s), 1452 (w), 1421 (w), 1388 (w), 1308 (w), 1228 (m), 1168 (m), 1141 (s), 969 (w), 852 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{39}BNO_4$; $[M+H]^+$: calculated: 404.2967, found: 404.2976.

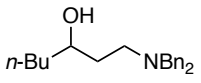


2-Methyl-3-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)cyclohex-2-en-1-one (**3.106**). The title compound was prepared according to *General Procedure D* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxaborolane (72.83 mg, 0.20 mmol), 3-bromo-2-methyl-cyclohex-2-en-1-one (45.4 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol) and styrene (20.83 mg, 0.20 mmol). The yellow oil residue was purified by silica gel chromatography to afford the product as colorless oil (52.2 mg, 0.15 mmol, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 – 2.32 (m, 2H), 2.29 (dt, *J* = 6.1, 3.1 Hz, 2H), 2.18 – 2.12 (m, 2H), 1.92 – 1.86 (m, 4H), 1.73 (s, 3H), 1.66 – 1.57 (m, 3H), 1.36 – 1.31 (m, 2H), 1.31 – 1.27 (m, 2H), 1.25 (s, 12H), 1.17 – 1.09 (m, 1H), 0.93 (td, *J* = 12.5, 3.2 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.5, 159.9, 130.3, 83.1, 38.0, 37.7, 35.1, 31.7, 30.9, 26.6, 25.0, 24.93, 24.92, 22.6, 10.3.; IR: ν_{max} 2974 (w), 2922 (s), 2849 (w), 1663 (s), 1626 (w), 1450 (w), 1378 (m), 1304 (m), 1233 (w), 1139 (s), 968 (w), 858 (w) cm^{-1}.; HRMS (DART) for $C_{21}H_{36}BO_3$; $[M+H]^+$: calculated: 347.2752, found: 347.2752.

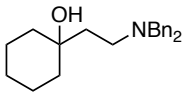


Methyl 3-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)propanoate (**3.107**). The title compound was prepared according

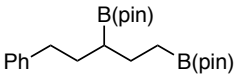
to *General Procedure D* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxaborolane (72.8 mg, 0.20 mmol), methyl chloroformate (22.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), styrene (62.5 mg, 0.6 mmol). The colorless oil mixture was purified by silica gel chromatography to afford the product as colorless oil (42.2 mg, 0.14 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.33 – 2.25 (m, 2H), 1.84 (d, *J* = 12.8 Hz, 2H), 1.67 – 1.56 (m, 4H), 1.32 – 1.20 (m, 16H), 0.97 – 0.86 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 83.1, 51.4, 35.3, 34.8, 30.5, 26.5, 25.1, 24.8. IR(neat) ν_{max} 2977 (m), 2925 (s), 2852 (m), 1741 (s), 1454 (w), 1379 (m), 1371 (m), 1337 (m), 1139 (s), 859 (w). HRMS (DART) $[M+H]^+$ calcd. for $C_{16}H_{30}BO_4$ 297.2237, found 297.2249.



1-(Dibenzylamino)heptan-3-ol (**3.108**). The title compound was prepared according to *General Procedure G* with 2,2'-(heptane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (70.42 mg, 0.20 mmol), (dibenzylamino) 4-(diethylamino)benzoate (93.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), cesium fluoride (91.1 mg, 0.6 mmol). The white solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as colorless oil (42.3 mg, 0.13 mmol, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 8H), 7.30 – 7.24 (m, 2H), 5.62 (s, 1H), 3.84 (d, *J* = 13.1 Hz, 2H), 3.64 – 3.53 (m, 1H), 3.31 (d, *J* = 13.2 Hz, 2H), 2.74 (ddd, *J* = 13.5, 10.3, 3.6 Hz, 1H), 2.59 (ddd, *J* = 13.0, 5.2, 3.6 Hz, 1H), 1.76 – 1.66 (m, 1H), 1.61 – 1.52 (m, 1H), 1.44 – 1.23 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.0, 129.3, 128.4, 127.3, 73.2, 58.5, 52.6, 37.0, 32.2, 27.8, 22.8, 14.1.; IR: ν_{max} 3323 (br), 3060 (w), 2927 (m), 2854 (w), 1493 (w), 1451 (m), 1365 (w), 1074 (w), 1027 (w), 746 (s), 698 (s) cm^{-1}.; HRMS (DART) for $C_{21}H_{30}NO$; $[M+H]^+$: calculated: 312.2322, found: 312.2322.

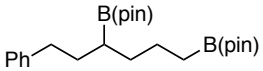


1-(2-(Dibenzylamino)ethyl)cyclohexan-1-ol (**3.109**). The title compound was prepared according to *General Procedure G* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxaborolane (72.83 mg, 0.20 mmol), (dibenzylamino) 4-(diethylamino)benzoate (93.2 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), cesium fluoride (91.1 mg, 0.6 mmol). The yellow solid mixture was oxidized according to $NaOH/H_2O_2$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (49.3 mg, 0.15 mmol, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 8H), 7.30 – 7.22 (m, 2H), 5.96 (s, 1H), 3.55 (s, 4H), 2.72 – 2.64 (m, 2H), 1.68 – 1.62 (m, 2H), 1.61 – 1.42 (m, 3H), 1.32 – 1.12 (m, 5H), 1.11 – 1.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9, 129.6, 128.4, 127.3, 71.8, 58.5, 49.1, 37.6, 35.8, 26.0, 22.1.; IR: ν_{max} 3300 (br), 3025 (w), 2925 (s), 2851 (w), 1494 (w), 1450 (m), 1373 (w), 1252 (w), 1163 (w), 1110 (w), 1075 (w), 970 (w), 890 (w), 749 (m), 698 (s) cm^{-1}.; HRMS (DART) for $C_{22}H_{30}NO$; $[M+H]^+$: calculated: 324.2322, found: 324.2319.

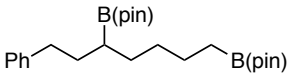


2,2'-(5-Phenylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.110**). The title compound was prepared according to *General Procedure E* with 2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.93 g, 5.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.2g, 5.25 mmol), copper cyanide (44.8 mg, 0.5 mmol) The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (1.86 g, 4.7 mmol, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 7.19 – 7.10 (m, 3H), 2.65 – 2.52 (m, 2H), 1.76 – 1.48 (m, 4H), 1.27 – 1.19 (m, 24H), 1.06 – 0.98 (m, 1H), 0.86 – 0.71 (m, 2H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.2, 128.4, 128.1, 125.4, 82.85, 82.79, 35.5, 33.2, 25.2, 24.9, 24.82, 24.79.; IR: ν_{max} 2975 (w), 2925 (w), 2856 (w), 1453 (w), 1370 (m), 1313 (m), 1270 (w), 1213 (w), 1142 (s),

967 (w), 847 (w), 748 (w), 699 (w) cm^{-1}.; HRMS (DART) for $C_{23}H_{39}B_2O_4$; $[M+H]^+$: calculated: 401.3029, found: 401.3038.

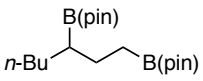


2,2'-(6-Phenylhexane-1,4-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.111). The title compound was prepared according to *General Procedure E* with 2,2'-(5-phenylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (0.78 g, 2.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (448.0 mg, 2.0 mmol), copper cyanide (17.6 mg, 0.20 mmol). The white solid mixture was purified by silica gel chromatography to afford the product as white solid (0.73 g, 1.8 mmol, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.20 – 7.13 (m, 3H), 2.66 – 2.51 (m, 2H), 1.78 – 1.34 (m, 6H), 1.28 – 1.22 (m, 24H), 1.08 – 1.00 (m, 1H), 0.80 – 0.73 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 128.4, 128.2, 125.5, 82.84, 82.78, 35.6, 33.9, 33.3, 24.9, 24.81, 24.79, 23.6.; IR: ν_{max} 2975 (w), 2924 (w), 2857 (w), 1454 (w), 1370 (m), 1315 (m), 1237 (w), 1213 (w), 1143 (s), 967 (w), 847 (w), 747 (w), 699 (w) cm^{-1}.; HRMS (DART) for $C_{24}H_{41}B_2O_4$; $[M+H]^+$: calculated: 415.3186, found: 415.3195.

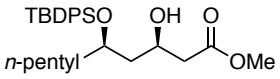


2,2'-(7-Phenylheptane-1,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.112). The title compound was prepared according to *General Procedure E* with 2,2'-(6-phenylhexane-1,4-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (82.84 g, 0.2 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (46.4 mg, 0.21 mmol), copper cyanide (1.8 mg, 0.02 mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (81.3 mg, 0.19 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.20 – 7.15 (m, 3H), 2.65 – 2.53 (m, 2H), 1.77 – 1.52 (m, 2H), 1.49 – 1.28 (m, 6H), 1.28 – 1.20 (m, 24H), 1.07 – 1.00 (m, 1H), 0.77 (t, J = 7.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 128.4, 128.2, 125.5, 82.85, 82.78, 35.7,

33.5, 32.0, 31.0, 24.9, 24.8, 24.3.; IR: ν_{max} 2975 (w), 2923 (w), 2855 (w), 1454 (w), 1370 (m), 1314 (m), 1213 (w), 1143 (s), 967 (w), 846 (w), 698 (w) cm^{-1}.; HRMS (DART) for $C_{25}H_{43}B_2O_4$; $[M+H]^+$: calculated: 429.3342, found: 429.3351.



2,2'-(Heptane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**3.159**). The title compound was prepared according to *General Procedure E* with 2,2'-(hexane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.01 g, 3.0 mmol), 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (729.0 mg, 3.3 mmol), copper cyanide (26.9 mg, 0.30 mmol) The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (0.98 g, 2.8 mmol, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57 – 1.32 (m, 4H), 1.31 – 1.18 (m, 28H), 0.98 – 0.89 (m, 1H), 0.86 (t, *J* = 7.0 Hz, 3H), 0.81 – 0.70 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.74, 82.69, 31.4, 30.89, 30.85, 25.4, 24.82, 24.79, 23.0, 14.1.; IR: ν_{max} 2975 (w), 2922 (w), 2856 (w), 1465 (w), 1369 (m), 1311 (m), 1214 (w), 1142 (s), 968 (w), 865 (w), 847 (w), 670 (w) cm^{-1}.; HRMS (DART) for $C_{19}H_{39}B_2O_4$; $[M+H]^+$: calculated: 353.3029, found: 353.3035.



Methyl (3*R*,5*R*)-5-((*tert*-butyldiphenylsilyl)oxy)-3-hydroxydecanoate. (**3.116**) The title compound was prepared according to *General Procedure D* with (((2*S*,4*R*)-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nonan-4-yl)oxy)(*tert*-butyl)diphenylsilane (247.3 mg, 0.4 mmol), methyl chloroformate (44.2 mg, 0.47 mmol), copper cyanide (7.0 mg, 0.08 mmol), styrene (122mg, 1.2 mmol). The colorless oil mixture was oxidized according to $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as pale-yellow oil (107 mg, 0.24 mmol, 60% yield). Note: The unoxidized boronic ester product (methyl (3*R*,5*R*)-5-((*tert*-butyldiphenylsilyl)oxy)-3-(4,4,5,5-tetramethyl-1,3,2-

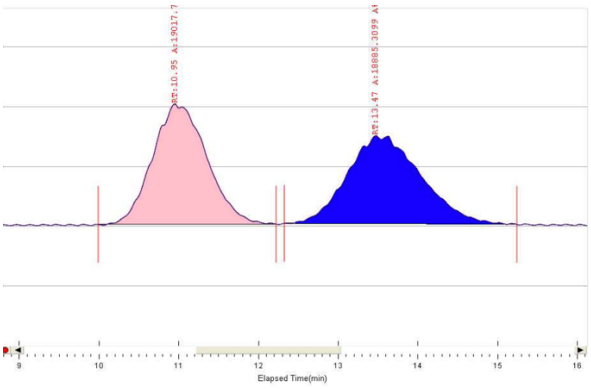
dioxaborolan-2-yl)decanoate), despite being bench stable, is susceptible to oxidation. Purification by silica gel chromatography would oxidize it to alcohol with full conversion. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 4H), 7.47 – 7.36 (m, 6H), 4.27 – 4.15 (m, 1H), 4.01 – 3.90 (m, 1H), 3.69 (s, 3H), 3.17 (s, 1H), 2.42 – 2.31 (m, 2H), 1.74 (dt, *J* = 14.9, 7.6 Hz, 1H), 1.63 (dt, *J* = 14.1, 4.9 Hz, 1H), 1.49 – 1.35 (m, 2H), 1.27 – 1.10 (m, 4H), 1.07 (s, 9H), 1.04 – 0.98 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 135.9, 134.3, 133.9, 129.7, 129.6, 127.6, 127.5, 72.3, 66.3, 51.6, 42.6, 41.4, 36.8, 31.6, 27.0, 24.4, 22.4, 19.3, 13.9.; IR: ν_{max} 3524 (br), 2951 (m), 2855 (m), 1736 (m), 1462 (w), 1263 (w), 1196 (w), 1109 (s), 1053 (w), 821 (w), 702 (s), 611 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{27}H_{41}O_4Si$; $[M+H]^+$: calculated: 457.2769, found: 457.2771. $[\alpha]_D^{20}$: –14.5 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

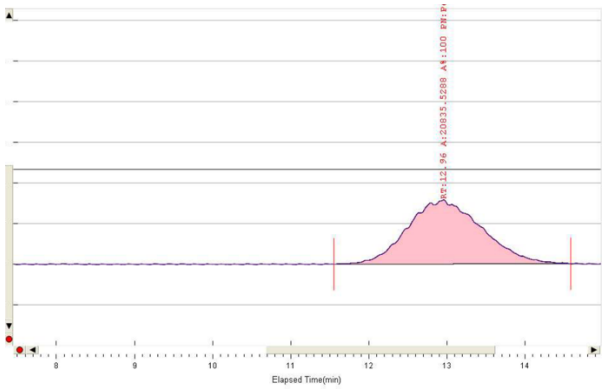
Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 5-((tert-butyldiphenylsilyl)oxy)-3-hydroxydecanoate

Racemic Compound

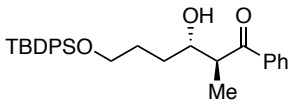


Peak No	% Area	Area	RT (min)
1	50.1747	19017.7485	10.95
2	49.8253	18885.3099	13.47
Total:	100	37903.0584	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	100	20835.5288	12.96
Total:	100	20835.5288	



(2*S*,3*S*)-6-((*tert*-Butyldiphenylsilyl)oxy)-3-hydroxy-2-methyl-1-phenylhexan-1-one (**3.117**). The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)diphenylsilane (118.5 mg, 0.20 mmol, 98:2 er), benzoyl chloride (33.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol). The yellow oil residue was oxidized according to $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (53.7 mg, 0.12 mmol, 58% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.0 Hz, 2H), 7.66 (d, *J* = 6.5 Hz, 4H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.44 – 7.35 (m, 6H), 3.94 – 3.88 (m, 1H), 3.71 (hept, *J* = 5.1, 4.6 Hz, 2H), 3.61 – 3.54 (m, 1H), 3.07 (s, 1H), 1.84 – 1.66 (m, 3H), 1.59 – 1.50 (m, 1H), 1.26 (d, *J* = 7.2 Hz, 3H), 1.04 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.5, 136.8, 135.6, 135.5, 133.8, 133.3, 129.6, 128.7, 128.4, 127.6, 73.7, 63.9, 45.9, 31.3, 28.8, 26.8, 19.2, 15.2.; IR: ν_{max} 3441 (br), 2928 (w), 2855 (w), 1678 (w), 1426 (w), 1286 (w), 1209 (w), 1109 (s), 970 (w), 822 (w), 702 (s), 505 (m) cm^{-1}.; HRMS (DART) for $C_{29}H_{37}O_3Si$; $[M+H]^+$: calculated: 461.2507, found: 461.2514. $[\alpha]_D^{20}$: +16.6 (c = 1.0, $CHCl_3$, *l* = 50 mm).

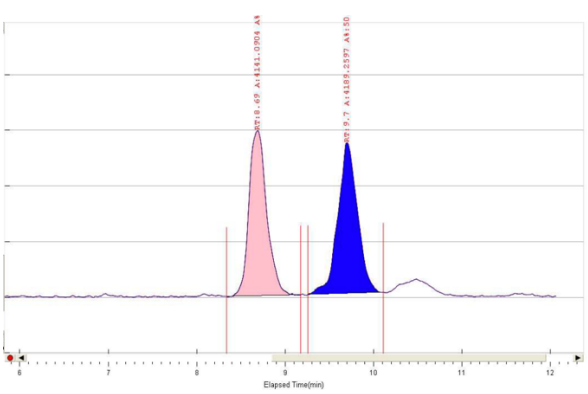
With AdLi activation: The title compound was prepared according to *General Procedure E* with (((4*S*,5*S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)diphenylsilane (118.5 mg, 0.20 mmol, 93:7 er), benzoyl chloride (33.7 mg, 0.24 mmol), copper cyanide (3.6 mg, 0.04 mmol), 1-*tert*-butyl-4-(4-*tert*-butylphenyl)benzene (106.6 mg, 0.4 mmol), lithium (13.9 mg, 2.0 mmol), adamantyl chloride (34.1 mg, 0.2 mmol), styrene (20.8 mg, 0.2 mmol). The yellow solid mixture was oxidized according to $NaBO_3/H_2O$ protocol and was purified by silica gel chromatography to afford the product as yellow oil (40.7 mg, 0.088 mmol, 44% yield).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

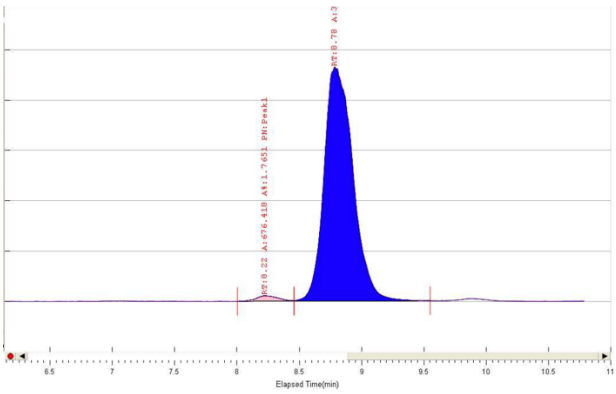
Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 6-((tert-butyldiphenylsilyl)oxy)-3-hydroxy-2-methyl-1-phenylhexan-1-one

Racemic Compound



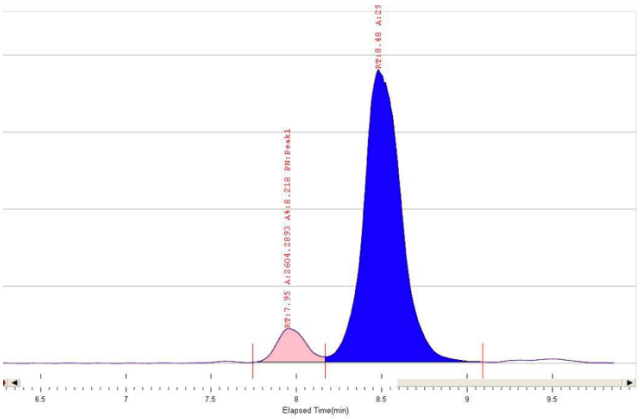
Peak No	% Area	Area	RT (min)
1	49.7109	4141.0904	8.69
2	50.2891	4189.2597	9.7
Total:	100	8330.3501	

Standard Conditions

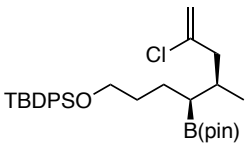


Peak No	% Area	Area	RT (min)
1	1.7651	676.418	8.22
2	98.2349	37644.3293	8.78
Total:	100	38320.7473	

Conditions with AdLi activation (starting material 93:7 er)

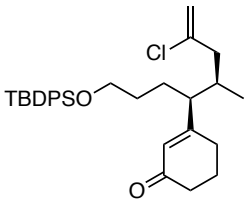


Peak No	% Area	Area	RT (min)
1	8.218	2604.2893	7.95
2	91.782	29085.7148	8.48
Total:	100	31690.0041	



***tert*-Butyl(((4*S*,5*R*)-7-chloro-5-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)oxy)diphenylsilane (3.120)**. The title compound was prepared according to *General Procedure D* with (((4*S*,5*S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)oxy)(*tert*-butyl)diphenylsilane (2.26 g, 3.81 mmol, 98:2 er), 2,3-dichloroprop-1-ene (507.9 mg, 4.6 mmol), copper cyanide (68.3 mg, 0.8

mmol). The colorless oil residue was purified by silica gel chromatography to afford the product as colorless oil (1.83 g, 3.4 mmol, 89% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 – 7.65 (m, 4H), 7.44 – 7.34 (m, 6H), 5.16 – 5.13 (m, 1H), 5.08 (s, 1H), 3.66 (t, *J* = 6.3 Hz, 2H), 2.43 (dd, *J* = 13.9, 4.3 Hz, 1H), 2.12 (dd, *J* = 13.9, 9.8 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.66 – 1.59 (m, 1H), 1.56 – 1.43 (m, 3H), 1.23 (d, *J* = 2.6 Hz, 12H), 1.05 (s, 9H), 0.99 – 0.95 (m, 1H), 0.90 (d, *J* = 6.7 Hz, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.5, 135.6, 134.19, 134.17, 129.4, 127.5, 113.0, 82.9, 64.2, 45.1, 32.6, 31.9, 26.9, 24.9, 24.8, 24.1, 19.2, 18.1.; IR: ν_{max} 2928 (w), 2856 (w), 1632 (w), 1426 (w), 1378 (w), 1317 (w), 1142 (m), 1109 (s), 971 (w), 877 (w), 822 (w), 739 (w), 701 (s), 613 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{31}H_{47}BO_3SiCl$; $[M+H]^+$: calculated: 541.3071, found: 541.3085. $[\alpha]_D^{20}$: +2.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).



3-((4*S*,5*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)-7-chloro-5-methyloct-7-en-4-yl)cyclohex-2-en-1-one (**3.121**). The title compound was prepared according to *General Procedure D* with *tert*-butyl(((4*S*,5*R*)-7-chloro-5-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)oxy)diphenylsilane (1.81 g, 3.35 mmol), 3-iodocyclohex-2-en-1-one (891.3 mg, 4.0 mmol), copper cyanide (59.9 mg, 0.67 mmol) with styrene (348 mg, 3.35 mmol). The yellow oil mixture was purified by silica gel chromatography to afford the product as yellow gel (0.98 g, 1.9 mmol, 58% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 4H), 7.45 – 7.40 (m, 2H), 7.39 – 7.35 (m, 4H), 5.81 (s, 1H), 5.18 (s, 1H), 5.09 (s, 1H), 3.67 – 3.58 (m, 2H), 2.36 (t, *J* = 7.0 Hz, 2H), 2.31 – 2.26 (m, 1H), 2.25 – 2.15 (m, 2H), 2.00 – 1.88 (m, 5H), 1.74 – 1.65 (m, 1H), 1.47 – 1.37 (m, 2H), 1.35 – 1.28 (m, 1H), 1.04 (s, 9H), 0.89 (d, *J* = 5.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.4, 167.5, 141.4, 135.5, 133.9, 133.8, 129.6, 128.2, 127.6, 114.0, 63.5, 52.8, 45.1, 37.8, 32.9, 30.7, 26.9, 25.3, 22.8, 19.2, 16.0.; IR: ν_{max} 2928 (m), 2855 (w), 1670 (s), 1633 (w), 1458 (w), 1426 (w), 1240 (w), 1109 (s),

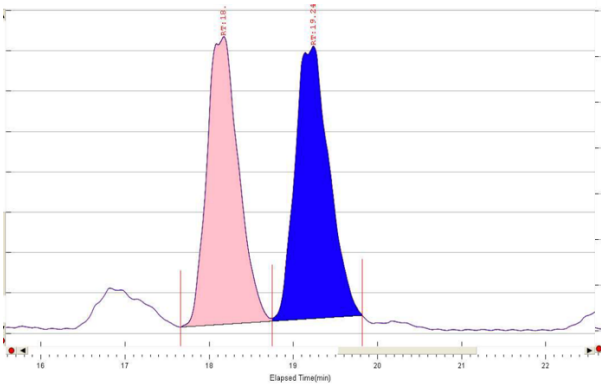
888 (w), 823 (w), 740 (w), 702 (s), 613 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{31}H_{42}O_2SiCl$; $[M+H]^+$: calculated: 509.2637, found: 509.2639. $[\alpha]_D^{20}$: –1.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described. Absolute stereochemistry was assigned by analogy.

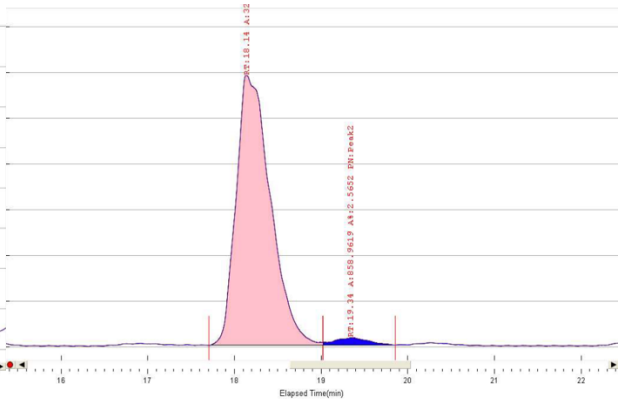
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 3-(1-((tert-butyldiphenylsilyl)oxy)-7-chloro-5-methyloct-7-en-4-yl)cyclohex-2-en-1-one.

Racemic Compound

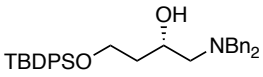


Peak No	% Area	Area	RT (min)
1	49.4349	18759.3972	18.17
2	50.5651	19188.3082	19.24
Total:	100	37947.7054	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.4348	32626.2796	18.14
2	2.5652	858.9619	19.34
Total:	100	33485.2415	



(*S*)-4-((*tert*-Butyldiphenylsilyl)oxy)-1-(dibenzylamino)butan-2-ol (**3.123**). To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (6.7 mg, 0.25 mol%), (*R,R*)-L (7.2 mg, 0.30 mol%), and $B_2(pin)_2$ (761.8 mg, 3.0 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added by syringe, and the mixture was heated to 80 ºC, and was

allwed to stir for 30 min. The mixture was then allowed cooled to room temperature and charged with (but-3-en-1-yloxy)(*tert*-butyl)diphenylsilane (1.06 g, 3.45 mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC for 24 h. The mixture was allowed to cool to room temperature, and was diluted to 0.4 M. It was confirmed by TLC that $B_2(pin)_2$ was fully consumed.

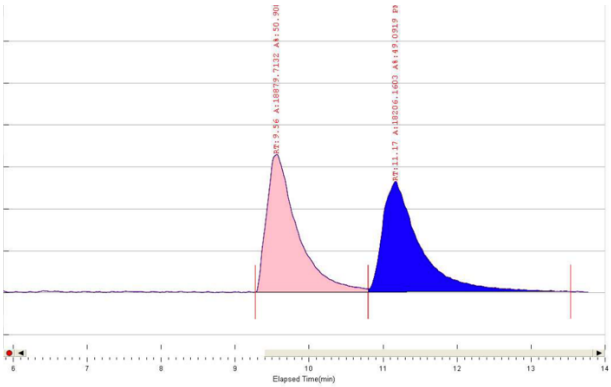
The solution was cooled to –78 ºC, *tert*-butyllithium (3.0 mmol, solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to warm to room temperature and to stir for 25 min. The reaction flask was transferred into glovebox again, The reaction vial was transferred into glovebox again, cesium fluoride 1.37 g, 9.0 mmol), copper cyanide (53.7 mg, 0.6 mmol) and (dibenzylamino)4-(diethylamino)benzoate (1.4 g, 3.6 mmol) were added. The flask was sealed with septum cap and removed from glovebox. The mixture was heated to 60 ºC (oil bath) and allowed to stir for 12 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug with diethyl ether as eluent. Solvents were removed under reduced pressure. The yellow solid residue was oxidized with $NaOH/H_2O_2$ and purified by silica gel chromatography to furnish the title compound as a colorless gel (1.0 g, 1.9 mmol, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.66 (m, 4H), 7.48 – 7.40 (m, 6H), 7.38 – 7.33 (m, 8H), 7.32 – 7.26 (m, 2H), 4.08 – 4.00 (m, 1H), 3.91 – 3.77 (m, 4H), 3.52 (d, J = 13.5 Hz, 2H), 2.55 (d, J = 7.0 Hz, 2H), 1.75 – 1.60 (m, 2H), 1.10 (s, 9H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.8, 135.60, 135.58, 133.7, 133.6, 129.7, 129.1, 128.4, 127.7, 127.2, 65.7, 61.5, 59.8, 58.6, 37.3, 26.9, 19.2.; IR: ν_{max} 3469 (br), 3025 (w), 2928 (w), 2854 (w), 1426 (w), 1370 (w), 1110 (m), 822 (w), 737 (m), 700 (s), 614 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{34}H_{42}NO_2Si$; $[M+H]^+$: calculated: 524.2979, found: 524.2982. $[\alpha]_D^{20}$: +26.2 (c = 1.0, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Procedure D* with (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-butyl)diphenylsilane. Absolute stereochemistry was assigned by analogy.

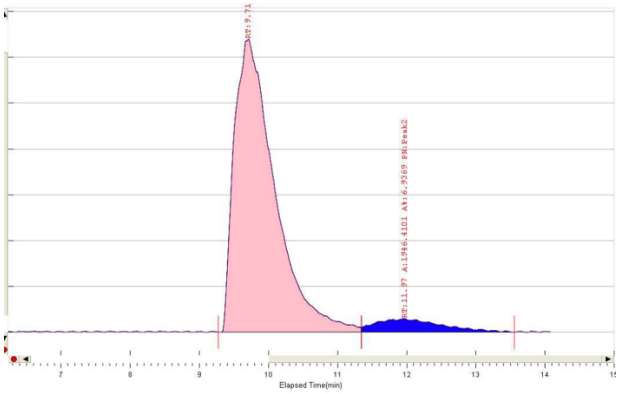
Chiral SFC (AD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of 4-((tert-butyldiphenylsilyl)oxy)-1-(dibenzylamino)butan-2-ol.

Racemic Compound

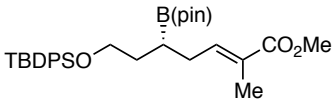


Peak No	% Area	Area	RT (min)
1	50.9081	18879.7132	9.56
2	49.0919	18206.1603	11.17
Total:	100	37085.8735	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.0631	26112.1803	9.71
2	6.9369	1946.4101	11.97
Total:	100	28058.5904	



Methyl (*R*,*E*)-7-((*tert*-butyldiphenylsilyl)oxy)-2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enoate (**3.124**). To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (6.7 mg, 0.25 mol%), (*R,R*)-L (7.2 mg, 0.30 mol%), and $B_2(pin)_2$ (761.8 mg, 3.0 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added by syringe, and the mixture was heated to 80 ºC, and was allwed to stir for 30 min. The mixture was then cooled to room temperature and charged with (but-3-en-1-yloxy)(*tert*-butyl)diphenylsilane (1.06 g, 3.45

mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC for 24 h. The reaction was allowed to cool to room temperature, and was diluted to 0.4 M. It was confirmed by TLC that $B_2(pin)_2$ was fully consumed.

The solution was cooled to –78 ºC, *tert*-butyllithium (3.0 mmol, solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to warm to room temperature and to stir for 25 min. The reaction flask was transferred into glovebox again, styrene (312.5 mg, 3.0 mmol), copper cyanide (53.7 mg, 0.6 mmol) and methyl (*E*)-3-bromo-2-methylacrylate (644.4 mg, 3.6 mmol) were added. The flask was sealed with septum cap and removed from glovebox. The mixture was heated to 60 ºC and was allowed to stir for 12 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug. Solvents were removed under reduced pressure. The yellow oil residue was purified by silica gel chromatography to furnish the title compound as yellow oil (1.07 g, 2.0 mmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.65 (m, 4H), 7.43 – 7.35 (m, 6H), 6.83 – 6.72 (m, 1H), 3.72 (s, 3H), 3.71 – 3.62 (m, 2H), 2.26 (t, *J* = 8.4 Hz, 2H), 1.81 (s, 3H), 1.80 – 1.72 (m, 1H), 1.71 – 1.64 (m, 1H), 1.36 – 1.28 (m, 1H), 1.17 (d, *J* = 3.6 Hz, 12H), 1.05 (s, 10H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 142.5, 135.5, 134.0, 129.5, 129.4, 127.6, 127.5, 83.2, 63.2, 51.6, 33.6, 30.0, 26.9, 24.7, 24.6, 19.2, 12.5.; IR: ν_{max} 2928 (w), 2855 (w), 1713 (m), 1461 (w), 1378 (w), 1259 (w), 1142 (m), 1108 (s), 822 (w), 702 (s), 613 (w), 505 (m) cm^{-1}.; HRMS (DART) for $C_{31}H_{46}BO_5Si$; $[M+H]^+$: calculated: 537.3202, found: 537.3227. $[\alpha]_D^{20}$: –2.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

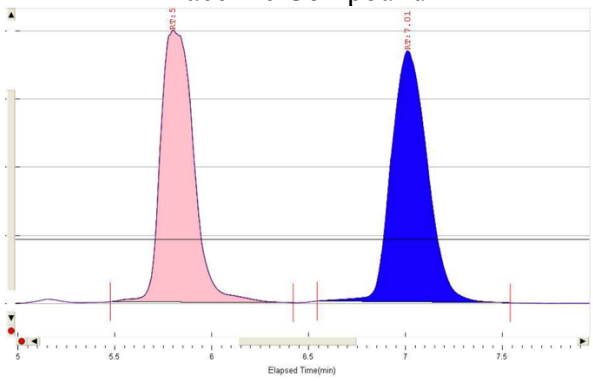
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Procedure A* with (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-

butyl)diphenylsilane. Material was oxidized according to the $NaBO_3/H_2O$ protocol and subjected to SFC without purification. Absolute stereochemistry was assigned by analogy.

Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 ºC, 210–270 nm) – analysis of methyl (E)-7-((tert-butyldiphenylsilyl)oxy)-5-hydroxy-2-methylhept-2-enoate.

Racemic Compound



Peak No	% Area	Area	RT (min)
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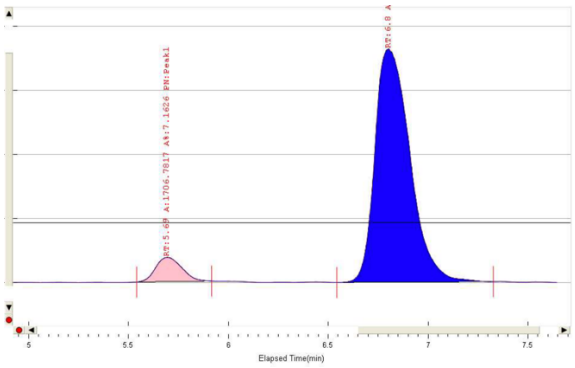
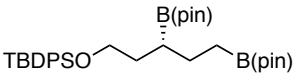
2	50.2148	23854.5169	7.01
Total:	100	47504.9945	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.1626	1706.7817	5.69
2	92.8374	22122.3273	6.8
Total:	100	23829.109	

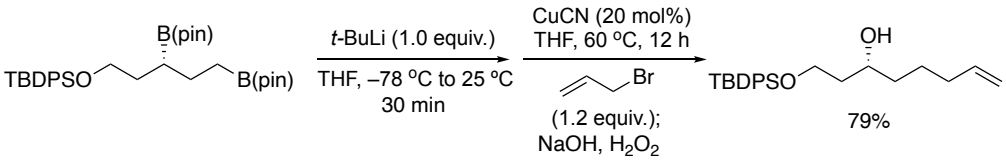


(*R*)-((3,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)(*tert*-butyl)diphenylsilane (**3.125**). To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (6.7 mg, 0.25 mol%), (*R,R*)-L (7.2 mg, 0.30 mol%), and $B_2(pin)_2$ (761.8 mg, 3.0 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.0 M) was added by syringe, and the mixture was heated to 80 ºC, and was allowed to stir for 30 min. The mixture was then cooled to room temperature and charged with (but-3-en-1-yloxy)(*tert*-butyl)diphenylsilane (1.06 g, 3.45 mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC for 24 h. The reaction was allowed to cool to room temperature, and was diluted to 0.4 M. It was confirmed by TLC that $B_2(pin)_2$ was fully consumed.

The solution was cooled to –78 ºC, *tert*-butyllithium (3.15 mmol, solution in pentane) was added dropwise by a syringe. The mixture was allowed to stir at –78 ºC for 5 min and then allowed to warm to room temperature and allowed to stir for 25 min. The reaction flask was transferred into glovebox again, copper cyanide (26.9 mg, 0.3 mmol) and 2-(bromomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (795.2 mg, 3.6 mmol) were added. The flask was sealed with septum cap and removed from glovebox. The mixture was allowed to stir at 25 ºC for 2 h. The mixture was diluted with diethyl ether and was passed through a silica gel plug with diethyl ether as eluent. Solvents were removed under reduced pressure. The colorless oil residue was purified by silica gel chromatography to furnish the title compound as colorless oil (1.52 g, 2.6 mmol, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.63 (m, 4H), 7.42 – 7.33 (m, 6H), 3.74 – 3.59 (m, 2H), 1.76 – 1.68 (m, 2H), 1.57 – 1.46 (m, 2H), 1.23 (s, 12H), 1.15 (d, *J* = 3.7 Hz, 12H), 1.04 (s, 9H, overlapped with m, 1H), 0.78 (td, *J* = 9.8, 6.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 134.3, 129.3, 127.5, 82.8, 82.8, 63.8, 34.0, 26.9, 25.4, 24.8, 24.8, 24.7, 19.2. IR: ν_{max} 2974 (w), 2927 (w), 2855 (w), 1470 (w), 1369 (s), 1313 (s), 1214 (w), 1142 (s), 1108 (s), 967 (w), 823 (w), 738 (w), 701 (s), 504 (m) cm^{-1}.; HRMS (DART) for $C_{33}H_{53}B_2O_5Si$; $[M+H]^+$: calculated: 579.3843, found: 579.3864. $[\alpha]_D^{20}$: –0.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

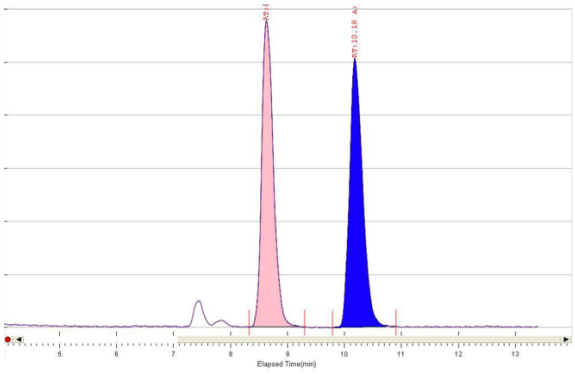
Analysis of Stereochemistry:

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to *General Procedure B* with (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)(*tert*-butyl)diphenylsilane. Material was derived with method described below. Absolute stereochemistry was assigned by analogy.



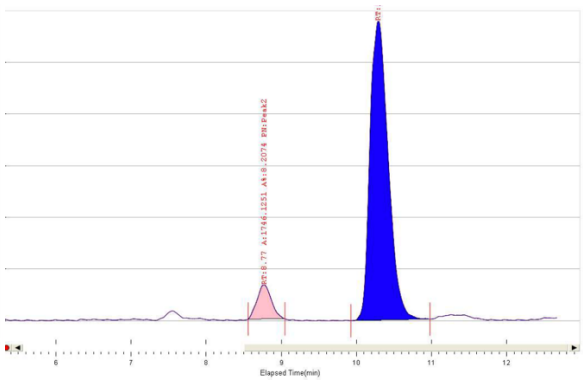
Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210–270 nm) – analysis of 1-((tert-butyldiphenylsilyl)oxy)oct-7-en-3-ol.

Racemic Compound



Peak No	% Area	Area	RT (min)
1	50.3205	16407.7712	8.63
2	49.6795	16198.791	10.18
Total:	100	32606.5622	

Standard Conditions



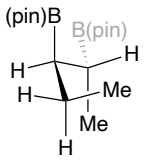
Peak No	% Area	Area	RT (min)
1	8.2074	1746.1251	8.77
2	91.7926	19528.8961	10.29
Total:	100	21275.0212	

3.6.4 Computational Methods and Data

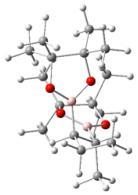
3.6.4.1 Computational methods

All calculations were conducted with density functional theory (DFT) implemented in Gaussian 16 suite of program.[79] All molecular structures were optimized by B3LYP[80] functional with 6-31G* basis sets. Frequency calculations were performed at the same level of theory to characterize the stationary points (no imaginary frequencies for local minima). Molecular structure visualizations were obtained with Gaussview.[81]

3.6.4.2 Cartesian coordinates of computed structures



3.129-1



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H	3.13620400	4.16322700	0.73764700
C	1.80679800	3.11016400	-0.63222400
H	1.36199500	4.03268200	-1.02668500
H	2.63439300	2.86082400	-1.30877500
C	0.76796100	1.95996400	-0.68670500
B	1.46729300	0.58874700	-0.35828200
O	1.24151900	-0.13334300	0.79202400

[79] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16 Rev. C.01*, Wallingford, CT, 2016.

[80] Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch. M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.

[81] GaussView, Version 6, Dennington, R.; Keith, T. A.; Millam, J. M. Semichem Inc., Shawnee Mission, KS, 2016.

O	2.40072600	0.00193500	-1.17975000
C	2.64089200	-1.34283000	-0.67009500
C	1.72016900	-2.27441100	-1.46327900
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H	1.85875600	-3.32083700	-1.17451400
H	0.67150400	-2.00135600	-1.31743800
C	4.10138000	-1.70494700	-0.90665000
H	4.33127900	-2.68224400	-0.46861400
H	4.29741000	-1.76070700	-1.98195700
H	4.77546600	-0.96189000	-0.47522600
C	2.22899500	-1.20489700	0.83847100
C	1.58316700	-2.44497300	1.44297100
H	2.28525000	-3.28561400	1.43693500
H	1.30060700	-2.24517900	2.48129600
H	0.68562600	-2.73929000	0.89556700
C	3.36788000	-0.70943100	1.73399500
H	2.95763400	-0.43757400	2.71108700
H	4.12832700	-1.48248700	1.88082300
H	3.84937900	0.17586400	1.30764500
H	0.43074300	1.89134000	-1.73235300
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H	-2.13644200	3.59593200	0.47759800
H	-0.61437300	4.37618800	0.02922700
H	-1.54974800	3.50218300	-1.19100500
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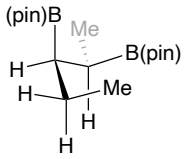
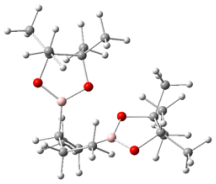
C	-3.05298800	-0.55648600	0.73200000
C	-2.65129600	-0.78478300	-0.76818600
C	-2.35437200	-1.51964400	1.69583200
H	-2.73593300	-2.54020900	1.59374300
H	-1.27441600	-1.52527500	1.52491000
H	-2.53388300	-1.18555400	2.72221100
C	-4.55236000	-0.52591000	0.99852200
H	-5.00953600	-1.48627600	0.73684700
H	-4.73340200	-0.34296500	2.06227800
H	-5.04657200	0.26311400	0.42771600
C	-3.65993300	-0.19972700	-1.76042500
H	-3.22036200	-0.21321900	-2.76222400
H	-4.58631900	-0.78168700	-1.78147600
H	-3.90458000	0.83690200	-1.50904000
C	-2.32570400	-2.22743800	-1.13284300
H	-3.20547600	-2.86562700	-0.99709100
H	-2.02368500	-2.28366500	-2.18331700

H	-1.51242700	-2.62428300	-0.52204800



3.129-2



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H	-0.28721300	3.15698500	-2.85858200
C	-0.78457700	3.10069800	-0.74572500
H	-0.20517100	4.00777100	-0.52056500
H	-1.81110200	3.43855400	-0.94388700
C	-0.82049000	2.21909900	0.53247700
B	-1.61877500	0.88914700	0.27388700
O	-1.06145100	-0.23038300	-0.29845800
O	-2.94886400	0.72142900	0.57501900
C	-3.37203300	-0.54507900	-0.01640300
C	-4.40514300	-1.19209400	0.89649500
H	-5.30790400	-0.57420100	0.92938800
H	-4.68436100	-2.18130200	0.51778800
H	-4.02880500	-1.30182800	1.91562900
C	-3.99291900	-0.20948200	-1.37487400
H	-4.39615800	-1.10257700	-1.86177900
H	-4.81084800	0.50163500	-1.22585100
H	-3.25828500	0.25027700	-2.04326300
C	-2.01401700	-1.32117000	-0.13372600
C	-1.62327500	-2.05342900	1.15303000
H	-2.23976800	-2.94406400	1.30884300
H	-0.57560900	-2.35578800	1.08442200
H	-1.72589600	-1.40053000	2.02521600
C	-1.90604100	-2.25388600	-1.33256200
H	-0.92875900	-2.74684900	-1.33148300
H	-2.67668700	-3.03065800	-1.28472000
H	-2.01338300	-1.71160700	-2.27432800
H	-1.41014500	2.79955700	1.25801400
C	0.56835700	1.97888200	1.20909500
H	1.13053900	2.92240500	1.11711000
C	0.36499700	1.69438000	2.71052700
H	-0.19377700	0.76243700	2.86063800
H	1.32043600	1.58223700	3.23497500
H	-0.19685900	2.50282000	3.19486900
O	1.64403900	-0.38966500	1.14723300

O	2.29983000	1.04107400	-0.51171800
B	1.48521800	0.85329000	0.58204500
C	2.75780400	-1.04643900	0.48205800
C	2.86101000	-0.25472000	-0.87190500
C	3.97756600	-0.85948600	1.38900700
H	3.75130300	-1.27270800	2.37658200
H	4.85745400	-1.37499600	0.99213100
H	4.21940400	0.20080600	1.51098700
C	2.43482200	-2.52850900	0.33294000
H	2.34945500	-2.98792200	1.32276900
H	1.49311000	-2.68192700	-0.19764700
H	3.23146100	-3.04442100	-0.21402300
C	4.27973800	-0.04229600	-1.38620200
H	4.76040900	-1.00333000	-1.59908500
H	4.25067500	0.53534600	-2.31547800
H	4.89345400	0.50216700	-0.66537200
C	1.97259300	-0.82939400	-1.97872200
H	1.96767800	-0.13546900	-2.82490900
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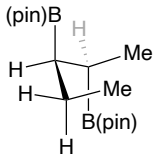

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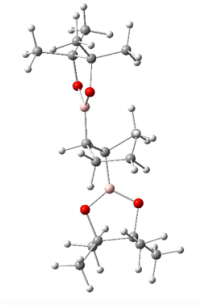

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C	-0.10978300	2.45397500	-0.16226500
H	-0.87031100	2.27907500	0.60478500
H	0.86048500	2.56452400	0.33327000
H	-0.34973400	3.40623200	-0.65010400
C	-0.07676800	1.31725600	-1.18913300
H	-1.07984400	1.20014000	-1.62147300
H	0.57542500	1.61336200	-2.02056100
C	0.40845200	-0.05664000	-0.67047100
B	1.95691300	-0.09800500	-0.38696400
O	2.59460600	-1.20216500	0.13037600
O	2.82022400	0.94044800	-0.64485700
C	4.10973100	0.59629800	-0.05721300
C	5.21573200	1.13728000	-0.95467300
H	5.17905200	2.23106900	-0.96545600
H	6.19894800	0.83411700	-0.57907500

H	5.10981100	0.78244700	-1.98192600
C	4.15743800	1.27667700	1.31392800
H	5.12176300	1.11871700	1.80633600
H	4.00991600	2.35255300	1.18050600
H	3.36503400	0.90381200	1.96997300
C	4.02985400	-0.97016500	0.02766500
C	4.49727900	-1.66956500	-1.25180300
H	5.58174700	-1.59384000	-1.37695600
H	4.22949400	-2.72886000	-1.19511800
H	4.01361500	-1.24245800	-2.13570800
C	4.71033900	-1.58332600	1.24530500
H	4.58385700	-2.67034400	1.22898000
H	5.78379300	-1.36597300	1.23711100
H	4.28434700	-1.20454500	2.17672100
H	0.25444200	-0.75724800	-1.50733000
C	-0.40846400	-0.66179100	0.52801900
H	-0.22506200	-1.74587400	0.48630200
C	0.04376300	-0.19171800	1.92393600
H	-0.54400400	-0.68631900	2.70577800
H	1.09743700	-0.43534700	2.09841100
H	-0.08124300	0.88541500	2.06001600
O	-2.60900200	-0.92816700	-0.82190700
O	-2.77931100	0.21621300	1.15473400
C	-4.03724400	-0.73687500	-0.60180000
C	-4.06232700	0.39761900	0.48622800
C	-4.05160500	1.80953500	-0.10631300
H	-5.00861300	2.05166600	-0.57842800
H	-3.87111800	2.52952900	0.69741100
H	-3.25690800	1.92429600	-0.84899300
C	-4.68981500	-0.36743800	-1.92836500
H	-4.61060100	-1.20823000	-2.62451800
H	-5.75244400	-0.14317200	-1.78584900
H	-4.20823400	0.49979800	-2.38500800
C	-5.17340100	0.27032700	1.52145600
H	-5.09944400	1.08972000	2.24326900
H	-6.15566900	0.32875600	1.04052600
H	-5.10807300	-0.67260800	2.06823400
C	-4.58414000	-2.07414900	-0.09458100
H	-5.66897200	-2.03759900	0.04395400
H	-4.35585500	-2.85192100	-0.82935200
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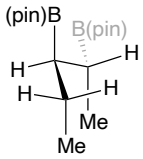
B	-1.95069700	-0.45973700	0.29143700



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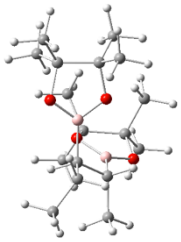

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C	-1.85558700	3.10086100	-0.19822800
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B	-1.49988000	0.57910300	0.05842200
O	-1.22128500	-0.34905500	-0.91985200
O	-2.47968900	0.15784700	0.92688500
C	-2.70940200	-1.25765000	0.66668700
C	-1.84082800	-2.02633200	1.66654900
H	-2.12317100	-1.72996300	2.68129200
H	-1.97839600	-3.10787000	1.57248000
H	-0.78271200	-1.78928600	1.52595100
C	-4.18401100	-1.56638800	0.89144500
H	-4.40207200	-2.60909000	0.63619400
H	-4.43495100	-1.41583300	1.94608300
H	-4.82693000	-0.91838300	0.29196200
C	-2.22085300	-1.40565500	-0.81778700
C	-1.56433600	-2.73996600	-1.14733200
H	-2.27944100	-3.56048500	-1.02457900
H	-1.22491500	-2.73751200	-2.18780700
H	-0.70158300	-2.93372000	-0.50705100
C	-3.30549300	-1.07772500	-1.84743600
H	-2.84432100	-1.00302400	-2.83676300
H	-4.07437900	-1.85548500	-1.88223300
H	-3.78688900	-0.12104600	-1.62228100
H	-0.53648000	2.12797900	1.20826200
C	0.47361900	2.04118300	-0.70057400
H	0.18680600	1.89336100	-1.75283700
C	1.23400000	3.38260000	-0.62083300
H	2.15315600	3.34784400	-1.21683300
H	0.62889800	4.21544100	-0.99533300
H	1.51593800	3.61599700	0.41381800
B	1.45317300	0.86568500	-0.33375300
O	2.52009000	0.50054100	-1.12022600
O	1.36665500	0.12626500	0.82426300
C	3.05518100	-0.74085600	-0.57447900
C	2.57779300	-0.67987200	0.91998600
C	2.40522100	-1.87669600	-1.36953000
H	2.78128400	-2.85530500	-1.05581400

H	1.31797800	-1.86038600	-1.25464100
H	2.63628700	-1.74287900	-2.43064200
C	4.56640100	-0.75140700	-0.76466000
H	5.00604100	-1.63879900	-0.29661000
H	4.80353600	-0.77833700	-1.83278400
H	5.03243400	0.13732400	-0.33387600
C	3.53873200	0.08806000	1.83163800
H	3.05001000	0.26303400	2.79472400
H	4.46033800	-0.47457300	2.00884800
H	3.80021400	1.05925400	1.40028800
C	2.22688100	-2.02801400	1.53612000
H	3.10851200	-2.67735500	1.56639400
H	1.87446100	-1.88489100	2.56234000
H	1.44178400	-2.53642200	0.97307800
H	-1.72653100	3.38733100	-1.25092100
C	-1.77602500	4.34389100	0.69523400
H	-1.97063700	4.07656500	1.74096100
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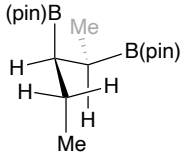
H	-2.51851300	5.09481400	0.39897500



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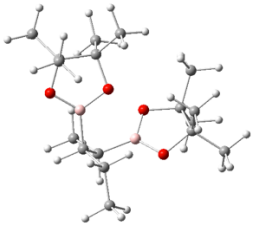

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C	-0.66605700	2.15185500	0.34792000
B	-1.59665800	0.90383300	0.13118200
O	-1.15350300	-0.23173500	-0.50860000
O	-2.90516600	0.80765000	0.53417400
C	-3.45106400	-0.41608800	-0.04917600
C	-4.44237200	-1.02621500	0.93302500
H	-5.30284800	-0.36032800	1.05139300
H	-4.80680700	-1.98959100	0.56047300
H	-3.99176700	-1.18007300	1.91563800
C	-4.16110400	-0.00571100	-1.34172200
H	-4.65861200	-0.85890300	-1.81284600
H	-4.91798400	0.74864400	-1.10743700
H	-3.45725800	0.42746100	-2.05910000
C	-2.15719600	-1.26763900	-0.29945600
C	-1.71701500	-2.06986200	0.92785600
H	-2.37445900	-2.92786600	1.09871100
H	-0.69782700	-2.43020400	0.77061300

H	-1.71450800	-1.44800600	1.82774400
C	-2.19974900	-2.16116900	-1.53208700
H	-1.25555300	-2.70748400	-1.62393900
H	-3.00879200	-2.89466100	-1.44833000
H	-2.34746400	-1.57971500	-2.44457600
H	-1.24441800	2.93297100	0.86488500
C	0.53550300	1.78331000	1.27825000
H	1.15343200	2.68747200	1.38214700
C	0.03516500	1.40042500	2.68156400
H	-0.55905600	0.47921800	2.65851100
H	0.86924600	1.22611100	3.37027600
H	-0.59666000	2.19065000	3.10634700
O	1.58259500	-0.60258300	1.15757700
O	2.30374600	0.90145100	-0.41109200
B	1.47230900	0.67365000	0.66174500
C	2.68965400	-1.25239800	0.47044600
C	2.83630400	-0.38740100	-0.83427300
C	3.89876700	-1.15289200	1.40481100
H	3.64494200	-1.61572600	2.36328300
H	4.77056100	-1.66946400	0.99178200
H	4.16778200	-0.10871500	1.59167900
C	2.32652400	-2.71290100	0.23111700
H	2.20802900	-3.22510900	1.19116000
H	1.39204200	-2.80763400	-0.32543200
H	3.11919800	-3.21996800	-0.32954500
C	4.26877200	-0.18780700	-1.31459300
H	4.72316800	-1.14845800	-1.58045800
H	4.27129400	0.44679200	-2.20638800
H	4.88750200	0.29195100	-0.55321200
C	1.95017000	-0.87059300	-1.98630900
H	1.98414500	-0.12859700	-2.79036800
H	2.30178300	-1.82627600	-2.38771300
H	0.91140900	-0.97359500	-1.66322300
H	0.26042800	1.94044700	-1.60869700
C	0.64156000	3.96127800	-0.96685200
H	0.79606100	4.38399600	-1.96657300
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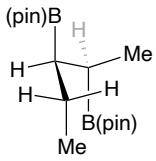

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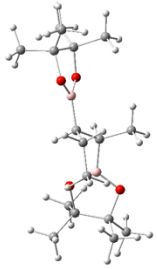

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B	-2.01079400	0.25507800	0.17667700
O	-2.42388100	-1.01684700	-0.14477700
O	-3.06063300	1.09669100	0.46141600
C	-4.26613000	0.28072000	0.54737400
C	-4.48023700	-0.03041000	2.03121500
H	-4.54709500	0.91075200	2.58503600
H	-5.40486600	-0.59272000	2.19323700
H	-3.64491500	-0.60788000	2.43912000
C	-5.43964500	1.08341300	-0.00030700
H	-6.34797100	0.47162800	-0.02075900
H	-5.62741600	1.94805400	0.64396700
H	-5.24108300	1.44765000	-1.01044600
C	-3.87280800	-0.98143400	-0.29971600
C	-4.45143700	-2.29919200	0.20008100
H	-5.54594800	-2.27631100	0.16620000
H	-4.10910300	-3.11815200	-0.44027300
H	-4.13821600	-2.51320200	1.22408100
C	-4.14623100	-0.81311700	-1.79708900
H	-3.66246100	-1.63085300	-2.33951800
H	-5.21820000	-0.83987300	-2.01522200
H	-3.73787700	0.13150300	-2.16951300
H	-0.15958200	0.48465000	1.25630500
C	0.37833400	-0.18048300	-0.72189600
H	0.05001500	-1.21966100	-0.55451400
C	0.13550700	0.12748000	-2.20757700
H	0.68362700	-0.57189400	-2.84756000
H	-0.92978000	0.04919700	-2.45910600
H	0.46715400	1.13703000	-2.47425700
O	2.33094500	-0.28530400	0.97996400
O	2.93524900	-0.22676400	-1.22859500
C	3.74669200	-0.62669800	0.95434600
C	4.18460400	-0.15269000	-0.47999800
C	4.64412200	1.30683400	-0.52497900
H	5.61843400	1.43219600	-0.04278700
H	4.73429800	1.61745400	-1.57028100
H	3.92521000	1.96767500	-0.03394100
C	4.44178900	0.08807200	2.10689300
H	4.06025100	-0.29284500	3.05938600
H	5.52182500	-0.09176000	2.07712800
H	4.26633900	1.16545100	2.07581200
C	5.21251100	-1.04585400	-1.16527000
H	5.44183800	-0.64715000	-2.15843800
H	6.14297200	-1.07550400	-0.58817700

H	4.84321500	-2.06652600	-1.28478300
C	3.83282400	-2.14416500	1.14281400
H	4.87159400	-2.48482000	1.19132300
H	3.33667000	-2.41360300	2.07997700
H	3.33023100	-2.67351300	0.32741400
B	1.89949300	-0.20335700	-0.32487300
H	-0.78327800	2.48852600	-0.96756700
C	1.06877500	2.75496200	0.10103000
H	1.53924700	2.46881700	1.04850000
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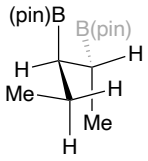

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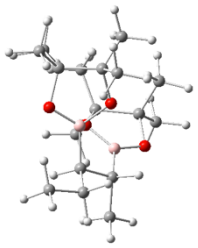

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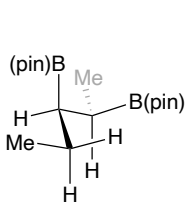
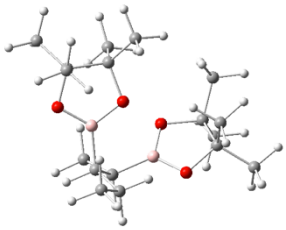
C	-0.86660100	2.04106600	0.22658800
B	-1.45482600	0.58546000	0.11964200
O	-1.22063900	-0.23572700	-0.96138500
O	-2.30936900	0.02405100	1.03797200
C	-2.50755100	-1.36992100	0.65928300
C	-1.52582800	-2.18780800	1.50126300
H	-1.73378100	-2.00953600	2.56067300
H	-1.62255100	-3.26037500	1.30679900
H	-0.49689100	-1.87961700	1.30223200
C	-3.94382000	-1.76441500	0.97946300
H	-4.14477300	-2.78819300	0.64559400
H	-4.10407200	-1.72272800	2.06128000
H	-4.66207800	-1.09442100	0.50219100
C	-2.15144700	-1.35388100	-0.87034900
C	-1.46306200	-2.61266900	-1.38178800
H	-2.12472900	-3.47968300	-1.28127800
H	-1.21647000	-2.49379400	-2.44145200
H	-0.53933800	-2.81704500	-0.83704100
C	-3.34197800	-0.99833000	-1.76550900
H	-2.97911900	-0.81282000	-2.78085400
H	-4.07384200	-1.81090400	-1.80278800
H	-3.84450900	-0.09231300	-1.41269000
H	-0.66433800	2.24992900	1.28805200
C	0.46528200	2.17091600	-0.55785300
H	0.23145200	2.14666900	-1.63273200

C	1.20824200	3.49613700	-0.26919000
H	2.13772300	3.55959200	-0.84600500
H	0.60307400	4.37374300	-0.52129600
H	1.47053000	3.57080100	0.79408100
B	1.46119100	0.98695900	-0.27752200
O	2.53767700	0.70880700	-1.08606500
O	1.40241000	0.17191500	0.83149700
C	3.12897200	-0.53503100	-0.60856500
C	2.65813600	-0.57060000	0.88740600
C	2.52405400	-1.65561200	-1.45845900
H	2.94685400	-2.63125000	-1.20005100
H	1.43826900	-1.69542700	-1.33526500
H	2.73849200	-1.45522600	-2.51245800
C	4.63814300	-0.47074600	-0.80439100
H	5.11727300	-1.36275100	-0.38632600
H	4.86988100	-0.43067500	-1.87328300
H	5.06880100	0.41275900	-0.32843000
C	3.57978900	0.20972300	1.82889700
H	3.08937100	0.31192000	2.80150600
H	4.53356500	-0.30631900	1.97470100
H	3.78202000	1.21299800	1.44129900
C	2.39317000	-1.96306800	1.44346900
H	3.31846100	-2.54900600	1.45928300
H	2.02165100	-1.88676800	2.46999600
H	1.65243800	-2.50282600	0.85087200
H	-2.21191700	2.81440200	-1.29260700
H	-1.48195500	4.06226500	-0.30040300
C	-3.18531500	3.12368000	0.61566600
H	-3.89194000	3.87073800	0.23607000
H	-3.69863800	2.15774600	0.65536000
H	-2.92801400	3.39887000	1.64597900



3.129-8

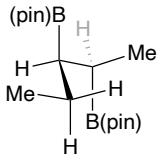


0 1

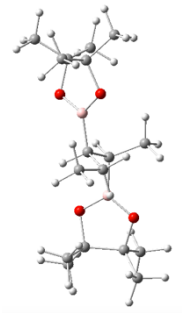
C	-0.40843700	2.85040500	-0.71666400
C	-0.75063500	2.08926700	0.58202600
B	-1.56793200	0.78141300	0.27138900
O	-1.09044000	-0.21248100	-0.55188200
O	-2.80630900	0.49338500	0.78791500
C	-3.29456300	-0.70647800	0.11390200
C	-4.09077500	-1.53603300	1.11324100

H	-4.98886100	-0.98769500	1.41427800
H	-4.40619500	-2.48292900	0.66201900
H	-3.50708500	-1.75370800	2.00997700
C	-4.20029500	-0.23304700	-1.02592100
H	-4.66388400	-1.07787700	-1.54437400
H	-4.99396100	0.39573100	-0.61180000
H	-3.64238900	0.35967800	-1.75712500
C	-1.96269300	-1.37018300	-0.38687400
C	-1.31111700	-2.27371500	0.66250800
H	-1.88138300	-3.19780500	0.79786700
H	-0.30083800	-2.52962100	0.33748500
H	-1.23005900	-1.76706200	1.62835600
C	-2.06381700	-2.09502300	-1.72260900
H	-1.08668200	-2.50943200	-1.99040700
H	-2.77760800	-2.92319700	-1.65843100
H	-2.37963700	-1.42190500	-2.52237800
H	-1.38732700	2.74786800	1.19261500
C	0.51748000	1.76376800	1.43626300
H	1.05588400	2.71691200	1.56561800
C	0.12324600	1.24755200	2.83031100
H	-0.39923800	0.28563700	2.76738900
H	1.00308100	1.09437600	3.46493900
H	-0.54501300	1.95299400	3.33987000
O	1.73607100	-0.51686500	1.08477800
O	2.32116900	1.17530100	-0.34250600
B	1.52338600	0.78779700	0.70953300
C	2.89518000	-1.00351800	0.34791500
C	2.95012900	-0.02488900	-0.87941600
C	4.09574400	-0.86480800	1.28872000
H	3.89348000	-1.42477800	2.20674100
H	5.00967900	-1.26168400	0.83631800
H	4.26623700	0.18196000	1.55863400
C	2.67433900	-2.46754000	-0.01105700
H	2.59877300	-3.06422800	0.90342400
H	1.75868800	-2.60709000	-0.58845400
H	3.51652200	-2.84969200	-0.59810400
C	4.35369000	0.33122600	-1.35407800
H	4.88111700	-0.56391400	-1.70125300
H	4.29100800	1.03360200	-2.19114900
H	4.94240100	0.79737900	-0.56113900
C	2.08703800	-0.48184700	-2.05935000
H	2.04257800	0.32673900	-2.79583800
H	2.51154300	-1.36524400	-2.54665600
H	1.06668200	-0.70221700	-1.73568700
H	0.22664600	2.22495900	-1.35229200
H	0.19299500	3.73488600	-0.46245000

C	-1.64939000	3.28769200	-1.50014100
H	-1.37583800	3.87204300	-2.38601800
H	-2.23059700	2.42278200	-1.84401900
H	-2.31266200	3.90477600	-0.88166900



3.129-9

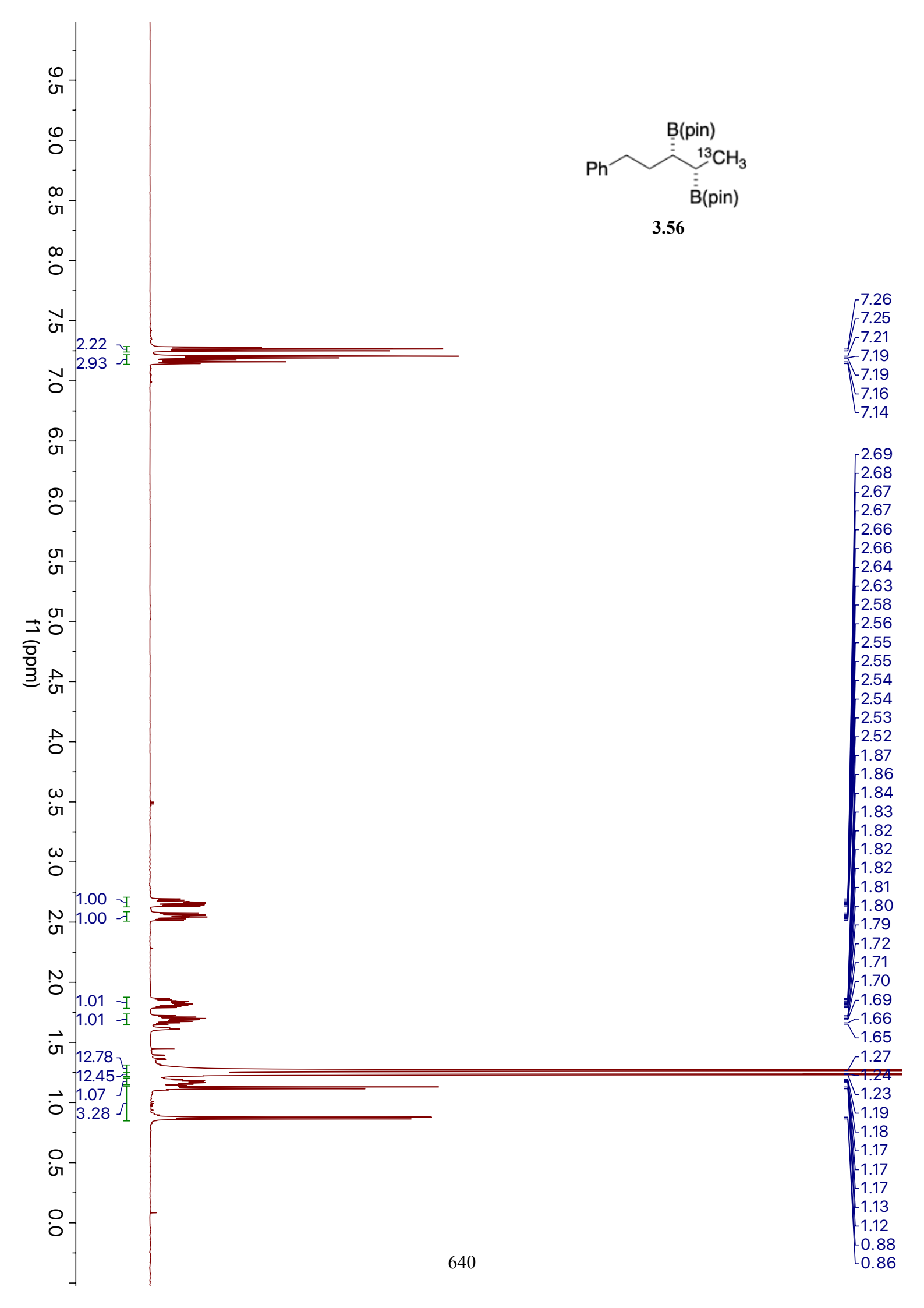


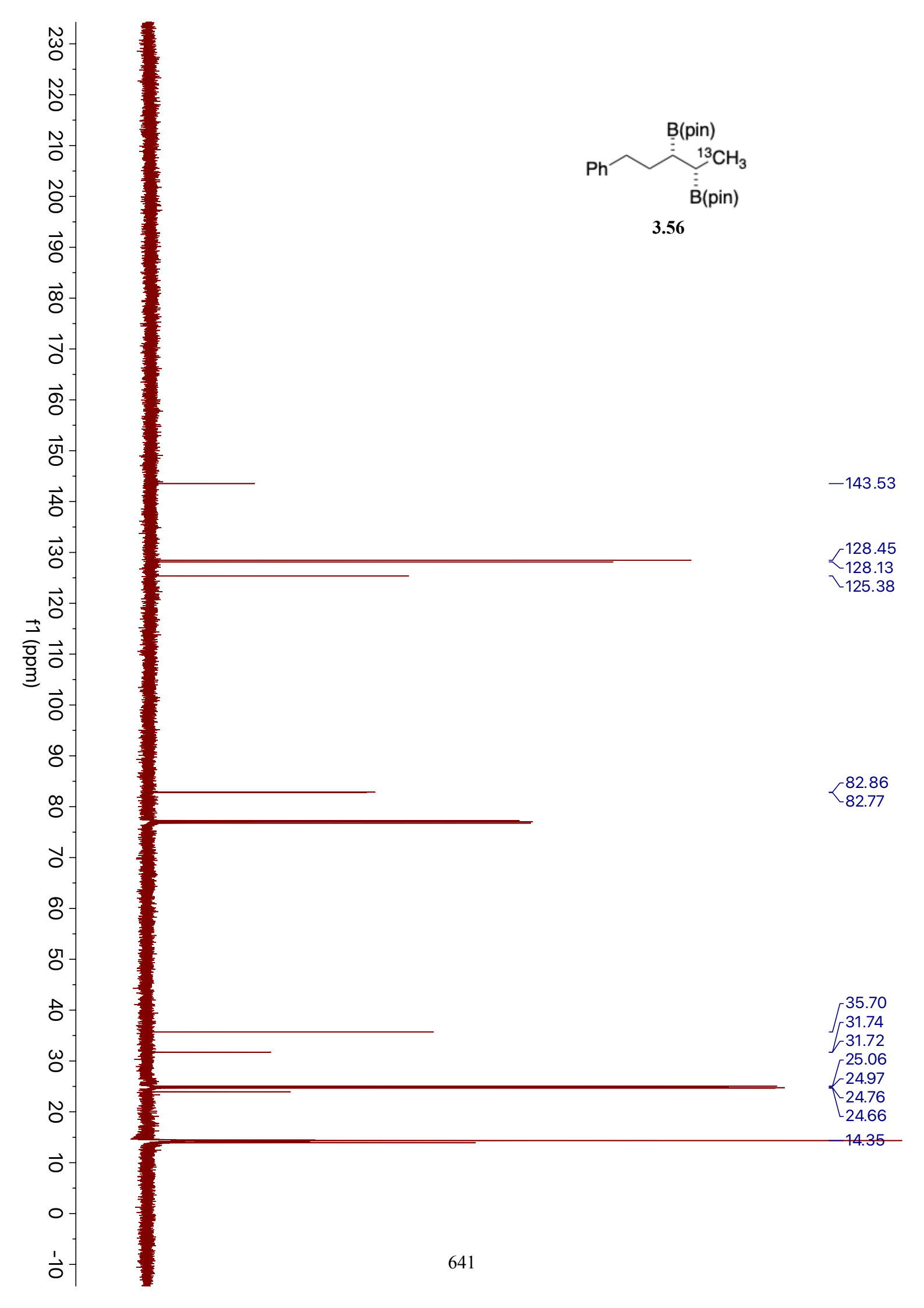
0 1

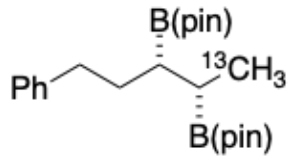
C	-0.00326900	1.46765100	-1.21969300
C	-0.33860000	0.49665600	-0.07219600
B	-1.88134400	0.22196500	0.06414900
O	-2.46345500	-0.21994200	1.22897900
O	-2.78183200	0.34814300	-0.96700200
C	-4.03920200	-0.24618300	-0.52699300
C	-5.19084800	0.56189600	-1.11172900
H	-5.18781600	0.47089400	-2.20240400
H	-6.15112100	0.18644100	-0.74212300
H	-5.10868200	1.62076800	-0.85769600
C	-4.06256600	-1.67681800	-1.07242300
H	-5.00854300	-2.17696100	-0.84353100
H	-3.94344100	-1.64406800	-2.15949100
H	-3.24414400	-2.27266300	-0.65728900
C	-3.90872300	-0.18182500	1.03683000
C	-4.39262100	1.14486500	1.62901000
H	-5.48228500	1.23176000	1.58027100
H	-4.08865600	1.19685700	2.67868500
H	-3.95082400	1.99718400	1.10359900
C	-4.53320600	-1.35375000	1.78374400
H	-4.37589900	-1.23010600	2.85977100
H	-5.61237500	-1.39526900	1.60099400
H	-4.09086700	-2.30538700	1.48180500
H	-0.00131800	0.95502800	0.86940400
C	0.42118200	-0.87661900	-0.18785700
H	0.09098000	-1.48702400	0.66541100
C	0.10049800	-1.63559200	-1.48561200
H	0.55506900	-2.63270600	-1.47651400
H	-0.97895600	-1.75919900	-1.63119100
H	0.49357000	-1.10964600	-2.36155200
O	2.50696800	-0.26293900	1.21583700
O	2.87301200	-0.58261100	-1.02295500

C	3.84681600	0.25126100	0.95819100
C	4.19301600	-0.40213000	-0.42780100
C	5.03038000	0.46715100	-1.35768600
H	6.00455000	0.68558600	-0.90715100
H	5.20320700	-0.06162500	-2.30024700
H	4.53019600	1.41132900	-1.58323400
C	3.72368200	1.77660600	0.89458000
H	3.29166100	2.13645000	1.83311900
H	4.69955900	2.25241200	0.75833900
H	3.06674400	2.08883200	0.07680900
C	4.81020900	-1.79738400	-0.30194000
H	4.83320400	-2.26572300	-1.29044200
H	5.83399600	-1.74938300	0.08133700
H	4.21799100	-2.43322000	0.36329800
C	4.75791100	-0.15806500	2.10874900
H	5.78953700	0.15328100	1.91267400
H	4.42628400	0.32843300	3.03135500
H	4.74343900	-1.23818200	2.26861900
B	1.95681500	-0.59781400	0.00043900
H	-0.42955300	1.09092300	-2.15704600
H	1.08429700	1.50404000	-1.37320200
C	-0.52699000	2.88326400	-0.96354800
H	-0.27199200	3.56049400	-1.78672600
H	-1.61809100	2.88329800	-0.85708100
H	-0.10063200	3.29927200	-0.04212500

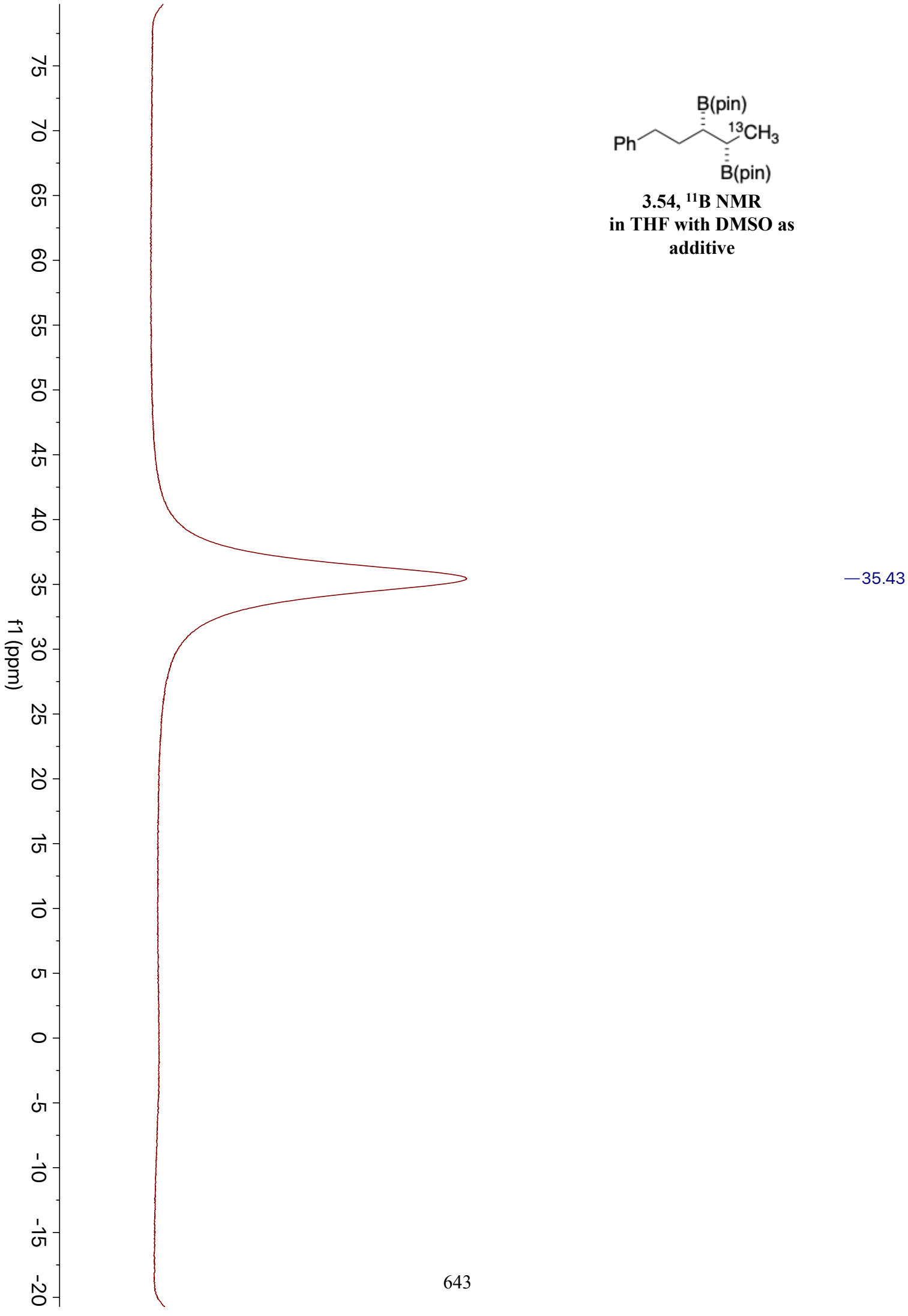
3.7 Spectra


B(pin)
Ph
13CH3
B(pin)
3.56
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.22
2.93
1.00
1.00
1.01
1.01
12.78
12.45
1.07
3.28
7.26
7.25
7.21
7.19
7.19
7.16
7.14
2.69
2.68
2.67
2.67
2.66
2.66
2.64
2.63
2.58
2.56
2.55
2.55
2.54
2.54
2.53
2.52
1.87
1.86
1.84
1.83
1.82
1.82
1.82
1.81
1.80
1.79
1.72
1.71
1.70
1.69
1.66
1.65
1.27
1.24
1.23
1.19
1.18
1.17
1.17
1.17
1.13
1.12
0.88
0.86

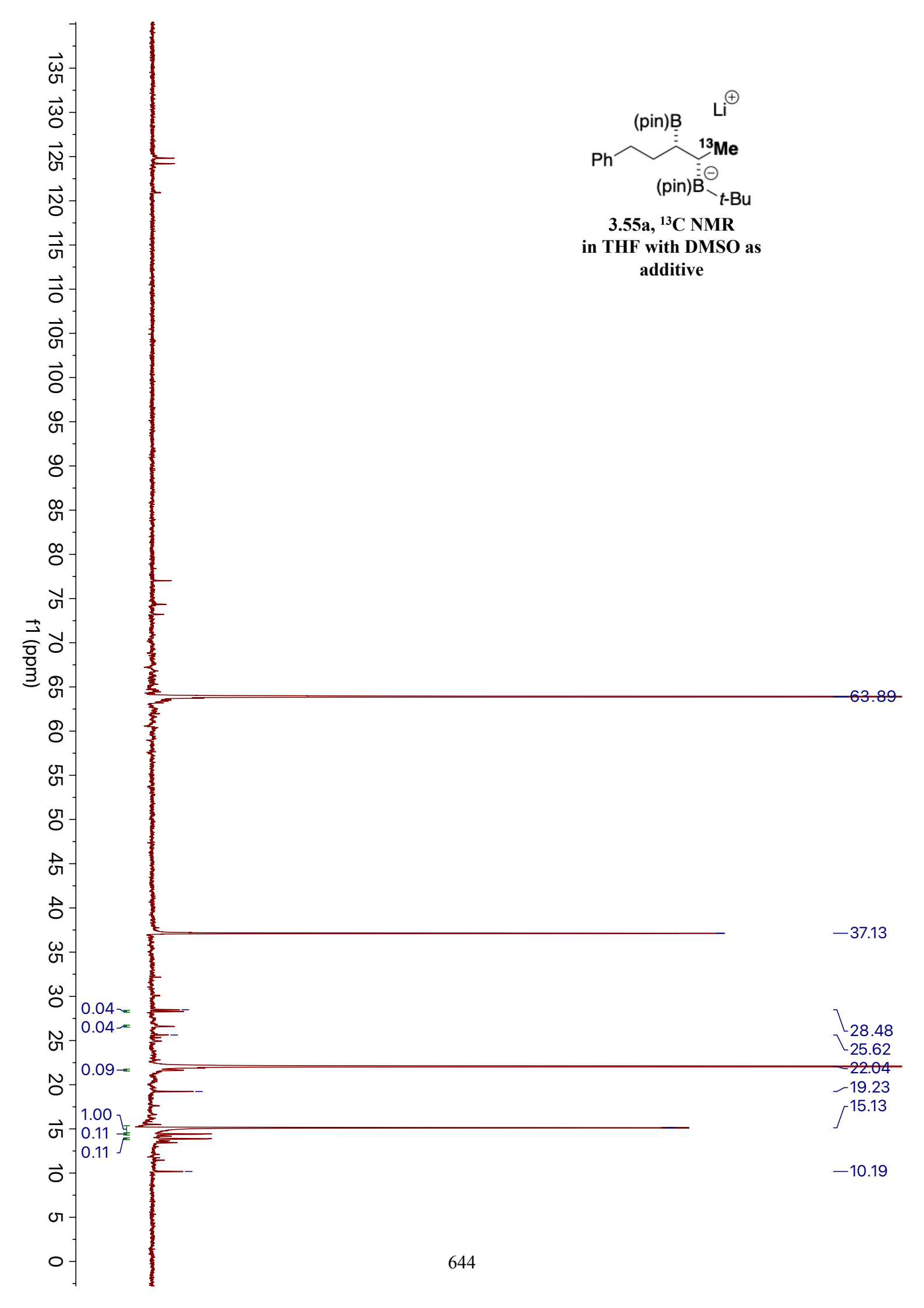

B(pin)
Ph
13CH3
B(pin)
3.56
143.53
128.45
128.13
125.38
82.86
82.77
35.70
31.74
31.72
25.06
24.97
24.76
24.66
14.35
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

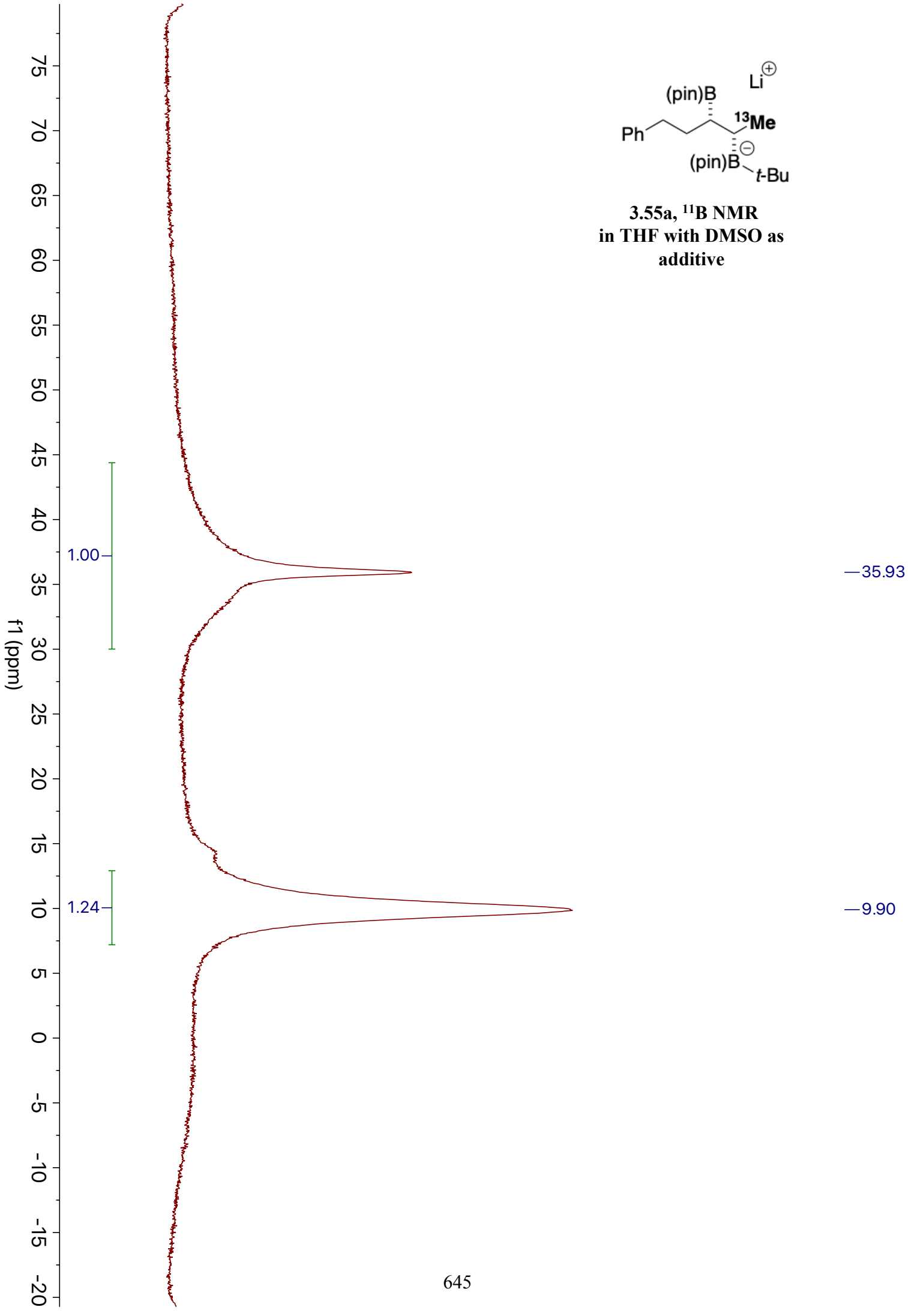


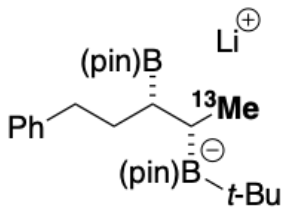
3.54, ^{13}C NMR in THF with DMSO as additive



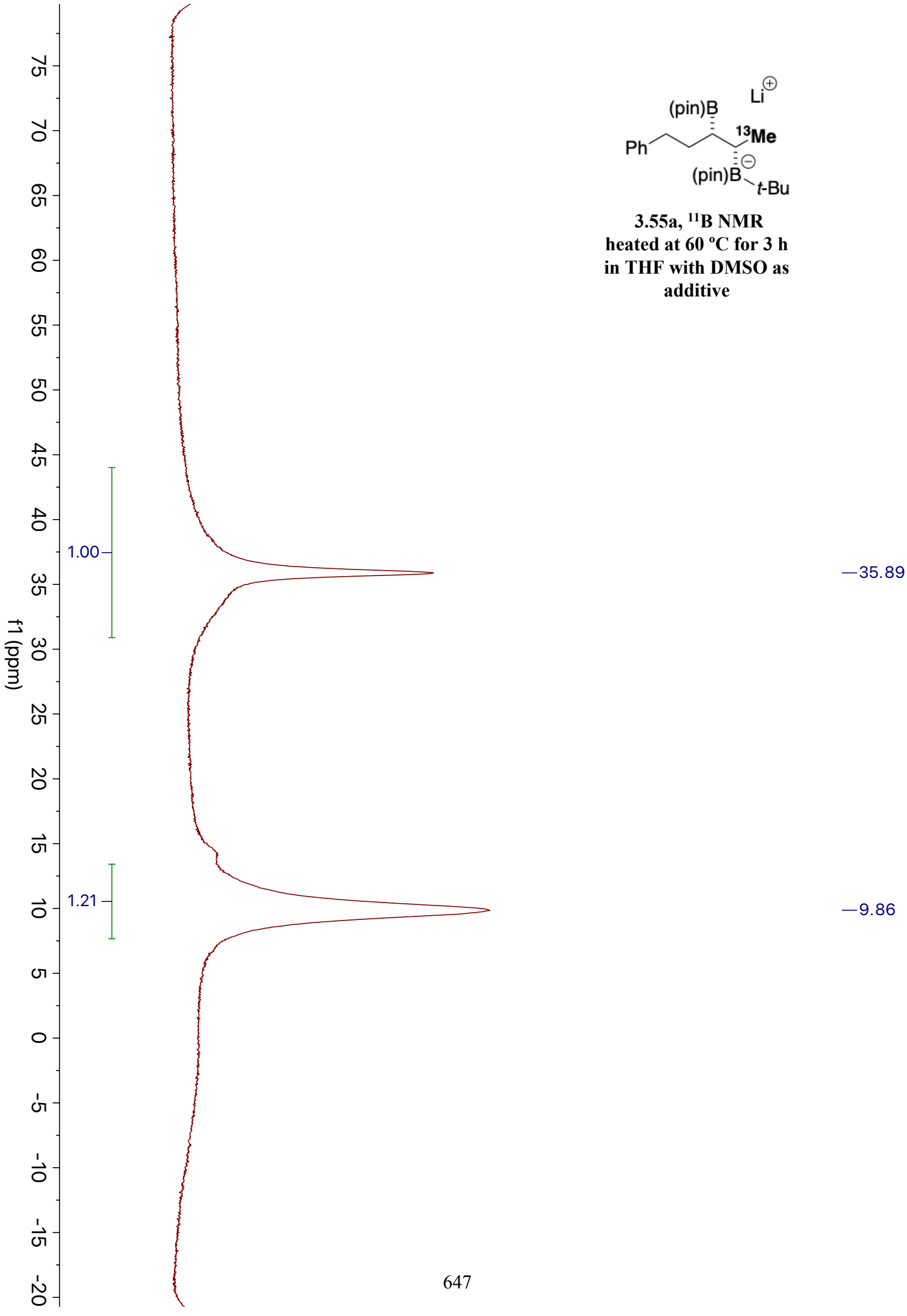
3.54, ^{11}B NMR in THF with DMSO as additive

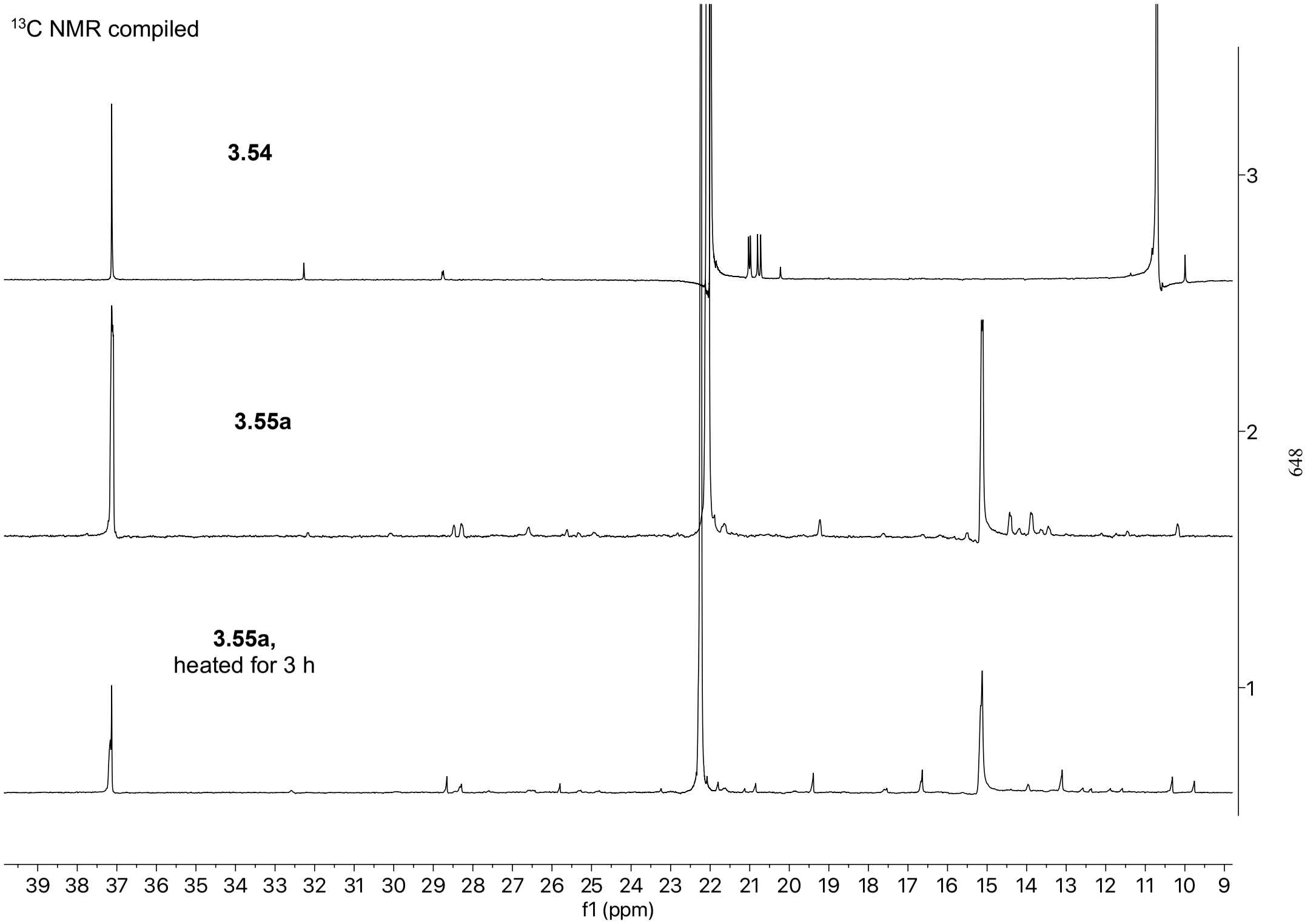

Li
(pin)B
Ph
13Me
(pin)B
t-Bu
3.55a, 13C NMR
in THF with DMSO as
additive
f1 (ppm)
135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
63.89
37.13
28.48
25.62
22.04
19.23
15.13
10.19
0.04
0.04
0.09
1.00
0.11
0.11


Li
(pin)B
13Me
Ph
(pin)B
t-Bu
3.55a, 11B NMR
in THF with DMSO as
additive
1.00
1.24
35.93
9.90
f1 (ppm)
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20

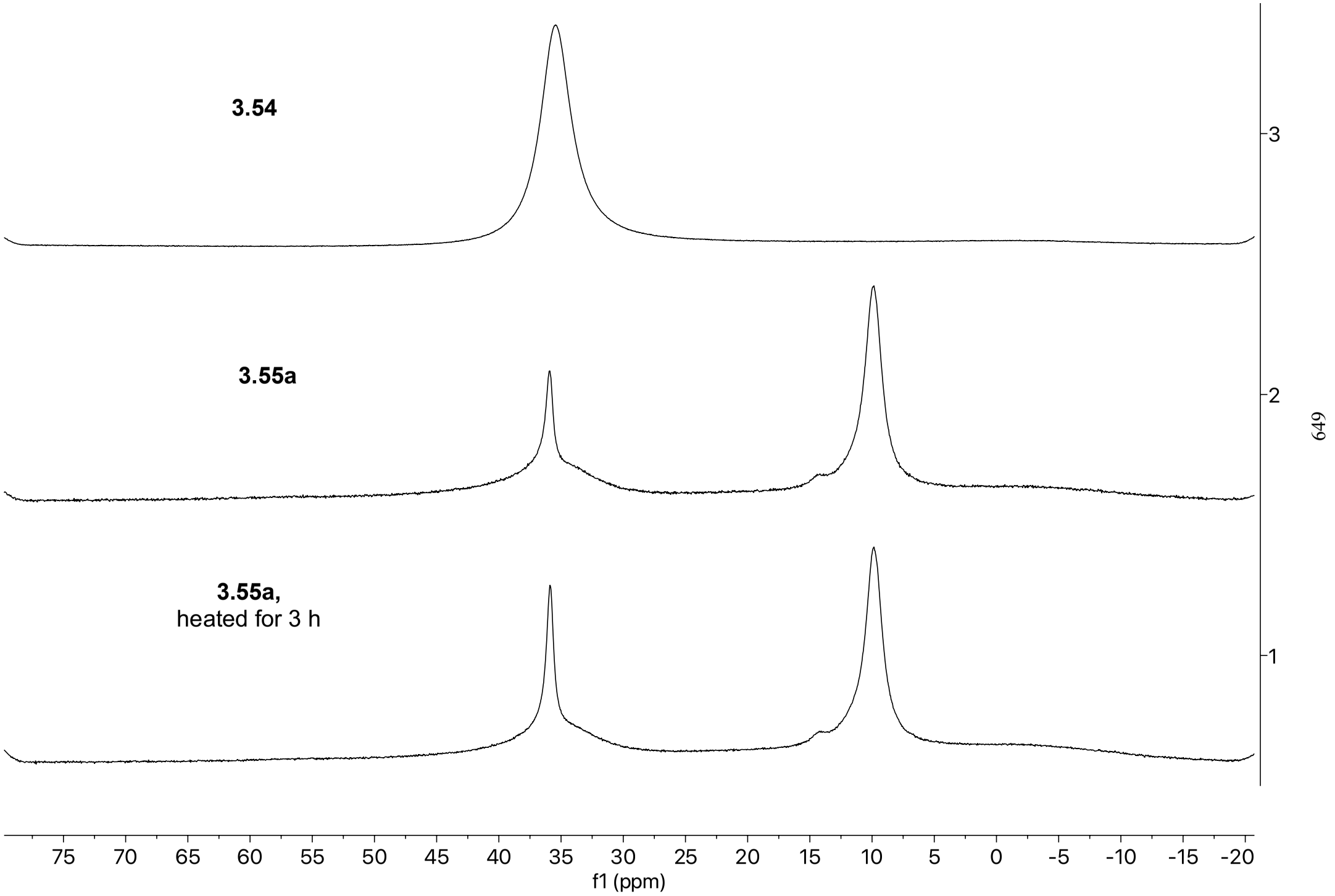


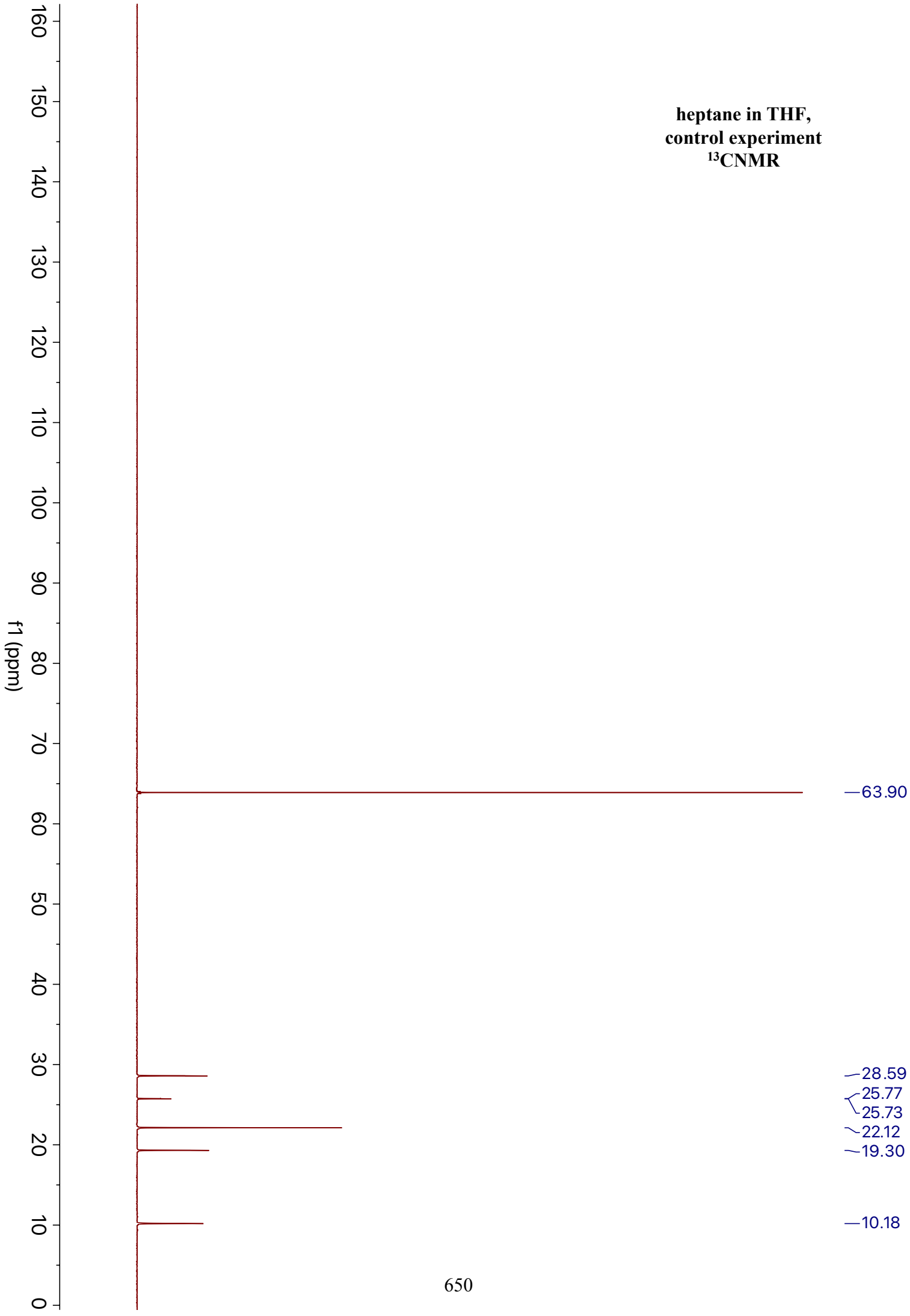
3.55a, ^{13}C NMR heated at 60 ºC for 3 h in THF with DMSO as additive

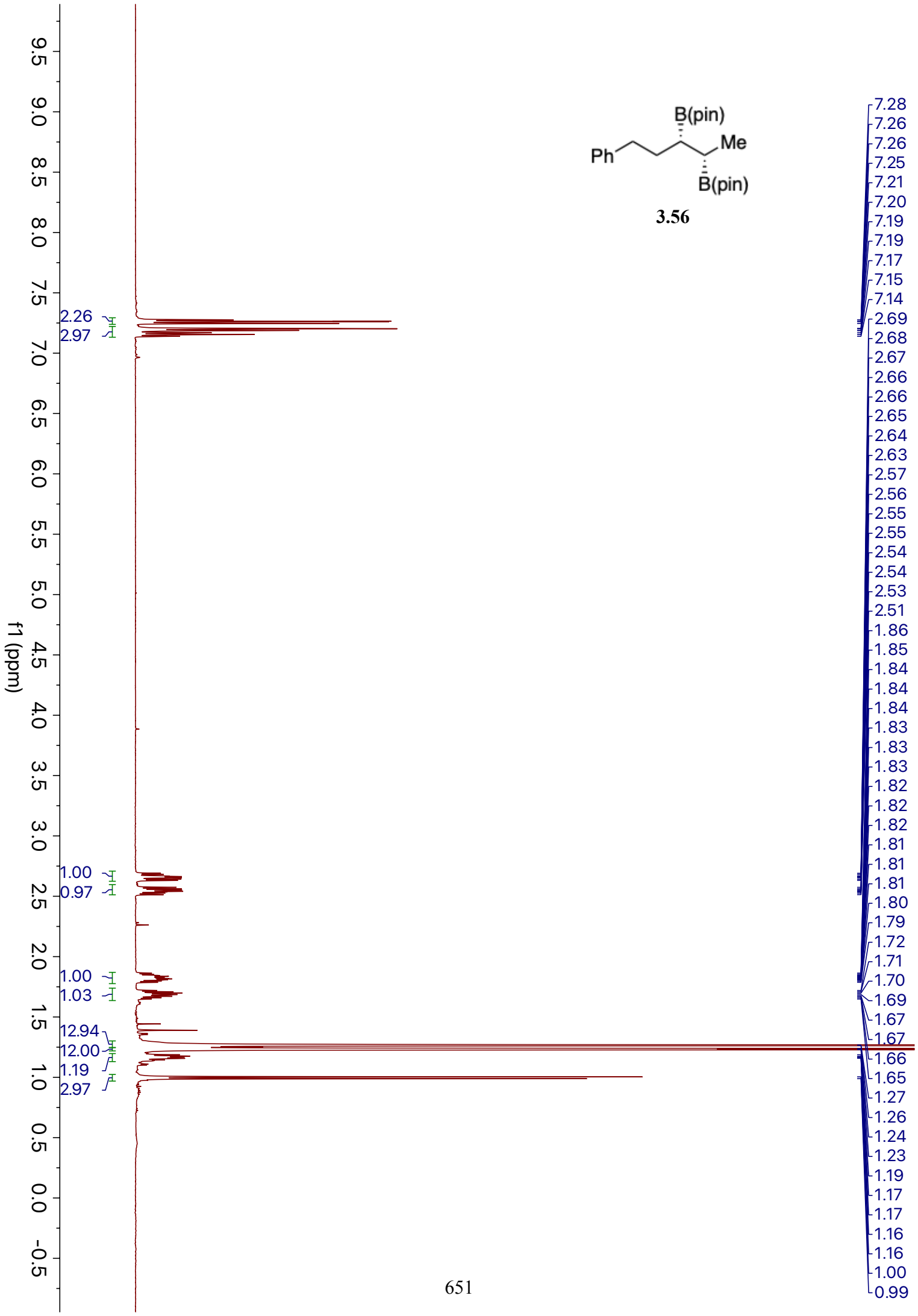

Li
(pin)B
Ph
13Me
(pin)B
t-Bu
3.55a, 11B NMR
heated at 60 ºC for 3 h
in THF with DMSO as
additive
1.00
1.21
35.89
9.86
f1 (ppm)
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20

