1,2-Oxaborines: Synthesis, Properties, and Reactivity

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A thesis

submitted to the Faculty of

the department of Chemistry

in partial fulfillment

of the requirements for the degree of

Master of Science

Boston College
Morrissey College of Arts and Sciences
Graduate School

December 2017

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Despite extensive research in B–N-containing aromatic systems (most notably 1,2-azaborines) for their potential use in biomedicine and materials science, development of their oxygen counterparts, 1,2-oxaborines, remains underdeveloped. Presented herein is a straightforward route to access 1,2-oxaborines via a ring-closing metathesis strategy. Attempts to utilize the 1,2-oxaborine as a 1,3-diene in the Diels–Alder cycloaddition for potential application as a 4C + 1O synthon are also presented. Lastly, investigations regarding the aromaticity of the B–O heterocycles is probed using computations and isothermal reaction calorimetry.

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BCl_3	boron trichloride
BIPHEP	2,2'-Bis(diphenylphosphino)biphenyl
br	broad
Bu	*n*-butyl
CH_2Cl_2	dichloromethane
COD	1,5-cyclooctadiene
d	doublet
D	debye
DART	direct analysis in real time
dd	doublet of doublets
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL-H	diisobutylaluminum hydride
DMAD	dimethyl acetylenedicarboxylate
DMSO	dimethyl sulfoxide
dq	doublet of quartets
dtbpy	4,4'-Di-*tert*-butyl-2,2'-dipyridyl
equiv	equivalents
Et_2O	diethyl ether
Et_3N	triethylamine
h	hour(s)

H_2	hydrogen gas
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene)
$(i\text{Pr})_2\text{NH}$	diisopropylamine
KHMDS	Potassium bis(trimethylsilyl)amide
m	multiplet
MeOH	methanol
n-BuLi	*n*-butyllithium
NMR	nuclear magnetic resonance spectroscopy
PCy_3	tricyclohexylphosphine
Ph	phenyl
PPh_3	triphenylphosphine
PV	pressure vessel
Py	pyridine
q	quartet
RSE	resonance stabilization energy
RT	room temperature
s	singlet
t	triplet
THF	tetrahydrofuran
TMSCl	trimethylsilyl chloride

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my adviser, Professor Liu, for providing the opportunity to join his research group and pursue a new, rather unexplored area of chemistry. His understanding and guidance has allowed me to grow as a scientist, and recognize additional areas I hope to improve. I would also like to thank all members of the Liu group, with additional appreciation for Dr. Jacob Ishibashi and Zachary Giustra, who routinely provided advice on executing experiments. Additionally, Yuanzhe Zhang, has made my time in the Liu group enjoyable with his light-hearted demeanor and sense of humor.

I would like to acknowledge Professor Morken and Professor Byers for serving on my thesis committee. Special thanks are due to Professor Liu and Professor Morken who have greatly aided in my transition from graduate school to a career.

Prior to beginning graduate studies, my time in the lab of Professor Suzanne Blum was instrumental in solidifying my desire to pursue research. Professor Blum has since remained an invaluable mentor and provided unwavering support in both my academic and professional pursuits. Also while in the Blum lab, I had the opportunity to work alongside a formative mentor and friend, Dr. Darius Faizi, whose advice is still much appreciated.

Beyond BC, I must thank the multinational and multifaceted brunch crew, past and present members: Marie, Edith, Vivianna, Jayne, Sandra, Tony, Max, Emilie, and Charlotte. Our adventures, in and around the city, have been the highlight of my time in

Boston. In particular, special thanks is owed to Marie, who made difficult times bearable through her resolute commitment to our friendship and willingness to listen.

Lastly, I would like to thank my family who has provided ceaseless encouragement, support, and love. To my brothers, Michael and Chris, your unspoken support and interactions from afar have provided a piece of home during times of hardship. To my brother and roommate, Dr. Matthew Nava, your fortitude and compassion for all that you do, especially science, is unmatched. Growing up you've served as a testament to all that can be achieved through hard work, and the past two years have proven no exception. Despite your aversion to household duties and your lack of a green thumb, you've made my time in Boston more enjoyable than I could have ever imagined. To Bryan, your companionship and love has made the past two years possible. Your presence and calls have meant more than you can imagine. To my dad, Bill, I have appreciated your support and constant praise, even when it was unwarranted. And to my mother, Jean, I owe all that I've accomplished to your selflessness and sacrifice. All that you've done and continue to do for my brothers and I does not go unnoticed or unappreciated.

INTRODUCTION

The concept of isosterism was first introduced by Langmuir in 1919.[1] By this definition, molecules possessing the same number and arrangement of electrons were considered "isosteric". Furthermore, he declared isosteres with the same overall charge as isoelectronic. Nitrous oxide and carbon dioxide serve as a classic pair that is both isosteric and isoelectronic. Each molecule, comprised of a total of three atoms, has twenty-two electrons and an overall neutral charge. As observed by Langmuir, these similar electronic and structural features gave rise to markedly similar physical properties (**Table 1.1**).[2]

Table 1.1 Physical Properties of Isosteric N_2O and CO_2 Pair

	N_2O	CO_2
Critical Temperature (°C)	35.4	31.9
Critical Pressure (atm)	75	77
Density (g/mL)	0.856	0.858
Viscosity (Pa·s)	148×10^{-6}	148×10^{-6}
Formula of Hydrate	$N_2O{\cdot}6H_2O$	$CO_2{\cdot}6H_2O$

By analogy, ammonia-borane serves as an isostere of ethane. However, despite their identical electron count, ammonia-borane is a solid under standard conditions, exhibits a dipole moment of 5.2 D, and has a bond dissociation energy of 27.2 kcal/mol.[3,4]

[1] Langmuir, I. *J. Am. Chem. Soc.* **1919**, *41*, 1543–1559.
[2] Bradlow, H. L.; Vanderwerf, C. A.; Kleinberg, *J. Chem. Ed.* **1947**, *24*, 433–435.
[3] Thorne, L. R.; Suenram, R. D.; Lovas, F. J. *J. Chem Phys.* **1983**, *78*, 167–171.
[4] Grant, D. J.; Dixon, D. A. *J. Phys. Chem. A* **2006**, *110*, 12955–12962.

In stark contrast, ethane is a gas under standard conditions, exhibits no effective dipole moment, and has a bond dissociation energy of 90.1 kcal/mol.[5,6] These differences in physical properties also hold true for the isosteric and isostructural ethene and aminoborane pair as well. Under standard conditions, aminoborane largely exists in polymeric/oligomeric form. It has a net dipole moment of 1.844 D and has a bond dissociation energy of 139.7 kcal/mol.[4,7] As is the case with ethane, ethene is a gas under standard conditions, possesses no effective dipole moment, and has a bond dissociation energy of 174. 1 kcal/mol.[5,6] The unique physical and chemical properties imparted by replacement of a C–C bond with the complementary B–N bond, namely CC/BN isosterism, has resulted in a thrust of research geared toward the potential application of these heteroaromatic molecules in biomedicine and materials science.[8,9]

[5] Pritchard, R. H.; Kern, C. W. *J. Am. Chem. Soc.* **1969**, *91*, 1631–1635.
[6] Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255–263.
[7] Sugie, M.; Takeo, H.; Matsumura, C. *Chem. Phys. Lett.* **1979**, *64*, 573–575.
[8] Baker, S. J.; Tomsho, S. W.; Benkovic, S. J. *J. Chem. Soc. Rev.* **2011**, *40*, 4279–4285.
[9] Hudson, Z. M.; Wang, S. *Dalton Trans*. **2011**, *40*, 7805–7816.

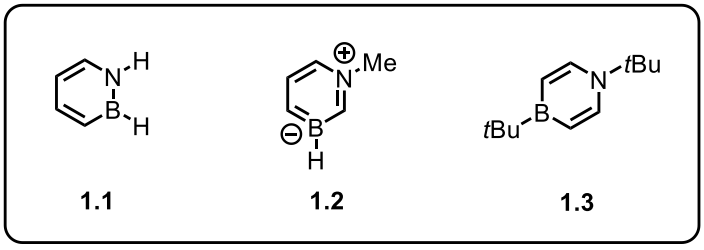
1.0 CHAPTER 1

1.1 FIRST REPORTS OF CC/BN ISOSTERISM

Alfred Stock reported the synthesis of the first CC/BN isosteric arene, borazine ($B_3N_3H_6$), in 1926.[10] Though commonly referred to as the "inorganic benzene", borazine possesses significantly less aromatic character relative to its organic counterpart.[11] This reduced aromaticity is presumed to be a result of the large electronegativity difference between boron and nitrogen, with much of the electron density localized on nitrogen, rather than delocalized around the ring.[12] Subsequent approaches utilizing CC/BN isosterism have generally involved the replacement of a singular C–C bond with a B–N unit.

The organic/inorganic hybrid 1,2-azaborine **1.1** evaded isolation until 2009 when Liu and co-workers devised an innovative "protection/deprotection" strategy to access and characterize the molecule.[13]

Figure 1.1 Isolated Azaborine Isomers



1.1 **1.2** **1.3**

Shortly after, the Liu group reported the synthesis and isolation of the first 1,3-

[10] Stock, A.; Pohland, E. *Ber. Dtsch. Chem. Ges.* **1926**, *59*, 2210–2215.
[11] (a) Hohnstedt, L. F.; Schaeffer, G. W. *Advances in Chemistry* **1961**, *32*, 232–240. (b) Chiavarino, B.; Crestoni, M. E.; Di Mariso, A.; Fornarini, S.; Rosi, M. *J. Am. Chem. Soc.* **1999**, *121*, 11204–11210. (c) Kiran, B.; Phukan, A. K.; Jemmis, E. D. Inorg. Chem. 2001, 40, 3615–3618. (d) Madura, I.; Krygowski, T. M.; Cyrański, M. K. *Tetrahedron* **1998**, *54*, 14913–14918.
[12] Lisovenko, A. S.; Timoshkin, A. Y. *Inorg. Chem.* **2010**, *49*, 10357–10369.
[13] Marwitz, A. J. V.; Matus, M. H. Zakharov, L. N.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2009**, *48*, 973–977.

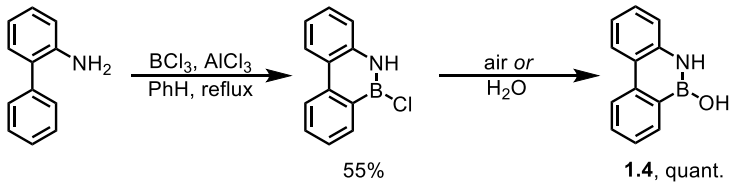
azaborine **1.2**.[14] That same year, Braunschweig and co-workers provided a route to access the simplest known 1,4-azaborine **1.3** via cyclotrimerization of acetylene with iminoborane, *t*BuN≡B*t*Bu, in the presence of a dimeric Rh(I) complex.[15] Theoretical studies completed on each of the three B–N constitutional isomers suggest the 1,2-azaborine is the most thermodynamically stable, and the 1,3-azaborine the least stable.[16] However, the 1,3-azaborine possesses the greatest aromaticity, followed by the 1,2-, and 1,4-azaborine, the difference between the 1,2- and the 1,4-azaborine being relatively small.[16]

[14] Xu, S.; Zakharov, L. N.; Liu, S.-Y. *J. Am. Chem. Soc.* **2011**, *113*, 20152–20155.
[15] Braunschweig, H.; Damme, A.; Jimenez-Halla, J. O. C.; Pfaffinger, B.; Radacki, K.; Wolf, J. *Angew. Chem. Int. Ed.* **2012**, *51*, 10034–10037.
[16] (a) Kranz, M.; Clark, T. *J. Org. Chem.* **1992**, *57*, 5492–5500. (b) Xu, S.; Mikulas, T. C.; Zakharov, L. N.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 7527–7531. (c) Matus, M. H.; Liu, S.-Y.; Dixon, D. A. *J. Phys. Chem. A.* **2010**, *114*, 2644–2654. (d) Baranac-Stojanovic, M. *Chem. Eur. J.* **2014**, *20*, 16558–16565.

1.2 PIONEERING STUDIES IN AZABORINE CHEMISTRY

In 1958, Dewar and co-workers reported the synthesis of a novel class of B–N-containing compounds, 9,10-azaboraphenanthrenes.[17] These isostructural and isoelectronic analogues of phenanthrene, whereby the C–C double bond between C9 and C10 was replaced with a B–N unit, represented the first neutral, aromatic B–N-containing compounds, save for borazine. Preparation of the 9,10-azaboraphenanthrene commenced by heating 2-aminobiphenyl in the presence of boron trichloride to generate the intermediate 2-biphenylaminoboron dichloride (**Scheme 1.1**). Upon heating with aluminum chloride, the aromatic compound was generated. The ultraviolet spectra of the hydroxyl derivative **1.4** of the 9,10-azaboraphenanthrene shows a bathochromic shift relative to the all-carbon counterpart, phenanthrene. The marked differences in the spectra suggest the compounds behave as aromatic analogues of phenanthrene rather than cyclic boron amides.[17]

Scheme 1.1 Dewar's Synthesis of 9,10-azaboraphenanthrenes

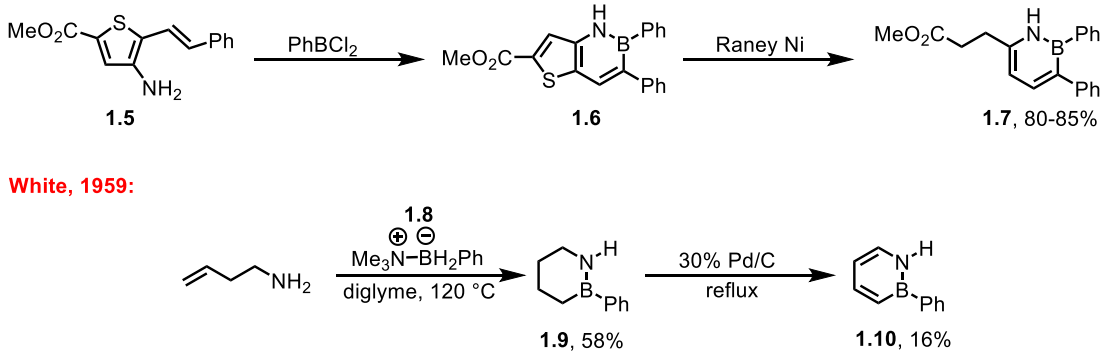


55% **1.4**, quant.

[17] Dewar, M. J. S.; Kubba, V. P.; Pettit, R. *J. Chem. Soc.* **1958**, *0*, 3073–3076.

Following this seminal report, in 1962 Dewar et al. described the synthesis of the first monocyclic 1,2-azaborine via a desulfurization strategy (**Scheme 1.2**).[18] Condensation of **1.5** with dichlorophenylborane gave 2-carbomethoxy-5,6-diphenyl-5,4-borazarobenzothiophene **1.6**. Reduction using Raney nickel afforded the 3,6-disubstituted 1,2-azaborine **1.7**. The recalcitrant nature of **1.7** to acidic and basic solutions suggested considerable stability, even after prolonged periods. Shortly after Dewar's landmark synthesis, White reported the isolation of the *B*-Ph-1,2-azaborine. Using a more general approach, White and co-workers envisioned accessing the azaborine core via a dehydrogenation of the cyclic 1,2-azaboracyclohexane **1.9**.[19] **1.9** was prepared by reaction of 3-butenylamine with **1.8**. The authors propose formation of the ring by initial generation of a tertiary amine adduct of phenylborane. These adducts have previously been shown to be competent intermediates in hydroboration reactions.[20] The dehydrogenation was then facilitated by Pd/C to generate **1.10**. Again, the resistance of the 1,2-azaborine to oxidation and solvolysis was attributed to the aromatic stabilization gained following dehydrogenation.

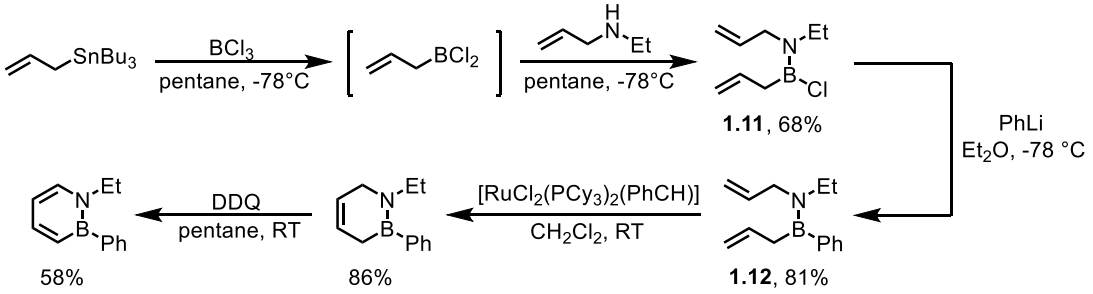
Scheme 1.2 Pioneering Strategies to Access Monocyclic 1,2-Azaborines



[18] Dewar, M. J. S.; Marr, P. A. *J. Am. Chem. Soc.* **1962**, *84*, 3782.
[19] White, D. G. *J. Am Chem. Soc.* **1963**, *85*, 3634–3636.
[20] Ashby, E. C. *J. Am. Chem. Soc.* **1959**, *81*, 4791–4795.

1.3 ADVANCES IN AZABORINE SYNTHESIS

Scheme 1.3 Ashe's Initial Synthetic Route to 1,2-Azaborines

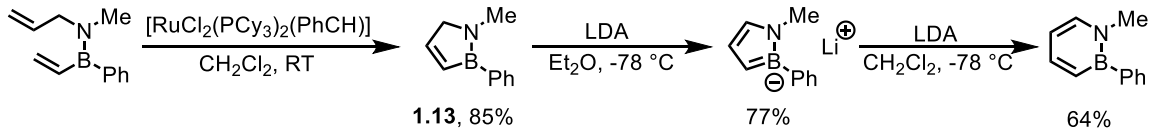


Despite the pioneering work completed by Dewar and White on both polycyclic and monocyclic 1,2-azaborines, progress in the field was hampered by the lack of a straightforward and modular synthesis to access the heteraromatic core. A new approach was reported by Ashe and co-workers leveraging the ruthenium-based olefin metathesis catalyst recently developed by Grubbs.[21,22] In this vein, allyltributyltin was treated with boron trichloride to generate the allylboron dichloride *in situ* (**Scheme 1.3**). Addition of ethyl allylamine generated the diene moiety necessary for the key transformation and subsequent addition of phenyllithium was used to convert **1.11** to the less electrophilic species **1.12**. The six-membered ring was then generated using Grubbs' first generation catalyst and oxidized to the 1,2-azaborine using DDQ.

[21] Ashe, A. J.; Fang, X. *Org. Lett.* **2000**, *2*, 2089–2091.
[22] (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039–2041. (b) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118,* 100–110.

Shortly thereafter, the Ashe group presented another method to access 1,2-azaborines from the five-membered azaborole **1.13** which could be prepared using an analogous ring-closing approach (**Scheme 1.4**).[23] Upon deprotonation, the azaborolide could undergo carbene insertion to generate the ring expanded 1,2-azaborine.

Scheme 1.4 Ashe's Ring-Expansion Protocol Towards the Synthesis of 1,2-Azaborines

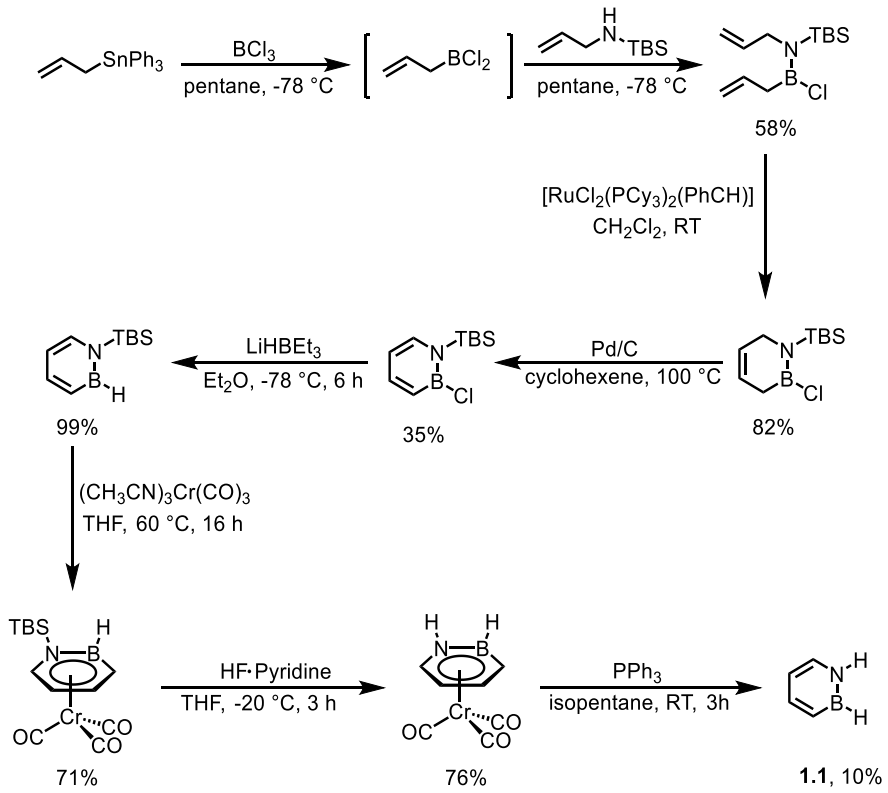


1.13, 85% 77% 64%

Contributions by the Liu group towards the general synthesis of 1,2-azaborines included a route that carried a versatile *B*-Cl moiety throughout the ring-closing and oxidation protocols (**Scheme 1.5**).[13] Once the aromatic molecule was generated, the boron substituent could be easily exchanged by treatment with an array of nucleophiles. The presence of the silyl protecting group on the nitrogen aided in the isolation of the parent 1,2-azaborine **1.1** by the Liu group in 2009, albeit in low yield.[13] Due to subsequent difficulties removing the silyl group, Liu et al. sought to develop a protecting group-free synthesis of the nitrogen heterocycles.[24]

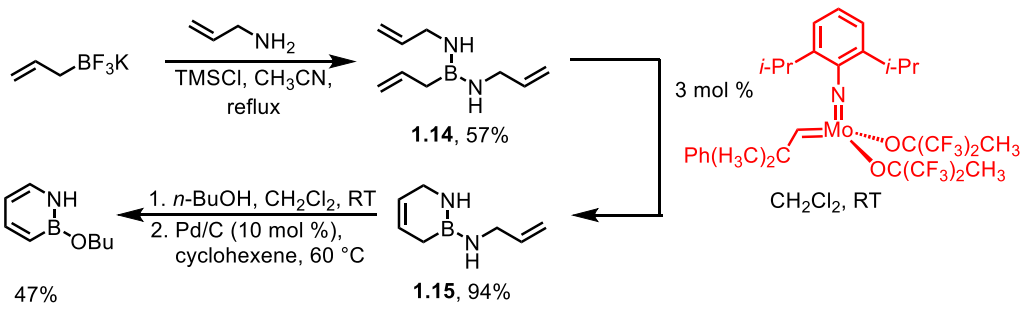
[23] Ashe, A. J.; Fang, X.; Fang, X.; Kampf, J. W. *Organometallics* **2001**, *20*, 5413–5418.
[24] Abbey, E. R.; Lamm, A. N.; Baggett, A. W.; Zakharov, L. N.; Liu, S.-Y. *J. Am. Chem. Soc.* **2013**, *135* (34), 12908–12913.

Scheme 1.5 Contibutions from Liu Group Using Versatile B-Cl Intermediate



Utilizing the method outlined in **Scheme 1.6**, allylboron dichloride was generated *in situ* by treatment of the potassium allyltrifluoroborate salt with TMSCl. Following generation of the allylborane, addition of two equivalents of allylamine furnished triene **1.14**. Ring-closing metathesis of **1.14** with Schrock's Mo catalyst afforded **1.15**, which upon exchange and oxidation delivered the *B*–OBu-1,2-azaborine. From this versatile synthon, several 1,2-azaborine derivatives could be isolated through routine transformations.

Scheme 1.6 Protecting Group-Free Strategy to Versatile B-OBu Moiety

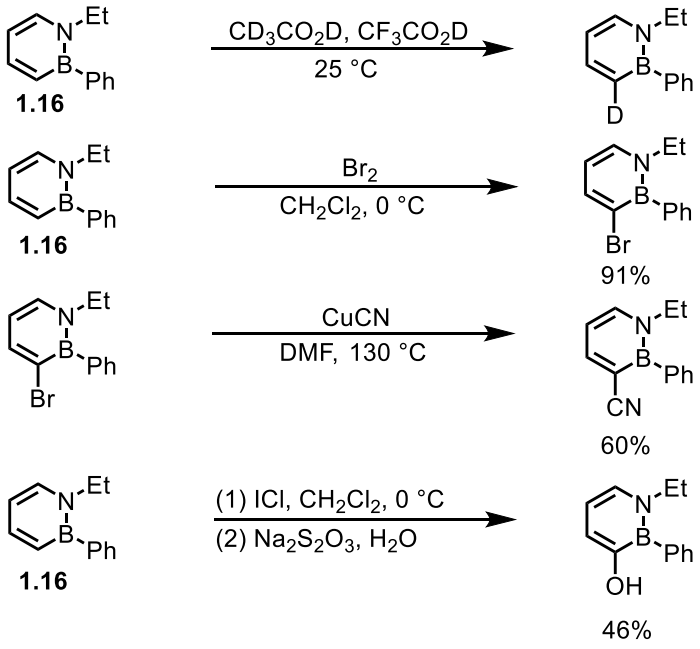


1.4 ELABORATION OF THE AZABORINE CORE

1.4.1 Functionalization Reactions of 1,2-Azaborines

Despite the methods described above to access the 1,2-azaborine core, investigations into their functionalization and subsequent reactivity were not thoroughly explored until 2007. In this regard, Ashe and co-workers disclosed various functionalization reactions of the *B*-Ph-*N*-Et-1,2-azaborine via electrophilic substitution reactions.[25] Simple acid-catalyzed proton–deuterium isotope exchange using a 1:3 w/w mixture of trifluoroacetic acid-d_1 and acetic acid-d_4 provided the C3-deuterated heterocycle (**Scheme 1.7**). After prolonged reaction times in the acidic mixture, however, generation of phenylboroxine was observed.

Scheme 1.7 Electrophilic Aromatic Substitution of 1,2-Azaborines

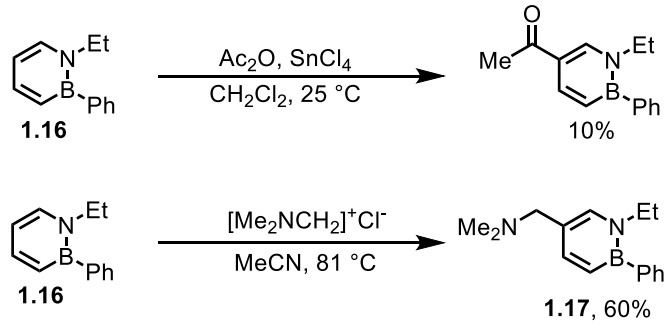


[25] Pan, J.; Kampf, J. K.; Ashe, A. J. *Org. Lett.* **2007**, *9*, 679–681.

