# ENANTIOSELECTIVE SYNTHESIS OF TERTIARY BORONIC ESTERS THROUGH CONJUNCTIVE CROSS-COUPLING AND CYCLOBUTENE DIBORATION

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**Abstract:** This dissertation will present three main projects focusing on the catalytic enantioselective synthesis and stereospecific functionalization of tertiary alkylboronates. In the first project, acyl chlorides were incorporated as a new class of electrophile in conjunctive cross-coupling, from which, a variety of tertiary β-boryl amides were successfully synthesized with high enantioselectivity. The utility of the tertiary alkylboronates products was also demonstrated through several orthogonal functionalizations of the boronic ester group and amide groups. The project culminated in the enantioselective total synthesis of natural product (+)-Adalinine that leveraged this newly developed methodology. In the second project, a conjunctive cross-coupling enabled ring closure was developed to synthesize tertiary alkylboronates residing on carbocyclic and heterocyclic scaffolds. A Phosphinooxazoline (Phox) ligand was identified as a non-expensive ligand that catalyzed the conjunctive cyclization reaction with high enantioselectivity. A Series of synthetically challenging enantimerically enriched spirocyclic and aryl bicyclic tertiary alkylboronates were efficiently generated using this method, and several cyclopentyl boronic esters with two continuous stereogenic centers were synthesized with high diastereoselectivity. In the third project, a Rh-catalyzed diboration reaction was successfully employed to diborate monosubstituted cyclobutenes with excellent enantioselectivity. The less sterically hindered secondary boronic ester units in the diboron products can be regioselectively functionalized using the newly developed tert-butyllithium activation-transmetallation strategy. As a result, a variety of stereochemically defined β-substituted cyclobutyl tertiary boronic esters were synthesized with high efficiency.

ACKNOWLEDGEMENT

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Joining Jim's group initially seemed like a venture into "cool chemistry." However, it became evident that Jim's influence extended beyond academic pursuits. His decisions, each strategically altering my trajectory, guided me from a novice to a seasoned researcher. Jim's leadership, marked by positive influences, weekly invaluable advice, and an uplifting lab environment, contributed significantly to my growth and the group's success.

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LIST OF ABBREVIATIONS

| | |
|---|---|
| Ac | Acetyl |
| $\beta_3$-AR | $\beta_3$-Adrenergic receptors |
| Boc | *tert*-butyloxycarbonyl |
| BBN | Borabicyclo[3.3.1]nonane |
| bDNA | branched DNA |
| Bn | Benzyl |
| bpy | Bipyrdine |
| cat | Catechol |
| Cbz | Benzyloxycarbonyl |
| CB1 | Cannabinoid receptor 1 |
| CB1 | Cannabinoid receptor 2 |
| CDI | 1,1'-carbonyldiimidazole |
| COD | Cyclooctadiene |
| conv. | Conversion |
| CPhos | 2-Dicyclohexylphosphino-2,6-bis(N,N-dimethylamino)biphenyl |
| dan | Naphthalene-1,8-diamine |
| DABCO | 1,4-diazabicyclo[2.2.2]octane |
| dba | Dibenzylideneacetone |
| DCM | Dichloromethane |
| DIBAL | Diisopropylaluminum hydride |
| diglyme | bis(2-methoxyethyl) ether |
| DiPP | 2,5-diisopropyl phenyl |
| DOT1L | DOT1 like histone lysine methyltransferase |
| dr | Diastereomeric Ratio |
| DMA | Dimethylacetamide |
| dme | Dimethyl ethylene |
| DMSO | Dimethyl sulfone |
| dtbbpy | 4,4'-di-tert-butyl-2,2'-bipyridine |
| $EC_{50}$ | Half maximal effective concentration |
| $EC_{90}$ | 90% maximal effective concentration |
| ee | Enantiomeric excess |
| equiv | Equivalent |
| er | Enantiomeric ratio |
| Et | Ethyl |
| $Et_2O$ | Diethyl ether |
| EtOAc | Ethyl acetate |
| hac | (1R,2S)-1,2-dihydroacenaphthylene-1,2-diol |
| *i*- | *iso* |
| $IC_{50}$ | Half maximal inhibitory co-ncentration |
| JAK1 | Janus kinase inhibitor 1 |
| JAK1 | Janus kinase inhibitor 2 |
| $K_i$ | Inhibitor constant (measuring the inhibitor's potency, smaller $K_i$ indicates higher potency) |
| $K_d$ | Equilibrium dissociation c-onstant (measuring the ligand's affinity towards certain receptor, smaller $K_d$ indicates higher affinity) |

| | |
|---|---|
| mac | (1R,2S)-1,2-dimethyl-1,2-dihydroacenaphthylene-1,2-diol |
| Mes | Mesityl |
| *m*- | *meta*- |
| neo | Neopentyl Glycol |
| $H_2N$-NMM | 1-amino-1-methylpiperidin-1-ium iodide |
| *o*- | *ortho*- |
| OAc | Acetoxy Group |
| OAmyl | 2-methylbutanoate |
| OMs | Methanesulfonate |
| OTf | Trifluoromethanesulfonate |
| *p*- | *para*- |
| PB2 | Polymerase basic 2 |
| Pd-G3 | Buchwald Third Generation Precatalysts |
| pin | Pinacol |
| PDE10A | Phosphodiesterase 10A |
| PK | Pharmacokinetic |
| PMB | *para*-Methoxy benzyl |
| PMP | *para*-Methoxy phenyl |
| RuPhos | 2-Dicyclohexylphosphino-2,6-diisopropoxybiphenyl |
| SPhos | 2-Dicyclohexylphosphino-2,6-dimethoxybiphenyl |
| *t*- | *tert*- |
| TBDPS | *tert*-Butyldphenylsilyl |
| TBS | *tert*-Butyldimethylsilyl |
| TEMPO | 2,2,6,6-tetramethyl-1-piperidinyloxy |
| TFA | Trifluoroacetyl |
| THF | Tetrahydrofuran |
| $TI_{avg}$ | Average therapeutic index |
| TIPS | Triisopropylsilyl |
| TMEDA | N,N,N,N-tetramethyl ethylenediamine |
| TMS | Trimethylsilyl |
| TNKS1 | Tankyrase 1 |
| Tol | Toluene |
| Ts | Toluenesulfonyl |
| XPhos | 2-Dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl |

# Table of Contents

# Chapter 1 Enantioselective Synthesis of Tertiary β-Boryl Amides by Conjunctive Cross-Coupling of Alkenyl Boronates and Carbamoyl Chlorides

## 1.1 Introduction

Carbonyl functional groups are widely present in organic molecules. Due to the high electronegativity of the oxygen atom, the carbon-oxygen double bond is typically polarized towards the oxygen, resulting in the carbon atom becoming electrophilic and highly reactive.[1] As a result, building blocks containing carbonyl groups are extensively utilized by both nature and industry to construct more complex structures.[2] Reactions involving acyl groups generally occur via two different modes: addition-elimination[3] or direct cleavage/formation of the acyl bond.[4] The addition-elimination mode is more commonly applicable to various classes of acyl groups. Examples include esterification[5] or amidation of carboxylic acids[6], as well as hydrolysis of esters, acyl halides, and acid anhydrides.[7] On the other hand, direct cleavage or formation of the acyl C–X bond occurs less frequently and often requires the involvement of reactive catalysts.[8] Despite being less general, catalytic direct cleavage/formation of acyl C–X bonds plays a vital role in the industrial-scale synthesis of carbonyl-containing molecules. For instance, in industrial settings, catalytic hydroacylation of alkenes is carried out to synthesize complex aldehyde-containing chemical feedstocks on a multimillion-ton scale annually.[9] In the setting of pharmaceutical reagents R&D, acyl chlorides can be used as electrophiles in Suzuki-Miyaura cross-coupling reactions to synthesize acyl aromatic motifs found in a variety of pharmaceutically relevant molecules.[10] Both processes rely on the direct cleavage of acyl C–X bonds (C–H bond for hydroacylation and C–Cl bond for acylative Suzuki-Miyaura coupling) and the direct formation of acyl C–C bonds, facilitated by the oxidative addition and reductive elimination of transition metals.

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[1] Wiberg, B. K. *Acc. Chem. Res.* **1999**, *32*, 922–929.
[2] Berthier, G.; Serre, J. *General and theoretical aspects of the carbonyl group*. **1966**.
[3] Murov, S. *J. Chem. Educ.* **2007**, *84*, 1224.
[4] Yamaguchi, J. *Chem. Soc. Rev*. **2017**, *46*, 5864–5888.
[5] Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, 52, 1989–1993.
[6] Swiderek, K.; Marti, S.; Tunon, I.; Moliner, V.; Bertran, J. *J. Am. Chem. Soc.* **2015**, 137, 12024–12034.
[7] Kevill, D. N. *Chloroformate esters and related compounds.* **1972**.
[8] Fu, Z.; Wang, X.; Tao, S.; Bu, Q.; Wei, D.; Liu, N. *J. Org. Chem.* **2021**, *86*, 2339–2358.
[9] Franke, R.; Selent, D.; Borner, A. *Chem. Rev.* **2012**, *112*, 5675–5732.
[10] Blangetti, M.; Rosso, H.; Prandi, C.; Deagostino, A.; Venturello, P. *Molecules* **2013**, *18*, 1188–1213.

In addition to these well-established examples, numerous transformations based on this reaction mechanism have been discovered and investigated.[11] Interestingly, if new stereogenic centers are formed through catalytic acylation processes (such as migratory insertion of an alkene[12] or desymmetrization of meso anhydride[13]), the stereochemistry of the reaction can be controlled by a careful chiral catalyst design. In this chapter, a palladium-catalyzed reaction between a tetrasubstituted alkenyl boronate complex and acyl electrophiles is employed to synthesize enantiomerically enriched β-boryl carbonyl compounds.[14] The reaction mechanism, condition screening, substrate scope, as well as the utility of the reaction products, will be discussed.

### 1.1.1 Acylative Suzuki-Miyaura cross-coupling

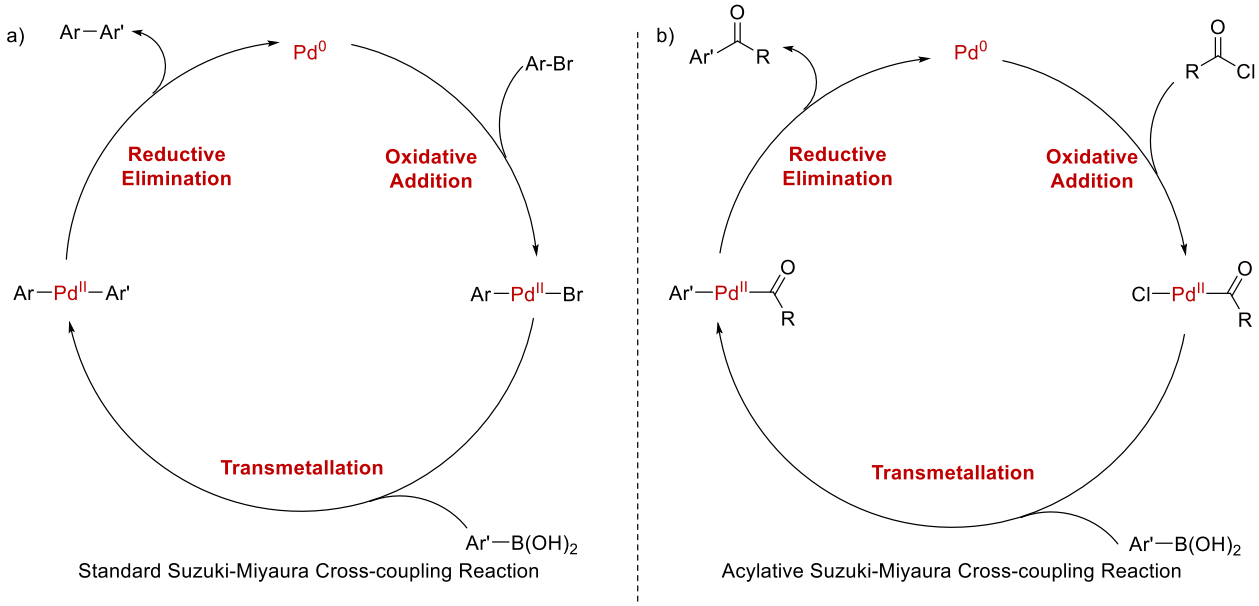



***Figure 1.1.*** Comparison Between Standard and Acylative Suzuki-Miyaura Cross-coupling Reactions

The Suzuki-Miyaura cross-coupling is a palladium catalyzed C–C bond-forming reaction between an organoboron and an aryl or alkenyl halide or triflate electrophile.[15] The reaction is proposed to access by an oxidative addition, transmetallation and reductive elimination catalytic

[11] Rodriguez, N.; Goossen, L. J. *Chem. Soc. Rev.* **2011**, *40*, 5030–5048.
[12] Nozaki, K. *Pure and Applied Chemistry* **2004**, *76*, 541–546.
[13] Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 174–175.
[14] Wilhelmsen, C. A.; Zhang, X.; Myhill, J. A.; Morken, J. P. *Angew. Chem. Int. Ed.* **2022**, *61*, e202116784.
[15] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.

cycle (Figure 1.1a).[16] If an acyl electrophile is used to substitute the aryl or alkenyl halide, an acylative version of Suzuki-Miyaura cross-coupling can be achieved, and carbonyl containing molecules can be generated (Figure 1.1b).[17] Several types of acyl electrophiles have been studied, including acyl chlorides, acyl fluorides, esters, amides, chloroformates and carbamoyl chlorides.

### 1.1.1.1 Acyl halides and anhydrides as electrophiles

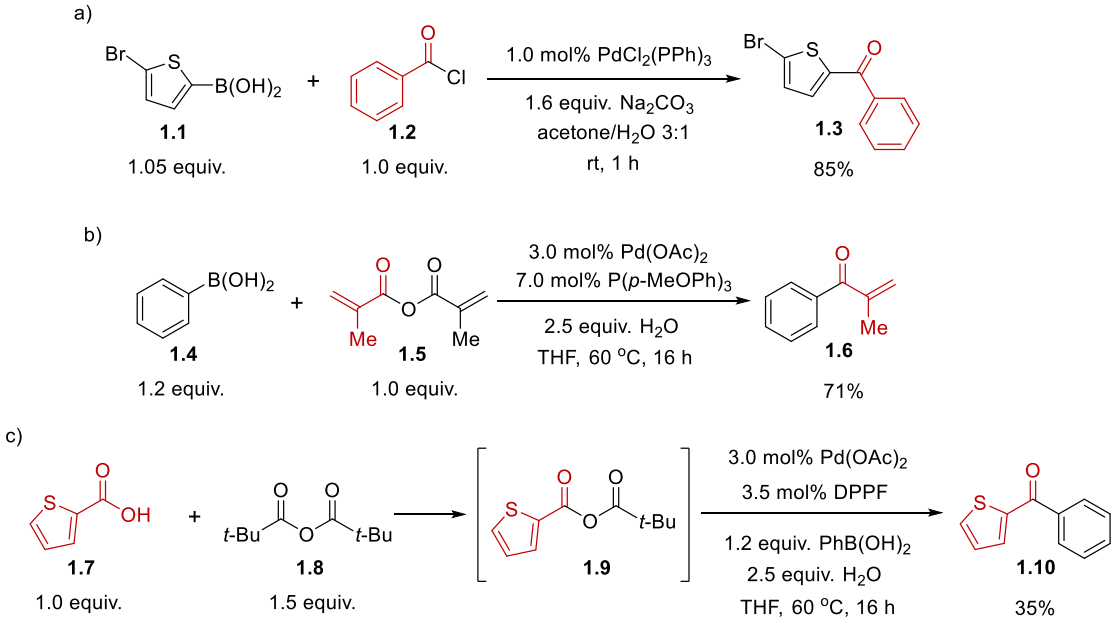



***Figure 1.2.*** Acylative Suzuki-Miyaura Cross-Coupling with Acyl Chloride or Acid Anhydride Electrophiles

The first acylative Suzuki-Miyaura cross-coupling between an aryl boronic acid and an acyl halide was developed by Bumagin in 1999, which showcased the high efficiency of this coupling reaction. [18] Due to the high electrophilicity of acyl chlorides, the oxidative addition can occur with a phospine-free Pd(0) complex at room temperature (Figure 1.2a). Interestingly, the oxidative addition of acyl chlorides is faster than that of aryl bromides as **1.1** can be used as the acyl electrophile without cross-coupling happening to the aryl bromide. In 2001, Gooβen developed the cross-coupling using acid anhydrides as electrophiles.[19] Using triphenylphosphine-ligated Pd(0), symmetrical anhydrides bearing aryl or alkyl substituents could be coupled with aryl

[16] Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461–470.
[17] Dieter, P. K. *Tetrahedron* **1999**, *55*, 4177–4236.
[18] Bumagin, N. A.; Korolev, D. N. *Tetrahedron Lett.* **1999**, *40*, 3057–3060.
[19] Gooβen, L. J.; Ghosh, K. *Eur. J. Org. Chem.* **2002**, 3254–3267.

boronic esters at room temperature (Figure 1.2b). Also, it was found that when an non-symmetric anhydride bearing a bulky *t*-Bu group is used (**1.9**), the oxidative addition will only occur on the less hindered acyl group. This feature makes it possible to cross-couple specific acyl groups from carboxylic acids after being converted to pivalic anhydride (Figure 1.2c).

### 1.1.1.2 Chloroformates and carbamoyl chlorides as electrophiles

Besides alkyl and aryl ketones, Suzuki-type coupling reactions can also be used to synthesize esters and amides. Duan and Deng demonstrated a cross-coupling between aryl boronic esters and chloroformates or carbamoyl chlorides.[20] Using $Pd(PPh_3)_4$ as catalyst, aryl esters and amides can be generated in moderate to good yield. It was found that the addition of $Cu_2O$ facilitated transmetallation between aryl boronic acid and acylated Pd complex (Figure 1.3).

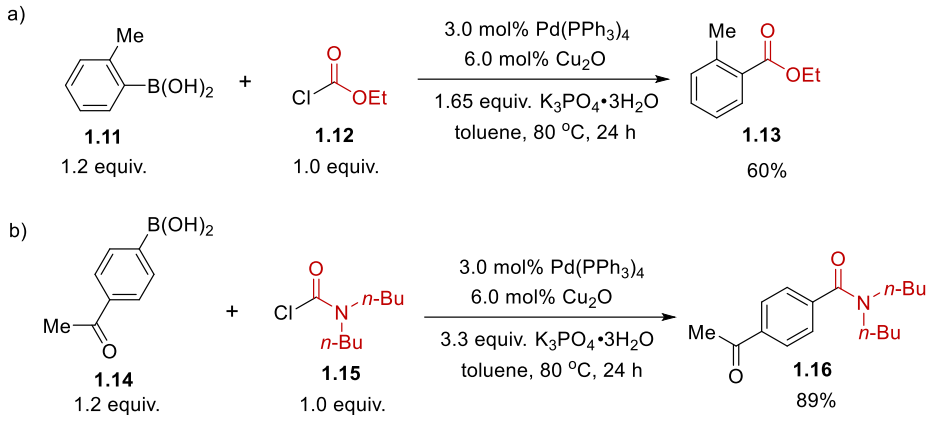



***Figure 1.3.*** Acylative Suzuki-Miyaura Cross-coupling with Chloroformate and Carbamoyl Chlorides Electrophiles

### 1.1.1.3 Esters and amides as electrophiles

Although acyl halides and anhydrides are widely used in acylative coupling reactions, they are among the least stable forms of carboxylic acid derivatives. Many are sensitive to air and moisture and therefore not suitable for long term storage under ambient conditions.[21] In comparison, amides and esters are much more abundant and stable. Therefore, significant effort has been focused towards the development of the activation of the acyl group in esters and amides.[22] Aryl esters

[20] Duan, Y.; Deng, M. *Synlett*. **2005**, *2*, 355-357.
[21] Meng, G.; Szostak, M. *Org. Lett.* **2015**, *17*, 4364–4367.
[22] Dander, J. E.; Garg, N. *ACS Catal.* **2017**, *7*, 1413–1423.

have been shown to be suitable electrophiles for the Suzuki-Miyaura cross-coupling reaction, owing to their relatively high electrophilicity compared to alkyl esters. However, reports from Shi[23] and Itami[24] have shown that both the C(aryl)–O bond (Figure 1.4a) and the C(acyl)–O bond (Figure 1.4b) can be cleaved by transition metal such as $Ni^0$.

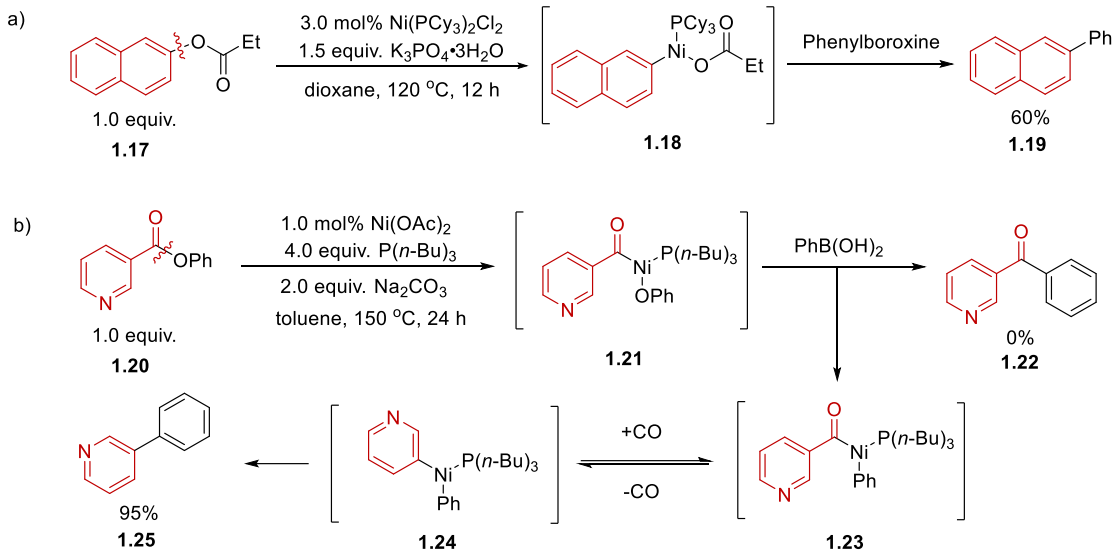



***Figure 1.4.*** Ni-catalyzed Activation of Aryl Esters in Suzuki-Miyaura Cross-Coupling

The regioselectivity of oxidative addition can be controlled by choosing different substituents on the acyl moiety: when an alkyl substituted acyl group is used (such as **1.17**), the oxidative addition will perferrentially occur with the C(aryl)–O bond, while when aryl substituted acyl group is used (such as **1.20**), the oxidative addition will perferrentially occur with the C(acyl)–O bond. The different regioselectivity should lead to either biaryl coupling product **1.19** or acyl-aryl coupling product **1.22**, however, an acyl-$Ni^{II}$ species will undergo a reversible decarbonylation, leading to the formation of decarbonylative aryl-aryl coupling product **1.25**. Similar reactions were also reported by Rueping in 2017, when Ni-catalyzed Negishi cross-couplings were carried out using pivalic aryl esters or benzoyl aryl esters electrophiles.[25]

[23] Guan, B.; Wang, Y.; Li, B.; Yu, D.; Shi, Z. *J. Am. Chem. Soc.* **2008**, *130*, 14468–14470.
[24] Muto, K.; Yamaguchi, J.; Musaev, D. G.; Itami, K. *Nature Comm.* **2015**, 7508.
[25] Liu, X.; Jia, J.; Rueping, M. *ACS Catal.* **2017**, *7*, 4491–4496.

In order to avoid decarbonylation and achieve an authentic acyl-aryl coupling using ester electrophiles, a NHC-ligated Pd complex was used as catalyst in Newman's work.[26] Due to the electron-rich nature of the NHC-$Pd^0$ complex, activation of the ester can be accomplished under milder conditions (90 °C *vs* 150 °C in Ni-catalysis). Moreover, through DFT calculations, Newman discovered that the oxidative addition of NHC-$Pd^0$ complex to the C(acyl)–O bond could be preferred over the C(aryl)–O bond with much lower transition state energy (by 15.5 kcal/mol). This was confirmed experimentally by Szostak, who discovered that an C(acyl)–O bond oxidative addition will perferrentially occur, and an acyl-aryl coupling can be accomplished when a phenyl decanoate ester was used as electrophile.

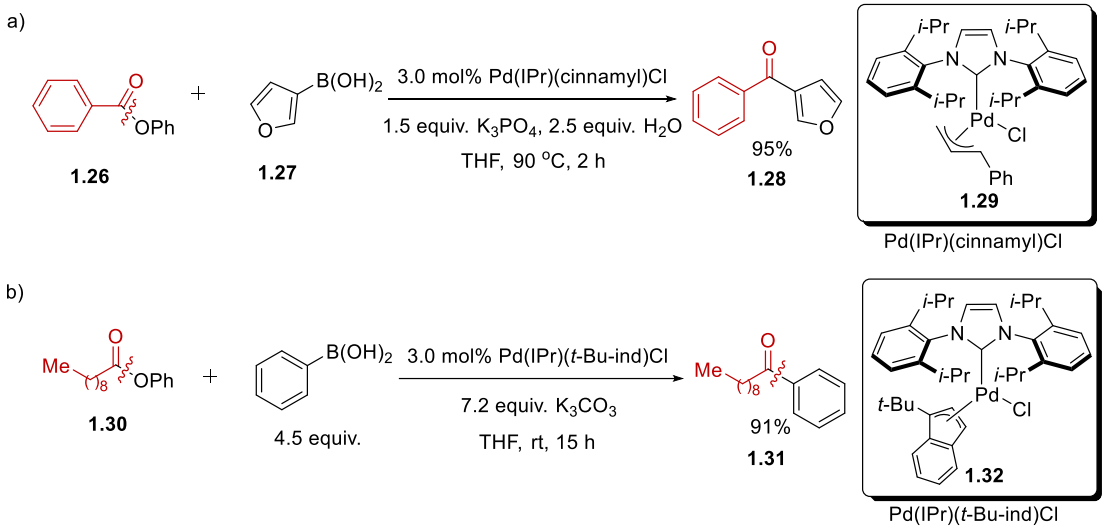



***Figure 1.5.*** Pd(NHC)-catalyzed Suzuki-Miyaura Cross-Coupling using Aryl or Alkyl Phenoxide Esters as Electrophiles

[26] Halima, T. B.; Zhang, W.; Yalaoui, I.; Hong, X.; Yang, Y.; Houk, K. N.; Newman, S. G. *J. Am. Chem. Soc.* **2017**, *139*, 1311–1318.

As the most stable type of carboxylate derivative, amides are considered as the most challenging electrophiles in transition metal-catalyzed cross-coupling reactions.[27] It was not until 2015 that the first example of C(acyl)–N bond cleavage in amides was discovered by Garg.[28] He has shown that an NHC-Ni$^0$ complex can oxidatively insert into C(acyl)–N bond in amides that

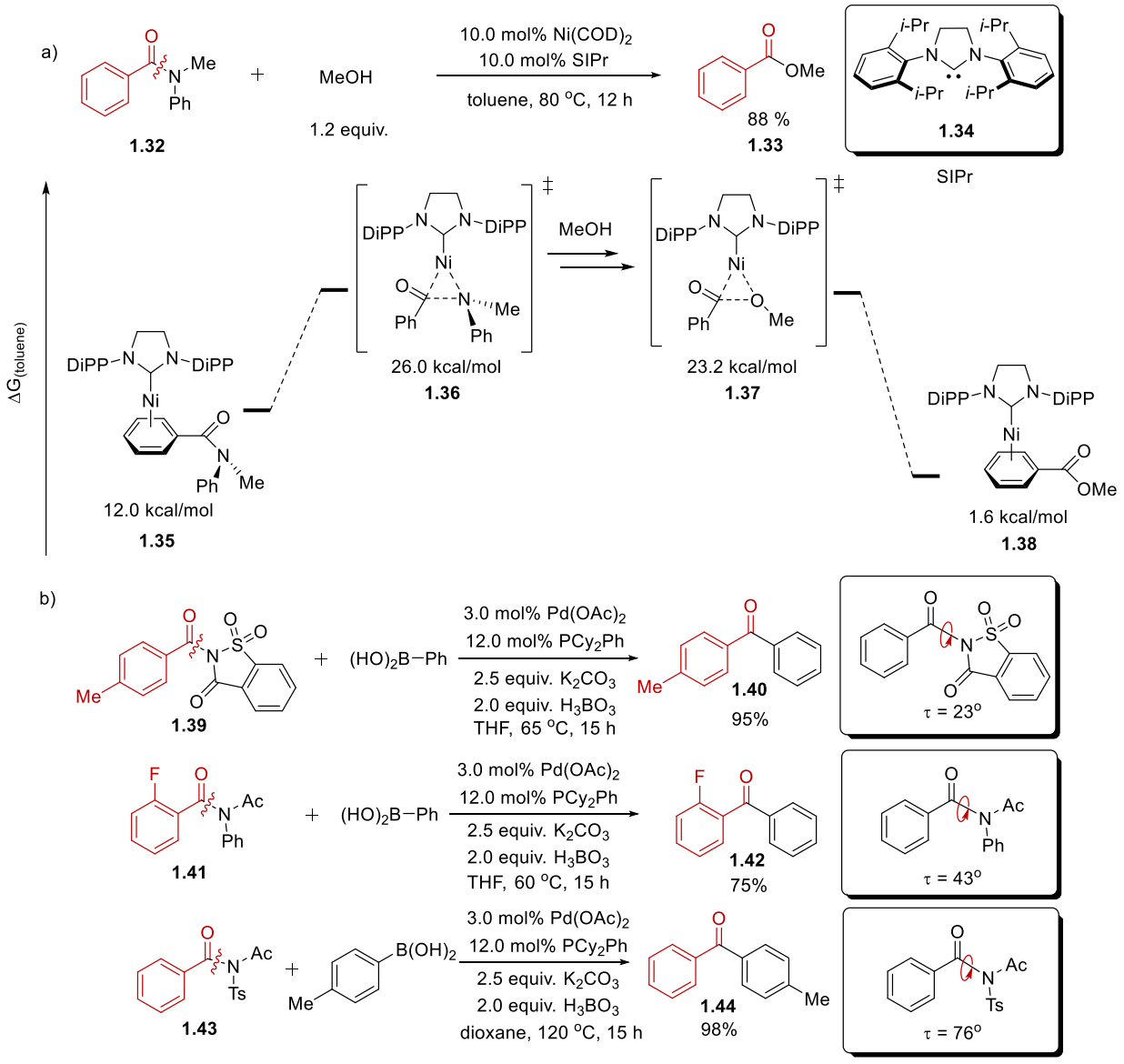



***Figure 1.6.*** Transition Metal-catalyzed Suzuki-Miyaura Cross-coupling using Activated Amide Electrophiles.

[27] Boit, T. B.; Weires, N. A.; Kim, J.; Garg, N. *ACS Catal.* **2018**, *8*, 1003–1008.
[28] Hie, L.; Nathel, N. F.; Shah, T. K.; Baker, E. L.; Liu, P.; Houk, K. N.; Grag, N. *Nature* **2015**, *524*, 79–83.

are slightly activated by one aryl substituent on the nitrogen (such as **1.32**). The acylated $Ni^{II}$ can subsequently react with methanol to deliver methyl ester **1.33**. Through DFT calculations, it was found that the energy barrier between phenyl-stabilized (NHC)$Ni^0$ **1.35** and three-membered ring transition state **1.36** for C(acyl)–N bond oxidative addition is 14 kcal/mol, which is much lower than the transition state energy barrier for C(acyl)–O bond activation (**1.37** to **1.38**, 21.6 kcal/mol). This calculation result indicates that the aryl substituent on N can significantly destabilize the amide bond by pyramidalizing the conformation of nitrogen atom through electronic and steric effects. Szostak further develop this strategy and show that a variety of amides with different Winkler-Duntiz distortion angles (τ angles)[29] can be used as electrophiles in Suzuki-Miyaura cross-coupling reactions, including acyl saccharin **1.39** (τ = 23°)[30], N-acetyl phenyl amides **1.41** (τ = 43°)[31] and N-acetyl tosyl amides **1.43** (τ = 76°).[32]

### 1.1.2 Conjunctive cross-coupling reaction

In 2016, Morken[33] sought to merge the traditional Suzuki-Miyaura cross-coupling with a 1,2-migration of tetrasubstituted boronate complex, to facilitate a conjunctive cross-coupling, which produces secondary boronic esters as versatile building blocks for complex molecule synthesis. The secondary boronate can be generated highly enantioselectively, when a very bulky ($S_p$, $S_p$)-Mandyphos **1.47** is used as the optimal ligand. While in the beginning of the discovery of conjuctive cross-coupling, traditional $Csp^2$ electrophiles were used to install aryl (**1.48**-**1.52**) or alkenyl (**1.53**) functional groups on the β-positon of the boronic ester, after a few years of development, variety of other types of electrophiles were found to be compatible as well, including propargyl acetates, allyl halides, alkyl halides and acyl chlorides.

[29] Meng, G.; Shi, S.; Lalancette, R.; Szostak, R.; Szostak, M. *J. Am. Chem. Soc.* **2018**, *140*, 727–734.
[30] Liu, G.; Meng, G.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett*. **2016**, *18*, 4194–4197.
[31] Liu, C.; Li, G.; Shi, S.; Meng, G.; Lalancette, R.; Szostak, R.; Szostak, M. *ACS Catal.* **2018**, *8*, 9131–9139.
[32] Liu, S.; Shi, S.; Liu, Y.; Liu, R.; Lalancette, R.; Szostak, R.; Szostak, M. *Org. Lett.* **2018**, *20*, 7771–7774.
[33] Zhang, L.; Lovinger, G. L.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science*, **2016**, *351*, 70-74.

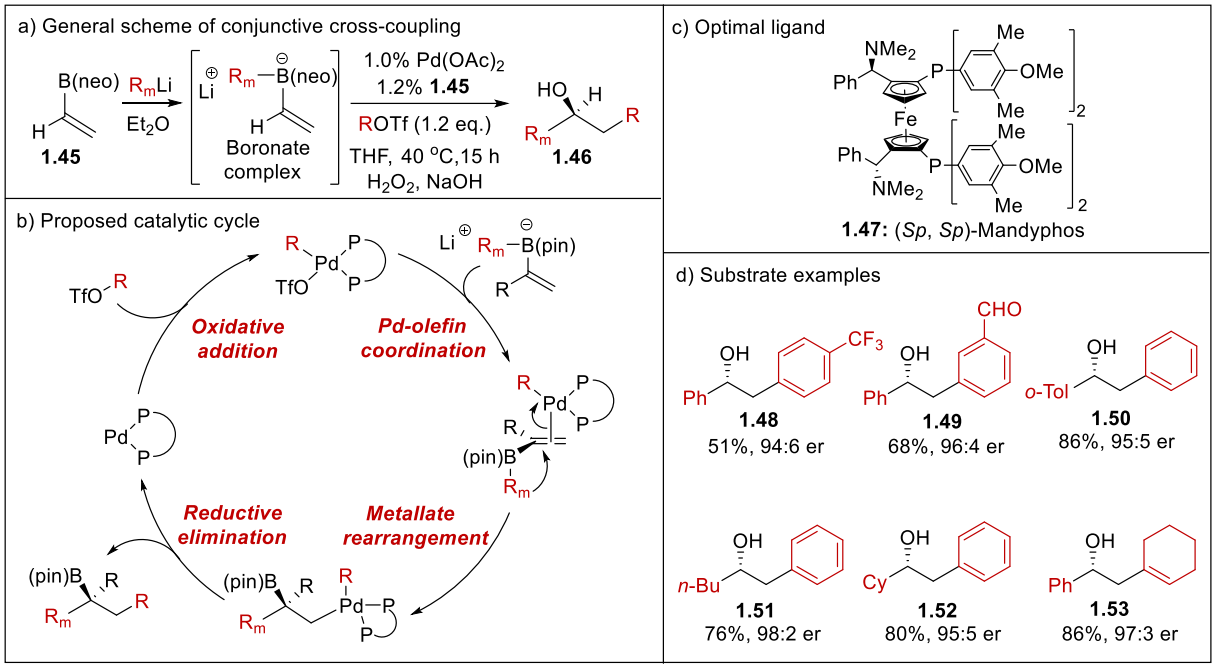



***Figure 1.7.*** General Scheme of Conjunctive Cross-coupling Reaction

### 1.1.2.1 Conjunctive cross-coupling with propargyl electrophiles

In 2019, Aparece demonstrated that propargyl carbonates **1.55** are suitable electrophiles for conjunctive cross-coupling reactions to generate enantiomerically enriched β-boroallenes.[34] In this reaction, different types of migrating groups can be incorporated, including electron-rich arenes (**1.57**), electron-poor arenes (**1.58)** and primary or secondary alkyl migrating groups such as **1.59** and **1.60**. On the electrophile side, the substituent on the alkyne was most commonly a C($sp^2$) group, such as an arene or alkene. Although a methoxy methyl group substituent on the terminal alkyne can be tolerated (**1.62**), a more general *n*-butyl substituent in **1.63** drastically decreased the yield of the reaction. On the propargylic position, a pair of symmetrical alkyl substituents were tested and showed good reactivity and enantioselectivity. However, the three substituents $R_1$, $R_2$ and $R_3$ on electrophile **1.56** appearred to be necessary, as the author noted that replacing any of these three substituents with a hydrogen atom would significantly decrease the yield of the reaction.

[34] Aparece, M. D.; Hu, W.; Morken, J. P. *ACS Catal.* **2019**, *12*, 11381–11385.

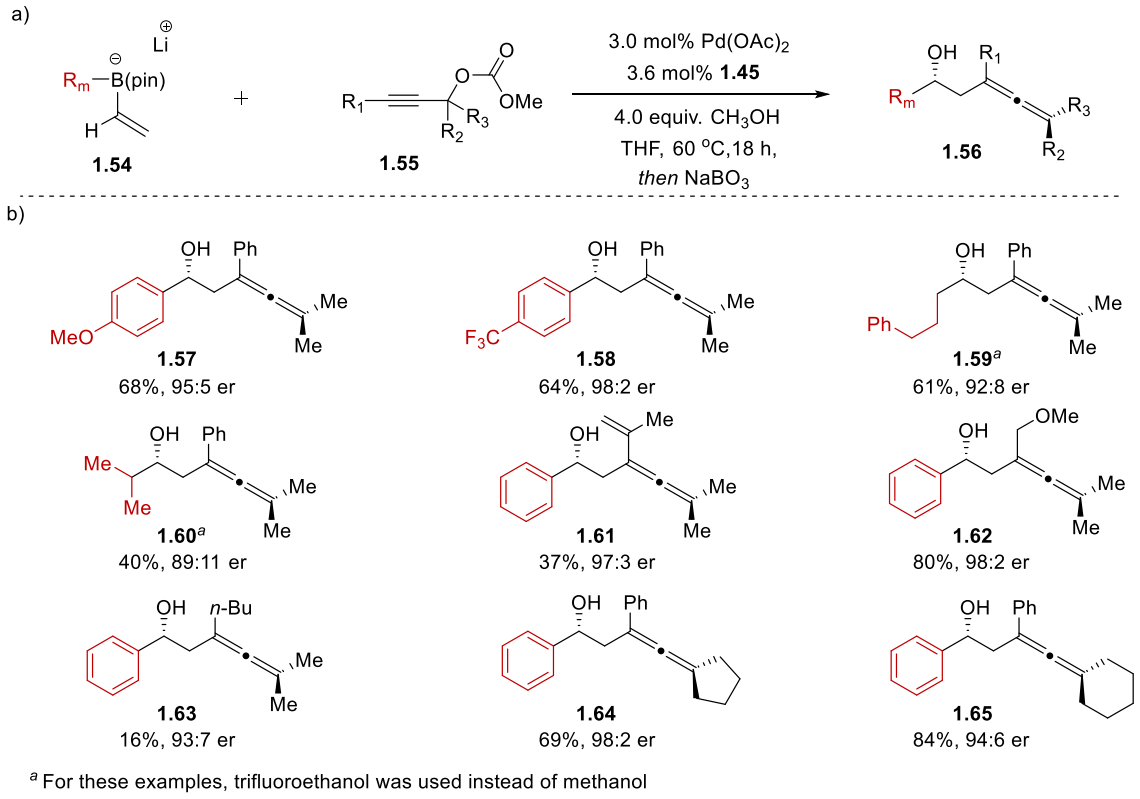
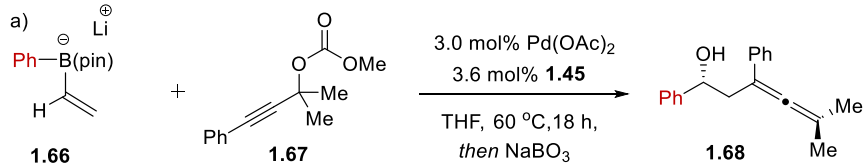



***Figure 1.8.*** Conjunctive Cross-coupling with Propargyl Electrophiles: General Scheme and Substrate Examples.

Additionally, Aparece discovered that methanol, which was generated by an undesired β-hydride elimination side reaction, could increase the yield and enantioselectivity of the reaction. Indeed, by adding additional amounts of methanol, the performance of the reaction was improved from 45% yield and 92:8 er to 83% yield and 96:4 er (Figure 1.8a, entry 1 *vs* entry 4). To understand the function of the alcohol in the conjuctive cross-coupling reaction, an $^{1}$H NMR study on the reaction between boronate complex (**1.66**) and methanol was carried out (Figure 1.8b). It was found that a ligand exchange between boronate complex (**1.66**) and methanol occurs and quickly reaches equilibrium, where 68% of pinacol ligated boronate complex **1.66** was converted to the dimethoxy boronate complex **1.69**. It was proposed that this ligand exchange event facilitated the conjunctive cross-coupling, both improving the yield and the enantioselectivity, when propargyl carbonate **1.67** was used as electrophile.




| entry | X equivalence of 1.67 | additive | 1.68(%) | er |
|---|---|---|---|---|
| 1 | 1.2 equiv. | none | 45 | 92:8 |
| 2 | 2.0 equiv. | none | 60 | 93:7 |
| 3 | 3.0 equiv. | none | 83 | 93:7 |
| 4 | 1.2 equiv. | 4.0 equiv. MeOH | 83 | 96:4 |

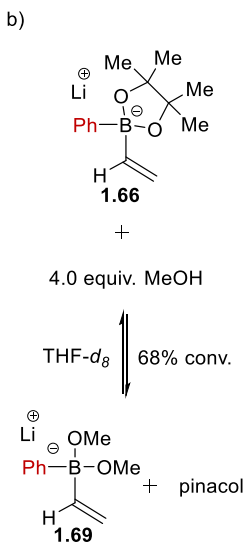



***Figure 1.9.*** The Effect of Methanol on Conjunctive Cross-coupling with Propargyl Carbonate Electrophile.

### 1.1.2.2 Conjunctive cross-coupling with allyl electrophiles

To date, the Pd-catalyzed conjunctive cross-coupling reaction with allyl electrophiles, such as allyl halides, acetates and carbonates, has not yet been developed. Aparece attempted to incorporate an allyl acetate electrophile in the conjunctive cross-coupling.[35] They discovered that after 1,2-migration, the mono-dentate ligated $Pd^{II}$ in **1.68** (Figure 10) is prone to β-hydride elimination reaction, leading to alkenyl boronate **1.70** as major product.

[35] Aparece, M. D.; Gao, C.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 592 –595.

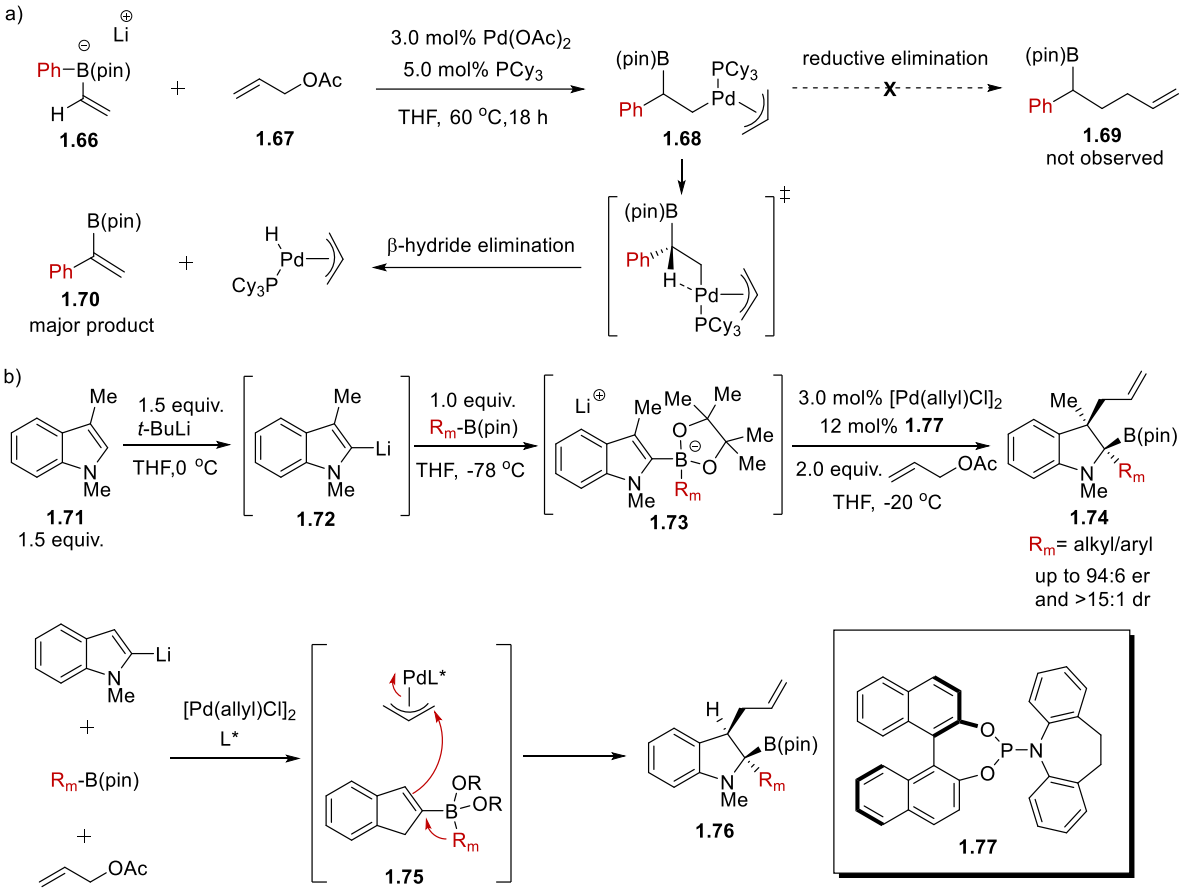



***Figure 1.10.*** Pd–catalyzed Conjunctive Cross-Coupling on Alkene or Indole Substituted Boronic Esters with Allyl Electrophiles.

In 2017, the Ready group discovered that the β-hydride elimination reaction can be avoided by using an indole as a substrate.[36] They firstly performed a directed lithiation on indole **1.71**. Then, the lithiated indole **1.72** was treated with alkyl/aryl boronic ester to form boronate complex **1.73**. By treating this indole substituted boronate complex with allyl acetate in the presence of a chiral Pd-catalyst with ligand **1.77**, 1,2-migration of the $R_m$ in the boronate complex can be triggered by the Pd-allyl complex. The mechanism of this transformation was proposed to occur by outer-sphere pathway[37], where the electrophilic π* of Pd-allyl complex interacts with the π bond of the indole to induce 1,2-migration (as shown in **1.75**).

[36] Panda, S.; Ready, J. M. *J. Am. Chem. Soc.* **2018**, *140*, 13242–13252.
[37] Panda, S.; Ready, J. M. *J. Am. Chem. Soc.* **2017**, *139*, 6038–604.

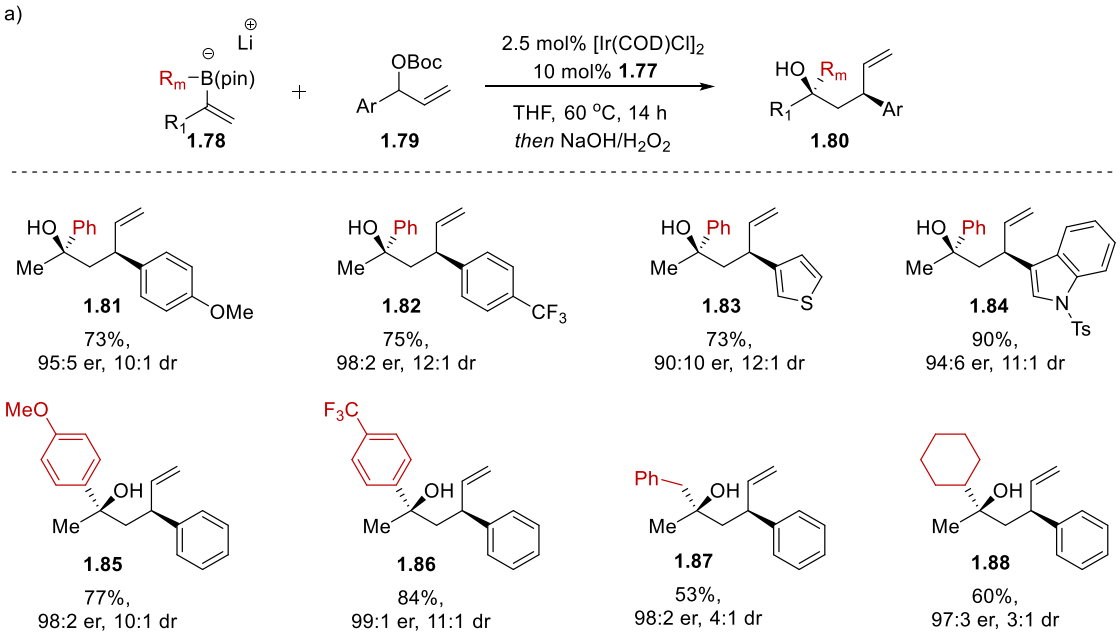



***Figure 1.11.*** Ir–catalyzed Conjunctive Cross-Coupling on Alkene or Indole Substituted Boronic Esters with Allyl Electrophiles.

In 2021, the Ready group shows that an Ir-catalyst can be used to induce 1,2-migration on a more general α-substituted alkenyl boronate complex (Figure 1.11).[38] The reaction was found to be both enantioselective and diastereoselective; when an aryl substituted carbonate protected allyl alcohol was used, good to high level of er and dr of the allylation product can be achieved. A variety of aryl substituents on the allylic position of the electrophile could be accounted general; electron rich arenes, electron deficient arenes as well as heteroatoms can be incorporated. Surprisingly, challenging migrating groups such as electron deficient arenes and benzyl groups can be used in this reaction, as well as electron rich arenes and secondary alkyl groups such as cyclohexanes.

[38] Davis, C. R.; Luvaga, I. K.; Ready, J. M. *J. Am. Chem. Soc.* **2021**, *143*, 4921–4927.

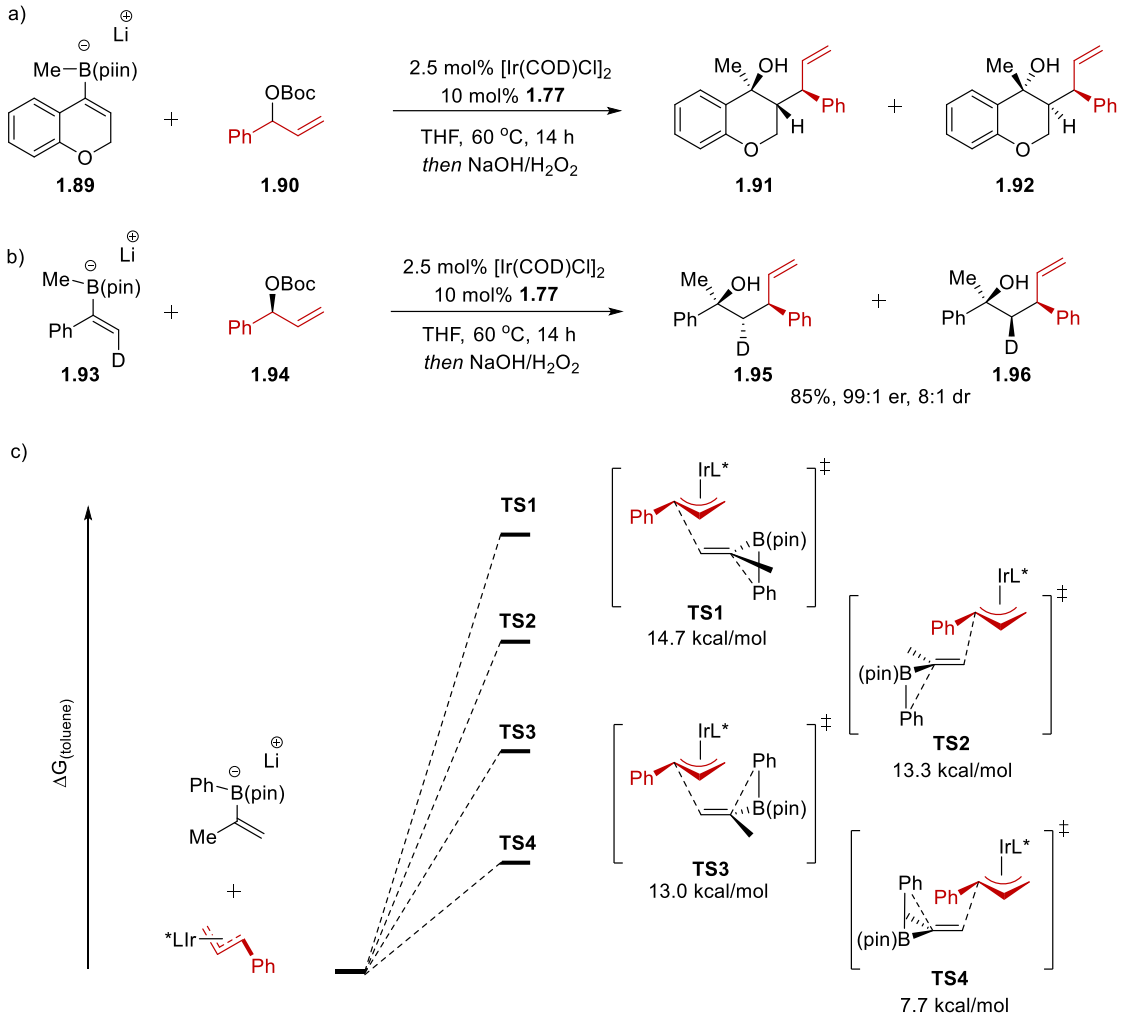



***Figure 1.12.*** Ir–Catalyzed Allyl Conjunctive Cross-Coupling Mechanistic Study Using Deuterium Labelling and DFT Calculations.

Based on discoveries during their mechanistic study[39], Ready proposed that the Ir-allyl complex induced a 1,2-migration of alkenyl boronate complex through a *syn* addition across the alkene. Ready conducted the standard Ir-catalyzed allylation on cyclic alkenyl boronate complex **1.89**, from which it was observed that the reaction would produce a pair of diastereomers **1.91** and **1.92**, in which the migrating group was *cis* to the allyl group. This result suggested a possible *syn* addition was under operation when the 1,2-migration occurred. This mode of action was also confirmed by a deuterium-labeling experiment. The Ready group synthesized deuterium labeled alkenyl boronic ester and generated the corresponding boronate complex (**1.93**) by treating this

[39] Davis, C. R.; Fu, Y.; Liu, P.; Ready, J. M. *J. Am. Chem. Soc.* **2022**, *144*, 16118–16130.

boronic ester with methyllithium. After subjecting **1.93** to the standard allylation conditions, the major product **1.95** was found to have the deuterium atom *cis* relative to the hydroxyl group, which supported the hypothesis that the 1,2-migration occurred by a *syn* addition mechanism. The *syn* addition mechanism was further supported by DFT calculations, where the 1,2-migration transition state with the lowest energy barrier (Figure 1.11c, **TS4**) was the *syn* addition reaction path.

### 1.1.2.3 Conjunctive cross-coupling with alkyl electrophiles

Recent advances in cross-coupling reactions involving alkyl halide electrophiles utilize a nickel catalyst, and this demonstrated remarkable efficiency.[40, 41] The nickel complex has the ability to activate a range of alkyl halides, transforming them into corresponding alkyl radicals through halogen atom abstraction reactions.[42, 43] Exploiting this feature, the Morken research group endeavored to integrate alkyl halide electrophiles in conjunctive cross-coupling reactions using a nickel-based system.

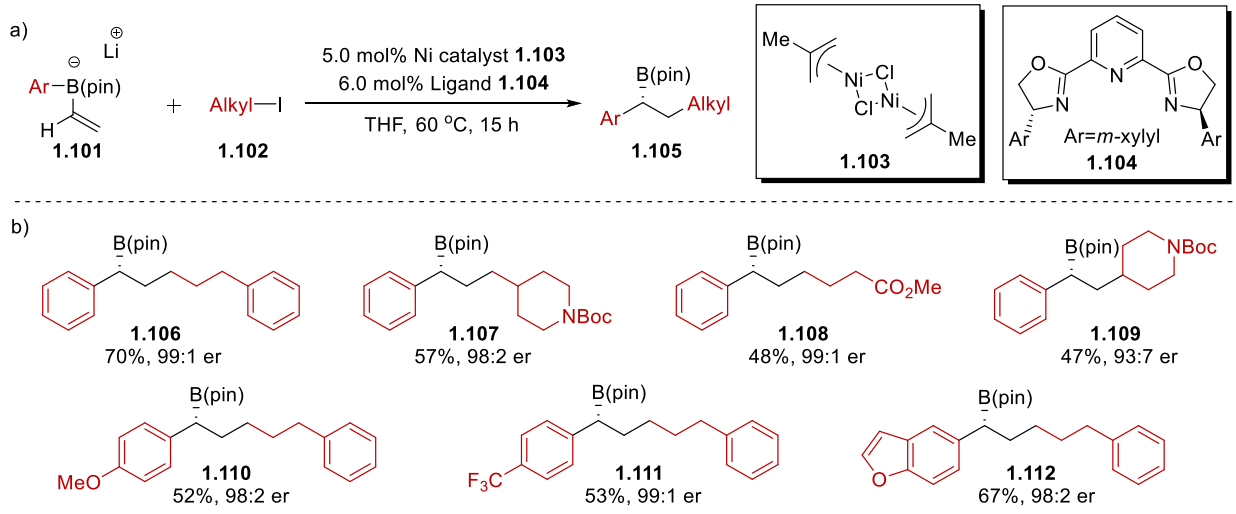



***Figure 1.13.*** Ni-catalyzed Enantioselective Conjunctive Cross-Coupling with Alkyl Halide Electrophiles: Example of Substrates.

In 2017, Lovinger discovered that chiral pybox **1.104** in conjunction with Ni complexes can catalyze an enantioselective conjunctive cross-coupling reaction between boronate complex **1.101**

[40] Zhou, J, Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340–1341.
[41] Choi, J.; Fu, G. C. *Science* **2017**, *356*, **e**aaf7230.
[42] Li, Z.; Jiang, Y.; Fu, Y. *Chem. Eur. J.* **2012**, *18*, 4345–4357.
[43] Biswas, S.; Weix, D. J. *J. Am. Chem. Soc.* **2013**, *135*, 16192–16197.

and alkyl iodide **1.102**. [44]It was found that, only aryl migrating groups could be incorporated, although the electronic nature of the migrating arenes can be varied; both electron-rich (**1.110**) and deficient arenes (**1.111**), as well as heterocycles (**1.112**) can be employed. In the case of electrophiles, both primary alkyl groups, such as **1.106** to **1.108**, as well as secondary alkyl group in **1.109** can be incorporated with moderate to good yield and high enantioselectivity.

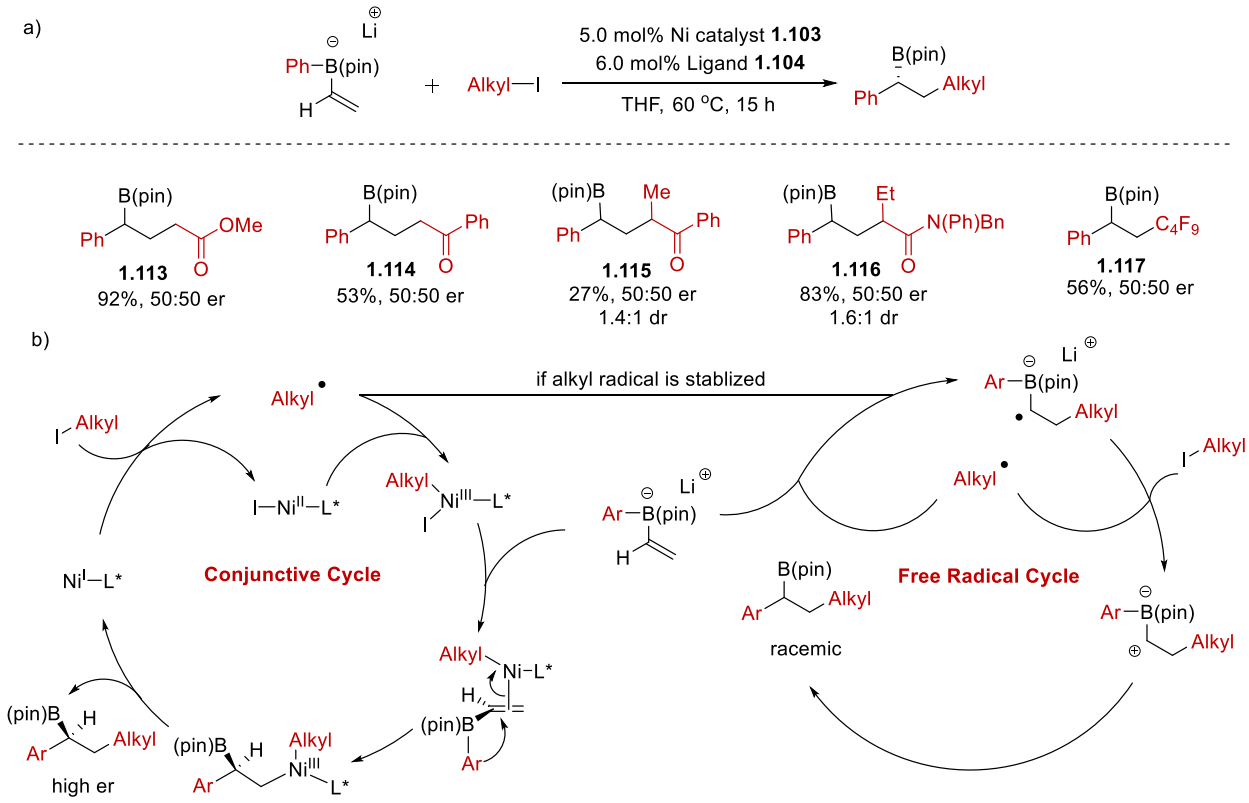



***Figure 1.14.*** Ni-catalyzed Racemic Conjunctive Cross-coupling When a Stable Alkyl Radical is Generated: Examples and Proposed Mechanism

Of note, a range of other alkyl iodide electrophiles were found to give conjunctive cross-coupling products with low levels of enantioselectivity as shown in Figure 1.13a. It was proposed that the low enantioselectivity arose due to the high stability of the alkyl radical. As shown in Figure 1.13b, after halogen atom abstraction by Ni complex, if the carbon-centered radical generated in this process was stabilized by electronic effects, instead of recombining with the Ni catalyst, it would react directly with the electron-rich boronate complex through a radical addition

[44] Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 17293–17296.

mechanism. The α-boryl radical generated in this process may initiate a radical chain reaction, from which the conjunctive coupling product would form in racemic manner.

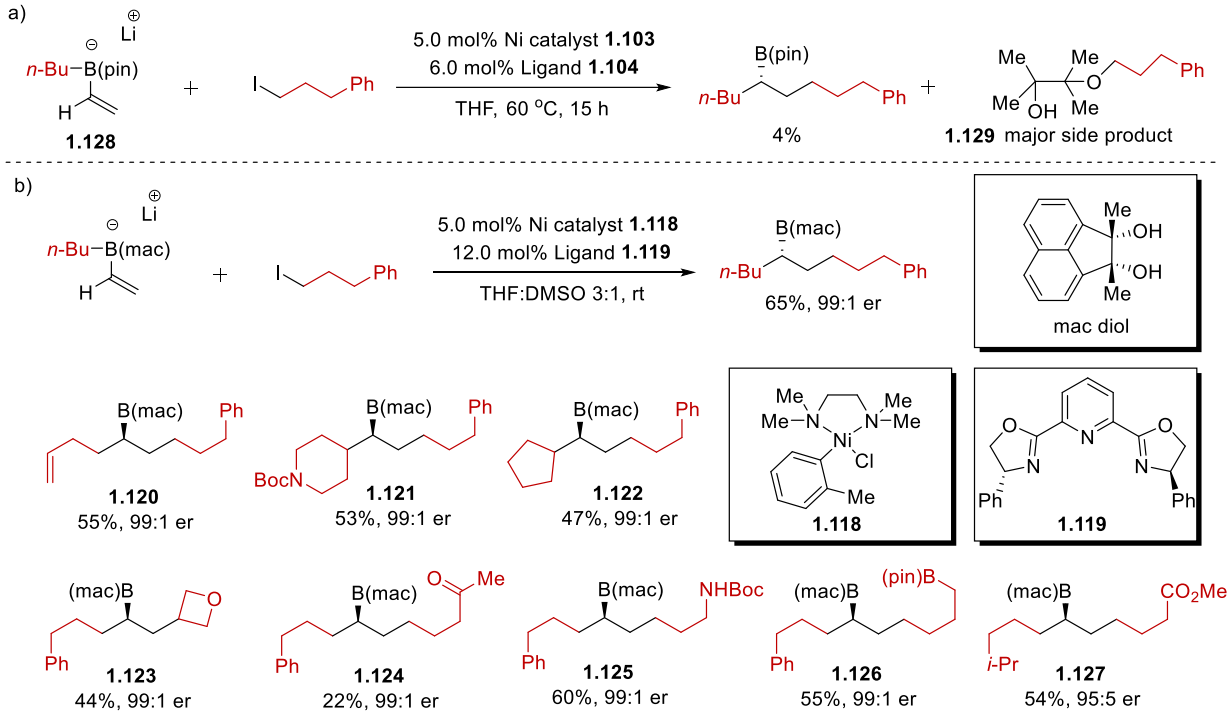



***Figure 1.15.*** Ni-catalyzed Alkyl-B(mac) Boronate Complex Coupling with Alkyl Iodides

While Lovinger's work majorly focused on aryl migration reactions, Koo was able to show that with modified conditions, alkyl migrating groups can be incorporated as well. [45] Using reaction conditions developed by Lovinger, Koo observed that when *n*-butyl-substituted boronate complex **1.128** was used as starting material, the reaction would only produce the desired product in a trace amount. A significant amount of alkylated pinacol **1.129** was observed as a byproduct, which indicated that an undesired alkylation of the oxygen atoms in the boronate complex was occurring. To prevent this side reaction, a more hindered methylated acenaphthoquinone (mac diol) ligand was synthesized and ligated on boron.[46] After optimization, the Ni complex induced 1,2-migration of *n*-butyl-B(mac) boronate complex can be achieved with conditions shown in Figure 1.15b. The reaction can tolerate primary, secondary and tertiary alkyl migrating groups, and also

[45] Koo, S. M.; Vendola, A. J.; Momm, S. N.; Morken, J. P. *Org. Lett.* **2020**, *22*, 666–669.
[46] a) Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 15181–15185.
b) Meng, Y.; Kong, Z.; Morken, J. P. *Angew. Chem. Int. Ed.* **2020**, *59*, 8456–8459.
c) Law, C.; Kativhu, E.; Wang, J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2020**, *59*, 10311–10315.
d) Zhang, C.; Hu, W.; Lovinger, G. J.; Jin, J.; Chen, J.; Morken, J. P. *J. Am. Chem. Soc.* **2021**, *143*, 14189–14195.

applied to a range of electrophiles; alkyl groups containing functional groups such as protected amines, ketones, methyl esters as well as boronic esters can be introduced. Remarkably, the reaction can generate all these secondary alkylboronates with excellent enantioselectivity (> 97:3).

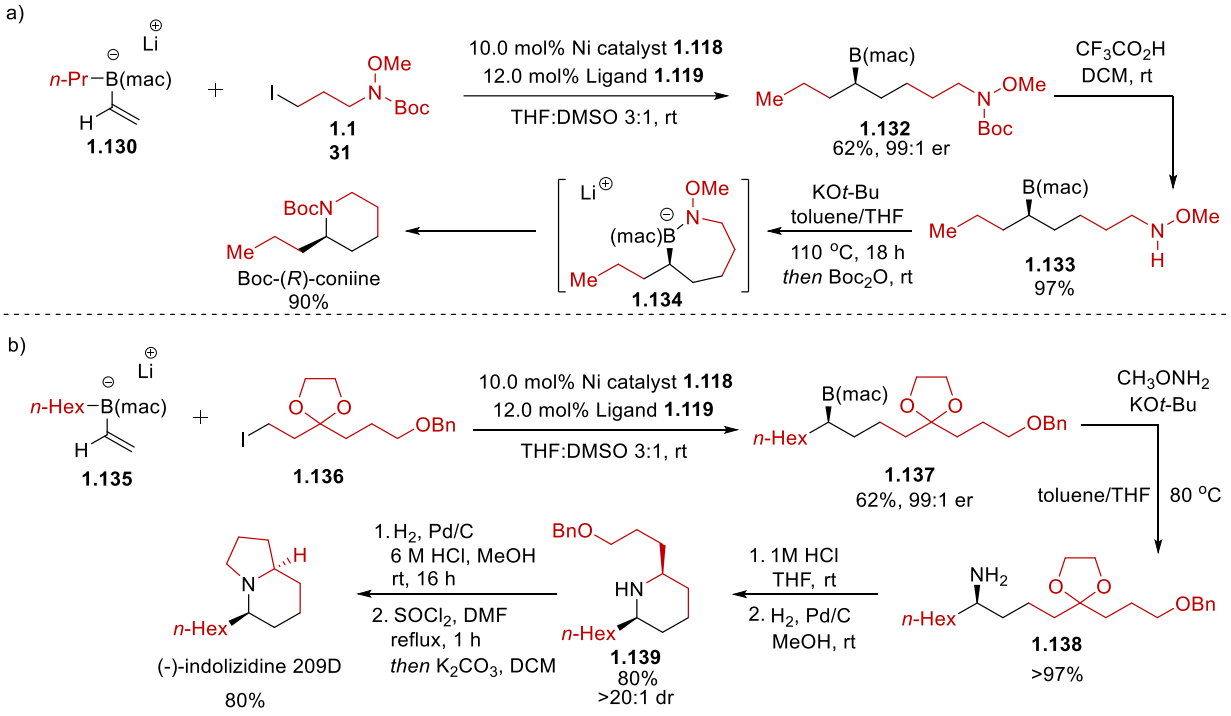



***Figure 1.16.*** Ni-Catalyzed Alkyl-B(mac) Boronate Complex Coupling with Alkyl Iodides

To showcase the utility of the alkyl-alkyl conjunctive cross-coupling reaction, Koo conducted a total synthesis of natural product derivatives Boc-(*R*)-coniine[47] and (-)-indolizidine 209D.[48] In the synthesis of Boc-(*R*)-coniine, the key intermediate secondary boronic ester **1.132** was constructed from the conjunctive coupling in 62% yield as a single enantiomer. Subsequently, the deprotected methoxyl amine underwent an intramolecular amination with the secondary boronate to yield the target molecule in 90% yield.[49] In the synthesis of (-)-indolizidine 209D, **1.136** was

[47] Isolation: a) Hotti, H.; Rischer, H. *Molecules* **2017**, *22*, 1962–1965. Recent synthesis: b) Reding, M. T.; Buchwald, S. L. *J. Org. Chem.* **1998**, *63*, 6344-6346. c) Friestad, G. K.; Marié, J.-C.; Suh, Y.; Qin, J. *J. Org. Chem.* **2006**, *71*, 7016–7018. d) Daly, M.; Gill, K.; Sime, M.; Simpson, G.L.; Sutherland, A. *Org. Biomol. Chem.* **2011**, *9*, 6761–6763.
[48] Isolation: a) Daly, J. W.; Spande, T. F.; Garraffo, H. M. *J. Nat. Prod.* **2005**, *68*, 1556–1558. Recent syntheses: b) Kim, G.; Shim, J. H.; Kim, J. H. Bull. *Korean Chem. Soc.* **2003**, *24*, 1832–1835. c) Coia, N.; Mokhtari, N.; Vasse, J.-L.; Szymoniak, *J. Org. Lett.* **2011**, *13*, 6292–6295. d) Chiou, W.-H.; Chen, H.-Y. *RSC Adv.* **2017**, *7*, 684–686.
[49] a) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett.* **2018**, *29*, 1749−1752. b) Liu, X. X.; Zhu, Q.; Chen, D.; Wang, L.; Jin, L. Q.; Liu, C. *Angew. Chem. Int. Ed.* **2020**, *59*, 2745−2749. For intramolecular version: c) Xu, P.; Zhang, M.; Ingoglia, B.; Allais, C.; Dechert-Schmitt, A.-M. R.; Singer, R. A.; Morken, J. P. *Org. Lett.* **2021**, *23*, 3379–3383.

used as electrophile in conjunctive cross-coupling reaction. Then, **1.137** was subjected to amination reaction to yield free amine **1.138** in quantitative yield. Deprotection of the ketal group followed by reductive the amination reaction yielded cyclic amine **1.139** in 80% yield. Lastly, deprotection and chlorination of the benzyl protected alcohol was carried out followed by an *in situ* $S_N2$, where the bicyclic natural product (-)-indolizidine 209D can be generated with 80% yield.

### 1.1.2.4 Conjunctive cross-coupling with acyl electrophiles

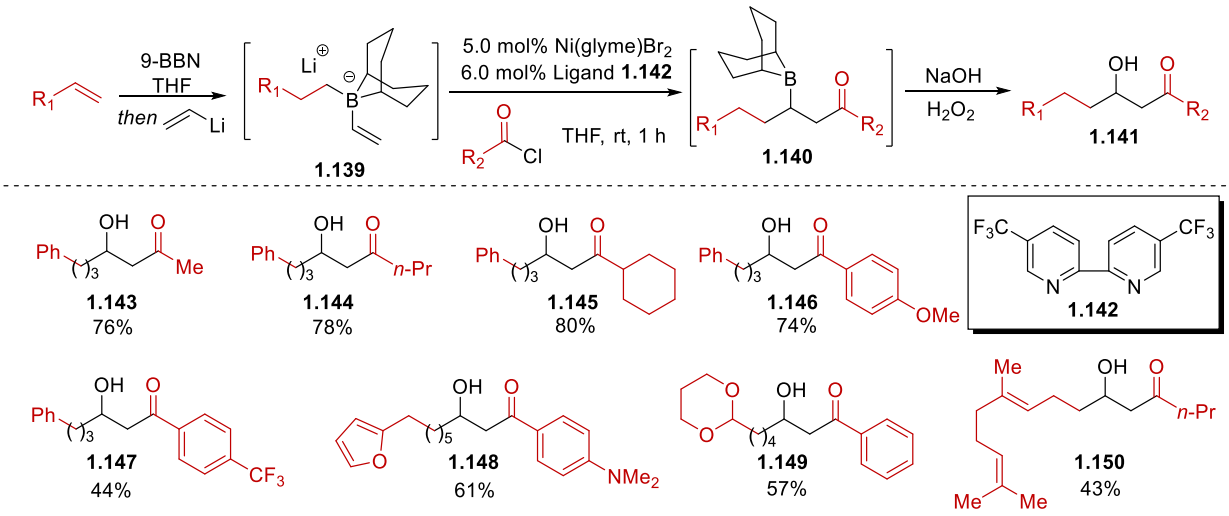



***Figure 1.17.*** Ni-catalyzed Acylative Conjunctive Cross-coupling with 9-BBN Derived Alkenyl Boronate Complex.

Based on the detailed development of the acylative Suzuki-Miyaura cross-coupling reaction, as well as the recent success of incorporating different electrophiles in conjunctive cross-coupling reaction, Law decided to investigate the potential of using acyl chlorides as electrophiles in conjunctive cross-coupling.[50] In this case, an alkenyl 9-BBN derived boronate complex was synthesized as the nucleophile[51], while bipyridine (**1.142**)-Ni complex was employed as the catalyst.[52] An acylative conjunctive cross-coupling was found to deliver a variety of 9-BBN

[50] Law, C.; Meng, Y.; Koo, S. M.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 6654–6658.
[51] For more 9-BBN derived boronate complex reactions: a) Yamamoto, Y.; Toi, H.; Murahashi, S.; Moritani, I. *J. Am. Chem. Soc.* **1975**, *97*, 2558–2559. b) Fang, G. Y.; Wallner, O. A.; Blaso, N. D.; Ginesta, X.; Harvey, J. N.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2007**, *129*, 14632–14639. c) Fang, G. Y.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2007**, *46*, 359 –362.
[52] For more Ni-catalyzed transformation with acyl electrophiles: a) Joe, C. L.; Doyle, A. G. *Angew. Chem. Int. Ed.* **2016**, *55*, 4040–4043. b) Wotal, A. C.; Weix, D. *Org. Lett.* **2012**, *14*, 1476–1479. c) Zhao, C.; Jia, X.; Wang, X.; Gong, H. *J. Am. Chem. Soc.* **2014**, *136*, 17645–17651. d) Cerney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442–7445.

derived β-boryl ketones (**1.140**) that can be oxidized to the corresponding β-hydroxyl ketones **1.141** *in situ*. The reaction was found to apply to many electrophiles: Ketones containing methyl groups (**1.143**), n-alkyl substituents (**1.144**), secondary alkyl groups (**1.145**), as well as a varity of aryl groups (**1.146-1.148**) can be synthesized with moderate to good yields. Functional groups such as protected aldehydes (**1.149**) did not inhibit the reaction. Moreover, the hydroboration of polyene substrates was found to be regioselective for the terminal alkene over more substituted alkenes (**1.150**).

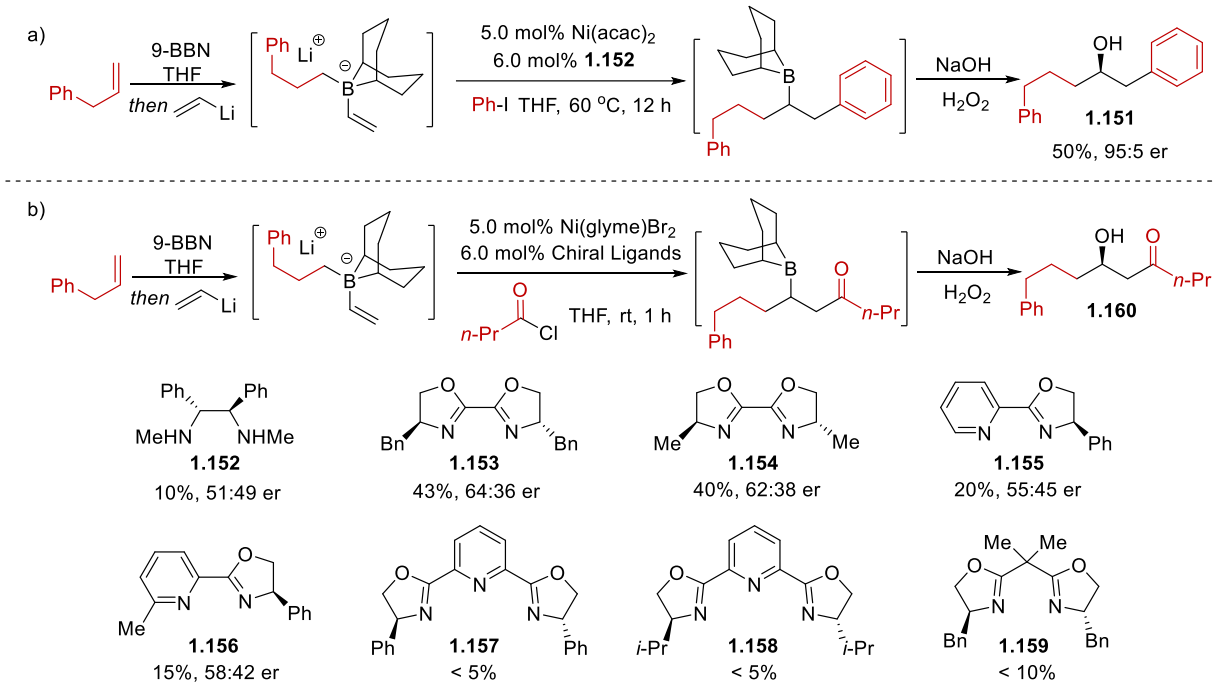



***Figure 1.18.*** Attempted Enantioselective Ni-Catalyzed Acylative Conjunctive Cross-Coupling with 9-BBN Derived Boronate Complexes

Prior to Law's study on acylative conjunctive coupling reactions with 9-BBN derived boronate complexes, Chierchia had shown that with a enantio-enriched chiral diamine (**1.52**)-Ni complex, the same boronate complex can be coupled with phenyl iodide enantioselectively to yield secondary[53] alcohol **1.151** with high er (Figure 1.18a). Law found that the chiral diamine ligand **1.152** could not induce high enantioselectivity when an acyl electrophile was used (51:49 er). To improve the enantioselectivity, the performance of a variety of chiral ligands, including bisoxazolines (**1.153**, **1.154** and **1.159**), pyridine-oxazolines (**1.155** and **1.156**), pybox ligands

[53] Chierchia, M.; Law, C.; Morken, J. P. *Angew. Chem. Int. Ed.* **2017**, *56*, 11870–11874.

(**1.157** and **1.158**) were examined. Highest enantiomeric ratio (64:36) was achieved when **1.153** was used.

### 1.1.3 β-Boryl Carbonyl Compounds

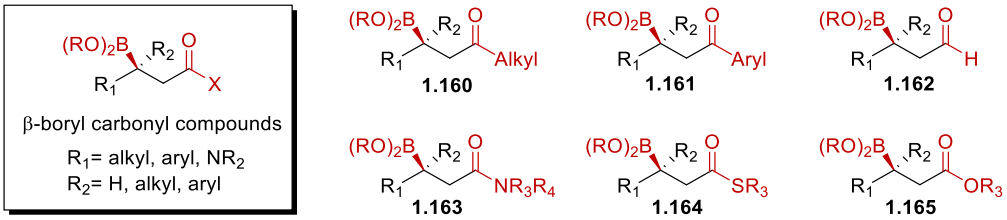



***Figure 1.19.*** Structure of Precedential Asymmetrically Synthesized β-Boryl Carbonyl Compounds

β -Boryl carbonyl compounds constitute a class of chemical compounds featuring boronic ester functional groups located at the β-position of the carbonyl moiety. To date, nearly 400 distinct β-boryl carbonyl compounds have been successfully synthesized through enantioselective methods. As shown in Figure 1.19, a variety of different carbonyl groups were incorporated, including ketones (**1.160** and **1.161**), aldehyde (**1.162)**, amide (**1.163)**, thioester (**1.164)**, as well as esters (**1.165)**. These boron-containing molecules are versatile building blocks due to the high modularity of both the boronic ester group and the carbonyl group. As shown in Law's work, conjunctive cross-coupling with acyl electrophiles will generate β-boryl carbonyl compounds as products. In this section, the utility and reported synthesis method of β-boryl carbonyl compounds will be discussed.

#### 1.1.3.1 Orthogonal Transformations of β-Boryl Carbonyl Compounds

Despite the presence of a highly reactive carbonyl group, there are still numerous orthogonal transformations that can be applied to the boronic ester moiety in β-boryl carbonyl compounds. As shown in Figure 1.20, beside a simple oxidation of the boron to generate secondary or tertiary alcohols, efficient transformations such as amination, halogenation, silylation, and carbonylation have been developed that can replace the boron atom in β-boryl carbonyl compounds with a variety of useful functional groups. Liu [54] discovered that the amination protocol they developed using aminoazanium salts can be applied to β-boryl esters. By treating β-boryl esters with $H_2N$-NMM in

[54] Xu, J.; Qin, Y.; Liu, C. *Synlett.* **2023**, *34*, doi: 10.1055/a-2028-5646.

the present of base at 100 ℃, the boronate atom can be aminated to generate β-amino esters **1.170** in 69% yield. Beside amination, Tong reported a hyrazination of β-boryl esters. [55] By treating 1,1-disubstituted hydrazine with $MnO_2$ and β-boryl ester, the *in situ* generated 1,1-diazine can form a boronate complex with the boronic ester, which then underwent 1,2-migration to yield **1.171** in 80% yield. In 2020, Xu showed that dialkylamide groups in β-boryl amides can be tolerated in Matteson homologation reaction.[56] In the present of a β-boryl amide, chloromethyl lithium can be generated by treating chloroiodomethane with *n*-BuLi, which can selectively react with the boron atom in β-boryl amide. After oxidation, homologated primary alcohol **1.175** can be synthesized in 82% yield with perfect enantiospecificity. Li found that the boronic ester in β-boryl ketones can be converted to fluoride by using Selectfluor as fluorine source and $AgNO_3$ as catalyst.[57] Evidence has shown that the reaction occurs through the intermediacy of a secondary radical intermediate, which renders **1.172** without stereospecificity. Additionally, Hu discovered that the boronic ester in β-boryl ketones can be transformed to silyl groups.[58] By activating the benzylic boronic ester with tert-butoxide, a phenyl stabilized carbanion can be generated, which could react with TIPSCl to generate **1.173** in 85% yield with no stereospecificity.

The pinacol boronic ester in β-boryl carbonyl compounds can be easily converted to a more reactive trifluoroborate salt,[59] which can be further transformed into a range of functional groups. For example, as shown by Bao et al.[60] the oxidizable trifluoroborate moiety in β-boryl ester **1.67** can react with a photosensitizer under blue light to generate secondary radical, which can subsequently be trapped by a $Ni^{II}$-amidyl radical that was generated between Ni catalyst and tosyl azide. Tosyl protected amine **1.169** was formed as the product with 66% yield. Additionally, the trifluoroborate group also undergo transmetallation towards a variety of transition metals. Based on Miyaura's report [61], Yun demonstrated that a tertiary carbon substituted trifluoroborate transmetallated to $Rh^{I}$ in the presence of water. The organo-rhodium species can then react with

[55] Wang, J.; Wang, D.; Tong, X. *Org. Biomol. Chem.* **2021**, *19*, 5762–5766.
[56] a) Matteson, D. S. *Chem. Rev.* **1989**, 89, 1535–1551. b) Matteson, D. S.; Collins, B. S. L.; Aggarwal, V. K.; Ciganek, E. *Organic Reactions* **2021**, *105*, 427–860.
[57] Li, Z.; Wang, Z.; Zhu, L.; Tan, X.; Li, C. *J. Am. Chem. Soc.* **2014**, *136*, 16439−16443.
[58] Tang, M.; Zhu, W.; Sun, H.; Wang, J.; Jing, S.; Wang, M.; Shi, Z.; Hu, J. *Chem. Sci.* **2023**, *14*, 7355–7360.
[59] Zhou, L.; Han, B.; Zhang, Y.; Li, B.; Wang, L.; Wang, J.; Wang, X.; Zhu, L. *Cata. Lett.* **2021**, *151*, 3220–3229.
[60] Zhou, S.; Lv, K.; Fu, Rui.; Zhu, C.; Bao, X. *ACS Catal.* **2021**, *11*, 5026−5034.
[61] Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem. Int. Ed.* **1998**, *37*, 3279−3270.

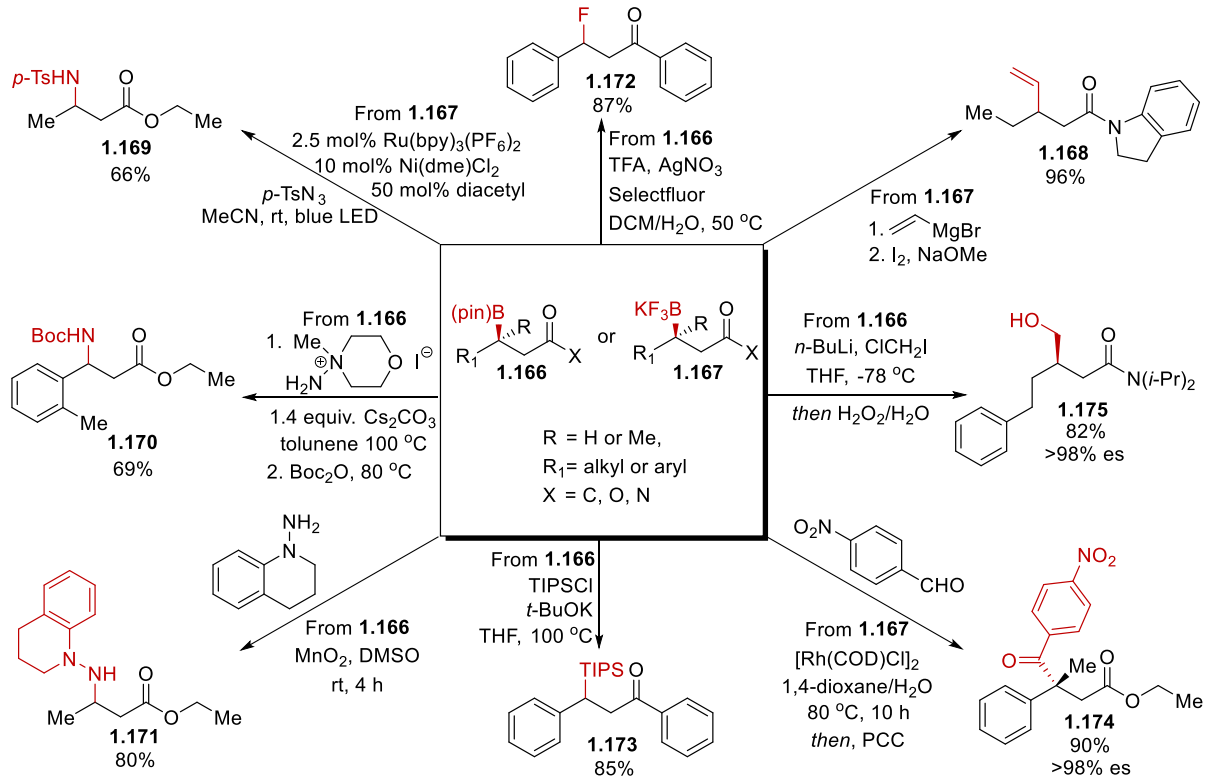



***Figure 1.20.*** Miscellaneous Transformation of Boronate Functional Group in β-Boryl Carbonyl Compounds

the aldehyde to generate a secondary alcohol, which was subsequently oxidized to ketone (**1.174**) to achieve a stereospecific acylation of the boron atom in a β-boryl ester.[62]

Exploiting the photoredox-active and transmetallation-active properties of trifluoroborate groups in β-boryl carbonyls, researchers can also cross-couple the borate with aryl halides to synthesize a variety of β-aryl carbonyl compounds. In 2010, Molander [63]reported the first example of Suzuki-Miyaura cross-coupling of the trifluoroborate form of β-boryl amides (Figure 1.21a). In his report, an XPhos-Pd complex was used as the catalyst, and a variety of aryl chlorides were used as electrophiles. The reaction can incorporate electron-rich arenes such as **1.178**, as well as aryl groups bearing electron withdrawing groups such as **1.179** to **1.181**. Additionally, Molander also discovered that such a cross-coupling would invert the boron-containing stereogenic center. As shown in Figure 1.21b, starting from enantiomerically enriched trifluoroborates **1.182**, the

[62] Feng, X.; Yun, J. *Chem. Eur. J.* **2010**, *16*, 13609–13612.
[63] a) Sandrock, D. L.; Gerard, L.; Chen, C.; Dreher, S. D.; Molander, G. A. *J. Am. Chem. Soc.* **2010**, *132*, 17108–17110. b) Molander, G. A.; Wisniewski, S. R.; Sarvari, M. *Adv. Synth. Catal.* **2013**, *355*, 3037–3057.

borylated carbon was proposed to transmetallate to Pd complex with inversion through an open-shell $S_E2$ transition state (**1.184**). After reductive elimination, the corresponding β-aryl amide **1.183** was formed with inverted stereochemistry. A similar transmetallation mode was also observed by Hall et al.[64], when they selectively cross-coupled the $BF_3K$ group in a β-diboryl ester **1.185** with phenyl bromide: the stereogenic center in the arylated product **1.187** was inverted when compared to the starting material. After converting the B(dan) group into the $BF_3K$ group in **1.188**, the subsequent coupling was also invertive in stereochemistry, giving diarylated product **1.190** with high stereospecificity.

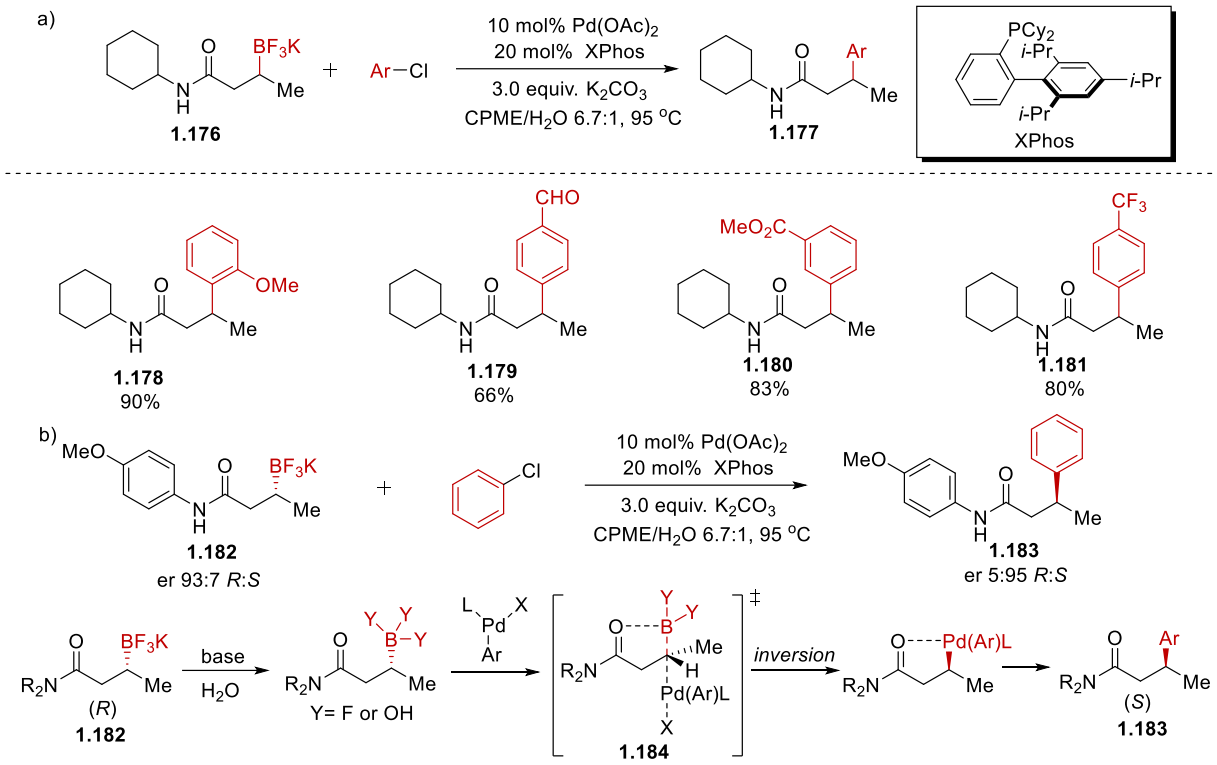



***Figure 1.21.*** Suzuki-Miyaura Cross-coupling of trifluoroborates with Aryl Chlorides and The Stereochemistry Analysis

While secondary alkyl trifluoroborates are usually reactive nucleophiles in stereospecific Suzuki-Miyaura cross-coupling reactions, examples of tertiary borates that undergo cross-coupling are rare, presumably because of the high steric hindrance of tertiary carbons making the

[64] Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nature Chem.* **2011**, *3*, 894–899.

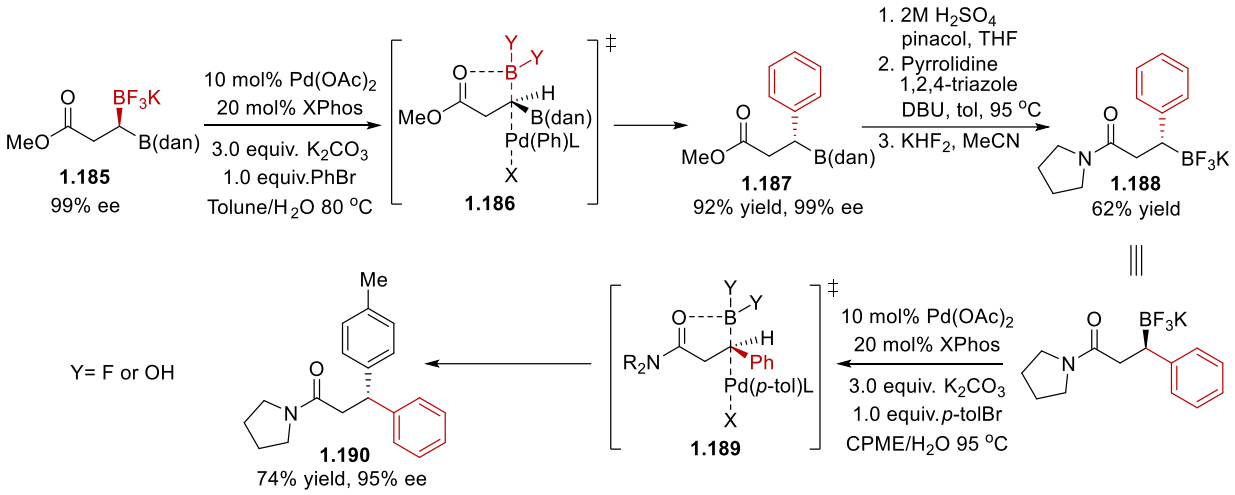



***Figure 1.22.*** Suzuki-Miyaura Cross-Coupling of β-Diboryl Carbonyl with Aryl Halides.

transmetallation reaction difficult to occur.[65] To date, there are still no reported stereospecific cross-couplings of the boron atom in a tertiary β-boryl carbonyl compounds. However, leveraging the redox-active property of tertiary alkyl trifluoroborates, non-stereospecific transformations of the borate were achieved by several researchers. In 2016, Molander demonstrated the photoredox/Ni dual catalysis cross-coupling of secondary β-trifluoroboratoketone **1.191** with aryl bromides through an alkyl radical transfer pathway (Figure 1.23a).[66] In this reaction, photocatalyst **1.193** was found to be optimal for energy transfer between the Ni catalyst and the borate substrate. Once oxidized, a secondary alkyl radical can be generated, which will subsequently be trapped by $Ni^{II}(Ar)$. Upon reductive elimination, β-aryl ketone **1.192** can be generated in high yield. Molander subsequently discovered that with modified conditions where a $Ni(TMHD)_2$ complex was employed as catalyst and $ZnBr_2$ was used as additive, the reaction can be applied to a tertiary β-trifluoroboratoketone **1.194** to achieve non-stereospecific coupling of tertiary carbon with aryl halides.[67] Recently, Molander also employed this well established reaction to synthesize bicyclopentane (BCP) bioisosteres bearing novel substituents.[68] As shown in Figure 1.23c, the tertiary alkyl radical generated from photo-redox activation of β-trifluoroboratoketone can be

[65] a) Joshi-Pangu, A.; Biscoe, M. R. *Synlett.* **2012**, *23*, 1103–1107. b) Yang, S.; Jiang, W.; Xiao, B. *Chem. Commun.* **2021**, *57*, 8143–8146.
[66] Tellis, J. C.; Amani, J.; Molander, G. A. *Org. Lett.* **2016**, *18*, 2994−2997.
[67] Primer, D. N.; Molander, G. A. *J. Am. Chem. Soc.* **2017**, *139*, 9847−9850.
[68] Huang, W.; Keess, S.; Molander G. A. *J. Am. Chem. Soc.* **2022**, *144*, 12961−12969. For more information on BCP bioisosteres, see review: a) Shire, B. R.; Anderson, E. A. *JACS Au* **2023**, *3*, 1539–1553. b) Anderson, J. M.; Measom, N. D.; Murphy, J. A.; Poole, D. L. *Angew. Chem. Int. Ed.* **2021**, *133*, 24958–24973.

trapped by tricyclopentane **1.197** to yield a BCP radical, which can subsequently react with $Ni^{II}(Ar)$ to generate BCP inserted β-aryl ketone **1.198** in 48% yield.

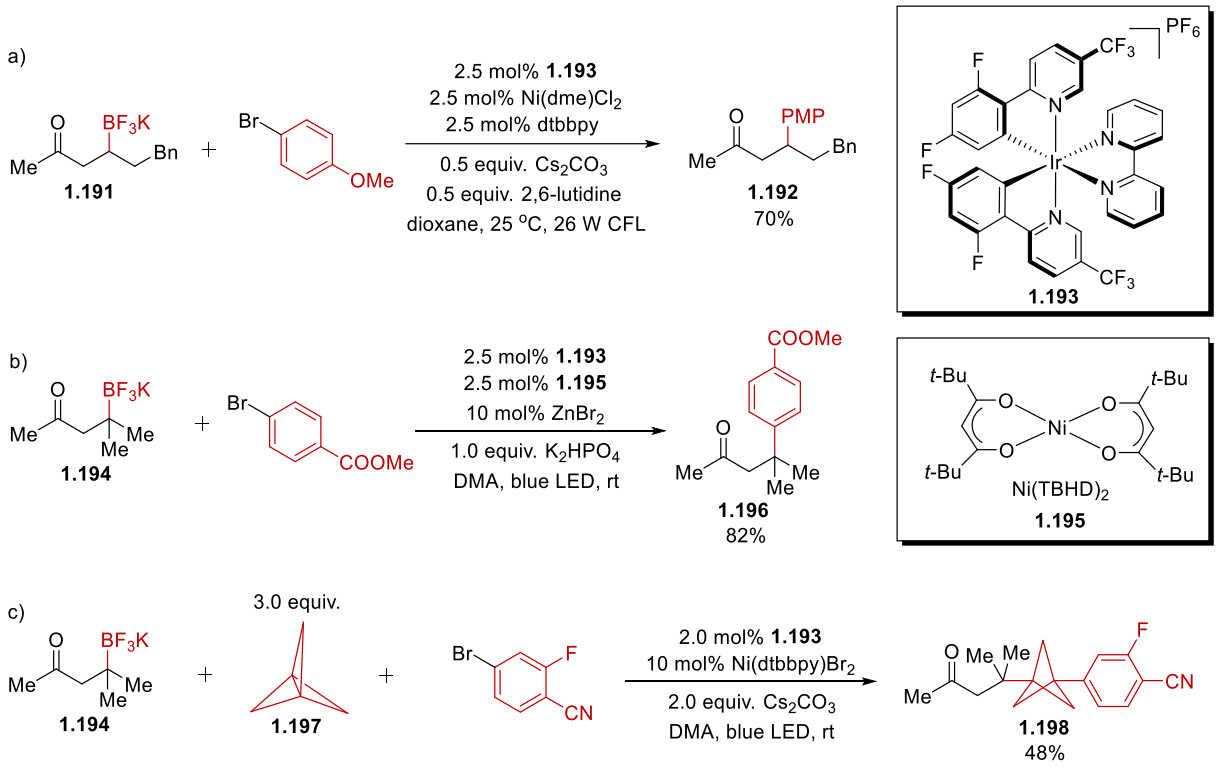



***Figure 1.23.*** Photocatalytic Activation and Transformation of β-Trifluoroboratoketones

### 1.1.3.2 β-Boryl Carbonyls Synthesis by Conjugate Borylation

Another common method to synthesize enantiomerically enriched β-boryl carbonyls is through enantioselective conjugate borylation of α,β-unsaturated carbonyls. Such a reaction has been thoroughly studied by many researchers. The first example of this enantioselective transformation was reported by Yun in 2008.[69] After a extensive optimization, they found that using either chiral Josiphos or chiral Mandyphos ligated copper catalyst, in the presence of a catalytic amount of NaO*t*-Bu and a stoichiometric amount of MeOH, the unsaturated ester can be successfully borylated with excellent yield and enantioselectivity (as shown in Figure 1.24a). Since this discovery, Yun quickly expanded the substrate scope, developing conditions to borylate a range of different types of unsaturated carbonyl compounds. In the case of α,β-unsaturated amides, since

[69] Lee, J.; Yun, J. *Angew. Chem. Int. Ed.* **2008**, *47*, 145 –147.

the substrate is much less reactive, it was found beneficial to increase the catalyst loading.[70] A similar catalytic system can be applied to linear ketones as well; using a Josiphos ligand, phenyl, methyl, isopropyl and tert-butyl-substituted unsaturated ketones can all be borylated with high yield and enantioselectivity.[71] However, when cyclic ketones were used as substrate, ligand **1.217** or **1.218** did not provide satisfying enantioselectivity. Instead, (*R*,*S*)-Taniaphos (**1.232)** was used as a more efficient ligand to borylate cyclic unsaturated ketones with good to high enantioselectivity.[72]

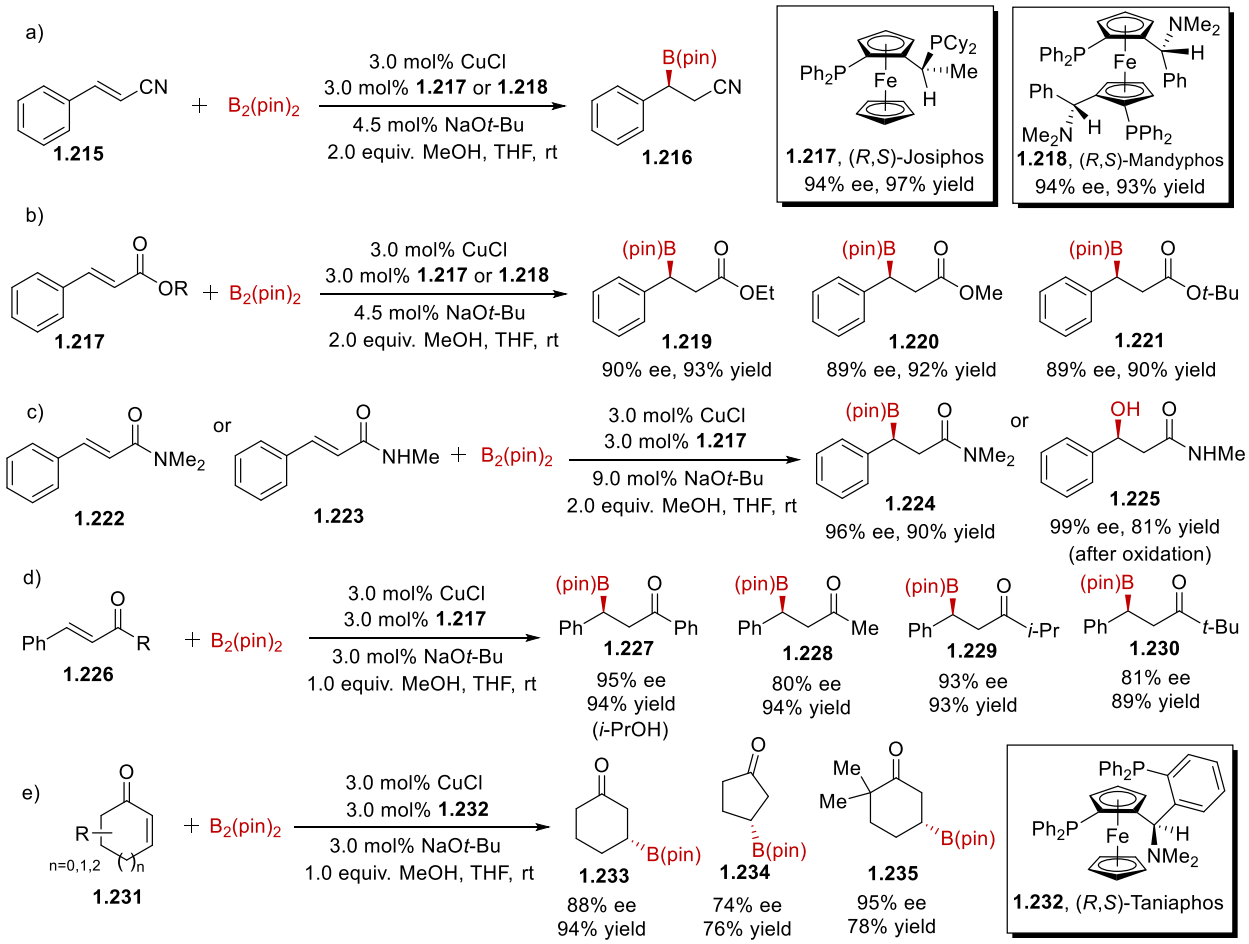



***Figure 1.24.*** Yun's Enantioselective Conjugate Borylation of α,β-Unsaturated Carbonyls Catalyzed by Cu-diphosphine Complexes

[70] Chea, H.; Sim, H.; Yun, J. *Adv. Synth. Catal.* **2009**, *351*, 855 – 858.
[71] Sim, H.; Feng, X.; Yun, J. *Chem. Eur. J.* **2009**, *15*, 1939 – 1943.
[72] Feng, X.; Yun, J. *Chem. Commun.* **2009**, 6577–6579.

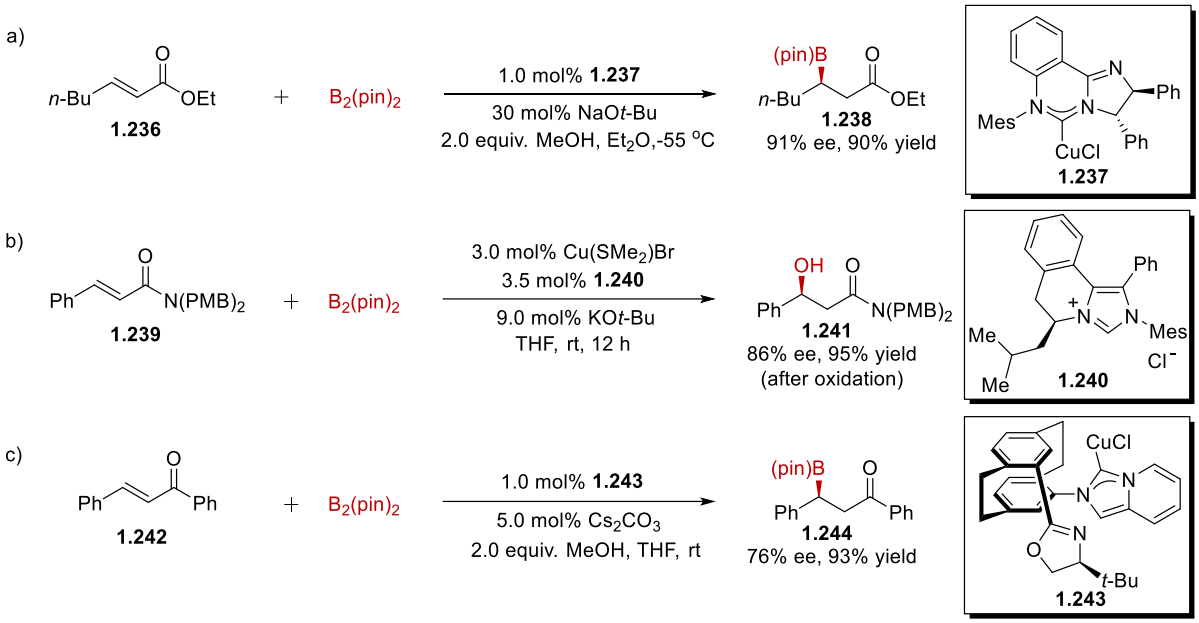



***Figure 1.25.*** Enantioselective Conjugate Borylation of α,β-Unsaturated Carbonyls Catalyzed by Cu-NHC Complex

Besides chiral diphosphine ligands, a range of other types of chiral ligands were also capable of catalyzing the reaction with high yield and enantioselectivity. One class of ligand found effective is chiral NHC ligand. McQuade et al.[73] synthesized a novel 6-NHC-Cu complex **1.237**, which was found capable of catalyzing the conjugate borylation of α,β-unsaturated esters with high yield and er. Soon after, Hong et al.[74]were able to broaden the substrate scope to incorporate α,β-unsaturated amides by using a chiral 5-NHC ligand **1.240**. For α,β-unsaturated ketones, Song et al. [75] employed synthesize another chiral NHC ligand **1.243**, which contains an oxazoline substituted paracyclophane backbone.

P,N ligands were employed to catalyze enantioselective conjugate borylation as well. In 2009, Fernandez[76] discovered that chiral P,N ligand (*S*)-Quinap **1.246** was a suitable ligand for Cu-catalyzed conjugate borylation of α,β-unsaturated ester **1.245**, which enabled a reaction with high yield and a moderate 79% ee. In 2023, Wu et al.[77] showed that another type of P,N ligands, (**1.249**)

[73] Park, J. K.; Lackey, H. H.; Rexford, M. D.; Shatruk, M.; McQuade, T. M. *Org. Lett.* **2010**, *21*, 5008–5011.
[74] Hirsch-Weil, D.; Abboud, K. A.; Hong, S. *Chem. Commun.* **2010**, *46*, 7525–7527.
[75] Hong, D.; Ma, Y.; Zhao, L.; Duang, W.; He, F.; Song, C. *Tetrahedron*: *Asymmetry* **2011**, *22*, 1055–1062.
[76] Fleming, W. J.; Muller-Bunz, H.; Lillo, V.; Fernandez, E.; Guiry, P. J. *Org. Biomol. Chem.* **2009**, *7*, 2520–2524.
[77] Yan, H.; Sha, F.; Wu, X. *Tetrahedron Lett.* **2023**. *117*. 154364-154369.

was effective for catalyzing the conjugate borylation of α,β-unsaturated amide **1.248**. The special pyridine functional group on the nitrogen was found to be important to deliver borylated products with high enantioselectivity. Beside P,N ligands, N,N ligands were also tested by Kobayashi. A bipyridine ligand (**1.252**) was found to be optimal.[78] Remarkably, the reaction catalyzed by **1.252**-Cu complex was capable of converting a large range of unsaturated ketones in water under ambient atmosphere.

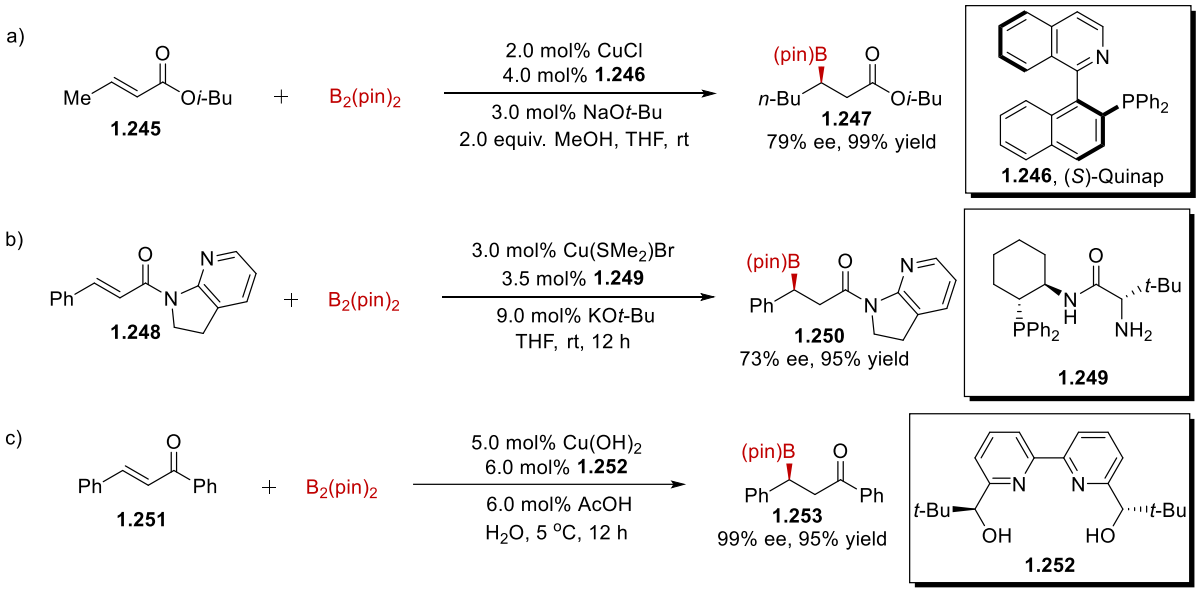



***Figure 1.26.*** Enantioselective Conjugate Borylation of α,β-Unsaturated Carbonyls Catalyzed by P,N or N,N ligand-Cu Complexes

Compared to β-monosubstituted unsaturated carbonyls, β,β-disubstituted unsaturated carbonyls are usually more challenging substrates because of the increased steric hindrance and stablility of the the alkene.[79] Moreover, when the two substituents on the β-position are similar in size, it becomes more dfficult for the chiral catalyst to differentiate the two prochiral faces of the alkene substrate, leading to lower enantioselectivity in construction of the boron-substituted quaternary carbon stereocenter. Indeed, when Yun utilized Josiphos **1.217**-Cu complex to catalyze the borylation of β,β-disubstituted unsaturated ester **1.254**, a drastic decrease in yield was observed (15% for **1.256** compared to 93% for **1.219**, in Figure 1.24b). Through ligand screening, Yun eventually discovered that with MeDuphos **1.255**, the yield of the reaction was recovered, and the

[78] Kobayashi, S.; Xu, P.; Endo, T.; Ueno, M.; Kitsanosono, T. *Angew. Chem. Int. Ed.* **2012**, *51*, 12763–12766.
[79] Feng, X.; Yun, J. *Chem. Eur. J.* **2010**, *16*, 13609–13612.

tertiary alkylboronate can be generated with high enantioselectivity. Although a range of ester substrates can be borylated with high yield and selectivity, both alkyl (**1.258**) or aryl (**1.259**) substituted unsaturated ketones gave much lower enantiomeric ratios when subjected to the borylation conditions.

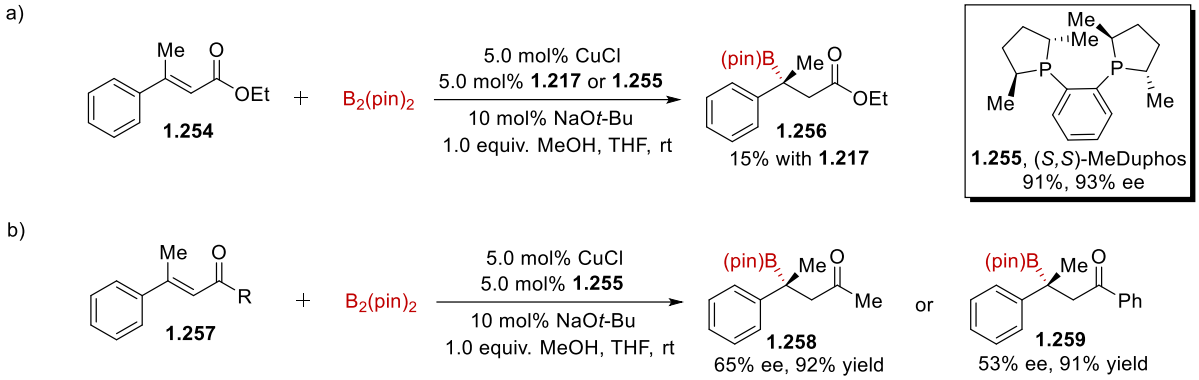



***Figure 1.27.*** Enantioselective Conjugate Borylation of β,β-Disubstituted Unsaturated Carbonyls Catalyzed by Diphosphine Ligated Cu

In 2010, Hoveyda et al.[80] developed a chiral NHC-Cu catalyst that also catalyzed the borlylation of β,β-disubstituted unsaturated ester with high enantioselectivity. Additionaly, the chiral NHC-Cu catalyst system was able to borylate ketone substrates with higher ers comparing to diphosphine ligated Cu complexes. Impressively, Kobayashi et al.[81] has shown that the dipyridine-Cu catalyst system was able to borylate more challenging β,β-disubstituted unsaturated carbonyls as well. A spectrum of different types of carbonyl compounds can be incorporated, including esters, linear and cyclic ketones as well as amides, and the enantioselectivity was found to be higher than 93:7 er across all types of substrates. Again, all of these reactions can be done in water under ambient atmosphere.

[80] O'Brien J. M.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630–10633.
[81] Kobayashi, S.; Xu, P.; Endo, T.; Ueno, M.; Kitsanosono, T. *Angew. Chem. Int. Ed.* **2012**, *51*, 12763–12766.

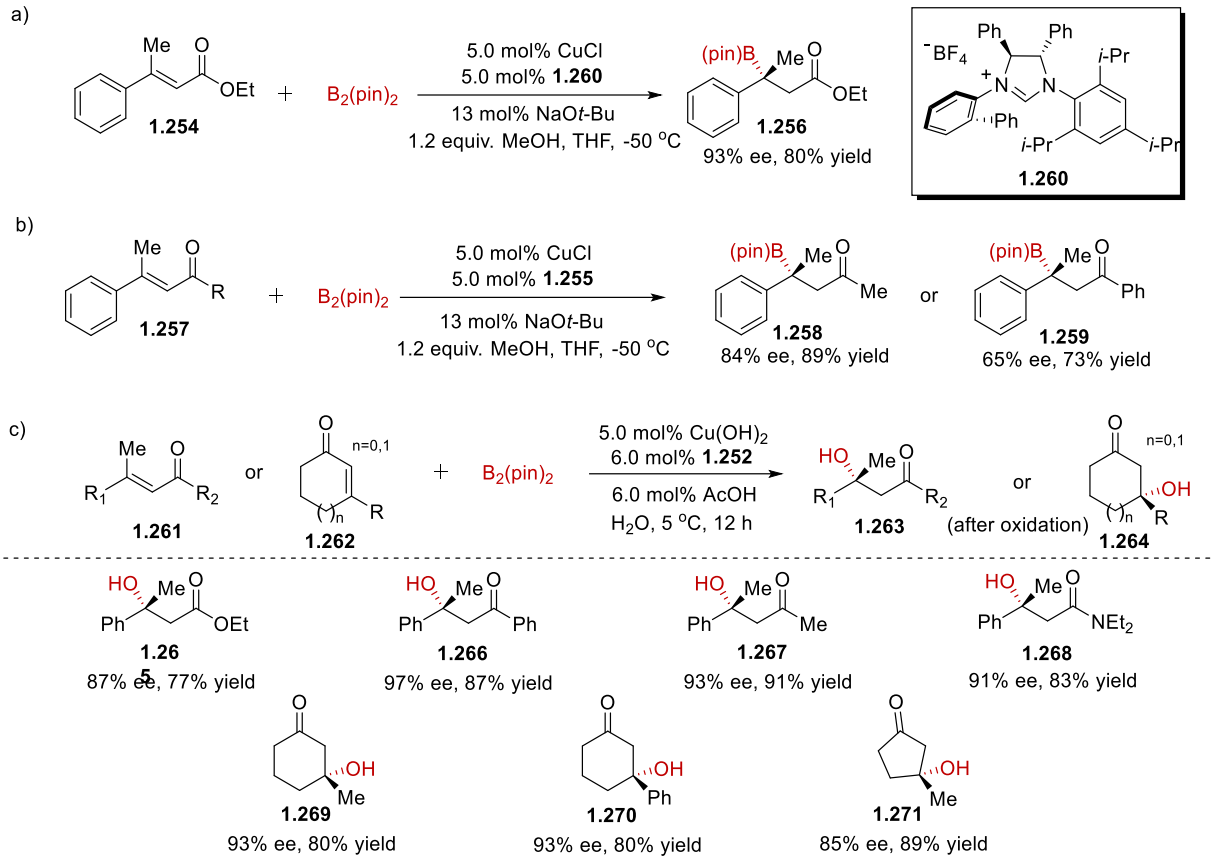



***Figure 1.27.*** Enantioselective Conjugate Borylation of β,β-Disubstituted Unsaturated Carbonyls Catalyzed by NHC-Cu or Bipyridine-Cu Complexes

### 1.1.3.3 β-Boryl Carbonyl Synthesis by Hydroboration

Besides conjugate borylation, Li discovered that a Rh-catalyzed hydroboration of α,β-unsaturated amides also delivered the β-boryl amides with high enantioselectivity.[82] After testing a large library of diphosphine ligands, Li found that most would afford the Rh catalyzed hydroboration product with undesired regioselectivity: the nucleophilic hydride would add to the electrophilic β-carbon and the boron atom would add to the α-carbon. However, ligand **1.273** was found to reverse the regioselectivity and deliver the desired β-boryl amide **1.274** with 71% yield and 97% ee. Importantly, whereas it was found challenging to control the α-carbon stereocenter in the conjugate borylation reaction [83], in the case of hydroboration, because the migratory insertion

[82] Gao, T.; Zhang, Wen.; Sun, X.; Lu, H.; Li, B. *J. Am. Chem. Soc.* **2019**, *141*, 4670−4677.
[83] For more discussion on α-carbon stereochemistry control: a) Xie, J.; Lin,S.; Li, G. *Org. Lett.* **2016**, *18*, 3926–3929. b) Zuo, Y.; Zhong, Z.; Fan, Y.; Li, X.; Chen, X.; Chang, Y.; Song, R.; Fu, X.; Zhang, A.; Zhong, C. *Org. Biomol. Chem.* **2018**,*16*, 9237-9242. c) He, Z.; Zhao, Y.; Tian, P.; Wang, C.; Dong, H.; Lin, G. *Org. Lett.* **2014**, *16*, 1426–1429.

of hydride onto the α-carbon happens first, the stereochemistry of α-carbon could be controlled. Indeed, Li discovered that when there is a substituent on the α-carbon of the unsaturated amide, the hydroboration can deliver the β-boryl amide with excellent diastereoselectivity as shown in Figure 1.28b (**1.276**-**1.278**).

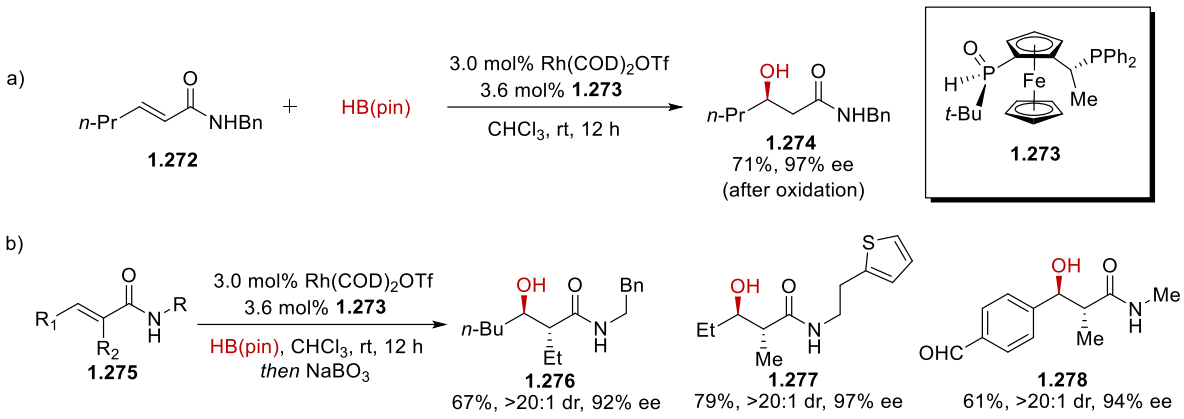



***Figure 1.28.*** Regio-reversed Stereoselective Hydroboration of α, β-Unsaturated Amides

To probe the reason behind the distinctly different catalytic behavior of ligand **1.273** and monodentate phosphine ligands, Li et al.[84] carried out DFT calculations to determine the detailed energy profiles for each step in the proposed reaction mechanism. It was found that for the desired regio-reveresed α-carbon hydride insertion (Figure 1.29, in red), $PPh_3$ ligands and ligand **1.273** give similar transition-state energy (3.6 kcal/mol for $PPh_3$ and 3.5 kcal/mol for **1.273**). However, ligand **1.273** significantly increased the transition-state energy for the undesired β-carbon hydride insertion (1.9 kcal/mol for $PPh_3$ and 4.4 kcal/mol for **1.273**). That is instead of promoting the desired regioselective reaction, ligand **1.273** inhibits the undesired migratory insertion mode and decreases the amount of the undesired α-boration product.

[84] Gao, T.; Zhang, Wen.; Sun, X.; Lu, H.; Li, B. *J. Am. Chem. Soc.* **2019**, *141*, 4670−4677.

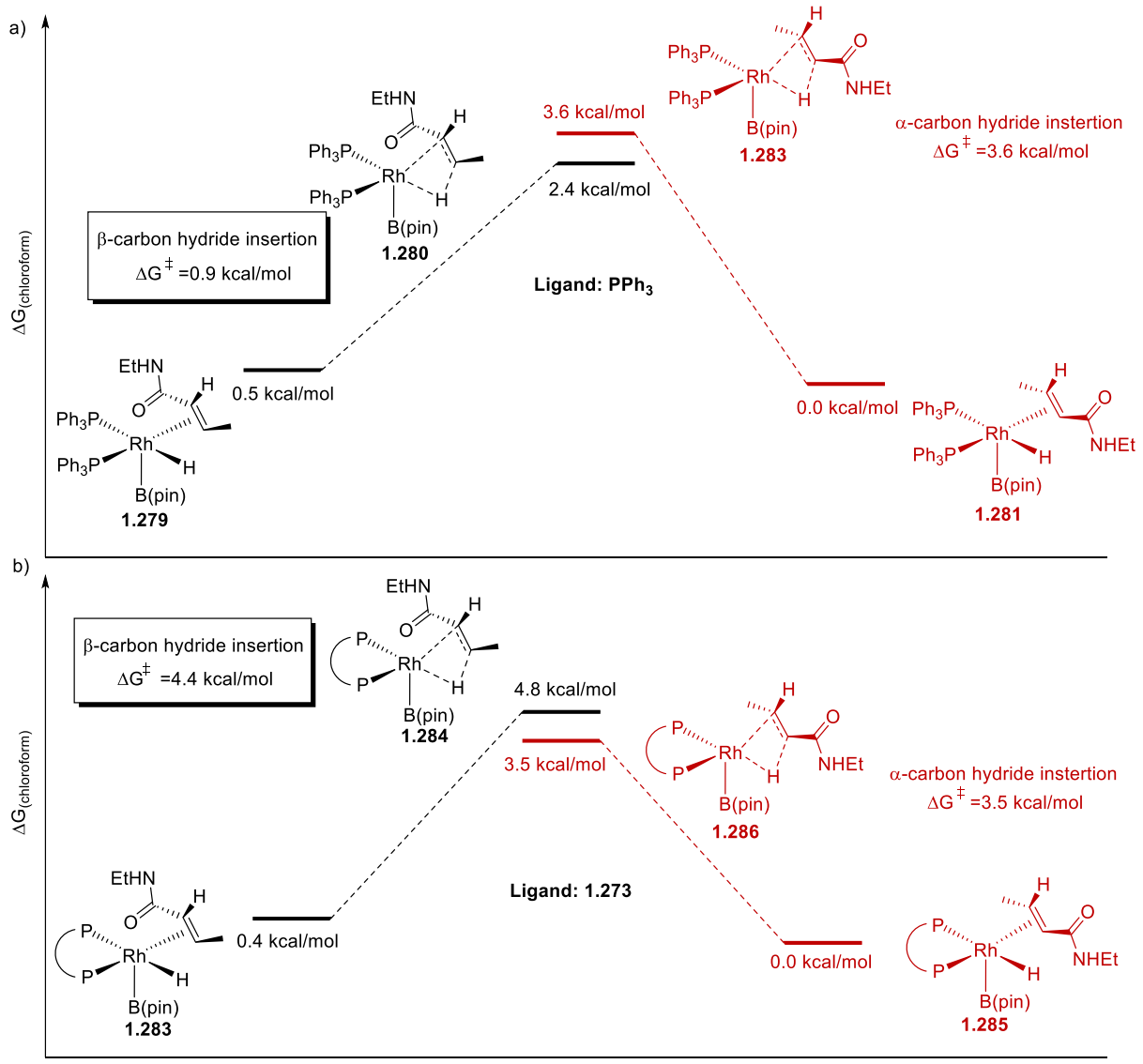



***Figure 1.29.*** DFT calculation Results for Transition-state Energy Profiles in Two Modes of Migratory Insertion with Different Rh Complexes

Additionally, Li also utilized this Rh-catalyzed hydroboration reaction to borylate more challenging β,β-disubstituted unsaturated amides, from which a verity of tertiary β-boryl amides were synthesized with generally high yields and enantioselectivity. [85] Notably, when the two substituents on the β-carbon were structurally similar (for example substrate **1.295-1.297** in Figure 1.30) the tertiary boronic ester can still be generated with high er, which suggested that the chiral

[85] Gao, T.; Lu, H.; Gao, P.; Li, B. *Nature Commun.* **2021**, *12*, 3776.

Rh complex differentiates the two prochiral faces of the substrate based on the orientation of the carbonyl, instead of the steric difference between the two β-substituents.

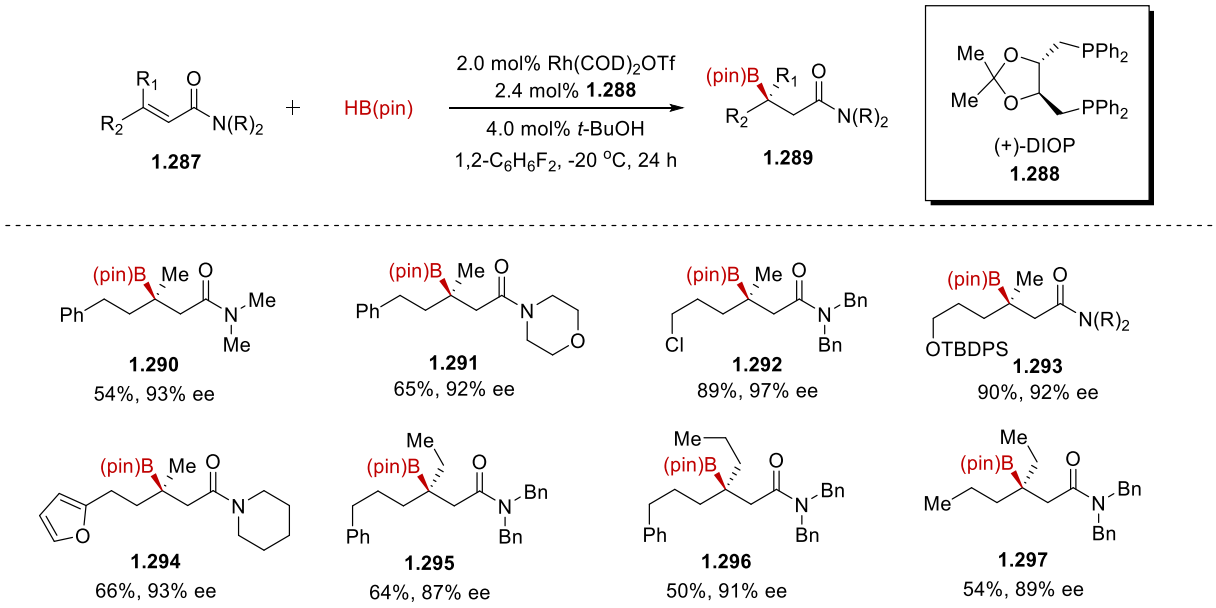



***Figure 1.30.*** Regio-reversed Stereoselective Hydroboration of β,β-disubstituted α,β-Unsaturated Amides

### 1.1.3.4 Total Synthesis Using β-Boryl Carbonyls as Key Intermediates

Herein, to further demonstrate the importance of β-boryl carbonyl compounds, a total synthesis of natural product $\Delta^{12}$-prostaglandin $J_3$ accomplished by Aggarwal will be discussed. [86] Leveraging an aldol condensation reaction, target molecule **1.199** can be divided into two fragments: northern fragment **1.200** and southern fragment **1.201**. To synthesize the β-boryl aldehyde southern fragment **1.201**, β,γ-unsaturated aldehyde **1.203** was firstly prepared from homoallylic alcohol **1.202** by DMP oxidation in the presence of catalytic amount of TEMPO. Then, a Wittig reaction was applied to aldehyde **1.203** to synthesize α,β-unsaturated ester **1.204** as a substrate for conjugate borylation. The enantioselective borylation was carried out using the reaction conditions developed by Yun. [87] Josiphos-Cu complex catalyzed this conjugate borylation with good enantioselectivity (93:7 er) and excellent yield (85%). Subsequently, the ester group in the β-boryl

[86] Lee, J.; Yun, J. *Angew. Chem. Int. Ed.* **2008**, *47*, 145 –147.
[87] Jing, C.; Aggarwal, V. K. *Org. Lett.* **2020**, *22*, 6505–6509.

ester **1.205** was reduced to the aldehyde by treatment with DIBAL to give southern fragment **1.201** in 93% yield.

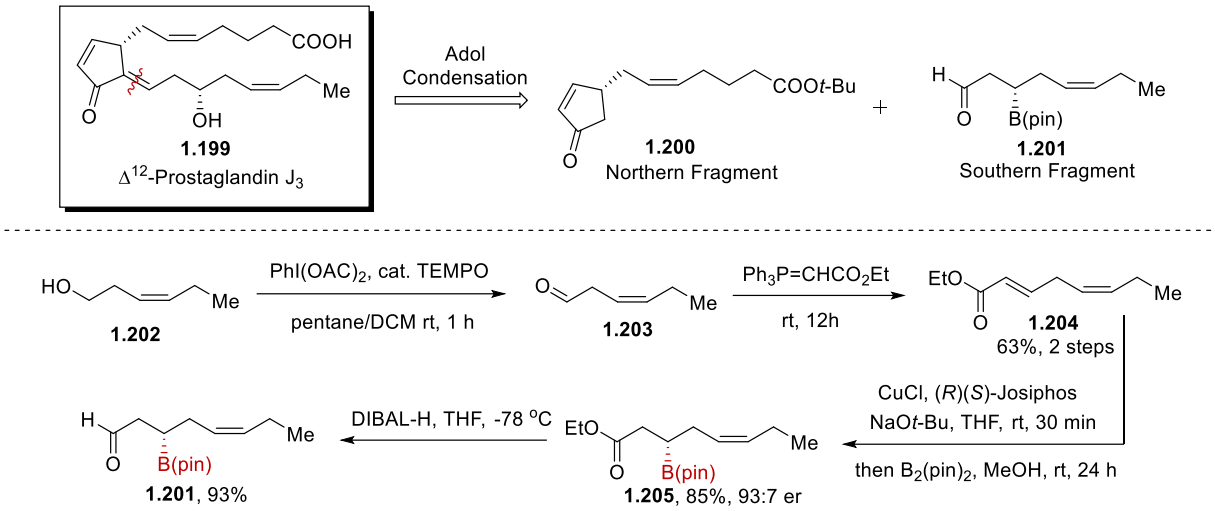



***Figure 1.31.*** Δ[12]-prostaglandin J3 Southern Fragment Synthesis

To synthesize the enone northern fragment, an enantioselective dimerization of butanedial **1.206** was firstly carried out. Using (L)-proline as a catalyst, the aldol addition between two molecules of **1.206** proceeds with high enantioselectivity (99:1 er). Subsequently, with catalyst **1.215**, a condensation catalyst developed by Aggarwal et al., a Robinson annulation occurs to furnish the enal **1.207** in 29% overall yield. Then, the hemiacetal was oxidized to lactone **1.208** while under the same condition the aldehyde group was oxidized to a carboxylic acid. Following activation of carboxylic acid group with ethyl chloroformate and treatment with sodium azide allowed acyl azide **1.209** was to be synthesized in 80% yield. Subsequently, by treating **1.209** with heat, a Curtis rearrangement occurred. After by alcoholysis with benzyl alcohol, a Cbz-protected enamine **1.210** was synthesized in 90% yield. To install the (*Z*)-olefin moiety, **1.210** was firstly reduced to hemiacetal **1.211** by treating with DIBAL, and then, by subjecting **1.211** to an excess amount of alkyl ylide, a (*Z*)-selective Wittig reaction was carried out to generate alkene-containing product **1.212**. Subsequently, by treating the secondary alcohol with acid, followed by protection of the carboxylic acid group as a *t*-butyl ester, northern fragment **1.200** can be synthesized in 66% yield over three steps.

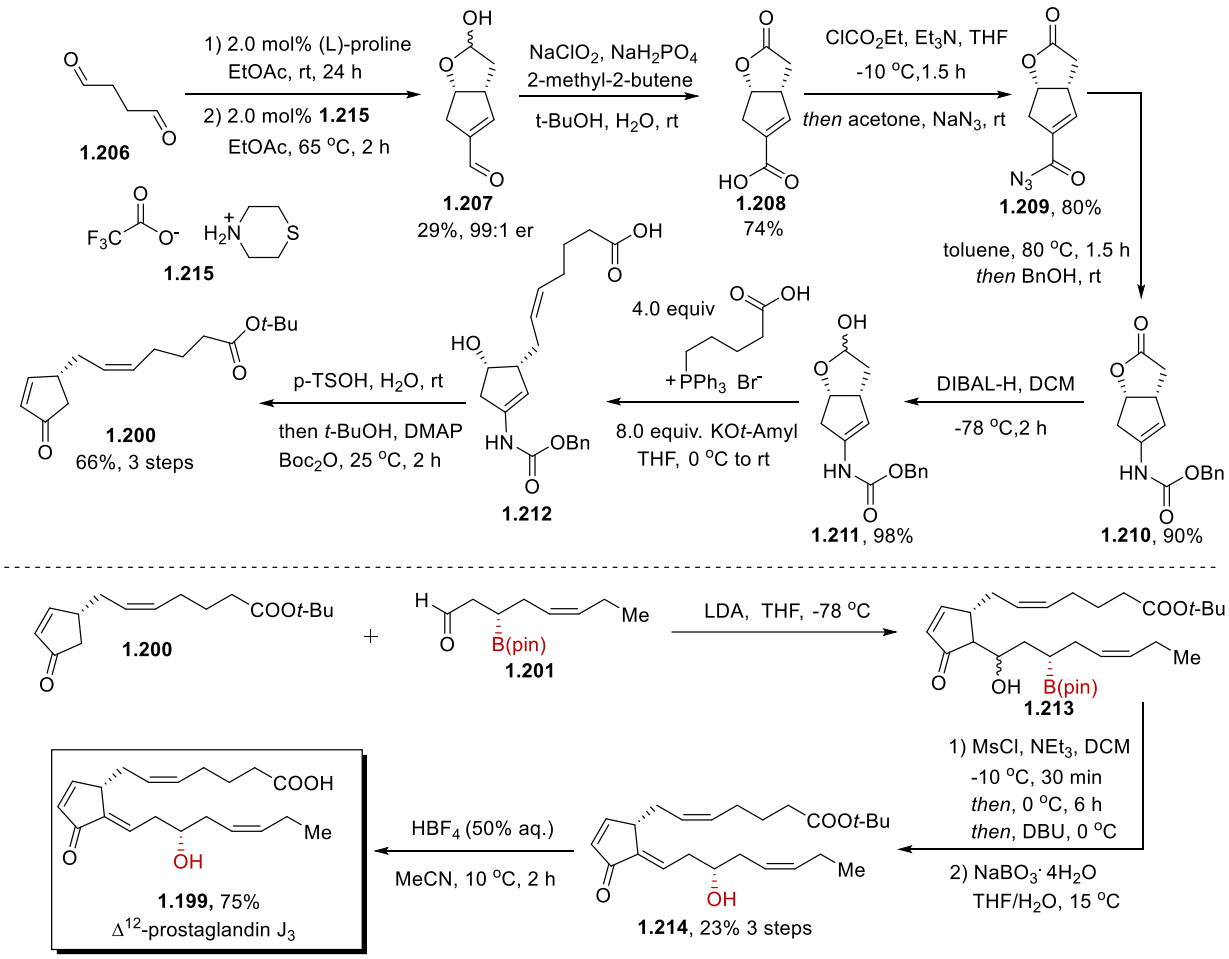



***Figure 1.32.*** Δ[12]-Prostaglandin J$_3$ Northern Fragment Synthesis and End Game

To join the two fragments and complete the total synthesis, **1.200** was deprotonated by LDA, then reacted with **1.201** to yield secondary alcohol **1.213**. Subsequent elimination of the hydroxyl group and oxidation of the boronic ester yielded **1.214** in 23% overall yield. Following deprotection of the *t*-butyl ester by treatment with acid, the target molecule Δ[12]-prostaglandin J$_3$ was synthesized in 75% yield.

## 1.2 Reaction Design

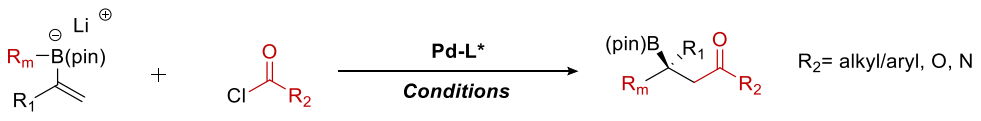



***Figure 1.33.*** Reaction Design for Pd-Catalyzed Enantioselective Conjunctive Cross-Coupling Between α-Substituted Alkenyl Boronate Complexes and Acyl Electrophiles

As discussed above, using conjugate borylation, secondary β-boryl carbonyls can be easily accessed with high stereochemical control. However, reactions that can produce tertiary boronates at the β-position of the carbonyl are still rare, due to the low reactivity and high symmetry of the alkene substrate. Additionally, only few examples where the borylated tertiary carbon contains two substituents with similar steric properties (for example, two *n*-alkyl chains) have been reported.[88] We considered that by reacting acyl electrophiles and α-substituted alkenyl boronic esters, an enantioselective conjunctive cross-coupling could be a complementary method to access these challenging tertiary alkylboronates. In the previous Ni-catalyzed conjunctive cross-coupling between 9-BBN derived boronate complexes and acyl chlorides, only β-boryl ketones were synthesized.[89] We wanted to further explore the possibility of incorporating chloroformate electrophiles as well as carbamoyl chloride electrophiles into this reaction to deliver ester and amide products.[90]

## 1.3 Results and Discussion

### 1.3.1 Alkyl/Aryl Substituted Acyl Electrophiles

#### 1.3.1.1 Alkyl/Aryl Substituted Acyl Chlorides

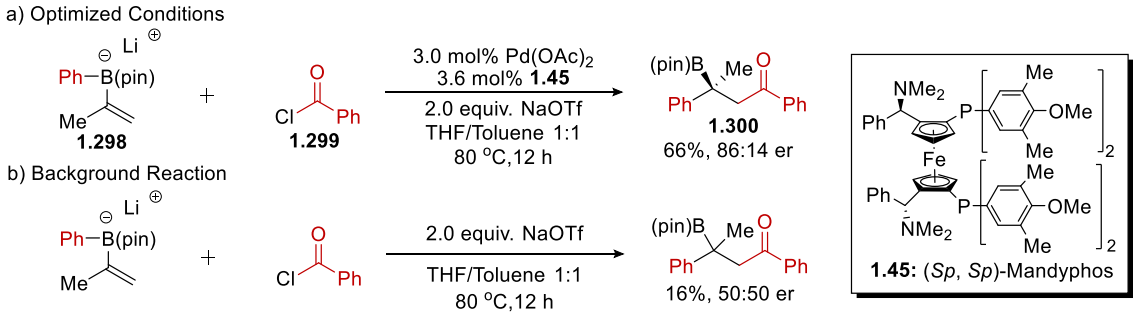



***Figure 1.34.*** Performance of Benzoyl Chloride Electrophile

We firstly investigated the performance of simple benzoyl chloride as an electrophile. As shown in Figure 1.34a, after thorough condition optimization, with the previously superior

[88] a) O'Brien J. M.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630–10633. b) Gao, T.; Lu, H.; Gao, P.; Li, B. *Nature Commun.* **2021**, *12*, 3776.
[89] Law, C.; Meng, Y.; Koo, S. M.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 6654–6658.
[90] Wilhelmsen, C. A.; Zhang, X.; Myhill, J. A.; Morken, J. P. *Angew. Chem. Int. Ed.* **2022**, *61*, e202116784.

Mandyphos ligand **1.45**, a moderate 86:14 er was achieved in synthesizing the desired tertiary β-boryl ketone (**1.300**). Additionally, during the optimization of this reaction, it was found that the benzoyl chloride electrophile can induce the 1,2-migration of boronate complex, presumably through a polar induced rearrangement mechanism discovered by Aggarwal and Studer. [91] Noticing that an acyl chloride electrophile could be over reactive, we decided to look for a more stable alternative electrophile.

### 1.3.1.2 Alkyl/Aryl Substituted Acyl Saccharins

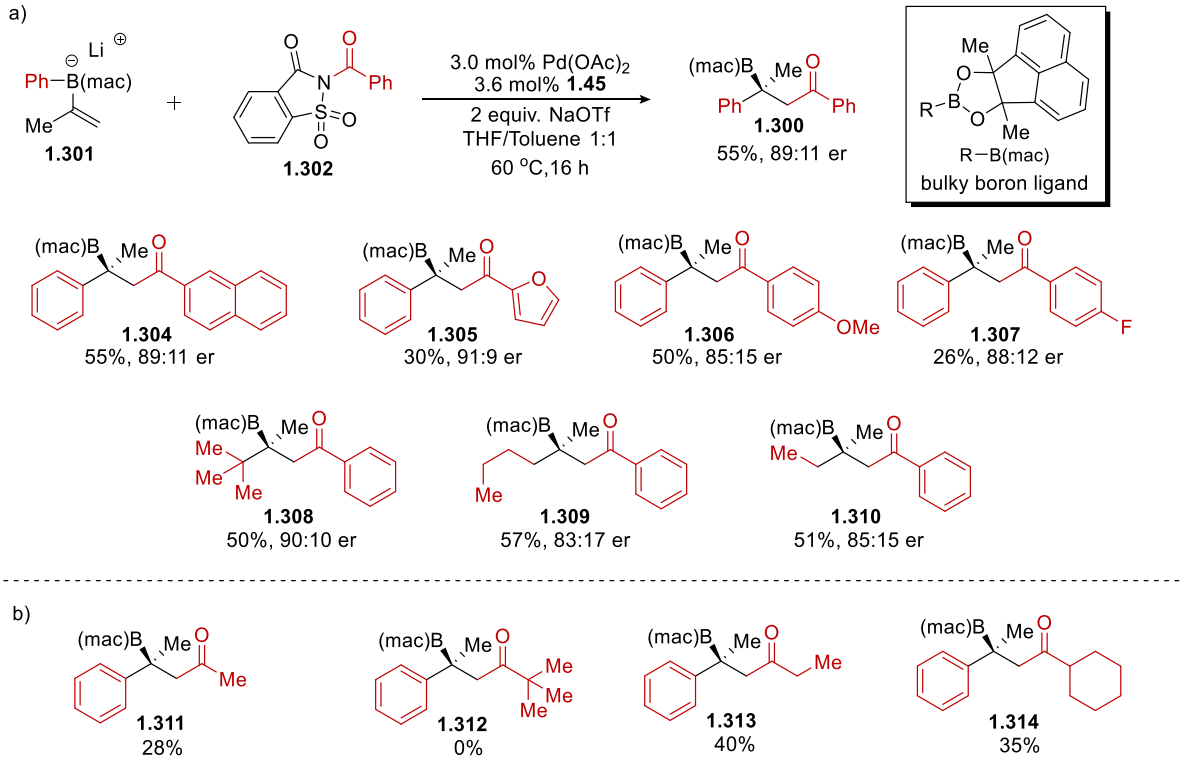



***Figure 1.35.*** Performance of Acyl Saccharin Electrophiles

Inspired by the work published by Szostak (see section **1.1.1.2**), we decided to use twisted amide electrophiles as alternatives to acyl chlorides. Additionally, in order to prevent undesired side-reaction pathways, a more bulky "mac" diol ligand was synthesized and installed onto the boronate complex.[92] As shown in Figure 1.35a, we discovered that benzoyl saccharin **1.302** could be a superior electrophile, as reaction with it produces ketone product **1.300** with higher er than

[91] Detail of this reaction mode will be discussed in Chapter 2.
[92] Detail for the function of mac diol boron ligand will be discussed in Chapter 2, Introduction.

with benzoyl chlorides. A variety of aryl substituents can be installed onto the ketone (substrates **1.304-1.307**). The reaction can tolerate both aryl and alkyl migrating groups, though the alkyl migration reactions typically give lower enantioselectivity (substrates **1.308-1.310**). However, with the alkyl substituted acyl saccharin electrophile, the yields of the conjuctive cross-coupling product are significantly lower. In these reactions (substrates **1.311-1.314**), the undesired Suzuki-Miyaura product becomes the major product.

### 1.3.2 Chloroformate Electrophiles

Based on the presedent of applying chloroformates in Suzuki-Miyaura cross-coupling reactions to synthesize esters, we also attempted to incorporate chloroformates in conjuctive cross-coupling, hoping to synthesize a variety of tertiary β-boryl esters.

#### 1.3.2.1 Preparation of Chloroformates

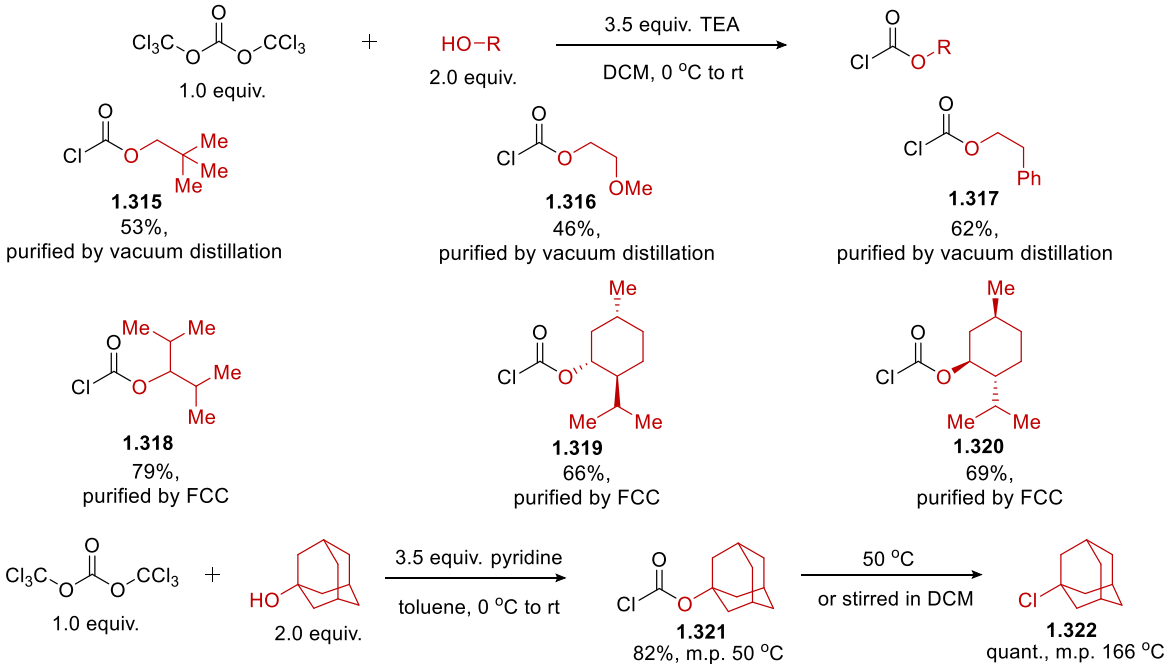



***Figure 1.36.*** Preparation of Chloroformates

Primary alkyl substituted chloroformates can be synthesized by treating the corresponding primary alcohol with triphosgene. [93]The ratio between alcohol loading and triphosgene loading is

[93] Gerard, S.; Dive, G; Clamot, B.; Touillaux, R.; Marchand-Brynaert, J. *Tetrahedron* **2002**, *58*,2423–2433.

usually 2.0:1.0. In the present of excess amount of TEA or pyridine as an acid scavenger, the primary alkyl substituted chloroformate can be generated with full conversion of the alcohol. To purify the product vacuum distillation was carried out for each primary alkyl substituted chloroformate. For secondary alkyl substituted chloroformates such as **1.318**, **1.319** and **1.320**, column chromatography with silica gel solid phase was used, due to the thermal instability of these compounds. [94] For tertiary carbon substituted chloroformate, we found that tert-butyl chloroformate are very challenging to prepare, as it readily eliminates to isopropene upon treatment with base. Adamantyl chloroformate is more stable and will not eliminate due to the bridged ring structure, however, it was found prone to fragmentation when treating with heat or being dissolved in polar solvents such as DCM.[95] Therefore, the reaction to synthesize adamantyl chloroformate was carried out in tolunene. Upon completion, the reaction was filtered to remove pyridine-HCl salt. Then, tolunene was removed by vacuum distillation without heating. The crystalline solid acquired through this process should be the desired chloroformate with >90% purity with a melting point of 50 ºC. If decomposition occurred, the undesired side product admantyl chloride has a higher melting point at 166 ºC. [96]

#### 1.3.2.2 Chloroformate Electrophile Substrate Scope

With a variety chloroformates either purchased or freshly prepared, the conjuctive cross-couplings with these electrophiles was examined. For primary alkyl substituted chloroformates, the enantioselectivity of the conjunctive cross-coupling reactions are around 85:15 er. Secondary alkyl groups such as cyclopentane in **1.330** reacted with higher enantioselectivity (90:10). When (-)-menthol derived chloroformate was used, reaction gave 2.4:1 dr on the boron containing stereocenter, while (+)-menthol derived chloroformate would invert the configuration of the boron containing stereocenter (0.8:1 dr), which indicated a strong interaction between the carbonyl group and alkenyl boronate complex substrate during the alkene binding step.

[94] Hajra, S.; Bhowmick, M.; Maji, B.; Sinha, D. *J. Org. Chem.* **2007**, *72*, 4872–4876.
[95] Haas, W. L.; Krumkalns, E. V.; Gerzon, K. *J. Am. Chem. Soc.* **1966**, *88*, 1988–1992.
[96] Kevill, D. N.; Weitl, F. L. *J. Am. Chem. Soc.* **1968**, *90*, 6416–6420.

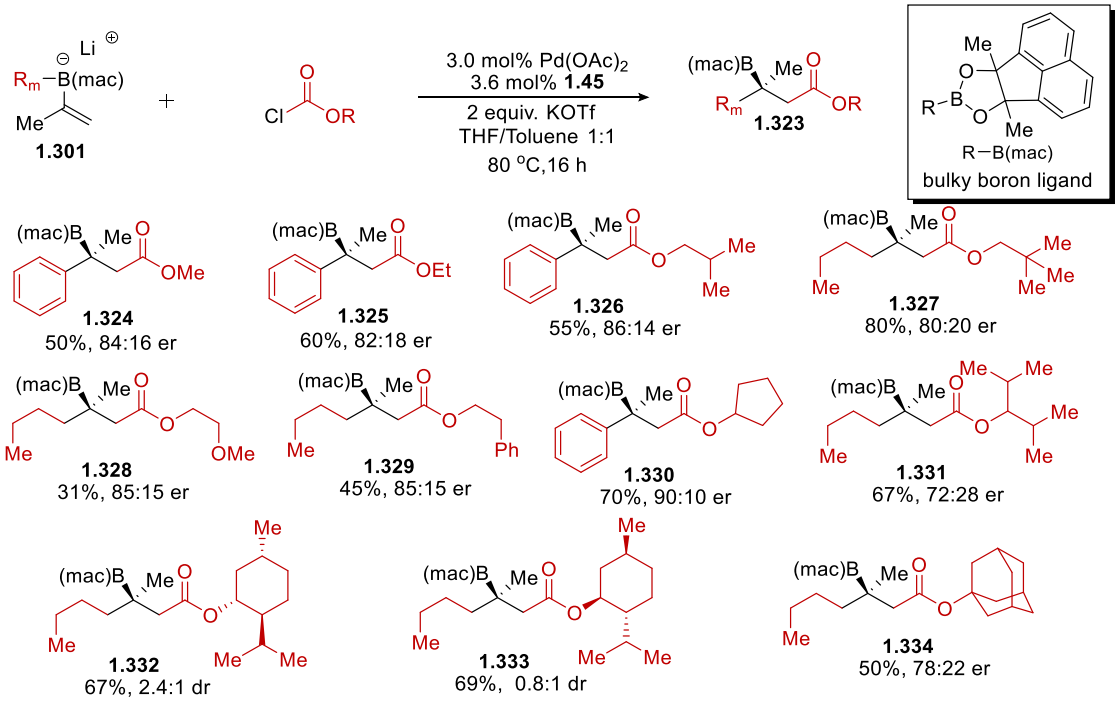



***Figure 1.37.*** Performance of Chloroformate Electrophiles

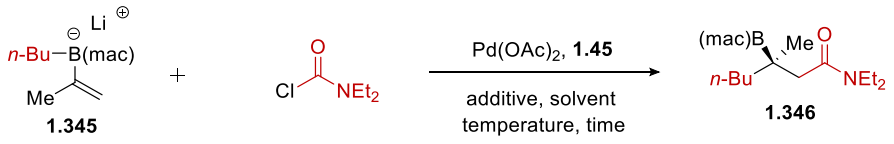
### 1.3.3 Carbamoyl Chloride Electrophiles

As shown above, when acyl chloride, acyl saccharin and chloroformate electrophiles are used in conjunctive cross-coupling, we were not able to achieve a single reaction that gave the desired tertiary β-boryl carbonyls with higher then 80% ee, despite an immense amount of optimizing the conditions and the electrophile/migrating group. We hypothesized that the low enantioselectivity is due to the high electrophilicity of these acyl electrophiles, therefore, we moved on to test carbamoyl chloride electrophiles, which are significantly less electrophilic yet have shown good performance in acylative Suzuki-Miyaura cross-coupling reaction (see section **1.1.1.2**).

#### 1.3.3.1 Carbamoyl Chloride Electrophile Reaction Optimization

Using N,N-diethyl carbamoyl chloride, we examined reaction conditions (Table 1.38). Employing the previously optimal conditions for acyl saccharin electrophiles or chloroformates, reaction entry 1 showed that the carbamoyl chloride gave low enantioselectivity with 70:30 er. However, we found that by changing the salt additive from KOTf to CsF, under the same conditions, the enantioselectivity can be improved to 81:19 er (Figure 1.38, entry 2). As shown in entry 7, replacing CsF with KF resulted in a much lower enantioselectivity that is comparable to entry 1.

Therefore, we believe the cesium cation played a central role in regulating the transition state structure for the Pd-alkene binding step. Lowering the reaction temperature and prolonging the reaction time could further improve the er to 87:13 (entry 3). By further lowering the temperature to room temperature and prolonging the reaction time to 48 h, the enantioselectivity could be increased to 91:9 er, while with increased catalyst loading, the reaction can now produce the β-boryl amide with 85% yield and 92:8 er (entry 4, 5). Taking consideration of the high expense of the catalyst (particularly the chiral Mandyphos ligand **1.45**) we decided to optimize the catalyst loading. It was found that 3.0 mol% catalyst loading is sufficient to give a useful amount of product (entry 6). With this catalyst loading, we proceeded to optimize from other aspects of the reaction. It was found that due to its low solubility in THF, CsF would settle at the bottom of reaction vessel as a crystalline solid for a long period of reaction time, which might diminish the reactivity as well as impact the enantioselectivity of the reaction. To enhance the solubility of CsF, 3.0 equivalents of water were added at the beginning of the reaction, which was found to improve the conversion and the enantioselectivity (entry 8).

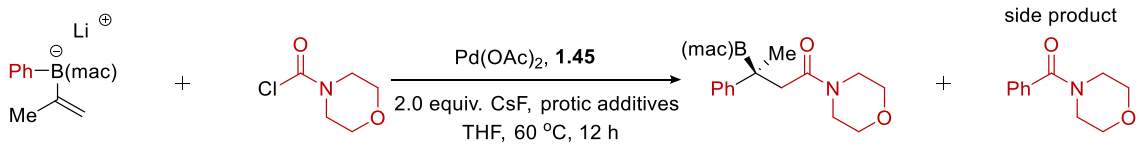



| entry | catalyst loading | additive | solvent | temperature | time | yield | er |
|---|---|---|---|---|---|---|---|
| 1 | 1.0 mol% | 2.0 eq. KOTf | THF/Tol | 80 °C | 12 h | 62% | 70:30 |
| 2 | 1.0 mol% | 2.0 eq. CsF | THF/Tol | 80 °C | 12 h | 59% | 81:19 |
| 3 | 1.0 mol% | 2.0 eq. CsF | THF | 40 °C | 24 h | 64% | 87:13 |
| 4 | 1.0 mol% | 2.0 eq. CsF | THF | rt | 48 h | 27% | 91:9 |
| 5 | 5.0 mol% | 2.0 eq. CsF | THF | rt | 48 h | 85% | 92:8 |
| 6 | 3.0 mol% | 2.0 eq. CsF | THF | rt | 72 h | 45% | 92:8 |
| 7 | 3.0 mol% | 2.0 eq. KF | THF | 80 °C | 12 h | 56% | 72:28 |
| 8 | 3.0 mol% | 2.0 eq. CsF, 3.0 eq. $H_2O$ | THF | rt | 72 h | 86% | 94:6 |

***Table 1.38.*** Reaction Condition Optimization Table

### 1.3.3.2 Protic Additives' Effects on The Reaction

As demonstrated in Figure 1.381, protic additive such a water has significant effects on the performance of the conjucntive cross-coupling reaction. Besides water, we investigate other protic additives' effect on the reaction. As presented in Table 1.381, in a reaction with phenyl migrating group, reaction without any protic additive (entry 1) resulted in significantly lower yield on the conjunctive cross-coupling product. 3.0 equivalent of methanol did not improve the yield of the reaction. A much higher yield was achieved when water as added, as demonstrated by entry 3. More acidic protic additive such as trifluoroethanol (entry 4, pKa=12.5) or phenol (entry 5, pKa=9.95) resulted in partial or complete decomposition of boronate complex. Through this investigation, water as a protic additive was found superior and significantly improved the reaction yield by inhibiting the undesired Suzuki-Miyaura cros-coupling side reaction. The effect of water was also more drastic on reaction with aryl migrating groups.




| entry | protic additive | pKa | amount | product yield | side product yield |
|---|---|---|---|---|---|
| 1 | none | N/A | N/A | 10% | 80% |
| 2 | methanol | 15.5 | 3.0 eq. | 0% | 10% |
| 3 | water | 15.7 | 3.0 eq. | 85% | <10% |
| 4 | trifluoroethanol | 12.5 | 3.0 eq. | 55% | <10% |
| 5 | phenol | 9.95 | 3.0 eq. | 0% | <10% |

***Table 1.381.*** Protic Additives' Effects on The Reaction

### 1.3.3.3 NMR study on The Interaction Between Water and Boronate Complex

We delved deeper into unraveling the role of water through NMR analysis, as illustrated in Figure 1.382. The $^{1}$H NMR findings indicate that water plays a pivotal role in expediting the diastereomeric isomerization of a significant "ate" complex. Introducing 1.0 equiv. of water led to noticeable changes in the concentration of each diastereomer over time, resulting in an almost 1:1

diastereomeric ratio within just an hour. In stark contrast, when the experiment was conducted without water, an identical setup yielded only a 0.2:1 diastereomeric ratio after 36 hours. These observations, coupled with heightened chemoselectivity in conjunctive cross-coupling, propose that water might function as an H-bond donor to the oxygens of the ate complex, thereby facilitating the observed isomerization. While numerous possibilities exist regarding the multifaceted roles of water, one plausible scenario is that a specific diastereomer proves essential for efficient catalysis, and water serves as a catalyst in promoting this diastereomeric preference under catalytic conditions.

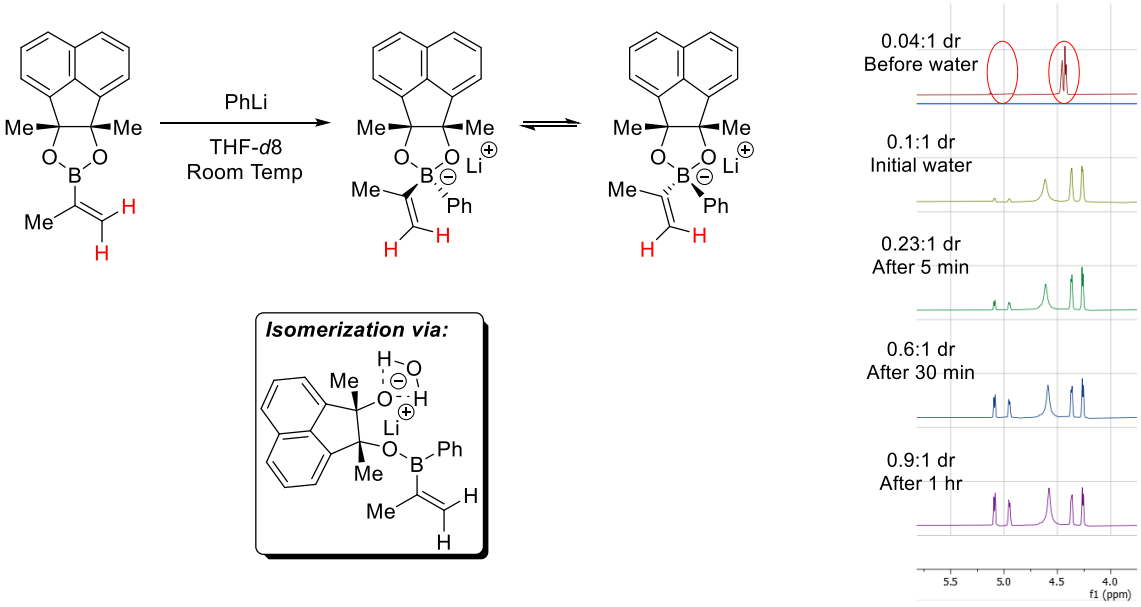
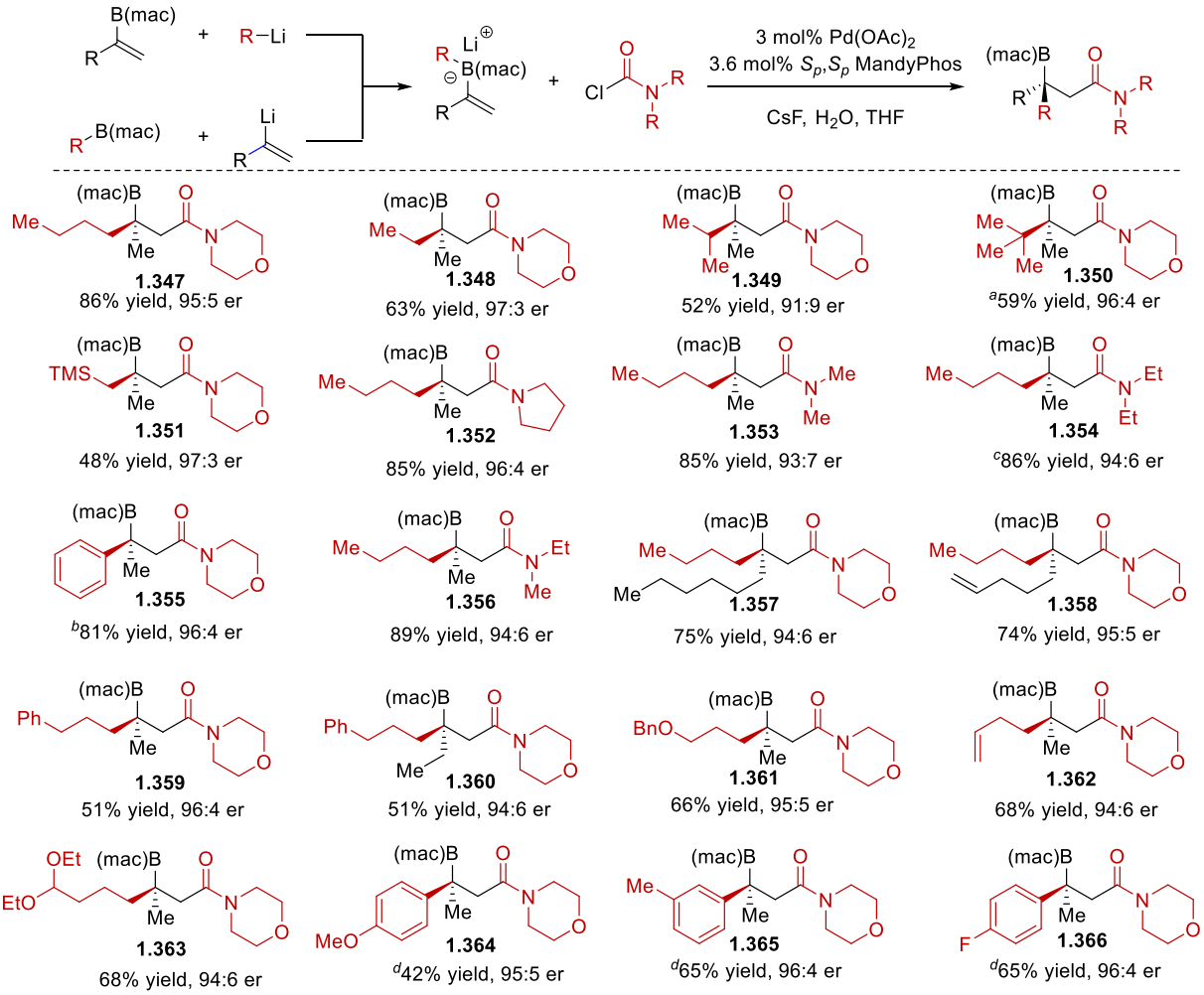



***Figure 1.382.*** Interaction Between Water and Boronate Complex

### 1.3.3.4 Carbamoyl Chloride Electrophiles Reaction Substrate Scope

With the optimal reaction conditions in hand, we explored the scope of this conjuctive cross-coupling reaction. (Figure 1.39). In the case of alkyl migration, we found a variety of alkyl groups, including primary carbon (**1.347**, **1.348**), secondary carbon (**1.349**) as well as tertiary carbon (**1.350**) can be incorporated. The reaction can also tolerate a variety of functional groups, including alkene (**1.362**), benzyl protected alcohol (**1.361**) as well as an acetal group (**1.363**). Impressively, β-boryl amides with quaternary carbon substituted by two primary alkyl chains were also

synthesized with high enantioselectivity, for example **1.357**, **1.358** and **1.360**, all with around 90% ee. Aryl migrating groups such as *p*-methoxyl phenyl (**1.364**), *p*-fluorophenyl (**1.366**) and *m*-tolyl (**1.365**) were all incorporated with high enantioselectivity and good yields.

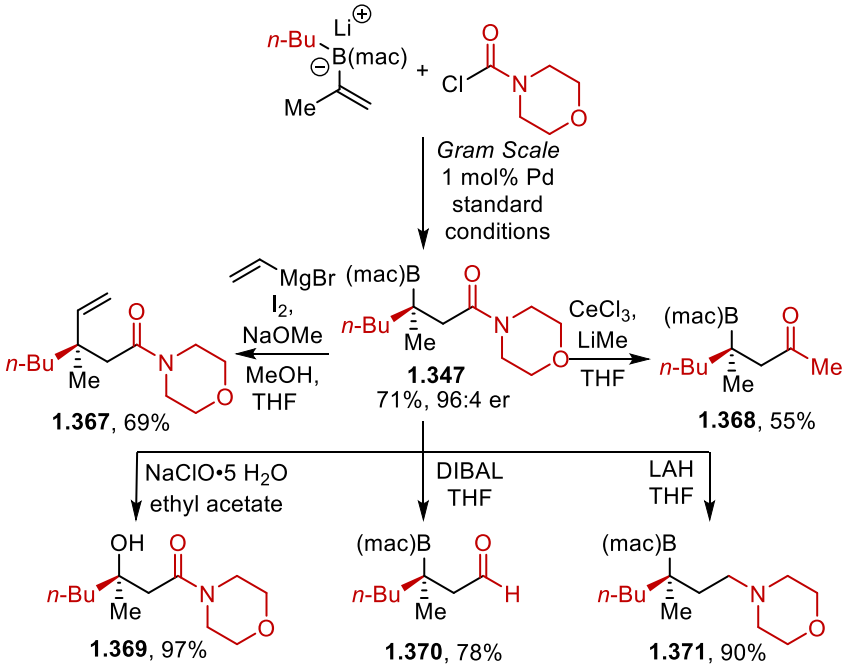


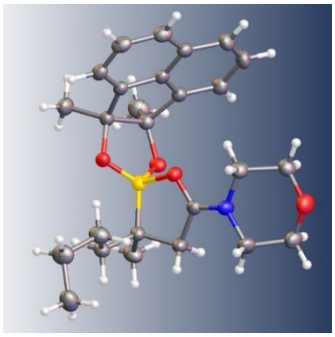

Yields are isolated yields of purified material and represent an average yield of two separate experiments. Enantiomeric ratios were determined by SFC analysis on a chiral stationary phased and are in comparison to authentic racemic materials. For commercial organolithiums, reaction was conducted with 3% Pd and 3.6% (*Sp*,*Sp*-MandyPhos) in THF (0.22 M) with 2 equiv. carbamoyl chloride, 2 equiv. CsF, 1 equiv. water at room temperature for 2 days. [a]Reaction conducted at 40 °C for 3 days. [b]Reaction conducted in .166 M THF at 60 °C for 12 hours. [c]Reaction conducted at rt for 3 days. For lithium halogen exchange, reaction was conducted with 3% Pd and 3.6% (*Sp*,*Sp*-MandyPhos) in THF (0.22 M) with 2 equiv. carbamoyl chloride, 3 equiv. CsF, 6 equiv. water at room temperature for 2 days. [d]Reaction conducted in .166 M THF at 60 °C for 12 hours. [e]Pentyllithium derived "ate" was made from pentylbromide and lithium metal (see section supporting information for details)

***Figure 1.39.*** Reaction Substrate Scope

### 1.3.3.5 Derivatization of β-boryl Amides

Substrate **1.347** was synthesized in gram scale with 71% yield and 96:4 er. This compound was purified into a crystalline material, from which a single crystal was acquired and the crystal structure was obtained through X-ray crystallography. From the crystal structure, an unambiguous carbonyl-boron chelation was identified. With the boron atom serving as an intramolecular Lewis acid activating the amide group, we proposed that transformation of the amide could be conducted orthogonal to the boronic ester. Indeed, methylation (**1.347** to **1.368**), reduction (**1.347** to **1.370**), or decarbonylation (**1.347** to **1.371**) can be performed on the amide moiety with good to excellent yield. Additionally, the B(mac) functional group can be derivatized orthogonally as well. Zweifel olefination (**1.347** to **1.367**), or oxidation (**1.347** to **1.369**) were conducted with high yields.



Crystal Stucture of **1.347**

***Figure 1.40.*** Boronic Ester Functionalization

### 1.3.3.6 Total Synthesis of Natural Product (+)-Adalinine

Lastly, to further demonstrate the utility of these newly synthesized enantiomerically enriched tertiary β-boryl amides, a total synthesis of (+)-adalinine **1.388** was conducted. (-)-Adalinine was

firstly isolated in 1996 from the European two-spotted ladybird beetle *Adalia bipunctata*.[97] It contains a challenging amide substituted quaternary carbon stereocenter. So far, there are three reported enantioselective total synthesis of (-)-adalinine, where the quaternary carbon stereocenter was constructed enantioselectively through three distinct approaches. In the total synthesis reported by Kibayashi in 1999, carboxylic acid **1.372** was treated with chiral auxiliary **1.373** to synthesize lactam **1.374**.[98] Then a Sakurai allylation was carried out on **1.374**. The allyl silane addition to iminium was found to be highly diastereoselective, giving the desired lactam **1.375** with 76% yield and 16:1 dr.

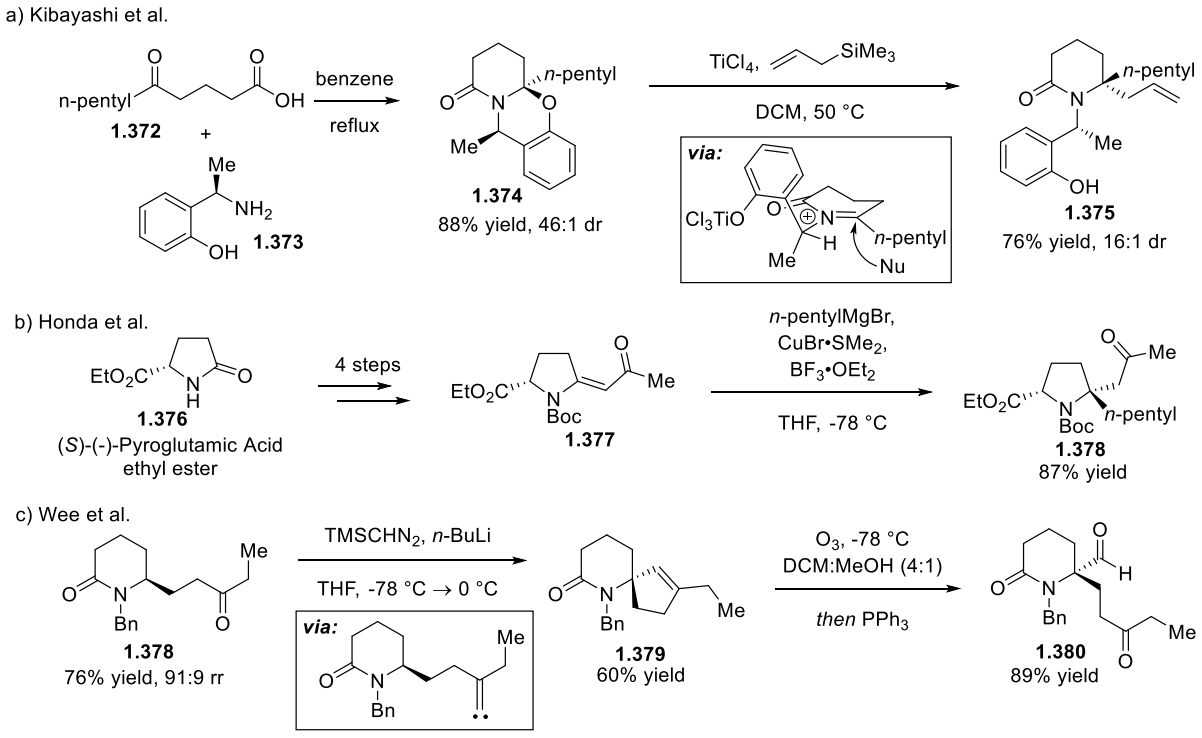
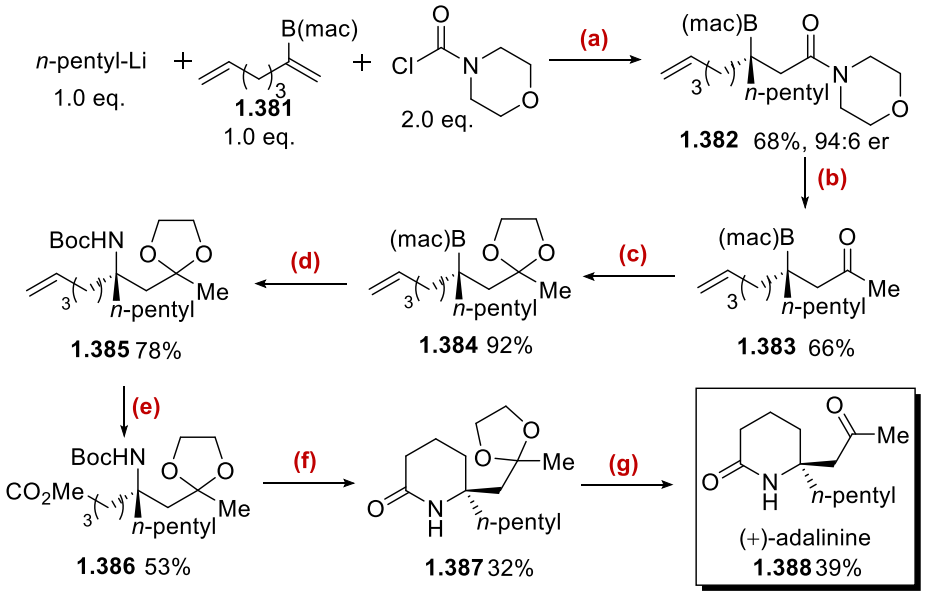



***Figure 1.41.*** Reported Synthesis of Natural Product (-)-Adalinine Key Intermediate

In Honda's synthesis, [99] enantiomerically pure cyclic amine **1.377** was synthesized from commercially available **1.376**. in four steps. Then, a diastereoselective conjugate addition was performed on the unsaturated ketone in **1.377**, from which the cyclic amine **1.378** was generated

[97] Lognay, G., Hemptinne, J. L., Chan, F. Y., Gaspar, C. H., Marlier, M., Braekman, J. C., Daloze, D., Pasteels, J. M. *J. Nat. Prod.* **1996**, *59*, 510–515.
[98] Yamazaki, N., Ito, T., Kibayashi, C. *Tetrahedron Letters* **1999**, *40*, 739–745.
[99] Honda, T., Kimura, M. *Org. Lett.* **2000**, *2*, 3925–3930.

in 87% yield as a single diastereomer. In Wee's synthesis, [100] an alkylidene carbene insertion of α-amino C–H was conducted to convert ketone **1.378** to spiro cyclic alkene **1.379** as a single diastereomer. Subsequent ozonolysis of **1.379** will cleave the alkene group to generate the desired tertiary carbon substituted amine **1.380** in 89% yield.




Conitions: **(a)**: 3 mol% $Pd(OAc)_2$, 3.6 mol% ($R_p$,$R_p$)-**L1**,2 equiv. CsF, 6.0 equiv. $H_2O$, THF, rt, 48 h. **(b)**: 3.0 equiv. "$MeCeCl_2$", 30 min at -78 °C, 30 min at 0 °C, THF. **(c)**:5 equiv. $(HOCH_2)_2$ 2.5 equiv. $HC(OMe)_3$, 0.1 equiv. *p*TSA, rt, PhMe, 12 h. **(d)**: 3 equiv. $MeONH_2$, 5 equiv. KO*t*-Bu, PhMe, 100 °C, 24 h, *then* $NaHCO_3$ (aq), 5 eq. $Boc_2O$, 80 °C, 5 h. **(e)**: $O_3$, 2.5 M NaOH in MeOH, DCM, -78 °C, 15 min. **(f)**: TFA, DCM, rt, 1 h *then* PhMe, 110 °C, 12 h. **(g)**: *p*TSA, acetone, rt, 12 h

***Figure 1.42.*** Total Synthesis of (+)-Adalinine

Utilizing the newly developed conjunctive cross-coupling, the tertiary amine on the β-position of the carbonyl can be installed enantioselectively. Indeed, from alkenyl B(mac) **1.381**, by adding *n*-pentyllithium to form the corresponding boronate complex, the conjunctive cross-coupling with chloroacyl morpholine under standard conditions can give amide **1.382** in 68% yield and 94:6 er. Then, the previously mentioned orthogonal methylation of the morpholine amide was carried out to prepare methyl ketone **1.383** in 66% yield. We attempted to aminate the boronate in the presence of an amide or ketone functional group. However, perhaps due to the carbonyl-boron

[100] Annadi, K., Wee, A. G. H. *J. Org. Chem.* **2016**, *81*, 1021–1027.

chelation found in the crystal structure of **1.347**, the amination occurred with low conversion of the starting material. Therefore, a ketal protection of the methyl ketone was protected as ketal to give **1.384**. Subsequently, the B(mac) was converted to the desired amine **1.385** in 78% yield. By oxidative ozonolysis of terminal alkene methyl ester **1.386** can be generated in 53% yield. By heating ester **1.386**, lactamization occurred to furnish cyclic amide **1.387** in 32% yield. Subsequent deprotection of the methyl ketone delivered the natural product (+)-Adalinine **1.388** in 39% yield.

## 1.4 Supporting Information

### 1.4.1 General Information

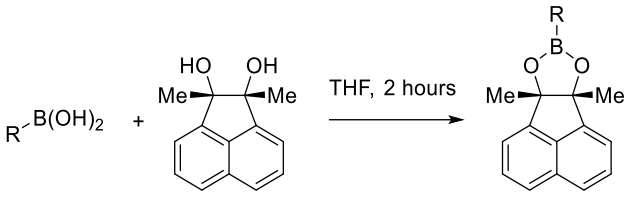
$^{1}$H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). $^{13}$C NMR spectra were recorded on either a Varian Gemini-500 (126 MHz), Varian Gemini-600 (151 MHz) or a Varian Inova-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). $^{11}$B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer. $^{19}$F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers ($cm^{-1}$) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), or potassium permanganate stain ($KMnO_4$, sodium carbonate, and water), or para-anisaldehyde stain (ethanol, sulfuric acid, and *p*-anisaldehyde).

Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

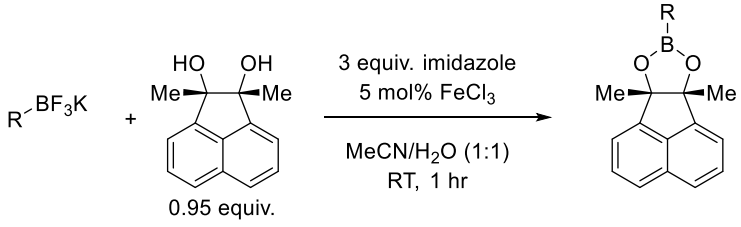
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. All carbamoyl chlorides were purchased from commercial sources and were distilled using a short path distillation apparatus. All other reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without further purification.

### 1.4.2 Experimental Details

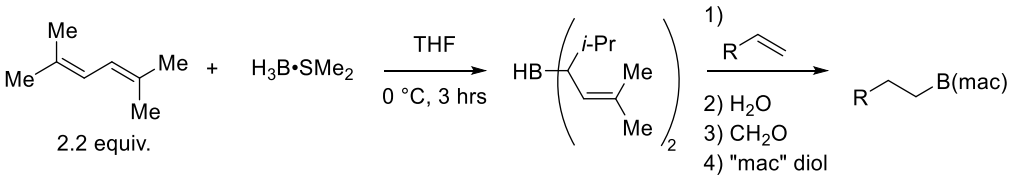
#### 1.4.2.1 Procedures for Preparation of Boronic Esters




*Method A:* To a 50 mL round bottom flask equipped with a magnetic stir bar was charged with boronic acid (2.0 mmol, 1.0 equiv.), "mac" diol (2.0 mmol, 1.0 equiv.), and THF (10 mL). Reaction was allowed to stir at room temperature and open to air. Reaction conversion was monitored by TLC (within 2 hours). Upon completion, reaction mixture was concentrated under vacuum. The crude product was purified by a silica gel plug using dichloromethane as an eluten. *This method can be used with conveniently available and easily handled boronic acids.*

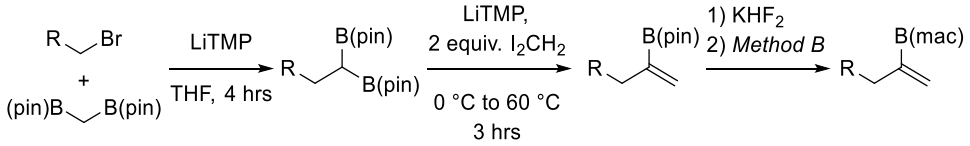


*Method B:* Organoboronates were prepared according to a modified literature procedure, as follows.[1] To a 250 mL round bottom flask equipped with a magnetic stir bar was charged open to air and at room temperature with potassium trifluroborate (8.0 mmol, 1.0 equiv.) and 1:1 acetonitrile:water (60 mL). Iron trichloride (0.4 mmol, 0.05 equiv.), imidazole (24.0 mmol, 3 equiv.), and "mac" diol (7.6 mmol, 0.95 equiv.) were added sequentially. Reaction mixture was allowed to stir vigorously for 1 hour. Reaction was diluted with water and ethyl acetate. Reaction mixture was transferred to a separatory funnel and collected the organic layer. The aqueous layer was washed three times with ethyl acetate. The collected organic layers were washed with brine, dried with sodium sulfate, filtered into a round bottom flask, and concentrated under vacuum. A silica plug eluted with DCM was used to purify the resulting crude. The crude can be further purified by recrystallization using hot ethyl acetate. *This method can be used when the corresponding boronic acid is unavailable or difficult to handle.*

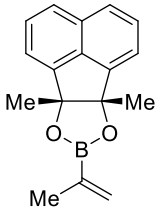



*Method C:* Organoboronates were prepared according to a modified literature procedure, as follows.[2] To a flame-dried 100 mL round bottom flask equipped with a magnetic stir bar was charged with 2mL THF and 2,5-dimethylhexa-2,4-diene (4.4 mmol, 2.2 equiv.). The resulting solution was chilled in an ice bath and borane dimethylsulfide (2 mmol, 1 equiv.) was added dropwise. Upon the completion of the dropwise addition, the reaction was allowed to stir at that temperature for 3 hours. After, alkene (2 mmol, 1 equiv.) was added dropwise and, upon completion, allowed to stir at room temperature for 2 hours. Then, the reaction was cooled by an ice bath and water (14 mmol, 7 equiv.) was added dropwise to the reaction. Paraformaldehyde (2 mmol, 1 equiv.) was added directly at room temperature and was allowed to stir for 2 hours. After, "mac" diol (2 mmol, 1 equiv.) was added directly. The diol slowly disappears over the course of an hour and then resulting mixture was subject an aqueous work up. Reaction was washed with water. The aqueous layer was washed with ethyl acetate times. The organic layers were collected and washed with brine, dried with sodium sulfate, filtered and concentrated under vacuum. Crude

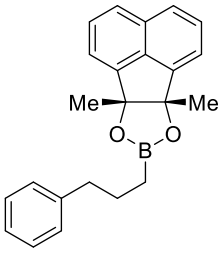
is purified using silica gel chromatography. *This method can be used to gain access to alkyl boronic esters from available terminal alkene.*



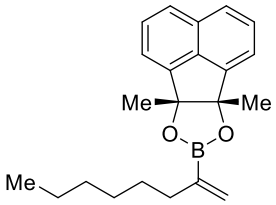

*Method D*: 1,1 bisboronates are prepared using the following methodology precedent.[3] The following boron-wittig reaction was performed using the following methodology precedent.[4] The same alpha substituted alkenyl B(pin) used in this publication were prepared as the previously mentioned literature precedent and obtained intermediate NMR spectra are in good agreement with reported spectra. Transformation from the B(pin) to the corresponding B(mac) was performed from a literature precedent[5] and *Method B*.




**(6bR,9aS)-6b,9a-dimethyl-8-(prop-1-en-2-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-1).** The title compound was prepared according to *Method B* with potassium isopropenyltrifluoroborate (4.83 g, 32.67 mmol, 1 equiv.), 1,2-dimethylacenaphthylene-1,2-diol, "mac", (7.00 g, 32.67 mmol, 1 equiv.), iron (III) chloride (265 mg, 1.63 mmol, 0.05 equiv.), and imidazole (6.67 g, 98.01 mmol, 3 equiv.) in 250 mL water: acetonitrile mixture in 1:1 ratio. The resulting crude was purified by recrystallization using hot ethyl acetate to yield the title compound (6.42 g, 24.6 mmol, 74% yield) as a white crystalline solid. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, $J$ = 7.9, 1.1 Hz, 2H), 7.63 – 7.54 (m, 4H), 5.72 (dq, $J$ = 3.9, 1.3 Hz, 1H), 5.57 (dq, $J$ = 3.6, 1.7 Hz, 1H), 1.80 (s, 6H), 1.75 (t, $J$ = 1.5 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.0, 134.9, 131.5, 130.6, 128.6, 125.3, 119.7, 92.2, 22.3, 21.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.91.; IR (neat): $\nu_{max}$ 2991.17 (w), 2974.88 (w), 1620.42 (m), 1301.58 (s), 1175.17 (m), 1115.72 (m), 1076.48 (m) cm$^{-1}$. HRMS (DART) for $C_{17}H_{18}BO_2$ $[M+H]^+$: Calc'd: 265.13944, found: 265.14002.

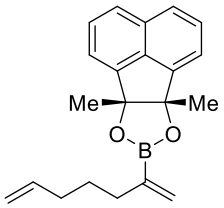


**(6bR,9aS)-6b,9a-dimethyl-8-(3-phenylpropyl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-2).** The title compound was prepared according to *Method C* with 2,5-dimethylhexa-2,4-diene (1.57 mL, 11.00 mmol, 2.2 equiv.), 1,2-dimethylacenaphthylene-1,2-diol (1.07 g, 2.00 mmol, 1 equiv.), allylbenzene (0.662 mL, 5.00 mmol, 1 equiv.), borane dimethylsulfide (0.474 mL, 5.00 mmol, 1.00 equiv.), paraformaldehyde (150.2 mg, 5.00 mmol, 1.00 equiv.), and water (0.625 mL, ~35.0 mmol, ~7 equiv.) in 5 mL THF. The resulting crude was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (1.30 g, 3.78 mmol, 76% yield) as a white solid. Product Rf = 0.6 in 10% ethylacetate:hexanes (UV active and stains green with *para*-anisaldehyde stain).; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.64 – 7.51 (m, 4H), 7.24 – 7.17 (m, 2H), 7.15 – 7.03 (m, 3H), 2.50 (t, *J* = 7.7 Hz, 2H), 1.76 (s, 6H), 1.67 (p, *J* = 7.9 Hz, 2H), 0.78 (t, *J* = 7.9 Hz, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.0, 142.7, 134.8, 131.5, 128.6, 128.6, 128.2, 125.6, 125.4, 119.5, 91.8, 38.5, 26.1, 22.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.13.; IR (neat): $\nu_{max}$ 3022.89 (w), 2969.40 (w), 2928.92 (w), 1369.86 (m), 1114.50 (m), 1075.89 (m), 824.16 (m), 776.59 (m) $cm^{-1}$. HRMS (DART) for $C_{23}H_{24}BO_2$ $[M+H]^+$: Calc'd: 343.18639, found: 343.18711.

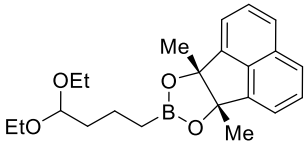


**(6bR,9aS)-6b,9a-dimethyl-8-(oct-1-en-2-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-3).** The title compound was prepared according to *Method D* with trifluoro-(1-methyleneheptyl)-potassio-boron (2.49 g, 11.42 mmol, 1 equiv.), iron (III) trichloride (92.6 mg, 0.57 mmol, 0.05 equiv.), imidazole (2.33 g, 34.3 mmol, 3 equiv.), and 1,2-dimethylacenaphthylene-1,2-diol (2.45 g, 11.42 mmol, 1 equiv.) in a 85 mL 1:1 water: acetonitrile mixture. The resulting crude was purified by silica gel column chromatography using 25% DCM:hexanes (unoptimized column conditions) to isolate the title compound (484 mg, 1.45 mmol, 13% yield) as a white solid. Product Rf = 0.8 in 50% DCM:hexanes (UV active and stains with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.9, 1.1 Hz, 2H), 7.70 – 7.48 (m, 4H), 5.82 – 5.70 (m, 1H), 5.56 (dt, *J* = 3.5, 1.6 Hz, 1H), 2.10 (tt, *J* = 7.4, 1.3 Hz, 2H), 1.81 (s, 6H), 1.35 (dt, *J* = 12.4, 4.5 Hz, 2H), 1.27 – 1.18 (m, 6H), 0.90 – 0.81 (m, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.1, 134.9, 131.5, 129.1, 128.6, 125.3, 119.6, 92.1, 35.2, 31.9, 29.1, 24.9, 22.7, 22.3, 14.23, 14.22.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.26.; IR (neat): $\nu_{max}$ 2922.51 (w),

1362.82 (m), 1114.30 (m), 1075.82 (m), 823.21 (m), 775.26 (m) $cm^{-1}$. HRMS (DART) for $C_{22}H_{28}BO_2$ $[M+H]^+$: Calc'd: 335.21769, found: 335.21699.




**(6bR,9aS)-8-(hepta-1,6-dien-2-yl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-4).** The title compound was prepared according to *Method D* with trifluoro-(1-methylenehex-5-enyl)-potassio-boron (1.68 g, 8.33 mmol, 1 equiv.), iron (III) trichloride (67.6 mg, 0.42 mmol, 0.05 equiv.), imidazole (1.7 g, 25 mmol, 3 equiv.), and 1,2-dimethylacenaphthylene-1,2-diol (1.78 g, 8.33 mmol, 1 equiv.) in 62 mL 1:1 water: acetonitrile mixture. The resulting crude was purified by silica gel column chromatography using 25% DCM:hexanes (unoptimized column conditions) to isolate the title compound (824 mg, 2.59 mmol, 31% yield) as a white solid. Product Rf = 0.7 in 50% DCM:hexanes (UV active and stains with potassium permanganate stain).; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.62 – 7.54 (m, 4H), 5.82 – 5.72 (m, 2H), 5.57 – 5.53 (m, 1H), 4.99 – 4.92 (m, 1H), 4.90 (ddd, *J* = 10.0, 2.1, 1.1 Hz, 1H), 2.10 (t, *J* = 7.7 Hz, 2H), 1.99 (q, *J* = 7.2 Hz, 2H), 1.80 (s, 6H), 1.49 – 1.41 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.0, 139.1, 134.8, 131.4, 129.6, 128.5, 125.3, 119.6, 114.3, 92.1, 34.7, 33.5, 28.4, 24.9, 22.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.33.; IR (neat): $\nu_{max}$ 3059.03 (w), 2972.49 (w), 2925.66 (w), 1297.80 (m), 1114.14 (m), 1075.33 (m), 775.76 (m) $cm^{-1}$. HRMS (DART) for $C_{21}H_{24}BO_2$ $[M+H]^+$: Calc'd: 319.18639, found: 319.18765.

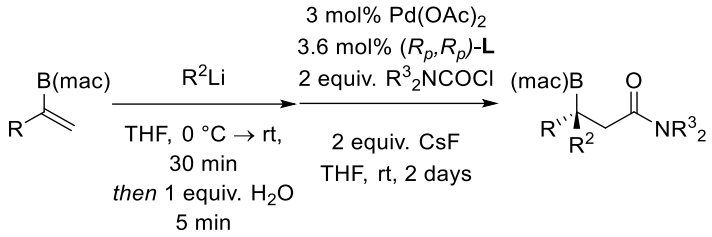



**Compound (6bR,9aS)-8-(4,4-diethoxybutyl)-6b,9a-dimethyl-6b, 9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-5).** The title com pound was prepared according to *Method C* with 2,5-dimethylhexa-2,4-diene (0.63 mL, 4.4 mmol, 2.2 equiv.), 1,2-dimethylacenaphthylene-1,2-diol (428.5 mg, 2 mmol, 1 equiv.), 4,4-diethoxybut-1-ene (0.339 mL, 2 mmol, 1 equiv.), borane dimethylsulfide (0.19 mL, 2 mmol, 1 equiv.), paraformaldehyde (60 mg, 2 mmol, 1 equiv.), and water (0.625 mL, ~35 mmo l, ~7 equiv.) in 2 mL THF. The resulting crude was purified by silica gel column chromatography using 10% ethyl acetate:hexanes to isolate the title compound (420 mg, 1.14 mmol, 57% yield) a s a white solid. Product Rf = 0.2 in 10% ethylacetate:hexanes (UV active and stains green with *p ara*-anisaldehyde stain).; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.87 – 7.70 (m, 2H), 7.63 – 7.50 (m, 4H) , 4.41 (t, J = 5.7 Hz, 1H), 3.55 (dq, J = 9.5, 7.1 Hz, 2H), 3.40 (dq, J = 9.5, 7.1 Hz, 2H), 1.77 (s, 6 H), 1.55 – 1.50 (m, 2H), 1.41 (dt, J = 15.5, 7.6 Hz, 2H), 1.15 (t, J = 7.1 Hz, 6H), 0.75 (t, J = 7.8 H

z, 2H).; $^{13}$C NMR (600 MHz, $CDCl_3$) δ 145.0, 134.7, 131.5, 128.7, 128.42, 125.44, 125.2, 119.7, 119.4, 102.9, 102.7, 91.8, 77.4, 77.2, 76.9, 60.9, 60.72, 60.68, 60.51, 36.0, 22.28, 22.20, 19.3, 15. 7, 15.5, 15.3, 15.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 36.3.; IR (neat): $\nu_{max}$, 2974.12 (m), 2934.96 ( m), 2876.52 (m), 1724.83 (s), 1374.35(m), 1117.10 (s), 1078.41 (s). HRMS (DART) for $C_{20}H_{24}B O_3$ $[M\text{-}C_2H_5O^-]^+$: Calc'd 323.18130, found: 323.18212.

### 1.4.2.2 General Procedures for Conjunctive Cross Coupling

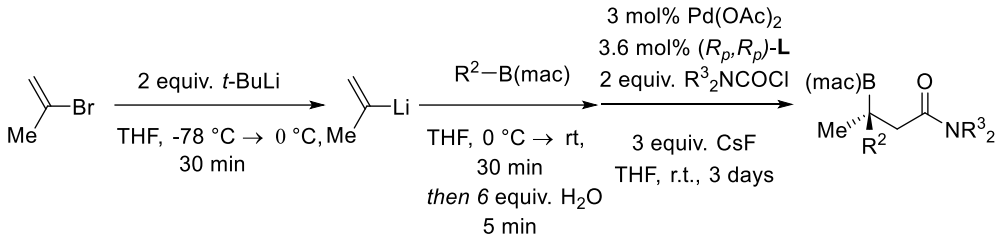
*Method A*:




To an oven-dried 2-dram vial equipped with a magnetic stir bar in an argon-filled glovebox was added alkenyl boronic acid "mac" ester (0.2 mmol, 1.0 equiv.) and THF (0.4 mL). This vial was sealed with a septum cap, and then removed from the glovebox. The vial was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. Commercial alkyllithium solution (0.2 mmol, 1.0 equiv.) was added dropwise to the stirring solution often resulting in a color change. Upon completion of addition, reaction was allowed to warm to room temperature and stirred for 30 minutes at that temperature. Then, deionized water (0.2 mmol, 1 equiv.) was added via syringe and allowed to stir for an additional 5 minutes usually resulting a colorless solution. The solvent was carefully removed under reduced pressure to yield a white solid and was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (0.0072 mmol, 0.036 equiv.), and 0.2 mL THF. This palladium solution was allowed to stir for 15 minutes at room temperature. Cesium fluoride (0.4 mmol, 2 equiv.) was added to the white solid "ate" vial, followed by palladium solution, then 0.4 mL THF, and finally carbamoyl chloride (0.4 mmol, 2 equiv.) by mass. The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox. The reaction was stirred at room temperature for 2 days. The resulting mixture was filtered through

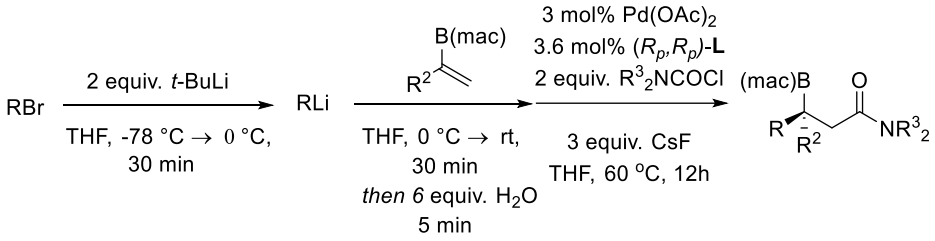
a silica plug eluted with diethyl ether and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography to afford the desired product.

*Method B*:




To an oven-dried 2-dram vial equipped with a magnetic stir bar in an argon-filled glovebox was added alkyl boronic acid "mac" ester (0.2 mmol, 1.0 equiv.) and THF (0.4 mL). This vial was sealed with a septum cap, and then removed from the glovebox. The vial was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. To a separate oven-dried 10 ml round bottom flask equipped with a magnetic stir bar was added isopropenyl bromide (1.0 mmol, 5.0 equiv.) and THF (2.5 ml) under argon. Commercial *tert*-butyllithium solution (2.0 mmol, 2 equiv. to isopropenyl bromide) was added dropwise to the stirring solution under nitrogen at -78 ˚C. Reaction was stirred at this temperature for 30 min then slowly warmed to and kept at 0 ˚C. Concentration of this alkenyllithium solution was titrated by BHT using 1,10-phenathroline as indicator. Suitable amount of this aryllithium solution (0.2 mmol, 1 equiv.) was added into boronic ester solution via syringe at 0 ˚C. The rest of procedure is identical to *Method A*, except for stirring the reaction at room temperature for 3 days.

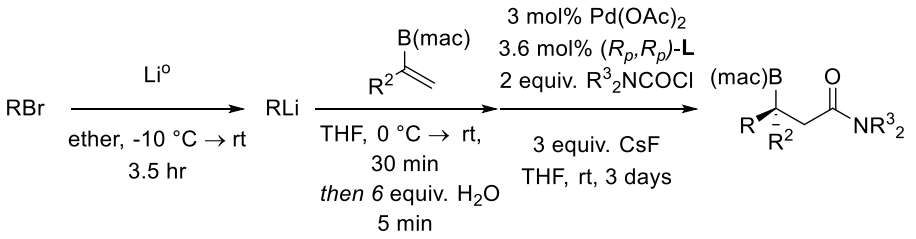
*Method C*:




To an oven-dried 2-dram vial equipped with a magnetic stir bar in an argon-filled glovebox was added alkenyl boronic acid "mac" ester (0.2 mmol, 1.0 equiv.) and THF (0.4 mL). This vial was sealed with a septum cap, and then removed from the glovebox. The vial was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. To a separate oven-dried 10 ml round bottom flask equipped with a magnetic stir bar was added aryl bromide (1.0 mmol, 5.0 equiv.) and

THF (2.5 ml) under argon. Commercial tert-butyllithium solution (2.0 mmol, 2 equiv. to RBr) was added dropwise to the stirring solution under nitrogen at -78 ˚C. Reaction was stirred at this temperature for 30 min then slowly warmed to and kept at 0 ˚C. Concentration of this aryllithium solution was titrated by BHT using 1,10-phenathroline as indicator. Suitable amount of this aryllithium solution (0.2 mmol, 1 equiv.) was added into boronic ester solution via syringe at 0 ˚C. Reaction was allowed to warm up to room temperature and stirred for 30 min. Then, deionized water (1.2 mmol, 6 equiv.) was added via syringe and allowed to stir for an additional 5 minutes. The solvent was carefully removed under reduced pressure and was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (0.0072 mmol, 0.036 equiv.), and 0.2 mL THF. This palladium solution was allowed to stir for 15 minutes at room temperature. Cesium fluoride (0.6 mmol, 3 equiv.) was added to the "ate" vial, followed by palladium solution, 0.4 mL THF, and finally carbamoyl chloride (0.4 mmol, 2 equiv.). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox. The reaction was stirred at 60 ˚C for 12h. The resulting mixture was filtered through a silica plug eluted with diethyl ether and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography to afford the desired product.

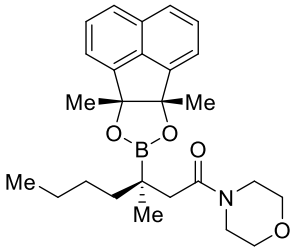
*Method D:*




To an oven-dry, round bottom flask equipped with a magnetic stirring bar was added freshly prepared lithium slots (277.6 mg, 40 mmol) and diethyl ether (5 mL) in the glovebox. The mixture was cooled in a brine /ice bath and stirred vigorously as solution of pentyl bromide (1.24 mL, 10 mmol) in diethyl ether (5 mL) was added slowly over 120 min using a syringe pump. After the addition, the mixture was allowed to warm to room temperature and stirred for an additional 90 min. Mixture was titrated using L-menthol and using 1,10-phenathroline as indicator. To an oven-dried vial and magnetic stir bar, was added alkenyl boronic acid "mac" ester (0.2 mmol, 1 equiv.)

and THF in the glovebox. This vial was sealed with a septum cap, and then removed from the glovebox. The vial was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. Alkyllithium solution (0.2 mmol, 1.0 equiv.) was added dropwise to the stirring solution often resulting in a color change. Upon completion of addition, reaction was allowed to warm to room temperature and stirred for 30 minutes at that temperature. Then, deionized water (1.2 mmol, 6 equiv.) was added via syringe and allowed to stir for an additional 5 minutes usually resulting a colorless solution. The solvent was carefully removed under reduced pressure to yield a white solid and was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (0.0072 mmol, 0.036 equiv.), and 0.2 mL THF. This palladium solution was allowed to stir for 15 minutes at room temperature. Cesium fluoride (0.6 mmol, 3 equiv.) was added to the white solid "ate" vial, followed by palladium solution, then 1.0 mL THF, and finally carbamoyl chloride (0.4 mmol, 2 equiv.) by mass. The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox. The reaction was stirred at room temperature for 3 days. The resulting mixture was filtered through a silica plug eluted with diethyl ether and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography to afford the desired product.

### 1.4.2.3 Characterization of Conjunctive Cross Coupling Products



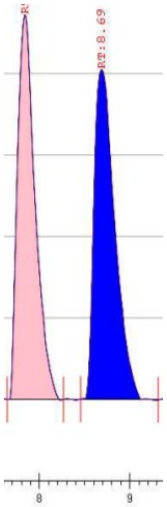
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (3).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in hexanes, 0.08 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to afford a white solid (75.5 mg, 86.7% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.68 (m, 2H), 7.59 – 7.46 (m, 4H), 3.68 – 3.52 (m, 4H), 3.45 – 3.34 (m, 4H), 2.41 (d, $J$ = 16.5 Hz, 2H), 2.11 (d, $J$ = 16.6 Hz, 2H), 1.76 (d, $J$ = 20.4 Hz, 6zH), 1.29 – 1.18 (m, 1H), 1.03 (td, $J$ = 12.4, 4.3 Hz, 1H), 0.96 – 0.80 (m, 6H), 0.68 – 0.54 (m, 1H), 0.46 (t, $J$ = 7.1 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.4, 146.8, 146.6, 135.2, 131.3, 128.4, 128.3, 124.6, 124.5, 119.03, 118.99, 90.9, 90.8, 66.9, 66.6, 45.9, 44.9, 42.7, 38.9, 27.5, 23.4, 22.4, 22.2, 22.1, 13.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.50.; IR (neat): $\nu_{max}$ 2958.36 (m), 2924.25 (m), 2854.17 (m), 1631.30 (s), 1115.11 (s), 781.52 (s) cm$^{-1}$. HRMS (DART) for $C_{26}H_{35}BNO_4$ $[M+H]^+$: Calc'd: 436.26537, found: 436.26719. $[\alpha]^{20}_D$: 0.764 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

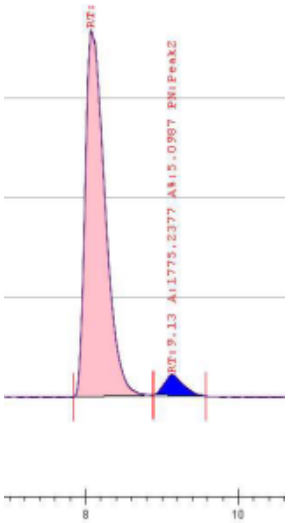
*Chiral SFC (AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one*

Racemic

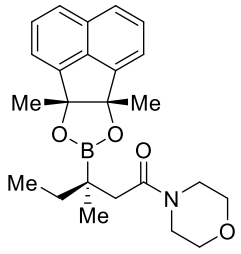


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.8614 | 12781.9478 | 7.84 |
| 2 | 50.1386 | 12853.0154 | 8.69 |
| Total: | 100 | 25634.9632 | |

Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 94.9013 | 33042.3678 | 8.07 |
| 2 | 5.0987 | 1775.2377 | 9.13 |
| Total: | 100 | 34817.6055 | |



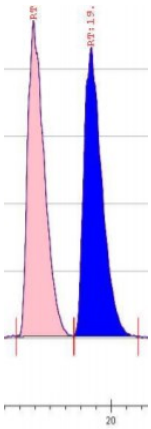
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinopentan-1-one (4).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), ethyllithium (0.5 M in benzene, 0.40 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography eluted with 20% ethyl acetate:hexanes to isolate the title compound (51.1 mg, 0.125 mmol, 63% yield) as a white solid. Product Rf = 0.4 in 40% ethyl acetate: hexanes (UV active and stains blue with *para*-anisaldehyde stain). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.68 (m, 2H), 7.59 – 7.48 (m, 4H), 3.67 – 3.50 (m, 4H), 3.43 – 3.32 (m, 4H), 2.40 (d, $J$ = 16.5 Hz, 1H), 2.12 (d, $J$ = 16.5 Hz, 1H), 1.77 (s, 3H), 1.74 (s, 3H), 1.35 – 1.25 (m, 1H), 1.17 – 1.06 (m, 1H), 0.84 (s, 3H), 0.50 (t, $J$ = 7.5 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.3, 146.8, 146.6, 135.2, 131.3, 128.4, 128.3, 124.6, 124.5, 119.0, 90.9, 90.8, 66.9, 66.6, 45.9, 44.4, 42.6, 31.4, 22.4, 22.1, 21.6, 9.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.57.; IR (neat): $\nu_{max}$ 3038.45 (w), 2963.49 (m), 2920.65 (m), 2855.46 (m), 1630.97 (s), 1458.89 (m), 1115.31 (s), 781.21 (m) cm$^{-1}$. HRMS (DART) for $C_{24}H_{31}BNO_4$ $[M+H]^+$: Calc'd: 408.23407, found: 408.23393. $[\alpha]^{20}_D$: -1.158 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

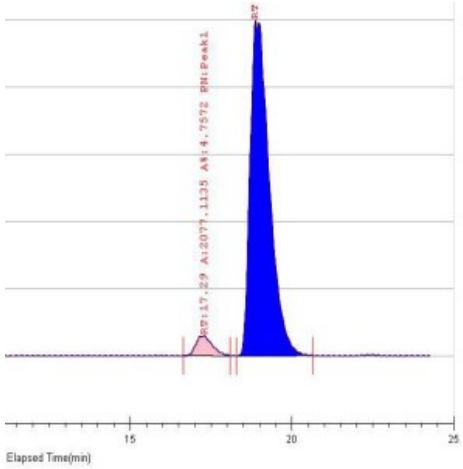
*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinopentan-1-one*

Racemic

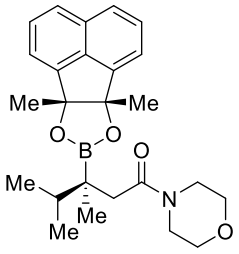


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.2044 | 35423.6397 | 17.45 |
| 2 | 49.7956 | 35135.2579 | 19.35 |
| Total: | 100 | 70558.8976 | |

Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 4.7572 | 2077.1135 | 17.29 |
| 2 | 95.2428 | 41585.0067 | 18.86 |
| Total: | 100 | 43662.1202 | |

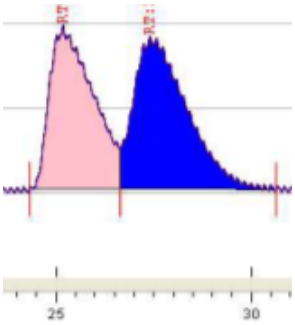


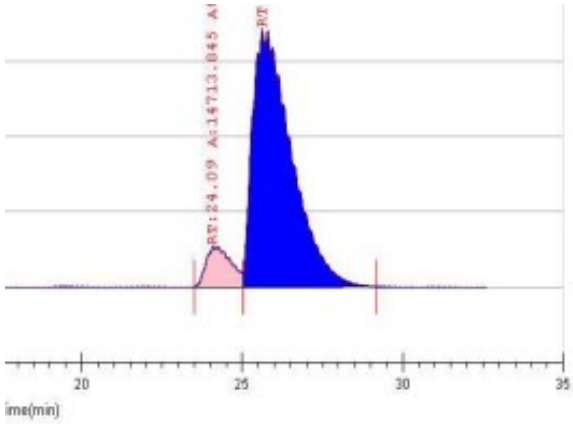
**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3,4-dimethyl-1-morpholinopentan-1-one (5).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), isopropyllithium (0.7 M in pentane, 0.285 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (44.9 mg, 0.106 mmol, 53% yield) as a white solid. Product Rf = 0.5 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.70 (t, *J* = 8.5 Hz, 2H), 7.58 – 7.47 (m, 4H), 3.74 – 3.52 (m, 3H), 3.51 – 3.45 (m, 1H), 3.40 – 3.34 (m, 2H), 3.33 – 3.22 (m, 2H), 2.41 (d, *J* = 16.5 Hz, 1H), 2.14 (d, *J* = 16.5 Hz, 1H), 1.77 (s, 3H), 1.73 (s, 3H), 1.61 (hept, *J* = 7.0 Hz, 1H), 0.77 (s, 3H), 0.63 (d, *J* = 6.9 Hz, 3H), 0.44 (d, *J* = 6.7 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.9, 147.3, 146.8, 135.3, 131.2, 128.4, 128.2, 124.5, 124.3, 118.93, 118.88, 90.6, 90.5, 66.8, 66.5, 45.9, 44.0, 42.7, 33.8, 22.6, 22.2, 19.1, 17.3, 16.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.16. IR (neat): $\nu_{max}$ 3041.66 (w), 2957.17 (m), 2924.93 (m), 1610.73 (s), 1114.45 (s), 751.42 (m) cm$^{-1}$. HRMS (DART) for $C_{25}H_{33}BNO_4$ $[M+H]^+$: Calc'd: 422.24972, found: 422.24937. $[\alpha]^{20}_D$: -1.109 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

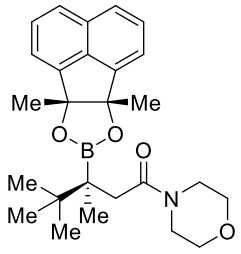
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3,4-dimethyl-1-morpholinopentan-1-one*




| Peak No | % Area | Area | RT (min) | Peak No | % Area | Area | RT (min) |
|---|---|---|---|---|---|---|---|
| 1 | 46.7015 | 7435.5062 | 25.18 | 1 | 9.2566 | 14713.845 | 24.09 |
| 2 | 53.2985 | 8485.8432 | 27.4 | 2 | 90.7434 | 144242.1529 | 25.62 |
| Total: | 100 | 15921.3494 | | Total: | 100 | 158955.9979 | |



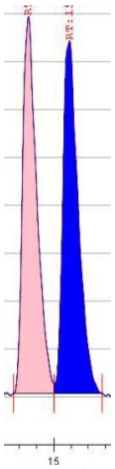
**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3,4,4-trimethyl-1-morpholinopentan-1-one (6).** The reaction was performed according to the general procedure *Method A* at 40 °C using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium (1.7 M in pentane, 0.117 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (51.2 mg, 0.118 mmol, 59% yield) as a white solid. Product Rf = 0.5 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.72 (t, *J* = 7.2 Hz, 2H), 7.61 – 7.46 (m, 4H), 3.72 – 3.54 (m, 4H), 3.51 – 3.32 (m, 4H), 2.64 (d, *J* = 16.2 Hz, 1H), 2.03 (d, *J* = 16.2 Hz, 1H), 1.80 (s, 3H), 1.73 (s, 3H), 0.91 (3, 2H), 0.61 (s, 9H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.3, 146.7, 146.4, 135.1, 131.2, 128.3, 128.3, 124.6, 124.5, 119.1, 119.0, 91.1, 90.8, 67.0, 66.6, 45.8, 42.4, 39.4, 33.9, 26.9, 22.3, 22.0, 19.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.87.; IR (neat): $\nu_{max}$ 3039.63 (w), 2964.30 (m), 2856.85 (m), 1632.87 (s), 1433.38 (m), 1214.53 (m), 1115.72 (s), 782.20 (m) cm$^{-1}$. HRMS (DART) for $C_{26}H_{35}BNO_4$ $[M+H]^+$: Calc'd: 436.26537, found: 436.26514. $[\alpha]^{20}_D$: -14.961 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

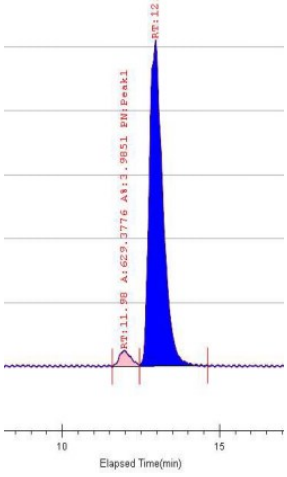
*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3,4,4-trimethyl-1-morpholinopentan-1-one*

Racemic

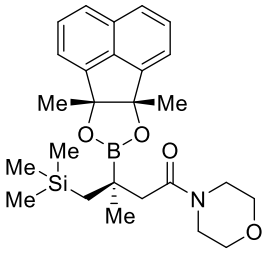


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.6785 | 22549.8309 | 14.26 |
| 2 | 50.3215 | 22841.6879 | 15.46 |
| Total: | 100 | 45391.5188 | |

Enriched




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 3.9851 | 629.3776 | 11.98 |
| 2 | 96.0149 | 15163.6949 | 12.96 |
| Total: | 100 | 15793.0725 | |



**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholino-4-(trimethylsilyl)butan-1-one (7)**. The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), $TMSCH_2Li$ (1.0 M in pentane, 0.2 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to afford a white solid (45.4 mg, 48.8% yield). Product Rf = 0.7 in 2% triethylamine:38% acetone:60% hexanes (stains blue with *para*-anisaldehyde stain and UV active).; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.72 (dd, $J$ = 8.0, 4.5 Hz, 2H), 7.58 – 7.49 (m, 4H), 3.67 – 3.51 (m, 4H), 3.43 – 3.34 (m, 4H), 2.46 (d, $J$ = 16.3 Hz, 1H), 2.21 (d, $J$ = 16.3 Hz, 1H), 1.80 (s, 3H), 1.74 (s, 3H), 0.93 (s, 3H), 0.67 (d, $J$ = 14.5 Hz, 1H), 0.49 (d, $J$ = 14.5 Hz, 1H), -0.35 (s, 9H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 172.5, 146.32, 146.29, 135.5, 131.3, 128.34, 128.28, 124.7, 124.6, 119.2, 119.1, 91.30, 91.25, 67.0, 66.7, 48.2, 45.9, 42.3, 27.8, 24.9, 22.3, 22.2, 0.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.11. IR (neat): $\nu_{max}$ 3043.43 (w), 2965.72 (m), 2913.22 (m), 2852.48 (m), 1624.02 (s), 1115.38 (s), 834.20 (s) cm$^{-1}$. HRMS (DART) for $C_{26}H_{36}BNO_4Si$ $[M+H]^+$: Calc'd: 466.25794 , found: 466.25735. $[\alpha]^{20}_D$: -0.350 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

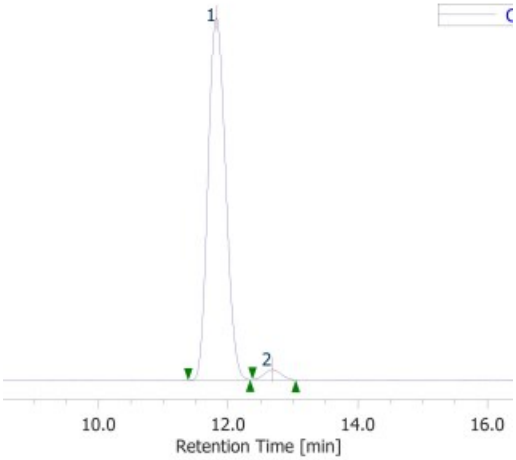
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (AD-H, 10% IPA, 1 mL/min, 100 bar, 35 °C, 210-270 nm) - 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholino-4-(trimethylsilyl)butan-1-one*

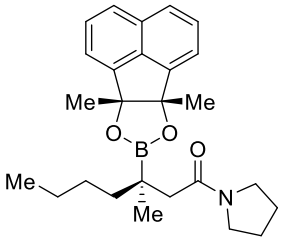
Racemic


| tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|
| 12.053 | 925972 | 52546 | 51.837 |
| 12.910 | 860338 | 47421 | 48.163 |

Enriched




| tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|
| 11.817 | 20166942 | 1072189 | 97.361 |
| 12.677 | 546667 | 29978 | 2.639 |



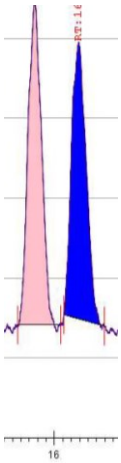
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-(pyrrolidin-1-yl)heptan-1-one (8).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in hexanes, 0.08 mL, 0.2 mmol, 1.0 equiv.), 1-pyrrolidinecarbonyl chloride (53.4 mg, 0.4 mmol, 2 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound ( 70.3 mg, 0.167 mmol, 83.8% yield) as a white solid. Product Rf = 0.45 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.5, 1.3 Hz, 2H), 7.58 – 7.47 (m, 4H), 3.45 – 3.21 (m, 4H), 2.41 (d, *J* = 16.8 Hz, 1H), 2.05 (d, *J* = 16.8 Hz, 1H), 1.89 (pd, *J* = 7.0, 6.6, 5.1 Hz, 2H), 1.85 – 1.71 (m, 8H), 1.16 (ddd, *J* = 12.9, 11.3, 4.3 Hz, 1H), 1.00 (td, *J* = 12.5, 4.1 Hz, 1H), 0.93 – 0.73 (m, 6H), 0.63 – 0.52 (m, 1H), 0.44 (t, *J* = 7.0 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.3, 147.5, 147.27, 147.26, 135.2, 131.3, 128.23, 128.22, 124.3, 124.2, 118.9, 118.8, 90.4, 90.3, 46.9, 46.6, 46.2, 38.7, 27.5, 25.8, 24.5, 23.4, 22.7, 22.4, 22.3, 13.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 26.41.; IR (neat): $\nu_{max}$ 3037.54 (w), 2951.87 (m), 2924.79 (m), 2868.52 (m), 1619.44 (s), 1447.82 (m), 1115.92 (s), 1080.74 (m), 780.53 (m) $cm^{-1}$. HRMS (DART) for $C_{26}H_{35}BNO_3$ $[M+H]^+$: Calc'd: 420.27045, found: 420.27052. $[\alpha]^{20}_D$: 1.750 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

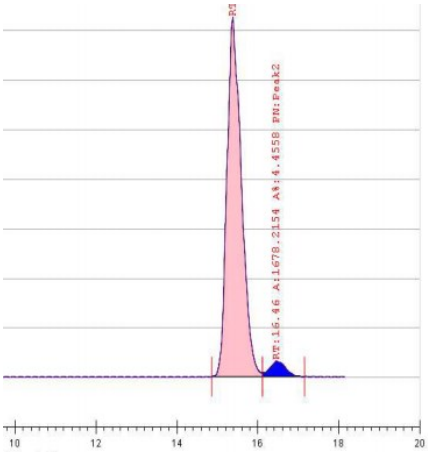
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (ODR-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-(pyrrolidin-1-yl)heptan-1-one*

Racemic

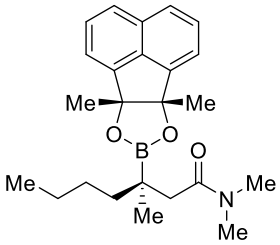


Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 51.751 | 4461.181 | 15.54 |
| 2 | 48.249 | 4159.2896 | 16.57 |
| Total: | 100 | 8620.4706 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 95.5442 | 35985.6187 | 15.38 |
| 2 | 4.4558 | 1678.2154 | 16.46 |
| Total: | 100 | 37663.8341 | |



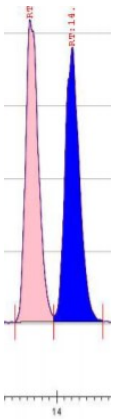
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N,N,3-trimethylheptanamide (9).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in hexanes, 0.08 mL, 0.2 mmol, 1.0 equiv.), dimethylcarbamyl chloride (43.0 mg, 0.4 mmol, 2 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (66.4 mg, 0.168 mmol, 84% yield) as a white solid. Product Rf = 0.5 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.62 (m, 2H), 7.57 – 7.46 (m, 4H), 2.91 (s, 3H), 2.79 (s, 3H), 2.41 (d, *J* = 16.8 Hz, 1H), 2.13 (d, *J* = 16.9 Hz, 1H), 1.77 (s, 3H), 1.73 (s, 3H), 1.19 (td, *J* = 12.1, 4.4 Hz, 1H), 1.02 (td, *J* = 12.5, 4.0 Hz, 1H), 0.96 – 0.75 (m, 6H), 0.61 (qq, *J* = 10.3, 5.8, 3.3 Hz, 1H), 0.47 (t, *J* = 7.0 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 176.2, 147.6, 147.3, 135.2, 131.3, 128.3, 128.2, 124.3, 124.2, 118.9, 118.8, 90.3, 90.2, 45.5, 38.7, 37.3, 36.0, 27.5, 23.5, 22.7, 22.5, 13.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 26.12.; IR (neat): $\nu_{max}$ 3039.72 (w), 2951.95 (m), 2924.44 (m), 1628.73 (s), 1115.27 (s), 1080.98 (m), 780.72 (m) cm$^{-1}$. HRMS (DART) for $C_{24}H_{33}BNO_3$ $[M+H]^+$: Calc'd: 394.25480, found: 394.25579. $[\alpha]^{20}_D$: 0.789 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

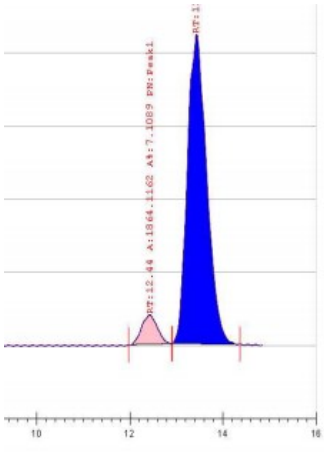
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N,N,3-trimethylheptanamide*

Racemic

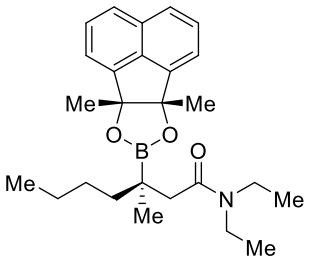


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.8769 | 20381.4443 | 13.27 |
| 2 | 50.1231 | 20482.0161 | 14.42 |
| Total: | 100 | 40863.4604 | |

Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 7.1089 | 1864.1162 | 12.44 |
| 2 | 92.8911 | 24358.1538 | 13.43 |
| Total: | 100 | 26222.27 | |



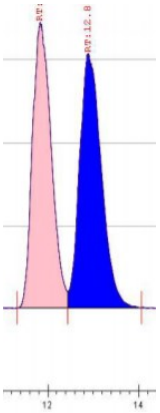
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N,N-diethyl-3-methylheptanamide (10).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in pentane, 0.080 mL, 0.2 mmol, 1.0 equiv.), diethylcarbamoyl chloride (54.2 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (69.6 mg, 0.165 mmol, 83% yield) as a white solid. Product Rf = 0.7 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 2H), 7.54 – 7.46 (m, 4H), 3.27 – 3.19 (m, 2H), 3.18 – 3.10 (m, 1H), 3.01 – 2.92 (m, 1H), 2.41 (d, *J* = 16.7 Hz, 1H), 2.10 (d, *J* = 16.7 Hz, 1H), 1.74 (s, 3H), 1.72 (s, 3H), 1.32 – 1.19 (m, 1H), 1.10 (t, *J* = 7.2, 1.4 Hz, 3H), 1.08 – 1.02 (m, 1H), 1.00 – 0.87 (m, 3H), 0.85 (t, *J* = 7.2 Hz, 3H), 0.79 (s, 3H), 0.78 – 0.71 (m, 1H), 0.55 (t, *J* = 7.0 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 176.6, 148.3, 148.0, 135.3, 131.2, 128.22, 128.16, 123.96, 123.93, 118.7, 89.7, 89.7, 45.4, 42.6, 41.6, 38.4, 27.6, 23.6, 23.0, 22.8, 22.5, 14.0, 13.8, 12.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 22.65. IR (neat): $\nu_{max}$ 3038.37 (w), 2962.00 (m), 2926.54 (m), 1612.60 (s), 1459.92 (m), 1116.46 (s), 780.66 (m) cm$^{-1}$. HRMS (DART) for $C_{26}H_{37}BNO_3$ $[M+H]^+$: Calc'd: 422.28610, found: 422.28726. $[\alpha]^{20}_D$: -17.896 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

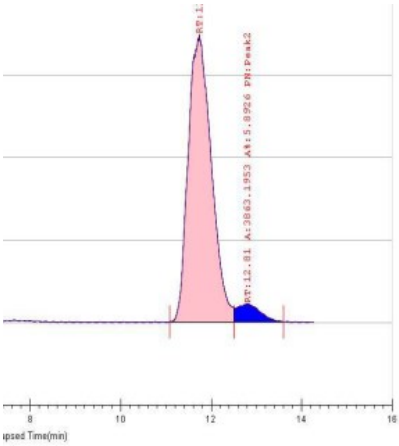
*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N,N-diethyl-3-methylheptanamide*

Racemic

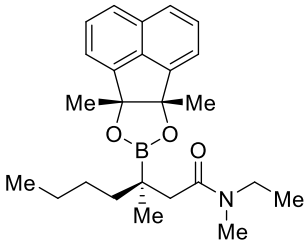


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.1834 | 49469.1302 | 11.83 |
| 2 | 50.8166 | 51111.8831 | 12.89 |
| Total: | 100 | 100581.0133 | |

Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 94.1074 | 61697.0746 | 11.74 |
| 2 | 5.8926 | 3863.1953 | 12.81 |
| Total: | 100 | 65560.2699 | |



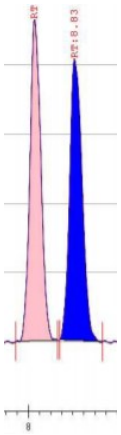
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N-ethyl-N,3-dimethylheptanamide (11).** The reaction was performed according to the general procedure *Method A* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in pentane, 0.080 mL, 0.2 mmol, 1.0 equiv.), methylethylcarbamoyl chloride (48.6 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (72.0 mg, 0.177 mmol, 88% yield) as a white solid. Product Rf = 0.45 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.65 (m, 2H), 7.57 – 7.47 (m, 4H), 3.28 (tq, J = 13.9, 7.2 Hz, 1H), 3.22 – 3.04 (m, 1H), 2.81 (d, J = 57.0 Hz, 3H), 2.41 (dd, J = 19.7, 16.8 Hz, 1H), 2.11 (t, J = 16.9 Hz, 1H), 1.75 (d, J = 1.8 Hz, 3H), 1.72 (d, J = 3.8 Hz, 3H), 1.32 – 1.15 (m, 1H), 1.11 (t, J = 7.2 Hz, 1.5H), 1.08 – 0.98 (m, 1H), 0.97 – 0.83 (m, 4.5H), 0.79 (d, J = 13.2 Hz, 3H), 0.74 – 0.60 (m, 1H), 0.55 – 0.46 (m, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 176.4, 147.9, 147.9, 147.61, 147.60, 135.28, 135.25, 131.3, 128.23, 128.19, 124.15, 124.13, 124.08, 118.77, 118.74, 118.73, 90.02, 89.98, 45.9, 45.1, 44.8, 43.6, 38.6, 38.6, 34.8, 33.4, 27.54, 27.51, 23.51, 23.50, 22.8, 22.6, 22.5, 22.4, 13.97, 13.96, 13.2, 12.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 24.51.; IR (neat): $\nu_{max}$ 3034.49 (w), 2958.52 (m), 2926.22 (m), 1622.61 (s), 1116.41 (s), 1082.17 (m), 780.557 (m) cm$^{-1}$. HRMS (DART) for $C_{25}H_{35}BNO_3$ $[M+H]^+$: Calc'd: 408.27045, found: 408.27120. $[\alpha]^{20}_D$: -2.742 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

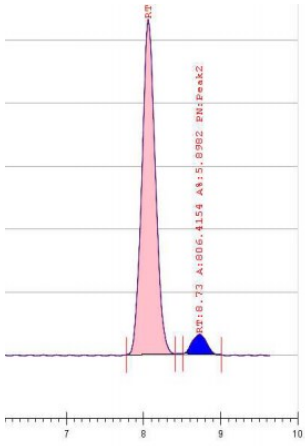
*Chiral SFC (ODR-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-N-ethyl-N,3-dimethylheptanamide*

Racemic

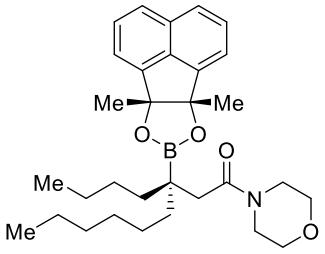


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.9839 | 6331.9047 | 8.11 |
| 2 | 50.0161 | 6335.9956 | 8.83 |
| Total: | 100 | 12667.9003 | |

Enriched



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 94.1018 | 12865.813 | 8.06 |
| 2 | 5.8982 | 806.4154 | 8.73 |
| Total: | 100 | 13672.2284 | |



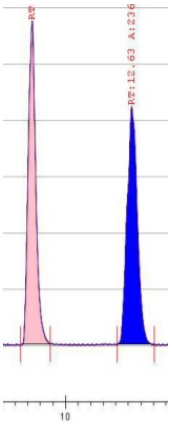
**(R)-3-butyl-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholinononan-1-one (12).** The reaction was performed according to the general procedure *Method A* using alkenyl B(mac) (**S-3**) (66.9 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in pentane, 0.080 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to isolate the title compound (73.3 mg, 0.145 mmol, 73% yield) as a white solid. Product Rf = 0.8 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, $J$ = 8.0 Hz, 2H), 7.57 – 7.47 (m, 4H), 3.62 (t, $J$ = 4.8 Hz, 2H), 3.57 (t, $J$ = 4.9 Hz, 2H), 3.43 – 3.37 (m, 4H), 2.28 (s, 2H), 1.75 (s, 6H), 1.34 – 1.15 (m, 4H), 1.10 – 0.84 (m, 10H), 0.78 (t, $J$ = 7.3 Hz, 3H), 0.75 – 0.68 (m, 2H), 0.61 (t, $J$ = 7.3 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.7, 146.91, 146.88, 135.2, 131.3, 128.3, 124.47, 124.46, 119.0, 90.7, 66.9, 66.7, 46.0, 42.8, 41.0, 33.7, 33.2, 31.8, 30.1, 26.4, 24.1, 23.5, 22.6, 22.34, 22.30, 14.20, 14.15.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.67.; IR (neat): $\nu_{max}$ 2952.73 (m), 2922.96 (m), 2852.40 (m), 1631.22 (s), 1115.08 (s), 781.34 (m) cm$^{-1}$. HRMS (DART) for $C_{31}H_{45}BNO_4$ $[M+H]^+$: Calc'd: 506.34362, found: 506.34187. $[\alpha]^{20}_D$: 0.754 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

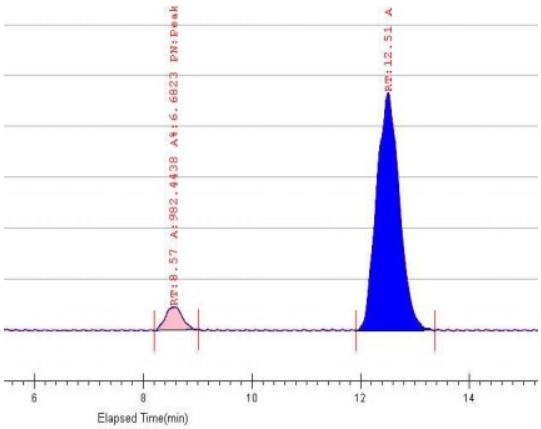
*Chiral SFC (AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-butyl-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholinononan-1-one*

Racemic

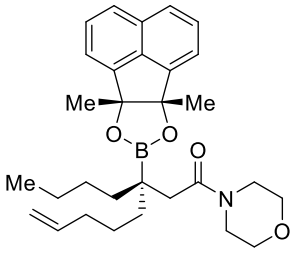


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.3539 | 24020.049 | 8.68 |
| 2 | 49.6461 | 23682.3939 | 12.63 |
| Total: | 100 | 47702.4429 | |

Enriched




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 6.6823 | 982.4438 | 8.57 |
| 2 | 93.3177 | 13719.8128 | 12.51 |
| Total: | 100 | 14702.2566 | |



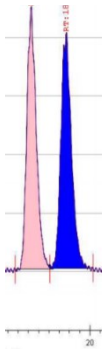
**(R)-3-butyl-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholinooct-7-en-1-one (13).** The reaction was performed according to the general procedure *Method A* using alkenyl B(mac) (**S-4**) (63.4 mg, 0.2 mmol, 1.0 equiv.), *n*-butyllithium (2.5 M in pentane, 0.080 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (3.6 µL, 0.2 mmol, 1 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 1% triethylamine: 10% acetone: 89% hexanes) to isolate the title compound (75.0 mg, 0.153 mmol, 76% yield) as a white solid. Product Rf = 0.6 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).;$^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, $J$ = 7.9 Hz, 2H), 7.60 – 7.44 (m, 4H), 5.50 (ddt, $J$ = 17.1, 10.4, 6.6 Hz, 1H), 4.81 – 4.77 (m, 1H), 4.76 (t, $J$ = 1.4 Hz, 1H), 3.62 (t, $J$ = 4.9 Hz, 2H), 3.56 (t, $J$ = 4.8 Hz, 2H), 3.38 (q, $J$ = 4.8 Hz, 4H), 2.28 (d, $J$ = 2.1 Hz, 2zH), 1.80-1.72 (m, 8H), 1.34 – 1.14 (m, 4H), 1.08 – 0.82 (m, 5H), 0.82 – 0.69 (m, 1H), 0.61 (t, $J$ = 7.3 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.9, 146.94, 146.92, 139.4, 135.2, 131.3, 128.3, 124.45, 124.43, 118.9, 113.8, 90.59, 90.57, 66.8, 66.6, 66.3, 46.0, 42.8, 41.1, 34.5, 33.3, 33.2, 26.5, 23.7, 23.5, 22.4, 22.3, 14.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 28.87. IR (neat): $\nu_{max}$ 2951.95 (m), 2924.15 (m), 2854.90 (m), 1635.36 (s), 1115.79 (s), 781.86 (s) cm$^{-1}$. HRMS (DART) for $C_{30}H_{41}BNO_4$ $[M+H]^+$: Calc'd: 490.31232, found: 490.31170. $[\alpha]^{20}_D$: -3.012 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

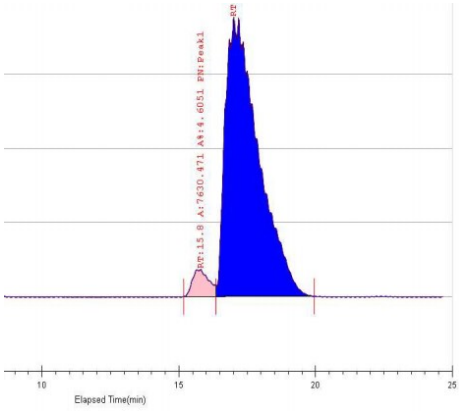
*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-butyl-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1 morpholinooct-7-en-1-one*

Racemic

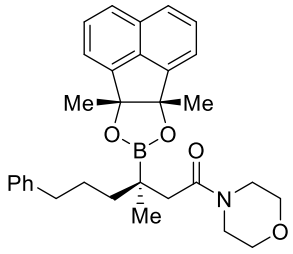


| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.5859 | 7099.1143 | 17.15 |
| 2 | 50.4141 | 7217.6763 | 18.85 |
| Total: | 100 | 14316.7906 | |

Enriched




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 4.6051 | 7630.471 | 15.8 |
| 2 | 95.3949 | 158064.9338 | 17.01 |
| Total: | 100 | 165695.4048 | |



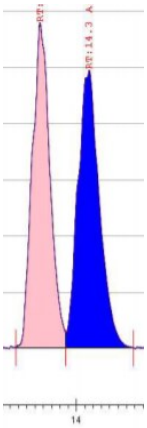
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholino-6-phenylhexan -1-one (14).** The reaction was performed according to the general procedure *Method B* using phenylpropyl B(mac) (**S-2**) (68.5 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium (1.7 M in pentane, 0.235 mL, 0.4 mmol, 2.0 equiv.), 2-bromopropene (24.2 mg, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.1 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (eluted with 10% acetone:hexanes) to afford a white solid (52.1 mg, 52.4% yield). Product Rf. = 0.1 in 20% ethyl acetate:hexanes (UV active and stains blue green with PAA). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 11.2, 7.9 Hz, 2H), 7.61 – 7.48 (m, 4H), 7.19 – 7.05 (m, 3H), 6.70 (d, *J* = 7.3 Hz, 2H), 3.71 – 3.52 (m, 4H), 3.48 – 3.30 (m, 4H), 2.42 (d, *J* = 16.5 Hz, 1H), 2.20 (t, *J* = 7.2 Hz, 2H), 2.12 (d, *J* = 16.5 Hz, 1H), 1.77 (d, *J* = 26.4 Hz, 6H), 1.35 – 1.23 (m, 2H), 1.16 – 0.97 (m, 2H), 0.86 (s, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.3, 146.8, 146.5, 142.8, 135.1, 131.3, 128.38, 128.35, 128.2, 128.1, 125.4, 124.7, 124.5, 119.1, 119.0, 91.0, 90.9, 66.9, 66.6, 45.9, 45.0, 42.7, 39.1, 36.6, 27.1, 22.4, 22.3, 22.1.; $^{11}$B NMR (160 MHz, cdcl$_3$) δ 27.34. IR (neat): $\nu_{max}$ 2965.68 (m), 2926.24 (m), 2853.77 (m), 1625.83 (s), 1114.5 (s), 749.03 (s) cm$^{-1}$. HRMS (DART) for $C_{31}H_{37}BNO_4$ $[M+H]^+$: Calc'd: 498.28102, found: 498.28230. $[\alpha]^{20}_D$: 4.017 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

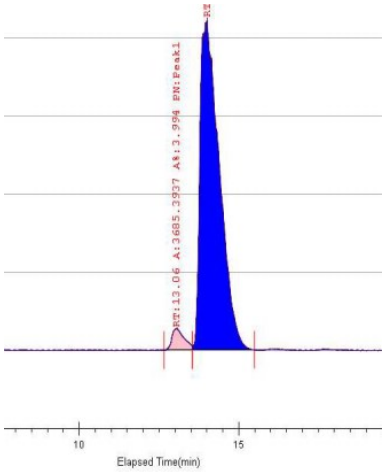
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (AD-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) - 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholino-6-phenylhexan -1-one*

Racemic

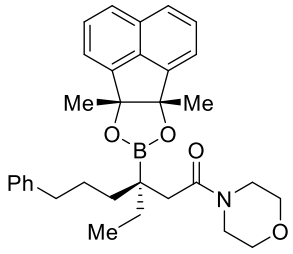


Enriched




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.0635 | 17155.3916 | 13.12 |
| 2 | 50.9365 | 17810.3047 | 14.3 |
| Total: | 100 | 34965.6963 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 3.994 | 3685.3937 | 13.06 |
| 2 | 96.006 | 88588.3607 | 14.01 |
| Total: | 100 | 92273.7544 | |



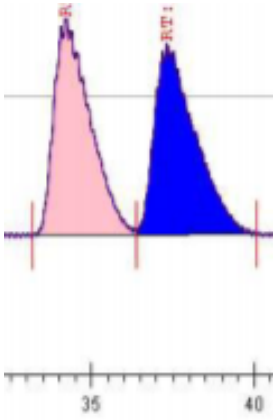

**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-ethyl-1-morpholino-6-phenylhexan-1-one (15).** The reaction was performed according to the general procedure *Method B* using phenylpropyl B(mac) (**S-2**) (68.5 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium (1.7 M in pentane, 0.235 mL, 0.4 mmol, 2.0 equiv.), 2-bromobut-1-ene (27.0 mg, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.1 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M).. The crude mixture was purified by silica gel chromatography eluted with 10% acetone:hexanes to isolate the title compound (52.7 mg, 0.103 mmol, 51% yield) as a white solid. Product Rf = 0.6 in 30% acetone: 70% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.9, 4.1 Hz, 2H), 7.60 – 7.47 (m, 4H), 7.17 (t, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 2H), 3.61 (t, *J* = 4.9 Hz, 2H), 3.56 (t, *J* = 4.9 Hz, 2H), 3.40 – 3.35 (m, 4H), 2.35 – 2.21 (m, 4H), 1.76 (d, *J* = 8.9 Hz, 6H), 1.48 – 1.18 (m, 5H), 1.16 – 1.06 (m, 1H), 0.55 (t, *J* = 7.4 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.8, 146.94, 146.91, 143.0, 135.2, 131.3, 128.33, 128.32, 128.3, 128.1, 125.4, 124.51, 124.47, 119.0, 118.9, 90.63, 90.60, 66.8, 66.6, 45.9, 42.8, 40.8, 36.7, 33.5, 26.4, 25.7, 22.4, 22.3, 8.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 27.42.; IR (neat): $\nu_{max}$ 2968.52 (m), 2938.22 (m), 2820.51 (m), 1628.66 (s), 1115.37 (s), 781.37 (s) cm$^{-1}$. HRMS (DART) for $C_{32}H_{39}BNO_4$ $[M+H]^+$: Calc'd: 512.29667, found: 512.29809. $[\alpha]^{20}_D$: 3.845 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

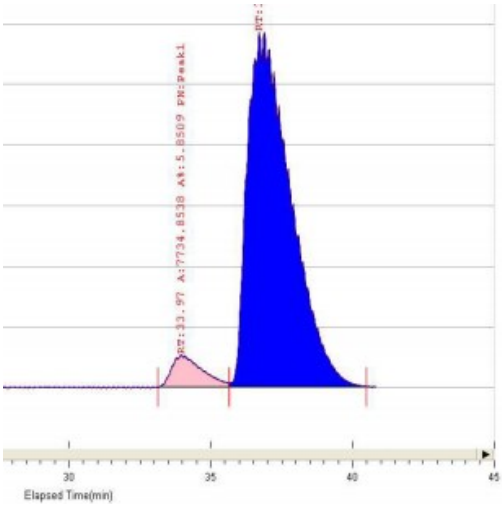
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (AD-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) - 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-ethyl-1-morpholino-6-phenylhexan-1-one*

Racemic

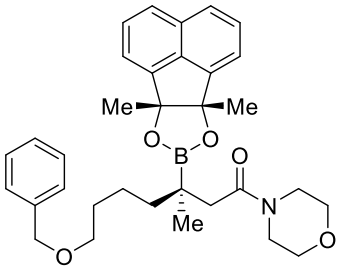



Enriched




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.3249 | 11948.8765 | 34.22 |
| 2 | 49.6751 | 11794.5779 | 37.31 |
| Total: | 100 | 23743.4544 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 5.8509 | 7734.8538 | 33.97 |
| 2 | 94.1491 | 124465.0053 | 36.7 |
| Total: | 100 | 132199.8591 | |



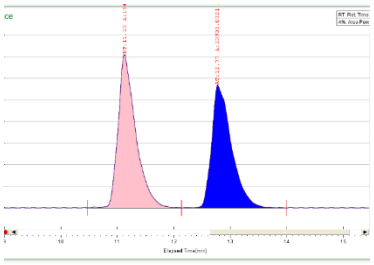

**(S)-7-(benzyloxy)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (16).** The reaction was performed according to the general procedure *Method B* using 1-benzyloxyl butyl B(mac) (77.2 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% ethyl acetate:hexanes) to isolate the title compound (74.1 mg, 0.137 mmol, 68.5% yield) as a white solid. Product Rf = 0.60 in 2% triethylamine: 20% acetone: 78% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.5 Hz, 2H), 7.53 – 7.47 (m, 4H), 7.34 – 7.31 (m, 2H), 7.26 (dd, *J* = 8.0, 6.0 Hz, 3H), 4.32 (s, 2H), 3.62 – 3.52 (m, 4H), 3.42 – 3.31 (m, 4H), 3.04 – 2.89 (m, 2H), 2.40 (d, *J* = 16.6 Hz, 1H), 2.11 (d, *J* = 16.6 Hz, 1H), 1.74 (d, *J* = 22.4 Hz, 6H), 1.22 (dq, *J* = 12.9, 7.3, 5.5 Hz, 2H), 1.15 (dq, *J* = 13.0, 7.2 Hz, 1H), 1.09 – 0.99 (m, 2H), 0.83 (s, 3H), 0.66 (ddp, *J* = 12.3, 7.1, 4.5, 4.1 Hz, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.7, 146.9, 146.6, 128.38, 128.33, 128.27, 127.7, 127.5, 124.5, 124.4, 119.0, 118.9, 90.75, 90.69, 72.8, 70.5, 66.8, 66.5, 47.3, 45.9, 44.9, 42.8, 38.9, 30.3, 29.8, 22.1, 22.1, 21.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 28.4.; IR (neat): $\nu_{max}$, 2967.42 (m), 2927.64 (m), 2856.12 (m), 1624.96 (s), 1462.80 (m), 1115.49 (s), 1082.27 (s), 782.46 (s) $cm^{-1}$. HRMS (DART) for $C_{33}H_{40}BNO_5$ $[M+H]^+$: Calc'd: 542.30723, found: 542.30691. $[\alpha]^{20}_D$: 6.789 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

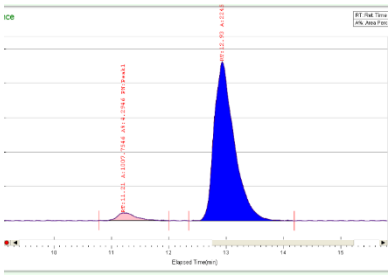
*Chiral SFC (Chiralcel AD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-7-(benzyloxy)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho-[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one*

Race

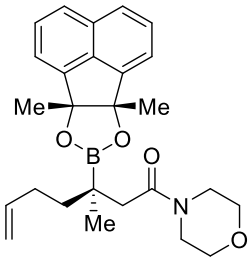


| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 52.537 | 15424.7692 | 11.13 |
| 2 | 47.463 | 13935.0321 | 12.77 |
| Total | 100 | 29359.8013 | |

Enric



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 4.2946 | 1007.7546 | 11.21 |
| 2 | 95.7054 | 22457.9527 | 12.93 |
| Total | 100 | 23465.7073 | |



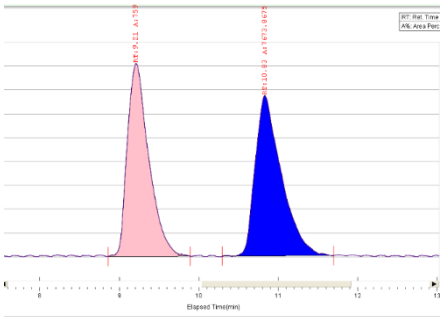

**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinohept-6-en-1-one (17).** The reaction was performed according to the general procedure *Method B* using 1-butenyl B(mac) (55.6 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% ethyl acetate:hexanes) to isolate the title compound (59.6 mg, 0.138 mmol, 68.8% yield) as a white solid. Product Rf = 0.60 in 2% triethylamine: 30% acetone: 68% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.71 (dd, $J$ = 8.0, 4.6 Hz, 2H), 7.56 – 7.47 (m, 4H), 5.47 (ddt, $J$ = 16.9, 10.1, 6.7 Hz, 1H), 4.64 – 4.45 (m, 2H), 3.58 (d, $J$ = 33.8 Hz, 4H), 3.36 (d, $J$ = 4.4 Hz, 4H), 2.41 (d, $J$ = 16.5 Hz, 1H), 2.14 (d, $J$ = 16.6 Hz, 1H), 1.74 (d, $J$ = 22.4 Hz, 7H), 1.49 (s, 1H), 1.32 (td, $J$ = 12.4, 4.7 Hz, 1H), 1.15 (td, $J$ = 12.5, 5.0 Hz, 1H), 0.84 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.6, 146.9, 146.6, 139.8, 135.2, 131.3, 128.4, 128.3, 124.6, 124.5, 119.0, 113.5, 90.8, 90.7, 66.8, 66.6, 45.9, 44.9, 42.8, 38.6, 29.9, 22.4, 22.2, 22.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 28.2. IR (neat): $\nu_{max}$, 2969.72 (m), 2925.36 (m), 2857.31 (m), 1622.65 (s), 1464.55 (m), 1116.37 (s), 1082.78 (s), 782.54 (s) $cm^{-1}$. HRMS (DART) for $C_{26}H_{32}BNO_4$ $[M+H]^+$: Calc'd: 434.24972, found: 434.25053. $[\alpha]^{20}_D$: 1.899 (c = 1.0 g/mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

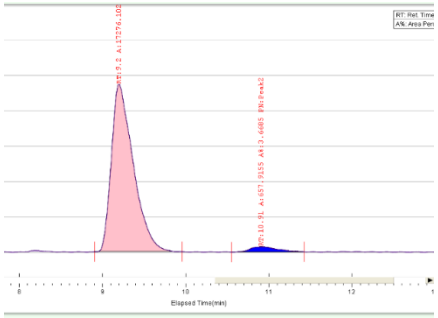
*Chiral SFC (Chiralcel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]-dioxaborol-8-yl)-3-methyl-1-morpholinohept-6-en-1-one.*

Race

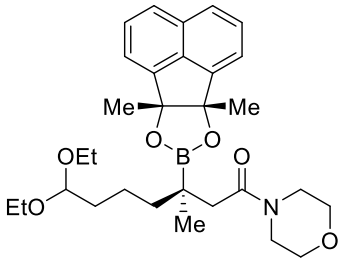


| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.7446 | 7595.8763 | 9.21 |
| 2 | 50.2554 | 7673.8675 | 10.83 |
| Total | 100 | 15269.7438 | |

Enric



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 96.3315 | 17276.102 | 9.20 |
| 2 | 3.6685 | 657.9155 | 10.91 |
| Total | 100 | 17934.0175 | |

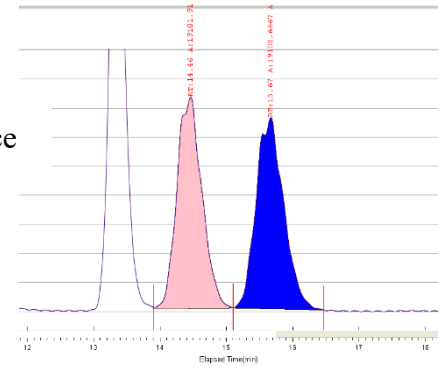



**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-7,7-diethoxy-3-methyl-1-morpholinoheptan-1-one (18).** The reaction was performed according to the general procedure *Method B* using 5,5-diethoxypentyl B(mac) (**S-5**) (73.6 mg, 0.2 mmol, 1.0 equiv.), isopropenyllithium (0.50 mL, 0.4 M, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 20% ethyl acetate:hexanes) to isolate the title compound (61.0 mg, 0.116 mmol, 58.3% yield) as an off-white solid. Product Rf = 0.50 in 2% triethylamine: 20% ethyl acetate: 78% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.56 – 7.49 (m, 4H), 3.99 (t, J = 5.7 Hz, 1H), 3.63 – 3.43 (m, 6H), 3.39 – 3.25 (m, 6H), 2.41 (d, J = 16.6 Hz, 1H), 2.13 (d, J = 16.6 Hz, 1H), 1.75 (d, J = 17.2 Hz, 6H), 1.30 – 1.18 (m, 4H), 1.11 (dq, J = 14.1, 7.1 Hz, 8H), 0.84 (s, 3H).; 13C NMR (151 MHz, $CDCl_3$) δ 173.6, 146.9, 146.7, 135.1, 131.2, 128.34, 128.25, 124.5 124.4, 118.96, 118.94, 103.2, 90.8, 90.7, 77.4, 77.2, 76.9, 66.8, 66.5, 61.3, 60.7, 45.9, 44.7, 42.7, 38.8, 34.5, 30.4, 22.4, 22.2, 22.1, 20.6, 15.5, 15.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 28.4.; IR (neat): $\nu_{max}$, 2968.45 (m), 2927.12 (m), 2860.33 (m), 1654.11 (s), 1462.10 (m), 1111.50 (s), 1088.47 (s). HRMS (DART) for $C_{28}H_{37}BNO_5$ $[M\text{-}C_2H_5O^-]^+$: Calc'd 478.27593, found: 478.27607. $[\alpha]^{20}_D$: 8.030 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst. Crude material was used for SFC without purification.

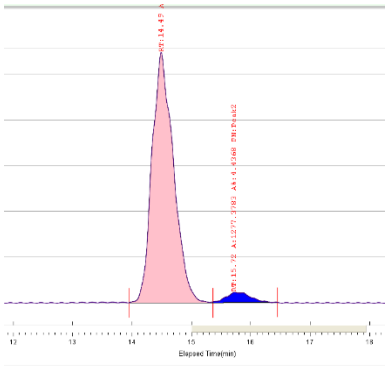
*Chiral SFC (Chiralcel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho-[1,2-d][1,3,2]dioxaborol-8-yl)-7,7-diethoxy-3-methyl-1-morpholinoheptan-1-one*

Race

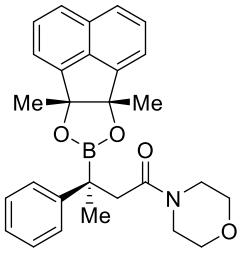


| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.1035 | 19181.9141 | 14.46 |
| 2 | 49.8965 | 19102.6667 | 15.67 |
| Total | 100 | 38284.5808 | |

Enric



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 95.5632 | 27513.1068 | 14.49 |
| 2 | 4.4368 | 1277.3783 | 15.72 |
| Total | 100 | 28790.4851 | |



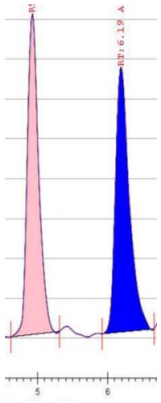
**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-phenylbutan-1-one (19).** The reaction was performed according to the general procedure *Method A* at 60 °C using isopropenyl B(mac) (XX) (52.8 mg, 0.2 mmol, 1.0 equiv.), phenyllithium (1.9 M in dibutyl ether, 0.105 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.4 mmol, 2.0 equiv.), and water (10.8 µL, 0.6 mmol, 3 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 2% triethylamine, 20% acetone, 78% hexanes) to isolate the title compound (74.2 mg, 0.162 mmol, 81% yield) as a white solid. Product Rf = 0.3 in 3% triethylamine: 30% acetone: 67% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.71 (t, *J* = 7.2 Hz, 2H), 7.52 (dt, *J* = 23.1, 6.8 Hz, 3H), 7.42 (d, *J* = 6.9 Hz, 1H), 7.04 – 6.92 (m, 5H), 3.70 – 3.56 (m, 3H), 3.53 – 3.47 (m, 1H), 3.44 (t, *J* = 4.9 Hz, 2H), 3.32 (t, *J* = 5.0 Hz, 2H), 3.03 (d, *J* = 16.4 Hz, 2H), 2.55 (d, *J* = 16.5 Hz, 2H), 1.73 (d, *J* = 12.8 Hz, 6H), 1.22 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 174.8, 148.2, 147.4, 146.9, 135.4, 131.2, 128.4, 128.1, 127.8, 126.5, 124.7, 124.2, 119.0, 118.7, 90.5, 90.4, 66.6, 66.4, 46.1, 43.6, 43.4, 26.9, 22.6, 22.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 24.77. IR (neat): $\nu_{max}$ 2964.82 (m), 2924.49 (m), 2855.63 (m), 1610.994 (s), 1113.43 (s), 1082.75 (s), 752.21 (s) cm$^{-1}$. HRMS (DART) for $C_{28}H_{31}BNO_4$ $[M+H]^+$: Calc'd: 456.23407, found: 456.23432. $[\alpha]^{20}_D$: -33.002 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

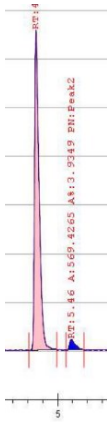
Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

*Chiral SFC (AD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-phenylbutan-1-one*

Race

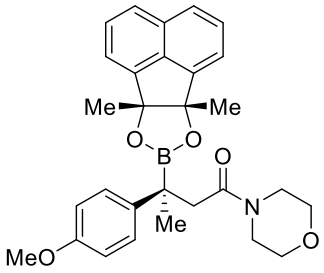


Enric



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.846 | 18104.0436 | 4.92 |
| 2 | 50.154 | 18215.8814 | 6.19 |
| Total: | 100 | 36319.925 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 96.0651 | 13901.8187 | 4.27 |
| 2 | 3.9349 | 569.4265 | 5.46 |
| Total: | 100 | 14471.2452 | |



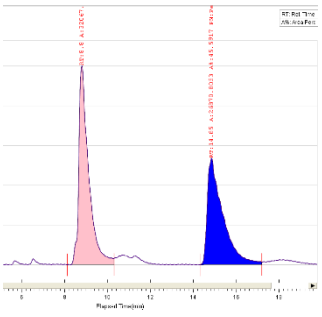

**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-(4-methoxyphenyl)butan-1-one (20).** The reaction was performed according to the general procedure *Method C* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 20% ethyl acetate:hexanes) to isolate the title compound ( 39.9 mg, 0.085 mmol, 42.5% yield) as a white solid. Product Rf = 0.50 in 2% triethylamine: 30% acetone: 68% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, $J$ = 8.1, 6.1 Hz, 2H), 7.50 (dt, $J$ = 22.2, 7.0 Hz, 3H), 7.41 (d, $J$ = 6.9 Hz, 1H), 6.88 (d, $J$ = 8.6 Hz, 2H), 6.52 (d, $J$ = 8.5 Hz, 2H), 3.68 (s, 3H), 3.59 (s, 3H), 3.51 (s, 1H), 3.42 (t, $J$ = 4.9 Hz, 2H), 3.32 (t, $J$ = 4.9 Hz, 1H), 2.95 (d, $J$ = 16.4 Hz, 1H), 2.51 (d, $J$ = 16.4 Hz, 1H), 1.72 (s, 6H), 1.17 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$): δ 174.5, 156.8, 147.3, 146.9, 140.3, 135.3, 131.2, 128.4, 128.1, 127.4, 124.2, 119.0, 118.8, 113.2, 90.5, 90.4, 66.7, 66.4, 55.2, 47.3, 46.0, 44.0, 43.3, 29.8, 26.7, 22.6, 22.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 26.7.; IR (neat): $\nu_{max}$, 2967.16 (m), 2926.18 (m), 2856.57 (m), 1611.09 (s), 1511.37 (m), 1114.97 (s), 1084.11 (s), 783.13 (s) cm$^{-1}$. HRMS (DART) for $C_{29}H_{32}BNO_4$ $[M+H]^+$: Calc'd: 486.24463, found: 486.24476. $[\alpha]^{20}_D$: 12.287 (c = 1.0 g/mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and 50% ($S_p$, $S_p$)-L1 :50% ($R_p$, $R_p$)-L1 (3.6 mol%) as the catalyst. Crude material was used for SFC without purification.