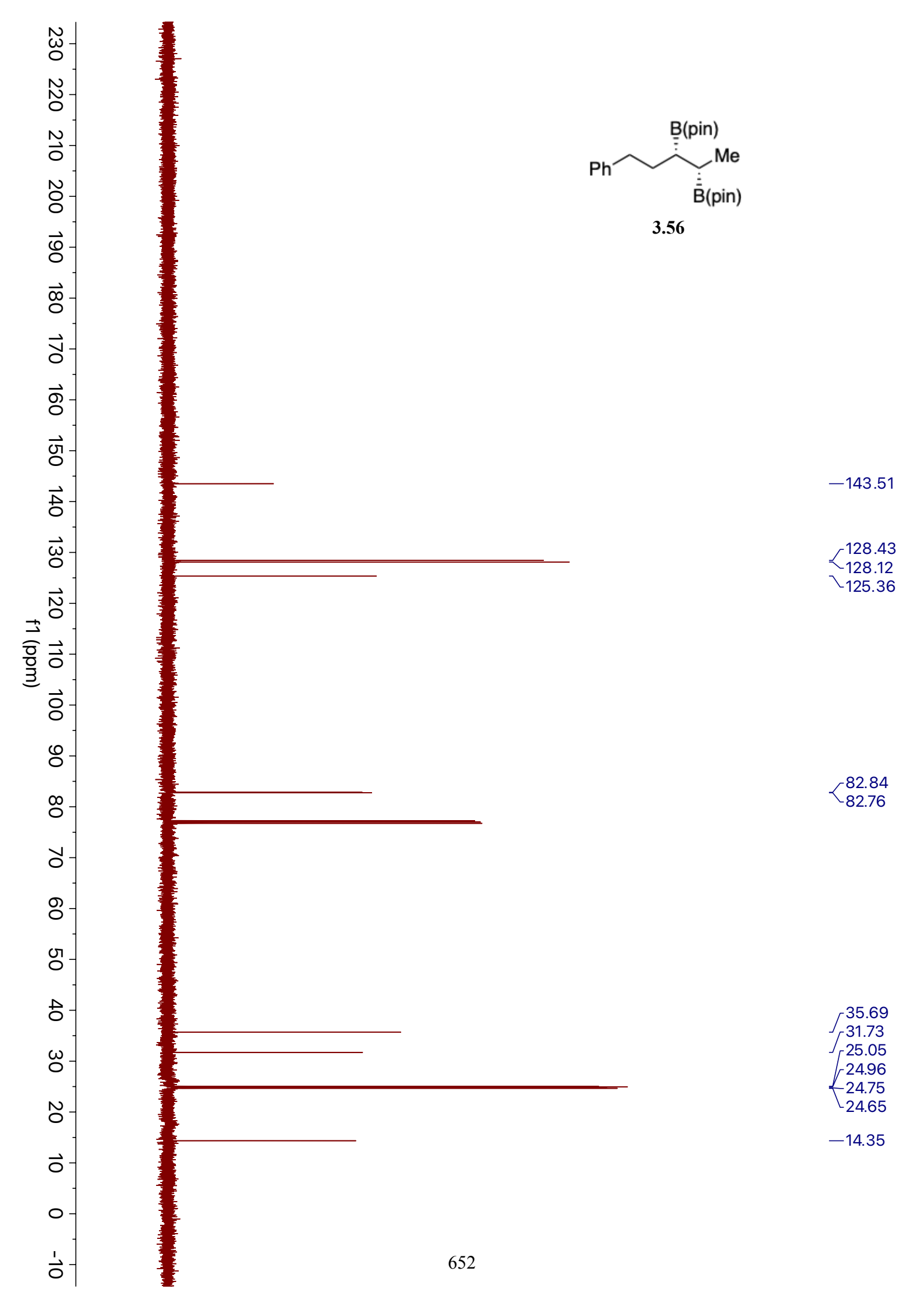

^{13}C NMR compiled
3.54
3.55a
3.55a,
heated for 3 h
3
2
1
648
39 38 37 36 35 34 33 32 31 30 29 28 27 26 25 24 23 22 21 20 19 18 17 16 15 14 13 12 11 10 9
f1 (ppm)

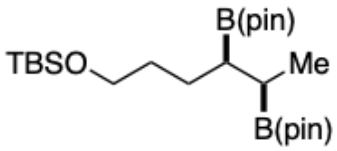
^{11}B NMR compiled



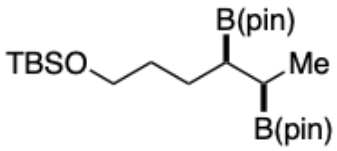

heptane in THF,
control experiment
13CNMR
f1 (ppm)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
63.90
28.59
25.77
25.73
22.12
19.30
10.18


B(pin)
Ph
Me
B(pin)
3.56
f1 (ppm)
2.26
2.97
1.00
0.97
1.00
1.03
12.94
12.00
1.19
2.97


B(pin)
Ph
Me
B(pin)
3.56
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
143.51
128.43
128.12
125.36
82.84
82.76
35.69
31.73
25.05
24.96
24.75
24.65
14.35

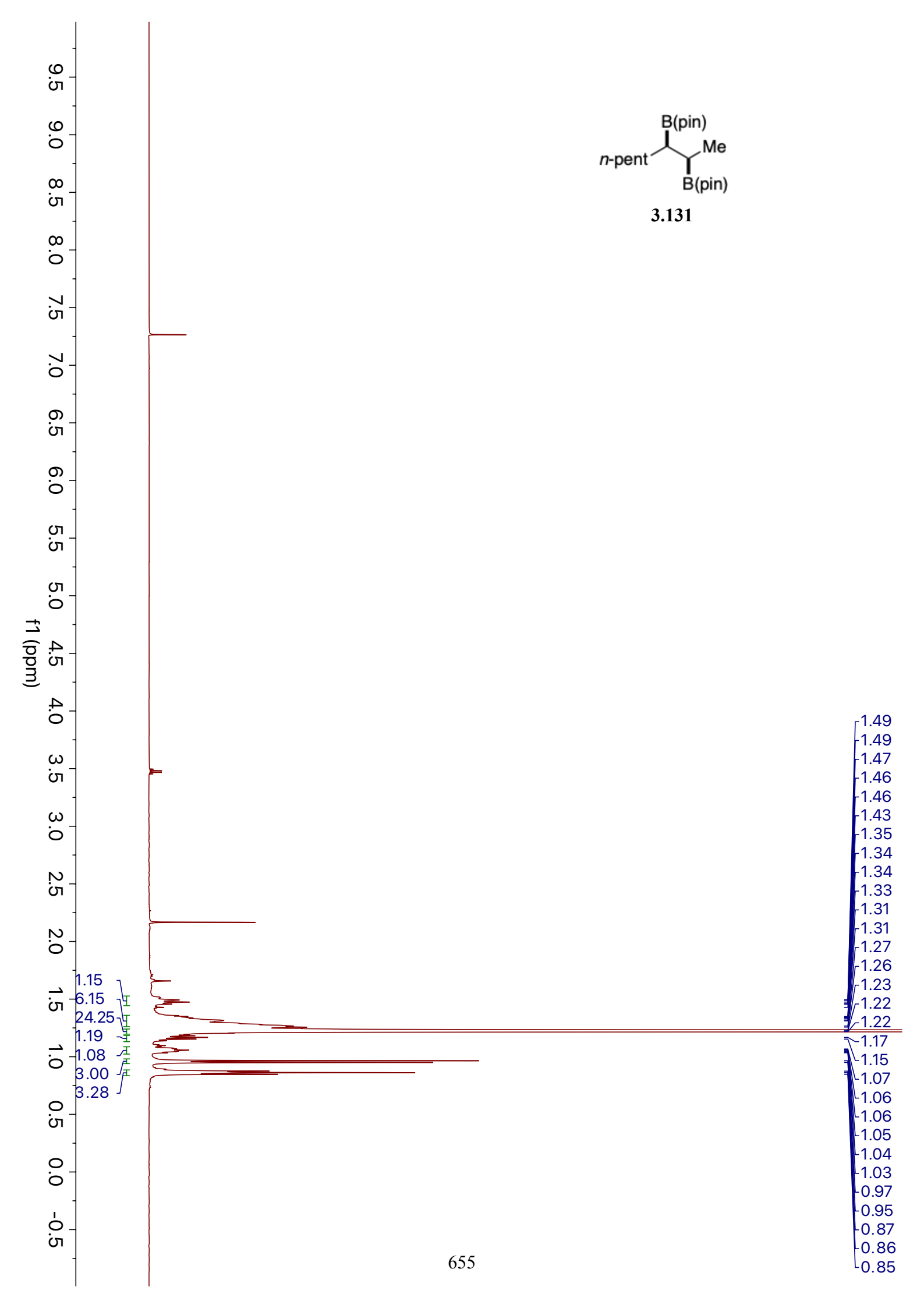


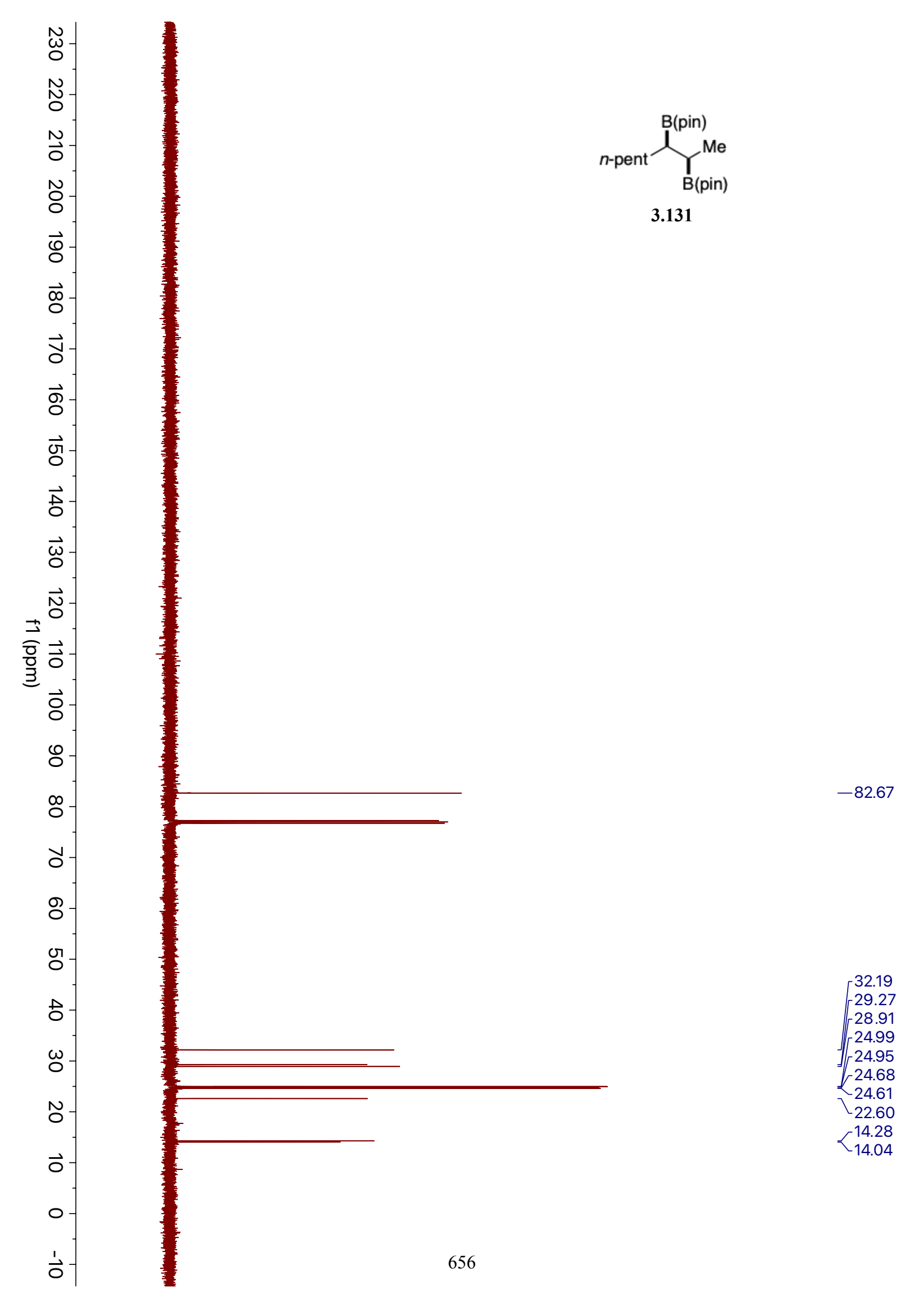
3.130

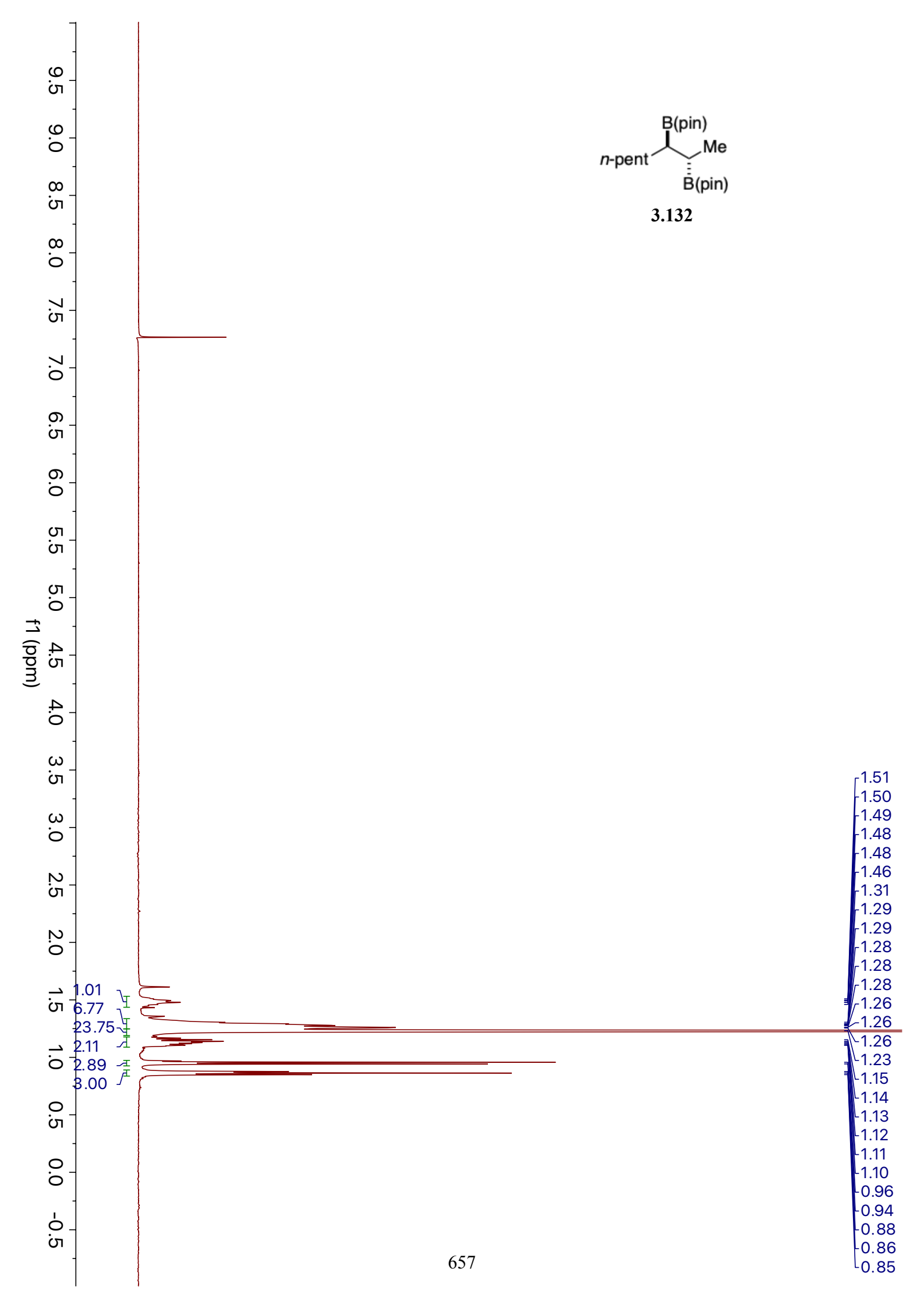

B(pin)
TBSO
Me
B(pin)

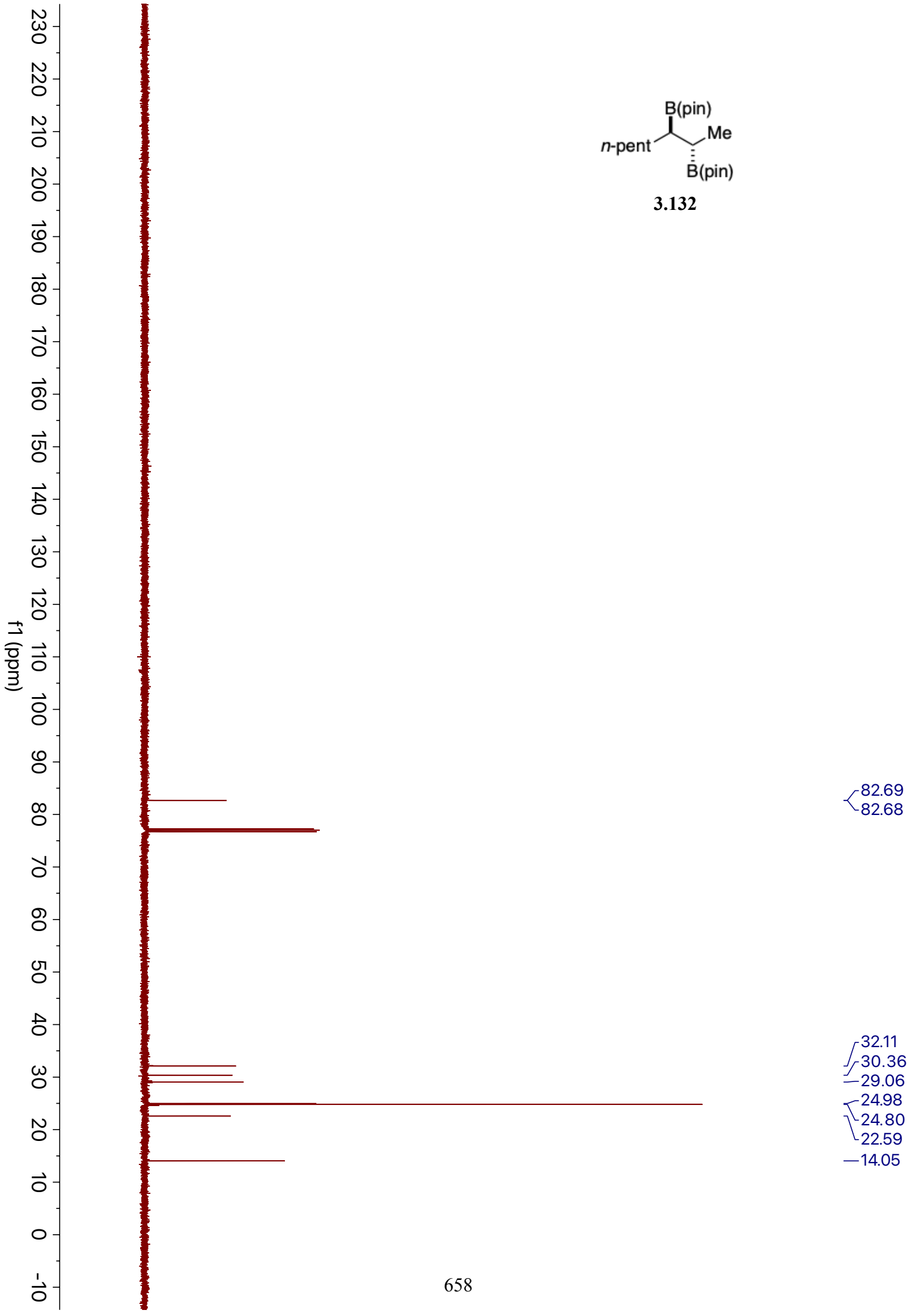
3.130

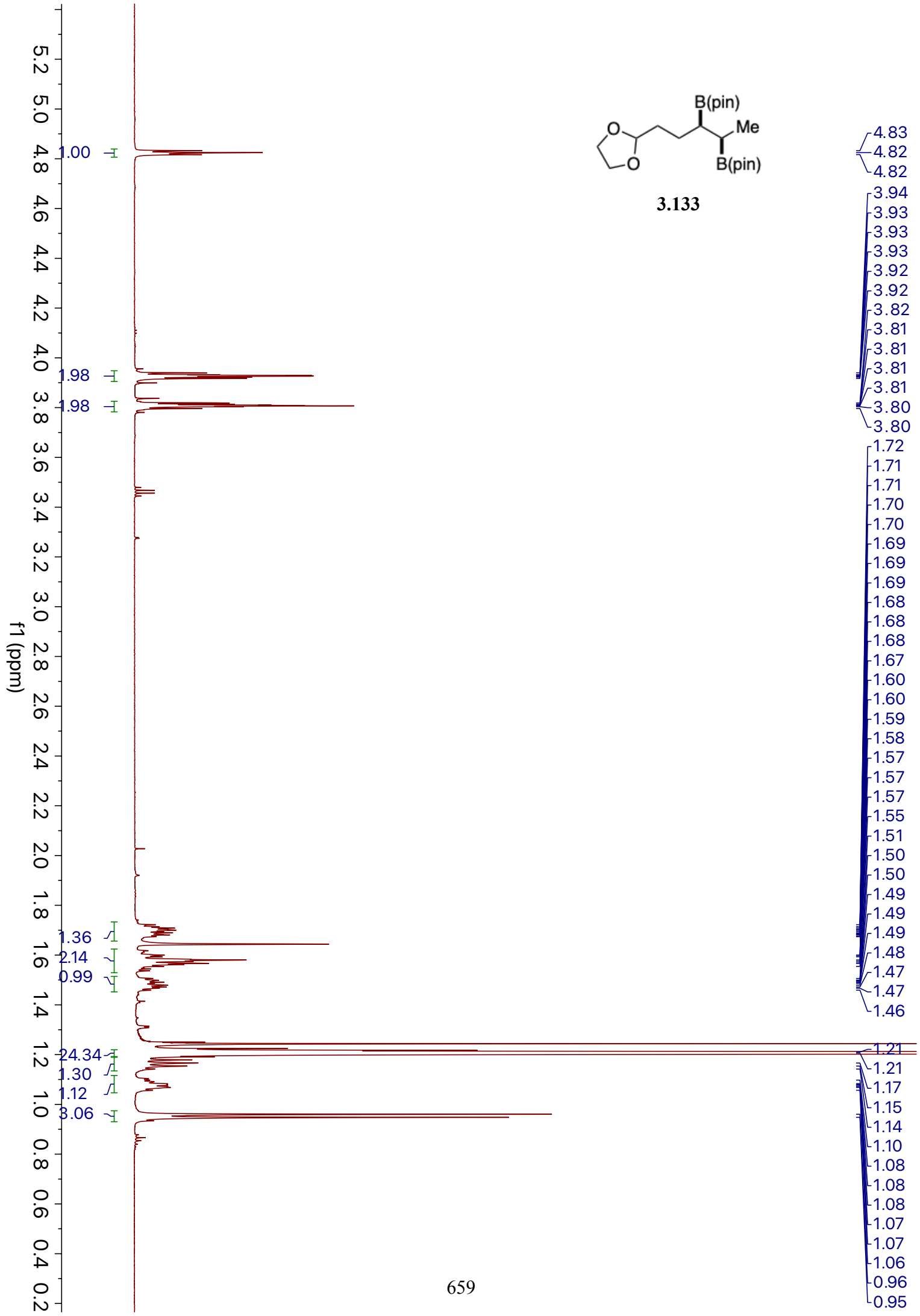
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
82.72
82.68
63.82
32.63
25.99
25.52
24.99
24.94
24.69
24.63
18.34
14.28
-5.23

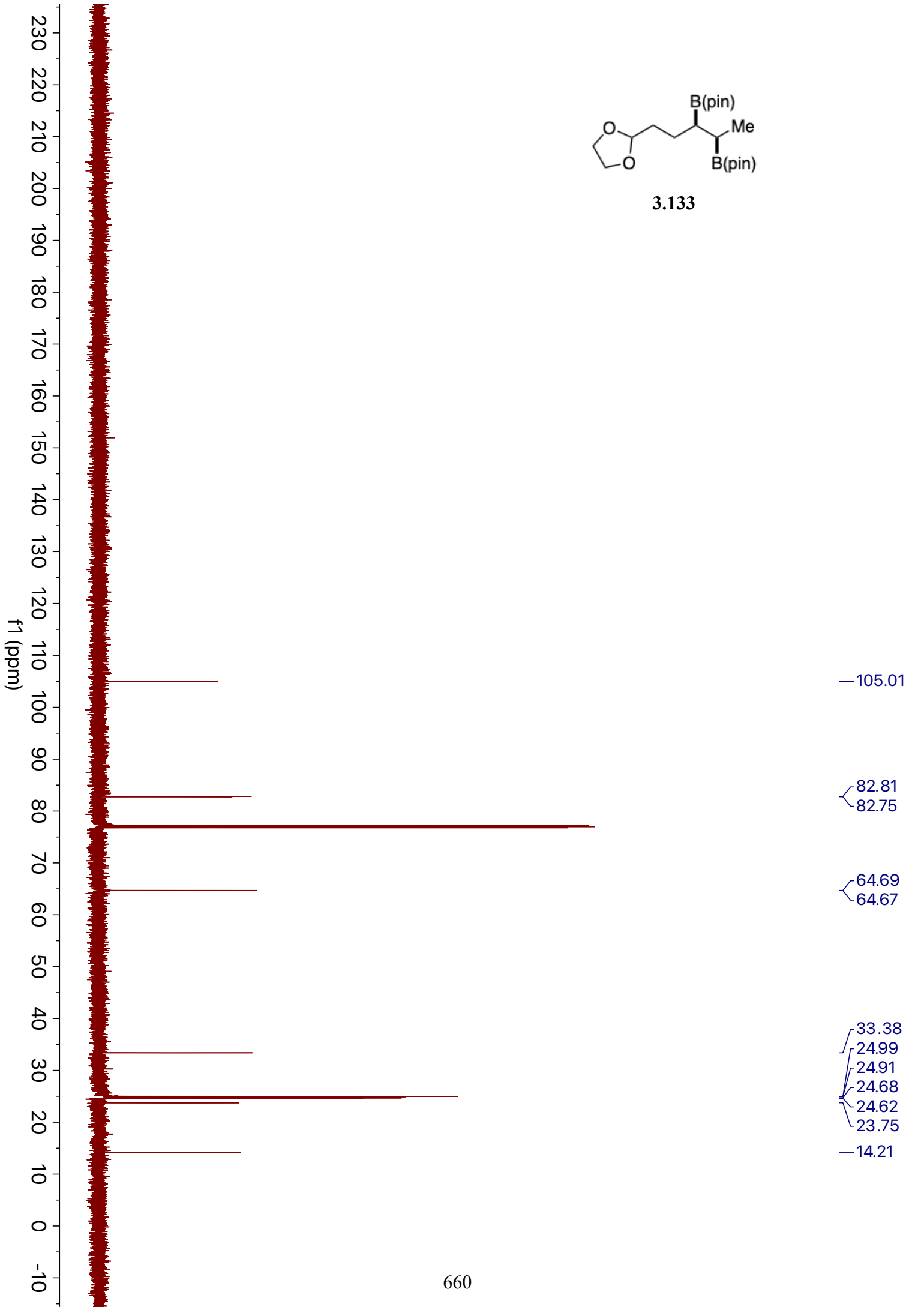

B(pin)
n-pent
Me
B(pin)
3.131
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.15
6.15
24.25
1.19
1.08
3.00
3.28
1.49
1.49
1.47
1.46
1.46
1.43
1.35
1.34
1.34
1.33
1.31
1.31
1.27
1.26
1.23
1.22
1.22
1.17
1.15
1.07
1.06
1.06
1.05
1.04
1.03
0.97
0.95
0.87
0.86
0.85

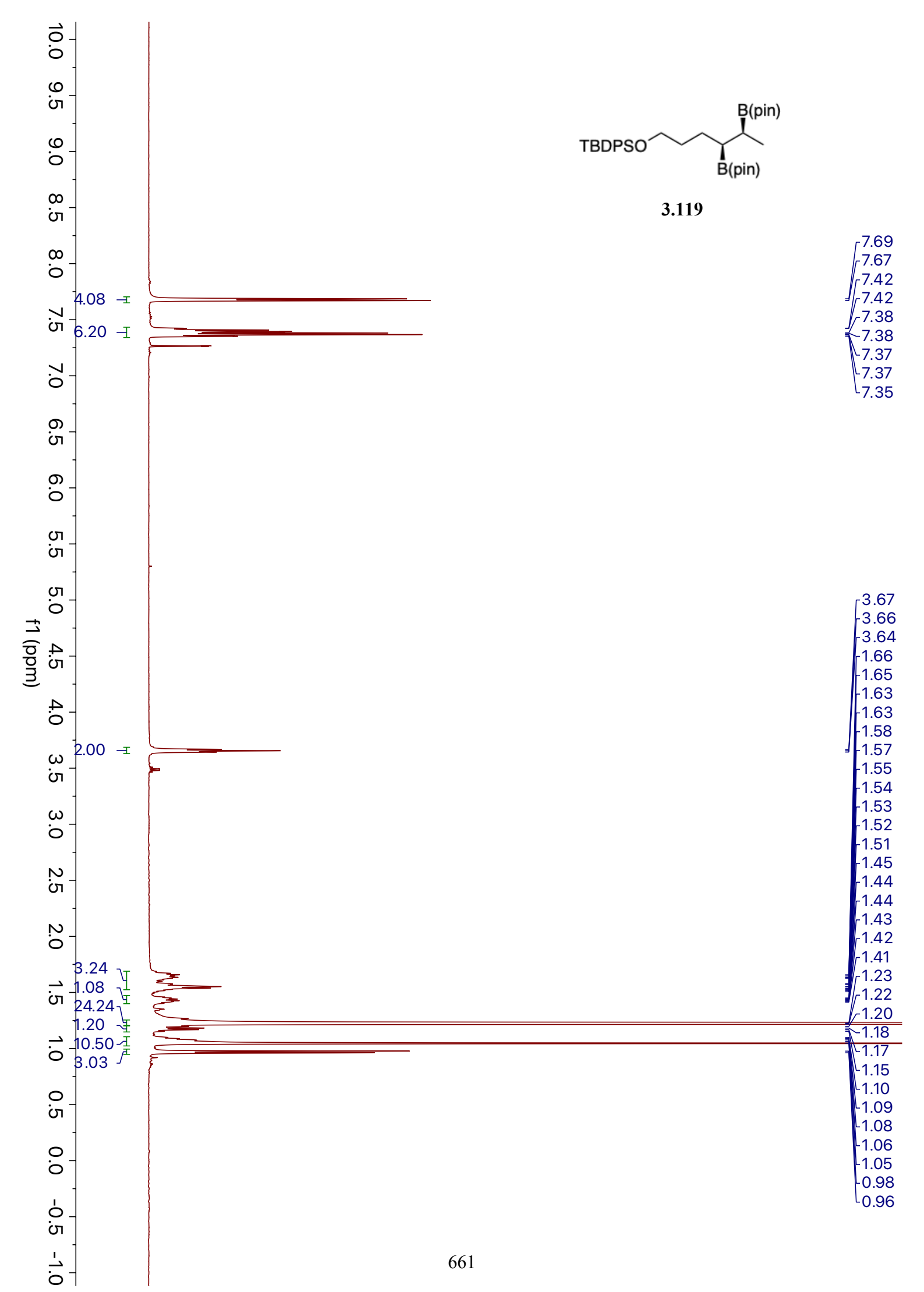

B(pin)
n-pent
Me
B(pin)
3.131
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
82.67
32.19
29.27
28.91
24.99
24.95
24.68
24.61
22.60
14.28
14.04

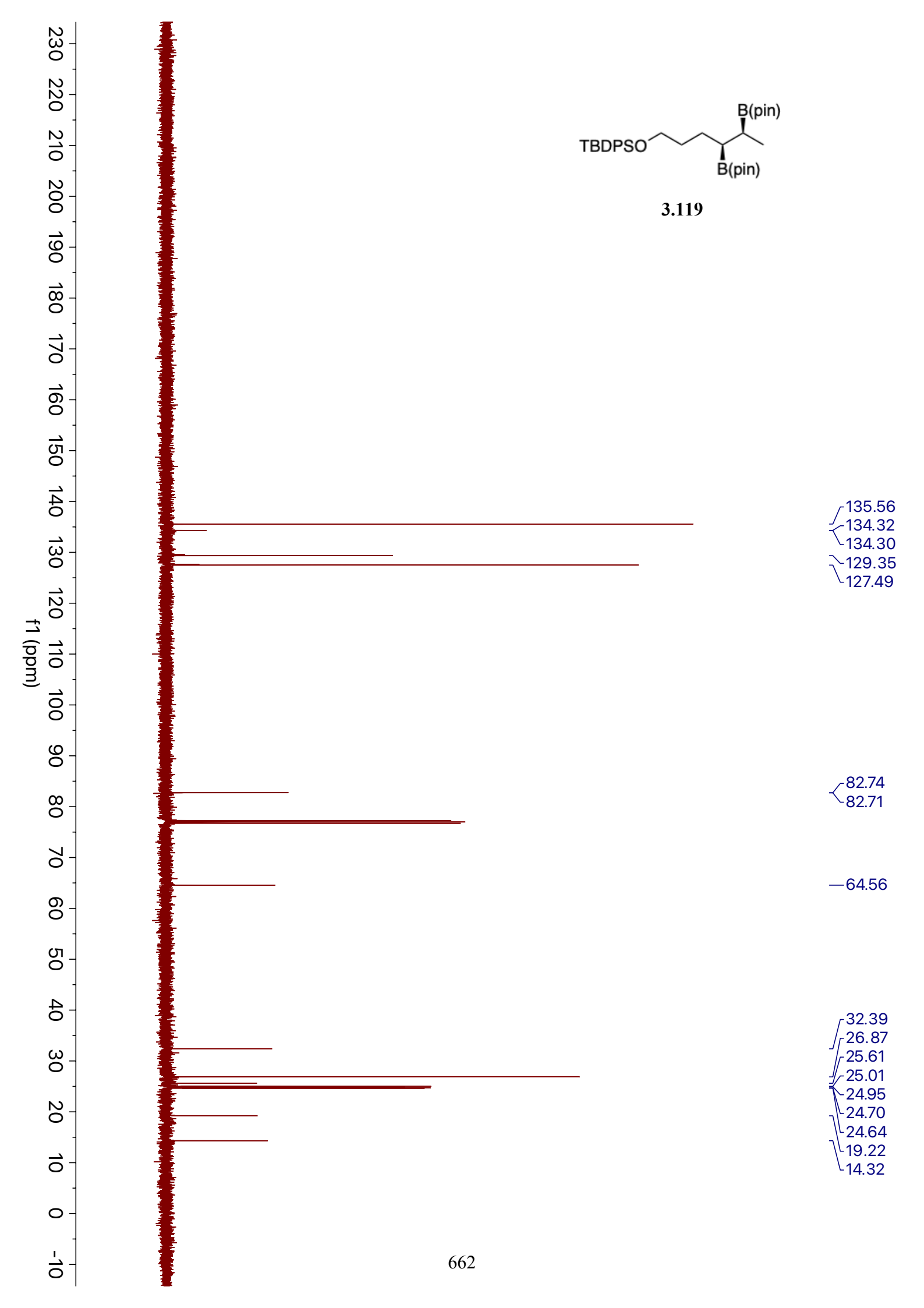

B(pin)
n-pent
Me
B(pin)
3.132
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.01
6.77
23.75
2.11
2.89
3.00
1.51
1.50
1.49
1.48
1.48
1.46
1.31
1.29
1.29
1.28
1.28
1.28
1.26
1.26
1.26
1.23
1.15
1.14
1.13
1.12
1.11
1.10
0.96
0.94
0.88
0.86
0.85

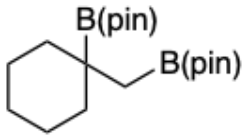

B(pin)
n-pent
Me
B(pin)
3.132
82.69
82.68
32.11
30.36
29.06
24.98
24.80
22.59
14.05
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


B(pin)
Me
B(pin)
O
O
3.133
f1 (ppm)
5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2
1.00
1.98
1.98
1.36
2.14
0.99
24.34
1.30
1.12
3.06
4.83 4.82 4.82
3.94 3.93 3.93 3.93 3.92 3.92 3.82 3.81 3.81 3.81 3.81 3.80 3.80
1.72 1.71 1.71 1.70 1.70 1.69 1.69 1.69 1.68 1.68 1.68 1.67 1.60 1.60 1.59 1.58 1.57 1.57 1.57 1.55 1.51 1.50 1.50 1.49 1.49 1.49 1.48 1.47 1.47 1.46
1.21 1.21 1.17 1.15 1.14 1.10 1.08 1.08 1.08 1.07 1.07 1.06 0.96 0.95

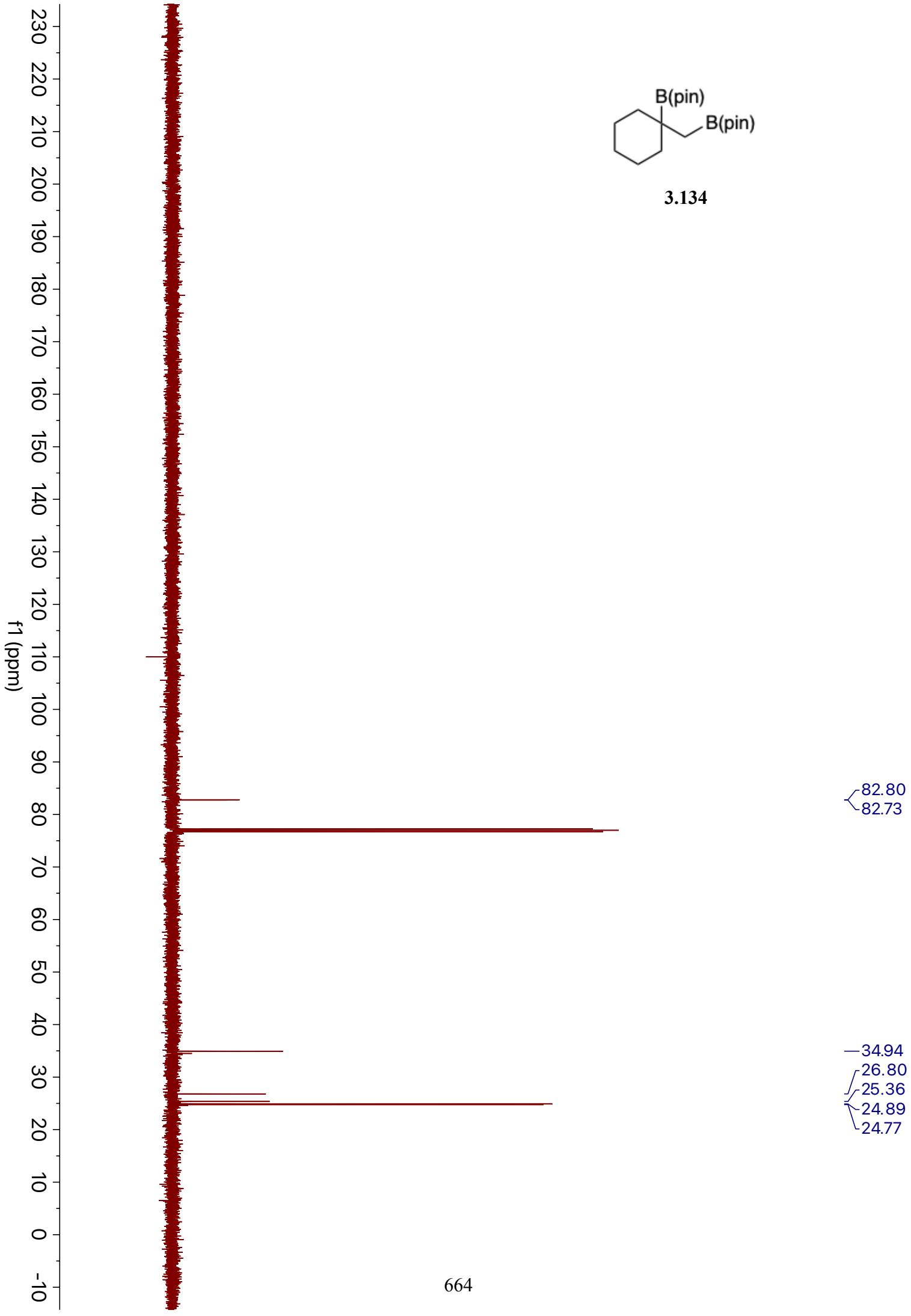

B(pin)
Me
B(pin)
O
O
3.133
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
105.01
82.81
82.75
64.69
64.67
33.38
24.99
24.91
24.68
24.62
23.75
14.21

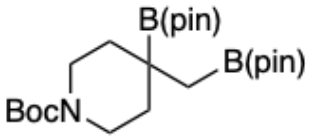

B(pin)
TBDPSO
B(pin)
3.119
7.69
7.67
7.42
7.42
7.38
7.38
7.37
7.37
7.35
4.08
6.20
2.00
3.24
1.08
24.24
1.20
10.50
3.03
3.67
3.66
3.64
1.66
1.65
1.63
1.63
1.58
1.57
1.55
1.54
1.53
1.52
1.51
1.45
1.44
1.44
1.43
1.42
1.41
1.23
1.22
1.20
1.18
1.17
1.15
1.10
1.09
1.08
1.06
1.05
0.98
0.96
f1 (ppm)


B(pin)
TBDPSO
B(pin)
3.119
135.56
134.32
134.30
129.35
127.49
82.74
82.71
64.56
32.39
26.87
25.61
25.01
24.95
24.70
24.64
19.22
14.32
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



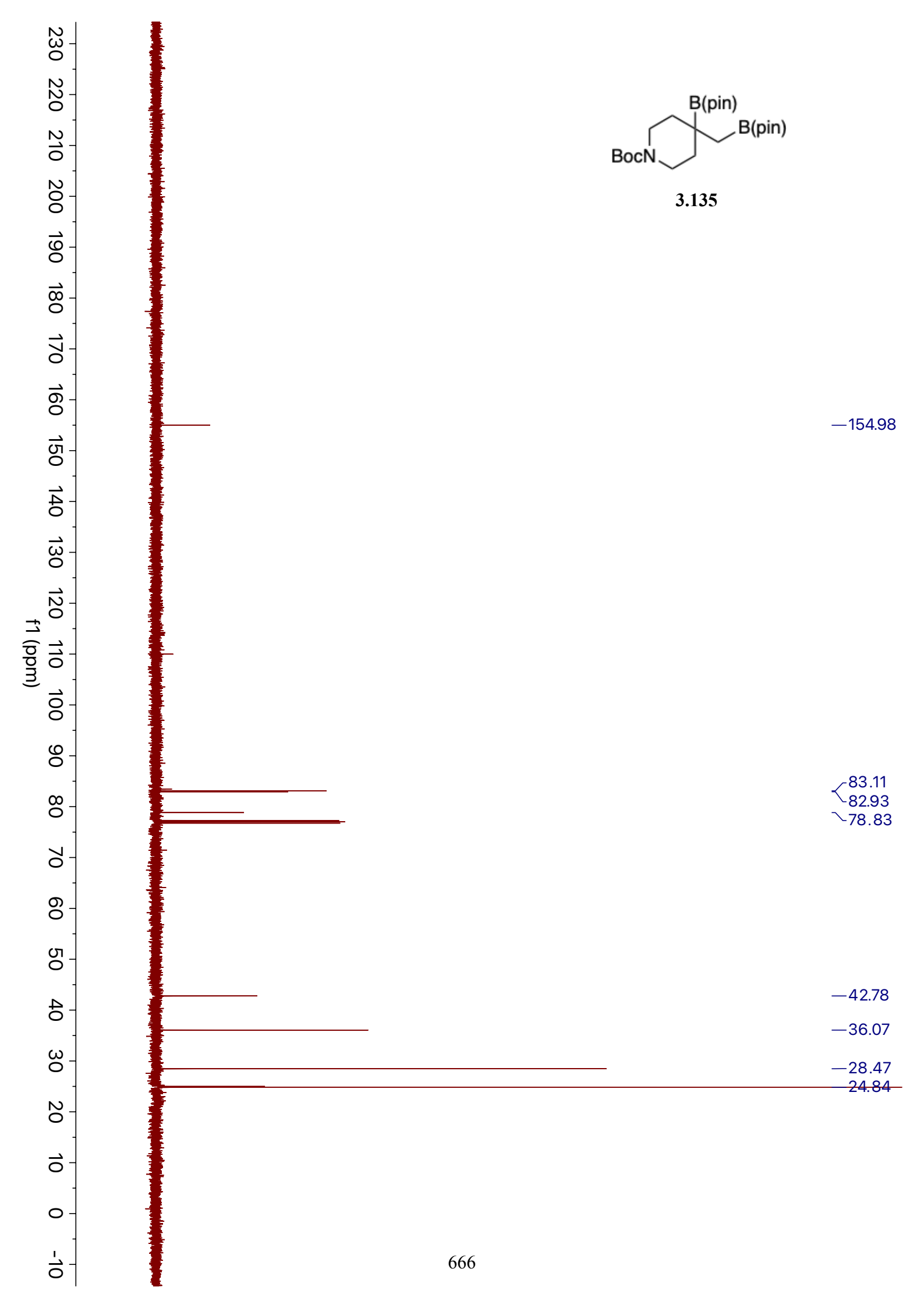
3.134

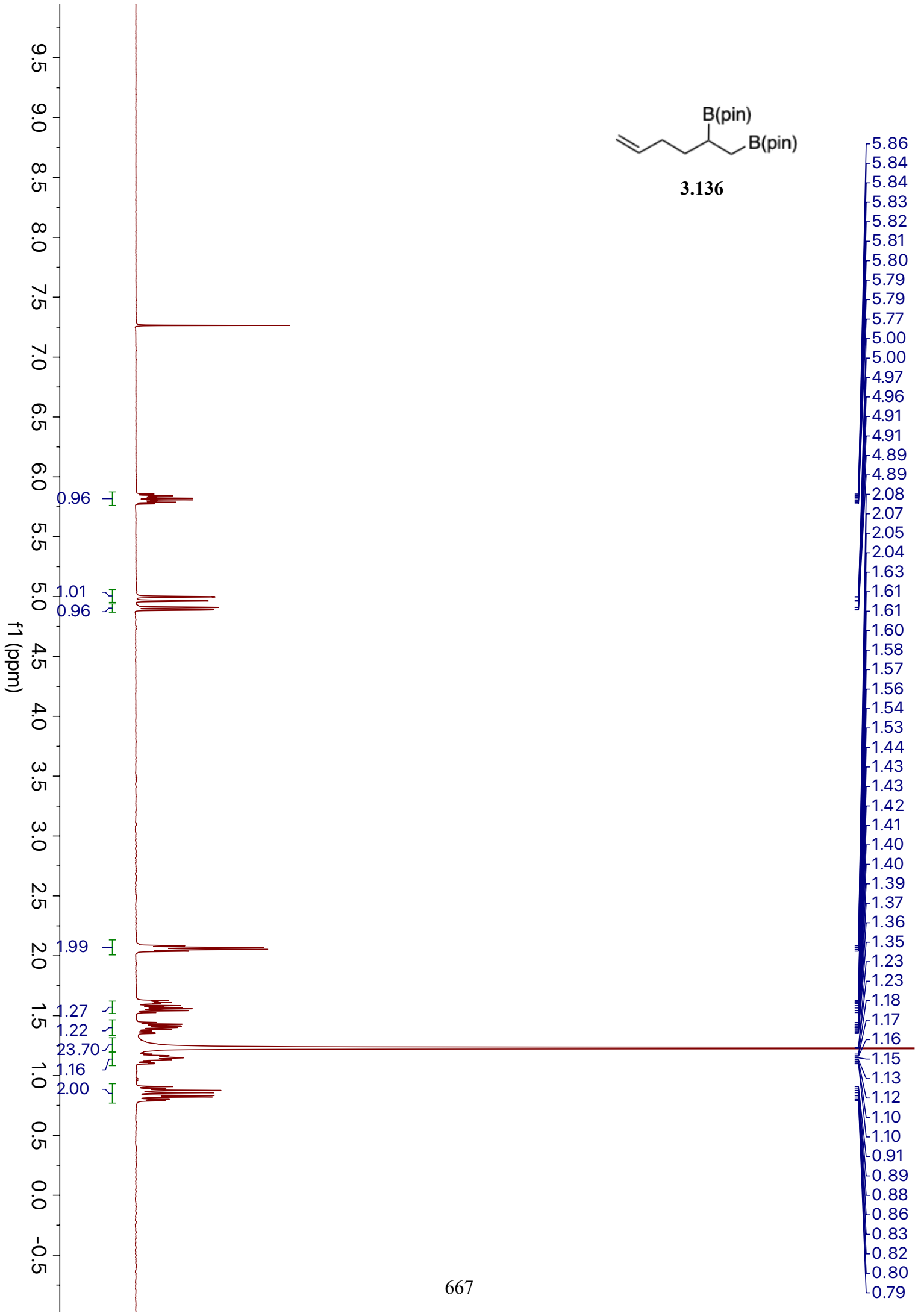

B(pin)
B(pin)
3.134
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
82.80
82.73
34.94
26.80
25.36
24.89
24.77

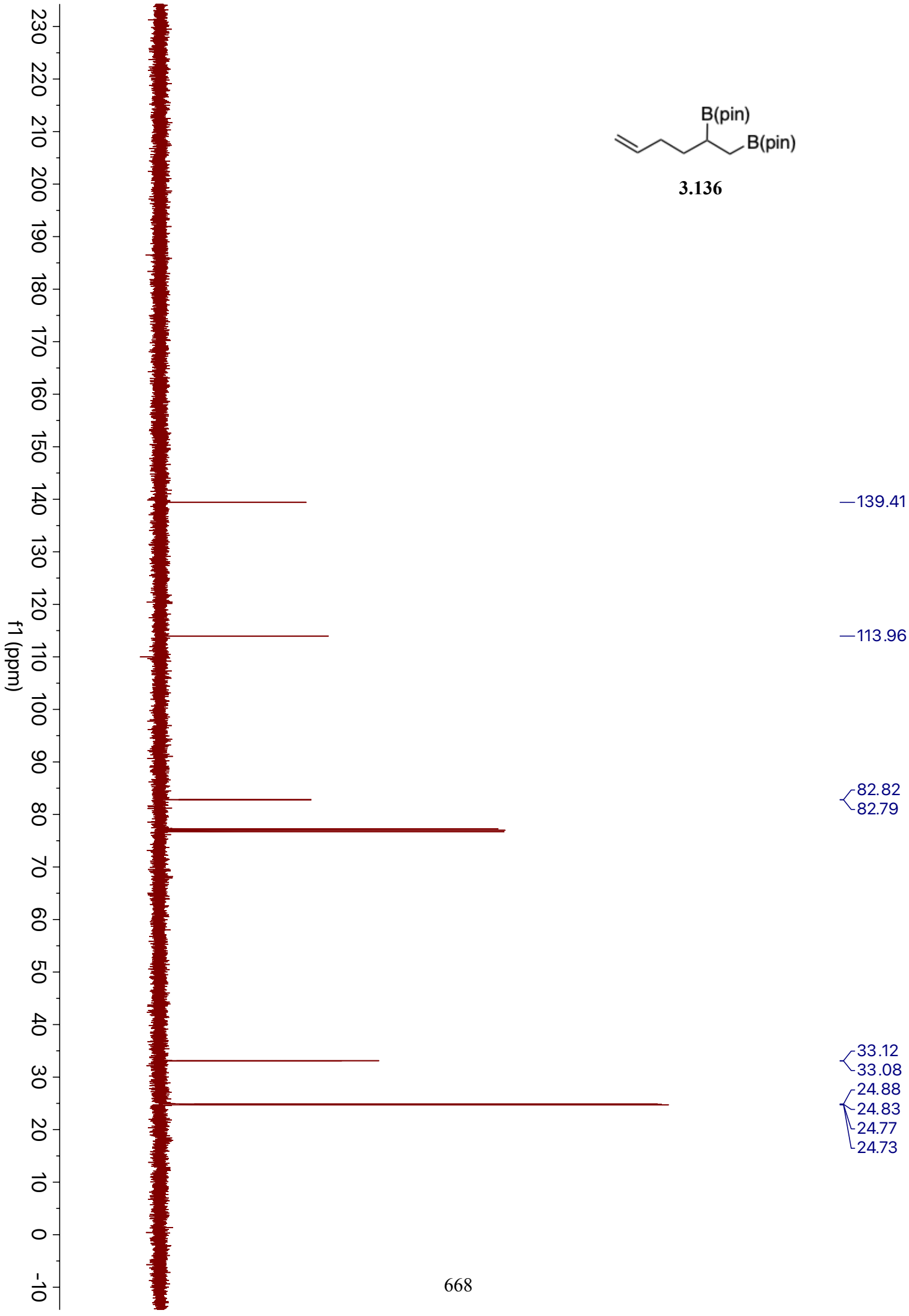

B(pin)
B(pin)
BocN

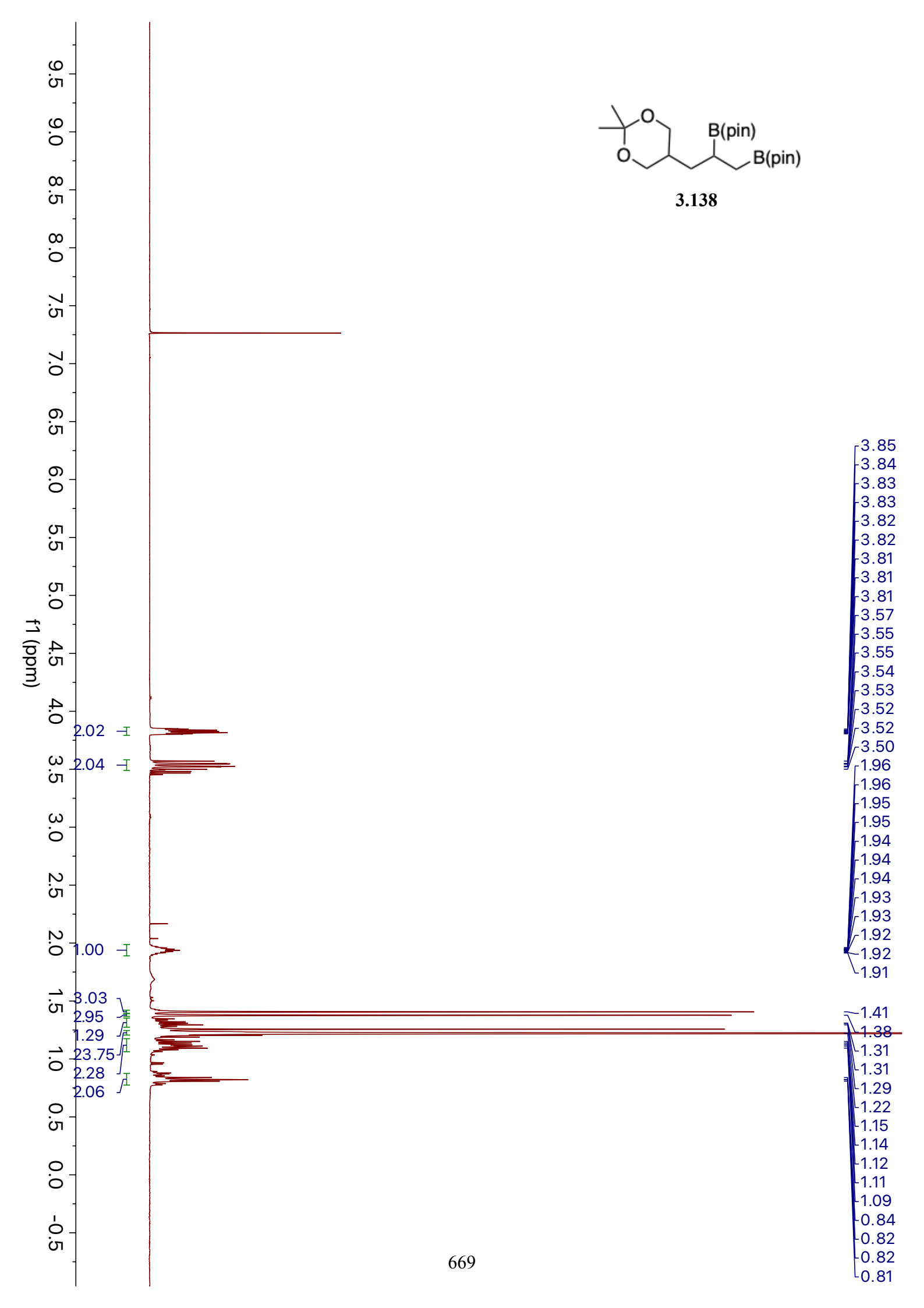
3.135

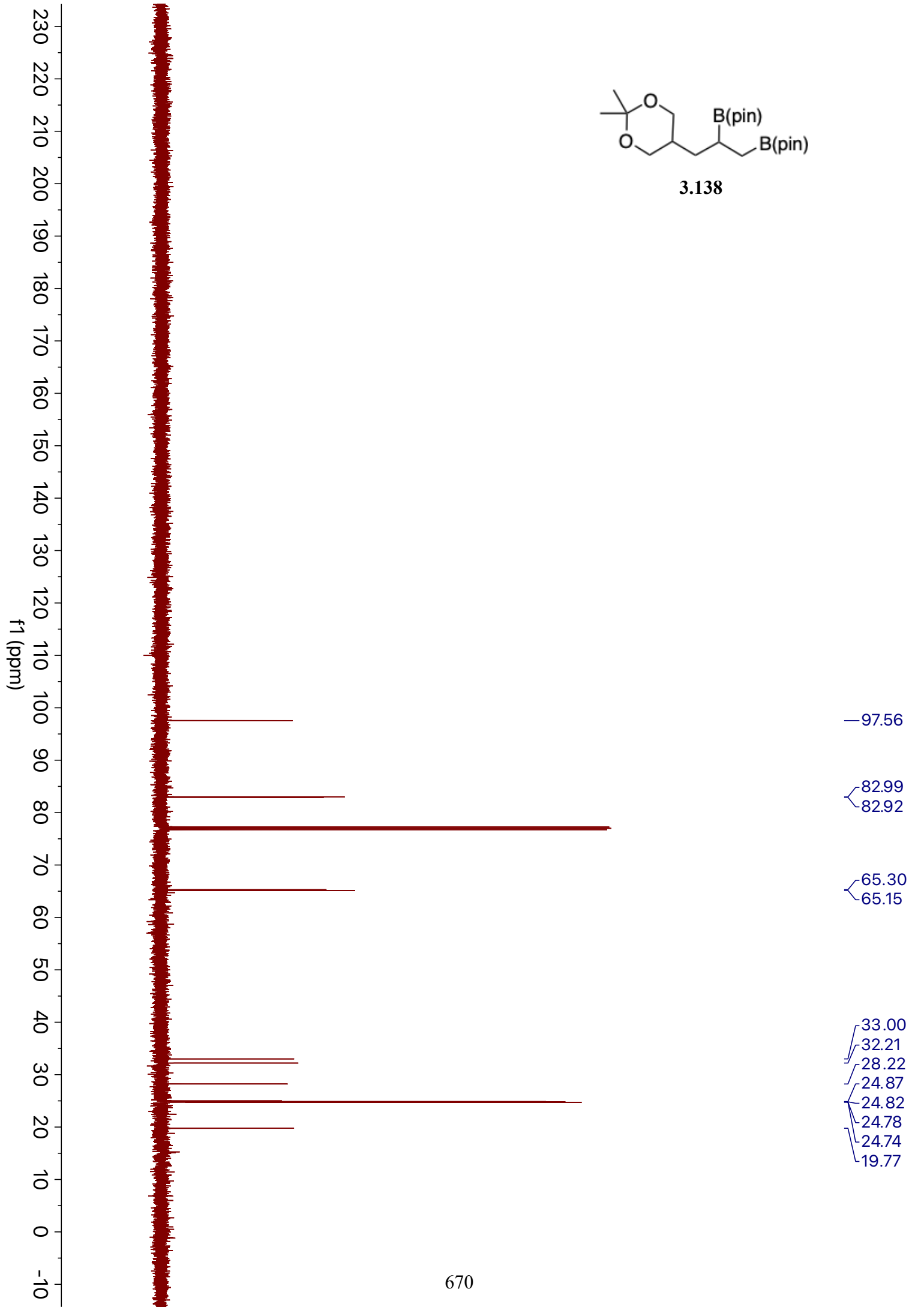
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.00
1.99
2.02
9.21
12.47
11.64
1.78
2.02
3.88
3.85
2.90
2.90
2.88
2.88
2.85
2.85
1.85
1.83
1.44
1.25
1.22
1.19
1.19
1.18
1.16
1.15
0.83

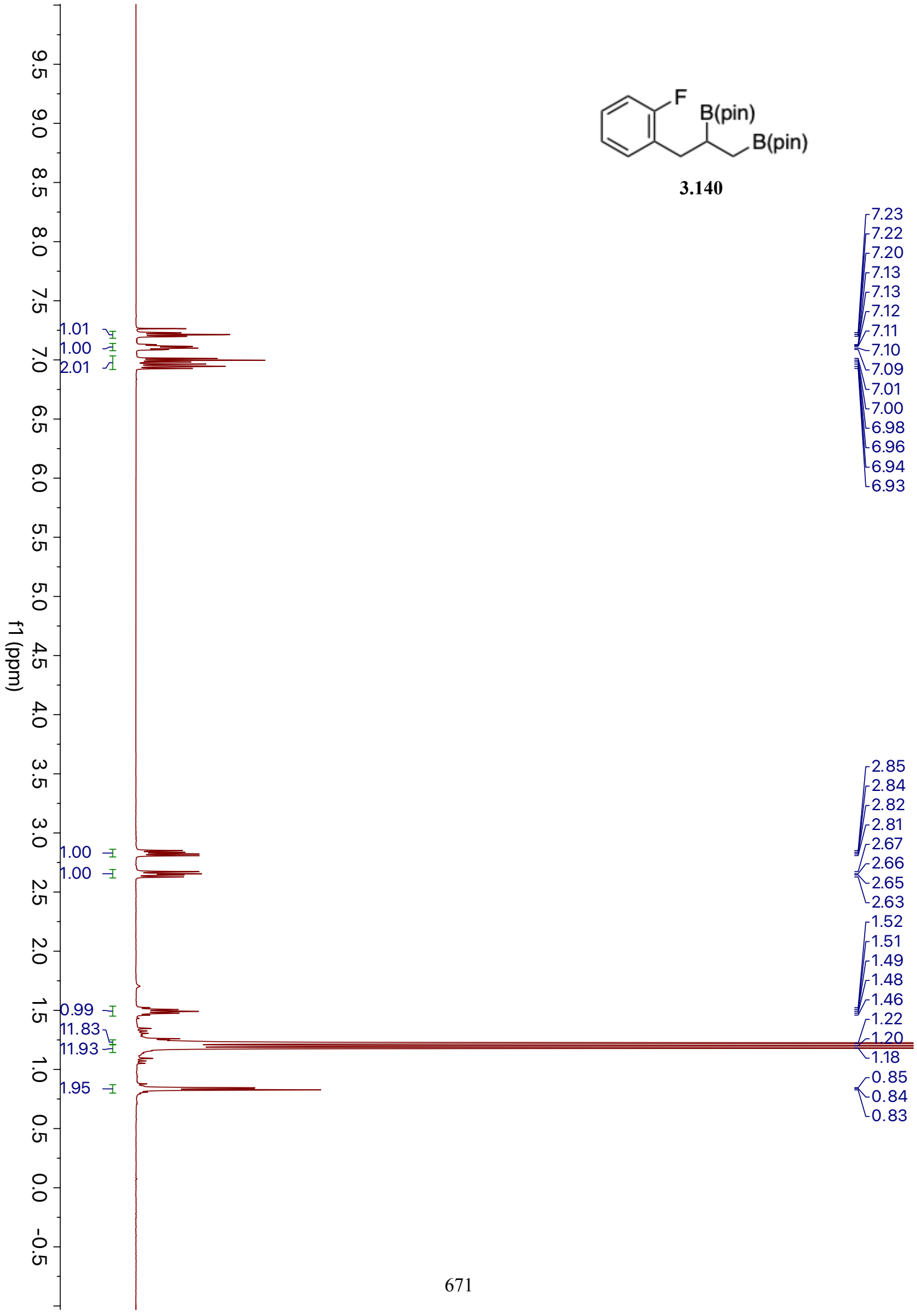

B(pin)
B(pin)
BocN
3.135
154.98
83.11
82.93
78.83
42.78
36.07
28.47
24.84
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

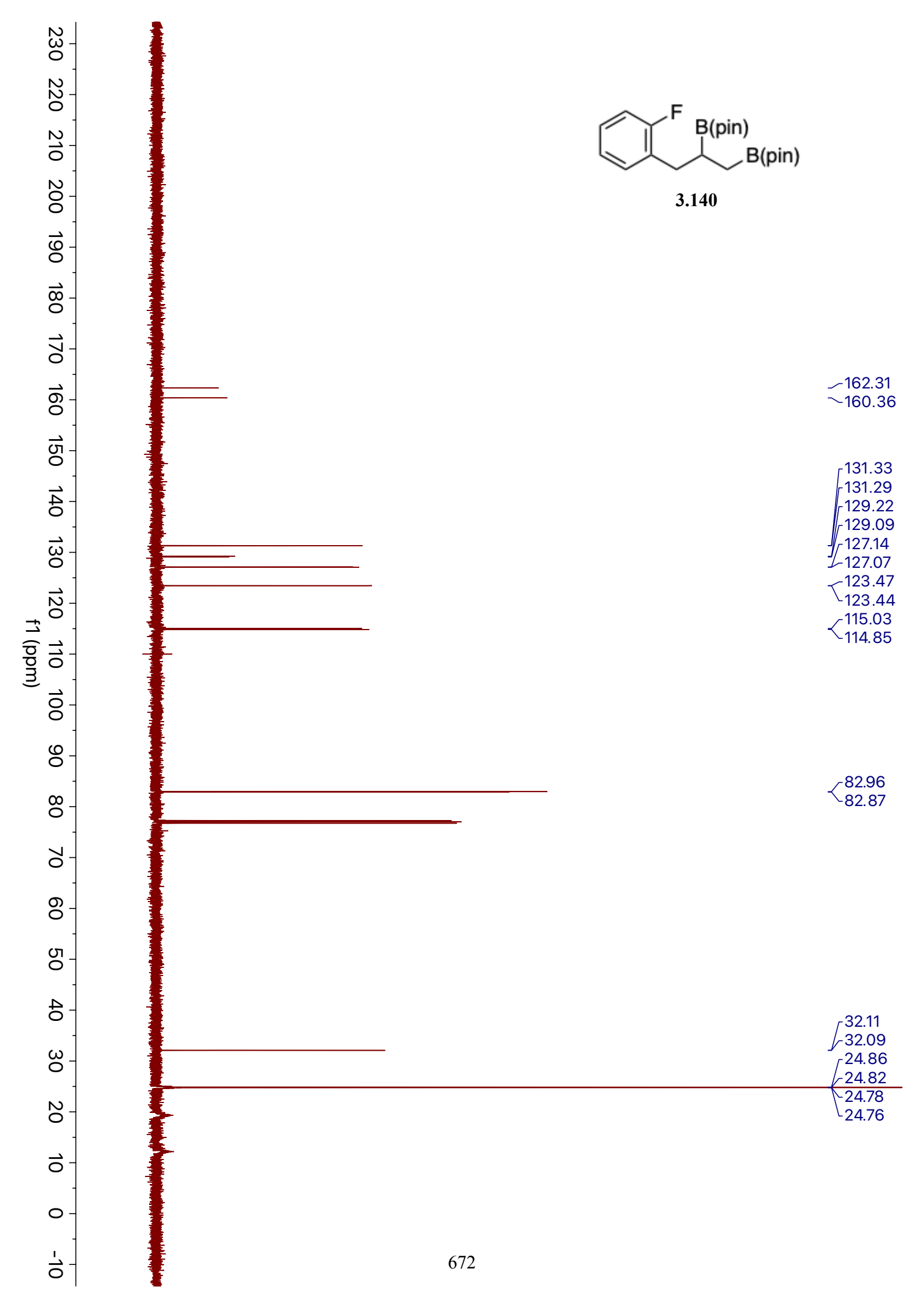

B(pin)
B(pin)
3.136
f1 (ppm)
0.96
1.01
0.96
1.99
1.27
1.22
23.70
1.16
2.00

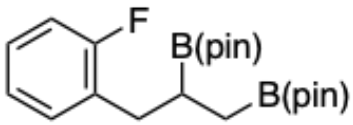

B(pin)
B(pin)
3.136
139.41
113.96
82.82
82.79
33.12
33.08
24.88
24.83
24.77
24.73
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


B(pin)
B(pin)
O
O
3.138
f1 (ppm)
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
2.02
2.04
1.00
3.03
2.95
1.29
23.75
2.28
2.06
3.85 3.84 3.83 3.83 3.82 3.82 3.81 3.81 3.81 3.57 3.55 3.55 3.54 3.53 3.52 3.52 3.50
1.96 1.96 1.95 1.95 1.94 1.94 1.94 1.93 1.93 1.92 1.92 1.91
1.41 1.38 1.31 1.31 1.29 1.22 1.15 1.14 1.12 1.11 1.09 0.84 0.82 0.82 0.81


B(pin)
B(pin)
O
O
3.138
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
97.56
82.99
82.92
65.30
65.15
33.00
32.21
28.22
24.87
24.82
24.78
24.74
19.77

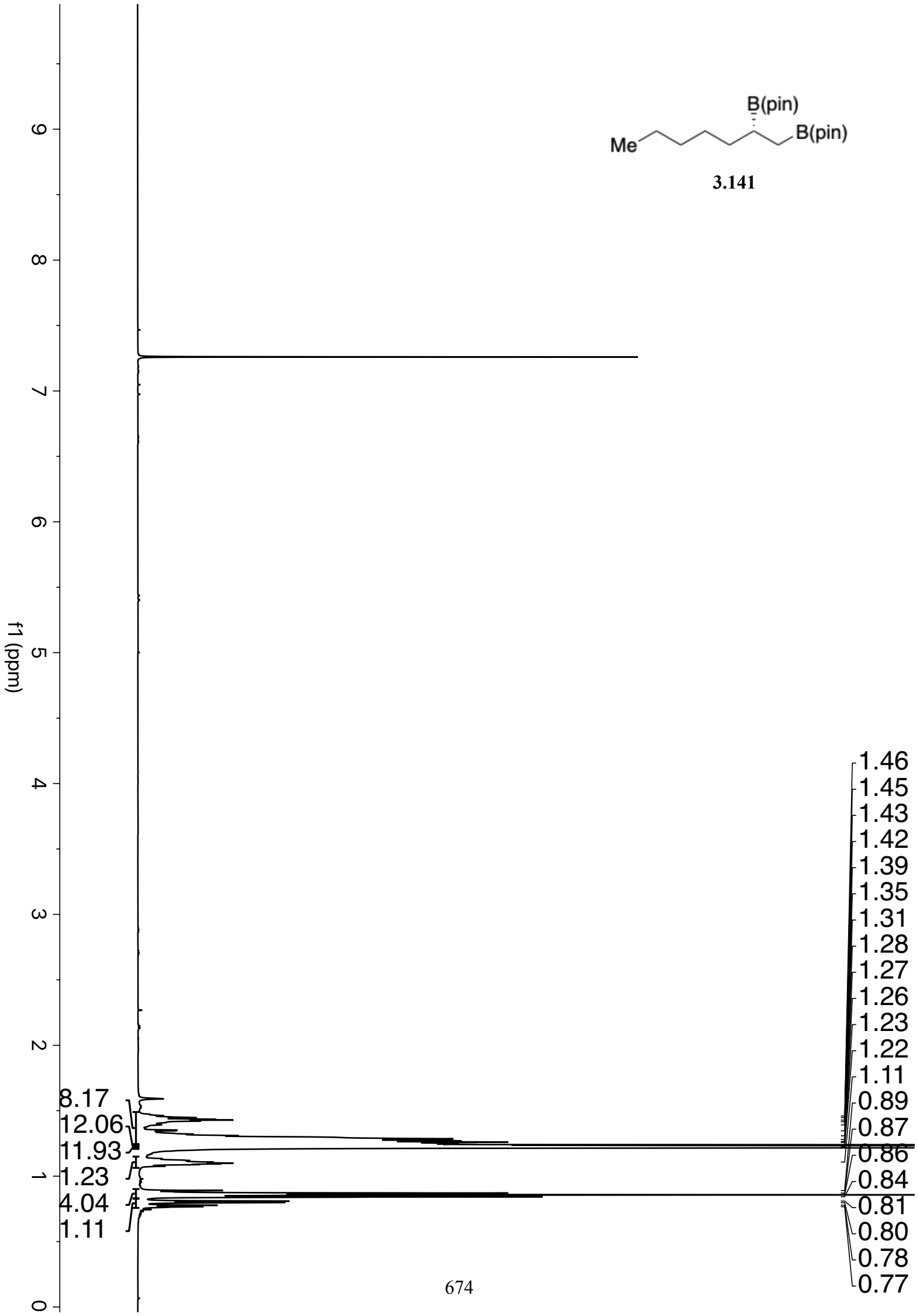

F
B(pin)
B(pin)
3.140
7.23
7.22
7.20
7.13
7.13
7.12
7.11
7.10
7.09
7.01
7.00
6.98
6.96
6.94
6.93
2.85
2.84
2.82
2.81
2.67
2.66
2.65
2.63
1.52
1.51
1.49
1.48
1.46
1.22
1.20
1.18
0.85
0.84
0.83
1.01
1.00
2.01
1.00
1.00
0.99
11.83
11.93
1.95
f1 (ppm)

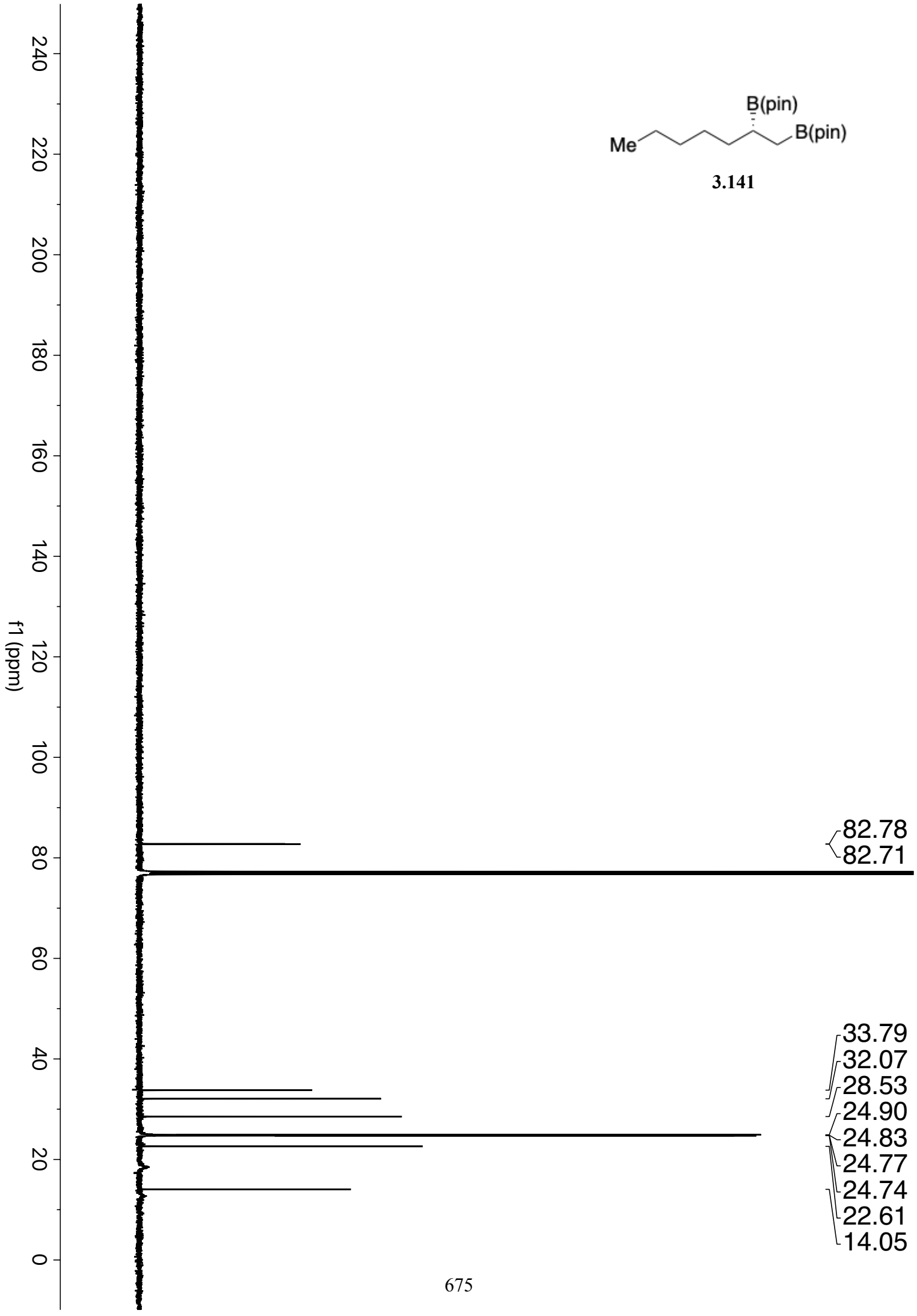

F
B(pin)
B(pin)
3.140
162.31
160.36
131.33
131.29
129.22
129.09
127.14
127.07
123.47
123.44
115.03
114.85
82.96
82.87
32.11
32.09
24.86
24.82
24.78
24.76
f1 (ppm)

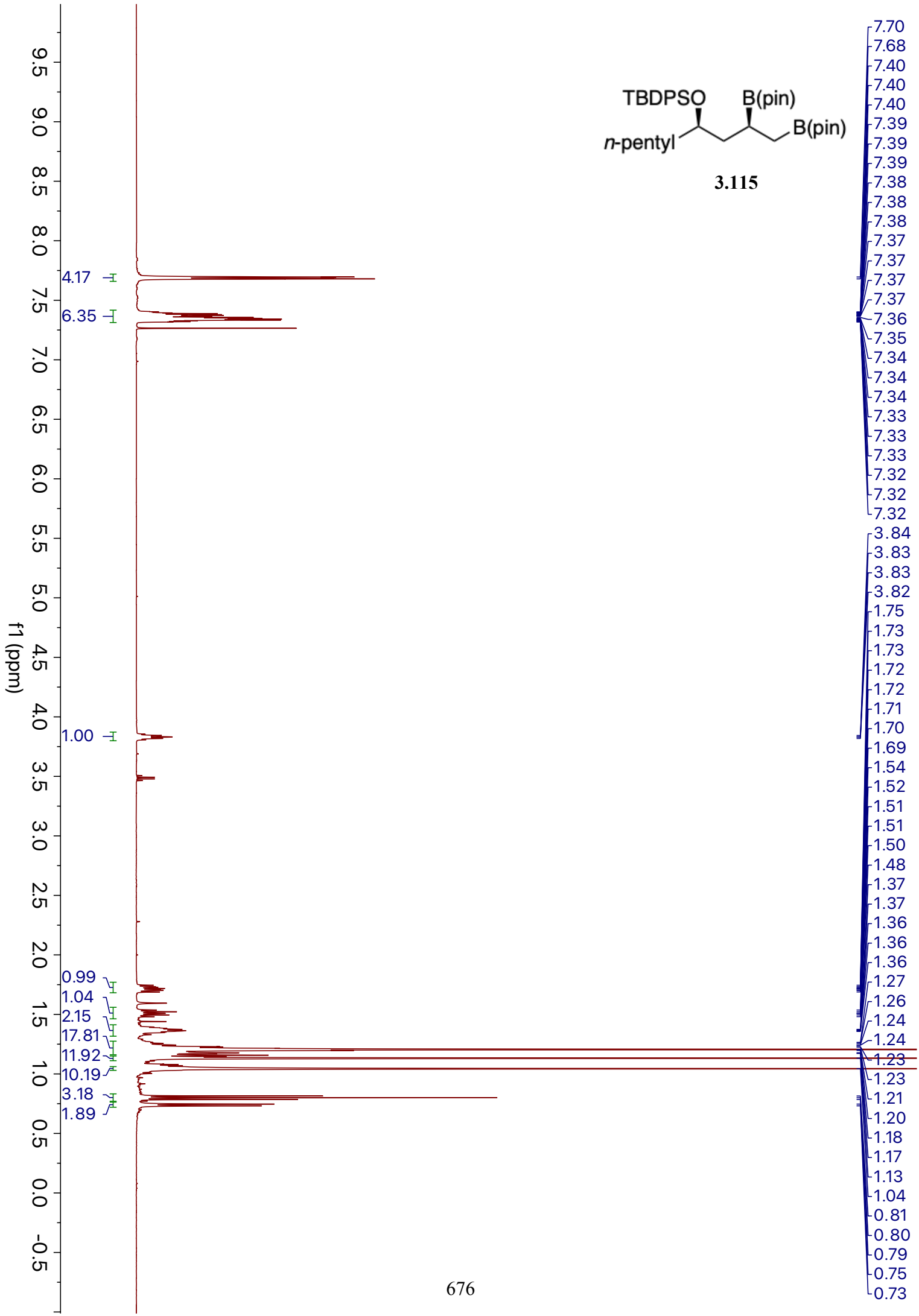

F
B(pin)
B(pin)

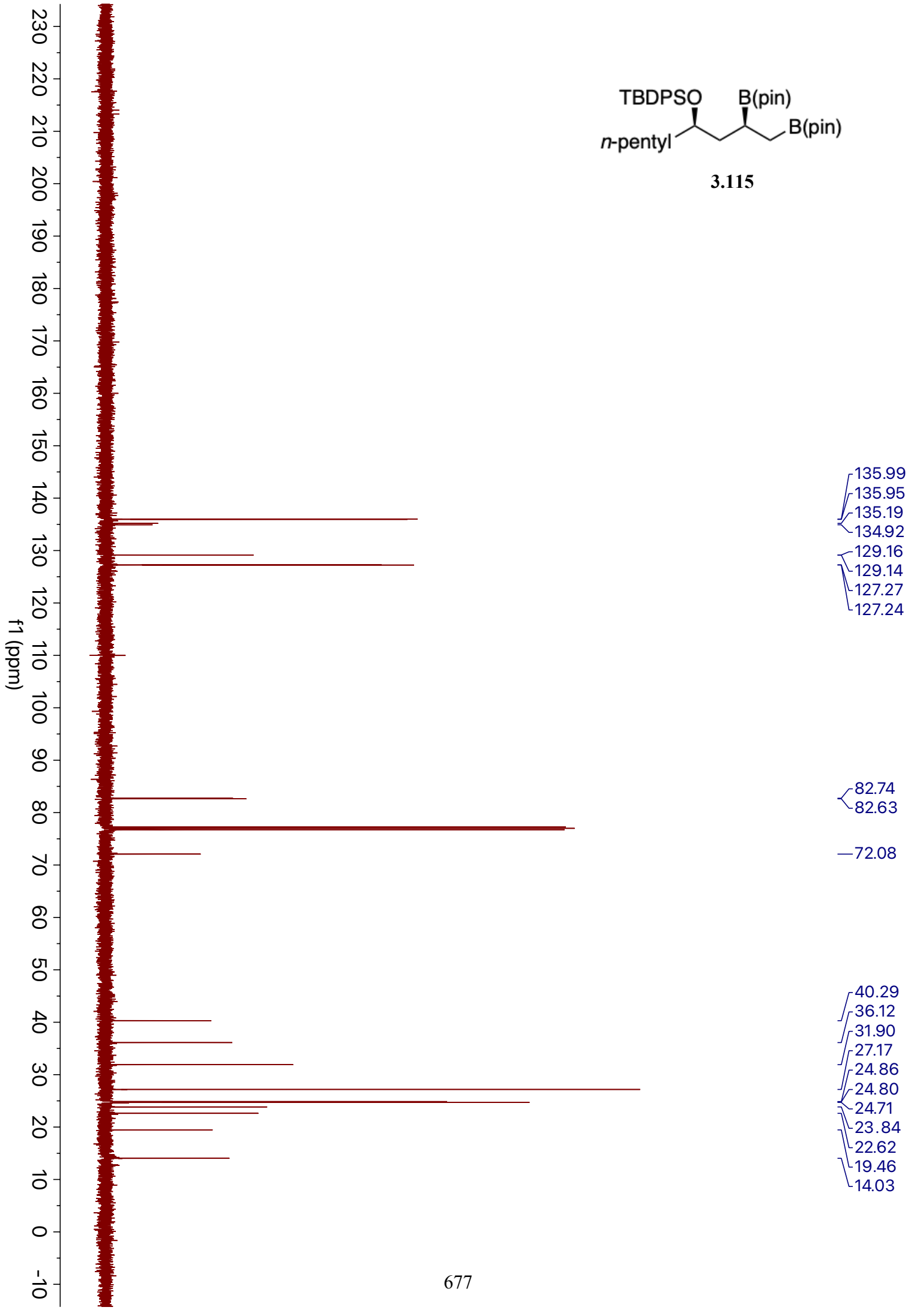
3.140

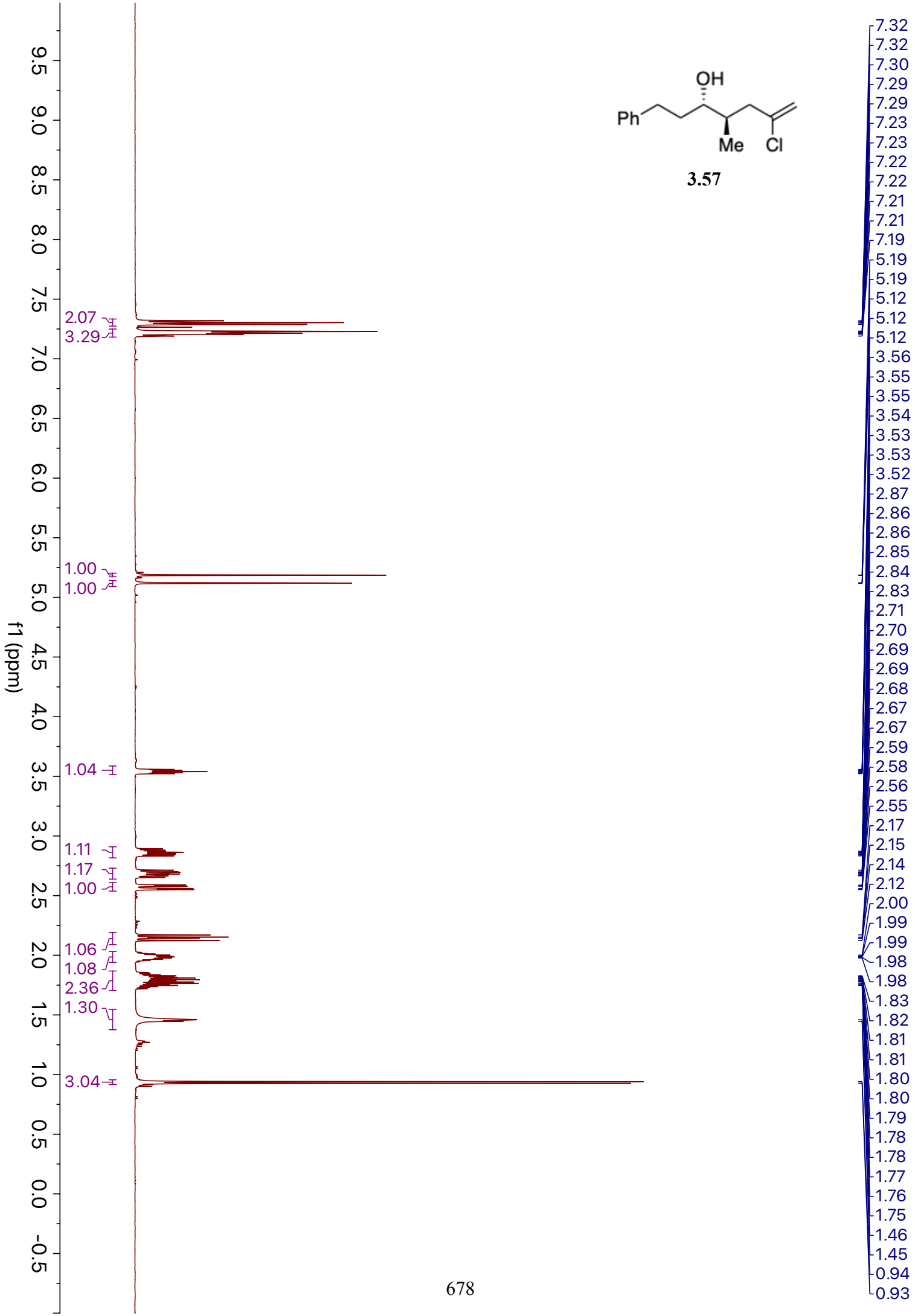
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)
-117.61

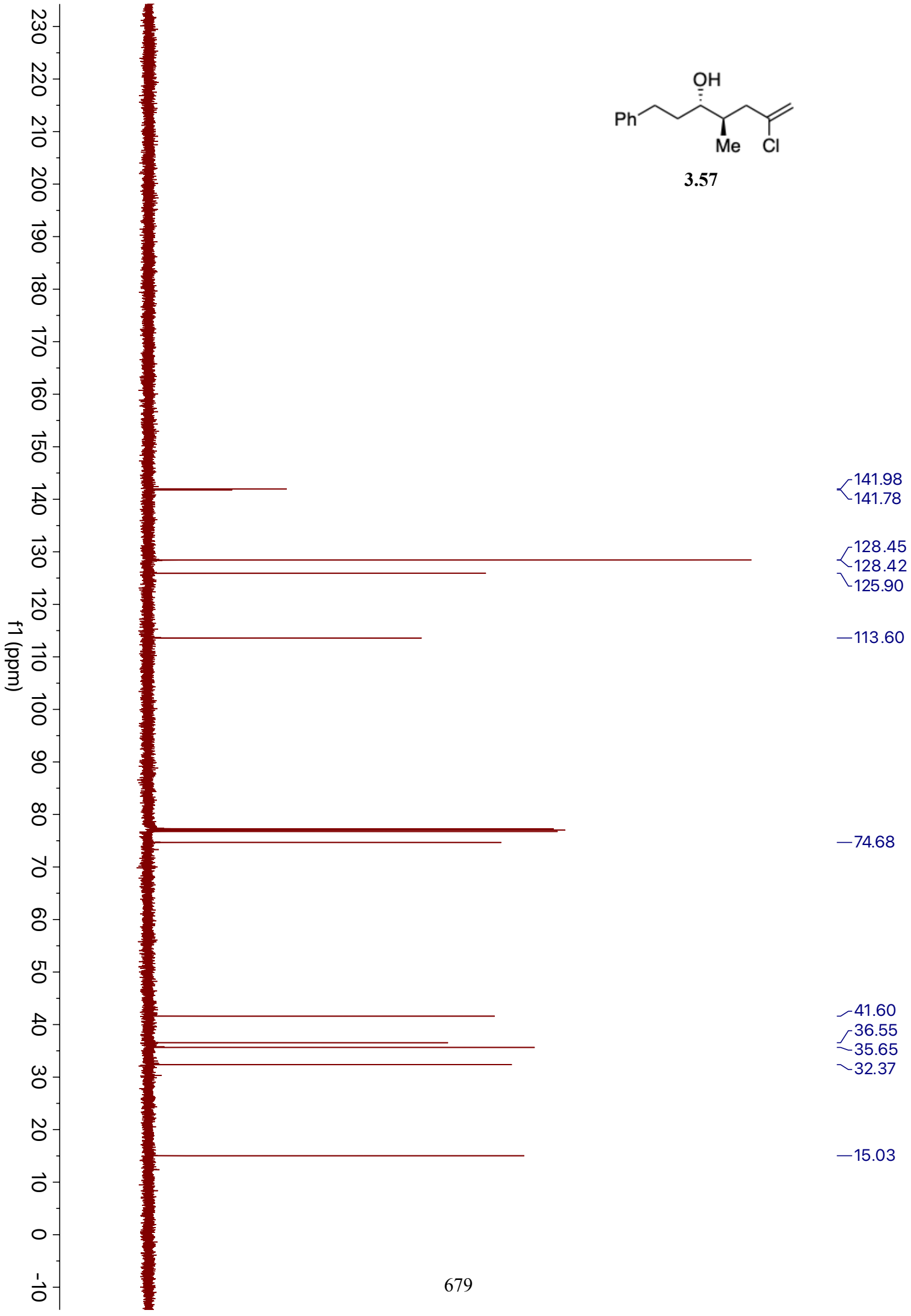

B(pin)
Me
B(pin)
3.141
f1 (ppm)
0
1
2
3
4
5
6
7
8
9
8.17
12.06
11.93
1.23
4.04
1.11
1.46
1.45
1.43
1.42
1.39
1.35
1.31
1.28
1.27
1.26
1.23
1.22
1.11
0.89
0.87
0.86
0.84
0.81
0.80
0.78
0.77

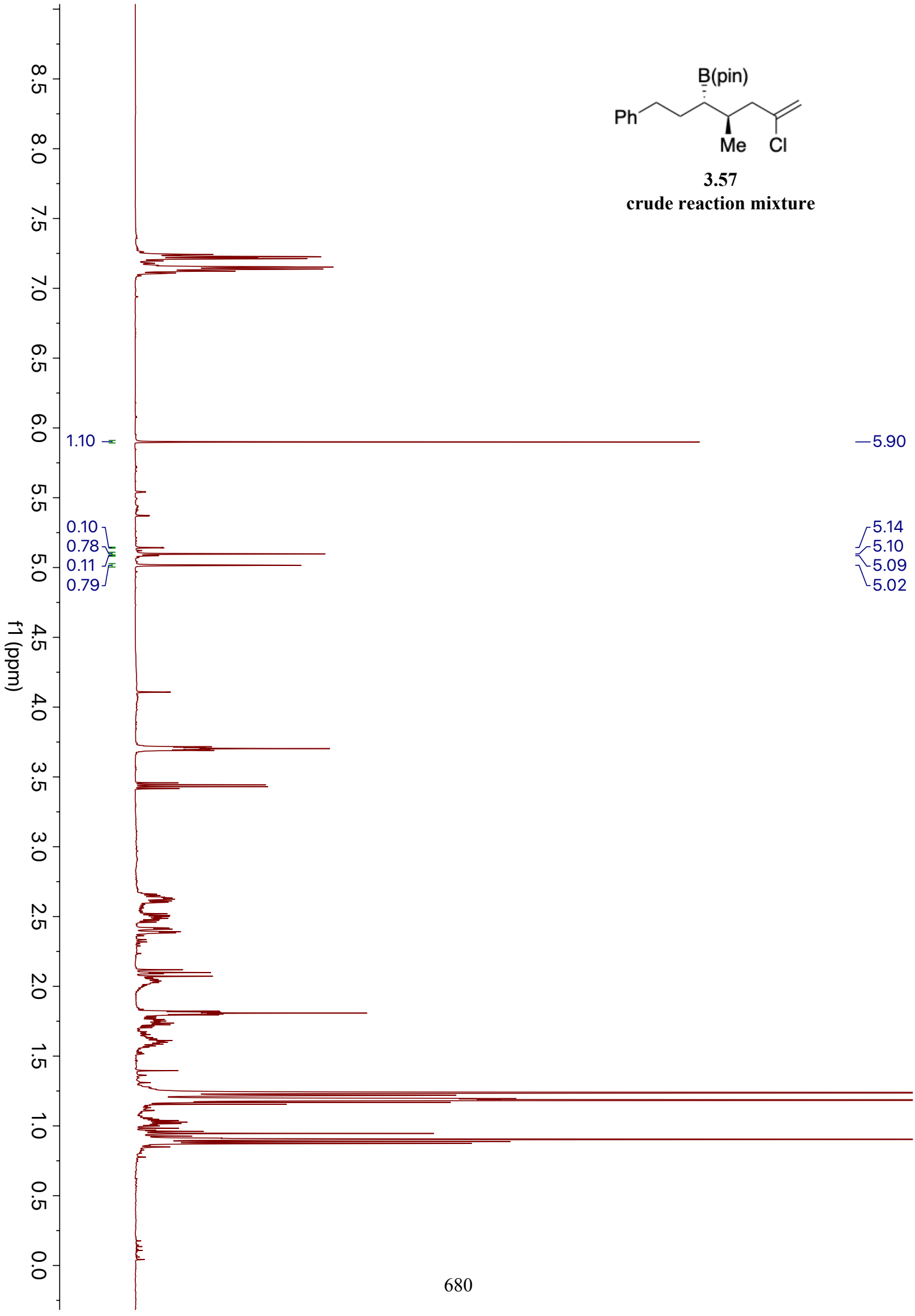

B(pin)
B(pin)
Me
3.141
f1 (ppm)
240
220
200
180
160
140
120
100
80
60
40
20
0
82.78
82.71
33.79
32.07
28.53
24.90
24.83
24.77
24.74
22.61
14.05

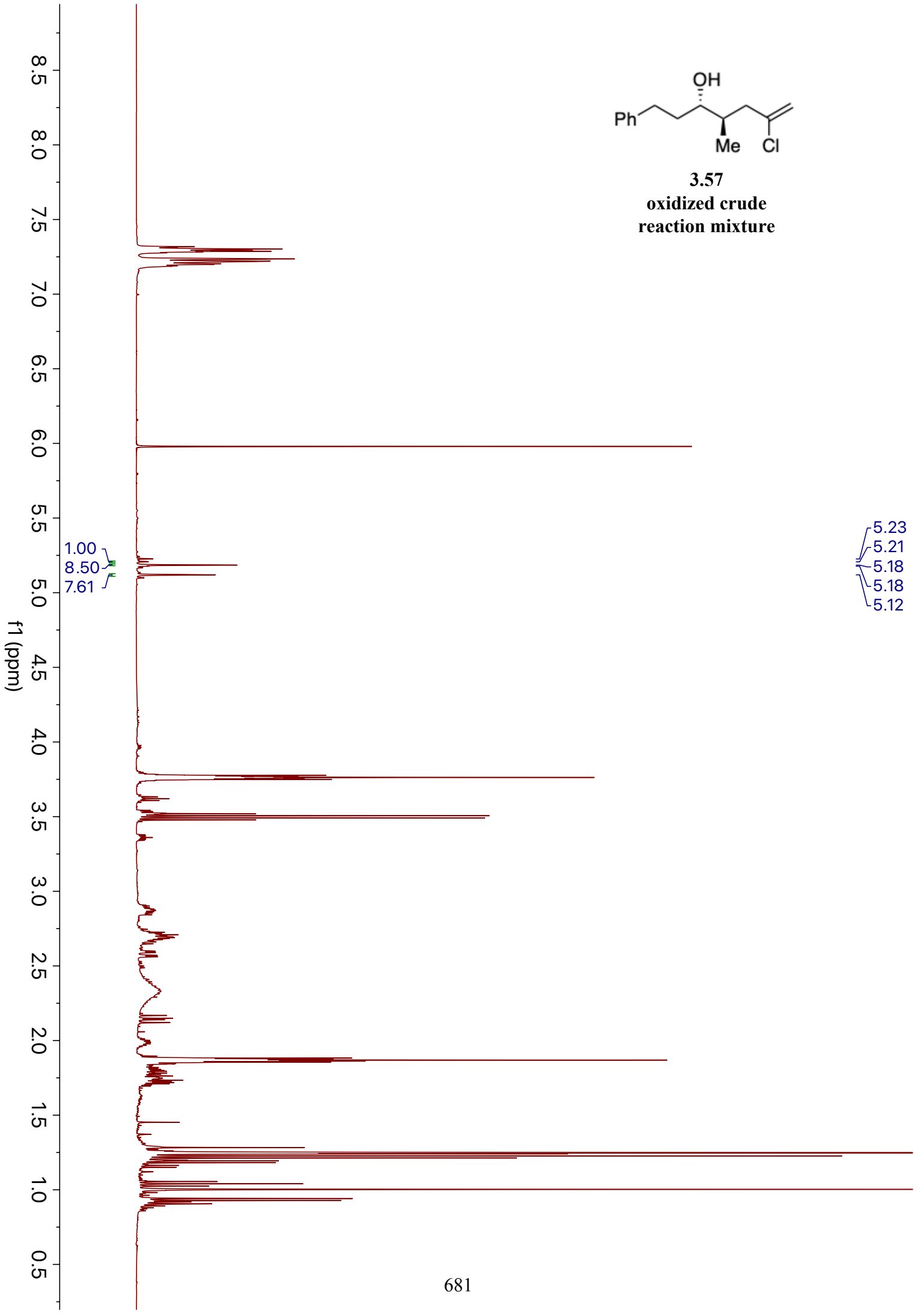

TBDPSO
B(pin)
B(pin)
n-pentyl
3.115
f1 (ppm)
4.17
6.35
1.00
0.99
1.04
2.15
17.81
11.92
10.19
3.18
1.89

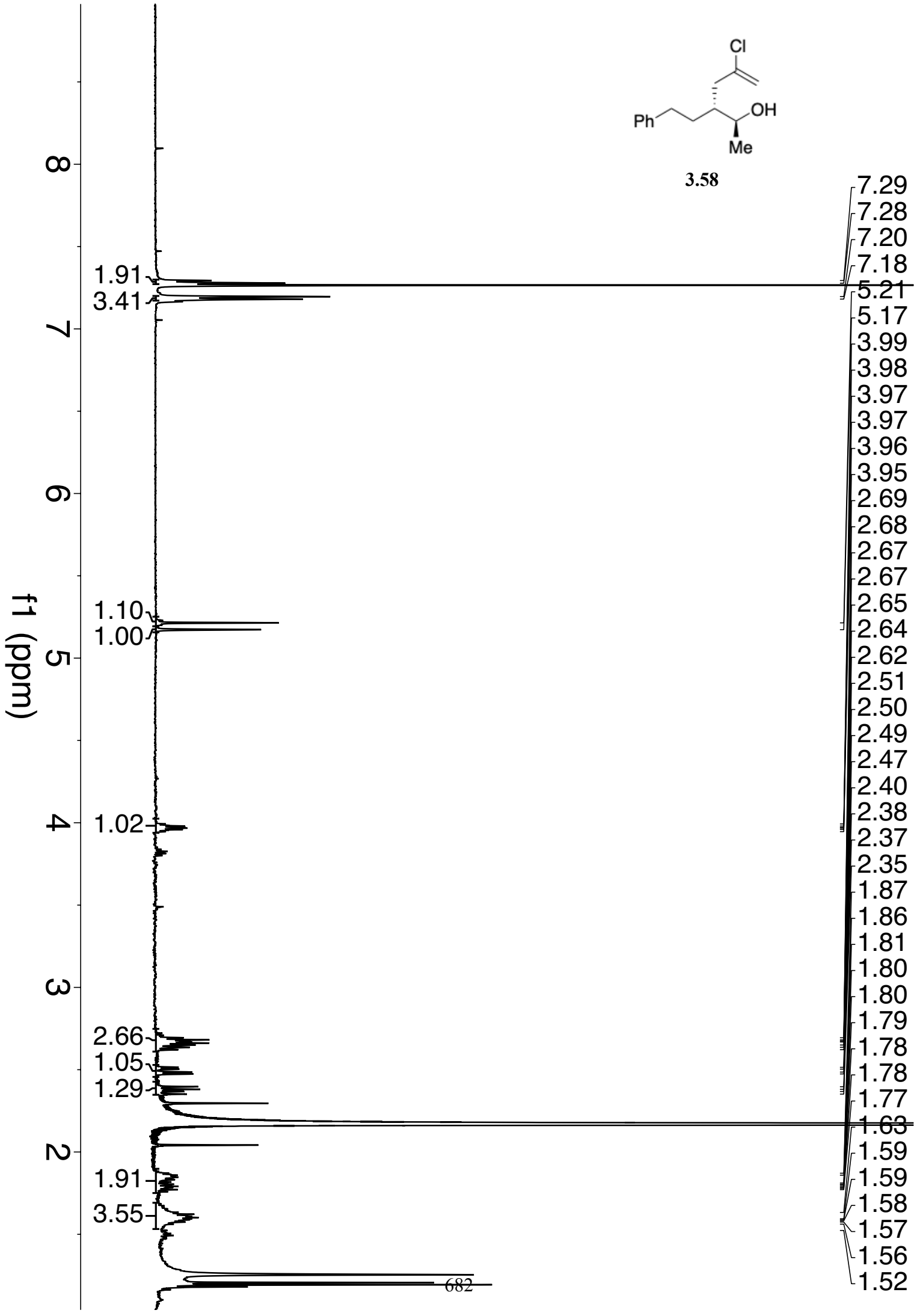

TBDPSO
B(pin)
B(pin)
n-pentyl
3.115
135.99
135.95
135.19
134.92
129.16
129.14
127.27
127.24
82.74
82.63
72.08
40.29
36.12
31.90
27.17
24.86
24.80
24.71
23.84
22.62
19.46
14.03
f1 (ppm)