Consistent with the sufficiently nucleophilic character at the C3-position, facile bromination was also observed.[13,25] Ashe *et al*. subsequently showed that conversion of the bromide to the nitrile could be achieved by addition of CuCN in DMF at 130 °C. Similarly, the 3-hydroxy-1,2-azaborine could be generated first by reaction of **1.16** with iodine monochloride followed by quenching in the presence of $Na_2S_2O_3$ (**Scheme 1.7**).

Substitution was also observed at the 5-position of the 1,2-azaborine (**Scheme 1.8**). Upon treatment of **1.16** with acetic anhydride and $SnCl_4$, the acetylated product was isolated, however, the production of a number of byproducts resulted in a poor yield. In this same manner, the aminated product **1.17** was generated by addition of **1.16** to the iminium chloride. The results of the Ashe group experimentally confirmed the findings of previously completed MO calculations which revealed significant electron-density at the C3- and C5-positions.[26]

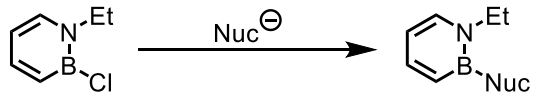
Scheme 1.8 Electrophilic Aromatic Substitution at C5



[26] (a) Kranz, M.; Clark, T. *J. Org. Chem.* **1992**, *57*, 5492–5500. (b) Kar, T.; Elmore, D. E.; Scheiner, S. *J. Mol. Struct.* **1997**, *392*, 65–74.

Shortly after the publication by the Ashe group, the Liu group presented a general method to synthesize *B*-substituted 1,2-azaborines through nucleophilic exchange.[27] Using **1.18** as a precursor, alkyl-, vinyl-, aryl-, and alkynyl-substituted azaborines were isolated after treatment with the corresponding organolithium or Grignard reagent. Furthermore, heteroatom-based nucleophiles could be used to synthesize several unprecedented products including those generated from nucleophiles shown in entries **5** and **6** (**Table 1.2**).

Table 1.2 Nucleophilic Addition to *B*-Cl-1,2-Azaborine



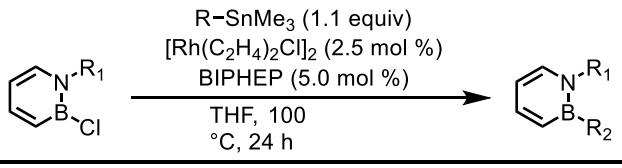
1.18

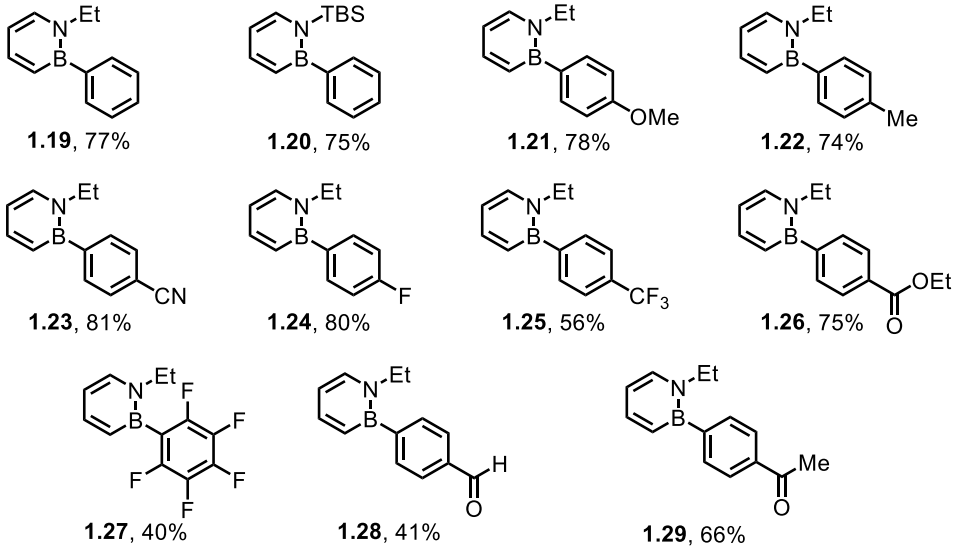
Entry	Nucleophile (Nuc)	Yield
1	Li—Bu	79%
2	Li—vinyl	50%
3	BrMg—Ph	76%
4	BrMg—≡—Ph	83%
5	Li—NMe_2	66%
6	K–SBn	80%
7	K–O*t*Bu	71%
8	Et_3BLi—H	92%

Later, in 2013 the Liu group described methods for the rhodium-catalyzed boron arylation of 1,2-azaborines.[28] Though arylation was previously described using nucleophilic substitution at boron (*vide supra*), the scope was limited to functional groups that were compatible with the organolithium and organomagnesium reagents. Seeking to address this limitation, a rhodium-catalyzed cross-coupling reaction of *B*-Cl-1,2-azaborines and arylstannanes was developed (**Scheme 1.9**).

[27] Marwitz, A. J. V.; Abbey, E. R.; Jenkins, J. T.; Zakharov, L. N.; Liu, S.-Y. *Org. Lett.* **2007**, *9*, 4905–4908.
[28] Rudebusch, G. E.; Zakharov, L. N; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 9316–9319.

Scheme 1.9 Rhodium-Catalyzed Boron Arylation of 1,2-Azaborines



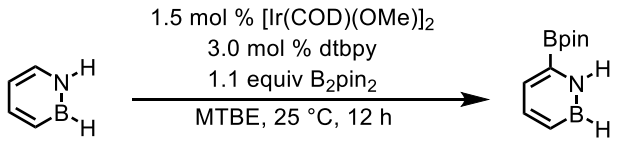


With chlorobis(ethylene)rhodium(I) dimer identified as the optimal catalyst and BIPHEP as the optimal supporting ligand, the scope of the arylation protocol was explored. Electron-donating and electron-withdrawing groups at the *para*-position were well tolerated, however, the electron-deficient pentafluorostannane **1.27** gave low yields of product. Arylstannanes **1.28** and **1.29** bearing electrophilic moieties incompatible with the previously described method could be isolated in 41% and 66% yield, respectively.

In attempts to further develop methods for the functionalization of the 4-, 5-, and 6-positions of the 1,2-azaborine backbone, it was envisioned by the Liu group that installation of chelating groups at the 6-position would present the opportunity to synthesize BN-containing bidentate ligands. As such, Ir-catalyzed C–H borylation of 1,2-azaborines was investigated due to the success of this reaction for other nitrogen-containing

heterocycles. Using a 1:2 ratio of $[Ir(COD)(OMe)]_2$ and dtbpy, borylation was regioselective for the 6-position of the parent 1,2-azaborine **1.1** (**Scheme 1.10**).[29]

Scheme 1.10 C6-Borylation of Parental 1,2-Azaborine



1.1

1.4.2 Applications of 1,2-Azaborines in Organic Synthesis

Beyond their synthesis and functionalization, the chemistry of monocyclic 1,2-azaborines is limited. Prior work conducted by the Liu group, namely isothermal reaction calorimetry, revealed the resonance stabilization energy of 1,2-azaborines to be approximately 17 kcal/mol.[30] Though essentially half that of benzene (RSE ~32 kcal/mol), this result is on par with other heteroaromatic compounds including pyrrole (RSE ~21 kcal/mol), thiophene (RSE ~20 kcal/mol), and furan (RSE ~15 kcal/mol).[31,32] The participation of these heterocycles in various [4+2] cycloaddition reactions served as the impetus for exploring the competency of the 1,2-azaborine as a 1,3-diene in the Diels–Alder reaction. As such, it was envisioned by Liu and co-workers that the 1,2-azaborine motif could potentially serve as a 4C + 1N synthon in organic synthesis.[33]

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[29] Baggett, A. W.; Vasiliu, M.; Li, B..; Dixon, D. A.; Liu, S.-Y. *J. Am. Chem. Soc.* **2015**, *137*, 5536–5541.

[30] Campbell, P. G.; Abbey, E. R.; Neiner, D.; Grant, D. J.; Dixon, D. A.; Liu, S.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 18048–18050.

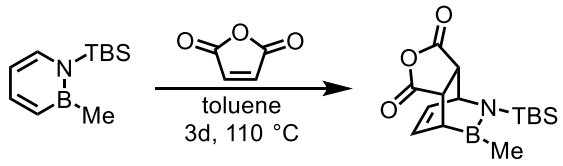
[31] The RSE values are predicted computationally using the following exchange reaction (benzene as an example): $C_6H_6 + C_6H_{10} \rightarrow 2C_6H_8$

[32] Burford, R. J.; Li, B.; Vasiliu, M.; Dixon, D. A.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 7823–7827.

[33] (a) Kozmin, S. A.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 5252–5253. (b) Janey, J. M.; Iwama, T.; Kozmin, S. A.; Rawal, V. H. *J. Org. Chem.* **2000**, *65*, 9059–9068.

This would ultimately narrow the gap within the literature regarding the reactivity of 1,2-azaborines, and impressively, result in the generation of functionally complex allylic amines.

Scheme 1.11 Thermal Diels-Alder Cycloaddition of 1,2-Azaborines

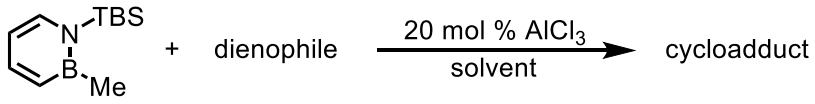


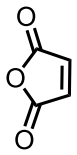
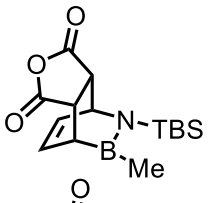
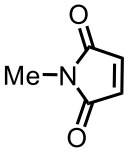
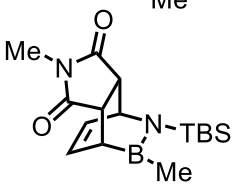
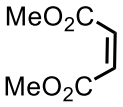
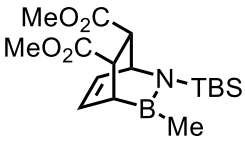
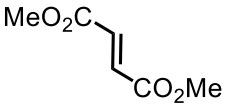
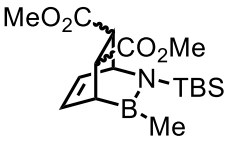
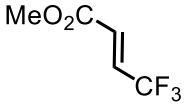
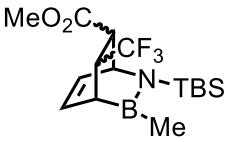
Reaction of *B*-Me-*N*-TBS-1,2-azaborine with maleic anhydride at 110 °C proceeded to completion, but required extended reaction times. As such, a number of Lewis acids were screened with $AlCl_3$ proving optimal.

With established conditions, a survey of substituent effects revealed the importance of the *N*–TBS substituent for Diels–Alder reactivity. Furthermore, the boron substituent was found to exert significant influence as well. Both methyl and isopropoxy substituents on boron were effective for the cyclization, while the *N*-TBS-*B*-Ph-1,2-azaborine was intermediate in reactivity, delivering the endo diastereomer in 62% yield. The *sp*-hybridized *B*-alkynyl and *B*-H-substituted 1,2-azaborines furnished only trace amounts of the cycloaddition product. These results reveal that the observed Diels–Alder reactivity directly correlates with the aromaticity of the heterocycle; the more aromatic the molecule, the lower the thermodynamic driving force for the cycloaddition to occur.

When probing the dienophile scope, high diastereoselectivity was achieved for (*Z*)-dienophiles. However, (*E*)-dienophiles gave approximately 1:1 mixtures of diastereomers (**Table 1.3**). When dimethylmaleate and dimethylfumurate were utilized, full conversion to the cycloadduct was not achieved, despite altering the reaction parameters. This observation suggested the possibility of a reversible reaction.[34] To probe this hypothesis,

methyl acrylate was used as a less electron-deficient dienophile. Under the reaction conditions, cycloaddition of **1.30** with methyl acrylate delivered two diasteromeric products, *endo*-**1.31** and *exo*-**1.31**. Addition of one equivalent on *N*-Methylmaleimide resulted in complete conversion to the cycloadduct, further supporting the claims of a reversible reaction (**Scheme 1.12**).



Dienophile	Cycloadduct	NMR Yield (%)
		96[a] >95:5 d.r.
		95[a] >95:5 d.r.
		9[b] >95:5 d.r.
		43[b] 1.1:1 d.r.
		90[b] 1.1:1 d.r.

[a]Monitored after 12 h at room temperature in toluene.
[b]Monitored after 12 h at 50 °C in CH_2Cl_2.

[34] (a) Hirsch, A. K. H.; Reutenauer, P.; Le Moignan, M.; Ulrich, S.; Boul, P. J.; Harrowfield, J. M.; Jarowski, P. D.; Lehn, J.-M. *Chem. Eur. J.* **2014**, *20*, 1073–1080. (b) Kotha, S.; Banerjee, S. *RSC Adv*. **2013**, *3*, 7642–7666.

Scheme 1.12 Reversible Cycloaddition Using Methyl Acrylate as Dienophile

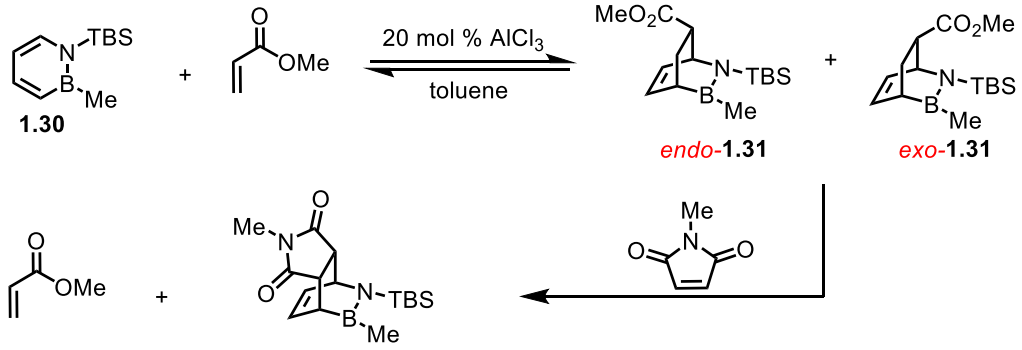
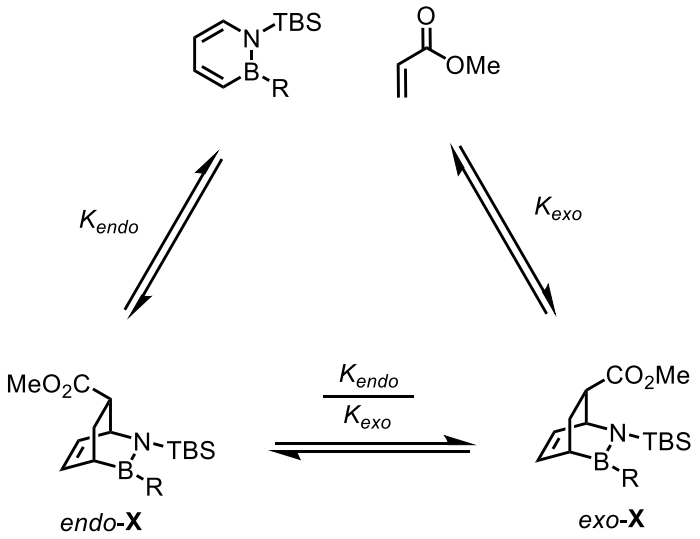


Figure 1.2 Thermodynamic Parameters for Diels-Alder Reaction Involving 1,2-Azaborines



Adduct	R	ΔG_{298K} (kcal/mol)	K	ΔH (kcal/mol)	ΔS (e.u.)
endo-**1.31**	Me	-2.0 ± 0.1 (-2.3)	30.1	-13.4 ± 0.5 (-17.8)	-38.0 ± 2.0 (-44.9)
exo-**1.31**	Me	-1.7 ± 0.1 (-1.4)	19.1	-14.3 ± 0.9 (-19.2)	-42.0 ± 3.0 (-51.5)
endo-**1.32**	≡—H	-0.4 ± 0.1 (-0.6)	2.1	-12.0 ± 1.0 (-16.6)	-39.0 ± 3.0 (-46.4)
exo-**1.32**	≡—H	-0.2 ± 0.1 (+0.2)	1.4	-15.0 ± 1.0 (-16.9)	-51.0 ± 4.0 (-49.1)

Determination of the equilibrium constants for the formation of each diastereomer allowed for the subsequent determination of the free energy (ΔG) for the formation for each diastereomer as well as the reaction enthalpy (ΔH) and entropy (ΔS). Analysis of the reaction parameters revealed a larger driving force for the formation of the *endo* diastereomer and a larger driving force for cycloadduct formation for the *B*-Me-1,2-azaborine relative to the *B*-alkynyl substituted 1,2-azaborine **1.32**.

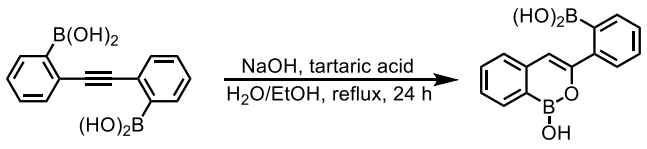
This work completed by the Liu group represents the first use of 1,2-azaborines as intermediates in organic synthesis, and paves the way for exploring additional reactivity of these BN-containing heterocycles, and related compounds.

2.0 CHAPTER 2

2.1 INITIAL METHODS FOR THE SYNTHESIS OF 1,2-OXABORINES

The first benzofused oxaborine was serendipitously discovered by Nazy and co-workers upon heating mildly basic solutions of 2,2'-tolandiboronic acid, **2.1**.[35] Elemental analysis revealed the byproduct was an isomer of **2.1** and neutralization indicated the presence of one remaining boronic acid group. The formation of **2.2** was further corroborated by the appearance of a sharp band in the C=C region of the IR spectrum.

Scheme 2.1 Formation of 1,2-Oxaborine by Rearrangement of Diboronic Acid



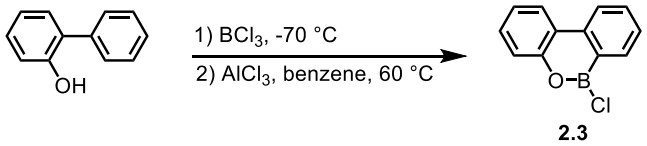
2.1 **2.2**, 90%

Following the report by Nazy, Dewar and co-workers described the synthesis of 9,10-boroxarophenanthrene, a heteroaromatic derivative of phenanthrene.[36] Treatment of 2-phenylphenol with boron trichloride delivered the dichlorophenoxyborane intermediate and subsequent addition of $AlCl_3$ at 60 °C afforded **2.3**. The spectra of the hydroxyl derivative of **2.3** bears close resemblance to those of the previously synthesized 9,10-azaboraphenanthrenes, which the authors imply is a consequence of the considerable

[35] Letsinger, R. L.; Nazy, J. R. *J. Am. Chem. Soc.* **1959**, *81*, 3013–3017.
[36] Dewar, M. J. S.; Dietz, R. *Tetrahedron Lett.* **1959**, *1*, 21–23.

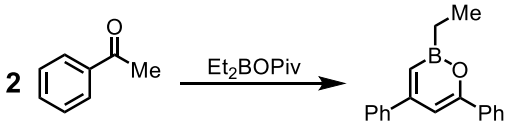
aromatic character. Additionally, the reluctance of 10-hydroxy-10,9-boroxarophenanthrene to undergo hydrolysis of the C–B bond and oxidation was attributed to significant π-delocalization.

Scheme 2.2 Dewar's Synthetic Strategy to Access 9,10-boroxarophenanthrene



2.3

Scheme 2.3 Isolation of First Monocyclic 1,2-Oxaborine



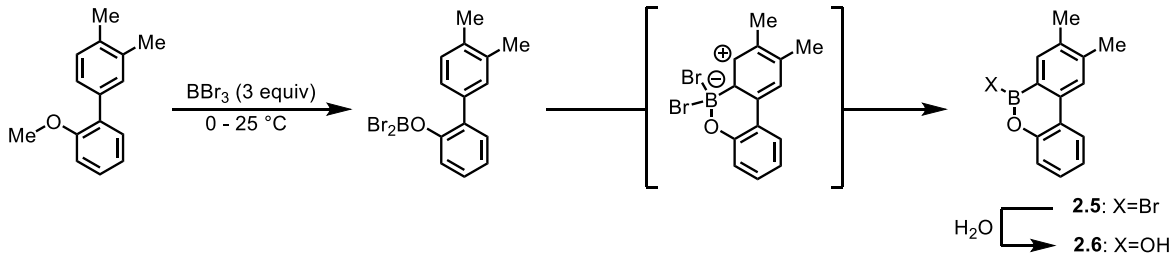
2.4

The first monocyclic 1,2-oxaborine **2.4** was inadvertently generated upon condensation of acetophenone and diethylboryl pivalate by Köster et al.[37] However, after isolation of the monocyclic 1,2-oxaborine **2.4**, synthesis of boron- and oxygen-containing aromatic systems was largely limited to fused-ring derivatives of naphthalene and phenanthrene. In this vein, Dolle and co-workers synthesized various analogues of the 10-hydroxy-10,9-boroxarophenanthrenes previously reported by Dewar.[38] A similar strategy was employed to access these derivatives involving demethylation of 2-methoxybiaryls by boron tribromide. In the absence of a methyl substituent at the 3' position, the authors observe conversion to the phenol upon hydrolysis. In contrast, the presence of a methyl group in the 3' position provides access to the title compound **2.6** following intramolecular electrophilic aromatic substitution, rearomatization, and hydrolysis. In addition to accessing these motifs through demethylation of 2-methoxybiaryls, Dolle et al. streamlined

[37] Köster, R.; Pourzal, A.-A. *Synthesis* **1973**, *11*, 674–676.
[38] Zhou, Q. J.; Worm, K.; Dolle, R. E. *J. Org. Chem.* **2004**, *69*, 5147–5149.

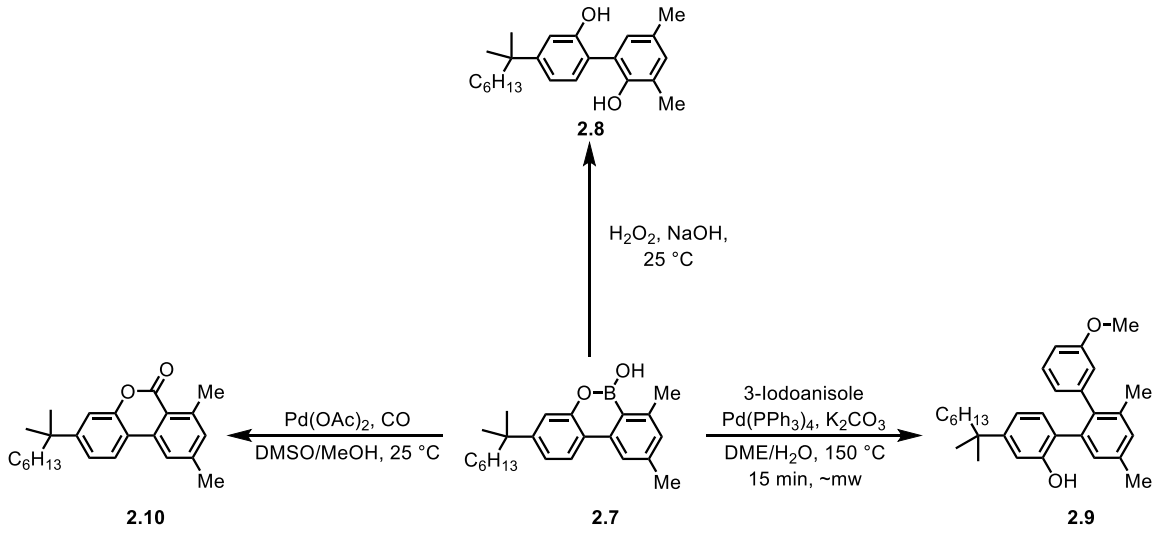
the conditions developed by Dewar to synthesize 10-hydroxy-10,9-boroxarophenanthrenes from 2-hydroxybiphenyls bearing varying substitution patterns.

Scheme 2.4 Demethylation Strategy for the Synthesis of Benzofused 1,2-Oxaborines



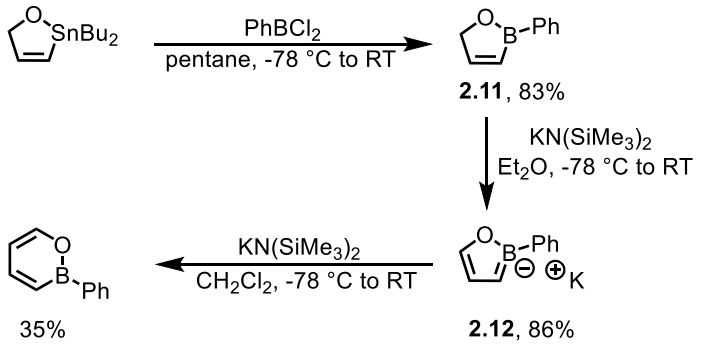
Interestingly, Dolle and co-workers also sought to utilize the boroxarene **2.7** as a synthetic intermediate. Oxidation of **2.7** gave the dihydroxy compound **2.8**, while Suzuki cross-coupling allowed for the isolation of triaryl product **2.9**. Lastly, through the intermediacy of **2.7**, the benzofused lactone **2.10** could be synthesized by palladium-catalyzed carbonylation.