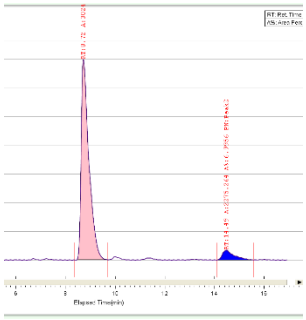
*Chiral SFC (Chiralcel AD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]-dioxaborol-8-yl)-1-morpholino-3-(4-methoxyphenyl)butan-1-one.*

Race

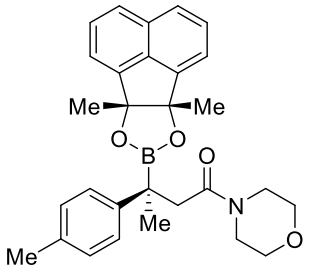


| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 54.4083 | 32067.1859 | 8.8 |
| 2 | 45.5917 | 26870.8053 | 14.85 |
| Total | 100 | 58937.9912 | |

Enric



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 93.0044 | 30248.742 | 8.72 |
| 2 | 6.9956 | 2275.264 | 14.10 |
| Total | 100 | 32524.006 | |



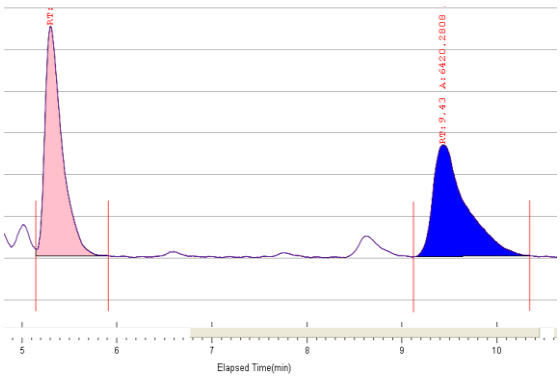

**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-(p-tolyl)butan-1-one (21).** The reaction was performed according to the general procedure *Method C* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 20% ethyl acetate:hexanes) to isolate the title compound (57.7 mg, 0.123 mmol, 61.5% yield) as a white solid. Product Rf = 0.40 in 2% triethylamine: 40% acetone: 58% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, $J$ = 8.0, 4.7 Hz, 2H), 7.53 – 7.46 (m, 3H), 7.41 (d, $J$ = 6.6 Hz, 1H), 6.87 (d, $J$ = 8.2 Hz, 2H), 6.79 (d, $J$ = 7.9 Hz, 2H), 3.66 – 3.56 (m, 3H), 3.50 (d, $J$ = 6.2 Hz, 1H), 3.43 (t, $J$ = 4.8 Hz, 2H), 3.34 – 3.29 (m, 2H), 2.97 (d, $J$ = 16.4 Hz, 1H), 2.52 (d, $J$ = 16.5 Hz, 1H), 2.18 (s, 3H), 1.72 (d, $J$ = 6.2 Hz, 6H), 1.19 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$): δ 174.5, 147.3, 146.9, 145.1, 135.4, 134.0, 131.2, 128.6, 128.4, 128.1, 126.3, 124.3, 119.0, 118.8, 90.6, 90.5, 66.7, 66.5, 46.0, 43.2, 29.8, 26.7, 22.6, 22.5, 20.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 26.66.; IR (neat): $\nu_{max}$, 2968.42 (m), 2923.58 (m), 2857.29 (m), 1613.81 (s), 1445.53 (m), 1116.82 (s), 1084.44 (s), 782.76 (s) cm$^{-1}$. HRMS (DART) for $C_{29}H_{32}BNO_4$ $[M+H]^+$: Calc'd: 470.24972, found: 470.25116. $[\alpha]^{20}_D$: 12.287 (c = 1.0 g/mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst. Crude material was used for SFC without purification.

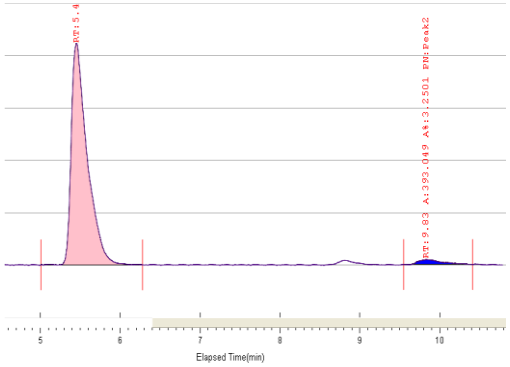
*Chiral SFC (Chiralcel AD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho-[1,2-d][1,3,2]-dioxaborol-8-yl)-1-morpholino-3-(p-tolyl)butan-1-one.*

Race

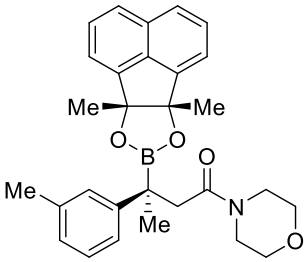



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 51.805 | 6901.1975 | 5.3 |
| 2 | 48.195 | 6420.2808 | 9.43 |
| Total | 100 | 13321.4783 | |

Enric




| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 96.7499 | 11700.4772 | 5.45 |
| 2 | 3.2501 | 393.049 | 9.83 |
| Total | 100 | 12093.5262 | |



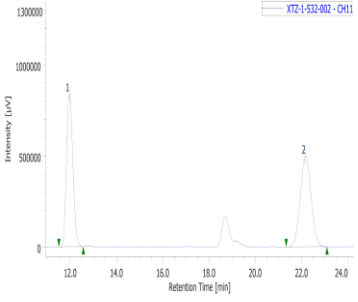
**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-(m-tolyl)butan-1-one (22).** The reaction was performed according to the general procedure *Method C* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 20% ethyl acetate:hexanes) to isolate the title compound ( 61.7 mg, 0.132 mmol, 65.8% yield) as a white solid. Product Rf = 0.40 in 2% triethylamine: 40% acetone: 58% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.70 (t, $J$ = 8.2 Hz, 2H), 7.57 – 7.46 (m, 3H), 7.42 (d, $J$ = 6.6 Hz, 1H), 6.89 (t, $J$ = 7.6 Hz, 1H), 6.81 – 6.72 (m, 2H), 6.68 (d, $J$ = 2.0 Hz, 1H), 3.69 – 3.59 (m, 3H), 3.55 – 3.50 (m, 1H), 3.45 (t, $J$ = 4.8 Hz, 2H), 3.38 (t, $J$ = 4.9 Hz, 2H), 2.99 (d, $J$ = 16.4 Hz, 1H), 2.55 (d, $J$ = 16.5 Hz, 1H), 1.95 (s, 3H), 1.73 (s, 6H), 1.20 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 174.6, 148.1, 147.4, 146.8, 137.1, 135.3, 131.2, 128.4, 128.2, 127.7, 127.6, 125.5, 124.3, 123.3, 119.0, 118.8, 90.6, 90.5, 66.7, 66.5, 46.1, 43.6, 43.3, 29.8, 27.0, 22.5, 21.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 26.2.; IR (neat): $\nu_{max}$, 2966.32 (m), 2923.45 (m), 2855.91 (m), 1607.14 (s), 1458.33 (m), 1115.59 (s), 1083.84 (s), 782.14 (s) cm$^{-1}$. HRMS (DART) for $C_{29}H_{32}BNO_5$ $[M+H]^+$: Calc'd: 470.24972, found: 470.25025. $[\alpha]^{20}_D$: 16.398 (c = 1.0 g/mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

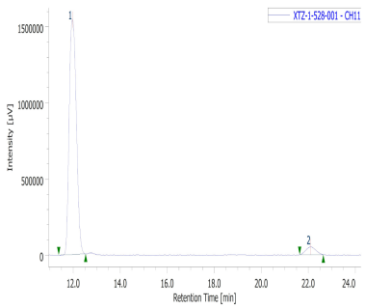
*Chiral SFC (Chiralcel AD-H, 15% IPA, 1 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho-[1,2-d][1,3,2]-dioxaborol-8-yl)-1-morpholino-3-(m-tolyl)butan-1-one*

Race




| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.715 | 15995171 | 11.97 |
| 2 | 50.285 | 16178867 | 22.18 |
| Total | 100 | 32174038 | |

Enric




| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 95.605 | 32804267 | 11.96 |
| 2 | 4.395 | 1508131 | 22.10 |
| Total | 100 | 34312398 | |

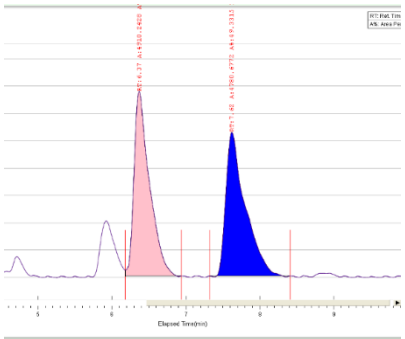
**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-(4-fluorophenyl)butan-1-one (23).** The reaction was performed according to the general procedure *Method C* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), 4-morpholine carbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.2 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (0.6 mL, 0.33 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 20% ethyl acetate:hexanes) to isolate the title compound ( 62.0 mg, 0.131 mmol, 65.5% yield) as a white solid. Product Rf = 0.50 in 2% triethylamine: 30% acetone: 68% hexanes (UV active and stains blue with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.1, 6.0 Hz, 2H), 7.56 – 7.48 (m, 3H), 7.38 (d, *J* = 6.8 Hz, 1H), 6.86 (dd, *J* = 8.6, 5.5 Hz, 2H), 6.61 (t, *J* = 8.8 Hz, 2H), 3.68 – 3.58 (m, 3H), 3.54 (dt, *J* = 11.8, 5.0 Hz, 1H), 3.47 (t, *J* = 5.0 Hz, 2H), 3.38 (t, *J* = 4.9 Hz, 2H), 3.01 (d, *J* = 16.5 Hz, 1H), 2.54 (d, *J* = 16.5 Hz, 1H), 1.72 (s, 6H), 1.17 (s, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$): δ 174.8, 148.2, 147.4, 146.9, 135.4, 131.2, 128.4, 128.1, 127.8, 126.5, 124.7, 124.2, 119.0, 118.7, 90.5, 90.4, 66.8, 66.7, 66.5, 47.4, 46.1, 43.6, 43.4, 26.9, 22.7, 22.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 24.4.; $^{19}$F NMR (470 MHz, $CDCl_3$) δ -112.9.; IR (neat): $\nu_{max}$, 2966.59 (m), 2923.55 (m), 2855.36 (m), 1616.33 (s), 1508.68 (m), 1115.30 (s), 1084.33 (s), 782.30 (s) cm$^{-1}$. HRMS (DART) for $C_{28}H_{29}BF\,NO_4$ $[M+H]^+$: Calc'd: 474.22464, found: 474.22438. $[\alpha]^{20}_D$: 10.499 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst. Crude material was used for SFC without purification.

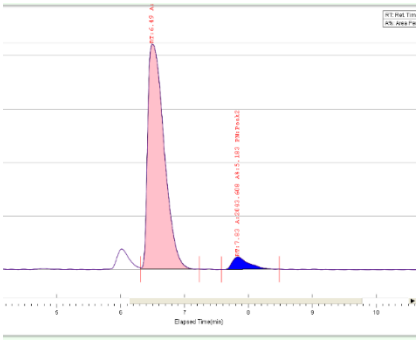
*Chiral SFC (Chiralcel AD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]-dioxaborol-8-yl)-1-morpholino-3-(4-fluoroxyphenyl)butan-1-one.*

Race

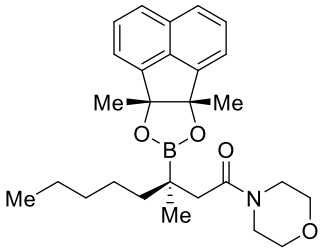


| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.6685 | 4910.2428 | 6.37 |
| 2 | 49.3315 | 4780.6772 | 7.62 |
| Total | 100 | 9690.92 | |

Enric



| Peak No. | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 94.817 | 37385.3649 | 6.49 |
| 2 | 5.183 | 2043.608 | 7.83 |
| Total | 100 | 39428.9729 | |



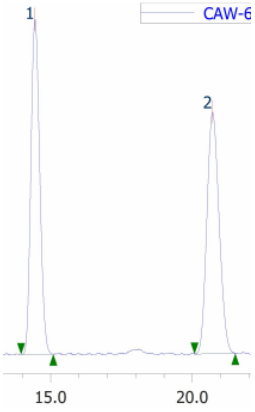
**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinooctan-1-one (26).** The reaction was performed according to the general procedure *Method D* using isopropenyl B(mac) (**S-1**) (52.8 mg, 0.2 mmol, 1.0 equiv.), pentyllithium (0.83 M in ether, 0.244 mL, 0.2 mmol, 1.0 equiv.), 4-morpholinecarbonyl chloride (59.8 mg, 0.4 mmol, 2.0 equiv.), palladium (II) acetate (1.35 mg, 0.006 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (91.1 mg, 0.6 mmol, 3.0 equiv.), and water (21.6 µL, 1.2 mmol, 6 equiv.) in THF (1.2 mL, 0.13 M). The crude mixture was purified by silica gel chromatography (deactivated silica using 2% triethylamine:hexanes, eluted with 10% acetone:hexanes) to afford a white solid (60.8 mg, 67.7% yield). Product Rf = 0.45 in 2% triethylamine:29% acetone:70% hexanes (stains blue with *para*-anisaldehyde stain and UV active).; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.68 (m, 2H), 7.58 – 7.48 (m, 4H), 3.66 – 3.51 (m, 4H), 3.45 – 3.33 (m, 4H), 2.41 (d, $J$ = 16.5 Hz, 1H), 2.11 (d, $J$ = 16.5 Hz, 1H), 1.76 (d, $J$ = 21.0 Hz, 6H), 1.25 – 1.17 (m, 1H), 1.07 – 0.99 (m, 1H), 0.99 – 0.75 (m, 8H), 0.69 – 0.60 (m, 1H), 0.57 (t, $J$ = 7.0 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.3, 146.8, 146.5, 135.2, 131.3, 128.32, 128.26, 124.6, 124.5, 119.01, 118.97, 90.9, 90.8, 66.9, 66.6, 45.9, 45.0, 42.6, 39.2, 32.5, 24.9, 22.40, 22.38, 22.2, 22.1, 13.9.; $^{11}$B NMR (192 MHz, $CDCl_3$) δ 28.91.; IR (neat): $\nu_{max}$ 3040.36 (w), 2956.84 (m), 2922.60 (m), 2853.61 (m), 1632.62 (s), 1415.01 (m), 1213.07 (m), 1115.10 (s), 781.42 (w) cm$^{-1}$. HRMS (DART) for $C_{27}H_{27}BNO_4$ $[M+H]^+$: Calc'd: 450.28102 found: 450.28026. $[\alpha]^{20}_D$: -0.725 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

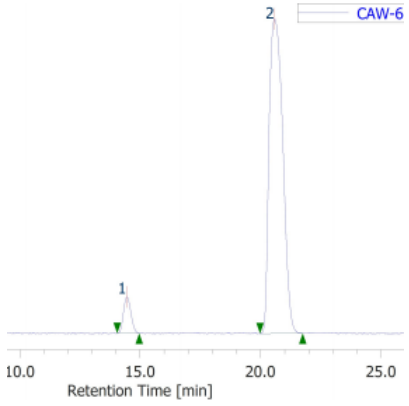
*Chiral SFC (AD-H, 10% IPA, 1 mL/min, 100 bar, 35 °C, 210-270 nm) - 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinooctan-1-one*

Racemic




| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|---|---|---|
| 1 | Unknown | 11 | 14.447 | 6564595 | 303341 | 50.087 |
| 2 | Unknown | 11 | 20.707 | 6541692 | 218807 | 49.913 |

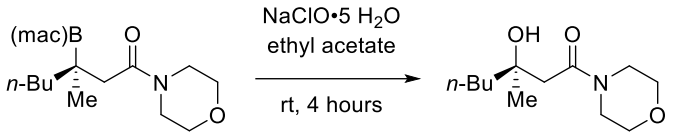
Enriched




| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|---|---|---|
| 1 | Unknown | 11 | 14.450 | 4520529 | 210467 | 5.926 |
| 2 | Unknown | 11 | 20.577 | 71765271 | 1816991 | 94.074 |

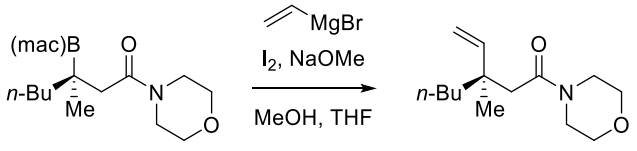
### 1.4.2.4 Transformations of Product

***Oxidation***




**(R)-3-hydroxy-3-methyl-1-morpholinoheptan-1-one (31).** The title compound was prepared according to a literature procedure with slight modification.[7] 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (**3**) (43.5 mg, 0.1 mmol, 1 equiv.) was dissolved in 1 mL ethyl acetate and one drop of water was cooled to 0 ˚C using a ice/water bath. Solid sodium hypochlorite pentahydrate (49.4 mg, 0.3 mmol, 3 equiv.) was added directly. Reaction was allowed to warm to room temperature and stir vigorously for 4 hours. Reaction was quenched with 1 mL saturated aqueous sodium thiosulfate and 1 mL saturated aqueous ammonium chloride. Aqueous layer was extracted three times with ethyl acetate. The collected organic layers were washed with brine, dried with magnesium sulfate, filtered, and concentrated under vacuum. Crude mixture was purified using silica gel column chromatography (silica was deactivated with 2% triethylamine:hexanes and eluted with 40% ethyl acetate:hexanes) to yield the desired product as clear oil (22.2 mg, 96.8% yield). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 3.75 – 3.60 (m, 6H), 3.53 – 3.44 (m, 2H), 2.46 – 2.36 (m, 2H), 1.58 – 1.47 (m, 2H), 1.34 – 1.27 (m, 4H), 1.25 (s, 1H), 1.23 (s, 3H), 0.91 (t, $J$ = 7.0 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 171.7, 71.4, 67.0, 66.7, 46.2, 42.3, 41.8, 41.3, 27.1, 26.4, 23.4, 14.3.; IR (neat): $\nu_{max}$ 3424.76 (bm), 2955.09 (m), 2923.37 (m), 2853.99 (m), 1617.23 (s), 1115.24 (s) cm$^{-1}$. HRMS (DART) for $C_{12}H_{24}NO_3$ $[M+H]^+$: Calc'd: 230.17507, found: 230.17604. $[\alpha]^{20}_D$: 2.060 (c = 4.3 mg/mL, $CHCl_3$, $l$ = 50 mm).

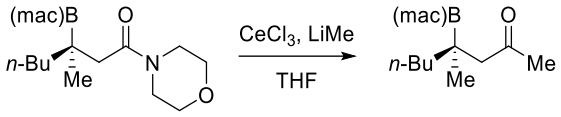
***Olefination***




**(R)-3-methyl-1-morpholino-3-vinylheptan-1-one (30).** The title compound was prepared according to a literature procedure with slight modification.[8] To an oven dry vial and stir bar was

added 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (**3**) (87.1 mg, 0.2 mmol, 1 equiv.) and 2 mL dry THF under nitrogen atmosphere. The resulting was chilled to 0 ˚C using a ice/water bath. Vinyl magnesium bromide solution 1M in THF (0.8 mL, 0.8 mmol, 4 equiv.) was added dropwise via syringe. Reaction was allowed to warm up to room temperature and stir for 30 minutes. The resulting orange solution was then cooled to -78 ˚C using a dry ice/acetone bath and a solution of iodine (203 mg, 0.8 mmol, 4 equiv.) in 1.5 mL anhydrous MeOH was added dropwise via syringe. The resulting red mixture was allowed to stir for 30 minutes at that temperature. A solution of sodium methoxide (86.4 mg, 1.6 mmol, 8 equiv.) in 2 mL anhydrous methanol was added dropwise via syringe. The resulting mixture was allowed to warm to room temperature and stir for 1 hour. Reaction was quenched with saturated aqueous sodium thiosulfate. The aqueous layer was extracted three times with ethyl acetate. The collected organics were dried with magnesium sulfate, filtered and concentrated under vacuum to yield an orange oil. The crude mixture was purified using silica gel chromatography (eluted with 50% diethyl ether:pentane) to yield a clear oil (33.1 mg, 69.1% yield). $^{1}$H NMR (400 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.02 (d, *J* = 10.8 Hz, 1H), 4.95 (d, *J* = 17.5 Hz, 1H), 3.77 – 3.55 (m, 6H), 3.55 – 3.41 (m, 2H), 2.42 – 2.27 (m, 2H), 1.56 – 1.40 (m, 2H), 1.35 – 1.16 (m, 4H), 1.13 (s, 3H), 0.88 (t, *J* = 7.1 Hz, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 170.0, 146.4, 112.1, 67.2, 66.8, 47.2, 42.8, 41.9, 40.9, 39.9, 26.5, 23.5, 23.1, 14.3.; IR (neat): $\nu_{max}$ 2955.24 (m), 2925.66 (m), 2855.78 (m), 1636.43 (s), 1456.33 (m), 1419.09 (m), 1115.47 (s) $cm^{-1}$. HRMS (DART) for $C_{14}H_{26}NO_2$ $[M+H]^+$: Calc'd: 240.19581, found: 240.19561. $[\alpha]^{20}_D$: -6.019 (c = 1g/100 mL, $CHCl_3$, *l* = 50 mm).

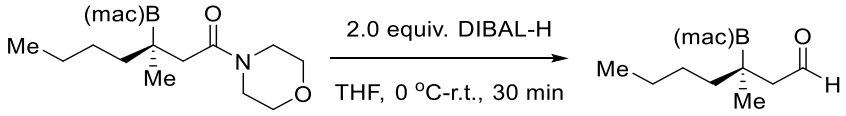
***Methylation***




**(S)-4-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-4-methyloctan-2-one (29)**. The title compound was prepared according to a literature procedure with slight modification.[9] In the glovebox, an oven-dried 25 mL round bottom flask and magnetic stir bar was charged with cerium chloride (296 mg, 1.2 mmol) and 5 mL of anhydrous THF. Out of the glovebox, the white slurry was placed under positive pressure of nitrogen

atmosphere and cooled to -78 ˚C using a dry ice/acetone bath. 1.6 M methyllithium in diethyl ether solution (075 mL, 1.2 mmol) was added dropwise via syringe at that temperature. After stirring for 10 minutes, the mixture was warmed 0 ˚C using an ice/water bath and stir for an additional 10 minutes. This mixture was cooled to -78 ˚C without stirring and the supernatant was used. This supernatant (0.2 M "$MeCeCl_2$", 3 mL, 0.6 mmol, 6 equiv.) was added dropwise to a solution of 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (**3**) (43.5 mg, 0.1 mmol, 1 equiv.) in 0.5 mL THF that was chilled to -78 ˚C. After allowing the reaction to stir at -78 ˚C for 15 minutes and was quenched with 1 mL methanol. At room temperature was diluted with water and the aqueous layer was extracted three times with ethyl acetate. The collected organics were washed with brine, dried with magnesium sulfate, filtered, and concentrated under vacuum. The crude mixture was purified using silica gel chromatography (eluted with 5% acetone:hexanes) to yield a white solid (20.1 mg, 55.1% yield) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.46 (m, 4H), 2.61 (d, *J* = 17.8 Hz, 1H), 2.31 (d, *J* = 17.8 Hz, 1H), 2.04 (s, 3H), 1.83 (s, 3H), 1.74 (s, 3H), 1.33 – 1.20 (m, 1H), 1.19 – 1.07 (m, 1H), 1.03 – 0.95 (m, 1H), 0.96 – 0.73 (m, 5H), 0.61 – 0.47 (m, 1H), 0.41 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 209.3, 145.5, 135.0, 131.4, 128.5, 125.0, 119.4, 91.82, 91.77, 55.15, 38.99, 30.18, 27.37, 23.17, 21.94, 21.88, 21.45, 13.78. $^{11}$B NMR (160 MHz, $CDCl_3$) δ 35.04. IR (neat): $\nu_{max}$ 3041.97 (w), 2953.67 (m), 2953.367 (m), 2867.94 (m), 1709.60 (s), 1116.56 (s), 781.19 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{29}BO_3$ $[M+H]^+$: Calc'd: 364.22825, found: 365.22882. $[\alpha]^{20}_D$: 3.599 (c = 1g/100 mL, $CHCl_3$, *l* = 50 mm).

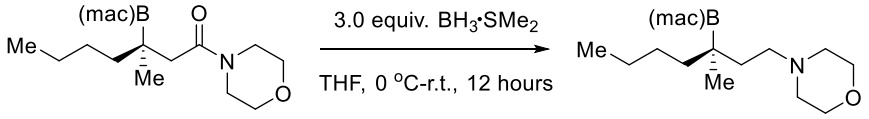
***Reduction to Aldehyde***




**(S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methylheptanal (32).** To an oven-dried 2-dram vial equipped with a magnetic stir bar in an argon-filled glovebox was added 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (**3**) (43.5 mg, 0.1 mmol, 1.0 equiv.) and THF (1.0 mL). This flask was sealed with a septum, and then removed from the glovebox. The flask was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. Commercial

DIBAL-H solution (1 M in hexane, 0.20 mL, 2.0 equiv.) was added dropwise. Reaction was allowed to warm up to room temperature and stirred for 30 min. Then, reaction was quenched by 0.5 mL methanol and filtered through a silica plug eluted with diethyl ether and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (eluted with 5% ethyl acetate in hexane) to isolate the title compound (25.0 mg, 0.0714 mmol, 70.5% yield) as a white solid. Product Rf = 0.55 in 10% ethyl acetate: 90% hexane (UV active and stains pale yellow with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.60 – 7.51 (m, 4H), 2.53 (d, *J* = 17.1 Hz, 1H), 2.23 (d, *J* = 17.1 Hz, 1H), 1.77 (d, *J* = 23.6 Hz, 6H), 1.25 – 1.19 (m, 2H), 1.17 – 1.11 (m, 1H), 0.95 – 0.92 (m, 2H), 0.89 (s, 3H), 0.80 – 0.74 (m, 1H), 0.53 (t, *J* = 7.1 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 203.4, 145.1, 145.0, 134.9, 131.4, 128.51, 128.49, 125.25, 125.23, 119.49, 119.44, 92.1, 54.2, 39.3, 27.6, 23.2, 22.1, 22.0, 21.9, 13.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 31.9.; IR (neat): $\nu_{max}$, 2955.93 (m), 2928.01 (m), 2870.23 (m), 1719.90 (s), 1467.28 (m), 1117.15 (s), 1087.32 (s), 781.85 (s) cm$^{-1}$. HRMS (DART) for $C_{22}H_{27}BO_3$ $[M+H]^+$: Calc'd: 351.21260, found: 351.21289. $[\alpha]^{20}_D$: 2.001 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

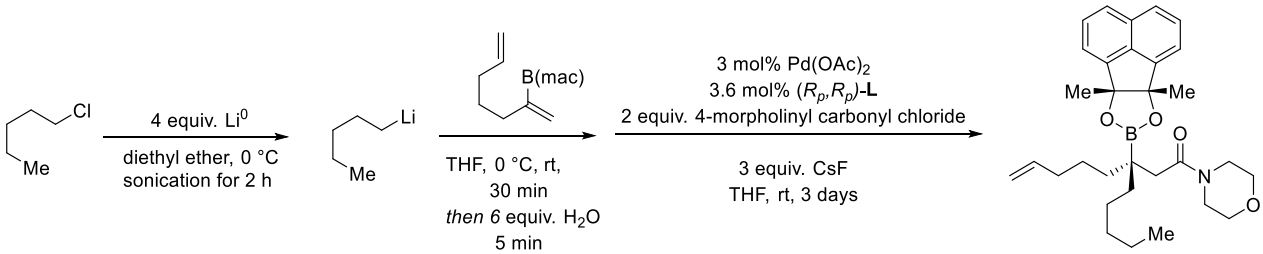
***Reduction to Amine***




**4-((S)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methylheptyl)morpholine (33).** To an oven-dried 2-dram vial equipped with a magnetic stir bar in an argon-filled glovebox was added 3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-3-methyl-1-morpholinoheptan-1-one (**3**) (43.5 mg, 0.1 mmol, 1.0 equiv.) and THF (1.0 mL). This flask was sealed with a septum, and then removed from the glovebox. The flask was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. Borane dimethyl sulfide (neat, 22.8 mg, 0.30 mmol, 3.0 equiv.) was added. Reaction was allowed to warm up to room temperature and stirred for 12 hours. Then, reaction was quenched by 3 mL $H_2O$ and extracted with diethyl ether for 3 times. Ether solution was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (eluted with 10% ethyl acetate in hexane) to isolate the title

compound (36.8 mg, 0.0873mmol, 87.3% yield) as a colorless oil. Product Rf = 0.55 in 20% ethyl acetate: 80% hexane (UV active and stains pale yellow with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.1 Hz, 2H), 7.62 – 7.53 (m, 4H), 3.87 (q, *J* = 8.7 Hz, 2H), 3.23 (dd, *J* = 31.7, 12.5 Hz, 2H), 2.60 (dd, *J* = 25.3, 12.3 Hz, 2H), 2.41 (td, *J* = 12.2, 4.7 Hz, 1H), 2.17 (td, *J* = 12.3, 3.8 Hz, 1H), 2.06 (q, *J* = 9.6 Hz, 2H), 1.77 (s, 6H), 1.68 – 1.63 (m, 1H), 1.55 – 1.51 (m, 1H), 1.39 (d, *J* = 7.6 Hz, 1H), 1.16 (d, *J* = 9.5 Hz, 4H), 1.03 (dd, *J* = 12.0, 7.1 Hz, 1H), 0.87 (s, 3H), 0.78 (t, *J* = 6.8 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 145.0, 144.9, 134.6, 131.5, 128.64, 128.57, 125.53, 125.46, 119.64, 119.58, 92.1, 61.66, 61.55, 57.9, 56.6, 39.2, 31.9, 27.9, 23.4, 22.1, 21.9, 21.1, 14.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 35.5.; IR (neat): $\nu_{max}$, 2956.71 (m), 2929.81 (m), 2870.72 (m), 2367.40 (br), 1459.80 (m), 1116.51 (s), 1077.45 (s), 783.15 (s) $cm^{-1}$. HRMS (DART) for $C_{26}H_{36}BNO_3$ $[M+H]^+$: Calc'd: 422.28610, found: 422.28687. $[\alpha]^{20}_D$: 10.998 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

### 1.4.2.5 Synthesis of (+)-Adalinine




**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-pentyloct-7-en-1-one (34).** To an oven-dried 25 ml round bottom flask equipped with a magnetic stir bar in an argon-filled glovebox was added 6bR,9aS)-8-(hepta-1,6-dien-2-yl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (**S-4**) (632.2 mg, 2.0 mmol, 1.0 equiv.) and THF (4.0 mL). This flask was sealed with a septum, and then removed from the glovebox. The flask was placed under a nitrogen atmosphere and cooled to 0 ˚C using an ice bath. To a separate oven-dried 25.0 ml round bottom flask equipped with a magnetic stir bar was added n-pentyl chloride (532.97 mg, 5.0 mmol) and diethyl ether (10.0 ml) under argon. Lithium metal (154.10 mg, 20.0 mmol) was added at room temperature. Reaction was cooled down to 0 ˚C and sonicated at this temperature for 2 hours. Concentration of n-pentyllithium solution was determined to be 0.44 M (88% conversion from n-pentyl chloride) by using BHT titration and 1,10-phenathroline as indicator. Suitable amount of this n-pentyllithium solution (4.54 mL, 2.0

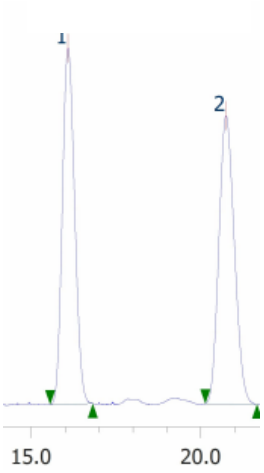
mmol, 1 equiv.) was added into boronic ester solution via syringe at 0 ˚C. Reaction was allowed to warm up to room temperature and stirred for 30 min. Then, deionized water (0.216 mL, 12.0 mmol, 6 equiv.) was added via syringe and allowed to stir for an additional 5 minutes. The solvent was carefully removed under reduced pressure and was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (13.5 mg, 0.06 mmol, 0.03 equiv.), ($R_p$,$R_p$)-**L** (75.8 mg, 0.072 mmol, 0.036 equiv.), and 2 mL THF. This palladium solution was allowed to stir for 15 minutes at room temperature. Cesium fluoride (911.3 mg, 6.0 mmol, 3 equiv.) was added to the "ate" flask, followed by palladium solution, then 10 mL THF, and finally carbamoyl chloride (593.3 mg, 4.0 mmol, 2 equiv.) by mass. The reaction flask was sealed with a rubber septum, taped, and brought out of the glovebox. The reaction was stirred at room temperature for 3 days. The resulting mixture was filtered through a silica plug eluted with diethyl ether and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (eluted with 40% diethyl ether: toluene) to isolate the title compound (693.0 mg, 1.37 mmol, 68.5% yield) as a white solid. Product Rf = 0.60 in 50% diethyl ether: 50% toluene (UV active and stains pale yellow with potassium permanganate stain).; $^1$H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.52 (dd, *J* = 16.4, 7.3 Hz, 4H), 5.51 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 4.84 – 4.73 (m, 2H), 3.59 (dt, *J* = 32.3, 4.8 Hz, 4H), 3.38 (t, *J* = 4.9 Hz, 4H), 2.29 (d, *J* = 1.8 Hz, 2H), 1.75 (d, *J* = 1.3 Hz, 8H), 1.33 – 1.18 (m, 4H), 1.05 – 0.86 (m, 7H), 0.78 (ddq, *J* = 11.4, 7.0, 4.4 Hz, 1H), 0.68 (t, *J* = 7.0 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 173.8, 146.9, 139.4, 135.1, 131.2, 128.3, 124.4, 118.91, 118.89, 113.8, 90.6, 66.8, 66.5, 45.9, 42.8, 41.11, 41.10, 34.5, 33.5, 33.1, 32.6, 23.8, 23.6, 22.6, 22.32, 22.31, 14.03.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.6.; IR (neat): $\nu_{max}$, 2968.22 (m), 2926.03 (m), 2855.75 (m), 1633.18 (s), 1457.99 (m), 1114.54 (s), 1081.15 (s), 781.28 (s) cm$^{-1}$. HRMS (DART) for $C_{31}H_{42}BNO_4$ $[M+H]^+$: Calc'd: 504.32797, found: 504.32885. $[\alpha]^{20}_D$: 12.789 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with $Pd(OAc)_2$ (3 mol%) and BrettPhos (3.6 mol%) as the catalyst.

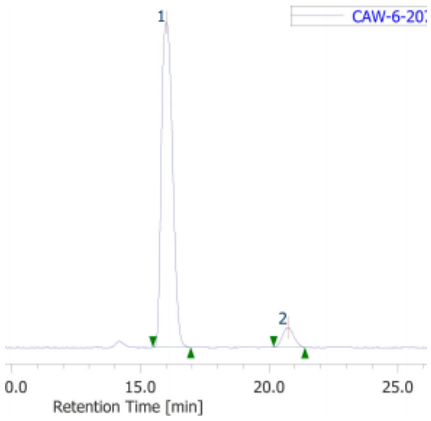
*Chiral SFC (Chiralcel AD-H, 10% IPA, 1.0 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho-[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-pentyloct-7-en-1-one*

Racemic

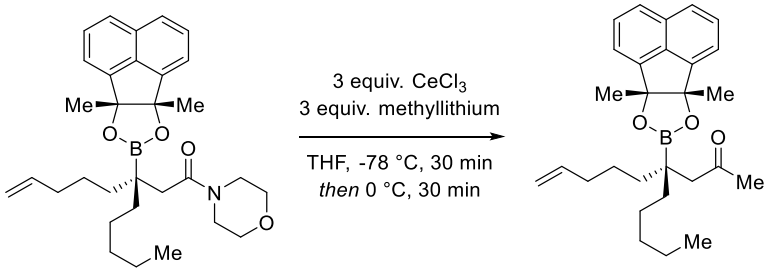



| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|---|---|---|
| 1 | Unknown | 11 | 16.080 | 4680576 | 186078 | 49.549 |
| 2 | Unknown | 11 | 20.733 | 4765772 | 150720 | 50.451 |

Enriched

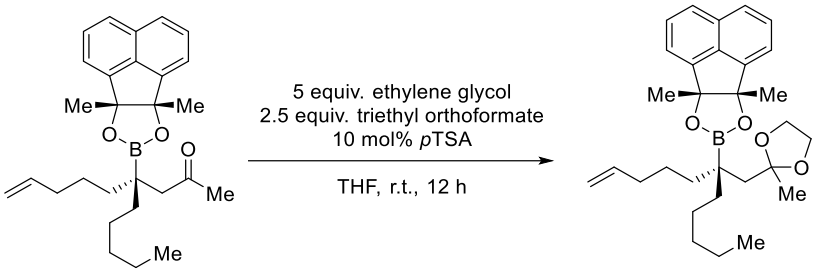



| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% |
|---|---|---|---|---|---|---|
| 1 | Unknown | 11 | 15.997 | 46973169 | 1560917 | 94.126 |
| 2 | Unknown | 11 | 20.720 | 2931329 | 94493 | 5.874 |



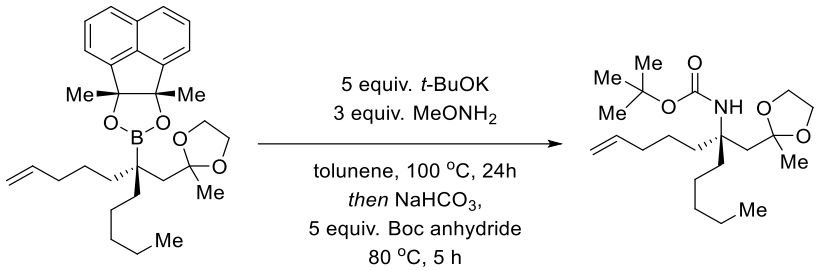

**(R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-pentyloct-7-en-1-one (35)** To an oven-dried 25 ml round bottom flask equipped with a magnetic stir bar in an argon-filled glovebox was added $CeCl_3$ (1.21 g, 4.85 mol) and 20.0 mL THF. This flask was sealed with a septum, and then removed from the glovebox. The flask was placed under a nitrogen atmosphere and cooled to -78 ˚C using an acetone-dry ice bath. Commercial methyllithium solution (1.6 M in ether, 3 mL, 4.8 mol) was added dropwise via syringe. Reaction was stirred at -78 ˚C for 15 min and then at 0 ˚C for 10 min. Then, reaction was cooled to and kept at -78 ˚C without stirring. Supernatant of this solution was deemed as a 0.2 M methylcerium solution. To a separate 50 mL round bottom flask was added (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-

pentyloct-7-en-1-one (**34**) (700.0 mg, 1.39 mmol, 1.0 equiv.) and 4.0 mL THF under argon. Reaction was cooled down to -78 ˚C. Then, the freshly prepared methylcerium solution was added (20.8 mL, 4.2 mmol, 3 equiv.) while stirring. Reaction was stirred at -78 ˚C for 30 min and then at 0 ˚C for another 30 min. The reaction was then quenched using 1.0 mL methanol and filtered through a silica plug eluted with diethyl ether and concentrated under reduced pressure. The resulting crude mixture was purified by silica gel chromatography (eluted with 3% ethyl acetate: hexane) to isolate the title compound (402.0 mg, 0.930 mmol, 66.2% yield) as a white solid. Product Rf = 0.50 in 10% ethyl acetate: 90% hexane (UV active and stains yellow with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.59 – 7.50 (m, 4H), 5.46 (ddt, *J* = 17.1, 11.2, 6.7 Hz, 1H), 4.80 – 4.70 (m, 2H), 2.50 (s, 2H), 2.04 (s, 3H), 1.78 (d, *J* = 4.3 Hz, 6H), 1.72 (dd, *J* = 15.0, 7.2 Hz, 2H), 1.27 – 1.17 (m, 4H), 1.02 (dd, *J* = 13.3, 6.3 Hz, 1H), 0.93 (ddd, *J* = 28.4, 8.0, 4.1 Hz, 5H), 0.84 (dt, *J* = 12.6, 6.8 Hz, 1H), 0.73 – 0.68 (m, 1H), 0.63 (t, *J* = 6.9 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 209.3, 145.6, 139.1, 134.9, 131.4, 128.4, 125.0, 119.3, 114.0, 91.68, 91.67, 51.2, 34.3, 33.7, 33.1, 32.42, 32.41, 30.2, 23.9, 23.7, 22.5, 21.9, 13.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 35.4.; IR (neat): $\nu_{max}$, 2927.75 (m), 2857.64 (m), 1710.57 (s), 1458.53 (m), 1116.96 (s), 1078.96 (s), 825.10 (s), 781.07 (s) cm$^{-1}$. HRMS (DART) for $C_{28}H_{37}BO_3$ $[M+H]^+$: Calc'd: 433.29085, found: 433.29090. $[\alpha]^{20}_D$: 9.299 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).



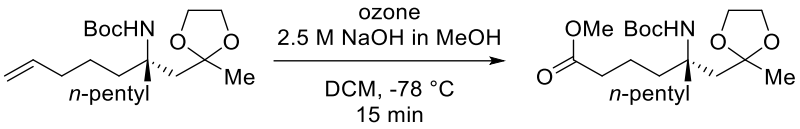

**((6bR,9aS)-6b,9a-dimethyl-8-((R)-6-((2-methyl-1,3-dioxolan-2-yl)methyl)undec-1-en-6-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-6)**. To an oven dried 2-dram vial and stir bar was charged with (R)-3-((6bR,9aS)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-1-morpholino-3-pentyloct-7-en-1-one (**35**) (370 mg, 0.856 mmol, 1.0 equiv.), 2 ml dry toluene, 4-methylbenzenesulfonic acid monohydrate (16.28 mg, 0.0856 μmol, 10 mmol%), triethyl orthoformate (317.03 mg, 2.14 mmol, 2.5 equiv.) and then lastly ethylene glycol (265.56 mg, 4.28 mmol, 5.0 equiv.). Reaction was allowed to stir for 12 hours. The resulting mixture was filtered through a silica plug eluted with diethyl ether and concentrated under reduced

pressure. The resulting crude mixture was purified by silica gel chromatography (eluted with 3% ethyl acetate: hexane) to isolate the title compound (370.0 mg, 0.776 mmol, 90.7% yield) as a white solid. Product Rf = 0.45 in 10% ethyl acetate: 90% hexane (UV active and stains yellow with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.7 Hz, 2H), 7.61 – 7.50 (m, 4H), 5.74 – 5.61 (m, 1H), 4.95 – 4.79 (m, 2H), 3.26 (dt, *J* = 14.2, 8.1 Hz, 4H), 1.88 (q, *J* = 7.1 Hz, 2H), 1.75 (d, *J* = 14.2 Hz, 8H), 1.30 (dd, *J* = 18.7, 7.9 Hz, 6H), 1.13 (dt, *J* = 12.4, 7.7 Hz, 5H), 1.00 (s, 4H), 0.77 (t, *J* = 6.9 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 145.93, 145.90, 139.5, 135.2, 131.2, 128.39, 128.37, 124.77, 124.76, 119.3, 113.9, 109.8, 91.3, 63.45, 63.41, 44.7, 34.6, 33.0, 32.7, 32.2, 25.2, 23.2, 22.9, 22.7, 22.5, 22.25, 22.23, 14.19, 14.15.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.2.; IR (neat): $\nu_{max}$, 2928.24 (m),1377.94 (m), 1293.32 (s), 1263.54 (m), 1115.86 (s), 1079.16 (s), 825.56 (s), 780.51 (s) $cm^{-1}$. HRMS (DART) for $C_{30}H_{41}BO_4$ $[M+H]^+$: Calc'd: 477.31707, found: 477.31931. $[\alpha]^{20}_D$: 11.998 (c = 1.0 g/mL, $CHCl_3$, *l* = 50 mm).



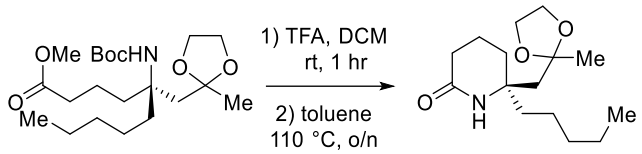

**tert-butyl (S)-(6-((2-methyl-1,3-dioxolan-2-yl)methyl)undec-1-en-6-yl)carbamate (36)**. The title compound was prepared according to a literature procedure with slight modification.[10] In the glovebox, an oven dried 4-dram vial was added *t*-BuOK (280.52 mg, 2.50 mmol, 5 equiv.), ((6bR,9aS)-6b,9a-dimethyl-8-((R)-6-((2-methyl-1,3-dioxolan-2-yl)methyl)undec-1-en-6-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (**S-6**) (238.23 mg, 0.5 mmol) and THF (5.0 mL). Vial was sealed by a septum cap and removed out of glovebox. Previously prepared $MeONH_2$ solution (2.0 M, 0.750 mL, 3 equiv.) was taken out of the freezer and allowed to warm to room temperature before adding to the reaction mixture via syringe. Reaction was slowly heated to 100 ˚C and allowed to stir at that temperature for 24 hours. Then, reaction was allowed to cool to 80 ˚C. Then, Boc anhydride (545.62 mg, 2.5 mmol, 5.0 equiv.) was added, followed by 1 mL saturated $NaHCO_3$ water solution. Reaction was stirred at 80 ˚C for 5 hours. Then reaction was quenched with water and extracted three times with ether. The collected organics were washed with brine, dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The resulting crude mixture was purified by silica gel chromatography (eluted with 10% ethyl acetate: hexane) to isolate the title compound (145.5 mg, 0.394 mmol, 78.5% yield) as a white solid. Product Rf = 0.6 in 20% ethyl acetate: 80% toluene (UV inactive but stains yellow with potassium permanganate stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.0, 10.2, 6.6 Hz, 1H), 5.11 –

4.91 (m, 3H), 3.93 (s, 4H), 2.07 – 1.97 (m, 4H), 1.71 (s, 4H), 1.41 (s, 9H), 1.34 (s, 4H), 1.30 – 1.20 (m, 7H), 0.87 (t, $J$ = 7.1 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 156.9, 139.0, 114.4, 110.3, 81.6, 64.4, 64.09, 64.08, 56.8, 34.1, 32.2, 28.5, 28.3, 26.3, 25.6, 23.1, 23.0, 22.7, 14.1.; IR (neat): $\nu_{max}$, 3393.87 (br), 2931.02 (m), 1717.78 (s), 1498.95 (s), 1365,20 (s), 1116.74 (s), 1082.15 (s), 908.98 (s), 779.91 (s) $cm^{-1}$. HRMS (DART) for $C_{21}H_{39}NO_4$ $[M+H]^+$: Calc'd: 370.29519, found: 370.29484. $[\alpha]^{20}_D$: 11 (c = 1.0 g/mL, $CHCl_3$, $l$ = 50 mm).

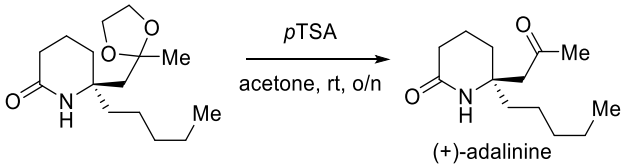



**methyl(S)-5-((tert-butoxycarbonyl)amino)-5-((2-methyl-1,3-dioxolan-2-yl)methyl)decanoate (37).** The title compound was prepared according to a literature procedure with slight modification.[11] A 2.5 M methanolic NaOH was freshly prepared by mixing pulverized solid NaOH and dry methanol under a nitrogen in an oven dry vial equipped with a magnetic stir bar. Mixture was allowed to stir for 1 hour at room temperature. A solution tert-butyl (S)-(6-((2-methyl-1,3-dioxolan-2-yl)methyl)undec-1-en-6-yl)carbamate (**36**) (115 mg, 311.20 µmol, 1 equiv.) in 15 mL dry dichloromethane and 2.5 M methanolic NaOH (0.622 mL, 1.56 mmol, 5 equiv.)was stirred at -78 ˚C using dry an ice/acetone bath. Ozone was passed through the solution. Clear solution changed to an orange color and an orange precipitate formed. After about 10 minutes, orange solution changed to a blue color, indicating reaction completion. The reaction mixture was diluted with diethyl ether and water and allowed to warm to room temperature. The aqueous layer was extracted three times with ether and collect organic layers were dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude mixture was purified by silica gel chromatography with deactivated silica (2% triethylamine:98% hexanes) and eluted with 10% ethyl acetate:hexanes to isolate the title compound (65.3 mg, 0.163 mmol, 52.3% yield) as a clear oil. Product Rf = 0.4 in 20% ethyl acetate: 80% hexanes (not UV active and stains blue with *para*-anisaldehyde stain).; $^1$H NMR (500 MHz, $CDCl_3$) δ 5.15 (s, 1H), 3.93 (s, 3H), 3.66 (s, 3H), 2.29 (t, $J$ = 7.5 Hz, 2H), 1.99 (s, 2H), 1.82 – 1.51 (m, 6H), 1.41 (s, 10H), 1.35 – 1.17 (m, 9H), 0.88 (t, $J$ = 7.3 Hz, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 174.3, 110.4, 64.19, 64.18, 56.9, 51.6, 41.3, 34.5, 34.1, 32.3, 32.1, 28.6, 28.5, 25.7, 23.3, 22.8, 19.4, 19.0, 14.22. IR (neat): $\nu_{max}$, 3381.54 (bm), 2952.02 (m), 2928.94 (m), 2869.76 (m), 1736.51 (s), 1715.18 (s), 1501.05 (m), 1364.00 (m),

1166.11 (s) $cm^{-1}$. HRMS (DART) for $C_{21}H_{40}NO_6$ $[M+H]^+$: Calc'd: 402.28501, found: 402.28522. $[\alpha]^{20}_D$: 5.5 (c = 1.0 g/ 100 mL, $CHCl_3$, *l* = 50 mm).




**(S)-6-((2-methyl-1,3-dioxolan-2-yl)methyl)-6-pentylpiperidin-2-one (38).** To an oven-dried vial equipped with a magnetic stir bar and septum under nitrogen was charged with methyl 5-(tert-butoxycarbonylamino)-5-[(2-methyl-1,3-dioxolan-2-yl)methyl]decanoate (120.6 mg, 300.35 μmol, 1 equiv.) (**37**) and 5 mL dry dichloromethane. Trifluoroacetic acid (0.440 mL, 5.7 mmol, 20 equiv.) was added via syringe dropwise at room temperature. Reaction was allowed stir at that temperature for 1 hour. Reaction was quenched with saturated sodium bicarbonate (aqueous). Aqueous layer was extracted 3 times with ethyl ether. Collected organics were washed with brine, dried with magnesium sulfate, filtered, and concentrated under vacuum to yield a clear oil. The resulting oil was dissolved in 5 mL dry toluene in an oven-dried vial equipped with a magnetic stir bar and enclosed with a telfon lined hard cap and sealed with electrical tape. Solution was heated to 110 ˚C and allowed to stir overnight at that temperature. The resulting solution was allowed to cool to room temperature and concentrated under vacuum. The crude mixture was purified with neutral alumina chromatography eluted with 100% ethyl acetate to isolate the title compound (25.9 mg, 0.096 mmol, 32% yield) as a clear oil. Product Rf is 0.4 in 10% methanol:ethyl acetate (silica TLC plate) (not UV active, stains red with *para*-anisaldehyde stain).; $^1$H NMR (600 MHz, $CDCl_3$) δ 6.71 (s, 1H), 4.07 – 3.90 (m, 4H), 2.35 – 2.24 (m, 2H), 2.03 (d, *J* = 15.2 Hz, 1H), 1.89 (d, *J* = 15.3 Hz, 1H), 1.83 – 1.49 (m, 6H), 1.37 – 1.17 (m, 9H), 0.89 (t, *J* = 7.2 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 171.8, 110.1, 64.1, 63.7, 57.0, 45.9, 40.1, 32.5, 32.4, 30.9, 25.9, 24.0, 22.7, 17.0, 14.2.; IR (neat): $\nu_{max}$ 2950.64 (m), 2929.16 (m), 2869.37 (m), 1656.60 (s), 1457.11 (m), 1401.74 (m), 1374.53 (m), 1040.84 (m) $cm^{-1}$. HRMS (DART) for $C_{15}H_{28}NO_3$ $[M+H]^+$: Calc'd: 270.20637, found: 270.20688. $[\alpha]^{20}_D$: 14 (c = 0.2 g/ 100 mL, $CHCl_3$, *l* = 50 mm)



**(S)-6-(2-oxopropyl)-6-pentylpiperidin-2-one (38).** A vial equipped with a magnetic stir bar was charged with 6-[(2-methyl-1,3-dioxolan-2-yl)methyl]-6-pentyl-piperidin-2-one (20.6 mg, 76.47 μmol, 1 equiv.) and 10 mL of wet acetone. 4-methylbenzenesulfonic acid monohydrate (145.46 mg, 764.72 μmol, 10 equiv.) was added directly at room temperature and reaction was allowed to stir for 8 hours. Reaction was quenched with 1 mL saturated sodium carbonate (aqueous). The aqueous layer was extracted ethyl acetate three times. The collected organics were washed with brine, dried with magnesium sulfate, filtered, and concentrated to yield a clear oil. The crude mixture was purified using neutral alumina chromatography by eluting with 100% ethyl acetate and then 5% methanol:95% ethyl acetate. Product Rf is 0.3 in 10% methanol:ethyl acetate (silica TLC plate) (not UV active, stains red with *para*-anisaldehyde stain).; $^{1}$H NMR (600 MHz, $CDCl_3$) δ 6.57 (s, 1H), 2.69 (d, $J$ = 17.8 Hz, 1H), 2.63 (d, $J$ = 17.8 Hz, 1H), 2.36 – 2.23 (m, 2H), 2.13 (s, 3H), 1.85 – 1.67 (m, 4H), 1.67 – 1.52 (m, 2H), 1.34 – 1.08 (m, 6H), 0.87 (t, $J$ = 7.0 Hz, 3H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 207.3, 171.6, 56.3, 51.4, 39.4, 32.1, 32.0, 31.5, 31.4, 24.0, 22.6, 17.4, 14.1.; IR (neat): $\nu_{max}$ 2950.70 (m), 2928.58 (m), 2858.05 (m), 1704.60 (m), 1656.58 (s), 1455.59 (m), 1401.68 (m), 1361.75 (m) cm$^{-1}$. HRMS (DART) for $C_{13}H_{24}NO_2$ $[M+H]^+$: Calc'd: 226.18016, found: 226.17989 $[\alpha]^{20}_D$: 21 (c = 0.2 g/100 mL, $CHCl_3$, $l$ = 50 mm)

### 1.4.3 Supporting Information References

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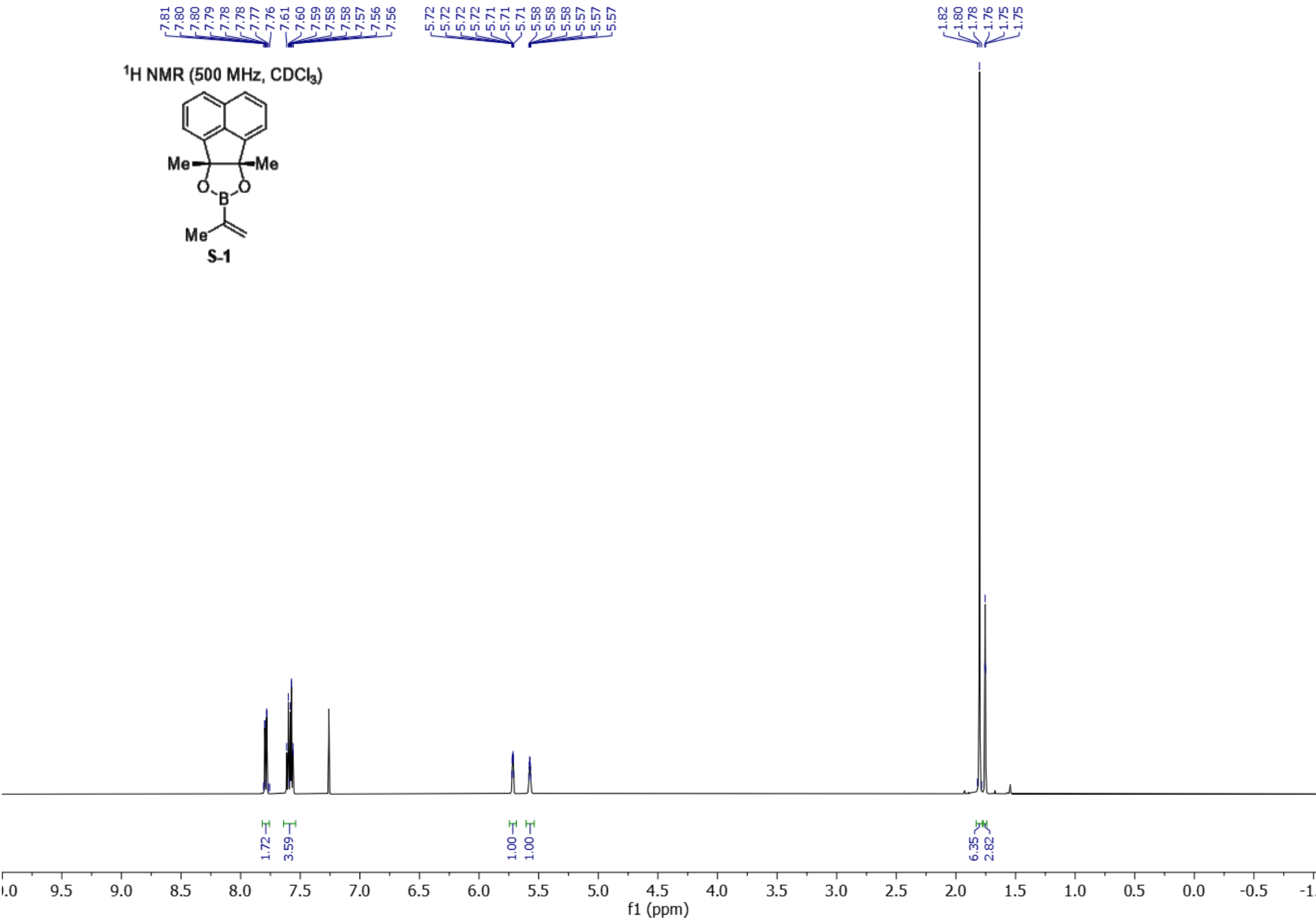
### 1.4.4 NMR Spectra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7.80
7.80
7.79
7.78
7.78
7.77
7.76
7.61
7.60
7.59
7.58
7.58
7.57
7.56
7.56
5.72
5.72
5.72
5.72
5.71
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5.58
5.57
5.57
5.57
1.82
1.80
1.78
1.76
1.75
1.75
1H NMR (500 MHz, CDCl3)
Me
Me
O
B
O
Me
S-1
1.72
3.59
1.00
1.00
6.35
2.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
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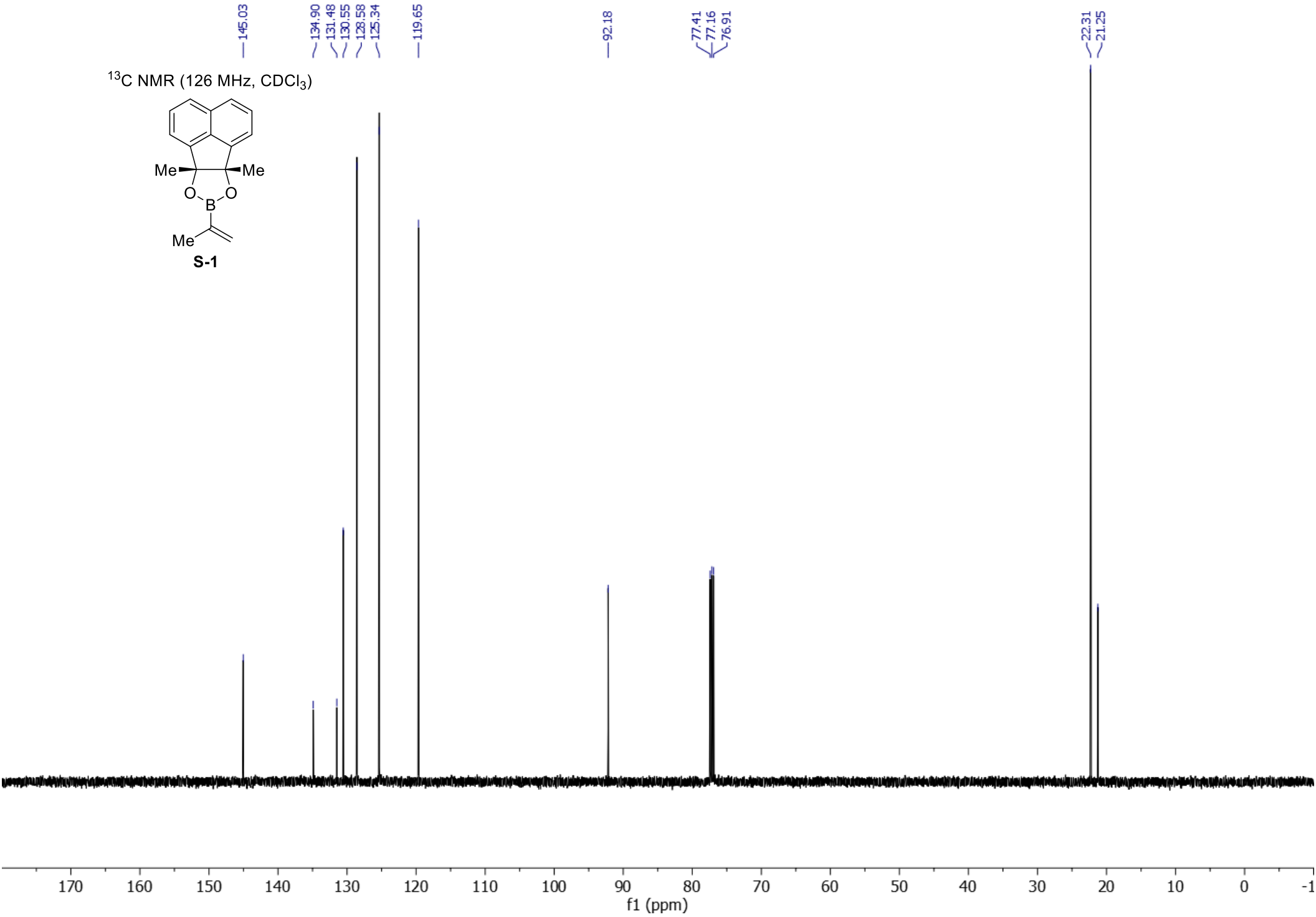
0.5
0.0
-0.5
f1 (ppm)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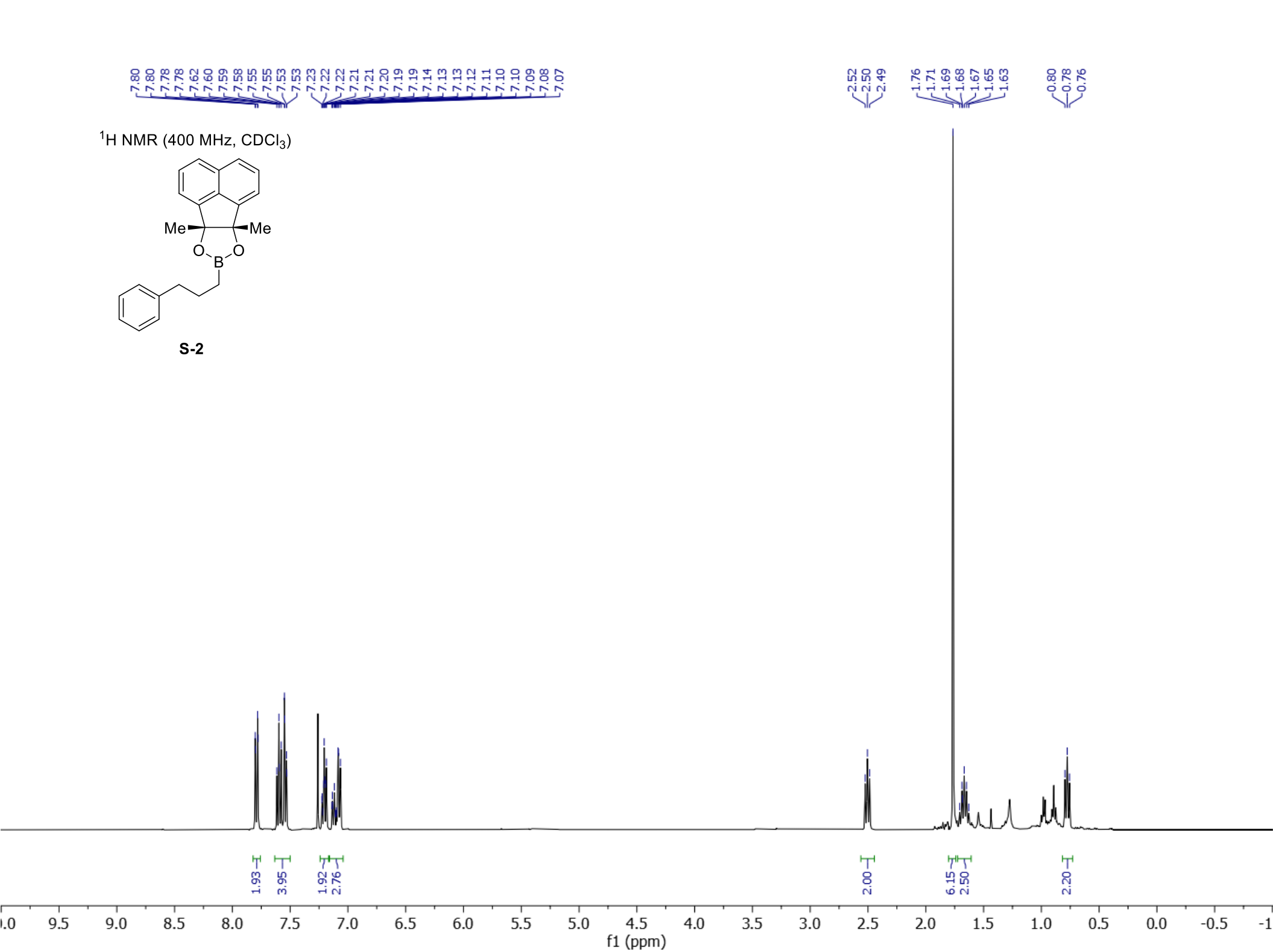
134.90
131.48
130.55
128.58
125.34
119.65
92.18
77.41
77.16
76.91
22.31
21.25
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
O
O
B
Me
S-1
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.80
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7.59
7.58
7.55
7.55
7.53
7.53
7.23
7.22
7.22
7.21
7.21
7.20
7.19
7.19
7.14
7.13
7.13
7.12
7.11
7.10
7.10
7.09
7.08
7.07
2.52
2.50
2.49
1.76
1.71
1.69
1.68
1.67
1.65
1.63
0.80
0.78
0.76
1H NMR (400 MHz, CDCl3)
Me
Me
O
O
B
S-2
1.93
3.95
1.92
2.76
2.00
6.15
2.50
2.20
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
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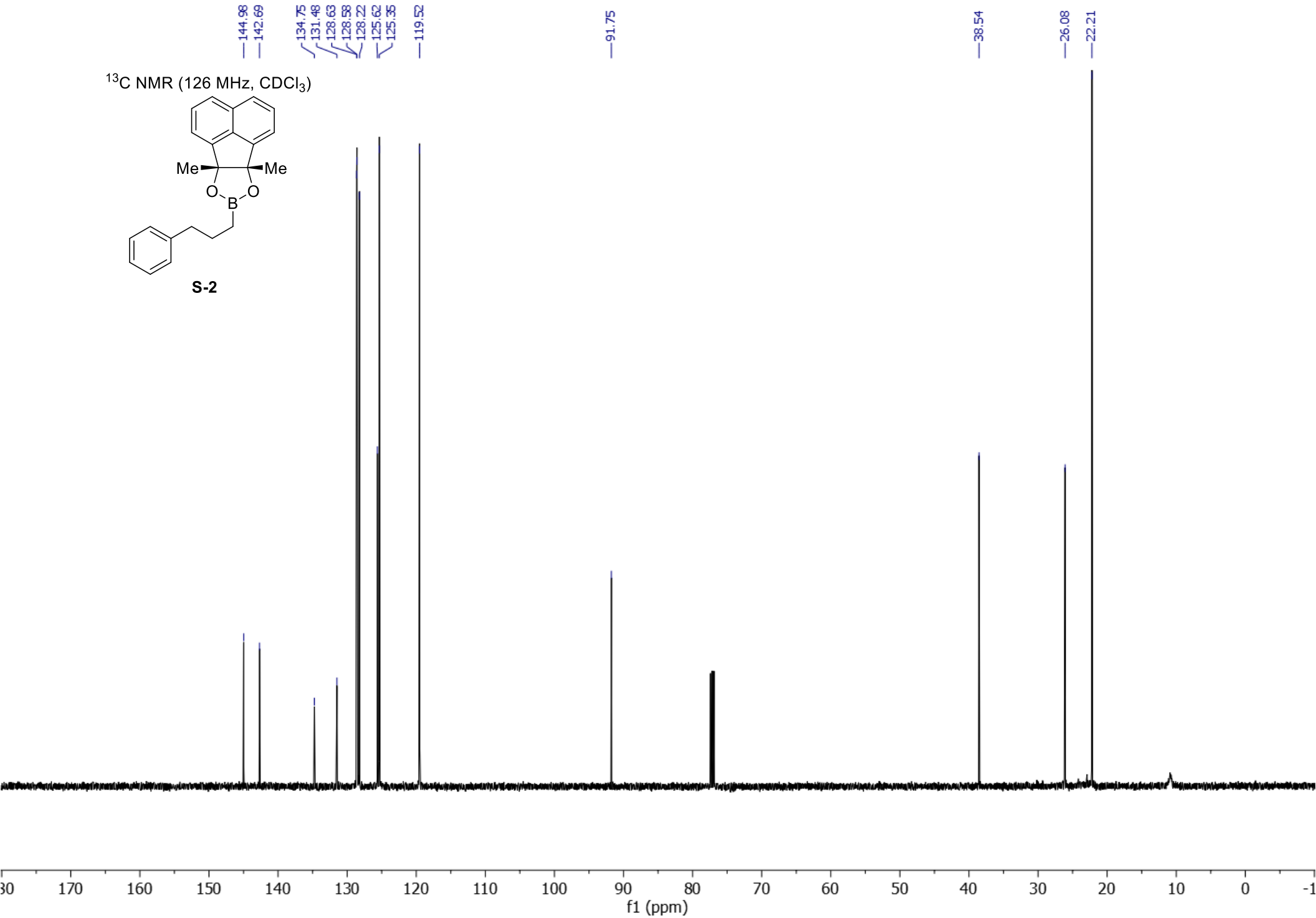
1.0
0.5
0.0
-0.5
f1 (ppm)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119.52
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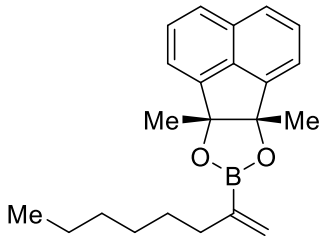
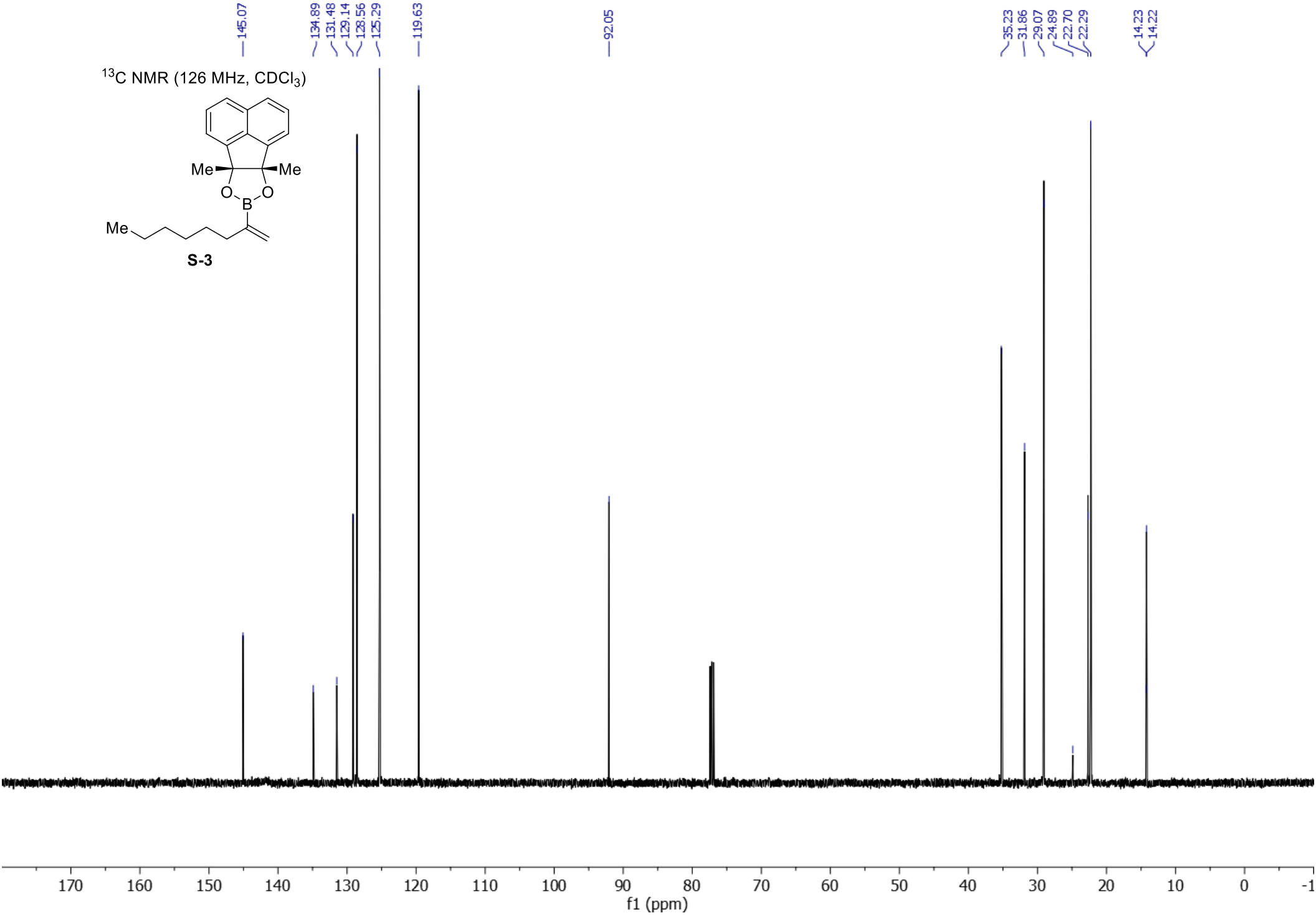
26.08
22.21
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
S-2
f1 (ppm)

$^1$H NMR (600 MHz, $CDCl_3$)




**S-3**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128.56
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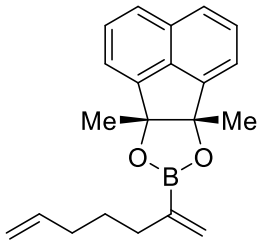
24.89
22.70
22.29
14.23
14.22
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
Me
S-3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

$^1$H NMR (600 MHz, $CDCl_3$)

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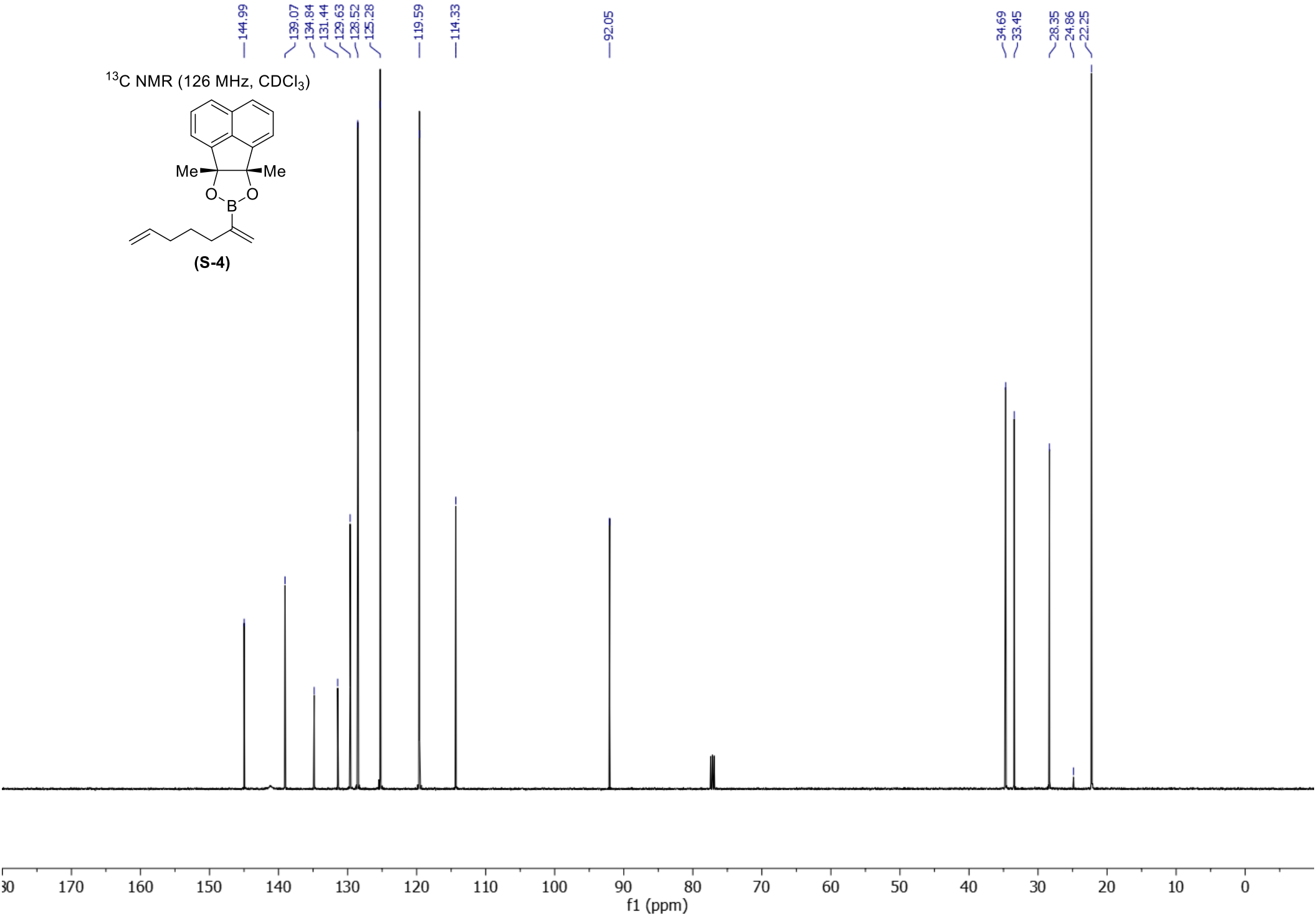
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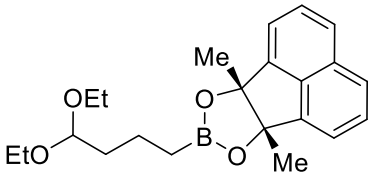
114.33
92.05
34.69
33.45
28.35
24.86
22.25
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
O
B
O
(S-4)
f1 (ppm)

$^1$H NMR (500 MHz, $CDCl_3$)

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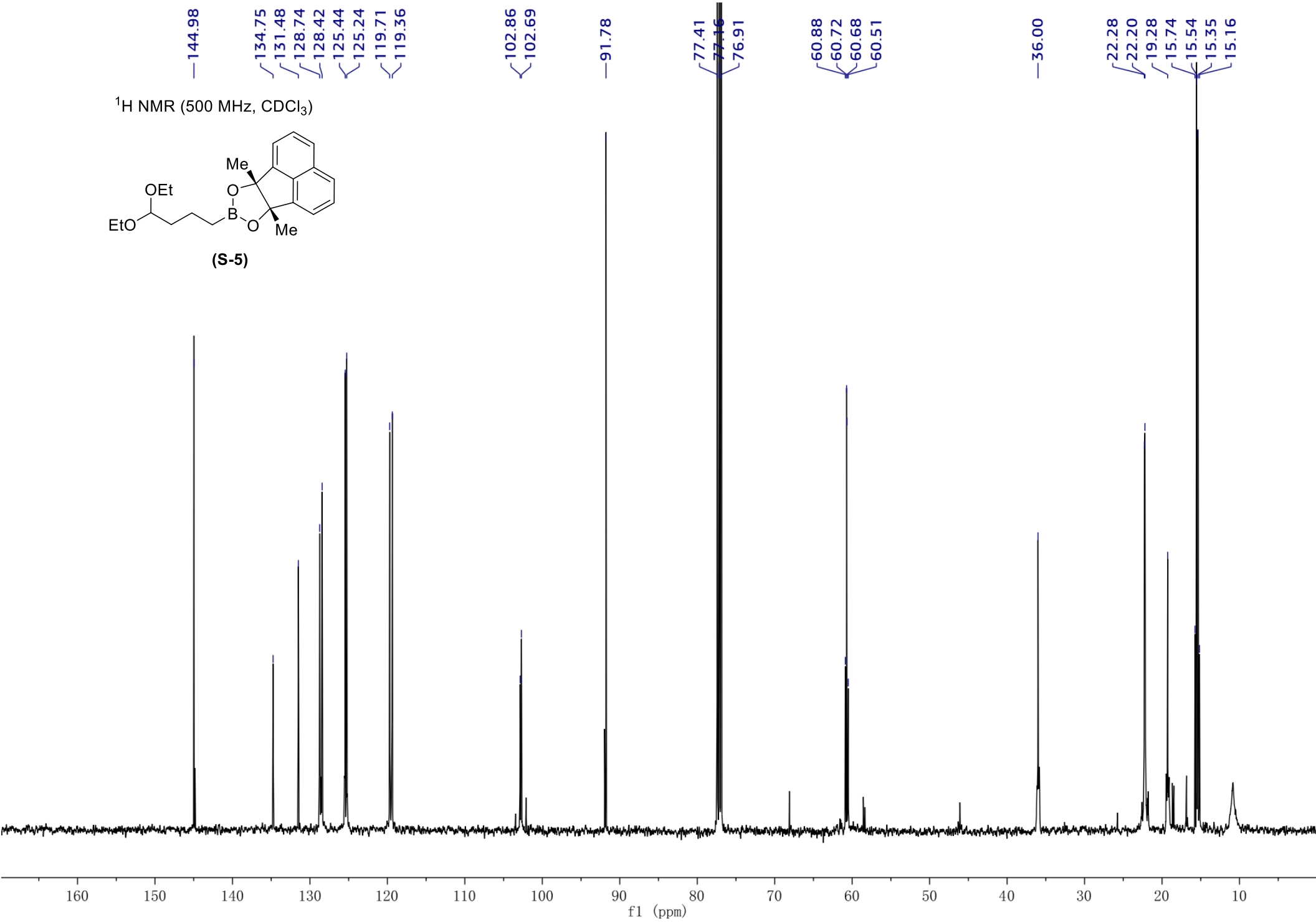
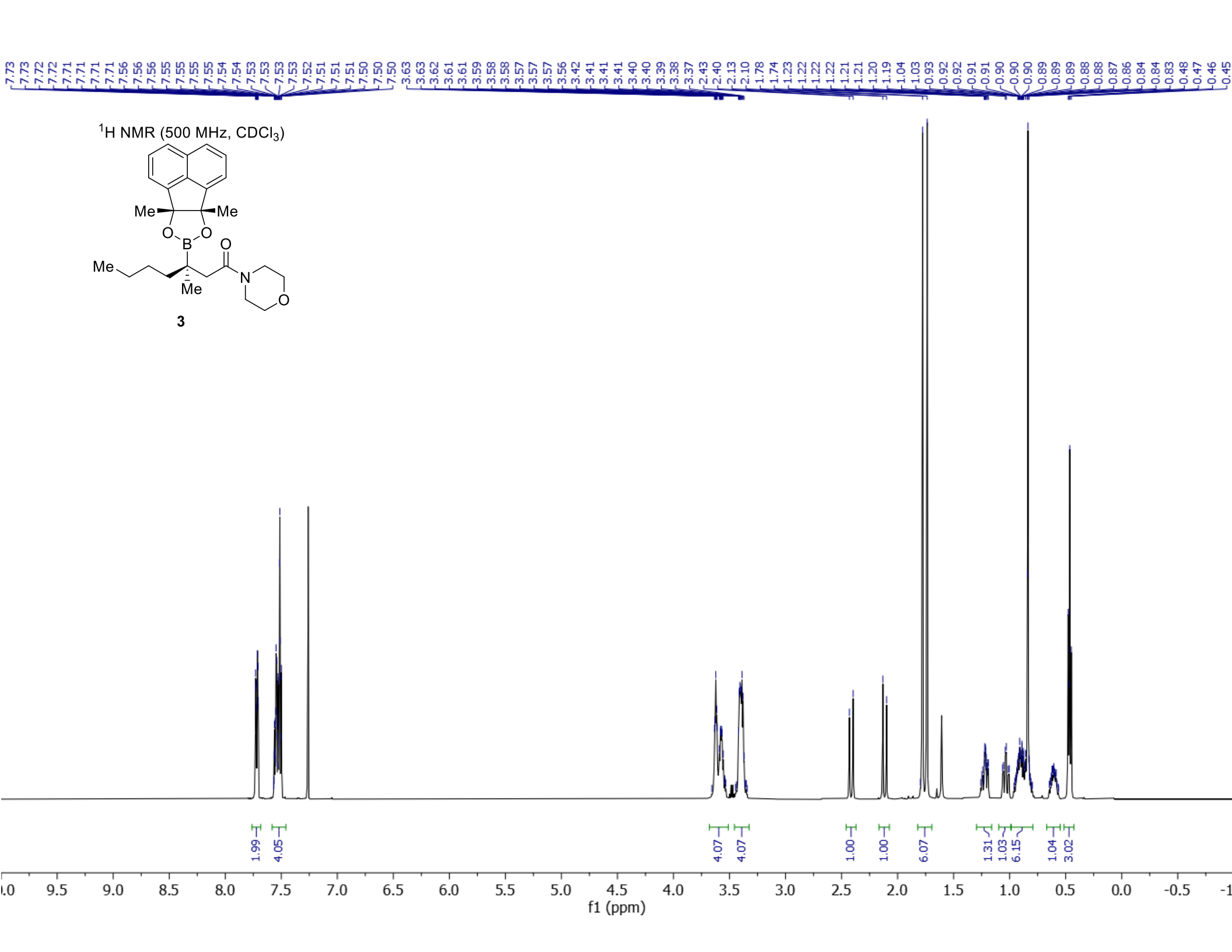
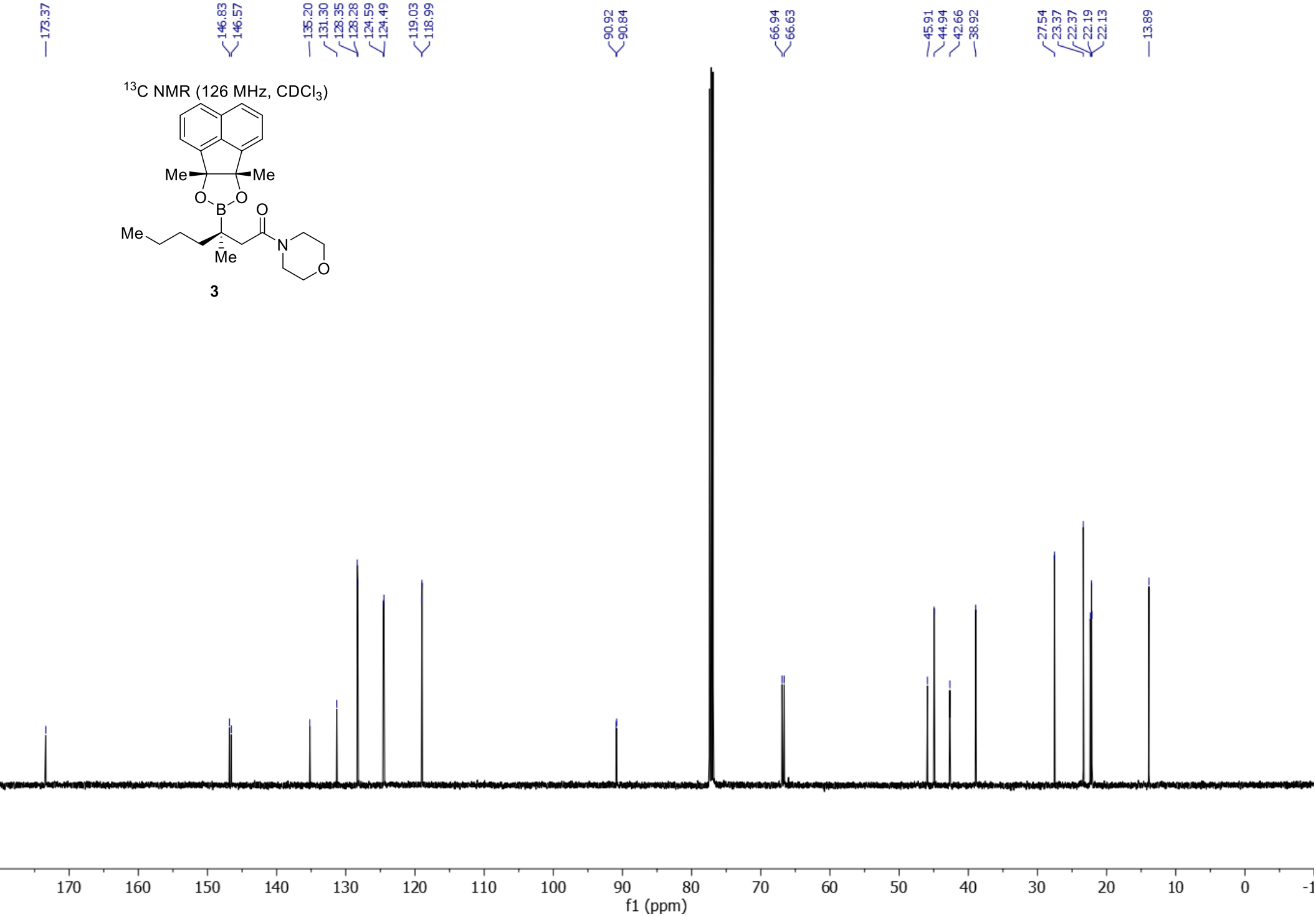



$^1$H NMR (500 MHz, $CDCl_3$)

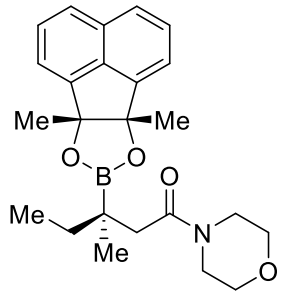



**(S-5)**

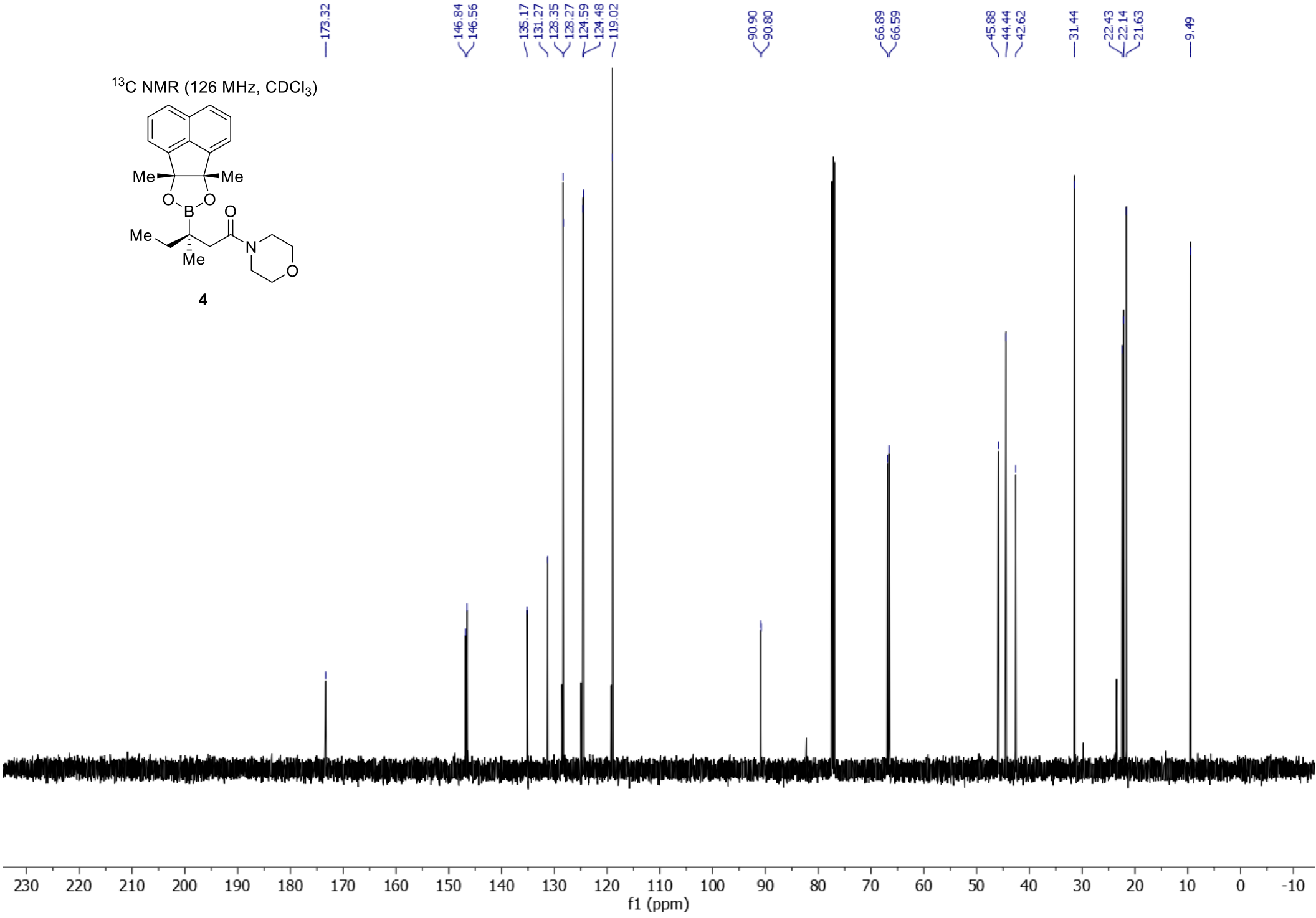

$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
O
B
O
O
Me
Me
N
O
3
f1 (ppm)


173.37
146.83
146.57
135.20
131.30
128.35
128.28
124.59
124.49
119.03
118.99
90.92
90.84
66.94
66.63
45.91
44.94
42.66
38.92
27.54
23.37
22.37
22.19
22.13
13.89
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
N
O
3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

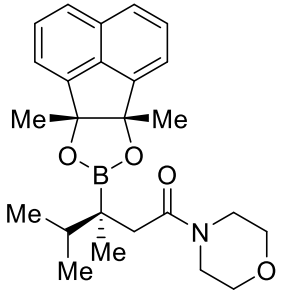
$^1$H NMR (500 MHz, $CDCl_3$)



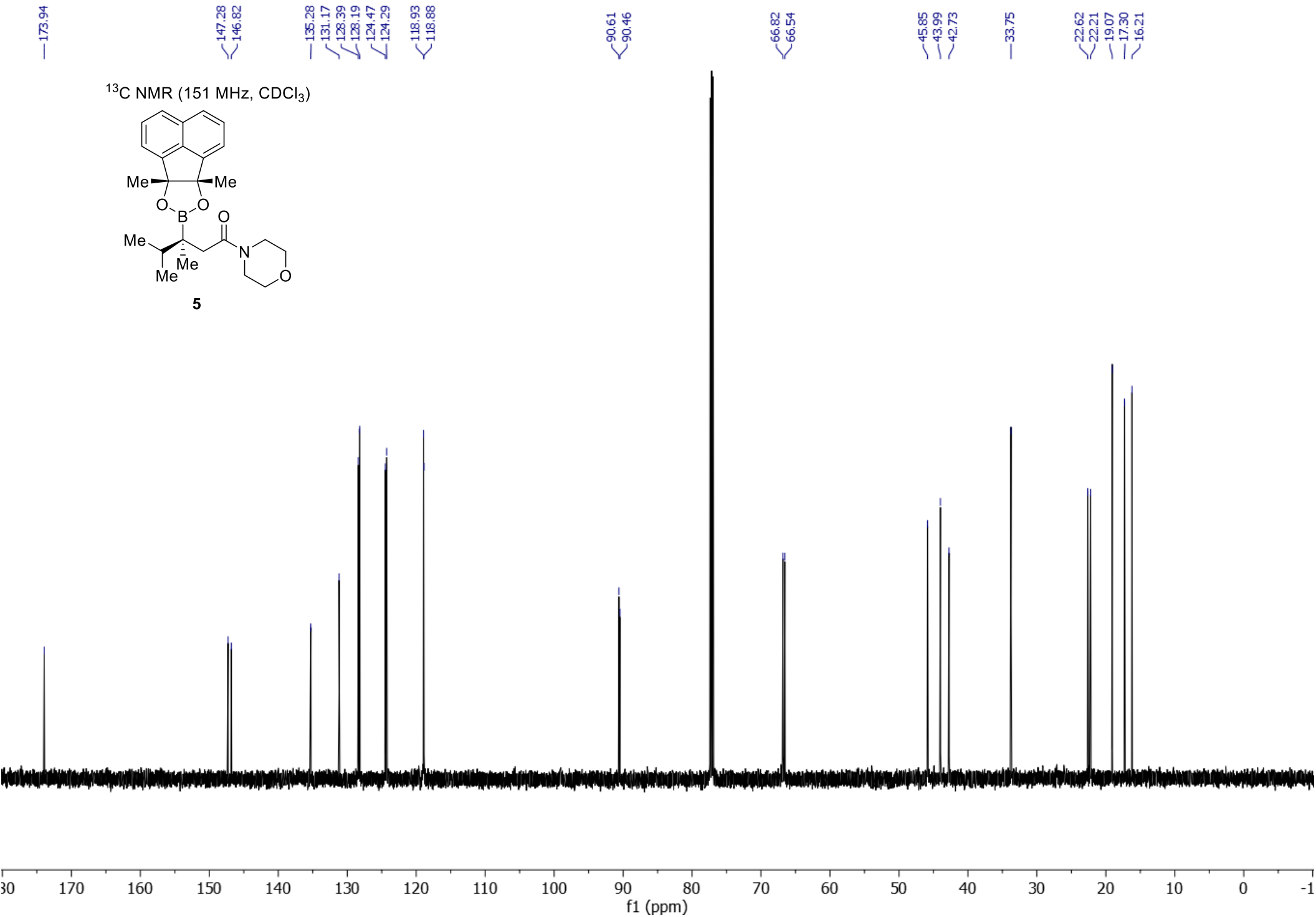

**4**


173.32
146.84
146.56
135.17
131.27
128.35
128.27
124.59
124.48
119.02
90.90
90.80
66.89
66.59
45.88
44.44
42.62
31.44
22.43
22.14
21.63
9.49
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
Me
O
4
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

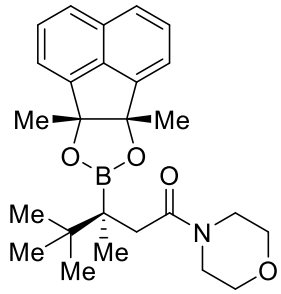
$^1$H NMR (600 MHz, $CDCl_3$)



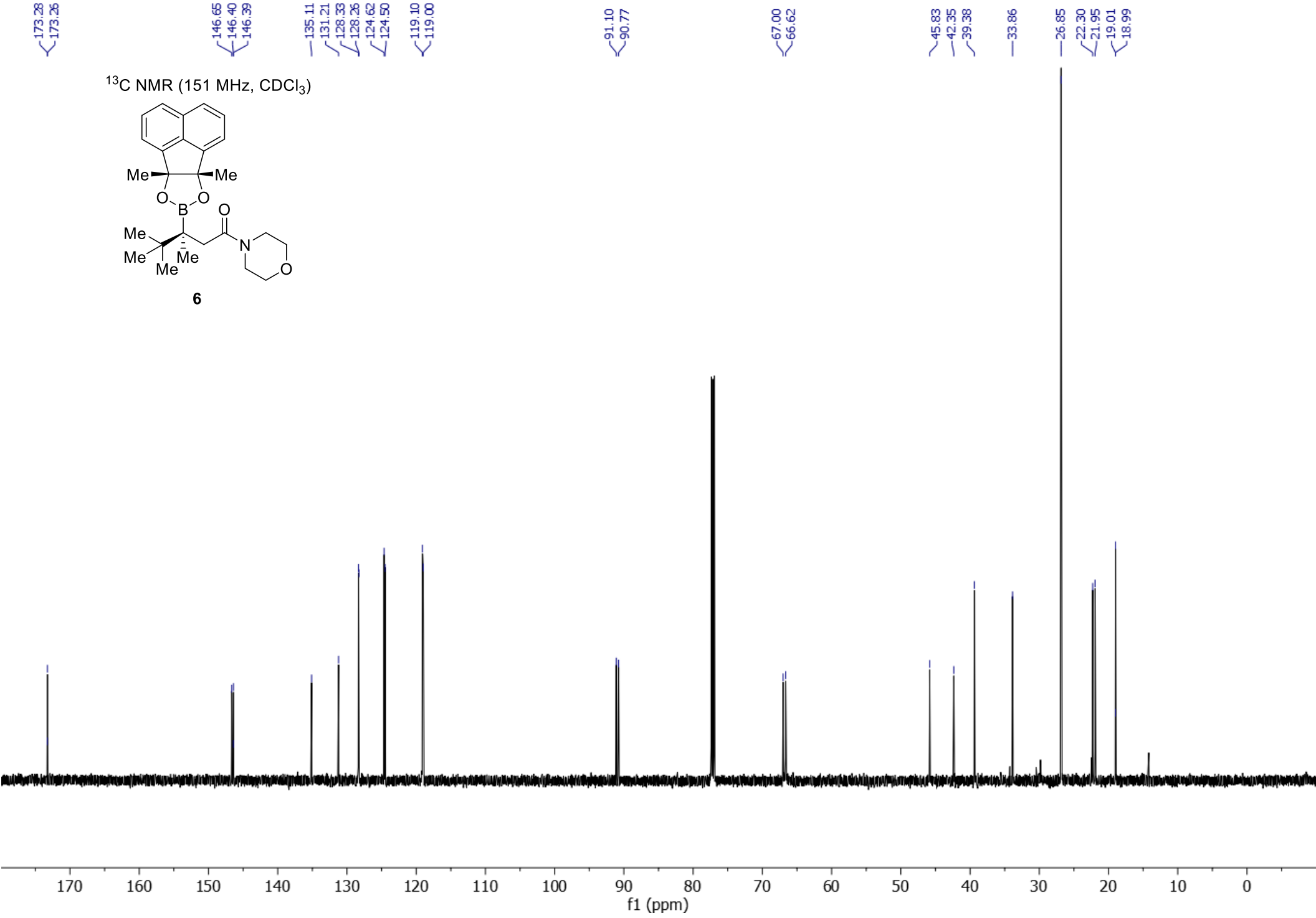

**5**


173.94
147.28
146.82
135.28
131.17
128.39
128.19
124.47
124.29
118.93
118.88
90.61
90.46
66.82
66.54
45.85
43.99
42.73
33.75
22.62
22.21
19.07
17.30
16.21
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
Me
N
O
5
f1 (ppm)

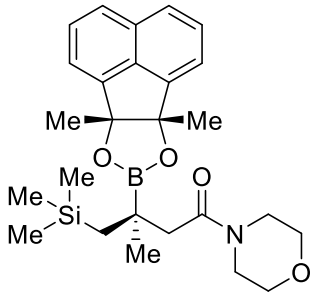
$^1$H NMR (600 MHz, $CDCl_3$)



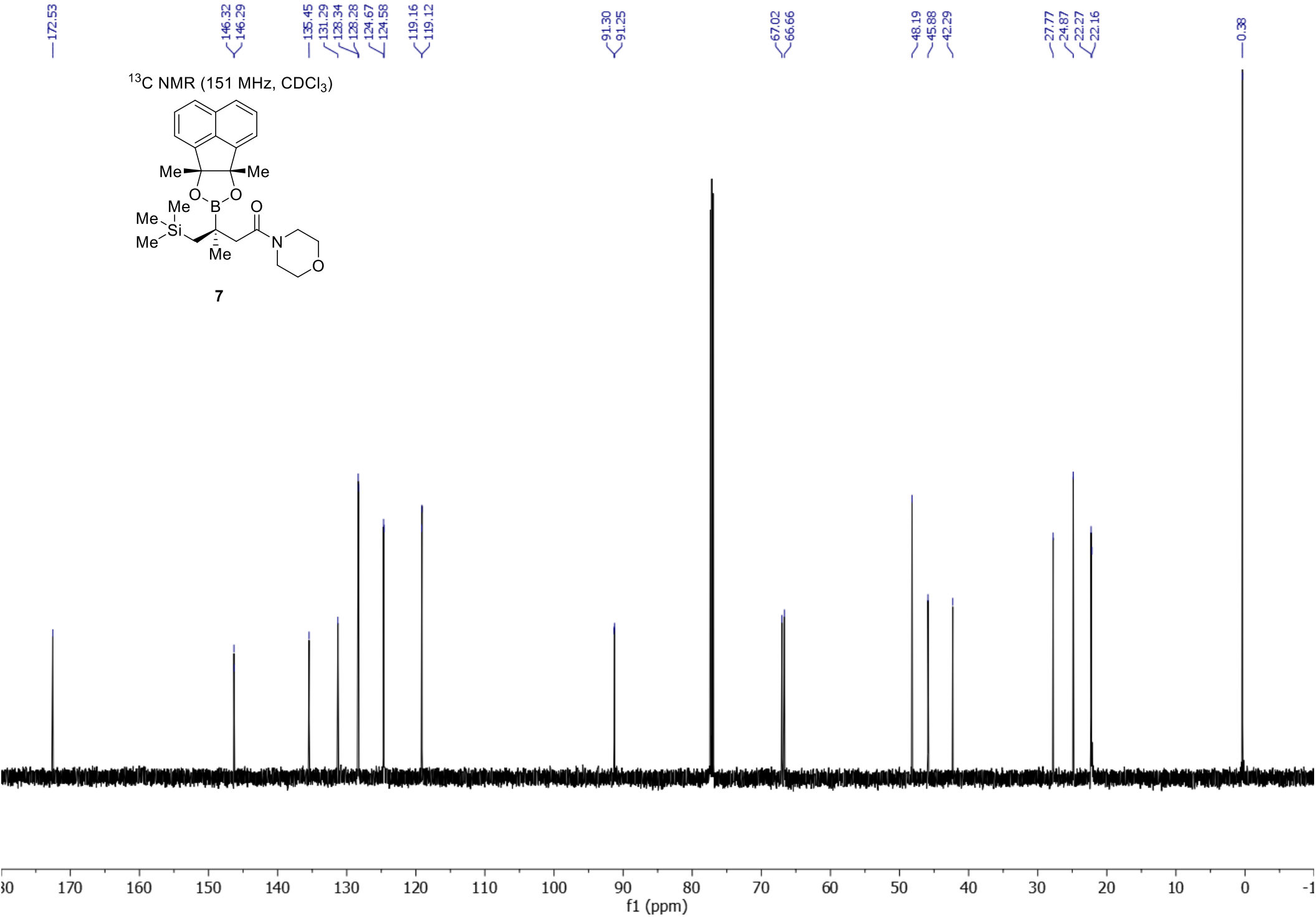

**6**


173.28
173.26
146.65
146.40
146.39
135.11
131.21
128.33
128.26
124.62
124.50
119.10
119.00
91.10
90.77
67.00
66.62
45.83
42.35
39.38
33.86
26.85
22.30
21.95
19.01
18.99
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
Me
Me
N
O
6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

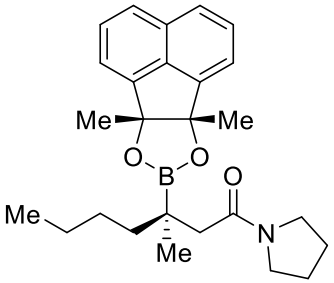
$^1$H NMR (600 MHz, $CDCl_3$)



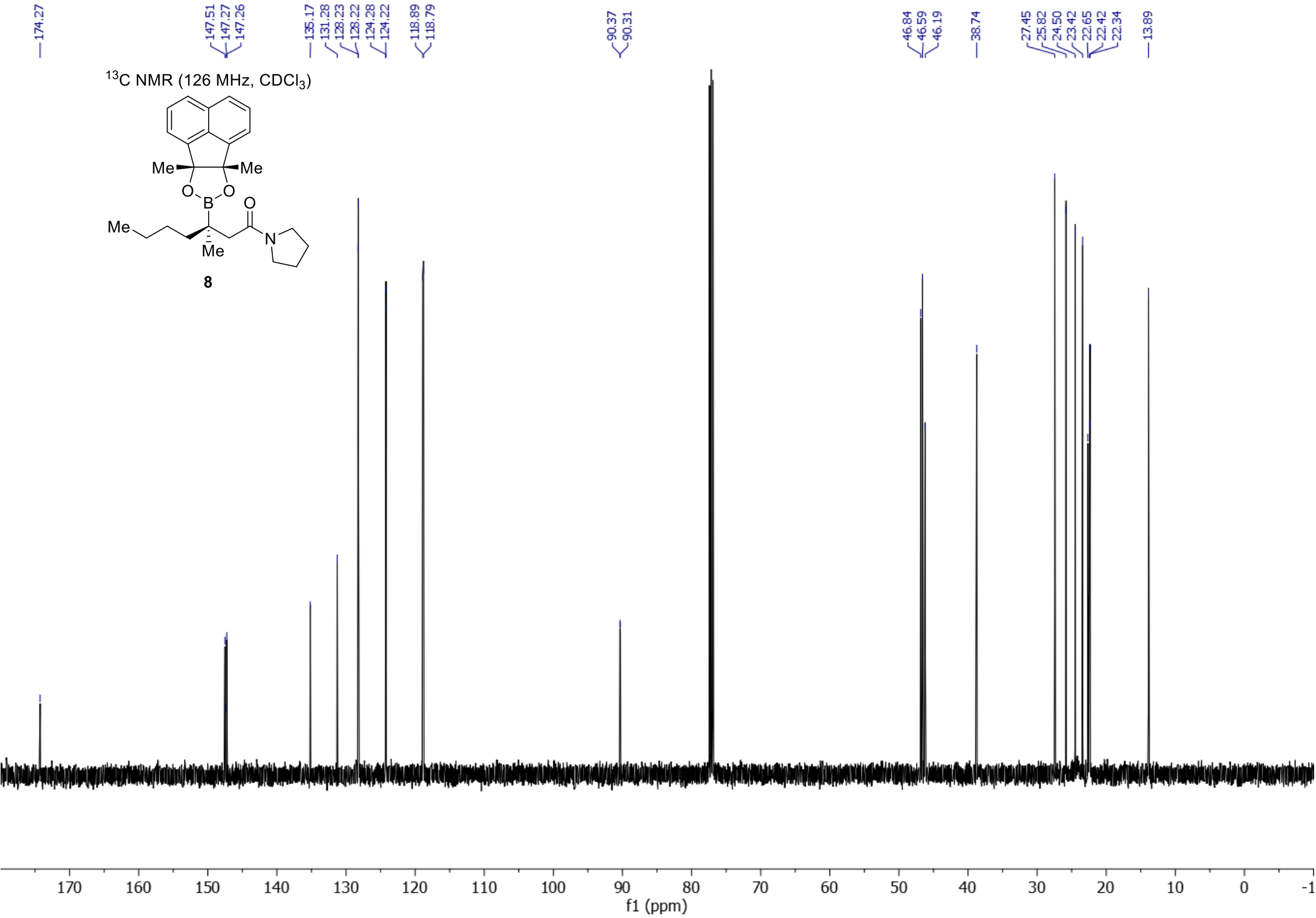

**7**


172.53
146.32
146.29
135.45
131.29
128.34
128.28
124.67
124.58
119.16
119.12
91.30
91.25
67.02
66.66
48.19
45.88
42.29
27.77
24.87
22.27
22.16
0.38
13C NMR (151 MHz, CDCl3)
Me
Me
O
O
B
Me
O
Me
Si
Me
Me
N
O
7
f1 (ppm)

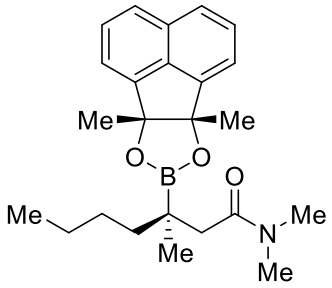
$^1$H NMR (500 MHz, $CDCl_3$)



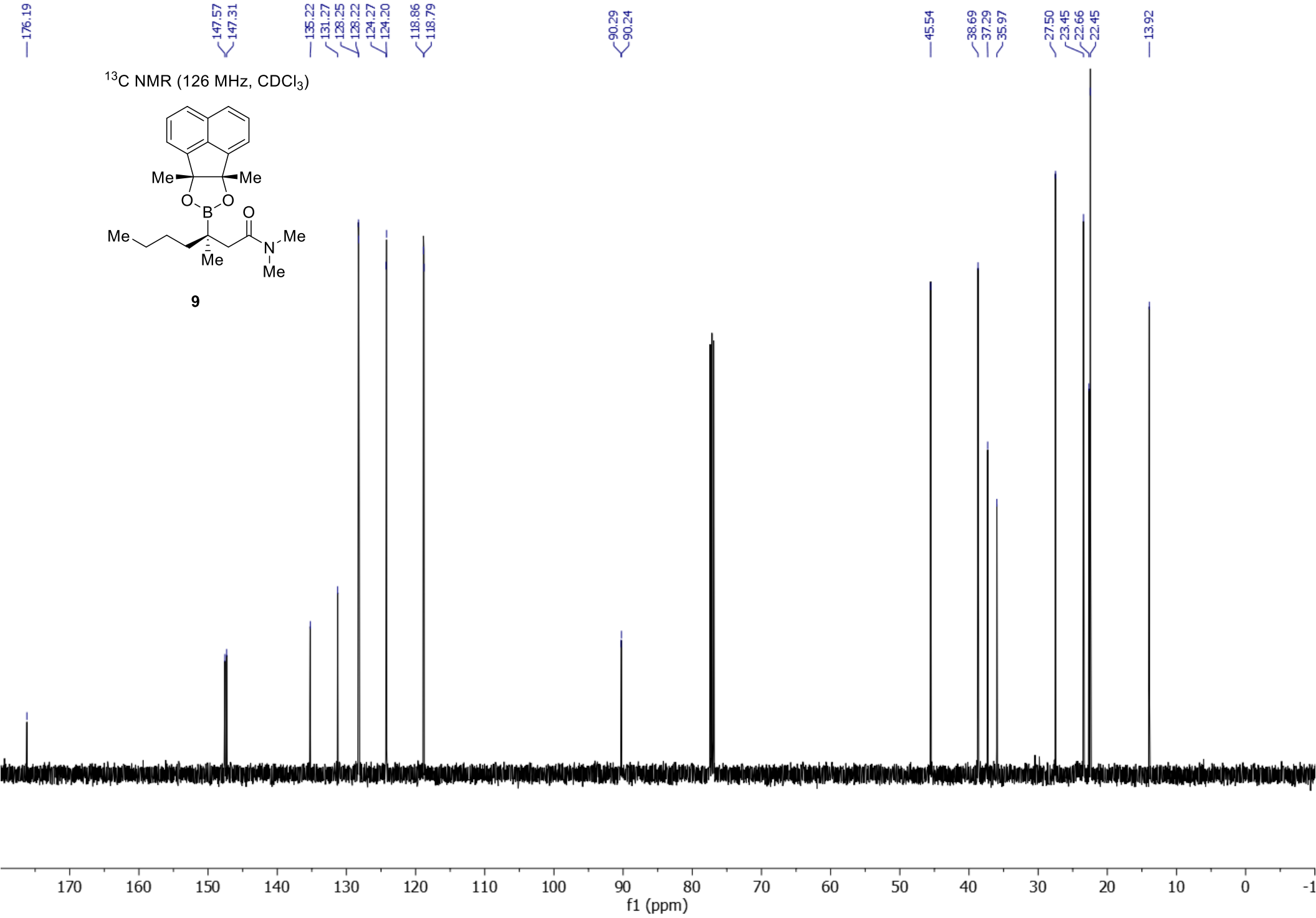

**8**


174.27
147.51
147.27
147.26
135.17
131.28
128.23
128.22
124.28
124.22
118.89
118.79
90.37
90.31
46.84
46.59
46.19
38.74
27.45
25.82
24.50
23.42
22.65
22.42
22.34
13.89
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
N
8
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

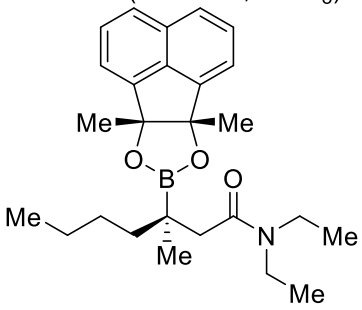
$^1$H NMR (500 MHz, $CDCl_3$)



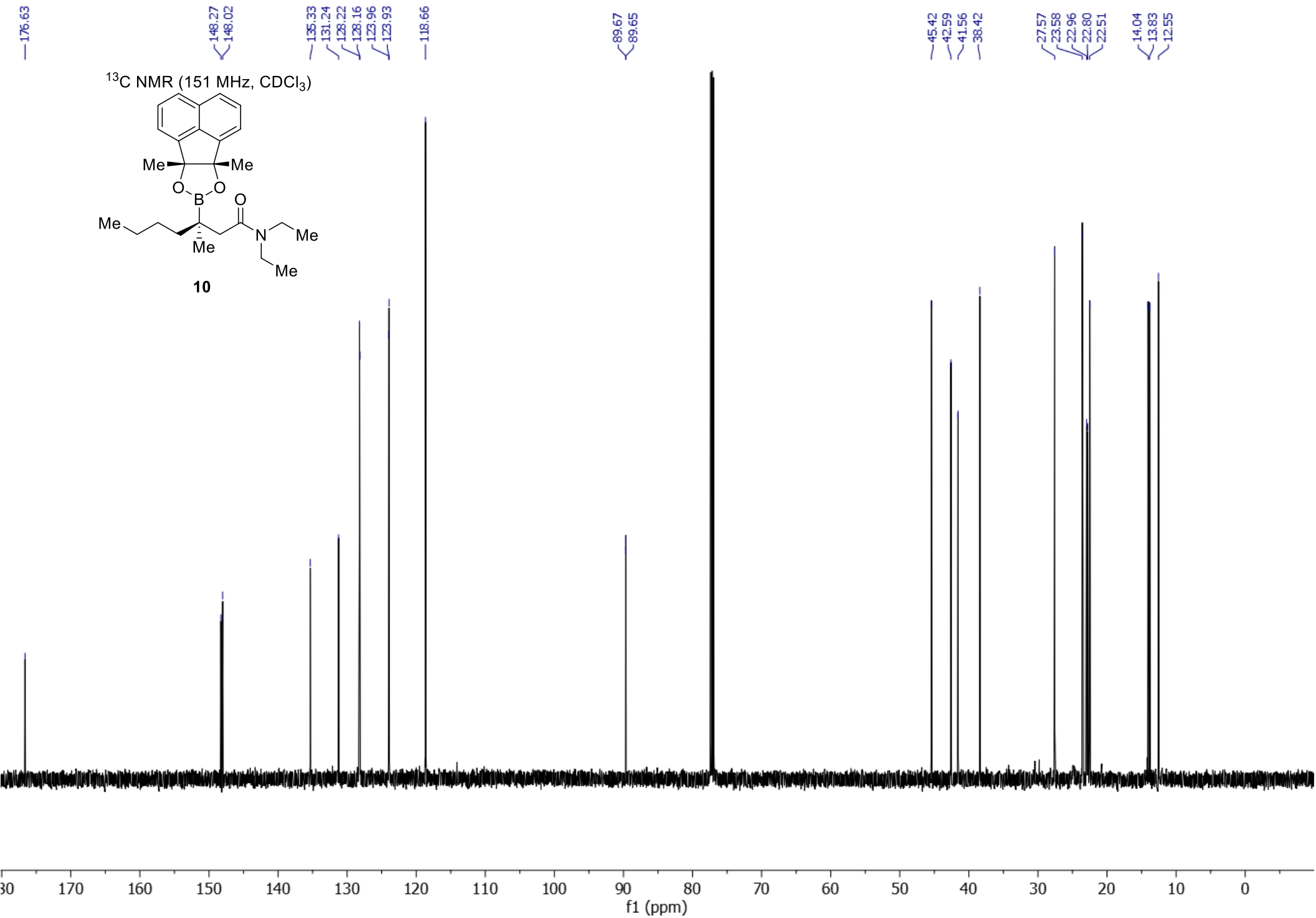

**9**


176.19
147.57
147.31
135.22
131.27
128.25
128.22
124.27
124.20
118.86
118.79
90.29
90.24
45.54
38.69
37.29
35.97
27.50
23.45
22.66
22.45
13.92
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
O
B
O
O
Me
N
Me
Me
Me
9
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

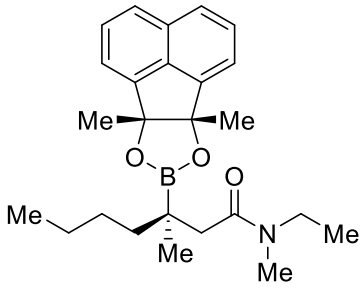
$^1$H NMR (600 MHz, $CDCl_3$)



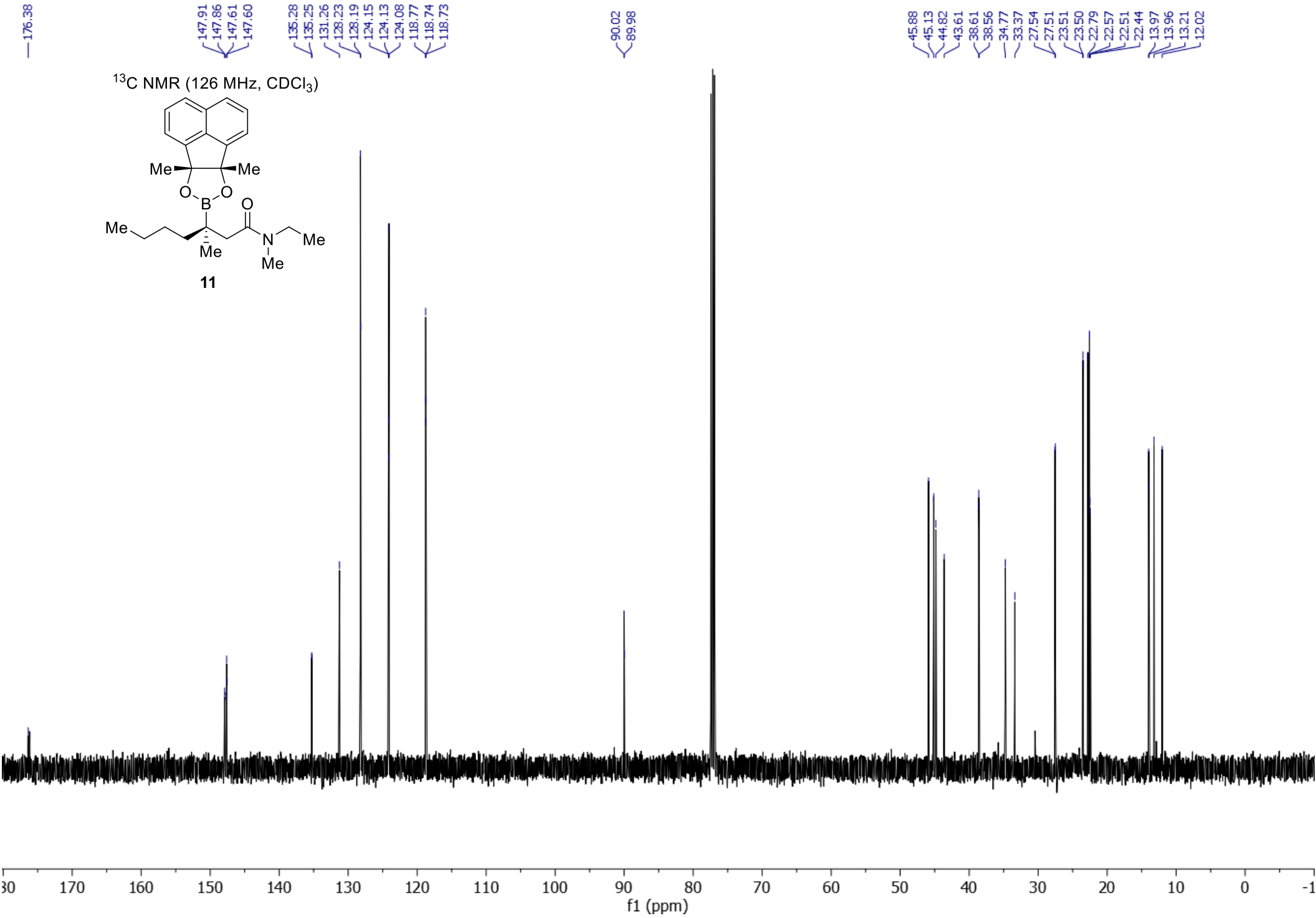

**10**


176.63
148.27
148.02
135.33
131.24
128.22
128.16
123.96
123.93
118.66
89.67
89.65
45.42
42.59
41.56
38.42
27.57
23.58
22.96
22.80
22.51
14.04
13.83
12.55
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
Me
Me
Me
10
f1 (ppm)

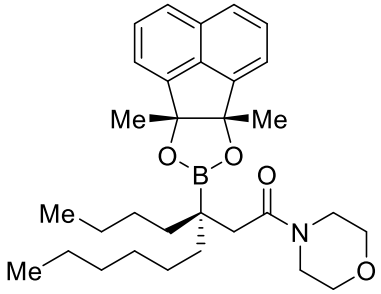
$^1$H NMR (500 MHz, $CDCl_3$)



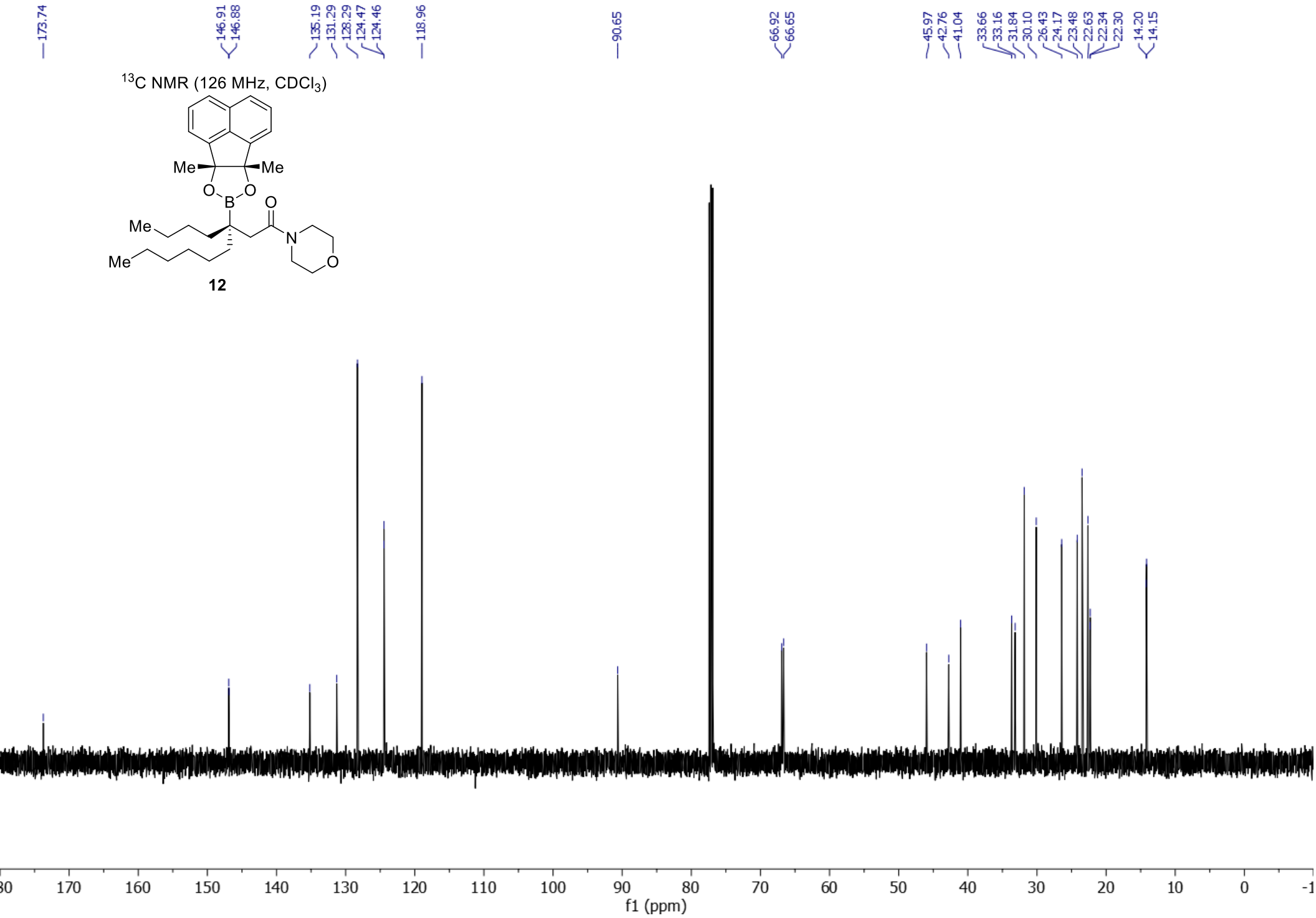

**11**


176.38
147.91
147.86
147.61
147.60
135.28
135.25
131.26
128.23
128.19
124.15
124.13
124.08
118.77
118.74
118.73
90.02
89.98
45.88
45.13
44.82
43.61
38.61
38.56
34.77
33.37
27.54
27.51
23.51
23.50
22.79
22.57
22.51
22.44
13.97
13.96
13.21
12.02
$^{13}$C NMR (126 MHz, CDCl$_3$)
Me
Me
O
B
O
O
Me
N
Me
Me
Me
11
f1 (ppm)

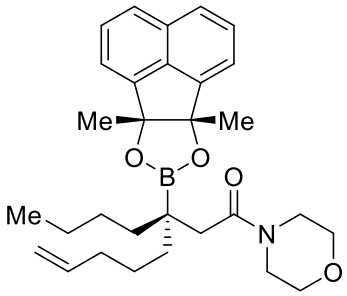
$^1$H NMR (500 MHz, $CDCl_3$)



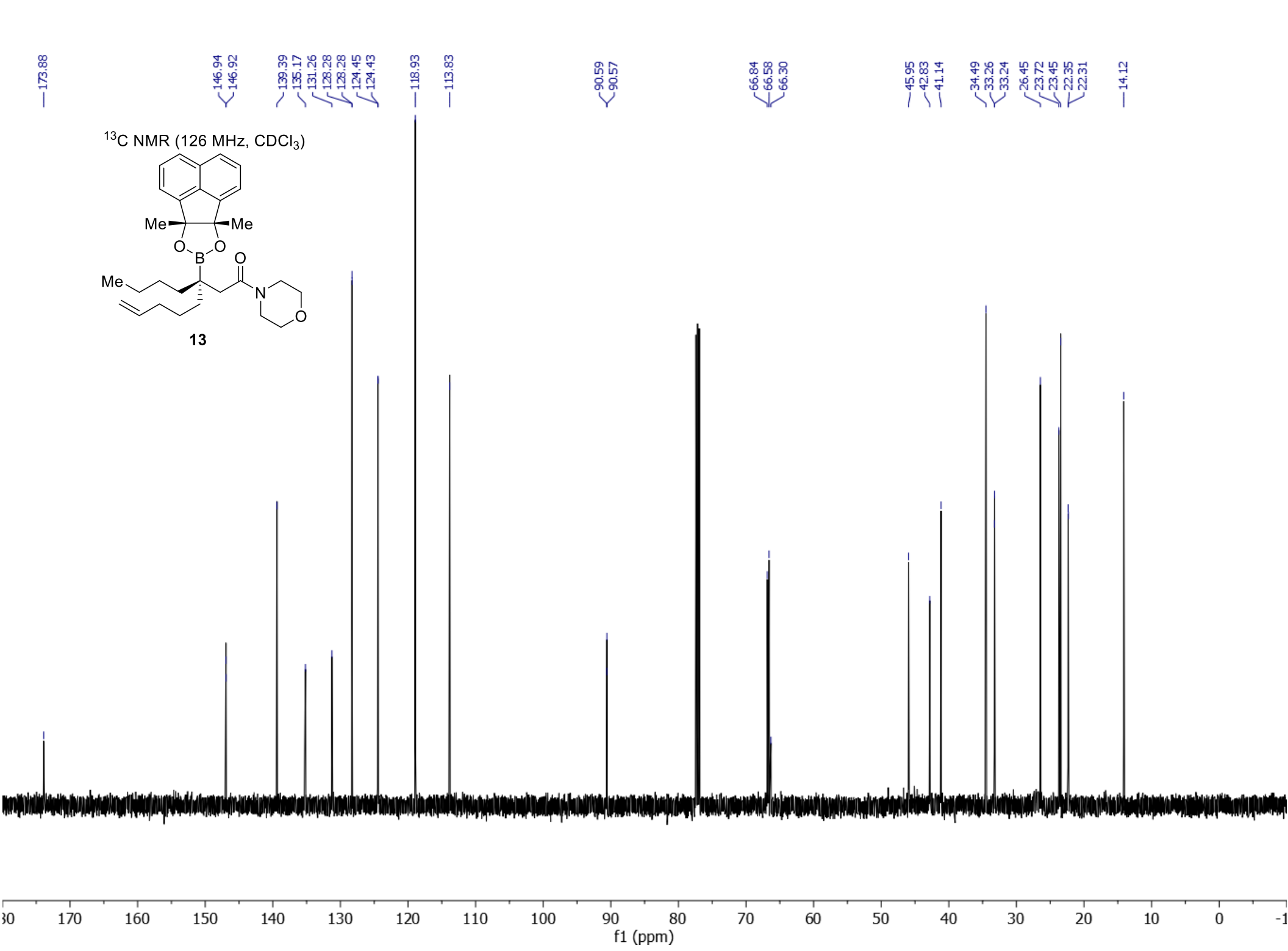

**12**


173.74
146.91
146.88
135.19
131.29
128.29
124.47
124.46
118.96
90.65
66.92
66.65
45.97
42.76
41.04
33.66
33.16
31.84
30.10
26.43
24.17
23.48
22.63
22.34
22.30
14.20
14.15
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
Me
O
12
f1 (ppm)

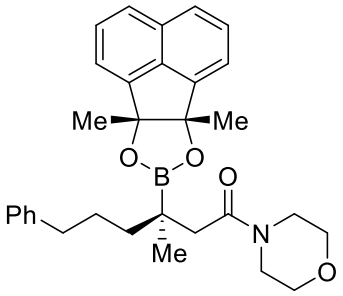
$^1$H NMR (500 MHz, $CDCl_3$)



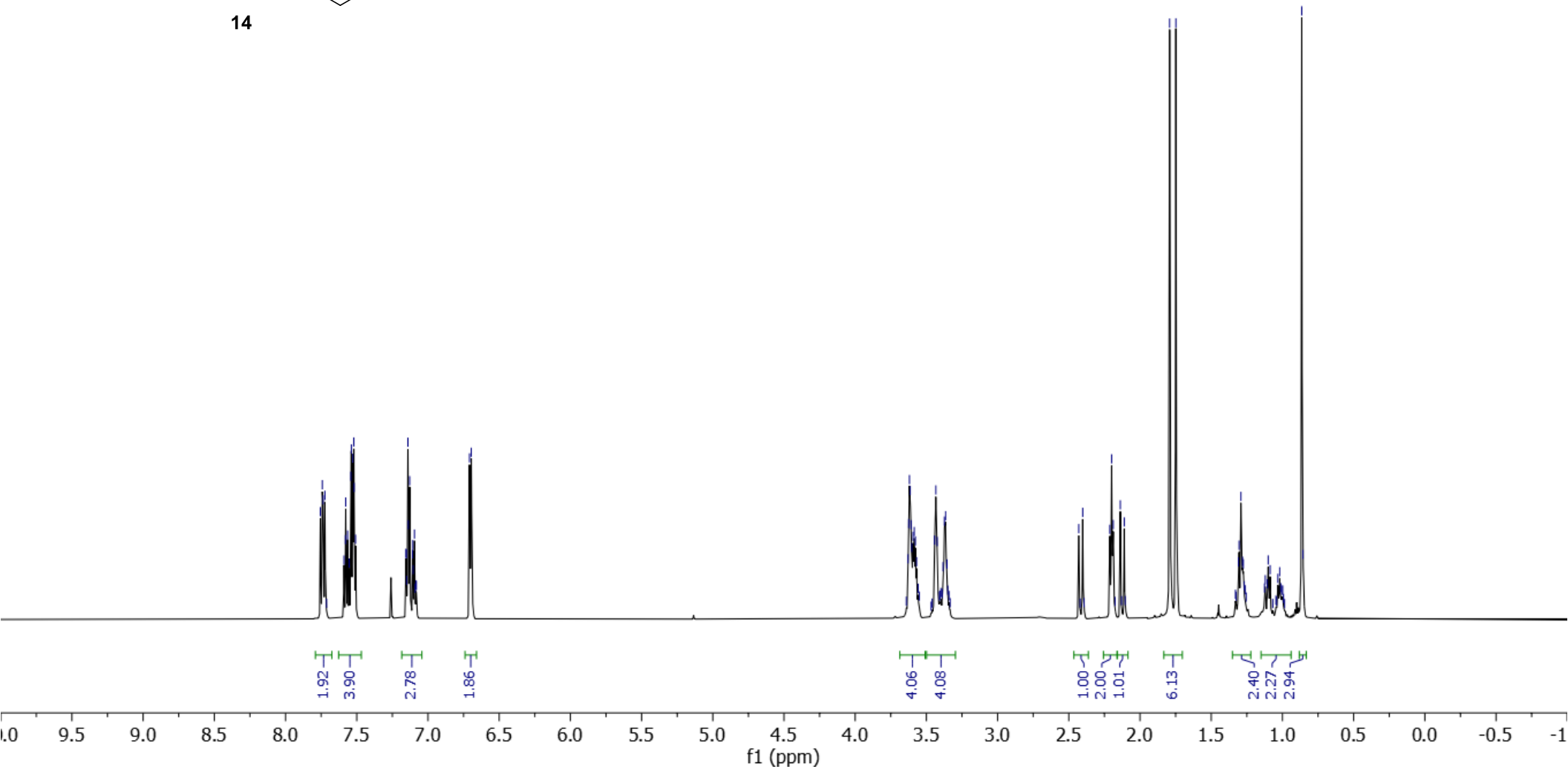

**13**

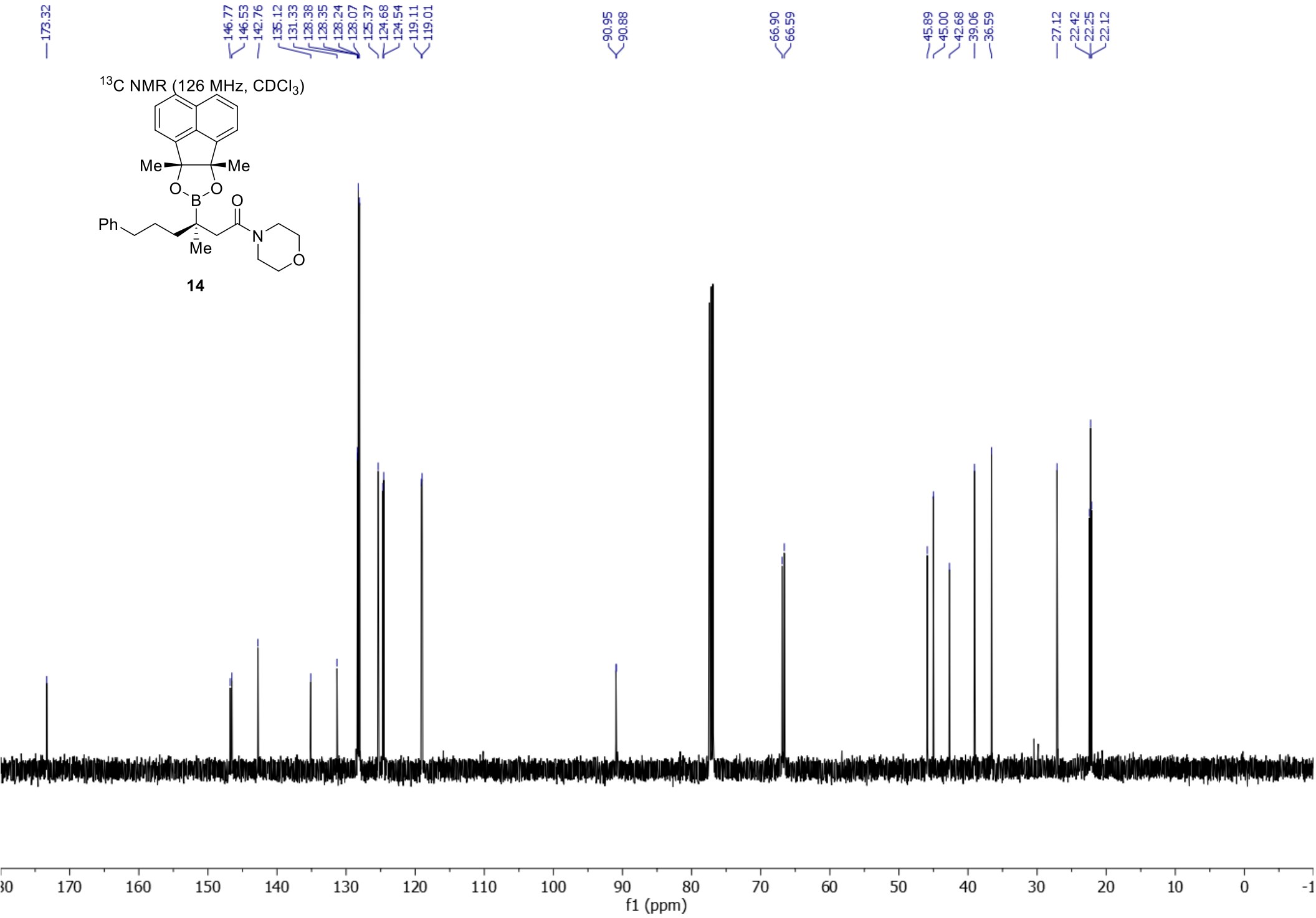

173.88
146.94
146.92
139.39
135.17
131.26
128.28
128.28
124.45
124.43
118.93
113.83
90.59
90.57
66.84
66.58
66.30
45.95
42.83
41.14
34.49
33.26
33.24
26.45
23.72
23.45
22.35
22.31
14.12
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
O
13
f1 (ppm)

$^1$H NMR (600 MHz, $CDCl_3$)

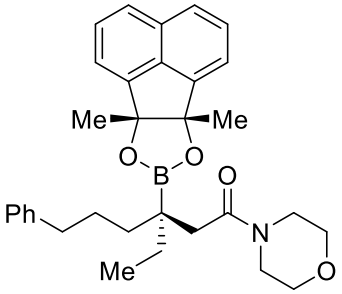



**14**

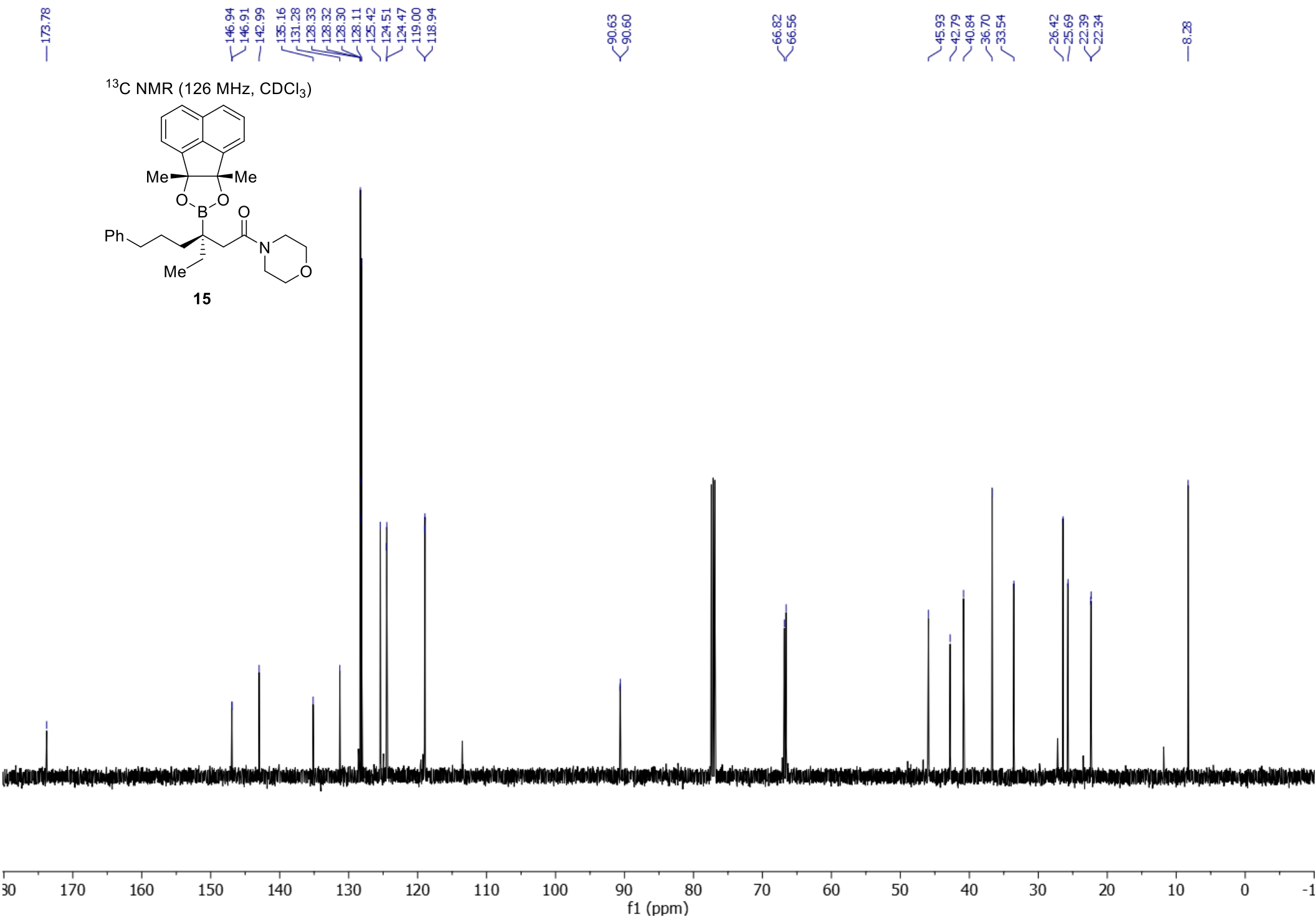



173.32
146.77
146.53
142.76
135.12
131.33
128.38
128.35
128.24
128.07
125.37
124.68
124.54
119.11
119.01
90.95
90.88
66.90
66.59
45.89
45.00
42.68
39.06
36.59
27.12
22.42
22.25
22.12
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Ph
N
Me
O
14
f1 (ppm)

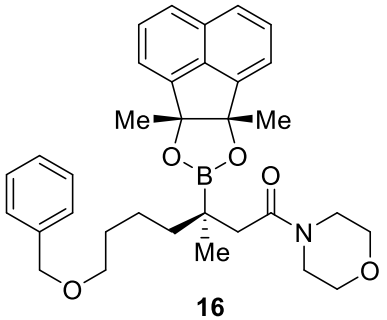
$^1$H NMR (600 MHz, $CDCl_3$)



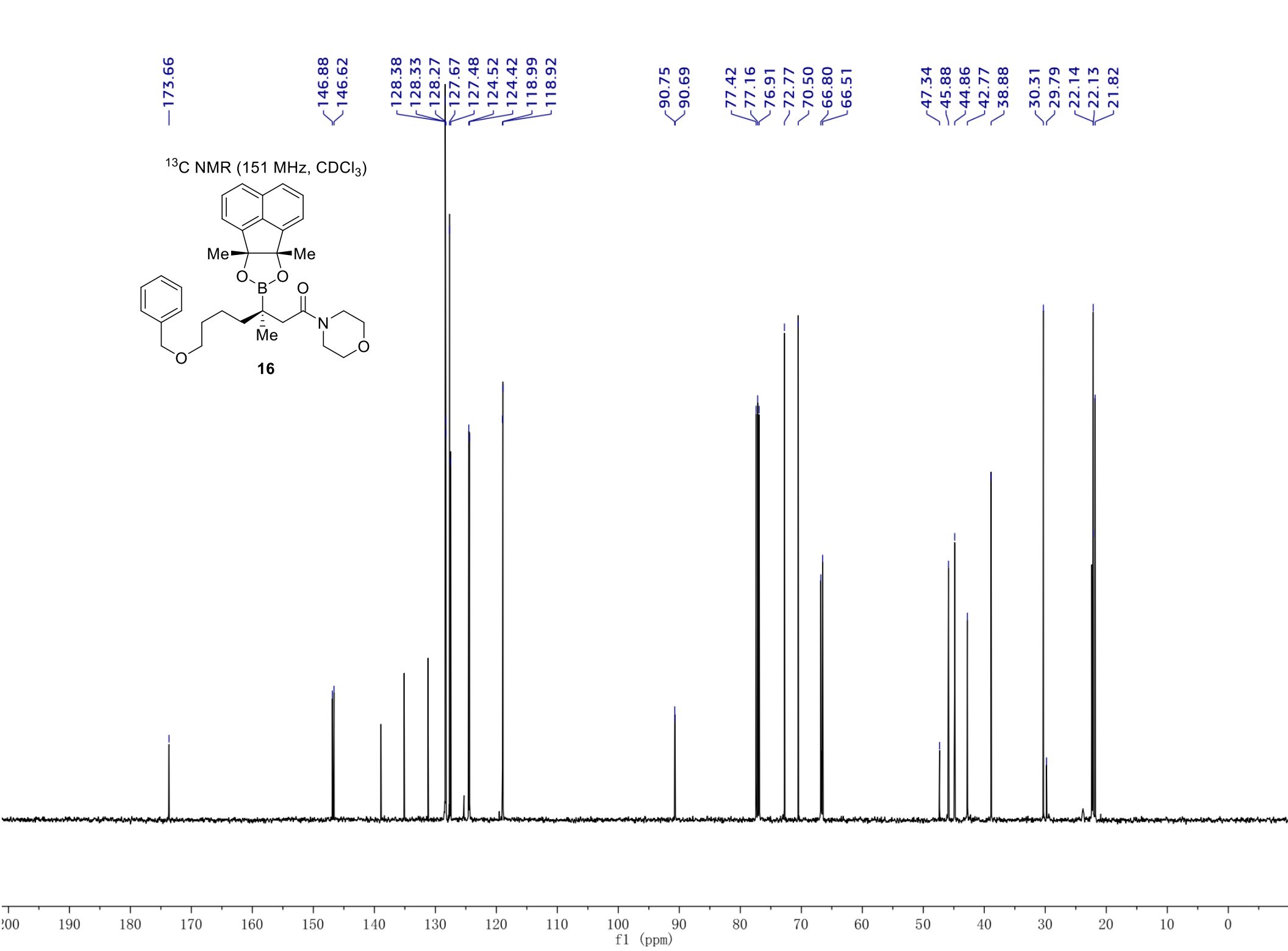

**15**


173.78
146.94
146.91
142.99
135.16
131.28
128.33
128.32
128.30
128.11
125.42
124.51
124.47
119.00
118.94
90.63
90.60
66.82
66.56
45.93
42.79
40.84
36.70
33.54
26.42
25.69
22.39
22.34
8.28
13C NMR (126 MHz, CDCl3)
Me
Me
O
B
O
O
Ph
N
Me
O
15
f1 (ppm)

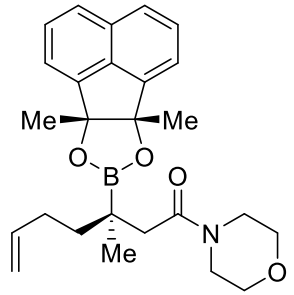
$^1$H NMR (600 MHz, $CDCl_3$)



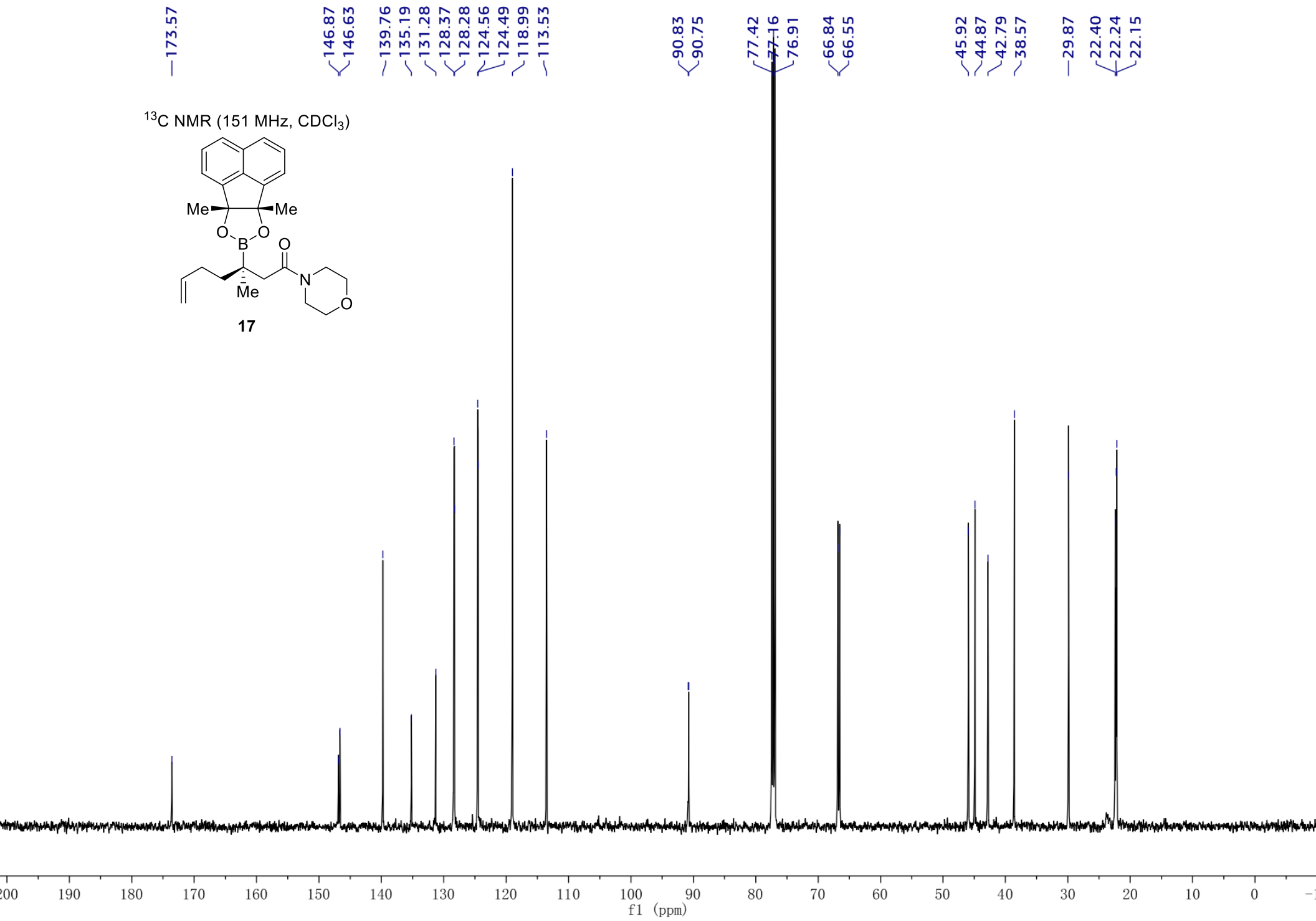

**16**


173.66
146.88
146.62
128.38
128.33
128.27
127.67
127.48
124.52
124.42
118.99
118.92
90.75
90.69
77.42
77.16
76.91
72.77
70.50
66.80
66.51
47.34
45.88
44.86
42.77
38.88
30.31
29.79
22.14
22.13
21.82
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
N
O
Me
O
16
f1 (ppm)

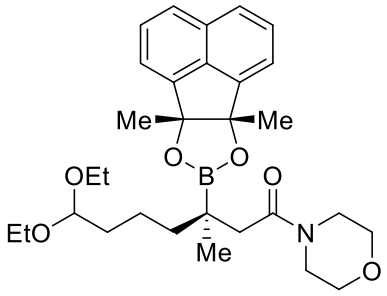
$^1$H NMR (600 MHz, $CDCl_3$)



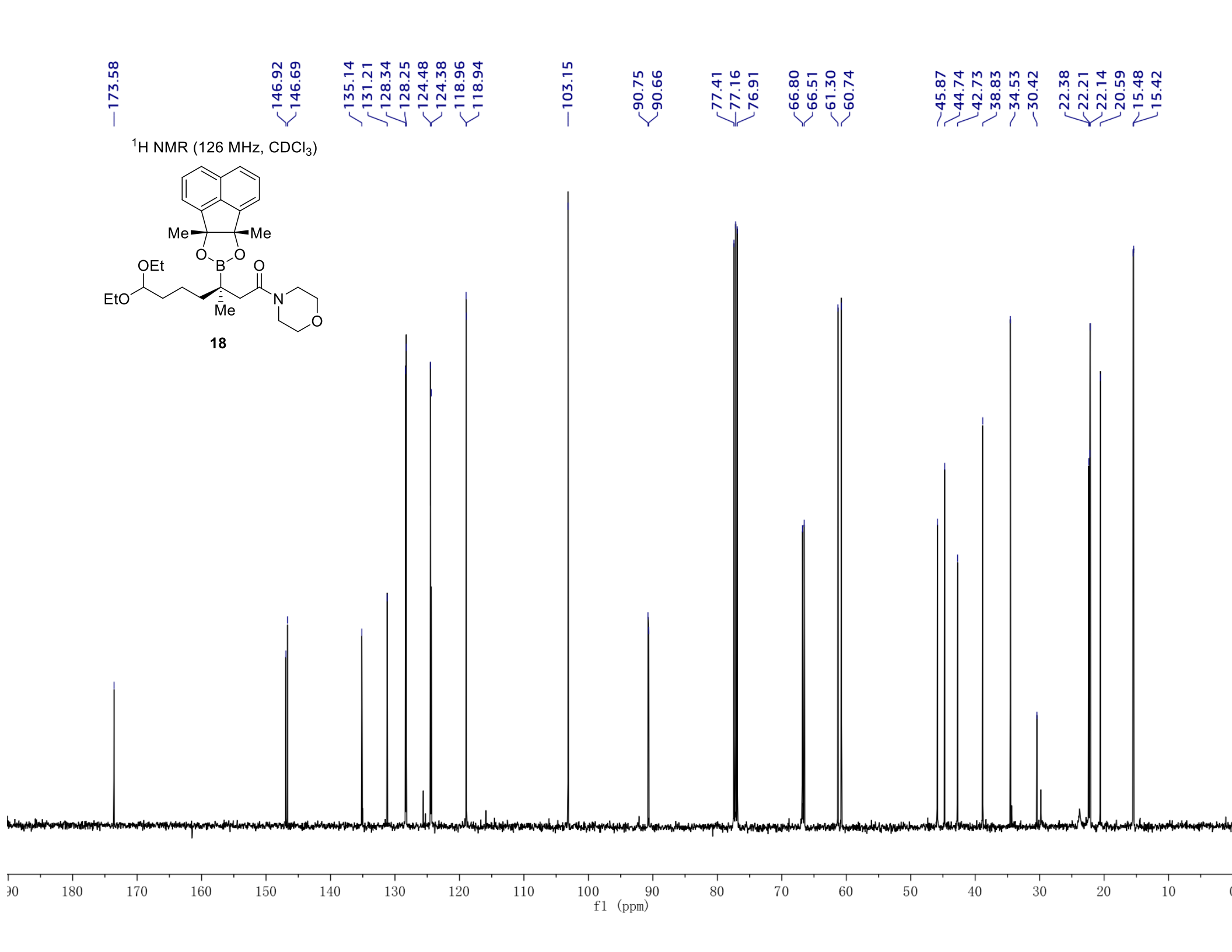

**17**


173.57
146.87
146.63
139.76
135.19
131.28
128.37
128.28
124.56
124.49
118.99
113.53
90.83
90.75
77.42
77.16
76.91
66.84
66.55
45.92
44.87
42.79
38.57
29.87
22.40
22.24
22.15
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
N
Me
O
17
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

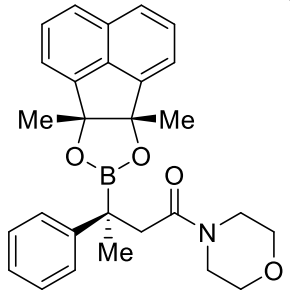
$^1$H NMR (500 MHz, $CDCl_3$)



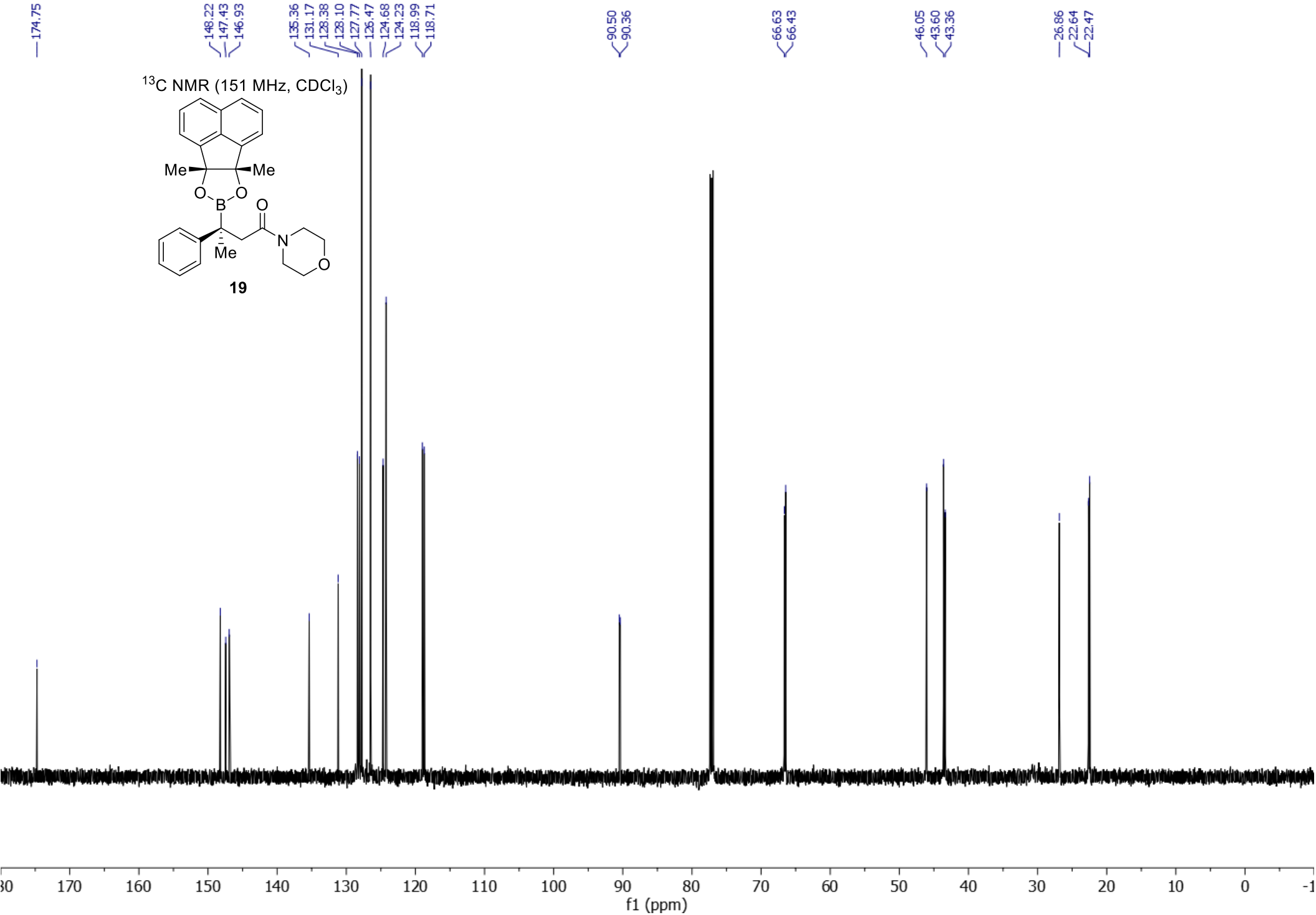

**18**


173.58
146.92
146.69
135.14
131.21
128.34
128.25
124.48
124.38
118.96
118.94
103.15
90.75
90.66
77.41
77.16
76.91
66.80
66.51
61.30
60.74
45.87
44.74
42.73
38.83
34.53
30.42
22.38
22.21
22.14
20.59
15.48
15.42
1H NMR (126 MHz, CDCl3)
Me
Me
O
B
O
OEt
O
EtO
N
Me
O
18
f1 (ppm)

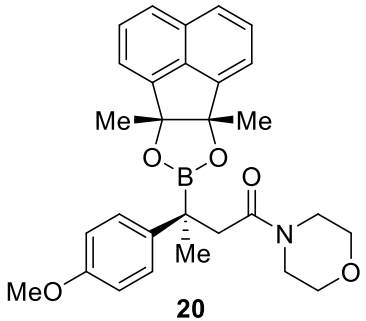
$^1$H NMR (500 MHz, $CDCl_3$)



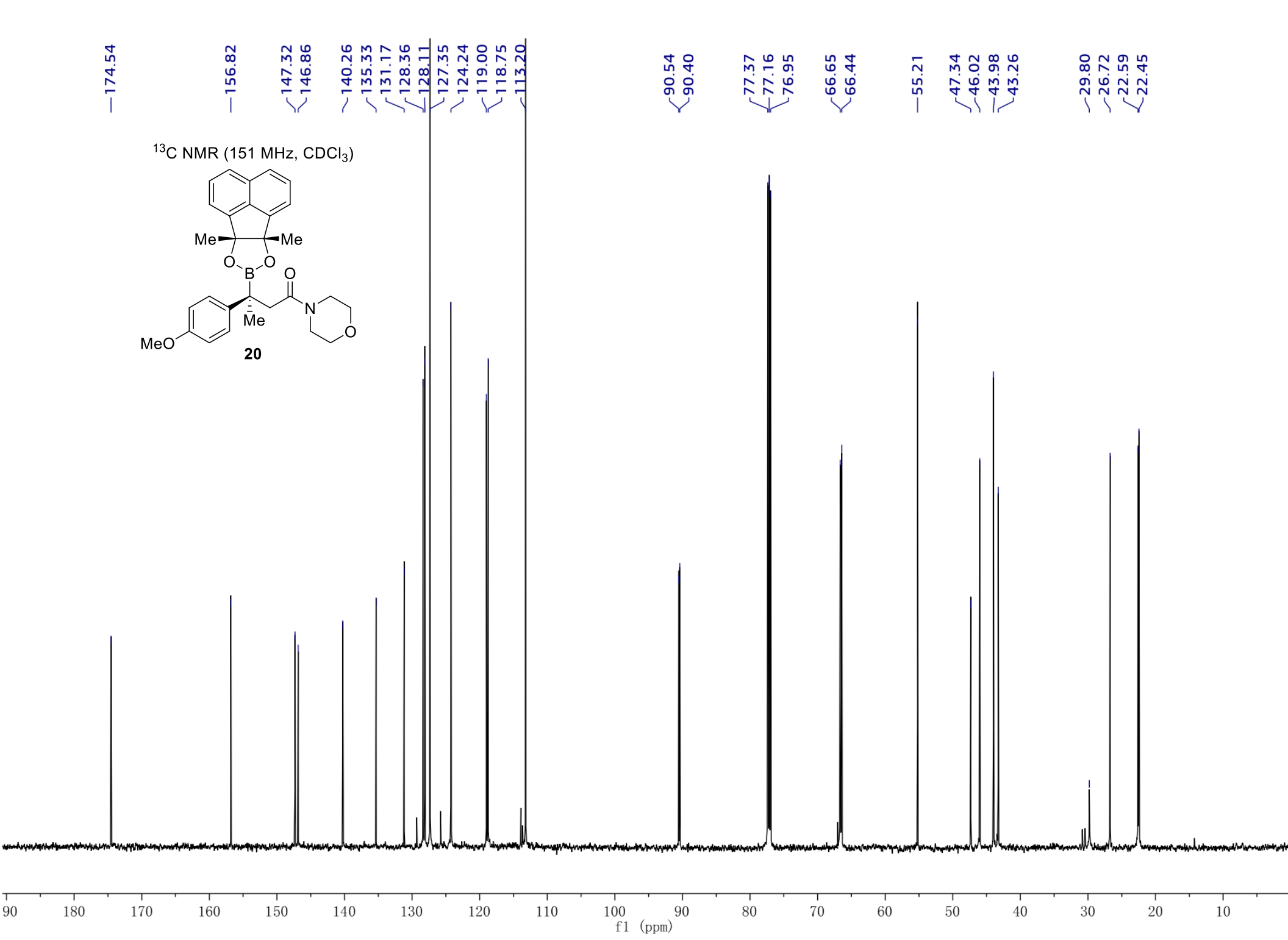

**19**

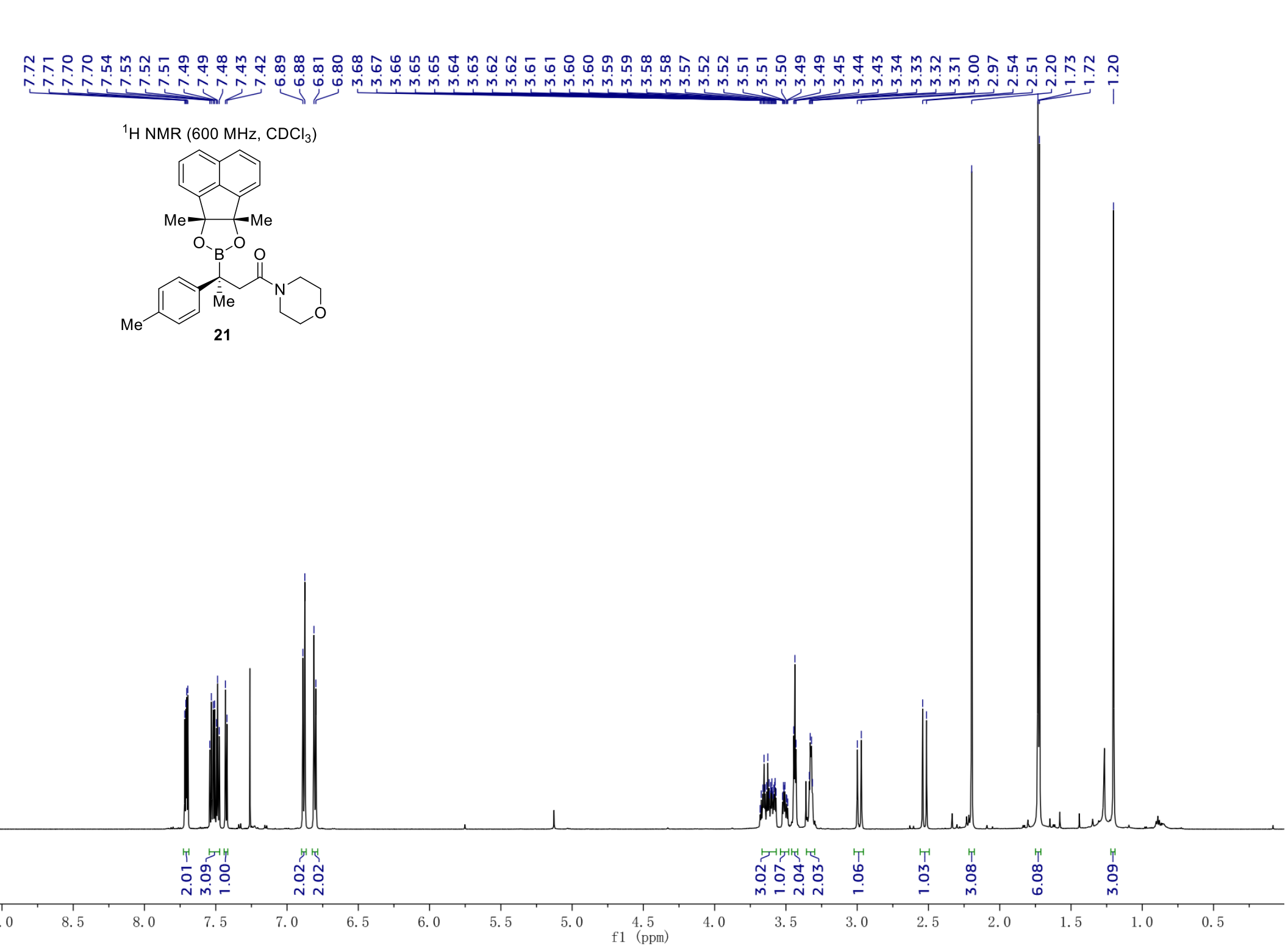

174.75
148.22
147.43
146.93
135.36
131.17
128.38
128.10
127.77
126.47
124.68
124.23
118.99
118.71
90.50
90.36
66.63
66.43
46.05
43.60
43.36
26.86
22.64
22.47
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
N
O
Me
19
f1 (ppm)

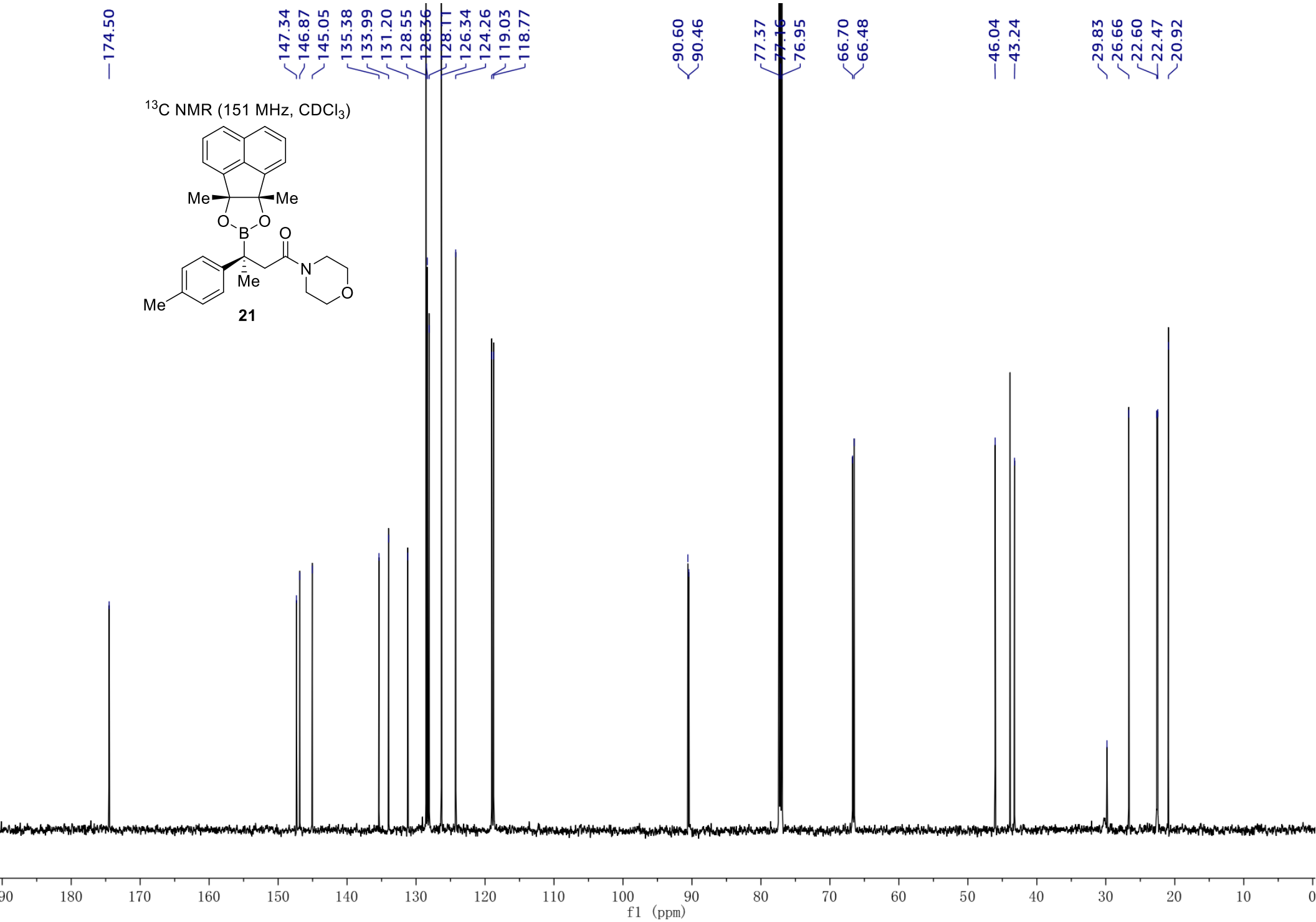
$^1$H NMR (600 MHz, $CDCl_3$)



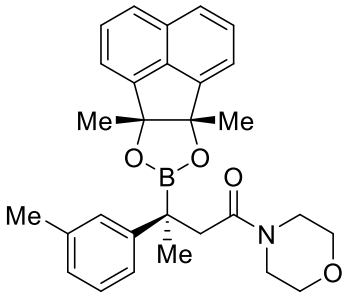

**20**


174.54
156.82
147.32
146.86
140.26
135.33
131.17
128.36
128.11
127.35
124.24
119.00
118.75
113.20
90.54
90.40
77.37
77.16
76.95
66.65
66.44
55.21
47.34
46.02
43.98
43.26
29.80
26.72
22.59
22.45
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
O
MeO
20
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

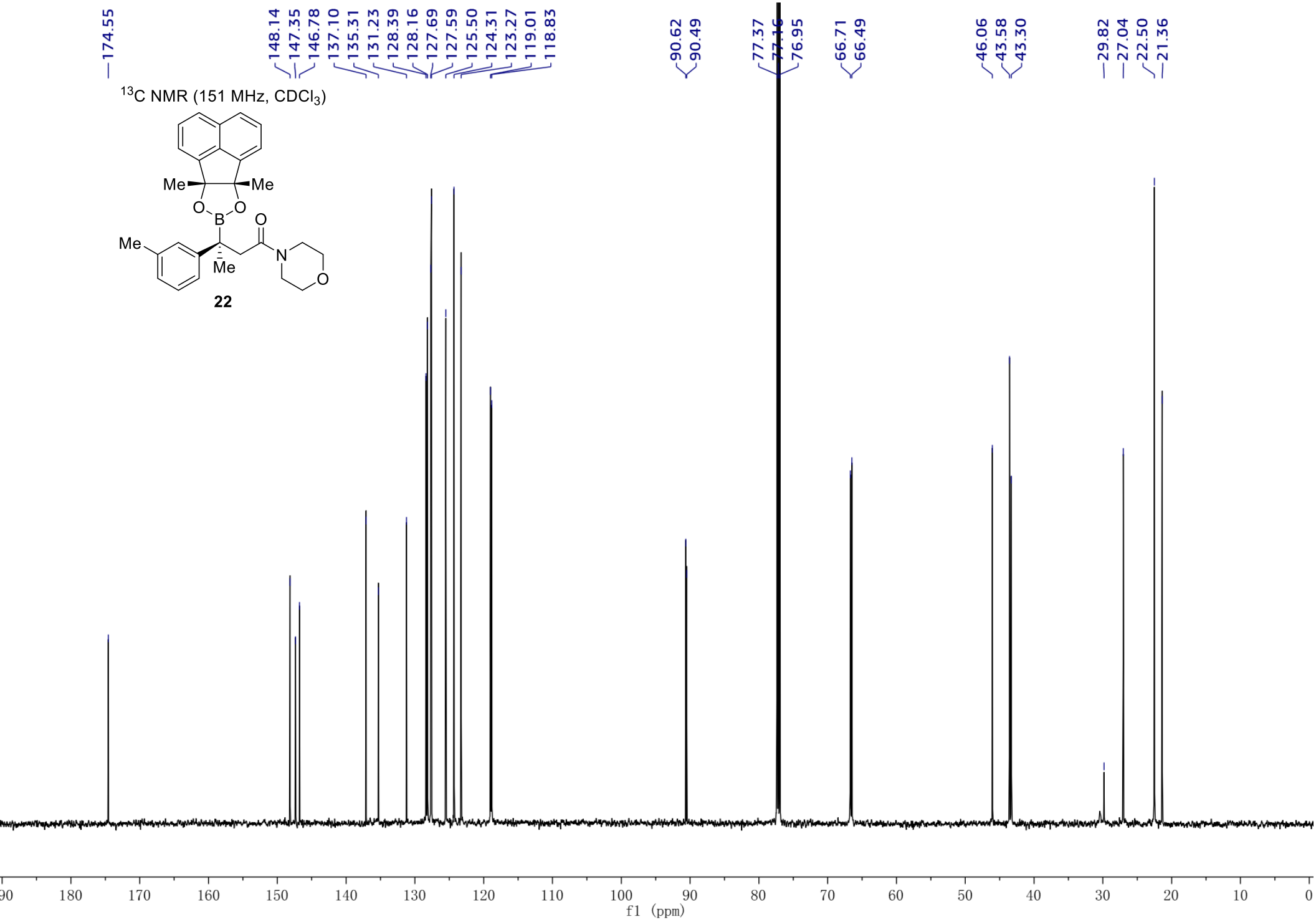

7.72 7.71 7.70 7.70 7.54 7.53 7.52 7.51 7.49 7.49 7.48 7.43 7.42 6.89 6.88 6.81 6.80 3.68 3.67 3.66 3.65 3.65 3.64 3.63 3.62 3.62 3.61 3.61 3.60 3.60 3.59 3.59 3.58 3.58 3.57 3.52 3.52 3.51 3.51 3.50 3.49 3.49 3.45 3.44 3.43 3.34 3.33 3.32 3.31 3.00 2.97 2.54 2.51 2.20 1.73 1.72 1.20
1H NMR (600 MHz, CDCl3)
Me
Me
O
B
O
O
N
Me
Me
O
21
2.01 3.09 1.00 2.02 2.02 3.02 1.07 2.04 2.03 1.06 1.03 3.08 6.08 3.09
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
f1 (ppm)


174.50
147.34
146.87
145.05
135.38
133.99
131.20
128.55
128.36
128.11
126.34
124.26
119.03
118.77
90.60
90.46
77.37
77.16
76.95
66.70
66.48
46.04
43.24
29.83
26.66
22.60
22.47
20.92
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
N
O
Me
21
f1 (ppm)

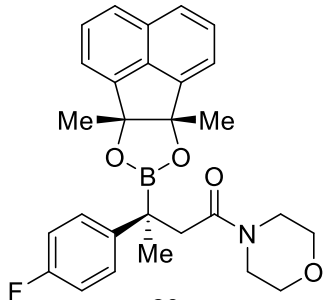
$^1$H NMR (600 MHz, $CDCl_3$)



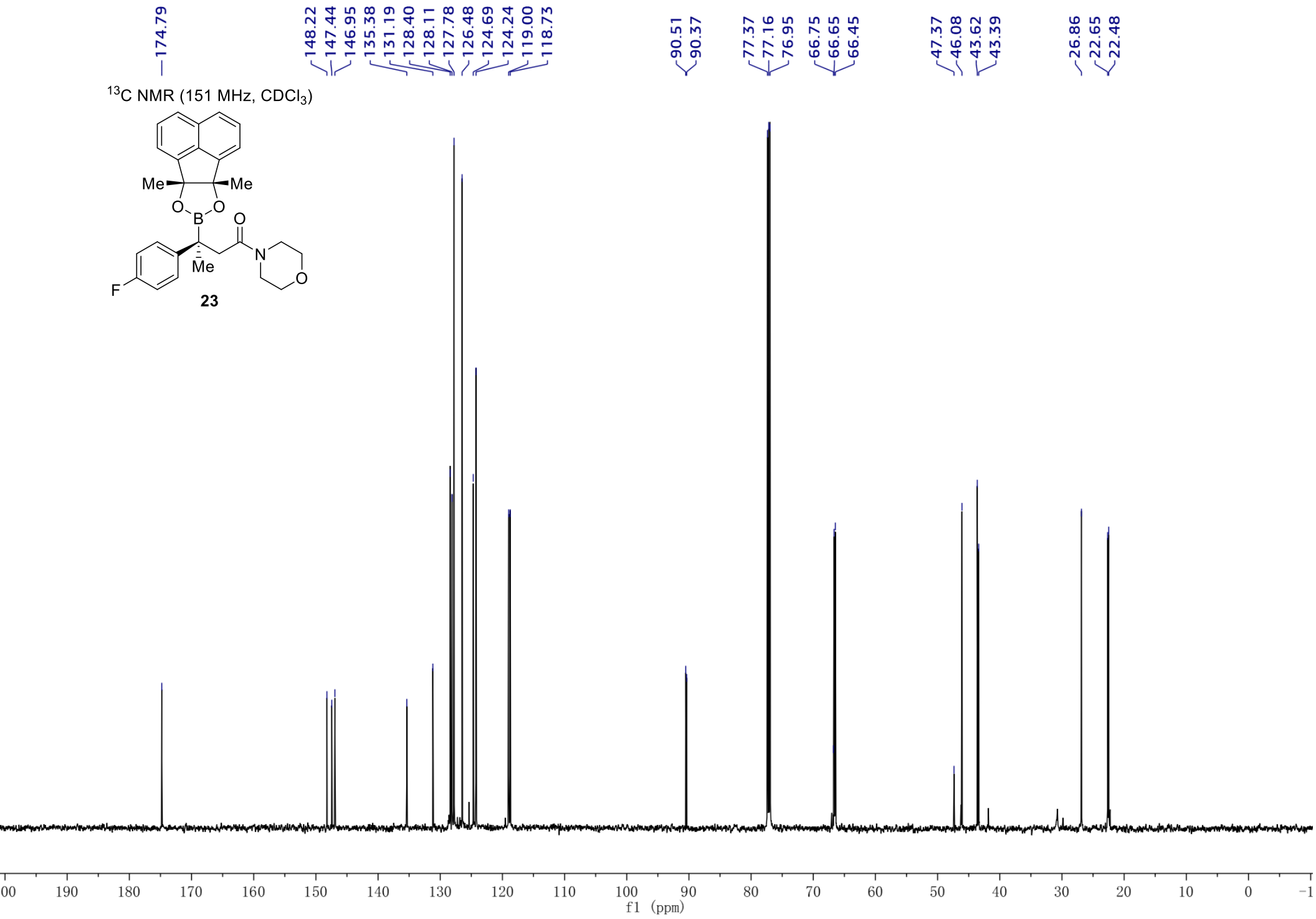

**22**


174.55
148.14
147.35
146.78
137.10
135.31
131.23
128.39
128.16
127.69
127.59
125.50
124.31
123.27
119.01
118.83
90.62
90.49
77.37
77.16
76.95
66.71
66.49
46.06
43.58
43.30
29.82
27.04
22.50
21.36
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
N
O
22
f1 (ppm)

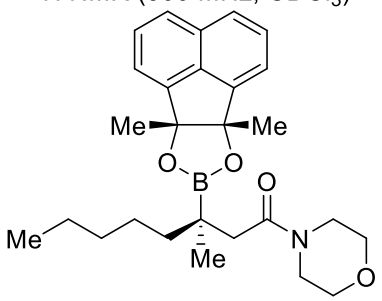
$^1$H NMR (600 MHz, $CDCl_3$)



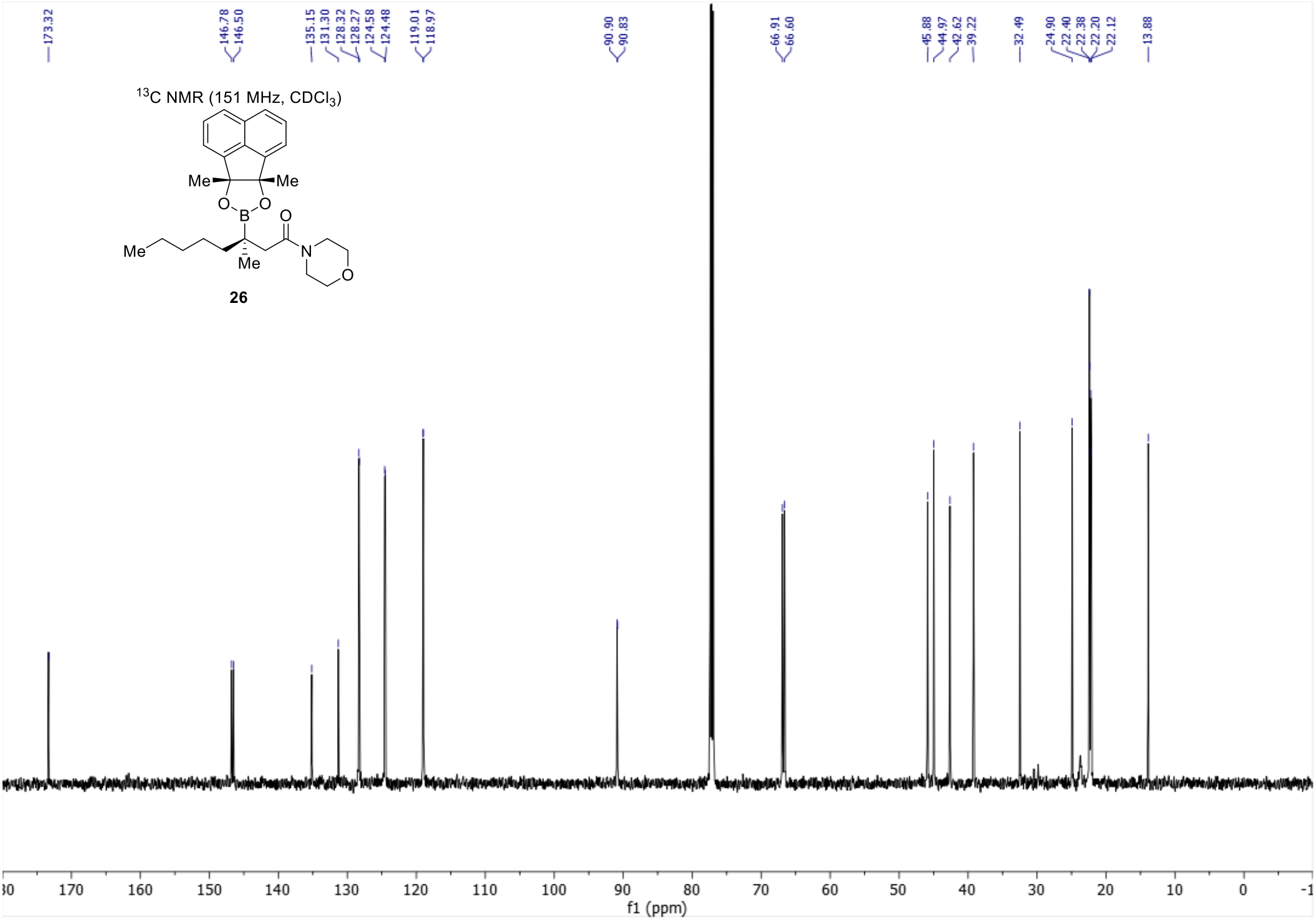

**23**


174.79
148.22
147.44
146.95
135.38
131.19
128.40
128.11
127.78
126.48
124.69
124.24
119.00
118.73
90.51
90.37
77.37
77.16
76.95
66.75
66.65
66.45
47.37
46.08
43.62
43.39
26.86
22.65
22.48
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
N
O
Me
F
23
f1 (ppm)

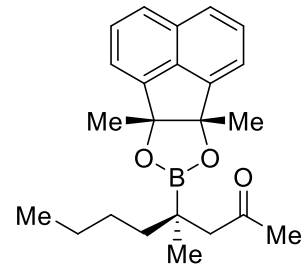
$^1$H NMR (500 MHz, $CDCl_3$)




**26**


173.32
146.78
146.50
135.15
131.30
128.32
128.27
124.58
124.48
119.01
118.97
90.90
90.83
66.91
66.60
45.88
44.97
42.62
39.22
32.49
24.90
22.40
22.38
22.20
22.12
13.88
$^{13}$C NMR (151 MHz, CDCl$_3$)
Me
Me
O
B
O
O
Me
Me
N
O
26
f1 (ppm)

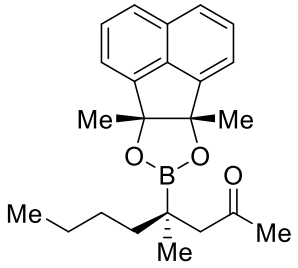
$^1$H NMR (500 MHz, $CDCl_3$)



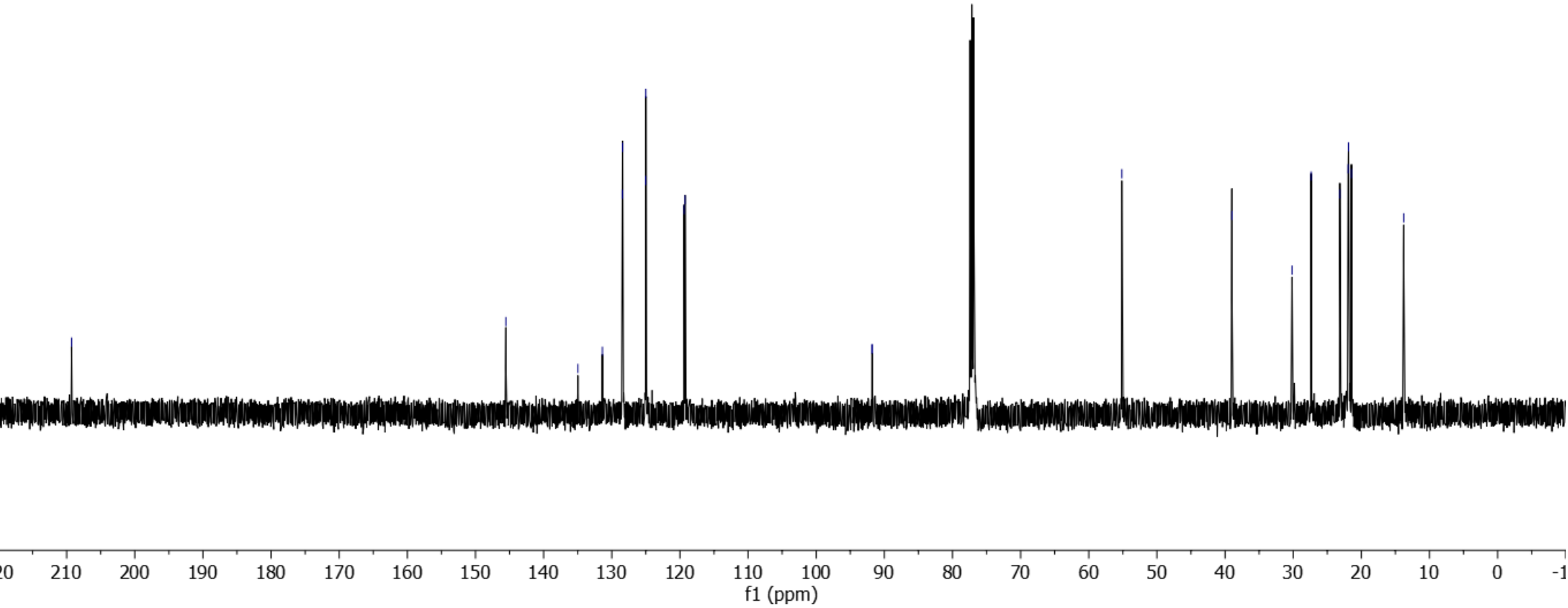

**29**

209.27
145.53
134.98
131.37
128.45
128.41
125.02
125.00
119.38
119.25
91.82
91.77
55.15
38.99
30.18
27.37
23.17
21.94
21.88
21.45
13.78

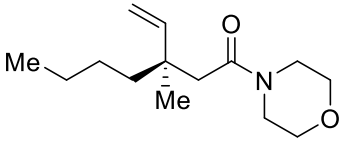
$^{13}$C NMR (126 MHz, $CDCl_3$)



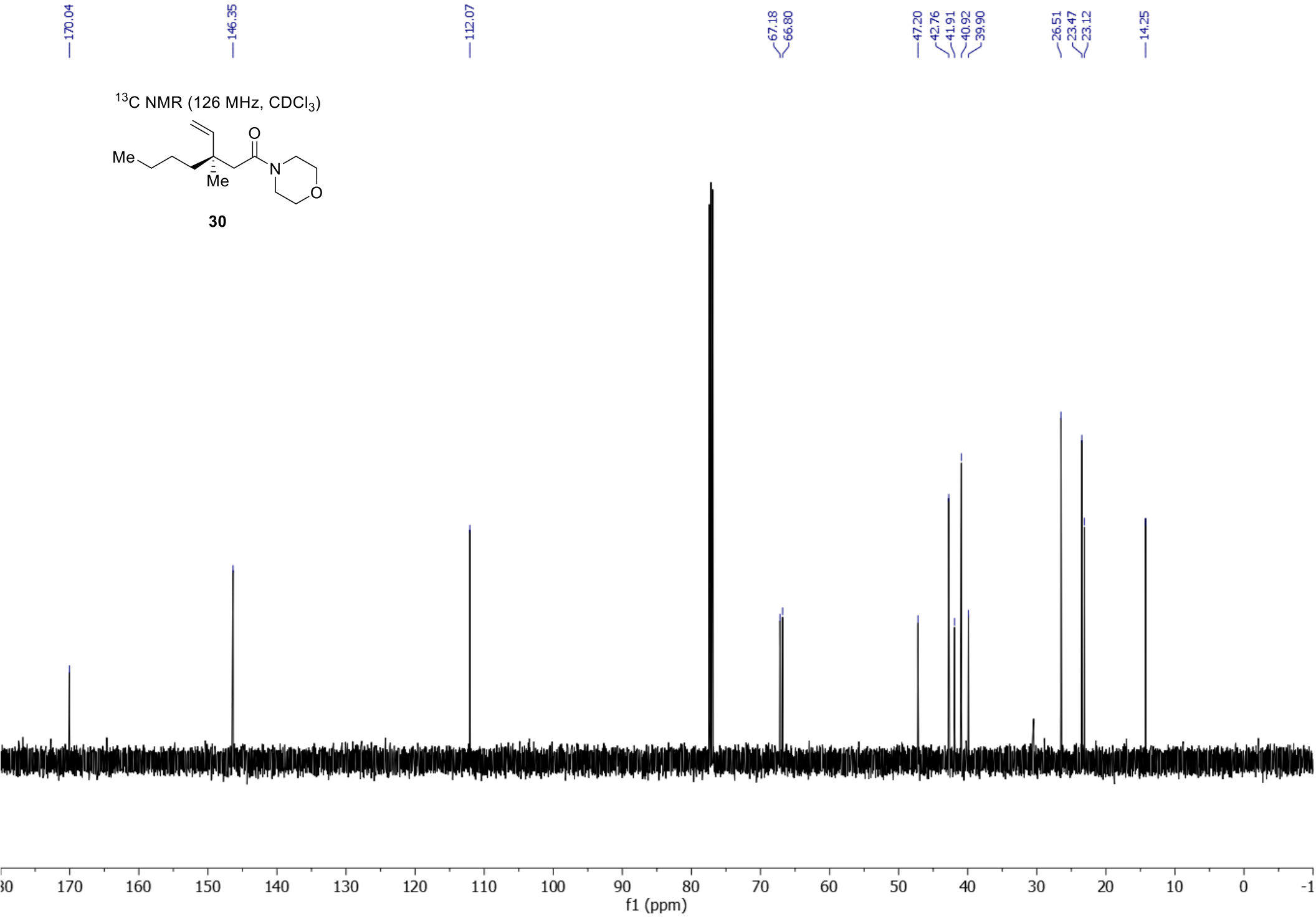

**29**



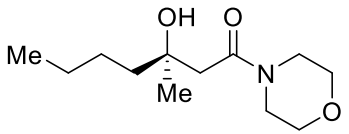
$^1$H NMR (400 MHz, $CDCl_3$)



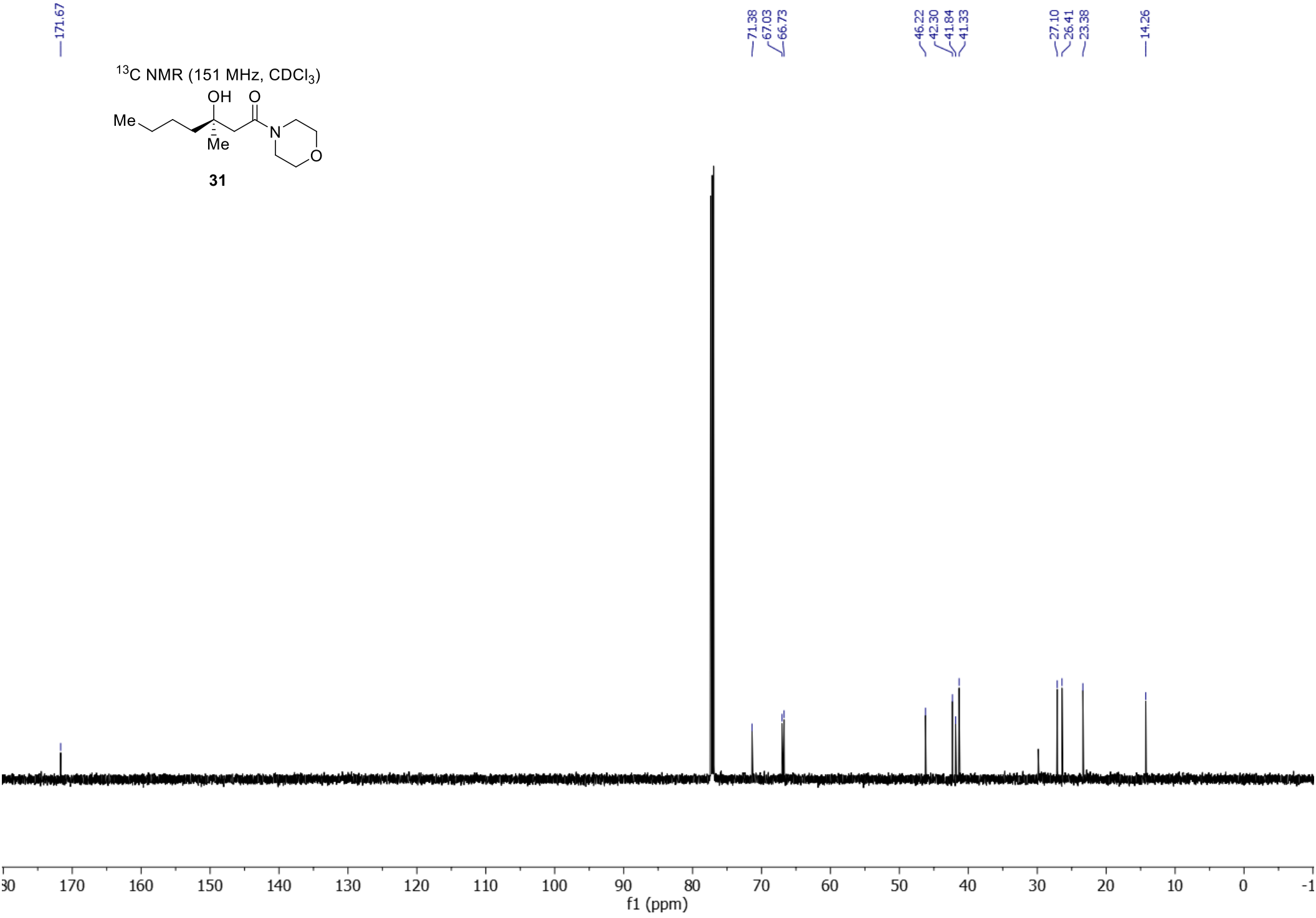

**30**

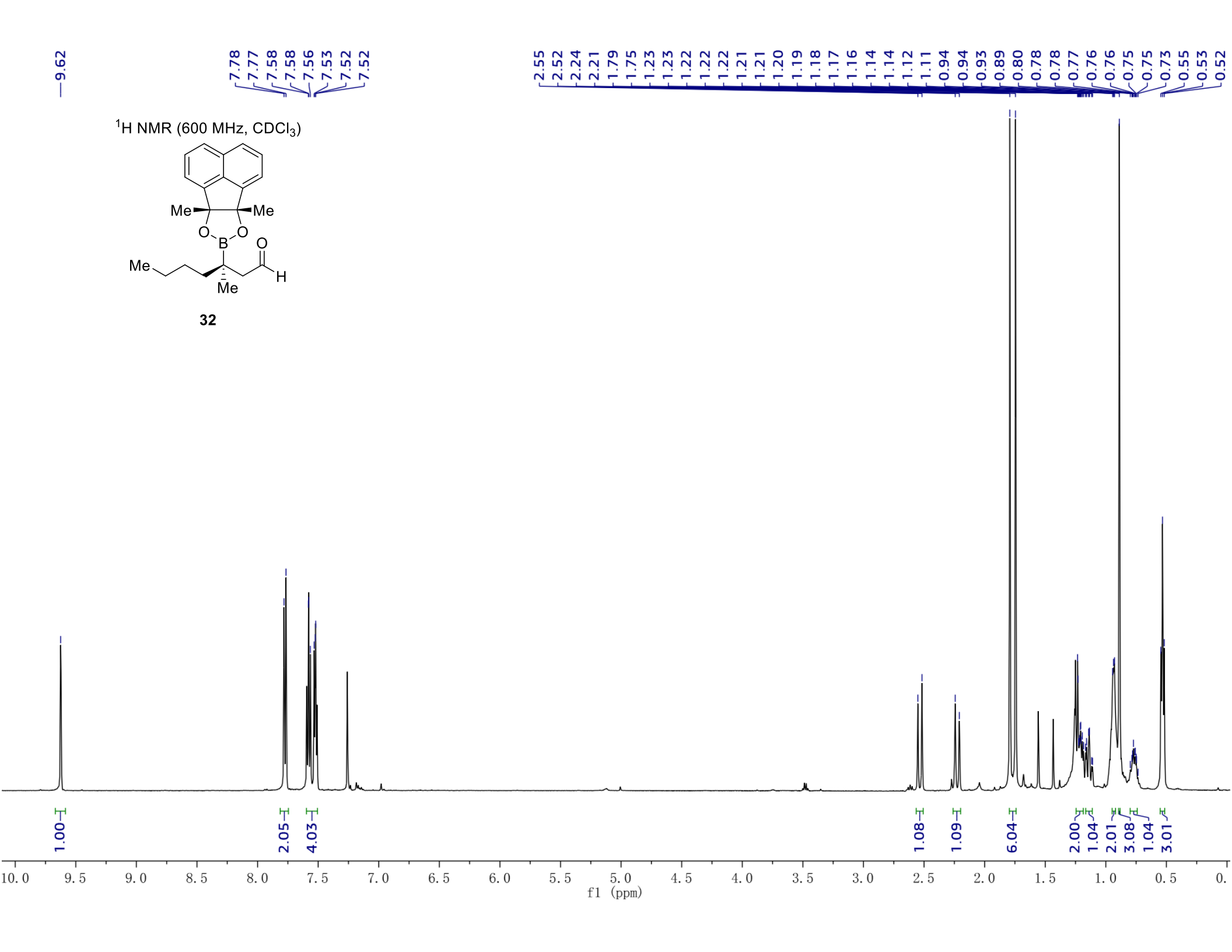

170.04
146.35
112.07
67.18
66.80
47.20
42.76
41.91
40.92
39.90
26.51
23.47
23.12
14.25
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
O
N
O
30
f1 (ppm)

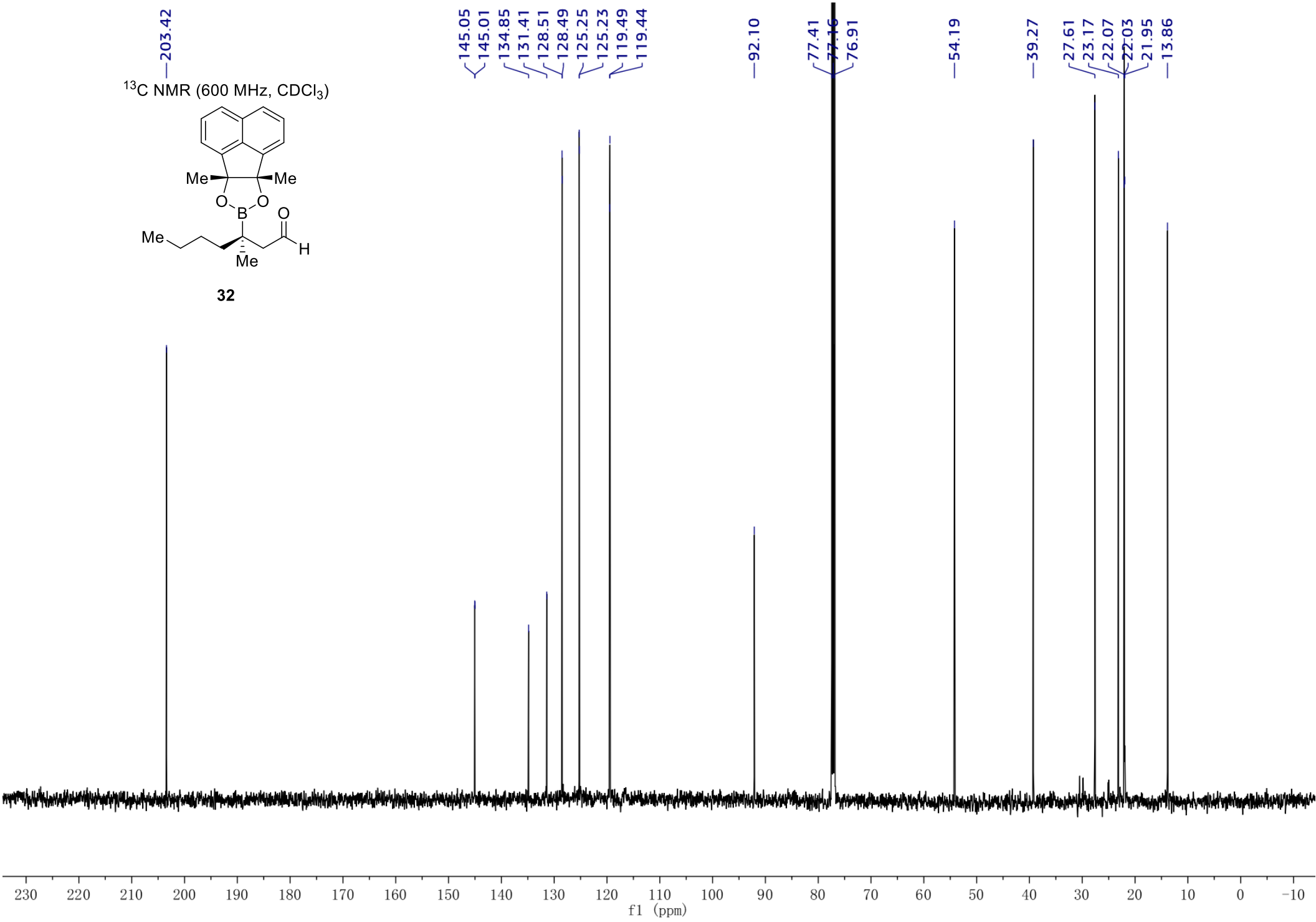
$^1$H NMR (600 MHz, $CDCl_3$)



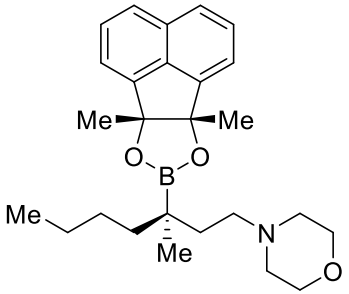

**31**


171.67
71.38
67.03
66.73
46.22
42.30
41.84
41.33
27.10
26.41
23.38
14.26
13C NMR (151 MHz, CDCl3)
OH
O
Me
Me
N
O
31
f1 (ppm)

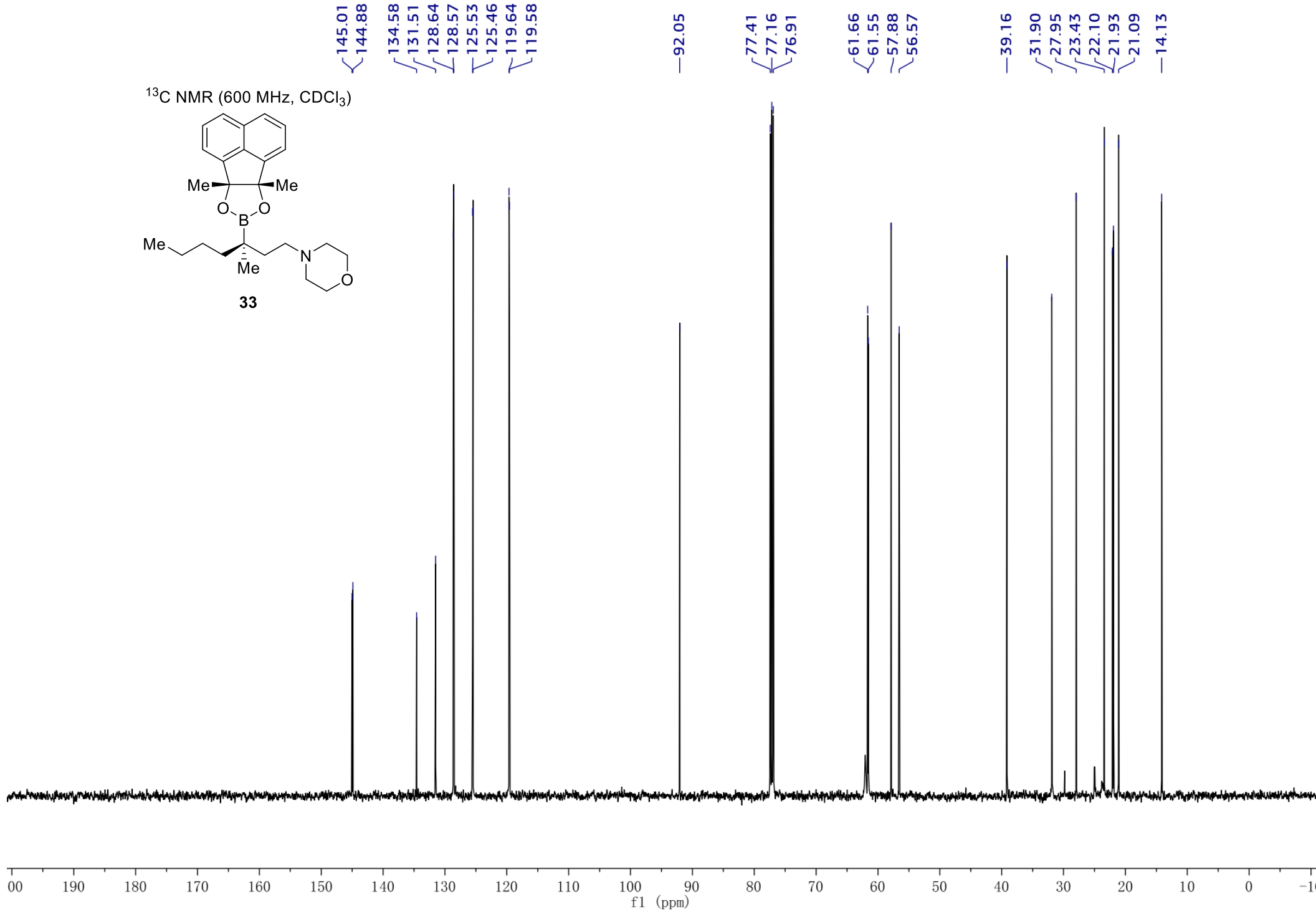

9.62
7.78
7.77
7.58
7.58
7.56
7.53
7.52
7.52
2.55
2.52
2.24
2.21
1.79
1.75
1.23
1.23
1.22
1.22
1.22
1.21
1.21
1.20
1.19
1.18
1.17
1.16
1.14
1.14
1.12
1.11
0.94
0.94
0.93
0.89
0.80
0.78
0.78
0.77
0.76
0.76
0.75
0.75
0.73
0.55
0.53
0.52
1H NMR (600 MHz, CDCl3)
Me
Me
O
B
O
O
Me
H
Me
32
1.00
2.05
4.03
1.08
1.09
6.04
2.00
1.04
2.01
3.08
1.04
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


203.42
145.05
145.01
134.85
131.41
128.51
128.49
125.25
125.23
119.49
119.44
92.10
77.41
77.16
76.91
54.19
39.27
27.61
23.17
22.07
22.03
21.95
13.86
13C NMR (600 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
H
32
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

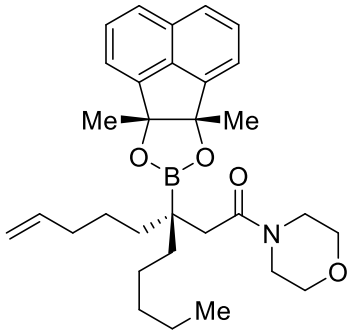
$^1$H NMR (600 MHz, $CDCl_3$)



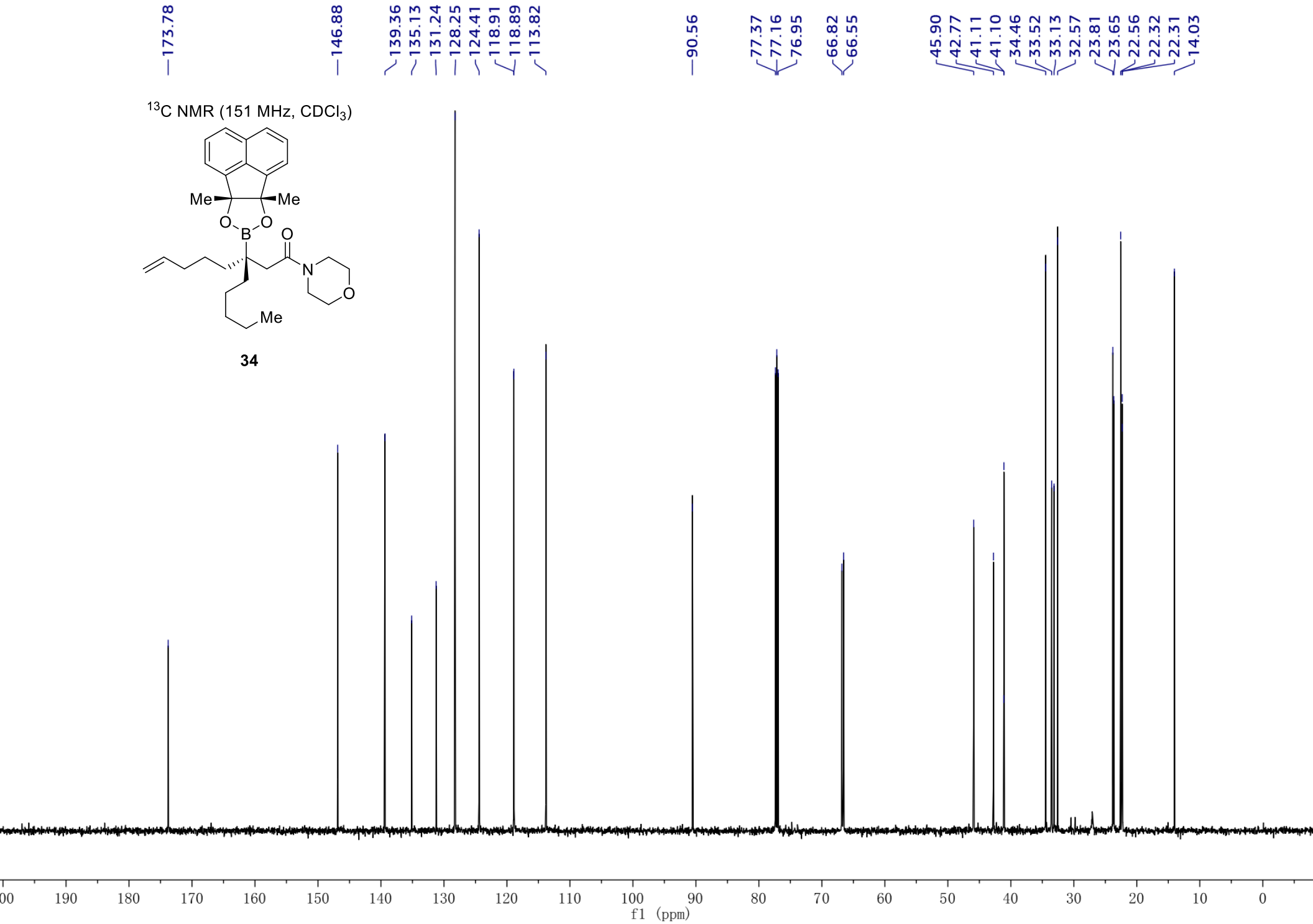

**33**


145.01
144.88
134.58
131.51
128.64
128.57
125.53
125.46
119.64
119.58
92.05
77.41
77.16
76.91
61.66
61.55
57.88
56.57
39.16
31.90
27.95
23.43
22.10
21.93
21.09
14.13
13C NMR (600 MHz, CDCl3)
Me
Me
O
B
O
Me
Me
N
O
33
f1 (ppm)

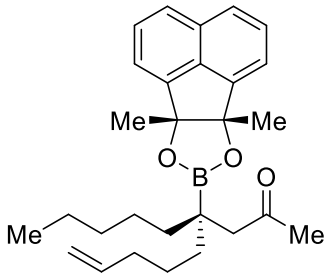
$^1$H NMR (600 MHz, $CDCl_3$)



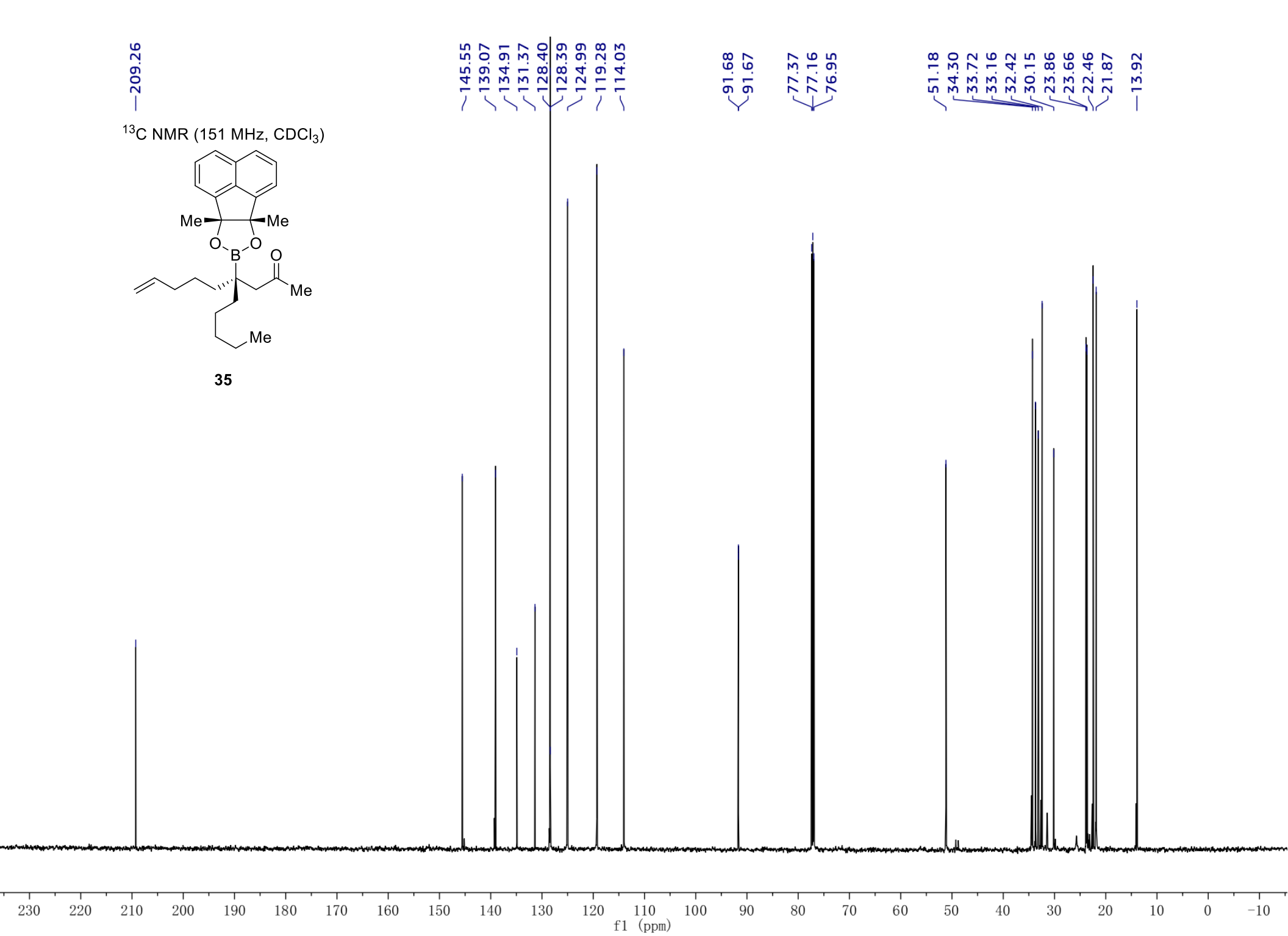

**34**


173.78
146.88
139.36
135.13
131.24
128.25
124.41
118.91
118.89
113.82
90.56
77.37
77.16
76.95
66.82
66.55
45.90
42.77
41.11
41.10
34.46
33.52
33.13
32.57
23.81
23.65
22.56
22.32
22.31
14.03
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
N
O
Me
34
f1 (ppm)

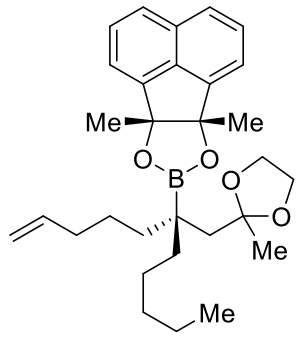
$^1$H NMR (400 MHz, $CDCl_3$)



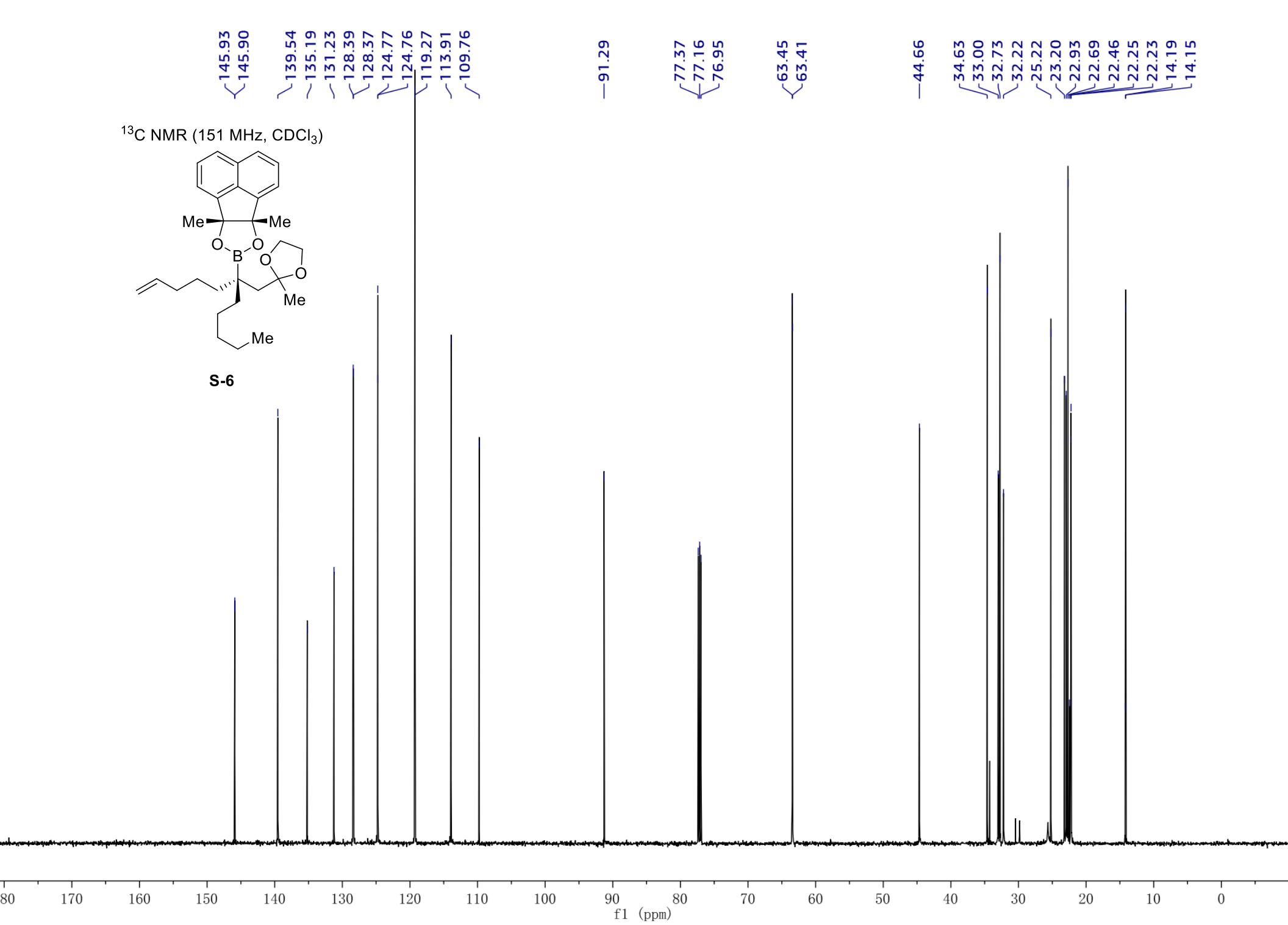

**35**


209.26
145.55
139.07
134.91
131.37
128.40
128.39
124.99
119.28
114.03
91.68
91.67
77.37
77.16
76.95
51.18
34.30
33.72
33.16
32.42
30.15
23.86
23.66
22.46
21.87
13.92
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
Me
Me
35
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

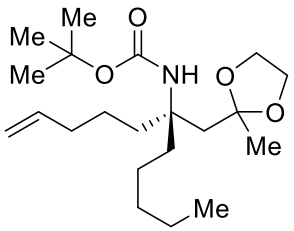
$^1$H NMR (600 MHz, $CDCl_3$)



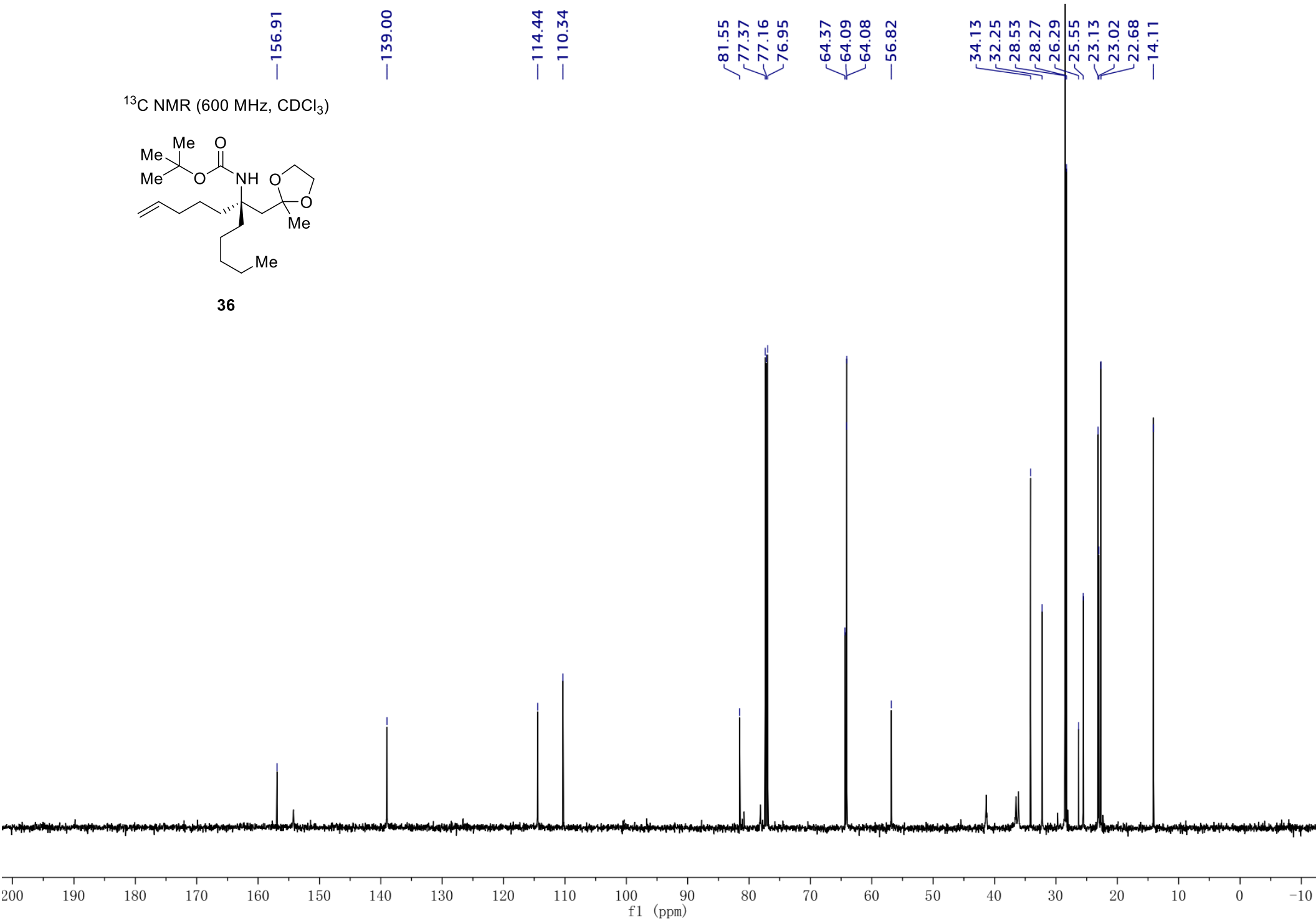

**S-6**


145.93
145.90
139.54
135.19
131.23
128.39
128.37
124.77
124.76
119.27
113.91
109.76
91.29
77.37
77.16
76.95
63.45
63.41
44.66
34.63
33.00
32.73
32.22
25.22
23.20
22.93
22.69
22.46
22.25
22.23
14.19
14.15
13C NMR (151 MHz, CDCl3)
Me
Me
O
B
O
O
O
Me
Me
S-6
f1 (ppm)

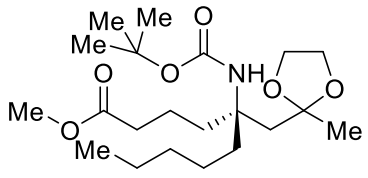
$^1$H NMR (600 MHz, $CDCl_3$)



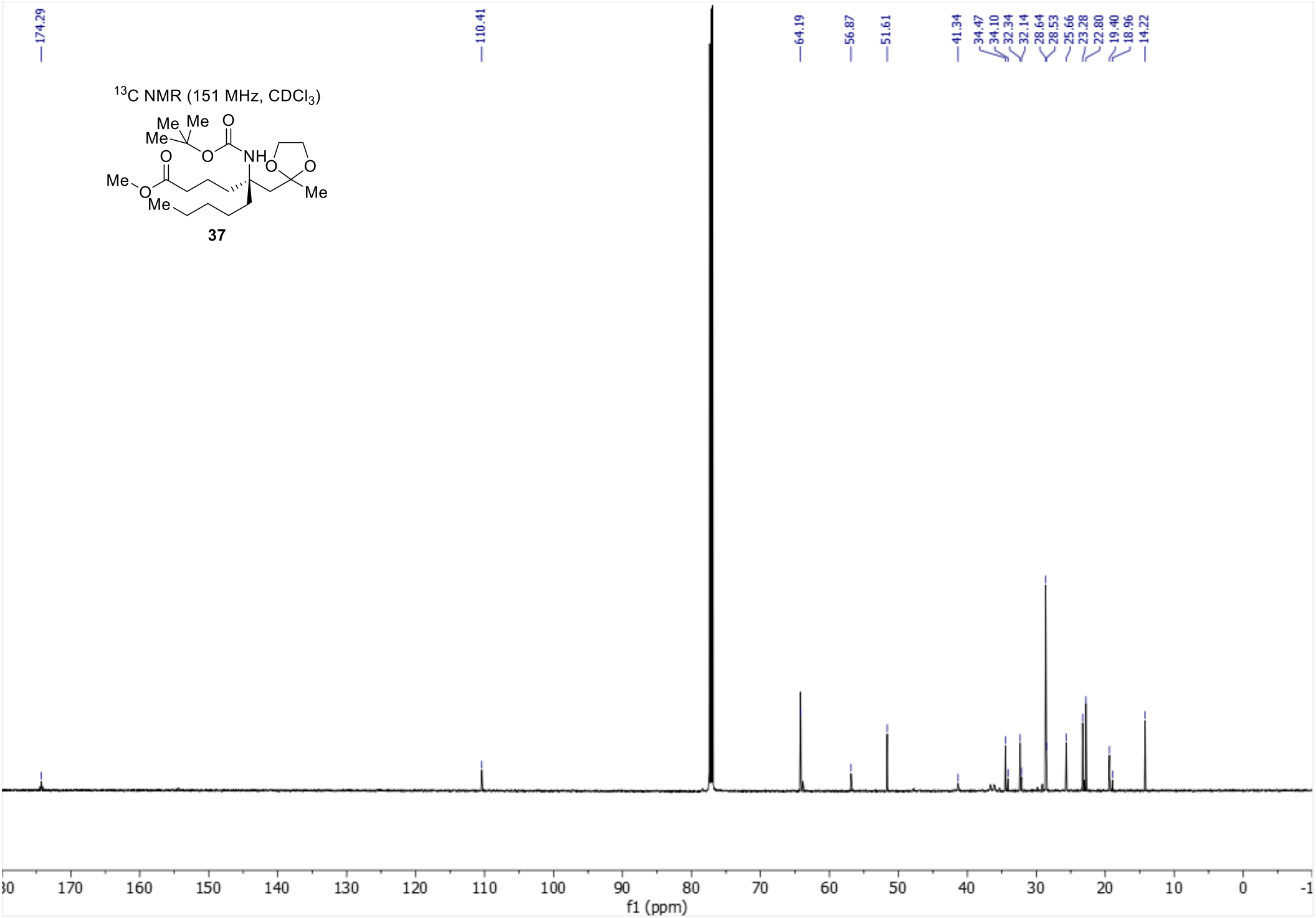

**36**


156.91
139.00
114.44
110.34
81.55
77.37
77.16
76.95
64.37
64.09
64.08
56.82
34.13
32.25
28.53
28.27
26.29
25.55
23.13
23.02
22.68
14.11
13C NMR (600 MHz, CDCl3)
Me
Me
Me
O
O
NH
O
O
Me
Me
36
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

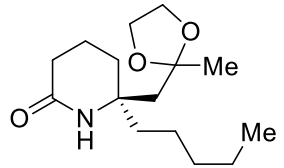
$^1$H NMR (500 MHz, $CDCl_3$)



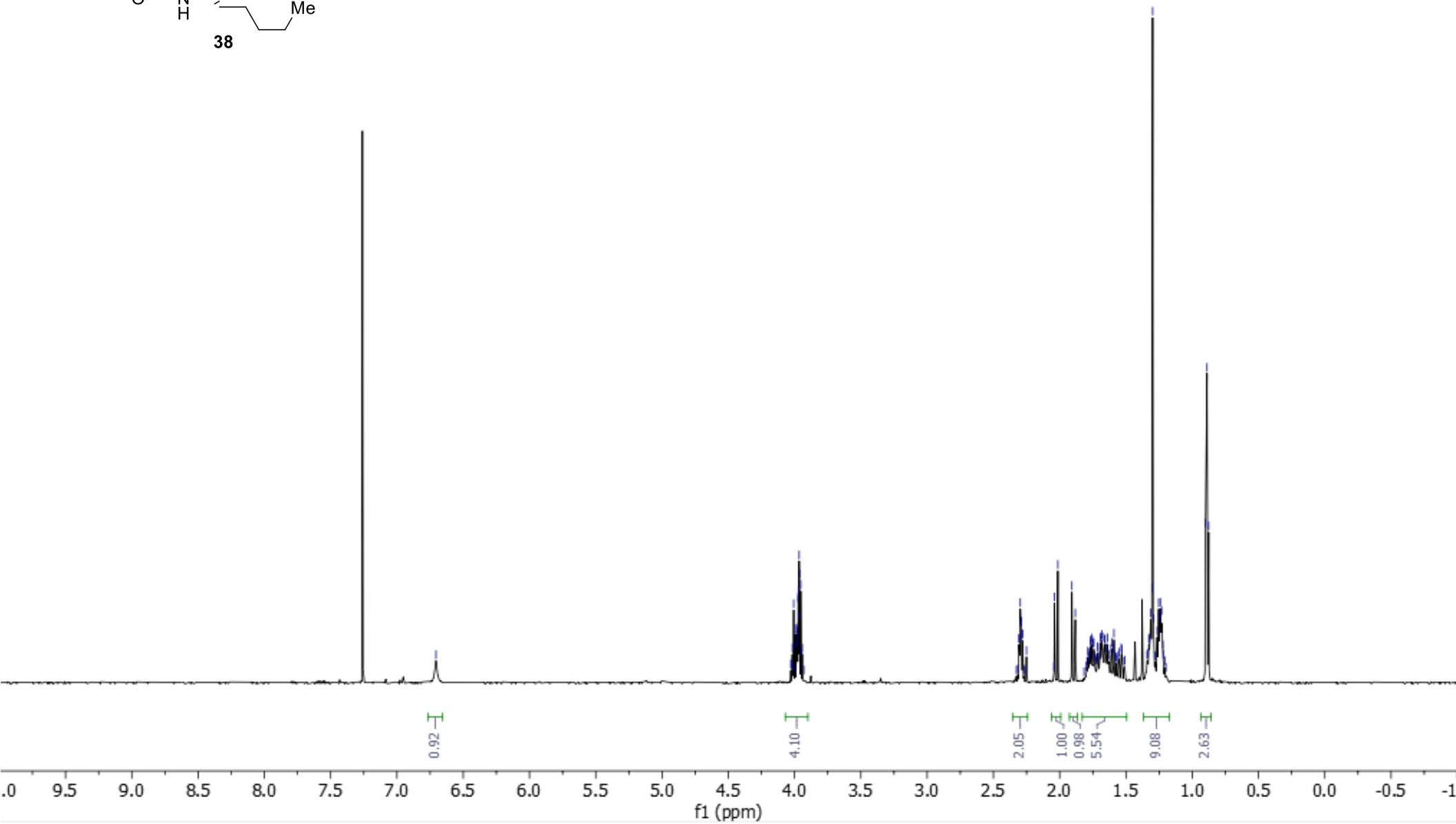

**37**

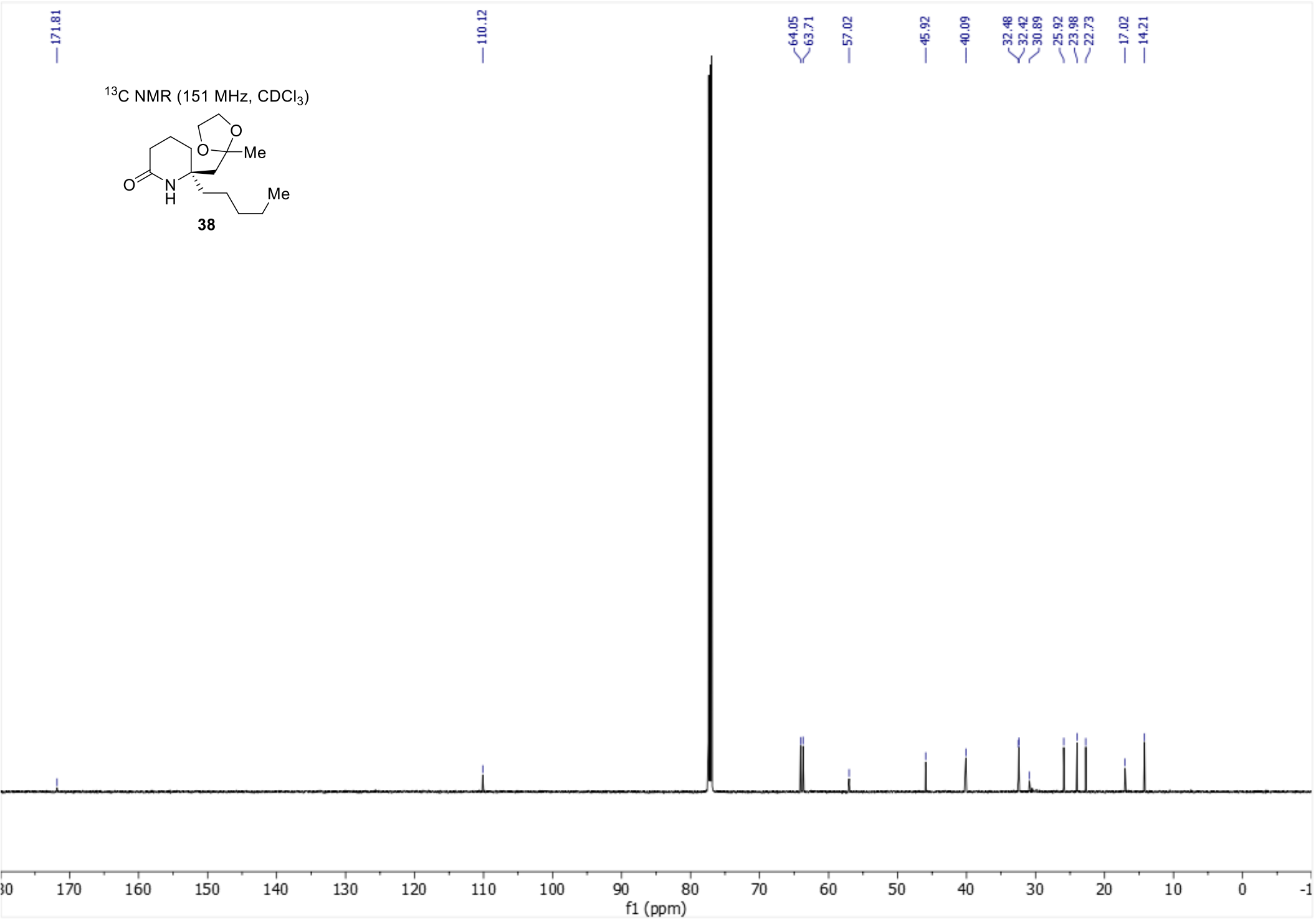

174.29
110.41
64.19
56.87
51.61
41.34
34.47
34.10
32.34
32.14
28.64
28.53
25.66
23.28
22.80
19.40
18.96
14.22
13C NMR (151 MHz, CDCl3)
Me
Me
Me
O
O
NH
O
O
Me
O
Me
Me
37
f1 (ppm)

$^1$H NMR (600 MHz, $CDCl_3$)

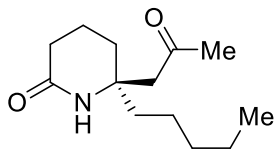



**38**



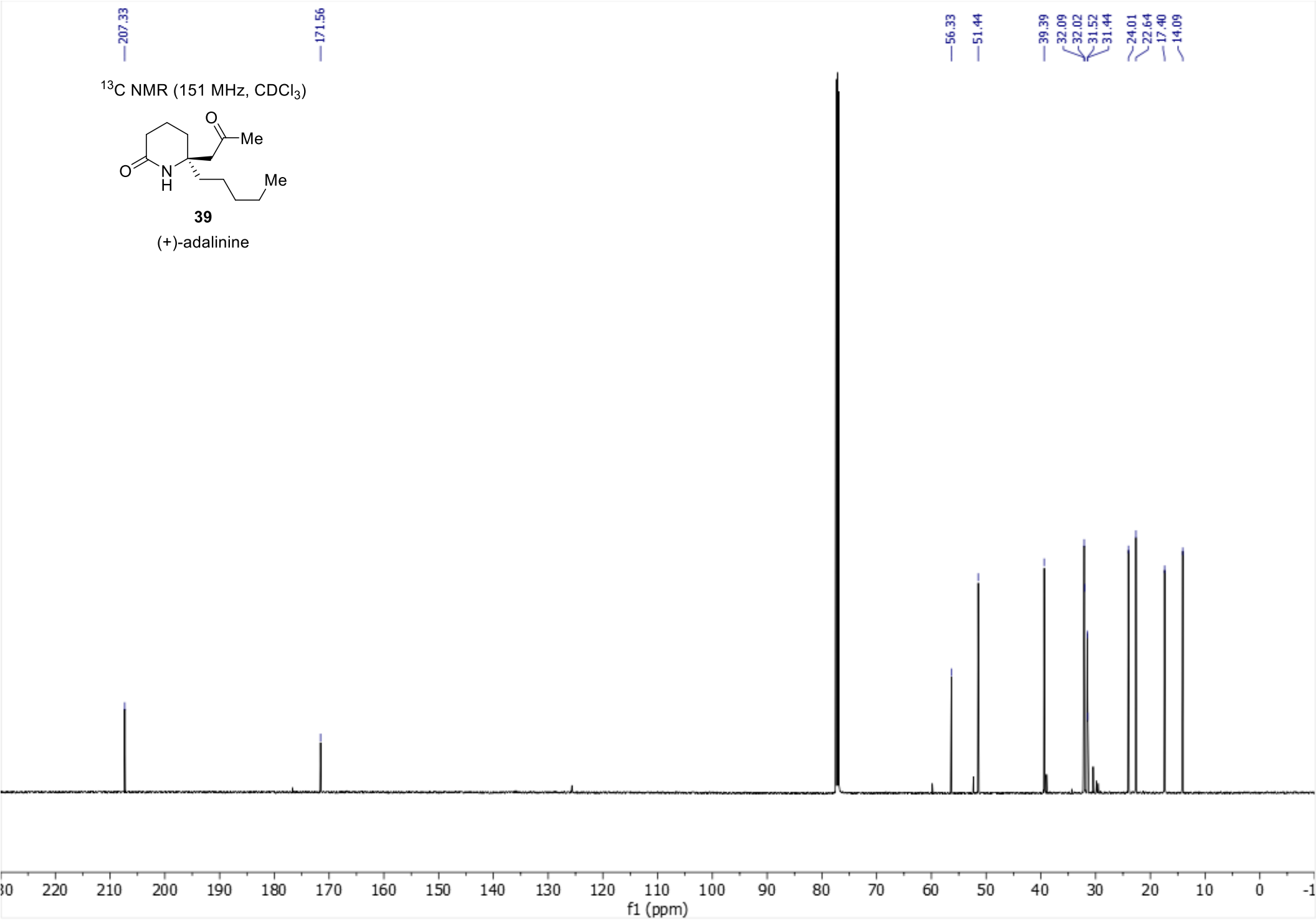

171.81
110.12
64.05
63.71
57.02
45.92
40.09
32.48
32.42
30.89
25.92
23.98
22.73
17.02
14.21
13C NMR (151 MHz, CDCl3)
O
O
Me
O
N
H
Me
38
f1 (ppm)

$^1$H NMR (600 MHz, $CDCl_3$)



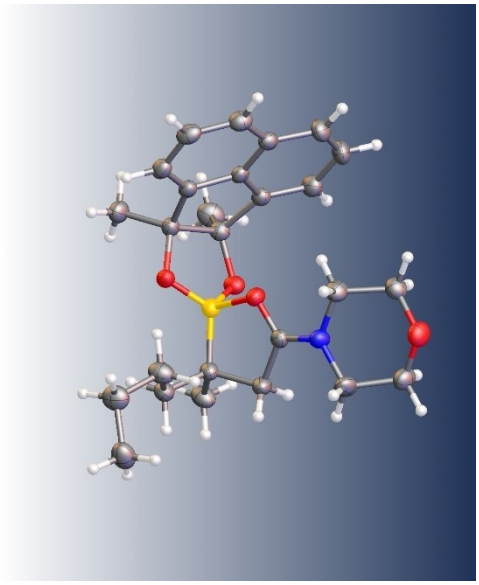

**39**

(+)-adalinine


207.33
171.56
56.33
51.44
39.39
32.09
32.02
31.52
31.44
24.01
22.64
17.40
14.09
$^{13}$C NMR (151 MHz, $CDCl_3$)
O
Me
O
N
H
Me
39
(+)-adalinine
f1 (ppm)

### 1.4.5 X-ray Crystallography Data

Table 1. Crystal data and structure refinement for C26H34BNO4.



| | | |
|---|---|---|
| Identification code | C26H34BNO4 | |
| Empirical formula | C26 H34 B N O4 | |
| Formula weight | 435.35 | |
| Temperature | 173(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 9.4672(7) Å | α= 90°. |
| | b = 13.2370(9) Å | β= 90°. |
| | c = 18.5559(13) Å | γ = 90°. |
| Volume | 2325.4(3) $Å^3$ | |
| Z | 4 | |
| Density (Calc'd) | 1.244 $Mg/m^3$ | |
| Absorption coefficient | 0.652 $mm^{-1}$ | |
| F(000) | 936 | |
| Crystal size | 0.360 x 0.180 x 0.120 $mm^3$ | |
| Theta range for data collection | 4.102 to 66.465°. | |
| Index ranges | -11<=h<=11, -15<=k<=15, -22<=l<=21 | |
| Reflections collected | 55923 | |

| | |
|---|---|
| Independent reflections | 4073 [R(int) = 0.0394] |
| Completeness to theta = 66.465° | 99.3 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.7528 and 0.6825 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 4073 / 0 / 289 |
| Goodness-of-fit on $F^2$ | 1.054 |
| Final R indices [I>2sigma(I)] | R1 = 0.0292, wR2 = 0.0756 |
| R indices (all data) | R1 = 0.0315, wR2 = 0.0790 |
| Absolute structure parameter | -0.01(4) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.120 and -0.166 e.$Å^{-3}$ |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for C26H34BNO4. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 4071(1) | 5266(1) | 6404(1) | 29(1) |
| O(2) | 1140(2) | 3000(1) | 4972(1) | 41(1) |
| O(3) | 5458(1) | 6614(1) | 7048(1) | 28(1) |
| O(4) | 5864(1) | 4949(1) | 7358(1) | 30(1) |
| N(1) | 3227(2) | 4341(1) | 5486(1) | 32(1) |
| B(1) | 5660(2) | 5628(2) | 6768(1) | 27(1) |
| C(1) | 6506(3) | 7693(2) | 4173(1) | 48(1) |
| C(2) | 5878(3) | 7935(2) | 4904(1) | 46(1) |
| C(3) | 5519(2) | 6995(2) | 5353(1) | 40(1) |
| C(4) | 6824(2) | 6449(1) | 5621(1) | 32(1) |
| C(5) | 6625(2) | 5471(1) | 6058(1) | 28(1) |
| C(6) | 5808(2) | 4689(2) | 5606(1) | 35(1) |
| C(7) | 4287(2) | 4778(1) | 5832(1) | 28(1) |
| C(8) | 1776(2) | 4411(2) | 5747(1) | 36(1) |
| C(9) | 1078(2) | 3383(2) | 5689(1) | 35(1) |
| C(10) | 2570(2) | 2878(2) | 4760(1) | 40(1) |
| C(11) | 3361(2) | 3865(2) | 4773(1) | 39(1) |
| C(12) | 8100(2) | 5070(2) | 6245(1) | 40(1) |
| C(13) | 5183(2) | 5370(1) | 7975(1) | 28(1) |
| C(14) | 3677(2) | 4974(1) | 8055(1) | 26(1) |
| C(15) | 3176(2) | 4025(1) | 8202(1) | 33(1) |
| C(16) | 1695(2) | 3885(2) | 8237(1) | 39(1) |
| C(17) | 744(2) | 4655(2) | 8130(1) | 36(1) |
| C(18) | 1239(2) | 5645(1) | 7981(1) | 29(1) |
| C(19) | 425(2) | 6530(2) | 7876(1) | 34(1) |
| C(20) | 1084(2) | 7443(2) | 7753(1) | 35(1) |
| C(21) | 2569(2) | 7539(1) | 7708(1) | 31(1) |
| C(22) | 3380(2) | 6692(1) | 7803(1) | 25(1) |
| C(23) | 2715(2) | 5767(1) | 7948(1) | 25(1) |
| C(24) | 4965(2) | 6537(1) | 7776(1) | 27(1) |
| C(25) | 6070(2) | 5149(2) | 8637(1) | 42(1) |

| | | | | |
|---|---|---|---|---|
| C(26) | 5764(2) | 7299(2) | 8230(1) | 38(1) |

Table 3. Bond lengths [Å] and angles [°] for C26H34BNO4.

| | |
|---|---|
| O(1)-C(7) | 1.260(2) |
| O(1)-B(1) | 1.717(2) |
| O(2)-C(10) | 1.419(3) |
| O(2)-C(9) | 1.425(3) |
| O(3)-B(1) | 1.419(2) |
| O(3)-C(24) | 1.432(2) |
| O(4)-C(13) | 1.427(2) |
| O(4)-B(1) | 1.430(3) |
| N(1)-C(7) | 1.324(3) |
| N(1)-C(8) | 1.461(3) |
| N(1)-C(11) | 1.470(3) |
| B(1)-C(5) | 1.616(3) |
| C(1)-C(2) | 1.516(3) |
| C(1)-H(1A) | 0.9800 |
| C(1)-H(1B) | 0.9800 |
| C(1)-H(1C) | 0.9800 |
| C(2)-C(3) | 1.535(3) |
| C(2)-H(2A) | 0.9900 |
| C(2)-H(2B) | 0.9900 |
| C(3)-C(4) | 1.515(3) |
| C(3)-H(3A) | 0.9900 |
| C(3)-H(3B) | 0.9900 |
| C(4)-C(5) | 1.538(3) |
| C(4)-H(4A) | 0.9900 |
| C(4)-H(4B) | 0.9900 |
| C(5)-C(12) | 1.533(3) |
| C(5)-C(6) | 1.541(3) |
| C(6)-C(7) | 1.505(3) |
| C(6)-H(6A) | 0.9900 |
| C(6)-H(6B) | 0.9900 |
| C(8)-C(9) | 1.516(3) |
| C(8)-H(8A) | 0.9900 |
| C(8)-H(8B) | 0.9900 |
| C(9)-H(9A) | 0.9900 |

| | |
|---|---|
| C(9)-H(9B) | 0.9900 |
| C(10)-C(11) | 1.506(3) |
| C(10)-H(10A) | 0.9900 |
| C(10)-H(10B) | 0.9900 |
| C(11)-H(11A) | 0.9900 |
| C(11)-H(11B) | 0.9900 |
| C(12)-H(12A) | 0.9800 |
| C(12)-H(12B) | 0.9800 |
| C(12)-H(12C) | 0.9800 |
| C(13)-C(25) | 1.516(3) |
| C(13)-C(14) | 1.527(3) |
| C(13)-C(24) | 1.602(3) |
| C(14)-C(15) | 1.370(3) |
| C(14)-C(23) | 1.404(3) |
| C(15)-C(16) | 1.416(3) |
| C(15)-H(15A) | 0.9500 |
| C(16)-C(17) | 1.374(3) |
| C(16)-H(16A) | 0.9500 |
| C(17)-C(18) | 1.419(3) |
| C(17)-H(17A) | 0.9500 |
| C(18)-C(23) | 1.408(3) |
| C(18)-C(19) | 1.416(3) |
| C(19)-C(20) | 1.379(3) |
| C(19)-H(19A) | 0.9500 |
| C(20)-C(21) | 1.414(3) |
| C(20)-H(20A) | 0.9500 |
| C(21)-C(22) | 1.370(3) |
| C(21)-H(21A) | 0.9500 |
| C(22)-C(23) | 1.403(2) |
| C(22)-C(24) | 1.516(3) |
| C(24)-C(26) | 1.517(3) |
| C(25)-H(25A) | 0.9800 |
| C(25)-H(25B) | 0.9800 |
| C(25)-H(25C) | 0.9800 |
| C(26)-H(26A) | 0.9800 |
| C(26)-H(26B) | 0.9800 |

| | |
|---|---|
| C(26)-H(26C) | 0.9800 |
| | |
| C(7)-O(1)-B(1) | 109.38(13) |
| C(10)-O(2)-C(9) | 109.79(15) |
| B(1)-O(3)-C(24) | 108.90(13) |
| C(13)-O(4)-B(1) | 107.95(14) |
| C(7)-N(1)-C(8) | 121.59(16) |
| C(7)-N(1)-C(11) | 123.95(17) |
| C(8)-N(1)-C(11) | 114.02(16) |
| O(3)-B(1)-O(4) | 108.41(16) |
| O(3)-B(1)-C(5) | 119.55(15) |
| O(4)-B(1)-C(5) | 117.84(15) |
| O(3)-B(1)-O(1) | 106.43(14) |
| O(4)-B(1)-O(1) | 104.11(14) |
| C(5)-B(1)-O(1) | 98.03(13) |
| C(2)-C(1)-H(1A) | 109.5 |
| C(2)-C(1)-H(1B) | 109.5 |
| H(1A)-C(1)-H(1B) | 109.5 |
| C(2)-C(1)-H(1C) | 109.5 |
| H(1A)-C(1)-H(1C) | 109.5 |
| H(1B)-C(1)-H(1C) | 109.5 |
| C(1)-C(2)-C(3) | 113.6(2) |
| C(1)-C(2)-H(2A) | 108.8 |
| C(3)-C(2)-H(2A) | 108.8 |
| C(1)-C(2)-H(2B) | 108.8 |
| C(3)-C(2)-H(2B) | 108.8 |
| H(2A)-C(2)-H(2B) | 107.7 |
| C(4)-C(3)-C(2) | 112.62(18) |
| C(4)-C(3)-H(3A) | 109.1 |
| C(2)-C(3)-H(3A) | 109.1 |
| C(4)-C(3)-H(3B) | 109.1 |
| C(2)-C(3)-H(3B) | 109.1 |
| H(3A)-C(3)-H(3B) | 107.8 |
| C(3)-C(4)-C(5) | 118.34(17) |
| C(3)-C(4)-H(4A) | 107.7 |
| C(5)-C(4)-H(4A) | 107.7 |

| | |
|---|---|
| C(3)-C(4)-H(4B) | 107.7 |
| C(5)-C(4)-H(4B) | 107.7 |
| H(4A)-C(4)-H(4B) | 107.1 |
| C(12)-C(5)-C(4) | 107.37(16) |
| C(12)-C(5)-C(6) | 110.32(16) |
| C(4)-C(5)-C(6) | 109.82(17) |
| C(12)-C(5)-B(1) | 112.04(16) |
| C(4)-C(5)-B(1) | 113.00(15) |
| C(6)-C(5)-B(1) | 104.29(14) |
| C(7)-C(6)-C(5) | 106.00(15) |
| C(7)-C(6)-H(6A) | 110.5 |
| C(5)-C(6)-H(6A) | 110.5 |
| C(7)-C(6)-H(6B) | 110.5 |
| C(5)-C(6)-H(6B) | 110.5 |
| H(6A)-C(6)-H(6B) | 108.7 |
| O(1)-C(7)-N(1) | 120.68(17) |
| O(1)-C(7)-C(6) | 115.50(16) |
| N(1)-C(7)-C(6) | 123.74(16) |
| N(1)-C(8)-C(9) | 109.23(16) |
| N(1)-C(8)-H(8A) | 109.8 |
| C(9)-C(8)-H(8A) | 109.8 |
| N(1)-C(8)-H(8B) | 109.8 |
| C(9)-C(8)-H(8B) | 109.8 |
| H(8A)-C(8)-H(8B) | 108.3 |
| O(2)-C(9)-C(8) | 111.59(17) |
| O(2)-C(9)-H(9A) | 109.3 |
| C(8)-C(9)-H(9A) | 109.3 |
| O(2)-C(9)-H(9B) | 109.3 |
| C(8)-C(9)-H(9B) | 109.3 |
| H(9A)-C(9)-H(9B) | 108.0 |
| O(2)-C(10)-C(11) | 111.79(18) |
| O(2)-C(10)-H(10A) | 109.3 |
| C(11)-C(10)-H(10A) | 109.3 |
| O(2)-C(10)-H(10B) | 109.3 |
| C(11)-C(10)-H(10B) | 109.3 |
| H(10A)-C(10)-H(10B) | 107.9 |

| | |
|---|---|
| N(1)-C(11)-C(10) | 110.07(17) |
| N(1)-C(11)-H(11A) | 109.6 |
| C(10)-C(11)-H(11A) | 109.6 |
| N(1)-C(11)-H(11B) | 109.6 |
| C(10)-C(11)-H(11B) | 109.6 |
| H(11A)-C(11)-H(11B) | 108.2 |
| C(5)-C(12)-H(12A) | 109.5 |
| C(5)-C(12)-H(12B) | 109.5 |
| H(12A)-C(12)-H(12B) | 109.5 |
| C(5)-C(12)-H(12C) | 109.5 |
| H(12A)-C(12)-H(12C) | 109.5 |
| H(12B)-C(12)-H(12C) | 109.5 |
| O(4)-C(13)-C(25) | 108.96(16) |
| O(4)-C(13)-C(14) | 111.45(15) |
| C(25)-C(13)-C(14) | 111.81(16) |
| O(4)-C(13)-C(24) | 104.46(14) |
| C(25)-C(13)-C(24) | 116.38(16) |
| C(14)-C(13)-C(24) | 103.50(14) |
| C(15)-C(14)-C(23) | 119.32(17) |
| C(15)-C(14)-C(13) | 131.13(17) |
| C(23)-C(14)-C(13) | 109.55(15) |
| C(14)-C(15)-C(16) | 118.13(18) |
| C(14)-C(15)-H(15A) | 120.9 |
| C(16)-C(15)-H(15A) | 120.9 |
| C(17)-C(16)-C(15) | 123.06(19) |
| C(17)-C(16)-H(16A) | 118.5 |
| C(15)-C(16)-H(16A) | 118.5 |
| C(16)-C(17)-C(18) | 119.78(18) |
| C(16)-C(17)-H(17A) | 120.1 |
| C(18)-C(17)-H(17A) | 120.1 |
| C(23)-C(18)-C(19) | 116.06(17) |
| C(23)-C(18)-C(17) | 116.24(17) |
| C(19)-C(18)-C(17) | 127.68(18) |
| C(20)-C(19)-C(18) | 120.10(18) |
| C(20)-C(19)-H(19A) | 119.9 |
| C(18)-C(19)-H(19A) | 119.9 |

| | |
|---|---|
| C(19)-C(20)-C(21) | 122.61(18) |
| C(19)-C(20)-H(20A) | 118.7 |
| C(21)-C(20)-H(20A) | 118.7 |
| C(22)-C(21)-C(20) | 118.41(17) |
| C(22)-C(21)-H(21A) | 120.8 |
| C(20)-C(21)-H(21A) | 120.8 |
| C(21)-C(22)-C(23) | 119.18(17) |
| C(21)-C(22)-C(24) | 131.42(17) |
| C(23)-C(22)-C(24) | 109.39(15) |
| C(14)-C(23)-C(22) | 112.92(16) |
| C(14)-C(23)-C(18) | 123.47(17) |
| C(22)-C(23)-C(18) | 123.60(17) |
| O(3)-C(24)-C(22) | 110.16(15) |
| O(3)-C(24)-C(26) | 108.31(15) |
| C(22)-C(24)-C(26) | 112.61(16) |
| O(3)-C(24)-C(13) | 104.16(14) |
| C(22)-C(24)-C(13) | 104.52(14) |
| C(26)-C(24)-C(13) | 116.68(16) |
| C(13)-C(25)-H(25A) | 109.5 |
| C(13)-C(25)-H(25B) | 109.5 |
| H(25A)-C(25)-H(25B) | 109.5 |
| C(13)-C(25)-H(25C) | 109.5 |
| H(25A)-C(25)-H(25C) | 109.5 |
| H(25B)-C(25)-H(25C) | 109.5 |
| C(24)-C(26)-H(26A) | 109.5 |
| C(24)-C(26)-H(26B) | 109.5 |
| H(26A)-C(26)-H(26B) | 109.5 |
| C(24)-C(26)-H(26C) | 109.5 |
| H(26A)-C(26)-H(26C) | 109.5 |
| H(26B)-C(26)-H(26C) | 109.5 |

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Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C26H34BNO4. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 28(1) | 28(1) | 30(1) | -7(1) | 4(1) | -1(1) |
| O(2) | 34(1) | 42(1) | 45(1) | -8(1) | -7(1) | -3(1) |
| O(3) | 34(1) | 24(1) | 26(1) | -1(1) | 5(1) | -3(1) |
| O(4) | 30(1) | 27(1) | 33(1) | 2(1) | 6(1) | 4(1) |
| N(1) | 32(1) | 37(1) | 28(1) | -6(1) | 4(1) | -5(1) |
| B(1) | 25(1) | 24(1) | 32(1) | -2(1) | 2(1) | -1(1) |
| C(1) | 56(2) | 50(1) | 38(1) | 6(1) | -2(1) | -13(1) |
| C(2) | 50(1) | 44(1) | 43(1) | 9(1) | 1(1) | 7(1) |
| C(3) | 35(1) | 46(1) | 40(1) | 7(1) | 5(1) | 6(1) |
| C(4) | 30(1) | 31(1) | 34(1) | -1(1) | 4(1) | -2(1) |
| C(5) | 27(1) | 25(1) | 33(1) | -3(1) | 6(1) | -1(1) |
| C(6) | 33(1) | 32(1) | 39(1) | -9(1) | 10(1) | -4(1) |
| C(7) | 32(1) | 25(1) | 27(1) | -1(1) | 4(1) | -3(1) |
| C(8) | 29(1) | 38(1) | 40(1) | -5(1) | 1(1) | 1(1) |
| C(9) | 30(1) | 37(1) | 39(1) | 1(1) | 0(1) | -2(1) |
| C(10) | 38(1) | 43(1) | 38(1) | -12(1) | -1(1) | -4(1) |
| C(11) | 45(1) | 48(1) | 25(1) | -9(1) | 3(1) | -9(1) |
| C(12) | 31(1) | 38(1) | 49(1) | 7(1) | 7(1) | 5(1) |
| C(13) | 27(1) | 29(1) | 29(1) | 1(1) | 0(1) | 2(1) |
| C(14) | 30(1) | 26(1) | 23(1) | -1(1) | 2(1) | 0(1) |
| C(15) | 37(1) | 26(1) | 36(1) | 3(1) | 2(1) | 2(1) |
| C(16) | 43(1) | 27(1) | 46(1) | 0(1) | 4(1) | -9(1) |
| C(17) | 31(1) | 36(1) | 41(1) | -3(1) | 1(1) | -8(1) |
| C(18) | 29(1) | 32(1) | 25(1) | -5(1) | 1(1) | -2(1) |
| C(19) | 30(1) | 38(1) | 33(1) | -3(1) | -2(1) | 6(1) |
| C(20) | 40(1) | 34(1) | 31(1) | 0(1) | 0(1) | 13(1) |
| C(21) | 41(1) | 24(1) | 29(1) | -1(1) | 2(1) | 2(1) |
| C(22) | 31(1) | 24(1) | 21(1) | -2(1) | 2(1) | 0(1) |
| C(23) | 31(1) | 24(1) | 20(1) | -3(1) | 1(1) | -1(1) |
| C(24) | 31(1) | 25(1) | 26(1) | -2(1) | 2(1) | -4(1) |
| C(25) | 38(1) | 53(1) | 37(1) | 8(1) | -6(1) | 3(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(26) | 38(1) | 39(1) | 35(1) | -9(1) | 0(1) | -8(1) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for C26H34BNO4.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 6710 | 8323 | 3916 | 73 |
| H(1B) | 7383 | 7309 | 4236 | 73 |
| H(1C) | 5832 | 7290 | 3893 | 73 |
| H(2A) | 5008 | 8337 | 4835 | 55 |
| H(2B) | 6556 | 8356 | 5178 | 55 |
| H(3A) | 4937 | 7199 | 5771 | 48 |
| H(3B) | 4951 | 6525 | 5055 | 48 |
| H(4A) | 7368 | 6927 | 5923 | 38 |
| H(4B) | 7416 | 6285 | 5197 | 38 |
| H(6A) | 5911 | 4837 | 5085 | 42 |
| H(6B) | 6168 | 4000 | 5700 | 42 |
| H(8A) | 1245 | 4910 | 5457 | 43 |
| H(8B) | 1772 | 4639 | 6255 | 43 |
| H(9A) | 1557 | 2905 | 6019 | 43 |
| H(9B) | 79 | 3438 | 5841 | 43 |
| H(10A) | 2603 | 2592 | 4267 | 47 |
| H(10B) | 3038 | 2393 | 5089 | 47 |
| H(11A) | 4371 | 3744 | 4664 | 47 |
| H(11B) | 2976 | 4322 | 4399 | 47 |
| H(12A) | 8010 | 4445 | 6524 | 59 |
| H(12B) | 8622 | 4933 | 5799 | 59 |
| H(12C) | 8609 | 5576 | 6530 | 59 |
| H(15A) | 3805 | 3476 | 8279 | 40 |
| H(16A) | 1342 | 3229 | 8340 | 46 |
| H(17A) | -242 | 4525 | 8157 | 43 |
| H(19A) | -577 | 6495 | 7891 | 40 |
| H(20A) | 518 | 8030 | 7697 | 42 |
| H(21A) | 2993 | 8175 | 7613 | 38 |
| H(25A) | 5610 | 5436 | 9063 | 64 |
| H(25B) | 6166 | 4417 | 8696 | 64 |

| | | | | |
|---|---|---|---|---|
| H(25C) | 7008 | 5452 | 8578 | 64 |
| H(26A) | 5440 | 7257 | 8731 | 56 |
| H(26B) | 6777 | 7152 | 8209 | 56 |
| H(26C) | 5590 | 7981 | 8044 | 56 |

Table 6. Torsion angles [°] for C26H34BNO4.

| | |
|---|---|
| C(24)-O(3)-B(1)-O(4) | -23.2(2) |
| C(24)-O(3)-B(1)-C(5) | -162.14(16) |
| C(24)-O(3)-B(1)-O(1) | 88.31(16) |
| C(13)-O(4)-B(1)-O(3) | 25.90(19) |
| C(13)-O(4)-B(1)-C(5) | 165.69(16) |
| C(13)-O(4)-B(1)-O(1) | -87.11(15) |
| C(7)-O(1)-B(1)-O(3) | 141.66(15) |
| C(7)-O(1)-B(1)-O(4) | -103.92(16) |
| C(7)-O(1)-B(1)-C(5) | 17.54(17) |
| C(1)-C(2)-C(3)-C(4) | 70.6(3) |
| C(2)-C(3)-C(4)-C(5) | -178.03(18) |
| C(3)-C(4)-C(5)-C(12) | 178.82(18) |
| C(3)-C(4)-C(5)-C(6) | 58.8(2) |
| C(3)-C(4)-C(5)-B(1) | -57.1(2) |
| O(3)-B(1)-C(5)-C(12) | 102.4(2) |
| O(4)-B(1)-C(5)-C(12) | -32.8(2) |
| O(1)-B(1)-C(5)-C(12) | -143.48(14) |
| O(3)-B(1)-C(5)-C(4) | -19.0(2) |
| O(4)-B(1)-C(5)-C(4) | -154.27(17) |
| O(1)-B(1)-C(5)-C(4) | 95.07(16) |
| O(3)-B(1)-C(5)-C(6) | -138.26(18) |
| O(4)-B(1)-C(5)-C(6) | 86.5(2) |
| O(1)-B(1)-C(5)-C(6) | -24.16(17) |
| C(12)-C(5)-C(6)-C(7) | 145.12(17) |
| C(4)-C(5)-C(6)-C(7) | -96.73(18) |
| B(1)-C(5)-C(6)-C(7) | 24.6(2) |
| B(1)-O(1)-C(7)-N(1) | 174.03(16) |
| B(1)-O(1)-C(7)-C(6) | -3.0(2) |
| C(8)-N(1)-C(7)-O(1) | 0.4(3) |
| C(11)-N(1)-C(7)-O(1) | 172.28(18) |
| C(8)-N(1)-C(7)-C(6) | 177.09(19) |
| C(11)-N(1)-C(7)-C(6) | -11.0(3) |
| C(5)-C(6)-C(7)-O(1) | -14.1(2) |
| C(5)-C(6)-C(7)-N(1) | 169.02(18) |

| | |
|---|---|
| C(7)-N(1)-C(8)-C(9) | -136.51(19) |
| C(11)-N(1)-C(8)-C(9) | 50.8(2) |
| C(10)-O(2)-C(9)-C(8) | 61.5(2) |
| N(1)-C(8)-C(9)-O(2) | -55.9(2) |
| C(9)-O(2)-C(10)-C(11) | -60.6(2) |
| C(7)-N(1)-C(11)-C(10) | 137.2(2) |
| C(8)-N(1)-C(11)-C(10) | -50.4(2) |
| O(2)-C(10)-C(11)-N(1) | 54.4(2) |
| B(1)-O(4)-C(13)-C(25) | -142.76(16) |
| B(1)-O(4)-C(13)-C(14) | 93.37(17) |
| B(1)-O(4)-C(13)-C(24) | -17.75(18) |
| O(4)-C(13)-C(14)-C(15) | 66.2(3) |
| C(25)-C(13)-C(14)-C(15) | -56.0(3) |
| C(24)-C(13)-C(14)-C(15) | 177.98(19) |
| O(4)-C(13)-C(14)-C(23) | -113.39(16) |
| C(25)-C(13)-C(14)-C(23) | 124.37(17) |
| C(24)-C(13)-C(14)-C(23) | -1.66(19) |
| C(23)-C(14)-C(15)-C(16) | 0.2(3) |
| C(13)-C(14)-C(15)-C(16) | -179.39(19) |
| C(14)-C(15)-C(16)-C(17) | 0.0(3) |
| C(15)-C(16)-C(17)-C(18) | -0.3(3) |
| C(16)-C(17)-C(18)-C(23) | 0.4(3) |
| C(16)-C(17)-C(18)-C(19) | -178.1(2) |
| C(23)-C(18)-C(19)-C(20) | -0.1(3) |
| C(17)-C(18)-C(19)-C(20) | 178.27(19) |
| C(18)-C(19)-C(20)-C(21) | 1.5(3) |
| C(19)-C(20)-C(21)-C(22) | -1.2(3) |
| C(20)-C(21)-C(22)-C(23) | -0.5(3) |
| C(20)-C(21)-C(22)-C(24) | 178.75(18) |
| C(15)-C(14)-C(23)-C(22) | 179.91(17) |
| C(13)-C(14)-C(23)-C(22) | -0.4(2) |
| C(15)-C(14)-C(23)-C(18) | -0.2(3) |
| C(13)-C(14)-C(23)-C(18) | 179.50(17) |
| C(21)-C(22)-C(23)-C(14) | -178.12(16) |
| C(24)-C(22)-C(23)-C(14) | 2.5(2) |
| C(21)-C(22)-C(23)-C(18) | 2.0(3) |

| | |
|---|---|
| C(24)-C(22)-C(23)-C(18) | -177.45(16) |
| C(19)-C(18)-C(23)-C(14) | 178.49(16) |
| C(17)-C(18)-C(23)-C(14) | -0.1(3) |
| C(19)-C(18)-C(23)-C(22) | -1.6(3) |
| C(17)-C(18)-C(23)-C(22) | 179.79(17) |
| B(1)-O(3)-C(24)-C(22) | -100.31(17) |
| B(1)-O(3)-C(24)-C(26) | 136.12(17) |
| B(1)-O(3)-C(24)-C(13) | 11.28(19) |
| C(21)-C(22)-C(24)-O(3) | -71.3(2) |
| C(23)-C(22)-C(24)-O(3) | 108.05(16) |
| C(21)-C(22)-C(24)-C(26) | 49.7(3) |
| C(23)-C(22)-C(24)-C(26) | -130.93(17) |
| C(21)-C(22)-C(24)-C(13) | 177.36(19) |
| C(23)-C(22)-C(24)-C(13) | -3.31(19) |
| O(4)-C(13)-C(24)-O(3) | 4.07(18) |
| C(25)-C(13)-C(24)-O(3) | 124.23(17) |
| C(14)-C(13)-C(24)-O(3) | -112.70(15) |
| O(4)-C(13)-C(24)-C(22) | 119.69(15) |
| C(25)-C(13)-C(24)-C(22) | -120.15(18) |
| C(14)-C(13)-C(24)-C(22) | 2.92(18) |
| O(4)-C(13)-C(24)-C(26) | -115.24(17) |
| C(25)-C(13)-C(24)-C(26) | 4.9(3) |
| C(14)-C(13)-C(24)-C(26) | 128.00(17) |

Symmetry transformations used to generate equivalent atoms:

# Chapter 2 Enantioselective Construction of Cyclic Tertiary Boronic Esters by Conjunctive Cross-Coupling Reaction

## 2.1 Introduction

Tertiary functional groups such as tertiary alcohols, tertiary carbon substituted amines and quaternary carbons are pervasive in natural products and therapeutic agents. The stereoselective construction of these versatile tertiary and quaternary carbon stereogenic centers represents a paramount challenge in the field of organic synthesis.[1] Among the methodologies aimed at achiving this mission, the stereospecific transformation of tertiary alkyl boronic esters has emerged as a versatile tool for the constructing tertiary functional groups.[2] Several stoichiometric and catalytic processes have been developed to construct tertiary boronates,[3] wherein metallate shift-based reactions of $\alpha$-substituted alkenyl boronate complexes have proven highly effective for forging new C–C and C–electrophile bonds.[4] For instance, Aggarwal and Studer groups have demonstrated that various electrophiles can induce such rearrangement through radical or radical-polar crossover pathways.[5]

In catalytic enantioselective approaches to construct enantiomerically enriched secondary and tertiary organoboronic esters, the Morken group has employed chiral palladium and nickel catalyst for the conjunctive coupling of alkenyl boronate complexes. The stereochemical outcome of these

[1] For recent advances in catalytic asymmetric synthesis of carbocyclic tertiary alcohols, α-tertiary amines and quaternary carbon centers, see: (a) Liu, Y. L.; Lin, X. T.*Adv. Synth. Catal.* **2019**, *361*, 876–918. (b) Liu, H. C.; Lau, V. H.; Xu, M. P.; Chan, T. H.; Huang, Z. X. *Nat. Commun.* **2022**, *13*, 4759 (c) Qiao, Y.; Bai, S. M.; Wu, X. F.; Yang, Y. Y.; Meng, H.; Ming, J. L. *Org. Lett.* **2022**, *24*, 1556–1560.