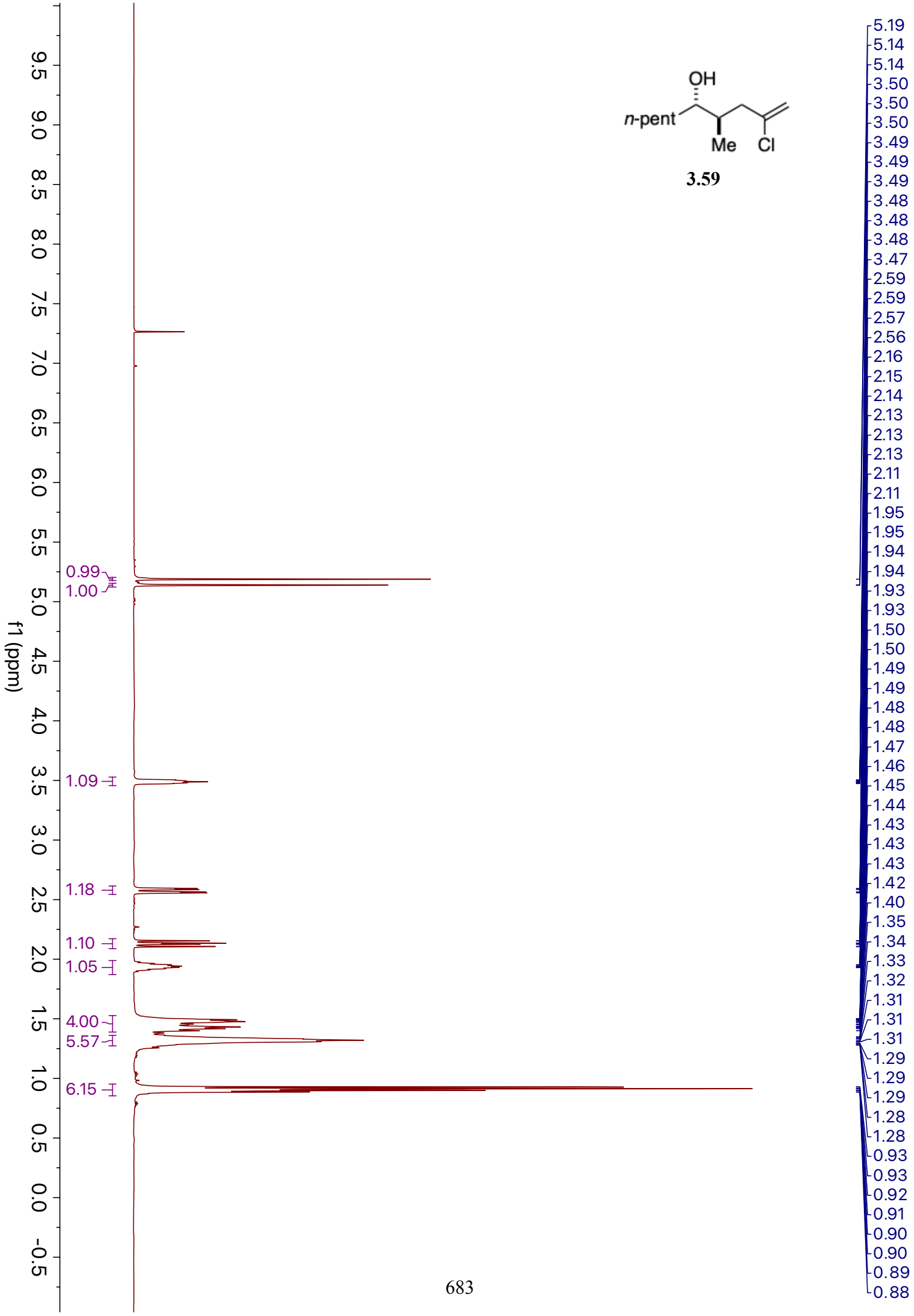

OH
Ph
Me
Cl
3.57
2.07
3.29
1.00
1.00
1.04
1.11
1.17
1.00
1.06
1.08
2.36
1.30
3.04
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
7.32 7.32 7.30 7.29 7.29 7.23 7.23 7.22 7.22 7.21 7.21 7.19 5.19 5.19 5.12 5.12 5.12 3.56 3.55 3.55 3.54 3.53 3.53 3.52 2.87 2.86 2.86 2.85 2.84 2.83 2.71 2.70 2.69 2.69 2.68 2.67 2.67 2.59 2.58 2.56 2.55 2.17 2.15 2.14 2.12 2.00 1.99 1.99 1.98 1.98 1.83 1.82 1.81 1.81 1.80 1.80 1.79 1.78 1.78 1.77 1.76 1.75 1.46 1.45 0.94 0.93

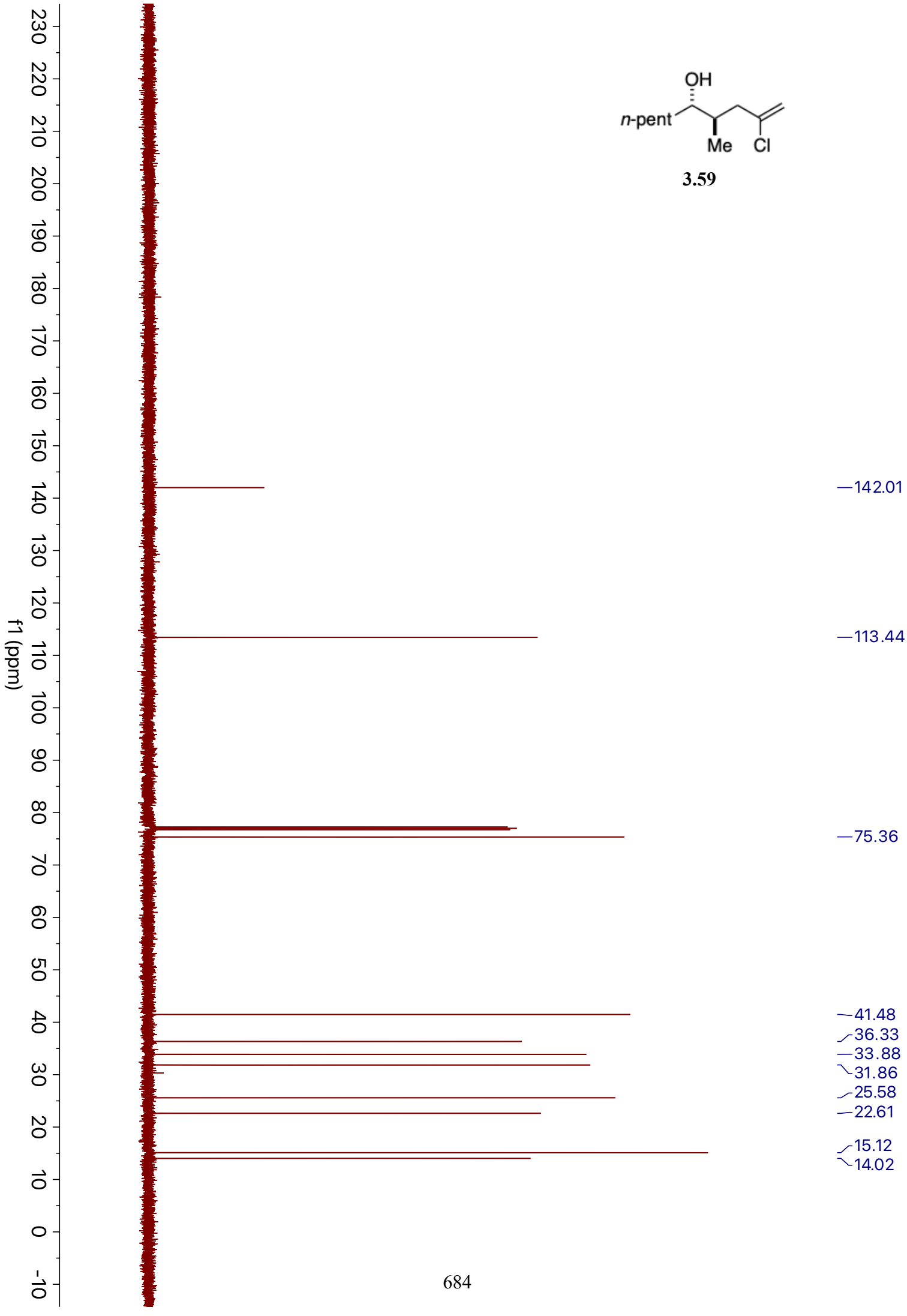

OH
Ph
Me
Cl
3.57
141.98
141.78
128.45
128.42
125.90
113.60
74.68
41.60
36.55
35.65
32.37
15.03
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

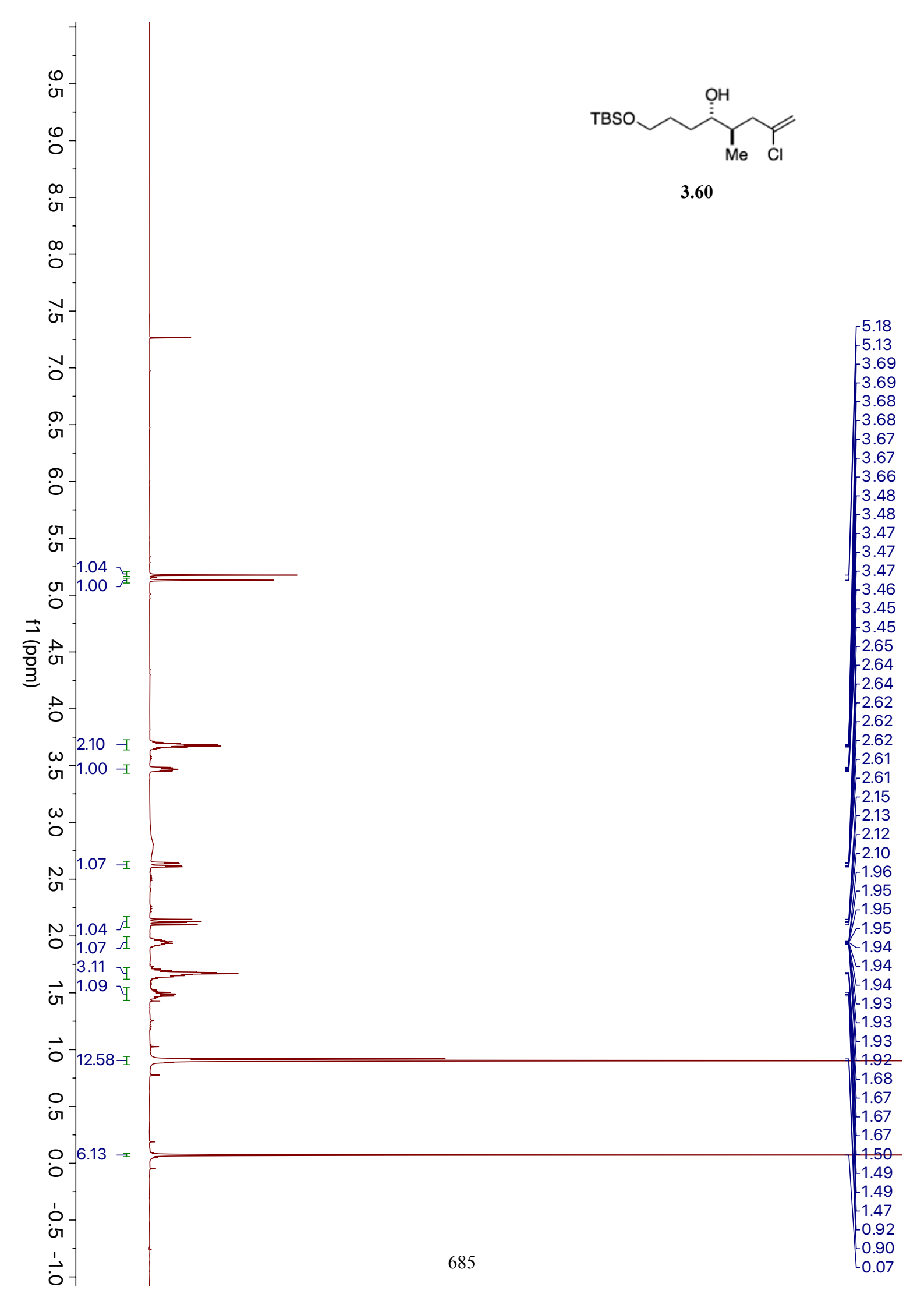

B(pin)
Ph
Me
Cl
3.57
crude reaction mixture
1.10
0.10
0.78
0.11
0.79
5.90
5.14
5.10
5.09
5.02
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

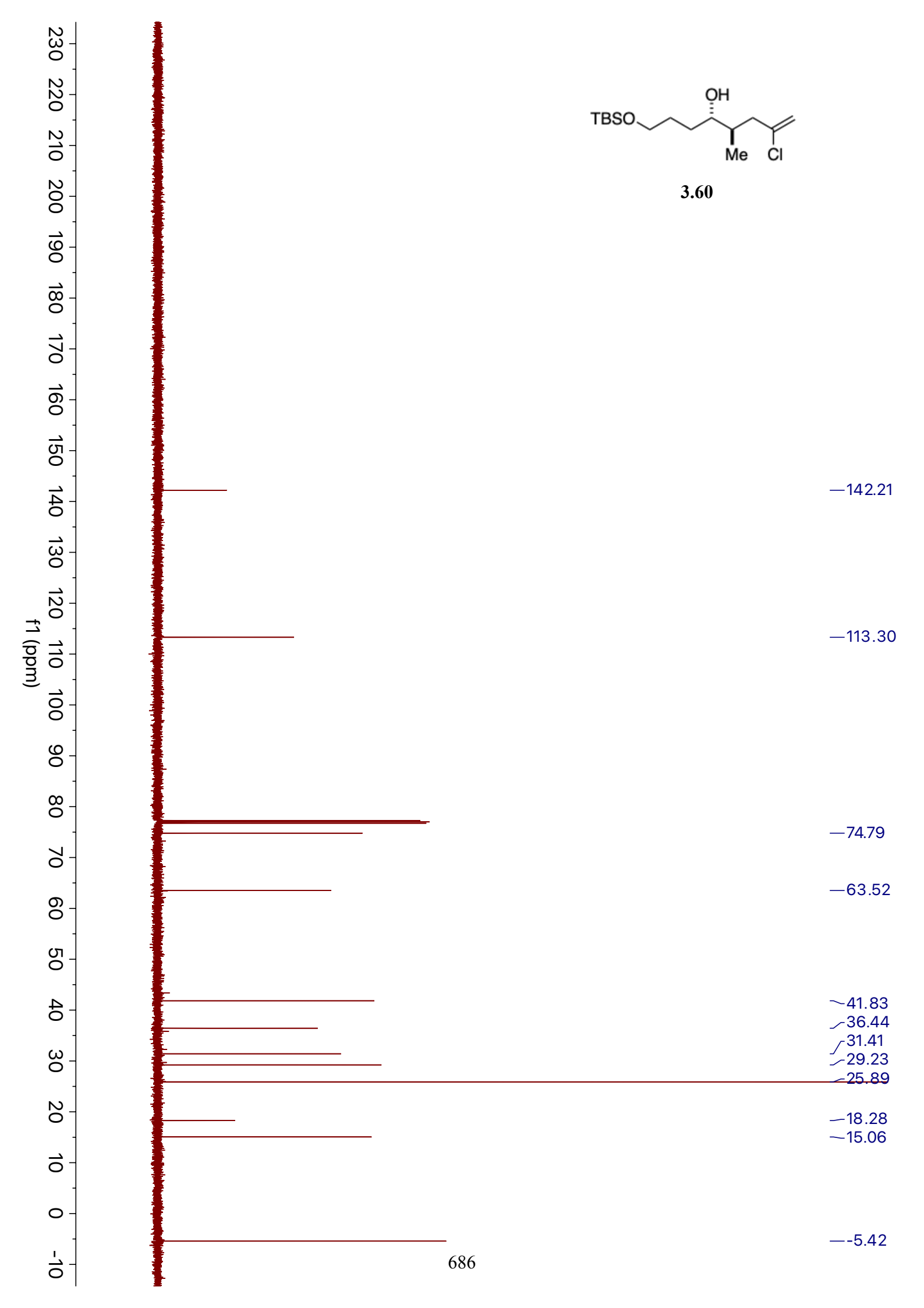

OH
Ph
Me
Cl
3.57
oxidized crude
reaction mixture
1.00
8.50
7.61
5.23
5.21
5.18
5.18
5.12
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

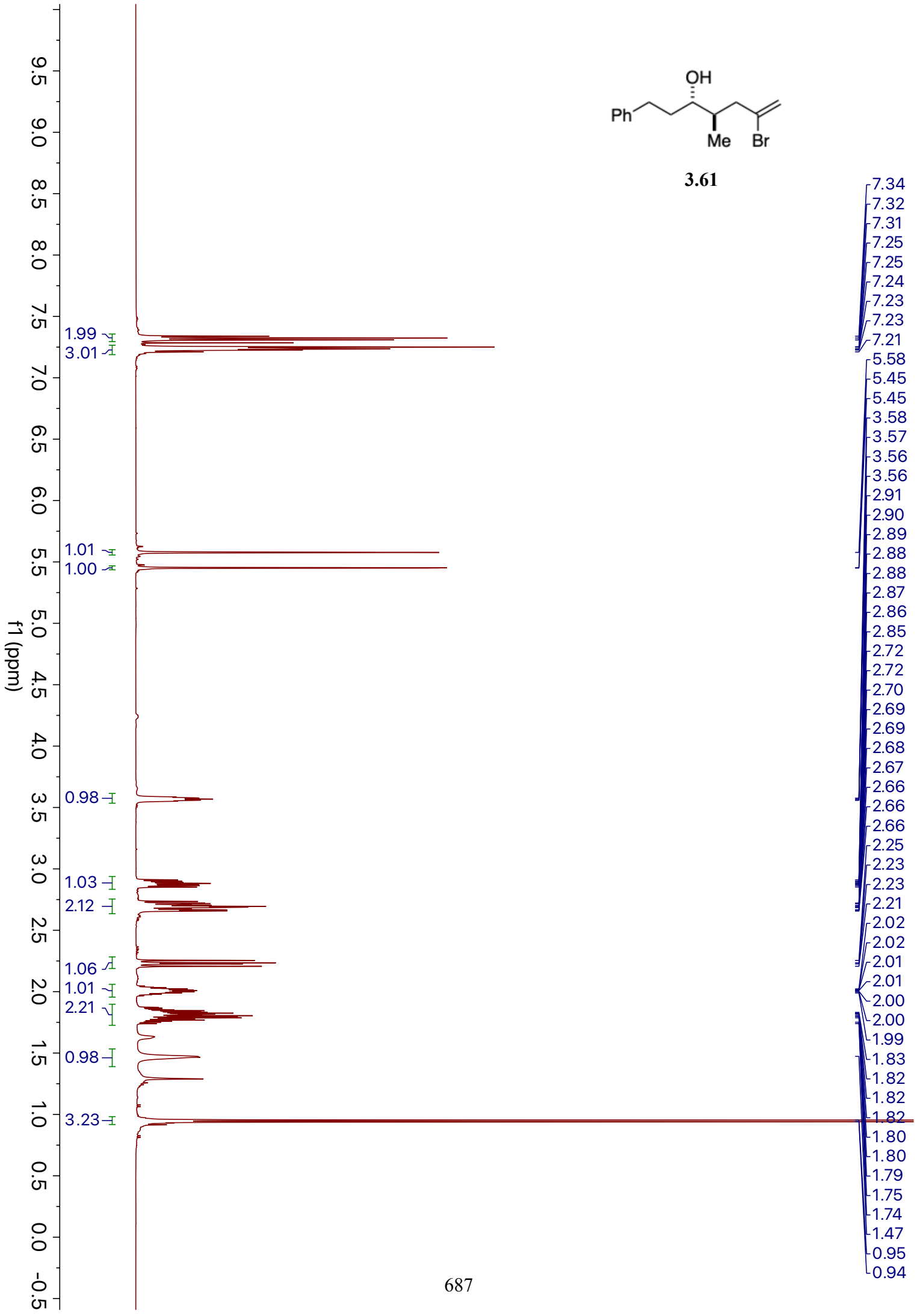

Cl
Ph
OH
Me
3.58
f1 (ppm)
8
7
6
5
4
3
2
1.91
3.41
1.10
1.00
1.02
2.66
1.05
1.29
1.91
3.55
7.29
7.28
7.20
7.18
5.21
5.17
3.99
3.98
3.97
3.97
3.96
3.95
2.69
2.68
2.67
2.67
2.65
2.64
2.62
2.51
2.50
2.49
2.47
2.40
2.38
2.37
2.35
1.87
1.86
1.81
1.80
1.80
1.79
1.78
1.78
1.77
1.63
1.59
1.59
1.58
1.57
1.56
1.52

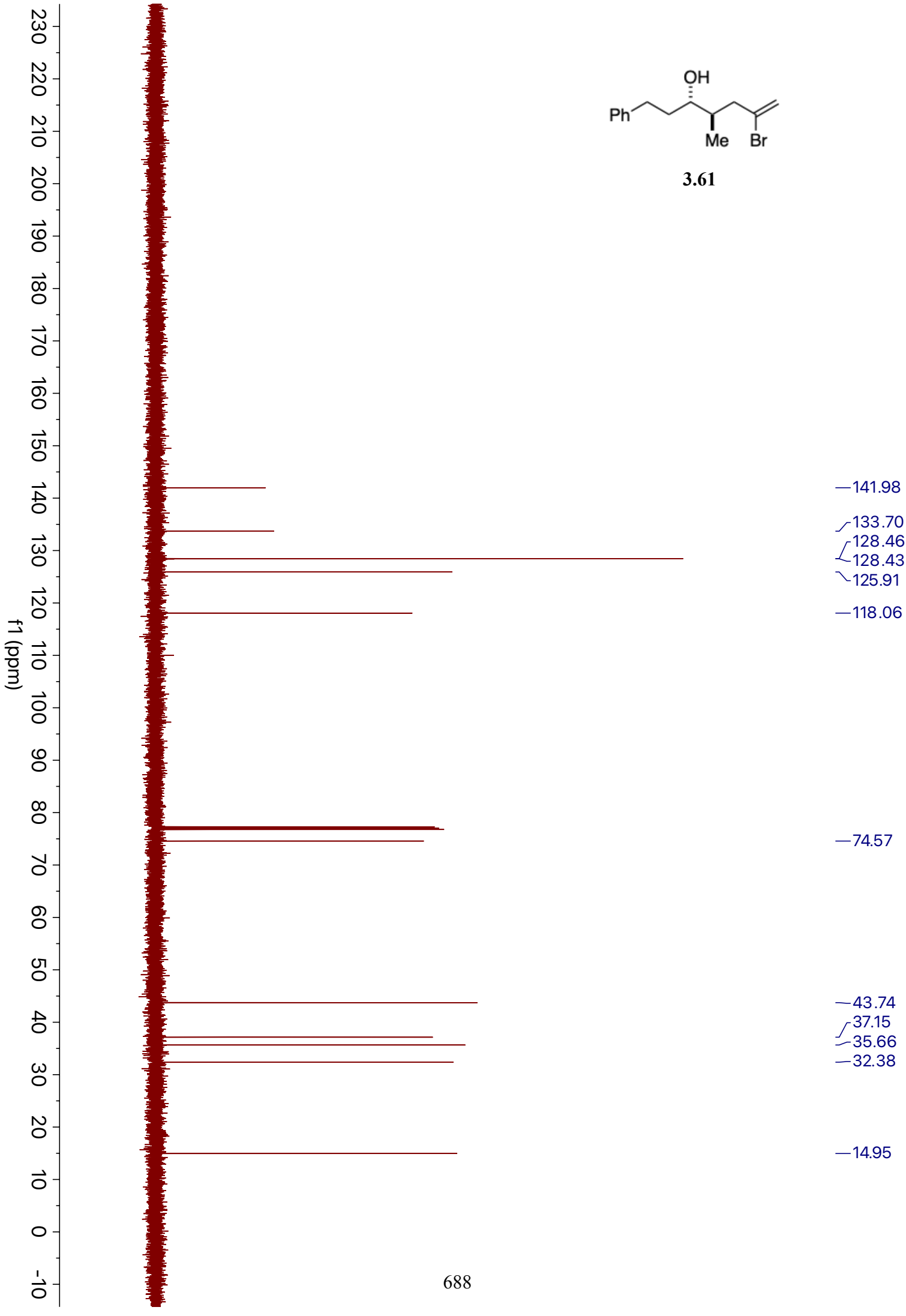

OH
n-pent
Me
Cl
3.59
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
0.99
1.00
1.09
1.18
1.10
1.05
4.00
5.57
6.15
5.19 5.14 5.14 3.50 3.50 3.50 3.49 3.49 3.49 3.48 3.48 3.48 3.47 2.59 2.59 2.57 2.56 2.16 2.15 2.14 2.13 2.13 2.13 2.11 2.11 1.95 1.95 1.94 1.94 1.93 1.93 1.50 1.50 1.49 1.49 1.48 1.48 1.47 1.46 1.45 1.44 1.43 1.43 1.43 1.42 1.40 1.35 1.34 1.33 1.32 1.31 1.31 1.31 1.29 1.29 1.29 1.28 1.28 0.93 0.93 0.92 0.91 0.90 0.90 0.89 0.88

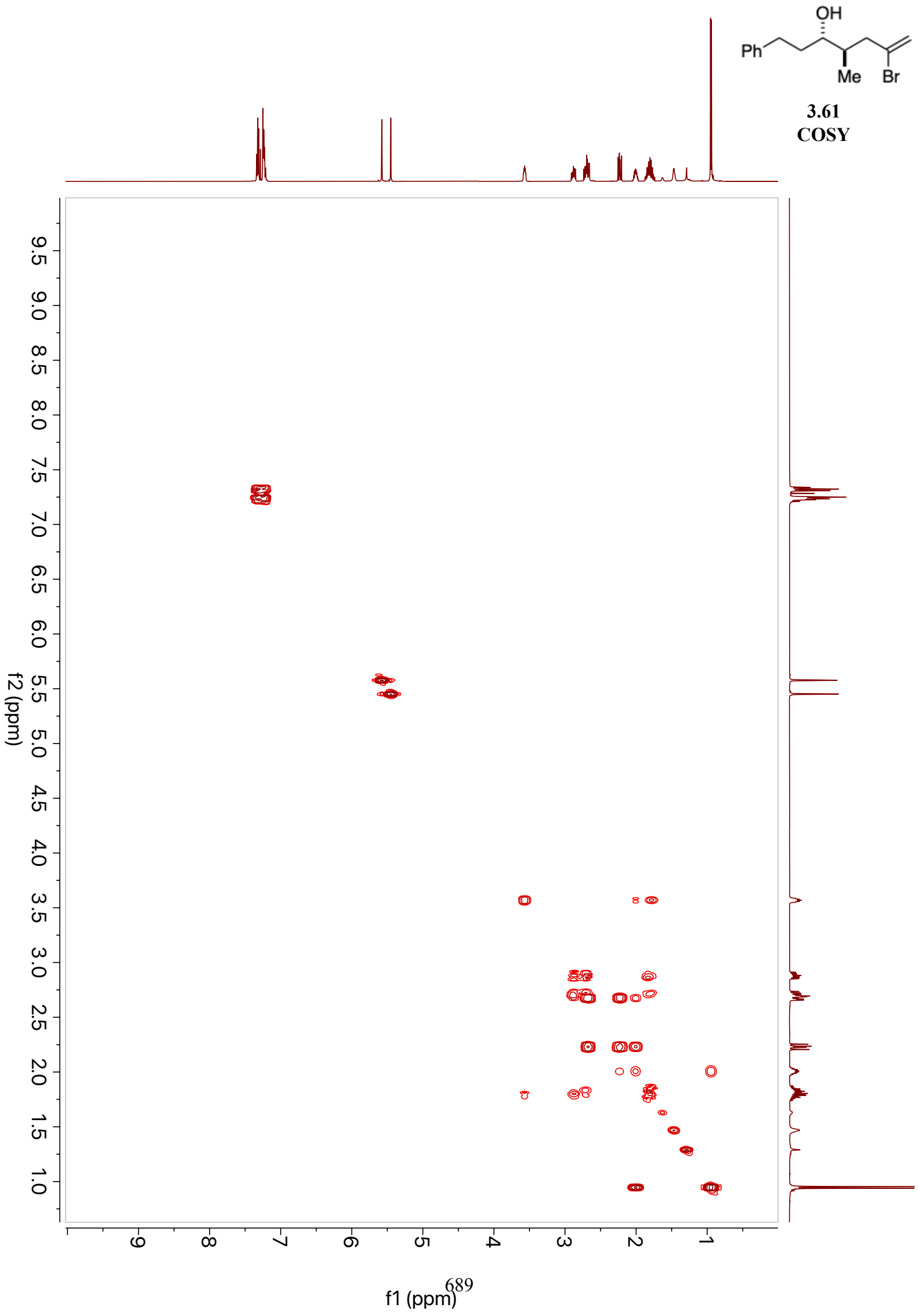

OH
n-pent
Me
Cl
3.59
142.01
113.44
75.36
41.48
36.33
33.88
31.86
25.58
22.61
15.12
14.02
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

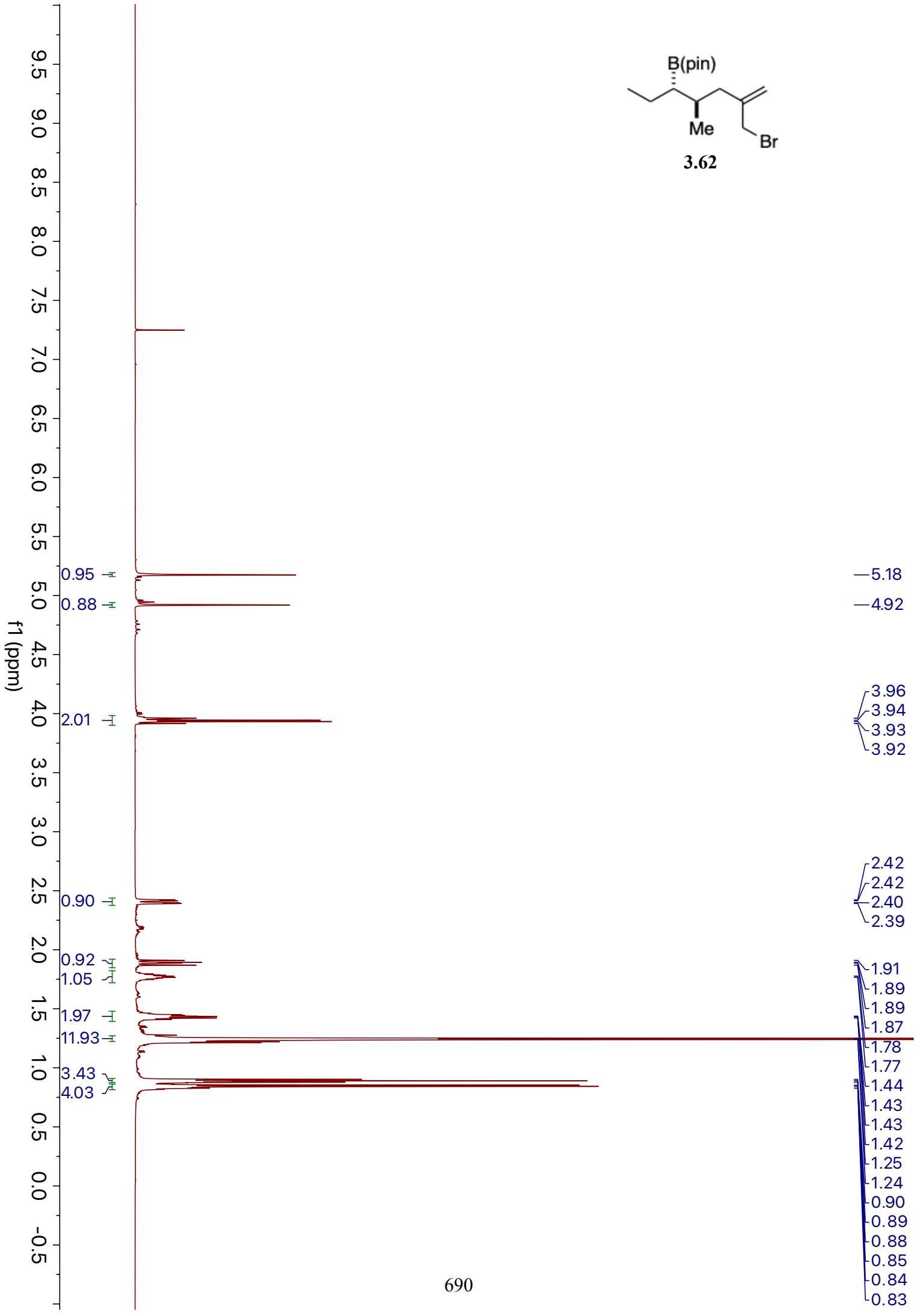

OH
TBSO
Me
Cl
3.60
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1.04
1.00
2.10
1.00
1.07
1.04
1.07
3.11
1.09
12.58
6.13
5.18
5.13
3.69
3.69
3.68
3.68
3.67
3.67
3.66
3.48
3.48
3.47
3.47
3.47
3.46
3.45
3.45
2.65
2.64
2.64
2.62
2.62
2.62
2.61
2.61
2.15
2.13
2.12
2.10
1.96
1.95
1.95
1.95
1.94
1.94
1.94
1.93
1.93
1.93
1.92
1.68
1.67
1.67
1.67
1.50
1.49
1.49
1.47
0.92
0.90
0.07

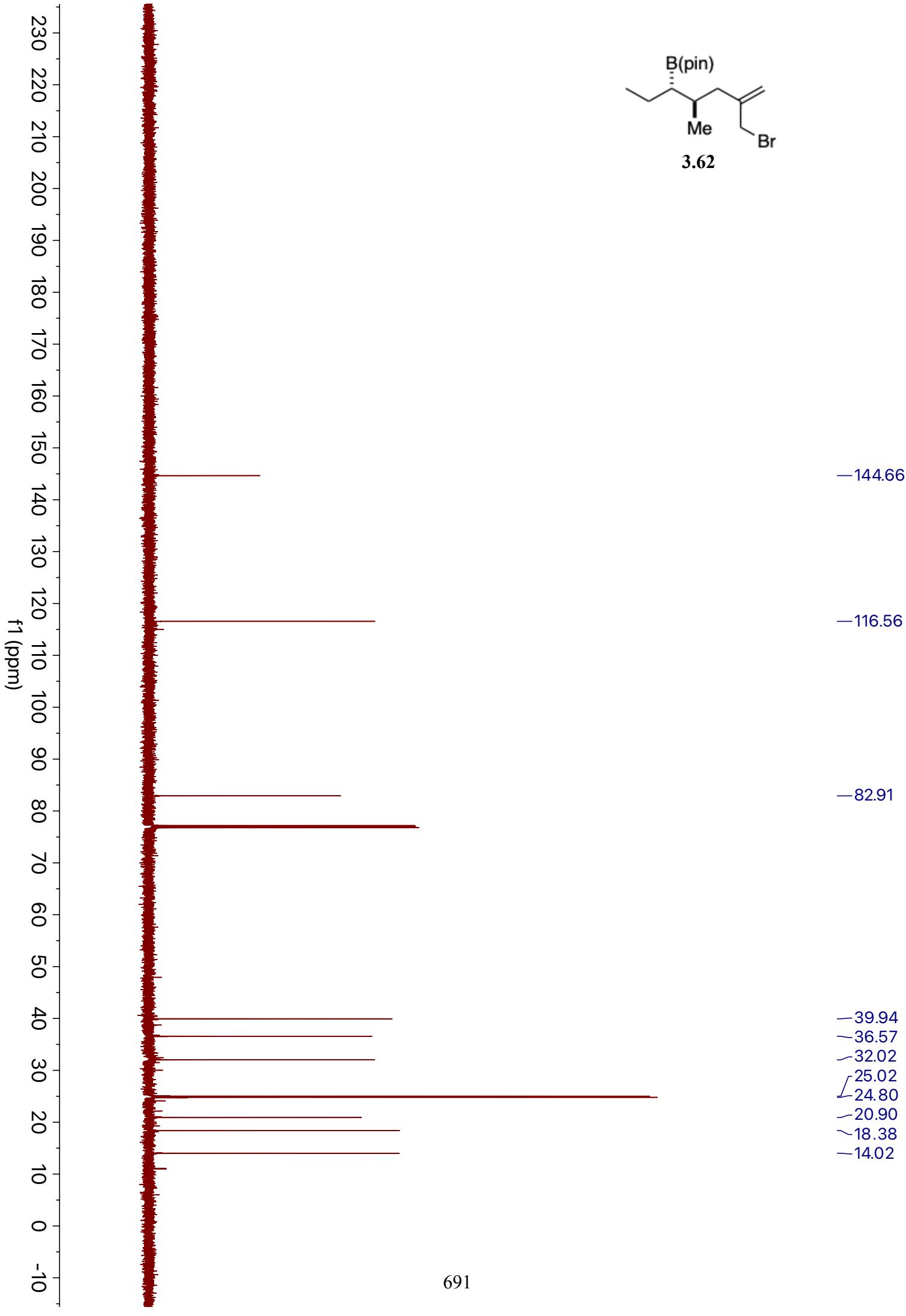

OH
TBSO
Me
Cl
3.60
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
142.21
113.30
74.79
63.52
41.83
36.44
31.41
29.23
25.89
18.28
15.06
-5.42

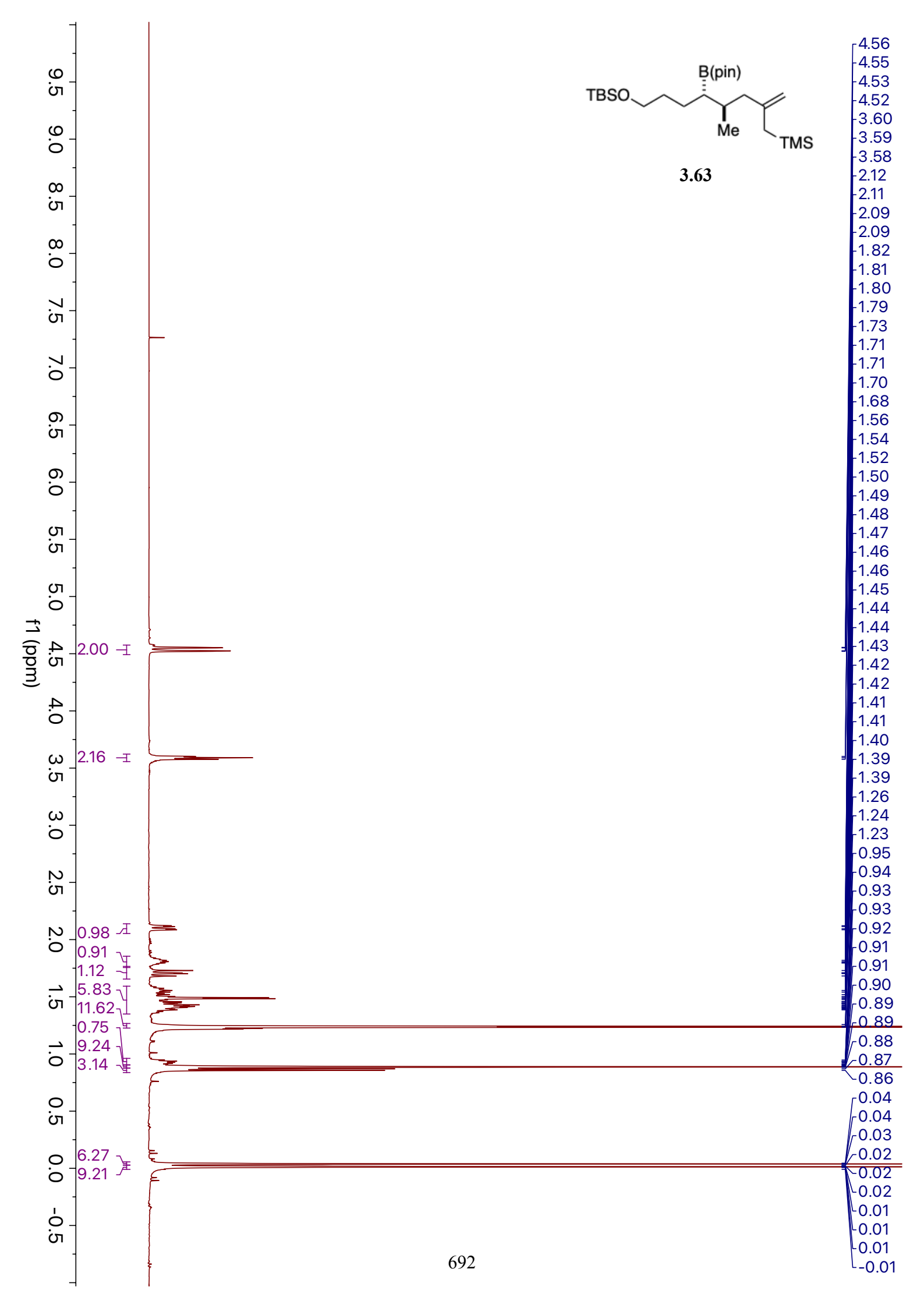

OH
Ph
Me
Br
3.61
f1 (ppm)
1.99
3.01
1.01
1.00
0.98
1.03
2.12
1.06
1.01
2.21
0.98
3.23
7.34
7.32
7.31
7.25
7.25
7.24
7.23
7.23
7.21
5.58
5.45
5.45
3.58
3.57
3.56
3.56
2.91
2.90
2.89
2.88
2.88
2.87
2.86
2.85
2.72
2.72
2.70
2.69
2.69
2.68
2.67
2.66
2.66
2.66
2.25
2.23
2.23
2.21
2.02
2.02
2.01
2.01
2.00
2.00
1.99
1.83
1.82
1.82
1.82
1.80
1.80
1.79
1.75
1.74
1.47
0.95
0.94

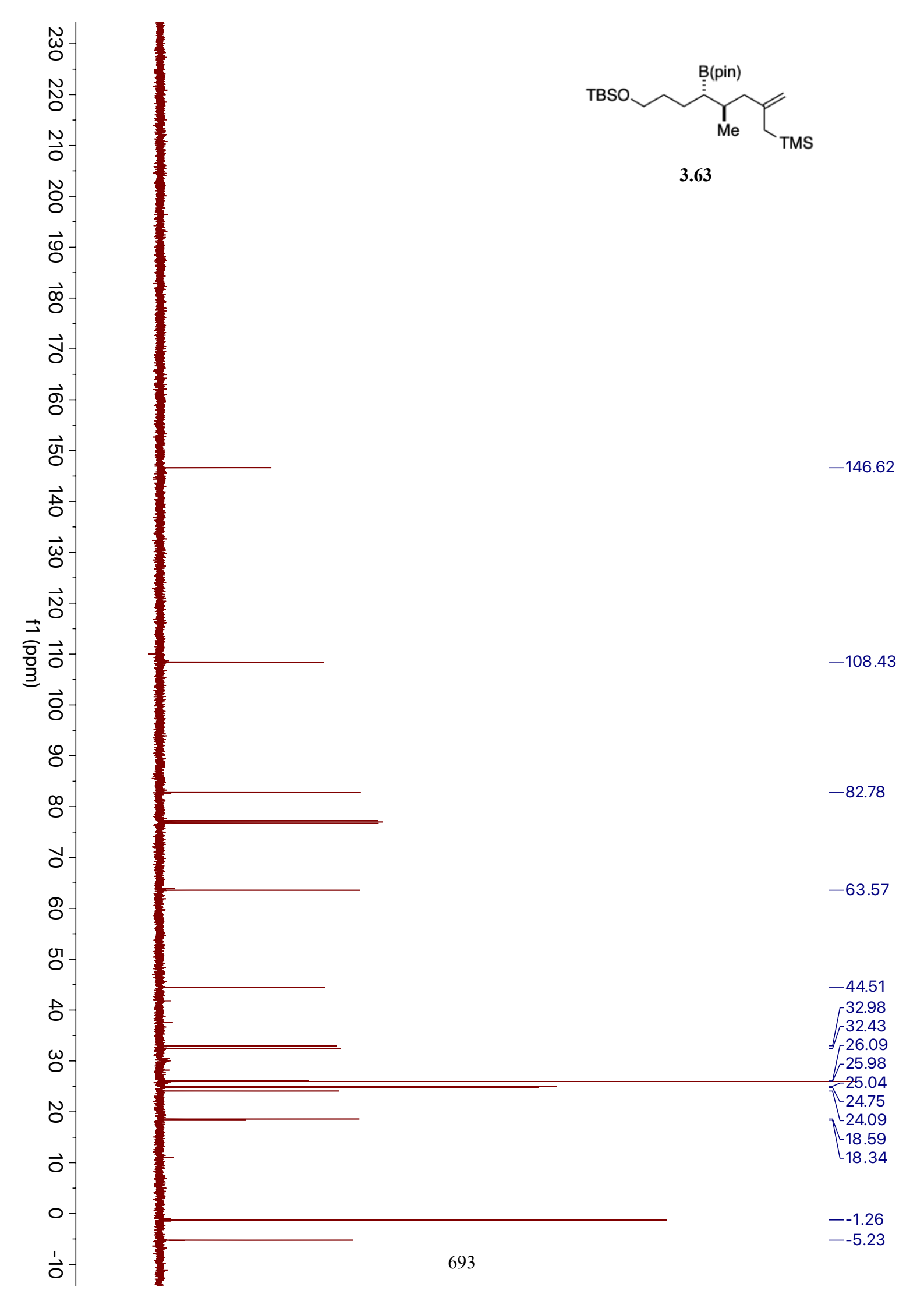

OH
Ph
Me
Br
3.61
141.98
133.70
128.46
128.43
125.91
118.06
74.57
43.74
37.15
35.66
32.38
14.95
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

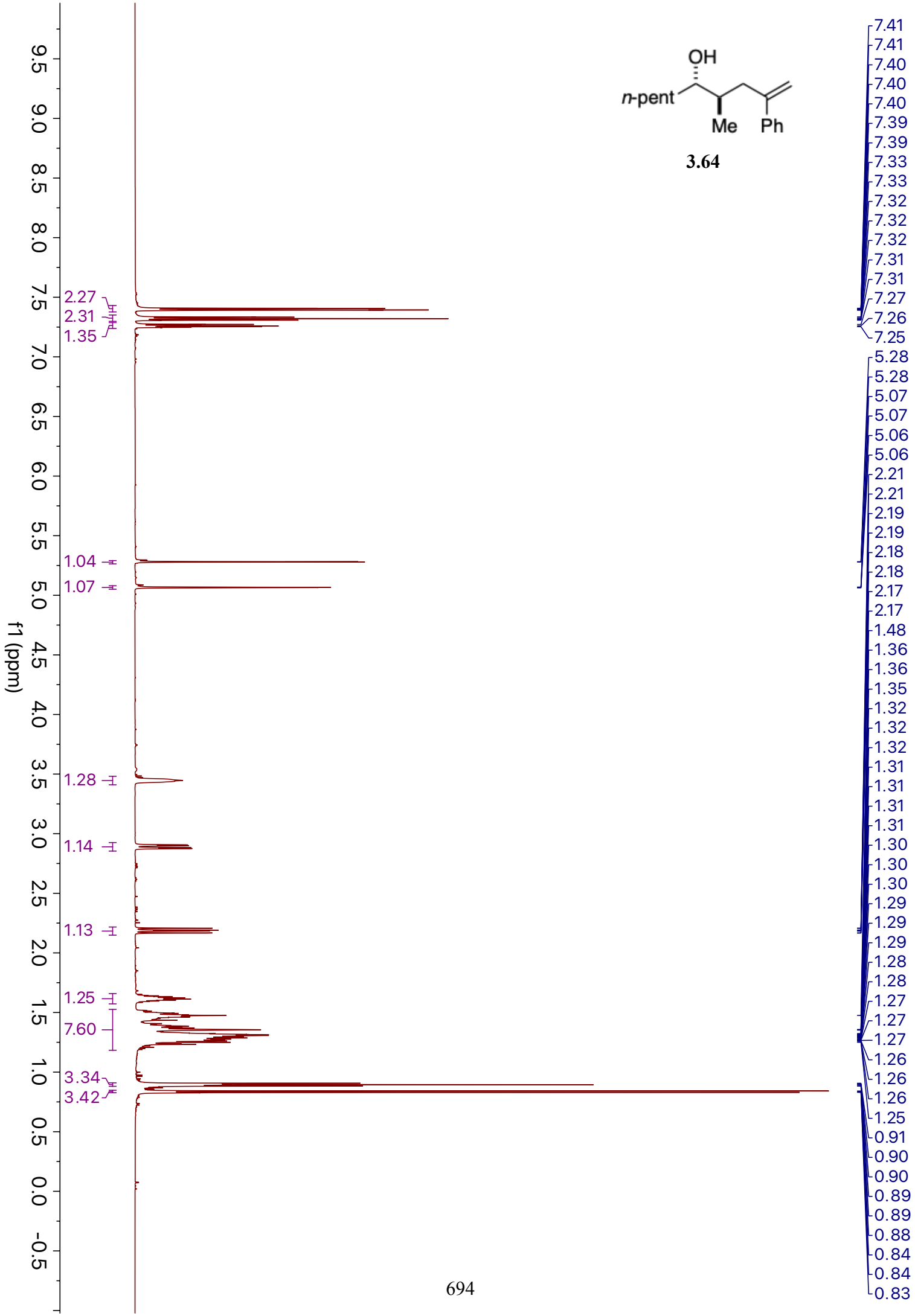

OH
Ph
Me
Br
3.61
COSY
f2 (ppm)
f1 (ppm)

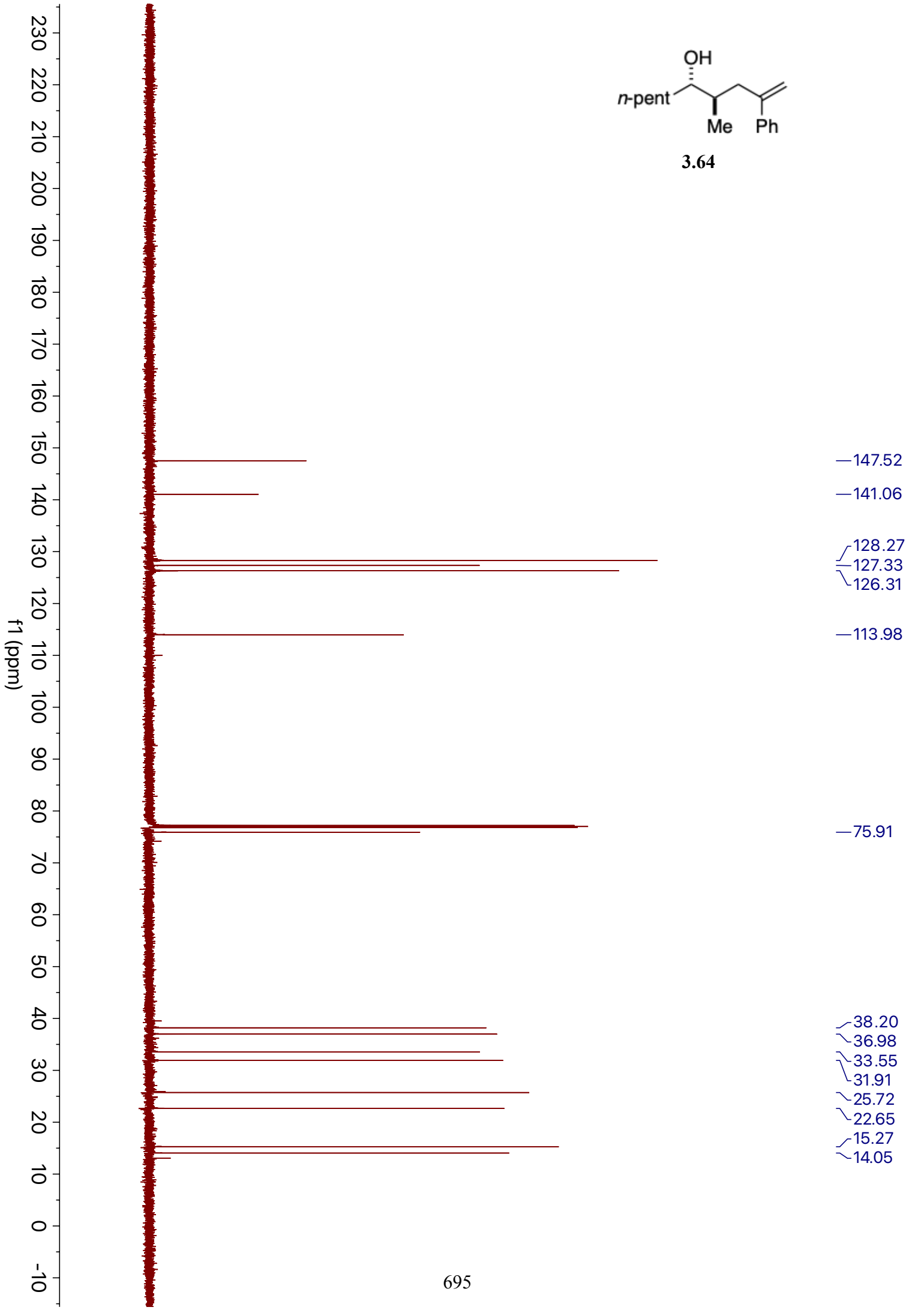

B(pin)
Me
Br
3.62
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0.95
0.88
2.01
0.90
0.92
1.05
1.97
11.93
3.43
4.03
5.18
4.92
3.96
3.94
3.93
3.92
2.42
2.42
2.40
2.39
1.91
1.89
1.89
1.87
1.78
1.77
1.44
1.43
1.43
1.42
1.25
1.24
0.90
0.89
0.88
0.85
0.84
0.83

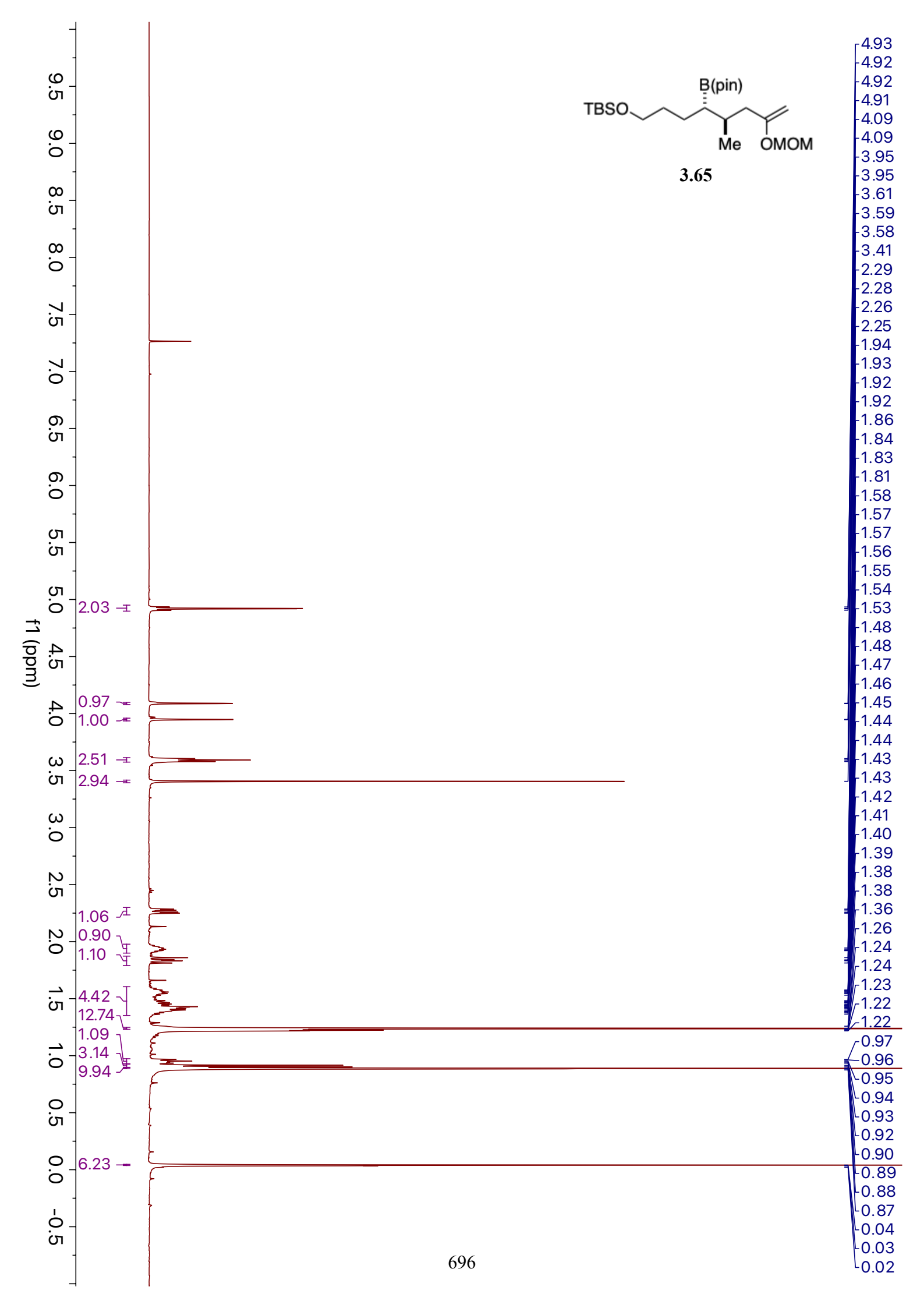

B(pin)
Me
Br
3.62
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
144.66
116.56
82.91
39.94
36.57
32.02
25.02
24.80
20.90
18.38
14.02

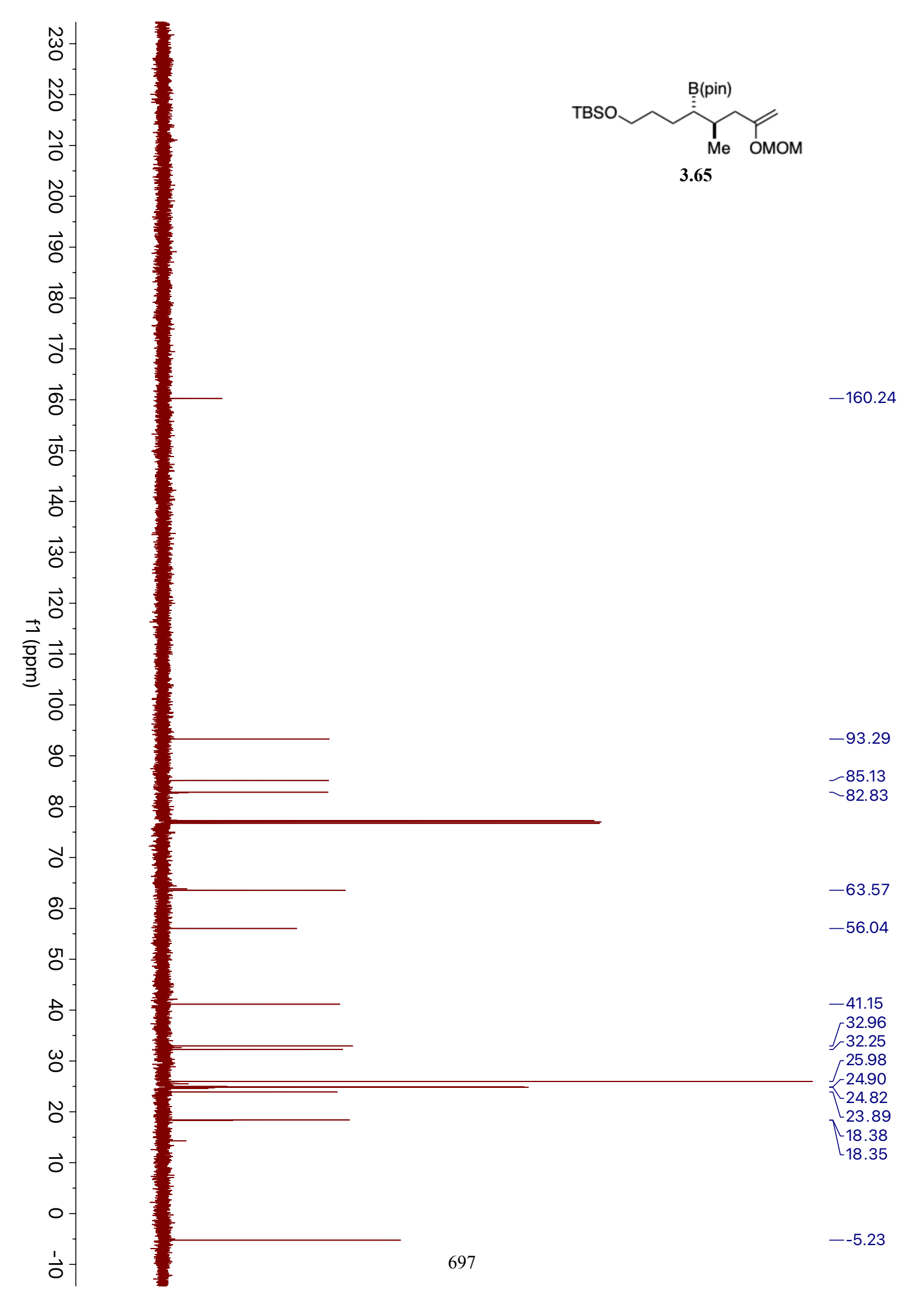

B(pin)
TBSO
Me
TMS
3.63
f1 (ppm)
2.00
2.16
0.98
0.91
1.12
5.83
11.62
0.75
9.24
3.14
6.27
9.21

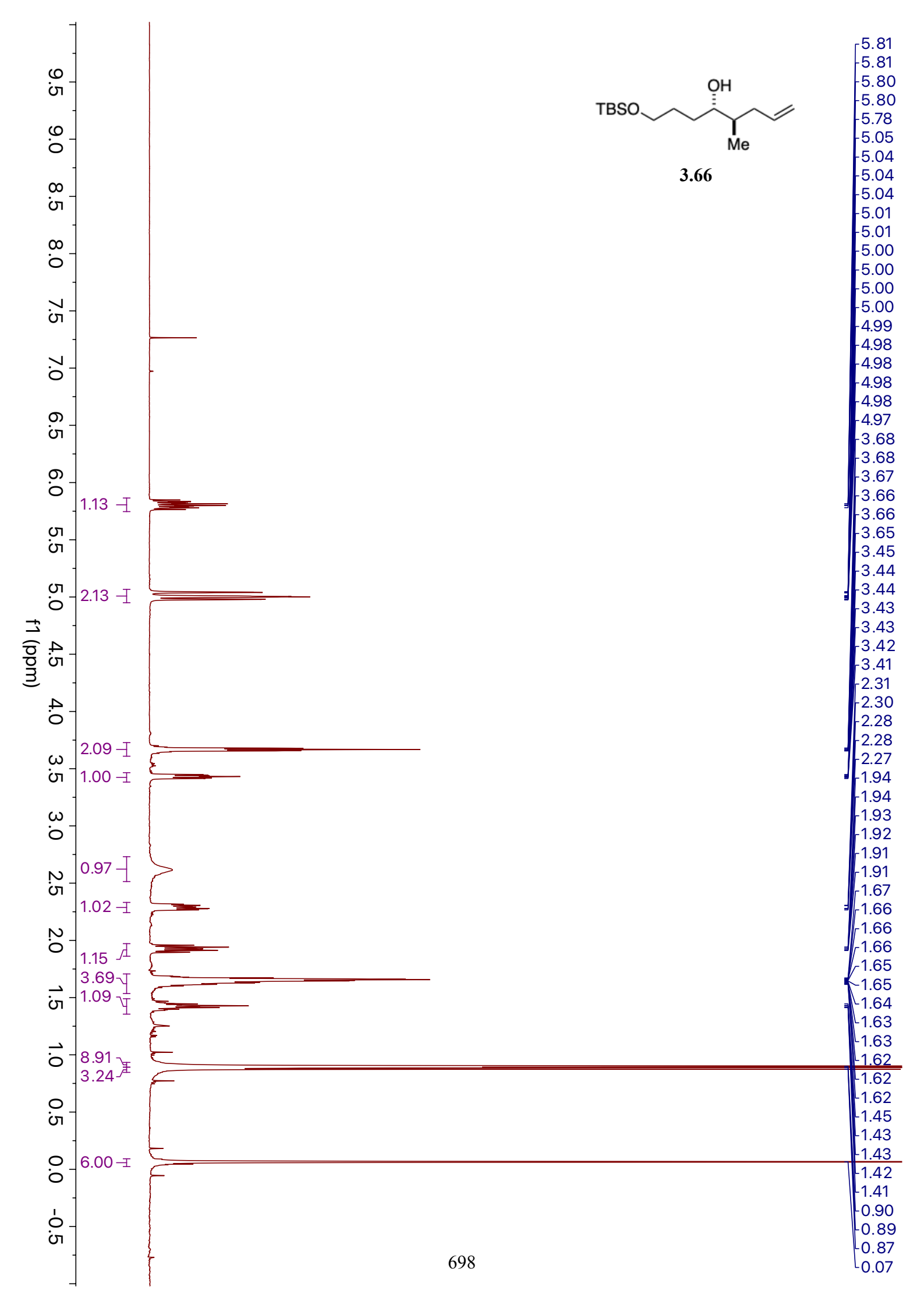

B(pin)
TBSO
Me
TMS
3.63
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
146.62
108.43
82.78
63.57
44.51
32.98
32.43
26.09
25.98
25.04
24.75
24.09
18.59
18.34
-1.26
-5.23

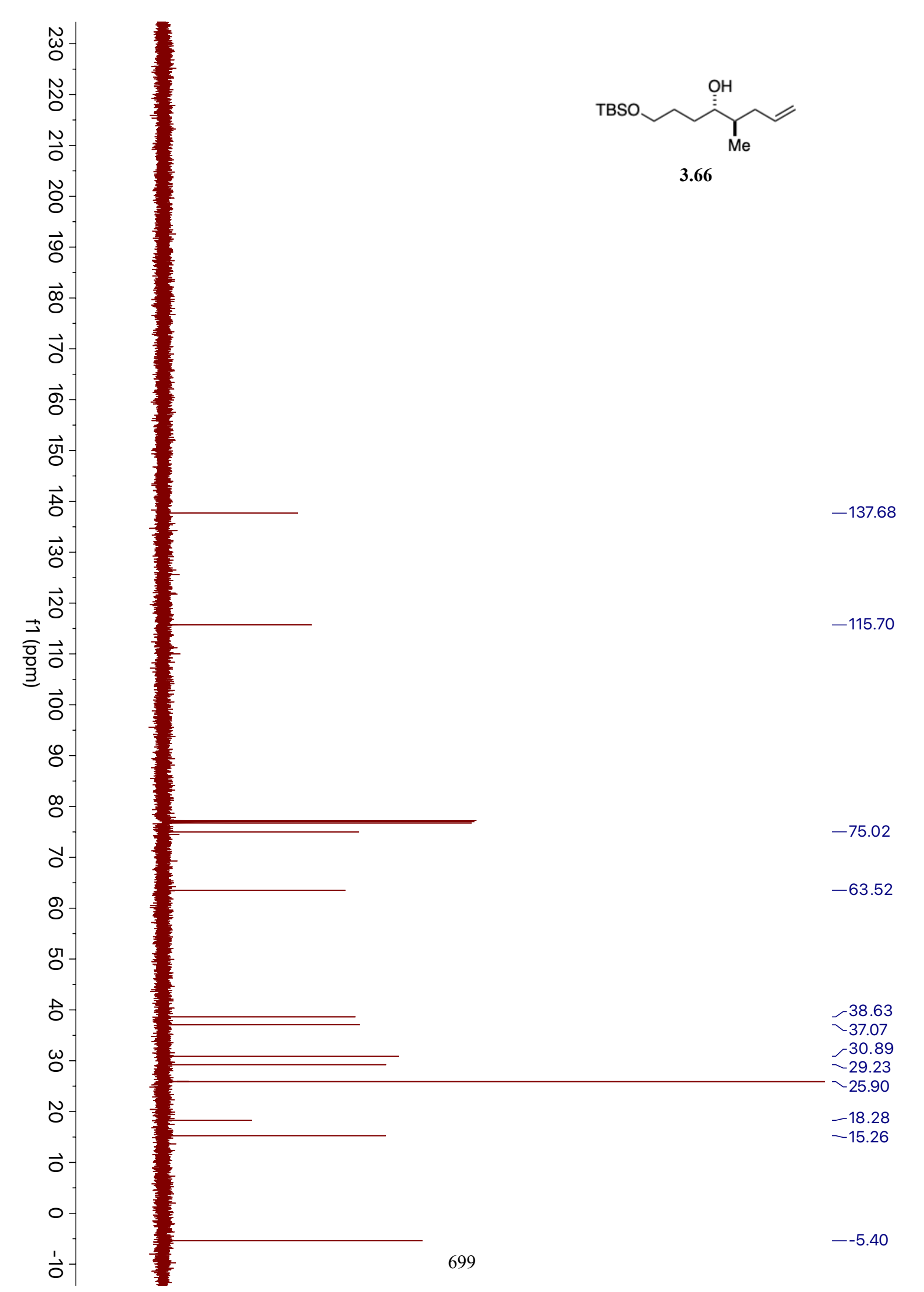

OH
n-pent
Me
Ph
3.64
f1 (ppm)
2.27
2.31
1.35
1.04
1.07
1.28
1.14
1.13
1.25
7.60
3.34
3.42

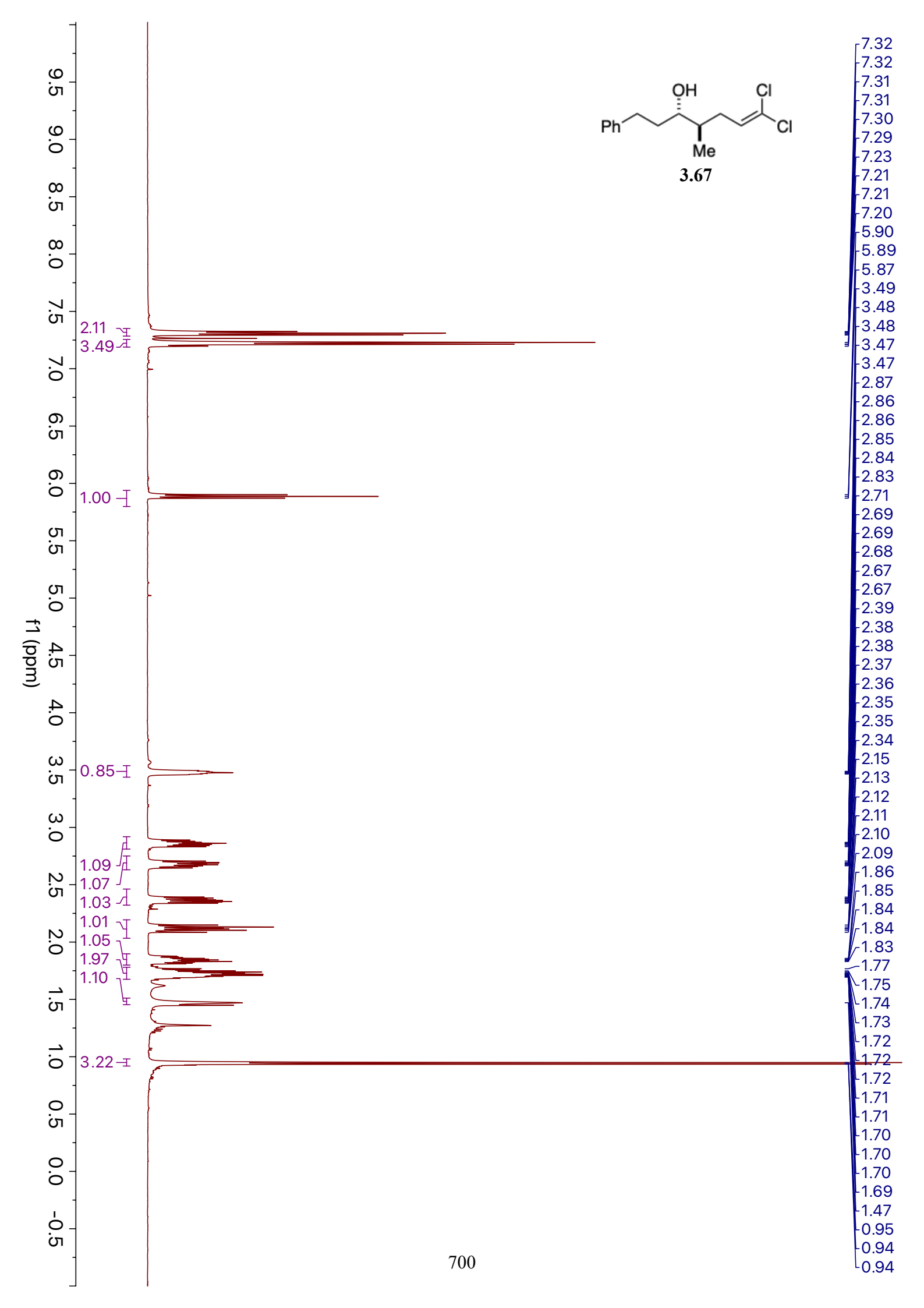

OH
n-pent
Me
Ph
3.64
147.52
141.06
128.27
127.33
126.31
113.98
75.91
38.20
36.98
33.55
31.91
25.72
22.65
15.27
14.05
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

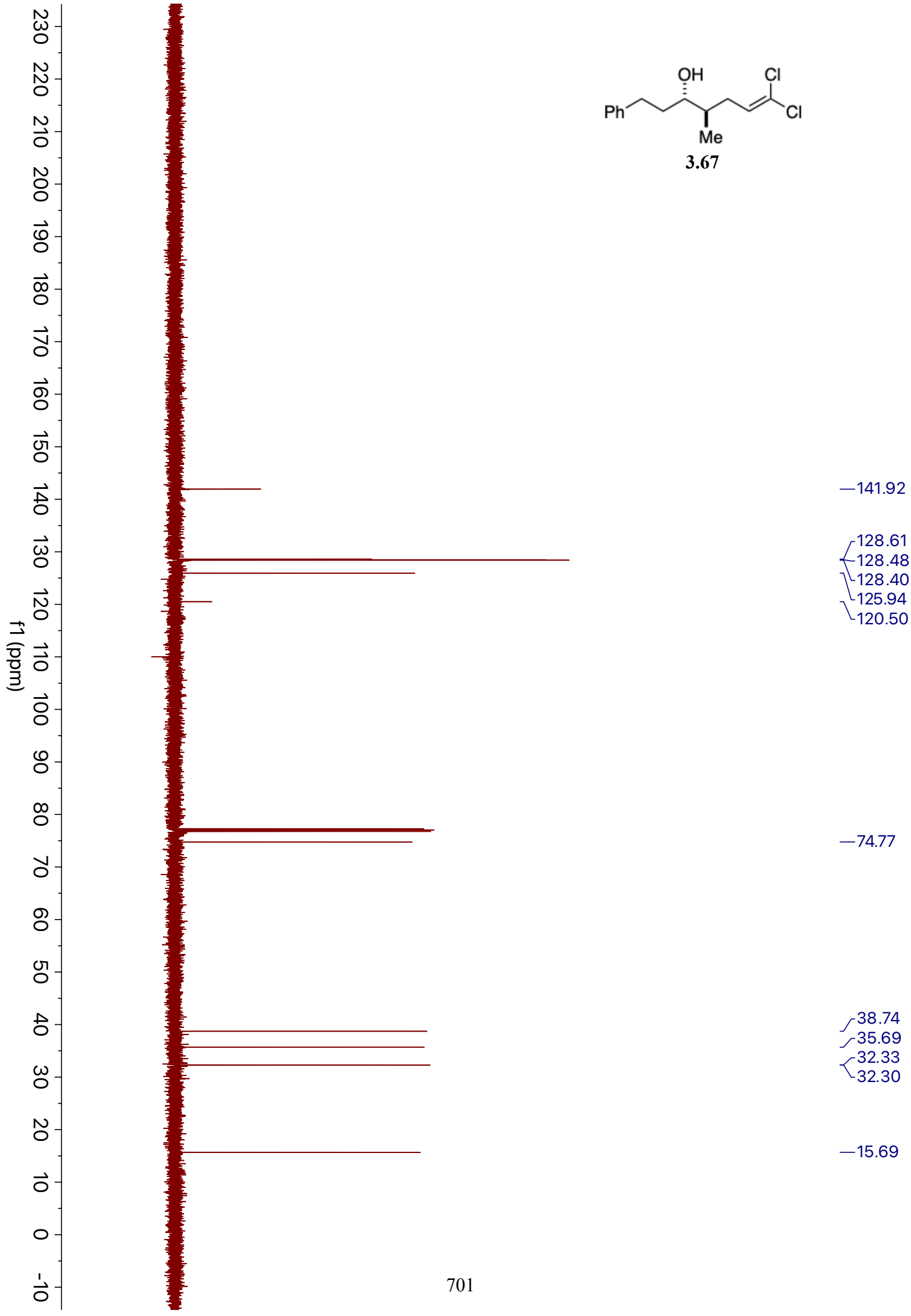

B(pin)
TBSO
Me
OMOM
3.65
f1 (ppm)
2.03
0.97
1.00
2.51
2.94
1.06
0.90
1.10
4.42
12.74
1.09
3.14
9.94
6.23

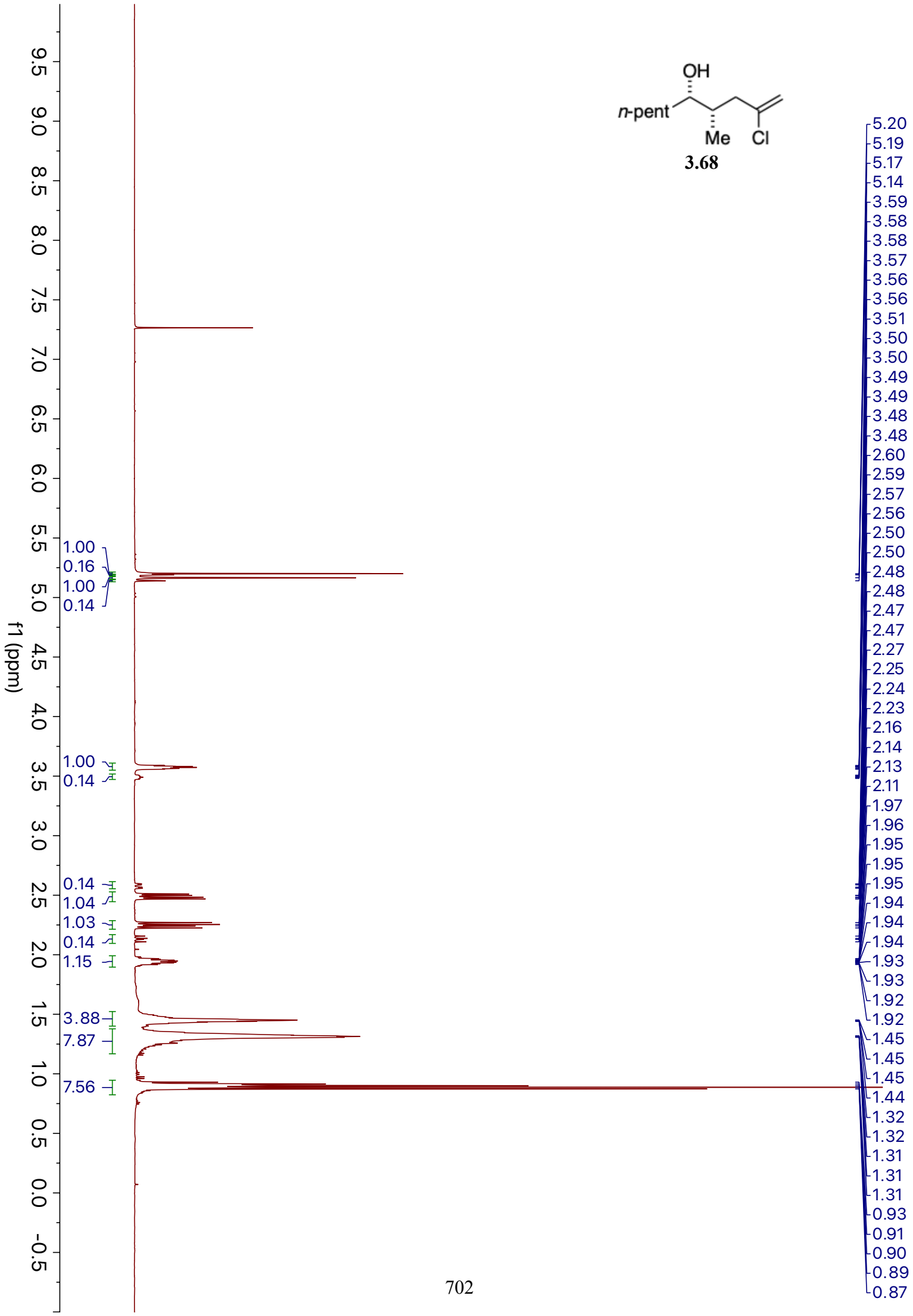

B(pin)
TBSO
Me
OMOM
3.65
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
160.24
93.29
85.13
82.83
63.57
56.04
41.15
32.96
32.25
25.98
24.90
24.82
23.89
18.38
18.35
-5.23

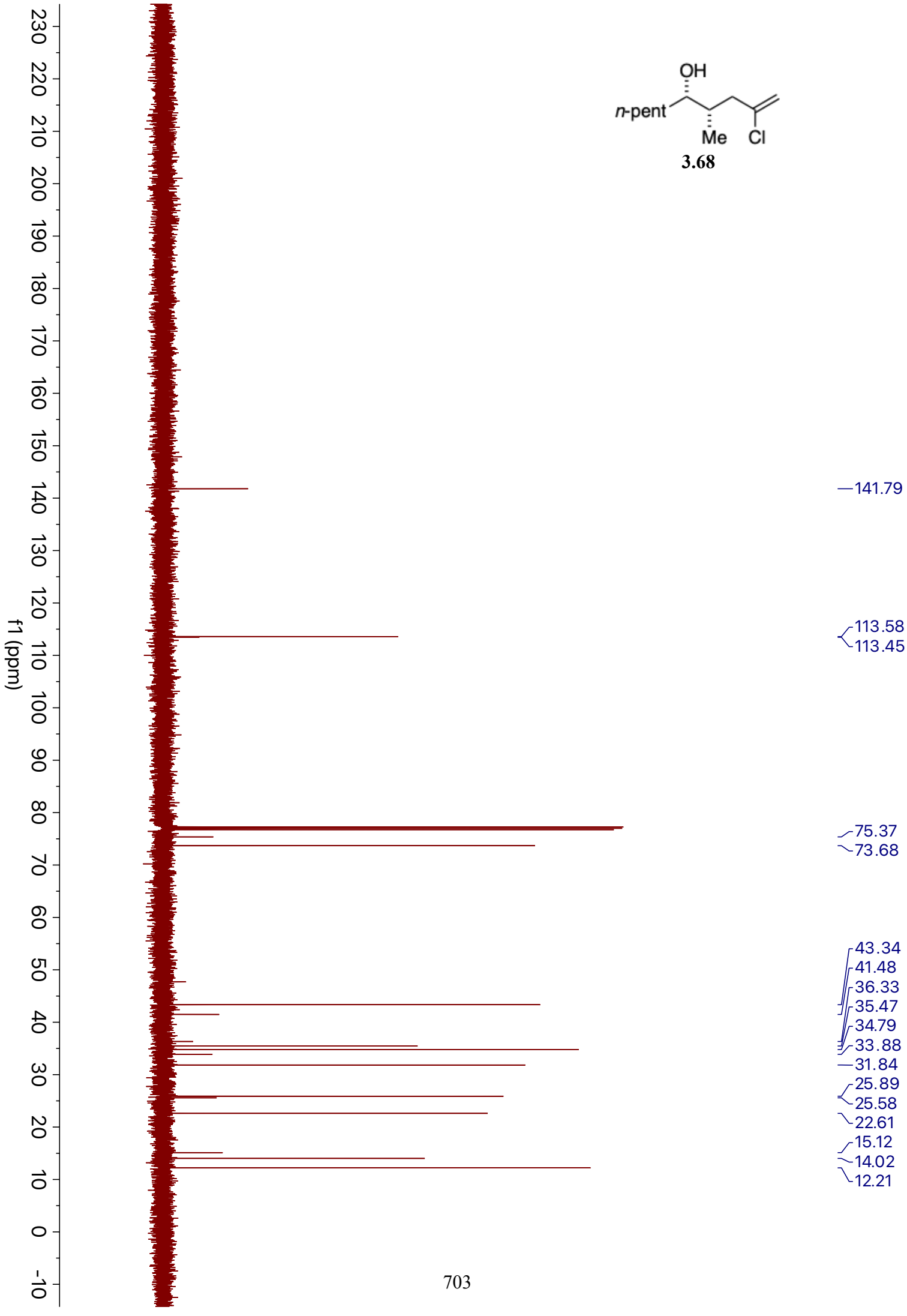

TBSO
OH
Me
3.66
f1 (ppm)
1.13
2.13
2.09
1.00
0.97
1.02
1.15
3.69
1.09
8.91
3.24
6.00

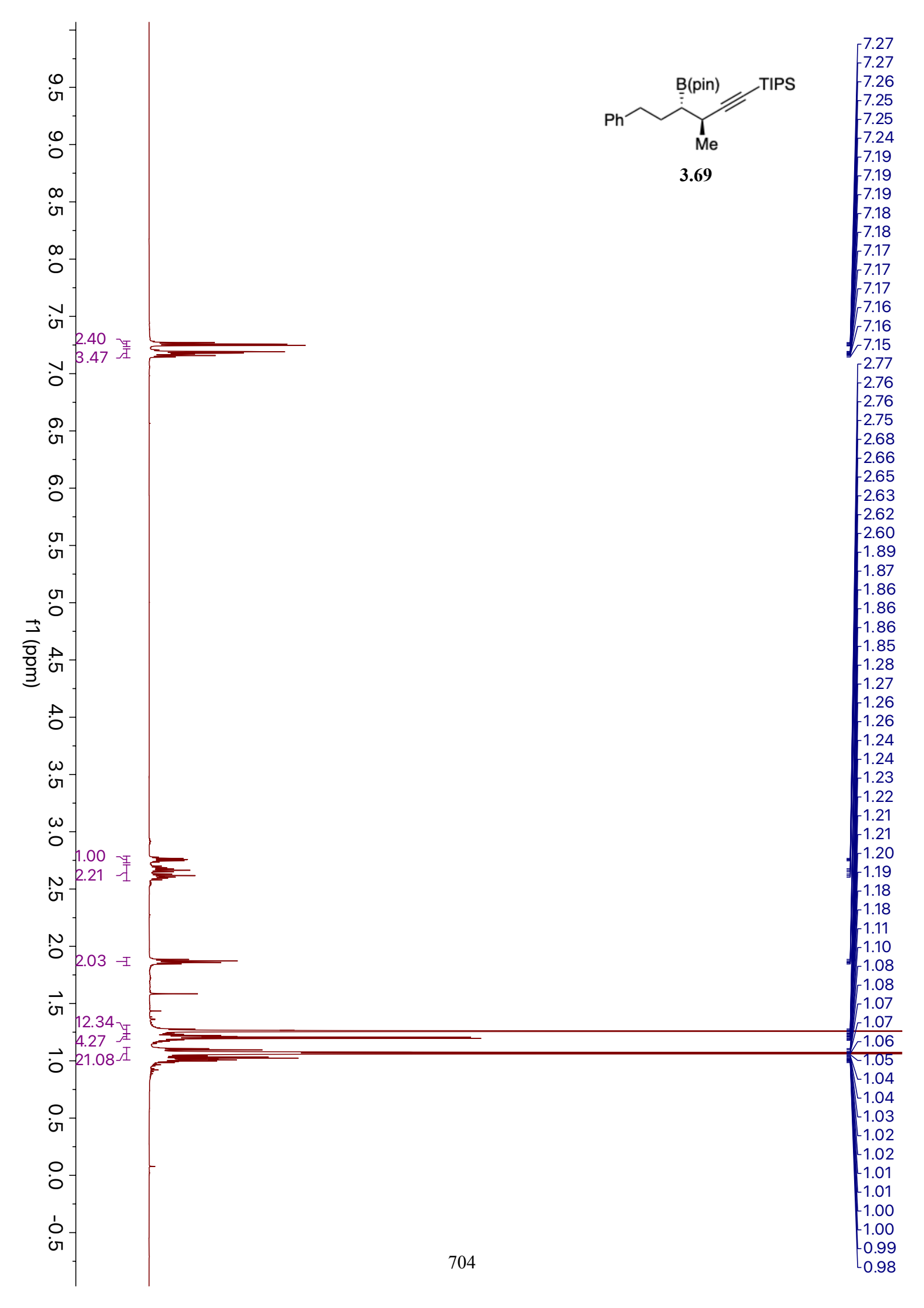

OH
TBSO
Me
3.66
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
137.68
115.70
75.02
63.52
38.63
37.07
30.89
29.23
25.90
18.28
15.26
-5.40

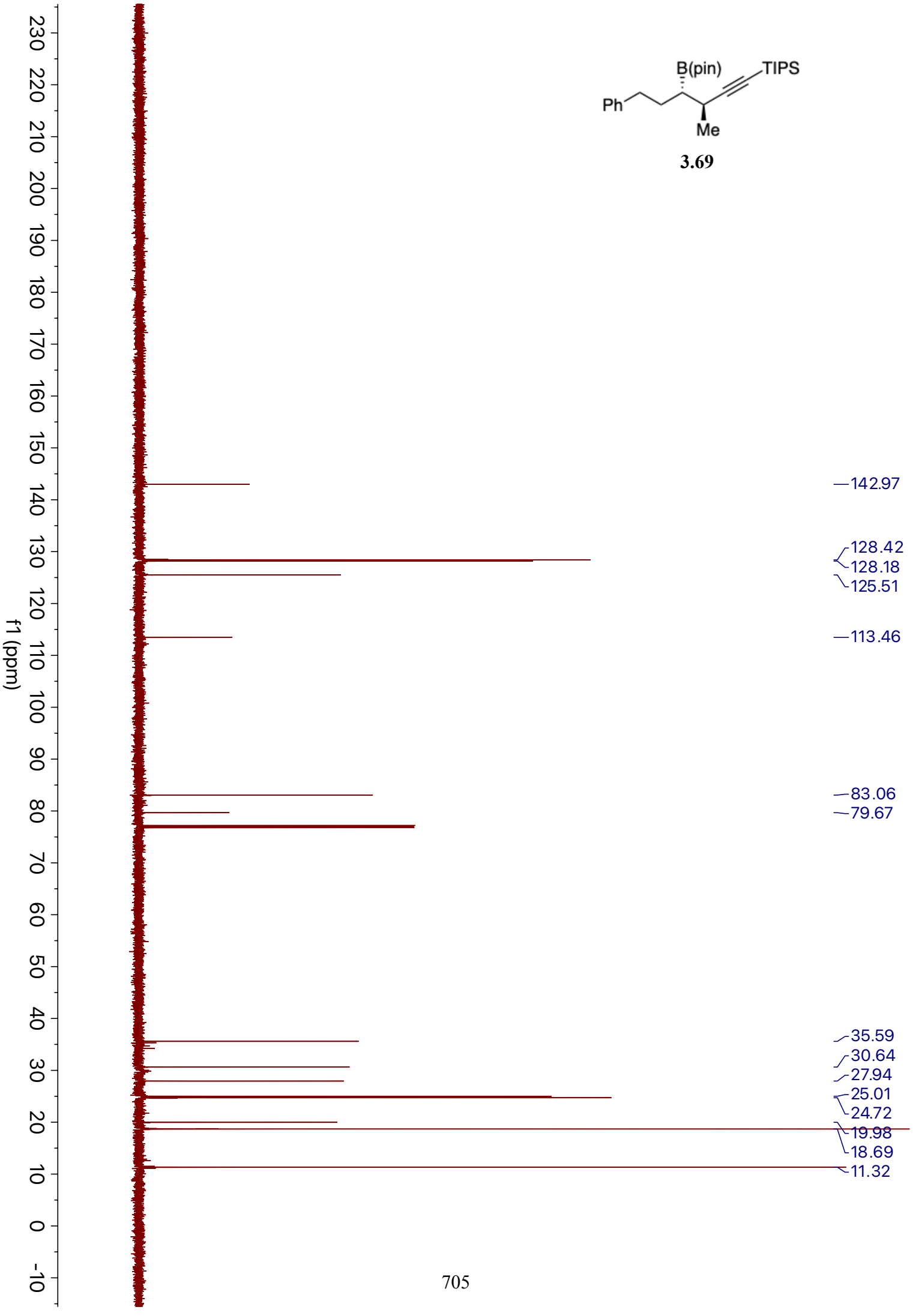

OH
Cl
Ph
Cl
Me
3.67
f1 (ppm)
2.11
3.49
1.00
0.85
1.09
1.07
1.03
1.01
1.05
1.97
1.10
3.22

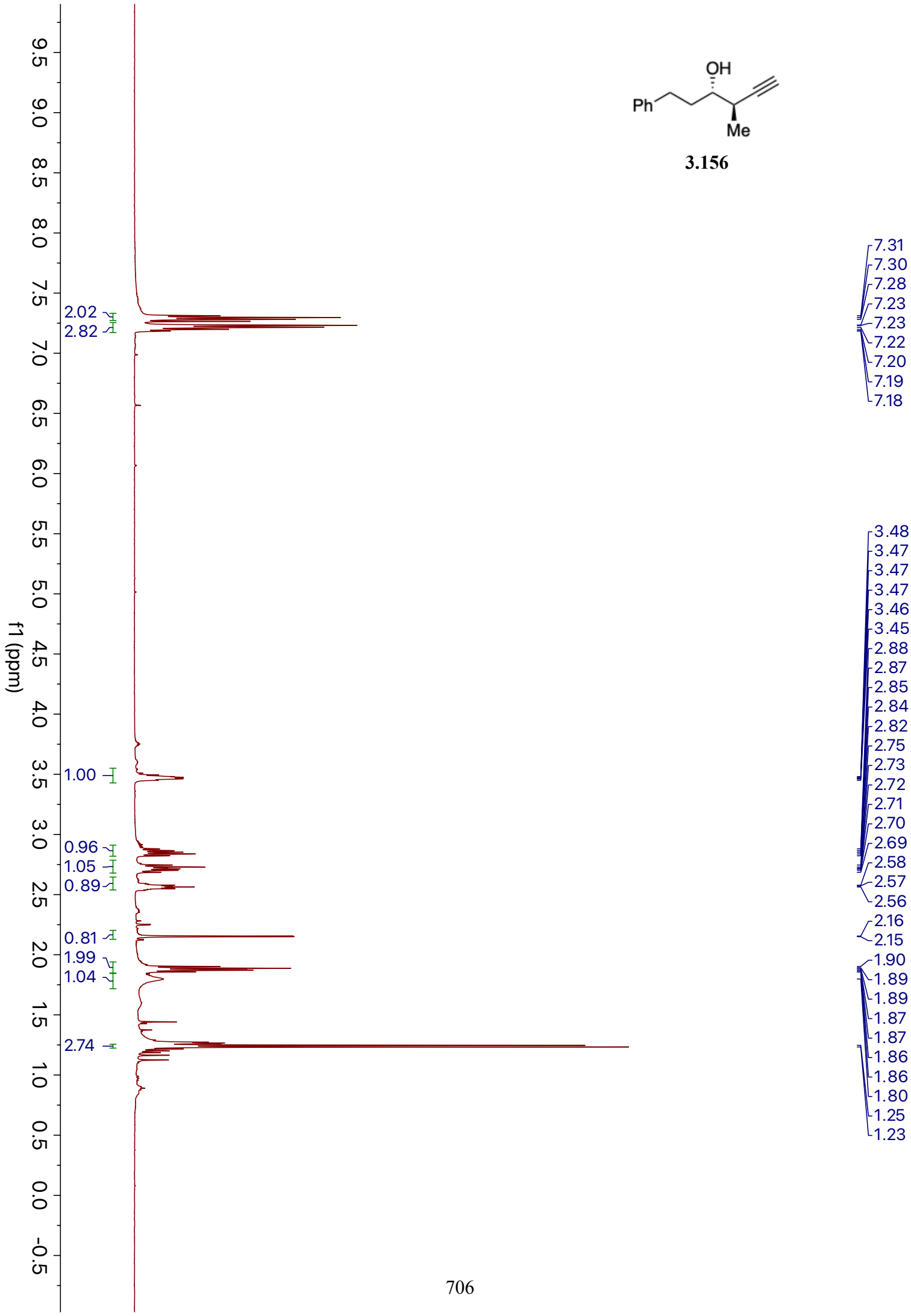

OH
Cl
Ph
Cl
Me
3.67
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
141.92
128.61
128.48
128.40
125.94
120.50
74.77
38.74
35.69
32.33
32.30
15.69

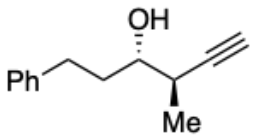

OH
n-pent
Me
Cl
3.68
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1.00
0.16
1.00
0.14
1.00
0.14
0.14
1.04
1.03
0.14
1.15
3.88
7.87
7.56
5.20
5.19
5.17
5.14
3.59
3.58
3.58
3.57
3.56
3.56
3.51
3.50
3.50
3.49
3.49
3.48
3.48
2.60
2.59
2.57
2.56
2.50
2.50
2.48
2.48
2.47
2.47
2.27
2.25
2.24
2.23
2.16
2.14
2.13
2.11
1.97
1.96
1.95
1.95
1.95
1.94
1.94
1.94
1.93
1.93
1.92
1.92
1.45
1.45
1.45
1.44
1.32
1.32
1.31
1.31
1.31
0.93
0.91
0.90
0.89
0.87


OH
n-pent
Me
Cl
3.68
141.79
113.58
113.45
75.37
73.68
43.34
41.48
36.33
35.47
34.79
33.88
31.84
25.89
25.58
22.61
15.12
14.02
12.21
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


B(pin)
TIPS
Ph
Me
3.69
f1 (ppm)
2.40
3.47
1.00
2.21
2.03
12.34
4.27
21.08

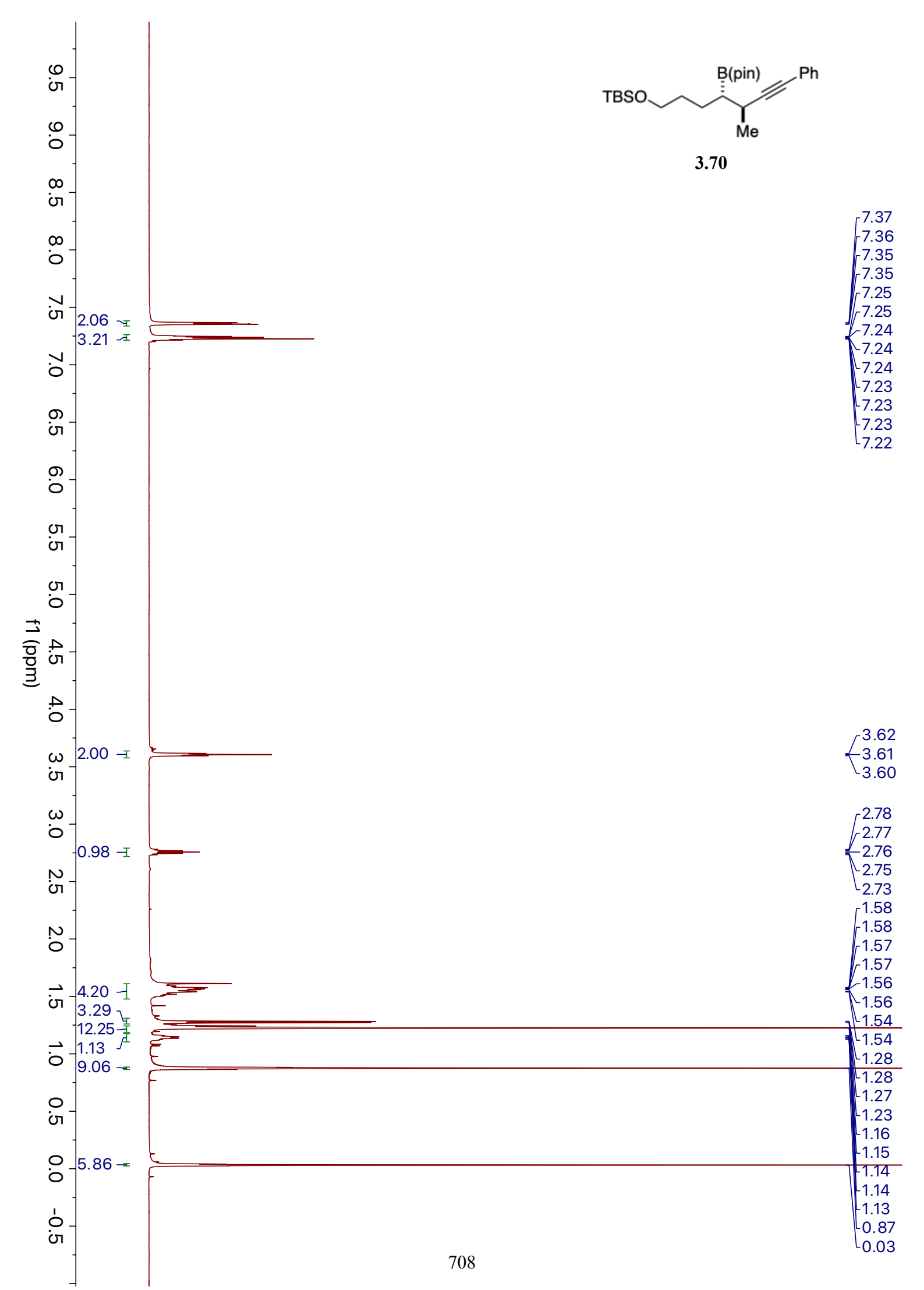

B(pin)
TIPS
Ph
Me
3.69
142.97
128.42
128.18
125.51
113.46
83.06
79.67
35.59
30.64
27.94
25.01
24.72
19.98
18.69
11.32
f1 (ppm)

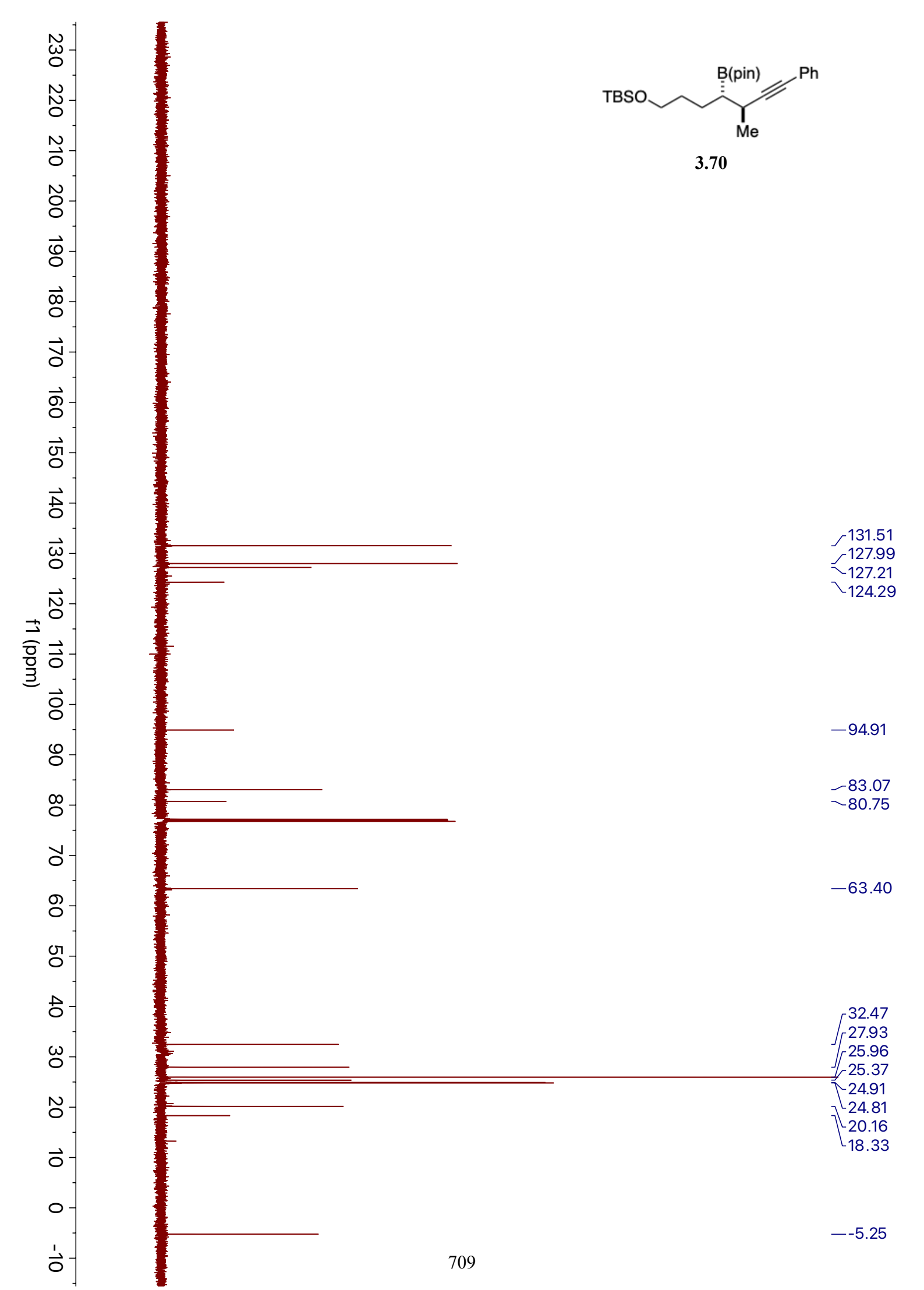

OH
Ph
Me
3.156
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
2.02
2.82
1.00
0.96
1.05
0.89
0.81
1.99
1.04
2.74
7.31
7.30
7.28
7.23
7.23
7.22
7.20
7.19
7.18
3.48
3.47
3.47
3.47
3.46
3.45
2.88
2.87
2.85
2.84
2.82
2.75
2.73
2.72
2.71
2.70
2.69
2.58
2.57
2.56
2.16
2.15
1.90
1.89
1.89
1.87
1.87
1.86
1.86
1.80
1.25
1.23