Scheme 2.5 Dolle's Downstream Functionalization of Benzofused 1,2-Oxaborines



2.2 ADVANCEMENTS IN OXABORINE SYNTHESES

Scheme 2.6 Ashe's Route to Generate Minimally-Substituted 1,2-Oxaborines



In 2007, the Ashe group implemented a route, previously developed by their lab for the synthesis of 1,2-azaborines, in order to access minimally substituted 1,2-oxaborines in a straightforward manner.[39] Synthesis of the oxaborolide intermediate **2.12** was achieved by transmetallation of the oxastannole with dichlorophenylborane. Deprotonation of the 2-substituted-2,5-dihydro-1,2-oxaborole **2.11** generated the oxaborolide. Once the oxoborolide was obtained, the 1,2-oxaborine was formed via a carbenoid ring-expansion mediated by CH_2Cl_2 and KHMDS. Use of deuterated solvent resulted in complete deuterium incorporation at the 3-position, consistent with the proposed *in situ* generation of chlorocarbene followed by insertion adjacent to boron, and loss of chloride.[39]

2.2.1 Reactivity Investigations of 1,2-Oxaborines Enabled by the Ashe Synthesis

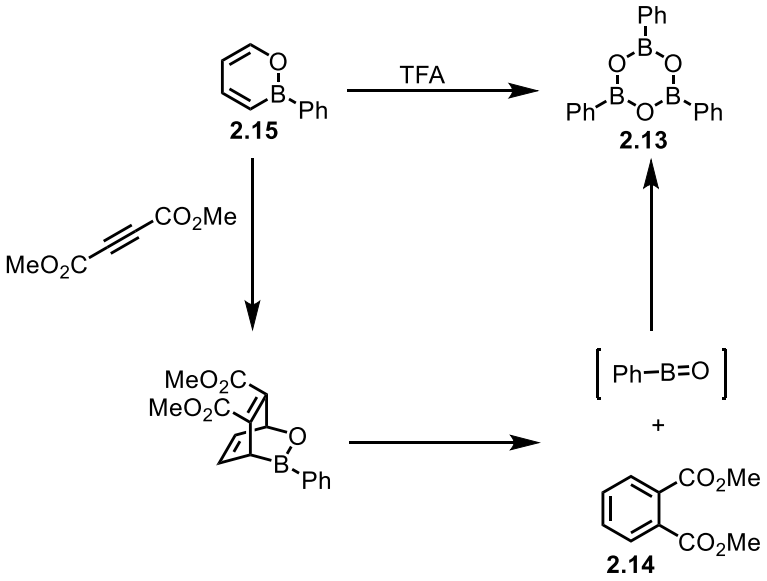
The synthesis of the *B*-Ph-1,2-oxaborine by the Ashe group provided important

[39] Ashe, A. J.; Fang, X. D.; Fang, X. G.; Kampf, J. W. *Organometallics* **2001**, *20*, 5413–5418.

insights regarding the aromaticity of the small molecule. The ^{1}H, ^{11}B, and ^{13}C NMR spectra of the 1,2-oxaborine were found to display chemical shifts similar to those of the complementary 1,2-azaborine, previously established to possess classical aromatic properties.[25] Additionally, complexation of the *B*-Ph-1,2-oxaborine with $Cr(CO)_3(CH_3CN)_3$ revealed exclusive binding of the phenyl substituent with the metal center, as opposed to the heteroaromatic core.[40] This observation is in contrast to the 1,2-azaborine case in which the heteroaromatic core coordinates with the chromium center. It should, however, be noted that upon heating the phenyl-coordinated 1,2-azaborine complex is generated. Comparison of the endocyclic and exocyclic B–C bond lengths of the *B*-Ph-1,2-oxaborine metal complex, 1.481(8) Å and 1.567(7) Å, respectively, are consistent with electron delocalization within the ring. Lastly, the Ashe group utilized the 1,2-oxaborine as a 1,3-diene in the Diels–Alder reaction with DMAD, giving phenylboronic anhydride **2.13** and dimethyl phthalate **2.14**. Compound **2.13** was similarly generated upon treatment of **2.15** with trifluoroacetic acid. Despite the aromatic properties of the 1,2-oxaborine, the observed reactivity is distinct from that previously established with the 1,2-azaborine.

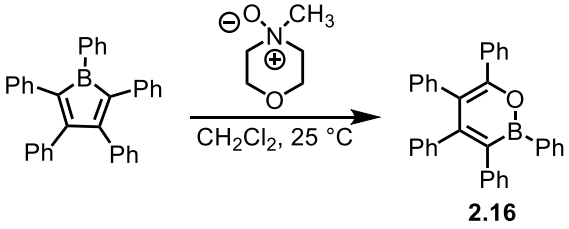
[40] Pan, J.; Kampf, J. W.; Ashe, A. J. *Organometallics.* **2007**, *26*, 1563–1564.

Scheme 2.7 Generation of Phenyl Boroxine from 1,2-Oxaborine Precursor

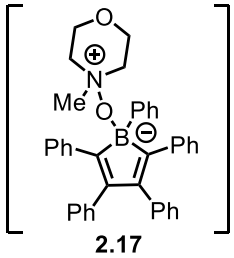


2.2.2 Martin and Co-Workers' Route to Oxaborines

Scheme 2.8 1,2-Oxaborine Formation via 1,1-Insertion Mechanism



A subsequent report by the Martin group presented another route to access 1,2-oxaborines, and provided further insight into the aromatic nature of this class of heterocycles.[41] The pentaphenyl-1,2-oxaborine **2.16** was prepared via oxygen-atom insertion into the pentaphenyl borole with *N*-methylmorpholine-*N*-oxide. The tetracoordinate boron intermediate **2.17** gave rise to a sharp peak at 6.4 ppm by ^{11}B NMR, but full



2.17

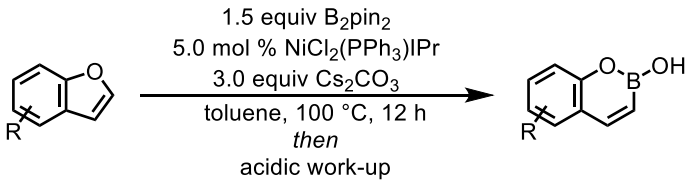
[41] Yruegas, S.; Patterson, D. C.; Martin, C. D. *Chem. Commun.* **2016**, *52*, 6658–6661.

conversion to a broad singlet at 38.4 ppm, signaling generation of **2.16**, was achieved after 30 minutes. The isolation of the *B*-biphenyl-1,2-oxaborine confirmed the endocyclic carbon bonds lie between single and double bonds, with slightly more diene-like character than that reported for 1,2-azaborines.

Nucleus-independent chemical shifts were completed on the pentaphenyl-1,2-oxaborine as well as the biphenyl derivative to computationally gauge the aromaticity of the heterocycles relative to other aromatic molecules. The values suggest that the parent 1,2-oxaborine is slightly less aromatic than the parent 1,2-azaborine. Both heteroaromatic rings have reduced aromaticity relative to benzene. Introduction of a phenyl substituent at the boron center further resulted in a reduction in the aromaticity of the 1,2-oxaborine. This trend holds true for the phenyl-substituted derivatives, synthesized by Martin and co-workers.

2.2.3 Yorimitsu's Nickel-Catalyzed Boron-Insertion of Benzofurans

Scheme 2.9 Nickel-Catalyzed Boron-Atom Insertion of Benzofurans



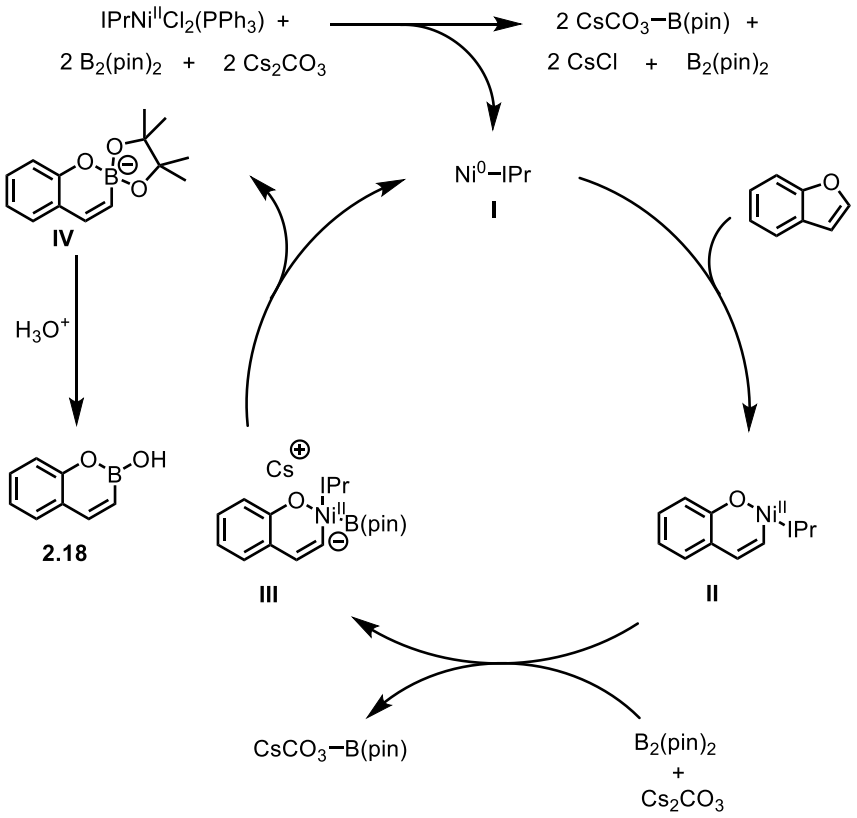
A later report by Yorimitsu et al. describes the nickel-catalyzed boron insertion into the C–O bond of benzofurans for the preparation of benzofused oxaborine analogues.[42] The success of the reaction hinged on the use of an *N*-heterocyclic carbene ligand, IPr, and

[42] Saito, H.; Otsuka, S.; Nogi, K.; Yorimitsu, H. *J. Am. Chem. Soc.* **2016**, *138*, 15315–15318.

$B_2(pin)_2$ as the diboron reagent.[43] With optimal conditions established, a variety of substituted benzofurans were transformed into the heteroaromatic naphthalene derivatives. Notably, substrates containing methoxy, ester, and fluoro substituents at the 5-position, groups potentially reactive under nickel catalysis, proceeded smoothly to afford the desired product. π-extended systems could also be accessed using the developed route.

The authors propose the active IPrNi(0) species **I** is generated by reduction of the Ni(II) precatalyst by $B_2(pin)_2$. Oxidative addition into the C–O bond of the benzofuran

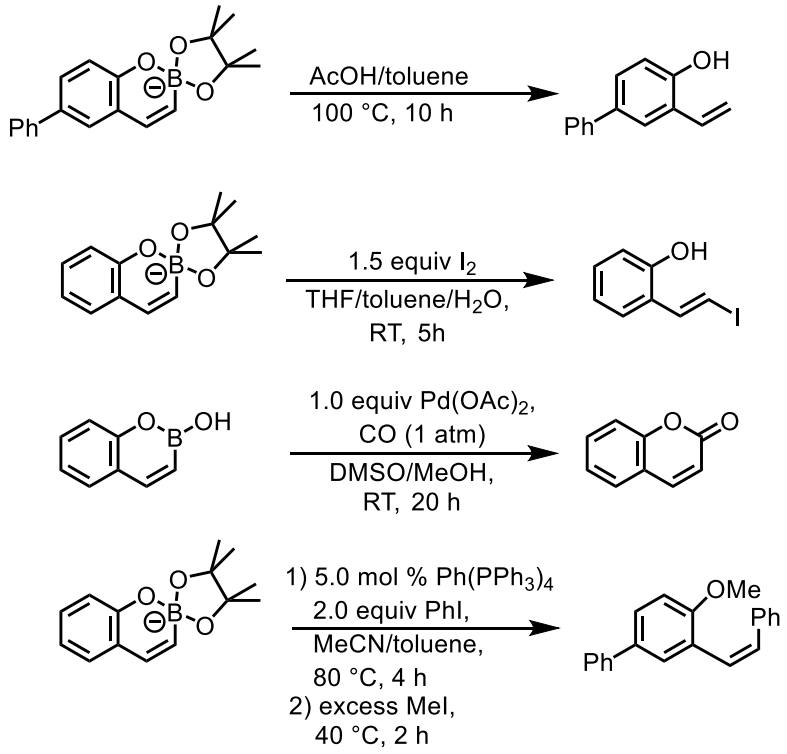
Figure 2.1 Proposed Mechanism for Nickel-Catalyzed Boron-Insertion



[43]Matsubara, K.; Ueno, K.; Shibata. Y. *Organometallics*, **2006**, *25*, 3422–3427.
[44] (a) Wenkert, E.; Michelotti, L. E.; Swindell, C. S. *J. Am. Chem. Soc*. **1979**, *101*, 2246–2247. (b) Cornella, J.; Martin, R. *Org. Lett*. **2013**, *15*, 6298–6301. (c) Tobisu, M.; Takahira, T.; Morioka, T.; Chatani, N. *J. Am. Chem. Soc*. **2016**, *138*, 6711–6714. (d) Guo, L.; Leindecker, M.; Hsiso, C.-C.; Baumann, C.; Rueping, M. *Chem. Commun*. **2015**, *51*, 1937–1940.

affords the Ni(II) intermediate **II**, which undergoes metalate formation to generate **III** and migratory insertion into boron.[44] Lastly, reductive elimination of **III** followed by intramolecular B–O bond formation furnishes **IV**. Upon work-up, the spirocyclic borate **IV** is transformed into the cyclic boronic ester. To demonstrate the utility of **2.18** and its derivatives, these borates were used as synthetic intermediates in a variety of transformations ranging from carbonylation to iodination, as illustrated in **Scheme 2.10**.[38,45] Attempts by the authors to complete boron insertion into dibenzofuran, 2-benzylfuran, and 2,3-dihydrofuran using the established protocol were met with no success. As such, facile access to monocyclic 1,2-oxaborines must be achieved through alternative methods.

Scheme 2.10 Functionalization of Boronate Esters and 1,2-Oxaborines



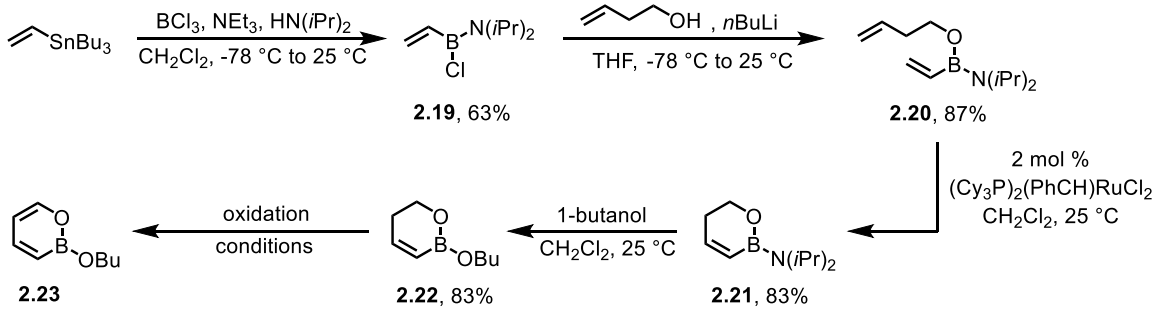
[45]Brown, H. C.; Hamaoka, T. Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 5786–5788.

2.3 LIU GROUP EFFORTS TOWARDS THE ISOLATION AND STUDY OF MONOCYCLIC 1,2-OXABORINES

Initial attempts to synthesize the 1,2-oxaborine core by our group relied on a cross metathesis strategy between 3-butenal 1,1-diethylacetal and pinacol vinylboronate followed by deprotection and intramolecular cyclization. However, isolation of the 1,2-oxaborine was not achieved through this route.

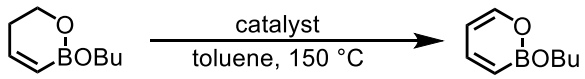
In an effort to rapidly gain access to 1,2-oxaborine derivatives for reactivity studies, I pursued a ring-closing metathesis route analogous to that developed by Ashe for the synthesis of 1,2-azaborines (**Scheme 2.11**). Initial attempts utilized a diisopropylamino(vinyl)borane intermediate synthesized by the transmetallation of boron trichloride with tributyl(vinyl)tin and subsequent addition of diisopropylamine. Nucleophilic addition of the homoallylic alkoxide to the borane furnished the diene. Ring-closing metathesis of **2.20** with Grubbs first generation catalyst provided the B–O six-membered ring **2.21**. Oxidation attempts of the diisopropylamino-substituted heterocycle **2.21** were unsuccessful. However, exchange of the boron substituent with 1-butanol to produce **2.22** facilitated the subsequent dehydrogenation to the 1,2-oxaborine.

Scheme 2.11 Liu's Initial Route to Access 1,2-Oxaborines



Despite observing conversion to product, the oxidation required long reaction times and consistently proved low-yielding. In an effort to circumvent the production of the saturated B–O six-membered ring, various hydrogen acceptors were analyzed including cyclohexene, norbornadiene, *tert*-butylethylene, and *trans*-stilbene. In the case of cyclohexene and norbornadiene, the 1,2-oxaborine proved to be a superior hydrogen acceptor than the additives; the saturated B–O six-membered ring was observed by ^{1}H NMR with the alkene resonances of the additives still persisting. Once *trans*-Stilbene was identified as the optimum additive, various catalysts were screened for the dehydrogenation (**Table 2.1**). As was observed with 1,2-azaborines, Pd/C was found to be the most efficient catalyst for the dehydrogenation delivering the 1,2-oxaborine in 48.2% NMR yield.

Table 2.1 Catalyst Screen for Oxidation to 1,2-Oxaborine



2.22

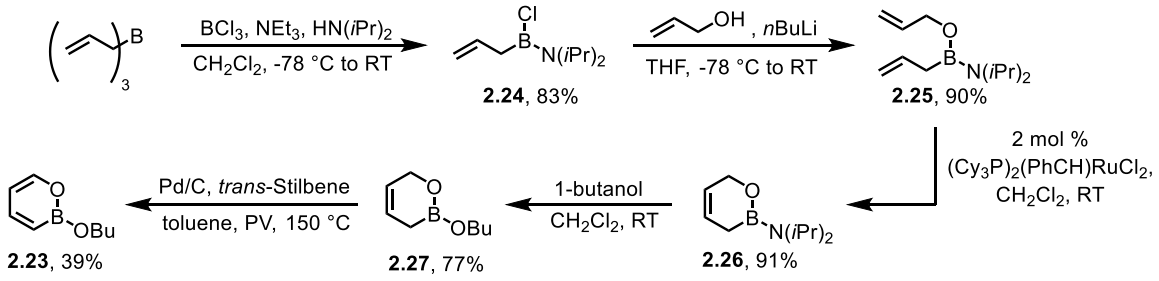
Catalyst	NMR Yield[a]
DDQ	0%
Pd/C[b]	48.2%
Pd Black[b]	34.3%
Rh/C[b]	5.1%
Co(TPP)/*p*-$NO_2C_6H_4SO_2N_3$	0%

[a]NMR yields determined using mesitylene as an internal standard.
[b]*trans*-Stilbene (5.0 equiv) was added to the reaction mixture as a hydrogen acceptor.

Later efforts were directed at accessing the 1,2-oxaborine via the allylic ether **2.27**, in an attempt to provide sufficient material for reactivity studies (**Scheme 2.12**). A strategy similar to the ring-closing metathesis one described above was utilized, using triallylborane as the allyl source.[46] Comproportionation with BCl_3 generated the allyl boron dichloride *in situ,* which upon successive treatment with diisopropylamine and triethylamine, generated

the diisopropylamino allylborane **2.24**. Addition of the lithium allylalkoxide followed by ring-closing metathesis and substituent exchange, furnished the six-membered ring **2.27**. It was posited that this olefin isomer could be more efficiently oxidized to the 1,2-oxaborine, as intermediate **2.27** would be less thermodynamically stable than **2.22**. The aromatic heterocycle was isolated in 39 % yield. Although the isolation of **2.23** appears to be more facile using this route, under the reaction conditions, isomerization to the B-vinyl isomer was observed in combination with the fully reduced B–O six-membered ring.

Scheme 2.12 Liu's Revised Synthesis to Access 1,2-Oxaborines

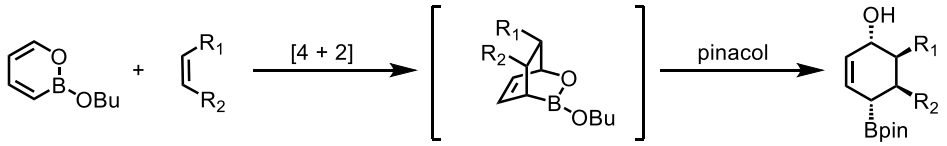


[46] (a) Bubnov, Y. N.; Tsyban, A. V.; Mikhailov, B. M. *Izv. Akad. Mauk. SSR, Ser. Khim*. **1967**, 472. (b) Bubnov, Y. N.; Bogdanov, V. S.; Mikhailov, B. M.. *Zh. Obsh. Khim*. **1968**, *38*, 260.

2.3.1 Diels–Alder Cycloaddition of 1,2-Oxaborines

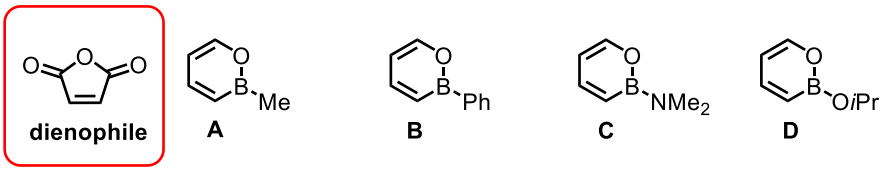
Following the isolation of the *B*-OBu-1,2-oxaborine, its competency as a 1,3-diene in the Diels–Alder cycloaddition was probed in an effort to generate stereochemically complex cyclohexene derivatives (**Scheme 2.13**).[47] Complementary Diels–Alder reactivity has been observed with 1,2-azaborines, however, use of less electron-deficient substrates, such as methyl acrylate, results in a reversible reaction.[32] Density Functional Theory calculations completed in collaboration with the Dixon group at the University of Alabama indicate the reaction of a *B*-O*i*Pr-1,2-oxaborine with methyl acrylate and maleic anhydride is a thermodynamically downhill process (**Table 2.2** and **Table 2.3**). Bearing this in mind, the *B*-OBu-1,2-oxaborine was chosen as a model substrate for the cycloaddition reaction.

Scheme 2.13 Proposed Cycloaddition Reaction Using 1,2-Oxaborines as 1,3-Dienes



[47] (a) Bertozzi, F.; Olsson, R.; Frejd, T. *Org. Lett*. **2000**, *2*, 1283–1286. (b) Sudo, Y.; Shirasaki, S. H.; Nishida, A. *J. Am. Chem. Soc.* **2008**, *130*, 12588–12589.

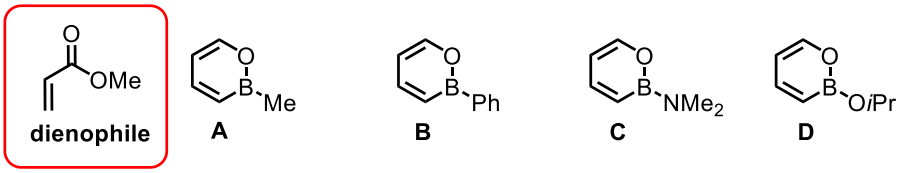
Table 2.2 Calculated Thermodynamic Parameters for 1,2-Oxaborine Cycloaddition at 298 K Using Maleic Anhydride as the Dienophile



$Adduct_{endo}$	G3MP2			M06/DZVP2	G3MP2
	ΔG_{gas}	ΔH_{gas}	ΔS_{gas}	ΔG_{solv}[a]	ΔG_{solv}[a]
A	-11.1	-24.2	-44.1	-13.4	-10.6
B	-10.6	-25.1	-48.7	-12.0	-9.5
C	-13.1	-27.8	-49.1	-14.9	-12.3
D	-12.2	-26.4	-47.9	-14.0	-11.1

[a]Toluene used as solvent.

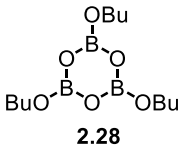
Table 2.3 Calculated Thermodynamic Parameters for 1,2-Oxaborine Cycloaddition at 298 K Using Methyl Acrylate as the Dienophile



$Adduct_{endo}$	G3MP2			M06/DZVP2	G3MP2
	ΔG_{gas}	ΔH_{gas}	ΔS_{gas}	ΔG_{solv}[a]	ΔG_{solv}[a]
A	-7.5	-20.6	-44.0	-9.4	-6.5
B	-6.9	-21.6	-48.5	-8.1	-5.6
C	-8.4	-23.0	-49.0	-10.0	-7.4
D	-8.3	-22.5	-47.9	-10.3	-7.0

[a]Toluene used as solvent.

Attempts to conduct the reaction thermally using maleic anhydride and methyl acrylate were met with little success. Conducting the reaction at room temperature resulted in no conversion of starting material. As the temperature was increased, consumption of starting material was observed, with formation of a broad peak at δ 18.9 by ^{11}B NMR. Analysis of the reaction mixture revealed no formation of the desired cycloadduct, but rather generation of what was presumed to be the *B*-OBu boroxine **2.28**. The *B*–Ph-1,2-oxaborine was also assessed as a diene in the [4 +2]

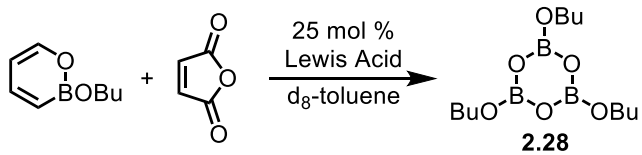


2.28

cycloaddition reaction. Nonetheless, as before, a broad peak was observed by ^{11}B NMR using both maleic anhydride and methyl acrylate as dienophiles.

In an effort to prevent the deleterious retro-Diels–Alder process, we envisioned conducting the cycloaddition under more mild reaction conditions. In this vein, we sought to utilize Lewis acids to promote the reaction at room temperature (**Table 2.4**).[48] Screening several Lewis acids in the reaction between the 1,2-oxaborine and maleic anhydride, instead promoted the undesired reactivity. In addition to the boroxine, the reaction mixture was largely comprised of unreacted starting material.

Table 2.4 Lewis Acid Screen for Diels-Alder Cycloaddition



2.28

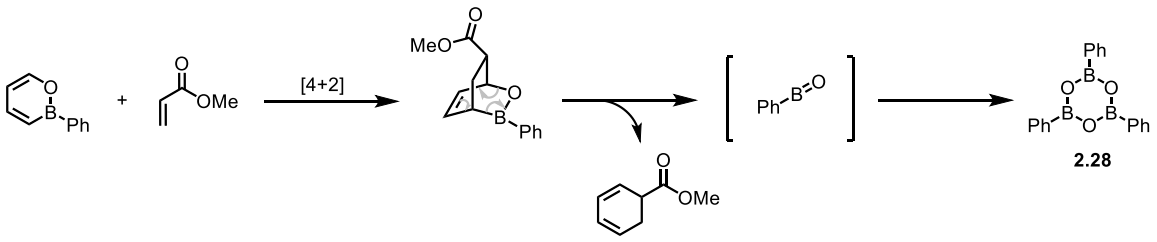
Lewis Acid	Conversion to 2.28
$SnCl_2$	21.7%
MgI_2	19.6%
$AlCl_3$	75.8%
$Sc(OTf)_3$	54.9%

To unambiguously confirm the formation of boroxine, the *B*–Ph derivative, synthesized via Grignard addition to the *B*–OBu-1,2-oxaborine, was subjected to the $AlCl_3$-catalyzed conditions for 15 h. Upon conclusion of the 15 h, a ^1H NMR was acquired before spiking the reaction mixture with independently prepared *B*–Ph boroxine, **2.28**. Analysis of the reaction mixture by ^1H NMR immediately following the addition of **2.28** revealed a

[48] (a) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc*. **1983**, *105*, 3716–3717. (b) Thamapipol, S.; Bernardinelli, G.; Besnard, C.; Kundig, E. P. *Org. Lett.* **2010**, *12*, 5604–5607. (c) Yakelis, N. A.; Roush, W. R. *Org. Lett*. **2001**, *3*, 957–960. (d) Twin, H.; Batey, R. A. *Org. Lett*. **2004**, *6*, 4913–4916.

notable increase in a characteristic downfield peak at 8.22 ppm. As reported by Ashe and co-workers, the boroxine could be generated by the initial Diels–Alder cycloaddition between the 1,2-oxaborine and dienophile, followed by a rapid retro-Diels–Alder process.[40] Subsequent trimerization of the oxyborane provides the boroxine **2.28**. Peaks consistent with the generation of the diene were observed, however, significant decomposition prevented the unambiguous detecharacterization.