[2] For stereospecific amination of tertiary alkylboronates: (a) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett*. **2018**, *29*, 1749–1752. (b) Liu, X. X.; Zhu, Q.; Chen, D.; Wang, L.; Jin, L. Q.; Liu, C. *Angew. Chem. Int. Ed.* **2020**, *59*, 2745–2749. For stereospecific construction of quaternary carbon centers from tertiary boronic esters: (a) Mykura, R. C.; Songara, P.; Luc, E.; Rogers, J.; Stammers, E.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2021**, *50*, 11436–11441. (b) Odachowski, M.; Bonet, A.; Essafi, S.; Ramsden, P.; Harvey, J. N.; Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2016**, *138*, 9521−9532. (c) Sanford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481–5494.

[3] (a) Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Nature* **2008**, *456*, 778−782. (b) O'Brien, J. M.; Lee, K.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010***, 132,* 10630–10633. (c) Kubota, K.; Yamamoto, E.; Ito, H. *J. Am. Chem. Soc.* **2015***, 137,* 420−424.

[4] Namirembe, S.; Morken, J. P. *Chem. Soc. Rev.* **2019**, *48*, 3464–3474.

[5] For 1,2-migration of α-substituted alkenyl boronate complex using radical-polar crossover strategies: (a) You, C.; Studer, A. *Angew. Chem. Int. Ed.* **2020**, *59*, 17245–17249. (b) Armstrong, R. J.; Niwetmarin, W.; Aggarwal, V. K. *Org. Lett.,* **2017**, *19*, 2762–2765. (c) Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, *139*, 5736–5739. (d) You, C.; Studer, A. *Chem. Sci.* **2021**, 12, 15765–15769. For a review, see: (e) Wang, H.; Jing, C. C.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2020**, *59*, 16859–16872.

reactions indicates an *anti* migration mechanism.[6] In contrast, Ready has demonstrated that Ir(allyl)-induced metallate shift may occur by *syn* migration.[7] To extend the scope of metal-catalyzed conjunctive coupling reactions for the construction of cyclic molecules, we explored reactions involving cyclic boronate complexes. In addition to enantiodiscrimination, a critical concern arises regarding whether the cyclic constraint of substrates precludes necessary alignment of the rearranging B–C bond and the alkene. If these two features are too far out of alignment, the activation barrier for the metalate shift may be raised sufficiently, making direct Suzuki-Miyaura reaction becomes the predominant reaction pathway. In this chapter, we demonstrate that Pd-catalyzed conjunctive coupling can indeed operate efficiently on cyclic boronate complexes and provides access to a range of enantiomerically-enriched spirocycles and benzo-fused carbocycles and heterocycles in an efficient fashion.

### 2.1.1 Stereospecific Functionalization of Tertiary Alkylboronates

To date, numerous reports have been published demonstrating the conversion of tertiary alkylboronates into a variety of functional groups, encompassing alcohols, amines, as well as carbon-based functional groups like alkenes and arenes. Many of these transformations have been documented as stereospecific. This section delves into a detailed discussion of the stereospecific transformation of tertiary alkyl-boronates.

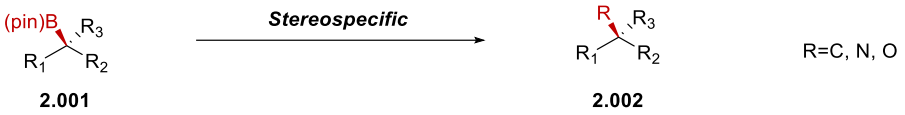



***Figure 2.1.*** General Scheme for Tertiary Alkylboronate Stereospecific Transformation

#### 2.1.1.1 Stereospecific Oxidation of Tertiary Alkylboronates

One of the most prevalent stereospecific functionalizations of tertiary boronates is hydroxyl-lation, facilitated by peroxide-induced 1,2-migration. This process has proven highly efficient, furnishing tertiary alcohols with both high yields (usually higher than 90%) and complete stereospecificity. Various oxidants have demonstrated the capability to achieve this transformation

[6] For detail, see Chapter 1, section 1.1.2.
[7] Davis, C. R.; Luvaga, I. K.; Ready, J. M. *J. Am. Chem. Soc.* **2021**, *143*, 4921–4927.

(see Figure 2.2). For example, Aggarwal synthesized a stereodefined tertiary alcohol, **2.005**, by treating an enantiomerically enriched tertiary alkylboronate with $H_2O_2$ in the presence of NaOH. [8] The same conditions were applied to oxidize more hindered tertiary boronic esters, as demonstrated by Brown, who oxidized a tertiary boron atom that contained a bulky *cis*-phenyl substituent on the β-carbon (the synthesis of **2.010**). [9] In situations requiring less basic conditions,

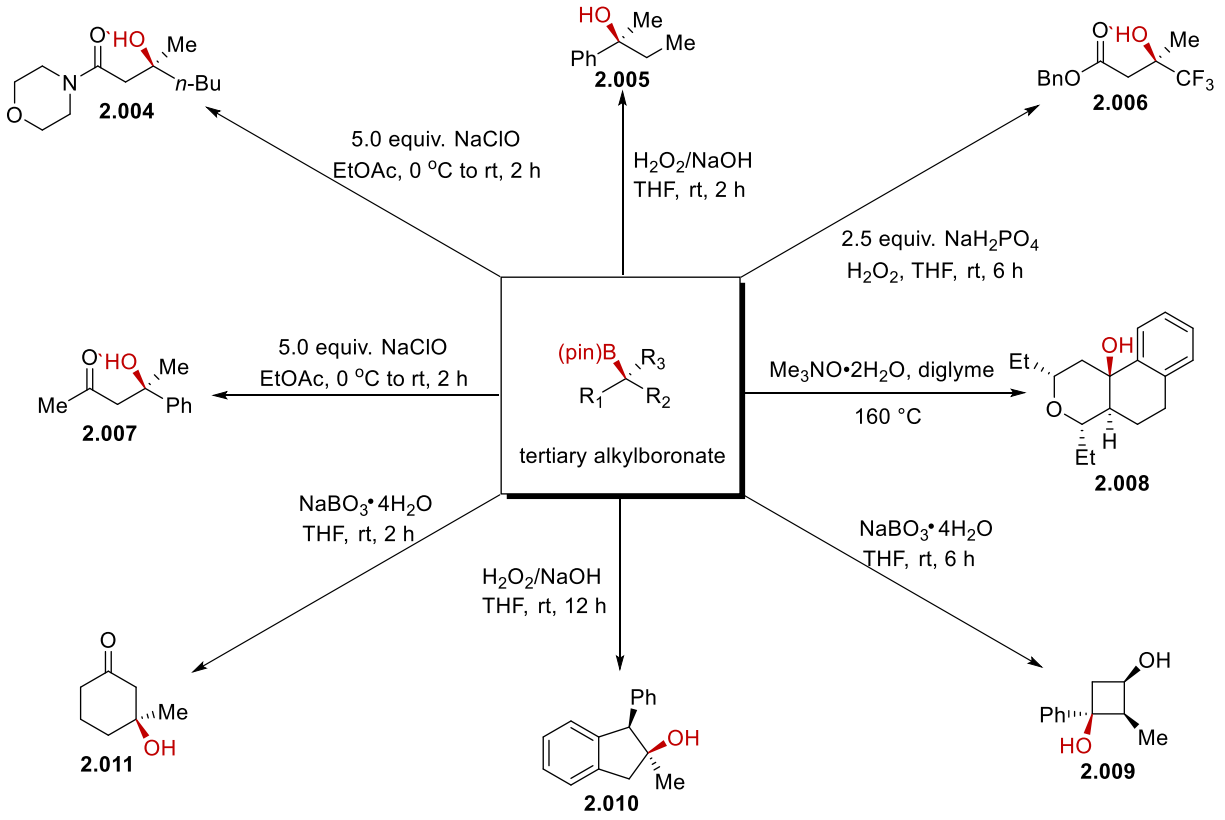



***Figure 2.2.*** Stereospecific Oxidation of Tertiary Alkylboronates Under Various conditions

$NaBO_3$ was often used as an oxidant. For example, Kobayashi used $NaBO_3 \cdot 4H_2O$ to oxidize a tertiary cyclic β-boryl ketone, producing enantiomerically enriched tertiary alcohol **2.011**.[10] The same oxidant was effective in oxidizing more hindered tertiary boronates, as shown by Hall , who used $NaBO_3 \cdot 4H_2O$ to oxidize a stererodefined cyclobutyl tertiary boronic ester containing a *cis* β-stereocenter, resulting in the synthesize of diol **2.009**. Environmental friendly oxidants were also explored. For example, in Hovedya's work on conjugate borylation of α,β-unsaturated ketones[11],

[8] Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Nature*, **2008**, *456*, 778–782.
[9] Chen, L.; Lear, A. R.; Gao, Pin.; Brown, K. *Angew. Chem. Int. Ed.* **2019**, *58*, 10956–10960.
[10] Kitanosono, T.; Xu, P.; Kobayashi, S. *Chem. Asian J.* **2014**, *9*, 179–188.
[11] Radomkit, S.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2014**, *53*, 3387–3391.

household bleach $NaClO \cdot 5H_2O$ was used to oxidize the enantiomerically enriched tertiary β-boryl ketone to generate alcohol **2.007**. For substrates that are even more sensitive to pH, for example the α-$CF_3$ substituted tertiary boronate synthesized by Zhang [12], a less basic salt ($NaH_2PO_4$) was used to control the pH of the oxidation process, in order to generate tertiary alcohol **2.006** without triggering β-elimination. Ito also demonstrated the oxidation of a challenging bridgehead tertiary boron using TMAO as oxidant at much higher temperature (160 °C) to synthesize tertiary alcohol **2.008**. [13]

### 2.1.1.2 Stereospecific Amination of Tertiary Alkylboronates

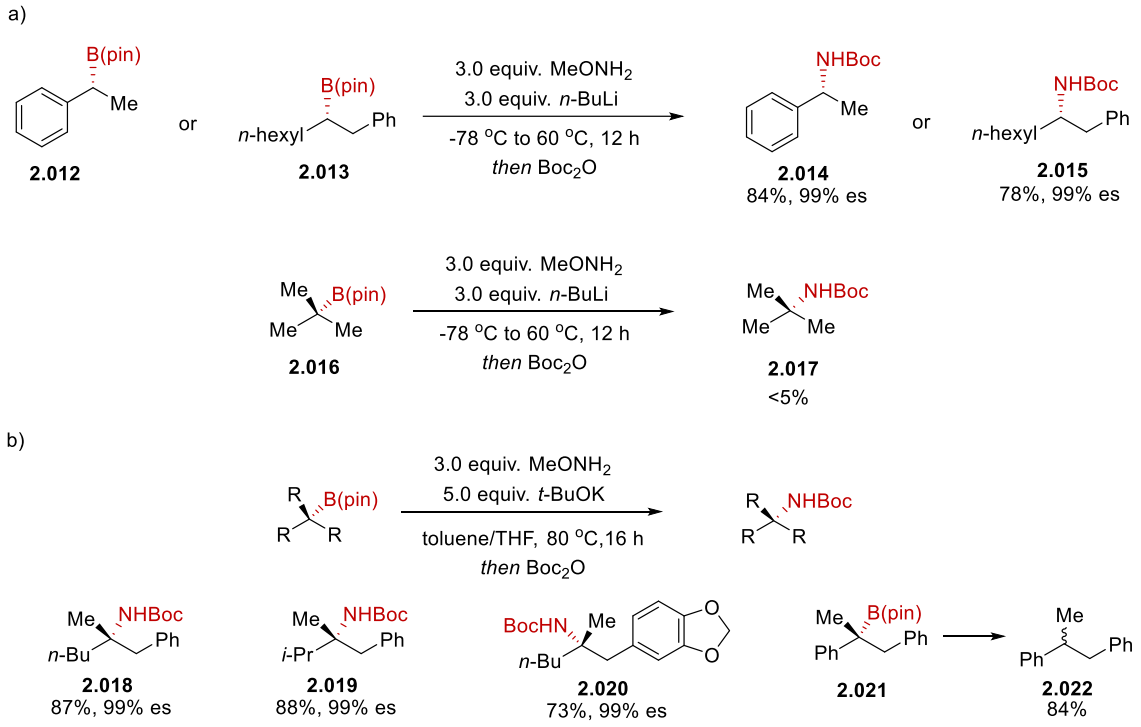



***Figure 2.3.*** Morken 's Stereospecific Amination of Alkyl boronates

Morken pioneered a method for the direct conversion of alkyl boronic esters to amino groups with high stereospecificity, utilizing methoxy amine as the amination reagent (see Figure 2.3a). [14] This process involves deprotonating methoxy amine with n-butyllithium reagent, forming a boronate complex with the alkylboronate. Subsequent 1,2-migration results in the generation of desired tertiary carbon-substituted amines in high yield and stereospecificity, especially for

[12] Liu, B.; Wu, H.; Zhang, J. *ACS Catal.* **2018**, *8*, 8318−8323.
[13] Suginome, M.; Ohmori, Y.; Ito, Y. *Chem. Commun.* **2001**, 1090–1091.
[14] Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449−16451.

secondary alkyl boronic esters like substrates **2.012** and **2.013**. However, the standard reaction conditions failed to yield the desired amination product for tertiary alkyl boronate **2.016**. To overcome this limitation in the amination of tertiary boronates, an alternative protocol was developed.[15] Morken found that by using t-BuOK as a base to deprotonate methoxy amine, the reaction efficiently converts various tertiary boronates to tertiary carbon-substituted amines with high stereospecificity (refer to Figure 2.3b, substrates **2.018**, **2.019**, and **2.020**). Nevertheless, when subjecting a benzylic tertiary boronic ester, such as **2.021**, to the standard amination conditions, only the protodeborylation product **2.022** formed in a non-stereospecific manner.

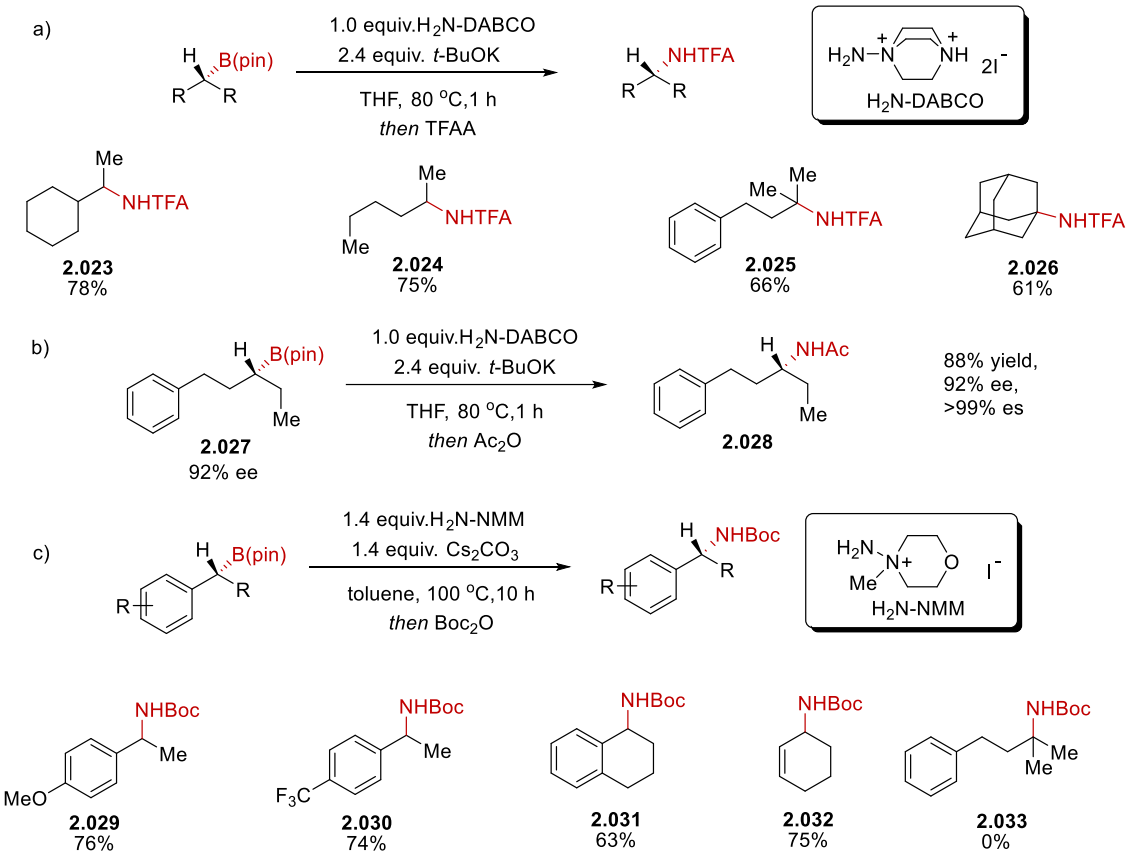



***Figure 2.4.*** Liu 's Stereospecific Amination of Alkyl boronates by Aminoazanium Salt

Liu introduced an alternative protocol for the amination of alkyl boronic esters utilizing aminoazanium salts, specifically amino-DABCO, as the amination reagent.[16] Illustrated in Figure 2.4a, this method demonstrated efficient amination of various secondary and tertiary alkyl

[15] Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett* **2018**, *29*, 1749–1752.
[16] Liu, X.; Zhu, Q.; Chen, D.; Wang, Lu.; Jin, L.; Liu, C. *Angew. Chem. Int. Ed.* **2020**, *59*, 2745 –2749.

boronates under optimized conditions. To showcase the stereospecificity, the amination of enantiomerically enriched secondary alkyl boronic ester **2.027** was performed, resulting in the desired secondary amine **2.028** with an 88% yield and perfect enantiospecificity. Notably, the amino-DABCO amination conditions proved unsuitable for benzylic boronic esters, leading to a significant protodeborylation side-reaction. Consequently, a distinct set of reaction conditions employing amino-NMM (N-methyl morpholine) as the amination reagent was employed for benzylic boronates (**2.029**-**2.032**).[17] While these conditions successfully borylated a series of secondary benzylic alkylboronates, tertiary benzylic alkylboronate **2.033** remained a challenging substrate for amination under optimized conditions. As of now, a reliable method for the amination of tertiary benzylic alkyl boronates is yet to be established.

### 2.1.1.3 Stereospecific Olefination of Tertiary Alkylboronates

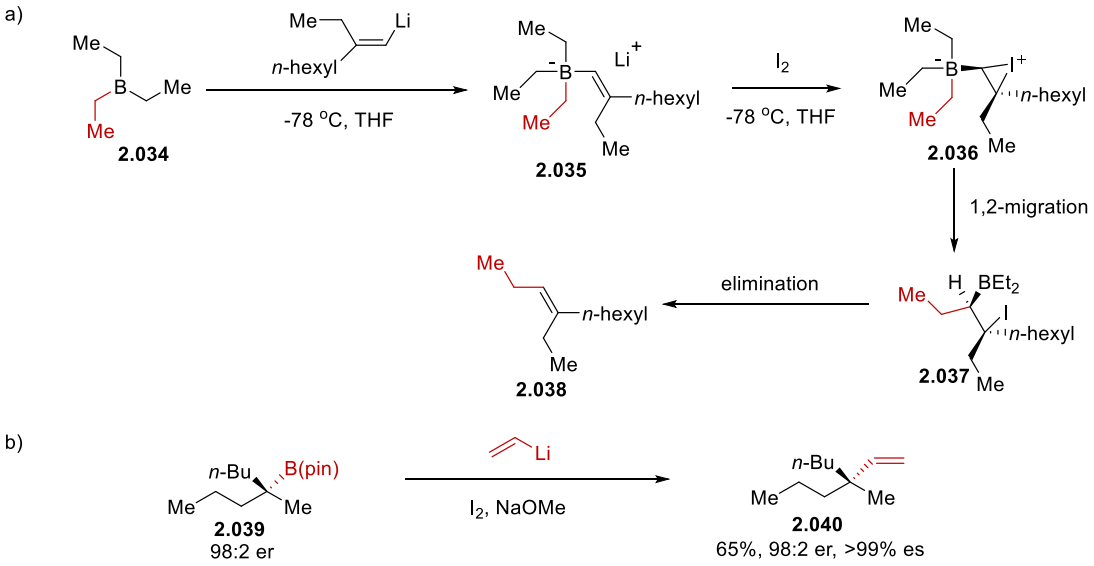



***Figure 2.5.*** Zweifel Olefination of Trialkyl Borane and Tertiary Alkylboronate

Zweifel initially reported an olefination process for dicyclohexylborane.[18] Levy later extended this method into a general protocol for the olefination of trialkylboranes.[19] Treating triethylborane (**2.034**) with alkenyllithium produces a tetrasubstituted borate complex (**2.035**). Upon treatment with molecular iodine, an iodonium ion (**2.036**) is formed, inducing 1,2-migration to generate β-

[17] Xu, J.; Qin, Y.; Liu, C. *Synlett.* **2023**, *34*, A–E.
[18] Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652–3653.
[19] LaLima, N. J.; Levy, A. B. *J. Org. Chem.* **1978**, *43*, 1279–1281.

iodo borane (**2.037**). Subsequently, an E2 elimination occurs, yielding the desired olefinated product (**2.038**). Aggarwal demonstrated the applicability of the Zweifel olefination process to tertiary alkylboronic esters.[20] For instance, enantiomerically enriched alkylboronate **2.039**, when subjected to standard Zweifel olefination conditions, yielded product **2.040** with a 66% yield and perfect stereospecificity. Additionally, Aggarwal reported that the same reaction can be achieved using a more readily available vinyl Grignard reagent.[21] Monitoring the reaction by $^{11}$B NMR revealed that treating boronic ester **2.041** with an excess of vinyl Grignard reagent leads to the exchange of the pinacol ligand on boron into alkenyl groups, resulting in a trialkenyl alkyl borane complex (**2.042**). Subsequent treatment of this borane complex with iodine and base produces the olefination product **2.043**.

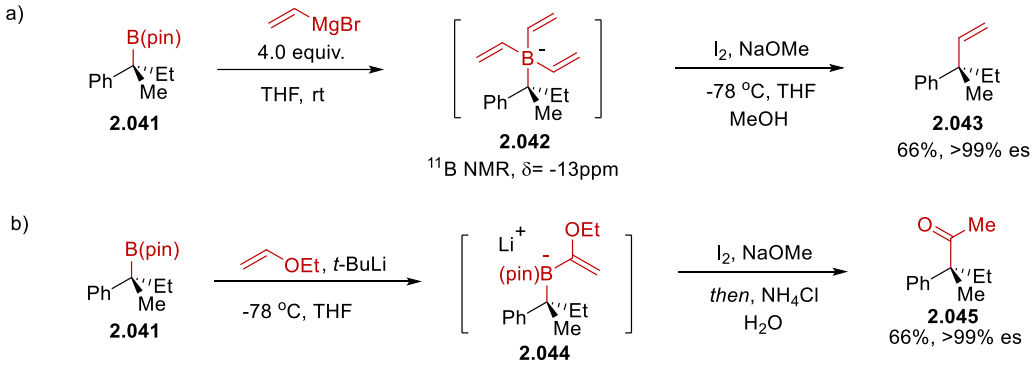



***Figure 2.6.*** Zweifel Olefination of Tertiary Alkylboronate Using Vinyl Grignard or Ethyoxyl Alkenyllithium

Aggarwal introduced a modified Zweifel olefination process involving a one-step acetylation of the boronic ester.[21] In this variation, the olefination reagent was changed from vinyl lithium to α-ethoxy alkenyl lithium, obtained by treating ethyl vinyl ether with *t*-BuLi, resulting in the formation of an α-ethoxy alkenyl boronate complex (**2.044**). Subsequently, employing the standard Zweifel olefination protocol, an ethyl enolate was stereospecifically generated, followed by hydrolysis upon treatment with acid to yield the desired acetylation product (**2.045**) in high yield.

[20] Pulis, A. P.; Blair, D. J.; Torres, E.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2013**, *135*, 16054–16057.
[21] Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 3760–3763.

### 2.1.1.4 Stereospecific Homologation of Tertiary Alkylboronates

The one-carbon homologation of alkyl boronic ester was initially discovered by Matteson [22] In this process, dichloromethylithium adds to the empty p-orbital of boronic ester **2.046**, forming the boronate complex **2.047**. Subsequent treatment with $ZnCl_2$ results in the departure of one chloride, inducing 1,2-migration and generating the homologated α-chloro boronic ester **2.048**. This compound can then react with a Grignard reagent to produce the new secondary boronic ester **2.049**. Aggarwal extended the applicability of this reaction to tertiary boronic esters, provided that

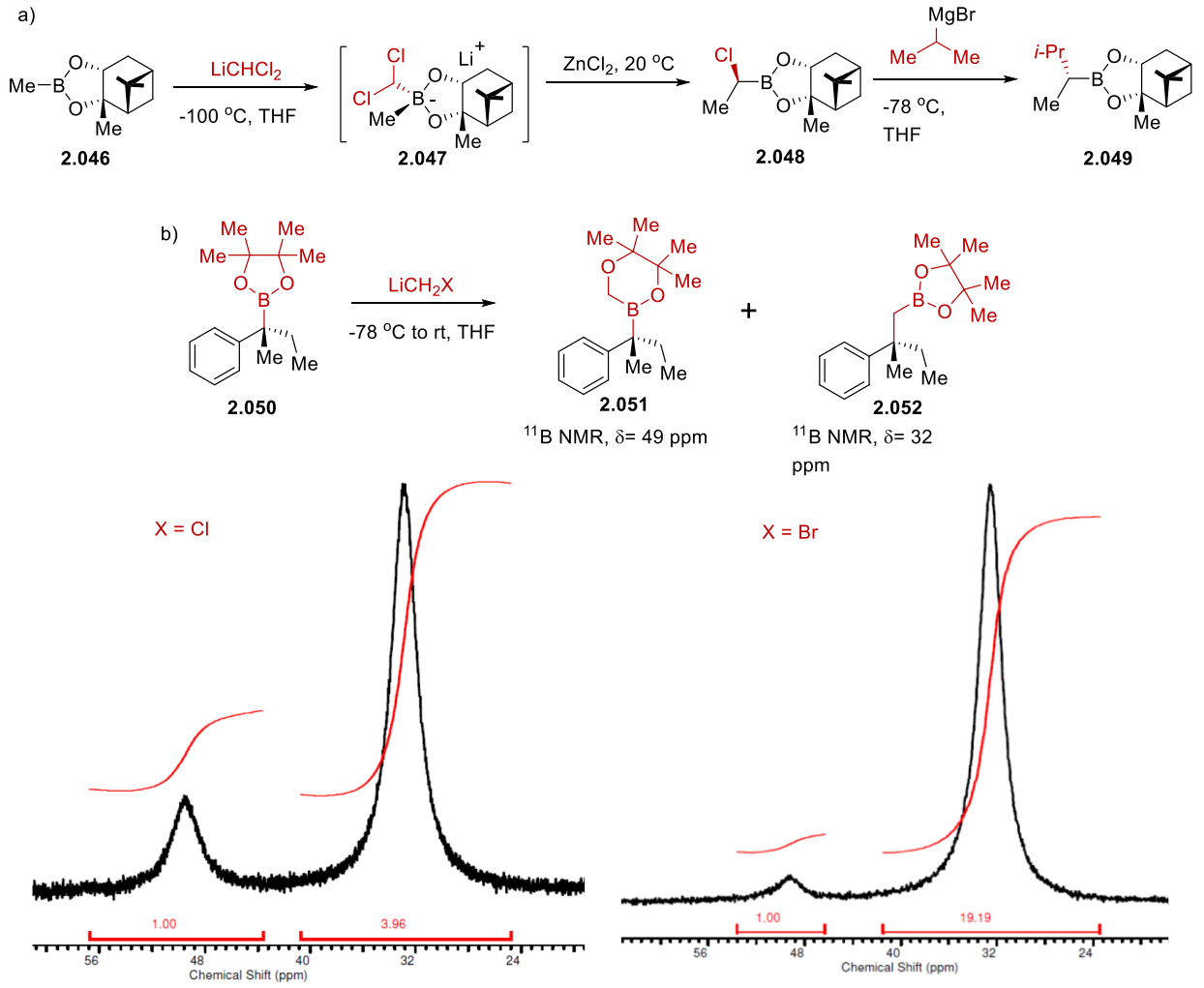



***Figure 2.7.*** Matteson Homologation

[22] Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810–819. For review: a) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535–1551. b) Matteson, D. S.; Collins, B. S. L.; Aggarwal, V. K.; Ciganek, E. *Organic Reactions* **2021**, *105*, 427–860.

the boron is located on a benzylic carbon (see Figure 2.7b).[13] When chloromethyllithium is used as the homologation reagent, approximately 20% of the oxygen-migrating side product was observed in the $^{11}B$ NMR spectrum (**2.051**). Substituting chloromethyllithium with bromomethyllithium significantly reduces the side product, furnishing the desired homologated primary alkyl boronic ester **2.052** in higher yield and perfect stereospecificity.

### 2.1.1.5 Stereospecific Transmetallation of Tertiary Alkylboronates

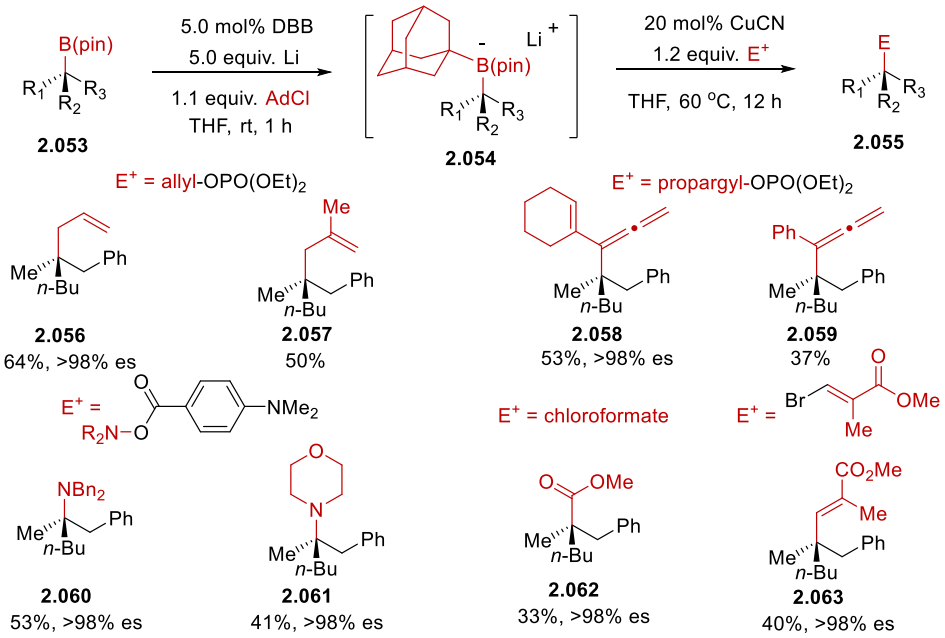



***Figure 2.8.*** Stereospecific Transmetallation of Tertiary Alkylboronates: Substrate Scope

As highlighted in section 1.1.3.1, the transmetallation of tertiary alkylboronates poses a significant challenge due to steric hindrance. Typically, achieving transmetallation of the tertiary carbon from boron to another metal requires homolytic cleavage of the C–B bond and the formation of a tertiary carbon radical, leading to a non-stereospecific transmetallation process. For instance, as depicted in Figure 1.23b and c, Molander developed a cross-coupling reaction between the photoredox-active tertiary alkyl $BF_3K$ salt and aryl halides using this radical-mediated strategy. To attain a stereospecific transmetallation of the tertiary alkyl group in a boronic ester, activation of the boron atom by a strong activator is essential. Morken [23] introduced a novel adamantyllithium reagent that functions as a potent activator for the stereospecific transmetallation of tertiary

[23] Liang, H.; Morken J. P. *J. Am. Chem. Soc.* **2023**, *145*, 20755–20760.

alkylboronates.

In the presence of a catalytic amount of ditert-butylbenzene (DBB), chloroadamantane undergoes lithiation by lithium metal to generate adamantyllithium *in situ*. The exposure of enantiomerically enriched tertiary alkylboronate **2.053** to this reactive intermediate leads to the formation of boronate complex **2.054**. Subsequent reaction of **2.054** with various electrophiles, catalyzed by CuCN, results in several cross-coupling reactions characterized by moderate yields and high stereospecificity. Effective electrophiles, as illustrated in Figure 2.8, include allylphosphate (**2.056** and **2.057**), propargylphosphate (**2.058** and **2.059**), carboxyl amine (**2.060** and **2.061**), chloroformate (**2.062**), and β-bromoenone (**2.063**).

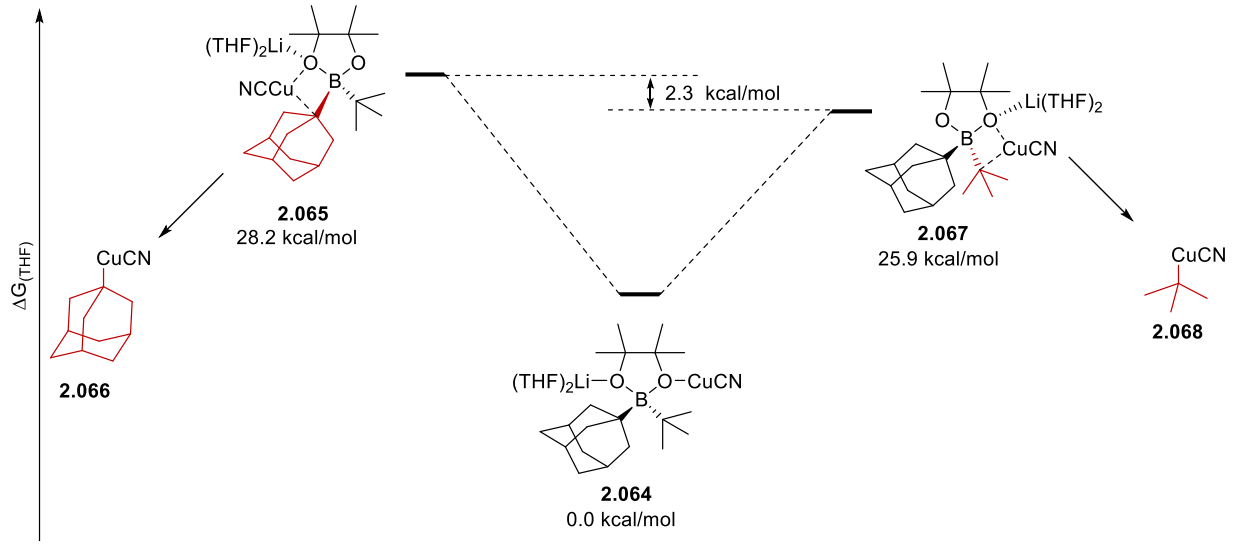



***Figure 2.9.*** Stereospecific Transmetallation of Tertiary Alkylboronates: DFT Calculation

Morken conducted DFT calculations to explore the role of the adamantyllithium activator. From CuCN and lithium cation-ligated boronate complex **2.064**, the energy barrier for the transmetallation reaction towards *tert*-butyl cuprate **2.068** was determined to be 25.9 kcal/mol, while a similar transmetallation reaction leading to adamantyl cuprate **2.066** was determined to have a 28.2 kcal/mol energy barrier. The transmetallation of *tert*-butyl group requires less energy than adamantyl group by 2.3 kcal/mol, making the transmetallation selective towards the formation of tertiary alkyl cuprate rather than adamantyl cuprate.

### 2.1.2 Conjunctive Cross-Coupling with Various Alkene Backbones

In section 1.1.2., detailed discussions on conjunctive cross-coupling reactions involving various electrophiles are presented. In this chapter, we will delve into conjunctive cross-coupling reactions with different alkene backbones, covering α-alkyl substituted alkenes, β-alkyl substituted alkenes, β-silylalkenes, as well as enynes.

#### 2.1.2.1 Conjunctive Cross-Coupling with α-Alkyl Substituted Alkenyl Boronates

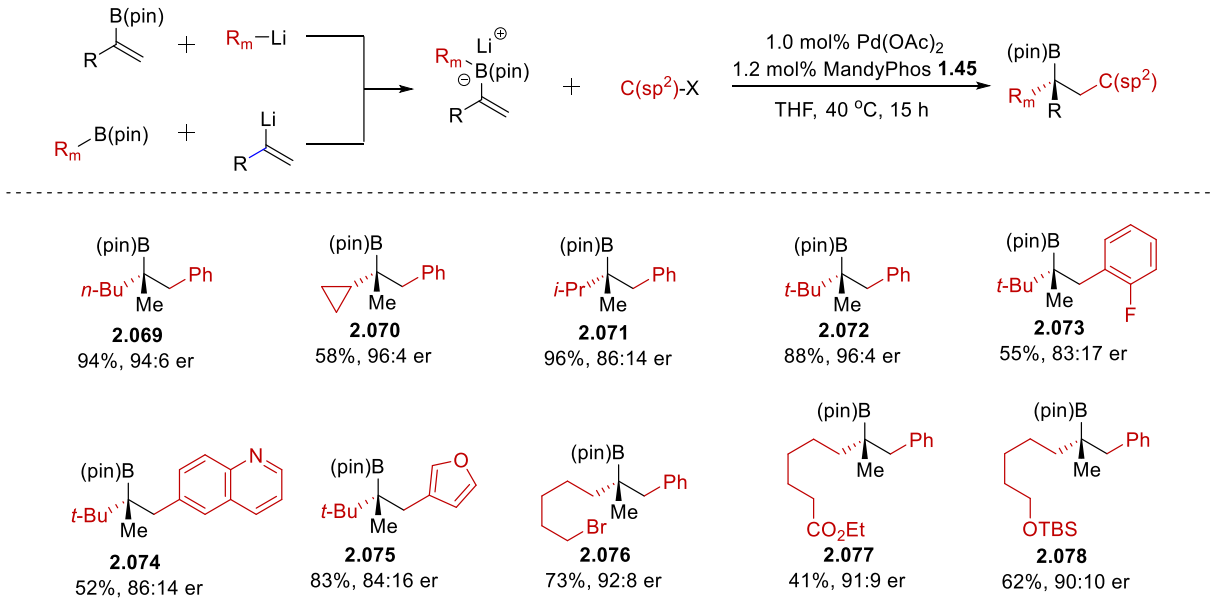



***Figure 2.10.*** Conjunctive Cross-Coupling with α-Alkyl Substituted Alkenyl Boronates: Selected Substrates

In 2018, Morken introduced the conjunctive cross-coupling reaction with α-alkyl substituted alkenyl boronates. Illustrated in Figure 2.10, the use of the optimal diphosphine ligand Mandyphos enabled the synthesis of various tertiary alkyl boronic esters with high yields and enantioselectivity. The reaction's tolerance to functional groups, particularly with *n*-alkyl migration, was explored.[24] Primary alkyl groups containing bromide (**2.076**), ester (**2.077**), or TBS-protected alcohol (**2.078**) could be incorporated, yielding the desired tertiary alkylboronates with moderate to good yield and higher than 80% ee. Secondary migrating groups, such as a cyclobutyl group in **2.070** or an isopropyl group in **2.071**, were also successfully incorporated. Impressively, *t*-butyl group

[24] Myhill, J. A.; Zhang, L.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2018**, *57,* 12799–12803.

migration was efficient, allowing the construction of alkylboronates with two contiguous quaternary carbon centers, as exemplified by substrate **2.072**, with high yield and enantioselectivity. Exploring the scope of aryl electrophiles with a *t*-butyl migrating group revealed incorporation of *ortho*-fluorine substitution (**2.073**), as well as heterocycles such as quinoline (**2.074**) and furan (**2.075**), albeit with diminished enantioselectivity.

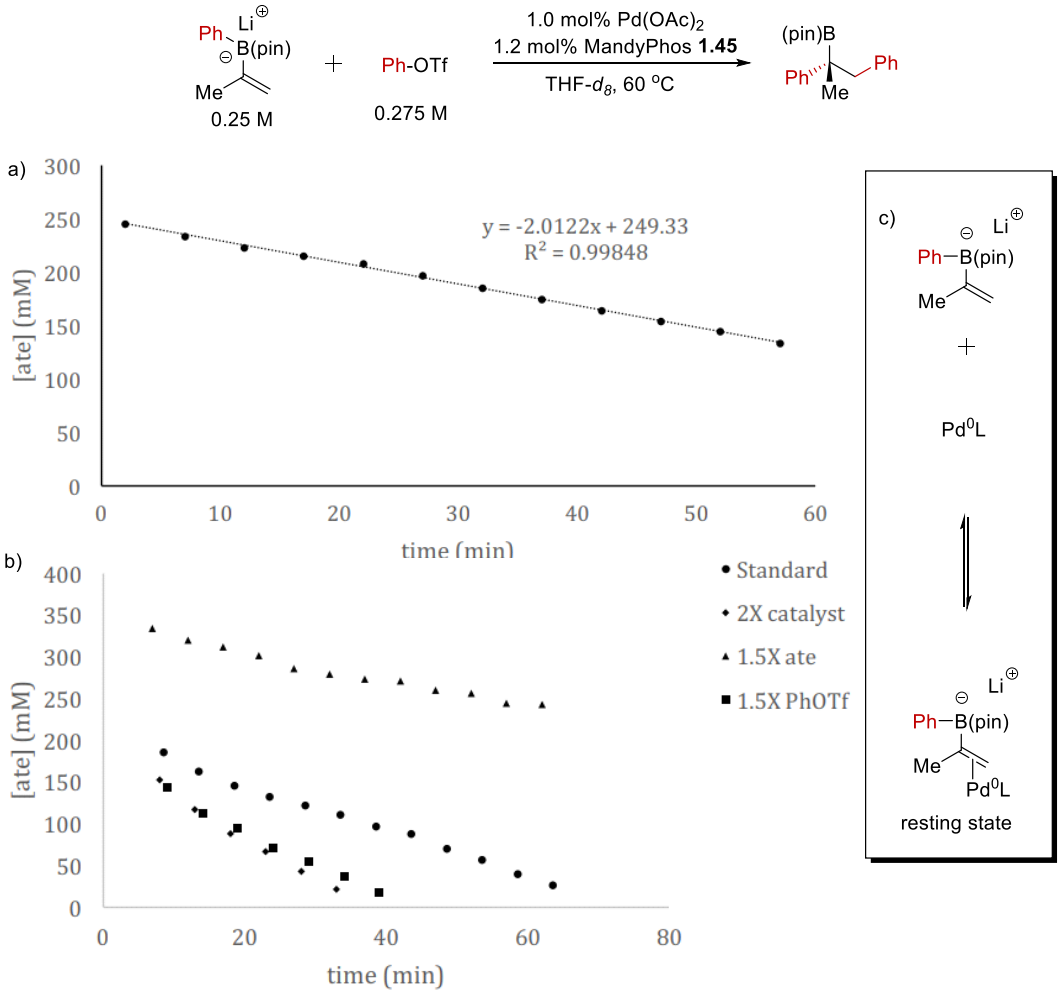
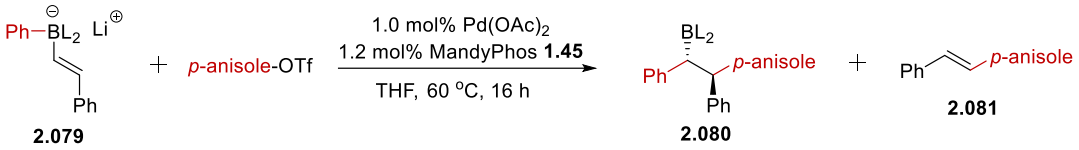



***Figure 2.11.*** Conjunctive Cross-Coupling with α-Alkyl Substituted Alkenyl Boronates: Kinetic Study

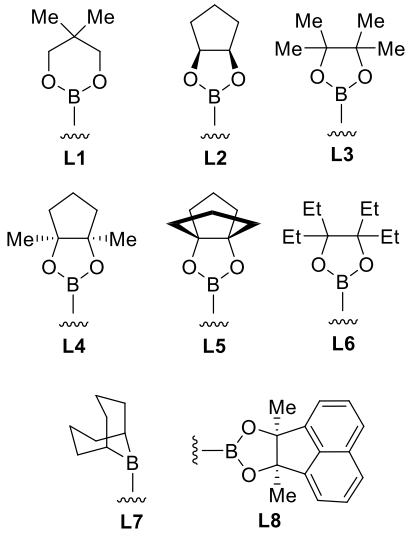
Investigation of the kinetic profile of the conjunctive cross-coupling reaction with phenyl-isopropenyl boronate complex allowed notable observations. As depicted in Figure 2.11a, the concentration of the boronate starting material exhibited a linear decrease over time, indicating a zero-order reaction with a coefficient value ($R^2$) of 0.99848. Furthermore, Figure 2.11b revealed that the reaction has a first-order dependence on the phenyltriflate electrophile and palladium

catalyst, while displaying an inverse order in respect to the boronate complex starting material. The combination of these phenomena suggested that the boronate complex can decelerate the reaction rate by coordinating with the $Pd^0$ catalyst, forming a stable resting state, as illustrated in Figure 2.11c.

### 2.1.2.2 Conjunctive Cross-Coupling with β-Substituted Alkenyl Boronates




| entry | $BL_2$ | 2.080:2.081 | yield of 2.080 | dr | er |
|---|---|---|---|---|---|
| 1 | **L1** (neo) | 1:5.8 | 13% | >20:1 | 99:1 |
| 2 | **L2** | 1:>20 | <5% | nd | nd |
| 3 | **L3** (pin) | 1:2 | 35% | >20:1 | 98:2 |
| 4 | **L4** | 1.7:1 | 56% | >20:1 | 99:1 |
| 5 | **L5** | 1:2 | 30% | >20:1 | nd |
| 6 | **L6** | 1:3 | 20% | >20:1 | nd |
| 7 | **L7** (9-BBN) | >20:1 | 92% | >20:1 | 67:33 |
| 8 | **L8** (mac) | 2.5:1 | 75% | >20:1 | 99:1 |
| 9* | **L8** (mac) | 4.2:1 | 83% | >20:1 | 99:1 |




* Optimized condition: 40 °C, 1.0 equiv. CsF

***Figure 2.12.*** Boron Ligand Optimization for β-Substituted Alkenyl Boronate Complex Conjuctive Cross-Coupling Reaction

Morken extended their work by developing the conjunctive cross-coupling with β-substituted alkenyl boronates.[25] In a standard conjunctive cross-coupling condition with the Mandyphos ligand **1.45**, reactions involving β-substituted alkenyl boron ligated by *neo*-pentyl glycol (Figure 2.12, entry 1) or pinacol (entry 3) were found to be inefficient, resulting in a significant amount of Suzuki-Miyaura cross-coupling byproduct **2.081**. Proposing that the transmetallation event was influenced by palladium-oxygen binding, a range of boron ligands was explored to identify a

[25] Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 15181–15185.

structure capable of shielding the oxygen atoms in the boronate complex and inhibiting the undesired oxygen binding-transmetallation pathway.[26] Among the tested diols, "mac diol" **L8** proved most effective, yielding product **2.080** to **2.081** with a ratio of 2.5:1. Through further optimization of reaction conditions, the reaction was ultimately refined to predominantly yield the desired conjunctive coupling product with excellent diastereomer and enantiomer ratios (Figure 2.12, entry 9).

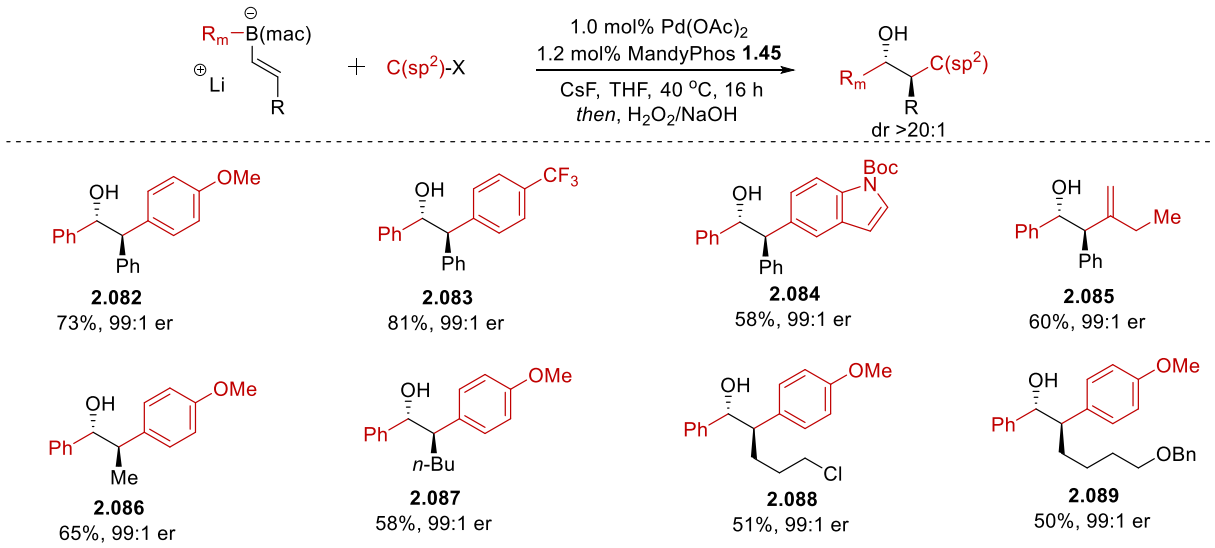



***Figure 2.13.*** β-Substituted Alkenyl Boronate Complex Conjuctive Cross-Coupling Reaction: Substrate Scope

With effective reaction conditions in hand, Morken further investigated the substrate scope of the reaction. As shown in Figure 2.13, with β-phenyl alkenyl B(mac) derived boronate complex and phenyl migrating group, a variety of C($sp^2$) electrophiles can be incorporated, including electron-rich methoxyl phenyl group in **2.082**, electron withdrawing group such as $CF_3$ in **2.083**. Heterocycle electrophiles such as indole **2.084** was also incorporated. Beside aryl electrophiles, alkenyl bromides can also serve as coupling partners, for example, *iso*-butenyl group can be installed in substrate **2.085**. Additionally, β-alkyl substituted alkenyl B(mac) derived boronate complex could also serve as nucleophiles in conjunctive cross-coupling. Several alkyl groups were

[26] (a) Huang, Y.-L.; Weng, C.-M.; Hong, F.-E. *Chem. Eur. J.* **2008**, *14*, 4426. (b) Thomas, A. A.; Wang, H.; Zahrt, A. F.;Denmark, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 3805. (c) Thomas,A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 4401. (d) Thomas, A. A.; Denmark, S. E. *Science* **2016**, *352*, 329. (e) Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116. (f) Amatore, C.; Jutand, A.; Le Duc, G. *Chem. Eur. J.* **2011**, *17*, 2492. (g) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.

shown to give desired conjunctive coupling with moderate yield, including methyl group in **2.086** and *n*-butyl group in **2.087**. Functional groups such as primary alkyl chloride (**2.088**) and benzyl protected alcohol (**2.089**) were also well tolerated. Impressively, all examples of substrates can be synthesized with greater than 20:1 dr and 99:1 er, demonstrating the remarkable stereochemical control of this conjunctive cross-coupling.

### 2.1.2.3 Conjunctive Cross-Coupling with β-Silyl Alkenyl Boronates

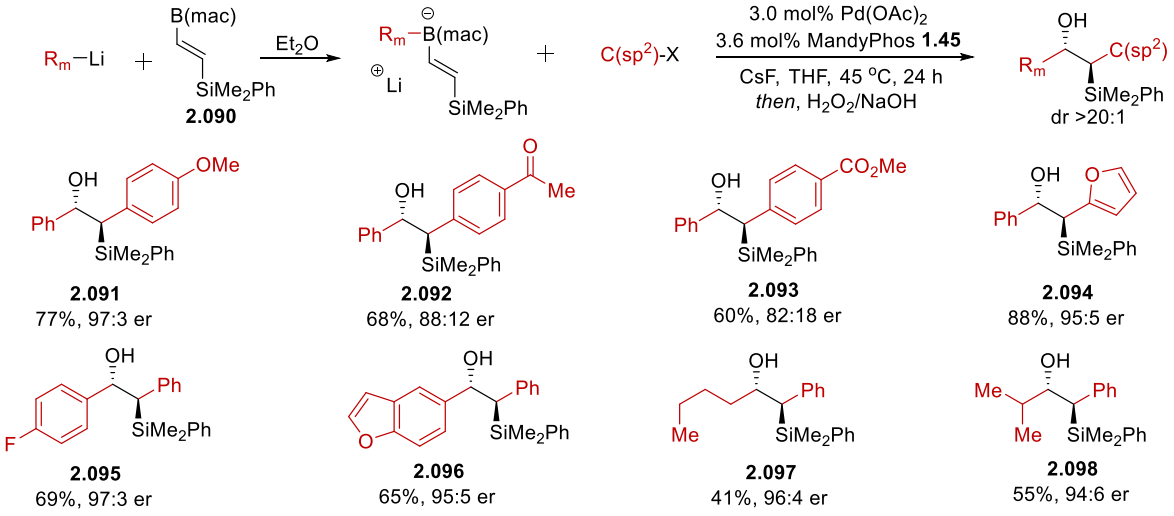



***Figure 2.14.*** β-Silyl Alkenyl Boronate Complex Conjuctive Cross-Coupling Reaction: Substrate Scope

Morken expanded the application of conjunctive cross-coupling to synthesize a series of modular vicinal bimetallic as β-boryl silanes.[27] By introducing a silyl substituent on the β-position of the alkenyl boronate, the *trans*-1-silyl-2-boryl alkene **2.090** can be used as alkene backbone for conjunctive cross-coupling to construct a variety of β-boryl silanes, as illustrated in Figure 2.14. In comparison to the β-alkyl/aryl version, conjunctive couplings for β-silyl alkenylboronates exhibited lower enantioselectivity, especially when more electron-deficient aryl halides were used as electrophiles. As seen in substrates **2.092** and **2.093**. These reactions occurred with less than 80% ee. However, with electron-rich aryl groups like p-methoxyphenyl in **2.091** or furan group in **2.094**, higher enantioselectivity was achieved. Regarding migration groups, both electron-rich and

[27] Meng, Y.; Kong, Z.; Morken, J. P. *Angew. Chem. Int. Ed.* **2020**, *59*, 8456 –8459.

electron-poor aryl groups could migrate, yielding silane products **2.095** or **2.096** with good yield and higher than 90% ee.

### 2.1.2.4 Conjunctive Cross-Coupling with Enynes

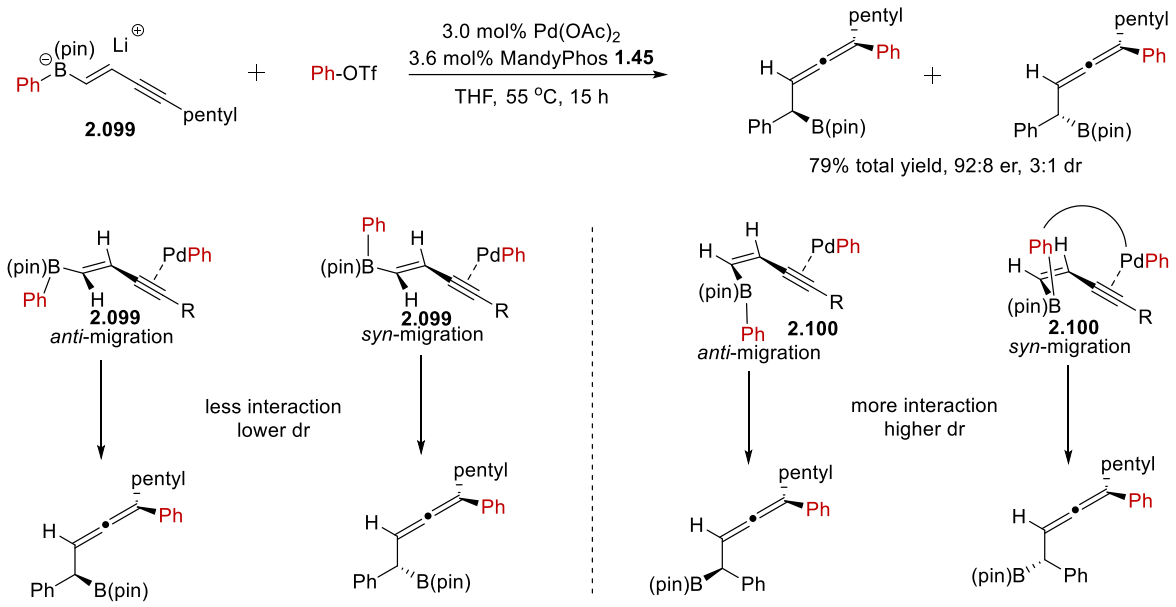



***Figure 2.15.*** Enynyl Boronate complex Conjunctive Coupling: Stereochemistry Controlled by Substrate Design

In 2020, Morken presented their findings on the conjunctive cross-coupling reaction of enynyl boronic esters. [28] This study resulted in the synthesis of a diverse array of β-allenyl alkylboronates with high stereoselectivity. The process involved treating a *trans*-alkynyl alkenyl B(pin) with phenyllithium to generate the boronate complex **2.099**. Applying the standard conjunctive cross-coupling on **2.099** yielded a pair of diastereomers of allenes with a 3:1 diastereomeric ratio (dr), indicating an exclusive alkyne binding during 1,2-migration. To improve diastereoselectivity, Morken proposed the use of a *cis*-alkenyl B(pin) instead of a trans-alkene. This modification led to higher diastereomeric ratios, as the bulky boronate group could now be positioned closer to the alkyne, inhibiting the *syn*-migration pathway through steric repulsion.

[28] Law, C.; Kativhu, E.; Wang, J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2020**, *59*, 10311–10315.

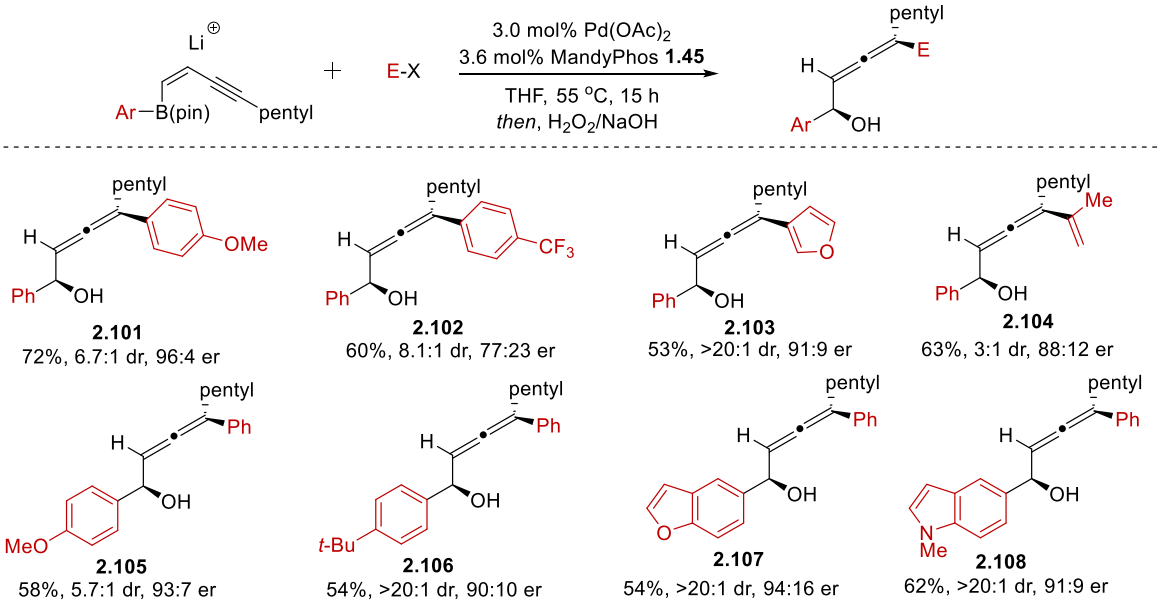



***Figure 2.16.*** Enynyl Boronate complex Conjunctive Coupling: Aryl Migration Substrate Scope

Indeed, utilizing cis-alkenyl B(pin) as the starting material, a diverse array of β-allenyl alkylboronates was synthesized with high diastereomeric ratios, as depicted in Figure 2.16. The incorporation of various aryl electrophiles was explored, encompassing both electron-rich (**2.101**) and electron-poor (**2.102**) arenes. Heterocycles (**2.103**) and alkenyl (**2.104**) electrophiles were also successfully incorporated. Regarding the migrating groups, a range of aryl groups was tested, including electron-rich arenes such as *p*-anisole **2.105**, and *p*-tert-butyl phenyl group **2.106**. Additionally, heterocycles such as benzofuran (**2.107**) and indoles (**2.108**) could also serve as migrating groups. The stereoselectivity outcomes of the reactions varied: electron-withdrawing groups on the electrophile significantly diminished the enantiomeric ratio (er), as demonstrated by substrate **2.102**. In most cases, the diastereoselectivity was higher than 5:1, except when an alkenyl electrophile was employed, as seen in substrate **2.104**, where the diastereomeric ratio dropped to 3:1.

Morken then investigated the migration of alkyl substituents, as shown in Figure 2.17. When applying the standard conditions to an alkyl-substituted *cis*-enynyl B(pin) boronate complex (**2.109**), a modest enantiomeric ratio of 56:44 was obtained. In order to improve the enantioselectivity of the reaction outcome, different boron ligands were installed. While the mac ligand 2.110 did not improve the enantiomeric ratio, the "hac" variant **2.111** significantly increased the enantiomeric ratio to 92:8, albeit with a slight reduction in yield. Subsequent investigations

revealed a dimethyl-substituted version of hac, "hac*" **2.112**, which not only improved the enantiomeric ratio but also maintained an acceptable level of yield. Consequently, hac* ligand **2.112** was adopted for exploring the substrate scope of alkyl migration. This exploration resulted in the incorporation of various alkyl substituents, all exhibiting higher than 20:1 dr and good enantiomeric ratio, exemplified by Figure 2.17 substrates **2.113** to **2.116**.

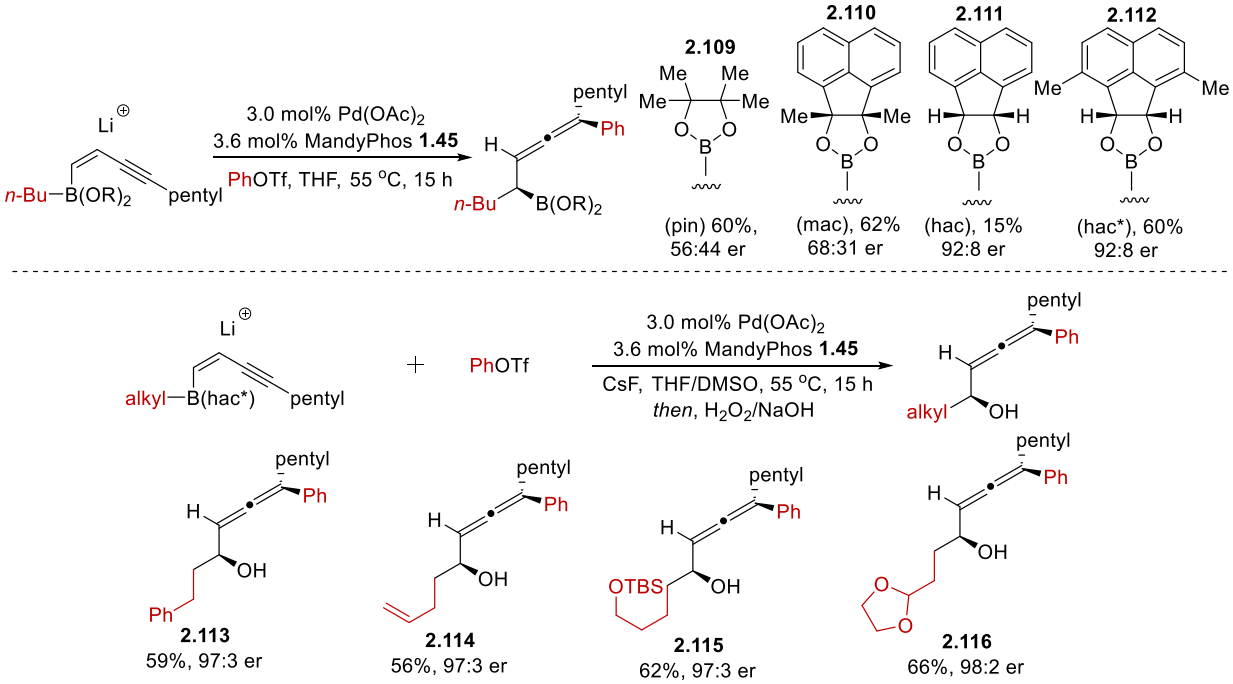



***Figure 2.17.*** Enynyl Boronate complex Conjunctive Coupling: Alkyl Migration Enabled by Boron Ligand Design

### 2.1.3 Conjunctive Cross-Coupling with P,N-Ligand

As detailed in Chapter 1, section 1.12, and Chapter 2, section 2.12, all preceding instances of conjunctive cross-coupling reactions depended exclusively on a single optimal ligand: Mandyphos **1.45**. This paradigm shifted when P,N ligands proved equally or even more effective in catalyzing conjunctive cross-coupling reactions. [29]

As depicted in Figure 2.18a, a classic conjunctive cross-coupling with a boronate complex derived from vinyl B(pin), using the Pd-Mandyphos **1.45** catalyst, exhibited remarkable efficiency. The yields of the reaction is up to 85% while the enantiomeric ratio is up to 96:4. In contrast,

[29] Gao, C.; Wilhelmson, C. A.; Morken, J. P. *J. Org. Chem.* **2023**, *88*, 1828−1835.

Figure 2.18b illustrates that, when a series of P,N ligands were employed in conjunction with $Pd_2(dba)_3$ as the palladium source, the yields and enantiomeric ratios of the conjunctive cross-coupling reaction varied based on different ligand structures. The use of phosphine-sulfonamide ligands **L1** and **L3** resulted in much lower reaction yields. When an Ullman's auxiliary-derived phosphine-imine ligand **L2** was applied, the reaction yielded conjunctive products with moderate enantiomeric ratio. Subsequent findings revealed that Phox ligand **L5** and Quinap ligand **L7** effectively catalyzed the reaction with decent yield and high enantiomeric ratio. Due to the high modularity and cost-effectiveness of Phox ligands, it was chosen as the prefered ligand for further exploration.

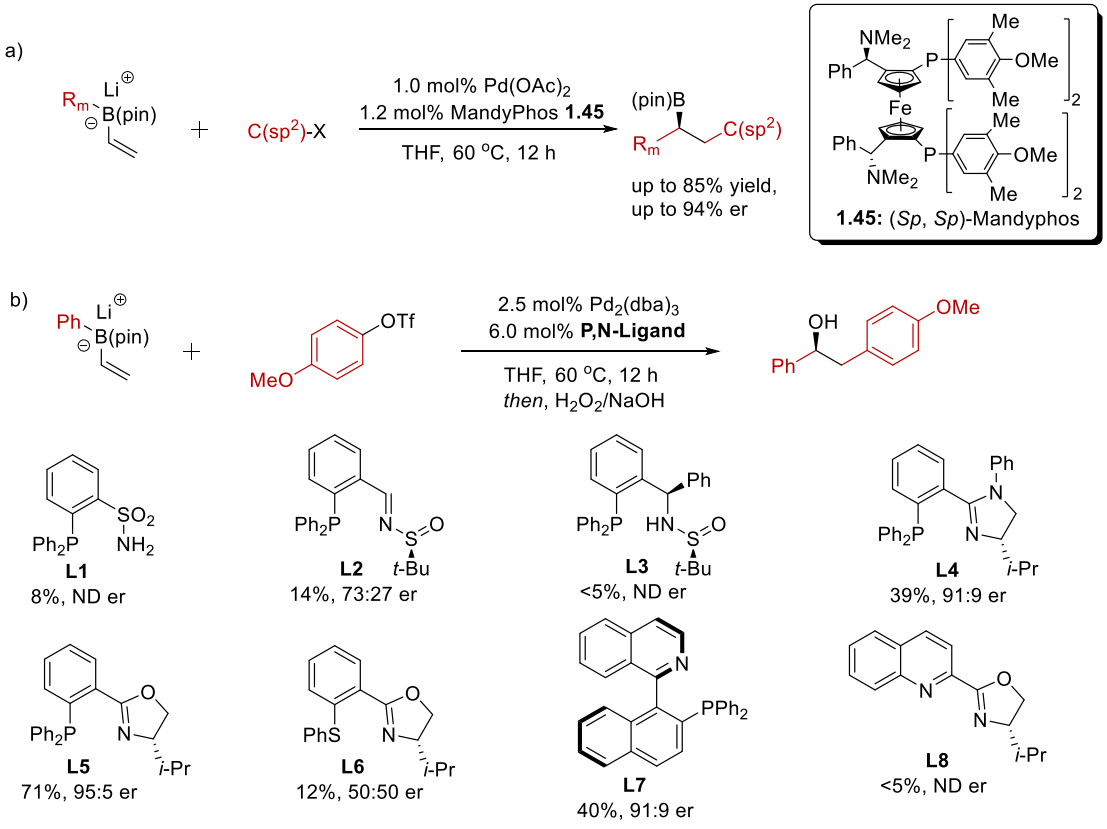
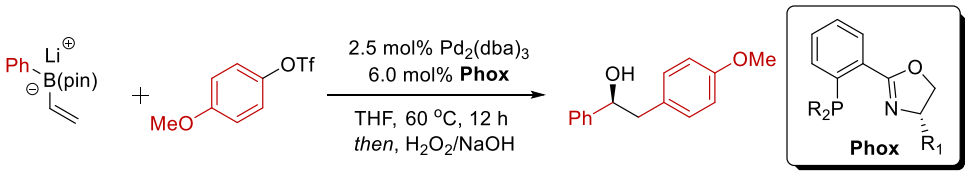



***Figure 2.18.*** Classic Conjunctive Cross-Coupling with P,N-Ligands

To pinpoint the optimal substitution pattern on the Phox ligand, a library of Phox ligands featuring various substituents on the oxazoline and phosphine moieties was synthesized. As illustrated in Figure 2.19, the functional group attached to the oxazoline side of the Phox ligands appeared to have minimal impact on the reaction outcome. Altering the substituents from isopropyl in **L5** to tert-butyl in **L9**, methyl in **L10**, or phenyl in **L11** all resulted in reactions with similarly

high yields and 90% ee. Conversely, substituents on the phosphine exerted a more substantial influence on the reaction outcome. Changing the diphenyl phosphine group in **L5** to either dimesityl phosphine in **L13** or di-o-tolyl phosphine in **L14** significantly reduced the reaction yield. Dicyclohexyl phosphine in **L15** further decreased the yield to 55%. Eventually, di(3,5-xylyl) was identified as the optimal phosphine substituent, while phenyl was selected as the optimal functional group on the oxazoline, rendering **L16** as the optimal Phox ligand.




| entry | Ligand | $R_{1\ (oxazoline)}$ | $R_{(phosphine)}$ | yield | er |
|---|---|---|---|---|---|
| 1 | **L5** | *i*-Pr | Ph | 71% | 95:5 |
| 2 | **L9** | *t*-Bu | Ph | 70% | 95:5 |
| 3 | **L10** | Me | Ph | 75% | 95:5 |
| 4 | **L11** | Ph | Ph | 83% | 97:3 |
| 5 | **L12** | Ph | 2-furyl | 85% | 93:7 |
| 6 | **L13** | Ph | mesityl | 13% | 93:7 |
| 7 | **L14** | Ph | *o*-tolyl | trace | NA |
| 8 | **L15** | Ph | Cy | 55% | 94:6 |
| 9 | **L16** | Ph | 3,5-xylyl | 84% | 97:3 |

***Figure 2.19.*** P,N-Ligands Optimization

In the previously reported study on conjunctive cross-coupling using organo-magnesium-derived boronate complexes, it was revealed that a stoichiometric amount of sodium triflate salt additive was necessary to act as a halide scavenger. This was essential because the conjunctive cross-coupling reaction could be significantly inhibited by free chloride or bromide anions dissolved in THF.[30] However, one notable advantage of replacing Mandyphos ligand **1.45** with Phox ligand **L16** was the apparent elimination of the need for a halogen scavenger. A range of organo-magnesium bromide-derived boronate complexes was synthesized and subjected to

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

conjunctive cross-coupling with Phox **L16** as the Pd-ligand. Remarkably, the reaction proceeded smoothly, yielding the desired conjunctive cross-coupling product without the addition of any halide scavenger additive, as illustrated in Figure 2.20. Utilizing phenylpropyl Grignard reagent-derived boronate complexes, various C($sp^2$) electrophiles were tested, including bromoanisole, bromopyridine, bromothiophene, as well as alkenyl bromide. These reactions all produced the desired conjunctive cross-coupling products with yields exceeding 70% and enantioselectivity exceeding 80%.

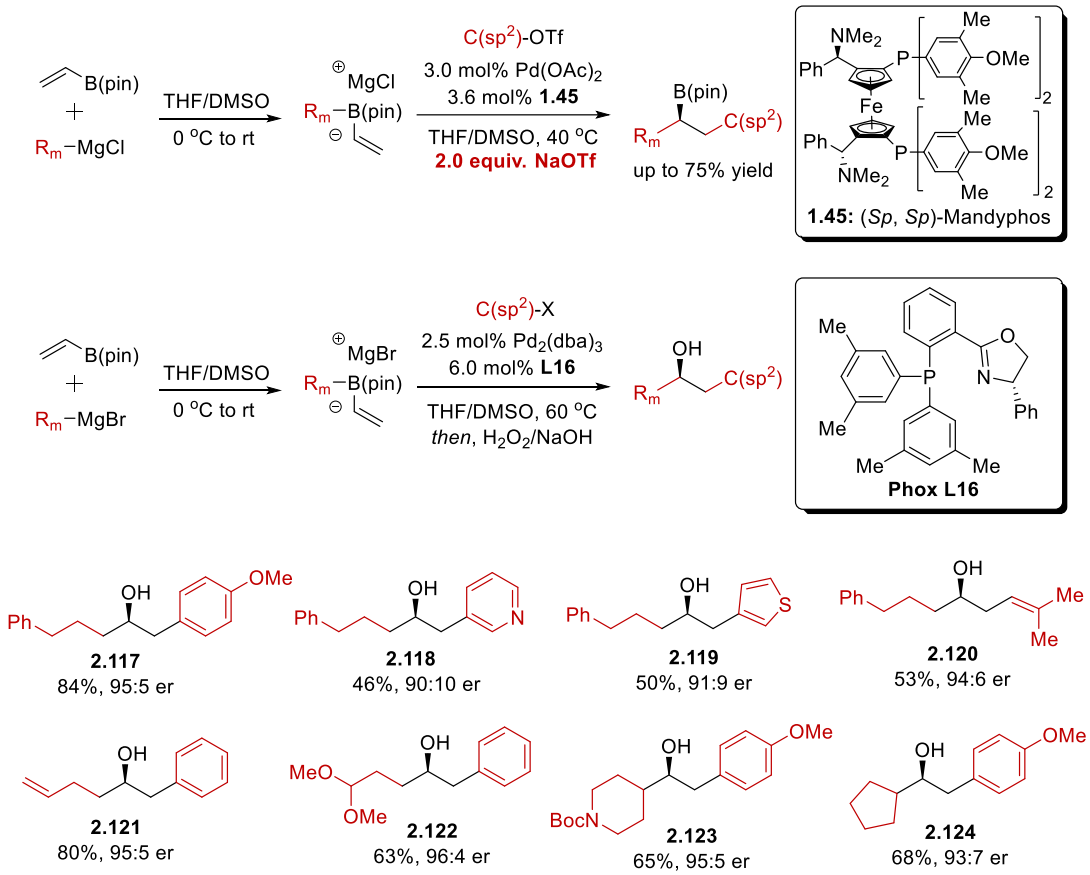



***Figure 2.20.*** P,N-Ligands Catalyzed Conjunctive Cross-Coupling Substrate Scope

### 2.1.4 Cyclization Reactions *via* 1,2-Migration of Alkenylborornate

In the preceding discussion, the 1,2-migration of alkenylboronate complexes, whether through conjunctive cross-coupling reactions or radical-polar crossover strategies, was primarily employed for the synthesis of linear secondary or tertiary alkyl boronic esters. However, it's noteworthy that this mode of reaction has also been explored for constructing cyclic alkylboronates. In this section,

we will delve into examples of cyclization reactions facilitated by the 1,2-migration of alkenylboronates.

### 2.1.4.1 Total Synthesis of (-)-Filiformin *via* Zweifel Olefination Cyclization

In 2014, Aggarwal achieved a concise total synthesis of (-)-filiformin employing a Zweifel olefination as a pivotal step.[31] Initially, bromomethyl B(pin) **2.171** was treated with zinc powder to generate α-boryl methylzinc. The organozinc compound was then coupled with dibromopropene to yield alkenyl bromide **2.172** in 81% yield. Utilizing the enantiomerically enriched Cbz-protected secondary alcohol **2.173**, a stereospecific deprotonation and lithiation were performed to synthesize organolithium reagent **2.174**. The combination of **2.174** and **2.172** underwent an Aggarwal homologation reaction, as described in section 2.1.1.4., to produce the enantiomerically enriched tertiary boronic ester **2.175** in 78% yield. Subsequently, another Aggarwal homologation was executed. The secondary organolithium reagent used in this step was customized into a Cbx -protected alcohol to form a more stable boronate complex. Allyl bromide was introduced as a scavenger for other organolithium species generated by the fragmentation of the boronate complex. Under these optimized conditions, the homologated secondary boronic ester **2.177** was obtained in 45% yield. Subsequent Zwiefel olefination cyclization ensued. Treating **2.177** with *t*-butyllithium triggered a lithium-halogen exchange, and the *in situ* generated alkenyllithium added onto the empty p-orbital of the secondary boronate to form the cyclic boronate complex intermediate **2.178**. Under standard Zweifel olefination conditions, a ring contraction occurred, furnishing the five-membered ring exocyclic alkene **2.179** in 97% yield. Following deprotection of the phenol and acid-promoted cyclization, the bridged-ring-containing intermediate **2.180** was obtained with a yield of 60%. Finally, by treating 2.180 with bromine, a site-selective bromination yielded the natural product (-)-filiformin in 85% yield.

[31] Blair, D. J.; Fletcher, C.J.; Wheelhouse, K. M. P.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2014**, *53*, 5552 –5555.

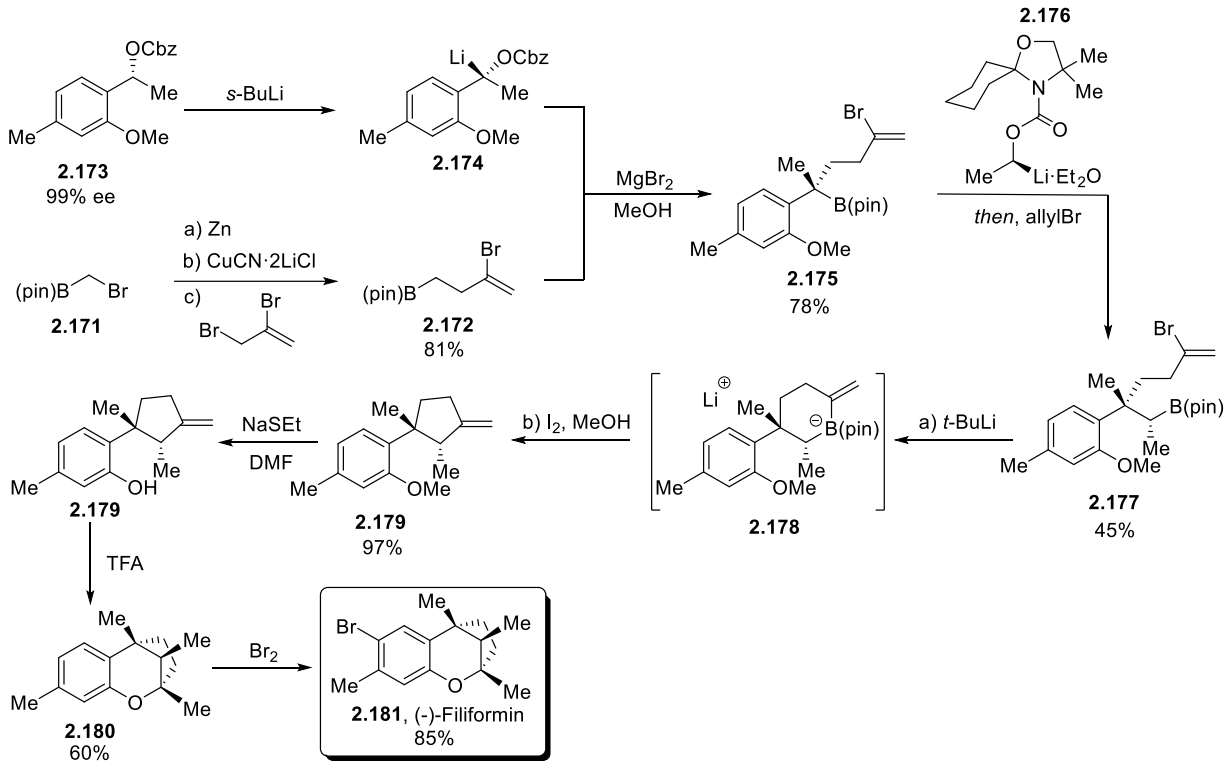



***Figure 2.21.*** Total Synthesis of (-)-Filiformin

### 2.1.4.2 Photoredox Synthesis of Cyclobutane from Cyclic Alkenylboronates

Aggarwal and colleagues envisioned that the radical-polar crossover-induced 1,2-migration reaction could also facilitate a cyclization process on a cyclic alkenyl boronate complex.[32] As depicted in Figure 2.22, employing radical-induced 1,2-migration allowed 5-membered ring cyclic boronate complexes to undergo ring contraction, producing various cyclobutanyl boronic esters. In the substrate scope, cyclobutanes without stereocenters were synthesized with moderate to good yields (substrate **2.182** to **2.187**). Different α-iodo carbonyls proved effective as electrophiles, encompassing phenyl ketones, esters, amides, and sulfones. When cyclobutanes with two continuous stereocenters were formed, the reaction proceeded with high diastereomeric ratios, as illustrated in substrates **2.188** to **2.193**. Notably, these reactions exhibited high stereospecificity for the pre-existing boron-containing stereocenter, resulting in densely substituted cyclobutanes with elevated enantiomeric ratios.

[32] Davenport, R.; Silvi, M.; Noble, A.; Hosni, Z.; Fey, N.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2020**, *59*, 6525–6528

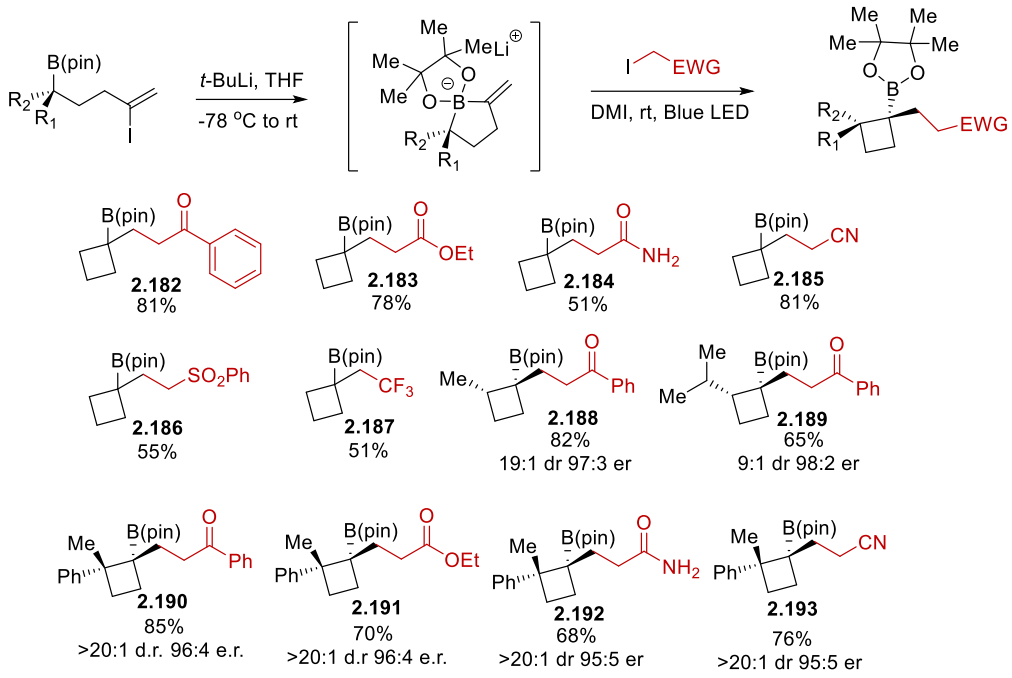



***Figure 2.22.*** Substrate Scope for Photoredox Induced Cyclobutanation *via* 1,2-Migration of Cyclic Alkenylboronates

Leveraging DFT calculations, Aggarwal and colleagues developed a theoretical framework to elucidate the origin of the high diastereoselectivity observed in substrates **2.188** to **2.193**. According to the computational results, when treating a cyclic boronate complex with only a methyl substituent on the α-carbon of the boronate with a carboradical, a radical addition product would predominantly take on two distinct conformations: **2.194** and **2.195**. The equilibrium between these conformations slightly favored **2.194**, where the larger methyl group is *gauche* to the B(pin) moiety, causing steric repulsion. Consequently, the SET process from **2.195** to **2.197** is disfavored, leading to the formation of **2.199** as the minor product. A parallel argument was made for substrate **2.200** derived from a phenyl and methyl-substituted tertiary boronic ester, except that the smaller group on the α-carbon of the boronate was replaced by a phenyl group. Interestingly, in **2.201** and **2.202**, both the phenyl group and the methyl group could be at the *gauche* position to the B(pin) unit. However, the *gauche* methyl-B(pin) conformation **2.202** appeared to be significantly disfavored, with its ground state energy found to be 2.7 kcal/mol higher than the *gauche* phenyl-B(pin) conformation **2.201**. This observation aligns well with the experimental data, as substrates **2.190** to **2.197** exclusively yielded the predicted diastereomer with a ratio greater than 20:1.

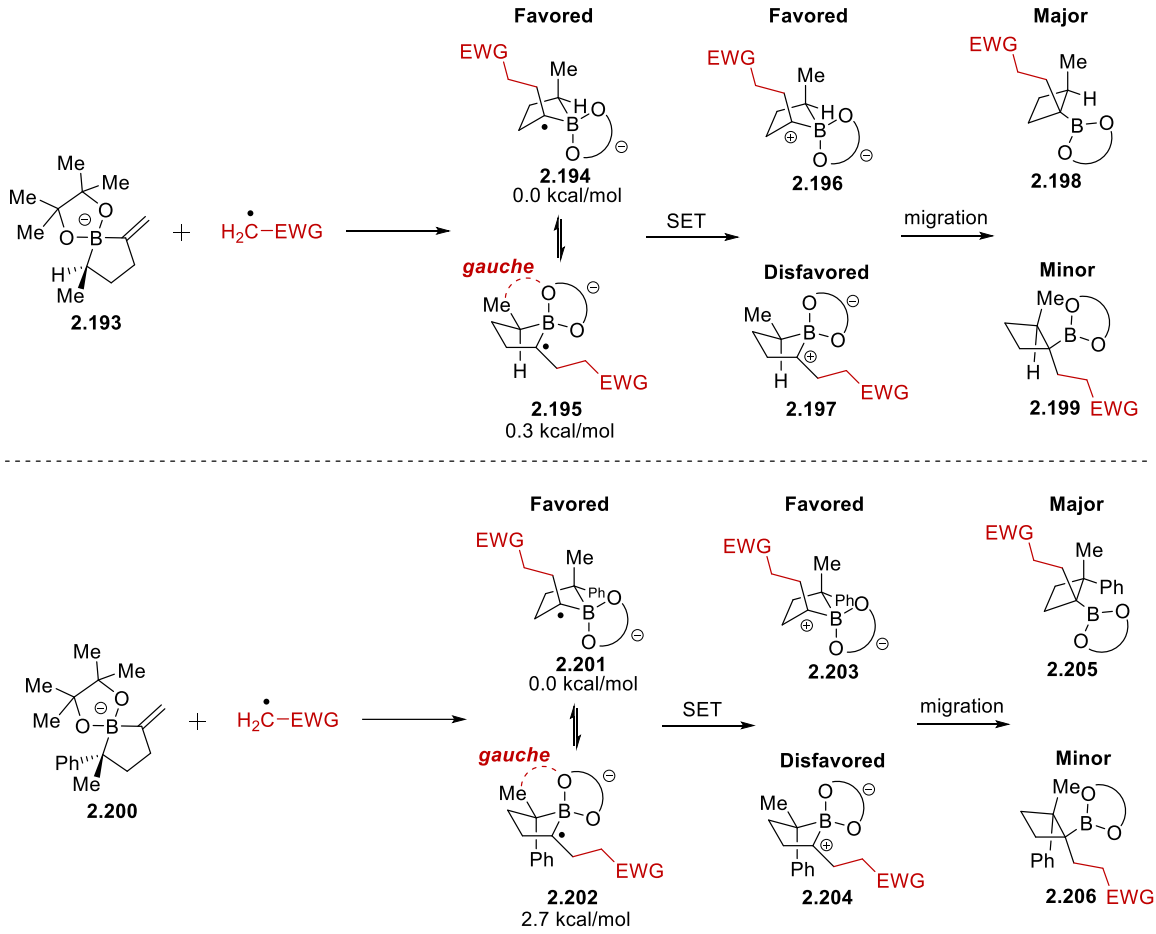



***Figure 2.23.*** Rational for The Origin of Diastereoselectivity Supported by DFT Calculation

### 2.1.4.3 Polar Induced 1,2-Migration Cyclic Alkenylboronates

Aggarwal also presented a similar reaction for constructing cyclopentanyl boronic esters, utilizing polar-induced 1,2-migration of cyclic alkenylboronates instead of radicals.[33] In Figure 2.24, starting from pre-synthesized enantiomerically enriched tertiary boronic ester, a lithium-halogen exchange and intramolecular addition led to the formation of the desired 6-membered ring boronate complex. Treatment of this cyclic boronate with electrophiles, such as Eschenmoser's salt, induced a polar 1,2-migration, yielding the desired cyclopentanyl boronic esters in good to high yield. Two sets of conditions were applied to the reaction, resulting in the preferential formation of opposite diastereomers. Condition A favored the diastereomer with boron cis to the aryl substituent, while condition B favored the opposite diastereomer. Various aryl substituents on the

[33] Fairchild, M. E.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2022**, *61*, e202205816.

α-carbon of the boronic ester were tested, including arenes with electron-donating or -withdrawing groups. Additionally, cyclic boronate substrates derived from enantiomerically enriched secondary boronic esters were tested. In this case, only one diastereomer of the product was formed preferentially, with the alkyl side-arm favoring the trans-position to the B(pin) moiety, consistent with previously reported cyclobutanation results in section 2.1.5.2.

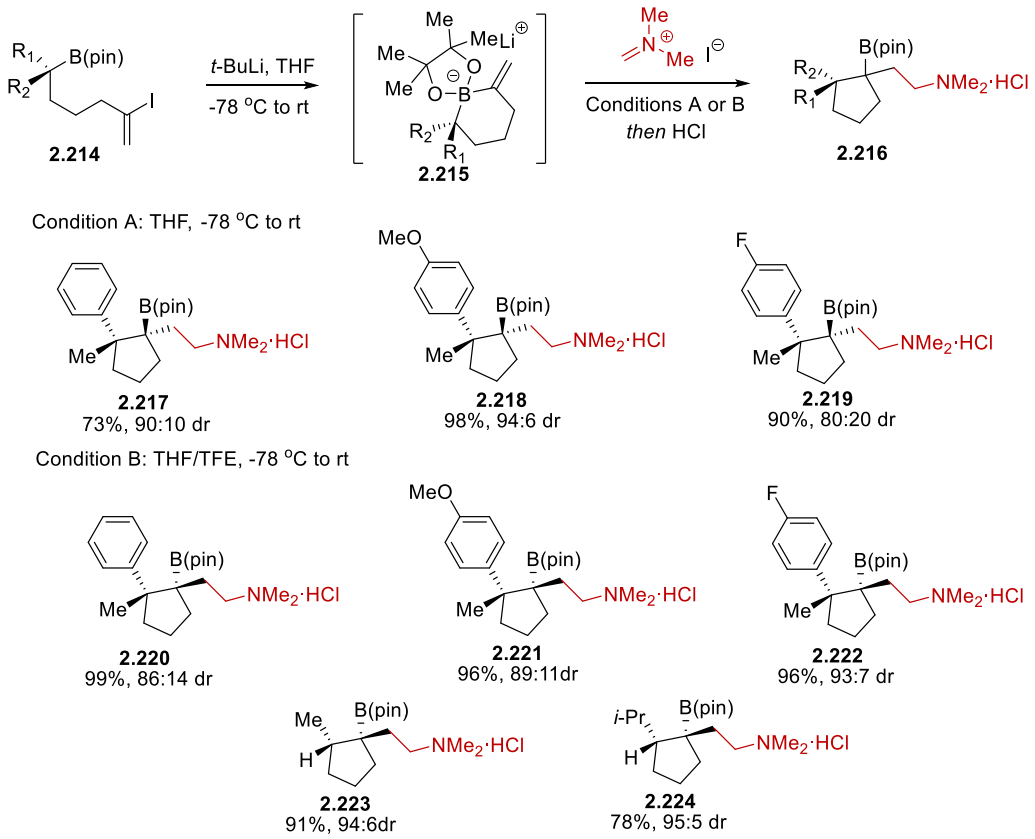



***Figure 2.24.*** Cyclopentanation *via* 1,2-Migration of Cyclic Alkenylboronate Induced by Eschenmoser's salt

In addition to Eschenmoser's salt, other electrophilic reagents demonstrated the ability to interact with these cyclic boronate complexes and induce the 1,2-migration reaction. Across the substrate scope presented in Figure 2.25, diverse carbocyclic tertiary boronic esters were synthesized, featuring distinct substituents on the β-carbon. Notable examples include a heptatriene group (**2.225**), a thioacetal (**2.226**), bromide and iodide derivatives (**2.227** and **2.228**), a thioether (**2.229**), and a simple proton (**2.230**). All these tertiary boronic esters were obtained with good to high levels of diastereoselectivities. While this study did not involve DFT calculations

to rationalize the high diastereoselectivity, particularly the diastereodivergent nature of reactions with Eschenmoser's salt as the electrophile, Aggarwal provided a similar argument to the one discussed in section 2.1.5.2. They proposed that the disfavored *gauche* interaction between the large side-arm and the B(pin) moiety drove the observed high diastereoselectivities.

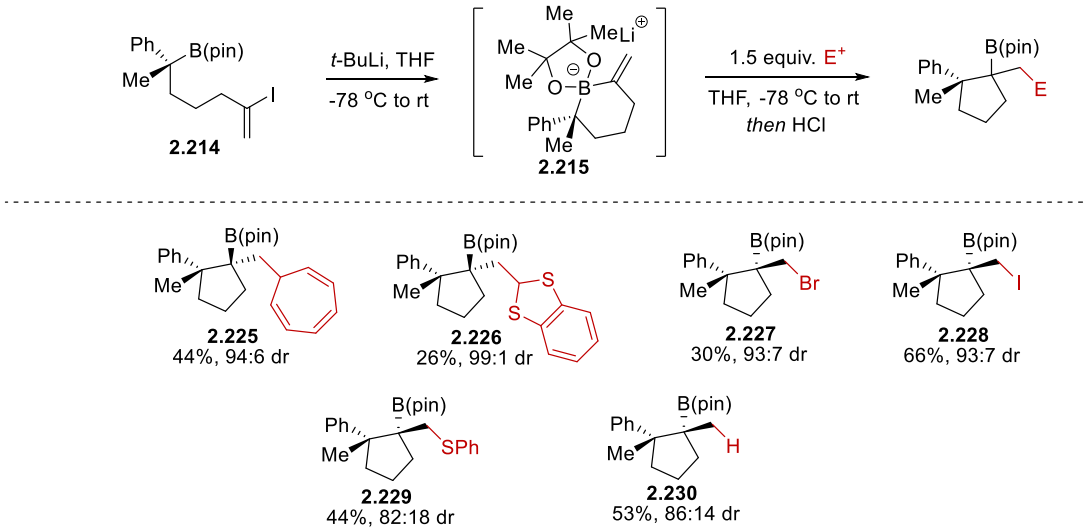



***Figure 2.25.*** Electrophiles Scope Other Than Eschenmoser's salt

## 2.2 Reaction design

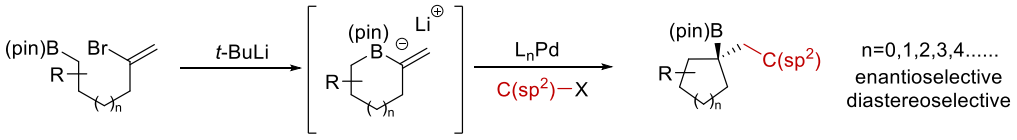



***Figure 2.26.*** General Scheme for Conjunctive Cyclization Reaction Design

In addition to Zweifel olefination or radical-polar crossover for inducing 1,2-migration of alkenylboronate complexes, transition metal catalysis, as highlighted in the introduction sections of chapter 1 and chapter 2, has proven to be another robust strategy for promoting the 1,2-migration of linear alkenylboronates. The promising outcomes from these reactions with linear substrates prompt the exploration of transition metal catalysis for the analogous 1,2-migration in cyclic alkenylboronates. As depicted in Figure 2.26, the development of such a transition metal-catalyzed reaction offers a pathway to synthesize a diverse array of tertiary boronic esters within cyclic frameworks, including carbocycles and heterocycles. Importantly, the incorporation of $C(sp^2)$

groups on the β-carbon now becomes feasible, a feature often challenging to achieve through radical-polar crossover strategies.

## 2.3 Results and Discussion

### 2.3.1 Conjunctive Cyclization Reaction with Primary Alkyl Boronic Esters

#### 2.3.1.1 Starting Material Synthesis

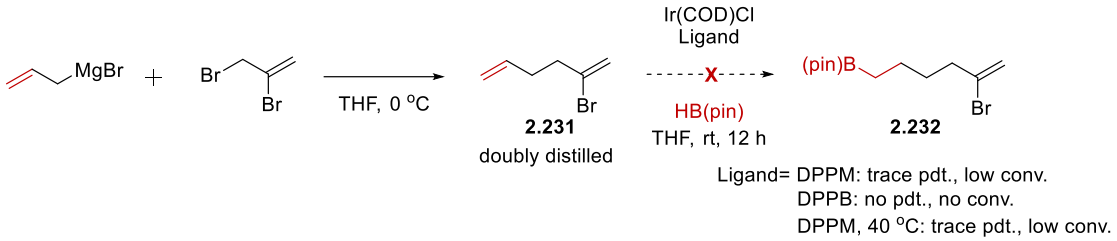



***Figure 2.27.*** Failed Attempt on Ir-catalyzed Hydroboration of Diene **2.231**

Following a similar approach to that employed by Aggarwal , our investigation commenced with a straightforward synthesis involving a primary B(pin) group positioned four carbons away from an alkenyl bromide unit. However, our route to the synthesis of the starting material differed. Initially, we explored an Ir-catalyzed hydroboration of diene **2.231**, anticipating a regioselective hydroboration favoring the less hindered terminal alkene to yield the desired alkyl B(pin) starting material. [34] Unfortunately, the reaction conditions, typically effective for clean hydroboration products according to literature, proved ineffective for substrate **2.231**. Utilizing Ir-DPPM complex or Ir-DPPB complex as catalysts, the reaction yielded only trace amounts of the desired boronic ester after 12 hours of stirring together the catalyst, HB(pin), and diene substrate in THF at room temperature. The reaction was ineffective, resulting in the predominant recovery of the diene starting material. Even under elevated temperatures, the conversion of the reaction remained unsatisfactory (see Figure 2.27).

[34] Fiorito, D.; Mazet, C. *ACS Catal.* **2018**, *10*, 9382–9387.

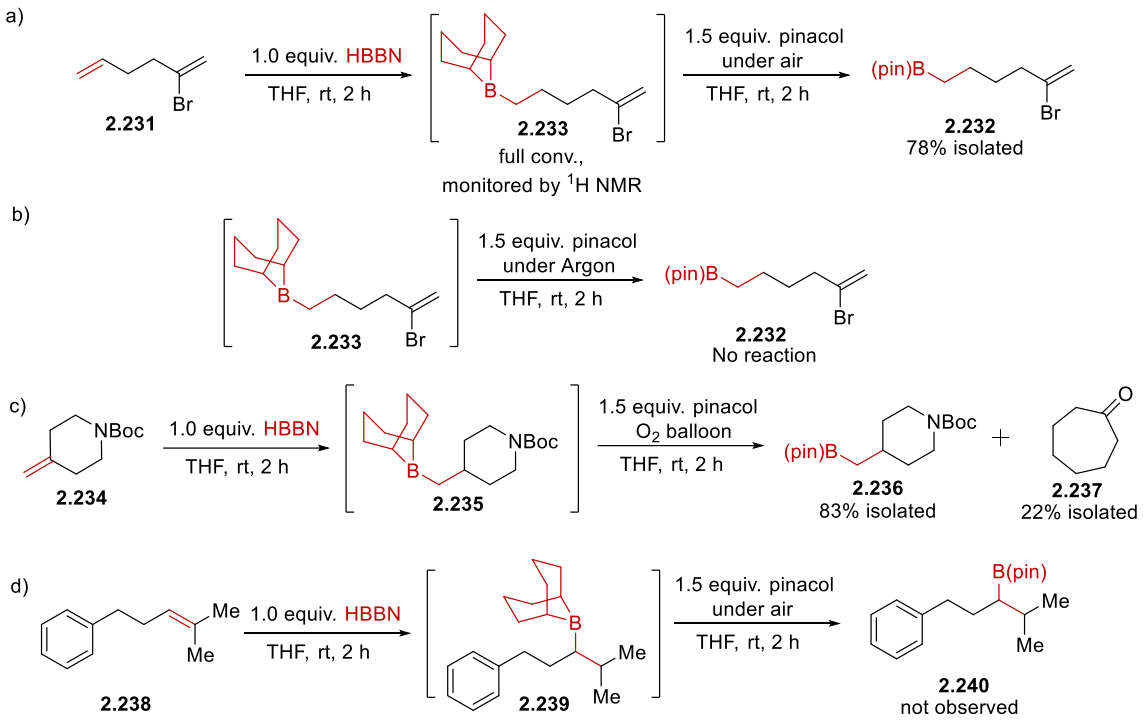



***Figure 2.28.*** Hydroboration Using HBBN and Pinacol Exchange

Suspecting that the sluggish reaction observed might be attributed to the presence of another alkene group capable of chelating onto the Ir(I), hindering oxidative addition with HB(pin), we turned our attention to hydroboration reactions not reliant on transition metal catalysts. The hydroboration with HBBN emerged as a promising candidate, as it is typically transition metal-free, and evidence indicates that hydroboration with HBBN on substrates containing multiple alkenes can exhibit regioselectivity, favoring the least hindered terminal alkene. As illustrated in Figure 2.28a, when diene **2.231** was treated with 1.0 equiv. of HBBN in THF for 2 h at room temperature, followed by the addition of 1.5 equiv. of pinacol and stirring under air for an additional 2 h, the desired primary alkyl B(pin) **2.232** was successfully synthesized, giving an isolated yield of 78%. The anticipated regioselectivity of HBBN hydroboration was in line with previous reports; however, the subsequent ligand exchange between the cyclooctyl group and pinacol took us by surprise. Subsequent investigations, as illustrated in Figure 2.28b, revealed that the reaction necessitated the presence of air, particularly $O_2$, as ligand exchange under an argon atmosphere did not transpire. Further analysis of the reaction products components for the exocyclic alkene substrate **2.234** unveiled a volatile side-product, cyclooctanone **2.237** (isolated yield: 22%, Figure 2.28c), originating from the cyclooctyl group formerly attached to the boron

atom. Additionally, the ligand exchange was found to be effective only with primary alkyl BBN, as substrate **2.238** failed to yield the desired secondary B(pin) **2.240**, despite complete consumption of the starting material alkene.

### 2.3.1.2 Conjunctive Cyclization Reaction with Primary Alkyl B(pin)

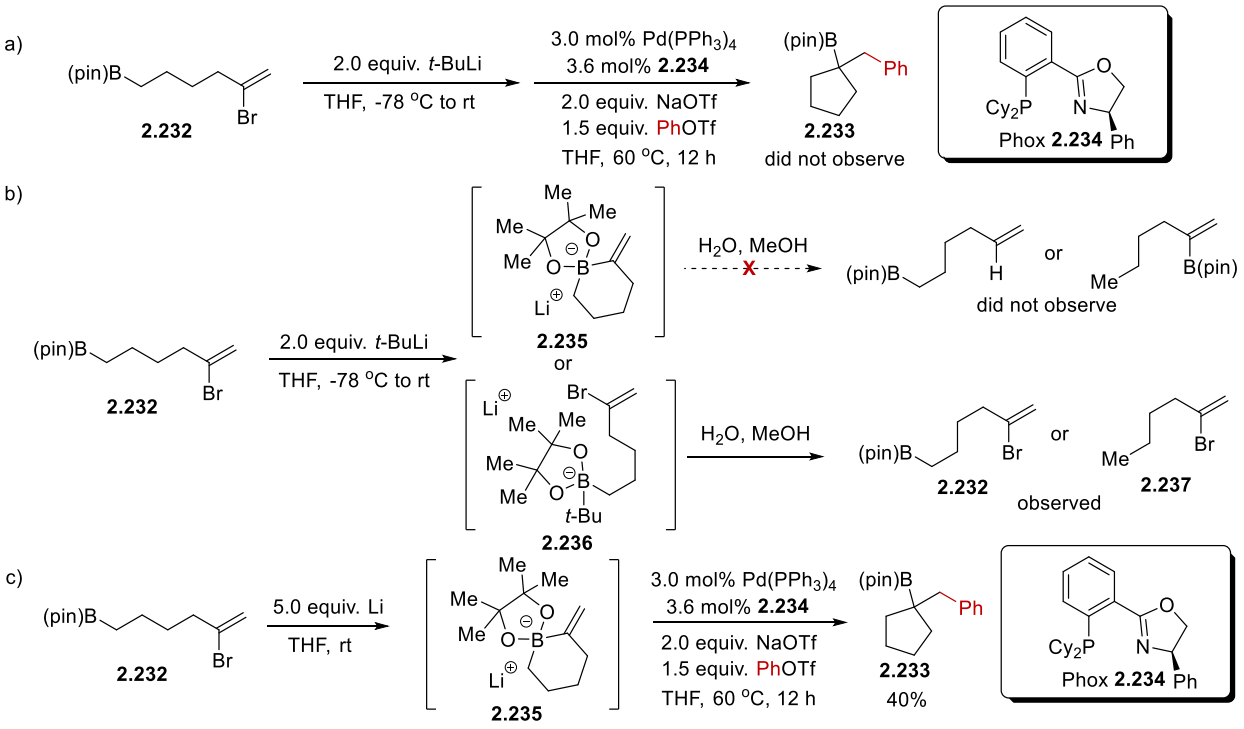



***Figure 2.29.*** Conjunctive Cyclization with Primary Alkylboronate

With the primary alkyl B(pin) starting material **2.232** in hand, we proceeded to investigate the formation of the cyclic alkenylboronate complex **2.235** and the conjunctive cross-coupling on such a cyclic boronate, abbreviated as the conjunctive cyclization reaction. As illustrated in Figure 2.29a, treating **2.232** with 2.0 equiv. *t*-BuLi at -78 °C revealed a tetracoordinated boronate complex, observed on $^{11}$B NMR. However, when this boronate complex was subjected to standard conjunctive cross-coupling conditions, it failed to yield the desired cyclization product. Instead, a complex mixture was obtained after workup, which included a small amount of unreacted starting material, protodeborylation, and cross-coupling of the phenyl triflate with the primary B(pin). Notably, the alkenyl bromide moiety in most of these side-products remained untouched, indicating the absence of the desired lithium-halogen exchange. Upon closer inspection (Figure 2.29b), treating **2.232** with only 1.0 equiv. *t*-BuLi resulted in the same tetra-coordinated boronate

complex, but notably not the desired cyclic alkenyl boronate **2.235**. Subsequent hydrolysis of this boronate complex produced either the starting material **2.232** or protodeborylation of primary B(pin) **2.237**, with the alkenyl bromide remaining unreacted. It became apparent that the *t*-BuLi, instead of reacting with the bromide atom on the alkene, might be reacting with the unhindered and electrophilic empty p-orbital of the boron to form the undesired *t*-butyl boronate complex **2.236**. To address this issue, a lithiation with metallic lithium was employed on **2.232**, as depicted in Figure 2.29c. Treating **2.232** with an excess amount of lithium metal at room temperature resulted in the formation of the desired cyclic boronate complex **2.236**. Subsequent treatment of the resulting complex with standard conjunctive cross-coupling conditions indeed yielded the cyclized tertiary boronic ester **2.233** with a 40% isolated yield.

### 2.3.2 Conjunctive Cyclization Reaction Towards Cyclobutane Synthesis

#### 2.3.2.1 Starting Material Synthesis

Encouraged by the success of conjunctive cyclization with primary alkylboronates, our investigation extended to reactions involving secondary alkylboronates. Departing from the methodology employed by Aggarwal, we pursued an alternative approach for the synthesis of starting materials. Starting with a terminal alkene (**2.236**), we employed a Fernandez diboration to access the racemic vicinal diboron compound **2.237**. Utilizing a newly developed Cu-catalyzed cross-coupling reaction (elaborated in chapter 3), this vicinal diboron underwent coupling with dibromopropene, resulting in the synthesis of a secondary boron moiety situated three carbons away from an alkenylbromide unit (**2.238**). For the synthesis of enantiomerically enriched secondary boronic esters (**2.240**), a carbohydrate-catalyzed enantioselective diboration was employed to yield the precursor vicinal diboron **2.239** with a 95:5 er.

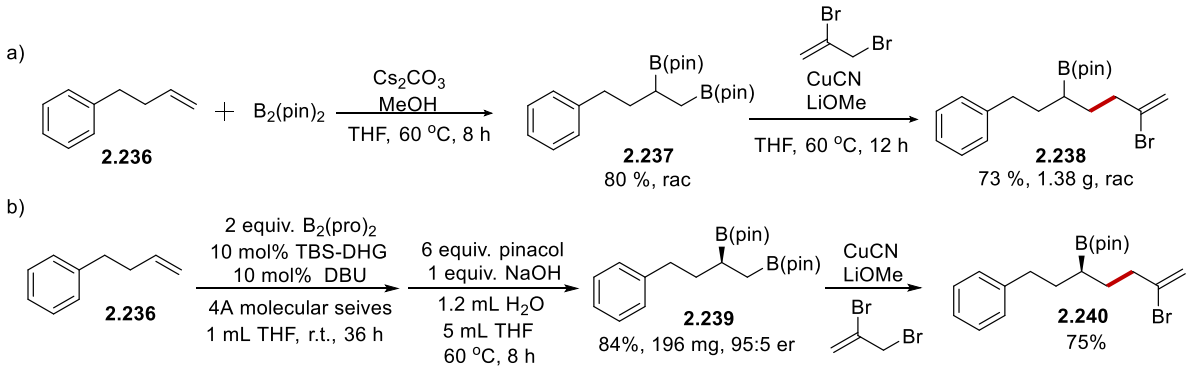


***Figure 2.30.*** Racemic and Enantiomerically Enrich Starting Material Synthesis

### 2.3.2.2 Conjunctive Cyclization for Synthesis of Cyclobutanes

To our satisfaction, the secondary alkylboronate, **2.241**, exhibited a significantly less electrophilic p-orbital on boron, attributed to both steric hindrance and electronic effects (elaborated in detail in chapter 3 concerning the rate difference in *t*-BuLi addition to primary and secondary alkylboronates). Upon treatment of **2.241** with 2.0 equiv. *t*-BuLi, the lithium-halogen exchange ensued, yielding the racemic pair of desired cyclic alkenylboronate complexes. Employing standard conjunctive cross-coupling reaction conditions with the Mandyphos ligand **1.45**, the ensuing cyclization afforded the cyclobutanyl tertiary boronate product, **2.243**, as a sole diastereomer with an enantiomeric ratio of 90:10. Notably, the reaction produced a modest amount (25%) of the conjunctive cyclization product, with the major product being the Suzuki-Miyaura cross-coupling product, **2.244**, enantioenriched at 62:38. Remarkably, considering the formation of an enantiomerically enriched product even with racemic starting material, we posit that the reaction proceeded through a kinetic resolution-type transformation. One enantiomer of the cyclic boronate complex was primarily converted to the conjunctive cyclization product **2.243**, while the other was predominantly transformed into the Suzuki-Miyaura cross-coupling product **2.244**.

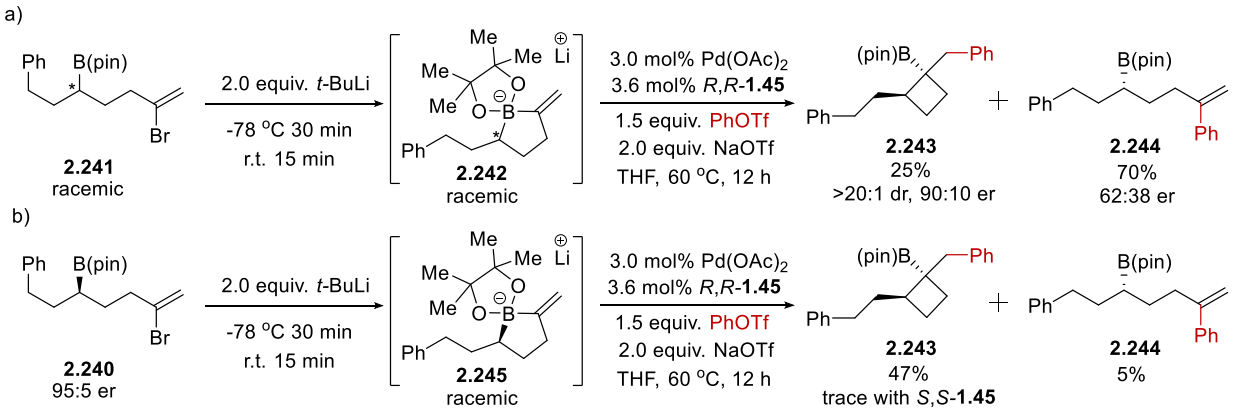



***Figure 2.31.*** Conjunctive Cyclization for Cyclobutane Synthesis

This hypothesis was further supported by the reaction with enantiomerically enriched cyclic boronate **2.245**. The chirality of ligand **1.45** appeared to match with the chirality of **2.245**, producing the desired cyclic boronic ester **2.243** with higher yield (47%). While the other enantiomer of the same ligand *S*,*S*-**1.45** produced **2.243** in only trace amount.

### 2.3.3 Conjunctive Cyclization Reaction Towards Cyclopentane Synthesis

#### 2.3.3.1 Starting Material Synthesis

The results from the formation of cyclobutanes encouraged us to further investigate the reaction with larger ring sizes. We developed another sequence to produce secondary boronic ester with boron located four carbons away from the alkenylbromide unit. A regioselective diboration was carried out on diene **2.246**. Then the same Cu-catalyze cross-coupling reaction was carried out to couple the terminal B(pin) in **2.247** with an allyl group, from which the desired secondary boronic ester **2.248** was prepared with 74% yield as a pair of racemates.

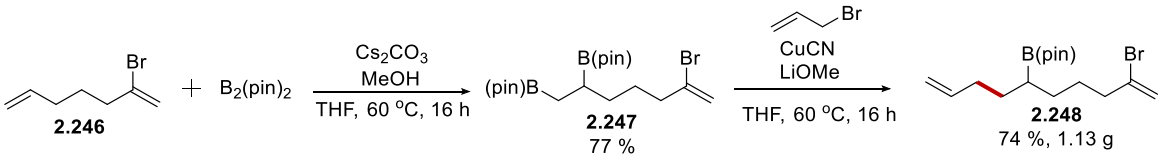



***Figure 2.32.*** Starting Material Synthesis

#### 2.3.3.2 Conjunctive Cyclization Reaction for Synthesis of Cyclopentanes

With the secondary boronic ester **2.248** in hand, our focus shifted to investigating the conjunctive cyclization of such starting material. Illustrated in Figure 2.33a, the use of ligand **1.45** with the racemic pair of cyclic boronate substrate exhibited significantly improved chemoselectivity compared to the cyclobutanation counterpart. The desired cyclobutyl boronic ester was obtained with a 65% isolated yield, while the Suzuki-Miyaura cross-coupling byproduct was formed only in trace amounts. However, further exploration of the stereochemistry of the product, facilitated by $^{1}$H NMR and SFC data (to be discussed in later sections), unveiled the presence of four stereoisomers of the product in this conjunctive cyclization: **2.252** generated in 34%, **2.253** generated in 1%, **2.254** generated in 18%, and **2.255** generated in 12%.

The stereochemical outcome of the reaction can be elucidated as follows: the strong substrate control, akin to the stereochemistry control observed by Aggarwal in radical-induced cyclization reaction (sections 2.1.5.2. and 2.1.5.3.), induces a stereochemistry preference. Both enantiomers of **2.249** preferentially form one of the diastereomers, with S-**2.249** giving rise to **2.252** and R-**2.249** leading to **2.254**. In these diastereomers, the B(pin) unit is positioned trans to the alkyl sidearm on the β-carbon. Simultaneously, the formation of the boron-containing stereocenter is

influenced by the chiral ligand **1.45**, favoring an R configuration with the B(pin) pointing inward and the benzyl group pointing outward. When S-**2.249** is involved in the reaction, the substrate control (B(pin) trans to the sidearm) aligns with the ligand control (B(pin) pointing inward), resulting in an enhanced overall stereochemistry of 34:1. This leads to the formation of the highly preferred R-configuration boronic ester **2.252**, which bears an S configuration alkyl sidearm on the β-carbon. Conversely, when R-**2.249** is engaged in the reaction, a conflict arises between substrate and ligand control. The substrate control necessitates the reaction to generate a product where B(pin) points outward to remain trans to the alkyl sidearm, while the R,R-Mandyphos **1.45** ligand still prefers the formation of an R configuration on the boron-containing stereocenter, where the B(pin) group should point inward. This conflict results in diminished diastereoselectivity, producing two diastereomers, **2.254** and **2.255**, from R-**2.249** in close to equal amounts (18:12).

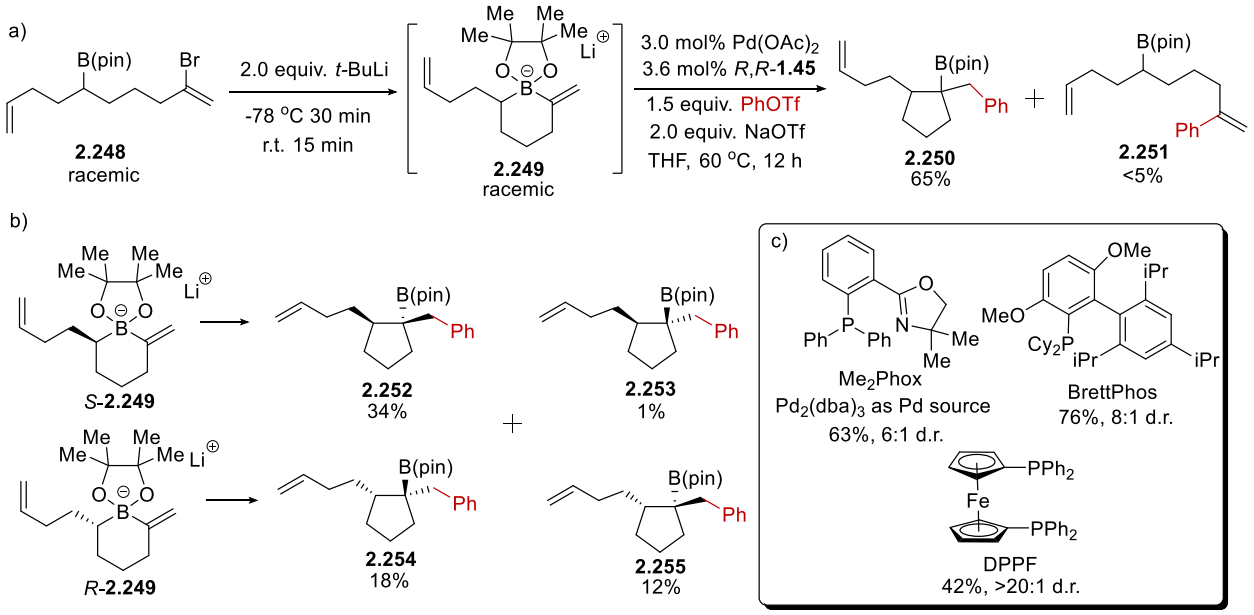



***Figure 2.33.*** Conjunctive Cyclization towards Cyclopentanes

Additionally, we investigated the performance of several achiral ligands on this cyclization reaction. As shown in Figure 2.33c, $Me_2$Phox ligand improved the diastereoselectivity to 6:1, while Brettphos improved to 8:1 and DPPF gave only one diastereomer as the product, albeit with lower yield.

### 2.3.4 Conjunctive Cyclization Reaction of Tertiary Alkylboronates

As we faced challenges in developing a high-yielding and enantioselective transformation using either primary or secondary alkylboronates as starting materials, we proceeded to explore modifications in the substitution pattern on the boronic ester. Our aim was to identify a specific type of starting material that could reliably give an enantioselective transformation. Tertiary alkyl boronic esters with identical α-substituents emerged as a promising candidate. This achiral starting material, devoid of stereogenic centers, presented an opportunity for the conjunctive cyclization reaction to yield a pair of enantiomers of the cyclic tertiary boronic ester. With only one stereocenter to be constructed, our hope was that the stereochemistry could be exclusively controlled by the chiral catalyst.

#### 2.3.4.1 Starting Material Synthesis for tertiary boronic esters

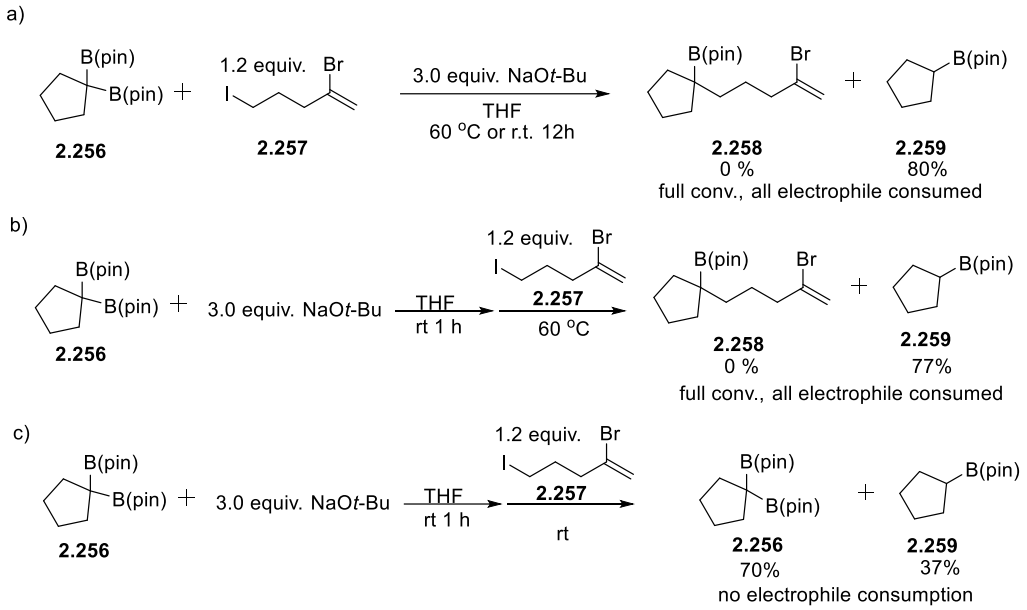



***Figure 2.34.*** Failed Attempt on Synthesizing Tertiary Boronic Ester Using Cross-Coupling Between Geminal Diboron and Alkyl Iodide

While the concept of utilizing an achiral tertiary boronic ester for achieving enantioselective conjunctive cyclization appeared promising, practical implementation revealed challenges in synthesizing the starting material. Initially, we intended to synthesize the targeted molecule using

a substitution reaction reported by Moken in 2014.[35] Excess NaO*t*-Bu was added to germinal diboron **2.256** to generate the corresponding α-boryl carbanion. Subsequently, this carbanion was treated with alkyl iodide electrophile **2.257**, with the anticipation of an $S_N2$ reaction yielding the desired tertiary boronic ester **2.258**, complete with an attached alkenyl bromide unit. However, this approach proved ineffective, resulting only in the formation of protodeborylation side product **2.259** and the complete decomposition of electrophile **2.257**. Attempts to enhance the reaction yield, such as pre-stirring the base with germinal diboron or lowering the reaction temperature, exhibited little to no improvement (Figure 2.34b and c).

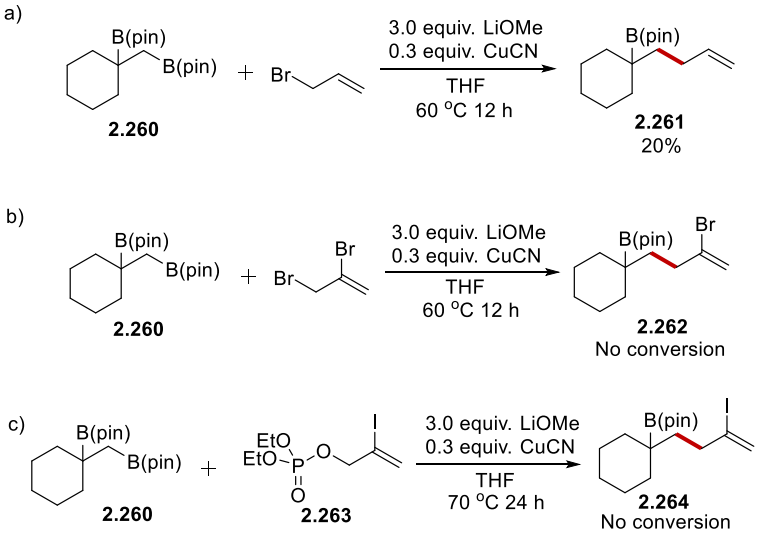



***Figure 2.35.*** Failed Attempt on Synthesizing Tertiary Boronic Ester Using Cross-Coupling Between Vicinal Diboron and Allyl Electrophiles

Considering the challenge posed by the diminished nucleophilicity of tertiary carbanions due to high steric hindrance in the previously mentioned cross-coupling reaction, we explored the feasibility of utilizing the newly developed cross-coupling method between vicinal diboron and allyl electrophiles to synthesize substrate **2.262**.[36] The initial attempt seemed promising, as substrate **2.260** could be successfully coupled with allyl bromide to yield terminal alkene **2.261**, albeit with a lower yield compared to other diboron substrates. However, when substituting the allyl bromide with dibromopropene electrophile, the reaction yield plummeted to 0%, with the

[35] Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581-10585.
[36] Xu, N.; Kong, Z.; Wang, J. Z.; Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 17815–17823.

major side product being the protodeborylation of the primary B(pin) unit. Further attempts to employ a potentially more electrophilic allyl phosphate electrophile **2.263** were unhelpful.

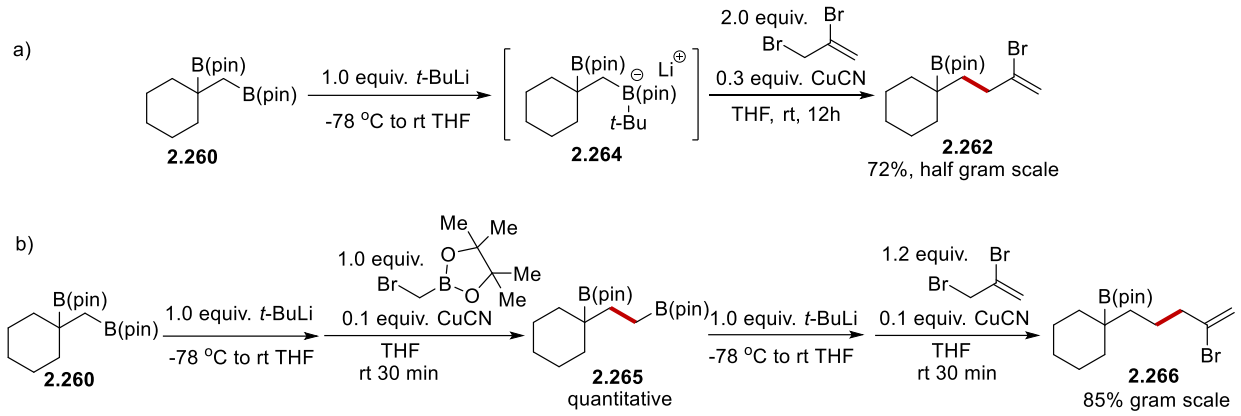



***Figure 2.36.*** Starting Material Synthesis *via* *t*-BuLi Activated Bisboronates

At this juncture, a new strategy was required for synthesizing the desired starting material, **2.258**. Drawing inspiration from Aggarwal 's work (for further details, refer to chapter 3), coupled with our own discoveries presented in sections 2.3.1 and 2.3.2, we contemplated utilizing an organolithium reagent instead of an alkoxide base to activate the vicinal diboron and thereby facilitate the previously challenging vicinal diboron-allyl coupling. As demonstrated in section 2.3.1, the reaction between *t*-BuLi and substrate **2.232** showcased that the *t*-Bu anion could efficiently add to the empty p-orbital of the primary B(pin) group at a rate faster than its reaction with the bromine atom on the alkene. While the *t*-Bu anion reacting with the secondary B(pin) group was notably slower than lithium-halogen exchange, as highlighted in section 2.3.2., it is now reasonable to deduce that by adding 1.0 equiv. *t*-BuLi to vicinal diboron **2.260**, it should selectively add to the more accessible primary B(pin) group, activate the primary carbon, and facilitate the subsequent cross-coupling reaction.

Indeed, the addition of *t*-BuLi to **2.260** proved to be regioselective when conducted at -78 °C. Upon treating the selectively activated 1,2-bisboronate **2.264** with CuCN and dibromopropene, an allylation reaction ensued, yielding the desired alkenylbromide **2.262** with a 72% yield. Importantly, this reaction demonstrated scalability, facilitating successful gram-scale synthesis. To synthesize the homologated alkenyl bromide **2.266**, the activated 1,2-bisboronate **2.264** underwent a site-selective homologation reaction with bromomethyl B(pin), resulting in the formation of 1,3-diboron **2.265**. Subsequently, the same strategy was employed to introduce the alkenylbromide

moiety: 1,3-diboron **2.265** underwent treatment with *t*-BuLi to activate the less hindered primary B(pin) unit, which was then coupled with dibromopropene to yield **2.266** with an 85% yield.

### 2.3.4.2 Reaction Optimization

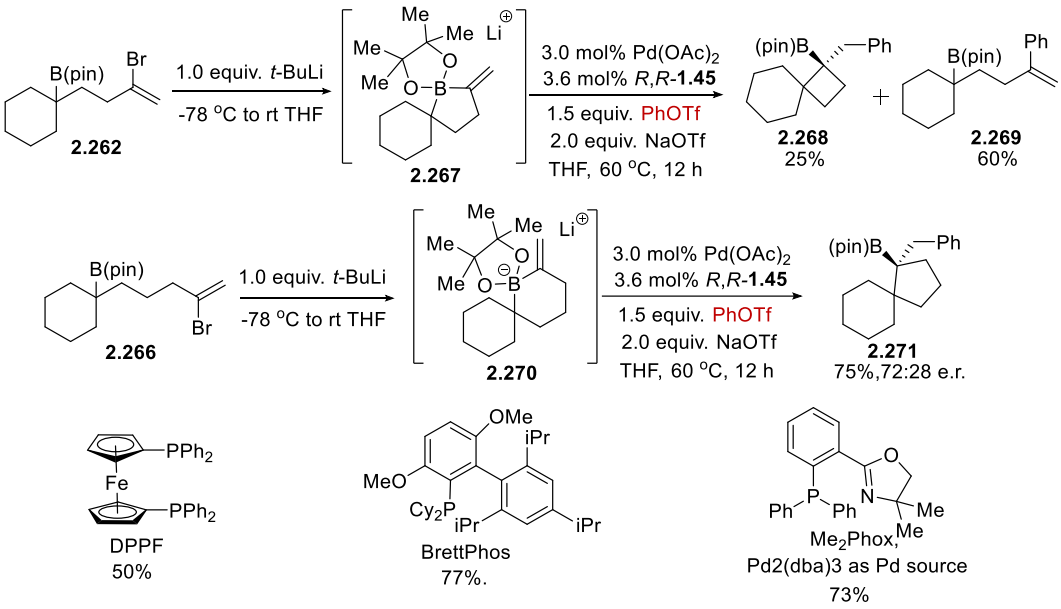
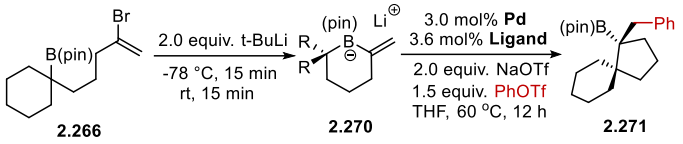



***Figure 2.37.*** Preliminary Results on Cyclization with Tertiary Boronic Esters

With the correct starting material in hand, we delved into the conjunctive cyclization of these compounds. The treatment of alkenylbromide **2.262** with 2.0 equiv. *t*-BuLi indeed generated the cyclic boronate complex as anticipated (Figure 2.37, **2.267**). However, utilizing this complex for the subsequent 1,2-migration under standard conjunctive cross-coupling conditions resulted in a mere 25% yield of the desired cyclobutanyl boronic ester. Moreover, the preparation of a racemic sample proved cumbersome, precluding the determination of enantioselectivity for the reaction. Similar to the cyclobutanation reaction detailed in section 2.3.2.2., this cyclization process suffered from significant side reactions, yielding large amount of the undesired Suzuki-Miyaura cross-coupling byproduct.

We proceeded to explore the cyclopentanation from **2.266**, expecting intrinsically better chemoselectivity in formation of the conjunctive cross-coupling product. Utilizing a standard conjunctive cyclization protocol with *R,R*-Mandyphos ligand **1.45**, the cyclopentane substrate was indeed formed with good yield with only minimal Suzuki-Miyaura cross-coupling side-product observed. However, after obtaining a racemic sample of **2.271** via a similar reaction with various




| entry | Pd source | ligand | yield 2.271 (%) | er |
|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | **1.45** | 75 | 72:28 |
| 2 | $Pd_2(dba)_3$ | **L2** | 83 | 65:35 |
| 3 | $Pd_2(dba)_3$ | **L3** | 79 | 55:45 |
| 4 | $Pd_2(dba)_3$ | **L4** | 86 | 65:35 |
| 5 | $Pd_2(dba)_3$ | **L5** | 69 | 72:28 |
| 6 | $Pd_2(dba)_3$ | **L6** | 77 | 52:48 |
| 7 | $Pd_2(dba)_3$ | **L7** | 80 | 72:28 |
| 8 | $Pd_2(dba)_3$ | **L8** | 55 | 80:20 |
| 9 | $Pd_2(dba)_3$ | **2.272** | 30 | 90:10 |
| 10 | $Pd(ACN)_2Cl_2$ | **2.272** | 72 | 86:14 |
| 11 | $Pd(PPh_3)_4$ | **2.272** | 77 | 91:9 |
| 12 | $Pd(PPh_3)_4$ | **2.273** | 72 | 95:5 |

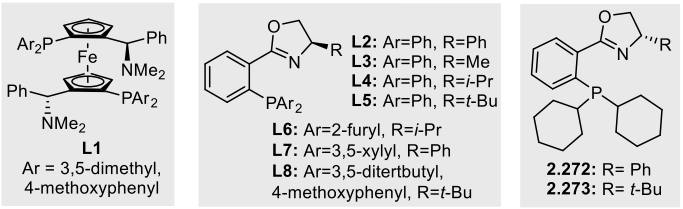



***Table 2.38.*** Ligand and Pd-source Screening

achiral ligands, we determined the enantioselectivity of the reaction with *R,R*-Mandyphos ligand **1.45** to be 72:28 er. In contrast to the discussion in section 2.1.2.1, where a very similar conjunctive cross-coupling reaction was explored and a tertiary migrating group did not necessarily lower the enantioselectivity (as demonstrated by substrate **2.072** with 96:4 er), it appears that the rigid and confined conformation of the cyclic boronate complex in this case made it more challenging for the Pd-*R,R*-Mandyphos complex to differentiate the prochiral faces of the alkene unit, consequently reducing the enantiomeric ratio. At this juncture, ligand screening was conducted to identify the more efficient ligand that can significantly improve the enantioselectivity.

As demonstrated in section 2.1.3, Phox ligands were found to be equal to or even better than Mandyphos for conjunctive cross-coupling reactions. Therefore, we proceeded with ligand screening, focusing on Phox ligands. As depicted in Table 2.38, when compared to ligand **1.45** in entry 1, most Phox ligands with diaryl substituents on the phosphine failed to enhance enantioselectivity (**L2** to **L7**). Only when a significantly hindered ligand like L8 was applied did the enantiomeric ratio improve. Phox with dicyclohexyl-substituted phosphine significantly enhanced the enantioselectivity (entry 9, ligand **2.272**, 90:10 er). Further screening revealed that $Pd(PPh_3)_4$ was the optimal Pd source, and Phox **2.273** with a *t*-Bu-substituted oxazoline was the optimal ligand (entry 12, 72% yield, 95:5 er).

### 2.3.4.3 Substrate Synthesis

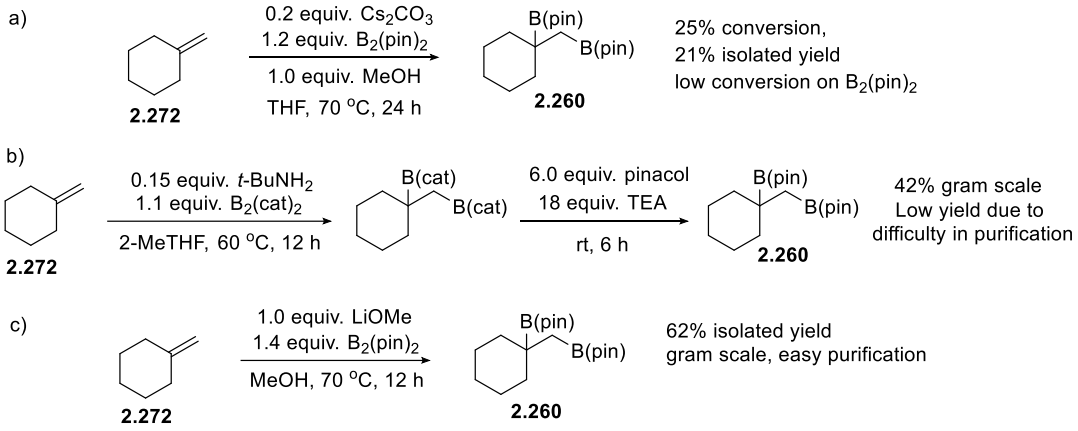



***Figure 2.39.*** Condition Scouting for Exocyclic Alkene Diboration

To implement the strategy outlined in Figure 2.36 for the synthesis of each substrate, a reliable method for preparing the exocyclic 1,2-bisboronates **2.260** was crucial. Initially, we explored the use of standard Fernandez diboration to achieve this diboron reagent (Figure 2.39a). However, the reaction proved sluggish, converting only a small amount of the exocyclic alkene to the desired diboron even under extended reaction times. Subsequently, we tested the diboration conditions employed by Aggarwal to diborate similar substrates. [37] This reaction was indeed effective in converting the exocyclic alkene **2.272** to the bisboronate **2.260** with an acceptable yield (Figure 2.39b). Nevertheless, the reaction required a large excess of pinacol for exchanging the catechol

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

ligand on the boron atom at the end of the reaction, making it challenging to purify when attempted on a large scale.

Finally, we adopted a improved diboration condition discovered by Fernandez [38], which still utilized pinacolato diboron but under a much more basic environment, using an alkoxide base instead of $Cs_2CO_3$. This new reaction condition, as shown in Figure 2.39c, rapidly converted the alkene **2.272** to the diboron product **2.260**. Additionally, the purification process was found to be much more manageable, enabling easy scaling up of the reaction. With this protocol, a library of diboron substrates, as illustrated in Figure 2.40, was efficiently developed with good yields and good quantities. However, certain substrates posed challenges, particularly those containing heteroatom substituents on the β-carbon to the exocyclic alkene, such as substrate **2.281** and **2.282**, which were unable to yield the desired diboron due to a high tendency for β-elimination processes under strongly basic conditions.

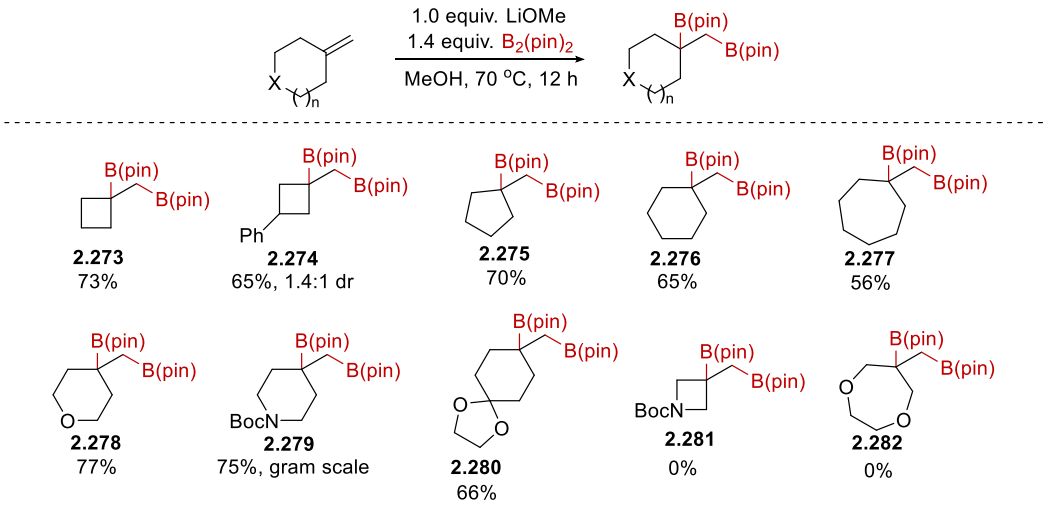



***Figure 2.40.*** 1,2-Bisboronate Synthesis

Having obtained the necessary 1,2-bisboronates, we proceeded with the site-selective homologation and allylation sequence. For substrates containing only hydrocarbon skeletons (**2.283** to **2.286**), the reaction could be conducted at room temperature. However, substrates containing heteroatoms (**2.287** to **2.290**) required heating (Figure 2.41, **2.87**-**2.90**). Ultimately, all the 1,2-bisboronates were successfully transformed into the desired alkenyl bromide-attached

[38] Bonet, A.; Pubil-Ulldemolins, C.; Bo, C.; Gulyas, H.; Fernandez, E. *Angew. Chem. Int. Ed.* **2011**, *50*, 7158–7161.

tertiary alkyl boronic esters, achieving good to high two-step yields. Notably, substrate **2.290**, featuring a doubly homologated alkyl tether, was obtained by cnductiong the site-selective homologation process twice. Furthermore, for the geminal dimethyl substrate **2.291**, a boronate complex rearrangement reaction developed by Studer [39] was employed to rapidly prepare the 1,3-bisboronate in a single step (Figure 2.41b). This intermediate then underwent the same site-selective allylation process, yielding the desired alkenyl B(pin) in 85% yield.

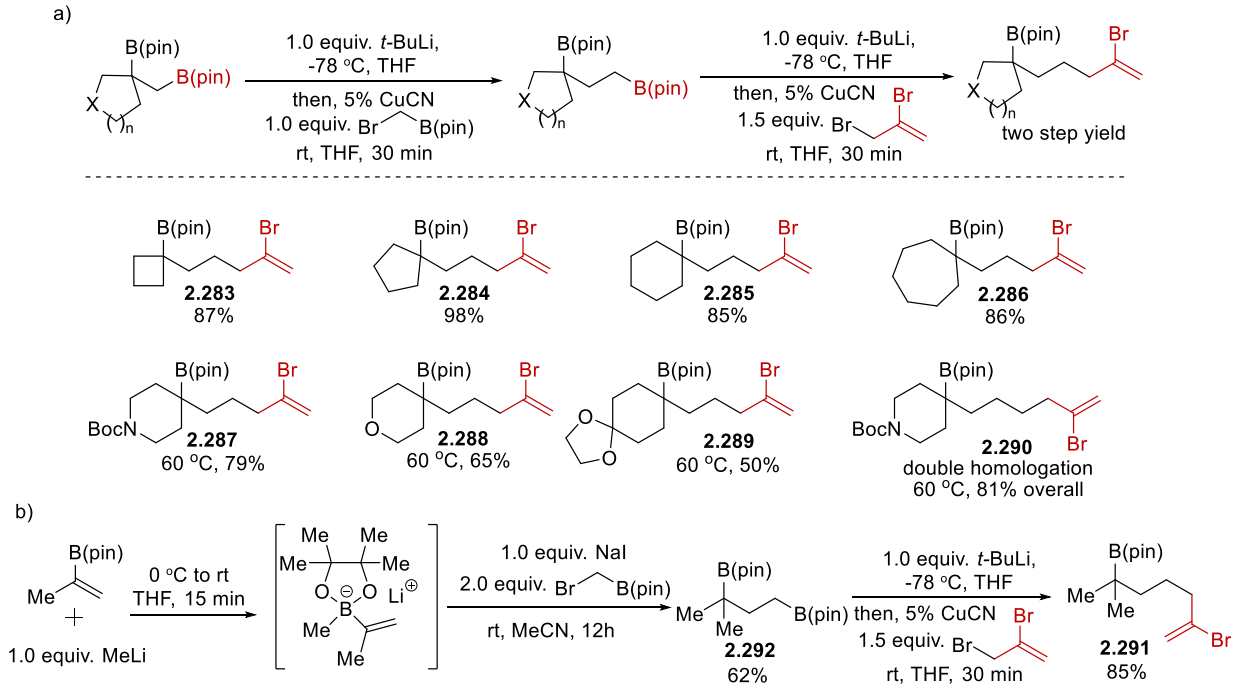



***Figure 2.41.*** Alkenylbromide synthesis

### 2.3.4.4 Conjunctive Cyclization Reaction

Having obtained the necessary starting materials, we applied the optimized conjunctive cyclization reaction conditions to these substrates. As illustrated in Figure 2.42, all the starting materials acquired in Figure 2.41 were successfully transformed into the desired spirocyclic or monocyclic tertiary boronic esters with high yields and enantioselectivities. Notably, using substrates **2.284** and **2.287**, the scope of electrophiles was investigated as well. The reaction not only tolerated aryl electrophiles but also incorporated alkenyl bromide (**2.299**), alkynyl bromide (**2.300**), as well as benzyl bromide (**2.301**). A single crystal of substrate **2.307** was obtained through

[39] You, C.; Studer, A. *Angew. Chem. Int. Ed*. **2020**, *59*, 17245 –17249.

recrystallization for X-ray crystallography study, revealing the absolute configuration of the boron-containing stereogenic center to be in the *R* configuration. Beyond cyclization to cyclopentanes, successful six-membered ring closure was achieved, as demonstrated by substrate **2.305**, where the enantioselectivity appeared to be indifferent towards the ring size.

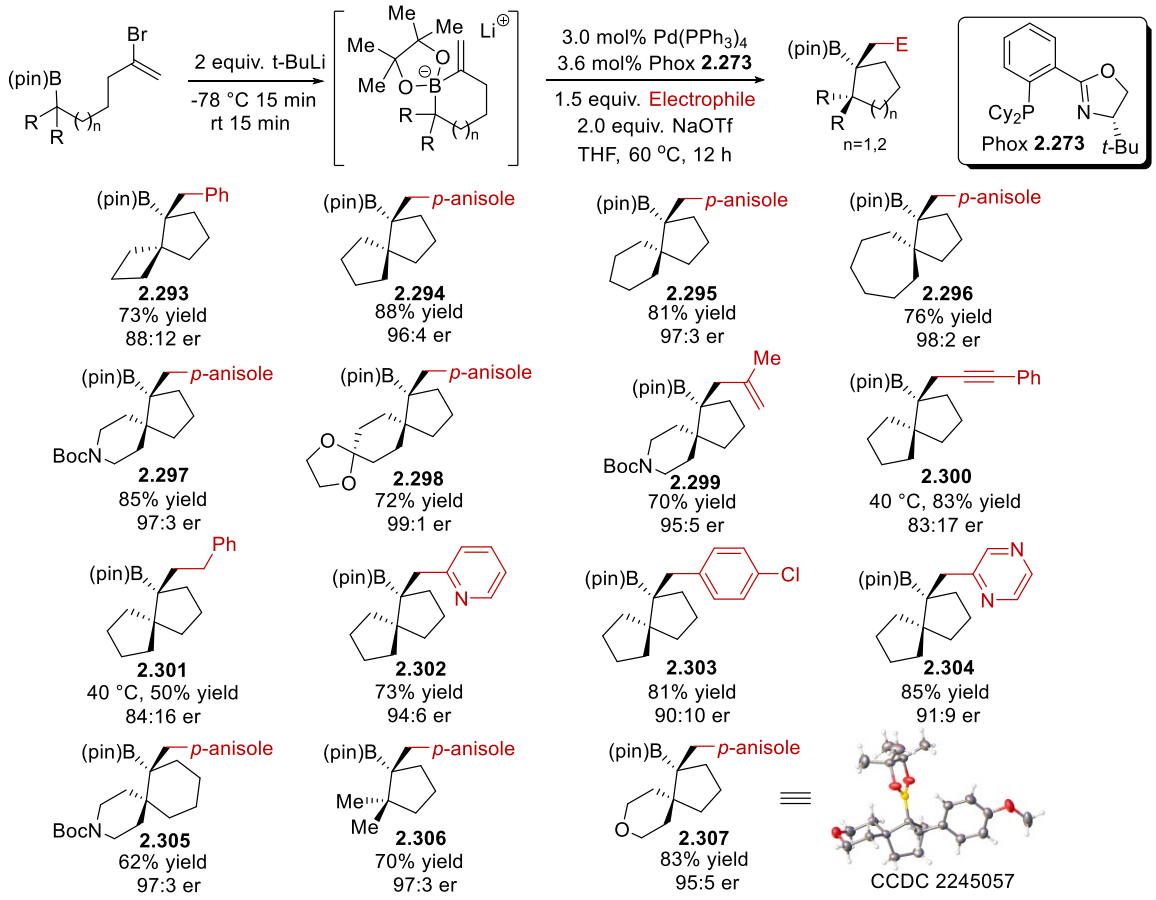



***Figure 2.42.*** Substrate Scope for Tertiary alkylboronate Conjunctive Cyclization

### 2.3.5 Conjunctive Cyclization for Aryl Bicycloalkanes Syntheses

Building on the inspiration drawn from Aggarwal 's work (as discussed in section 2.1.5.2), we envisioned the potential application of the conjunctive cyclization reaction for the synthesis of aryl bicyclic tertiary boronic esters. In contrast to radical-induced cyclization methods, the conjunctive cyclization presented a distinctive opportunity to impart enantioselectivity to these reactions, given that the cyclization process is now governed by a chiral catalyst.

### 2.3.5.1 Formation of Cyclic Alkenylboronate Complexes

As outlined in section 2.3.1.2, the rate of *t*-BuLi addition to the empty p-orbital of boron in the boronic ester can, in certain cases, exceed the rate of lithium-halogen exchange. With this in mind, we intentionally synthesized two distinct starting materials that could potentially yield the same cyclic alkenylboronate complex. One of these materials featured an aryl B(pin) and alkenyl bromide (**2.308**), while the other featured an alkenyl B(pin) and aryl bromide (**2.309**). Interestingly, upon analyzing the hydrolysis product compositions of the resulting boronate complexes, namely **2.310** and **2.311**, markedly different outcomes were observed. It was revealed that, due to the formation of **2.314** and **2.313** during hydrolysis, the boronate complex **2.310** generated from **2.308** was actually a *t*-butyl-substituted boron, where the alkenyl bromide did not react. The appearance of 40% **2.312** could be attributed to lithium-halogen exchange; however, the alkenyl lithium appeared to undergo facile β-elimination before its addition to B(pin), ultimately yielding the phenol **2.312** as the final product. In contrast, the protonation of **2.311** yielded only **2.315**, one of the potential products resulting from the protonation of the actual cyclic alkenylboronate complex. The difference in reactivity between the two boron empty p-orbitals in **2.308** and **2.309** can be explained as follows: when the B(pin) unit is located on the arene *ortho* to the alkenyl bromide group, steric clash necessitates the B(pin) group to adopt a perpendicular orientation. This configuration renders the empty p-orbital no longer in conjugation with the π-system of the arene, making it much more electrophilic than the one in **2.309**. Armed with this insight, we proceeded to synthesize substrates featuring alkenyl B(pin) units rather than aryl B(pin) units.

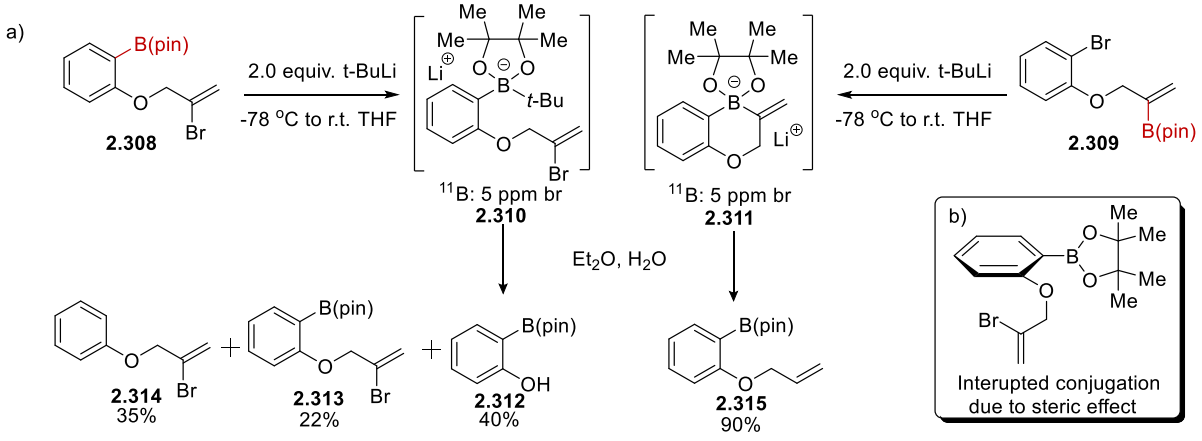



***Figure 2.43.*** Formation of Cyclic Boronate Complexes from Different Starting Materials

### 2.3.5.2 Substrate Synthesis

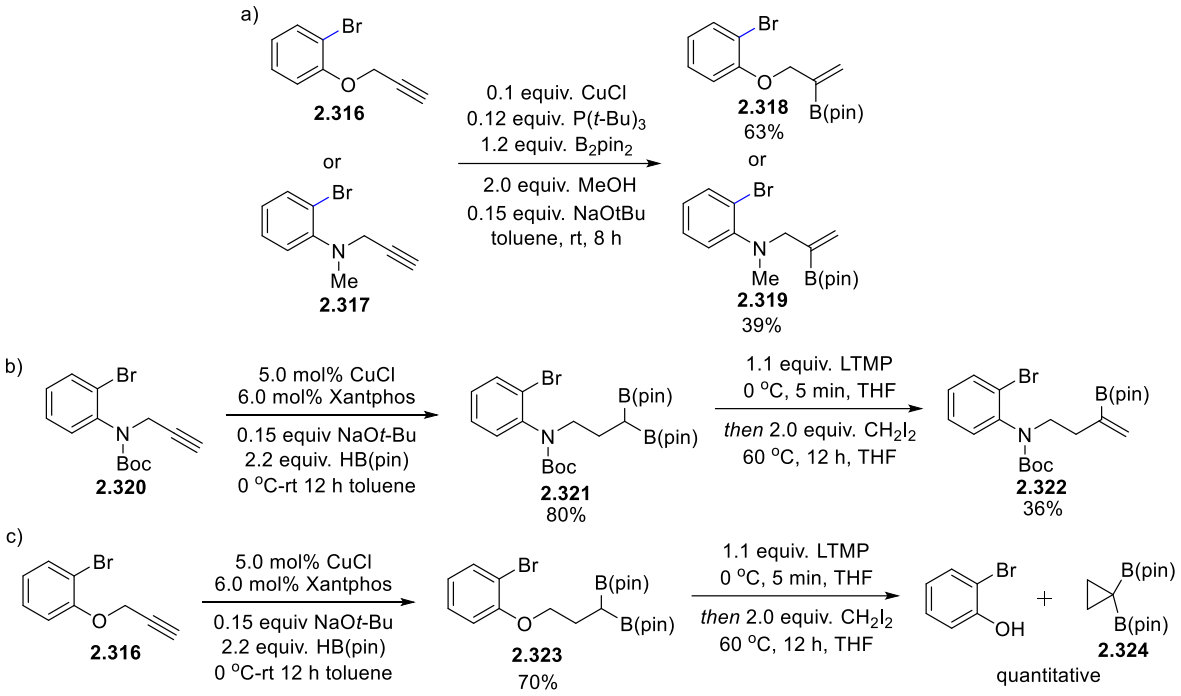



***Figure 2.44.*** Preliminary Substrate Synthesis

Continuing with the synthesis of the required alkenyl boronic esters for substrate scope investigation, we employed a sequential approach. Beginning with 2-bromophenol or 2-bromo-N-methyl-aniline, we conducted propargylation to obtain the corresponding alkynes, **2.316** and **2.317**. Subsequently, a Cu-catalyzed protoboration was employed to introduce the alkenylB(pin) units in **2.318** and **2.319**.[40] However, for one-carbon homologated substrate **2.322**, a different strategy was necessary due to the inefficiency of the Cu-catalyzed protoboration, which became less regioselective, resulting in a challenging-to-purify crude mixture. For **2.322**, the approach involved a Cu-catalyzed double hydroboration of the terminal alkyne 2.320 to generate geminal diboron **2.321**.[41] A boron-Wittig reaction was then implemented to install the alkenylboronate functional group in **2.322**.[42] Attempting to extend this strategy to synthesize oxygen-tethered substrates, as illustrated in Figure 2.44c, posed challenges. During the boron-Wittig step, the diboryl carbanion generated from deprotonation underwent a rapid intramolecular $S_N2$ reaction. This intramolecular

[40] Jang, H.; Zhugranlin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859–7871.
[41] Lee, S.; Li, D.; Jaesook Yun, J. *Chem. Asian. J.* **2014**, *9*, 2440–2445.
[42] Coombs, J. R.; Zhang, L.; Morken, J. P. *Org. Lett.* **2015**, *7*, 1708-1712.

reaction utilized the 2-bromophenoxyl group as a leaving group, resulting in the formation of the cyclopropane byproduct **2.325**. This process proved to be facile, yielding the undesired side-products **2.325** and 2-bromophenol in quantitative yield. The ease of this undesired reaction made it challenging to identify more potent electrophiles to override it, as changing the electrophile from diiodomethane to formaldehyde or Eschenmoser's salt failed to produce any desired olefination product.

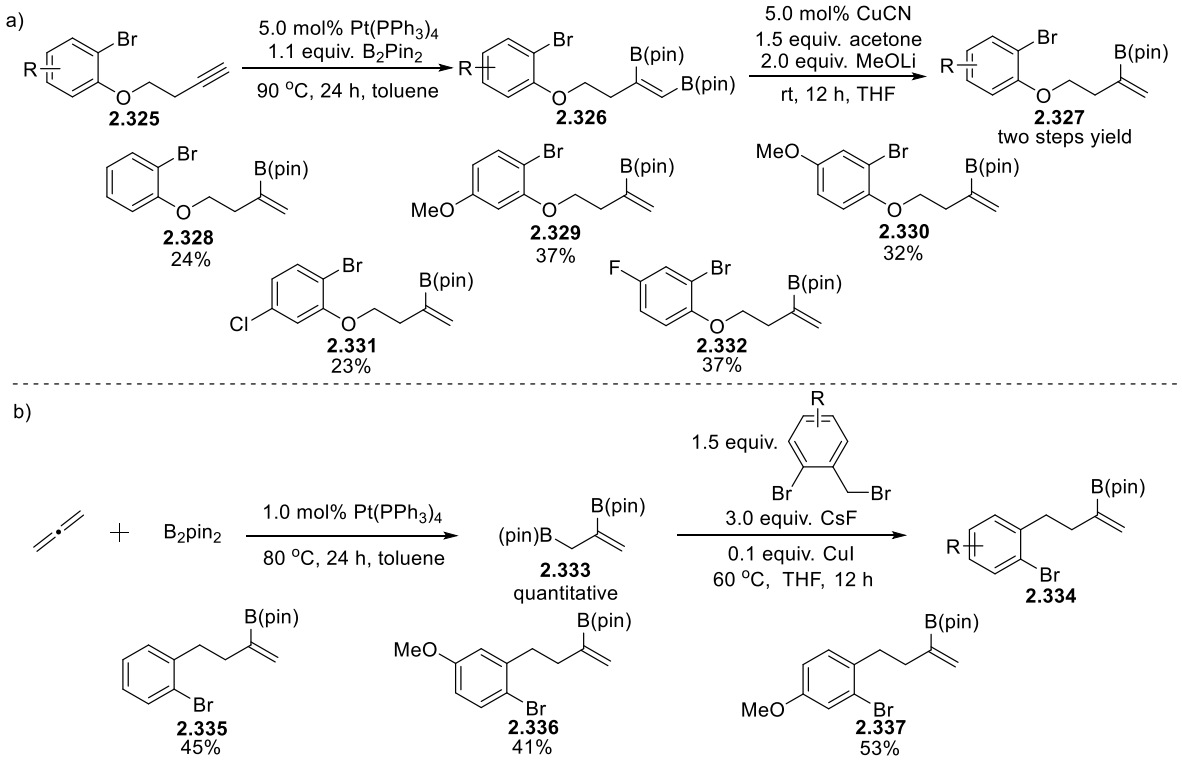



***Figure 2.45.*** Aryl Bicyclic Substrate Synthesis

To overcome the challenges in synthesizing oxygen-tethered alkenyl bromides, we implemented a novel strategy developed within our research group. Starting with alkynes **2.325**, easily obtained from 2-bromophenol through Mitsunobu reaction, a Pt-catalyzed diboration reaction was performed to generate alkenyl vicinal diborons **2.326**. Subsequently, the alkene bearing vicinal boronate substituents underwent a site-selective protodeborylation reaction, resulting in the desired alkenylboronates **2.327**. Although the yields were moderate, the regioselectivities achieved were excellent. Additionally, we employed an allyl-benzyl coupling between the diboron and benzyl bromide to synthesize two-carbon-tethered alkenylboronates **2.334**. Given the commercial availability of substituted benzyl bromides and the ease of

synthesizing diboron **2.333** from the diboration of allene on a ten-gram scale, this process demonstrated high efficiency in substrate synthesis.

### 2.3.5.3 Scope on Aryl Bicyclic Tertiary Boronic Ester Synthesis

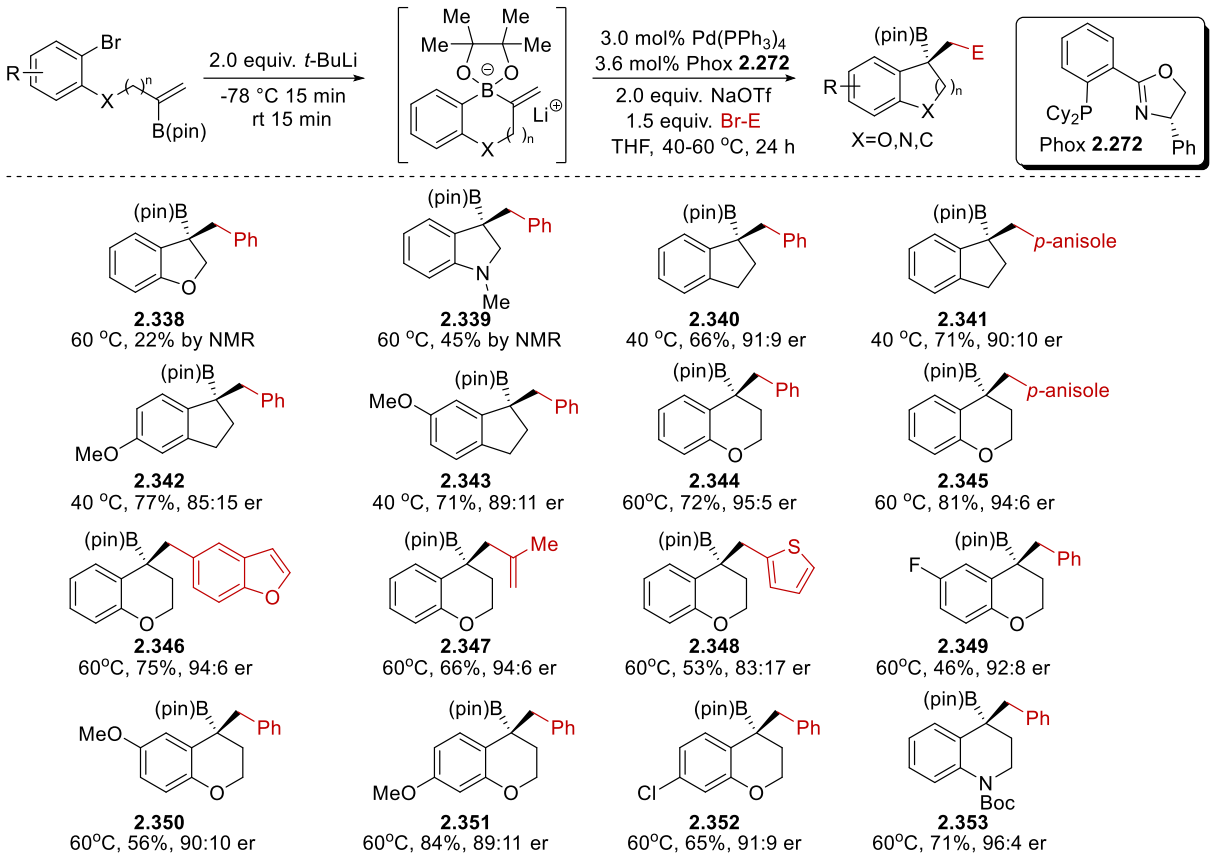


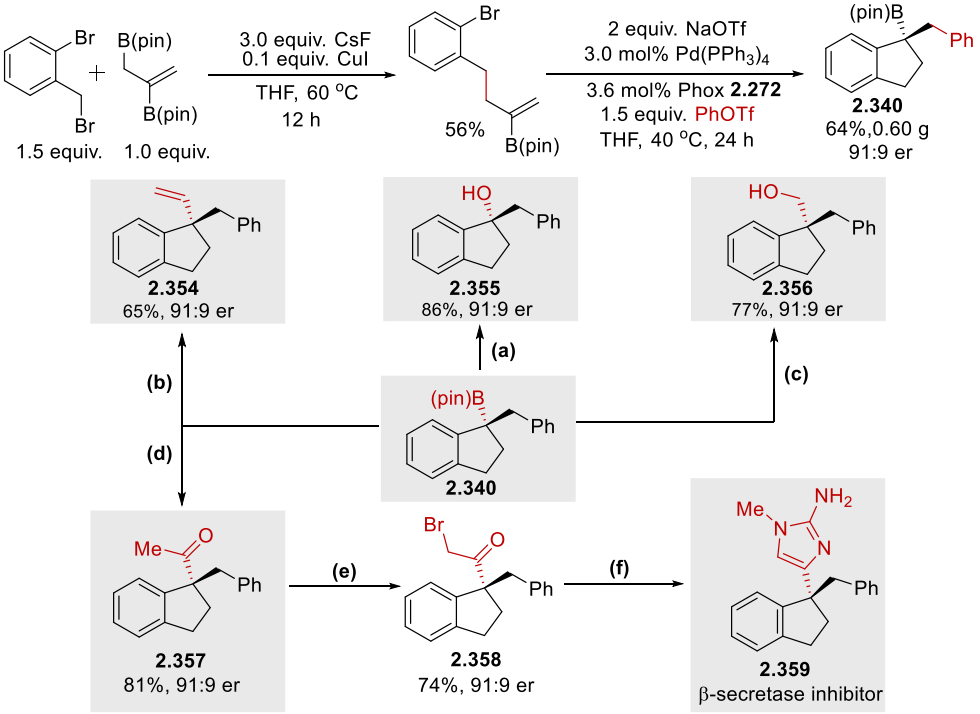

***Figure 2.46.*** Aryl Bicyclic Substrate Scope

We then embarked on the investigation of the cyclization reaction for the synthesized aromatic alkenylboronates. Utilizing Phox ligand **2.272** (Figure 2.46), we successfully synthesized a range of aryl bicyclic tertiary boronic esters, each displaying varied yields and enantioselectivities. Although **2.338** and **2.339** were detected in crude NMR spectra, they proved unstable and quickly oxidized upon exposure to air, making purification challenging. Conversely, tertiary boronates with indane skeletons exhibited stability under ambient conditions and could be isolated through column chromatography. Consequently, substrates **2.340**, **2.341**, **2.342**, and **2.343** were synthesized with satisfactory yield and enantioselectivity. Furthermore, hydrochromanes featuring these tertiary boron stereogenic centers were successfully synthesized, attaining good yields or

enantioselectivities (as depicted in Figure 2.46, substrates **2.344** to **2.352**). Finally, substrate **2.353**, incorporating an amine on the tether, was successfully generated with a 71% yield and 96:4 er.

### 2.3.5.4 Product Derivatization

To showcase the versatility of the newly synthesized aryl bicyclic tertiary boronic esters, we initiated the derivatization of the boron atom in substrate **2.340**. As illustrated in Figure 2.47, we initially conducted a gram-scale synthesis of **2.340**, yielding comparable results to the small-scale reaction in terms of both yield and enantiomeric ratio. Subsequently, we performed a stereospecific oxidation to generate the tertiary alcohol, utilizing the conditions outlined in section 2.1.1.1. Despite the hindered nature of the boronic ester in **2.340**, the oxidation process was remarkably efficient, yielding **2.355** with a high yield and perfect stereospecificity in a brief reaction time.




Conitions: **(a)**: For 0.2 mmol reaction, 0.5 mL $H_2O_2$, 0.5 mL 3M NaOH, 0.5 mL THF, rt, 1 h. **(b)**: 4.0 equiv. vinyl magnesium bromide, 5.0 equiv. $I_2$, 5.0 equiv. MeOLi in 1 mL MeOH, in THF, -78 °C to rt **(c)**: 4.0 equiv. $CH_2Br_2$, 3.0 equiv. *n*-BuLi, -78 °C to rt 2 h. *then*, 0.5 mL $H_2O_2$, 0.5 mL 3M NaOH, 0.5 mL THF, rt, 1 h. **(d)**: 4.0 equiv. ethyl vinyl ether, 2.5 equiv. *t*-BuLi, 3.0 equiv. $I_2$, 8.0 equiv. MeOLi in 1 mL MeOH. *then*, quanch with 3M HCl **(e)**: $Br_2$, MeOH, 0 °C to rt, 3 h **(f)**: Following known procedure in reference

***Figure 2.47.*** Aryl Bicyclic Substrate Derivatization

We further proceeded with a Zweifel olefination reaction, following the conditions discussed in section 2.1.1.3, leading to the formation of **2.354** with a 65% yield and impeccable

stereospecificity. Additionally, a Matteson homologation reaction was carried out using a modified condition from section 2.1.1.4, successfully homologating the benzylic tertiary alkylboronate and furnishing primary alcohol **2.356** after oxidation, with good yield and stereospecificity. Finally, an acetylation of the boron was performed using the modified Zweifel olefination conditions from section 2.1.1.4, resulting in the desired methyl ketone product **2.357** with an excellent yield. Notably, a site-selective bromination of the methyl ketone **2.357** produced intermediate 2.358, which has been reported as a precursor to the drug lead molecule **2.359**. Impressively, the previously reported synthesis of **2.359** was racemic, whereas the newly developed conjunctive cyclization and stereospecific transformations offer the potential for an asymmetric synthesis of **2.359**.

### 2.3.6 Revisiting Diastereoselective Conjunctive Cyclization Reactions

Following the exploration of diastereoselective conjunctive cyclizations for the synthesis of cyclobutanes and cyclopentanes with two continuous stereogenic centers in sections 2.3.2 and 2.3.3, we gained valuable insights. Building on the success of developing an enantioselective version of this reaction using tertiary alkylboronate and arylboronate substrates, we opted to revisit the diastereoselective version of conjunctive cyclization. The goal was to determine whether it is feasible to enhance the performance of these reactions and achieve improved diastereoselectivity.

#### 2.3.6.1 Cyclopentyl Tertiary Alkylboronate Synthesis

In our previous investigations using chiral Mandyphos ligand **1.45** on cyclopentane synthesis, controlling the stereochemistry proved challenging. Considering the superior stereoselectivity exhibited by Phox ligands **2.272** and **2.273**, we sought to explore the potential of improving stereoselectivity with Phox ligands. However, as depicted in Figure 2.48a, repeating the reaction from section 2.1.3 with optimal Phox ligand **2.272** did not enhance stereoselectivity, yielding cyclopentane product **2.250** with similar diastereoselectivity and enantioselectivity. Undeterred, we synthesized the enantiomerically enriched secondary alkylboronate **2.363** with the aim of achieving highly diastereoselective transformations by aligning substrate chirality with ligand chirality. Subsequently, substrate **2.366** was formed with improved diastereoselectivity (10:1 dr), where the crystal structure revealed a preference for generating a boronic ester with the B(pin) unit trans to the phenethyl sidearm. This stereochemistry preference aligns with the radical-induced

ring closure reported by Aggarwal (section 2.1.5.2 and 2.1.5.3). Moreover, this diastereoselective reaction exhibited a broad scope, successfully incorporating various electrophiles such as alkenyl bromides (**2.367**), alkenyl iodide (**2.368**), brominated heterocycles (**2.369** and **2.370**), and alkynyl bromide (**2.371**).

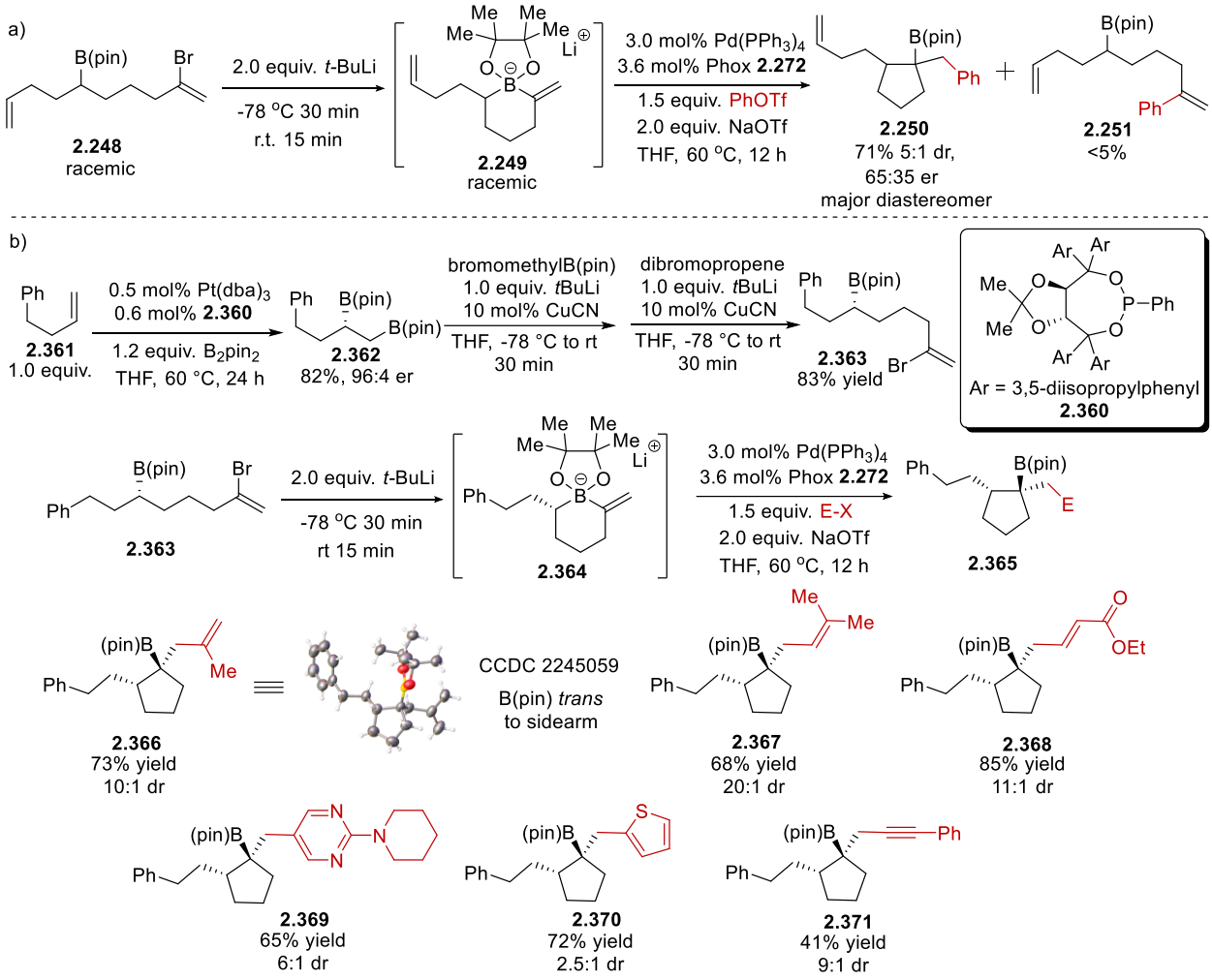



***Figure 2.48.*** Diastereoselective Conjunctive Cyclization for Cyclopentane Synthesis

### 2.3.6.2 Cyclobutyl Tertiary Alkylboronate Synthesis

Lastly, we revisited the cyclobutane tertiary alkylboronate synthesis, using Phox **2.272** as optimal ligand. Unfortunately, even when using the enantiomerically enriched secondary boronic ester **2.372**, the reaction failed to generate synthetically useful amounts of the desired cyclobutane product. The production of **2.373**, even with a conventional phenyl triflate electrophile, suffered from low yields. Other electrophiles, such as alkenyl bromide (**2.274**), chloroformate (**2.275**), and

alkynyl bromide (**2.276**), resulted in only trace amounts of product. Further investigation into the cyclobutanation reaction using DFT calculations indicated a more challenging transformation. Comparing the ring contraction from six to five-membered rings (**2.277** to **2.278**), the ring contraction from **2.279** to **2.280** encountered a 2.2 kcal/mol higher transition state barrier, likely due to the high ring strain in cyclobutanes. Additionally, as shown in **2.279**, the five-membered ring cyclic alkenylboronate preferred a flat conformation, where the migrating C−B bond did not align with the π* of the alkene moiety. This conformational preference likely made the 1,2-migration even more challenging. Currently, efficient conditions for achieving the conjunctive cyclization of cyclobutanes with high yields and stereochemistry control remain elusive.

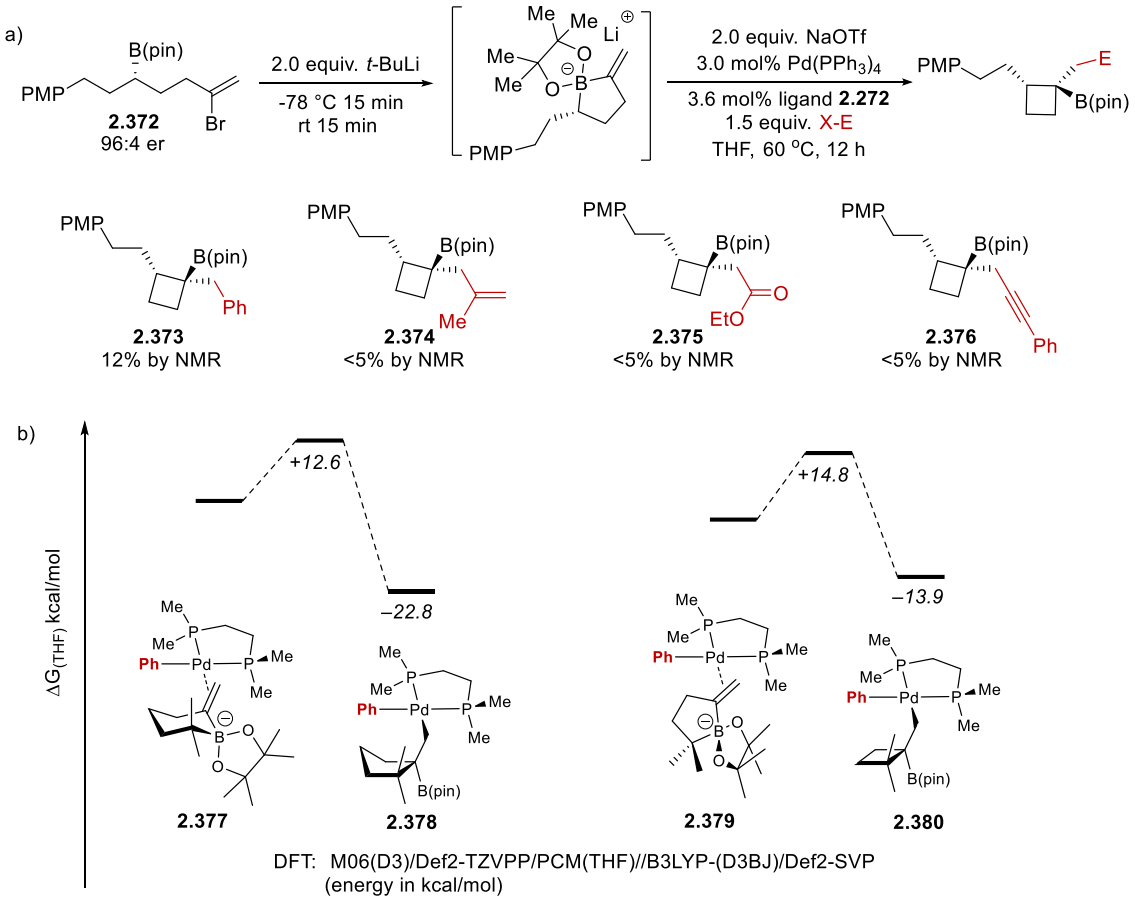



***Figure 2.49.*** Attempts on Cyclobutane synthesis

## 2.4 Supporting Information

### 2.4.1 General Information

$^{1}$H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). $^{13}$C NMR spectra were recorded on either a Varian Gemini-500 (126 MHz), Varian Gemini-600 (151 MHz) or a Varian Inova-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). $^{11}$B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer. $^{19}$F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers ($cm^{-1}$) as follows: strong (s), broad (br), medium (m), and weak (m). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel ($SiO_2$, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), or potassium permanganate stain ($KMnO_4$, sodium carbonate, and water), or para-anisaldehyde stain (ethanol, sulfuric acid, and *p*-anisaldehyde).

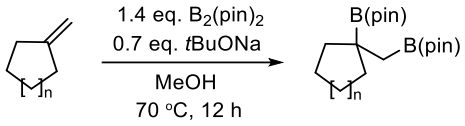
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector, with isopropanol or methanol as the modifier.

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

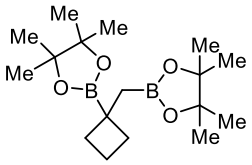
nitrogen. All reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without further purification.

### 2.4.2 Experimental Procedures

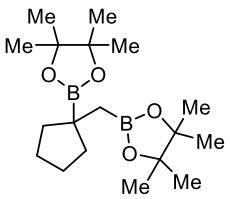
#### 2.4.2.1 General Procedure for Diboration of 1,1-Disubstituted Exocyclic Alkenes



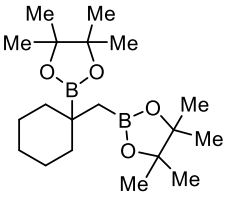

In an argon-filled glovebox, a 25 mL pressure vessel was equipped with a magnetic stir bar and charged with exocyclic alkene (1.0 equiv.), $B_2(pin)_2$ (1.4 equiv.), sodium *tert*-butoxide (0.7 equiv.) and anhydrous MeOH. The pressure vessel was sealed properly with Teflon cap and brought out of glovebox. Reaction was stilled at 70 °C for 12 hours. Upon completion, reaction mixture was concentrated under vacuum, re-dissolved in 15 mL of diethyl ether and filtered through a short silica gel plug. The crude material was concentrated under vacuum and analyzed by $^1$H NMR. Crude product was purified using silica gel chromatography.



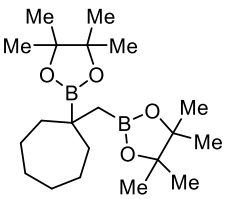
**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclobutyl)methyl)-1,3,2-dioxaborolane** (**S-1**) The title compound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclobutene (0.136 g, 2.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.711 g, 2.8 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.134 g, 1.4 mmol, 0.7 equiv.) in 5 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.40 g, 1.24 mmol, 62% yield) as a clear oil. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (500 MHz, $CDCl_3$) δ 2.22 – 2.14 (m, 2H), 1.92 – 1.85 (m, 2H), 1.72 – 1.62 (m, 2H), 1.26 (s, 12H), 1.20 (s, 12H), 1.10 (s, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 82.93, 82.85, 32.6, 25.0, 24.8, 18.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.85.; IR (neat) $\nu_{max}$ 2980 (m), 1380 (s), 1360 (m), 1305 (s), 1213 (m), 1147 (s) cm$^{-1}$.; HRMS (DART) for $C_{17}H_{33}B_2O_4$ $[M+H]^+$: Calc'd: 323.25595, found: 323.25729.



**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclopentyl)methyl)-1,3,2-dioxaborolane** (**S-2**) The title compound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclobutene (0.164 g, 2.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.711 g, 2.8 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.134 g, 1.4 mmol, 0.7 equiv.) in 5 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.5 g, 1.5 mmol, 75% yield) as a clear oil. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (500 MHz, $CDCl_3$) δ 1.85 – 1.76 (m, 2H), 1.67 – 1.49 (m, 2H), 1.31 – 1.24 (m, 4H), 1.23 (s, 12H), 1.21 (s, 12H), 0.89 (s, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 82.90, 82.87, 37.7, 25.3, 25.0, 24.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.01.; IR (neat) $\nu_{max}$ 2977 (m), 2945 (m), 1379 (m), 1370 (m), 1317 (m), 1142 (s), 847 (m) cm$^{-1}$.; HRMS (DART) for $C_{18}H_{35}B_2O_4$ $[M+H]^+$: Calc'd: 337.27160, found: 337.27288.

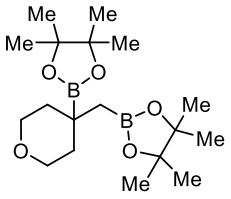


**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclohexyl)methyl)-1,3,2-dioxaborolane** (**S-3**) The title compound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclohexane (0.77 g, 8.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (2.84 g, 11.2 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.56 g, 5.6 mmol, 0.7 equiv.) in 10 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (1.9 g, 5.4 mmol, 67% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 1.85 (d, J = 12.7 Hz, 2H), 1.60 – 1.53 (m, 3H), 1.32 (ddt, J = 15.0, 11.8, 3.3 Hz, 2H), 1.23 (d, J = 18.0 Hz, 24H), 1.15 – 1.10 (m, 1H), 1.02 (td, J = 12.4, 3.3 Hz, 2H), 0.80 (s, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 82.73, 82.68, 37.2, 26.5, 25.0, 24.8, 24.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.44.; IR (neat): $\nu_{max}$ 2977 (m), 2922 (m), 2850 (m), 1449 (m), 1370 (m), 1140 (s), 1109 (s), 970 (s) cm$^{-1}$. HRMS (DART) for $C_{19}H_{37}B_2O_4$ $[M+H]^+$: Calc'd: 351.28725, found: 351.28850.

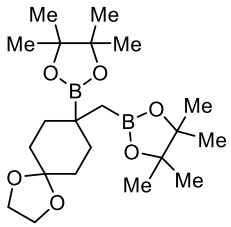


**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cycloheptyl)methyl)-1,3,2-dioxaborolane** (**S-4**) The title compound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclohexane (0.55 g, 5.0 mmol, 1.0 equiv.),

$B_2(pin)_2$ (1.78 g, 7.0 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.34 g, 3.5 mmol, 0.7 equiv.) in 8 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (1.1 g, 3.0 mmol, 60% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 1.86 – 1.78 (m, 2H), 1.56 – 1.39 (m, 8H), 1.33 – 1.27 (m, 2H), 1.23 (d, *J* = 14.9 Hz, 24H), 0.84 (s, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 82.65, 82.58, 38.3, 29.7, 24.8, 24.7, 24.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) 34.91.; IR (neat): $\nu_{max}$ 2976.34 (m), 2919.4 (m), 2853.40 w), 1460.14 (m), 1303.08 (s), 1257.48 (s), 1139.81 (m) cm$^{-1}$. HRMS (DART) for $C_{20}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 365.30290, found:365.30315.

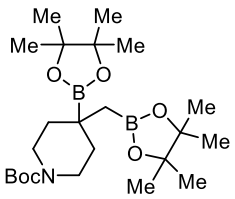


**4,4,5,5-tetramethyl-2-(4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) methyl)tetrahydro-2H-pyran-4-yl)-1,3,2-dioxaborolane** (**S-5**) The titled com-pound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclohexane (0.11 g, 1.1 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.39 g, 1.5 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.074 g, 0.77 mmol, 0.7 equiv.) in 2 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 10-20% ethyl acetate:hexanes to isolate the title compound (0.19 g, 0.53 mmol, 48% yield) as a white solid. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 3.82 (dt, *J* = 11.6, 3.3 Hz, 2H), 3.46 (td, *J* = 11.6, 1.8 Hz, 2H), 1.82 (d, *J* = 14.5 Hz, 2H), 1.35 (td, *J* = 12.3, 11.8, 4.0 Hz, 2H), 1.24 (d, *J* = 17.3 Hz, 24H), 0.85 (s, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 83.1, 82.9, 66.9, 37.0, 24.77, 24.75.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.86; IR (neat): $\nu_{max}$ 2976.7 (m), 2928.66 (m), 1441.97 (s), 1370.50 (m), 1212.55 (s), 1105.22 (s) cm$^{-1}$. HRMS (DART) for $C_{18}H_{35}B_2O_5$ $[M+H]^+$: Calc'd: 353.26651, found: 353.26801.



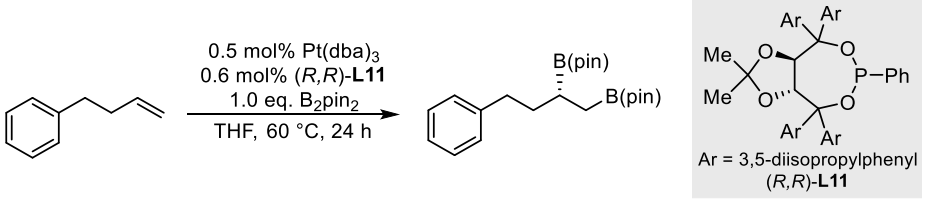
**4,4,5,5-tetramethyl-2-((8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-dioxaspiro[4.5]decan-8-yl)methyl)-1,3,2-dioxaborolane** (**S-6**) The title com-pound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclobutene (0.308 g, 2.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.711 g, 2.8 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.134 g, 1.4 mmol, 0.7 equiv.) in 5 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound

(0.6 g, 1.5 mmol, 74% yield) as a white solid. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 3.91 (s, 4H), 1.91 (d, *J* = 3.5 Hz, 2H), 1.69 – 1.59 (m, 4H), 1.39 – 1.30 (m, 2H), 1.25 (s, 12H), 1.22 (s, 12H), 0.84 (s, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 109.4, 83.1, 83.0, 34.3, 33.4, 25.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.92.; IR (neat) $\nu_{max}$ 2976 (m), 2929 (m), 1447 (m), 1354 (m), 1305 (m), 1274 (m), 1185 (s), 1164 (s), 1062 (m), 702 (m) cm$^{-1}$.; HRMS (DART) for $C_{21}H_{39}B_2O_6$ $[M+H]^+$: Calc'd: 409.29273, found: 409.29292.



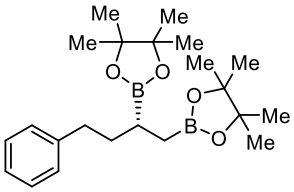

**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclopentyl)methyl)-1,3,2-dioxaborolane** (**S-7**) The title compound was prepared according to *General procedure for diboration of 1,1-disubstituted exocyclic alkenes* with methylenecyclobutene (0.394 g, 2.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.711 g, 2.8 mmol, 1.4 equiv.), sodium *tert*-butoxide (0.134 g, 1.4 mmol, 0.7 equiv.) in 5 mL MeOH. The resulting crude product was purified by silica gel column chromatography using 5 to 10% ethyl acetate:hexanes to isolate the title compound (0.65 g, 1.5 mmol, 72% yield) as a sticky oil. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 2H), 2.87 (s, 2H), 1.84 (d, *J* = 13.0 Hz, 2H), 1.44 (s, 9H), 1.24 (s, 12H), 1.22 (s, 12H), 1.19 – 1.04 (m, 2H), 0.83 (s, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 155.1, 83.2, 83.1, 78.9, 36.2, 28.6, 25.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.46.; IR (neat) $\nu_{max}$ 2976 (m), 1688 (m), 1420 (m), 1388 (m), 1363 (m), 1321 (m), 1227 (s), 1138 (s), 1061 (m), 862 (m) cm$^{-1}$.; HRMS (DART) for $C_{23}H_{44}B_2NO_6$ $[M+H]^+$: Calc'd: 452.33493, found: 452.33644.

### 2.4.2.2 Procedure for Enantioselective Terminal Alkene Diboration




In an argon-filled glovebox, a 25 mL pressure vessel was equipped with a magnetic stir bar and charged with $B_2(pin)_2$ (1.27 g, 5.0 mmol, 1.0 equiv.), $Pt(dba)_3$ (22.45 mg, 0.5 mol%) and (*R*,*R*)-**L11** (27.28 mg, 0.6 mol%) and 5.0 mL anhydrous THF. The pressure vessel was sealed properly with Teflon cap and brought out of glovebox. Reaction was stirred at 80 °C for 2 hours. Then, the reaction was cooled to 0 °C and 4-phenyl-1-butene (660.5 mg, 5.0 mmol, 1.0 equiv.) was added.

The reaction was stirred at 60 ℃ for 24 hours. Upon completion, reaction mixture was concentrated under vacuum, re-dissolved in 15 mL of diethyl ether and filtered through a short silica gel plug. The crude material was concentrated under vacuum and analyzed by $^{1}$H NMR. Crude product was purified using silica gel chromatography.

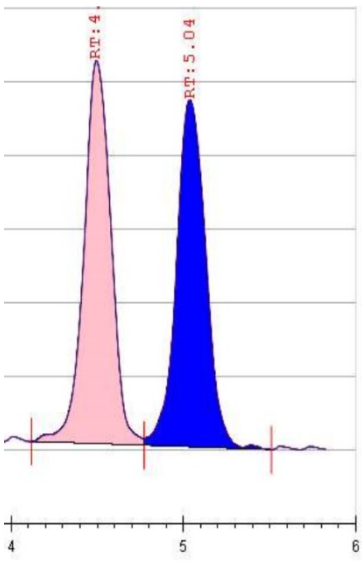


**(R)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)** (**S-8**) The title compound was prepared according to *Procedure for platinum catalyzed enantioselective terminal alkene diboration.* The resulting crude product was purified by silica gel column chromatography using 1 to 5% ethyl acetate:hexanes to isolate the title compound (1.70 g, 4.4 mmol, 88% yield) as a sticky oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). δ 7.28 – 7.24 (m, 2H), 7.21 – 7.12 (m, 3H), 2.62 (t, *J* = 8.3 Hz, 2H), 1.86 – 1.73 (m, 1H), 1.64 (ddd, *J* = 12.4, 7.3, 1.9 Hz, 1H), 1.25 (d, *J* = 8.8 Hz, 25H), 0.97 – 0.85 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 143.3, 128.4, 128.1, 125.4, 82.9, 35.9, 35.3, 24.91, 24.89, 24.79, 24.78.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.46.; IR (neat) $\nu_{max}$ 2977.34 (s), 2930.49 (s), 149.31(s), 1371.00 (s), 1315.40 (s), 1141.57 (s) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{36}B_2O_4$ $[M+H]^+$: Calc'd: 387.14664, found: 387.14678.

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to Fernandez's diboration protocol.

*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane).*




**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
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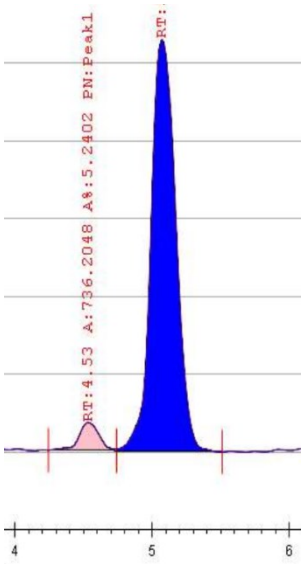
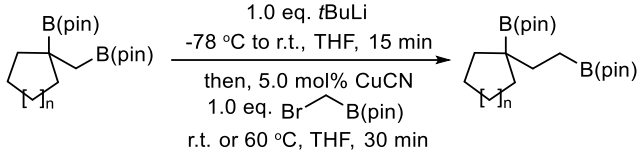
| 2 | 49.5044 | 2788.4225 | 5.04 |
| Total: | 100 | 5632.6762 | |



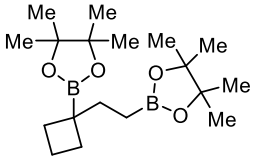

**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 5.2402 | 736.2048 | 4.53 |
| 2 | 94.7598 | 13313.077 | 5.07 |
| Total: | 100 | 14049.2818 | |

### 2.4.2.3 General Procedure for Diboron Site-Selective Homologation

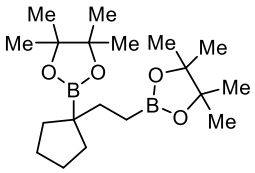



In an argon-filled glovebox, a 10 mL round bottom flask was equipped with a magnetic stir bar and charged with vicinal diboron (1.0 equiv.) and anhydrous THF. The round bottom flask was sealed properly with rubber septum and brought out of glovebox. Reaction was cooled to -78 °C using dry ice-acetone bath. *tert*-Butyllithium (1.0 equiv as a stock solution in pentane, concentration was determined from titration with BHT and 1,10-phenanthroline as indicator) was added dropwise via syringe. Upon completion, reaction was stirred at -78 °C for 15 min and then warmed to room temperature. The round bottom flask was brought back to glovebox where CuCN (around 5.0 mol%) and bromomethyl B(pin) (1.0 equiv.) was added to the reaction. The reaction was stirred at room temperature or 60 °C for 30 min. Reaction was then diluted with diethyl ether and filtered through a short silica gel plug. The crude material was concentrated under vacuum and side product *tert*-butylB(pin) was removed by this means as well. The crude product was either used for next step without purification, or purified using silica gel chromatography.

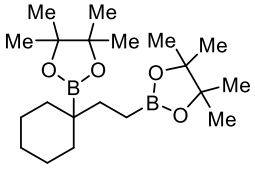


**4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)ethyl)-1,3,2-dioxaborolane** (**S-9**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)methyl)-1,3,2-dioxaborolane (**S-1)** (0.322 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.63 mL, 1.0 mmol, 1.0 equiv.), bromomethyl B(pin) (0.221 g, 1.0 mmol, 1.0 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The only side product *tert*-butylB(pin) was removed by vacuum. Pure product (0.337 g, 1.0 mmol, quantitative yield) as a clear oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 2.10 – 2.02 (m, 2H), 1.90 – 1.81 (m, 2H), 1.70 – 1.57 (m, 4H), 1.23 (s, 12H), 1.22 (s, 12H), 0.66 – 0.59 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 83.0, 82.9, 33.6, 29.7, 24.9, 24.8, 17.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.27.; IR (neat) $\nu_{max}$ 2976

(m), 1369 (s), 1302 (m), 1211 (s), 1141 (m), 966 (m), 847 (m) $cm^{-1}$.; HRMS (DART) for $C_{18}H_{35}B_2O_4$ $[M+H]^+$: Calc'd: 337.27160, found: 337.27178.

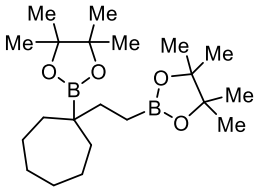


**4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)ethyl)-1,3,2-dioxaborolane** (**S-10**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (**S-2)** (0.336 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.63 mL, 1.0 mmol, 1.0 equiv.), bromomethyl B(pin) (0.221 g, 1.0 mmol, 1.0 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The only side product *tert*-butylB(pin) was removed by vacuum. Pure product (0.350 g, 1.0 mmol, quantitative yield) as a clear oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.79 – 1.73 (m, 2H), 1.62 – 1.41 (m, 6H), 1.29 – 1.23 (m, 2H), 1.22 (s, 12H), 1.21 (s, 12H), 0.77 – 0.68 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 82.91, 82.89, 35.0, 32.5, 25.5, 24.94, 24.85.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.52.; IR (neat) $\nu_{max}$ 2944 (m), 2866 (m), 1629 (m), 1408 (m), 1371 (m), 1165 (s), 857 (m) $cm^{-1}$.; HRMS (DART) for $C_{19}H_{37}B_2O_4$ $[M+H]^+$: Calc'd: 351.28725, found: 351.28855.

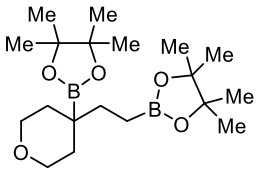


**4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxaborolane** (**S-11**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclohexyl)methyl)-1,3,2-dioxaborolane (**S-3)** (1.63 g, 4.7 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 2.9 mL, 4.7 mmol, 1.0 equiv.), bromomethyl B(pin) (1.03 g, 4.7 mmol, 1.0 equiv.), CuCN (0.0209 g, 0.23 mmol, 5.0 mol%) in 10 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (1.56 g, 4.3 mmol, 91% yield) as a clear oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 1.86 (d, $J$ = 12.7 Hz, 2H), 1.67 – 1.54 (m, 4H), 1.39 – 1.34 (m, 2H), 1.23 (d, $J$ = 6.4 Hz, 25H), 1.09 (ddd, $J$ = 16.1, 8.0, 3.8 Hz, 1H), 0.87 (td, $J$ = 12.7, 3.3 Hz, 2H), 0.74 – 0.68 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 82.8, 82.7, 34.9, 34.5, 26.7, 25.3, 24.8, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) 34.78; IR (neat): $\nu_{max}$ 2977.29 (s), 2923.80 (m), 2850.15 (m), 1452.40 (s), 1387.80 (s),

1232.45 (s), 1107.70 (s) $cm^{-1}$. HRMS (DART) for $C_{20}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 365.30290, found: 365.30333.

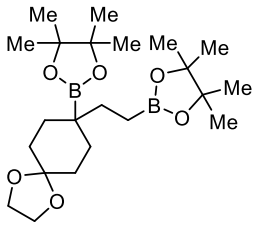


**4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cycloheptyl)ethyl)-1,3,2-dioxaborolane** (**S-12**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cycloheptyl)methyl)-1,3,2-dioxaborolane (**S-4)** (0.073 g, 0.20 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.125 mL, 0.20 mmol, 1.0 equiv.), bromomethyl B(pin) (0.044 g, 0.20 mmol, 1.0 equiv.), CuCN (0.0090 g, 0.01 mmol, 5.0 mol%) in 1.2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.072 g, 0.19 mmol, 95% yield) as a clear oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 1.79 (dd, $J$ = 13.4, 7.5 Hz, 2H), 1.58 – 1.36 (m, 11H), 1.22 (d, $J$ = 1.1 Hz, 25H), 0.73 – 0.66 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 82.6, 35.7, 33.7, 29.8, 24.73, 24.68, 24.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.27; IR (neat): $\nu_{max}$ 2976.22 (m), 2924.65 (m), 2853.57 (s), 1379.06 (s), 1447.69 (m), 1222.43 (s), 1143.18 (s), 1056.33 (s) $cm^{-1}$. HRMS (DART) for $C_{21}H_{41}B_2O_4$ $[M+H]^+$: Calc'd: 379.31855, found: 379.31879.

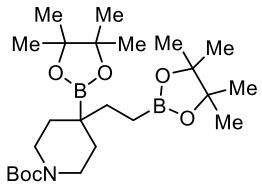


**4,4,5,5-tetramethyl-2-(4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)tetrahydro-2H-pyran-4-yl)-1,3,2-dioxaborolane** (**S-13**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-(4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)tetrahydro-2H-pyran-4-yl)-1,3,2-dioxaborolane (**S-5)** (0.070 g, 0.20 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.125 mL, 0.20 mmol, 1.0 equiv.), bromomethyl B(pin) (0.044 g, 0.20 mmol, 1.0 equiv.), CuCN (0.0090 g, 0.01 mmol, 5.0 mol%) in 1.2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.070 g, 0.19 mmol, 95% yield) as a white solid. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 3.87 – 3.82 (m, 2H), 3.36 (td, $J$ = 12.1, 1.6 Hz, 2H), 1.80 – 1.74 (m, 2H), 1.42 – 1.37 (m, 2H), 1.21 (d, $J$ = 9.8 Hz, 26H), 0.73 – 0.66 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 83.1, 82.7, 67.3, 34.8, 34.2, 24.8, 24.6.; $^{11}$B NMR (160 MHz,

$CDCl_3$) 35.04; IR (neat): $\nu_{max}$ 2976.73 (m), 2926.53 (m), 2838.42 (m), 1450.26 (m), 1369.05 (s), 1196.37 (s), 1140.23 (s), 855.51 (s) $cm^{-1}$. HRMS (DART) for $C_{19}H_{37}B_2O_5$ $[M+H]^+$: Calc'd: 367.28216, found: 367.28305.

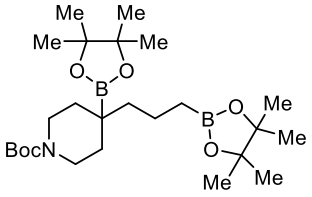


**4,4,5,5-tetramethyl-2-(2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-dioxaspiro[4.5]decan-8-yl)ethyl)-1,3,2-dioxaborolane** (**S-14**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with 4,4,5,5-tetramethyl-2-((8-(4,4,5,5-tetra methyl-1,3,2-dioxaborolan-2-yl)-1,4-dioxaspiro[4.5]decan-8-yl)methyl)-1,3,2-dioxaborolane (**S-6)** (0.408 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.63 mL, 1.0 mmol, 1.0 equiv.), bromomethyl B(pin) (0.221 g, 1.0 mmol, 1.0 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The only side product *tert*-butylB(pin) was removed by vacuum. Pure product (0.423 g, 1.0 mmol, quantitative yield) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 4H), 1.93 – 1.83 (m, 2H), 1.74 – 1.64 (m, 2H), 1.62 – 1.50 (m, 4H), 1.46 – 1.38 (m, 2H), 1.24 (s, 12H), 1.23 (s, 12H), 0.78 – 0.67 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 109.6, 83.2, 82.9, 64.22, 64.19, 33.8, 31.9, 25.0, 24.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.93.; IR (neat) $\nu_{max}$ 2976 (m), 2930 (m), 1370 (s), 1303 (m), 1275 (m), 1214 (m), 1165 (s), 1141 (m), 1035 (m), 864 (m) $cm^{-1}$.; HRMS (DART) for $C_{22}H_{41}B_2O_6$ $[M+H]^+$: Calc'd: 423.30838, found: 423.30998.

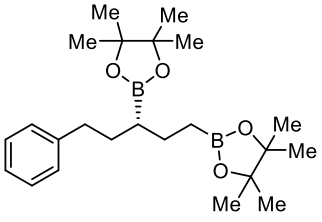


**tert-butyl4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate** (**S-15**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* (copper catalyzed homologation was performed at 60 °C due to low solubility of boronate complex in THF) with 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (**S-7**) (0.451 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.63 mL, 1.0 mmol, 1.0 equiv.), bromomethyl B(pin) (0.221 g, 1.0 mmol, 1.0 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The only side product *tert*-butylB(pin) was removed by vacuum. Pure product (0.464 g, 1.0 mmol, quantitative yield) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 2H), 2.74 (s, 2H), 1.83 (d, $J$ = 13.0 Hz, 2H), 1.44 (s, 9H), 1.42 – 1.32 (m, 2H), 1.23 (s, 12H), 1.23 (s, 12H), 1.12 – 1.02 (m, 2H), 0.76 – 0.65 (m, 2H).; $^{13}$C NMR

(151 MHz, $CDCl_3$) δ 155.2, 83.4, 83.0, 79.1, 34.0, 28.6, 25.1, 24.9.; $^{11}B$ NMR (160 MHz, $CDCl_3$) δ 33.05.; IR (neat) $\nu_{max}$ 2979 (m), 1686 (m), 1422 (m), 1366 (s), 1308 (m), 1264 (m), 1166 (m), 1077 (m), 737 (s) $cm^{-1}$.; HRMS (DART) for $C_{24}H_{46}B_2NO_6$ $[M+H]^+$: Calc'd: 466.35058, found: 466.35299.



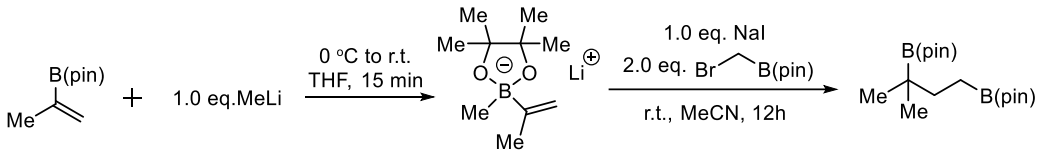
**tert-butyl4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)piperidine-1-carboxylate** (**S-16**) The title compound was prepared according to *General procedure for diboron site-selective homologation* (copper catalyzed homologation was performed at 60 °C due to low solubility of boronate complex in THF) with tert-butyl4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate (**S-15**) (0.093 g, 0.20 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.125 mL, 0.20 mmol, 1.0 equiv.), bromomethyl B(pin) (0.044 g, 0.20 mmol, 1.0 equiv.), CuCN (0.0090 g, 0.01 mmol, 5.0 mol%) in 1.2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.088 g, 0.18 mmol, 92% yield) as a clear oil. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1H$ NMR (600 MHz, $CDCl_3$) δ 3.93 (s, 2H), 2.71 (t, $J$ = 11.0 Hz, 2H), 1.80 (d, $J$ = 12.7 Hz, 2H), 1.42 (d, $J$ = 1.1 Hz, 9H), 1.38 – 1.31 (m, 2H), 1.23 – 1.18 (m, 26H), 1.06 (t, $J$ = 12.5 Hz, 2H), 0.70 (t, $J$ = 7.1 Hz, 2H).; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 154.9, 83.1, 82.7, 78.8, 43.0, 34.2, 28.3, 26.8, 24.8, 24.7, 24.5, 19.8.; $^{11}B$ NMR (160 MHz, $CDCl_3$) 32.44; IR (neat): $\nu_{max}$ 2976.40 (m), 2930.42 (m), 1892.11 (s), 1420.24 (m), 1368.46 (m), 1307.96 (s), 1142.24 (s), 967.15 (s) $cm^{-1}$. HRMS (DART) for $C_{25}H_{48}B_2NO_6$ $[M+H]^+$: Calc'd: 480.36623, found: 480.36722.



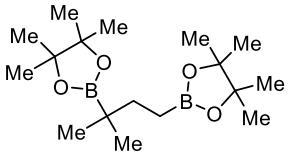
**(R)-2,2'-(5-phenylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)** (**S-17**) The titled compound was prepared according to *General procedure for diboron site-selective homologation* with (R)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-diox aboro lane) (**S-8**) (0.774 g, 2.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 1.26 mL, 2.0 mmol, 1.0 equiv.), bromomethyl B(pin) (0.442 g, 2.0 mmol, 1.0 equiv.), CuCN (0.0090 g, 0.010 mmol, 5.0 mol%) in 4 mL THF. The only side product *tert*-butylB(pin) was removed by vacuum. Pure product (0.801 g, 2.0 mmol, quantitative yield) as a clear oil. δ 7.28 – 7.23 (m, 2H),

7.20 – 7.12 (m, 3H), 2.60 (dtd, *J* = 14.1, 7.0, 6.4, 3.3 Hz, 2H), 1.84 – 1.48 (m, 4H), 1.25 (d, *J* = 14.2 Hz, 24H), 1.03 (ddd, *J* = 8.7, 6.1, 2.5 Hz, 1H), 0.86 – 0.73 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 143.2, 128.43, 128.40, 128.36, 128.2, 125.45, 125.40, 82.87, 82.82, 82.80, 35.5, 33.2, 25.2, 24.91, 24.88, 24.84, 24.80, 24.78.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.27.; IR (neat) 2977.58 (m), 2927.01 (m), 1454.86 (m), 1370.82 (m), 1315.16 (s), 1143.68 (s) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 401.17354, found: 401.172989.

#### 2.4.2.4 General Procedure for Electrophile Induced 1,2-Migration



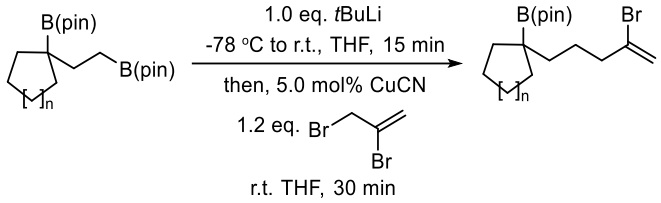

The iodo methyl B(pin) induced 1,2-migration of boronate complex was reported by the Studer group.[2] In an argon-filled glovebox, a 25 mL round bottom flask was equipped with a magnetic stir bar and charged with isopropenyl B(pin) (1.0 equiv.) and anhydrous THF. The round bottom flask was sealed properly with rubber septum and brought out of glovebox. Reaction was cooled to 0 °C using dry ice-acetone bath. Methyllithium-THF solution (1.0 equiv.) was added dropwise via syringe. Upon completion, reaction was stirred at 0 °C for 15 min and then warmed to room temperature. Solvent was evacuated under vaccum. The round bottom flask was brought back to glovebox and added MeCN, NaI (1.5 equiv.) and bromomethyl B(pin) (1.5 equiv.) and stirred at room temperature for 12 h. Reaction was then diluted with diethyl ether and filtered through a short silica gel plug. The crude material was concentrated under vacuum and analyzed by $^1$H NMR. Crude product was purified using silica gel chromatography.



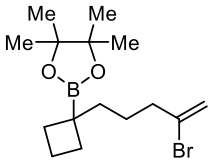
**2,2'-(3-methylbutane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxa borolane)** (**S-18**) The title compound was prepared according to *General procedure for electrophile induced 1,2-migration* with isopropenyl B(pin) (0.84 g, 5 mmol, 1.0 equiv.), methyllithium-THF solution (1.6 M, 3.1 mL, 5 mmol, 1.0 equiv.), bromomethyl B(pin) (2.21 g, 10.0 mmol, 2.0 equiv.), NaI (0.83 g, 5 mmol, 1.0equiv.) in 10 mL MeCN. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (1.02 g, 3.12 mmol, 62% yield) as a clear oil.

Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 1.40 – 1.36 (m, 2H), 1.22 (d, *J* = 11.1 Hz, 24H), 0.90 (s, 6H), 0.74 – 0.69 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 82.69, 82.67, 34.5, 24.7, 24.6, 24.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.43; IR (neat): $\nu_{max}$ 2976.61 (m), 2876.80 (m),1473.60 (m), 1370.06 (s), 1143.01 (s) $cm^{-1}$. HRMS (DART) for $C_{17}H_{35}B_2O_4$ $[M+H]^+$: Calc'd: 325.27160, found: 325.27158.

### 2.4.2.5 General Procedure for Diboron Site-Selective Allylation

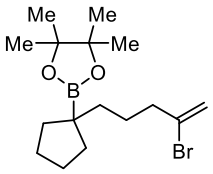



In an argon-filled glovebox, a 25 mL round bottom flask was equipped with a magnetic stir bar and charged with 1,3-diboron (1.0 equiv.) and anhydrous THF. The round bottom flask was sealed properly with rubber septum and brought out of glovebox. Reaction was cooled to -78 °C using dry ice-acetone bath. *tert*-Butyllithium-pentane solution (concentration determined from titration with BHT and 1,10-phenanthroline as indicator, 1.0 equiv.) was added dropwise via syringe. Upon completion, reaction was stirred at -78 °C for 15 min and then warmed to room temperature. The round bottom flask was brought back to glovebox where CuCN (around 5.0 mol%) and 2,3-dibromopropene (1.0 equiv.) was added and the reaction was stirred at room temperature for 30 min. Reaction was then diluted with diethyl ether and filtered through a short silica gel plug. The crude material was concentrated under vacuum and analyzed by $^{1}$H NMR. Crude product was purified using silica gel chromatography.

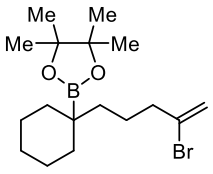



**2-(1-(4-bromopent-4-en-1-yl)cyclobutyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-19**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)ethyl)-1,3,2-dioxabor olane (**S-9**) (0.336 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.625 mL, 1.0 mmol, 1.0 equiv.), 2,3-dibromopropene (0.24 g, 1.2 mmol, 1.2 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column

chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.285 g, 0.87 mmol, 87% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.55 (d, *J* = 1.4 Hz, 1H), 5.37 (d, *J* = 1.5 Hz, 1H), 2.39 (t, *J* = 7.2 Hz, 2H), 2.16 – 2.08 (m, 2H), 1.97 – 1.83 (m, 2H), 1.72 – 1.64 (m, 2H), 1.57 – 1.52 (m, 2H), 1.47 – 1.40 (m, 2H), 1.26 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 135.1, 116.3, 83.2, 42.0, 38.8, 30.4, 25.3, 24.9, 18.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.86.; IR (neat) $\nu_{max}$ 2975 (m), 2932 (m), 1629 (m), 1386 (m), 1343 (m), 1164 (s), 1142 (m), 883 (m) cm$^{-1}$.; HRMS (DART) for $C_{15}H_{27}BO_2Br$ $[M+H]^+$: Calc'd: 329.12820, found: 329.12975.

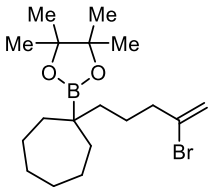



**2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-20**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)ethyl)-1,3,2-dioxabo rolane (**S-10**) (0.350 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.625 mL, 1.0 mmol, 1.0 equiv.), 2,3-dibromopropene (0.24 g, 1.2 mmol, 1.2 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.270 g, 0.79 mmol, 79% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.55 (d, *J* = 1.5 Hz, 1H), 5.37 (d, *J* = 1.5 Hz, 1H), 2.40 (t, *J* = 6.9 Hz, 2H), 1.85 – 1.78 (m, 2H), 1.66 – 1.48 (m, 6H), 1.40 – 1.33 (m, 2H), 1.30 – 1.25 (m, 2H), 1.24 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 135.1, 116.3, 83.1, 42.4, 37.8, 35.5, 26.5, 25.4, 24.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 35.00.; IR (neat) $\nu_{max}$ 2976 (m), 2942 (m), 1629 (m), 1408 (m), 1370 (m), 1213 (s), 1111 (m), 579 (m) cm$^{-1}$.; HRMS (DART) for $C_{16}H_{29}BO_2Br$ $[M+H]^+$: Calc'd: 343.14385, found: 343.14366.

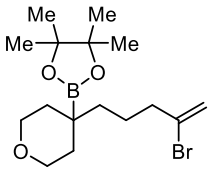



**2-(1-(4-bromopent-4-en-1-yl)cyclohexyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-21**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethyl)-1,3,2-dioxabo rolane (**S-11**) (0.57 g, 1.6 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 1.0 mL, 1.6 mmol, 1.0 equiv.), 2,3-dibromopropene (0.375 g, 1.9 mmol, 1.2 equiv.), CuCN (0.0073 g, 0.23 mmol, 5.0 mol%) in 10 mL THF. The resulting crude product was purified by silica gel column

chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.43 g, 1.2 mmol, 77% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.53 (s, 1H), 5.35 (s, 1H), 2.36 (t, *J* = 7.3 Hz, 2H), 1.87 (d, *J* = 12.7 Hz, 2H), 1.61 (t, *J* = 14.4 Hz, 3H), 1.52 (dd, *J* = 16.4, 8.1 Hz, 2H), 1.25 (s, 16H), 1.14 (d, *J* = 7.8 Hz, 1H), 0.90 (t, *J* = 12.1 Hz, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 134.8, 116.2, 82.9, 42.3, 39.7, 35.3, 26.6, 25.2, 24.9, 24.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) 32.11; IR (neat): $\nu_{max}$ 2977.01 (m), 2925.00 (m), 2851.24 (m), 1776.04 (s), 1729.85 (m), 1629.30 (s), 1388.50 (m), 1141.52 (s), 1037.60 (s) $cm^{-1}$. HRMS (DART) for $C_{17}H_{31}BBrO_2$ $[M+H]^+$: Calc'd: 357.15950, found: 357.16023.

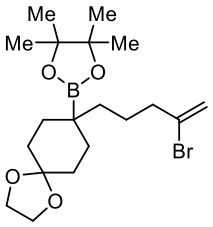



**2-(1-(4-bromopent-4-en-1-yl)cycloheptyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-22**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cycloheptyl)ethyl)-1,3,2-dioxabo rolane (**S-12**) (0.19 g, 0.50 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.33 mL, 0.50 mmol, 1.0 equiv.), 2,3-dibromopropene (0.12 g, 0.60 mmol, 1.2 equiv.), CuCN (0.0023 g, 0.025 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.16 g, 0.43 mmol, 86% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.53 (s, 1H), 5.36 (s, 1H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.84 – 1.79 (m, 2H), 1.48 (ddt, *J* = 23.6, 16.6, 9.5 Hz, 10H), 1.24 (s, 16H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 134.8, 116.1, 82.8, 42.3, 39.0, 38.3, 36.1, 29.6, 24.7, 24.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) 33.23; IR (neat): $\nu_{max}$ 2976.58 (m), 2921.91 (m), 2852.43 (m), 1626.77 (s), 1460.15 (m), 1387.60 (m), 1305.11 (s), 1143.40 (s). HRMS (DART) for $C_{18}H_{33}BBrO_2$ $[M+H]^+$: Calc'd: 371.17515, found: 371.17498.

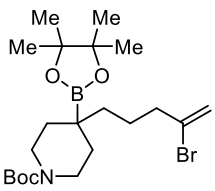



**2-(4-(4-bromopent-4-en-1-yl)tetrahydro-2H-pyran-4-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane** (**S-23**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)tetrahy dro-2H-pyran-4-yl)-1,3,2-dioxaborolane (**S-13**) (0.35 g, 0.95 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.59 mL, 0.95 mmol, 1.0 equiv.), 2,3-dibromopropene (0.23 g, 1.14 mmol, 1.2 equiv.), CuCN (0.0043 g, 0.047 mmol, 5.0 mol%) in 3 mL THF. The

resulting crude product was purified by silica gel column chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.22 g, 0.62 mmol, 65% yield) as a clear oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.54 (s, 1H), 5.37 (s, 1H), 3.87 (d, *J* = 13.5 Hz, 2H), 3.40 (t, *J* = 11.5 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.80 (d, *J* = 13.2 Hz, 2H), 1.57 – 1.46 (m, 2H), 1.26 (s, 16H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 134.4, 116.4, 83.3, 67.2, 42.0, 39.5, 35.2, 24.8, 23.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) 32.46; IR (neat): $\nu_{max}$ 2976.15 (m), 2929.17 (m), 2837.98 (m), 1629.14 (s), 1445.54 (s), 1378.45 (s), 1307.29 (s), 1140.03 (m), $cm^{-1}$. HRMS (DART) for $C_{16}H_{29}BBrO_3$ $[M+H]^+$: Calc'd: 359.13876, found: 359.13989.

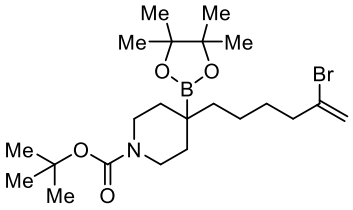



**2-(8-(4-bromopent-4-en-1-yl)-1,4-dioxaspiro[4.5]decan-8-yl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane** (**S-24**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 4,4,5,5-tetramethyl-2-(2-(8-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-dioxaspiro[4.5]decan-8-yl)ethyl)-1,3,2-dioxaborolane (**S-14**) (0.422 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.625 mL, 1.0 mmol, 1.0 equiv.), 2,3-dibromopropene (0.24 g, 1.2 mmol, 1.2 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.207 g, 0.50 mmol, 50% yield) as a clear oil. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.53 (d, *J* = 1.5 Hz, 1H), 5.36 (d, *J* = 1.5 Hz, 1H), 3.92 (s, 4H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.93 – 1.46 (m, 10H), 1.32 – 1.26 (m, 2H), 1.25 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 134.8, 116.5, 109.5, 83.5, 64.31, 64.28, 42.4, 33.8, 32.3, 25.1, 24.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.73.; IR (neat) $\nu_{max}$ 2976 (m), 2933 (m), 1448 (m), 1379 (m), 1371 (m), 1349 (m), 1229 (s), 1164 (s), 1036 (m), 884 (m) $cm^{-1}$.; HRMS (DART) for $C_{19}H_{33}BO_4Br$ $[M+H]^+$: Calc'd: 415.16498, found: 415.16541.

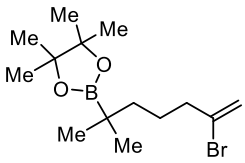



**tert-butyl 4-(4-bromopent-4-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxabo rolan-2-yl)piperidine-1-carboxylate** (**S-25**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with tert-butyl4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(2-(4,4,5,5-tetramethyl -1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate (**S-15**) (0.465 g, 1.0 mmol,

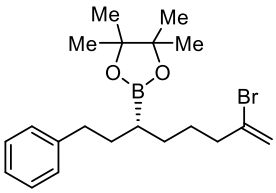
1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.625 mL, 1.0 mmol, 1.0 equiv.), 2,3-dibromopropene (0.24 g, 1.2 mmol, 1.2 equiv.), CuCN (0.0045 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.361 g, 0.79 mmol, 79% yield) as a clear oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.52 (d, *J* = 1.4 Hz, 1H), 5.35 (d, *J* = 1.6 Hz, 1H), 3.96 (s, 2H), 2.74 (s, 2H), 2.36 (t, *J* = 7.2 Hz, 2H), 1.89 – 1.80 (m, 2H), 1.57 – 1.46 (m, 2H), 1.43 (s, 9H), 1.31 – 1.24 (m, 2H), 1.24 (s, 12H), 1.12 – 1.02 (m, 2H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 155.1, 134.6, 116.7, 83.6, 79.2, 42.2, 39.2, 28.6, 25.1, 24.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.50.; IR (neat) $\nu_{max}$ 2976 (m), 1687 (s), 1448 (m), 1389 (m), 1308 (m), 1308 (m), 1276 (m), 1108 (s), 767 (m), 669 (m) cm$^{-1}$.; HRMS (DART) for $C_{21}H_{38}BNO_4Br$ $[M+H]^+$: Calc'd: 458.20718, found: 458.20649.




**tert-butyl 4-(5-bromohex-5-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2 -dioxaborolan-2-yl)piperidine-1-carboxylate** (**S-26**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with tert-butyl4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)piperidine-1-carboxylate (**S-16**) (0.15 g, 0.30 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.19 mL, 0.30 mmol, 1.0 equiv.), 2,3-dibromopropene (0.073 g, 0.36 mmol, 1.2 equiv.), CuCN (0.0014 g, 0.015 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.12 g, 0.25 mmol, 81% yield) as a clear oil. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.52 (s, 1H), 5.35 (s, 1H), 3.93 (s, 2H), 2.73 (s, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 1.81 (d, *J* = 12.9 Hz, 2H), 1.49 (p, *J* = 7.1 Hz, 2H), 1.43 (s, 9H), 1.23 (d, *J* = 6.3 Hz, 16H), 1.06 (t, *J* = 12.7 Hz, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.8, 134.5, 116.3, 83.2, 78.9, 41.0, 39.9, 34.2, 28.4, 28.3, 24.8, 24.8, 24.5, 24.4, 24.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.23; IR (neat): $\nu_{max}$ 2970.40 (m), 2930.42 (m), 1692.11 (s), 1420.24 (m), 1388.46 (s), 1227.83 (m), 1142.24 (m) cm$^{-1}$. HRMS (DART) for $C_{22}H_{40}BBrNO_4$ $[M+H]^+$: Calc'd: 472.22283, found: 472.22387.

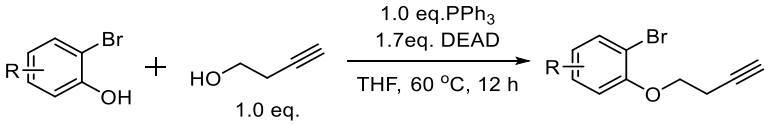


**2-(6-bromo-2-methylhept-6-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-27**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with 2,2'-(3-methylbutane-1,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxa borolane) (**S-18**) (0.20 g, 0.62 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.40 mL, 0.62 mmol, 1.0 equiv.), 2,3-dibromopropene (0.15 g, 0.74 mmol, 1.2 equiv.), CuCN (0.0029 g, 0.031 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 5% ethyl acetate:hexanes to isolate the title compound (0.17 g, 0.53 mmol, 85% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 5.55 (s, 1H), 5.36 (s, 1H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.56 – 1.47 (m, 2H), 1.23 (s, 14H), 0.93 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 134.9, 116.0, 82.9, 42.1, 39.8, 26.8, 24.8, 24.7, 24.6, 24.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.65; IR (neat): $\nu_{max}$ 2977.06 (m), 2937.33 (m), 2861.66 (m), 1629.36 (s), 1474.26 (m), 1369.64 (m), 1306.24 (m), 1138.02 $cm^{-1}$. HRMS (DART) for $C_{14}H_{27}BBrO_2$ $[M+H]^+$: Calc'd: 317.12820, found: 317.12817.

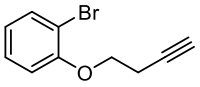


**4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) cyclopentyl)methyl)-1,3,2-dioxaborolane** (**49**) The title compound was prepared according to *General procedure for diboron site-selective allylation* with (R)-2,2'-(5-phenylpentane-1,3-diyl)bis(4,4,5,5-tetramethyl -1,3,2-dioxaborolane) (**S-17**) (0.40 g, 1.0 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.63 mL, 1.0 mmol, 1.0 equiv.), 2,3-dibromopropene (0.24 g, 1.2 mmol, 1.2 equiv.), CuCN (0.0032 g, 0.005 mmol, 5.0 mol%) in 2 mL THF. The resulting crude product was purified by silica gel column chromatography using 2% ethyl acetate:hexanes to isolate the title compound (0.605 g, 1.53 mmol, 77% yield) as a clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). δ 7.32 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 5.55 (d, *J* = 1.4 Hz, 1H), 5.38 (d, *J* = 1.6 Hz, 1H), 2.63 (tdt, *J* = 13.6, 10.2, 7.0 Hz, 2H), 2.51 – 2.41 (m, 2H), 1.83 – 1.64 (m, 4H), 1.35 – 1.17 (m, 14H), 1.14 – 1.06 (m, 1H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.8, 134.9, 128.4, 128.3, 125.6, 116.3, 83.1, 40.9, 35.4, 33.2, 29.5, 24.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) 35.65; IR (neat): $\nu_{max}$ 2988.17 (m), 2934.88 (m), 1611.42 (m), 1305.58 (s), 1106.12 (m), 1111.27 (m), $cm^{-1}$. HRMS (DART) for $C_{20}H_{31}BBrO_2$ $[M+H]^+$: Calc'd: 394.172395, found: 394.172401.

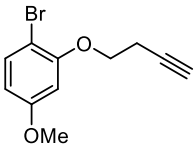
### 2.4.2.6 General Procedure for Preparing Butynyl Aryl Ether



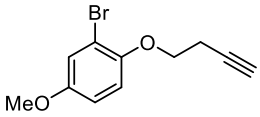

A 100 mL round bottom flask was equipped with a magnetic stir bar and charged with 2-bromohydroxyl arenes (1.0 equiv.), 3-butynyl-1-ol (1.0 equiv.), triphenylphosphine (1.0 equiv.) and anhydrous THF. The round bottom flask was sealed properly with rubber septum cooled to 0 °C using ice water bath. Diethyl azodicarboxylate (DEAD) (1.7 equiv.) was added dropwise via syringe. Upon completion, reaction was stirred at 0 °C for 15 min and then warmed to room temperature. Reaction was then stirred at room temperature for 12 h. Upon completion, reaction was then diluted with diethyl ether. Triphenylphosphine oxide was precipitated out and filtered off through a short silica gel plug. To remove the leftover bromophenol, the crude material was washed twice with 6M NaOH water solution and dried over sodium sulfate. The crude product was concentrated under vacuum and analyzed by $^{1}$H NMR. Crude product was then purified using silica gel chromatography.



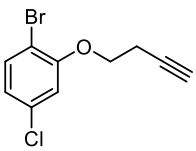

**1-bromo-2-(but-3-yn-1-yloxy)benzene** (**S-29**) The title compound was prepared according to *General procedure for preparing butynyl aryl ether using Mitsunobu reaction* with 2-bromophenol (8.65 g, 50.0 mmol, 1.0 equiv.), 3-butynyl-1-ol (3.50 g, 50.0 mmol, 1.0 equiv.), triphenylphosphine (11.1 g, 50.0 mmol, 1.0 equiv.), diethyl azodicarboxylate (DEAD) (14.8 g, 85.0 mmol, 1.7 equiv.) in 20 mL THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (4.71 g, 20.8 mmol, 41% yield) as a clear oil. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with potassium permanganese stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.9 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 1H), 4.14 (t, *J* = 7.2 Hz, 2H), 2.73 (t, *J* = 7.2 Hz, 2H), 2.05 (t, *J* = 2.7 Hz, 1H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.7, 133.4, 128.4, 122.3, 113.7, 112.4, 79.9, 70.1, 67.2, 19.4.; IR (neat): $\nu_{max}$ 3294.63 (m), 2949.16 (m), 1587.07 (m), 1477.26 (s), 1276.77 (m), 1244.45 (s), 1052.25 (s), 1029.45 (s) $cm^{-1}$. HRMS (DART) for $C_{10}H_9BrO$ $[M+H]^+$: Calc'd: 225.08546, found: 225.08499.




**1-bromo-2-(but-3-yn-1-yloxy)-4-methoxybenzene** (**S-30**) The title compound was prepared according to *General procedure for preparing butynyl aryl ether using Mitsunobu reaction* with 2-bromo-5-methoxyphenol (1.01 g, 5.0 mmol, 1.0 equiv.), 3-butynyl-1-ol (0.35 g, 5.0 mmol, 1.0 equiv.), triphenylphosphine (1.11 g, 5.0 mmol, 1.0 equiv.), diethyl azodicarboxylate (DEAD) (1.48 g, 8.50 mmol, 1.7 equiv.) in 8 mL THF. SThe resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.711 g, 2.80 mmol, 56% yield) as a white solid. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with potassium permanganese stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.7 Hz, 1H), 6.49 (d, *J* = 2.7 Hz, 1H), 6.42 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.12 (t, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 2.74 (td, *J* = 7.2, 2.7 Hz, 2H), 2.05 (t, *J* = 2.7 Hz, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 160.3, 155.7, 133.5, 107.0, 103.4, 101.7, 80.2, 70.4, 67.4, 55.8, 19.6.; IR (neat) $\nu_{max}$ 3292 (m), 1581 (s), 1487 (s), 1305 (s), 1281 (s), 1167 (s), 633 (m) cm$^{-1}$.; HRMS (DART) for $C_{11}H_{12}O_2Br$ $[M+H]^+$: Calc'd: 255.00152, found: 255.00295.

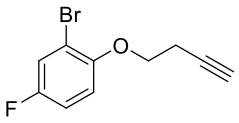



**2-bromo-1-(but-3-yn-1-yloxy)-4-methoxybenzene** (**S-31**) The title compound was prepared according to *General procedure for preparing butynyl aryl ether using Mitsunobu reaction* with 2-bromo-4-metho xyphenol (1.01 g, 5.0 mmol, 1.0 equiv.), 3-butynyl-1-ol (0.35 g, 5.0 mmol, 1.0 equiv.), triphenylphosphine (1.11 g, 5.0 mmol, 1.0 equiv.), diethyl azodicarboxylate (DEAD) (1.48 g, 8.50 mmol, 1.7 equiv.) in 8 mL THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.635 g, 2.5 mmol, 50% yield) as a white solid. Product Rf = 0.4 in 10% ethyl acetate:hexanes (stains with potassium permanganese stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 2.9 Hz, 1H), 6.89 (d, *J* = 8.9 Hz, 1H), 6.80 (dd, *J* = 8.9, 3.0 Hz, 1H), 4.10 (t, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 2.71 (td, *J* = 7.2, 2.7 Hz, 2H), 2.05 (t, *J* = 2.7 Hz, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 154.8, 149.3, 118.9, 116.1, 114.0, 113.5, 80.3, 70.2, 68.7, 56.0, 19.7.; IR (neat) $\nu_{max}$ 3294 (m), 1494 (s), 1470 (m), 1274 (m), 1215 (s), 1040 (s), 644 (m) cm$^{-1}$.; HRMS (DART) for $C_{11}H_{12}O_2Br$ $[M+H]^+$: Calc'd: 255.00152, found: 255.00099.



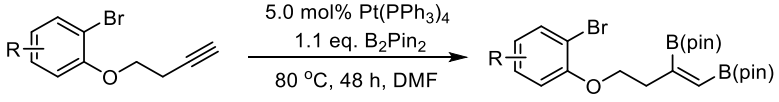

**1-bromo-2-(but-3-yn-1-yloxy)-4-chlorobenzene** (**S-32**) The title compound was prepared according to *General procedure for preparing butynyl aryl ether using Mitsunobu reaction* with 2-bromo-5-chlorophenol (1.04 g, 5.0 mmol, 1.0

equiv.), 3-butynyl-1-ol (0.35 g, 5.0 mmol, 1.0 equiv.), triphenylphosphine (1.11 g, 5.0 mmol, 1.0 equiv.), diethyl azodicarboxylate (DEAD) (1.48 g, 8.50 mmol, 1.7 equiv.) in 8 mL THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.671 g, 2.6 mmol, 52% yield) as a white solid. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with potassium permanganese stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.6 Hz, 1H), 7.21 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 4.11 (t, *J* = 7.2 Hz, 2H), 2.73 (td, *J* = 7.1, 2.7 Hz, 2H), 2.06 (t, *J* = 2.7 Hz, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 153.9, 133.1, 128.4, 126.7, 114.5, 113.1, 79.9, 70.4, 67.7, 19.5.; IR (neat) $\nu_{max}$ 3299 (m), 1480 (s), 1386 (m), 1287 (m), 1098 (s), 871 (m), 717 (m), 651 (m) $cm^{-1}$.; HRMS (DART) for $C_{10}H_9OClBr$ $[M+H]^+$: Calc'd: 258.95198, found: 258.95261.

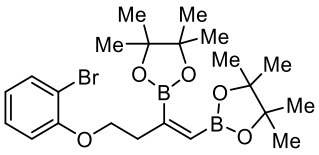



**2-bromo-1-(but-3-yn-1-yloxy)-4-fluorobenzene** (**S-33**) The title compound was prepared according to *General procedure for preparing butynyl aryl ether using Mitsunobu reaction* with 2-bromo-4-fluorophenol (0.98 g, 5.0 mmol, 1.0 equiv.), 3-butynyl-1-ol (0.35 g, 5.0 mmol, 1.0 equiv.), triphenylphosphine (1.11 g, 5.0 mmol, 1.0 equiv.), diethyl azodicarboxylate (DEAD) (1.48 g, 8.50 mmol, 1.7 equiv.) in 8 mL THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.631 g, 2.45 mmol, 49% yield) as a white solid. Product Rf = 0.6 in 10% ethyl acetate:hexanes (stains with potassium permanganese stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 7.8, 3.0 Hz, 1H), 6.97 (td, *J* = 8.4, 3.0 Hz, 1H), 6.86 (dd, *J* = 9.1, 4.8 Hz, 1H), 4.11 (t, *J* = 7.1 Hz, 2H), 2.72 (td, *J* = 7.1, 2.7 Hz, 2H), 2.06 (t, *J* = 2.7 Hz, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 157.1 (d, *J* = 243.9 Hz), 151.7 (d, *J* = 2.8 Hz), 120.6 (d, *J* = 25.4 Hz), 114.9 (d, *J* = 4.7 Hz), 114.8 (d, *J* = 9.3 Hz), 112.9 (d, *J* = 9.8 Hz), 80.1, 70.3, 68.3, 19.6.; $^{19}$F NMR (564 MHz, $CDCl_3$) δ -120.85 (td, *J* = 7.7, 4.6 Hz, 1F).; IR (neat) $\nu_{max}$ 3300 (m), 1489 (s), 1470 (m), 1290 (m), 1260 (s), 1046 (m), 864 (m) $cm^{-1}$.; HRMS (DART) for $C_{10}H_9OFBr$ $[M+H]^+$: Calc'd: 242.98153, found: 242.98245.

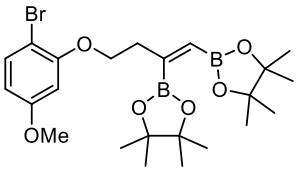
### 2.4.2.7 General Procedures for Terminal Alkyne Diboration



In glovebox, an oven-dried 25 mL round bottom flask was equipped with a magnetic stir bar and charged with butynyl aryl ether (1.0 equiv.), $B_2(pin)_2$ (1.1 equiv.), $Pt(PPh_3)_4$ (1.5 mol%) and anhydrous DMF. The round bottom flask was sealed with rubber septum, brought out of glovebox and heated to 80 °C. Reaction was stirred at this temperature for 48 h. Upon completion, reaction was then diluted with water and extracted with diethyl ether twice. The mixture was dried over sodium sulfate, concentrated under vacuum and analyzed by $^1$H NMR. Crude product was then purified using silica gel chromatography.

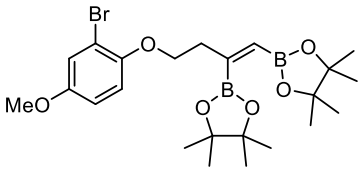



**(E)-2,2'-(4-(2-bromophenoxy)but-1-ene-1,2-diyl)bis(4,4,5,5-tetra methyl-1,3,2-dioxaborolane) (S-34**)The title compound was prepared according to *General procedures for terminal alkyne diboration* with 1-bromo-2-(but-3-yn-1-yloxy)benzene (**S-29**) (2.0 g, 8.89 mmol, 1.0 equiv.), $B_2(pin)_2$ (2.48 g, 9.77 mmol, 1.1 equiv.), $Pt(PPh_3)_4$ (0.166g, 0.133 mmol, 1.5 mol%) in 15 mL DMF. The resulting crude product was purified by silica gel column chromatography using 5 to 10% ethyl acetate:hexanes to isolate the title compound (2.22 g, 4.63 mmol, 52% yield) as a white solid. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.9 Hz, 1H), 7.22 (t, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 6.79 (t, *J* = 7.6 Hz, 1H), 6.10 (s, 1H), 4.12 – 4.07 (m, 2H), 2.75 (t, *J* = 7.9 Hz, 2H), 1.31 – 1.28 (m, 24H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 155.1, 133.2, 128.2, 121.4, 113.2, 112.1, 83.8, 83.4, 68.2, 38.5, 24.8, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 31.06. IR (neat): $\nu_{max}$ 2976.98 (m), 2930.74 (m), 1617.86 (m), 1587.97 (s), 1468.08 (m), 1334.71 (m), 1138.35 (m) cm$^{-1}$. HRMS (DART) for $C_{22}H_{34}B_2BrO_5$ $[M+H]^+$: Calc'd: 479.17702, found: 479.17541.

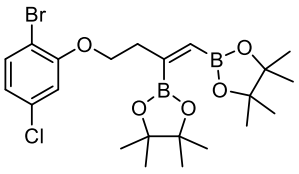



**(E)-2,2'-(4-(2-bromo-5-methoxyphenoxy)but-1-ene-1,2-diyl)bis (4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S-35**) The title compound was prepared according to *General procedures for terminal alkyne diboration* with 1-bromo-2-(but-3-yn-1-yloxy)-4-methoxybenzene (**S-30**) (0.23 g, 1.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.28 g, 1.10 mmol, 1.1 equiv.), $Pt(PPh_3)_4$ (0.0186g, 0.015 mmol, 1.5 mol%) in 3 mL DMF. The resulting crude product was purified by silica gel column chromatography using 5 to 20% ethyl acetate:hexanes to isolate the title compound (0.32 g, 0.63 mmol, 63% yield) as white solid. Product Rf = 0.6 in 20% ethyl acetate:hexanes (stains with CAM

stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 1H), 6.52 (d, *J* = 2.8 Hz, 1H), 6.36 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.10 (s, 1H), 4.05 (t, 2H), 3.76 (s, 3H), 2.74 (t, 2H), 1.30 (s, 12H), 1.28 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 160.4, 156.1, 133.3, 106.4, 103.1, 101.1, 84.1, 83.8, 68.5, 55.7, 38.8, 25.2, 25.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.24.; IR (neat) $\nu_{max}$ 2977 (m), 1593 (m), 1444 (s), 1280 (s), 1167 (m), 1060 (m), 967 (s) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{36}B_2O_6Br$ $[M+H]^+$: Calc'd: 509.18759, found: 509.18936.

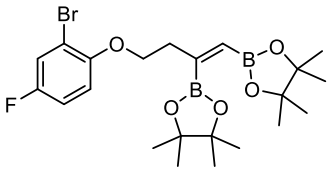



**(E)-2,2'-(4-(2-bromo-4-methoxyphenoxy)but-1-ene-1,2-diyl)bis (4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S-36)** The title compound was prepared according to *General procedures for terminal alkyne diboration* with 2-bromo-1-(but-3-yn-1-yloxy)-4-methoxybenzene (**S-31**) (0.25 g, 1.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.28 g, 1.10 mmol, 1.1 equiv.), $Pt(PPh_3)_4$ (0.0186g, 0.015 mmol, 1.5 mol%) in 3 mL DMF. The resulting crude product was purified by silica gel column chromatography using 5 to 20% ethyl acetate:hexanes to isolate the title compound (0.312 g, 0.62 mmol, 62% yield) as white solid. Product Rf = 0.6 in 20% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 3.0 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.76 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.07 (s, 1H), 4.06 – 3.99 (m, 2H), 3.74 (s, 3H), 2.72 (t, *J* = 7.8 Hz, 2H), 1.30 (s, 12H), 1.28 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 154.1, 149.8, 118.9, 114.9, 113.7, 112.9, 84.0, 83.6, 69.4, 56.0, 39.0, 25.00, 24.96.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.19.; IR (neat) $\nu_{max}$ 2977 (m), 1494 (s), 1404 (m), 1337 (s), 1312 (s), 1273 (m), 850 (m) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{36}B_2O_6Br$ $[M+H]^+$: Calc'd: 509.18759, found: 509.18754.



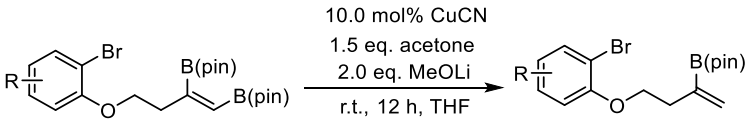

**(E)-2,2'-(4-(2-bromo-5-chloro)but-1-ene-1,2-diyl)bis(4,4,5,5-tetrame thyl-1,3,2-dioxaborolane)** (**S-37**) The title compound was prepared according to *General procedures for terminal alkyne diboration* with 1-bromo-2-(but-3-yn-1-yloxy)-4-chlorobenzene (**S-32**) (0.26 g, 1.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.28 g, 1.10 mmol, 1.1 equiv.), $Pt(PPh_3)_4$ (0.0186g, 0.015 mmol, 1.5 mol%) in 3 mL DMF. The resulting crude product was purified by silica gel column chromatography using 5 to 20% ethyl acetate:hexanes to isolate the title compound (0.251 g, 0.49 mmol, 49% yield) as white solid. Product Rf = 0.6 in 20% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 2.5 Hz, 1H), 7.17 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.09 (s, 1H), 4.09 – 4.01 (m, 2H), 2.71 (t, *J* = 7.1 Hz, 2H), 1.29 (s, 12H), 1.27

(s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 154.3, 132.8, 128.2, 125.8, 114.0, 112.7, 84.0, 83.6, 68.7, 38.6, 24.98, 24.95.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.02.; IR (neat) $\nu_{max}$ 2978 (m), 1480 (m), 1466 (m), 1379 (s), 1371 (s), 1287 (s), 1245 (m), 1111(m) $cm^{-1}$.; HRMS (DART) for $C_{22}H_{33}B_2O_5ClBr$ $[M+H]^+$: Calc'd: 513.13805, found: 513.13751.

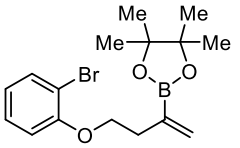


**(E)-2,2'-(4-(2-bromo-4-fluoro)but-1-ene-1,2-diyl)bis(4,4,5,5-tetra methyl-1,3,2-dioxaborolane)** (**S-38**) The title compound was prepared according to *General procedures for terminal alkyne diboration* with 2-bromo-1-(but-3-yn-1-yloxy)-4-fluorobenzene (**S-33**) (0.24 g, 1.0 mmol, 1.0 equiv.), $B_2(pin)_2$ (0.28 g, 1.10 mmol, 1.1 equiv.), $Pt(PPh_3)_4$ (0.0186g, 0.015 mmol, 1.5 mol%) in 3 mL DMF. The resulting crude product was purified by silica gel column chromatography using 5 to 20% ethyl acetate:hexanes to isolate the title compound (0.347 g, 0.70 mmol, 70% yield) as white solid. Product Rf = 0.6 in 20% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.26 (m, 1H), 6.94 (ddd, J = 9.1, 7.8, 3.0 Hz, 1H), 6.87 (dd, J = 9.1, 4.8 Hz, 1H), 6.10 (s, 1H), 4.08 – 4.02 (m, 2H), 2.76 – 2.70 (m, 2H), 1.30 (s, 12H), 1.29 (s, 12H).; $^{13}$C NMR (151 MHz, CDCl3) δ 156.7 (d, J = 242.7 Hz), 152.1 (d, J = 2.5 Hz), 120.5 (d, J = 25.5 Hz), 114.7 (d, J = 22.5 Hz), 114.1 (d, J = 8.3 Hz), 112.4 (d, J = 9.8 Hz), 84.1, 83.7, 69.2, 38.8, 25.05, 25.02.; $^{19}$F NMR (470 MHz, $CDCl_3$) δ -122.32 (td, J = 7.9, 4.9 Hz).; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.10.; IR (neat) νmax 2978 (m), 1491 (s), 1470 (m), 1389 (s), 1379 (s), 1311 (s), 1191 (m), 859 (m) cm-1.; HRMS (DART) for $C_{22}H_{33}B_2O_5FBr$ $[M+H]^+$: Calc'd: 497.16760, found: 497.1689.

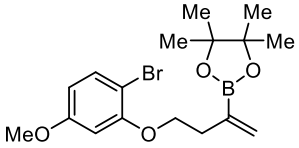
### 2.4.2.8 General Procedures for Alkenyl Diboron Site-Selective Protodeborylation




In glovebox, an oven-dried 3-dram vial was equipped with a magnetic stir bar and charged with alkenyl diboron (1.0 equiv.), lithium methoxide (2.0 equiv.), CuCN (10.0 mol%), acetone (1.5 equiv.) and anhydrous THF. The vial was sealed properly with cap and tapes, brought out of glovebox and stirred at room temperature for 48 h. Upon completion, reaction was then diluted with diethyl ether filtered through a short silica pad, concentrated under vacuum and analyzed by $^1$H NMR. Crude product was then purified using silica gel chromatography.

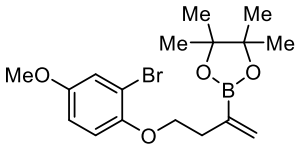


**2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-39**) The title compound was prepared according to *General procedures for alkenyl diboron site-selective protodeborylation* with (E)-2,2'-(4-(2-bromophenoxy)but-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxa borolane) (**S-34**) (0.225 g, 0.470 mmol, 1.0 equiv.), lithium methoxide (0.357 g, 0.940 mmol, 2.0 equiv.), CuCN (0.0042 g, 0.0470 mmol, 10.0 mol%), acetone (0.0410 g, 0.704 mmol, 1.5 equiv.) in 3.0 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.0750 g, 0.212 mmol, 45% yield) as white crystals. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.26 – 7.21 (m, 1H), 6.96 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.80 (td, *J* = 7.6, 1.1 Hz, 1H), 5.94 (d, *J* = 3.2 Hz, 1H), 5.82 (s, 1H), 4.12 (t, *J* = 7.3 Hz, 2H), 2.69 (t, *J* = 7.2 Hz, 2H), 1.27 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 155.3, 133.2, 132.5, 128.2, 121.4, 113.2, 112.2, 83.5, 68.4, 34.8, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.23. IR (neat): $\nu_{max}$ 2976.70 (m), 2928.96 (m), 1618.15 (m), 1587.24 (s), 1487.35 (m), 1310.72 (s), 1275.77 (s), 1139.40 (s), 1051.09 (s) $cm^{-1}$. HRMS (DART) for $C_{16}H_{23}BBrO_3$ $[M+H]^+$: Calc'd: 353.06300, found: 353.09220.

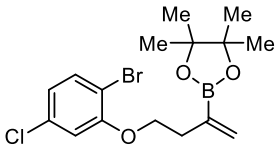


**2-(4-(2-bromo-5-methoxyphenoxy)but-1-en-2-yl)-4,4,5,5-tetramethy l-1,3,2-dioxaborolane** (**S-40**) The title compound was prepared according to *General procedures for alkenyl diboron site-selective protodeborylation* with (E)-2,2'-(4-(2-bromo-5-methoxyphenoxy)but-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S-35**) (0.203 g, 0.40 mmol, 1.0 equiv.), lithium methoxide (0.304 g, 0.80 mmol, 2.0 equiv.), CuCN (0.0036 g, 0.040 mmol, 10.0 mol%), acetone (0.0348 g, 0.60 mmol, 1.5 equiv.) in 2.0 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.0840 g, 0.22 mmol, 55% yield) as white solid. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.7 Hz, 1H), 6.56 (d, *J* = 2.8 Hz, 1H), 6.37 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.94 (d, *J* = 3.3 Hz, 1H), 5.85 – 5.79 (m, 1H), 4.08 (t, *J* = 7.3 Hz, 2H), 3.78 (s, 3H), 2.68 (t, *J* = 7.4 Hz, 2H), 1.27 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 160.3, 156.2, 133.2, 132.9, 106.0, 103.2, 101.3, 83.8, 68.6, 55.7, 35.0, 25.0.; $^{11}$B

NMR (160 MHz, $CDCl_3$) δ 30.12.; IR (neat) $\nu_{max}$ 2977(m), 1594 (m), 1425 (m), 1282 (s), 1140 (m), 1026 (m), 684 (m) $cm^{-1}$.; HRMS (DART) for $C_{17}H_{25}BO_4Br$ $[M+H]^+$: Calc'd: 383.10238, found: 383.10166.