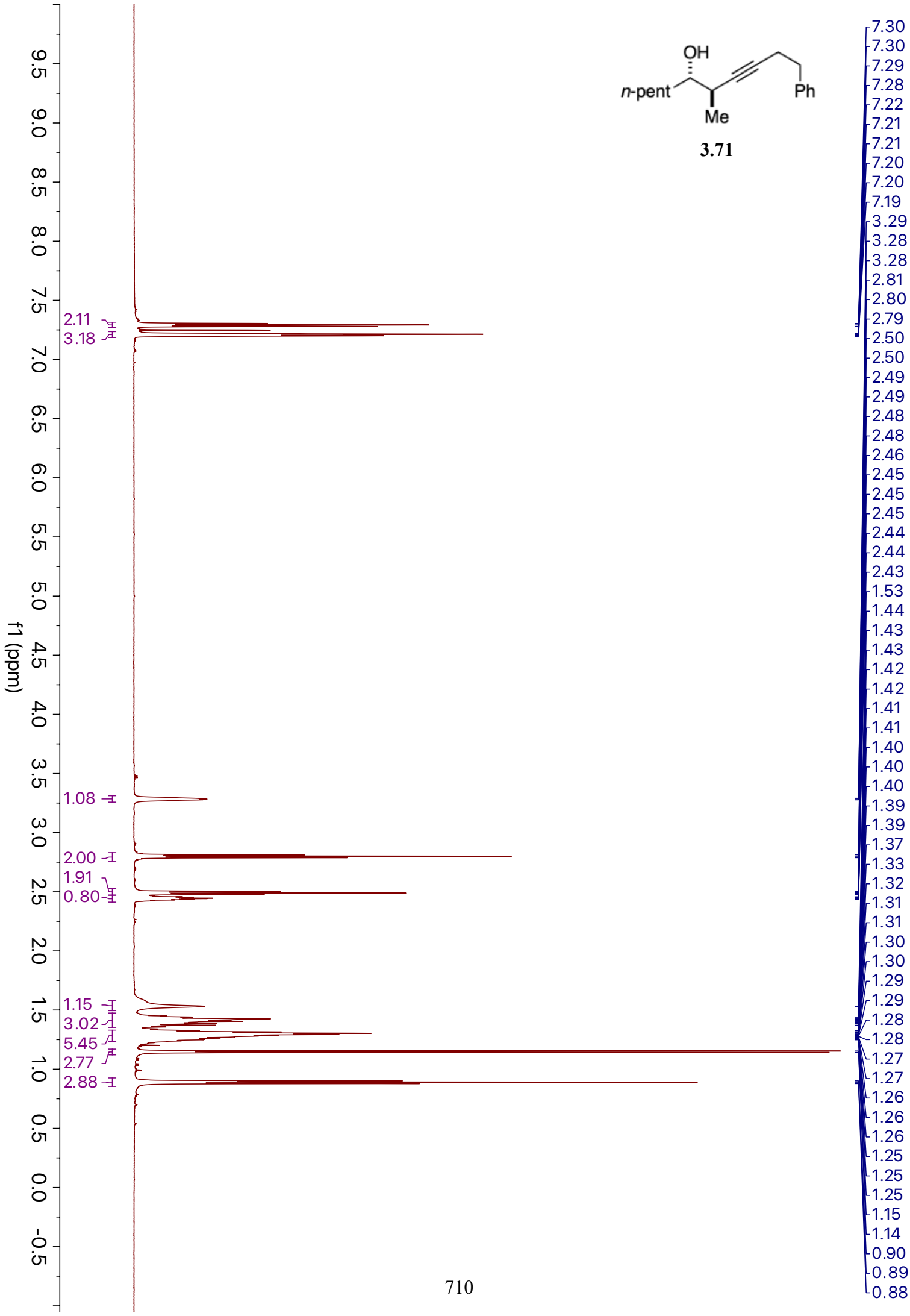

OH
Ph
Me

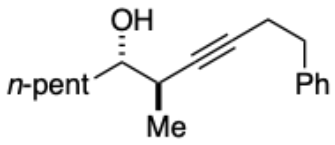
3.156

f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
141.85
128.44
128.40
125.86
84.98
73.44
71.16
36.85
33.09
32.05
17.38


B(pin)
Ph
TBSO
Me
3.70
f1 (ppm)
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
2.06
3.21
2.00
0.98
4.20
3.29
12.25
1.13
9.06
5.86
7.37
7.36
7.35
7.35
7.25
7.25
7.24
7.24
7.24
7.23
7.23
7.23
7.22
3.62
3.61
3.60
2.78
2.77
2.76
2.75
2.73
1.58
1.58
1.57
1.57
1.56
1.56
1.54
1.54
1.28
1.28
1.27
1.23
1.16
1.15
1.14
1.14
1.13
0.87
0.03

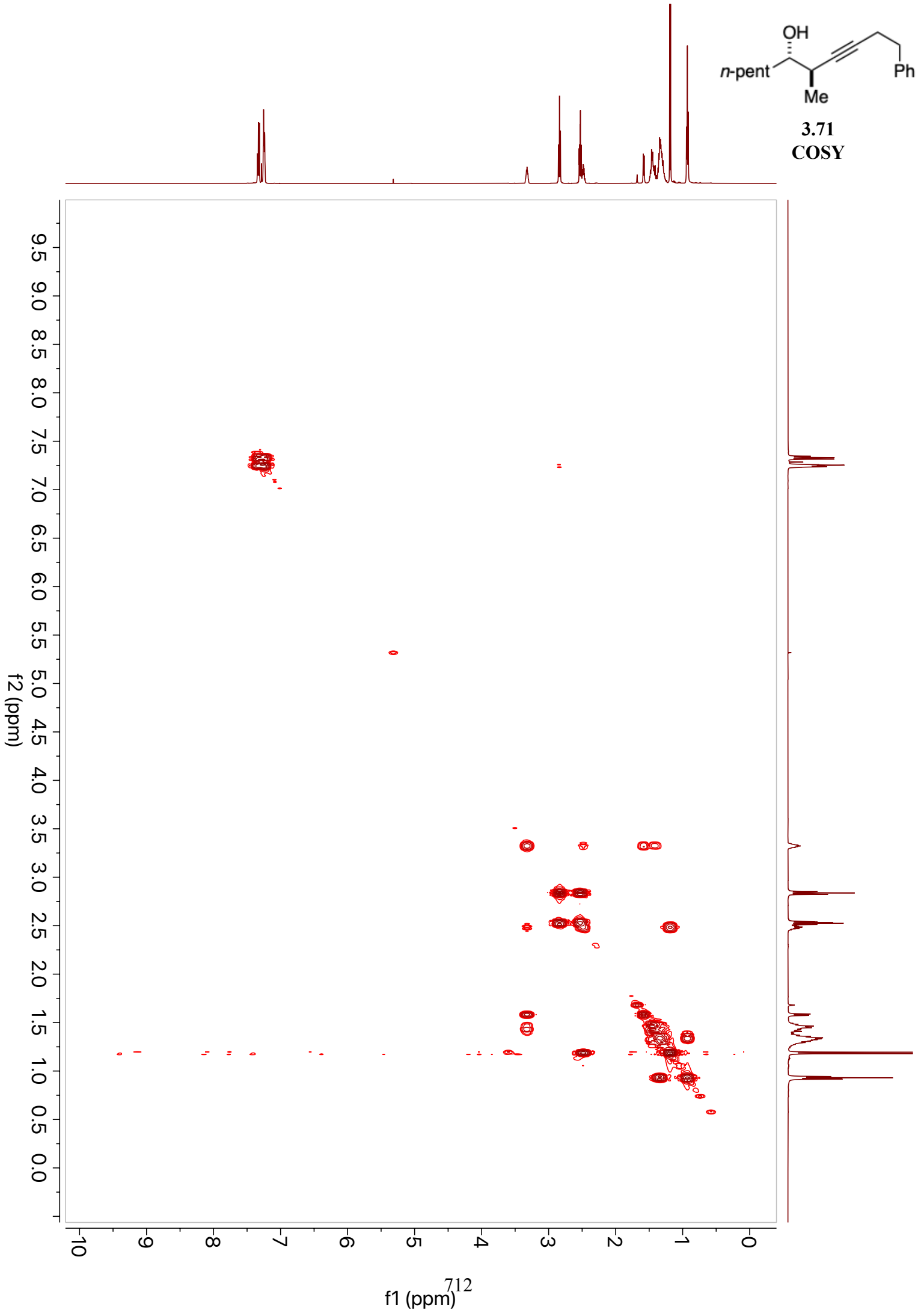

B(pin)
Ph
TBSO
Me
3.70
131.51
127.99
127.21
124.29
94.91
83.07
80.75
63.40
32.47
27.93
25.96
25.37
24.91
24.81
20.16
18.33
-5.25
f1 (ppm)

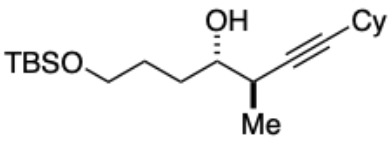

OH
n-pent
Me
Ph
3.71
f1 (ppm)
2.11
3.18
1.08
2.00
1.91
0.80
1.15
3.02
5.45
2.77
2.88


OH
n-pent
Ph
Me

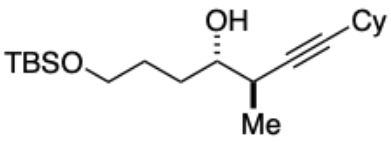
3.71

f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
140.67
128.44
128.33
126.28
82.50
81.56
74.52
35.26
35.22
33.18
31.82
25.44
22.63
20.81
17.99
14.04


OH
n-pent
Ph
Me
3.71
COSY
f2 (ppm)
f1 (ppm)

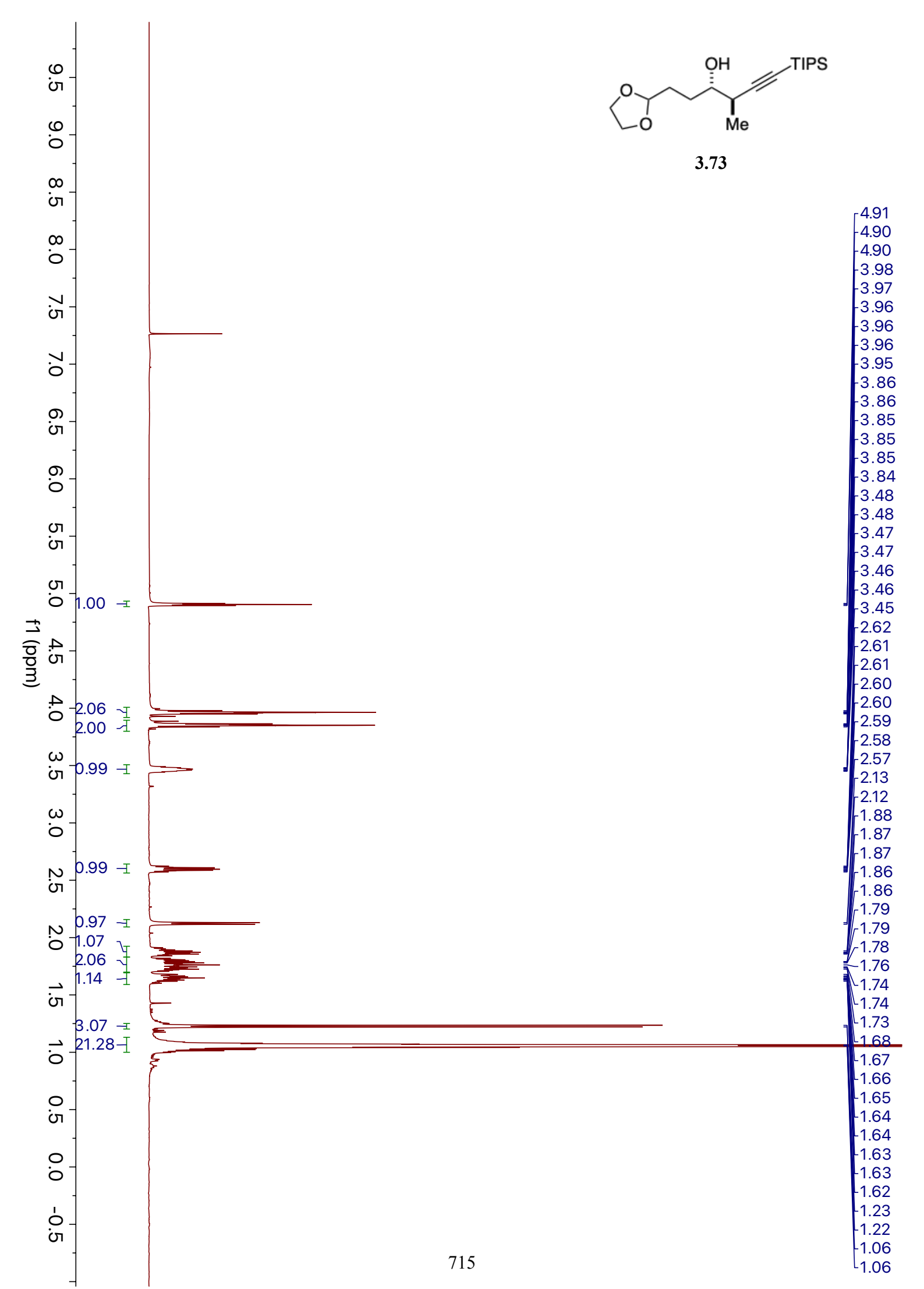


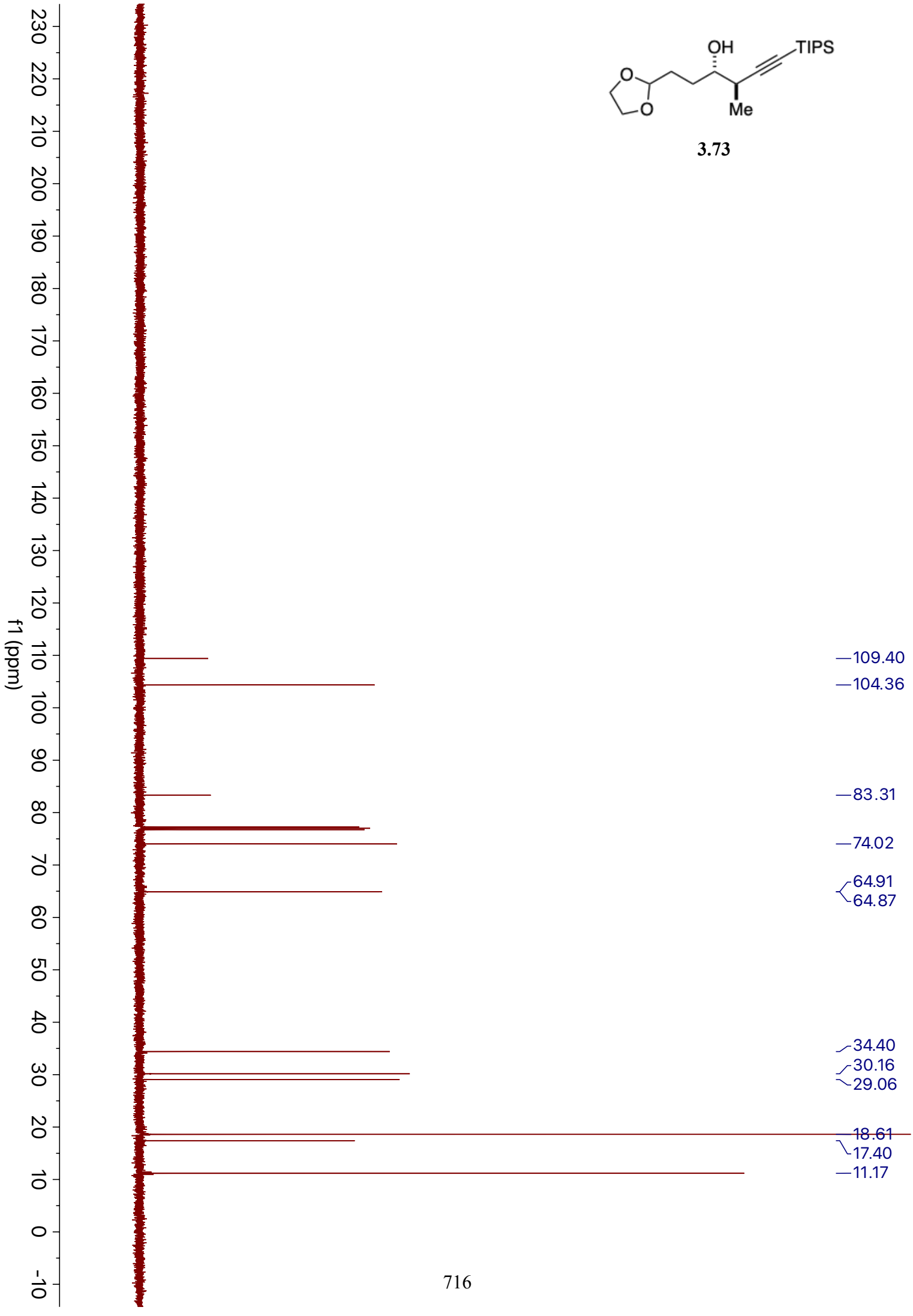
3.72

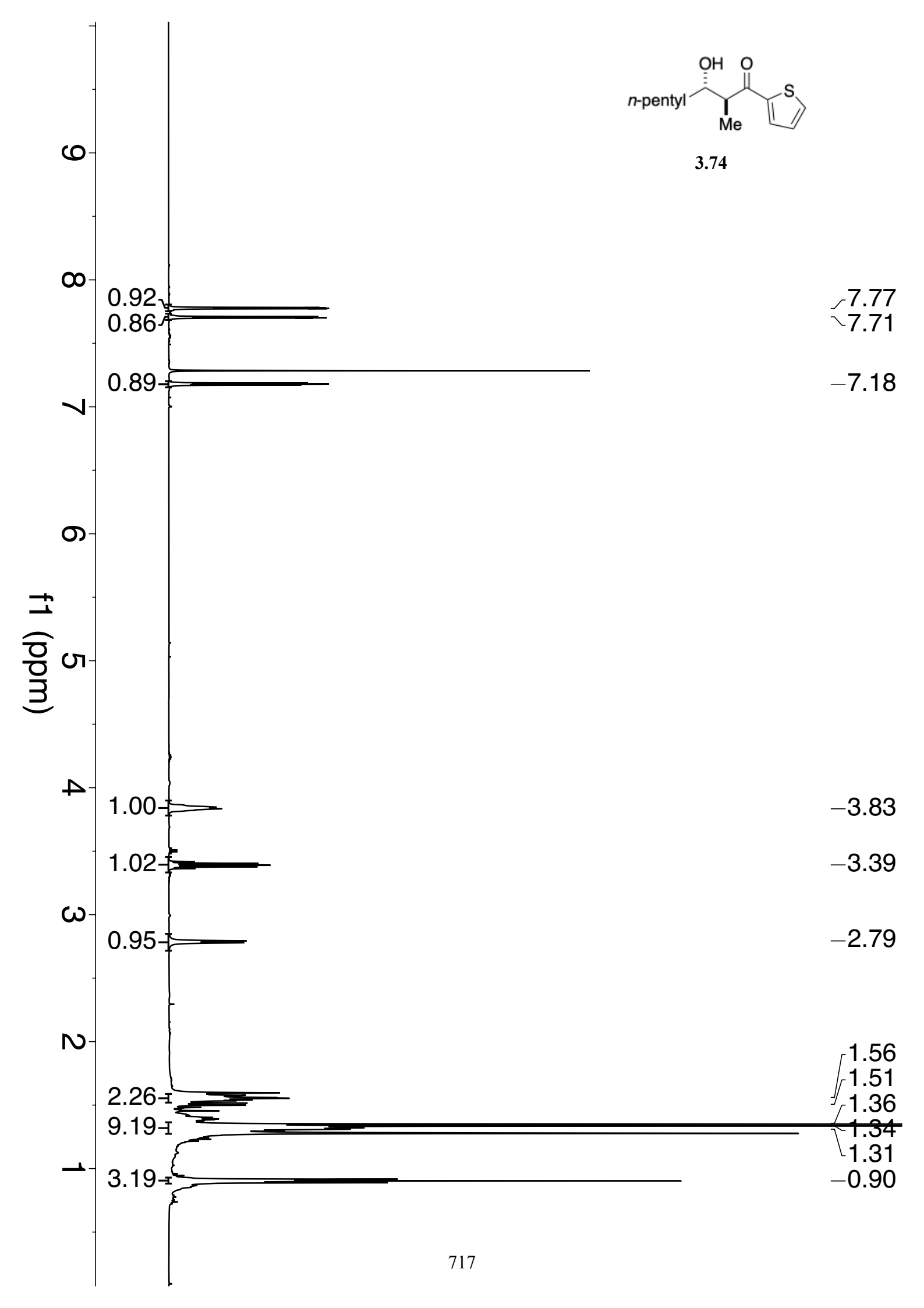

OH
Cy
TBSO
Me

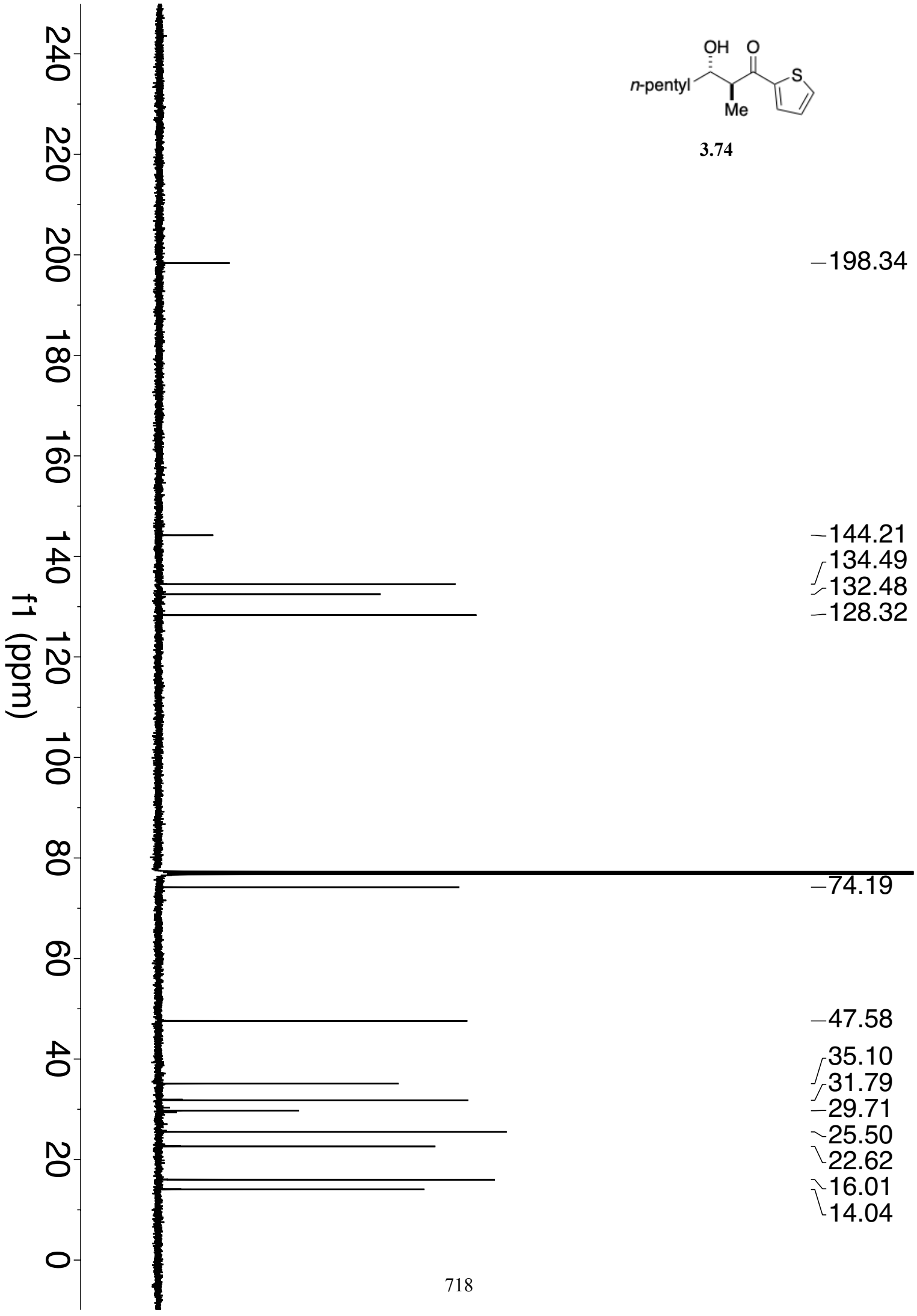
3.72

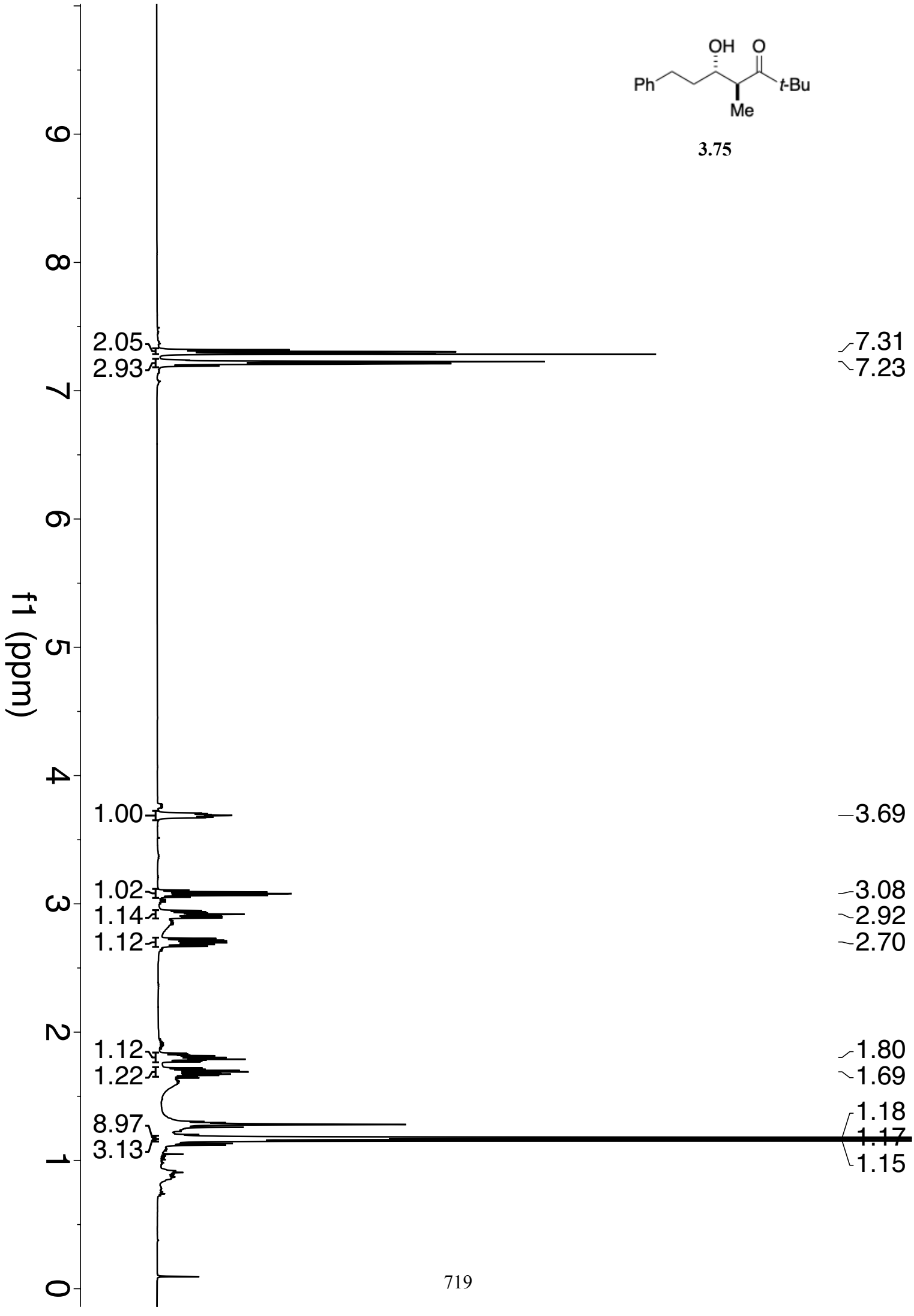
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
87.72
80.55
74.35
63.22
33.17
33.07
31.65
29.20
29.01
25.92
25.90
24.82
18.30
17.74
-5.34

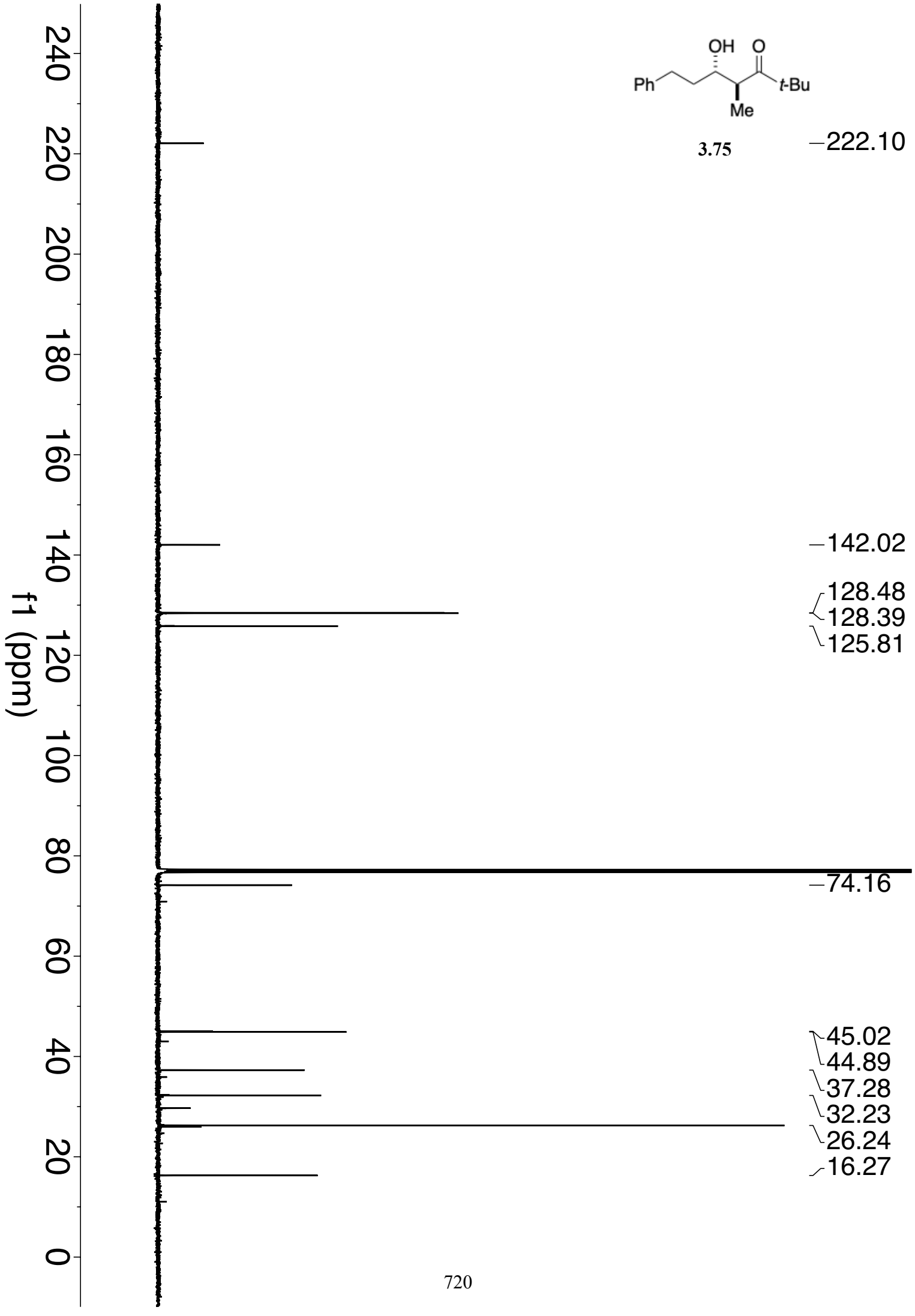

OH
TIPS
O
O
Me
3.73
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
1.00
2.06
2.00
0.99
0.99
0.97
1.07
2.06
1.14
3.07
21.28
4.91 4.90 4.90 3.98 3.97 3.96 3.96 3.96 3.95 3.86 3.86 3.85 3.85 3.85 3.84 3.48 3.48 3.47 3.47 3.46 3.46 3.45 2.62 2.61 2.61 2.60 2.60 2.59 2.58 2.57 2.13 2.12 1.88 1.87 1.87 1.86 1.86 1.79 1.79 1.78 1.76 1.74 1.74 1.73 1.68 1.67 1.66 1.65 1.64 1.64 1.63 1.63 1.62 1.23 1.22 1.06 1.06

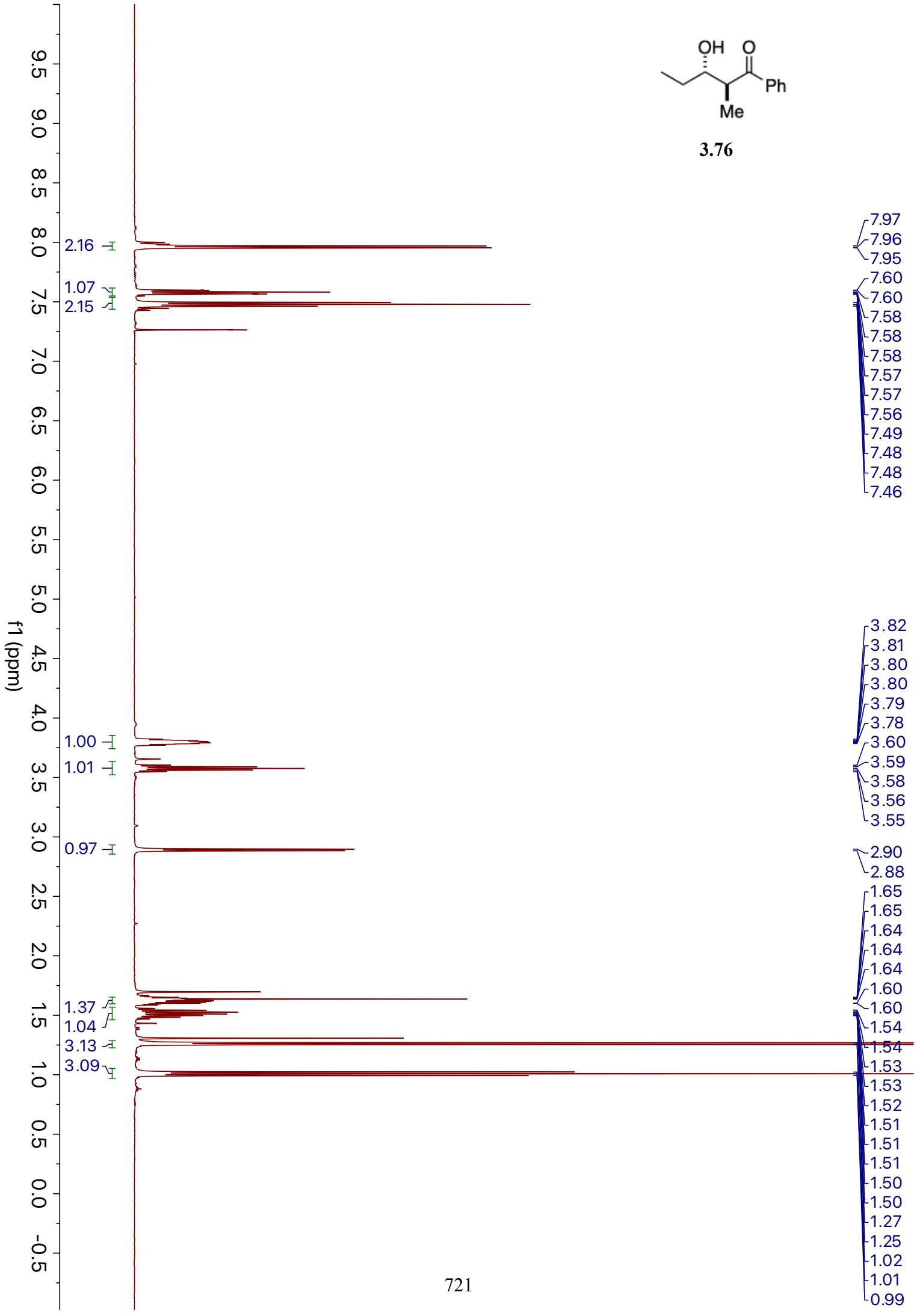

OH
TIPS
O
O
Me
3.73
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
109.40
104.36
83.31
74.02
64.91
64.87
34.40
30.16
29.06
18.61
17.40
11.17

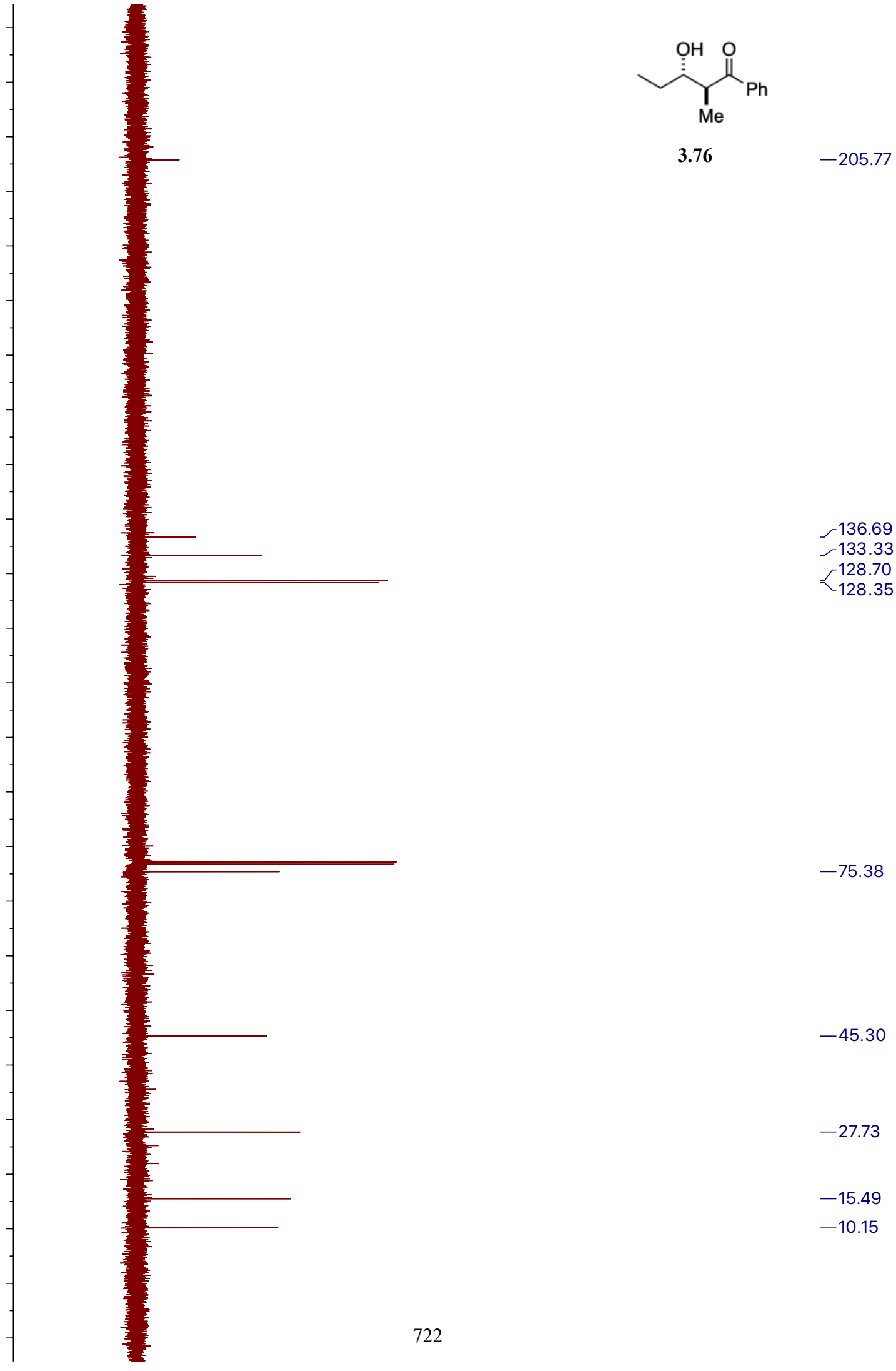

OH
O
n-pentyl
S
Me
3.74
f1 (ppm)
9
8
7
6
5
4
3
2
1
0.92
0.86
0.89
1.00
1.02
0.95
2.26
9.19
3.19
7.77
7.71
7.18
3.83
3.39
2.79
1.56
1.51
1.36
1.34
1.31
0.90

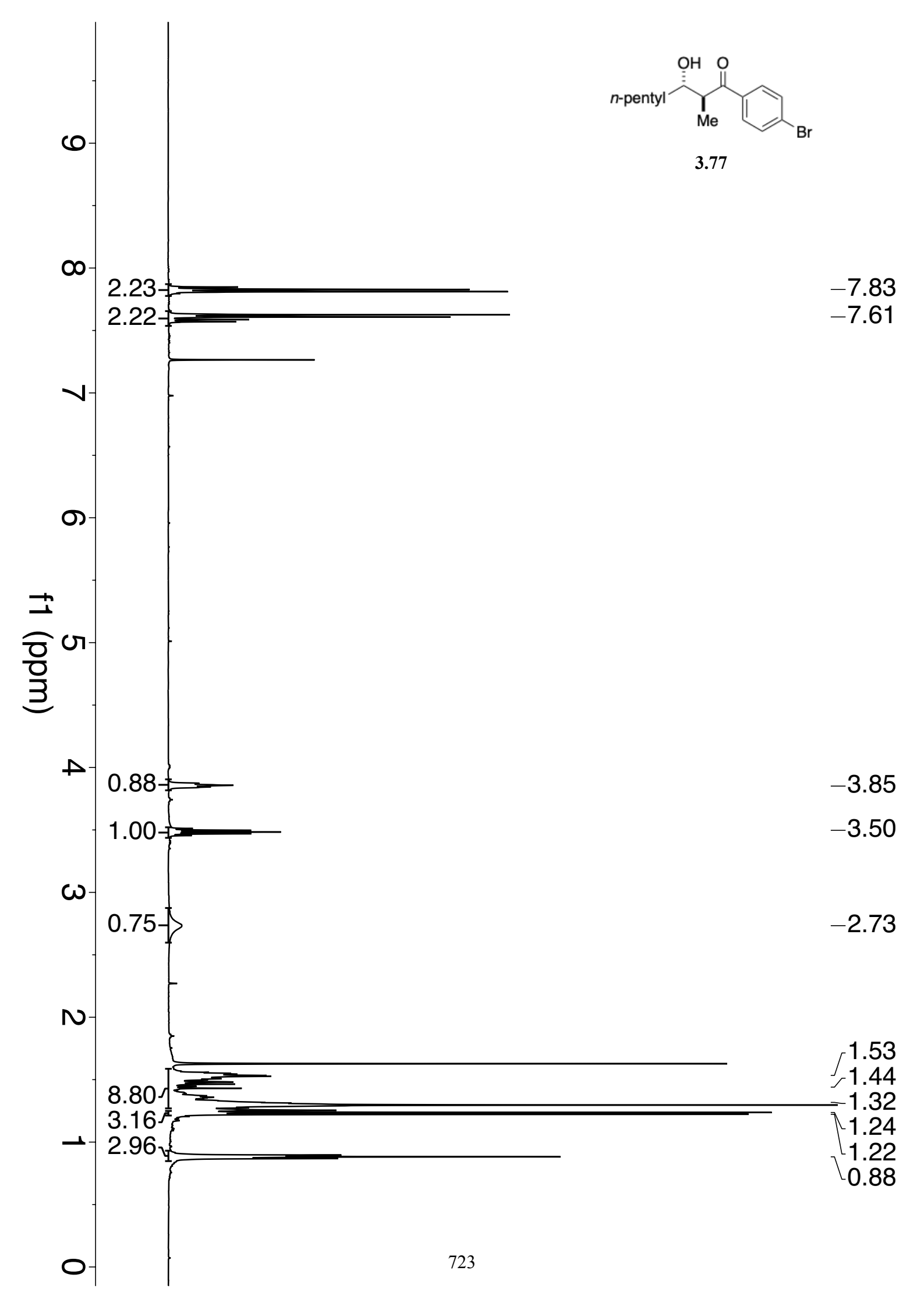

OH
O
S
n-pentyl
Me
3.74
198.34
144.21
134.49
132.48
128.32
74.19
47.58
35.10
31.79
29.71
25.50
22.62
16.01
14.04
f1 (ppm)
240
220
200
180
160
140
120
100
80
60
40
20
0

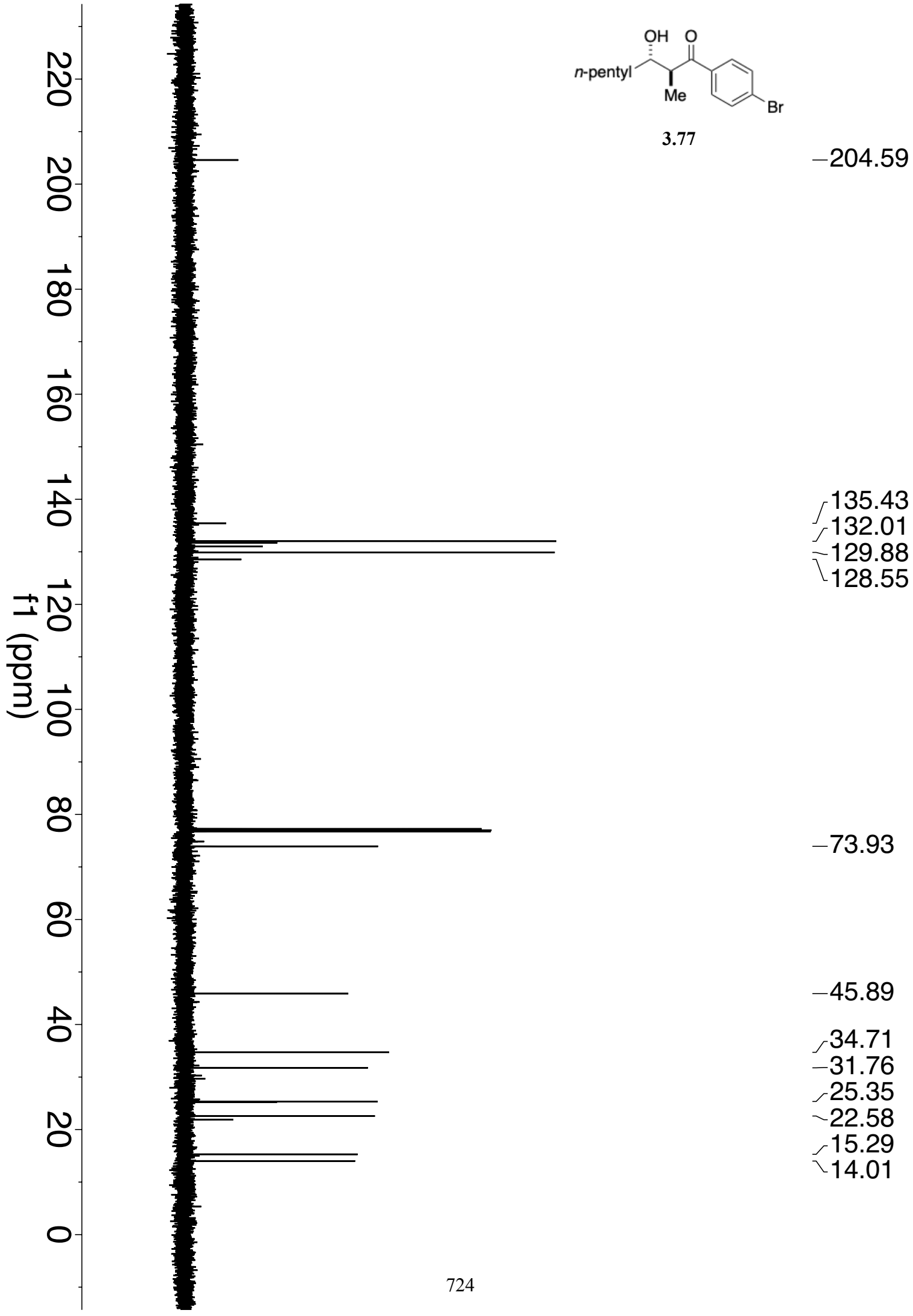

OH
O
Ph
t-Bu
Me
3.75
2.05
2.93
7.31
7.23
1.00
3.69
1.02
1.14
1.12
3.08
2.92
2.70
1.12
1.22
1.80
1.69
8.97
3.13
1.18
1.17
1.15
f1 (ppm)
0
1
2
3
4
5
6
7
8
9

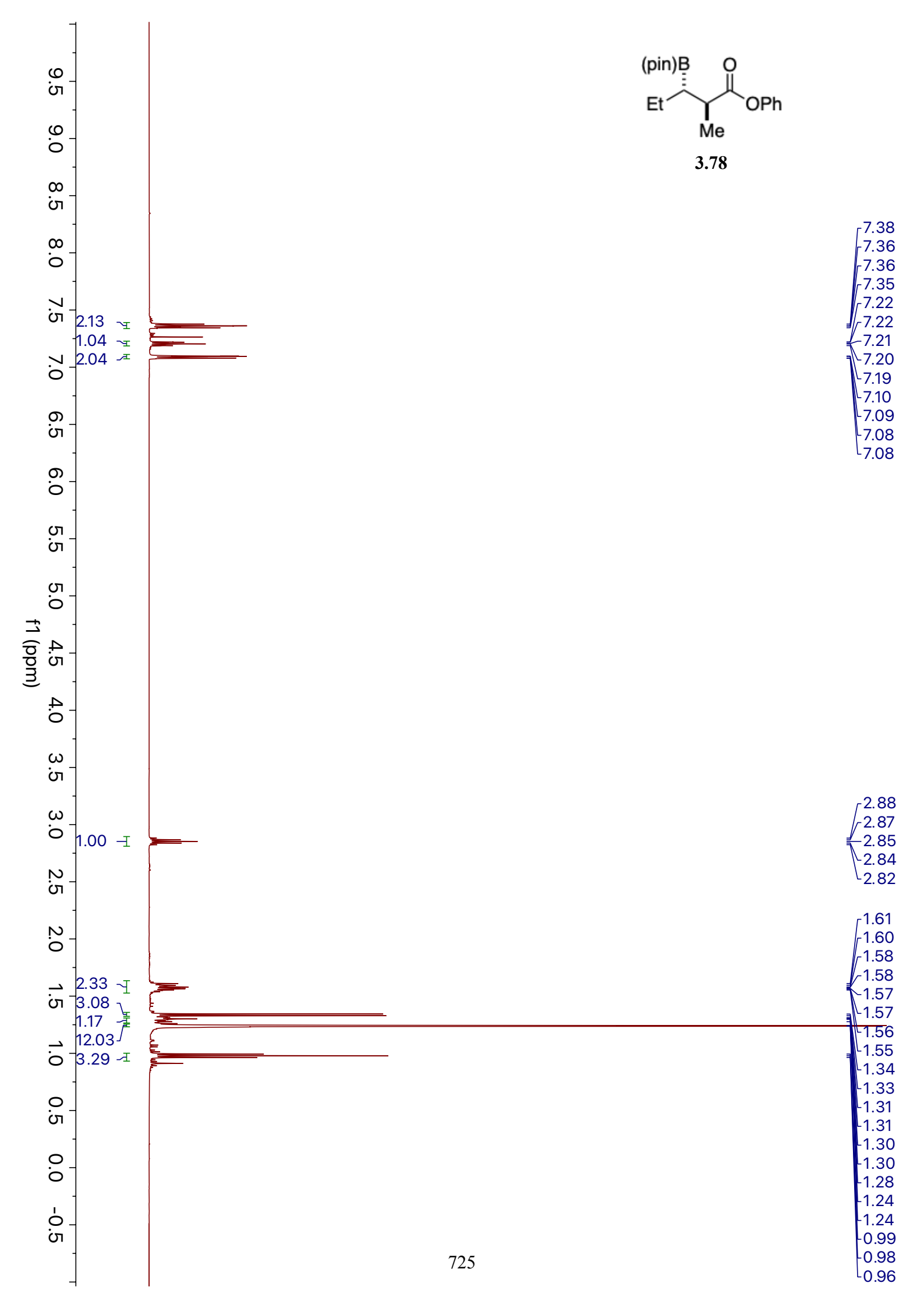

OH
O
Ph
t-Bu
Me
3.75
222.10
142.02
128.48
128.39
125.81
74.16
45.02
44.89
37.28
32.23
26.24
16.27
f1 (ppm)
240
220
200
180
160
140
120
100
80
60
40
20
0

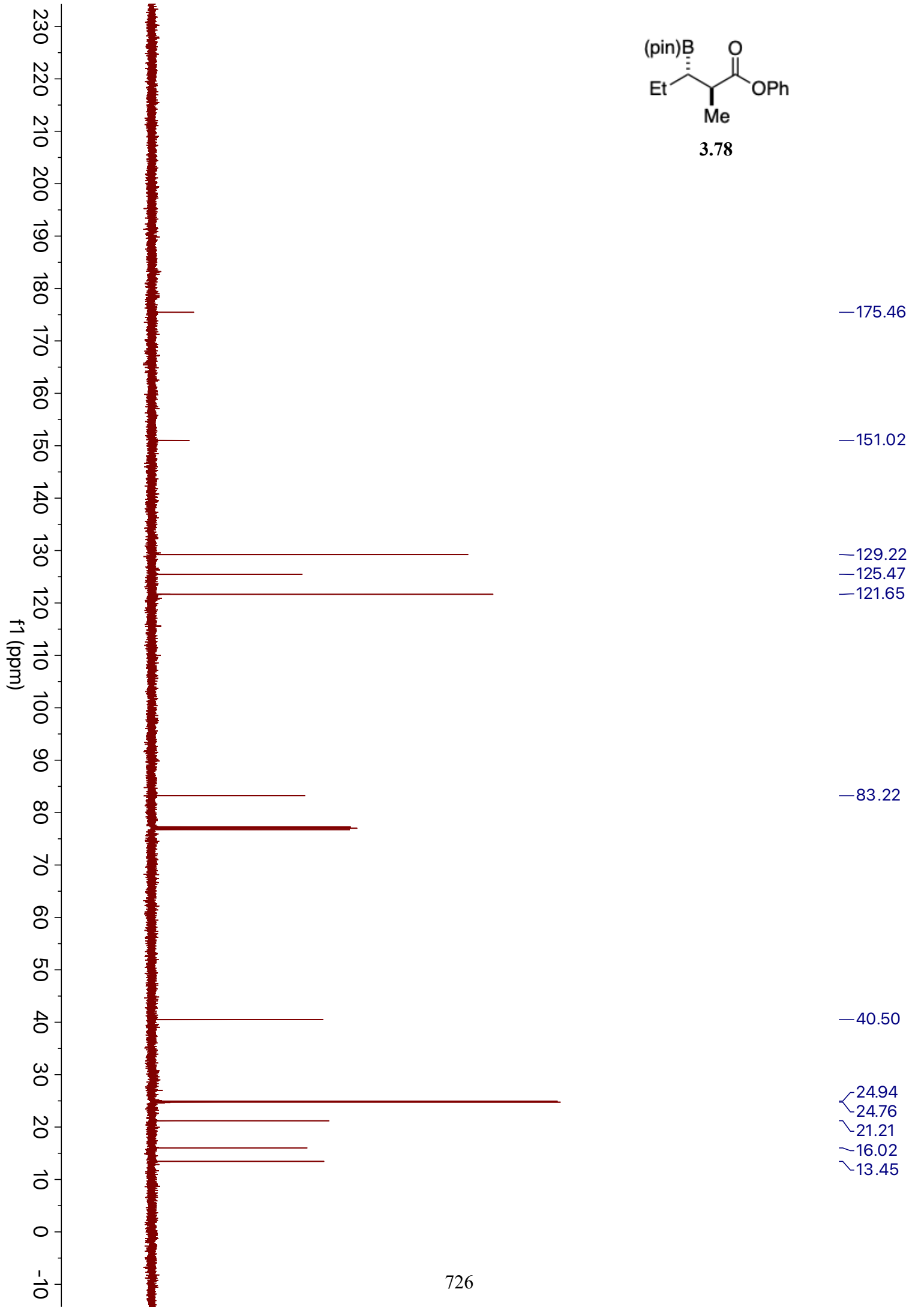

OH
O
Ph
Me
3.76
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.16
1.07
2.15
1.00
1.01
0.97
1.37
1.04
3.13
3.09
7.97
7.96
7.95
7.60
7.60
7.58
7.58
7.58
7.57
7.57
7.56
7.49
7.48
7.48
7.46
3.82
3.81
3.80
3.80
3.79
3.78
3.60
3.59
3.58
3.56
3.55
2.90
2.88
1.65
1.65
1.64
1.64
1.64
1.60
1.60
1.54
1.54
1.53
1.53
1.52
1.51
1.51
1.51
1.50
1.50
1.27
1.25
1.02
1.01
0.99

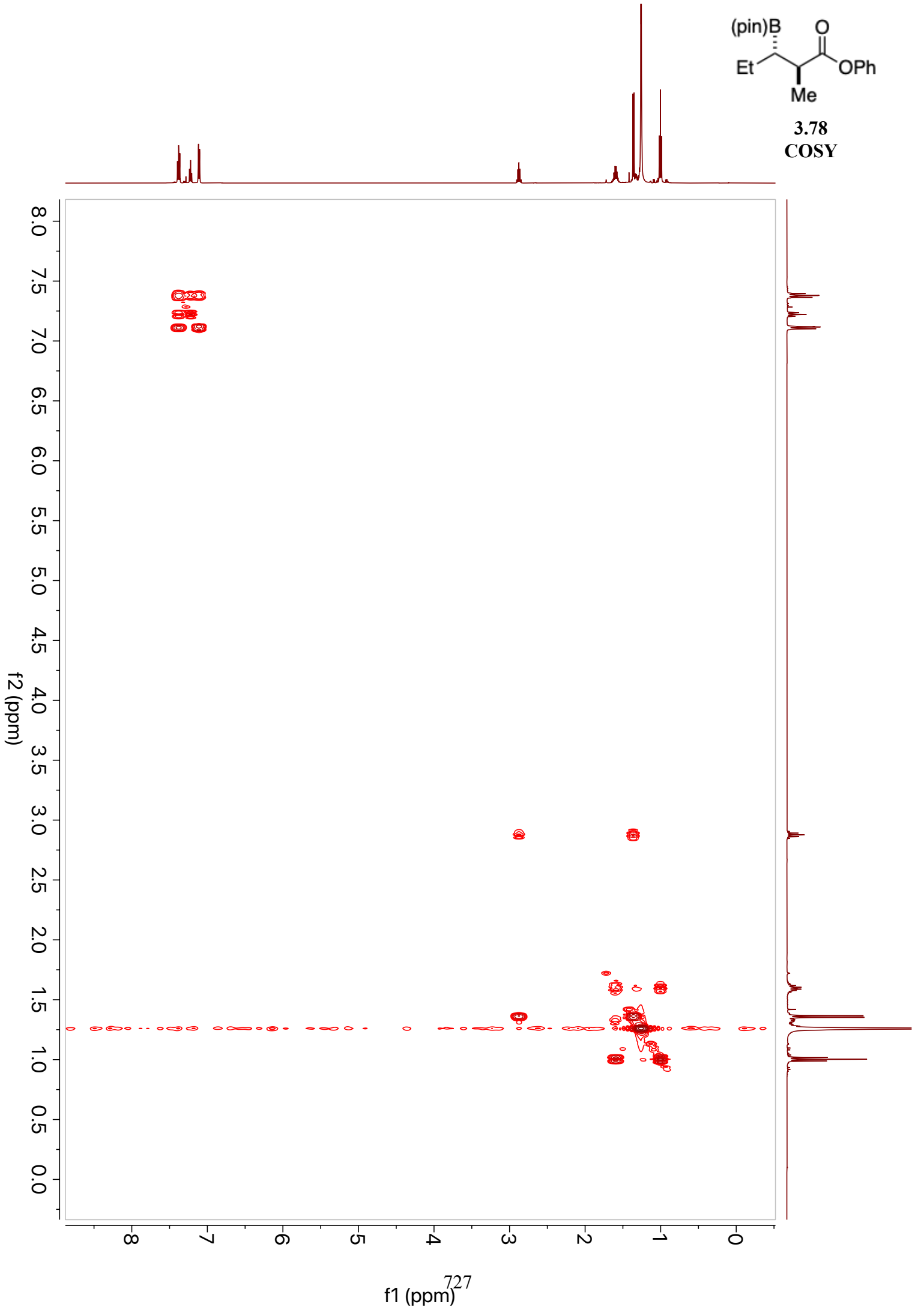

OH
O
Ph
Me
3.76
205.77
136.69
133.33
128.70
128.35
75.38
45.30
27.73
15.49
10.15
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

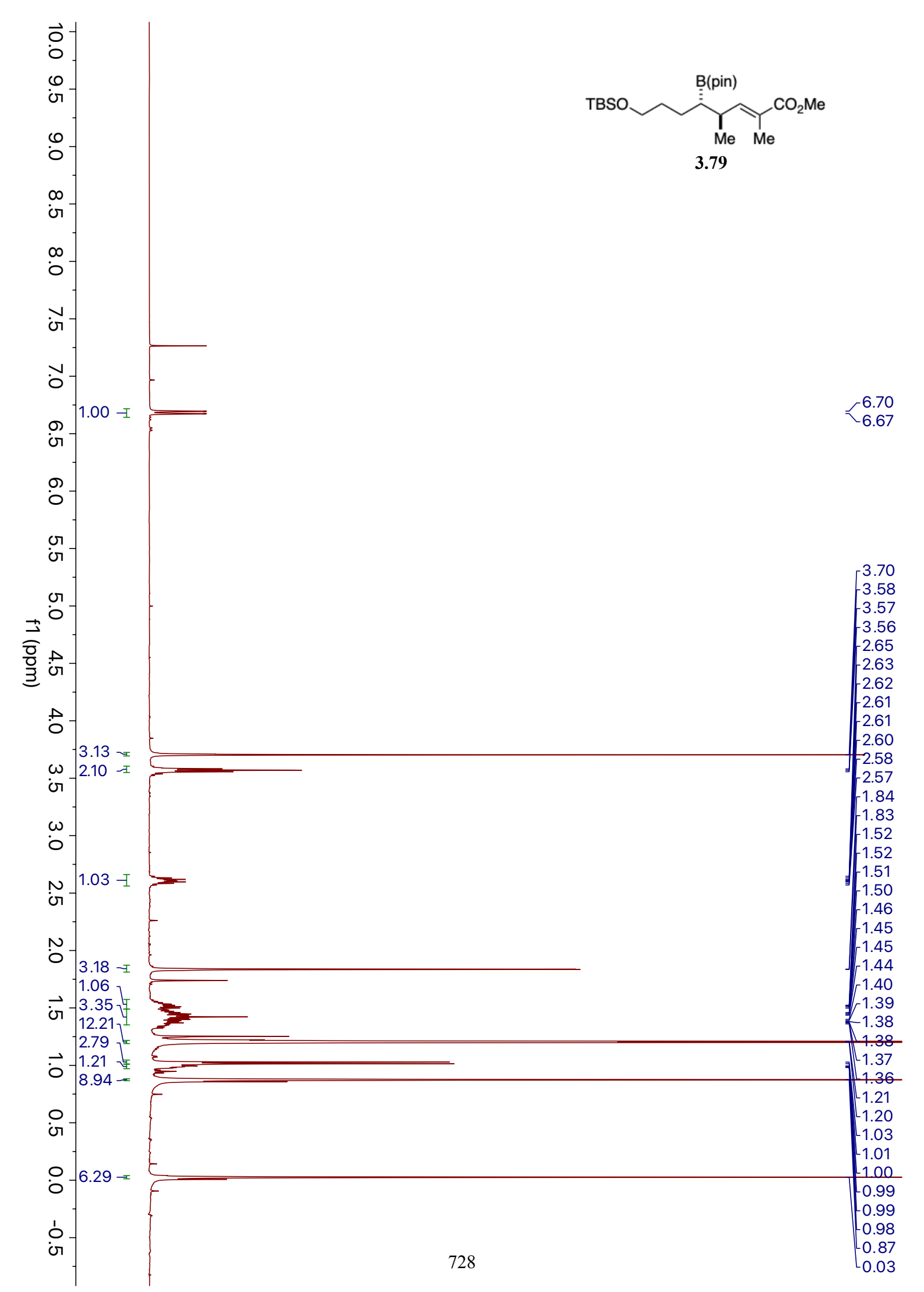

OH
O
n-pentyl
Me
Br
3.77
f1 (ppm)
2.23
2.22
0.88
1.00
0.75
8.80
3.16
2.96
7.83
7.61
3.85
3.50
2.73
1.53
1.44
1.32
1.24
1.22
0.88

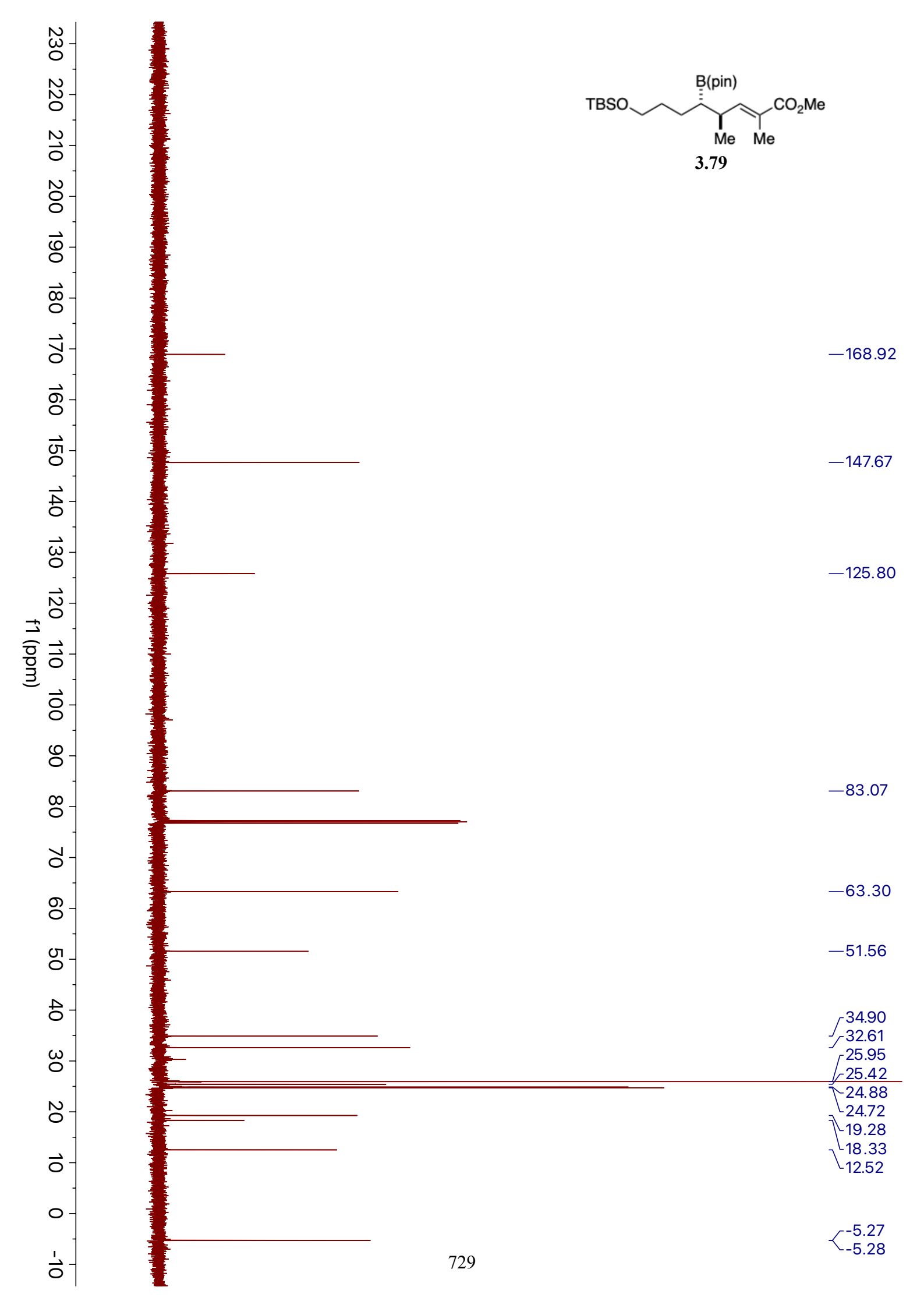

OH
O
n-pentyl
Me
Br
3.77
204.59
135.43
132.01
129.88
128.55
73.93
45.89
34.71
31.76
25.35
22.58
15.29
14.01
f1 (ppm)
220
200
180
160
140
120
100
80
60
40
20
0

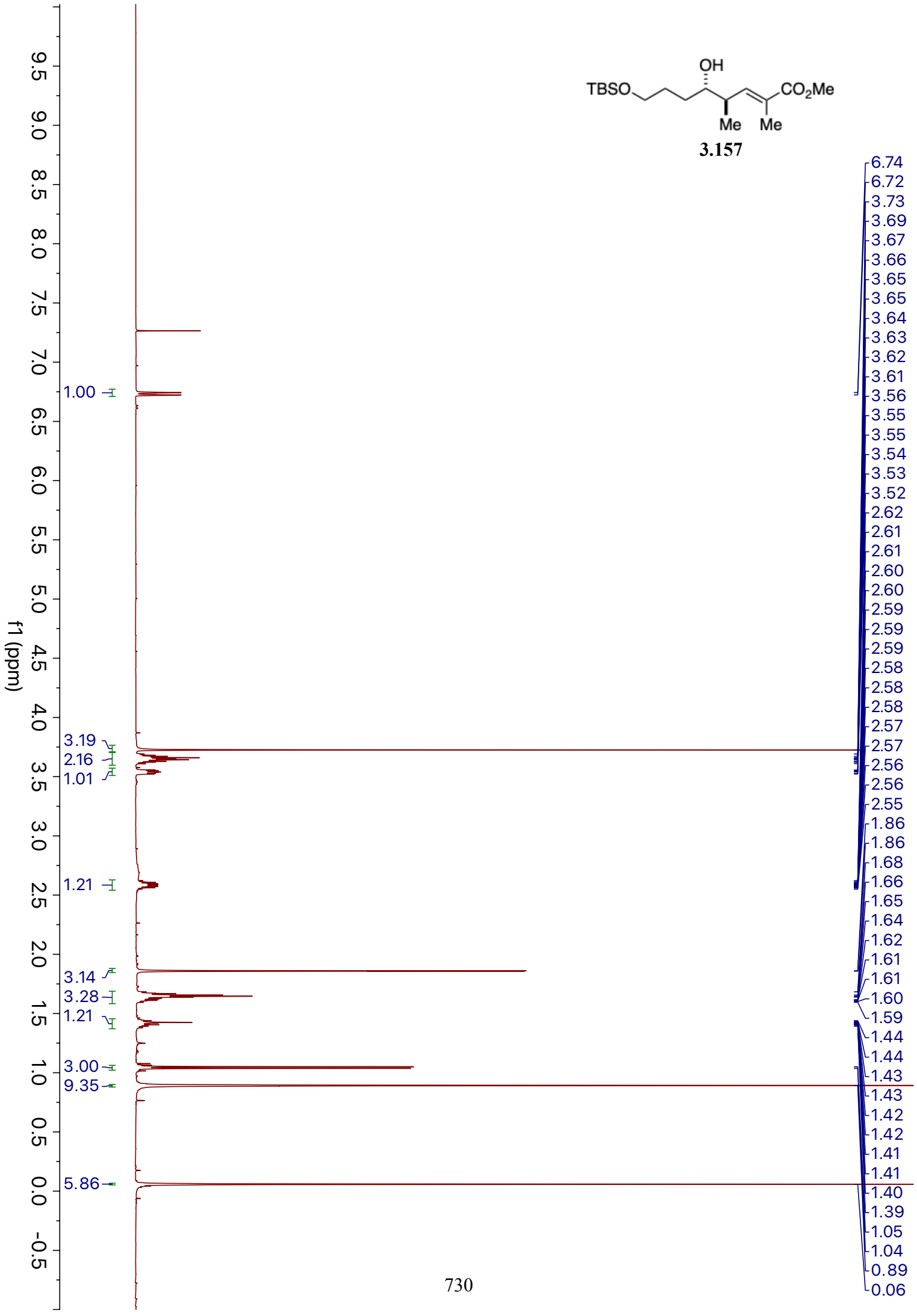

(pin)B
O
Et
OPh
Me
3.78
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.13
1.04
2.04
1.00
2.33
3.08
1.17
12.03
3.29
7.38
7.36
7.36
7.35
7.22
7.22
7.21
7.20
7.19
7.10
7.09
7.08
7.08
2.88
2.87
2.85
2.84
2.82
1.61
1.60
1.58
1.58
1.57
1.57
1.56
1.55
1.34
1.33
1.31
1.31
1.30
1.30
1.28
1.24
1.24
0.99
0.98
0.96

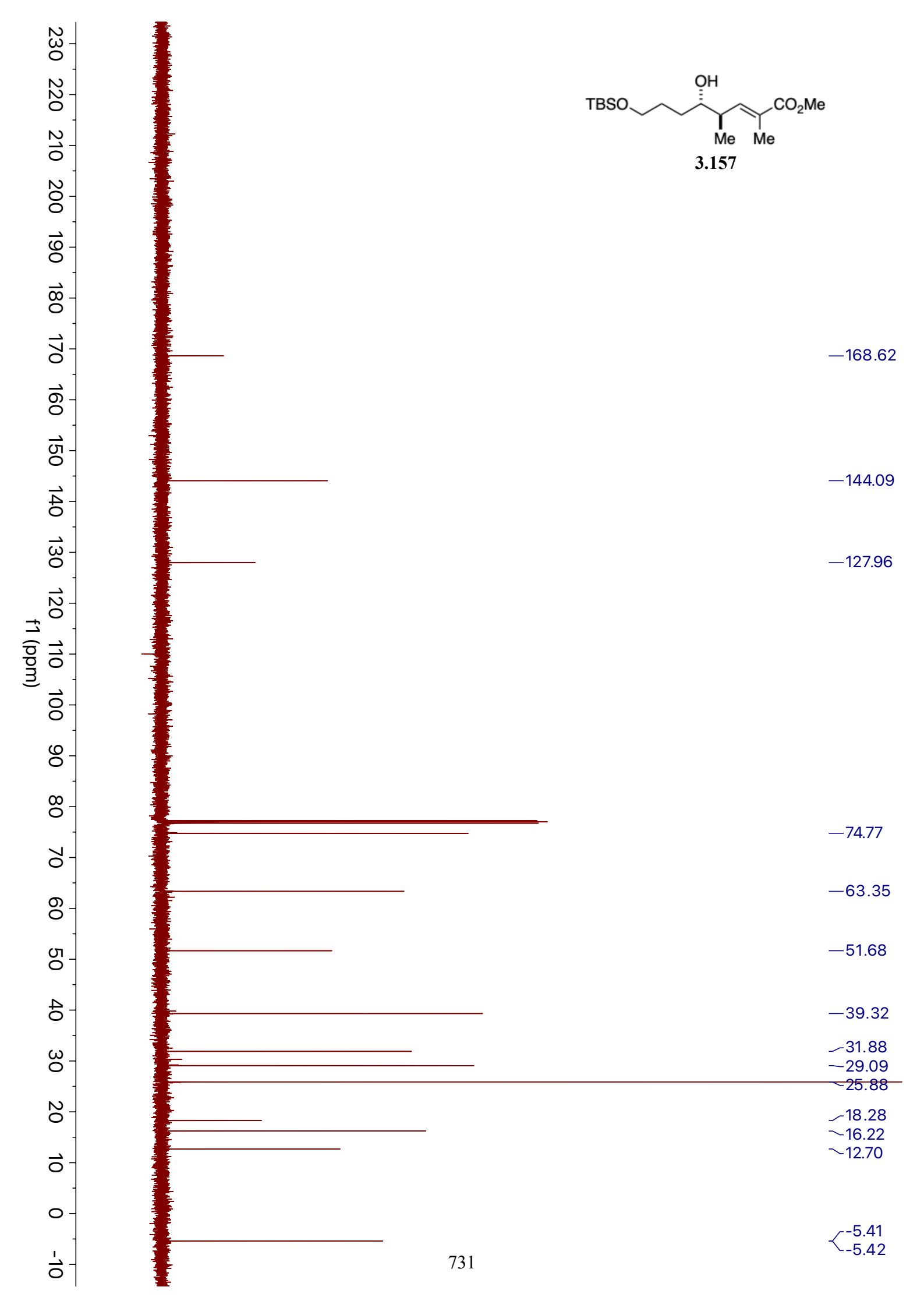

(pin)B
O
Et
OPh
Me
3.78
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
175.46
151.02
129.22
125.47
121.65
83.22
40.50
24.94
24.76
21.21
16.02
13.45

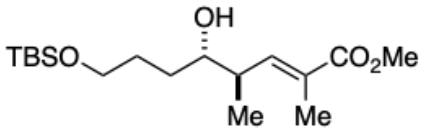

(pin)B
O
Et
OPh
Me
3.78
COSY
f2 (ppm)
f1 (ppm)


B(pin)
TBSO
CO2Me
Me
Me
3.79
f1 (ppm)
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
3.13
2.10
1.03
3.18
1.06
3.35
12.21
2.79
1.21
8.94
6.29
6.70
6.67
3.70
3.58
3.57
3.56
2.65
2.63
2.62
2.61
2.61
2.60
2.58
2.57
1.84
1.83
1.52
1.52
1.51
1.50
1.46
1.45
1.45
1.44
1.40
1.39
1.38
1.38
1.37
1.36
1.21
1.20
1.03
1.01
1.00
0.99
0.99
0.98
0.87
0.03


B(pin)
TBSO
CO2Me
Me
Me
3.79
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.92
147.67
125.80
83.07
63.30
51.56
34.90
32.61
25.95
25.42
24.88
24.72
19.28
18.33
12.52
-5.27
-5.28


OH
TBSO
CO2Me
Me
Me
3.157
f1 (ppm)
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
3.19
2.16
1.01
1.21
3.14
3.28
1.21
3.00
9.35
5.86
6.74
6.72
3.73
3.69
3.67
3.66
3.65
3.65
3.64
3.63
3.62
3.61
3.56
3.55
3.55
3.54
3.53
3.52
2.62
2.61
2.61
2.60
2.60
2.59
2.59
2.59
2.58
2.58
2.58
2.57
2.57
2.56
2.56
2.55
1.86
1.86
1.68
1.66
1.65
1.64
1.62
1.61
1.61
1.60
1.59
1.44
1.44
1.43
1.43
1.42
1.42
1.41
1.41
1.40
1.39
1.05
1.04
0.89
0.06

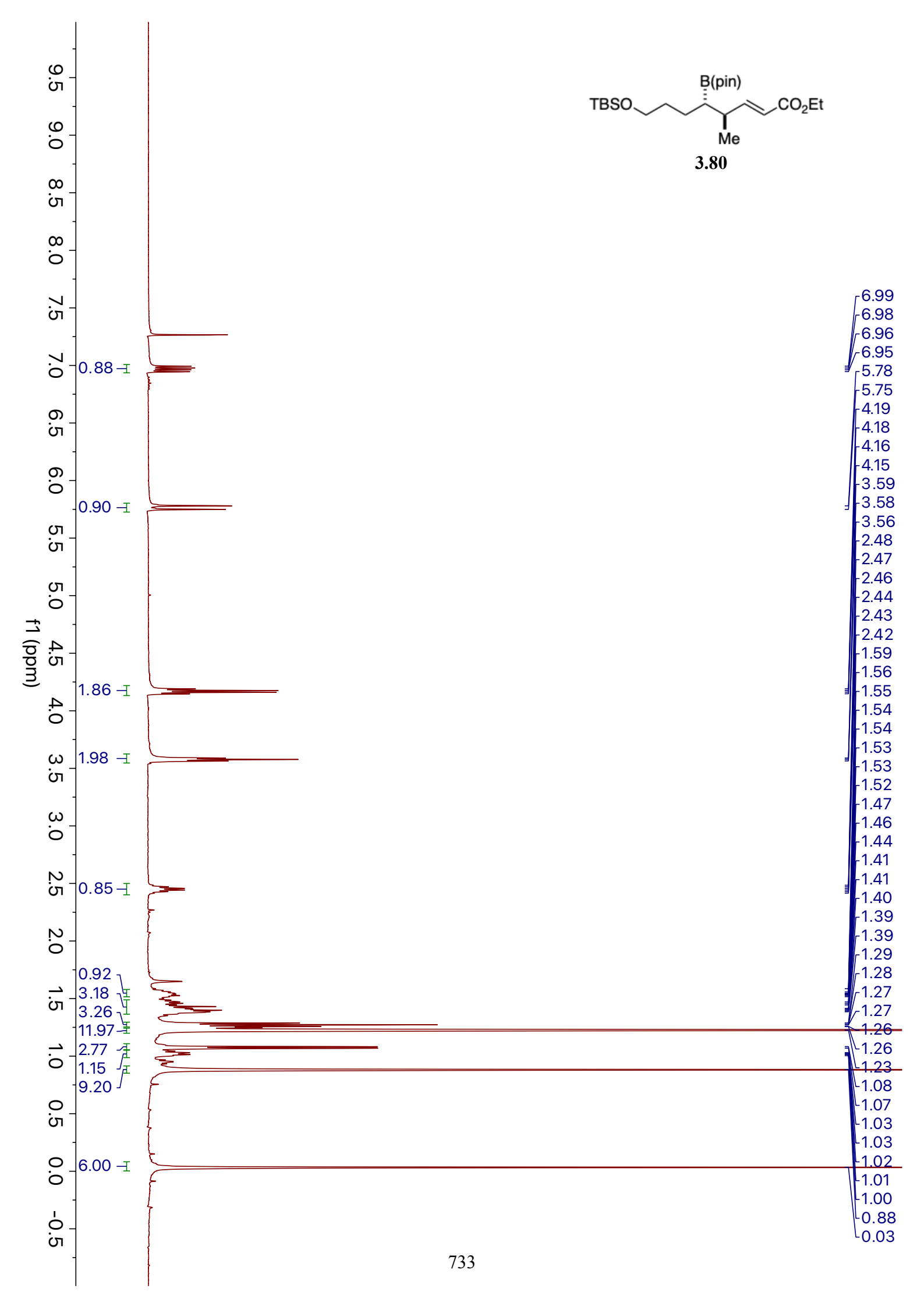

OH
TBSO
CO2Me
Me
Me
3.157
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.62
144.09
127.96
74.77
63.35
51.68
39.32
31.88
29.09
25.88
18.28
16.22
12.70
-5.41
-5.42

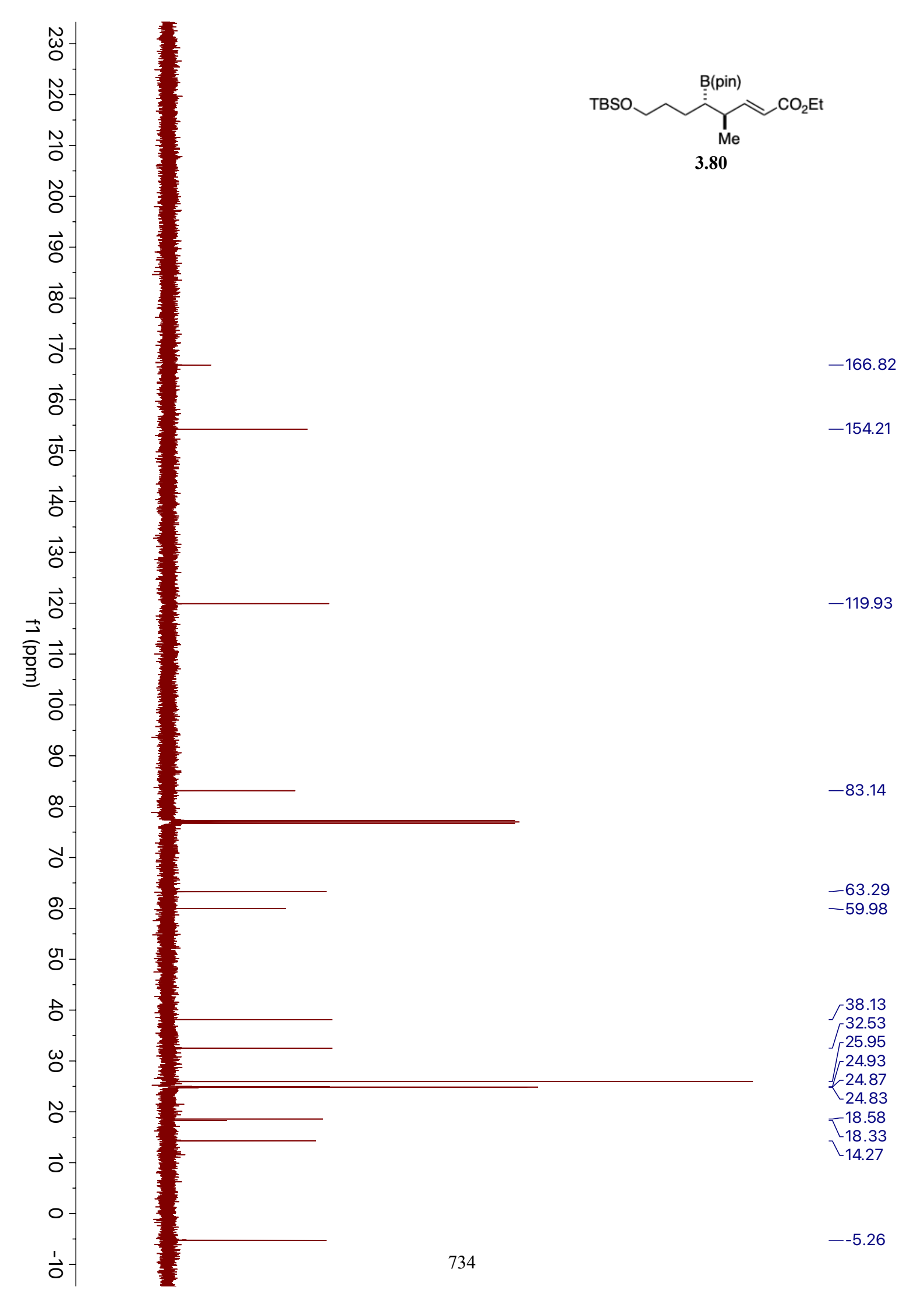


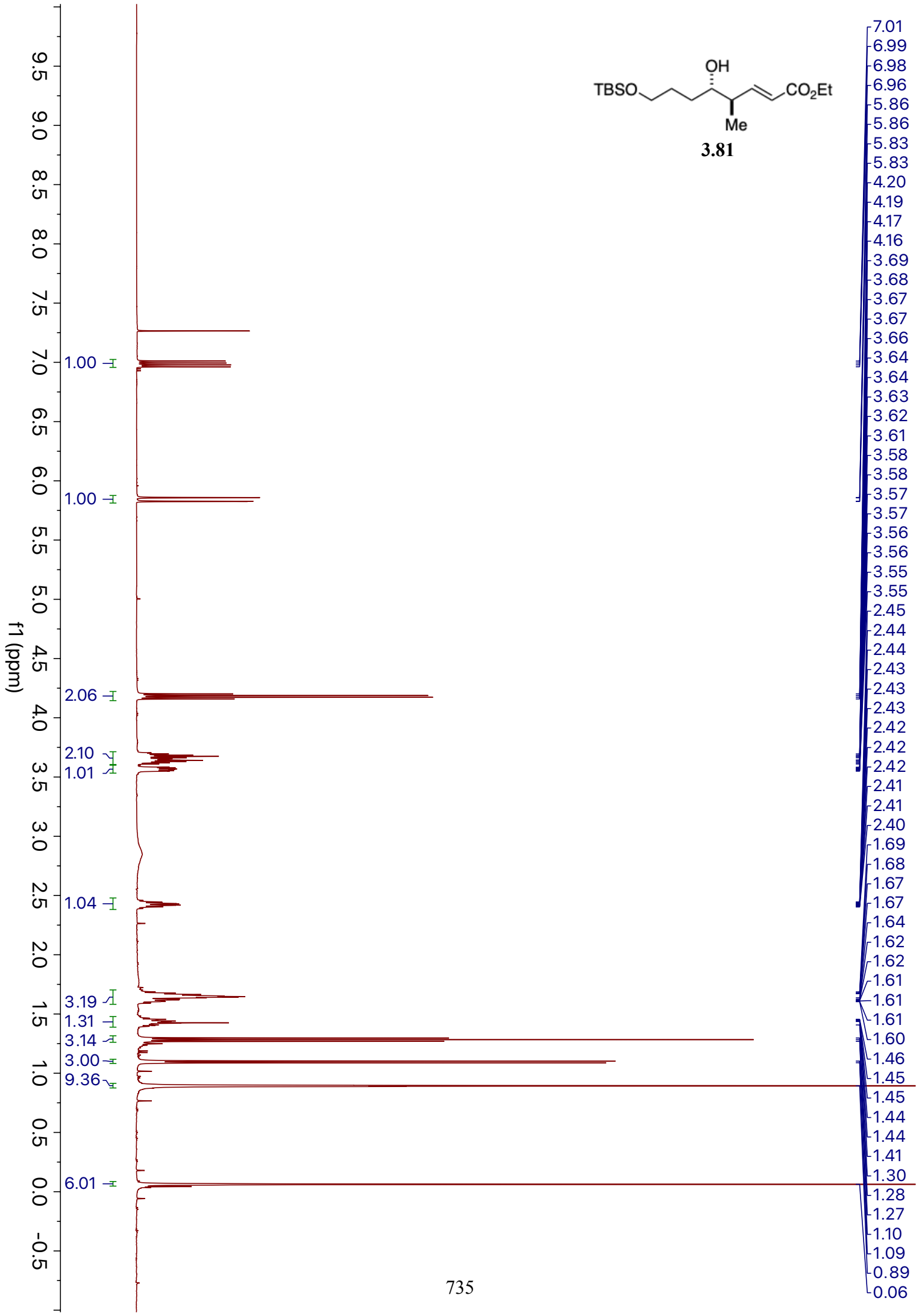
3.157
COSY

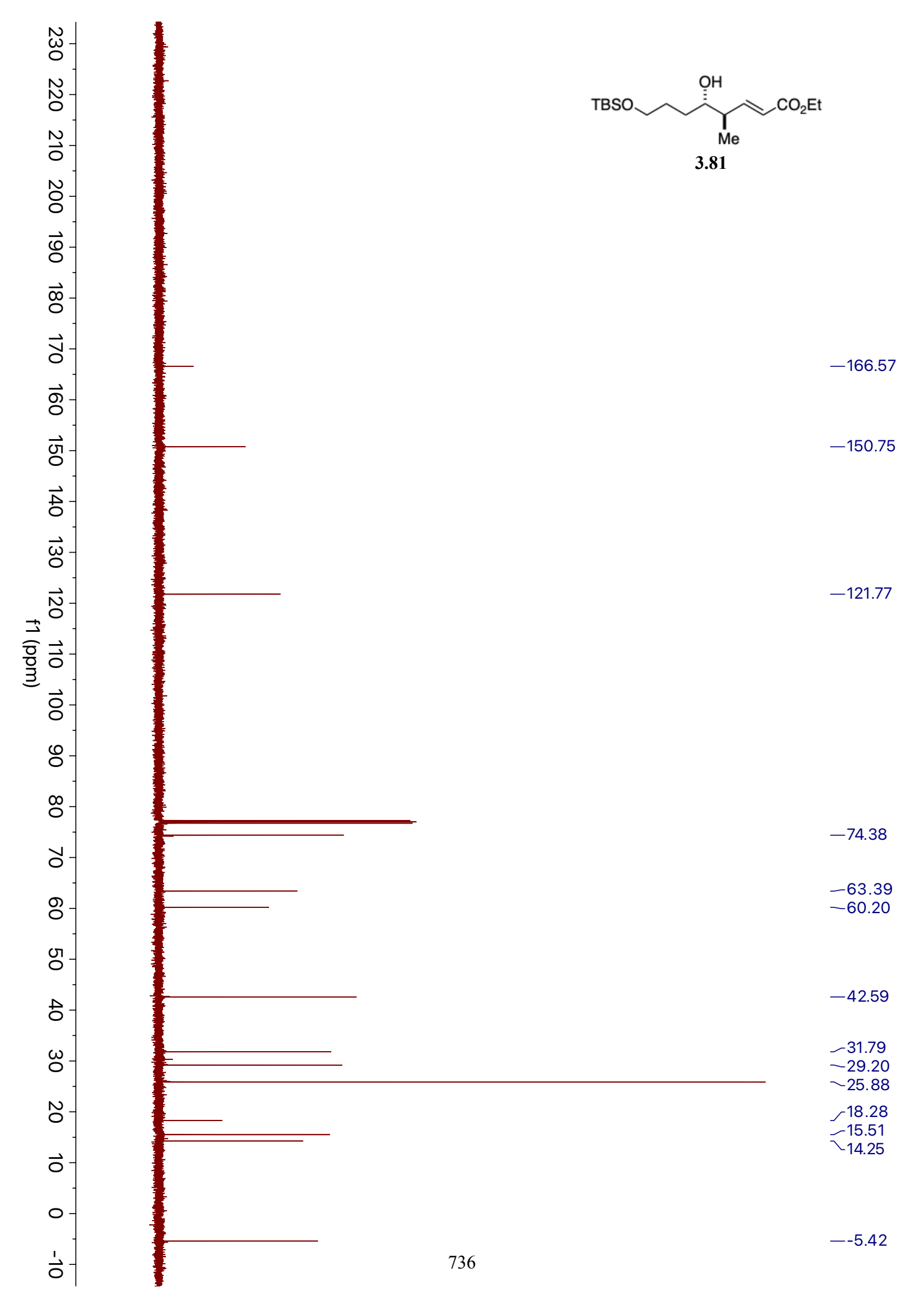
f2 (ppm)

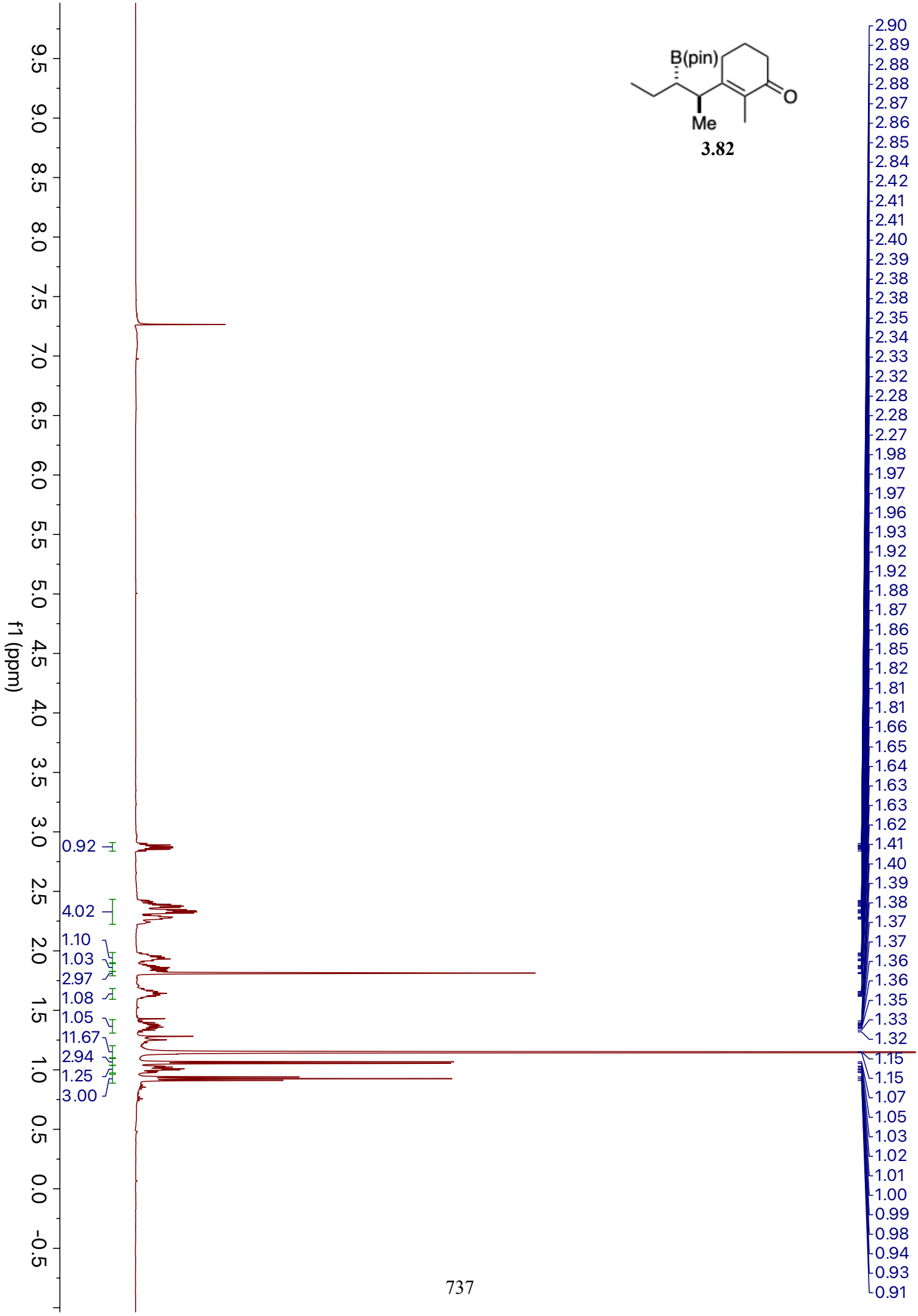
f1 (ppm)

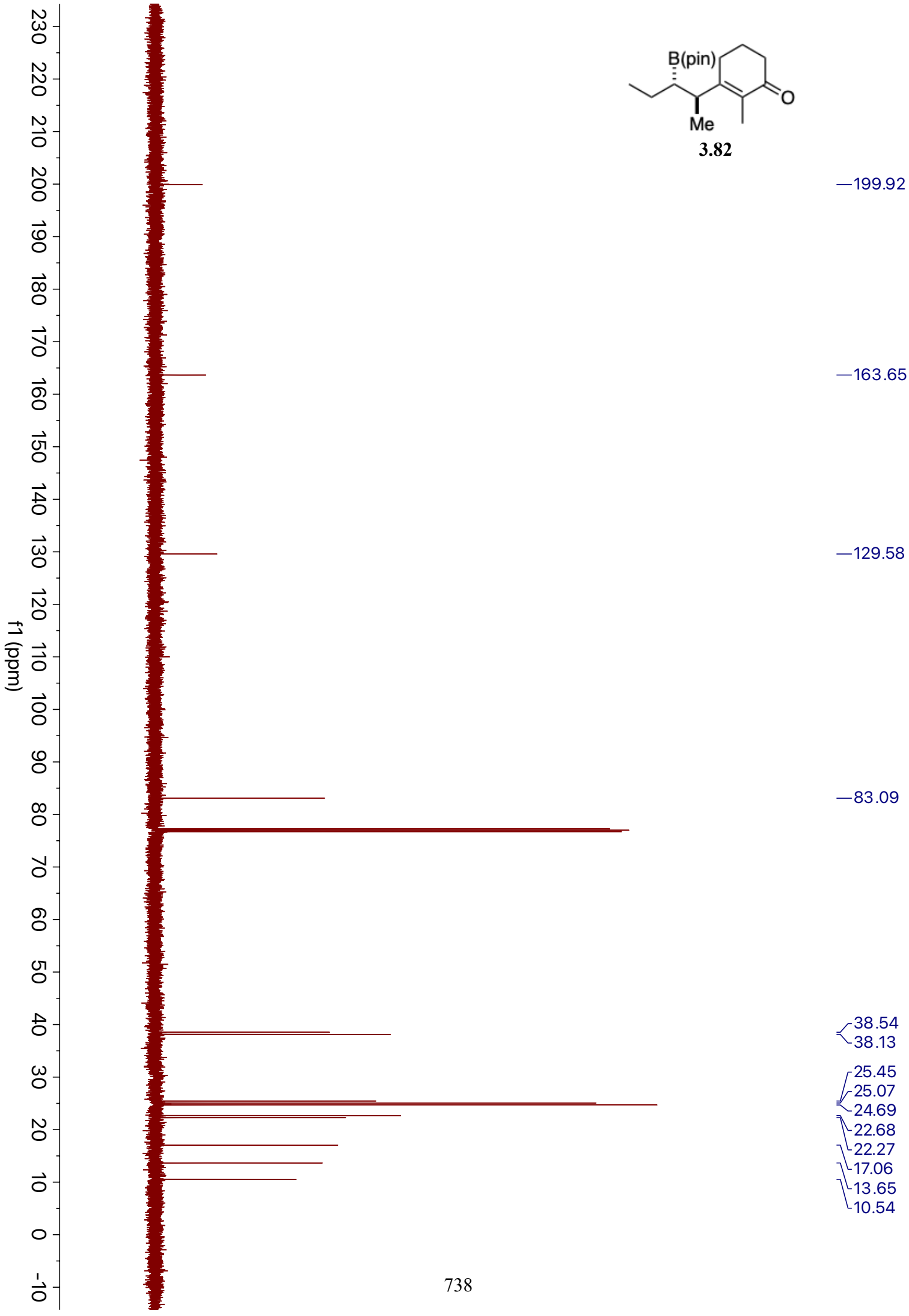

B(pin)
TBSO
CO2Et
Me
3.80
f1 (ppm)
0.88
0.90
1.86
1.98
0.85
0.92
3.18
3.26
11.97
2.77
1.15
9.20
6.00
6.99
6.98
6.96
6.95
5.78
5.75
4.19
4.18
4.16
4.15
3.59
3.58
3.56
2.48
2.47
2.46
2.44
2.43
2.42
1.59
1.56
1.55
1.54
1.54
1.53
1.53
1.52
1.47
1.46
1.44
1.41
1.41
1.40
1.39
1.39
1.29
1.28
1.27
1.27
1.26
1.26
1.23
1.08
1.07
1.03
1.03
1.02
1.01
1.00
0.88
0.03

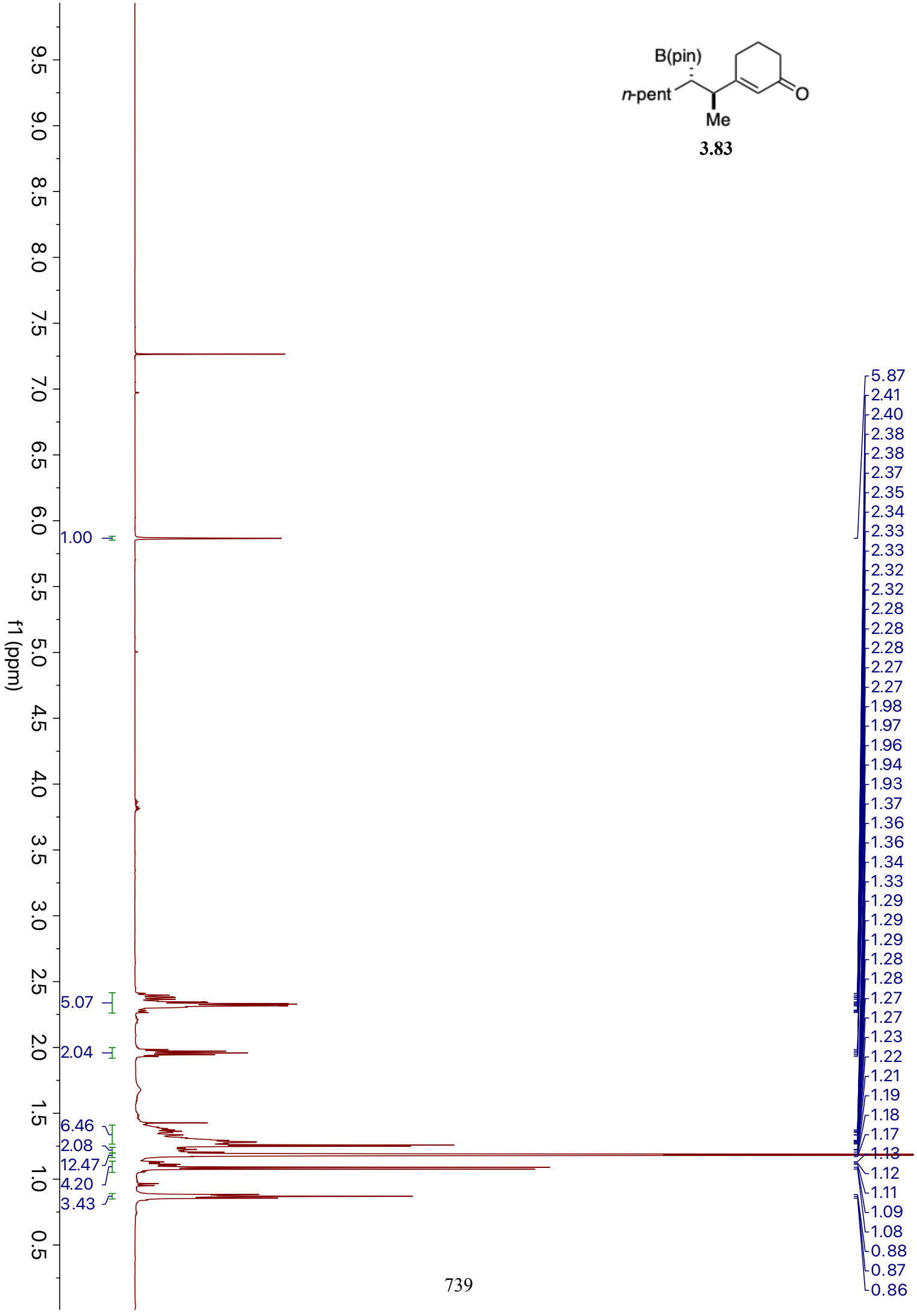

B(pin)
TBSO
CO2Et
Me
3.80
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
166.82
154.21
119.93
83.14
63.29
59.98
38.13
32.53
25.95
24.93
24.87
24.83
18.58
18.33
14.27
-5.26

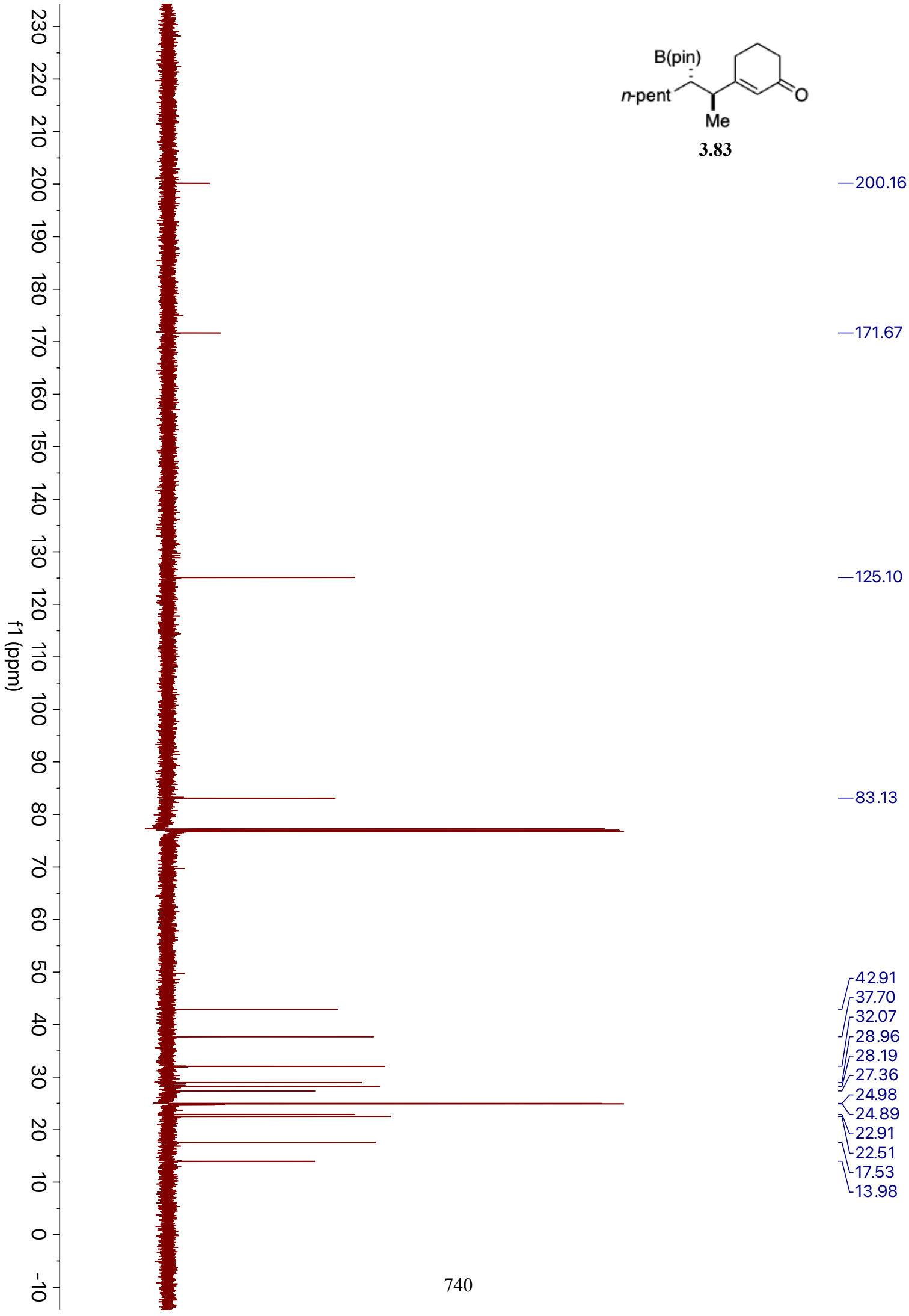

OH
TBSO
CO2Et
Me
3.81
f1 (ppm)
1.00
1.00
2.06
2.10
1.01
1.04
3.19
1.31
3.14
3.00
9.36
6.01