Scheme 2.14 Proposed Mechanism for Generation of *B*-Ph Boroxine



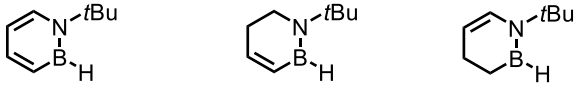
2.4 PROGRESS TOWARDS THE RESONANCE STABILIZATION ENERGY DETERMINATION OF 1,2-OXABORINES

To better understand the observed reactivity of the 1,2-oxaborines, we sought to quantify their aromaticity through the determination of the resonance stabilization energy. Since the isolation of benzene in the early 1800s, energetic, geometric, and magnetic properties have been developed to quantitatively determine the aromaticity of small

[49] (a) Sondheimer, F. *Pure Appl. Chem*. **1963**, *68*, 209–218. (b) Slayden, S. W.; Liebman, J. F. *Chem. Rev*. **2001**, *101*, 1541–1566. (c) Cyrański, M. K. *Chem. Rev*. **2005**, *105*, 3773–3811.
[50] (a) Dewar, M. J. S. *Tetrahedron Suppl*. **1966**, *8*, 75. (b) Krygowski, T. M.; Cyrański, M. K. *Chem. Rev*. **2001**, *101*, 1385–1419.
[51] (a) Elvidge, J. A.; Jackman, L. M. *J. Chem. Soc*. **1961**, *0*, 859–866. (b) Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev*. **2005**, *105*, 3842–3888. (c) Mitchell, R. H. *Chem. Rev*. **2001**, *101*, 1301–1315. (d) Gomes, J. A.; Mallion, R. B. *Chem. Rev*. **2001**, *101*, 1421–1449.

molecules.[49,50,51] One such method involves comparing the heat of hydrogenation of an aromatic molecule with the heats of hydrogenation of suitable, non-aromatic reference compounds. In doing so, the resonance stabilization energy, a marker of aromaticity, can be deduced. This method was first utilized by Kistiakowsky and co-workers to elucidate the RSE of benzene as 36 kcal/mol.[52] Similarly, the Liu group determined the RSE of 1,2-azaborines by comparing the heat of hydrogenation of aromatic molecule **2.29** with the corresponding B(vinyl) **2.30** and N(vinyl) **2.31** olefin isomers using isothermal reaction calorimetry (**Figure 2.2**).[30]

Figure 2.2 BN Heterocycles Utilized for Resonance Stabilization Energy Determination



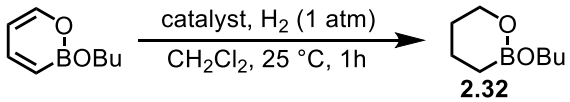
2.29 **2.30** **2.31**

Given the restrictions of the calorimeter, predominantly the lack of stirring capabilities, various homogeneous catalysts were screened for the hydrogenation of the *B*–OBu-1,2-oxaborine (**Table 2.5**). Entries 1-3 showed modest conversion to the saturated six-membered ring by ^{1}H NMR. On the other hand, use of Crabtree's catalyst exclusively generated **2.32**. Given the results obtained with [(COD)Ir(py)(PCy_3)]PF_6, other cationic metal complexes were examined, but all provided inferior results under the screening conditions. Several catalysts provided improved conversion to the B–O six-membered ring at higher pressures of H_2, namely Wilkinson's catalyst, however, complete hydrogenation was not observed at 15 bar after 5.5 hours. Use of coordinating solvents such as methanol provided reduced conversion presumably due to occupation of the catalyst's open coordination sites, rendering the oxidative addition of hydrogen kinetically slow.[53]

[52] Kistiakowsky, G. B.; Ruhoff, J. R.; Smith, H. A. Vaughan, W. E. *J. Am. Chem. Soc*. **1936**, *58*, 146–153.
[53]Crabtree, R. *Acc. Chem. Res*. **1979**, *12*, 331–337.

Subsequent evaluation of the catalyst loading revealed 1.25 mol % to be optimum for hydrogenation of the *B*–OBu-1,2-oxaborine within one hour. At lower catalyst loadings, complete hydrogenation was not observed after one hour, and importantly, the heat-flow measurements acquired on the calorimeter plateaued.

Table 2.5 Homogeneous Hydrogenation Catalyst Screen



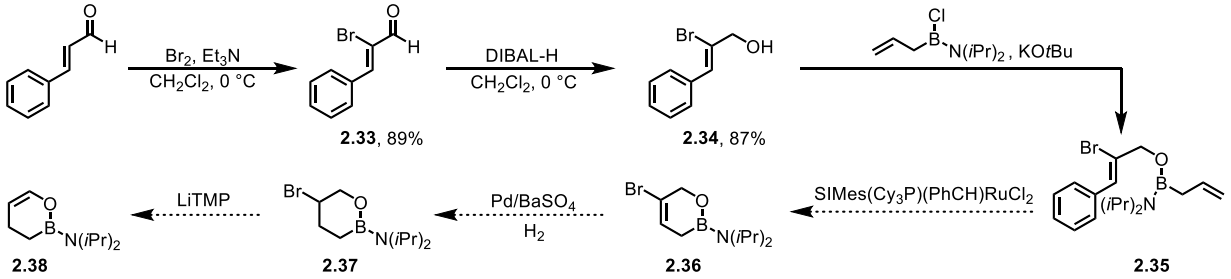
2.32

Entry	Catalyst	Conversion
1	$Rh(H)(CO)(PPh_3)_3$	21%
2	$Cl_2Ru(PPh_3)_3$	0%
3	$RhCl(PPh_3)_3$	38%
4	$[(COD)Ir(py)(PCy_3)]PF_6$	100%
5	$[Rh(nbd)_2]BF_4$, PCy_3	18%
6	$[Rh(COD)_2]BF_4$, PCy_3	15%
7	$[Rh(COD)_2]OTf$, PCy_3	0%
8	$[Rh(COD)_2]BF_4$, PPh_3	14%

To complete the series of olefin isomers necessary for the hydrogenation studies, potential routes to access the enol ether six-membered ring **2.39** were investigated. It was postulated that a similar ring-closing metathesis reaction could be utilized.[54] Once **2.36** was generated, hydrogenation to the alkane using $Pd/BaSO_4$ and elimination was predicted to generate the desired olefin (**Scheme 2.15**).[55] It was presumed that the presence of a halogen β to the oxygen atom of the B–O six-membered ring would facilitate the elimination upon deprotonation α to oxygen.[56]

[54] Gatti, M.; Drinkel, E.; Wu, L.; Pusterla, I.; Gaggia, F.; Dorta, R. *J. Am. Chem. Soc*. **2010**, *132*, 15179–15181.
[55]Cowell, D. B.; Davis, A. K.; Mathieson, D. W.; Nicklin, P. D. *J. Chem. Soc. Perkin Trans. 1* **1974**, *0*, 1505–1513.
[56] Smith III, A. B.; Fukui, M.; Vaccaro, H. A.; Empfield, J. R. *J. Am. Chem. Soc*. **1991**, *113*, 2071–2092.

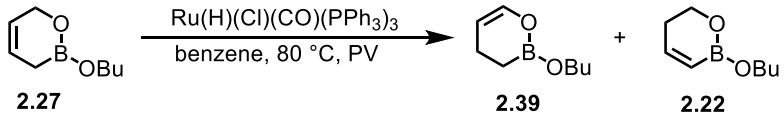
Scheme 2.15 Proposed Route to Synthesize Enol Ether Isomer for Calorimetry Studies



Work conducted in the groups of Weinreb and Dorta revealed use of the commercially available Grubbs 2nd generation catalyst allows for the formation of cyclic alkenyl halides from the requisite diene precursors.[54,57] In particular, efforts by Dorta et al. revealed substitution of the alkenyl halide moiety is essential to prevent catalyst degradation.[58] As a result, *trans*-Cinnamaldehyde was selected to generate the bromo-substituted allylic alcohol. Bromination to generate **2.33** was facile, as was the reduction to generate **2.34**. Despite screening a number of conditions to generate the diene **2.35**, full conversion was not observed. Furthermore, attempts to isolate **2.35** returned only the starting alcohol.

Given the instability of **2.35** to isolation on small-scale, isomerization of the allylic ether **2.27** was explored (**Scheme 2.16**). In the presence of $Ru(H)(Cl)(CO)(PPh_3)_3$ an equilibrium mixture of the B(vinyl) and enol ether olefin isomers was acquired. Analysis of other metal hydride catalysts provided inferior results.[59]

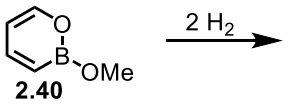
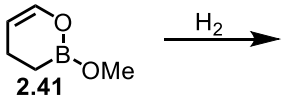
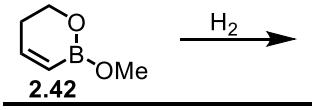
Scheme 2.16 Isomerization to Enol Ether Isomer Using Metal-Hydride



[57] Chao, W.; Weinreb, S. M. *Org. Lett*. **2003**, *5*, 2505–2507.
[58] Macnaughton, M. L.; Johnson, M. J. A.; Kampf, J. W. *J. Am. Chem. Soc*. **2007**, *129*, 7708–7709.
[59] Abbey, E. R.; Zakharov, L. N.; Liu, S.-Y. *J. Am. Chem. Soc*. **2008**, *130*, 7250–7252.

With each of the necessary olefin isomers in hand for reaction calorimetry, the expected heats of hydrogenation were computed at the G3MP2 level by using the Gaussian 09 program.[60] Comparing the heat of hydrogenation of the aromatic *B*–OBu-1,2-oxaborine to the sum of the O-vinyl and B-vinyl reference compounds, the resonance stabilization energy can be estimated using the equation RSE = $\Delta H_{2.40} - (\Delta H_{2.41} + \Delta H_{2.42})$. Utilizing this equation and the computationally derived ΔH values, it was found that the RSE of the 1,2-oxaborine is 9.22 kcal/mol, substantially lower than that of benzene (RSE ~ 36 kcal/mol) and the parental 1,2-azaborine **1.1** (RSE ~ 17 kcal/mol).[30,50]

Table 2.6 Computationally Determined Heats of Hydrogenation

Reaction	ΔH_{calc} (kcal/mol)
 **2.40**	-40.56
 **2.41**	-24.85
 **2.42**	-24.93

2.5 CONCLUSIONS

Building off prior work by the Ashe and Liu groups, a modular synthesis to deliver the *B*–OBu-1,2-oxaborine was developed. Investigations into the reactivity of 1,2-oxaborines as 1,3-dienes within the Diels–Alder reaction reveal that although they readily undergo the [4+2] cycloaddition, the retro-Diels–Alder reaction is particularly facile, preventing isolation of the desired cycloadduct. The propensity for these B–O heterocycles to engage in [4+2] cycloadditions is further supported by the computationally-determined

RSE. The RSE of 1,2-oxaborines, approximately 9.22 kcal/mol, suggests these molecules are "diene-like", rather than considerably aromatic molecules. The experimental RSE remains to be determined via isothermal reaction calorimetry, however, methods to access the necessary reference compounds **2.39** and **2.22** have been developed. Additionally, Crabtree's catalyst has been identified as the optimal hydrogenation catalyst for the calorimetry measurements.

[60] Gaussian 09, Revision B.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

3.0 EXPERIMENTAL

Unless otherwise stated, reactions were conducted in oven-dried glassware under an atmosphere of nitrogen or using a glove box. THF, Et_2O, CH_2Cl_2, toluene, benzene, and pentane were purified by passing through a neutral alumina column under argon. All reagents were purchased from commercial vendors and used as received unless otherwise noted. Diisopropylamine was dried over CaH_2 and distilled before use.

^1H NMR spectra were recorded on a Varian Gemini-500 (500 MHz) or Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm and reported relative to deuterated solvent signals (C_6D_6: 7.16 ppm). Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dq = doublet of quartets, t = triplet, tt = triplet of triplets, tdd = triplet of doublet of doublets, ddt = doublet of doublet of triplets, q = quartet, p = pentet, m = multiplet, br = broad), integration and coupling constants (Hz). ^{11}B NMR spectra were recorded on a Varian Unity/Inova 500 spectrometer (160 MHz) or Varian Unity/Inova 600 (192 MHz) spectrometer at ambient temperature. ^{11}B NMR chemical shifts are externally referenced BF_3•Et_2O (δ 0). ^{13}C NMR spectra were recorded on a Varian Unity/Inova 500 (125 MHz) or Unity/Inova 600 (150 MHz) spectrometer with complete proton decoupling. High-resolution mass spectroscopy data were obtained at the Boston College mass spectrometry facility on a JEOL AccuTOF instrument (JEOL USA, Peabody, MA), equipped with a DART ion source (IonSense, Inc., Danvers, MA) in positive ion mode.

Experimental calorimetry measurements were acquired using a Setaram C80 Calvet calorimeter with Setsoft 2000 software. A stock solution of Crabtree's catalyst was prepared in CH_2Cl_2 (0.002 M). In a nitrogen-filled glove box, the B-O six-membered ring (15.0 mg, 0.097 mmol, 1.0 equiv) was weighed in a 4 mL vial before transferring to the sample cell (Hastelloy, approx. 5 mL capacity) using CH_2Cl_2 (0.87 mL). To the sample cell was then added the catalyst solution (0.6 mL) via syringe before sealing, and removing from the glove box. Both cells were then loaded into the Setaram C80 calorimeter and a H_2 inlet was connected to the sample cell. The sample and reference cells were then equilibrated at 28 °C for approximately 2.5 hrs, or until zero heat-flow was visualized. Once equilibrated, data collection was initiated and the sample cell was purged with H_2 before charging with 20 psi of H_2. All valves were then closed and left closed for the remainder of the experiment. Data collection was allowed to proceed until the heat-flow reached zero, or stabilized near zero. The sample cell was then transferred to the glove box, and a crude NMR was acquired to ensure complete hydrogenation. Using the Setaram software, SetSoft 2000, integration of the graph of heat-flow vs. time gave the corresponding enthalpy of hydrogenation.

Computational Details

Molecules were initially optimized with B3LYP exchange-correlation functional at the density functional theory level and the DGDZVP2 basis set with Gaussian 09 program system. These coordinates were then used as input to the composite G3MP2 calculations. The B3LYP/DGDZVP2 optimized coordinated are given below.

Optimized Cartesian Coordinates (B3LYP-DGDZVP2)

B-OMe vinyl

C	1.834681	1.051470	0.069715

C	0.573808	1.427771	-0.219371
C	1.174543	-1.311082	-0.328602
C	2.144871	-0.387482	0.385626
H	2.654453	1.768953	0.112830
H	0.355315	2.472300	-0.426858
H	1.316617	-2.351569	-0.025621
H	3.166194	-0.644120	0.080495
H	2.089930	-0.556801	1.469750
H	1.332518	-1.241191	-1.411871
O	-0.194872	-0.985804	-0.043490
B	-0.536416	0.347151	-0.102349
C	-2.830844	-0.320289	0.160495
H	-3.804171	0.170699	0.164967
H	-2.781387	-1.035754	-0.663204
H	-2.686422	-0.857552	1.100730
O	-1.848044	0.707923	0.006409

B-OMe enol ether

C	-1.929134	-0.872704	0.352299
C	-0.647530	-1.364988	-0.335213
C	-1.105247	1.417104	-0.124052
C	-2.137363	0.587975	0.065678
H	-2.799992	-1.449979	0.024049
C	-0.831234	-1.427752	-1.416869
H	-1.202760	2.477720	-0.329617
H	-3.138234	1.006798	0.028140
O	0.223131	1.027401	-0.059372
B	0.514692	-0.329231	-0.114759
C	2.826646	0.287229	0.160545
H	3.778441	-0.238226	0.235477
H	2.844702	0.963408	-0.696661
H	2.654256	0.870732	1.067137
O	1.813963	-0.713464	-0.001413
H	-1.854365	-1.027259	1.438136
H	-0.365255	-2.368483	-0.005259

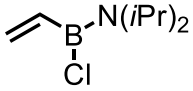
B-OMe cyclohexane

C	1.922856	0.909486	-0.278656
C	0.537436	1.467447	0.058539
C	1.088370	-1.446750	-0.161621
C	2.094633	-0.451776	0.387447
H	2.023820	0.785771	-1.364729
H	0.268252	2.311342	-0.585452
H	1.136043	-2.397772	0.377092
H	3.101995	-0.855200	0.228492
O	-0.270690	-0.993732	-0.063243

B	-0.570518	0.345146	-0.005930
C	-2.886992	-0.316285	0.022082
H	-3.854596	0.185466	0.051048
H	-2.813691	-0.922266	-0.883755
H	-2.787060	-0.972243	0.889967
O	-1.888500	0.707173	0.036320
H	1.299029	-1.649709	-1.218926
H	1.952614	-0.353483	1.470945
H	2.719871	1.594225	0.031955
H	0.542007	1.867882	1.081638

B-OMe 1,2-oxaborine

C	1.396205	1.357055	-0.000283
C	0.038636	1.195685	-0.000185
C	1.760988	-1.028121	0.000060
C	2.276184	0.225774	-0.000158
H	1.842916	2.350871	-0.000458
H	-0.587238	2.084263	-0.000286
H	2.357815	-1.934772	0.000166
H	3.353324	0.349339	-0.000236
B	-0.497668	-0.235156	0.000063
O	0.435838	-1.277313	0.000170
C	-2.842350	0.296752	0.000111
H	-3.783941	-0.252878	0.000244
H	-2.799163	0.930443	0.891203
H	-2.799258	0.930176	-0.891175
O	-1.795100	-0.668254	0.000200



1-chloro-*N,N*-diisopropyl-1-vinylboranamine 2.19

The procedure for the preparation of the vinylborane **2.19** was a slight modification of a literature procedure.[21] A 500 mL round-bottom flask was charged with a 1.0 M solution of BCl_3 in hexanes (85.5 mL, 85.5 mmol, 1.0 equiv) and a magnetic stir bar under an atmosphere of N_2. Simultaneously, in a nitrogen-filled glovebox, to a 250 mL oven-dried round-bottom flask was added tributyl(vinyl)stannane (25.0 mL, 85.5 mmol, 1.0 equiv) and anhydrous pentane (100 mL). The flask was then capped with septa, removed from glovebox, and immediately placed under N_2. The BCl_3 solution was cooled to -78 °C before the dropwise addition of the tin solution. The reaction mixture was allowed

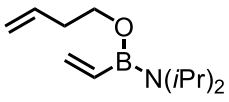
to stir at -78 °C for 3 h after which time diisopropylamine (12.0 mL, 85.5 mmol, 1.0 equiv) and triethylamine (11.9 mL, 85.5 mmol, 1.0 equiv) were added sequentially. The reaction mixture was then allowed to warm to room temperature over course of 18 h. The reaction mixture was transferred to a glovebox where solids were removed via filtration before removing solvent under reduced pressure. The crude product was purified via vacuum distillation (60 °C, 100 mTorr) to afford a clear, colorless oil (9.37 g, 63%).

^{1}H NMR (600 MHz, C_6D_6) δ 6.46 - 6.33 (m, 2H), δ 5.92 (dd, *J* = 12.6, 4.8 Hz, 1H), δ 4.04 (br, 1H), δ 3.38 (br, 1H), δ 1.09 - 1.04 (m, 6H), δ 0.96 (d, *J* = 7.0 Hz, 6H)

^{11}B NMR (600 MHz, C_6D_6) δ 34.5

^{13}C NMR (125 MHz, C_6D_6) δ 135.4, 49.1, 47.9, 23.9, 22.5

HRMS (DART+) *m/z* calc'd for $C_8H_{17}BClN$ $[M + H]^+$: 174.1221; found 174.1224.



1-(but-3-en-1-yloxy)-*N*,*N*-diisopropyl-1-vinylboranamine 2.20

To an oven-dried 100 mL round-bottom equipped with a stir bar was added vinylborane **2.19** (9.37 g, 54.02 mmol, 1.0 equiv) and anhydrous THF (3.5 mL) in a nitrogen-filled glovebox. A separate 100 mL oven-dried round-bottom flask was charged with 3-Buten-1-ol (4.65 mL, 54.02 mmol, 1.0 equiv) and anhydrous THF (20.0 mL). Both flasks were capped with septa, removed from glovebox, and immediately placed under N_2. The flask containing the alcohol solution was then cooled to -78 °C before the slow addition of *n*BuLi (21.61 mL, 54.02 mmol, 1.0 equiv). Once addition was complete, the solution was allowed to warm to room temperature over course of 1 h. The homoallyl alkoxide solution was then transferred to the vinylborane solution at -78 °C. Following addition, the reaction mixture was gradually warmed to RT over a period of 3 h. The reaction mixture

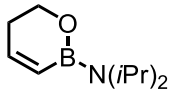
was transferred to a glovebox where solids were removed via filtration before removing solvent under reduced pressure. The crude product was purified via vacuum distillation (45 °C, 190 mTorr) to afford a clear, colorless oil (9.77 g, 86.5 %).

^{1}H NMR (600 MHz, C_6D_6) δ 6.05 (dd, *J* = 20.5, 15.0 Hz, 1H), δ 5.84 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H), δ 5.69 (dd, *J* = 15.2 Hz, 3.9 Hz, 1H), δ 5.46 (dd, *J* = 20.4, 3.9 Hz, 1H), δ 5.10 – 5.00 (m, 2H), δ 3.79 (t, *J* = 6.6 Hz, 2H), δ 3.18 – 3.13 (m, 1H), 2.28 – 2.21 (m, 2H), δ 1.40 (br, 6H), δ 1.04 – 0.97 (br, 6H)

^{11}B NMR (192 MHz, C_6D_6) δ 30.19

^{13}C NMR (150 MHz, C_6D_6) δ 136. 46, 127.24, 116.74, 65.36, 48.47, 44.32, 37.56, 24.34, 22.78

HRMS (DART+) *m/z* calc'd for $C_{12}H_{24}BNO$ $[M + H]^+$: 210.2029; found 210.2033.



***N,N*-diisopropyl-5,6-dihydro-2*H*-1,2-oxaborinin-2-amine 2.21**

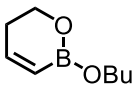
In a nitrogen-filled glovebox, an oven-dried 500 mL round-bottom flask was charged with Grubbs first generation catalyst (0.77 g, 0.93 mmol, 0.02 equiv), anhydrous CH_2Cl_2 (234 mL), and a magnetic stir bar. Diene **2.20** (9.77 g, 46.72, 1.0 equiv) was then added via pipette and reaction mixture was allowed to stir for 10 min before capping flask with septa, removing from glovebox, and immediately placing under N_2. Reaction mixture was stirred at 23 °C for 18 h after which time, volatiles were removed under reduced pressure. The crude product was purified via vacuum distillation (35 °C, 120 mTorr) to afford a clear, colorless oil (6.98 g, 82.5%).

^{1}H NMR (500 MHz, C_6D_6) δ 6.61 (dt, *J* = 12.6, 4.2 Hz, 1H), δ 6.04 (dt, *J* = 12.4, 1.8 Hz, 1H), δ 3.86 (t, *J* = 6.8 Hz, 2H), δ 3.59 (h, *J* = 6.8 Hz, 2H), δ 1.90 (tdd, *J* = 6.0, 4.1, 1.7 Hz, 2H), δ 1.33 (d, *J* = 6.8 Hz, 6H), δ 1.08 (d, *J* = 6.8 Hz, 6H)

^{11}B NMR (160 MHz, C_6D_6) δ 27.41

^{13}C NMR (150 MHZ, C_6D_6) δ 145.98, 126.56, 62.61, 46.32, 44.46, 29.55, 23.90, 23.83

HRMS (DART+) *m/z* calc'd for $C_{10}H_{20}BNO$ $[M + H]^+$: 182.1716; found 182.1715.



2-butoxy-5,6-dihydro-2*H*-1,2-oxaborinine 2.22

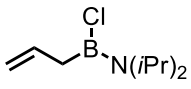
An oven-dried 50 mL round-bottom flask equipped with a stir bar was charged with B–N(*i*Pr)$_2$ six-membered ring **2.21** (6.98 g, 38.54 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (15.4 mL). 1-butanol (3.88 mL, 42.39 mmol, 1.1 equiv) was then added via syringe. The reaction mixture was then stirred at 23 °C for 17 h. Volatiles were removed under reduced pressure and the crude product was purified by fractional distillation (36 °C, 120 mTorr) to deliver the desired product as a clear, colorless oil (4.91 g, 82.7%).

^{1}H NMR (500 MHz, C_6D_6) δ 6.58 (dt, *J* = 12.0, 3.7 Hz, 1H), δ 5.89 (dt, *J* = 12.0, 1.7 Hz, 1H), δ 4.01 (t, *J* = 6.6 Hz, 2H), δ 3.79 (t, *J* = 6.3 Hz, 2H), δ 1.79 (tdd, *J* = 6.2, 4.0, 1.7 Hz, 2H), δ 1.56 (ddt, *J* = 8.9, 7.9, 6.4 Hz, 2H), δ 1.41 – 1.28 (m, 2H), δ 0.84 (t, *J* = 7.4 Hz, 3H)

^{11}B NMR (160 MHz, C_6D_6) δ 26.08

^{13}C NMR (125 MHz, C_6D_6) δ 149.82, 125.05, 63.64, 62.80, 34.45, 29.44, 19.82, 14.36

HRMS (DART+) *m/z* calc'd for $C_8H_{15}BO_2H$ $[M + H]^+$: 155.1243; found 155.1246.



1-allyl-1-chloro-*N*,*N*-diisopropylboranamine 2.24

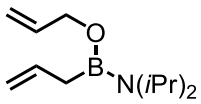
To an oven-dried 1.0 L round-bottom flask equipped with a stir bar was added triallylborane (6.70 g, 50.0 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (250 mL). The solution was then cooled to -78 °C before the dropwise addition of boron trichloride (100.0 mL, 100.0 mmol, 2.0 equiv) via cannula. The reaction was allowed to stir for 4 hrs at -78 °C before the sequential addition of diisopropylamine (21.02 mL, 150.0 mmol, 3.0 equiv) and triethylamine (20.91 mL, 150.0 mmol, 3.0 equiv). Following the addition, the reaction was gradually warmed to room temperature over course of 18 hrs, after which it was filtered over a bed of Celite with repeated CH_2Cl_2 rinsings. Volatiles were removed under reduced pressure and the crude product was purified via distillation (65 °C, 100 mTorr) to give a clear, colorless oil (23.33 g, 82.9%).