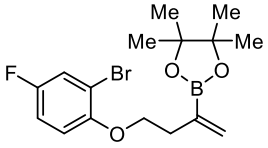


**2-(4-(2-bromo-4-methoxyphenoxy)but-1-en-2-yl)-4,4,5,5-tetramethy l-1,3,2-dioxaborolane** (**S-41**) The title compound was prepared according to *General procedures for alkenyl diboron site-selective protodeborylation* with (E)-2,2'-(4-(2-bromo-4-methoxyphenoxy)but-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**S-36**) (0.203 g, 0.40 mmol, 1.0 equiv.), lithium methoxide (0.304 g, 0.80 mmol, 2.0 equiv.), CuCN (0.0036 g, 0.040 mmol, 10.0 mol%), acetone (0.0348 g, 0.60 mmol, 1.5 equiv.) in 2.0 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.0802 g, 0.21 mmol, 51% yield) as white solid. Product Rf = 0.5 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 3.0 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.79 (dd, *J* = 9.0, 3.0 Hz, 1H), 5.93 (d, *J* = 3.3 Hz, 1H), 5.82 – 5.78 (m, 1H), 4.05 (t, *J* = 7.2 Hz, 2H), 3.75 (s, 3H), 2.70 – 2.63 (m, 2H), 1.27 (s, 12H).; $^{13}C$ NMR (151 MHz, $CDCl_3$) δ 154.0, 149.8, 132.4, 118.8, 114.8, 113.7, 112.8, 83.6, 69.5, 55.9, 35.2, 24.8.; $^{11}B$ NMR (160 MHz, $CDCl_3$) δ 29.97.; IR (neat) $\nu_{max}$ 2977 (m), 1494 (s), 1469 (m), 1410 (s), 1273 (s), 1141 (m), 951 (m) $cm^{-1}$.; HRMS (DART) for $C_{17}H_{25}BO_4Br$ $[M+H]^+$: Calc'd: 383.10238, found: 383.10186.



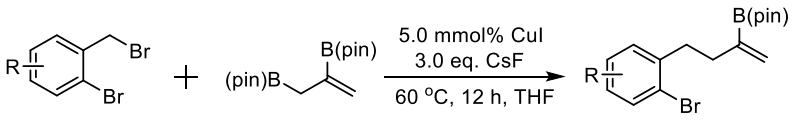
**2-(4-(2-bromo-5-chloro)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-diox aborolane** (**S-42**) The title compound was prepared according to *General procedures for alkenyl diboron site-selective protodeborylation* with (E)-2,2'-(4-(2-bromo-5-chloro)but-1-ene-1,2-diyl)bis(4,4,5,5-tetrame thyl-1,3,2-dioxaborolane) (**S-37**) (0.204 g, 0.40 mmol, 1.0 equiv.), lithium methoxide (0.304 g, 0.80 mmol, 2.0 equiv.), CuCN (0.0036 g, 0.040 mmol, 10.0 mol%), acetone (0.0348 g, 0.60 mmol, 1.5 equiv.) in 2.0 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.0695 g, 0.18 mmol, 46% yield) as white solid. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.5 Hz, 1H), 7.20 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 5.95 (d, *J* = 3.3 Hz, 1H), 5.82 – 5.79 (m, 1H), 4.09 (t, *J* = 7.2 Hz, 2H), 2.70 –

2.64 (m, 2H), 1.27 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 154.4, 132.9, 132.9, 128.2, 125.7, 114.0, 112.8, 83.7, 69.0, 35.0, 24.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.95.; IR (neat) $\nu_{max}$ 2977 (m), 1480 (m), 1465 (m), 1369 (m), 1311(s), 1245 (s), 1167 (m), 951 (m) $cm^{-1}$.; HRMS (DART) for $C_{16}H_{22}BO_3ClBr$ $[M+H]^+$: Calc'd: 387.05284, found: 387.05274.



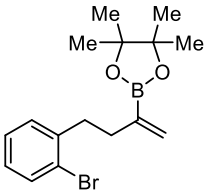
**2-(4-(2-bromo-4-fluoro)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane** (**S-43**) The title compound was prepared according to *General procedures for alkenyl diboron site-selective protodeborylation* with (E)-2,2'-(4-(2-bromo-4-fluoro)but-1-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2 -dioxaborolane) (**S-38**) (0.198 g, 0.40 mmol, 1.0 equiv.), lithium methoxide (0.304 g, 0.80 mmol, 2.0 equiv.), CuCN (0.0036 g, 0.040 mmol, 10.0 mol%), acetone (0.0348 g, 0.60 mmol, 1.5 equiv.) in 2.0 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.0777 g, 0.21 mmol, 53% yield) as white solid. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 1H), 6.95 (ddd, *J* = 9.0, 7.7, 3.0 Hz, 1H), 6.90 (dd, *J* = 9.1, 4.9 Hz, 1H), 5.94 (d, *J* = 3.3 Hz, 1H), 5.82 – 5.79 (m, 1H), 4.08 (t, *J* = 7.2 Hz, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 1.27 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 156.61 (d, *J* = 242.2 Hz), 152.17 (d, *J* = 2.8 Hz), 132.75, 120.38, 114.63 (d, *J* = 22.5 Hz), 114.00 (d, *J* = 8.2 Hz), 112.45 (d, *J* = 9.9 Hz), 83.74, 69.42, 35.10, 24.94.; $^{19}$F NMR (564 MHz, $CDCl_3$) δ -122.44 (td, *J* = 7.7, 4.8 Hz).; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.00.; IR (neat) $\nu_{max}$ 2925 (m), 1491 (s), 1469 (m), 1431 (m), 1402 (m), 1291 (m), 1260 (s), 1191 (m), 861 (m) $cm^{-1}$.; HRMS (DART) for $C_{16}H_{22}BO_3FBr$ $[M+H]^+$: Calc'd: 371.08239, found: 371.08384.

### 2.4.2.9 General Procedures for 2,3-Diborylpropene Site-Selective Benzylation

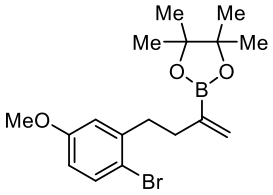



In glovebox, an oven-dried 50 mL round bottom flask was equipped with a magnetic stir bar and charged with 2,3-diborylpropene (1.0 equiv.), 2-bromoarylbromide (1.5 equiv.), CuI (5.0 mol%), CsF (3.0 equiv.) and anhydrous THF. The flask was sealed properly with a rubber septum, brought out of glovebox and stirred at 60 ℃ for 12 h. Large amount of solid precipitation formed during the first hour of stirring, which typically caused the reaction to stop stirring. Upon

completion, reaction was then diluted with diethyl ether and quenched with 3M HCl. The mixture was extracted with ether for 3 times, dried over sodium sulfate for 2 times, concentrated under vacuum and analyzed by $^1$H NMR. Crude product was then purified using silica gel chromatography.

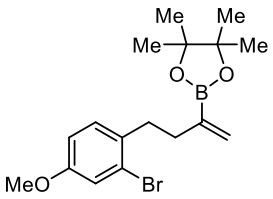



**2-(4-(2-bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborol ane** (**40**) The title compound was prepared according to *General procedures for 2,3-diborylpropene site-selective benzylation* with 3-diborylpropene (**39**) (1.76 g, 6.0 mmol, 1.0 equiv.), 2-bromoarylbromide (**38**) (2.25 g, 9.0 mmol, 1.5 equiv.), CuI (0.0571 g, 0.30 mmol, 5.0 mol%), CsF (2.73 g, 18.0 mmol, 3.0 equiv.) in 30 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 2 to 5% ethyl acetate:hexanes to isolate the title compound (0.988 g, 2.93 mmol, 45% yield) as clear oil. Product Rf = 0.7 in 10% ethyl acetate:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, $J$ = 8.0 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.03 (dt, $J$ = 8.2, 4.3 Hz, 1H), 5.81 (d, $J$ = 2.8 Hz, 1H), 5.62 (s, 1H), 2.91 – 2.84 (m, 2H), 2.51 – 2.41 (m, 2H), 1.28 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 141.5, 132.5, 130.4, 129.6, 127.2, 127.1, 124.4, 83.3, 35.7, 35.3, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 31.13. IR (neat): $\nu_{max}$ 2976.31 (m), 1616.81 (s), 1470.06 (s), 1438.16 (m), 1388.64 (s), 1309.08 (s), 1137.81 (s) cm$^{-1}$. HRMS (DART) for $C_{16}H_{23}BBrO_2$ $[M+H]^+$: Calc'd: 337.09690, found: 337.09680.



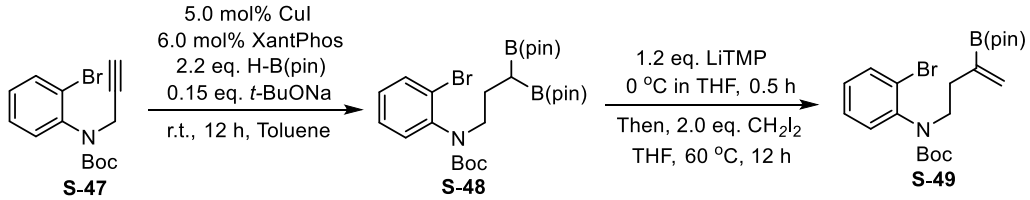

**2-(4-(2-bromo-5-methoxyphenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**S-45**) The title compound was prepared according to *General procedures for 2,3-diborylpropene site-selective benzylation* with 2,3-diborylpropene (0.588 g, 2.0 mmol, 1.0 equiv.), 2-bromo-5-methoxyl-benzylbromide (0.840 g, 3.0 mmol, 1.5 equiv.), CuI (0.0191 g, 0.10 mmol, 5.0 mol%), CsF (0.911 g, 6.0 mmol, 3.0 equiv.) in 15 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 50 to 80% DCM:hexanes. Side product (typically homocoupling of electrophile) must be removed, otherwise the subsequent conjunctive cross-coupling reaction would perform much worse. Titled compound was isolated as white crystals (0.303 g, 0.825 mmol, 41% yield). Product Rf = 0.6 in 50% DCM:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, $J$ = 8.8 Hz, 1H), 6.77 (d, $J$ = 3.1 Hz, 1H),

6.60 (dd, $J$ = 8.7, 3.1 Hz, 1H), 5.81 (d, $J$ = 3.3 Hz, 1H), 5.63 (s, 1H), 3.77 (s, 3H), 2.86 – 2.78 (m, 2H), 2.49 – 2.40 (m, 2H), 1.28 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 158.7, 142.5, 133.0, 129.5, 116.1, 114.9, 112.9, 83.3, 55.3, 35.9, 35.3, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 29.98. IR (neat): $\nu_{max}$ 2976.88 (m), 1584.94 (m), 1471.35 (s), 1370,07 (s), 1139.46 (s), 1056.65 (s) $cm^{-1}$. HRMS (DART) for $C_{17}H_{25}BBrO_3$ $[M+H]^+$: Calc'd: 367.10746, found: 367.10848.




**2-(4-(2-bromo-5-methoxyphenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**S-46**) The title compound was prepared according to *General procedures for 2,3-diborylpropene site-selective benzylation* with 2,3-diborylpropene (0.588 g, 2.0 mmol, 1.0 equiv.), 2-bromo-4-methoxyl-benzylbromide (0.840 g, 3.0 mmol, 1.5 equiv.), CuI (0.0191 g, 0.10 mmol, 5.0 mol%), CsF (0.911 g, 6.0 mmol, 3.0 equiv.) in 15 mL anhydrous THF. The resulting crude product was purified by silica gel column chromatography using 50 to 80% DCM:hexanes. Side product (typically homocoupling of electrophile) must be removed, otherwise the subsequent conjunctive cross-coupling reaction would perform much worse. Titled compound was isolated as white crystals (0.390 g, 1.06 mmol, 53% yield). Product Rf = 0.6 in 50% DCM:hexanes (stains with CAM stain). $^1$H NMR (600 MHz, $CDCl_3$) δ 7.10 (d, $J$ = 8.5 Hz, 1H), 7.07 (d, $J$ = 2.6 Hz, 1H), 6.77 (dd, $J$ = 8.4, 2.7 Hz, 1H), 5.80 (d, $J$ = 3.3 Hz, 1H), 5.61 (s, 1H), 3.76 (s, 3H), 2.83 – 2.77 (m, 2H), 2.44 – 2.39 (m, 2H), 1.28 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 158.0, 133.4, 130.6, 129.5, 124.4, 117.6, 113.3, 83.3, 55.4, 35.6, 34.8, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.59. IR (neat): $\nu_{max}$ 2976.53 (m), 1804.82 (s), 1491.38 (s), 1307.88 (s), 1185.64 (m), 1038.05 (m) $cm^{-1}$. HRMS (DART) for $C_{17}H_{25}BBrO_3$ $[M+H]^+$: Calc'd: 367.10746, found: 367.10701.

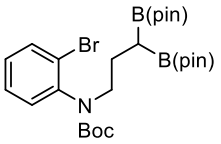
### 2.4.2.10 General Procedures for The Synthesis of N-tethered Starting Material



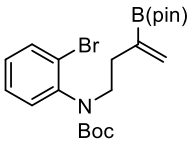

**S-47** was synthesized according to literature report. [4] To prepare compound **S-48**, **S-47** went through a Cu catalyzed double hydroboration [5] using following procedure: In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with CuI (9.9 mg, 0.1 mmol,

5.0 mol%), XantPhos (69.4 mg, 0.12 mmol, 6.0 mol%), *t*-BuONa (28.8 mg, 0.3 mmol, 0.15 equiv.) and 2 mL toluene. The reaction was stirred for 15 min before adding in H-B(pin) by mass (563.1 mg, 4.4 mmol, 2.2 equiv.). The reaction was stirred for additional 10 min. **S-47** was added by mass (620.4 mg, 2.0 mmol, 1.0 equiv.). The vial was sealed by cap, taped and brought out of glovebox and stirred at room temperature for 12 h. Reaction was deluted with ether before being loaded onto a short silica gel pluged and filtered through with large amount of ether. The crude product was concentrated on vaccum and purified using column chromatography. Rf: 0.4 in acetate:hexane 2:8. Isolated 1.01 g pure product as sticky oil (88%).

**S-49** was synthesized from **S-48** by deprotonation and alkylation with $CH_2I_2$ using previously reported method: [6] In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with LiTMP (88.3 mg, 0.6 mmol, 1.2 equiv.) and 1.0 mL THF. The vial was caped with Teflon cap and taped and brought outside the glovebox. The reaction was cooled to 0 ºC and charged with 1.0 M THF solution of **S-48** (0.5 mL, 0.5 mmol, 1.0 equiv.) via syringe. Reaction was stirred at 0 ºC for 30 min. Then diiodomethane was added by volumn (0.08mL, 1.0 mmol, 2.0 equiv.). Reaction was stirred at 60 ºC for 12 h. Then, reaction was quenched with 3 M HCl and extracted with ether. The crude product was dried over sodium sulfate and concentrated on vaccum. The crude product was purified by column chromatography (Rf: 0.2 in DCM-hexane 1:1) using 1:1 to 4:1 DCM-hexane as eluent to yield 59.6 mg of pure compound **S-49** as colorless oil with 52% isolated yield.



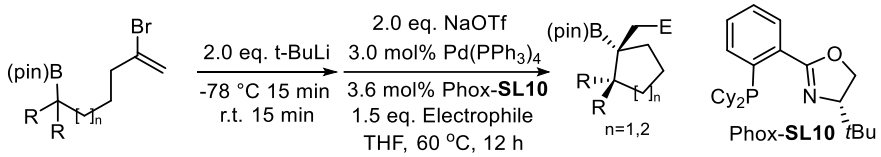

**tert-butyl (3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)(2-bromophenyl)carbamate** (**S-48**) $^1$H NMR (600 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 14.8, 7.1 Hz, 1H), 7.31 – 7.21 (m, 2H), 7.13 – 7.04 (m, 1H), 3.86 – 3.67 (m, 1H), 3.23 – 3.08 (m, 1H), 1.85 – 1.69 (m, 2H), 1.51 (s, 3H), 1.32 (d, *J* = 11.0 Hz, 6H), 1.23 – 1.11 (m, 24H), 0.93 – 0.60 (m, 1H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 156.9, 154.0, 141.4, 140.8, 133.25, 133.22, 133.1, 132.8, 132.7, 132.6, 131.2, 131.1, 130.9, 130.8, 130.7, 128.6, 128.4, 128.3, 128.1, 128.1, 128.0, 128.0, 127.7, 127.7, 127.6, 123.8, 123.64, 123.61, 83.0, 82.92, 82.90, 80.2, 80.0, 79.6, 53.2, 52.1, 51.6, 50.8, 28.4, 28.3, 28.1, 24.8, 24.7, 24.6, 24.5, 24.3, 24.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.52. IR (neat): $\nu_{max}$ 2916.23 (m), 1704.82 (s), 1422.09 (s), 1207.11 (s), 1112.14 (m), 1041.45 (m) cm$^{-1}$. HRMS (DART) for $C_{26}H_{43}B_2BrNO_6$ $[M+H]^+$: Calc'd: 566.23816, found: 566.23769.




**tert-butyl (2-bromophenyl)(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) but-3-en-1-yl)carbamate (S-49)** $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 13.5, 7.9 Hz, 1H), 7.34 – 7.18 (m, 2H), 7.12 (q, *J* = 7.7, 5.8 Hz, 1H), 5.82 (d, *J* = 3.5 Hz, 1H), 5.73 – 5.63 (m, 1H), 4.05 – 3.78 (m, 1H), 3.45 – 3.25 (m, 1H), 2.51 – 2.32 (m, 2H), 1.54 (s, 3H), 1.32 (s, 6H), 1.19 (d, *J* = 10.0 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.2, 141.5, 132.9, 131.5, 131.1, 130.8, 128.5, 128.2, 128.0, 127.6, 123.8, 83.3, 79.8, 50.4, 48.6, 35.0, 34.1, 28.5, 28.2, 24.7, 24.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.74. IR (neat): $\nu_{max}$ 2976.53 (m), 1804.82 (s), 1491.38 (s), 1307.88 (s), 1185.64 (m), 1038.05 (m) $cm^{-1}$. HRMS (DART) for $C_{21}H_{32}BBrNO_4$ $[M+H]^+$: Calc'd: 452.15295, found: 452.15431.

### 2.4.2.11 General Procedures for Conjunctive Cross-Coupling

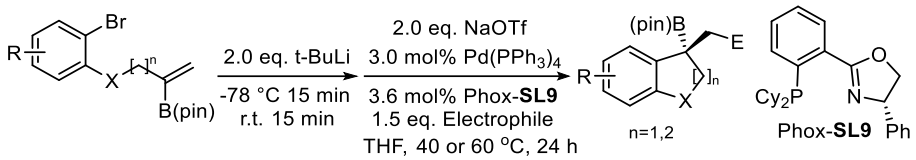
*Method A*:




In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with bromoalkenylboronic ester (0.2 mmol, 1.0 equiv.) and 0.4 mL anhydrous THF. The 2-dram vial was sealed properly with a Teflon cap, brought out of glovebox and cooled to -78 ℃ using dry ice-acetone bath. *tert*-Butyllithium-pentane solution (concentration determined from titration with BHT and 1,10-phenanthroline, 0.4 mmol, 2.0 equiv.) was added via syringe. Reaction was stirred at -78 ℃ for 15 min and then warmed to room temperature to stir for another 15 min. Solvent was removed using high vacuum. Then, the vial was moved into a glovebox. In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with $Pd(PPh_3)_4$ (6.9 mg, 0.006 mmol, 3.0 mol%) and Phox ligand (0.1 M stock solution in THF, 0.072 mL, 0.0072 mmol, 3.6 mol%) followed by 0.53 mL anhydrous THF. The catalyst solution was premixed for 1 hour at room temperature. Then, the vial with boronate complex was opened under Ar and added NaOTf (68.8 mg, 0.4 mmol, 2.0 equiv.) followed by 0.6 mL THF and prepared catalyst solution. At last, electrophile (0.3 mmol, 1.5 equiv.) was added. The vial was then sealed with cap, taped and stirred at 60 ℃ for 12 hours. Upon completion, reaction was diluted with hexane and flushed

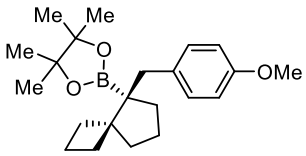
through a silica gel plug using diethyl ether. Crude mixture was concentrated under vacuum and analyzed by NMR. Pure product was isolated using silica gel chromatography.

*Method B*:




In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with bromoalkenylboronic ester (0.2 mmol, 1.0 equiv.) and 0.4 mL anhydrous THF. The 2-dram vial was sealed properly with a Teflon cap, brought out of glovebox and cooled to -78 ℃ using dry ice-acetone bath. *tert*-Butyllithium-pentane solution (concentration determined from titration with BHT and 1,10-phenanthroline, 0.4 mmol, 2.0 equiv.) was added via syringe. Reaction was stirred at -78 ℃ for 15 min and then warmed to room temperature to stir for another 15 min. Solvent was removed using high vacuum. Then, the vial was moved into a glovebox. In glovebox, an oven-dried 2-dram vial was equipped with a magnetic stir bar and charged with $Pd(PPh_3)_4$ (6.9 mg, 0.006 mmol, 3.0 mol%) and Phox ligand (0.1 M stock solution in THF, 0.072 mL, 0.0072 mmol, 3.6 mol%) followed by 0.53 mL anhydrous THF. The catalyst solution was premixed for 1 hour at room temperature. Then, the vial with boronate complex was opened under Ar and added NaOTf (68.8 mg, 0.4 mmol, 2.0 equiv.) followed by 0.6 mL THF and prepared catalyst solution. At last, electrophile (0.3 mmol, 1.5 equiv.) was added. The vial was then sealed with cap, taped and stirred at 40 or 60 ℃ for 24 hours. Upon completion, reaction was diluted with hexane and flushed through a silica gel plug using diethyl ether. Crude mixture was concentrated under vacuum and analyzed by NMR. Pure product was isolated using silica gel chromatography.

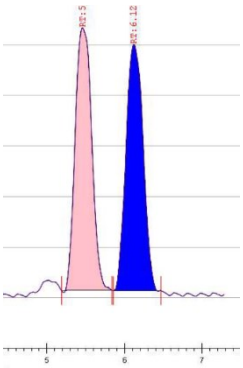
### 2.4.3 Characterization of Conjunctive Coupling Products



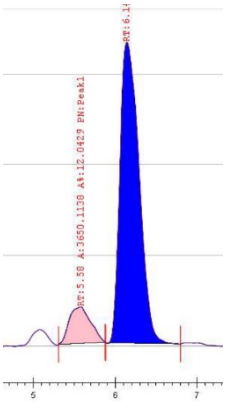

**(R)-2-(5-(4-methoxybenzyl)spiro[3.4]octan-5-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane** (**4**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclobutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-19**) (65.8 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (51.7 mg, 0.145 mmol, 72.7% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, $J$ = 8.6 Hz, 2H), 6.76 (d, $J$ = 8.6 Hz, 2H), 3.76 (s, 3H), 2.83 (d, $J$ = 13.2 Hz, 1H), 2.45 – 2.36 (m, 1H), 2.21 (d, $J$ = 13.3 Hz, 1H), 2.12 – 2.03 (m, 1H), 1.96 – 1.83 (m, 1H), 1.83 – 1.69 (m, 3H), 1.70 – 1.56 (m, 4H), 1.51 – 1.43 (m, 1H), 1.19 (s, 6H), 1.08 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 157.8, 133.9, 131.1, 113.3, 83.0, 55.4, 52.7, 38.5, 37.2, 32.2, 30.7, 27.9, 25.8, 24.9, 20.7, 16.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.77.; IR (neat) $\nu_{max}$ 2972 (m), 1541 (s), 1489 (m), 1388 (m), 1340 (m), 1210 (m), 1177 (m) cm$^{-1}$.; HRMS (DART) for $C_{22}H_{34}BO_3$ $[M+H]^+$: Calc'd: 357.25955, found: 357.25959.; $[\alpha]^{20}_D$: -0.6 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm

***Analysis of Stereochemistry:***

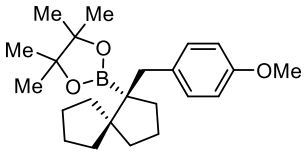
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand. *Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(5-(4-methoxybenzyl)spiro[3.4]octan-5-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane.*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.8443 | 3849.2674 | 5.46 |
| 2 | 49.1557 | 3721.4307 | 6.12 |
| Total: | 100 | 7570.6981 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 12.0429 | 3650.1138 | 5.58 |
| 2 | 87.9571 | 26659.2459 | 6.14 |
| Total: | 100 | 30309.3597 | |

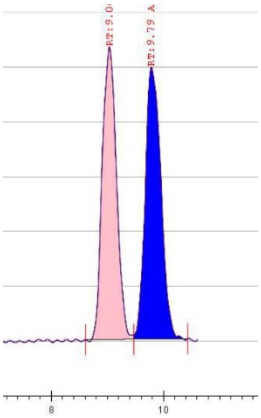


**(R)-2-(1-(4-methoxybenzyl)spiro[4.4]nonan-1-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane** (**5**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (59.8 mg, 0.162 mmol, 80.8% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, $J$ = 8.6 Hz, 2H), 6.76 (d, $J$ = 8.6 Hz, 2H), 3.77 (s, 3H), 2.84 (d, $J$ = 13.2 Hz, 1H), 2.33 (d, $J$ = 13.2 Hz, 1H), 1.96 – 1.86 (m, 1H), 1.83 – 1.47 (m, 11H), 1.46 – 1.37 (m, 2H), 1.19 (s, 6H), 1.07 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 157.8, 133.9, 131.2, 113.3, 83.0, 57.2, 55.4, 38.0, 37.8, 37.0, 33.3, 31.4, 25.9, 24.9, 24.7, 24.5, 21.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.71.; IR (neat) $\nu_{max}$ 2949 (m), 1511 (s), 1454 (m), 1388 (s), 1370 (m), 1246 (s), 1209 (m), 1039 (m), 852 (m) cm$^{-1}$.; HRMS (DART) for $C_{23}H_{36}BO_3$ $[M+H]^+$: Calc'd: 371.27520, found: 371.27662.; $[\alpha]^{20}_D$: 3.2 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

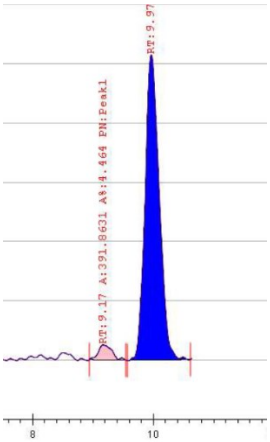
***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

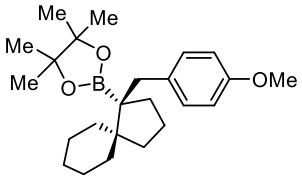
*Chiral SFC (OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)spiro[4.4]nonan-1-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane.*




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.4006 | 9391.4203 | 9.04 |
| 2 | 50.5994 | 9619.3083 | 9.79 |
| Total: | 100 | 19010.7286 | |




| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 4.464 | 391.8631 | 9.17 |
| 2 | 95.536 | 8386.392 | 9.97 |
| Total: | 100 | 8778.2551 | |

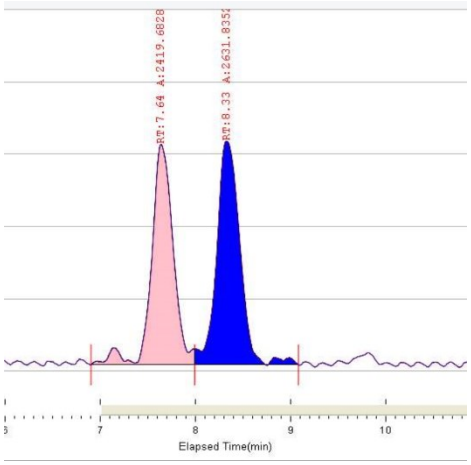


**(*R*)-2-(1-(4-methoxybenzyl)spiro[4.5]decan-1-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane** (**6**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclohexyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-21**) (71.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford a white solid (63.3 mg, 0.17 mmol, 82.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) 7.16 (d, $J$ = 8.5 Hz, 2H), 6.76 (d, $J$ = 8.4 Hz, 2H), 3.77 (s, 3H), 2.89 (d, $J$ = 13.0 Hz, 1H), 2.25 (d, $J$ = 13.0 Hz, 1H), 1.83 – 1.54 (m, 15H), 1.23 (s, 7H), 1.13 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.6, 133.9, 131.2, 113.1, 82.9, 55.2, 49.0, 36.0, 35.2, 32.2, 31.9, 29.3, 26.8, 26.0, 24.8, 23.9, 23.3, 21.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.03.; IR (neat): $\nu_{max}$ 2927.95 (m), 2856.20 (m), 2854.17 (m), 1611.19 (s), 1511.94 (s), 1370.56 (s), 1247.01 (s), 1143.81 (s) $cm^{-1}$. HRMS (DART) for $C_{24}H_{37}BO_3$ $[M+H]^+$: Calc'd: 384.36756, found: 384.36707. $[\alpha]^{20}_D$: 0.7 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

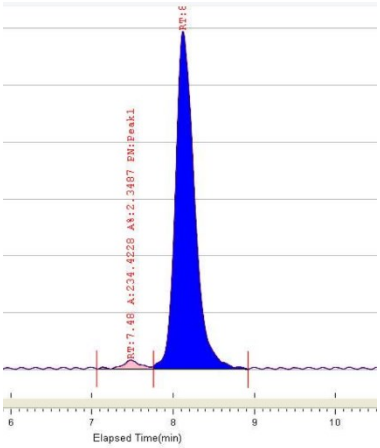
***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

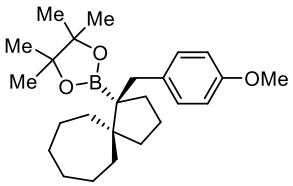
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)spiro[4.5]decan-1-yl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 47.9001 | 2419.6828 | 7.64 |
| 2 | 52.0999 | 2631.8352 | 8.33 |
| Total: | 100 | 5051.518 | |




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 2.3487 | 234.4228 | 7.48 |
| 2 | 97.6513 | 9746.5675 | 8.12 |
| Total: | 100 | 9980.9903 | |

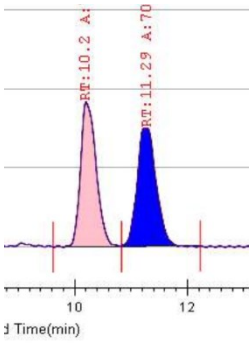


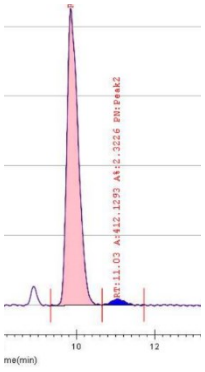
**(*R*)-2-(1-(4-methoxybenzyl)spiro[4.6]undecan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**7**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cycloheptyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-22**) (74.2 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford a clear oil (60.0 mg, 0.15 mmol, 75.0% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 3H), 2.94 (d, *J* = 12.9 Hz, 1H), 2.28 (d, *J* = 12.9 Hz, 1H), 1.90 – 1.83 (m, 2H), 1.62 (dq, *J* = 13.1, 6.2 Hz, 11H), 1.46 (dd, *J* = 19.2, 7.4 Hz, 5H), 1.20 (s, 6H), 1.11 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.5, 133.9, 131.2, 112.9, 82.8, 55.1, 51.9, 38.3, 37.5, 37.4, 34.7, 30.9, 30.0, 29.8, 25.6, 24.8, 24.5, 24.1, 20.7.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.89.; IR (neat): $\nu_{max}$ 2925.06 (m), 2856.99 (m), 1610.75 (s), 1462.70 (m), 1369.73 (m), 1143.62 (s) cm$^{-1}$. HRMS (DART) for $C_{25}H_{40}BO_3$ $[M+H]^+$: Calc'd: 399.30650, found: 399.30855. $[\alpha]^{20}_D$: 2.1 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

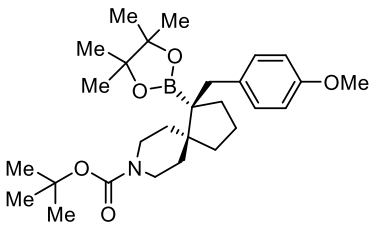
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)spiro[4.6]undecan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.0995 | 7056.7441 | 10.2 |
| 2 | 49.9005 | 7028.724 | 11.29 |
| Total: | 100 | 14085.4681 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 97.6774 | 17332.1345 | 9.84 |
| 2 | 2.3226 | 412.1293 | 11.03 |
| Total: | 100 | 17744.2638 | |

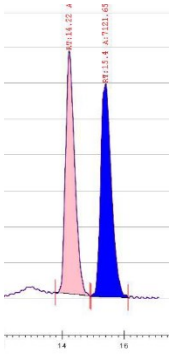


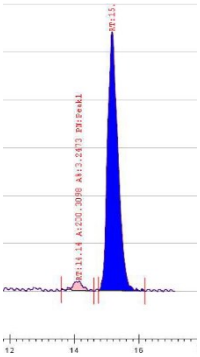
**tert-butyl-(*R*)-1-(4-methoxybenzyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-azaspiro[4.5]decane-8-carboxylate** (**8**) The reaction was performed according to the general procedure *Method A* using tert-butyl 4-(4-bromopent-4-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate (**S-25**) (91.0 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 5 to 10% ethyl acetate:hexanes) to afford a white solid (86.9 mg, 0.179 mmol, 89.5% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, $J$ = 8.6 Hz, 2H), 6.77 (d, $J$ = 8.6 Hz, 2H), 4.16 – 3.88 (m, 2H), 3.77 (s, 3H), 2.85 (d, $J$ = 12.9 Hz, 1H), 2.80 – 2.67 (m, 2H), 2.25 (d, $J$ = 13.0 Hz, 1H), 1.90 – 1.54 (m, 10H), 1.46 (s, 9H), 1.22 (s, 6H), 1.10 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 157.9, 155.0, 133.3, 131.3, 113.3, 83.3, 76.95, 55.4, 28.6, 26.1, 24.9, 21.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.62.; IR (neat) $\nu_{max}$ 2959 (m), 2941 (m), 1692 (s), 1512 (m), 1472 (m), 1456 (m), 1365 (s), 1316 (m), 1144 (m), 1036 (m), 801 (m) $cm^{-1}$.; HRMS (DART) for $C_{28}H_{45}BNO_5$ $[M+H]^+$: Calc'd: 486.33853, found: 486.33909.; $[\alpha]^{20}_D$: -2.4 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

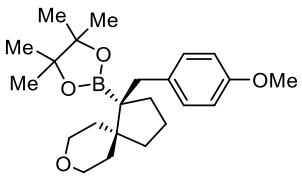
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl-(R)-1-(4-methoxybenzyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-azaspiro[4.5]decane-8-carboxylate.*





| Peak No | % Area | Area | RT (min) | Peak No | % Area | Area | RT (min) |
|---|---|---|---|---|---|---|---|
| 1 | 49.1674 | 6888.3503 | 14.22 | 1 | 3.2473 | 200.3098 | 14.14 |
| 2 | 50.8326 | 7121.6523 | 15.4 | 2 | 96.7527 | 5968.2164 | 15.17 |
| Total: | 100 | 14010.0026 | | Total: | 100 | 6168.5262 | |



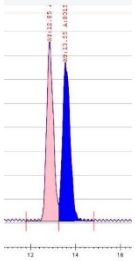
**(*R*)-2-(1-(4-methoxybenzyl)-8-oxaspiro[4.5]decan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**9**) The reaction was performed according to the general procedure *Method A* using 2-(4-(4-bromopent-4-en-1-yl)tetrahydro-2H-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-23**) (71.8 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a white solid (64.2 mg, 0.16 mmol, 82.5% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 3.90 (dd, *J* = 11.3, 4.1 Hz, 1H), 3.84 – 3.76 (m, 4H), 3.57 (t, *J* = 11.6 Hz, 1H), 3.47 (t, *J* = 11.7 Hz, 1H), 2.87 (d, *J* = 13.0 Hz, 1H), 2.25 (d, *J* = 13.0 Hz, 1H), 2.05 (td, *J* = 13.0, 4.8 Hz, 1H), 1.87 (dd, *J* = 17.3, 9.4 Hz, 1H), 1.80 (d, *J* = 8.8 Hz, 1H), 1.71 (s, 1H), 1.60 (dt, *J* = 13.5, 6.3 Hz, 3H), 1.44 – 1.33 (m, 3H), 1.23 (s, 6H), 1.13 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.7, 133.1, 131.2, 113.1, 83.1, 65.8, 65.0, 55.2, 46.6, 35.4, 35.4, 32.5, 31.3, 28.94, 25.9, 24.8, 24.7, 20.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.87.; IR (neat): $\nu_{max}$ 2951.96 (m), 2929.11 (m), 2868.79 (m), 1611.24 (s), 1512.07 (s), 1464.55 (m), 1371.33 (s), 1247.35 (s), 1143.41 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{36}BO_4$ $[M+H]^+$: Calc'd: 387.27012, found: 387.27132. $[\alpha]^{20}_D$: 7.6 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

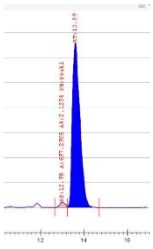
Absolute configuration was determined by x-ray crystallography.

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

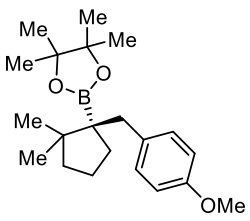
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)-8-oxaspiro[4.5]decan-1-yl)-4,4,5,5-tetr amethyl-1,3,2-dioxaborolane.*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.1536 | 6434.2672 | 29.21 |
| 2 | 50.8464 | 6655.8486 | 30.57 |
| Total: | 100 | 13090.1158 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 97.9434 | 19349.3718 | 29.3 |
| 2 | 2.0566 | 406.3024 | 30.89 |
| Total: | 100 | 19755.6742 | |

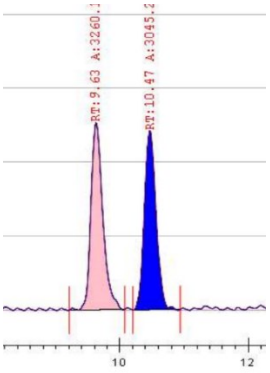


***(R)*-2-(1-(4-methoxybenzyl)-2,2-dimethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane** (**11**) The reaction was performed according to the general procedure *Method A* using 2-(6-bromo-2-methylhept-6-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-27**) (63.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford a clear oil (48.4 mg, 0.141 mmol, 70.3% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, $J$ = 8.6 Hz, 2H), 6.76 (d, $J$ = 8.7 Hz, 2H), 3.77 (s, 3H), 2.89 (s, 1H), 2.25 (d, $J$ = 13.1 Hz, 1H), 1.90 (dt, $J$ = 13.0, 7.7 Hz, 1H), 1.66 (ddd, $J$ = 36.0, 13.8, 7.6 Hz, 4H), 1.45 – 1.40 (m, 1H), 1.20 (s, 6H), 1.11 (s, 6H), 1.07 (s, 3H), 1.00 (s, 3H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.5, 133.9, 131.0, 113.0, 82.9, 55.2, 44.9, 40.0, 37.3, 30.4, 27.8, 25.7, 24.8, 23.8, 21.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.21.; IR (neat): $\nu_{max}$ 2953.96 (m), 2868.65 (m), 1611.37 (s), 1511.40 (s), 1465.13 (m), 1370.15 (s), 1245.74 (s), 1142.47 (s) cm$^{-1}$. HRMS (DART) for $C_{21}H_{34}BO_3$ $[M+H]^+$: Calc'd: 345.25955, found: 345.26004. $[\alpha]^{20}_D$: -3.9 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

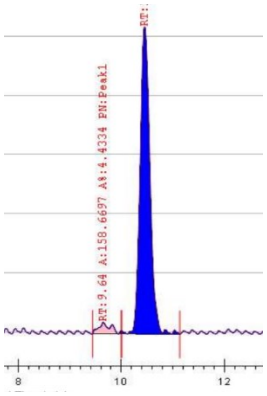
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

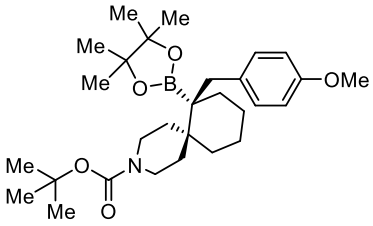
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)-2,2-dimethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 51.704 | 3260.1782 | 9.63 |
| 2 | 48.296 | 3045.2936 | 10.47 |
| Total: | 100 | 6305.4718 | |




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 4.4334 | 158.6697 | 9.64 |
| 2 | 95.5666 | 3420.3294 | 10.45 |
| Total: | 100 | 3578.9991 | |

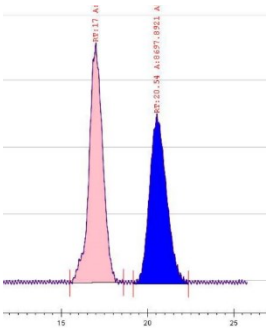


***tert*-butyl-(*R*)-7-(4-methoxybenzyl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-azaspiro[5.5]undecane-3-carboxylate** (**12**) The reaction was performed according to the general procedure *Method A* using tert-butyl 4-(5-bromohex-5-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate (**S-26**) (97.3 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 5 to 10% ethyl acetate:hexanes) to afford a clear oil (64.2 mg, 0.125 mmol, 62.3% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, $J$ = 8.6 Hz, 2H), 6.75 (d, $J$ = 8.7 Hz, 2H), 3.75 (s, 5H), 2.93 – 2.69 (m, 4H), 2.05 (td, $J$ = 13.1, 5.0 Hz, 2H), 1.87 – 1.80 (m, 1H), 1.68 – 1.63 (m, 2H), 1.50 – 1.41 (m, 14H), 1.25 – 1.21 (m, 8H), 1.04 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.6, 154.6, 132.5, 131.6, 131.1, 113.0, 83.0, 78.8, 70.8, 55.1, 40.0, 38.9, 35.7, 33.0, 32.0, 28.4, 26.1, 24.6, 24.4, 21.9, 20.8.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.86.; IR (neat): $\nu_{max}$ 2927.61 (m), 2861.13 (m), 1689.81 (m), 1511.52 (s), 1200.09 (s), 1141.98 (s) $cm^{-1}$. HRMS (DART) for $C_{29}H_{47}BNO_5$ $[M+H]^+$: Cal c'd: 500.35418, found: 500.35426. $[\alpha]^{20}_D$: 0.764 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

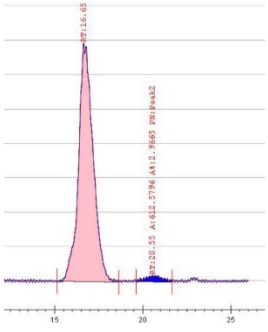
***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

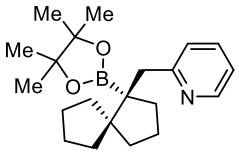
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl-(R)-7-(4-methoxybenzyl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-azaspiro[5.5]undecane-3-carboxylate*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 53.1491 | 9867.1545 | 17 |
| 2 | 46.8509 | 8697.8921 | 20.54 |
| Total: | 100 | 18565.0466 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 97.0335 | 20037.5147 | 16.65 |
| 2 | 2.9665 | 612.5796 | 20.55 |
| Total: | 100 | 20650.0943 | |

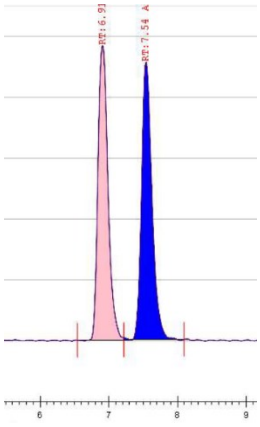


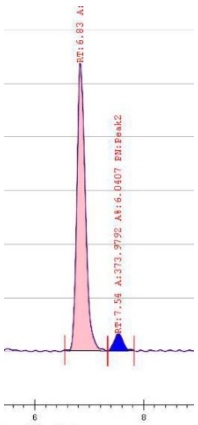
**(*R*)-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl)pyridine** (**13**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromopyridine (47.4 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (50.0 mg, 0.162 mmol, 73.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, $J$ = 4.8 Hz, 1H), 7.53 (td, $J$ = 7.6, 1.8 Hz, 1H), 7.14 (d, $J$ = 7.8 Hz, 1H), 7.09 – 7.04 (m, 1H), 3.14 (d, $J$ = 14.7 Hz, 1H), 2.63 (d, $J$ = 14.7 Hz, 1H), 1.93 – 1.79 (m, 2H), 1.71 – 1.48 (m, 9H), 1.47 – 1.34 (m, 3H), 1.24 (s, 12H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 162.1, 147.4, 136.3, 123.9, 120.8, 82.4, 56.6, 41.7, 38.1, 36.2, 33.9, 32.3, 26.0, 25.5, 24.7, 24.5, 20.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 30.94.; IR (neat) $\nu_{max}$ 2949 (s), 2869 (m), 1569 (m), 1477 (m), 1369 (s), 1299 (m), 1199 (m), 1144 (s), 1096 (m), 853 (m), 749 (m) $cm^{-1}$.; HRMS (DART) for $C_{21}H_{33}BO_2N$ $[M+H]^+$: Calc'd: 342.25989, found: 342.26071.; $[\alpha]^{20}_D$: 16.2 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

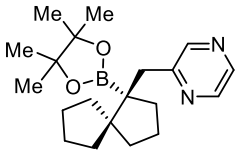
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl)pyridine.*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.5703 | 4898.5399 | 6.91 |
| 2 | 49.4297 | 4788.0586 | 7.54 |
| Total: | 100 | 9686.5985 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 93.9593 | 5817.039 | 6.83 |
| 2 | 6.0407 | 373.9792 | 7.54 |
| Total: | 100 | 6191.0182 | |

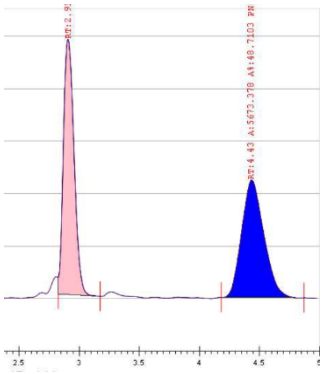


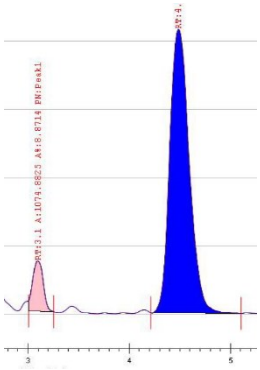
**(*R*)-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl)pyrazine** (**14**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromopyrazine (47.7 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (52.0 mg, 0.152 mmol, 76.0% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.5 Hz, 1H), 8.43 – 8.41 (m, 1H), 8.33 (d, *J* = 2.6 Hz, 1H), 3.14 (d, *J* = 14.4 Hz, 1H), 2.65 (d, *J* = 14.4 Hz, 1H), 1.98 – 1.80 (m, 2H), 1.73 – 1.55 (m, 9H), 1.51 – 1.37 (m, 3H), 1.21 (s, 6H), 1.21 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.0, 145.7, 143.2, 141.6, 83.1, 56.8, 38.6, 38.0, 36.5, 33.7, 31.7, 25.6, 25.1, 24.7, 24.5, 20.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.83.; IR (neat) $\nu_{max}$ 2948 (m), 2869 (m), 1474 (m), 1450 (m), 1388 (s), 1301 (m), 1266 (m), 1211 (s), 1142 (m), 855 (m) $cm^{-1}$.; HRMS (DART) for $C_{20}H_{32}BO_2N_2$ $[M+H]^+$: Calc'd: 343.25514, found: 343.25654.; $[\alpha]^{20}_D$: 10.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

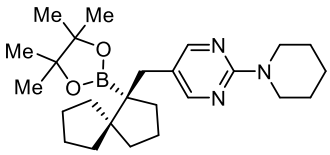
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl)pyrazine.*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 51.2897 | 5973.8169 | 2.91 |
| 2 | 48.7103 | 5673.378 | 4.43 |
| Total: | 100 | 11647.1949 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 8.8714 | 1074.8825 | 3.1 |
| 2 | 91.1286 | 11041.4039 | 4.49 |
| Total: | 100 | 12116.2864 | |

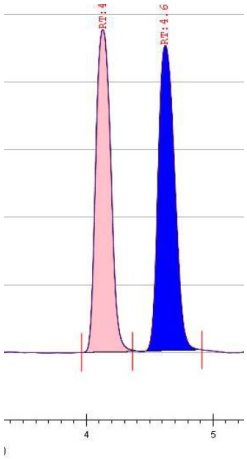


**(*R*)-2-(piperidin-1-yl)-5-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl)pyrimidine** (**15**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 5-bromo-2-(piperidin-1-yl)pyrimidine (72.6 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (58.8 mg, 0.138 mmol, 69.1% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 2H), 3.71 (dd, *J* = 6.5, 4.6 Hz, 4H), 2.66 (d, *J* = 13.6 Hz, 1H), 2.17 (d, *J* = 13.5 Hz, 1H), 1.94 – 1.32 (m, 20H), 1.19 (s, 6H), 1.08 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.9, 121.5, 83.2, 57.0, 45.2, 37.9, 36.9, 33.3, 32.4, 31.3, 25.8, 25.8, 25.1, 24.9, 24.6, 24.4, 20.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.96.; IR (neat) $\nu_{max}$ 2976 (m), 2927 (m), 1691 (s), 1451 (m), 1423 (m), 1390 (m), 1276 (m), 1247 (m), 1228 (m), 700 (m) $cm^{-1}$.; HRMS (DART) for $C_{25}H_{41}BO_2N_3$ $[M+H]^+$: Calc'd: 426.32863, found: 426.32786.; $[\alpha]^{20}_D$: -1.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

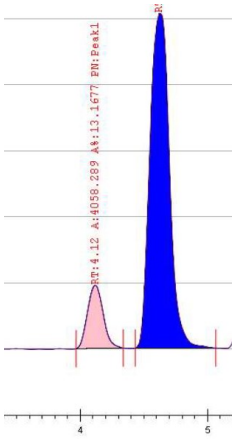
***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

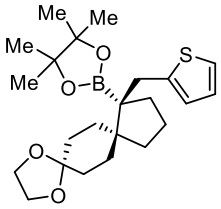
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(piperidin-1-yl)-5-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl) pyrimidine.*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.0456 | 19432.8351 | 4.13 |
| 2 | 50.9544 | 20189.1513 | 4.62 |
| Total: | 100 | 39621.9864 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 13.1677 | 4058.289 | 4.12 |
| 2 | 86.8323 | 26761.7498 | 4.62 |
| Total: | 100 | 30820.0388 | |

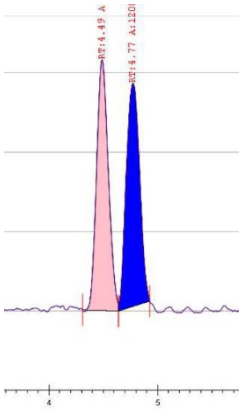


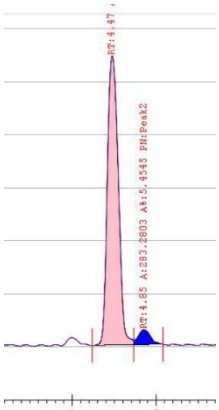
**(*R*)-4,4,5,5-tetramethyl-2-(9-(thiophen-2-ylmethyl)-1,4-dioxadispiro[4.2.4$^8$.2$^5$]tetradecan-9-yl)-1,3,2-dioxaborolane** (**16**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (82.8 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromothiophene (48.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 4% ethyl acetate:hexanes) to afford a white solid (66.3 mg, 0.159 mmol, 79.3% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.06 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.86 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.81 (dd, *J* = 3.5, 1.1 Hz, 1H), 3.97 – 3.86 (m, 4H), 3.18 (d, *J* = 14.0 Hz, 1H), 2.55 (d, *J* = 14.0 Hz, 1H), 2.08 – 1.82 (m, 2H), 1.78 – 1.47 (m, 12H), 1.20 (s, 6H), 1.15 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 144.2, 126.33, 126.28, 123.2, 109.1, 83.4, 64.3, 64.1, 48.0, 32.39, 32.37, 32.3, 32.0, 31.7, 30.5, 29.2, 25.9, 24.8, 21.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.25.; IR (neat) $\nu_{max}$ 2945 (m), 2871 (m), 1440 (m), 1372 (s), 1305 (m), 1209 (s), 1165 (m), 1107 (m), 1039 (m), 690 (m) cm$^{-1}$.; HRMS (DART) for $C_{23}H_{36}BO_4S$ $[M+H]^+$: Calc'd: 419.24219, found: 419.24250.; $[\alpha]^{20}_D$: 8.6 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

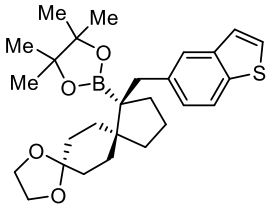
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(9-(thiophen-2-ylmethyl)-1,4-dioxadispiro[4.2.48.25]tetradecan-9-yl)-1,3,2-dioxaborolane*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.6955 | 1186.1778 | 4.49 |
| 2 | 50.3045 | 1200.715 | 4.77 |
| Total: | 100 | 2386.8928 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 94.5455 | 4910.1995 | 4.47 |
| 2 | 5.4545 | 283.2803 | 4.85 |
| Total: | 100 | 5193.4798 | |

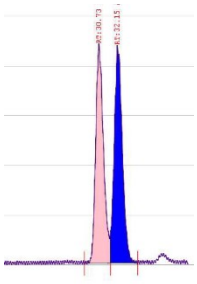


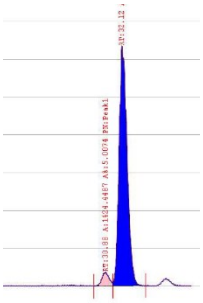
**(*R*)-2-(9-(benzo[b]thiophen-5-ylmethyl)-1,4-dioxadispiro[4.2.4$^8$.2$^5$]tetradecan-9-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**17**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-20**) (82.8 mg, 0.2 mmol, 1j.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromothiophene (48.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 4% ethyl acetate:hexanes) to afford a white solid (68.6 mg, 0.146 mmol, 73.2% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.68 (m, 2H), 7.37 (d, $J$ = 5.4 Hz, 1H), 7.26 – 7.20 (m, 1H), 3.98 – 3.87 (m, 4H), 3.09 (d, $J$ = 12.9 Hz, 1H), 2.44 (d, $J$ = 12.9 Hz, 1H), 2.01 (ddd, $J$ = 14.9, 13.3, 4.1 Hz, 1H), 1.89 – 1.48 (m, 13H), 1.23 (s, 6H), 1.10 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 139.7, 137.8, 137.2, 127.4, 126.2, 125.1, 123.7, 121.6, 109.2, 64.3, 64.1, 48.2, 37.4, 34.0, 32.5, 32.27, 32.0, 31.5, 29.6, 29.4, 26.0, 24.9, 24.8, 21.2.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.54.; IR (neat) $\nu_{max}$ 2940 (m), 2870 (m), 1463 (m), 1371 (s), 1330 (m), 1208 (s), 1164 (m), 1038 (m), 966 (m), 876 (m) cm$^{-1}$.; HRMS (DART) for $C_{27}H_{38}BO_4S$ $[M+H]^+$: Calc'd: 469.25784, found: 469.25850.; $[\alpha]^{20}_D$: -14.0 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

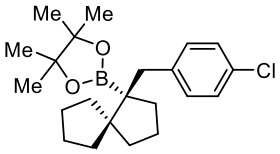
Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-(9-(benzo[b]thiophen-5-ylmethyl)-1,4-dioxadispiro[4.2.48.25]tetradecan-9-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.*





| Peak No | % Area | Area | RT (min) | Peak No | % Area | Area | RT (min) |
|---|---|---|---|---|---|---|---|
| 1 | 49.2836 | 9238.8549 | 30.73 | 1 | 5.0074 | 1424.4487 | 30.88 |
| 2 | 50.7164 | 9507.4523 | 32.15 | 2 | 94.9926 | 27022.4296 | 32.12 |
| Total: | 100 | 18746.3072 | | Total: | 100 | 28446.8783 | |

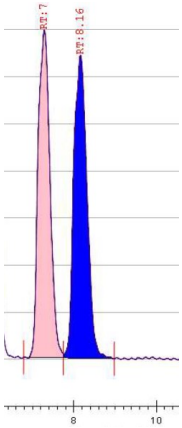


**(*R*)-2-(1-(4-chlorobenzyl)spiro[4.4]nonan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**18**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 1-bromo-4-chlorobenzene (57.4 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford clear oil (57.4 mg, 0.138 mmol, 69.1% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 2H), 3.71 (dd, *J* = 6.5, 4.6 Hz, 4H), 2.66 (d, *J* = 13.6 Hz, 1H), 2.17 (d, *J* = 13.5 Hz, 1H), 1.94 – 1.32 (m, 20H), 1.19 (s, 6H), 1.08 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.9, 121.5, 83.2, 57.0, 45.2, 37.9, 36.9, 33.3, 32.4, 31.3, 25.8, 25.8, 25.1, 24.9, 24.6, 24.4, 20.9.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.96.; IR (neat) $\nu_{max}$ 2976 (m), 2927 (m), 1691 (s), 1451 (m), 1423 (m), 1390 (m), 1276 (m), 1247 (m), 1228 (m), 700 (m) $cm^{-1}$.; HRMS (DART) for $C_{25}H_{41}BO_2N_3$ $[M+H]^+$: Calc'd: 426.32863, found: 426.32786.; $[\alpha]^{20}_D$: -1.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand.

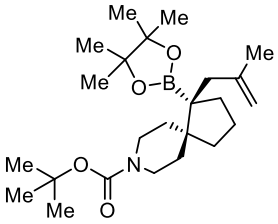
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(piperidin-1-yl)-5-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[4.4]nonan-1-yl)methyl) pyrimidine.*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.1556 | 13839.9307 | 7.28 |
| 2 | 50.8444 | 14315.4227 | 8.16 |
| Total: | 100 | 28155.3534 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 9.7961 | 3055.6942 | 7.02 |
| 2 | 90.2039 | 28137.2384 | 7.88 |
| Total: | 100 | 31192.9326 | |

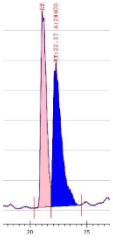


***tert*-butyl-(*R*)-1-(2-methylallyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-azaspiro[4.5]decane-8-carboxylate** (**19**) The reaction was performed according to the general procedure *Method A* using tert-butyl 4-(4-bromopent-4-en-1-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate (**S-25**) (91.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), isopropylbromide (36.3 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (59.1 mg, 0.140 mmol, 70.5% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 4.70 (d, *J* = 18.3 Hz, 2H), 3.99 (d, *J* = 31.8 Hz, 2H), 2.72 (d, *J* = 60.9 Hz, 2H), 2.27 (d, *J* = 14.1 Hz, 1H), 1.94 – 1.88 (m, 1H), 1.83 (d, *J* = 14.1 Hz, 1H), 1.71 (d, *J* = 21.8 Hz, 4H), 1.67 – 1.54 (m, 4H), 1.44 (s, 10H), 1.40 – 1.35 (m, 2H), 1.23 (d, *J* = 6.9 Hz, 13H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.7, 145.0, 111.9, 83.1, 78.9, 47.5, 39.2, 30.5, 28.4, 25.6, 25.1, 25.1, 24.8, 24.0, 21.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ33.21.; IR (neat): $\nu_{max}$ 2975.57 (m), 2940.07 (m), 2871.95 (m), 1694.21 (s), 1423.97 (s), 1389.92 (s), 1144.73 $cm^{-1}$. HRMS (DART) for $C_{24}H_{43}BNO_4$ $[M+H]^+$: Calc'd: 420.32797, found: 420.32682. $[\alpha]^{20}_D$: 0.764 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

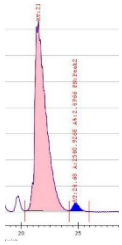
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above racemic Phox-L10 as the ligand. In order to enhance the UV absorbance of the product, the nitrogen on the pipyridine was deprotected by stirring it with 0.1 equiv. TFA in THF at 60 °C for 3 hours. Then the nitrogen was acylated with benzoyl chloride. Enantioselectivity was determined by chiral SFC.

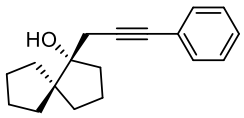
*Chiral SFC (OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl-(R)-1-(2-methylallyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-azaspiro[4.5]decane-8-carboxylate.*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 47.8485 | 22570.6159 | 21.05 |
| 2 | 52.1515 | 24600.3396 | 22.27 |
| Total: | 100 | 47170.9555 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 97.5034 | 99233.4778 | 21.49 |
| 2 | 2.4966 | 2540.9268 | 24.68 |
| Total: | 100 | 101774.4046 | |

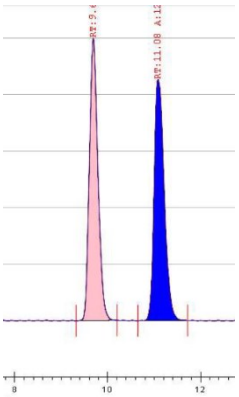


**(*S*)-1-(3-phenylprop-2-yn-1-yl)spiro[4.4]nonan-1-ol** (**20'**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), (bromoethynyl)benzene (54.0mg, 0.3 mmol, 1.5 equiv.). For easier purification, the crude material containing substrate **20** was oxidized to alcohol **20'** by treating with a mixture of 1.0 mL THF, 0.5 mL 30% hydrogen peroxide water solution and 0.5 mL of 3 M NaOH at 60 ºC for 3 hours. The crude mixture was then extracted with EtOAc three times and concentrated on vaccum. The crude product was purified by silica gel chromatography (eluted with 1 to 5% ethyl acetate:hexanes) to afford clear oil (42.4 mg, 0.166 mmol, 83.1% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H), 7.33 – 7.27 (m, 3H), 2.73 – 2.61 (m, 2H), 1.98 – 1.36 (m, 14H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 131.8, 128.4, 128.0, 123.6, 86.9, 83.4, 82.3, 56.7, 38.3, 38.2, 34.6, 32.4, 27.9, 25.3, 24.8, 19.1.; IR (neat) $\nu_{max}$ 3476 (br), 2953 (s), 2870 (m), 1714 (m), 1490 (m), 1360 (m), 1176 (m), 756 (m), 711 (m), 691 (m) $cm^{-1}$.; HRMS (DART) for $C_{18}H_{21}$ $[M+H-H_2O]^+$: Calc'd: 237.16378, found: 237.16505.; $[\alpha]^{20}_D$: -6.8 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

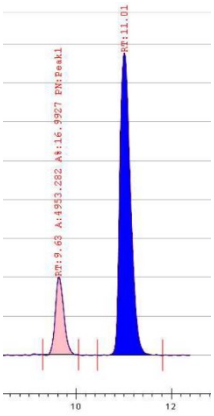
***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand.

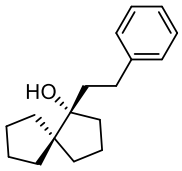
*Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(3-phenylprop-2-yn-1-yl)spiro[4.4]nonan-1-ol.*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.7821 | 12722.5973 | 9.69 |
| 2 | 50.2179 | 12833.9877 | 11.08 |
| Total: | 100 | 25556.585 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 16.9927 | 4953.282 | 9.63 |
| 2 | 83.0073 | 24196.1314 | 11.01 |
| Total: | 100 | 29149.4134 | |

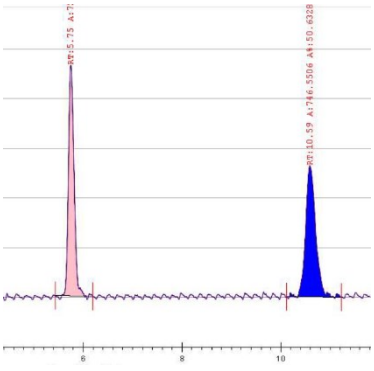


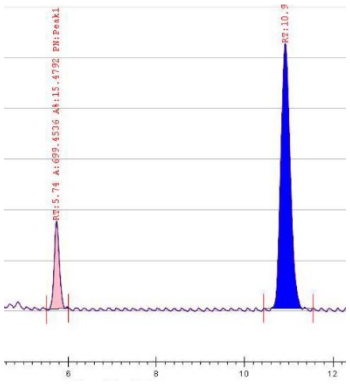
**(*S*)-1-phenethylspiro[4.4]nonan-1-ol** (**21'**) The reaction was performed according to the general procedure *Method A* using 2-(1-(4-bromopent-4-en-1-yl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-20**) (68.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), benzylbromide (51.3 mg, 0.3 mmol, 1.5 equiv.). For easier purification, the crude material containing **21** was oxidized to alcohol **21'** by treating with a mixture of 1.0 mL THF, 0.5 mL 30% hydrogen peroxide water solution and 0.5 mL of 3 M NaOH at 60 ºC for 3 hours. The crude mixture was then extracted with EtOAc three times and concentrated on vaccum. The crude product was purified by silica gel chromatography (eluted with 1 to 5% ethyl acetate:hexanes) to afford clear oil (42.4 mg, 0.166 mmol, 83.1% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.24 – 7.16 (m, 3H), 2.93 – 2.86 (m, 1H), 2.72 – 2.62 (m, 1H), 1.87 – 1.67 (m, 8H), 1.66 – 1.54 (m, 7H), 1.50 – 1.38 (m, 1H), 1.28 – 1.18 (m, 1H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 143.3, 128.5, 125.8, 84.4, 57.8, 38.0, 37.8, 36.7, 34.6, 32.2, 31.1, 25.5, 25.1, 19.4.; IR (neat) $\nu_{max}$ 3451 (br), 2951 (s), 2865 (m), 1452 (m), 699 (m), 539 (m) $cm^{-1}$.; HRMS (DART) for $C_{17}H_{23}$ [M+H-$H_2O$]$^+$: Calc'd: 227.17943, found: 227.17968. ; $[\alpha]^{20}_D$: 9.8 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand.

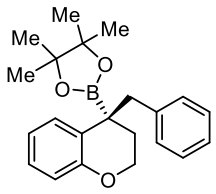
*Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-phenethylspiro[4.4]nonan-1-ol.*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.3672 | 727.8903 | 5.75 |
| 2 | 50.6328 | 746.5506 | 10.59 |
| Total: | 100 | 1474.4409 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 15.4792 | 699.4536 | 5.74 |
| 2 | 84.5208 | 3819.222 | 10.92 |
| Total: | 100 | 4518.6756 | |



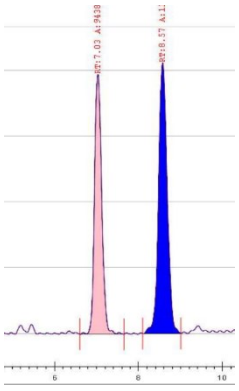
***(S)*-2-(4-benzylchroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (24)**

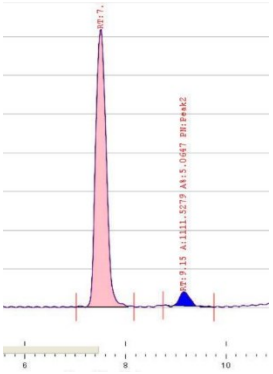
The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-39**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford a wihte solid (51.0 mg, 0.145 mmol, 72.8% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.49 (dd, $J$ = 7.9, 1.7 Hz, 1H), 7.25 – 7.16 (m, 5H), 7.10 – 7.04 (m, 1H), 6.88 (t, $J$ = 7.5 Hz, 1H), 6.80 (d, $J$ = 8.1 Hz, 1H), 4.21 (ddd, $J$ = 10.8, 8.3, 2.6 Hz, 1H), 4.10 (ddd, $J$ = 10.4, 6.7, 3.2 Hz, 1H), 3.44 (d, $J$ = 13.3 Hz, 1H), 2.82 (d, $J$ = 13.3 Hz, 1H), 1.99 (ddd, $J$ = 14.0, 6.7, 2.7 Hz, 1H), 1.82 (ddd, $J$ = 14.0, 8.2, 3.1 Hz, 1H), 1.21 (s, 6H), 1.14 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.6, 139.3, 130.1, 129.5, 127.8, 126.7, 126.6, 126.1, 126.0, 119.9, 117.0, 83.6, 63.6, 45.0, 30.2, 29.0, 24.8, 24.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.37.; IR (neat): $\nu_{max}$ 2977.43 (m), 2930.77 (m), 1602.75 (s), 1486.70 (s), 1361.89 (m), 1318.26 (s), 1142.54 (s) cm$^{-1}$. HRMS (DART) for $C_{22}H_{28}BO_3$ $[M+H]^+$: Calc'd: 351.21260, found: 351.21293. $[\alpha]^{20}_D$: 8.8 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

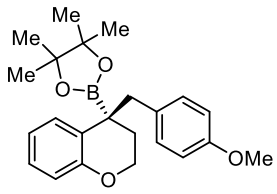
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxybenzyl)-2,2-dimethylcyclopentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane.*





| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 44.5513 | 9438.8406 | 7.03 |
| 2 | 55.4487 | 11747.6107 | 8.57 |
| Total: | 100 | 21186.4513 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 94.9353 | 20835.0457 | 7.51 |
| 2 | 5.0647 | 1111.5279 | 9.15 |
| Total: | 100 | 21946.5736 | |

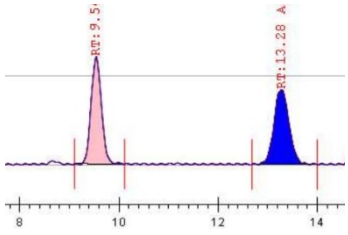


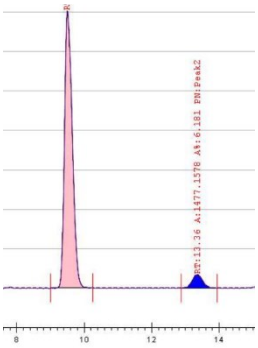
***(S)*-2-(4-(4-methoxybenzyl)chroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**25**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-39**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (61.9 mg, 0.163 mmol, 81.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.08 – 7.03 (m, 1H), 6.90 – 6.84 (m, 1H), 6.81 – 6.74 (m, 3H), 4.20 (ddd, *J* = 10.9, 8.2, 2.8 Hz, 1H), 4.09 (ddd, *J* = 10.5, 6.8, 3.2 Hz, 1H), 3.36 (d, *J* = 13.5 Hz, 1H), 2.76 (d, *J* = 13.4 Hz, 1H), 1.99 (ddd, *J* = 14.0, 6.8, 2.8 Hz, 1H), 1.81 (ddd, *J* = 14.0, 8.1, 3.2 Hz, 1H), 1.17 (d, *J* = 28.9 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.9, 154.6, 131.4, 131.1, 129.5, 126.8, 126.5, 119.8, 116.9, 113.2, 83.6, 63.6, 55.1, 44.0, 28.9, 24.8, 24.33, 24.31.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.15.; IR (neat): $\nu_{max}$ 2975.87 (m), 2931.23 (m), 1610.35 (m), 1511.49 (s), 1300.85 (s), 1142.11 (s) cm$^{-1}$. HRMS (DART) for $C_{23}H_{30}BO_4$ $[M+H]^+$: Calc'd: 381.22317, found: 381.22313. $[\alpha]^{20}_D$: 6.3 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

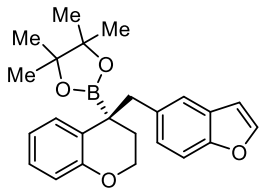
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (R)-2-(4-(4-methoxybenzyl)chroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 49.2722 | 3486.8281 | 9.54 |
| 2 | 50.7278 | 3589.8429 | 13.28 |
| Total: | 100 | 7076.671 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 93.819 | 22421.3792 | 9.5 |
| 2 | 6.181 | 1477.1578 | 13.36 |
| Total: | 100 | 23898.537 | |

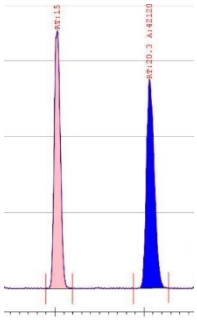


***(S)*-2-(4-(benzofuran-5-ylmethyl)chroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (26)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-39**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 5-bromobenzofuran (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (61.9 mg, 0.163 mmol, 81.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 2.1 Hz, 1H), 7.51 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.17 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.11 – 7.04 (m, 1H), 6.92 – 6.86 (m, 1H), 6.80 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.68 (q, *J* = 1.1 Hz, 1H), 4.21 (ddd, *J* = 10.9, 8.0, 2.7 Hz, 1H), 4.11 (ddd, *J* = 10.6, 6.8, 3.2 Hz, 1H), 3.54 (d, *J* = 13.4 Hz, 1H), 2.89 (d, *J* = 13.4 Hz, 1H), 1.99 (ddd, *J* = 14.2, 6.9, 2.8 Hz, 1H), 1.85 (ddd, *J* = 14.1, 8.1, 3.2 Hz, 1H), 1.21 (s, 6H), 1.14 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.7, 153.8, 145.0, 133.8, 129.6, 127.2, 126.9, 126.7, 126.6, 122.5, 120.0, 117.1 110.5, 106.4, 83.7, 63.7, 45.0, 29.1, 24.9, 24.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 31.89.; IR (neat): $\nu_{max}$23975.67 (m), 2923.53 (m), 2853.98 (m), 2380.35 (s), 1487.07 (s), 1142.77 (s) $cm^{-1}$. HRMS (DART) for $C_{24}H_{28}BO_4$ $[M+H]^+$: Calc'd: 391.20752, found: 391.20860. $[\alpha]^{20}_D$: 0.764 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

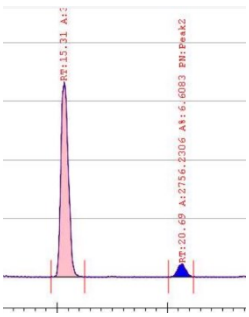
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

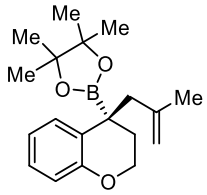
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (R)-2-(4-(benzofuran-5-ylmethyl)chroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 49.3807 | 41089.8392 | 15.14 |
| 2 | 50.6193 | 42120.502 | 20.3 |
| Total: | 100 | 83210.3412 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 93.3917 | 38952.2242 | 15.31 |
| 2 | 6.6083 | 2756.2306 | 20.69 |
| Total: | 100 | 41708.4548 | |

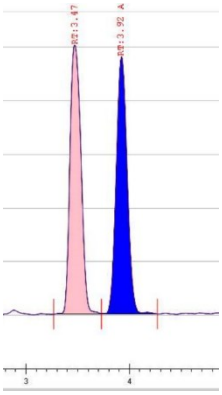


***(S)*-4,4,5,5-tetramethyl-2-(4-(2-methylallyl)chroman-4-yl)-1,3,2-dioxaboro lane** (**27**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-39**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), isopropylbromide (36.3 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 2% ethyl acetate:hexanes) to afford a clear oil (41.5 mg, 0.132 mmol, 66.2% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.08 – 6.97 (m, 1H), 6.88 – 6.71 (m, 2H), 4.75 (d, *J* = 43.1 Hz, 2H), 4.19 (dddd, *J* = 52.5, 10.5, 7.7, 2.9 Hz, 2H), 2.86 (d, *J* = 14.0 Hz, 1H), 2.30 (d, *J* = 14.0 Hz, 1H), 2.11 (ddd, *J* = 14.1, 6.3, 2.6 Hz, 1H), 1.83 (ddd, *J* = 13.9, 8.6, 3.2 Hz, 1H), 1.66 (s, 3H), 1.18 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.5, 143.5, 129.2, 127.2, 126.4, 119.9, 116.9, 113.4, 83.5, 63.8, 47.1, 30.2, 29.6, 28.5, 24.7, 24.7, 24.4, 23.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.05.; IR (neat): $\nu_{max}$ 2976.22 (m), 2924.65 (m), 2853.57 (s), 1379.06 (s), 1143.18 (s) $cm^{-1}$. HRMS (DART) for $C_{19}H_{28}BO_3$ $[M+H]^+$: Calc'd: 315.21260, found: 315.21359. $[\alpha]^{20}_D$: 7.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

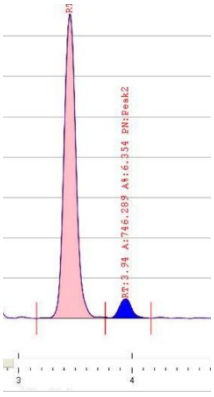
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

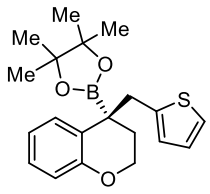
*Chiral SFC (OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (R)-4,4,5,5-tetramethyl-2-(4-(2-methylallyl)chroman-4-yl)-1,3,2-dioxaboro lane.*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 51.1688 | 3676.6925 | 3.47 |
| 2 | 48.8312 | 3508.7274 | 3.92 |
| Total: | 100 | 7185.4199 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 93.646 | 10998.8975 | 3.45 |
| 2 | 6.354 | 746.289 | 3.94 |
| Total: | 100 | 11745.1865 | |

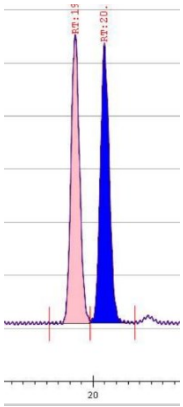


***(R)*-4,4,5,5-tetramethyl-2-(4-(thiophen-2-ylmethyl)chroman-4-yl)-1,3,2-dioxaborolane** (**28**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenoxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (**S-39**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromothiophene (48.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (38.2 mg, 0.107 mmol, 53.6% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.8 Hz, 1H), 7.11 – 7.05 (m, 2H), 6.90 – 6.85 (m, 2H), 6.79 (dd, *J* = 11.1, 5.7 Hz, 2H), 4.22 (ddd, *J* = 11.0, 8.2, 2.9 Hz, 1H), 4.08 (ddd, *J* = 10.6, 6.7, 3.3 Hz, 1H), 3.56 (d, *J* = 14.6 Hz, 1H), 3.09 (d, *J* = 14.6 Hz, 1H), 2.08 – 2.04 (m, 1H), 1.84 (dq, *J* = 11.6, 4.2, 3.2 Hz, 1H), 1.20 (d, *J* = 16.3 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.8, 141.3, 129.0, 126.8, 126.7, 126.2, 126.1, 123.8, 120.0, 117.1, 83.8, 63.5, 38.9, 29.6, 28.7, 24.9, 24.3.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.43.; IR (neat): $\nu_{max}$ 2923.46 (m), 2852.77 (m), 1716.53 (m), 1606.13 (s), 148.83 (s), 1222.41 (s) $cm^{-1}$. HRMS (DART) for $C_{20}H_{26}BO_3S$ $[M+H]^+$: Calc'd: 357.16902, found: 357.17080. $[\alpha]^{20}_D$: 7.7 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

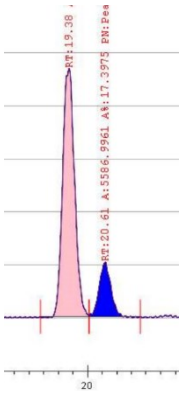
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

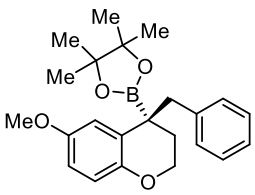
*Chiral SFC (OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-4,4,5,5-tetramethyl-2-(4-(thiophen-2-ylmethyl)chroman-4-yl)-1,3,2-dioxaborolane.*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 49.8823 | 14140.3943 | 19.24 |
| 2 | 50.1177 | 14207.1266 | 20.49 |
| Total: | 100 | 28347.5209 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 82.6025 | 26526.6991 | 19.38 |
| 2 | 17.3975 | 5586.9961 | 20.61 |
| Total: | 100 | 32113.6952 | |

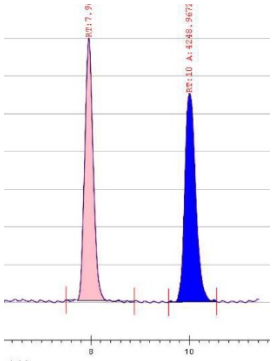


***(S)*-2-(4-benzyl-6-methoxychroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**29**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromo-4-methoxyphenoxy)but-1-en-2-yl)-4,4,5,5-tetramethy l-1,3,2-dioxaborolane (**S-41**) (76.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 3% ethyl acetate:hexanes) to afford a colorless oil (42.4 mg, 0.111 mmol, 55.7% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 1H), 7.24 – 7.15 (m, 5H), 6.49 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.36 (d, *J* = 2.7 Hz, 1H), 4.20 (ddd, *J* = 10.9, 8.1, 2.8 Hz, 1H), 4.08 (ddd, *J* = 10.5, 6.9, 3.2 Hz, 1H), 3.76 (s, 3H), 3.39 (d, *J* = 13.2 Hz, 1H), 2.77 (d, *J* = 13.2 Hz, 1H), 1.97 (ddd, *J* = 14.0, 6.9, 2.8 Hz, 1H), 1.79 (ddd, *J* = 14.1, 8.1, 3.2 Hz, 1H), 1.20 (s, 6H), 1.14 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.6, 155.6, 139.6, 130.4, 128.1, 126.3, 119.1, 107.3, 101.7, 83.8, 64.0, 55.3, 45.3, 29.2, 25.1, 24.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.09.; IR (neat) $\nu_{max}$ 2975 (m), 1614 (m), 1500 (s), 1443 (m), 1379 (m), 1315 (m), 1280 (s), 1196 (s), 1101 (m), 797 (m) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{30}BO_4$ $[M+H]^+$: Calc'd: 381.22317, found: 381.22408.; $[\alpha]^{20}_D$: 5.0 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

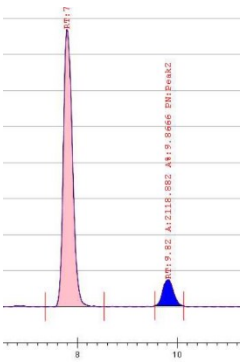
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

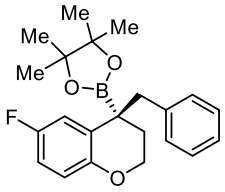
*Chiral SFC (OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-benzyl-6-methoxychroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane..*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.319 | 4134.7741 | 7.96 |
| 2 | 50.681 | 4248.9672 | 10 |
| Total: | 100 | 8383.7413 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 90.1334 | 19356.469 | 7.79 |
| 2 | 9.8666 | 2118.882 | 9.82 |
| Total: | 100 | 21475.351 | |

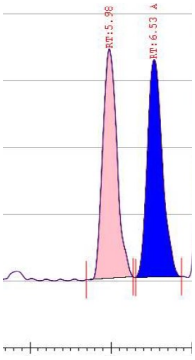


***(S)*-2-(4-benzyl-6-fluorochroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (30)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromo-4-fluoro)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-43**) (74.0 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 3% ethyl acetate:hexanes) to afford a colorless oil (33.8 mg, 0.092 mmol, 45.9% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 1H), 7.25 – 7.18 (m, 5H), 6.81 – 6.69 (m, 2H), 4.15 (ddd, *J* = 11.0, 8.2, 2.8 Hz, 1H), 4.06 (ddd, *J* = 10.8, 6.7, 3.3 Hz, 1H), 3.36 (d, *J* = 13.3 Hz, 1H), 2.81 (d, *J* = 13.3 Hz, 1H), 1.97 (ddd, *J* = 14.1, 6.7, 2.8 Hz, 1H), 1.80 (ddd, *J* = 14.1, 8.2, 3.3 Hz, 1H), 1.21 (s, 6H), 1.15 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.0, 156.0, 150.9, 139.1, 133.9 (d, *J* = 19.5 Hz), 132.2, 129.3 (d, *J* = 334.2 Hz), 128.7 (d, *J* = 36.3 Hz), 126.5, 117.9 (d, *J* = 8.1 Hz), 115.6 (d, *J* = 23.3 Hz), 113.7 (d, *J* = 23.4 Hz), 84.1, 64.0, 45.2, 29.0, 25.07, 24.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.14.; $^{19}$F NMR (470 MHz, $CDCl_3$) δ -124.15 (ddd, *J* = 9.9, 7.5, 5.1 Hz).; IR (neat) $\nu_{max}$ 2977 (m), 1491 (s), 1445 (m), 1353 (m), 1257 (m), 1215 (s), 1178 (m), 856 (m), 811 (m) $cm^{-1}$.; HRMS (DART) for $C_{22}H_{27}BO_3F$ $[M+H]^+$: Calc'd: 369.20318, found: 369.20496.; $[\alpha]^{20}_D$: -26.4 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

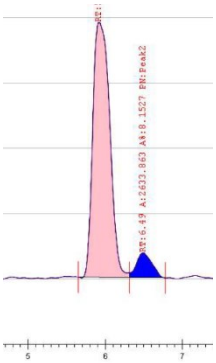
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

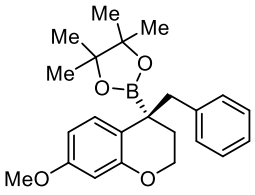
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-benzyl-6-fluorochroman-4-yl)-4,4,5,5-tetramethyl-1,3, 2-dioxaborolane..*



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 49.885 | 8371.7216 | 5.98 |
| 2 | 50.115 | 8410.3123 | 6.53 |
| Total: | 100 | 16782.0339 | |



| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 91.8473 | 29672.8003 | 5.91 |
| 2 | 8.1527 | 2633.863 | 6.49 |
| Total: | 100 | 32306.6633 | |

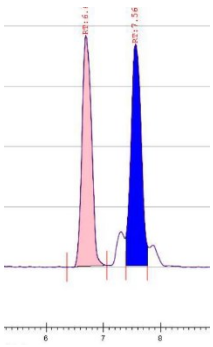


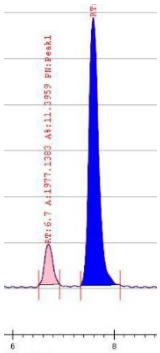
***(S)*-2-(4-benzyl-7-methoxychroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (31)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromo-5-methoxyphenoxy)but-1-en-2-yl)-4,4,5,5-tetramethy l-1,3,2-dioxaborolane (**S-40**) (76.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 3% ethyl acetate:hexanes) to afford a colorless oil (64.1 mg, 0.169 mmol, 84.3% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 1H), 7.24 – 7.15 (m, 5H), 6.49 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.36 (d, *J* = 2.7 Hz, 1H), 4.20 (ddd, *J* = 10.9, 8.1, 2.8 Hz, 1H), 4.08 (ddd, *J* = 10.5, 6.9, 3.2 Hz, 1H), 3.76 (s, 3H), 3.39 (d, *J* = 13.2 Hz, 1H), 2.77 (d, *J* = 13.2 Hz, 1H), 1.97 (ddd, *J* = 14.0, 6.9, 2.8 Hz, 1H), 1.79 (ddd, *J* = 14.1, 8.1, 3.2 Hz, 1H), 1.20 (s, 6H), 1.14 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 158.6, 155.6, 139.6, 130.4, 128.1, 126.3, 119.1, 107.3, 101.7, 83.8, 64.0, 55.3, 45.3, 29.2, 25.1, 24.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.09.; IR (neat) $\nu_{max}$ 2975 (m), 1614 (m), 1500 (s), 1443 (m), 1379 (m), 1315 (m), 1280 (s), 1196 (s), 1101 (m), 797 (m) $cm^{-1}$.; HRMS (DART) for $C_{23}H_{30}BO_4$ $[M+H]^+$: Calc'd: 381.22317, found: 381.22408.; $[\alpha]^{20}_D$: 5.0 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

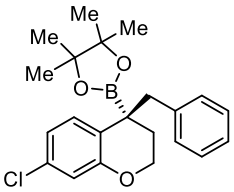
Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

*Chiral SFC (OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-benzyl-7-methoxychroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane*





| Peak No | % Area | Area | RT (min) | Peak No | % Area | Area | RT (min) |
|---|---|---|---|---|---|---|---|
| 1 | 49.029 | 22007.5744 | 6.69 | 1 | 11.3959 | 1977.1383 | 6.7 |
| 2 | 50.971 | 22879.3084 | 7.56 | 2 | 88.6041 | 15372.4312 | 7.59 |
| Total: | 100 | 44886.8828 | | Total: | 100 | 17349.5695 | |

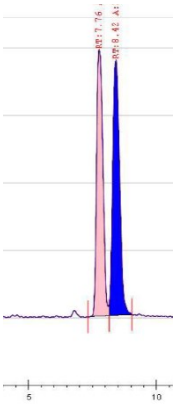


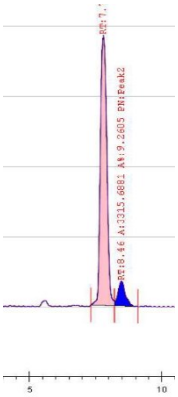
***(S)*-2-(4-benzyl-7-chlorochroman-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (32)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromo-5-chloro)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-diox aborolane (**S-42**) (77.2 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 3% ethyl acetate:hexanes) to afford a colorless oil (50.3 mg, 0.131 mmol, 65.5% yield). $^{1}$H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 2.6 Hz, 1H), 7.26 – 7.17 (m, 5H), 7.01 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.72 (d, *J* = 8.7 Hz, 1H), 4.17 (ddd, *J* = 10.9, 8.1, 2.8 Hz, 1H), 4.07 (ddd, *J* = 10.6, 6.9, 3.2 Hz, 1H), 3.38 (d, *J* = 13.3 Hz, 1H), 2.80 (d, *J* = 13.3 Hz, 1H), 1.97 (ddd, *J* = 14.1, 6.9, 2.8 Hz, 1H), 1.79 (ddd, *J* = 14.1, 8.1, 3.2 Hz, 1H), 1.22 (s, 6H), 1.15 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 153.5, 139.1, 130.4, 129.4, 128.7, 128.2, 126.9, 126.5, 124.8, 118.6, 84.2, 63.9, 45.1, 28.7, 25.1, 24.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.09.; IR (neat) $\nu_{max}$ 2976 (m), 1483 (s), 1467 (m), 1371 (m), 1361 (m), 1322 (m), 1227 (s), 849 (m), 726 (m) $cm^{-1}$.; HRMS (DART) for $C_{22}H_{27}BO_3Cl$ $[M+H]^+$: Calc'd: 385.17363, found: 385.17405.; $[\alpha]^{20}_D$: -8.4 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

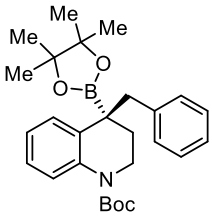
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-benzyl-7-chlorochroman-4-yl)-4,4,5,5-tetramethyl-1,3, 2-dioxaborolane*





| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 48.7122 | 33761.8693 | 7.76 |
| 2 | 51.2878 | 35547.0109 | 8.42 |
| Total: | 100 | 69308.8802 | |

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 90.7395 | 32488.8701 | 7.79 |
| 2 | 9.2605 | 3315.6881 | 8.46 |
| Total: | 100 | 35804.5582 | |

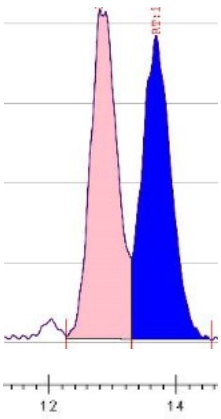


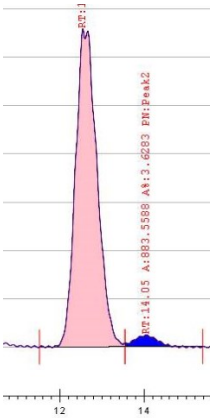

***tert-butyl (S)-4-benzyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydroquinoline-1(2H)-carboxylate*** (**33**) The reaction was performed according to the general procedure *Method B* using **S-49** (74.0 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 1 to 3% ethyl acetate:hexanes) to afford a colorless oil (53.1 mg, 0.142 mmol, 70.9% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.49 (m, 2H), 7.24 – 7.10 (m, 6H), 7.05 (dd, *J* = 7.7, 1.4 Hz, 1H), 3.74 – 3.61 (m, 2H), 3.36 (d, *J* = 13.4 Hz, 1H), 2.88 (d, *J* = 13.3 Hz, 1H), 1.96 (ddd, *J* = 13.5, 5.9, 4.0 Hz, 1H), 1.73 – 1.69 (m, 1H), 1.47 (s, 9H), 1.19 (s, 6H), 1.13 (s, 6H).; $^{13}$C NMR (151 MHz, $CDCl_3$) δ 153.7, 139.3, 138.7, 133.8, 130.3, 130.2, 128.4, 127.8, 126.1, 125.1, 124.7, 123.2, 115.3, 83.7, 80.3, 44.6, 42.3, 30.2, 29.7, 28.4, 24.9, 24.7, 24.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.14.;; IR (neat) $\nu_{max}$ 2975 (m), 1493 (s), 1771 (m), 1523 (m), 1115 (m), 1015 (s), 1008 (m) $cm^{-1}$.; HRMS (DART) for $C_{27}H_{37}BNO_4$ $[M+H]^+$: Calc'd: 450.27374, found: 450.27401.; $[\alpha]^{20}_D$: -21.0 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with a mixture of (R) and (S) Phox-L10 as the ligand. Enantioselectivity was determined by chiral SFC.

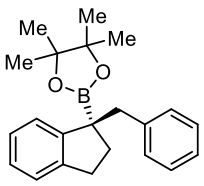
*Chiral SFC (OJ-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-benzyl-6-fluorochroman-4-yl)-4,4,5,5-tetramethyl-1,3, 2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.6013 | 16280.3312 | 12.89 |
| 2 | 49.3987 | 15893.416 | 13.93 |
| Total: | 100 | 32173.7472 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 96.3717 | 23468.0348 | 12.54 |
| 2 | 3.6283 | 883.5588 | 14.05 |
| Total: | 100 | 24351.5936 | |

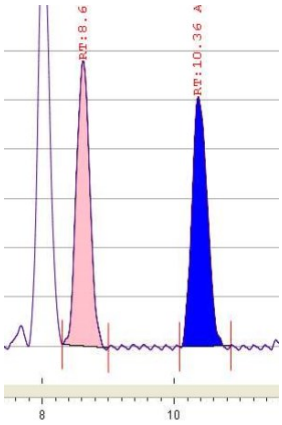


***(R)*-2-(1-benzyl-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (34)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**40**) (67.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (44.3 mg, 0.133 mmol, 66.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, $J$ = 7.4 Hz, 1H), 7.21 – 7.08 (m, 8H), 3.27 (d, $J$ = 13.3 Hz, 1H), 2.84 (dt, $J$ = 15.2, 7.4 Hz, 1H), 2.74 – 2.68 (m, 2H), 2.24 (ddd, $J$ = 12.4, 8.6, 6.2 Hz, 1H), 1.94 (ddd, $J$ = 12.5, 8.5, 6.4 Hz, 1H), 1.14 (d, $J$ = 10.6 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.45, 144.09, 140.48, 129.82, 127.75, 125.93, 125.90, 125.80, 124.38, 124.30, 83.42, 43.69, 33.36, 31.38, 24.78, 24.76, 24.51.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ32.33.; IR (neat): $\nu_{max}$ 2977.10 (m), 2928.95 (m), 1705.53 (s), 1454.41 (s), 1141.71 (s) cm$^{-1}$. HRMS (DART) for $C_{22}H_{27}BO_2$ $[M+H]^+$: Calc'd: 335.26612, found: 335.26590. $[\alpha]^{20}_D$: 7.5 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

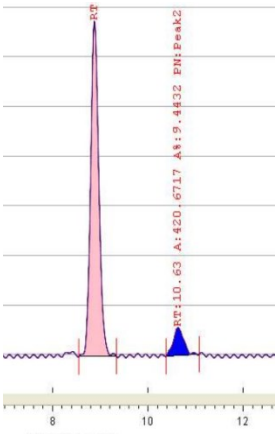
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

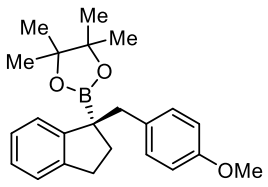
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-2-(1-benzyl-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.*




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.1272 | 1652.0006 | 8.62 |
| 2 | 49.8728 | 1643.618 | 10.36 |
| Total: | 100 | 3295.6186 | |




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 90.5568 | 4034.0906 | 8.87 |
| 2 | 9.4432 | 420.6717 | 10.63 |
| Total: | 100 | 4454.7623 | |

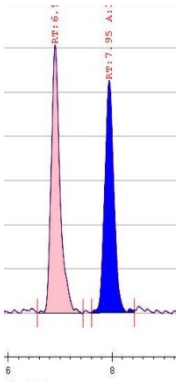


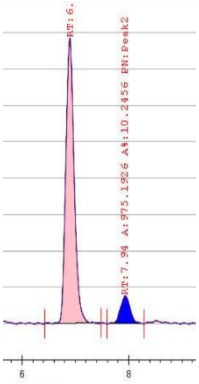

***(R)*-2-(1-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**35**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**40**) (67.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (51.6 mg, 0.141 mmol, 70.6% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.19 – 7.02 (m, 5H), 6.75 (d, *J* = 8.3 Hz, 2H), 3.78 (s, 3H), 3.20 (d, *J* = 13.4 Hz, 1H), 2.84 (dt, *J* = 15.2, 7.4 Hz, 1H), 2.76 – 2.66 (m, 2H), 2.24 (ddd, *J* = 12.8, 8.4, 6.4 Hz, 1H), 1.93 (ddd, *J* = 12.7, 8.2, 6.5 Hz, 1H), 1.15 (d, *J* = 7.5 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.83, 148.49, 144.12, 132.59, 130.73, 125.88, 125.86, 124.40, 124.28, 113.14, 83.38, 55.19, 42.75, 33.28, 31.37, 24.77, 24.54.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.23.; IR (neat): $\nu_{max}$ 2975.95 (m), 2925.26 (m), 1511.89 (s), 1247.59 (s), 1142.00 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{30}BO_3$ $[M+H]^+$: Calc'd: 365.22855, found: 365.22942. $[\alpha]^{20}_D$: 8.1 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

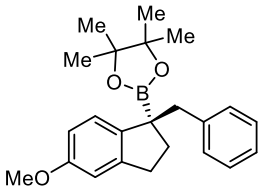
Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-2-(1-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.*





| Peak Info | | | | Peak Info | | | |
|---|---|---|---|---|---|---|---|
| **Peak No** | **% Area** | **Area** | **RT (min)** | **Peak No** | **% Area** | **Area** | **RT (min)** |
| 1 | 52.4588 | 3599.0118 | 6.9 | 1 | 89.7544 | 8542.9527 | 6.9 |
| 2 | 47.5412 | 3261.6357 | 7.95 | 2 | 10.2456 | 975.1926 | 7.94 |
| Total: | 100 | 6860.6475 | | Total: | 100 | 9518.1453 | |

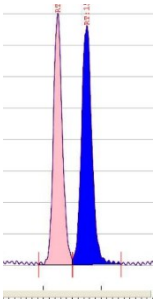


***(R)*-2-(1-benzyl-5-methoxy-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane (36)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromo-5-methoxyphenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-45**) (70.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), phenyltriflate (67.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (61.9 mg, 0.163 mmol, 81.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 2.1 Hz, 1H), 7.51 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.46 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.17 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.11 – 7.04 (m, 1H), 6.92 – 6.86 (m, 1H), 6.80 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.68 (q, *J* = 1.1 Hz, 1H), 4.21 (ddd, *J* = 10.9, 8.0, 2.7 Hz, 1H), 4.11 (ddd, *J* = 10.6, 6.8, 3.2 Hz, 1H), 3.54 (d, *J* = 13.4 Hz, 1H), 2.89 (d, *J* = 13.4 Hz, 1H), 1.99 (ddd, *J* = 14.2, 6.9, 2.8 Hz, 1H), 1.85 (ddd, *J* = 14.1, 8.1, 3.2 Hz, 1H), 1.21 (s, 6H), 1.14 (s, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.7, 153.8, 145.0, 133.8, 129.6, 127.2, 126.9, 126.7, 126.6, 122.5, 120.0, 117.1 110.5, 106.4, 83.7, 63.7, 45.0, 29.1, 24.9, 24.4.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.22.; IR (neat): $\nu_{max}$ 2976.38 (m), 2930.37 (m), 1700.53 (m), 1620.34 (s), 1453.83 (s), 1142.56 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{30}BO_3$ $[M+H]^+$: Calc'd: 365.22825, found: 365.22935. $[\alpha]^{20}_D$: 9.0 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

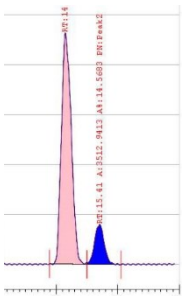
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

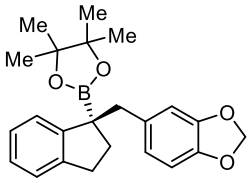
*Chiral SFC (OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) –(S)-2-(1-benzyl-5-methoxy-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane*



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 47.0596 | 8677.042 | 14.5 |
| 2 | 52.9404 | 9761.3735 | 15.51 |
| Total: | 100 | 18438.4155 | |



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 85.4317 | 20600.5746 | 14.29 |
| 2 | 14.5683 | 3512.9413 | 15.41 |
| Total: | 100 | 24113.5159 | |

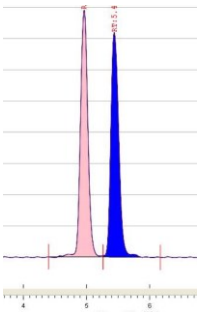


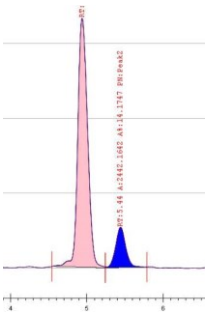
***(S)*-2-(1-(benzo[d][1,3]dioxol-5-ylmethyl)-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (38)** The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**40**) (67.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 5-bromobenzo[d][1,3]dioxole (60.3 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (55.3 mg, 0.146 mmol, 73.2% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 1H), 7.19 – 7.10 (m, 3H), 6.72 – 6.65 (m, 2H), 6.62 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.90 (s, 2H), 3.20 (d, *J* = 13.3 Hz, 1H), 2.89 – 2.82 (m, 1H), 2.76 (ddd, *J* = 15.4, 8.4, 6.2 Hz, 1H), 2.64 (d, *J* = 13.3 Hz, 1H), 2.24 (ddd, *J* = 12.6, 8.5, 6.2 Hz, 1H), 1.93 (ddd, *J* = 12.5, 8.4, 6.5 Hz, 1H), 1.16 (d, *J* = 6.9 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.3, 147.1, 145.6, 144.0, 134.3, 126.0, 125.9, 124.3, 122.7, 110.2, 107.6, 100.6, 83.4, 43.4, 33.2, 31.4, 24.8, 24.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.26.; IR (neat): $\nu_{max}$ 2914.16 (m), 2926.97 (m), 2877.33 (m), 1573.45 (s), 1101.55 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{28}BO_4$ $[M+H]^+$: Calc'd: 379.20752, found: 379.20794. $[\alpha]^{20}_D$: 22.4 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

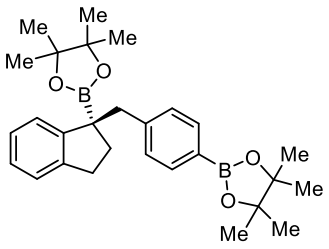
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-2-(1-(benzo[d][1,3]dioxol-5-ylmethyl)-2,3-dihydro-1H-inden-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (38)*





| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.6713 | 6383.3616 | 4.96 |
| 2 | 49.3287 | 6214.2354 | 5.44 |
| Total: | 100 | 12597.597 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 85.8253 | 14786.8841 | 4.94 |
| 2 | 14.1747 | 2442.1642 | 5.44 |
| Total: | 100 | 17229.0483 | |

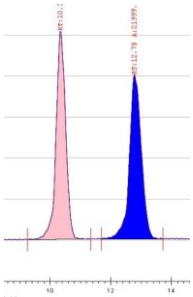


***(R)*-4,4,5,5-tetramethyl-2-(4-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3-dihydro-1H-inden-1-yl)methyl)phenyl)-1,3,2-dioxaborolane** (**39**) The reaction was performed according to the general procedure *Method B* using 2-(4-(2-bromophenyl)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**40**) (67.4 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-(4-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (84.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 2 to 5% ethyl acetate:hexanes) to afford a clear oil (62.9 mg, 0.136 mmol, 68.4% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.9 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.20 – 7.08 (m, 5H), 3.31 (d, *J* = 13.2 Hz, 1H), 2.89 – 2.81 (m, 1H), 2.79 – 2.70 (m, 2H), 2.22 (ddd, *J* = 12.5, 8.5, 6.1 Hz, 1H), 1.91 (ddd, *J* = 12.5, 8.4, 6.5 Hz, 1H), 1.35 (s, 12H), 1.15 (d, *J* = 3.9 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.3, 147.1, 145.6, 144.0, 134.3, 126.0, 125.9, 124.3, 122.7, 110.2, 107.6, 100.6, 83.4, 43.4, 33.2, 31.4, 24.8, 24.5.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 31.54.; IR (neat): $\nu_{max}$ 2973.82 (m), 2947.27 (m), 2815.36 (m), 1597.09 (s), 1118.12 (s) cm$^{-1}$. HRMS (DART) for $C_{28}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 461.30290, found: 461.30380. $[\alpha]^{20}_D$: 16.8 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

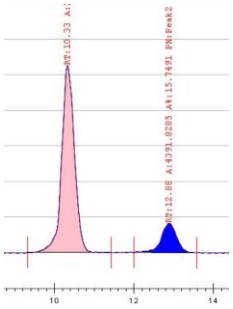
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Phox-L10 ligand. Enantioselectivity was determined by chiral SFC.

*Chiral SFC (AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-4,4,5,5-tetramethyl-2-(4-((1-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)-2,3-dihydro-1H-inden-1-yl)methyl)phenyl)-1,3,2-dioxaborolane (39)*

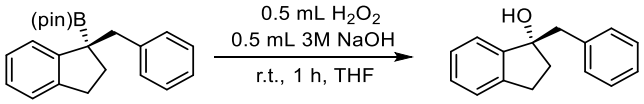


| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.4871 | 22432.7569 | 10.34 |
| 2 | 49.5129 | 21999.9348 | 12.78 |
| Total: | 100 | 44432.6917 | |

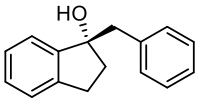


| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 84.2509 | 23494.3492 | 10.33 |
| 2 | 15.7491 | 4391.8285 | 12.88 |
| Total: | 100 | 27886.1777 | |

### 2.4.4 General Procedures for Tertiary Boronic Ester Oxidation



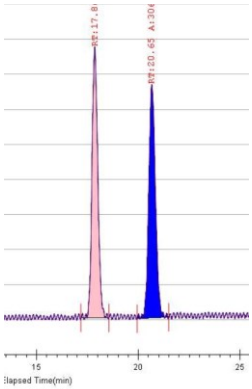

In 2-dram vial was charged with boronic ester solution in THF (0.4 mL, 0.25 M, 0.2 mmol), 0.5mL 3M NaOH water solution and 0.5 mL 30 wt% $H_2O_2$. Reaction was stirred at room temperature for 1 h. Then reaction was extracted with ether and dryed over sodium sulfate and concentrated to acquire crude mixture.

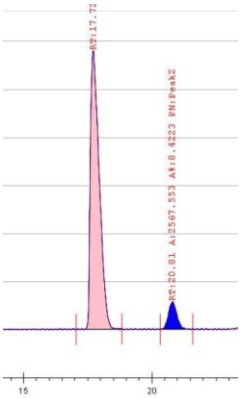



**(*S*)-1-benzyl-2,3-dihydro-1H-inden-1-ol** (**43**) The crude mixture was purified by silica gel chromatography (eluted with 2% ethyl acetate:hexanes) to afford a clear oil (38.8 mg, 0.173 mmol, 86.5% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.18 (m, 7H), 7.14 (dd, *J* = 7.5, 2.1 Hz, 2H), 3.15 (d, *J* = 13.3 Hz, 1H), 3.04 (d, *J* = 13.4 Hz, 1H), 2.91 (ddd, *J* = 15.9, 8.6, 3.8 Hz, 1H), 2.61 (dt, *J* = 15.8, 7.8 Hz, 1H), 2.40 (ddd, *J* = 13.0, 8.0, 3.7 Hz, 1H), 2.07 – 1.91 (m, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 147.1, 143.0, 137.1, 130.5, 128.3, 128.0, 126.6, 126.5, 124.8, 123.1, 83.5, 46.6, 40.1, 29.4.; IR (neat): $\nu_{max}$ 2955.71 (m), 2913.13 (m), 2822.11(m), 1677.89 (s), 1115.91 (s), 1004.38 (s) cm$^{-1}$. HRMS (DART) for $C_{16}H_{15}$ $[M+H-H2O]^+$: Calc'd: 207.11683, found: 207.11559. $[\alpha]^{20}_D$: 20.3 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S) 1-benzyl-2,3-dihydro-1H-inden-1-ol (41)*

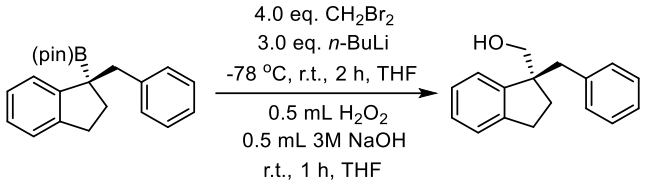




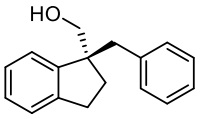
| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 50.1697 | 3083.8963 | 17.86 |
| 2 | 49.8303 | 3063.0334 | 20.65 |
| Total: | 100 | 6146.9297 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 91.5777 | 27917.6054 | 17.72 |
| 2 | 8.4223 | 2567.553 | 20.81 |
| Total: | 100 | 30485.1584 | |

### 2.4.5 General Procedures for Tertiary Boronic Ester Homologation



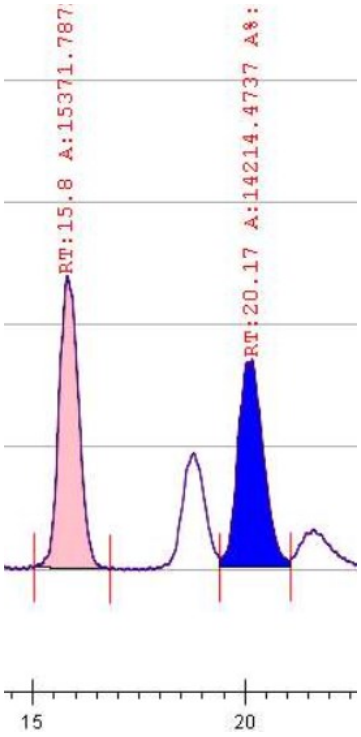

In glovebox, to an oven dried 2-dram vial was charged with boronic ester solution in THF (0.4 mL, 0.25 M, 0.2 mmol) and dibromomethane (139.04 mg, 0.8 mmol. 4.0 equiv.). The vial was sealed with tefflon cap and taped and then moved outside glovebox. The reaction was cooled to -78 °C using dry ice-acetone bath. Then, *n*-BuLi hexane solution (0.24 mL, 2.5 M, 0.6 mmol, 3.0 equiv.) was added dropwise. Reaction was stirred at -78 °C for 1 h then warm to room temperature to stir for 1 h. Then, reaction was diluted with diethyl ether and filtered through a plug of silica gel with ether and concentrated under vaccum. To oxidize the homologated primary boron, the crude product was treated with 0.5 mL hydrogen peroxide, 0.5 mL 3 M NaOH and stirred at room temperature for 1 h. The mixture was extracted with diethylether and dryed with sodium sulfate and concentrated under vaccum to afford the crude mixture.

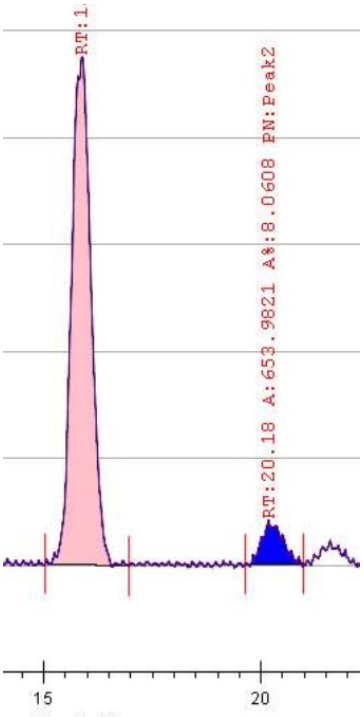



**(*S*)-(1-benzyl-2,3-dihydro-1H-inden-1-yl)methanol** (**44**) The crude mixture was purified by silica gel chromatography (eluted with 1:9 ethylacetate:hexanes) to afford a clear oil (37.1 mg, 0.156 mmol, 77.8% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.11 (m, 7H), 7.09 – 6.92 (m, 2H), 3.74 (dd, *J* = 10.9, 5.1 Hz, 1H), 3.63 (dd, *J* = 10.9, 6.5 Hz, 1H), 3.05 (d, *J* = 13.2 Hz, 1H), 2.87 (d, *J* = 13.2 Hz, 1H), 2.79 (ddd, *J* = 15.0, 8.8, 5.5 Hz, 1H), 2.57 (ddd, *J* = 15.7, 8.7, 6.5 Hz, 1H), 2.09 (dddd, *J* = 12.9, 8.8, 5.5, 1.0 Hz, 1H), 2.03 – 1.91 (m, 1H), 1.56 (d, *J* = 1.0 Hz, 2H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.2, 145.0, 138.2, 130.3, 127.8, 127.3, 126.2, 126.1, 124.9, 123.7, 67.9, 54.2, 42.5, 33.1, 30.3, 24.8.; IR (neat): $\nu_{max}$ 2955.09(m), 2913.13 (m), 2889.31(m), 1620.44 (s), 1355.59 (s), 1112.52 (s) cm$^{-1}$. HRMS (DART) for $C_{17}H_{17}$ $[M+H-H2O]^+$: Calc'd: 221.13248, found: 221.13170. $[\alpha]^{20}_D$: 22.1 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

*Chiral SFC (AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S) -(1-benzyl-2,3-dihydro-1H-inden-1-yl)methanol (42)*

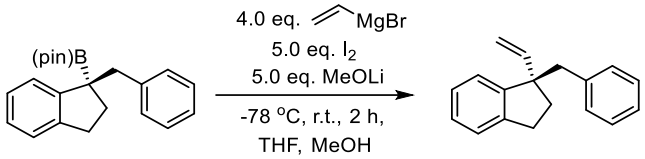


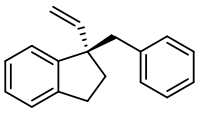

| Peak Info | | | |
|---|---|---|---|
| **Peak No** | **% Area** | **Area** | **RT (min)** |
| 1 | 51.9558 | 15371.7872 | 15.8 |
| 2 | 48.0442 | 14214.4737 | 20.17 |
| Total: | 100 | 29586.2609 | |

| Peak Info | | | |
|---|---|---|---|
| **Peak No** | **% Area** | **Area** | **RT (min)** |
| 1 | 91.9392 | 7459.1553 | 15.88 |
| 2 | 8.0608 | 653.9821 | 20.18 |
| Total: | 100 | 8113.1374 | |

### 2.4.6 General Procedures for Tertiary Boronic Ester Olefination



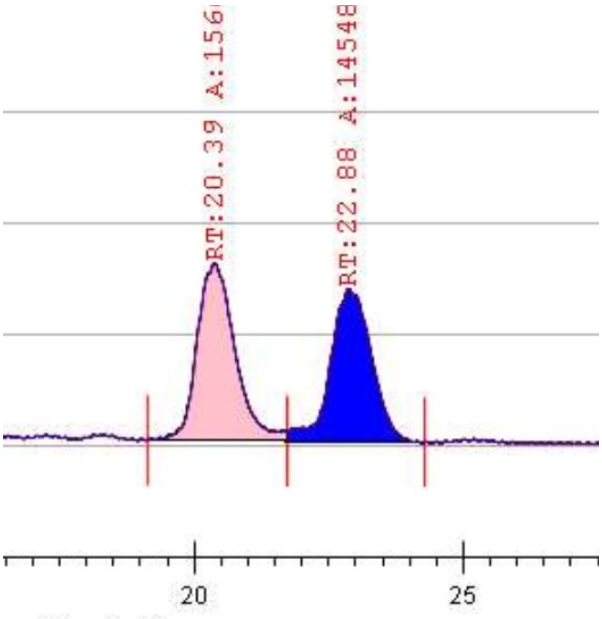

In glovebox, to an oven dried 2-dram vial was charged with boronic ester solution in THF (0.4 mL, 0.25 M, 0.2 mmol). The vial was sealed with tefflon cap and taped and then moved outside glovebox. The reaction was cooled to -78 °C using dry ice-acetone bath. Then, vinyl magnesium bromide diethyl ether solution (0.27 mL, 3 M, 0.8 mmol, 4.0 equiv.) was added dropwise. Reaction was stirred at -78 °C for 30 min. Then $I_2$ THF solution was added (0.5 mL, 4 M, 1.0 mmol, 5.0 equiv.) dropwise. Reaction was stirred at -78 °C for another 30 min and then warm to room temperature to stir for 15 min and then cooled to -78 °C again. To the reaction was added LiOMe methanol solution (1.0 mL, 1 M, 5.0 equiv.) dropwise. Then the cooling bath was removed and the reaction was stirred at room temperature for 1 h. Then, the reaction was quenched with 3 M HCl and extracted with diethyl ether. The ether solution was dried over sodium sulfate and concentrated under vaccum to afford the curde mixture



**(*R*)-1-benzyl-1-vinyl-2,3-dihydro-1H-indene** (**45**) The crude mixture was purified by silica gel chromatography (eluted with hexanes) to afford a clear oil (30.7 mg, 0.131 mmol, 65.4% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.12 (m, 7H), 6.99 (t, *J* = 3.7 Hz, 2H), 6.11 (dd, *J* = 17.4, 10.6 Hz, 1H), 5.03 (d, *J* = 10.7 Hz, 1H), 4.85 (d, *J* = 17.4 Hz, 1H), 3.05 (d, *J* = 13.1 Hz, 1H), 2.97 (d, *J* = 13.1 Hz, 1H), 2.72 (ddd, *J* = 15.0, 8.3, 6.2 Hz, 1H), 2.48 (ddd, *J* = 15.1, 8.1, 6.1 Hz, 1H), 2.16 (ddd, *J* = 13.7, 8.1, 6.1 Hz, 1H), 2.03 (ddd, *J* = 12.8, 8.3, 6.0 Hz, 1H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 147.6, 144.8, 144.1, 138.3, 130.4, 127.6, 126.8, 126.0, 124.6, 124.1, 112.3, 55.0, 46.1, 36.5, 30.3, 30.1, 29.7.; IR (neat): $\nu_{max}$ 2999.18 (m), 2902.25 (m), 2866.37(m), 1710.10 (s), 1295.49 (s), 1017.82 (s) cm$^{-1}$. HRMS (DART) for $C_{18}H_{19}$ $[M+H]^+$: Calc'd: 235.14813, found: 235.14786. $[\alpha]^{20}_D$: 13.4 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

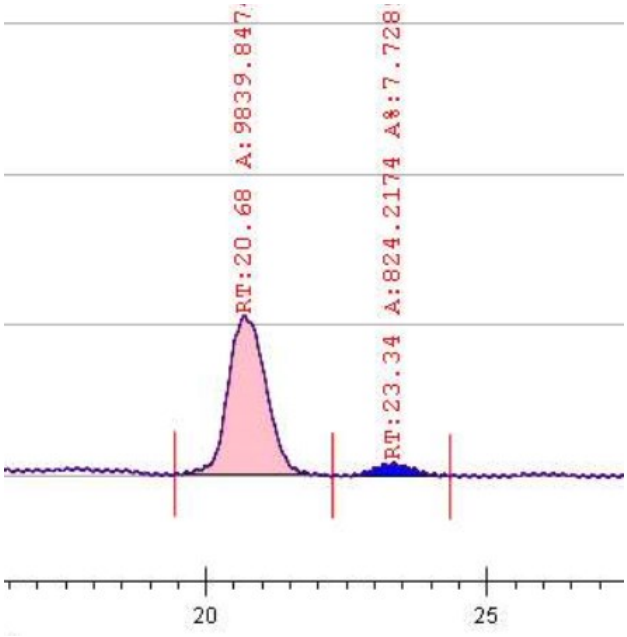
***Analysis of Stereochemistry:***

*(S)-1-benzyl-1-vinyl-2,3-dihydro-1H-indene (43) was firstly treated with 1 mL 1M THF solution of H-BBN and then oxidized with 0.5 mL $H_2O_2$ water solution, 0.5 mL NaOH. The generated primary alcohol was then filtered through silica gel plug before loaded on to SFC. Chiral SFC (AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*




**Peak Info**

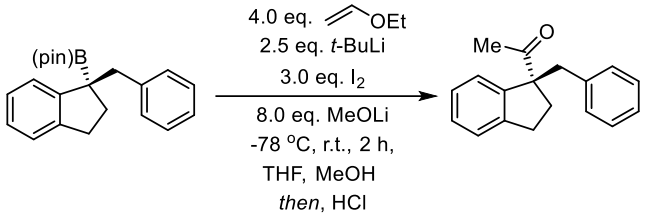
| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 51.8468 | 15664.7723 | 20.39 |
| 2 | 48.1532 | 14548.8262 | 22.88 |
| Total: | 100 | 30213.5985 | |



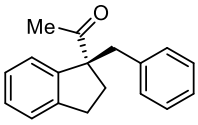

**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 92.2711 | 9839.8474 | 20.68 |
| 2 | 7.7289 | 824.2174 | 23.34 |
| Total: | 100 | 10664.0648 | |

### 2.4.7 General Procedures for Tertiary Boronic Ester Acetylation



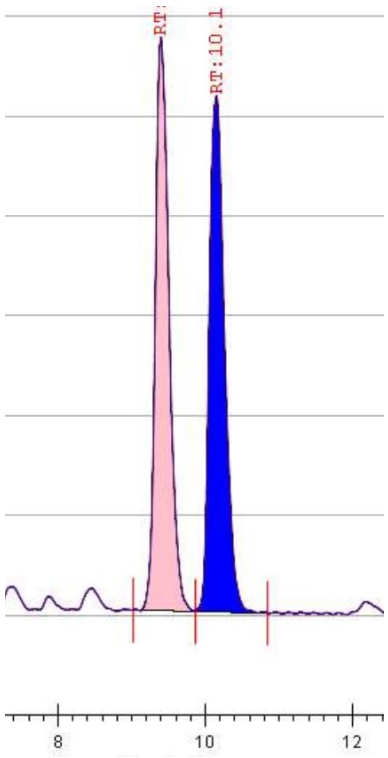

In glovebox, to an oven dried 2-dram vial was charged with ethyl vinyl ether (57.7 mg, 0.8 mmol, 4.0 equiv.) and 0.5 mL THF. The vial was sealed with tefflon cap and taped and then moved outside glovebox. The reaction was cooled to -78 ºC using dry ice-acetone bath. Then, *t*-BuLi pentane solution (0.33 mL, 1.5 M, 0.5 mmol, 2.5 equiv.) was added dropwise. Reaction was stirred at this temperature for 30 min, warm to 0 ºC to stir for additional 10 min and then cooled to -78 ºC again. Boronic ester solution in THF (0.4 mL, 0.25 M, 0.2 mmol) was added dropwise. Reaction was stirred at this temperature for 30 min, warm to 0 ºC to stir for additional 10 min and then cooled to -78 ºC again. Then, $I_2$ THF solution (0.6 mL, 1 M, 0.6 mmol, 3.0 equiv.) was added dropwise. Reaction was stirred at -78 ºC for another 30 min and then warm to room temperature to stir for 15 min and then cooled to -78 ºC again. To the reaction was added LiOMe methanol solution (1.0 mL, 1.6 M, 8.0 equiv.) dropwise. Then the cooling bath was removed and the reaction was stirred at room temperature for 1 h. Then, the reaction was quenched with 3 M HCl and stirred for 30 min and extracted with diethyl ether. The ether solution was dried over sodium sulfate and concentrated under vaccum to afford the curde mixture

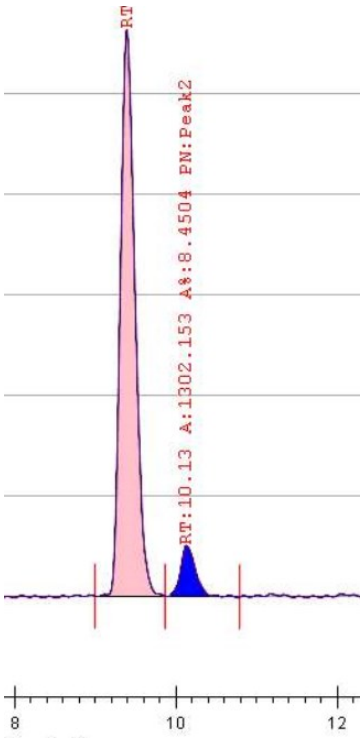



**(*S*)-1-(1-benzyl-2,3-dihydro-1H-inden-1-yl)ethan-1-one** (**46**) The crude mixture was purified by silica gel chromatography (eluted with 0.5:9.5 ethylacetate:hexanes) to afford a clear oil (40.6 mg, 0.162 mmol, 81.2% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.12 (m, 7H), 6.94 – 6.86 (m, 2H), 3.36 (d, *J* = 13.7 Hz, 1H), 3.10 (d, *J* = 13.7 Hz, 1H), 2.91 – 2.81 (m, 1H), 2.57 – 2.48 (m, 1H), 2.43 (ddd, *J* = 13.3, 8.9, 6.3 Hz, 1H), 2.17 – 2.05 (m, 4H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 209.8, 144.9, 144.3, 137.9, 130.1, 127.9, 127.8, 126.6, 126.3, 124.8, 124.7, 66.2, 42.6, 33.4, 31.0, 26.6.; IR (neat): $\nu_{max}$ 2911.32(m), 2811.84 (m), 2739.33(m), 1720.14 (s), 1656.99 (s), 1133.55(s) cm$^{-1}$. HRMS (DART) for $C_{18}H_{19}O$ $[M+H]^+$: Calc'd: 251.14304, found: 251.14202. $[\alpha]^{20}_D$: 27.7 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

***Analysis of Stereochemistry:***

*Chiral SFC (OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – (S)-1-(1-benzyl-2,3-dihydro-1H-inden-1-yl)ethan*



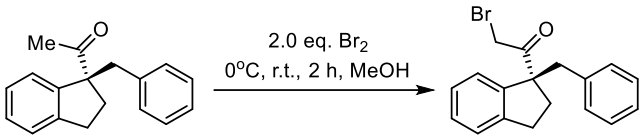

**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 50.0806 | 14821.8093 | 9.4 |
| 2 | 49.9194 | 14774.1225 | 10.15 |
| Total: | 100 | 29595.9318 | |

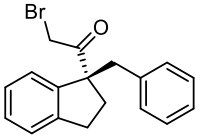
**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 91.5496 | 14107.2194 | 9.39 |
| 2 | 8.4504 | 1302.153 | 10.13 |
| Total: | 100 | 15409.3724 | |

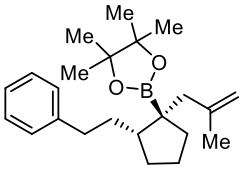
### 2.4.8 General Procedures for Bromination of Methyl Ketone




In 2-dram vial was charged with boronic ester solution in MeOH (0.4 mL, 0.25 M, 0.2 mmol). The reaction was cooled to 0 °C. Molecular bromine (63.9 mg, 0.4 mmol, 2.0 equiv.) was added dropwise. Reaction was stirred at 0 °C for 1.5 h and room temperature for 30 min. Then reaction was concentrated under vaccum to acquire crude mixture.

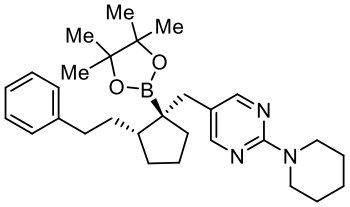



**(*S*)-1-(1-benzyl-2,3-dihydro-1H-inden-1-yl)-2-bromoethan-1-one** (**47**) The crude mixture was purified by silica gel chromatography (eluted with 0.5:9.5 ethylacetate:hexanes) to afford a clear oil (48.9 mg, 0.149 mmol, 74.5% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.12 (m, 7H), 6.94 – 6.81 (m, 2H), 3.97 (s, 2H), 3.35 (d, *J* = 13.7 Hz, 1H), 3.16 (d, *J* = 13.7 Hz, 1H), 2.87 (ddd, *J* = 16.1, 9.0, 4.9 Hz, 1H), 2.58 – 2.50 (m, 1H), 2.47 – 2.41 (m, 1H), 2.22 (ddd, *J* = 13.7, 8.8, 5.0 Hz, 1H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 202.5, 144.8, 143.0, 137.1, 130.2, 128.4, 128.0, 126.9, 126.5, 125.1, 124.7, 65.7, 42.8, 33.7, 33.4, 30.9.; IR (neat): $\nu_{max}$ 2943.11(m), 2903.23 (m), 2811.41(m), 1728.94 (s), 1655.19 (s), 1100.56 (s) cm$^{-1}$. HRMS (DART) for $C_{18}H_{16}OBr$ $[M+H]^+$: Calc'd: 327.03790, found: 327.03900.

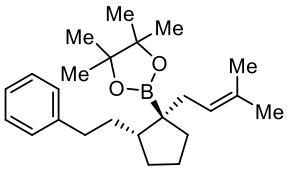



**4,4,5,5-tetramethyl-2-((1S,2R)-1-(2-methylallyl)-2-phenethylcyclopent yl)-1,3,2-dioxaborolane** (**50**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborola-ne (**47**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromopropene (36.3 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (51.7 mg, 0.146 mmol, 72.9% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.27 (t, *J* = 7.6 Hz, 2H), 7.17 (dd, *J* = 13.3, 7.3 Hz, 3H), 4.71 (s, 1H), 4.64 (s, 1H), 2.72 (ddd, *J* = 14.2, 9.7, 5.0 Hz, 1H), 2.48 (ddd, *J* = 13.5, 9.2, 7.4 Hz, 1H), 2.23 (d, *J* = 14.4 Hz, 1H), 2.00 – 1.91 (m, 2H), 1.87 – 1.72 (m, 3H), 1.68 (s, 3H), 1.60 (dddd, *J* = 18.9, 11.1,

6.3, 3.4 Hz, 3H), 1.52 – 1.45 (m, 1H), 1.43 – 1.36 (m, 1H), 1.17 (d, $J$ = 23.4 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.4, 143.0, 128.4, 128.2, 128.2, 125.5, 111.3, 82.9, 46.5, 37.8, 35.5, 32.5, 32.3, 30.1, 24.79, 24.71, 23.6, 23.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.34.; IR (neat): $\nu_{max}$ 2974.31 (m), 2914.35 (m), 2844.13 (m), 1635.03 (s), 1215.12 (s), 1047.56 (s) cm$^{-1}$. HRMS (DART) for $C_{23}H_{36}BO_2$ $[M+H]^+$: Calc'd: 355.28029, found: 355.28098. $[\alpha]^{20}_D$: 2.8 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm)

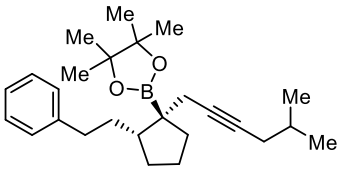


**5-(((1S,2R)-2-phenethyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaboro lan-2-yl)cyclopentyl)methyl)-2-(piperidin-1-yl)pyrimidine** (**52**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxa-borolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 5-bromo-2-(piperidin-1-yl)pyrimidine (72.6 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (62.9 mg, 0.132 mmol, 66.2% yield). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 2H), 7.29 – 7.25 (m, 3H), 7.21 – 7.14 (m, 3H), 3.74 (t, $J$ = 5.3 Hz, 4H), 2.74 (ddd, $J$ = 14.3, 9.6, 5.1 Hz, 1H), 2.65 (d, $J$ = 13.7 Hz, 1H), 2.53 (ddd, $J$ = 13.6, 9.3, 7.1 Hz, 1H), 2.06 – 1.91 (m, 3H), 1.72 – 1.56 (m, 10H), 1.53 – 1.44 (m, 2H), 1.15 (d, $J$ = 3.1 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.8, 128.4, 128.30, 128.27, 128.2, 125.6, 121.4, 83.2, 47.1, 45.0, 35.5, 33.0, 31.8, 29.8, 28.4, 25.7, 25.0, 24.9, 24.9, 24.8, 24.7, 22.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 34.69.; IR (neat): $\nu_{max}$ 2948.78 (m), 2904.85 (m), 2814.33(m), 1601.60 (s), 1105.19 (s), 1071.72 (s) cm$^{-1}$. HRMS (DART) for $C_{29}H_{43}BN_3O_2$ $[M+H]^+$: Calc'd: 476.34428, found: 476.34474. $[\alpha]^{20}_D$: 12.2 (c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm).

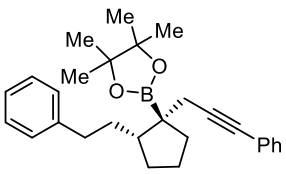


**4,4,5,5-tetramethyl-2-((1S,2R)-1-(3-methylbut-2-en-1-yl)-2-pheneth ylcyclopentyl)-1,3,2-dioxaborolane** (**53**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborola-ne (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 1-bromo-2-methylprop-1-ene (40.5 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography

(eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (50.5 mg, 0.137 mmol, 68.3% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.18 (dd, *J* = 17.6, 7.3 Hz, 3H), 5.11 (t, *J* = 7.2 Hz, 1H), 2.71 (ddd, *J* = 14.3, 10.0, 4.9 Hz, 1H), 2.52 (ddd, *J* = 13.7, 8.3, 4.8 Hz, 1H), 2.09 (dd, *J* = 14.3, 6.2 Hz, 1H), 1.96 – 1.80 (m, 4H), 1.69 (q, *J* = 7.1, 5.7 Hz, 5H), 1.61 – 1.50 (m, 6H), 1.42 – 1.37 (m, 1H), 1.18 (d, *J* = 16.1 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 143.2, 128.4, 128.2, 125.5, 123.9, 82.8, 46.1, 35.5, 32.8, 32.8, 30.5, 29.7, 28.3, 26.0, 24.7, 24.6, 22.9, 18.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 33.55.; IR (neat): $\nu_{max}$ 2944.26 (m), 2901.23(m), 2854.14 (m), 1611.36 (s), 1125.17 (s), 1090.22 (s) cm$^{-1}$. HRMS (DART) for $C_{24}H_{38}BO_2$ $[M+H]^+$: Calc'd: 369.29594, found: 369.29577. $[\alpha]^{20}_D$: 4.1 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

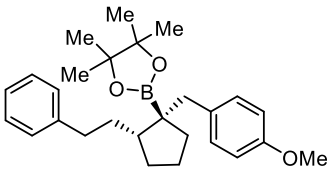



**4,4,5,5-tetramethyl-2-((1S,2R)-1-(5-methylhex-2-yn-1-yl)-2-phenethylcyclopentyl)-1,3,2-dioxaborolane** (**S-53**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborola-ne (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 1-bromo-4-methylpent-1-yne (48.3 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (59.6 mg, 0.151 mmol, 75.7% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.6 Hz, 2H), 7.21 – 7.13 (m, 3H), 2.71 (ddd, *J* = 15.0, 10.5, 5.0 Hz, 1H), 2.54 (ddd, *J* = 13.8, 10.1, 6.4 Hz, 1H), 2.44 – 2.36 (m, 1H), 2.09 (d, *J* = 16.4 Hz, 1H), 2.05 – 1.98 (m, 2H), 1.90 (dqt, *J* = 16.3, 6.7, 3.1 Hz, 3H), 1.74 (dq, *J* = 13.1, 6.6 Hz, 2H), 1.68 – 1.55 (m, 3H), 1.49 (ddd, *J* = 15.5, 10.5, 5.4 Hz, 1H), 1.40 – 1.34 (m, 1H), 1.22 (s, 12H), 0.95 (d, *J* = 6.6 Hz, 6H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 143.0, 128.2, 128.1, 125.4, 83.0, 80.1, 79.4, 48.4, 35.4, 34.6, 34.2, 32.0, 28.3, 28.1, 26.2, 25.0, 24.7, 23.0, 22.0.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 35.42.; IR (neat): $\nu_{max}$ 2988.31 (m), 2914.45 (m), 2814.47 (m), 1601.30 (s), 1155.12 (s), 1093.33 (s) cm$^{-1}$. HRMS (DART) for $C_{26}H_{40}BO_2$ $[M+H]^+$: Calc'd: 395.31159, found: 395.31219. $[\alpha]^{20}_D$: 3.3 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

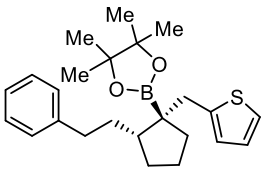



**4,4,5,5-tetramethyl-2-((1S,2R)-1-(3-methylbut-2-en-1-yl)-2-pheneth ylcyclopentyl)-1,3,2-dioxaborolane** (**54**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-

yl)cyclopentyl)methyl)-1,3,2-dioxaborola-ne (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), (bromoethynyl)benzene (54.4 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (45.7 mg, 0.110 mmol, 55.2% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.26 (dt, *J* = 5.8, 3.1 Hz, 5H), 7.20 – 7.14 (m, 4H), 2.74 (ddd, *J* = 14.7, 10.4, 5.0 Hz, 1H), 2.67 – 2.52 (m, 3H), 2.33 (d, *J* = 16.7 Hz, 1H), 2.00 – 1.92 (m, 3H), 1.78 – 1.68 (m, 2H), 1.64 (d, *J* = 7.4 Hz, 1H), 1.55 (td, *J* = 10.5, 9.4, 5.3 Hz, 1H), 1.43 – 1.38 (m, 1H), 1.22 (s, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.9, 131.5, 128.4, 128.3, 128.2, 128.2, 128.1, 127.2, 125.5, 124.4, 90.0, 83.2, 81.0, 48.6, 35.4, 34.7, 34.4, 32.1, 27.0, 25.0, 24.7, 23.1.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 36.42.; IR (neat): $\nu_{max}$ 2966.37 (m), 2904.15 (m), 2855.18 (m), 1691.31 (s), 1175.81 (s), 1055.99 (s) $cm^{-1}$. HRMS (DART) for $C_{28}H_{36}BO_2$ $[M+H]^+$: Calc'd: 415.28029, found: 415.28069. $[\alpha]^{20}_D$: 8.7 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)




**2-((1S,2R)-1-(4-methoxybenzyl)-2-phenethylcyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane** (**S-54**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 4-methoxylphenylbromide (56.1 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (67.9 mg, 0.162 mmol, 80.8% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 7.23 – 7.13 (m, 5H), 6.80 – 6.72 (m, 2H), 3.77 (d, *J* = 1.1 Hz, 3H), 2.84 (d, *J* = 13.3 Hz, 1H), 2.76 (ddd, *J* = 14.2, 9.7, 4.9 Hz, 1H), 2.53 (dt, *J* = 13.7, 8.3 Hz, 1H), 2.21 (d, *J* = 13.3 Hz, 1H), 2.07 – 1.99 (m, 2H), 1.91 – 1.84 (m, 1H), 1.66 – 1.57 (m, 3H), 1.51 (d, *J* = 12.2 Hz, 2H), 1.15 (d, *J* = 1.2 Hz, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.5, 143.0, 133.9, 130.8, 128.4, 128.2, 125.6, 113.2, 83.0, 55.2, 46.9, 35.5, 33.9, 32.9, 31.9, 30.0, 24.7, 22.6.; $^{11}$B NMR (160 MHz, $CDCl_3$) δ 32.76.; IR (neat): $\nu_{max}$ 2933.32 (m), 2914.15 (m), 2814.11 (m), 1611.31 (s), 1111.13 (s), 1011.51 (s) $cm^{-1}$. HRMS (DART) for $C_{27}H_{38}BO_3$ $[M+H]^+$: Calc'd: 420.28303, found: 420.28502. $[\alpha]^{20}_D$: 6.5 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)



**4,4,5,5-tetramethyl-2-((1S,2R)-2-phenethyl-1-(thiophen-2-ylmethyl) cyclopentyl)-1,3,2-dioxaborolane** (**S-55**) The reaction was performed according to the general procedure *Method C* using 4,4,5,5-tetramethyl-2-((1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)methyl)-1,3,2-dioxaborolane (**49**) (78.6 mg, 0.2 mmol, 1.0 equiv.), *tert*-butyllithium-pentane solution (1.6 M, 0.25 mL, 0.4 mmol, 2.0 equiv.), 2-bromothiophene (48.9 mg, 0.3 mmol, 1.5 equiv.). The crude mixture was purified by silica gel chromatography (eluted with 0 to 1% ethyl acetate:hexanes) to afford a clear oil (54.1 mg, 0.137 mmol, 68.3% yield). $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 3H), 7.19 (td, *J* = 10.6, 8.8, 5.5 Hz, 3H), 7.07 (t, *J* = 4.9 Hz, 1H), 6.87 (dq, *J* = 6.7, 3.5 Hz, 1H), 6.83 – 6.71 (m, 1H), 3.22 – 3.04 (m, 1H), 2.75 (ddd, *J* = 14.2, 9.8, 4.9 Hz, 1H), 2.64 – 2.52 (m, 2H), 2.04 – 1.91 (m, 3H), 1.79 – 1.62 (m, 3H), 1.60 – 1.54 (m, 2H), 1.19 – 1.15 (m, 12H).; $^{13}$C NMR (126 MHz, $CDCl_3$) δ 144.3, 143.5, 142.9, 128.43, 128.39, 128.35, 128.26, 128.2, 126.2, 126.15, 126.06, 125.7, 125.6, 125.5, 123.1, 123.0, 83.3, 83.1, 49.5, 46.8, 37.4, 35.49, 35.47, 34.8, 34.6, 32.9, 32.5, 31.6, 30.1, 29.8, 29.7, 25.1, 24.9, 24.8, 24.7, 22.8, 22.7.; IR (neat): $\nu_{max}$ 2966.37 (m), 2911.22 (m), 2833.11 (m), 1611.31 (s), 1144.14 (s), 1091.92 (s) $cm^{-1}$. HRMS (DART) for $C_{24}H_{34}BO_2S$ $[M+H]^+$: Calc'd: 397.23671, found: 397.23895. $[\alpha]^{20}_D$: 10.1 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm)

### 2.4.9 Computational Method and Data

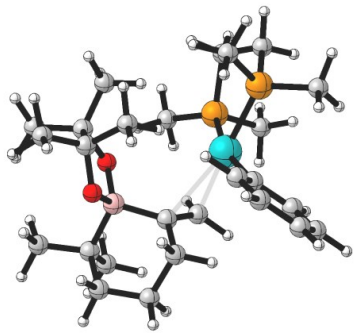
Computational methods [9]

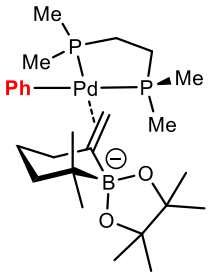
All calculations were conducted using density functional theory (DFT) implemented in Gaussian 16.

Geometries of intermediates and transition states were optimized using the dispersion-corrected B3LYP-D3 function with Def2-SVP basis set in tetrahydrofuran as solvent using the PCM model. Frequency calculations were performed at the same level of theory to characterize the stationary points (no imaginary frequencies for local minima and one imaginary frequency for transition state structures). Intrinsic Reaction Coordinate (IRC) calculations were performed followed by subsequent optimization of the end points with the previously mentioned optimization method. Single-point energy calculations were carried out using the dispersion-corrected M06-D3 function with the Def2-TZVPP basis set for all atoms.

Molecular structure visualizations were obtained using CYLview.

Computational data






B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.683017 au

Thermal correction to Energy= 0.721826 au

Thermal correction to Enthalpy= 0.722770 au

Thermal correction to Gibbs Free Energy= 0.616147 au

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -2004.748486 au

0 1

| | | | |
|---|---|---|---|
| C | -0.52771900 | 2.72198100 | 1.82262900 |
| H | -0.22768800 | 2.98180900 | 2.84994000 |

| | | | |
|---|---|---|---|
| H | -0.23820600 | 3.56894400 | 1.18078300 |
| C | -2.03446800 | 2.46170100 | 1.72058000 |
| H | -2.61022100 | 3.38798100 | 1.87571100 |
| H | -2.36256500 | 1.73872700 | 2.48338300 |
| P | 0.47029300 | 1.25974800 | 1.24291500 |
| P | -2.42387400 | 1.72230100 | 0.06214200 |
| C | 2.11006300 | 1.95568000 | 0.83894700 |
| H | 2.80086300 | 1.12950300 | 0.62283600 |
| H | 2.49177900 | 2.55552000 | 1.67868800 |
| C | 0.75259900 | 0.26587800 | 2.75271400 |
| H | 1.33230000 | -0.62961700 | 2.49091500 |
| H | 1.30235200 | 0.85832900 | 3.49952000 |
| H | -0.21269800 | -0.05069500 | 3.16951400 |
| C | -4.22198100 | 1.36611300 | 0.03285900 |
| H | -4.76235000 | 2.00483300 | 0.74707000 |
| H | -4.59811500 | 1.56962300 | -0.98038800 |
| H | -4.37027900 | 0.29925400 | 0.24793200 |
| C | -2.25480300 | 3.15682000 | -1.07770600 |
| H | -2.47442500 | 2.82028500 | -2.10150500 |
| H | -2.95187700 | 3.96365800 | -0.80362600 |
| H | -1.22438800 | 3.53850200 | -1.05786800 |
| Pd | -0.68466400 | 0.17650300 | -0.40733200 |
| H | 2.02487700 | 2.58325500 | -0.05932500 |

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|---|---|---|---|
| C | 3.60153600 | -1.71289900 | -1.78356600 |
| C | 2.96932000 | -2.26092400 | -0.66400500 |
| C | 1.73452100 | -1.75920000 | -0.23098100 |
| C | 1.09932200 | -0.70776300 | -0.90775100 |
| C | 1.75345800 | -0.16002200 | -2.02670700 |
| C | 2.98677500 | -0.65675200 | -2.46487500 |
| H | 4.56442300 | -2.10365400 | -2.12233500 |
| H | 3.43704600 | -3.08781100 | -0.12153100 |
| H | 1.26108300 | -2.21484300 | 0.63930700 |
| H | 1.29527300 | 0.66761000 | -2.57732700 |
| H | 3.46916500 | -0.21622700 | -3.34237600 |
| C | -4.87776300 | -4.35565000 | -1.36983400 |
| H | -5.66253100 | -3.75512700 | -0.88502000 |
| H | -5.37063400 | -4.98246100 | -2.13846800 |
| H | -4.44561400 | -5.02527200 | -0.61119200 |
| C | -3.79997900 | -3.46101300 | -1.99285700 |
| C | -2.80218400 | -4.36886200 | -2.74778400 |
| C | -1.58981200 | -3.64881300 | -3.34440500 |
| H | -2.43988600 | -5.13184400 | -2.03860400 |
| H | -3.32540100 | -4.91894400 | -3.55613900 |
| C | -0.80597400 | -2.80750600 | -2.30837100 |
| H | -0.90193400 | -4.38165700 | -3.80042200 |
| H | -1.91218000 | -2.98009400 | -4.16149100 |

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|---|---|---|---|
| H | 0.01021800 | -2.26903300 | -2.81261700 |
| H | -0.36540100 | -3.48053300 | -1.55697000 |
| C | -1.79191400 | -1.88214100 | -1.65297000 |
| C | -1.92348700 | -0.59400600 | -2.14071400 |
| H | -1.32365700 | -0.25964900 | -2.99989600 |
| H | -2.86699300 | -0.06661600 | -1.99149400 |
| B | -2.92946400 | -2.67870900 | -0.77662800 |
| O | -2.37128400 | -3.71761600 | 0.11618700 |
| O | -3.70617100 | -1.79750000 | 0.13131700 |
| C | -2.44217800 | -3.29673600 | 1.45820200 |
| C | -3.64961900 | -2.26935900 | 1.46871800 |
| C | -2.65527400 | -4.52013000 | 2.35349100 |
| H | -2.79055800 | -4.23077200 | 3.40795200 |
| H | -3.52944400 | -5.10223100 | 2.03424800 |
| H | -1.77283500 | -5.17636500 | 2.29202400 |
| C | -1.10973100 | -2.63844900 | 1.84356600 |
| H | -1.06375800 | -2.35508900 | 2.90544200 |
| H | -0.29996300 | -3.35569600 | 1.64490900 |
| H | -0.92663900 | -1.74340900 | 1.23010900 |
| C | -4.99165900 | -2.92262700 | 1.83520000 |
| H | -5.04374700 | -3.18717800 | 2.90283900 |
| H | -5.79972800 | -2.20625100 | 1.61941500 |
| H | -5.17425000 | -3.82586400 | 1.24304900 |

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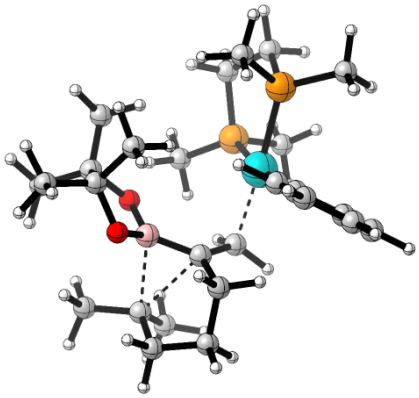
|---|---|---|---|
| C | -3.42488200 | -1.09259200 | 2.42597900 |
| H | -4.30510500 | -0.43200100 | 2.43638500 |
| H | -3.26044100 | -1.44515800 | 3.45617000 |
| H | -2.55555900 | -0.49822300 | 2.12021100 |
| C | -4.50077800 | -2.49579200 | -2.95918800 |
| H | -5.11823800 | -3.04371000 | -3.69733200 |
| H | -5.17306200 | -1.81481200 | -2.41007900 |
| H | -3.79960900 | -1.86732800 | -3.52767100 |



B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.681614 au

Thermal correction to Energy= 0.720491 au

Thermal correction to Enthalpy= 0.721435 au

Thermal correction to Gibbs Free Energy= 0.613049 au

Frequency= -230.49

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -2004.728399 au

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| | | | |
|---|---|---|---|
| C | -0.58410100 | 2.80869800 | 1.77370800 |
| H | -0.29766600 | 3.05711600 | 2.80791400 |
| H | -0.34002300 | 3.68591600 | 1.15317900 |
| C | -2.07766100 | 2.47738900 | 1.66435200 |

| | | | |
|---|---|---|---|
| H | -2.70095200 | 3.36391000 | 1.86429500 |
| H | -2.36188200 | 1.70501000 | 2.39665500 |
| P | 0.46333200 | 1.40282600 | 1.13823300 |
| P | -2.45216800 | 1.77976200 | -0.01905800 |
| C | 2.08609300 | 2.16804600 | 0.77340700 |
| H | 2.78882300 | 1.37097600 | 0.49179200 |
| H | 2.47583300 | 2.71796100 | 1.64353900 |
| C | 0.79579600 | 0.38777900 | 2.63066100 |
| H | 1.42743600 | -0.46529700 | 2.34626100 |
| H | 1.30579500 | 0.98208000 | 3.40422500 |
| H | -0.15117700 | 0.00012300 | 3.03071000 |
| C | -4.22928400 | 1.34000400 | 0.01882300 |
| H | -4.82135600 | 2.11305600 | 0.53144500 |
| H | -4.58295800 | 1.24511200 | -1.01870600 |
| H | -4.33997300 | 0.36033000 | 0.49831800 |
| C | -2.42539200 | 3.27381900 | -1.09467600 |
| H | -2.67485200 | 2.97348200 | -2.12305600 |
| H | -3.14954500 | 4.02871500 | -0.75032900 |
| H | -1.41642500 | 3.71007200 | -1.10247200 |
| Pd | -0.68524500 | 0.31828800 | -0.55692900 |
| H | 1.97863600 | 2.85241200 | -0.08035600 |
| C | 3.51569400 | -1.84712000 | -1.85651500 |
| C | 2.84902700 | -2.27770800 | -0.70488200 |

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|---|---|---|---|
| C | 1.64004000 | -1.68229000 | -0.32369400 |
| C | 1.05333800 | -0.64873400 | -1.07704100 |
| C | 1.74511500 | -0.22799900 | -2.22970100 |
| C | 2.95629000 | -0.81547600 | -2.61815400 |
| H | 4.45890400 | -2.31044400 | -2.15796900 |
| H | 3.27005600 | -3.08665700 | -0.09979000 |
| H | 1.13675700 | -2.05578300 | 0.57078800 |
| H | 1.32859200 | 0.57050600 | -2.85221200 |
| H | 3.46406400 | -0.46737800 | -3.52306700 |
| C | -4.80810800 | -3.94918400 | -1.45517200 |
| H | -5.43265600 | -3.18969100 | -0.96436300 |
| H | -5.46264300 | -4.51658300 | -2.14825800 |
| H | -4.44446900 | -4.64890800 | -0.69020300 |
| C | -3.66609300 | -3.31841000 | -2.23626800 |
| C | -2.79352100 | -4.37526500 | -2.89794800 |
| C | -1.47386200 | -3.79594300 | -3.39133800 |
| H | -2.58537400 | -5.17297000 | -2.16459800 |
| H | -3.34640000 | -4.85429600 | -3.73261200 |
| C | -0.81729100 | -3.03613600 | -2.22520200 |
| H | -0.80073400 | -4.58275800 | -3.77203500 |
| H | -1.65098100 | -3.10207100 | -4.23089400 |
| H | 0.04869900 | -2.46673700 | -2.58621500 |
| H | -0.45297600 | -3.76473400 | -1.48374600 |

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|---|---|---|---|
| C | -1.81203500 | -2.09817600 | -1.57917000 |
| C | -1.86058700 | -0.73288800 | -2.05459100 |
| H | -1.41811500 | -0.56287400 | -3.04947200 |
| H | -2.84316800 | -0.26175600 | -1.97378900 |
| B | -2.65902900 | -2.61603200 | -0.43434500 |
| O | -2.33867200 | -3.78436900 | 0.30588400 |
| O | -3.47854900 | -1.78088900 | 0.36705500 |
| C | -2.46185800 | -3.44561900 | 1.68926200 |
| C | -3.59256100 | -2.33841500 | 1.68376800 |
| C | -2.80026900 | -4.70027300 | 2.48563100 |
| H | -2.97139000 | -4.46067600 | 3.54657400 |
| H | -3.69451400 | -5.19877800 | 2.08978000 |
| H | -1.96166500 | -5.41085200 | 2.42725900 |
| C | -1.10752500 | -2.88530000 | 2.14583600 |
| H | -1.08751900 | -2.65424500 | 3.22087300 |
| H | -0.32925600 | -3.63391500 | 1.93712500 |
| H | -0.85886700 | -1.97381500 | 1.58364400 |
| C | -5.00115900 | -2.90664700 | 1.88206700 |
| H | -5.16373200 | -3.21460600 | 2.92599000 |
| H | -5.73683800 | -2.12548300 | 1.63684000 |
| H | -5.19038700 | -3.76790000 | 1.23222500 |
| C | -3.36744900 | -1.22184800 | 2.70514500 |
| H | -4.20659400 | -0.51026700 | 2.67741700 |

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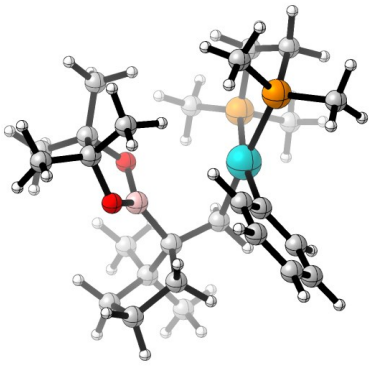
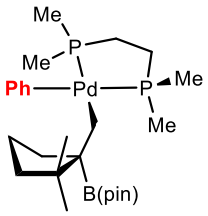
|---|---|---|---|
| H | -3.30421100 | -1.62619100 | 3.72695500 |
| H | -2.44612500 | -0.66772000 | 2.48822100 |
| C | -4.22183900 | -2.28840400 | -3.19984700 |
| H | -4.99142100 | -2.74882500 | -3.85163500 |
| H | -4.71079900 | -1.46241600 | -2.65755600 |
| H | -3.45878800 | -1.84430400 | -3.85354100 |






B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.684600 au

Thermal correction to Energy= 0.723464 au

Thermal correction to Enthalpy= 0.724409 au

Thermal correction to Gibbs Free Energy= 0.616794 au

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -2004.784787 au

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|---|---|---|---|
| C | -0.54978700 | 2.84855900 | 1.83483000 |
| H | -0.20784500 | 3.21122200 | 2.81741300 |
| H | -0.36567200 | 3.65864600 | 1.11049300 |
| C | -2.03877400 | 2.48129800 | 1.85533400 |
| H | -2.67086200 | 3.36577900 | 2.03712300 |

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|---|---|---|---|
| H | -2.24821600 | 1.75945500 | 2.66244000 |
| P | 0.48188100 | 1.39595500 | 1.28075600 |
| P | -2.51477700 | 1.64322700 | 0.26254700 |
| C | 2.08706300 | 2.14656000 | 0.80695500 |
| H | 2.78801600 | 1.33476900 | 0.56379000 |
| H | 2.50328200 | 2.76663900 | 1.61571200 |
| C | 0.88475100 | 0.54947600 | 2.86471100 |
| H | 1.49429300 | -0.34091600 | 2.65503600 |
| H | 1.43889800 | 1.22059200 | 3.53898200 |
| H | -0.04341100 | 0.22564200 | 3.35559900 |
| C | -4.26905400 | 1.17314600 | 0.50546700 |
| H | -4.87382500 | 2.04642700 | 0.79389200 |
| H | -4.65221100 | 0.75461400 | -0.43590900 |
| H | -4.33438400 | 0.39068500 | 1.26873700 |
| C | -2.65104000 | 3.04656700 | -0.92199000 |
| H | -2.97843500 | 2.65166400 | -1.89530600 |
| H | -3.37159400 | 3.80344100 | -0.57454400 |
| H | -1.66468600 | 3.51208100 | -1.05927800 |
| Pd | -0.73986700 | 0.24690600 | -0.38082300 |
| H | 1.94556900 | 2.75957000 | -0.09480400 |
| C | 3.39952900 | -1.79123400 | -2.06137800 |
| C | 2.94146500 | -2.09719000 | -0.77541300 |
| C | 1.74763500 | -1.53980200 | -0.30055600 |

| | | | |
|---|---|---|---|
| C | 0.95721200 | -0.67670500 | -1.08675600 |
| C | 1.44472300 | -0.38539200 | -2.37661100 |
| C | 2.64442500 | -0.92489100 | -2.85852500 |
| H | 4.33225600 | -2.22125200 | -2.43645600 |
| H | 3.51755700 | -2.77410600 | -0.13644600 |
| H | 1.42134200 | -1.80296700 | 0.70847200 |
| H | 0.86909600 | 0.27041600 | -3.03709300 |
| H | 2.98773000 | -0.67307000 | -3.86710200 |
| C | -4.72415100 | -2.30045600 | -2.19618400 |
| H | -4.83867900 | -1.20711700 | -2.11795900 |
| H | -5.50739600 | -2.66874100 | -2.87986600 |
| H | -4.91458100 | -2.72304400 | -1.20067200 |
| C | -3.33494700 | -2.67147900 | -2.72205100 |
| C | -3.09862600 | -4.19620000 | -2.69788600 |
| C | -1.56707000 | -4.38564300 | -2.76237300 |
| H | -3.48941000 | -4.60137400 | -1.74914600 |
| H | -3.63684700 | -4.71463700 | -3.50871600 |
| C | -0.95613200 | -3.02482700 | -2.34591700 |
| H | -1.24415700 | -5.19733200 | -2.09305300 |
| H | -1.24480000 | -4.66732900 | -3.77744800 |
| H | -0.49099400 | -2.52536400 | -3.20956800 |
| H | -0.16525600 | -3.13336800 | -1.59593200 |
| C | -2.13267400 | -2.15806300 | -1.82414400 |

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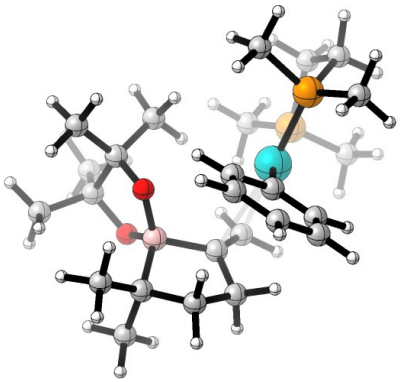
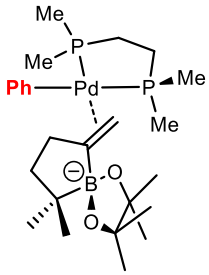
|---|---|---|---|
| C | -1.87435300 | -0.64209700 | -1.92666700 |
| H | -1.34710600 | -0.41304400 | -2.86829900 |
| H | -2.84411400 | -0.11986800 | -1.96349100 |
| B | -2.37043000 | -2.50147600 | -0.29967200 |
| O | -1.68180400 | -3.49355800 | 0.36171400 |
| O | -3.27606400 | -1.88058500 | 0.53512200 |
| C | -1.95720000 | -3.37967200 | 1.77545600 |
| C | -3.33151200 | -2.61245400 | 1.78076600 |
| C | -1.99406600 | -4.77261300 | 2.38874200 |
| H | -2.28305600 | -4.72344500 | 3.44979800 |
| H | -2.69857800 | -5.42909100 | 1.86211900 |
| H | -0.99438600 | -5.22810500 | 2.32844100 |
| C | -0.81989100 | -2.55654600 | 2.37976100 |
| H | -0.92946200 | -2.43578300 | 3.46667700 |
| H | 0.13331700 | -3.06753600 | 2.18272700 |
| H | -0.77531900 | -1.56501500 | 1.90736400 |
| C | -4.54165700 | -3.54608700 | 1.70262100 |
| H | -4.69316000 | -4.09427500 | 2.64381500 |
| H | -5.44143900 | -2.94597500 | 1.50257900 |
| H | -4.43012100 | -4.27519000 | 0.88717300 |
| C | -3.49974100 | -1.63173900 | 2.93511500 |
| H | -4.49721000 | -1.16947000 | 2.89522700 |
| H | -3.41020700 | -2.15079700 | 3.90135700 |

| | | | |
|---|---|---|---|
| H | -2.74825600 | -0.83299000 | 2.89566600 |
| C | -3.21186300 | -2.14614400 | -4.16327600 |
| H | -3.98501800 | -2.60625900 | -4.80083300 |
| H | -3.35031500 | -1.05518900 | -4.20256300 |
| H | -2.23264100 | -2.37261500 | -4.61011600 |






B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.653333 au

Thermal correction to Energy= 0.691268 au

Thermal correction to Enthalpy= 0.692212 au

Thermal correction to Gibbs Free Energy= 0.586925 au

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -1965.442084 au

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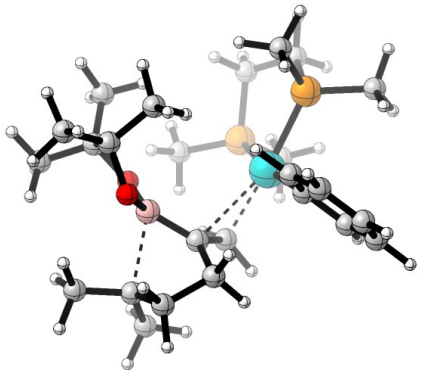
| | | | |
|---|---|---|---|
| C | 0.32852600 | 3.07642200 | 1.14896100 |
| H | 0.90212600 | 3.59330800 | 1.93448700 |
| H | 0.56456700 | 3.57308400 | 0.19407700 |
| C | -1.17533500 | 3.11564100 | 1.42189200 |
| H | -1.56920600 | 4.14245700 | 1.36200100 |

| | | | |
|---|---|---|---|
| H | -1.39893300 | 2.73742700 | 2.43279000 |
| P | 0.93551300 | 1.32798800 | 0.99616600 |
| P | -2.06946700 | 2.00272700 | 0.23475100 |
| C | 2.61032500 | 1.49800200 | 0.29010300 |
| H | 3.12309600 | 0.52894100 | 0.33697300 |
| H | 3.17559000 | 2.25164600 | 0.85882900 |
| C | 1.21567700 | 0.77894600 | 2.71807500 |
| H | 1.54796800 | -0.26792100 | 2.70564500 |
| H | 1.97987300 | 1.40723700 | 3.19973900 |
| H | 0.27559600 | 0.84313200 | 3.28268800 |
| C | -3.79067800 | 1.98795500 | 0.86603700 |
| H | -4.17796500 | 3.01447900 | 0.95087100 |
| H | -4.42954700 | 1.41725600 | 0.17744200 |
| H | -3.81691100 | 1.50275600 | 1.85121400 |
| C | -2.18367600 | 2.98939900 | -1.30938400 |
| H | -2.75133300 | 2.41504400 | -2.05594900 |
| H | -2.68352800 | 3.95392900 | -1.13265100 |
| H | -1.17382700 | 3.16457600 | -1.70769700 |
| Pd | -0.65232000 | 0.10192700 | -0.06201000 |
| H | 2.53552500 | 1.80481200 | -0.76212500 |
| C | 3.15034300 | -2.88748300 | -0.77098100 |
| C | 2.41405200 | -2.97421000 | 0.41483700 |
| C | 1.30595600 | -2.14353900 | 0.62400600 |

| | | | |
|---|---|---|---|
| C | 0.91710600 | -1.20712100 | -0.34493500 |
| C | 1.66989300 | -1.12125900 | -1.52716400 |
| C | 2.76903900 | -1.96073500 | -1.74669600 |
| H | 4.01213000 | -3.53925700 | -0.93618700 |
| H | 2.69163800 | -3.70653200 | 1.17858300 |
| H | 0.69795300 | -2.26857600 | 1.52049500 |
| H | 1.40330900 | -0.38890500 | -2.29567900 |
| H | 3.33400600 | -1.88311800 | -2.68015600 |
| C | -1.32988400 | -5.64899200 | 0.35914500 |
| H | -2.10248000 | -6.05977900 | 1.02987000 |
| H | -0.51910200 | -5.26333900 | 0.99595000 |
| C | -0.80204800 | -4.09113900 | -1.54318300 |
| C | -1.26118200 | -2.74858000 | -2.12570100 |
| H | -0.59645600 | -4.83813000 | -2.33457600 |
| H | 0.14212900 | -3.93529800 | -0.99910100 |
| H | -1.99057500 | -2.92019100 | -2.93925600 |
| H | -0.44393300 | -2.15921900 | -2.56593100 |
| B | -2.32860100 | -3.13011800 | 0.22484700 |
| C | -2.00857000 | -2.04288100 | -1.01432700 |
| C | -2.61304900 | -0.82939600 | -1.19892000 |
| H | -2.57513500 | -0.28805900 | -2.15579300 |
| H | -3.39216600 | -0.51868600 | -0.49791000 |
| O | -3.74500200 | -2.98247600 | 0.63034100 |

| | | | |
|---|---|---|---|
| O | -1.57686500 | -2.92836200 | 1.48947800 |
| C | -3.86597600 | -3.01849400 | 2.03503900 |
| C | -2.44372100 | -2.53481200 | 2.53151400 |
| C | -5.02293700 | -2.10636700 | 2.45470400 |
| H | -5.97160900 | -2.51806300 | 2.07511100 |
| H | -5.10146200 | -2.02792600 | 3.55108300 |
| H | -4.90770900 | -1.09709600 | 2.03730700 |
| C | -4.19054600 | -4.45232100 | 2.48783400 |
| H | -3.36739400 | -5.13710300 | 2.25019300 |
| H | -4.39797100 | -4.51545800 | 3.56759300 |
| H | -5.08384900 | -4.79642500 | 1.94422100 |
| C | -2.37786700 | -1.00792700 | 2.69415100 |
| H | -2.97455200 | -0.64130400 | 3.54404100 |
| H | -1.33015700 | -0.71773200 | 2.85633600 |
| H | -2.72330800 | -0.51366200 | 1.77964700 |
| C | -1.97780600 | -3.18003200 | 3.84020900 |
| H | -1.87220300 | -4.26782900 | 3.73579500 |
| H | -0.99351700 | -2.77320700 | 4.12312900 |
| H | -2.67903800 | -2.97188200 | 4.66454700 |
| H | -0.92927200 | -6.50221500 | -0.22416100 |
| C | -1.89286400 | -4.55578100 | -0.55068600 |
| C | -3.09473700 | -5.11969000 | -1.32161100 |
| H | -2.81534700 | -5.99664500 | -1.93898800 |

| | | | |
|---|---|---|---|
| H | -3.89042000 | -5.43409300 | -0.62773400 |
| H | -3.54657700 | -4.37441500 | -1.99723800 |



B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.651826 au

Thermal correction to Energy= 0.689955 au

Thermal correction to Enthalpy= 0.690900 au

Thermal correction to Gibbs Free Energy= 0.584421 au

Frequency= -233.77

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -1965.418439 au

0 1

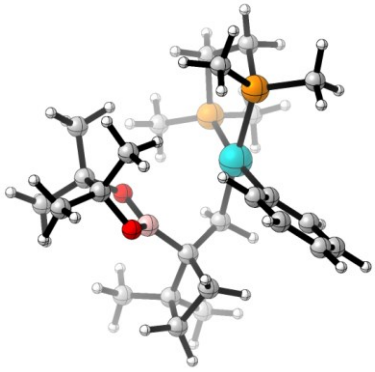
| | | | |
|---|---|---|---|
| C | -0.60080100 | 3.01513100 | 1.29780200 |
| H | -0.31615900 | 3.53592000 | 2.22558600 |
| H | -0.45788100 | 3.72937200 | 0.47103400 |
| C | -2.05678400 | 2.53493700 | 1.34145900 |

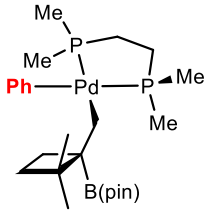
| | | | |
|---|---|---|---|
| H | -2.75991100 | 3.38310400 | 1.36400900 |
| H | -2.24292900 | 1.92959300 | 2.24395000 |
| P | 0.55957000 | 1.59023900 | 0.98091500 |
| P | -2.39877300 | 1.43516700 | -0.11821300 |
| C | 2.08853300 | 2.36764800 | 0.34163200 |
| H | 2.84990000 | 1.58400100 | 0.21987300 |
| H | 2.46036300 | 3.14554900 | 1.02568100 |
| C | 1.02977300 | 1.02818600 | 2.66249700 |
| H | 1.72039600 | 0.17821800 | 2.57435700 |
| H | 1.51410500 | 1.84110300 | 3.22466000 |
| H | 0.13219500 | 0.69313200 | 3.20008800 |
| C | -4.12237500 | 0.85377600 | 0.09465000 |
| H | -4.76961200 | 1.65531500 | 0.48136500 |
| H | -4.50091700 | 0.52899900 | -0.88579300 |
| H | -4.12334000 | -0.01808000 | 0.75971700 |
| C | -2.53336100 | 2.62710400 | -1.51363000 |
| H | -2.77339200 | 2.06922000 | -2.43071300 |
| H | -3.31913900 | 3.37550600 | -1.32628900 |
| H | -1.57060800 | 3.13538600 | -1.66583200 |
| Pd | -0.53032600 | 0.01945800 | -0.32860200 |
| H | 1.88401000 | 2.80833300 | -0.64468200 |
| C | 3.84732100 | -2.08227800 | -0.99323300 |
| C | 3.17892100 | -2.25136000 | 0.22389100 |

| | | | |
|---|---|---|---|
| C | 1.91173200 | -1.68711000 | 0.41751100 |
| C | 1.27125200 | -0.94223300 | -0.59009200 |
| C | 1.96257700 | -0.78464800 | -1.80605700 |
| C | 3.23053200 | -1.34534300 | -2.00974300 |
| H | 4.83604200 | -2.52196200 | -1.14899200 |
| H | 3.64388100 | -2.83081600 | 1.02743200 |
| H | 1.40610100 | -1.85499400 | 1.37166100 |
| H | 1.50414600 | -0.21753700 | -2.62266900 |
| H | 3.73800200 | -1.20776300 | -2.96960100 |
| C | -3.56413200 | -5.31283600 | -0.11234600 |
| H | -4.55441400 | -4.84539000 | 0.01035200 |
| H | -3.15569000 | -5.53476200 | 0.88349000 |
| C | -1.19352700 | -4.96716100 | -1.05631300 |
| C | -0.37329600 | -3.66641900 | -1.16057000 |
| H | -1.05143500 | -5.66426100 | -1.90580600 |
| H | -0.92127900 | -5.51435800 | -0.14146900 |
| H | -0.08476100 | -3.43279100 | -2.19720900 |
| H | 0.55268900 | -3.67895300 | -0.56781100 |
| B | -2.14346500 | -2.98659900 | 0.61702000 |
| C | -1.38063000 | -2.64392400 | -0.65038700 |
| C | -1.67575500 | -1.47399600 | -1.43025400 |
| H | -1.34954500 | -1.49836900 | -2.48166600 |
| H | -2.70428500 | -1.11644100 | -1.33016800 |

| | | | |
|---|---|---|---|
| O | -3.17723300 | -2.15823300 | 1.12194900 |
| O | -1.63537500 | -3.78675000 | 1.67281100 |
| C | -3.34507200 | -2.41471300 | 2.52390100 |
| C | -1.99655700 | -3.14454100 | 2.89825600 |
| C | -3.55249400 | -1.08745800 | 3.25322300 |
| H | -4.52552600 | -0.65258500 | 2.97878300 |
| H | -3.54799700 | -1.23619300 | 4.34413100 |
| H | -2.77027200 | -0.36134700 | 2.99687600 |
| C | -4.58302400 | -3.29427100 | 2.72324300 |
| H | -4.44793100 | -4.28598000 | 2.27599400 |
| H | -4.82413100 | -3.41916600 | 3.78970000 |
| H | -5.44081500 | -2.81183900 | 2.23047700 |
| C | -0.87723400 | -2.15139500 | 3.24079200 |
| H | -1.04385500 | -1.64222800 | 4.20135200 |
| H | 0.07418700 | -2.70004800 | 3.30171400 |
| H | -0.77927200 | -1.39438600 | 2.44901400 |
| C | -2.12110700 | -4.19167200 | 3.99853400 |
| H | -2.81929800 | -4.99021500 | 3.71600100 |
| H | -1.13793100 | -4.65023900 | 4.18484300 |
| H | -2.46862000 | -3.73620100 | 4.93895100 |
| H | -3.72592000 | -6.28062100 | -0.63340700 |
| C | -2.62989800 | -4.44232100 | -0.92573700 |
| C | -3.26974600 | -4.05074400 | -2.24086400 |

| | | | |
|---|---|---|---|
| H | -3.60886000 | -4.95071200 | -2.79425500 |
| H | -4.15818100 | -3.41607900 | -2.07847900 |
| H | -2.58803500 | -3.49877100 | -2.90427300 |






B3LYP-(D3BJ)/Def2-SVP/PCM(THF)

*Optimization and Frequency Calculation:*

Zero-point correction= 0.653027 au

Thermal correction to Energy= 0.691051 au

Thermal correction to Enthalpy= 0.691995 au

Thermal correction to Gibbs Free Energy= 0.586486 au

M06(D3)/Def2-TZVPP/PCM(THF)

*Single Point Calculation:*

Electronic Energy= -1965.464234 au

0 1

| | | | |
|---|---|---|---|
| C | -1.33941200 | 3.95313400 | 0.01118500 |
| H | -1.14145000 | 4.74059700 | 0.75590900 |
| H | -1.07050300 | 4.36707200 | -0.97435300 |
| C | -2.81216300 | 3.52305800 | 0.02173100 |
| H | -3.47483500 | 4.34565100 | -0.29299200 |
| H | -3.12235900 | 3.22453500 | 1.03718400 |

| | | | |
|---|---|---|---|
| P | -0.21949800 | 2.48704100 | 0.29345800 |
| P | -3.05165300 | 2.02922900 | -1.06374300 |
| C | 1.42213700 | 3.05623700 | -0.29390900 |
| H | 2.15579700 | 2.26593000 | -0.07755800 |
| H | 1.73178900 | 3.99364000 | 0.19308300 |
| C | -0.01188100 | 2.46600400 | 2.12177100 |
| H | 0.63157800 | 1.61973700 | 2.40159700 |
| H | 0.44113600 | 3.40377500 | 2.47868200 |
| H | -0.99086100 | 2.32930300 | 2.60162700 |
| C | -4.80648400 | 1.56240600 | -0.82039000 |
| H | -5.47298000 | 2.42269000 | -0.98564300 |
| H | -5.05582700 | 0.76284800 | -1.53272900 |
| H | -4.93912000 | 1.16156100 | 0.19010300 |
| C | -3.06673500 | 2.74420700 | -2.76007000 |
| H | -3.24778800 | 1.93261000 | -3.48036900 |
| H | -3.84890700 | 3.51150900 | -2.87074500 |
| H | -2.08456300 | 3.18456200 | -2.98406000 |
| Pd | -1.19376900 | 0.62947900 | -0.78298600 |
| H | 1.38347400 | 3.19923900 | -1.38350700 |
| C | 3.11459300 | -1.72886500 | -0.76729800 |
| C | 2.45881600 | -1.45832600 | 0.43847900 |
| C | 1.21946400 | -0.80625200 | 0.43691500 |
| C | 0.57942700 | -0.41531000 | -0.75623000 |

| | | | |
|---|---|---|---|
| C | 1.26418800 | -0.69836100 | -1.95492600 |
| C | 2.50990100 | -1.33930100 | -1.96686900 |
| H | 4.08333800 | -2.23598800 | -0.77193500 |
| H | 2.91504300 | -1.75700200 | 1.38776400 |
| H | 0.73562500 | -0.61508700 | 1.39718000 |
| H | 0.80982200 | -0.43020400 | -2.91390300 |
| H | 3.00808200 | -1.54302100 | -2.92020100 |
| C | -4.44401500 | -3.73113200 | -1.19554700 |
| H | -5.11238500 | -2.87644200 | -1.39109500 |
| H | -4.43190300 | -3.89937700 | -0.10812200 |
| C | -1.92275900 | -4.43588000 | -1.26955500 |
| C | -0.97515900 | -3.23249600 | -1.08380000 |
| H | -1.62020700 | -5.22392000 | -1.97946100 |
| H | -2.17721300 | -4.91084800 | -0.30868500 |
| H | -0.32656200 | -3.22766900 | -0.19844500 |
| H | -0.34473600 | -3.05612200 | -1.96719200 |
| B | -2.68320900 | -1.96615300 | 0.39209300 |
| C | -2.20430300 | -2.27871200 | -1.07282800 |
| C | -2.09799800 | -0.95812500 | -1.83989500 |
| H | -1.50977800 | -1.09408300 | -2.76343800 |
| H | -3.11045300 | -0.64098000 | -2.14133500 |
| O | -3.76304600 | -1.16764400 | 0.70778500 |
| O | -2.07933100 | -2.46660600 | 1.52250400 |

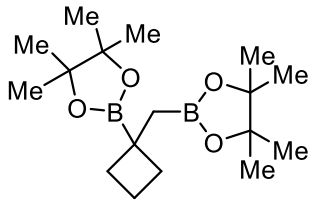
| | | | |
|---|---|---|---|
| C | -3.99812500 | -1.24868800 | 2.13251400 |
| C | -2.61159600 | -1.76890700 | 2.67133400 |
| C | -4.39674900 | 0.12626800 | 2.65656800 |
| H | -5.38776500 | 0.40421000 | 2.26811000 |
| H | -4.45839200 | 0.11865400 | 3.75533200 |
| H | -3.67769400 | 0.89725800 | 2.35194200 |
| C | -5.14207800 | -2.24078600 | 2.35182000 |
| H | -4.86634200 | -3.25149200 | 2.02066200 |
| H | -5.43674800 | -2.28938300 | 3.41010100 |
| H | -6.01243800 | -1.91521800 | 1.76338600 |
| C | -1.63674700 | -0.63382200 | 2.98468100 |
| H | -1.94745500 | -0.05347700 | 3.86484700 |
| H | -0.64446800 | -1.06180100 | 3.18608000 |
| H | -1.54578800 | 0.03953000 | 2.12087300 |
| C | -2.69987900 | -2.73555200 | 3.84432100 |
| H | -3.27162000 | -3.63604700 | 3.58581800 |
| H | -1.68771500 | -3.04862300 | 4.14089000 |
| H | -3.17579100 | -2.25289200 | 4.71161300 |
| H | -4.89088500 | -4.62514000 | -1.66424800 |
| C | -3.04401400 | -3.47060000 | -1.74030500 |
| C | -3.09019400 | -3.37302800 | -3.26508500 |
| H | -3.49023400 | -4.30821200 | -3.69314200 |
| H | -3.73814900 | -2.54559600 | -3.59531200 |

### 2.4.10 NMR Spectra


7.26
2.20
2.19
2.19
2.18
2.18
2.17
2.16
2.15
1.91
1.91
1.90
1.89
1.88
1.87
1.87
1.69
1.69
1.67
1.67
1.66
1.65
1.65
1.63
1.10
1H NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
O
Me
Me
Me
Me
2.00
2.09
2.21
12.77
12.21
1.89
f1 (ppm)

E

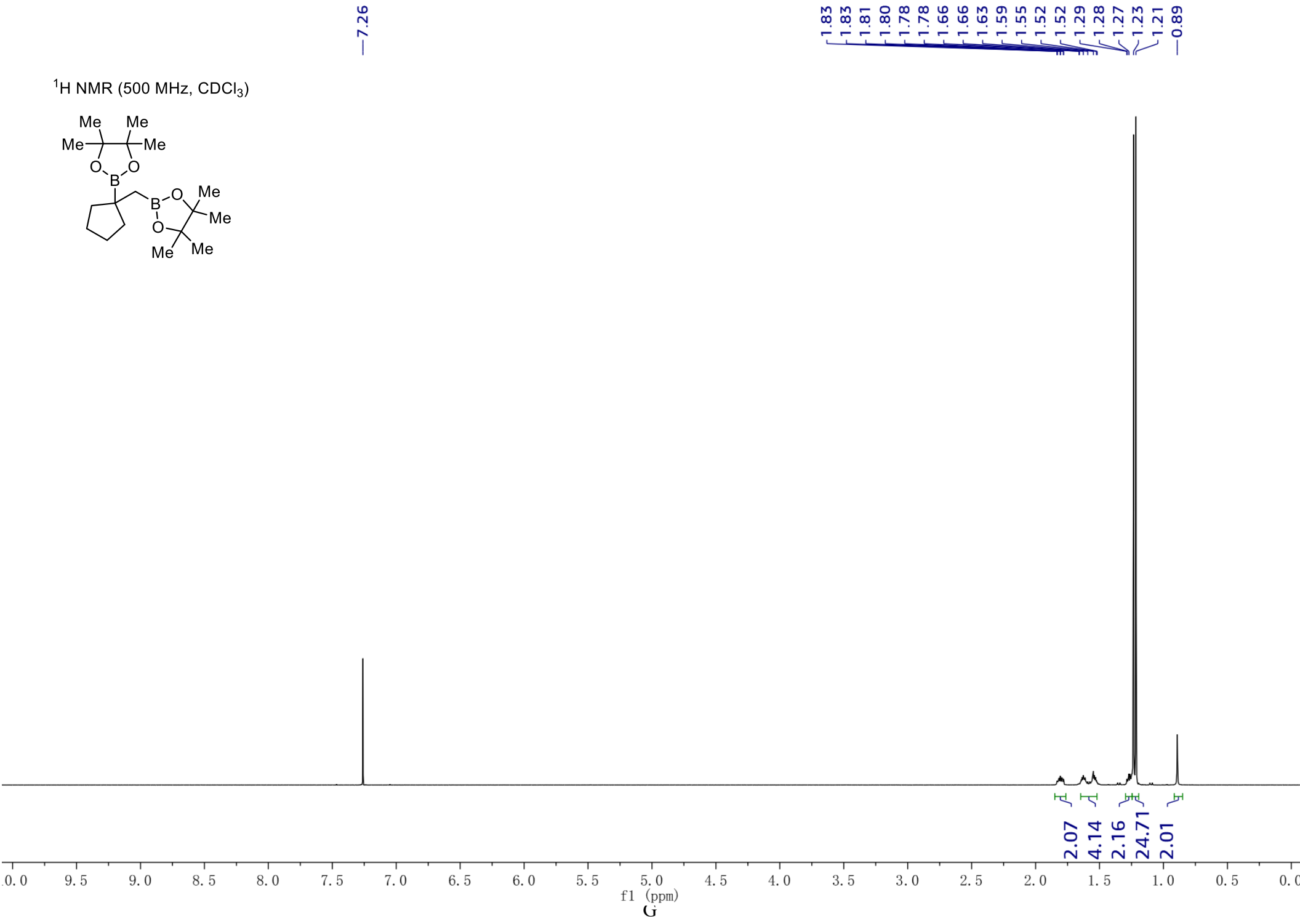
$^{13}$C NMR (126 MHz, $CDCl_3$)







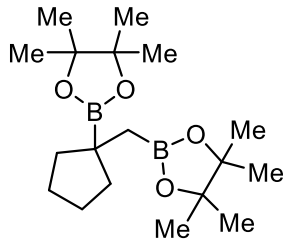
G
E


7.26
1.83
1.83
1.81
1.80
1.78
1.78
1.66
1.66
1.63
1.59
1.55
1.52
1.52
1.29
1.28
1.27
1.23
1.21
0.89
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
2.07
4.14
2.16
24.71
2.01
f1 (ppm)

G

E

$^{13}$C NMR (126 MHz, $CDCl_3$)

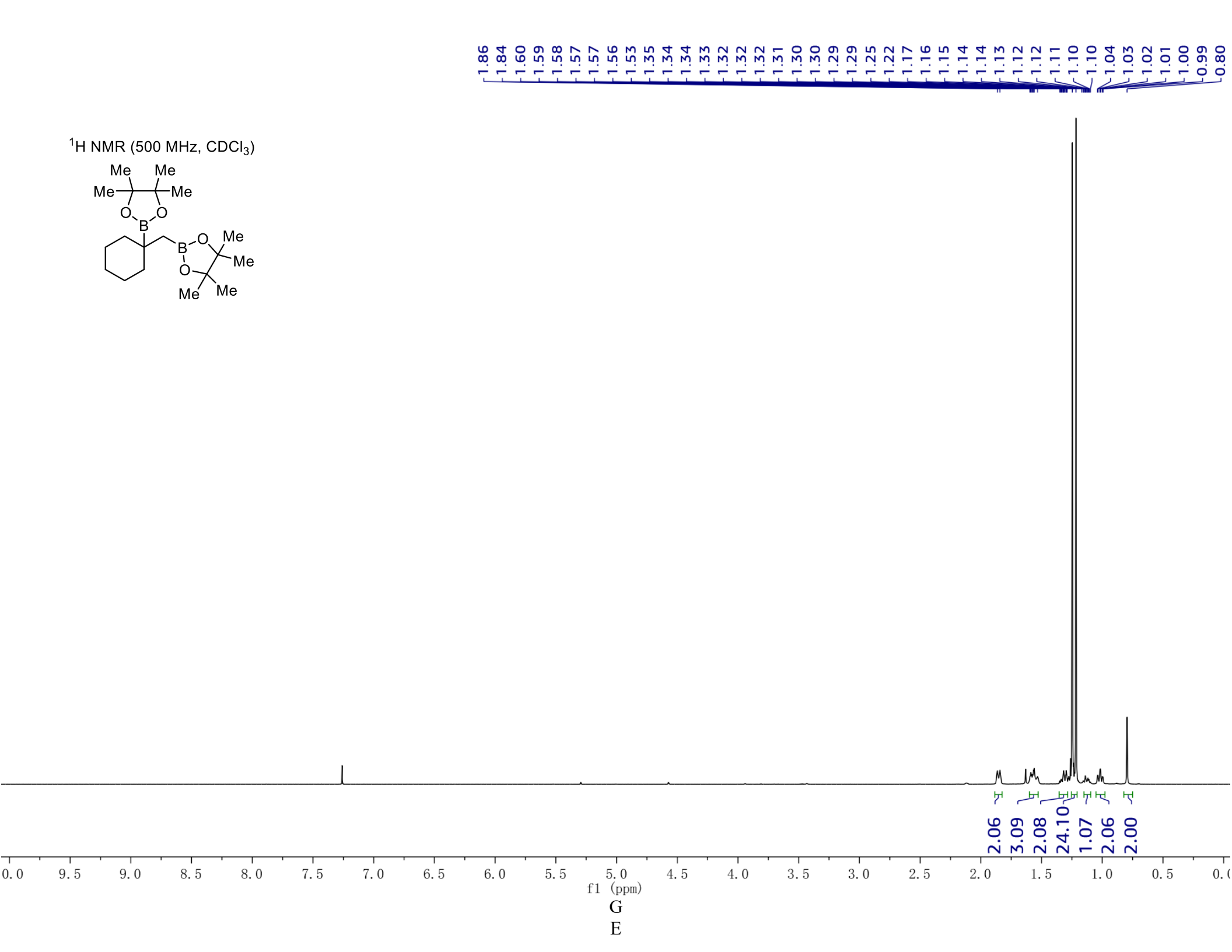






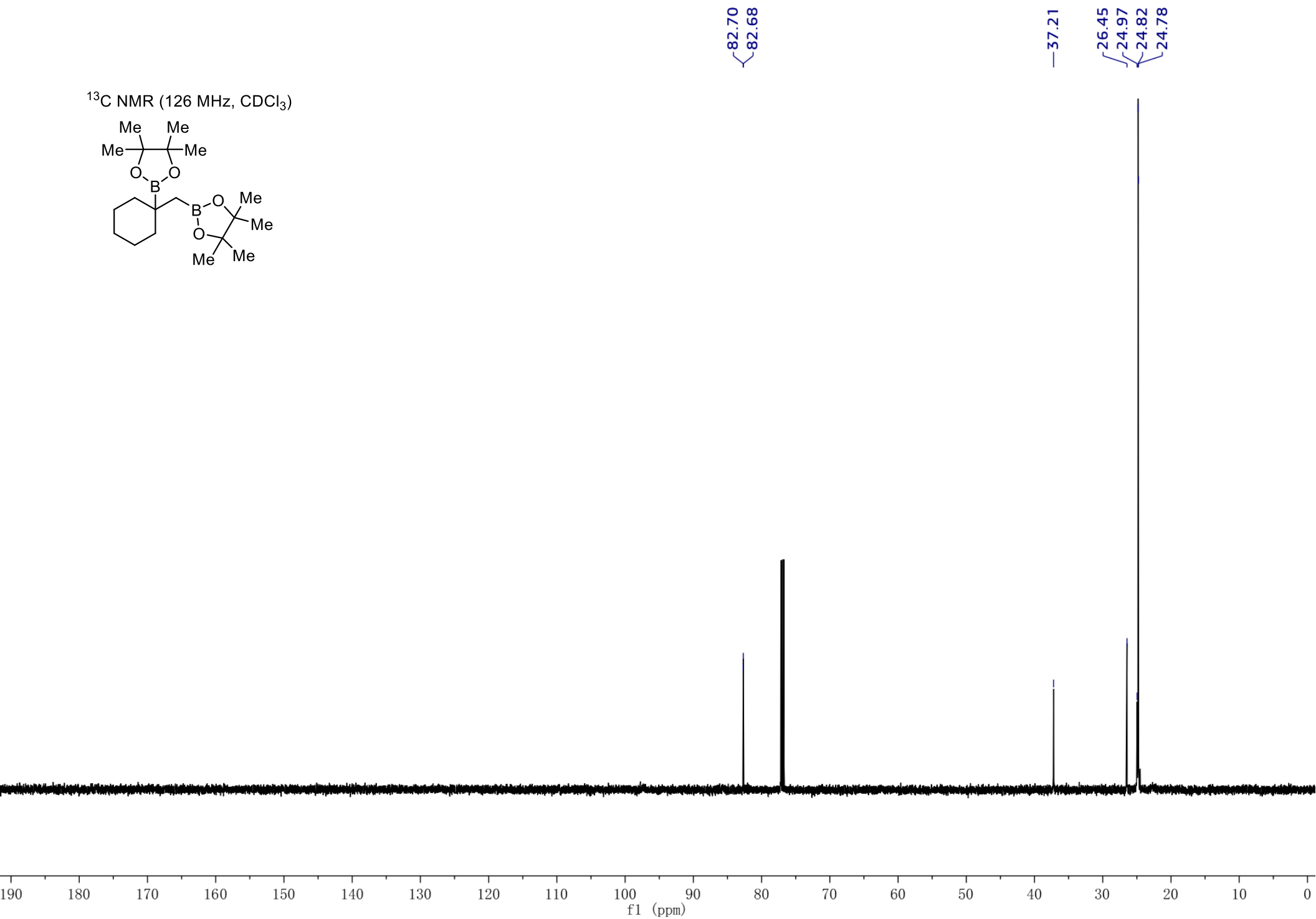
G

E


1.86 1.84 1.60 1.59 1.58 1.57 1.57 1.56 1.53 1.35 1.34 1.34 1.33 1.32 1.32 1.32 1.31 1.30 1.30 1.29 1.29 1.25 1.22 1.17 1.16 1.15 1.14 1.14 1.13 1.12 1.12 1.11 1.10 1.10 1.04 1.03 1.02 1.01 1.00 0.99 0.80
$^1$H NMR (500 MHz, $CDCl_3$)
Me Me Me Me O O B B O Me Me O Me Me
2.06 3.09 2.08 24.10 1.07 2.06 2.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

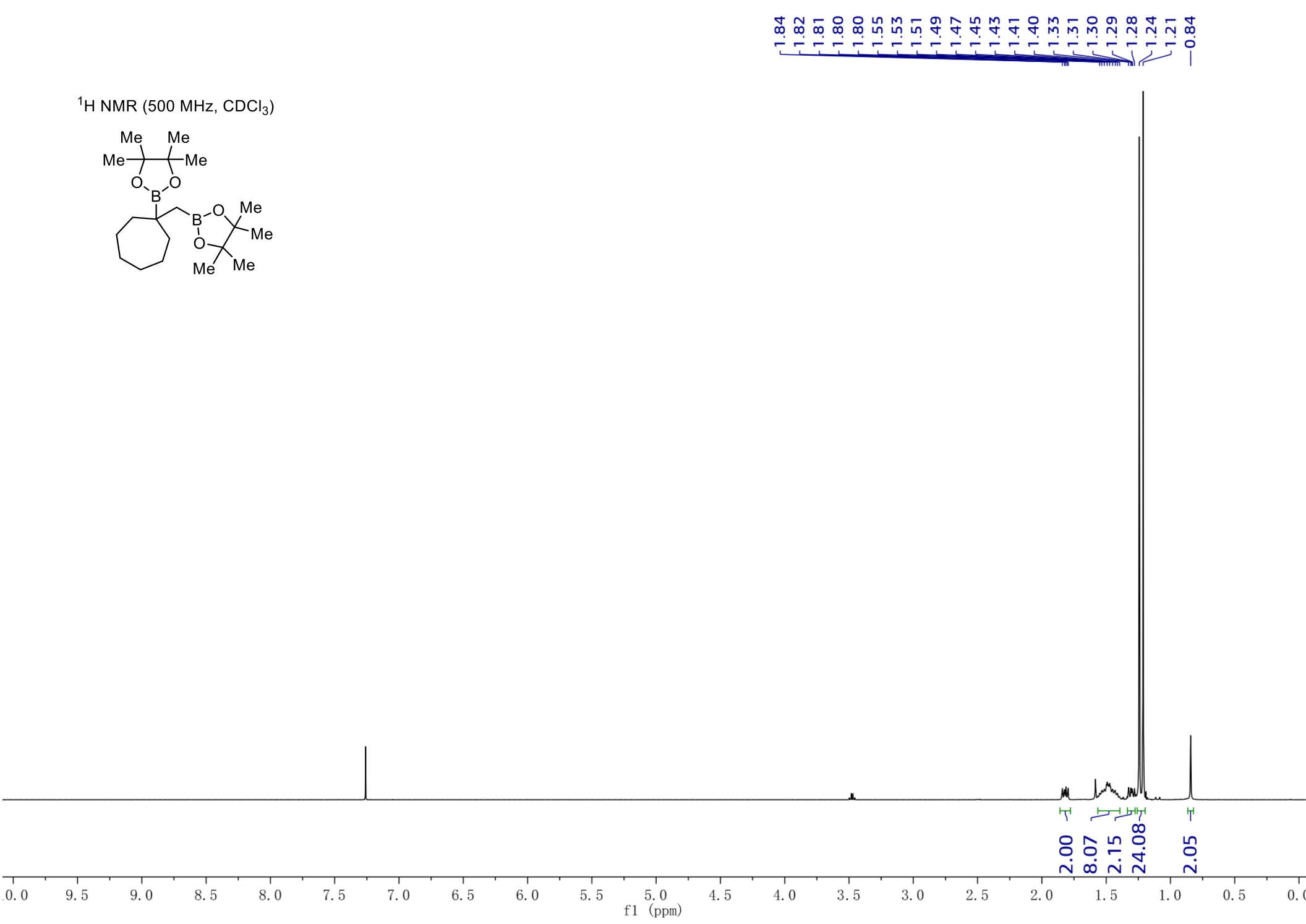
G

E


82.70
82.68
37.21
26.45
24.97
24.82
24.78
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

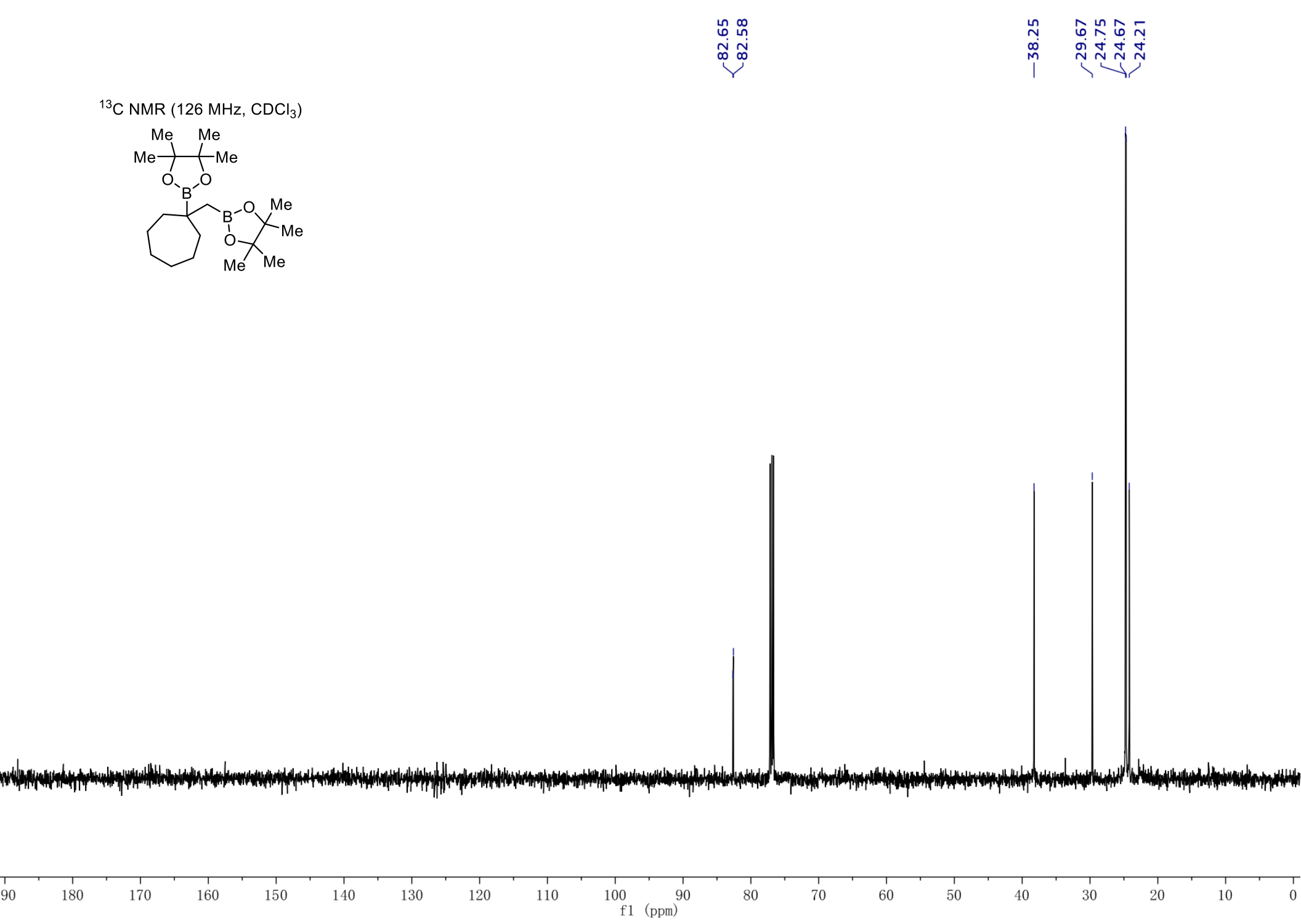
G

E


1.84
1.82
1.81
1.80
1.80
1.55
1.53
1.51
1.49
1.47
1.45
1.43
1.41
1.40
1.33
1.31
1.30
1.29
1.28
1.24
1.21
0.84
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
2.00
8.07
2.15
24.08
2.05
f1 (ppm)

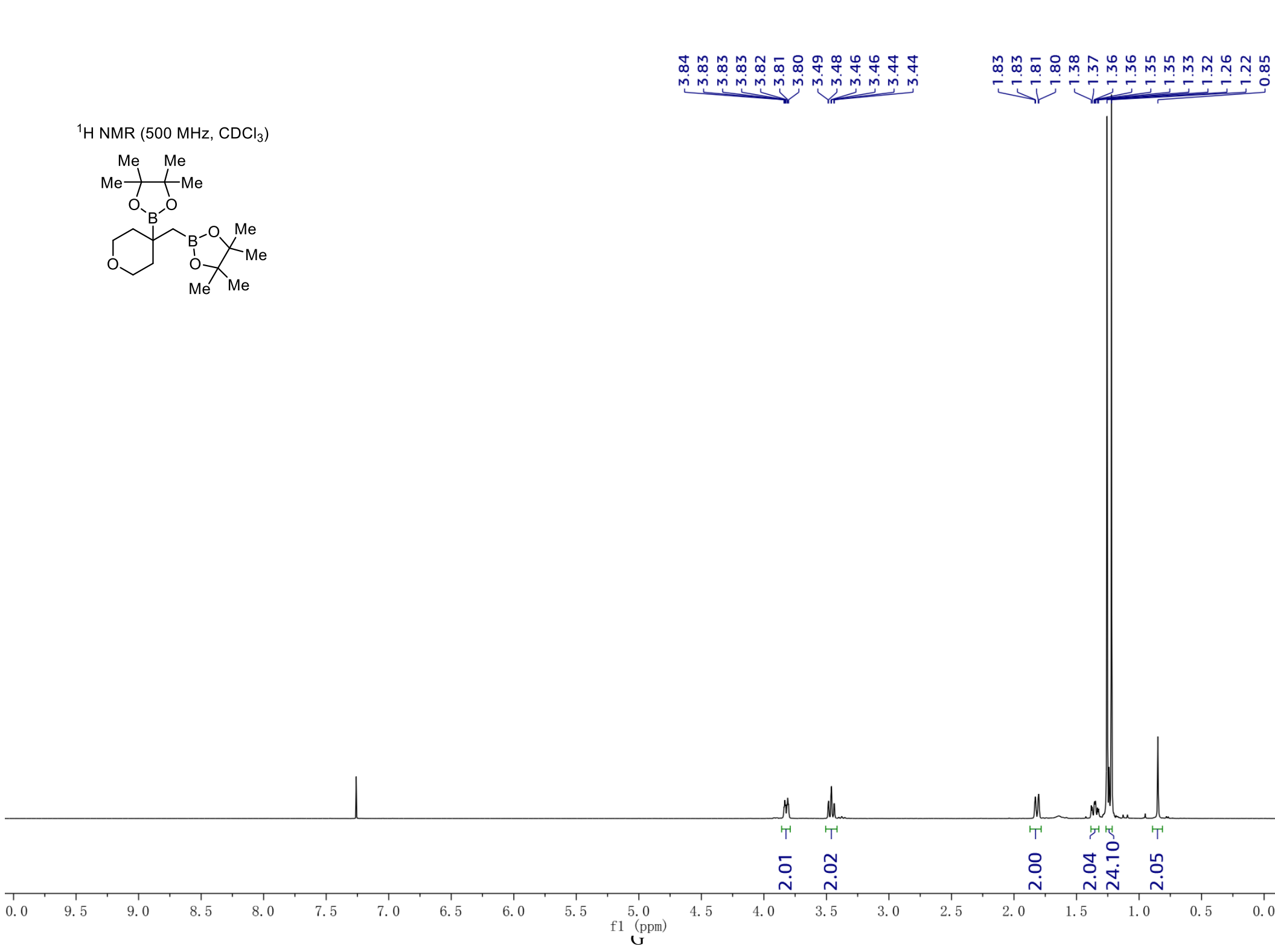
G

E


82.65
82.58
38.25
29.67
24.75
24.67
24.21
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

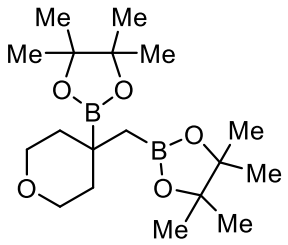
E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
O
B
Me
Me
O
O
Me
Me
3.84
3.83
3.83
3.83
3.82
3.81
3.80
3.49
3.48
3.46
3.46
3.44
3.44
1.83
1.83
1.81
1.80
1.38
1.37
1.36
1.36
1.35
1.35
1.33
1.32
1.26
1.22
0.85
2.01
2.02
2.00
2.04
24.10
2.05
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E

$^{13}$C NMR (126 MHz, $CDCl_3$)

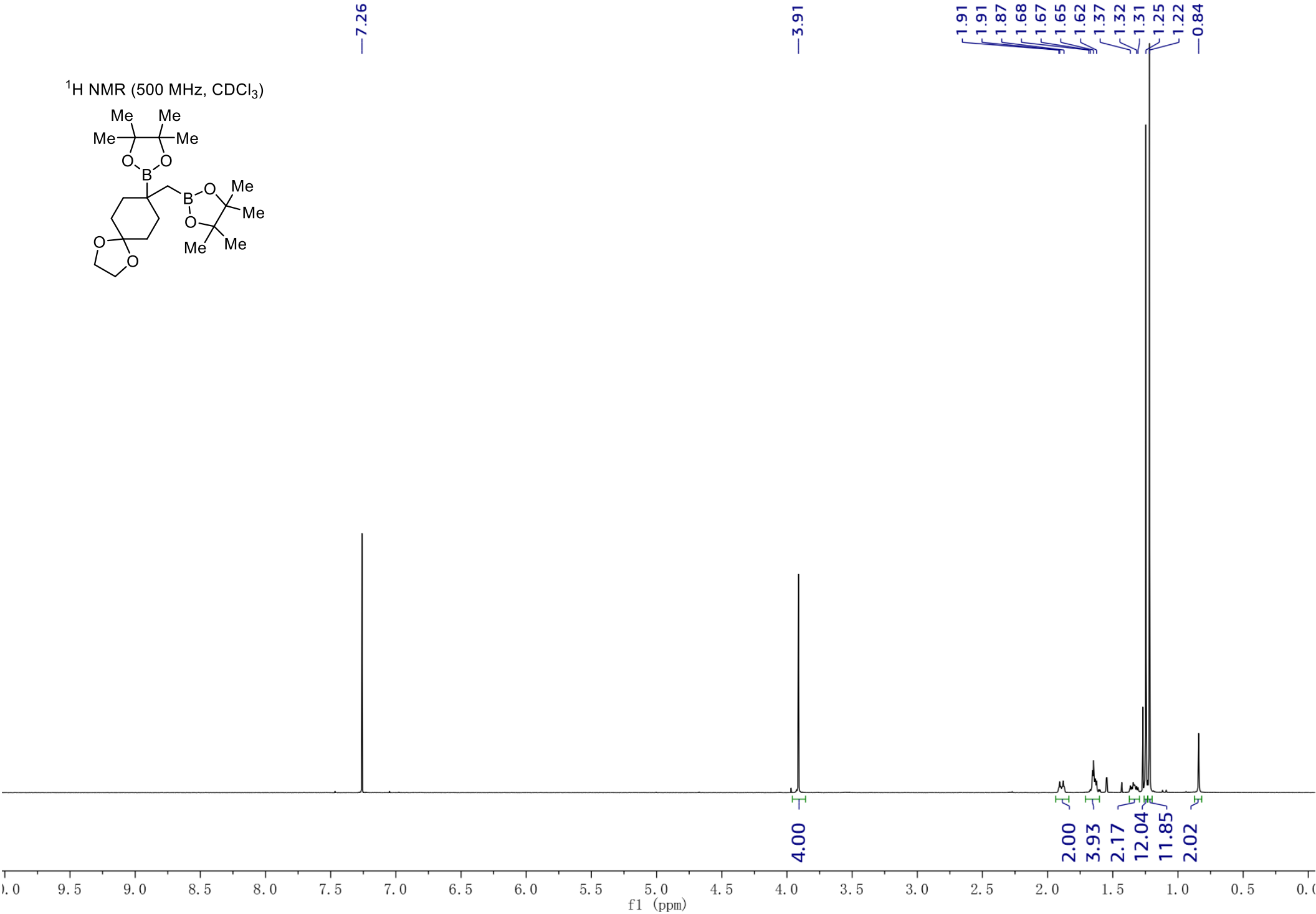






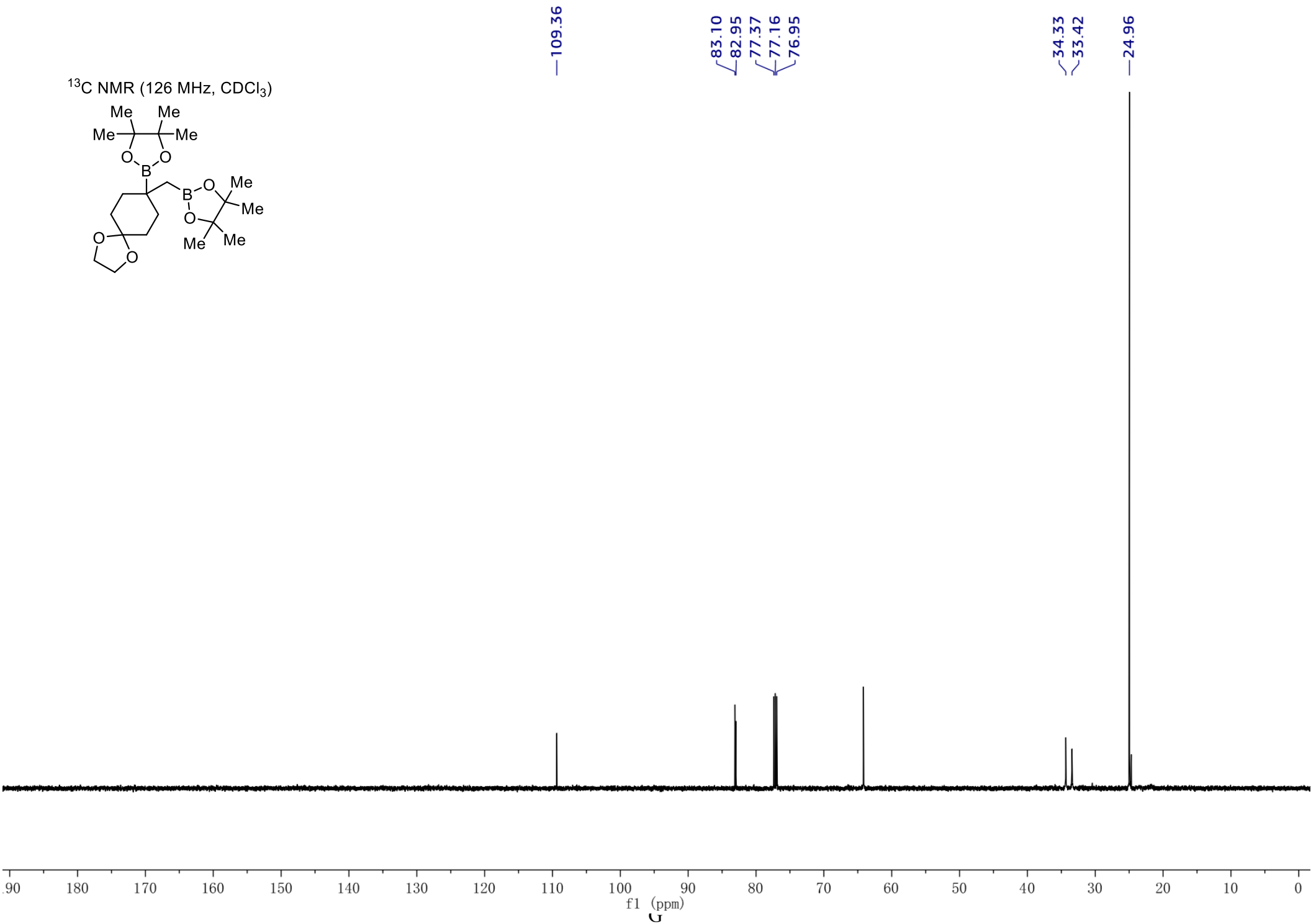
G

E


7.26
3.91
1.91
1.91
1.87
1.68
1.67
1.65
1.62
1.37
1.32
1.31
1.25
1.22
0.84
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
B
O
B
O
Me
Me
O
O
Me
Me
O
4.00
2.00
3.93
2.17
12.04
11.85
2.02
f1 (ppm)

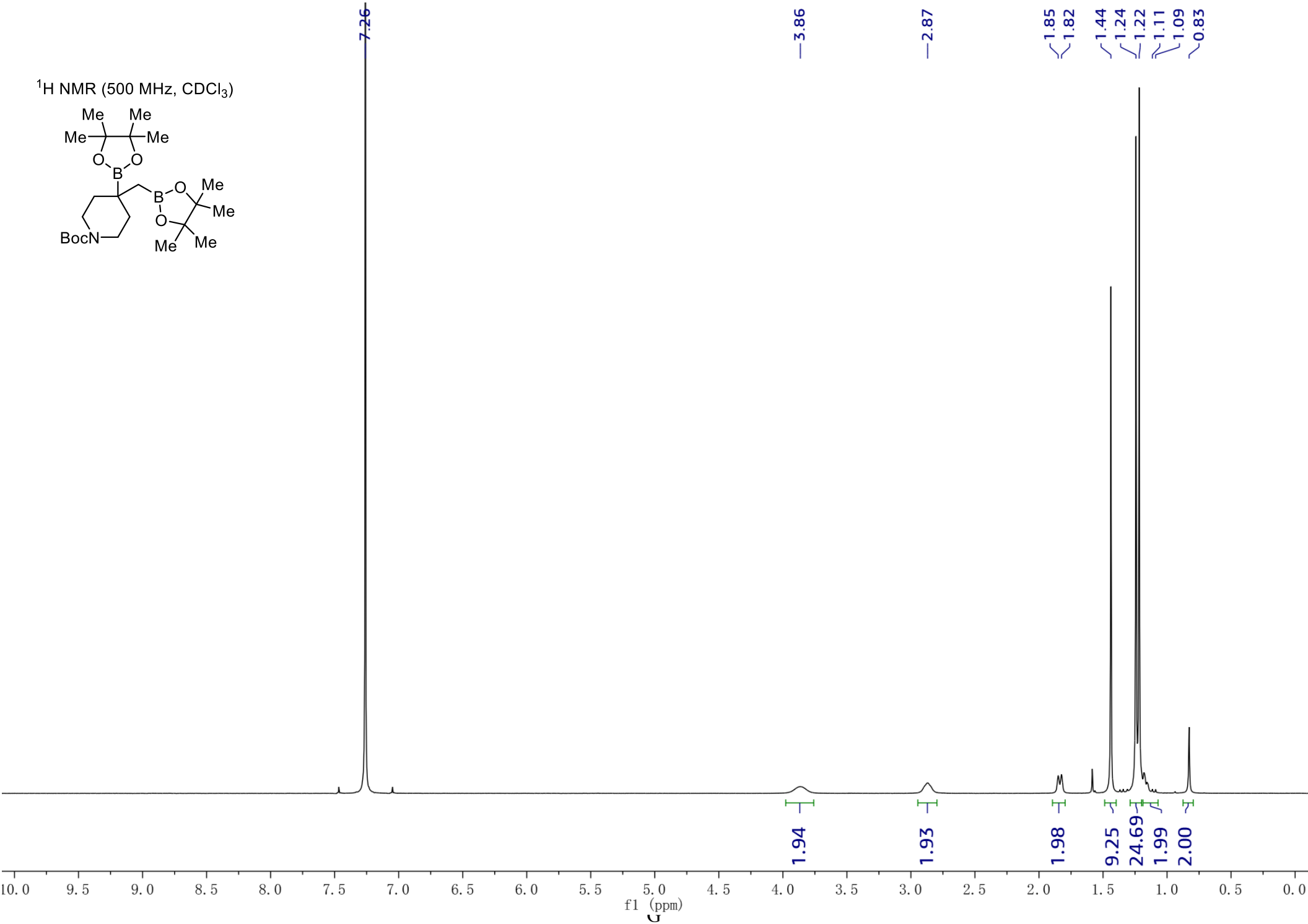
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
109.36
83.10
82.95
77.37
77.16
76.95
34.33
33.42
24.96
f1 (ppm)

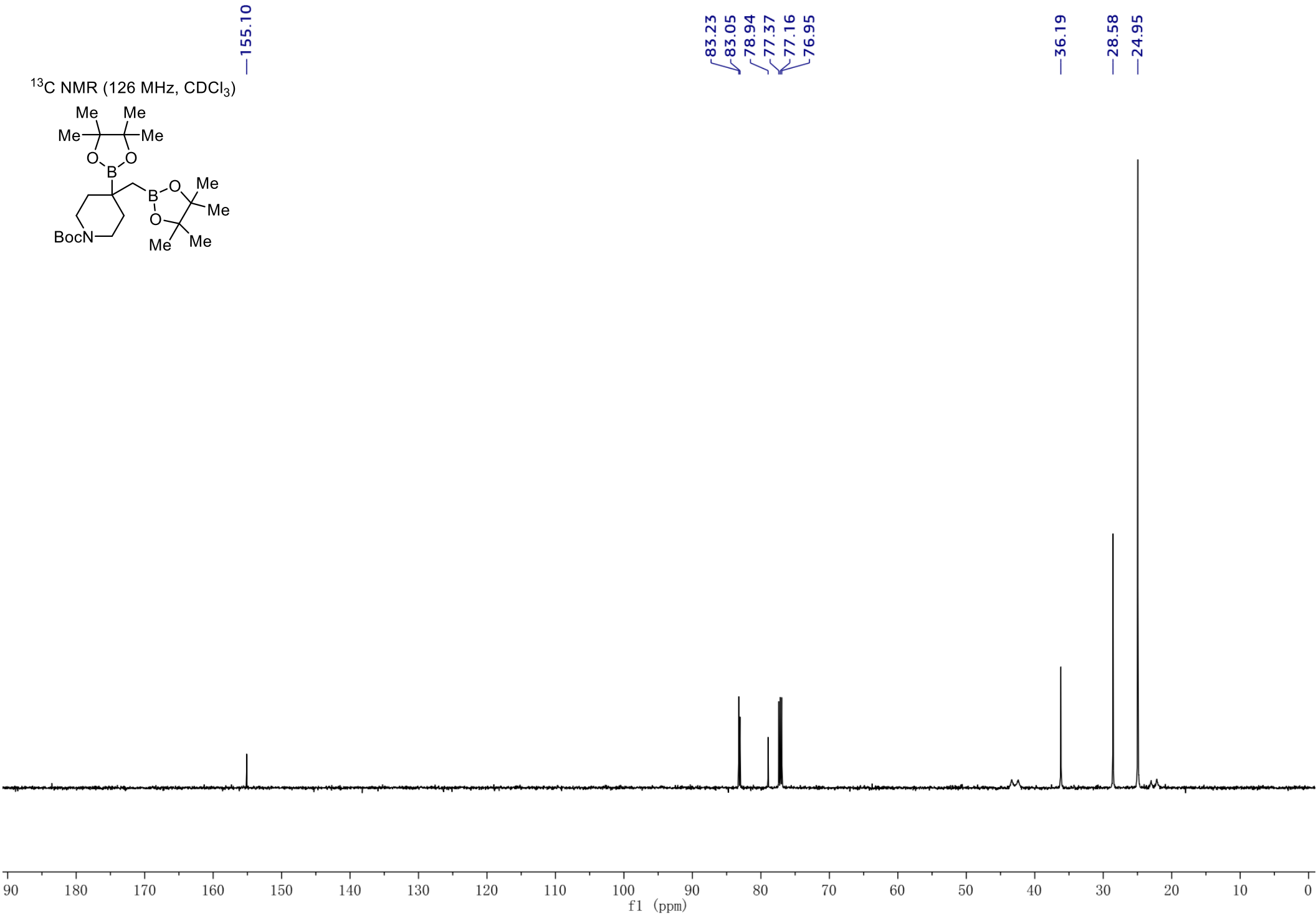
G

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
B
O
B
O
Me
Me
O
Me
Me
BocN
7.26
3.86
2.87
1.85
1.82
1.44
1.24
1.22
1.11
1.09
0.83
1.94
1.93
1.98
9.25
24.69
1.99
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

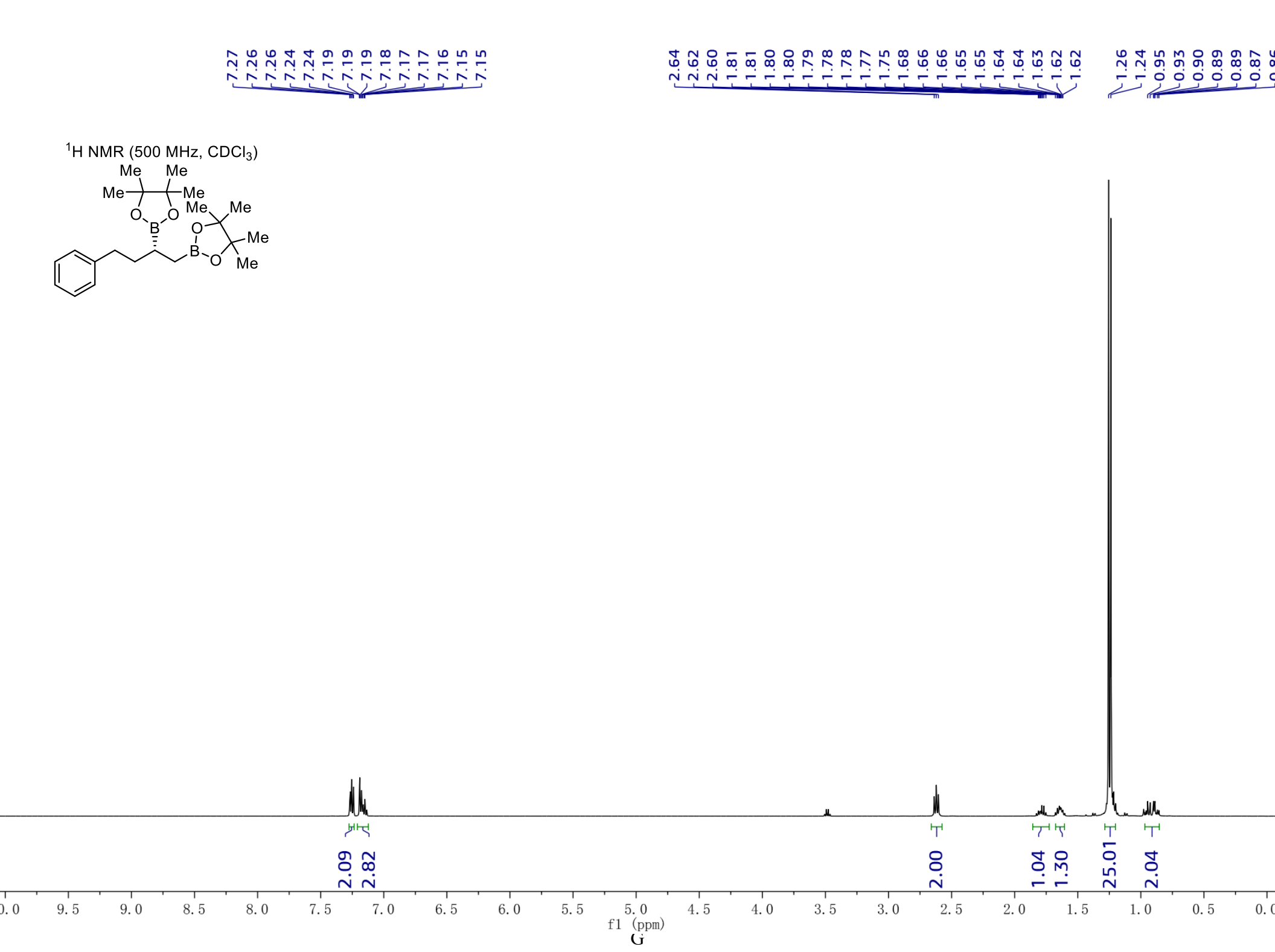
G

E


155.10
83.23
83.05
78.94
77.37
77.16
76.95
36.19
28.58
24.95
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
BocN
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

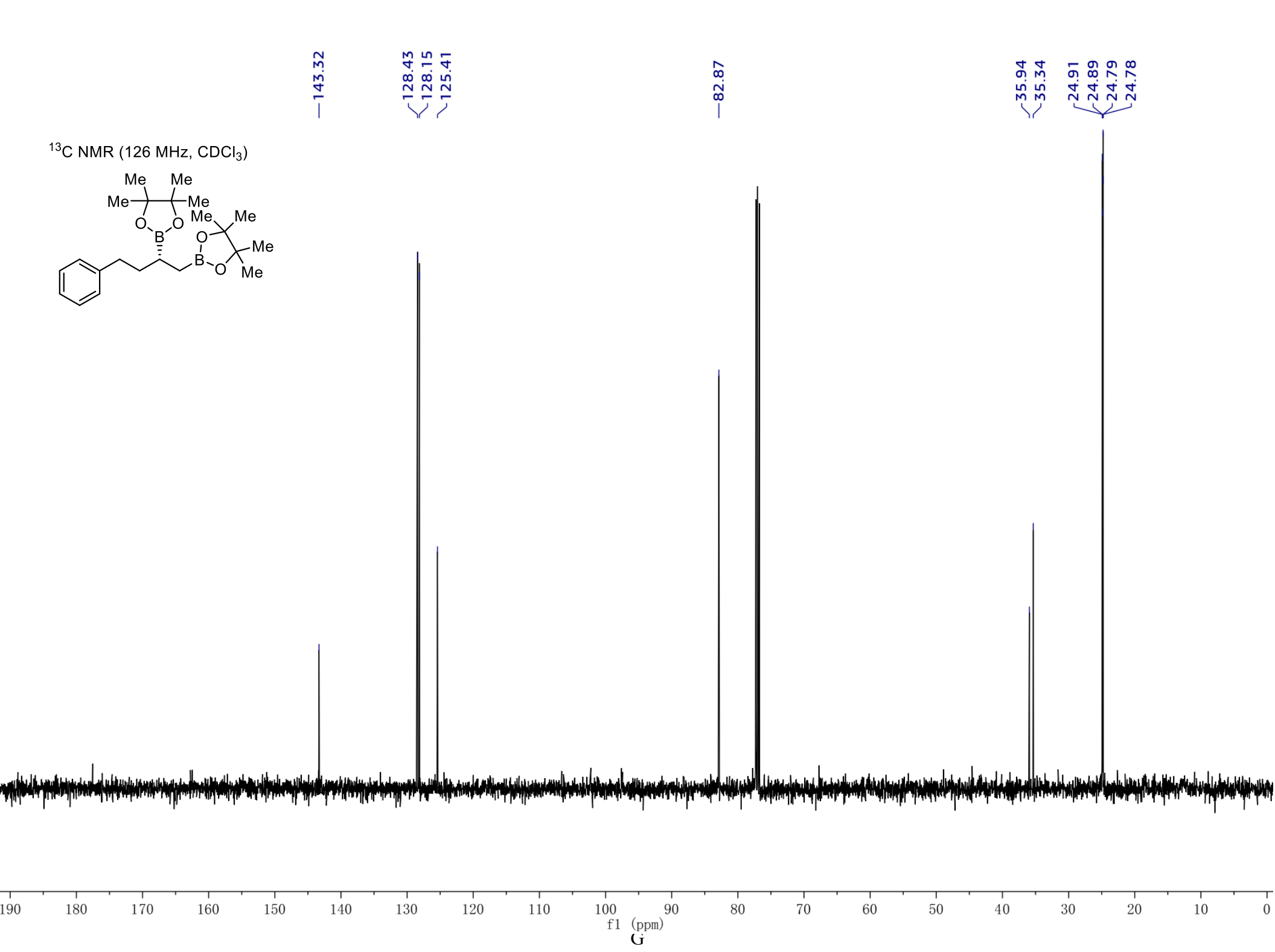
G

E


7.27
7.26
7.26
7.24
7.24
7.19
7.19
7.19
7.18
7.17
7.17
7.16
7.15
7.15
2.64
2.62
2.60
1.81
1.81
1.80
1.80
1.79
1.78
1.78
1.77
1.75
1.68
1.66
1.66
1.65
1.65
1.64
1.64
1.63
1.62
1.62
1.26
1.24
0.95
0.93
0.90
0.89
0.89
0.87
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
Me
Me
Me
2.09
2.82
2.00
1.04
1.30
25.01
2.04
f1 (ppm)

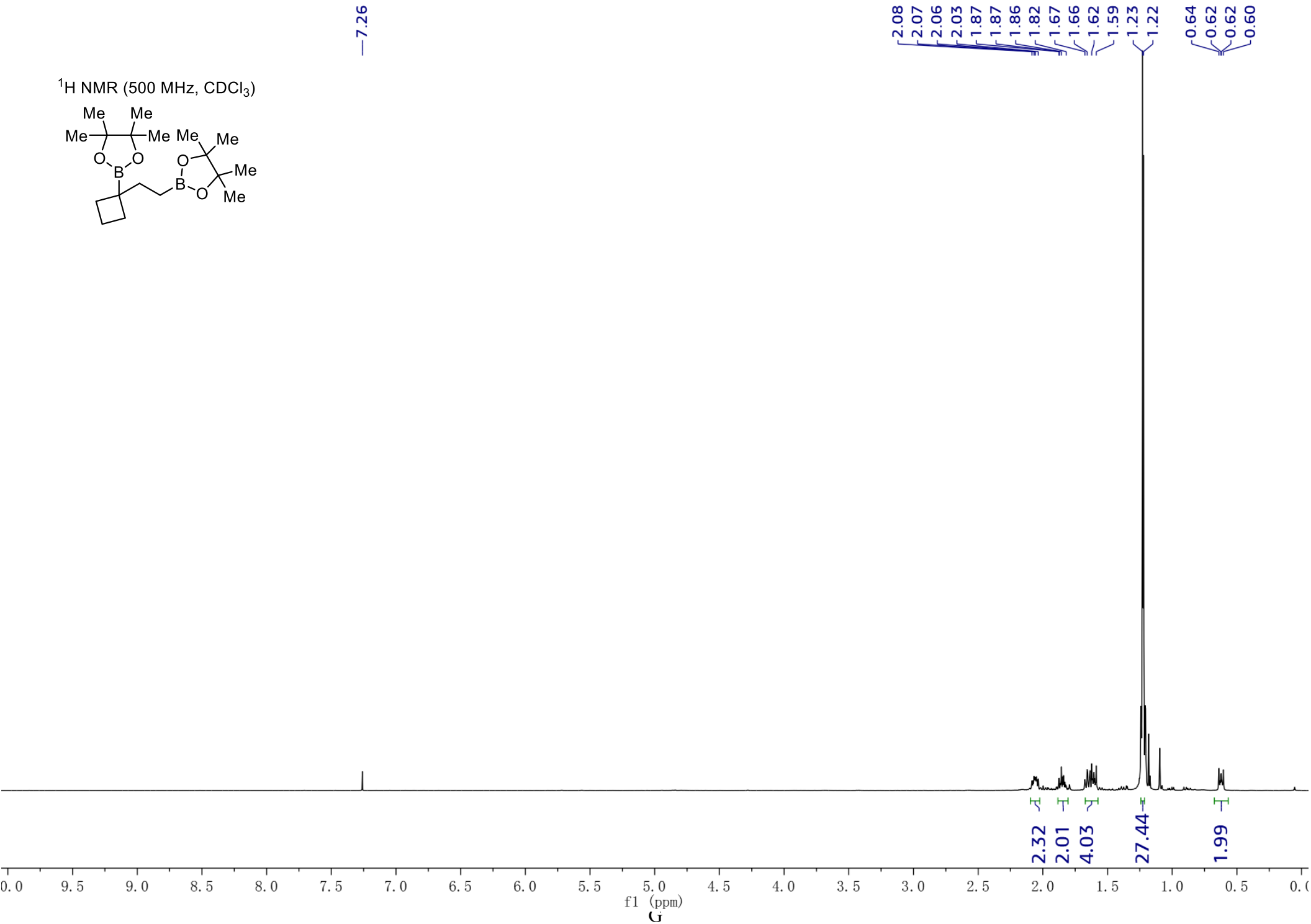
G

E


143.32
128.43
128.15
125.41
82.87
35.94
35.34
24.91
24.89
24.79
24.78
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Me
Me
O
B
O
O
B
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

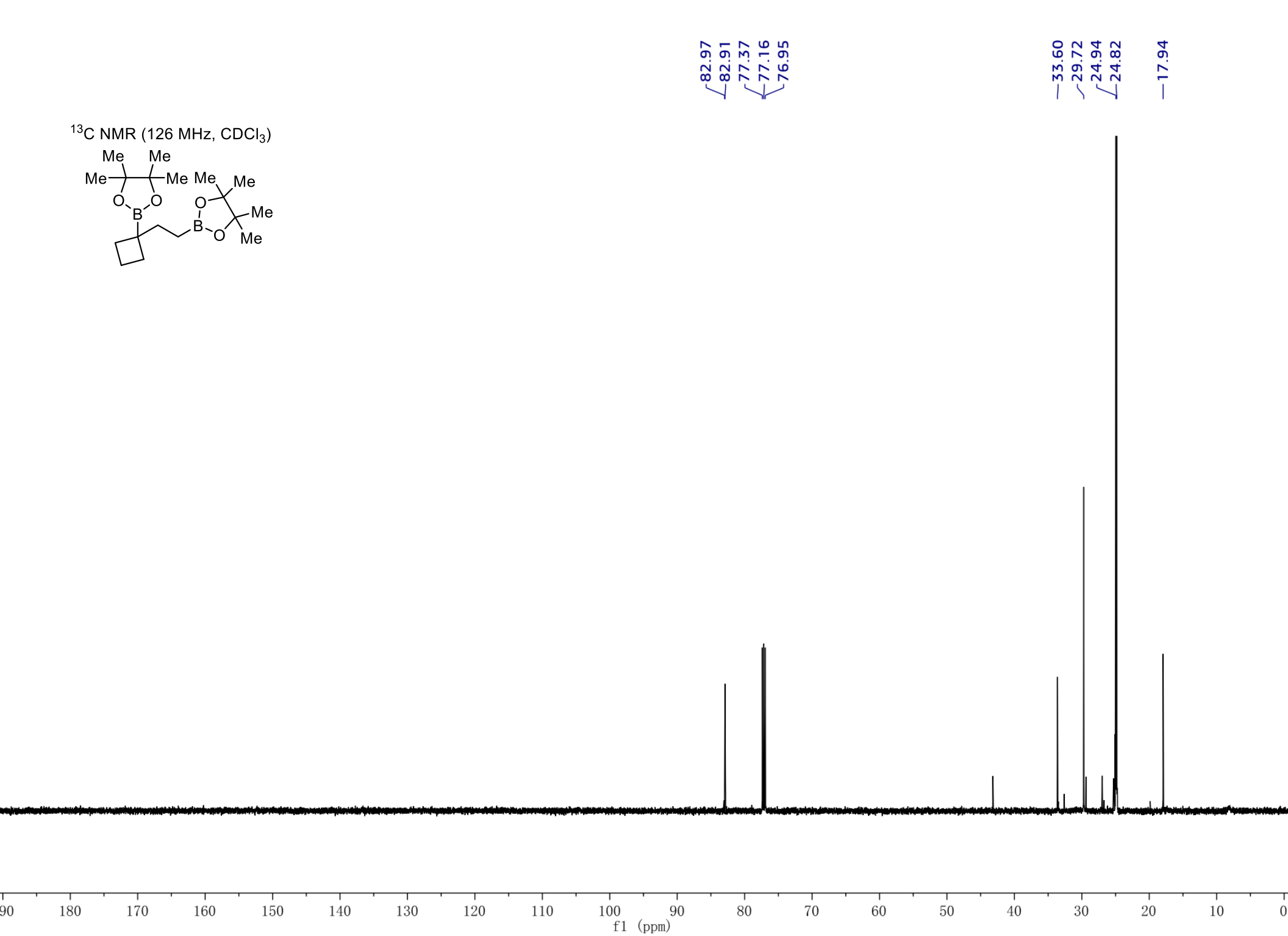
G

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
O
B
O
7.26
2.08
2.07
2.06
2.03
1.87
1.87
1.86
1.82
1.67
1.66
1.62
1.59
1.23
1.22
0.64
0.62
0.62
0.60
2.32
2.01
4.03
27.44
1.99
f1 (ppm)

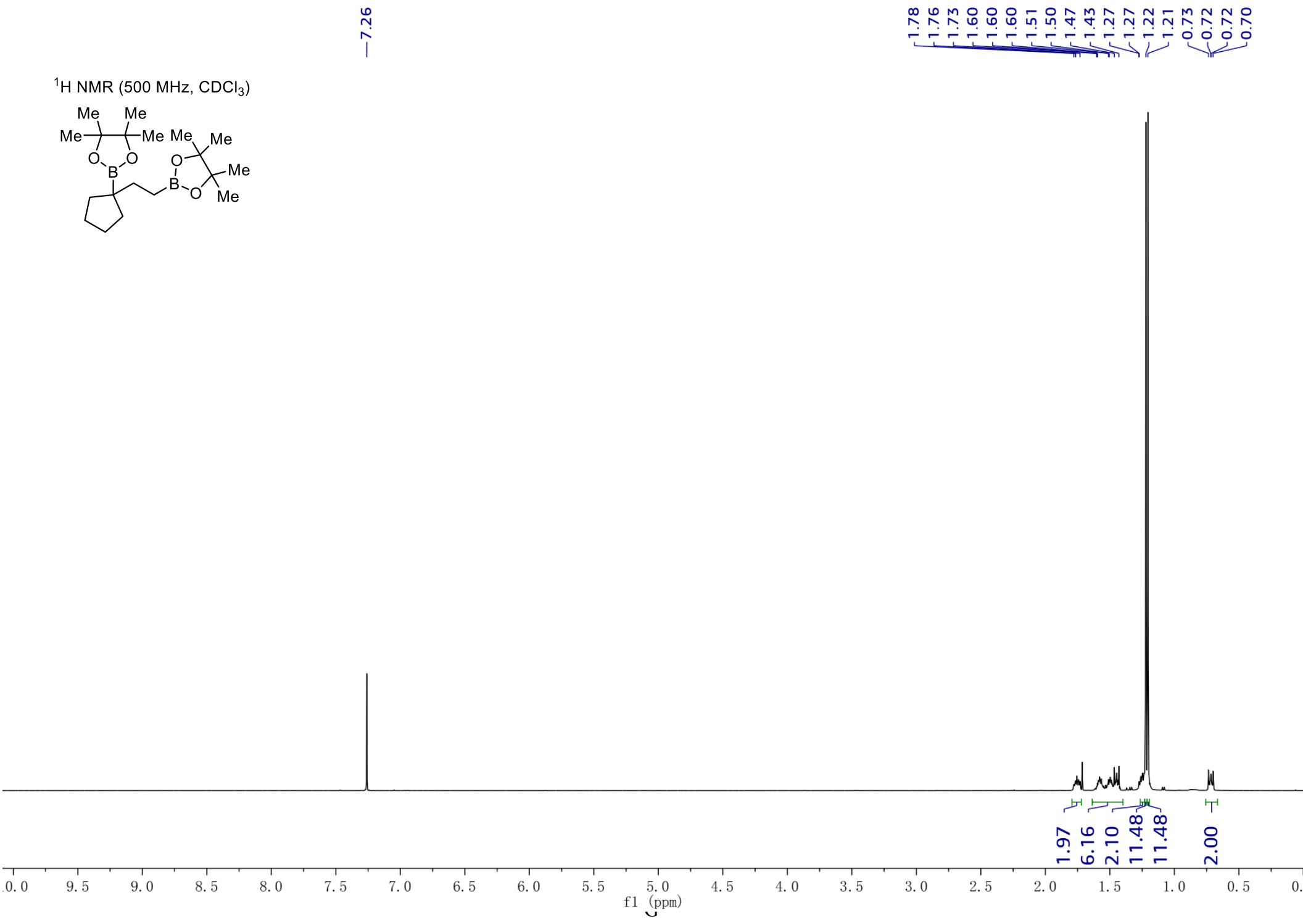
G

E

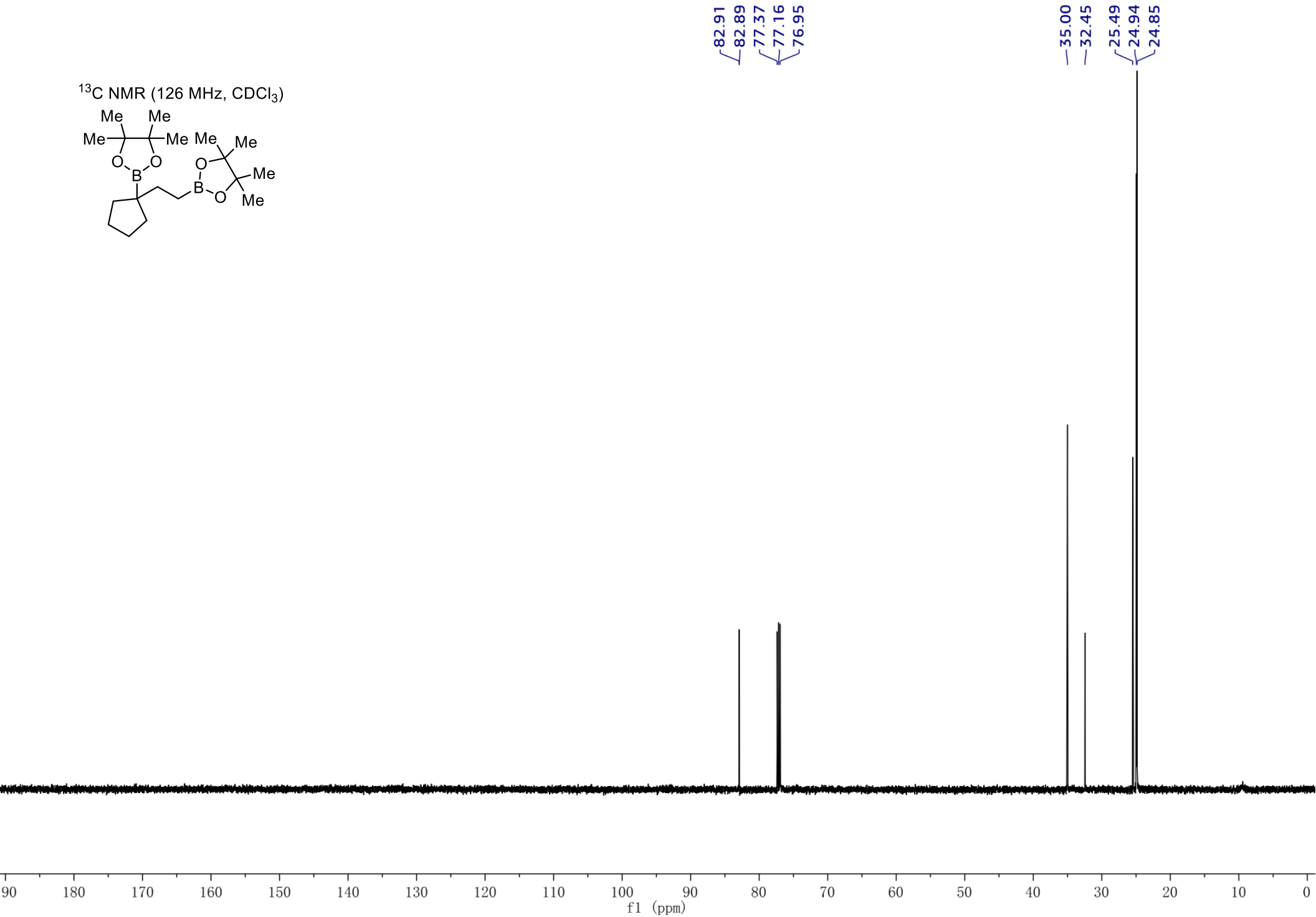

82.97
82.91
77.37
77.16
76.95
33.60
29.72
24.94
24.82
17.94
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
Me
Me
Me
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

E

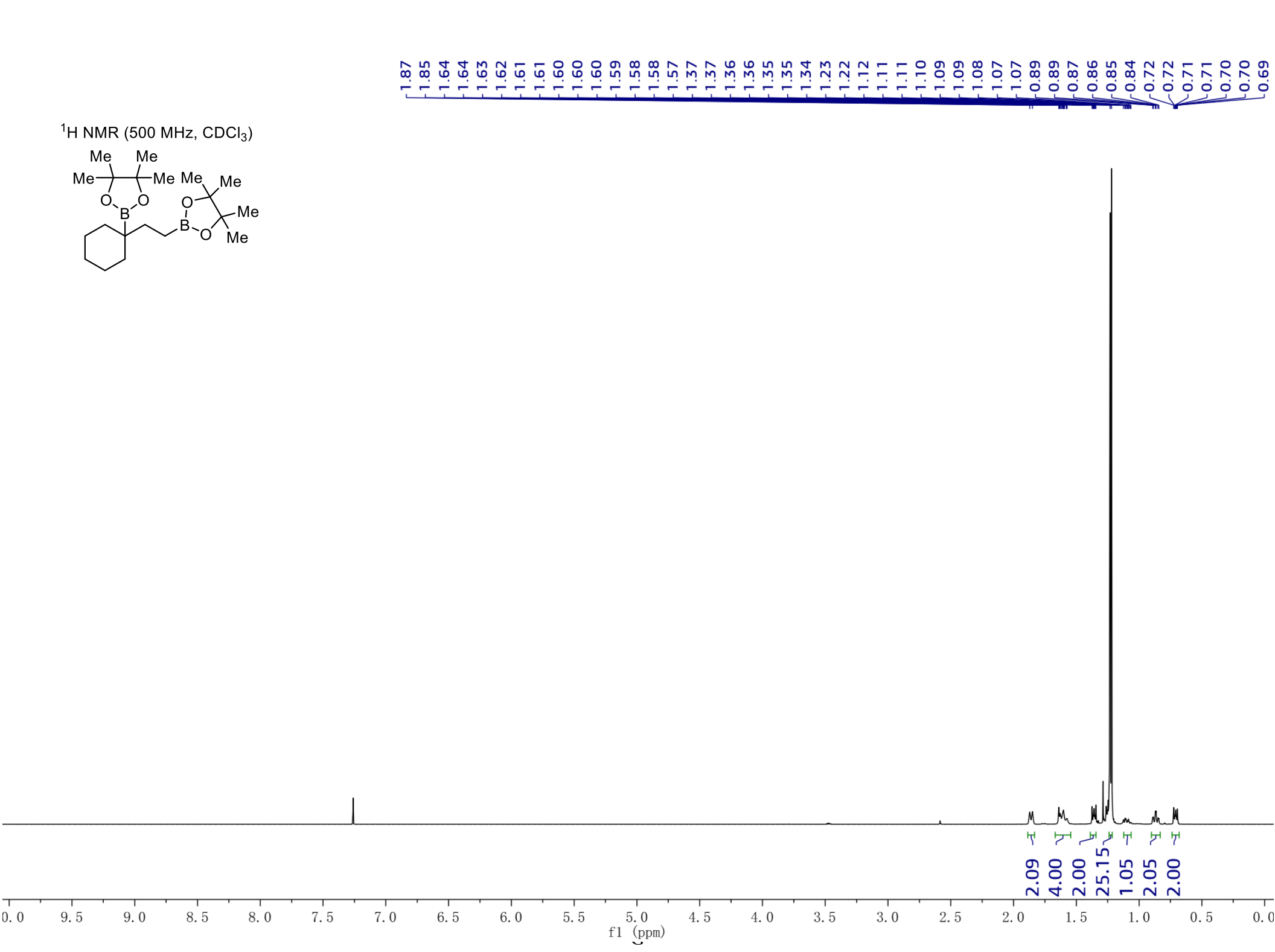

7.26
1.78
1.76
1.73
1.60
1.60
1.60
1.51
1.50
1.47
1.43
1.27
1.27
1.22
1.21
0.73
0.72
0.72
0.70
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
O
B
O
Me
Me
1.97
6.16
2.10
11.48
11.48
2.00
f1 (ppm)

E

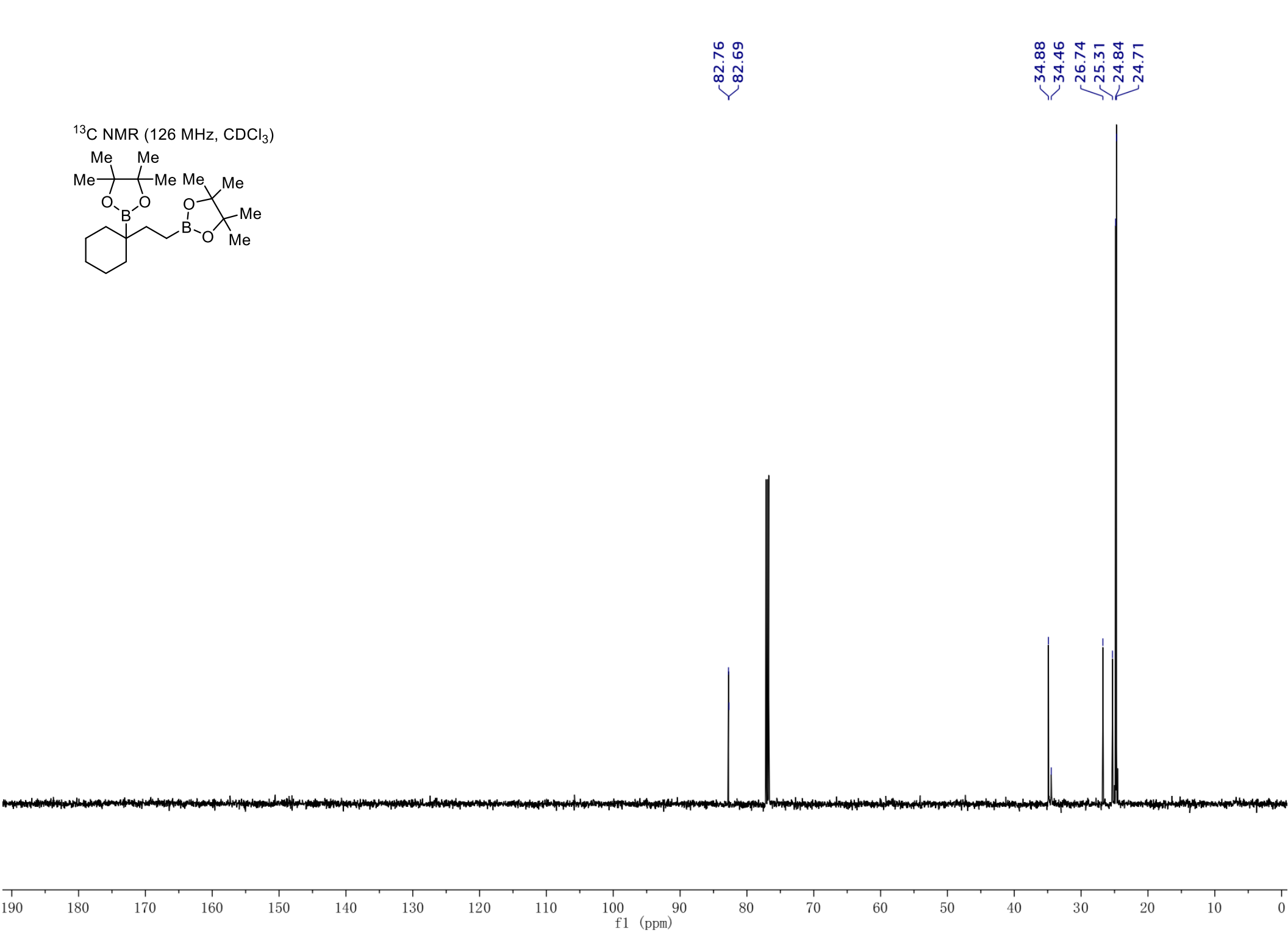

82.91
82.89
77.37
77.16
76.95
35.00
32.45
25.49
24.94
24.85
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

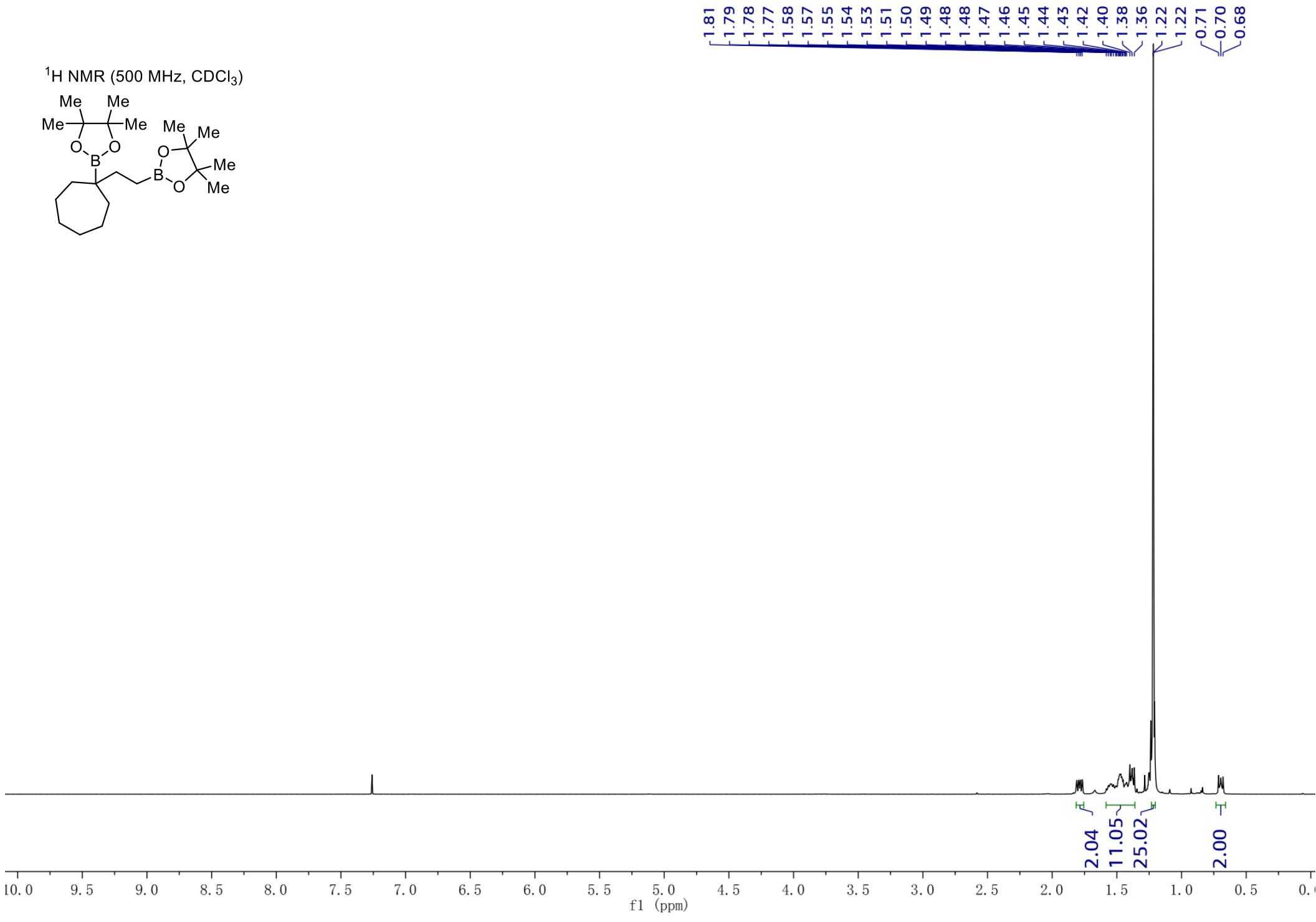
E


1.87 1.85 1.64 1.64 1.63 1.62 1.61 1.61 1.60 1.60 1.60 1.59 1.58 1.58 1.57 1.37 1.37 1.36 1.36 1.35 1.35 1.34 1.23 1.22 1.12 1.11 1.11 1.10 1.09 1.09 1.08 1.07 1.07 0.89 0.89 0.87 0.86 0.85 0.84 0.72 0.72 0.71 0.71 0.70 0.70 0.69
1H NMR (500 MHz, CDCl3)
Me Me Me Me Me Me O O B O B O Me Me Me
2.09 4.00 2.00 25.15 1.05 2.05 2.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

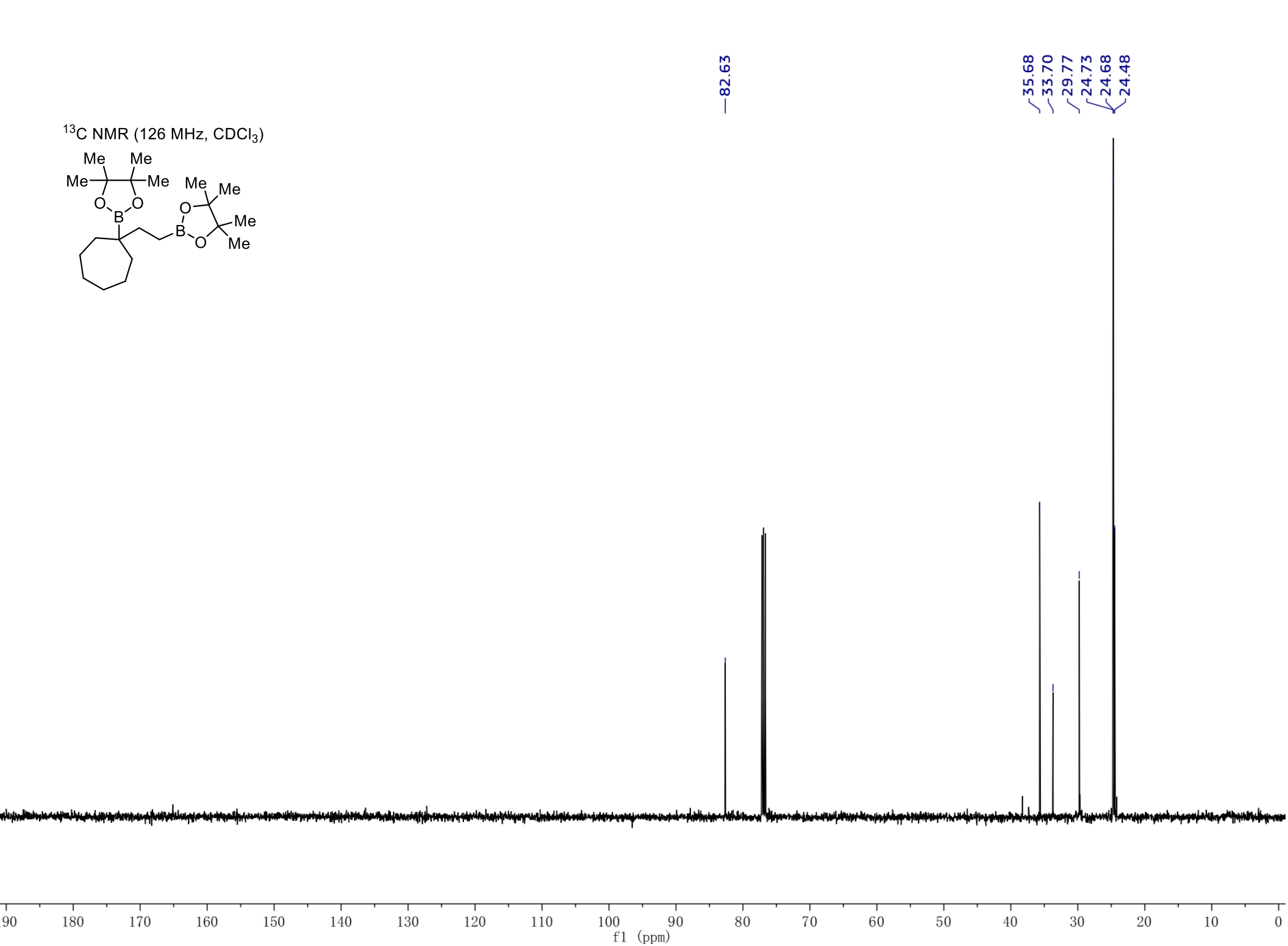
E


82.76
82.69
34.88
34.46
26.74
25.31
24.84
24.71
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
Me
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G
E

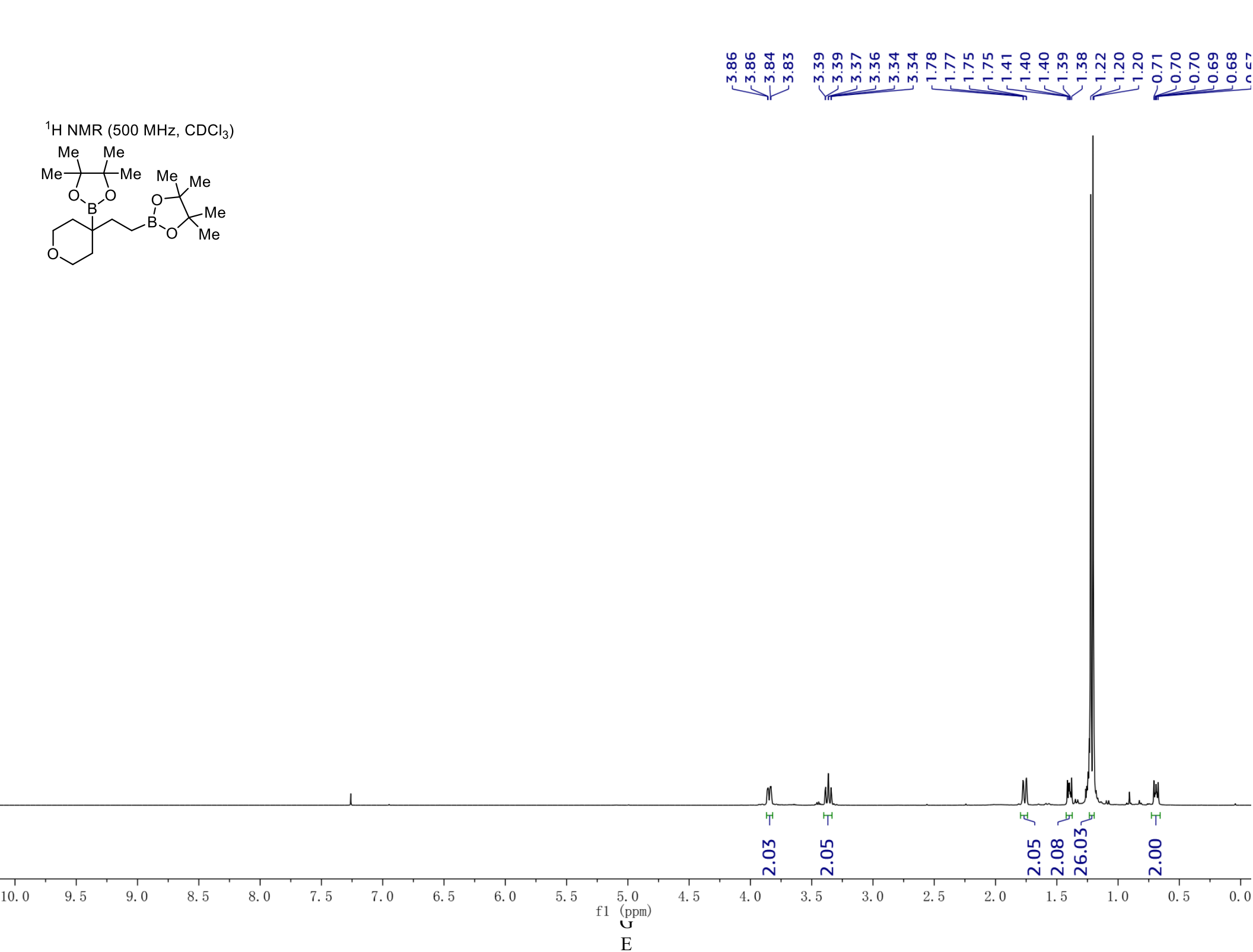

1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
1.81
1.79
1.78
1.77
1.58
1.57
1.55
1.54
1.53
1.51
1.50
1.49
1.48
1.48
1.47
1.46
1.45
1.44
1.43
1.42
1.40
1.38
1.36
1.22
1.22
0.71
0.70
0.68
2.04
11.05
25.02
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

E


82.63
35.68
33.70
29.77
24.73
24.68
24.48
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
f1 (ppm)

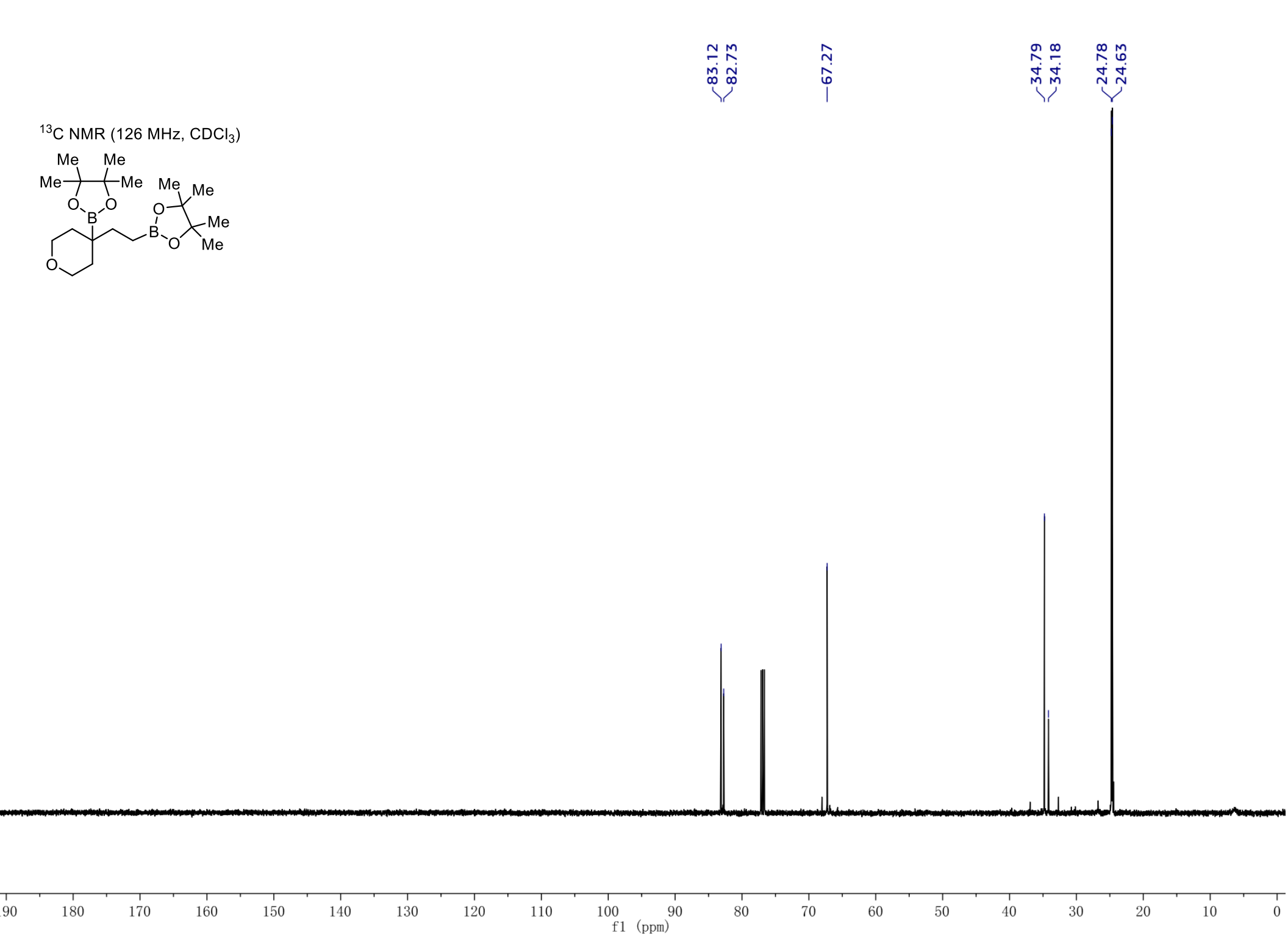
G

E


$^1$H NMR (500 MHz, $CDCl_3$)
3.86
3.86
3.84
3.83
3.39
3.39
3.37
3.36
3.34
3.34
1.78
1.77
1.75
1.75
1.41
1.40
1.40
1.39
1.38
1.22
1.20
1.20
0.71
0.70
0.70
0.69
0.68
2.03
2.05
2.05
2.08
26.03
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