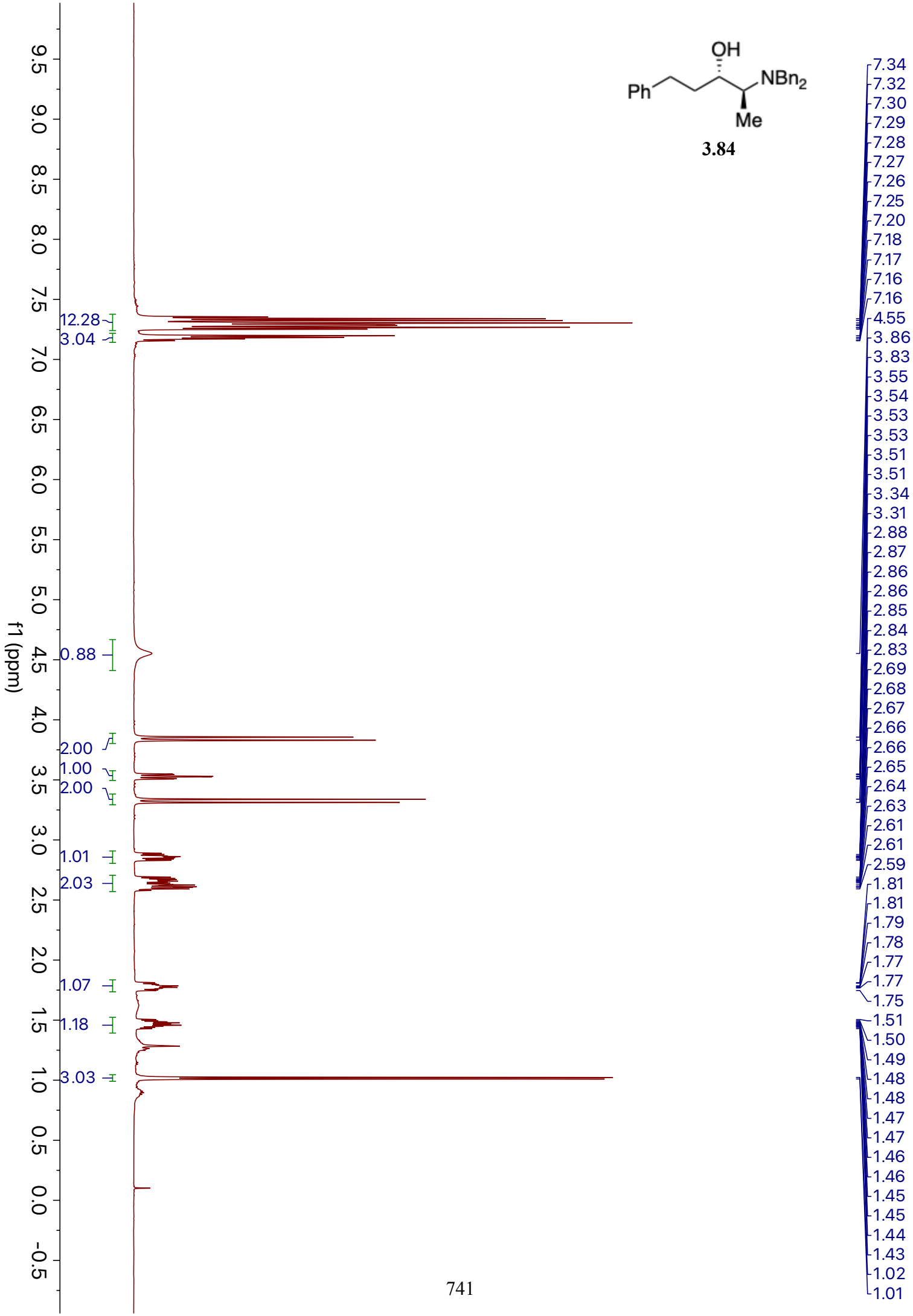

OH
TBSO
CO2Et
Me
3.81
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
166.57
150.75
121.77
74.38
63.39
60.20
42.59
31.79
29.20
25.88
18.28
15.51
14.25
-5.42

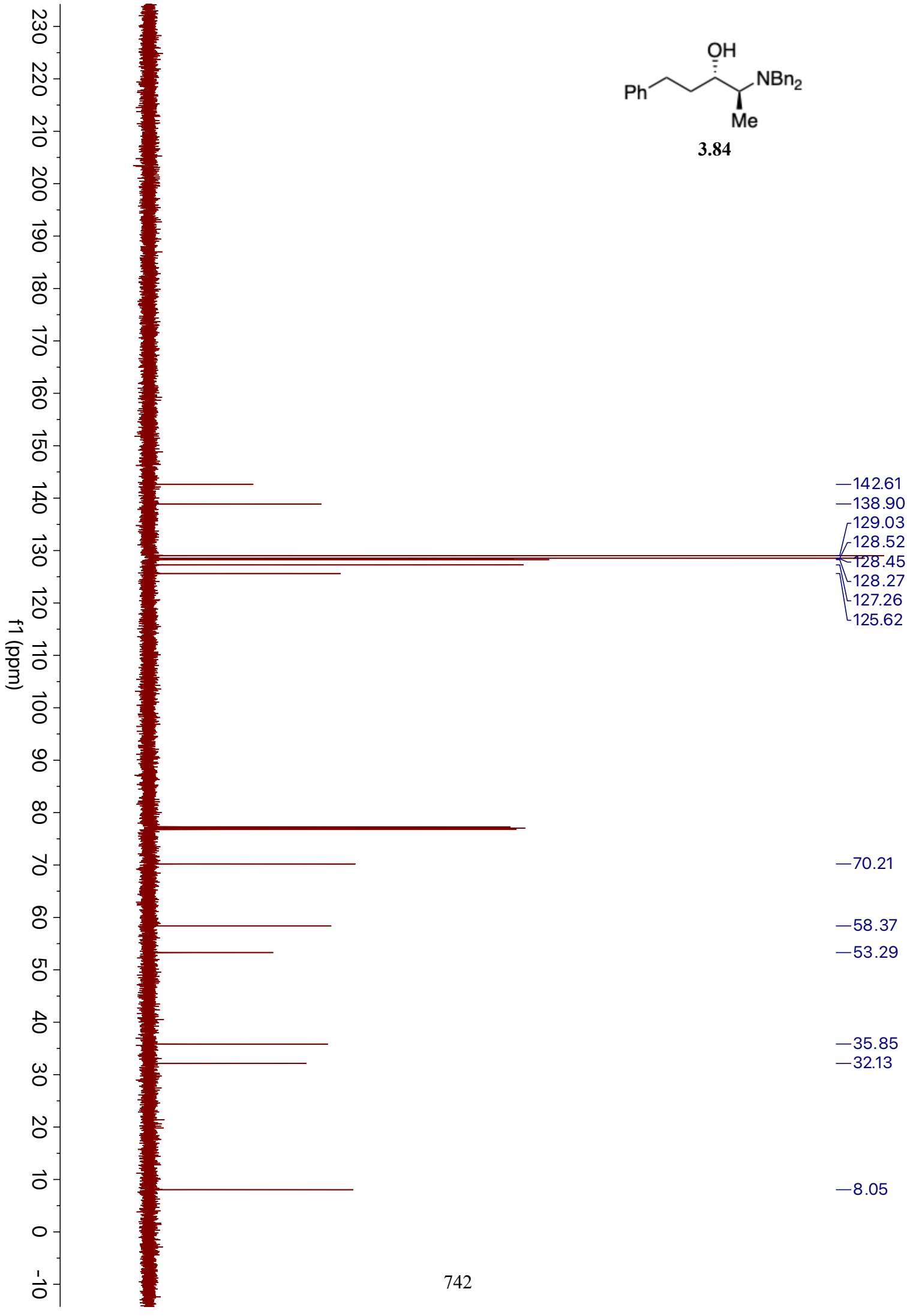

B(pin)
Me
O
3.82
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
0.92
4.02
1.10
1.03
2.97
1.08
1.05
11.67
2.94
1.25
3.00
2.90 2.89 2.88 2.88 2.87 2.86 2.85 2.84 2.42 2.41 2.41 2.40 2.39 2.38 2.38 2.35 2.34 2.33 2.32 2.28 2.28 2.27 1.98 1.97 1.97 1.96 1.93 1.92 1.92 1.88 1.87 1.86 1.85 1.82 1.81 1.81 1.66 1.65 1.64 1.63 1.63 1.62 1.41 1.40 1.39 1.38 1.37 1.37 1.36 1.36 1.35 1.33 1.32 1.15 1.15 1.07 1.05 1.03 1.02 1.01 1.00 0.99 0.98 0.94 0.93 0.91

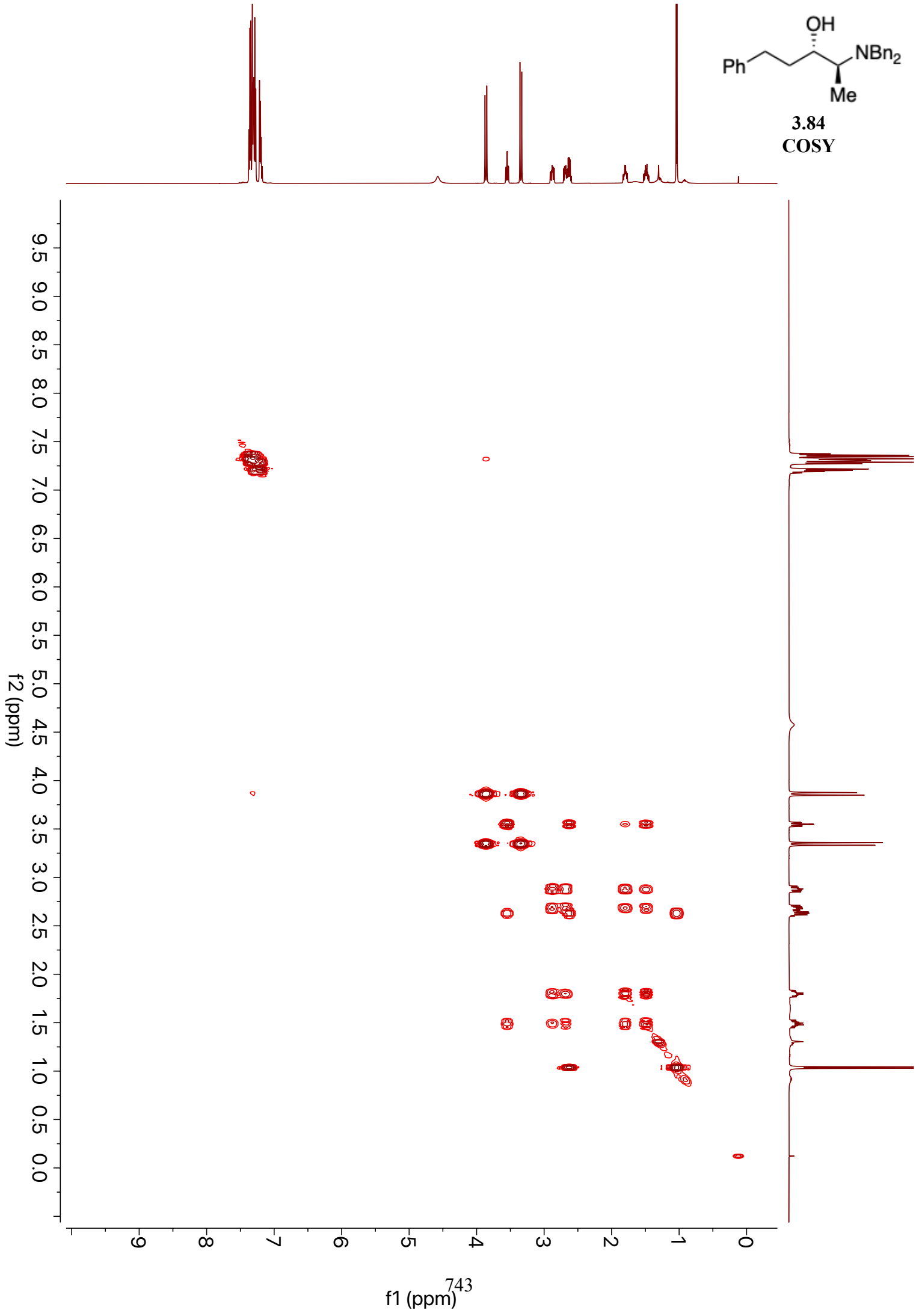

B(pin)
O
Me
3.82
199.92
163.65
129.58
83.09
38.54
38.13
25.45
25.07
24.69
22.68
22.27
17.06
13.65
10.54
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

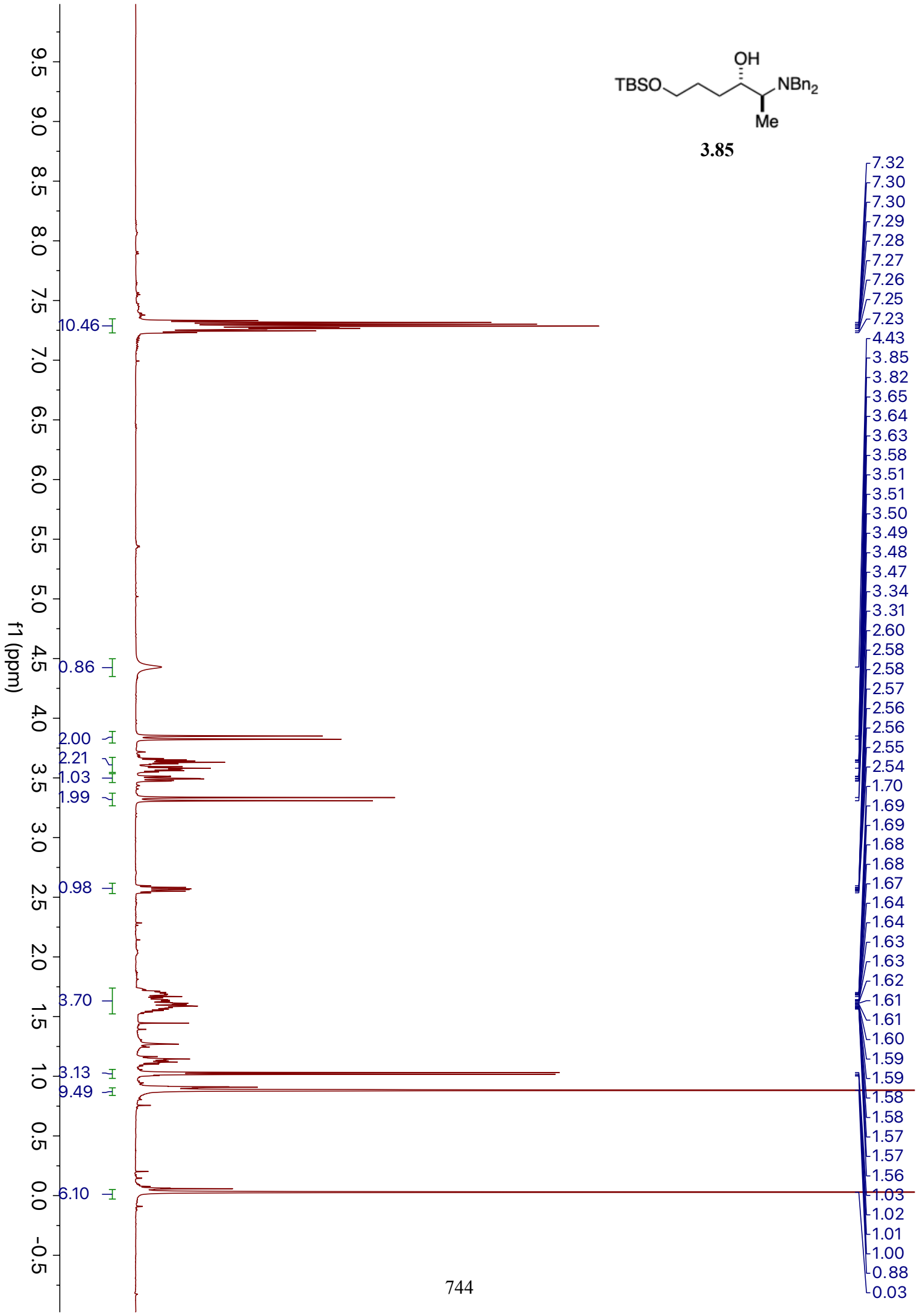

B(pin)
n-pent
Me
O
3.83
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.00
5.07
2.04
6.46
2.08
12.47
4.20
3.43
5.87
2.41
2.40
2.38
2.38
2.37
2.35
2.34
2.33
2.33
2.32
2.32
2.28
2.28
2.28
2.27
2.27
1.98
1.97
1.96
1.94
1.93
1.37
1.36
1.36
1.34
1.33
1.29
1.29
1.29
1.28
1.28
1.27
1.27
1.23
1.22
1.21
1.19
1.18
1.17
1.13
1.12
1.11
1.09
1.08
0.88
0.87
0.86

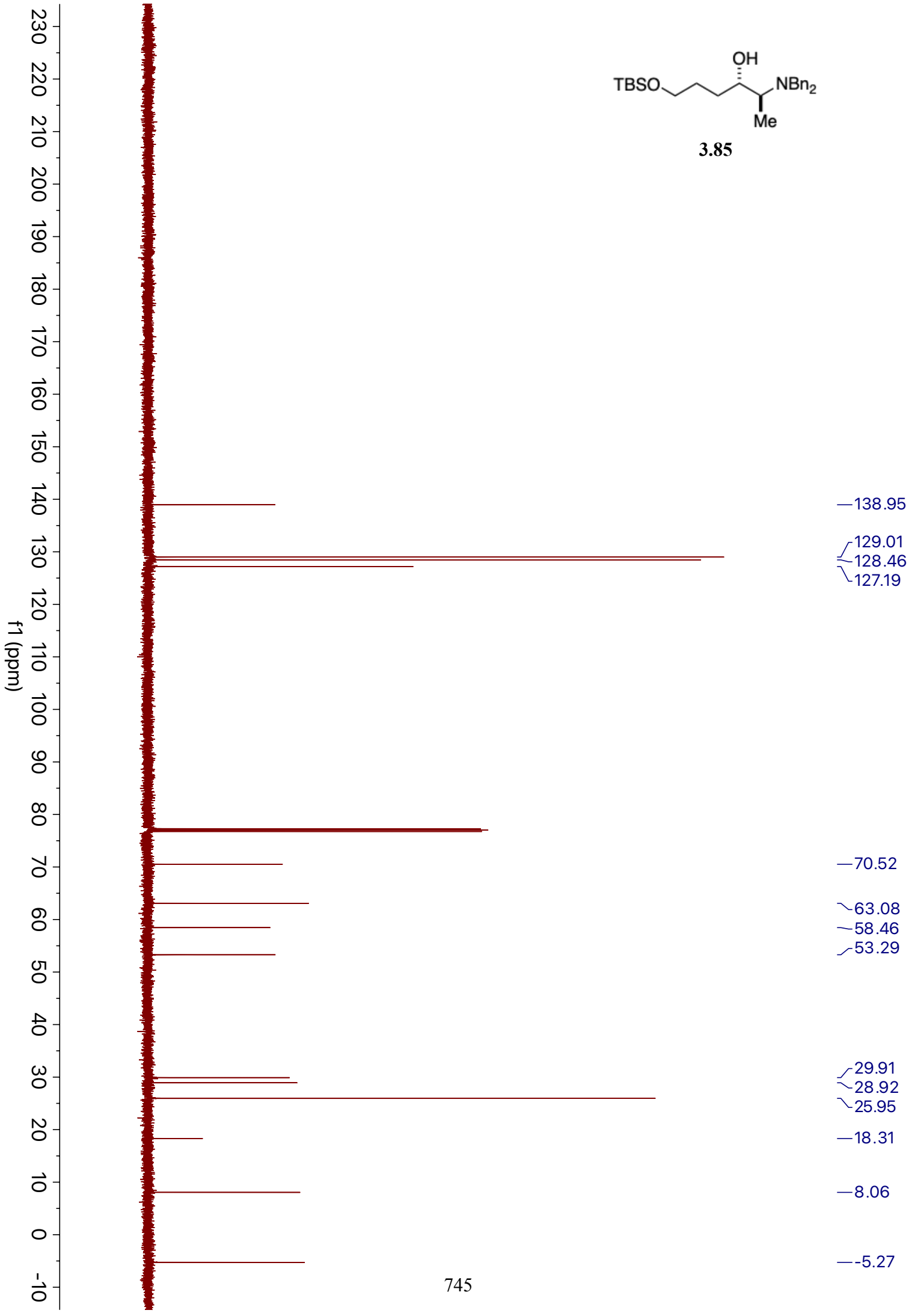

B(pin)
n-pent
Me
O
3.83
200.16
171.67
125.10
83.13
42.91
37.70
32.07
28.96
28.19
27.36
24.98
24.89
22.91
22.51
17.53
13.98
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

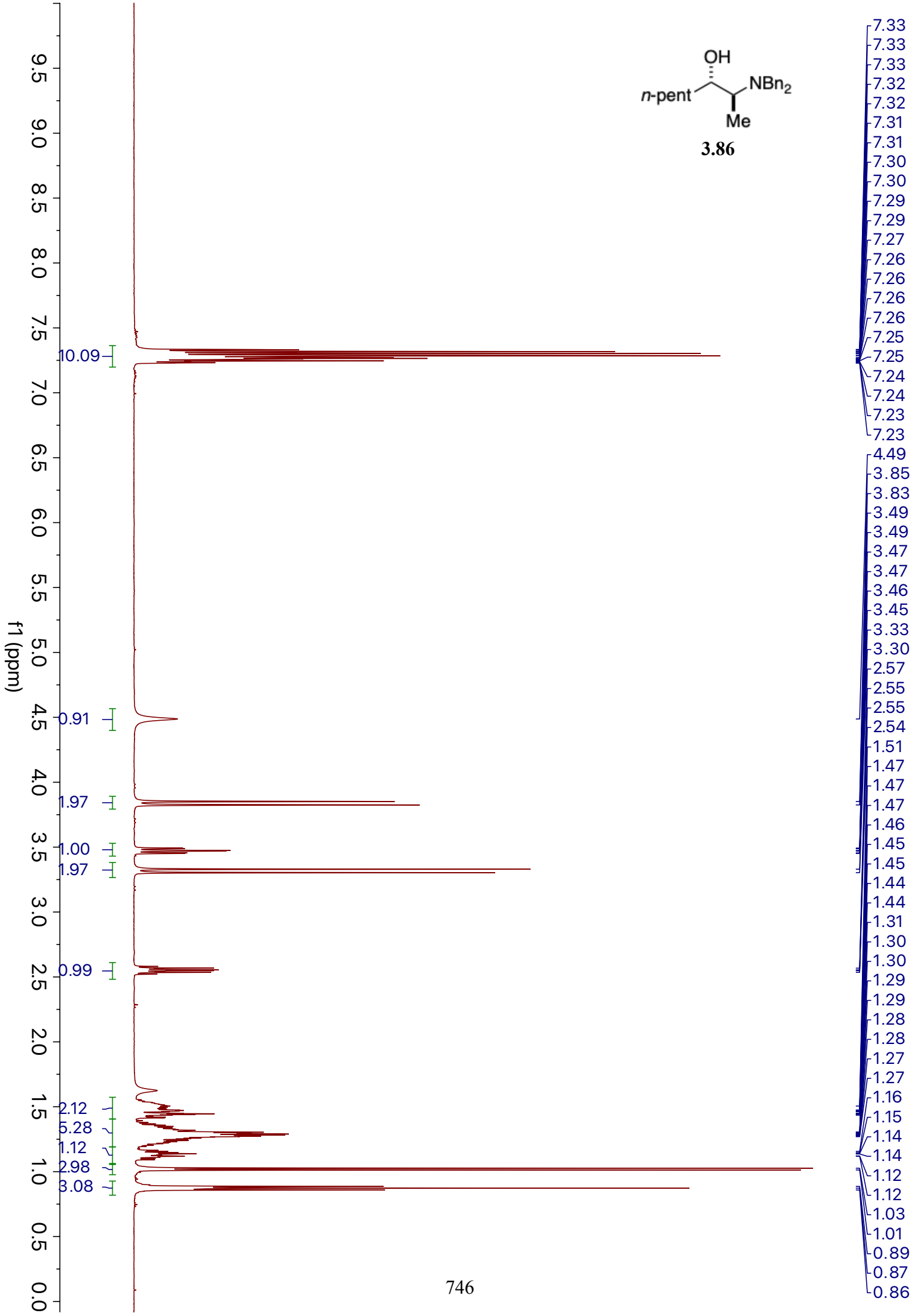

OH
NBn2
Ph
Me
3.84
f1 (ppm)
12.28
3.04
0.88
2.00
1.00
2.00
1.01
2.03
1.07
1.18
3.03

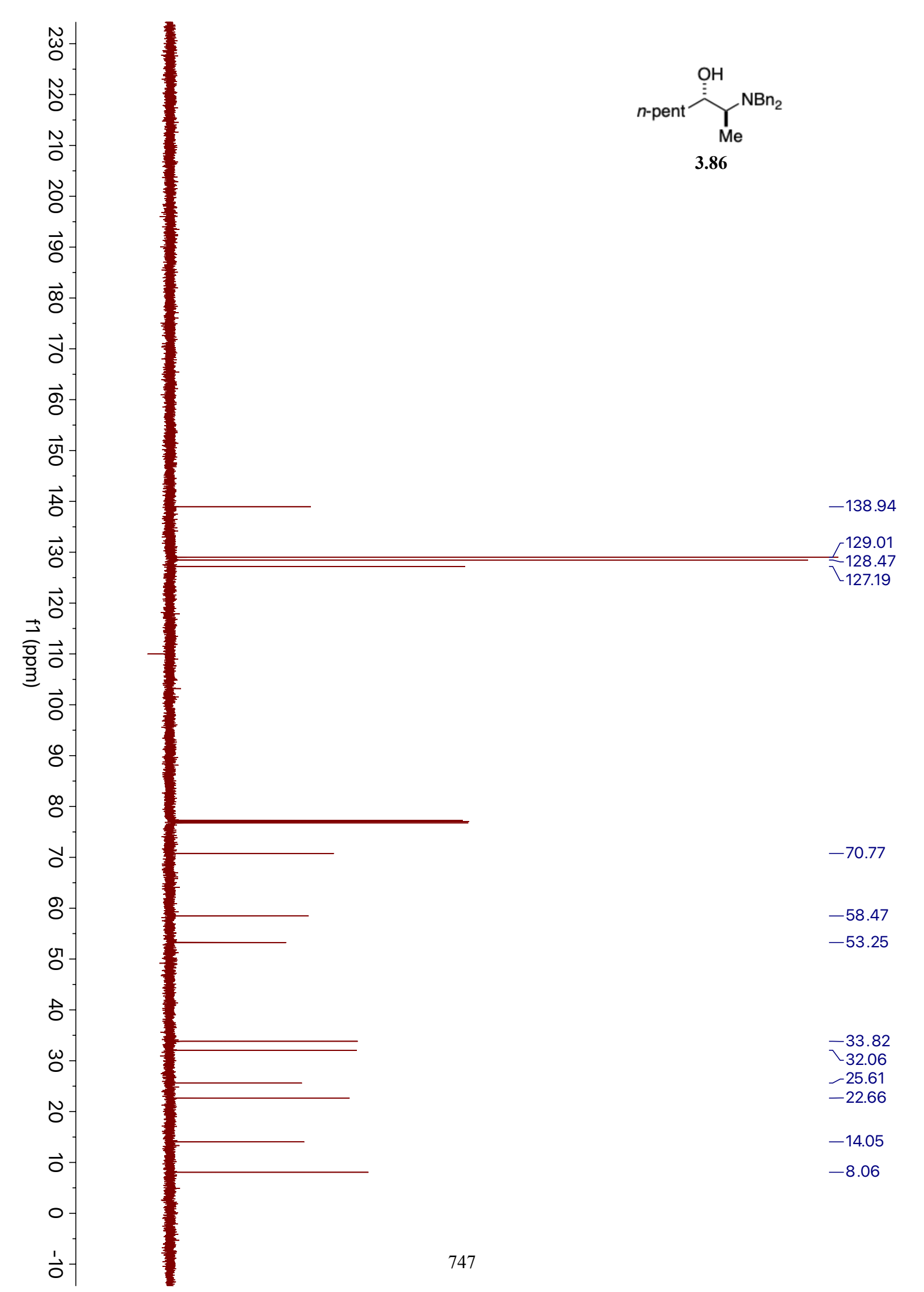

OH
Ph
NBn2
Me
3.84
142.61
138.90
129.03
128.52
128.45
128.27
127.26
125.62
70.21
58.37
53.29
35.85
32.13
8.05
f1 (ppm)

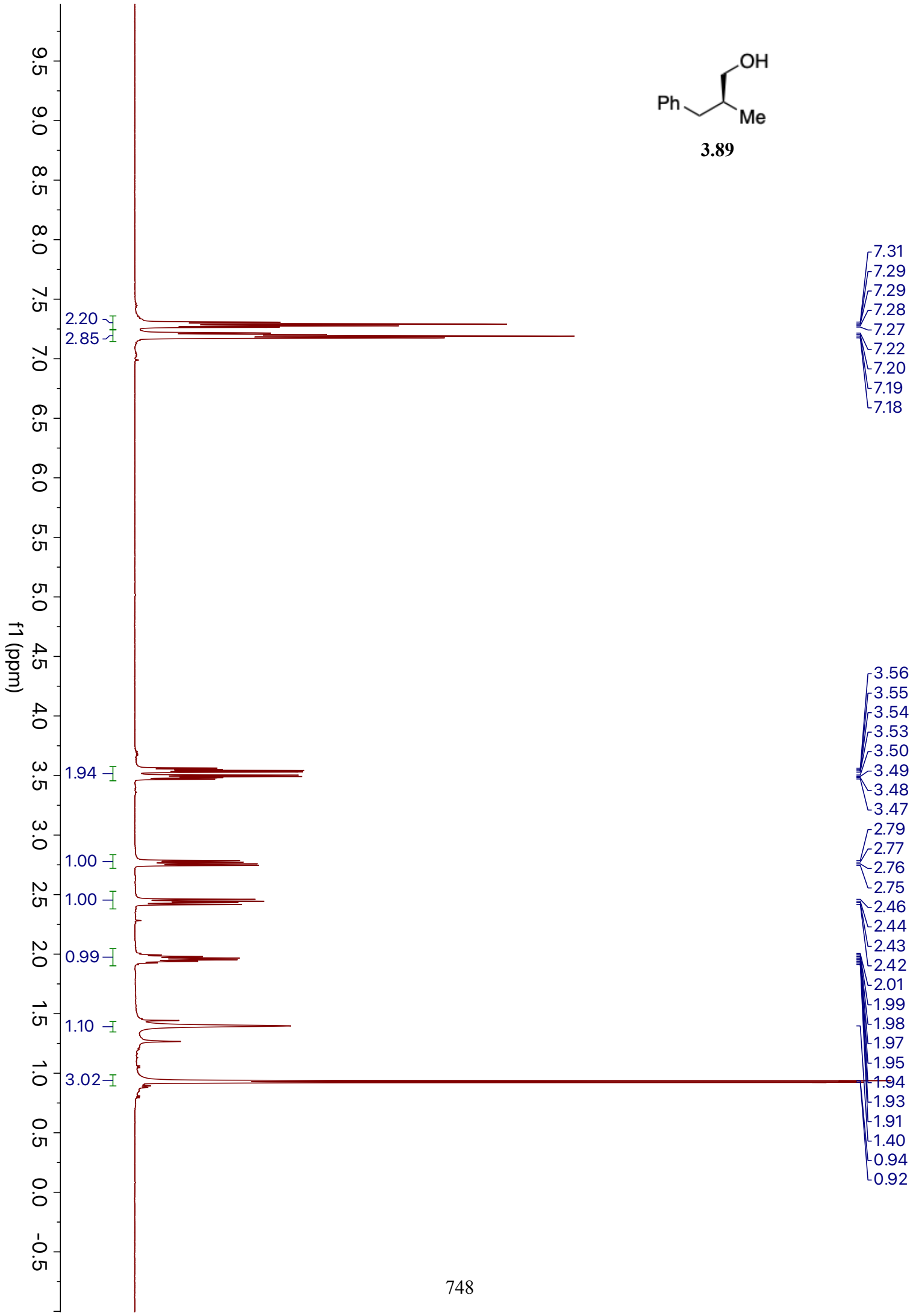

OH
NBn2
Ph
Me
3.84
COSY
f2 (ppm)
f1 (ppm)

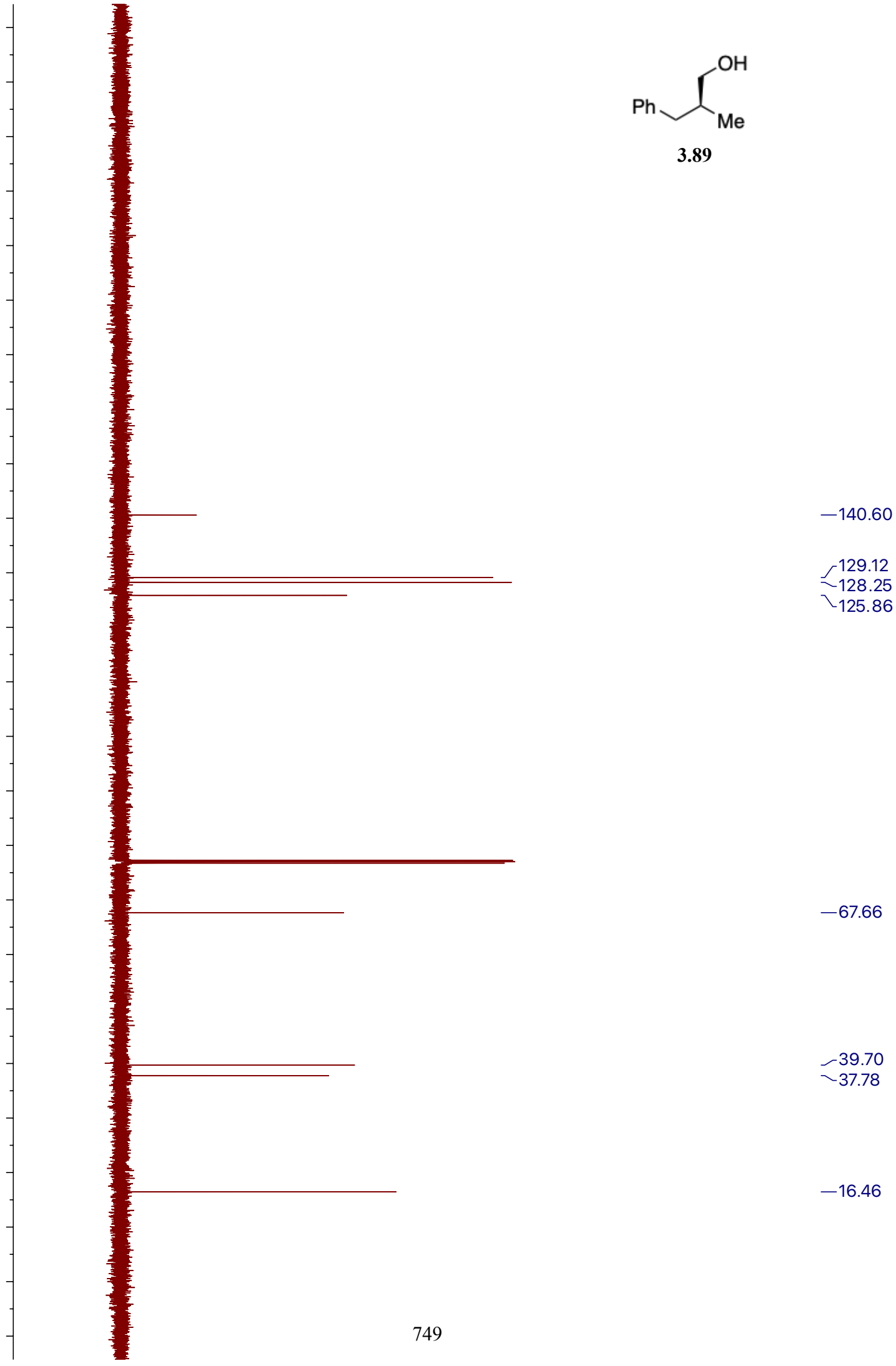

OH
TBSO
NBn2
Me
3.85
f1 (ppm)
10.46
0.86
2.00
2.21
1.03
1.99
0.98
3.70
3.13
9.49
6.10

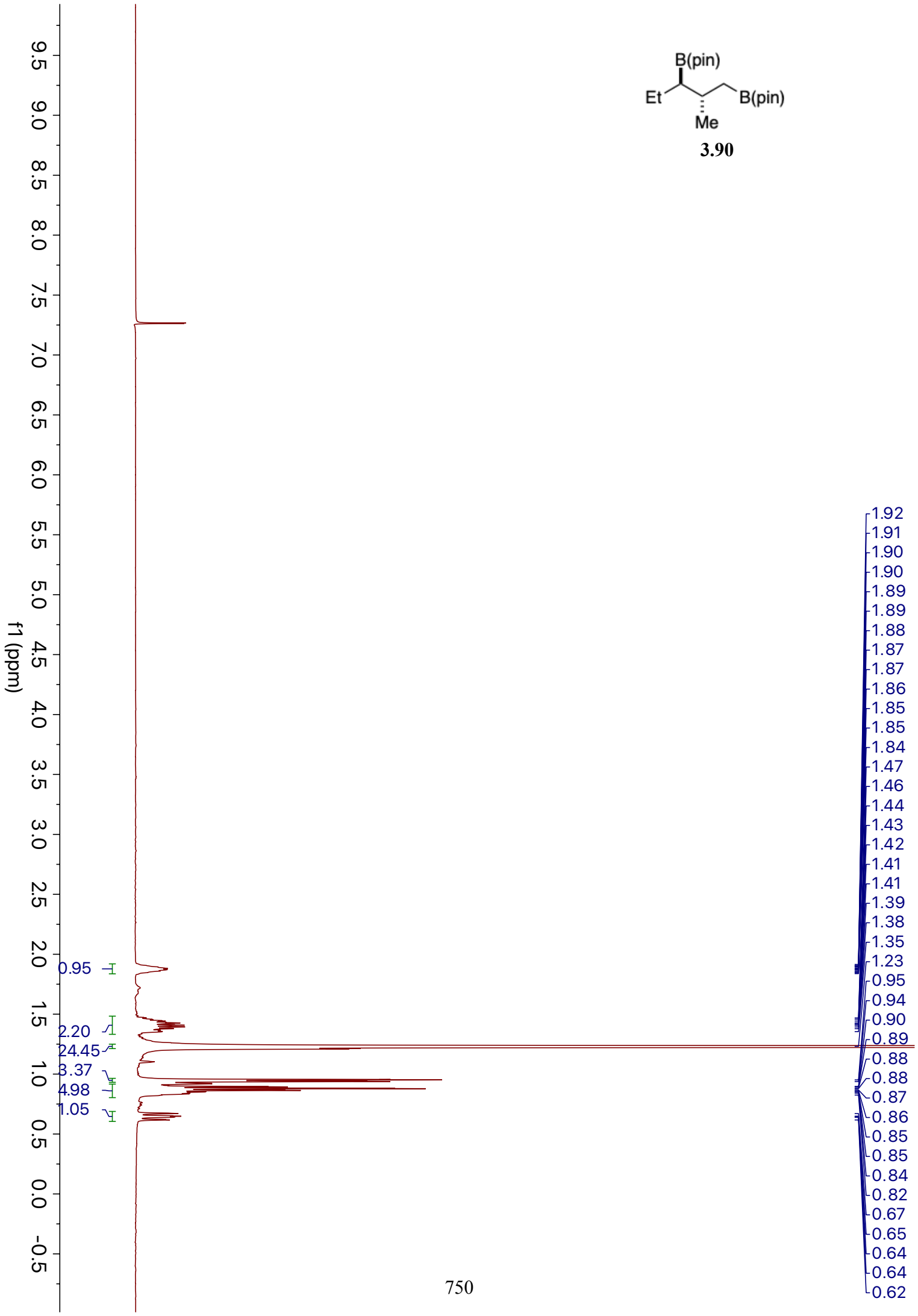

OH
TBSO
NBn2
Me
3.85
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
138.95
129.01
128.46
127.19
70.52
63.08
58.46
53.29
29.91
28.92
25.95
18.31
8.06
-5.27

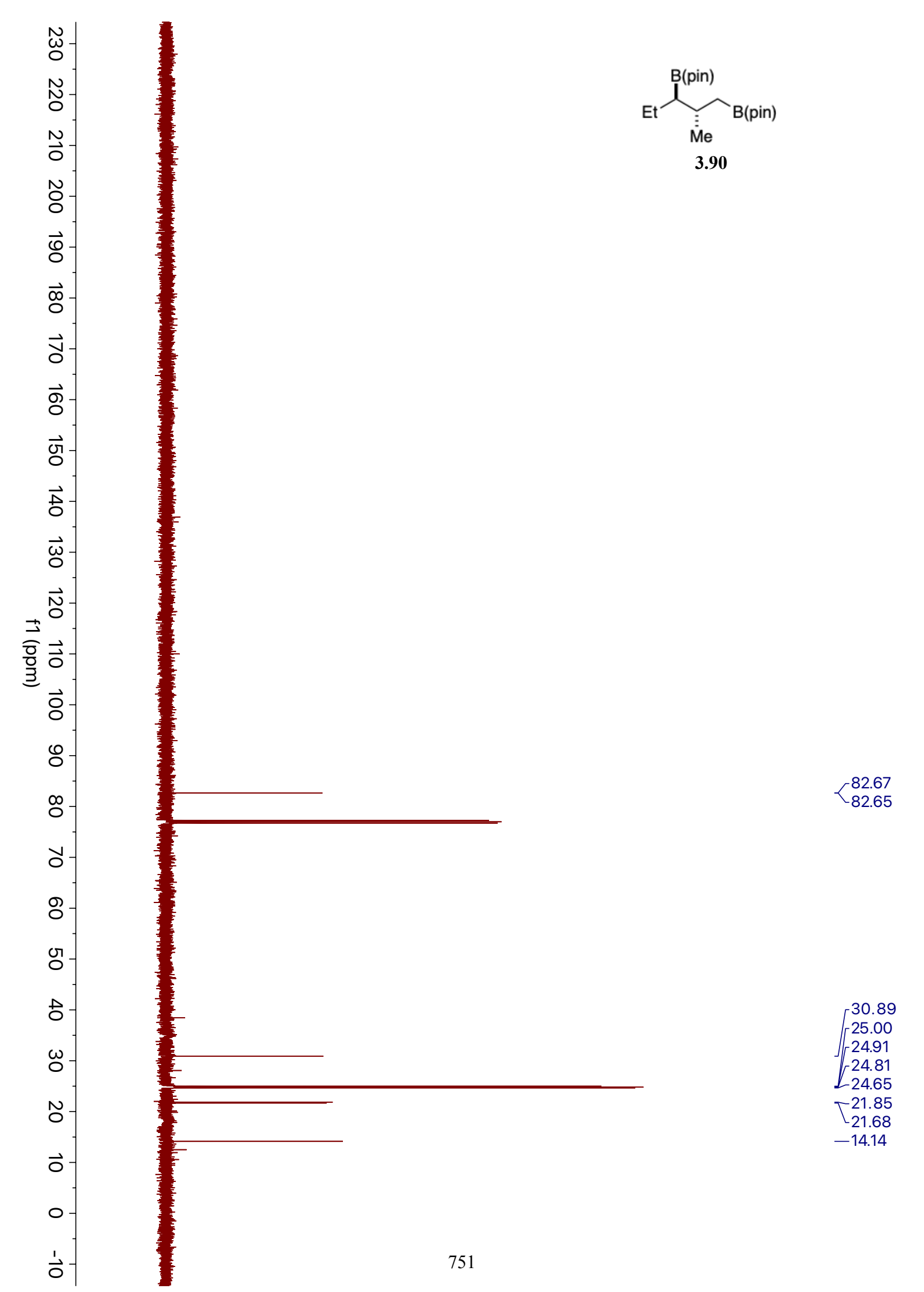

OH
n-pent
NBn2
Me
3.86
f1 (ppm)
10.09
0.91
1.97
1.00
1.97
0.99
2.12
5.28
1.12
2.98
3.08

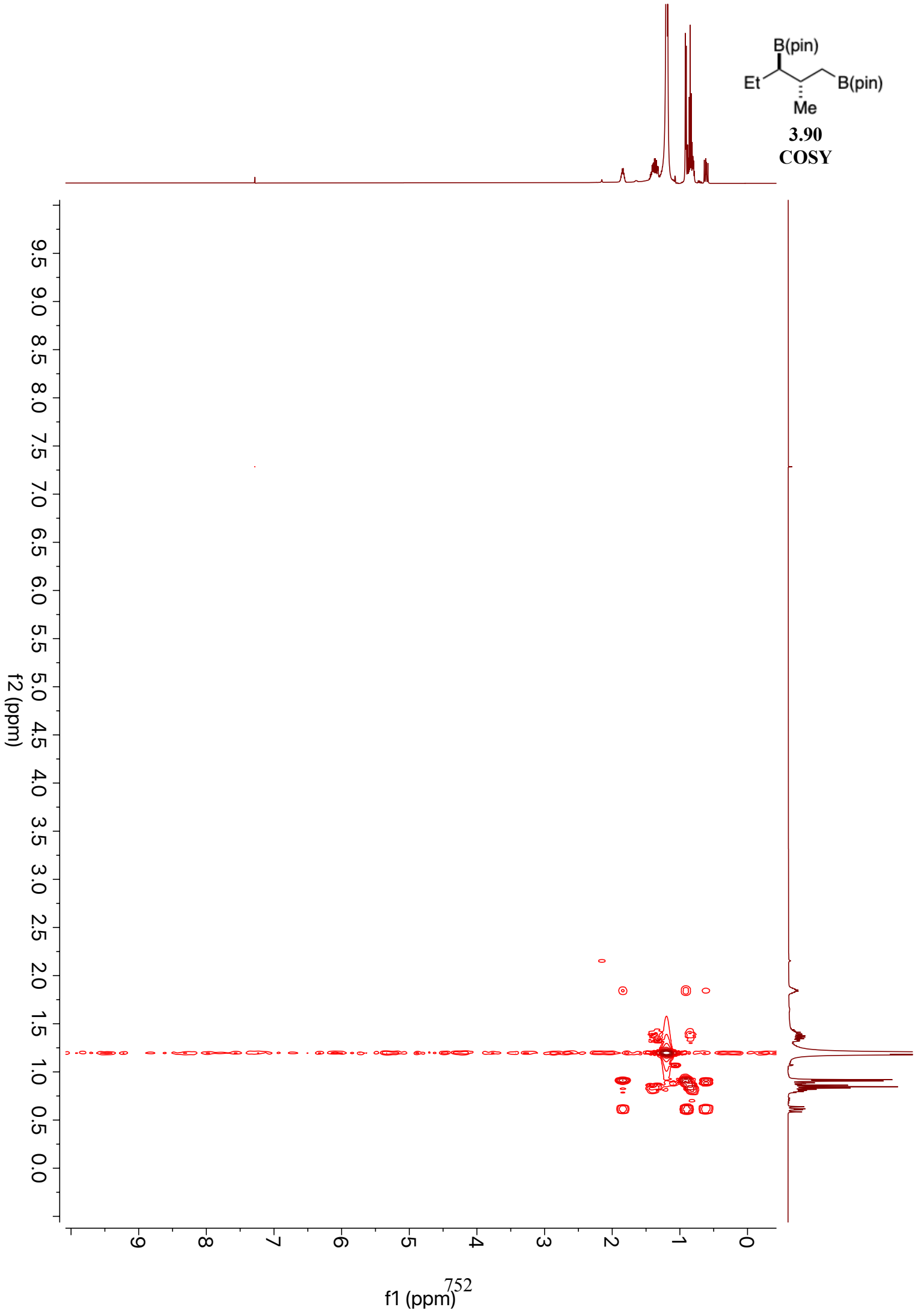

OH
n-pent
NBn2
Me
3.86
138.94
129.01
128.47
127.19
70.77
58.47
53.25
33.82
32.06
25.61
22.66
14.05
8.06
f1 (ppm)

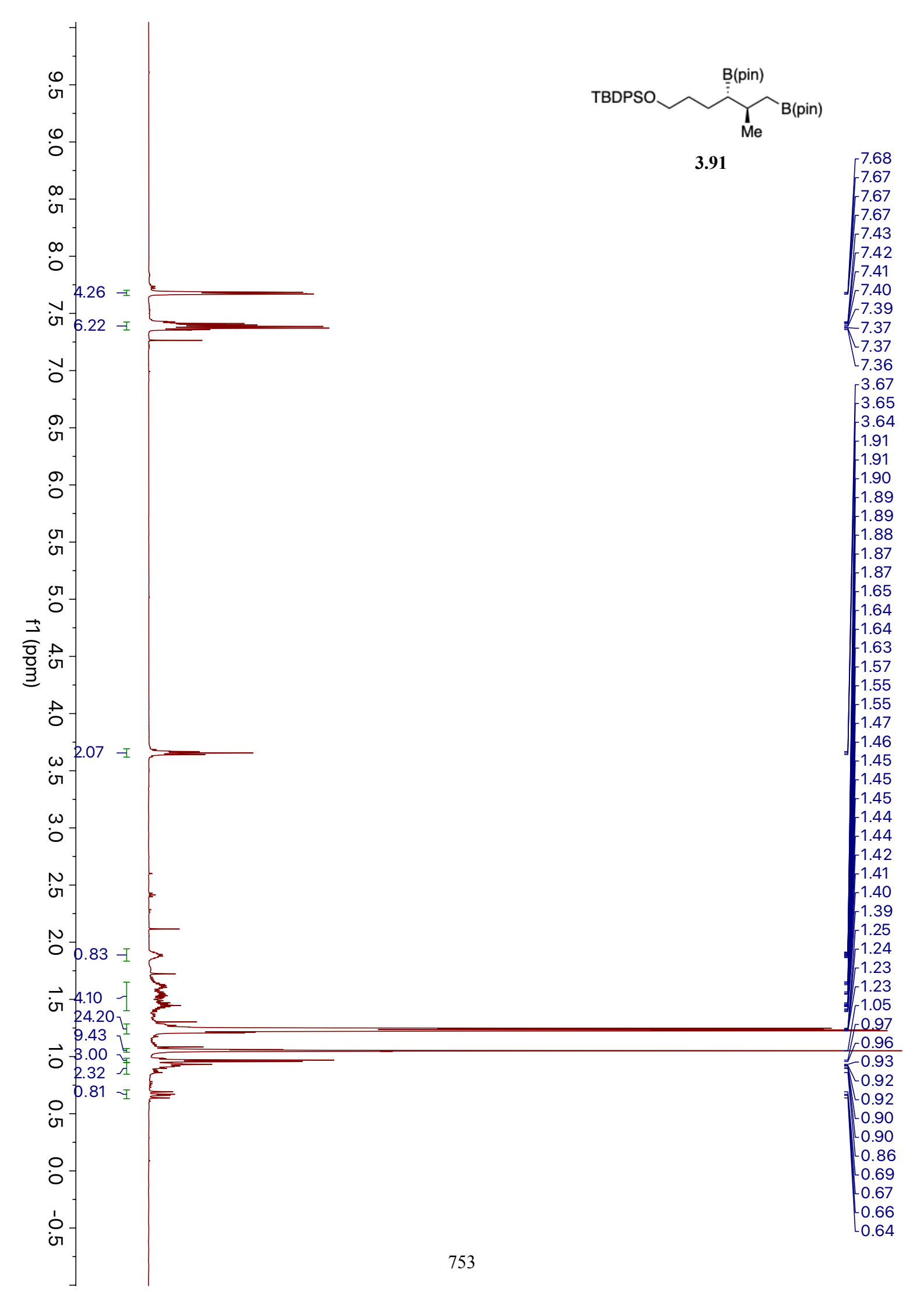

OH
Ph
Me
3.89
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
2.20
2.85
1.94
1.00
1.00
0.99
1.10
3.02
7.31
7.29
7.29
7.28
7.27
7.22
7.20
7.19
7.18
3.56
3.55
3.54
3.53
3.50
3.49
3.48
3.47
2.79
2.77
2.76
2.75
2.46
2.44
2.43
2.42
2.01
1.99
1.98
1.97
1.95
1.94
1.93
1.91
1.40
0.94
0.92

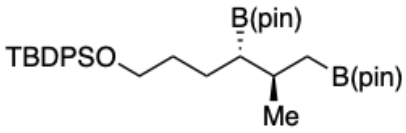

OH
Ph
Me
3.89
140.60
129.12
128.25
125.86
67.66
39.70
37.78
16.46
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


B(pin)
Et
B(pin)
Me
3.90
f1 (ppm)
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
0.95
2.20
24.45
3.37
4.98
1.05
1.92
1.91
1.90
1.90
1.89
1.89
1.88
1.87
1.87
1.86
1.85
1.85
1.84
1.47
1.46
1.44
1.43
1.42
1.41
1.41
1.39
1.38
1.35
1.23
0.95
0.94
0.90
0.89
0.88
0.88
0.87
0.86
0.85
0.85
0.84
0.82
0.67
0.65
0.64
0.64
0.62


B(pin)
Et
B(pin)
Me
3.90
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
82.67
82.65
30.89
25.00
24.91
24.81
24.65
21.85
21.68
14.14

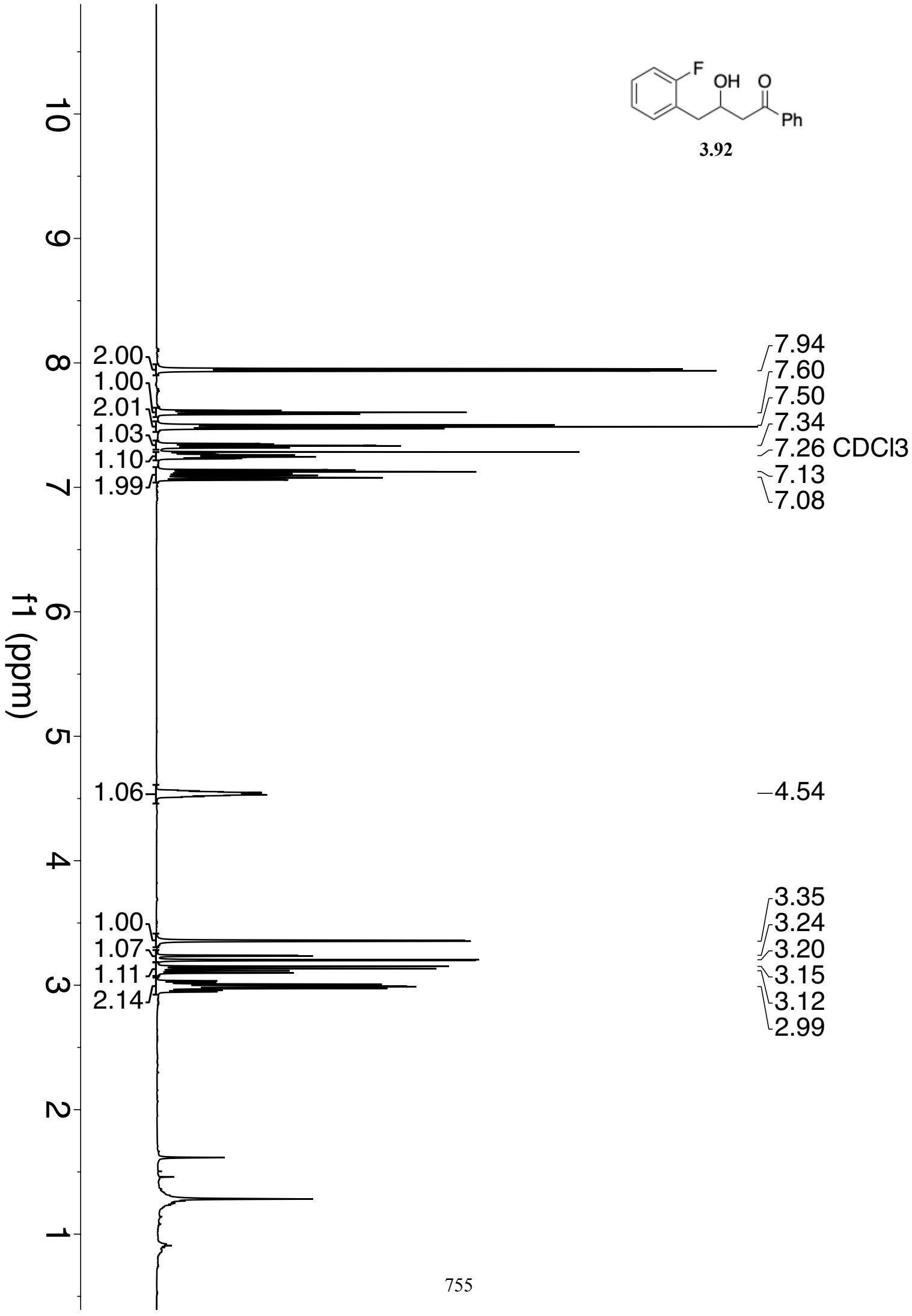

B(pin)
Et
B(pin)
Me
3.90
COSY
f2 (ppm)
f1 (ppm)

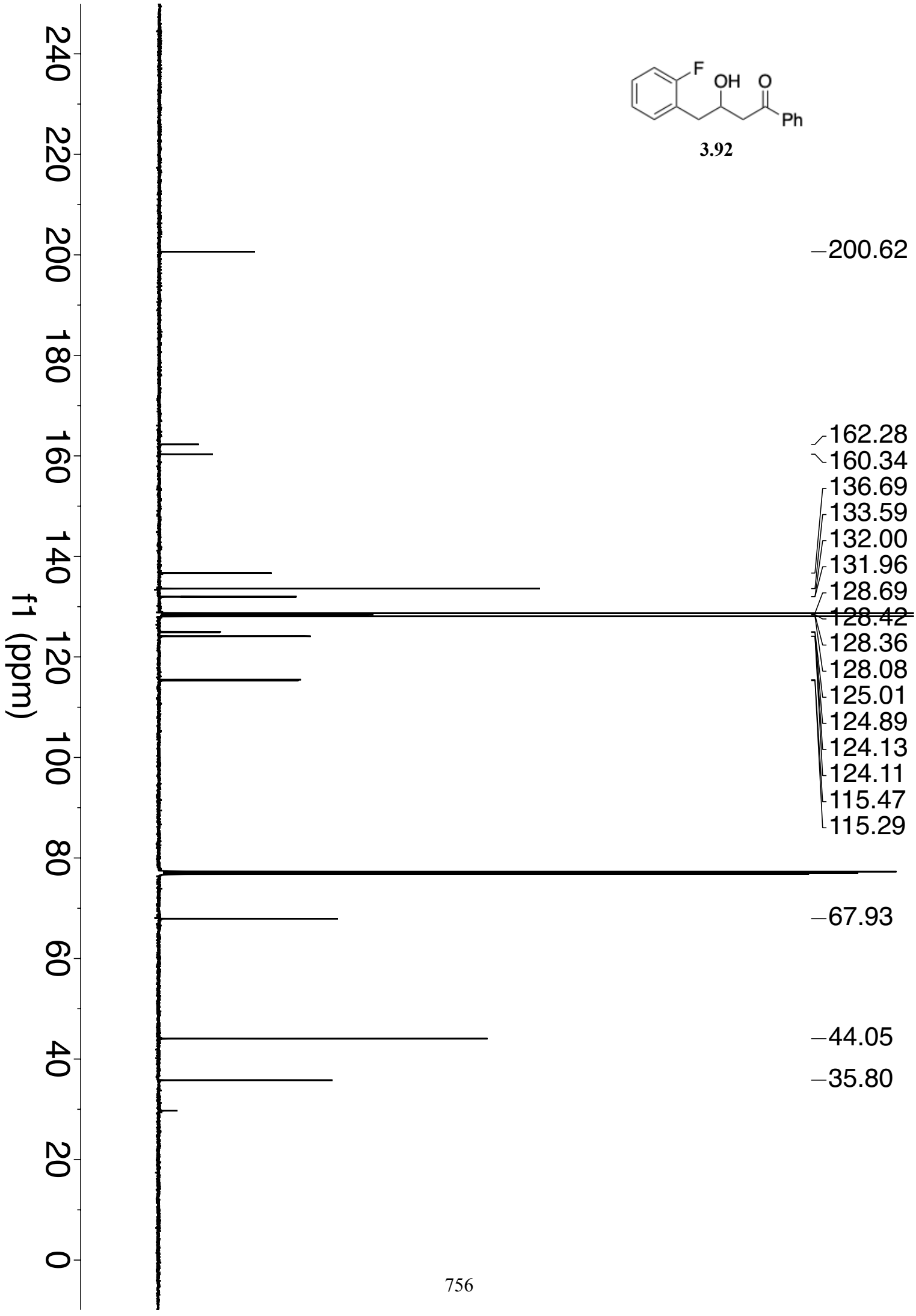

B(pin)
TBDPSO
B(pin)
Me
3.91
f1 (ppm)
4.26
6.22
2.07
0.83
4.10
24.20
9.43
3.00
2.32
0.81
7.68
7.67
7.67
7.67
7.43
7.42
7.41
7.40
7.39
7.37
7.37
7.36
3.67
3.65
3.64
1.91
1.91
1.90
1.89
1.89
1.88
1.87
1.87
1.65
1.64
1.64
1.63
1.57
1.55
1.55
1.47
1.46
1.45
1.45
1.45
1.44
1.44
1.42
1.41
1.40
1.39
1.25
1.24
1.23
1.23
1.05
0.97
0.96
0.93
0.92
0.92
0.90
0.90
0.86
0.69
0.67
0.66
0.64

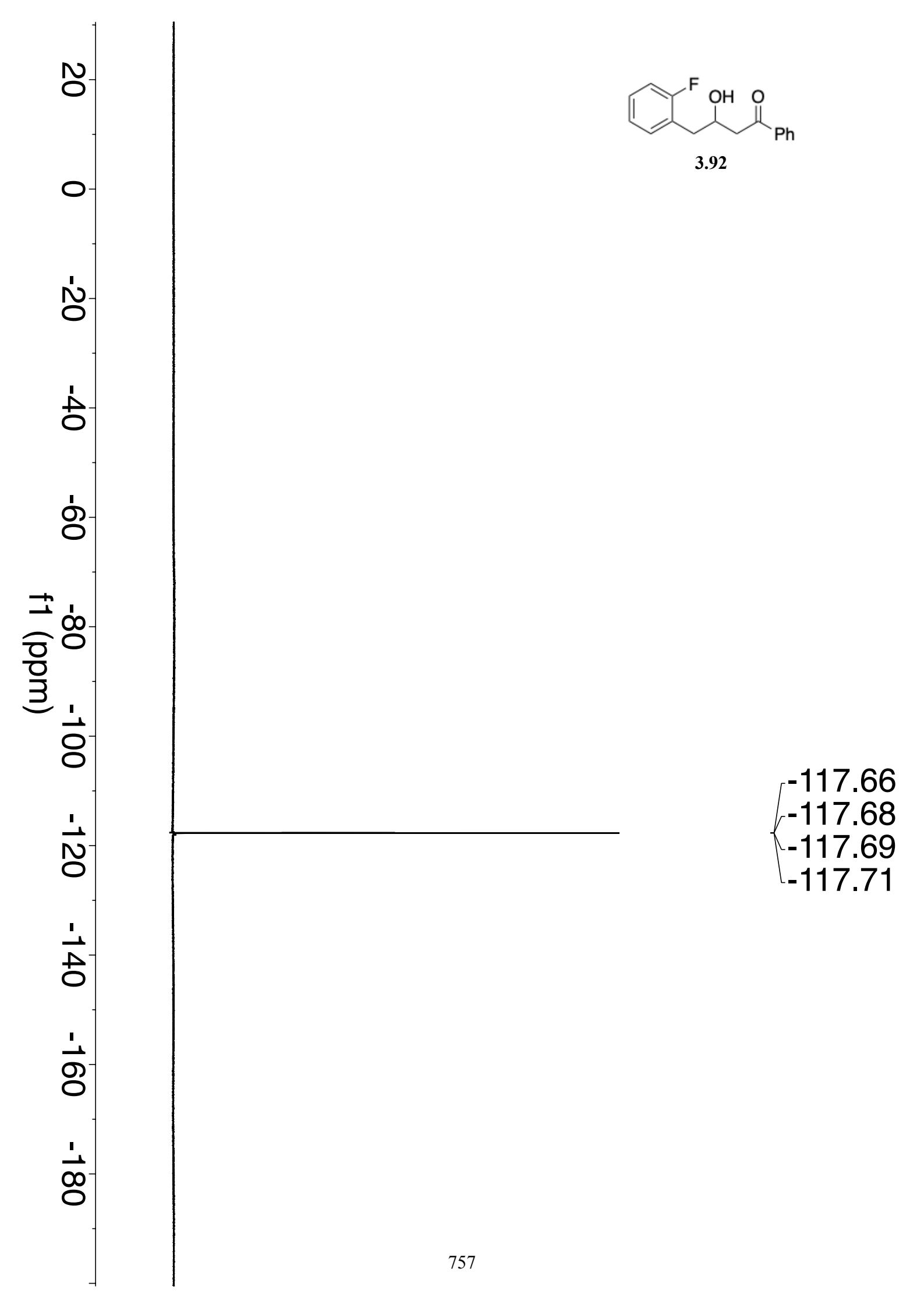

B(pin)
TBDPSO
B(pin)
Me

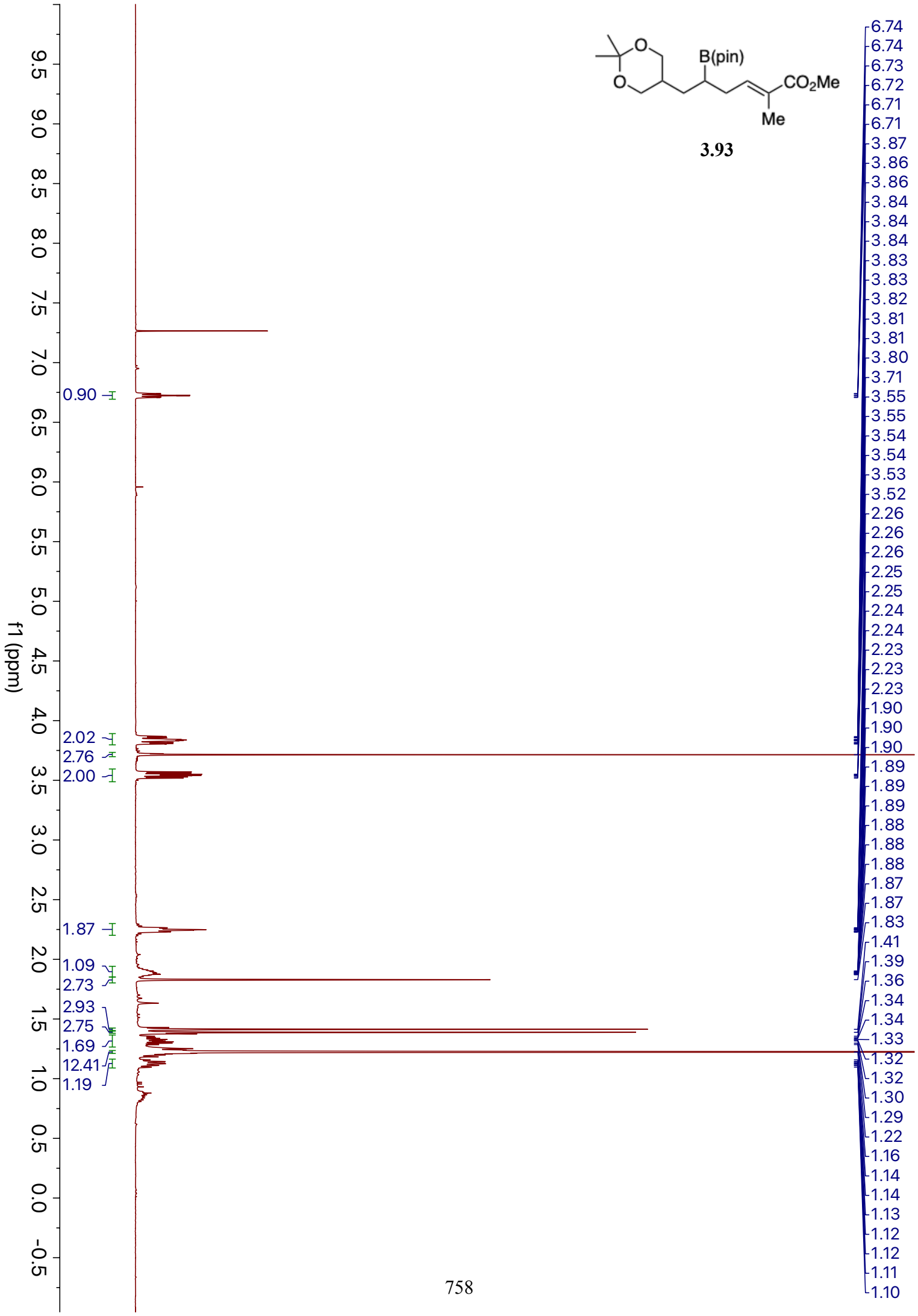
3.91

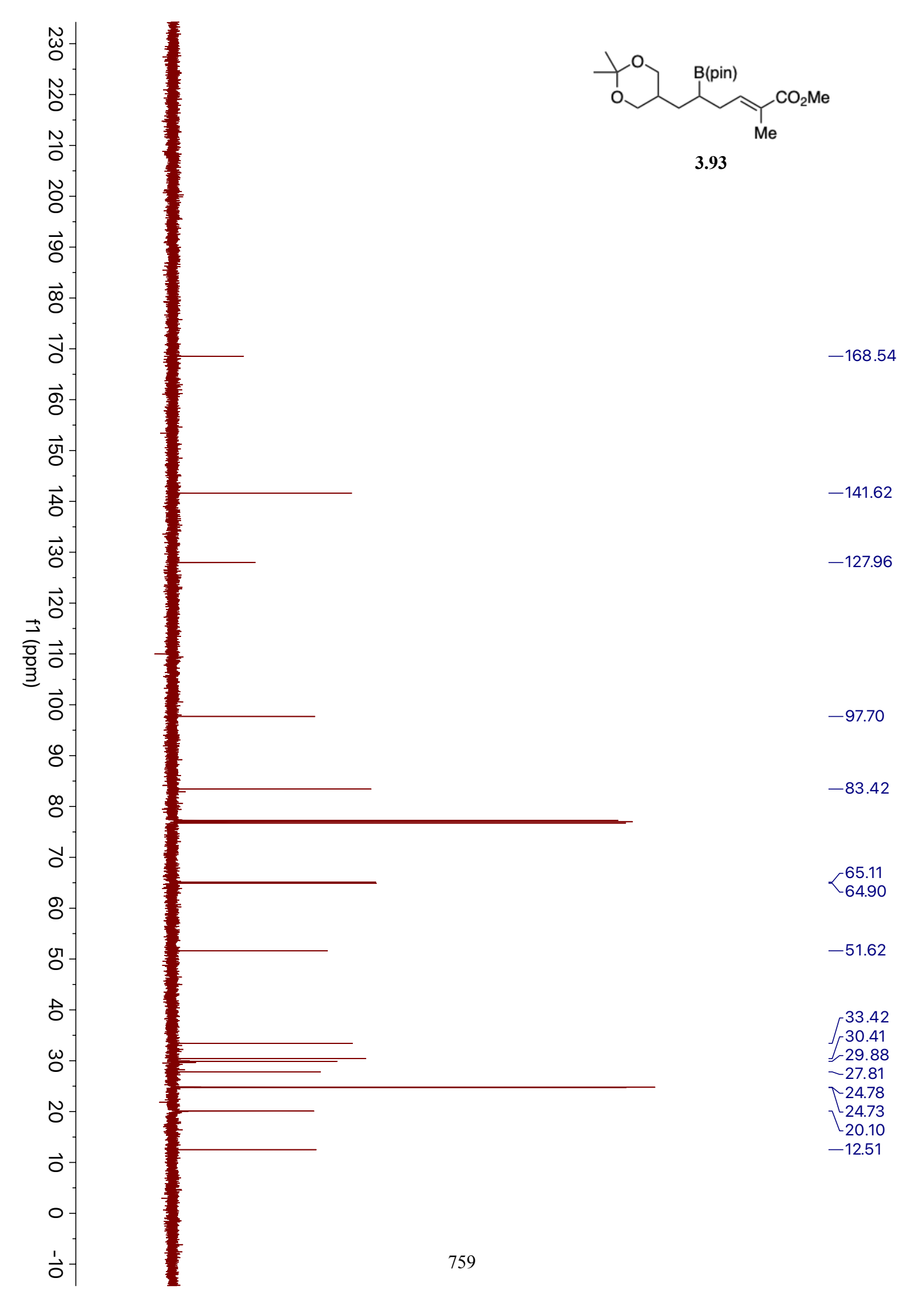
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
135.56
134.29
134.27
129.38
127.52
82.69
64.40
32.73
30.98
26.89
25.00
24.94
24.83
24.68
21.84
19.23

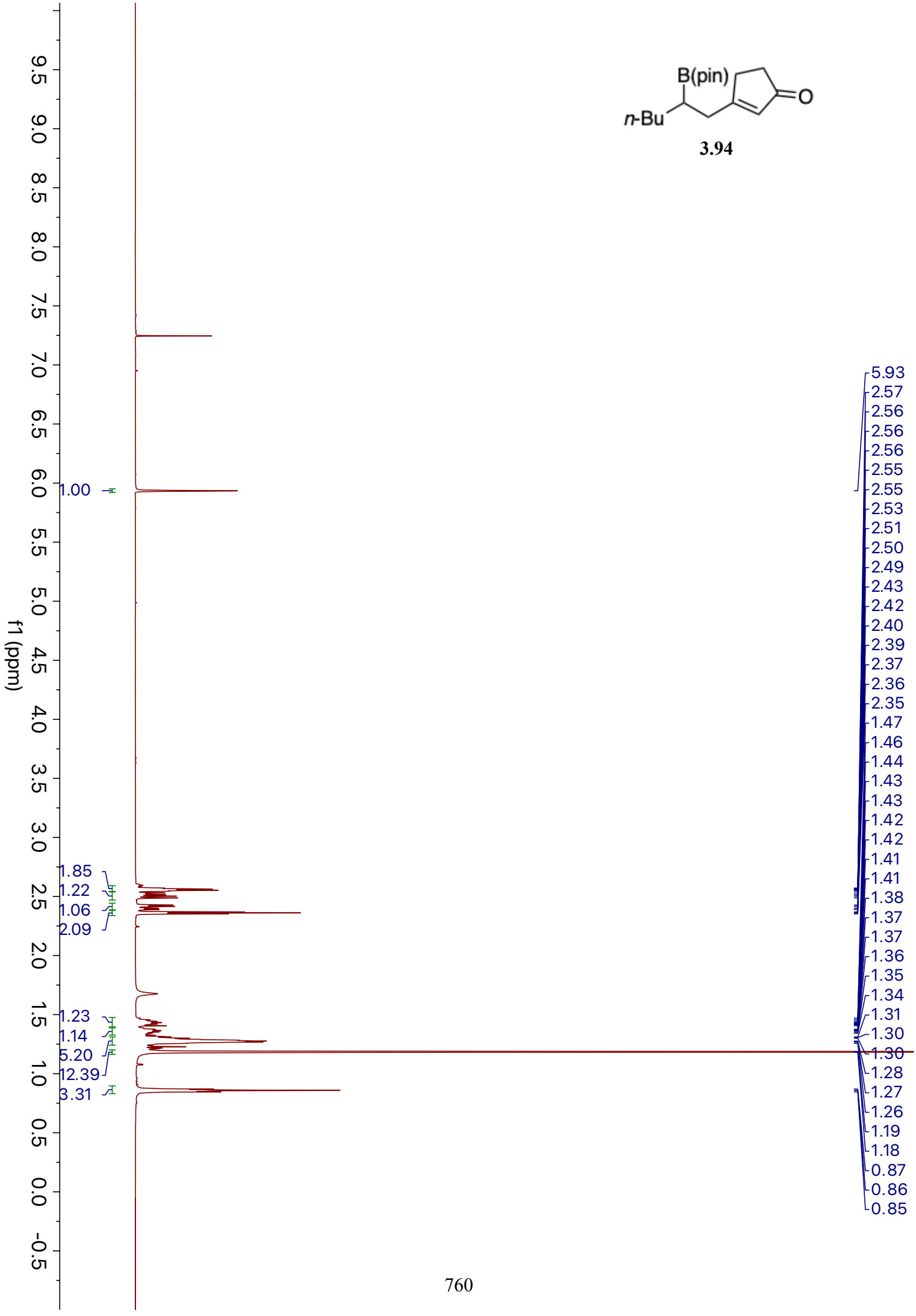

F
OH
O
Ph
3.92
2.00
1.00
2.01
1.03
1.10
1.99
1.06
1.00
1.07
1.11
2.14
7.94
7.60
7.50
7.34
7.26 CDCl3
7.13
7.08
4.54
3.35
3.24
3.20
3.15
3.12
2.99
f1 (ppm)

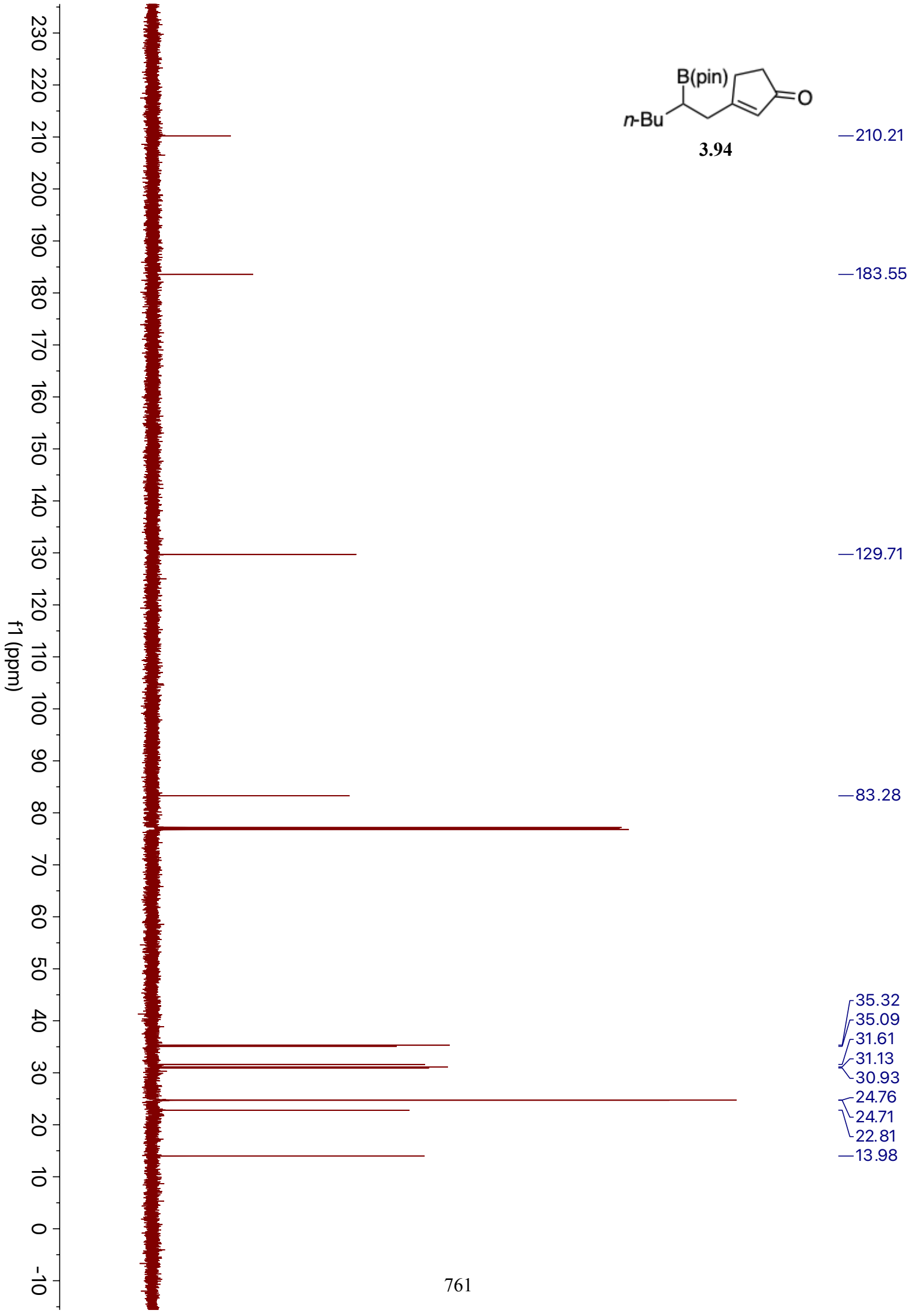

F
OH
O
Ph
3.92
200.62
162.28
160.34
136.69
133.59
132.00
131.96
128.69
128.42
128.36
128.08
125.01
124.89
124.13
124.11
115.47
115.29
67.93
44.05
35.80
f1 (ppm)
240
220
200
180
160
140
120
100
80
60
40
20
0

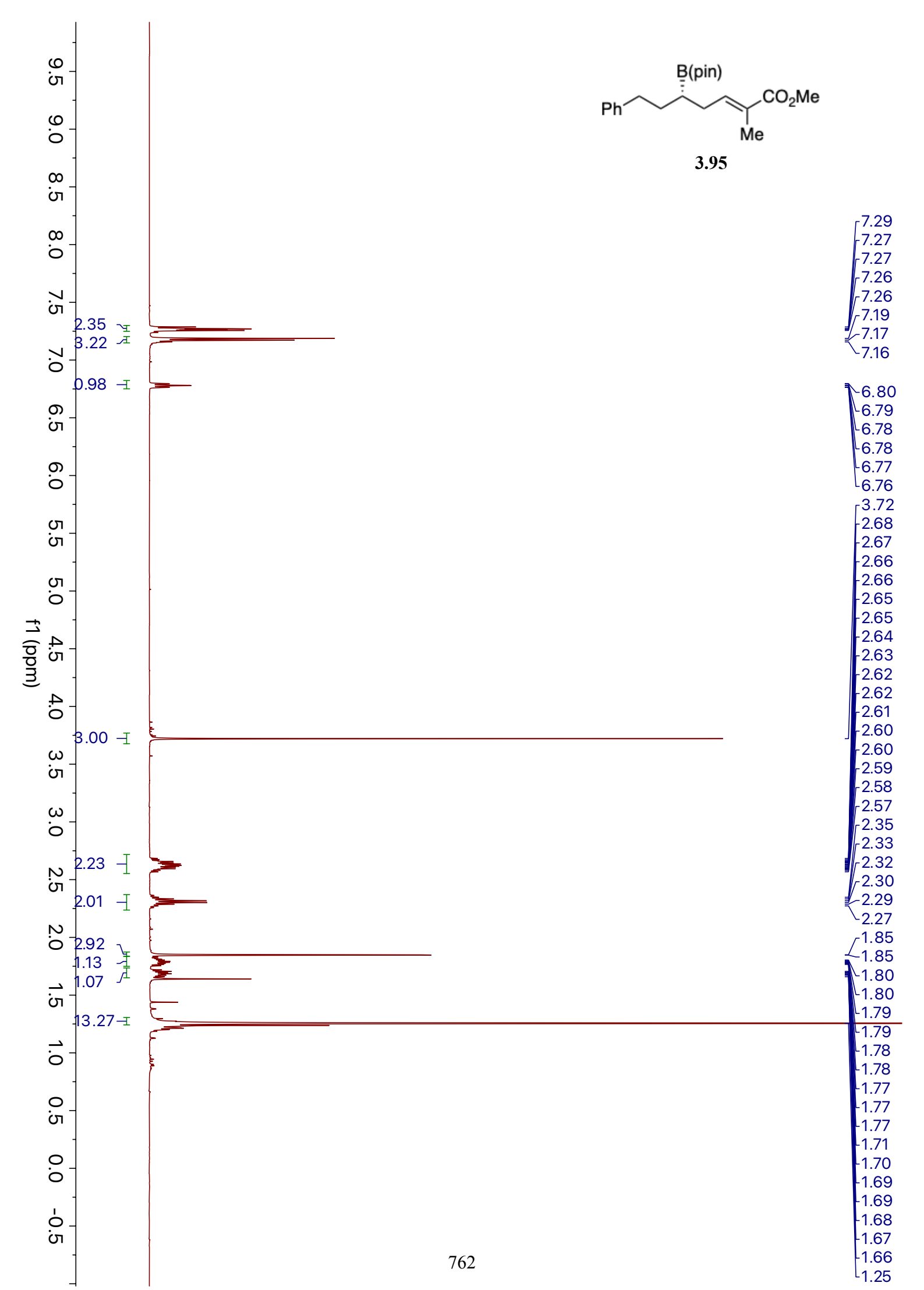

F
OH
O
Ph
3.92
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
f1 (ppm)
-117.66
-117.68
-117.69
-117.71

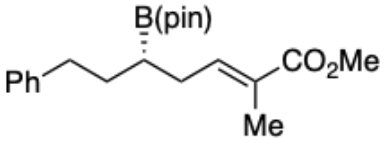

B(pin)
CO2Me
Me
3.93
f1 (ppm)
0.90
2.02
2.76
2.00
1.87
1.09
2.73
2.93
2.75
1.69
12.41
1.19


B(pin)
CO2Me
Me
3.93
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.54
141.62
127.96
97.70
83.42
65.11
64.90
51.62
33.42
30.41
29.88
27.81
24.78
24.73
20.10
12.51


B(pin)
n-Bu
O
3.94
f1 (ppm)
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
1.85
1.22
1.06
2.09
1.23
1.14
5.20
12.39
3.31
5.93
2.57
2.56
2.56
2.56
2.55
2.55
2.53
2.51
2.50
2.49
2.43
2.42
2.40
2.39
2.37
2.36
2.35
1.47
1.46
1.44
1.43
1.43
1.42
1.42
1.41
1.41
1.38
1.37
1.37
1.36
1.35
1.34
1.31
1.30
1.30
1.28
1.27
1.26
1.19
1.18
0.87
0.86
0.85

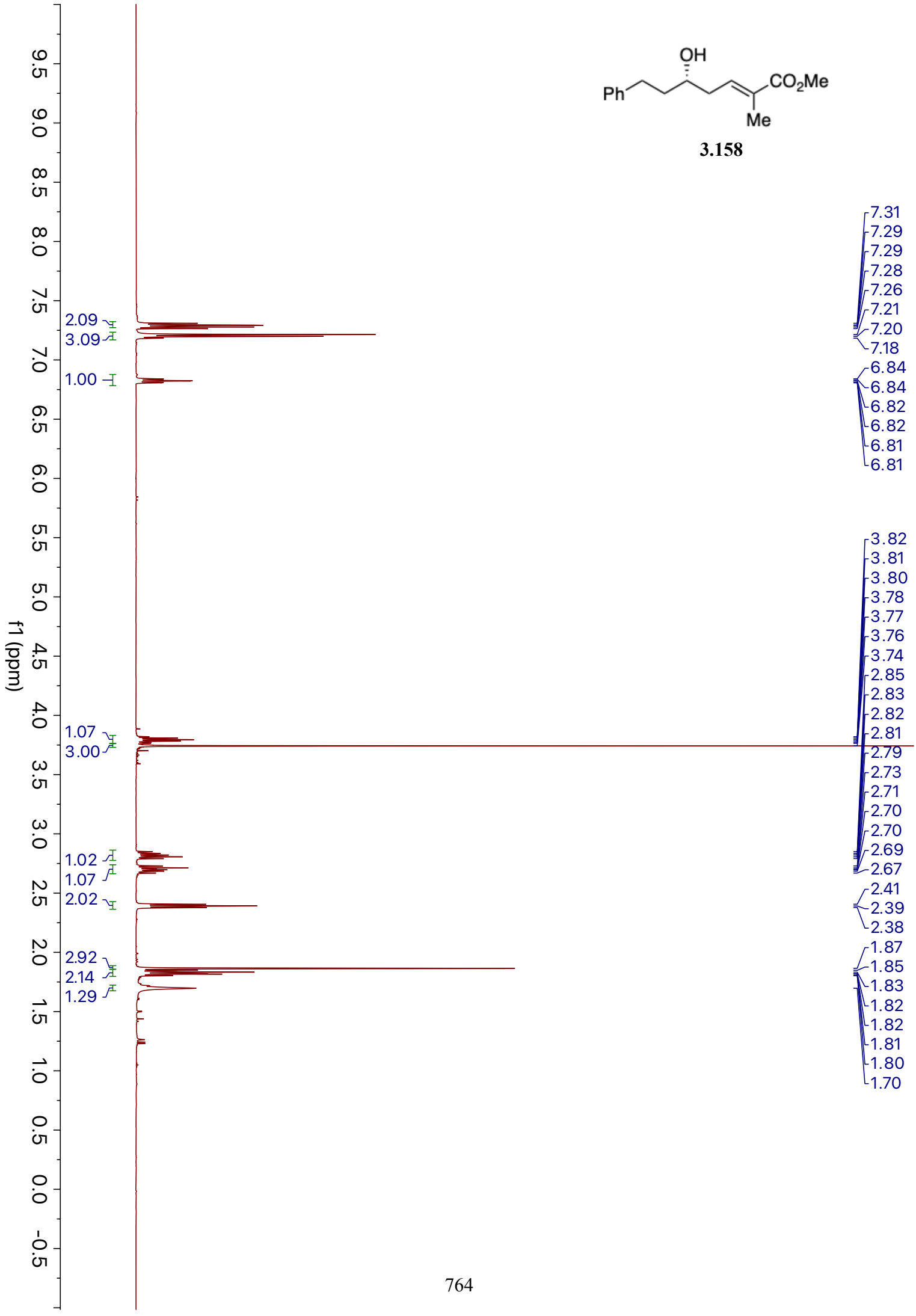

B(pin)
n-Bu
O
3.94
210.21
183.55
129.71
83.28
35.32
35.09
31.61
31.13
30.93
24.76
24.71
22.81
13.98
f1 (ppm)

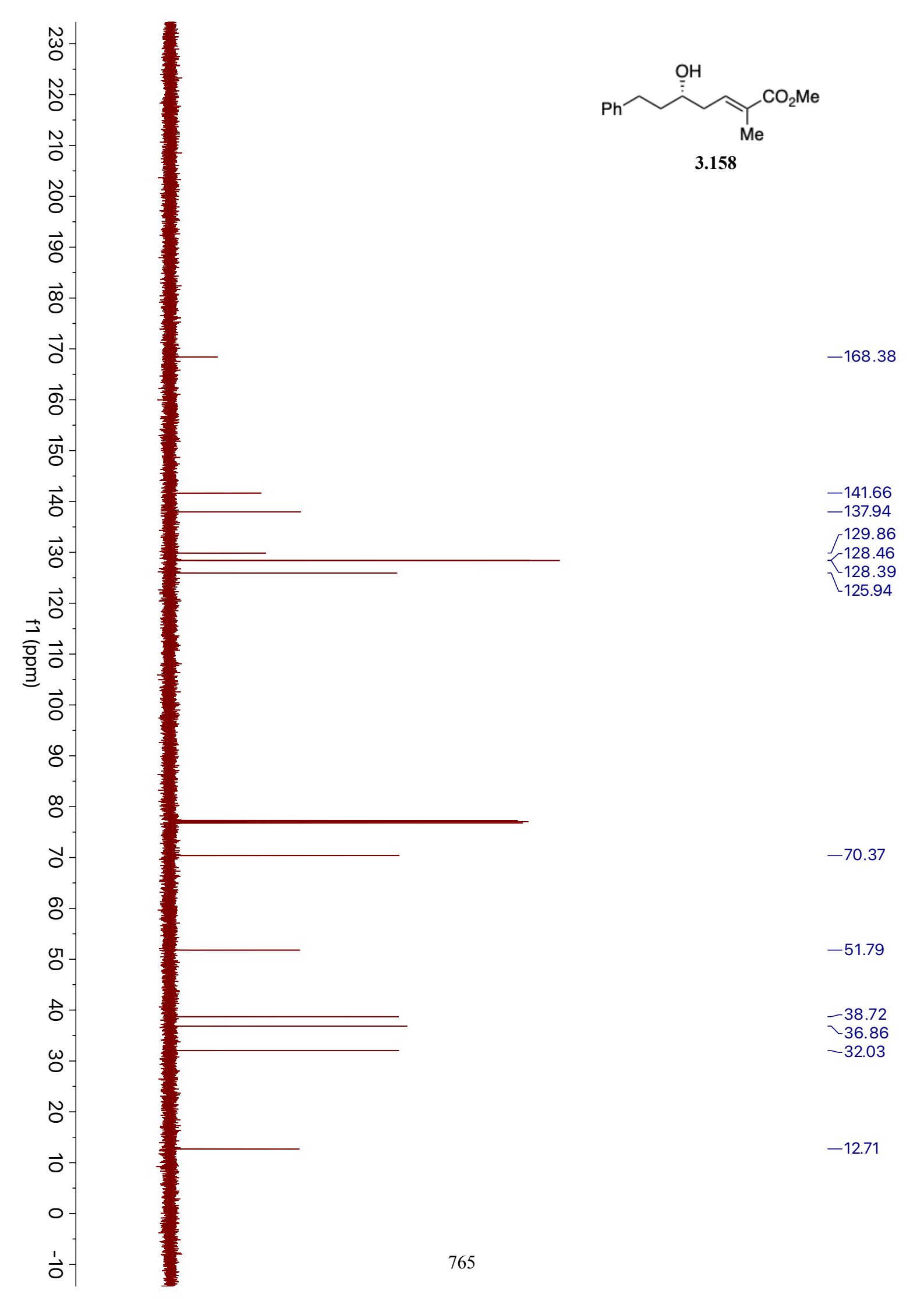

B(pin)
Ph
CO2Me
Me
3.95
f1 (ppm)
2.35
3.22
0.98
3.00
2.23
2.01
2.92
1.13
1.07
13.27
7.29
7.27
7.27
7.26
7.26
7.19
7.17
7.16
6.80
6.79
6.78
6.78
6.77
6.76
3.72
2.68
2.67
2.66
2.66
2.65
2.65
2.64
2.63
2.62
2.62
2.61
2.60
2.60
2.59
2.58
2.57
2.35
2.33
2.32
2.30
2.29
2.27
1.85
1.85
1.80
1.80
1.79
1.79
1.78
1.78
1.77
1.77
1.77
1.71
1.70
1.69
1.69
1.68
1.67
1.66
1.25

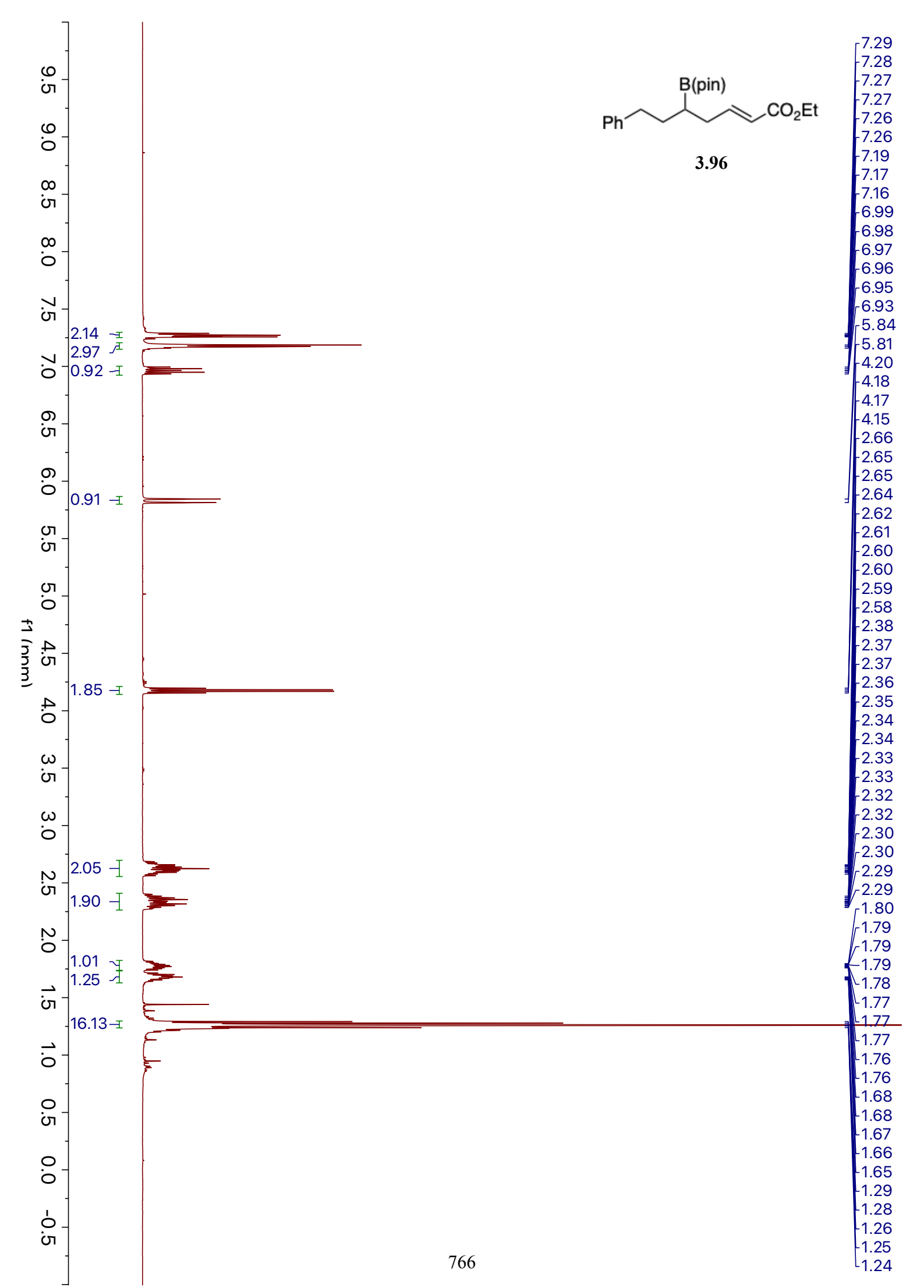

B(pin)
Ph
CO2Me
Me

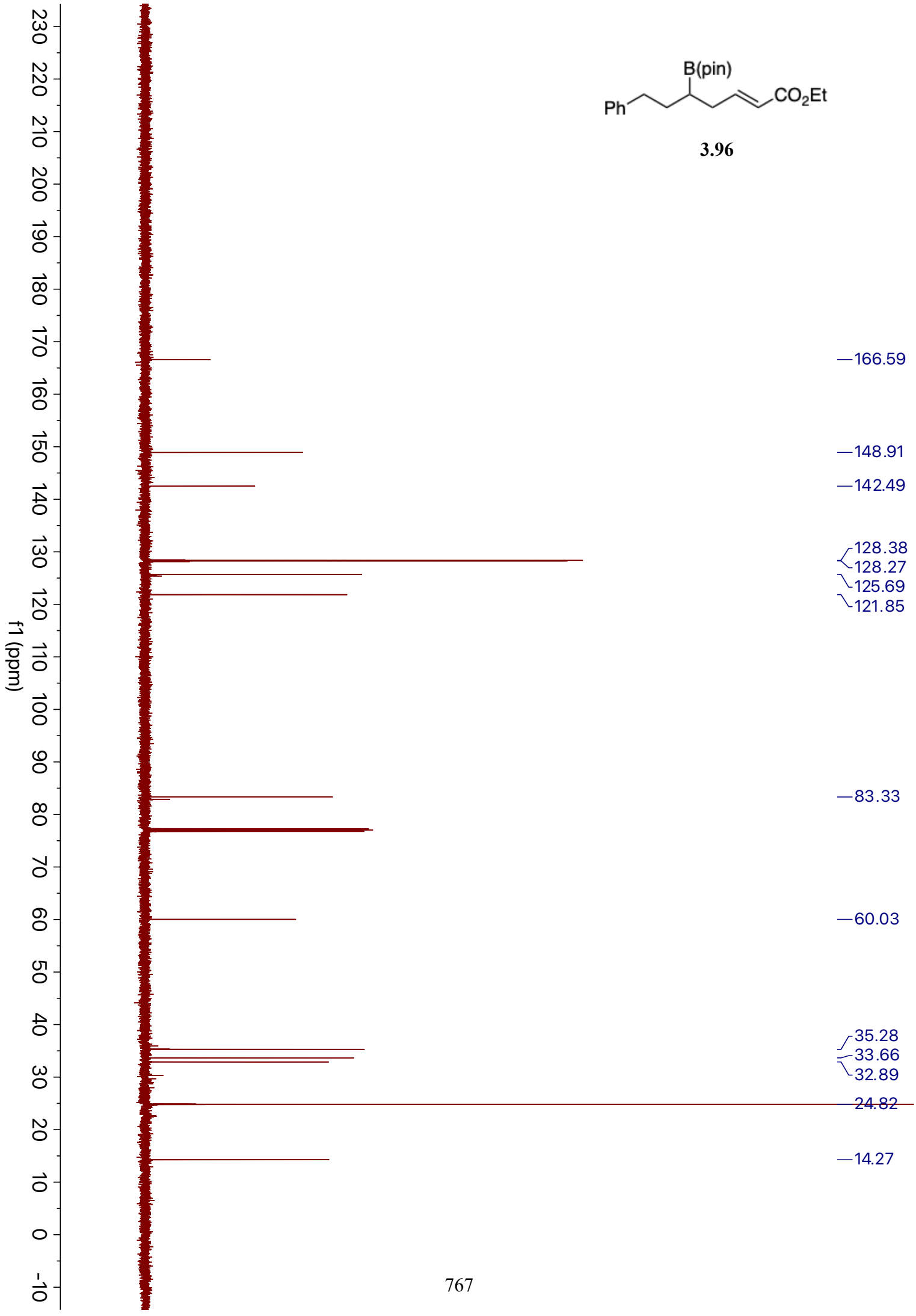
3.95

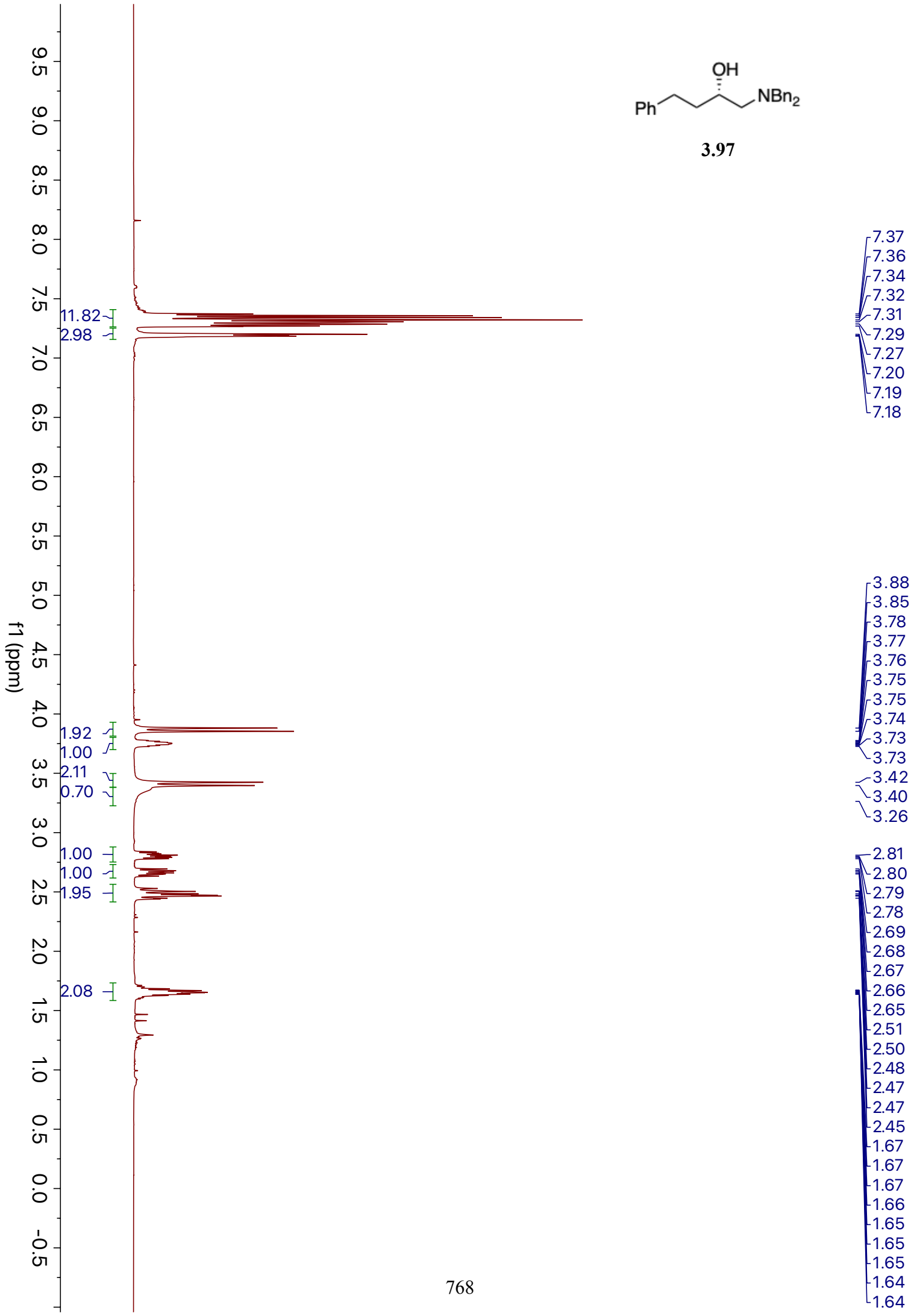
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
168.68
142.56
142.36
128.37
128.26
127.61
125.67
83.27
51.60
35.41
33.06
30.12
24.81
24.76
12.50


OH
Ph
CO2Me
Me
3.158
f1 (ppm)
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
2.09
3.09
1.00
1.07
3.00
1.02
1.07
2.02
2.92
2.14
1.29
7.31
7.29
7.29
7.28
7.26
7.21
7.20
7.18
6.84
6.84
6.82
6.82
6.81
6.81
3.82
3.81
3.80
3.78
3.77
3.76
3.74
2.85
2.83
2.82
2.81
2.79
2.73
2.71
2.70
2.70
2.69
2.67
2.41
2.39
2.38
1.87
1.85
1.83
1.82
1.82
1.81
1.80
1.70


OH
Ph
CO2Me
Me
3.158
168.38
141.66
137.94
129.86
128.46
128.39
125.94
70.37
51.79
38.72
36.86
32.03
12.71
f1 (ppm)


B(pin)
Ph
CO2Et
3.96
2.14
2.97
0.92
0.91
1.85
2.05
1.90
1.01
1.25
16.13
f1 (ppm)


B(pin)
Ph
CO2Et
3.96
166.59
148.91
142.49
128.38
128.27
125.69
121.85
83.33
60.03
35.28
33.66
32.89
24.82
14.27
f1 (ppm)


OH
Ph
NBn2
3.97
f1 (ppm)
11.82
2.98
1.92
1.00
2.11
0.70
1.00
1.00
1.95
2.08
7.37
7.36
7.34
7.32
7.31
7.29
7.27
7.20
7.19
7.18
3.88
3.85
3.78
3.77
3.76
3.75
3.75
3.74
3.73
3.73
3.42
3.40
3.26
2.81
2.80
2.79
2.78
2.69
2.68
2.67
2.66
2.65
2.51
2.50
2.48
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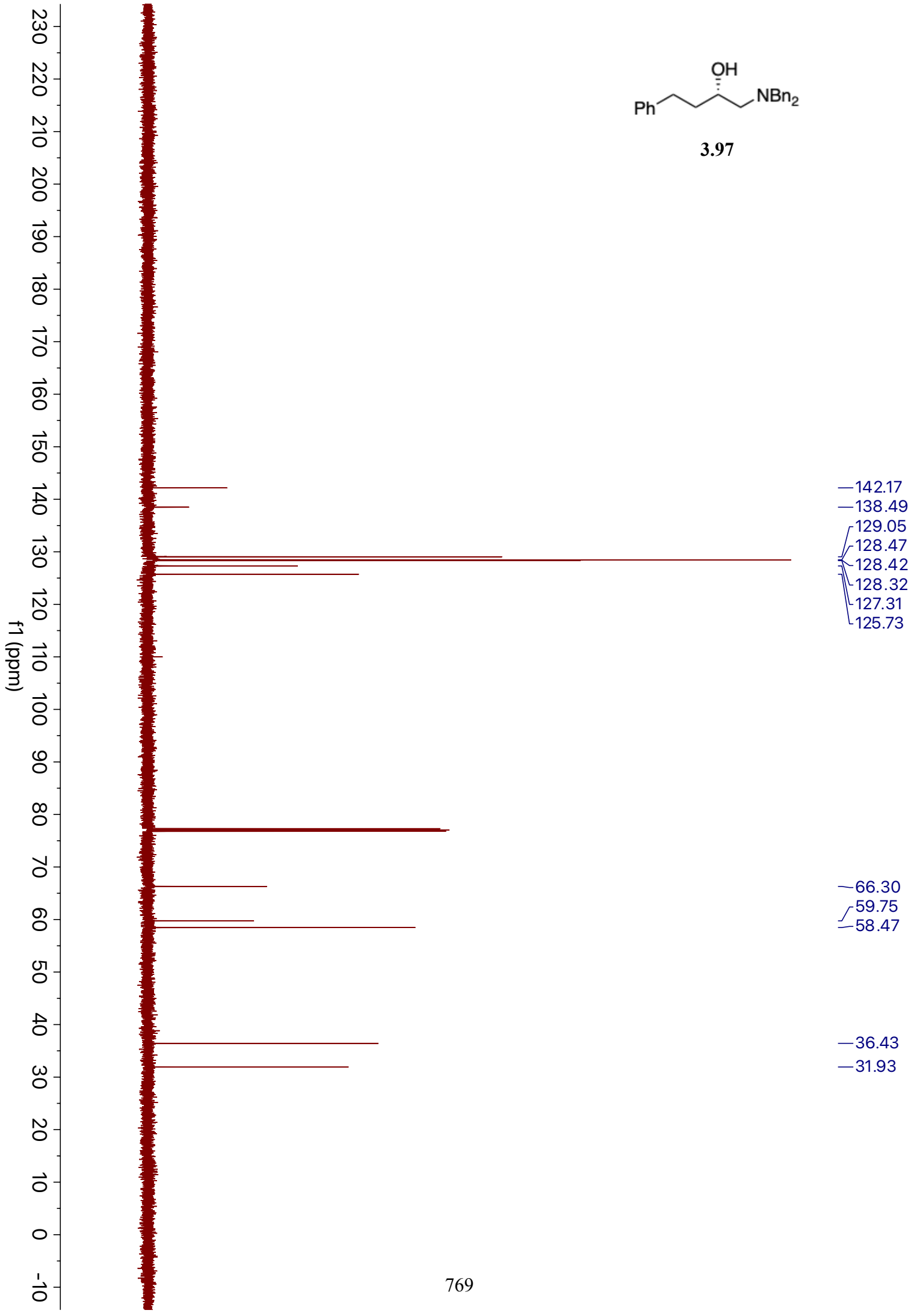
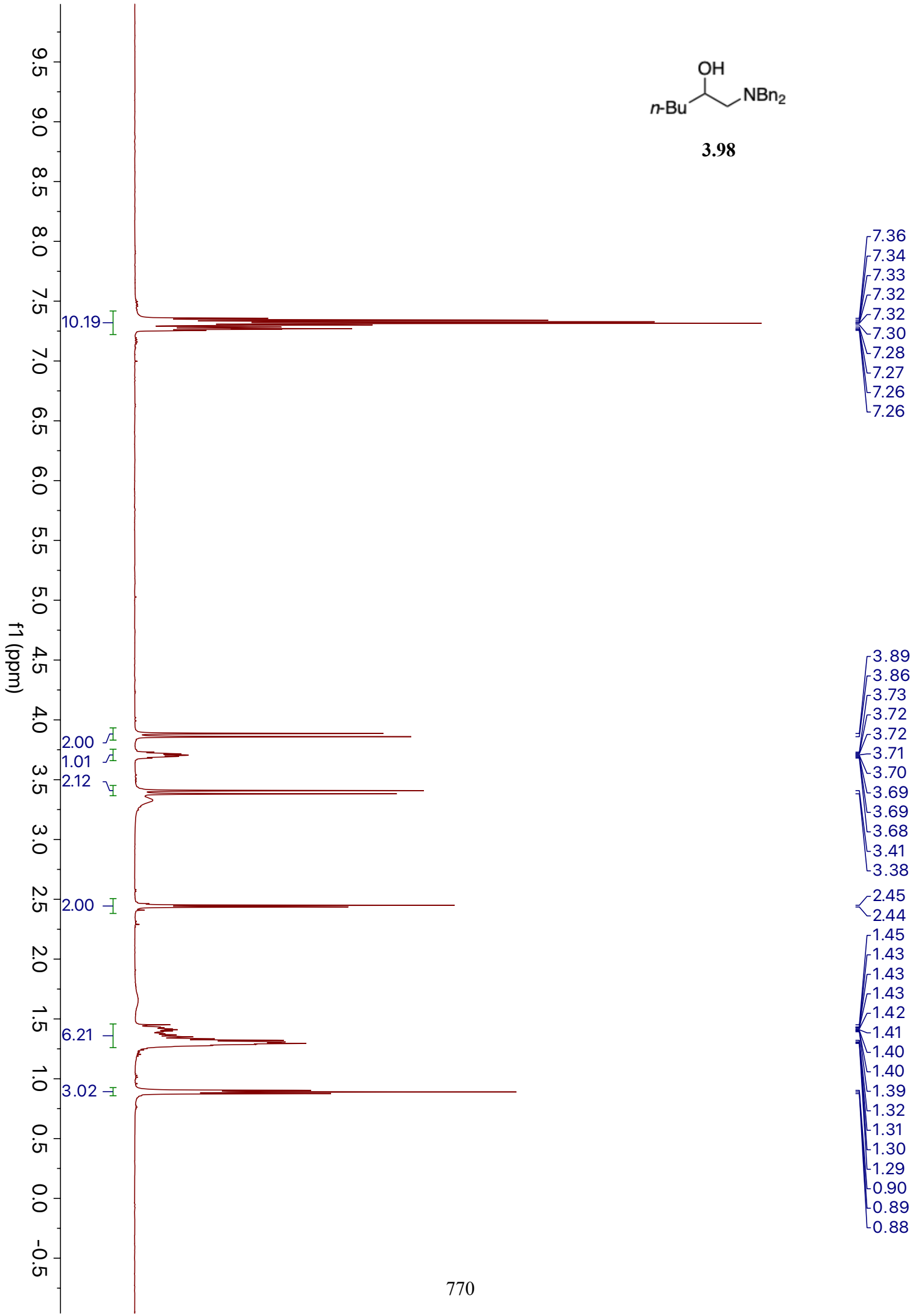
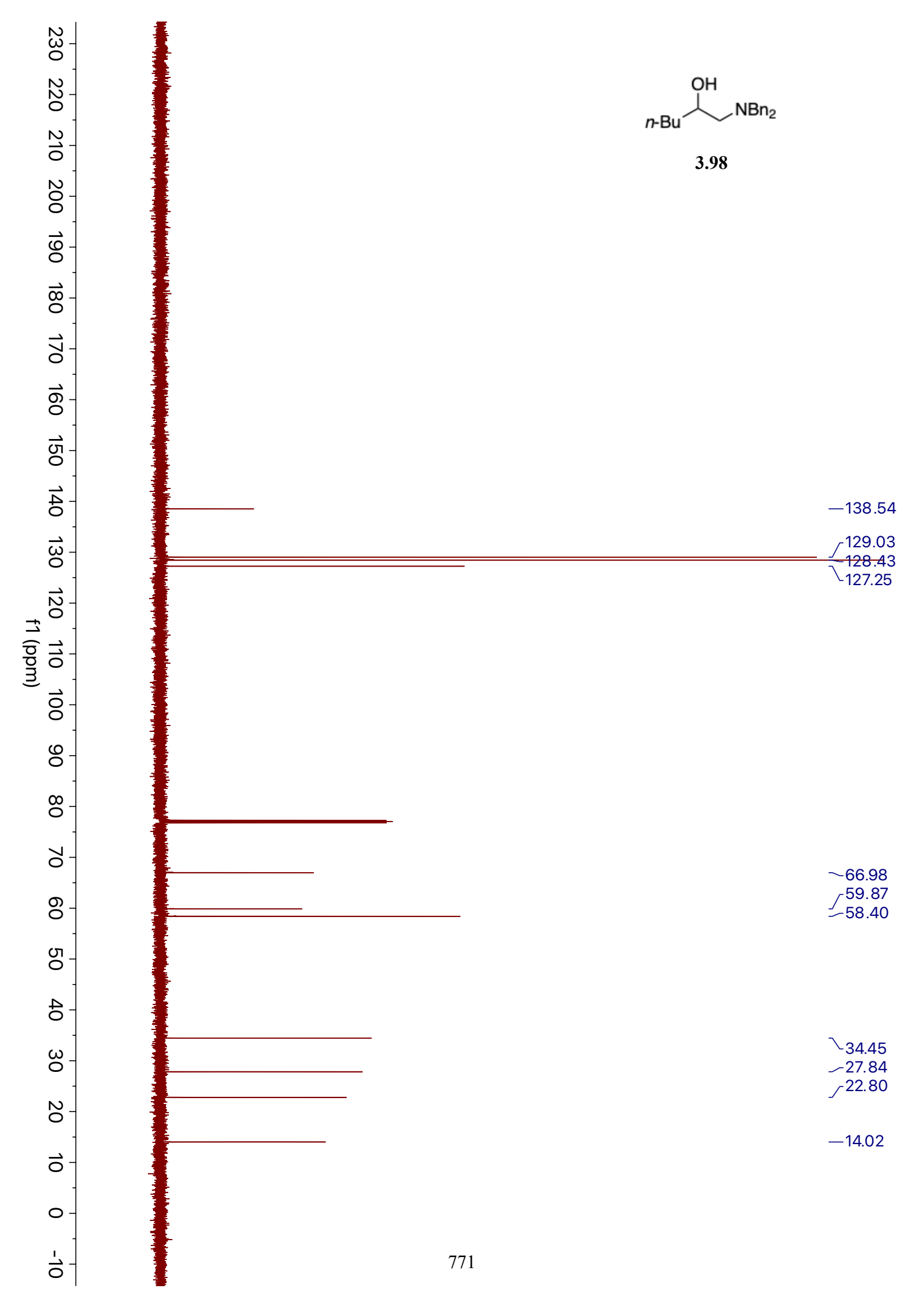
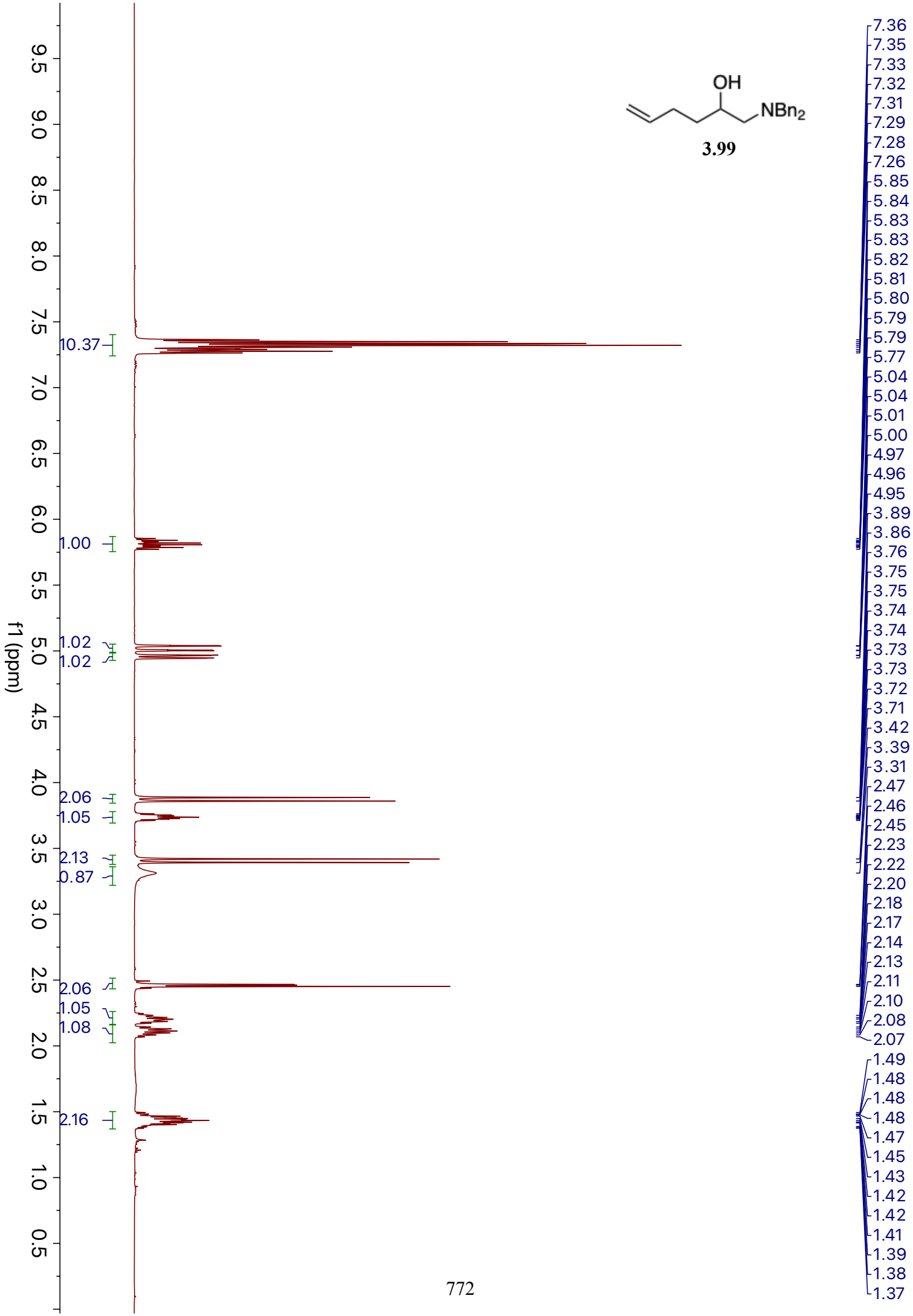
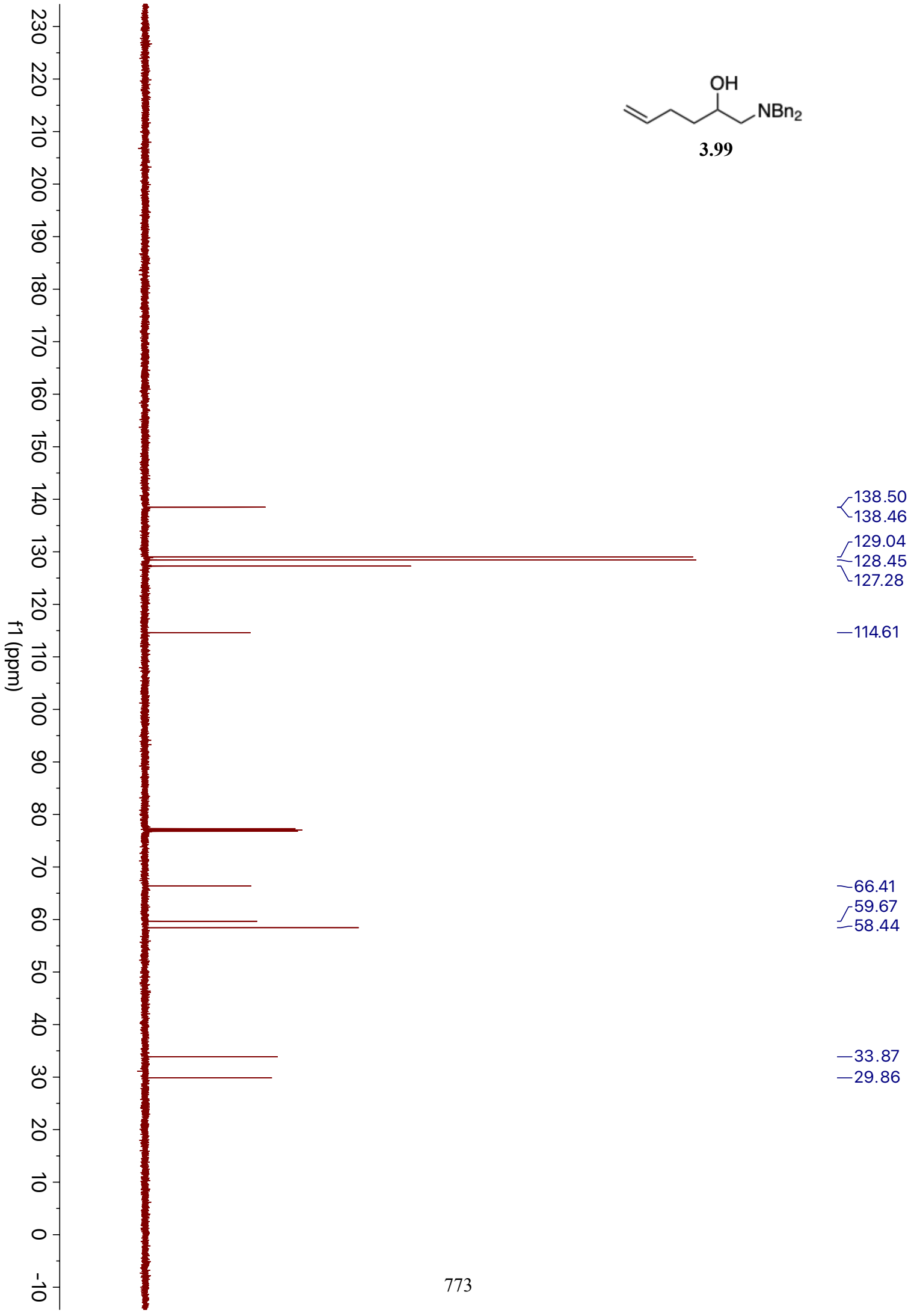
1.66
1.65
1.65
1.65
1.64
1.64

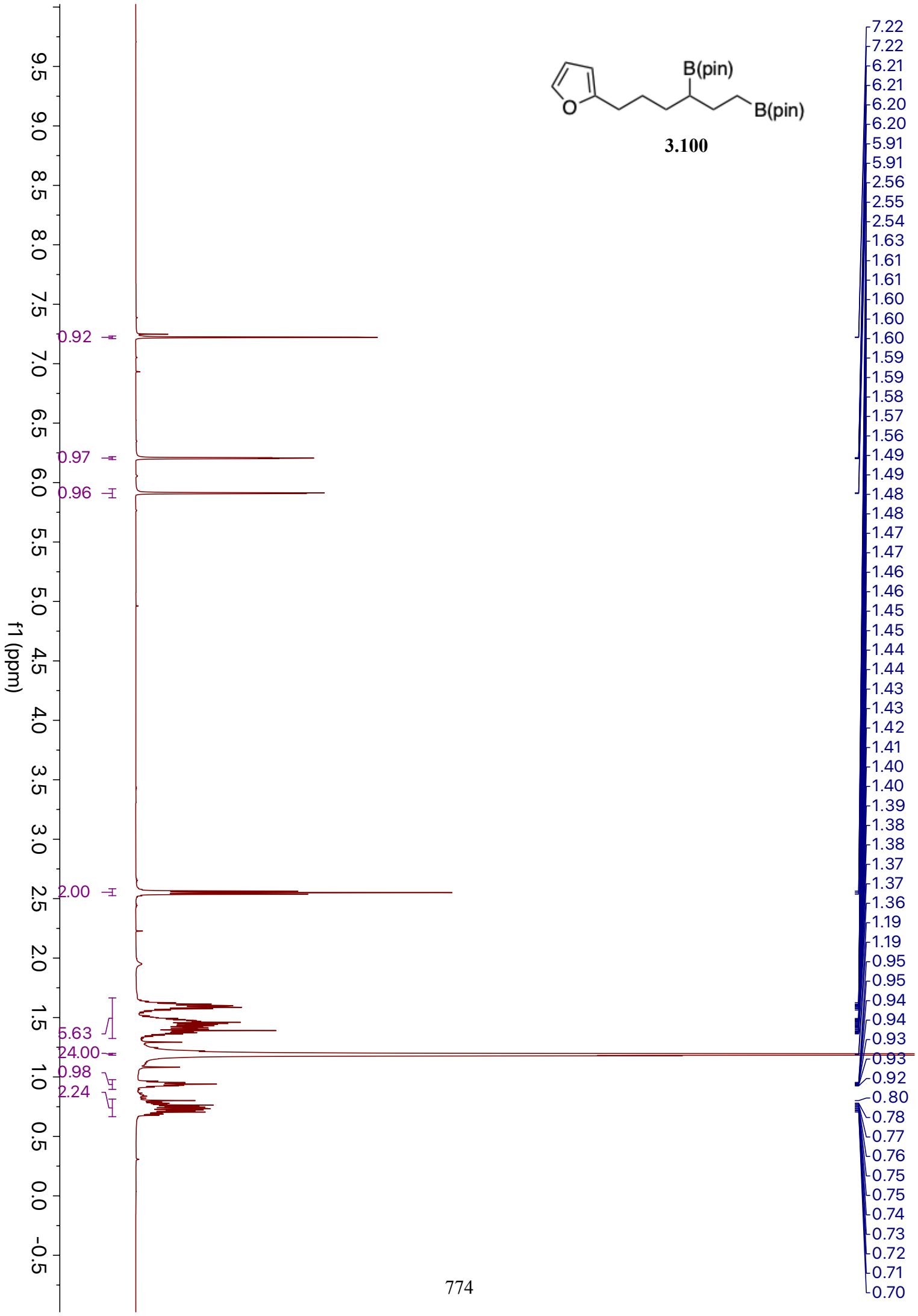

OH
Ph
NBn2
3.97
142.17
138.49
129.05
128.47
128.42
128.32
127.31
125.73
66.30
59.75
58.47
36.43
31.93
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

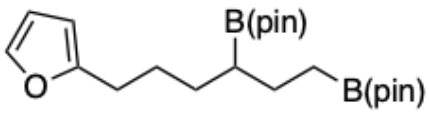

OH
n-Bu
NBn2
3.98
f1 (ppm)
10.19
2.00
1.01
2.12
2.00
6.21
3.02
7.36
7.34
7.33
7.32
7.32
7.30
7.28
7.27
7.26
7.26
3.89
3.86
3.73
3.72
3.72
3.71
3.70
3.69
3.69
3.68
3.41
3.38
2.45
2.44
1.45
1.43
1.43
1.43
1.42
1.41
1.40
1.40
1.39
1.32
1.31
1.30
1.29
0.90
0.89
0.88


OH
n-Bu
NBn2
3.98
138.54
129.03
128.43
127.25
66.98
59.87
58.40
34.45
27.84
22.80
14.02
f1 (ppm)


OH
NBn2
3.99
f1 (ppm)
10.37
1.00
1.02
1.02
2.06
1.05
2.13
0.87
2.06
1.05
1.08
2.16
7.36
7.35
7.33
7.32
7.31
7.29
7.28
7.26
5.85
5.84
5.83
5.83
5.82
5.81
5.80
5.79
5.79
5.77
5.04
5.04
5.01
5.00
4.97
4.96
4.95
3.89
3.86
3.76
3.75
3.75
3.74
3.74
3.73
3.73
3.72
3.71
3.42
3.39
3.31
2.47
2.46
2.45
2.23
2.22
2.20
2.18
2.17
2.14
2.13
2.11
2.10
2.08
2.07
1.49
1.48
1.48
1.48
1.47
1.45
1.43
1.42
1.42
1.41
1.39
1.38
1.37

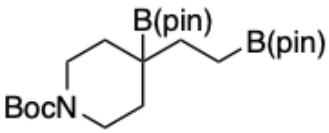

OH
NBn2
3.99
138.50
138.46
129.04
128.45
127.28
114.61
66.41
59.67
58.44
33.87
29.86
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


B(pin)
B(pin)
O
3.100
f1 (ppm)
0.92
0.97
0.96
2.00
5.63
24.00
0.98
2.24


B(pin)
O
B(pin)

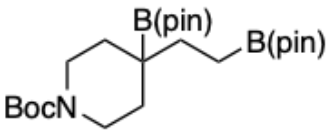
3.100

f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
156.52
140.44
109.90
104.38
82.75
82.72
30.66
28.20
27.44
25.28
24.80
24.76


B(pin)
B(pin)
BocN

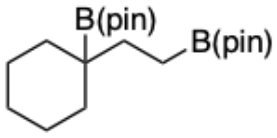
3.101

f1 (ppm)
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
1.98
2.00
2.02
9.10
2.09
23.86
2.16
1.96
3.98
3.95
2.76
2.76
2.74
2.73
2.71
2.71
1.84
1.81
1.44
1.42
1.40
1.38
1.23
1.23
1.09
1.08
1.06
1.06
1.04
1.03
0.73
0.71
0.69


B(pin)
B(pin)
BocN

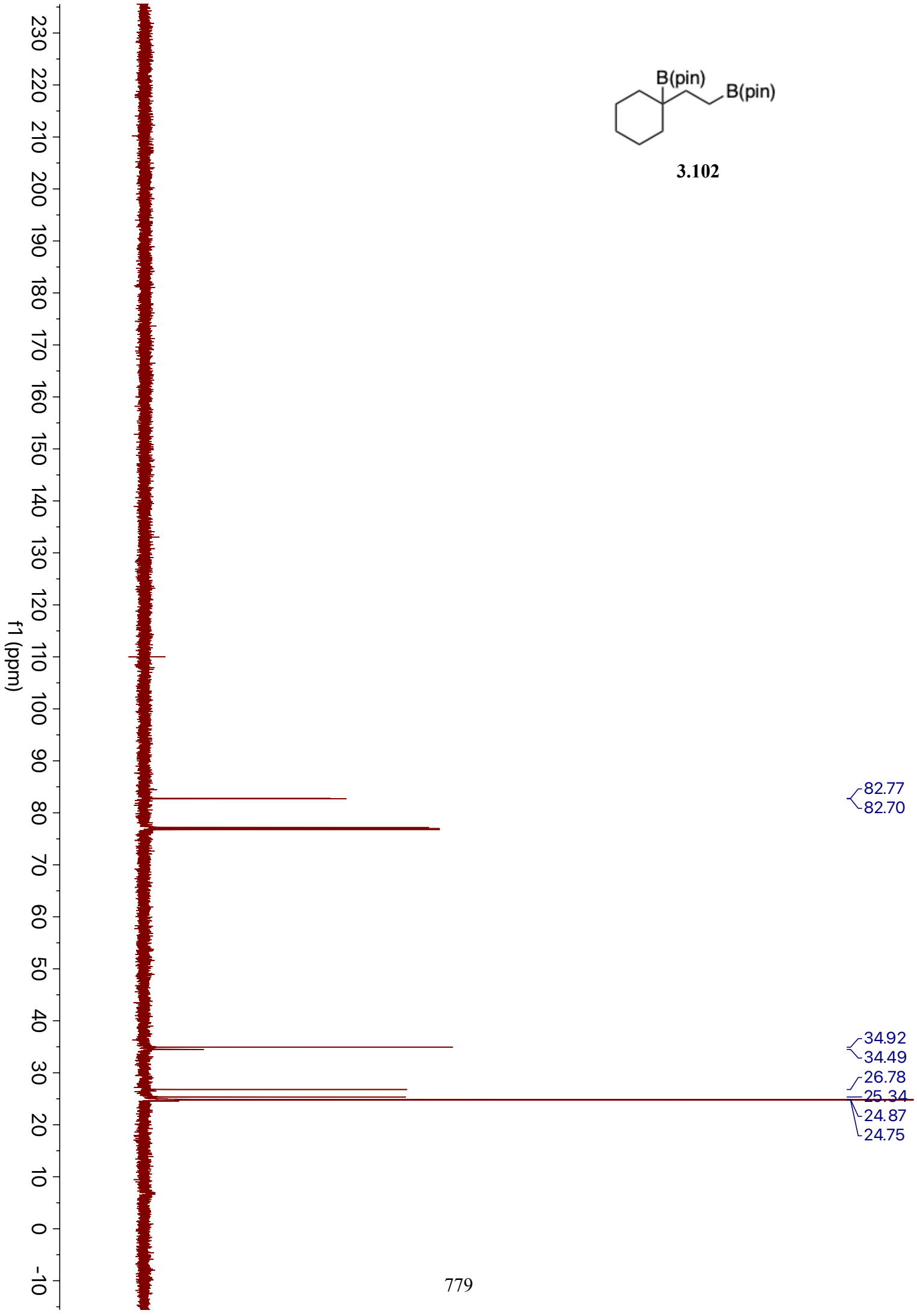
3.101

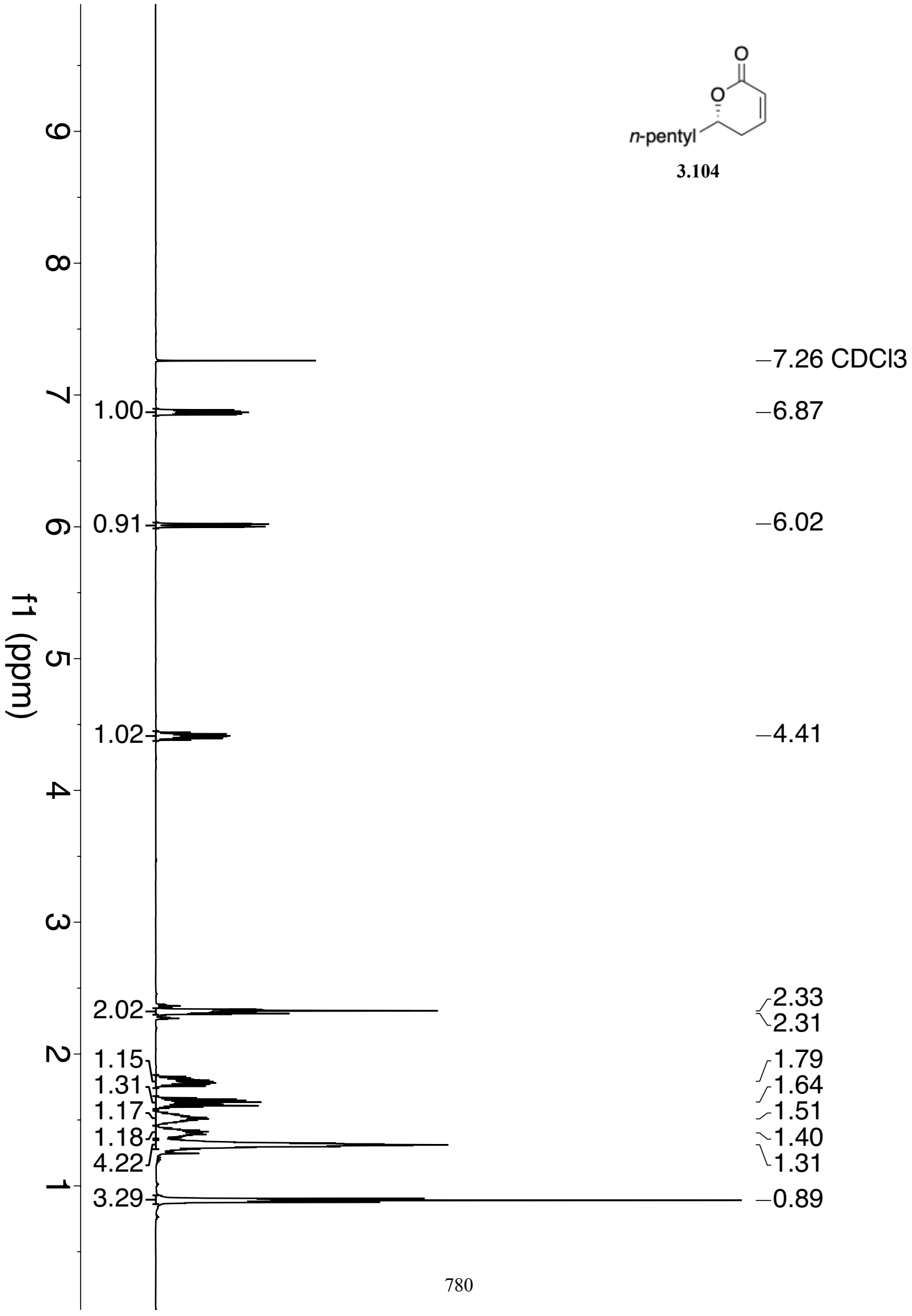
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
155.01
83.24
82.87
78.93
43.16
33.93
33.79
28.48
24.92
24.76

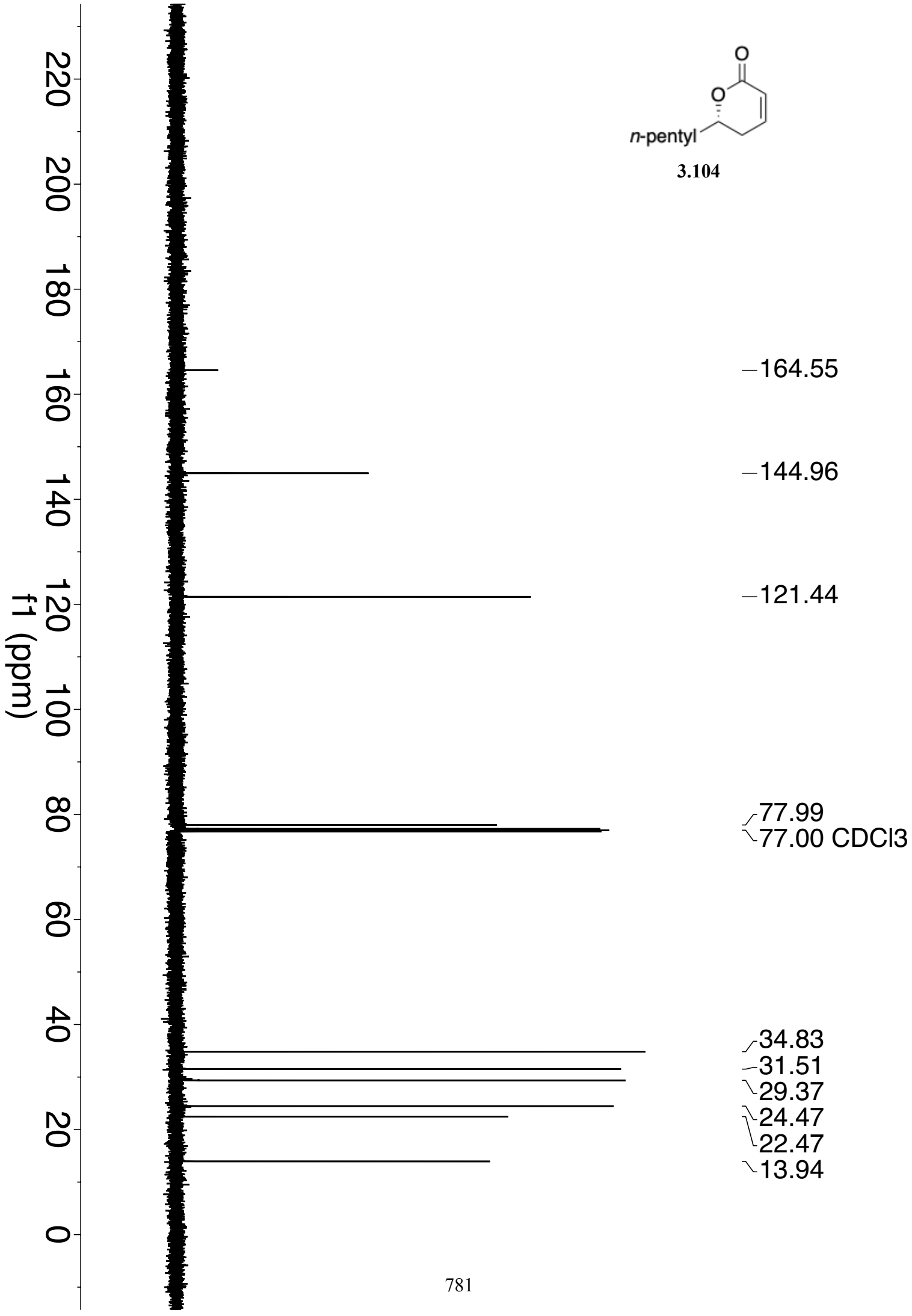

B(pin)
B(pin)

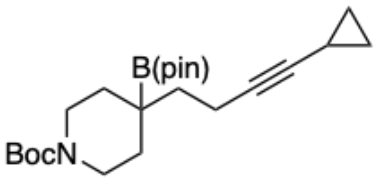
3.102

f1 (ppm)
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
2.00
3.07
2.17
26.32
1.26
2.06
1.93
1.86
1.83
1.61
1.59
1.58
1.56
1.36
1.36
1.34
1.33
1.33
1.22
1.21
1.21
1.20
1.10
1.09
1.09
1.09
1.07
1.07
1.07
0.87
0.87
0.85
0.85
0.83
0.83
0.71
0.69
0.68

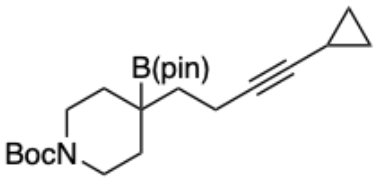

B(pin)
B(pin)
3.102
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
82.77
82.70
34.92
34.49
26.78
25.34
24.87
24.75


n-pentyl
3.104
f1 (ppm)
9
8
7
6
5
4
3
2
1
1.00
0.91
1.02
2.02
1.15
1.31
1.17
1.18
4.22
3.29
7.26 CDCl3
6.87
6.02
4.41
2.33
2.31
1.79
1.64
1.51
1.40
1.31
0.89


O
O
n-pentyl
3.104
164.55
144.96
121.44
77.99
77.00 CDCl3
34.83
31.51
29.37
24.47
22.47
13.94
f1 (ppm)
220
200
180
160
140
120
100
80
60
40
20
0



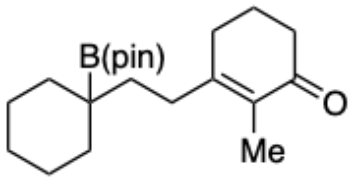
3.105



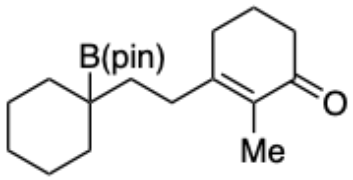
3.105

f1 (ppm)

154.92
83.44
82.92
79.06
75.86
39.67
33.88
28.45
24.89
14.98
7.86
-0.49

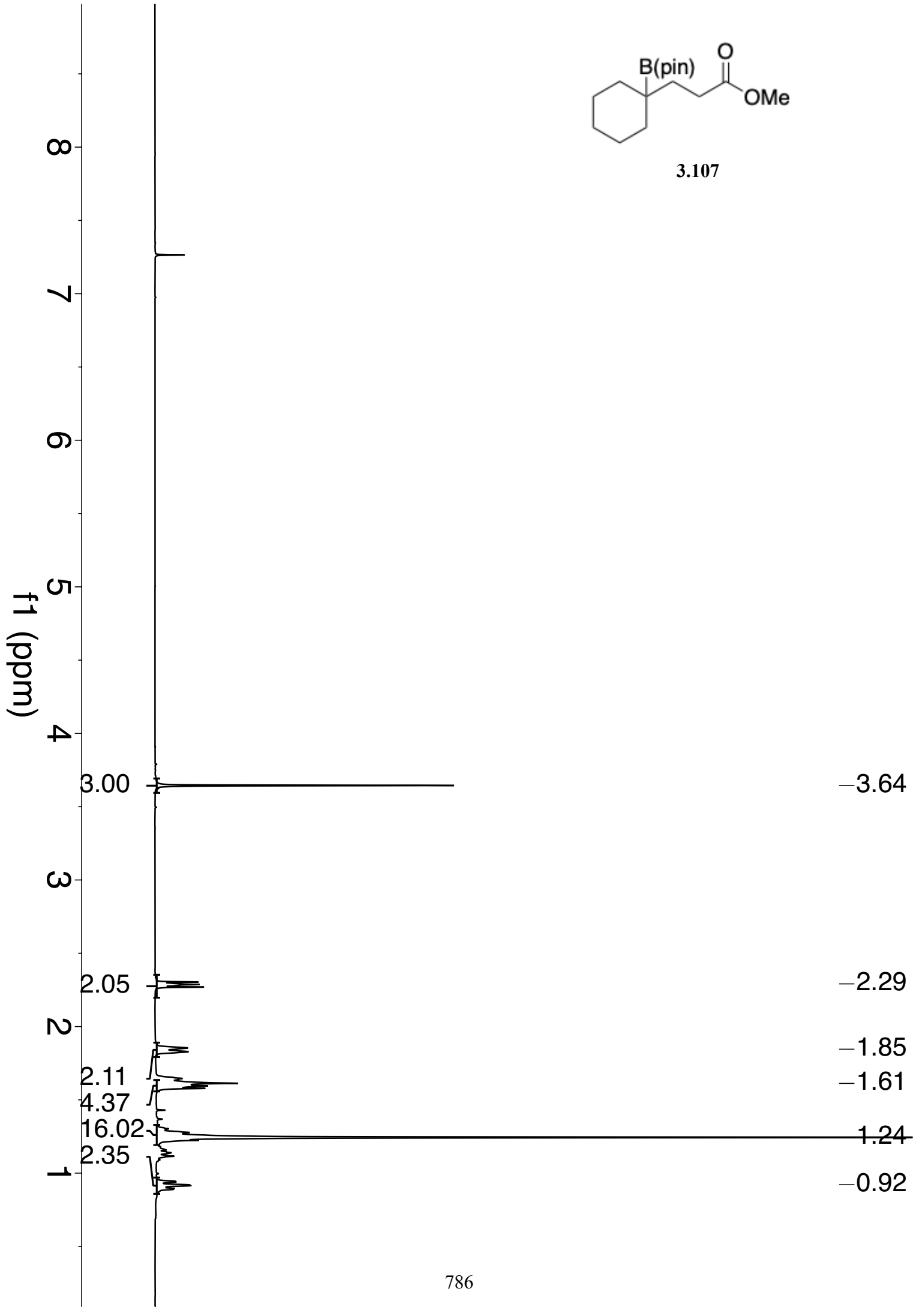


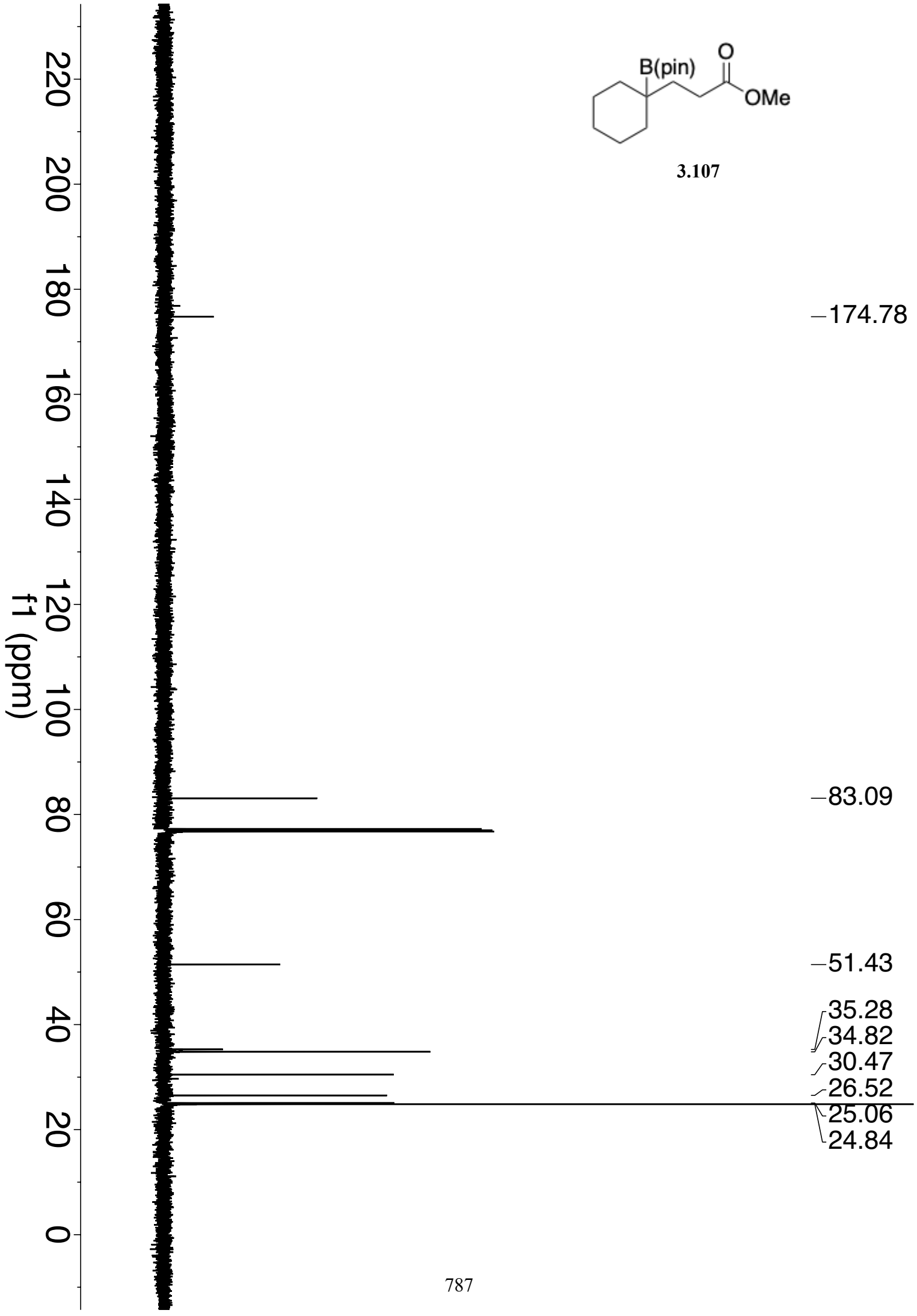
3.106

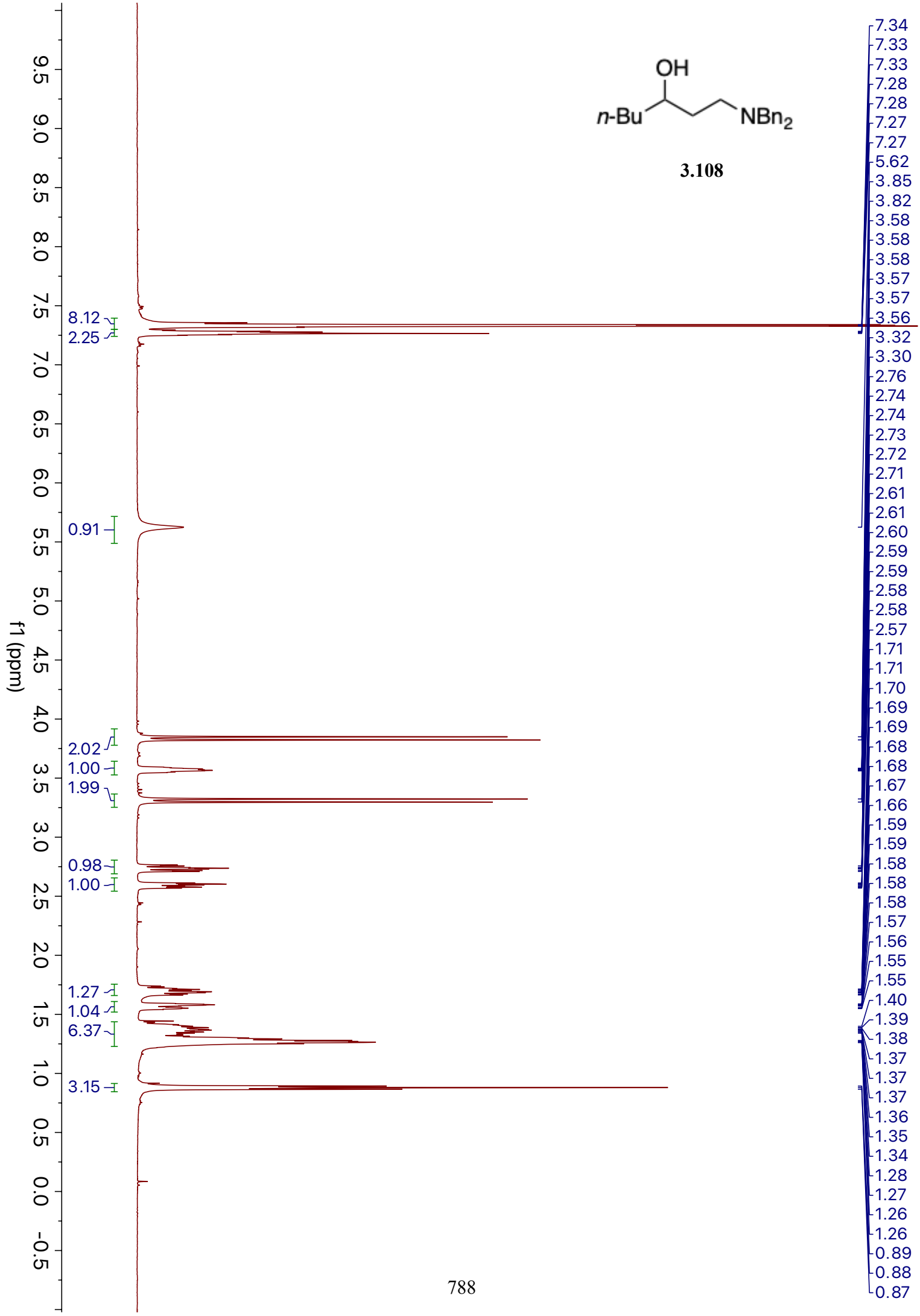

B(pin)
O
Me

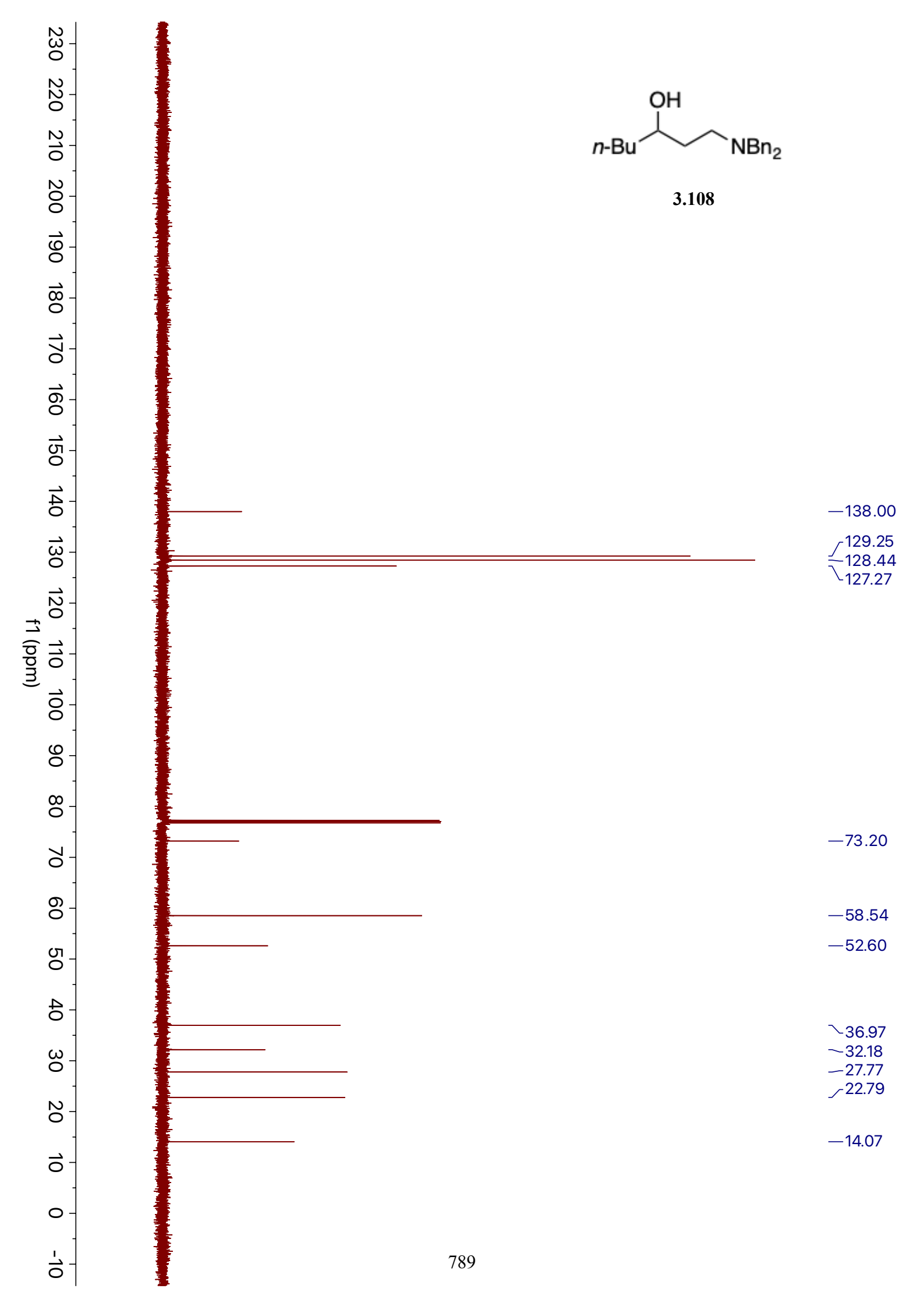
3.106

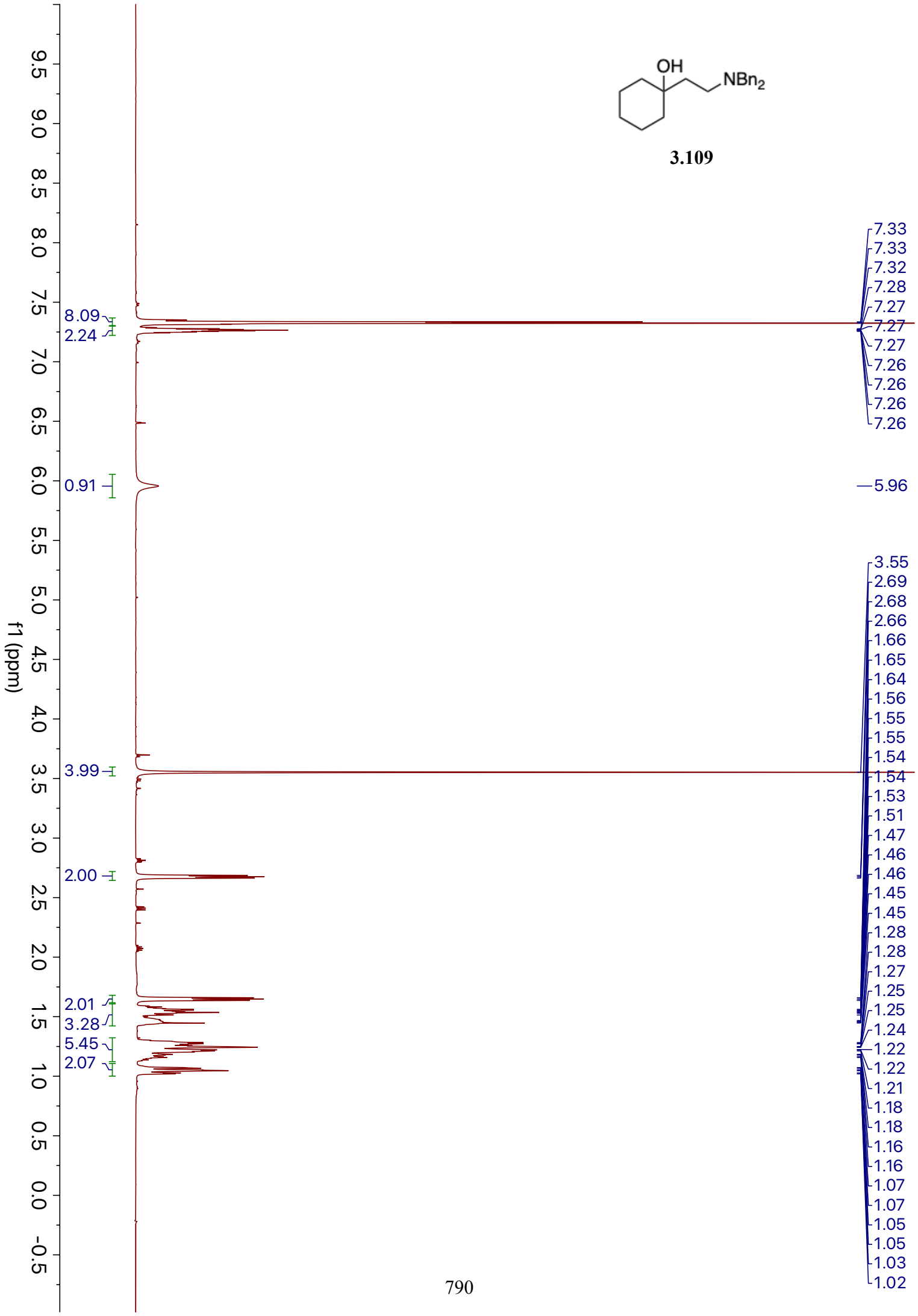
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
199.51
159.94
130.35
83.07
37.99
37.69
35.06
31.75
30.89
26.59
24.97
24.93
24.92
22.57
10.34

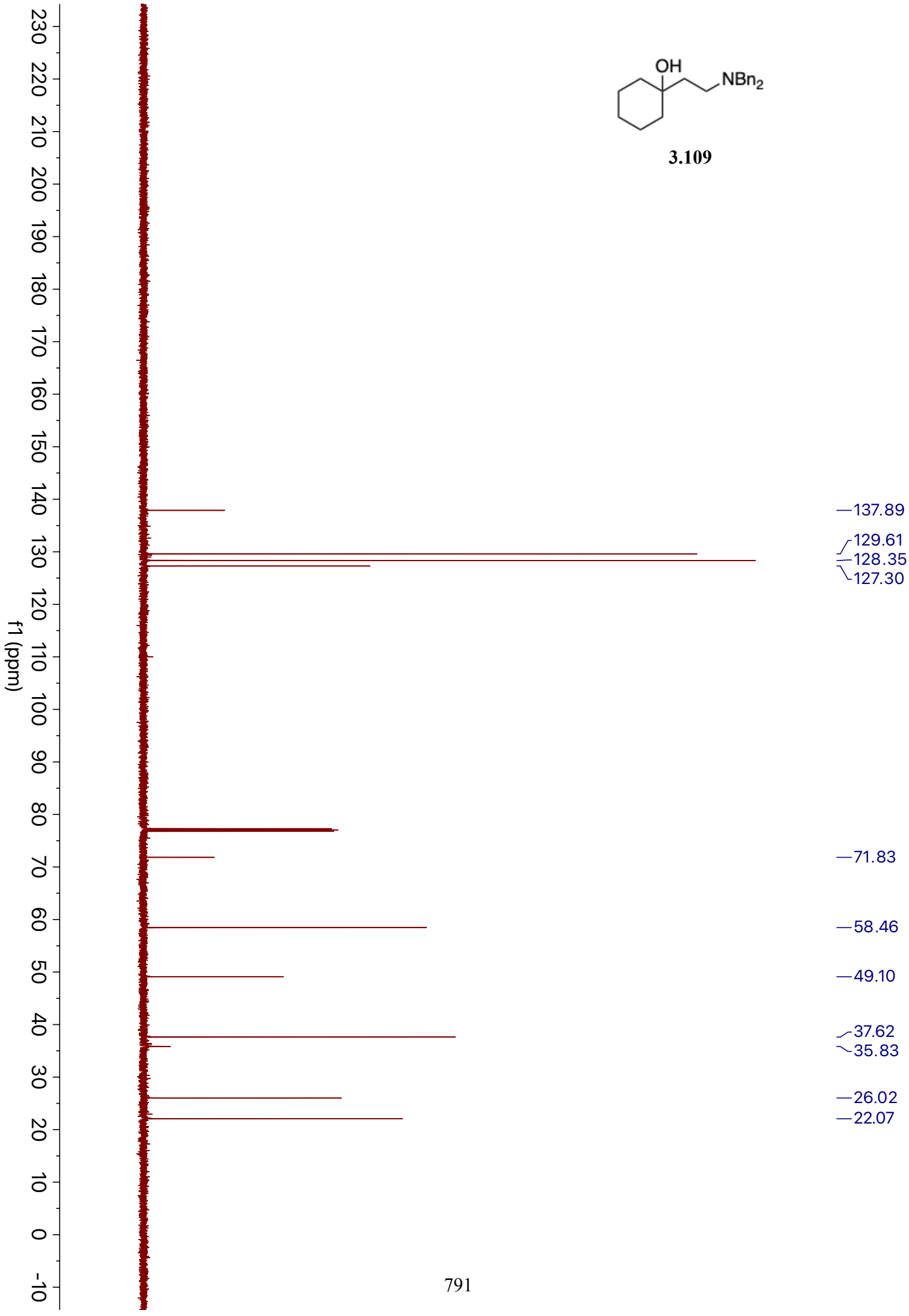

B(pin)
O
OMe
3.107
f1 (ppm)
8
7
6
5
4
3
2
1
3.00
2.05
2.11
4.37
16.02
2.35
3.64
2.29
1.85
1.61
1.24
0.92

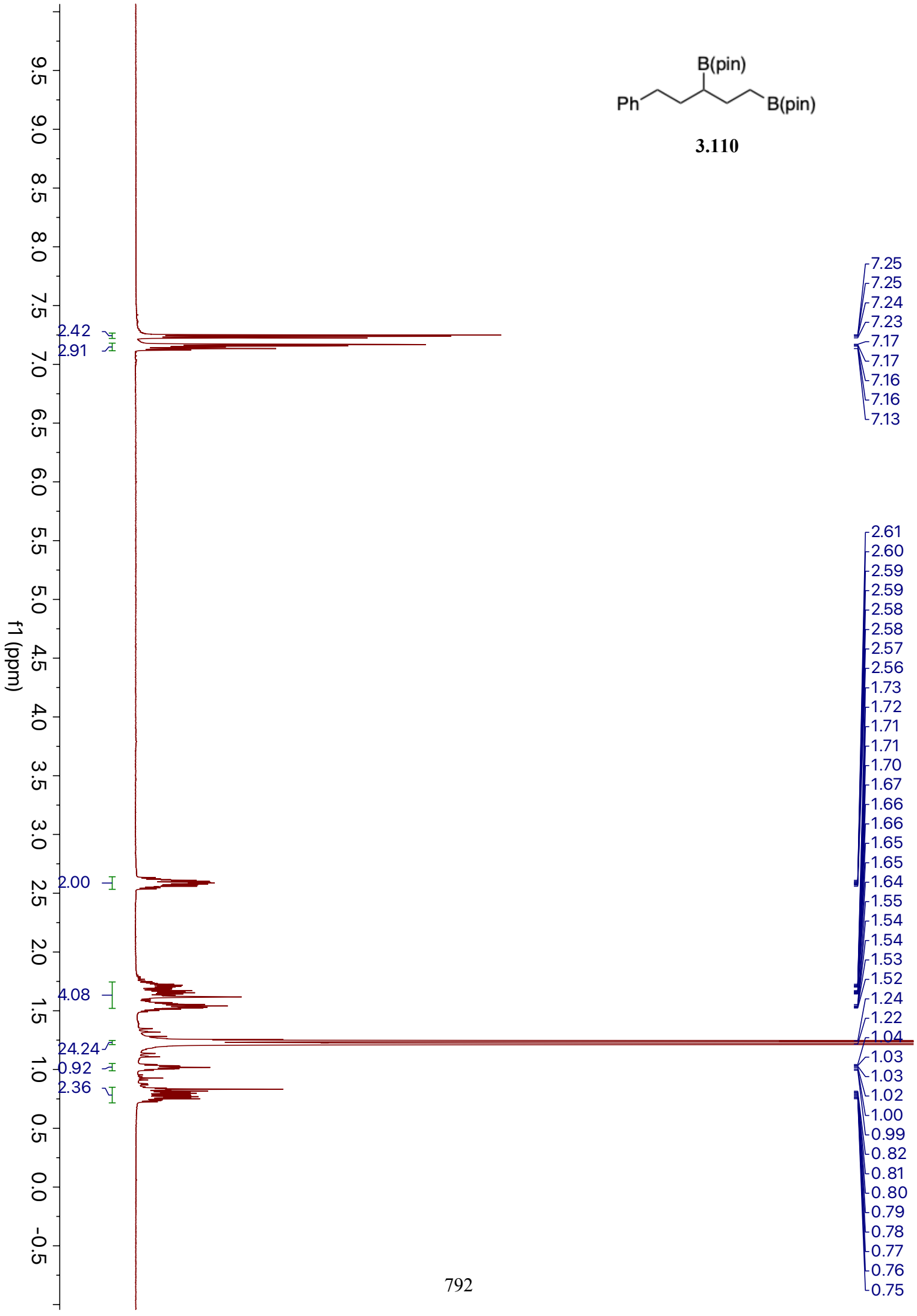

B(pin)
O
OMe
3.107
174.78
83.09
51.43
35.28
34.82
30.47
26.52
25.06
24.84
f1 (ppm)
220
200
180
160
140
120
100
80
60
40
20
0

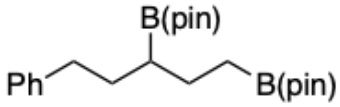

OH
n-Bu
NBn2
3.108
f1 (ppm)
8.12
2.25
0.91
2.02
1.00
1.99
0.98
1.00
1.27
1.04
6.37
3.15


OH
n-Bu
NBn2
3.108
138.00
129.25
128.44
127.27
73.20
58.54
52.60
36.97
32.18
27.77
22.79
14.07
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


OH
NBn2
3.109
f1 (ppm)
8.09
2.24
0.91
3.99
2.00
2.01
3.28
5.45
2.07
7.33
7.33
7.32
7.28
7.27
7.27
7.27
7.26
7.26
7.26
7.26
5.96
3.55
2.69
2.68
2.66
1.66
1.65
1.64
1.56
1.55
1.55
1.54
1.54
1.53
1.51
1.47
1.46
1.46
1.45
1.45
1.28
1.28
1.27
1.25
1.25
1.24
1.22
1.22
1.21
1.18
1.18
1.16
1.16
1.07
1.07
1.05
1.05
1.03
1.02

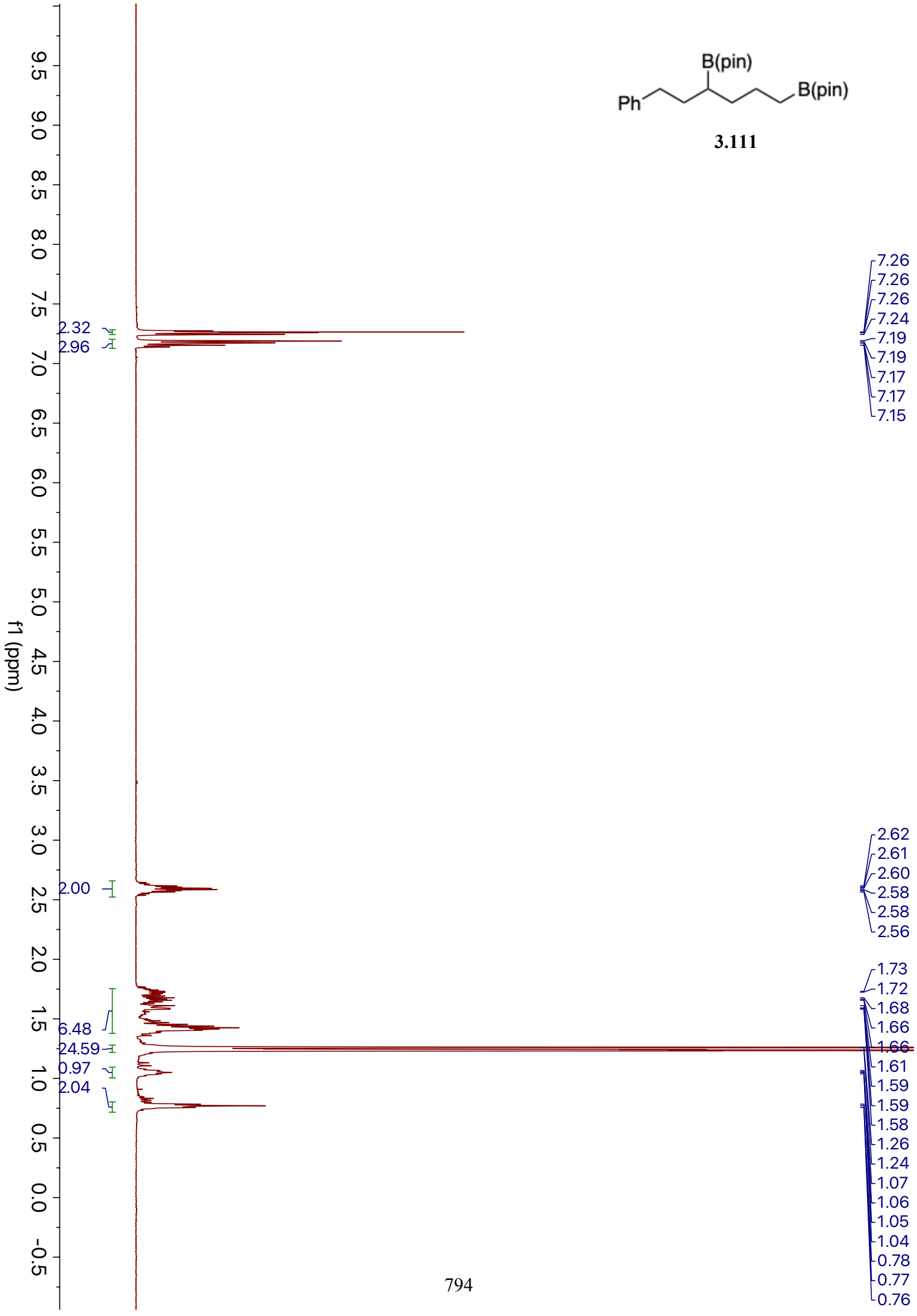

OH
NBn2
3.109
137.89
129.61
128.35
127.30
71.83
58.46
49.10
37.62
35.83
26.02
22.07
f1 (ppm)

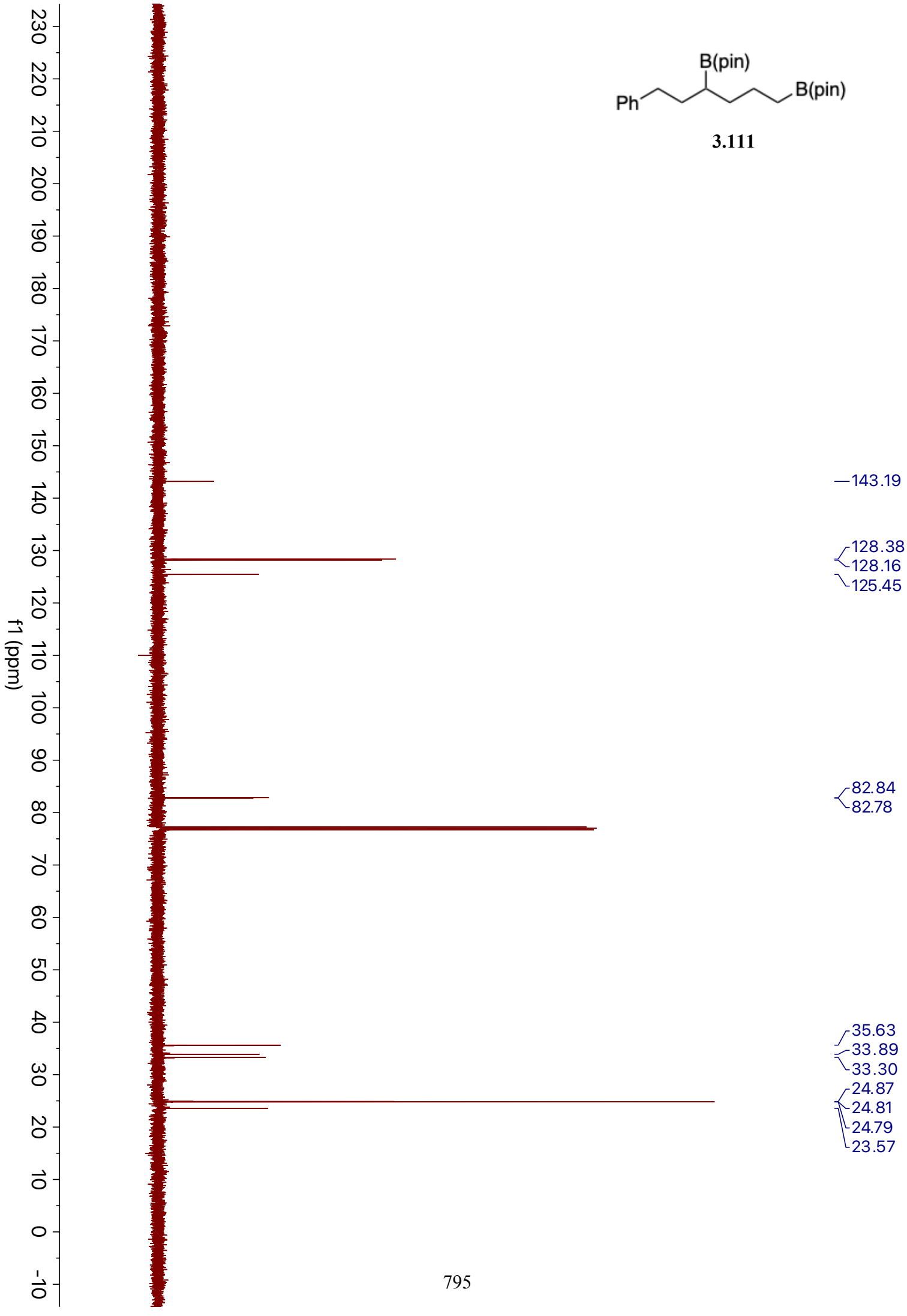

B(pin)
Ph
B(pin)
3.110
f1 (ppm)
2.42
2.91
2.00
4.08
24.24
0.92
2.36
7.25
7.25
7.24
7.23
7.17
7.17
7.16
7.16
7.13
2.61
2.60
2.59
2.59
2.58
2.58
2.57
2.56
1.73
1.72
1.71
1.71
1.70
1.67
1.66
1.66
1.65
1.65
1.64
1.55
1.54
1.54
1.53
1.52
1.24
1.22
1.04
1.03
1.03
1.02
1.00
0.99
0.82
0.81
0.80
0.79
0.78
0.77
0.76
0.75

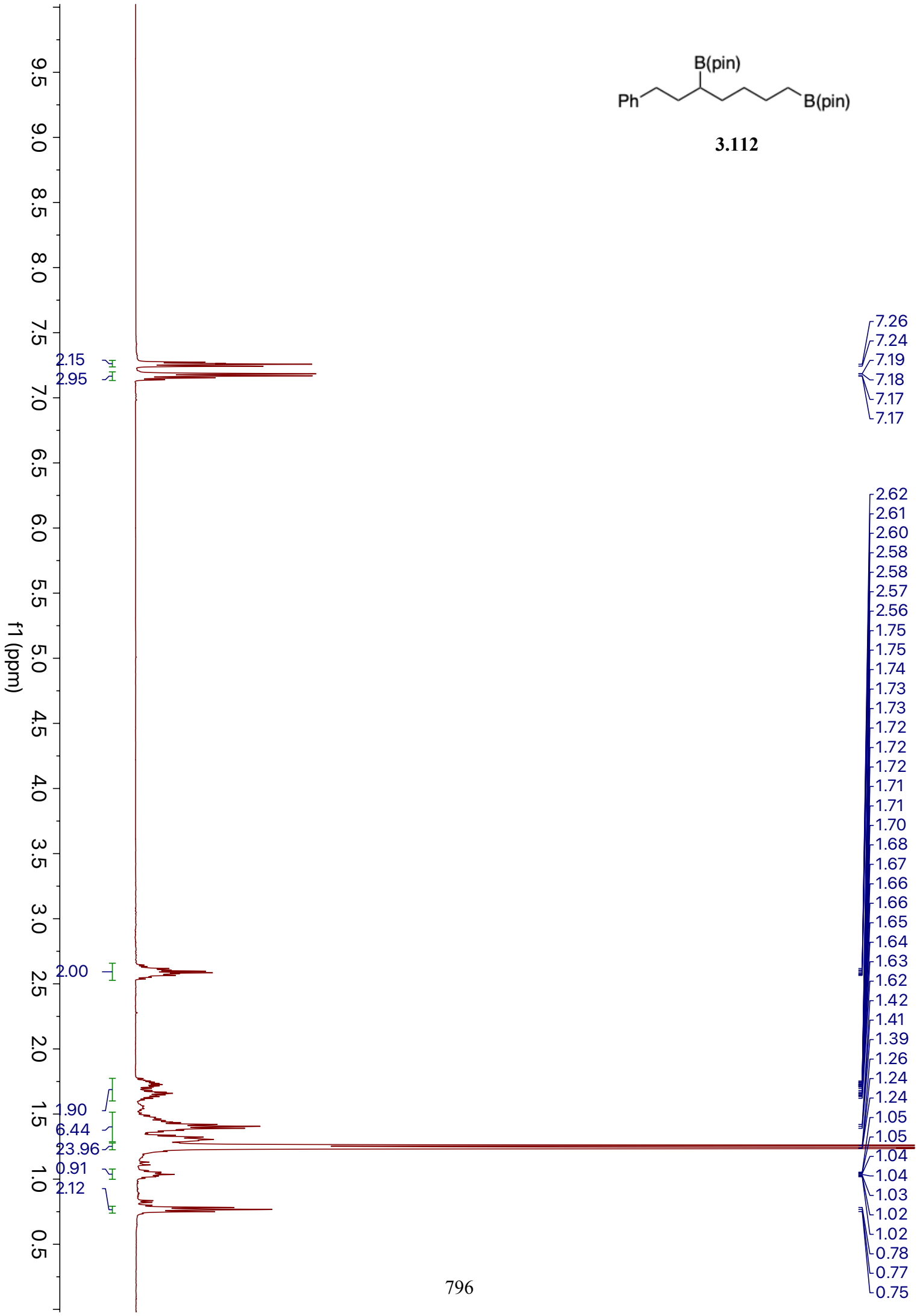

B(pin)
Ph
B(pin)

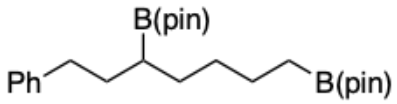
3.110

f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
143.17
128.37
128.13
125.42
82.85
82.79
35.52
33.22
25.21
24.89
24.82
24.79


B(pin)
Ph
B(pin)
3.111
f1 (ppm)
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
2.32
2.96
2.00
6.48
24.59
0.97
2.04
7.26
7.26
7.26
7.24
7.19
7.19
7.17
7.17
7.15
2.62
2.61
2.60
2.58
2.58
2.56
1.73
1.72
1.68
1.66
1.66
1.61
1.59
1.59
1.58
1.26
1.24
1.07
1.06
1.05
1.04
0.78
0.77
0.76


B(pin)
Ph
B(pin)
3.111
f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
143.19
128.38
128.16
125.45
82.84
82.78
35.63
33.89
33.30
24.87
24.81
24.79
23.57


B(pin)
Ph
B(pin)
3.112
f1 (ppm)
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
2.15
2.95
2.00
1.90
6.44
23.96
0.91
2.12
7.26
7.24
7.19
7.18
7.17
7.17
2.62
2.61
2.60
2.58
2.58
2.57
2.56
1.75
1.75
1.74
1.73
1.73
1.72
1.72
1.72
1.71
1.71
1.70
1.68
1.67
1.66
1.66
1.65
1.64
1.63
1.62
1.42
1.41
1.39
1.26
1.24
1.24
1.05
1.05
1.04
1.04
1.03
1.02
1.02
0.78
0.77
0.75


B(pin)
Ph
B(pin)

3.112

f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
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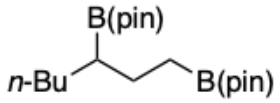
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B(pin)

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1.46
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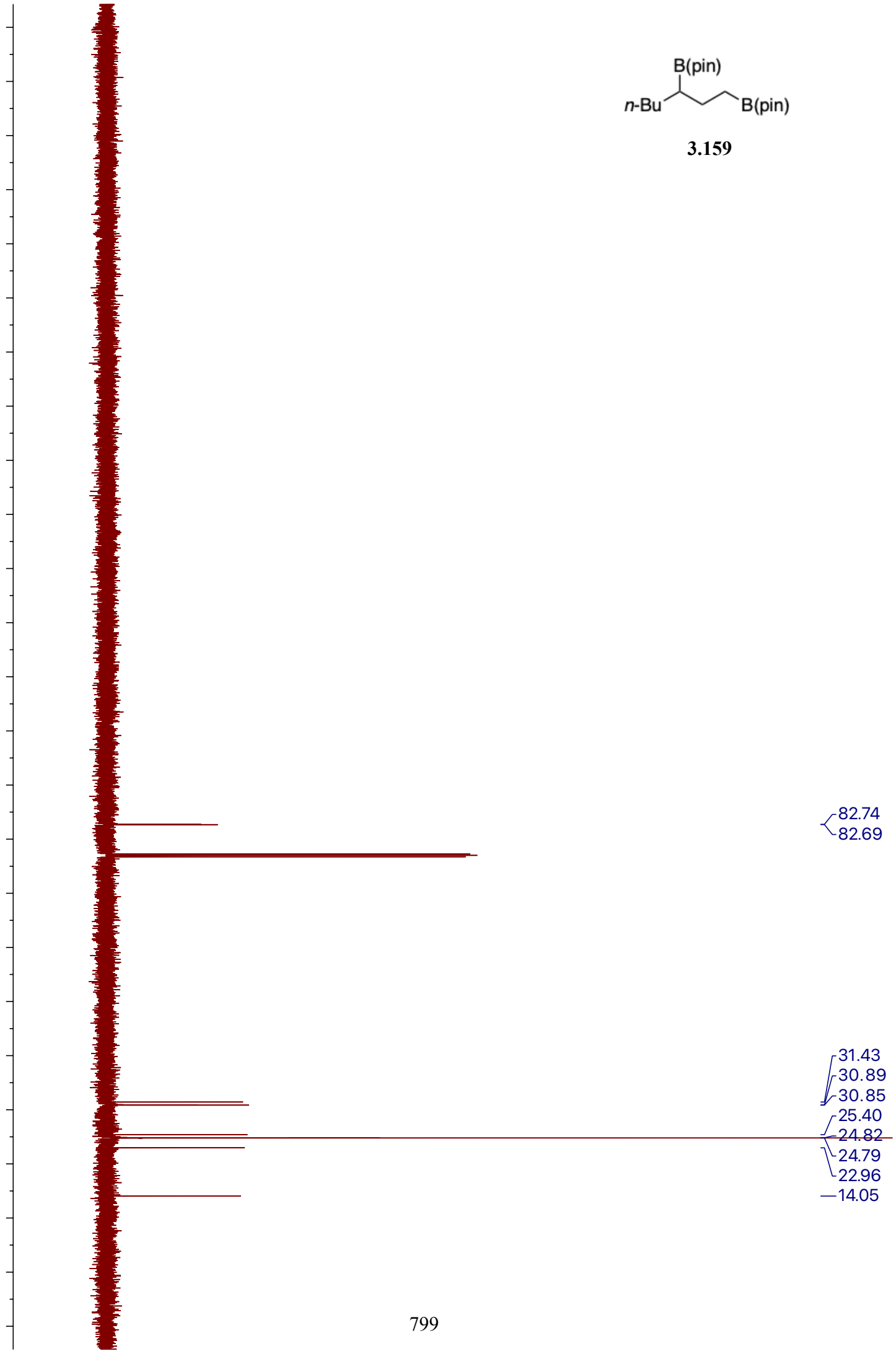
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80
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60
50
40
30
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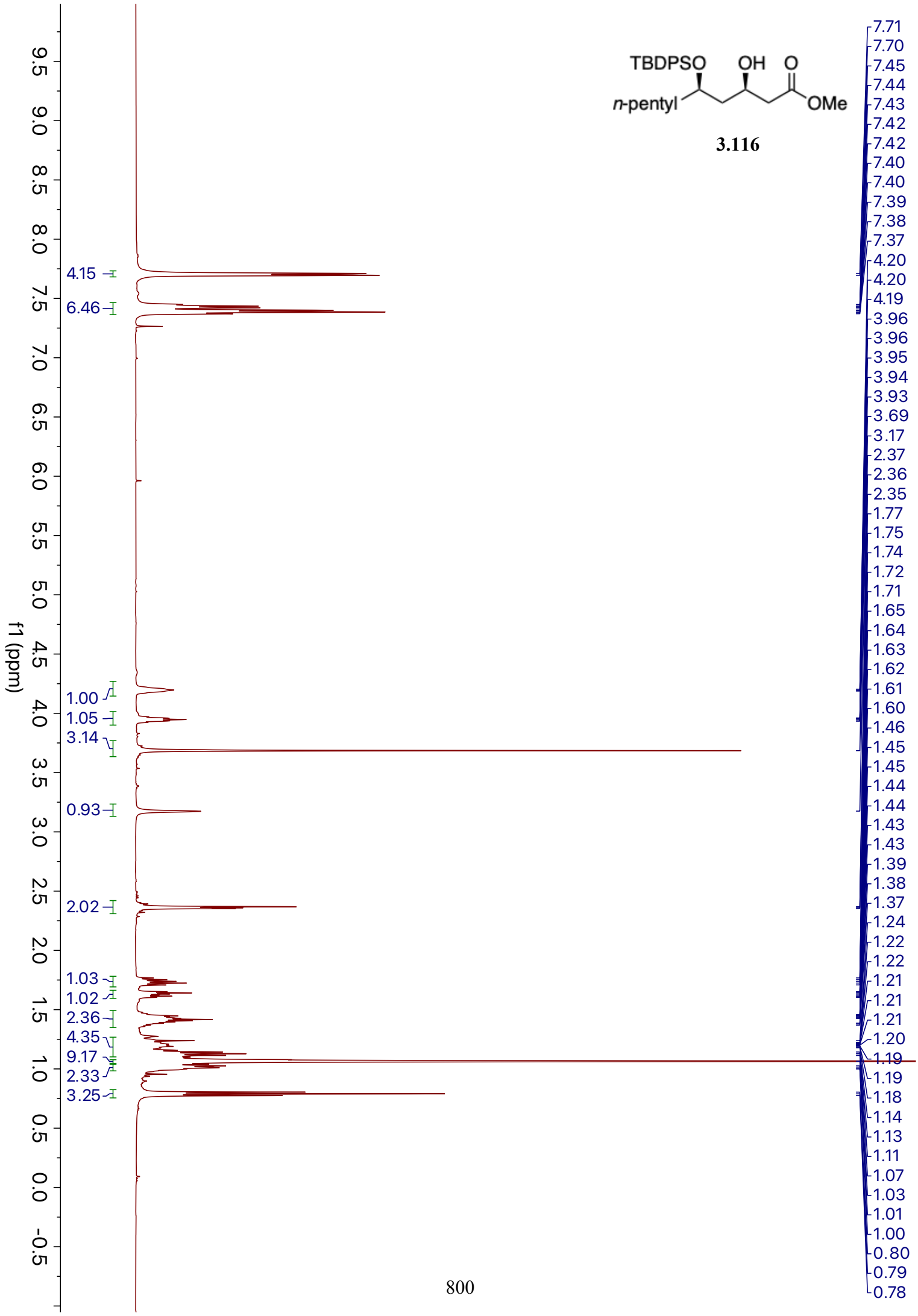
14.05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1.02
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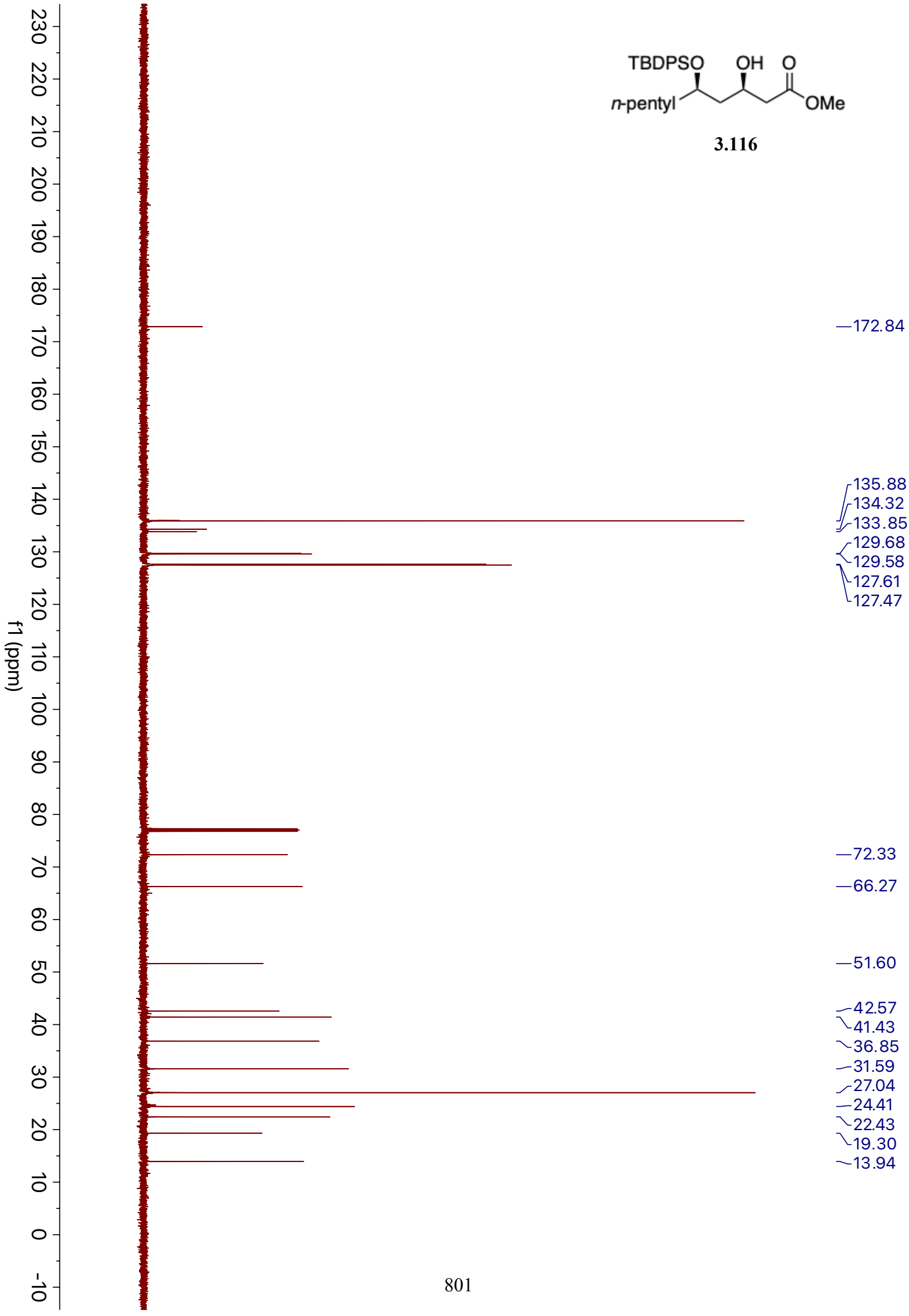
3.25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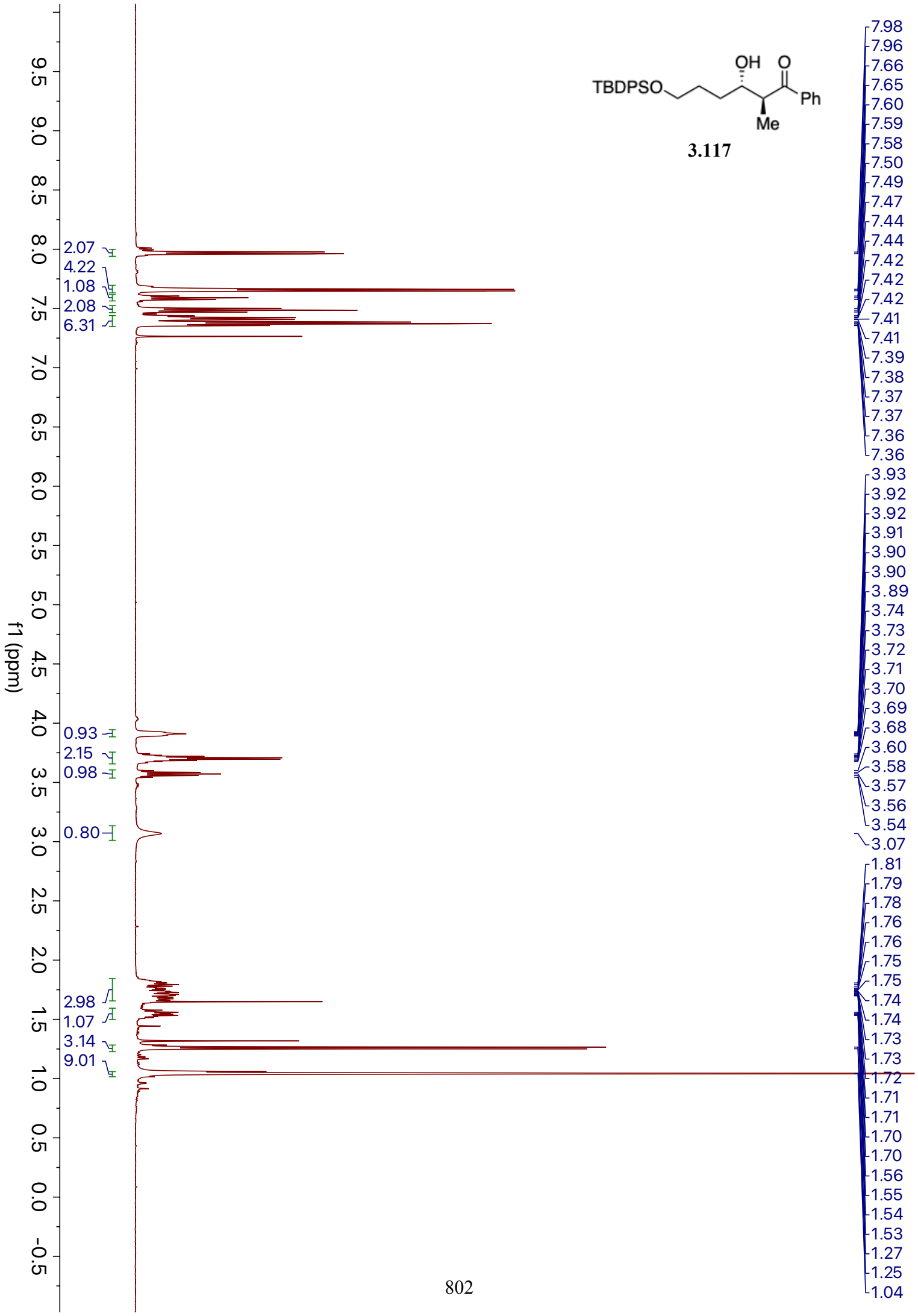
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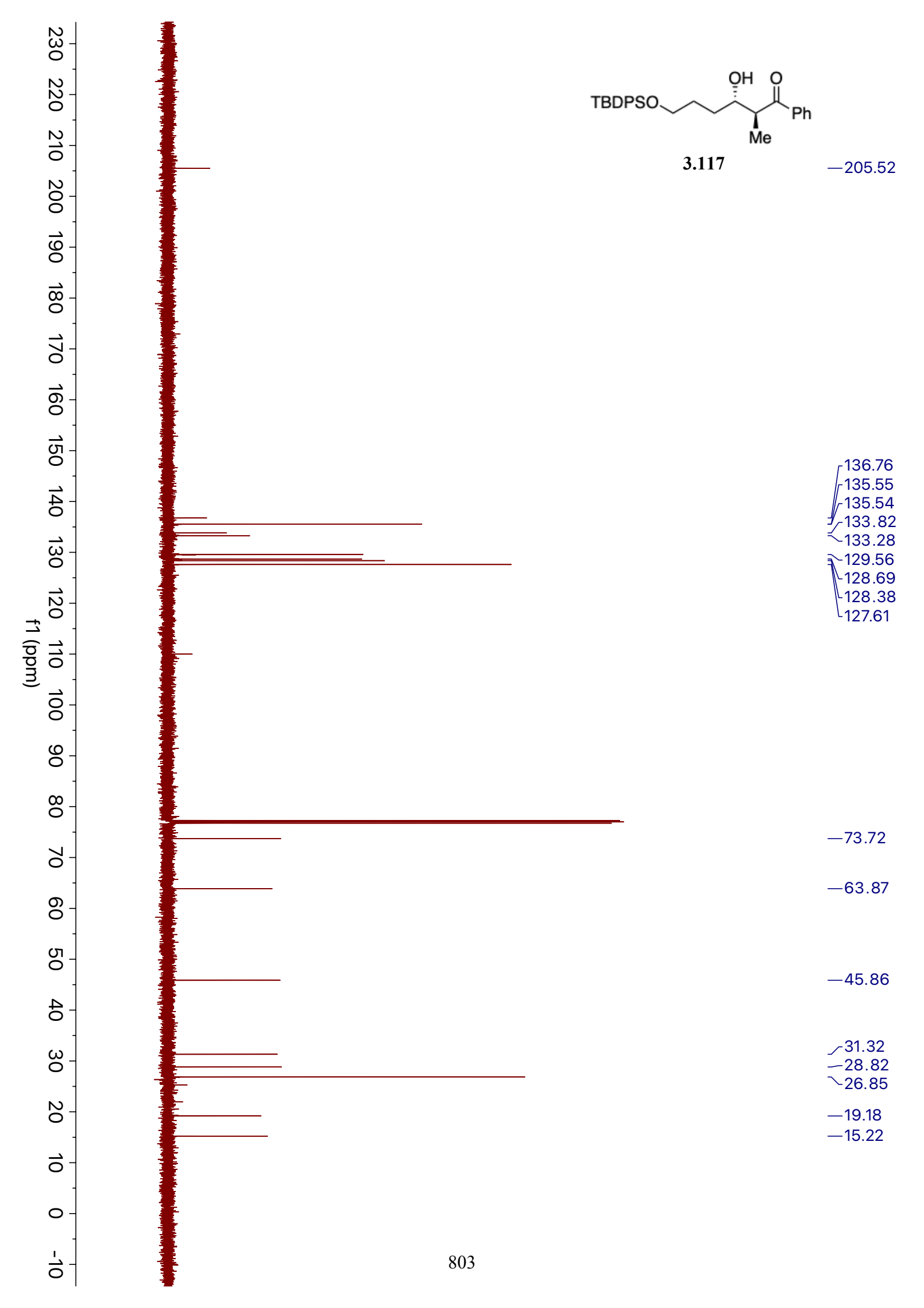
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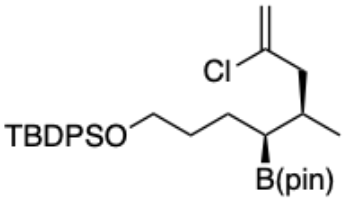
f1 (ppm)



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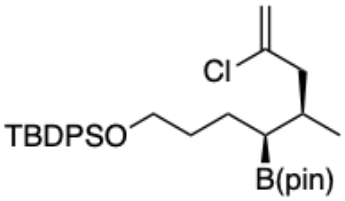
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-10
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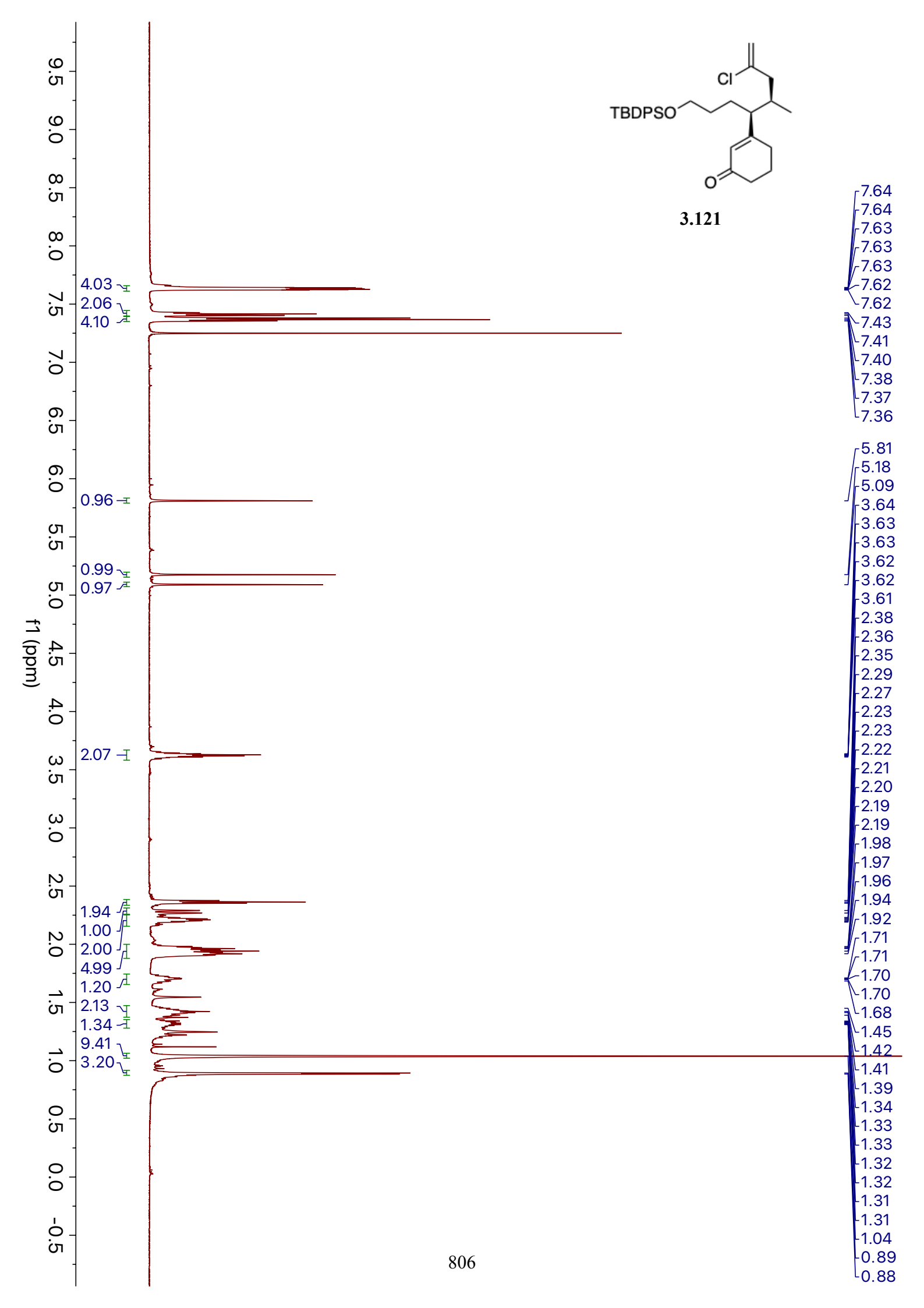
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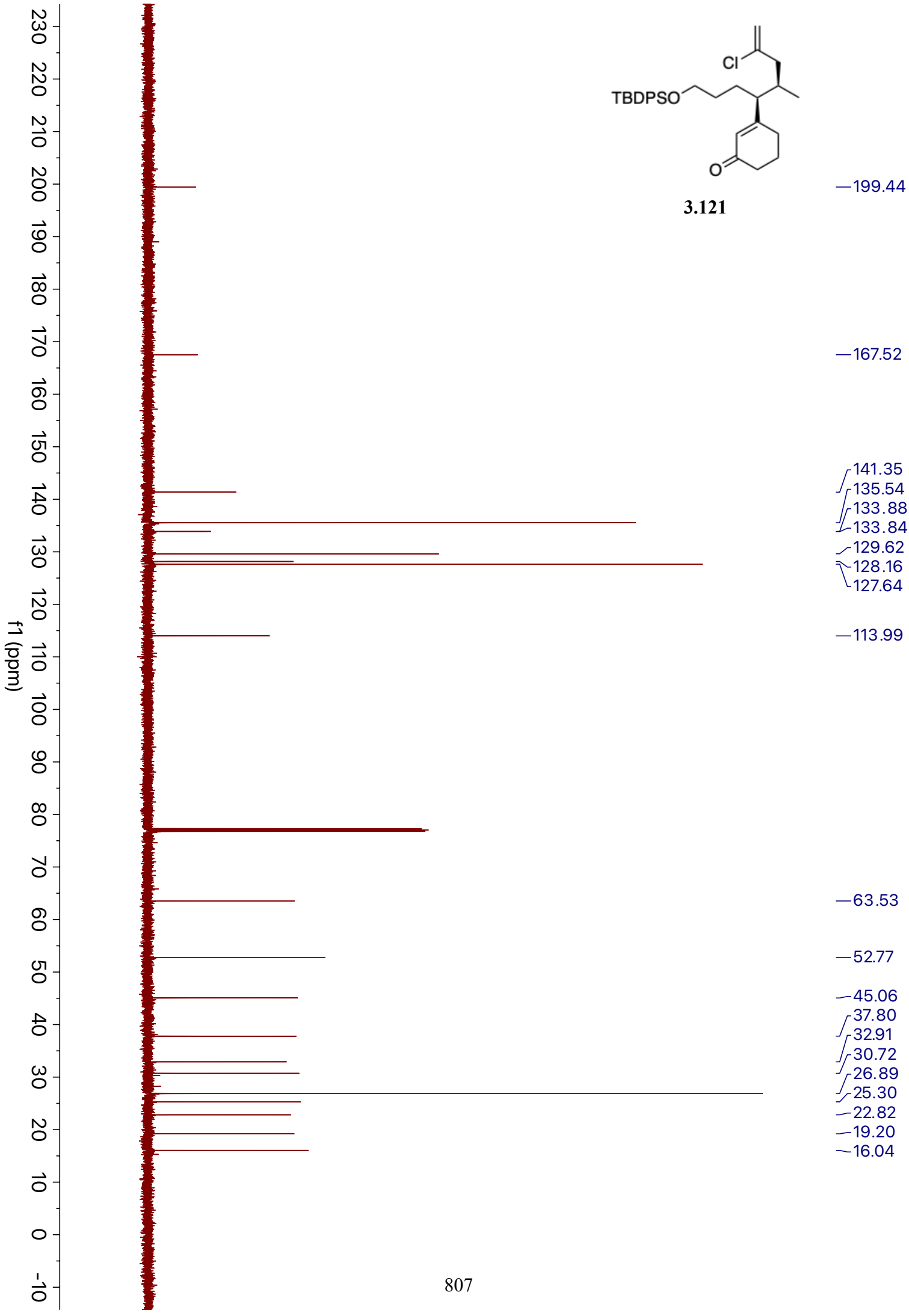
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113.99
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22.82
19.20
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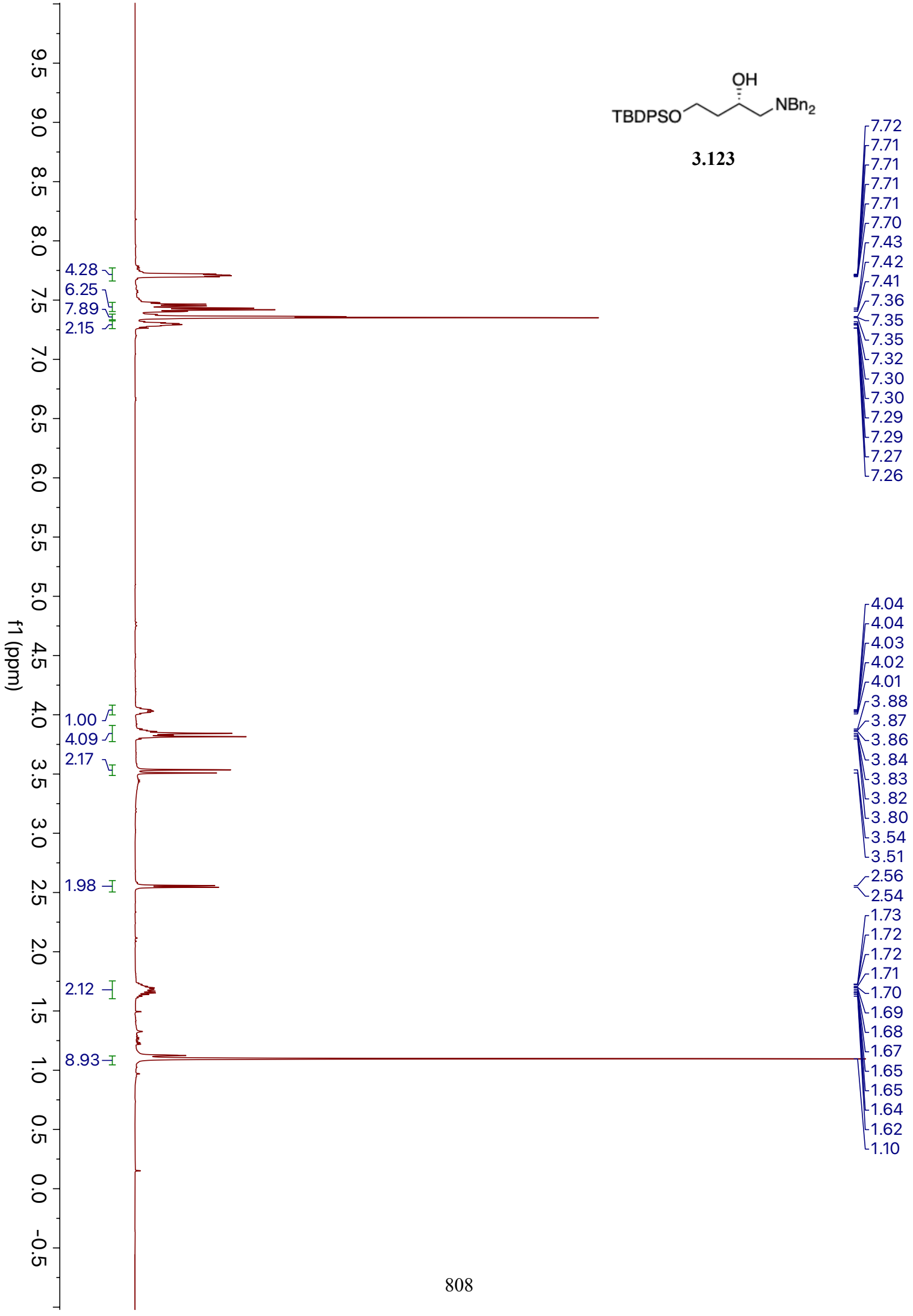
f1 (ppm)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1.5
1.0
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7.35
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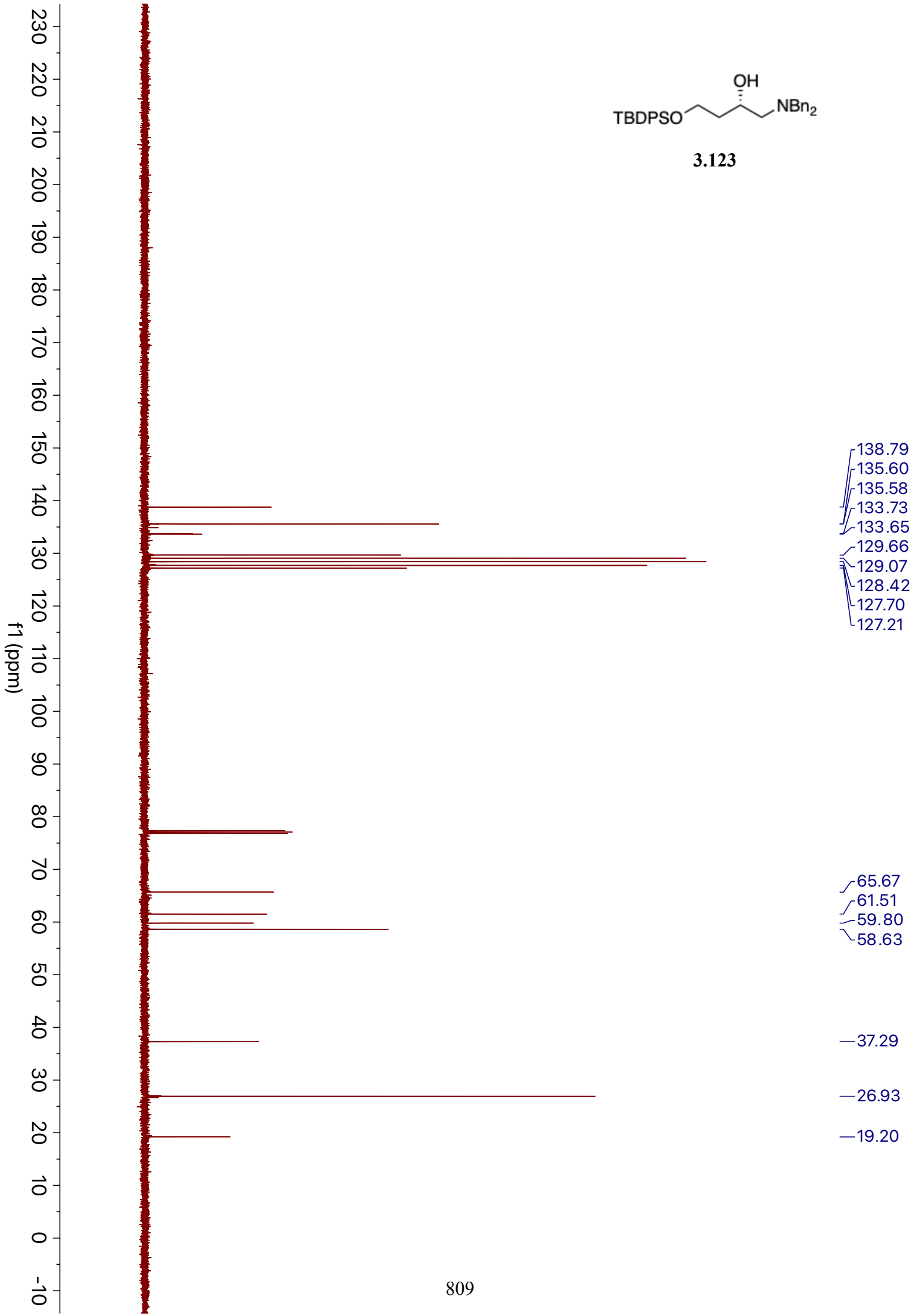
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37.29
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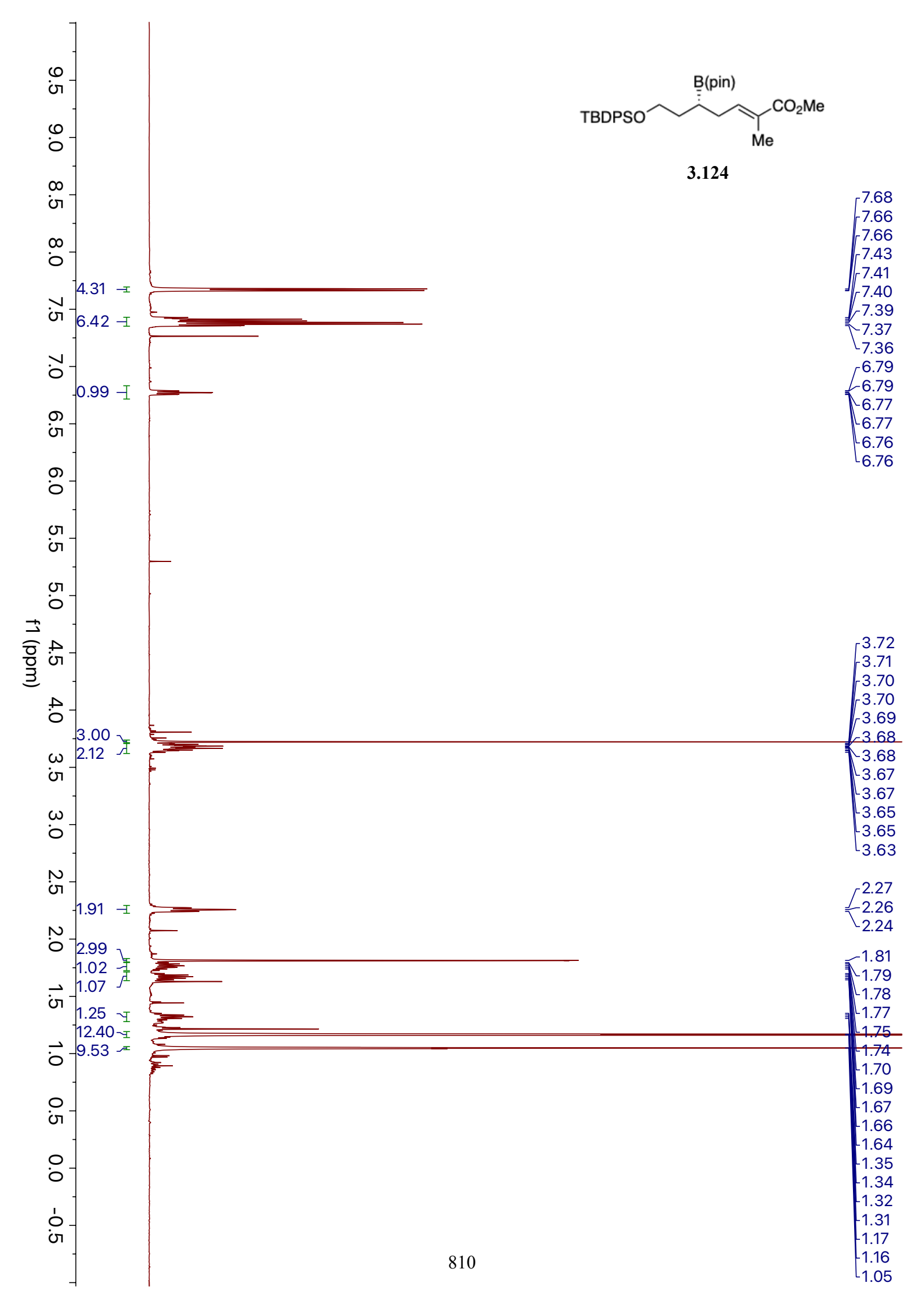
19.20
f1 (ppm)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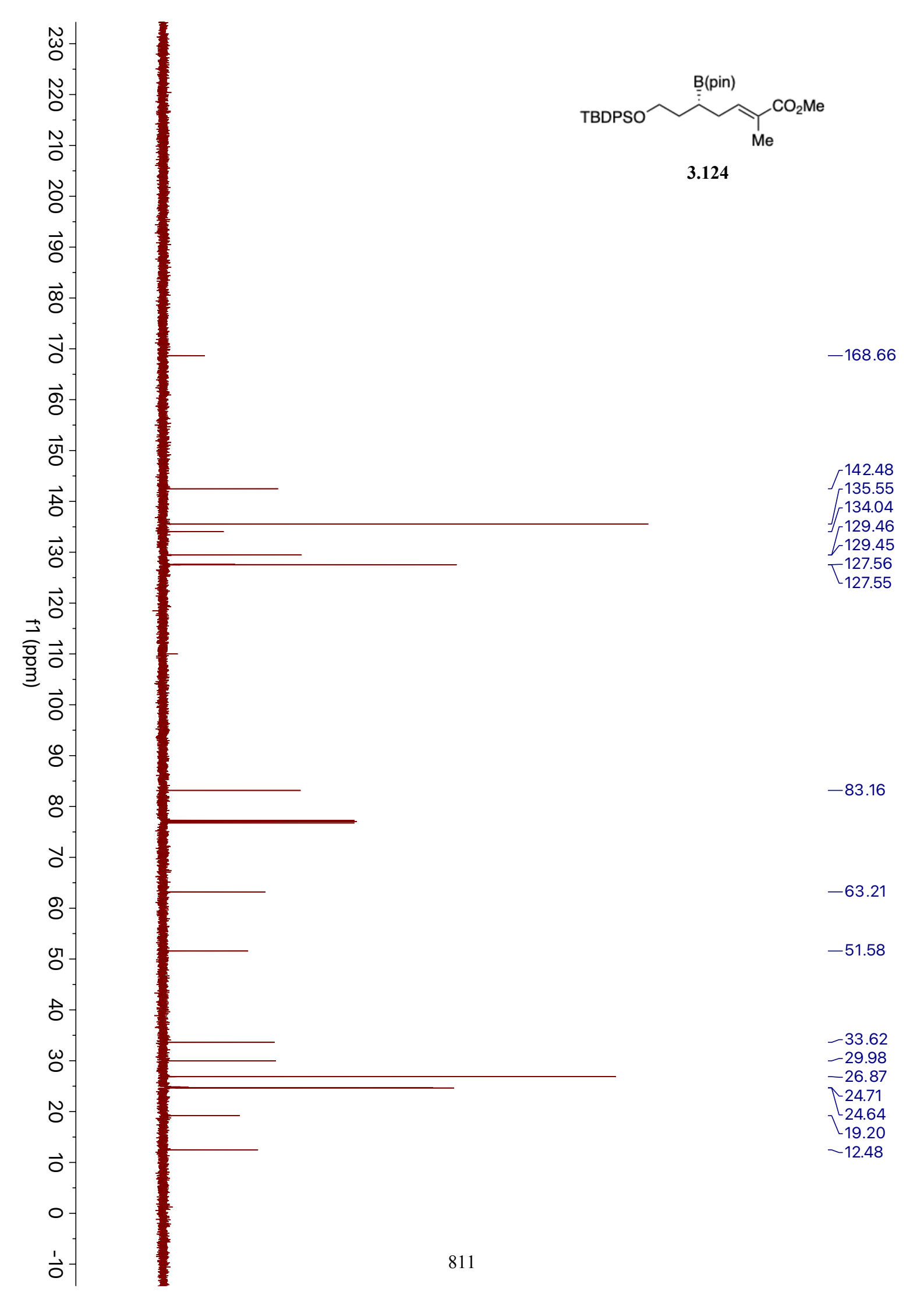
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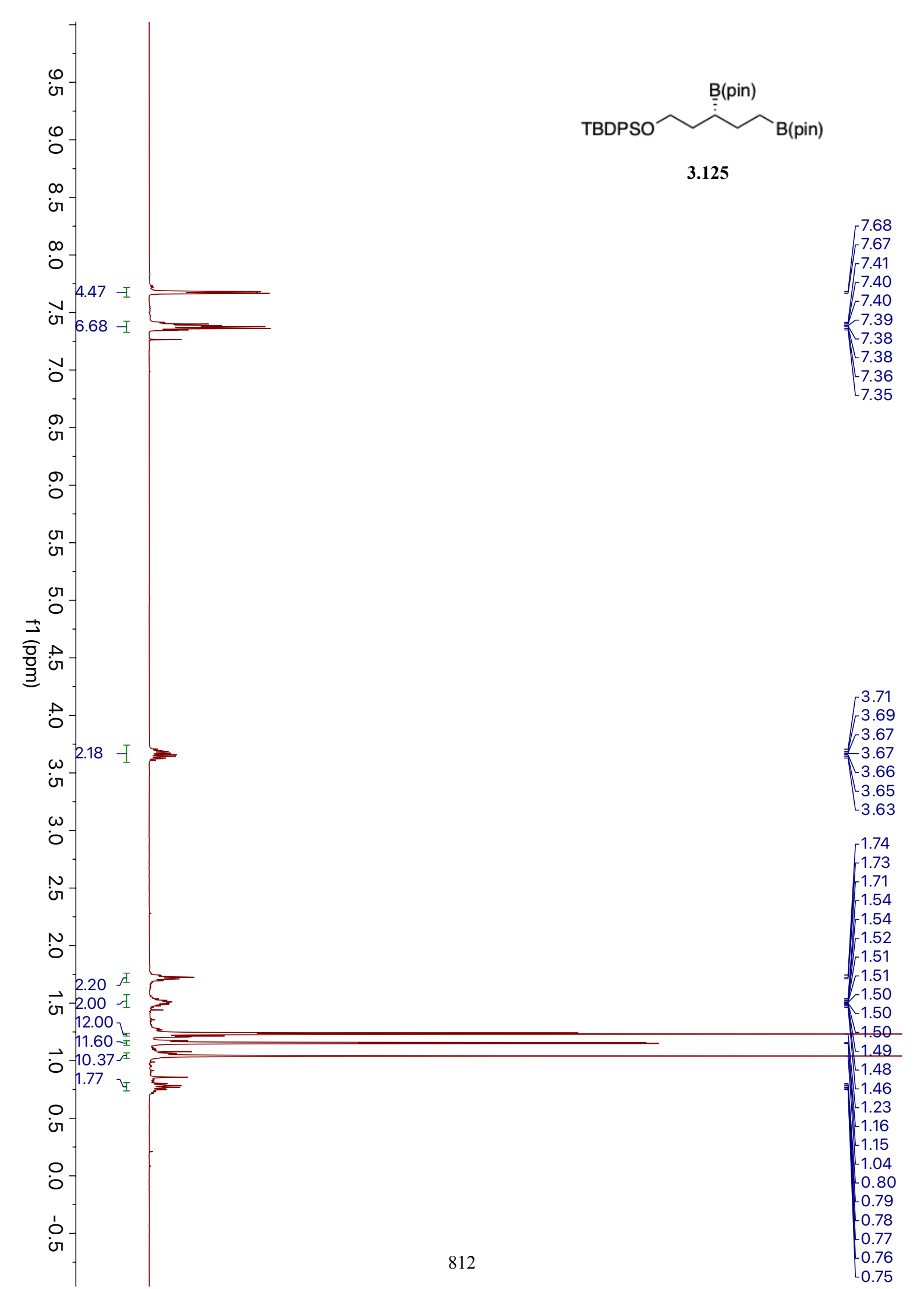
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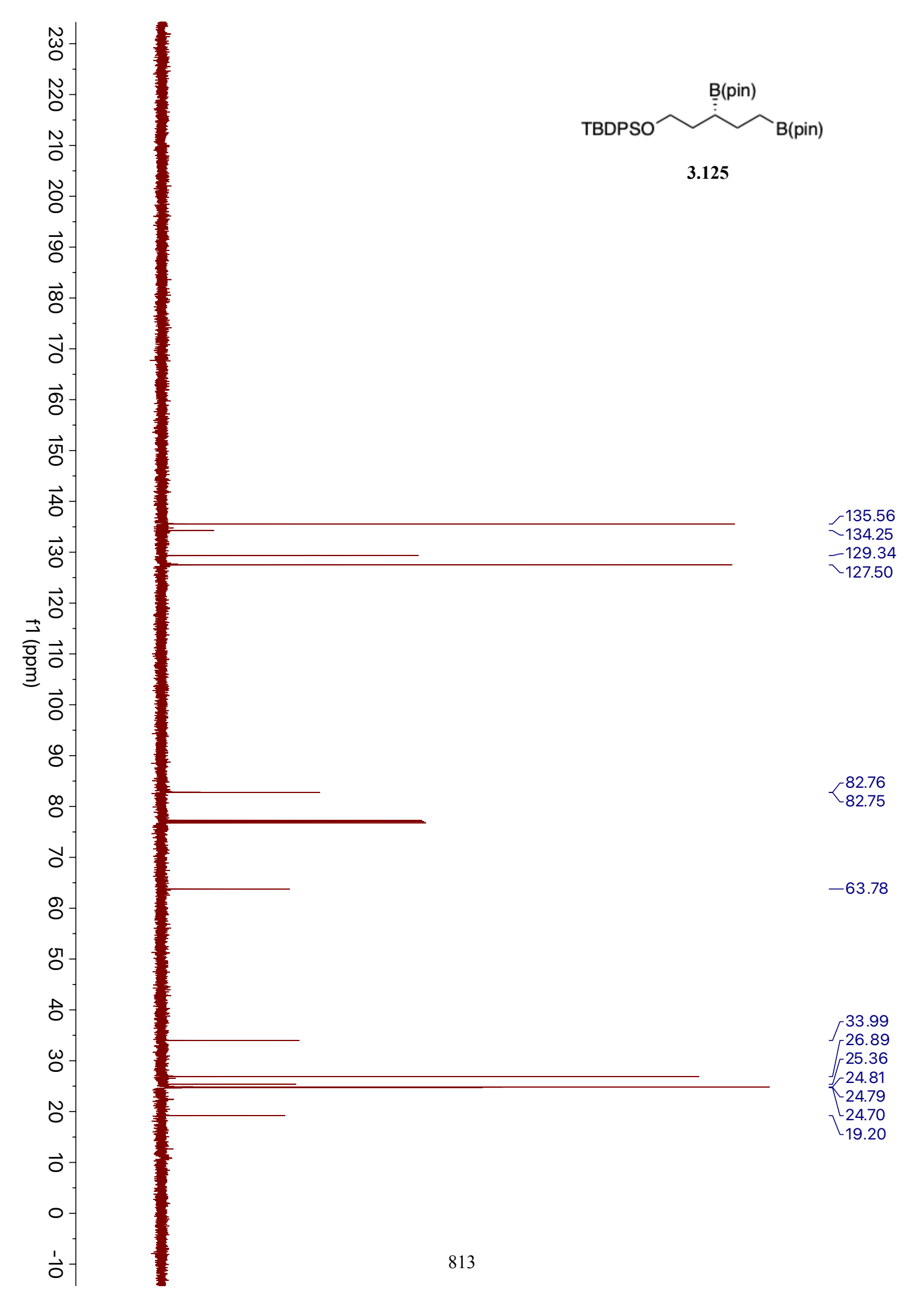
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B(pin)
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33.99
26.89
25.36
24.81
24.79
24.70
19.20
f1 (ppm)
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200
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180
170
160
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140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

APPENDIX

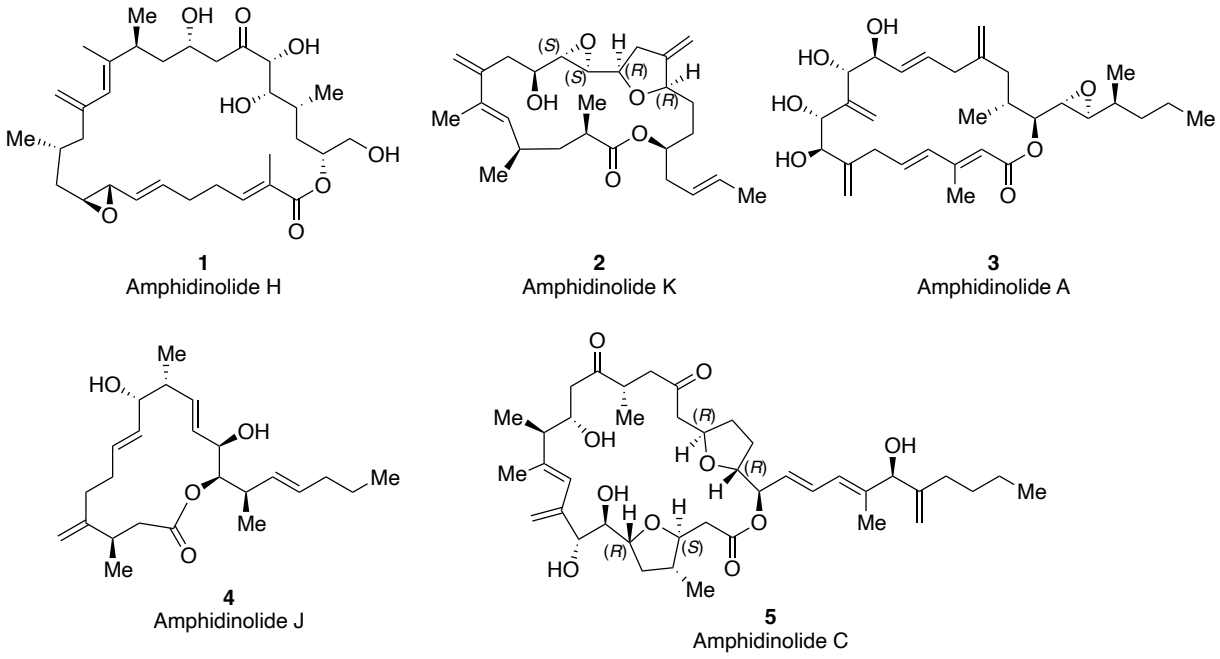
Proposal and Preliminary Results: Design and Synthesis of an Amphidinolide H Analog

Introduction

Amphidinolides are a family of structurally intriguing and biologically interesting bioactive macrolides and polyketides isolated from dinoflagellates *Amphidinium spp*.[1] So far, 34 macrolides have been isolated by the Kobayashi group (Scheme 1). These natural products are designated A–H, J–Y, G2, G3, H2–H5, T2–T5 and vary in their macrolactone cores (12–27 memebered) and side chains.

[1] For selected reviews on amphidinolides, see: (a) Kobayashi, J.; Ishibashi, M. *Chem. Rev.* **1993**, *93*,1753–1769. (b) Kobayashi, J.; Ishibashi, M. *Heterocycles* **1997**, *44*, 543–572. (c) Kobayashi, J.; Tsuda, M.; Ishibashi, M. *Pure. Appl. Chem.* **1999**, *71*, 1123–1126. (d) Kobayashi, J.; Shimbo, K.; Kubota, T.; Tsuda, M. *Pure. Appl. Chem.* **2003**, *75*, 337–342. (e) Kobayashi, J.; Tsuda, M. *Nat. Prod. Rep.* **2004**, *21*, 77–93. (f) Kobayashi, J.; Kubota, T. J. *Nat. Prod.* **2007**, *70*, 451–460. (f) Kobayashi, J. *J. Antibiot.* **2008**, *61*, 271–284.

Scheme 1. Representative Examples of Amphidinolide Natural Products



Background

Isolation and Structure Determination of Ampidinolide H

During the Kobayashi group's exploration of bioactive compounds derived from the Okinawan marine organism *Amphiscolops breviviridis*, they delved into the study of symbiotic microalgae *Amphidinium sp*. associated with marine invertebrates. From the cultured dinoflagellates, they isolated five novel cytotoxic macrolides named amphidinolides A-E.[2] Their ongoing pursuit of pharmacologically valuable substances from cultured dinoflagellates of the genus *Amphidinium*,

[2] (a) Kobayashi, J.; Ishibashi, M.; Nakamura, H.; Ohizumi, Y.; Yamasu, T.; Sasaki, T.; Hirata, Y. *Tetrahedron Lett*. **1986**, 27, 5755-5788. (b) Ishibashi, M.; Ohizumi, Y.; Hamashima, M.; Nakamura, H.; Hirata, Y.; Sasaki, T.; Kobayashi, J. *J. Chem. Soc., Chem. Commun.* **1987**, 1127-1129. (c) Kobayashi, J.; Ishibashi, M.; WSlchli, M. R.; Nakamura, H.; Hirata, Y.; Sasaki, T.; Ohizumi, Y. *J. Am. Chem. Soc.* **1988**, *110*, 490-494. (d) Kobayashi, J.; Ishibashi, M.; Nakamura, H.; Ohizumi, Y.; Yamasu, T.; Hirata, Y.; Sasaki, T.; Ohta, T.; Nozoe, S. *J. Nat. Prod.* **1989**, *52*, 1036-1041. (e) Kobayashi, J.; Ishibashi, M.; Murayama, T.; Takamatsu, M.; Iwamura, M.; Ohizumi, Y.; Sasaki, T. *J. Org. Chem*. **1990**, *55*, 3421-3423.

particularly the Y-25 strain, resulted in the discovery of a new cytotoxic macrolide designated amphidinolide H (**1**), which exhibited remarkably potent cytotoxic activity.[3]

The harvested cells (70 g) were extracted with methanol/toluene (3:1), and the extracts were dissolved in toluene and washed with 1.0 M aqueous solution of NaCl. The organic fraction was purified by silica gel chromatography with $CHCl_3$/MeOH (95:5) followed by reversed-phase HPLC to give amphidinolide H **1** as colorless amorphous powder (0.0017%).

The gross structure of **1** was elucidated primarily by 2D NMR, whereas the stereochemisty remained unsolved. In 2000, Kobayashi and co-workers reported that Y-72 strain of the genus *Amphidinium* produces relatively large amount of amphidinolide H (**1**). This discovery enabled them to determine the relative and absolute stereochemistry of amphidinolide H (**1**) on the basis of X-ray diffraction analysis (CCDC: 1217250).[4] The harvested algal cells (50 g) were extracted with MeOH/toluene (4:1), and the extracts were dissolved in toluene and washed with water. The toluene extracts were subjected to silica gel chromatogrphy followed by HPLC to afford amphidinolide H (0.082%). It was crystallized from hexanes/benzene as colorless needles.

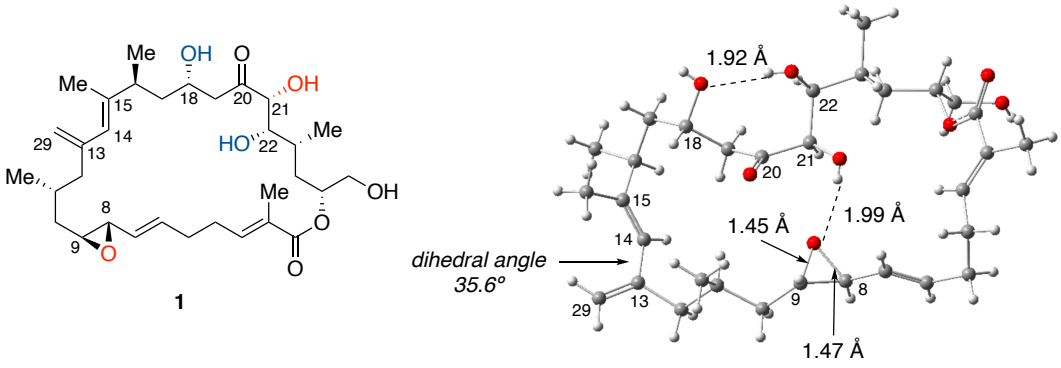
As illustrated in Scheme 2, the structure of amphidinolide H (**1**) adopts a rectangular shape, centrally bridged by an intramolecular hydrogen bond (1.99 Å) between the hydroxyl group (on C21) and the epoxide oxygen. Notably, the C8–O bond length (1.470 Å) within the epoxide ring exceeds that of the C9–O bond (1.448 Å), likely influenced by the intramolecular hydrogen bonding. Furthermore, intramolecular hydrogen bond (1.92 Å) between the hydroxyl group (on C22) and oxygen (on C18) facilitates the formation of an envelope-boat-shaped eight-membered

[3] Kobayashi, J.; Shigemori, H.; Ishibashi, M.; Yamasu, T.; Hirota, H.; Sasaki, T. *J. Org. Chem.* **1991**, *56*, 5221–5224.
[4] Kobayashi, J.; Shimbo, K.; Sato, M.; Shiro, M.; Tsuda, M. *Org. Lett.* **2000**, *2*, 2805–2807.

ring at the C18–C19–C20–C21–C22–O–H–O moiety. Remarkably, the *S-cis*-configured diene (C15–C14–C13–C29) adopts a twisted conformation with a torsion angle of 35.6º.

The elongation of the C8–O bond is speculated to augment the electrophilicity and reactivity of the conjugated epoxide, potentially enhancing the cytotoxicity of amphidinolide H.

Scheme 2. Crystal Structure and Analysis of Amphidinolide H



Biological Activity of Amphidinolide H

In 2002, Kobayashi and co-workers reported that amphidinolide H exhibits remarkably high cytotoxicity for both murine lymphoma L1210 (IC_{50}=0.00048 μg/mL) and human epidermoid carcinoma KB cell lines (IC_{50}=0.00052 μg/mL).[5]

In 2004, Saito and colleagues delved into the bioactivity of amphidinolide H, and uncovered its inhibitory effect on actin depolymerization through a mechanism that is distinct from other actin inhibitors.[6] Their findings shed light on a novel avenue of action for this compound. In the same year, Osada and co-workers elucidated further the cytotoxic mechanism of amphidinolide H.

[5] Kobayashi, J.; Shimbo, K.; Sato, M.; Tsuda, M. *J. Org. Chem.* **2002**, *67*, 6585–6592.

[6] Saito, S.; Feng, J.; Kira, A.; Kobayashi, J.; Ohizumi, Y. *Biochemical and Biophysical Research Communications* **2004**, *320*, 961–965.

Unlike previously documented F-actin stabilizers, amphidinolide H was found to covalently bind to actin. Through mass spectrometry analysis, they pinpointed the binding site of amphidinolide H to Tyr200 in actin subdomain 4.[7]

Previous Total Syntheses of Amphidinolide H

Because of its unique biological activity, combined with the low isolated amounts from nature, amphinidolide H has garnered continued interest in its total syntheses. To date, there have been three total syntheses of amphidinolide H by the Fürstner[8–9] and Nishiyama[10] groups.

Total Synthesis of Amphidinolide H by Alois Fürstner

In 2007, Fürstner and co-workers reported the first total synthesis of amphinidolide H.[8] Compound **1** was dissected into four fragments A–D, with fragment B being a characterized compound with established synthesis routes. These four fragments were strategically designed to be combined by a metal-catalyzed cross-coupling, an aldol reaction, an esterification, and an olefin metathesis (Scheme 3).

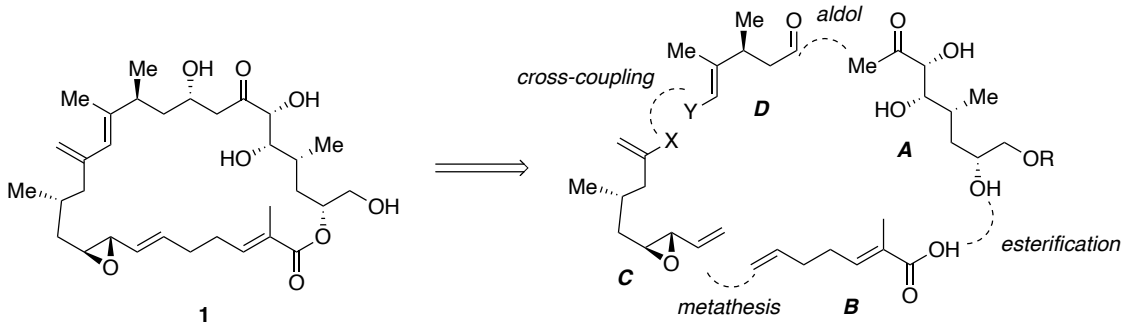
[7] Usui, T.; Kazami, S.; Dohmae, N.; Mashimo, Y.; Kondo, H.; Tsuda, M.; Terasaki, A. G.; Ohashi, K.; Kobayashi, J.; Osada, H. *Chemistry & Biology* **2004**, *11*, 1269–1277.

[8] Fürstner, A.; Bouchez, L. C.; Funel, J.; Liepins, V.; Porée, F.; Gilmour, R.; Beaufils, F.; Laurich, D.; Tamiya, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 9265–9270.

[9] Fürstner, A.; Bouchez, L. C.; Morency, L.; Funel, J.; Liepins, V.; Porée, F.; Gilmour, R.; Laurich, D.; Beaufils, F.; Tamiya, M. *Chem. Eur. J.* **2009**, *15*, 3983–4010.

[10] Hara, A.; Morimoto, R.; Iwasaki, Y.; Saitoh, T.; Ishikawa, Y.; Nishiyama, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 9877–9880.

Scheme 3. Fürstner's Retrosynthetic Analysis of Amphidinolide H in 2007



To commence the synthesis of fragment A (Scheme 4), Roche ester (**6**) was converted into enoate **7** in 69% yield. The following Sharpless epoxidation afforded **8** in 68% yield and 96.5:3.5 er.[11] Treatment with DIBAL followed by quenching with *t*-BuOH effectively opened the epoxide to give diol **9**. This process regioselectively delivered the hydride to the carbon atom on the γ position to the alcohol moiety.[12] Protecting-group interconversions furnished trisilylated triol **10** and the TES-protected primary alcohol underwent Swern oxidation to afford aldehyde **11** in high yield. This compound was subjected to boron glycolate aldol reaction with Evans *N*-oxazolidinone **12**.[13] **13** was furnished in 82% yield and excellent diastereoselectivity. The free alcohol in **13** was protected with TBS group, the compound was then converted into a thioester, which was treated with Me_2CuLi to afford methyl ketone **14** (fragment A) in 54% yield.[14]

[11] Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.

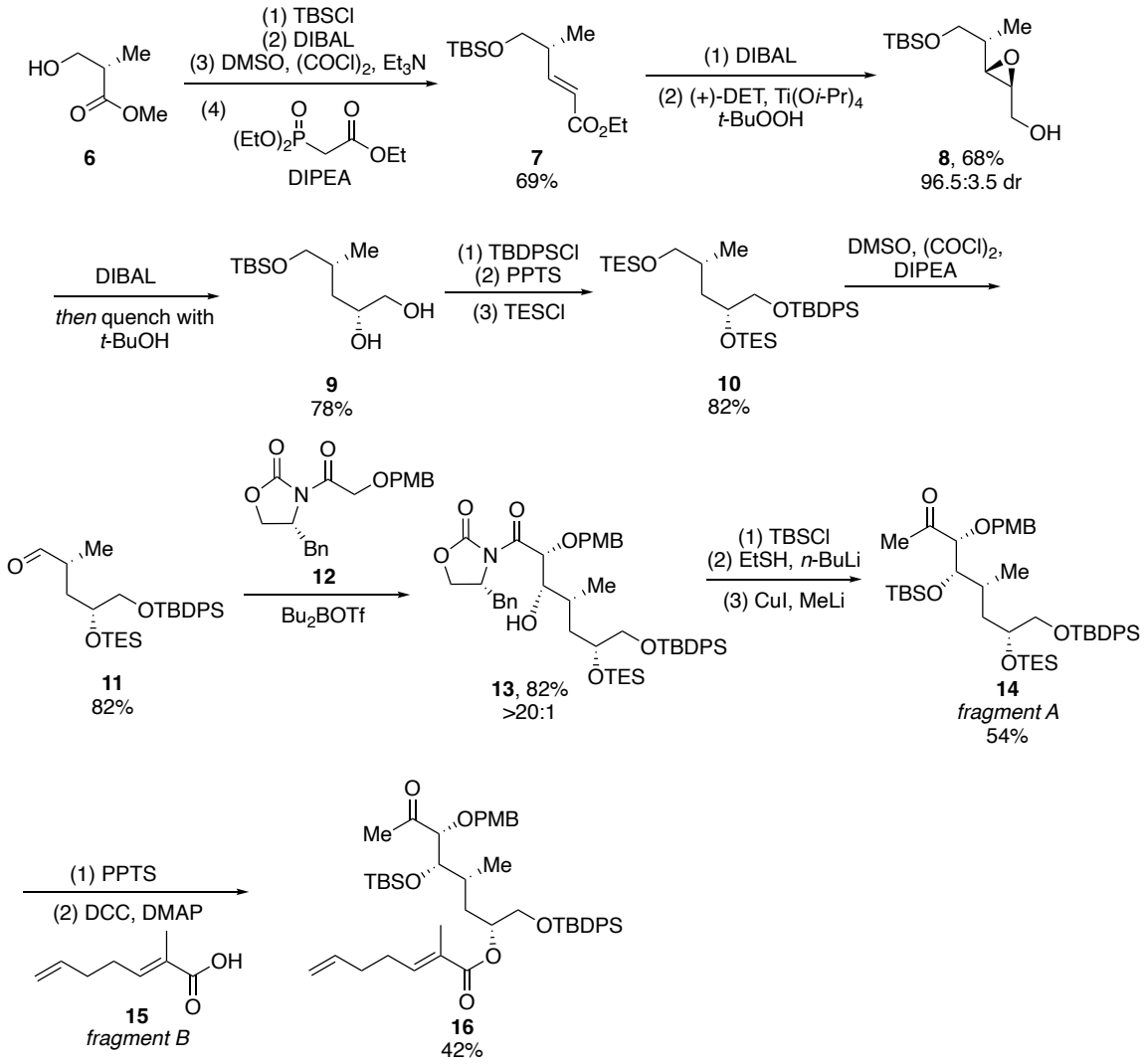
[12] Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719–2722.

[13] Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129.

[14] Anderson, R. J.; Henrick, C. A.; Rosenblum, L. D. *J. Am. Chem. Soc.* **1974**, *96*, 3654–3655.

Selective deprotection of TES in the presence of TBS- and TBDPS-protected alcohols was achieved with PPTS at low temperature. Subsequent esterification with readily available fragment B (**15**)[15] afforded **16** as the south-eastern fragment of **1**.

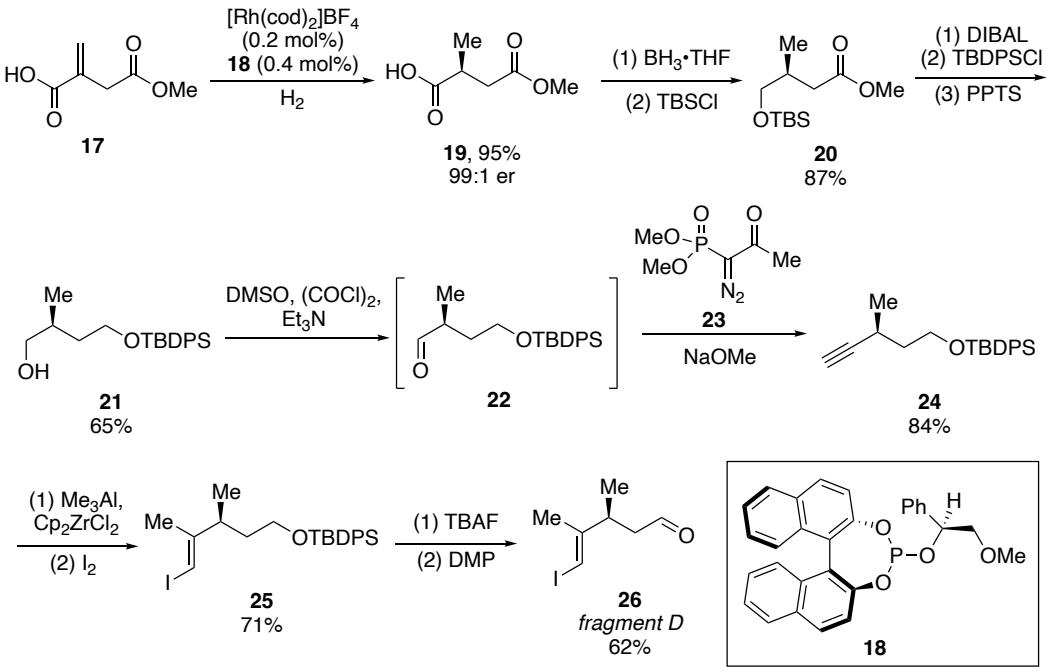
Scheme 4. Fürstner's Synthesis of the South-Eastern Fragment



[15] Savu, P. M.; Katzenellenbogen, J. A. *J. Org. Chem.* **1981**, *46*, 239–250.

Synthesis of fragment D is depicted in Scheme 5. Rh-catalyzed enantioselective hydrogenation of the itaconic acid monoester (**17**) afforded **19** in 95% yield and 99:1 er.[16] Oxidation state and protecting group management afforded aldehyde **22** over seven steps. Compound **22** was converted into terminal alkyne **24** through homologation with Ohira-Bestmann reagent (**23**).[17] A subsequent zirconium-induced carboalumination followed by quenching with I_2 installed the methyl group and iodide regioselectively.[18] Fragment D (**26**) was furnished through deprotection and oxidation of **25** in 62% yield.

Scheme 5. Fürstner's Synthesis of Fragment D



The authors started the synthesis of fragment C from the commercially available (*S*)-citronellal (Scheme 6). The carbonyl group was converted into a terminal alkyne with Ohira-Bestmann

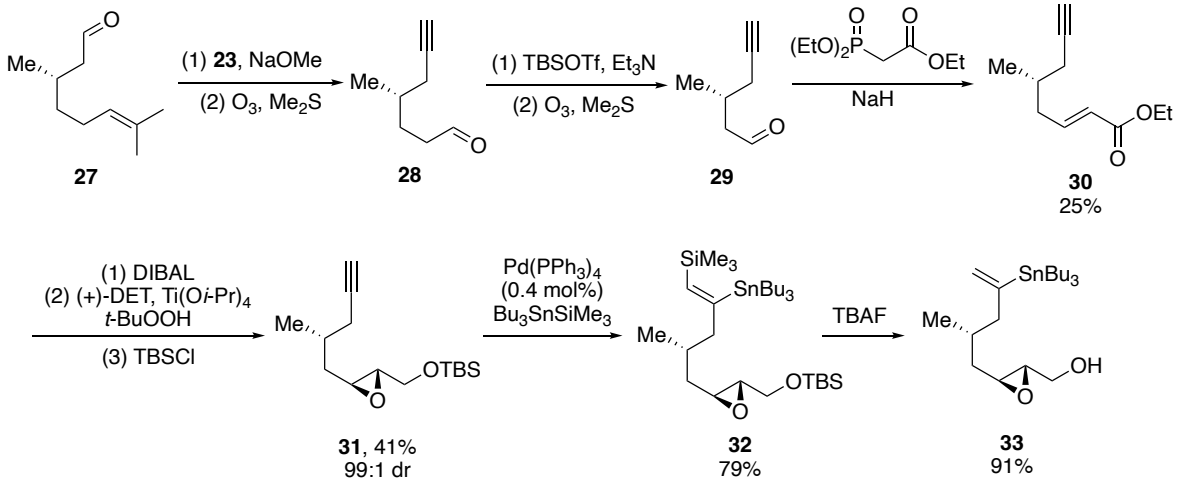
[16] Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889–3890.

[17] (a) Ohira, S. *Syn. Comm.* **1989**, *19*, 561–564; (b) Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521–522.

[18] Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem.* **1981**, *46*, 4093–4096.

reagent (**23**).[17] Ozonolysis of the trisubstituted olefin afforded aldehyde **28**, which was converted into **29** by ozonolysis of the corresponding silyl enol ether. A subsequent Horner-Wadsworth-Emmons reaction afforded **30** in 25% yield over five steps. Reduction of the ester **30** followed by Sharpless epoxidation[11] successfully installed the oxirane and afforded **31** in 41% yield and 99:1 dr. A Pd-catalyzed regioselective silylstannation of **31** afforded **32** in 79% yield.[19] Subsequent global desilylation with TBAF afforded fragment C (**33**) smoothly.

Scheme 6. Fürstner's Synthesis of Fragment C



Fragment D (**26**) was treated with lithium enolate derived from **16** to afford **34** in 70% yield. Compound **34** was isolated as a single diastereomer, and the high level of diastereoselectivity was ascribed to the strong 1,4-*anti*-induction by the OPMB substituent.[20] Protecting group management afforded **35** in 46% yield over three steps. A Pd-catalyzed Stille cross-coupling of the

[19] Chenard, B. L.; Van Zyl, C. M. *J. Org. Chem.* **1986**, *51*, 3561–3566.

[20] For selected reports on 1,4-*anti*-induction in aldol reactions, see: (a) Evans, D. A.; Carter, P. H.; Carreira, E. M.; Prunet, J. A.; Charette, A. B.; Lautens, M. *Angew. Chem., Int. Ed.***1998**, *37*, 2354–2359. (b) Evans, D. A.; Carter, P. H.; Carreira, E. M.; Charette, A. B.; Prunet, J. A.; Lautens, M. *J. Am. Chem. Soc.* **1999**, *121*, 7540–7552.

highly functionalized alkenyl iodide **35** with stannane **33** afforded the *cis*-diene **36** in 89% yield.[21] The epoxy alcohol **36** was then converted into vinyl oxirane **37** efficiently in two steps. **37** underwent ring-closing metathesis with Grubbs catalyst (second generation) under ambient temperature to afford **38** with high *E*-selectivity.[22] Finally, a global desilylation with TASF[23] furnished **1** in 55% yield.

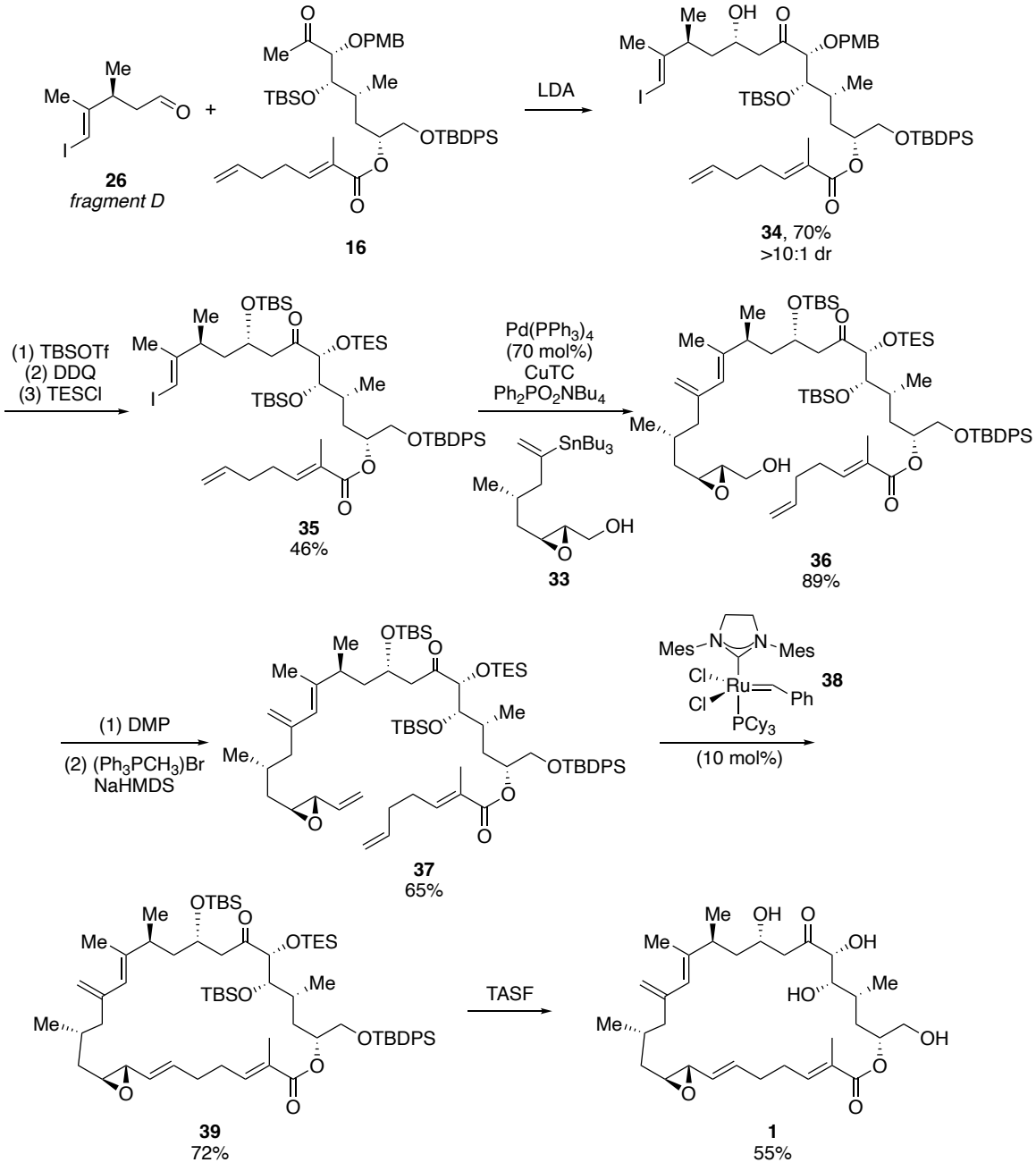
Following the success of synthesis of amphidinolide H, the Fürstner group applied the retro-synthetic disconnections (Scheme 3) to syntheses of other members of amphidinolide family with similar macrocyclic structure. They successfully synthesized amphidinolides G, B1, B4, and revised the structure of amphidinolide B2.[9]

[21] (a) Fürstner, A.; Nevado, C.; Waser, M.; Tremblay, M.; Chevrier, C.; Teplý, F.; Aïssa, C.; Moulin, E.; Müller, O. *J. Am. Chem. Soc.* **2007**, *129*, 9150–9161. (b) Fürstner, A.; Nevado, C.; Tremblay, M.; Chevrier, C.; Teplý, F.; Aïssa, C.; Waser, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5837–5842.

[22] For selected reports on metathesis reactions of vinyl epoxide: (a) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784. (b) Xiong, Z.; Corey, E. J. *J. Am. Chem. Soc.* **2000**, *122*, 4831–4832. (c) R. M. Garbaccio, S. J. Stachel, D. K. Baeschlin, S. J. Danishefsky, *J. Am. Chem. Soc.* **2001**, *123*, 10903–10908. (d) McDonald, F. E.; Wei, X. Concise, *Org. Lett.* **2002**, *4*, 593–595.

[23] Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 6436–6437.

Scheme 7. Fürstner's End Game towards the Synthesis of Amphidinolide H

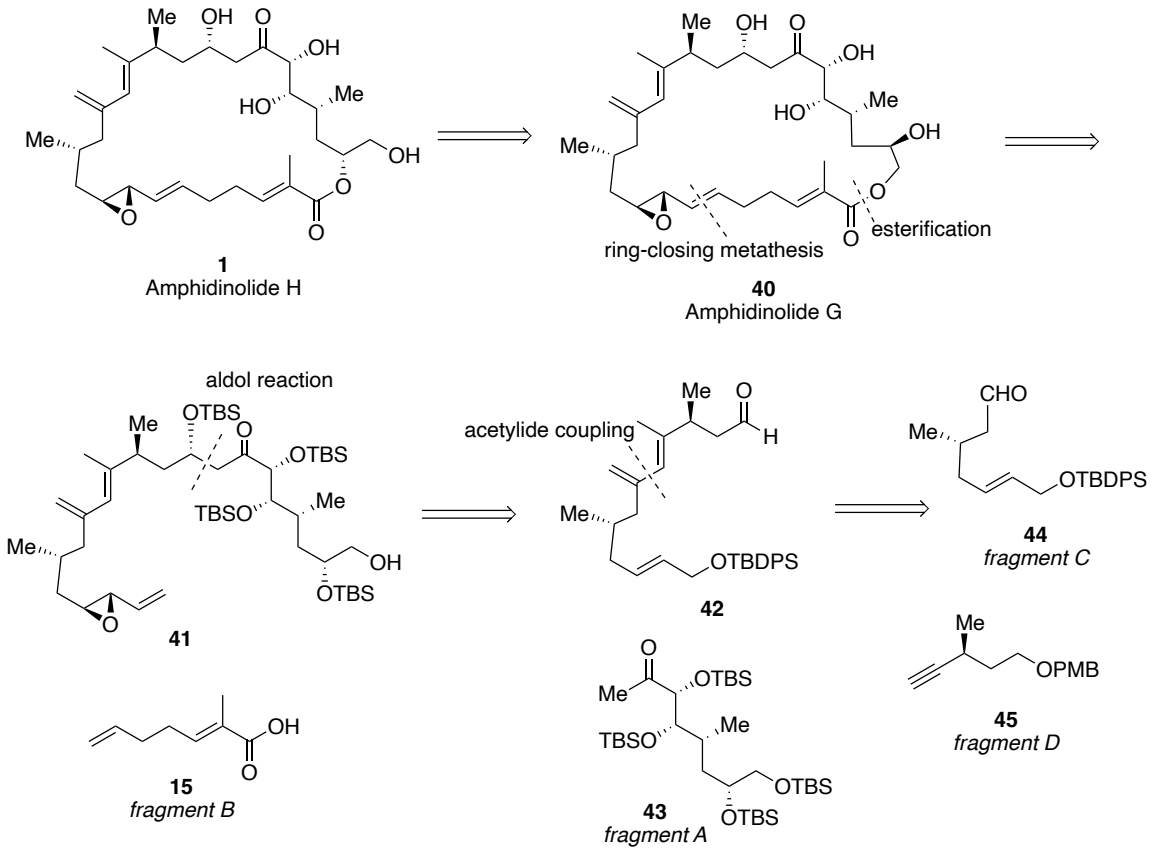


Total Synthesis of Amphidinolide H by Shigeru Nishiyama

In 2012, the Nishiyama group reported their synthesis of amphidinolide H.[10] The authors dissected the macrocycle into four fragments, similar to Fürstner's strategy. However, they

employed different reactions to assemble the fragments in a different order of assembly. The Nishiyama group started their assembly with the northwestern fragment (**42**), whereas the Fürstner group started theirs with the southeastern fragment (**16**). These four fragments would be combined by an acetylide coupling, an aldol reaction, an esterification, and a ring-closing metathesis (Scheme 8).

Scheme 8. Nishiyama's Retrosynthetic Analysis of Amphidinolide H in 2012



The Nishiyama group succeeded in synthesizing the northwestern fragment (**42**) and fragment A (**14**) in a previous report in 2011.[24] Synthesis of fragment D (**45**) started from the previously described alcohol **46** (Scheme 9).[25] Sharpless enantioselective epoxidation of **46** proceeded

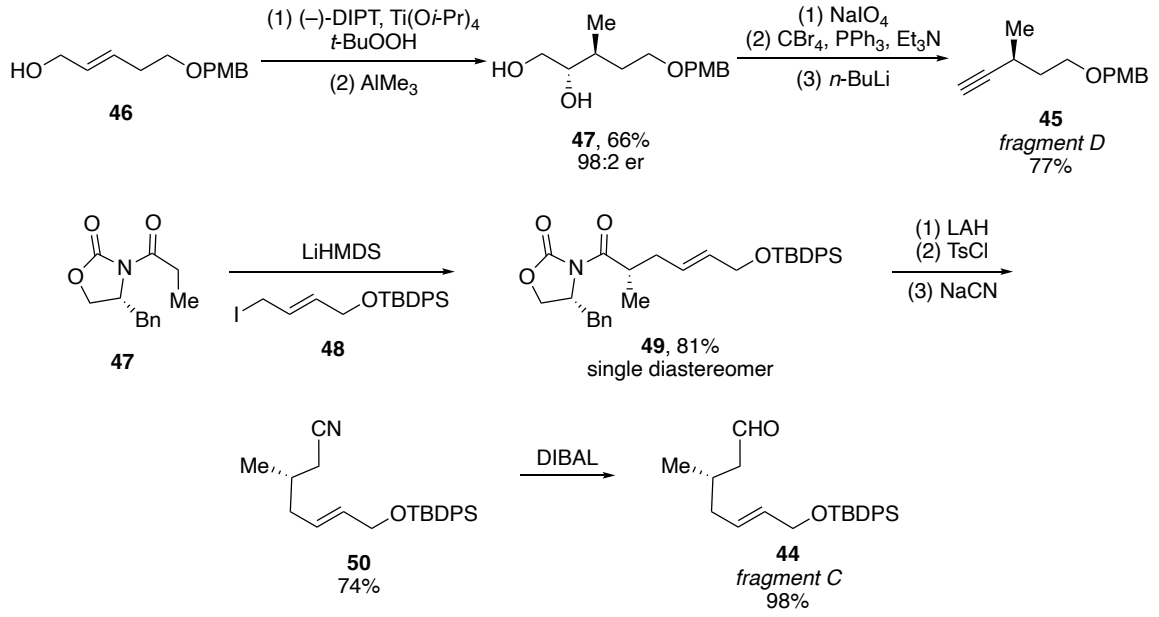
[24] Hara, A.; Morimoto, R.; Ishikawa, Y.; Nishiyama, S. *Org. Lett.* **2011**, *13*, 4036–4039.

[25] Oka, T.; Murai, A. *Tetrahedron* **1998**, *54*, 1–20.

smoothly to afford the corresponding epoxide. Treatment with $AlMe_3$ led to a directed regioselective addition of methyl group to open the epoxide, delivering diol **47** in 66% yield over two steps and 98:2 er. The 1,2-diol was then cleaved with $NaIO_4$ to generate the corresponding aldehyde, which was then converted into the terminal alkyne moiety of fragment D (**45**) with Corey-Fuchs reaction.[26]

Synthesis of the fragment C started with Evans alkylation of oxazolidinone **47** with iodide **48**. This reaction delivered **49** in 81% yield as a single diastereomer. Reductive removal of the chiral auxiliary with LAH was followed by the tosylation of the resulting alcohol and cyanide substitution of the tosylate. Nitrile **50** was afforded in 74% yield over three steps. Upon reduction of **50** by DIBAL, fragment C (**44**) was obtained in 98% yield.

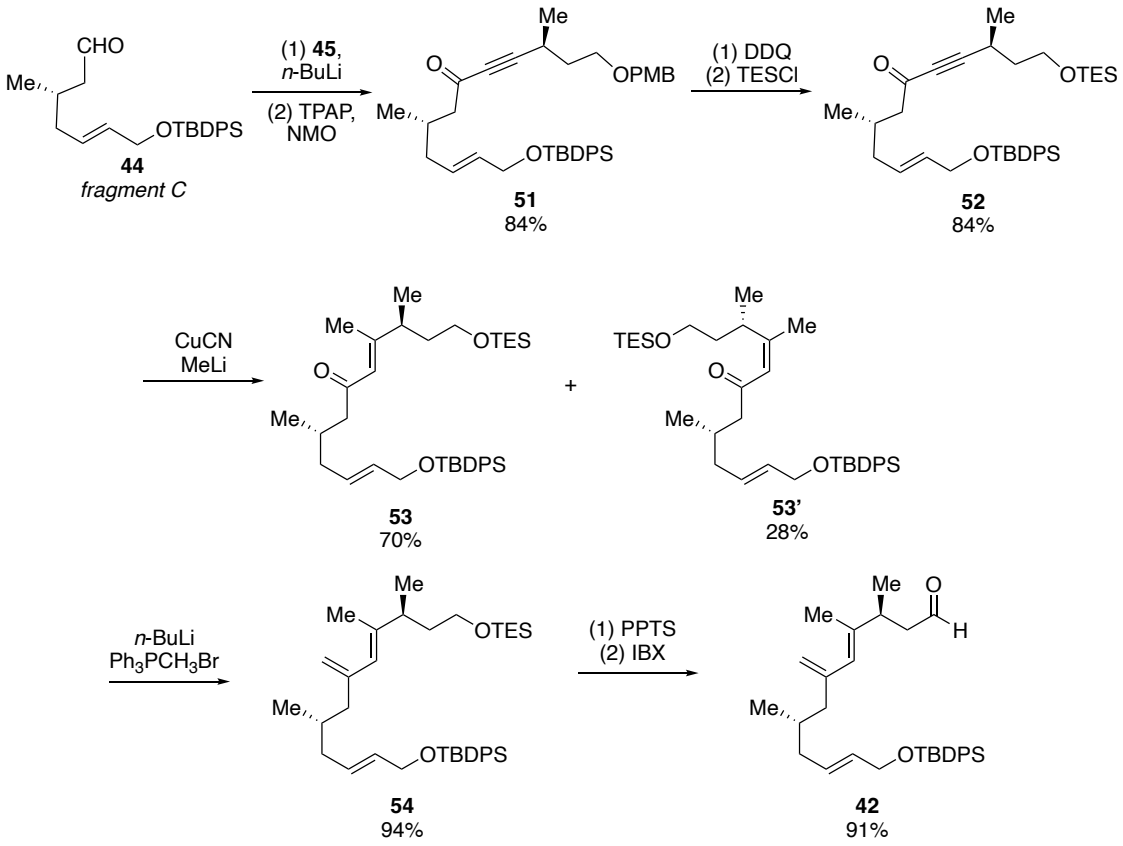
Scheme 9. Nishiyama's Synthesis of Fragments C and D



[26] Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769–3772.

The coupling reaction between the aldehyde fragment C (**44**) and the alkynyl fragment D (**45**) proceeded smoothly. *n*-BuLi was used to generate the key lithium acetylide from terminal alkyne **45** (Scheme 10). Ley-Griffith oxidation of the propargylic alcohol furnished the α,β-unsaturated ketone **51** in 84% yield over two steps. Protecting group management afforded **52** efficiently. Treatment of the α,β-unsaturated ketone **52** with the Gilman reagent furnished conjugate addition products, generating the desired (*E*)-enone **53** in 70% yield and the undesired (*Z*)-enone **53'** in 28% yield. Although the *E*/*Z* selectivity was moderate (2.5:1), the isomers **53** and **53'** could be easily separated with silica gel chromatography. The enone **53** was then converted into *cis*-diene **54** with Wittig reaction. Selective removal of the TES group was accomplished by subjecting **54** to PPTS at 0 ºC. Upon IBX oxidation, aldehyde **42** was afforded in 91% yield over two steps.

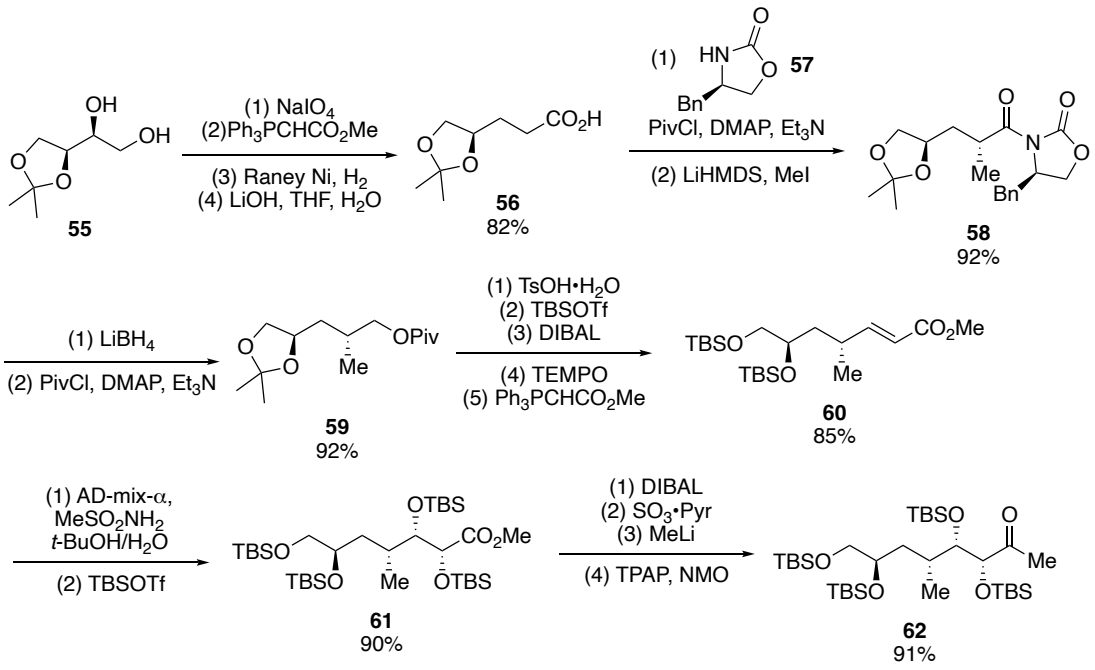
Scheme 10. Nishiyama's Synthesis of the Northwestern Fragment



Synthesis of fragment A began with diol **55**.[27] Cleavage of the diol moiety in **55** with $NaIO_4$ followed by a Wittig reaction introduced the acrylate moiety. Subsequent hydrogenation by Raney Ni and ester hydrolysis afforded carboxylic acid **56** in 82% yield over four steps (Scheme 11). Evans alkylation enabled stereoselective methylation, affording **58** in 92% yield. Reductive removal of the chiral auxiliary from **58** yielded the corresponding alcohol, which then underwent pivolate protection to afford **59**. Protecting group management of the diol, followed by removal of the pivolate group furnished the primary alcohol moiety. TEMPO oxidation of the alcohol, followed by a Wittig reaction furnished the acrylate ester **60**. Sharpless asymmetric dihydroxylation of the acrylate ester **60** afforded a single diastereomer of the corresponding diol, which underwent TBS protection to afford **61**. Then, DIBAL reduction of the ester moiety in **61**, followed by Parikh-Doering oxidation, addition of MeLi, and Ley-Griffith oxidation furnished the desired methyl ketone moiety in fragment A (**62**).

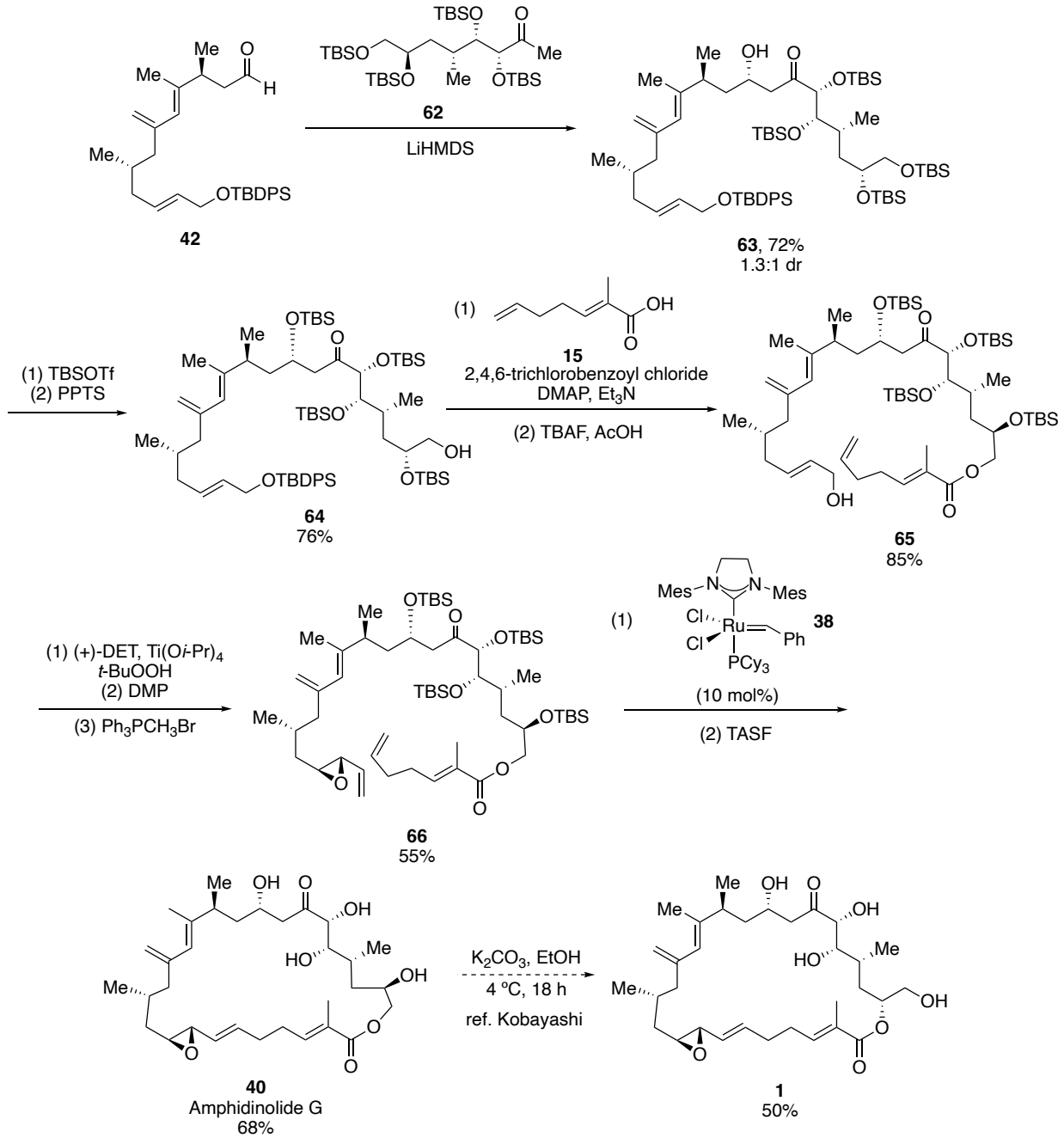
[27] Abushanab, E.; Raymond, P. P. *J. Org. Chem.* **1988**, *53*, 2598–2602.

Scheme 11. Nishiyama's Synthesis of Fragment A



Aldol reaction between northwestern fragment (**42**) and fragment A (**62**) afforded **63** in 72% yield and 1.3:1 dr (Scheme 12). Through protecting group management of **63**, primary alcohol **64** was obtained in 76% yield. Yamaguchi esterification with fragment B (**15**) proceeded smoothly, affording the corresponding ester. Treatment with TBAF selectively deprotected the TBDPS group on the primary alcohol, furnishing **65**. Subsequent Sharpless epoxidation, DMP oxidation, and Wittig reaction furnished the vinyl epoxide **66**. Finally, ring-closing metathesis was achieved through the use of Grubbs catalyst (second generation). Global desilylation with TASF furnished amphidinolide G (**40**) in 68% yield over two steps. Although the authors did not synthesize amphidinolide H, they referred to a report by Kobayashi and co-workers[4] stating that treatment with base would induce isomerization of **40** to afford amphidinolide H (**1**).

Scheme 12. Nishiyama's End Game towards the Synthesis of Amphidinolide H

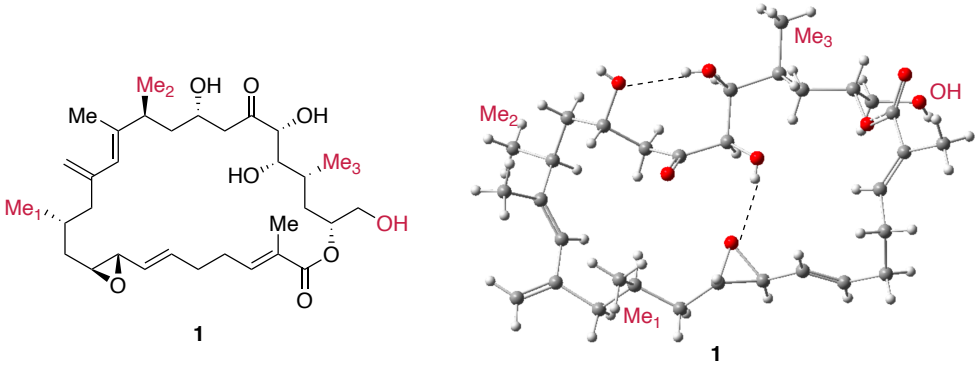


Analog Design for Amphidinolide H

Despite significant efforts directed towards the total synthesis of amphidinolide, its syntheses remain challenging due to the complex macrocyclic structure, which features nine stereogenic

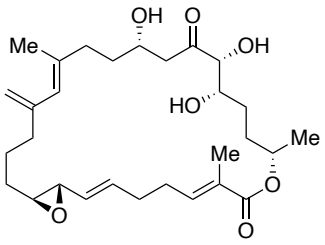
centers. In an attempt to simplify the synthesis process while retaining the bioactivity of amphidinolide H, we contemplated the removal of certain functional groups from the molecule. Specifically, we considered eliminating three stereogenic methyl groups and one hydroxyl group (highlighted in Scheme 13) that were determined to make no significant contribution to the key structural features of the molecule, as analyzed by Kobayashi and colleagues.[4]

Scheme 13. Analysis of Amphidinolide H Structure

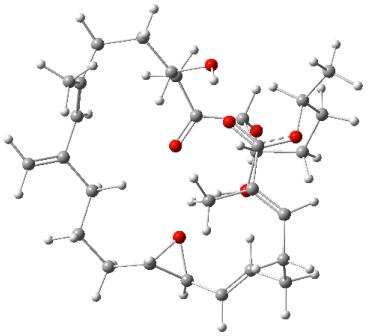


We performed a Monte-Carlo conformational search (MCMM) on the simplified analog of amphidinolide H, compound **67**. As depicted in Scheme 14, the two lowest energy conformers (**67-1**, **67-2**) adopted a "folded" conformation, whereas the next two lowest energy conformers (**67-3**, **67-4**) exhibited a "rectangular" conformation, akin to the crystal structure of **1**. Upon analysis of these four low-energy conformers by DFT calculations, it was found that the "folded" conformers possessed higher energies compared to the "rectangular" ones.

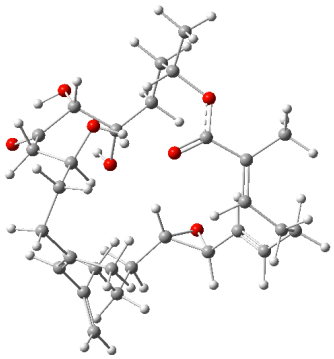
Scheme 14. Low Energy Conformers of Amphidinolide H Analog[a]



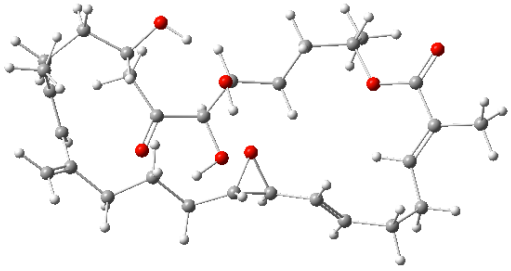
67



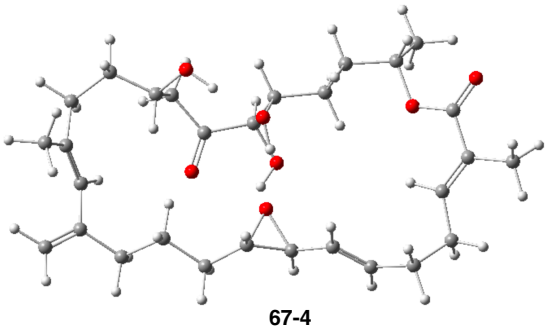
67-1
"folded"
MCMM: 0 kcal/mol
DFT: 6.13 kcal/mol



67-2
"folded"
MCMM: 0.52 kcal/mol
DFT: 8.40 kcal/mol



67-3
"rectangular"
MCMM: 0.65 kcal/mol
DFT: 0.56 kcal/mol



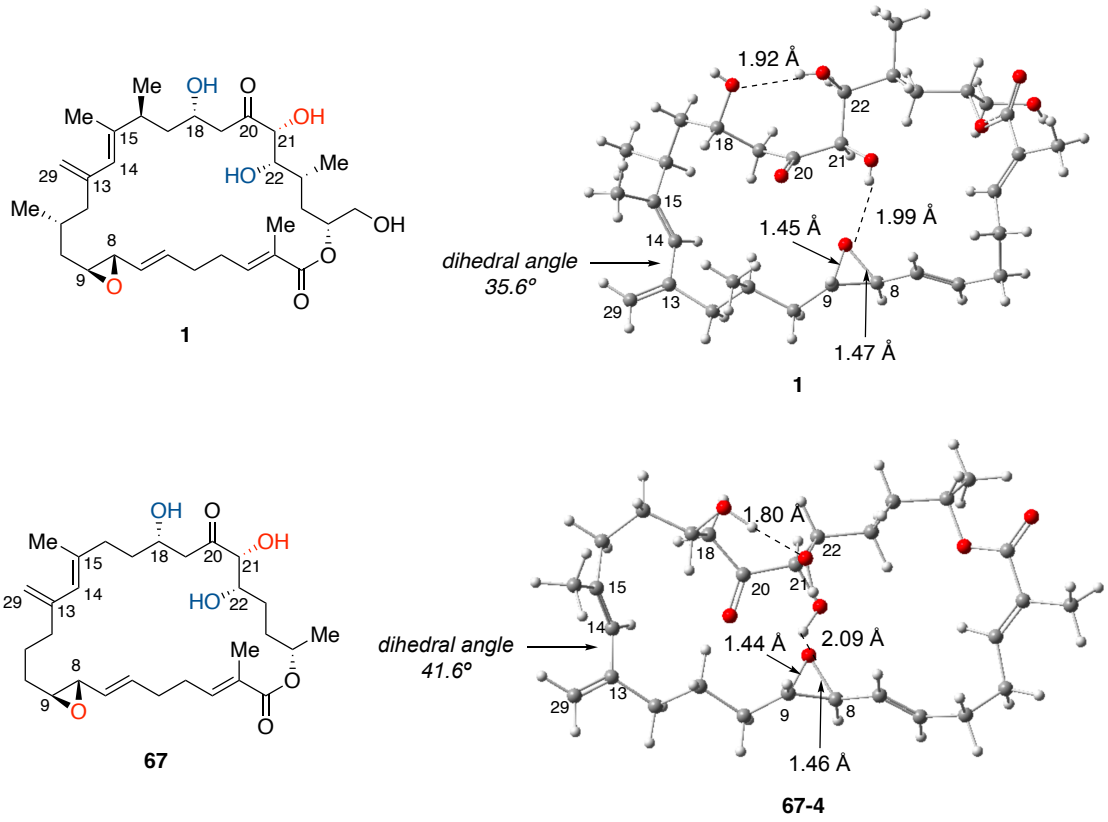
67-4
"rectangular"
MCMM: 0.79 kcal/mol
DFT: 0 kcal/mol

[a]Conformation search was performed with Monte Carlo Multiple Minimum (MCMM), the Mixed Torsional/Low-Mode sampling (MTLMOD) search method was used. Ground state geometries were optimized with DFT methodology. The B3LYP(GD3BJ) functional and 6-31G* basis sets were employed. Tetrahydrofuran solvation was modeled with the PCM model.

We then examined conformer **67-4**, which was determined to be the lowest energy conformer based on DFT calculations. **67-4** exhibited key structural characteristics reminiscent of the crystal structure of **1**: (1) It is centrally bridged by an intramolecular hydrogen bond (2.09 Å) between OH (on C21) and epoxide oxygen. (2) The bond length of C8–O bond (1.46 Å) within the epoxide is

longer than that of C9–O bond (1.44 Å). (3) An intramolecular hydrogen bond (1.80 Å) is formed between the hydroxyl group (on C22) and the oxygen atom (on C18) (4) The *S-cis* diene at C15–C14–C13–C29 is twisted, exhibiting a substantial torsion angle of 41.6º (Scheme 15).

Scheme 15. Comparison between Analog 67 and Amphidinolide H[a]



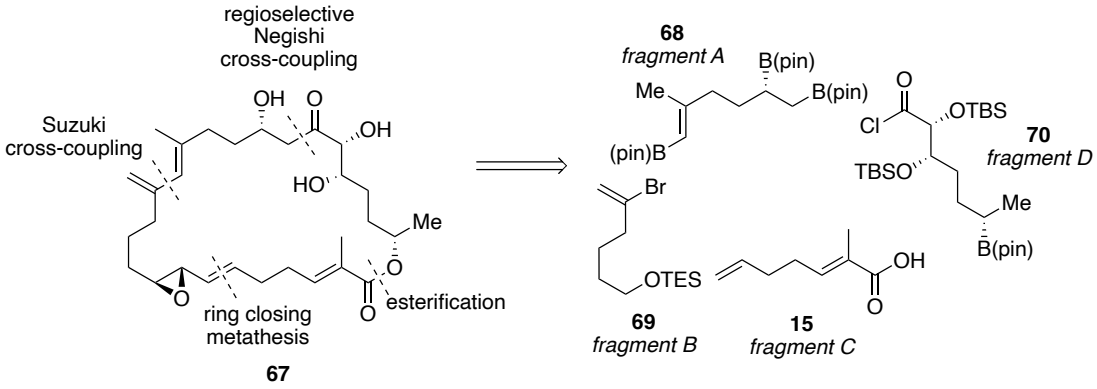
We regarded analog **67** as having a molecular shape similar to that of amphidinolide H. Additionally, Kobayashi and co-workers suggested that the elongation of the C8–O bond compared to the C9–O bond might contribute to the high bioactivity of amphidinolide H. We speculated that the similar elongation of the C8–O bond in **67** indicates potential high bioactivity.

Studies Towards the Synthesis of the Amphidinolide H Analog

Development of the Retrosynthesis

We envisioned a disconnection similar to previous syntheses[8–10] and dissected the macrocycle into four fragments (**68**–**70**) (Scheme 16). We considered employing alkylboronic esters as not only "masked" hydroxyl groups but also functionalization handles for regioselective and stereospecific C–C bond formation. The northwestern fragment would be synthesized first through a Suzuki cross-coupling between fragments A (**68**) and B (**69**). The primary boronic ester of the northwestern fragment would be functionalized with fragment D (**70**) through a regioselective Neigishi cross-coupling. Then, fragment C (**15**) would be installed by esterification. Finally, a ring-closing metathesis would close the macrocycle.

Scheme 16. Retrosynthetic Analysis of Amphidinolide H Analog



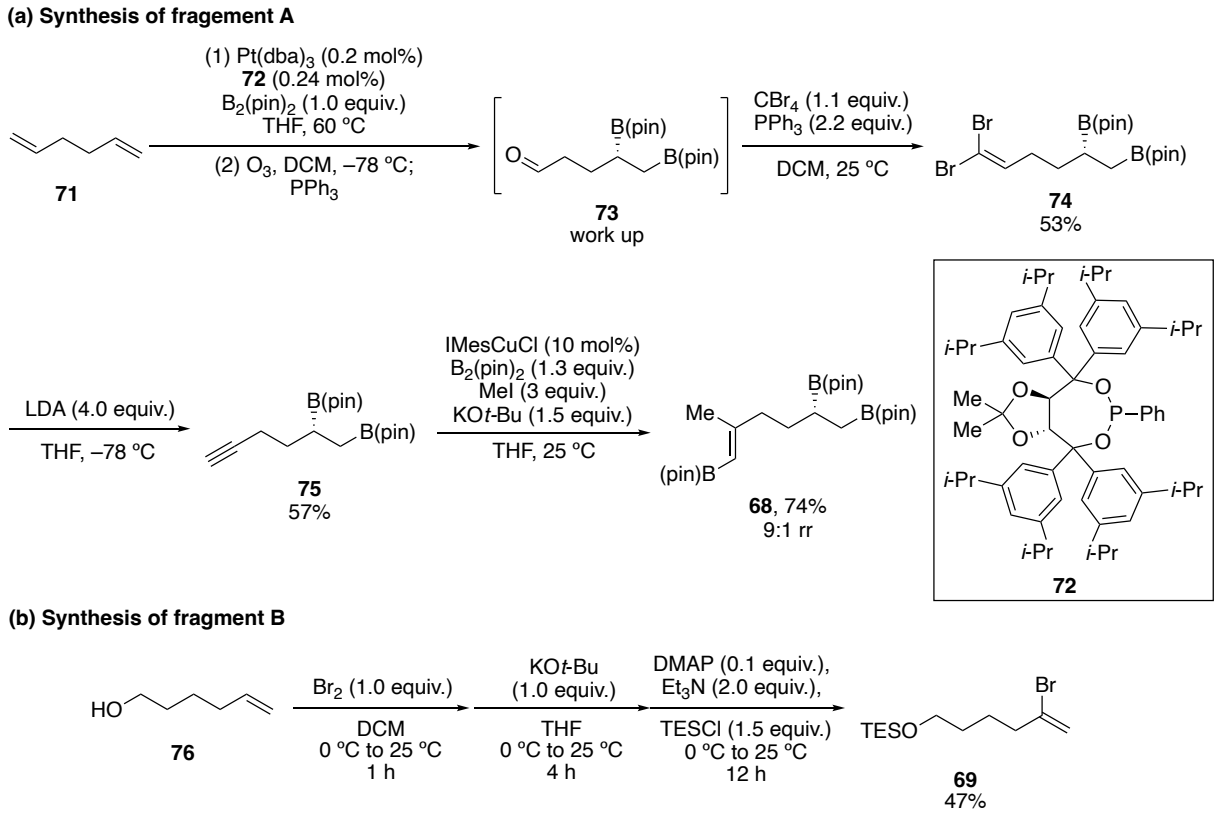
Progress towards the synthesis of Amphidinolide Analog

The synthesis of fragment A started with 1,5-hexadiene (**71**) (Scheme 17a). An enantioselective diboration[28] with low catalyst loading, followed by ozonolysis, successfully furnished **73**. It is

[28] Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222–11231.

noteworthy that ozonolysis proceeded smoothly in the presence of alkylboronic esters without decomposition or oxidation of boronic esters. A Corey-Fuchs reaction with LDA[29] converted the aldehyde moiety of **73** to terminal alkyne of **75**. Finally, an NHC–Cu-catalyzed regioselective methylborylation[30] of the terminal alkyne afforded fragment A (**68**) in 74% yield and 9:1 rr. Fragment B (**69**) was synthesized from 5-hexenol (**76**) in three consecutive steps (Scheme 17b).[31]

Scheme 17. Syntheses of Fragments A and B[a]



[a]Yields corresponded to isolated and purified products (±5%). Regioisomeric ratios (rr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

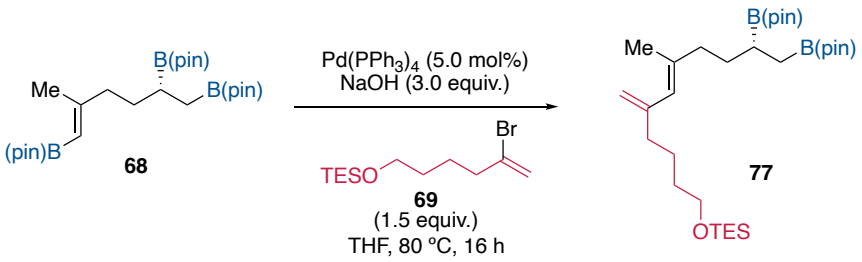
[29] Gibtner, T.; Hampel, F.; Gisselbrecht, J. -P.; Hirsch, A. *Chem. Eur. J.*, **2002**, *68*, 408–432.

[30] Mun, B.; Kim, S.; Yoon, H.; Kim, K. H.; Lee, Y. *J. Org. Chem.* **2017**, *82*, 6349–6357.

[31] Brandt, D.; Dittoo, A.; Bellosta, V.; Cossy, J. *Org. Lett.* **2015**, *17*, 816–819.

We conducted a survey of Suzuki cross-coupling conditions to assemble fragments A and B (Table 1). Despite reports of efficient Pd-catalyzed regioselective coupling of 1,2-bis(boronic esters),[32] we only observed coupling with the alkenyl boronic ester, and no coupling of the primary boronic ester. Although this reaction afforded 76% yield on small scale (entry 4), it afforded only 45% yield on gram-scale. The diminished yield indicates the need for further investigation and optimization to enhance the efficiency of this Suzuki cross-coupling reaction for large-scale applications.

Table 1. Optimization of Pd-Catalyzed Suzuki Cross-Coupling of Fragments A and B[a]



entry	changes made to condition	conv. (%)
1	none	69
2	1.0 equiv. of **69** was added	53
3	10 mol% $Pd(PPh_3)_4$, Na_2CO_3 was used instead of NaOH	40
4	2.0 equiv. of **69** was added	76
5	3.0 equiv. of **69** was added	63
6	10 mol% $Pd(PPh_3)_4$ was added	75
7	toluene was used instead of THF	47

[a]Reactions were carried out under argon atmosphere. Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

The synthesis of fragment D (**70**) commenced with an Evans aldol reaction between **78** and **79**, affording **80** in 70% yield and 17:1 dr (Scheme 18a).[33] Enantioselective diboration of the terminal

[32] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386–390.

[33] Chatterjee, S.; Guchhait, S.; Goswami, R. K. *J. Org. Chem.* **2014**, *79*, 7689–7695.

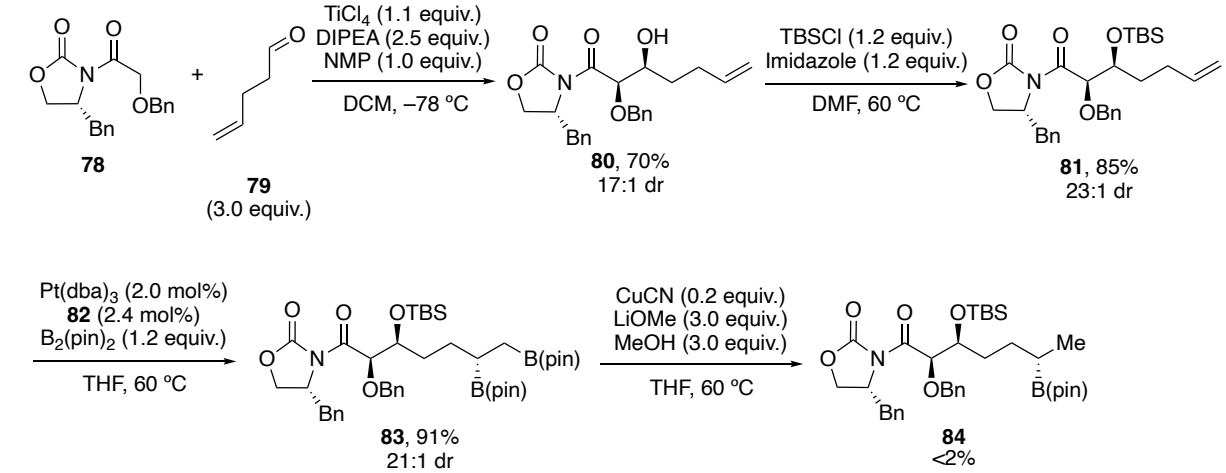
alkene **81** proceeded smoothly to afford **83** in 91% yield and 21:1 dr. However, attempts at Cu-catalyzed regioselective protonation of the 1,2-bis(boronic ester) of **83** led to substrate decomposition.[34] It is conceivable that the acidic proton of **83** intramolecularly protonated the organocopper species. To address this issue, we planned to conduct the diboration/protonation sequence before Evans aldol reaction (Scheme 18b). This sequence furnished the enantiomerically enriched secondary boronic ester **85** in 78% yield. Subsequent ozonolysis of the terminal alkene afforded aldehyde **86**.

We envisioned that an Evans aldol reaction between **78** and **86** would furnish **87**.[33] Conversion of the auxiliary to acyl chloride (**70**) or thiol ester (**88**) would furnish fragment D or its equivalent.

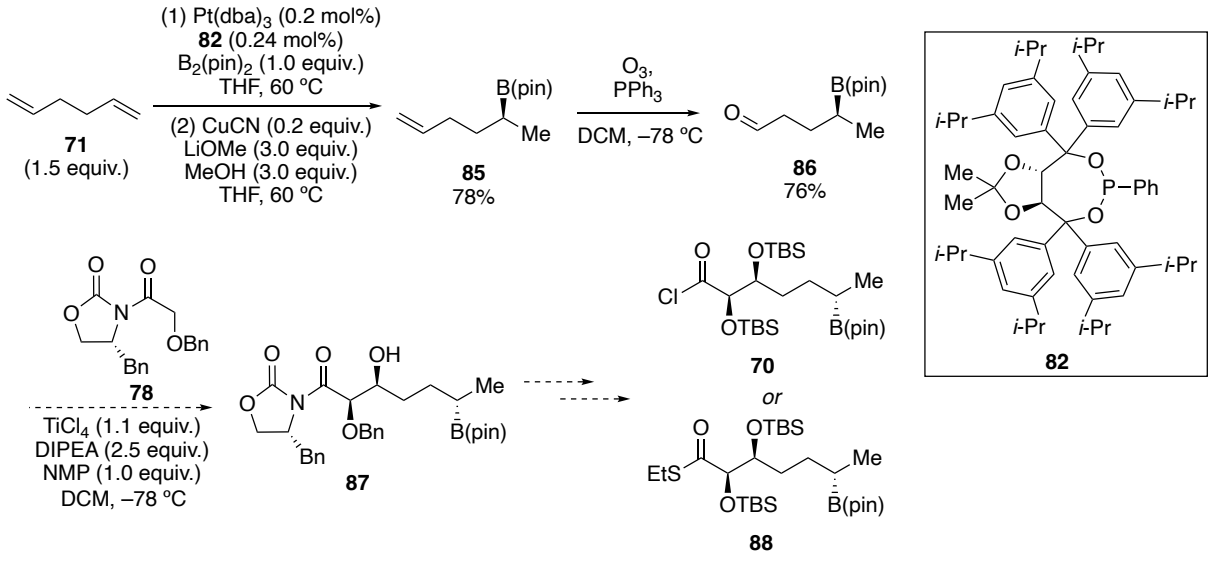
[34] Xu, N.; Kong, Z.; Wang, J. Z.; Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 17815–17823.

Scheme 18. Progress towards Synthesis of Fragments D[a]

(a) Attempt in synthesizing fragment D



(b) Revised route to fragment D



[a]Yields corresponded to isolated and purified products (±5%). Diastereomeric ratios (dr) were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%). Conversions to the desired product were determined by analysis of ^{1}H NMR spectra of unpurified mixtures (±2%).

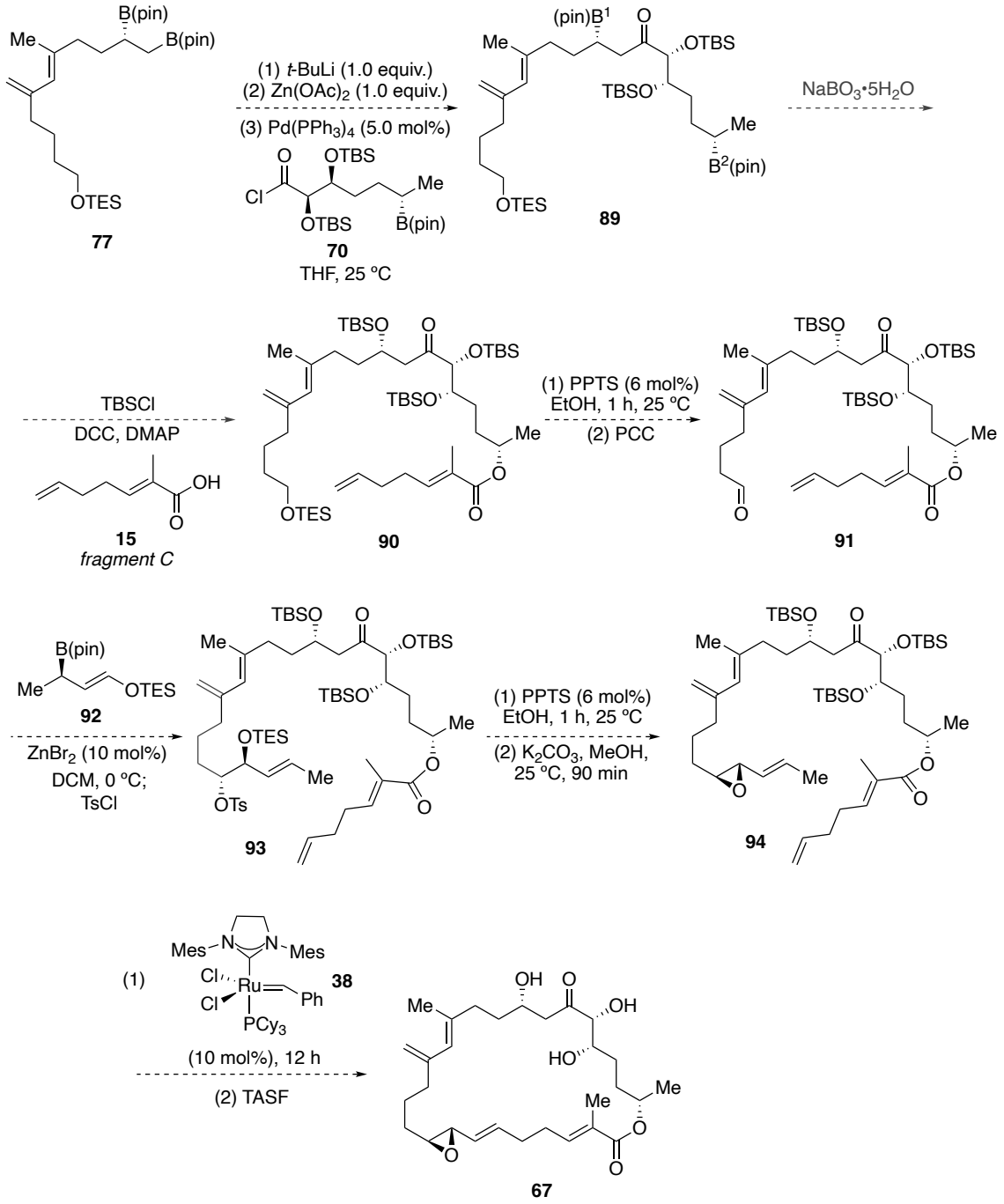
Future Directions

We plan to assemble northwestern fragment **77** and fragment D (**70**) with a *t*-BuLi activated regioselective Negishi cross-coupling[35] or Fukuyama coupling (Scheme 19). After oxidizing the two alkylboronic esters of **89**, our challenge will be to develop a regioselective protocol to protect OH^1 and to esterify OH^2 with fragment C (**15**). Selective removal of the TES group,[8] followed by oxidation, would yield the aldehyde moiety in **91**. A diastereoselective addition of enantiomerically enriched allyl boronic ester **92** to aldehyde **91** would afford the *trans*-diol moiety of **93**.[36] We anticipate obtaining the epoxide moiety of **94** through removal of the TES group followed by intramolecular nucleophilic substitution of the OTs group. Finally, akin to previous syntheses of amphidinolide H, we intend to employ ring-closing metathesis with Grubbs catalyst (2nd generation) to afford **67**.

[35] Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 9976–9981.

[36] Yamamoto, E.; Takenouchi, Y.; Ozaki, T.; Miya, T.; Ito, H. *J. Am. Chem. Soc.* **2014**, *136*, 16515–16521.

Scheme 19. Future Direction towards the Synthesis of Amphidinolide H Analog



Conclusions

In conclusion, we have devised a simplified analog of amphidinolide H that shows potential to preserve the natural product's overall structure and bioactivity. We envisioned a modular synthetic

route towards the intended analog. Furthermore, the extensive installation and functionalization of organoboronate compounds in the synthesis route presented an opportunity to explore their utility and robustness in chemical transformations.

Experimental Section

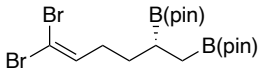
General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (126 MHz), Varian Gemini-600 (151 MHz) or a Varian Inova-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed with 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 aluminum-backed plates from Silicycle. Visualization was performed with ultraviolet light (254 nm), or potassium permanganate stain

($KMnO_4$, sodium carbonate, and water), or CAM stain (ammonium molybdate tetrahydrate, cerium ammonium sulfate dehydrate, sulfuric acid).

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified by Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. All other reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without purification.

Experimental Procedures and Characterization of Products

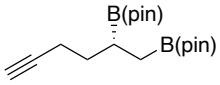


(*R*)-2,2'-(6,6-Dibromohex-5-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**74**). The title compound was prepared according to a literature procedure.[28] To an oven-dried round-bottom flask equipped with a magnetic stir bar in air was added $Pt(dba)_3$ (35.9 mg, 0.04 mmol), **72** (39.9 mg, 0.05 mmol), and $B_2(pin)_2$ (5.1 g, 20.0 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (20 mL, 1.0 M) was added by syringe, and the mixture was heated to 80 °C and was allowed to stir for 30 min. The flask was then allowed to cool to room temperature and was charged with 1,5-hexadiene (2.5 g, 30.0 mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC overnight.

The solvents were removed under reduced pressure. The yellow oil residue was dissolved in DCM (40 mL) and was treated with ozone at –78 ºC and was allowed to stir until completion (monitered with TLC). The mixture was flushed with air and argon and triphenylphopshine (6.8 g, 26.0 mmol) was added. The resulting solution was allowed to warm slowly to room temperature and allowed to stir for 2 h. DCM was removed under reduced prssure, then the pale-yellow mixture

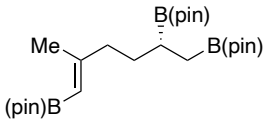
was diluted with hexanes and Et_2O. The mixture was then passed through a celiete plug. Huge amount of solid (PPh_3O) was filtered off. The solvents were removed under reduced prssure, the pale-yellow oil residue was used directly in the next step without purification.

PPh_3 (11.5 g, 44.0 mmol) was added at 0 ºC to a solution of CBr_4 (7.3 g, 22.0 mmol) in anhydrous DCM under N_2 atmosphere (20 mL). The mixture was allowed to stir for 10 min. At the same temperature, the residue from the previous step, dissolved in anhydrous DCM (20 mL), was dropped slowly into the stirring mixture at 0 ºC. The mixture was allowed to warm to room temperature and to stir overnight. DCM was removed under reduced prssure, then the mixture was diluted with hexanes and Et_2O. The mixture was then passed through a celiete plug. Huge amount of solid (PPh_3O) was filtered off. The solvents were removed under reduced prssure, the orange oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as yellow oil (5.26 g, 10.6 mmol, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.40 (t, J = 7.2 Hz, 1H), 2.15 – 2.06 (m, 2H), 1.63 – 1.53 (m, 1H), 1.49 – 1.38 (m, 1H), 1.23 (two singlets overlap, 24H), 1.18 – 1.09 (m, 1H), 0.89 (dd, J = 15.9, 9.4 Hz, 1H), 0.81 (dd, J = 15.9, 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 88.1, 83.0, 82.9, 32.4, 31.6, 24.89, 24.87, 24.79, 24.76.; IR: ν_{max} 2975 (m), 2924 (w), 1454 (w), 1369 (s), 1314 (s), 1270 (w), 1214 (w), 1142 (s), 967 (w), 846 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{33}B_2Br_2O_4$ $[M+H]^+$: calculated: 495.0906, found: 495.0913.; $[\alpha]_D^{20}$: –1.4 (c = 1.0, $CHCl_3$, l = 50 mm).