^{1}H NMR (400 MHz, C_6D_6) δ 6.09 (m, 1H), δ 5.15 – 4.99 (m, 2H), δ 3.49 – 3.79 (br, 1H), δ 3.41 – 3.31 (br, 1H), δ 2.08 (d, J = 7.3 Hz, 2H), δ 1.18 – 1.05 (br, 6H), δ 0.90 (d, J = 6.9 Hz, 6H)

^{11}B NMR (128 MHz, C_6D_6) δ 37.73

^{13}C NMR (100 MHz, C_6D_6) δ 136.18, 115.11, 48.41, 29.66 – 29.79, 23.18 – 22.80

HRMS (DART+) *m/z* calc'd for $C_9H_{19}BClN$ $[M + H]^+$: 188.1377; found 188.1383.



1-allyl-1-(allyloxy)-*N*,*N*-diisopropylboranamine 2.25

To an oven-dried 500 mL round-bottom flask equipped with stir bar was added allylborane **2.24** (23.40 g, 124.79 mmol, 1.0 equiv) and THF (40 mL). A separate 100 mL oven-dried round-bottom flask was charged with allyl alcohol (8.49 mL, 124. 79 mmol, 1.0 equiv) and THF (43 mL) before cooling to -78 °C. Once cooled, *n*BuLi (11.34 mL, 124.79 mmol, 1.0 equiv) was slowly added and reaction was allowed to gradually

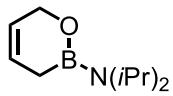
warm to room temperature over course of 40 min. Upon completion of 40 min, contents of the 100 mL round-bottom flask were transferred to the allylborane solution at -78 °C. The reaction was then allowed to warm to room temperature over course of 16 hrs after which time it was filtered using repeated pentane rinsings. Volatiles were removed under reduced pressure before purifying the crude product by vacuum distillation (48 °C, 80 mTorr) to afford a clear, colorless oil (23.53 g, 90.2%).

^{1}H NMR (500 MHz, C_6D_6) δ 5.96 – 5.78 (m, 2H), δ 5.32 (dq, *J* = 17.1, 2.0 Hz, 1H), δ 5.10 – 4.96 (m, 2H), δ 4.26 (dt, *J* = 4.1, 1.9 Hz, 2H), δ 3.62 (br, 1H), δ 3.15 (br, 1H), δ 1.72 (dt, *J* = 7.0, 1.8 Hz, 2H), δ 1.39 (br, 1H), δ 1.00 (br, 1H).

^{11}B NMR (MHz, C_6D_6) δ 31.52

^{13}C NMR (MHz, C_6D_6) δ 137.93, 136.66, 114.98, 114.25, 65.70, 47.85, 44.47, 24.32, 22.77, 20.77

HRMS (DART+) *m/z* calc'd for $C_{12}H_{24}BNO$ $[M + H]^+$: 210.2029; found 210.2023.



***N,N*-diisopropyl-3,6-dihydro-2*H*-1,2-oxaborinin-2-amine 2.26**

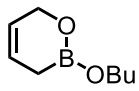
An oven-dried 500 mL round-bottom flask was charged with Grubbs first generation catalyst (1.85 g, 2.25 mmol, 0.02 equiv), CH_2Cl_2 (250.0 mL), and a stir bar. Diene **2.25** (23.53 g, 112.51 mmol, 1.0 equiv) was then added via pipette and vial was rinsed with CH_2Cl_2 (31.0 mL) to ensure complete transfer. Reaction mixture was allowed to stir for 16 hrs, after which time volatiles were removed under reduced pressure. The crude product was then purified by vacuum distillation to afford a clear, colorless oil (18.52 g, 90.9%).

^{1}H NMR (600 MHz, C_6D_6) δ 5.83 (dt, *J* = 10.3, 3.5 Hz, 1H), δ 5.46 (dt, *J* = 10.1, 2.5 Hz, 1H), δ 4.39 (pen, *J* = 3.2 Hz, 2H), δ 3.30 (br, 1H), δ 3.20 (br, 1H), δ 1.38 (d, *J* = 6.8 Hz, 6H), δ 0.95 (d, *J* = 6.8 Hz, 6H).

^{11}B NMR (192 MHz, C_6D_6) δ 30.98.

^{13}C NMR (126 MHZ, C_6D_6) δ 126.72, 125.61, 63.79, 49.97, 44.13, 24.34, 22.71, 12.14.

HRMS (DART+) *m/z* calc'd for $C_{10}H_{20}BNO$ $[M + H]^+$: 182.1716; found 182.1710.



2-butoxy-3,6-dihydro-2*H*-1,2-oxaborinine 2.27

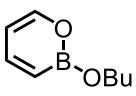
An oven-dried 250 mL round-bottom flask containing a stir bar was charged with *B*-N(*i*Pr)$_2$ six-membered ring **2.26** (18.03 g, 99.59 mmol, 1.0 equiv) and CH_2Cl_2 (40.0 mL). To the solution was then added 1-butanol (10.02 mL, 109.55 mmol, 1.1 equiv). Following addition of alcohol, reaction mixture was allowed to stir at RT for 17 hrs after which time the volatiles were removed under reduced pressure. The crude product was purified by fractional distillation (30 °C, 110 mTorr) to afford a clear, colorless oil (11.75 g, 76.6%)

^{1}H NMR (500 MHz, C_6D_6) δ 5.73 – 5.65 (m, 1H), δ 5.28 (dq, *J* = 10.1, 2.4 Hz, 1H), δ 4.33 (tt, *J* = 4.1, 2.4 Hz, 2H), δ 3.94 (t, *J* = 6.6 Hz, 2H), δ 1.53 (dq, *J* = 8.4, 6.7 Hz, 2H), δ 1.41 (br, 2H), δ 1.34 (sextet, *J* = 7.4 Hz, 2H), δ 0.85 (t, *J* = 7.4 Hz, 3H).

^{11}B NMR (160 MHz, C_6D_6) δ 30.05.

^{13}C NMR (126 MHz, C_6D_6) δ 126.00 – 125. 84, 65.59, 62.71, 34.44, 19.86, 14.37, 11.65 - 10.93.

HRMS (DART+) *m/z* calc'd for $C_8H_{15}BO_2$ $[M + H]^+$: 155.1243; found 155.1239.

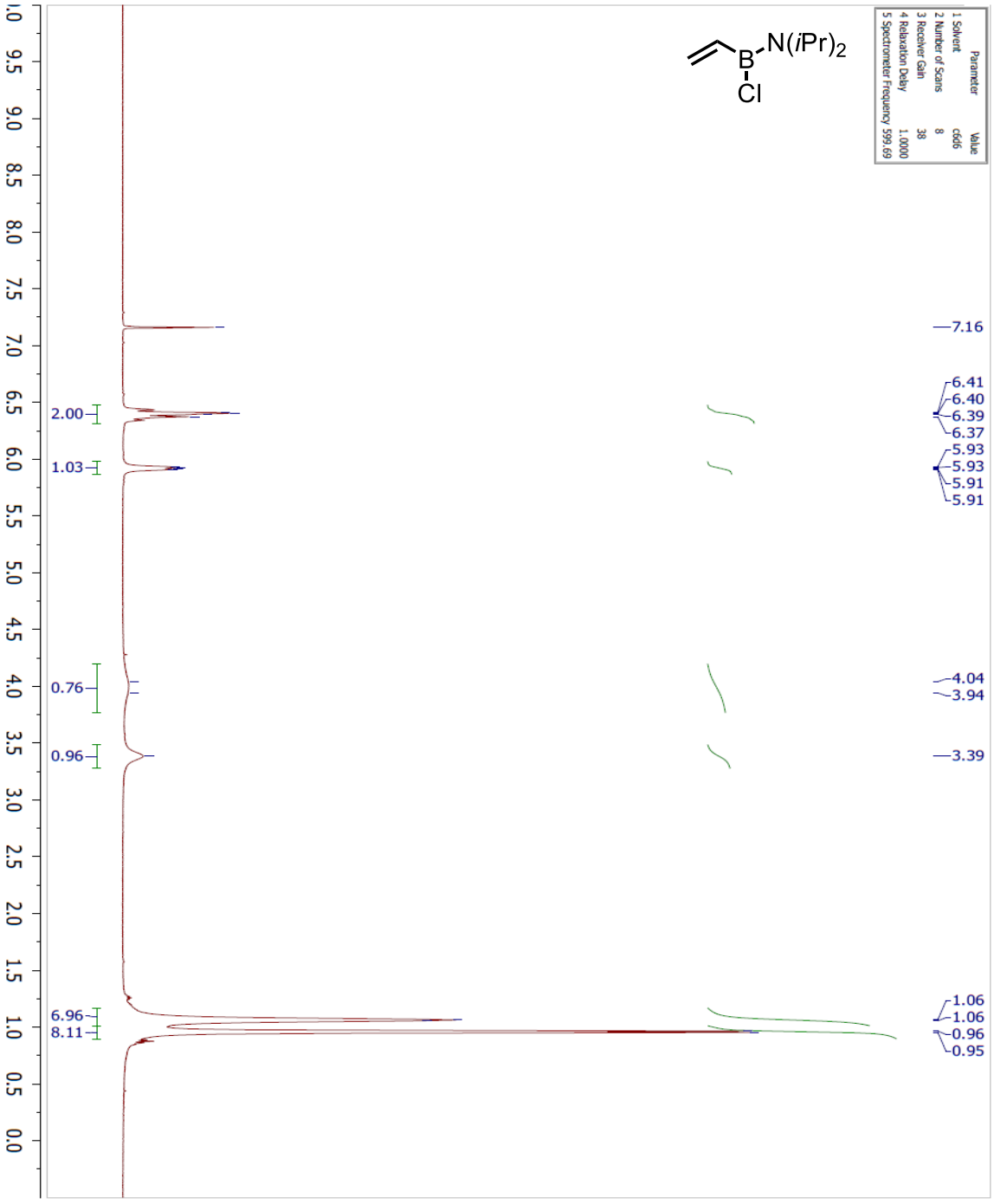


2-butoxy-2H-1,2-oxaborine 2.23

To an oven-dried 150 mL pressure vessel containing a stir bar was added 10 wt % Pd/C (0.35 g, 3.25 mmol, 0.20 equiv), trans-Stilbene (14.63 g, 81.15 mmol, 5.0 equiv), *B*-OBu six-membered ring **2.27** (2.50 g, 16.23 mmol, 1.0 equiv), and toluene (33.0 mL). The pressure vessel was then sealed and placed in a pre-heated 150 °C oil bath. Once ^{11}B NMR indicated full conversion, reaction mixture was filtered over a pad of Celite with repeated pentane rinsings. Volatiles were removed under reduced pressure and crude product was purified by distillation (65 °C, 400 mTorr) to afford a clear, colorless oil (953 mg, 38.6%).

^{1}H NMR (MHz, C_6D_6) δ 7.02 (br, 1H), δ 6.85 (d, J = 5.1 Hz, 1H), δ 6.21 (dt, J = 11.7, 1.2 Hz, 1H), δ 5.57 (ddd, J = 6.2, 5.1, 1.3 Hz, 1H), δ 3.94 (t, J = 6.6 Hz, 2H), δ 1.63 – 1.43 (m, 2H), δ 1.45 – 1.16 (m, 2H), δ 0.82 (t, J = 7.3 Hz, 3H)

^{11}B NMR (MHz, C_6D_6) δ 27.8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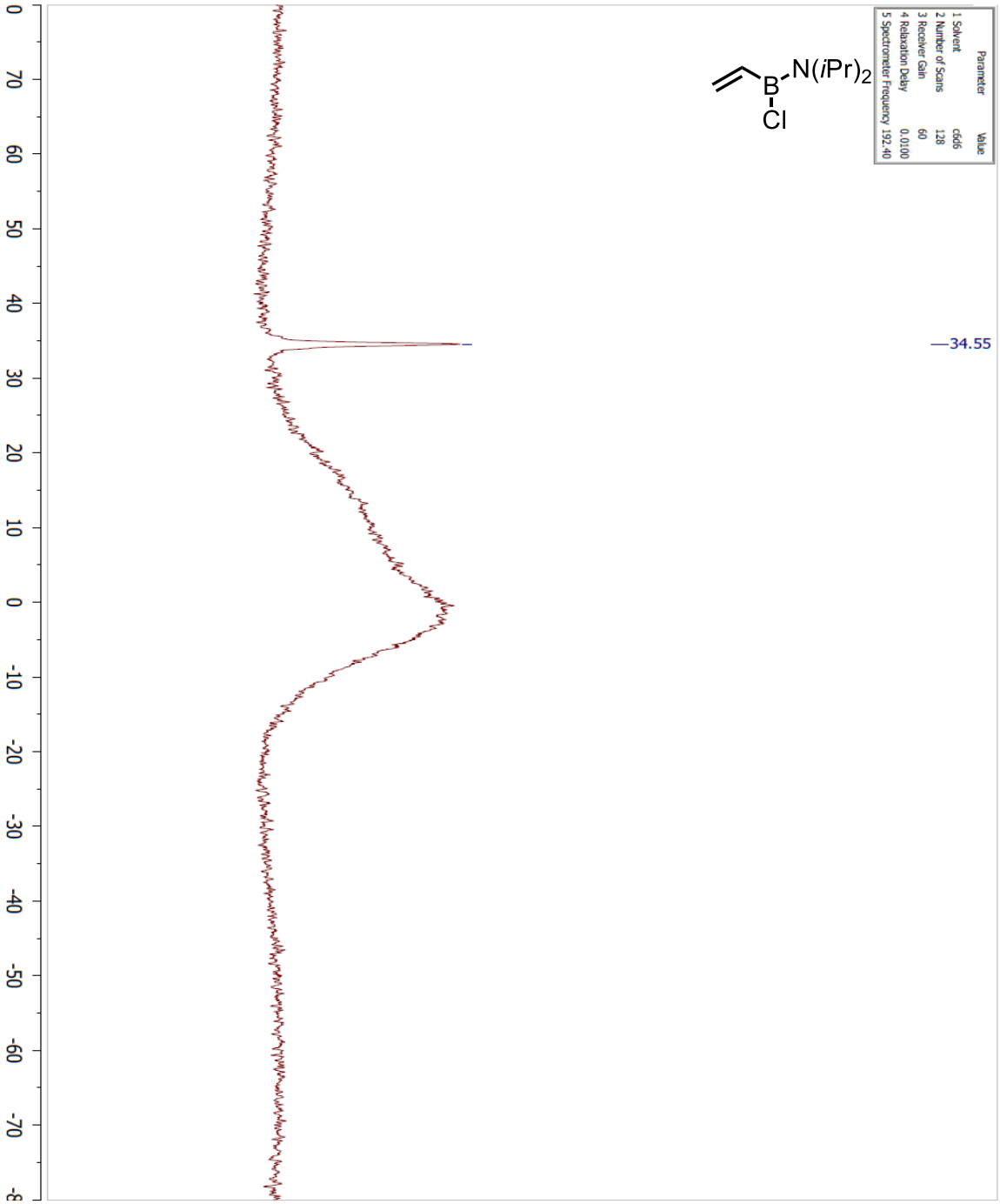
B
Cl
Parameter Value
1 Solvent c6d6
2 Number of Scans 8
3 Receiver Gain 38
4 Relaxation Delay 1.0000
5 Spectrometer Frequency 599.69
7.16
6.41
6.40
6.39
6.37
5.93
5.93
5.91
5.91
4.04
3.94
3.39
1.06
1.06
0.96
0.95
2.00
1.03
0.76
0.96
6.96
8.11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B
Cl
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50
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30
20
10
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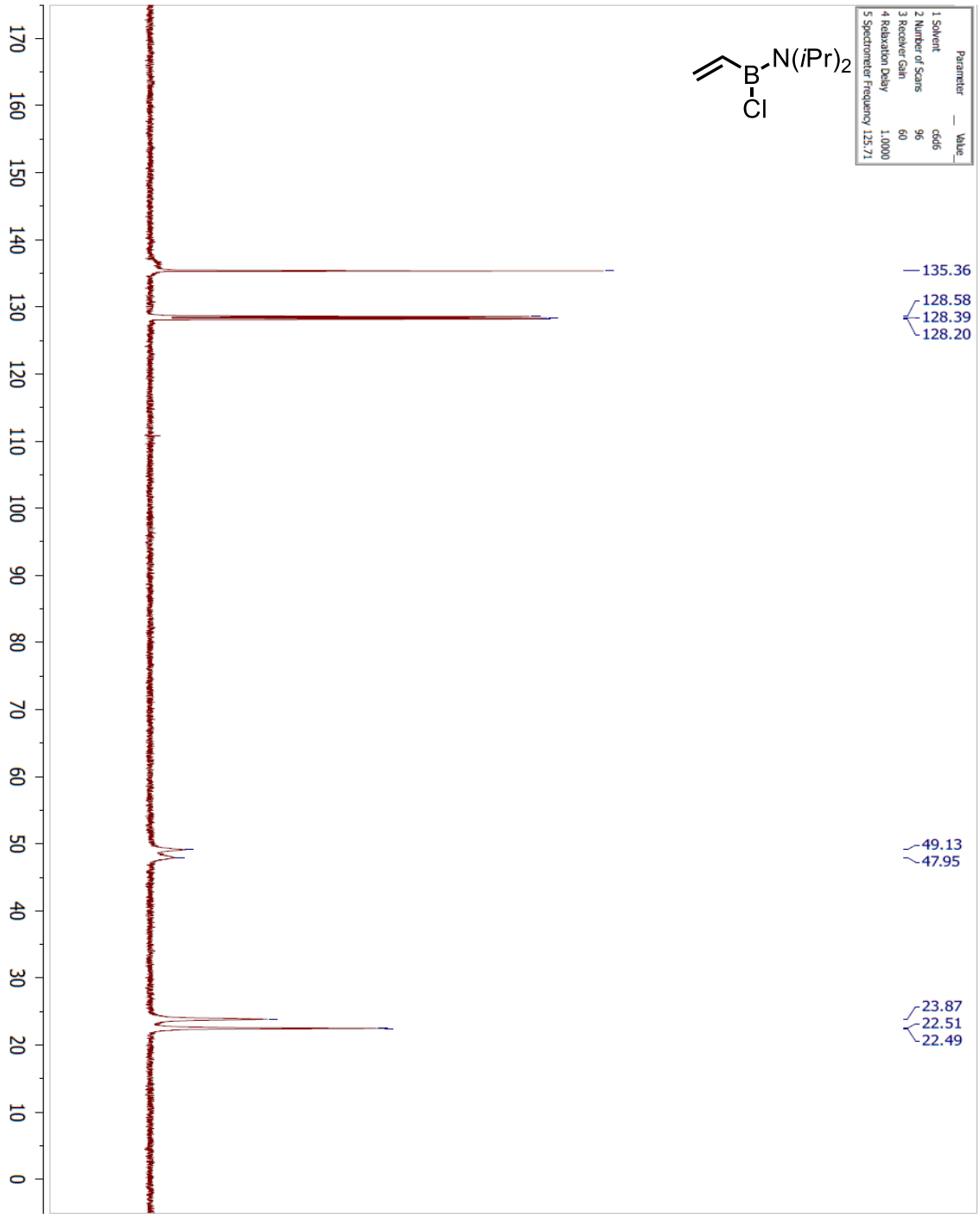
-20
-30
-40
-50
-60
-70


N(iPr)2
B
Cl
Parameter
Value
1 Solvent
c6d6
2 Number of Scans
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3 Receiver Gain
60
4 Relaxation Delay
1.0000
5 Spectrometer Frequency
125.71
135.36
128.58
128.39
128.20
49.13
47.95
23.87
22.51
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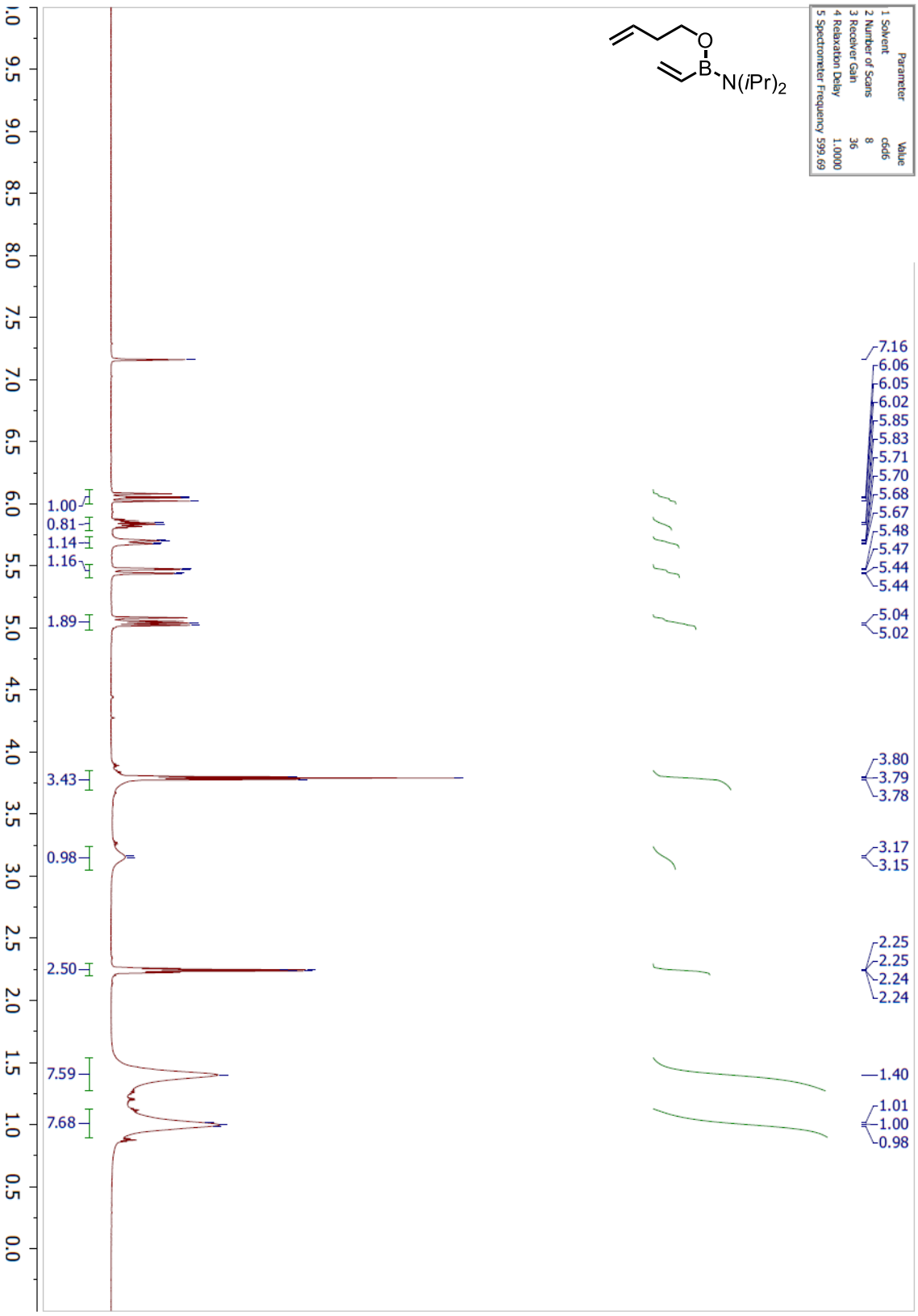
Parameter Value
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4 Relaxation Delay 1.0000
5 Spectrometer Frequency 599.69
N(iPr)2
7.16
6.06
6.05
6.02
5.85
5.83
5.71
5.70
5.68
5.67
5.48
5.47
5.44
5.44
5.04
5.02
3.80
3.79
3.78
3.17
3.15
2.25
2.25
2.24
2.24
1.40
1.01
1.00
0.98
1.00
0.81
1.14
1.16
1.89
3.43
0.98
2.50
7.59
7.68