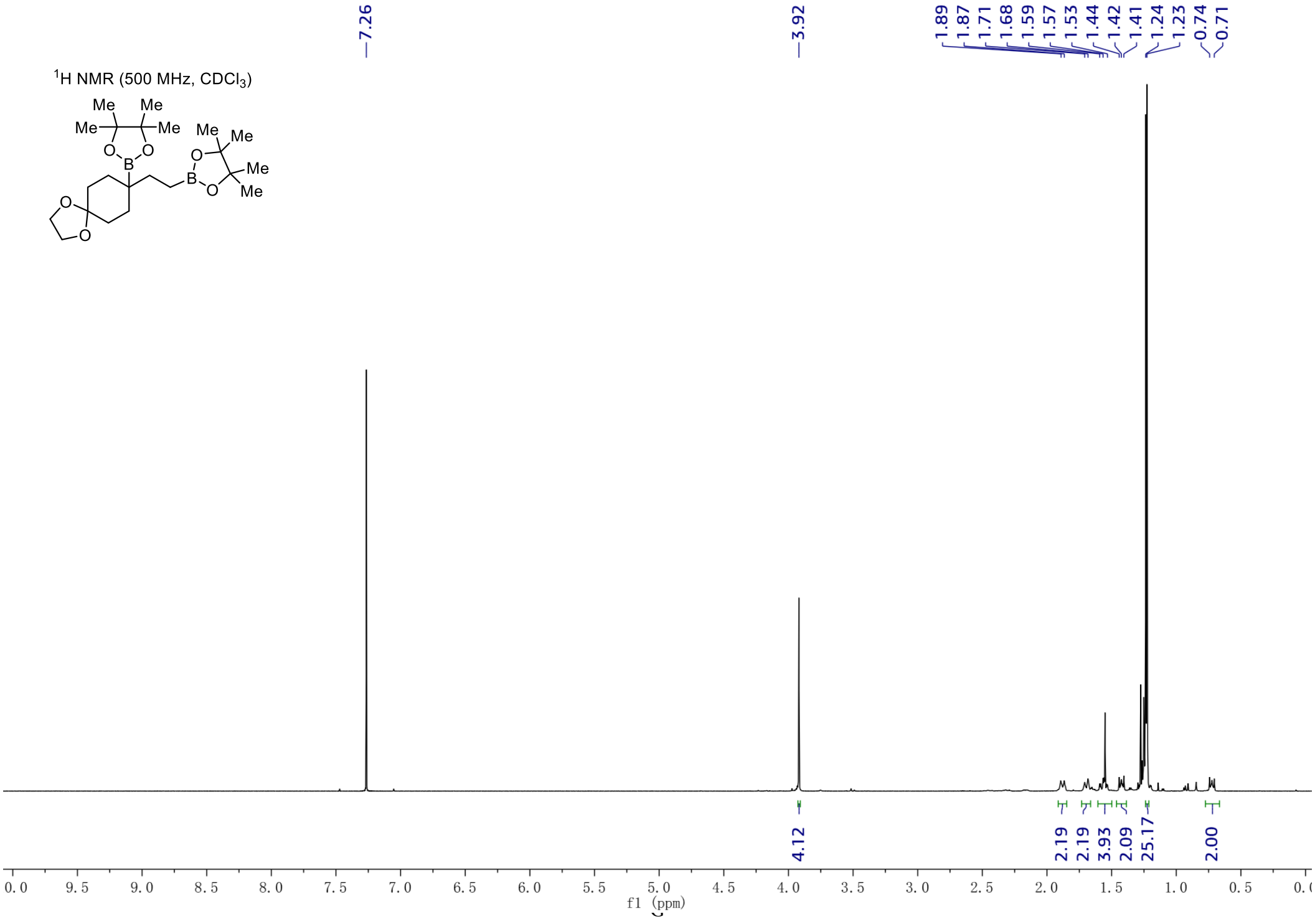
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
O
O
83.12
82.73
67.27
34.79
34.18
24.78
24.63
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

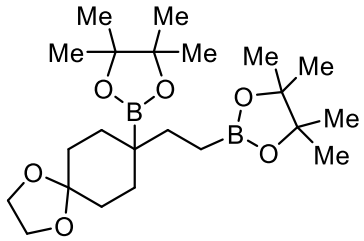
G

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
O
O
O
7.26
3.92
1.89
1.87
1.71
1.68
1.59
1.57
1.53
1.44
1.42
1.41
1.24
1.23
0.74
0.71
4.12
2.19
2.19
3.93
2.09
25.17
2.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

E

$^{13}$C NMR (126 MHz, $CDCl_3$)

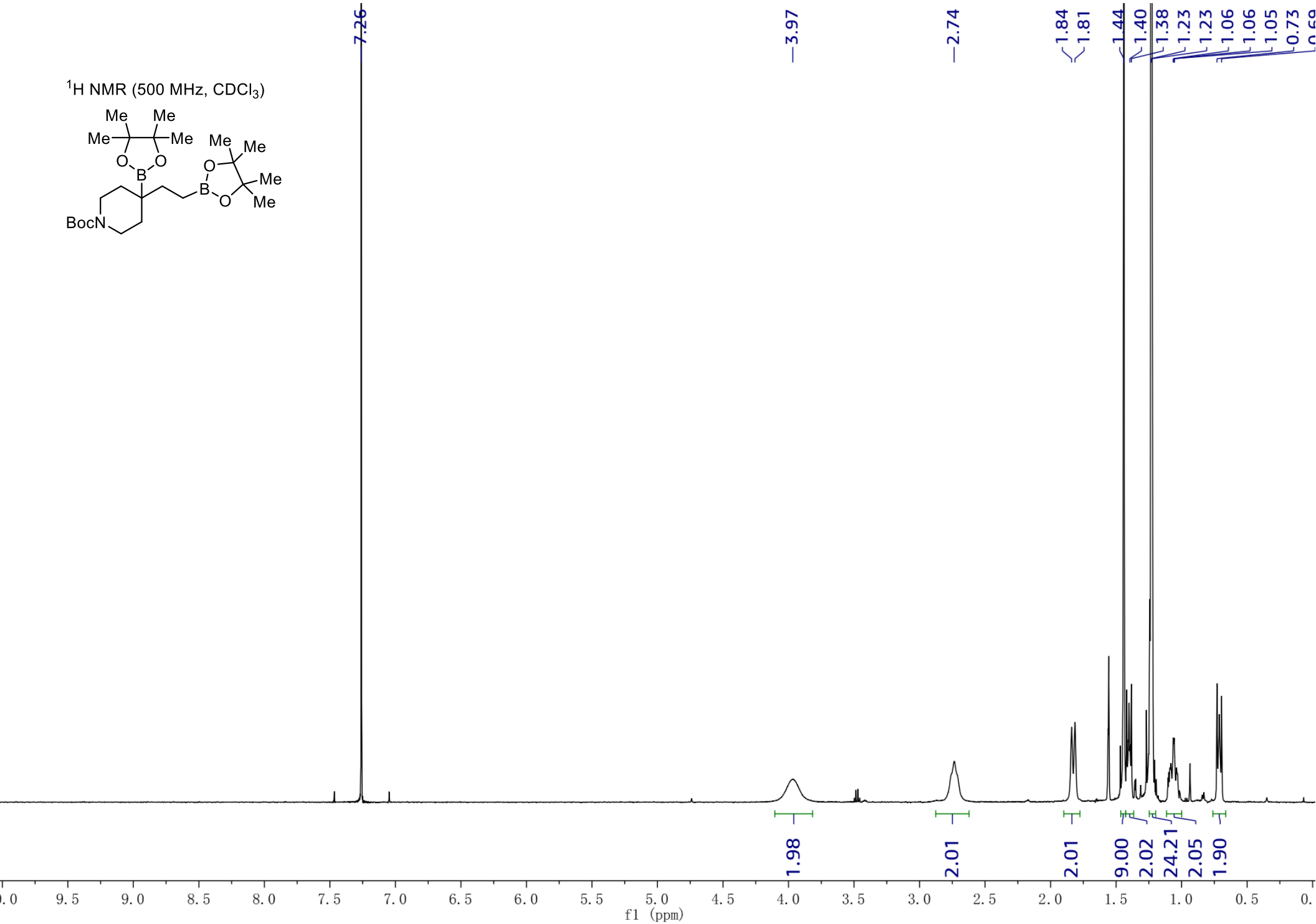




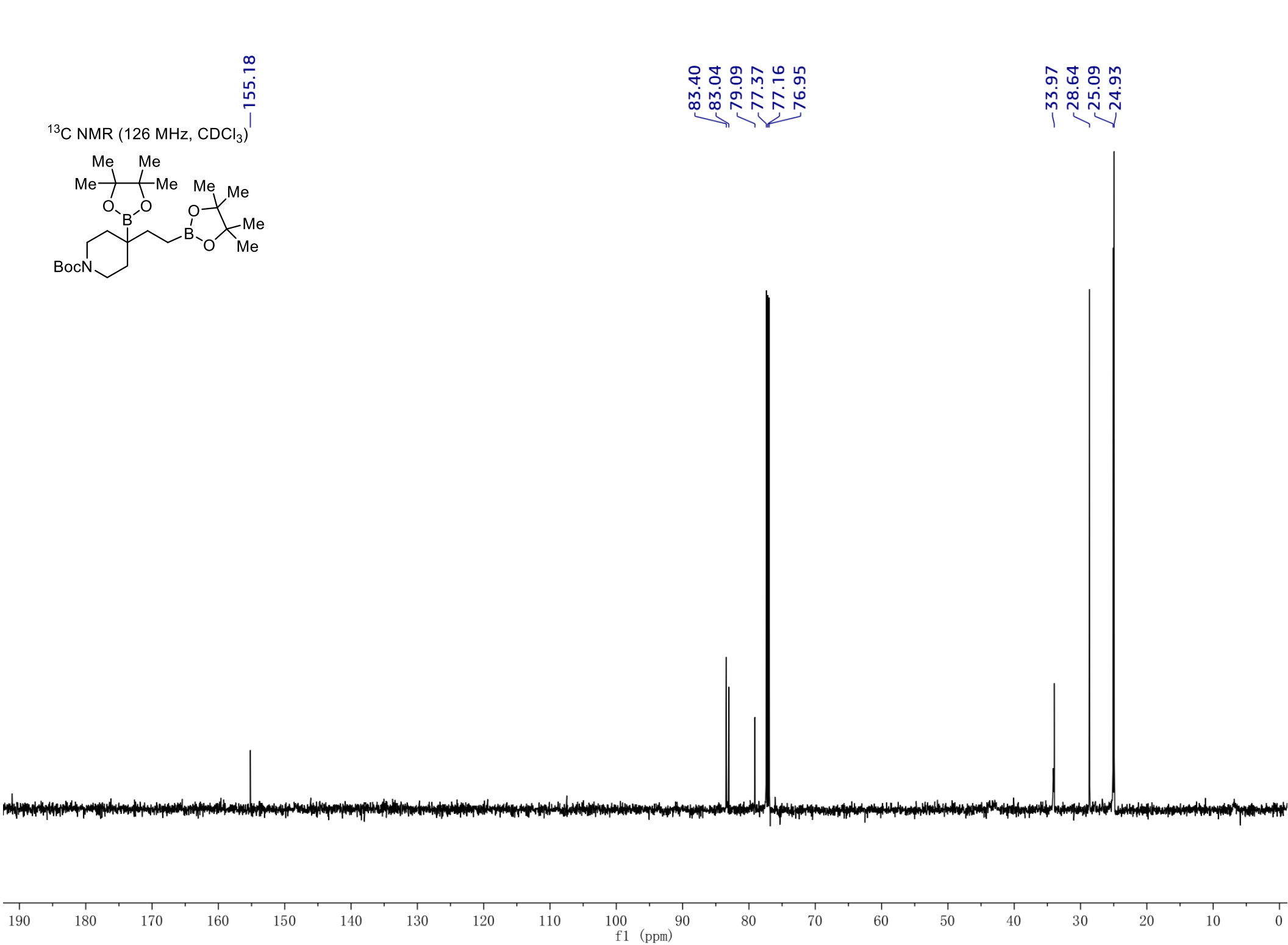


G

E

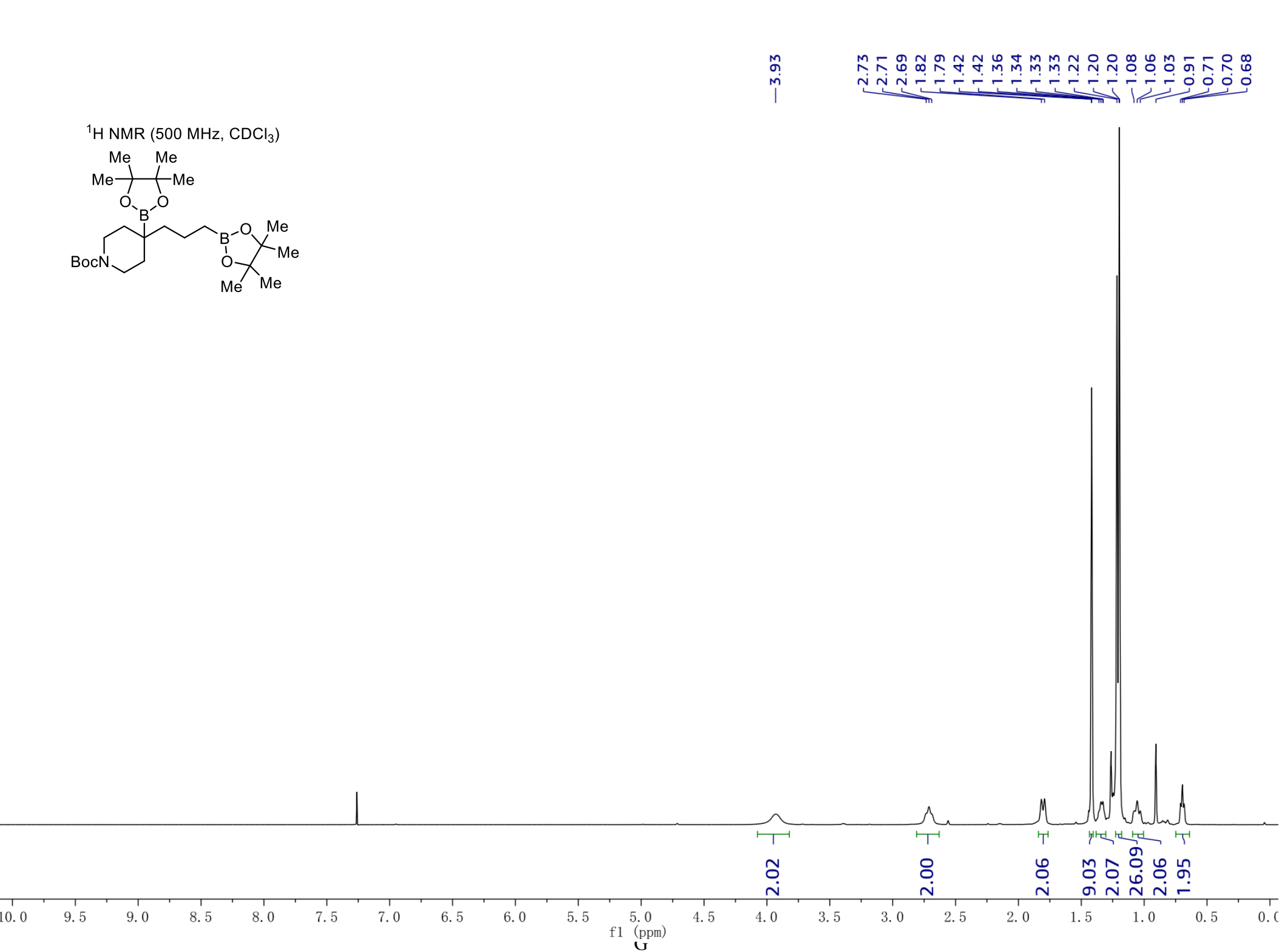

$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
Me
Me
Me
BocN
7.26
3.97
2.74
1.84
1.81
1.44
1.40
1.38
1.23
1.23
1.06
1.06
1.05
0.73
1.98
2.01
2.01
9.00
2.02
24.21
2.05
1.90
f1 (ppm)

E


155.18
83.40
83.04
79.09
77.37
77.16
76.95
33.97
28.64
25.09
24.93
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
O
O
B
O
B
O
Me
Me
BocN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

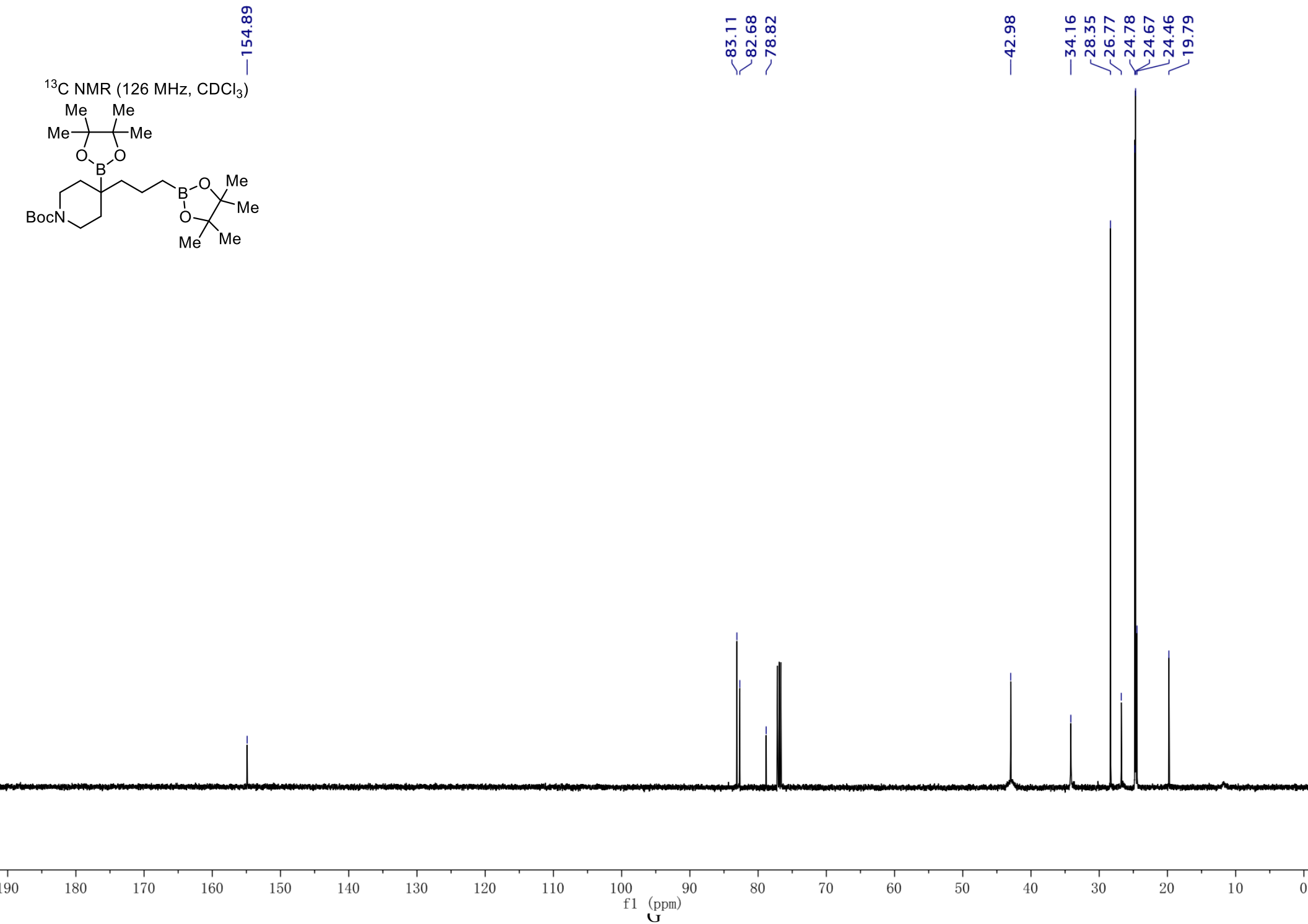
G

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
BocN
B
O
Me
Me
O
Me
Me
3.93
2.73
2.71
2.69
1.82
1.79
1.42
1.42
1.36
1.34
1.33
1.33
1.22
1.20
1.20
1.08
1.06
1.03
0.91
0.71
0.70
0.68
2.02
2.00
2.06
9.03
2.07
26.09
2.06
1.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

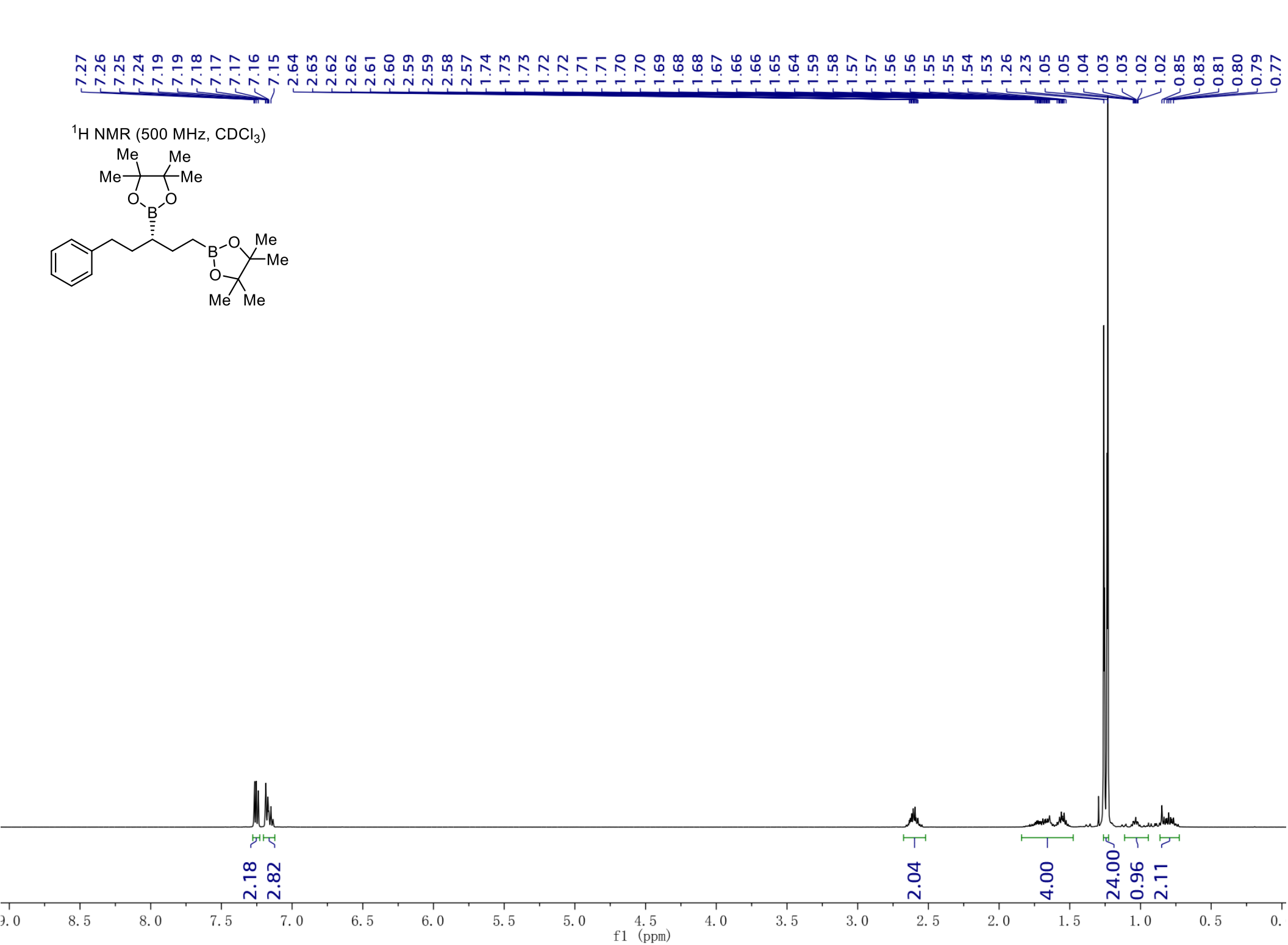
G

E


154.89
83.11
82.68
78.82
42.98
34.16
28.35
26.77
24.78
24.67
24.46
19.79
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
BocN
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

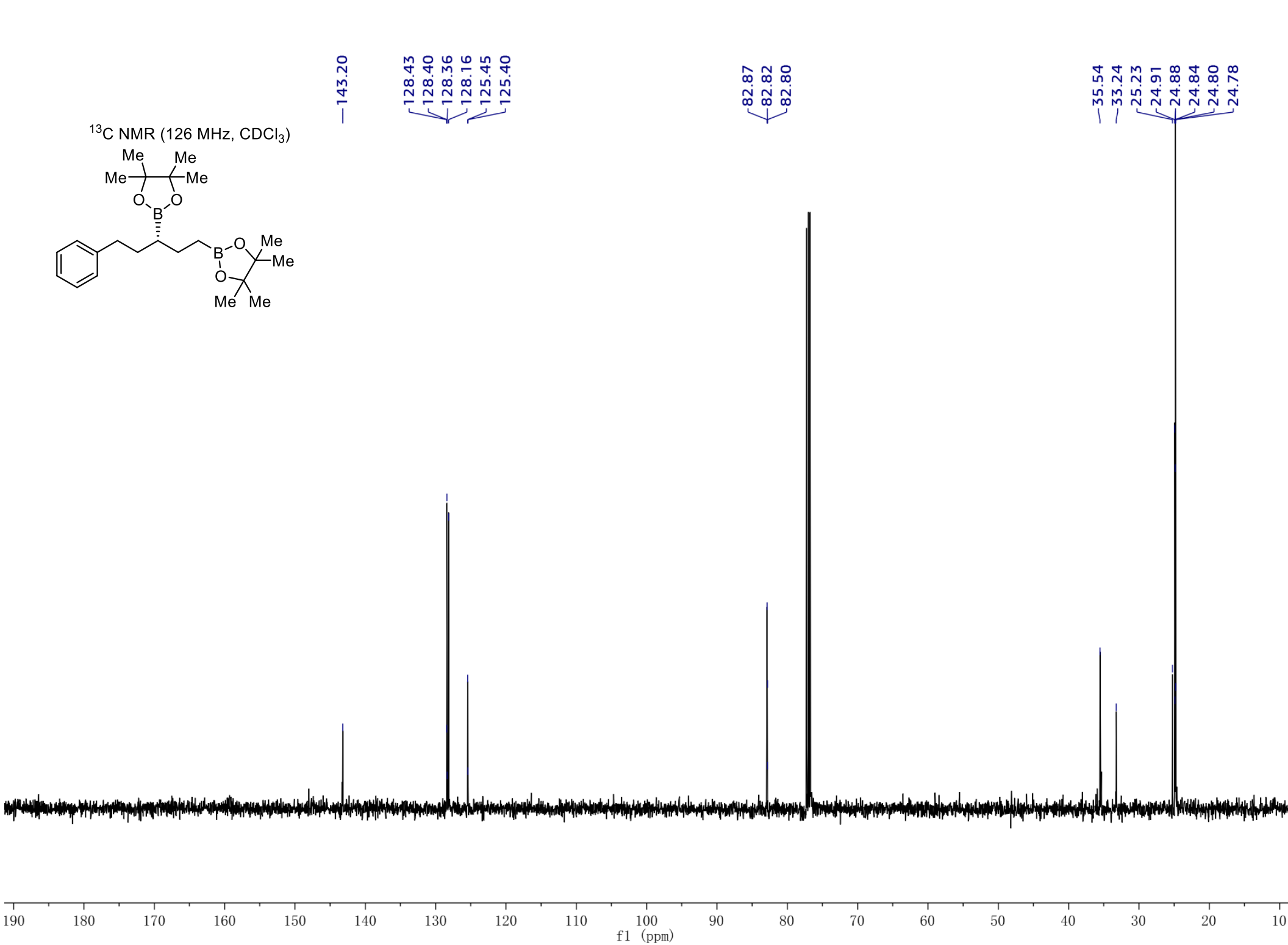
G

E


7.27 7.26 7.25 7.24 7.19 7.19 7.18 7.17 7.17 7.16 7.15 2.64 2.63 2.62 2.62 2.61 2.60 2.59 2.59 2.58 2.57 1.74 1.73 1.73 1.72 1.72 1.71 1.71 1.70 1.70 1.69 1.68 1.68 1.67 1.66 1.66 1.65 1.64 1.59 1.58 1.57 1.57 1.56 1.56 1.55 1.55 1.54 1.53 1.26 1.23 1.05 1.05 1.04 1.03 1.03 1.02 1.02 0.85 0.83 0.81 0.80 0.79 0.77
$^1$H NMR (500 MHz, $CDCl_3$)
Me Me Me Me O O B O B O Me Me O Me Me
2.18 2.82 2.04 4.00 24.00 0.96 2.11
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.
f1 (ppm)

G

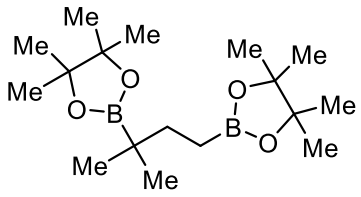
E


143.20
128.43
128.40
128.36
128.16
125.45
125.40
82.87
82.82
82.80
35.54
33.24
25.23
24.91
24.88
24.84
24.80
24.78
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
B
O
Me
Me
O
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

G

E

$^1$H NMR (500 MHz, $CDCl_3$)

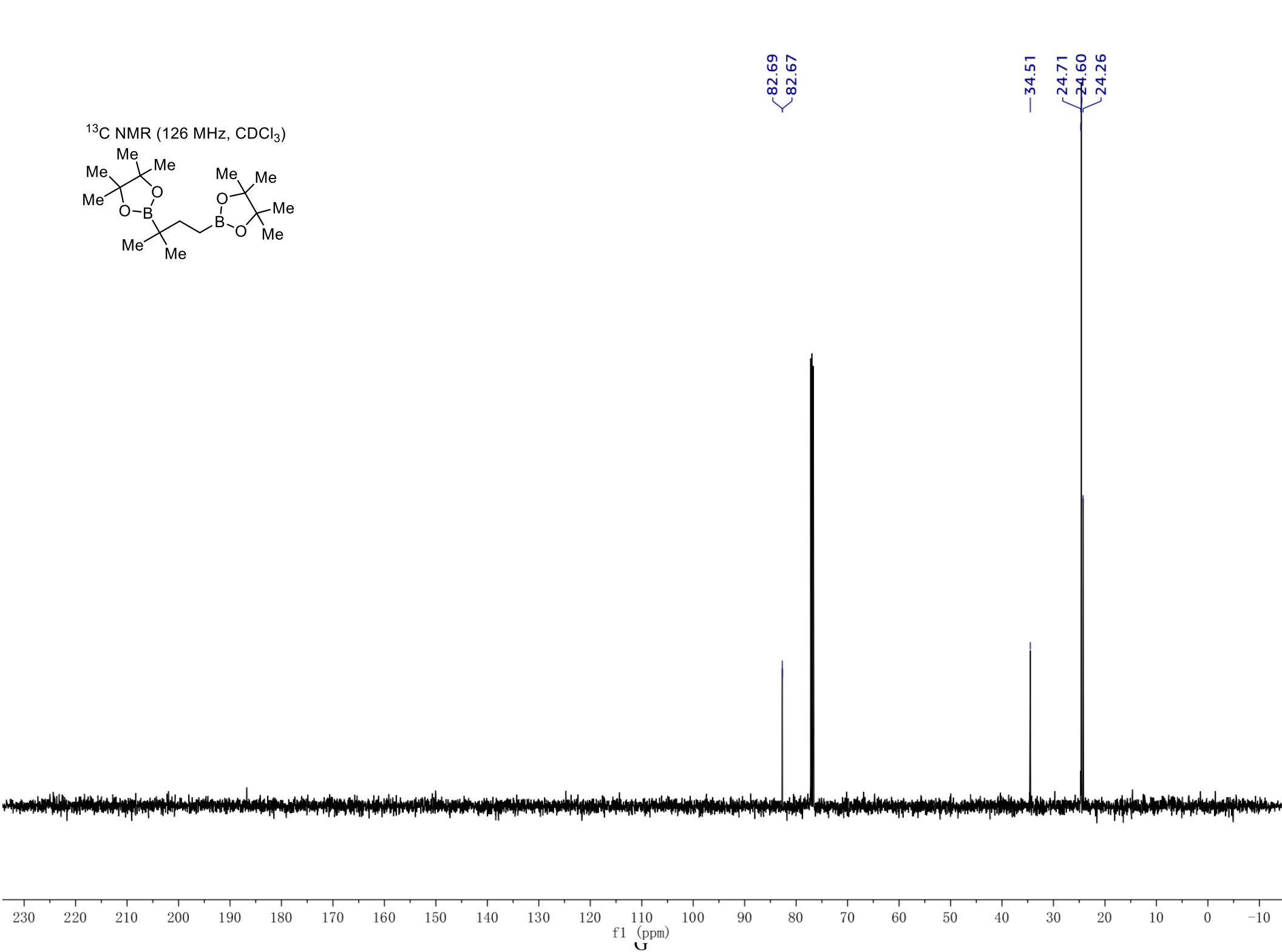




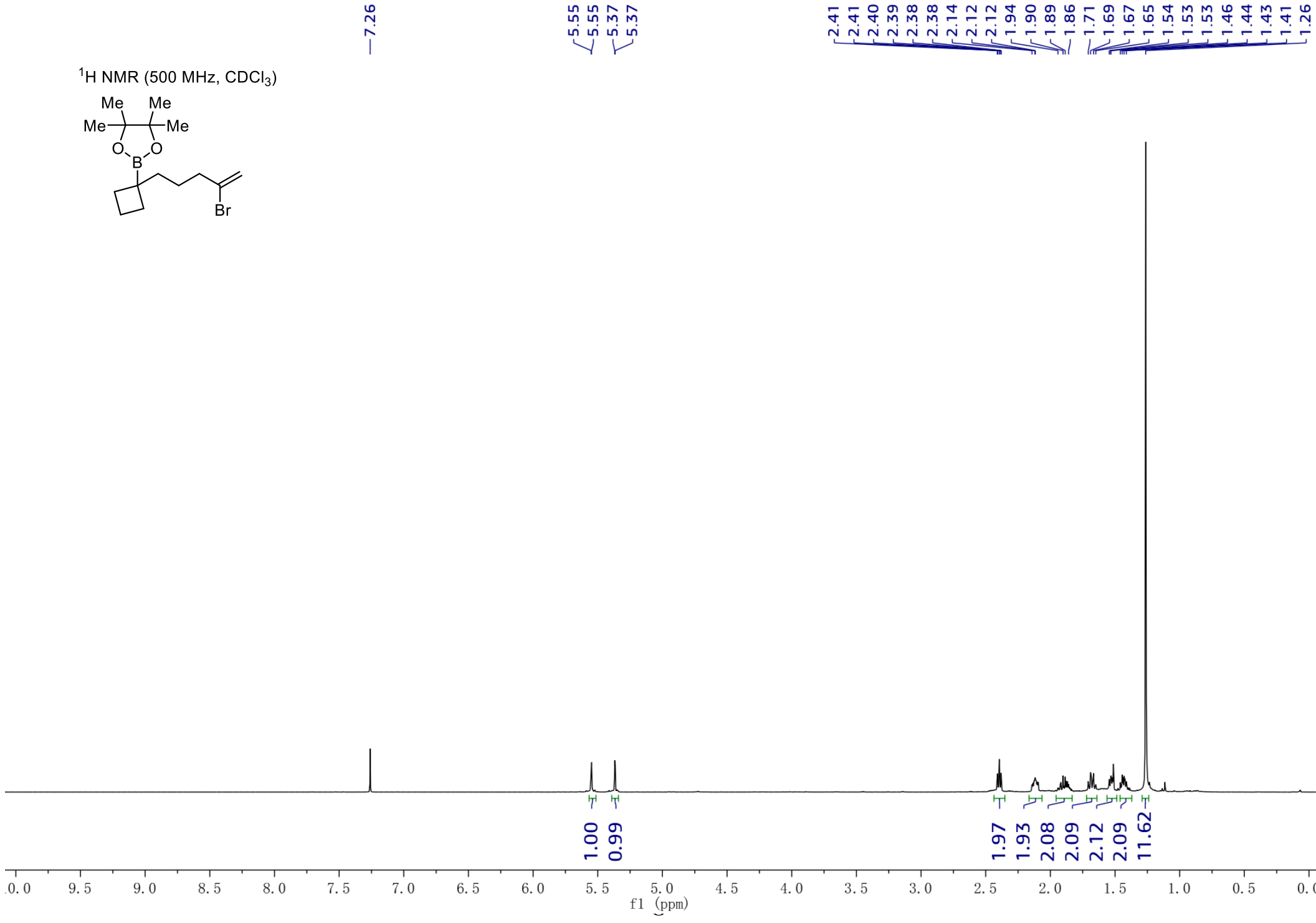


G

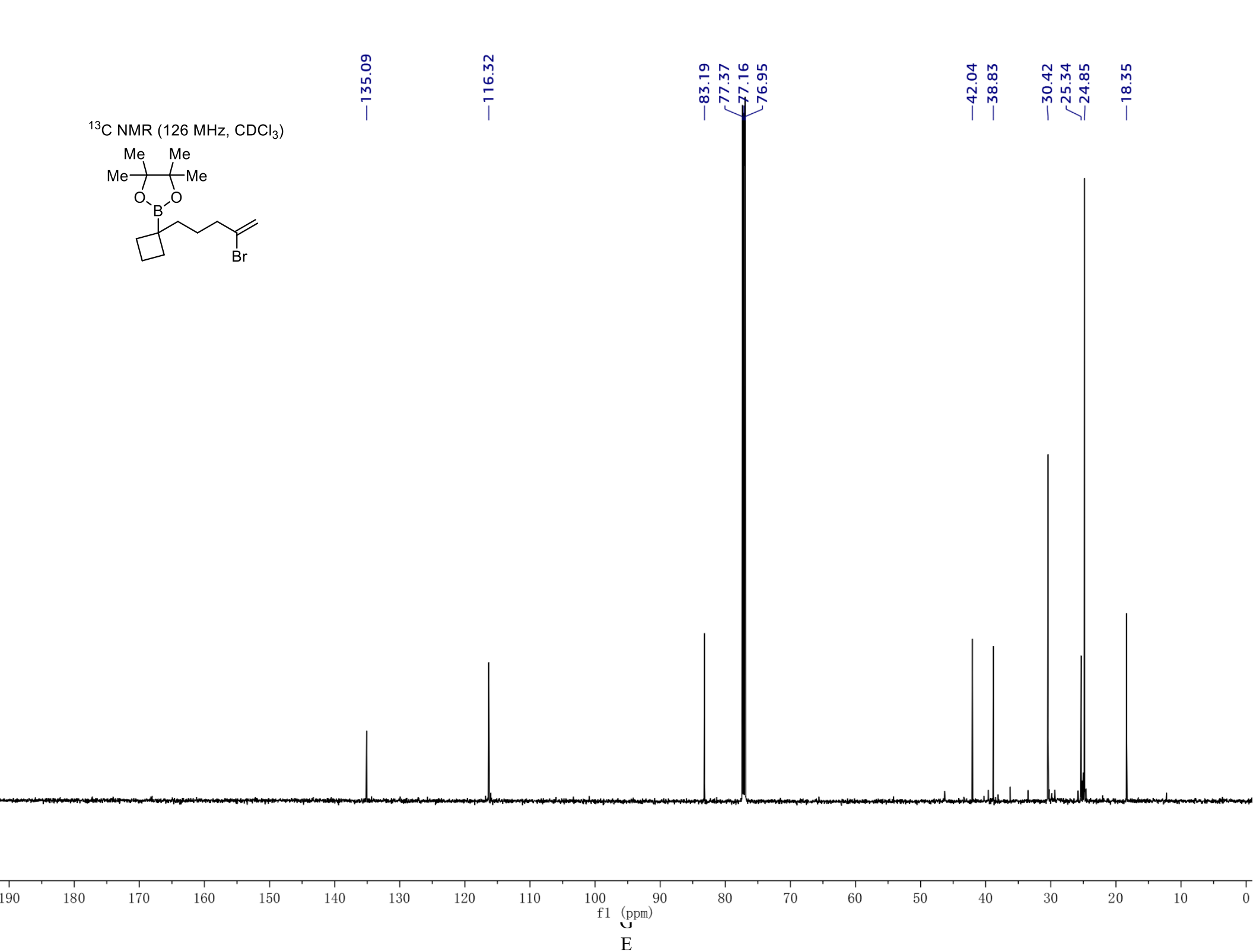
E



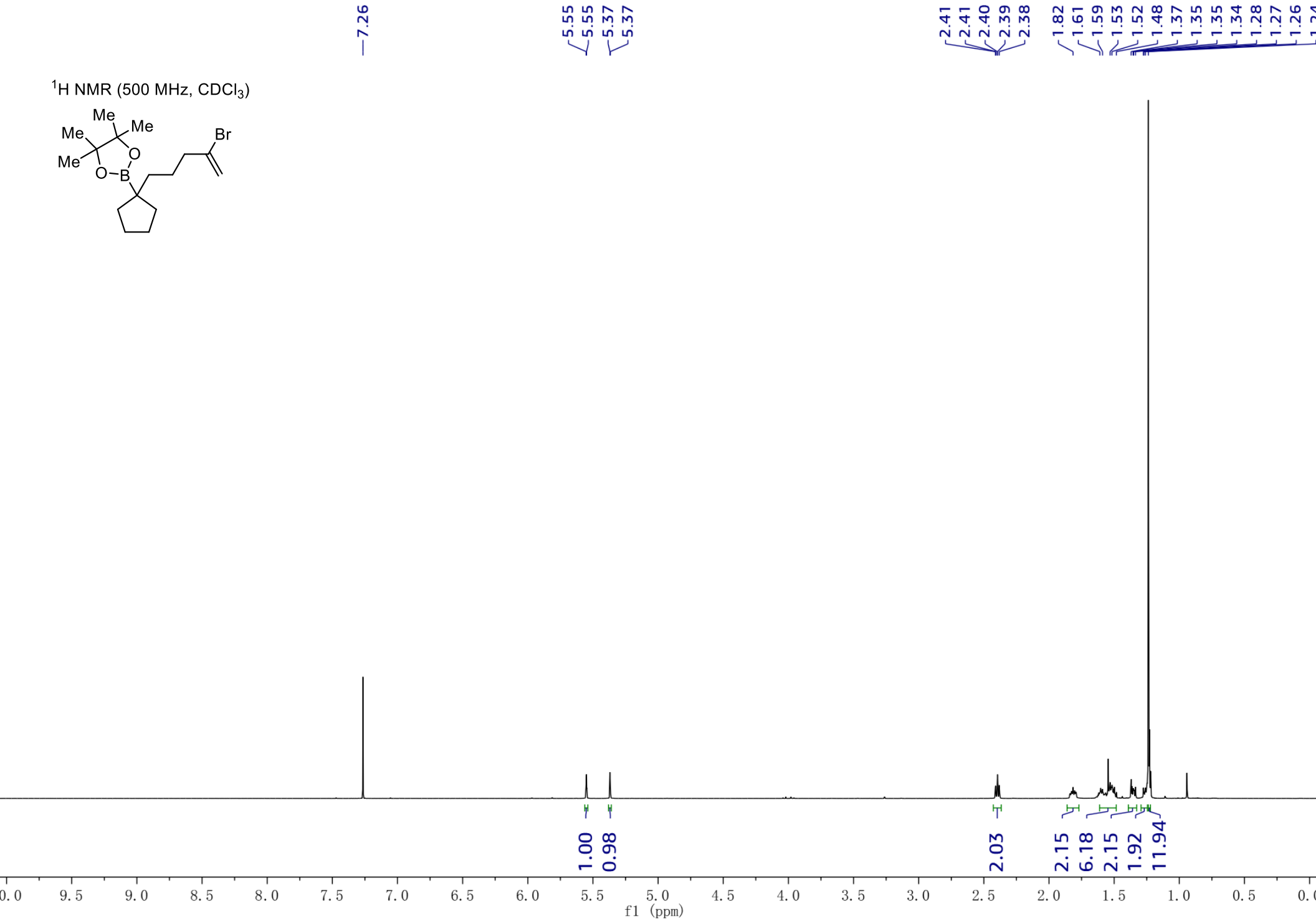

G
E


7.26
5.55
5.55
5.37
5.37
2.41
2.41
2.40
2.39
2.38
2.38
2.14
2.12
2.12
1.94
1.90
1.89
1.86
1.71
1.69
1.67
1.65
1.54
1.53
1.53
1.46
1.44
1.43
1.41
1.26
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
1.00
0.99
1.97
1.93
2.08
2.09
2.12
2.09
11.62
f1 (ppm)

E

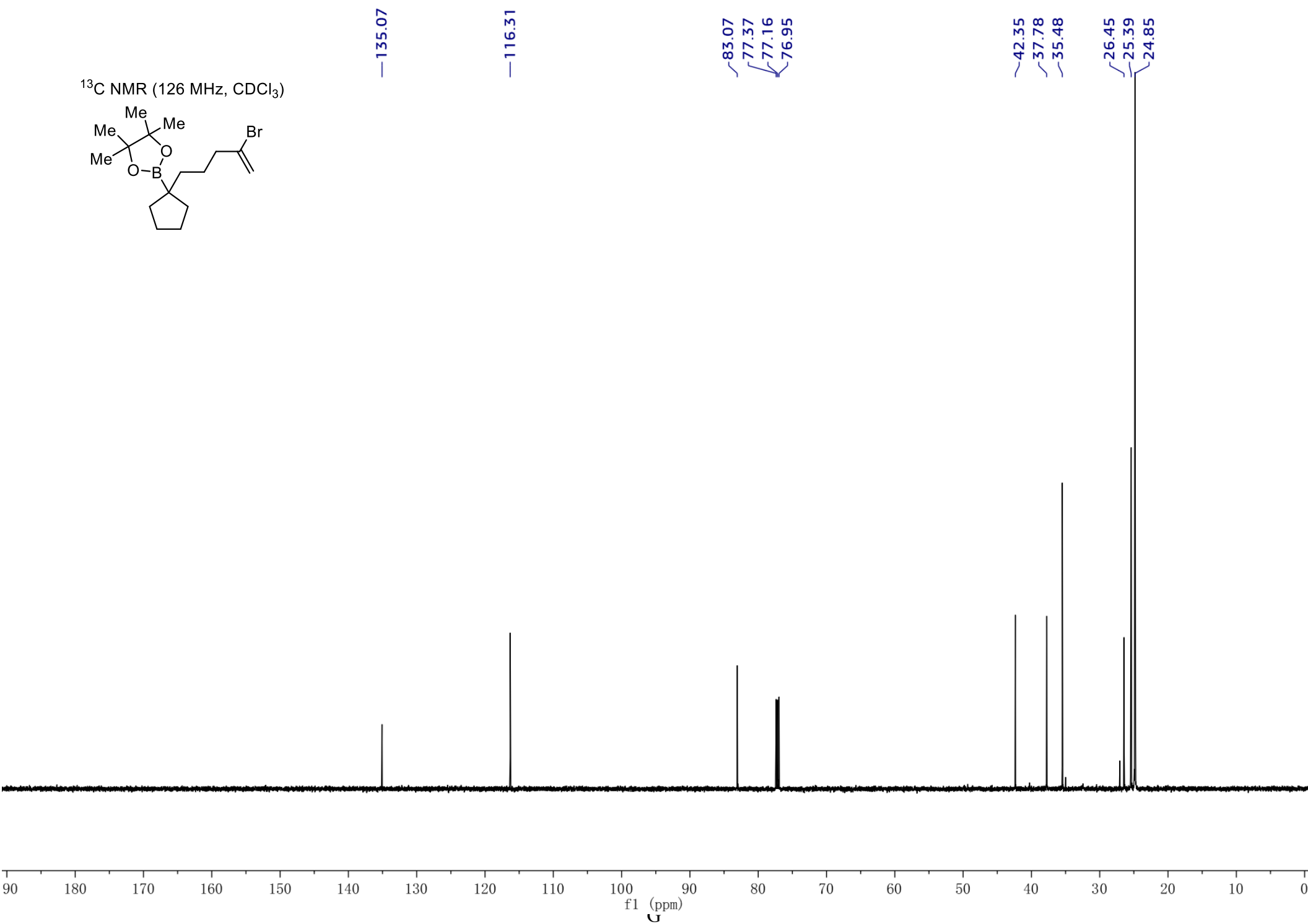

135.09
116.32
83.19
77.37
77.16
76.95
42.04
38.83
30.42
25.34
24.85
18.35
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.26
5.55
5.55
5.37
5.37
2.41
2.41
2.40
2.39
2.38
1.82
1.61
1.59
1.53
1.52
1.48
1.37
1.35
1.35
1.34
1.28
1.27
1.26
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
1.00
0.98
2.03
2.15
6.18
2.15
1.92
11.94
f1 (ppm)

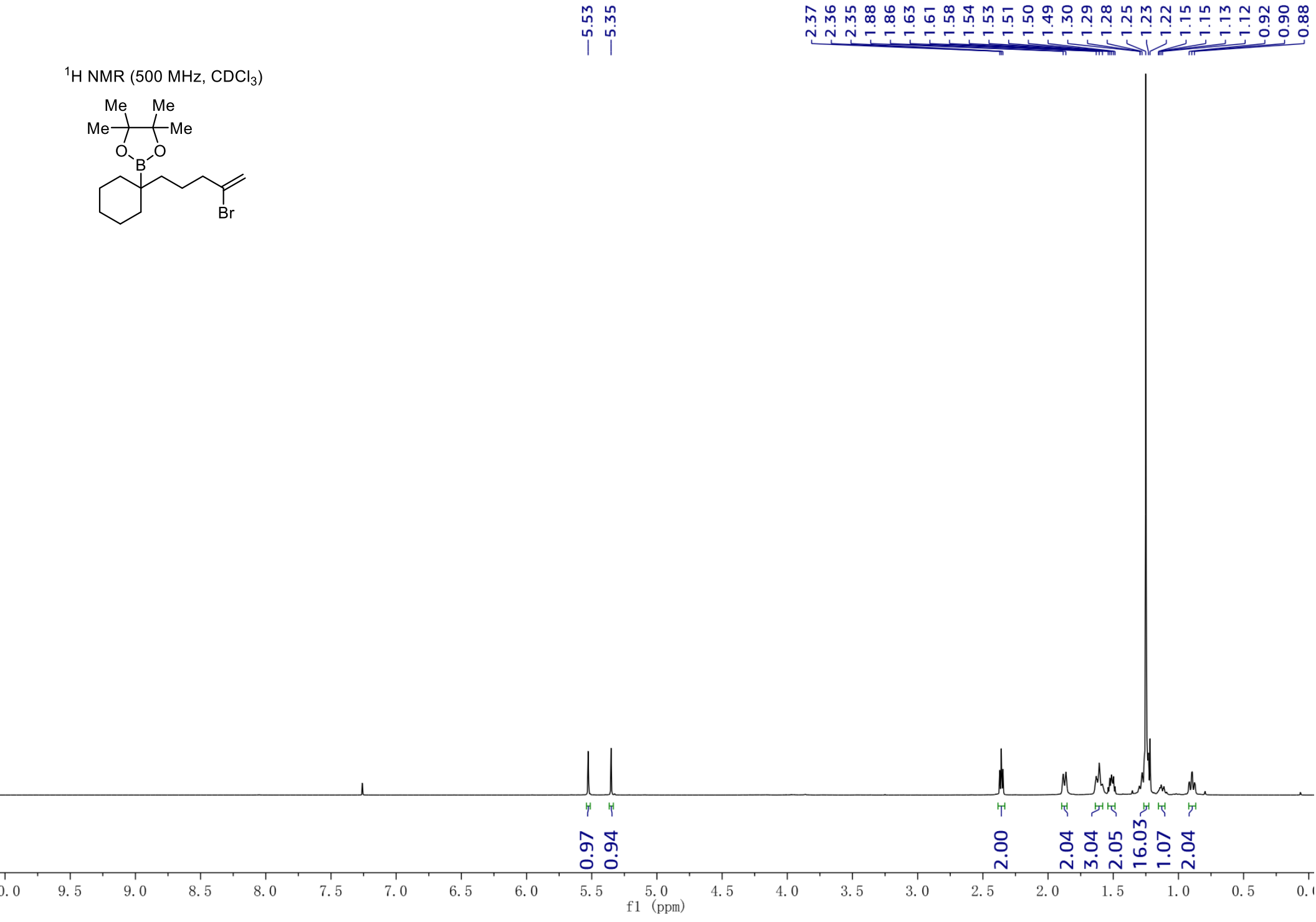
G

E

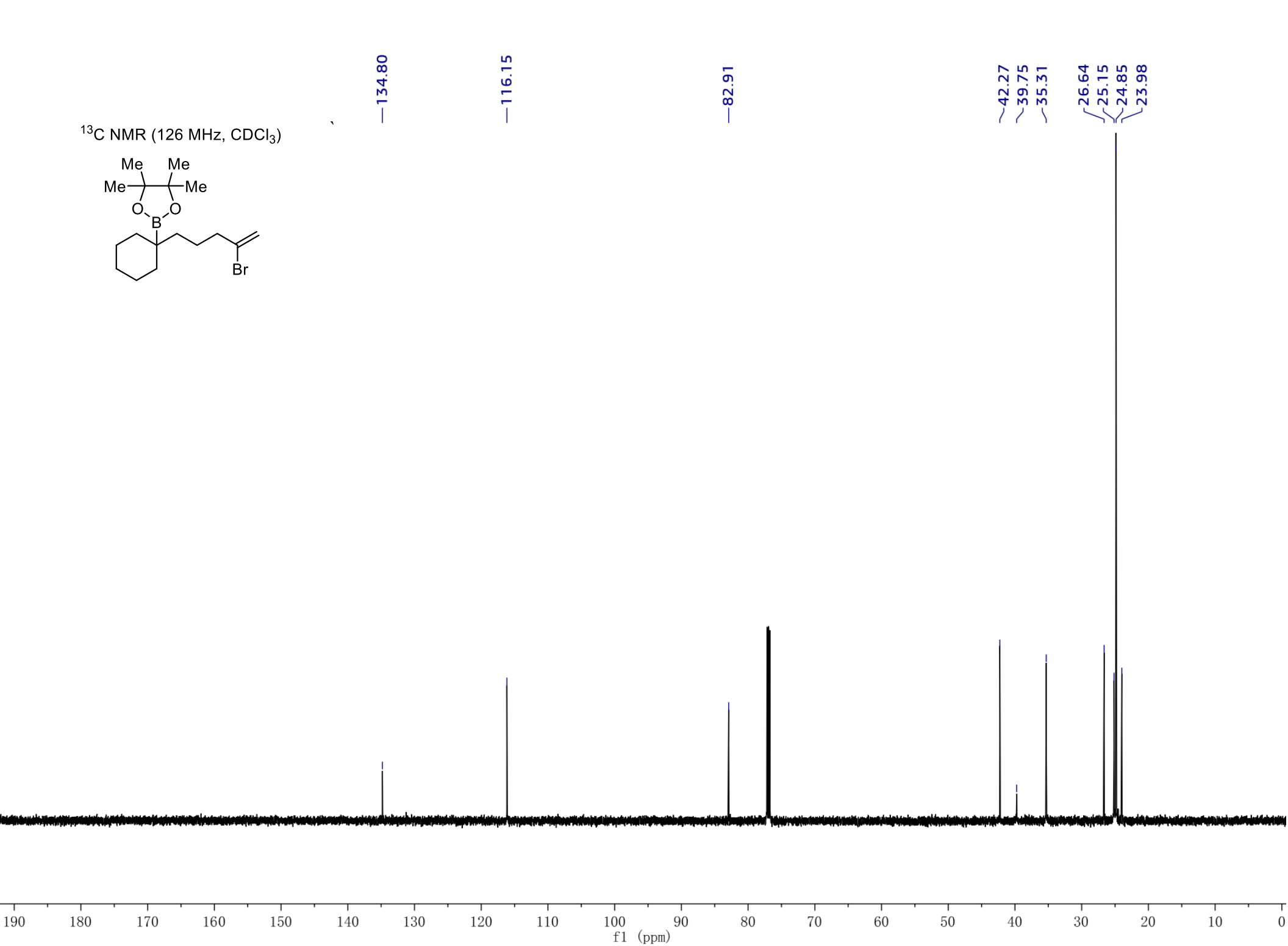

135.07
116.31
83.07
77.37
77.16
76.95
42.35
37.78
35.48
26.45
25.39
24.85
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
Br
5.53
5.35
2.37
2.36
2.35
1.88
1.86
1.63
1.61
1.58
1.54
1.53
1.51
1.50
1.49
1.30
1.29
1.28
1.25
1.23
1.22
1.15
1.15
1.13
1.12
0.92
0.90
0.88
0.97
0.94
2.00
2.04
3.04
2.05
16.03
1.07
2.04
f1 (ppm)

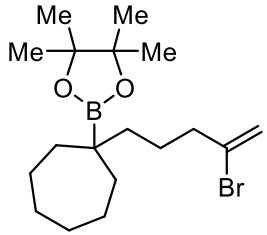
E


134.80
116.15
82.91
42.27
39.75
35.31
26.64
25.15
24.85
23.98
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

E

$^1$H NMR (500 MHz, $CDCl_3$)

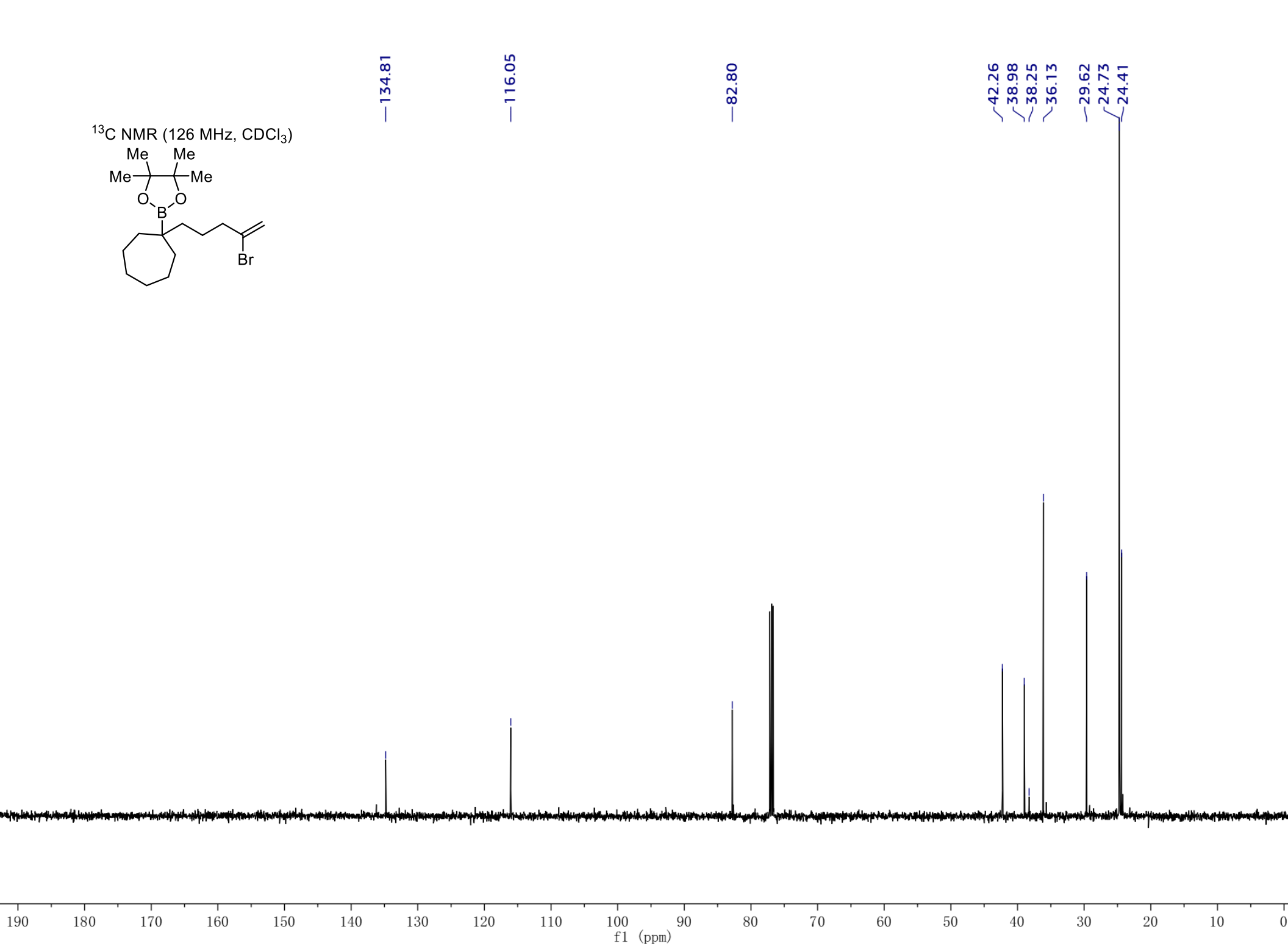






G

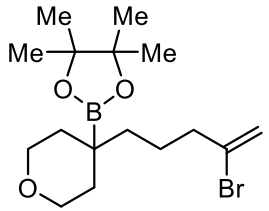
E


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
Br
134.81
116.05
82.80
42.26
38.98
38.25
36.13
29.62
24.73
24.41
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

E

$^1$H NMR (500 MHz, $CDCl_3$)

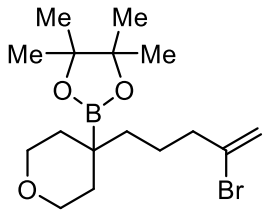






E

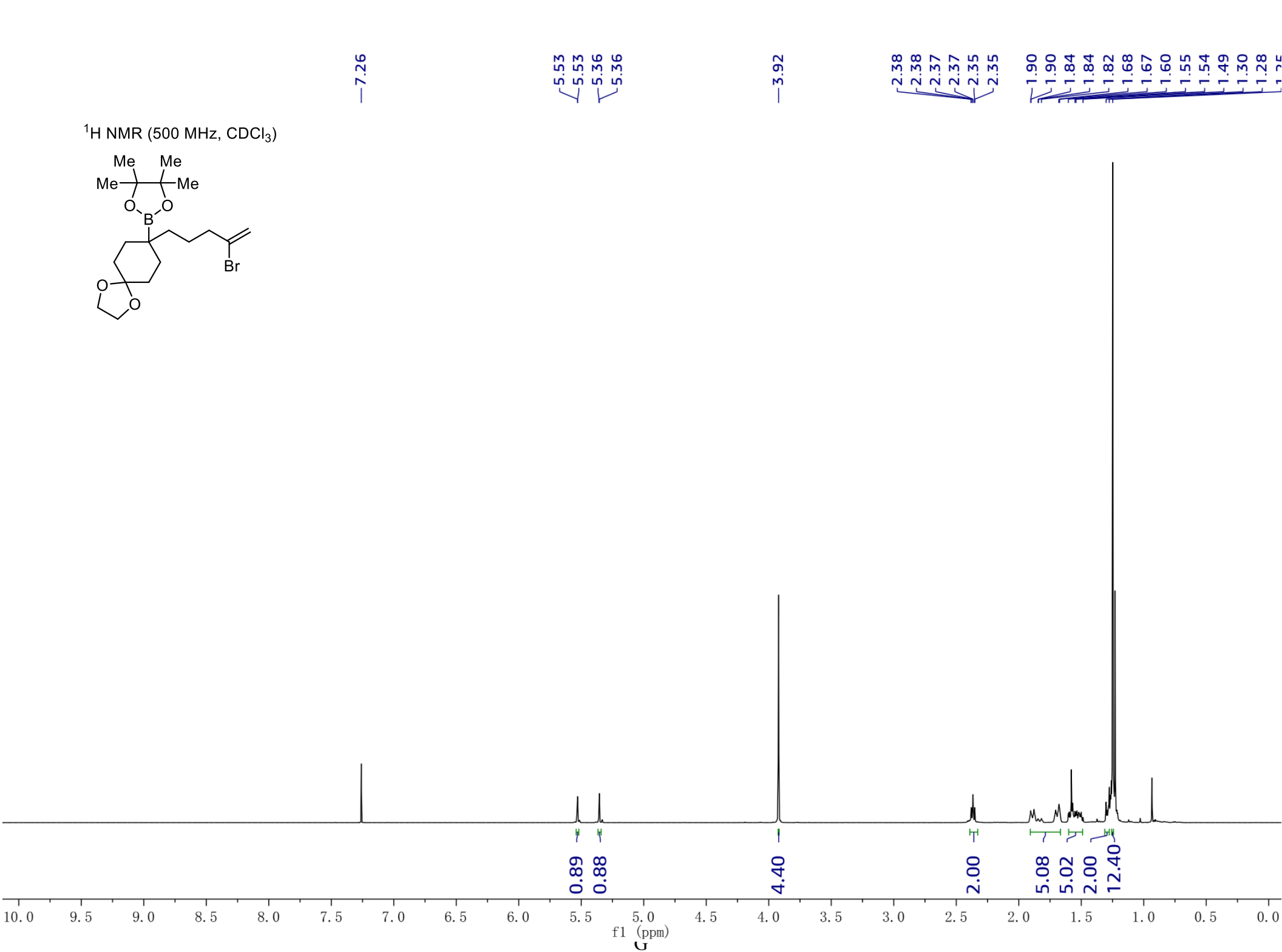
$^{13}$C NMR (126 MHz, $CDCl_3$)





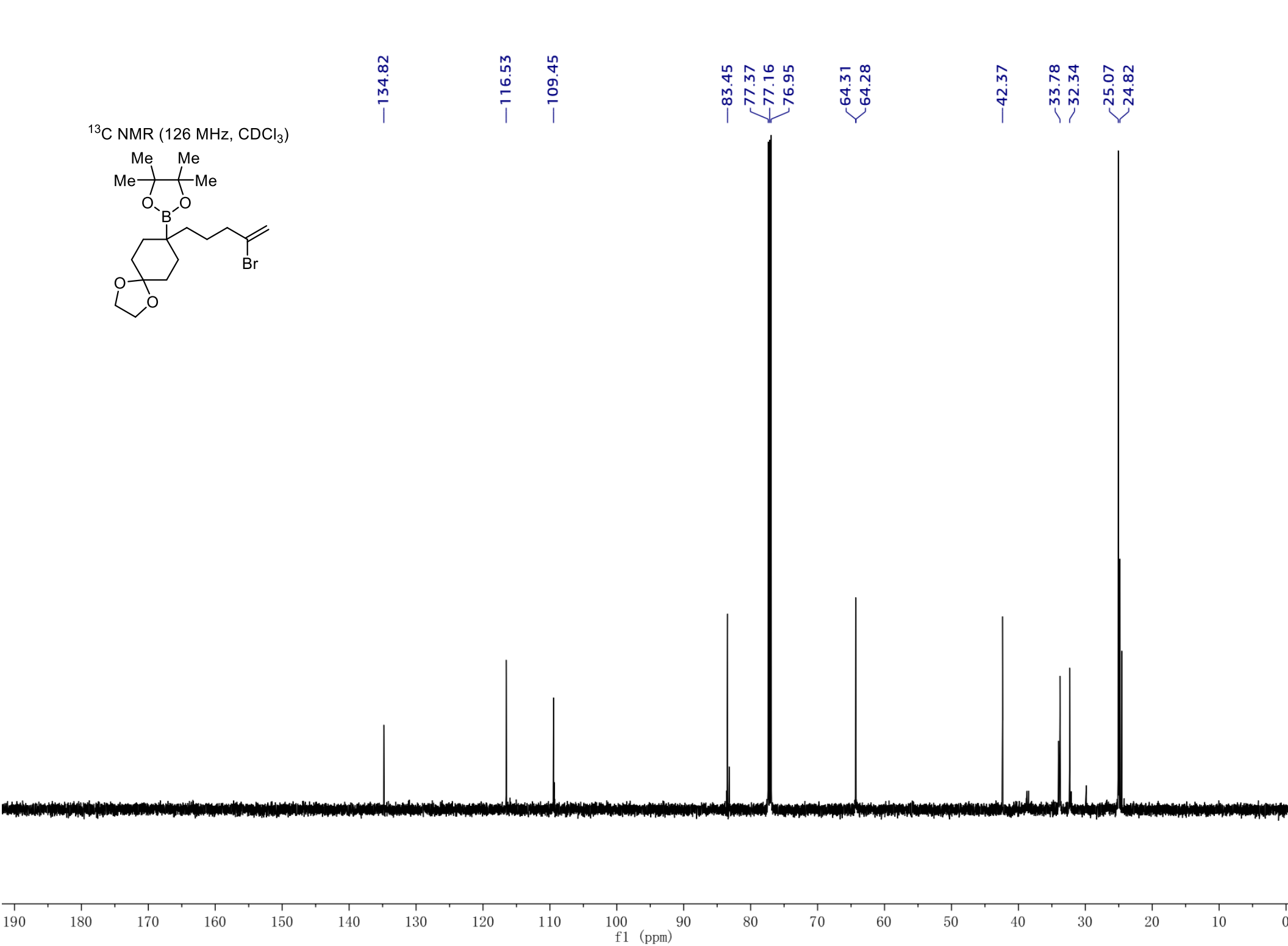


E


7.26
5.53
5.53
5.36
5.36
3.92
2.38
2.38
2.37
2.37
2.35
2.35
1.90
1.90
1.84
1.84
1.82
1.68
1.67
1.60
1.55
1.54
1.49
1.30
1.28
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
B
O
Br
O
O
0.89
0.88
4.40
2.00
5.08
5.02
2.00
12.40
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

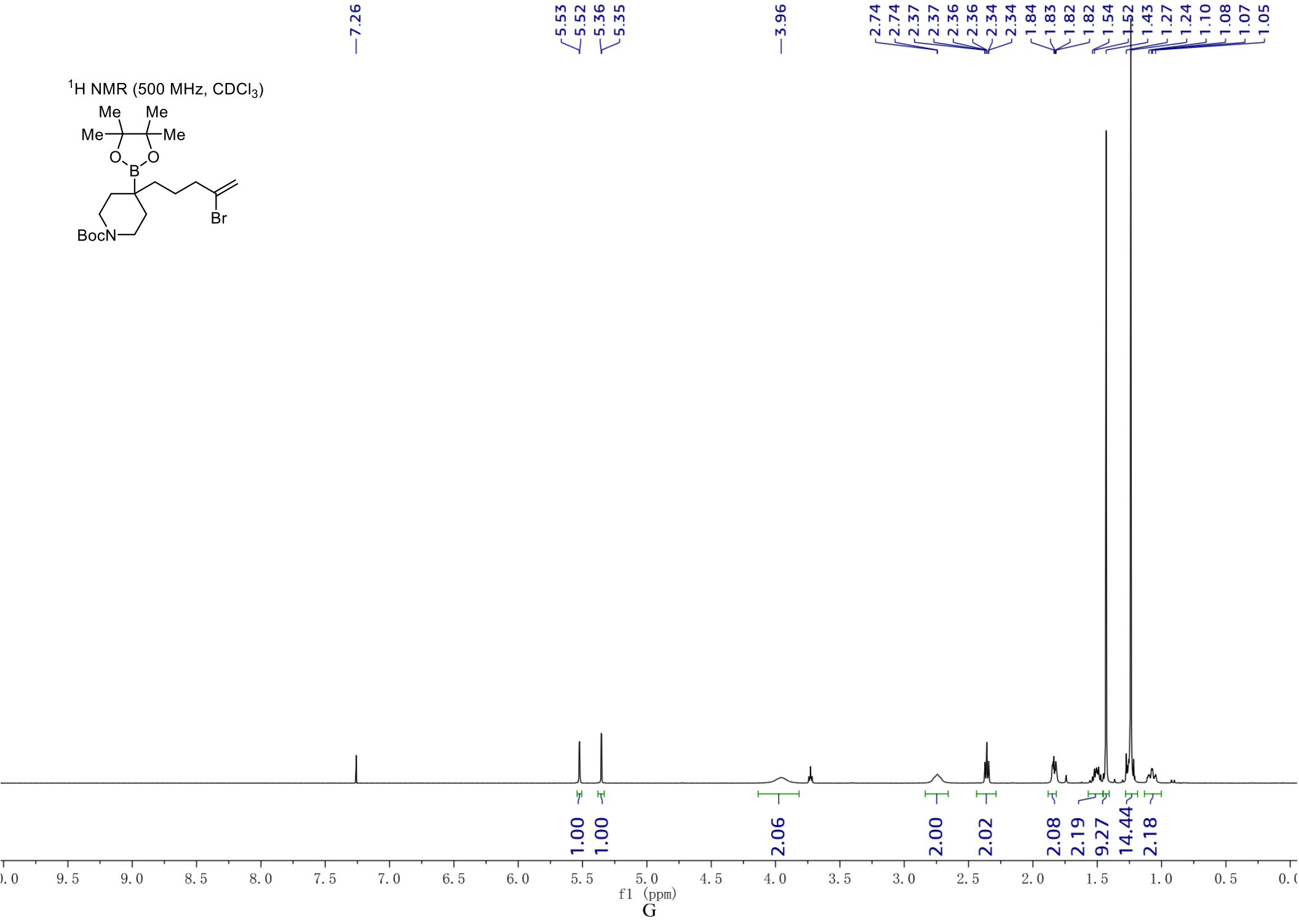
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
B
O
Br
O
O
134.82
116.53
109.45
83.45
77.37
77.16
76.95
64.31
64.28
42.37
33.78
32.34
25.07
24.82
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

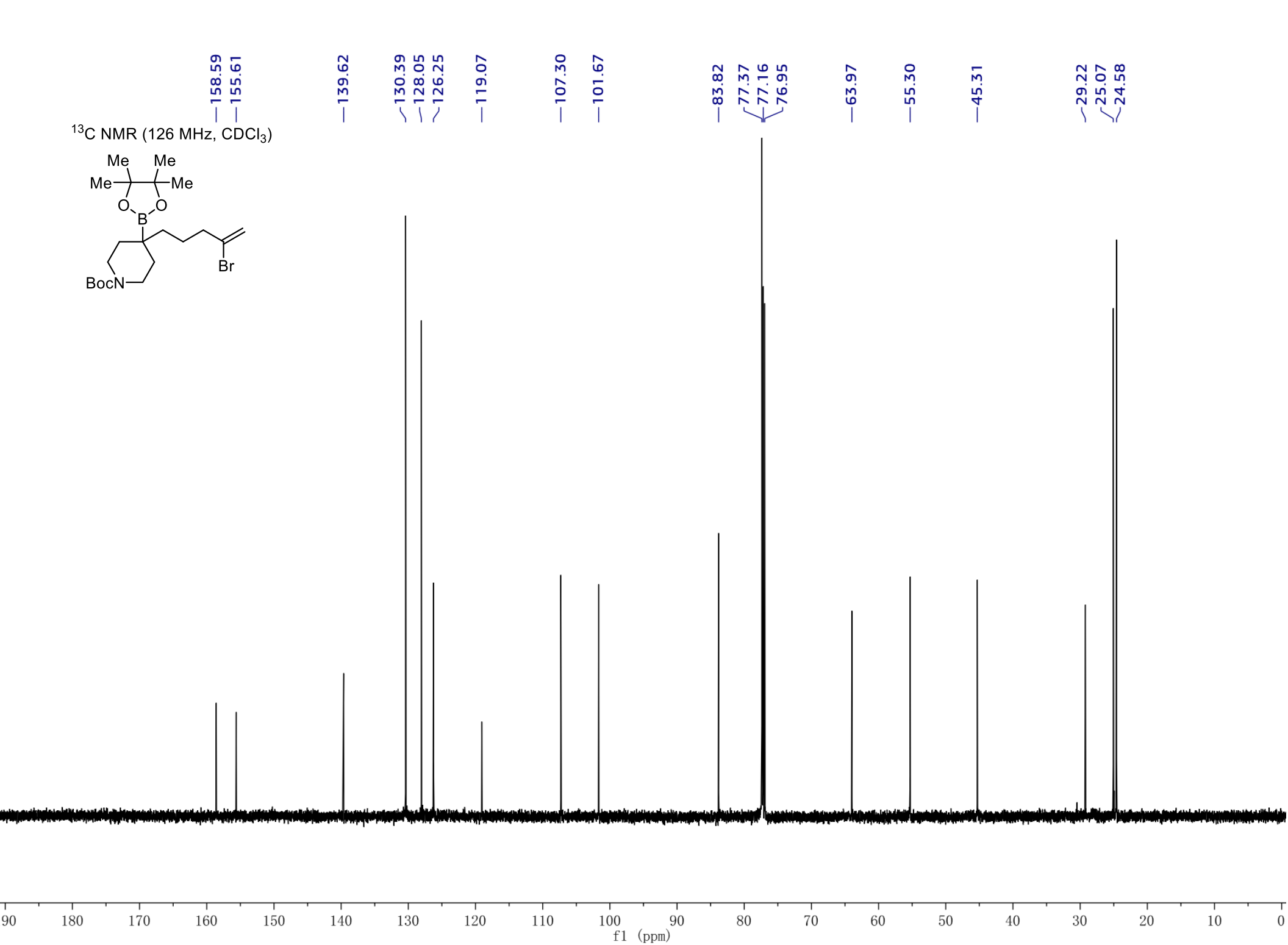
G

E


7.26
5.53
5.52
5.36
5.35
3.96
2.74
2.74
2.37
2.37
2.36
2.36
2.34
2.34
1.84
1.83
1.82
1.82
1.54
1.52
1.43
1.27
1.24
1.10
1.08
1.07
1.05
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
BocN
1.00
1.00
2.06
2.00
2.02
2.08
2.19
9.27
14.44
2.18
f1 (ppm)

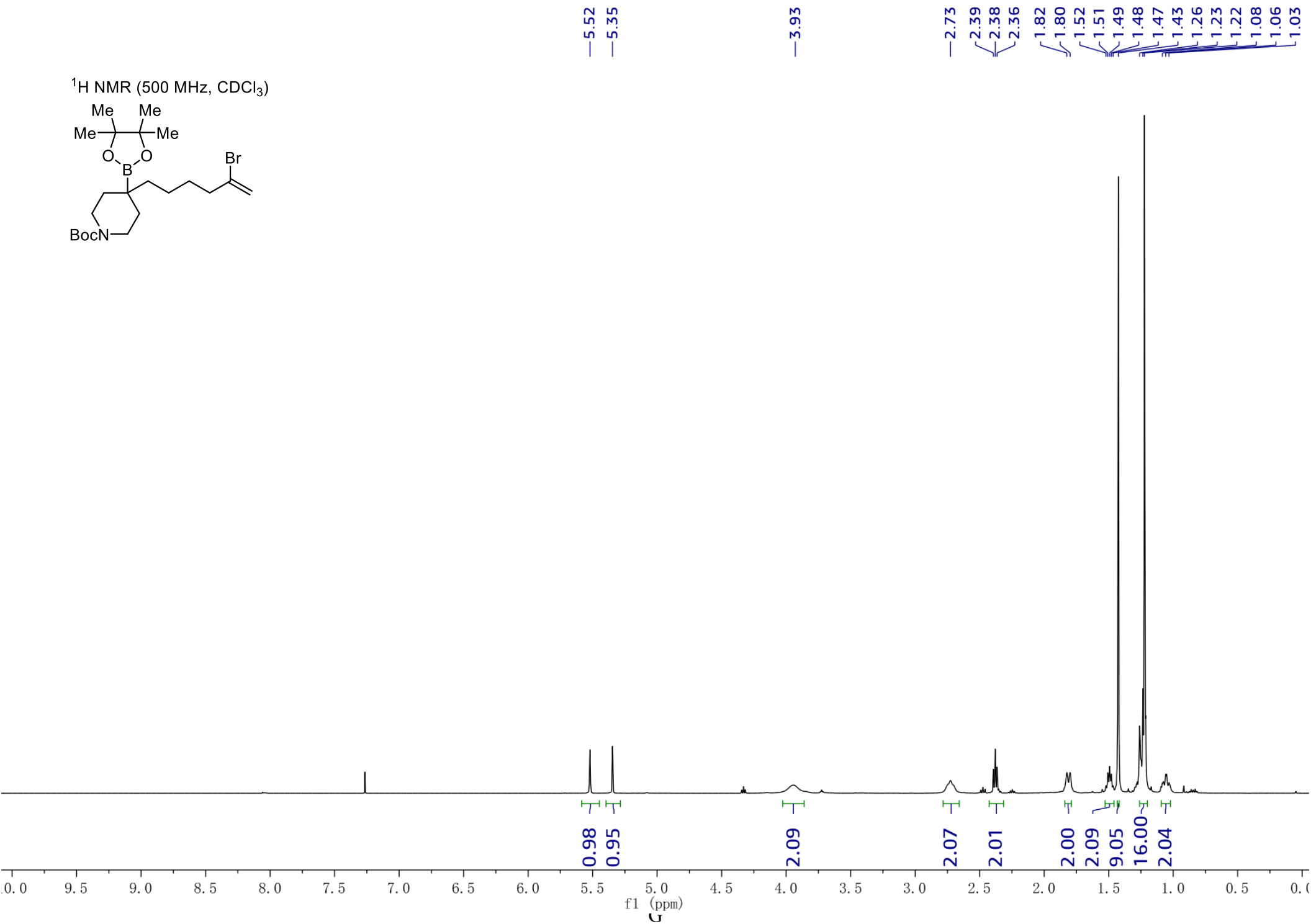
G

E


158.59
155.61
139.62
130.39
128.05
126.25
119.07
107.30
101.67
83.82
77.37
77.16
76.95
63.97
55.30
45.31
29.22
25.07
24.58
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
B
O
Br
BocN
f1 (ppm)

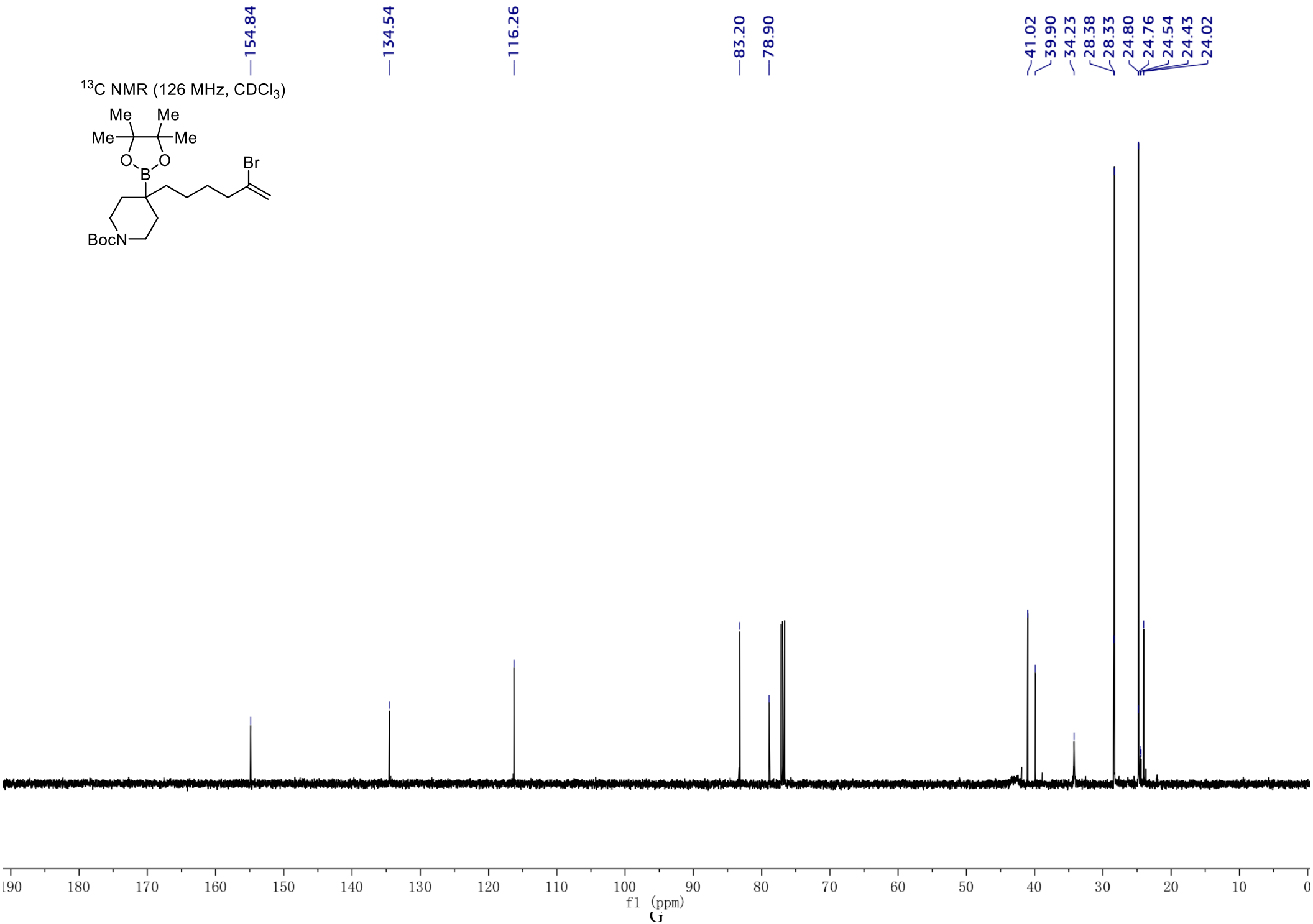
G

E


5.52
5.35
3.93
2.73
2.39
2.38
2.36
1.82
1.80
1.52
1.51
1.49
1.48
1.47
1.43
1.26
1.23
1.22
1.08
1.06
1.03
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
Br
BocN
0.98
0.95
2.09
2.07
2.01
2.00
2.09
9.05
16.00
2.04
f1 (ppm)

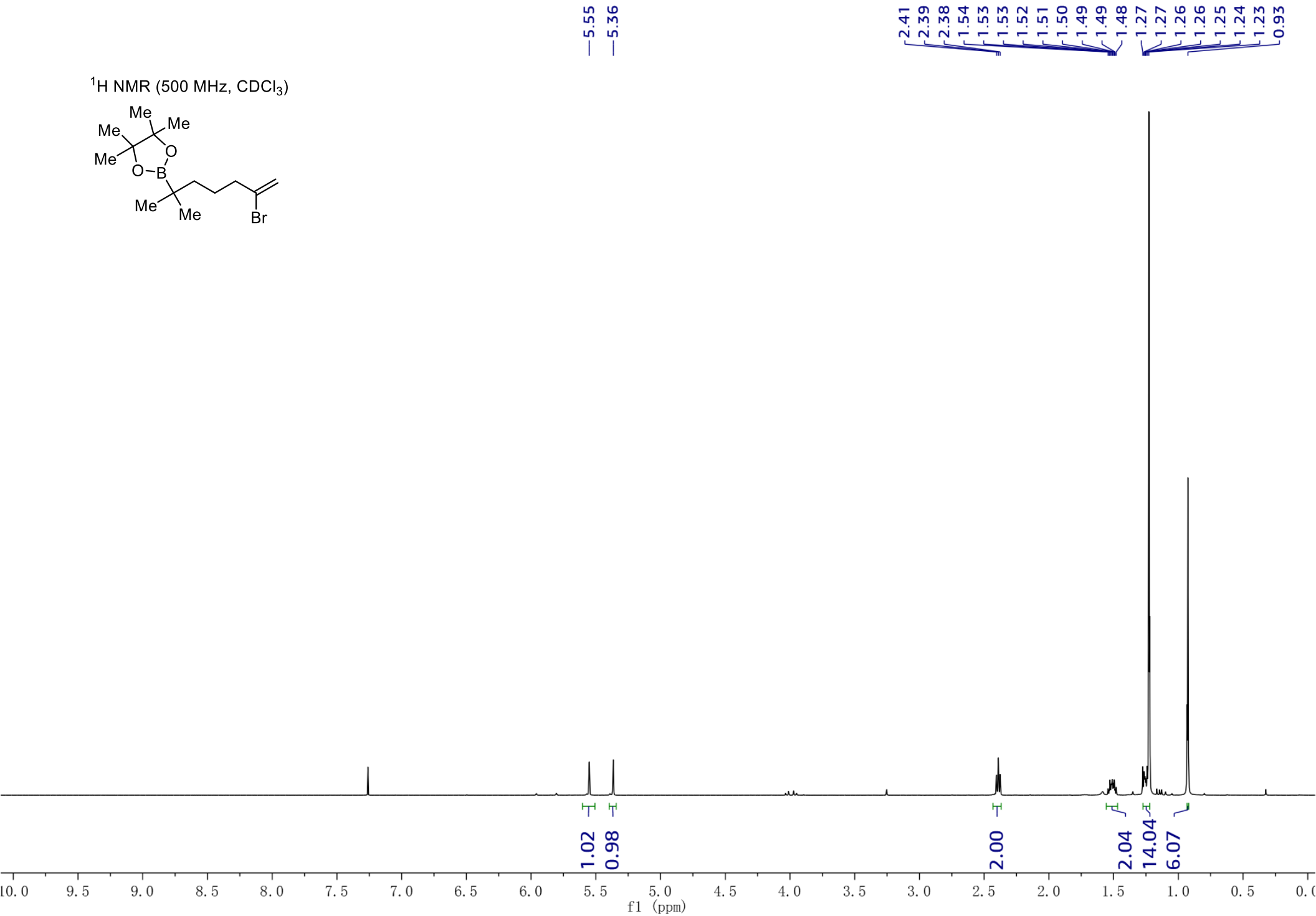
G

E


154.84
134.54
116.26
83.20
78.90
41.02
39.90
34.23
28.38
28.33
24.80
24.76
24.54
24.43
24.02
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
B
O
Br
BocN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

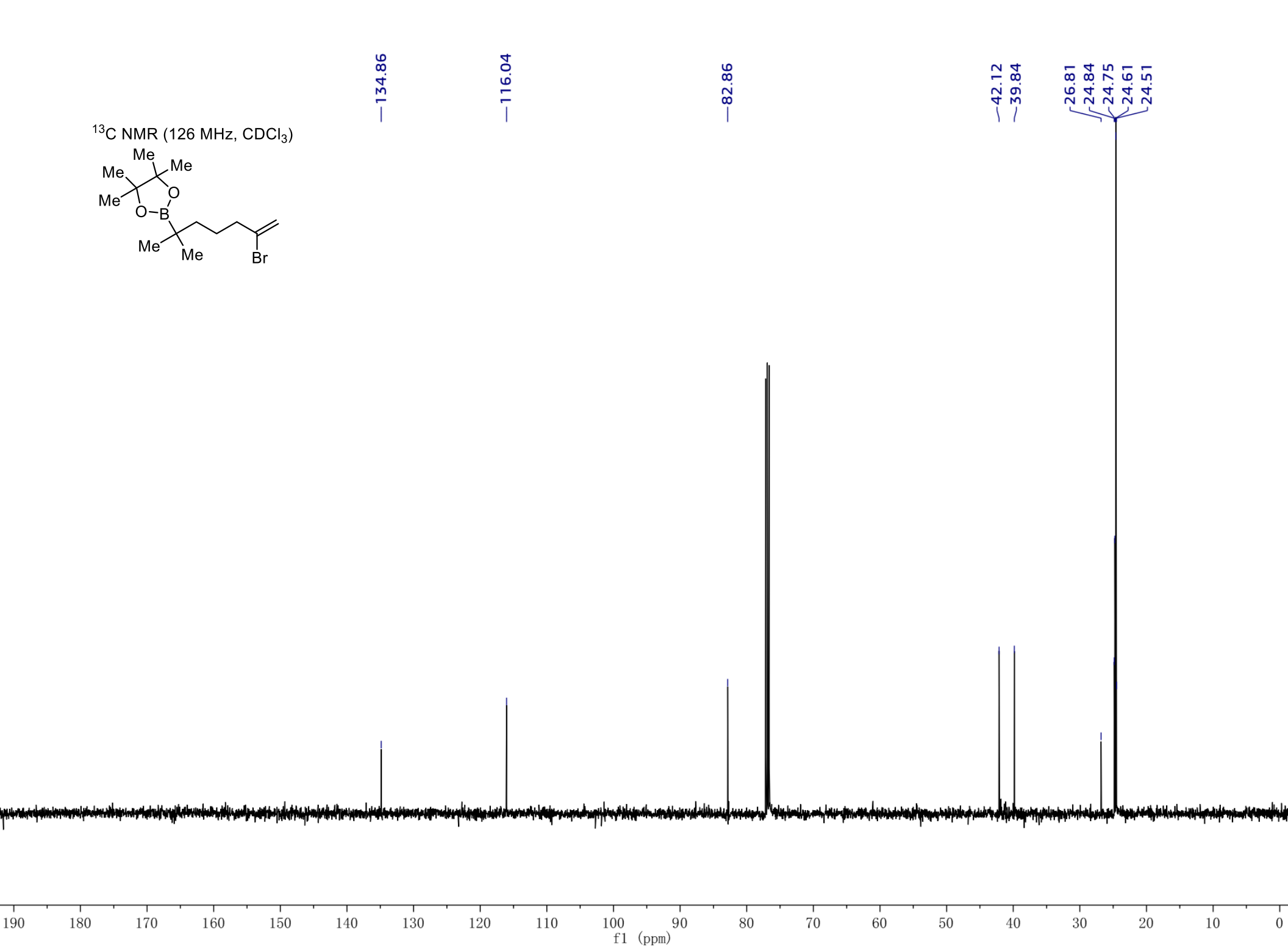
G

E


5.55
5.36
2.41
2.39
2.38
1.54
1.53
1.53
1.52
1.51
1.50
1.49
1.49
1.48
1.27
1.27
1.26
1.26
1.25
1.24
1.23
0.93
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
Me
Br
1.02
0.98
2.00
2.04
14.04
6.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

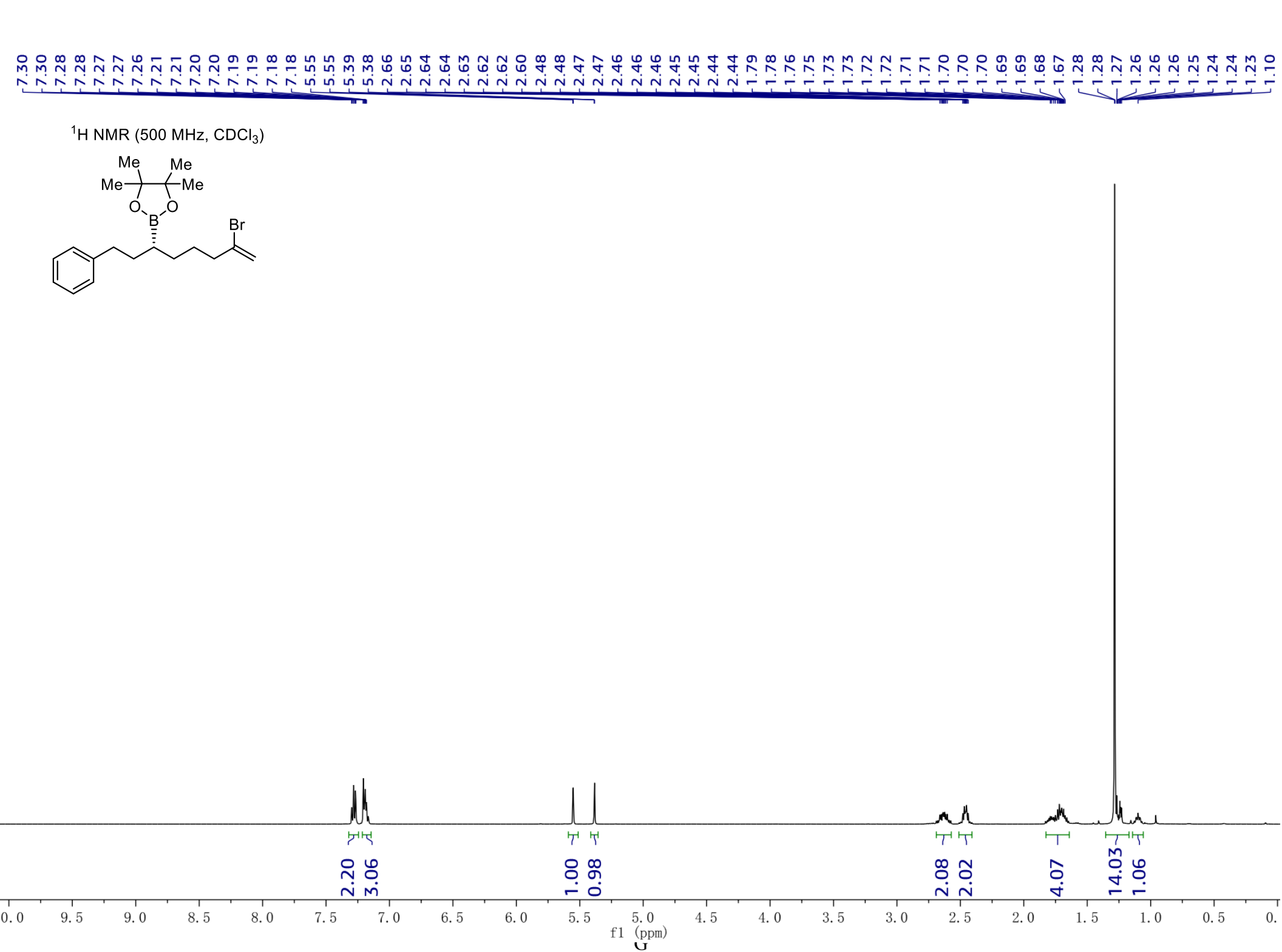
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
Me
Me
Br
134.86
116.04
82.86
42.12
39.84
26.81
24.84
24.75
24.61
24.51
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

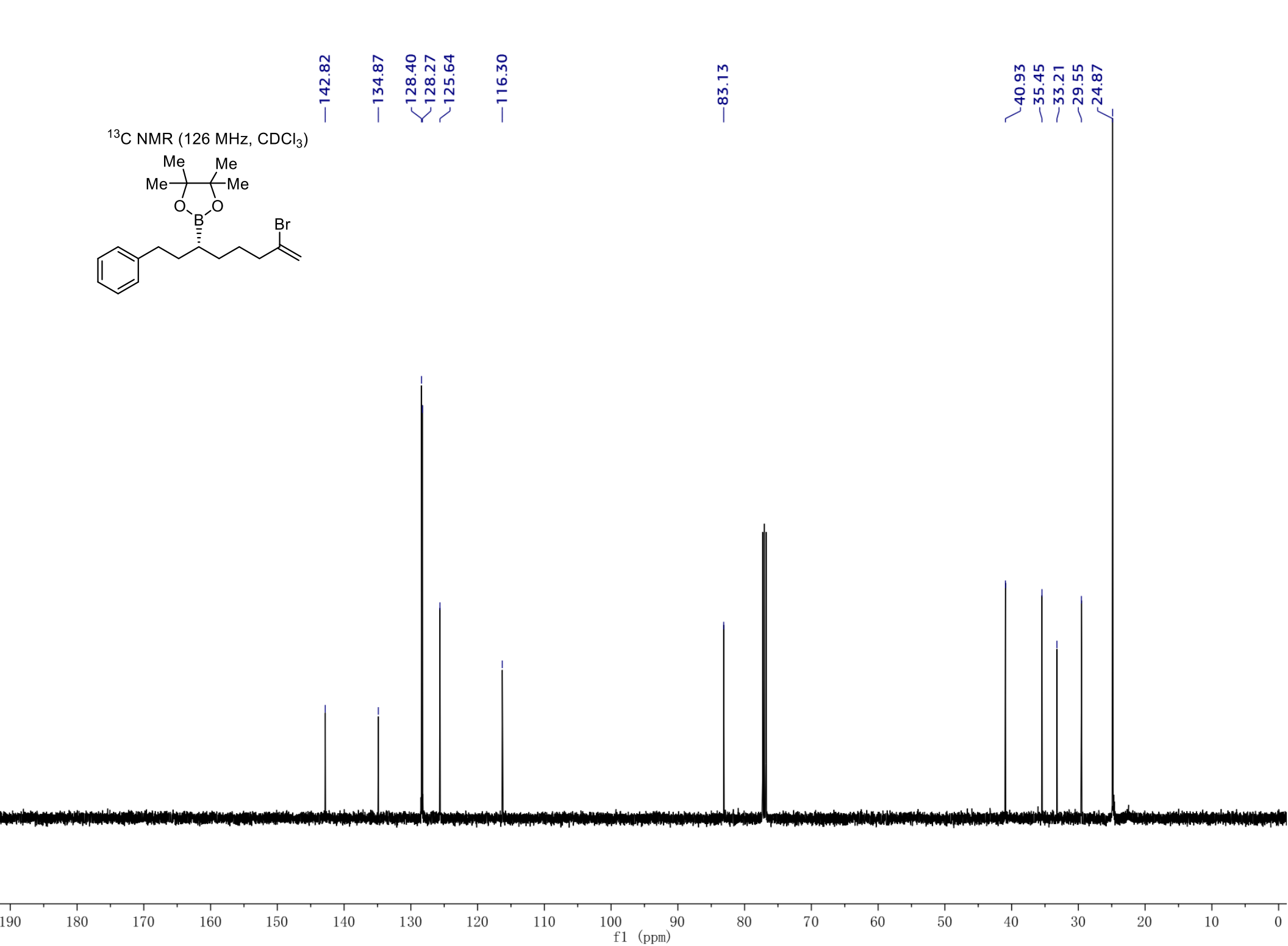
G

E


7.30 7.30 7.28 7.28 7.27 7.27 7.26 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.18 5.55 5.55 5.39 5.38 2.66 2.65 2.64 2.64 2.63 2.62 2.62 2.60 2.48 2.48 2.47 2.47 2.46 2.46 2.46 2.45 2.45 2.44 2.44 1.79 1.78 1.76 1.75 1.73 1.73 1.72 1.72 1.71 1.71 1.70 1.70 1.70 1.69 1.69 1.68 1.67 1.28 1.28 1.27 1.26 1.26 1.26 1.25 1.24 1.24 1.23 1.10
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
2.20
3.06
1.00
0.98
2.08
2.02
4.07
14.03
1.06
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

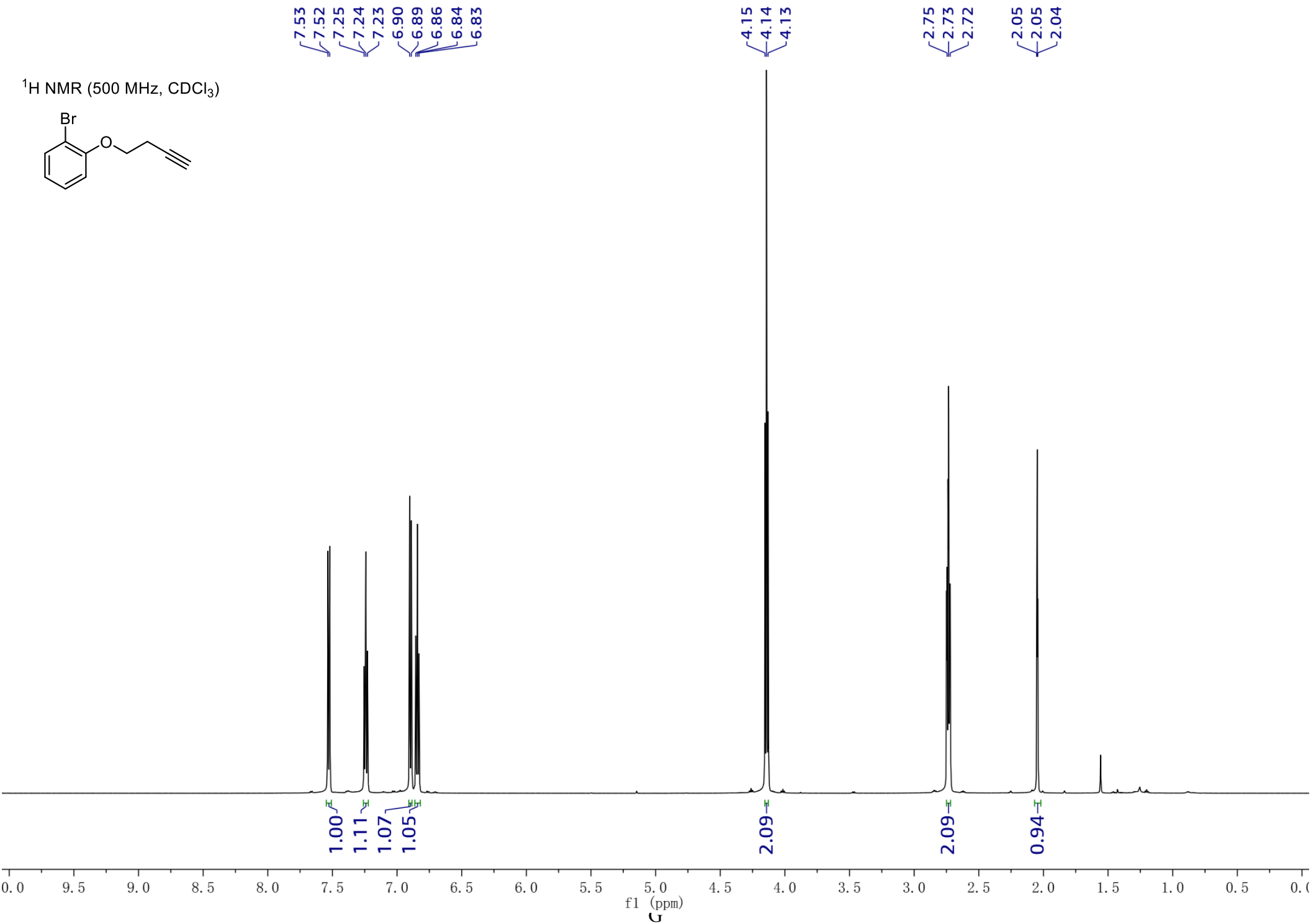
G

E


142.82
134.87
128.40
128.27
125.64
116.30
83.13
40.93
35.45
33.21
29.55
24.87
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

E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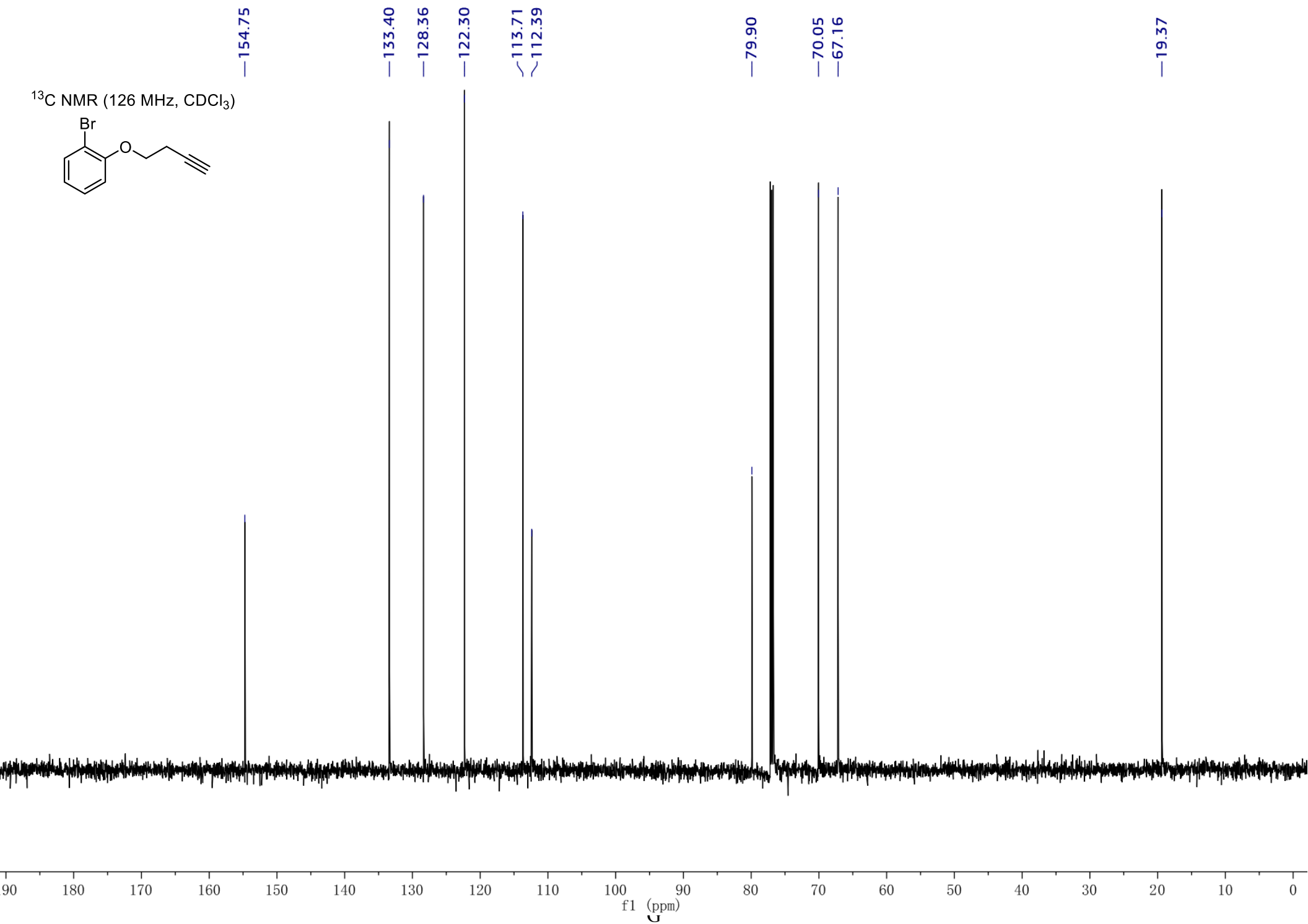
7.52
7.25
7.24
7.23
6.90
6.89
6.86
6.84
6.83
4.15
4.14
4.13
2.75
2.73
2.72
2.05
2.05
2.04
1H NMR (500 MHz, CDCl3)
Br
O
1.00
1.11
1.07
1.05
2.09
2.09
0.94
f1 (ppm)

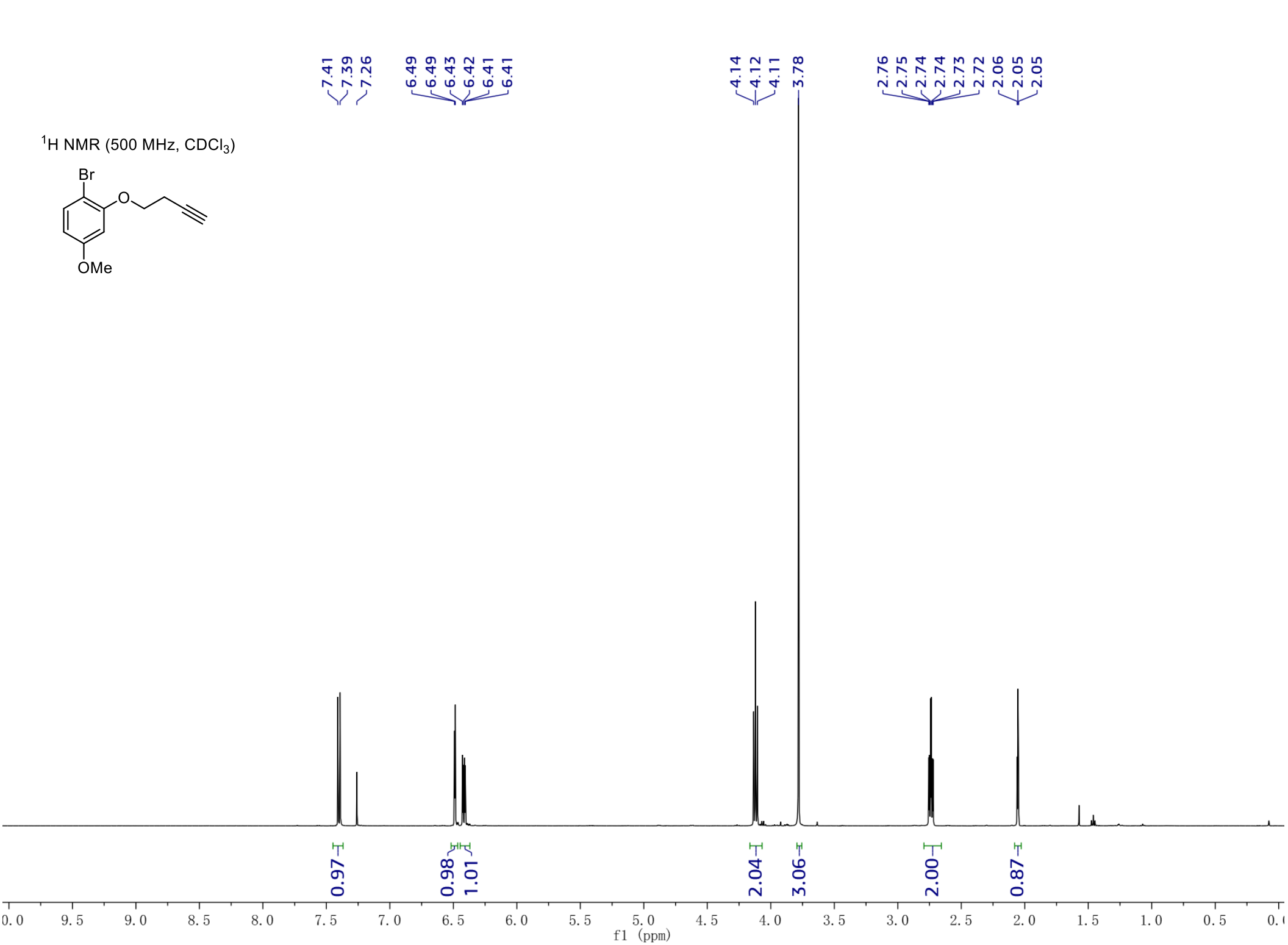
G

E


154.75
133.40
128.36
122.30
113.71
112.39
79.90
70.05
67.16
19.37
13C NMR (126 MHz, CDCl3)
Br
O
f1 (ppm)

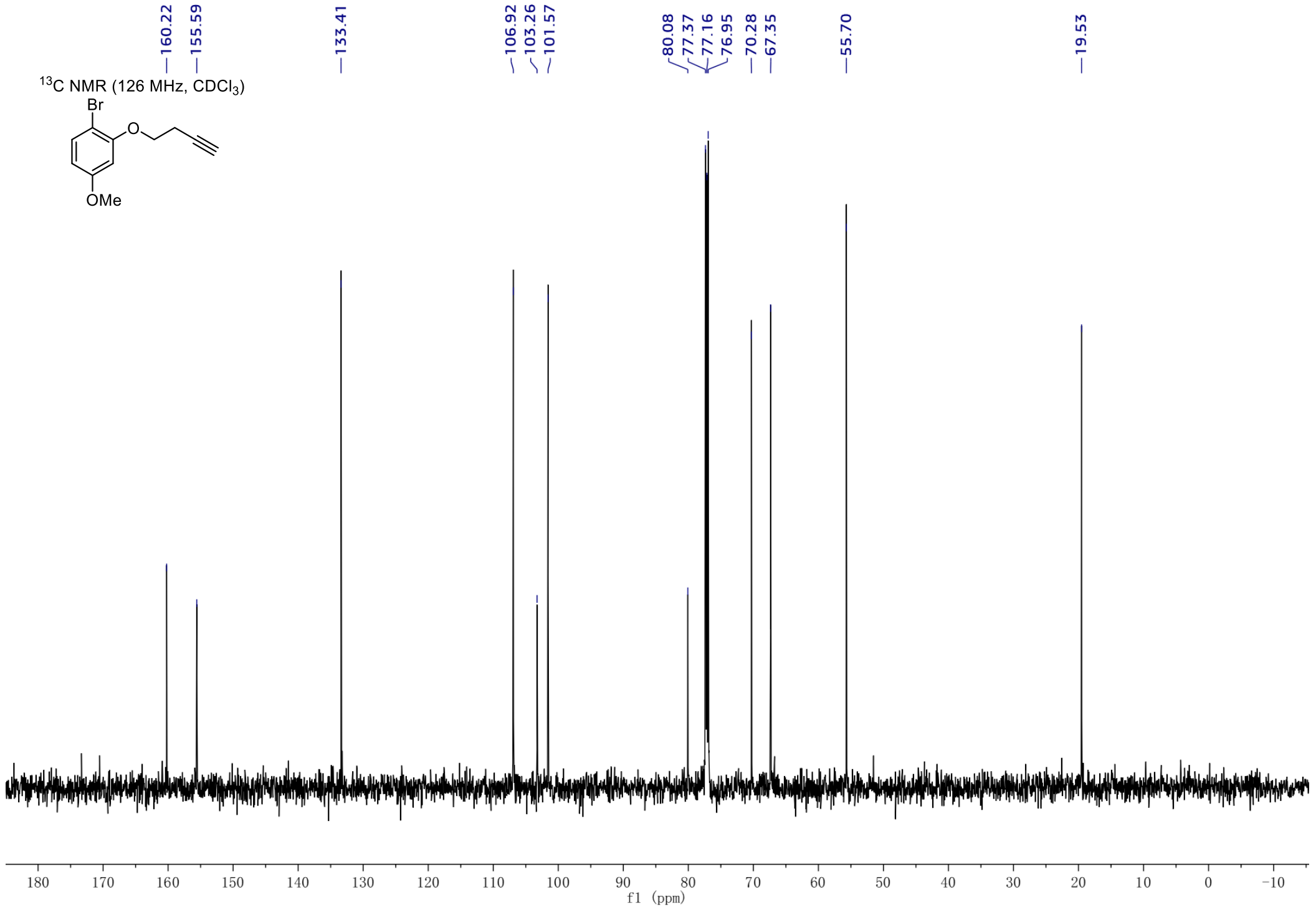
G

E


7.41
7.39
7.26
6.49
6.49
6.43
6.42
6.41
6.41
4.14
4.12
4.11
3.78
2.76
2.75
2.74
2.74
2.73
2.72
2.06
2.05
2.05
$^1$H NMR (500 MHz, CDCl$_3$)
Br
O
OMe
0.97
0.98
1.01
2.04
3.06
2.00
0.87
f1 (ppm)

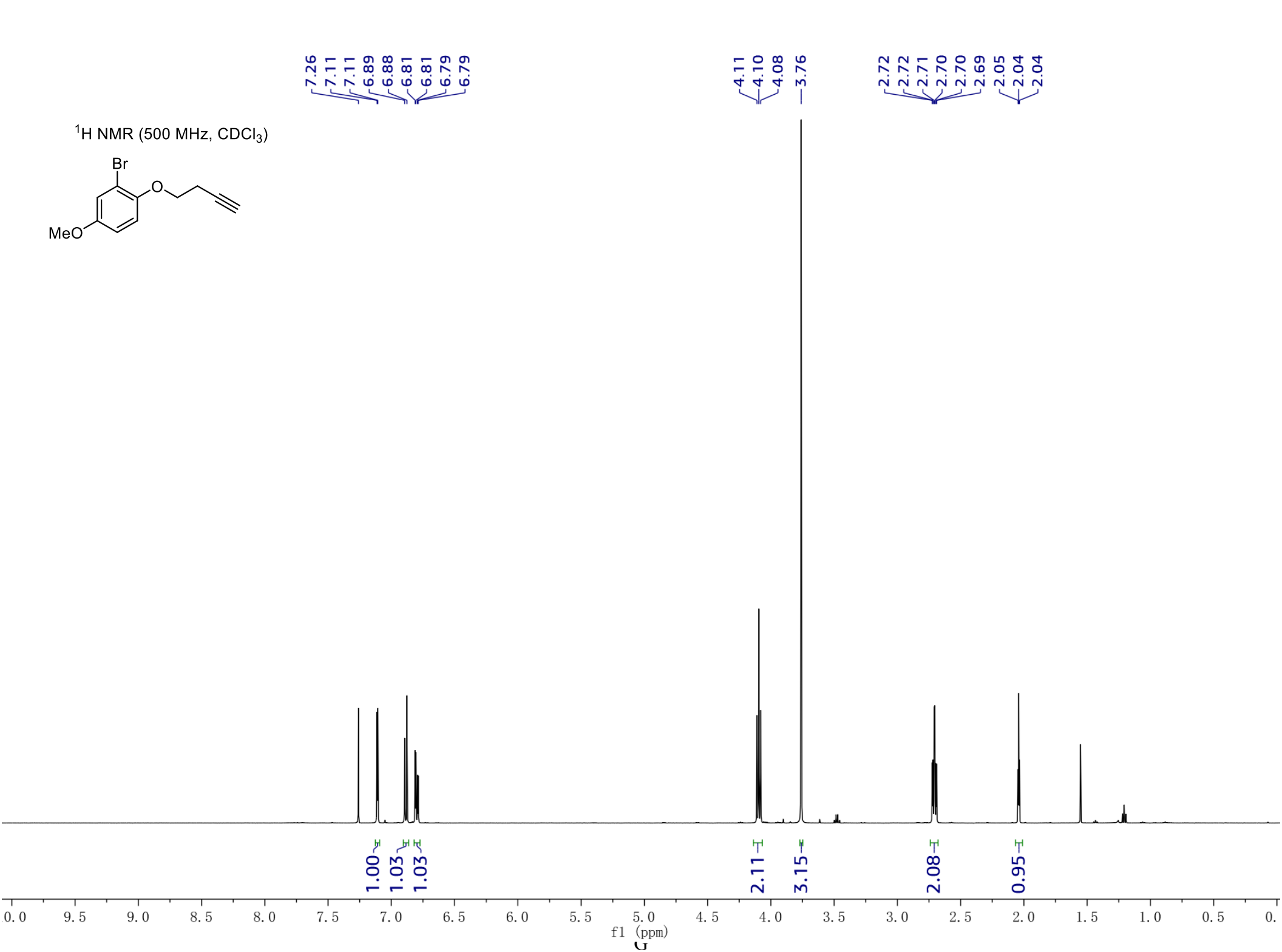
G

E


160.22
155.59
133.41
106.92
103.26
101.57
80.08
77.37
77.16
76.95
70.28
67.35
55.70
19.53
$^{13}$C NMR (126 MHz, CDCl$_3$)
Br
O
OMe
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

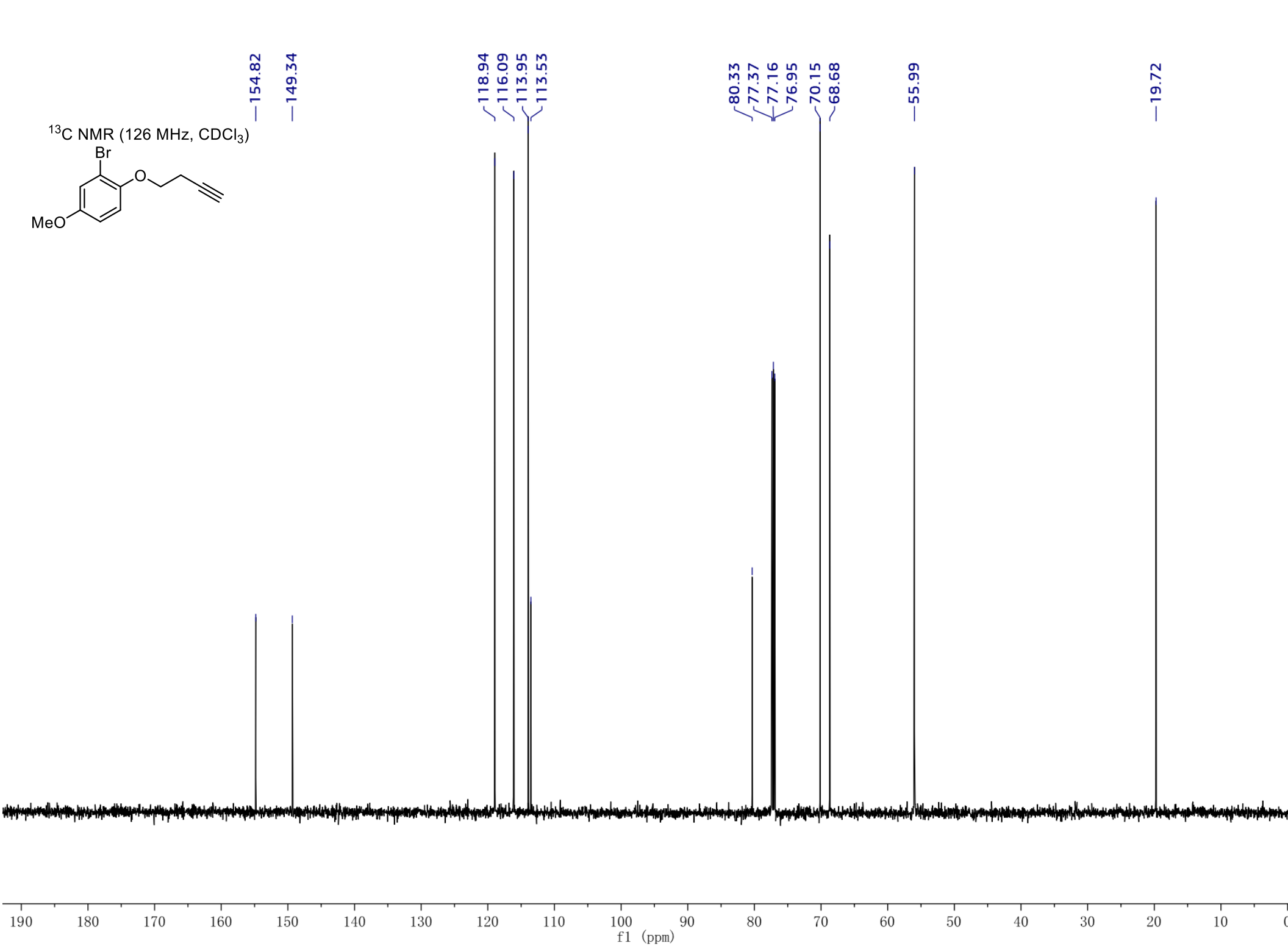
G

E


7.26
7.11
7.11
6.89
6.88
6.81
6.81
6.79
6.79
4.11
4.10
4.08
3.76
2.72
2.72
2.71
2.70
2.70
2.69
2.05
2.04
2.04
$^1$H NMR (500 MHz, $CDCl_3$)
Br
O
MeO
1.00
1.03
1.03
2.11
3.15
2.08
0.95
f1 (ppm)

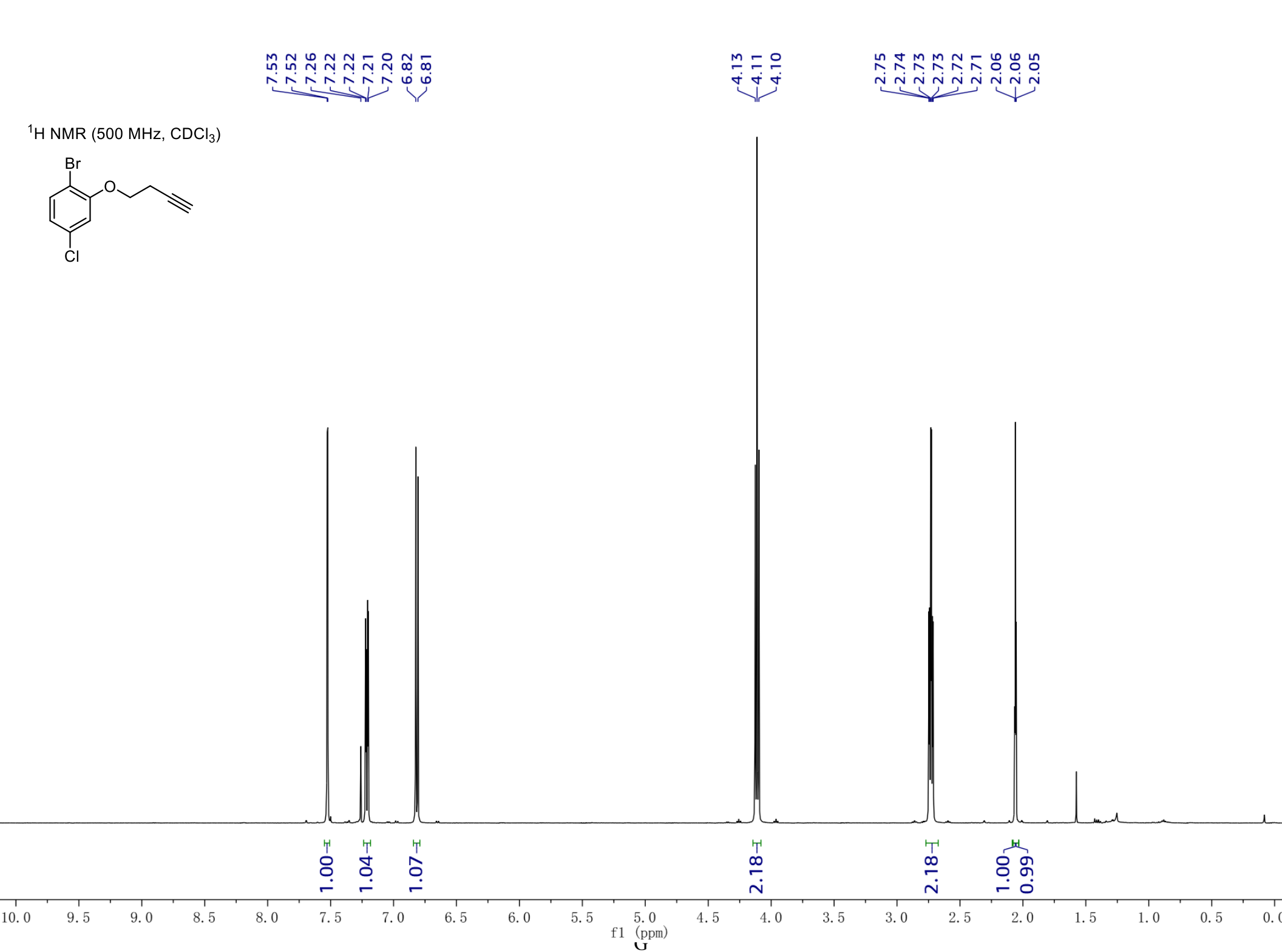
G

E


154.82
149.34
118.94
116.09
113.95
113.53
80.33
77.37
77.16
76.95
70.15
68.68
55.99
19.72
13C NMR (126 MHz, CDCl3)
Br
O
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

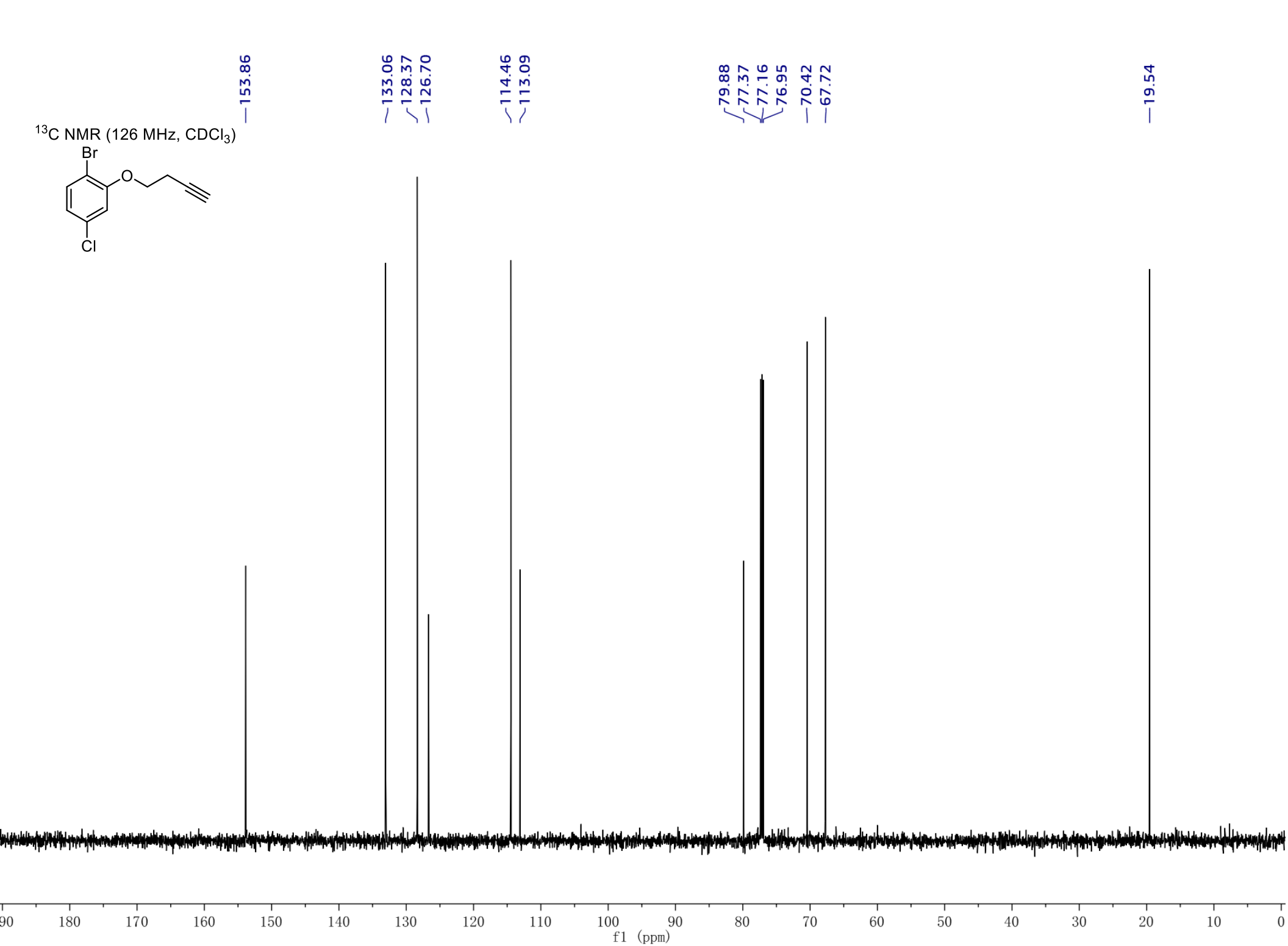
G

E


7.53
7.52
7.26
7.22
7.22
7.21
7.20
6.82
6.81
4.13
4.11
4.10
2.75
2.74
2.73
2.73
2.72
2.71
2.06
2.06
2.05
1H NMR (500 MHz, CDCl3)
Br
O
Cl
1.00
1.04
1.07
2.18
2.18
1.00
0.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

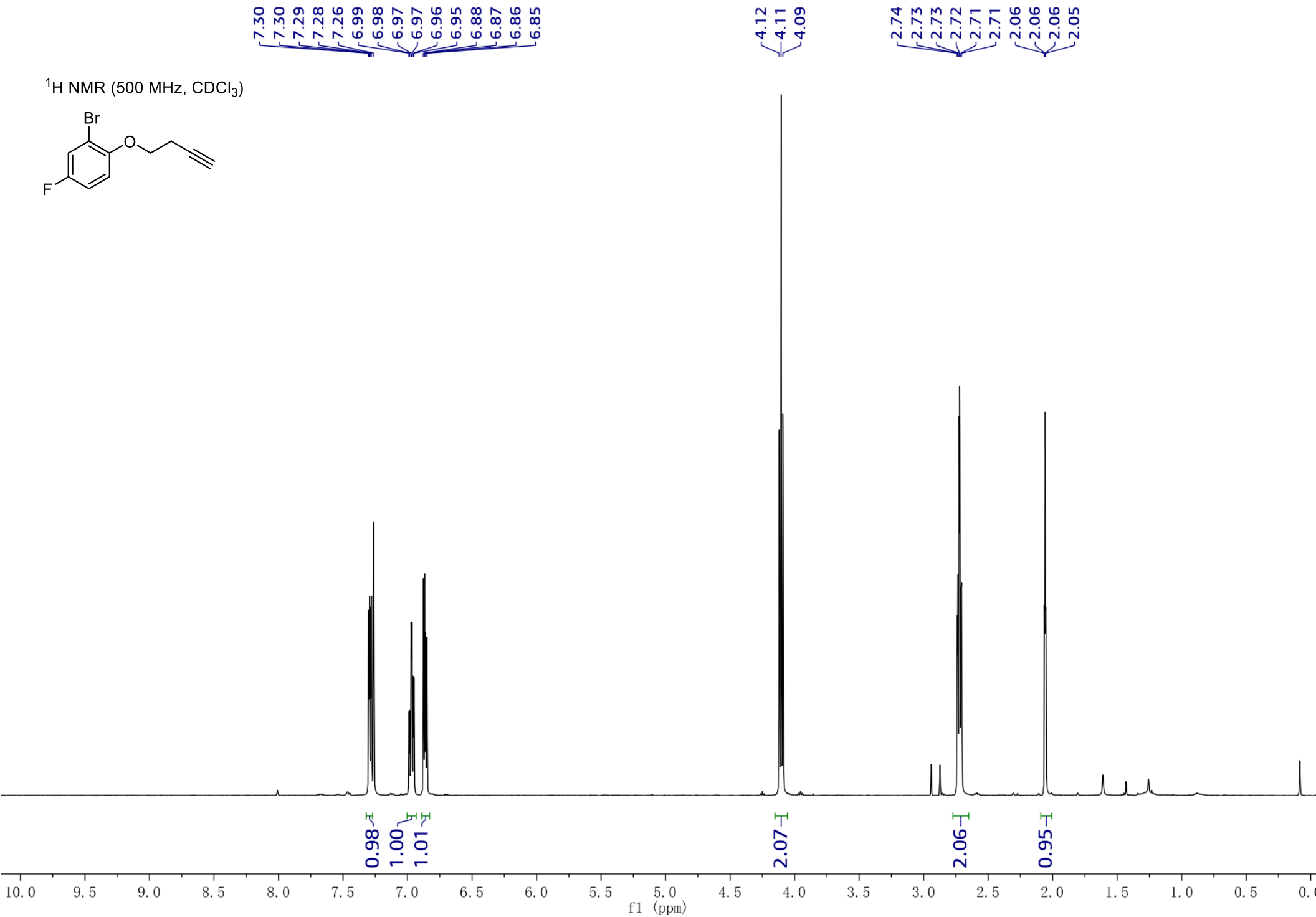
G

E


153.86
133.06
128.37
126.70
114.46
113.09
79.88
77.37
77.16
76.95
70.42
67.72
19.54
$^{13}$C NMR (126 MHz, CDCl$_3$)
Br
O
Cl
f1 (ppm)

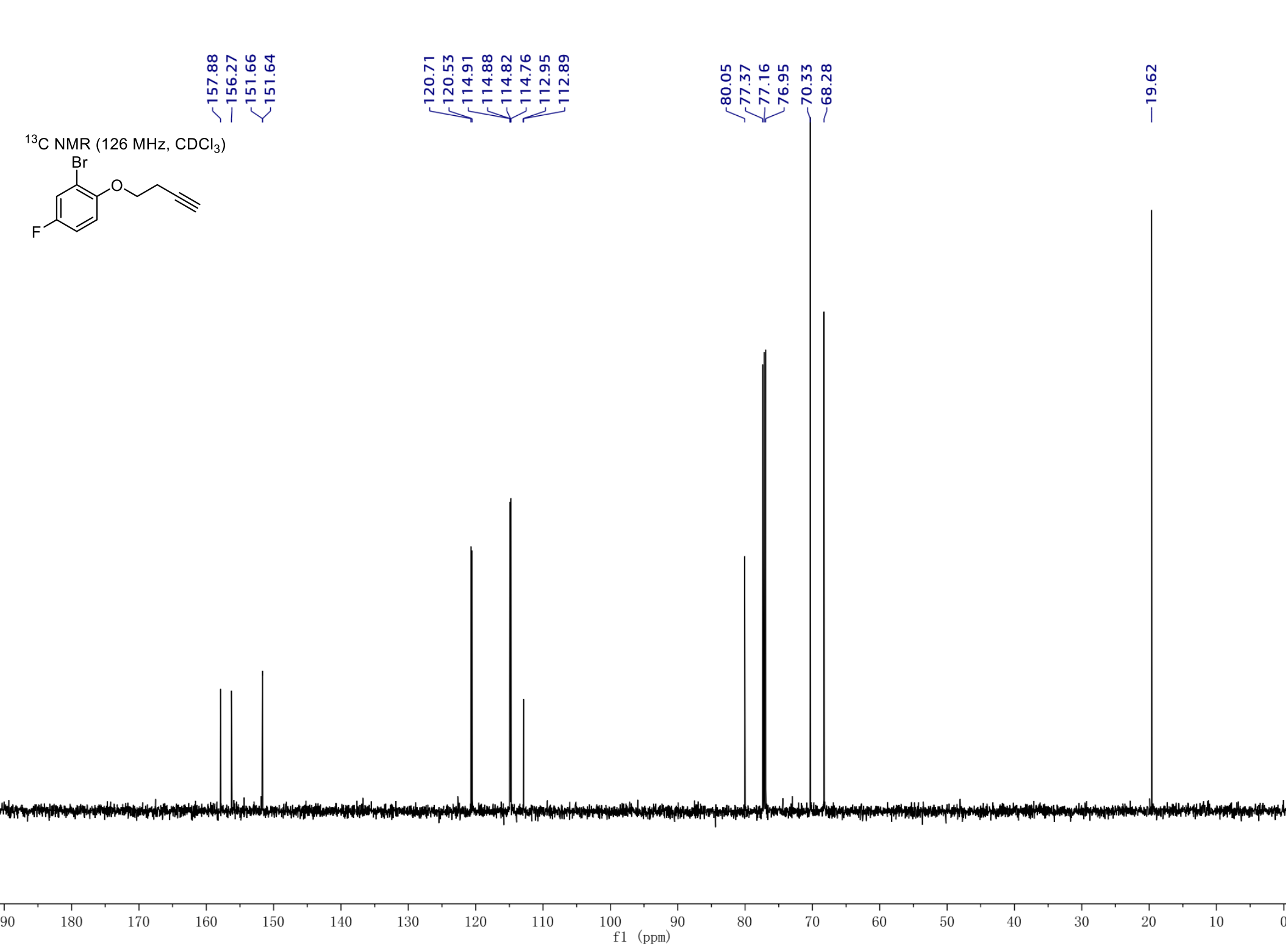
G

E


7.30
7.30
7.29
7.28
7.26
6.99
6.98
6.97
6.97
6.96
6.95
6.88
6.87
6.86
6.85
4.12
4.11
4.09
2.74
2.73
2.73
2.72
2.71
2.71
2.06
2.06
2.06
2.05
$^1$H NMR (500 MHz, $CDCl_3$)
Br
O
F
0.98
1.00
1.01
2.07
2.06
0.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

G

E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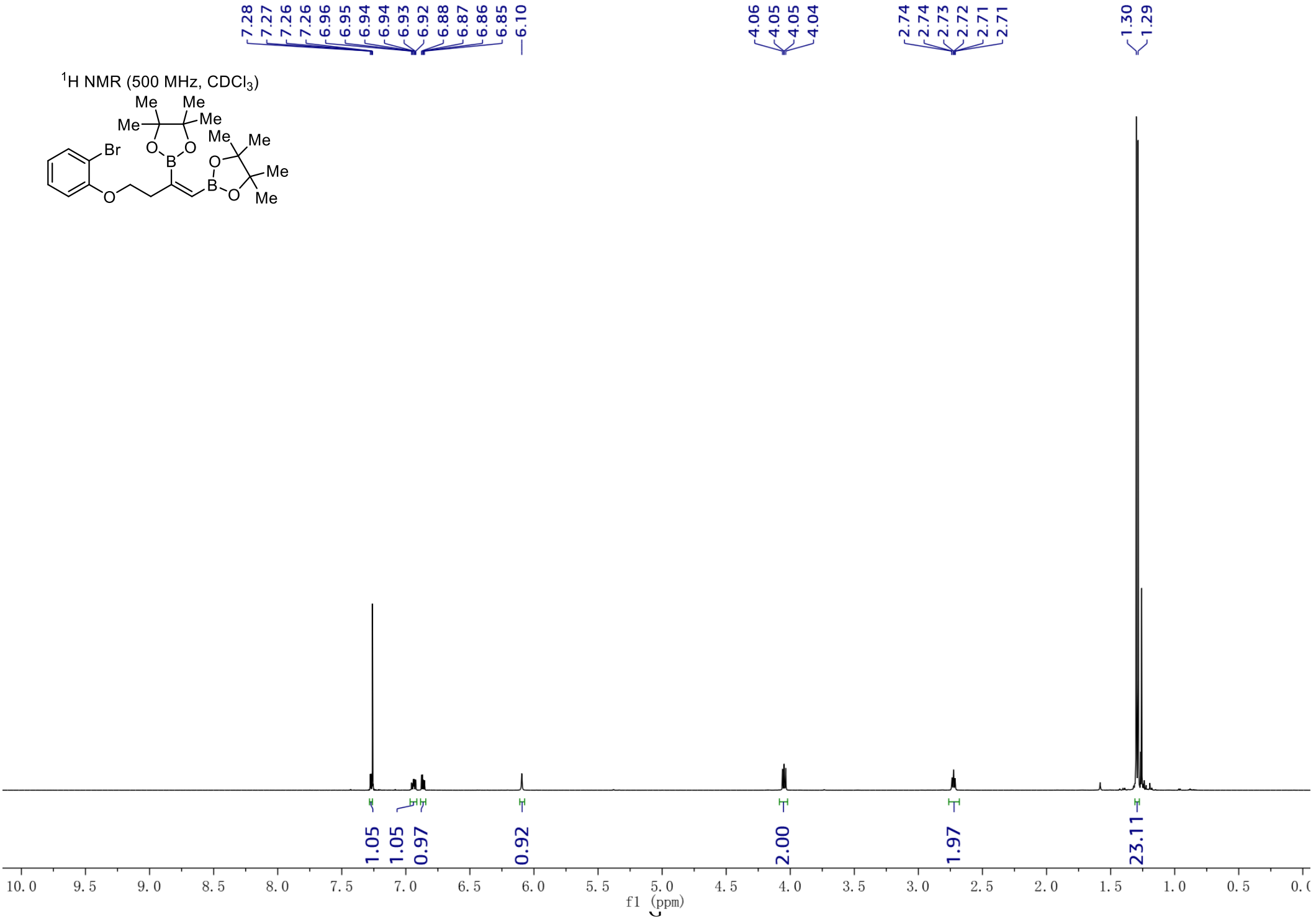
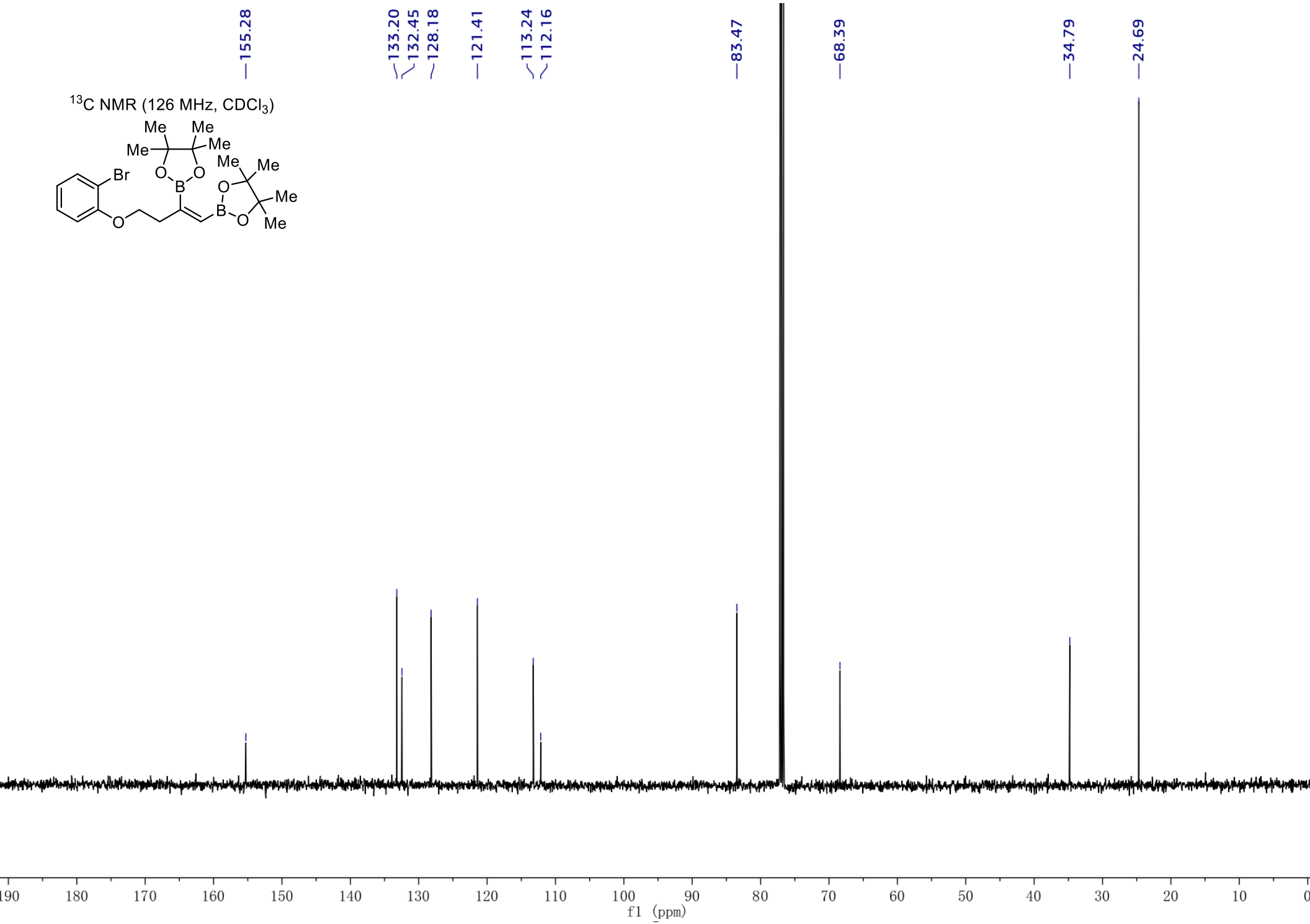
156.27
151.66
151.64
120.71
120.53
114.91
114.88
114.82
114.76
112.95
112.89
80.05
77.37
77.16
76.95
70.33
68.28
19.62
$^{13}$C NMR (126 MHz, $CDCl_3$)
Br
O
F
f1 (ppm)

G

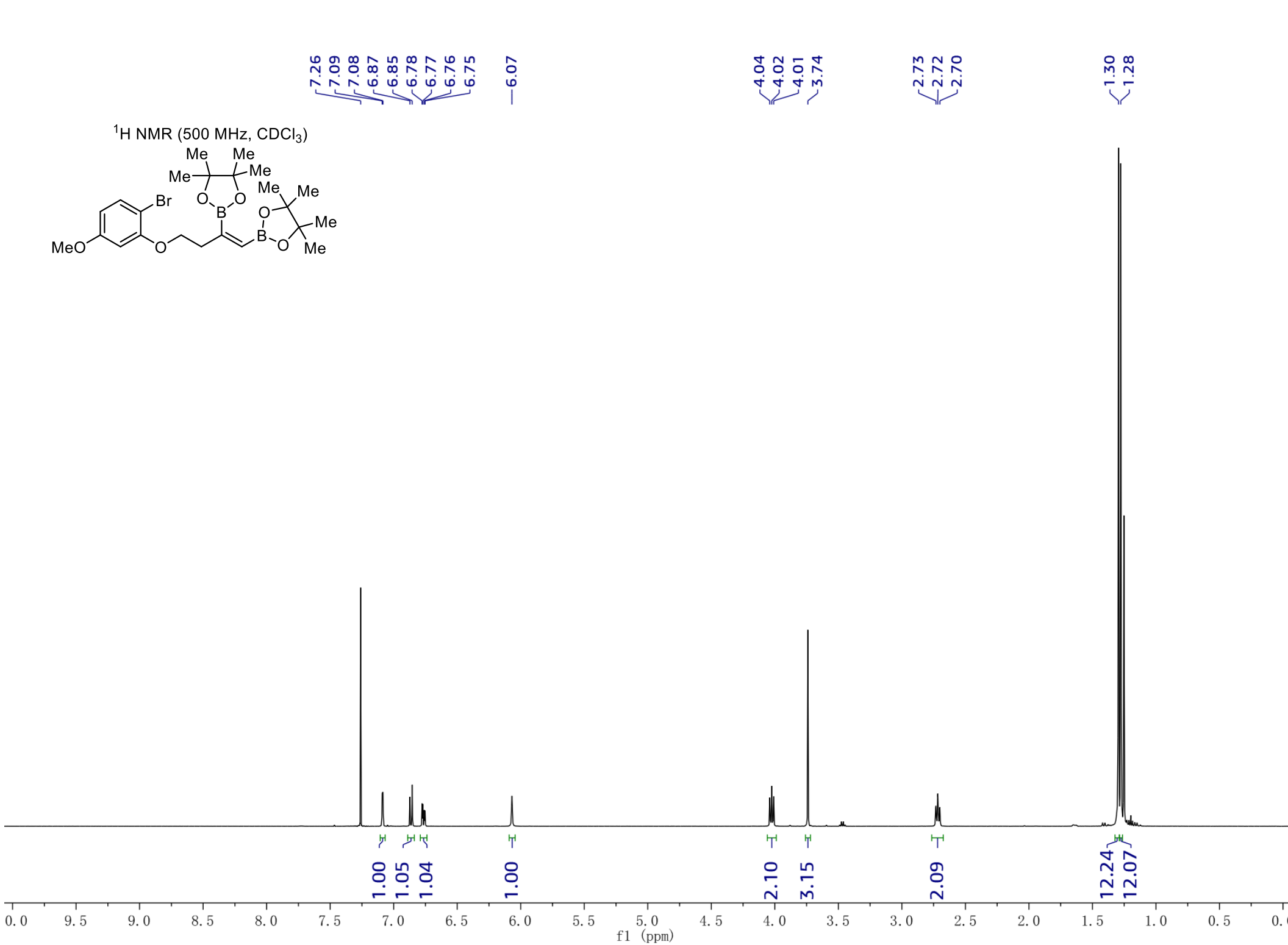
E


7.28
7.27
7.26
7.26
6.96
6.95
6.94
6.94
6.93
6.92
6.88
6.87
6.86
6.85
6.10
4.06
4.05
4.05
4.04
2.74
2.74
2.73
2.72
2.71
2.71
1.30
1.29
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Br
O
B
O
O
B
O
Me
Me
Me
O
1.05
1.05
0.97
0.92
2.00
1.97
23.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

E

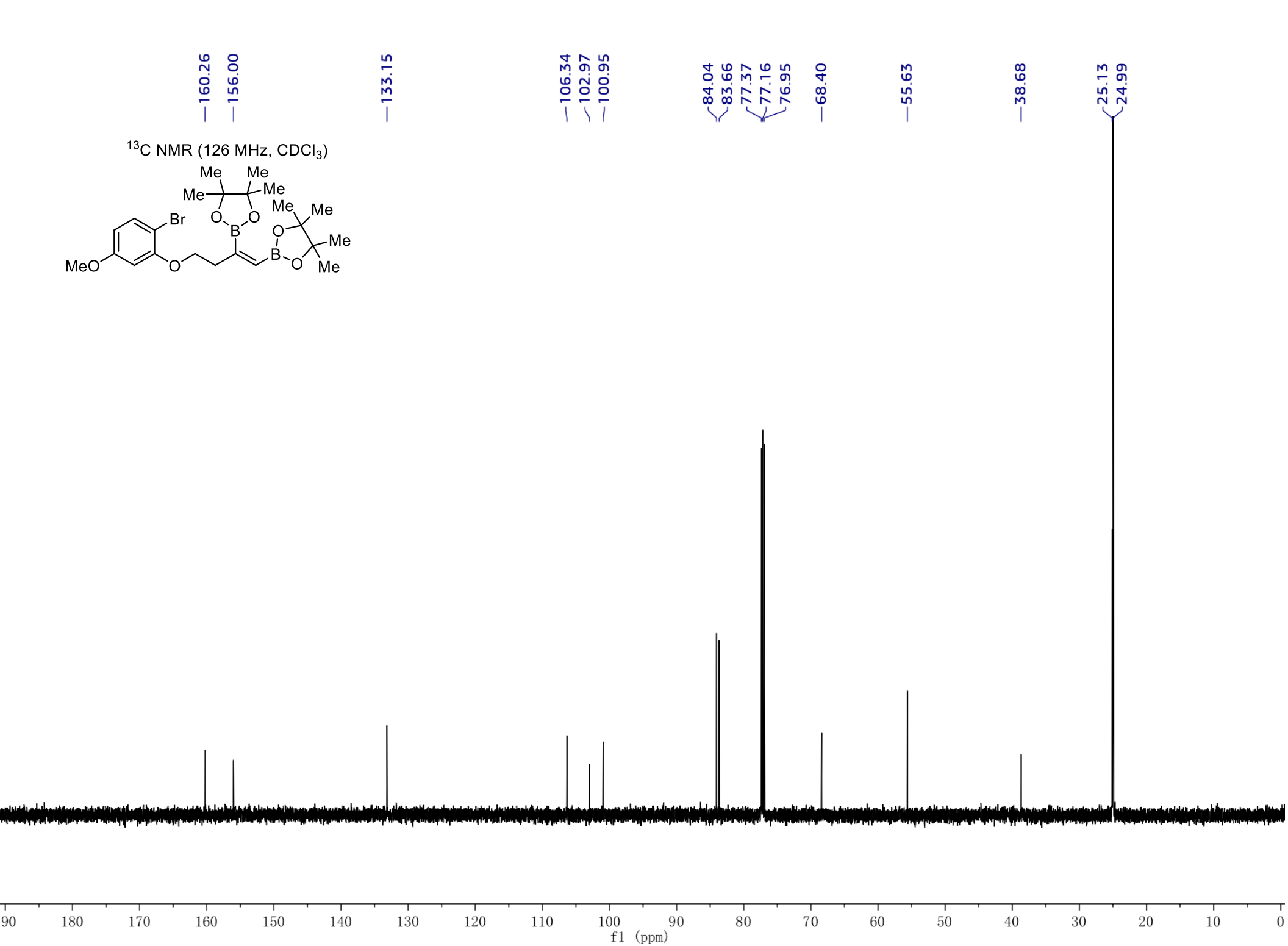

155.28
133.20
132.45
128.18
121.41
113.24
112.16
83.47
68.39
34.79
24.69
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Br
O
O
B
O
B
O
O
Me
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.26
7.09
7.08
6.87
6.85
6.78
6.77
6.76
6.75
6.07
4.04
4.02
4.01
3.74
2.73
2.72
2.70
1.30
1.28
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Br
O
O
B
O
B
O
Me
Me
Me
MeO
O
1.00
1.05
1.04
1.00
2.10
3.15
2.09
12.24
12.07
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

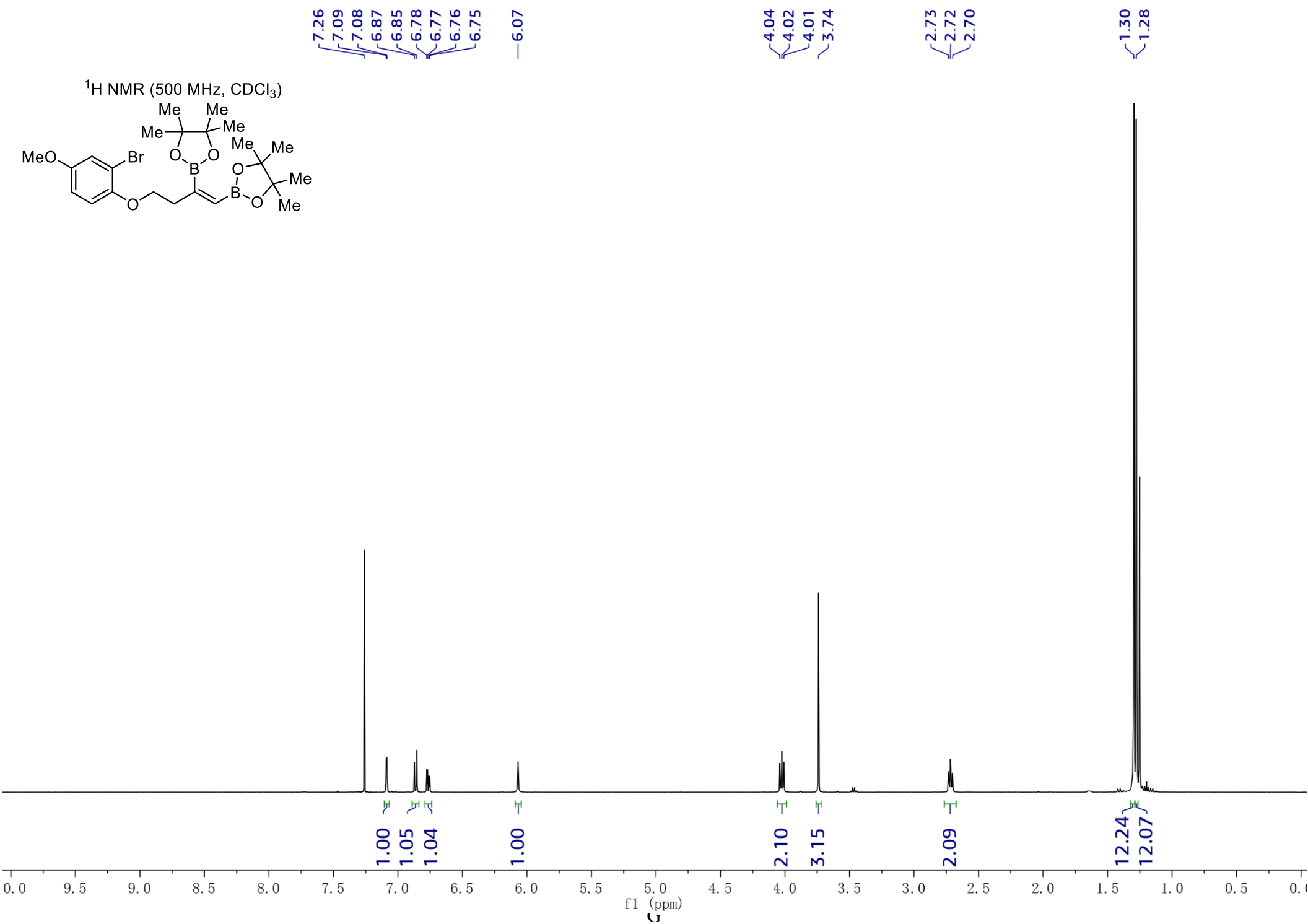
G

E


160.26
156.00
133.15
106.34
102.97
100.95
84.04
83.66
77.37
77.16
76.95
68.40
55.63
38.68
25.13
24.99
$^{13}$C NMR (126 MHz, CDCl$_3$)
Me
Me
Me
Me
Me
Me
Br
O
O
B
O
B
O
Me
Me
MeO
O
Me
f1 (ppm)

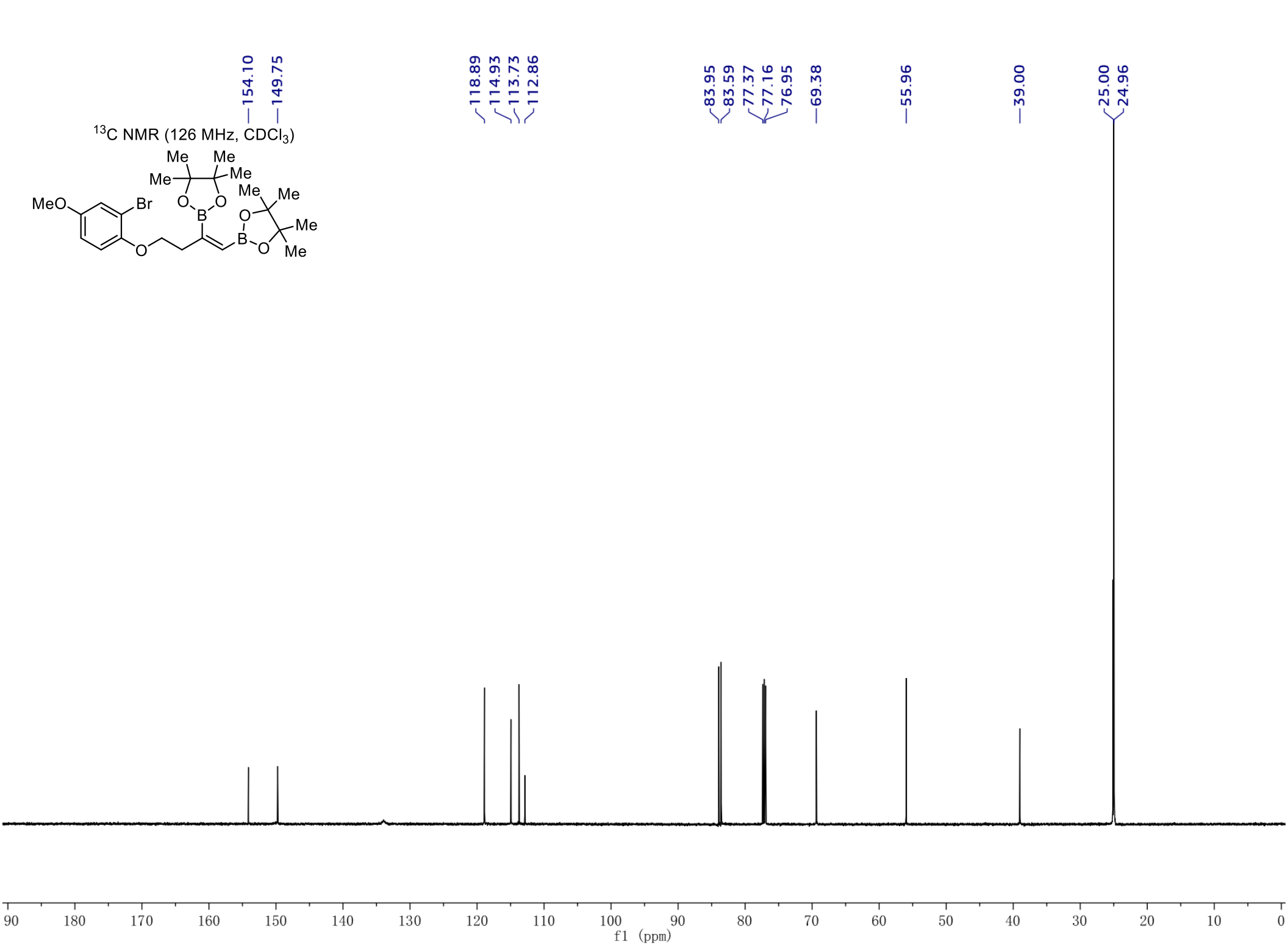
G

E


7.26
7.09
7.08
6.87
6.85
6.78
6.77
6.76
6.75
6.07
4.04
4.02
4.01
3.74
2.73
2.72
2.70
1.30
1.28
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
MeO
Br
O
B
O
O
B
O
Me
Me
O
Me
1.00
1.05
1.04
1.00
2.10
3.15
2.09
12.24
12.07
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

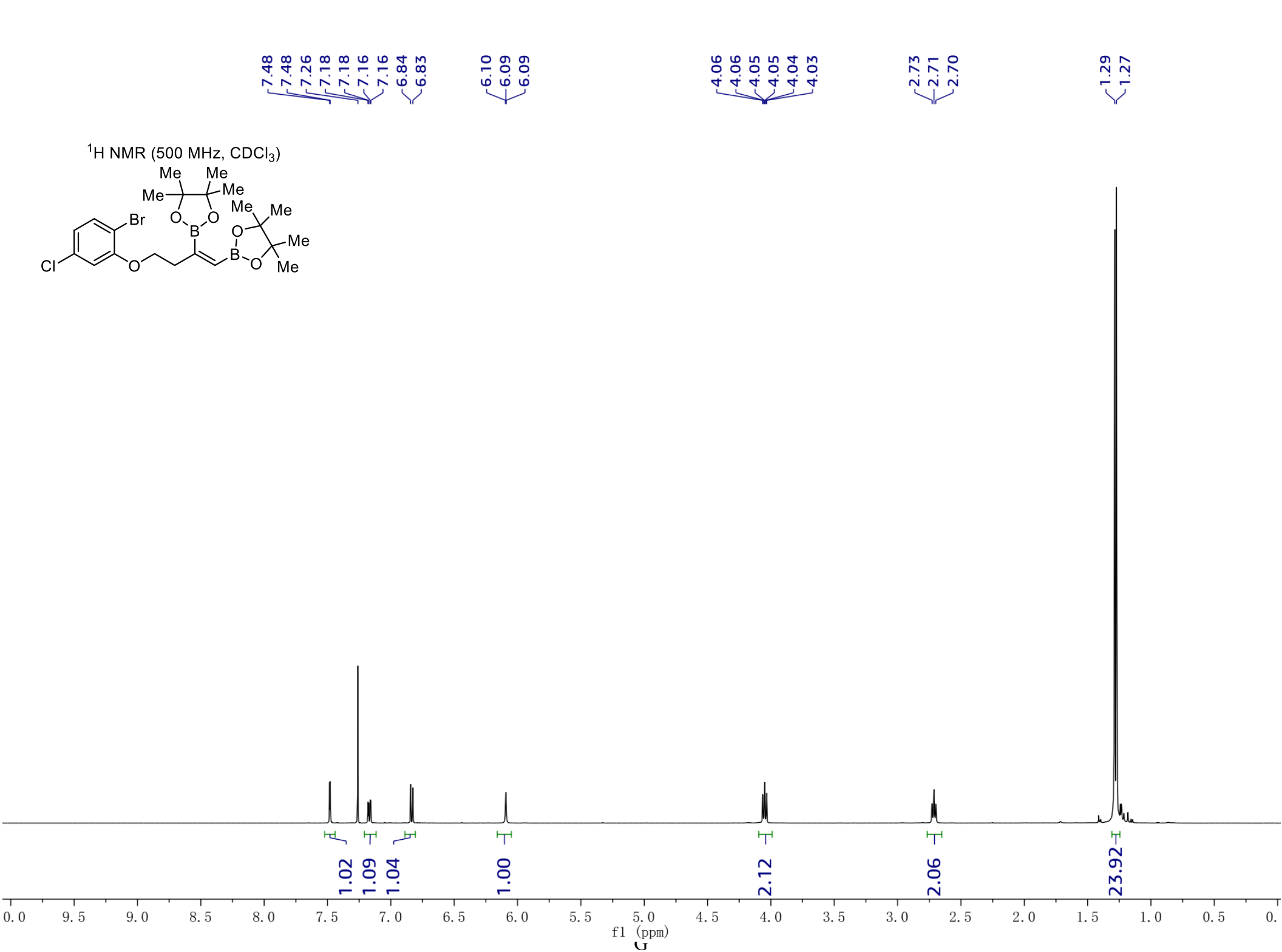
G

E


154.10
149.75
118.89
114.93
113.73
112.86
83.95
83.59
77.37
77.16
76.95
69.38
55.96
39.00
25.00
24.96
13C NMR (126 MHz, CDCl3)
MeO
Br
O
B
O
Me
Me
Me
Me
Me
Me
Me
Me
Me
f1 (ppm)

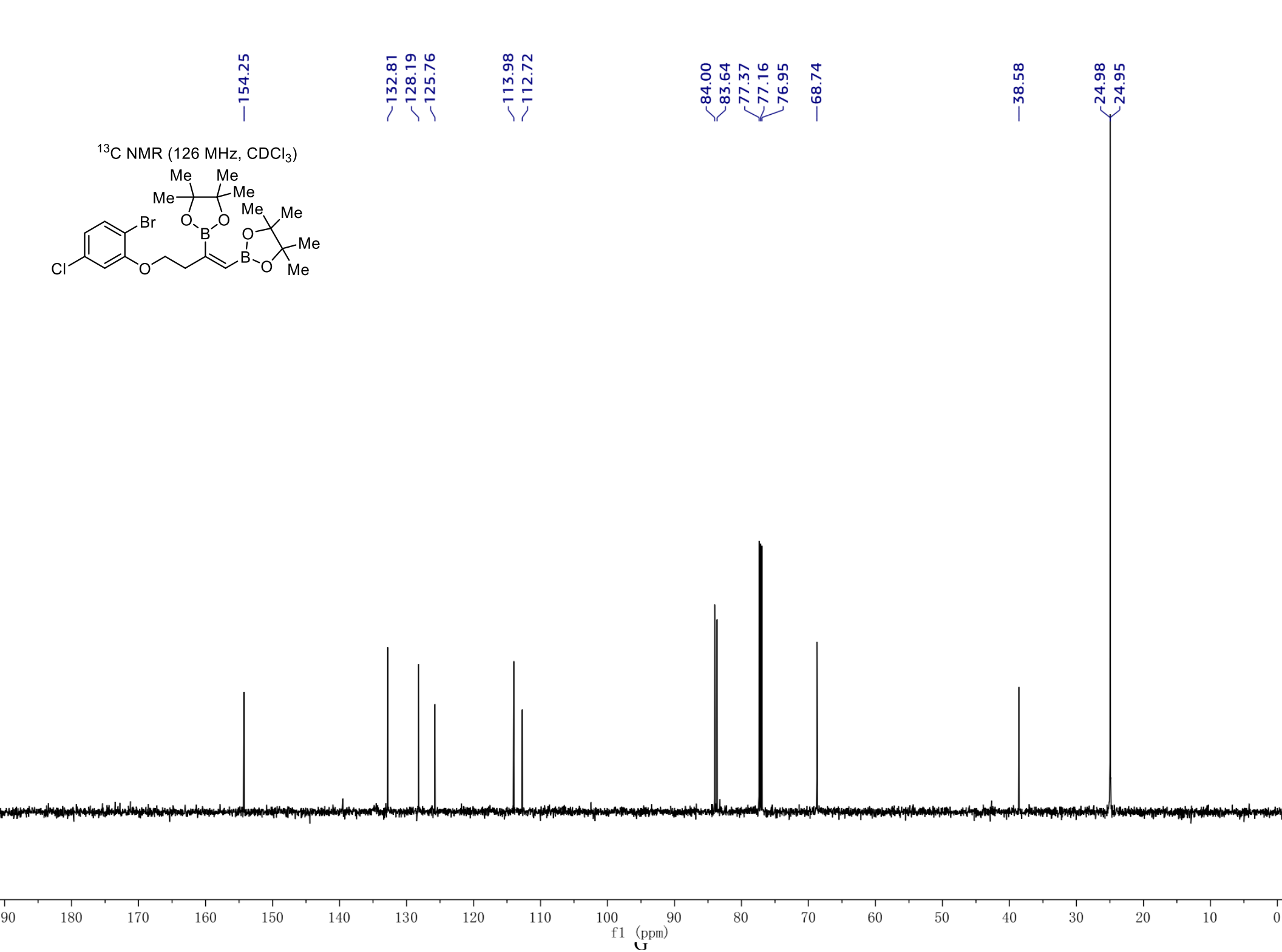
G

E


7.48
7.48
7.26
7.18
7.18
7.16
7.16
6.84
6.83
6.10
6.09
6.09
4.06
4.06
4.05
4.05
4.04
4.03
2.73
2.71
2.70
1.29
1.27
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
Me
Me
Br
O
O
B
O
B
O
Me
Me
Me
Cl
O
1.02
1.09
1.04
1.00
2.12
2.06
23.92
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

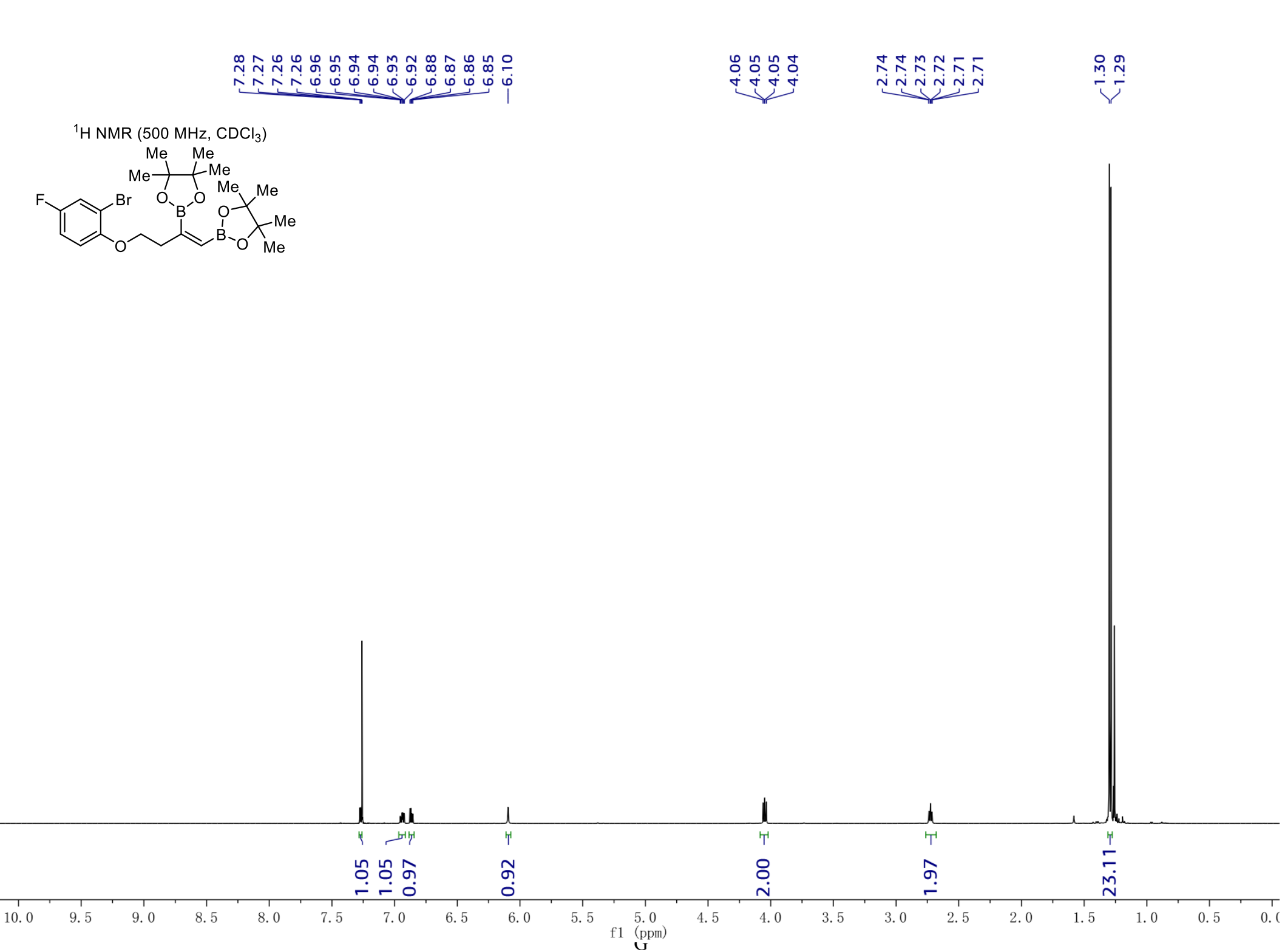
G

E


154.25
132.81
128.19
125.76
113.98
112.72
84.00
83.64
77.37
77.16
76.95
68.74
38.58
24.98
24.95
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
Br
O
B
O
O
Me
Me
Cl
O
B
O
Me
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

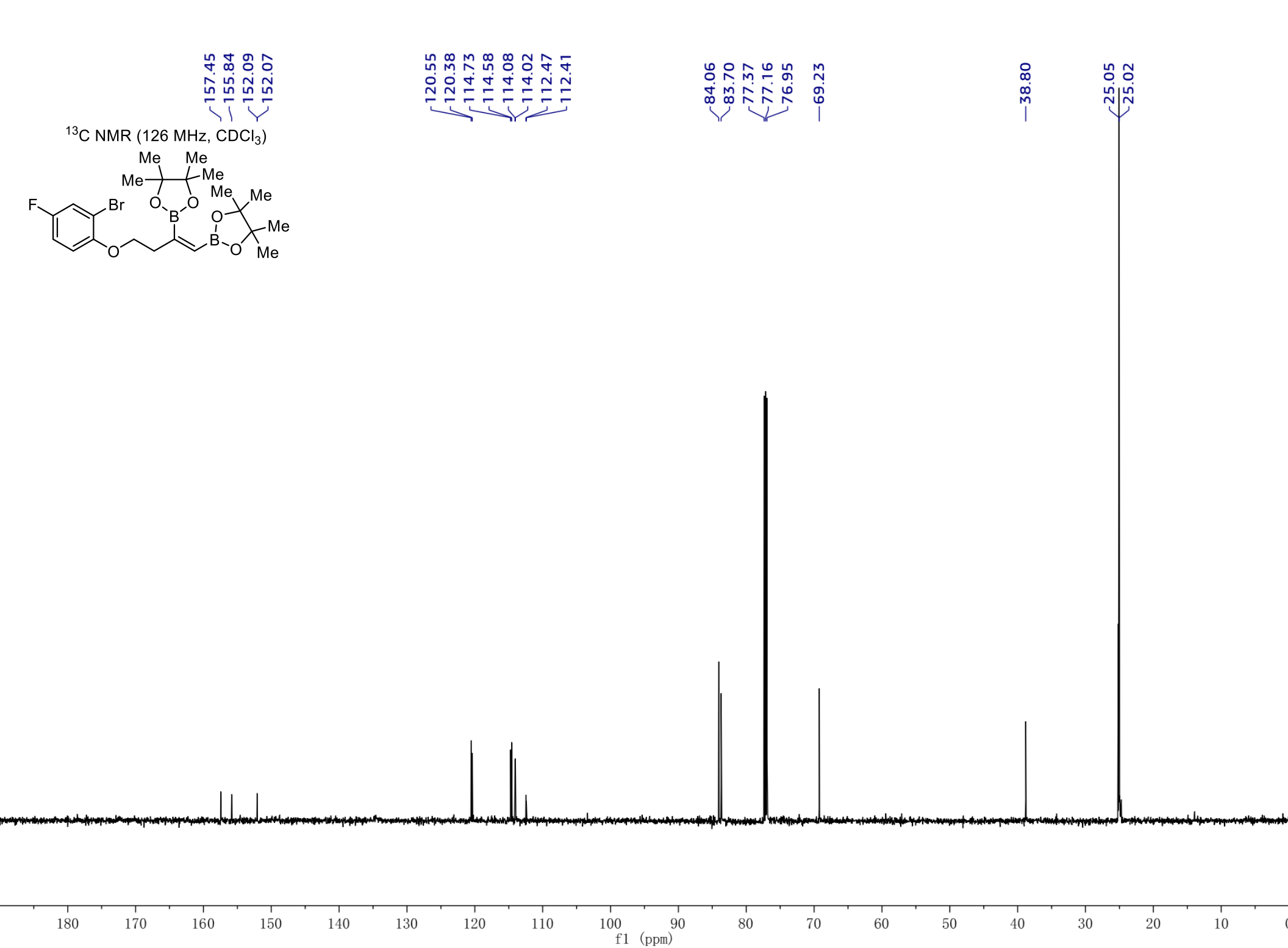
G

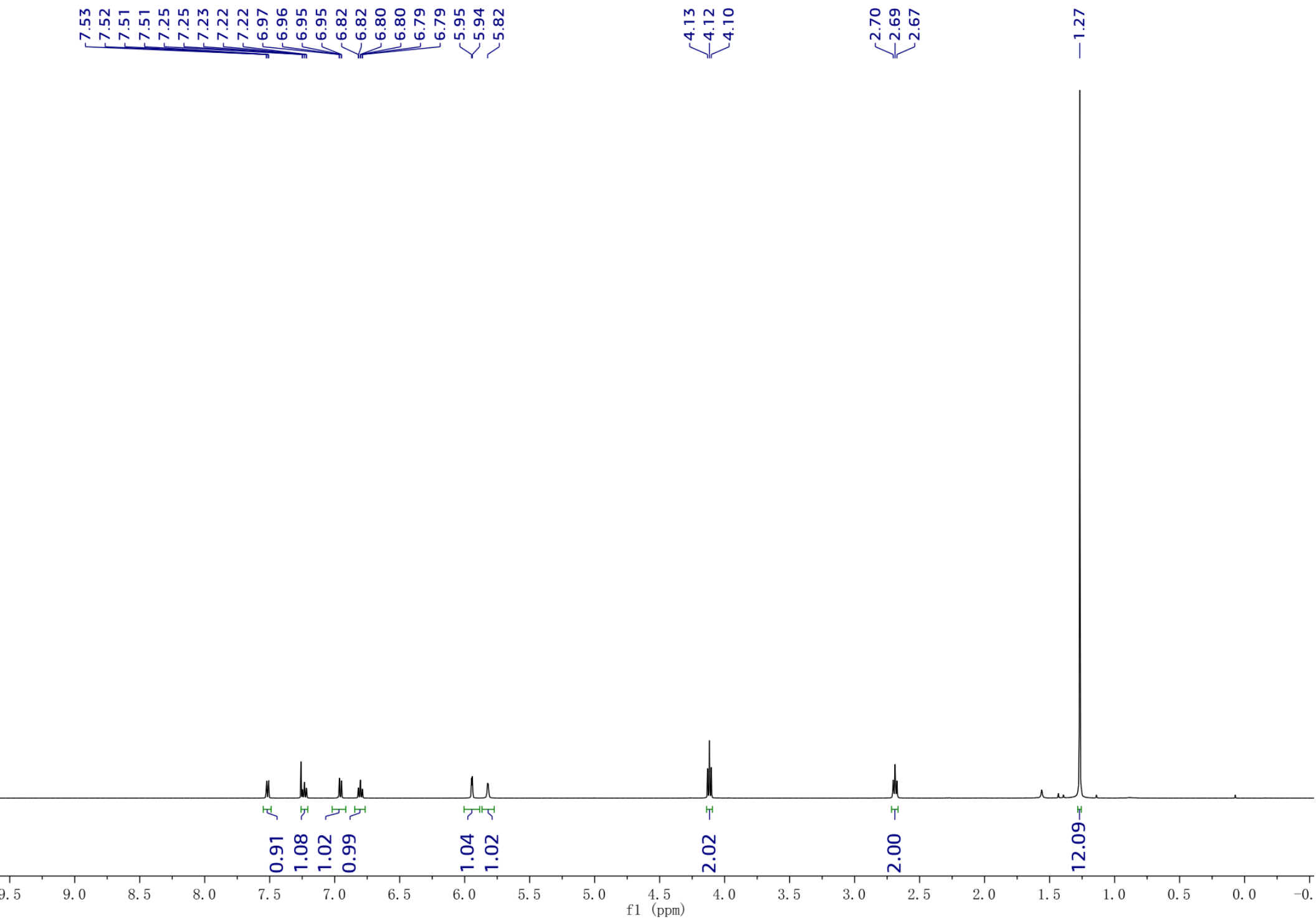
E


7.28
7.27
7.26
7.26
6.96
6.95
6.94
6.94
6.93
6.92
6.88
6.87
6.86
6.85
6.10
4.06
4.05
4.05
4.04
2.74
2.74
2.73
2.72
2.71
2.71
1.30
1.29
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
Me
Me
F
Br
O
B
O
O
B
O
Me
Me
Me
1.05
1.05
0.97
0.92
2.00
1.97
23.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

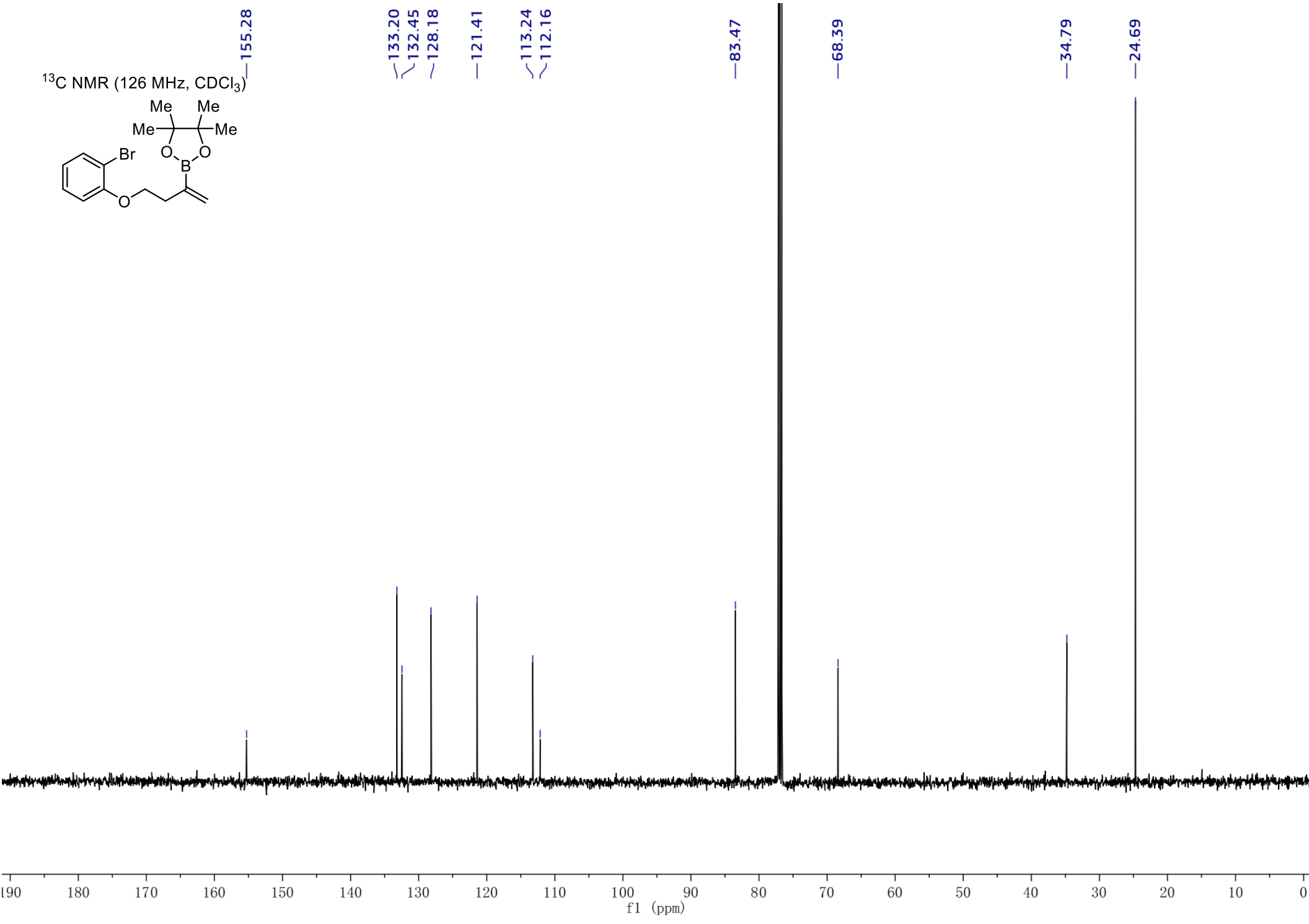
G

E

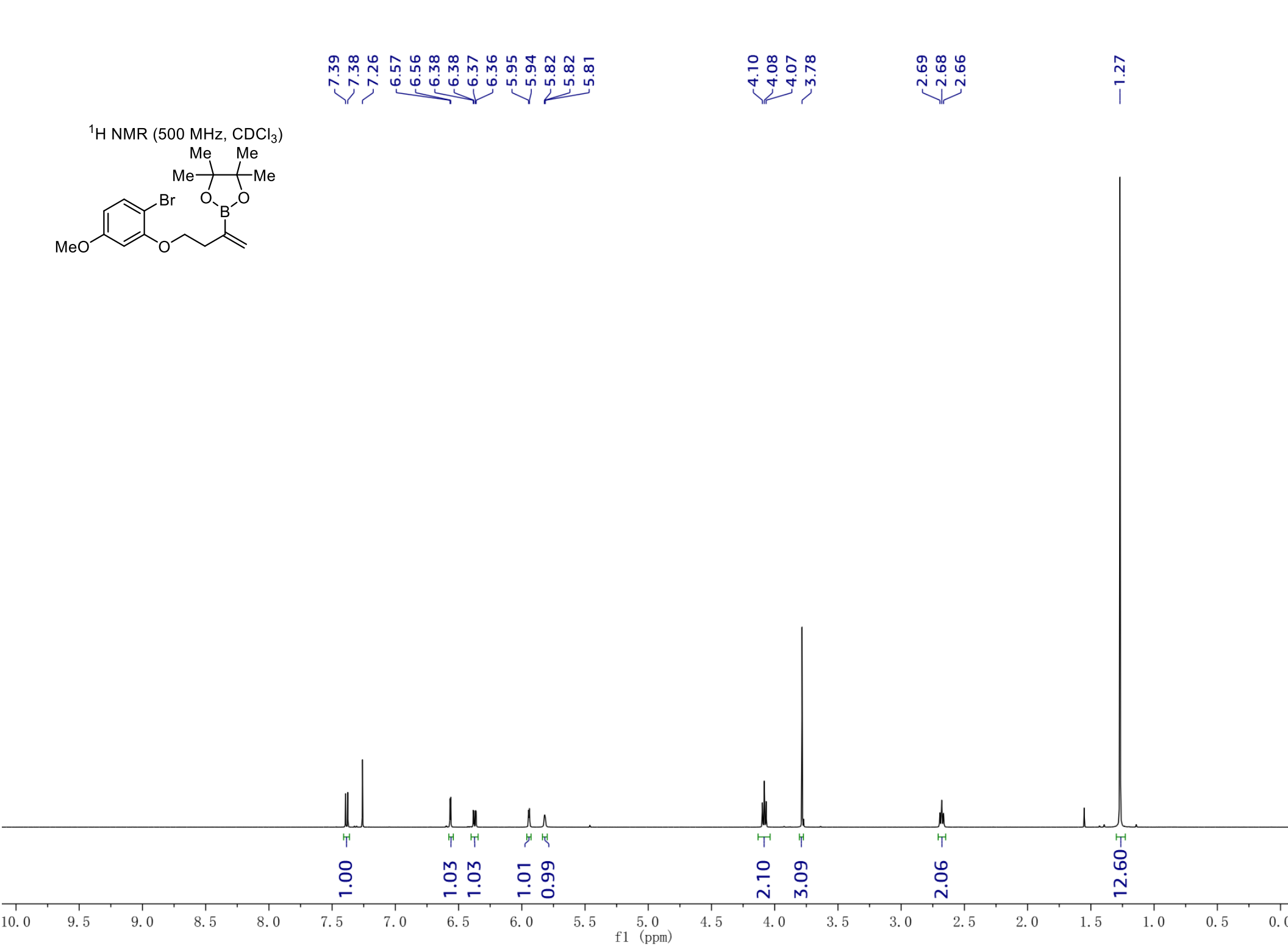

157.45
155.84
152.09
152.07
120.55
120.38
114.73
114.58
114.08
114.02
112.47
112.41
84.06
83.70
77.37
77.16
76.95
69.23
38.80
25.05
25.02
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Me
Me
F
Br
O
B
O
O
B
O
Me
Me
Me
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.53
7.52
7.51
7.51
7.25
7.25
7.23
7.22
7.22
6.97
6.96
6.95
6.95
6.82
6.82
6.80
6.80
6.79
6.79
5.95
5.94
5.82
4.13
4.12
4.10
2.70
2.69
2.67
1.27
0.91
1.08
1.02
0.99
1.04
1.02
2.02
2.00
12.09
f1 (ppm)

E

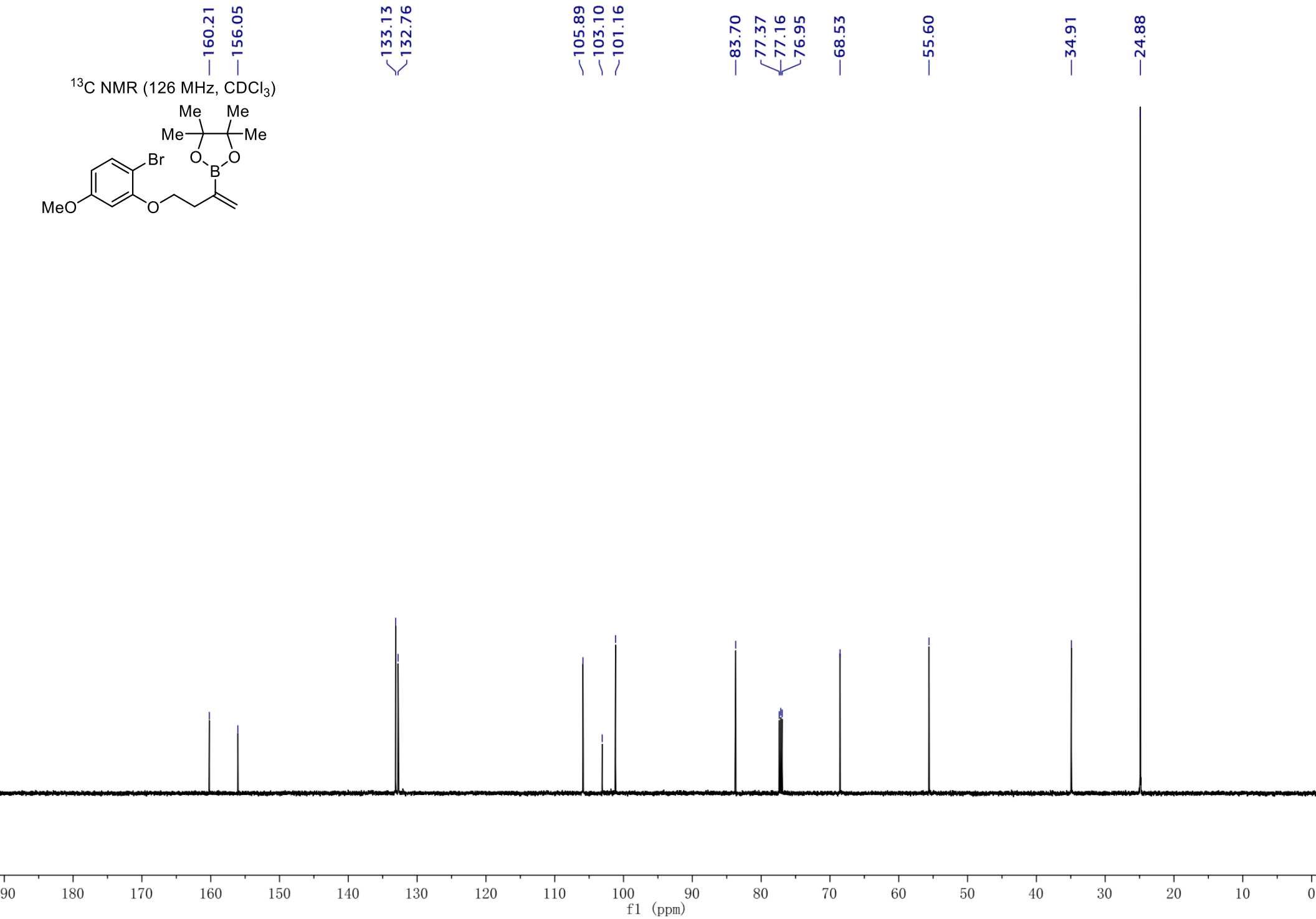

155.28
133.20
132.45
128.18
121.41
113.24
112.16
83.47
68.39
34.79
24.69
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Br
O
B
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.39
7.38
7.26
6.57
6.56
6.38
6.38
6.37
6.36
5.95
5.94
5.82
5.82
5.81
4.10
4.08
4.07
3.78
2.69
2.68
2.66
1.27
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
Br
O
O
B
MeO
O
1.00
1.03
1.03
1.01
0.99
2.10
3.09
2.06
12.60
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

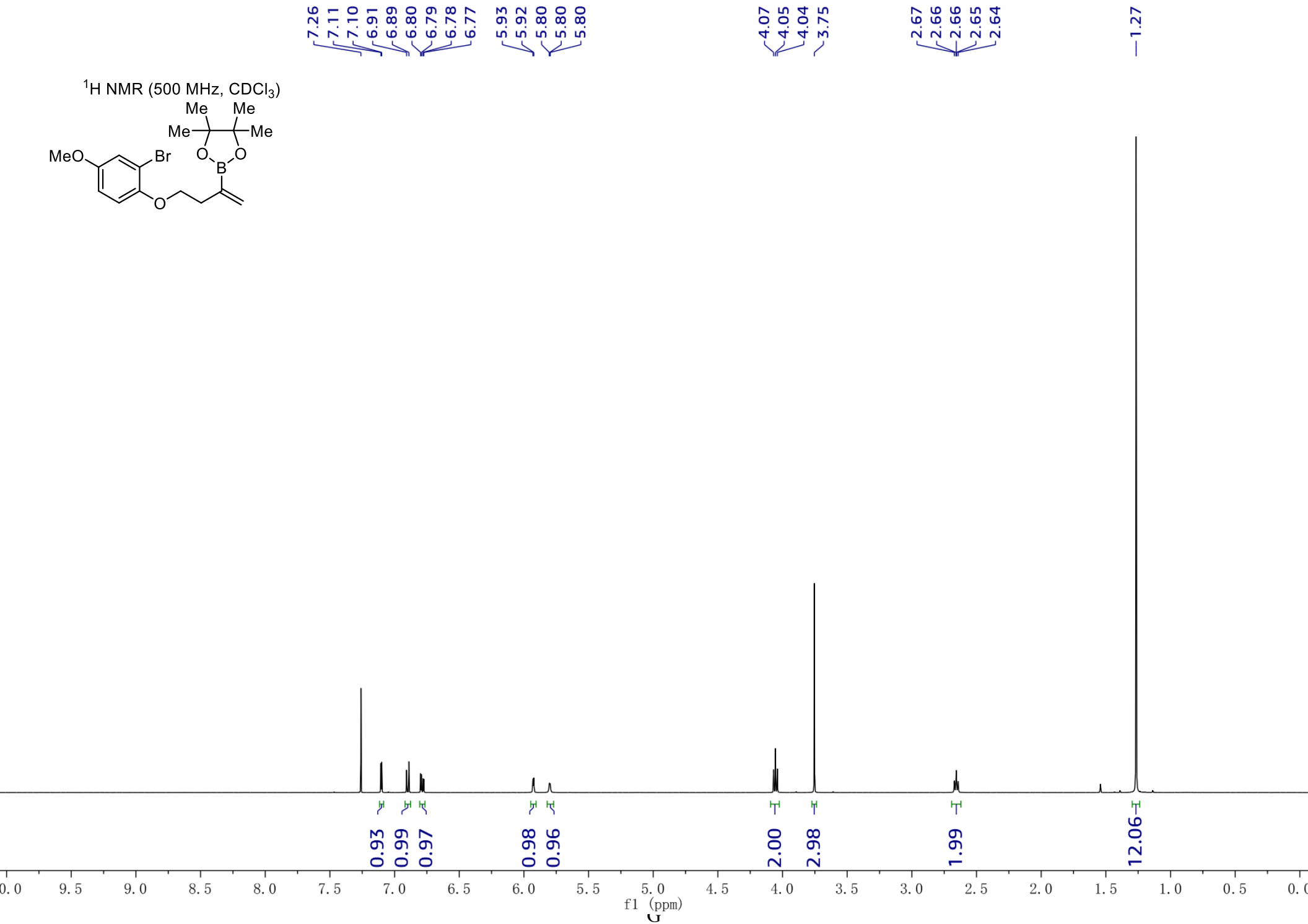
G

E


160.21
156.05
133.13
132.76
105.89
103.10
101.16
83.70
77.37
77.16
76.95
68.53
55.60
34.91
24.88
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
Br
O
O
B
MeO
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

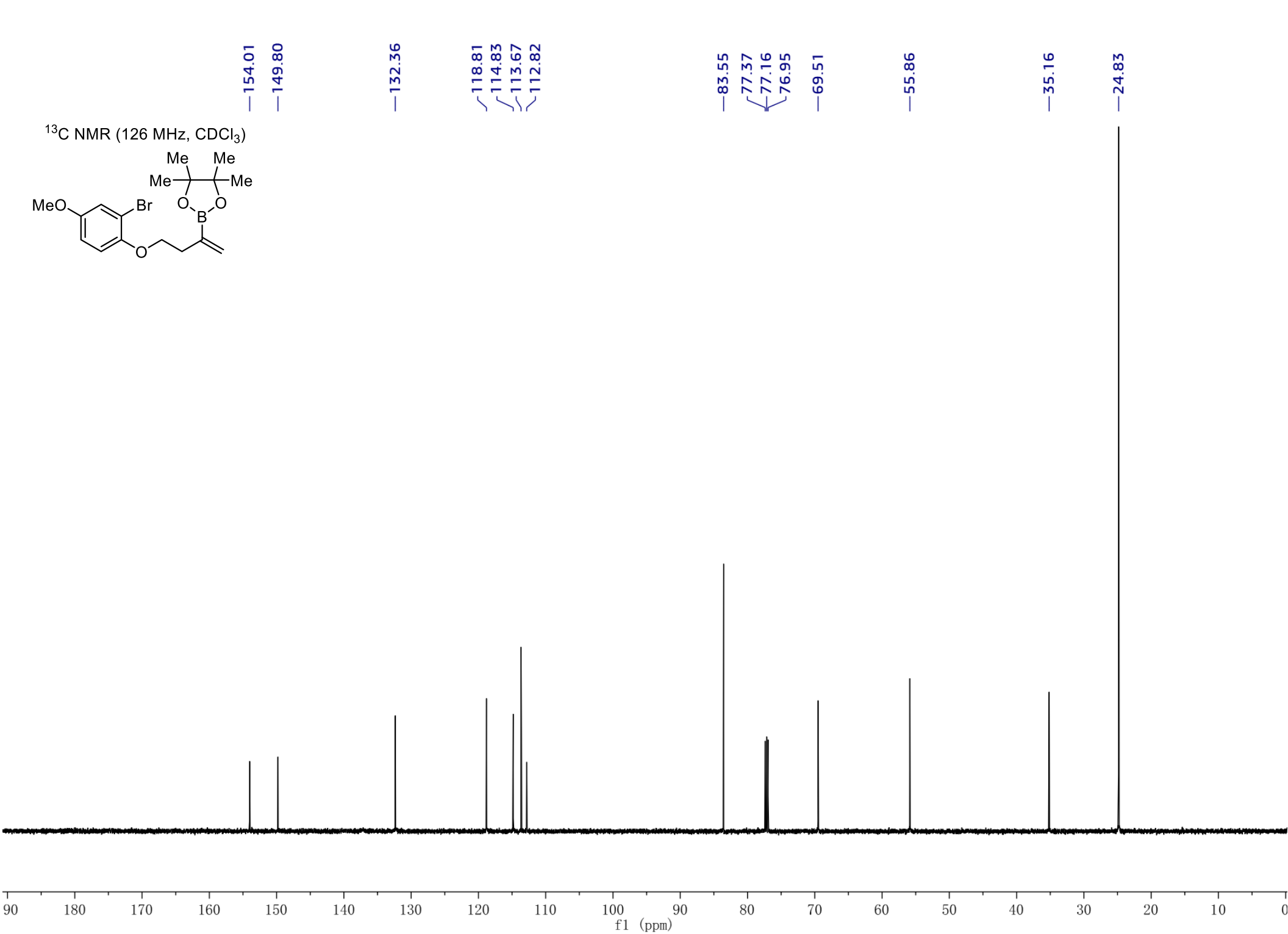
G

E


7.26
7.11
7.10
6.91
6.89
6.80
6.79
6.78
6.77
5.93
5.92
5.80
5.80
5.80
4.07
4.05
4.04
3.75
2.67
2.66
2.66
2.65
2.64
1.27
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
MeO
Br
O
B
O
O
0.93
0.99
0.97
0.98
0.96
2.00
2.98
1.99
12.06
f1 (ppm)

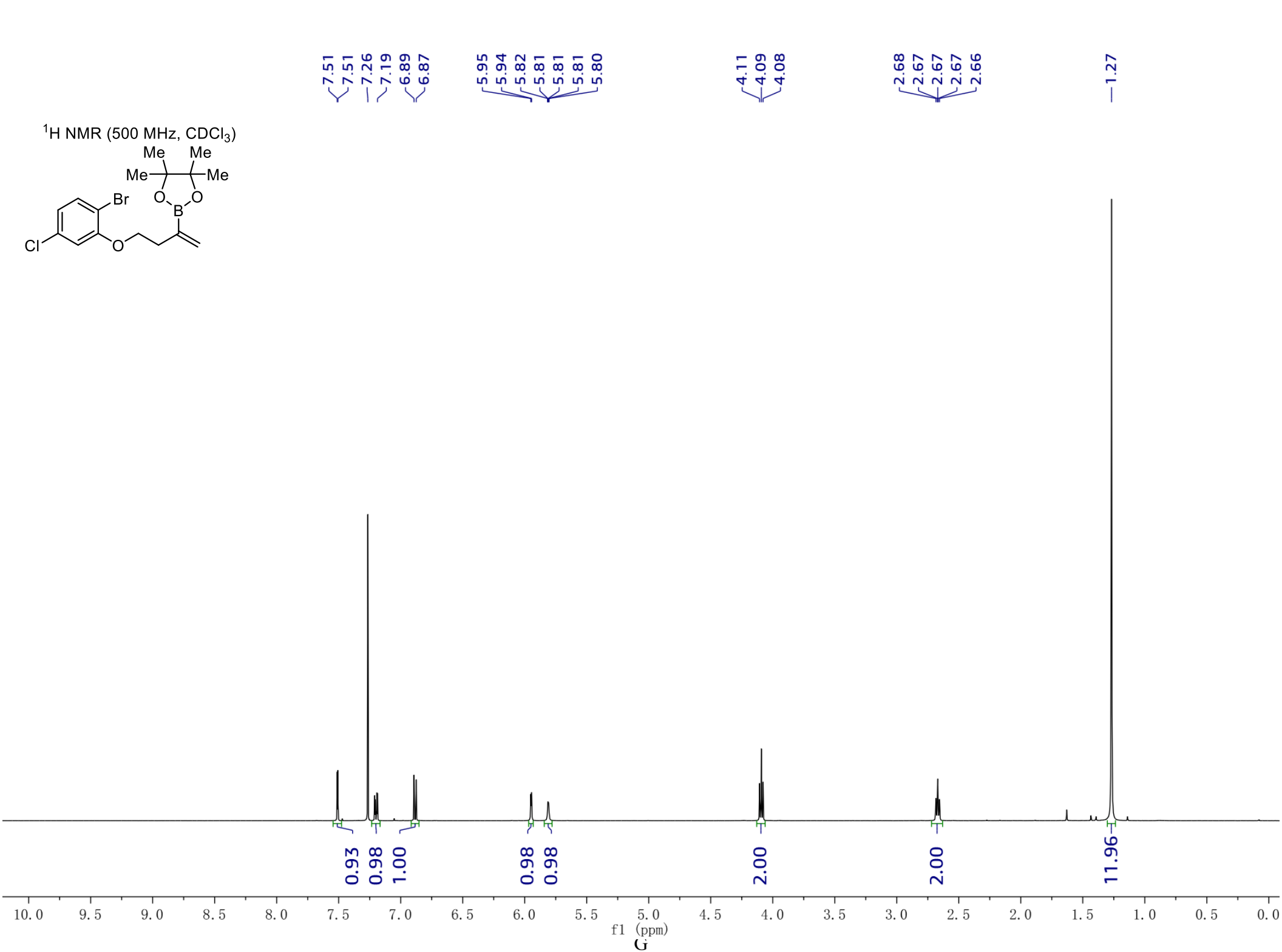
G

E


154.01
149.80
132.36
118.81
114.83
113.67
112.82
83.55
77.37
77.16
76.95
69.51
55.86
35.16
24.83
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
MeO
Br
O
B
O
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

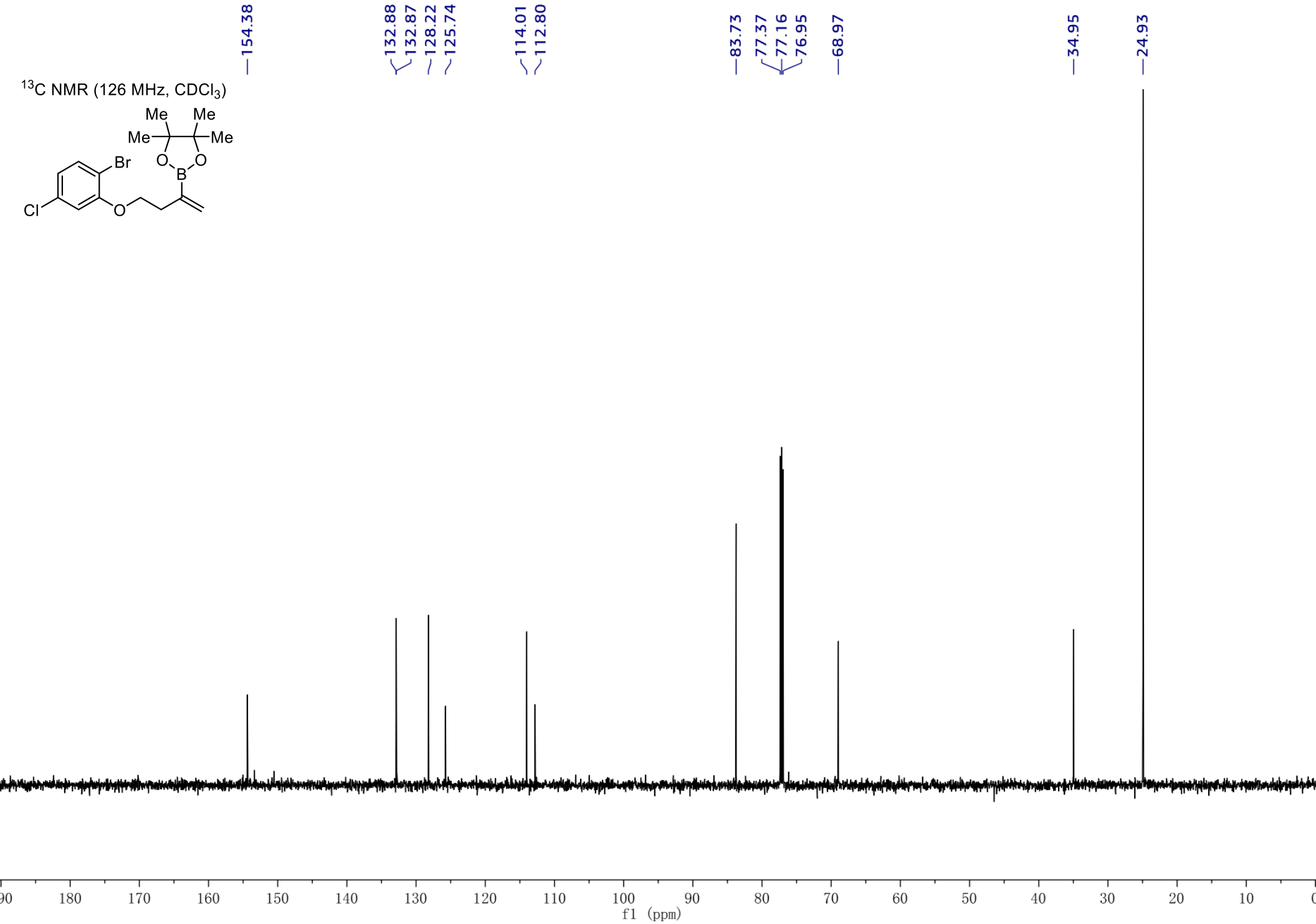
G

E

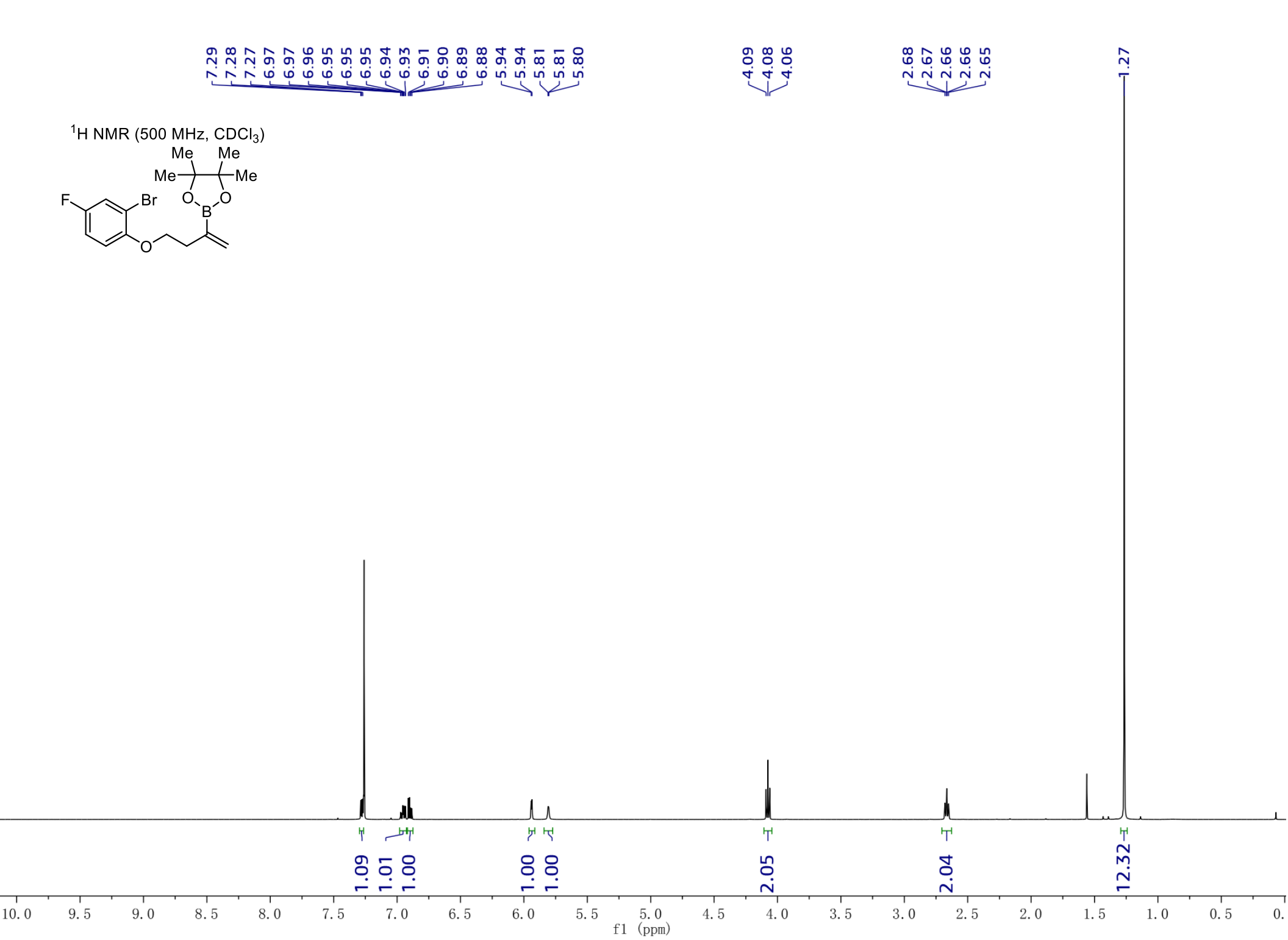

7.51
7.51
7.26
7.19
6.89
6.87
5.95
5.94
5.82
5.81
5.81
5.81
5.80
4.11
4.09
4.08
2.68
2.67
2.67
2.67
2.66
1.27
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
Br
O
O
B
Cl
O
0.93
0.98
1.00
0.98
0.98
2.00
2.00
11.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E

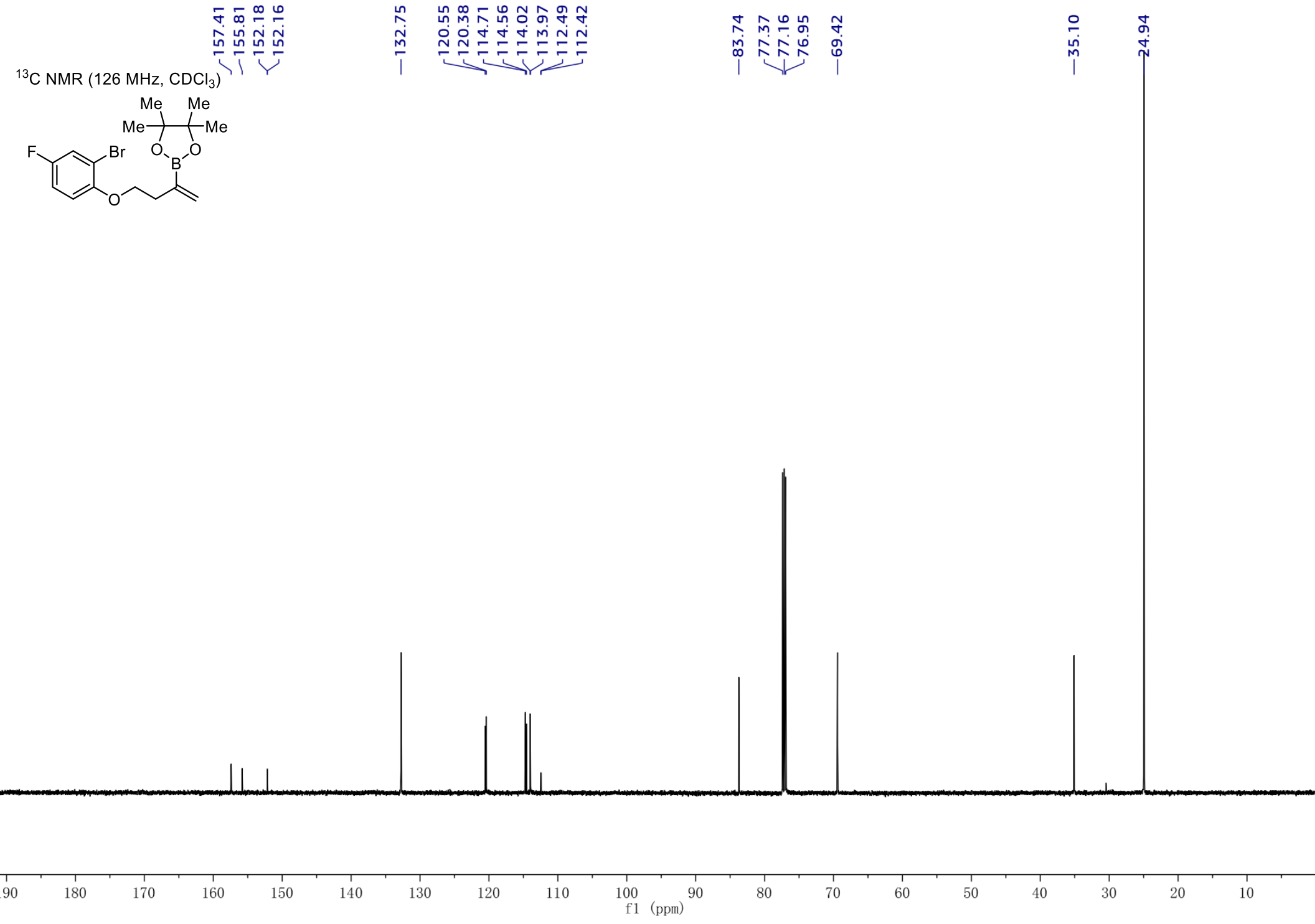

154.38
132.88
132.87
128.22
125.74
114.01
112.80
83.73
77.37
77.16
76.95
68.97
34.95
24.93
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Br
O
O
B
Cl
O
f1 (ppm)

E

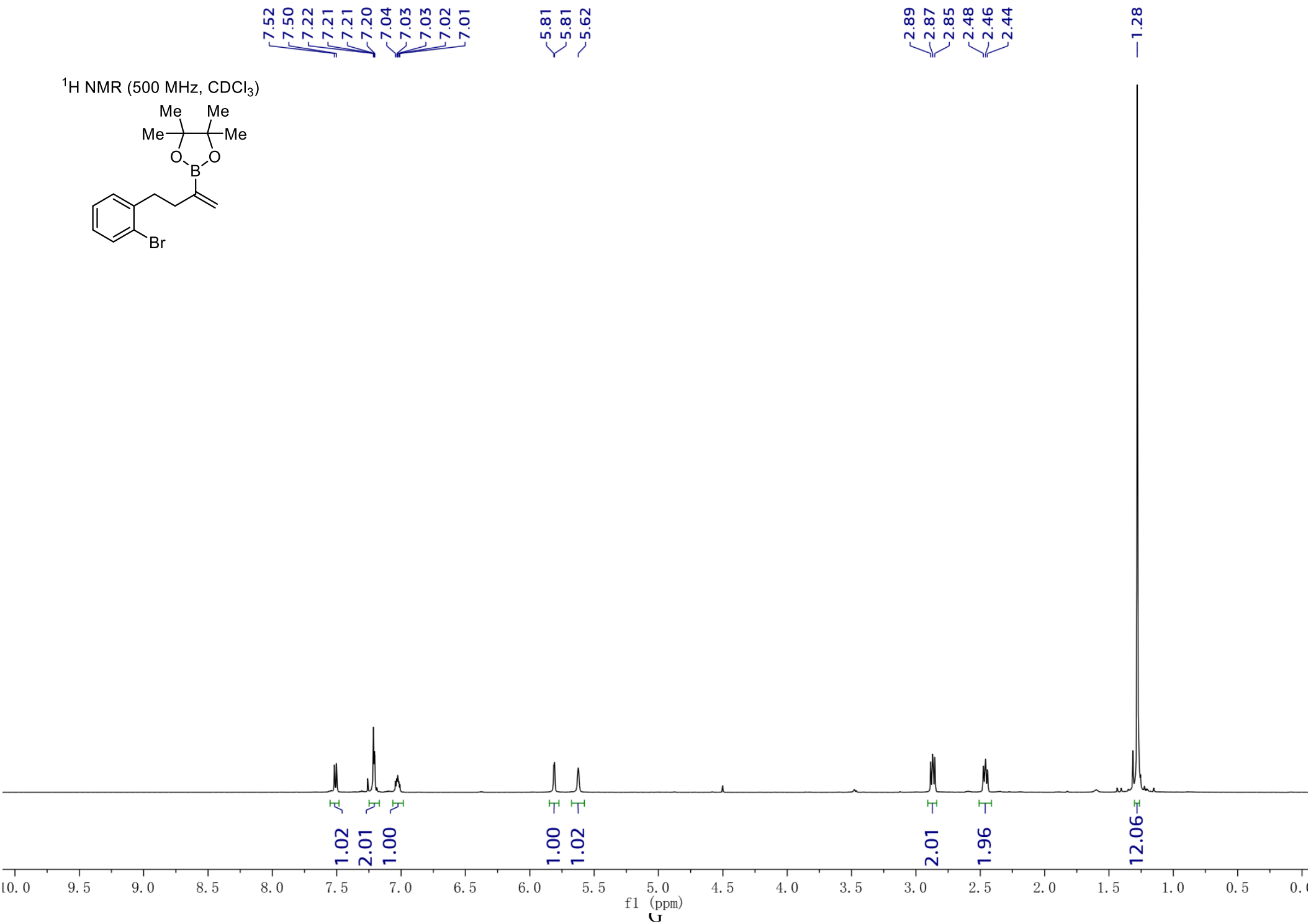

7.29
7.28
7.27
6.97
6.97
6.96
6.95
6.95
6.95
6.94
6.93
6.91
6.90
6.89
6.88
5.94
5.94
5.81
5.81
5.80
4.09
4.08
4.06
2.68
2.67
2.66
2.66
2.65
1.27
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
F
Br
O
O
B
O
1.09
1.01
1.00
1.00
1.00
2.05
2.04
12.32
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

G

E

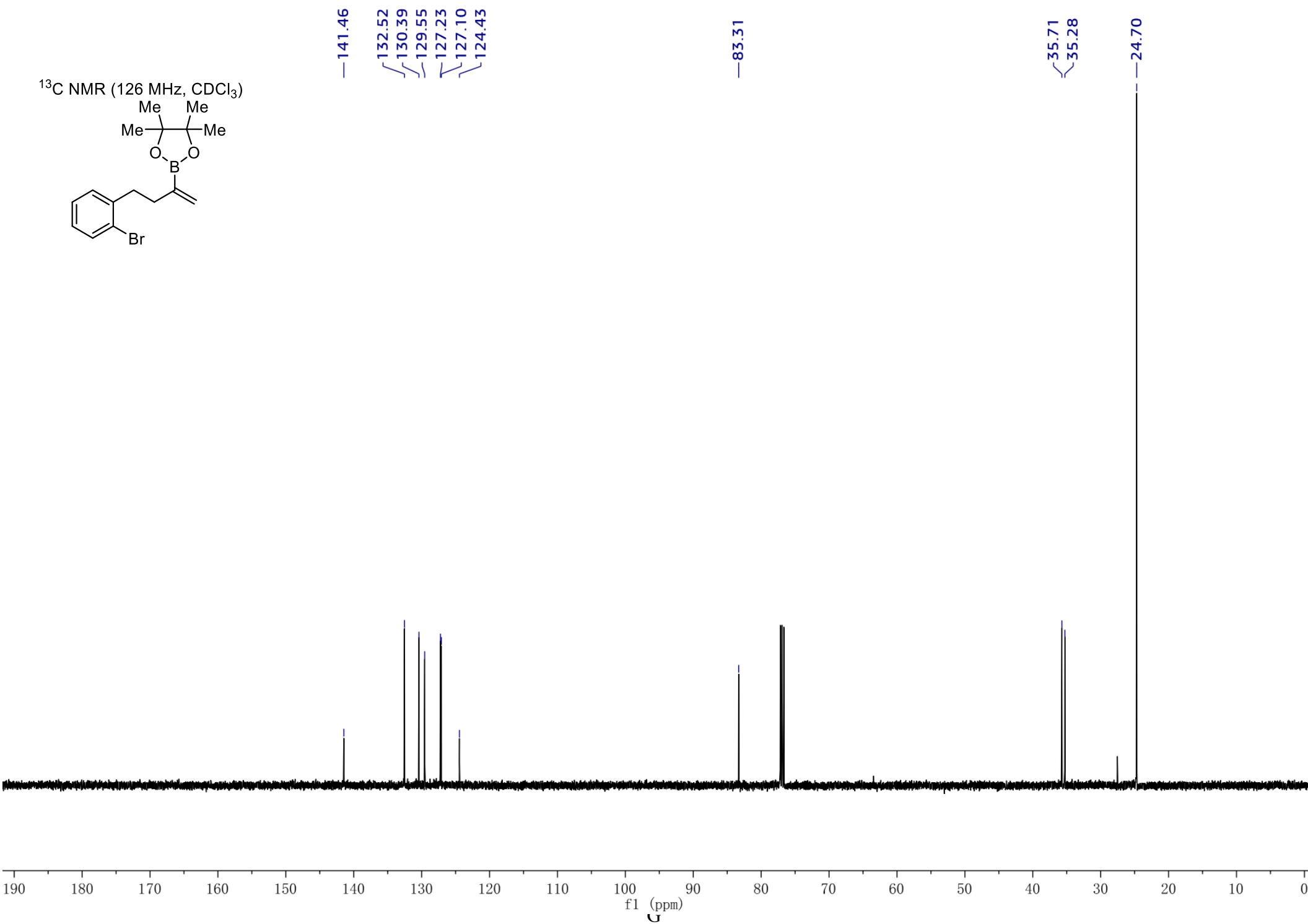

157.41
155.81
152.18
152.16
132.75
120.55
120.38
114.71
114.56
114.02
113.97
112.49
112.42
83.74
77.37
77.16
76.95
69.42
35.10
24.94
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
F
Br
O
O
B
O
O
f1 (ppm)

E


7.52
7.50
7.22
7.21
7.21
7.20
7.04
7.03
7.03
7.02
7.01
5.81
5.81
5.62
2.89
2.87
2.85
2.48
2.46
2.44
1.28
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
Br
1.02
2.01
1.00
1.00
1.02
2.01
1.96
12.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

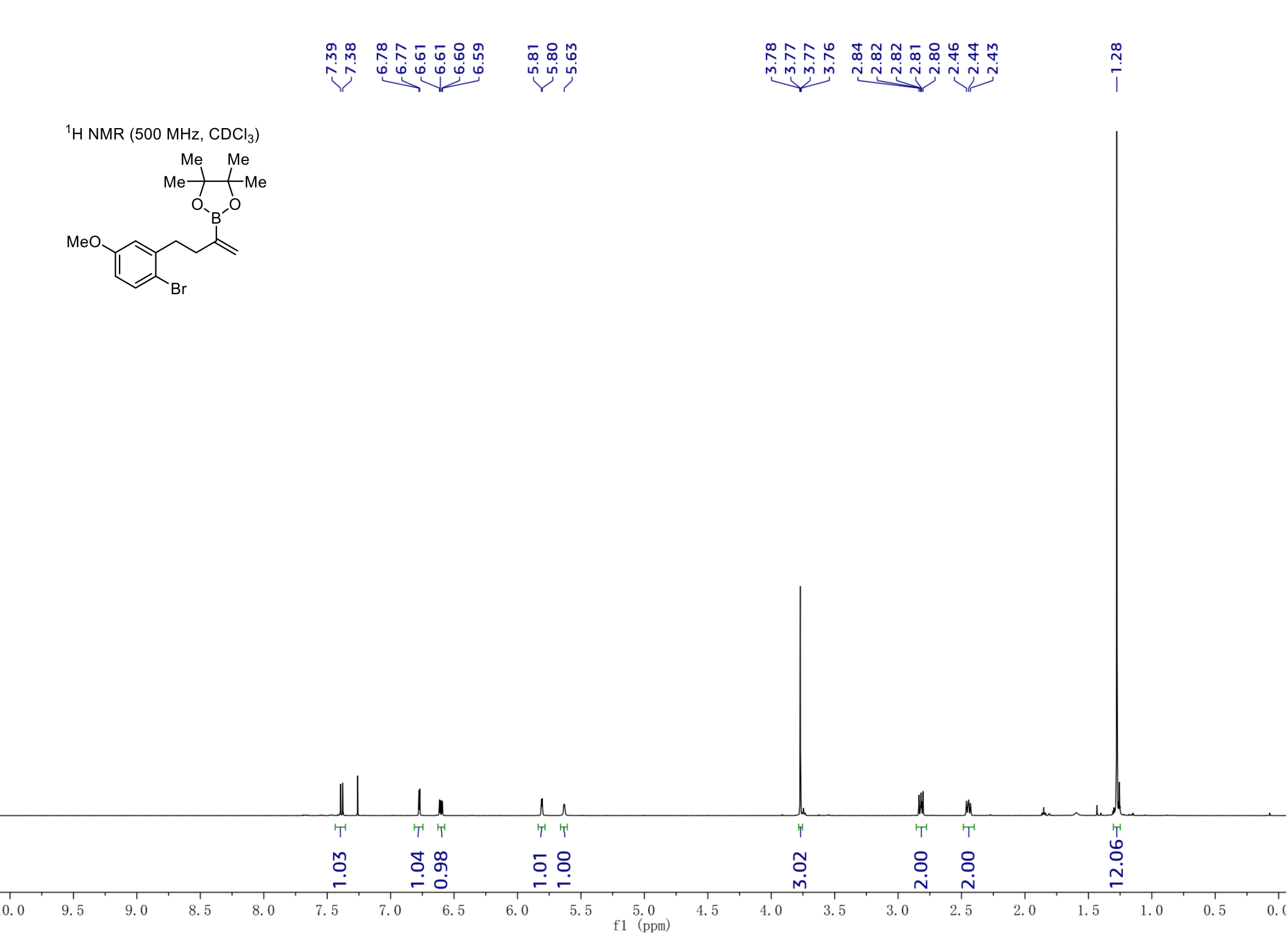
G

E


141.46
132.52
130.39
129.55
127.23
127.10
124.43
83.31
35.71
35.28
24.70
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

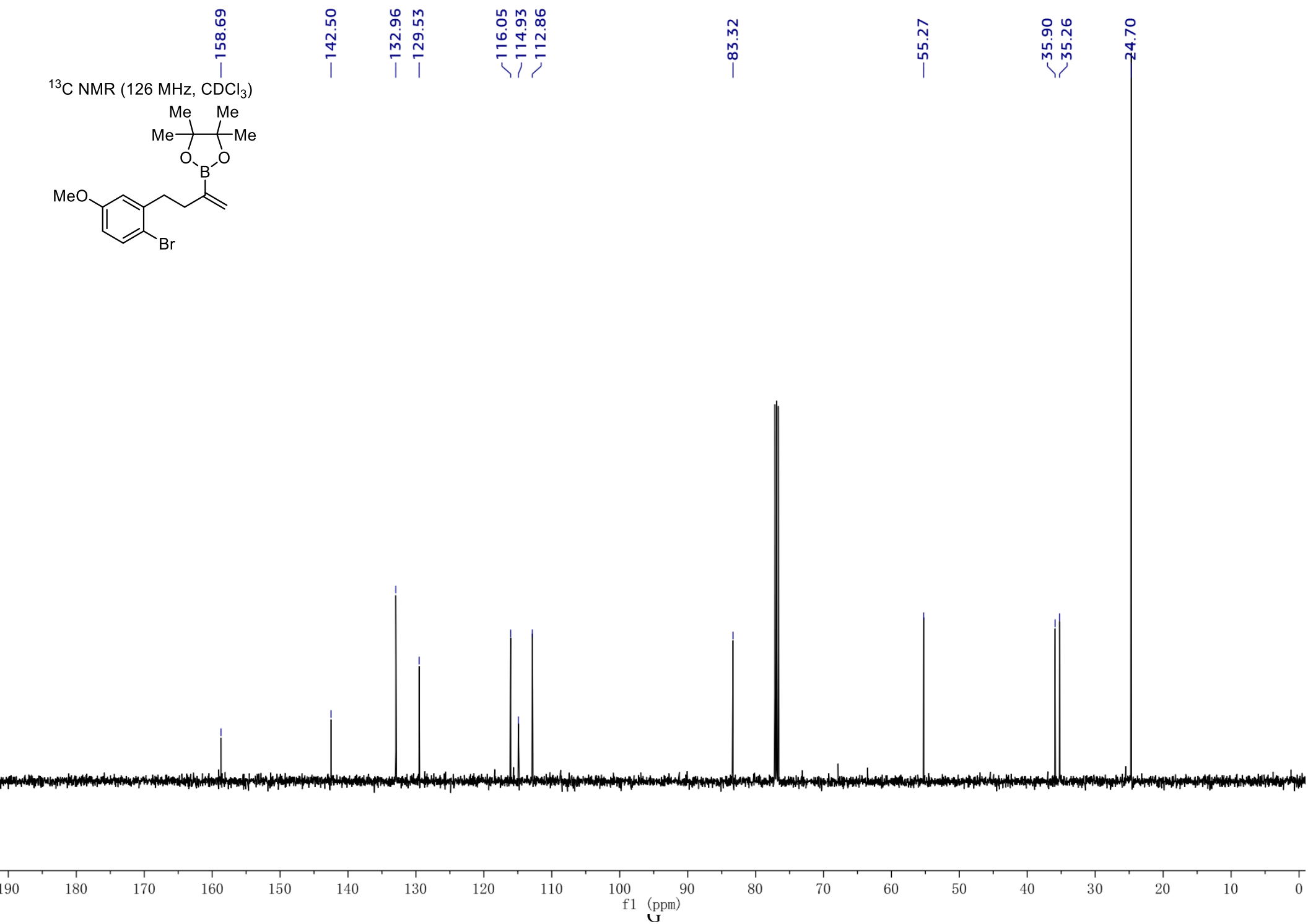
G

E


7.39
7.38
6.78
6.77
6.61
6.61
6.60
6.59
5.81
5.80
5.63
3.78
3.77
3.77
3.76
2.84
2.82
2.82
2.81
2.80
2.46
2.44
2.43
1.28
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
Br
1.03
1.04
0.98
1.01
1.00
3.02
2.00
2.00
12.06
f1 (ppm)

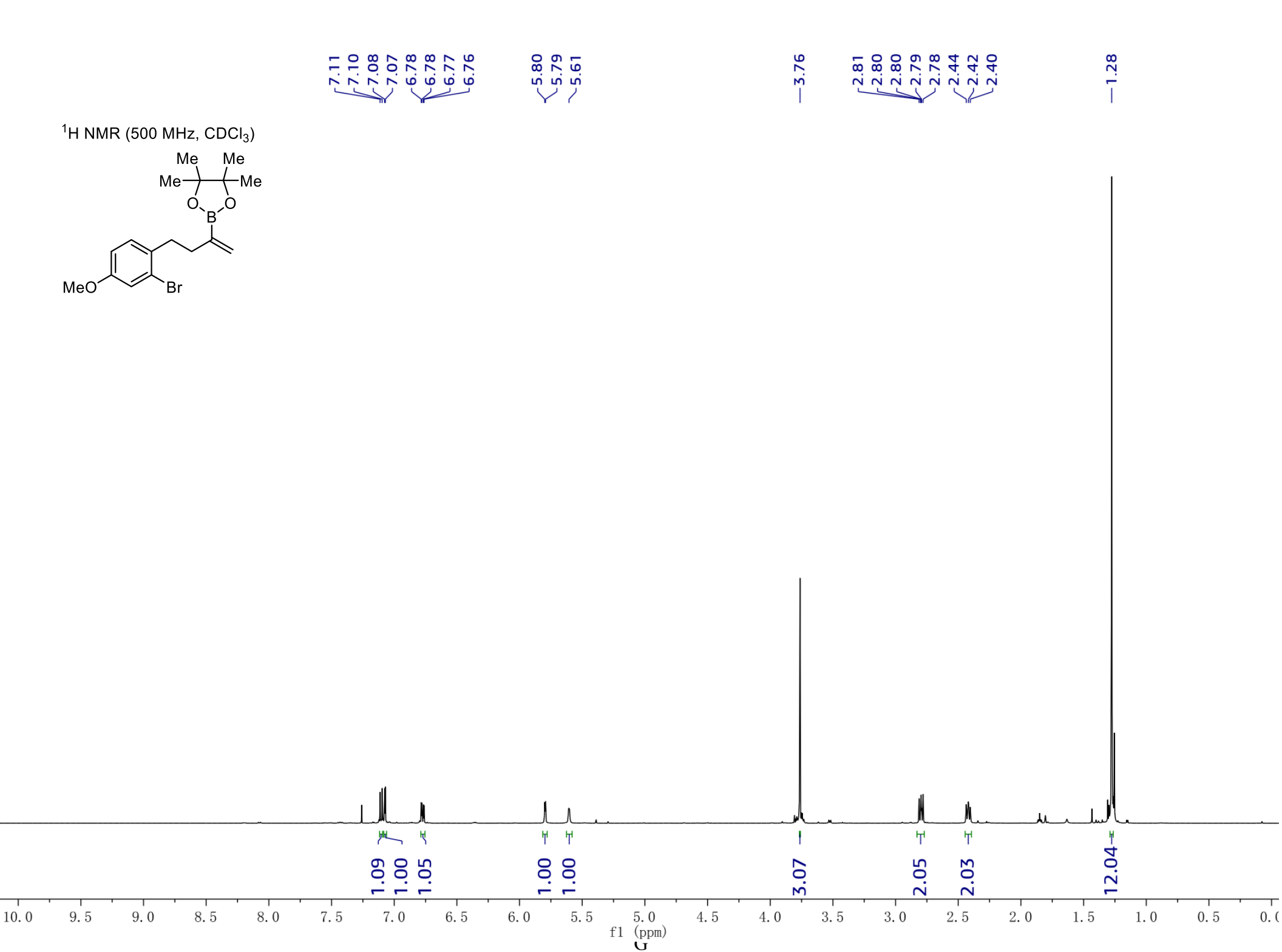
G

E


158.69
142.50
132.96
129.53
116.05
114.93
112.86
83.32
55.27
35.90
35.26
24.70
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

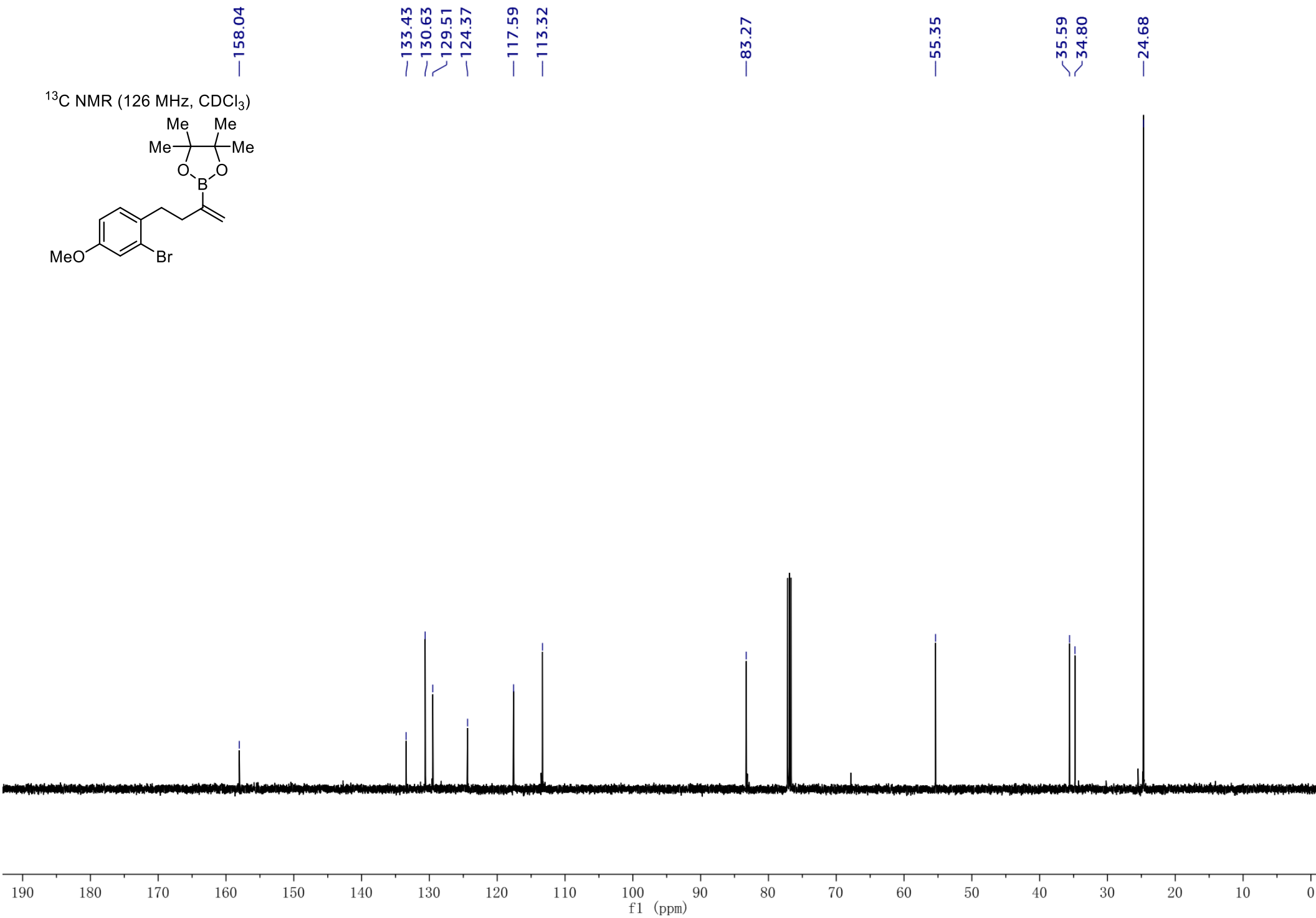
G

E


7.11
7.10
7.08
7.07
6.78
6.78
6.77
6.76
5.80
5.79
5.61
3.76
2.81
2.80
2.80
2.79
2.78
2.44
2.42
2.40
1.28
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
Br
1.09
1.00
1.05
1.00
1.00
3.07
2.05
2.03
12.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

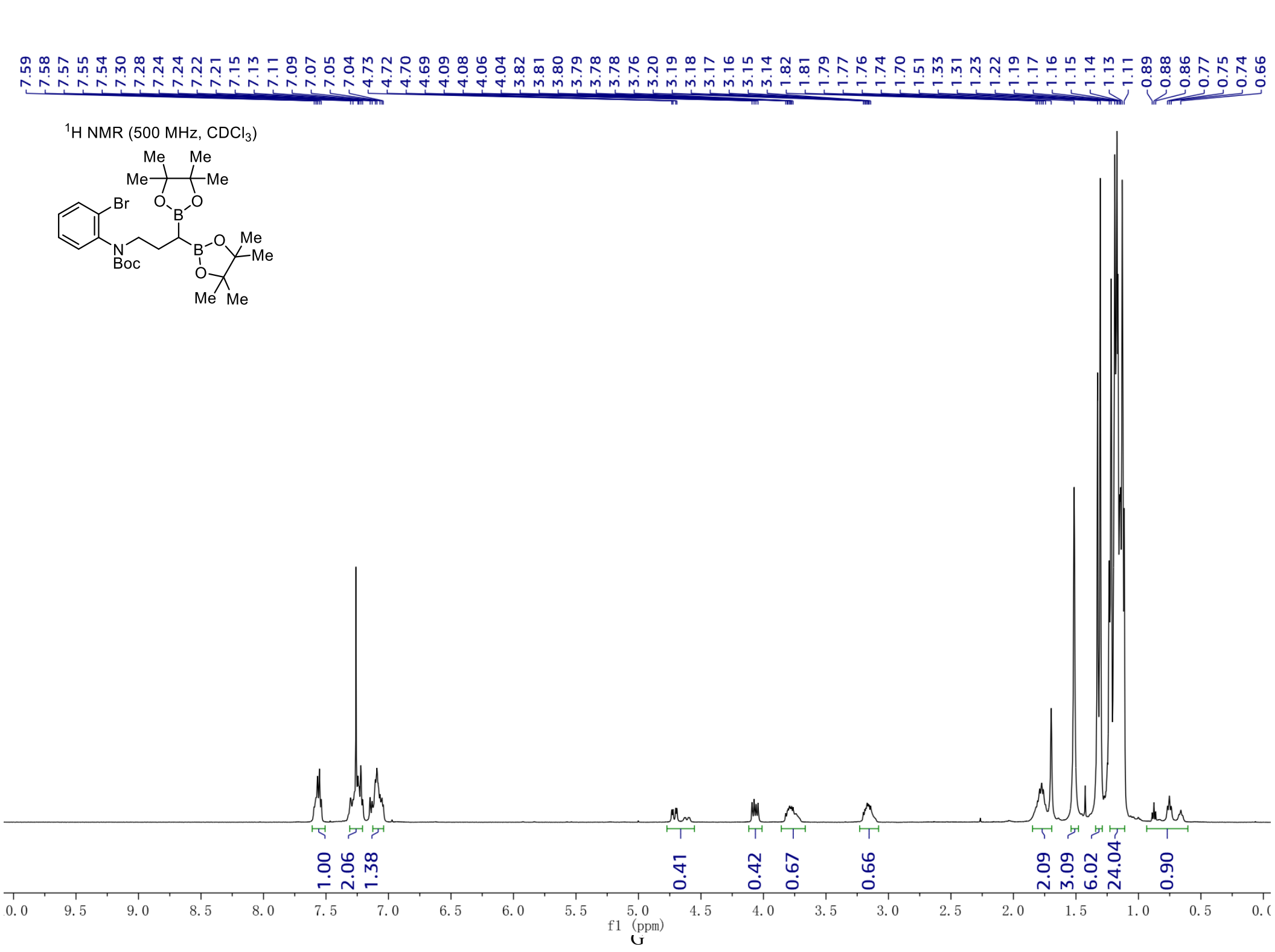
G

E


158.04
133.43
130.63
129.51
124.37
117.59
113.32
83.27
55.35
35.59
34.80
24.68
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

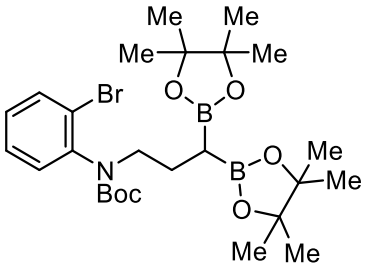
E


7.59 7.58 7.57 7.55 7.54 7.30 7.28 7.24 7.24 7.22 7.21 7.15 7.13 7.11 7.09 7.07 7.05 7.04 4.73 4.72 4.70 4.69 4.09 4.08 4.06 4.04 3.82 3.81 3.80 3.79 3.78 3.78 3.76 3.20 3.19 3.18 3.17 3.16 3.15 3.14 1.82 1.81 1.79 1.77 1.76 1.74 1.70 1.51 1.33 1.31 1.23 1.22 1.19 1.17 1.16 1.15 1.14 1.13 1.11 0.89 0.88 0.86 0.77 0.75 0.74 0.66
1H NMR (500 MHz, CDCl3)
Me Me Me Me Br O O B N Boc B O Me Me O Me Me
1.00 2.06 1.38 0.41 0.42 0.67 0.66 2.09 3.09 6.02 24.04 0.90
f1 (ppm)

G

E

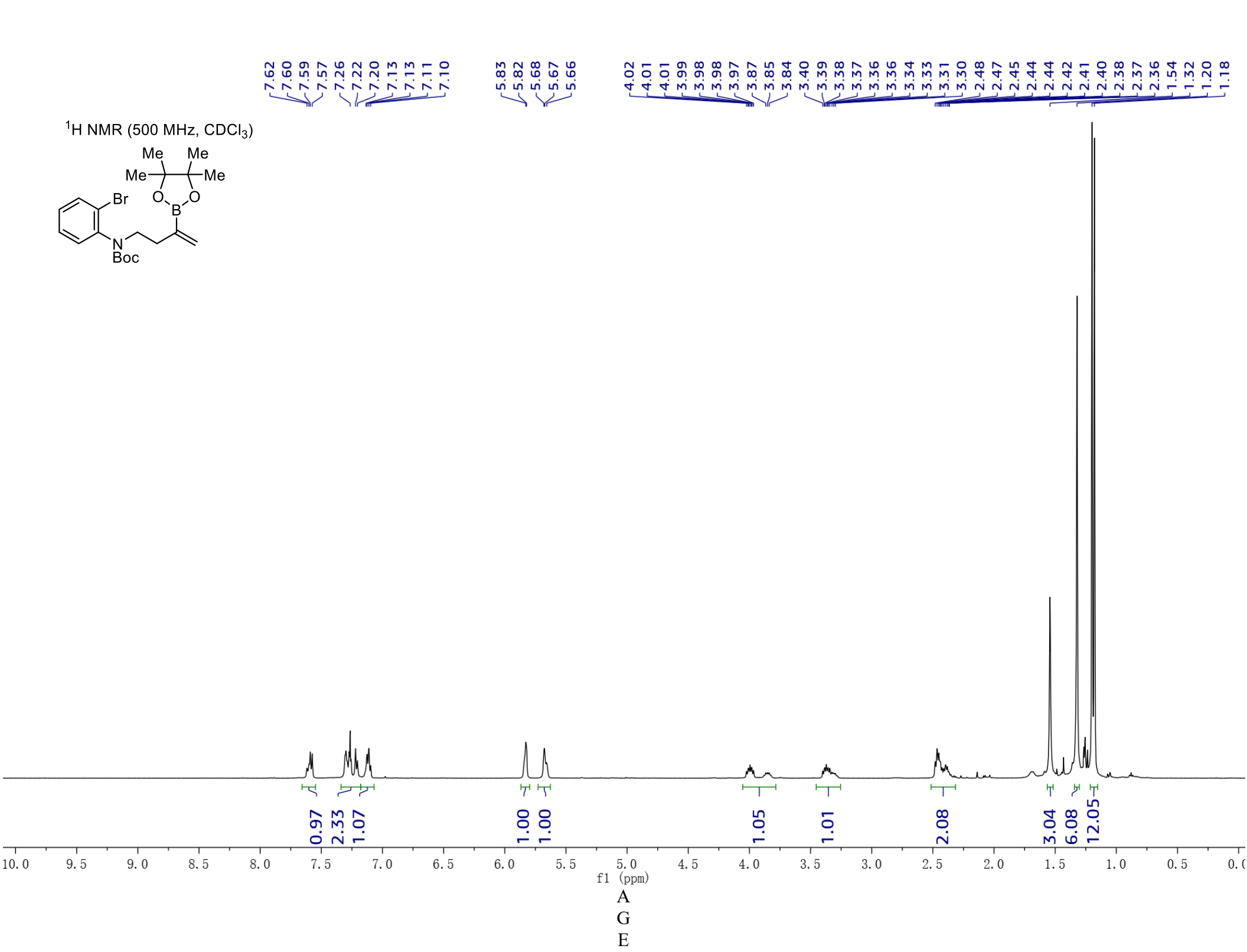
$^{13}$C NMR (126 MHz, $CDCl_3$)



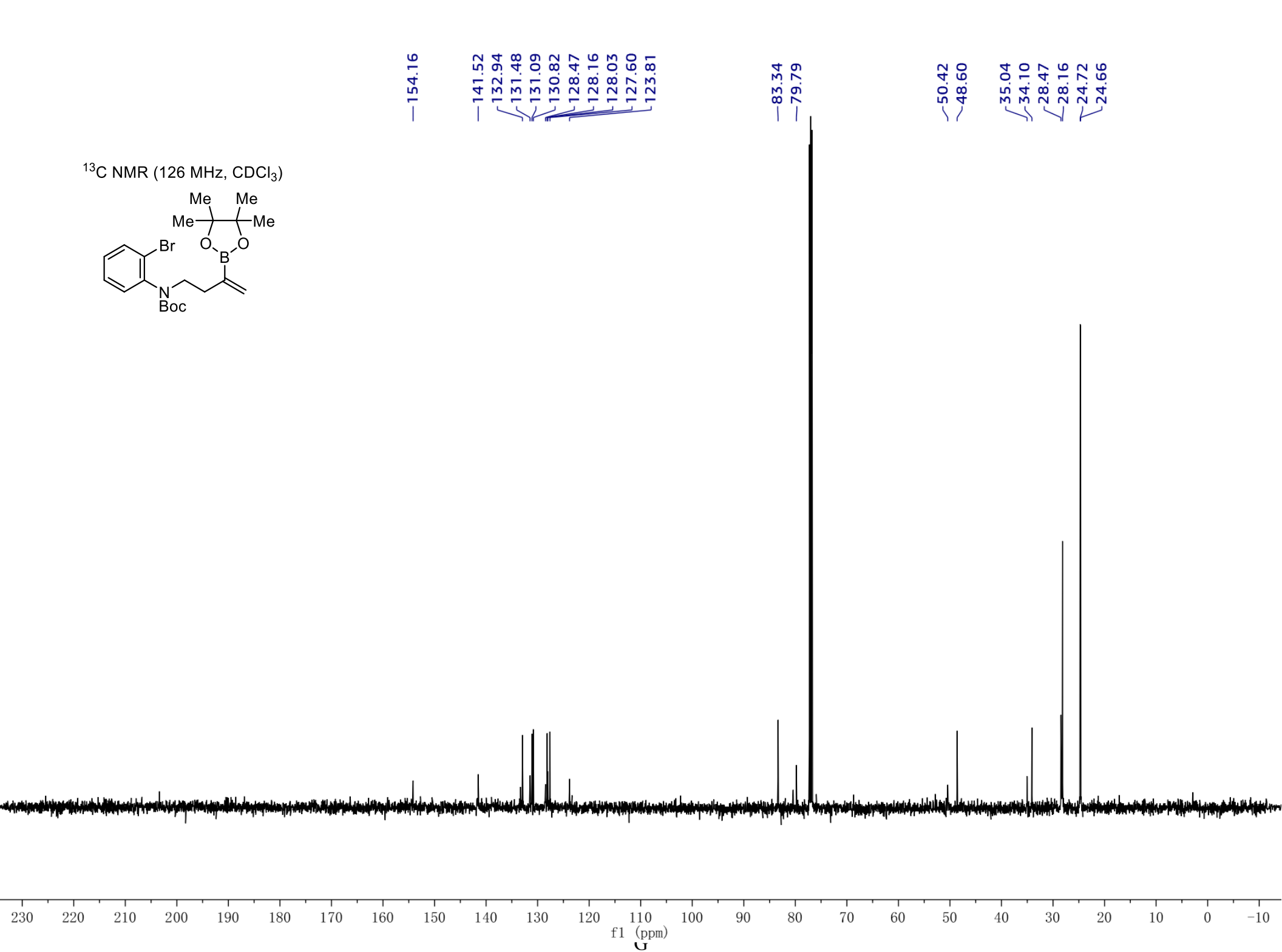

156.89
154.03
141.42
140.82
133.20
133.18
133.10
132.79
132.67
132.65
131.23
131.07
130.88
130.84
130.70
128.36
128.26
128.13
128.05
128.00
127.98
127.74
127.70
127.62
123.75
123.63
123.60
82.99
82.94
82.91
79.99
79.57
52.09
51.63
50.76
28.40
28.33
28.08
24.76
24.71
24.61
24.50
24.31




E

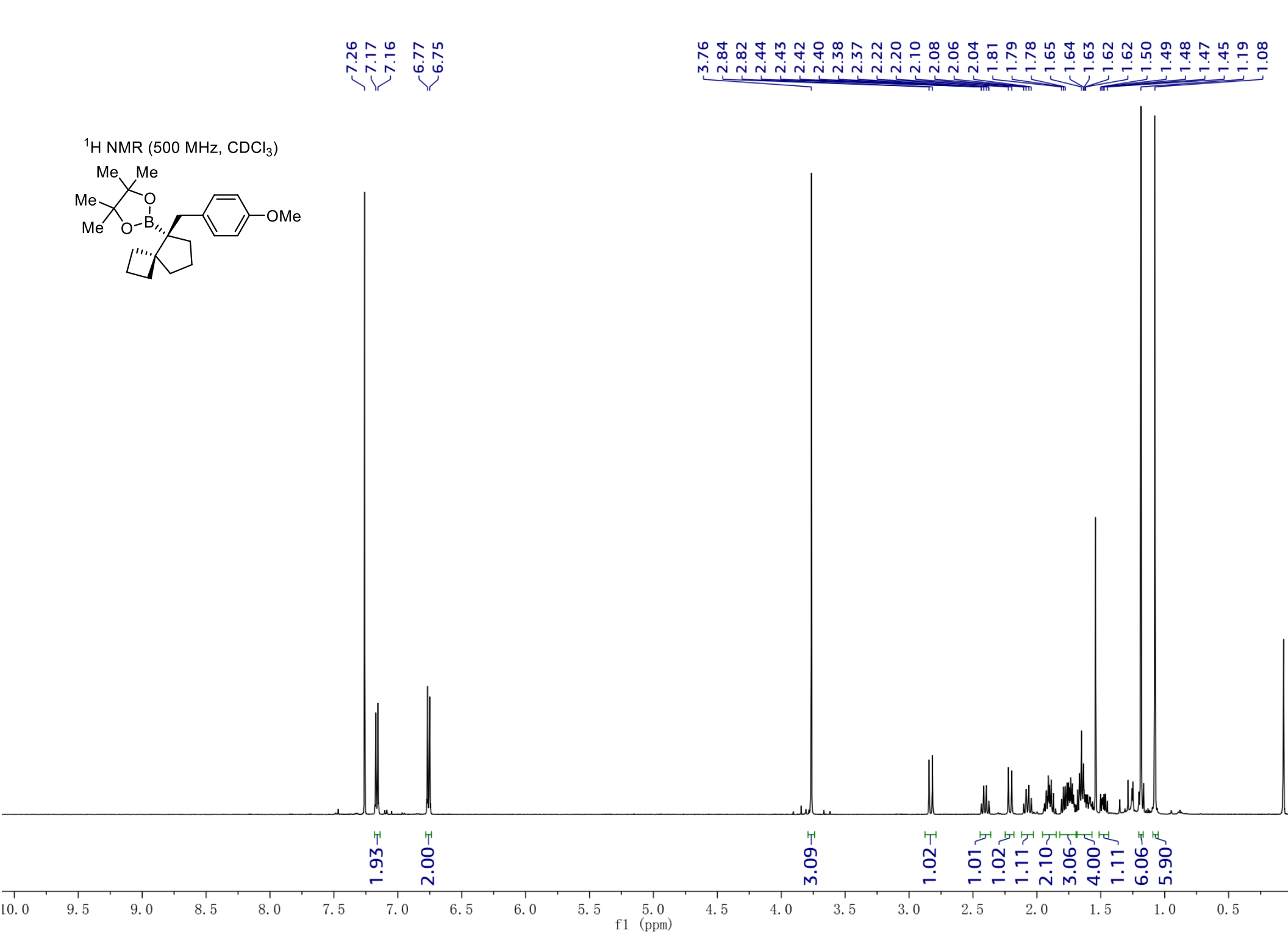

7.62
7.60
7.59
7.57
7.26
7.22
7.20
7.13
7.13
7.11
7.10
5.83
5.82
5.68
5.67
5.66
4.02
4.01
4.01
3.99
3.98
3.98
3.97
3.87
3.85
3.84
3.40
3.39
3.38
3.37
3.36
3.36
3.34
3.33
3.31
3.30
2.48
2.47
2.45
2.44
2.44
2.42
2.41
2.40
2.38
2.37
2.36
1.54
1.32
1.20
1.18
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
Br
O
O
B
N
Boc
0.97
2.33
1.07
1.00
1.00
1.05
1.01
2.08
3.04
6.08
12.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

A
G
E


154.16
141.52
132.94
131.48
131.09
130.82
128.47
128.16
128.03
127.60
123.81
83.34
79.79
50.42
48.60
35.04
34.10
28.47
28.16
24.72
24.66
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
Br
O
B
O
N
Boc
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

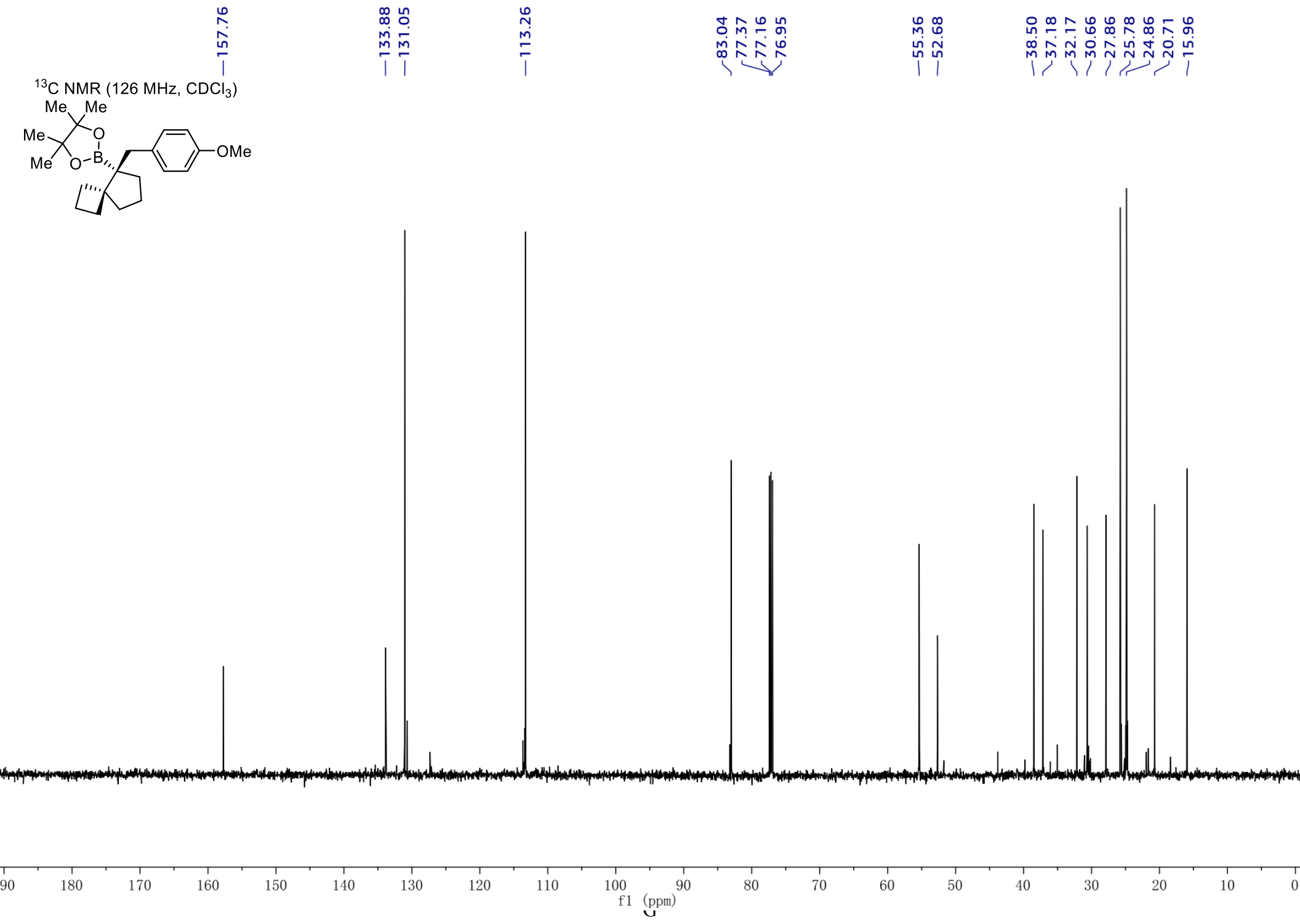
G

E


7.26
7.17
7.16
6.77
6.75
3.76
2.84
2.82
2.44
2.43
2.42
2.40
2.38
2.37
2.22
2.20
2.10
2.08
2.06
2.04
1.81
1.79
1.78
1.65
1.64
1.63
1.62
1.62
1.50
1.49
1.48
1.47
1.45
1.19
1.08
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
1.93
2.00
3.09
1.02
1.01
1.02
1.11
2.10
3.06
4.00
1.11
6.06
5.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

G

E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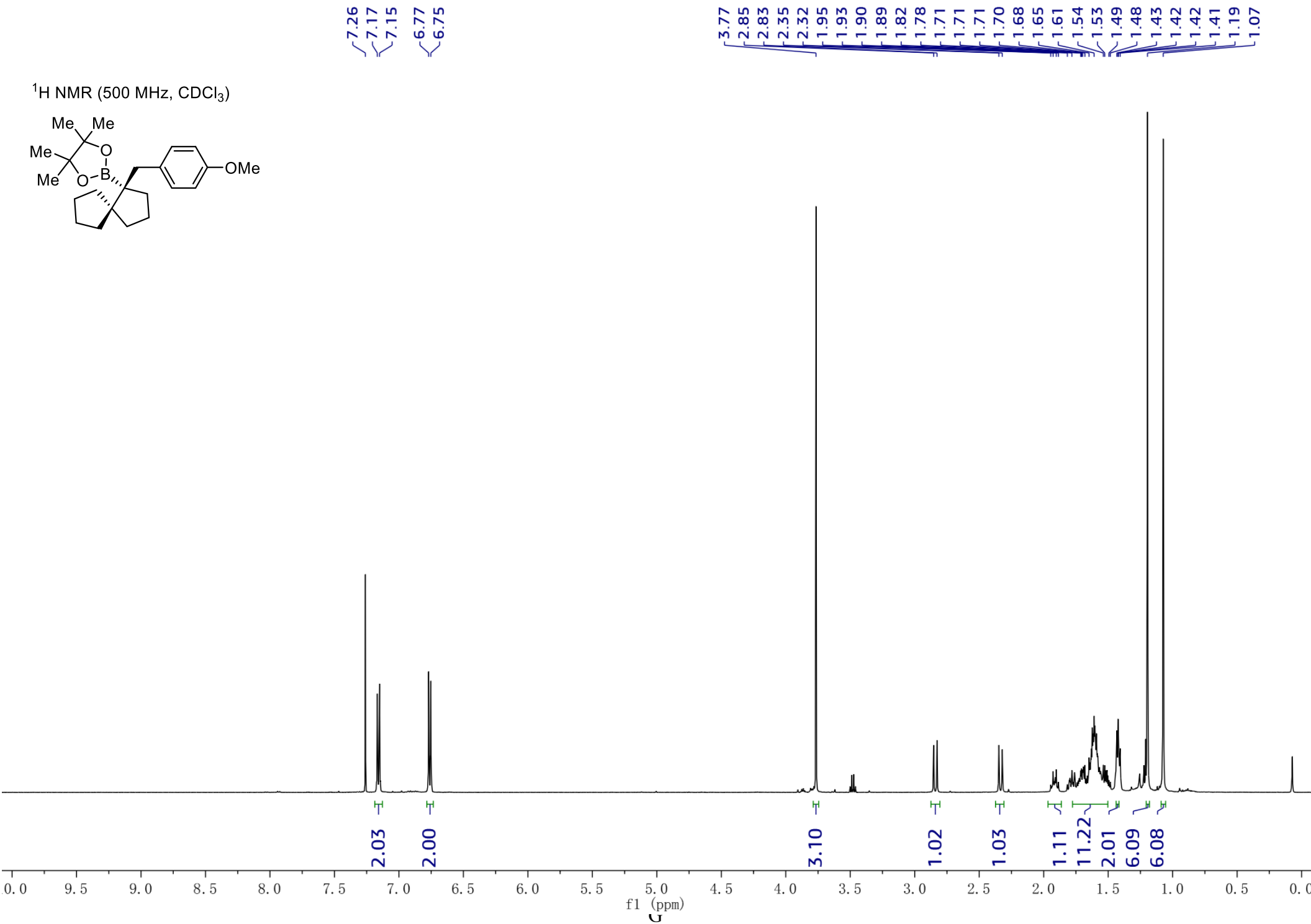
133.88
131.05
113.26
83.04
77.37
77.16
76.95
55.36
52.68
38.50
37.18
32.17
30.66
27.86
25.78
24.86
20.71
15.96
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
f1 (ppm)