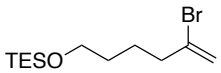
(*R*)-2,2'-(Hex-5-yne-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**75**). *n*-BuLi (2.7 M in hexanes, 42.4 mmol) was added to a solution of diisopropylamine (4.7 g, 46.6 mmol) in anhydrous THF (40 mL) at 0 ºC in an oven-dried three-necked flask under N_2 atmosphere (100 mL). The mixture was allowed to stir for 1 h, the resulting LDA solution was slowly added to a THF solution (10 mL) of (*R*)-2,2'-(6,6-dibromohex-5-ene-

1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**74**) (5.2 g, 10.6 mmol) at –78 ºC under N_2 atmosphere. The solution was allowed to stir at –78 ºC for 3 h. The reaction was quenched by the careful addition of an aqueous solution of HCl (10 %, 10 mL). The mixture was washed with Et_2O, and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the title compound as colorless oil (2.0 g, 6.0 mmol, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 – 2.15 (m, 2H), 1.91 (t, *J* = 2.6 Hz, 1H), 1.79 – 1.68 (m, 1H), 1.63 – 1.50 (m, 1H), 1.22 (s, 24H overlap with m, 1H), 0.90 – 0.78 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 85.1, 82.95, 82.91, 67.9, 32.5, 24.9, 24.83, 24.79, 24.7, 17.7.; IR: ν_{max} 3289 (w), 2975 (m), 2926 (w), 1369 (s), 1313 (s), 1214 (w), 1141 (s), 1107 (w), 967 (m), 845 (w), 670 (w), 628 (w) cm^{-1}.; HRMS (DART) for $C_{18}H_{33}B_2O_4$ $[M+H]^+$: calculated: 335.2560, found: 335.2574.; $[\alpha]_D^{20}$: –2.0 (c = 1.0, $CHCl_3$, *l* = 50 mm).



(*R*,*E*)-2,2',2''-(5-Methylhex-5-ene-1,2,6-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**68**). 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride (205.1 mg, 0.6 mmol) , CuCl (59.6 mg, 0.6 mmol) and KO*t*-Bu (1.35 g, 12.0 mmol) were added to an oven-dried round bottom flask equipped with a stirrer bar under argon atmosphere. Anhydrous THF (5 mL) was added, the mixture was allowed to stir at 25 ºC for 15 min. A solution of $B_2(pin)_2$ (1.99 g, 7.82 mmol) dissolved in THF (5 mL) was added at 0 ºC, the solution was allowed to stir at the same temperature for 10 min. A solution of (*R*)-2,2'-(hex-5-yne-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**75**) (2.0 g, 6.0 mmol) in THF (5 mL) and methyl iodide (2.6 g, 18.0 mmol) was added to the reation mixture at –78 ºC, the mixture was then allowed to warm to 25 ºC and allowed to stir for 3 h. The reaction was quenched by addition of H_2O (10 mL). The mixture was washed with Et_2O, and the combined organic layers were dried

over Na_2SO_4 and concentrated under reduced pressure. The yellow oil was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford colorless gel (2.13 g, 4.4 mmol, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37 (t, *J* = 7.2 Hz, 0.1H, minor regioisomer), 5.08 (s, 1H), 2.08 (t, *J* = 8.1 Hz, 2H), 1.94 (s, 3H), 1.64 – 1.54 (m, 1H), 1.53 – 1.42 (m, 1H), 1.23 (s, 12H), 1.20 (s, 24H), 1.13 – 1.04 (m, 2H), 0.85 (dd, *J* = 15.8, 9.7 Hz, 1H), 0.77 (dd, *J* = 15.8, 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 82.80, 82.77, 82.4, 41.6, 32.1, 24.9, 24.8, 24.75, 24.71, 21.2.; IR: ν_{max} 2975 (m), 2927 (w), 1636 (w), 1368 (s), 1312 (s), 1263 (m), 1214 (w), 1141 (s), 968 (m), 848 (w) cm^{-1}.; HRMS (DART) for $C_{25}H_{48}B_3O_6$ $[M+H]^+$: calculated: 477.3725, found: 477.3729.; $[\alpha]_D^{20}$: – 0.4 (c = 1.0, $CHCl_3$, *l* = 50 mm).

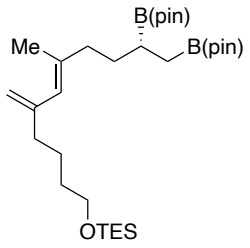


((5-Bromohex-5-en-1-yl)oxy)trimethylsilane (**69**). A solution of Br_2 (6.4 g, 40.0 mmol) in DCM (4 mL) was added to a solution of hex-5-en-1-ol (4.0 g, 40.0 mmol) in DCM (8 mL) at 0 ºC. The mixture was allowed to warm to room temperature and to stir for 1 h. The resulting mixture was concentrated *in vacuo* to afford the dibromide as brown liquid. The dibromide was used in the next step without purification.

A solution of KO*t*-Bu (4.5 g, 40.0 mmol) in anhydrous THF (20 mL) was added to a solution of the dibromide in THF (10 mL) under nitrogen atmosphere at 0 ºC. The mixture was allowed to warm to room temperature and to stir for 4 h before being quenched with water. The mixture was washed with Et_2O and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Alkenyl bromide was afforded as light brown liquid. The alkenyl bromide was used in the next step without purification.

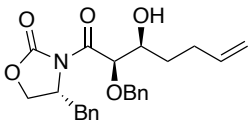
To a solution of the alkenyl bromide and DMAP (488.7 mg, 4.0 mmol) in DCM (20 mL) at 0 ºC were added Et_3N (8.1 g, 80.0 mmol) and triethylsilyl chloride (9.0 g, 60.0 mmol). The mixture was allowed to stir and warm to 25 ºC and to stir for 2 h. The reaction was quenched by addition

of water (10 mL), and the mixture was washed with Et_2O (3 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The brown oil residue was purified by silica gel chromatography (0–1% ethyl acetate in hexanes) to afford the product (5.5 g, 18.8 mmol, 47%) as colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.57 (s, 1H), 5.40 (s, 1H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 1.69 – 1.52 (m, 4H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.60 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.6, 116.4, 62.5, 41.2, 31.5, 24.3, 6.8, 4.4.; IR: ν_{max} 2950 (m), 2873 (m), 1628 (w), 1457 (w), 1236 (w), 1098 (s), 1004 (m), 882 (m), 774 (w), 727 (s) cm^{-1}.; HRMS (DART) for $C_{12}H_{26}OSiBr$ $[M+H]^+$: calculated: 293.0931, found: 293.0932.



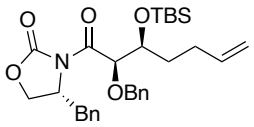
(*R*,*E*)-Triethyl((7-methyl-5-methylene-10,11-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)undec-6-en-1-yl)oxy)silane (**77**). (*R*,*E*)-2,2',2''-(5-Methylhex-5-ene-1,2,6-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**68**) (2.1 g, 4.5 mmol), ((5-bromohex-5-en-1-yl)oxy)trimethylsilane (**69**) (2.6 g, 9.0 mmol), $Pd(PPh_3)_4$ (258.5 mg, 0.22 mmol) and aqueous NaOH solution (4.5 mL, 3.0 M, 13.4 mmol) were added to a Schlenk flask, dissolved in 35 mL anhydrous THF under argon atmosphere. The mixture was heated to 80 ºC and allowed to stir for 12 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl, and the mixture was washed with EtOAc (10 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The light brown oil residue was purified by silica gel chromatography to afford the product (1.13 g, 2.0 mmol, 45%) as yellow gel. ^{1}H NMR (500 MHz, $cdcl_3$) δ 5.55 (s, 1H), 4.93 (s, 1H), 4.73 (s, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 2.09 – 2.01 (m, 4H), 1.75 (s, 3H), 1.63 – 1.39 (m, 6H), 1.23 (two singlets overlap, 24H), 1.17 – 1.06 (m, 1H), 0.95 (t, *J* = 8.0 Hz, 9H), 0.89 (dd, *J* = 10.0, 6.1 Hz, 1H), 0.82 (dd, *J* = 15.8, 6.1 Hz, 1H), 0.59 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126

MHz, $CDCl_3$) δ 146.4, 139.2, 125.4, 112.3, 82.82, 82.78, 62.8, 39.9, 37.5, 32.5, 32.4, 24.89, 24.86, 24.8, 24.7, 24.5, 17.9, 6.8, 4.4.; IR: ν_{max} 2974 (m), 2931 (m), 1368 (s), 1311 (s), 1214 (w), 1141 (s), 1102 (m), 1005 (w), 967 (m), 741 (m) cm^{-1}.; HRMS (DART) for $C_{31}H_{61}B_2O_5Si$ $[M+H]^+$: calculated: 563.4469, found: 563.4477.; $[\alpha]_D^{20}$: –1.8 (c = 1.0, $CHCl_3$, *l* = 50 mm).



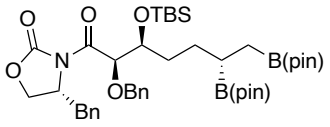
(*R*)-4-Benzyl-3-((2*R*,3*S*)-2-(benzyloxy)-3-hydroxyhept-6-enoyl)oxazolidin-2-one (**80**). The product was synthesized according to a literature procedure.[33] (*R*)-4-benzyl-3-(2-(benzyloxy)acetyl)oxazolidin-2-one (**78**) (1.3 g, 4.0 mmol) was dissolved in anhydrous CH_2Cl_2 (16 mL) under argon and was cooled to –78 ºC. $TiCl_4$ (843 mg, 4.4 mmol) and DIPEA (1.3 g, 10.0 mmol) were added and the solution was allowed to stir for 1 h at –78 ºC. Then NMP (397 mg, 4.0 mmol) was added and the mixture was allowed to stir for 45 min at the same temperature before addition of freshly distlled 4-pentenal (1.0 g, 12.0 mmol). After being allowed to stir for 1 h at the same temperature, the reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (20 mL). The mixture was washed with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The yellow oil residue was purified by silica gel chromatography to afford the product (1.15 g, 2.8 mmol, 70%) as colorless gel. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 – 7.24 (m, 9H), 7.22 – 7.18 (m, 2H), 5.79 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.28 (d, *J* = 6.7 Hz, 0.07H), 5.13 (d, *J* = 2.2 Hz, 1H), 5.02 (d, *J* = 17.0 Hz, 1H), 4.95 (d, *J* = 10.1 Hz, 1H), 4.75 (d, *J* = 11.4 Hz, 1H), 4.72 – 4.65 (m, 1H), 4.62 (d, *J* = 11.5 Hz, 0.07H, minor), 4.57 (d, *J* = 11.5 Hz, 0.07H, minor), 4.50 (d, *J* = 11.4 Hz, 1H), 4.27 – 4.21 (m, 1H), 4.19 (dd, *J* = 9.1, 2.3 Hz, 1H), 4.15 (dd, *J* = 9.1, 2.8 Hz, 0.07H, minor), 3.89 (q, *J* = 7.8 Hz, 1H), 3.29 (dd, *J* = 13.5, 3.4 Hz, 1H), 3.21 (dd, *J* = 13.5, 3.4 Hz, 0.07H), 2.76 (dd, *J* = 13.5, 9.6 Hz, 1H), 2.62 (dd, *J* = 13.5, 9.6 Hz, 0.07H), 2.36 – 2.13 (m, 2H), 2.11 – 2.00 (m, 1H), 1.81 – 1.73 (m, 1H), 1.73 – 1.66 (m, 1H) (17:1 dr).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6,

153.4, 138.0, 137.0, 135.0, 129.4, 129.0, 128.5, 128.4, 128.2, 127.5, 114.9, 79.3, 73.0, 72.0, 67.0, 55.6, 37.7, 33.3, 29.7.; IR: ν_{max} 3486 (br), 2921 (w), 1773 (s), 1706 (m), 1453 (w), 1388 (m), 1210 (m), 1109 (m), 913 (w), 699 (m) cm^{-1}.; HRMS (DART) for $C_{24}H_{28}NO_5$ $[M+H]^+$: calculated: 410.1962, found: 410.1961.; $[\alpha]_D^{20}$: –2.2 (c = 1.0, $CHCl_3$, *l* = 50 mm).



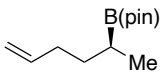
(*R*)-4-Benzyl-3-((2*R*,3*S*)-2-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)hept-6-enoyl)oxazolidin-2-one (**81**). To a solution of (*R*)-4-benzyl-3-((2*R*,3*S*)-2-(benzyloxy)-3-hydroxyhept-6-enoyl)oxazolidin-2-one (**80**) (240 mg, 0.59 mmol) and imidazole (47.9 mg, 0.70 mmol) in DMF (1.5 mL) was added *tert*-butyldimethylsilyl chloride (106 mg, 0.70 mmol). The mixture was allowed to stir at 60 ºC overnight. The reaction was quenched by addition of water (10 mL), and the mixture was washed with Et_2O (3 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The colorless oil was purified by silica gel chromatography (25% ethyl acetate in hexanes) to afford the product (262 mg, 0.50 mmol, 85%) as colorless gel. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.38 – 7.28 (m, 6H), 7.25 – 7.18 (m, 2H), 5.79 (td, *J* = 16.5, 6.4 Hz, 1H), 5.50 (d, *J* = 7.7 Hz, 0.05H, minor), 5.31 – 5.24 (m, 1H), 5.04 – 4.89 (m, 2H), 4.73 (d, *J* = 11.9 Hz, 1H), 4.63 – 4.53 (m, 2H), 4.19 – 4.11 (m, 2H), 4.10 – 4.03 (m, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.14 (d, *J* = 13.5 Hz, 0.05H, minor), 2.66 (dd, *J* = 13.3, 9.8 Hz, 1H), 2.59 – 2.51 (m, 0.05H, minor), 2.15 – 2.01 (m, 1H), 2.01 – 1.81 (m, 2H), 1.63 – 1.48 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H) (23:1 dr).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 153.1, 138.3, 137.6, 135.2, 129.4, 129.0, 128.44, 128.36, 127.9, 127.4, 114.6, 79.0, 73.1, 72.8, 66.5, 56.0, 37.6, 32.7, 29.6, 25.9, 18.1, -4.4, -4.6. IR: ν_{max} 2926 (w), 2854 (w), 1778 (s), 1707 (m), 1453 (w), 1384 (m), 1207 (m), 1105 (m), 911 (w), 836 (m), 776 (m), 699 (m) cm^{-1}.; HRMS (DART) for

$C_{30}H_{42}NO_5Si$ $[M+H]^+$: calculated: 524.2827, found: 524.2819.; $[\alpha]_D^{20}$: –26.4 (c = 1.0, $CHCl_3$, l = 50 mm).



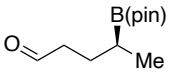
(*R*)-4-Benzyl-3-((2*R*,3*S*,6*S*)-2-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-6,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptanoyl)oxazolidin-2-one (**83**). The title compound was prepared according to a literature procedure.[28] To an oven-dried round-bottom flask equipped with a magnetic stir bar was added $Pt(dba)_3$ (25.9 mg, 0.029 mmol), **72** (31.5 mg, 0.035 mmol), and $B_2(pin)_2$ (439.9 mg, 1.7 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (1.5 mL) was added by syringe, and the mixture was allowed to stir at 80 °C for 30 min. The flask was then allowed to cool to room temperature and was charged with (*R*)-4-benzyl-3-((2*R*,3*S*)-2-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)hept-6-enoyl)oxazolidin-2-one (**81**) (756 mg, 1.4 mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC overnight. The mixture was passed through a silica gel plug and concentrated in *vacuo*. The yellow oil residue was purified by silica gel chromatography (40% ethyl acetate in hexanes) to afford the product (1.0 g, 1.3 mmol, 91%) as colorless gel. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.33 – 7.28 (m, 4H), 7.27 – 7.22 (m, 2H), 7.20 – 7.15 (m, 2H), 5.43 (d, J = 7.6 Hz, 0.05H, minor), 5.23 (d, J = 4.7 Hz, 1H), 4.72 – 4.58 (m, 2H), 4.50 (ddt, J = 9.6, 6.1, 2.9 Hz, 1H), 4.14 – 4.08 (m, 2H), 3.98 (q, J = 6.2 Hz, 1H), 3.16 (dd, J = 13.5, 3.2 Hz, 1H), 3.07 – 3.03 (m, 0.05H), 2.55 (dd, J = 13.5, 10.1 Hz, 1H), 2.42 (dd, J = 13.5, 10.1 Hz, 0.05H), 1.75 (tt, J = 11.8, 5.7 Hz, 1H), 1.50 – 1.33 (m, 3H), 1.20 (s, 12H), 1.19 – 1.18 (m, 12H), 1.11 – 1.03 (m, 1H), 0.84 (s, 9H), 0.82 – 0.73 (m, 2H), 0.03 (s, 3H), -0.01 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.3, 153.0, 137.8, 135.4, 129.4, 128.9, 128.4, 128.2, 127.7, 127.3, 82.80, 82.77, 79.5, 73.9, 73.2, 66.3, 55.9, 37.5, 32.6, 29.9, 25.9, 24.9, 24.82, 24.78, 24.7, 18.1, -4.4, -4.5 (21:1 dr).; IR: ν_{max} 2926 (w),

2854 (w), 1781 (s), 1706 (w), 1453 (w), 1369 (s), 1313 (s), 1210 (m), 1140 (s), 967 (w), 836 (m), 776 (w), 699 (w), 671 (w) cm^{-1}.; HRMS (DART) for $C_{42}H_{66}B_2NO_9Si$ $[M+H]^+$: calculated: 778.4688, found: 778.4722.; $[\alpha]_D^{20}$: –28.0 (c = 1.0, $CHCl_3$, l = 50 mm).



(*S*)-2-(Hex-5-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**85**). The title compound was prepared according to a literature procedure.[28] To an oven-dried round-bottom flask equipped with a magnetic stir bar was added $Pt(dba)_3$ (18.0 mg, 0.02 mmol), **72** (21.8 mg, 0.024 mmol), and $B_2(pin)_2$ (2.54 g, 10.0 mmol). The flask was sealed with a septum cap and purged with N_2. Tetrahydrofuran (10 mL, 1.0 M) was added by syringe, and the mixture was allowed to stir at 80 °C for 30 min. The mixture was then allowed to cool to room temperature and was charged with 1,5-hexadiene (1.23 g, 15.0 mmol). After purging once more with N_2, the mixture was allowed to stir at 60 ºC overnight.

The mixture was diluted with anhydrous THF (15 mL), CuCN (187 mg, 2.0 mmol), LiOMe (1.13 g, 30 mmol) and MeOH (961 mg, 30.0 mmol) were added under argon atmosphere, the mixture was allowed to stir at 60 ºC overnight. The yellow oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product (1.64 g, 7.8 mmol, 78%) as pale-yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.78 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 4.99 – 4.93 (m, 1H), 4.92 – 4.85 (m, 1H), 2.10 – 1.99 (m, 2H), 1.57 – 1.46 (m, 1H), 1.39 – 1.29 (m, 1H), 1.21 (s, 12H), 1.05 – 0.97 (m, 1H), 0.94 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.2, 114.1, 82.8, 33.1, 32.4, 24.71, 24.67, 15.3.; IR: ν_{max} 2975 (w), 2924 (w), 1639 (w), 1461 (w), 1369 (m), 1313 (s), 1228 (w), 1141 (s), 992 (w), 907 (w), 859 (w), 687 (w) cm^{-1}.; HRMS (DART) for $C_{12}H_{24}BO_2$ $[M+H]^+$: calculated: 211.1864, found: 211.1865.; $[\alpha]_D^{20}$: +3.2 (c = 1.0, $CHCl_3$, l = 50 mm).



(*S*)-4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pentanal (**86**). (*S*)-2-(Hex-5-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**85**) (1.64 g, 7.8 mmol) was dissolved in DCM (20 mL) and was treated with ozone at –78 ºC and was allowed to stir until completion (monitered with TLC). The mixture was flushed with air, triphenylphopshine (2.66 g, 10.2 mmol) was added. The resulting solution was allowed to warm to room temperature and to stir for 2 h. DCM was removed under reduced pressure, then the mixture was diluted with hexanes and Et_2O. The mixture was then passed through a celiete plug. Huge amount of solid (PPh_3O) was filtered off. The solvents were removed under reduced pressure. The colorless oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product (1.26 g, 5.9 mmol, 76%) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.69 (s, 1H), 2.39 (t, J = 7.7 Hz, 2H), 1.76 – 1.66 (m, 1H), 1.62 – 1.52 (m, 1H), 1.17 (s, 12H), 1.00 – 0.89 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.9, 83.0, 43.2, 25.3, 24.7, 24.6, 15.3.; IR: ν_{max} 2976 (w), 2870 (w), 2709 (w), 1724 (m), 1462 (w), 1370 (m), 1317 (m), 1214 (w), 1143 (s), 966 (w), 858 (w) cm^{-1}.; HRMS (DART) for $C_{11}H_{22}BO_3$ $[M+H]^+$: calculated: 213.1657, found: 213.1660.; $[\alpha]_D^{20}$: 3.6 (c = 1.0, $CHCl_3$, l = 50 mm).

Computational Methods and Data

Computational methods

The Monte Carlo Multiple Minimum (MCMM) and the Mixed torsional/Low-Mode sampling (MTLMOD) search methods implemented in Schrödinger software MacroModel[37] were run with 10,000 steps in total for one compound. The option of using a fixed number of steps per rotatable bond, as well as the Multi-Ligand option, were deselected. Torsional sampling of amides, esters,

[37] Schrödinger Release 2017–1: MacroModel, Schrödinger, LLC, New York, NY, 2017.

as well as all C–N and C–O single bonds and C=N and N=N double bonds, were allowed in the search ("extended sampling"). For energy minimizations, up to 50,000 steps of Truncated Newton minimization (TNCG)[38] with a gradient convergence criterion of 0.05 kJ $Å^{-1}$ mol^{-1} was used (the minimization terminates when the convergence criterion is met). The energy window for keeping conformers was set to 20.9 kJ mol^{-1} (5 kcal mol^{-1}). For MTLMOD, the probability of a torsion rotation/molecule translation was set to the default value of 0.5. Solvents were set to none. Also, the minimum and maximum distance for low-mode moves were kept at default values of 3.0 and 6.0 Å, respectively.

All calculations were conducted with density functional theory (DFT) implemented in Gaussian 16 suite of program.[39] All molecular structures were optimized by B3LYP[40] functional with 6-31G* basis sets and GD3BJ dispersion correction. Frequency calculations were performed at the same level of theory to characterize the stationary points (no imaginary frequencies for local minima). Molecular structure visualizations were obtained with Gaussview.[41]

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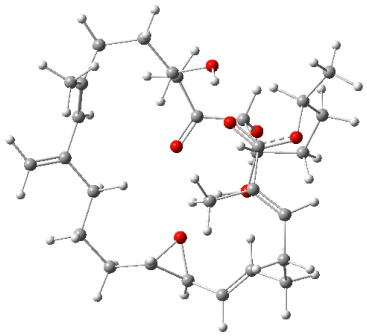
[40] Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch. M. J. *J. Phys. Chem.* **1994**, *98*, 11623–11627.

[41] GaussView, Version 6, Dennington, R.; Keith, T. A.; Millam, J. M. Semichem Inc., Shawnee Mission, KS, 2016.

Cartesian coordinates of computed structures



67-1

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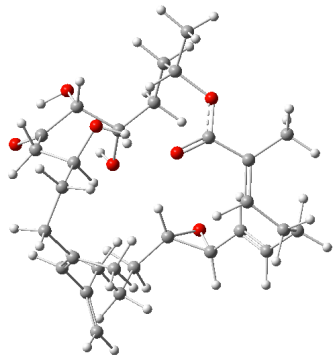

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O	3.87236600	-0.59736900	2.25278100
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C	-2.46160500	2.20118500	-1.51924600
C	-2.76041000	0.98496900	-2.01071500
C	-4.14454800	0.51111400	-2.35815300
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C	-2.06018500	-2.21847900	2.20726400
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C	0.32639400	-3.33805600	0.50462300
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C	3.50832500	-1.58465700	-2.65761500
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C	2.90431900	0.40615200	-1.12727500
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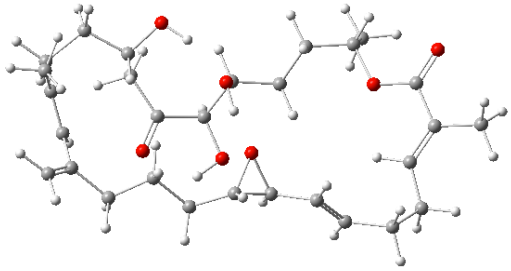

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C	5.38468500	1.06846300	0.23874400
C	5.73366900	2.47355000	0.62314800
C	4.67316300	3.48783800	0.11934500
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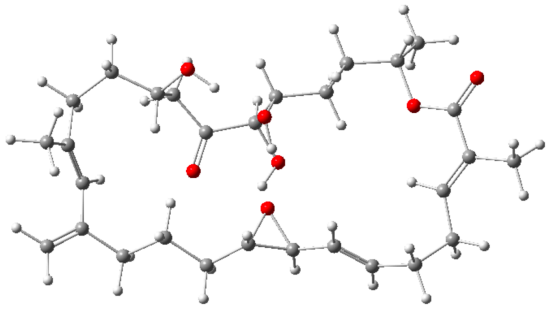

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C	5.70816500	-0.95437300	-0.70208100
C	6.07362700	0.48470500	-0.55731500
C	5.21680700	1.34497000	0.02102900
C	5.41125800	2.81512700	0.23450400
C	4.27708700	3.64994800	-0.41487600
C	2.95415400	3.46426300	0.26671000
C	1.87299900	2.90172900	-0.28230500
C	0.58751800	2.77857700	0.42721000
C	-0.70127400	2.67558800	-0.28435100
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C	-3.19514600	2.31443800	-0.24274400
C	-4.51241700	2.64148200	0.47620200
C	-5.68685000	1.84179000	-0.05124100
C	-5.60709900	0.38844600	0.17872100
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C	-4.51557100	-2.72645500	-0.85242700
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C	-2.79849400	-2.32420200	0.99532500
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H	0.56627500	3.16548800	1.44572200
H	-0.65623000	2.66551300	-1.37505500
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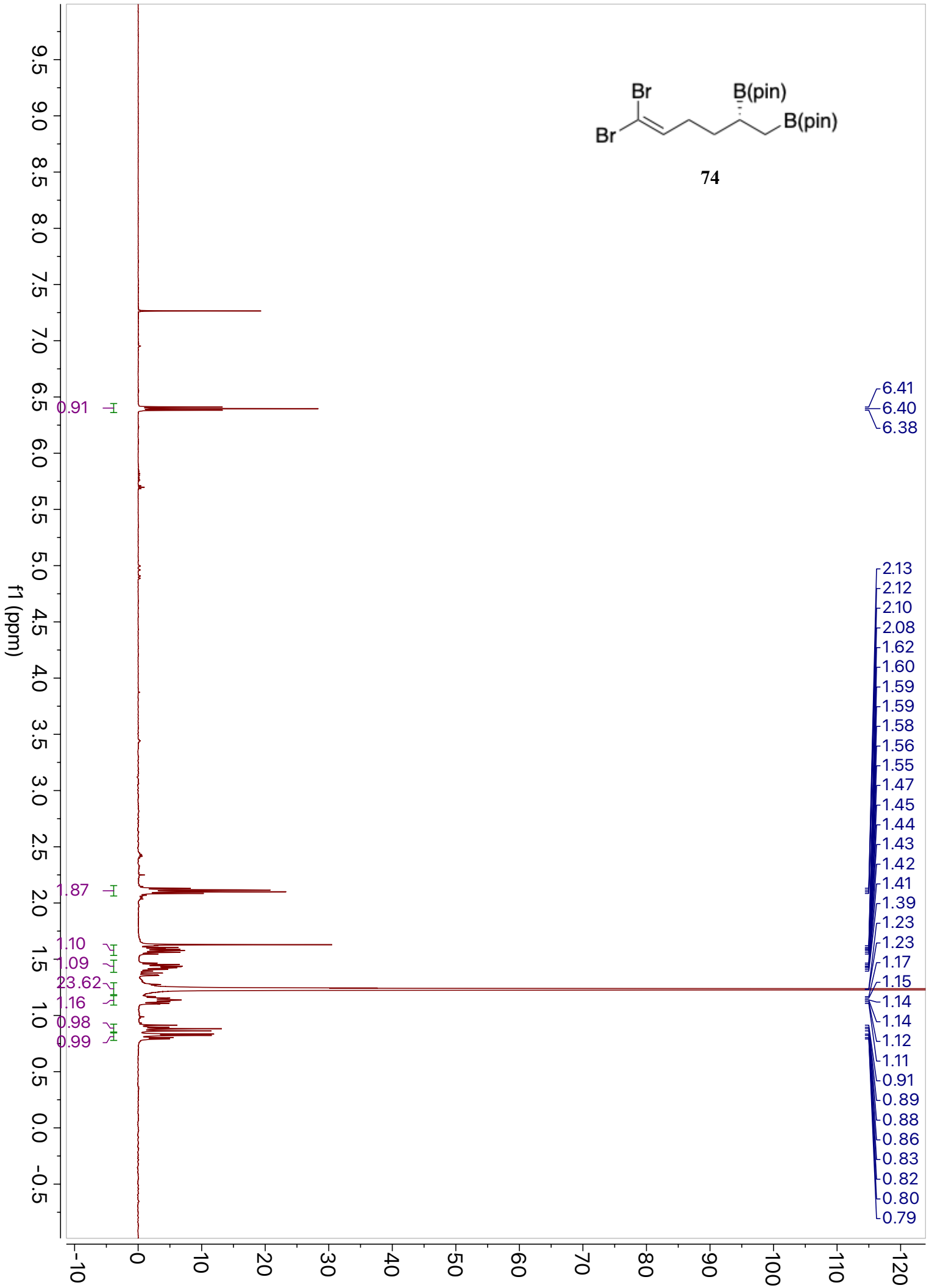
Spectra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6.40
6.38
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2.12
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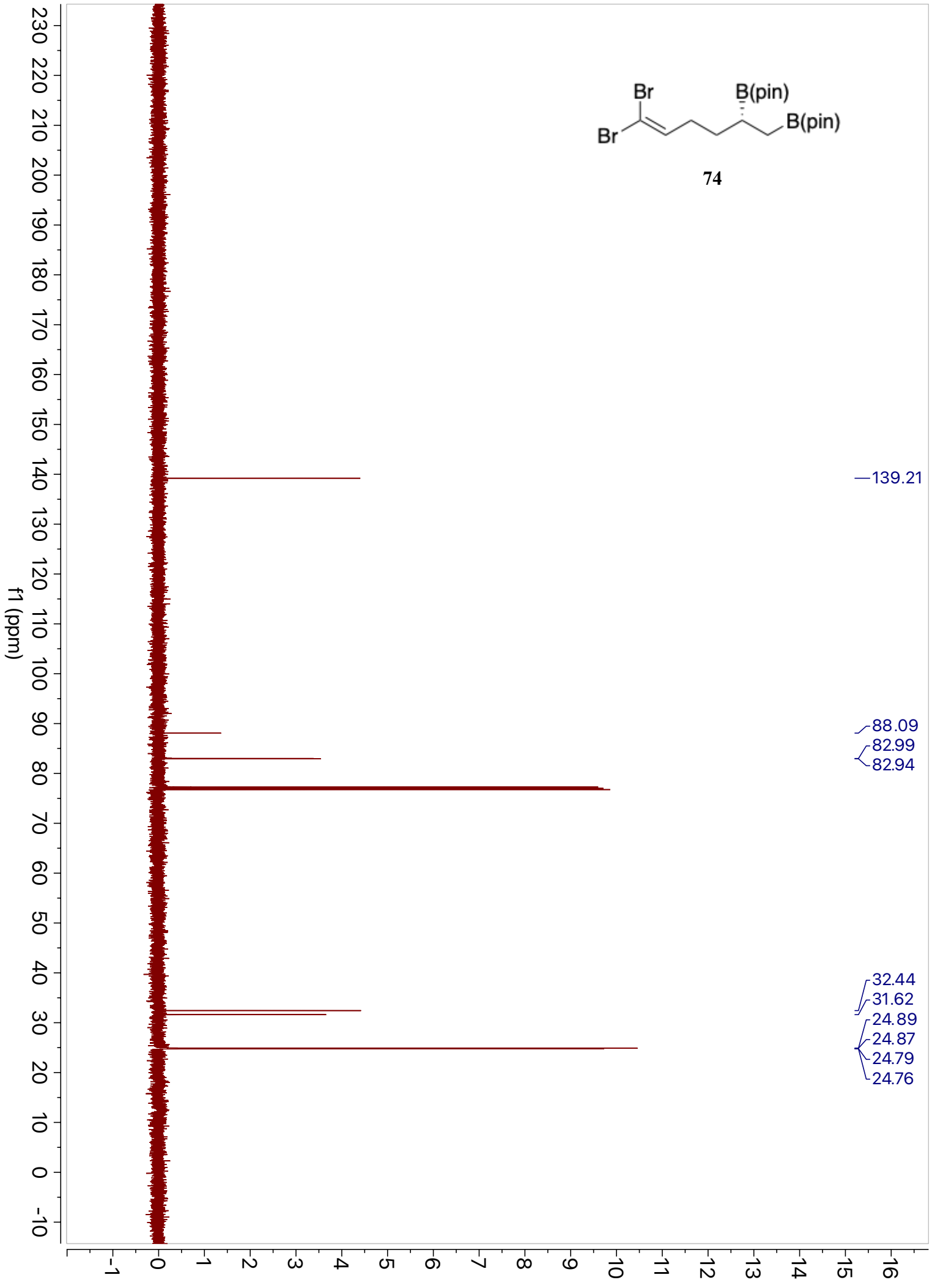
0.79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Br
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31.62
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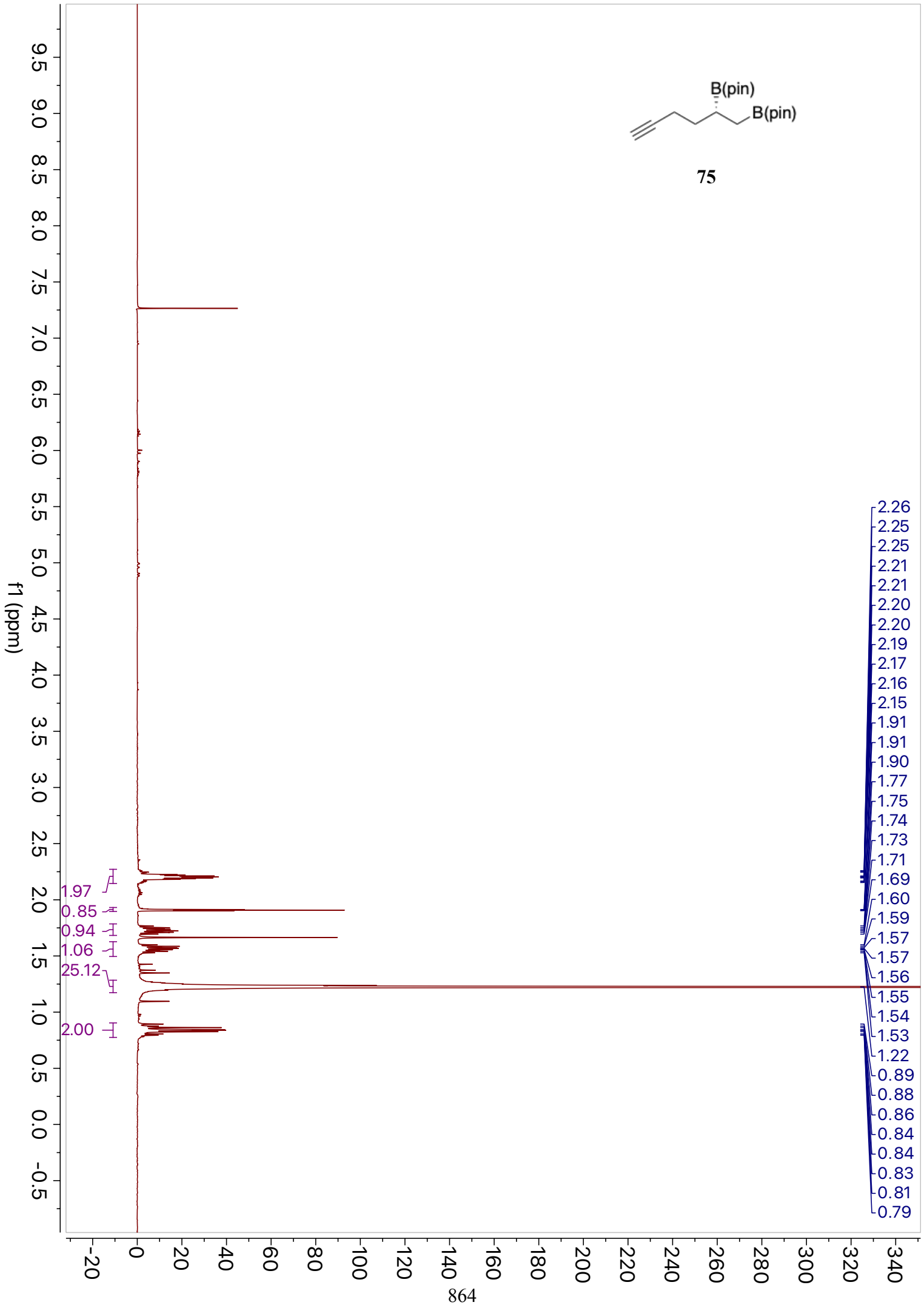
24.79
24.76
f1 (ppm)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2.25
2.21
2.21
2.20
2.20
2.19
2.17
2.16
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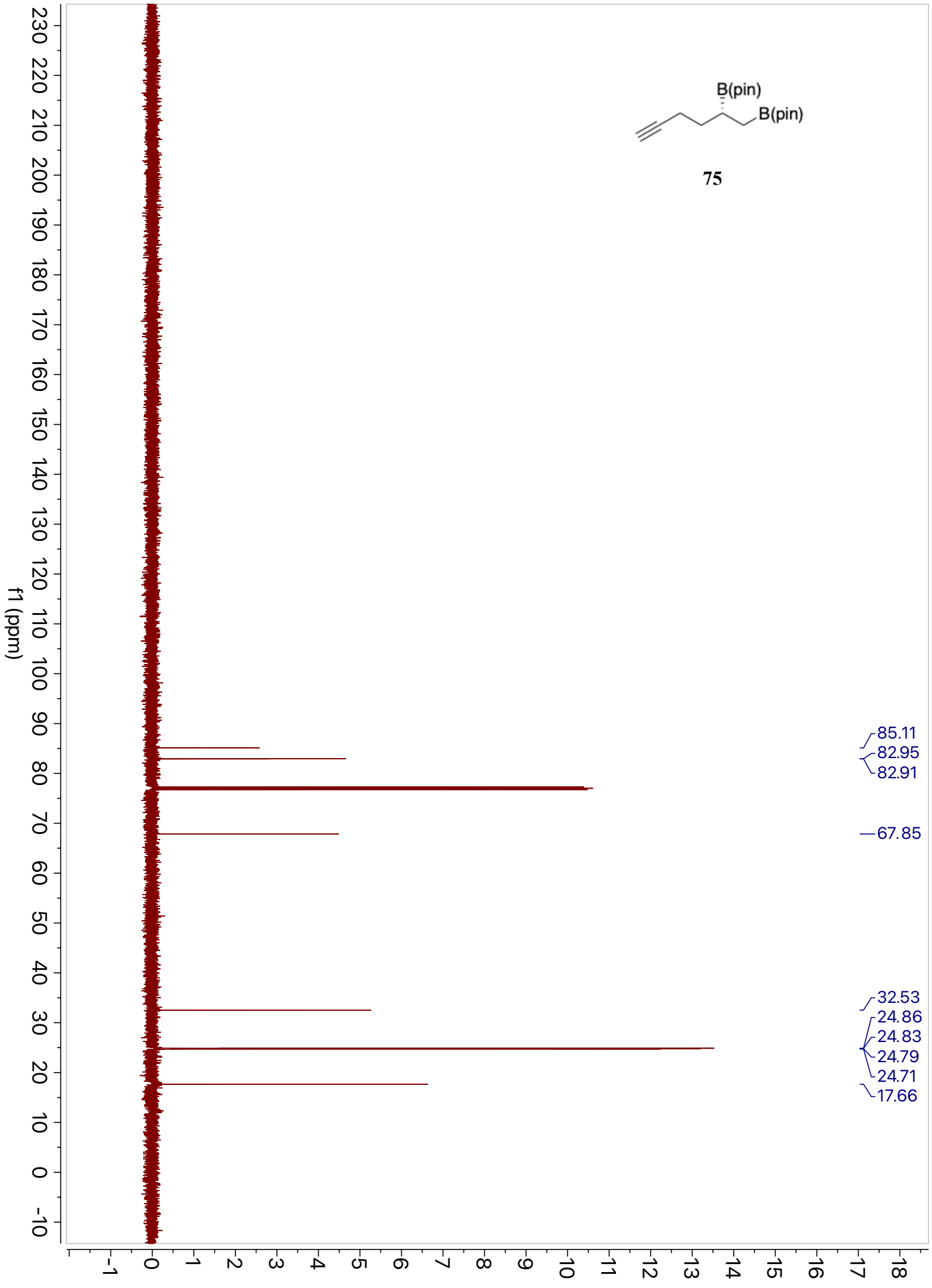
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B(pin)
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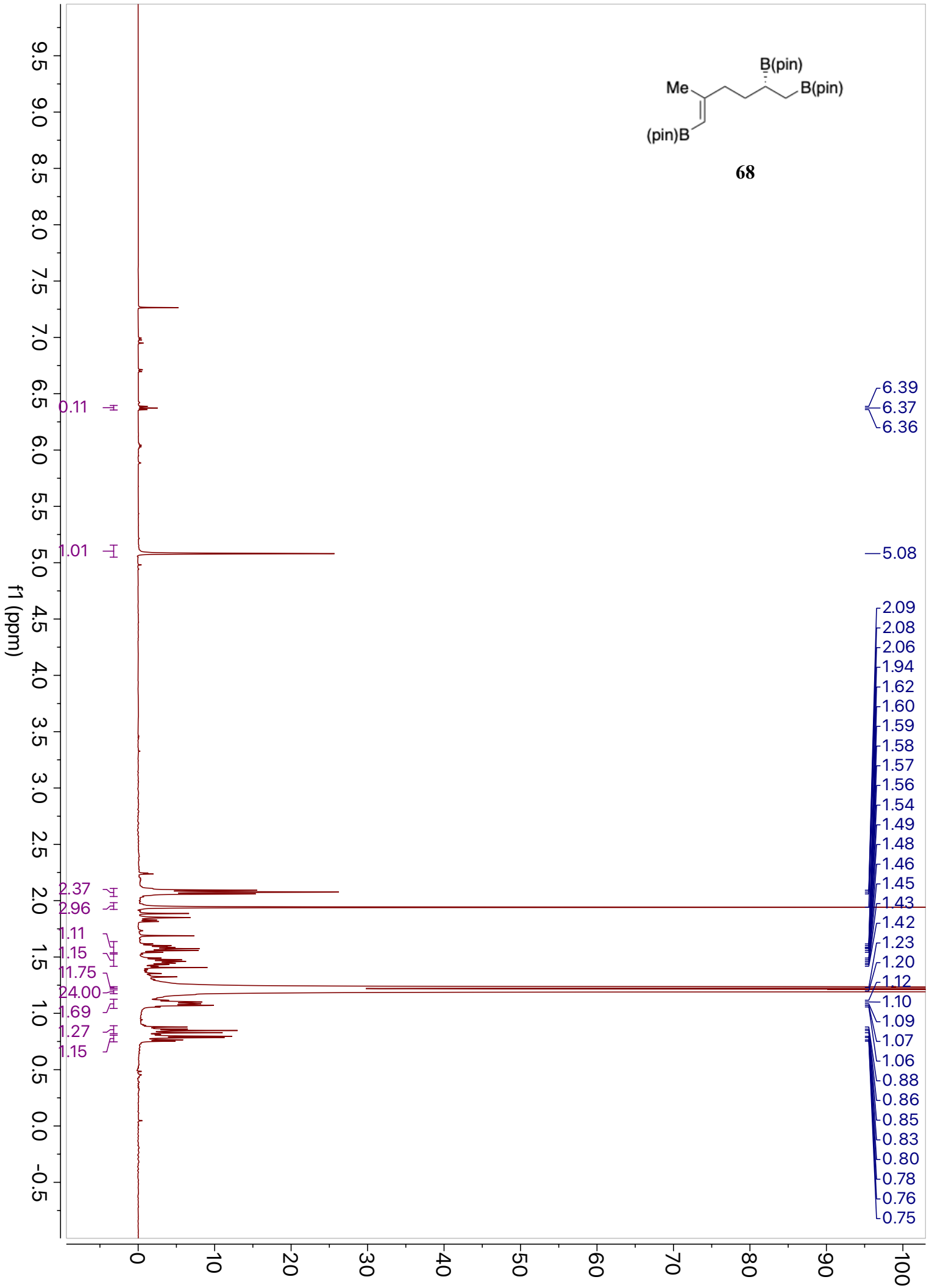
24.79
24.71
17.66
f1 (ppm)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Me
B(pin)
(pin)B
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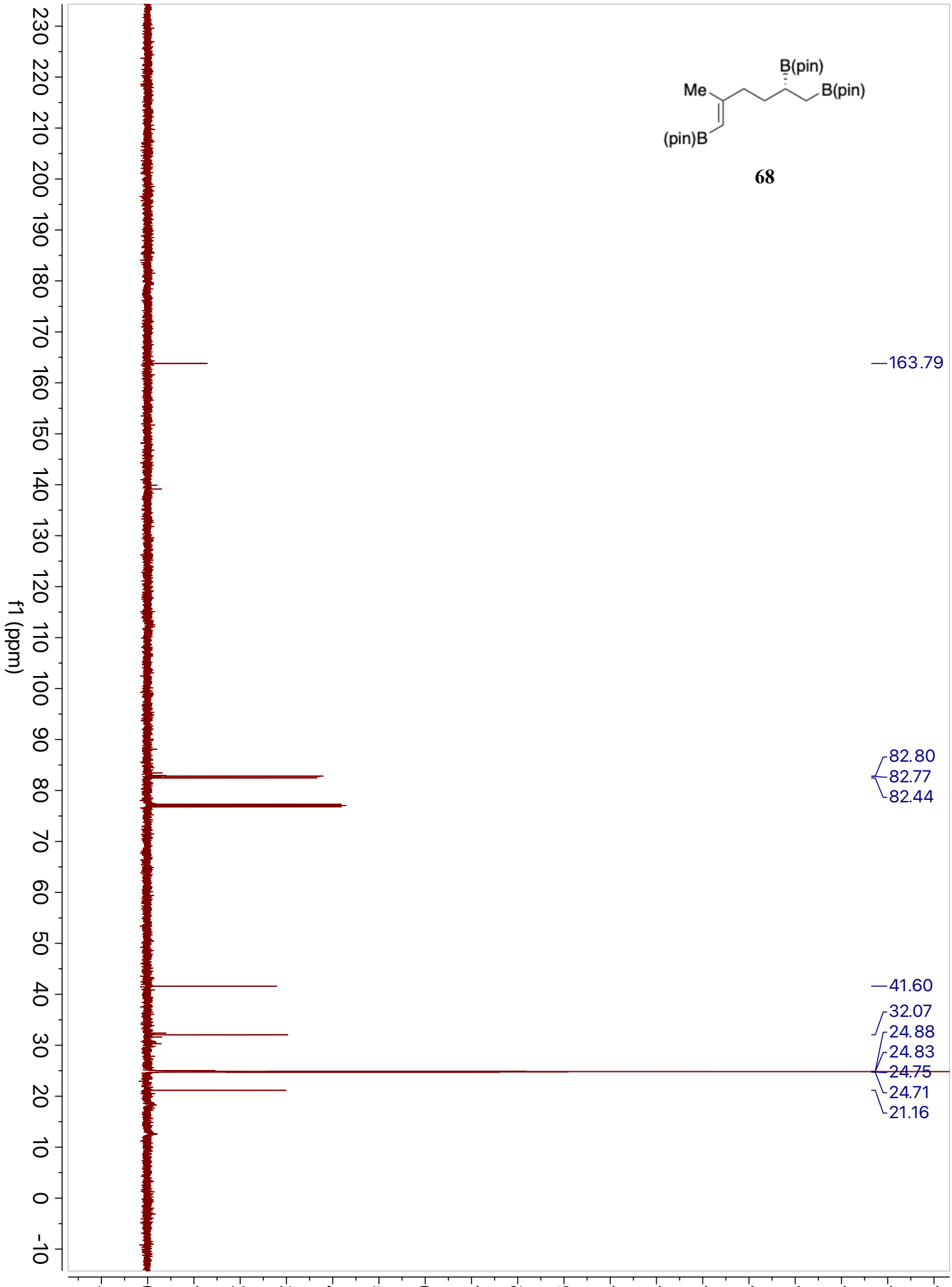
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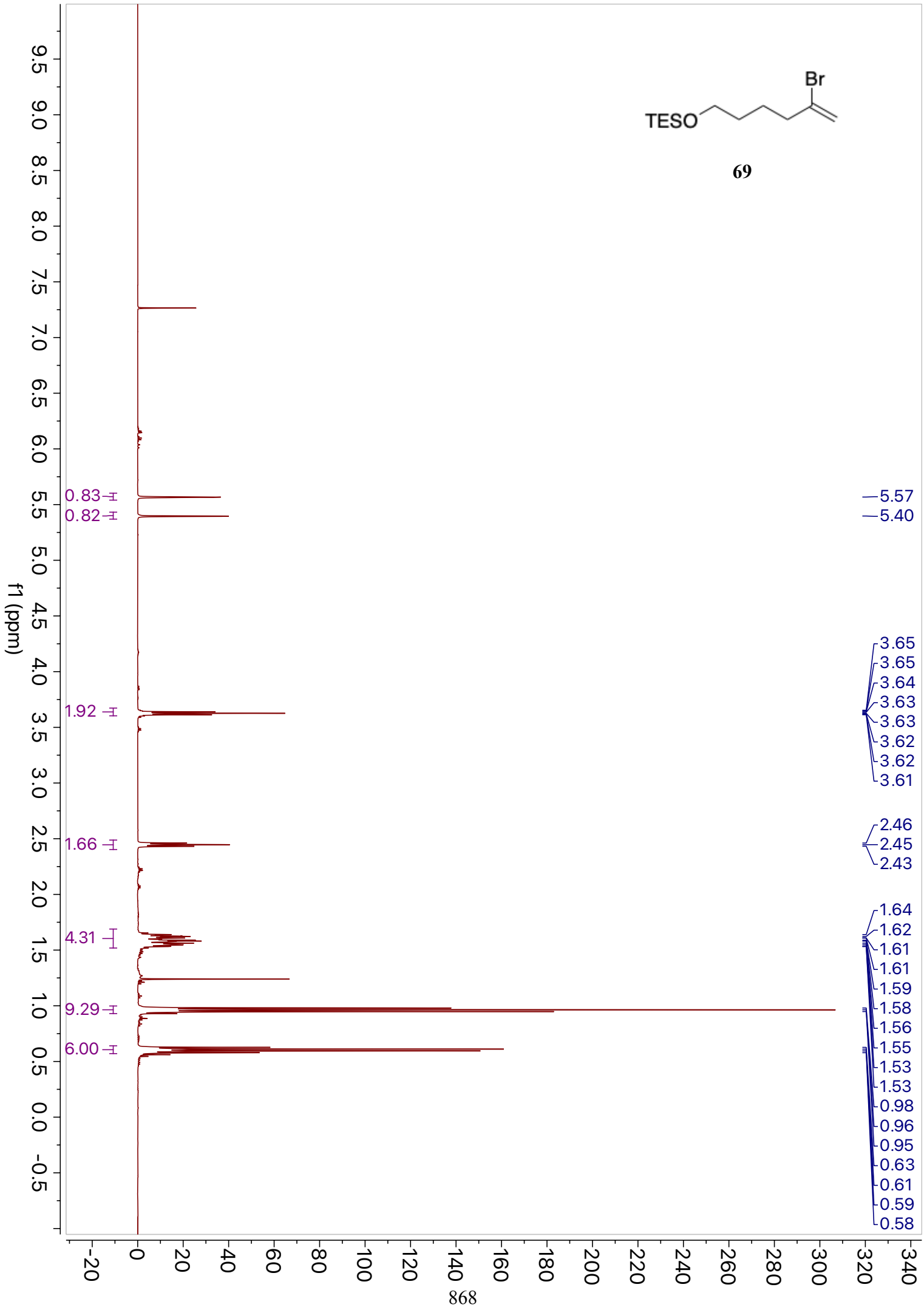
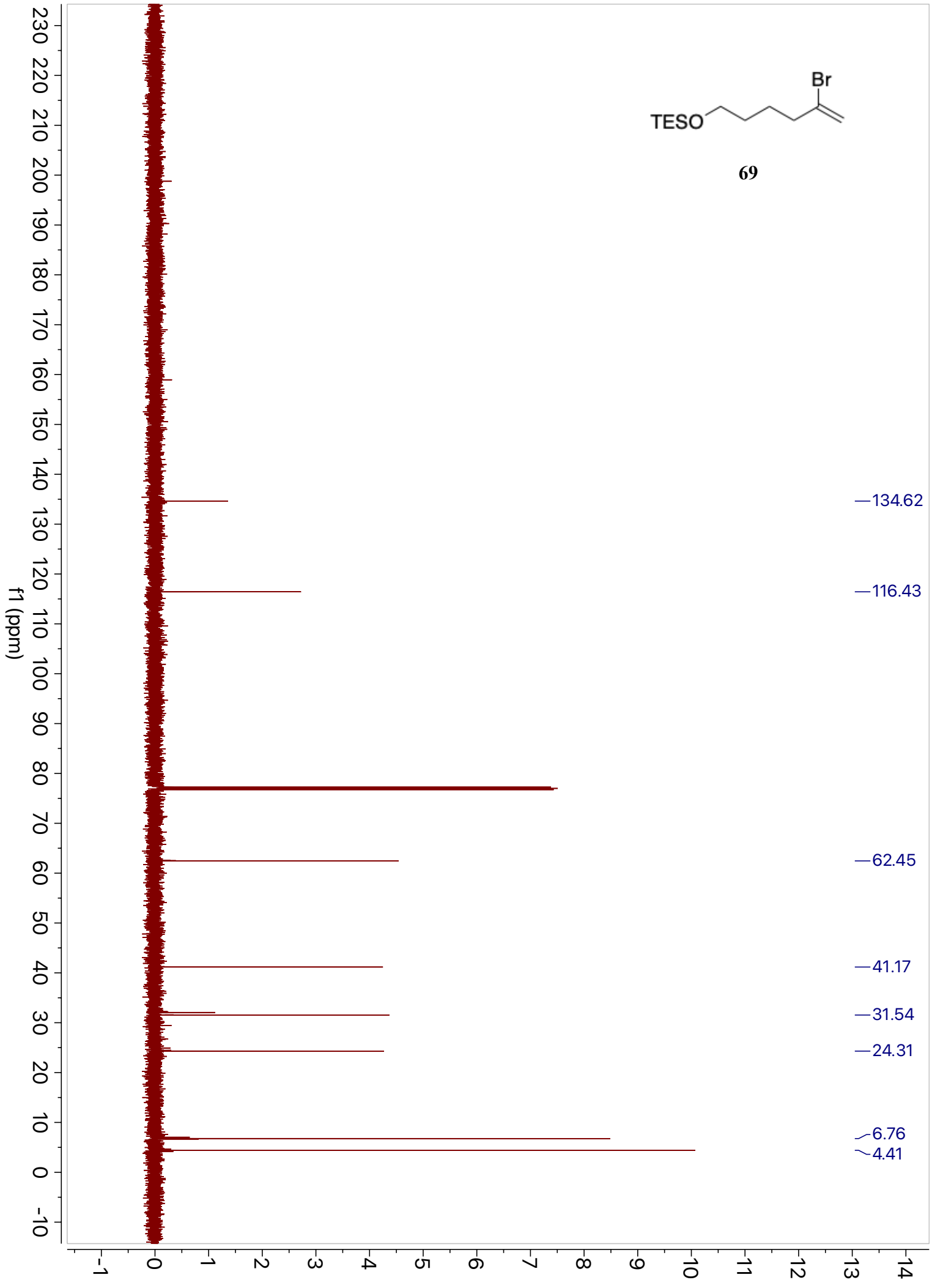
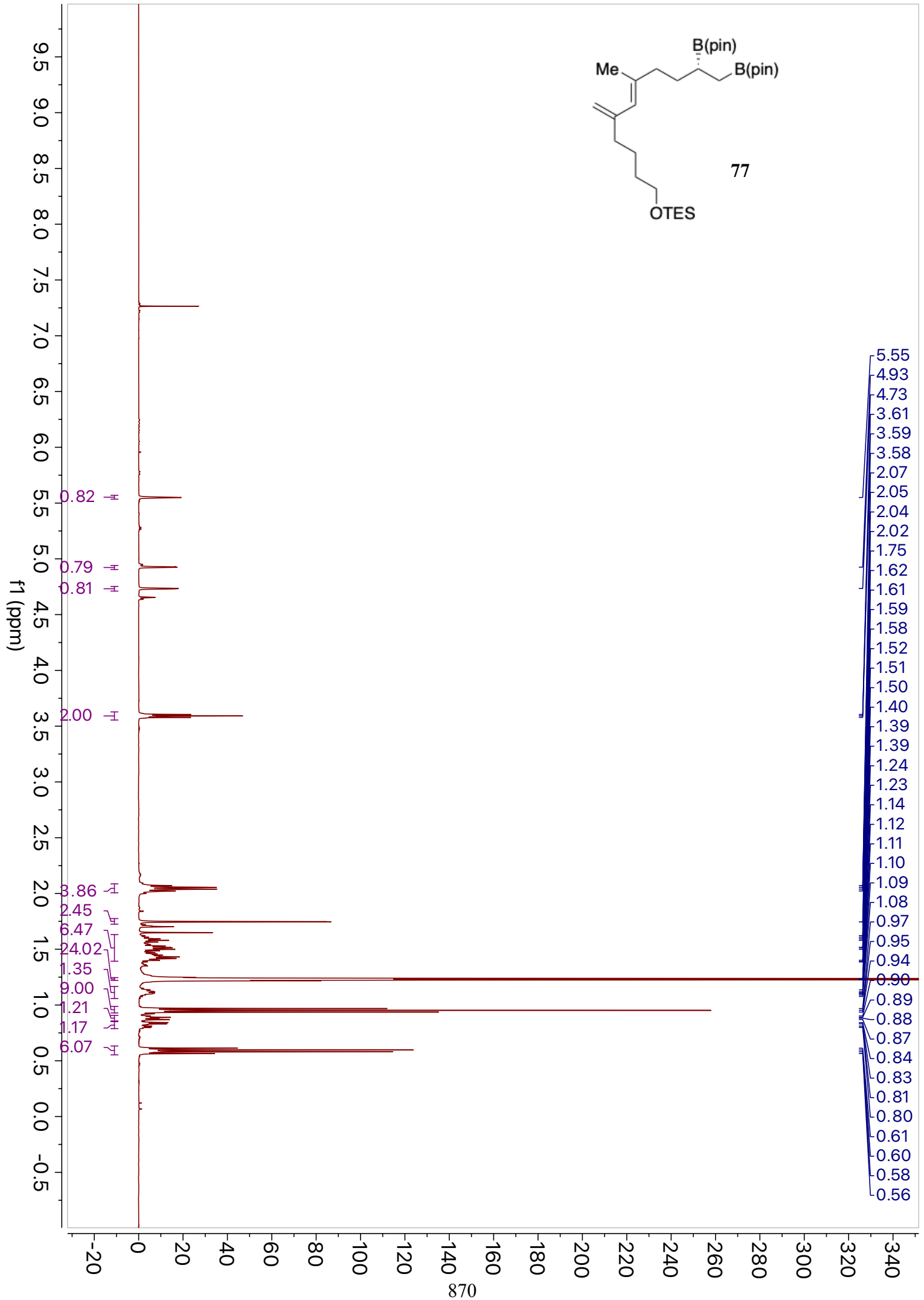
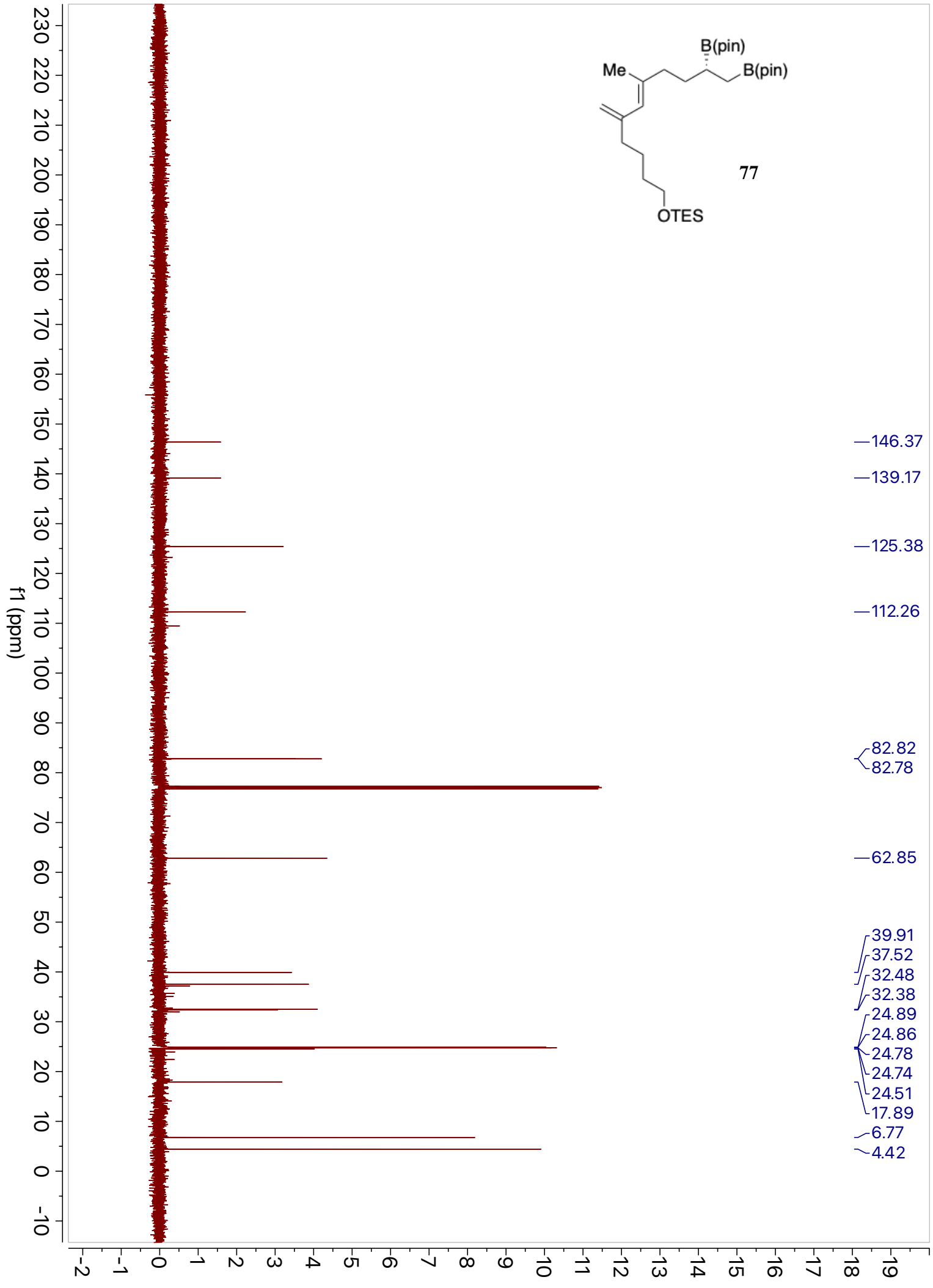
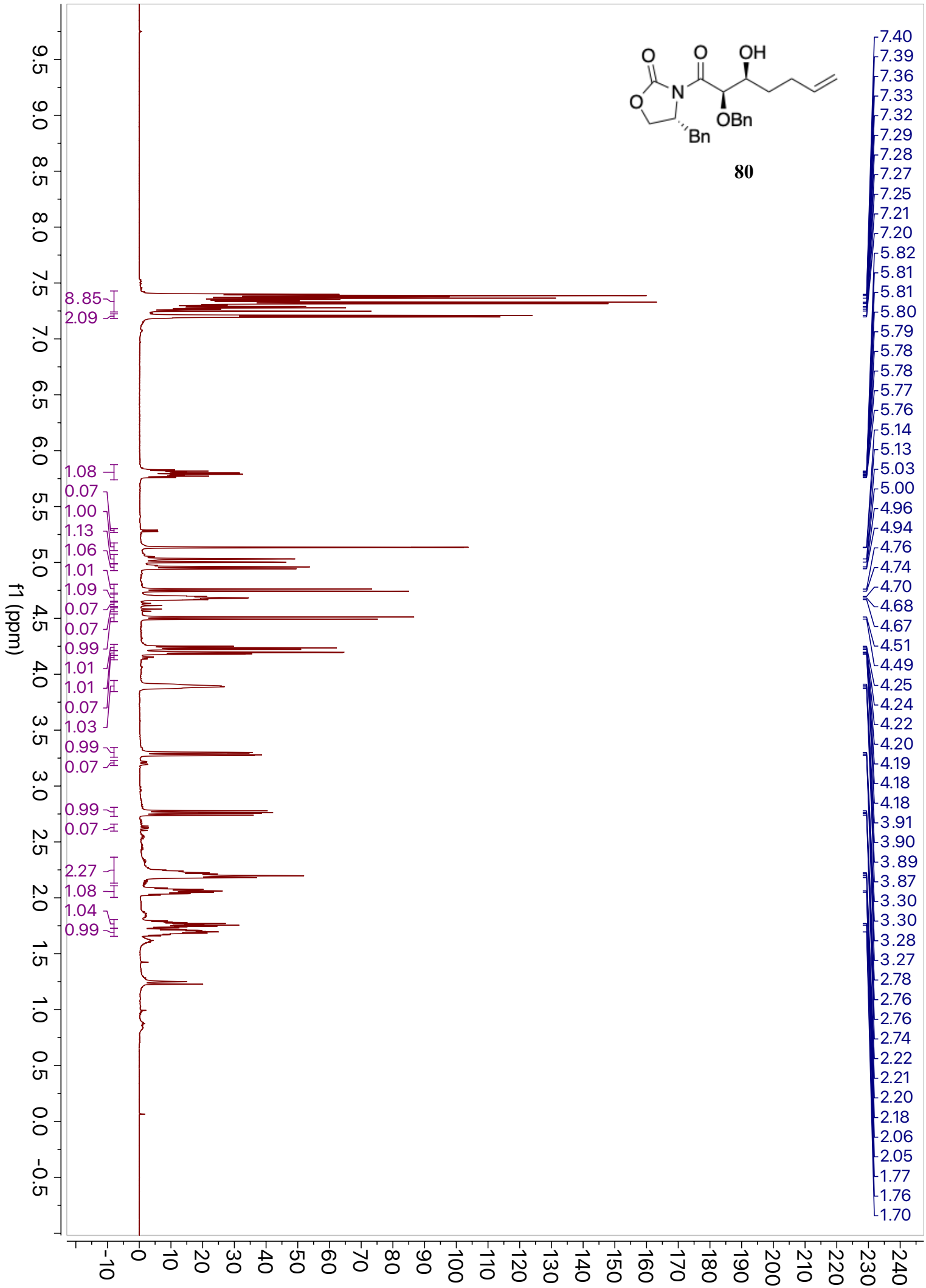
Me
B(pin)
(pin)B
68
163.79
82.80
82.77
82.44
41.60
32.07
24.88
24.83
24.75
24.71
21.16
f1 (ppm)

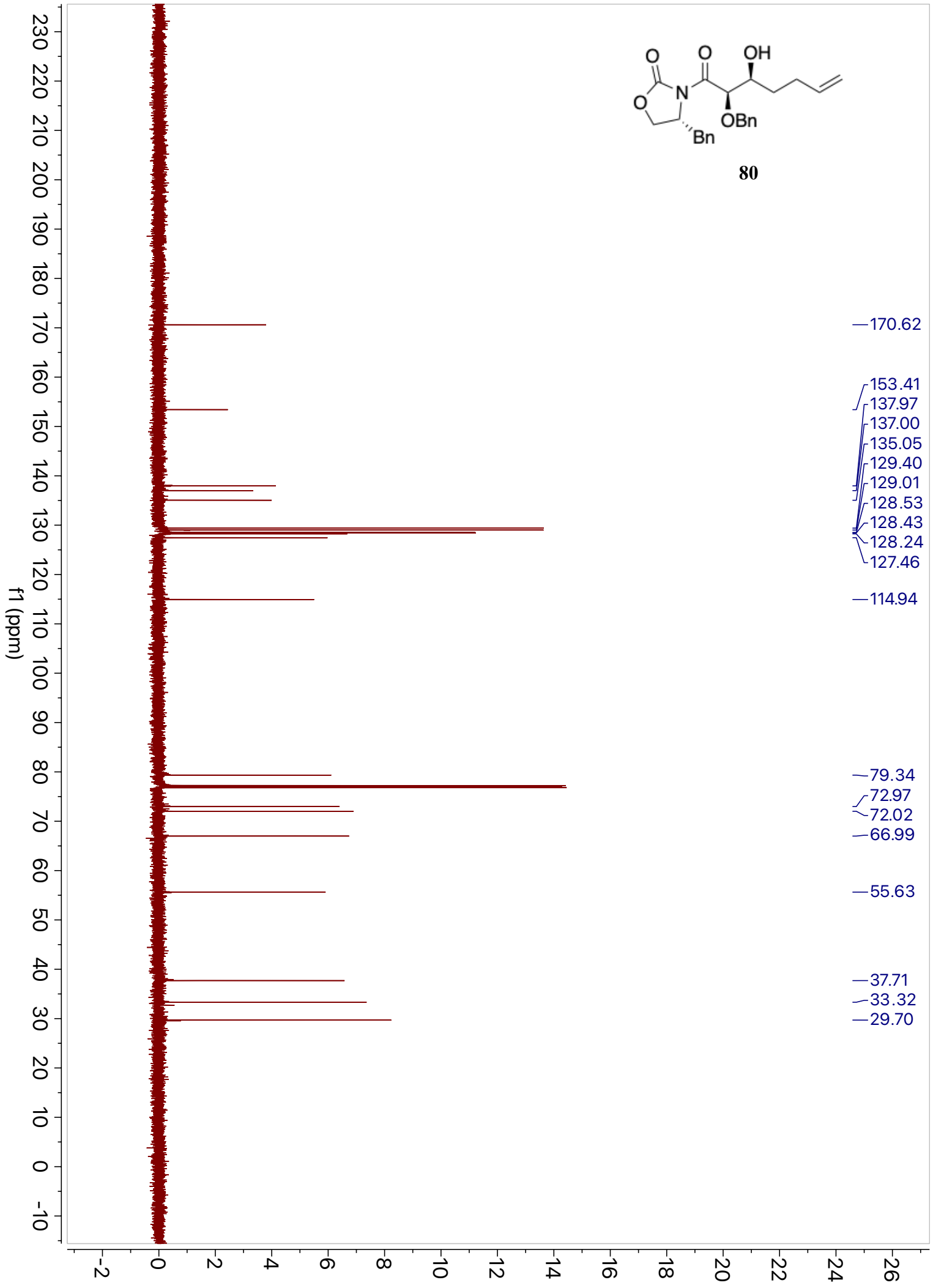

Br
TESO
69
0.83
0.82
1.92
1.66
4.31
9.29
6.00
5.57
5.40
3.65
3.65
3.64
3.63
3.63
3.62
3.62
3.61
2.46
2.45
2.43
1.64
1.62
1.61
1.61
1.59
1.58
1.56
1.55
1.53
1.53
0.98
0.96
0.95
0.63
0.61
0.59
0.58
f1 (ppm)

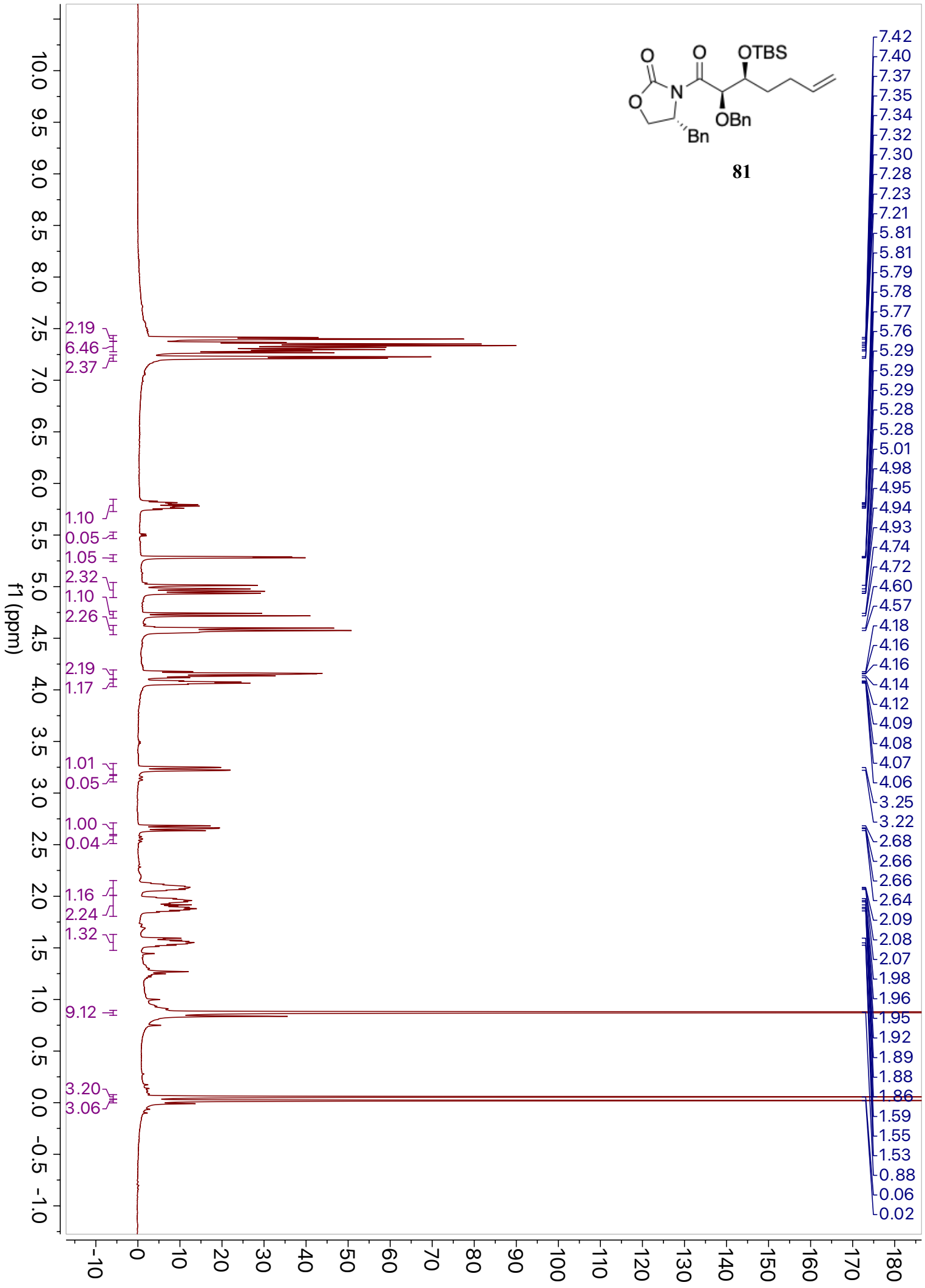

Br
TESO
69
134.62
116.43
62.45
41.17
31.54
24.31
6.76
4.41
f1 (ppm)

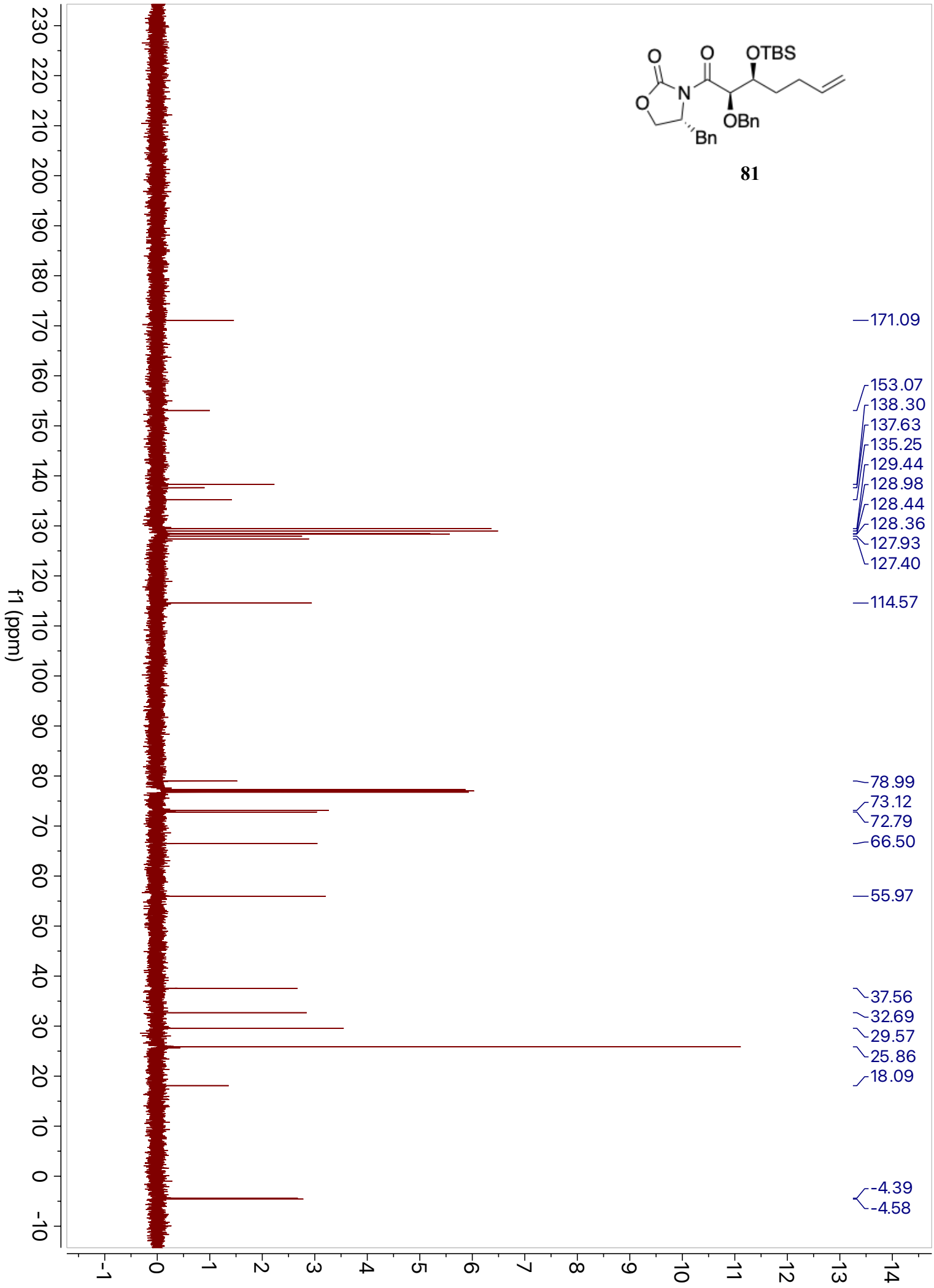

B(pin)
Me
B(pin)
OTES
77
f1 (ppm)
0.82
0.79
0.81
2.00
3.86
2.45
6.47
24.02
1.35
9.00
1.21
1.17
6.07
5.55
4.93
4.73
3.61
3.59
3.58
2.07
2.05
2.04
2.02
1.75
1.62
1.61
1.59
1.58
1.52
1.51
1.50
1.40
1.39
1.39
1.24
1.23
1.14
1.12
1.11
1.10
1.09
1.08
0.97
0.95
0.94
0.90
0.89
0.88
0.87
0.84
0.83
0.81
0.80
0.61
0.60
0.58
0.56

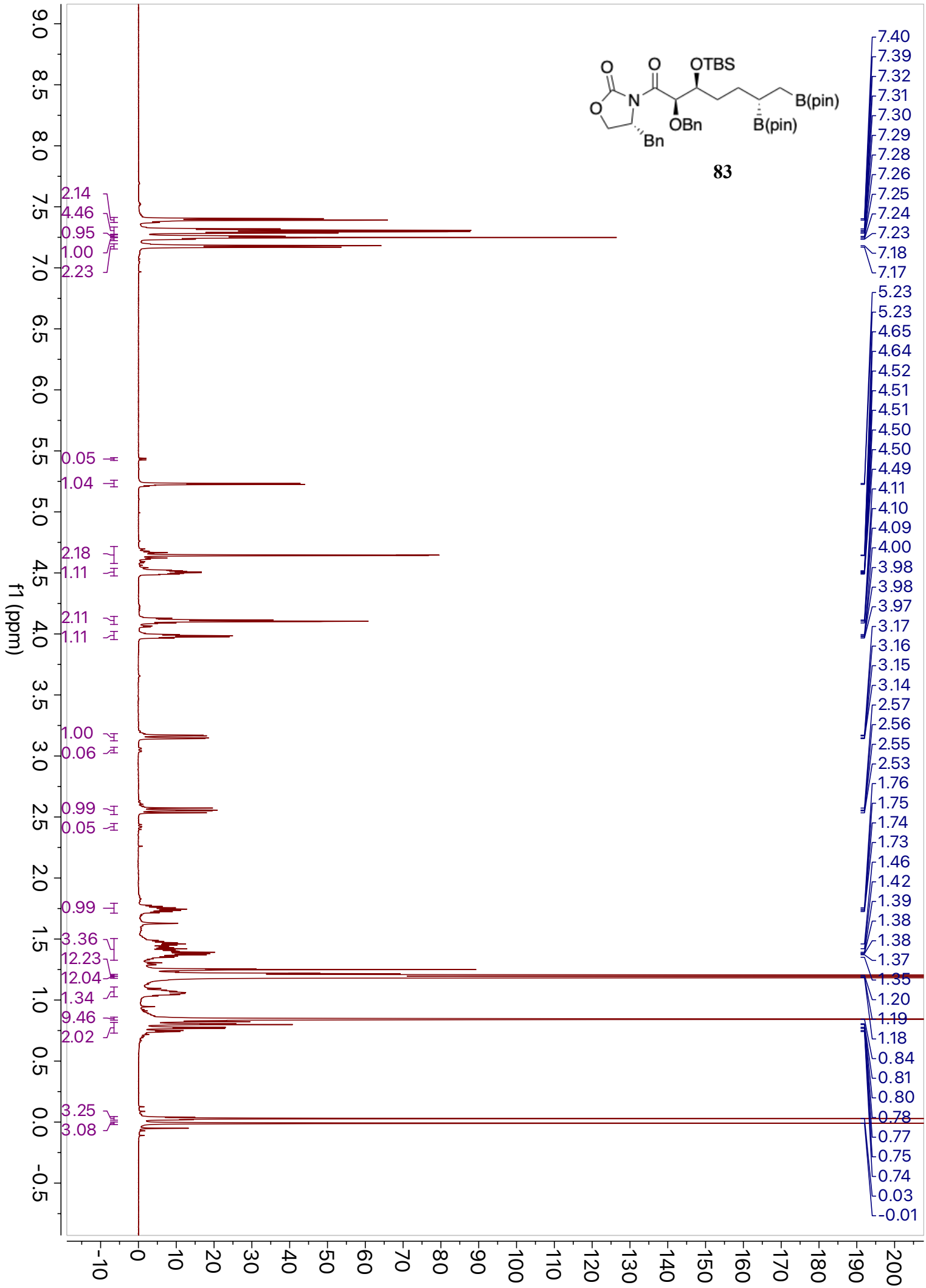

B(pin)
Me
B(pin)
77
OTES
146.37
139.17
125.38
112.26
82.82
82.78
62.85
39.91
37.52
32.48
32.38
24.89
24.86
24.78
24.74
24.51
17.89
6.77
4.42
f1 (ppm)

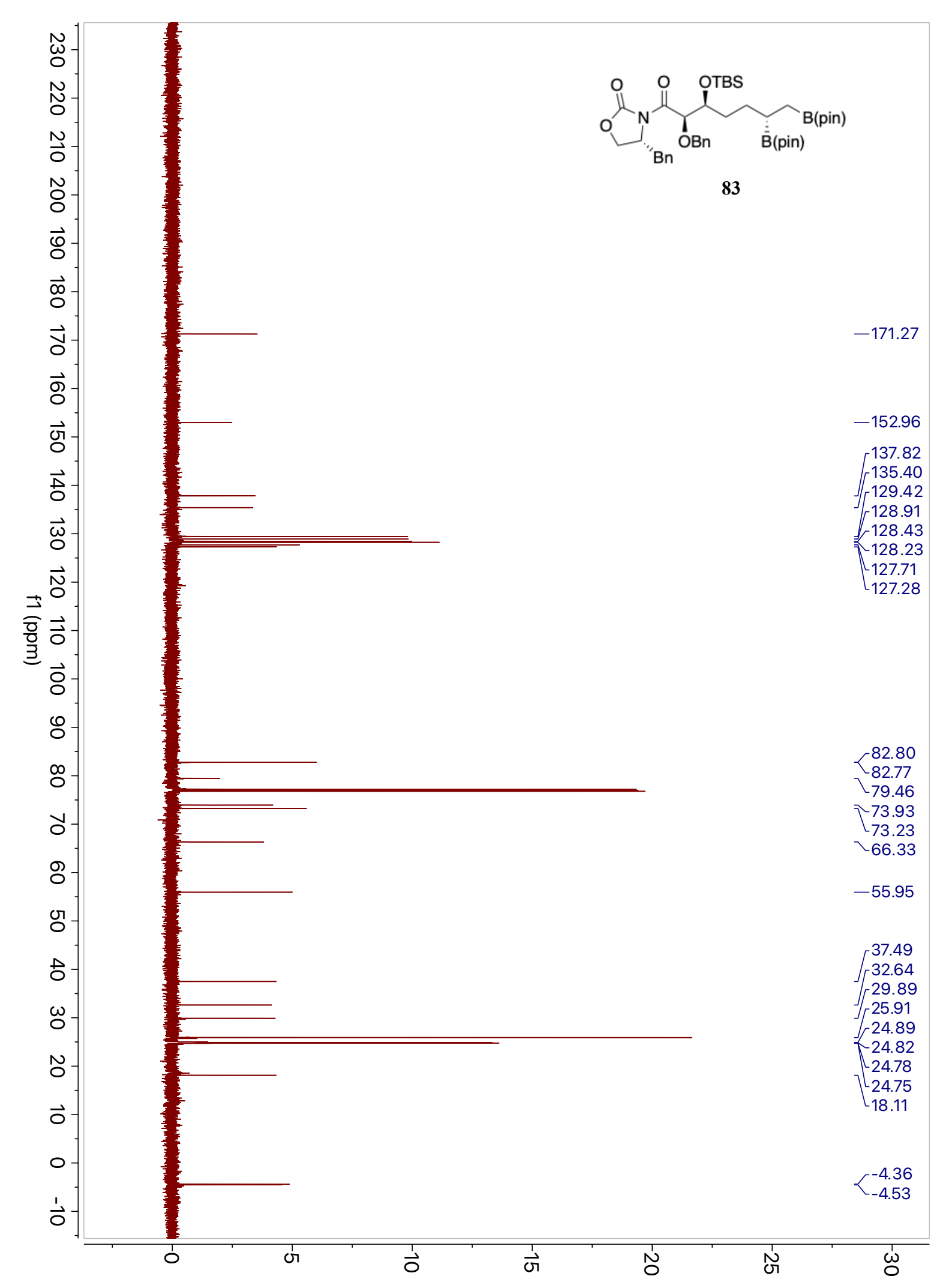

O
O
OH
N
O
OBn
Bn
80
f1 (ppm)
8.85
2.09
1.08
0.07
1.00
1.13
1.06
1.01
1.09
0.07
0.07
0.99
1.01
1.01
0.07
1.03
0.99
0.07
0.99
0.07
2.27
1.08
1.04
0.99
7.40
7.39
7.36
7.33
7.32
7.29
7.28
7.27
7.25
7.21
7.20
5.82
5.81
5.81
5.80
5.79
5.78
5.78
5.77
5.76
5.14
5.13
5.03
5.00
4.96
4.94
4.76
4.74
4.70
4.68
4.67
4.51
4.49
4.25
4.24
4.22
4.20
4.19
4.18
4.18
3.91
3.90
3.89
3.87
3.30
3.30
3.28
3.27
2.78
2.76
2.76
2.74
2.22
2.21
2.20
2.18
2.06
2.05
1.77
1.76
1.70

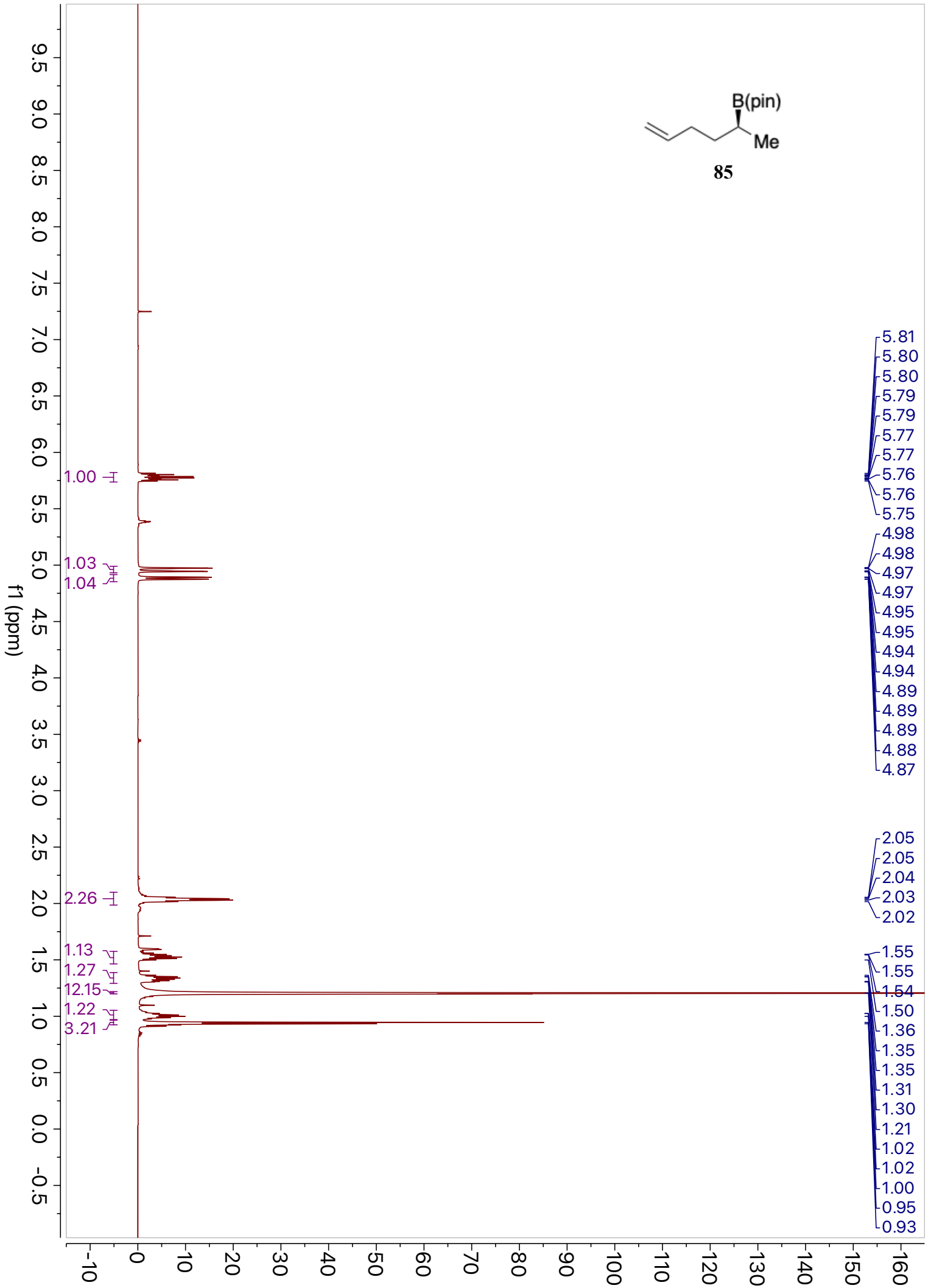

O
O
OH
N
O
OBn
Bn
80
170.62
153.41
137.97
137.00
135.05
129.40
129.01
128.53
128.43
128.24
127.46
114.94
79.34
72.97
72.02
66.99
55.63
37.71
33.32
29.70
f1 (ppm)

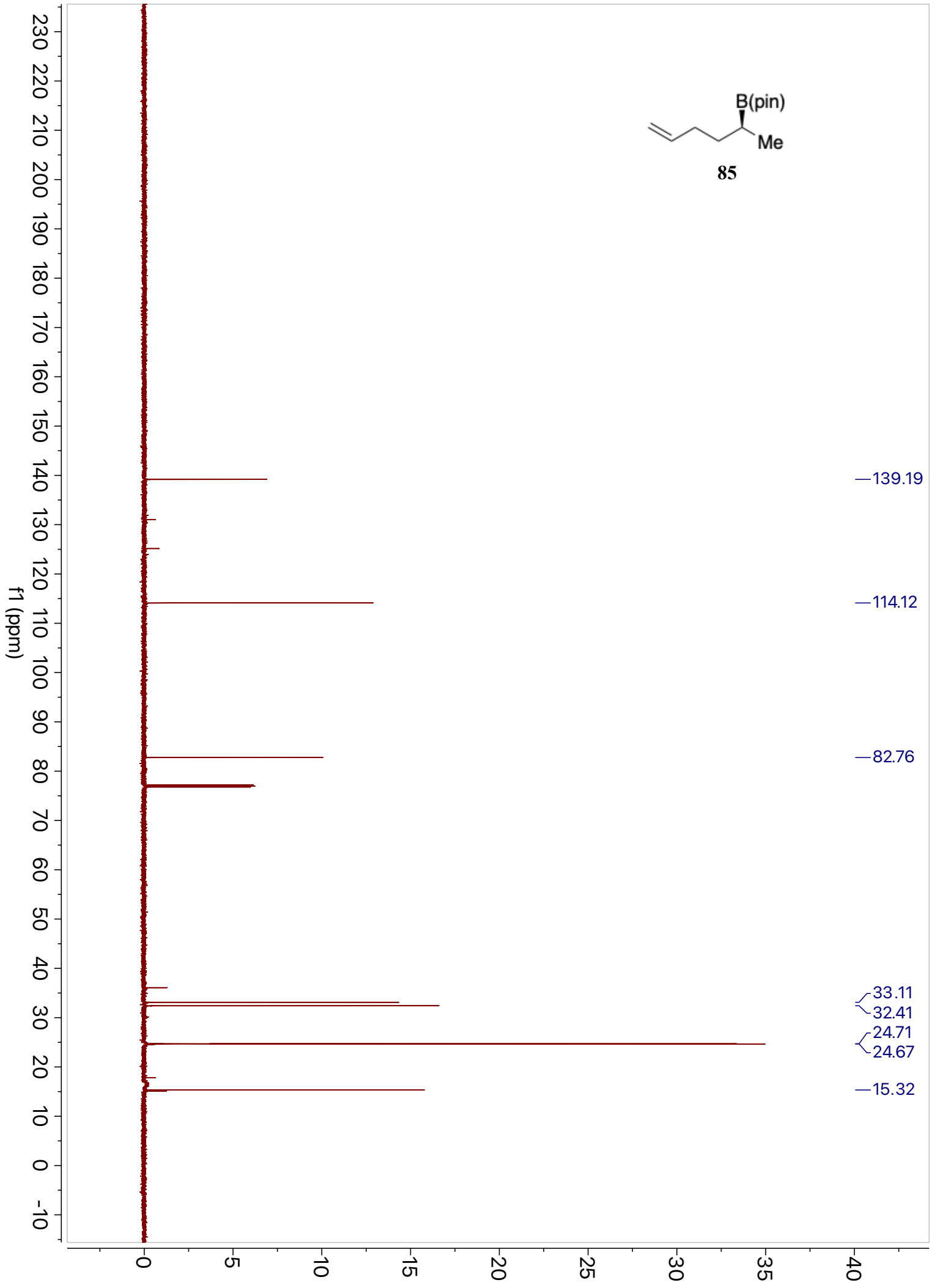

O
O
OTBS
N
O
OBn
Bn
81
f1 (ppm)
2.19
6.46
2.37
1.10
0.05
1.05
2.32
1.10
2.26
2.19
1.17
1.01
0.05
1.00
0.04
1.16
2.24
1.32
9.12
3.20
3.06
7.42
7.40
7.37
7.35
7.34
7.32
7.30
7.28
7.23
7.21
5.81
5.81
5.79
5.78
5.77
5.76
5.29
5.29
5.29
5.28
5.28
5.01
4.98
4.95
4.94
4.93
4.74
4.72
4.60
4.57
4.18
4.16
4.16
4.14
4.12
4.09
4.08
4.07
4.06
3.25
3.22
2.68
2.66
2.66
2.64
2.09
2.08
2.07
1.98
1.96
1.95
1.92
1.89
1.88
1.86
1.59
1.55
1.53
0.88
0.06
0.02

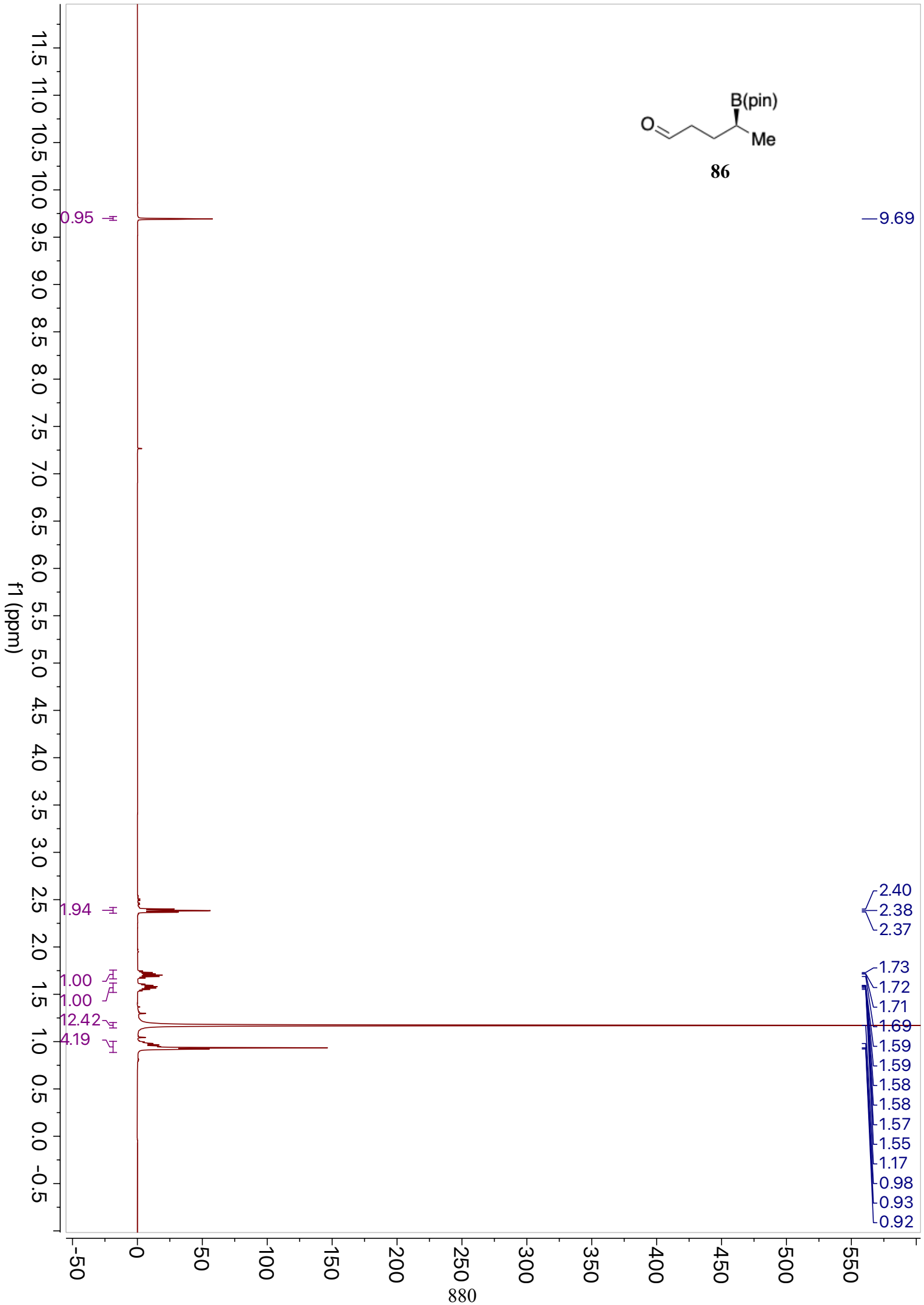

OTBS
O
O
N
O
OBn
Bn
81
171.09
153.07
138.30
137.63
135.25
129.44
128.98
128.44
128.36
127.93
127.40
114.57
78.99
73.12
72.79
66.50
55.97
37.56
32.69
29.57
25.86
18.09
-4.39
-4.58
f1 (ppm)

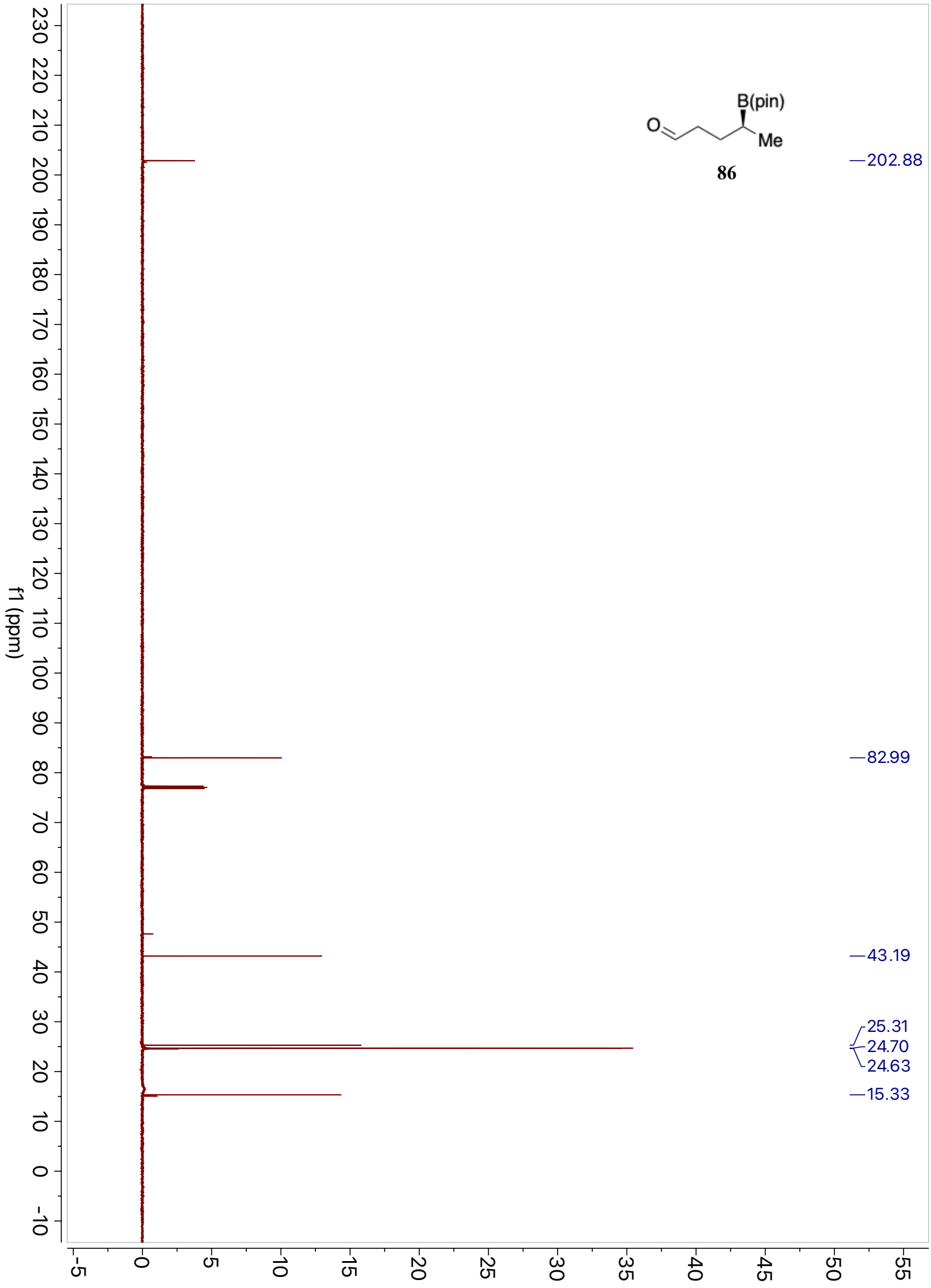

O
O
OTBS
N
O
B(pin)
OBn
B(pin)
Bn
83
f1 (ppm)


O
O
OTBS
N
O
B(pin)
OBn
B(pin)
Bn
83
171.27
152.96
137.82
135.40
129.42
128.91
128.43
128.23
127.71
127.28
82.80
82.77
79.46
73.93
73.23
66.33
55.95
37.49
32.64
29.89
25.91
24.89
24.82
24.78
24.75
18.11
-4.36
-4.53
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
0 5 10 15 20 25 30


B(pin)
Me
85
f1 (ppm)
1.00
1.03
1.04
2.26
1.13
1.27
12.15
1.22
3.21
5.81
5.80
5.80
5.79
5.79
5.77
5.77
5.76
5.76
5.75
4.98
4.98
4.97
4.97
4.95
4.95
4.94
4.94
4.89
4.89
4.89
4.88
4.87
2.05
2.05
2.04
2.03
2.02
1.55
1.55
1.54
1.50
1.36
1.35
1.35
1.31
1.30
1.21
1.02
1.02
1.00
0.95
0.93


B(pin)
Me
85
139.19
114.12
82.76
33.11
32.41
24.71
24.67
15.32
f1 (ppm)


B(pin)
O
Me
86
0.95
1.94
1.00
1.00
12.42
4.19
9.69
2.40
2.38
2.37
1.73
1.72
1.71
1.69
1.59
1.59
1.58
1.58
1.57
1.55
1.17
0.98
0.93
0.92
f1 (ppm)


B(pin)
O
Me
86
202.88
82.99
43.19
25.31
24.70
24.63
15.33
f1 (ppm)