Parameter Value
1 Solvent c6d6
2 Number of Scans 128
3 Receiver Gain 60
4 Relaxation Delay 0.0100
5 Spectrometer Frequency 192.40
O
B
N(iPr)2
30.24
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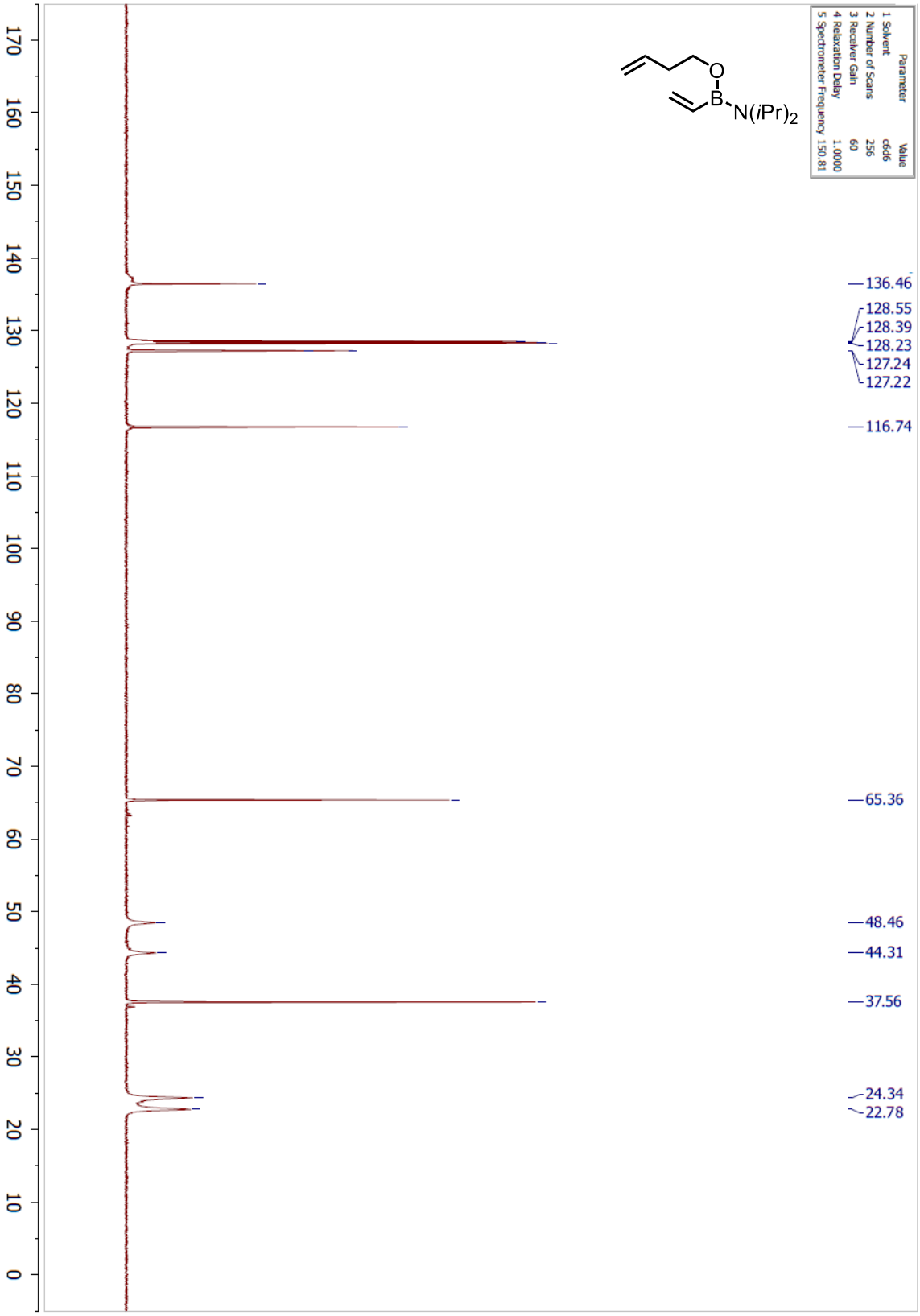
-8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B
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128.39
128.23
127.24
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37.56
24.34
22.78
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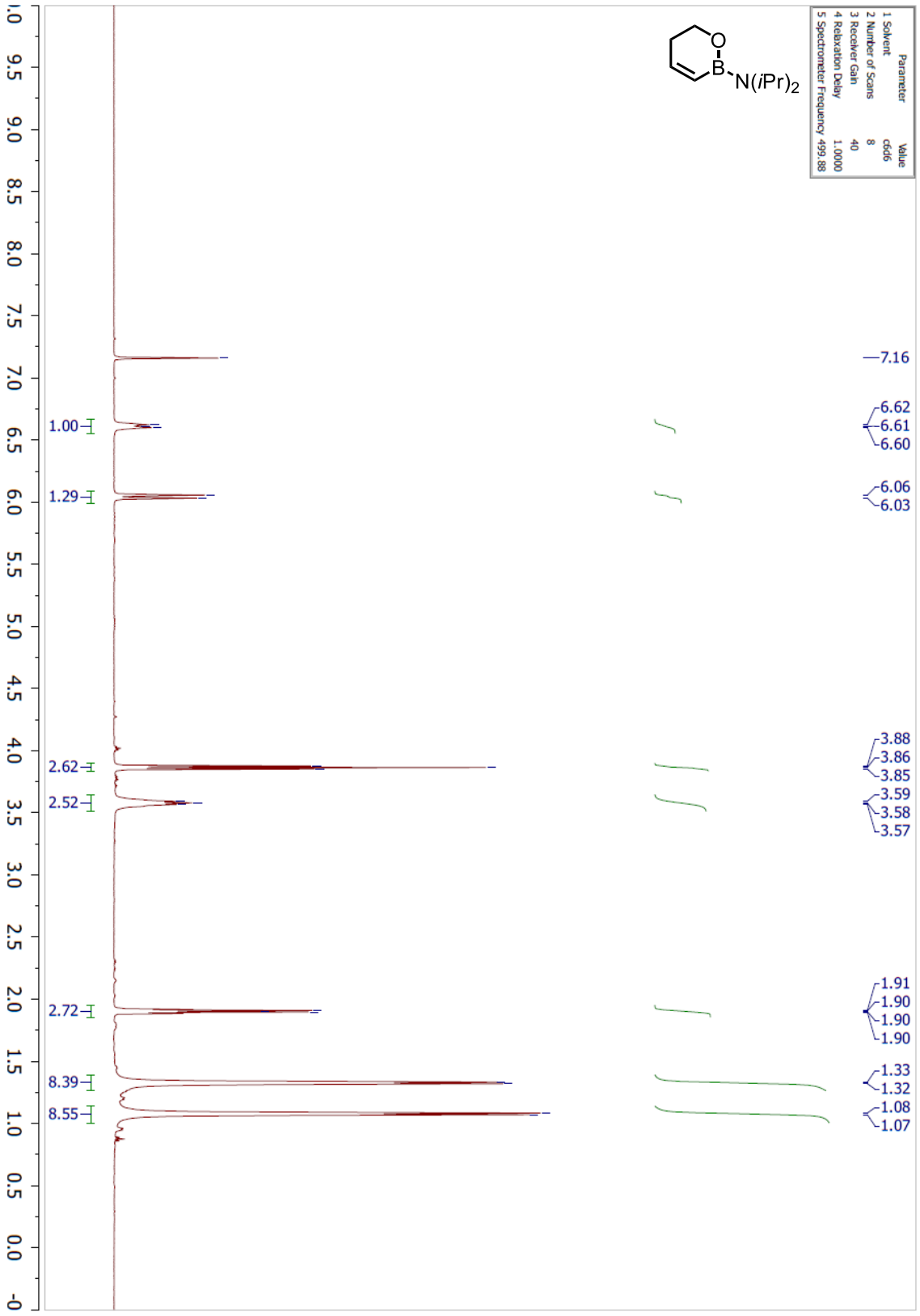
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4 Relaxation Delay 1.0000
5 Spectrometer Frequency 499.88
O
B
N(iPr)2
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6.62
6.61
6.60
6.06
6.03
3.88
3.86
3.85
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3.58
3.57
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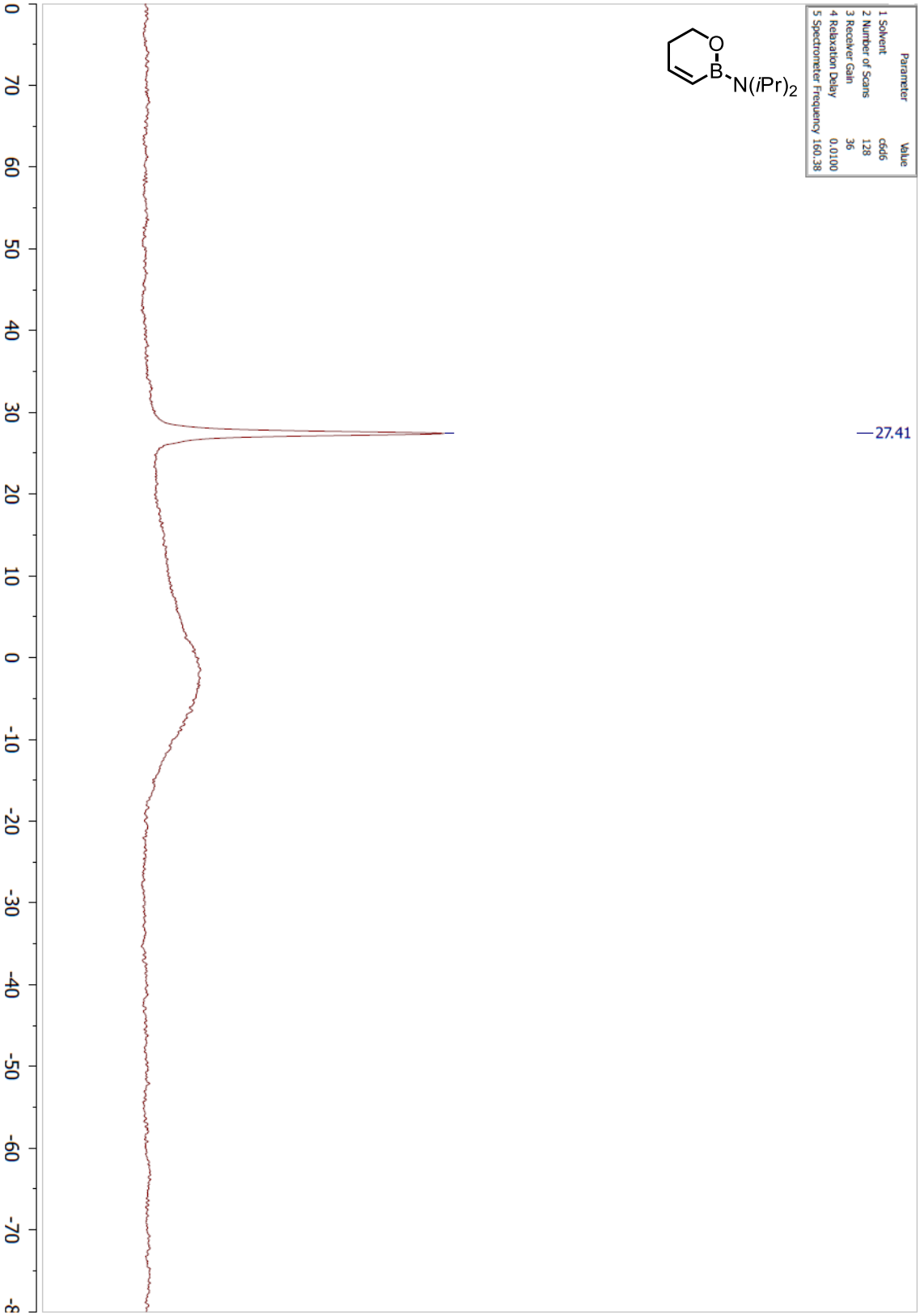
Parameter Value
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2 Number of Scans 128
3 Receiver Gain 36
4 Relaxation Delay 0.0100
5 Spectrometer Frequency 160.38
O
B
N(iPr)2
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60
50
40
30
20
10
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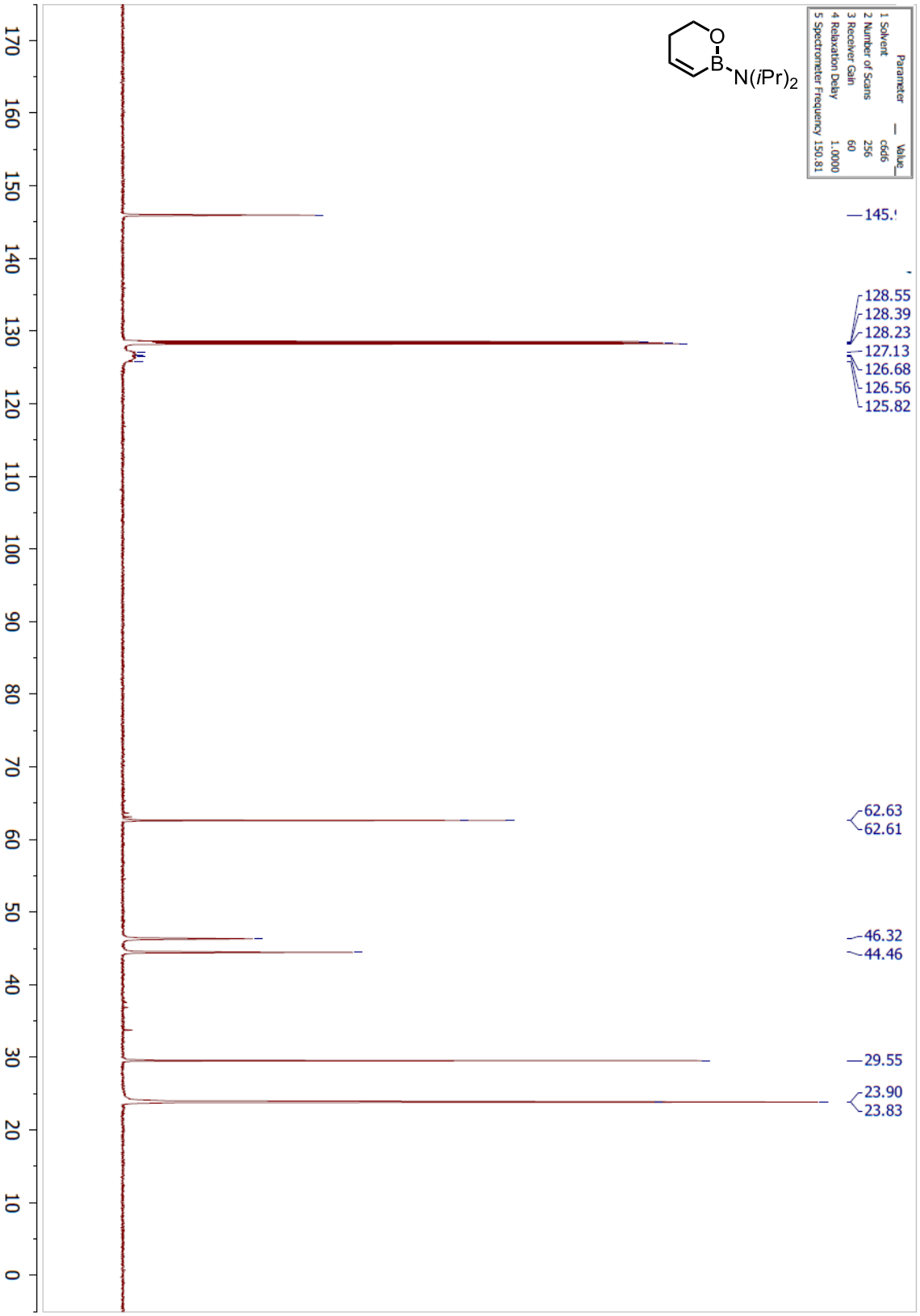
-50
-60
-70