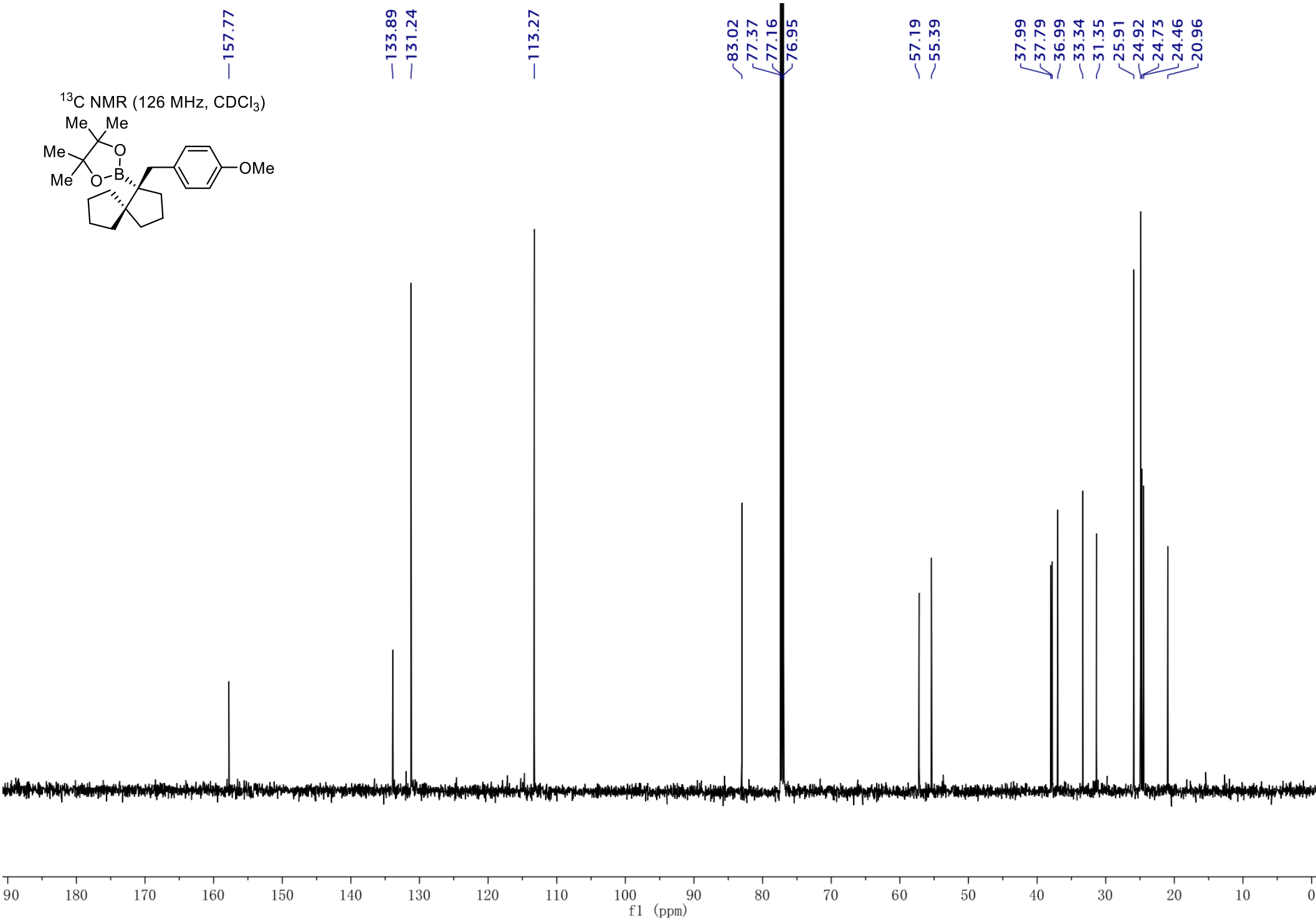
G

E

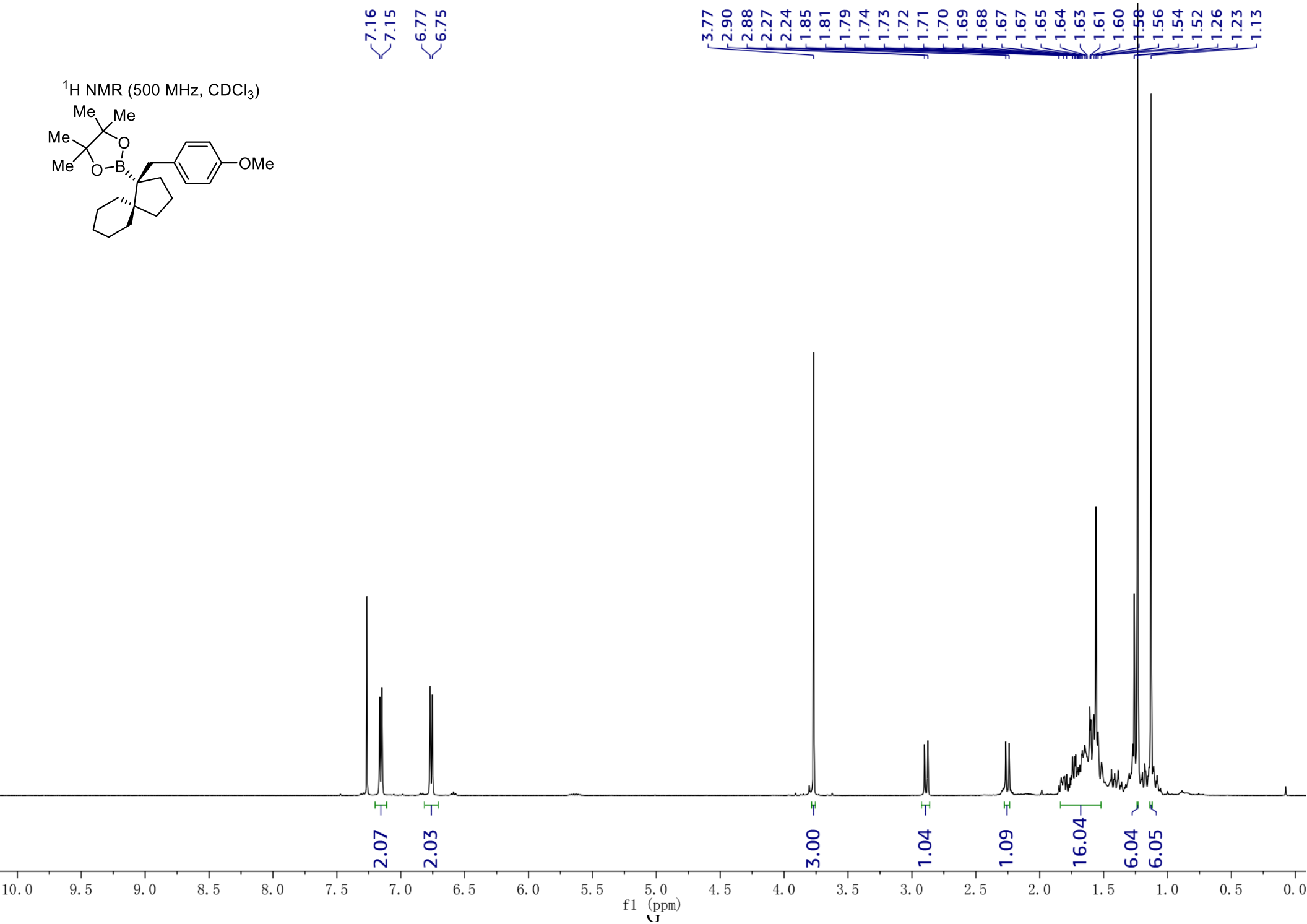

7.26
7.17
7.15
6.77
6.75
3.77
2.85
2.83
2.35
2.32
1.95
1.93
1.90
1.89
1.82
1.78
1.71
1.71
1.71
1.70
1.68
1.65
1.61
1.54
1.53
1.49
1.48
1.43
1.42
1.42
1.41
1.19
1.07
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
2.03
2.00
3.10
1.02
1.03
1.11
11.22
2.01
6.09
6.08
f1 (ppm)

G

E

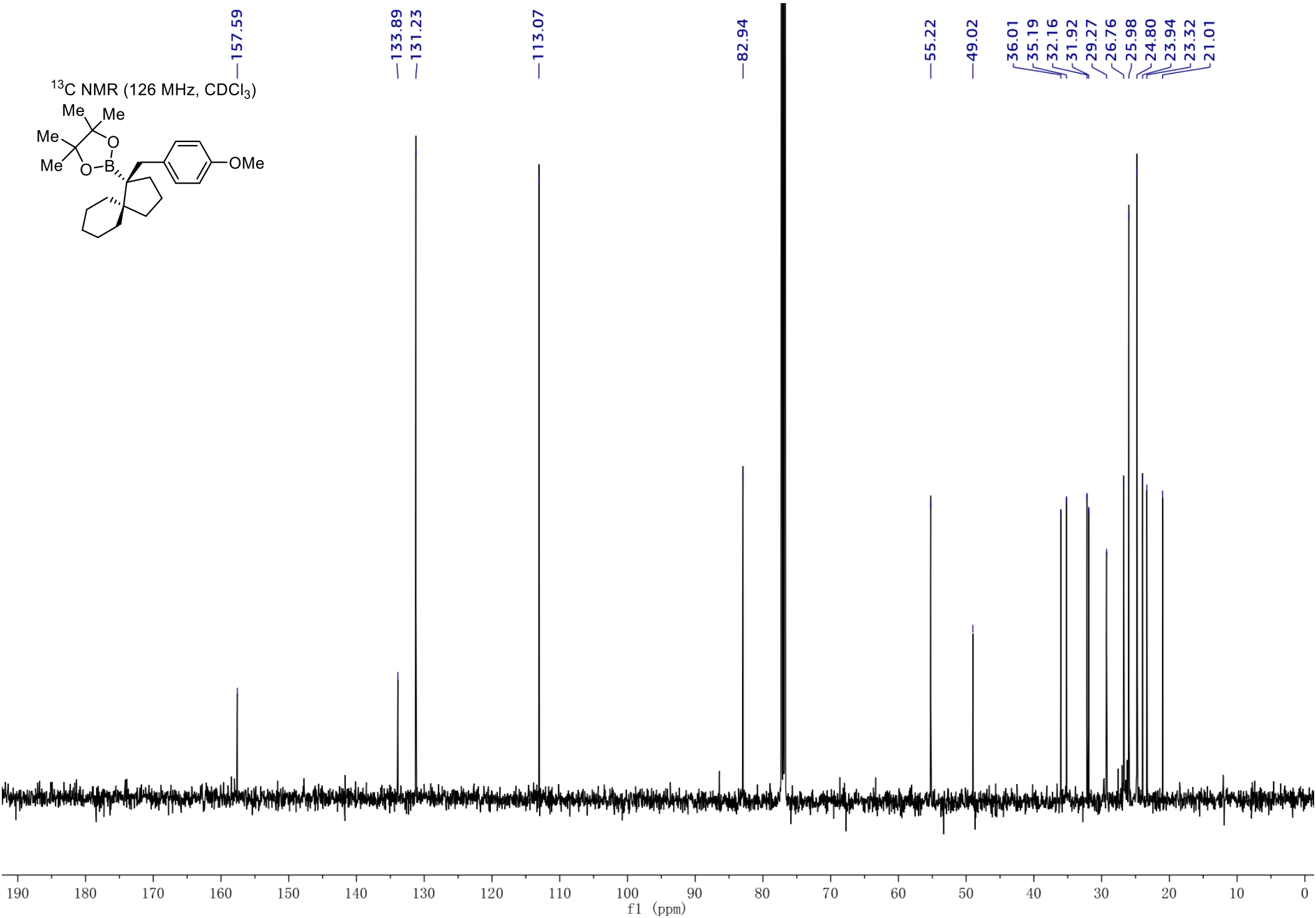

157.77
133.89
131.24
113.27
83.02
77.37
77.16
76.95
57.19
55.39
37.99
37.79
36.99
33.34
31.35
25.91
24.92
24.73
24.46
20.96
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
OMe
7.16
7.15
6.77
6.75
3.77
2.90
2.88
2.27
2.24
1.85
1.81
1.79
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.67
1.67
1.65
1.64
1.63
1.61
1.60
1.58
1.56
1.54
1.52
1.26
1.23
1.13
2.07
2.03
3.00
1.04
1.09
16.04
6.04
6.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

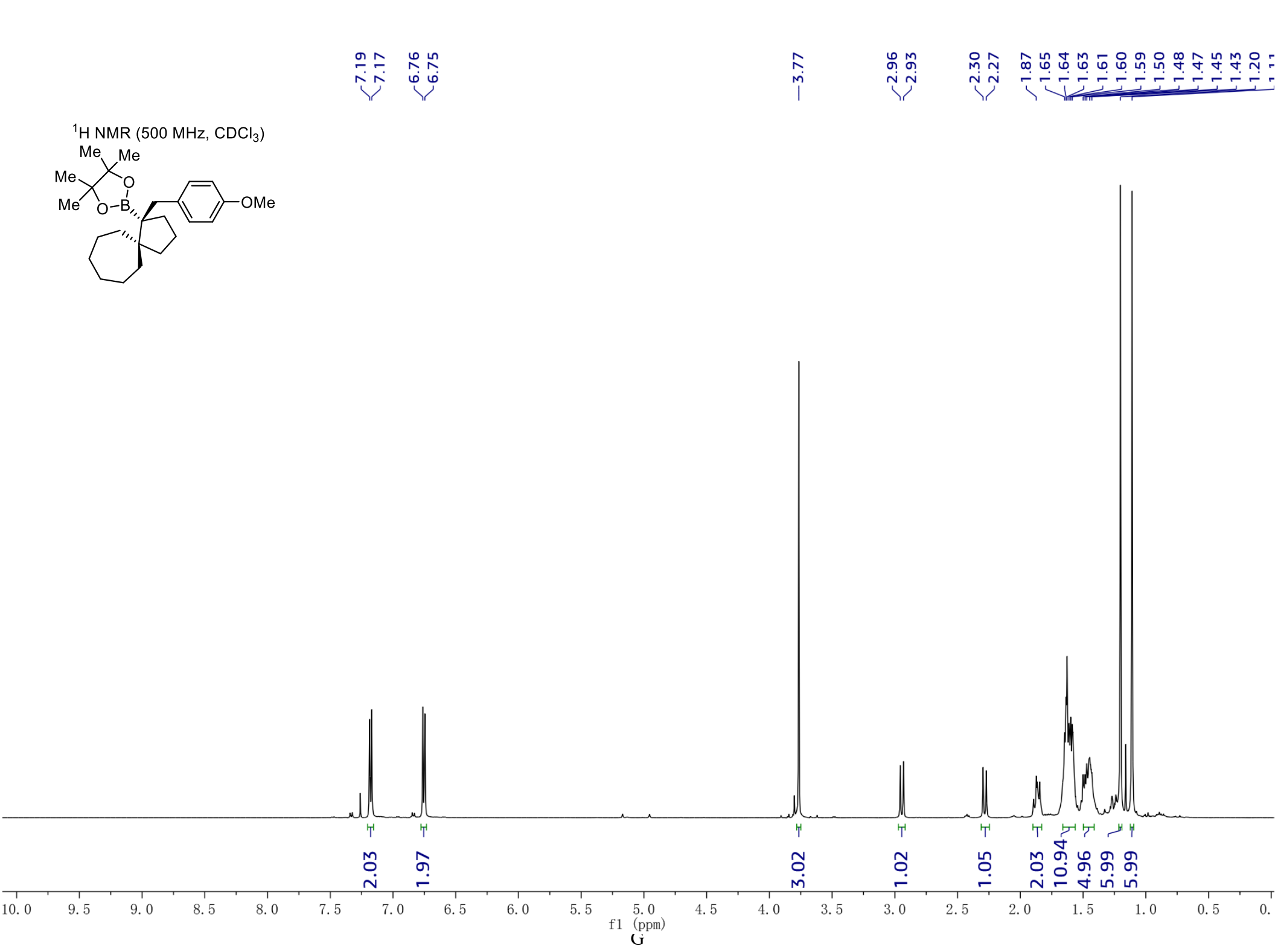
G

E


157.59
133.89
131.23
113.07
82.94
55.22
49.02
36.01
35.19
32.16
31.92
29.27
26.76
25.98
24.80
23.94
23.32
21.01
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

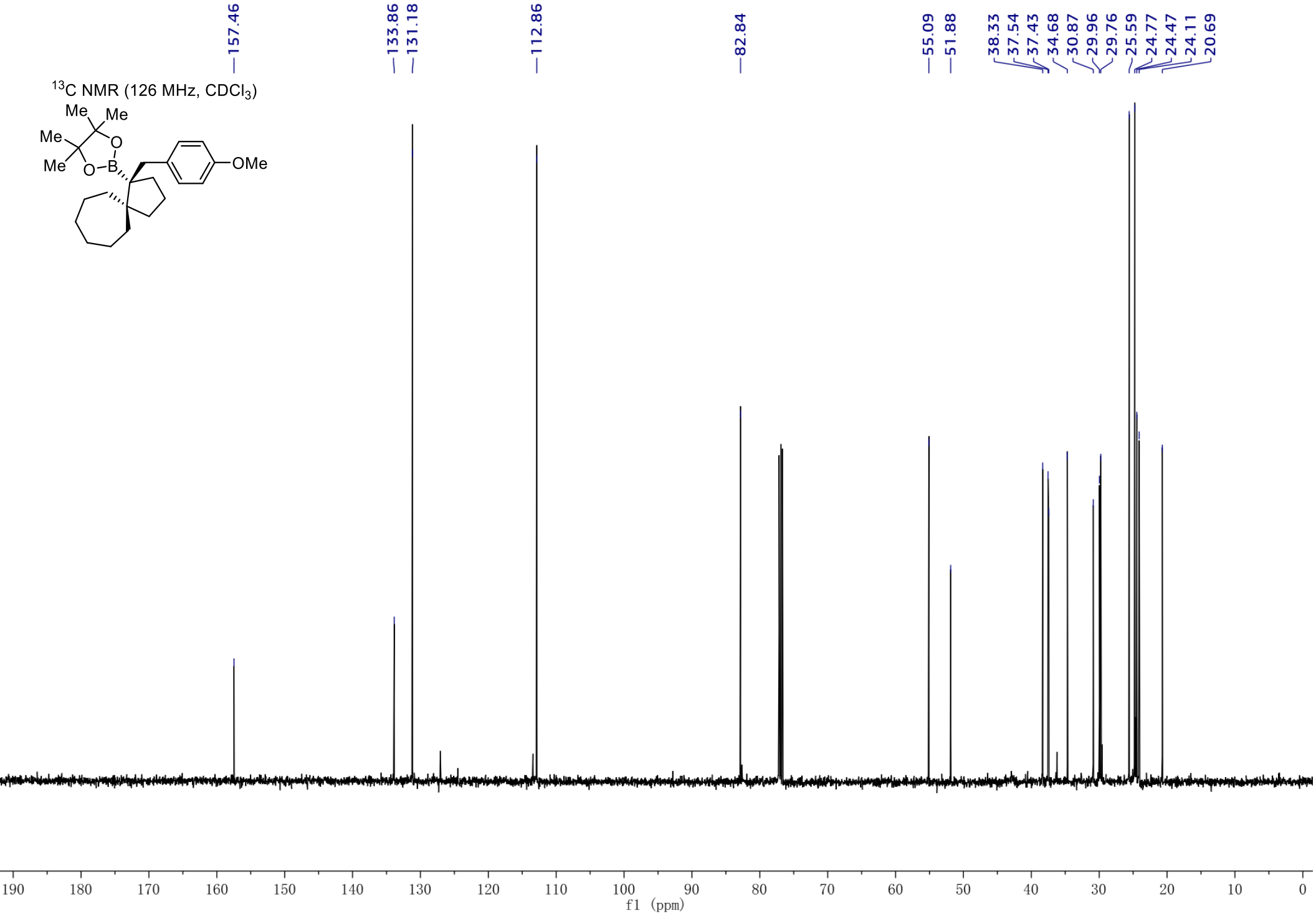
G

E

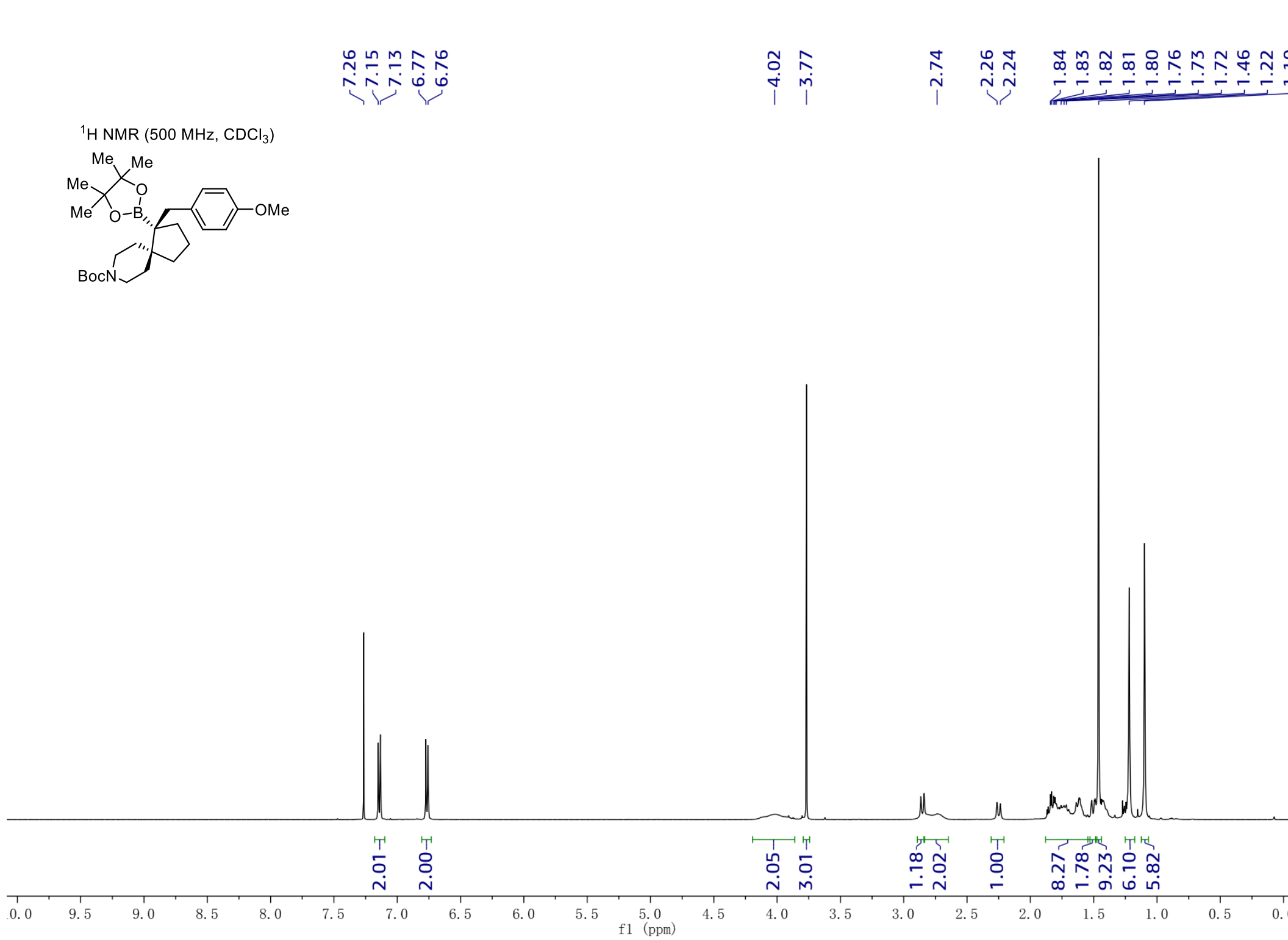

7.19
7.17
6.76
6.75
3.77
2.96
2.93
2.30
2.27
1.87
1.65
1.64
1.63
1.61
1.60
1.59
1.50
1.48
1.47
1.45
1.43
1.20
1H NMR (500 MHz, CDCl3)
Me
Me
Me
O
Me
O
B
OMe
2.03
1.97
3.02
1.02
1.05
2.03
10.94
4.96
5.99
5.99
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

G

E

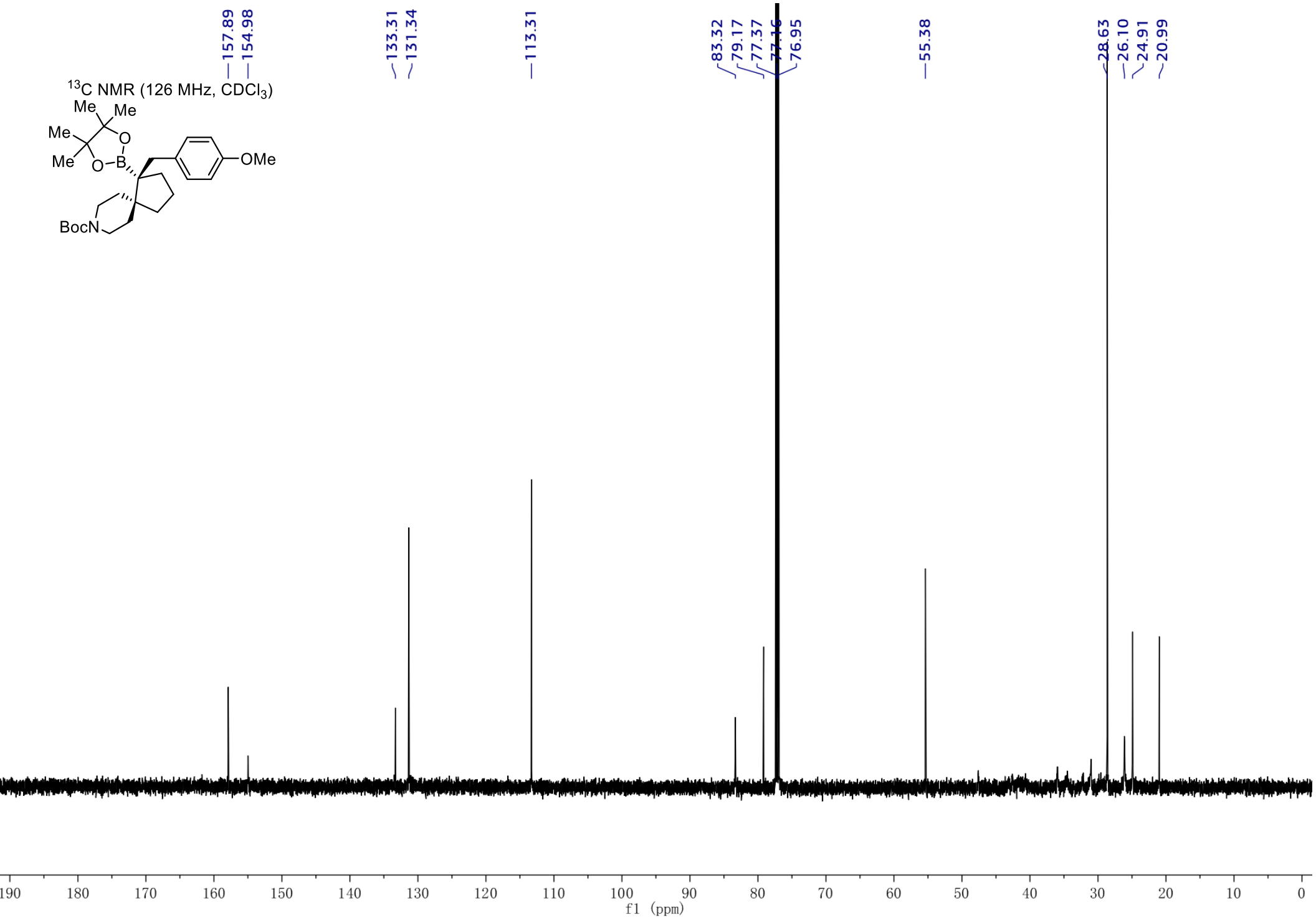

157.46
133.86
131.18
112.86
82.84
55.09
51.88
38.33
37.54
37.43
34.68
30.87
29.96
29.76
25.59
24.77
24.47
24.11
20.69
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.26
7.15
7.13
6.77
6.76
4.02
3.77
2.74
2.26
2.24
1.84
1.83
1.82
1.81
1.80
1.76
1.73
1.72
1.46
1.22
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
OMe
BocN
2.01
2.00
2.05
3.01
1.18
2.02
1.00
8.27
1.78
9.23
6.10
5.82
f1 (ppm)

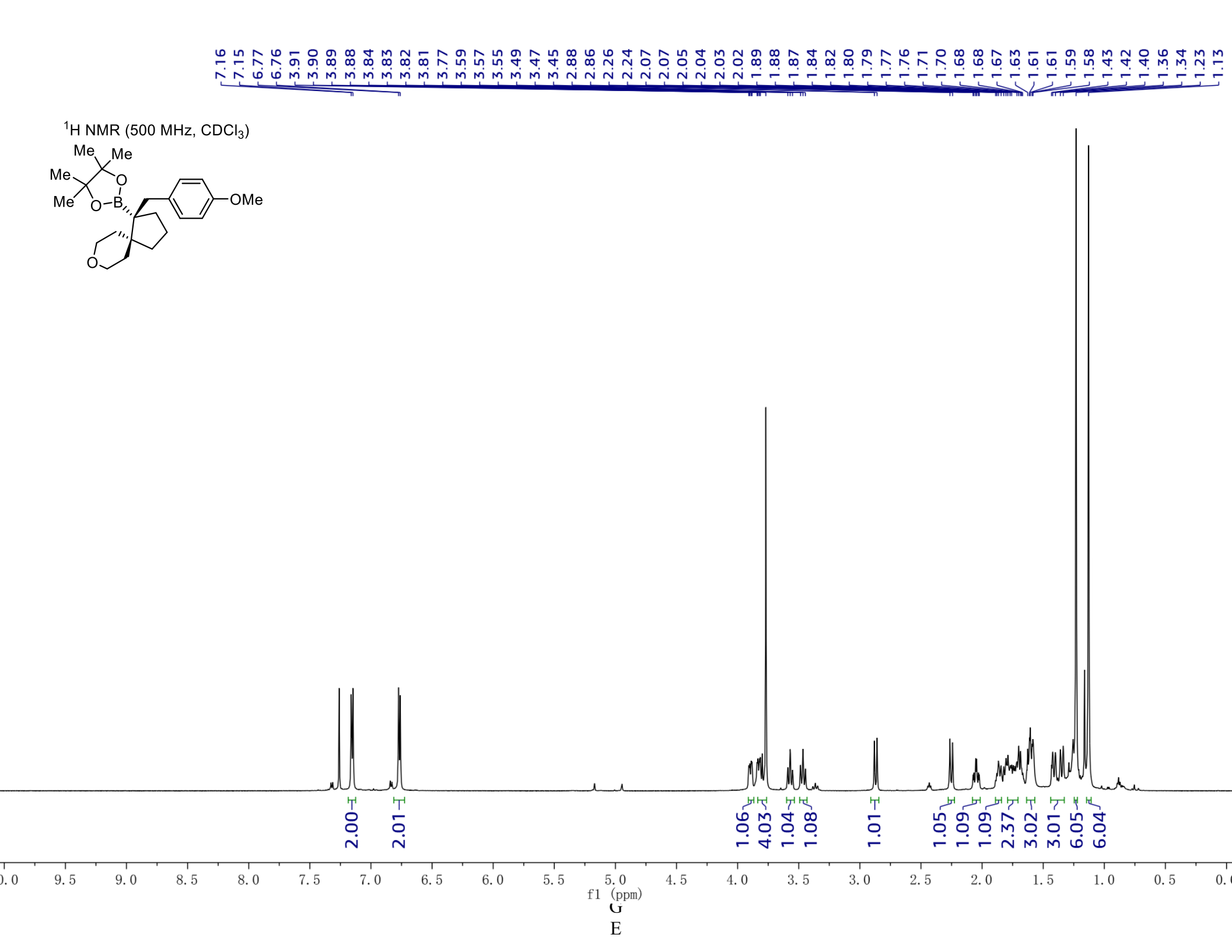
G

E


157.89
154.98
133.31
131.34
113.31
83.32
79.17
77.37
77.16
76.95
55.38
28.63
26.10
24.91
20.99
$^{13}$C NMR (126 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
OMe
BocN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

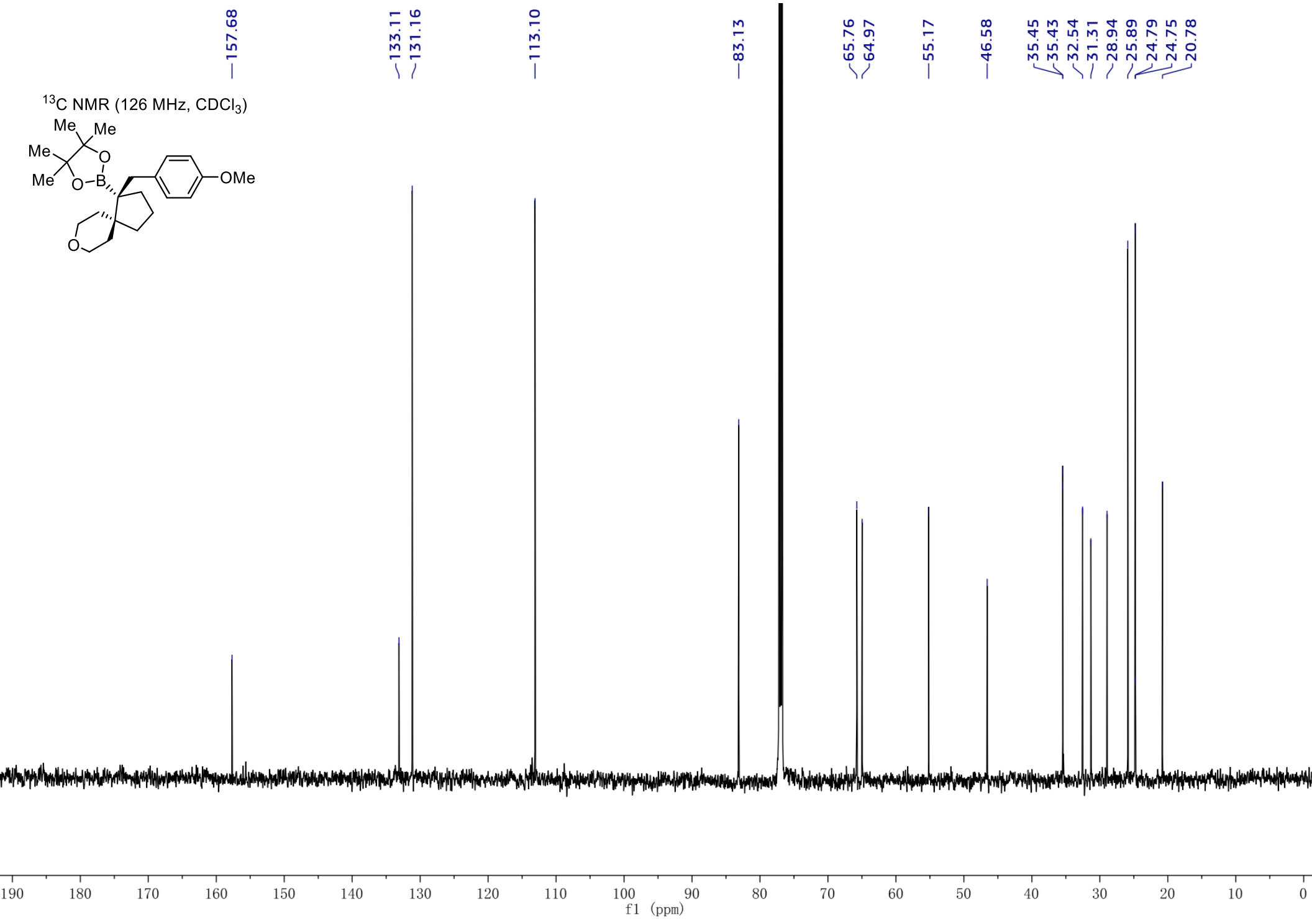
G

E

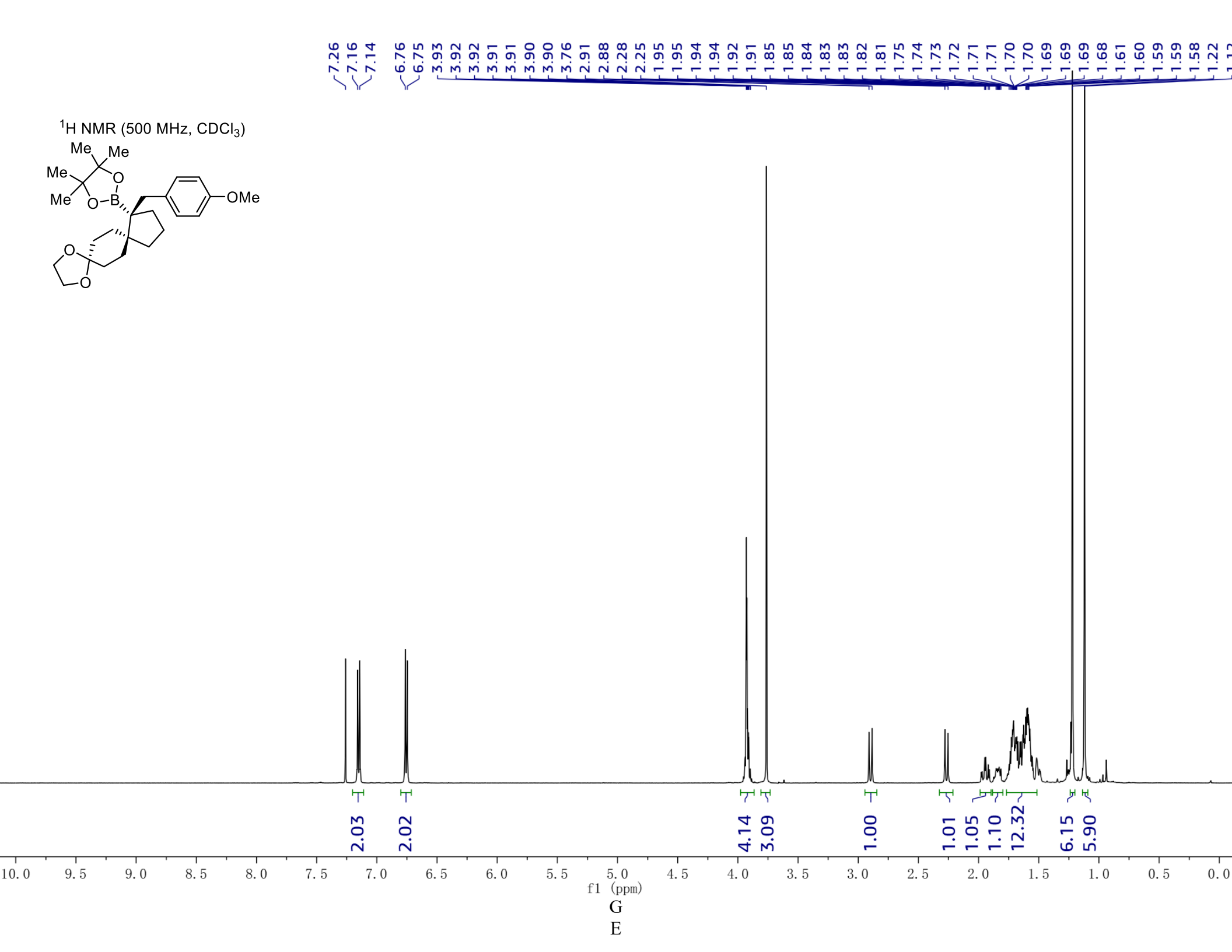

7.16 7.15 6.77 6.76 3.91 3.90 3.89 3.88 3.84 3.83 3.82 3.81 3.77 3.59 3.57 3.55 3.49 3.47 3.45 2.88 2.86 2.26 2.24 2.07 2.07 2.05 2.04 2.03 2.02 1.89 1.88 1.87 1.84 1.82 1.80 1.79 1.77 1.76 1.71 1.70 1.68 1.68 1.67 1.63 1.61 1.61 1.59 1.58 1.43 1.42 1.40 1.36 1.34 1.23 1.13
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
O
OMe
2.00
2.01
1.06
4.03
1.04
1.08
1.01
1.05
1.09
1.09
2.37
3.02
3.01
6.05
6.04
f1 (ppm)

G

E

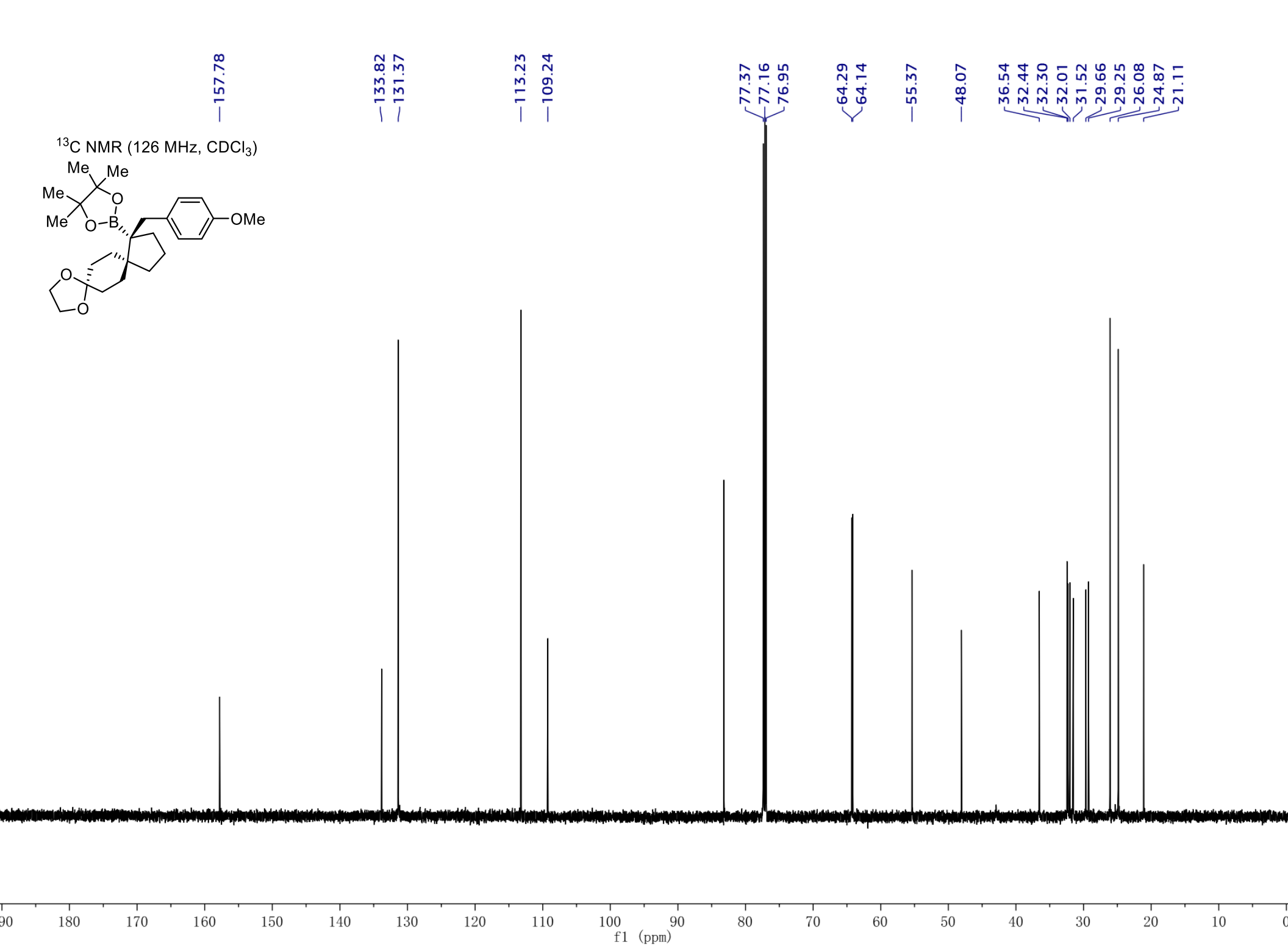

157.68
133.11
131.16
113.10
83.13
65.76
64.97
55.17
46.58
35.45
35.43
32.54
31.31
28.94
25.89
24.79
24.75
20.78
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
OMe
O
O
7.26
7.16
7.14
6.76
6.75
3.93
3.92
3.92
3.91
3.91
3.90
3.90
3.76
2.91
2.88
2.28
2.25
1.95
1.95
1.94
1.94
1.92
1.91
1.85
1.85
1.84
1.83
1.83
1.82
1.81
1.75
1.74
1.73
1.72
1.71
1.71
1.70
1.70
1.69
1.69
1.69
1.68
1.61
1.60
1.59
1.59
1.58
1.22
2.03
2.02
4.14
3.09
1.00
1.01
1.05
1.10
12.32
6.15
5.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E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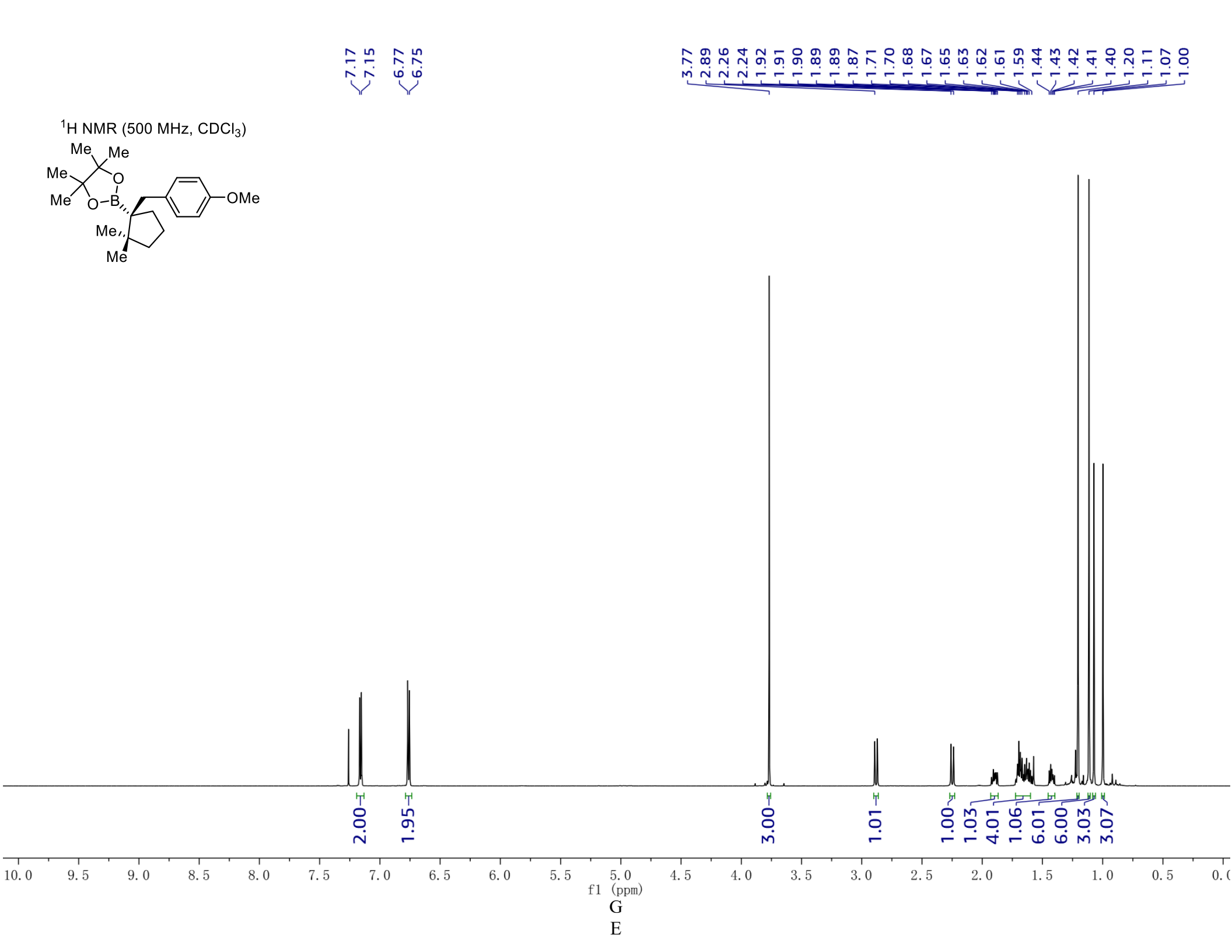
133.82
131.37
113.23
109.24
77.37
77.16
76.95
64.29
64.14
55.37
48.07
36.54
32.44
32.30
32.01
31.52
29.66
29.25
26.08
24.87
21.11
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
O
O
f1 (ppm)

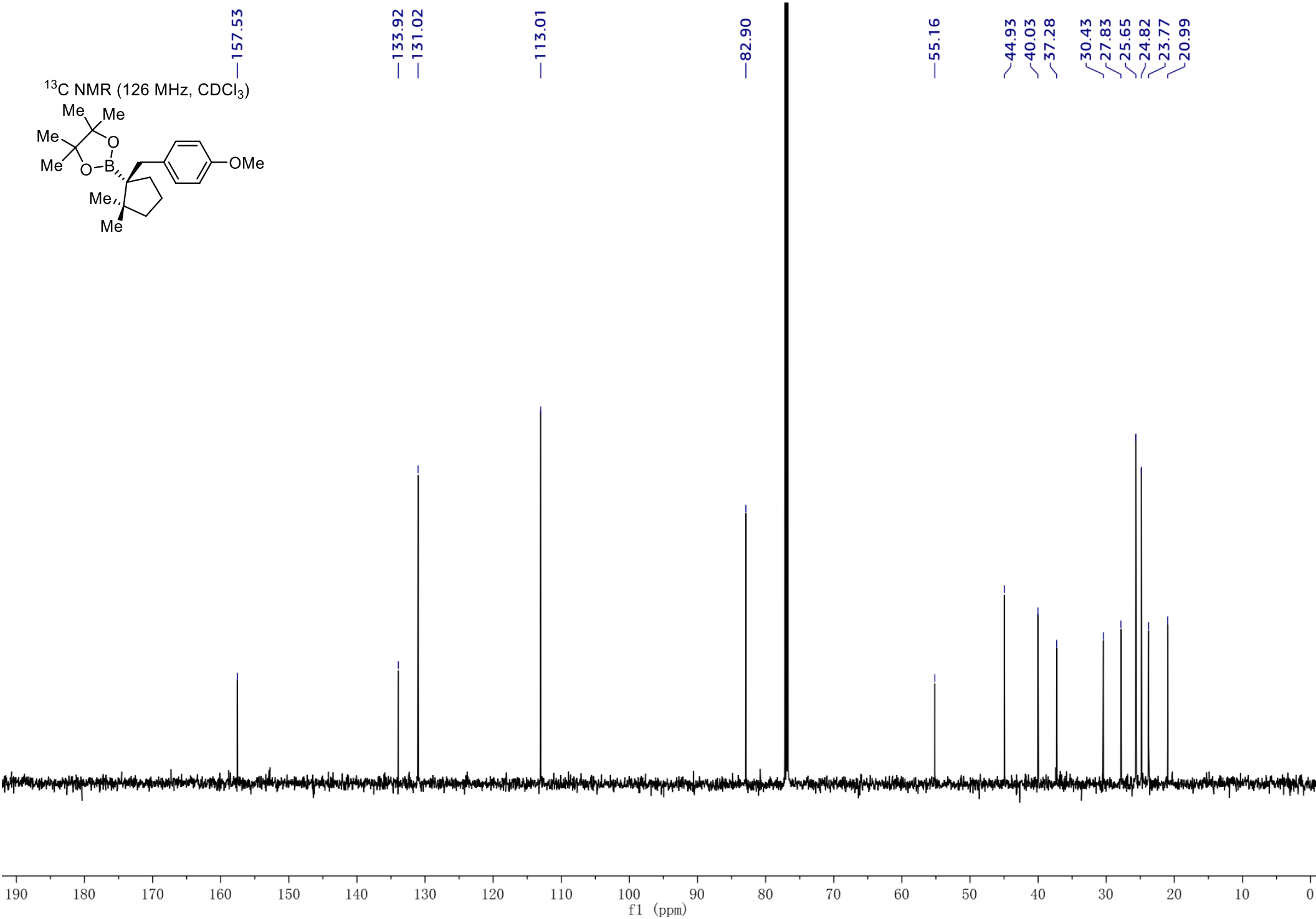
G

E


7.17
7.15
6.77
6.75
3.77
2.89
2.26
2.24
1.92
1.91
1.90
1.89
1.89
1.87
1.71
1.70
1.68
1.67
1.65
1.63
1.62
1.61
1.59
1.44
1.43
1.42
1.41
1.40
1.20
1.11
1.07
1.00
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
O
Me
O–B
OMe
Me
Me
2.00
1.95
3.00
1.01
1.00
1.03
4.01
1.06
6.01
6.00
3.03
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

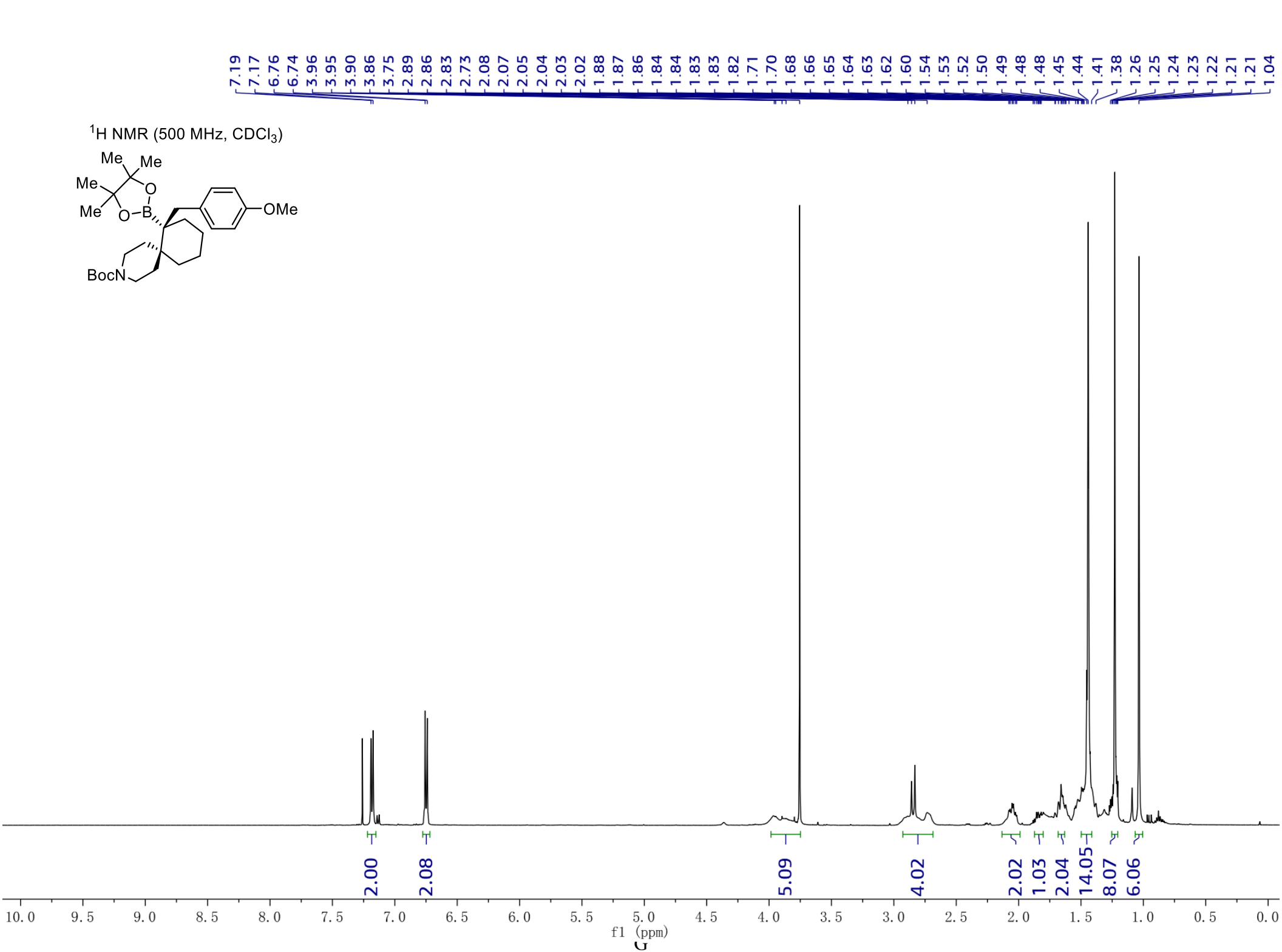
G

E


157.53
133.92
131.02
113.01
82.90
55.16
44.93
40.03
37.28
30.43
27.83
25.65
24.82
23.77
20.99
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
Me
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

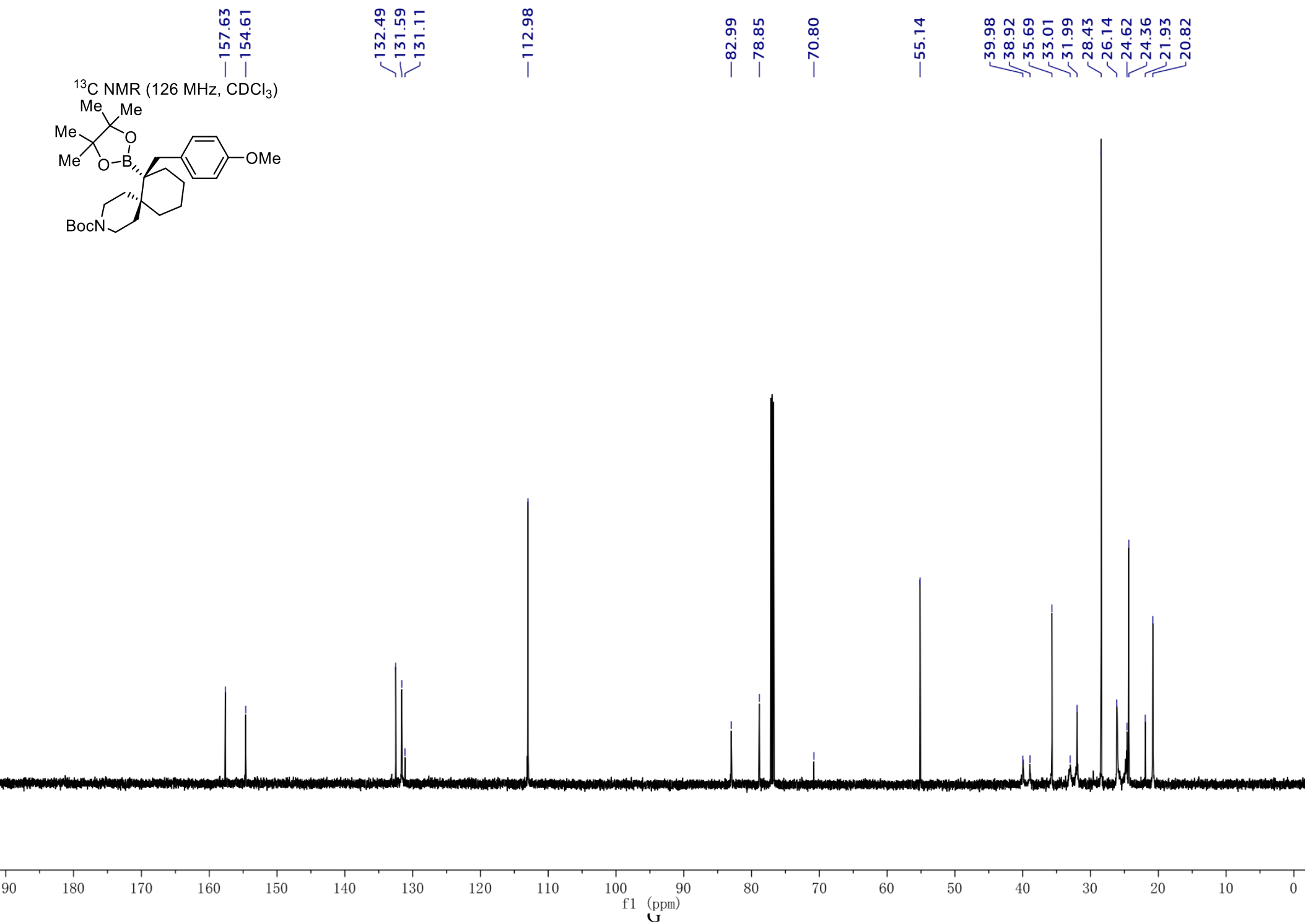
G

E


7.19 7.17 6.76 6.74 3.96 3.95 3.90 3.86 3.75 2.89 2.86 2.83 2.73 2.08 2.07 2.05 2.04 2.03 2.02 1.88 1.87 1.86 1.84 1.84 1.83 1.83 1.82 1.71 1.70 1.68 1.66 1.65 1.64 1.63 1.62 1.60 1.54 1.53 1.52 1.50 1.49 1.48 1.48 1.45 1.44 1.41 1.38 1.26 1.25 1.24 1.23 1.22 1.21 1.21 1.04
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O–B
OMe
BocN
2.00
2.08
5.09
4.02
2.02
1.03
2.04
14.05
8.07
6.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

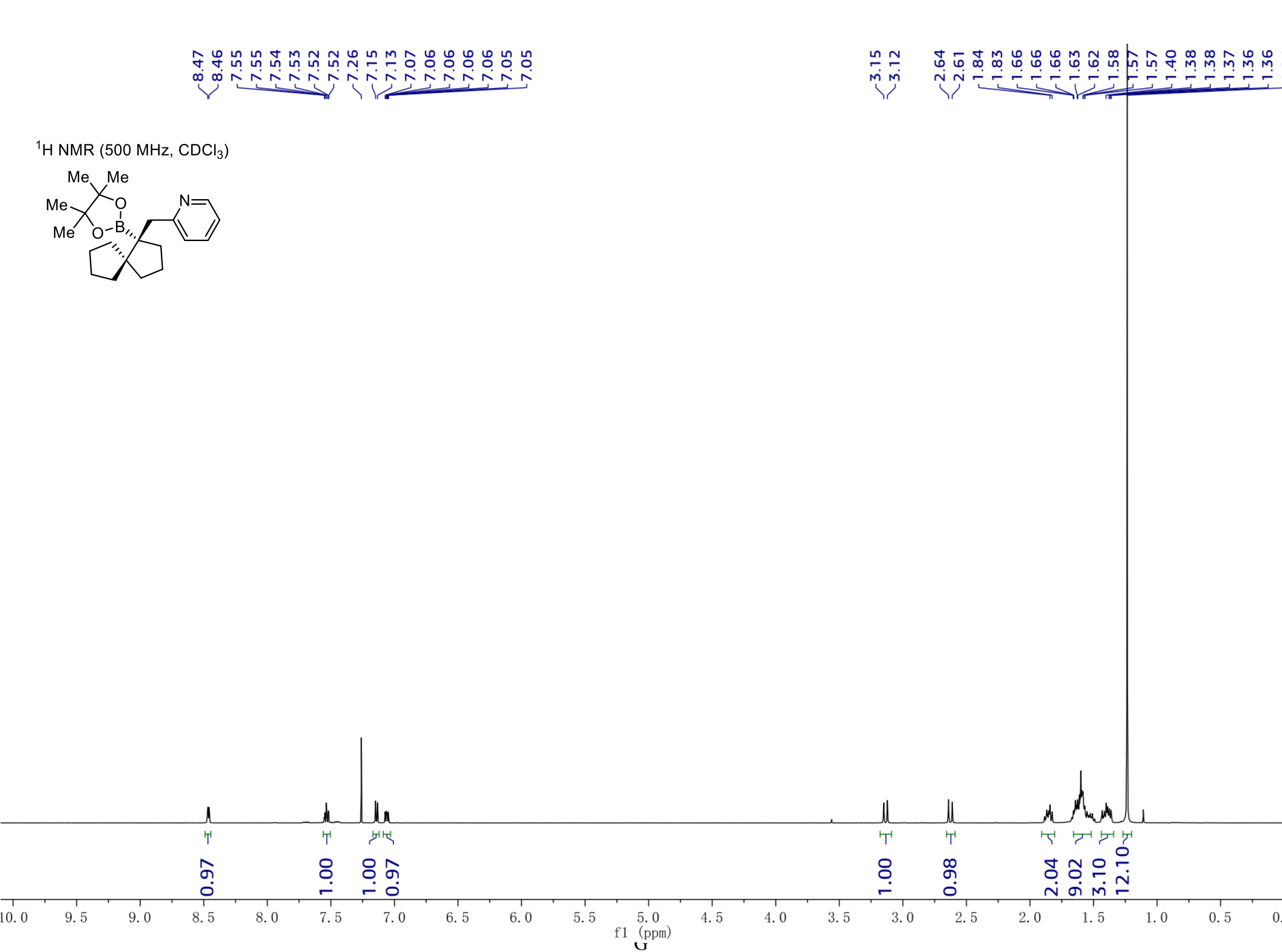
G

E


157.63
154.61
132.49
131.59
131.11
112.98
82.99
78.85
70.80
55.14
39.98
38.92
35.69
33.01
31.99
28.43
26.14
24.62
24.36
21.93
20.82
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
BocN
f1 (ppm)

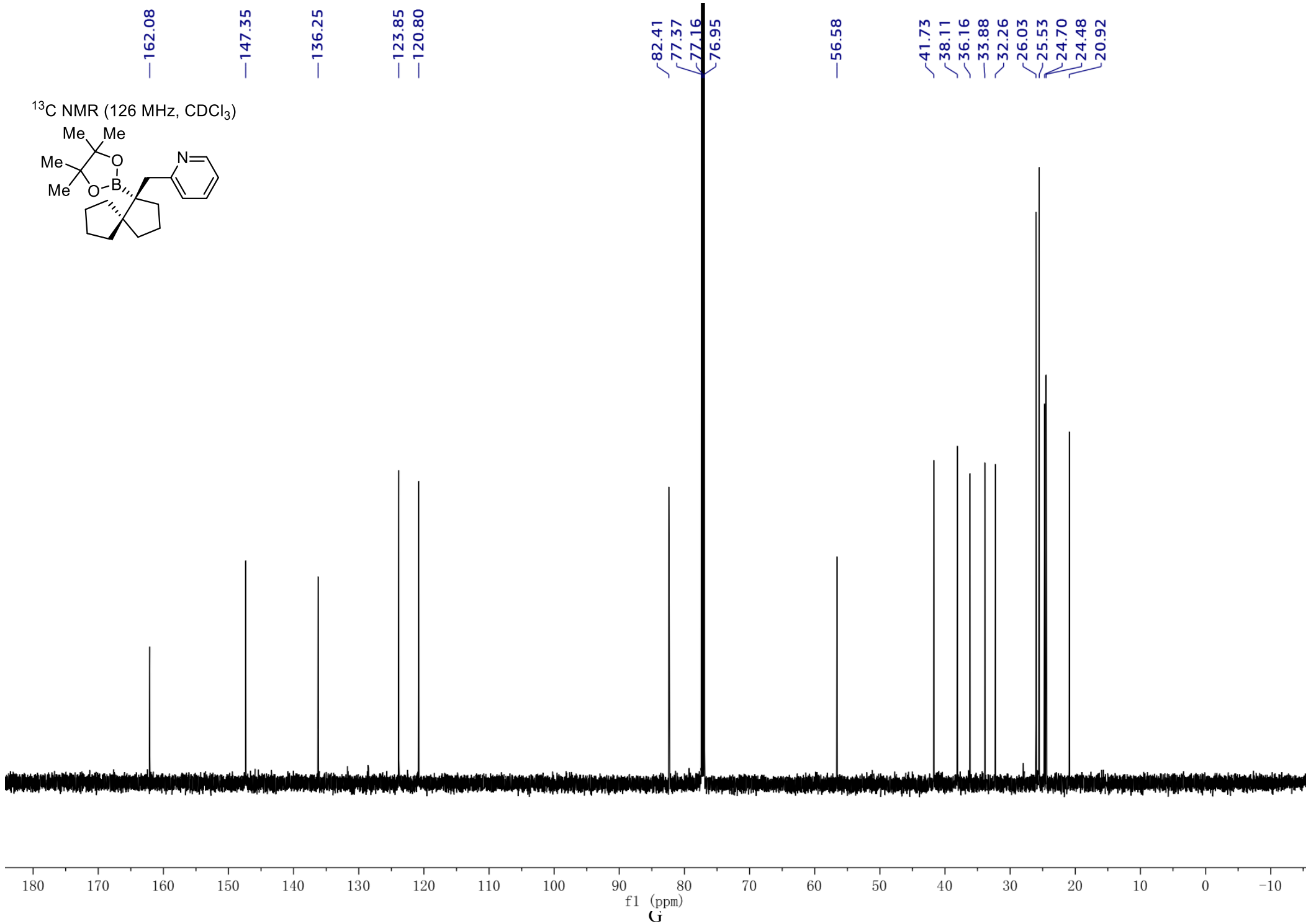
G

E


8.47
8.46
7.55
7.55
7.54
7.53
7.52
7.52
7.26
7.15
7.13
7.07
7.06
7.06
7.06
7.06
7.05
7.05
3.15
3.12
2.64
2.61
1.84
1.83
1.66
1.66
1.66
1.63
1.62
1.58
1.57
1.57
1.40
1.38
1.38
1.37
1.36
1.36
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
0.97
1.00
1.00
0.97
1.00
0.98
2.04
9.02
3.10
12.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

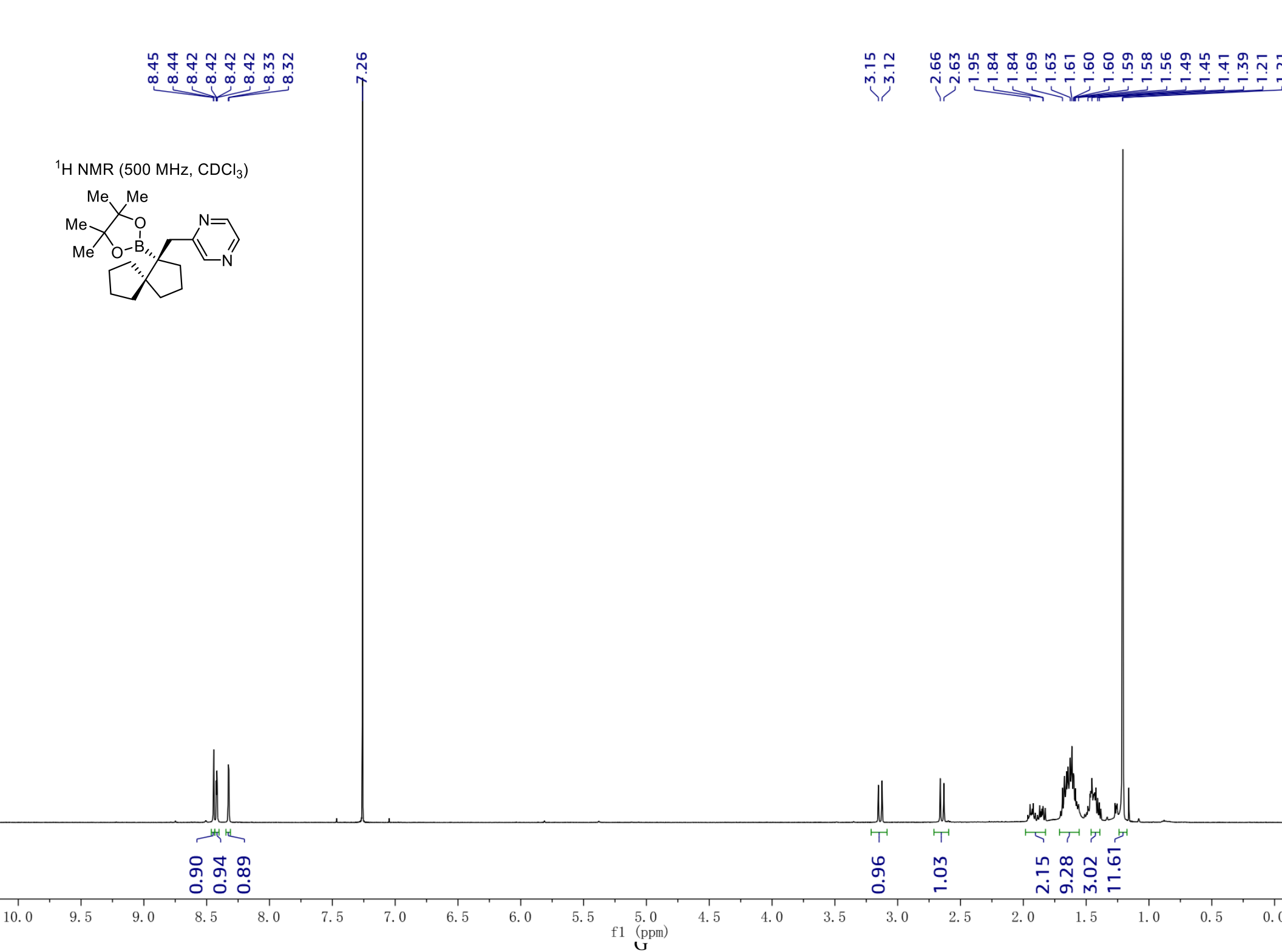
G

E


162.08
147.35
136.25
123.85
120.80
82.41
77.37
77.16
76.95
56.58
41.73
38.11
36.16
33.88
32.26
26.03
25.53
24.70
24.48
20.92
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
B
O
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

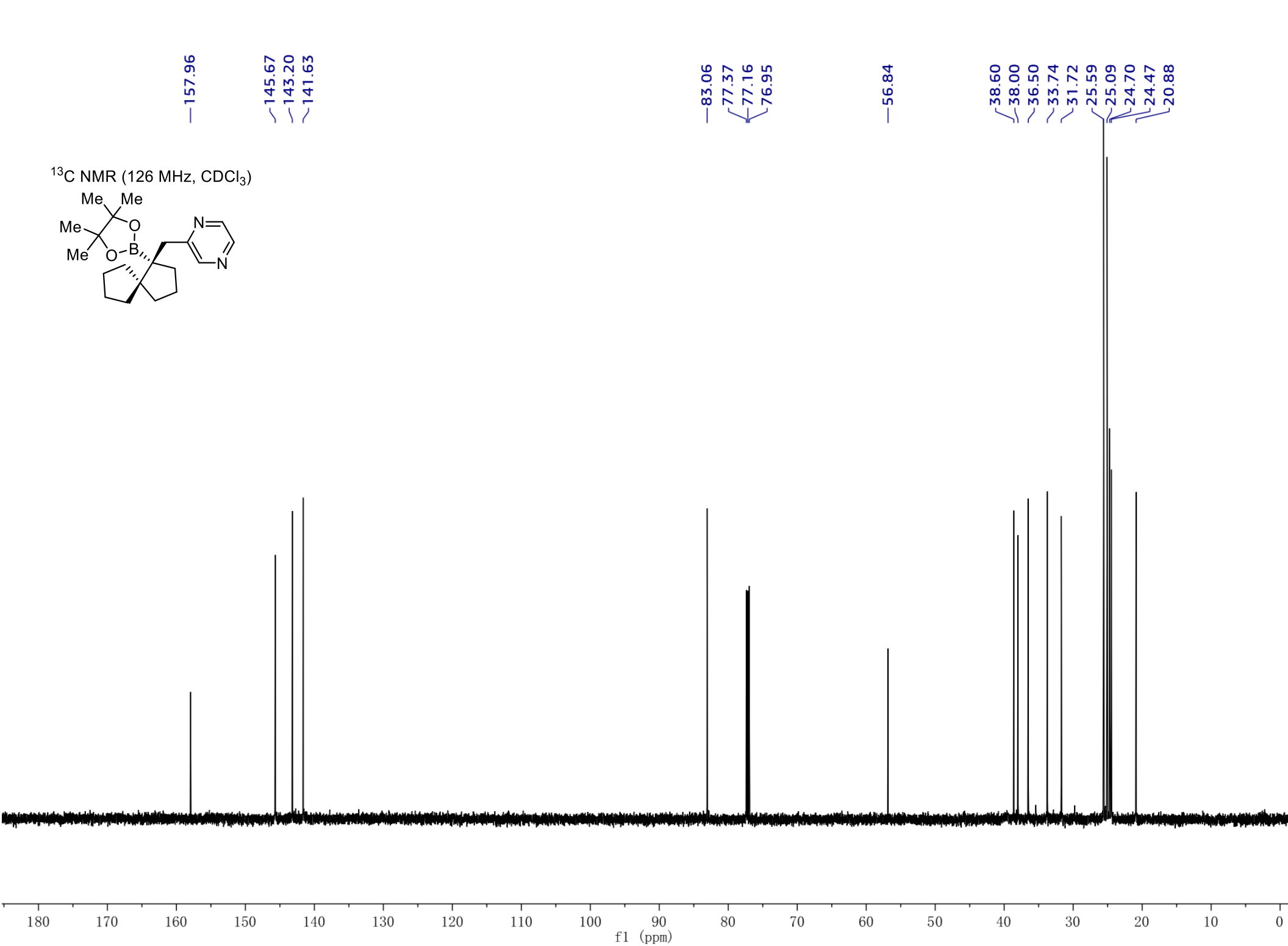
G

E


8.45
8.44
8.42
8.42
8.42
8.42
8.33
8.32
7.26
3.15
3.12
2.66
2.63
1.95
1.84
1.84
1.69
1.63
1.61
1.60
1.60
1.59
1.58
1.56
1.49
1.45
1.41
1.39
1.21
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
N
N
0.90
0.94
0.89
0.96
1.03
2.15
9.28
3.02
11.61
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

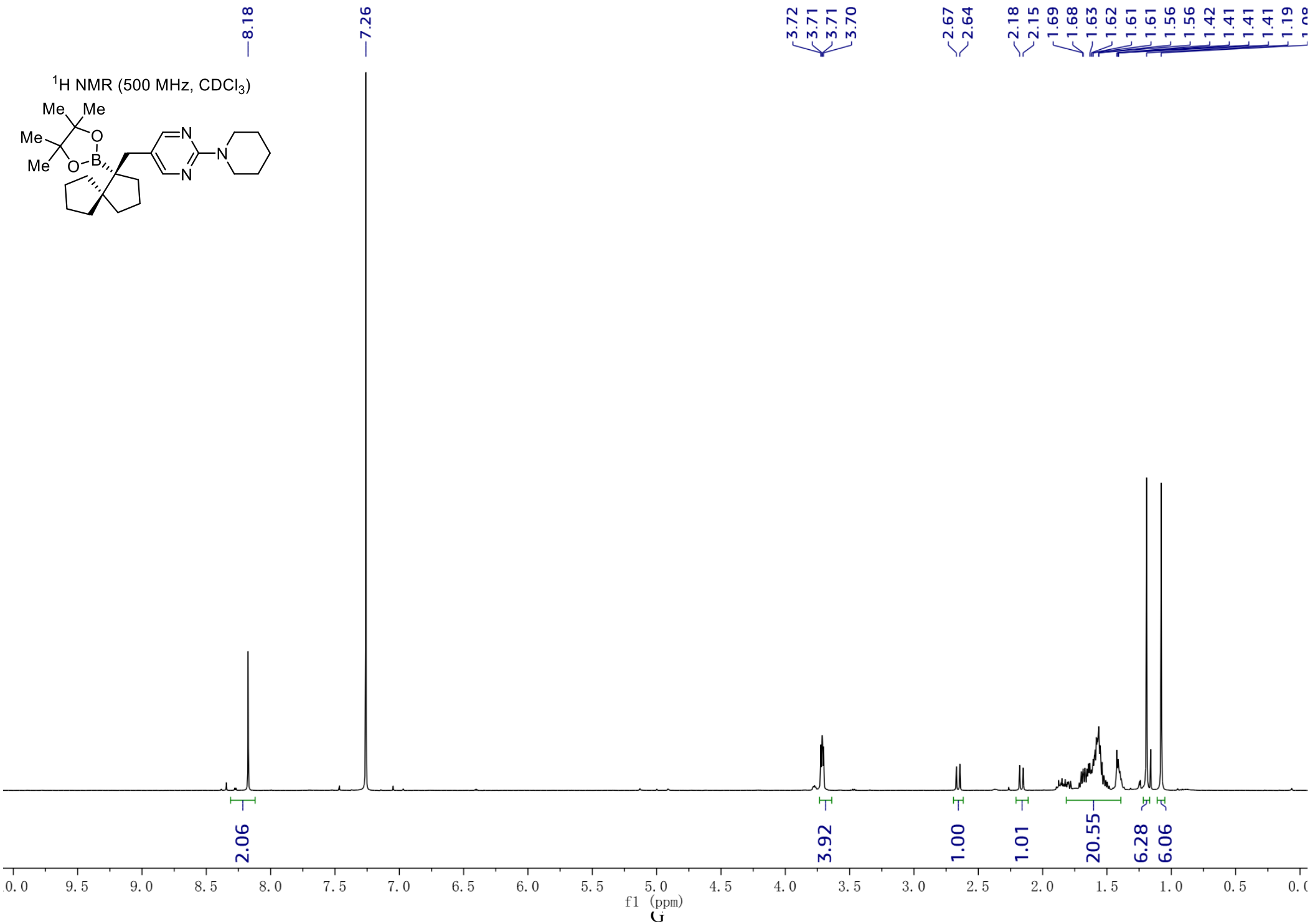
G

E


157.96
145.67
143.20
141.63
83.06
77.37
77.16
76.95
56.84
38.60
38.00
36.50
33.74
31.72
25.59
25.09
24.70
24.47
20.88
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

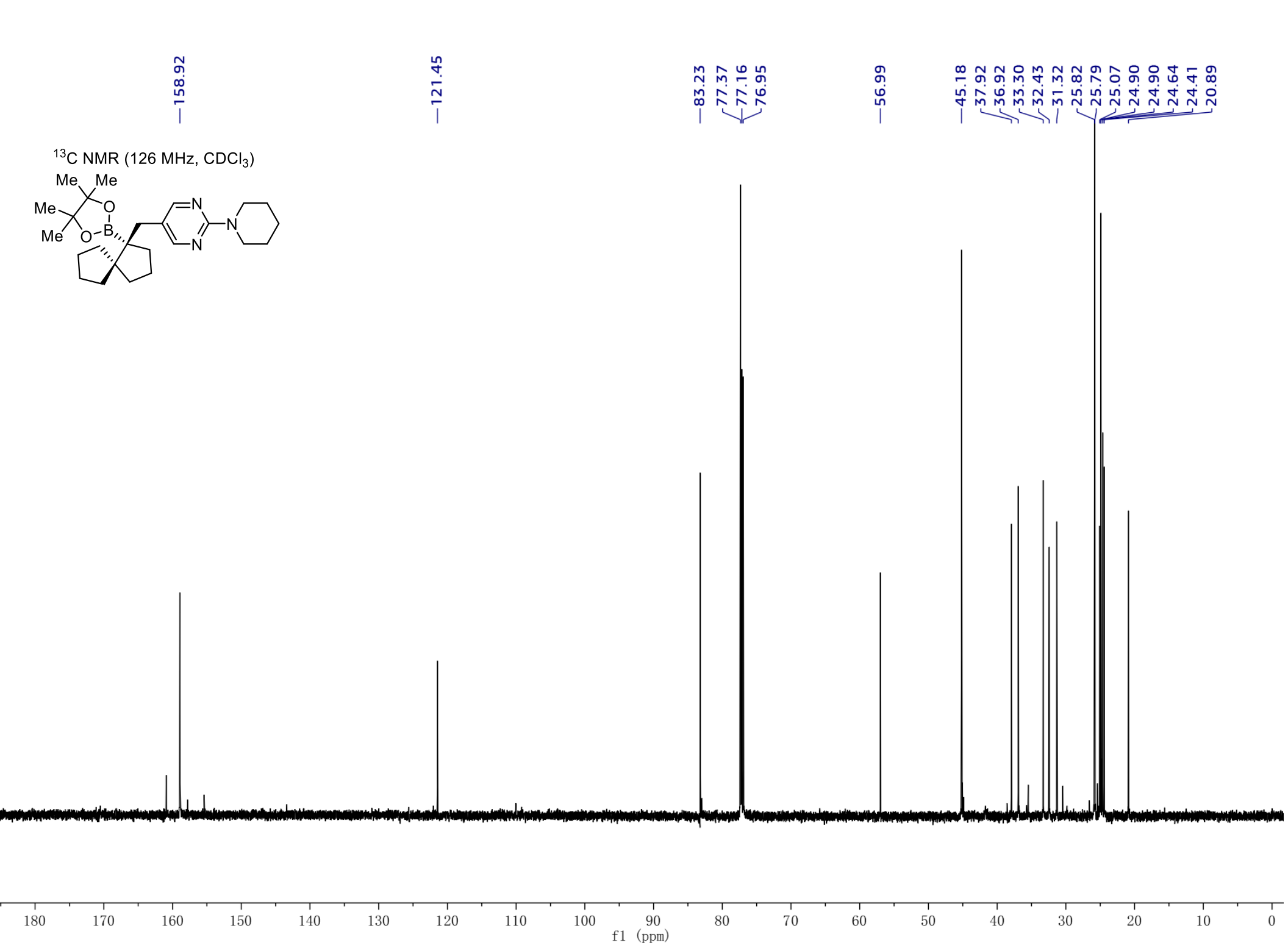
G

E


8.18
7.26
3.72
3.71
3.71
3.70
2.67
2.64
2.18
2.15
1.69
1.68
1.63
1.62
1.61
1.61
1.56
1.56
1.42
1.41
1.41
1.41
1.19
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
N
N
2.06
3.92
1.00
1.01
20.55
6.28
6.06
f1 (ppm)

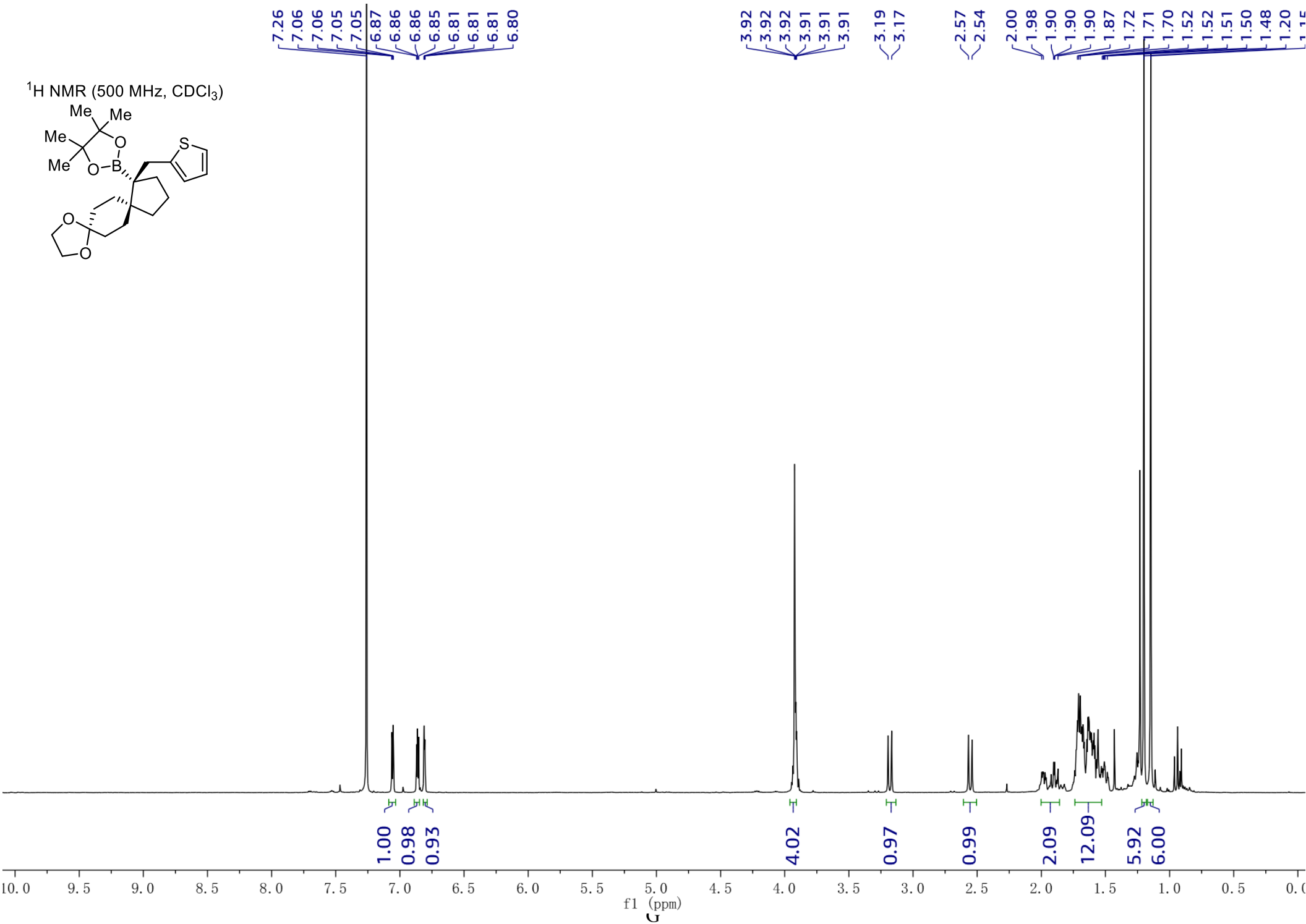
G

E


158.92
121.45
83.23
77.37
77.16
76.95
56.99
45.18
37.92
36.92
33.30
32.43
31.32
25.82
25.79
25.07
24.90
24.90
24.64
24.41
20.89
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
N
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

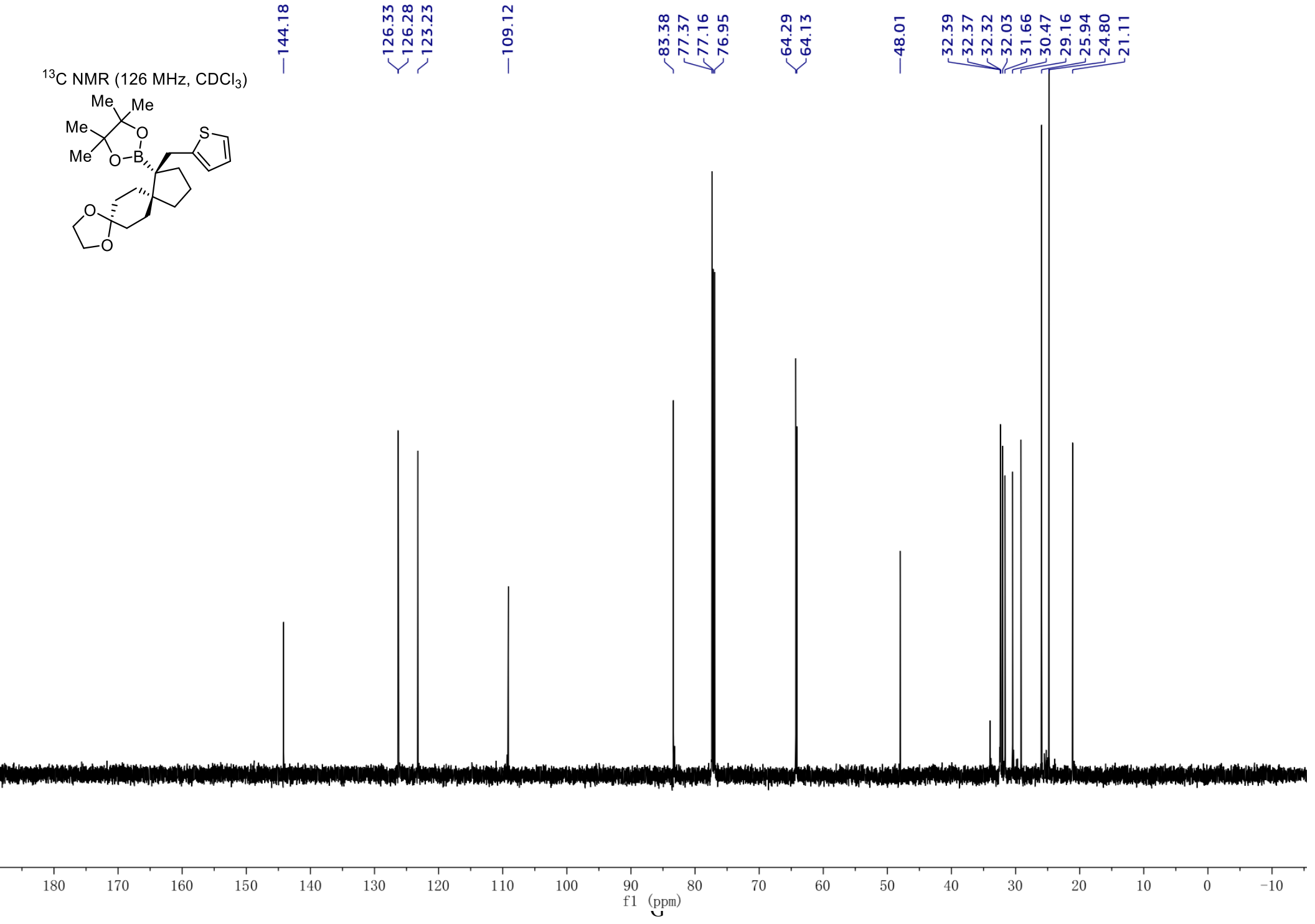
G

E

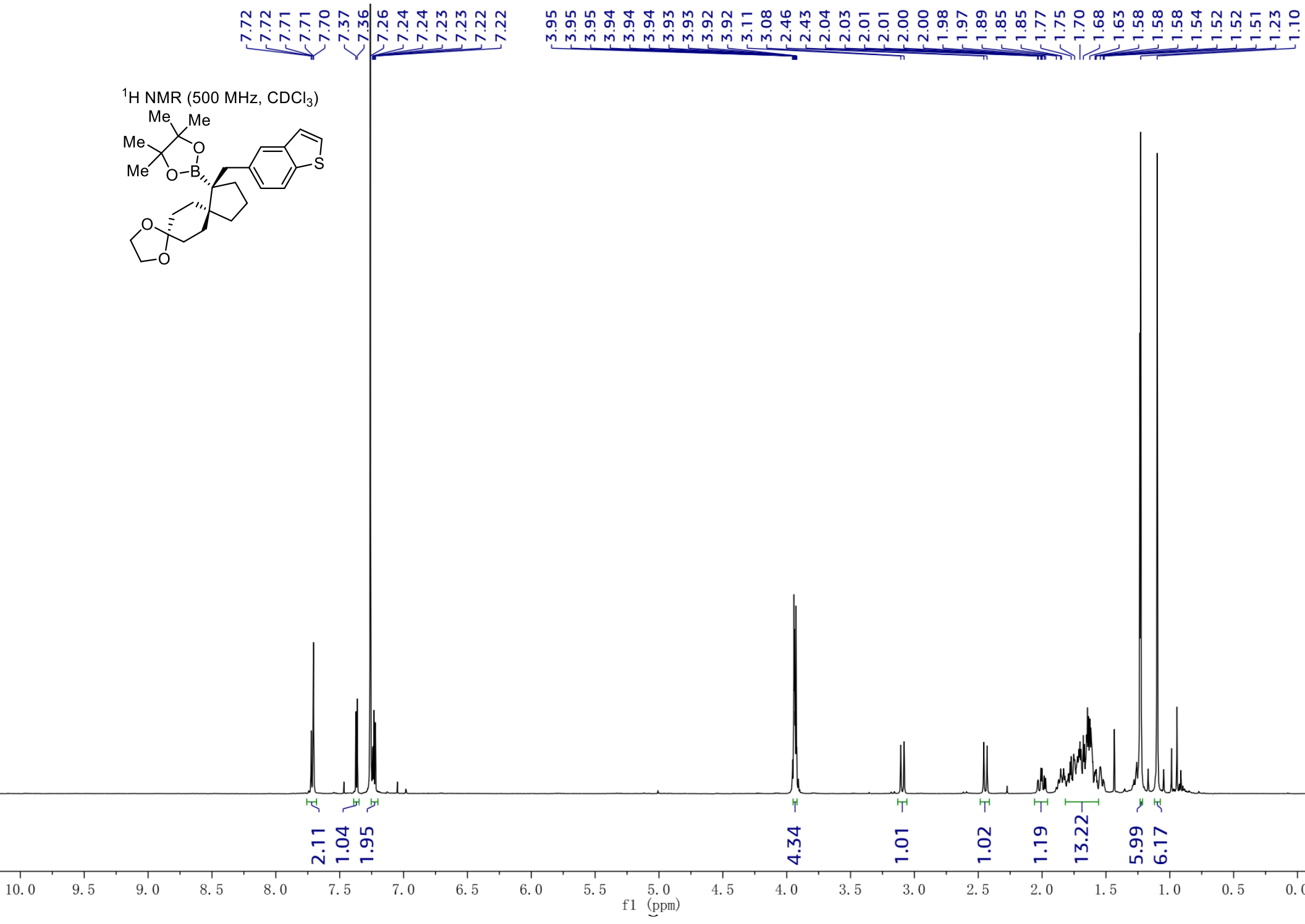

$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
S
O
O
7.26
7.06
7.06
7.05
7.05
6.87
6.86
6.86
6.85
6.81
6.81
6.81
6.80
3.92
3.92
3.92
3.91
3.91
3.91
3.19
3.17
2.57
2.54
2.00
1.98
1.90
1.90
1.90
1.87
1.72
1.71
1.70
1.52
1.52
1.51
1.50
1.48
1.20
1.00
0.98
0.93
4.02
0.97
0.99
2.09
12.09
5.92
6.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

G

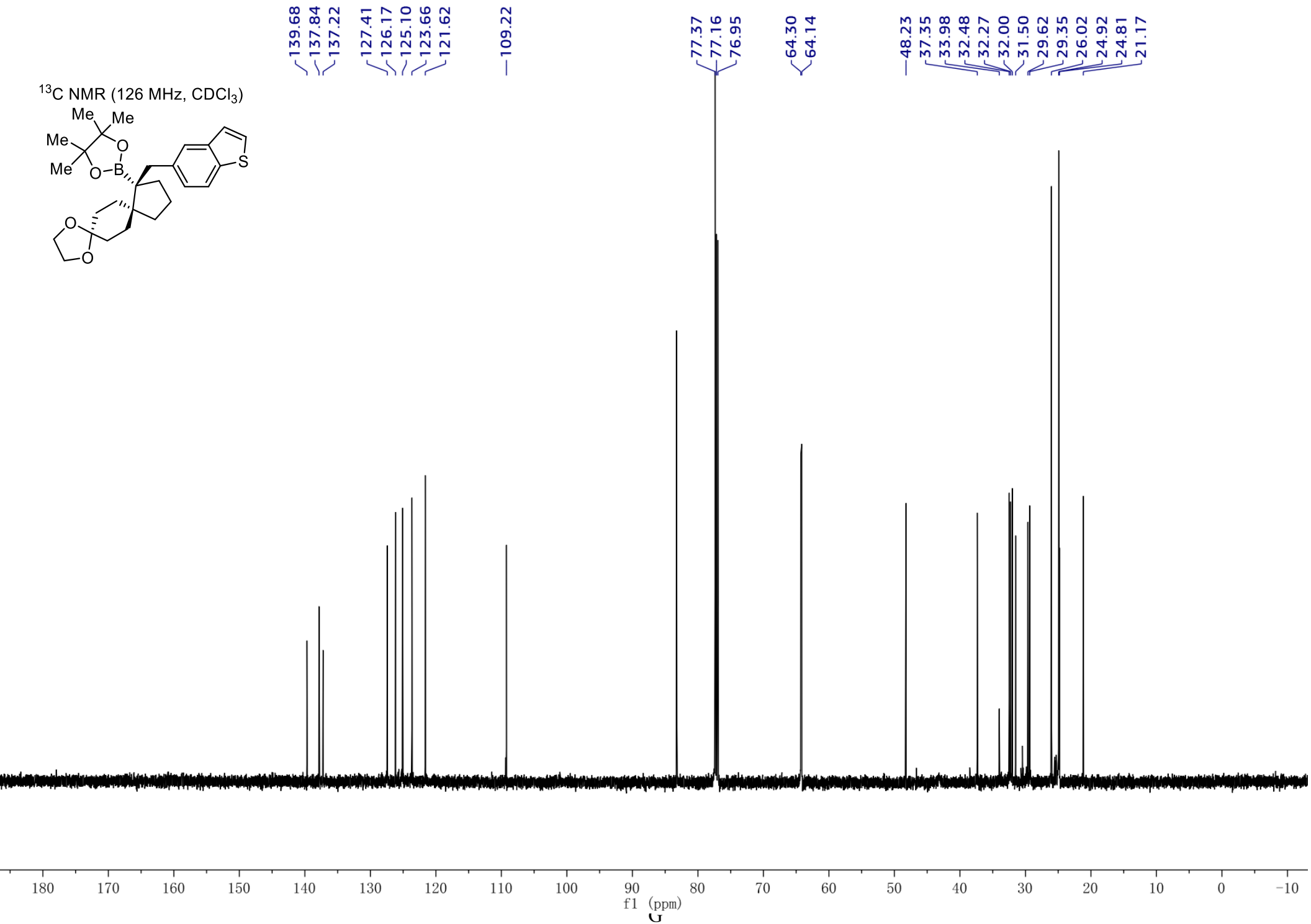
E


144.18
126.33
126.28
123.23
109.12
83.38
77.37
77.16
76.95
64.29
64.13
48.01
32.39
32.37
32.32
32.03
31.66
30.47
29.16
25.94
24.80
21.11
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

E


7.72 7.72 7.71 7.71 7.70 7.37 7.36 7.26 7.24 7.24 7.23 7.23 7.22 7.22
3.95 3.95 3.95 3.94 3.94 3.94 3.93 3.93 3.92 3.92 3.11 3.08 2.46 2.43 2.04 2.03 2.01 2.01 2.00 2.00 1.98 1.97 1.89 1.85 1.85 1.77 1.75 1.70 1.68 1.63 1.58 1.58 1.58 1.54 1.52 1.52 1.51 1.23 1.10
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
S
O
O
2.11
1.04
1.95
4.34
1.01
1.02
1.19
13.22
5.99
6.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

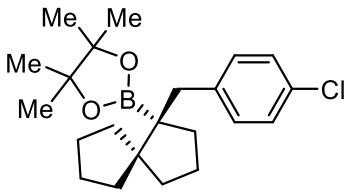
E

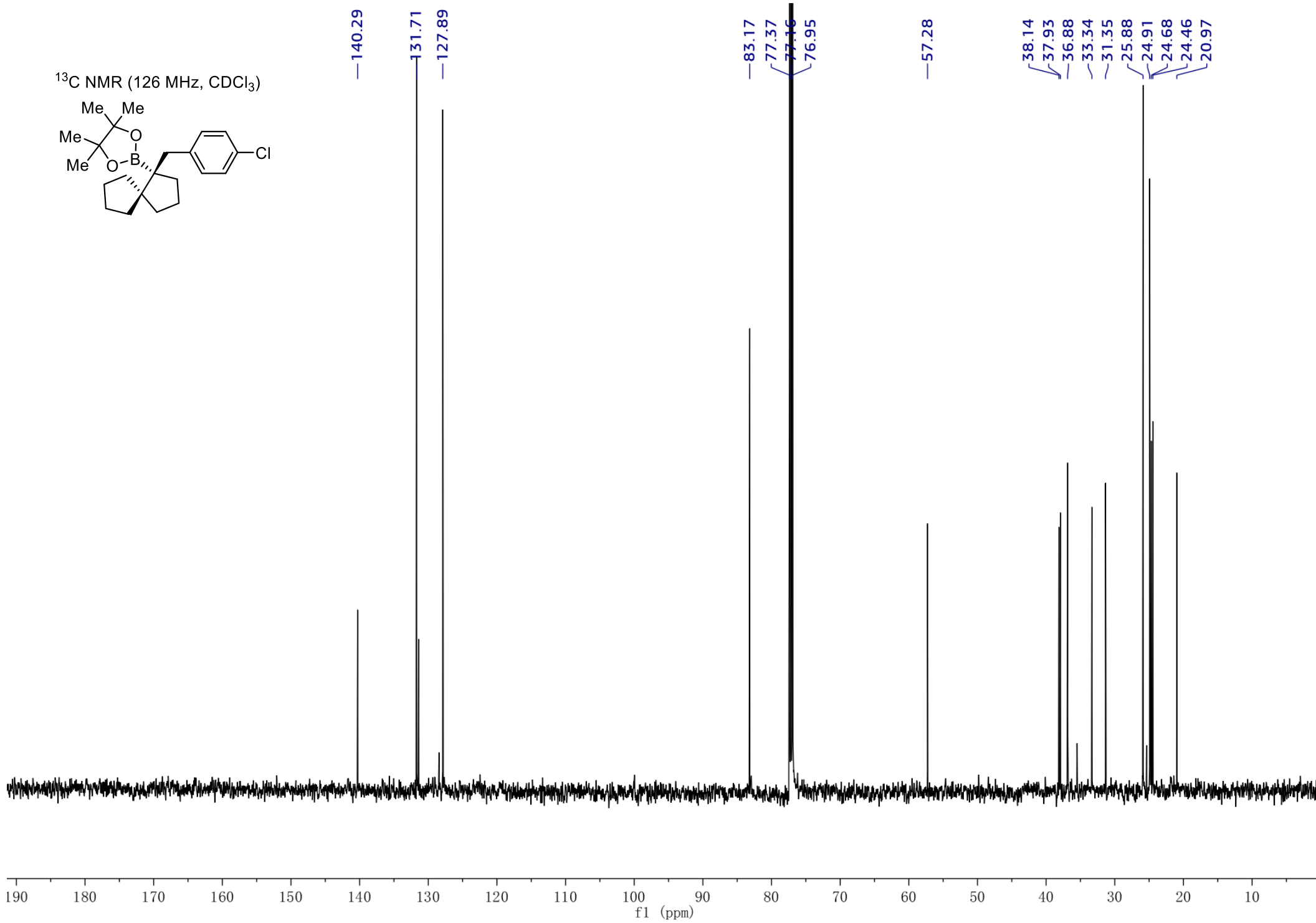

139.68
137.84
137.22
127.41
126.17
125.10
123.66
121.62
109.22
77.37
77.16
76.95
64.30
64.14
48.23
37.35
33.98
32.48
32.27
32.00
31.50
29.62
29.35
26.02
24.92
24.81
21.17
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

G

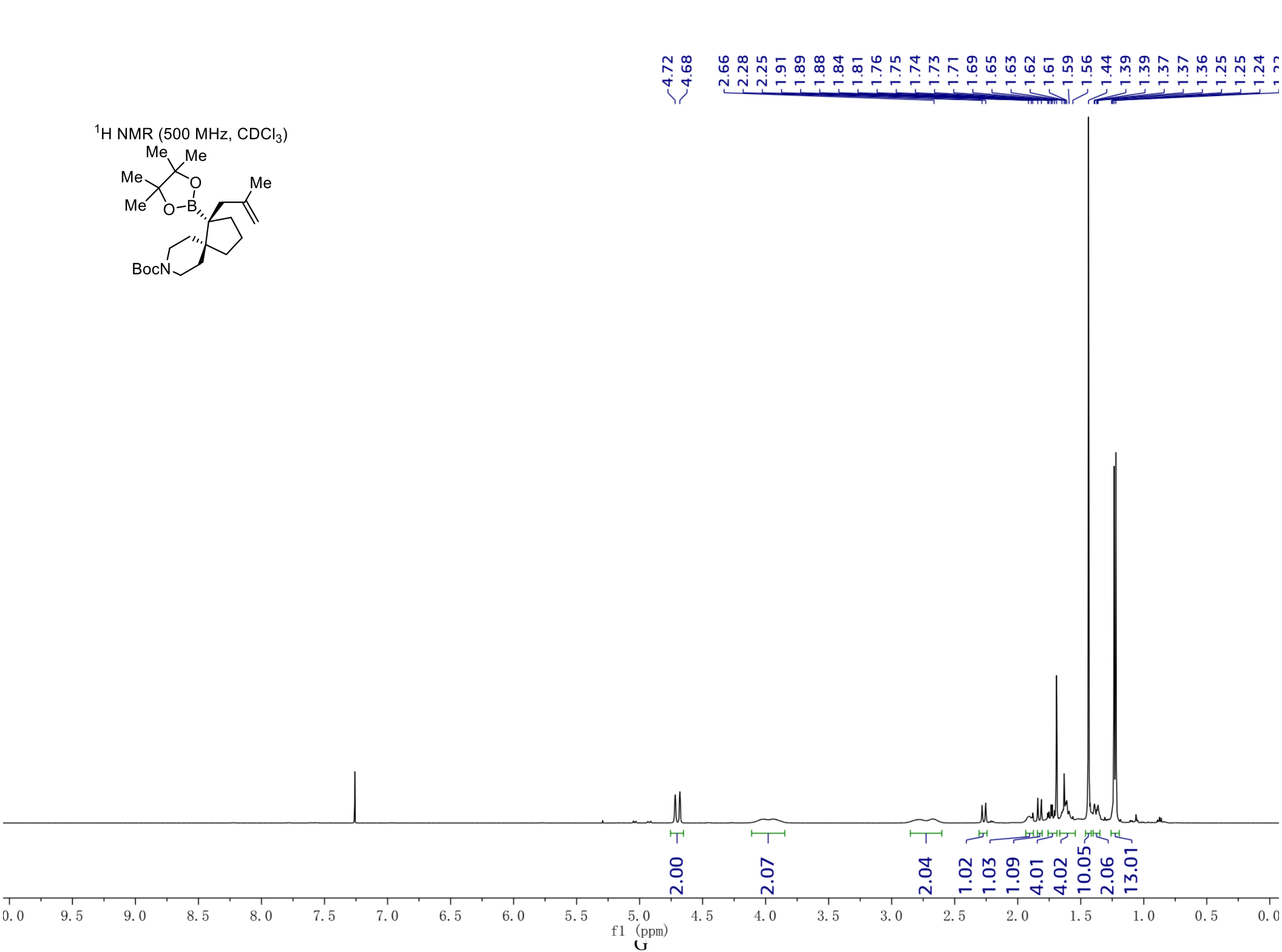
E

$^1$H NMR (500 MHz, $CDCl_3$)



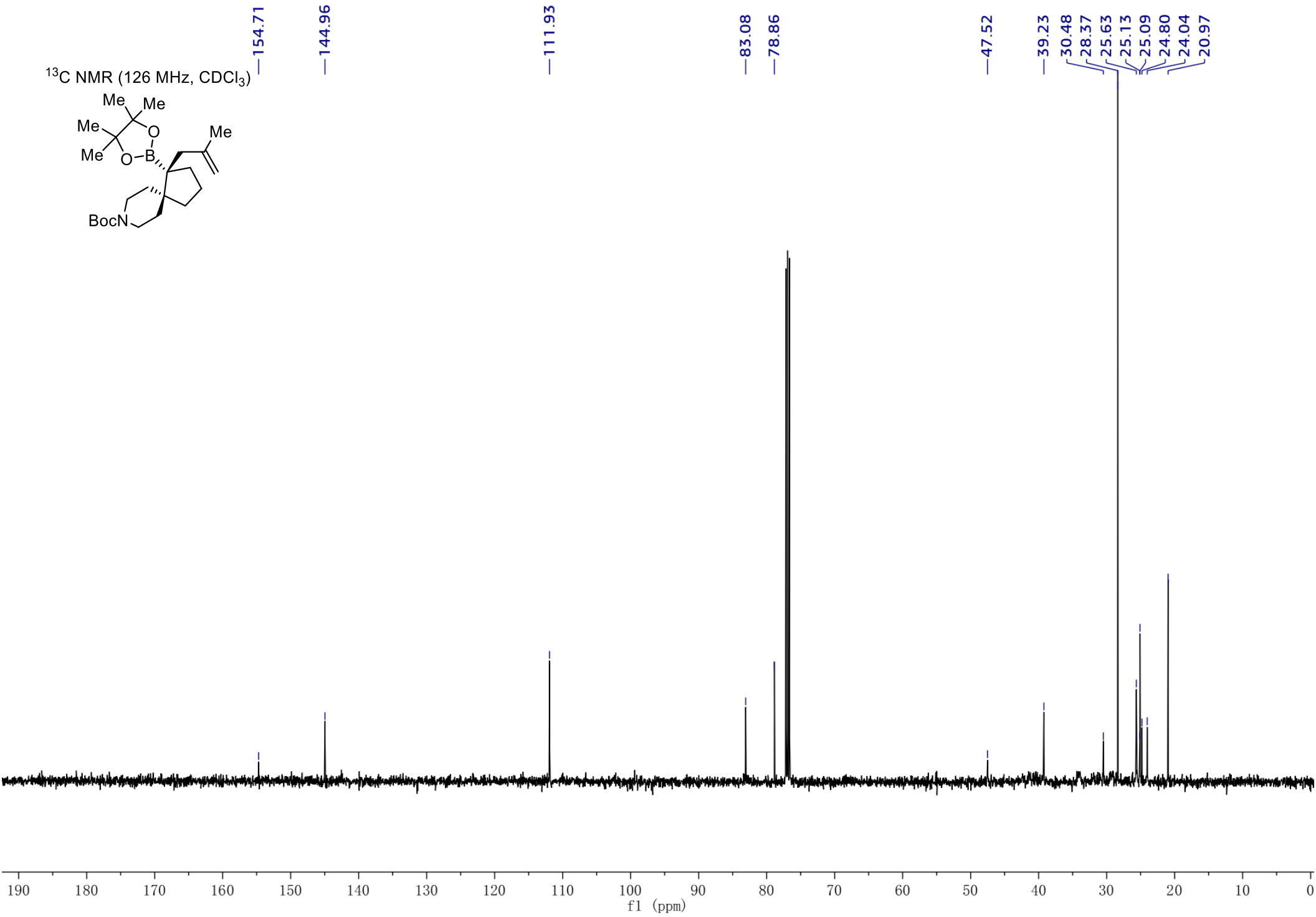

$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
Cl
140.29
131.71
127.89
83.17
77.37
77.16
76.95
57.28
38.14
37.93
36.88
33.34
31.35
25.88
24.91
24.68
24.46
20.97
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

E

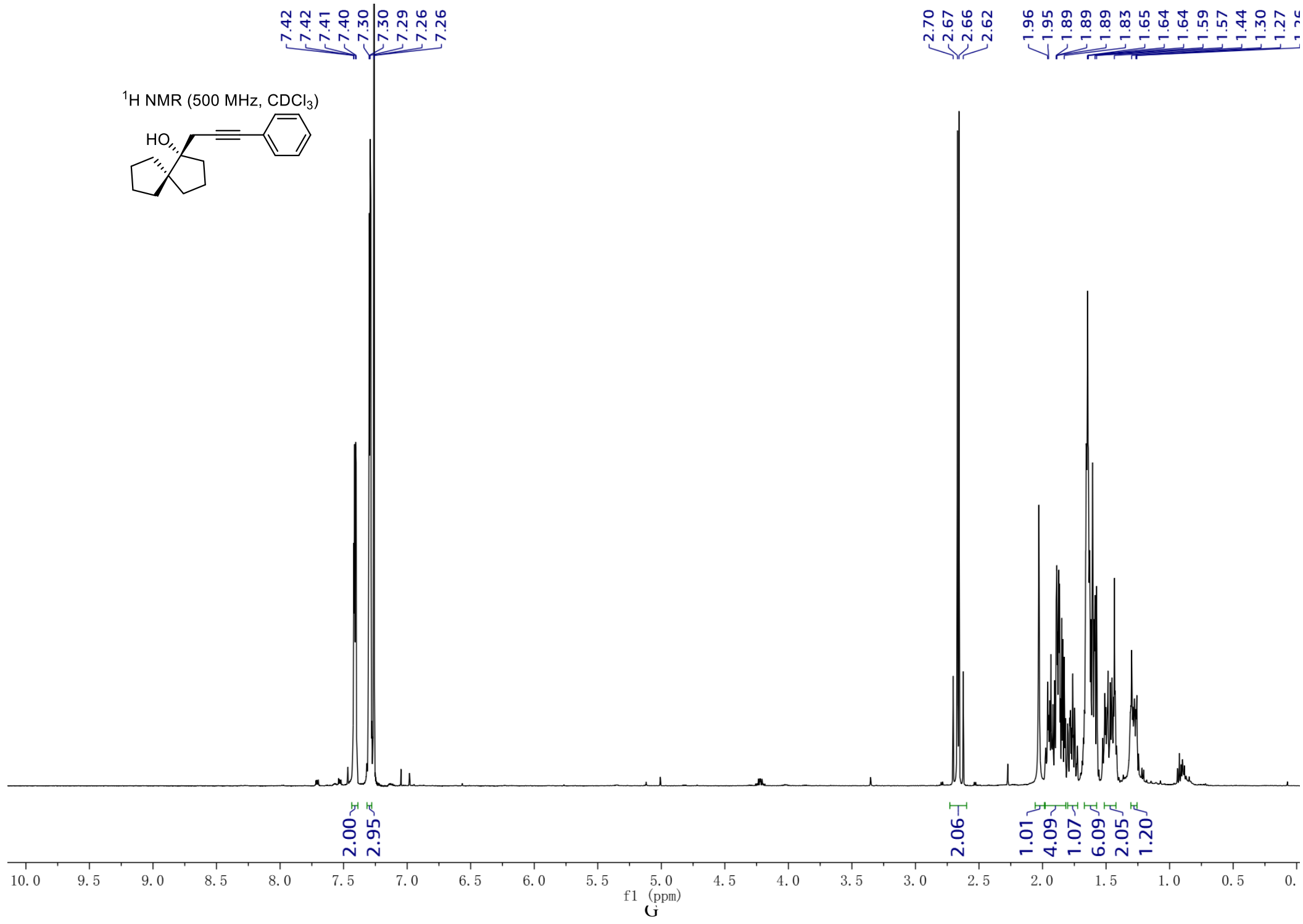

4.72
4.68
2.66
2.28
2.25
1.91
1.89
1.88
1.84
1.81
1.76
1.75
1.74
1.73
1.71
1.69
1.65
1.63
1.62
1.61
1.59
1.56
1.44
1.39
1.39
1.37
1.37
1.36
1.25
1.25
1.24
2.00
2.07
2.04
1.02
1.03
1.09
4.01
4.02
10.05
2.06
13.01
f1 (ppm)

G

E

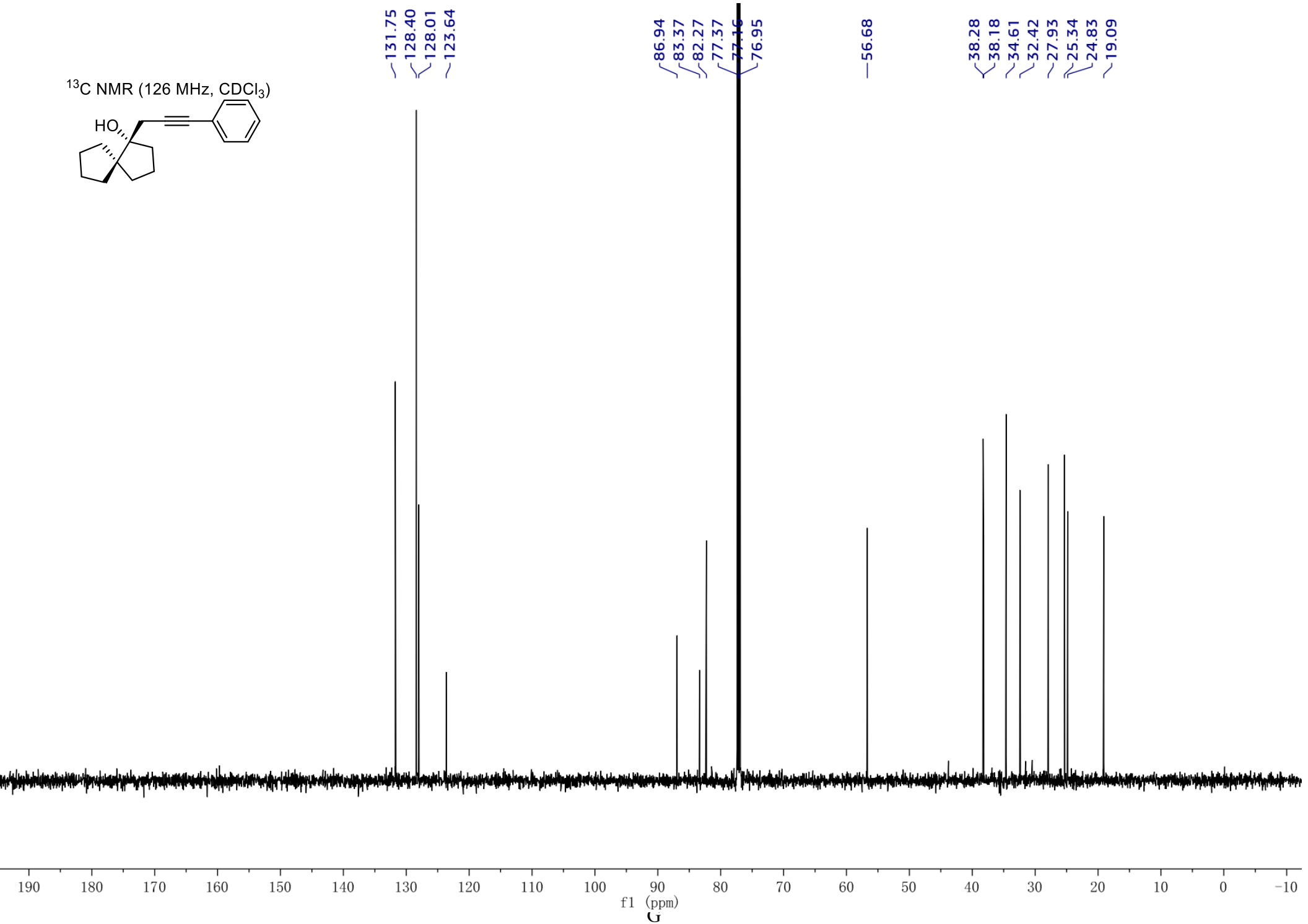

154.71
144.96
111.93
83.08
78.86
47.52
39.23
30.48
28.37
25.63
25.13
25.09
24.80
24.04
20.97
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
BocN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.42
7.42
7.41
7.40
7.30
7.30
7.29
7.26
7.26
2.70
2.67
2.66
2.62
1.96
1.95
1.89
1.89
1.89
1.83
1.65
1.64
1.64
1.59
1.57
1.44
1.30
1.27
$^1$H NMR (500 MHz, CDCl$_3$)
HO
2.00
2.95
2.06
1.01
4.09
1.07
6.09
2.05
1.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

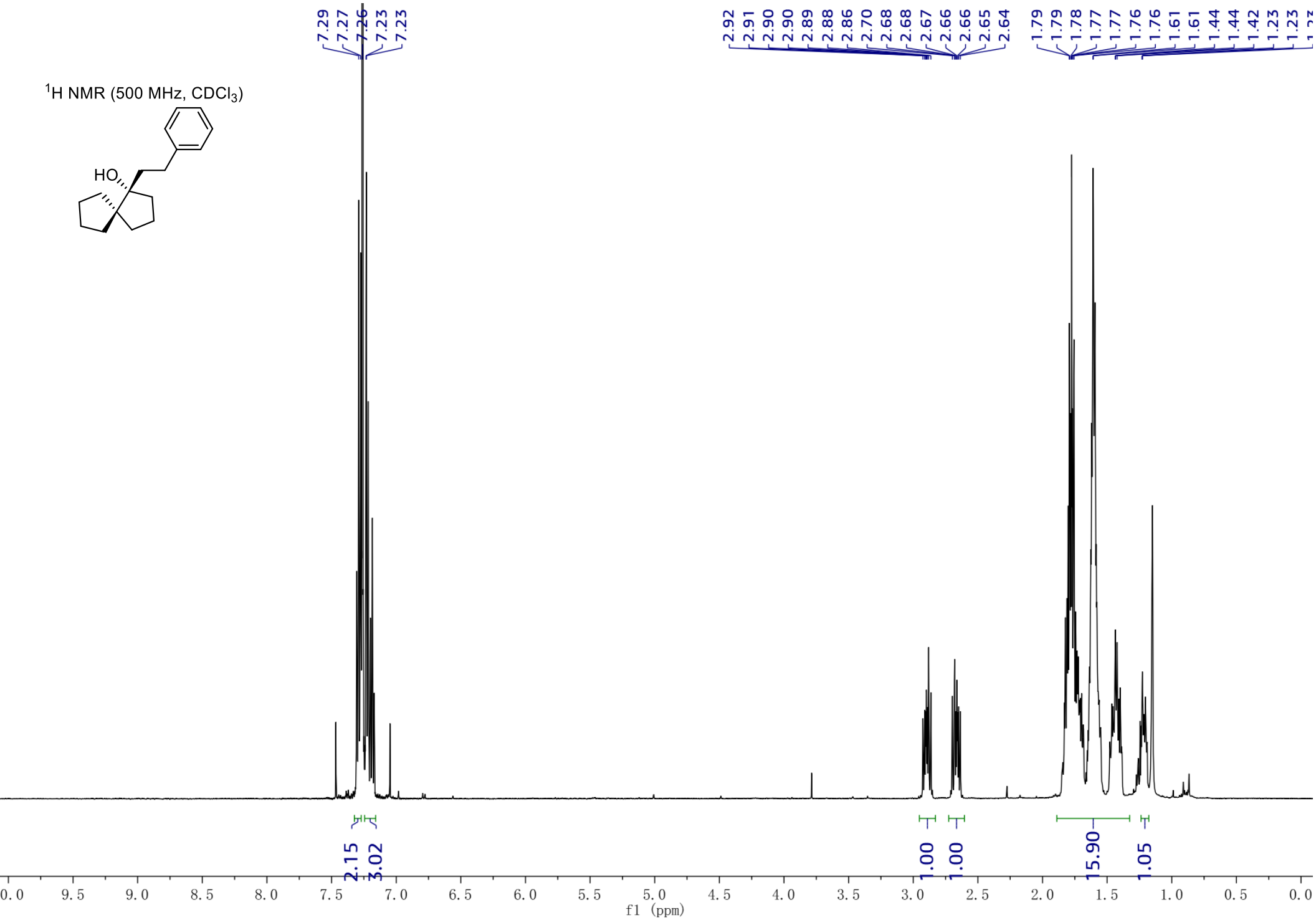
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
HO
131.75
128.40
128.01
123.64
86.94
83.37
82.27
77.37
77.16
76.95
56.68
38.28
38.18
34.61
32.42
27.93
25.34
24.83
19.09
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

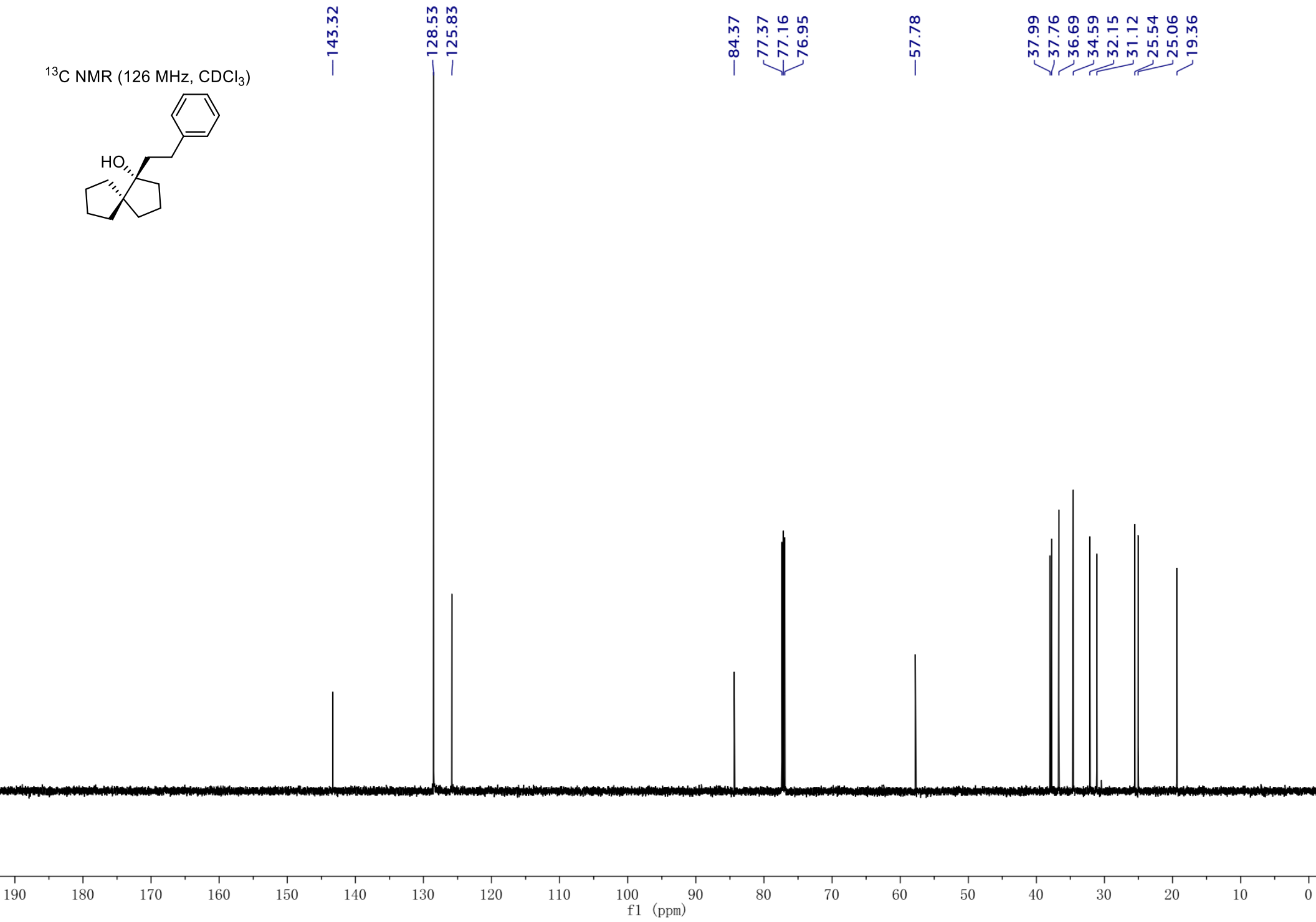
G

E

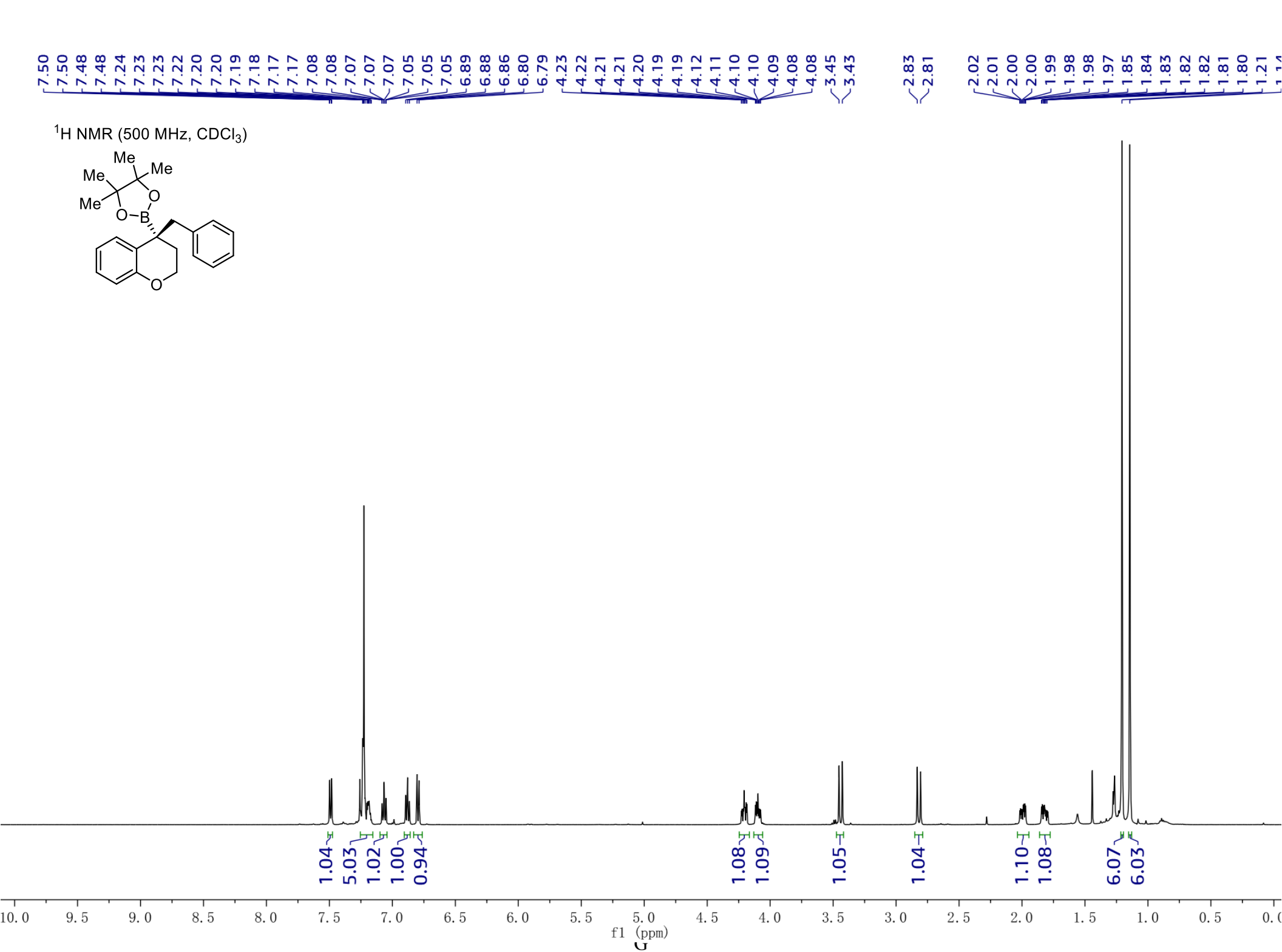

$^1$H NMR (500 MHz, $CDCl_3$)
HO
7.29
7.27
7.26
7.23
7.23
2.92
2.91
2.90
2.90
2.89
2.88
2.86
2.70
2.68
2.68
2.67
2.66
2.66
2.65
2.64
1.79
1.79
1.78
1.77
1.77
1.76
1.76
1.61
1.61
1.44
1.44
1.42
1.23
1.23
2.15
3.02
1.00
1.00
15.90
1.05
f1 (ppm)

G

E

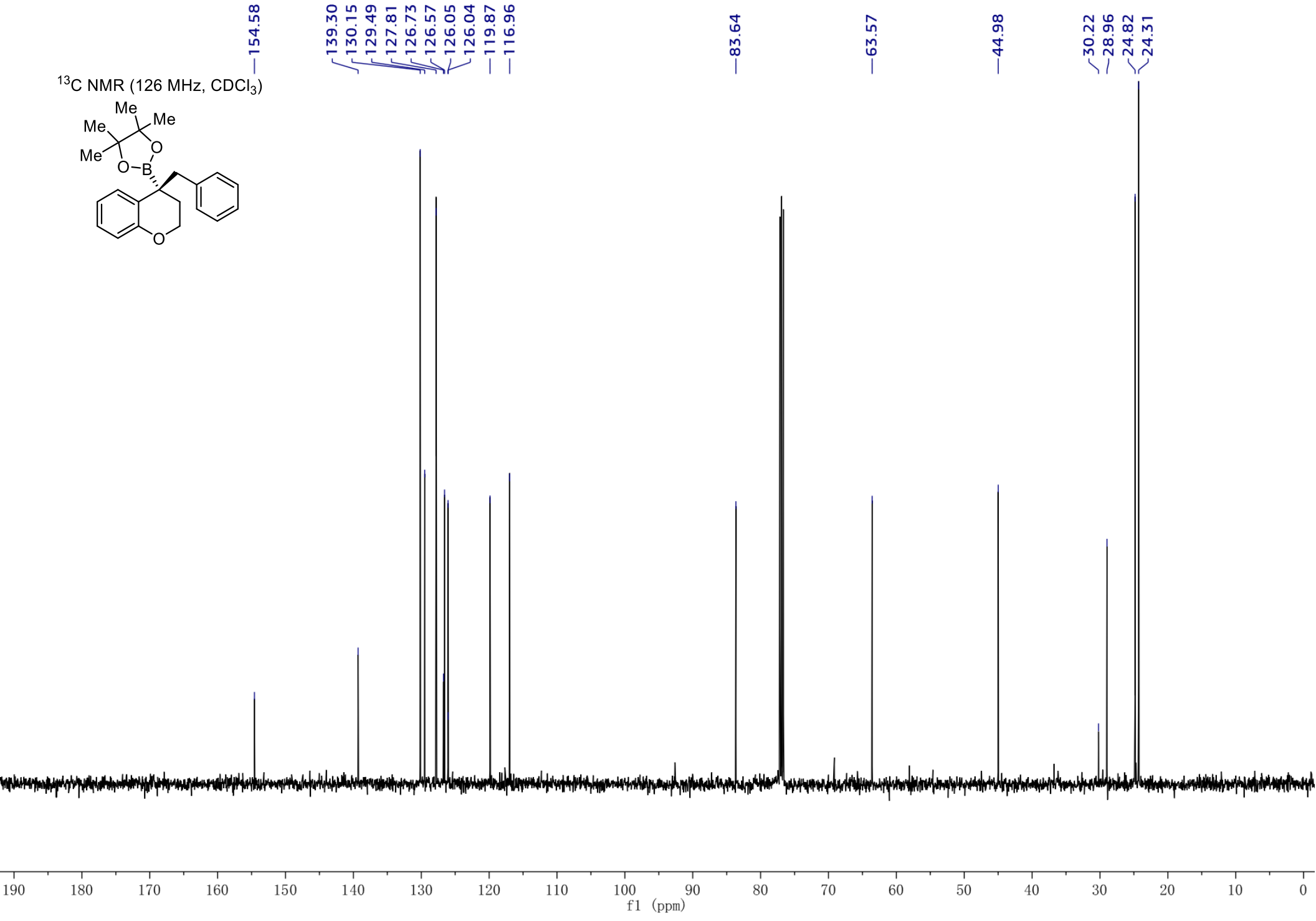

$^{13}$C NMR (126 MHz, $CDCl_3$)
HO
143.32
128.53
125.83
84.37
77.37
77.16
76.95
57.78
37.99
37.76
36.69
34.59
32.15
31.12
25.54
25.06
19.36
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E

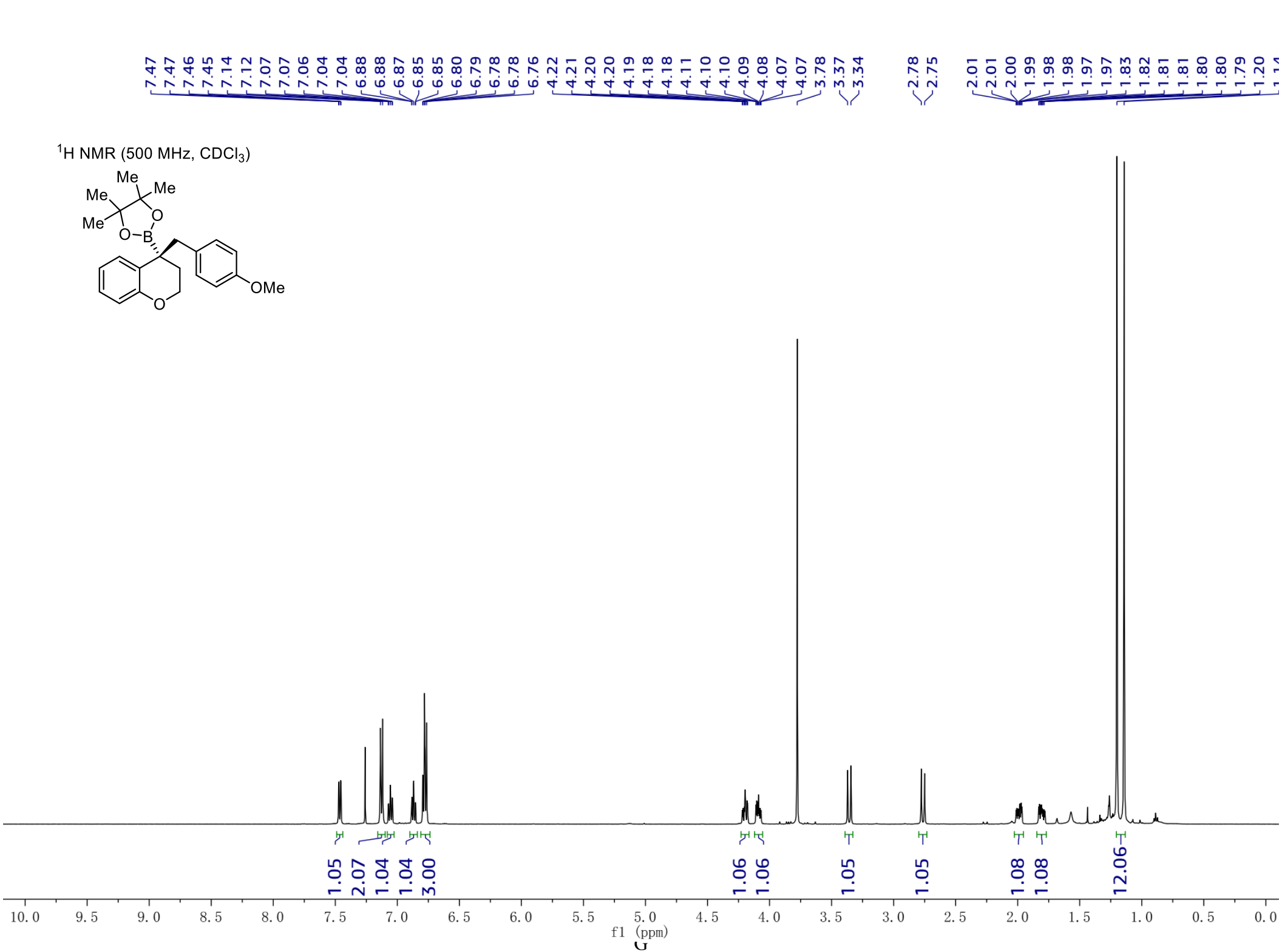

$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
O
7.50 7.50 7.48 7.48 7.24 7.23 7.23 7.22 7.20 7.20 7.19 7.18 7.17 7.17 7.08 7.08 7.07 7.07 7.07 7.05 7.05 7.05 6.89 6.88 6.86 6.80 6.79
4.23 4.22 4.21 4.21 4.20 4.19 4.19 4.12 4.11 4.10 4.10 4.09 4.08 4.08
3.45 3.43
2.83 2.81
2.02 2.01 2.00 2.00 1.99 1.98 1.98 1.97 1.85 1.84 1.83 1.82 1.82 1.81 1.80 1.21
1.04 5.03 1.02 1.00 0.94 1.08 1.09 1.05 1.04 1.10 1.08 6.07 6.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

G

E

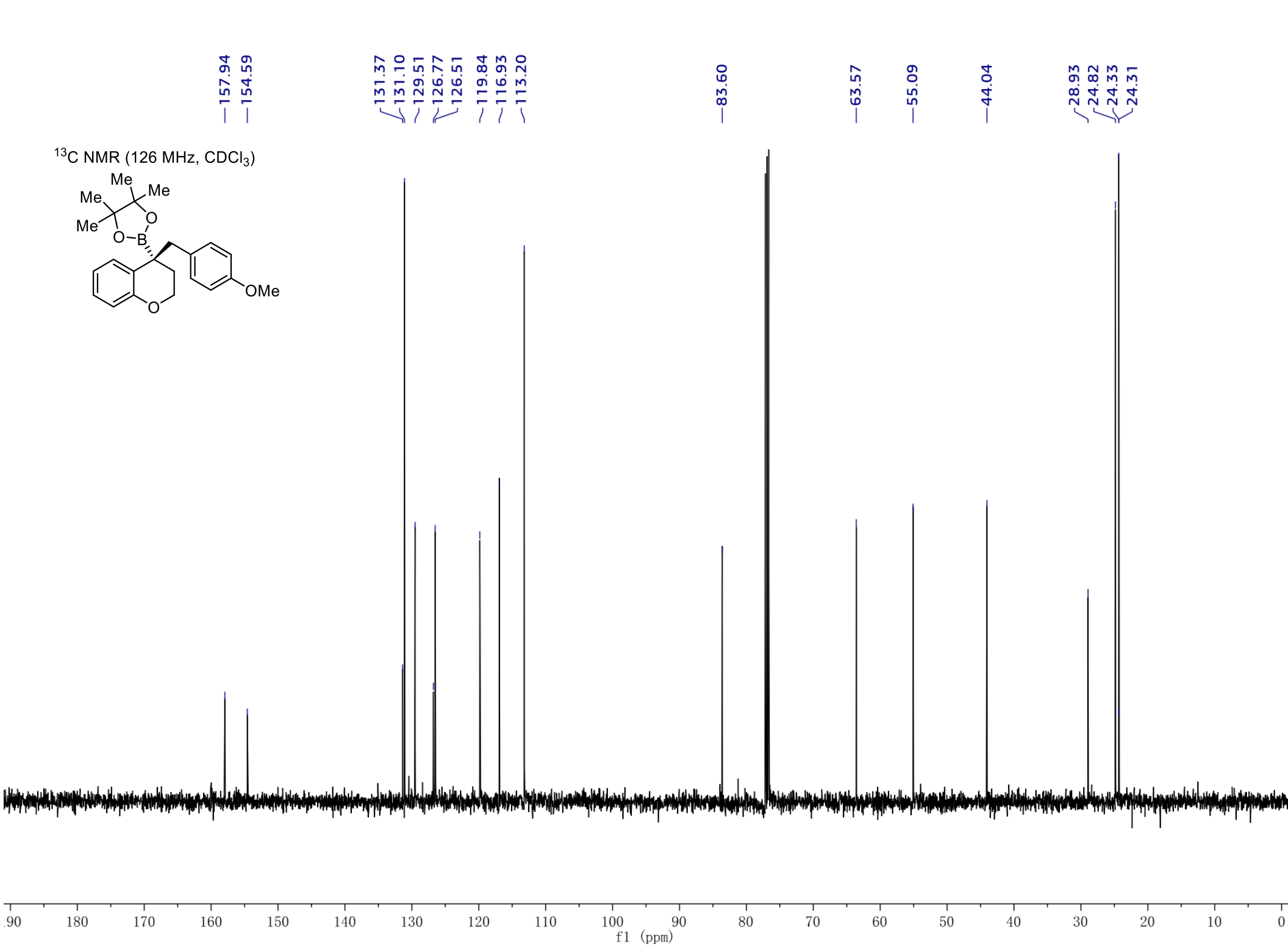

154.58
139.30
130.15
129.49
127.81
126.73
126.57
126.05
126.04
119.87
116.96
83.64
63.57
44.98
30.22
28.96
24.82
24.31
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


7.47 7.47 7.46 7.45 7.14 7.12 7.07 7.07 7.06 7.04 7.04 6.88 6.88 6.87 6.85 6.85 6.80 6.79 6.78 6.78 6.76
4.22 4.21 4.20 4.20 4.19 4.18 4.18 4.11 4.10 4.10 4.09 4.08 4.07 4.07 3.78 3.37 3.34
2.78 2.75
2.01 2.01 2.00 1.99 1.98 1.98 1.97 1.97 1.83 1.82 1.81 1.81 1.80 1.80 1.79 1.20
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
O
1.05 2.07 1.04 1.04 3.00 1.06 1.06 1.05 1.05 1.08 1.08 12.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

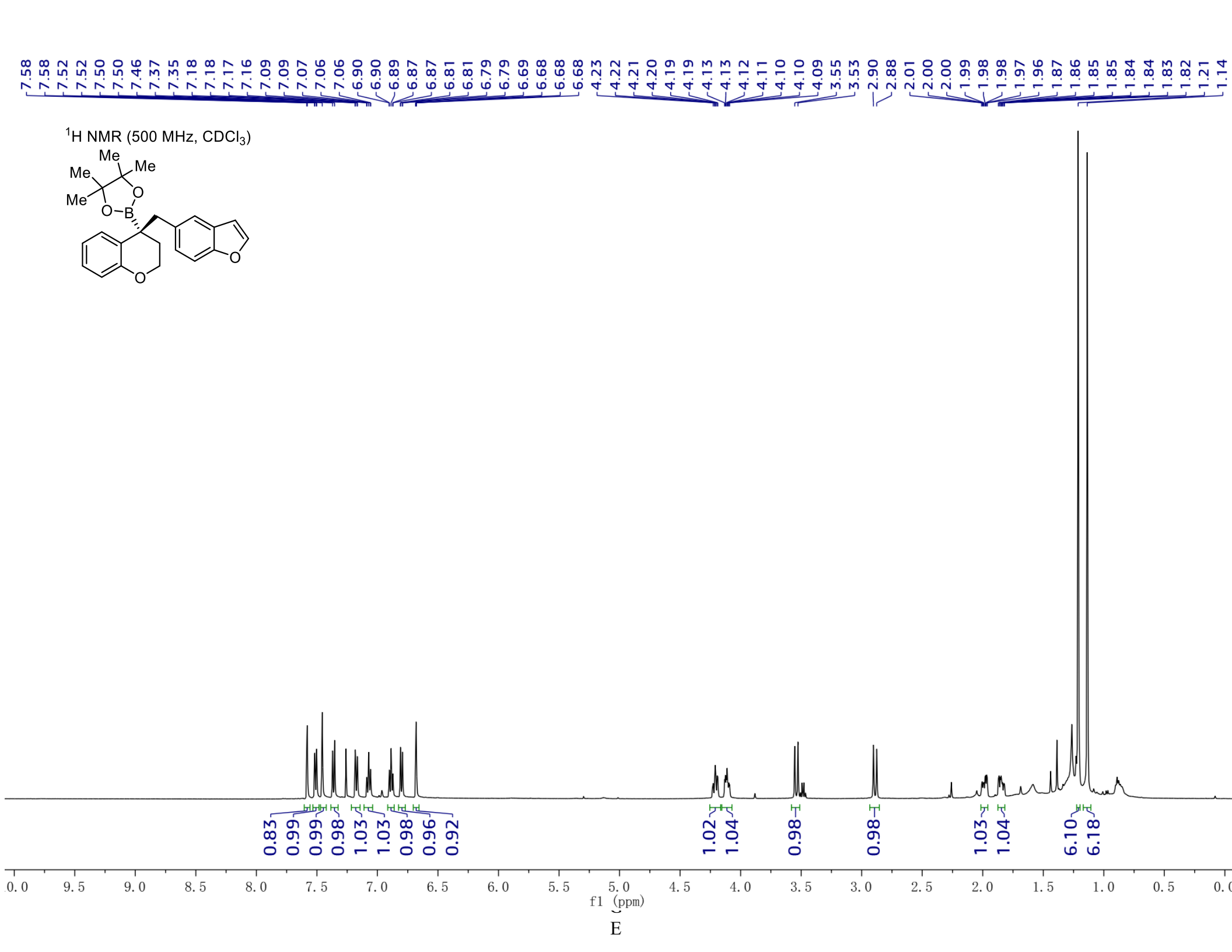
G

E

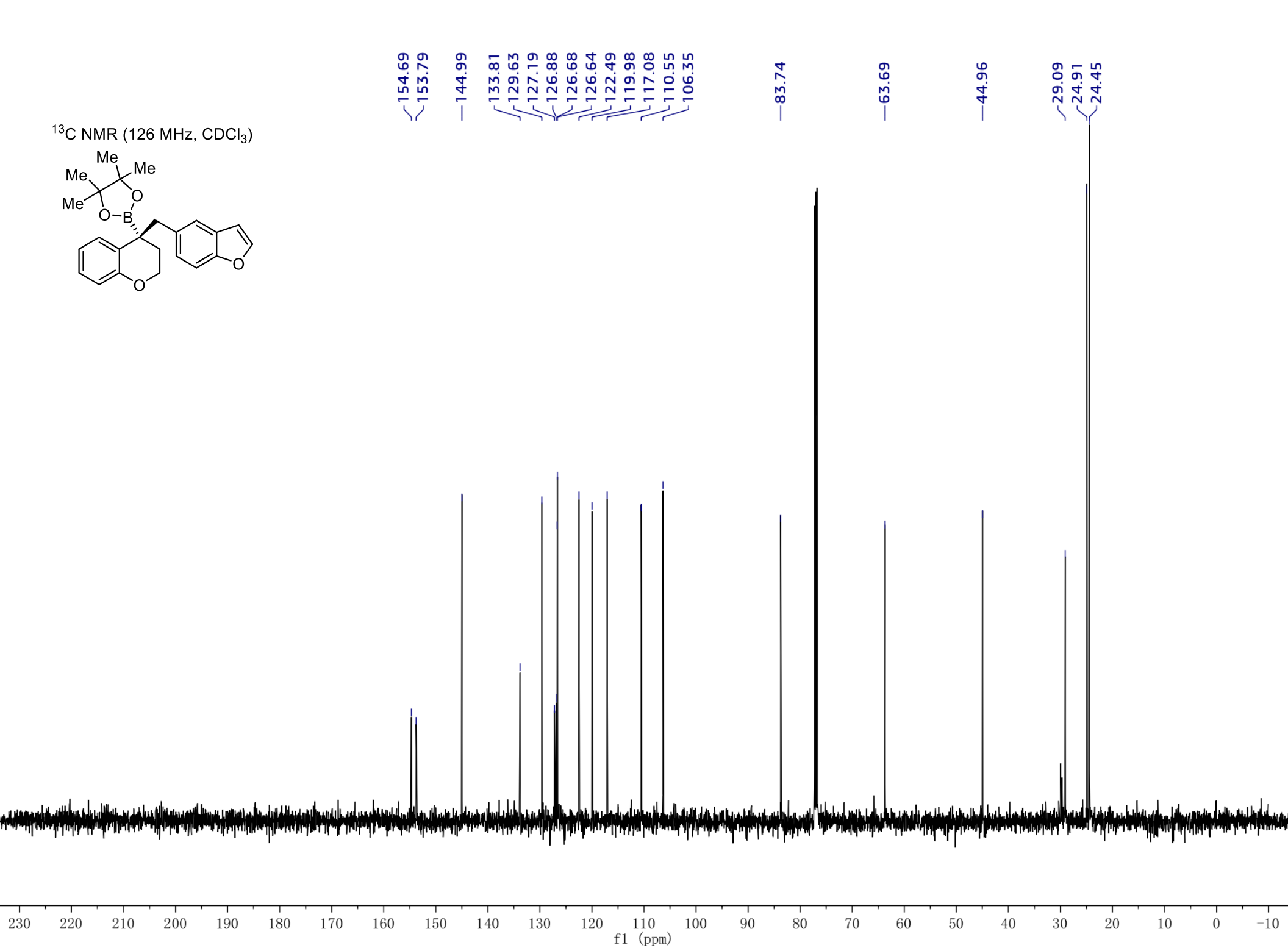

157.94
154.59
131.37
131.10
129.51
126.77
126.51
119.84
116.93
113.20
83.60
63.57
55.09
44.04
28.93
24.82
24.33
24.31
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
O
f1 (ppm)

G

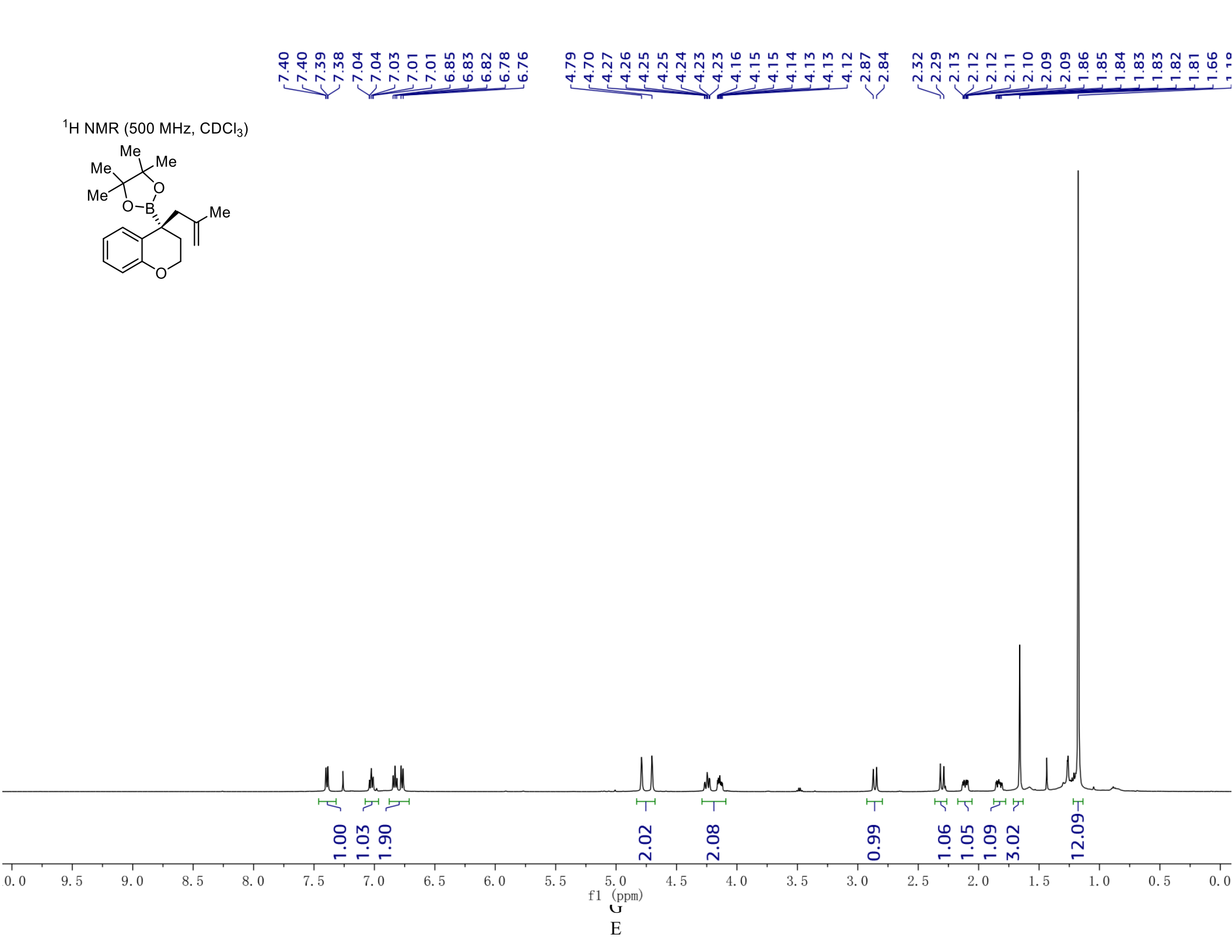
E


7.58 7.58 7.52 7.52 7.50 7.50 7.46 7.37 7.35 7.18 7.18 7.17 7.16 7.09 7.09 7.07 7.06 7.06 6.90 6.90 6.89 6.87 6.87 6.81 6.81 6.79 6.79 6.69 6.68 6.68 6.68
4.23 4.22 4.21 4.20 4.19 4.19 4.13 4.13 4.12 4.11 4.10 4.10 4.09 3.55 3.53 2.90 2.88
2.01 2.00 2.00 1.99 1.98 1.98 1.97 1.96 1.87 1.86 1.85 1.85 1.84 1.84 1.83 1.82 1.21 1.14
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
O
O
0.83 0.99 0.99 0.98 1.03 1.03 0.98 0.96 0.92
1.02 1.04 0.98 0.98 1.03 1.04 6.10 6.18
f1 (ppm)

E


154.69
153.79
144.99
133.81
129.63
127.19
126.88
126.68
126.64
122.49
119.98
117.08
110.55
106.35
83.74
63.69
44.96
29.09
24.91
24.45
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
O
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

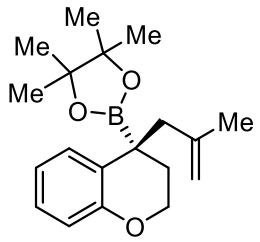
E


7.40 7.40 7.39 7.38 7.04 7.04 7.03 7.01 7.01 6.85 6.83 6.82 6.78 6.76
4.79 4.70 4.27 4.26 4.25 4.25 4.24 4.23 4.23 4.16 4.15 4.15 4.14 4.13 4.13 4.12 2.87 2.84
2.32 2.29 2.13 2.12 2.12 2.11 2.10 2.09 2.09 1.86 1.85 1.84 1.83 1.83 1.82 1.81 1.66
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
O
1.00 1.03 1.90 2.02 2.08 0.99 1.06 1.05 1.09 3.02 12.09
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

G

E

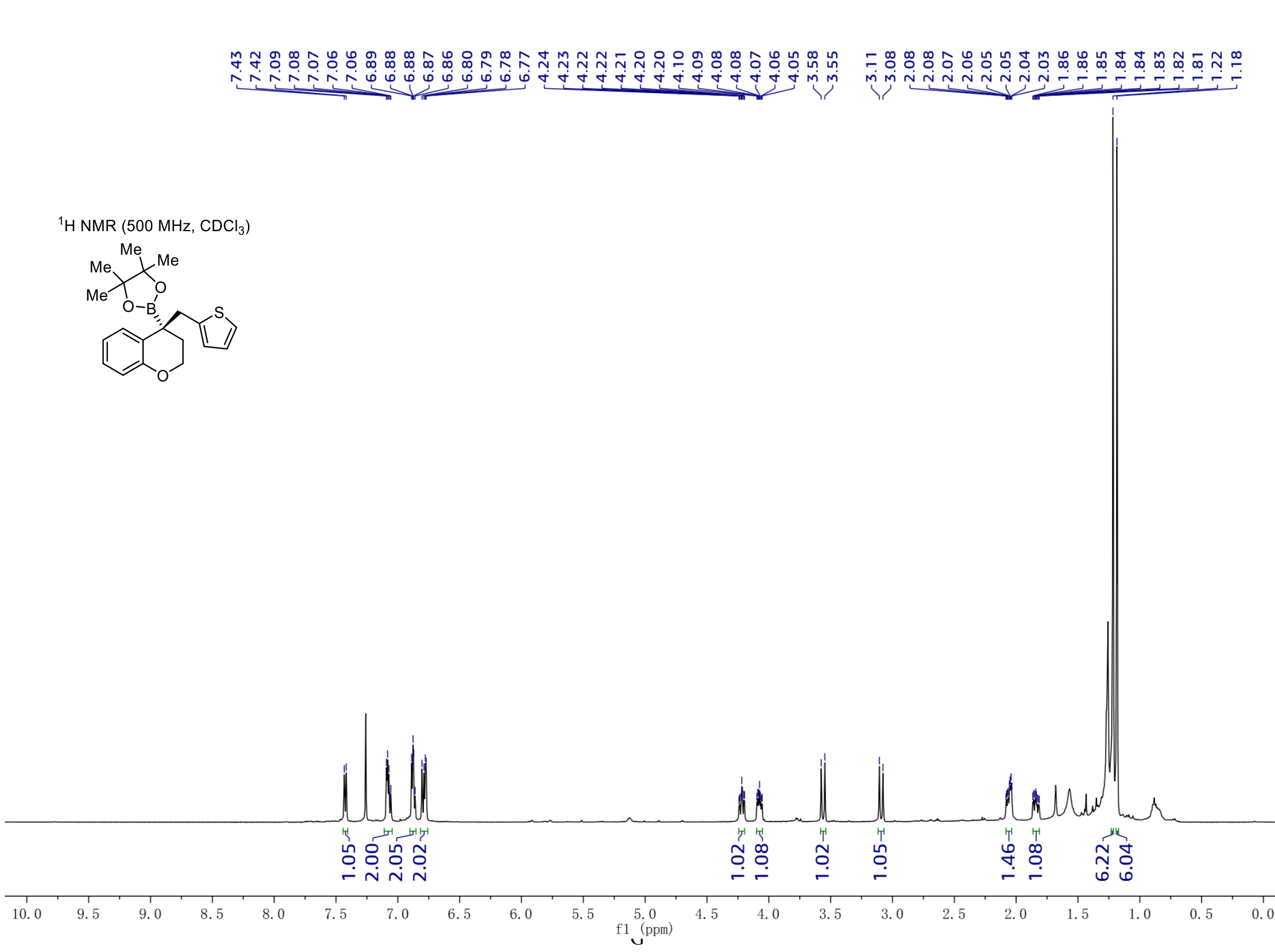
$^{13}$C NMR (126 MHz, $CDCl_3$)



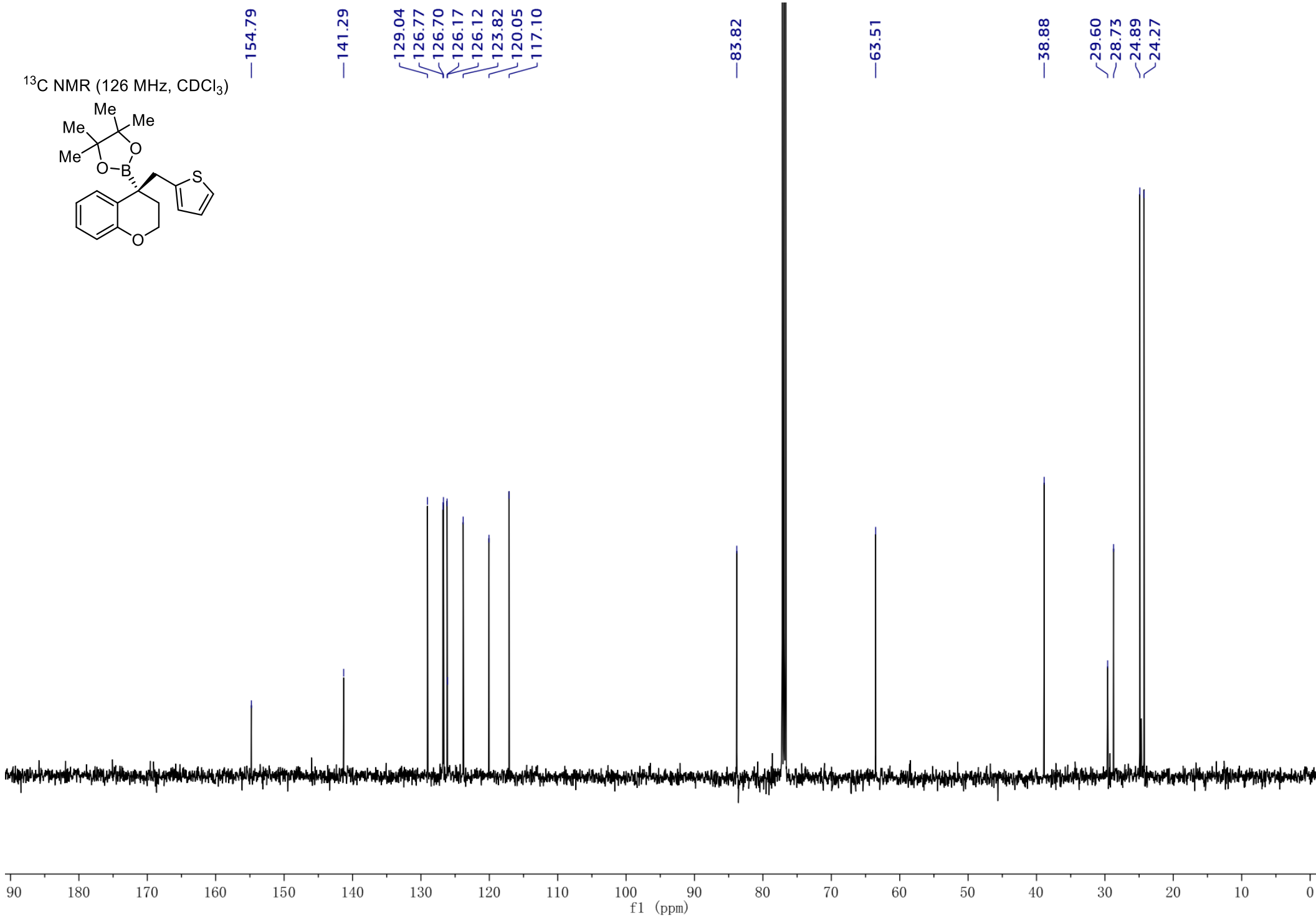

154.49
143.55
129.25
127.22
126.37
119.86
116.87
113.43
83.54
63.81
47.11
30.22
29.59
28.51
24.70
24.67
24.37
23.60



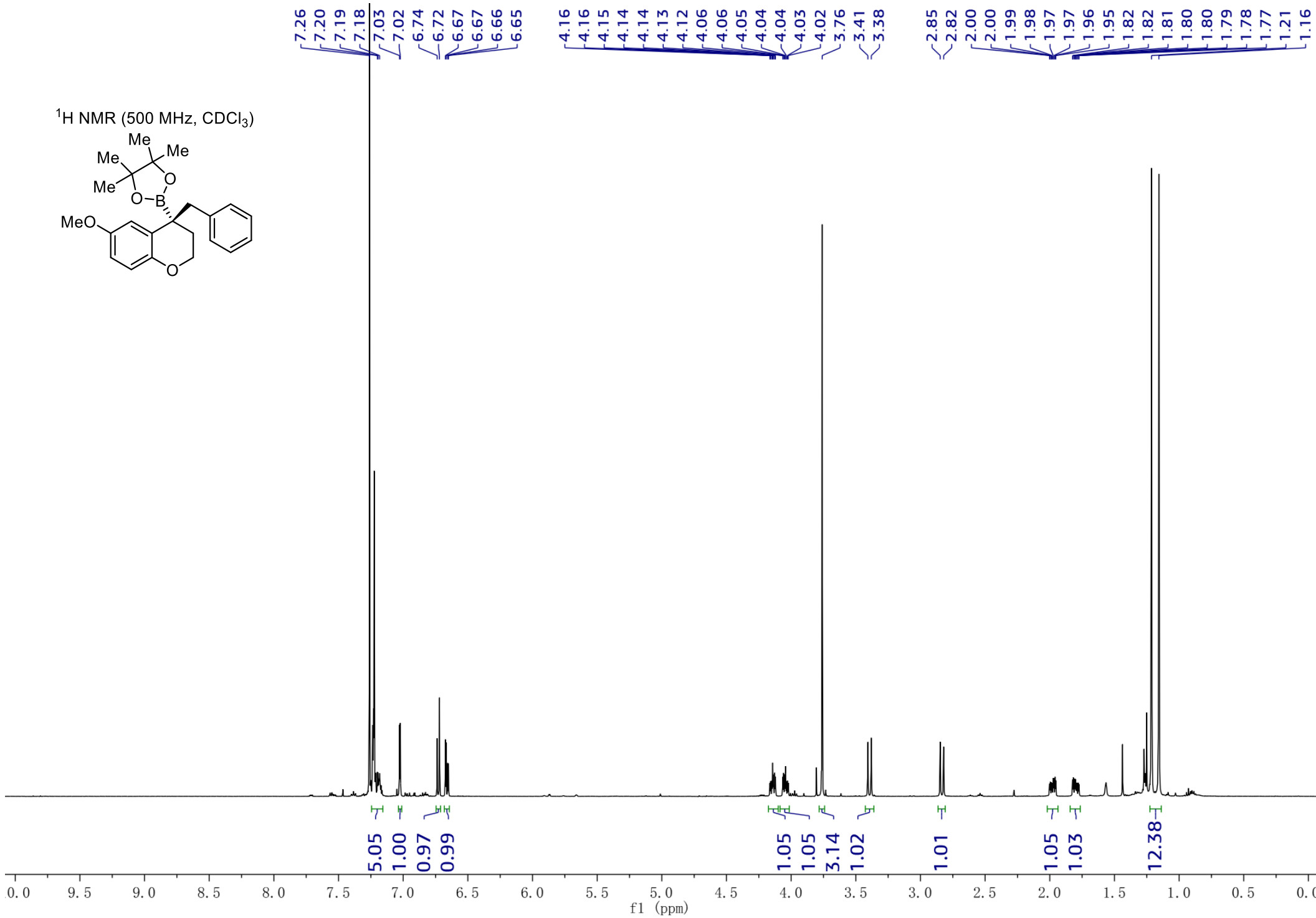

E


7.43
7.42
7.09
7.08
7.07
7.06
7.06
6.89
6.88
6.88
6.87
6.86
6.80
6.79
6.78
6.77
4.24
4.23
4.22
4.22
4.21
4.20
4.20
4.10
4.09
4.08
4.08
4.07
4.06
4.05
3.58
3.55
3.11
3.08
2.08
2.08
2.07
2.06
2.05
2.05
2.04
2.03
1.86
1.86
1.85
1.84
1.84
1.83
1.82
1.81
1.22
1.18
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
O
1.05
2.00
2.05
2.02
1.02
1.08
1.02
1.05
1.46
1.08
6.22
6.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

E

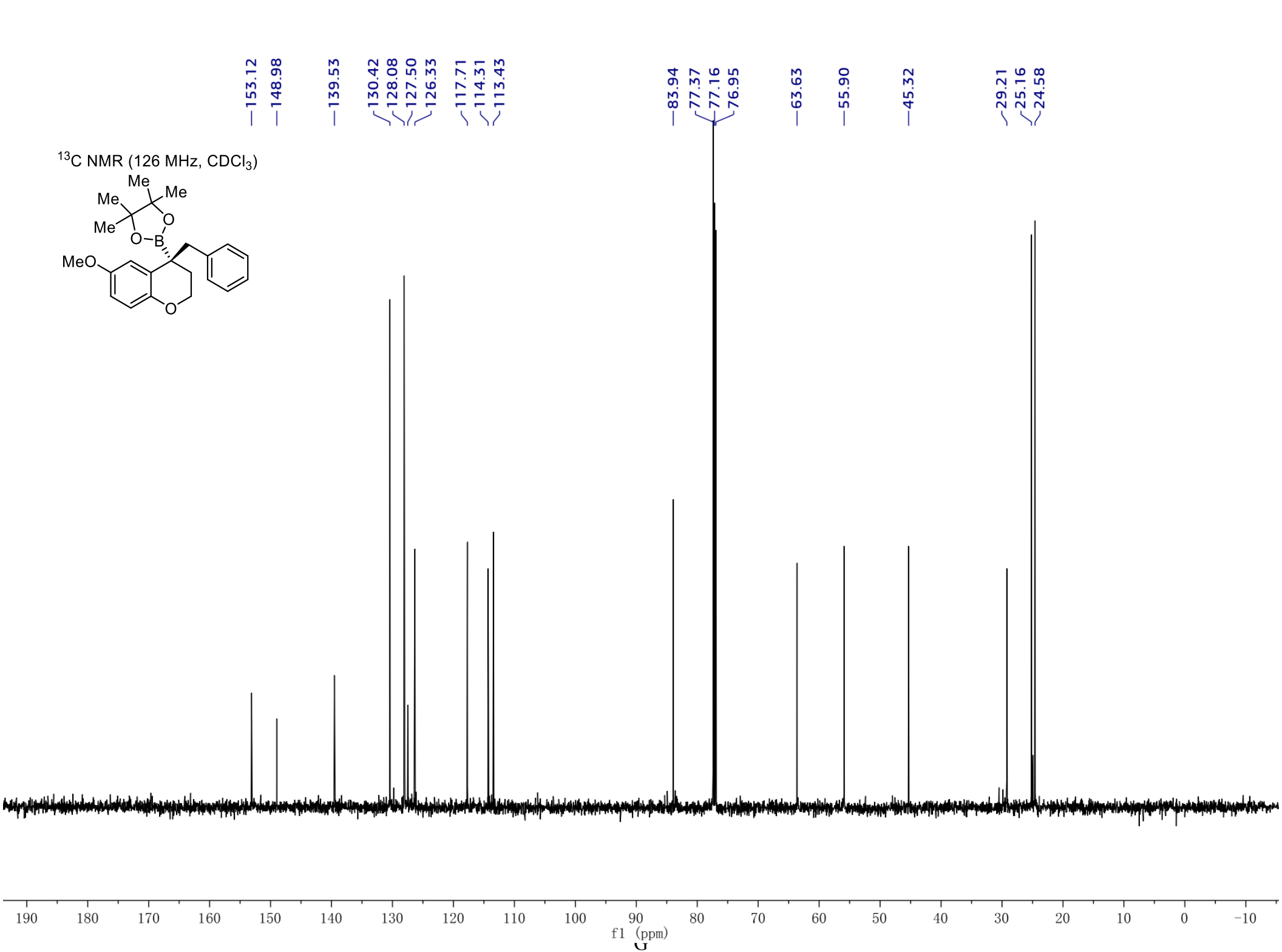

154.79
141.29
129.04
126.77
126.70
126.17
126.12
123.82
120.05
117.10
83.82
63.51
38.88
29.60
28.73
24.89
24.27
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
O
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E


$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
MeO
O
7.26 7.20 7.19 7.18 7.03 7.02 6.74 6.72 6.67 6.67 6.66 6.65
4.16 4.16 4.15 4.14 4.14 4.13 4.12 4.06 4.06 4.05 4.04 4.04 4.03 4.02 3.76 3.41 3.38
2.85 2.82 2.00 2.00 1.99 1.98 1.97 1.97 1.96 1.95 1.82 1.82 1.81 1.80 1.80 1.79 1.78 1.77 1.21 1.16
5.05 1.00 0.97 0.99 1.05 1.05 3.14 1.02 1.01 1.05 1.03 12.38
f1 (ppm)

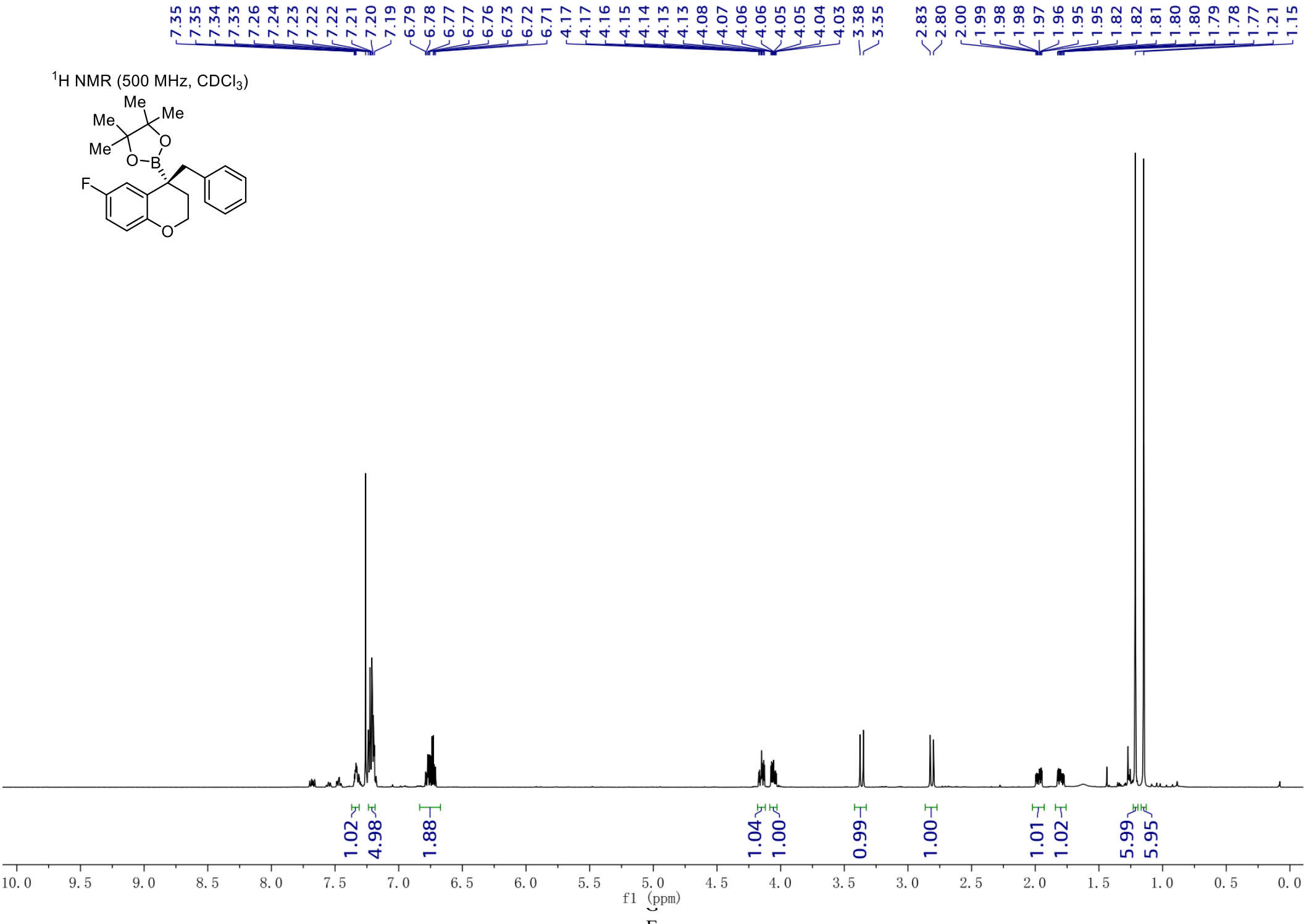
G

E

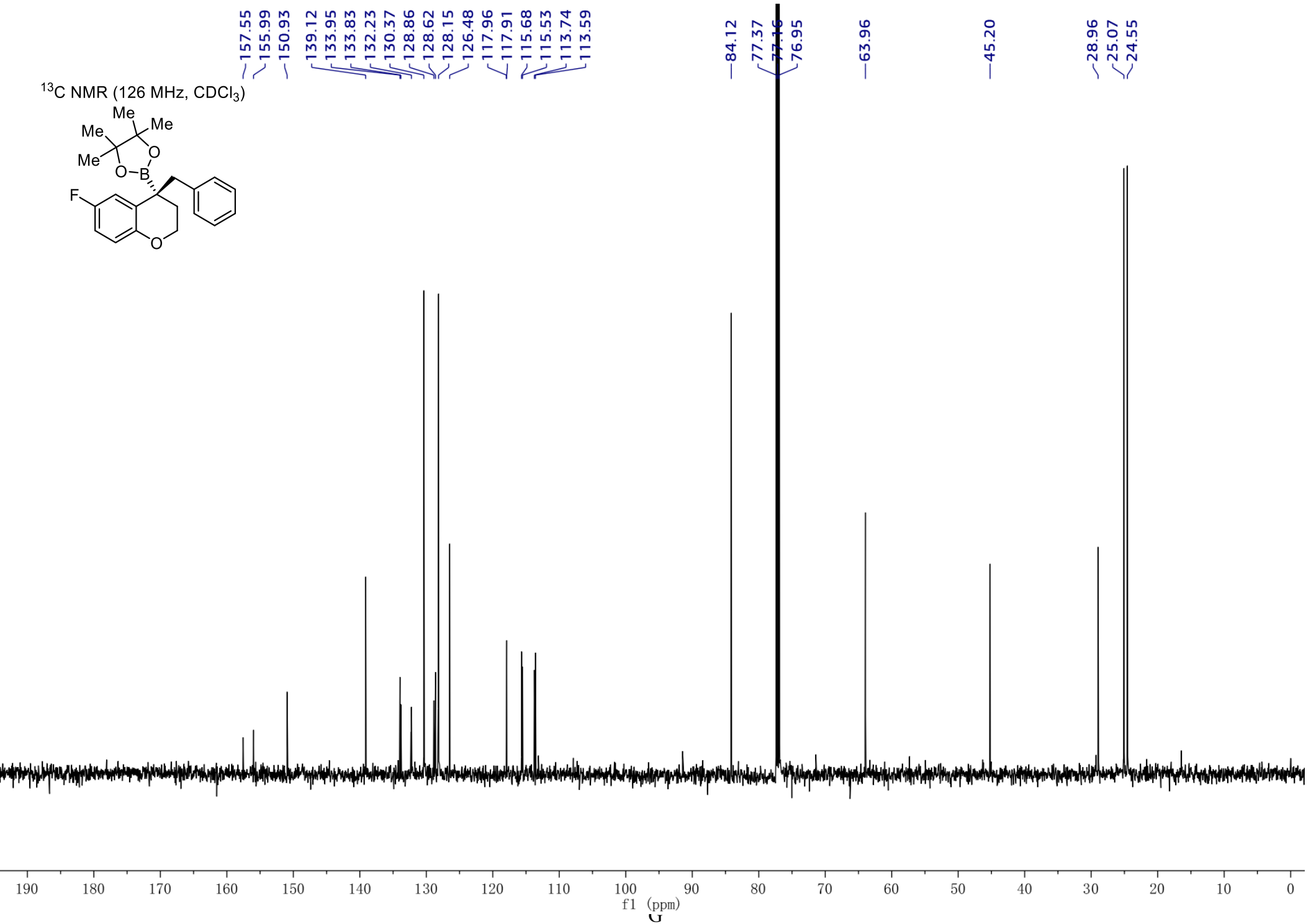

153.12
148.98
139.53
130.42
128.08
127.50
126.33
117.71
114.31
113.43
83.94
77.37
77.16
76.95
63.63
55.90
45.32
29.21
25.16
24.58
$^{13}$C NMR (126 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
MeO
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

G

E

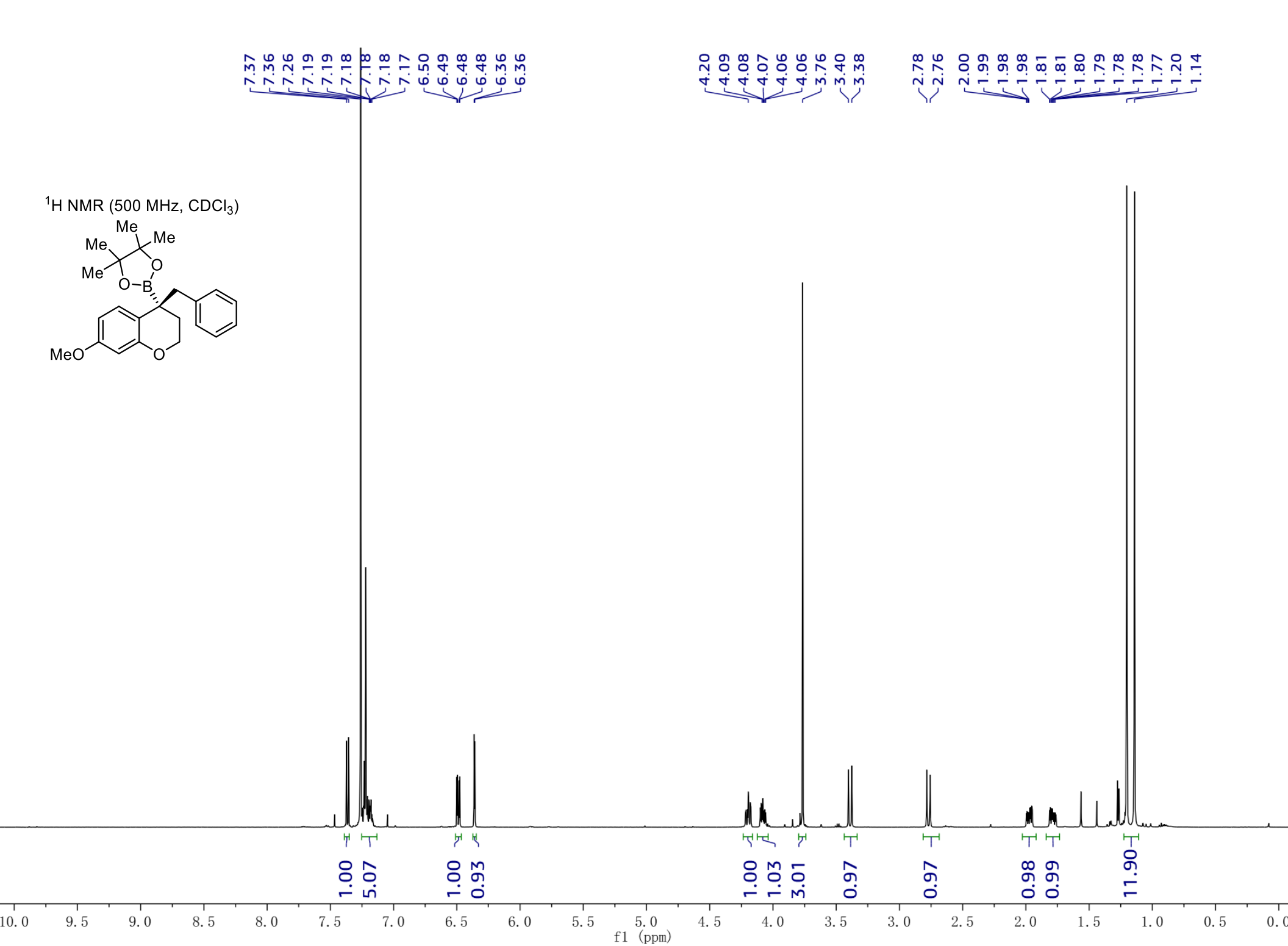

7.35 7.35 7.34 7.33 7.26 7.24 7.23 7.22 7.22 7.21 7.20 7.19 6.79 6.78 6.77 6.77 6.76 6.73 6.72 6.71 4.17 4.17 4.16 4.15 4.14 4.13 4.13 4.08 4.07 4.06 4.06 4.05 4.05 4.04 4.03 3.38 3.35 2.83 2.80 2.00 1.99 1.98 1.98 1.97 1.96 1.95 1.95 1.82 1.82 1.81 1.80 1.80 1.79 1.78 1.77 1.21 1.15
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
F
O
1.02 4.98 1.88 1.04 1.00 0.99 1.00 1.01 1.02 5.99 5.95
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

E


157.55
155.99
150.93
139.12
133.95
133.83
132.23
130.37
128.86
128.62
128.15
126.48
117.96
117.91
115.68
115.53
113.74
113.59
84.12
77.37
77.16
76.95
63.96
45.20
28.96
25.07
24.55
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
F
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

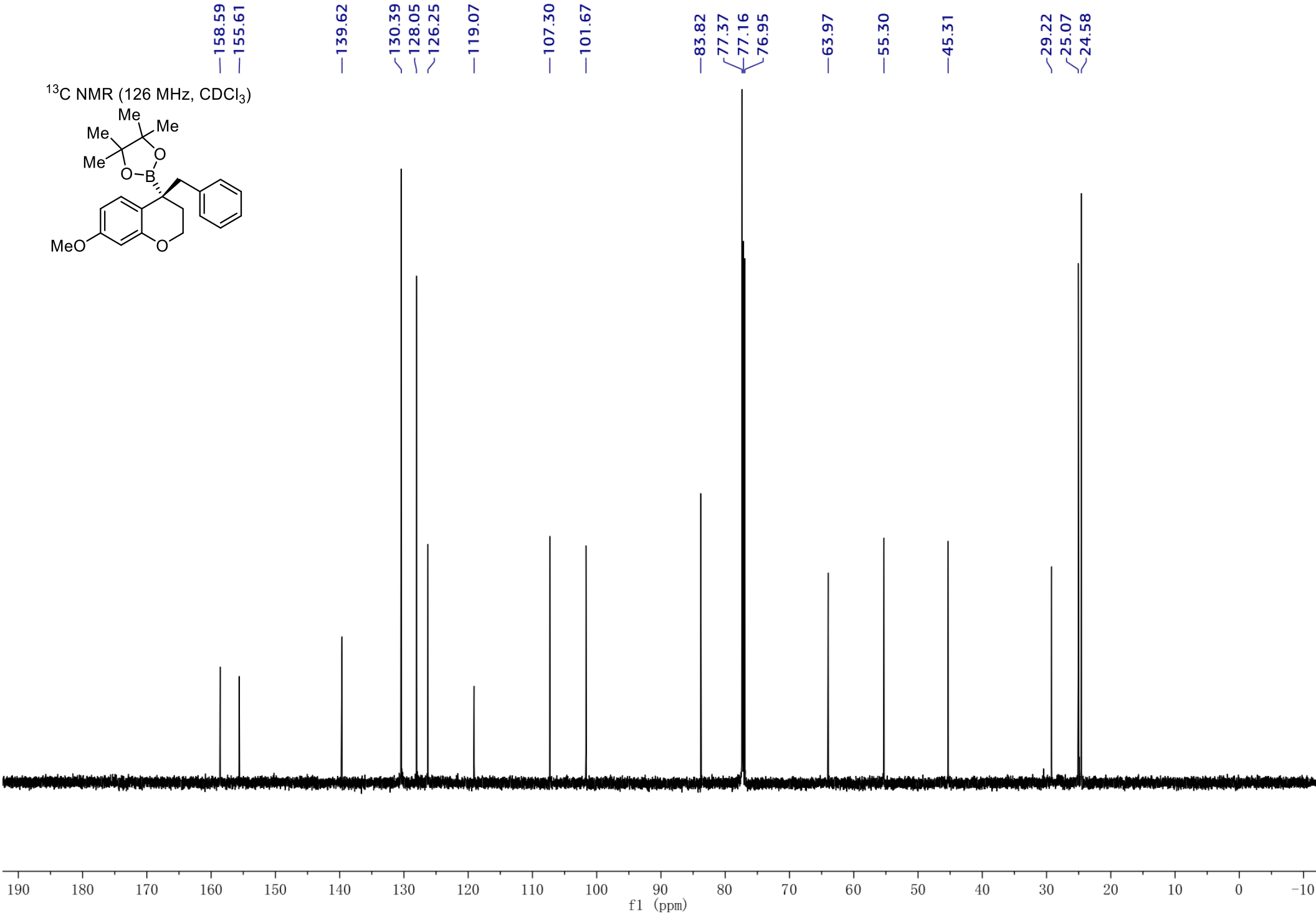
G

E

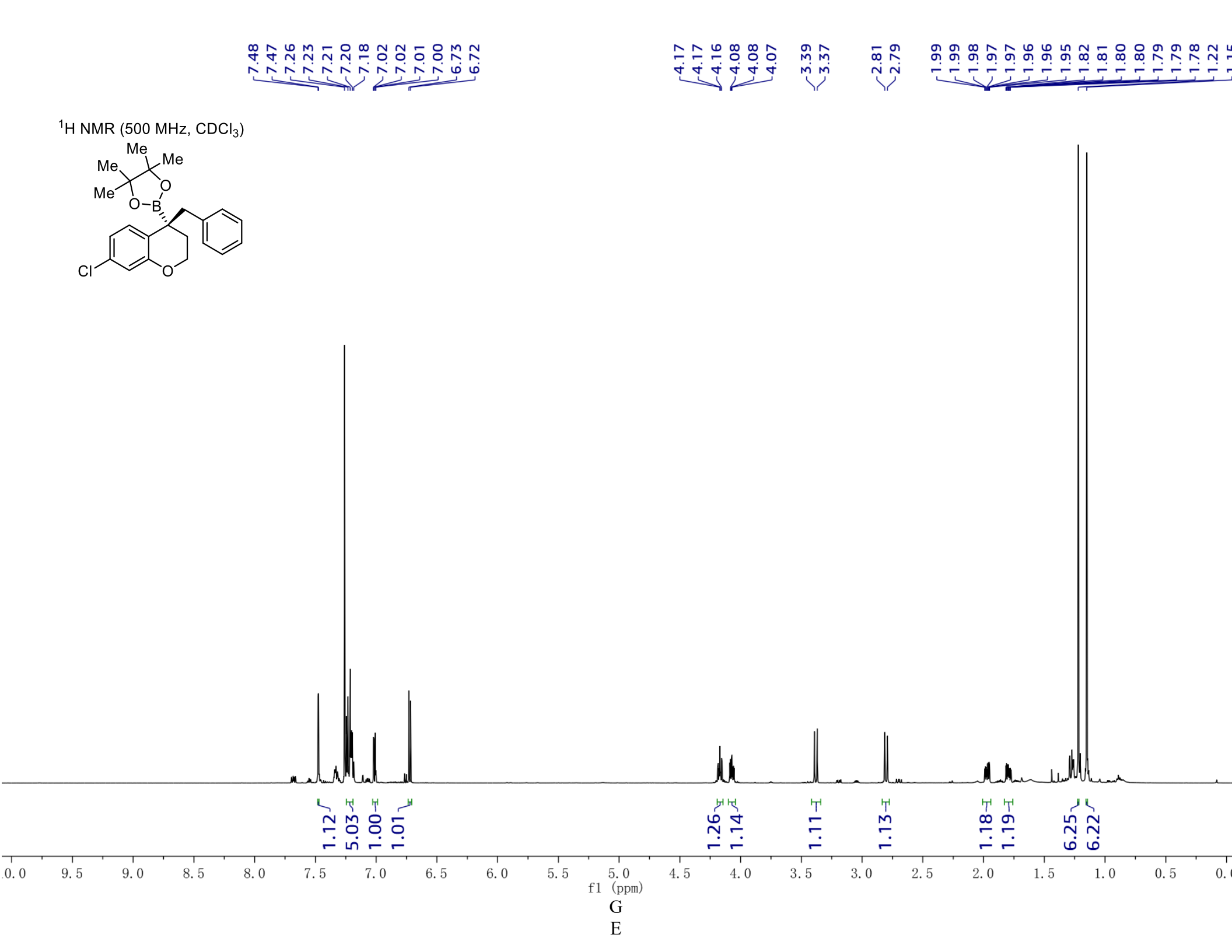

7.37
7.36
7.26
7.19
7.19
7.18
7.18
7.18
7.17
6.50
6.49
6.48
6.48
6.36
6.36
4.20
4.09
4.08
4.07
4.06
4.06
3.76
3.40
3.38
2.78
2.76
2.00
1.99
1.98
1.98
1.81
1.81
1.80
1.79
1.78
1.78
1.77
1.20
1.14
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
O
1.00
5.07
1.00
0.93
1.00
1.03
3.01
0.97
0.97
0.98
0.99
11.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E

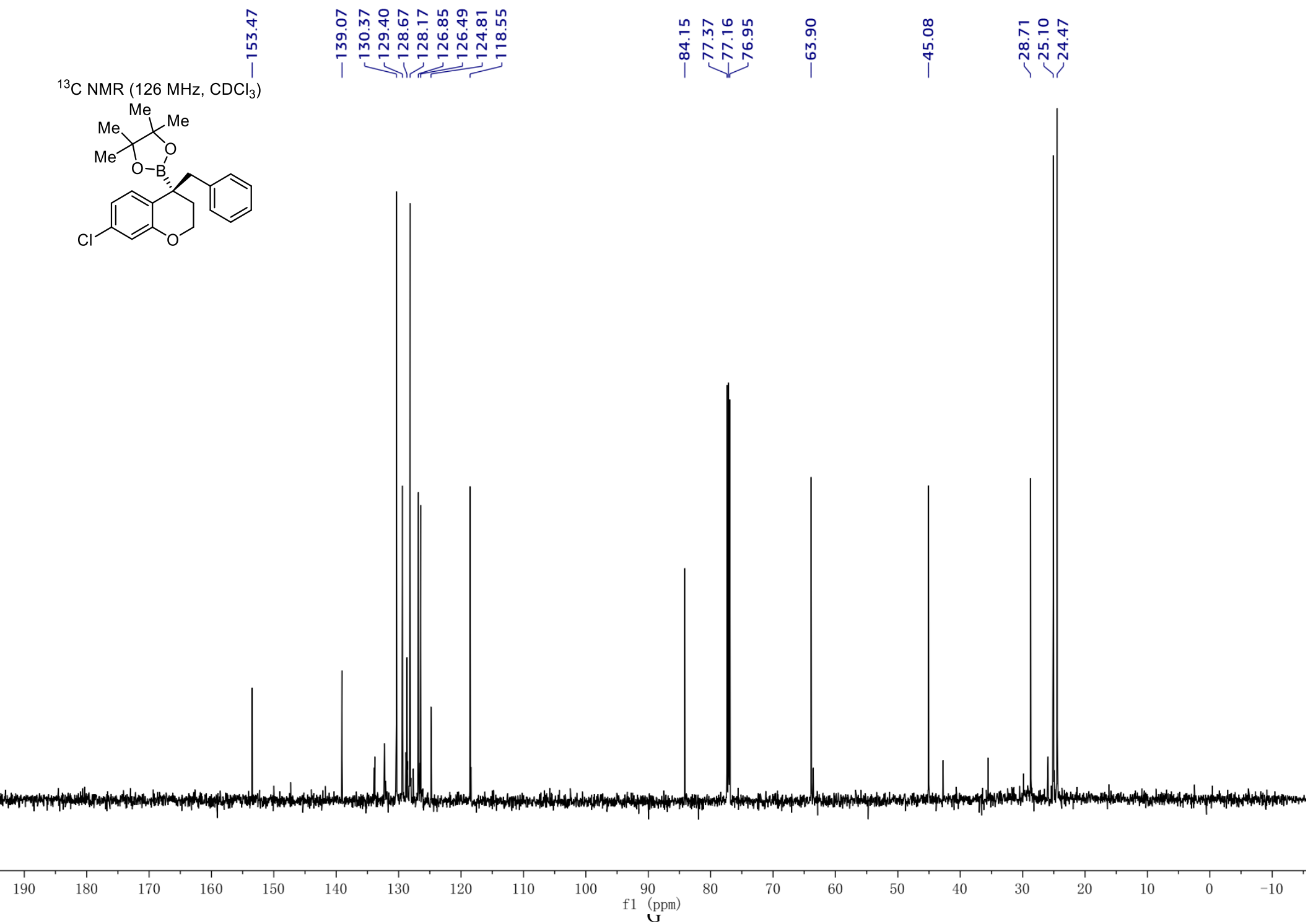

158.59
155.61
139.62
130.39
128.05
126.25
119.07
107.30
101.67
83.82
77.37
77.16
76.95
63.97
55.30
45.31
29.22
25.07
24.58
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O–B
MeO
O
f1 (ppm)

E


7.48
7.47
7.26
7.23
7.21
7.20
7.18
7.02
7.02
7.01
7.00
6.73
6.72
4.17
4.17
4.16
4.08
4.08
4.07
3.39
3.37
2.81
2.79
1.99
1.99
1.98
1.97
1.97
1.96
1.96
1.95
1.82
1.81
1.80
1.80
1.79
1.79
1.78
1.22
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Cl
O
1.12
5.03
1.00
1.01
1.26
1.14
1.11
1.13
1.18
1.19
6.25
6.22
f1 (ppm)

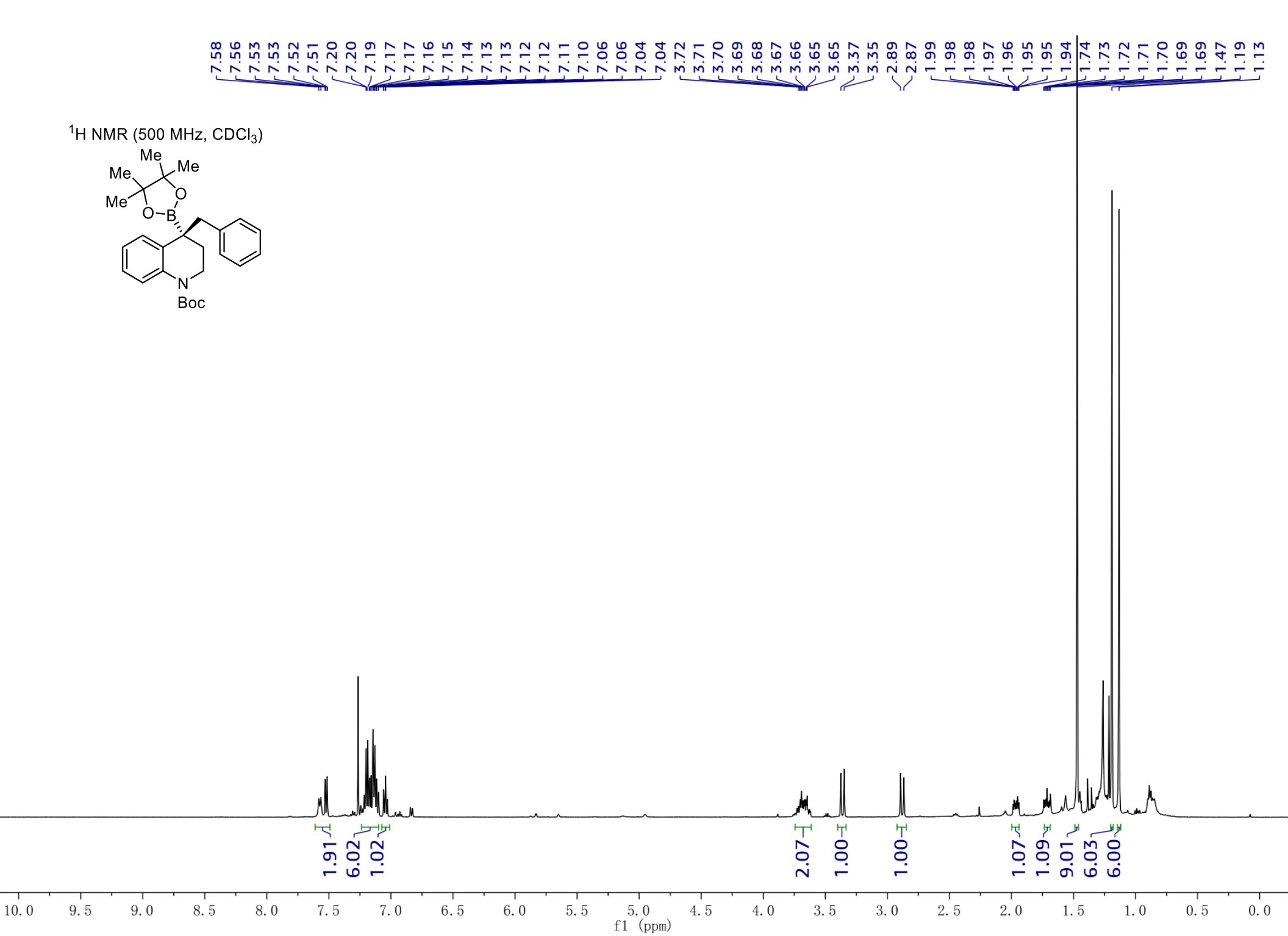
G

E


153.47
139.07
130.37
129.40
128.67
128.17
126.85
126.49
124.81
118.55
84.15
77.37
77.16
76.95
63.90
45.08
28.71
25.10
24.47
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Cl
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

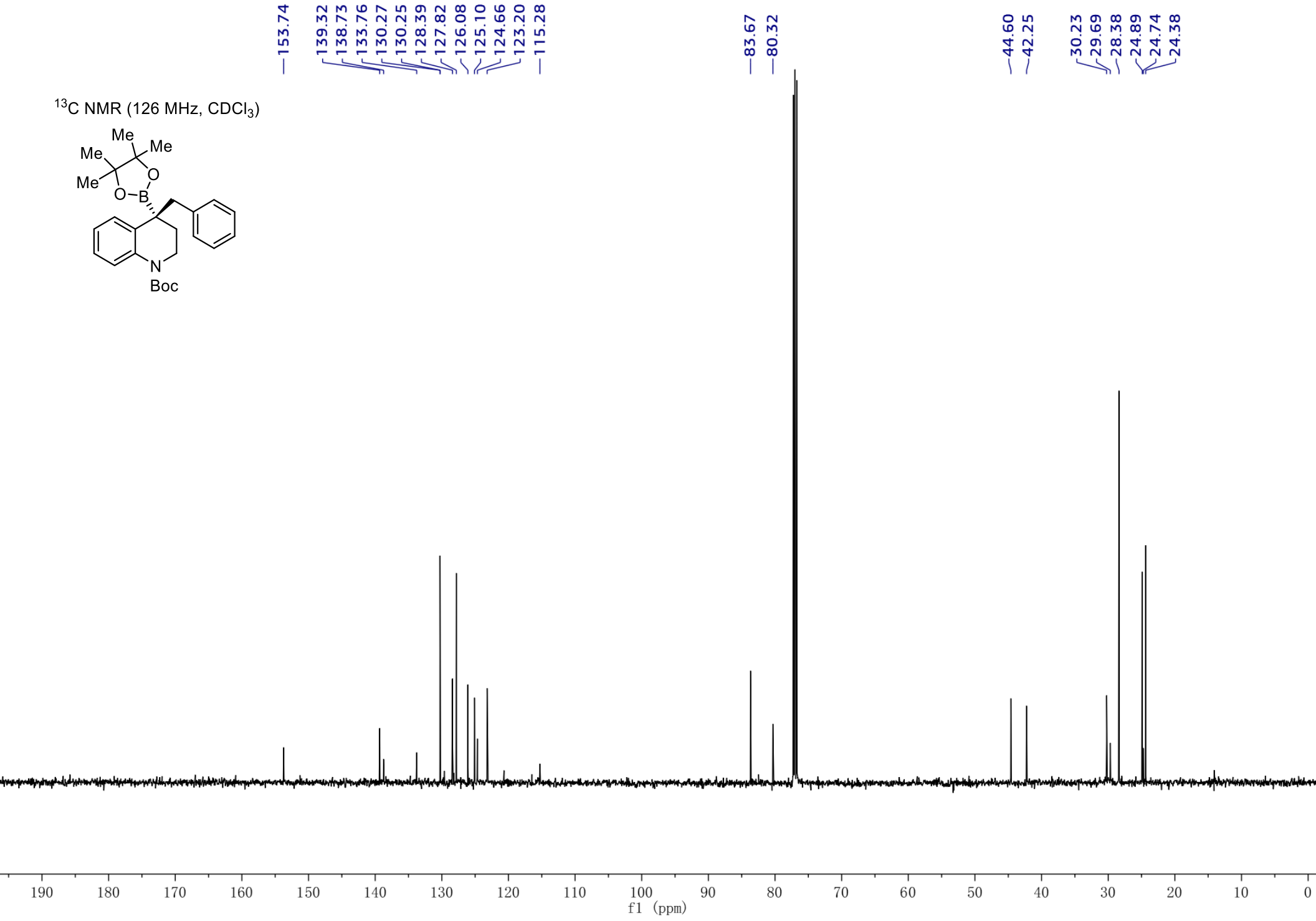
G

E

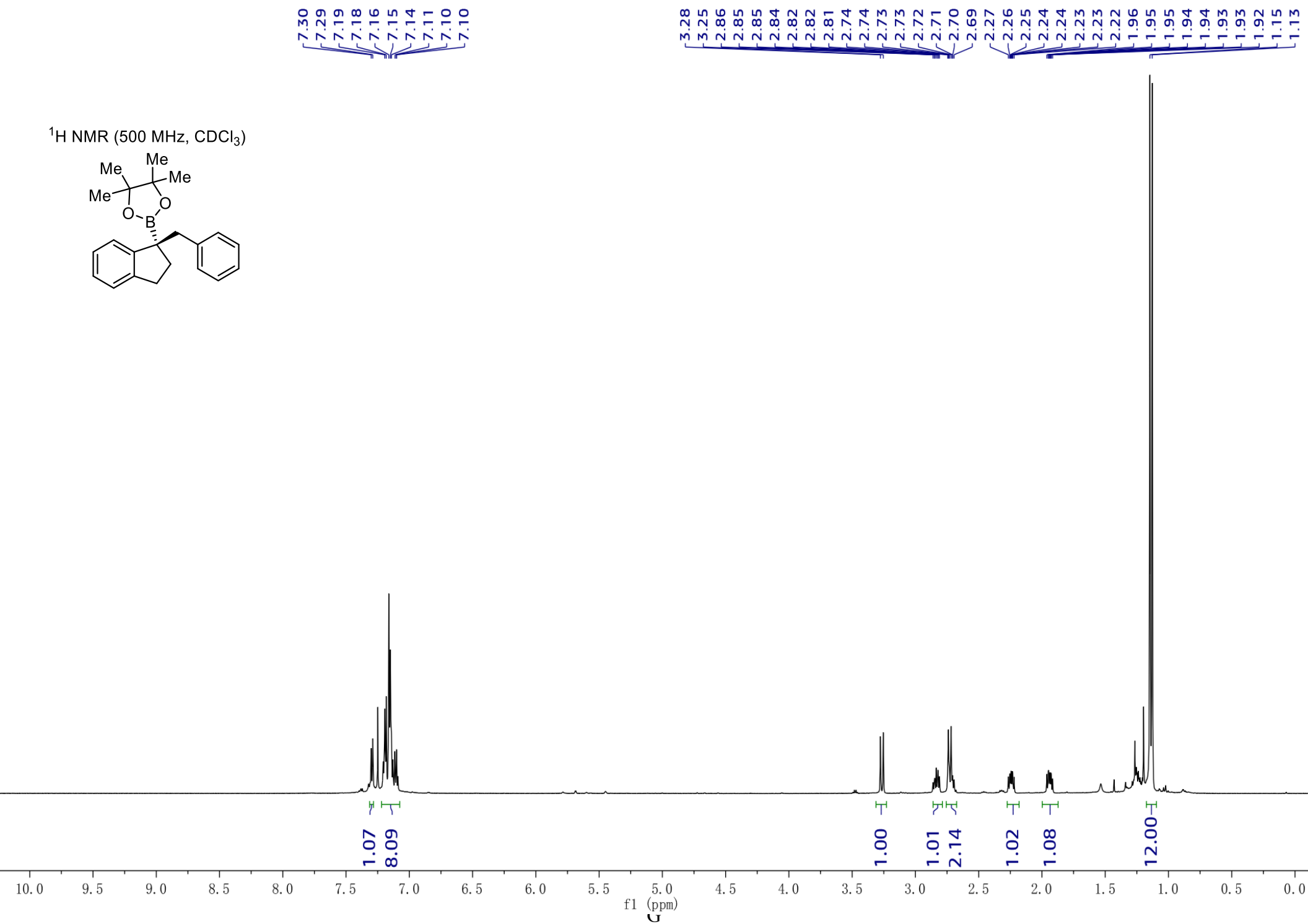

7.58 7.56 7.53 7.53 7.52 7.51 7.20 7.20 7.19 7.17 7.17 7.16 7.15 7.14 7.13 7.13 7.12 7.12 7.11 7.10 7.06 7.06 7.04 7.04
3.72 3.71 3.70 3.69 3.68 3.67 3.66 3.65 3.65 3.37 3.35 2.89 2.87
1.99 1.98 1.98 1.97 1.96 1.95 1.95 1.94 1.74 1.73 1.72 1.71 1.70 1.69 1.69 1.47 1.19 1.13
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
N
Boc
1.91 6.02 1.02 2.07 1.00 1.00 1.07 1.09 9.01 6.03 6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

G

E


153.74
139.32
138.73
133.76
130.27
130.25
128.39
127.82
126.08
125.10
124.66
123.20
115.28
83.67
80.32
44.60
42.25
30.23
29.69
28.38
24.89
24.74
24.38
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
Boc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

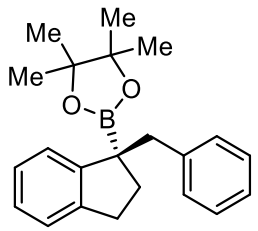
E


7.30
7.29
7.19
7.18
7.16
7.15
7.14
7.11
7.10
7.10
3.28
3.25
2.86
2.85
2.85
2.84
2.82
2.82
2.81
2.74
2.74
2.73
2.73
2.72
2.71
2.70
2.69
2.27
2.26
2.25
2.24
2.24
2.23
2.23
2.22
1.96
1.95
1.95
1.94
1.94
1.93
1.93
1.92
1.15
1.13
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
1.07
8.09
1.00
1.01
2.14
1.02
1.08
12.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E

$^{13}$C NMR (126 MHz, $CDCl_3$)

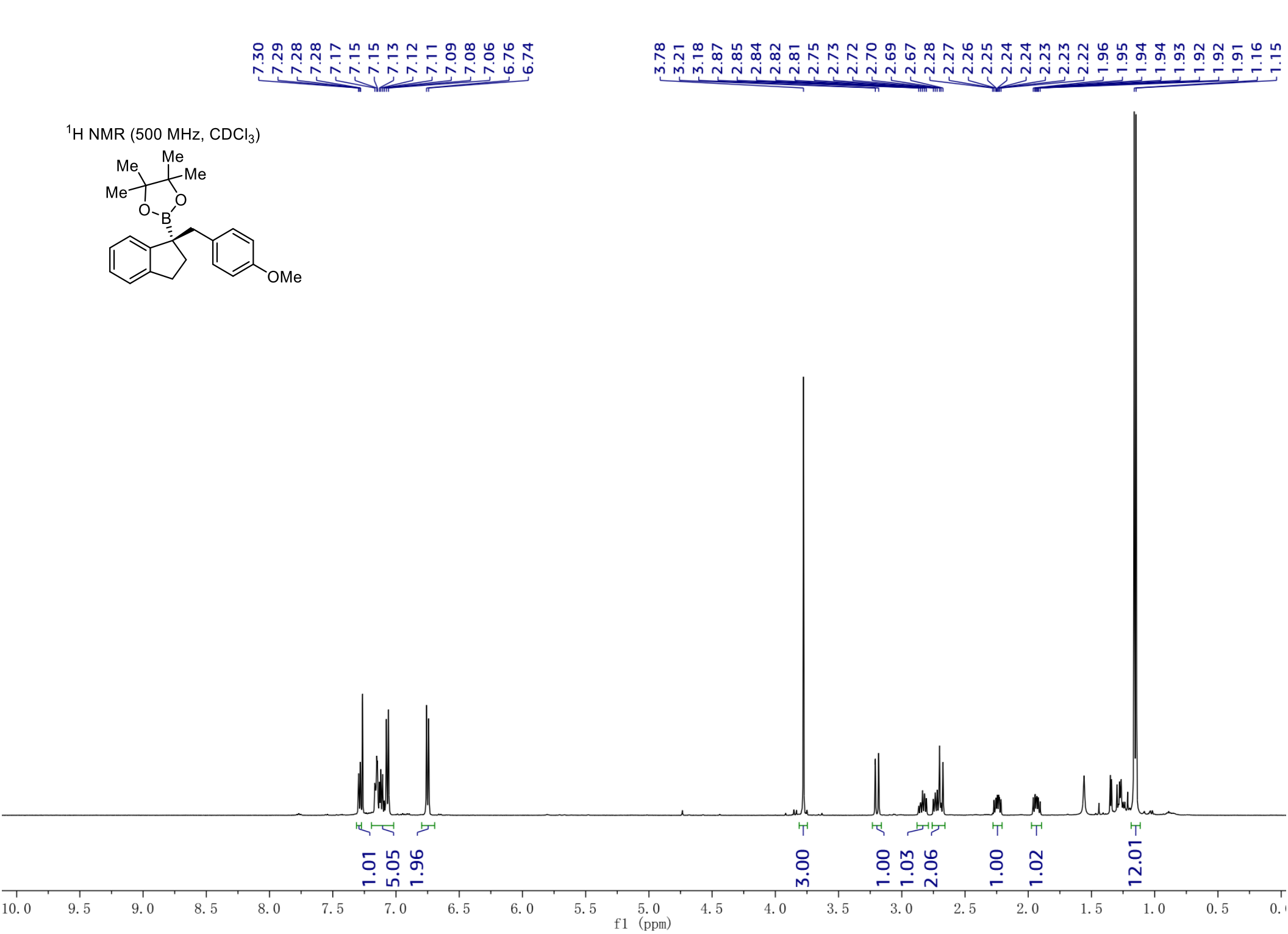



148.45
144.09
140.48
129.82
127.75
125.93
125.90
125.80
124.38
124.30
83.42
43.69
33.36
31.38
24.78
24.76
24.51

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

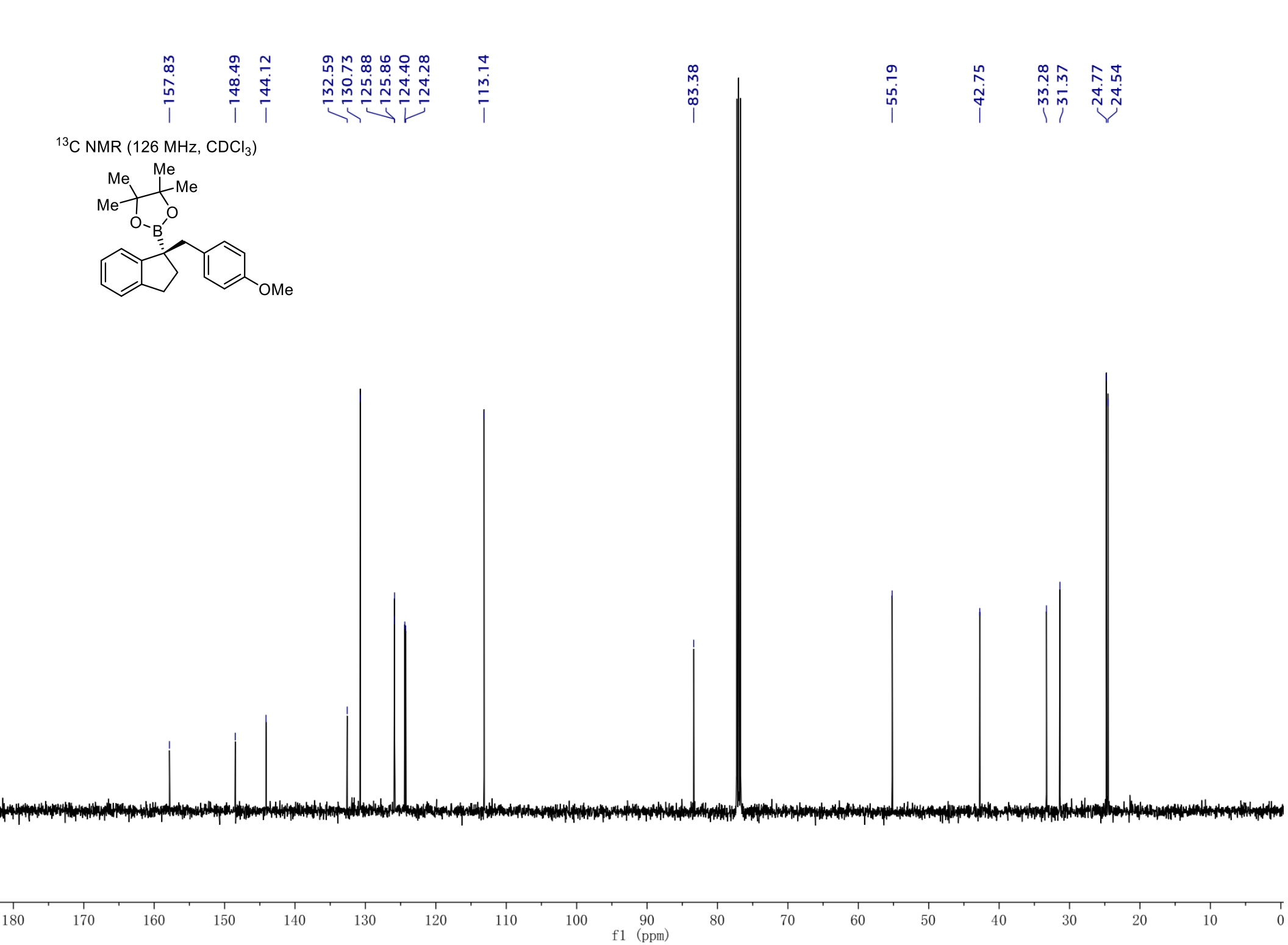
f1 (ppm)

E


7.30
7.29
7.28
7.28
7.17
7.15
7.15
7.13
7.12
7.11
7.09
7.08
7.06
6.76
6.74
3.78
3.21
3.18
2.87
2.85
2.84
2.82
2.81
2.75
2.73
2.72
2.70
2.69
2.67
2.28
2.27
2.26
2.25
2.24
2.24
2.23
2.23
2.22
1.96
1.95
1.94
1.94
1.93
1.92
1.92
1.91
1.16
1.15
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
1.01
5.05
1.96
3.00
1.00
1.03
2.06
1.00
1.02
12.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

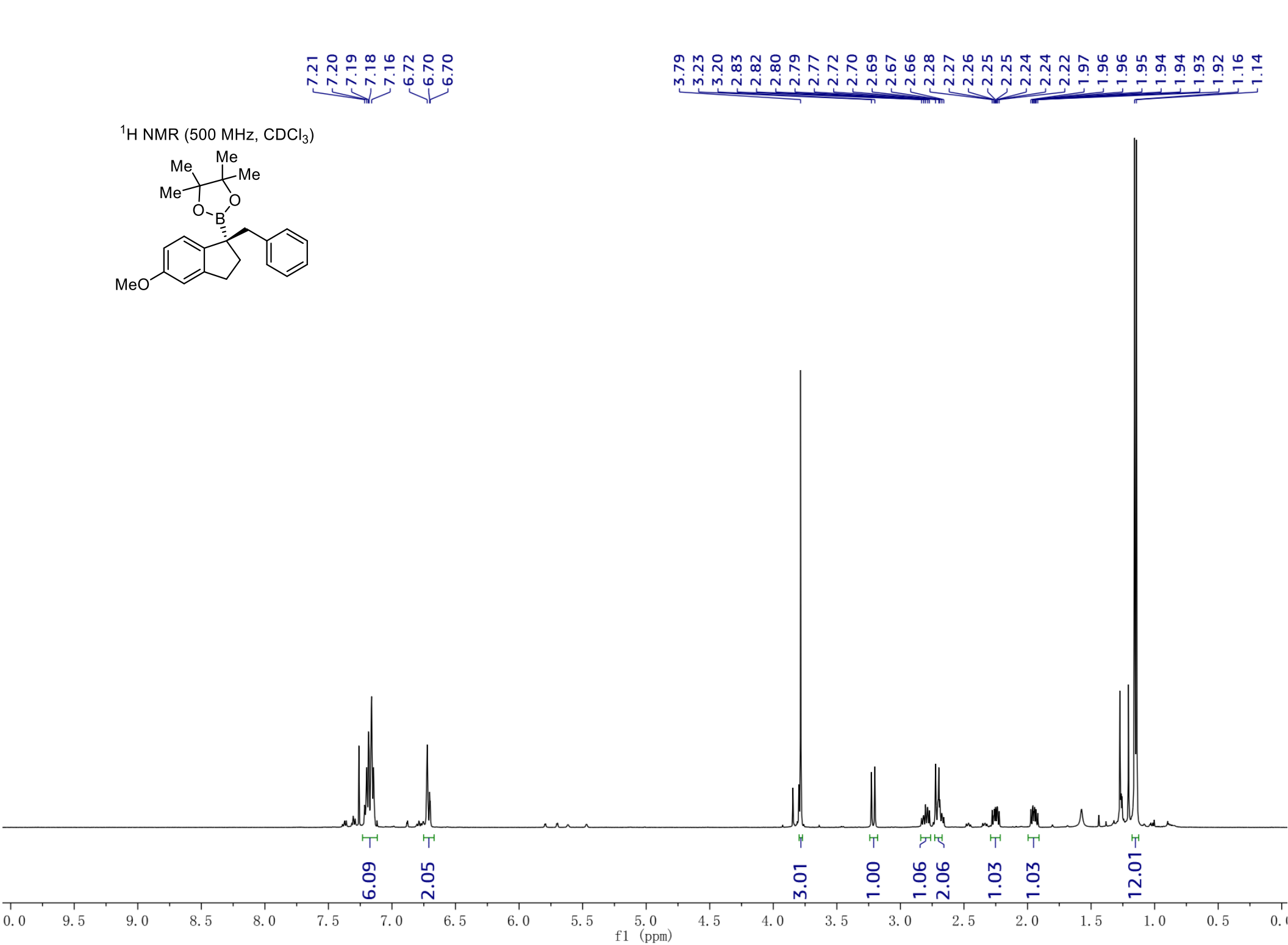
G

E


157.83
148.49
144.12
132.59
130.73
125.88
125.86
124.40
124.28
113.14
83.38
55.19
42.75
33.28
31.37
24.77
24.54
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
OMe
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

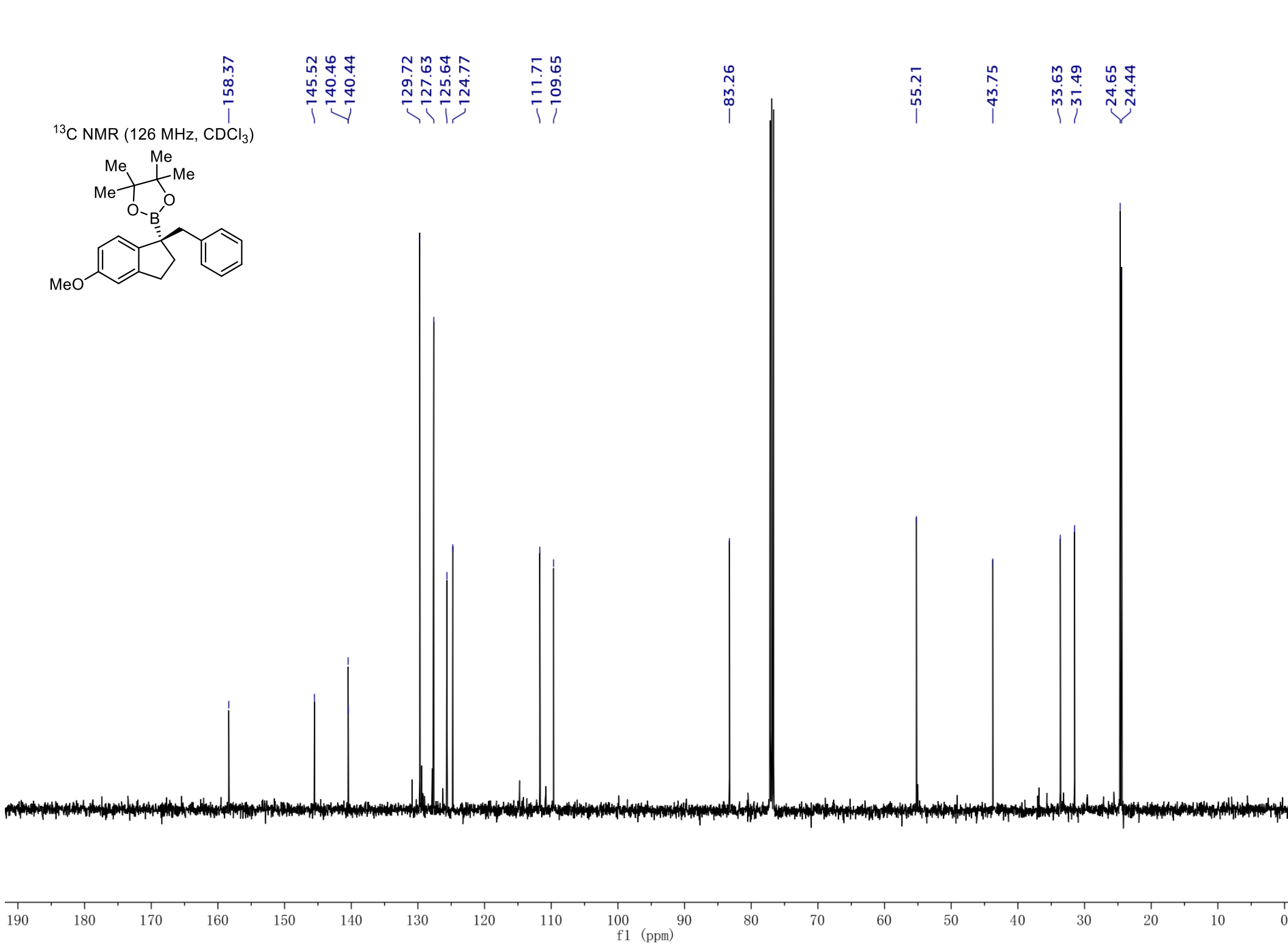
G

E


7.21
7.20
7.19
7.18
7.16
6.72
6.70
6.70
3.79
3.23
3.20
2.83
2.82
2.80
2.79
2.77
2.72
2.70
2.69
2.67
2.66
2.28
2.27
2.26
2.25
2.25
2.24
2.24
2.22
1.97
1.96
1.96
1.95
1.94
1.94
1.93
1.92
1.16
1.14
$^1$H NMR (500 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
MeO
6.09
2.05
3.01
1.00
1.06
2.06
1.03
1.03
12.01
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

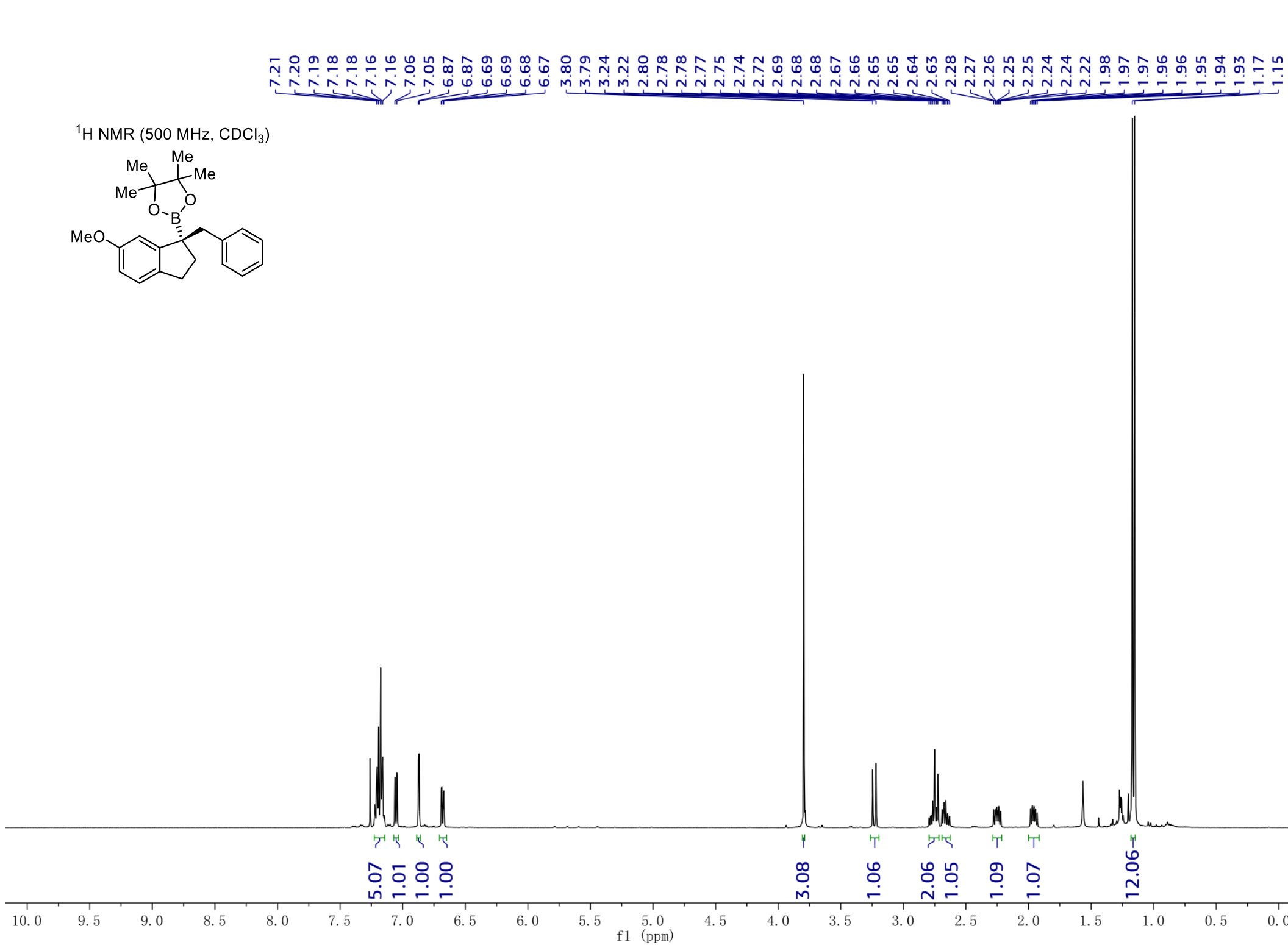
G

E


158.37
145.52
140.46
140.44
129.72
127.63
125.64
124.77
111.71
109.65
83.26
55.21
43.75
33.63
31.49
24.65
24.44
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

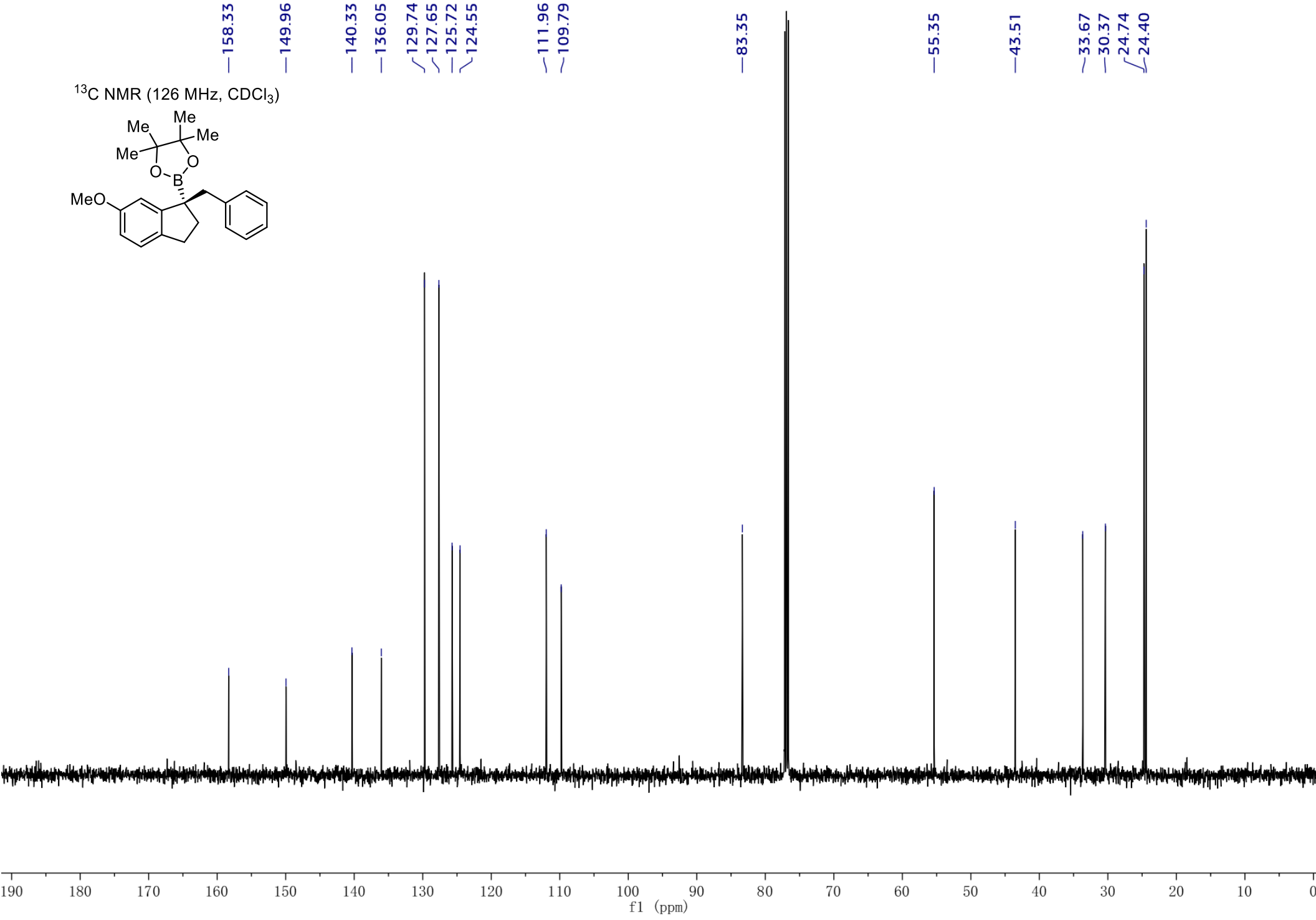
G

E

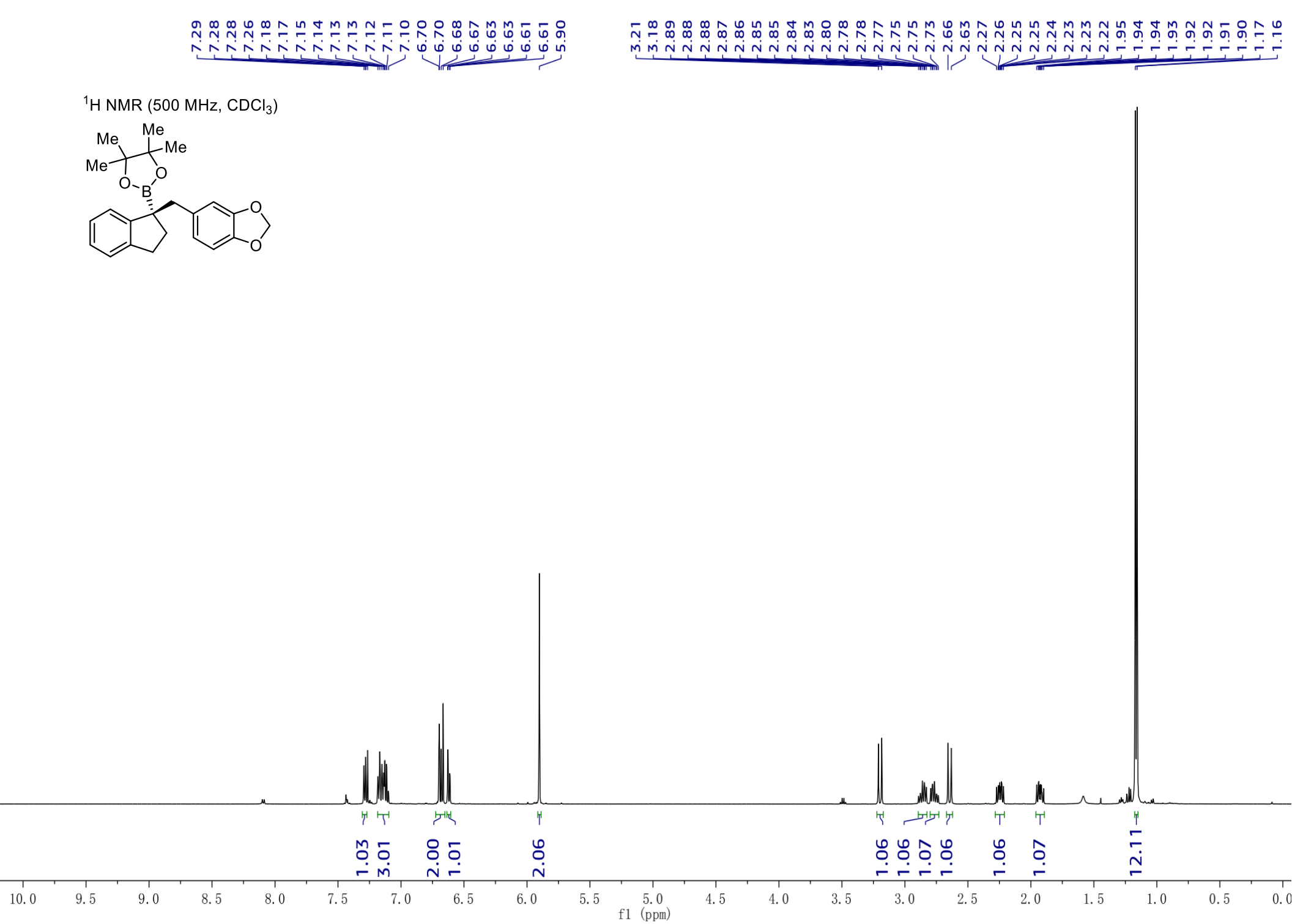

7.21 7.20 7.19 7.18 7.18 7.16 7.16 7.06 7.05 6.87 6.87 6.69 6.69 6.68 6.67 3.80 3.79 3.24 3.22 2.80 2.78 2.78 2.77 2.75 2.74 2.72 2.69 2.68 2.68 2.67 2.66 2.65 2.65 2.64 2.63 2.28 2.27 2.26 2.25 2.25 2.24 2.24 2.22 1.98 1.97 1.97 1.96 1.96 1.95 1.94 1.93 1.17 1.15
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
MeO
5.07
1.01
1.00
1.00
3.08
1.06
2.06
1.05
1.09
1.07
12.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

G

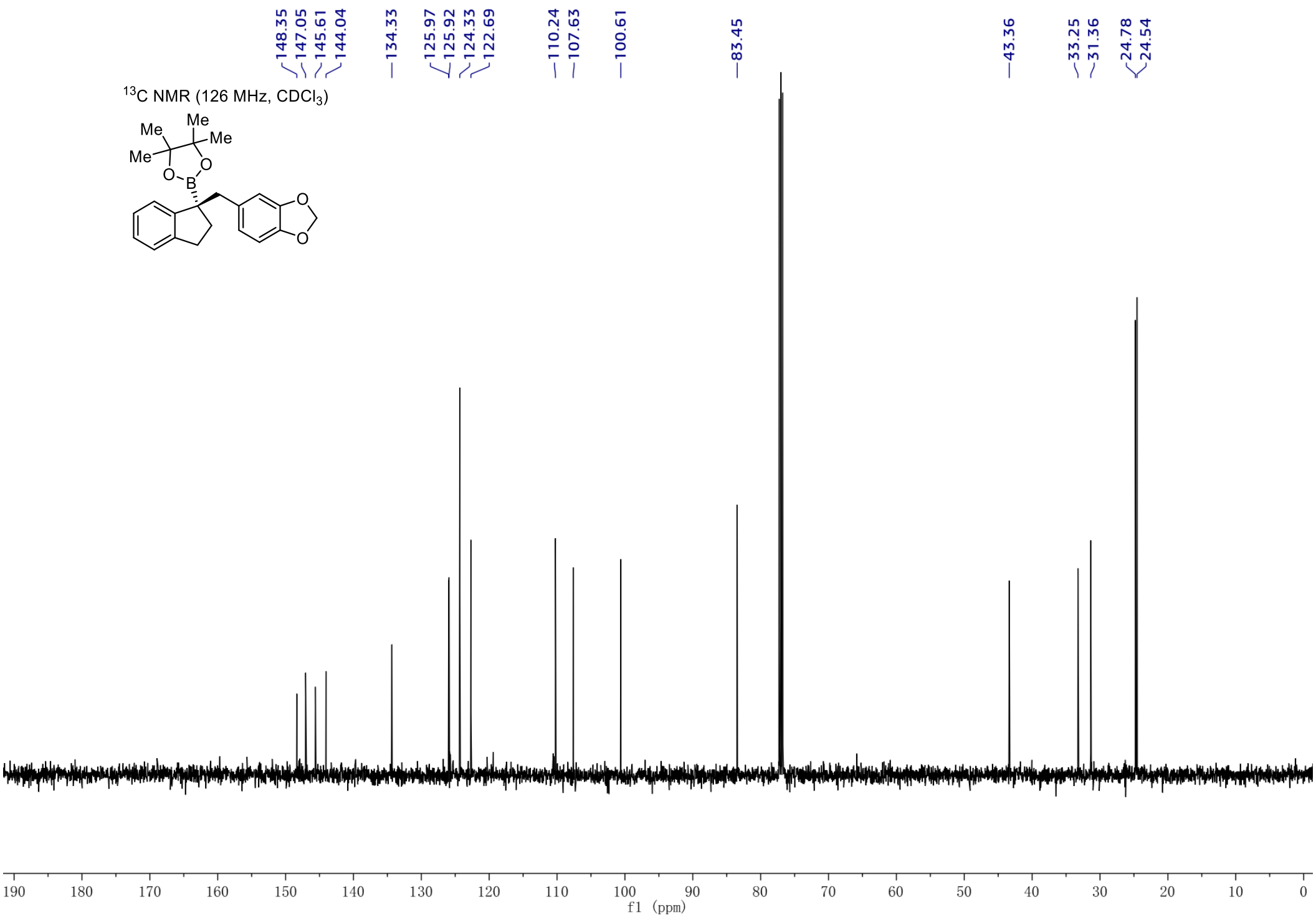
E


158.33
149.96
140.33
136.05
129.74
127.65
125.72
124.55
111.96
109.79
83.35
55.35
43.51
33.67
30.37
24.74
24.40
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

E

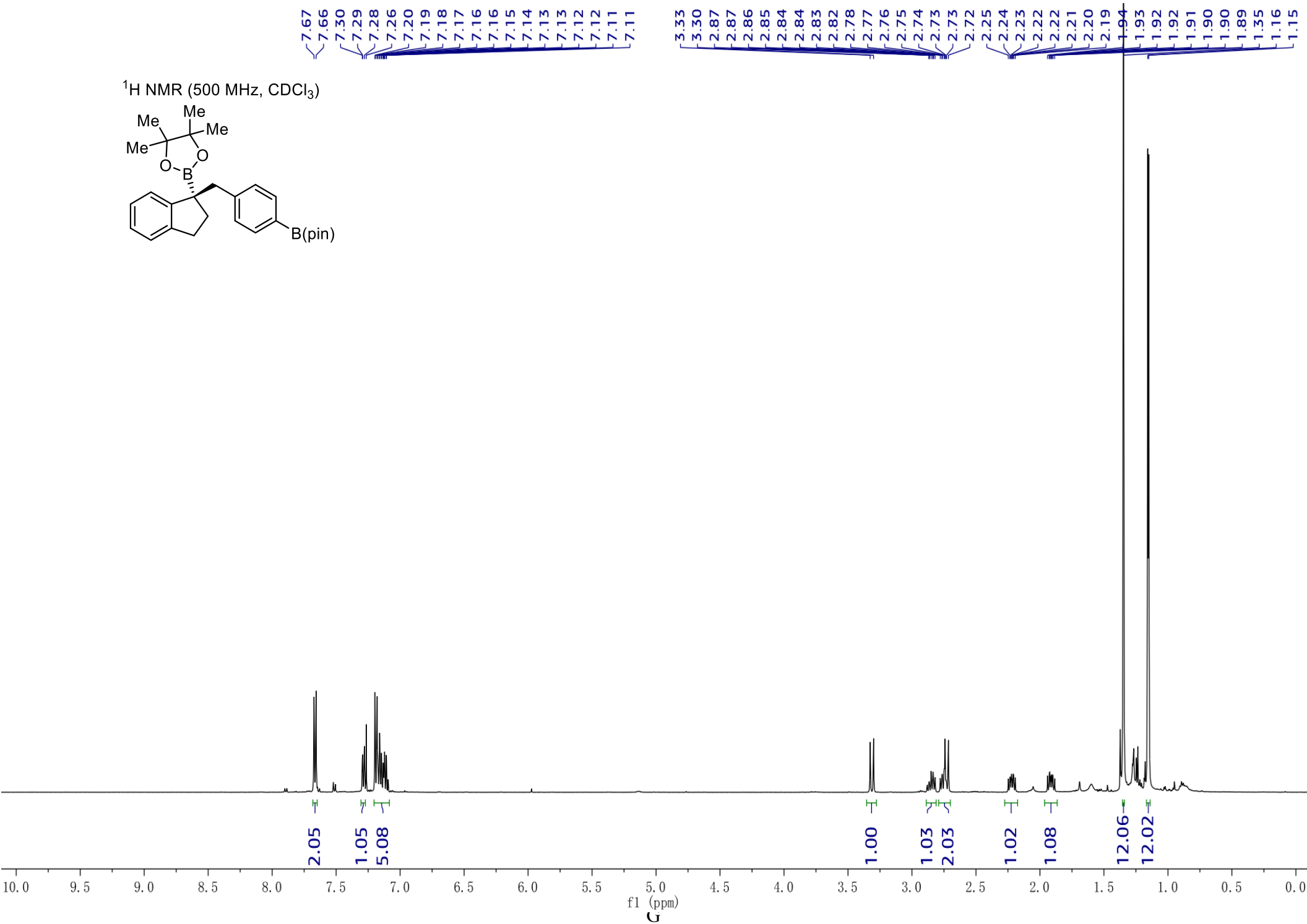

7.29 7.28 7.28 7.26 7.18 7.17 7.15 7.14 7.13 7.13 7.12 7.11 7.10 6.70 6.70 6.68 6.67 6.63 6.63 6.61 6.61 5.90
3.21 3.18 2.89 2.88 2.88 2.87 2.86 2.85 2.85 2.84 2.83 2.80 2.78 2.78 2.77 2.75 2.75 2.73 2.66 2.63 2.27 2.26 2.25 2.25 2.24 2.23 2.23 2.22 1.95 1.94 1.94 1.93 1.92 1.92 1.91 1.90 1.17 1.16
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
O
O
1.03 3.01 2.00 1.01 2.06 1.06 1.06 1.07 1.06 1.06 1.07 12.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

E


148.35
147.05
145.61
144.04
134.33
125.97
125.92
124.33
122.69
110.24
107.63
100.61
83.45
43.36
33.25
31.36
24.78
24.54
$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
O
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

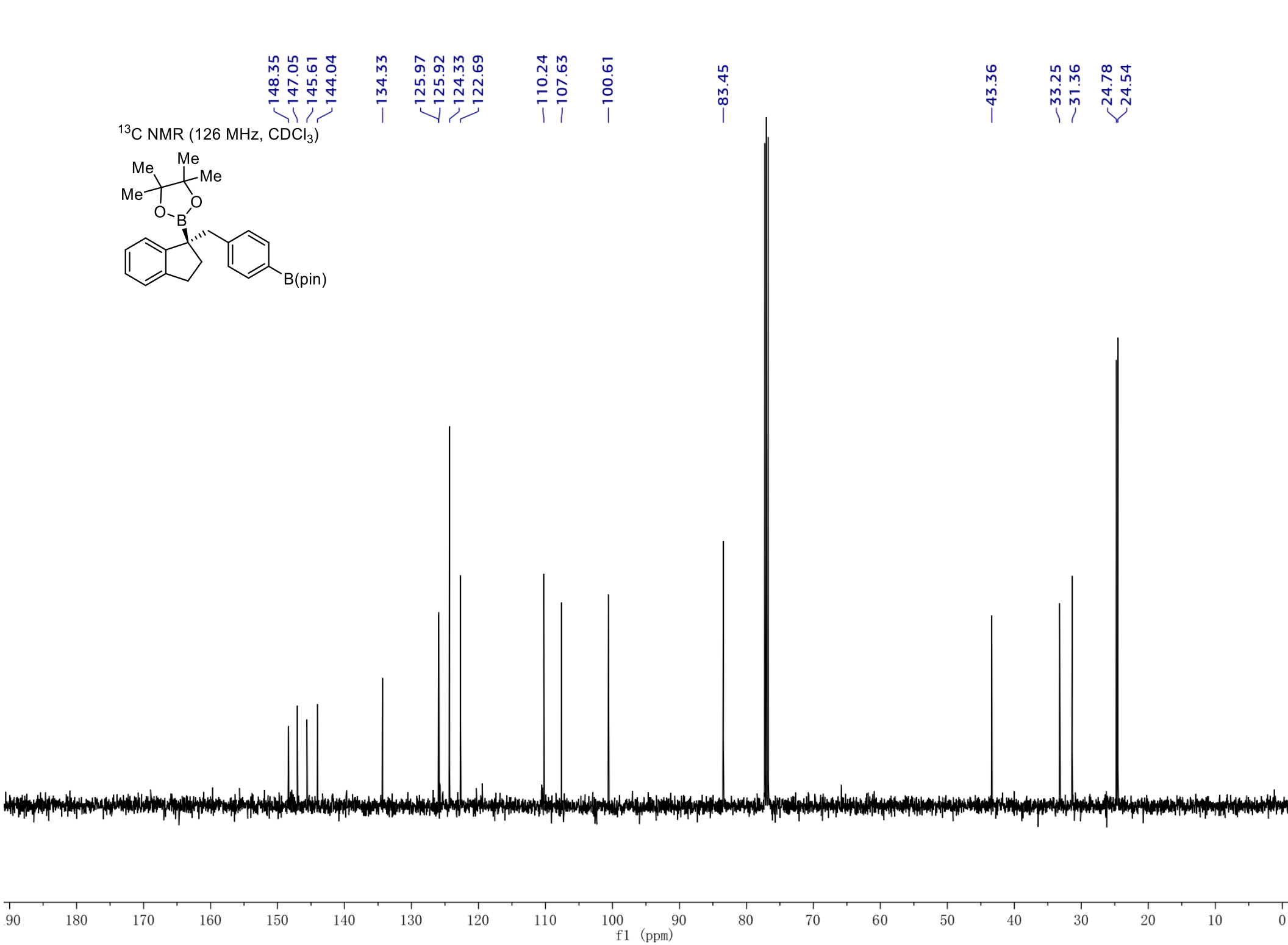
G

E


7.67 7.66 7.30 7.29 7.28 7.26 7.20 7.19 7.18 7.17 7.16 7.16 7.15 7.14 7.13 7.13 7.12 7.12 7.11 7.11
3.33 3.30 2.87 2.87 2.86 2.85 2.84 2.84 2.83 2.82 2.78 2.77 2.76 2.75 2.74 2.73 2.73 2.72 2.25 2.24 2.23 2.22 2.22 2.21 2.20 2.19 1.94 1.93 1.92 1.92 1.91 1.90 1.90 1.89 1.35 1.16 1.15
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
B(pin)
2.05
1.05
5.08
1.00
1.03
2.03
1.02
1.08
12.06
12.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

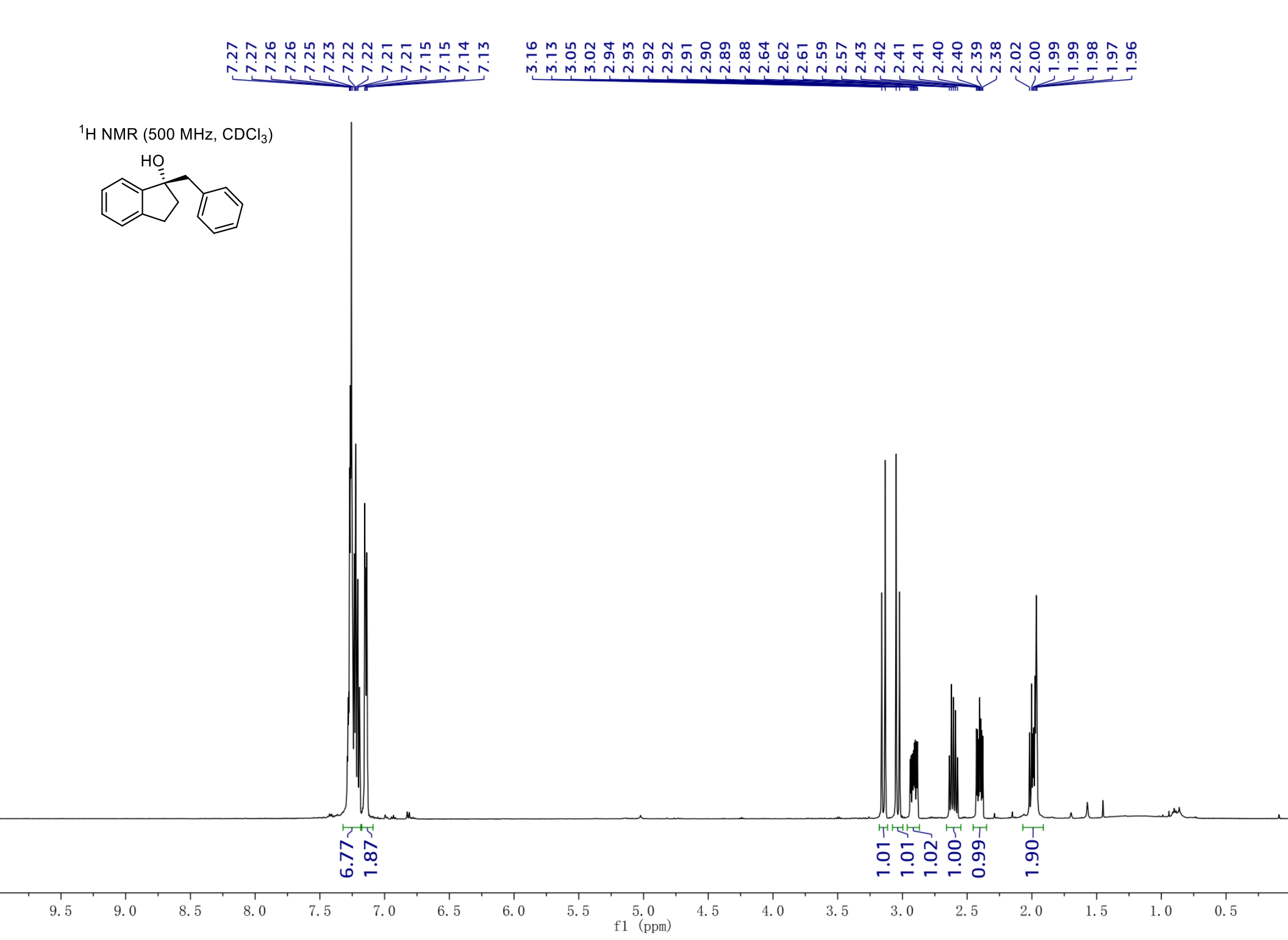
G

E


148.35
147.05
145.61
144.04
134.33
125.97
125.92
124.33
122.69
110.24
107.63
100.61
83.45
43.36
33.25
31.36
24.78
24.54
$^{13}$C NMR (126 MHz, CDCl$_3$)
Me
Me
Me
Me
O
O
B
B(pin)
f1 (ppm)

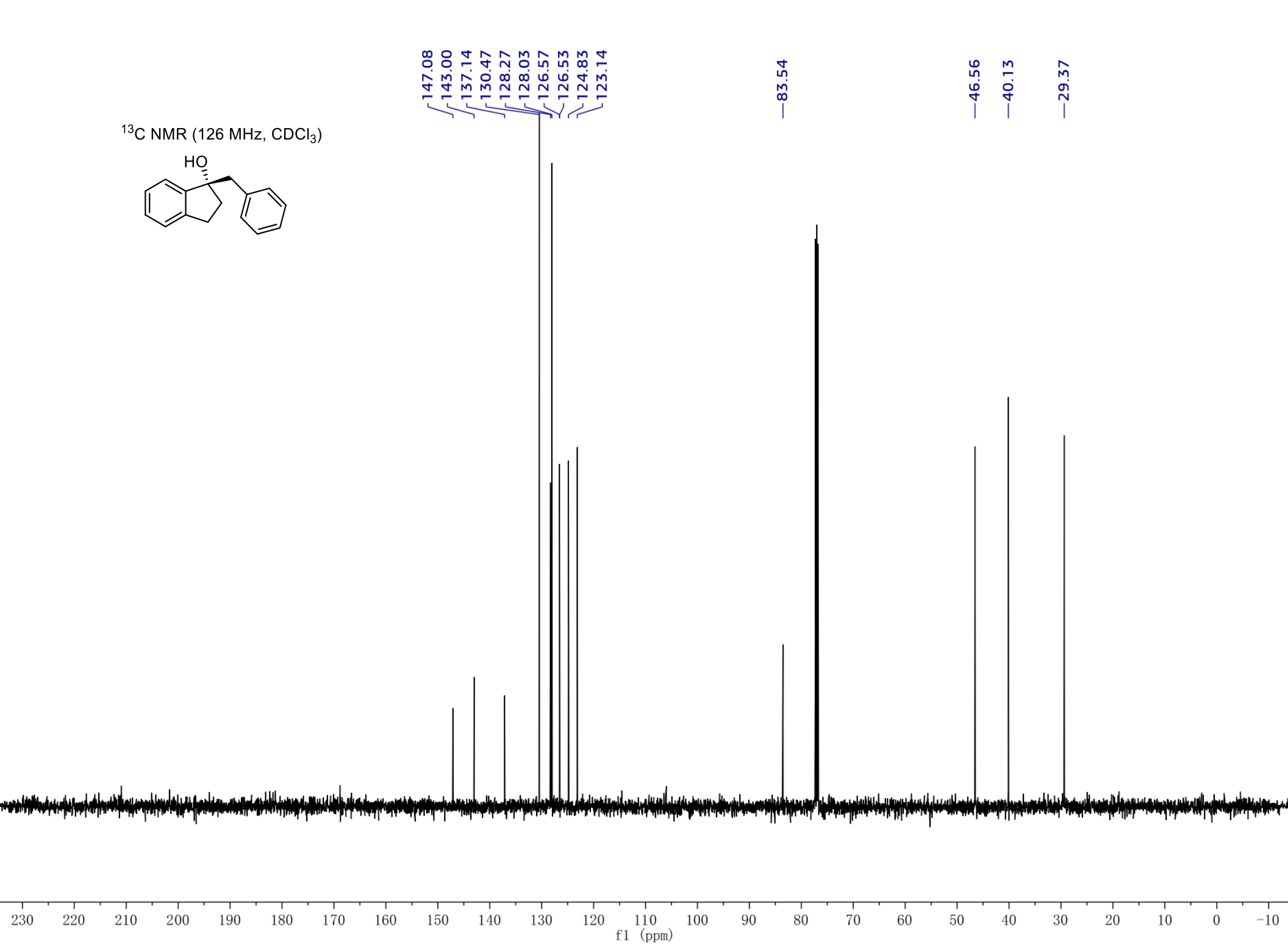
G

E


7.27 7.27 7.26 7.26 7.25 7.23 7.22 7.22 7.21 7.21 7.15 7.15 7.14 7.13
3.16 3.13 3.05 3.02 2.94 2.93 2.92 2.92 2.91 2.90 2.89 2.88 2.64 2.62 2.61 2.59 2.57 2.43 2.42 2.41 2.41 2.40 2.40 2.39 2.38 2.02 2.00 1.99 1.99 1.98 1.97 1.96
$^1$H NMR (500 MHz, $CDCl_3$)
HO
6.77
1.87
1.01
1.01
1.02
1.00
0.99
1.90
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
f1 (ppm)

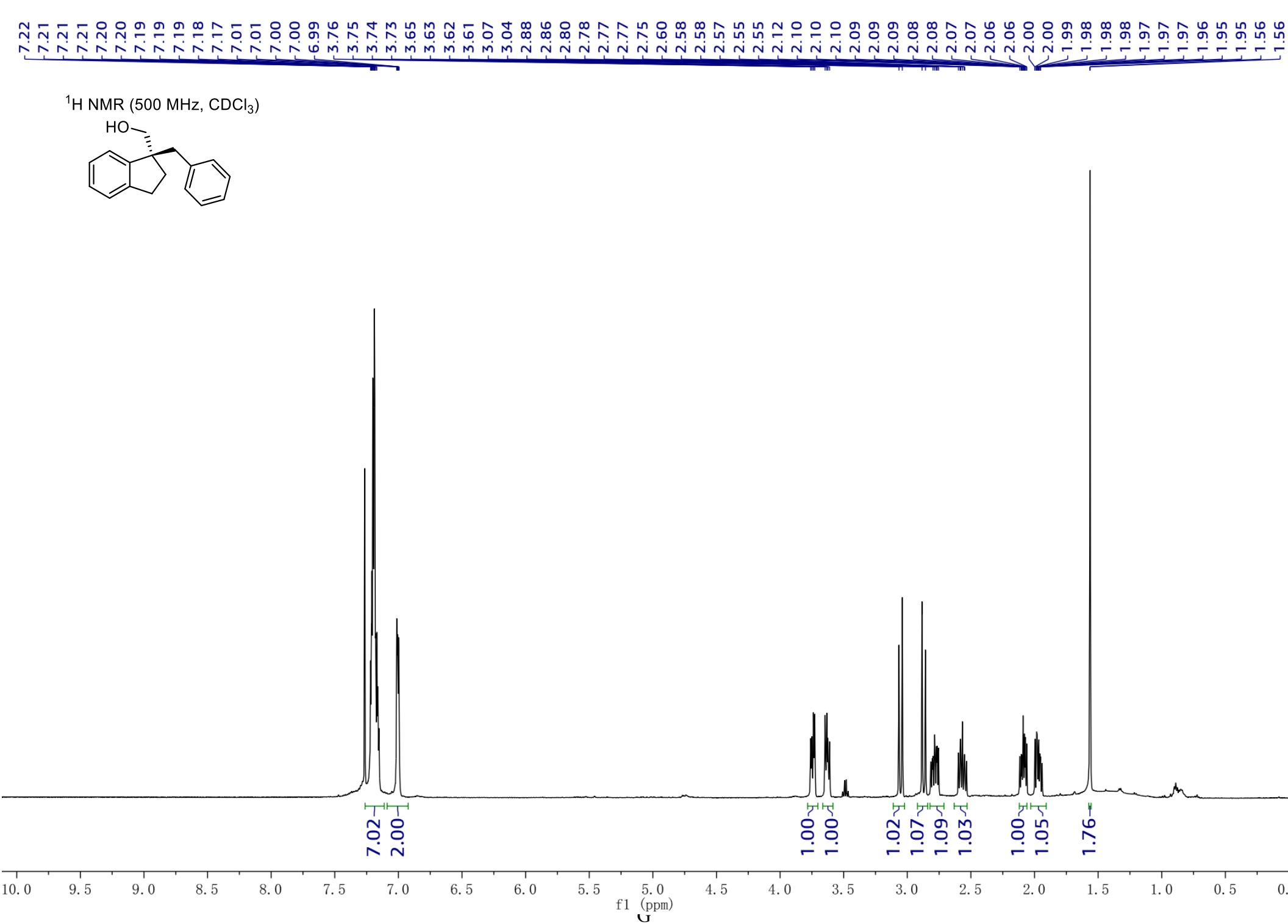
G

E


147.08
143.00
137.14
130.47
128.27
128.03
126.57
126.53
124.83
123.14
83.54
46.56
40.13
29.37
$^{13}$C NMR (126 MHz, $CDCl_3$)
HO
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