O
B
N(iPr)2
Parameter — Value
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3 Receiver Gain 60
4 Relaxation Delay 1.0000
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128.55
128.39
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127.13
126.68
126.56
125.82
62.63
62.61
46.32
44.46
29.55
23.90
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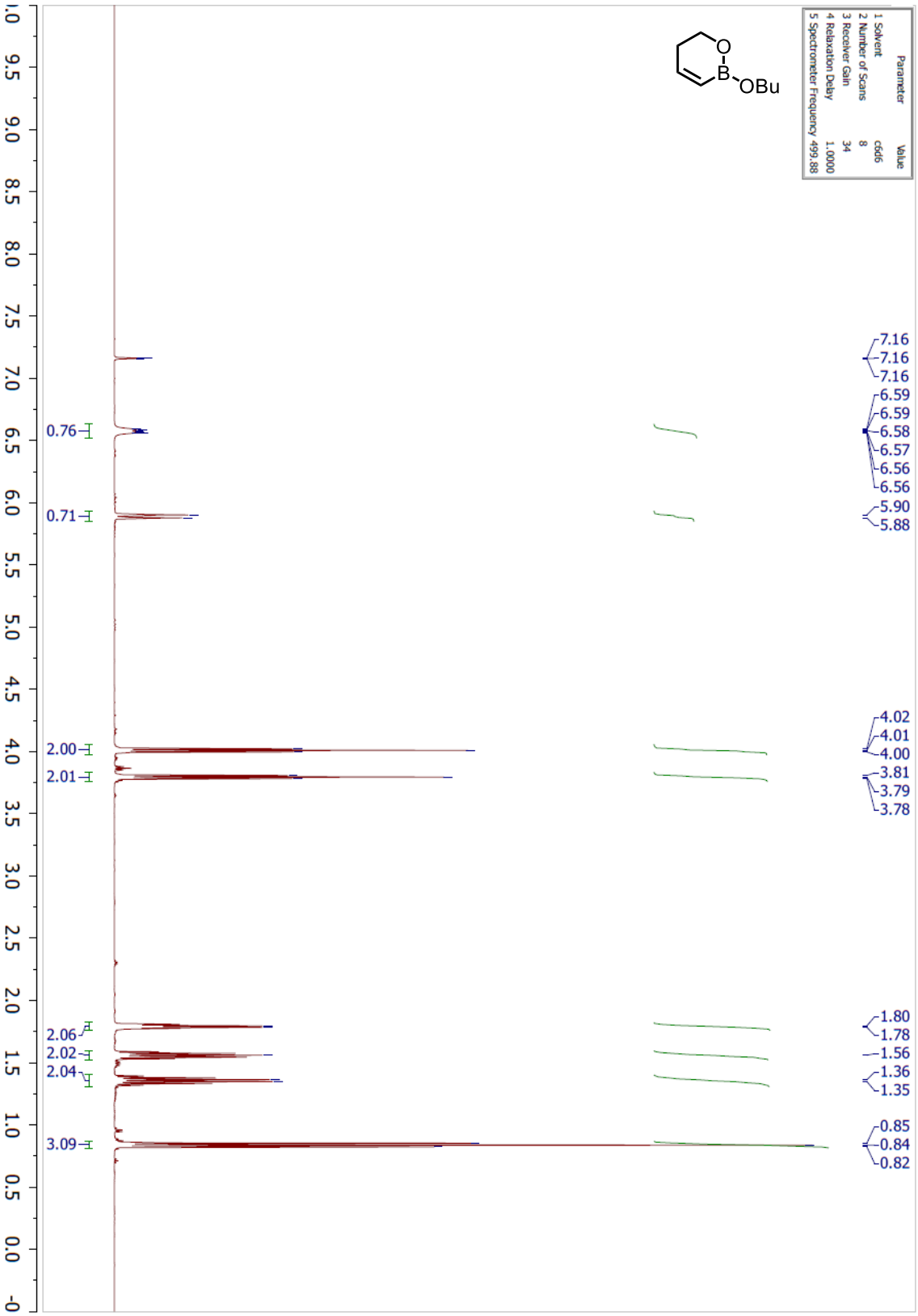
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2 Number of Scans 8
3 Receiver Gain 34
4 Relaxation Delay 1.0000
5 Spectrometer Frequency 499.88
O
B
OBu
7.16
7.16
7.16
6.59
6.59
6.58
6.57
6.56
6.56
5.90
5.88
4.02
4.01
4.00
3.81
3.79
3.78
1.80
1.78
1.56
1.36
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2.01
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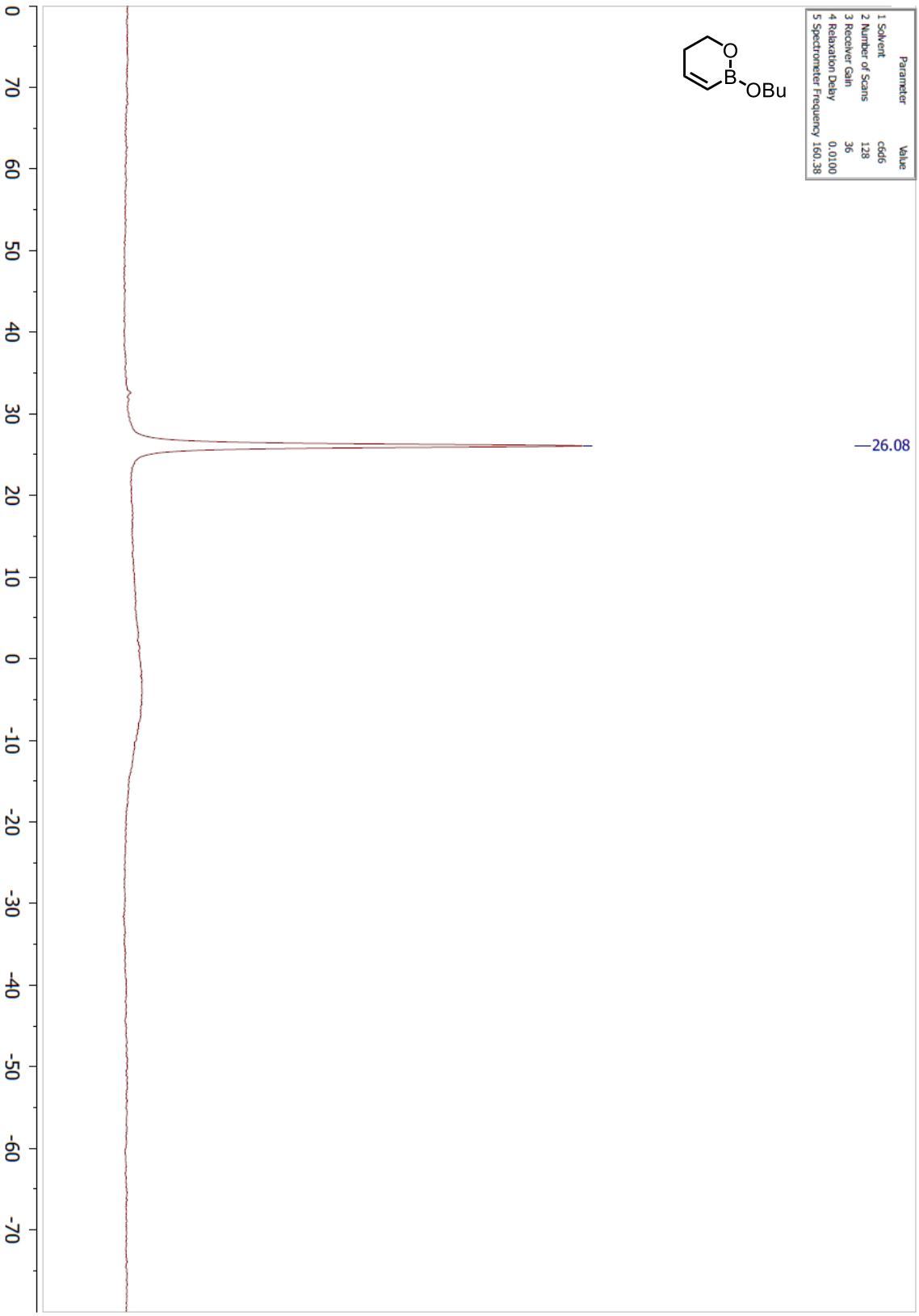
2.02
2.04
3.09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O
B
OBu
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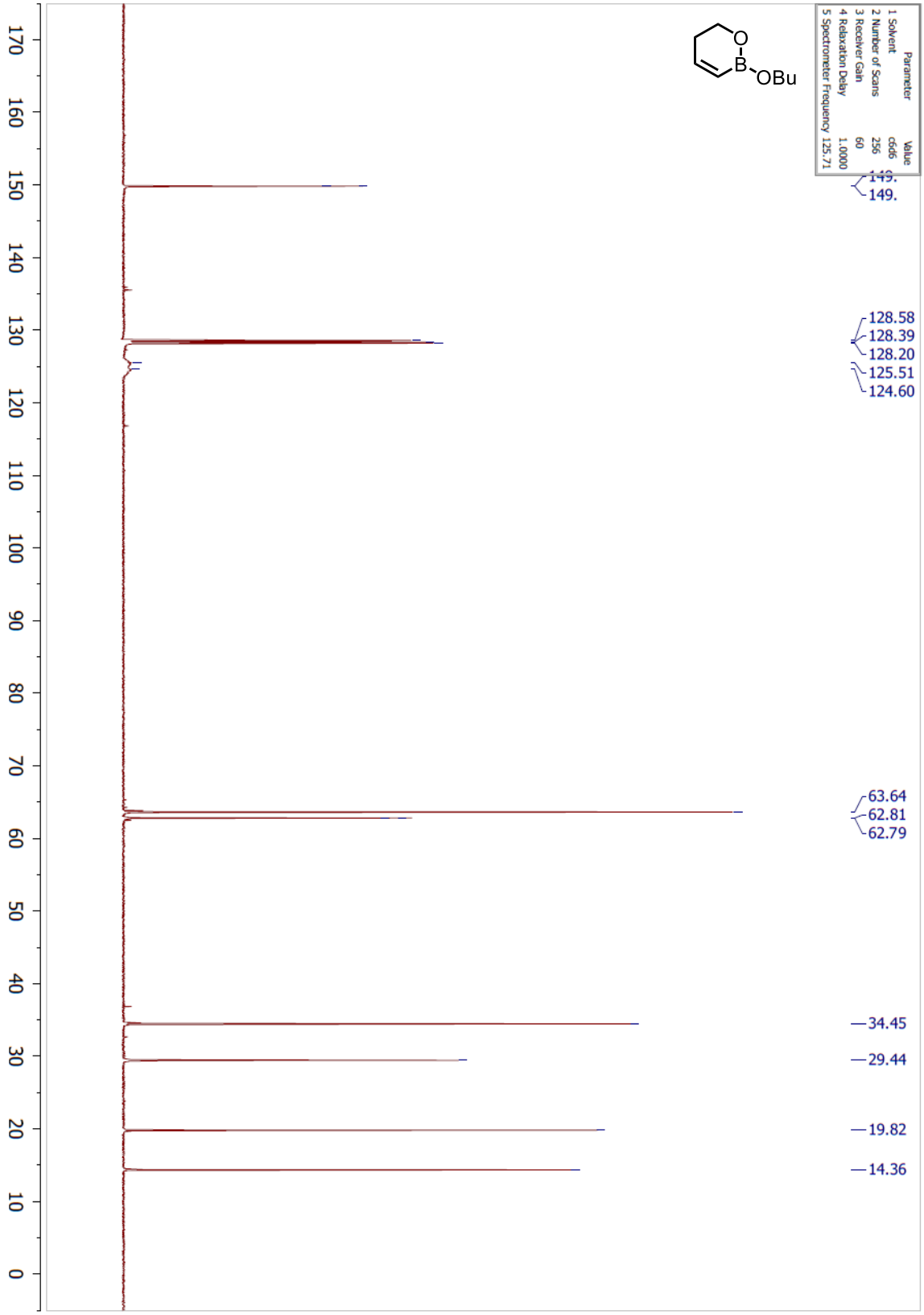
O
B
OBu
Parameter Value
1 Solvent c6d6
2 Number of Scans 256
3 Receiver Gain 60
4 Relaxation Delay 1.0000
5 Spectrometer Frequency 125.71
149.
149.
128.58
128.39
128.20
125.51
124.60
63.64
62.81
62.79
34.45
29.44
19.82
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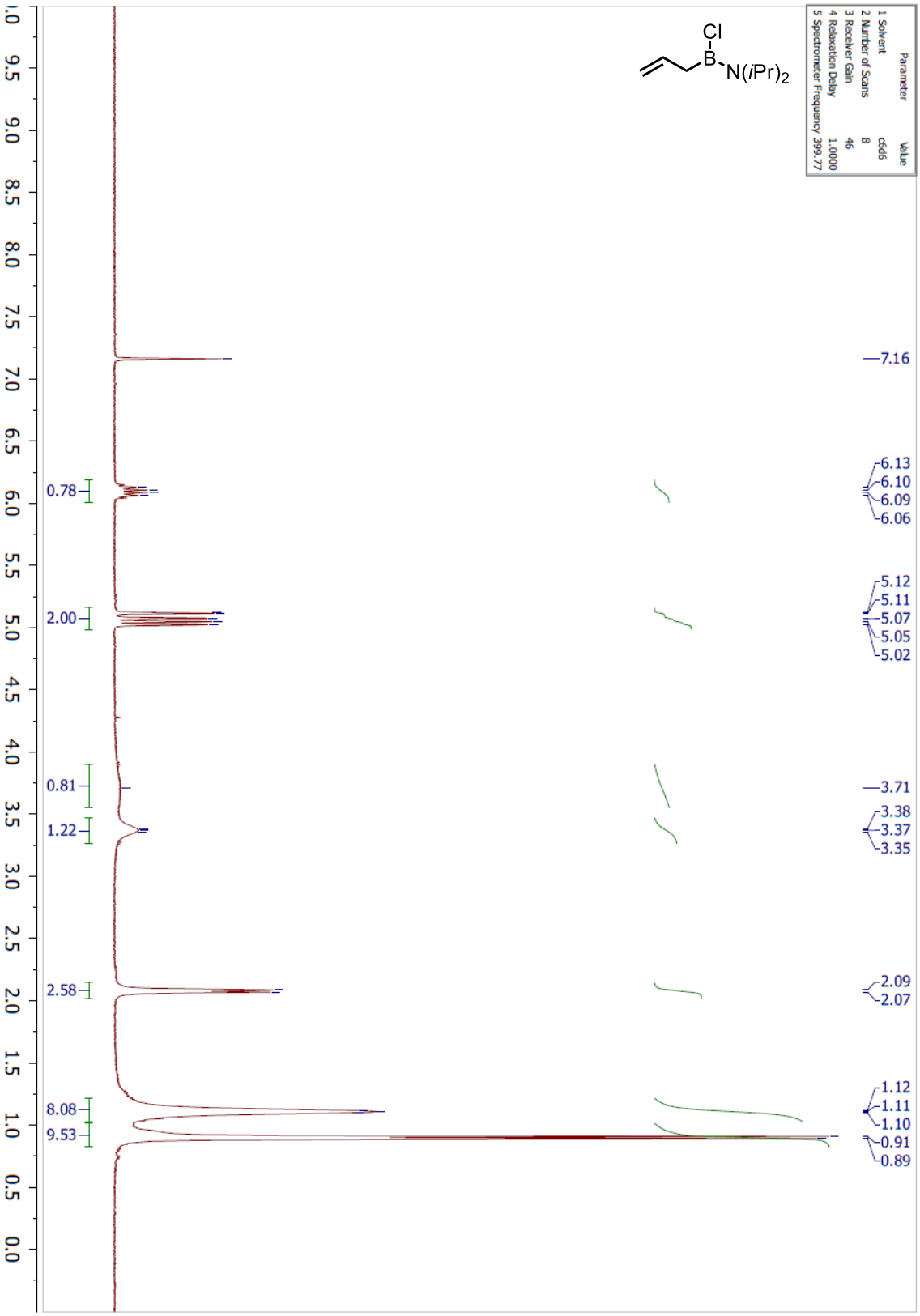
Cl
B
N(iPr)2
Parameter Value
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2 Number of Scans 8
3 Receiver Gain 46
4 Relaxation Delay 1.0000
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7.16
6.13
6.10
6.09
6.06
5.12
5.11
5.07
5.05
5.02
3.71
3.38
3.37
3.35
2.09
2.07
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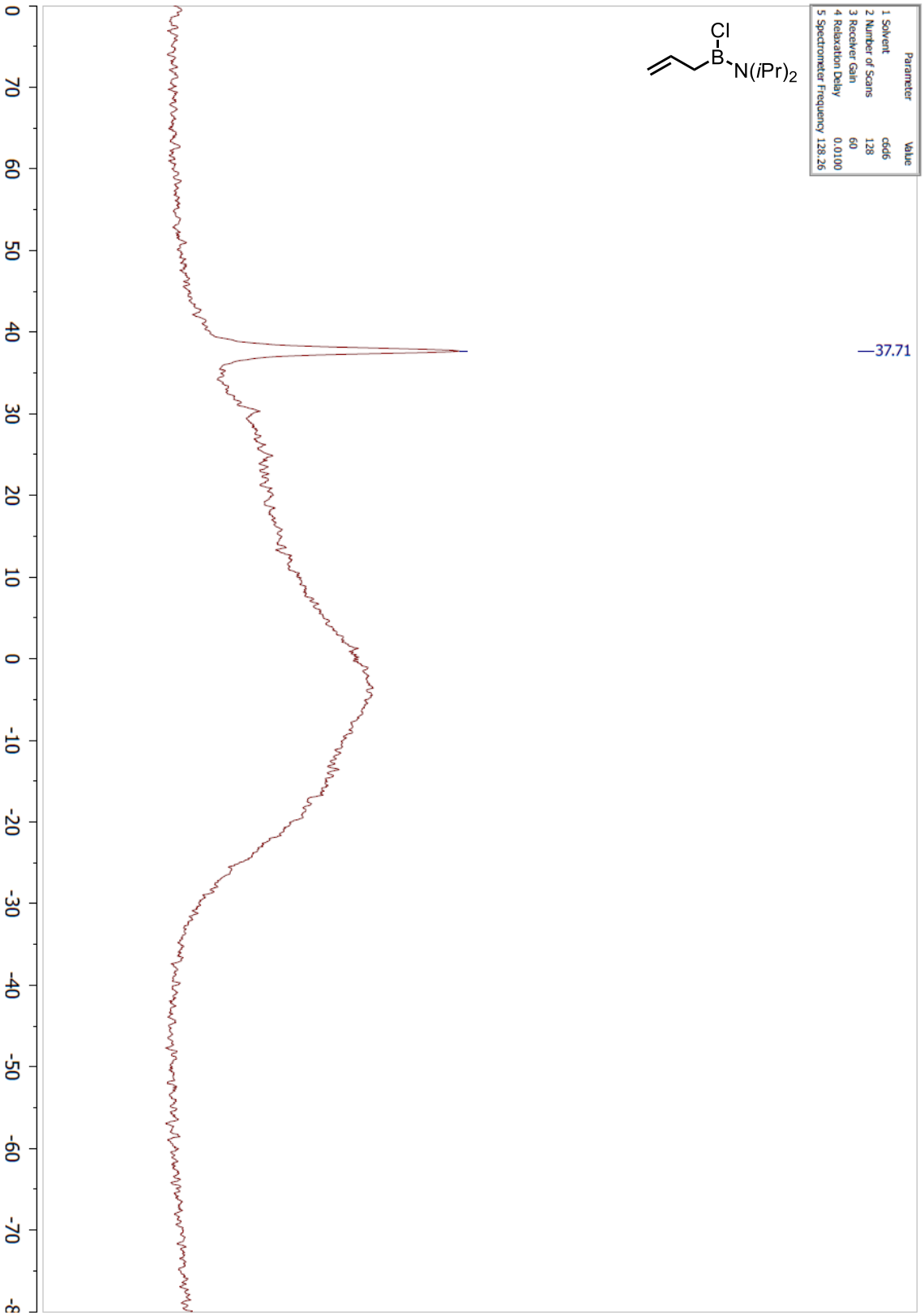
Cl
B
N(iPr)2
37.71
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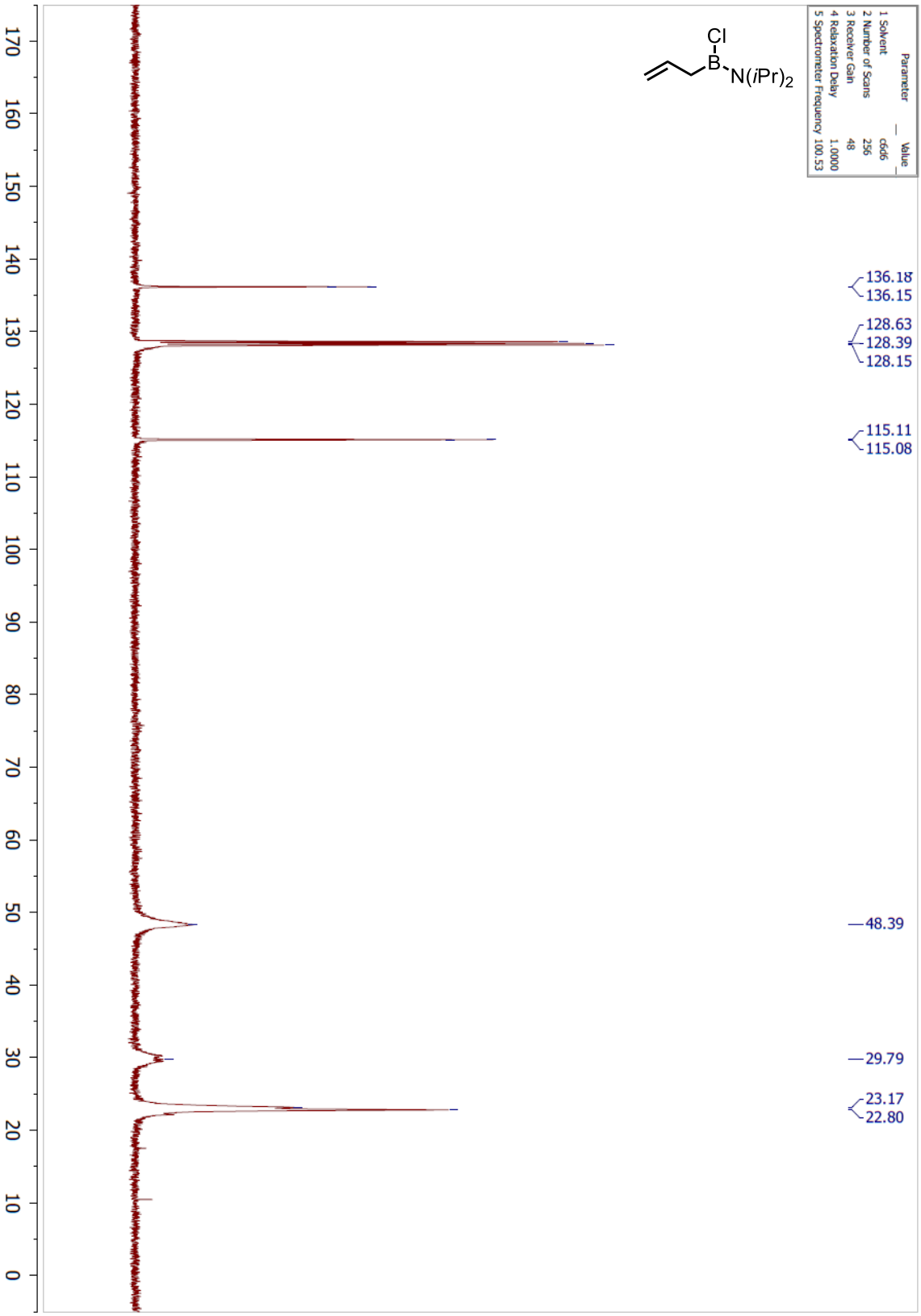
-8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N(iPr)2
Parameter
Value
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cd6
2 Number of Scans
256
3 Receiver Gain
48
4 Relaxation Delay
1.0000
5 Spectrometer Frequency
100.53
136.18
136.15
128.63
128.39
128.15
115.11
115.08
48.39
29.79
23.17
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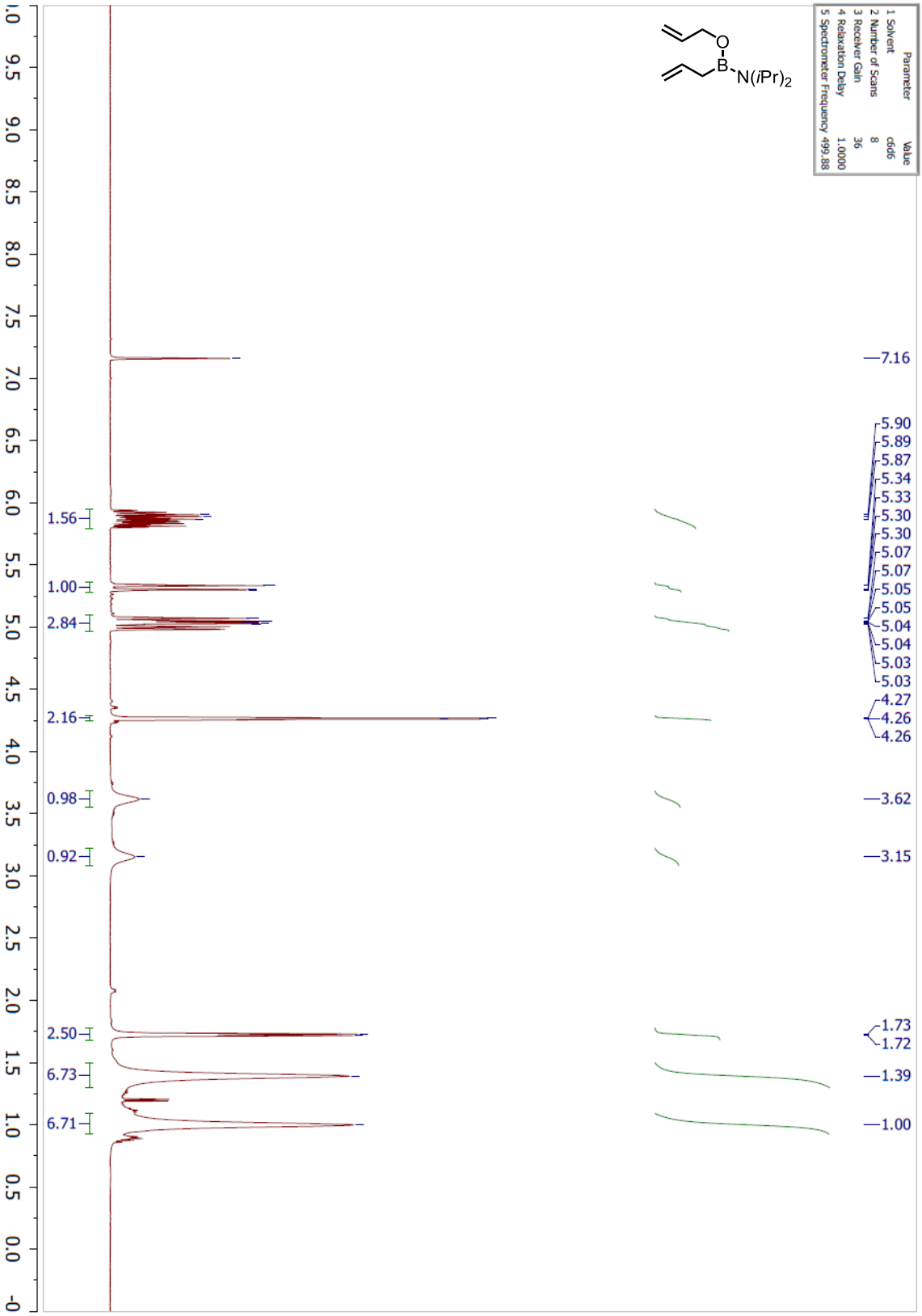
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3 Receiver Gain 36
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O
B
N(iPr)2
7.16
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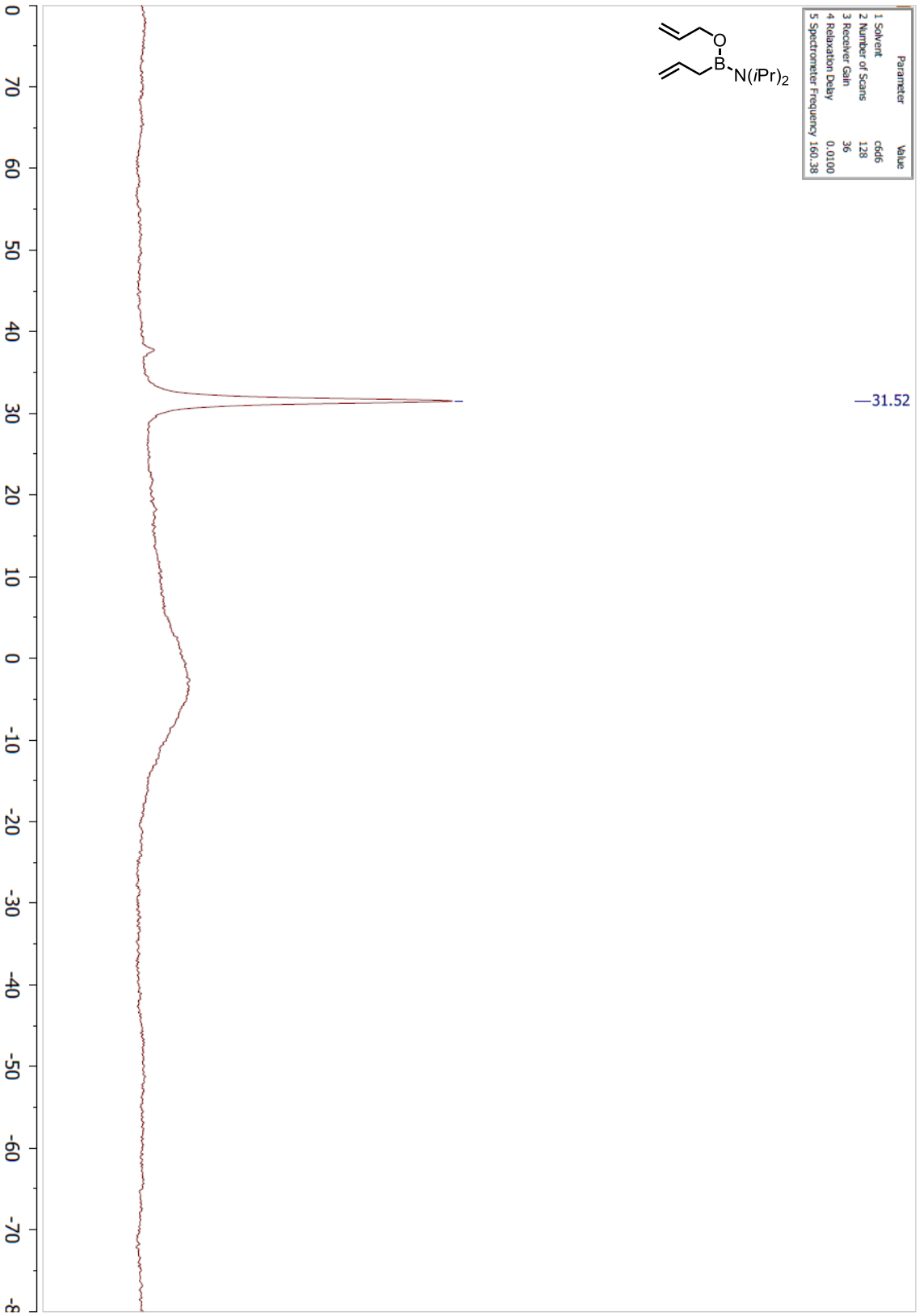
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N(iPr)2
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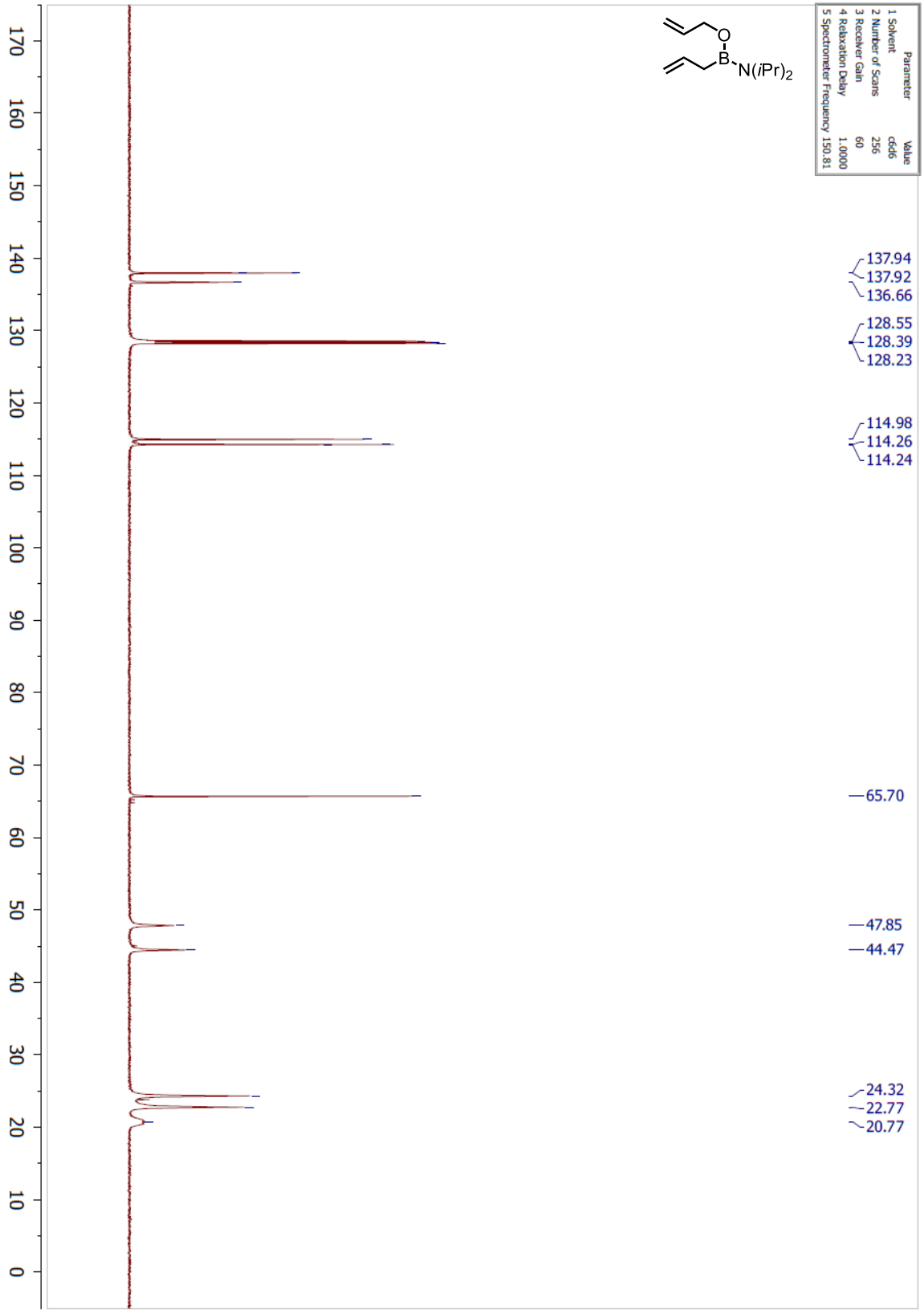
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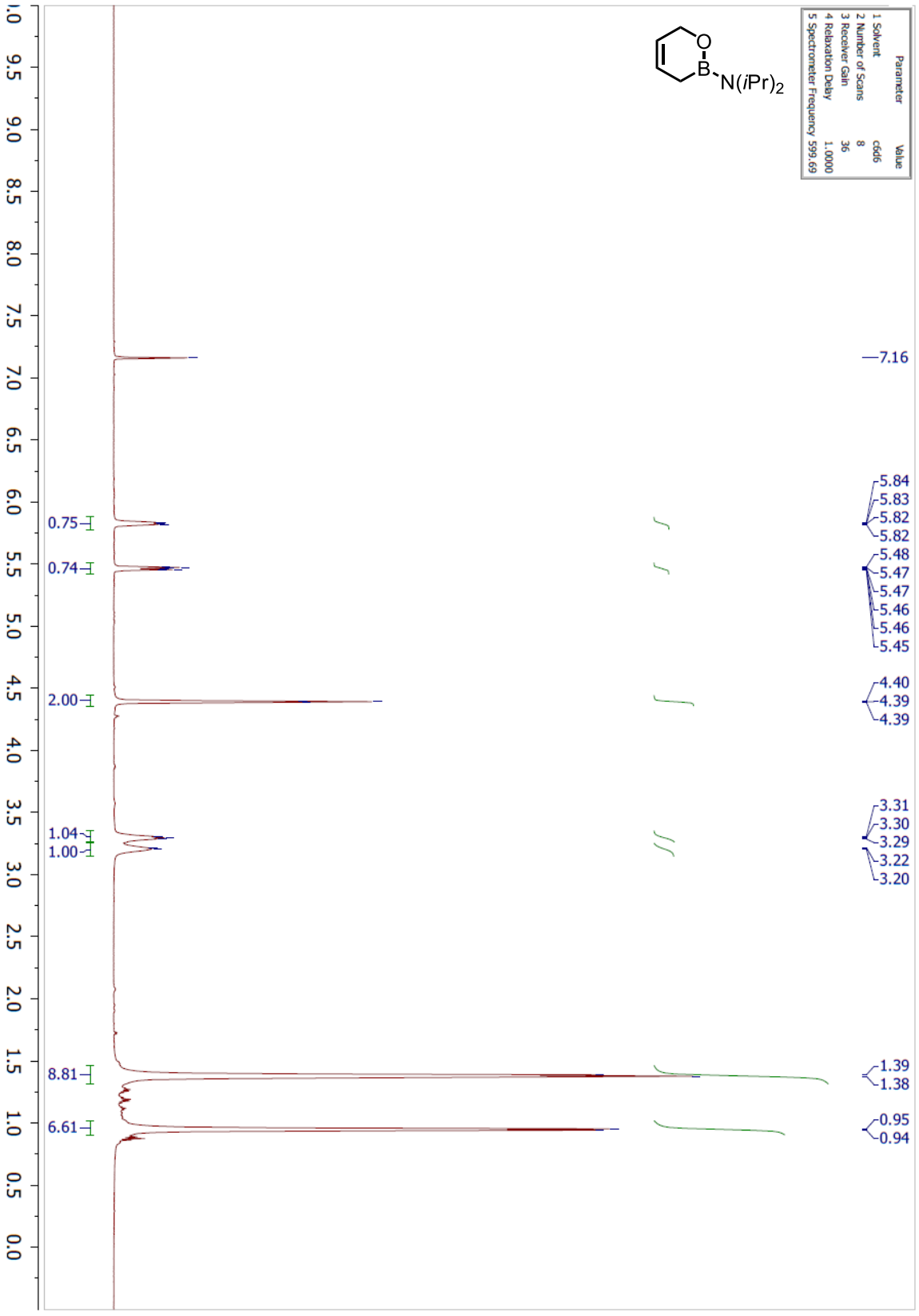
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N(iPr)2
7.16
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5.82
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5.47
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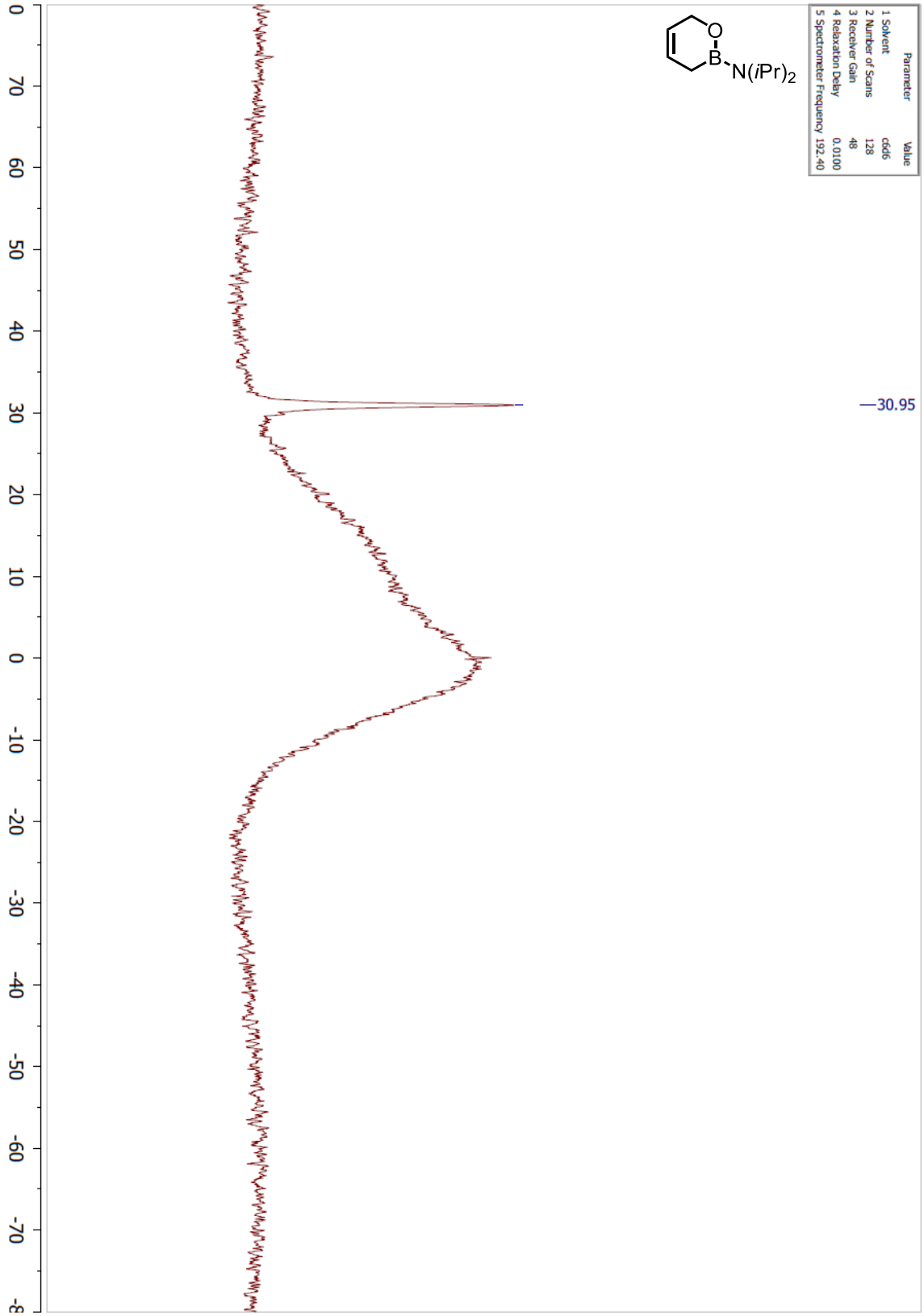
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B
N(iPr)2
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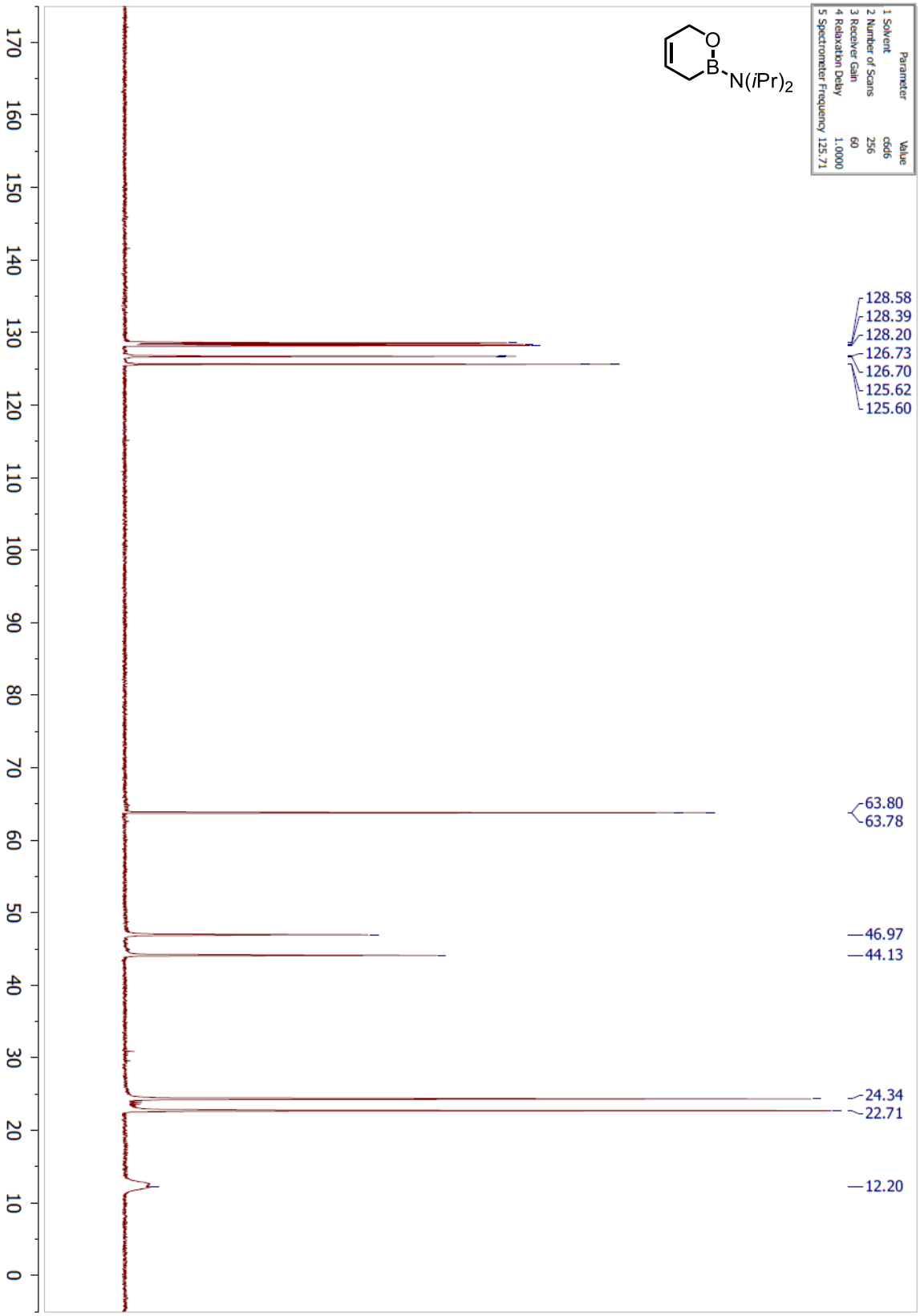
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B
N(iPr)2
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128.20
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126.70
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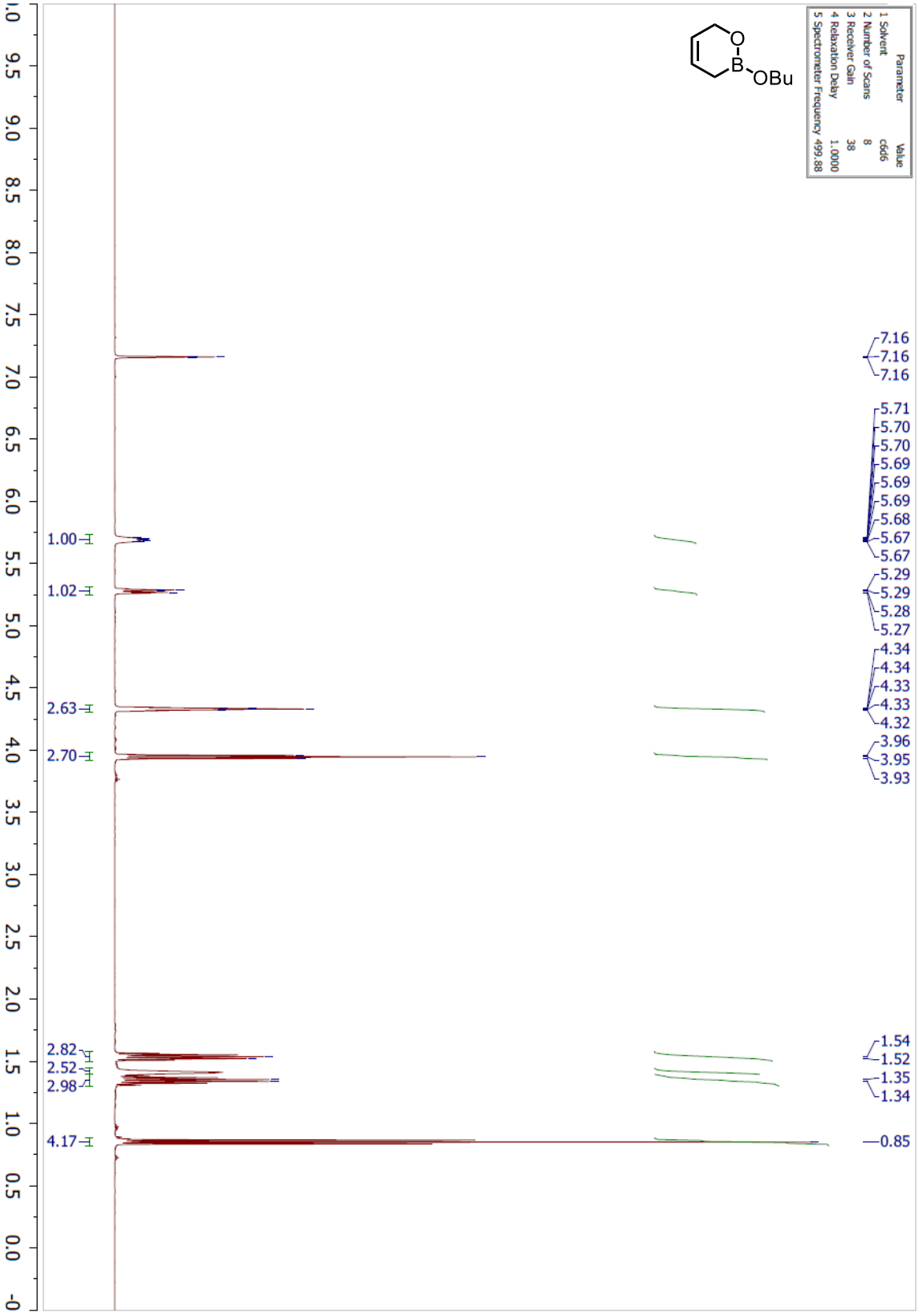
O
B
OBu
Parameter Value
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3 Receiver Gain 38
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5 Spectrometer Frequency 499.88
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7.16
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5.68
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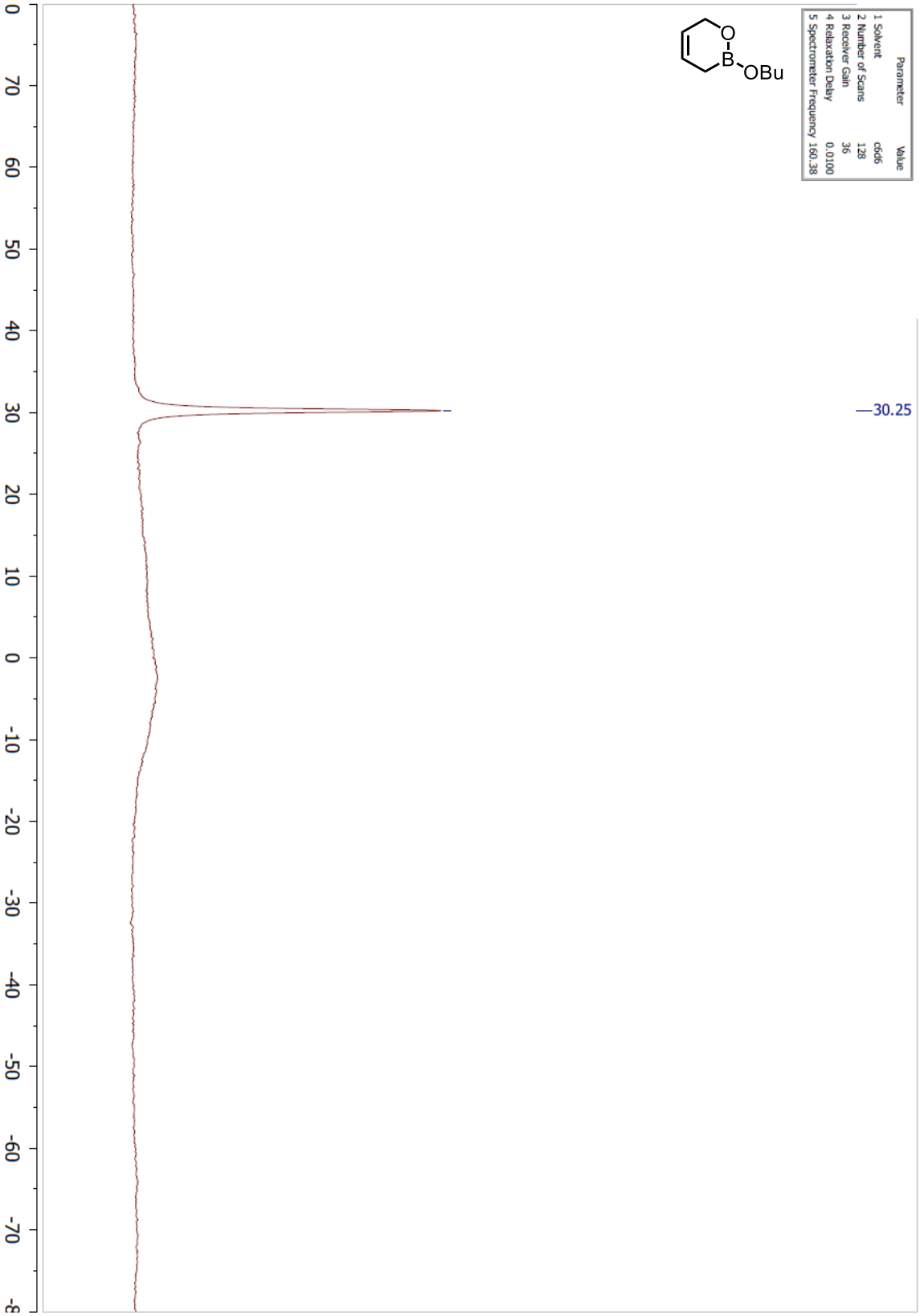
1.34
0.85
1.00
1.02
2.63
2.70
2.82
2.52
2.98
4.17
10 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0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3 Receiver Gain 36
4 Relaxation Delay 0.0100
5 Spectrometer Frequency 160.38
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B
OBu
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-10
-20
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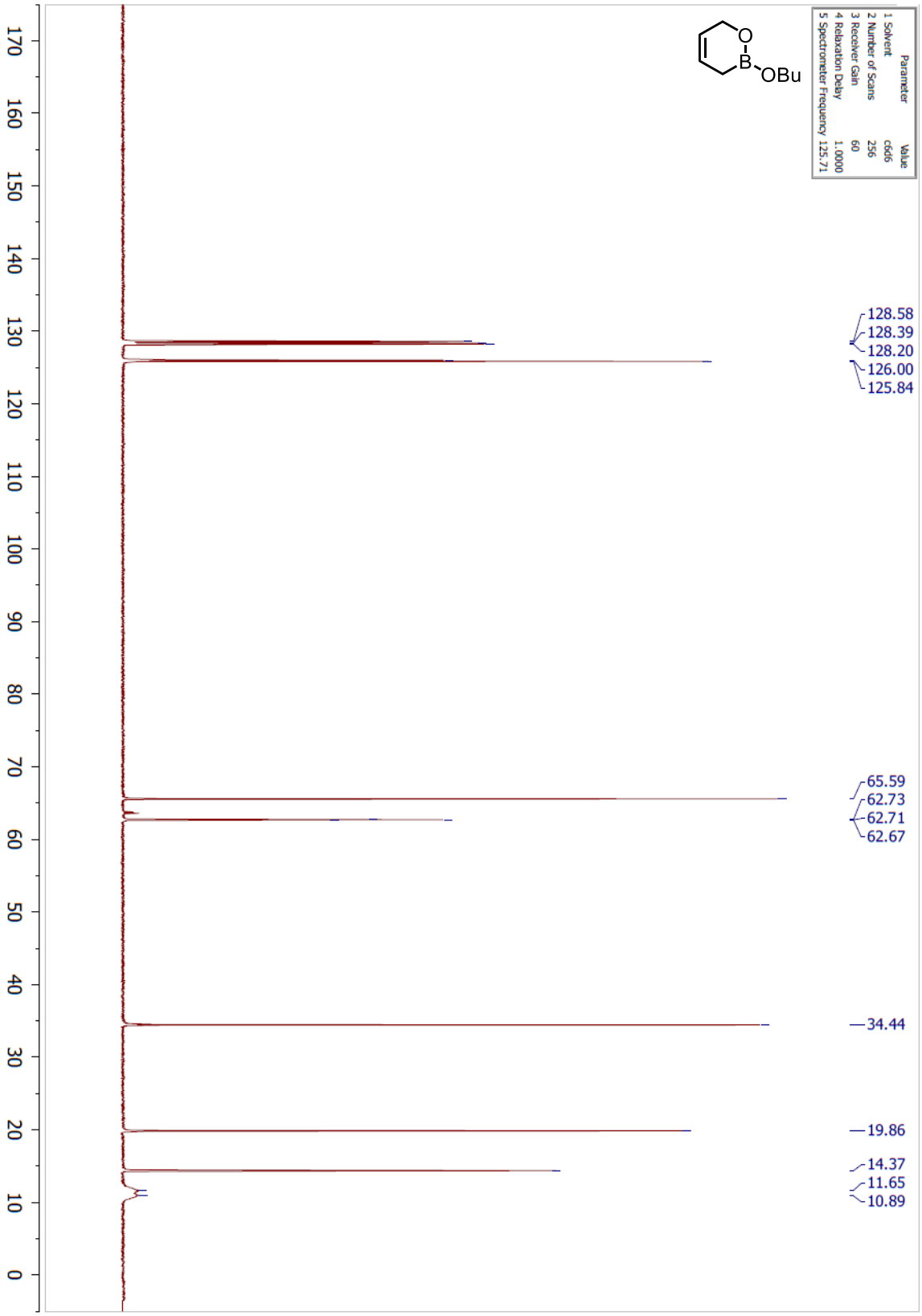
-70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B
OBu
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3 Receiver Gain 60
4 Relaxation Delay 1.0000
5 Spectrometer Frequency 125.71
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126.00
125.84
65.59
62.73
62.71
62.67
34.44
19.86
14.37
11.65
10.89
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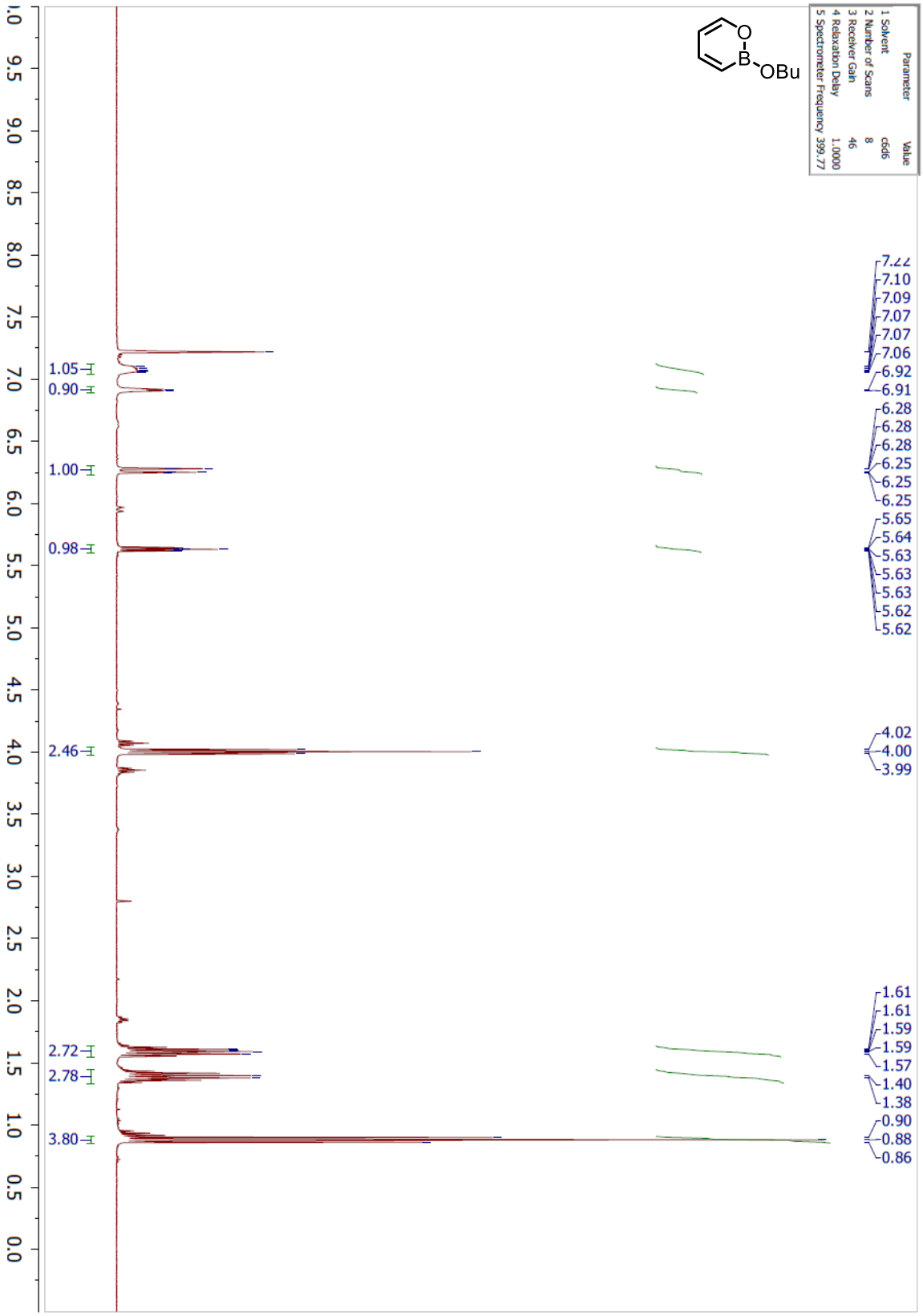
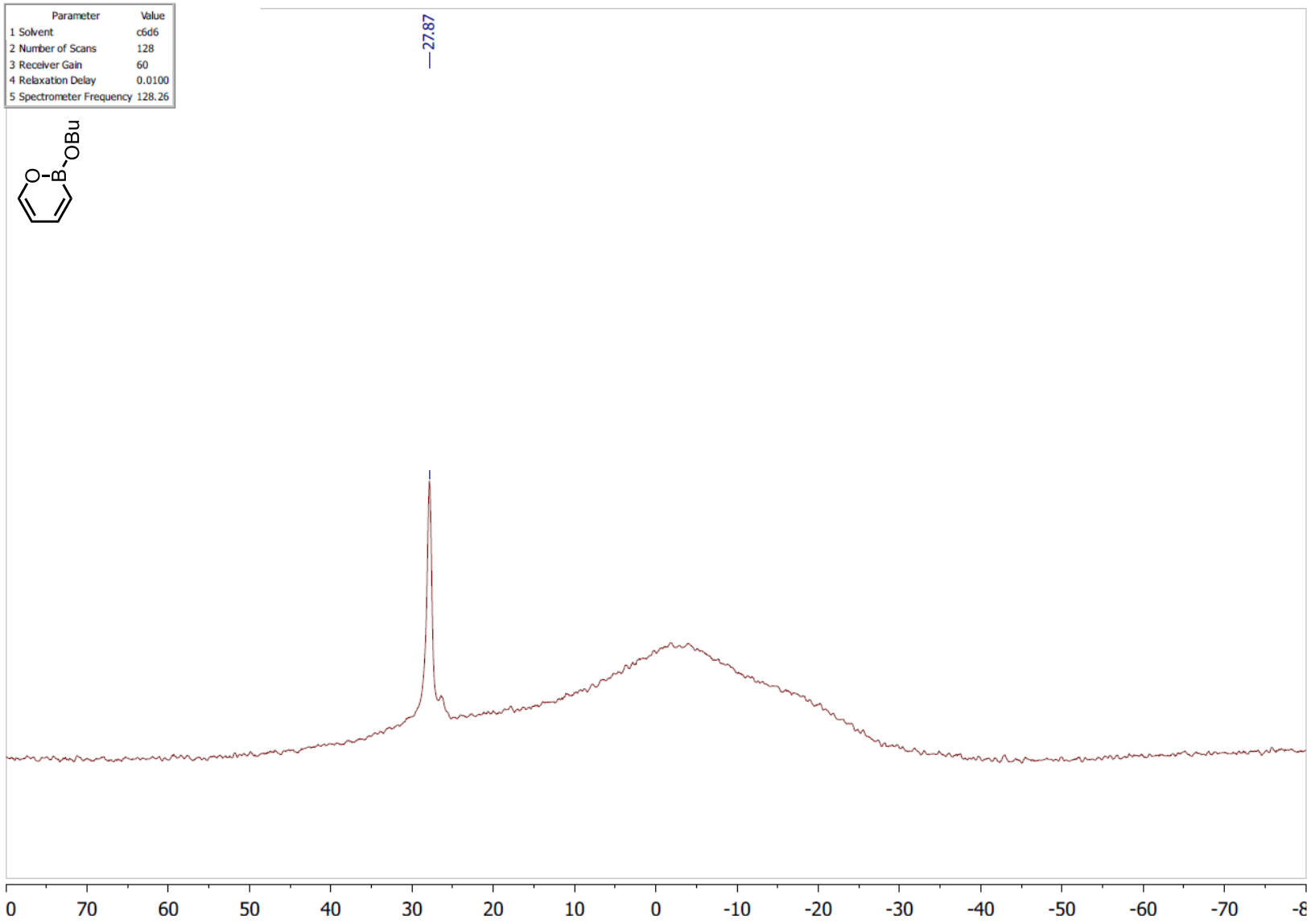
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


OBu
Parameter Value
1 Solvent c6d6
2 Number of Scans 8
3 Receiver Gain 46
4 Relaxation Delay 1.0000
5 Spectrometer Frequency 399.77
7.22
7.10
7.09
7.07
7.07
7.06
6.92
6.91
6.28
6.28
6.28
6.25
6.25
6.25
5.65
5.64
5.63
5.63
5.63
5.62
5.62
4.02
4.00
3.99
1.61
1.61
1.59
1.59
1.57
1.40
1.38
0.90
0.88
0.86
1.05
0.90
1.00
0.98
2.46
2.72
2.78
3.80


Parameter Value
1 Solvent c6d6
2 Number of Scans 128
3 Receiver Gain 60
4 Relaxation Delay 0.0100
5 Spectrometer Frequency 128.26
27.87
OBu
B
O
0
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70