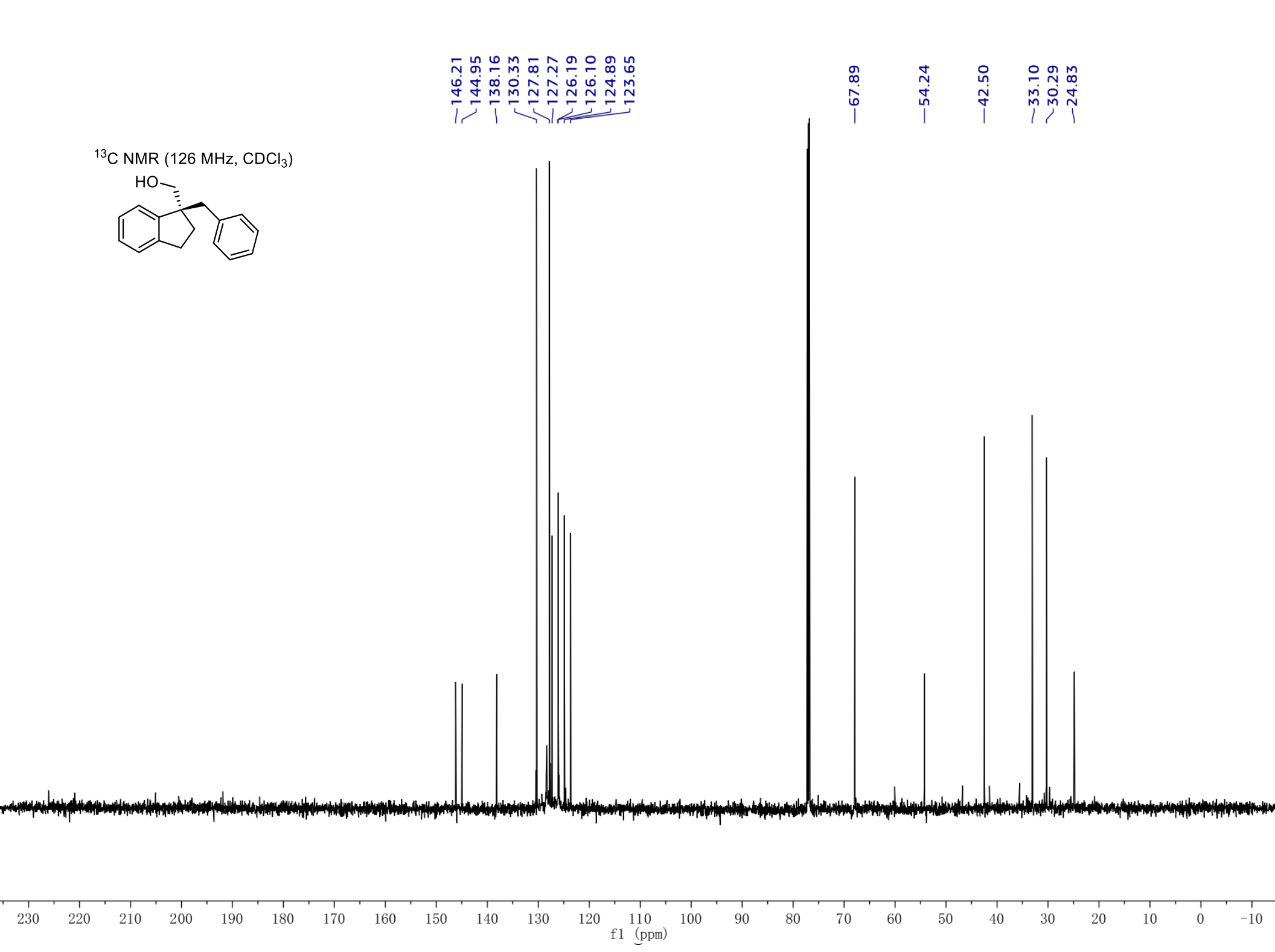
G

E


7.22 7.21 7.21 7.21 7.20 7.20 7.19 7.19 7.19 7.18 7.17 7.01 7.01 7.00 7.00 6.99 3.76 3.75 3.74 3.73 3.65 3.63 3.62 3.61 3.07 3.04 2.88 2.86 2.80 2.78 2.77 2.77 2.75 2.60 2.58 2.58 2.57 2.55 2.55 2.12 2.10 2.10 2.10 2.09 2.09 2.09 2.08 2.08 2.07 2.07 2.06 2.06 2.00 2.00 1.99 1.98 1.98 1.98 1.97 1.97 1.97 1.96 1.95 1.95 1.56 1.56
$^1$H NMR (500 MHz, $CDCl_3$)
HO
7.02
2.00
1.00
1.00
1.02
1.07
1.09
1.03
1.00
1.05
1.76
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

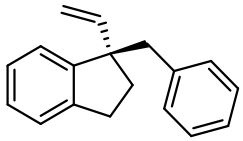
G

E


146.21
144.95
138.16
130.33
127.81
127.27
126.19
126.10
124.89
123.65
67.89
54.24
42.50
33.10
30.29
24.83
$^{13}$C NMR (126 MHz, $CDCl_3$)
HO
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

E

$^{1}$H NMR (500 MHz, $CDCl_3$)

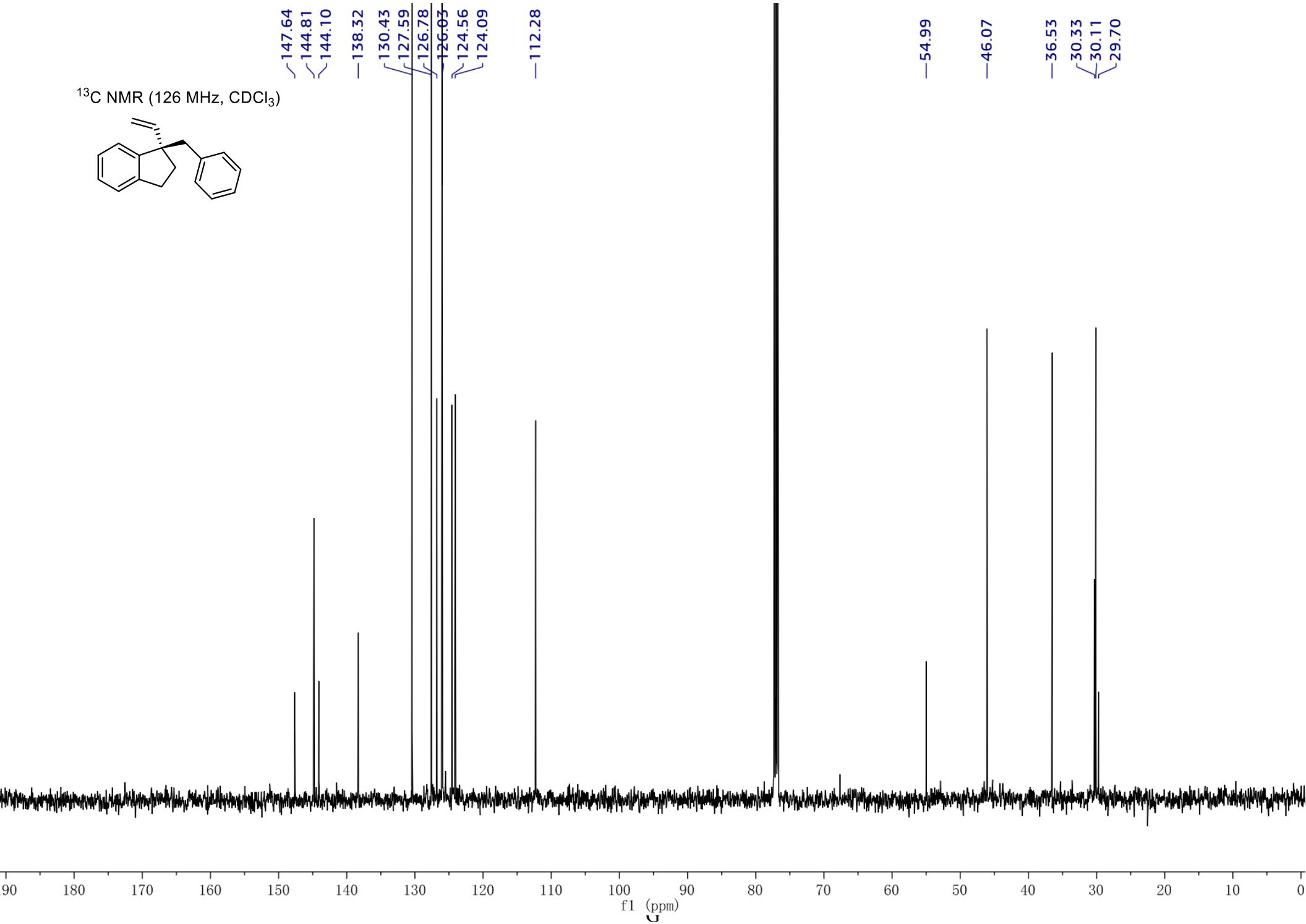


7.20 7.19 7.18 7.18 7.17 7.17 7.16 7.16 7.15 7.00 6.99 6.99 6.14 6.12 6.10 6.08 5.04 5.02 4.86 4.83 3.06 3.04 2.98 2.96 2.74 2.74 2.72 2.71 2.71 2.69 2.51 2.50 2.50 2.48 2.47 2.47 2.18 2.17 2.17 2.16 2.15 2.14 2.13 2.06 2.04 2.04 2.03 2.03 2.02

7.07 2.03 0.96 1.06 1.00 1.01 1.03 1.02 1.04 1.07 0.98

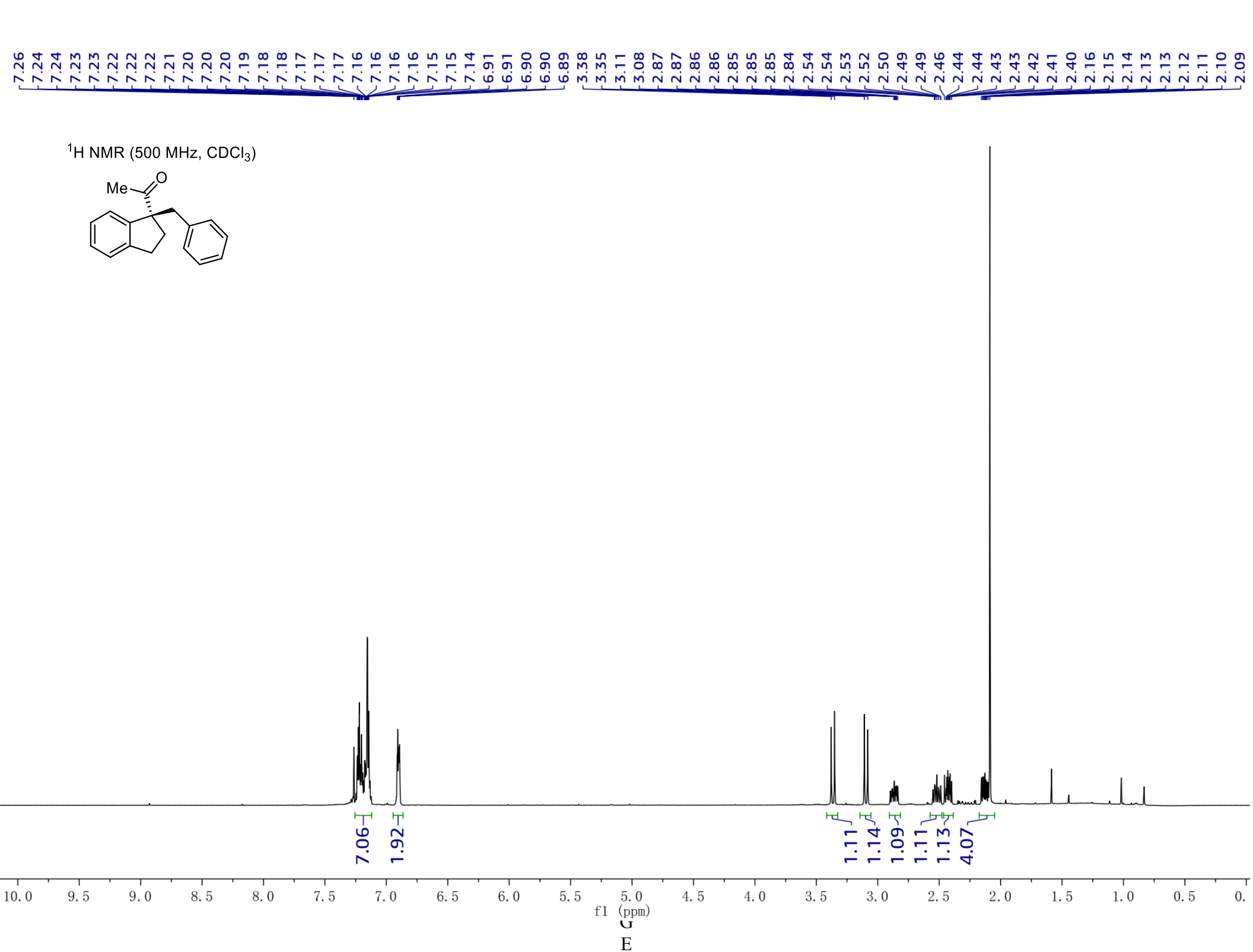
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)


147.64
144.81
144.10
138.32
130.43
127.59
126.78
126.03
124.56
124.09
112.28
54.99
46.07
36.53
30.33
30.11
29.70
13C NMR (126 MHz, CDCl3)
f1 (ppm)

G

E

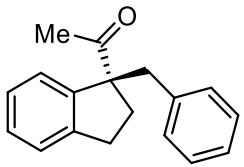

7.26 7.24 7.24 7.23 7.23 7.22 7.22 7.22 7.21 7.20 7.20 7.20 7.19 7.18 7.18 7.17 7.17 7.17 7.16 7.16 7.16 7.16 7.15 7.15 7.14 6.91 6.91 6.90 6.90 6.89
3.38 3.35 3.11 3.08 2.87 2.87 2.86 2.86 2.85 2.85 2.85 2.84 2.54 2.54 2.53 2.52 2.50 2.49 2.49 2.46 2.44 2.44 2.43 2.43 2.42 2.41 2.40 2.16 2.15 2.14 2.13 2.13 2.12 2.11 2.10 2.09
1H NMR (500 MHz, CDCl3)
Me
O
7.06
1.92
1.11
1.14
1.09
1.11
1.13
4.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

G

E

209.85
144.87
144.32
137.87
130.12
127.87
127.80
126.56
126.26
124.83
124.68
66.17
42.60
33.42
31.01
26.63

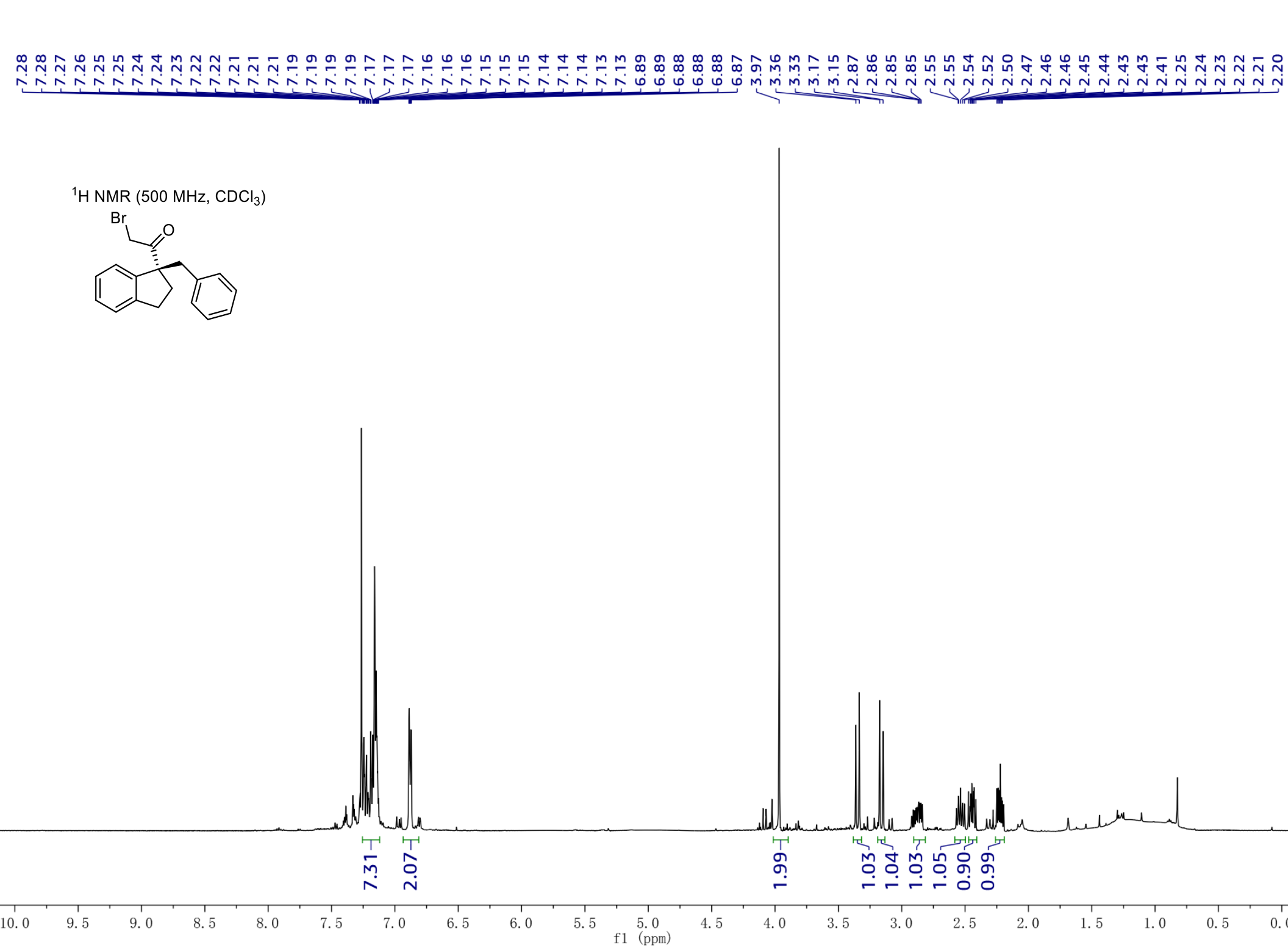
$^{13}$C NMR (126 MHz, $CDCl_3$)





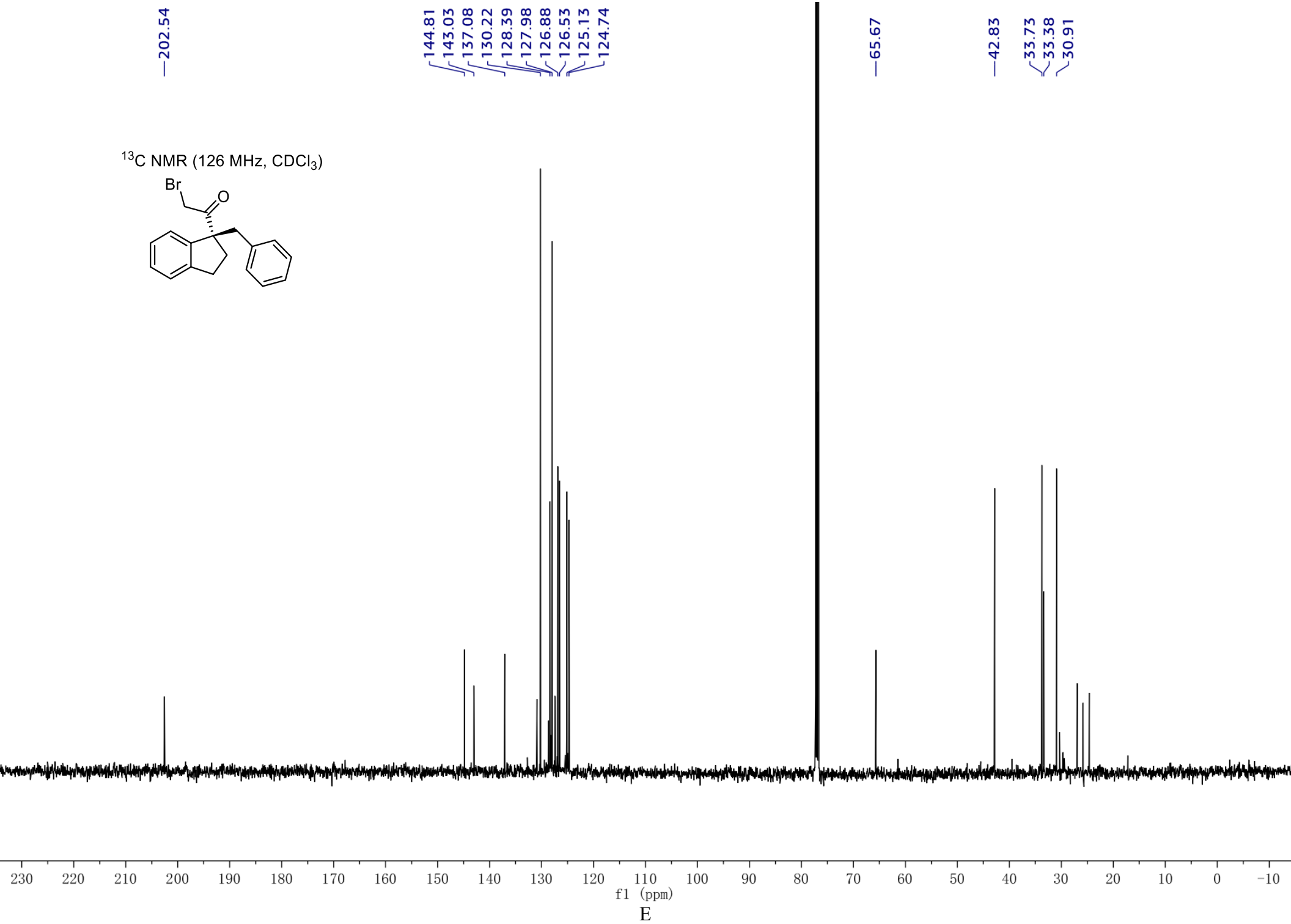


E

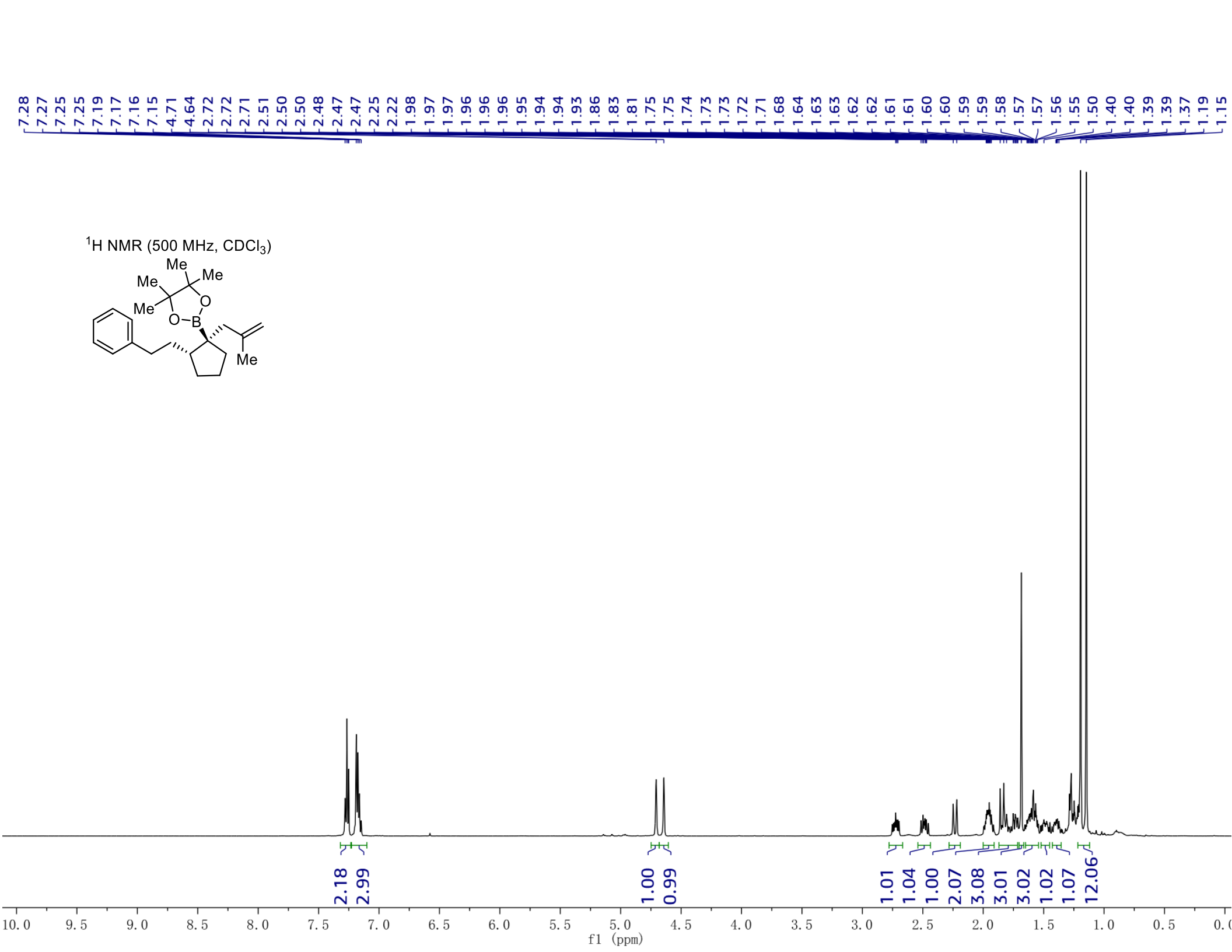

7.28 7.28 7.27 7.26 7.25 7.25 7.24 7.24 7.23 7.22 7.22 7.21 7.21 7.21 7.19 7.19 7.19 7.19 7.17 7.17 7.17 7.16 7.16 7.16 7.15 7.15 7.15 7.14 7.14 7.14 7.13 7.13 6.89 6.89 6.88 6.88 6.88 6.87 3.97 3.36 3.33 3.17 3.15 2.87 2.86 2.85 2.85 2.55 2.55 2.54 2.52 2.50 2.47 2.46 2.46 2.45 2.44 2.43 2.43 2.41 2.25 2.24 2.23 2.22 2.21 2.20
$^1$H NMR (500 MHz, $CDCl_3$)
Br
O
7.31
2.07
1.99
1.03
1.04
1.03
1.05
0.90
0.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

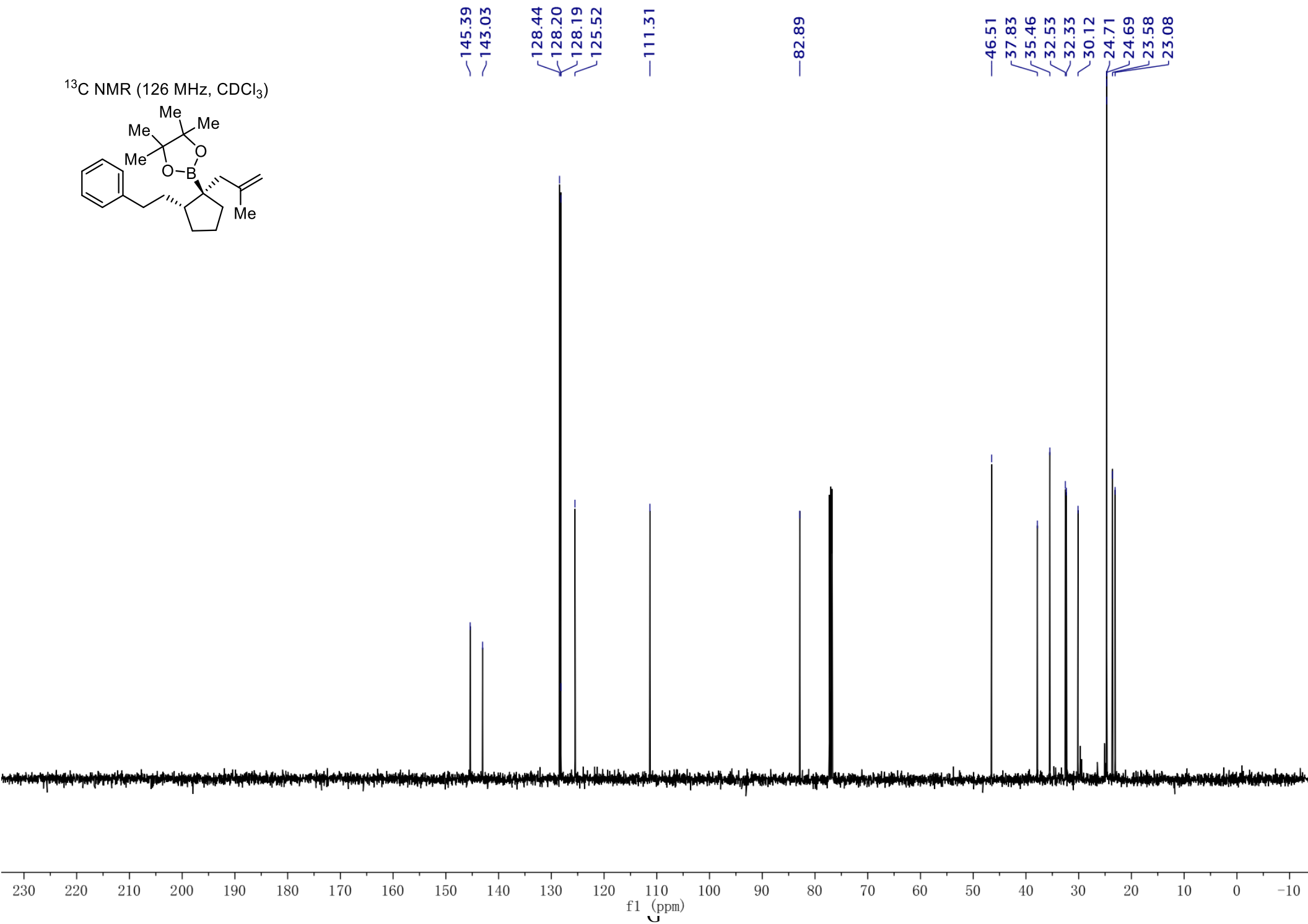
G

E


202.54
144.81
143.03
137.08
130.22
128.39
127.98
126.88
126.53
125.13
124.74
65.67
42.83
33.73
33.38
30.91
13C NMR (126 MHz, CDCl3)
Br
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

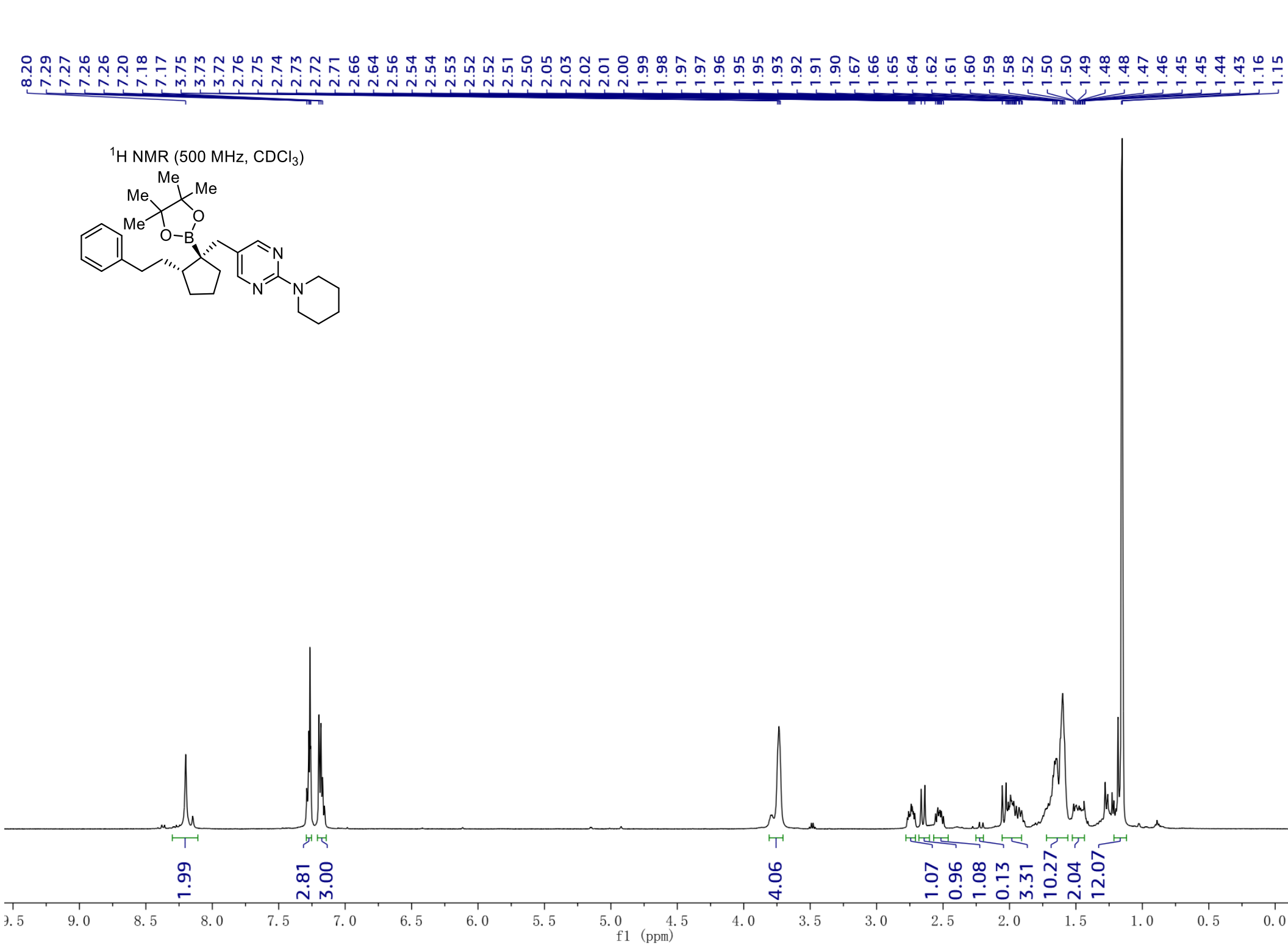
E


7.28 7.27 7.25 7.25 7.19 7.17 7.16 7.15 4.71 4.64 2.72 2.72 2.71 2.51 2.50 2.50 2.48 2.47 2.47 2.25 2.22 1.98 1.97 1.97 1.96 1.96 1.96 1.95 1.94 1.94 1.93 1.86 1.83 1.81 1.75 1.75 1.74 1.73 1.73 1.72 1.71 1.68 1.64 1.63 1.63 1.62 1.62 1.61 1.61 1.60 1.60 1.59 1.59 1.58 1.57 1.57 1.56 1.55 1.50 1.40 1.40 1.39 1.39 1.37 1.19 1.15
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
Me
2.18 2.99 1.00 0.99 1.01 1.04 1.00 2.07 3.08 3.01 3.02 1.02 1.07 12.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
Me
145.39
143.03
128.44
128.20
128.19
125.52
111.31
82.89
46.51
37.83
35.46
32.53
32.33
30.12
24.71
24.69
23.58
23.08
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

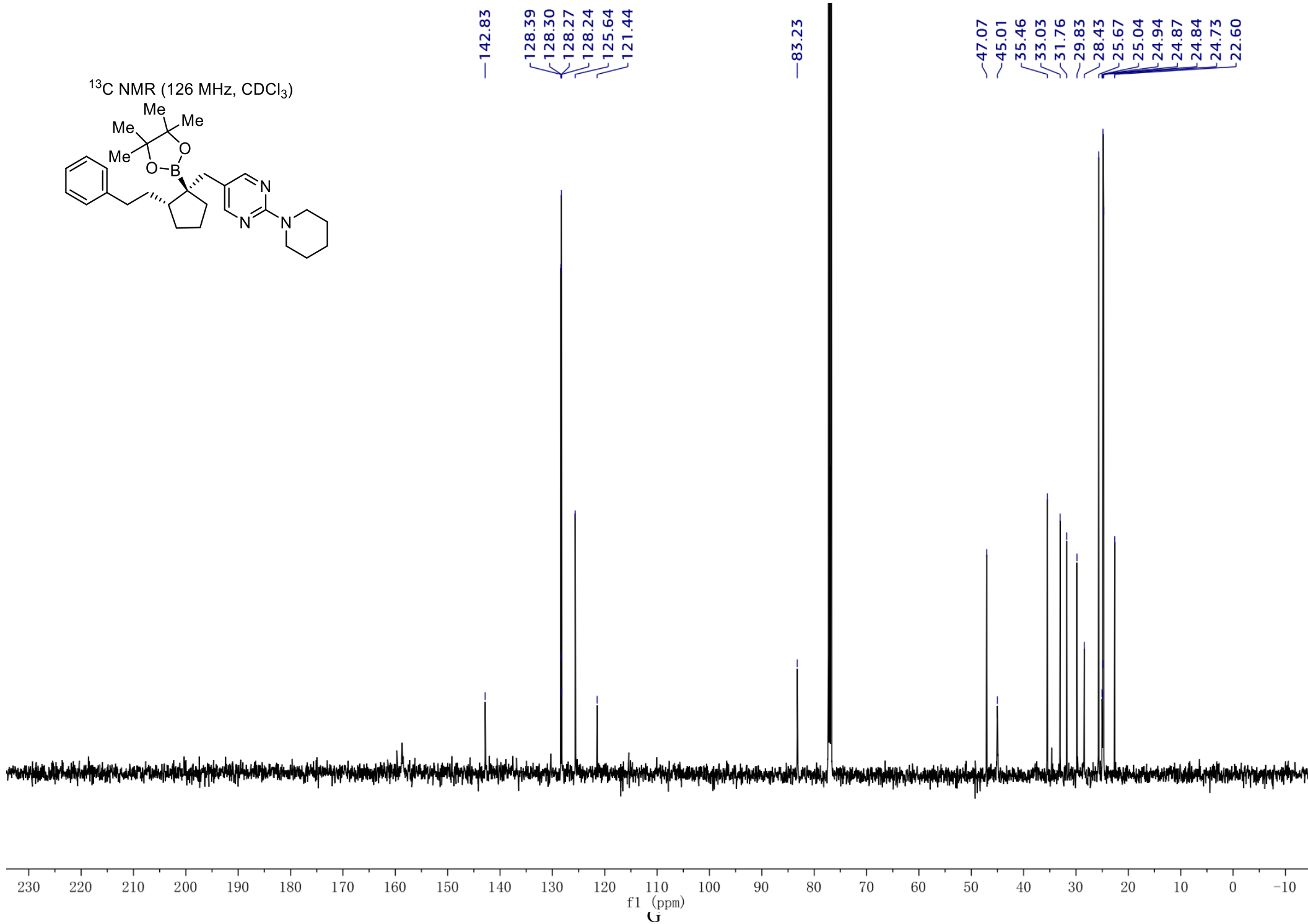
G

E


8.20 7.29 7.27 7.26 7.26 7.20 7.18 7.17 3.75 3.73 3.72 2.76 2.75 2.74 2.73 2.72 2.71 2.66 2.64 2.56 2.54 2.54 2.53 2.52 2.52 2.51 2.50 2.05 2.03 2.02 2.01 2.00 1.99 1.98 1.97 1.97 1.96 1.95 1.95 1.93 1.92 1.91 1.90 1.67 1.66 1.65 1.64 1.62 1.61 1.60 1.59 1.58 1.52 1.50 1.50 1.49 1.48 1.48 1.47 1.46 1.45 1.45 1.44 1.43 1.16 1.15
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
N
N
N
1.99
2.81
3.00
4.06
1.07
0.96
1.08
0.13
3.31
10.27
2.04
12.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

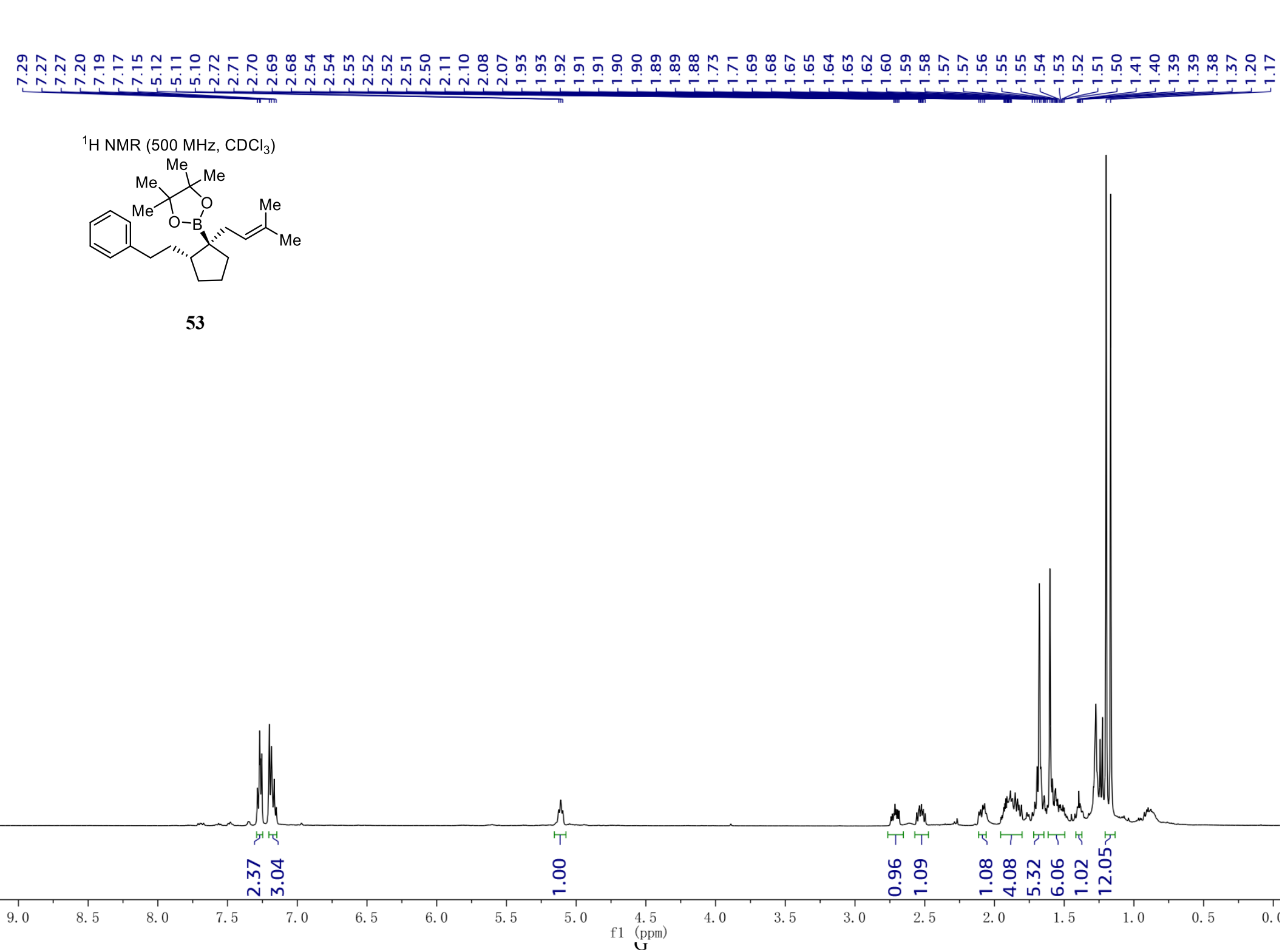
G

E


$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
N
N
N
142.83
128.39
128.30
128.27
128.24
125.64
121.44
83.23
47.07
45.01
35.46
33.03
31.76
29.83
28.43
25.67
25.04
24.94
24.87
24.84
24.73
22.60
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

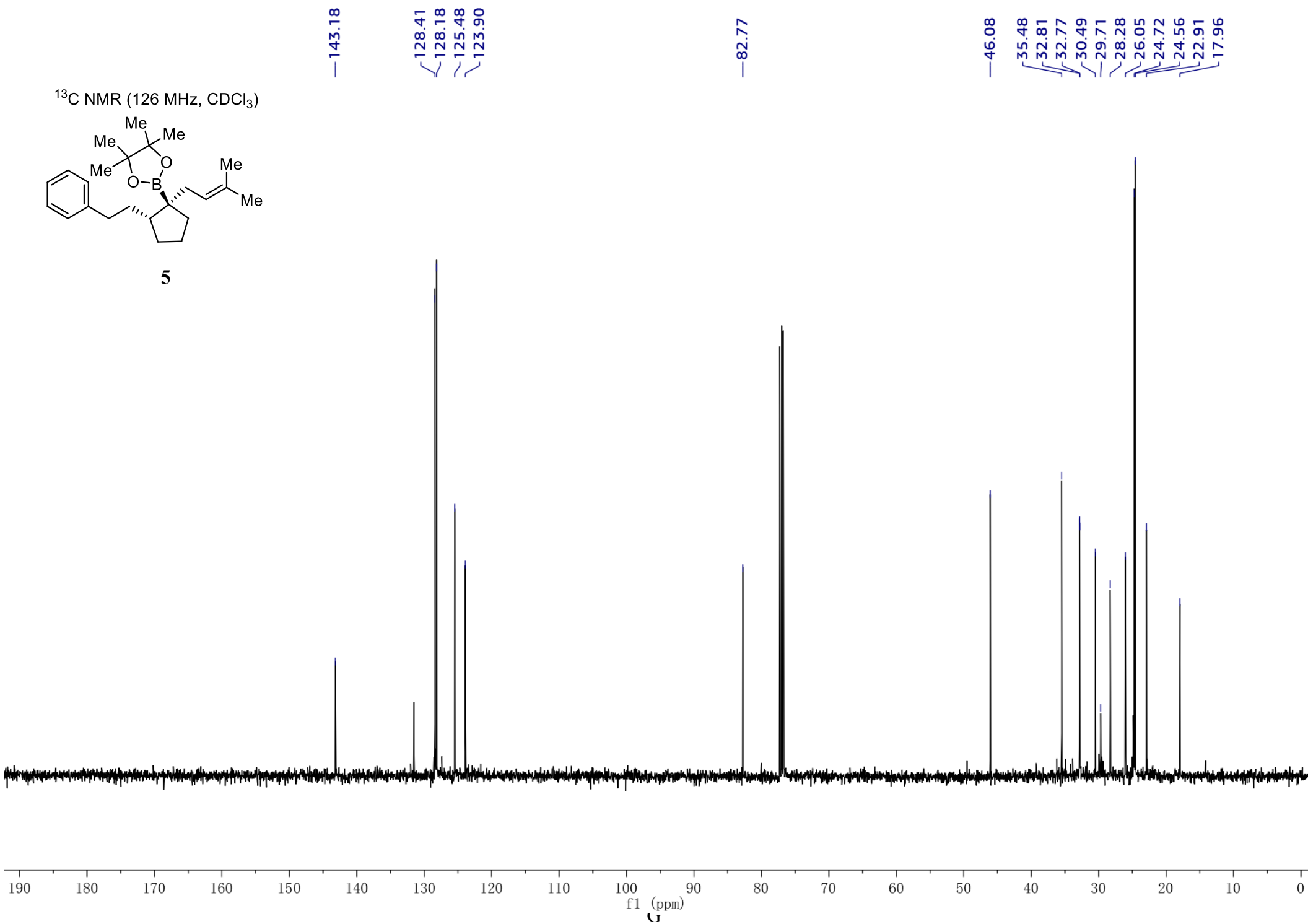
G

E


7.29 7.27 7.27 7.20 7.19 7.17 7.15 5.12 5.11 5.10 2.72 2.71 2.70 2.69 2.68 2.54 2.54 2.53 2.52 2.52 2.51 2.50 2.11 2.10 2.08 2.07 1.93 1.93 1.92 1.91 1.91 1.90 1.90 1.89 1.89 1.88 1.73 1.71 1.69 1.68 1.67 1.65 1.64 1.63 1.62 1.60 1.59 1.58 1.57 1.57 1.56 1.55 1.55 1.54 1.53 1.52 1.51 1.50 1.41 1.40 1.39 1.39 1.38 1.37 1.20 1.17
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O–B
Me
Me
53
2.37
3.04
1.00
0.96
1.09
1.08
4.08
5.32
6.06
1.02
12.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

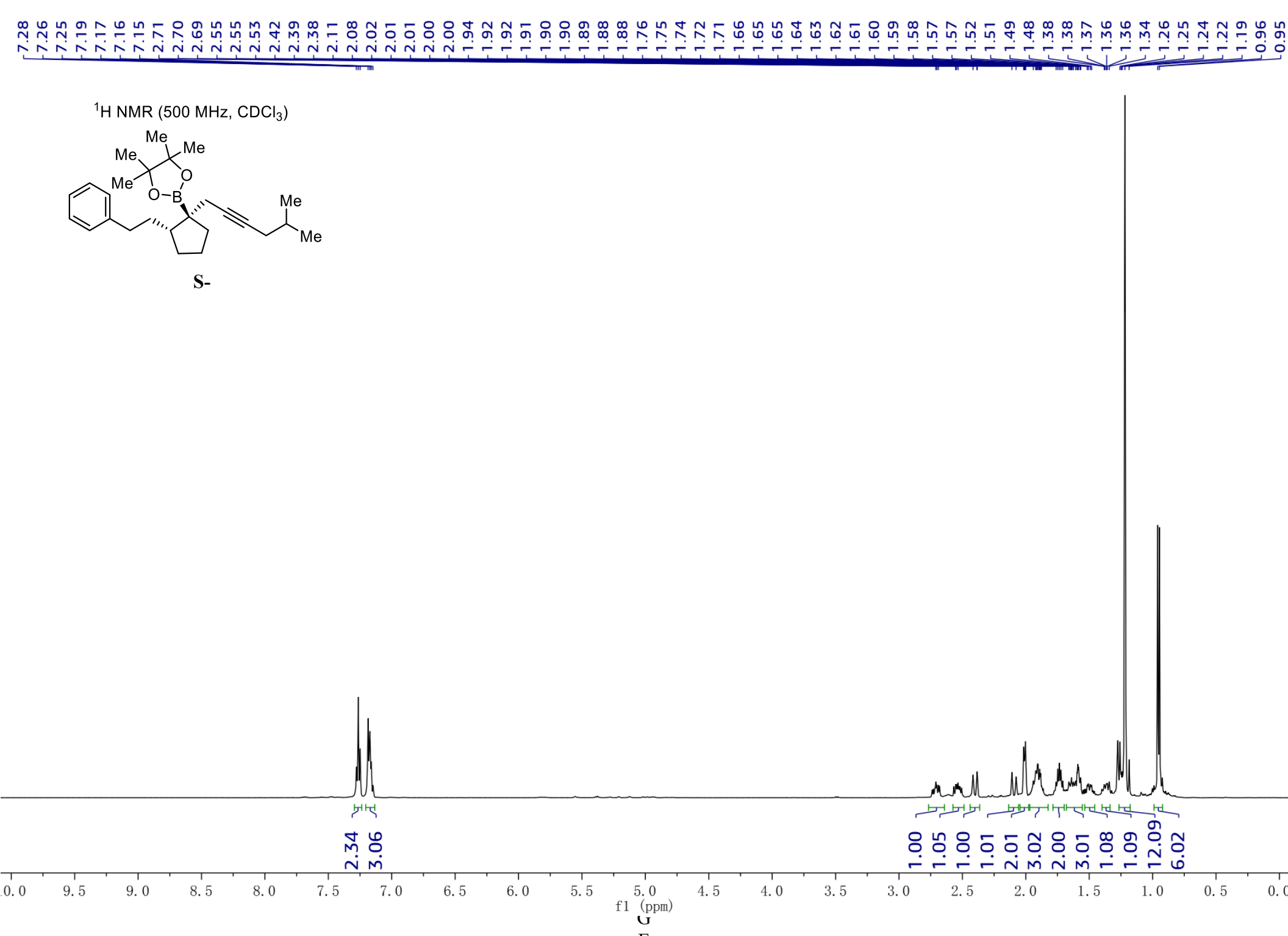
G

E


143.18
128.41
128.18
125.48
123.90
82.77
46.08
35.48
32.81
32.77
30.49
29.71
28.28
26.05
24.72
24.56
22.91
17.96
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
Me
5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

G

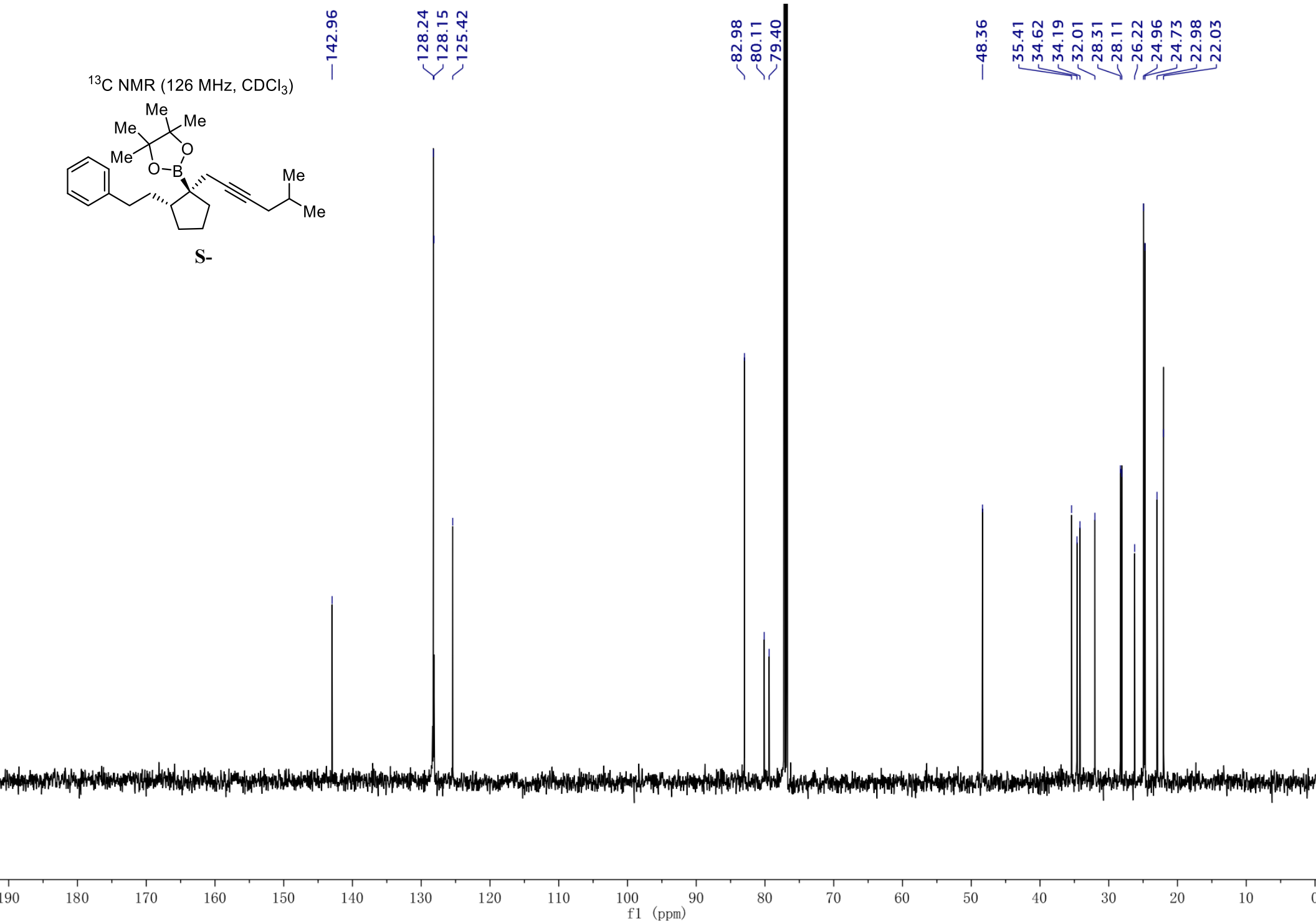
E


7.28 7.26 7.25 7.19 7.17 7.16 7.15 2.71 2.70 2.69 2.55 2.55 2.53 2.42 2.39 2.38 2.11 2.08 2.02 2.01 2.01 2.00 2.00 1.94 1.92 1.92 1.91 1.90 1.90 1.89 1.88 1.88 1.76 1.75 1.74 1.72 1.71 1.66 1.65 1.65 1.64 1.63 1.62 1.61 1.60 1.59 1.58 1.57 1.57 1.52 1.51 1.49 1.48 1.38 1.38 1.37 1.36 1.36 1.34 1.26 1.25 1.24 1.22 1.19 0.96 0.95
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
Me
2.34
3.06
1.00
1.05
1.00
1.01
2.01
3.02
2.00
3.01
1.08
1.09
12.09
6.02
f1 (ppm)

S-

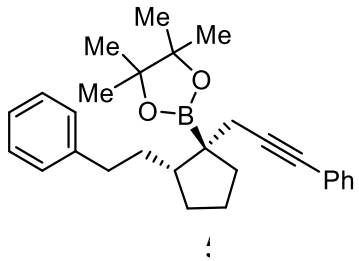
G

E


142.96
128.24
128.15
125.42
82.98
80.11
79.40
48.36
35.41
34.62
34.19
32.01
28.31
28.11
26.22
24.96
24.73
22.98
22.03
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Me
Me
S-
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

E

$^1$H NMR (500 MHz, $CDCl_3$)

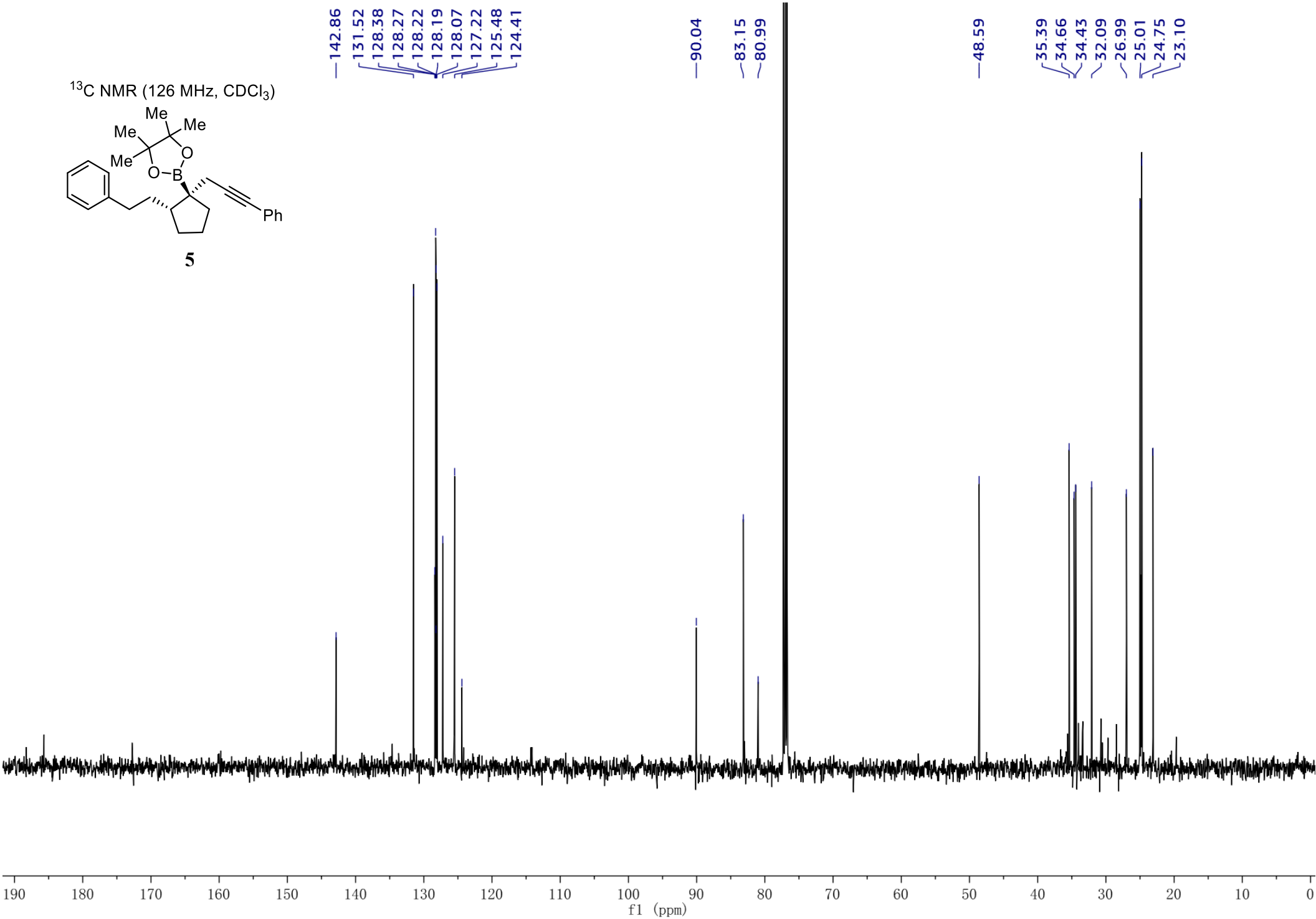



7.36 7.35 7.34 7.34 7.27 7.26 7.26 7.25 7.25 7.20 7.18 7.16 7.15 2.74 2.73 2.72 2.65 2.62 2.60 2.58 2.58 2.56 2.35 2.32 2.00 1.98 1.97 1.96 1.95 1.94 1.94 1.78 1.78 1.77 1.77 1.76 1.75 1.75 1.74 1.74 1.72 1.72 1.71 1.70 1.70 1.68 1.67 1.67 1.66 1.66 1.65 1.64 1.63 1.63 1.58 1.57 1.56 1.55 1.54 1.53 1.42 1.42 1.40 1.39 1.39 1.22

1.48 5.27 4.05 1.08 3.03 1.00 3.04 2.38 1.43 1.35 1.36 12.03

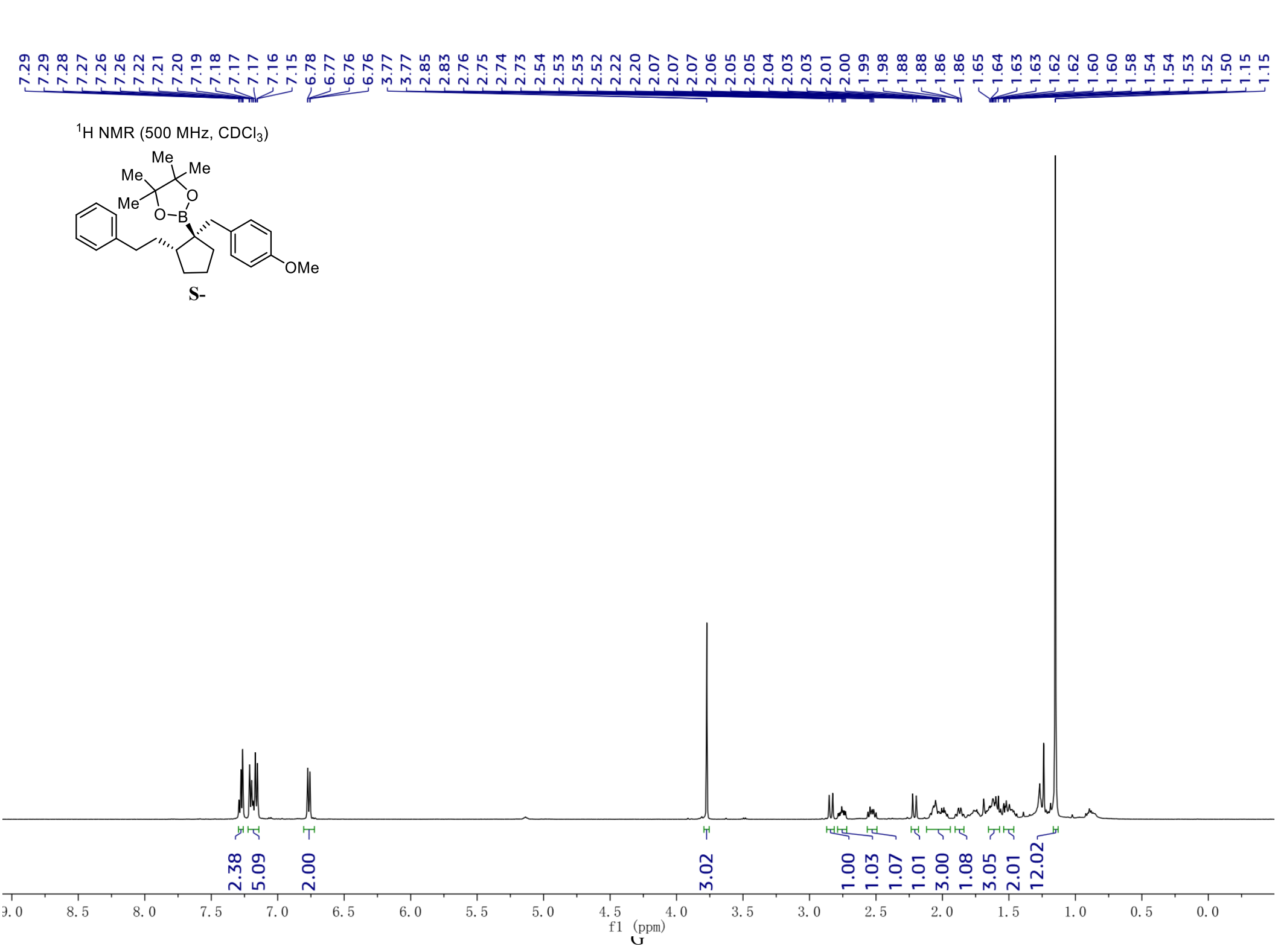
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)


142.86
131.52
128.38
128.27
128.22
128.19
128.07
127.22
125.48
124.41
90.04
83.15
80.99
48.59
35.39
34.66
34.43
32.09
26.99
25.01
24.75
23.10
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
Ph
5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

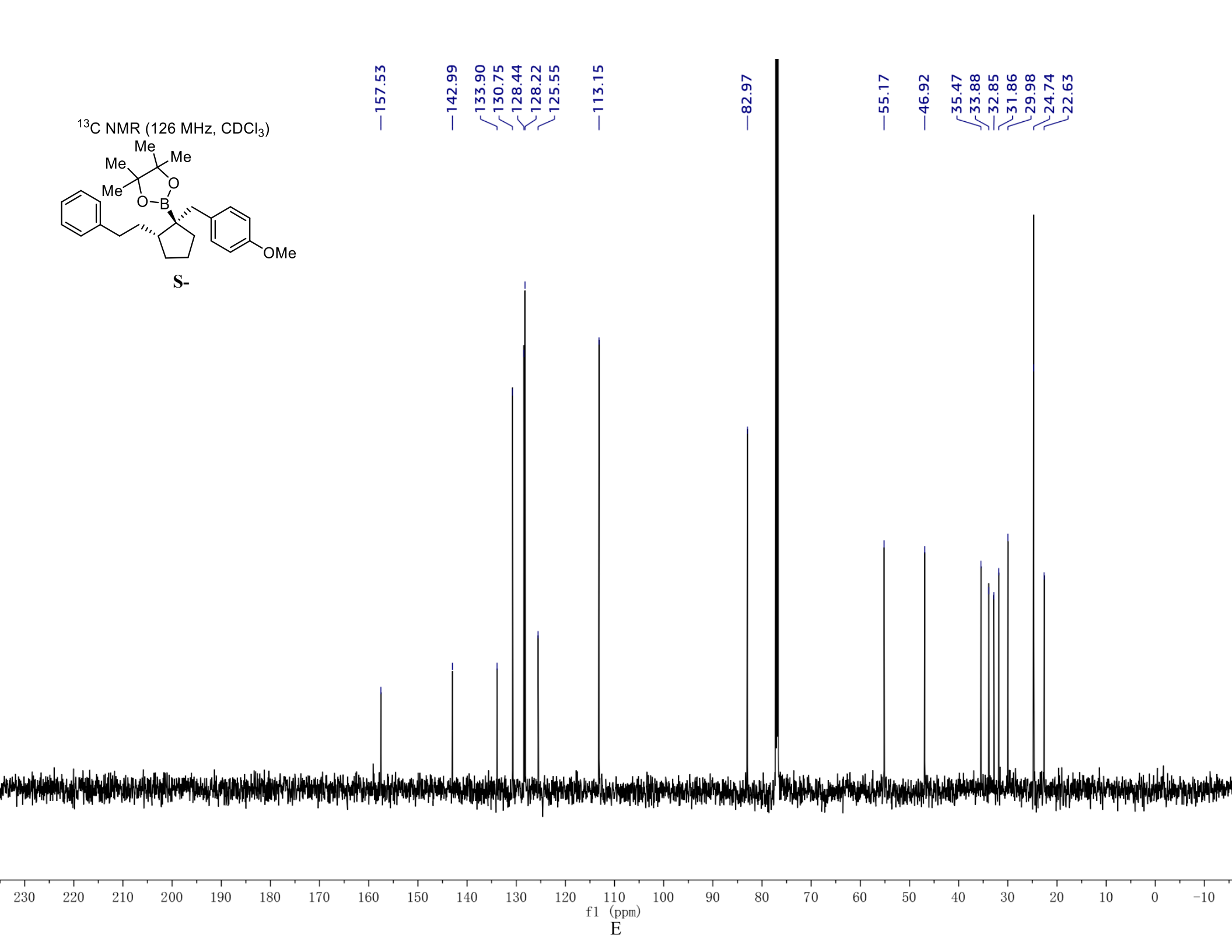
G

E

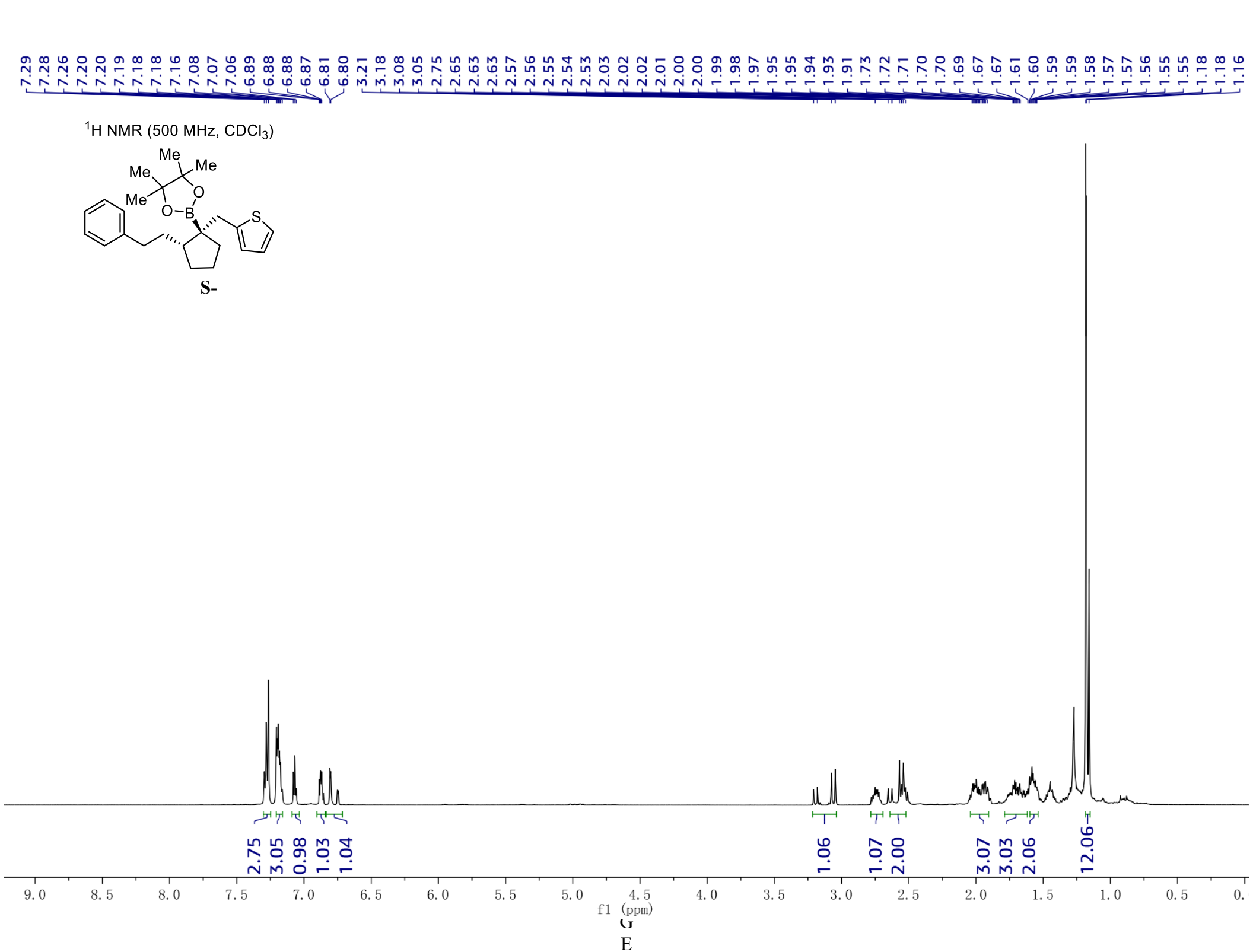

7.29 7.29 7.28 7.27 7.26 7.26 7.22 7.21 7.20 7.19 7.18 7.17 7.17 7.16 7.15 6.78 6.77 6.76 6.76 3.77 3.77 2.85 2.83 2.76 2.75 2.74 2.73 2.54 2.53 2.53 2.52 2.22 2.20 2.07 2.07 2.07 2.06 2.05 2.05 2.04 2.03 2.03 2.01 2.00 1.99 1.98 1.88 1.88 1.86 1.86 1.65 1.64 1.63 1.63 1.62 1.62 1.60 1.60 1.58 1.54 1.54 1.53 1.52 1.50 1.15 1.15
$^1$H NMR (500 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O
B
OMe
S-
2.38
5.09
2.00
3.02
1.00
1.03
1.07
1.01
3.00
1.08
3.05
2.01
12.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

G

E

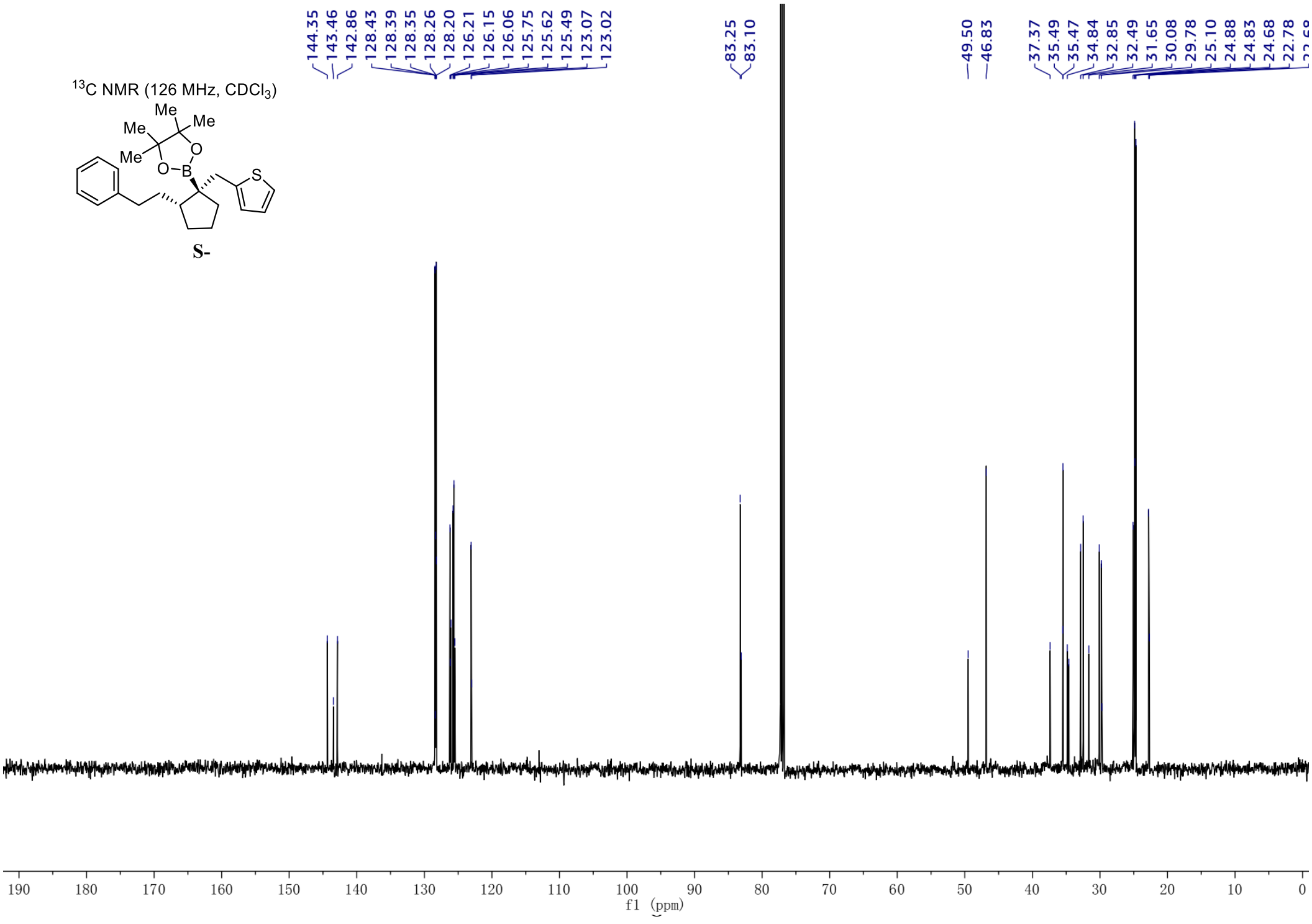

$^{13}$C NMR (126 MHz, $CDCl_3$)
Me
Me
Me
Me
O
O–B
OMe
S-
157.53
142.99
133.90
130.75
128.44
128.22
125.55
113.15
82.97
55.17
46.92
35.47
33.88
32.85
31.86
29.98
24.74
22.63
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

E


7.29 7.28 7.26 7.20 7.20 7.19 7.18 7.18 7.16 7.08 7.07 7.06 6.89 6.88 6.88 6.87 6.81 6.80
3.21 3.18 3.08 3.05 2.75 2.65 2.63 2.63 2.57 2.56 2.55 2.54 2.53 2.03 2.02 2.02 2.01 2.00 2.00 1.99 1.98 1.97 1.95 1.95 1.94 1.93 1.91 1.73 1.72 1.71 1.70 1.70 1.69 1.67 1.67 1.61 1.60 1.59 1.59 1.58 1.57 1.57 1.56 1.55 1.55 1.18 1.18 1.16
1H NMR (500 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
S-
2.75
3.05
0.98
1.03
1.04
1.06
1.07
2.00
3.07
3.03
2.06
12.06
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
f1 (ppm)

G

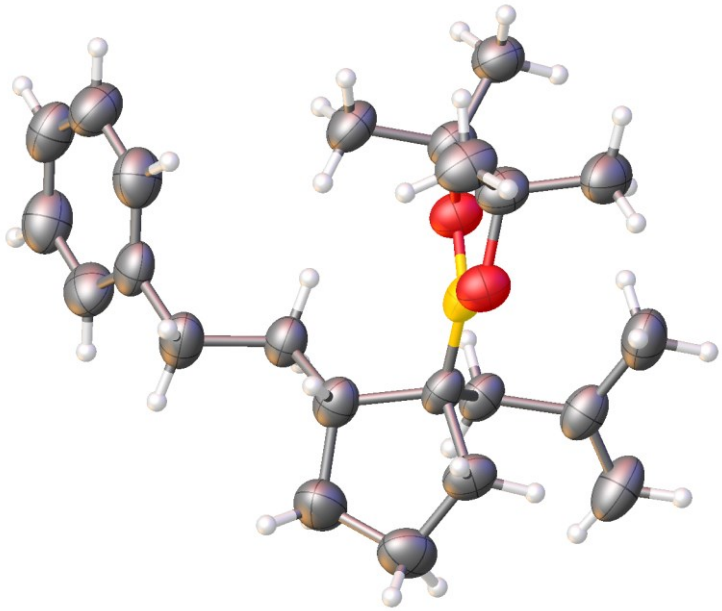
E


144.35
143.46
142.86
128.43
128.39
128.35
128.26
128.20
126.21
126.15
126.06
125.75
125.62
125.49
123.07
123.02
83.25
83.10
49.50
46.83
37.37
35.49
35.47
34.84
32.85
32.49
31.65
30.08
29.78
25.10
24.88
24.83
24.68
22.78
13C NMR (126 MHz, CDCl3)
Me
Me
Me
Me
O
O
B
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

**S-**

E

### 2.4.11 X-ray Crysatallography data



| | | |
|---|---|---|
| Identification code | C23H35BO2 | |
| Empirical formula | C23 H35 B O2 | |
| Formula weight | 354.32 | |
| Temperature | 173(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 9.5141(5) Å | □= 90°. |
| | b = 9.9905(5) Å | □= 90°. |
| | c = 22.6950(11) Å | □ = 90°. |
| Volume | 2157.17(19) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.091 $Mg/m^3$ | |
| Absorption coefficient | 0.508 $mm^{-1}$ | |
| F(000) | 776 | |
| Crystal size | 0.260 x 0.220 x 0.100 $mm^3$ | |
| Theta range for data collection | 3.895 to 66.967°. | |
| Index ranges | -11<=h<=11, -11<=k<=11, -26<=l<=26 | |
| Reflections collected | 31809 | |
| Independent reflections | 3820 [R(int) = 0.0727] | |
| Completeness to theta = 66.967° | 99.5 % | |
| Absorption correction | Semi-empirical from equivalents | |

| | |
|---|---|
| Max. and min. transmission | 0.7528 and 0.5731 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3820 / 0 / 240 |
| Goodness-of-fit on $F^2$ | 1.054 |
| Final R indices [I>2sigma(I)] | R1 = 0.0681, wR2 = 0.1998 |
| R indices (all data) | R1 = 0.0754, wR2 = 0.2077 |
| Absolute structure parameter | 0.0(2) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.297 and -0.181 e.$Å^{-3}$ |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for C23H35BO2. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 4178(3) | 5930(3) | 1909(1) | 52(1) |
| O(2) | 3494(4) | 4580(3) | 1152(1) | 55(1) |
| B(1) | 3267(6) | 5756(5) | 1446(2) | 46(1) |
| C(1) | 4696(7) | 8199(7) | 784(2) | 74(2) |
| C(2) | 3281(6) | 8796(4) | 884(2) | 55(1) |
| C(3) | 2773(8) | 9778(5) | 550(2) | 73(2) |
| C(4) | 2419(5) | 8236(4) | 1388(2) | 49(1) |
| C(5) | 2019(5) | 6738(4) | 1322(2) | 46(1) |
| C(6) | 1247(5) | 6499(5) | 732(2) | 54(1) |
| C(7) | -233(6) | 7068(6) | 826(2) | 70(2) |
| C(8) | -519(6) | 6959(7) | 1490(3) | 74(2) |
| C(9) | 813(5) | 6390(5) | 1770(2) | 54(1) |
| C(10) | 1065(5) | 6820(5) | 2406(2) | 51(1) |
| C(11) | 16(6) | 6224(6) | 2847(2) | 64(1) |
| C(12) | 418(5) | 6460(5) | 3483(2) | 56(1) |
| C(13) | -215(6) | 7434(5) | 3820(2) | 64(1) |
| C(14) | 196(7) | 7638(5) | 4400(2) | 69(1) |
| C(15) | 1239(7) | 6889(6) | 4645(2) | 67(1) |
| C(16) | 1883(7) | 5920(6) | 4317(2) | 72(2) |
| C(17) | 1476(6) | 5716(5) | 3736(2) | 67(1) |
| C(18) | 4894(5) | 4666(5) | 2003(2) | 53(1) |
| C(19) | 4796(6) | 4002(5) | 1387(2) | 58(1) |
| C(20) | 4070(6) | 3913(5) | 2473(2) | 61(1) |
| C(21) | 6373(6) | 4942(5) | 2212(2) | 61(1) |
| C(22) | 4636(7) | 2484(5) | 1393(2) | 70(1) |
| C(23) | 5992(6) | 4422(6) | 979(2) | 68(1) |

Table 3. Bond lengths [Å] and angles [°] for C23H35BO2.

| | |
|---|---|
| O(1)-B(1) | 1.374(6) |
| O(1)-C(18) | 1.451(6) |
| O(2)-B(1) | 1.368(6) |
| O(2)-C(19) | 1.466(6) |
| B(1)-C(5) | 1.566(7) |
| C(1)-C(2) | 1.490(9) |
| C(2)-C(3) | 1.331(7) |
| C(2)-C(4) | 1.515(6) |
| C(4)-C(5) | 1.552(6) |
| C(5)-C(6) | 1.546(6) |
| C(5)-C(9) | 1.572(6) |
| C(6)-C(7) | 1.533(8) |
| C(7)-C(8) | 1.534(8) |
| C(8)-C(9) | 1.528(8) |
| C(9)-C(10) | 1.525(6) |
| C(10)-C(11) | 1.535(6) |
| C(11)-C(12) | 1.510(7) |
| C(12)-C(17) | 1.376(8) |
| C(12)-C(13) | 1.377(7) |
| C(13)-C(14) | 1.387(8) |
| C(14)-C(15) | 1.363(9) |
| C(15)-C(16) | 1.367(8) |
| C(16)-C(17) | 1.390(8) |
| C(18)-C(21) | 1.510(7) |
| C(18)-C(20) | 1.522(7) |
| C(18)-C(19) | 1.551(6) |
| C(19)-C(22) | 1.525(7) |
| C(19)-C(23) | 1.526(8) |

| | |
|---|---|
| B(1)-O(1)-C(18) | 107.4(3) |
| B(1)-O(2)-C(19) | 107.1(4) |
| O(2)-B(1)-O(1) | 112.5(4) |
| O(2)-B(1)-C(5) | 124.8(4) |
| O(1)-B(1)-C(5) | 122.4(4) |
| C(3)-C(2)-C(1) | 122.5(5) |

| | |
|---|---|
| C(3)-C(2)-C(4) | 120.4(5) |
| C(1)-C(2)-C(4) | 117.1(4) |
| C(2)-C(4)-C(5) | 114.6(3) |
| C(6)-C(5)-C(4) | 110.4(3) |
| C(6)-C(5)-B(1) | 114.8(4) |
| C(4)-C(5)-B(1) | 113.6(4) |
| C(6)-C(5)-C(9) | 100.4(4) |
| C(4)-C(5)-C(9) | 109.2(4) |
| B(1)-C(5)-C(9) | 107.4(3) |
| C(7)-C(6)-C(5) | 104.9(4) |
| C(6)-C(7)-C(8) | 105.9(4) |
| C(9)-C(8)-C(7) | 106.7(4) |
| C(10)-C(9)-C(8) | 114.8(4) |
| C(10)-C(9)-C(5) | 115.8(4) |
| C(8)-C(9)-C(5) | 104.7(4) |
| C(9)-C(10)-C(11) | 114.0(4) |
| C(12)-C(11)-C(10) | 113.4(4) |
| C(17)-C(12)-C(13) | 118.0(5) |
| C(17)-C(12)-C(11) | 120.0(5) |
| C(13)-C(12)-C(11) | 122.0(5) |
| C(12)-C(13)-C(14) | 120.5(5) |
| C(15)-C(14)-C(13) | 120.9(5) |
| C(14)-C(15)-C(16) | 119.5(5) |
| C(15)-C(16)-C(17) | 119.7(6) |
| C(12)-C(17)-C(16) | 121.4(5) |
| O(1)-C(18)-C(21) | 109.0(4) |
| O(1)-C(18)-C(20) | 106.9(4) |
| C(21)-C(18)-C(20) | 110.5(4) |
| O(1)-C(18)-C(19) | 102.2(3) |
| C(21)-C(18)-C(19) | 114.7(4) |
| C(20)-C(18)-C(19) | 112.9(4) |
| O(2)-C(19)-C(22) | 108.1(4) |
| O(2)-C(19)-C(23) | 107.5(4) |
| C(22)-C(19)-C(23) | 110.7(5) |
| O(2)-C(19)-C(18) | 102.2(4) |
| C(22)-C(19)-C(18) | 115.1(4) |
| C(23)-C(19)-C(18) | 112.7(4) |

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C23H35BO2. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 63(2) | 47(2) | 46(2) | -4(1) | -9(1) | 3(1) |
| O(2) | 65(2) | 50(2) | 50(2) | -5(1) | -8(2) | 4(2) |
| B(1) | 61(3) | 44(2) | 34(2) | 2(2) | 1(2) | -9(2) |
| C(1) | 81(4) | 87(4) | 52(3) | 6(3) | 12(3) | -13(3) |
| C(2) | 80(3) | 44(2) | 40(2) | -3(2) | 3(2) | -7(2) |
| C(3) | 116(5) | 51(3) | 51(3) | 6(2) | 14(3) | 2(3) |
| C(4) | 66(3) | 49(2) | 33(2) | -1(2) | 2(2) | 2(2) |
| C(5) | 59(3) | 49(2) | 30(2) | 1(2) | -2(2) | -6(2) |
| C(6) | 66(3) | 55(2) | 43(2) | -6(2) | -11(2) | 2(2) |
| C(7) | 65(3) | 87(4) | 59(3) | -12(3) | -13(3) | 3(3) |
| C(8) | 58(3) | 102(4) | 62(3) | 2(3) | -4(2) | -4(3) |
| C(9) | 63(3) | 54(2) | 44(2) | -1(2) | 0(2) | -9(2) |
| C(10) | 58(3) | 54(2) | 42(2) | 1(2) | 4(2) | -9(2) |
| C(11) | 65(3) | 80(3) | 48(2) | 2(2) | 4(2) | -20(3) |
| C(12) | 64(3) | 57(3) | 46(2) | 6(2) | 9(2) | -15(2) |
| C(13) | 70(3) | 55(3) | 68(3) | 11(2) | 7(3) | 3(3) |
| C(14) | 88(4) | 56(3) | 64(3) | -5(2) | 18(3) | 0(3) |
| C(15) | 88(4) | 68(3) | 46(2) | -2(2) | 7(2) | -11(3) |
| C(16) | 84(4) | 77(3) | 54(3) | 9(3) | 1(3) | 9(3) |
| C(17) | 75(3) | 64(3) | 62(3) | -7(2) | 16(3) | 1(3) |
| C(18) | 63(3) | 53(2) | 42(2) | 0(2) | -3(2) | 3(2) |
| C(19) | 67(3) | 52(2) | 53(2) | -1(2) | -5(2) | 10(2) |
| C(20) | 78(3) | 60(3) | 46(2) | 10(2) | 2(2) | 6(3) |
| C(21) | 63(3) | 66(3) | 54(3) | 4(2) | -6(2) | 5(2) |
| C(22) | 93(4) | 54(3) | 62(3) | -6(2) | -7(3) | 15(3) |
| C(23) | 72(3) | 83(3) | 49(3) | 2(2) | 7(2) | 18(3) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for C23H35BO2.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 4590 | 7283 | 636 | 110 |
| H(1B) | 5217 | 8183 | 1157 | 110 |
| H(1C) | 5211 | 8737 | 495 | 110 |
| H(3A) | 3319 | 10125 | 234 | 88 |
| H(3B) | 1866 | 10134 | 627 | 88 |
| H(4A) | 1545 | 8767 | 1424 | 59 |
| H(4B) | 2957 | 8349 | 1758 | 59 |
| H(6A) | 1729 | 6969 | 405 | 65 |
| H(6B) | 1204 | 5531 | 639 | 65 |
| H(7A) | -934 | 6546 | 600 | 84 |
| H(7B) | -276 | 8014 | 697 | 84 |
| H(8A) | -736 | 7851 | 1657 | 89 |
| H(8B) | -1327 | 6358 | 1564 | 89 |
| H(9) | 713 | 5394 | 1772 | 64 |
| H(10A) | 1013 | 7809 | 2428 | 62 |
| H(10B) | 2027 | 6552 | 2523 | 62 |
| H(11A) | -923 | 6620 | 2776 | 77 |
| H(11B) | -57 | 5248 | 2778 | 77 |
| H(13) | -938 | 7971 | 3654 | 77 |
| H(14) | -257 | 8308 | 4628 | 83 |
| H(15) | 1517 | 7039 | 5042 | 81 |
| H(16) | 2607 | 5387 | 4485 | 86 |
| H(17) | 1937 | 5050 | 3508 | 80 |
| H(20A) | 4040 | 4446 | 2835 | 92 |
| H(20B) | 4528 | 3054 | 2553 | 92 |
| H(20C) | 3110 | 3754 | 2333 | 92 |
| H(21A) | 6818 | 5596 | 1950 | 91 |
| H(21B) | 6916 | 4108 | 2208 | 91 |
| H(21C) | 6345 | 5300 | 2614 | 91 |
| H(22A) | 3697 | 2248 | 1537 | 104 |
| H(22B) | 5348 | 2092 | 1653 | 104 |

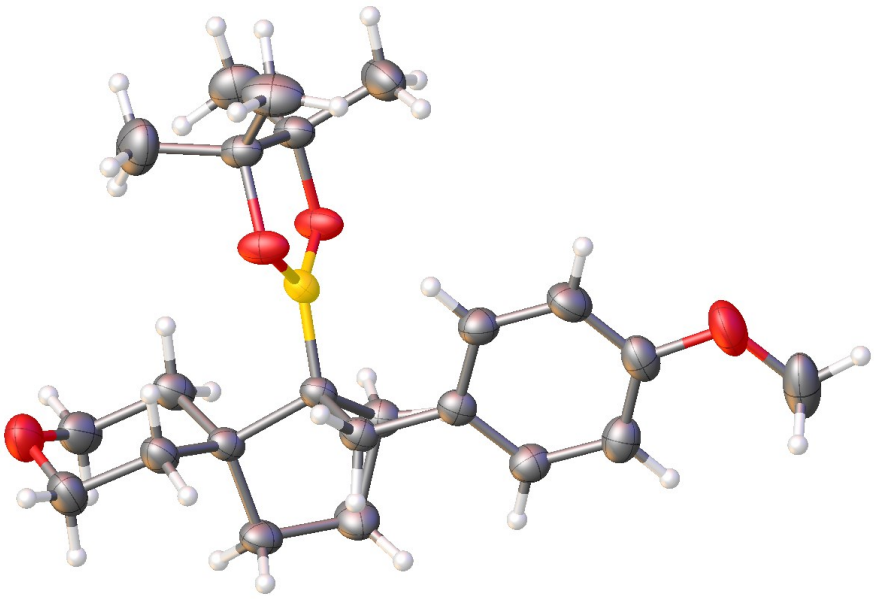
| | | | | |
|---|---|---|---|---|
| H(22C) | 4759 | 2135 | 993 | 104 |
| H(23A) | 5737 | 4217 | 570 | 102 |
| H(23B) | 6848 | 3932 | 1085 | 102 |
| H(23C) | 6158 | 5386 | 1019 | 102 |

Table 6. Torsion angles [°] for C23H35BO2.

| | |
|---|---|
| C(19)-O(2)-B(1)-O(1) | -8.5(5) |
| C(19)-O(2)-B(1)-C(5) | 177.8(4) |
| C(18)-O(1)-B(1)-O(2) | -11.4(5) |
| C(18)-O(1)-B(1)-C(5) | 162.4(4) |
| C(3)-C(2)-C(4)-C(5) | 117.0(5) |
| C(1)-C(2)-C(4)-C(5) | -62.9(6) |
| C(2)-C(4)-C(5)-C(6) | -55.2(5) |
| C(2)-C(4)-C(5)-B(1) | 75.4(5) |
| C(2)-C(4)-C(5)-C(9) | -164.7(4) |
| O(2)-B(1)-C(5)-C(6) | -15.5(6) |
| O(1)-B(1)-C(5)-C(6) | 171.4(4) |
| O(2)-B(1)-C(5)-C(4) | -144.0(4) |
| O(1)-B(1)-C(5)-C(4) | 43.0(5) |
| O(2)-B(1)-C(5)-C(9) | 95.1(5) |
| O(1)-B(1)-C(5)-C(9) | -78.0(5) |
| C(4)-C(5)-C(6)-C(7) | -74.9(5) |
| B(1)-C(5)-C(6)-C(7) | 155.1(4) |
| C(9)-C(5)-C(6)-C(7) | 40.3(5) |
| C(5)-C(6)-C(7)-C(8) | -27.3(6) |
| C(6)-C(7)-C(8)-C(9) | 2.5(6) |
| C(7)-C(8)-C(9)-C(10) | 151.0(5) |
| C(7)-C(8)-C(9)-C(5) | 22.9(6) |
| C(6)-C(5)-C(9)-C(10) | -166.2(4) |
| C(4)-C(5)-C(9)-C(10) | -50.1(5) |
| B(1)-C(5)-C(9)-C(10) | 73.6(5) |
| C(6)-C(5)-C(9)-C(8) | -38.6(5) |
| C(4)-C(5)-C(9)-C(8) | 77.5(5) |
| B(1)-C(5)-C(9)-C(8) | -158.9(4) |
| C(8)-C(9)-C(10)-C(11) | 69.2(6) |
| C(5)-C(9)-C(10)-C(11) | -168.4(4) |
| C(9)-C(10)-C(11)-C(12) | 170.1(4) |
| C(10)-C(11)-C(12)-C(17) | -76.0(6) |
| C(10)-C(11)-C(12)-C(13) | 102.0(6) |
| C(17)-C(12)-C(13)-C(14) | -0.9(8) |
| C(11)-C(12)-C(13)-C(14) | -179.0(5) |

| | |
|---|---|
| C(12)-C(13)-C(14)-C(15) | 0.6(9) |
| C(13)-C(14)-C(15)-C(16) | -0.4(9) |
| C(14)-C(15)-C(16)-C(17) | 0.5(9) |
| C(13)-C(12)-C(17)-C(16) | 1.1(8) |
| C(11)-C(12)-C(17)-C(16) | 179.2(5) |
| C(15)-C(16)-C(17)-C(12) | -0.9(9) |
| B(1)-O(1)-C(18)-C(21) | 146.6(4) |
| B(1)-O(1)-C(18)-C(20) | -93.9(4) |
| B(1)-O(1)-C(18)-C(19) | 24.9(5) |
| B(1)-O(2)-C(19)-C(22) | 144.9(4) |
| B(1)-O(2)-C(19)-C(23) | -95.6(5) |
| B(1)-O(2)-C(19)-C(18) | 23.2(4) |
| O(1)-C(18)-C(19)-O(2) | -28.8(4) |
| C(21)-C(18)-C(19)-O(2) | -146.6(4) |
| C(20)-C(18)-C(19)-O(2) | 85.6(5) |
| O(1)-C(18)-C(19)-C(22) | -145.6(4) |
| C(21)-C(18)-C(19)-C(22) | 96.6(6) |
| C(20)-C(18)-C(19)-C(22) | -31.2(7) |
| O(1)-C(18)-C(19)-C(23) | 86.2(5) |
| C(21)-C(18)-C(19)-C(23) | -31.5(6) |
| C(20)-C(18)-C(19)-C(23) | -159.3(4) |

Symmetry transformations used to generate equivalent atoms:



| | | |
|---|---|---|
| Identification code | C23H35BO4 | |
| Empirical formula | C23 H35 B O4 | |
| Formula weight | 386.32 | |
| Temperature | 100(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 10.0979(7) Å | □= 90°. |
| | b = 13.0805(9) Å | □= 90°. |
| | c = 16.4720(11) Å | □ = 90°. |
| Volume | 2175.7(3) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.179 $Mg/m^3$ | |
| Absorption coefficient | 0.616 $mm^{-1}$ | |
| F(000) | 840 | |
| Crystal size | 0.240 x 0.200 x 0.080 $mm^3$ | |
| Theta range for data collection | 4.316 to 66.633°. | |
| Index ranges | -11<=h<=11, -15<=k<=15, -19<=l<=19 | |
| Reflections collected | 63749 | |
| Independent reflections | 3820 [R(int) = 0.0715] | |
| Completeness to theta = 66.633° | 99.6 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7528 and 0.6553 | |

| | |
|---|---|
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3820 / 0 / 258 |
| Goodness-of-fit on $F^2$ | 1.054 |
| Final R indices [I>2sigma(I)] | R1 = 0.0334, wR2 = 0.0850 |
| R indices (all data) | R1 = 0.0350, wR2 = 0.0873 |
| Absolute structure parameter | 0.05(4) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.186 and -0.169 e.$Å^{-3}$ |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for C23H35BO4. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 7939(2) | 1287(1) | 3933(1) | 61(1) |
| O(2) | 4389(2) | 9057(1) | 4006(1) | 53(1) |
| O(3) | 6655(1) | 6081(1) | 2326(1) | 38(1) |
| O(4) | 7783(1) | 6561(1) | 3452(1) | 38(1) |
| B(1) | 6651(2) | 6146(2) | 3152(1) | 27(1) |
| C(1) | 7095(4) | 424(2) | 4010(2) | 65(1) |
| C(2) | 7375(2) | 2228(2) | 4076(1) | 41(1) |
| C(3) | 8215(2) | 3060(2) | 4007(1) | 45(1) |
| C(4) | 7745(2) | 4042(2) | 4138(1) | 37(1) |
| C(5) | 6427(2) | 4216(2) | 4346(1) | 30(1) |
| C(6) | 5614(2) | 3365(2) | 4422(1) | 36(1) |
| C(7) | 6066(2) | 2377(2) | 4284(1) | 40(1) |
| C(8) | 5901(2) | 5277(2) | 4484(1) | 30(1) |
| C(9) | 5430(2) | 5839(2) | 3696(1) | 28(1) |
| C(10) | 4592(2) | 6812(2) | 3934(1) | 30(1) |
| C(11) | 3253(2) | 6343(2) | 4200(1) | 38(1) |
| C(12) | 3093(2) | 5338(2) | 3723(2) | 44(1) |
| C(13) | 4389(2) | 5189(2) | 3245(1) | 34(1) |
| C(14) | 5236(2) | 7475(2) | 4590(1) | 36(1) |
| C(15) | 4489(3) | 8466(2) | 4730(2) | 49(1) |
| C(16) | 3687(3) | 8507(2) | 3402(2) | 47(1) |
| C(17) | 4374(2) | 7510(2) | 3183(1) | 37(1) |
| C(18) | 7920(2) | 6439(2) | 2015(1) | 33(1) |
| C(19) | 8592(2) | 6934(2) | 2782(1) | 34(1) |
| C(20) | 7640(3) | 7191(2) | 1334(2) | 52(1) |
| C(21) | 8632(3) | 5514(2) | 1681(2) | 52(1) |
| C(22) | 8513(3) | 8090(2) | 2816(2) | 62(1) |
| C(23) | 10001(2) | 6599(3) | 2938(2) | 57(1) |

Table 3. Bond lengths [Å] and angles [°] for C23H35BO4.

| | |
|---|---|
| O(1)-C(2) | 1.377(3) |
| O(1)-C(1) | 1.421(4) |
| O(2)-C(16) | 1.418(3) |
| O(2)-C(15) | 1.425(3) |
| O(3)-B(1) | 1.362(2) |
| O(3)-C(18) | 1.454(2) |
| O(4)-B(1) | 1.359(3) |
| O(4)-C(19) | 1.457(2) |
| B(1)-C(9) | 1.577(3) |
| C(1)-H(1A) | 0.9800 |
| C(1)-H(1B) | 0.9800 |
| C(1)-H(1C) | 0.9800 |
| C(2)-C(7) | 1.380(3) |
| C(2)-C(3) | 1.384(3) |
| C(3)-C(4) | 1.386(3) |
| C(3)-H(3) | 0.9500 |
| C(4)-C(5) | 1.394(3) |
| C(4)-H(4) | 0.9500 |
| C(5)-C(6) | 1.389(3) |
| C(5)-C(8) | 1.504(3) |
| C(6)-C(7) | 1.389(3) |
| C(6)-H(6) | 0.9500 |
| C(7)-H(7) | 0.9500 |
| C(8)-C(9) | 1.566(2) |
| C(8)-H(8A) | 0.9900 |
| C(8)-H(8B) | 0.9900 |
| C(9)-C(13) | 1.543(3) |
| C(9)-C(10) | 1.578(2) |
| C(10)-C(14) | 1.530(3) |
| C(10)-C(11) | 1.548(3) |
| C(10)-C(17) | 1.553(3) |
| C(11)-C(12) | 1.540(3) |
| C(11)-H(11A) | 0.9900 |
| C(11)-H(11B) | 0.9900 |
| C(12)-C(13) | 1.539(3) |

| | |
|---|---|
| C(12)-H(12A) | 0.9900 |
| C(12)-H(12B) | 0.9900 |
| C(13)-H(13A) | 0.9900 |
| C(13)-H(13B) | 0.9900 |
| C(14)-C(15) | 1.518(3) |
| C(14)-H(14A) | 0.9900 |
| C(14)-H(14B) | 0.9900 |
| C(15)-H(15A) | 0.9900 |
| C(15)-H(15B) | 0.9900 |
| C(16)-C(17) | 1.520(3) |
| C(16)-H(16A) | 0.9900 |
| C(16)-H(16B) | 0.9900 |
| C(17)-H(17A) | 0.9900 |
| C(17)-H(17B) | 0.9900 |
| C(18)-C(21) | 1.512(3) |
| C(18)-C(20) | 1.518(3) |
| C(18)-C(19) | 1.573(3) |
| C(19)-C(23) | 1.510(3) |
| C(19)-C(22) | 1.516(3) |
| C(20)-H(20A) | 0.9800 |
| C(20)-H(20B) | 0.9800 |
| C(20)-H(20C) | 0.9800 |
| C(21)-H(21A) | 0.9800 |
| C(21)-H(21B) | 0.9800 |
| C(21)-H(21C) | 0.9800 |
| C(22)-H(22A) | 0.9800 |
| C(22)-H(22B) | 0.9800 |
| C(22)-H(22C) | 0.9800 |
| C(23)-H(23A) | 0.9800 |
| C(23)-H(23B) | 0.9800 |
| C(23)-H(23C) | 0.9800 |

| | |
|---|---|
| C(2)-O(1)-C(1) | 116.6(2) |
| C(16)-O(2)-C(15) | 110.30(18) |
| B(1)-O(3)-C(18) | 109.49(15) |
| B(1)-O(4)-C(19) | 109.21(15) |
| O(4)-B(1)-O(3) | 112.72(17) |

| | |
|---|---|
| O(4)-B(1)-C(9) | 123.54(16) |
| O(3)-B(1)-C(9) | 123.63(17) |
| O(1)-C(1)-H(1A) | 109.5 |
| O(1)-C(1)-H(1B) | 109.5 |
| H(1A)-C(1)-H(1B) | 109.5 |
| O(1)-C(1)-H(1C) | 109.5 |
| H(1A)-C(1)-H(1C) | 109.5 |
| H(1B)-C(1)-H(1C) | 109.5 |
| O(1)-C(2)-C(7) | 124.4(2) |
| O(1)-C(2)-C(3) | 115.8(2) |
| C(7)-C(2)-C(3) | 119.8(2) |
| C(2)-C(3)-C(4) | 120.4(2) |
| C(2)-C(3)-H(3) | 119.8 |
| C(4)-C(3)-H(3) | 119.8 |
| C(3)-C(4)-C(5) | 121.1(2) |
| C(3)-C(4)-H(4) | 119.5 |
| C(5)-C(4)-H(4) | 119.5 |
| C(6)-C(5)-C(4) | 117.14(18) |
| C(6)-C(5)-C(8) | 121.17(17) |
| C(4)-C(5)-C(8) | 121.69(18) |
| C(5)-C(6)-C(7) | 122.45(19) |
| C(5)-C(6)-H(6) | 118.8 |
| C(7)-C(6)-H(6) | 118.8 |
| C(2)-C(7)-C(6) | 119.1(2) |
| C(2)-C(7)-H(7) | 120.4 |
| C(6)-C(7)-H(7) | 120.4 |
| C(5)-C(8)-C(9) | 114.49(15) |
| C(5)-C(8)-H(8A) | 108.6 |
| C(9)-C(8)-H(8A) | 108.6 |
| C(5)-C(8)-H(8B) | 108.6 |
| C(9)-C(8)-H(8B) | 108.6 |
| H(8A)-C(8)-H(8B) | 107.6 |
| C(13)-C(9)-C(8) | 110.35(16) |
| C(13)-C(9)-B(1) | 113.56(15) |
| C(8)-C(9)-B(1) | 110.71(15) |
| C(13)-C(9)-C(10) | 101.47(15) |
| C(8)-C(9)-C(10) | 109.60(15) |

| | |
|---|---|
| B(1)-C(9)-C(10) | 110.76(16) |
| C(14)-C(10)-C(11) | 113.30(16) |
| C(14)-C(10)-C(17) | 106.80(16) |
| C(11)-C(10)-C(17) | 109.59(16) |
| C(14)-C(10)-C(9) | 113.85(15) |
| C(11)-C(10)-C(9) | 102.62(15) |
| C(17)-C(10)-C(9) | 110.68(15) |
| C(12)-C(11)-C(10) | 106.58(16) |
| C(12)-C(11)-H(11A) | 110.4 |
| C(10)-C(11)-H(11A) | 110.4 |
| C(12)-C(11)-H(11B) | 110.4 |
| C(10)-C(11)-H(11B) | 110.4 |
| H(11A)-C(11)-H(11B) | 108.6 |
| C(13)-C(12)-C(11) | 106.27(17) |
| C(13)-C(12)-H(12A) | 110.5 |
| C(11)-C(12)-H(12A) | 110.5 |
| C(13)-C(12)-H(12B) | 110.5 |
| C(11)-C(12)-H(12B) | 110.5 |
| H(12A)-C(12)-H(12B) | 108.7 |
| C(12)-C(13)-C(9) | 105.24(16) |
| C(12)-C(13)-H(13A) | 110.7 |
| C(9)-C(13)-H(13A) | 110.7 |
| C(12)-C(13)-H(13B) | 110.7 |
| C(9)-C(13)-H(13B) | 110.7 |
| H(13A)-C(13)-H(13B) | 108.8 |
| C(15)-C(14)-C(10) | 112.36(18) |
| C(15)-C(14)-H(14A) | 109.1 |
| C(10)-C(14)-H(14A) | 109.1 |
| C(15)-C(14)-H(14B) | 109.1 |
| C(10)-C(14)-H(14B) | 109.1 |
| H(14A)-C(14)-H(14B) | 107.9 |
| O(2)-C(15)-C(14) | 111.78(18) |
| O(2)-C(15)-H(15A) | 109.3 |
| C(14)-C(15)-H(15A) | 109.3 |
| O(2)-C(15)-H(15B) | 109.3 |
| C(14)-C(15)-H(15B) | 109.3 |
| H(15A)-C(15)-H(15B) | 107.9 |

| | |
|---|---|
| O(2)-C(16)-C(17) | 111.97(19) |
| O(2)-C(16)-H(16A) | 109.2 |
| C(17)-C(16)-H(16A) | 109.2 |
| O(2)-C(16)-H(16B) | 109.2 |
| C(17)-C(16)-H(16B) | 109.2 |
| H(16A)-C(16)-H(16B) | 107.9 |
| C(16)-C(17)-C(10) | 112.35(17) |
| C(16)-C(17)-H(17A) | 109.1 |
| C(10)-C(17)-H(17A) | 109.1 |
| C(16)-C(17)-H(17B) | 109.1 |
| C(10)-C(17)-H(17B) | 109.1 |
| H(17A)-C(17)-H(17B) | 107.9 |
| O(3)-C(18)-C(21) | 106.71(17) |
| O(3)-C(18)-C(20) | 107.75(18) |
| C(21)-C(18)-C(20) | 109.74(19) |
| O(3)-C(18)-C(19) | 103.23(14) |
| C(21)-C(18)-C(19) | 114.67(18) |
| C(20)-C(18)-C(19) | 114.05(18) |
| O(4)-C(19)-C(23) | 107.58(18) |
| O(4)-C(19)-C(22) | 106.00(19) |
| C(23)-C(19)-C(22) | 109.4(2) |
| O(4)-C(19)-C(18) | 103.26(14) |
| C(23)-C(19)-C(18) | 115.07(19) |
| C(22)-C(19)-C(18) | 114.7(2) |
| C(18)-C(20)-H(20A) | 109.5 |
| C(18)-C(20)-H(20B) | 109.5 |
| H(20A)-C(20)-H(20B) | 109.5 |
| C(18)-C(20)-H(20C) | 109.5 |
| H(20A)-C(20)-H(20C) | 109.5 |
| H(20B)-C(20)-H(20C) | 109.5 |
| C(18)-C(21)-H(21A) | 109.5 |
| C(18)-C(21)-H(21B) | 109.5 |
| H(21A)-C(21)-H(21B) | 109.5 |
| C(18)-C(21)-H(21C) | 109.5 |
| H(21A)-C(21)-H(21C) | 109.5 |
| H(21B)-C(21)-H(21C) | 109.5 |
| C(19)-C(22)-H(22A) | 109.5 |

| | |
|---|---|
| C(19)-C(22)-H(22B) | 109.5 |
| H(22A)-C(22)-H(22B) | 109.5 |
| C(19)-C(22)-H(22C) | 109.5 |
| H(22A)-C(22)-H(22C) | 109.5 |
| H(22B)-C(22)-H(22C) | 109.5 |
| C(19)-C(23)-H(23A) | 109.5 |
| C(19)-C(23)-H(23B) | 109.5 |
| H(23A)-C(23)-H(23B) | 109.5 |
| C(19)-C(23)-H(23C) | 109.5 |
| H(23A)-C(23)-H(23C) | 109.5 |
| H(23B)-C(23)-H(23C) | 109.5 |

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Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C23H35BO4. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 80(1) | 39(1) | 65(1) | -8(1) | 6(1) | 20(1) |
| O(2) | 69(1) | 35(1) | 56(1) | 5(1) | 11(1) | 12(1) |
| O(3) | 34(1) | 56(1) | 26(1) | -9(1) | 5(1) | -11(1) |
| O(4) | 31(1) | 61(1) | 23(1) | -2(1) | 0(1) | -8(1) |
| B(1) | 28(1) | 30(1) | 24(1) | -1(1) | 1(1) | 6(1) |
| C(1) | 111(2) | 34(1) | 50(1) | -3(1) | -13(2) | 13(1) |
| C(2) | 52(1) | 37(1) | 35(1) | -2(1) | -2(1) | 11(1) |
| C(3) | 39(1) | 48(1) | 49(1) | 1(1) | 9(1) | 11(1) |
| C(4) | 33(1) | 39(1) | 40(1) | 4(1) | 3(1) | 1(1) |
| C(5) | 30(1) | 35(1) | 24(1) | 2(1) | -2(1) | 2(1) |
| C(6) | 31(1) | 39(1) | 37(1) | 4(1) | -2(1) | 1(1) |
| C(7) | 46(1) | 34(1) | 40(1) | 2(1) | -8(1) | -1(1) |
| C(8) | 29(1) | 35(1) | 24(1) | 0(1) | 0(1) | 2(1) |
| C(9) | 27(1) | 32(1) | 24(1) | 0(1) | 1(1) | 3(1) |
| C(10) | 28(1) | 33(1) | 28(1) | 2(1) | 2(1) | 6(1) |
| C(11) | 29(1) | 43(1) | 41(1) | 4(1) | 6(1) | 6(1) |
| C(12) | 29(1) | 48(1) | 56(1) | -4(1) | 1(1) | 0(1) |
| C(13) | 30(1) | 41(1) | 30(1) | -1(1) | -3(1) | -1(1) |
| C(14) | 41(1) | 36(1) | 30(1) | -1(1) | 4(1) | 5(1) |
| C(15) | 64(2) | 39(1) | 44(1) | -3(1) | 11(1) | 8(1) |
| C(16) | 50(1) | 44(1) | 48(1) | 13(1) | 8(1) | 15(1) |
| C(17) | 38(1) | 41(1) | 32(1) | 6(1) | 3(1) | 10(1) |
| C(18) | 31(1) | 40(1) | 28(1) | -2(1) | 5(1) | -4(1) |
| C(19) | 32(1) | 43(1) | 28(1) | -2(1) | 4(1) | -5(1) |
| C(20) | 55(2) | 66(2) | 35(1) | 8(1) | -4(1) | -2(1) |
| C(21) | 50(1) | 50(1) | 54(1) | -17(1) | 13(1) | -4(1) |
| C(22) | 84(2) | 44(1) | 59(2) | -9(1) | -2(2) | -9(1) |
| C(23) | 32(1) | 91(2) | 48(1) | -1(1) | -4(1) | -2(1) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for C23H35BO4.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 6778 | 374 | 4571 | 98 |
| H(1B) | 7587 | -198 | 3870 | 98 |
| H(1C) | 6337 | 498 | 3643 | 98 |
| H(3) | 9119 | 2957 | 3870 | 54 |
| H(4) | 8332 | 4606 | 4084 | 44 |
| H(6) | 4715 | 3462 | 4573 | 43 |
| H(7) | 5481 | 1811 | 4332 | 48 |
| H(8A) | 6601 | 5692 | 4745 | 35 |
| H(8B) | 5147 | 5238 | 4867 | 35 |
| H(11A) | 3255 | 6207 | 4791 | 45 |
| H(11B) | 2516 | 6817 | 4074 | 45 |
| H(12A) | 2946 | 4759 | 4099 | 53 |
| H(12B) | 2330 | 5383 | 3348 | 53 |
| H(13A) | 4286 | 5426 | 2678 | 40 |
| H(13B) | 4650 | 4459 | 3240 | 40 |
| H(14A) | 5271 | 7085 | 5104 | 43 |
| H(14B) | 6156 | 7635 | 4427 | 43 |
| H(15A) | 3588 | 8309 | 4932 | 59 |
| H(15B) | 4950 | 8871 | 5152 | 59 |
| H(16A) | 3606 | 8936 | 2909 | 57 |
| H(16B) | 2783 | 8357 | 3601 | 57 |
| H(17A) | 5241 | 7665 | 2932 | 45 |
| H(17B) | 3832 | 7140 | 2778 | 45 |
| H(20A) | 7177 | 6838 | 892 | 78 |
| H(20B) | 8477 | 7470 | 1131 | 78 |
| H(20C) | 7085 | 7748 | 1540 | 78 |
| H(21A) | 8811 | 5031 | 2122 | 77 |
| H(21B) | 9469 | 5727 | 1433 | 77 |
| H(21C) | 8075 | 5182 | 1270 | 77 |
| H(22A) | 7589 | 8305 | 2752 | 93 |
| H(22B) | 9048 | 8382 | 2378 | 93 |

| | | | | |
|---|---|---|---|---|
| H(22C) | 8849 | 8329 | 3341 | 93 |
| H(23A) | 10333 | 6934 | 3430 | 86 |
| H(23B) | 10557 | 6790 | 2475 | 86 |
| H(23C) | 10026 | 5856 | 3012 | 86 |

Table 6. Torsion angles [°] for C23H35BO4.

| | |
|---|---|
| C(19)-O(4)-B(1)-O(3) | 7.3(2) |
| C(19)-O(4)-B(1)-C(9) | -169.04(17) |
| C(18)-O(3)-B(1)-O(4) | 2.7(2) |
| C(18)-O(3)-B(1)-C(9) | 179.02(17) |
| C(1)-O(1)-C(2)-C(7) | -0.2(3) |
| C(1)-O(1)-C(2)-C(3) | 179.3(2) |
| O(1)-C(2)-C(3)-C(4) | 179.9(2) |
| C(7)-C(2)-C(3)-C(4) | -0.7(4) |
| C(2)-C(3)-C(4)-C(5) | 0.5(4) |
| C(3)-C(4)-C(5)-C(6) | 0.4(3) |
| C(3)-C(4)-C(5)-C(8) | -179.61(19) |
| C(4)-C(5)-C(6)-C(7) | -1.2(3) |
| C(8)-C(5)-C(6)-C(7) | 178.86(19) |
| O(1)-C(2)-C(7)-C(6) | 179.4(2) |
| C(3)-C(2)-C(7)-C(6) | 0.0(3) |
| C(5)-C(6)-C(7)-C(2) | 1.0(3) |
| C(6)-C(5)-C(8)-C(9) | -94.1(2) |
| C(4)-C(5)-C(8)-C(9) | 85.9(2) |
| C(5)-C(8)-C(9)-C(13) | 55.3(2) |
| C(5)-C(8)-C(9)-B(1) | -71.3(2) |
| C(5)-C(8)-C(9)-C(10) | 166.27(16) |
| O(4)-B(1)-C(9)-C(13) | -168.26(18) |
| O(3)-B(1)-C(9)-C(13) | 15.8(3) |
| O(4)-B(1)-C(9)-C(8) | -43.5(3) |
| O(3)-B(1)-C(9)-C(8) | 140.56(19) |
| O(4)-B(1)-C(9)-C(10) | 78.3(2) |
| O(3)-B(1)-C(9)-C(10) | -97.6(2) |
| C(13)-C(9)-C(10)-C(14) | 163.95(16) |
| C(8)-C(9)-C(10)-C(14) | 47.3(2) |
| B(1)-C(9)-C(10)-C(14) | -75.2(2) |
| C(13)-C(9)-C(10)-C(11) | 41.11(17) |
| C(8)-C(9)-C(10)-C(11) | -75.56(18) |
| B(1)-C(9)-C(10)-C(11) | 161.99(16) |
| C(13)-C(9)-C(10)-C(17) | -75.74(19) |
| C(8)-C(9)-C(10)-C(17) | 167.58(16) |

| | |
|---|---|
| B(1)-C(9)-C(10)-C(17) | 45.1(2) |
| C(14)-C(10)-C(11)-C(12) | -151.77(17) |
| C(17)-C(10)-C(11)-C(12) | 89.1(2) |
| C(9)-C(10)-C(11)-C(12) | -28.6(2) |
| C(10)-C(11)-C(12)-C(13) | 4.9(2) |
| C(11)-C(12)-C(13)-C(9) | 21.6(2) |
| C(8)-C(9)-C(13)-C(12) | 77.4(2) |
| B(1)-C(9)-C(13)-C(12) | -157.65(17) |
| C(10)-C(9)-C(13)-C(12) | -38.76(19) |
| C(11)-C(10)-C(14)-C(15) | -70.1(2) |
| C(17)-C(10)-C(14)-C(15) | 50.6(2) |
| C(9)-C(10)-C(14)-C(15) | 173.11(16) |
| C(16)-O(2)-C(15)-C(14) | 61.1(3) |
| C(10)-C(14)-C(15)-O(2) | -58.0(3) |
| C(15)-O(2)-C(16)-C(17) | -60.5(2) |
| O(2)-C(16)-C(17)-C(10) | 56.5(2) |
| C(14)-C(10)-C(17)-C(16) | -50.0(2) |
| C(11)-C(10)-C(17)-C(16) | 73.1(2) |
| C(9)-C(10)-C(17)-C(16) | -174.40(18) |
| B(1)-O(3)-C(18)-C(21) | 110.7(2) |
| B(1)-O(3)-C(18)-C(20) | -131.46(19) |
| B(1)-O(3)-C(18)-C(19) | -10.5(2) |
| B(1)-O(4)-C(19)-C(23) | -135.23(19) |
| B(1)-O(4)-C(19)-C(22) | 107.8(2) |
| B(1)-O(4)-C(19)-C(18) | -13.1(2) |
| O(3)-C(18)-C(19)-O(4) | 13.97(19) |
| C(21)-C(18)-C(19)-O(4) | -101.70(19) |
| C(20)-C(18)-C(19)-O(4) | 130.57(19) |
| O(3)-C(18)-C(19)-C(23) | 130.9(2) |
| C(21)-C(18)-C(19)-C(23) | 15.2(3) |
| C(20)-C(18)-C(19)-C(23) | -112.5(2) |
| O(3)-C(18)-C(19)-C(22) | -100.9(2) |
| C(21)-C(18)-C(19)-C(22) | 143.5(2) |
| C(20)-C(18)-C(19)-C(22) | 15.7(3) |

# Chapter 3 Enantioselective Diboration of Monosubstituted Cyclobutenes and Regioselective Diboron Functionalization

## 3.1 Introduction

Cyclobutanes, as a class of highly strained carbocycles, have been recognized as structurally intriguing motifs in both natural products [1] and drug molecules. [2] Thanks to their high conformational rigidity, cyclobutane skeletons offer unique advantages in drug design by securely locking a specified pharmacophore into a specific spatial orientation, resulting in molecules with significantly fewer possible conformers compared to other scaffolds. [3] However, although cyclobutanes are widely demonstrated to be valuable motifs, methods towards the synthesis of densely functionalized cyclobutanes are still quite limited, in contrast to methods for the synthesis of larger ring sizes, or even cyclopropanes. This is mainly because of two reasons: firstly, the high ring strain (26.3 kcal/mol for unsubstituted cyclobutane)[4] often renders it thermodynamically unfavourable for a four-membered ring closure to occur. [5] Additionally, as cycloalkenes are versatile precursors for the synthesis of corresponding cycloalkanes, the ring strain and nearly 90° C–C bond angles result in cyclobutenes to be synthetically challenging[6] and the π-bond less stable compared to higher ordered ring systems. Secondly, there are numerous methods for cyclopentane and cyclohexane formation, such as [2+3] and [2+4] cycloaddition reactions that could occur under

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therma-conditions.[7] Moreover, for [1+2] cyclopropanation, various methods leveraging the reaction between carbenes and alkenes have been developed.[8] However, the [2+2] cyclobutane synthesis is thermally forbidden according to Woodward-Hoffmann rules.[9] Therefore, in order to achieve such a reaction, a more technically demanding photochemistry is usually required.[10] Moreover, these photochemistry processes are often considered difficult in controlling the stereochemistry outcomes.[11] Despite these challenges, various novel transition-metal or small molecule catalysts systems have been developed to deliver these cyclobutanes, where the newly generated stereogenic centers on the cyclobutane ring can be precisely controlled. One example is Bach 's chiral photosensitizer-catalyzed [2+2] cycloaddition to quinolones[12], as well as similar cycloadditions controlled by chiral Lewis acid and hydrogen bond donors.[13] Chiral auxiliaries have been shown to render photocatalytic [2+2] cycloadditions stereospecific as well, for example the work done by Xia [14] More recently, List also developed an ion-pair enabled photocatalyt system to achieve a more general enantioselective [2+2] cycloaddition.[15] Beyond ring-closure reactions towards stereodefined substituted cyclobutanes, there are also reactions utilizing cyclobutenes as precursors for installing functional groups stereoselectively onto the cyclobutane ring.[16] In this Chapter, methods for constructing stereodefined substituted cyclobutanes will be thoroughly reviewed. In this context, a novel strategy for the synthesis of densely functionalized cyclobutanes that we developed will be introduced. This method leverages a strategy of enantioselective

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[13] For Lewis acid catalyzed cyclobutanation: a) Canales, E. Corey, E. J. *J. Am. Chem. Soc.* **2007**, *129*, 12686-12687. b) Brimioulle, R.; Guo, H.; Bach, T. *Chem. Eur. J.* **2012**, *18*, 7552–7560. c) Brimioulle, R.; Bach, T. *Science* **2013**, *342*. 840−843. For hydrogen bond donor controlled cyclobutanation: a) Vallavoju, N.; Selvakumar, S.; Jockush, S.; Sibi, M. P.; Sivaguru, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 5604–5608. b) Vallavoju, N.; Selvakumar, S.; Jockush, S.; Prabhakaran, M. T.; Sibi, M. P.; Sivaguru, J. *Adv. Synth. Catal.* **2014**, *356*, 2763–2768.

[14] Zhao, G.; Yang, C.; Sun, H.; Lin, R.; Xia, W. *Org. Lett.* **2012**, *14*, 776–779.

[15] Das, S.; Zhu, C.; Demirbas, D.; Bill, E.; Kanta, C.; List, B. *Science* **2023**. *379*, 494–499.

[16] For review on the synthesis of cyclobutenes: Xu, Y.; Conner, M. L.; Brown, M. K. *Angew. Chem. Int. Ed.* **2015**, *54*, 11918–11928. More detailed discussion will be held later. For the derivatization of cyclobutenes, see discussions later in this Chapter.

diboration of monosubstituted cyclobutenes and site-selective functionalization of resulted diboron. The optimization, substrate scope of the reaction, and the utility of the diboron products will be discussed in detail.

### 3.1.1 Examples of Cyclobutanes Synthesis in Natural Products

To date, there have been numerous reports on the asymmetric synthesis of complex natural products containing cyclobutane rings. As demonstrated in Ding 's review[1], the strategies for constructing such cyclobutane rings can be categorized into four types: intramolecular ring closure, cycloaddition, ring contraction, and ring expansion. In this context, representative works in each of these four classes of cyclobutane synthesis will be discussed.

#### 3.1.1.1 Intramolecular Ring Closure

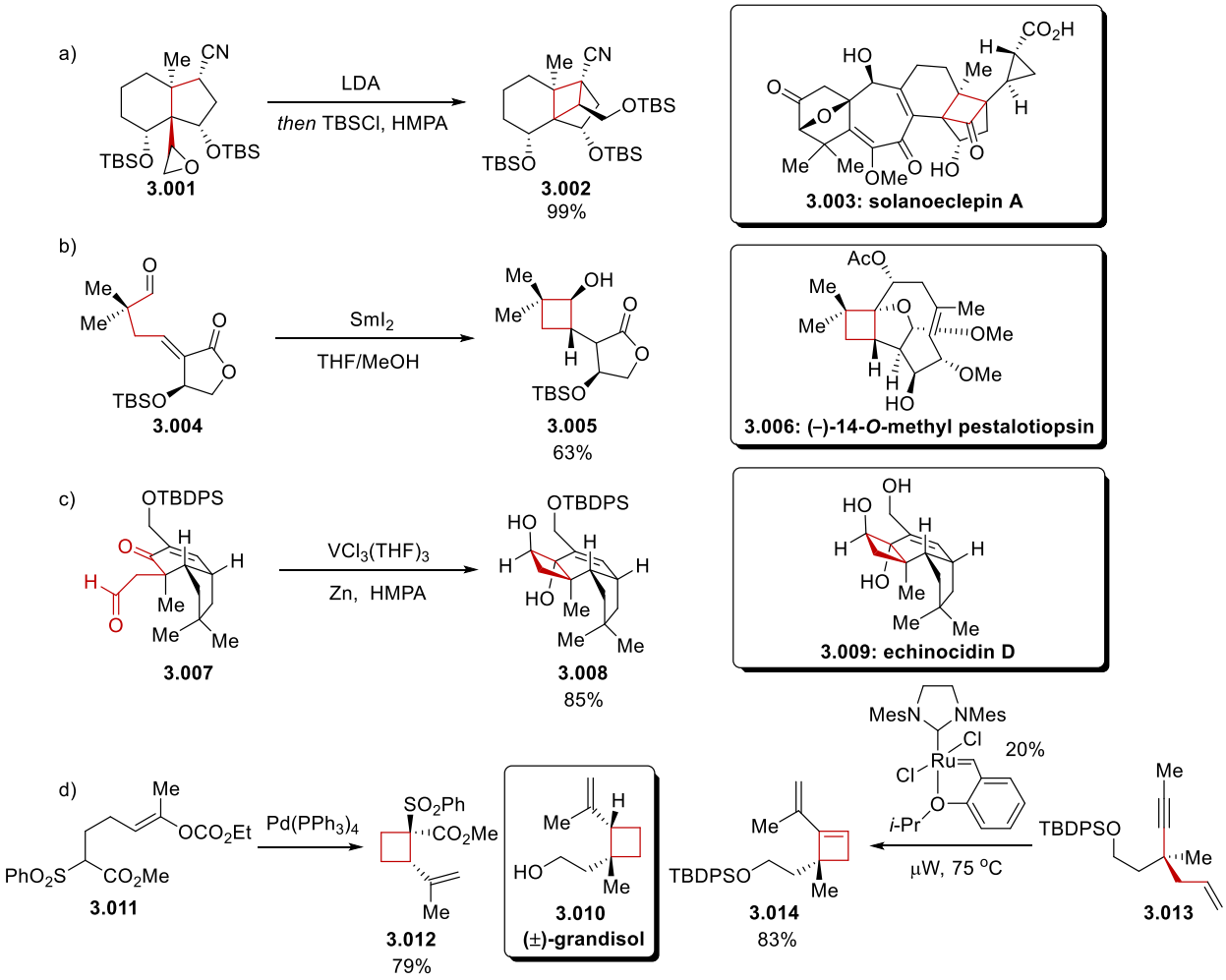


***Figure 3.1.*** Synthesis of Cyclobutanes Using Intramolecular Ring Closure Strategy

In the total synthesis of solanoeclepin A[17], Tanino utilized a nucleophilic intramolecular cyclization reaction to construct the bridged cyclobutane ring in **3.002**. After deprotonation of the nitrile-substituted carbon in **3.001**, the carbanion intramolecularly attacks the epoxide to furnish the desired cyclobutane product in quantitative yield. In addition to nucleophilic cyclization, radical-mediated ring closure was also found to be an effective strategy. An example of this approach is the total synthesis of (−)-14-O-methyl pestalotiopsin accomplished by Procter.[18] As shown in Figure 3.1b, by treating aldehyde **3.004** with samarium iodide, the aldehyde was reduced to an α-oxy carboradical, which intramolecularly adds to the Michael acceptor, producing the cyclobutane containing product **3.005** in 63% yield. Another illustration is the total synthesis of echinocidin D[19] accomplished by Scheidt (Figure 3.1c). Similarly, treating dicarbonyl **3.007** with a vanadium/zinc bimetallic reductant reduces the more exposed aldehyde moiety to the α-oxy carboradical, which then reacts with the metal-ligated ketone to furnish the cyclobutane **3.008** in 85% yield.

Transtion-metal catalyzed processes have also been shown to promote four membered ring closure as well. For example, Suh utilized a Pd-catalyzed allylic alkylation to close the cyclobutane ring in **3.012**, a key intermediate for the synthesis of (±)-grandisol.[20] The reaction from **3.011** to **3.012** was shown to be highly diastereoselective and in good yield (79%). In the synthesis of the same natural product (±)-grandisol, Goess took a different approach; the cyclobutane originating from a cyclobutene **3.014** was prepared from an intramolecular enyne metathesis on linear enyne **3.013**. The reaction was quite effective, considering the difficulty in overcoming possible side reactions such as intermolecular metathesis.[21] The Hoveyda-Grubbs II catalyst[22] was found to be the optimal catalyst for an effective cyclobutenation to occur.

[17] Tanino, K.; Takahashi, M.; Tomata, Y.; Uehara, T.; Narabu, T.; Miyashita, M. *Nature Chem*. **2011**, *3*, 484–488.
[18] Baker, T. M.; Edmonds, D. J.; Hamilton, D.; O'Brein, C. J.; Procter, D. J. *Angew. Chem. Int. Ed.* **2008**, *47*, 5631–5633.
[19] Hovey, M. T.; Cohen, D. T.; Walden, D. M.; Cheong, P. H.; Scheidt, K. A. *Angew. Chem. Int. Ed.* **2017**, *56*, 9864–9867.
[20] Han, Y. T.; Kim, N. J.; Jung, J. W.; Yun, H.; Lee, S.; Suh, Y. G. *Arch. Pharmacal Res.* **2011**, *34*, 1437–1442.
[21] Xie, J.; Wang, J.; Dong, G. *Org. Lett.* **2017**, *19*, 3017–3020.
[22] Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

### 3.1.1.2 [2+2] Cycloaddition

As an efficient way to approach cyclobutanes, [2+2] photocycloaddition has been widely used to prepare key intermediates in cyclobutane containing natural product synthesis.[23] In 2008, Nicolaou [24] reported the total synthesis of bielschowskysin (Figure 3.2a), where the cyclobutane core structure **3.016** was constructed by an intramolecular [2+2] photocycloaddition from macrocycle **3.015**. The reaction proved highly efficient, furnishing the desired multicyclization product **3.016** in 90% yield. Another example is the total synthesis of (+)-aquatolide by Takao , where the cyclobutane-containing cage ring system in **3.019** was synthesized by using an intramolecular crossed [2+2] photocycloaddition.[25] As shown in Figure 3.2b, the crossed cycloaddition from **3.018** successfully constructed the desired cage ring system in 37% yield.

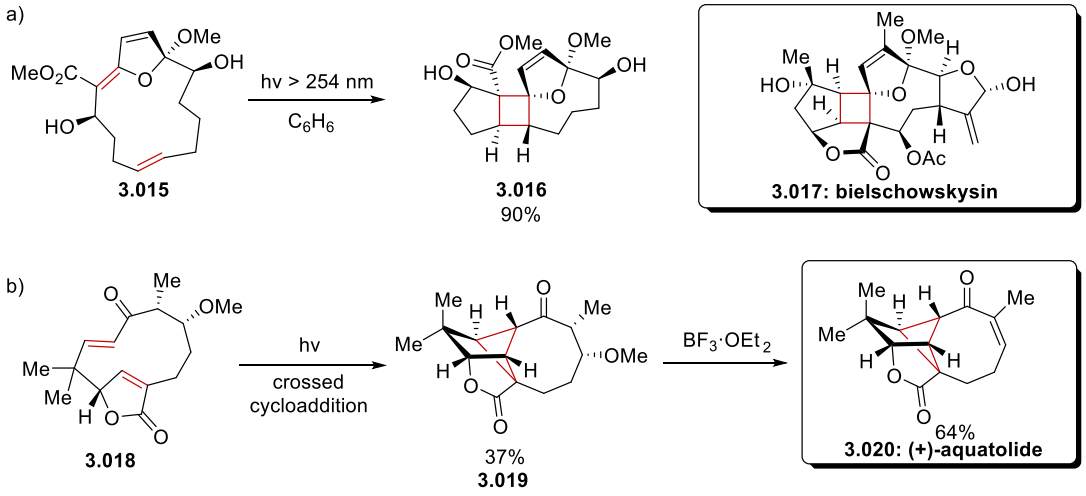


***Figure 3.2.*** Synthesis of Cyclobutanes Using Intramolecular [2+2] Cycloaddition

### 3.1.1.3 Ring Contraction Strategies

In Chapter 2, we introduced an example of cyclobutane synthesis using the ring contraction strategy, specifically Aggarwal's synthesis of cyclobutyl boronic ester *via* visible-light-driven ring contraction of cyclic alkenyl boronate complexes. In the earlier part of the Results and Discussion section of Chapter 2, we also attempted a similar ring contraction approach to synthesize

[23] Williams, M. J.; Deak, H. L.; Snapper, M. L. *J. Am. Chem. Soc.* **2007**, *129*, 486–487.
[24] Nicolaou, K. C.; Adsool, V. A.; Hale, C. R. H. *Angew. Chem. Int. Ed.* **2011**, *50*, 5149–5152.
[25] Takao, K.; Yamada, A.; Fukushima, Y.; Komatsu, D.; Ogura, A.; Yoshida, K. *Angew. Chem. Int. Ed.* **2019**, *58*, 9851–9855.

cyclobutanes using a conjunctive cross-coupling reaction. Besides these examples, numerous reports also exist on the synthesis of cyclobutanes employing various types of ring contraction reactions. For instance, Reisman utilized a Wolff rearrangement to construct the cyclobutane motif in the total synthesis of (+)-psiguadial B. [26] By subjecting diazo compound **3.022** and aminoquinoline to UV light in the present of (+)-cinchonine alkaloid, an enantioselective ring contraction delivered the cyclobutyl amide **3.023** with 62% yield and 79% ee. Another application of the Wolff rearrangement in constructing a cyclobutane ring is evident in Zhang's total synthesis of the cage-ring system in the natural product aquatolide, as shown in Figure 3.2b from **3.024** to **3.025**.[27] The Ramberg-Backlund ring contraction can also be employed to generate cyclobutenes. One example is the synthesis of ladderane reported by Burns. [28] The cyclobutene-cyclobutane bicyclic intermediate **3.028** can be generated from chlorinated sulfoxide by a ring contraction in 49% yield. Subsequently, intermediate underwent [2+2] photocycloaddition to yield the desired ladderane.

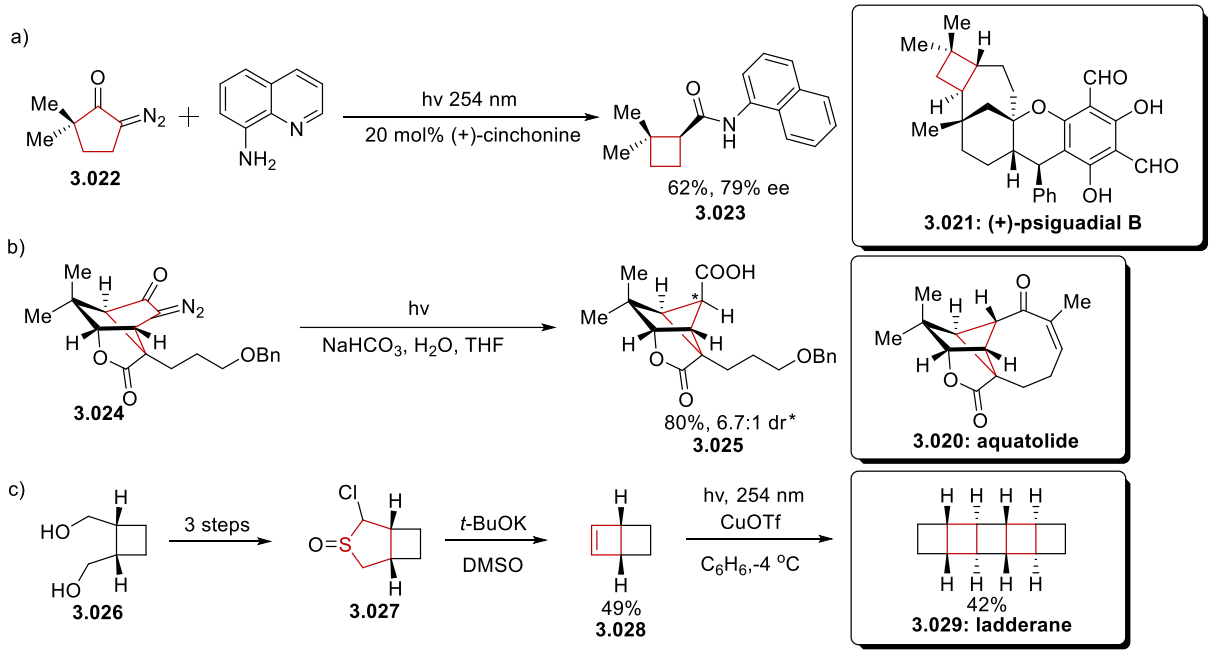


***Figure 3.3.*** Synthesis of Cyclobutanes Using Ring Contraction Reactions

[26] Chapman, L. M.; Beck, J. C.; Wu, L.; Reisman, S. E. *J. Am. Chem. Soc.* **2016**, *138*, 9803–9806.
[27] Taylor, R. J. K.; Casy, R. *The Ramberg-Backlund Reaction in Organic Reactions* **2004**, 359–475.
[28] Mercer, J. A. M.; Cohen, C. M.; Shuken, S. R.; Wager, A. M.; Smith, M. W.; Moss III, F. R.; Smith, M. D.; Vahala, R.; Martinez, A. G.; Boxer, S. G.; Burns, N. Z. *J. Am. Chem. Soc.* **2016**, *138*, 15845–15848.

### 3.1.1.4 Ring Expansion Strategies

As mentioned previously, despite the higher ring strain of cyclopropanes compared to cyclobutanes, they are more synthetically accessible due to advancements in cyclopropanation reactions involving carbene equivalents and alkenes. Consequently, researchers have directed their efforts towards synthesizing cyclobutanes from cyclopropane starting materials through ring expansion reactions. An illustrative example is the synthesis of pipercyclobutanamide A (Figure 3.4) reported by Tang and colleagues. [29] Cyclopropane **3.031** was initially synthesized through enantioselective cyclopropanation reaction. Subsequently, **3.031** was converted to hydrazine **3.032** in five steps, which then followed by rearrangement and ring expansion, resulting in the desired cyclobutane **3.033**—a core structure pivotal for the enantioselective total synthesis of pipercyclobutanamide A.

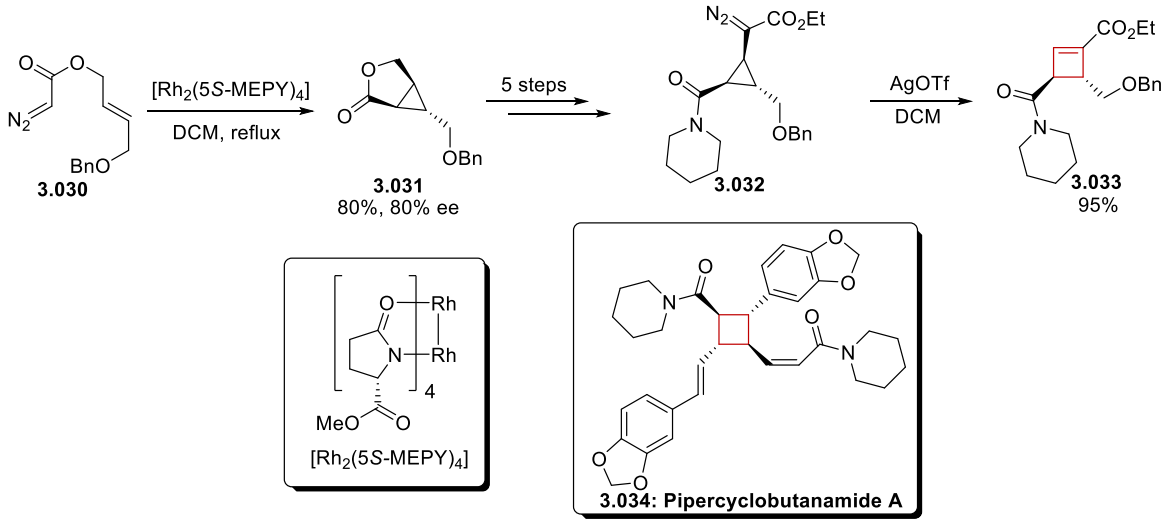


***Figure 3.4.*** Synthesis of Pipercyclobutanamide A Using Ring Expansion of Cyclopropane

In 2020, Aggarwal introduced a methodology for the diastereoselective construction of densely substituted cyclobutanes through the expansion of cyclopropane. [30] Beginning with bromocyclopropane and vinyl B(pin), an homologation was employed to synthesize vinyl cyclopropyl B(pin), denoted as **3.071**. [31] Subsequently, **3.071** underwent reaction with

[29] Liu, R.; Zhang, M.; Wyche, T. P.; Winston, G. N.; Bugni, T. S.; Tang, W. *Angew. Chem. Int. Ed.* **2012**, *51*, 7503–7506.
[30] Hari, D. P.; Abell, J.C.; Fasano, V.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2020**, *142*, 5515−5520.
[31] For detail of this reaction, see Chapter 2 section 2.1.1.2.

organolithium reagents to yield boronate complexes **3.072**. A polar-induced 1,2-migration ring expansion ensued upon treating **3.072** with Eschenmoser salt. This process consistently produced the desired cyclobutyl tertiary boronic esters in high yields and diastereomeric ratios, exemplified by the substrates in Figure 3.5 (**3.074-3.077**). The utility of this method was demonstrated in the synthesis of the natural product (±)-grandisol **3.010**, utilizing the methyl-migrating substrate **3.078** as the starting material.

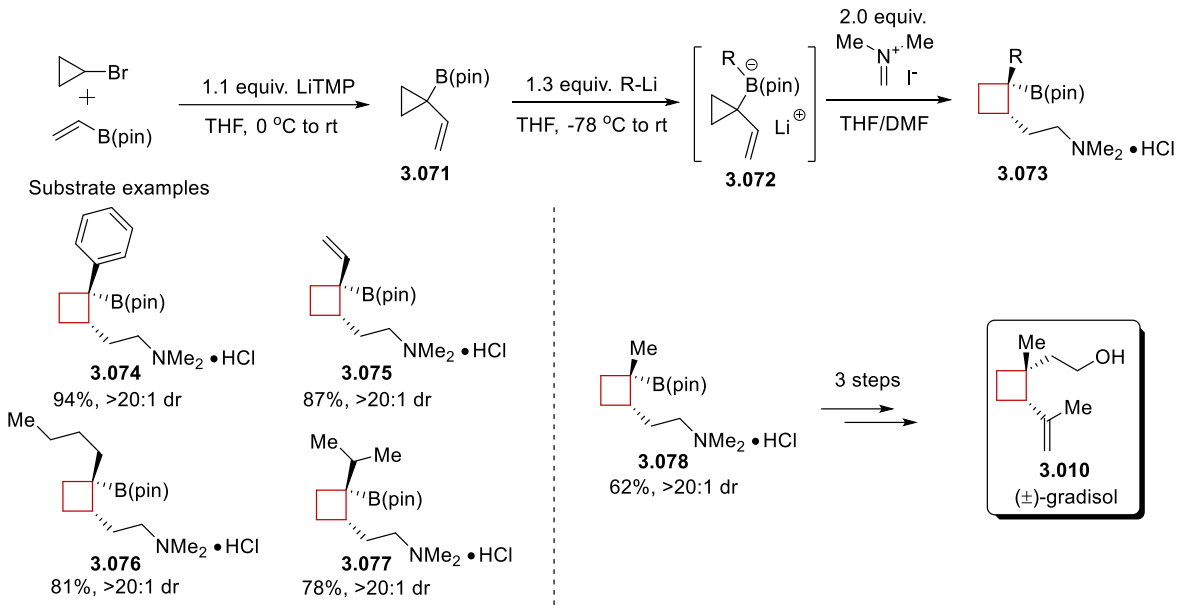


***Figure 3.5.*** Ring Expansion of Cyclopropane *via* Polar Crossover Induced 1,2-migration of Vinyl Cyclopropyl Boronate Complexes

### 3.1.2 The Applications of Cyclobutanes in Drug Design

Cyclobutanes play a crucial role as scaffolds in drug design, contributing to the enhancement of drug molecules in various ways.[32] Three well-recognized functions underscore the significance of cyclobutanes in drug design: (1) the rigid cyclobutane ring acts as a conformational restriction factor, imparting molecular rigidity. This rigidity is instrumental in directing pharmacophores conformation to achieve desired spatial orientations. (2) The hydrophobic nature of the cyclobutane ring enhances a drug's binding efficacy toward hydrophobic pockets in protein targets. (3) Cyclobutane serves as a bioisosteric replacement for *para*-substituted arenes and *cis*/trans olefins, thereby reducing the planarity of drug molecules. In this section, examples illustrating the

[32] Van der Kolk, M. R.; Janssen, M. A. C. H.; Rutjes, F. P. J. T.; Blanco-Ania, D. *ChemMedChem.* **2022**, *17*, e202200020.

use of cyclobutanes to enhance the performance of drug molecules through these three mechanisms will be presented and discussed.

### 3.1.2.1 Using Cyclobutanes as Conformational Restriction Factor

The ablility of cyclobutanes to rigidify a hydrocarbon aliphatic chain in a drug molecule has been exemplified by Nikas's development of the CB1 receptor antagonist Hexahydrocannabinol (HHC).[33] As depicted in Figure 3.6a, the insertion of a 1,1-disubstituted cyclobutane into the *n*-pentane domain of HHC resulted in the rigidified structure **3.035**, which exhibits a significantly lower inhibition constant against CB1 and heightened selectivity against CB2. Another illustrative example is the DOT1L inhibitor **3.037**, developed by Daigle.[34] Seeking to enhance the performance of a known aminonucleoside inhibitor (**3.036** in Figure 3.6b), Daigle synthesized **3.037**, incorporating a trans-configured 1,3-disubstituted cyclobutane onto the propane linker and modifying the urea motif into benzimidazole. Consequently, **3.037** demonstrated a substantially lower $K_i$, improved residence time, and enhanced selectivity compared to its original drug lead.

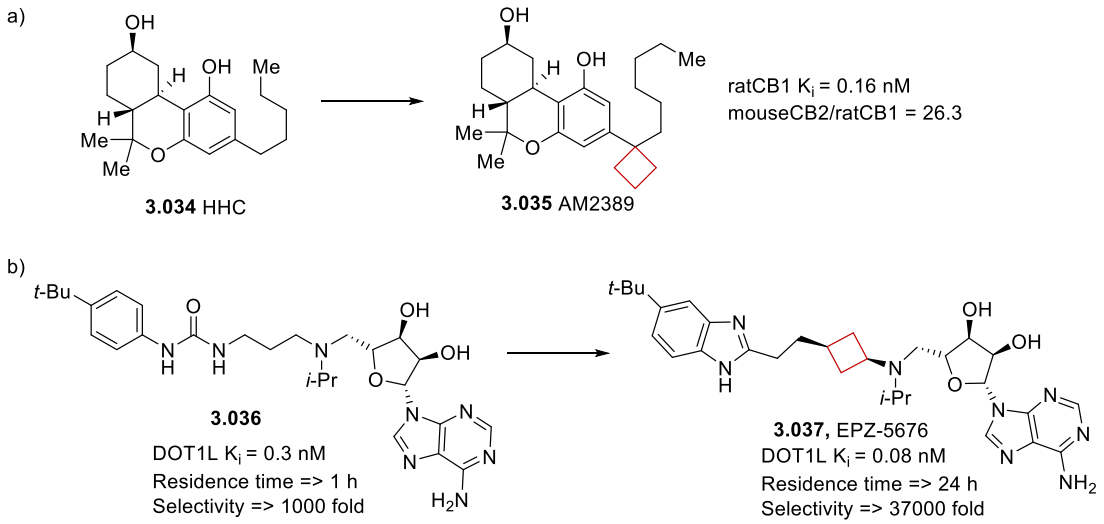


***Figure 3.6.*** Examples of Enhancing Drug Molecule Rigidity by Introducing Cyclobutane Ring to Aliphatic Chains

[33]. Nikas, S. P.; Alapafuja, S. O.; Papanastasiou, I.; Paronis, C. A.; Shukla, V. G.; Papahatjis, D. P.; Bowman, A. L.; Halikhedkar, A. Han, X.; Makriyannis, A.; *J. Med. Chem.* **2010**, 53, 6996–17010.

[34] Daigle, S. R.; Olhava, E. J.; Therkelsen, C. A.; Basavapathruni, A.; Jin, L.; Boriack-Sjodin, P. A.; Allain, C. J.; Klaus, C. R.; Raimondi, A.; Scott, M. P.; Waters, N. J.; Chesworth, R.; Moyer, M. P.; Copeland, R. A.; Richon, V. M.; Pollock, R. M. *Blood* **2013**, *122*, 1017–1025.

In addition to utilizing cyclobutanes for the configuration restriction effect to enhance the rigidity of drug molecules, researchers have employed cyclobutanes as scaffolds to guide pharmacophores toward desired spatial orientations. A notable example is the JAK1 receptor inhibitor **3.039**, developed by Vazquez. [35] The discovery of **3.039** was rooted in the pre-existing drug tofacitinib, as depicted in Figure 3.7a, with substantial modifications to its aliphatic ring system. Specifically, the α-cyano carbonyl was replaced with sulfonamide, and the flexible piperidine scaffold was substituted with a rigid cyclobutane linker. These modifications not only maintained high potencies comparable to the original drug but also significantly improved its selectivity towards JAK1 over JAK2.

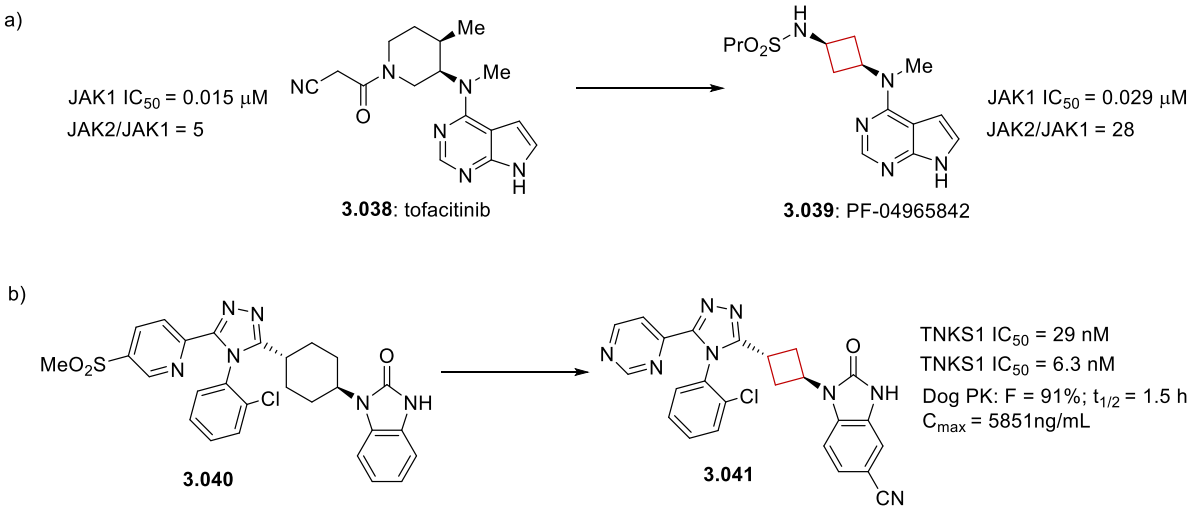


***Figure 3.7.*** Examples Using Cyclobutane to Restrict Spatial Orientation of Pharmacophores

Further investigations revealed that the enhanced selectivity of **3.039** is attributed to the puckered conformation of the cyclobutane, which positions the sulfonamide group to form strong hydrogen bonds with functional groups in the JAK1 binding pocket. As another example, the TNKS inhibitor **3.041**, developed by Anumala, also employed a similar strategy. [36] In the original lead molecule **3.040**, *trans*-1,4-cyclohexane served as a linker for the two heterocyclic

[35] Vazquez, M. L.; Kaila, N.; Strohbach, J. W.; Trzupek, J. D.; Brown, M. F.; Flanagan, M. E.; Mitton-Fry, M. J. Johnson, T. A.; TenBrink, R. E.; Arnold, E. P.; Basak, A.; Heasley, S. E.; Kwon, S.; Langille, J.; Parikh, M. D.; Griffin, S. H.; Casavant, J. M.; Duclos, B. A.; Fenwick, A. E.; Harris, T. M.; Han, S.; Caspers, N.; Dowty, M. E.; Yang, X.; Banker, M. E.; Hegen, M.; Symanowicz, P. T.; Li. L.; Wang, L.; Lin, T. H.; Jussif, J.; Clark, J. D.; Telliez, J .B.; Robinson, R. P.; Unwalla, R.; J. Med. Chem. 2018, 61, 1130–1152.

[36] Anumala, U. R.; Waaler, J.; Nkizinkiko, Y. Ignatev, A.; Lazarow, K.; Lindemann, P.; Olsen, P. A.; Murthy, S.; Obaji, E.; Majouga, A. G.; Leonov, S.; von Kries, J. P.; Lehtio, L.; Krauss, S.; Nazare, M. J. Med. Chem. **2017**, *60*, 10013–10025.

pharmacophores. The substitution from a flexible cyclohexane to a more rigid cyclobutane resulted in the repositioning of the two pharmacophore groups with shorter distances between them. This adjustment effectively locked them in position, significantly enhancing binding affinity and pharmacokinetic performance.

### 3.1.2.2 Using Cyclobutanes to Improve Hydrophobicity

As an aliphatic ring system, cyclobutanes can be utilized to augment the hydrophobicity of a drug molecule thereby enhancing its binding to hydrophobic domains within a given binding pocket. An illustrative case is the development of the β3-AR inhibitor **3.043**, depicted in Figure 3.8a. According to research conducted by Wada [37], the original lead molecule **3.042** encountered challenges such as poor metabolic stability and inadequate pharmacokinetics. By changing the methyl group on the sulfonamide to a cyclobutane group, the similarly high binding affinity was maintained. A further study shows that the cyclobutyl ring in **3.045** fits the hydrophobic pocket of targeted protein more effectively.

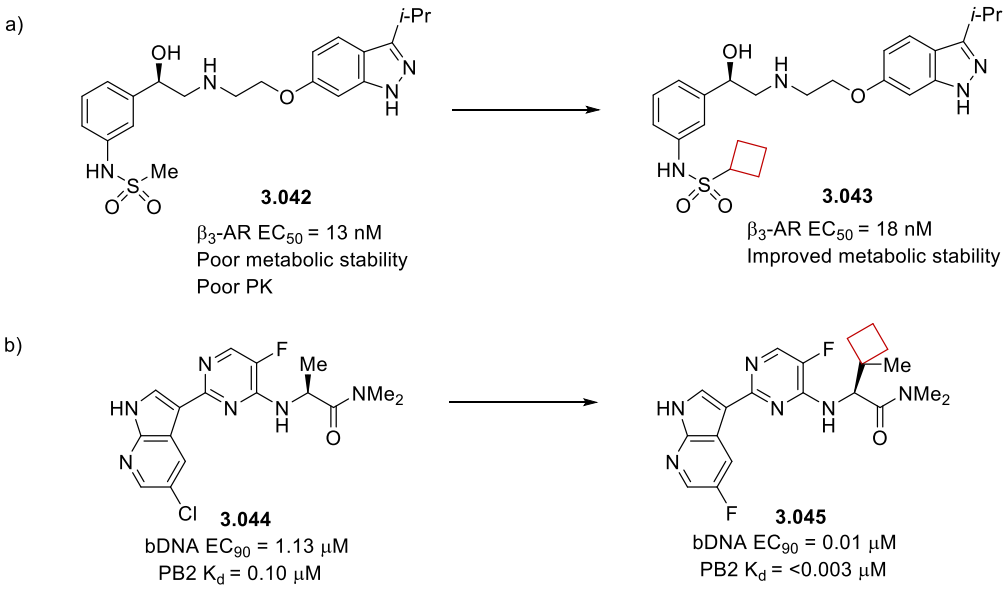


***Figure 3.8.*** Examples of Enhancing Drug Molecule Hydrophobicity by Introducing Cyclobutane Rings

[37] Wada, Y.; Nakano, S.; Morimoto, A.; Kasahara, K.; Hayashi, T.; Takada, Y.; Suzuki, H.; Niwwa-Sakai, M.; Ohashi, S.; Mori, M.; Hirokawa, T.; Shuto, S.; *J. Med. Chem.* **2017**, *60*, 3252–3265.

Notably, this modification substantially increased the molecule's stability, resulting in **3.043** exhibiting improved metabolic stability and pharmacokinetics. Another instance is the development of the PB2 binder **3.045** by Farmer. [38] Their findings indicated that incorporating an additional cyclobutyl group onto the methyl amide **3.044** enhanced the molecule's fit within the hydrophobic domain of the targeted enzyme's binding site. Consequently, this modification significantly improved the molecule's binding affinity to both bDNA and PB2 protein.

### 3.1.2.3 Using Cyclobutanes as Bioisosteres

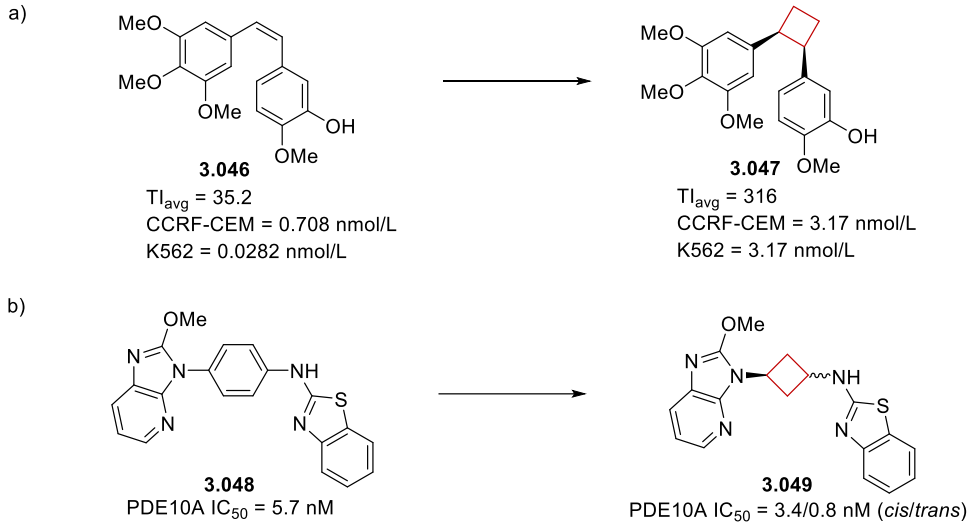


***Figure 3.9.*** Examples of Using Cyclobutanes as Bioisosteres

Cyclobutanes can serve as valuable bioisosteres due to their distinctive bond angles and rigid nature. Specifically, 1,2-disubstituted cyclobutanes closely mimic *cis* alkenes and *ortho*-substituted arenes, while 1,3-disubstituted cyclobutanes can be considered as isosteres for *para*-substituted arenes. An illustration of utilizing 1,2-disubstituted cyclobutane as a bioisostere for a *cis* alkene is exemplified in the development of the cancer treatment drug lead **3.047**, derived from the *cis* alkene-containing natural product **3.046**. Although natural product **3.046** demonstrated potency against various cancer cell lines, its *cis*-stilbene motif was prone to partial isomerization to the *trans* isomer under physiological conditions, diminishing the drug molecule's *in vivo* potency.

[38] Farmer, L. J.; Clark, M. P.; Boyd, M. J.; Perola, E.; Jones, S. M.; Tsai, A.; Jacobs, M. D.; Bandarage, U. K.; Ledeboer, M.W.; Wang, T.; Deng, H.; Ledford, B.; Gu, W.; Duffy, J. P.; Bethiel, R. S.; Shannon, D.; Byrn, R. A.; Leeman, J. R.; Rijnbrand, R.; Benett, H. B.; O'Brien, C.; Memmott, C.; Nti-Addae, K.; Bennani, Y. L.; Charifson, P. S.; *ACS Med. Chem. Lett.* **2017**, *8*, 256–260.

To counteract this isomerization, Nowikow introduced a 1,2-disubstituted cyclobutane to replace the alkene scaffold [39], thereby locking the aryl groups into the *cis* orientation. This modification significantly improved the drug molecule's therapeutic index (TI), as depicted in Figure 3.9a. Compound **3.047** exhibited comparable potency to the natural product against cancer cell lines such as CCRF-CEM and K562. Additionally, 1,3-disubstituted cyclobutane has been employed as a bioisostere for *para*-substituted arenes. An example is the discovery of the PDE10A inhibitor **3.049**. [40] In the original drug lead **3.048**, a *para*-substituted phenyl group oriented the imidazole[4,5,*b*]pyridine and the benzo[*d*]thiazol-2-amine unit linearly. By substituting the phenyl linker with either *cis* or *trans* 1,3-disubstituted cyclobutane, the binding affinity of **3.049** toward the target protein PDE10A increased. This improvement stemmed from reducing the molecule's planarity and thereby enhancing its occupancy in the target binding pocket.

### 3.1.3 Enantioselective [2+2] Cycloaddition

As outlined in Section 3.1, controlling the stereochemical outcomes of photochemical [2+2] cycloadditions are generally considered challenging, especially in terms of enantioselectivity. Various strategies have been developed to achieve enantioselective ring closure. Chiral catalysts, including chiral photosensitizers, chiral Lewis acids, and ion pairs, have demonstrated the ability to catalyze this enantioselective process. Additionally, chiral auxiliaries have been employed to induce enantioselectivity. This section will delve into the detailed discussion of the enantioselective synthesis of cyclobutanes through the aforementioned strategies.

#### 3.1.3.1 [2+2] Cycloaddition Controlled by Chiral Photosensitizer

Bach discovered that a chiral photosensitizer could effectively control the photochemical [2+2] cycloaddition.[41] The proposed catalytic cycle, illustrated in Figure 3.10a, outlines the interaction between photosensitizer **3.050** and substrate **3.051** through hydrogen bonding. Following the formation of the host-guest complex **3.052**, the complex could be excited by photons. In its excited triplet state, complex **3.053** underwent [2+2] cycloaddition, resulting in the formation of the

[39] Nowikow, C.; Fuerst, R.; Kauderer, M.; Dank, C.; Schmid, W.; Hajduch, M.; Rehulka, J.; Gurska, S.; Mokshyna, O.; Polishchuk, P.; Zupko, I.; Dzubak, P.; Rinner, U. *Bioorg. Med. Chem.* **2019**, *27*, 115032.
[40] Hu, E.; Andrews, K.; Chmait, S.; Zhao, X.; Davis, C.; Miller, S.; Puppa, G.; Dovlatyan, M.; Chen, H.; Lester-Zeiner, D.; Able, J.; Biorn, C.; Ma, J.; Shi, J.; Treanor, J.; Allen, J. R.; *ACS Med. Chem. Lett.* **2014**, *5*, 700–705.
[41] Wada, Y.; Nakano, S.; Morimoto, A.; Kasahara, K.; Hayashi, T.; Takada, Y.; Suzuki, H.; Niwwa-Sakai, M.; Ohashi, S.; Mori, M.; Hirokawa, T.; Shuto, S.; *J. Med. Chem.* **2017**, *60*, 3252–3265.

product-catalyst complex **3.054**. Subsequently, the desired cyclobutane product **3.055** dissociated from the complex, and the photocatalyst **3.050** regenerated. Under different conditions, the excited triplet state complex **3.053** might undergo energy transfer from the host to the guest substrate **3.056**, which would then dissociate from the host catalyst rather than immediately undergoing cyclization. In such a case, an uncontrolled cycloaddition would occur, yielding the racemic product **3.055**. Bach was able to use this strategy to control the intramolecular [2+2] cycloaddition of diene

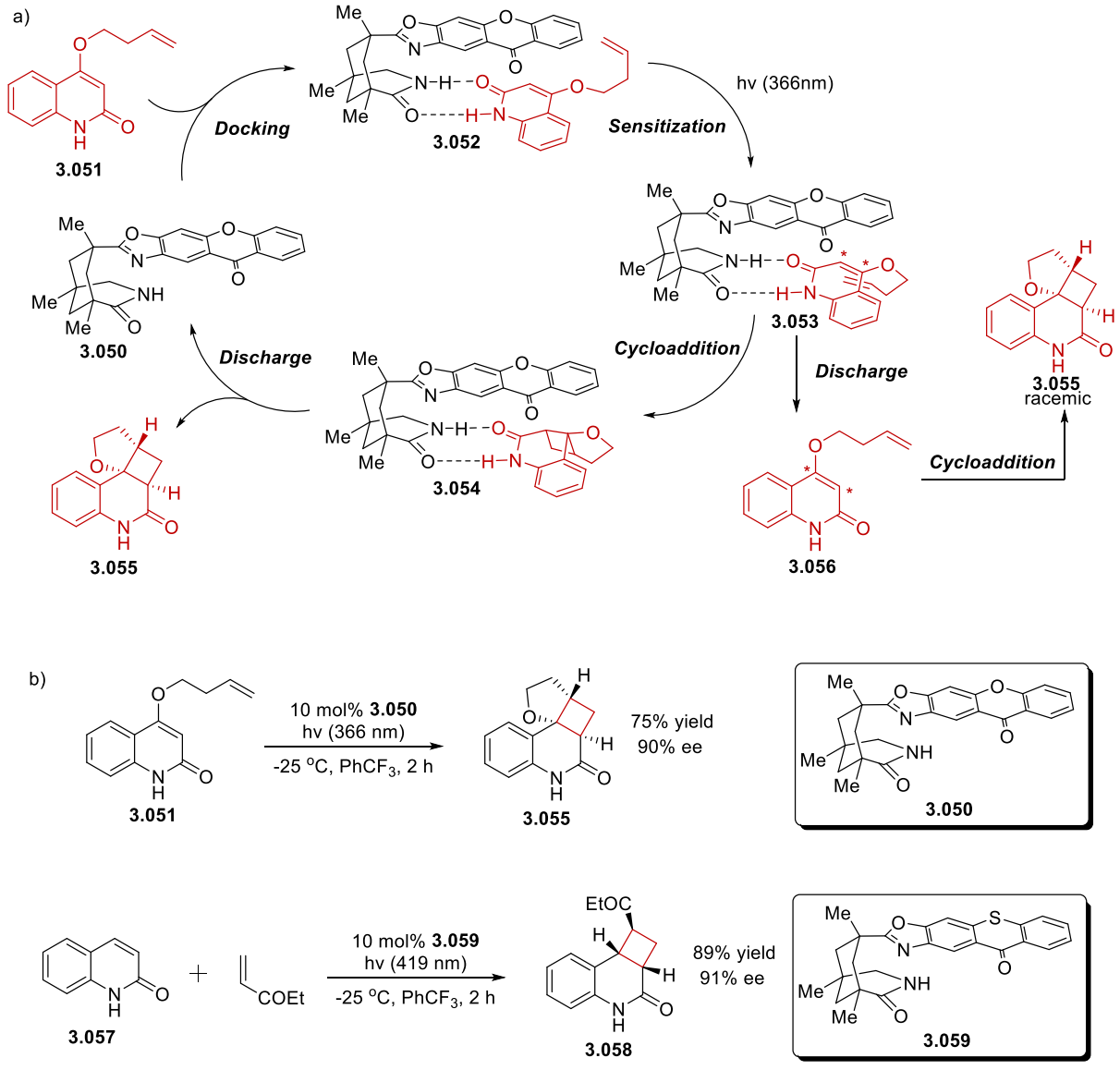


***Figure 3.10.*** Chiral Photosensitizer Catalyzed [2+2] Cycloaddition

substrate **3.051** with high level of enantioselectivity and yield (Figure 3.10b).[42] Additionally, the reaction system was used for the intermolecular [2+2] cycloaddition of **3.057** and ethyl acrylate, where the cyclization product **3.058** was formed with high yield and enantioselectivity as well.[43]

### 3.1.3.2 [2+2] Cycloaddition Controlled by Chiral Lewis Acid

Corey reported the pioneering instance of a chiral Lewis acid-catalyzed [2+2] cyclization reaction involving two general alkenes.[44] Their investigation revealed that treating a chiral boronate with tribromoaluminum yielded a robust chiral Lewis acid, denoted as **3.060**, which could strongly bind to the ester substrate **3.062**.[45] Upon activation, the Michael acceptor, now possessing enhanced electrophilicity, engaged with the enol ether substrate **3.061**. This interaction was followed by intramolecular ring closure, resulting in the desired cyclization product **3.063**. The reaction exhibited a broad substrate scope, accommodating various cyclic enol ethers with high yields and elevated enantiomeric excesses (**3.064** to **3.067**). Utilizing a two-electron stepwise process, the reaction did not necessitate light and could proceed under thermal conditions.

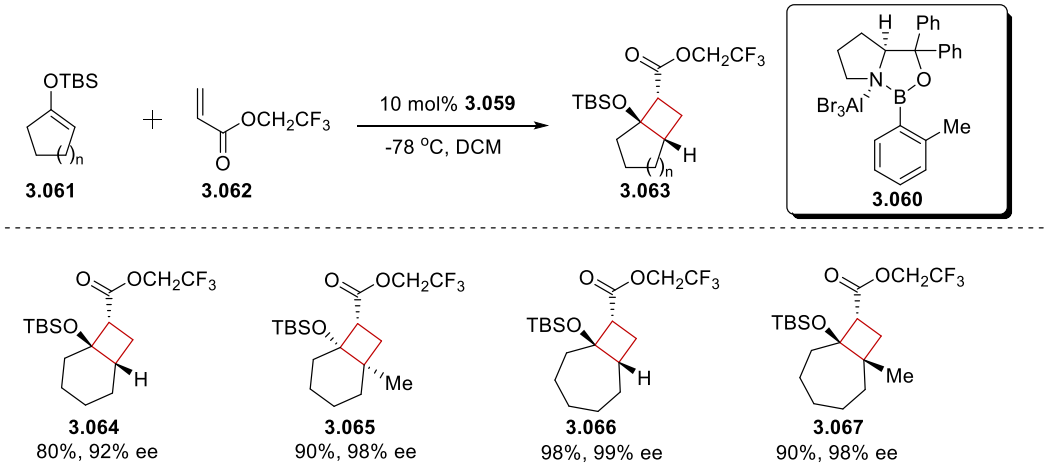


***Figure 3.11.*** Chiral Lewis Acid Controlled Stepwise [2+2] Cyclization Under Thermal Conditions

[42] Muller, C.; Bauer, A.; Maturi, M. M.; Cuquerella, M. C.; Miranda, M. A.; Bach, T. *J. Am. Chem. Soc.* **2011**, *133*, 16689–16697.
[43] Troster, A.; Alonso, R.; Bauer, A.; Bach, T. *J. Am. Chem. Soc.* **2016**, *138*, 7808−7811.
[44] Canales, E.; Corey, E. J. *J. Am. Chem. Soc.* **2007**, *129*, 12686−12687.
[45] For review on using CBS catalyst for cycloadditions: Schwinger, D. P.; Bach, T. *Acc. Chem. Res.* **2020**, *53*, 1933–1943.

Bach discovered that a similar Lewis acid catalyst, denoted as **3.069**, could also serve as a catalyst for photochemical cycloaddition processes. [46] They observed that cyclic unsaturated amide **3.068** exhibited photoactivity upon complexation with Lewis acids like boron trichloride, as indicated by a UV absorption band shift to higher wavelengths, as shown in Figure 3.12a. Consequently, Lewis acid **3.069** could bind to the amide substrate, become photochemically activated under light exposure, and catalyze the intramolecular [2+2] cycloaddition reaction of **3.068** with enantioselectivity control. Indeed, utilizing boronate **3.069** as the superior catalyst, the cyclization of the diene was accomplished with high yield and high enantiomeric excess.

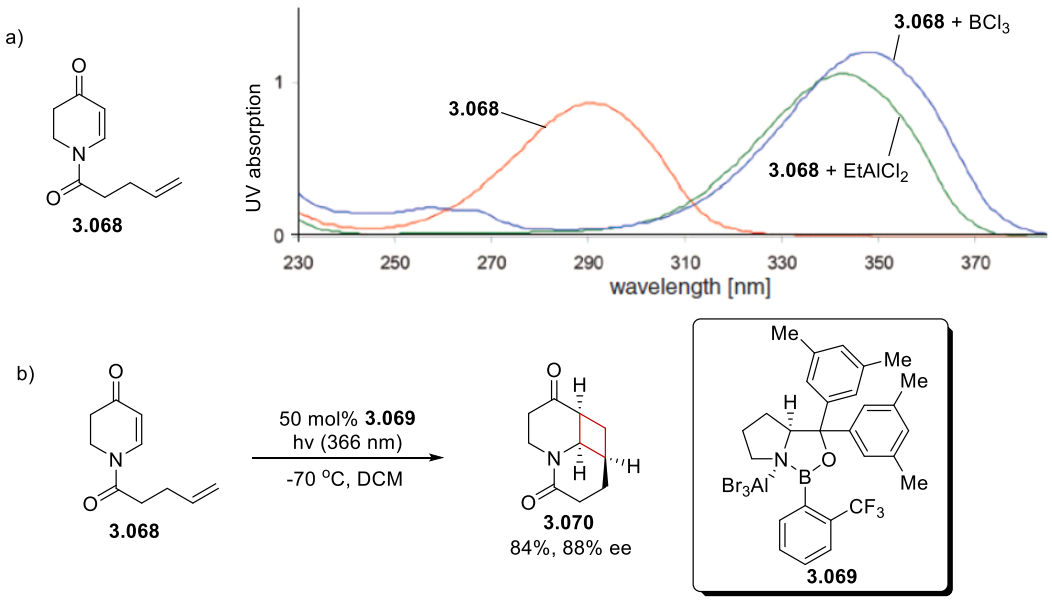


***Figure 3.12.*** Chiral Lewis Acid Controlled Photochemical [2+2] Cycloaddition

### 3.1.3.3 [2+2] Cycloaddition Controlled by Ion Pair

In Bach's illustration of catalytic photochemical [2+2] cycloaddition, the photosensitizer catalyst engaged the substrate through stable hydrogen bonding interactions. While this interaction provided strong stereochemistry control, it necessitated specially designed functional groups, such as an amide, on the substrate to form hydrogen bonds with the chiral catalyst, limiting the

[46] Brimioulle, R.; Bach, T. *Science*, **2013**, *342*, 840–843.

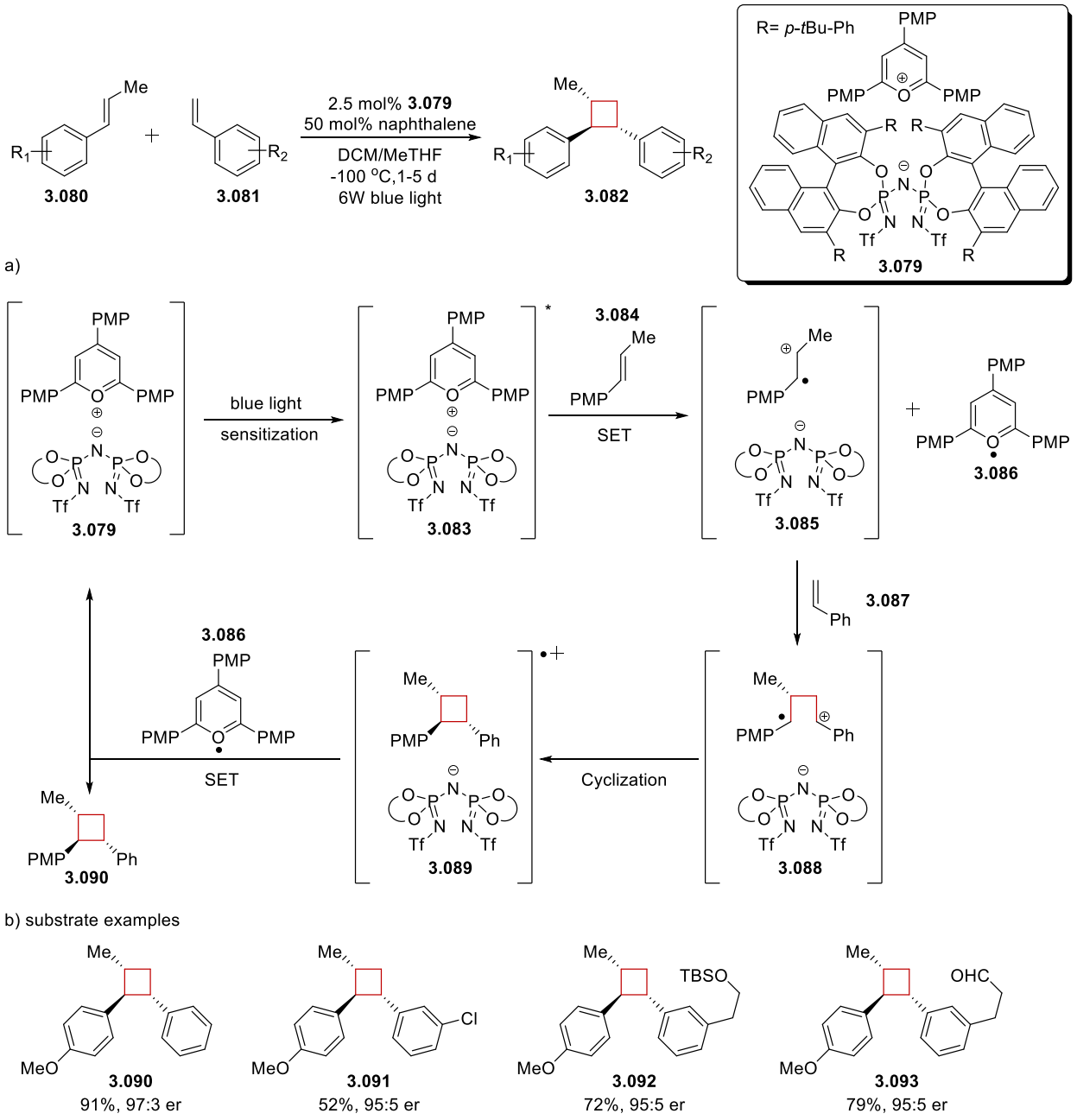


***Figure 3.13.*** Chiral Ion Pair Controlled [2+2] Cycloaddition

generality of this methodology. In 2023, List introduced a novel ion pair strategy to control the photochemical [2+2] cycloaddition process.[47] In this approach, the catalyst interacted with the substrate through electrostatic interactions, eliminating the need for specific functional groups on the substrate Following extensive screening, List identified an effective catalyst complex, denoted

[47] Das, S.; Zhu, C.; Demirbas, D.; Bill, E.; Kanta, C.; List, B. *Science* **2023**. *379*, 494–499.

as **3.079**, comprising a cationic pyrylium photosensitizer and an anionic imidodiphosphorimidate. The proposed mechanism involved the photosensitization of **3.079**, which would then react with the more electron-rich styrene substrate (e.g., **3.084**) through single electron transfer (SET). The pyrylium ion in the complex would be replaced by the radical cation form of substrate **3.084**, resulting in the generation of pyrylium radical **3.086**. This newly formed complex (**3.085**) would further react with another styrene-type substrate (**3.087**), yielding intermediate **3.088**. Subsequent spontaneous cyclization would produce radical cation complex **3.089**. In the presence of pyrylium radical **3.086**, another SET reaction would occur, releasing product **3.090** and regenerating catalyst **3.079**. With one alkene substrate fixed as para-methoxyl methyl styrene, the other alkene substrates exhibited broad scope, accommodating various substituents with high enantiomeric ratios (Figure 3.13, **3.090** to **3.093**).

### 3.1.3.4 [2+2] Cycloaddition Controlled by Chiral Auxiliary

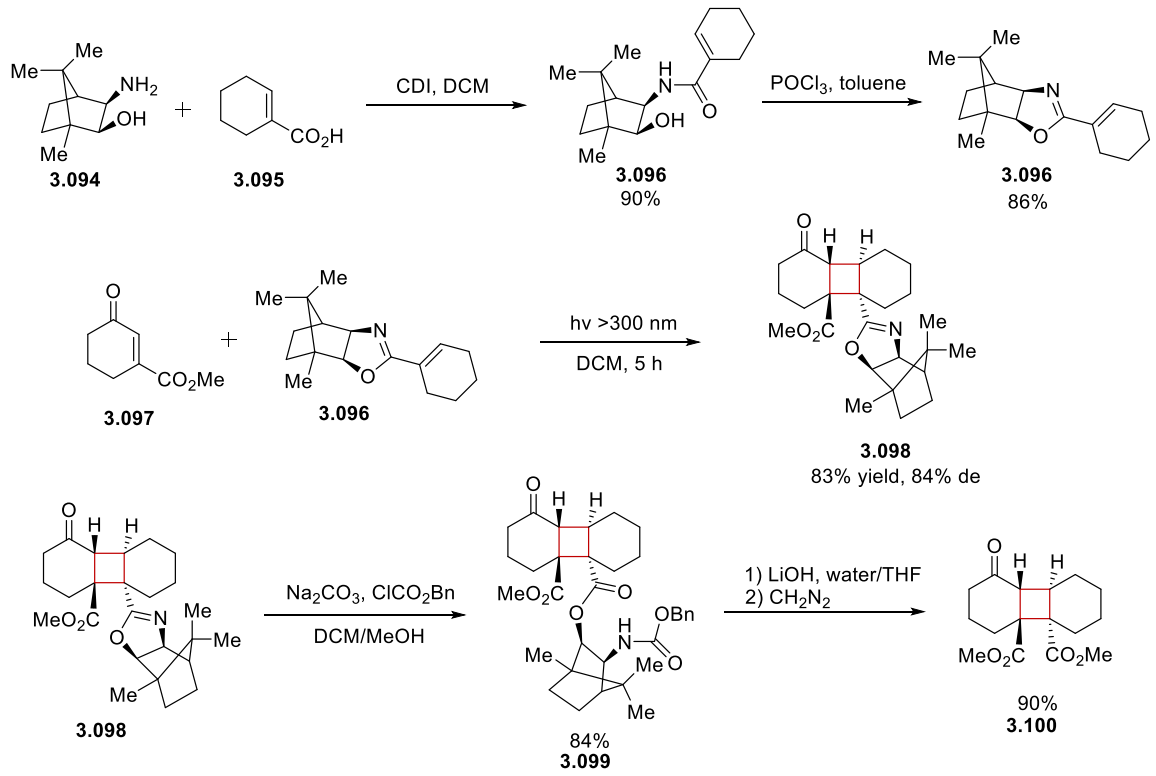


***Figure 3.14.*** Chiral Auxiliary Controlled Photochemical [2+2] Cycloaddition

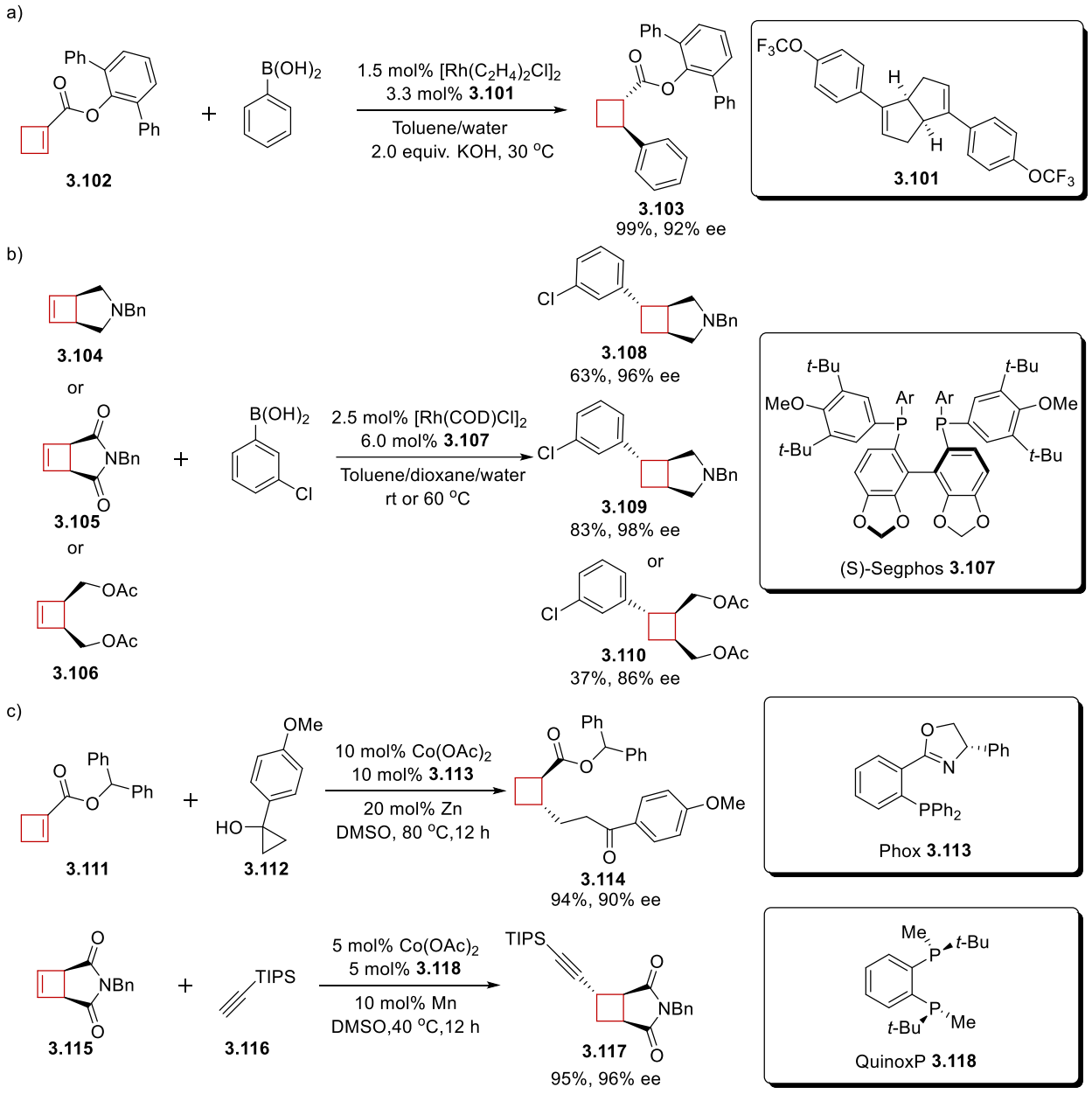


***Figure 3.15.*** Transition Metal Catalyzed Cross-coupling with Cyclobutenes

In addition to chiral catalysts, chiral auxiliaries have found application in controlling the stereochemical outcomes of photochemical [2+2] cycloaddition reactions. An illustrative example is the reaction system developed by Xia.[48] According to the author, β-amino alcohol **3.094** could be readily synthesized from (+)-camphor and condensed with carboxylic acid **3.095** to form

[48] Zhao, G.; Yang, C.; Sun, H.; Lin, R.; Xia, W. *Org. Lett.* **2012**, *14*, 776—779.

alkenyl oxazoline **3.096**. Upon treatment of **3.096** with cyclic enone **3.097** under photoirradiation, a photochemical [2+2] cycloaddition ensued, yielding the cyclobutane-containing product **3.098** with high diastereoselectivity. Additionally, the chiral oxazoline auxiliary on **3.098** can readily be removed from product. Subsequent treatment of **3.098** with base and benzyl chloroformate resulted in the degradation of the oxazoline into Cbz-protected amine **3.099** with an 84% yield. Following hydrolysis with water and methylation using diazomethane, diester **3.100** was obtained in a 90% yield.

### 3.1.4 Cyclobutane Synthesis via Functionalization of Cyclobutenes

Because controlling configuration of newly generated stereogenic centers during the formation of ring system in cyclobutanes synthesis could be challenging, the enantioselective functionalization of reactive alkene groups on cyclobutenes offers an alternative approach to stereodefined densely substituted cyclobutanes. In this section, several newly developed methodologies for enantioselective cyclobutene functionalization will be described.

#### 3.1.4.1 Transition Metal Catalyzed Cross-coupling of Cyclobutenes

Lin reported an example of Rh-catalyzed conjugate arylation of cyclobutenyl esters using aryl boronic esters as nucleophiles.[49] Under basic conditions, the aryl group on the boronic ester would transmetallate onto the $Rh^{I}$ catalyst complex. Then, the aryl rhodium complex would react with unsaturated ester **3.102** (Figure 3.15a) through conjugate addition, where the C–C bond was formed enantioselectively, and the Rh–C bond was protonated by water to generate the desired product and recycle the Rh-catalyst. A chiral diene ligand (**3.101**) was found optimal to effect the reaction with 99% yield and 98% ee. Fletcher further broadened the scope of this reaction.[50] By changing the catalyst system to $[Rh(COD)OH]_2$ and chiral (*S*)-Segphos ligand **3.107** as shown in Figure 3.15b, the reaction can now incorporate cyclic amines (**3.104**), cyclic amides (**3.105**) and diesters (**3.106**). Beside rhodium catalysis, early transition metals such as cobalt were also found to catalyze similar transformations. One example was reported by Meng in 2023.[51] As shown in Figure 3.15c, nuclophiles such as terminal alkynes and β-carbonyl alkyl groups generated *in situ*

[49] Chen, Y.; Hu, T.; Feng, C.; Lin, G. *Chem. Commun.* **2015**, *51*, 8773–8776.
[50] Goetzke F. W.; Hell, A. M. L.; Dijk, L.; Fetcher, S. P. *Nature Chem.* **2021**, *13*, 880–886.
[51] Liang, Z.; Wang, L.; Wang, Y.; Wang, L.; Chong, Q.; Meng, F. *J. Am. Chem. Soc.* **2023**, *145*, 3588−3598.

from hydroxyl cyclopropanes were successful incorporated. Phox ligand **3.113** was found optimal for hydroxyl cyclopropane nucleophile, while Quinoxp ligand **3.118** was found optimal for terminal alkynes.

### 3.1.4.2 Borylation of Cyclobutenes

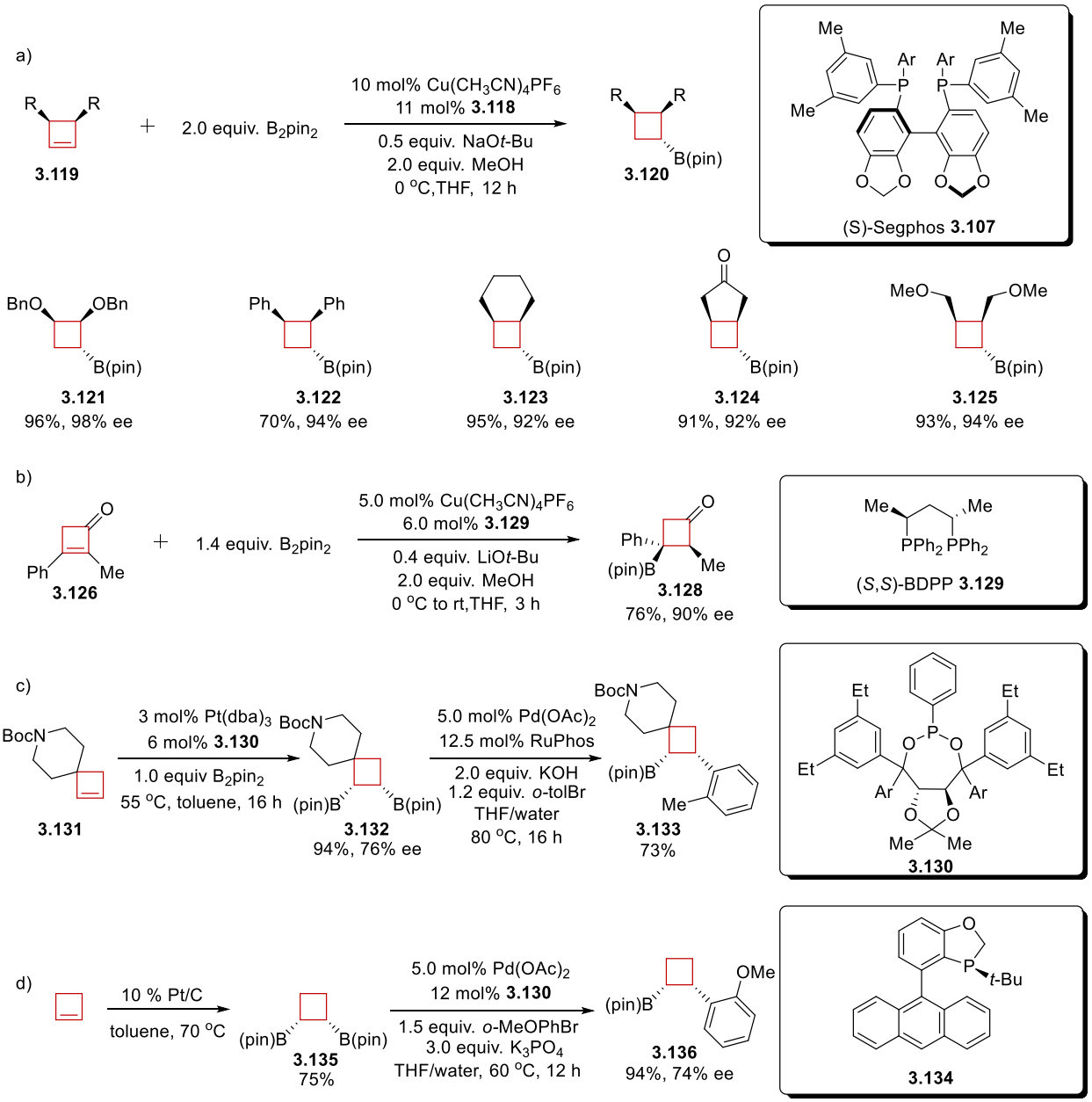


***Figure 3.16.*** The Enantioselective Syntheses of Cyclobutyl Boronic Esters

Various methods have been devised for the enantioselective borylation of cyclobutenes, encompassing protoboration and diboration. The pioneering instance of cyclobutene borylation

was reported by Tortosa in 2016.[52] Owing to the ground state destabilization effect arising from high ring strain, the alkene group in cyclobutenes exhibits sufficient reactivity for copper boration processes, as detailed in Chapter 1.

Tortosa discovered that by employing a Cu-Segphos complex as a catalyst and methanol as a proton source, protoboration could be successfully applied to a series of *meso* disubstituted cyclobutenes (**3.119**). The reaction was optimized under the catalysis of ligand **3.107**, yielding the desired borylated cyclobutanes in high yields and enantiomeric excesses (Figure 3.16a, **3.121** to **3.125**). Another instance of protoboration of cyclobutenes was reported by Hall, wherein α,β-disubstituted cyclobutenones (**3.126** in Figure 3.16b) were chosen as substrates for the generation of densely substituted cyclobutanes.[53] Through high-throughput screening, (*S*,*S*)-BDPP ligand **3.129** was identified as an effective ligand, leading to the borylation product **3.128** with a 76% yield and 90% ee. In addition to protoboration processes catalyzed by Cu complexes, the highly reactive alkene in cyclobutenes can also undergo Pt-catalyzed diboration reactions. Tortosa reported an enantioselective diboration of geminal disubstituted cyclobutene **3.131** using a chiral Pt catalyst.[54] In this case, chiral phosphite ligand **3.130** was identified as the optimal ligand, facilitating the formation of diboration product **3.132** with a high yield and moderate enantiomeric excess. The vicinal diboron product **3.132** was then subjected to a regioselective Suzuki-Miyaura cross-coupling reaction. This transformation, wherein the more exposed secondary B(pin) group located away from the geminal disubstituent was easily converted into an aryl group, yielded the mono boron-substituted cyclobutane product 3.133 in good yield (73%). In 2023, Morken presented another example of borylation of cyclobutenes through a diboration and regioselective Suzuki-Miyaura cross-coupling strategy.[55] In this work, a simple cyclobutene was initially diborated through Pt-catalysis, enabling the synthesis of *meso* cyclobutyl bisboronate **3.135** on a large scale. Subsequently, an enantioselective Suzuki-Miyaura cross-coupling desymmetrized **3.135**, wherein one of the B(pin) units was converted to an aryl group, resulting in the formation of cyclobutyl boronic ester **3.136** with a 94% yield and 74% ee. Both Tortosa and Morken's work exploited the concept of alkene diboration and regioselective functionalization.

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[52] Guisan-Ceinos, M.; Parra, A.; Martin-Heras, V.; Tortosa, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 6969–6972.
[53] Clement, H. A.; Bohi, M.; McDonald, R. M.; Bernier, L.; Coe, J. W.; Farrell, W.; Helal, C. J.; Reese, M. R.; Sach, N. W.; Lee, J. C.; Hall, D. G. *Angew. Chem. Int. Ed.* **2019**, *58*, 18405–18409.
[54] Novoa, L.; Trulli, L.; Parra, A.; Tortosa, M. *Angew. Chem. Int. Ed.* **2021**, *60*, 11763–11768.
[55] Zhang, M.; Lee, P. S.; Allias, C.; Rober, A, S.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 8308−8313.

### 3.1.4.3 Enantioselective Cycloaddition of Cyclobutenes

Cycloaddition reactions, such as [4+2] and [3+2] cycloadditions, prove to be efficient transformations that rapidly build structural complexity using simple alkene starting materials, researchers have explored their application in functionalizing cyclobutenes. To date, there are two reports on enantioselective cycloadditions using cyclobutene as starting materials. Liu discovered that the Lewis acid **3.060** developed by Corey could be successfully applied to the cycloaddition of cyclobutene as well.[56] Employing cyclobutenone **3.138** as the dienophile and chiral Lewis acid **3.060** as the catalyst, enantioselective [4+2] cycloaddition could be achieved with a variety of dienes **3.139**. As depicted in Figure 3.17a, example substrates **3.141** to **3.145** could all be synthesized using this method with high yield and enantioselectivity. In addition to [4+2] cycloaddition, enantioselective [3+2] cycloaddition has also been developed using cyclobutene as a starting material, as demonstrated by the work of Carretero. In this example, a chiral Cu complex with ligand **3.146** was employed as a catalyst to activate the dipole **3.148**. This catalytic system facilitated the cycloaddition with an 84% yield and 86% ee.[57]

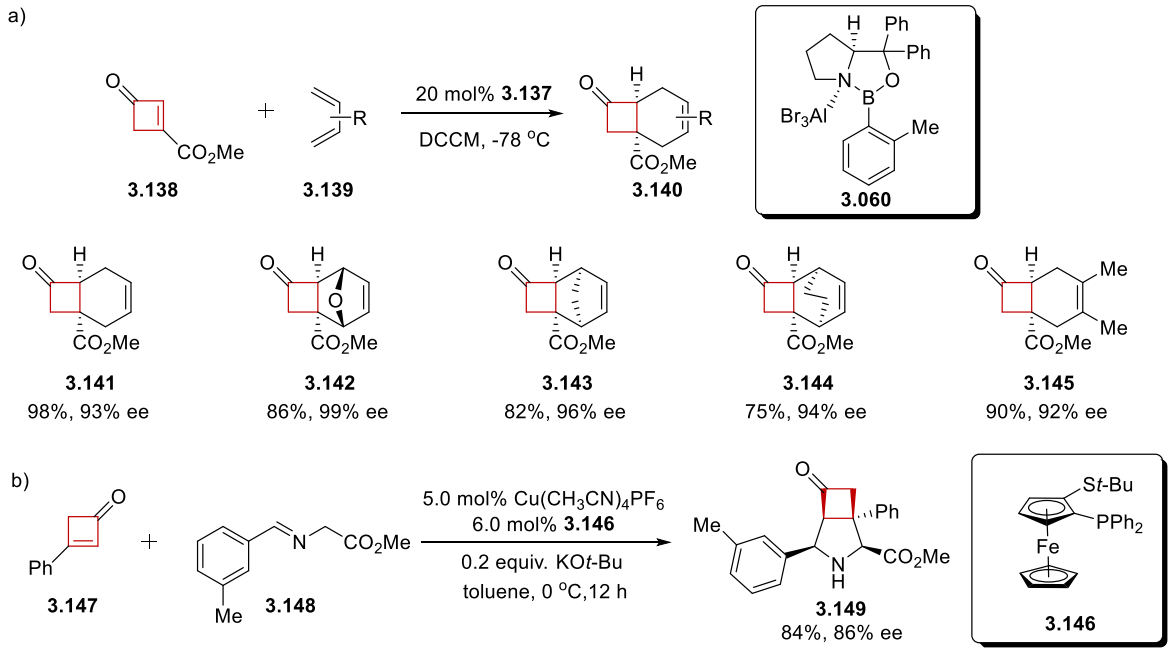



***Figure 3.17.*** The Enantioselective Cycloaddition with Cyclobutenones

[56] Yan, P.; Zhong, C.; Zhang, J.; Liu, Y.; Fang, H.; Liu, P. *Angew. Chem. Int. Ed.* **2021**, *60*, 4609–4613.
[57] Corpas, J.; Ponce, A.; Adrio, J.; Carretero, J. C. *Org. Lett.* **2018**, *20*, 3179−3182.

### 3.1.5 General Alkene Diboration and Regioselective Functionalization

#### 3.1.5.1 Pt-Catalyzed Enantioselective Diboration of Alkenes

As discussed in Section 3.1.4.2, diboration reactions provide a potent strategy for the difunctionalization of simple alkene starting materials. The Pt-catalyzed diboration reaction efficiently transforms cyclobutenes into densely substituted cyclobutane products with precise chemical control, representing a powerful approach. The development of enantioselective Pt-

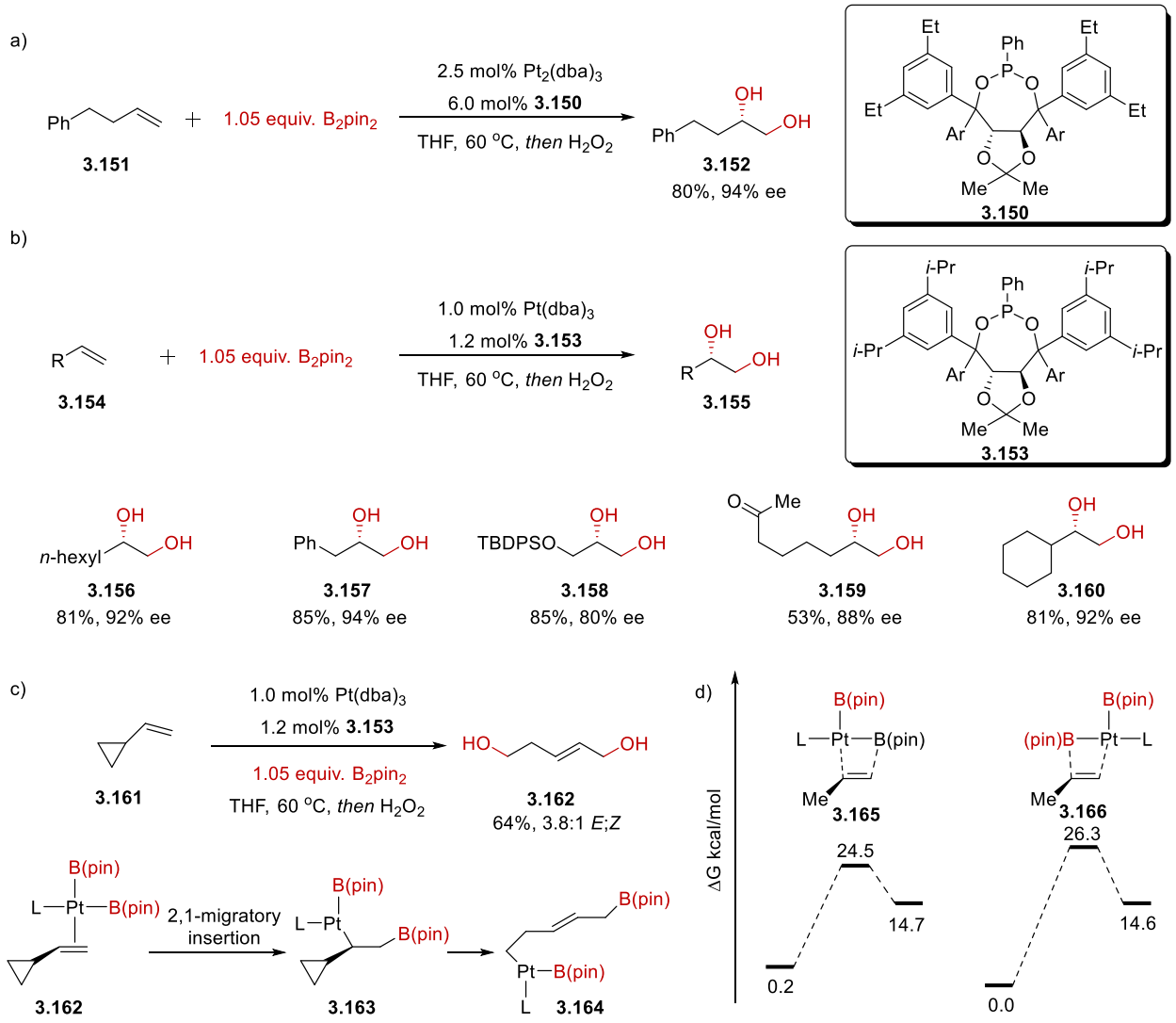



***Figure 3.18.*** Pt-catalyzed Enantioselective Diboration of Terminal Alkenes

catalyzed diboration reactions was pioneered by Morken, with the first reported enantioselective

diboration published in 2009.[58] In this seminal work, it was discovered that the phosphite ligand **3.150** could facilitate the reaction with high yield and enantioselectivity. Subsequently, Morken continued to study this reaction in detail, exploring optimal reaction conditions, potential substrate scope, and the mechanistic profile of the reaction.[59]

As illustrated in Figure 3.18b, another phosphonite ligand, **3.153**, was identified as capable of delivering a more efficient reaction with lower catalyst loading. Under the optimal conditions outlined in Figure 3.18b, a comprehensive substrate survey was conducted, with representative substrates listed (**3.156** to **3.160**). Interestingly, subsequent mechanistic studies revealed that the migratory insertion of Pt into the alkene substrate may proceed through an unusual 2,1-insertion. For instance, cyclobutyl alkene substrate **3.161** undergoes ring opening to yield diol **3.162**. This unusual 2,1-migratory insertion was further supported by DFT calculations. As depicted in Figure 3.18d, the transition state for 2,1-migratory insertion (**3.165**) exhibits a lower energy barrier (1.8 kcal/mol) compared to the 1,2-migratory insertion transition state **3.166**.

### 3.1.5.2 Rh-Catalyzed Enantioselective Diboration of Alkenes

Morken reported the pioneering example of terminal alkene enantioselective diboration using a Rh catalyst.[60] Following extensive screening, Quinap ligand **3.167** was identified as the optimal ligand for generating the desired vicinal diboron product **3.169** from terminal alkene substrates **3.168**, achieving good yields albeit with low enantiomeric excesses (as demonstrated by example substrates **3.170** to **3.174** in Figure 3.19a). Interestingly, Morken also discovered that this diboration reaction could be extended to 1,2-substituted *trans* internal olefins (**3.175**). This extension resulted in the formation of the desired vicinal diborons **3.176** with significantly higher enantioselectivities, as illustrated by substrates **3.177** to **3.180** in Figure 3.19b.

Nishiyama and Toribatake reported another instance of terminal alkene diboration utilizing a Rh catalyst.[61] In this study, the Rh-Phebox complex **3.182** was identified as the effective chiral catalyst, facilitating the diboration of terminal alkenes **3.181** with consistently high yields and enantioselectivities. Notably, the reaction could also be extended to α-methyl styrene, yielding a

[58] Kliman, L.T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *135*, 13210−13211.
[59] Coombs, J. R.; Haeffner, F.; Kliman, L.T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222−11231.
[60] a) Morgen, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702−8703. b) Trudeau, S.; Morgen, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538−9544.
[61] Toribatake, K.; Nishiyama, H. *Angew. Chem. Int. Ed.* **2013**, *52*, 11011–11015.

tertiary alcohol-containing product **3.188** with moderate enantiomeric excess. Furthermore, Nishiyama and Toribatake proposed that, unlike the Pt-catalyzed reaction, Rh-Phebox-catalyzed diboration processes might involve regular 1,2-migratory insertion, where the secondary carbon-

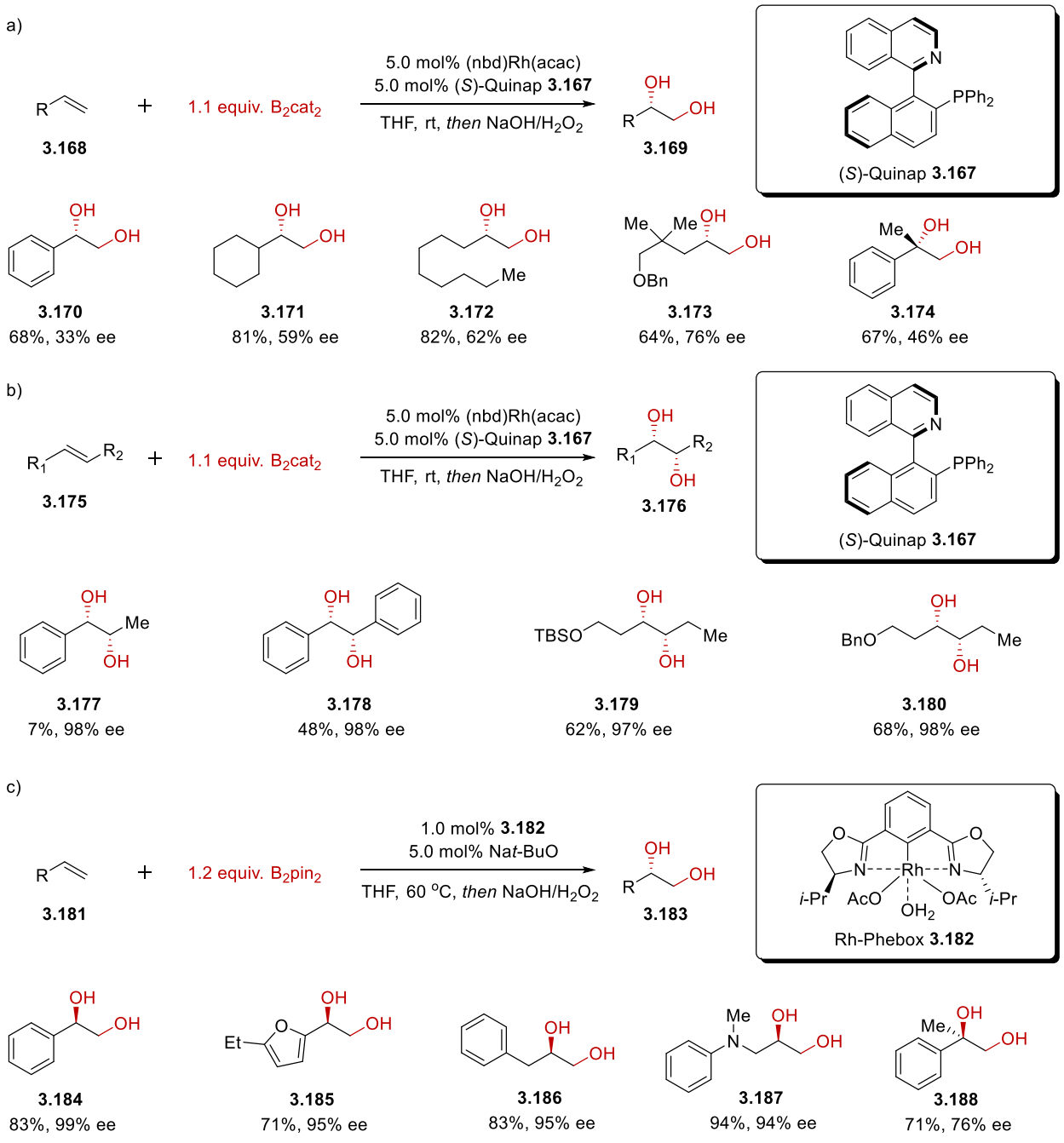



***Figure 3.19.*** Rh-catalyzed Enantioselective Diboration of Terminal and Internal Alkenes

boron bond is formed first.

### 3.1.5.3 Pd-catalyzed Regioselective Cross-coupling of 1,2-Bisboronate

As demonstrated in the previous discussion, alkyl boronic esters can serve as modular precursors for synthesis of molecules with different functionalities. Therefore, enantioselective diboration of alkenes can be considered a powerful method for the enantioselective difunctionalization of alkenes, provided that the two boron atoms in the diboration product can be transformed individually. Utilizing the slight steric and electronic differences between the primary B(pin) and secondary B(pin) in the 1,2-bisboronate **3.189**, Morken was able to develop a regioselective Suzuki-Miyaura cross-coupling of 1,2-bisboronate, where the more reactive primary B(pin) was transformed into an aryl group in **3.190** under Pd-catalysis.[62] The mechanism of this reaction and the origin of its regioselectivity are still under debate. In the work published in 2014, two possible modes of action were proposed: (1) as shown in Figure 3.20b, it was proposed that the boron atom on the internal secondary B(pin) group could serve as an intramolecular activator for the terminal primary boron. This activation effect rendered the primary B(pin) more electrophilic and prone to be activated by external base additives. (2) Base additives in the reaction could form a complex with the diboron substrate by bridging the two boron atoms, generating a cyclic boronate complex **3.192** as shown in Figure 3.20c. Although how such cyclic boronate would promote the subsequent transmetallation event was unclear at that time, the transmetallation would occur on the less hindered primary carbon, furnishing the regioselective Suzuki-Miyuara cross-coupling product.

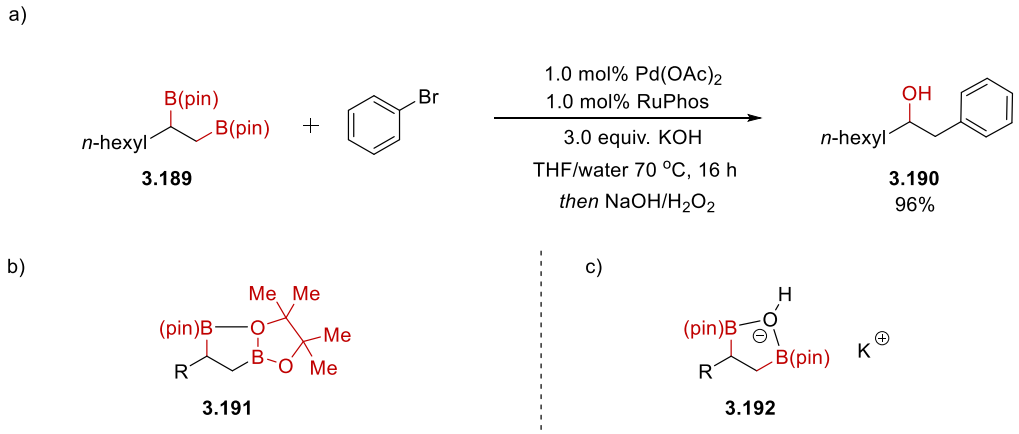



***Figure 3.20.*** Pd-catalyzed Regioselective Cross-coupling of 1,2-Bisboronate

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

### 3.1.5.4 Cu-catalyzed Regioselective Cross-coupling of 1,2-Bisboronate

In addition to transmetallation at the primary carbon of 1,2-bisboronate for Pd-catalyzed arylation, Morken also discovered that the primary carbon could undergo transmetallation with Cu, expanding the cross-coupling possibilities to a broader range of electrophiles.[63] By treating vicinal diboron **3.193** with excess LiOMe base and a catalytic amount of CuCN, cross-coupling of the primary boronic ester with various types of electrophiles, such as allyl bromide (**3.195**), propargyl bromide (**3.196**), alkynyl bromide (**3.197**), as well as regioselective protodeborylation (**3.198**), was achieved with overall high yields and perfect regioselectivity. In this work, Morken proposed that the mechanism of the Cu-catalyzed cross-coupling reaction is more likely to be the second scenario shown in section 3.1.5.3: the methoxide base binds to both boron atoms in 1,2-bisboronate, forming a bridged cyclic boronate complex that promotes the subsequent transmetallation. Detailed mechanistic studies and DFT calculations were carried out to support such a claim.

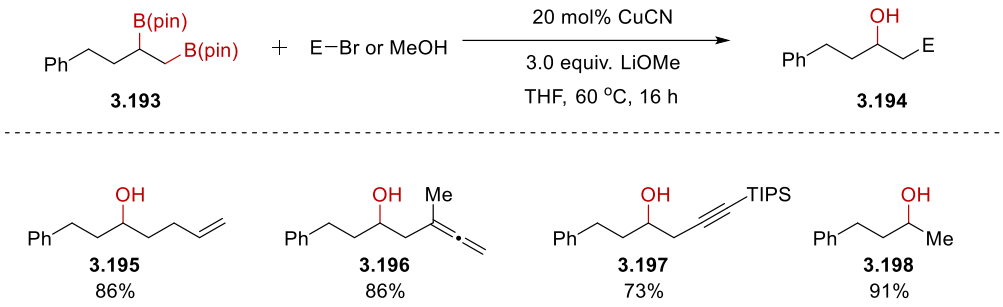



***Figure 3.21.*** Cu-catalyzed Regioselective Cross-coupling of 1,2-Bisboronate

In Chapter 2, we explored a fortuitous discovery that evolved into a novel strategy for site-selective bisboronate functionalization. At low temperatures, bulky organolithium reagents like *t*-BuLi demonstrated an ability to discern subtle steric and electronic disparities between primary and secondary boronic esters. This led to a selective reaction with the less hindered boron atom, forming the *t*-butylboronate complex **3.200**. Following site-selective activation, an efficient transmetallation and cross-coupling ensued when treating the *t*-butylboronate complex **3.200** with a Cu catalyst and an electrophile. This transformation exhibited considerable potential in synthesizing substrates for conjunctive cyclization reactions, as detailed in Chapter 2, Section 2.3.1. Further exploration of this transformation was undertaken by Morken, and here we present some

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

preliminary results. As depicted in Figure 3.22a, the boronate complex **3.200**, being highly stable and mildly basic, proved compatible with various highly reactive electrophiles. Examples include borylmethyl B(pin), acyl chloride, carboxyl amines, enabling the incorporation of these electrophiles to generate homologated 1,3-diboron (**3.202**), ketone (**3.203**), and ester (**3.204**), as well as amine-containing products (**3.206**) with good to high yields. Electrophiles effective in the cross-coupling of LiOMe-activated bisboronate could also be employed in this reaction, efficiently yielding the desired site-selective allylation **3.207**, alkynylation **3.208**, and allenylation **3.209** products.

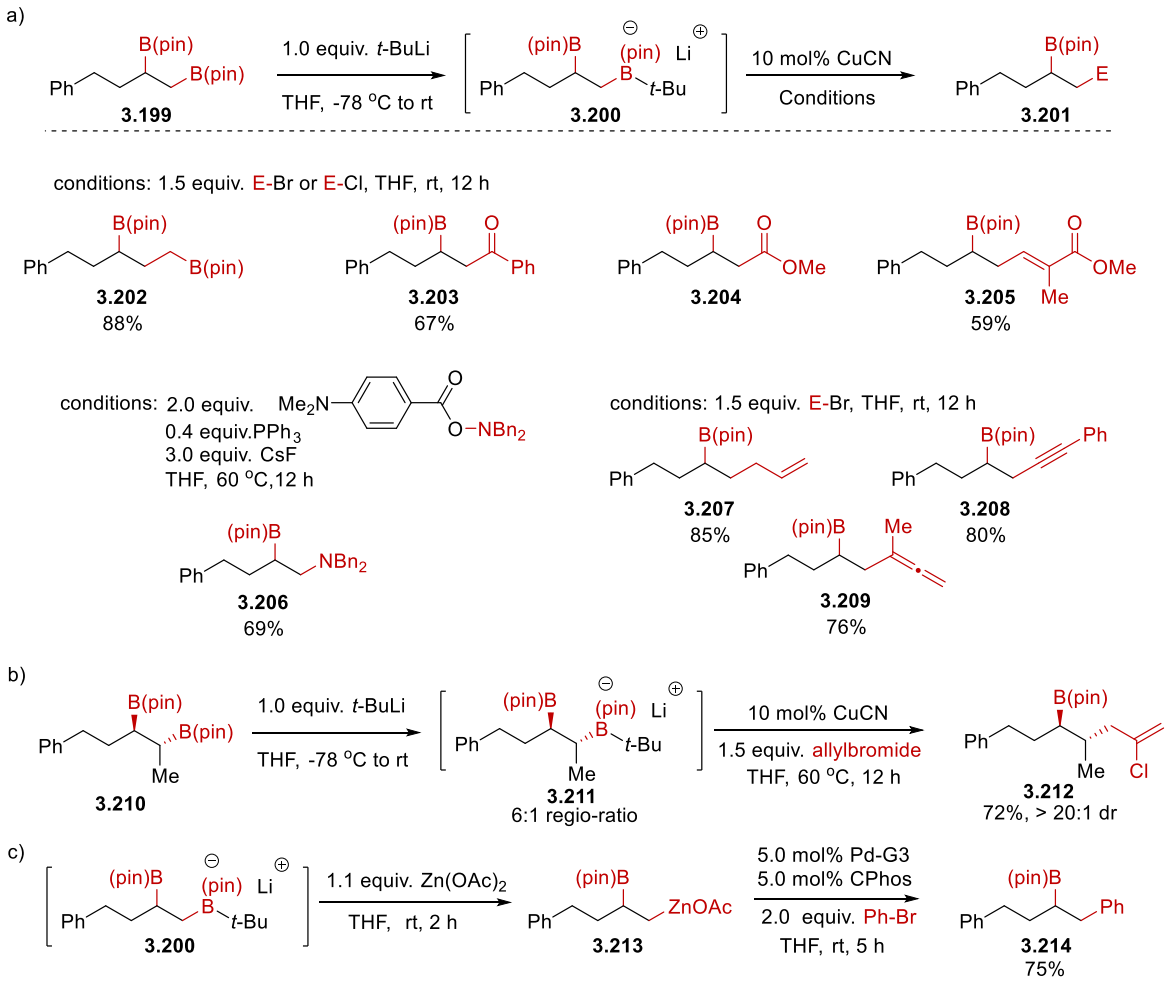



***Figure 3.22.*** Cu-catalyzed Regioselective Cross-coupling of 1,2-Bisboronate Enabled by *tert*-Butylithium Site-selective Activation

Moreover, it was observed that for the internal 1,2-bisboron **3.210**, featuring one secondary carbon with a smaller methyl substituent and another with a longer alkyl chain, *t*-BuLi activation

exhibited remarkable selectivity toward the less hindered secondary boron adjacent to the methyl group (**3.211**). Significantly, the subsequent transmetallation to Cu and coupling with an electrophile such as allyl bromide proved to be both high-yielding and highly stereospecific (**3.212**).[64] Finally, it was revealed that the primary carbon in the site-selectively activated *t*-butylboronate complex could undergo transmetallation to Zn (Figure 3.22c), giving rise to a novel β-boryl zinc reagent 3.213. This reagent could be utilized as a nucleophile in Negishi cross-coupling reactions, enabling an arylation analogous to the regioselective Suzuki-Miyaura cross-coupling described in Section 3.1.5.3.[65] In all, the *t*-BuLi activation strategy could provide a unified and ultimate solution to the site-selective functionalization of vicinal diborons.

## 3.2 Reaction Design

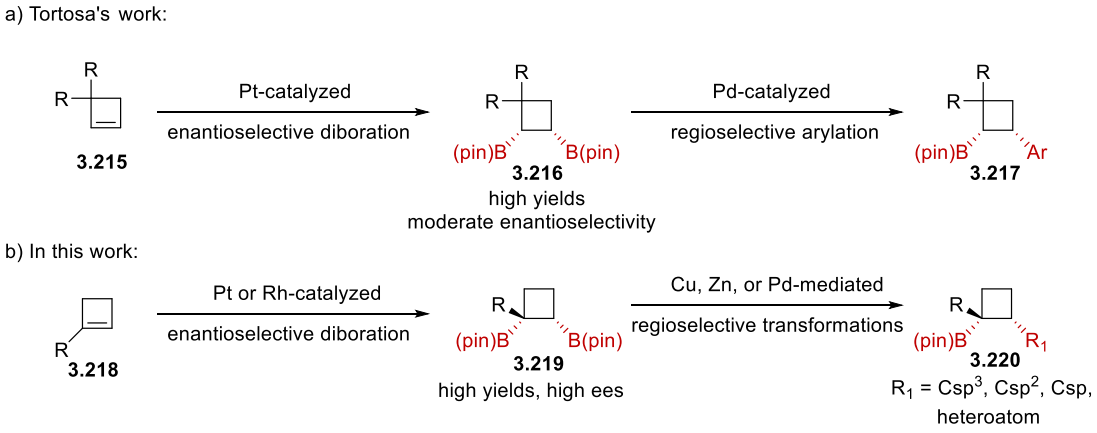



***Figure 3.23.*** Reaction Design Inspired by Tortosa's Work

Although Tortosa demonstrated the diboration of cyclobutenes and the regioselective functionalization of the resulting 1,2-bis(boronate), as detailed in Section 3.1.4.2, the focus was primarily on substrates without substituents on the alkenyl carbons. Additionally, only Pd-catalyzed Suzuki-Miyaura cross-coupling was employed for the derivatization of 1,2-bis(boronate), limiting the available transformations to arylations. We envisaged that by leveraging the ground state destabilization effect of ring strain in cyclobutenes, even more hindered substituted cyclobutenes could be diborated enantioselectively using Pt or Rh catalysis. Moreover, we aimed to explore the regioselective *t*-BuLi mediated diboron functionalization with these cyclobutyl 1,2-

[64] Xu, N.; Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2022**, *144*, 11546–11552.
[65] Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 9976–9981.

bis(boronates). This approach holds the potential to expand chemical possibilities further, as demonstrated in section 3.1.5.4.

## 3.3 Results and Discussion

### 3.3.1 Synthesis of Substituted Cyclobutenes

To secure a preparative-scale source of cyclobutene starting material for the methodology study, it is crucial to identify a synthetic route for the production of cyclobutenes **3.218** with various substituents on the alkene. This section outlines the attempted reactions for this purpose, providing a detailed discussion of their advantages and challenges.

#### 3.3.1.1 Organozirconium Mediated Formal [2+2] Reaction

In 1998, Takahashi reported a Zr-mediated cyclobutene formation reaction. [66] The proposed reaction mechanism (Figure 3.24a) involves the treatment of $Cp_2ZrCl_2$ complex with 2.0 equivalents of ethyl magnesium bromide to generate a zirconium metallacycle. The zirconocycle is then exposed to an alkynyl halide, leading to a regioselective migratory insertion that forms a ring-expanded zirconium metallacycle. Subsequently, an intramolecular $S_N2$ reaction takes place, generating the cyclobutenyl zirconium. Protonation of the organozirconium with HCl completes the reaction, yielding the desired monosubstituted cyclobutene as the final product. Given the ready availability of the required materials, this method was considered suitable for synthesizing cyclobutene substrates on a large scale. Indeed, using the Zr-mediated cyclobutene formation reaction, we successfully synthesized phenethyl cyclobutene **3.223** on a gram scale with a good yield (Figure 3.24b). The reaction did produce a small amount of alkyne byproduct (**3.222**), which could not be isolated through purification methods such as column chromatography. Instead, an additional alkoxide-promoted diboration was carried out on the mixture of **3.222** and **3.223** to borylate the alkyne, and then the boron-containing side product was easily removed through column chromotography (See Supporting Information section for details). However, it was observed that the reaction performed poorly on alkynyl bromide substrates containing Lewis basic functional groups, such as TBS-protected alcohol or an ester in compound **3.224** and **3.225**. Additionally, the reaction exhibited low efficiency on hindered substrates, such as secondary alkyl

[66] Kasai, K.; Liu Y.; Hara, R.; Takahashi, T. *Chem. Commun.*, **1998**, 1989–1990.

and phenyl-substituted alkynyl bromide substrates **3.226** and **3.227**. Nevertheless, the reaction tolerated alkyl bromides, as demonstrated by substrate **3.228**, offering an opportunity for late-stage functionalization of the pre-synthesized bromoethyl cyclobutene **3.229** to install groups not tolerated in the cyclization reaction. At this point, a borylation of the bromide was carried out, successfully delivering the primary B(pin) substrate **3.230**.

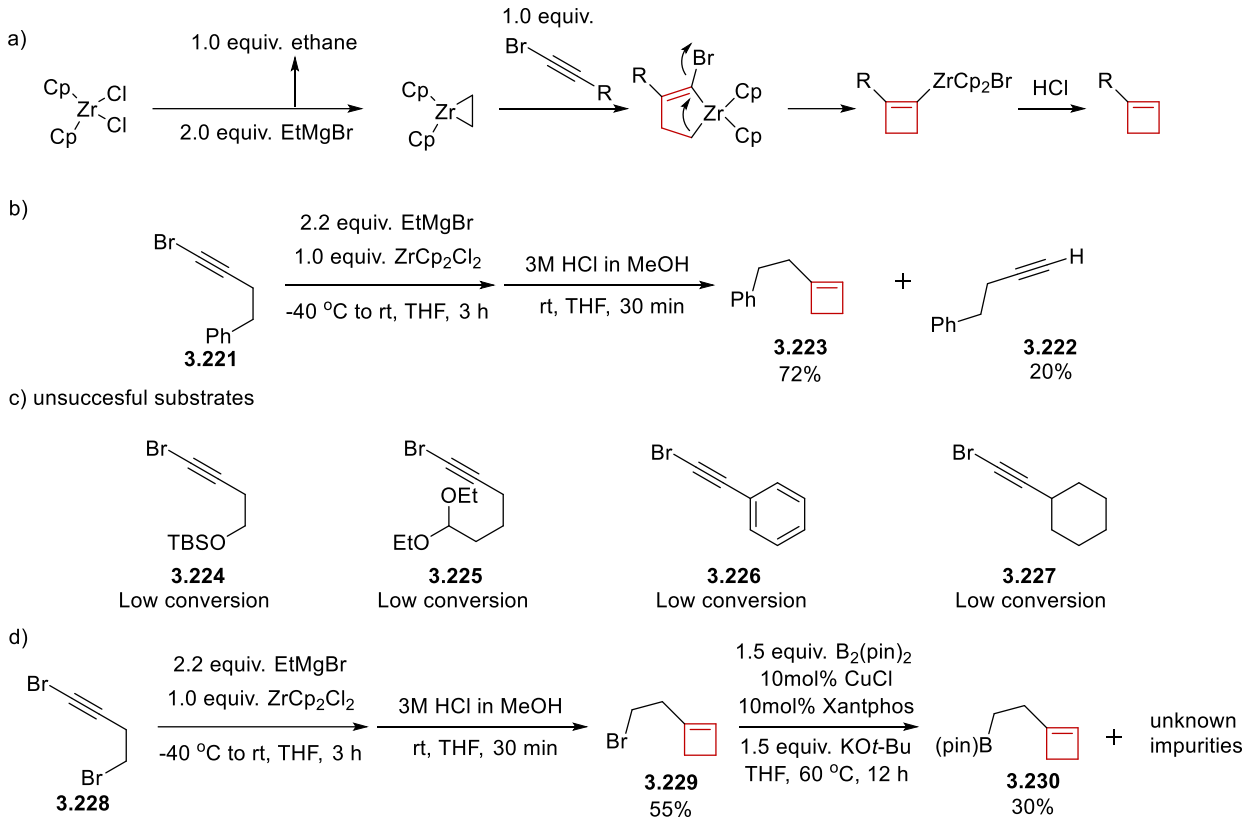



***Figure 3.24.*** Zirconium Mediated Cyclobutene Formation

### 3.3.1.2 Thioacetals Mediated Cyclobutene Formation Reaction

To expand the range of available cyclobutene substrates, we also utilized a thioacetal-mediated substituted cyclobutene synthesis developed by Cohen, Martin, and Knochel.[67] As depicted in Figure 3.25, the treatment of dithioacetal **3.231** with organolithium bases such as *n*-BuLi or *sec*-BuLi induced a cyclobutene formation reaction, yielding cyclobutenyl dithioether **3.232**. Subsequent oxidation of **3.232** produced disulfone **3.233**. Upon reaction with Grignard reagents,

[67] a) Cohen, T.; Ritter, R. H.; Ouellette, D. *J. Am. Chem. Soc.* **1982**, *104*, 7142–7148. b) Landen, H.; Martin, H.; Steigel, A. *Chem. Ber.* **1987**, *120*, 171–175. c) Knapp, K. M.; Goldfuss, B.; Knochel, P. *Chem. Eur. J.* **2003**, *9*, 5259–5265.

mono-arylation or alkylation occurred, leading to the formation of cyclobutenyl sulfone **3.234** (note that the nucleophiles must be organomagnesium reagents, as organolithium reagents only yielded undesired dialkylation or diarylation byproducts). Reduction of the sulfonyl group on **3.234** with magnesium powder in MeOH under sonication provided the final product by reductive cleavage of the sulfone. This approach exhibited good tolerance for functional groups and steric hindrance, enabling the successful preparation of a broader range of cyclobutene substrates (Figure 3.25, substrates **3.236** to **3.241**).

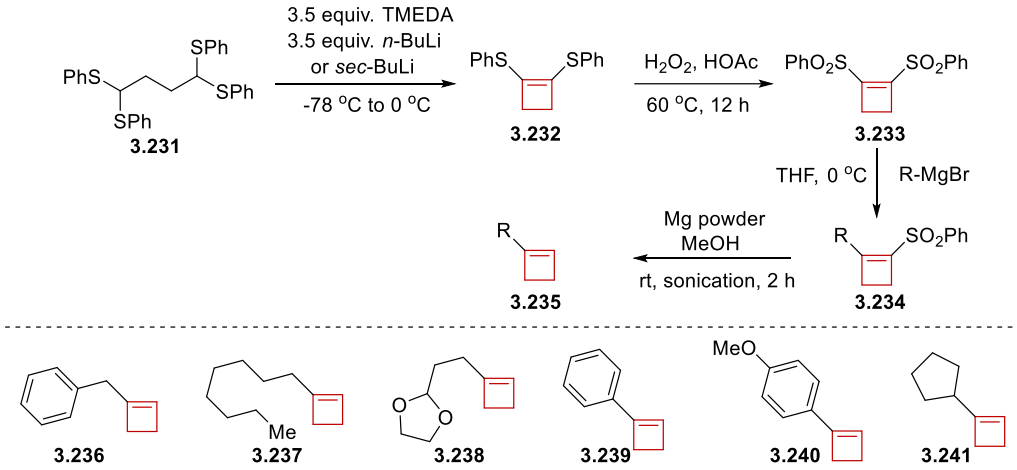



***Figure 3.25.*** Cyclobutenes Synthesis Using Dithioacetal

### 3.3.1.3 Cyclobutene Synthesis Through Alkene Isomerization

While the endocyclic alkenes in cyclobutenes are highly strained and often unstable, leading to thermodynamically disfavored products in exocyclic alkene-endocyclic alkene isomerization processes [68], Shefter demonstrated that under basic conditions in DMSO, the isomerization of **3.242** to **3.243** (Figure 3.26) was equilibrated towards the endocyclic alkene in a 1:6 ratio.[69] Exploiting this process, we successfully synthesized a significant quantity of methyl-substituted cyclobutene **3.243** using readily available cyclobutanone as the starting material, albeit with an approximately 15% impurity of exocyclic alkene **3.242**.

[68] Palani, V.; Wendlandt, A. E. *J. Am. Chem. Soc.* **2023**, *145*, 20053–20061.
[69] Batalin; Ldlis; Vilyatser; Zinenkov; Morzhakova; Fedulova; Shefter; *J. Appl. Chem. USSR* **1986**, *59*, 1684–1687. (only the abstract portion of this paper is available on Reaxys)

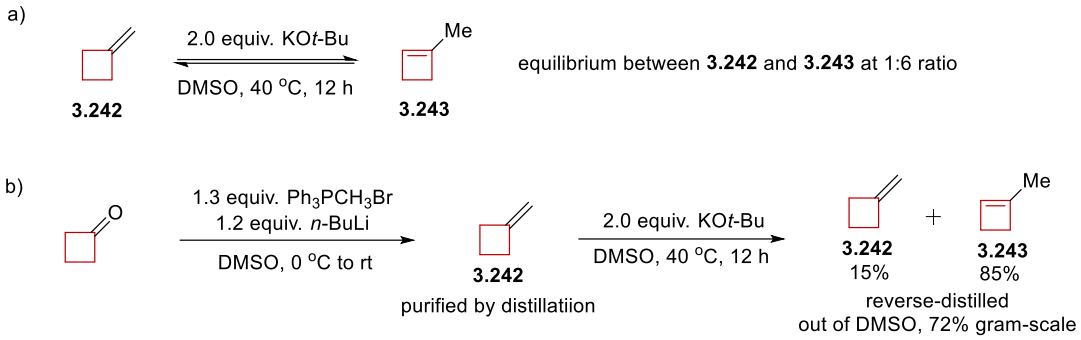



***Figure 3.26.*** Methyl Cyclobutene Synthesis Through Alkene Isomerization

### 3.3.2 Diboration of Monosubstituted Cyclobutenes

#### 3.3.2.1 Condition Optimization

We chose phenethyl cyclobutene **3.223** as the model substrate to optimize the diboration process. Initial attempts using the Fernandez diboration process and Pt-catalyzed enantioselective diboration processes, as depicted in Figure 3.27a, proved unsuccessful in converting the alkene **3.223** starting material to the diboron product **3.245**. Subsequently, we explored Rh-catalyzed diboration under the conditions outlined in section 3.1.5.2: Rh(nbd)(acac) served as the Rh source, (*S*)-Quinap **3.167** as the chiral ligand, and $B_2cat_2$ as the boron source. This approach efficiently transformed the alkene into the desired bis(boronate) **3.244**. Moreover, the catechol ligand on diboron **3.244** could be readily replaced by pinacol, yielding the pinacol-ligated bisboronate **3.245**, which could be isolated cleanly in 71% yield with excellent enantiomeric excess (99%). Despite achieving outstanding results with Rh-catalysis, we further explored other ligands to enhance our understanding of the reactivity of mono-substituted cyclobutenes. Tested ligands included P,N-Phox ligands **3.246** to **3.251**, monophosphine ligands such as phosphite **3.252** and (R)-BIDIME **3.256**, diphosphine ligands **3.253** and **3.254**, as well as pybox ligand **3.255**. Illustrated in Figure 3.27b, most of these ligands failed to convert the alkene starting material. Certain Phox ligands (**3.246** to **3.248**) and phosphite ligand **3.252** yielded the diboron in modest yield, although with a significantly lower enantiomeric excess compared to (S)-Quinap **3.167**. In an attempt to enhance the practicality of the reaction, we explored the direct use of $B_2pin_2$ as the diboron reagent, as shown in Figure 3.27c. However, when $B_2(pin)_2$ was employed, none of the ligands enabled effective reactions, indicating the necessity of $B_2(cat)_2$ diboron reagent.

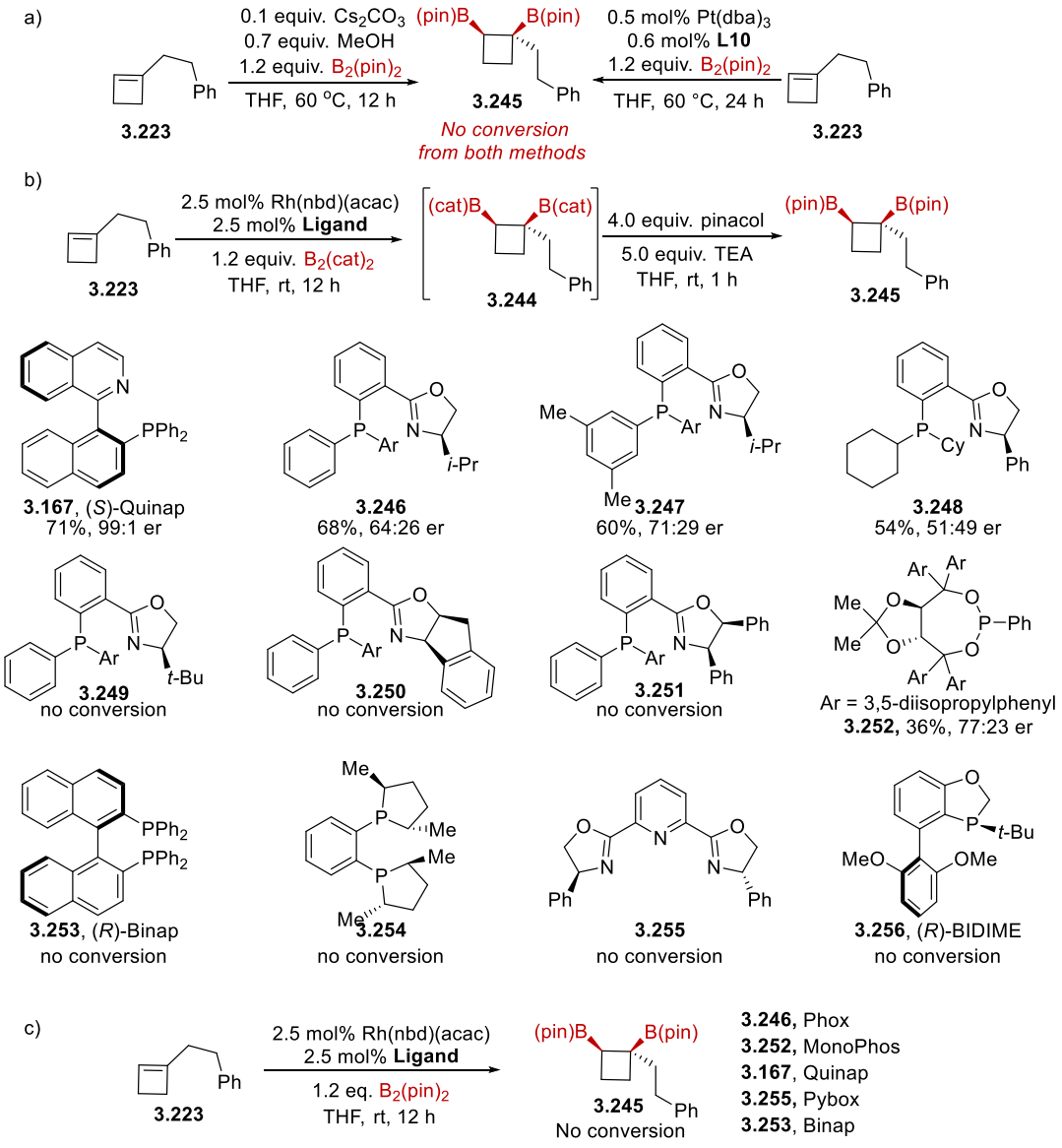



***Figure 3.27.*** Condition Optimization for Cyclobutene Diboration

### 3.3.2.2 Cyclobutene Diboration Substrate Scope

With the effective reaction conditions in hand, we proceeded to explore the scope of this diboration reaction. As illustrated in Figure 3.28, most of the monosubstituted cyclobutenes could be diborated under the optimal conditions with good to high yields and excellent enantiomeric excesses. Substrate **3.263** was contaminated by an exocyclic alkene diboration side product due to an inseparable impurity in the starting material. This diboron impurity posed a challenge to

removal through conventional purification methods. Therefore, a special procedure was applied to the mixture to eliminate this impurity, which will be detailed in the later section.

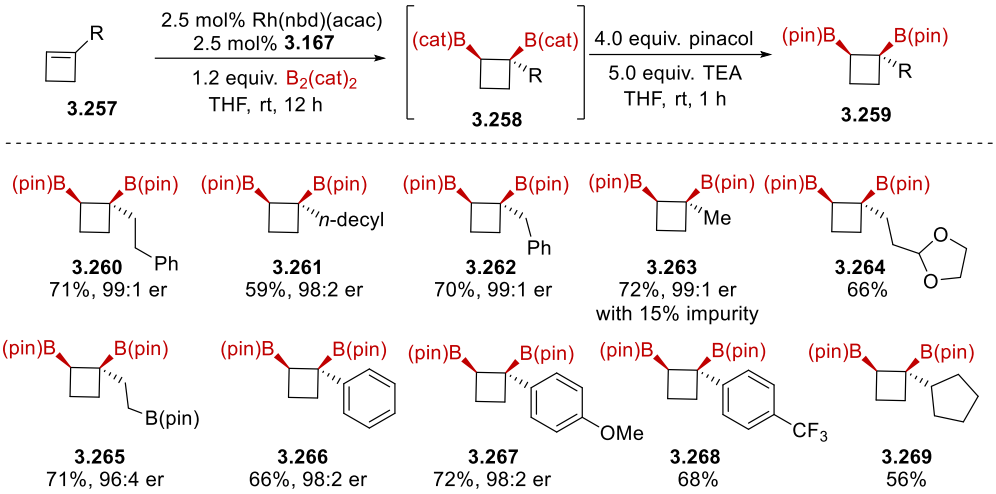



***Figure 3.28.*** Substrate Scope for Diboration of Cyclobutenes

### 3.3.3 Regioselective Functionalization of Cyclobutyl 1,2-Bisboronates

#### 3.3.3.1 Condition Optimization

With diboron **3.245** successfully synthesized on a large scale, we investigated the regioselective functionalization of the 1,2-bisboronate. As depicted in Figure 3.29, when the Pd-catalyzed regioselective Suzuki-Miyaura cross-coupling protocol was applied to **3.245**, no desired arylation product **3.270** was observed. Instead, cyclobutene **3.223** was identified as the major byproduct, indicating that a fast β-boryl elimination occurred after the secondary carbon had already transmetallated to palladium. In the LiOMe-promoted cross-coupling reaction using CuCN catalyst applied to **3.245**, no conversion to the desired allylation product **3.271** was observed as well. The cyclobutyl diboron **3.245** appeared to be too sterically hindered for the Cu-transmetallation process to occur. Lastly, the diboron functionalization strategy using *t*-BuLi as a site-selective activator was carried out on **3.245**. To our delight, at low temperature, *t*-BuLi was able to discriminate the steric difference between the tertiary boron and secondary boron in **3.245** and selectively form the boronate complex **3.272**. By treating the boronate complex with CuCN and allylbromide, the desired regioselective allylation product **3.271** was formed in a 64% isolated yield. The reaction only produced one diastereomer, showcasing the remarkable stereospecificity of this cross-coupling reaction.

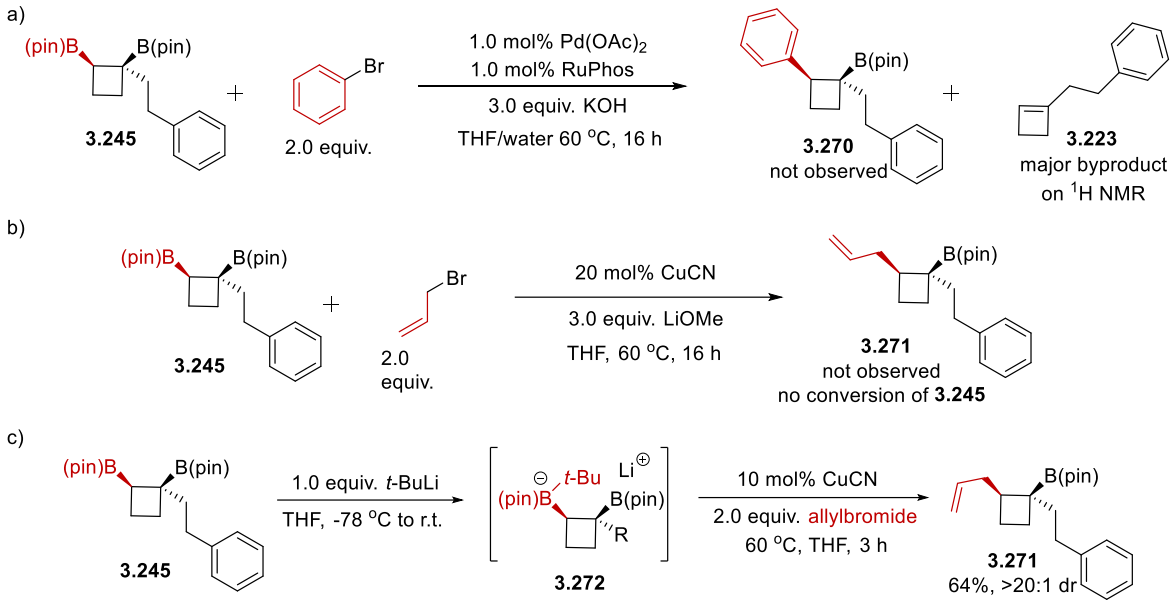



***Figure 3.29.*** Condition Optimization for Diboron Regioselective Functionalization

### 3.3.3.2 Cu-catalyzed Regioselective Functionalization of Diboron 3.245

With the initial success in regioselective allylation of diboron **3.245** using *t*-BuLi as the activator, we then explored the electrophile scope of this Cu-catalyzed cross-coupling reaction. As illustrated in Figure 3.30a, various halide-containing electrophiles were successfully incorporated, including bromomethylB(pin), ethyl chloroformate, benzoyl chloride, and alkynyl bromides. The reactions exhibited excellent stereospecificity in all cases. Additionally, with the reaction conditions demonstrated in section 3.1.5.4, regioselective amination was achieved, furnishing β-amino boronic ester **3.380** in moderate yield and excellent diastereomeric ratio. Regioselective phosphorylation was also achieved, where the secondary boron was converted to a diphenyl phosphine group using conditions kindly provided by Hao in the Morken group.[70]

[70] The reaction condition was provided by Liang Hao et al, which was unpublished when this thesis was written.

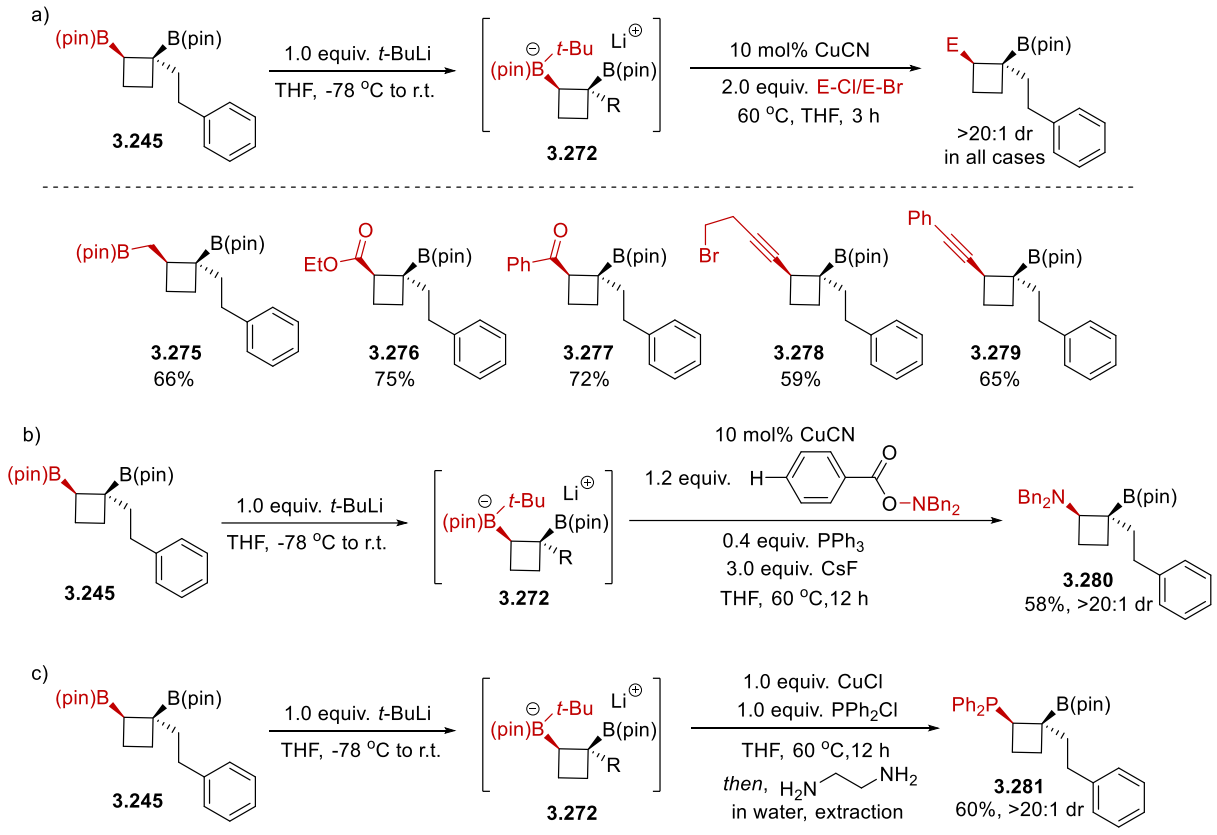



***Figure 3.30.*** Cu-Catalyzed Diboron **3.245** Regioselective Functionalization

### 3.3.3.3 Regioselective Synthesis of Organozinc from Diboron 3.245

Inspired by the Zn-mediated Pd-catalyzed Negishi coupling reaction demonstrated in Section 3.1.5.4, we explored the possibility of applying such a reaction to the cyclobutyl 1,2-bis(boronate) **3.245**. As depicted in Figure 3.31a, by treating the regioselectively formed t-butyl boronate complex **3.272** with $Zn(OAc)_2$, the desired stereospecific transmetallation occurred smoothly at room temperature, furnishing the β-boryl zinc species **3.282**. Monitored by $^{11}B$ NMR, a complete conversion of the boronate complex **3.272** to **3.282** was achieved within 30 minutes. In Figure 3.31b, the β-boryl zinc species **3.282** was subjected to Negishi cross-coupling reactions with both aryl and alkenyl bromide electrophiles, successfully installing the corresponding aryl or alkenyl groups at the β-position of tertiary boronic esters **3.284** to **3.286**. Additionally, **3.282** could be used as a starting material for the Pd-catalyzed acylation reaction, as shown in Figure 3.31c. Notably, acetyl chloride is considered a challenging electrophile for Cu-catalyzed cross-coupling reactions due to the highly acidic α-proton. With this newly developed Zn-transmetallation and Pd-catalyzed coupling reaction, the desired acetylation product **3.288** could now be synthesized with a high

yield. Lastly, using the reaction conditions developed by Liang Hao in the Morken group[71], a trifluoromethylation of β-boryl zinc **3.282** was achieved as well, enabling a net transformation of the secondary boron in **3.245** to a trifluoromethyl group in **3.289** with a 73% yield.

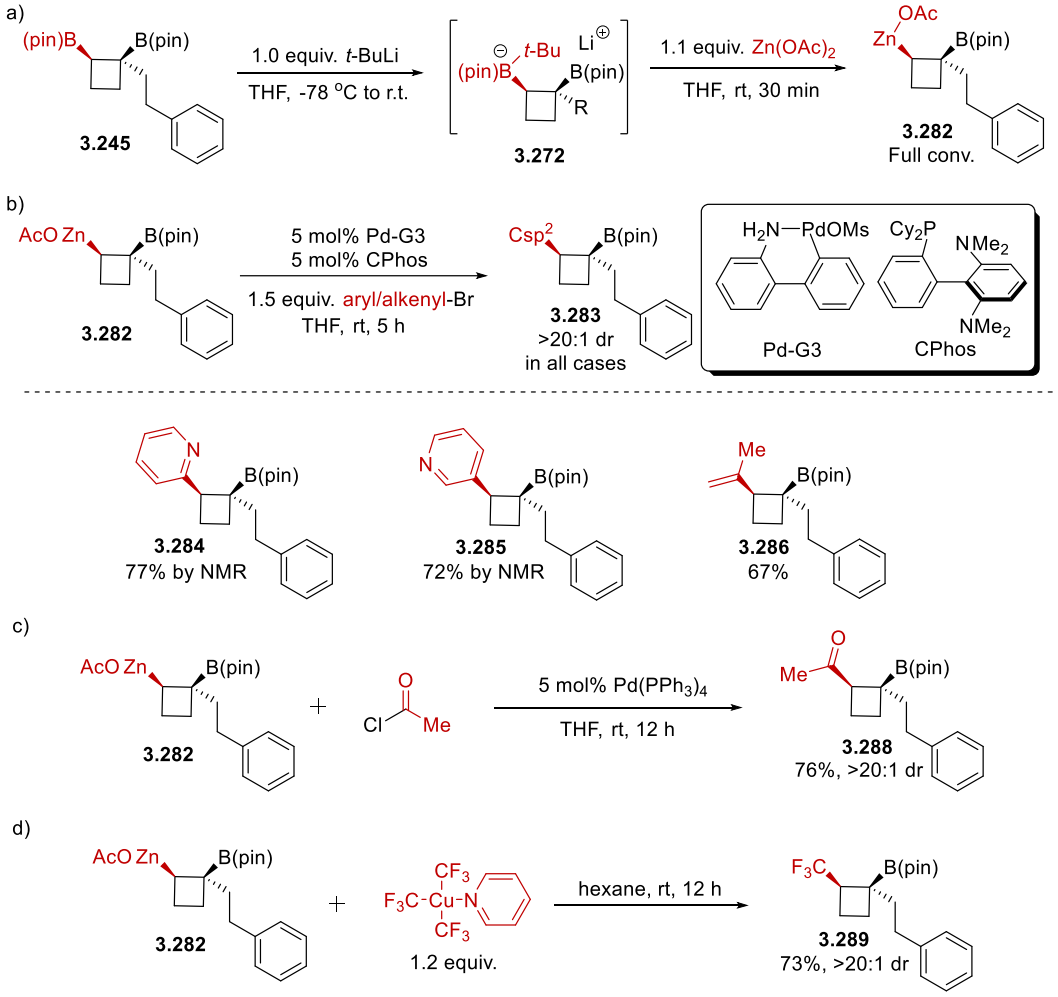



***Figure 3.31.*** Synthesis and Application of Organozinc from Diboron **3.245**

### 3.3.3.4 Purification and Functionalization of Substrate 3.263

In section 3.3.1.3 and 3.3.2.2, we discussed the challenges associated with synthesizing methyl substituted cyclobutyl 1,2-bisboronate **3.263**: as summarized in Figure 3.32a, because of the incomplete isomerization from exocyclic alkene **3.242** to the endocyclic alkene **3.243**, the diboration of this mixture yielded diboron product contaminated by **3.290**. In order to remove this impurity, a special treatment was carried out: the mixture of **3.290** and **3.263** was treated with 0.2

[71] Liang, H.; Morken, J. P. *J. Am. Chem. Soc.* **2023**, *145*, 9976–9981.

equivalents of *t*-BuLi at -78°C, where, due to the rate difference arising from the steric difference of boronates reacting with *t*-BuLi, only the primary B(pin) in **3.290** reacted with *t*-BuLi to form the boronate complex **3.291**. Then, the mixture was treated with $Zn(OAc)_2$ and then MeOH, where the primary boronate was transmetallated to zinc and then protonated to yield the monoboronate **3.294**. Due to the volatile nature of **3.294**, it could be easily removed by evaporation under high vacuum. Using this approach, **3.263** could be purified with 72% isolated yield. Later chromatography analysis on the derivative of **3.263** showed that the reaction was highly enantioselective as well, as **3.263** was generated with 99% ee. Despite the small size of methyl group in **3.263**, it was still hindered enough to ensure a regioselective activation to occur solely on the secondary boronic ester when activated with *t*-BuLi. The subsequent transmetallation to Zn and Negishi reaction was highly efficient as well, producing the alkenylation product **3.296** in 55% isolated yield.

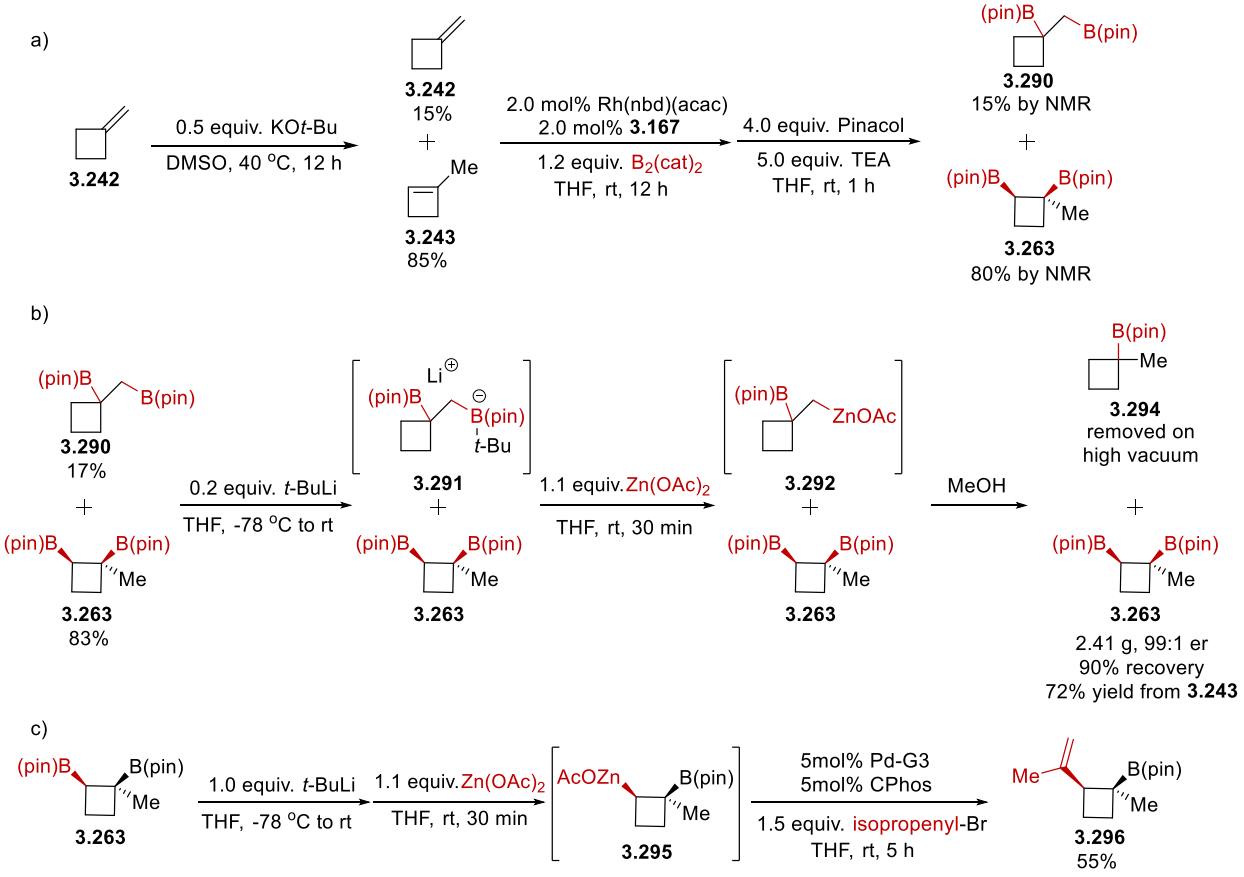



***Figure 3.32.*** Purification and Functionalization of Substrate **3.263**

### 3.3.3.5 Regioselective Functionalization of Triboron 3.265

Based on the discussion in section 3.1.2, an important application of cyclobutanes in designing pharmaceutical molecules is using their rigid backbone to direct pharmacophores to the active conformation. To accomplish such a mission, the syntheses of modular cyclobutane containing building blocks are in high demand, particularly for those with versatile handles that can be easily transformed into the desired pharmacophores. We considered triboron substrate **3.265** a suitable candidate for this role. The three boron atoms in **3.265** could be sequentially transformed into a large variety of functional groups according to their degree of steric hindrance: using the *t*-BuLi activation strategy, the 1° B(pin) could be function first, followed by the slightly more hindered 2° B(pin), and lastly, the 3° boron could then be functionalized using conditions demonstrated in section 2.1.1. To prove such concept, we performed a sequential difunctionalization of triboron **3.265**. As shown in Figure 3.33b, by treating **3.265** with 1.0 equiv. *t*-BuLi, the primary B(pin) was activated, forming the boronate complex **3.297**. Then, Cu-catalyzed allylation was applied and terminal alkene product **3.298** was acquired with 79% yield. The subsequent functionalization of secondary boronic ester was successful as well: the boronic ester was converted to isopropenyl group in **3.300** using Zn-mediated Pd-catalyzed Negishi coupling in 62% yield.

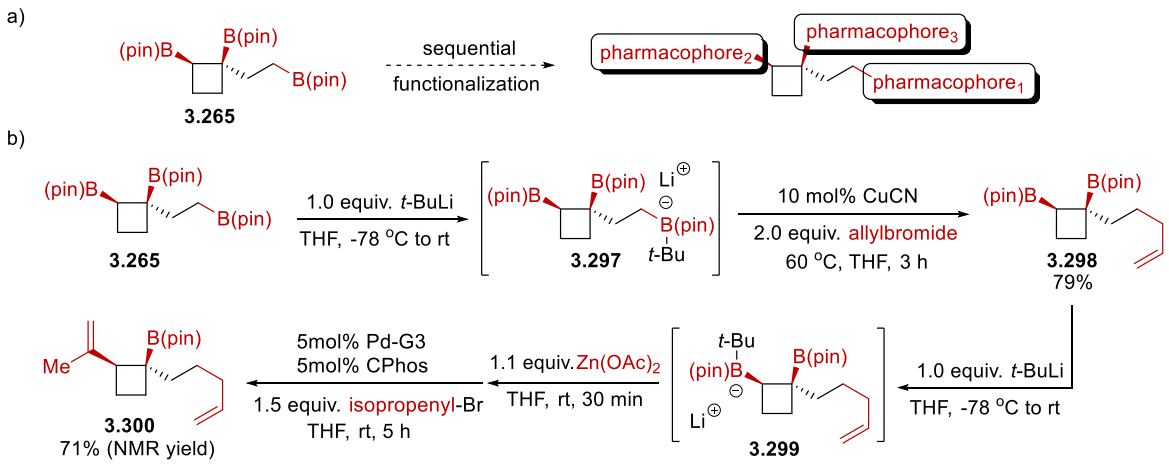



***Figure 3.32.*** Sequential Functionalization of Triboron **3.265**

### 3.3.4 Synthesis of Aliphatic Bicyclic Alkylboronates

In a final exploration, a crossover between the conjunctive cyclization reaction demonstrated in Chapter 2 and the regioselective diboration functionalization, as shown in this chapter, was conducted. Starting from the enantiomerically enriched diboron **3.245**, regioselective activation using *t*-BuLi was applied to synthesize the monoboronate complex **3.301**. This complex was then treated with a Cu-catalyst and bromomethylB(pin) to furnish the regioselective homologation product **3.302** in a 66% yield. Subsequently, a regioselective allylation was performed on **3.302**

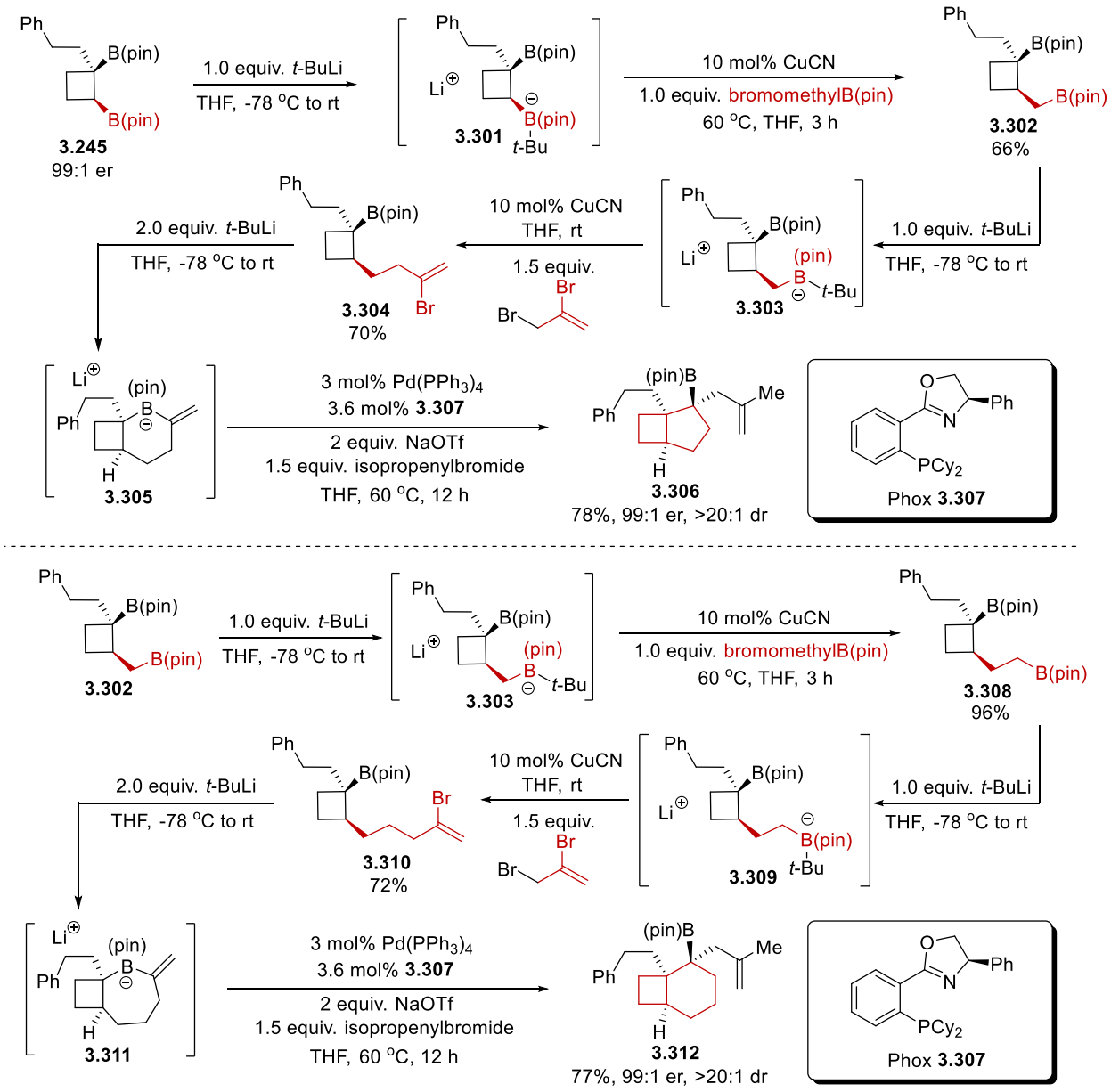



***Figure 3.33.*** Synthesis of Aliphatic Bicyclic Alkylboronates

using the same strategy. At this point, alkenyl bromide **3.304** was obtained, with a tertiary boronate intramolecularly tethered. Using *t*-BuLi to perform lithium-halogen exchange on **3.304** cleanly produced the cyclic boronate complex **3.305**, which was then treated with the optimal conjunctive cyclization condition as described in Chapter 2. The cyclization reaction yielded the [4,5]-bicyclic tertiary alkylboronate **3.306** with a 78% yield and >20:1 dr. Additionally, the 1,3-diboron **3.302** could undergo further regioselective homologation and allylation to yield the homologated alkenyl bromide **3.310**. From this, a [4,6]-bicyclic tertiary alkylboronate **3.312** was obtained with a 77% yield and >20:1 dr.

To understand the stereochemistry of this cyclization process, specifically from **3.304** to **3.306**, a correlation between the chirality of the substrate and the catalyst was identified. Utilizing the Phox ligand **3.307**, the aforementioned high yield and diastereoselectivity on **3.306** were achieved. Conversely, using the other enantiomer of the Phox ligand **3.307** resulted in approximately 50% lower yield and significantly more Suzuki-Miyaura byproduct. This outcome is attributed to a mismatch in chirality between **3.306** and the catalyst. By analyzing the X-ray crystallography data, the absolute and relative configuration of **3.306** were determined. The obtained crystal structure in Figure 3.34 reveals that the B(pin) unit is *trans* to the phenethyl group and *cis* to the cyclobutane. Due to the conformational restrictions on the cyclobutane, the cyclobutane motif in **3.306** is sterically less bulky than the free-rotating phenethyl sidearm. As a result, during the ring contraction, the cyclobutane adopts a *gauche* orientation to the B(pin) unit, favoring intermediates **3.315** and **3.316** due to their higher stability.

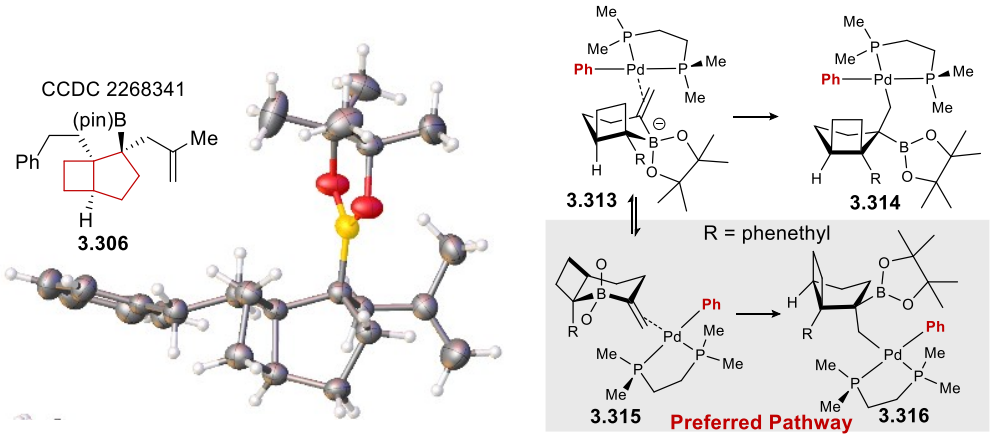



***Figure 3.34.*** Stereochemistry Analysis on The Bicyclic Alkylboronate Synthesis

## 3.4 Supporting Information

### 3.4.1 General Information

$^{1}$H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). $^{13}$C NMR spectra were recorded on either a Varian Gemini-500 (126 MHz), Varian Gemini-600 (151 MHz) or a Varian Inova-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). $^{11}$B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer. $^{19}$F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers ($cm^{-1}$) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), or potassium permanganate stain ($KMnO_4$, sodium carbonate, and water), or para-anisaldehyde stain (ethanol, sulfuric acid, and *p*-anisaldehyde).

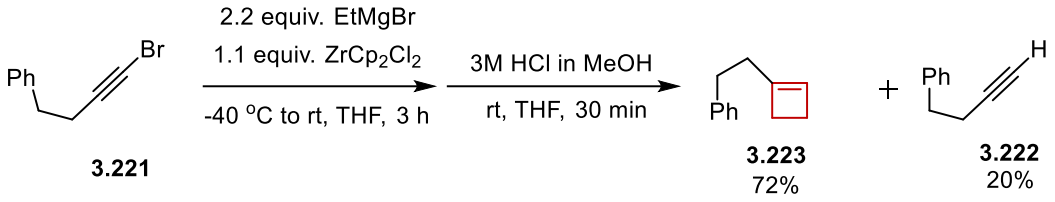
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. All carbamoyl chlorides were purchased from commercial sources and were distilled

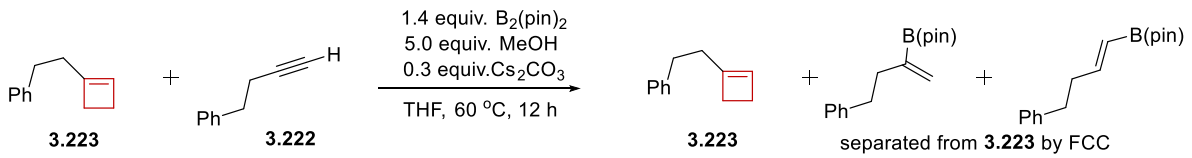
using a short path distillation apparatus. All other reagents were purchased from Aldrich, Alfa Aesar, Acros, Combi Blocks, TCI Chemicals or Oakwood Chemicals and used without further purification.

### 3.4.2 Cyclobutenes Diboration Experimental Details

#### 3.4.2.1 Procedures for Organozirconium Mediated Formal [2+2] Reaction

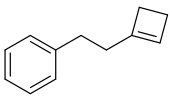



In glovebox, 3.22 g of $ZrCp_2Cl_2$ (11.0 mmol, 1.1 equiv.) was dissolved in 40 mL of anhydrous THF at room temperature (the complete dissolution of $ZrCp_2Cl_2$ is a key to successful reaction). Then, the reaction flask was brought outside the glovebox and cooled down to -40 °C with dry ice-acetonitrile bath. At this temperature, 7.3 mL of 3.0 M ethylmagnesium bromide-THF solution (22.0 mmol, 2.2 equiv.) was added dropwise. Upon completion, 1.0 equiv. of alkynyl bromides **3.221** (2.09 g, 10 mmol) was added as 2.0 mL THF solution via syringe. Then, the reaction was stirred at -40 °C for 1 h following by room temperature for 1 h. 5.0 mL 3.0 M HCl-MeOH solution was then added at room temperature dropwise. Reaction was then stirred at room temperature for 0.5 h. To workup the reaction, the mixture was diluted with 100 mL of hexane, from which the Zr salt would precipitate out and be removed by filtering the suspension through silica gel plug. The acquired clear solution was then concentrated under vacuum, and the crude mixture was subjected to column chromatography for initial purification (using hexane as eluent). From analyzing $^1H$ NMR of the purified material, around 20 mol% of alkyne impurity **3.222** was identified. The following procedure was used to remove such impurity and obtain purified substrate **3.223**.

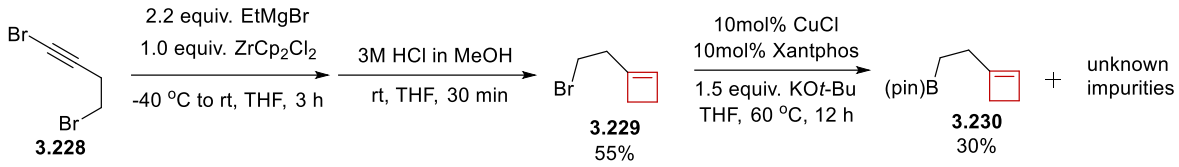



To the mixture of **3.223** and **3.222** (5.0 mmol in total, after pre-purification processes demonstrated above) was added 1.4 equiv. $B_2(pin)_2$ (7.0 mmol, 1.78 g) and 5.0 equiv. MeOH (1.0

mL). Then, 0.3 equiv. $Cs_2CO_3$ was added (1.5 mmol, 488 mg) along with 15 mL of THF. The flask was sealed with septum and heated to 60 °C with stirring for 12 h. Upon completion, the mixture was filtered through a plug of silica gel using diethyl ether. The crude was concentrated under vacuum and then subjected to flashed column chromatography (FCC) using hexane eluent, from which pure **3.223** was acquired (0.68 g, 4.3 mmol, 43% from **3.221**).

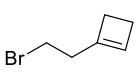


**(2-(cyclobut-1-en-1-yl)ethyl)benzene (3.223).** $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 3H), 7.18 (s, 2H), 5.69 (s, 1H), 2.75 (t, J = 7.8 Hz, 2H), 2.43 (dd, J = 3.4, 1.7 Hz, 2H), 2.33 (t, J = 6.9 Hz, 4H). (More characterization of this compound can be found in reference 66.)

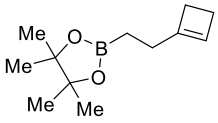



In glovebox, 3.22 g of $ZrCp_2Cl_2$ (11.0 mmol, 1.1 equiv.) was dissolved in 40 mL of anhydrous THF at room temperature (the complete dissolution of $ZrCp_2Cl_2$ is a key to successful reaction). Then, the reaction flask was brought outside the glovebox and cooled down to -40 °C with dry ice-acetonitrile bath. At this temperature, 7.3 mL of 3.0 M ethylmagnesium bromide-THF solution (22.0 mmol, 2.2 equiv.) was added dropwise. Upon completion, 1.0 equiv. of alkynyl bromides **3.228** (2.12 g, 10 mmol) was added as 2.0 mL THF solution via syringe. Then, the reaction was stirred at -40 °C for 1 h following by room temperature for 1 h. 5.0 mL 3.0 M HCl-MeOH solution was then added at room temperature dropwise. Reaction was then stirred at room temperature for 0.5 h. To workup the reaction, the mixture was diluted with 100 mL of pentane, from which the Zr salt would precipitate out and be removed by filtering the suspension through silica gel plug. Compound **3.229** has a boiling point close to THF. Therefore, the pentane-THF solution of **3.229** was carefully concentrated under low vacuum to remove most of the pentane solvent, and the resulting solution was used directly for the next step without further purification. The yield of this step was estimated to be around 55% through analyzing the $^1$H NMR of this pentane-THF-**3.229** mixture.

The solution of **3.229** was purged with $N_2$ and sealed in a 25 mL round-bottom-flask with septum. The flask was transferred into glovebox. Then, a pre-stirred 2.0 mL THF solution of CuCl and Xantphos (54.5 mg of CuCl and 318.2 mg of Xantphos, pre-stirred in THF for 30 min) was added into the flask via syringe followed by 15 mL THF, 925.2 mg KOt-Bu (1.5 equiv.) and 1.68 g $B_2(pin)_2$ (1.2 equiv.). The flask was sealed again and removed from glovebox and stirred at 60 °C for 12 h. Upon completion, the mixture was filtered through a plug of silia gel with diethyl ether and concentrated under vacuum. Crude mixture was purified with 10:1 hexane-ethyl acetate eluent to yield **3.230** as sticky oil in 30% yield.

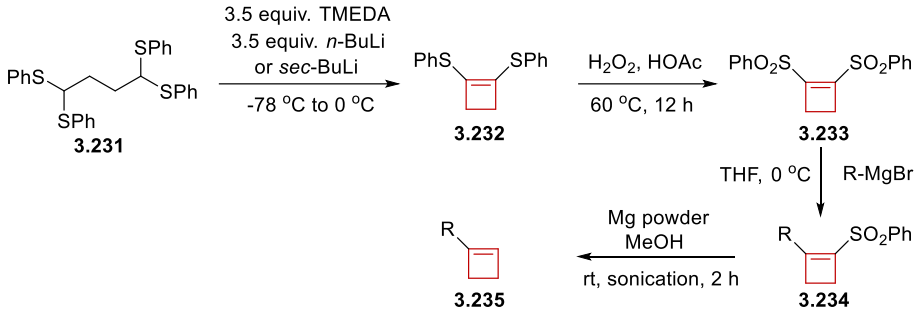



**1-(2-bromoethyl)cyclobut-1-ene (3.229).** $^1$H NMR (500 MHz, $CDCl_3$) δ 5.80 (t, $J$ = 1.3 Hz, 1H), 2.81 – 2.75 (m, 2H), 2.59 (ddt, $J$ = 7.2, 4.9, 1.2 Hz, 2H), 2.48 (tt, $J$ = 2.7, 1.2 Hz, 2H), 2.37 (ddt, $J$ = 4.3, 2.2, 1.1 Hz, 2H). (only $^1$H NMR of the mixture was provide for reference, further characterizaton was not carried out due to its low boiling point)

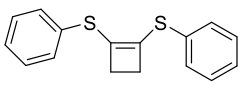


**2-(2-(cyclobut-1-en-1-yl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.230).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.65 (t, J = 0.9 Hz, 1H), 2.40 (dt, J = 3.2, 1.7 Hz, 2H), 2.34 – 2.26 (m, 2H), 2.11 (t, J = 7.1 Hz, 2H), 1.25 (s, 13H), 0.92 (t, J = 7.8 Hz, 2H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 152.3, 125.7, 83.0, 30.9, 26.1, 25.4, 24.8., $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.99, IR (neat): $\nu_{max}$ 2976.15 (w), 2920.04 (m), 2851.30 (m), 1310.21 (s), 1110.71 (s), 872.12 (s) $cm^{-1}$. HRMS (DART) for $C_{12}H_{22}BO_2$ $[M+H]^+$: Calc'd: 209.17156, found: 209.17074.

### 3.4.2.2 Procedures for Cyclobutane Synthesis Through Dithioacetals

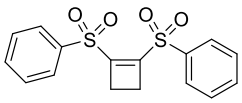



**3.231** was synthesized according to references (beware of the high odor hazard of thiophenol) 68. 1.0 equiv. **3.231** (6.2 g, 12.6 mmol) was dissolved in 250 mL of anhydrous diethyl ether. 3.5 equiv. TMEDA was added by volume (6.17 mL). The reaction flask was cooled to -78 °C. Then, 2.5 equiv. of *n*-BuLi or *sec*-BuLi was added as a stock solution in hexane. The reaction turned into a yellow slurry suspension during the addition of organolithium reagents. Upon completion, the reaction was warmed to 0 °C and stirred for additional 3 h, during which the reaction would gradually turn brown and transparent. Then, to remove lithium thiophenolate impurity, the reaction was washed with 200 mL 3 M NaOH solution. To remove TMEDA residue, the mixture was washed with 200 mL 3 M HCl. The organic layer after the washing process was gathered and concentrated under vacuum to yield **3.232** as sticky oil (2.8 g, 81% yield). No purification was conducted further.



**1,2-bis(phenylthio)cyclobut-1-ene (3.232).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 7.1, 1.2 Hz, 3H), 7.33 – 7.26 (m, 7H), 2.60 (d, *J* = 0.9 Hz, 4H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)

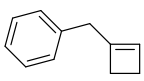
To oxidize **3.232** into **3.233**, **3.232** (2.8 g, 10.3 mmol) was dissolved in 10 mL HOAc and 15 mL 33 wt% hydrogen peroxide water solution. The reaction was heated to 60 ºC for 12 h (leave opening for $O_2$ generation, do not use sealed vessel). Then the reaction mixture was diluted with 100 mL water and quenched with concentrated NaOH solution at 0 ℃. Product **3.233** can be extracted from its water solution using large amount of DCM (more then 500 mL). The DCM solution of **3.233** was then concentrated under vacuum to gather a sticky hydroscopic white solid in 2.10 g. This crude material was dried over vacuum overnight and then subjected to the next step without further purification.



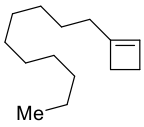
**1,2-bis(phenylsulfonyl)cyclobut-1-ene (3.233).** $^1$H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, $J$ = 8.4, 1.4 Hz, 3H), 7.70 (d, $J$ = 7.5 Hz, 2H), 7.64 – 7.57 (m, 5H), 2.73 (s, 4H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)

A THF solution of **3.233** (1.0 equiv., 1.0 mmol, used as 1.0 M THF stock solution) was transferred to a 2-dram vial in glovebox. The solution was diluted with additional 1.0 mL THF, and then, the vial was sealed with a septum and removed from glovebox. The reaction was cooled to 0 ℃ when the corresponding Grignard reagents (1.2 equiv.) were added *via* syringe. Then, the reaction was either warmed to rt (heating to 60 ℃ is required for **3.237**) to stir for an additional hour, before quenched with 3 M HCl and extracted with diethyl ether. The solution was then concentrated under vacuum to yield the crude material that was subjected directly to the reduction step without further purification.

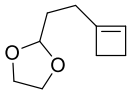
To reduce the monosulfone acquired from above, **3.234** (0.5 mmol) was dissolved in 2 mL of MeOH in 2-dram vial. Then, 5.0 equiv. Mg powder (2.5 mmol, 60.8 mg) was added. The vial was sealed with cap and placed in a sonicator to sonicate at room temperature for 2 h. Then, MeOH was removed under vacuum and the reaction was filtered through a plug of silica gel using diethyl ether. No further purifications were required and the obtained cyclobutenes were subjected to the diboration directly.



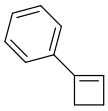
**(cyclobut-1-en-1-ylmethyl)benzene (3.235).** $^1$H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.21 (m, 5H), 5.67 (s, 1H), 3.36 (d, $J$ = 2.9 Hz, 2H), 2.45 (dd, $J$ = 3.2, 1.5 Hz, 2H), 2.36 (s, 2H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)



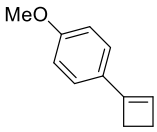

**1-octylcyclobut-1-ene (3.236).** $^1$H NMR (500 MHz, $CDCl_3$) δ 5.65 (s, 1H), 2.42 – 2.39 (m, 2H), 2.35 – 2.31 (m, 2H), 1.97 (d, *J* = 6.7 Hz, 3H), 1.47 – 1.21 (m, 31H), 0.89 (t, *J* = 6.8 Hz, 6H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)



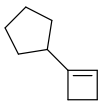

**1-octylcyclobut-1-ene (3.237).** $^1$H NMR (500 MHz, $CDCl_3$) δ 5.70 (s, 1H), 4.90 (t, *J* = 4.8 Hz, 1H), 4.02 – 3.94 (m, 2H), 3.91 – 3.78 (m, 2H), 2.46 – 2.40 (m, 2H), 2.33 (t, *J* = 3.1 Hz, 2H), 2.16 – 2.11 (m, 2H), 1.83 – 1.76 (m, 2H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 149.5, 127.0, 104.1, 64.9, 31.12, 31.16, 26.4, 25.6. IR (neat): $\nu_{max}$ 2938.33 (w), 2852.09 (m), 1467.11 (m), 1371.72 (m) cm$^{-1}$.



**cyclobut-1-en-1-ylbenzene (3.238).** $^1$H NMR (500 MHz, $CDCl_3$ δ 7.32 (dd, *J* = 8.1, 7.2 Hz, 3H), 7.25 (d, *J* = 14.6 Hz, 2H), 6.30 (t, *J* = 1.3 Hz, 1H), 2.84 – 2.81 (m, 2H), 2.54 (d, *J* = 1.3 Hz, 2H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)

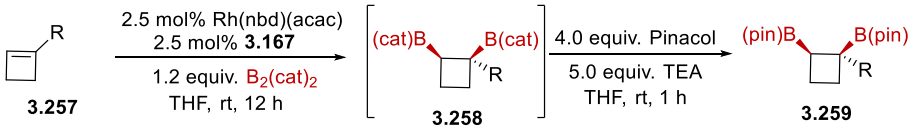



**1-(cyclobut-1-en-1-yl)-4-methoxybenzene (3.239).** $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.14 (t, J = 1.3 Hz, 1H), 3.80 (s, 3H), 2.84 – 2.74 (m, 2H), 2.57 – 2.47 (m, 2H). (Detailed characterization of this intermediate can be found in references 67 a,b and c.)



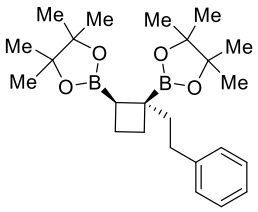
**cyclobut-1-en-1-ylcyclopentane (3.240).** $^1$H NMR (500 MHz, $CDCl_3$) δ 5.62 (s, 1H), 2.50 – 2.25 (m, 6H), 1.74 – 1.36 (m, 14H). (no further characterization on this compound was carried out due to its high volatility and high challenge to be isolated as its pure form.)

### 3.4.2.3 Procedures for Rh-catalyzed Diboration of Cyclobutenes




In glovebox, 1.0 equiv. **3.257** (0.1 mmol) was dissolved in 0.6 mL THF in a 2-dram vial to prepare a stock solution of **3.257**. In another 2-dram vial, 2.5 mol% of Rh(nbd)(acac) (0.8 mg, 2.5 μmol) along with 2.5 mol% (*S*)-Quinap **3.167** (1.1 mg, 2.5 μmol) was dissolved in 0.6 mL THF and stirred for 5 min. 1.2 equiv. $B_2(cat)_2$ (0.12 mmol, 28.5 mg) was then added to the catalyst

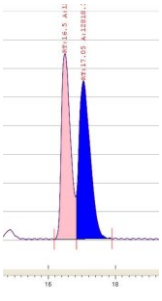
solution. The mixture was stirred for an additional 5 min before the stock solution of **3.257** was charged in. The vial was sealed by tape and removed from glovebox and stirred at rt for 12 h. Then, the vial was opened to air. 4.0 equiv. pinacol along with 5.0 equiv. TEA was added as a stock solution in THF (1.0 mL in volume, 0.4 M for pinacol, 0.5 M for TEA). The reaction was then stirred for an additional 1 h. Upon completion, the reaction mixture was diluted with diethyl ether and filtered through a plug of silica gel. The solution was then concentrated under vacuum to afford the crude product. The crude mixture was subjected to column chromatography for further purifications.



**2,2'-((1S,2R)-1-phenethylcyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.261).** 15.8 mg of **3.223** was used to produce 29.6 mg of **3.260** in 71.5% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 4H), 7.11 – 7.04 (m, 1H), 2.46 (ddd, $J$ = 9.7, 7.2, 1.9 Hz, 1H), 2.36 – 2.28 (m, 1H), 2.16 – 2.05 (m, 2H), 1.87 (dt, $J$ = 8.2, 1.7 Hz, 1H), 1.30 (d, $J$ = 7.8 Hz, 12H), 1.16 (d, $J$ = 6.8 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.8, 128.4, 128.4, 128.1, 125.3, 83.1, 82.8, 44.2, 33.0, 31.9, 25.0, 24.9, 24.9, 24.8, 20.1. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.55 ppm. IR (neat): $\nu_{max}$ 2976.45 (w), 2927.44 (m), 2859.31 (m), 1370.81 (s), 1311.11 (s), 1156.22 (s), 978.82 (s) $cm^{-1}$. HRMS (DART) for $C_{24}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 413.30474, found: 413.30290. $[\alpha]^{20}_D$: 7.8(c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm).

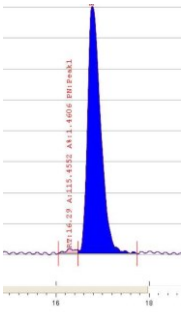
***Analysis of Stereochemistry:***

*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

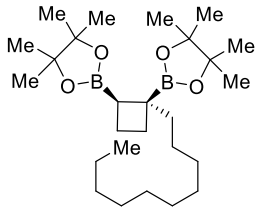


| Peak Info | | | |
|---|---|---|---|
| **Peak No** | **% Area** | **Area** | **RT (min)** |
| 1 | 48.7702 | 12202.9832 | 16.5 |
| 2 | 51.2298 | 12818.3904 | 17.05 |
| Total: | 100 | 25021.3736 | |

| Peak Info | | | |
|---|---|---|---|
| **Peak No** | **% Area** | **Area** | **RT (min)** |
| 1 | 1.4606 | 115.4552 | 16.29 |
| 2 | 98.5394 | 7789.4556 | 16.77 |
| Total: | 100 | 7904.9108 | |



Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was oxidized by hydrogen peroxide to the corresponding diol for easier SFC separation.



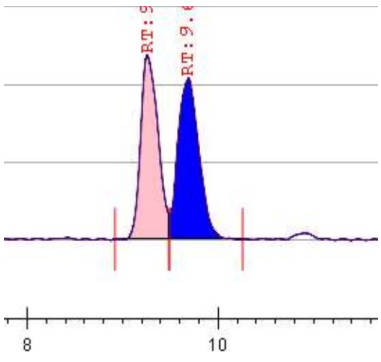
**2,2'-((1R,2R)-1-pentylcyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.261).** 19.4 mg of the corresponding cyclobutene was used to produce 26.3 mg of **3.261** in 58.6% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 2.08 – 2.02 (m, 1H), 1.90 (ddd, J = 16.3, 9.6, 2.9 Hz, 2H), 1.71 (d, J = 9.3 Hz, 1H), 1.52 (dd, J = 11.5, 7.9 Hz, 2H), 1.31 – 1.16 (m, 40H), 0.88 (t, J = 6.9 Hz, 4H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 82.9, 82.7, 42.0, 32.0, 31.9, 30.3, 29.7, 29.62, 29.58, 29.4, 26.3, 25.1, 24.8, 24.7, 22.7, 20.2, 14.1. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.3 ppm. IR (neat): $\nu_{max}$ 3038.33 (w), 2853.09 (m), 1485.91 (m), 1378.22 (m) cm$^{-1}$. HRMS (DART) for $C_{26}H_{51}B_2O_4$ $[M+H]^+$: Calc'd: 449.38952, found: 449.39157. $[\alpha]^{20}_D$: 20.3 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was oxidized by hydrogen peroxide to the corresponding diol, then reacted with 2.0 equiv. phenylboronic acid in THF for 1 h to generate the corresponding phenyl boronic ester to make it UV active.

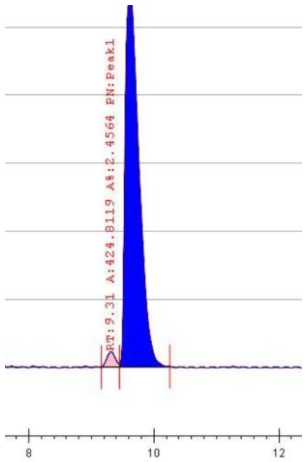
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

Racemic

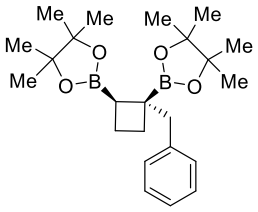



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 48.561 | 5965.9291 | 9.26 |
| 2 | 51.439 | 6319.5141 | 9.69 |
| Total: | 100 | 12285.4432 | |

Enriched




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 2.4564 | 424.8119 | 9.31 |
| 2 | 97.5436 | 16869.3733 | 9.63 |
| Total: | 100 | 17294.1852 | |



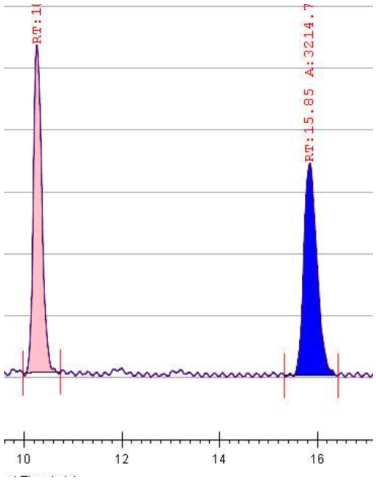
**2,2'-((1S,2R)-1-benzylcyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.262).** 10.8 mg of the corresponding cyclobutene was used to produce 21.0 mg of **3.262** in 70.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.11 (m, 5H), 2.89 (d, *J* = 13.7 Hz, 1H), 2.82 (d, *J* = 13.7 Hz, 1H), 2.16 – 2.07 (m, 1H), 2.00 – 1.90 (m, 2H), 1.86 – 1.79 (m, 1H), 1.70 (t, *J* = 9.4 Hz, 1H), 1.21 (d, *J* = 2.1 Hz, 12H), 1.18 (d, *J* = 9.5 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 140.6, 129.8, 127.6, 125.4, 83.1, 82.7, 45.7, 31.7, 30.3, 29.7, 25.0, 24.8, 24.8, 24.7, 24.7, 24.6, 20.4. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.4 ppm. IR (neat): $\nu_{max}$ 2976.17 (w), 2927.64 (m), 2855.31 (m), 1377.85 (s), 1309.14 (s), 1146.89 (s), 968.42 (s) cm$^{-1}$. HRMS (DART) for $C_{23}H_{37}B_2O_4$ $[M+H]^+$: Calc'd: 399.28845, found: 399.28725. $[\alpha]^{20}_D$: 31.4 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

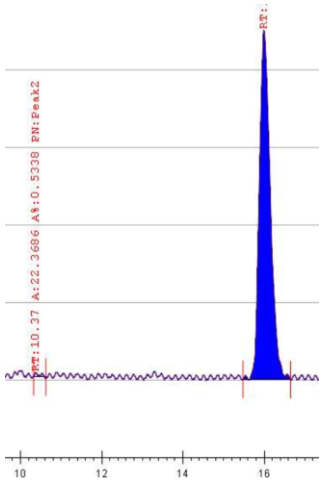
Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was oxidized by hydrogen peroxide to the corresponding diol for easier SFC separation.

*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

Racemic

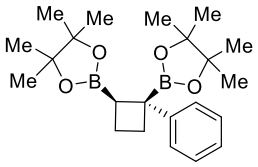



Enriched




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 49.9252 | 3205.1876 | 10.26 |
| 2 | 50.0748 | 3214.7947 | 15.85 |
| Total: | 100 | 6419.9823 | |

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 0.5338 | 22.3686 | 10.37 |
| 2 | 99.4662 | 4168.3656 | 15.99 |
| Total: | 100 | 4190.7342 | |



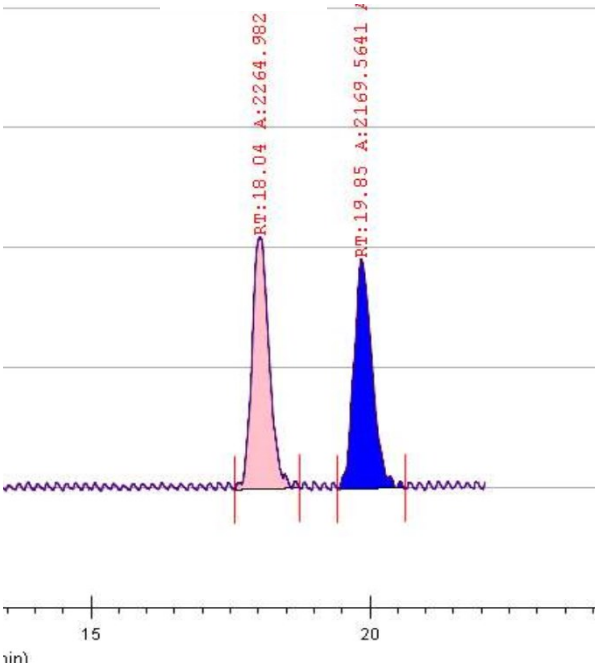
**2,2'-((1S,2R)-1-(2-(1,3-dioxolan-2-yl)ethyl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.266).** 26.2 mg of the corresponding cyclobutene was used to produce 51.2 mg of **3.266** in 66.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 4H), 7.11 – 7.03 (m, 1H), 2.46 (ddd, *J* = 9.7, 7.3, 1.9 Hz, 1H), 2.35 – 2.30 (m, 1H), 2.17 – 2.04 (m, 2H), 1.93 – 1.82 (m, 1H), 1.30 (d, *J* = 7.8 Hz, 12H), 1.16 (d, *J* = 6.8 Hz, 12H).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was oxidized by hydrogen peroxide to the corresponding diol for easier SFC separation.

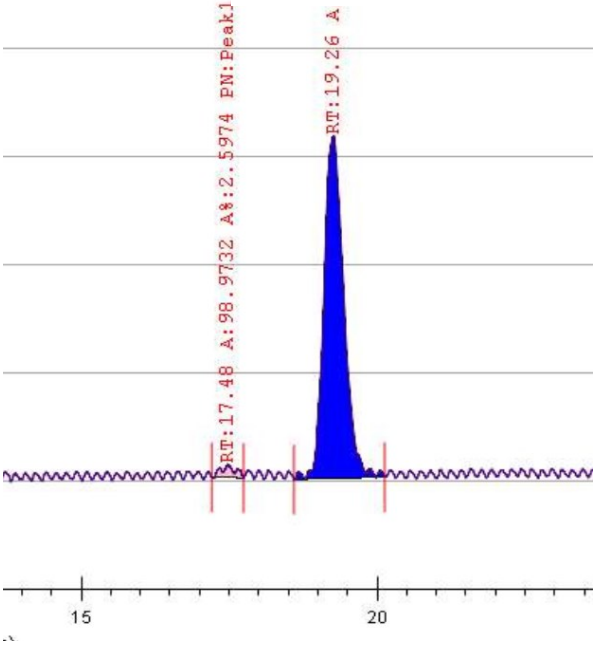
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

Racemic

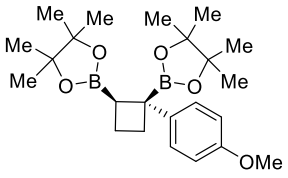



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 51.0759 | 2264.9826 | 18.04 |
| 2 | 48.9241 | 2169.5641 | 19.85 |
| Total: | 100 | 4434.5467 | |

Enriched




| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 2.5974 | 98.9732 | 17.48 |
| 2 | 97.4026 | 3711.4653 | 19.26 |
| Total: | 100 | 3810.4385 | |



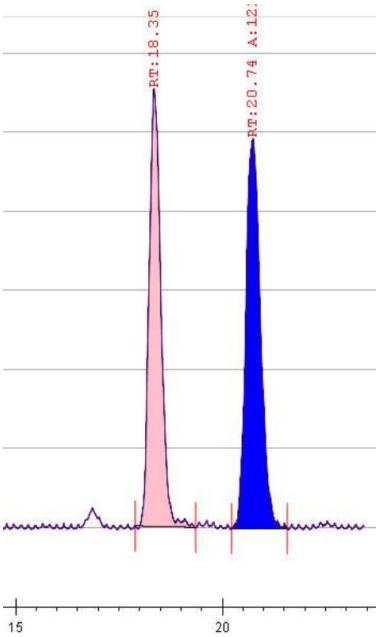
**2,2'-((1R,2R)-1-(4-methoxyphenyl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.267).** 16.0 mg of the corresponding cyclobutene was used to produce 30.2 mg of **3.267** in 72.1% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.78 (s, 3H), 2.44 (ddd, *J* = 9.8, 7.4, 2.0 Hz, 1H), 2.29 (td, *J* = 9.8, 7.4 Hz, 1H), 2.15 – 2.00 (m, 2H), 1.88 (dtd, *J* = 9.8, 8.3, 2.0 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 12H), 1.17 (d, *J* = 5.2 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 156.6, 142.1, 126.6, 113.3, 83.3, 83.0, 55.2, 33.2, 25.1, 24.9, 24.5, 20.6. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.6 ppm. IR (neat): $\nu_{max}$ 2981.75 (w), 2887.09 (s), 1475.98 (s), 1103.09 (s), 980.72 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{37}B_2O_5$ $[M+H]^+$: Calc'd: 415.27489, found: 415.27580. $[\alpha]^{20}_D$: -34.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was oxidized by hydrogen peroxide to the corresponding diol for easier SFC separation.

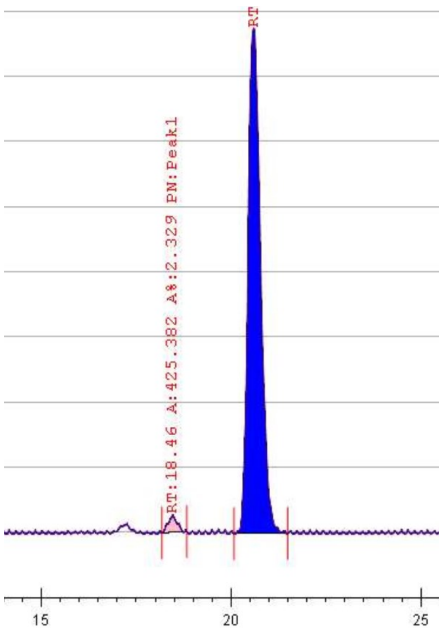
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

Racemic

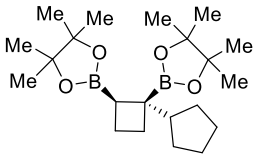



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 47.5171 | 10958.3728 | 18.35 |
| 2 | 52.4829 | 12103.5603 | 20.74 |
| Total: | 100 | 23061.9331 | |

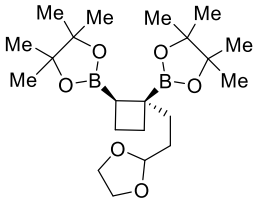
Enriched



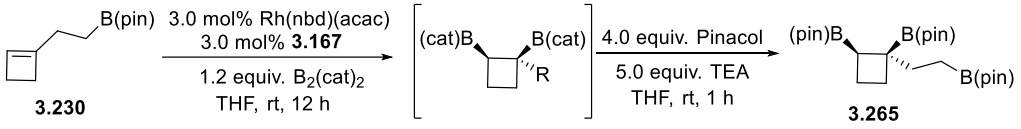

| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 2.329 | 425.382 | 18.46 |
| 2 | 97.671 | 17839.1022 | 20.6 |
| Total: | 100 | 18264.4842 | |



**2,2'-((1R,2R)-1-(4-methoxyphenyl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.269).** 15.1 mg of the corresponding cyclobutene was used to produce 24.2 mg of **3.269** in 55.7% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 2.07 – 1.74 (m, 5H), 1.72 – 1.42 (m, 8H), 1.28 – 1.22 (m, 24H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 82.8, 82.6, 48.6, 29.6, 28.5, 28.3, 25.7, 25.6, 25.1, 25.0, 24.9, 24.7, 24.6, 24.6, 20.0. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.1 ppm. IR (neat): $\nu_{max}$ 2971.45 (w), 2877.06 (s), 1474.13 (s), 1203.19 (s), 889.12 (s) cm$^{-1}$. HRMS (DART) for $C_{21}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 377.30393, found: 377.30390. $[\alpha]^{20}_D$: 10.2 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

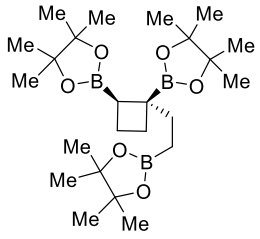


**2,2'-((1S,2R)-1-(2-(1,3-dioxolan-2-yl)ethyl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.264).** 15.4 mg of the corresponding cyclobutene was used to produce 21.0 mg of **3.264** in 70.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 4.87 – 4.80 (m, 1H), 3.99 – 3.91 (m, 2H), 3.88 – 3.79 (m, 2H), 2.07 – 1.87 (m, 3H), 1.77 – 1.66 (m, 3H), 1.59 – 1.52 (m, 2H), 1.25 (d, *J* = 5.0 Hz, 12H), 1.23 (d, *J* = 3.4 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 128.0, 105.2, 83.0, 82.8, 64.7, 35.9, 31.8, 30.6, 29.7, 24.9, 24.9, 24.9, 24.7, 19.9. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.5 ppm. IR (neat): $\nu_{max}$ 2977.34 (w), 2867.19 (s), 1466.54 (s), 1302.06 (s), 780.77 (s) cm$^{-1}$. HRMS (DART) for $C_{21}H_{39}B_2O_6$ $[M+H]^+$: Calc'd: 409.28545, found: 409.28435. $[\alpha]^{20}_D$: 15.7 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).




In glovebox, 1.0 equiv. **3.230** (0.314 mmol, 65.5 mg) was dissolved in 1.2 mL THF in a 3-dram vial to prepare a stock solution of **3.257**. In another 2-dram vial, 3.0 mol% of Rh(nbd)(acac) (2.9 mg, 9.5 μmol) along with 3.0 mol% (*S*)-Quinap **3.167** (4.2 mg, 9.5 μmol) was dissolved in 1.2 mL THF and stirred for 5 min. 1.2 equiv. $B_2(cat)_2$ (0.12 mmol, 90.0 mg) was then added to the catalyst solution. The mixture was stirred for an additional 5 min before the stock solution of **3.230** was charged in. The vial was sealed by tape and removed from glovebox and stirred at rt for 12 h. Then, the vial was opened to air. 4.0 equiv. pinacol along with 5.0 equiv. TEA was added as a stock

solution in THF (1.6 mL, 0.4 M for pinacol, 0.5 M for TEA). The reaction was then stirred for an additional 1 h. Upon completion, the reaction mixture was diluted with diethyl ether and filtered through a plug of silica gel. The solution was then concentrated under vacuum to afford the crude product. The crude mixture was subjected to column chromatography for further purification. Column condition: 95:5 volume ratio of hexane:ethyl acetate. Rf: 0.2 with 90:10 volume ratio of hexane:ethyl acetate. 116.4 mg **3.265** can be isolated cleanly in 80% isolated yield



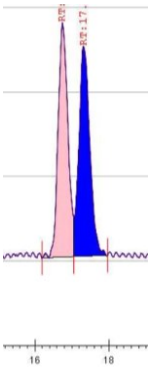
**2,2'-((1R,2R)-1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.265).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 1.99 (ddd, $J$ = 10.5, 8.2, 3.0 Hz, 1H), 1.95 – 1.80 (m, 2H), 1.72 – 1.67 (m, 1H), 1.62 – 1.59 (m, 1H), 1.50 (t, $J$ = 9.8 Hz, 1H), 1.24 – 1.20 (m, 37H), 0.85 (td, $J$ = 7.3, 5.9 Hz, 1H), 0.78 – 0.73 (m, 1H), 0.68 – 0.60 (m, 1H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 82.9, 82.7, 35.7, 31.3, 25.0, 24.8, 24.8, 24.8, 19.7. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.76 ppm. IR (neat): $\nu_{max}$ 2976.14 (w), 2857.29 (s), 1476.57 (s), 1312.08 (s), 880.17 (s) $cm^{-1}$. HRMS (DART) for $C_{24}H_{46}B_3O_6$ $[M+H]^+$: Calc'd: 463.35714, found: 463.35681. $[\alpha]^{20}_D$: 9.8(c = 1.0 g/100 mL, $CHCl_3$, $l$ = 50 mm).

***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was converted to **3.261** and oxidized to the diol for SFC separation

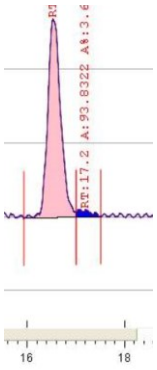
*Chiral SFC (OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm)*

Racemic



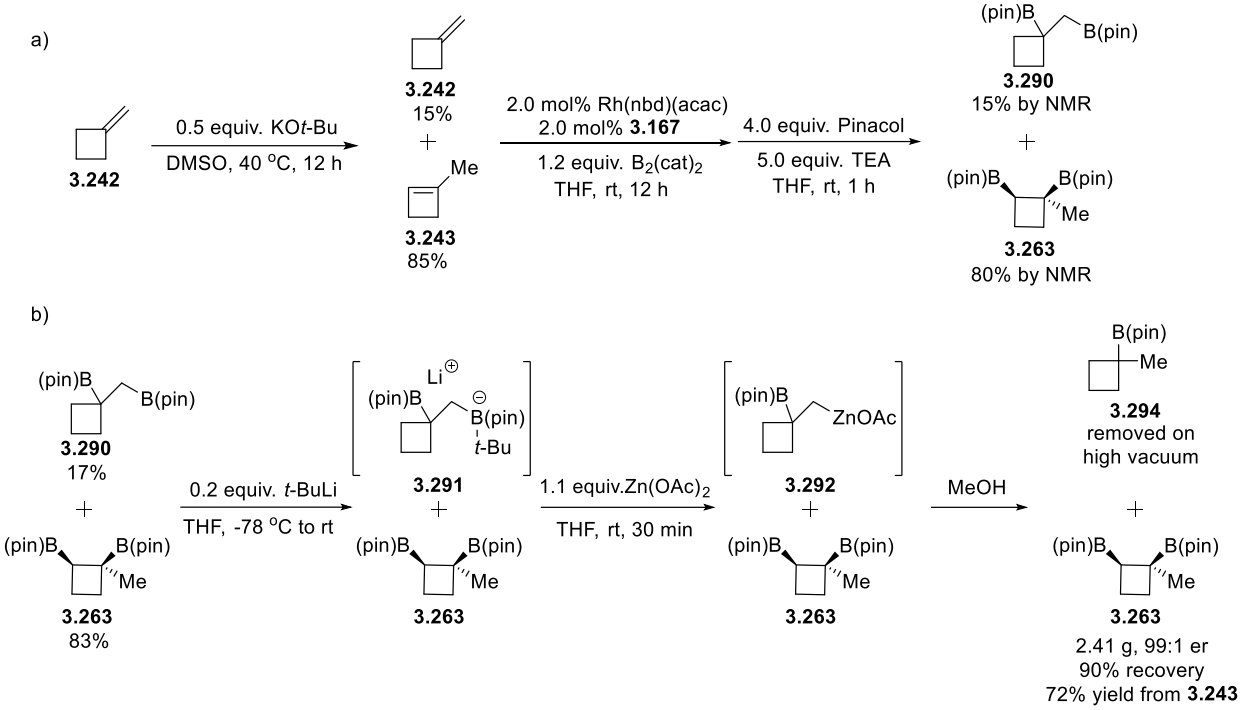
| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 49.807 | 2543.7441 | 16.74 |
| 2 | 50.193 | 2563.4608 | 17.31 |
| Total: | 100 | 5107.2049 | |

Enriched



| Peak Info | | | |
|---|---|---|---|
| Peak No | % Area | Area | RT (min) |
| 1 | 96.3903 | 2505.6262 | 16.53 |
| 2 | 3.6097 | 93.8322 | 17.2 |
| Total: | 100 | 2599.4584 | |

### 3.4.2.4 Procedures for Methylsubstituted Cyclobutyl Diboron Synthesis

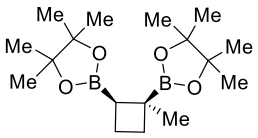



1.0 equiv. **3.242** (3.0 g, 44.0 mmol) was dissolved in 10 ml of DMSO in a 25 ml flask. Then, 0.5 equiv. KOt-Bu (22.0 mmol, 2.47 g) was added. The reaction was heated to 40 °C for 12 h. Then, the reaction was cooled to room temperature. A short-stem vacuum distillation head was added on the flask. Low vacuum was applied to the system, while the receiving vessel was cooled to -78 °C. The mixture of **3.242** and **3.243** was slowly distilled out and gathered in the receiving vessel in this manner. A total of 2.8 g was gathered in the end in 93% yield. $^1$H NMR analysis reveled that the mixture was composed of 85% of **3.243** and 15% of **3.242**.

In glovebox, the mixture of **3.242** and **3.243** (1.0 equiv., 7.17 g, 10 mmol.) was then dissolved in 1.0 mL THF in a 2-dram vial to prepare a stock solution of **3.257**. In a 50 mL flask, 2.0 mol% of Rh(nbd)(acac) (58.8 mg, 0.2mmol) along with 2.0 mol% (*S*)-Quinap **3.167** (87.9 mg, 0.2 mmol) was dissolved in 30 mL THF and stirred for 15 min. 1.2 equiv. $B_2(cat)_2$ (12.0 mmol, 2.85 g) was then added to the catalyst solution. The mixture was stirred for an additional 15 min before the stock solution of alkenes was charged in. The flask was sealed by tape and removed from glovebox and stirred at rt for 12 h. Then, the vial was opened to air. 3.0 equiv. pinacol along with 6.0 equiv. TEA was added as a stock solution in THF (30 mL, 1 M for pinacol, 2 M for TEA). The reaction was then stirred for an additional 2 h. Upon completion, the reaction mixture was diluted with

diethyl ether and filtered through a plug of silica gel. The solution was then concentrated under vacuum to afford the crude product. The crude mixture was subjected to column chromatography for further purification. Column condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. 2.59 g of the mixture of **3.263** and **3.290** can be isolated cleanly in 80.4% isolated yield.

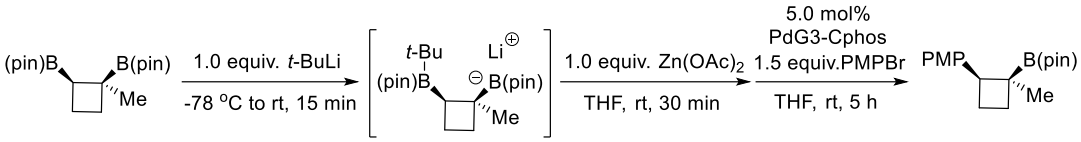
To remove **3.290** from **3.263**, following procedure was carried out. In glovebox, the mixture (2.59 g in total, containing 388 mg, 1.2 mmol of **3.290**) was charged into a 25 mL flask followed by 10 mL THF. The reaction was cooled to -78 ℃. 1.2 mmol of t-BuLi was added as a pentane stock solution. Reaction was stirred at -78 ℃ for 30 min before warmed to room temperature. The flask was transferred back to the glovebox, where 1.81 mmol, 331.6 mg of $Zn(OAc)_2$ was added. The reaction was stirred at room temperature of 1 h. Then the reaction flask was removed from glovebox. 4 mL of 3 M HCl methanol solution was added dropwise. Reaction was stirred for 2 h. Then, the solvents were removed under vacuum, and the reaction was diluted with diethyl ether and filtered through a plug of silica gel to remove Zinc salt. Then the mixture was concentrated under vacuum and then depressurized under high vacuum for 12 h to remove any volatile residues. At this point, all undesired **3.290** impurity was removed, and 1.94 g of the pure bisboronate **3.263** can be obtained in 88% recovery yield. The overall yield of this two-step sequence was 71%.




**2,2'-((1R,2R)-1-methylcyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.263).** $^1$H NMR (500 MHz, $CDCl_3$) δ 2.10 (dd, *J* = 10.5, 5.5 Hz, 1H), 1.95 (td, *J* = 9.2, 5.8 Hz, 2H), 1.73 – 1.66 (m, 1H), 1.50 (t, *J* = 9.6 Hz, 1H), 1.25 (dd, *J* = 5.0, 3.2 Hz, 24H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 82.9, 82.7, 33.3, 26.6, 24.9, 24.9, 24.8, 24.6, 19.7. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.5 ppm. IR (neat): $\nu_{max}$ 2911.36 (w), 2845.17 (s), 1106.43 (s), 1012.01 (s), 981.77 (s) cm$^{-1}$. HRMS (DART) for $C_{17}H_{33}B_2O_4$ $[M+H]^+$: Calc'd: 323.25595, found: 323.25749. $[\alpha]^{20}_D$: 3.7 (c = 1.0 g/100 mL, $CHCl_3$, *l* = 50 mm).

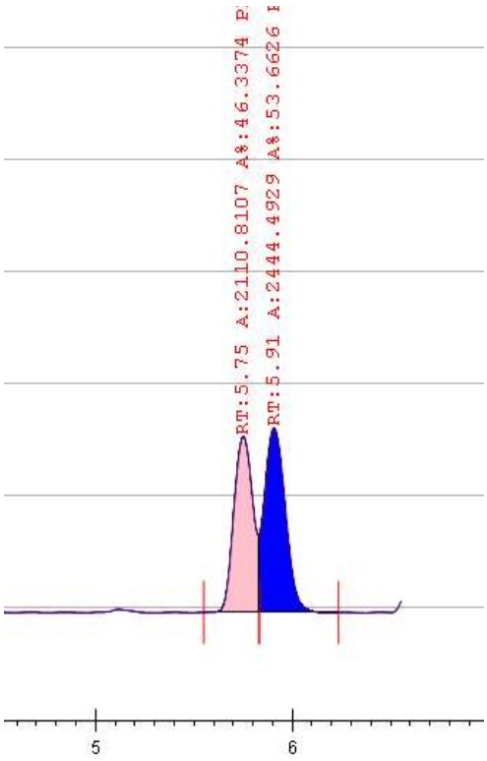
***Analysis of Stereochemistry:***

Racemic compound was prepared according to the procedure described above with racemic Quinap ligand. Enantioselectivity was determined by chiral SFC. The diboron was regioselectively arylated to the *p*-MeO phenyl boronic ester using the reaction shown below. The tertiary boronic ester was then oxidized to tertiary alcohol using peroxide and base for easier SFC separation.




*Chiral SFC (OJ-H, 3% IPA, 6 mL/min, 100 bar, 35 °C, 210-270 nm)*

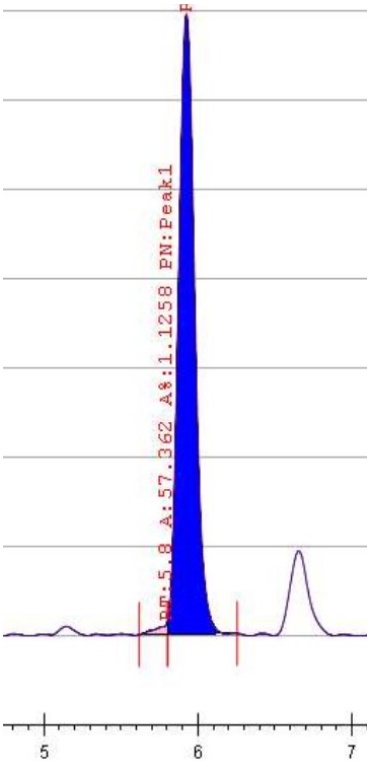
Racemic




**Peak Info**

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 46.3374 | 2110.8107 | 5.75 |
| 2 | 53.6626 | 2444.4929 | 5.91 |
| Total: | 100 | 4555.3036 | |

Enriched

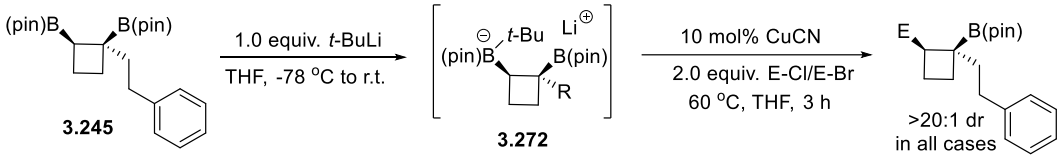



**Peak Info**

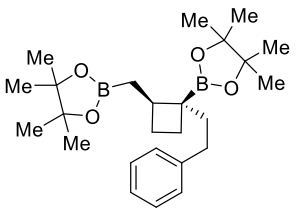
| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 1.1258 | 57.362 | 5.8 |
| 2 | 98.8742 | 5037.8844 | 5.93 |
| Total: | 100 | 5095.2464 | |

### 3.4.3 Diboron Functionalizations Experimental Details

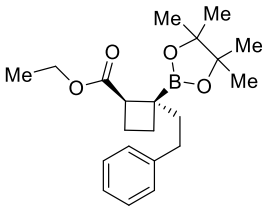
#### 3.4.3.1 Procedures for Cu-catalyzed Diboration Functionalization



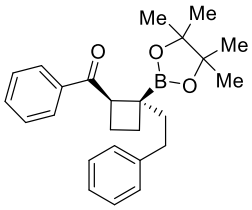

In glovebox, 1.0 equiv. **3.245** (0.1 mmol, 41.2 mg) was weighted in a 2-dram vial. 1.0 mL THF was then added followed by a magnetic stir bar. The vial was then sealed by septum cap and tape and removed from glovebox. The reaction was cooled down to -78 °C. Then, 1.0 equiv. t-BuLi (1.6 M stock solution in pentane) was added dropwise *via* syringe. The reaction was stirred at -78 °C for 10 min and then warmed to rt. Then, the vial was transferred into glovebox again, where around 10 mol% of CuCN (0.9 mg) was added in, along with 2.0 equiv. the designated electrophiles (electrophiles that were applicable to these reaction conditions are: allyl halides, alkynyl halides, acyl chlorides and bromomethyl B(pin)). Then, the vial was sealed again and removed from glovebox and heated to 60 °C for 3 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications.



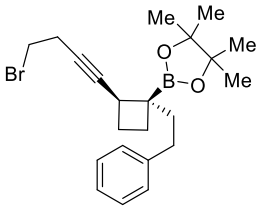
**4,4,5,5-tetramethyl-2-((1S,2R)-1-phenethyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclobutyl)-1,3,2-dioxaborolane (3.275).** 33.1 mg of the bromomethyl B(pin) electrophile was used to produce 65.9 mg of **3.275** in 66.3% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.5 Hz, 2H), 7.20 – 7.13 (m, 3H), 2.49 (ddd, *J* = 11.4, 9.3, 5.2 Hz, 2H), 2.23 (dd, *J* = 8.8, 6.4 Hz, 1H), 2.12 – 2.02 (m, 3H), 1.67 – 1.55 (m, 2H), 1.49 (dd, *J* = 10.2, 8.6 Hz, 1H), 1.30 (d, *J* = 2.0 Hz, 13H), 1.23 (d, *J* = 1.5 Hz, 12H), 1.06 (dd, *J* = 15.6, 6.2 Hz, 1H), 0.94 (dd, *J* = 15.6, 10.0 Hz, 1H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.7, 128.3, 128.3, 128.2, 128.1, 125.3, 83.1, 82.8, 65.8, 42.6, 41.6, 33.1, 27.1, 25.4, 25.0, 25.0, 24.9, 24.8, 24.8, 15.3. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.81 ppm. IR (neat): $\nu_{max}$ 2977.21(w), 2836.18 (s), 1665.71 (s), 1388.51 (s), 1113.226 (s), 965.17 (s) $cm^{-1}$. HRMS (DART) for $C_{25}H_{41}B_2O_4$ $[M+H]^+$: Calc'd: 427.31855, found: 427.31937.



**ethyl (1R,2S)-2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutane-1-carboxylate (3.276).** 16.3 mg of the ethyl chloroformate electrophile was used to produce 27.0 mg of **3.276** in 75.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.23 – 7.16 (m, 3H), 4.19 – 4.03 (m, 2H), 2.83 (t, *J* = 9.1 Hz, 1H), 2.59 (ddq, *J* = 25.6, 13.3, 6.6, 5.1 Hz, 2H), 2.33 – 2.25 (m, 1H), 2.13 – 2.00 (m, 3H), 1.84 (dt, *J* = 12.5, 6.2 Hz, 1H), 1.64 – 1.59 (m, 1H), 1.29 – 1.26 (m, 15H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 174.9, 143.1, 128.3, 128.2, 125.5, 83.4, 60.0, 47.2, 42.7, 32.7, 27.1, 25.0, 24.8, 20.9, 14.3. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.1 ppm. IR (neat): $\nu_{max}$ 2977.39 (w), 2855.84 (s), 1728.40 (s), 1376.43 (s), 1143.19 (s), 855.44 (s) cm$^{-1}$. HRMS (DART) for $C_{21}H_{32}BO_4$ $[M+H]^+$: Calc'd: 359.23882, found: 359.24019.

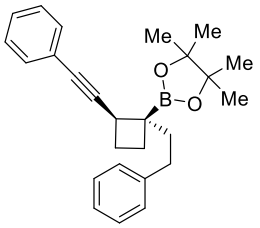


**((1R,2S)-2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)(phenyl)methanone (3.277).** 21.1 mg of the benzoyl chloride electrophile was used to produce 28.3 mg of **3.277** in 72.4% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.57 – 7.52 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.24 – 7.21 (m, 2H), 7.20 – 7.16 (m, 1H), 3.71 (t, *J* = 9.1 Hz, 1H), 2.62 (ddd, *J* = 25.9, 12.4, 5.0 Hz, 2H), 2.41 – 2.34 (m, 2H), 2.23 (ddd, *J* = 10.3, 7.9, 5.0 Hz, 1H), 2.10 (td, *J* = 12.4, 5.0 Hz, 1H), 1.87 (dd, *J* = 11.4, 6.4 Hz, 1H), 1.77 (dt, *J* = 10.5, 8.8 Hz, 1H), 1.33 (d, *J* = 3.7 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 201.0, 143.3, 132.7, 128.5, 128.4, 128.4, 128.4, 128.2, 125.5, 83.1, 52.7, 42.2, 32.6, 26.6, 25.2, 25.0, 23.5. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.9 ppm. IR (neat): $\nu_{max}$ 2975.23(w), 2856.11 (s), 1674.27 (s), 1378.11 (s), 1145.69 (s), 860.55 (s) cm$^{-1}$. HRMS (DART) for $C_{25}H_{32}BO_3$ $[M+H]^+$: Calc'd: 391.24390, found: 391.24355.



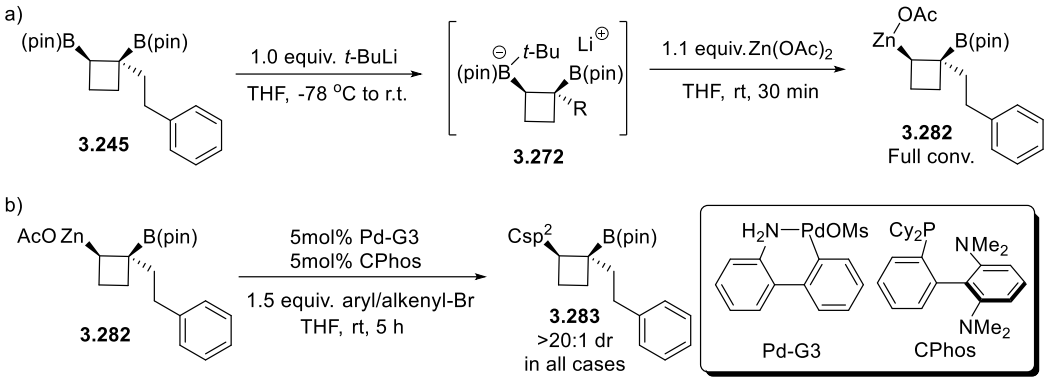
**2-((1S,2R)-2-(4-bromobut-1-yn-1-yl)-1-phenethylcyclobutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.278).** 31.8 mg of the alkynyl bromide electrophile was used to produce 25.0 mg of **3.278** in 59.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 7.6 Hz, 2H), 7.20 – 7.15 (m, 3H), 3.40 (t, *J* = 7.7 Hz, 2H), 2.76 – 2.68 (m, 3H), 2.54 – 2.48 (m, 2H), 2.19

– 2.03 (m, 4H), 1.66 (ddd, *J* = 12.8, 10.2, 7.0 Hz, 1H), 1.33 (d, *J* = 2.2 Hz, 15H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 201.0, 143.3, 132.7, 128.5, 128.4, 128.4, 128.4, 128.2, 125.5, 83.1, 52.7, 42.2, 32.6, 26.6, 25.2, 25.0, 23.5. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.9 ppm. IR (neat): $\nu_{max}$ 2975.23(w), 2856.11 (s), 1674.27 (s), 1378.11 (s), 1145.69 (s), 860.55 (s) $cm^{-1}$. HRMS (DART) for $C_{22}H_{31}BBrO_2$ $[M+H]^+$: Calc'd: 417.15950, found: 417.16060.

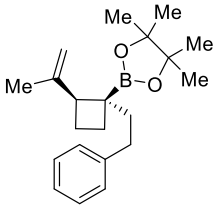



**4,4,5,5-tetramethyl-2-((1S,2R)-1-phenethyl-2-(phenylethynyl)cyclobutyl)-1,3,2-dioxaborolane (3.279).** 27.5 mg of the alkynyl bromide electrophile was used to produce 25.2 mg of **3.279** in 65.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.6 with 90:10 volume ratio of hexane:ethyl acetate. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.29 – 7.18 (m, 8H), 2.97 (t, *J* = 9.1 Hz, 1H), 2.58 (q, *J* = 3.9, 3.1 Hz, 1H), 2.30 – 2.14 (m, 4H), 1.79 – 1.70 (m, 1H), 1.63 – 1.58 (m, 1H), 1.31 (d, *J* = 12.6 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.0, 131.5, 128.4, 128.2, 128.1, 127.3, 125.6, 92.8, 83.5, 82.5, 53.4, 43.4, 42.6, 34.4, 32.8, 27.9, 26.2, 25.4, 24.8. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.72 ppm. IR (neat): $\nu_{max}$ 2976.28(w), 2856.08 (s), 1655.77 (s), 1386.41 (s), 1143.16 (s), 763.67 (s) $cm^{-1}$. HRMS (DART) for $C_{26}H_{32}BO_2$ $[M+H]^+$: Calc'd: 387.24899, found: 387.24966.

### 3.4.3.2 Procedures for Negishi Coupling Using Bisboronate

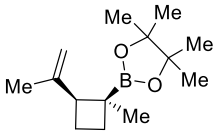



In glovebox, 1.0 equiv. **3.245** (0.1 mmol, 41.2 mg) was weighted in a 2-dram vial. 1.0 mL THF was then added followed by a magnetic stir bar. The vial was then sealed by septum cap and tape and removed from glovebox. The reaction was cooled down to -78 °C. Then, 1.0 equiv. t-BuLi (1.6 M stock solution in pentane) was added dropwise *via* syringe. The reaction was stirred at -78 °C for 10 min and then warmed to rt. Then, the vial was transferred into glovebox again, where 1.05 equiv. $Zn(OAc)_2$ (19.3 mg) was added in. The reaction was stirred at rt for 30 min, before 4.0 mg of Pd-G3-CPhos complex was added along with 1.5 equiv. the designated electrophiles (electrophiles that were applicable to these reaction conditions are: alkenyl halides and aryl halides). Then, the vial was sealed again and removed from glovebox and stirred at rt for 5 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications.



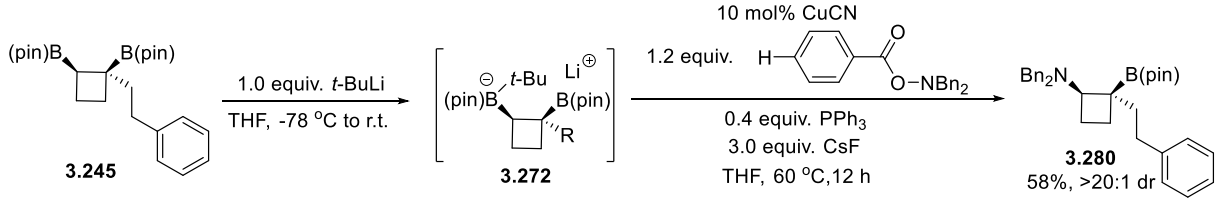

**4,4,5,5-tetramethyl-2-((1S,2R)-1-phenethyl-2-(prop-1-en-2-yl)cyclobutyl)-1,3,2-dioxaborolane (3.286).** 31.8 mg of the alkynyl bromide electrophile was used to produce 25.0 mg of **3.286** in 59.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 4H), 7.23 – 7.13 (m, 5H), 4.71 – 4.62 (m, 2H), 2.56 – 2.43 (m, 4H), 2.26 (d, $J$ = 5.1 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.99 – 1.82 (m, 4H), 1.77 – 1.70 (m, 4H), 1.64 (d, $J$ = 5.4 Hz, 1H), 1.58 – 1.49 (m, 2H), 1.32 – 1.25 (m, 23H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 147.8, 145.4, 143.3, 143.3, 128.5, 128.4, 128.3, 128.2, 128.2, 128.2, 125.5, 125.5, 108.3, 83.2, 52.1, 44.0, 42.0, 33.3, 33.2, 30.2, 26.4, 25.4, 24.9, 24.9, 24.7, 24.6, 22.3, 21.5, 18.2. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.41 ppm. IR (neat): $\nu_{max}$ 2986.18(w), 2857.18 (s),

1654.44 (s), 1381.11 (s), 1113.26 (s), 963.17 (s) $cm^{-1}$. HRMS (DART) for $C_{21}H_{32}BO_2$ $[M+H]^+$: Calc'd: 327.24899, found: 327.24974.



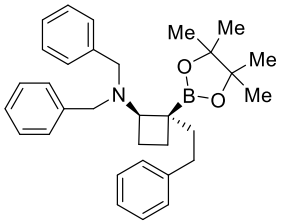
**4,4,5,5-tetramethyl-2-((1R,2R)-1-methyl-2-(prop-1-en-2-yl)cyclobutyl)-1,3,2-dioxaborolane (3.296).** 27.5 mg of the alkynyl bromide electrophile was used to produce 25.2 mg of **3.296** in 65.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. $^1H$ NMR (500 MHz, $CDCl_3$) δ 4.66 (t, *J* = 1.8 Hz, 1H), 4.62 (s, 1H), 2.44 (d, *J* = 9.3 Hz, 1H), 2.11 (ddd, *J* = 10.4, 8.8, 1.5 Hz, 1H), 1.99 (t, *J* = 9.3 Hz, 1H), 1.86 – 1.80 (m, 1H), 1.70 (s, 3H), 1.49 – 1.41 (m, 2H), 1.21 (d, *J* = 1.4 Hz, 12H). $^{13}C$ NMR (500 MHz, $CDCl_3$) δ 148.0, 109.9, 107.9, 82.9, 53.1, 28.6, 26.3, 25.0, 24.9, 24.6, 21.8, 21.4. $^{11}B$ NMR (500 MHz, $CDCl_3$) δ 34.3 ppm. IR (neat): $\nu_{max}$ 2976.95(w), 2860.91 (s), 1462.91 (s), 1371.42 (s), 1138.29 (s), 882.63 (s) $cm^{-1}$. HRMS (DART) for $C_{14}H_{26}BO_2$ $[M+H]^+$: Calc'd: 237.20204, found: 237.20250.

### 3.4.3.3 Miscellaneous Bisboronate Functionalization

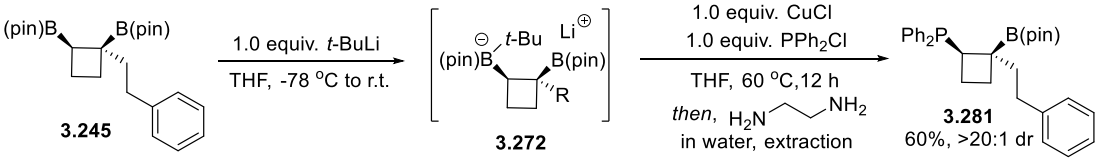



In glovebox, 1.0 equiv. **3.245** (0.1 mmol, 41.2 mg) was weighted in a 2-dram vial. 1.0 mL THF was then added followed by a magnetic stir bar. The vial was then sealed by septum cap and tape and removed from glovebox. The reaction was cooled down to -78 °C. Then, 1.0 equiv. t-BuLi (1.6 M stock solution in pentane) was added dropwise *via* syringe. The reaction was stirred at -78 °C for 10 min and then warmed to rt. Then, the vial was transferred into glovebox again, where around 10 mol% of CuCN (0.9 mg) was added in, along with 2.0 equiv. the amination electrophile (43.2mg, 0.12 mmol). Also, 0.4 equiv. $PPh_3$ (10.5 mg, 0.04 mmol) and 3.0 equiv. CsF (45.6 mg, 0.3 mmol) was added. Then, the vial was sealed again and removed from glovebox and heated to 60 °C for 12 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications. FCC condition: 98:2 volume ratio of hexane:ethyl

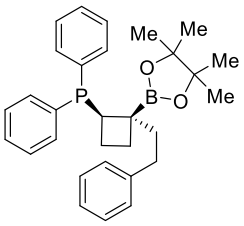
acetate to remove the non-polar component, then flush everything down with diethyl ether. Rf: 0.4 with 50:50 volume ratio of hexane:ethyl acetate. 28.0 mg of **3.280** was isolated in 58.2% yield.



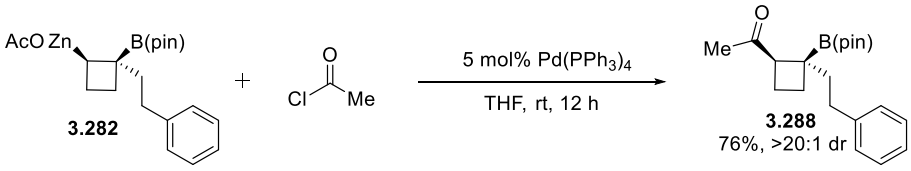

**(1R,2R)-N,N-dibenzyl-2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutan-1-amine (3.280).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 8.3 Hz, 5H), 7.27 – 7.23 (m, 7H), 7.19 – 7.16 (m, 3H), 3.71 (d, J = 14.1 Hz, 2H), 3.30 (d, J = 14.1 Hz, 2H), 2.95 (dd, J = 9.6, 7.7 Hz, 1H), 2.51 – 2.33 (m, 3H), 2.10 – 2.05 (m, 1H), 1.89 – 1.83 (m, 2H), 1.66 – 1.62 (m, 1H), 1.39 (s, 6H), 1.31 (s, 6H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.2, 139.0, 129.4, 128.4, 128.3, 128.2, 128.1, 127.7, 127.0, 126.5, 125.5, 83.3, 69.1, 54.6, 43.4, 33.1, 26.0, 25.8, 24.5, 23.8.. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.01 ppm. IR (neat): $\nu_{max}$ 2977.15(w), 2862.81 (s), 1457.19 (s), 1355.12 (s), 1118.17 (s), 887.64 (s) $cm^{-1}$. HRMS (DART) for $C_{32}H_{41}BNO_2$ $[M+H]^+$: Calc'd: 482.32249, found: 482.32205.



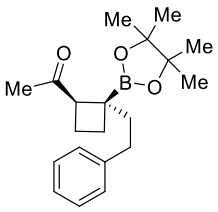

In glovebox, 1.0 equiv. **3.245** (0.1 mmol, 41.2 mg) was weighted in a 2-dram vial. 1.0 mL THF was then added followed by a magnetic stir bar. The vial was then sealed by septum cap and tape and removed from glovebox. The reaction was cooled down to -78 °C. Then, 1.0 equiv. t-BuLi (1.6 M stock solution in pentane) was added dropwise *via* syringe. The reaction was stirred at -78 °C for 10 min and then warmed to rt. In glovebox, 1.0 equiv. CuCl (9.9 mg, 0.1 mmol) and 1.0 equiv. diphenylphosphine chloride (22.6 mg, 1.0 mmol) was dissolved in 0.8 mL THF and stirred for 30 min. Then, the Cu solution was added to the boronate complex. Then, the vial was sealed again and removed from glovebox and heated to 60 °C for 12 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude was then washed with ethylene diamine water solution and extracted twice with diethyl ether. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. 25.1 mg of **3.281** was isolated in 59.5% yield



**((1R,2R)-2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)diphenylphosphane (3.281).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 2H), 7.39 – 7.34 (m, 2H), 7.29 – 7.23 (m, 8H), 7.16 (d, J = 7.5 Hz, 1H), 7.13 – 7.08 (m, 2H), 2.99 (ddd, J = 10.3, 8.4, 6.5 Hz, 1H), 2.44 – 2.34 (m, 3H), 2.13 – 2.04 (m, 1H), 1.96 – 1.89 (m, 2H), 1.81 – 1.75 (m, 1H), 1.59 – 1.53 (m, 1H), 1.38 (s, 6H), 1.34 (s, 6H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.1, 133.4, 133.3, 133.25, 133.21, 128.34, 128.30, 128.23, 128.21, 128.1, 128.05, 128.02, 125.5, 83.7, 43.4, 43.3, 42.8, 32.6, 30.0, 29.9, 25.8, 25.7, 25.0, 24.9, 23.4, 23.3. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.43 ppm. $^{31}$P NMR (500 MHz, $CDCl_3$) δ -12.33 ppm. IR (neat): $\nu_{max}$ 2979.65(w), 2863.61 (s), 1448.69 (s), 1345.21 (s), 1117.37 (s), 869.14 (s) $cm^{-1}$. HRMS (DART) for $C_{30}H_{37}BO_2P$ $[M+H]^+$: Calc'd: 471.26187, found: 471.26270.

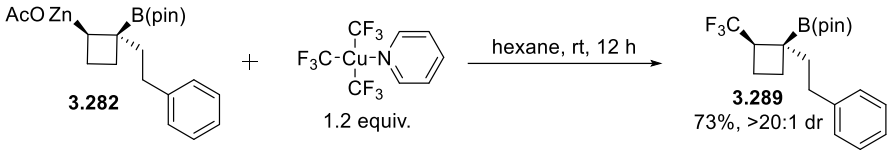



The β-boryl Zinc was prepared as described in section 3.4.3.2 in 0.1 mmol as 0.1 M stock solution in THF. To this solution was added 1.5 equiv. of acetyl chloride (9.4 mg, 0.15 mmol) and 5.0 mol% $Pd(PPh_3)_4$ (5.78 mg). The vial was then sealed by tape and removed from glovebox and stirred at room temperature for 12 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude was then washed with ethylene diamine water solution. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. 25.0 mg of **3.288** was isolated in 76.2% yield.

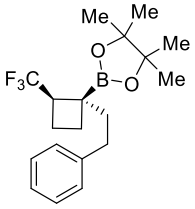


**1-((1R,2S)-2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutyl)ethan-1-one (3.288).** $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.6 Hz, 2H), 7.20 – 7.13 (m, 3H), 2.91 (t, *J* = 9.0 Hz, 1H), 2.59 – 2.48 (m, 2H), 2.24 – 2.17 (m, 1H), 2.10 – 2.02 (m, 6H), 1.78 (td, *J* = 12.4, 5.3 Hz, 1H), 1.27 (s, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$): δ 209.6, 143.0, 128.3, 128.3, 125.6, 83.4, 65.8, 56.2, 42.6,

32.7, 29.7, 28.1, 26.2, 25.1, 24.8, 20.6, 15.3. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.2 ppm. IR (neat): $\nu_{max}$ 2976.05(w), 2854.63 (s), 1705.66 (s), 1379.22 (s), 1143.07 (s), 871.72 (s) $cm^{-1}$. HRMS (DART) for $C_{20}H_{30}BO_3$ $[M+H]^+$: Calc'd: 329.22825, found: 329.22877.

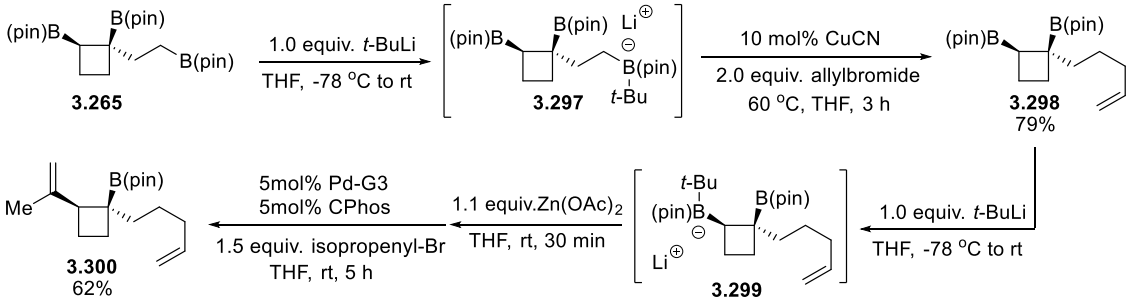



The β-boryl Zinc was prepared as described in section 3.4.3.2 in 0.1 mmol as 0.1 M stock solution in THF. The THF solvent in the reaction was evacuated under vacuum and the solid was redissolved in 1 mL hexane. Then 1.2 equiv. of the trifluoromethylation electrophile (42.0 mg, 0.12 mmol) was added.The vial was then sealed by tape and removed from glovebox and stirred at room temperature for 12 h. Then, the reaction mixture was diluted with diethyl ether and flashed through a plug of silica gel. The crude was then washed with ethylene diamine water solution. The crude material was then concentrated under vacuum and then subjected to column chromatography for further purifications. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.4 with 90:10 volume ratio of hexane:ethyl acetate. 25.0 mg of **3.288** was isolated in 76.2% yield

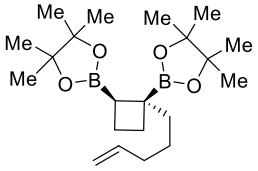



**4,4,5,5-tetramethyl-2-((1S,2R)-1-phenethyl-2-(trifluoromethyl)cyclobutyl)-1,3,2-dioxaborolane (3.289).** $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.19 (d, *J* = 7.2 Hz, 3H), 2.62 (q, *J* = 9.7 Hz, 1H), 2.56 – 2.43 (m, 2H), 2.26 (td, *J* = 9.5, 3.1 Hz, 1H), 2.18 – 2.12 (m, 1H), 2.06 (ddt, *J* = 9.6, 6.0, 3.3 Hz, 1H), 1.69 (td, *J* = 12.3, 11.4, 6.5 Hz, 1H), 1.59 (d, *J* = 9.8 Hz, 1H), 1.32 – 1.25 (m, 12H), 0.87 (td, *J* = 10.3, 8.4, 4.9 Hz, 1H). $^{19}$F NMR (500 MHz, $CDCl_3$) δ 69.58, 69.60 ppm. $^{13}$C NMR (500 MHz, $CDCl_3$) δ 142.5, 128.3, 128.3, 125.7, 83.8, 46.6, 43.0, 32.4, 26.6, 25.1, 24.9, 24.7, 18.4. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.9 ppm. IR (neat): $\nu_{max}$ 2978.48(w), 2855.98 (s), 1371.61 (s), 1323.32 (s), 1140.55 (s), 852.37 (s) $cm^{-1}$. HRMS (DART) for $C_{19}H_{27}BF_3O_2$ $[M+H]^+$: Calc'd: 355.20507, found: 355.20635.

### 3.4.3.4 Procedures for Triboron Functionalization

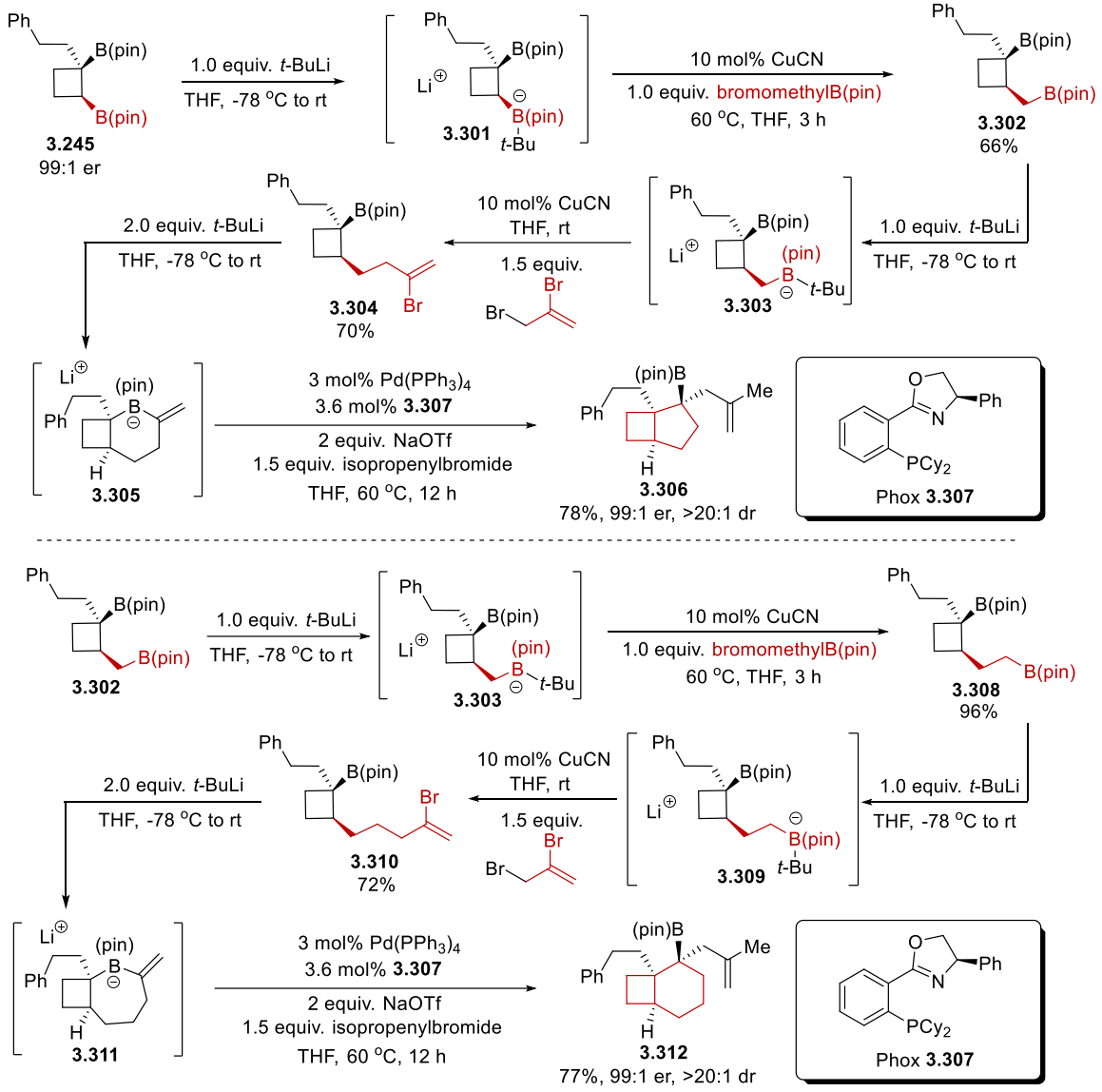



The reaction conditions are identical to the ones described in section 3.4.3.1 and 3.4.3.2.



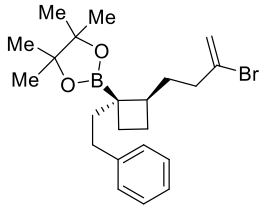
**2,2'-((1R,2R)-1-(pent-4-en-1-yl)cyclobutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.298).** 24.2 mg of the allyl bromide electrophile was used to produce 29.8 mg of **3.298** in 79.1% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.3 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 5.90 – 5.75 (m, 1H), 5.04 – 4.85 (m, 2H), 2.07 – 1.99 (m, 3H), 1.92 (ddd, $J$ = 28.1, 10.7, 8.1 Hz, 2H), 1.73 (t, $J$ = 9.4 Hz, 1H), 1.63 – 1.44 (m, 4H), 1.25 (dd, $J$ = 9.4, 3.7 Hz, 24H), 0.88 (tt, $J$ = 6.5, 2.8 Hz, 1H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 139.5, 113.7, 83.0, 82.7, 41.5, 34.4, 32.1, 25.6, 25.0, 24.8, 24.8, 20.1. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.6 ppm. IR (neat): $\nu_{max}$ 2976.49(w), 2855.38 (s), 1471.69 (s), 1377.31 (s), 1147.44 (s), 857.57 (s) cm$^{-1}$. HRMS (DART) for $C_{21}H_{39}B_2O_4$ $[M+H]^+$: Calc'd: 377.29562, found: 377.29570.

### 3.4.4 Aliphatic Bicyclic Boronates Syntheses Experimental Details

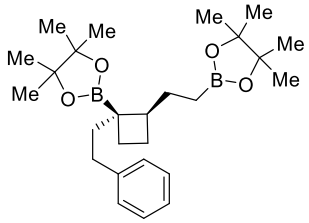



The diboron regioselective homologation reaction and allylation to install alkenyl bromide unit, as well as the conjunctive cyclization reaction conditions were similar to those described in Chapter 2 and Chapter 3. Adjustments were made only on the overall scale of the theses reactions in order to generate enough amount of intermediate for the reaction sequence. Noticeably, It is crucial to the match the chirality of the Quinap ligand for the enantioselective diboration reaction and the Phox ligand for the conjunctive cyclization reaction. (*S*)-Quinap should be paired with Phox **3.307**. Failed to do so will result in large amount of the Suzuki-Miyuara cross-coupling

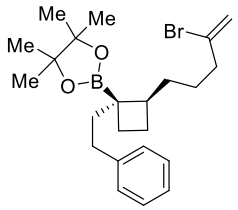
byproducts be generated in large amount during the conjunctive cyclization reaction, which were found difficult to remove through column chromatography purification.



**2-((1R,2R)-2-(3-bromobut-3-en-1-yl)-1-phenethylcyclobutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.304).** 49.0 mg of **3.304** was used to produce 40.0 mg of **3.279** in 83.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.6 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.20 – 7.15 (m, 3H), 5.53 (d, *J* = 1.4 Hz, 1H), 5.36 (d, *J* = 1.6 Hz, 1H), 2.52 – 2.40 (m, 3H), 2.34 (ddd, *J* = 9.6, 5.4, 1.2 Hz, 1H), 2.13 (ddd, *J* = 10.4, 8.8, 1.9 Hz, 1H), 2.05 – 1.96 (m, 3H), 1.74 (ddd, *J* = 13.2, 6.6, 3.3 Hz, 1H), 1.68 – 1.60 (m, 3H), 1.52 (dd, *J* = 10.4, 8.6 Hz, 1H), 1.31 (d, *J* = 3.2 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.3, 135.1, 128.3, 128.2, 125.5, 116.0, 83.2, 44.9, 43.3, 39.6, 33.7, 33.2, 27.2, 25.4, 24.9, 24.7. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 33.75 ppm. IR (neat): $\nu_{max}$ 2974.11(w), 2861.10 (s), 1449.91 (s), 1371.66 (s), 1114.31 (s), 887.15 (s) $cm^{-1}$. HRMS (DART) for $C_{22}H_{33}BBrO_2$ $[M+H]^+$: Calc'd: 419.17515, found: 419.17521.

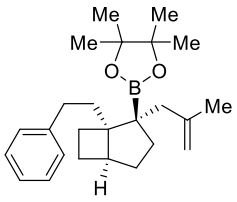


**4,4,5,5-tetramethyl-2-((1R,2S)-1-phenethyl-2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)cyclobutyl)-1,3,2-dioxaborolane (3.308).** 35.1 mg of **3.304** was used to produce 35.1 mg of **3.308** in 96.0% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.3 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.22 – 7.12 (m, 3H), 2.48 (ddd, *J* = 10.3, 5.8, 3.5 Hz, 2H), 2.13 – 1.91 (m, 4H), 1.67 – 1.55 (m, 3H), 1.51 – 1.43 (m, 2H), 1.30 (d, *J* = 4.5 Hz, 12H), 1.22 (d, *J* = 2.5 Hz, 12H), 0.72 (ddd, *J* = 9.3, 6.5, 5.2 Hz, 2H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.6, 128.3, 128.1, 125.3, 83.0, 82.7, 48.3, 43.3, 33.2, 29.6, 26.8, 25.2, 25.0, 24.8, 24.8, 24.6. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.21 ppm. IR (neat): $\nu_{max}$ 2986.11(w), 2856.10 (s), 1445.23 (s), 1368.16 (s), 1145.51 (s), 875.15 (s) $cm^{-1}$. HRMS (DART) for $C_{26}H_{43}B_2O_4$ $[M+H]^+$: Calc'd: 441.33420, found: 441.33495.

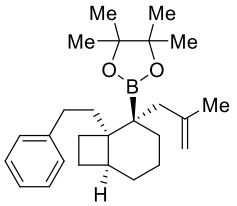


**2-((1R,2S)-2-(4-bromopent-4-en-1-yl)-1-phenethylcyclobutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.310).** 30.8 mg of **3.308** was used to produce 22.1 mg of **3.310** in 72.9% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.6 with 90:10 volume ratio of

hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.21 – 7.15 (m, 3H), 5.54 (q, *J* = 1.3 Hz, 1H), 5.37 (d, *J* = 1.6 Hz, 1H), 2.53 – 2.36 (m, 4H), 2.12 (ddd, *J* = 10.7, 8.9, 2.0 Hz, 1H), 2.07 – 1.95 (m, 3H), 1.62 (td, *J* = 10.8, 9.3, 5.8 Hz, 2H), 1.54 – 1.46 (m, 4H), 1.37 (tt, *J* = 8.2, 4.1 Hz, 1H), 1.30 (d, *J* = 3.9 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 143.4, 134.9, 128.3, 128.2, 125.4, 116.2, 83.1, 45.8, 43.3, 41.5, 33.9, 33.2, 27.1, 26.0, 25.3, 25.0, 24.9. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.11 ppm. IR (neat): $\nu_{max}$ 2977.91(w), 2868.21 (w), 1451.33 (s), 1370.77 (s), 1124.10 (s), 888.35 (s) $cm^{-1}$. HRMS (DART) for $C_{23}H_{35}BBrO_2$ $[M+H]^+$: Calc'd: 433.119080, found: 433.19119.



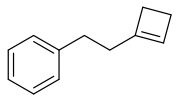

**4,4,5,5-tetramethyl-2-((1S,2S,5S)-2-(2-methylallyl)-1-phenethylbicyclo [3.2.0]heptan-2-yl)-1,3,2-dioxaborolane (3.306).** 19.0 mg of **3.304** was used to produce 13.5 mg of **3.306** in 78.2% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.6 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 4H), 7.22 – 7.17 (m, 1H), 4.74 – 4.68 (m, 1H), 4.64 (d, *J* = 2.6 Hz, 1H), 3.03 (td, *J* = 13.1, 5.0 Hz, 1H), 2.68 (td, *J* = 13.0, 4.5 Hz, 1H), 2.43 (s, 1H), 2.31 – 2.22 (m, 2H), 2.14 – 2.02 (m, 2H), 1.96 – 1.89 (m, 1H), 1.82 (ddd, *J* = 11.2, 7.7, 5.9 Hz, 2H), 1.77 – 1.73 (m, 1H), 1.69 (s, 3H), 1.40 – 1.35 (m, 2H), 1.32 (s, 1H), 1.23 (d, *J* = 8.3 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 145.0, 143.9, 128.4, 128.3, 125.5, 112.0, 83.1, 55.6, 42.1, 38.5, 36.8, 32.4, 31.0, 30.7, 26.0, 25.3, 25.0, 23.4, 22.3. $^{11}$B NMR (500 MHz, $CDCl_3$) δ 34.5 ppm. IR (neat): $\nu_{max}$ 2976.21(w), 2857.20 (s), 1455.93 (s), 1369.36 (s), 1144.60 (s), 885.75 (s) $cm^{-1}$. HRMS (DART) for $C_{25}H_{38}BO_2$ $[M+H]^+$: Calc'd: 381.29594, found: 381.9620.



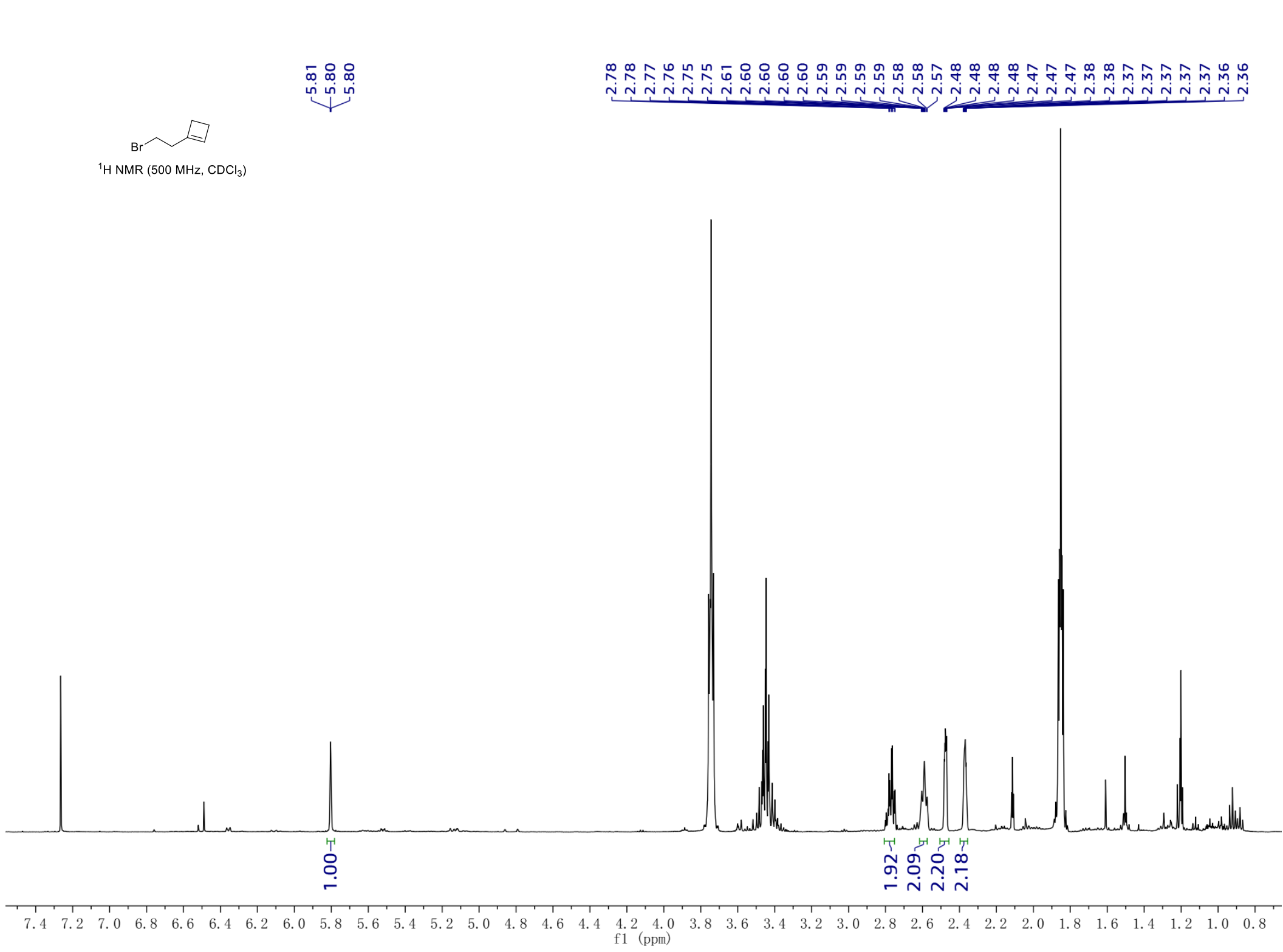

**4,4,5,5-tetramethyl-2-((1S,2S,6S)-2-(2-methylallyl)-1-phenethylbicyclo [4.2.0]octan-2-yl)-1,3,2-dioxaborolane (3.312).** 20.6 mg of of **3.310** was used to produce 14.5 mg of **3.312** in 77.3% isolated yield. FCC condition: 98:2 volume ratio of hexane:ethyl acetate. Rf: 0.6 with 90:10 volume ratio of hexane:ethyl acetate. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 4H), 7.21 – 7.17 (m, 1H), 4.74 (q, *J* = 1.5 Hz, 2H), 2.94 (td, *J* = 13.0, 4.9 Hz, 1H), 2.70 (td, *J* = 12.9, 4.5 Hz, 1H), 2.47 – 2.37 (m, 2H), 2.22 – 2.16 (m, 1H), 2.13 – 1.80 (m, 8H), 1.70 (s, 3H), 1.46 – 1.39 (m, 3H), 1.23 (d, *J* = 6.3 Hz, 12H). $^{13}$C NMR (500 MHz, $CDCl_3$) δ 145.7, 144.2, 128.4, 128.4, 128.3, 125.4, 112.9, 83.1, 43.4, 39.8, 39.6, 36.2, 32.2, 29.7, 28.7, 25.6, 25.4, 25.1, 25.0, 24.3, 23.8, 16.4. $^{11}$B NMR (500 MHz,

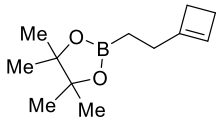
$CDCl_3$) δ 33.6 ppm. IR (neat): $\nu_{max}$ 2925.41(w), 2855.83 (s), 1456.03 (s), 1377.66 (s), 1143.72 (s), 885.58 (s) $cm^{-1}$. HRMS (DART) for $C_{26}H_{40}BO_2$ $[M+H]^+$: Calc'd: 395.31159, found: 395.31277.

### 3.4.5 NMR Spectra

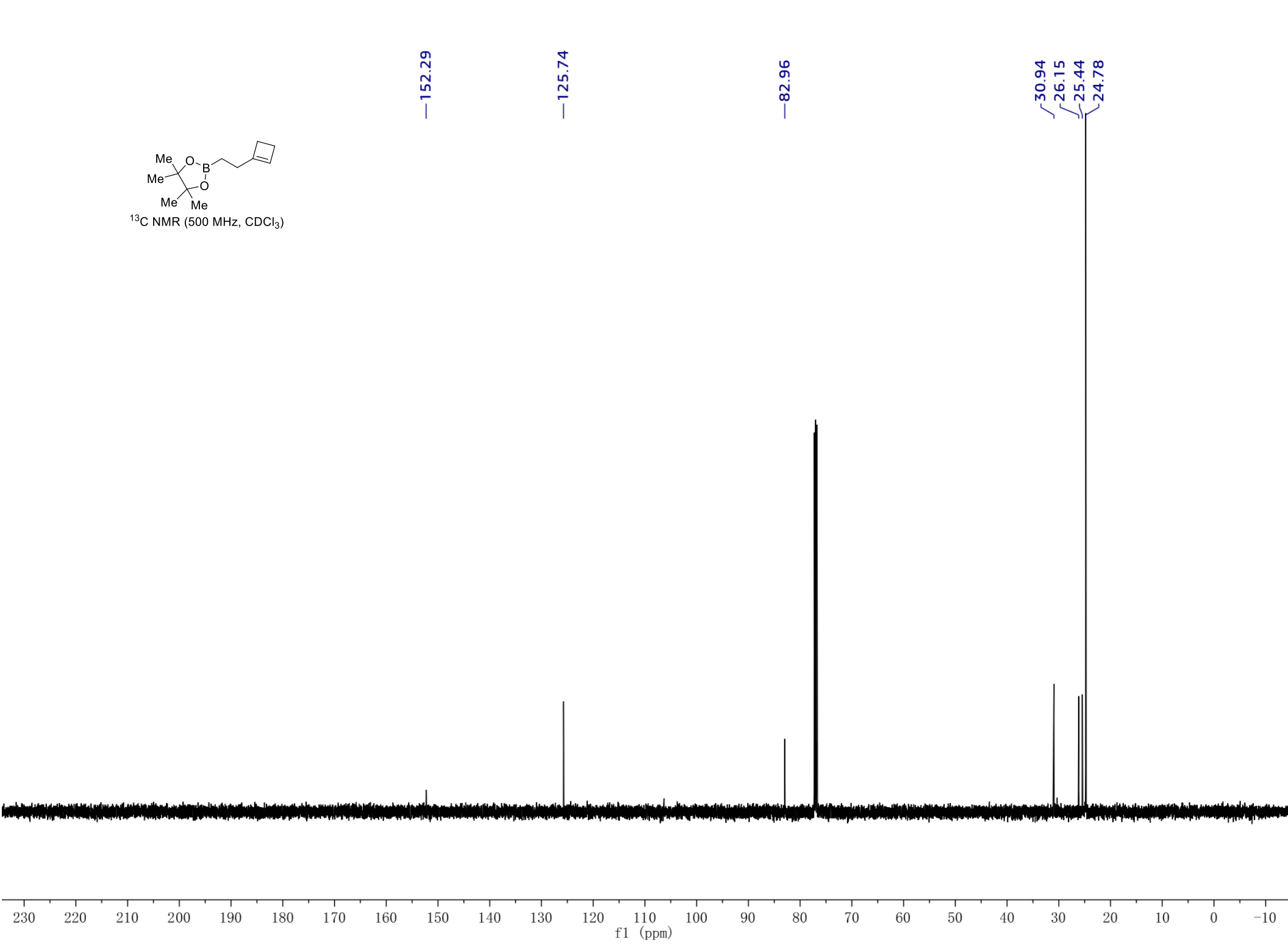


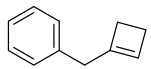
$^1$H NMR (500 MHz, $CDCl_3$)


Br
$^1$H NMR (500 MHz, $CDCl_3$)
5.81
5.80
5.80
2.78
2.78
2.77
2.76
2.75
2.75
2.61
2.60
2.60
2.60
2.60
2.59
2.59
2.59
2.59
2.58
2.58
2.57
2.48
2.48
2.48
2.48
2.47
2.47
2.47
2.38
2.38
2.37
2.37
2.37
2.37
2.37
2.36
2.36
1.00
1.92
2.09
2.20
2.18
7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f1 (ppm)

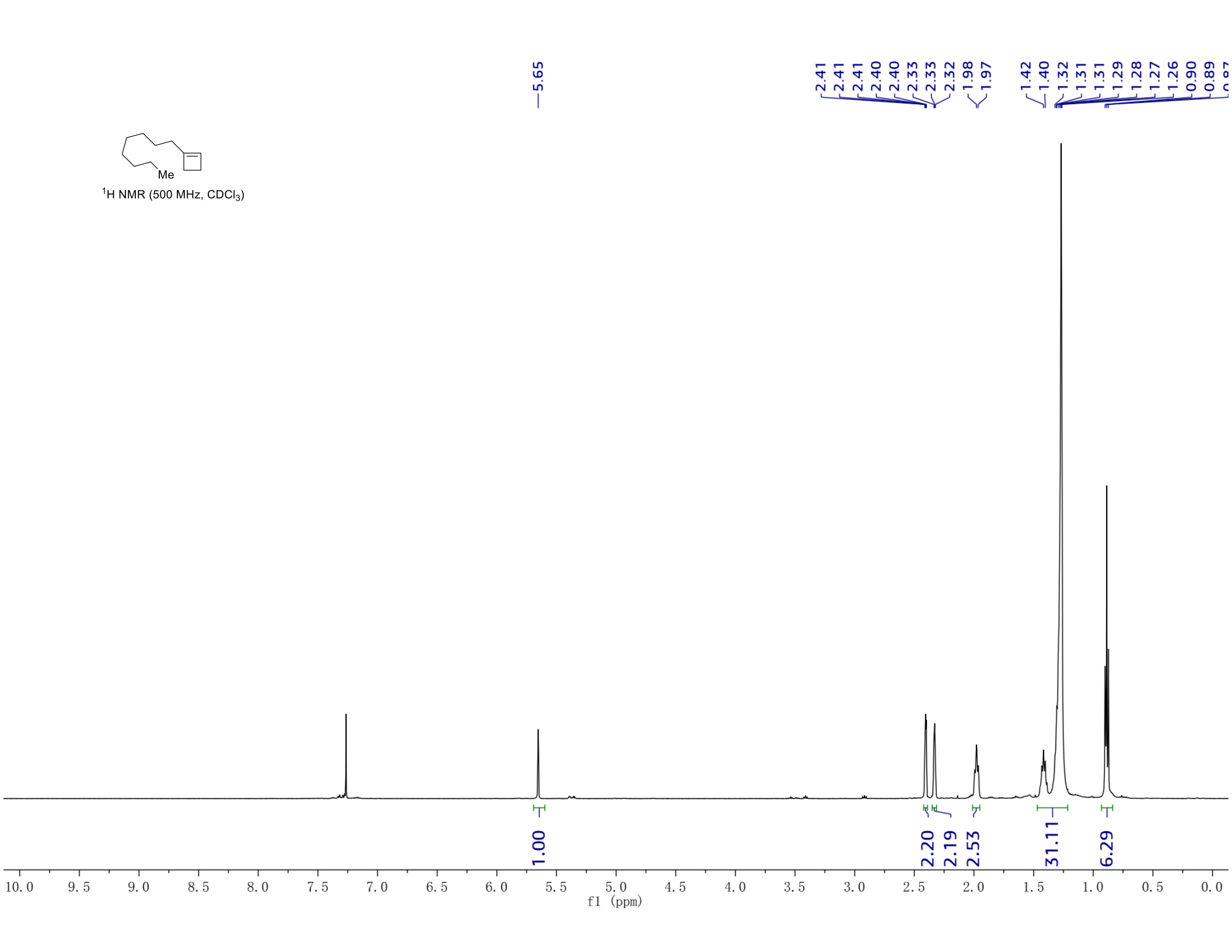


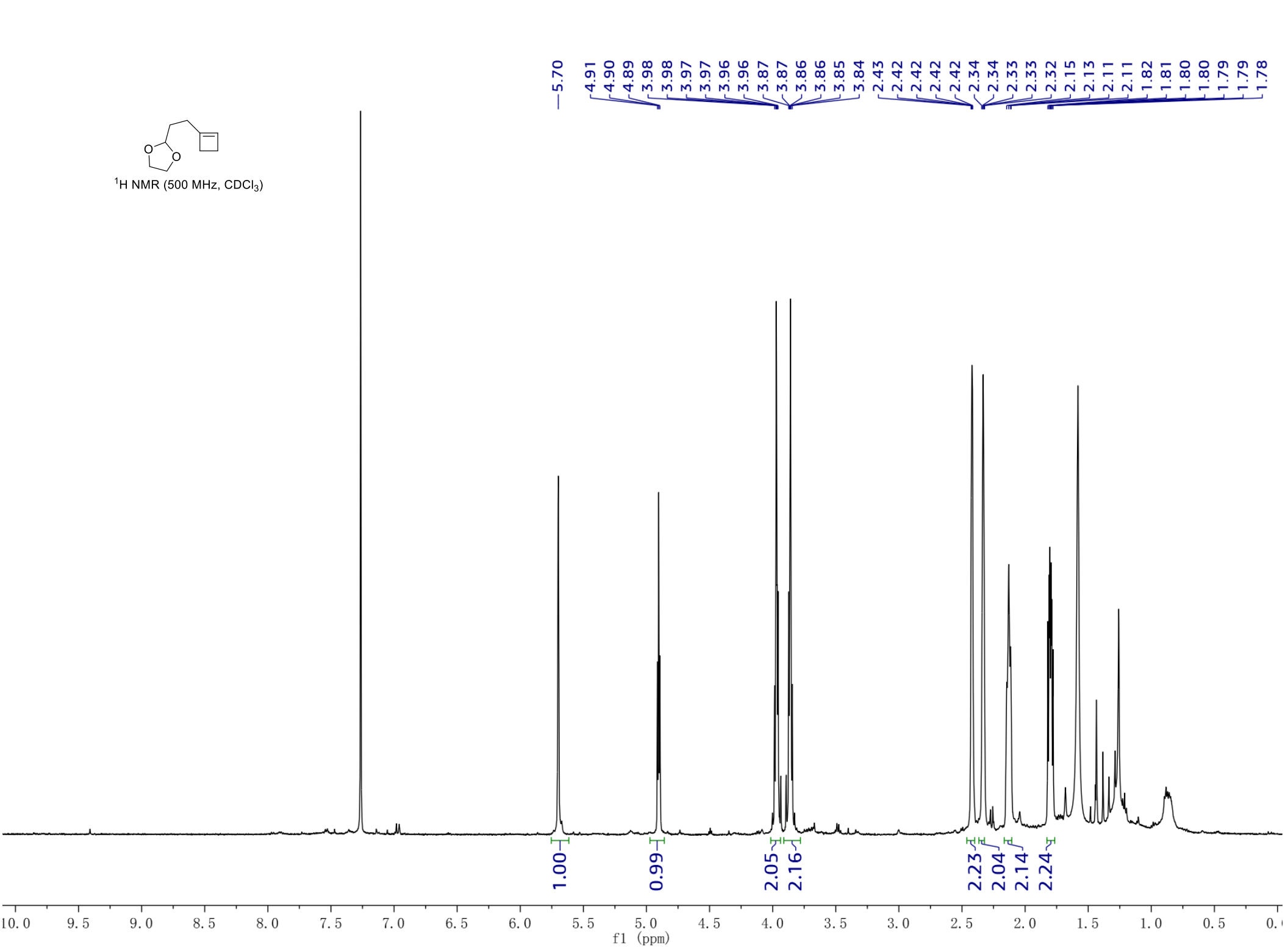

$^1$H NMR (500 MHz, $CDCl_3$)

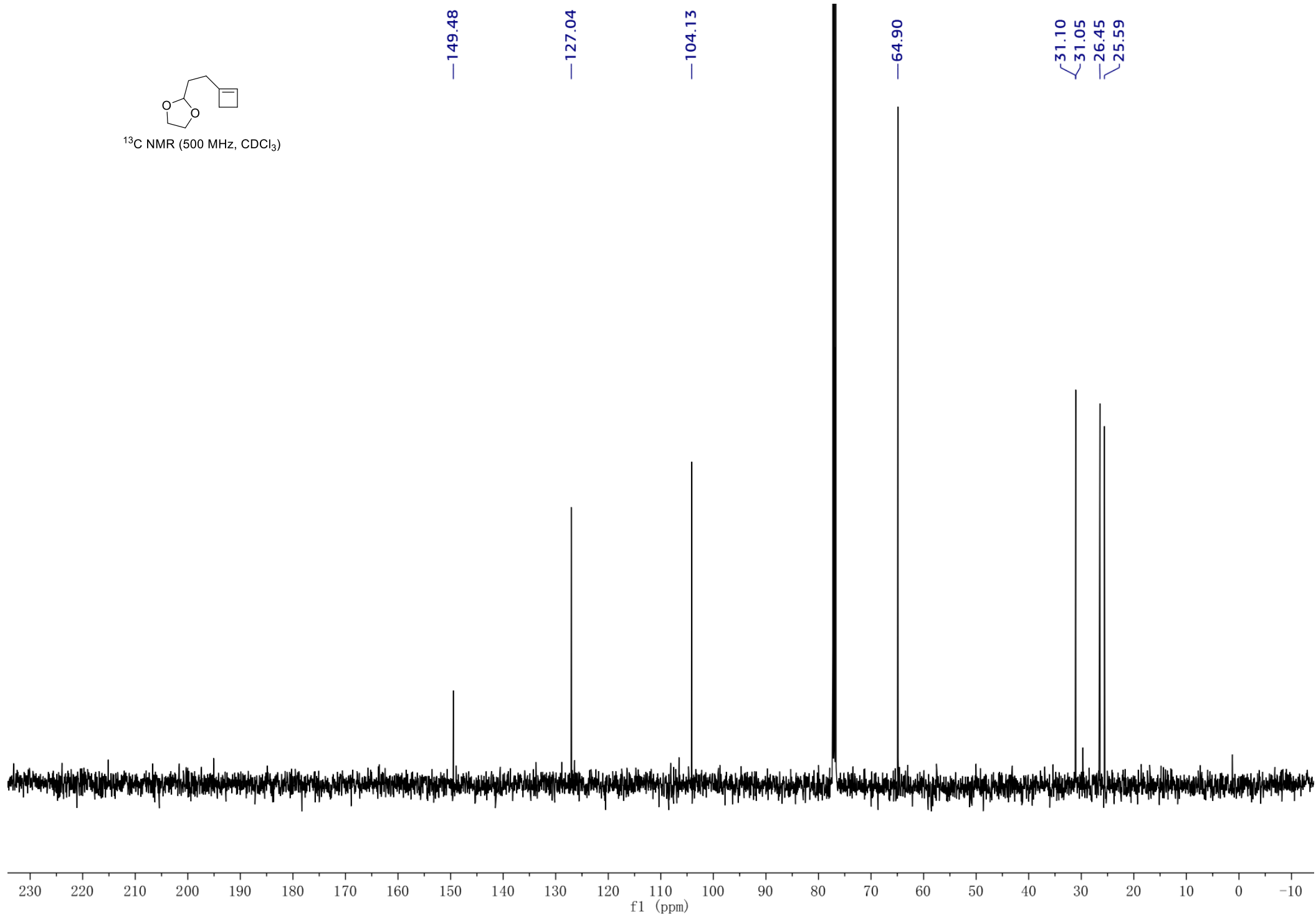

152.29
125.74
82.96
30.94
26.15
25.44
24.78
Me
O
B
Me
O
Me
Me
13C NMR (500 MHz, CDCl3)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

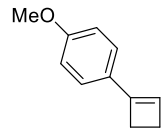


$^1$H NMR (500 MHz, $CDCl_3$)

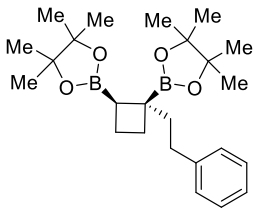

Me
$^1$H NMR (500 MHz, $CDCl_3$)
5.65
2.41
2.41
2.41
2.40
2.40
2.33
2.33
2.32
1.98
1.97
1.42
1.40
1.32
1.31
1.31
1.29
1.28
1.27
1.26
0.90
0.89
1.00
2.20
2.19
2.53
31.11
6.29
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


5.70
4.91
4.90
4.89
3.98
3.98
3.97
3.97
3.96
3.96
3.87
3.87
3.86
3.86
3.85
3.84
2.43
2.42
2.42
2.42
2.42
2.34
2.34
2.33
2.33
2.32
2.15
2.13
2.11
2.11
1.82
1.81
1.80
1.80
1.79
1.79
1.78
O
O
1H NMR (500 MHz, CDCl3)
1.00
0.99
2.05
2.16
2.23
2.04
2.14
2.24
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

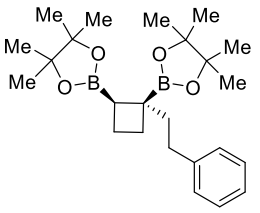

149.48
127.04
104.13
64.90
31.10
31.05
26.45
25.59
O
O
$^{13}$C NMR (500 MHz, $CDCl_3$)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)



$^1$H NMR (500 MHz, $CDCl_3$)

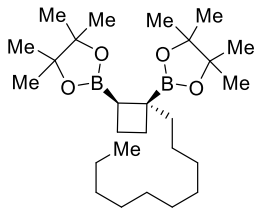



$^{13}C$ NMR (500 MHz, $CDCl_3$)

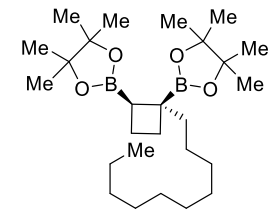
143.84
128.40
128.37
128.12
125.29
83.06
82.81
44.16
32.95
31.94
24.96
24.92
24.87
24.76
20.09

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)




$^{1}$H NMR (500 MHz, $CDCl_3$)

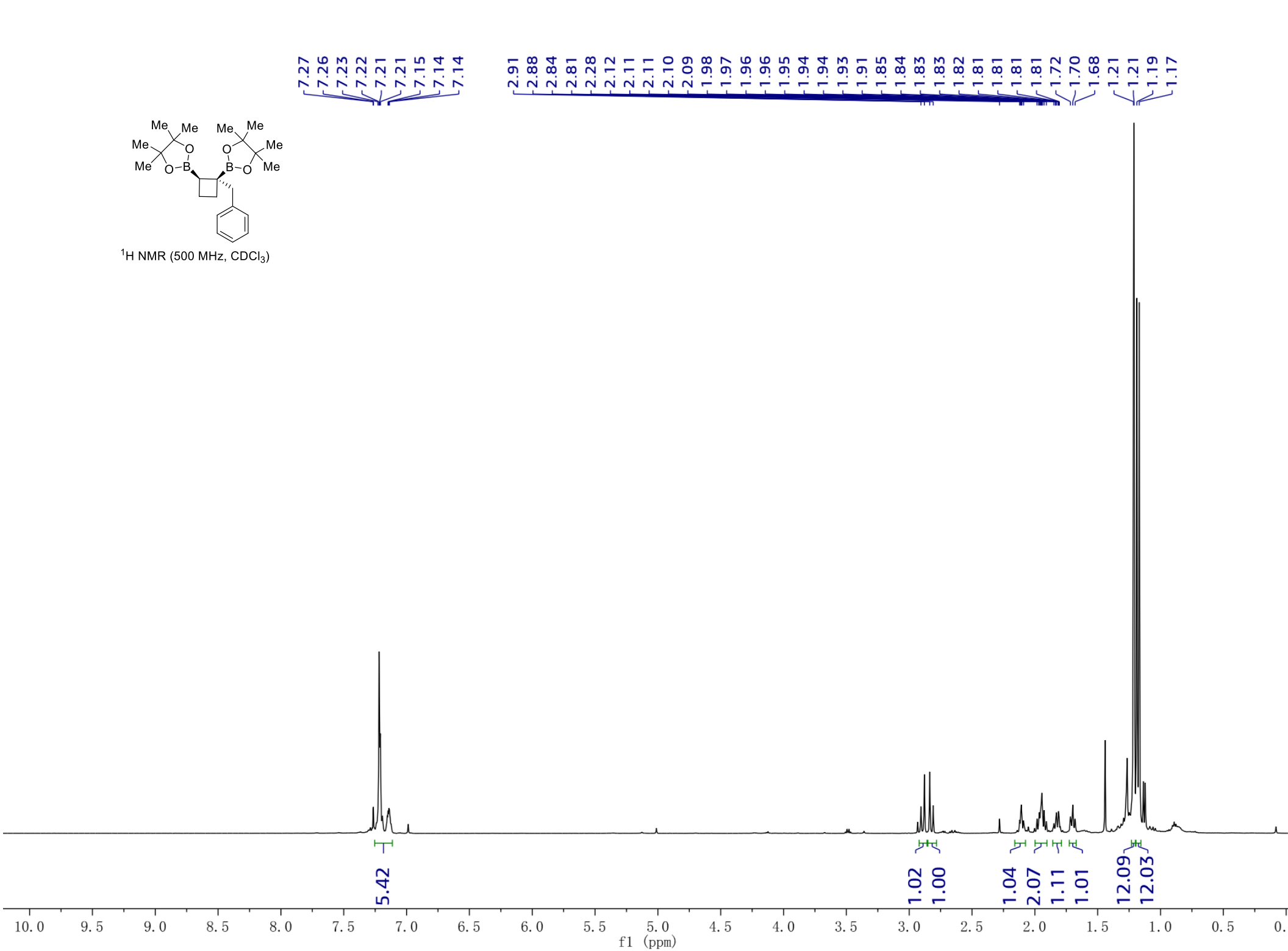


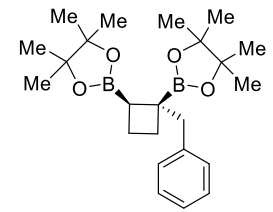

$^{13}C$ NMR (500 MHz, $CDCl_3$)

82.90
82.67
42.00
31.99
31.92
30.28
29.66
29.65
29.61
29.38
26.30
25.05
24.85
24.73
22.68
20.15
14.10

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)


7.27
7.26
7.23
7.22
7.21
7.21
7.15
7.14
7.14
2.91
2.88
2.84
2.81
2.28
2.12
2.11
2.11
2.10
2.09
1.98
1.97
1.96
1.96
1.95
1.94
1.94
1.93
1.91
1.85
1.84
1.83
1.83
1.82
1.81
1.81
1.81
1.81
1.72
1.70
1.68
1.21
1.21
1.19
1.17
Me
Me
Me
Me
O
O
B
B
O
O
Me
Me
Me
Me
1H NMR (500 MHz, CDCl3)
5.42
1.02
1.00
1.04
2.07
1.11
1.01
12.09
12.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

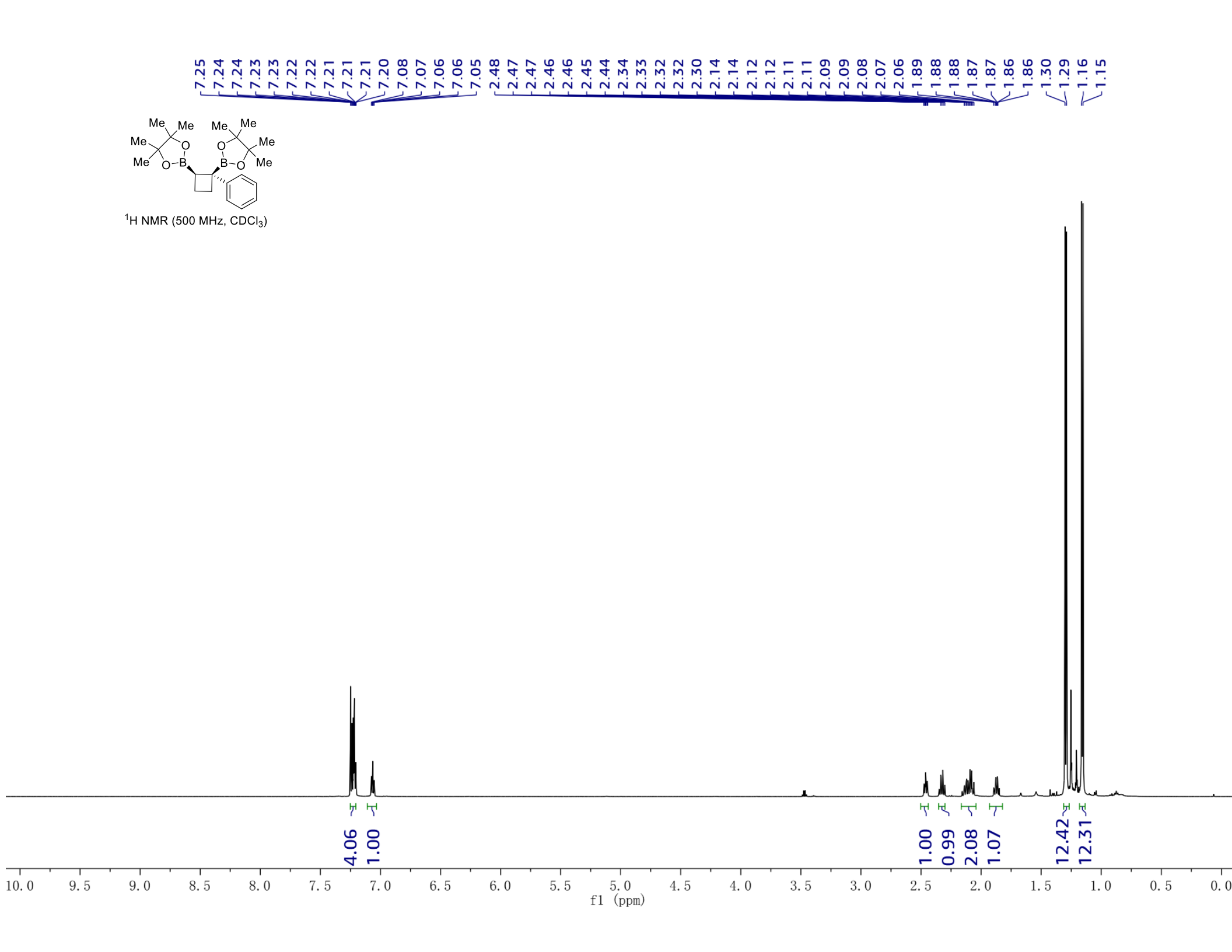


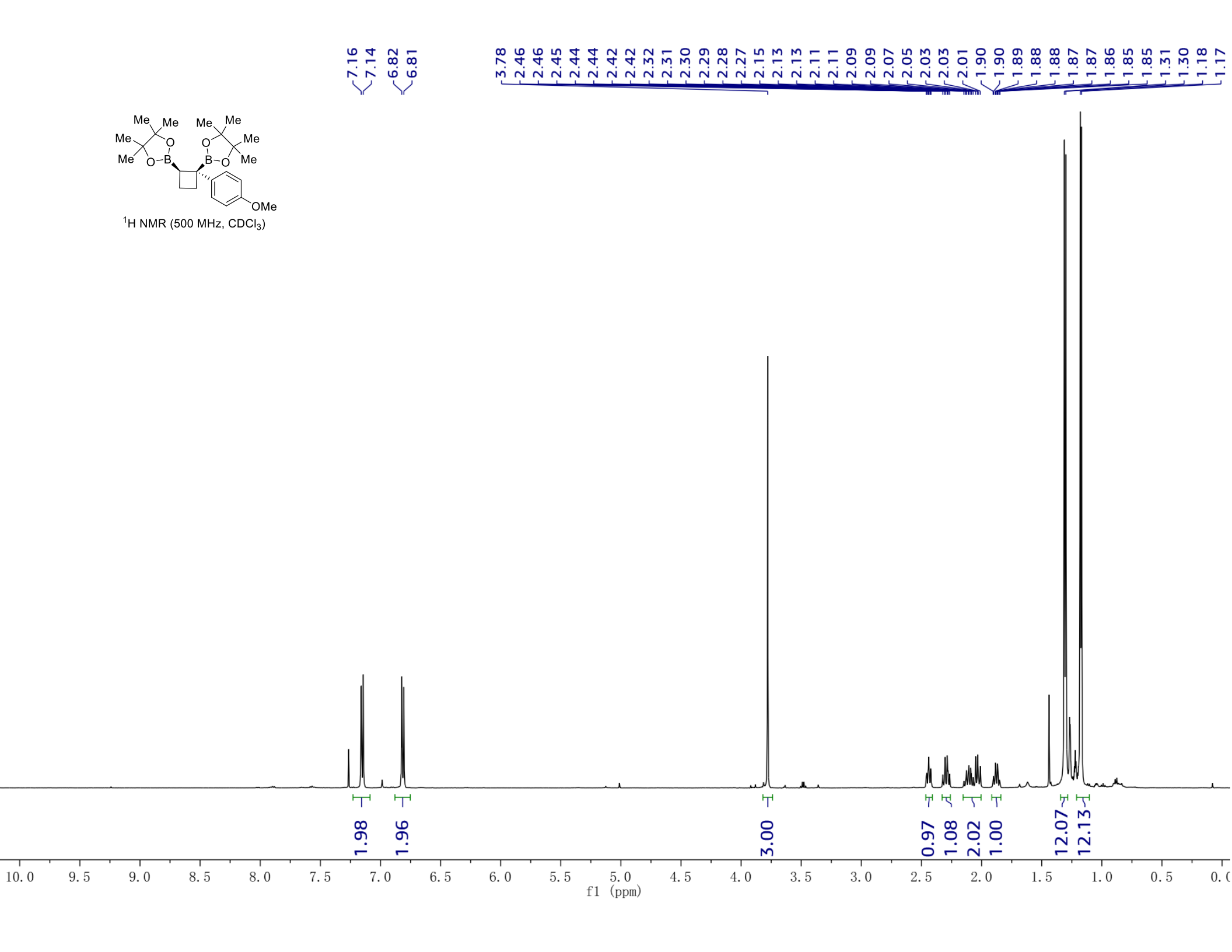

$^{13}C$ NMR (500 MHz, $CDCl_3$)

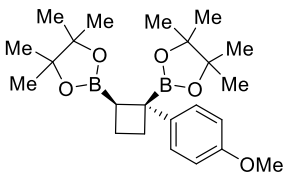
140.63
129.84
127.59
125.44
83.11
82.70
45.73
31.71
30.32
29.69
25.00
24.84
24.77
24.70
24.66
24.61
20.37

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

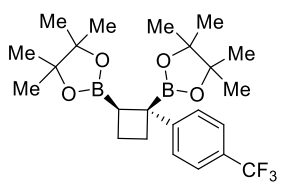
f1 (ppm)


7.25 7.24 7.24 7.23 7.23 7.22 7.22 7.21 7.21 7.21 7.20 7.08 7.07 7.06 7.06 7.05
2.48 2.47 2.47 2.46 2.46 2.45 2.44 2.34 2.33 2.32 2.32 2.30 2.14 2.14 2.12 2.12 2.11 2.11 2.09 2.09 2.08 2.07 2.06 1.89 1.88 1.88 1.87 1.87 1.86 1.86 1.30 1.29 1.16 1.15
Me Me Me Me Me Me O O O O B B
Me Me Me Me
1H NMR (500 MHz, CDCl3)
4.06 1.00 1.00 0.99 2.08 1.07 12.42 12.31
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


7.16
7.14
6.82
6.81
3.78
2.46
2.46
2.45
2.44
2.44
2.42
2.42
2.32
2.31
2.30
2.29
2.28
2.27
2.15
2.13
2.13
2.11
2.11
2.09
2.09
2.07
2.05
2.03
2.03
2.01
1.90
1.90
1.89
1.88
1.88
1.87
1.87
1.86
1.85
1.85
1.31
1.30
1.18
1.17
Me
Me
Me
O
O
Me
Me
O
B
B
O
Me
OMe
1H NMR (500 MHz, CDCl3)
1.98
1.96
3.00
0.97
1.08
2.02
1.00
12.07
12.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)




$^{13}$C NMR (500 MHz, $CDCl_3$)




$^1$H NMR (500 MHz, $CDCl_3$)

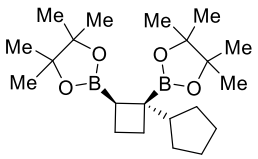
7.51 7.49 7.33 7.32

2.50 2.50 2.49 2.48 2.48 2.47 2.46 2.40 2.39 2.38 2.37 2.37 2.35 2.35 2.33 2.31 2.28 2.24 2.23 2.23 2.22 2.21 2.21 2.20 2.19 2.18 2.17 2.16 2.09 2.08 2.07 2.05 1.92 1.92 1.91 1.90 1.90 1.88 1.88 1.87 1.32 1.30 1.19 1.18

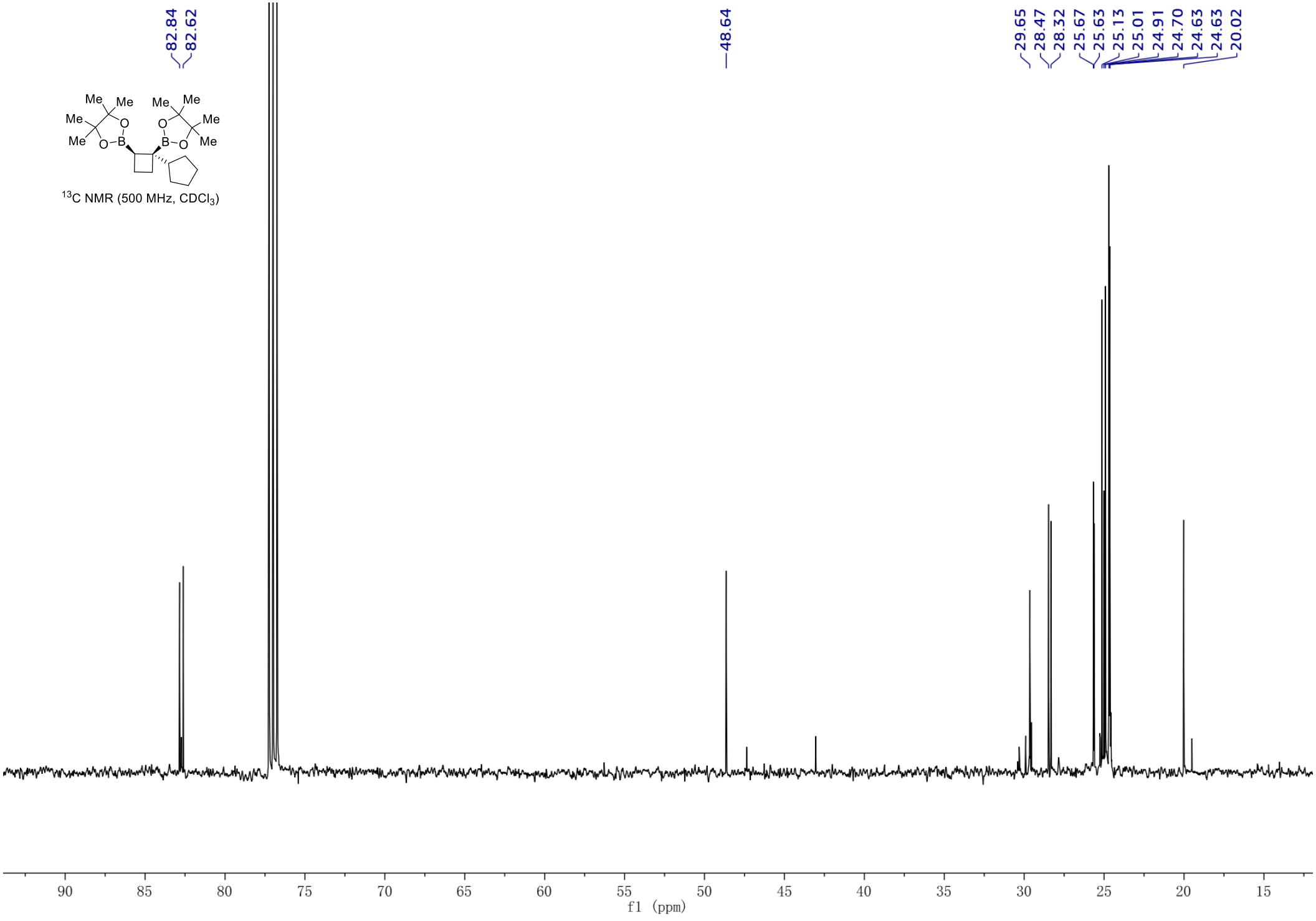
2.00 2.07 0.94 2.00 1.04 1.05 11.54 12.37

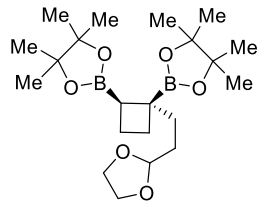
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0

f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)


82.84
82.62
48.64
29.65
28.47
28.32
25.67
25.63
25.13
25.01
24.91
24.70
24.63
24.63
20.02
Me
Me
Me
Me
O
O
B
Me
Me
Me
Me
O
O
B
Me
$^{13}$C NMR (500 MHz, $CDCl_3$)
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
f1 (ppm)



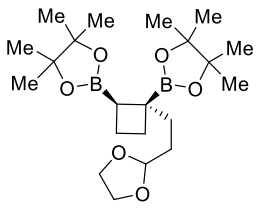
$^1$H NMR (500 MHz, $CDCl_3$)

4.84 4.83 4.82 3.97 3.96 3.96 3.95 3.95 3.94 3.84 3.84 3.83 3.83 3.83 2.04 2.04 2.02 2.02 2.00 1.98 1.96 1.96 1.91 1.90 1.89 1.89 1.89 1.77 1.75 1.74 1.70 1.69 1.68 1.68 1.67 1.67 1.60 1.59 1.58 1.58 1.58 1.57 1.56 1.54 1.52 1.25 1.24 1.23 1.22

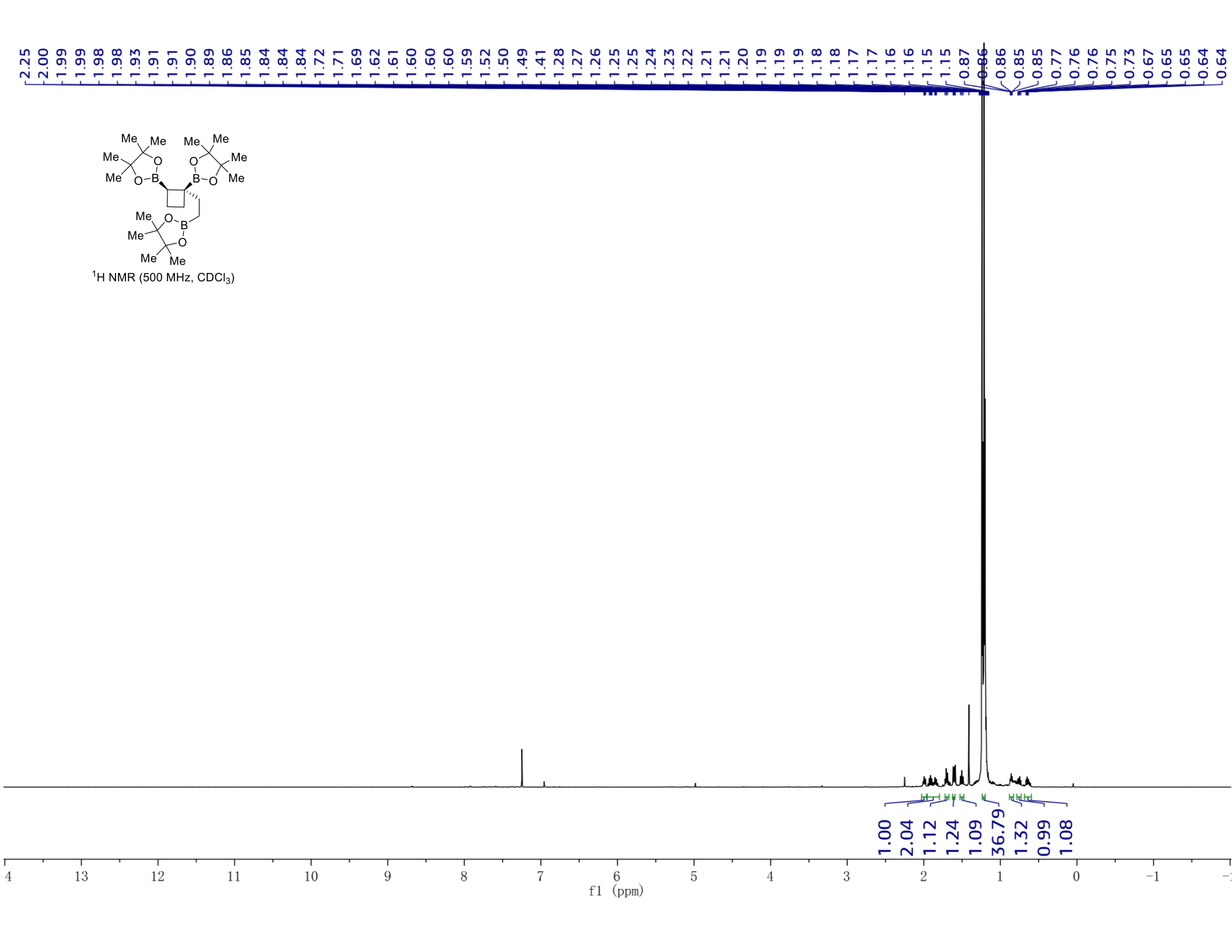
1.00 2.08 2.14 3.22 3.13 2.15 12.37 12.25

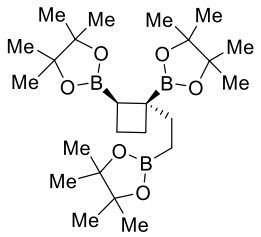
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

f1 (ppm)




$^{13}C$ NMR (500 MHz, $CDCl_3$)


2.25 2.00 1.99 1.99 1.98 1.98 1.93 1.91 1.91 1.90 1.89 1.86 1.85 1.84 1.84 1.84 1.72 1.71 1.69 1.62 1.61 1.60 1.60 1.60 1.59 1.52 1.50 1.49 1.41 1.28 1.27 1.26 1.25 1.25 1.24 1.23 1.22 1.21 1.21 1.20 1.19 1.19 1.19 1.18 1.18 1.17 1.17 1.16 1.16 1.15 1.15 0.87 0.86 0.86 0.85 0.85 0.77 0.76 0.76 0.75 0.73 0.67 0.65 0.65 0.64 0.64
Me Me Me Me Me Me O O O O B B Me Me Me Me Me Me O B O B Me
$^1$H NMR (500 MHz, $CDCl_3$)
1.00 2.04 1.12 1.24 1.09 36.79 1.32 0.99 1.08
4 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

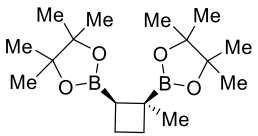



$^{13}$C NMR (500 MHz, $CDCl_3$)

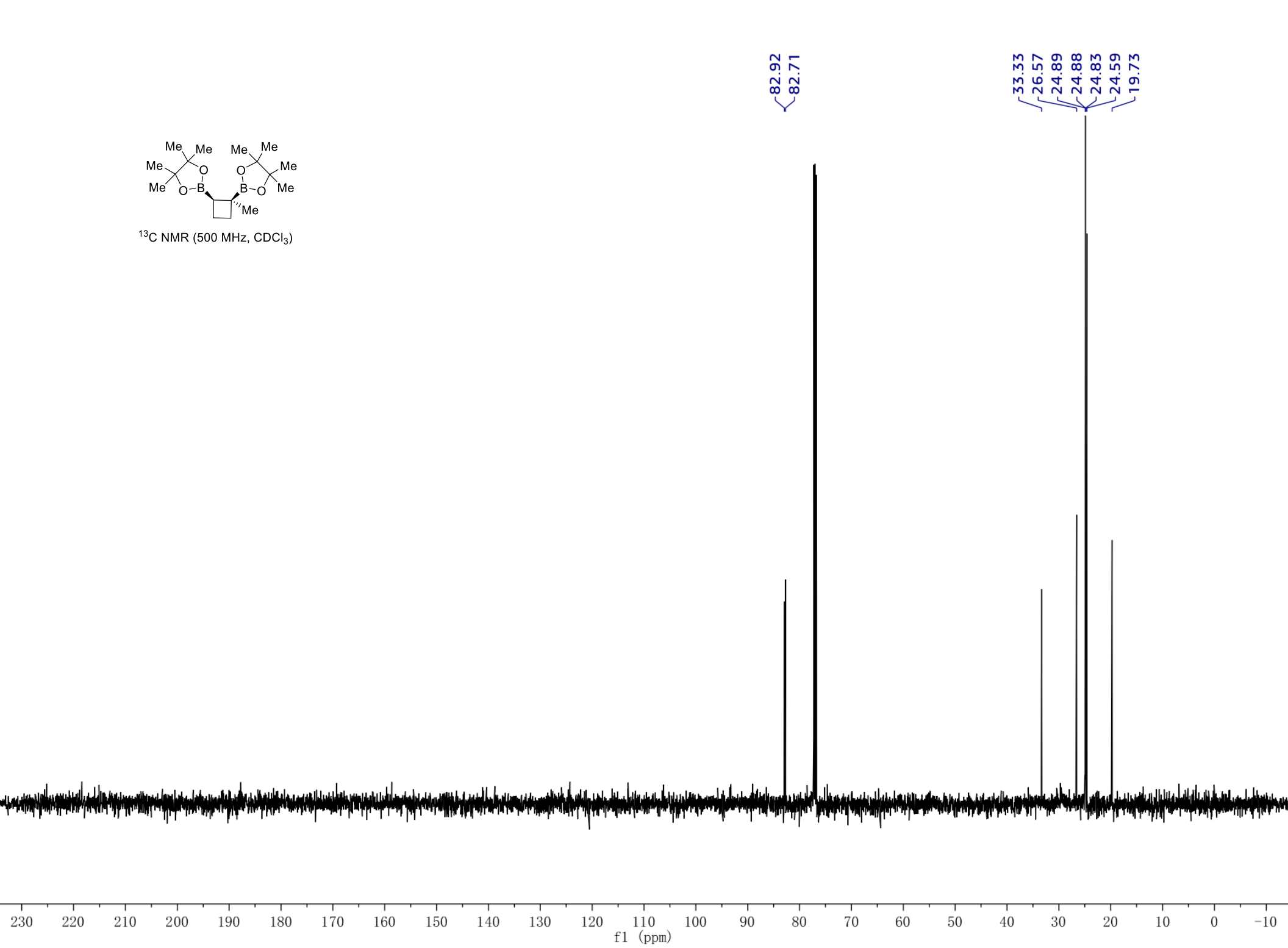
82.86
82.66
35.66
31.33
24.96
24.82
24.79
24.78
19.70

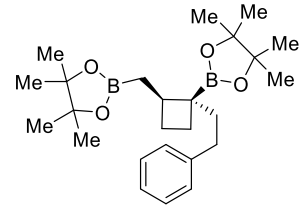
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)

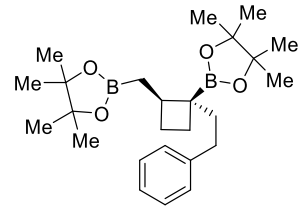



$^1$H NMR (500 MHz, $CDCl_3$)


82.92
82.71
33.33
26.57
24.89
24.88
24.83
24.59
19.73
Me
Me
Me
Me
Me
Me
O
O
B
B
O
O
Me
Me
13C NMR (500 MHz, CDCl3)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)



$^1$H NMR (500 MHz, $CDCl_3$)

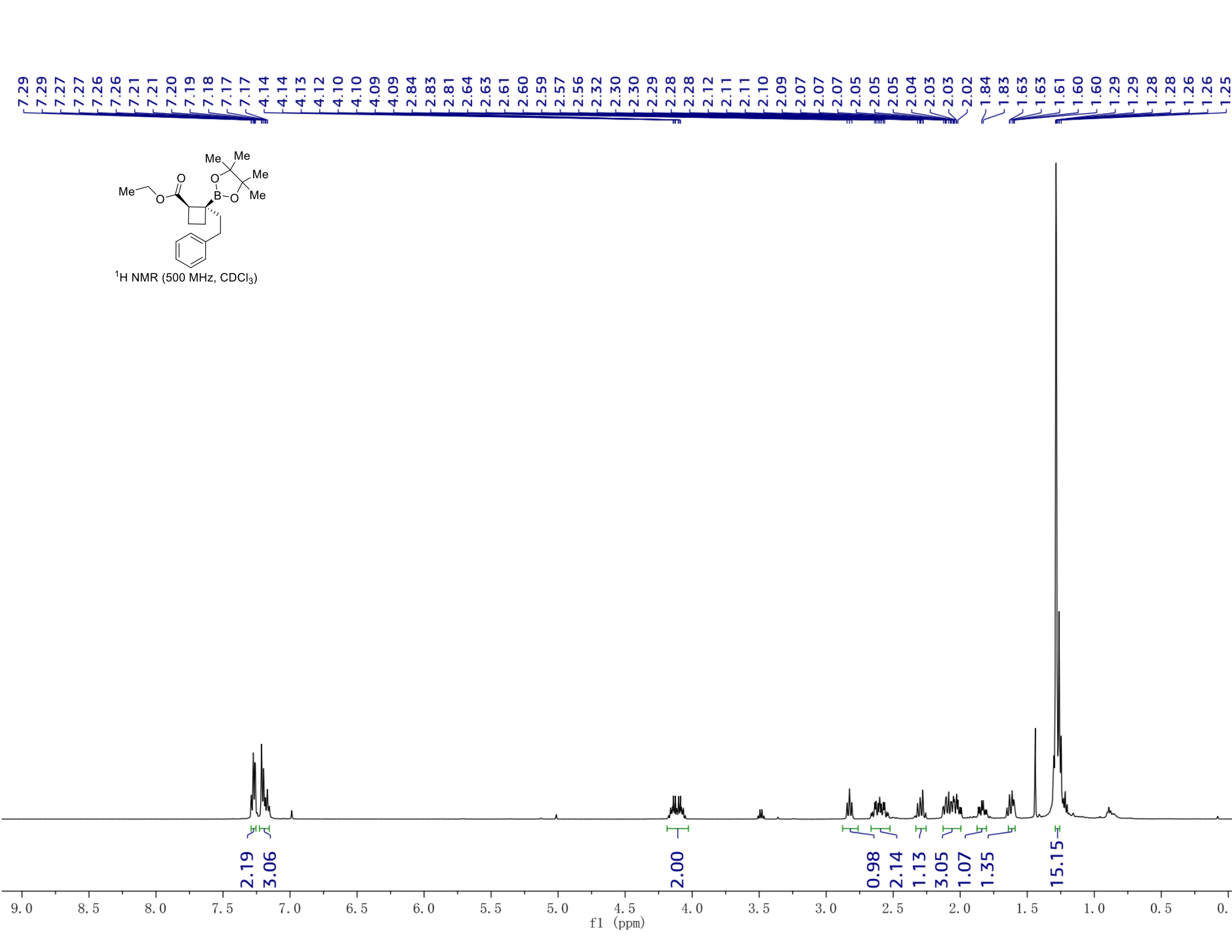


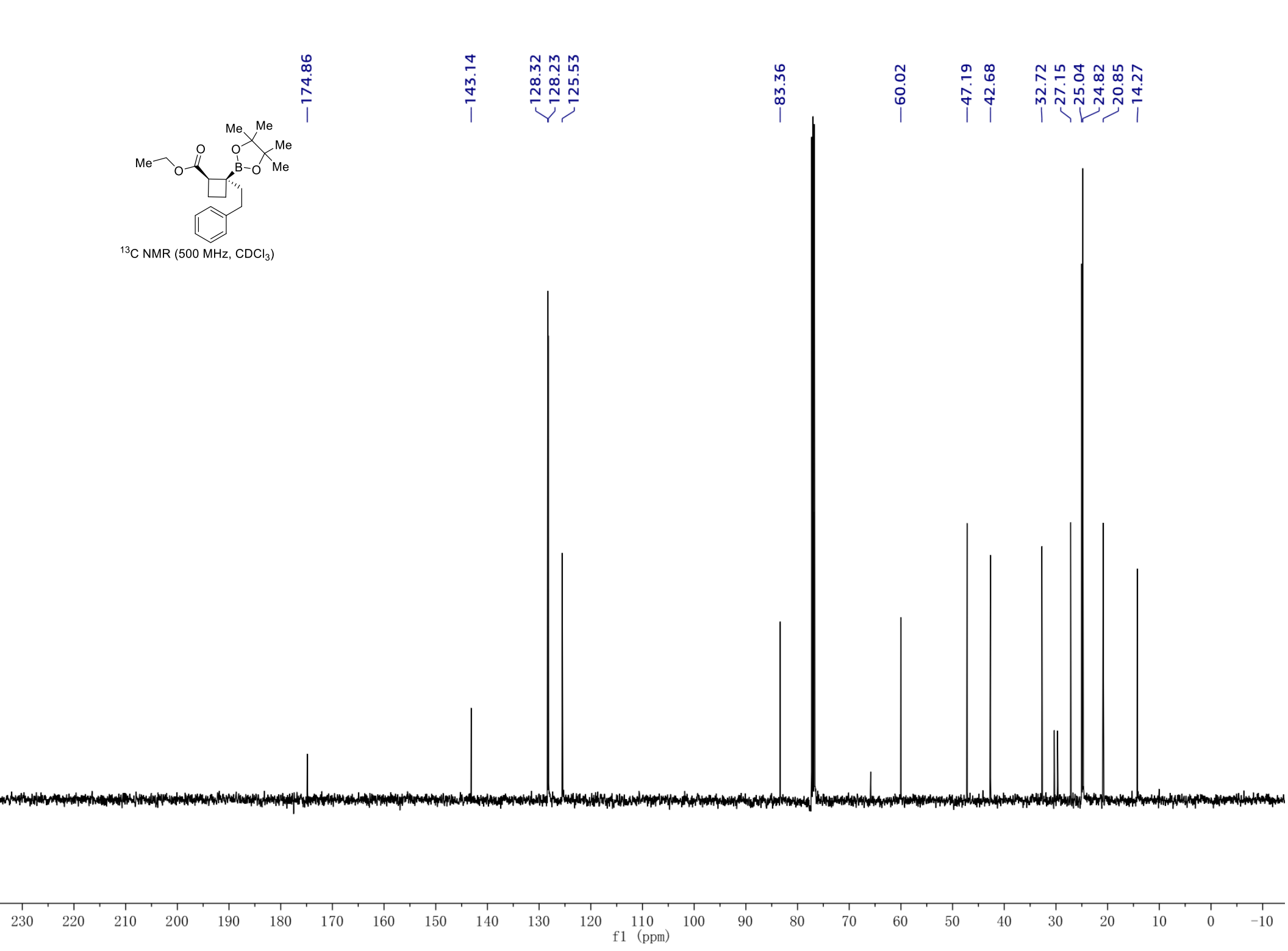

$^{13}C$ NMR (500 MHz, $CDCl_3$)

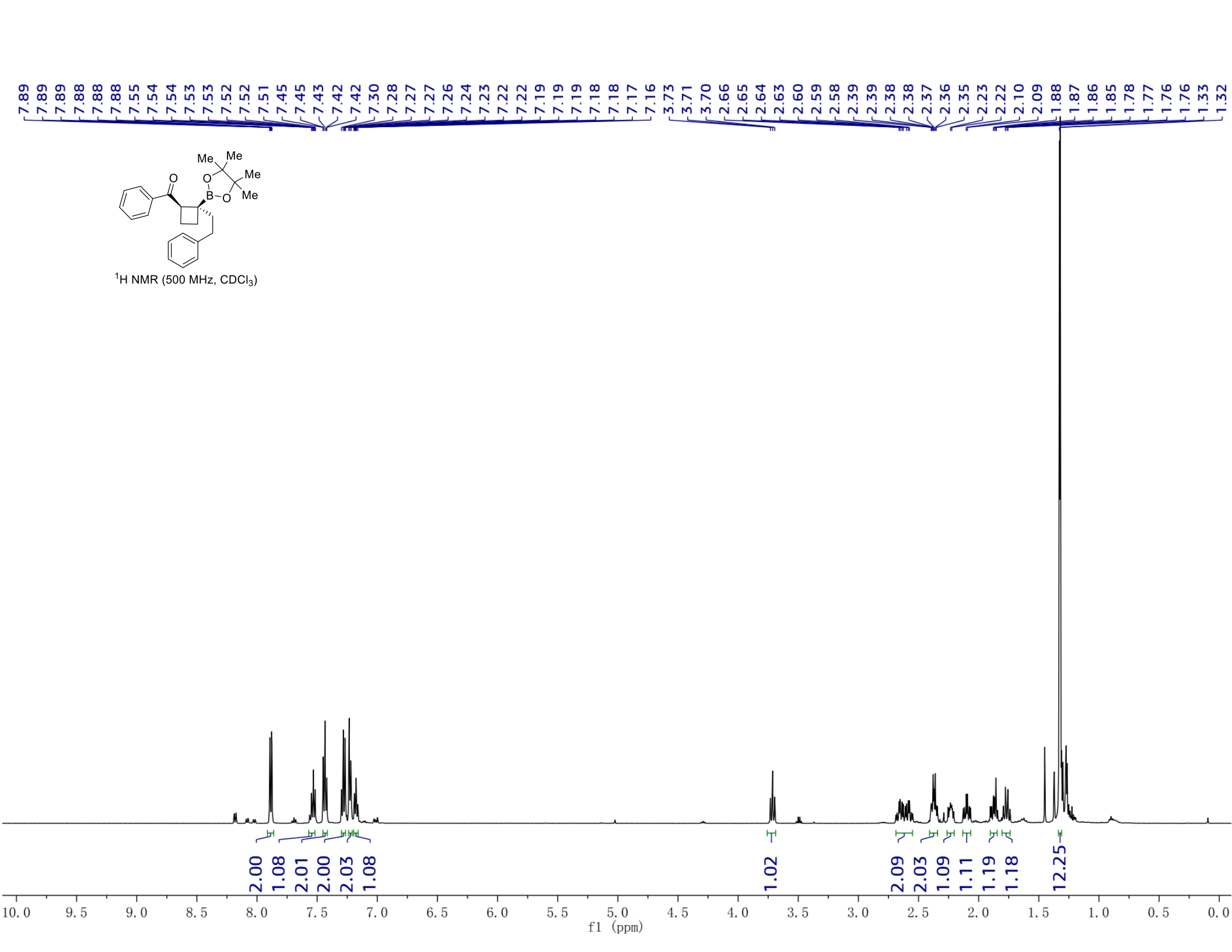
143.68
128.33
128.31
128.17
128.11
125.30
83.05
82.76
65.84
42.63
41.60
33.07
27.14
25.38
24.98
24.97
24.88
24.81
24.80
15.27

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

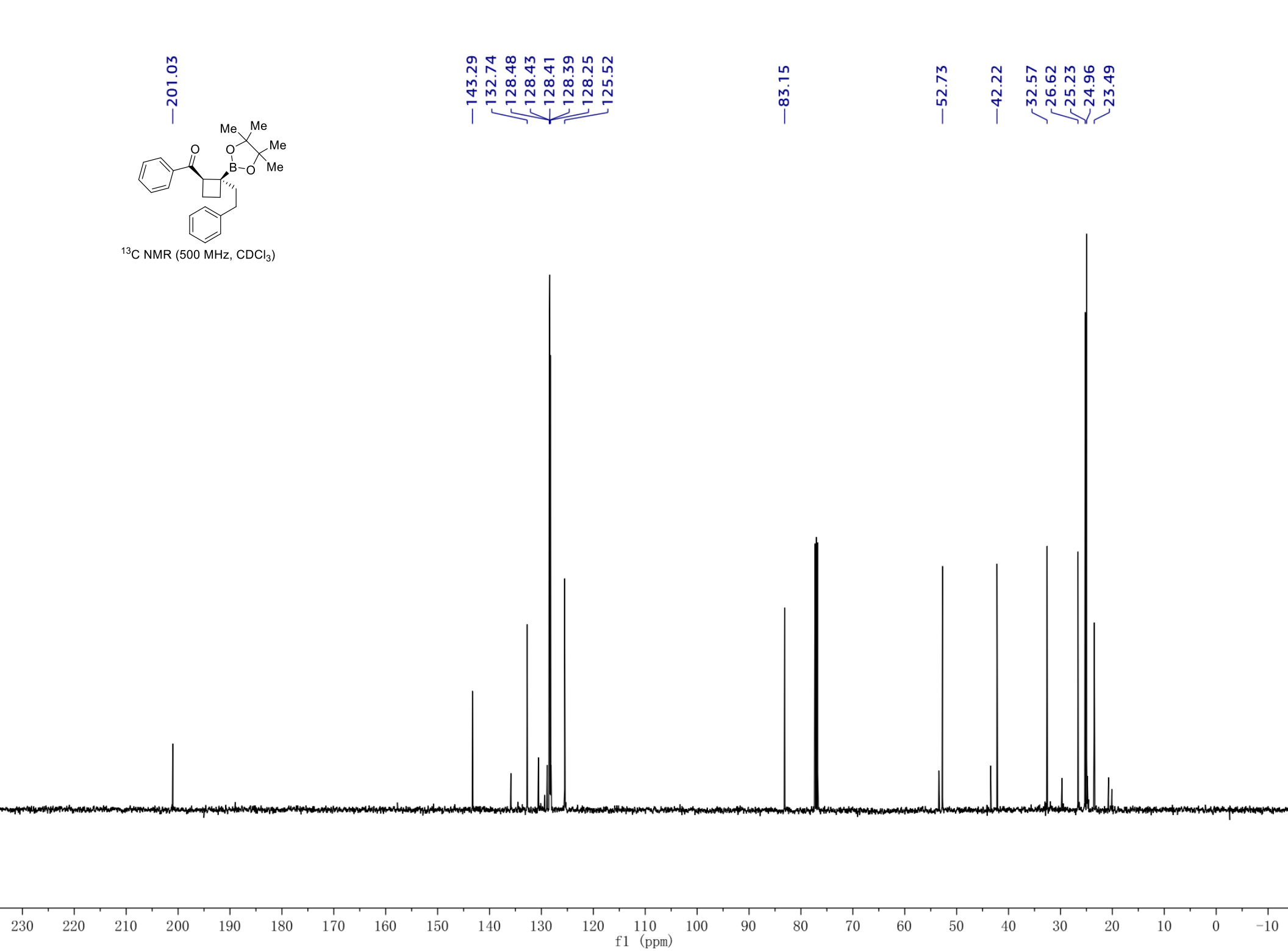
f1 (ppm)

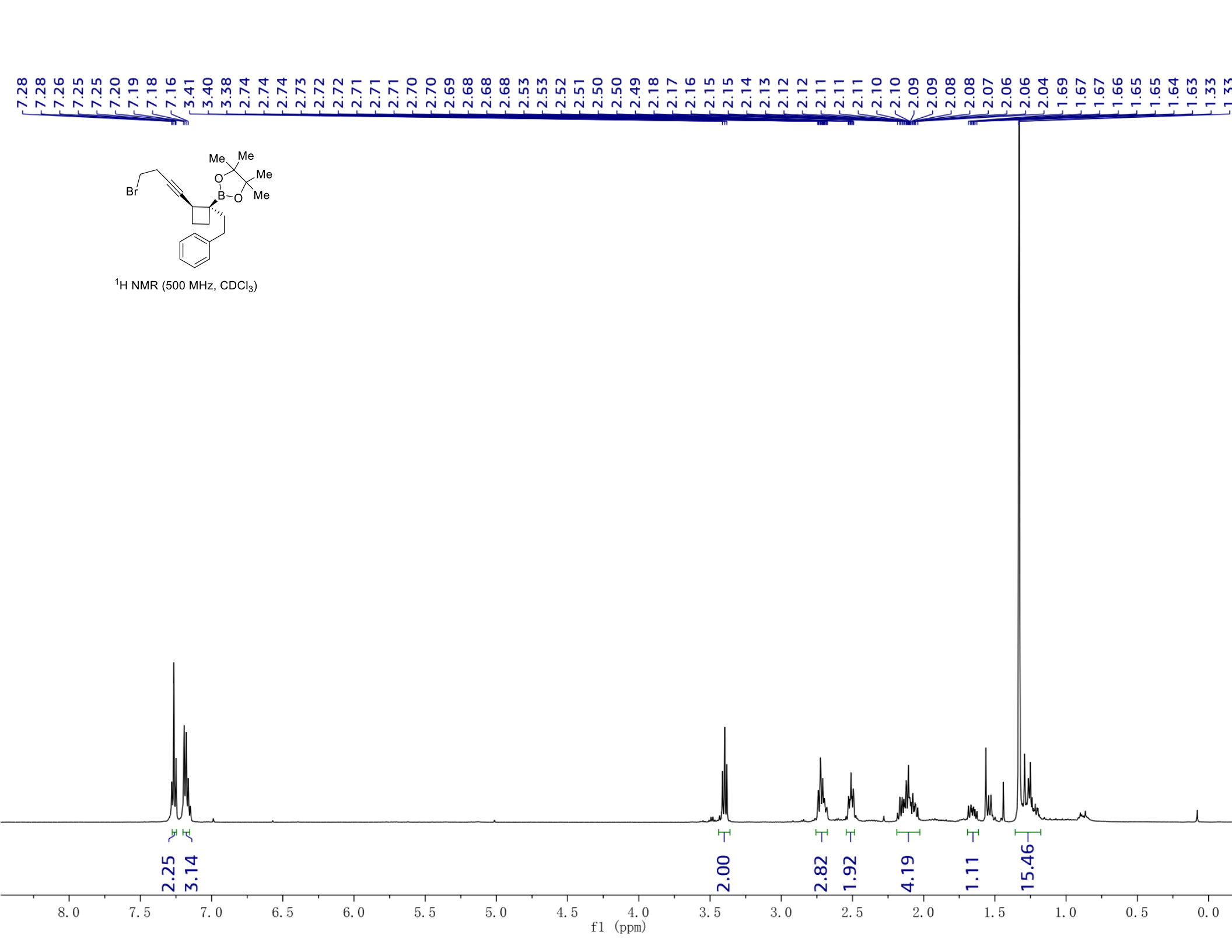

7.29 7.29 7.27 7.27 7.26 7.26 7.21 7.21 7.20 7.19 7.18 7.17 7.17 4.14 4.14 4.13 4.12 4.10 4.10 4.09 4.09 2.84 2.83 2.81 2.64 2.63 2.61 2.60 2.59 2.57 2.56 2.32 2.30 2.30 2.29 2.28 2.28 2.12 2.11 2.11 2.10 2.09 2.07 2.07 2.07 2.05 2.05 2.05 2.04 2.03 2.03 2.02 1.84 1.83 1.63 1.63 1.61 1.60 1.60 1.29 1.29 1.28 1.28 1.26 1.26 1.25
Me
Me
Me
Me
O
O
O
B
O
$^1$H NMR (500 MHz, CDCl$_3$)
2.19
3.06
2.00
0.98
2.14
1.13
3.05
1.07
1.35
15.15
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.
f1 (ppm)

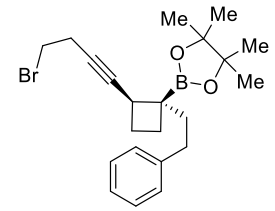

174.86
143.14
128.32
128.23
125.53
83.36
60.02
47.19
42.68
32.72
27.15
25.04
24.82
20.85
14.27
Me
Me
Me
Me
Me
O
O
O
B
O
$^{13}$C NMR (500 MHz, CDCl$_3$)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)


201.03
143.29
132.74
128.48
128.43
128.41
128.39
128.25
125.52
83.15
52.73
42.22
32.57
26.62
25.23
24.96
23.49
Me
Me
Me
Me
O
O
B
O
$^{13}$C NMR (500 MHz, $CDCl_3$)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


Me
Me
Me
O
B
O
Me
Br
$^1$H NMR (500 MHz, CDCl$_3$)
2.25
3.14
2.00
2.82
1.92
4.19
1.11
15.46
f1 (ppm)

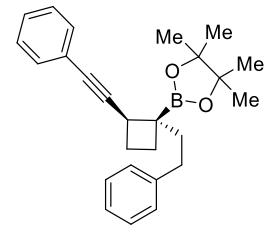



$^{13}C$ NMR (500 MHz, $CDCl_3$)

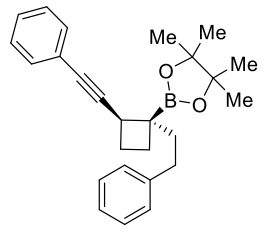
142.94
128.32
128.32
128.22
125.56
85.11
83.41
42.54
33.79
32.79
29.81
27.80
26.02
25.34
24.80
23.71
15.27

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)

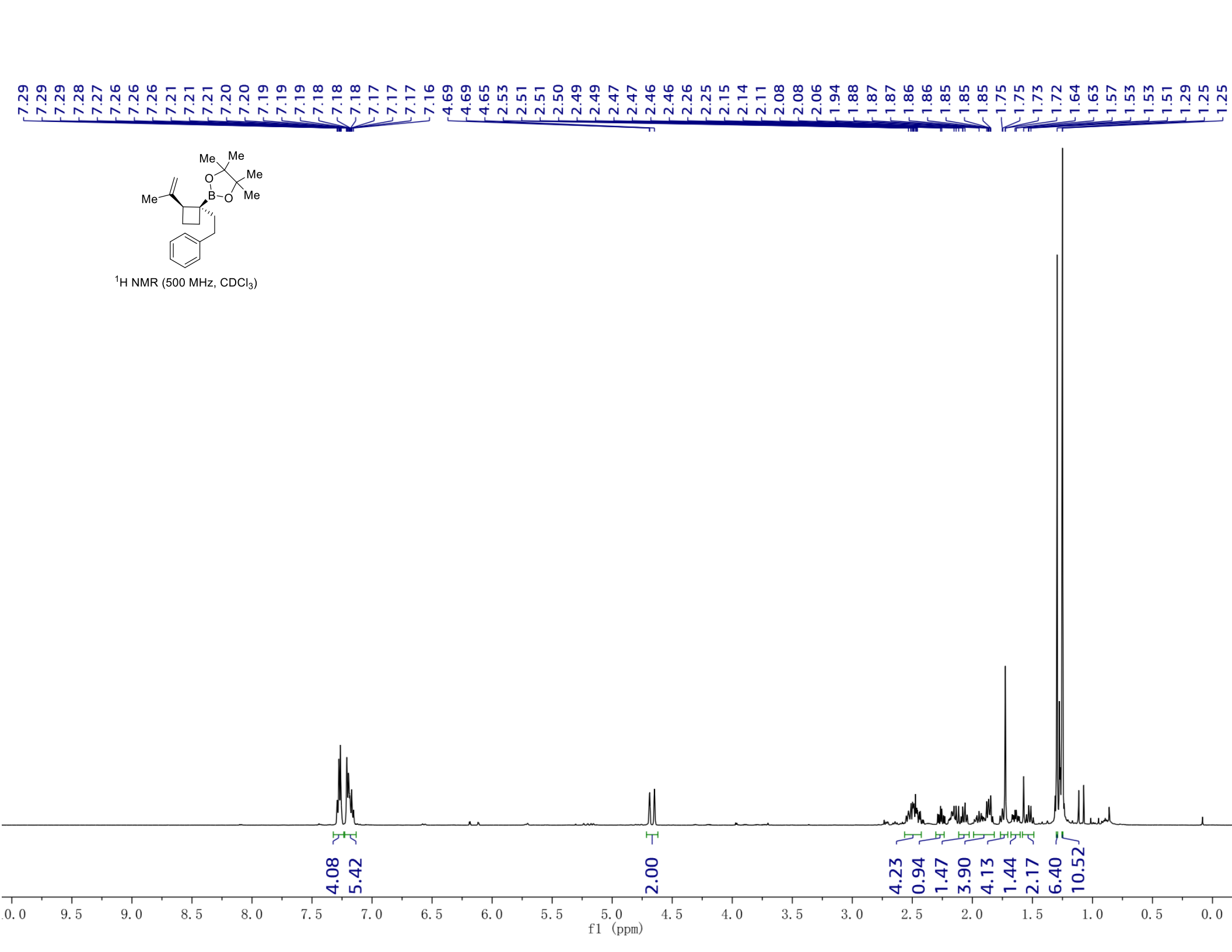


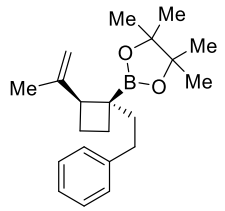

$^{13}C$ NMR (500 MHz, $CDCl_3$)

143.00
131.49
128.37
128.24
128.07
127.34
125.57
92.79
83.47
82.47
53.42
43.44
42.61
34.40
32.83
27.88
26.19
25.43
24.75

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)


7.29 7.29 7.29 7.28 7.27 7.26 7.26 7.26 7.21 7.21 7.21 7.20 7.20 7.19 7.19 7.19 7.18 7.18 7.18 7.17 7.17 7.17 7.16
4.69 4.69 4.65 2.53 2.51 2.51 2.50 2.49 2.49 2.47 2.47 2.46 2.46 2.26 2.25 2.15 2.14 2.11 2.08 2.08 2.06 1.94 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.85 1.75 1.75 1.73 1.72 1.64 1.63 1.57 1.53 1.53 1.51 1.29 1.25 1.25
Me
Me
O
Me
B
O
Me
Me
1H NMR (500 MHz, CDCl3)
4.08
5.42
2.00
4.23
0.94
1.47
3.90
4.13
1.44
2.17
6.40
10.52
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

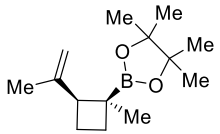



$^{13}C$ NMR (500 MHz, $CDCl_3$)

147.85
145.36
143.34
143.27
128.55
128.37
128.34
128.22
128.21
128.20
125.50
125.48
108.28
83.19
52.06
44.02
42.03
33.28
33.20
30.20
26.44
25.40
24.90
24.87
24.75
24.62
22.31
21.45
18.23

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)



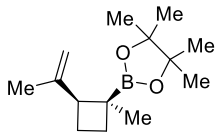

$^1$H NMR (500 MHz, $CDCl_3$)

4.67 4.67 4.66 4.66 4.66 4.62 2.45 2.43 2.13 2.13 2.11 2.11 2.10 2.09 2.09 2.01 1.99 1.97 1.86 1.85 1.84 1.84 1.83 1.83 1.82 1.82 1.70 1.67 1.48 1.48 1.46 1.44 1.44 1.42 1.42 1.21 1.21

0.96 0.91 0.92 1.00 1.00 1.09 3.05 1.62 12.50

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

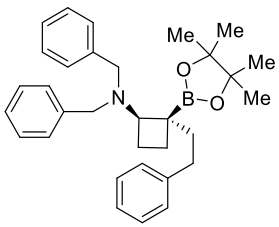



$^{13}C$ NMR (500 MHz, $CDCl_3$)

148.02
109.91
107.86
82.93
53.07
28.62
26.29
25.00
24.91
24.65
21.79
21.42

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)



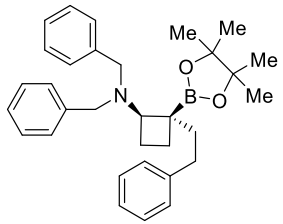

$^1$H NMR (500 MHz, $CDCl_3$)

7.37 7.36 7.35 7.34 7.32 7.29 7.29 7.27 7.27 7.27 7.26 7.25 7.24 7.24 7.23 7.23 7.19 7.18 7.18 7.17 7.17 7.17 7.17 7.16 7.15 3.72 3.70 3.31 3.29 2.96 2.95 2.95 2.93 2.46 2.45 2.44 2.43 2.42 2.39 2.38 2.37 2.36 2.35 2.07 2.07 2.06 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.84 1.66 1.65 1.64 1.64 1.63 1.62 1.39 1.31

5.15 7.08 3.45 2.27 2.00 0.98 2.98 1.01 2.11 0.99 5.97 5.91

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

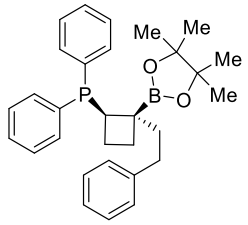



$^{13}$C NMR (500 MHz, $CDCl_3$)

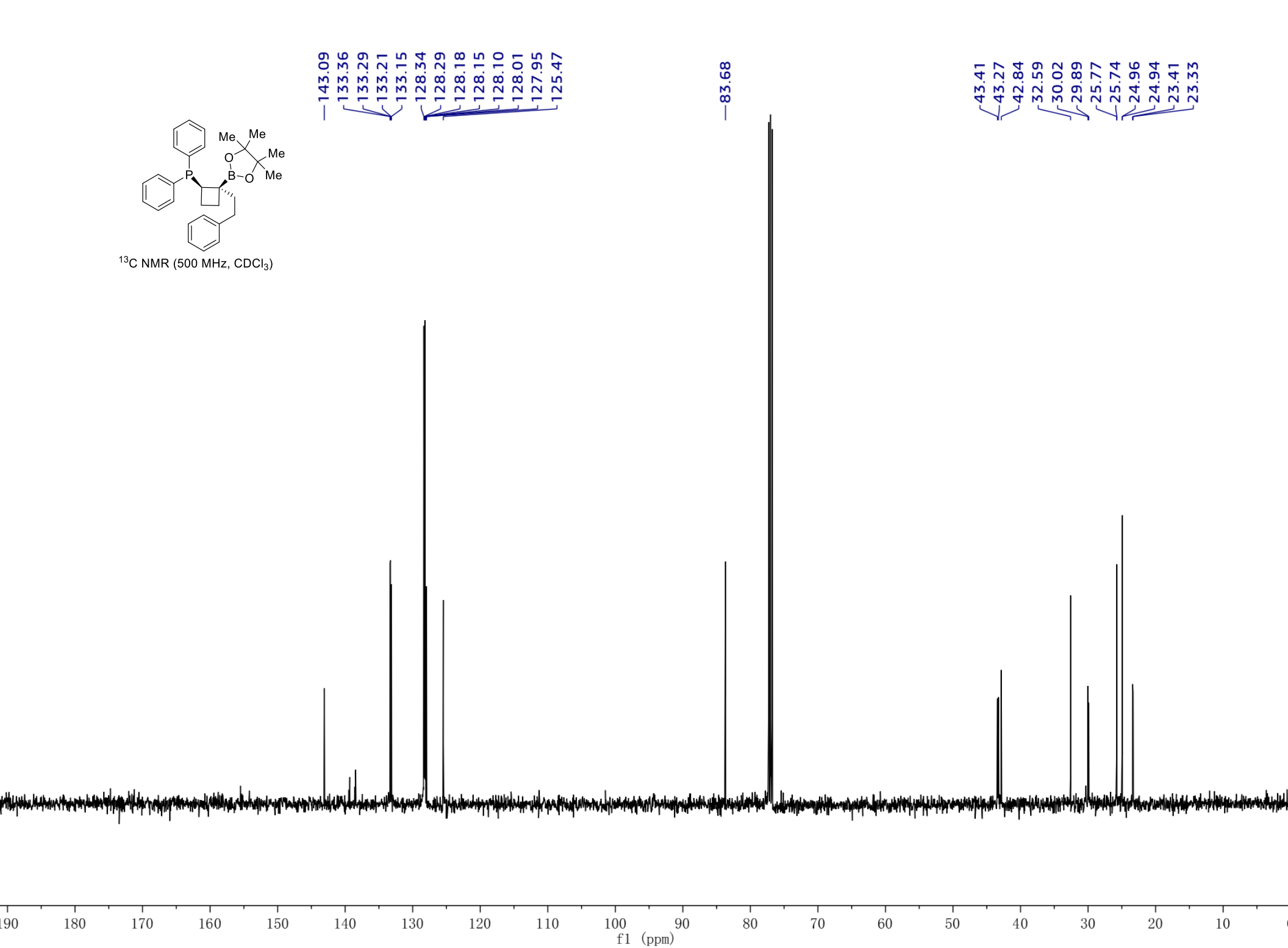
143.23
138.98
129.38
128.42
128.33
128.23
128.14
127.70
126.97
126.46
125.52
83.30
69.12
54.63
43.36
33.13
25.95
25.84
24.52
23.82

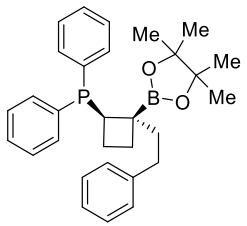
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

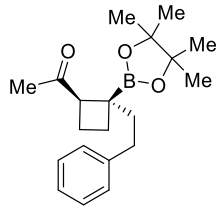



$^1$H NMR (500 MHz, $CDCl_3$)

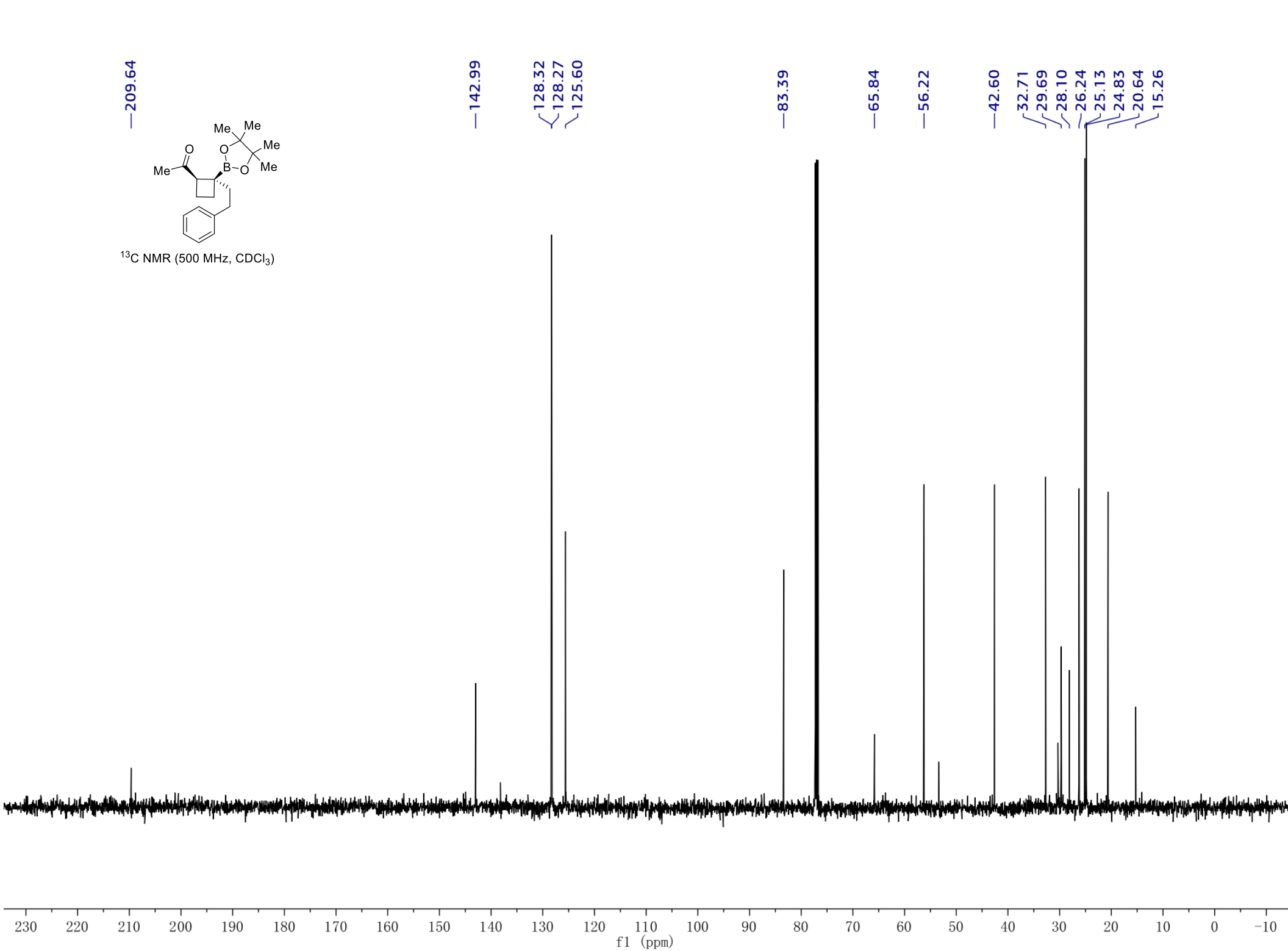

143.09
133.36
133.29
133.21
133.15
128.34
128.29
128.18
128.15
128.10
128.01
127.95
125.47
83.68
43.41
43.27
42.84
32.59
30.02
29.89
25.77
25.74
24.96
24.94
23.41
23.33
Me
Me
Me
Me
O
B
O
P
13C NMR (500 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

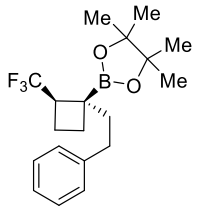



$^{31}$P NMR (500 MHz, $CDCl_3$)




$^1$H NMR (500 MHz, $CDCl_3$)


209.64
142.99
128.32
128.27
125.60
83.39
65.84
56.22
42.60
32.71
29.69
28.10
26.24
25.13
24.83
20.64
15.26
Me
Me
Me
Me
Me
O
O
B
O
$^{13}$C NMR (500 MHz, CDCl$_3$)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)



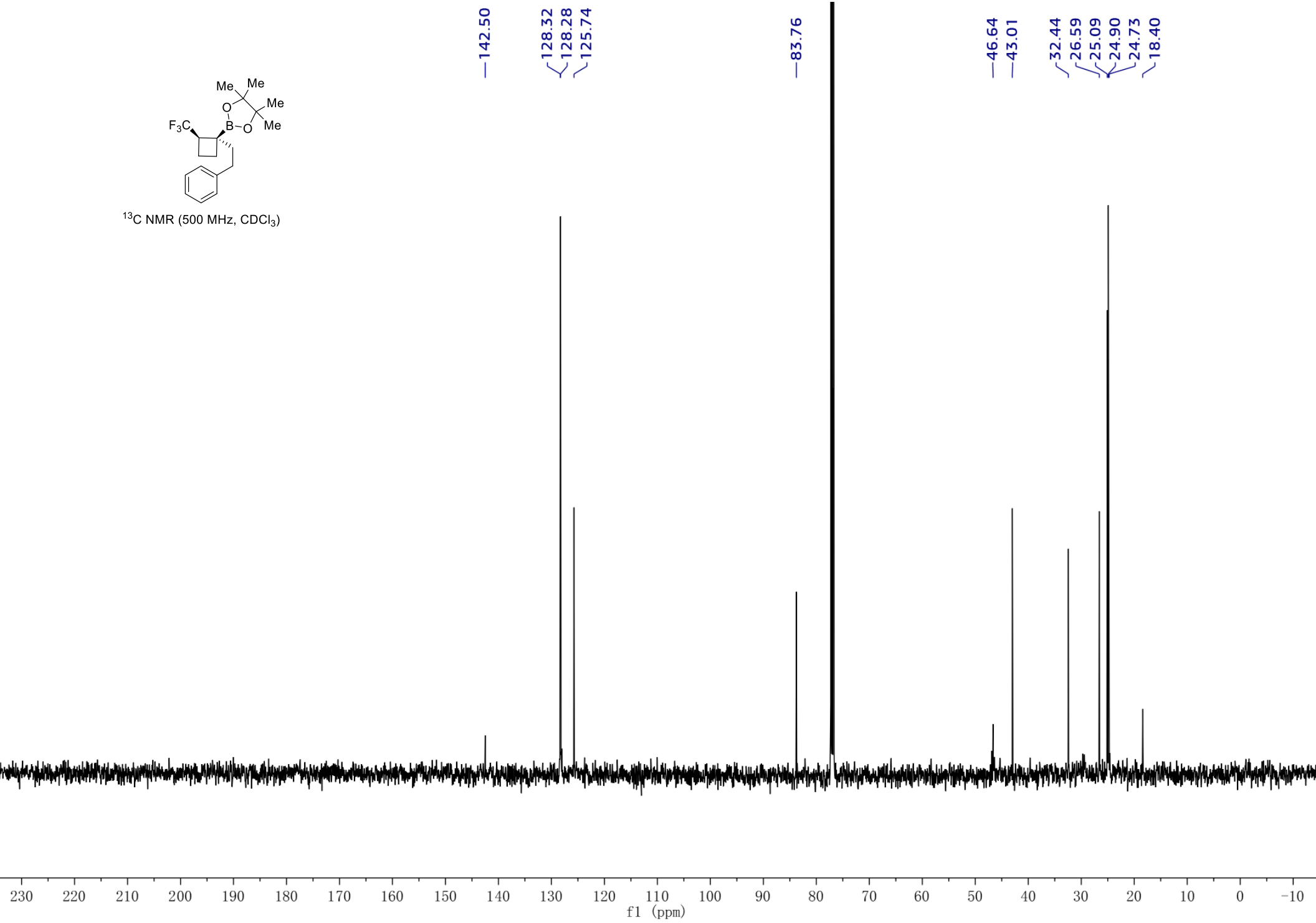

$^1$H NMR (500 MHz, $CDCl_3$)

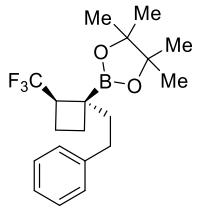
7.29 7.28 7.26 7.20 7.19 7.18 7.16 2.65 2.63 2.61 2.59 2.53 2.52 2.51 2.50 2.49 2.49 2.28 2.27 2.26 2.26 2.24 2.24 2.20 2.19 2.17 2.16 2.16 2.15 2.14 2.12 2.11 2.09 2.08 2.07 2.06 2.06 2.05 2.05 2.04 2.03 1.72 1.71 1.70 1.70 1.69 1.67 1.66 1.62 1.60 1.58 1.57 1.31 1.31 1.29 1.27 1.27 1.25 0.95 0.90 0.89 0.88 0.87 0.86 0.85

2.02 3.03 1.06 2.01 0.99 1.10 1.10 1.05 1.25 12.12 1.00

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)


142.50
128.32
128.28
125.74
83.76
46.64
43.01
32.44
26.59
25.09
24.90
24.73
18.40
Me
Me
Me
Me
O
B
O
F3C
13C NMR (500 MHz, CDCl3)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

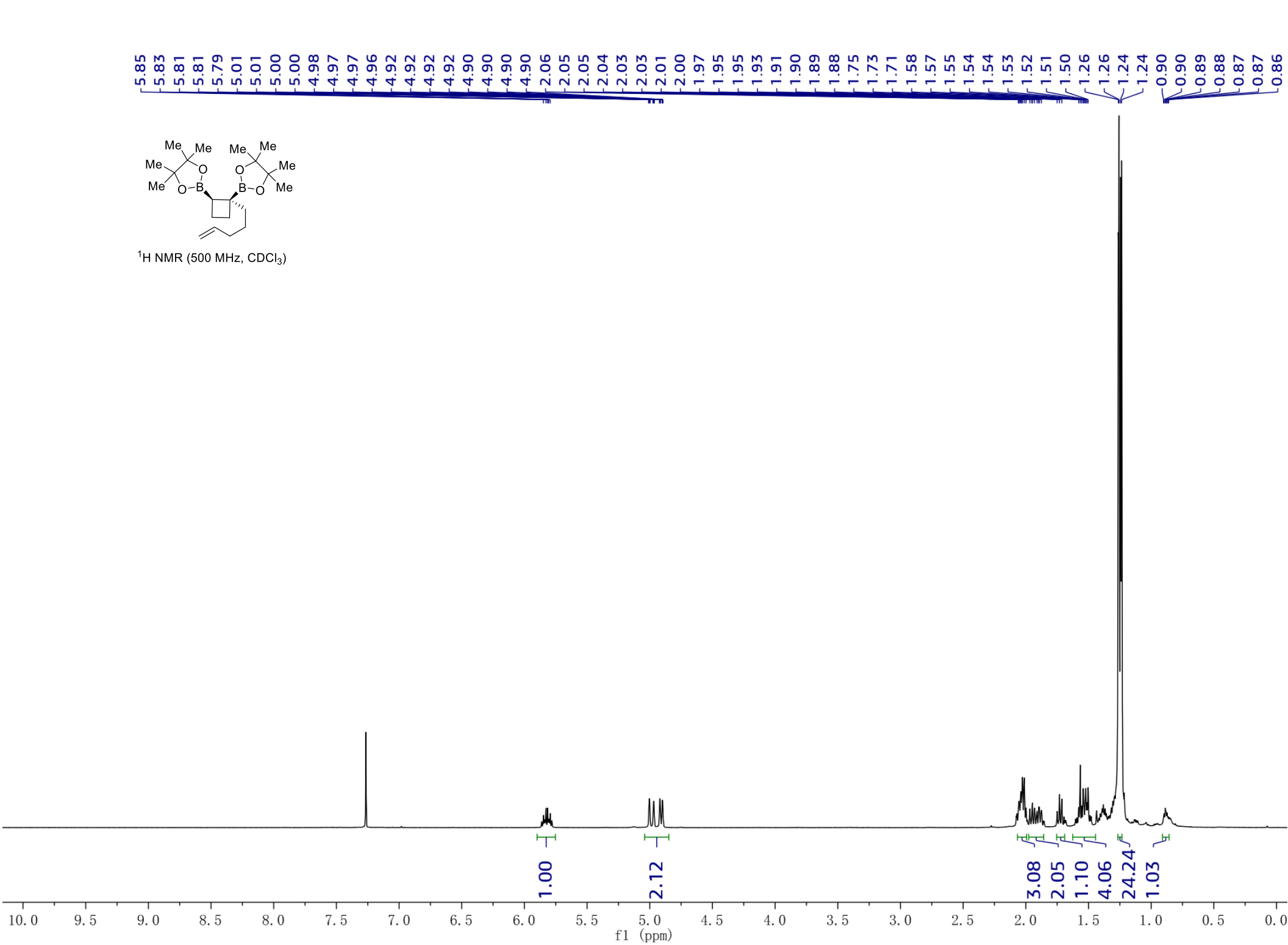


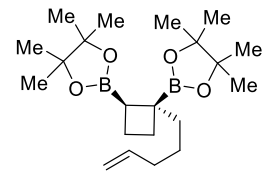

$^{19}$F NMR (500 MHz, $CDCl_3$)

-69.58
-69.60

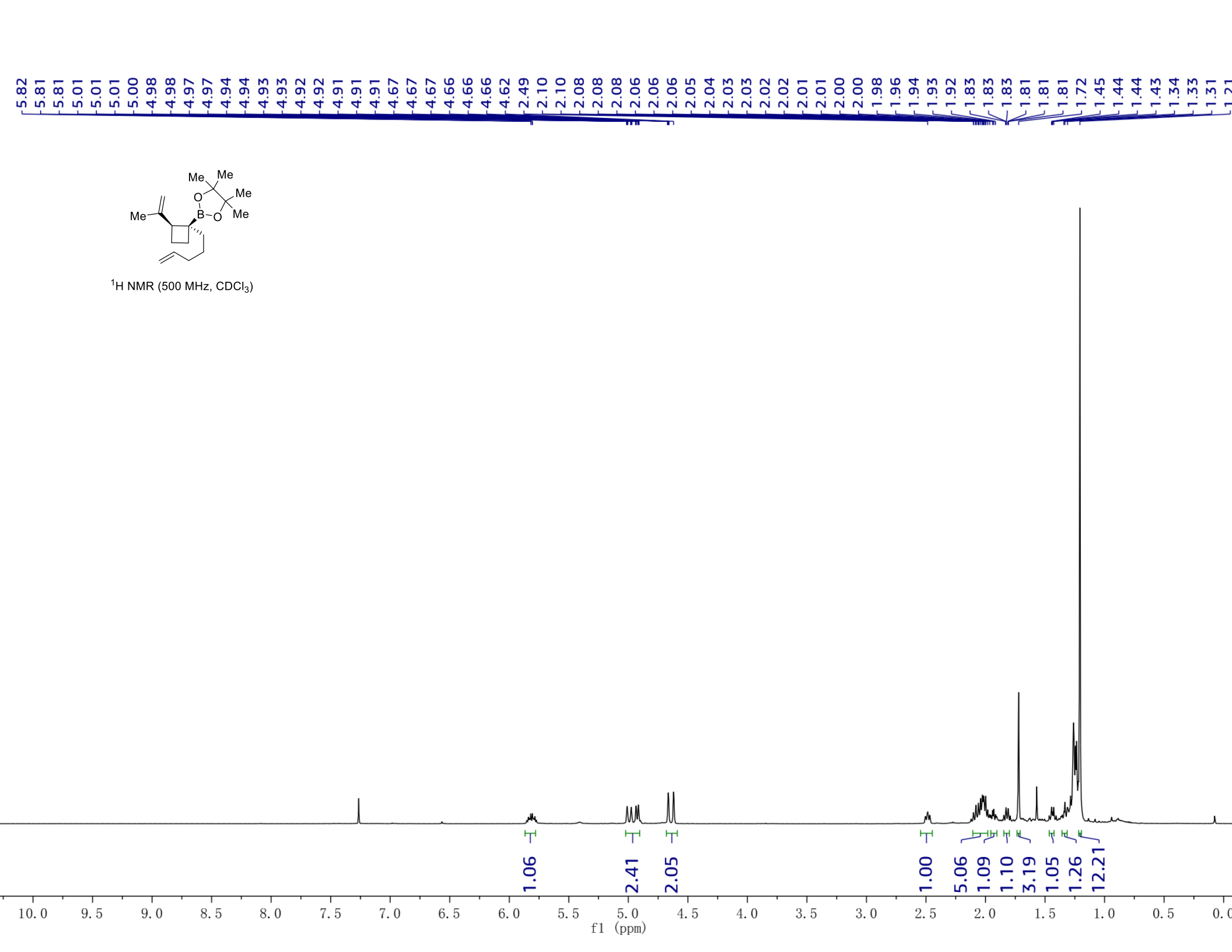
30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −20

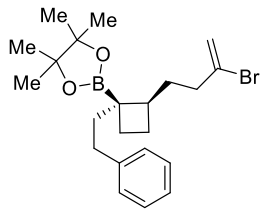
f1 (ppm)


5.85 5.83 5.81 5.81 5.79 5.01 5.01 5.00 5.00 4.98 4.97 4.97 4.96 4.92 4.92 4.92 4.92 4.90 4.90 4.90 4.90 2.06 2.05 2.05 2.04 2.03 2.03 2.01 2.00 1.97 1.95 1.95 1.93 1.91 1.90 1.89 1.88 1.75 1.73 1.71 1.58 1.57 1.55 1.54 1.54 1.53 1.52 1.51 1.50 1.26 1.26 1.24 1.24 0.90 0.90 0.89 0.88 0.87 0.87 0.86
Me Me Me Me Me Me O O B B O O Me Me
1H NMR (500 MHz, CDCl3)
1.00 2.12 3.08 2.05 1.10 4.06 24.24 1.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

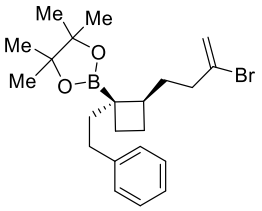



$^{13}C$ NMR (500 MHz, $CDCl_3$)


5.82 5.81 5.81 5.01 5.01 5.01 5.00 4.98 4.98 4.97 4.97 4.94 4.94 4.93 4.93 4.92 4.92 4.91 4.91 4.91 4.67 4.67 4.67 4.66 4.66 4.66 4.62 2.49 2.10 2.10 2.08 2.08 2.08 2.06 2.06 2.06 2.05 2.04 2.03 2.03 2.02 2.02 2.01 2.01 2.00 2.00 1.98 1.96 1.94 1.93 1.92 1.83 1.83 1.83 1.81 1.81 1.81 1.72 1.45 1.44 1.44 1.43 1.34 1.33 1.31
Me
Me
Me
O
B
O
Me
Me
1H NMR (500 MHz, CDCl3)
1.06
2.41
2.05
1.00
5.06
1.09
1.10
3.19
1.05
1.26
12.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)




$^{1}$H NMR (500 MHz, $CDCl_3$)

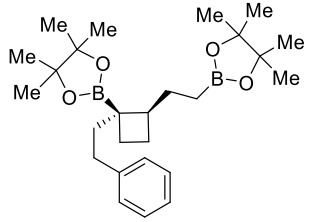



$^{13}C$ NMR (500 MHz, $CDCl_3$)

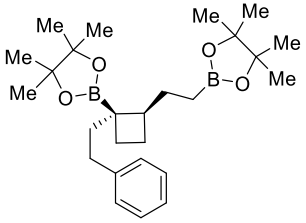
143.34
135.07
128.32
128.22
125.49
115.98
83.24
44.94
43.32
39.56
33.71
33.16
27.18
25.36
24.93
24.74

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)

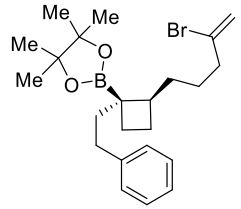



$^{13}C$ NMR (500 MHz, $CDCl_3$)

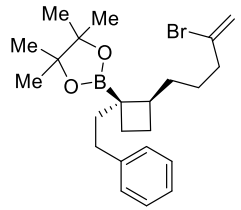
143.62
128.33
128.14
125.34
83.04
82.73
48.31
43.34
33.18
29.58
26.79
25.22
24.96
24.83
24.79
24.63

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)




$^1$H NMR (500 MHz, $CDCl_3$)

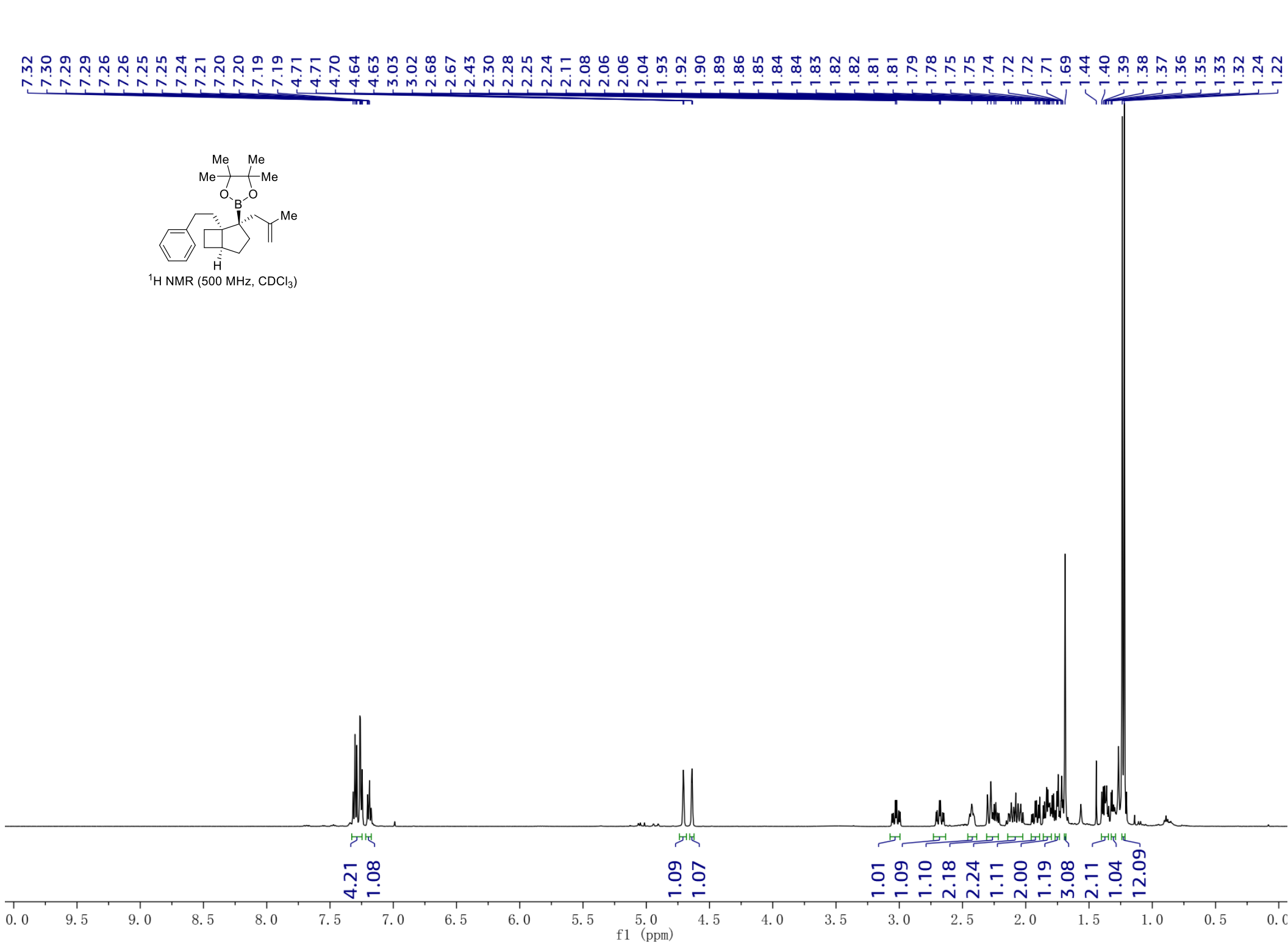


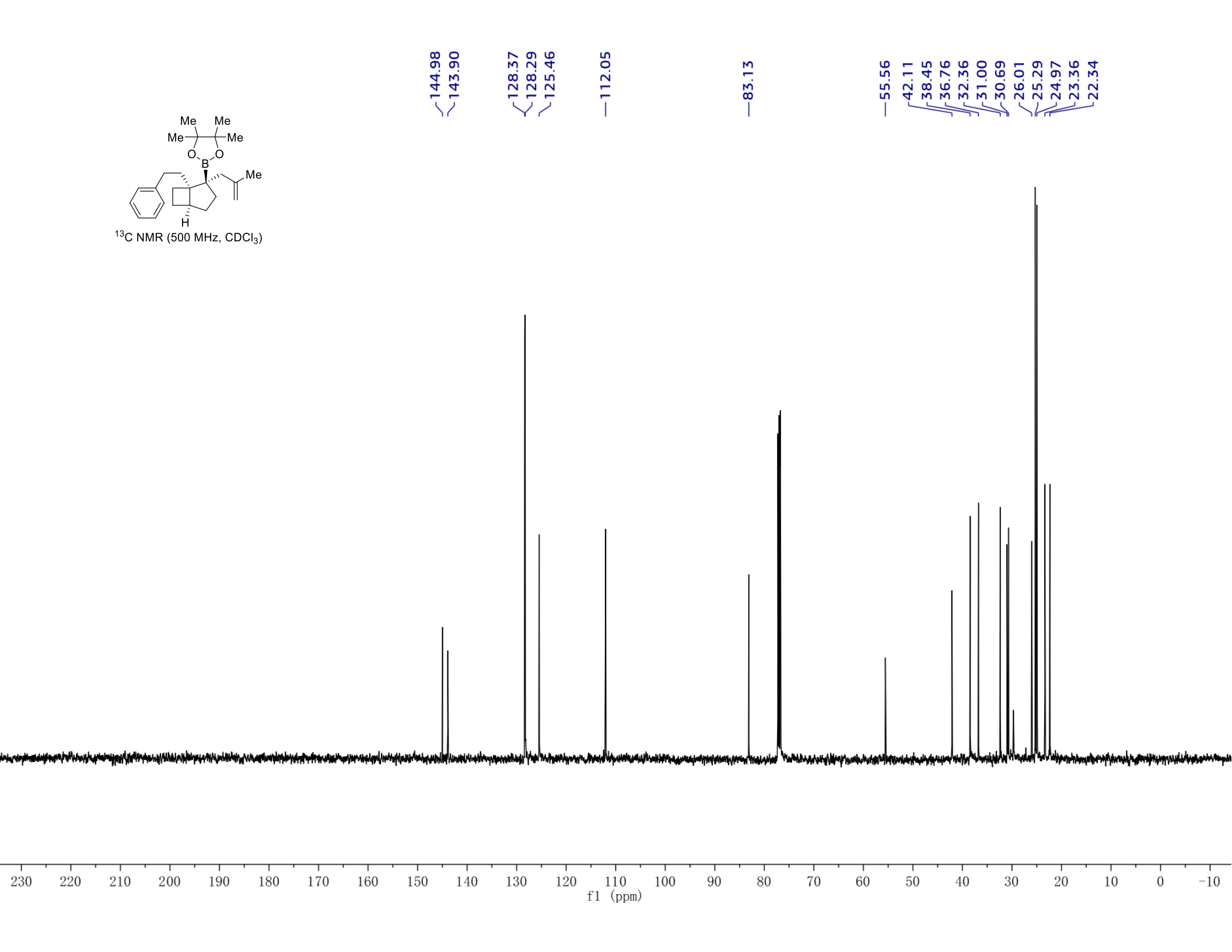

$^{13}C$ NMR (500 MHz, $CDCl_3$)

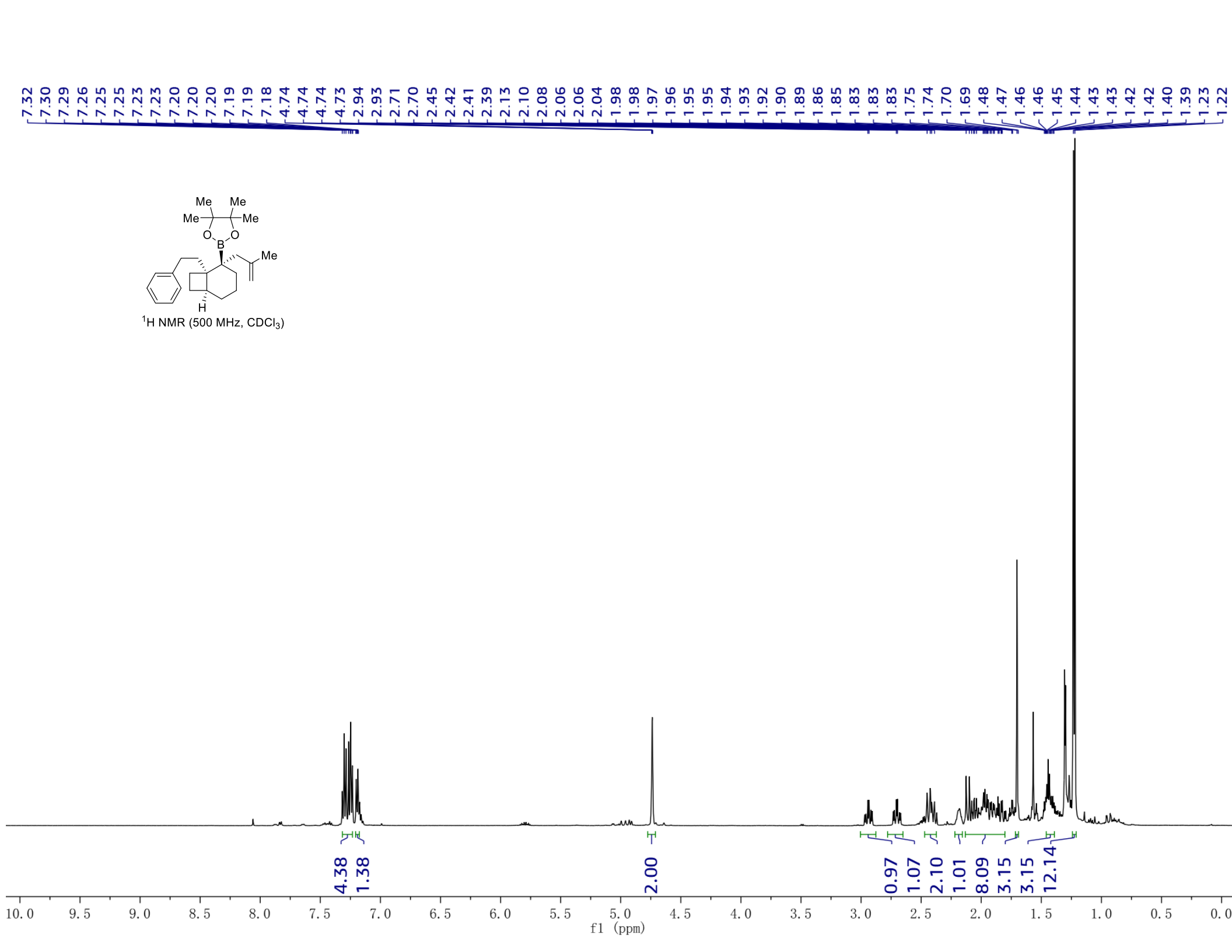
143.42
134.92
128.31
128.20
125.45
116.20
83.12
45.79
43.27
41.49
33.95
33.17
27.15
25.97
25.27
24.96
24.94

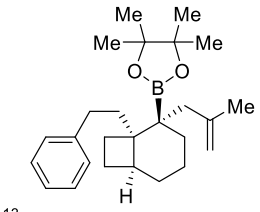
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10

f1 (ppm)


7.32 7.30 7.29 7.29 7.26 7.26 7.25 7.25 7.24 7.21 7.20 7.20 7.19 7.19 4.71 4.71 4.70 4.64 4.63 3.03 3.02 2.68 2.67 2.43 2.30 2.28 2.25 2.24 2.11 2.08 2.06 2.06 2.04 1.93 1.92 1.90 1.89 1.86 1.85 1.84 1.84 1.83 1.82 1.82 1.81 1.81 1.79 1.78 1.75 1.75 1.74 1.72 1.72 1.71 1.69 1.44 1.40 1.39 1.38 1.37 1.36 1.35 1.33 1.32 1.24 1.22
Me
Me
Me
Me
O
B
O
Me
H
1H NMR (500 MHz, CDCl3)
4.21
1.08
1.09
1.07
1.01
1.09
1.10
2.18
2.24
1.11
2.00
1.19
3.08
2.11
1.04
12.09
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


144.98
143.90
128.37
128.29
125.46
112.05
83.13
55.56
42.11
38.45
36.76
32.36
31.00
30.69
26.01
25.29
24.97
23.36
22.34
Me
Me
Me
Me
O
B
O
Me
H
13C NMR (500 MHz, CDCl3)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


7.32 7.30 7.29 7.26 7.25 7.25 7.23 7.23 7.20 7.20 7.20 7.19 7.19 7.18 4.74 4.74 4.74 4.73 2.94 2.93 2.71 2.70 2.45 2.42 2.41 2.39 2.13 2.10 2.08 2.06 2.06 2.04 1.98 1.98 1.97 1.96 1.95 1.95 1.94 1.93 1.92 1.90 1.89 1.86 1.85 1.83 1.83 1.83 1.75 1.74 1.70 1.69 1.48 1.47 1.46 1.46 1.45 1.44 1.43 1.43 1.42 1.42 1.40 1.39 1.23 1.22
Me
Me
Me
Me
O
B
O
Me
H
1H NMR (500 MHz, CDCl3)
4.38
1.38
2.00
0.97
1.07
2.10
1.01
8.09
3.15
3.15
12.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)




$^{13}C$ NMR (500 MHz, $CDCl_3$)

145.69
144.17
128.43
128.37
128.30
125.41
112.88
83.06
43.44
39.77
39.61
36.21
32.16
29.70
28.66
25.61
25.41
25.07
25.02
24.33
23.82
16.36

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

### 3.4.6 X-ray Crystallography data

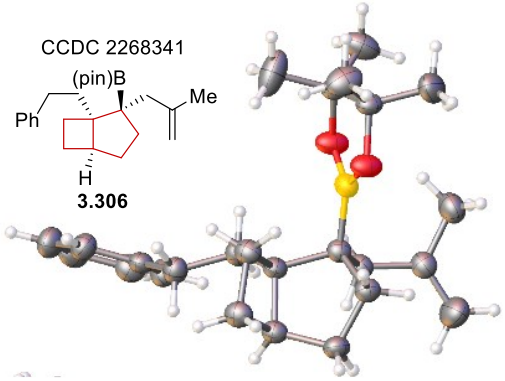



Table 1. Crystal data and structure refinement for C25H37BO2.

| | | |
|---|---|---|
| Identification code | C25H37BO2 | |
| Empirical formula | C25 H37 B O2 | |
| Formula weight | 380.35 | |
| Temperature | 173(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Monoclinic | |
| Space group | C2 | |
| Unit cell dimensions | a = 23.7725(8) Å | α= 90°. |
| | b = 7.1081(3) Å | β= 96.587(2)°. |
| | c = 26.5000(9) Å | γ = 90°. |
| Volume | 4448.3(3) $Å^3$ | |
| Z | 8 | |
| Density (calculated) | 1.136 $Mg/m^3$ | |
| Absorption coefficient | 0.525 $mm^{-1}$ | |
| F(000) | 1664 | |
| Crystal size | 0.260 x 0.220 x 0.140 $mm^3$ | |
| Theta range for data collection | 1.678 to 66.684°. | |
| Index ranges | -28<=h<=28, -8<=k<=8, -31<=l<=31 | |
| Reflections collected | 40813 | |
| Independent reflections | 7877 [R(int) = 0.1054] | |
| Completeness to theta = 66.684° | 100.0 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Max. and min. transmission | 0.7528 and 0.6312 | |
| Refinement method | Full-matrix least-squares on $F^2$ | |

| | |
|---|---|
| Data / restraints / parameters | 7877 / 1 / 506 |
| Goodness-of-fit on $F^2$ | 1.039 |
| Final R indices [I>2sigma(I)] | R1 = 0.0597, wR2 = 0.1410 |
| R indices (all data) | R1 = 0.0735, wR2 = 0.1503 |
| Absolute structure parameter | -0.1(3) |
| Extinction coefficient | 0.0023(3) |
| Largest diff. peak and hole | 0.273 and -0.260 e.$Å^{-3}$ |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for C25H37BO2. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 4096(1) | 7559(4) | 332(1) | 44(1) |
| O(2) | 3486(1) | 5098(5) | 315(1) | 52(1) |
| B(1) | 3874(2) | 6182(6) | 605(2) | 34(1) |
| C(1) | 5136(2) | 2679(9) | 1520(2) | 71(2) |
| C(2) | 4683(2) | 2983(6) | 1185(2) | 45(1) |
| C(3) | 4146(2) | 3784(6) | 1339(2) | 39(1) |
| C(4) | 4028(2) | 5912(5) | 1194(1) | 34(1) |
| C(5) | 4529(2) | 7147(6) | 1420(2) | 39(1) |
| C(6) | 4457(2) | 7313(7) | 1988(2) | 43(1) |
| C(7) | 3816(2) | 7417(6) | 2004(1) | 37(1) |
| C(8) | 3548(2) | 9364(6) | 1879(2) | 44(1) |
| C(9) | 3349(2) | 8722(6) | 1333(2) | 40(1) |
| C(10) | 3534(2) | 6645(6) | 1481(1) | 34(1) |
| C(11) | 3038(2) | 5276(6) | 1494(2) | 39(1) |
| C(12) | 2555(2) | 5933(6) | 1774(2) | 42(1) |
| C(13) | 2089(2) | 4495(6) | 1816(1) | 37(1) |
| C(14) | 2196(2) | 2573(6) | 1847(2) | 41(1) |
| C(15) | 1771(2) | 1305(6) | 1913(2) | 44(1) |
| C(16) | 1223(2) | 1936(7) | 1936(2) | 47(1) |
| C(17) | 1108(2) | 3847(7) | 1901(2) | 47(1) |
| C(18) | 1538(2) | 5106(7) | 1840(2) | 42(1) |
| C(19) | 4685(2) | 2458(8) | 636(2) | 62(1) |
| C(20) | 3374(2) | 5943(6) | -184(2) | 37(1) |
| C(21) | 3867(2) | 7378(6) | -200(1) | 40(1) |
| C(22) | 2798(2) | 6844(8) | -207(3) | 81(2) |
| C(23) | 3358(3) | 4368(8) | -567(2) | 62(1) |
| C(24) | 3687(2) | 9315(8) | -388(2) | 68(2) |
| C(25) | 4349(2) | 6695(10) | -482(2) | 68(2) |
| O(3) | 3416(1) | 4927(4) | 4715(1) | 48(1) |
| O(4) | 3990(1) | 2401(4) | 4680(1) | 45(1) |
| B(2) | 3713(2) | 3834(6) | 4419(2) | 35(1) |

| | | | | |
|---|---|---|---|---|
| C(26) | 4735(2) | 7417(9) | 3507(2) | 65(1) |
| C(27) | 4376(2) | 7073(6) | 3845(2) | 40(1) |
| C(28) | 3799(2) | 6263(5) | 3691(2) | 36(1) |
| C(29) | 3722(2) | 4144(6) | 3830(1) | 34(1) |
| C(30) | 4165(2) | 2923(6) | 3600(2) | 36(1) |
| C(31) | 3953(2) | 2793(6) | 3031(2) | 39(1) |
| C(32) | 3310(2) | 2690(6) | 3008(1) | 35(1) |
| C(33) | 3067(2) | 734(6) | 3118(2) | 43(1) |
| C(34) | 3014(2) | 1320(6) | 3666(2) | 40(1) |
| C(35) | 3155(2) | 3399(5) | 3537(1) | 33(1) |
| C(36) | 2653(2) | 4760(6) | 3528(2) | 37(1) |
| C(37) | 2100(2) | 4086(6) | 3238(2) | 40(1) |
| C(38) | 1630(2) | 5526(6) | 3173(1) | 36(1) |
| C(39) | 1069(2) | 4974(7) | 3174(2) | 46(1) |
| C(40) | 628(2) | 6240(8) | 3089(2) | 56(1) |
| C(41) | 735(2) | 8123(8) | 3006(2) | 53(1) |
| C(42) | 1290(2) | 8705(7) | 3009(2) | 49(1) |
| C(43) | 1730(2) | 7429(7) | 3091(2) | 46(1) |
| C(44) | 4530(2) | 7548(8) | 4393(2) | 55(1) |
| C(45) | 3418(2) | 4020(6) | 5210(1) | 36(1) |
| C(46) | 3908(2) | 2559(6) | 5214(1) | 39(1) |
| C(47) | 2840(2) | 3149(9) | 5209(3) | 79(2) |
| C(48) | 3501(3) | 5535(8) | 5606(2) | 63(1) |
| C(49) | 4465(2) | 3220(9) | 5495(2) | 62(1) |
| C(50) | 3766(2) | 615(8) | 5401(2) | 61(1) |

Table 3. Bond lengths [Å] and angles [°] for C25H37BO2.

| | |
|---|---|
| O(1)-B(1) | 1.358(5) |
| O(1)-C(21) | 1.457(5) |
| O(2)-B(1) | 1.367(6) |
| O(2)-C(20) | 1.449(5) |
| B(1)-C(4) | 1.575(6) |
| C(1)-C(2) | 1.331(7) |
| C(1)-H(1A) | 0.9500 |
| C(1)-H(1B) | 0.9500 |
| C(2)-C(3) | 1.497(6) |
| C(2)-C(19) | 1.504(7) |
| C(3)-C(4) | 1.578(5) |
| C(3)-H(3A) | 0.9900 |
| C(3)-H(3B) | 0.9900 |
| C(4)-C(5) | 1.543(6) |
| C(4)-C(10) | 1.561(5) |
| C(5)-C(6) | 1.537(6) |
| C(5)-H(5A) | 0.9900 |
| C(5)-H(5B) | 0.9900 |
| C(6)-C(7) | 1.530(6) |
| C(6)-H(6A) | 0.9900 |
| C(6)-H(6B) | 0.9900 |
| C(7)-C(8) | 1.544(6) |
| C(7)-C(10) | 1.568(5) |
| C(7)-H(7A) | 1.0000 |
| C(8)-C(9) | 1.538(6) |
| C(8)-H(8A) | 0.9900 |
| C(8)-H(8B) | 0.9900 |
| C(9)-C(10) | 1.577(6) |
| C(9)-H(9A) | 0.9900 |
| C(9)-H(9B) | 0.9900 |
| C(10)-C(11) | 1.531(6) |
| C(11)-C(12) | 1.511(6) |
| C(11)-H(11A) | 0.9900 |
| C(11)-H(11B) | 0.9900 |

| | |
|---|---|
| C(12)-C(13) | 1.521(6) |
| C(12)-H(12A) | 0.9900 |
| C(12)-H(12B) | 0.9900 |
| C(13)-C(18) | 1.389(6) |
| C(13)-C(14) | 1.391(6) |
| C(14)-C(15) | 1.381(6) |
| C(14)-H(14A) | 0.9500 |
| C(15)-C(16) | 1.385(6) |
| C(15)-H(15A) | 0.9500 |
| C(16)-C(17) | 1.387(7) |
| C(16)-H(16A) | 0.9500 |
| C(17)-C(18) | 1.382(6) |
| C(17)-H(17A) | 0.9500 |
| C(18)-H(18A) | 0.9500 |
| C(19)-H(19A) | 0.9800 |
| C(19)-H(19B) | 0.9800 |
| C(19)-H(19C) | 0.9800 |
| C(20)-C(22) | 1.506(7) |
| C(20)-C(23) | 1.509(6) |
| C(20)-C(21) | 1.558(6) |
| C(21)-C(24) | 1.509(7) |
| C(21)-C(25) | 1.518(6) |
| C(22)-H(22A) | 0.9800 |
| C(22)-H(22B) | 0.9800 |
| C(22)-H(22C) | 0.9800 |
| C(23)-H(23A) | 0.9800 |
| C(23)-H(23B) | 0.9800 |
| C(23)-H(23C) | 0.9800 |
| C(24)-H(24A) | 0.9800 |
| C(24)-H(24B) | 0.9800 |
| C(24)-H(24C) | 0.9800 |
| C(25)-H(25A) | 0.9800 |
| C(25)-H(25B) | 0.9800 |
| C(25)-H(25C) | 0.9800 |
| O(3)-B(2) | 1.358(6) |
| O(3)-C(45) | 1.461(5) |

| | |
|---|---|
| O(4)-B(2) | 1.359(5) |
| O(4)-C(46) | 1.456(5) |
| B(2)-C(29) | 1.579(6) |
| C(26)-C(27) | 1.328(7) |
| C(26)-H(26A) | 0.9500 |
| C(26)-H(26B) | 0.9500 |
| C(27)-C(44) | 1.495(6) |
| C(27)-C(28) | 1.500(6) |
| C(28)-C(29) | 1.567(5) |
| C(28)-H(28A) | 0.9900 |
| C(28)-H(28B) | 0.9900 |
| C(29)-C(30) | 1.544(6) |
| C(29)-C(35) | 1.567(5) |
| C(30)-C(31) | 1.536(5) |
| C(30)-H(30A) | 0.9900 |
| C(30)-H(30B) | 0.9900 |
| C(31)-C(32) | 1.526(6) |
| C(31)-H(31A) | 0.9900 |
| C(31)-H(31B) | 0.9900 |
| C(32)-C(33) | 1.547(6) |
| C(32)-C(35) | 1.573(5) |
| C(32)-H(32A) | 1.0000 |
| C(33)-C(34) | 1.530(6) |
| C(33)-H(33A) | 0.9900 |
| C(33)-H(33B) | 0.9900 |
| C(34)-C(35) | 1.562(6) |
| C(34)-H(34A) | 0.9900 |
| C(34)-H(34B) | 0.9900 |
| C(35)-C(36) | 1.534(6) |
| C(36)-C(37) | 1.523(6) |
| C(36)-H(36A) | 0.9900 |
| C(36)-H(36B) | 0.9900 |
| C(37)-C(38) | 1.510(6) |
| C(37)-H(37A) | 0.9900 |
| C(37)-H(37B) | 0.9900 |
| C(38)-C(39) | 1.391(6) |

| | |
|---|---|
| C(38)-C(43) | 1.394(6) |
| C(39)-C(40) | 1.381(7) |
| C(39)-H(39A) | 0.9500 |
| C(40)-C(41) | 1.385(8) |
| C(40)-H(40A) | 0.9500 |
| C(41)-C(42) | 1.382(7) |
| C(41)-H(41A) | 0.9500 |
| C(42)-C(43) | 1.381(6) |
| C(42)-H(42A) | 0.9500 |
| C(43)-H(43A) | 0.9500 |
| C(44)-H(44A) | 0.9800 |
| C(44)-H(44B) | 0.9800 |
| C(44)-H(44C) | 0.9800 |
| C(45)-C(48) | 1.501(6) |
| C(45)-C(47) | 1.506(7) |
| C(45)-C(46) | 1.560(6) |
| C(46)-C(49) | 1.517(6) |
| C(46)-C(50) | 1.518(7) |
| C(47)-H(47A) | 0.9800 |
| C(47)-H(47B) | 0.9800 |
| C(47)-H(47C) | 0.9800 |
| C(48)-H(48A) | 0.9800 |
| C(48)-H(48B) | 0.9800 |
| C(48)-H(48C) | 0.9800 |
| C(49)-H(49A) | 0.9800 |
| C(49)-H(49B) | 0.9800 |
| C(49)-H(49C) | 0.9800 |
| C(50)-H(50A) | 0.9800 |
| C(50)-H(50B) | 0.9800 |
| C(50)-H(50C) | 0.9800 |

| | |
|---|---|
| B(1)-O(1)-C(21) | 109.0(3) |
| B(1)-O(2)-C(20) | 108.7(3) |
| O(1)-B(1)-O(2) | 112.7(4) |
| O(1)-B(1)-C(4) | 123.7(4) |
| O(2)-B(1)-C(4) | 123.6(4) |

| | |
|---|---|
| C(2)-C(1)-H(1A) | 120.0 |
| C(2)-C(1)-H(1B) | 120.0 |
| H(1A)-C(1)-H(1B) | 120.0 |
| C(1)-C(2)-C(3) | 122.1(5) |
| C(1)-C(2)-C(19) | 120.8(5) |
| C(3)-C(2)-C(19) | 117.1(4) |
| C(2)-C(3)-C(4) | 115.5(3) |
| C(2)-C(3)-H(3A) | 108.4 |
| C(4)-C(3)-H(3A) | 108.4 |
| C(2)-C(3)-H(3B) | 108.4 |
| C(4)-C(3)-H(3B) | 108.4 |
| H(3A)-C(3)-H(3B) | 107.5 |
| C(5)-C(4)-C(10) | 102.2(3) |
| C(5)-C(4)-B(1) | 113.4(3) |
| C(10)-C(4)-B(1) | 109.8(3) |
| C(5)-C(4)-C(3) | 110.1(3) |
| C(10)-C(4)-C(3) | 108.9(3) |
| B(1)-C(4)-C(3) | 111.9(3) |
| C(6)-C(5)-C(4) | 104.8(3) |
| C(6)-C(5)-H(5A) | 110.8 |
| C(4)-C(5)-H(5A) | 110.8 |
| C(6)-C(5)-H(5B) | 110.8 |
| C(4)-C(5)-H(5B) | 110.8 |
| H(5A)-C(5)-H(5B) | 108.9 |
| C(7)-C(6)-C(5) | 104.7(3) |
| C(7)-C(6)-H(6A) | 110.8 |
| C(5)-C(6)-H(6A) | 110.8 |
| C(7)-C(6)-H(6B) | 110.8 |
| C(5)-C(6)-H(6B) | 110.8 |
| H(6A)-C(6)-H(6B) | 108.9 |
| C(6)-C(7)-C(8) | 115.2(4) |
| C(6)-C(7)-C(10) | 106.6(3) |
| C(8)-C(7)-C(10) | 90.0(3) |
| C(6)-C(7)-H(7A) | 114.2 |
| C(8)-C(7)-H(7A) | 114.2 |
| C(10)-C(7)-H(7A) | 114.2 |

| | |
|---|---|
| C(9)-C(8)-C(7) | 90.6(3) |
| C(9)-C(8)-H(8A) | 113.5 |
| C(7)-C(8)-H(8A) | 113.5 |
| C(9)-C(8)-H(8B) | 113.5 |
| C(7)-C(8)-H(8B) | 113.5 |
| H(8A)-C(8)-H(8B) | 110.8 |
| C(8)-C(9)-C(10) | 89.9(3) |
| C(8)-C(9)-H(9A) | 113.7 |
| C(10)-C(9)-H(9A) | 113.7 |
| C(8)-C(9)-H(9B) | 113.7 |
| C(10)-C(9)-H(9B) | 113.7 |
| H(9A)-C(9)-H(9B) | 110.9 |
| C(11)-C(10)-C(4) | 115.1(3) |
| C(11)-C(10)-C(7) | 117.1(3) |
| C(4)-C(10)-C(7) | 106.0(3) |
| C(11)-C(10)-C(9) | 114.1(3) |
| C(4)-C(10)-C(9) | 113.3(3) |
| C(7)-C(10)-C(9) | 88.3(3) |
| C(12)-C(11)-C(10) | 116.4(4) |
| C(12)-C(11)-H(11A) | 108.2 |
| C(10)-C(11)-H(11A) | 108.2 |
| C(12)-C(11)-H(11B) | 108.2 |
| C(10)-C(11)-H(11B) | 108.2 |
| H(11A)-C(11)-H(11B) | 107.3 |
| C(11)-C(12)-C(13) | 115.4(4) |
| C(11)-C(12)-H(12A) | 108.4 |
| C(13)-C(12)-H(12A) | 108.4 |
| C(11)-C(12)-H(12B) | 108.4 |
| C(13)-C(12)-H(12B) | 108.4 |
| H(12A)-C(12)-H(12B) | 107.5 |
| C(18)-C(13)-C(14) | 118.1(4) |
| C(18)-C(13)-C(12) | 119.5(4) |
| C(14)-C(13)-C(12) | 122.3(4) |
| C(15)-C(14)-C(13) | 121.1(4) |
| C(15)-C(14)-H(14A) | 119.4 |
| C(13)-C(14)-H(14A) | 119.4 |

| | |
|---|---|
| C(14)-C(15)-C(16) | 120.0(4) |
| C(14)-C(15)-H(15A) | 120.0 |
| C(16)-C(15)-H(15A) | 120.0 |
| C(15)-C(16)-C(17) | 119.6(4) |
| C(15)-C(16)-H(16A) | 120.2 |
| C(17)-C(16)-H(16A) | 120.2 |
| C(18)-C(17)-C(16) | 119.9(4) |
| C(18)-C(17)-H(17A) | 120.0 |
| C(16)-C(17)-H(17A) | 120.0 |
| C(17)-C(18)-C(13) | 121.2(4) |
| C(17)-C(18)-H(18A) | 119.4 |
| C(13)-C(18)-H(18A) | 119.4 |
| C(2)-C(19)-H(19A) | 109.5 |
| C(2)-C(19)-H(19B) | 109.5 |
| H(19A)-C(19)-H(19B) | 109.5 |
| C(2)-C(19)-H(19C) | 109.5 |
| H(19A)-C(19)-H(19C) | 109.5 |
| H(19B)-C(19)-H(19C) | 109.5 |
| O(2)-C(20)-C(22) | 106.6(4) |
| O(2)-C(20)-C(23) | 107.1(4) |
| C(22)-C(20)-C(23) | 109.7(4) |
| O(2)-C(20)-C(21) | 103.7(3) |
| C(22)-C(20)-C(21) | 113.8(4) |
| C(23)-C(20)-C(21) | 115.3(4) |
| O(1)-C(21)-C(24) | 107.4(4) |
| O(1)-C(21)-C(25) | 106.5(4) |
| C(24)-C(21)-C(25) | 109.3(4) |
| O(1)-C(21)-C(20) | 103.3(3) |
| C(24)-C(21)-C(20) | 114.9(4) |
| C(25)-C(21)-C(20) | 114.7(4) |
| C(20)-C(22)-H(22A) | 109.5 |
| C(20)-C(22)-H(22B) | 109.5 |
| H(22A)-C(22)-H(22B) | 109.5 |
| C(20)-C(22)-H(22C) | 109.5 |
| H(22A)-C(22)-H(22C) | 109.5 |
| H(22B)-C(22)-H(22C) | 109.5 |

| | |
|---|---|
| C(20)-C(23)-H(23A) | 109.5 |
| C(20)-C(23)-H(23B) | 109.5 |
| H(23A)-C(23)-H(23B) | 109.5 |
| C(20)-C(23)-H(23C) | 109.5 |
| H(23A)-C(23)-H(23C) | 109.5 |
| H(23B)-C(23)-H(23C) | 109.5 |
| C(21)-C(24)-H(24A) | 109.5 |
| C(21)-C(24)-H(24B) | 109.5 |
| H(24A)-C(24)-H(24B) | 109.5 |
| C(21)-C(24)-H(24C) | 109.5 |
| H(24A)-C(24)-H(24C) | 109.5 |
| H(24B)-C(24)-H(24C) | 109.5 |
| C(21)-C(25)-H(25A) | 109.5 |
| C(21)-C(25)-H(25B) | 109.5 |
| H(25A)-C(25)-H(25B) | 109.5 |
| C(21)-C(25)-H(25C) | 109.5 |
| H(25A)-C(25)-H(25C) | 109.5 |
| H(25B)-C(25)-H(25C) | 109.5 |
| B(2)-O(3)-C(45) | 108.5(3) |
| B(2)-O(4)-C(46) | 109.0(3) |
| O(3)-B(2)-O(4) | 112.9(3) |
| O(3)-B(2)-C(29) | 123.9(4) |
| O(4)-B(2)-C(29) | 123.2(4) |
| C(27)-C(26)-H(26A) | 120.0 |
| C(27)-C(26)-H(26B) | 120.0 |
| H(26A)-C(26)-H(26B) | 120.0 |
| C(26)-C(27)-C(44) | 120.6(4) |
| C(26)-C(27)-C(28) | 121.7(4) |
| C(44)-C(27)-C(28) | 117.7(4) |
| C(27)-C(28)-C(29) | 115.7(3) |
| C(27)-C(28)-H(28A) | 108.3 |
| C(29)-C(28)-H(28A) | 108.3 |
| C(27)-C(28)-H(28B) | 108.3 |
| C(29)-C(28)-H(28B) | 108.3 |
| H(28A)-C(28)-H(28B) | 107.4 |
| C(30)-C(29)-C(28) | 110.1(3) |

| | |
|---|---|
| C(30)-C(29)-C(35) | 101.6(3) |
| C(28)-C(29)-C(35) | 109.1(3) |
| C(30)-C(29)-B(2) | 113.5(3) |
| C(28)-C(29)-B(2) | 112.4(3) |
| C(35)-C(29)-B(2) | 109.5(3) |
| C(31)-C(30)-C(29) | 105.0(3) |
| C(31)-C(30)-H(30A) | 110.7 |
| C(29)-C(30)-H(30A) | 110.7 |
| C(31)-C(30)-H(30B) | 110.7 |
| C(29)-C(30)-H(30B) | 110.7 |
| H(30A)-C(30)-H(30B) | 108.8 |
| C(32)-C(31)-C(30) | 104.9(3) |
| C(32)-C(31)-H(31A) | 110.8 |
| C(30)-C(31)-H(31A) | 110.8 |
| C(32)-C(31)-H(31B) | 110.8 |
| C(30)-C(31)-H(31B) | 110.8 |
| H(31A)-C(31)-H(31B) | 108.8 |
| C(31)-C(32)-C(33) | 115.5(3) |
| C(31)-C(32)-C(35) | 106.5(3) |
| C(33)-C(32)-C(35) | 89.3(3) |
| C(31)-C(32)-H(32A) | 114.3 |
| C(33)-C(32)-H(32A) | 114.3 |
| C(35)-C(32)-H(32A) | 114.3 |
| C(34)-C(33)-C(32) | 90.5(3) |
| C(34)-C(33)-H(33A) | 113.6 |
| C(32)-C(33)-H(33A) | 113.6 |
| C(34)-C(33)-H(33B) | 113.6 |
| C(32)-C(33)-H(33B) | 113.6 |
| H(33A)-C(33)-H(33B) | 110.8 |
| C(33)-C(34)-C(35) | 90.4(3) |
| C(33)-C(34)-H(34A) | 113.6 |
| C(35)-C(34)-H(34A) | 113.6 |
| C(33)-C(34)-H(34B) | 113.6 |
| C(35)-C(34)-H(34B) | 113.6 |
| H(34A)-C(34)-H(34B) | 110.9 |
| C(36)-C(35)-C(34) | 114.5(3) |

| | |
|---|---|
| C(36)-C(35)-C(29) | 114.7(3) |
| C(34)-C(35)-C(29) | 113.9(3) |
| C(36)-C(35)-C(32) | 116.6(3) |
| C(34)-C(35)-C(32) | 88.3(3) |
| C(29)-C(35)-C(32) | 105.9(3) |
| C(37)-C(36)-C(35) | 115.8(3) |
| C(37)-C(36)-H(36A) | 108.3 |
| C(35)-C(36)-H(36A) | 108.3 |
| C(37)-C(36)-H(36B) | 108.3 |
| C(35)-C(36)-H(36B) | 108.3 |
| H(36A)-C(36)-H(36B) | 107.4 |
| C(38)-C(37)-C(36) | 115.4(3) |
| C(38)-C(37)-H(37A) | 108.4 |
| C(36)-C(37)-H(37A) | 108.4 |
| C(38)-C(37)-H(37B) | 108.4 |
| C(36)-C(37)-H(37B) | 108.4 |
| H(37A)-C(37)-H(37B) | 107.5 |
| C(39)-C(38)-C(43) | 117.0(4) |
| C(39)-C(38)-C(37) | 120.3(4) |
| C(43)-C(38)-C(37) | 122.6(4) |
| C(40)-C(39)-C(38) | 121.8(4) |
| C(40)-C(39)-H(39A) | 119.1 |
| C(38)-C(39)-H(39A) | 119.1 |
| C(39)-C(40)-C(41) | 120.4(5) |
| C(39)-C(40)-H(40A) | 119.8 |
| C(41)-C(40)-H(40A) | 119.8 |
| C(42)-C(41)-C(40) | 118.8(5) |
| C(42)-C(41)-H(41A) | 120.6 |
| C(40)-C(41)-H(41A) | 120.6 |
| C(43)-C(42)-C(41) | 120.6(5) |
| C(43)-C(42)-H(42A) | 119.7 |
| C(41)-C(42)-H(42A) | 119.7 |
| C(42)-C(43)-C(38) | 121.5(4) |
| C(42)-C(43)-H(43A) | 119.3 |
| C(38)-C(43)-H(43A) | 119.3 |
| C(27)-C(44)-H(44A) | 109.5 |

| | |
|---|---|
| C(27)-C(44)-H(44B) | 109.5 |
| H(44A)-C(44)-H(44B) | 109.5 |
| C(27)-C(44)-H(44C) | 109.5 |
| H(44A)-C(44)-H(44C) | 109.5 |
| H(44B)-C(44)-H(44C) | 109.5 |
| O(3)-C(45)-C(48) | 107.3(4) |
| O(3)-C(45)-C(47) | 105.8(4) |
| C(48)-C(45)-C(47) | 110.0(4) |
| O(3)-C(45)-C(46) | 103.1(3) |
| C(48)-C(45)-C(46) | 115.7(4) |
| C(47)-C(45)-C(46) | 114.0(4) |
| O(4)-C(46)-C(49) | 107.0(3) |
| O(4)-C(46)-C(50) | 107.8(4) |
| C(49)-C(46)-C(50) | 109.6(4) |
| O(4)-C(46)-C(45) | 103.1(3) |
| C(49)-C(46)-C(45) | 114.0(4) |
| C(50)-C(46)-C(45) | 114.5(4) |
| C(45)-C(47)-H(47A) | 109.5 |
| C(45)-C(47)-H(47B) | 109.5 |
| H(47A)-C(47)-H(47B) | 109.5 |
| C(45)-C(47)-H(47C) | 109.5 |
| H(47A)-C(47)-H(47C) | 109.5 |
| H(47B)-C(47)-H(47C) | 109.5 |
| C(45)-C(48)-H(48A) | 109.5 |
| C(45)-C(48)-H(48B) | 109.5 |
| H(48A)-C(48)-H(48B) | 109.5 |
| C(45)-C(48)-H(48C) | 109.5 |
| H(48A)-C(48)-H(48C) | 109.5 |
| H(48B)-C(48)-H(48C) | 109.5 |
| C(46)-C(49)-H(49A) | 109.5 |
| C(46)-C(49)-H(49B) | 109.5 |
| H(49A)-C(49)-H(49B) | 109.5 |
| C(46)-C(49)-H(49C) | 109.5 |
| H(49A)-C(49)-H(49C) | 109.5 |
| H(49B)-C(49)-H(49C) | 109.5 |
| C(46)-C(50)-H(50A) | 109.5 |

| | |
|---|---|
| C(46)-C(50)-H(50B) | 109.5 |
| H(50A)-C(50)-H(50B) | 109.5 |
| C(46)-C(50)-H(50C) | 109.5 |
| H(50A)-C(50)-H(50C) | 109.5 |
| H(50B)-C(50)-H(50C) | 109.5 |

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Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C25H37BO2. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 51(2) | 49(2) | 32(1) | 6(1) | 3(1) | -13(2) |
| O(2) | 63(2) | 60(2) | 32(2) | 4(1) | 3(1) | -22(2) |
| B(1) | 33(2) | 32(2) | 39(2) | 3(2) | 9(2) | 3(2) |
| C(1) | 57(3) | 69(4) | 83(4) | -1(3) | -6(3) | 17(3) |
| C(2) | 44(2) | 36(2) | 56(3) | 6(2) | 9(2) | 1(2) |
| C(3) | 45(2) | 32(2) | 40(2) | 5(2) | 10(2) | 1(2) |
| C(4) | 40(2) | 29(2) | 34(2) | 4(2) | 10(2) | -2(2) |
| C(5) | 44(2) | 37(2) | 36(2) | 2(2) | 4(2) | -5(2) |
| C(6) | 45(2) | 47(2) | 37(2) | 0(2) | 3(2) | -7(2) |
| C(7) | 45(2) | 36(2) | 30(2) | 0(2) | 5(2) | 0(2) |
| C(8) | 56(3) | 37(2) | 38(2) | -2(2) | 6(2) | 1(2) |
| C(9) | 47(2) | 37(2) | 37(2) | 5(2) | 7(2) | 6(2) |
| C(10) | 38(2) | 35(2) | 29(2) | 2(2) | 6(2) | -1(2) |
| C(11) | 43(2) | 36(2) | 38(2) | 1(2) | 7(2) | -4(2) |
| C(12) | 39(2) | 39(2) | 47(2) | 1(2) | 6(2) | 0(2) |
| C(13) | 36(2) | 45(2) | 29(2) | 1(2) | 4(2) | -1(2) |
| C(14) | 41(2) | 42(2) | 42(2) | -2(2) | 5(2) | 3(2) |
| C(15) | 52(3) | 38(2) | 43(2) | -1(2) | 5(2) | -6(2) |
| C(16) | 41(2) | 57(3) | 43(2) | 1(2) | 6(2) | -10(2) |
| C(17) | 37(2) | 57(3) | 46(2) | 3(2) | 6(2) | -1(2) |
| C(18) | 38(2) | 45(2) | 44(2) | 1(2) | 6(2) | 6(2) |
| C(19) | 66(3) | 59(3) | 66(3) | 7(3) | 27(2) | 15(3) |
| C(20) | 43(2) | 36(2) | 32(2) | 4(2) | 6(2) | 0(2) |
| C(21) | 43(2) | 50(3) | 28(2) | 6(2) | 6(2) | 0(2) |
| C(22) | 38(3) | 52(3) | 152(6) | 15(4) | 12(3) | 3(2) |
| C(23) | 93(4) | 51(3) | 44(3) | -6(2) | 16(3) | -11(3) |
| C(24) | 64(3) | 58(3) | 80(4) | 29(3) | 1(3) | -9(3) |
| C(25) | 49(3) | 106(5) | 52(3) | -16(3) | 19(2) | -7(3) |
| O(3) | 61(2) | 51(2) | 32(2) | 6(1) | 8(1) | 18(2) |
| O(4) | 54(2) | 50(2) | 32(1) | 8(1) | 6(1) | 15(2) |
| B(2) | 37(2) | 34(2) | 33(2) | 1(2) | 0(2) | -2(2) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(26) | 63(3) | 73(4) | 61(3) | 0(3) | 14(2) | -21(3) |
| C(27) | 44(2) | 36(2) | 41(2) | 3(2) | 2(2) | -2(2) |
| C(28) | 41(2) | 31(2) | 34(2) | 2(2) | 1(2) | 0(2) |
| C(29) | 36(2) | 32(2) | 32(2) | 3(2) | 3(2) | 2(2) |
| C(30) | 39(2) | 34(2) | 36(2) | 2(2) | 6(2) | 3(2) |
| C(31) | 41(2) | 44(2) | 33(2) | 0(2) | 8(2) | 2(2) |
| C(32) | 42(2) | 33(2) | 31(2) | 1(2) | 4(2) | 1(2) |
| C(33) | 52(3) | 36(2) | 41(2) | -2(2) | 6(2) | -3(2) |
| C(34) | 49(2) | 34(2) | 36(2) | 2(2) | 4(2) | -4(2) |
| C(35) | 37(2) | 35(2) | 27(2) | 2(2) | 2(2) | 2(2) |
| C(36) | 38(2) | 35(2) | 39(2) | -2(2) | 4(2) | 1(2) |
| C(37) | 37(2) | 40(2) | 44(2) | -2(2) | 5(2) | 0(2) |
| C(38) | 38(2) | 44(2) | 26(2) | -1(2) | 3(2) | 1(2) |
| C(39) | 41(2) | 49(3) | 48(3) | 2(2) | 9(2) | -2(2) |
| C(40) | 38(2) | 69(4) | 59(3) | 2(3) | 6(2) | 4(2) |
| C(41) | 50(3) | 61(3) | 48(3) | -1(2) | -1(2) | 15(2) |
| C(42) | 56(3) | 45(3) | 46(3) | 3(2) | 2(2) | 4(2) |
| C(43) | 43(2) | 47(3) | 47(2) | 6(2) | 3(2) | -4(2) |
| C(44) | 53(3) | 58(3) | 51(3) | -2(2) | -4(2) | -11(3) |
| C(45) | 42(2) | 38(2) | 29(2) | 3(2) | 6(2) | -1(2) |
| C(46) | 43(2) | 44(2) | 29(2) | 6(2) | 6(2) | 3(2) |
| C(47) | 42(3) | 58(3) | 139(6) | 18(3) | 20(3) | 1(2) |
| C(48) | 87(4) | 58(3) | 42(3) | -6(2) | 0(3) | 11(3) |
| C(49) | 43(3) | 91(4) | 52(3) | -4(3) | -3(2) | 5(3) |
| C(50) | 72(3) | 52(3) | 62(3) | 19(2) | 19(3) | 14(3) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for C25H37BO2.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 5124 | 2972 | 1868 | 85 |
| H(1B) | 5470 | 2168 | 1410 | 85 |
| H(3A) | 4154 | 3654 | 1712 | 47 |
| H(3B) | 3825 | 3022 | 1180 | 47 |
| H(5A) | 4895 | 6546 | 1373 | 47 |
| H(5B) | 4513 | 8402 | 1257 | 47 |
| H(6A) | 4619 | 6203 | 2177 | 52 |
| H(6B) | 4645 | 8462 | 2136 | 52 |
| H(7A) | 3683 | 6790 | 2306 | 44 |
| H(8A) | 3233 | 9667 | 2079 | 52 |
| H(8B) | 3827 | 10402 | 1897 | 52 |
| H(9A) | 3566 | 9290 | 1075 | 48 |
| H(9B) | 2937 | 8868 | 1236 | 48 |
| H(11A) | 2885 | 4985 | 1139 | 47 |
| H(11B) | 3188 | 4088 | 1652 | 47 |
| H(12A) | 2384 | 7063 | 1600 | 50 |
| H(12B) | 2712 | 6316 | 2121 | 50 |
| H(14A) | 2569 | 2124 | 1822 | 50 |
| H(15A) | 1854 | 0 | 1942 | 53 |
| H(16A) | 928 | 1065 | 1976 | 56 |
| H(17A) | 734 | 4291 | 1918 | 56 |
| H(18A) | 1455 | 6412 | 1815 | 50 |
| H(19A) | 4319 | 2782 | 447 | 93 |
| H(19B) | 4987 | 3147 | 493 | 93 |
| H(19C) | 4751 | 1103 | 608 | 93 |
| H(22A) | 2703 | 7437 | -539 | 121 |
| H(22B) | 2515 | 5883 | -156 | 121 |
| H(22C) | 2802 | 7800 | 60 | 121 |
| H(23A) | 3283 | 4888 | -910 | 93 |
| H(23B) | 3724 | 3716 | -531 | 93 |

| | | | | |
|---|---|---|---|---|
| H(23C) | 3058 | 3478 | -508 | 93 |
| H(24A) | 3530 | 9241 | -746 | 102 |
| H(24B) | 3398 | 9804 | -187 | 102 |
| H(24C) | 4015 | 10156 | -354 | 102 |
| H(25A) | 4214 | 6552 | -844 | 102 |
| H(25B) | 4658 | 7613 | -442 | 102 |
| H(25C) | 4486 | 5480 | -343 | 102 |
| H(26A) | 5094 | 7969 | 3613 | 78 |
| H(26B) | 4634 | 7111 | 3160 | 78 |
| H(28A) | 3711 | 6405 | 3319 | 43 |
| H(28B) | 3519 | 7016 | 3853 | 43 |
| H(30A) | 4544 | 3521 | 3652 | 43 |
| H(30B) | 4189 | 1658 | 3757 | 43 |
| H(31A) | 4070 | 3914 | 2848 | 47 |
| H(31B) | 4105 | 1654 | 2879 | 47 |
| H(32A) | 3102 | 3351 | 2709 | 43 |
| H(33A) | 2698 | 463 | 2918 | 51 |
| H(33B) | 3337 | -310 | 3090 | 51 |
| H(34A) | 3301 | 731 | 3918 | 48 |
| H(34B) | 2629 | 1154 | 3766 | 48 |
| H(36A) | 2586 | 5024 | 3882 | 45 |
| H(36B) | 2760 | 5961 | 3376 | 45 |
| H(37A) | 2177 | 3659 | 2897 | 48 |
| H(37B) | 1965 | 2982 | 3417 | 48 |
| H(39A) | 987 | 3691 | 3235 | 55 |
| H(40A) | 248 | 5817 | 3088 | 67 |
| H(41A) | 432 | 8998 | 2947 | 64 |
| H(42A) | 1370 | 9994 | 2955 | 59 |
| H(43A) | 2108 | 7858 | 3091 | 55 |
| H(44A) | 4217 | 7200 | 4585 | 83 |
| H(44B) | 4871 | 6852 | 4525 | 83 |
| H(44C) | 4602 | 8902 | 4428 | 83 |
| H(47A) | 2816 | 2514 | 5534 | 118 |
| H(47B) | 2550 | 4133 | 5160 | 118 |
| H(47C) | 2778 | 2231 | 4932 | 118 |
| H(48A) | 3504 | 4972 | 5944 | 94 |

| | | | | |
|---|---|---|---|---|
| H(48B) | 3862 | 6175 | 5582 | 94 |
| H(48C) | 3190 | 6446 | 5551 | 94 |
| H(49A) | 4427 | 3344 | 5857 | 94 |
| H(49B) | 4762 | 2302 | 5448 | 94 |
| H(49C) | 4567 | 4442 | 5360 | 94 |
| H(50A) | 3709 | 683 | 5761 | 92 |
| H(50B) | 3420 | 156 | 5204 | 92 |
| H(50C) | 4079 | -248 | 5359 | 92 |

Table 6. Torsion angles [°] for C25H37BO2.

| | |
|---|---|
| C(21)-O(1)-B(1)-O(2) | -3.0(5) |
| C(21)-O(1)-B(1)-C(4) | 179.3(4) |
| C(20)-O(2)-B(1)-O(1) | -8.1(5) |
| C(20)-O(2)-B(1)-C(4) | 169.6(4) |
| C(1)-C(2)-C(3)-C(4) | 104.8(5) |
| C(19)-C(2)-C(3)-C(4) | -77.5(5) |
| O(1)-B(1)-C(4)-C(5) | -9.6(6) |
| O(2)-B(1)-C(4)-C(5) | 173.0(4) |
| O(1)-B(1)-C(4)-C(10) | 104.1(4) |
| O(2)-B(1)-C(4)-C(10) | -73.4(5) |
| O(1)-B(1)-C(4)-C(3) | -134.9(4) |
| O(2)-B(1)-C(4)-C(3) | 47.6(5) |
| C(2)-C(3)-C(4)-C(5) | -56.3(5) |
| C(2)-C(3)-C(4)-C(10) | -167.6(4) |
| C(2)-C(3)-C(4)-B(1) | 70.8(5) |
| C(10)-C(4)-C(5)-C(6) | 39.4(4) |
| B(1)-C(4)-C(5)-C(6) | 157.5(3) |
| C(3)-C(4)-C(5)-C(6) | -76.2(4) |
| C(4)-C(5)-C(6)-C(7) | -36.4(4) |
| C(5)-C(6)-C(7)-C(8) | -79.5(4) |
| C(5)-C(6)-C(7)-C(10) | 18.5(4) |
| C(6)-C(7)-C(8)-C(9) | 99.8(4) |
| C(10)-C(7)-C(8)-C(9) | -8.6(3) |
| C(7)-C(8)-C(9)-C(10) | 8.5(3) |
| C(5)-C(4)-C(10)-C(11) | -158.5(3) |
| B(1)-C(4)-C(10)-C(11) | 80.8(4) |
| C(3)-C(4)-C(10)-C(11) | -42.0(4) |
| C(5)-C(4)-C(10)-C(7) | -27.4(4) |
| B(1)-C(4)-C(10)-C(7) | -148.1(3) |
| C(3)-C(4)-C(10)-C(7) | 89.1(4) |
| C(5)-C(4)-C(10)-C(9) | 67.7(4) |
| B(1)-C(4)-C(10)-C(9) | -53.0(4) |
| C(3)-C(4)-C(10)-C(9) | -175.8(3) |
| C(6)-C(7)-C(10)-C(11) | 135.7(4) |

| | |
|---|---|
| C(8)-C(7)-C(10)-C(11) | -108.0(4) |
| C(6)-C(7)-C(10)-C(4) | 5.8(4) |
| C(8)-C(7)-C(10)-C(4) | 122.1(3) |
| C(6)-C(7)-C(10)-C(9) | -108.0(4) |
| C(8)-C(7)-C(10)-C(9) | 8.3(3) |
| C(8)-C(9)-C(10)-C(11) | 110.6(4) |
| C(8)-C(9)-C(10)-C(4) | -115.1(4) |
| C(8)-C(9)-C(10)-C(7) | -8.4(3) |
| C(4)-C(10)-C(11)-C(12) | 179.3(3) |
| C(7)-C(10)-C(11)-C(12) | 53.7(5) |
| C(9)-C(10)-C(11)-C(12) | -47.3(5) |
| C(10)-C(11)-C(12)-C(13) | -175.6(3) |
| C(11)-C(12)-C(13)-C(18) | -150.2(4) |
| C(11)-C(12)-C(13)-C(14) | 31.8(6) |
| C(18)-C(13)-C(14)-C(15) | -1.7(6) |
| C(12)-C(13)-C(14)-C(15) | 176.4(4) |
| C(13)-C(14)-C(15)-C(16) | 1.7(6) |
| C(14)-C(15)-C(16)-C(17) | -1.0(7) |
| C(15)-C(16)-C(17)-C(18) | 0.3(7) |
| C(16)-C(17)-C(18)-C(13) | -0.3(7) |
| C(14)-C(13)-C(18)-C(17) | 0.9(6) |
| C(12)-C(13)-C(18)-C(17) | -177.2(4) |
| B(1)-O(2)-C(20)-C(22) | -105.5(4) |
| B(1)-O(2)-C(20)-C(23) | 137.1(4) |
| B(1)-O(2)-C(20)-C(21) | 14.8(4) |
| B(1)-O(1)-C(21)-C(24) | 133.7(4) |
| B(1)-O(1)-C(21)-C(25) | -109.3(4) |
| B(1)-O(1)-C(21)-C(20) | 11.8(4) |
| O(2)-C(20)-C(21)-O(1) | -15.9(4) |
| C(22)-C(20)-C(21)-O(1) | 99.5(5) |
| C(23)-C(20)-C(21)-O(1) | -132.6(4) |
| O(2)-C(20)-C(21)-C(24) | -132.5(4) |
| C(22)-C(20)-C(21)-C(24) | -17.2(6) |
| C(23)-C(20)-C(21)-C(24) | 110.7(5) |
| O(2)-C(20)-C(21)-C(25) | 99.6(4) |
| C(22)-C(20)-C(21)-C(25) | -145.0(5) |

| | |
|---|---|
| C(23)-C(20)-C(21)-C(25) | -17.1(6) |
| C(45)-O(3)-B(2)-O(4) | -9.0(5) |
| C(45)-O(3)-B(2)-C(29) | 169.1(4) |
| C(46)-O(4)-B(2)-O(3) | -3.5(5) |
| C(46)-O(4)-B(2)-C(29) | 178.3(4) |
| C(26)-C(27)-C(28)-C(29) | 105.8(5) |
| C(44)-C(27)-C(28)-C(29) | -76.2(5) |
| C(27)-C(28)-C(29)-C(30) | -56.2(4) |
| C(27)-C(28)-C(29)-C(35) | -166.9(3) |
| C(27)-C(28)-C(29)-B(2) | 71.4(5) |
| O(3)-B(2)-C(29)-C(30) | 170.6(4) |
| O(4)-B(2)-C(29)-C(30) | -11.4(6) |
| O(3)-B(2)-C(29)-C(28) | 44.8(5) |
| O(4)-B(2)-C(29)-C(28) | -137.2(4) |
| O(3)-B(2)-C(29)-C(35) | -76.6(5) |
| O(4)-B(2)-C(29)-C(35) | 101.4(4) |
| C(28)-C(29)-C(30)-C(31) | -75.5(4) |
| C(35)-C(29)-C(30)-C(31) | 40.0(4) |
| B(2)-C(29)-C(30)-C(31) | 157.5(3) |
| C(29)-C(30)-C(31)-C(32) | -36.4(4) |
| C(30)-C(31)-C(32)-C(33) | -79.8(4) |
| C(30)-C(31)-C(32)-C(35) | 17.5(4) |
| C(31)-C(32)-C(33)-C(34) | 98.6(4) |
| C(35)-C(32)-C(33)-C(34) | -9.4(3) |
| C(32)-C(33)-C(34)-C(35) | 9.5(3) |
| C(33)-C(34)-C(35)-C(36) | 109.4(4) |
| C(33)-C(34)-C(35)-C(29) | -116.0(4) |
| C(33)-C(34)-C(35)-C(32) | -9.3(3) |
| C(30)-C(29)-C(35)-C(36) | -158.7(3) |
| C(28)-C(29)-C(35)-C(36) | -42.5(4) |
| B(2)-C(29)-C(35)-C(36) | 81.0(4) |
| C(30)-C(29)-C(35)-C(34) | 66.8(4) |
| C(28)-C(29)-C(35)-C(34) | -177.0(3) |
| B(2)-C(29)-C(35)-C(34) | -53.6(4) |
| C(30)-C(29)-C(35)-C(32) | -28.6(4) |
| C(28)-C(29)-C(35)-C(32) | 87.7(4) |

| | |
|---|---|
| B(2)-C(29)-C(35)-C(32) | -148.9(3) |
| C(31)-C(32)-C(35)-C(36) | 136.1(4) |
| C(33)-C(32)-C(35)-C(36) | -107.5(4) |
| C(31)-C(32)-C(35)-C(34) | -107.2(3) |
| C(33)-C(32)-C(35)-C(34) | 9.2(3) |
| C(31)-C(32)-C(35)-C(29) | 7.2(4) |
| C(33)-C(32)-C(35)-C(29) | 123.6(3) |
| C(34)-C(35)-C(36)-C(37) | -46.7(5) |
| C(29)-C(35)-C(36)-C(37) | 179.0(3) |
| C(32)-C(35)-C(36)-C(37) | 54.4(5) |
| C(35)-C(36)-C(37)-C(38) | -172.4(3) |
| C(36)-C(37)-C(38)-C(39) | -145.8(4) |
| C(36)-C(37)-C(38)-C(43) | 36.7(6) |
| C(43)-C(38)-C(39)-C(40) | 1.1(6) |
| C(37)-C(38)-C(39)-C(40) | -176.6(4) |
| C(38)-C(39)-C(40)-C(41) | -0.8(7) |
| C(39)-C(40)-C(41)-C(42) | 0.0(7) |
| C(40)-C(41)-C(42)-C(43) | 0.5(7) |
| C(41)-C(42)-C(43)-C(38) | -0.1(7) |
| C(39)-C(38)-C(43)-C(42) | -0.6(6) |
| C(37)-C(38)-C(43)-C(42) | 177.0(4) |
| B(2)-O(3)-C(45)-C(48) | 139.1(4) |
| B(2)-O(3)-C(45)-C(47) | -103.4(4) |
| B(2)-O(3)-C(45)-C(46) | 16.5(4) |
| B(2)-O(4)-C(46)-C(49) | -107.2(4) |
| B(2)-O(4)-C(46)-C(50) | 134.9(4) |
| B(2)-O(4)-C(46)-C(45) | 13.4(4) |
| O(3)-C(45)-C(46)-O(4) | -17.7(4) |
| C(48)-C(45)-C(46)-O(4) | -134.6(4) |
| C(47)-C(45)-C(46)-O(4) | 96.4(5) |
| O(3)-C(45)-C(46)-C(49) | 98.0(4) |
| C(48)-C(45)-C(46)-C(49) | -18.9(6) |
| C(47)-C(45)-C(46)-C(49) | -147.9(5) |
| O(3)-C(45)-C(46)-C(50) | -134.6(4) |
| C(48)-C(45)-C(46)-C(50) | 108.6(5) |
| C(47)-C(45)-C(46)-C(50) | -20.5(6) |

Symmetry transformations used to generate equivalent atoms: