

# **Development of Methods for Boron Reagents**

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Dissertation submitted to the faculty of the Virginia Polytechnic Institute  
and State University in partial fulfillment of the requirements for the degree  
of

**Doctor of Philosophy  
in  
Chemistry**

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February 14, 2020  
Blacksburg, VA

Keywords: allene, semireduction, hydroboration, borylation, difluoroalkene

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## Abstract

Boron reagents are known to be valuable in the field of organic chemistry due to their abilities to undergo a variety of transformations, resulting in useful pharmaceuticals and synthetic intermediates. It has also been shown that diboron reagents can act as reaction mediators due to the unique properties of the boron atom. To that end, this dissertation discloses three novel methods of employing boron reagents.

Chapter 1 describes a method of utilizing a diboron reagent mediator in the palladium-catalyzed hydrogenation of allenes. In the presence of a palladium catalyst, tetrahydroxydiboron and stoichiometric water, allene semireduction proceeds in good yield. This semireduction is regioselective for the terminal alkene and results in the selective formation of *Z*-alkenes when used with unsymmetrical allenes (>80:20 *Z:E*). It is also compatible with more sterically hindered 1,1-diaryllallenes, resulting in tri-substituted alkenes in good yields (63-88%).

A borylation, defluorination of  $\alpha$ -trifluoromethyl- $\alpha,\beta$ -unsaturated esters is described in Chapter 2. The borylation is copper-catalyzed (10 mol %) and proceeds in the presence of stoichiometric bis(pinacolato)diboron and sodium tert-butoxide. The reaction affords compounds that contain two potentially useful functional handles: boronic esters and *gem*-difluoroalkenes. The products are obtained in moderate to good yield (up to 75%) with a large substrate scope including compounds with electron-donating, electron-withdrawing, heteroatom, and aryl substituents. In addition, the utility

of the products in further transformation is demonstrated. A proposed reaction mechanism that provides rationale for the formation of products is described along with experimental evidence.

Finally, Chapter 3 describes a transition-metal-free *trans* hydroboration of alkynoate esters and amides. The reaction is phosphine-catalyzed and proceeds with pinacolborane to afford (*E*)- $\beta$ -borylacrylates and (*E*)- $\beta$ -borylacrylamides in good to excellent yields. The reaction products are converted into novel oxaboroles through reduction with sodium borohydride. Theoretical calculations provide mechanistic insight for the transformation. The formation of a key phosphonocyclobutene intermediate is responsible for the observed stereoselectivity.

# **Development of Methods for Boron Reagents**

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## **General Audience Abstract**

Boron reagents are valuable in the field of organic chemistry due to their abilities to undergo and to facilitate a wide variety of chemical transformations. In some of these reactions, boron is transferred onto the final molecules. Compounds containing boron are valued both as pharmaceuticals and as intermediates toward the synthesis of other products. In other transformations, the diboron reagents act as reaction mediators. Often, incorporating diboron reagent mediators allows for replacement of less favorable reactants. This dissertation describes three novel uses for diboron reagents in the field of organic chemistry. The first method employs a diboron reagent mediator—replacing flammable hydrogen gas—in the hydrogenation of allenes. The second two methods are novel borylation reactions where boron is incorporated in the final molecules. These compounds are potentially useful in pharmaceuticals and organic synthesis.



## Acknowledgements

First and foremost, I would like to thank my advisor, Dr. Webster Santos, for his guidance, patience, and advice. He has been a fantastic mentor throughout my time at Virginia Tech. He challenged me to become an independent researcher, and to develop my critical thinking and leadership skills. The most important lesson I have learned from him is not to give up, no matter the road block. Without his guidance I would not be the scientist I am today.

I would also like to thank those who have served on my advisory committee, Dr. Felicia Etzkorn, Dr. John Matson, Dr. Tijana Grove, Dr. James Tanko, and Dr. Andrew Lowell. They have all been influential in the development of my writing and presentation skills. I would like to give a special thank you to Dr. Etzkorn for her guidance as a faculty mentor in the Graduate Women in Chemistry organization.

I would like to thank my colleagues in the Santos group—Elizabeth Childress, Cheryl Peck, Russell Snead, Hao Li, Ashley Peralta, Russell Fritzemeier, Eric Medici, Chris Sibley, Justin Grams, Jacob Murray, José Santiago-Rivera, Laura Wonilowicz, Chris Garcia, Daniel Foster, Johnathan Bowen, Connor Szwetkowski, Ariel Burgio, and Swetha Jos—for their support and for making my time here unforgettable. It has been a pleasure working with each and every one of you.

I would also like to thank several other friends and colleagues. To my first Virginia Tech friend and mentor, José Ángel Rodríguez Corrales—thank you for the seemingly endless time you spent teaching me new lab techniques and giving me feedback to improve my writing and presentation skills. Thank you to Elizabeth Childress, Kristýna Cagašová, and Curt Zanelotti for supporting me through my time

here. Words can't describe how much I appreciate you all. I will forever cherish the friendships I have made during my time in Blacksburg.

Finally, I would like to thank my family. To my husband, Dr. Loren Brown, thank you for your unconditional love and support. To my parents, Christopher Gates and Wanda Andrews, thank you for everything you have done to get me here and for always pushing me to be the best version of myself. Thank you to my sisters, brother, grandparents, aunts, and uncles for your encouragement throughout my time in graduate school.

## Table of Contents

Abstract.....	ii
General Audience Abstract.....	iv
Acknowledgements.....	v
List of Figures.....	x
List of Schemes.....	xi
List of Tables.....	xiii
Chapter 1. Regioselective diboron-mediated semireduction of terminal allenes.....	1
1.1 Contributions.....	1
1.2 Abstract.....	2
1.3 Allene hydrogenation in organic synthesis.....	3
1.4 Tetrahydroxydiboron mediated reductions.....	8
1.5 Optimization of reaction conditions.....	11
1.6 Substrate scope for the reduction of allenes.....	13
1.7 Proposed catalytic cycle.....	15
1.8 Conclusions.....	16
1.9 References.....	16
Chapter 2. Synthesis of borylated, <i>geminal</i> -difluoroalkenes from $\alpha,\beta$ -unsaturated esters.....	20
2.1 Contributions.....	20
2.2 Abstract.....	21
2.3 Boronic esters in organic synthesis and therapeutics.....	22
2.4 <i>gem</i> -Difluoroalkenes in organic synthesis and therapeutics.....	25
2.5 Synthesis of <i>gem</i> -difluoroalkenes.....	27

2.6	Optimization of reaction conditions for the borylation of methyl 3-phenyl-2-(trifluoromethyl)acrylate.....	29
2.7	Preparation of methyl 3-aryl-2-(trifluoromethyl)acrylates.....	32
2.8	Substrate scope for the borylation of methyl 3-aryl-2-(trifluoromethyl)acrylates.....	34
2.9	Proposed catalytic cycle and mechanistic insight into the borylation reaction.....	36
2.10	Applications.....	37
2.11	Conclusions.....	37
2.12	References.....	37
Chapter 3. Transition metal-free <i>trans</i> hydroboration of alkyneic acid derivatives: Experimental and theoretical studies.....		45
3.1	Contributions.....	45
3.2	Abstract.....	46
3.3	Hydroboration of alkynes.....	47
3.4	Results and Discussion.....	50
3.5	Applications.....	54
3.6	Mechanistic studies.....	55
3.7	Conclusions.....	59
3.8	References.....	59
Chapter 4. Experimental.....		65
4.1	General experimental methods.....	65
4.2	Instrumentation.....	65
4.3	Synthetic procedures and characterization of compounds for Chapter 1.....	66

4.4	Synthetic procedures and characterization of compounds for Chapter 2.....	83
4.5	Synthetic procedures and characterization of compounds for Chapter 3.....	106
4.6	References.....	126
Appendix A.....		133

## List of Figures

Figure 2.1 Structure of Velcade (bortezomib) 2.1 compared to the aldehyde analog 2.2.....	22
Figure 2.2 Difluoroalkenes as carbonyl mimics.....	27
Figure 2.3 Chiral ligands tested in borylation reaction.....	32
Figure 2.4 Substrates synthesized.....	33
Figure 3.1 Energy profile calculated at B3LYP/6-31G** for the proposed mechanism of <i>trans</i> hydroboration of methyl 3-phenylpropiolate.....	58

## List of Schemes

Scheme 1.1 Challenges in the reduction of allenes.....	3
Scheme 1.2 Semireduction of allenes resulting in chiral terminal alkenes.....	3
Scheme 1.3 Methods for semireduction of allenes.....	4
Scheme 1.4 Sodium-ammonia reduction of allenes.....	5
Scheme 1.5 Reduction of allenes with diimide.....	6
Scheme 1.6 Silyl-cupration/protodesilylation of allenes.....	6
Scheme 1.7 Hydrogenation of allenes with a Pd(Ar-BIAN)(alkene catalyst).....	7
Scheme 1.8 Hydrogenation of allenylphosphonates using a poisoned palladium catalyst.....	7
Scheme 1.9 Diboron-mediated production of molecular hydrogen.....	8
Scheme 1.10 Tetrahydroxydiboron mediated reduction of alkenes and alkynes.....	8
Scheme 1.11 Tetrahydroxydiboron mediated reductive amination reactions.....	9
Scheme 1.12 Diboron mediated reduction of heterocycles.....	10
Scheme 1.13 This work: Semireduction of allenes.....	10
Scheme 1.14 Substrate scope of the semireduction of 1,1-disubstituted allenes.....	13
Scheme 1.15 Substrate scope for the reduction of symmetrical allenes.....	14
Scheme 1.16 Proposed catalytic cycle.....	15
Scheme 2.1 Synthetic utility of boronic esters.....	23
Scheme 2.2 Allylboration of aldehydes.....	25
Scheme 2.3 Reactions of <i>gem</i> -difluoroalkenes.....	26
Scheme 2.4 Methods towards synthesis of <i>gem</i> -difluoroalkenes.....	27
Scheme 2.5 Methods towards synthesis of borylated <i>gem</i> -difluoroalkenes.....	28
Scheme 2.6 Synthesis of ester substrates.....	33

Scheme 2.7 Borylation of substituted 2-trifluoromethylacrylate derivatives.....	35
Scheme 2.8 Proposed catalytic cycle and mechanistic insight.....	36
Scheme 2.9 Transformations of product 2.37b.....	37
Scheme 3.1 Hydroboration of alkynes resulting in <i>cis</i> alkenes.....	47
Scheme 3.2 <i>Trans</i> hydroboration of terminal alkynes.....	47
Scheme 3.3 Transition-metal-catalyzed <i>trans</i> hydroboration of internal alkynes.....	48
Scheme 3.4 Transition-metal-free <i>trans</i> hydroboration of an internal alkyne.....	49
Scheme 3.5 Phosphine-catalyzed addition to alkynes.....	49
Scheme 3.6 This work: <i>trans</i> addition of pinacolborane to alkynoic acid derivatives.....	50
Scheme 3.7 Substrate scope for hydroboration of alkynoates.....	52
Scheme 3.8 Substrate scope for hydroboration of alkynamides.....	54
Scheme 3.9 Hydroboration of an MAO-inhibitor derivative.....	54
Scheme 3.10 Synthesis of 2-(5 <i>H</i> )-oxaboroles.....	55
Scheme 3.11 Mechanistic studies.....	56
Scheme 3.12 Proposed catalytic cycles.....	57



## List of Tables

Table 1.1 Optimization of reaction conditions for allene semireduction.....	12
Table 2.1 Optimization of reaction conditions for borylation.....	30
Table 2.2 Optimization of borylation conditions with chiral ligands.....	31
Table 3.1 Optimization of reaction conditions for hydroboration.....	51

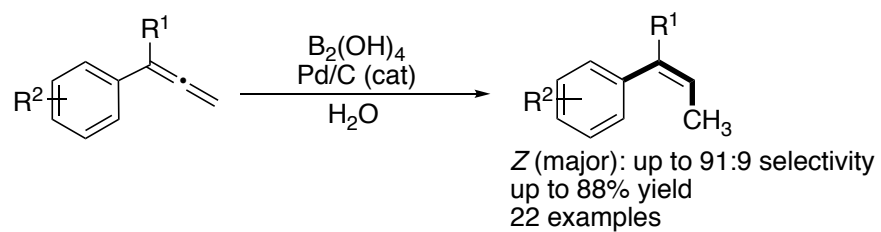
## Chapter 1. Regioselective diboron-mediated semireduction of terminal allenes

### 1.1 Contributions

The work described in this chapter was performed solely by the author. The final manuscript was prepared by the author in collaboration with Dr. Webster Santos. This work was published in *Synthesis* and is available online [Gates, A. M.; Santos, W. L. Regioselective Diboron-Mediated Semireduction of Terminal Allenes. *Synthesis*, **2019**, 51, 4619. Reproduced (adapted) with permission from Thieme.]

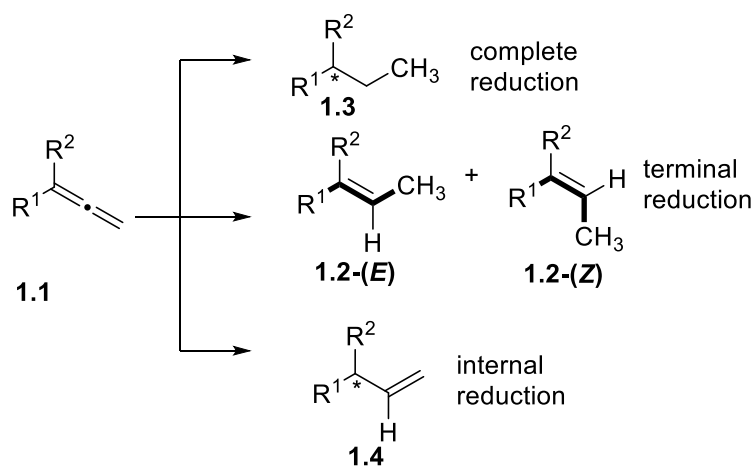
## 1.2 Abstract

A method for the regioselective reduction of the terminal double bond of 1,1-disubstituted allenes has been developed. In the presence of a palladium catalyst, tetrahydroxydiboron and stoichiometric water, allene semireduction proceeds in high yield to afford *Z*-alkenes selectively.



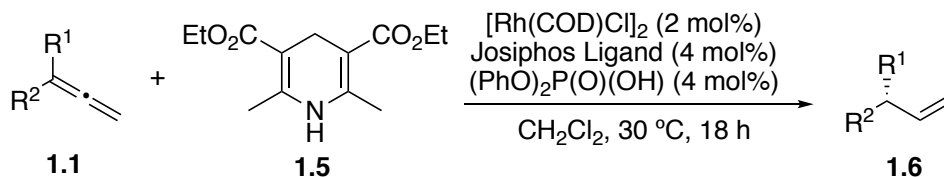
### 1.3 Allene hydrogenation in organic synthesis

Allenes are a special class of functional group because they possess unique reactivity, are important building blocks in chemical synthesis, and are a motif found in natural products.<sup>1-3</sup> Among many transformations, semireduction of allenes is challenging because of regio-, chemo- and stereoselectivity issues potentially affording up to four different products with two containing chiral centers (Scheme 1.1).



**Scheme 1.1** Challenges in the reduction of allenes

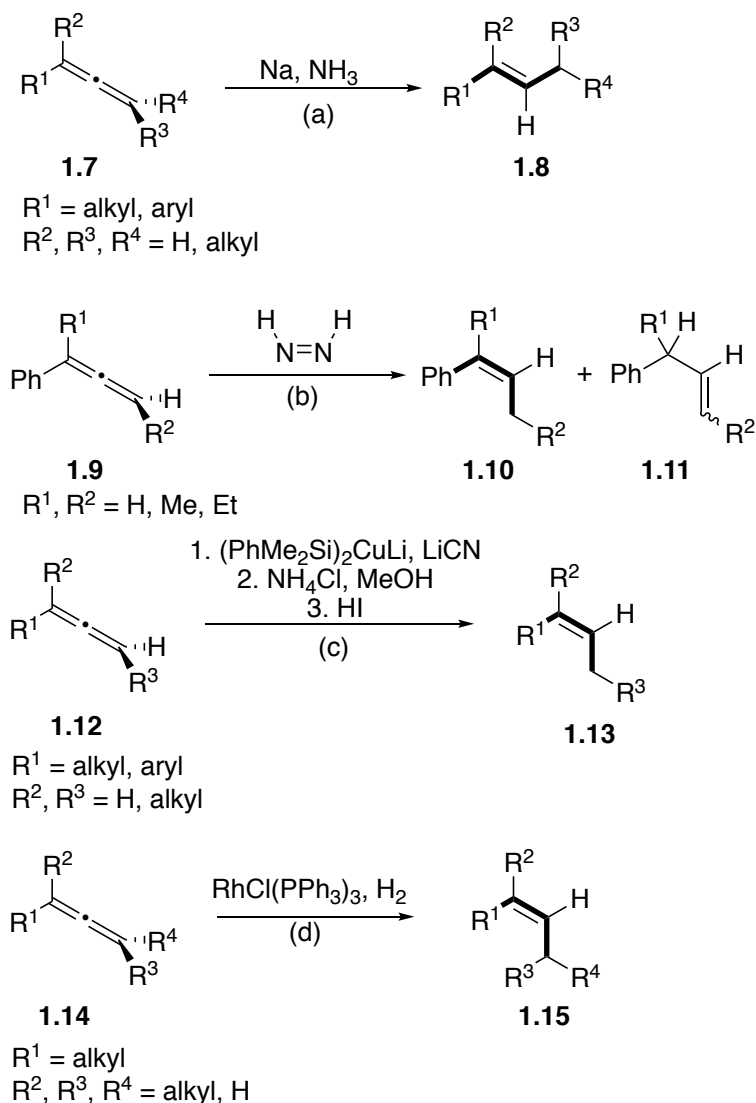
Controlling the extent of reduction such that only one equivalent of molecular hydrogen adds is difficult, and complete reduction leads to chiral alkanes. Successful semireduction of the terminal alkene leads to trisubstituted alkene **1.2**; however, the product can be confounded by a mixture of *E*- and *Z*-isomers. Furthermore, selective reduction of the internal alkene affords a chiral product bearing a terminal alkene. Toward this end, Dong and co-workers provided an approach



**Scheme 1.2** Semireduction of allenes resulting in chiral terminal alkenes.

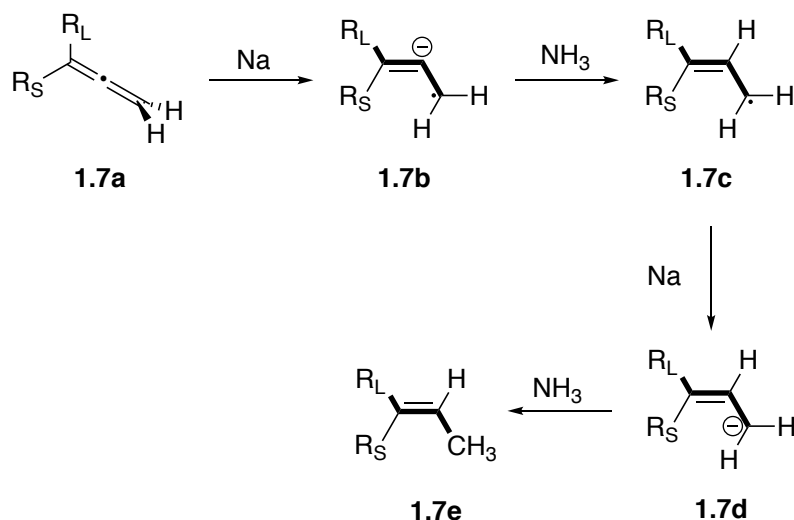
to enantioselective internal alkene reduction using a rhodium catalyst in the presence of Josiphos ligand and Hantzsch ester **1.5** as the reductant (Scheme 1.2).<sup>4</sup>

However, there are only a very limited number of investigations on the complementary terminal alkene reduction. Previously reported methods to achieve this transformation include sodium-ammonia,<sup>5</sup> diimide,<sup>6, 7</sup> silyl-cupration/protodesilylation,<sup>8</sup> and rhodium catalyzed hydrogenation (Scheme 1.3).<sup>9</sup> Unfortunately, these methods suffer from several limitations including severely narrow substrate scopes, low stereoselectivity, poor yields and/or harsh reaction conditions.



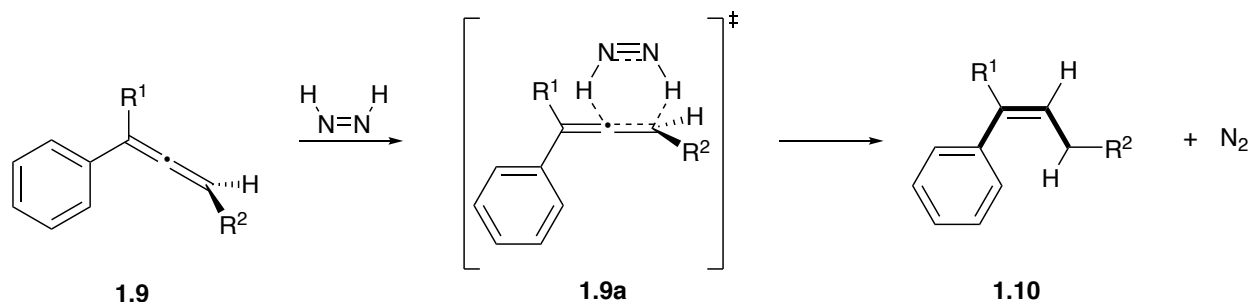
**Scheme 1.3.** Methods for semireduction of allenes.

Sodium-ammonia reduction of mono-, di-, and tetra-substituted allenes was studied in 1970 by Nagendrappa et al. (Scheme 1.3a).<sup>5</sup> The reaction proceeds through a radical mechanism which begins with the donation of an electron from sodium to the allene pi-bond. The formation of the more stable anion intermediate **1.7a**—where the larger R-group is oriented *cis* to the lone pair—drives reaction selectivity towards *trans*-alkene product **1.8** (>92:8 *trans*:*cis*).



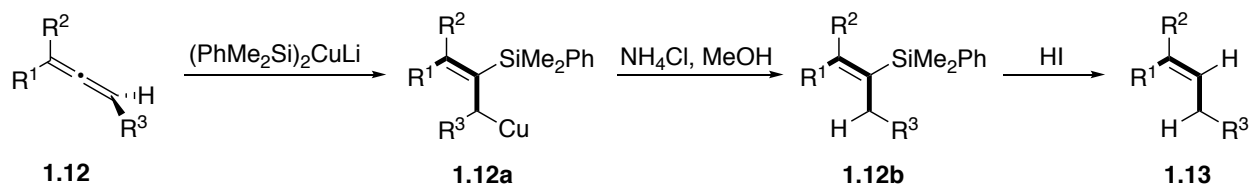
**Scheme 1.4.** Sodium-ammonia reduction of allenes.

Nagendrappa et al. also reported the semireduction of allenes with diimide in 1970.<sup>7</sup> In 1980, a more extensive study examining the effects of allene substituents was released by Fueno and co-workers.<sup>6</sup> The reaction proceeds through a 6-membered ring transition state, resulting in *Z*-alkene products (**1.10**, Scheme 1.5). It was found that for the monosubstituted allene and the 1,1-disubstituted allene, the reaction was selective for reduction of the terminal olefin, resulting in **1.10** as the major product. When an alkyl substituent was present in the R<sup>2</sup>-position, the alkene nearest the phenyl group was activated, resulting in a loss of regioselectivity and thus, a mixture of products **1.10** and **1.11** (Scheme 1.3b).



**Scheme 1.5.** Reduction of allenes with diimide.

Allenes also regioselectively undergo silyl-cupration as reported by Fleming and Rowley in 1988 (Scheme 1.3c).<sup>8</sup> Addition of a silyl-cuprate reagent across the terminal pi-bond results in copper-silyl species **1.12a** (Scheme 1.6). Protodecupration with ammonium chloride and methanol resulted in the vinyl silyl species **1.12b**. Protodesilylation with hydroiodic acid resulted in *Z*-alkene **1.13**.

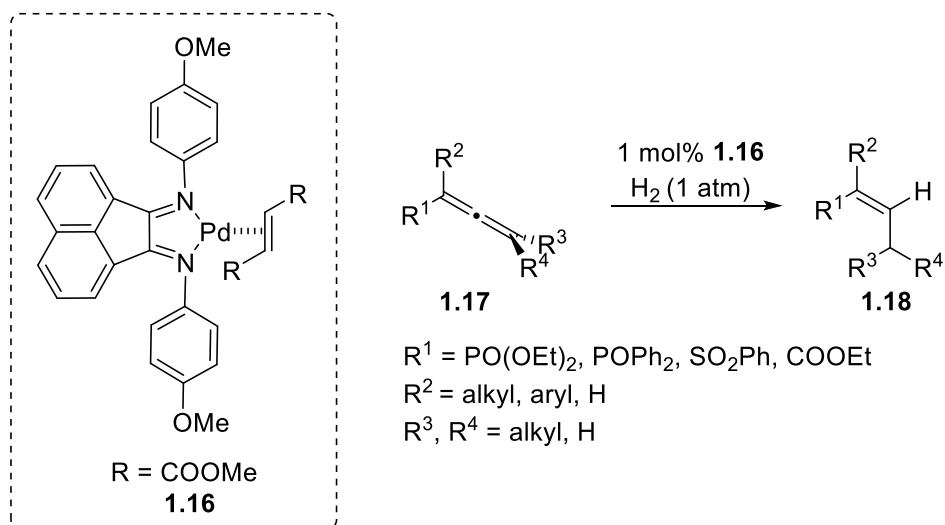


**Scheme 1.6.** Silyl-cupration/protodesilylation of allenes.

Transition-metal-catalyzed hydrogenation with a rhodium catalyst was published by Bhagwat and Devaprabhakara in 1972.<sup>9</sup> Seven alkyl allenes (**1.14**, Scheme 1.3d) were reduced to the corresponding *Z*-alkenes (**1.15**, Scheme 1.3d). The reaction was regioselective with hydrogenation of the least substituted alkene occurring preferentially. Interestingly, neither isomerization nor over-reduction to the saturated olefin were observed.

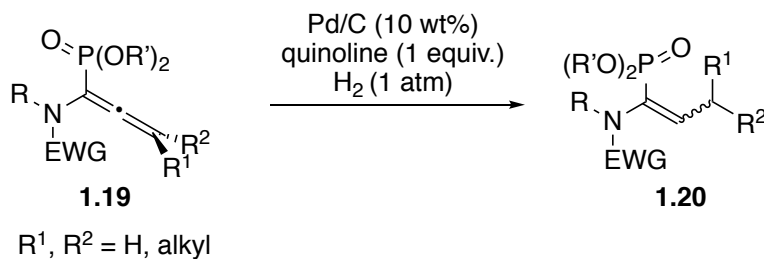
More recently, allenylphosphonates, phosphine oxides, sulfones and allenoates were shown to be efficient substrates in partial hydrogenations utilizing a [palladium(bis(arylimino)acenaphthene)(alkene)] complex (Scheme 1.7).<sup>10</sup> The reaction is *Z*-selective and products **1.18** were isolated in good to excellent yields (68-99%); however, the

reaction requires the use of a designer palladium complex (**1.16**) and the substrate scope was limited to the aforementioned functional groups.



**Scheme 1.7.** Hydrogenation of allenes with a Pd(Ar-BIAN)(alkene) catalyst.

In addition,  $\alpha$ -amino vinylphosphonates were synthesized by partial reduction of  $\alpha$ -amino allenylphosphonates (**1.19**, Scheme 1.8) with a poisoned palladium catalyst under a hydrogen atmosphere.<sup>11</sup> While the products (**1.20**) were isolated in moderate to excellent yields (47-97%), the *Z:E* selectivity was extremely variable (25:75 to 96:4) and highly dependent upon the sizes of the R and R' groups.



**Scheme 1.8.** Hydrogenation of allenylphosphonates using a poisoned palladium catalyst.

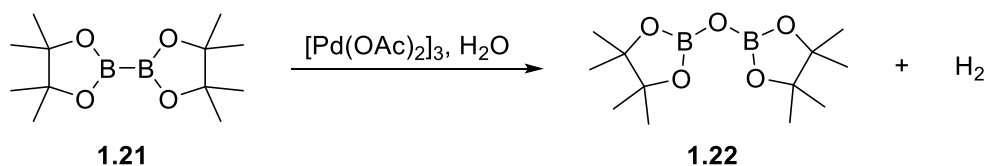
As described above, the current methods for the semireduction of allenes suffer from a variety of limitations, including extremely limited substrate scopes, harsh reaction conditions, and limited stereoselectivity. Our interest in the reactivity of allenes and their conversion into motifs



useful in medicinal and synthetic chemistry persuaded us to investigate a milder, diboron-mediated semireduction approach.<sup>12-14</sup>

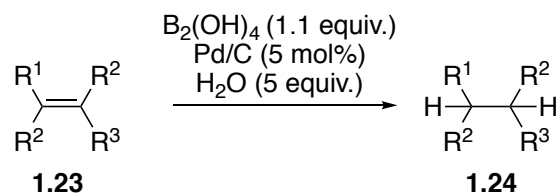
#### 1.4 Tetrahydroxydiboron mediated reductions

In 2016, Prabhu and co-workers demonstrated that molecular hydrogen could be released from water in the presence of bis(pinacolato)diboron and a palladium catalyst. The authors also found that the hydrogen generated could be used to hydrogenate a variety of olefins.<sup>15</sup> Diboron/water systems have been employed in a variety of applications including hydrogenation of alkenes and alkynes,<sup>16</sup> reductive amination,<sup>17-19</sup> hydrogenation of heterocycles<sup>20, 21</sup> and nitro reductions in DNA.<sup>22</sup>



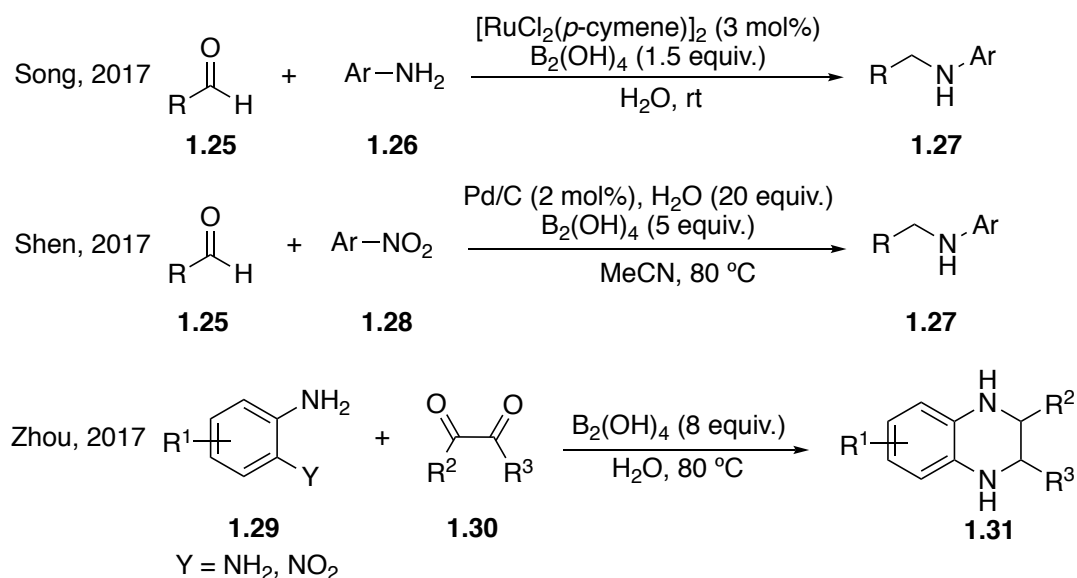
**Scheme 1.9.** Diboron-mediated production of molecular hydrogen.

Stokes and co-workers reported a diboron-mediated palladium-catalyzed hydrogenation of alkenes and alkynes using stoichiometric amounts of tetrahydroxydiboron to furnish the corresponding alkanes.<sup>16</sup> The reactions proceeded with excellent yields for a variety of aryl and alkyl substituted alkenes; however, decrease in yields was observed for styrenes with sensitive functional groups (such as nitro) and for alkenyl and aryl bromides due to a variety of side reactions (reduction of nitro-groups, styrene polymerization, etc).



**Scheme 1.10** Tetrahydroxydiboron mediated reduction of alkenes and alkynes.

There are several examples in the literature of the use of the tetrahydroxydiboron/water system to facilitate reductive amination (Scheme 1.11). Song<sup>17</sup> and co-workers published a rhodium-catalyzed reductive amination between aldehydes (**1.25**) and aryl amines (**1.26**). The reaction proceeded in good to excellent yield (73-92%) for a variety of aliphatic and aromatic aldehydes. Additionally, the authors were able to synthesize a series of  $\alpha$ -deuterated secondary amines by employing D<sub>2</sub>O as the solvent.



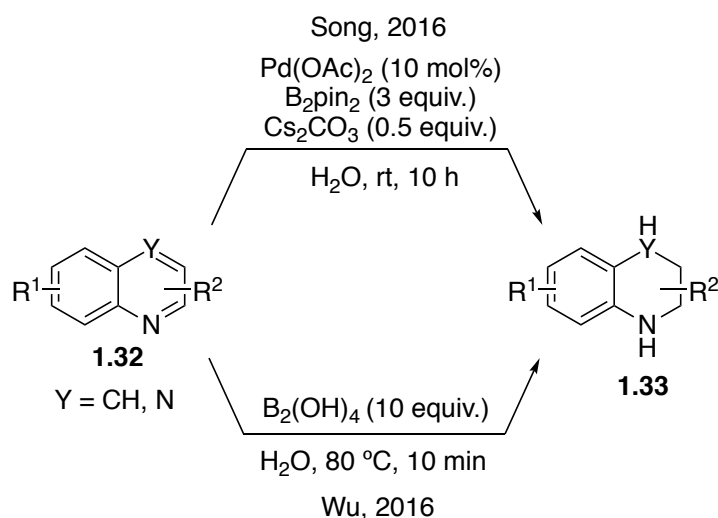
**Scheme 1.11.** Tetrahydroxydiboron mediated reductive amination reactions.

Shen<sup>19</sup> and co-workers published a palladium-catalyzed reductive amination between aldehydes (**1.25**) and nitroarenes (**1.28**, Scheme 1.11). When nitroarenes were exposed to the reaction conditions without aldehydes present, anilines were obtained in good to excellent yield (64-99%), indicating the first step of the reaction is the reduction of the nitroarene, followed by a reductive amination step.

A transition-metal-free reductive amination was achieved by Zhou and co-workers (Scheme 1.11).<sup>18</sup> Excess tetrahydroxydiboron was needed to facilitate the reduction of 2-

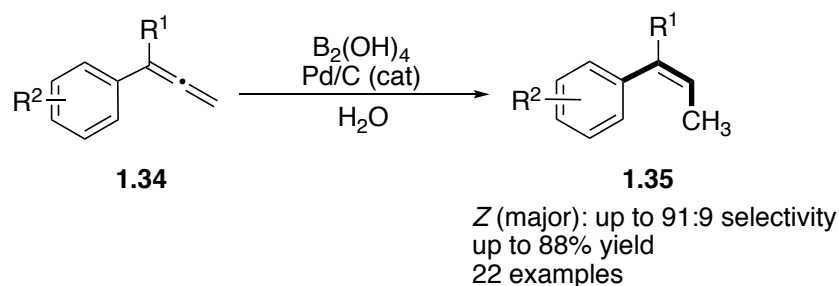
nitroanilines to 2-aminoanilines. Cyclization of the 2-aminoanilines with dicarbonyls (**1.30**) followed by hydrogenation led to the formation of tetrahydroquinoxalines (**1.31**).

Hydrogenation of heterocycles using diboron reagents has been shown to occur with and without transition-metal-catalysts. Song and Xuan's palladium-catalyzed reaction provided a variety of hydrogenated heterocycles (**1.33**, Scheme 1.12).<sup>21</sup> Without a transition-metal-catalyst, Wu and co-workers found a large excess of tetrahydroxydiboron and heat were necessary to facilitate the same types of transformations.<sup>20</sup>



**Scheme 1.12.** Diboron mediated reduction of heterocycles.

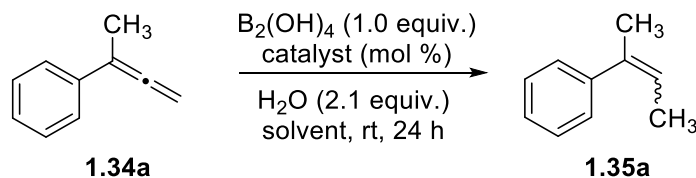
Inspired by these works, we investigated the applicability of diboron reagents in the semi-hydrogenation of allenes to produce *Z* alkenes (Scheme 1.13).



**Scheme 1.13.** This work: semireduction of allenes.

## 1.5 Optimization of reaction conditions

We began our study by using tetrahydroxydiboron, water and a palladium catalyst. The initial reaction conditions provided the desired product **1.35a** in good yield and *Z* selectivity (Table 1, entry 1). A variety of solvent conditions were subsequently screened. While methanol resulted in a very low yield (entry 2), diethylether and methyl *tert*-butylether afforded the product in good yield (entries 3, 4). Unfortunately, hexanes and THF resulted in poor yield and selectivity (entries 5, 6). Reducing the catalyst loading from 10 mol% to 5 mol% (entry 7) did not affect the yield. Next, a variety of palladium catalysts were evaluated. For example, Lindlar's catalyst and Pd(dppf)Cl<sub>2</sub> essentially shut down double bond hydrogenation (entries 8, 9). However, palladium hydroxide and palladium acetate restored activity, albeit in reduced yields (entries 10, 11). Switching to other transition metal catalysts, platinum on carbon and platinum oxide, induced an improvement in *Z/E* selectivity; however, these reactions suffered from poor yields and further optimization did not lead to substantial improvement (entries 12, 13). Rhodium did not afford any of the desired product (entry 14). When tetrahydroxydiboron and palladium catalyst were removed independently from the reaction, no product was observed suggesting their essential roles for the transformation (entries 15, 16). When exploring alternative diboron reagents, we found that bis(pinacolato)diboron and bis(catecholato)diboron were less effective mediators (entries 17, 18). As both dichloromethane and diethylether were equally efficient, we chose diethyl ether as the solvent and Pd/C as the transition metal catalyst (entry 3). The *E/Z* configuration was determined using nOe experiments. In general, additional tetrahydroxydiboron could be added to force the conversion of the reaction.

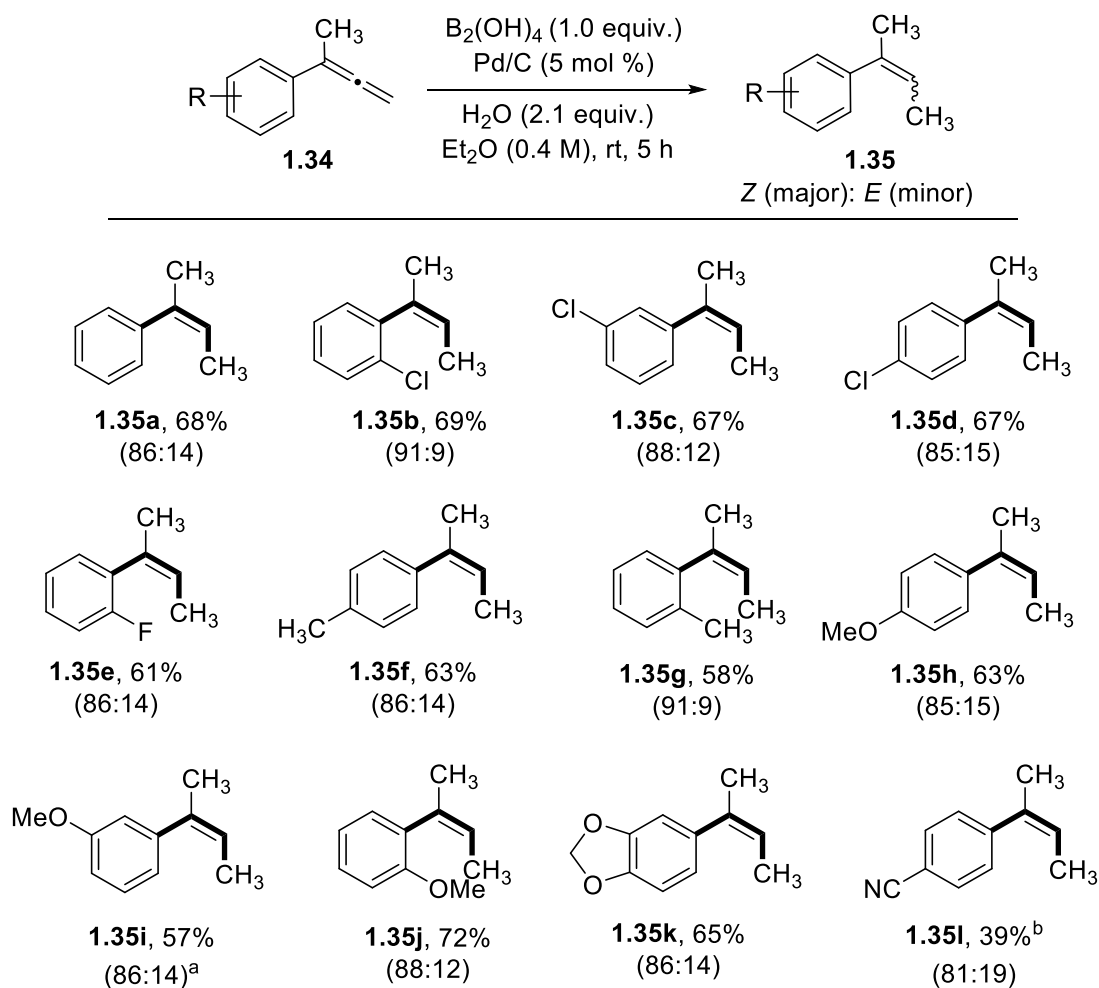
**Table 1.1.** Optimization of reaction conditions for allene semireduction.

Entry	Catalyst (mol %)	Solvent	<i>Z</i> : <i>E</i>	% Yield (%conversion)
1	Pd/C (10)	CH <sub>2</sub> Cl <sub>2</sub>	85:15	70 (99)
2	Pd/C (10)	MeOH	81:19	18 (56)
3	Pd/C (10)	Et <sub>2</sub> O	86:14	68 (93)
4	Pd/C (5)	MTBE	84:16	62 (82)
5	Pd/C (5)	hexanes	75:25	46 (99)
6	Pd/C (5)	CH <sub>2</sub> Cl <sub>2</sub>	85:15	69 (99)
7	Lindlar's cat (10)	CH <sub>2</sub> Cl <sub>2</sub>	-	0 (24)
8	Pd(dppf)Cl <sub>2</sub> (5)	CH <sub>2</sub> Cl <sub>2</sub>	-	0 (18)
9	Pd(OH) <sub>2</sub> /C (10)	CH <sub>2</sub> Cl <sub>2</sub>	83:17	54 (73)
10	Pd(OAc) <sub>2</sub> (10)	CH <sub>2</sub> Cl <sub>2</sub>	84:16	59 (88)
11	Pt/C (5)	CH <sub>2</sub> Cl <sub>2</sub>	89:11	29 (63)
12	PtO <sub>2</sub> (10)	CH <sub>2</sub> Cl <sub>2</sub>	91:9	33 (80)
13	Rh/C (5)	CH <sub>2</sub> Cl <sub>2</sub>	-	0 (27)
14 <sup>b</sup>	Pd/C (5)	CH <sub>2</sub> Cl <sub>2</sub>	-	0 (5)
15	-	CH <sub>2</sub> Cl <sub>2</sub>	-	0 (9)
16	Pd/C <sup>c</sup> (5)	CH <sub>2</sub> Cl <sub>2</sub>	85:15	32 (50)
17	Pd/C <sup>d</sup> (5)	CH <sub>2</sub> Cl <sub>2</sub>	87:13	37 (90)

<sup>a</sup>Buta-2,3-dien-2-ylbenzene (0.38 mmol), tetrahydroxydiboron (0.38 mmol), metal catalyst, and water (0.81 mmol) were dissolved in indicated solvent and stirred under inert atmosphere. Conversions and yields determined via <sup>1</sup>H NMR using 1,3,5-trimethoxybenzene as an internal standard. <sup>b</sup>Reaction performed without B<sub>2</sub>(OH)<sub>4</sub>. <sup>c</sup>Boron source was bis(pinacolato)diboron. <sup>d</sup>Boron source was bis(catecholato)diboron. MTBE = methyl *tert*-butylether

## 1.6 Substrate scope for the reduction of allenes

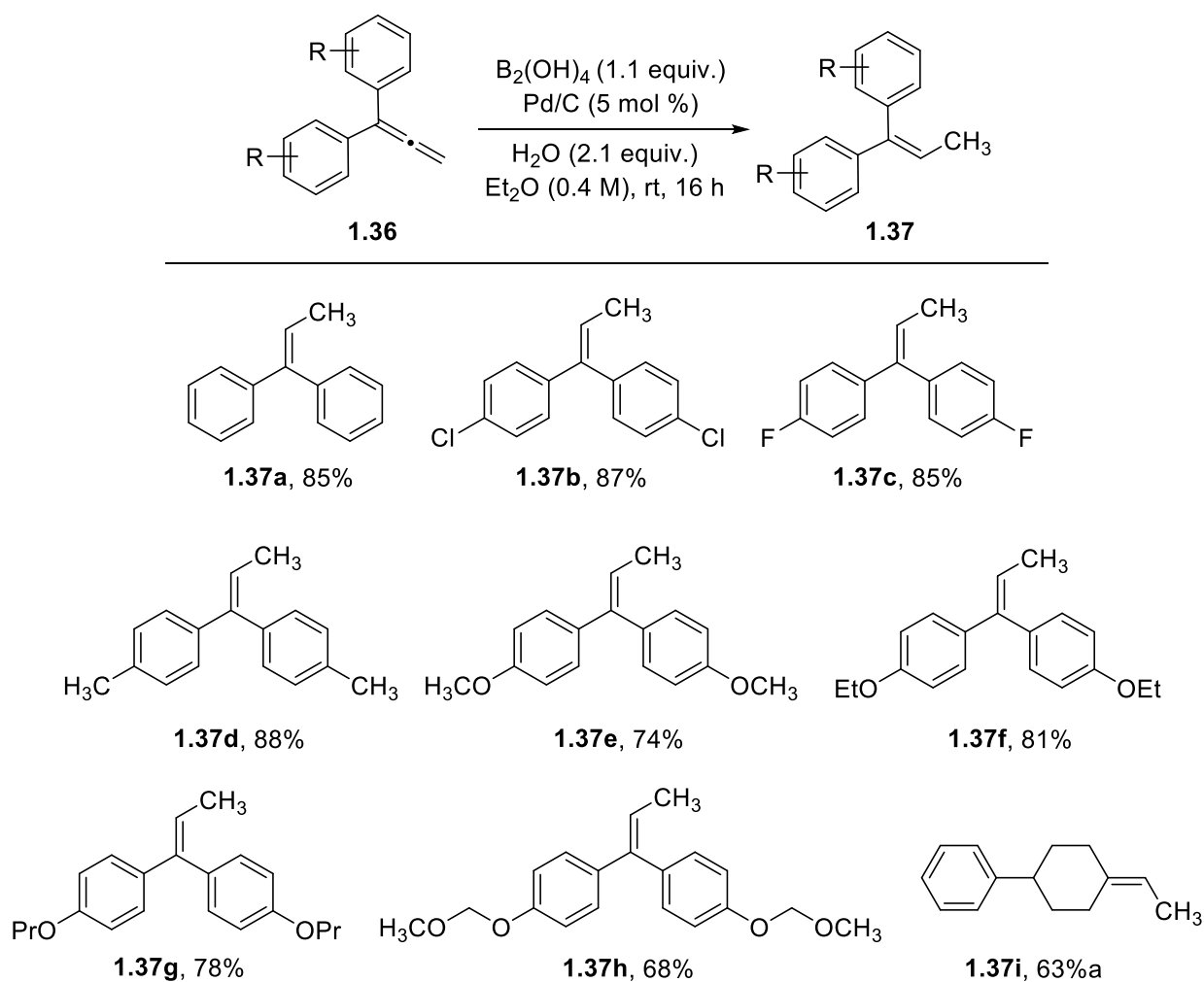
With optimized conditions in hand, a series of substrates was evaluated to determine the steric and electronic effects on the semireduction procedure (Scheme 1.14). Electron- withdrawing substituents, such as chlorine, were well tolerated in the *ortho*, *meta*, and *para* positions (**1.35b-d**). A fluorine atom in the *ortho* position was also an efficient substrate affording alkene **1.35e** in 61% yield. Electron-donating substituents such as methyl (**1.35f-g**) or methoxy (**1.35h-j**) also proved to be well-tolerated at various positions. An aryl ring with methylenedioxy substitution



**Scheme. 1.14.** Substrate scope of the semireduction of 1,1-disubstituted allenes. % Yield calculated via <sup>1</sup>H NMR using 1,3,5-trimethoxybenzene as an internal standard and refers to the sum of inseparable isomers. Reaction conversions are 94-100% unless stated otherwise. <sup>a</sup>90% conversion. <sup>b</sup>88% conversion.

(**1.35k**) also served as a good substrate. The presence of a cyano moiety in the *para* position resulted in a small reduction in yield and selectivity (**1.35l**). The stereoselectivity of the reaction was generally very good with 85-90% *Z* selectivity.

We also investigated a series of symmetrical, diaryl-substituted allenes (**1.36**, Scheme 1.15). These substrates resulted in much improved isolated yields, although longer reaction times (16 h) and a slight increase in the amount of tetrahydroxydiboron used (1.1 equiv instead of 1.0) were required. For example, 1,1-diphenyl allene (**1.36a**) reacted to afford **1.37a** in 85% yield. Electron-withdrawing groups, such as chloro and fluoro, produced the corresponding products

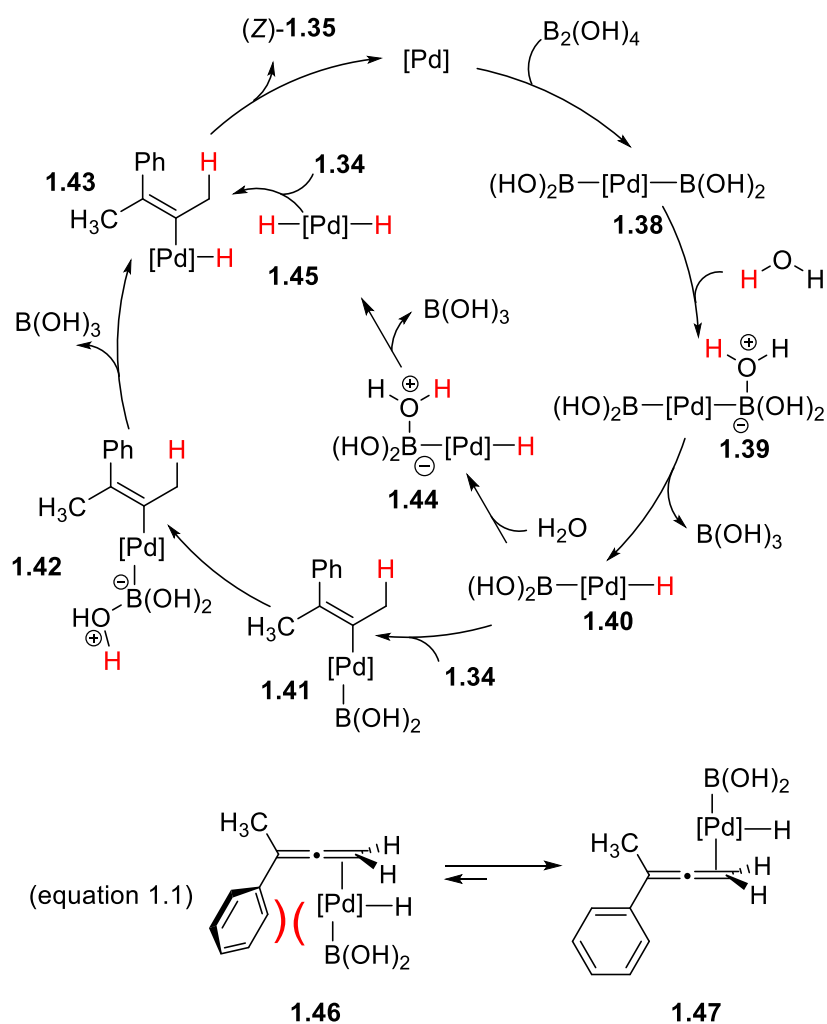


**Scheme 1.15.** Substrate scope for the reduction of symmetrical allenes. Isolated yields.

**1.37b**, **1.37c** in high yields. Electron-donating groups, such as methyl or alkyl ethers (**1.37d-g**), were also afforded in high yields. The current method is also compatible with protecting groups such as methoxymethyl (**1.37h**). Finally, an alkyl-substituted allene was tested and was reduced in good yield (**1.37i**).

## 1.7 Proposed catalytic cycle

The proposed catalytic cycle for allene semireduction is illustrated in Scheme 1.16.<sup>[10]</sup> First, palladium inserts into the B–B bond of tetrahydroxydiboron to generate intermediate **1.38**. A water molecule acts as a Lewis base to form a tetracoordinate boron (**1.39**) and a hydrogen atom is then



**Scheme 1.16.** Proposed catalytic cycle.



transferred to palladium forming **1.40** and releasing boric acid. We suspect that the stereoselectivity of the reaction is governed by the initial contact between the metal and allene, affording the *Z* configuration preferentially (Scheme 1.16, equation 1.1). Thus, the palladium hydride complex coordinates to allene **1.34** on the less sterically hindered side, i.e., on the side opposite of the phenyl ring. Palladium insertion on the allene yields **1.41**. Then, a second molecule of water coordinates to the boron atom, and the intermediate undergoes another hydrogen atom transfer to form palladium hydride complex **1.43**. Alternatively, dihydride formation could precede migratory insertion to generate **1.45**. Finally, reductive elimination of **1.43** forms the reduced product **1.35** and regenerates the active catalyst.

## 1.8 Conclusions

In conclusion, we have developed a method for the regioselective semireduction of terminal allenes. The semireduction of unsymmetrical allenes results in the formation of *Z*-alkenes in moderate to good yield. Semireduction of diaryl allenes proceeds in good yield. The protocol utilizes a diboron-mediated activation of water to generate catalytically competent palladium hydride for the reduction. The products generated could be useful as commodity materials for further chemical transformation.

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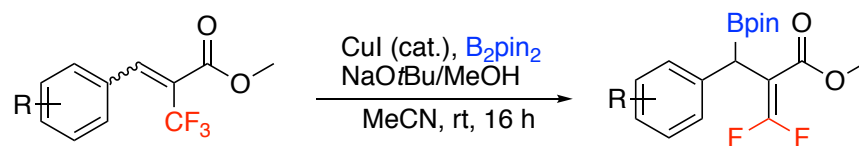
## Chapter 2. Synthesis of borylated, *geminal*-difluoroalkenes from $\alpha,\beta$ -unsaturated esters

### 2.1 Contributions

The work described in this chapter was performed in collaboration with Swetha Jos. The author is responsible for the optimization of borylation conditions, synthesis and characterization of substrates **2.36h-j**, **2.36l**, and **2.36p**, synthesis and characterization of compounds **2.37a-t**, the synthesis and characterization of substrate **2.38b** for the mechanistic study, and the synthesis and characterization of application products **2.45** and **2.46**. Swetha Jos synthesized and characterized substrates **2.36c-d**, **2.36g**, **2.36k**, **2.36o**, and **2.36q-u**. The syntheses of substrates **2.36a-b**, **2.36e-f**, **2.36m-n** were performed by the author and duplicated by Swetha Jos. The manuscript was prepared by the author and reviewed by Dr. Webster Santos in preparation for submission.

## 2.2 Abstract

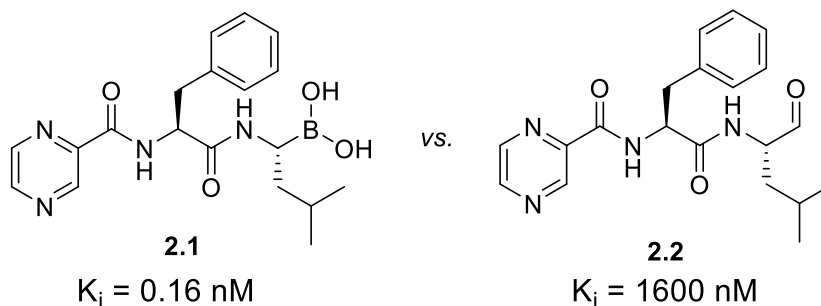
We report a copper-catalyzed  $\beta$ -borylation, defluorination of  $\alpha,\beta$ -unsaturated esters. The reaction affords borylated, *geminal*-difluoroalkenes in good yield. Products of the reaction exhibit dual functional handles that are known to be useful in the synthesis of small molecule building blocks. The synthetic utility of the products was demonstrated through nucleophilic substitution at the *gem*-difluoroalkene.



### 2.3 Boronic esters in organic synthesis and therapeutics

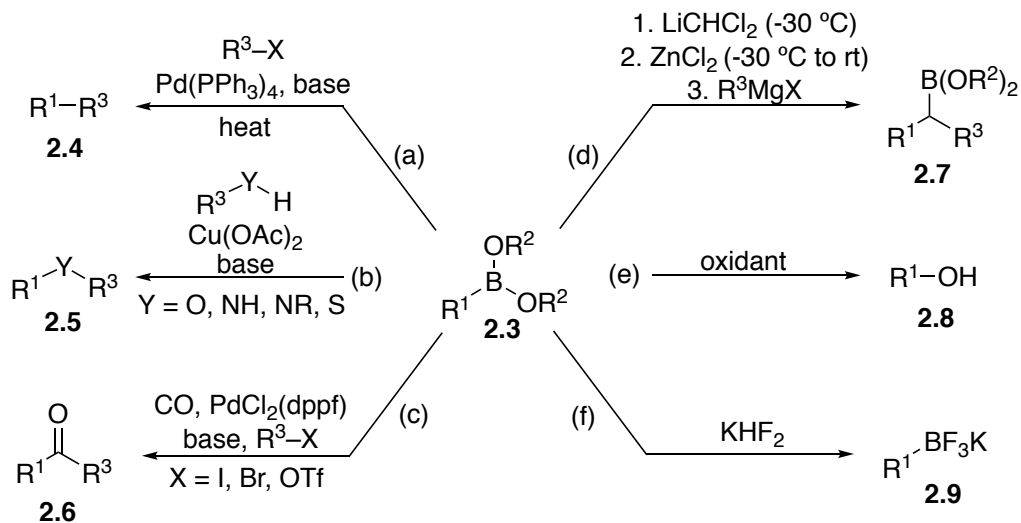
Compounds bearing boronic esters are known to be versatile small molecule building blocks as they readily undergo a variety of transformations. Although the first boronic acid was isolated in 1860,<sup>1</sup> the importance of this class of compounds was not realized for over a century. In 1979, the Suzuki-Miyaura cross-coupling reaction was reported and an exponential growth in boron chemistry followed.<sup>2</sup> While this newfound notoriety can be attributed to the introduction of the palladium-catalyzed cross-coupling reaction, boronic acid derivatives have since been shown to function as effective therapeutics as well as excellent building blocks in the synthesis of natural products and pharmaceuticals.<sup>3</sup>

Boronic acids made their debut in medicinal chemistry in 2003 with the introduction of Velcade (bortezomib, **2.1**), the first FDA-approved boronic acid-containing drug (Fig. 2.1).<sup>4</sup> The dipeptide is an effective proteasome inhibitor used in the treatment of multiple myeloma.<sup>5</sup> The reversible covalent interaction between the boron atom in the drug molecule and a threonine residue in the binding pocket of the 26S proteasome leads to cell apoptosis.<sup>6</sup> As demonstrated by the inhibition constants of **2.1** and **2.2**, the boron moiety provides far superior inhibition to that of the boronic acid's isostere **2.2**.<sup>4</sup> More recently, several boron-containing drugs have entered the market; therefore, investigations into new boron-containing molecules are warranted.



**Figure 2.1** Structure of Velcade (bortezomib) **2.1** compared to the aldehyde analog **2.2**.

As synthetic intermediates, boronic acids and their derivatives are utilized in a myriad of reactions for the formation of C–C, C–N, and C–O bonds (Scheme 2.1). The Suzuki-Miyaura cross-coupling reaction is perhaps one of the most useful reactions in the formation of C–C bonds commonly found in natural products and synthetic intermediates (Scheme 2.1a). The original study published in 1979 demonstrated the cross-coupling of boronic esters (such as **2.3**) with 1-alkenyl and 1-alkynyl halides;<sup>2</sup> however, the substrate scope has since been expanded upon so extensively that Suzuki, along with Heck and Negishi, was awarded the 2010 Nobel prize for the cross-coupling work.<sup>7</sup>



**Scheme 2.1.** Synthetic utility of boronic esters.

Another common transformation of boronic esters is the Chan-Evans-Lam cross-coupling reaction (Scheme 2.1b). The protocols published by Chan,<sup>8</sup> Evans,<sup>9</sup> and Lam<sup>10</sup> in 1998 described copper(II)-catalyzed reactions for the coupling of aryl boronic acids with amines, amides, and aryl alcohols using a base and atmospheric oxygen to form new C–O and C–N bonds. Since the original disclosure, it has been shown that thiols are also capable coupling partners as well.<sup>11</sup>



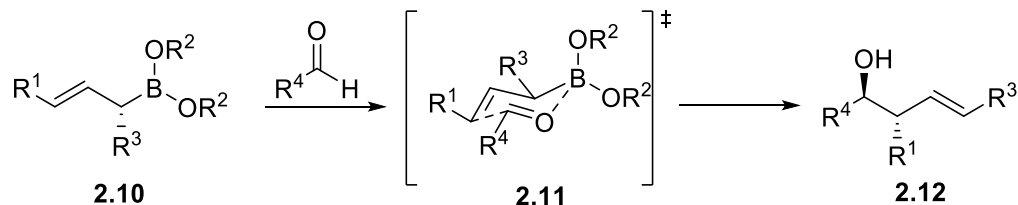
Boronic esters also undergo carbonylative coupling (Scheme 2.1c). Ishiyama et al. published the carbonylative coupling of boronic acids with aryl electrophiles, providing a milder alternative to the Friedel-Crafts acylation for the synthesis of unsymmetrical biaryl ketones.<sup>12</sup> Carbon monoxide acts as the C=O source in the palladium(0)-catalyzed method.

Homologation-alkylation reactions can introduce, with a high degree of stereoselectivity, a chiral center into a boronic ester-containing compound (Scheme 2.1d).<sup>13</sup> Due to the Lewis-acidity of boron, nucleophiles readily bind to boronic esters. If the nucleophile contains a leaving group on the  $\alpha$ -carbon, a 1,2-metallate rearrangement will occur. Subsequent treatment with a Grignard reagent results in alkylation and formation of the chiral boronic ester **2.7**.

Boronic esters also readily undergo oxidation to alcohols in the presence of a variety of different oxidants (Scheme 2.1e).<sup>14</sup> Commonly used reagents include Oxone<sup>15</sup> and hydrogen peroxide.<sup>16</sup> Oxidation in the presence of some more sensitive functional groups can be performed with sodium perborate.<sup>17</sup>

Finally, boronic esters can be converted into the more stable trifluoroborate salts (**2.9**, Scheme 2.1f).<sup>18</sup> Due to the tetracoordinate nature of the boron atom in the salt, as well as the strength of the B–F bond, these compounds are less reactive and are stable to air and moisture.

As with other boronic esters, allyl boronates also undergo a wide variety of synthetic transformations.<sup>19-21</sup> These organoborons have been used as substrates for many different reactions including oxidation, cross-coupling reactions,<sup>22-24</sup> and allylboration of carbonyls.<sup>25-31</sup> In an allylboration, allyl boronate **2.10** reacts with a carbonyl group. The stereoselectivity of the reaction is demonstrated through the 6-membered chair transition-state **2.11**. Stereoselectivity can be controlled by tailoring the size of the boronic ester.<sup>32</sup>



**Scheme 2.2.** Allylboration of aldehydes.

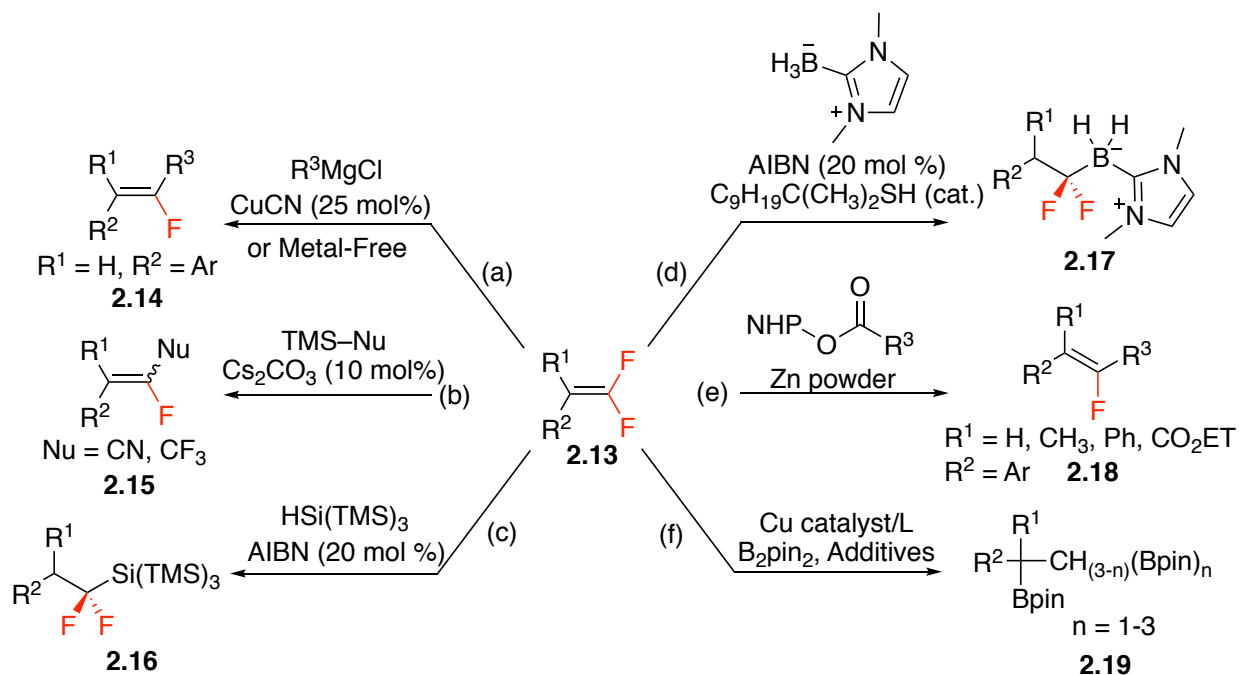
## 2.4 *Gem*-difluoroalkenes in organic synthesis and therapeutics

Like organoborons, *gem*-difluoroalkenes are valuable synthetic intermediates.<sup>33</sup> Some important transformations for the functional group include cross-coupling,<sup>34, 35</sup> nucleophilic substitution,<sup>36, 37</sup> hydroboration and hydrosilylation,<sup>38</sup> alkylation,<sup>39</sup> alkenylation,<sup>40</sup> and multiborylation.<sup>41</sup> Scheme 2.3 shows just a few examples of transformations of the functional group.

In a 2016 publication, Dai et al. reported a copper-catalyzed cross-coupling of *gem*-difluoroalkenes with primary, secondary, and tertiary Grignard reagents resulting exclusively in *Z*-alkene products **2.14** (Scheme 2.3a).<sup>34</sup> Secondary and tertiary alkylation proceeded under transition-metal-free conditions affording *Z*-alkenes; however, selectivity was lost for primary Grignard reagents under the metal-free conditions.<sup>34</sup>

Due to the electrophilicity of the carbon atom bearing the two fluorine atoms, *gem*-difluoroalkenes make excellent electrophiles for nucleophilic substitution reactions (Scheme 2.3b). Jiang et al. published a carbonate-catalyzed nucleophilic substitution using TMS-protected nucleophiles. The addition-elimination reaction occurs when the nucleophile ( $\text{CF}_3^-$  or  $\text{CN}^-$ ) displaces a fluorine atom, likely facilitated by TMS due to the fluorophilic nature of silicon atoms. For the cyanation reaction, *E*-isomers were the favored products due to the unfavorable electronic repulsion between a fluorine atom and the aryl  $\text{R}^1$  substituent in the intermediate. For trifluoromethylation, the steric and electronic repulsion between the  $\text{CF}_3$  group and the aryl group is more disfavored, resulting in the *Z*-isomers. When  $\text{R}^2$  is a hydrogen atom, the reaction exhibits

complete selectivity; however, when R<sup>2</sup> is larger than hydrogen, the selectivities for the cyanation and trifluoromethylation are E/Z = 7:1 and 1:6, respectively.



**Scheme 2.3.** Reactions of *gem*-difluoroalkenes.

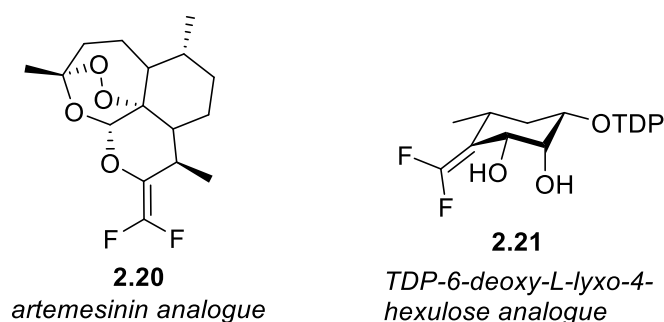
Liu et al. recently published methods for the radical hydrosilylation (Scheme 2.3c) and hydroboration (Scheme 2.3d) of *gem*-difluoroalkenes to form difluorinated alkylsilanes **2.16** and alkylboranes **2.17**, respectively.<sup>38</sup> Catalytic AIBN acts as the initiator for the reactions, which begin with a hydrogen abstraction from the borane or silane starting materials.

Sun and co-workers published a zinc-catalyzed decarboxylative alkylation of *gem*-difluoroalkenes with NHP (*N*-hydroxyphthalimide) esters (Scheme 2.3e).<sup>39</sup> The reaction proceeds through a radical mechanism, which is initiated by a single electron transfer from zinc to the NHP ester. The reaction is *Z*-selective due to the anticoplanar elimination of fluoride from the radical intermediate.

Finally, Hu et al. published a copper-catalyzed multi-borylation of *gem*-difluoroalkenes. By tailoring the copper catalyst, solvent (DMA or THF), base (lithium *tert*-butoxide or lithium

methoxide), and additives (methanol or formic acid), the authors found they could control the extent of borylation, such that they can selectively obtain di-, tri-, and tetra-alkylboronates.

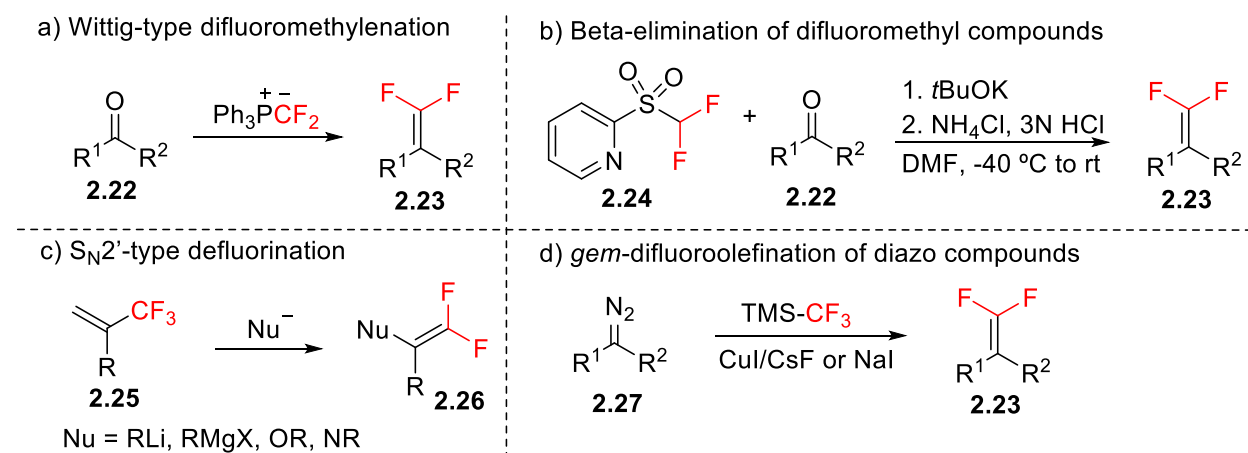
Not only valuable as synthetic intermediates, *gem*-difluoroalkenes are also valuable end products. It has been shown that the functional group, which acts as a carbonyl mimic, offers increases in lipophilicity and metabolic stability to drugs (Fig. 2.2).<sup>42-44</sup> Incorporation of both a boronic ester and a *gem*-difluoroalkene into a molecule would provide multiple functional handles that allow for further modification using both boron and fluorine chemistry.



**Figure 2.2** Difluoroalkenes as carbonyl mimics.

## 2.5 Synthesis of *gem*-difluoroalkenes

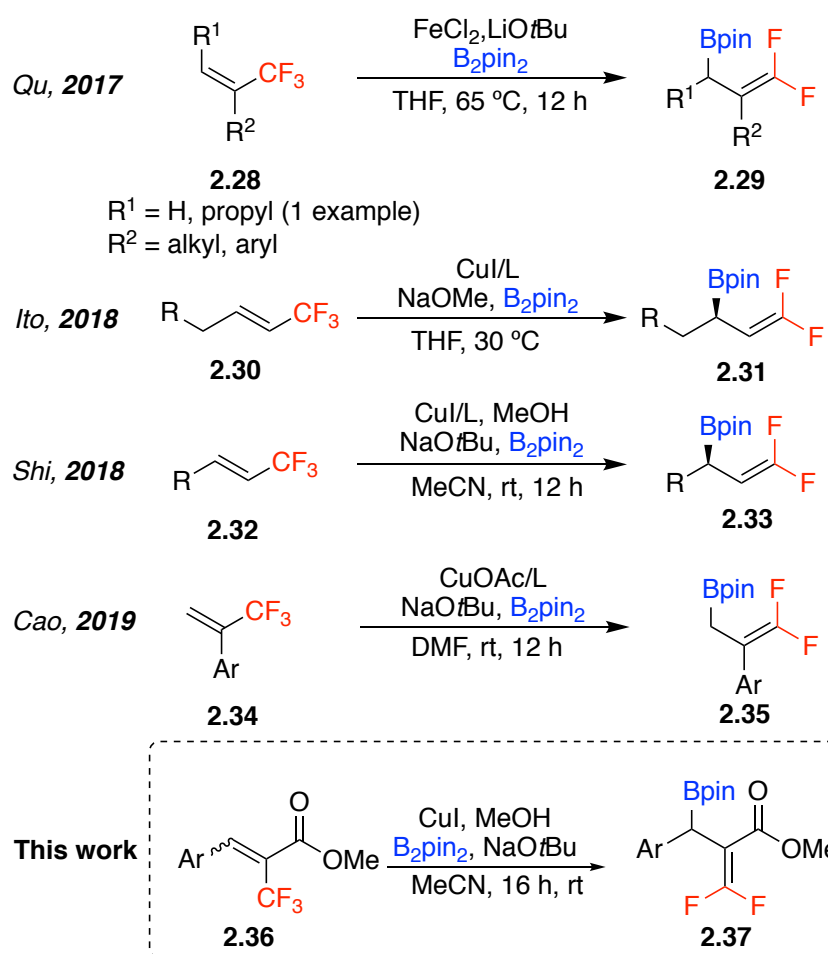
Common methods towards the formation of *gem*-difluoroalkenes include difluoromethylenation (Wittig-, Julia-, or Julia-Kocienski-type),<sup>45</sup>  $\beta$ -elimination of functionalized



**Scheme 2.4.** Methods towards synthesis of *gem*-difluoroalkenes.

difluoromethyl compounds,<sup>46</sup> S<sub>N</sub>2'-type defluorination of 2-trifluoromethyl-1-alkenes, and *gem*-difluoroolefination of diazo compounds (Scheme 2.4); however, these harsh reaction conditions are not amenable to many functional groups.<sup>47</sup>

Current efforts to form allyl boronate containing *gem*-difluoroalkenes include copper and iron-catalyzed reactions of trifluoromethyl alkenes (Scheme 2.5). In 2017, Qu and co-workers developed an iron(II)-catalyzed borylation/ $\beta$ -fluorine elimination reaction that gives rise to allylboryl *gem*-difluoroalkenes **2.29**. The reaction worked well for a variety of alkyl and aryl alkenes.<sup>48</sup> The reaction was not enantioselective for the substrate that resulted in a chiral center (R<sup>1</sup> = propyl).



**Scheme 2.5.** Methods towards synthesis of borylated *gem*-difluoroalkenes.

In 2018, Ito<sup>49</sup> and Shi<sup>50</sup> both published enantioselective copper-catalyzed borylation of CF<sub>3</sub>-substituted alkenes. Using chiral Josiphos-type ligands, they synthesized a variety of chiral allylboronates. Ito transformed the products through oxidation and allylation. Shi also demonstrated the synthetic utility of these products in a variety of transformations including oxidation, homologation, reduction, and hydrogenation. Cao and co-workers reported a similar copper-catalyzed method using a Xantphos ligand for borylation of trifluoromethyl styrenes.<sup>51</sup> With the exception of a handful of examples, these reactions are limited to disubstituted alkenes containing alkyl and aryl substituents.

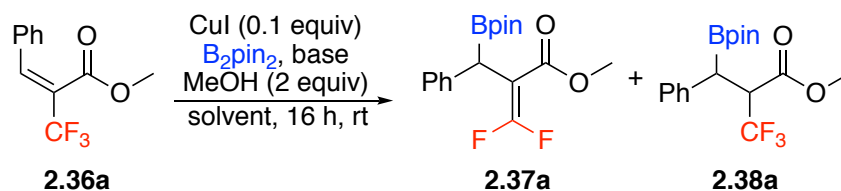
While  $\beta$ -borylation of  $\alpha,\beta$ -unsaturated esters<sup>52</sup> and borylation of trifluoromethyl alkenes are both known, there are no methods showing the transformation of  $\alpha$ -trifluoromethyl- $\alpha,\beta$ -unsaturated esters to boron-containing *gem*-difluoroalkenes. To our knowledge, this is the first reported borylation-defluorination of  $\alpha,\beta$ -unsaturated esters.

## 2.6 Optimization of reaction conditions for the borylation of methyl 3-phenyl-2-(trifluoromethyl)acrylate

We began our study with 10 mol% copper iodide and two equivalents each of bis(pinacolato)diboron, sodium *tert*-butoxide, and methanol. We were pleased to find the reaction was selective for the formation of the borylated *gem*-difluoroalkene **2.37a** in good yield (entry 1). Subsequent screening of bases demonstrated the importance of the sodium cation (entries 2-3). Interestingly, we found that the use of carbonate bases resulted in a change in selectivity towards borylated product **2.38a** (entries 4-5). The screening of additional solvents showed reduced yield and selectivity for product **2.37a** (entries 6-9). In order to improve the reaction atom economy, the diboron reagent was reduced to 1.5 equivalents and the base to 1 equivalent. While the yield and selectivity remained constant, incomplete conversion was observed (entry 10). It was found that

1.3 equivalents of base were needed for complete conversion of the ester (entry 11); however, side product **2.38a** was also formed. Addition of powdered 4 Å molecular sieves increased the yield of product **2.37a** (entry 12). Upon removal of copper iodide from the reaction, no product was formed

**Table 2.1. Optimization of reaction conditions for borylation**



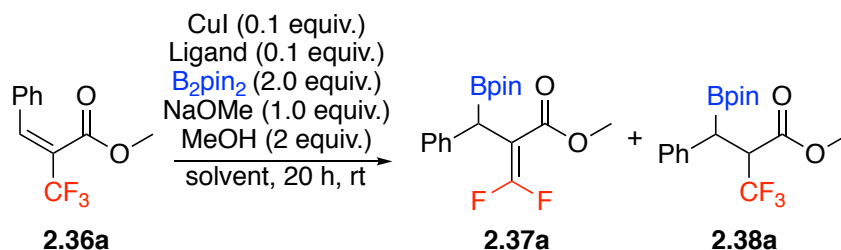
Entry	Solvent	$\text{B}_2\text{pin}_2$ equiv.	Base (equiv.)	%Yield <b>2.37a</b>	%Yield <b>2.38a</b> <sup>b</sup>	%Conversion <sup>b</sup>
1	MeCN	2	$\text{NaOtBu}$ (2)	62	4	100
2	MeCN	2	$\text{KOtBu}$ (2)	0	7	100
3	MeCN	2	$\text{LiOtBu}$ (2)	6	17	100
4	MeCN	2	$\text{Na}_2\text{CO}_3$ (2)	11	74	88
5	MeCN	2	$\text{Cs}_2\text{CO}_3$ (2)	0	22	100
6	dioxane	2	$\text{NaOtBu}$ (2)	45	14	97
7	toluene	2	$\text{NaOtBu}$ (2)	22	11	100
8	THF	2	$\text{NaOtBu}$ (2)	35	16	100
9	MTBE	2	$\text{NaOtBu}$ (1)	21	57	92
10 <sup>c</sup>	MeCN	1.5	$\text{NaOtBu}$ (1)	62	3	86
11 <sup>c</sup>	MeCN	1.5	$\text{NaOtBu}$ (1.3)	63	17	100
12 <sup>c,d</sup>	MeCN	1.5	$\text{NaOtBu}$ (1.3)	75	5	100
13 <sup>e</sup>	MeCN	1.05	$\text{NaOtBu}$ (1.2)	0	0	25

<sup>a</sup>General procedure: copper iodide (0.1 equiv, 0.020 mmol), bis(pinacolato)diboron, base, and methyl (*E*)-3-phenyl-2-(trifluoromethyl)acrylate **2.36a** were dissolved in the indicated solvent and stirred 16 h under inert atmosphere. <sup>b</sup>NMR yields and conversions ( $^{19}\text{F}$ ) given using 2-fluoro-4-iodoaniline as an internal standard. <sup>c</sup>(0.5:1) mixture of (*Z*)- and (*E*)- methyl 3-phenyl-2-(trifluoromethyl)acrylate used. <sup>d</sup>Powdered 4 Å molecular sieves (50 mg) added to reaction mixture. <sup>e</sup>Reaction run without copper.

(entry 13). As the syntheses of many substituted methyl 2-(trifluoromethyl)acrylates results in an inseparable mixture of *E/Z* isomers, the borylation was performed with a mixture of isomers, which resulted in no negative impact on yield (entries 10-12).

A series of chiral ligands were evaluated in the reaction (Table 2.2). First, a series of

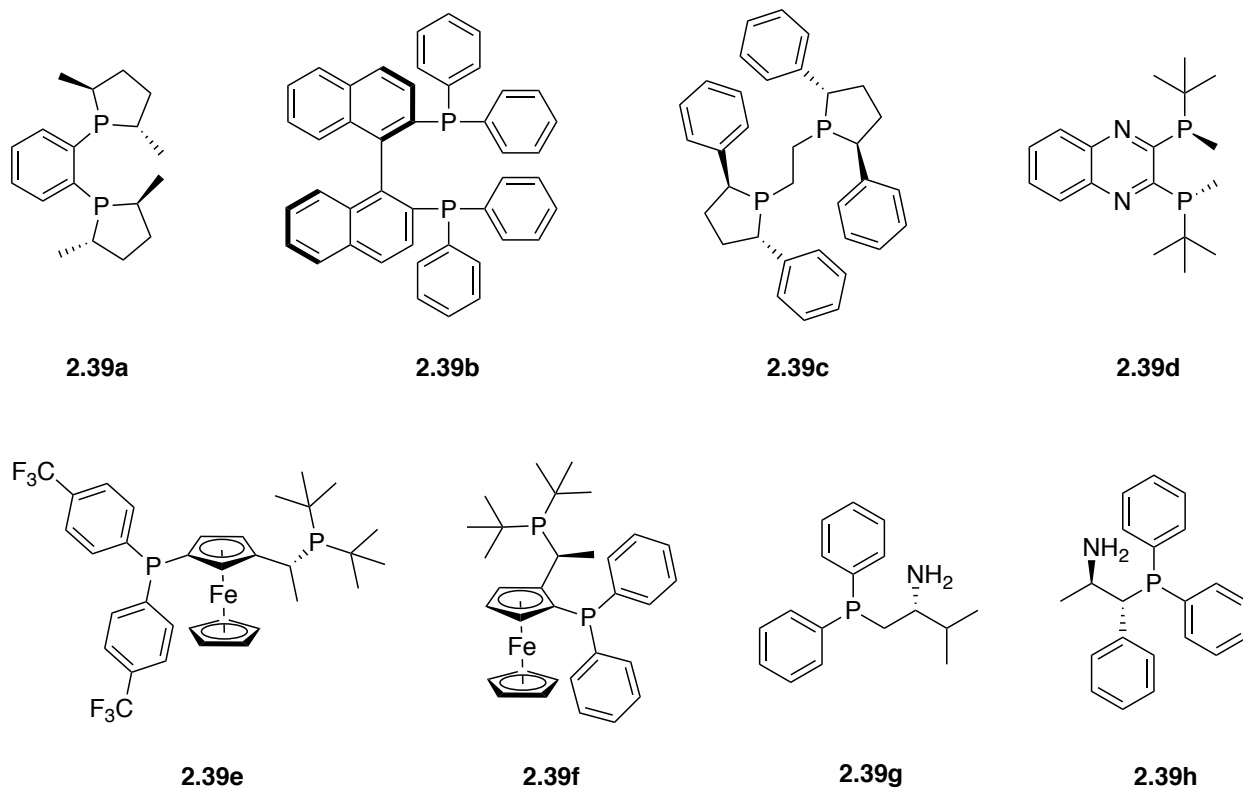
**Table 2.2. Optimization of borylation conditions with chiral ligands.**



Entry	Solvent	Ligand	%Yield 2.37a:2.38a <sup>b</sup>	%Conversion <sup>b</sup>
1	MeCN	<b>2.39a</b>	0:0	29
2	MeCN	<b>2.39b</b>	0:1	38
3	MeCN	<b>2.39c</b>	2:3	48
4	MeCN	<b>2.39d</b>	2:2	46
5	MeCN	<b>2.39e</b>	16:10	88
6	MeCN	<b>2.39f</b>	0:0	24
7	MeCN	<b>2.39g</b>	25:16	82
8	dioxane	<b>2.39g</b>	48:7	77
9	MeCN	<b>2.39h</b>	19:14	97
10 <sup>c</sup>	dioxane	<b>2.39h</b>	53:16	95

<sup>a</sup>General procedure: copper iodide (0.1 equiv, 0.020 mmol), base, and ligand **2.39** were dissolved in the indicated solvent and stirred under inert atmosphere for 10 min. Bis(pinacolato)diboron, and methyl (*E*)-3-phenyl-2-(trifluoromethyl)acrylate **2.36a** were then added to the reaction mixture. The reaction was stirred 20 h under inert atmosphere. <sup>b</sup>NMR yields and conversions (<sup>19</sup>F) given using bis(4-fluorophenyl)methanone as an internal standard. <sup>c</sup>Reaction performed with one equivalent sodium fluoride.



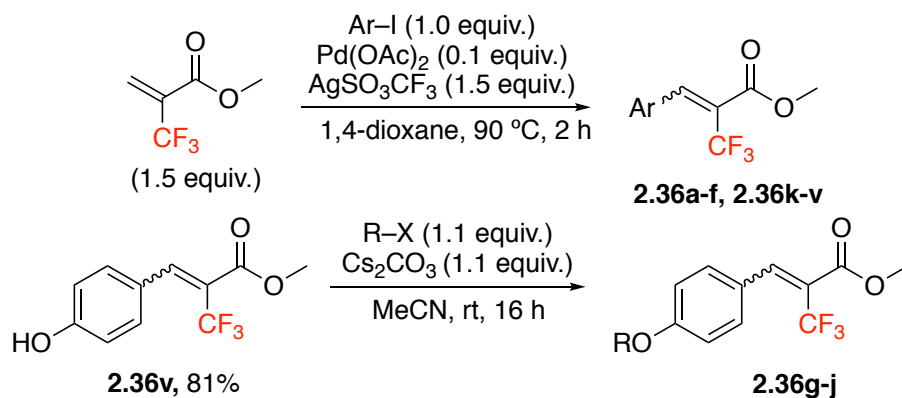


**Figure 2.3.** Chiral ligands tested in borylation reaction.

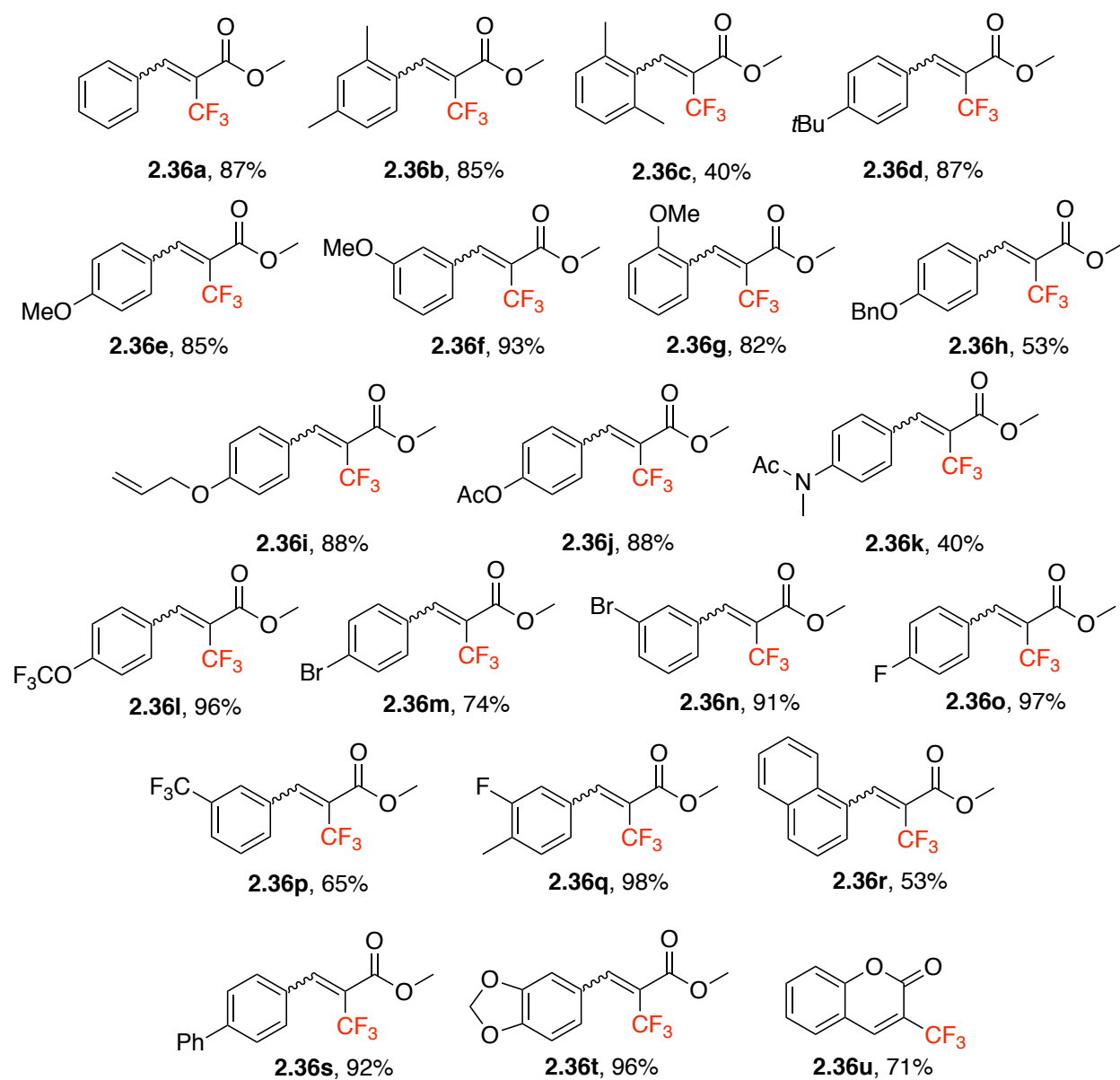
bidentate phosphine ligands were tested (Figure 2.3). *S,S*-Duphos (**2.39a**) and *R*-Binap (**2.39b**) resulted in no desired product formation (entries 1-2). Bidentate phosphine ligands **2.39c** and **2.39d** resulted in only trace product formation (entries 3-4). Two ferrocene ligands were tested, but resulted in little to no product formation (entries 5-6). Aminophosphine ligands **2.39g** and **2.39h** were more effective; however, further reaction optimization did not afford the desired product in good yield or selectivity.

## 2.7 Preparation of methyl 3-aryl-2-(trifluoromethyl)acrylates

The methyl 3-aryl-2-(trifluoromethyl)acrylate substrates **2.36** were not commercially available, and were synthesized using Xiao et al.'s published protocol.<sup>53</sup> Aryl iodides were reacted with methyl 2-(trifluoromethyl)acrylate, palladium (II) acetate, and silver trifluoromethane sulfonate in a Mizoroki-Heck reaction (Scheme 2.6). Substrates **2.36g-i** were synthesized from



**Scheme 2.6.** Synthesis of ester substrates.



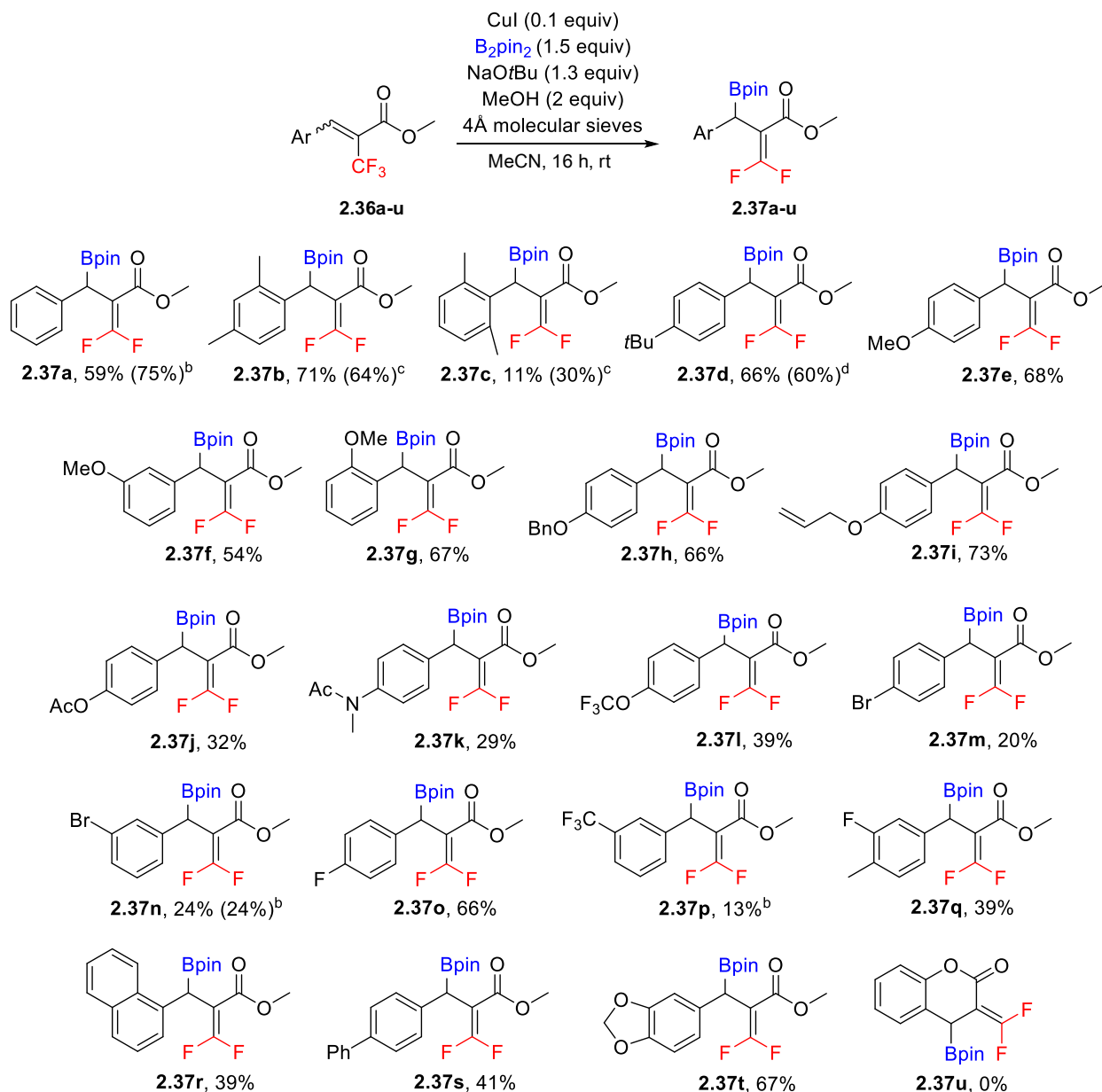
**Figure 2.4.** Substrates synthesized.

precursor **2.36v** via a Williamson ether synthesis using the corresponding alkyl bromides. Substrate **2.36j** was also synthesized from precursor **2.36v**, but was reacted with acetyl chloride. The substrates synthesized are shown in Figure 2.4.

## 2.8 Substrate scope for the borylation of methyl 3-aryl-2-(trifluoromethyl)acrylates

With optimized conditions in hand, we set out to investigate the substrate scope for the reaction (Scheme 2.7). We were pleased to find that methyl groups were well-tolerated in *ortho* and *para* positions on the phenyl ring (**2.37b-c**), with a moderate reduction in yield for the sterically hindered 2,5-dimethyl substituted ring (**2.37c**). The *tert*-butyl group in the *para* position was also well tolerated (**2.37d**). Substrates containing a methoxy group were borylated in good yield when the substitution occurred in the *para* and *ortho* positions (**2.37e**, **2.37g**); however, a slight reduction in yield occurred when the inductively withdrawing substituent was moved into the *meta*-position (**2.37f**). A phenyl group bearing a *para*-benzyl ether was also borylated in good yield (**2.37h**). Borylation of the allyl phenyl ether substrate **2.37i** demonstrated the chemoselectivity of the reaction for the internal alkene. Substrate **2.37j**, bearing a phenyl acetate group, was borylated with a reduction in yield due to the electron-withdrawing nature of the functional group. When the acetate group was substituted for an amide, substrate **2.37k** was isolated in 29% yield. Substrates containing electron withdrawing groups (**2.37l-q**) were borylated with a reduction in yield, with the exception of the substrate bearing a fluorine in the *para* position (**2.37o**). This reduction in yield was due to the formation of side products including protodeboronated products and side products **2.38**. The disubstituted substrate **2.36q**, with a fluorine atom in the *meta* position, was borylated in 39% yield. The reduction in yield when comparing **2.37o** and **2.37q** can be attributed to the increased electron-withdrawing nature of a fluorine atom in the *meta* position. Larger aryl groups such as naphthyl, biphenyl, and

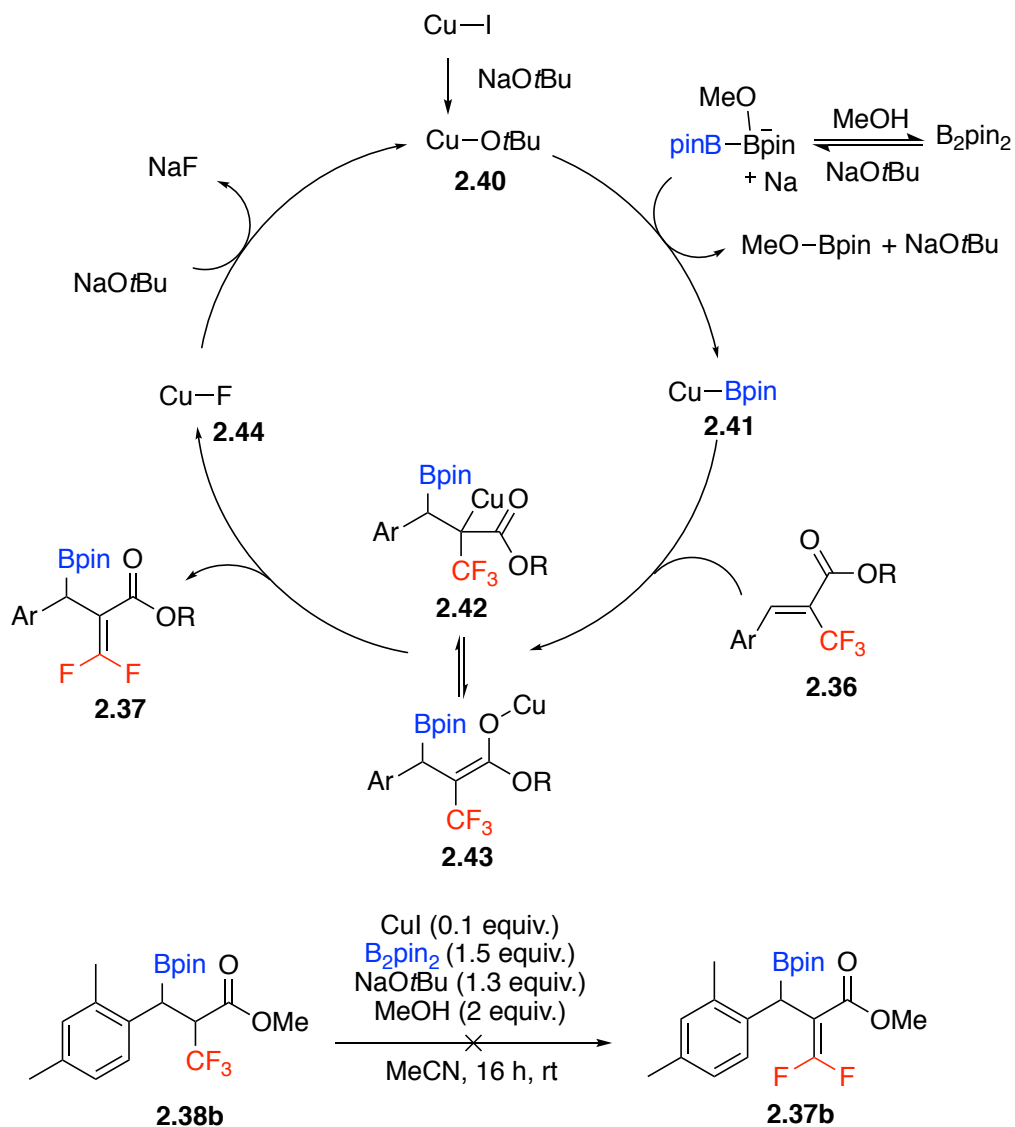
benzodioxolyl groups were well-tolerated (**2.37r-t**). Finally, borylation of the more conformationally restricted substrate **2.36u** was unsuccessful.



**Scheme 2.7.** Borylation of substituted 2-trifluoromethylacrylate derivatives <sup>a</sup>General procedure: to a vial containing powdered 4 Å molecular sieves (~50 mg) was added copper iodide (0.020 mmol), bis(pinacolato)diboron (0.300 mmol), sodium tert-butoxide (0.260 mmol), and substrate **2.36** (0.200 mmol). Dry acetonitrile (0.800 mL) and methanol (0.400 mmol) were added and the reaction was stirred 16 h under inert atmosphere. <sup>b</sup>NMR yield (<sup>19</sup>F) given using 2-fluoro-4-iodoaniline as an internal standard. <sup>c</sup>2.0 mmol scale. <sup>d</sup>1.0 mmol scale.

## 2.9 Proposed catalytic cycle and mechanistic insight into the borylation reaction

A proposed mechanism is given in Scheme 2.8 (top). Activation of  $B_2pin_2$  by a methoxide anion results in the formation of the copper-boryl species **2.41**. Addition of **2.41** across the double bond in **2.36** results in the formation of ester intermediate **2.42**, which can tautomerize to the copper bound enolate **2.43**. Elimination of copper fluoride forms product **2.37**. Reaction of additional base results in the regeneration of the active catalyst. Protonation of intermediate **2.42**

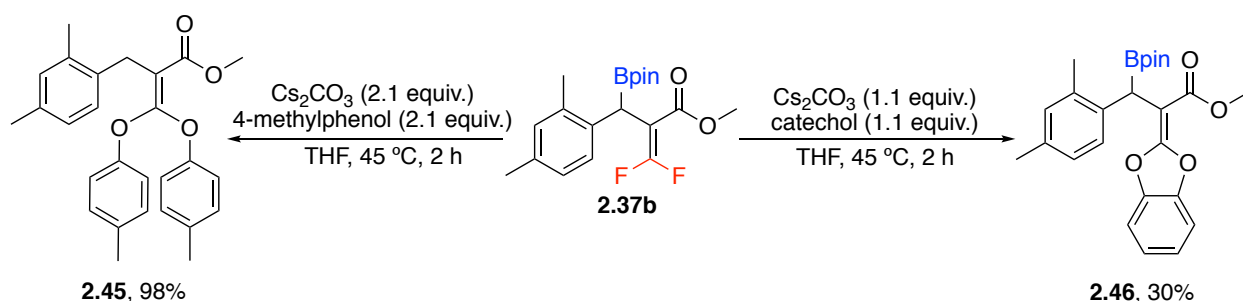


**Scheme 2.8.** Proposed catalytic cycle and mechanistic insight.

will result in the formation of side product **2.38**. A control experiment was performed showing **2.38b** is not an intermediate towards the formation of **2.37b** (Scheme 2.8 bottom).

## 2.10 Applications

In the presence of cesium carbonate and nucleophiles, allyl boronic ester **2.37b** undergoes substitution (Scheme 2.9).<sup>54</sup> Interestingly, when excess cesium carbonate was employed, the substituted, protodeborylated ester **2.45** was formed in excellent yield. When a single equivalent of cesium carbonate was used in the presence of the nucleophile catechol, the borylated ester **2.46** was formed in moderate yield.



**Scheme 2.9.** Transformations of product **2.37b**

## 2.11 Conclusions

In conclusion, a novel protocol for the synthesis of borylated *gem*-difluoroalkenes was developed. The reaction proceeds in good yield for a variety of substrates. A mechanism for the reaction was proposed, and the products were functionalized in the presence of a mild base and nucleophiles.

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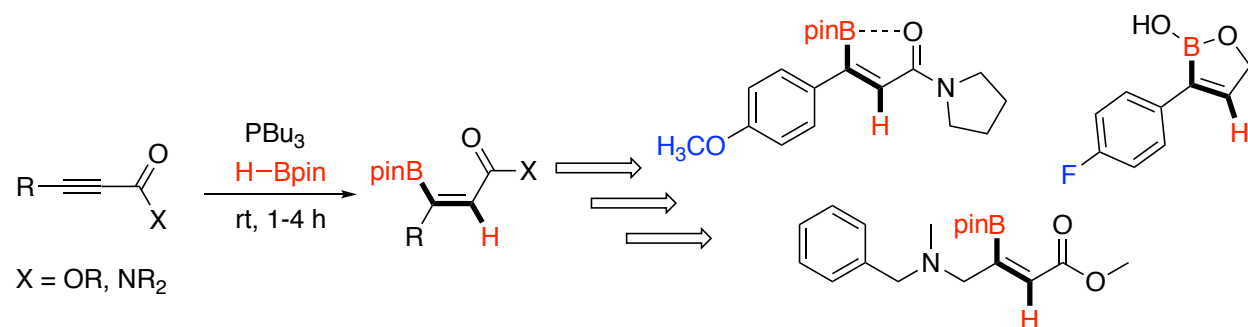
## Chapter 3. Transition metal-free *trans* hydroboration of alkynoic acid derivatives: Experimental and theoretical studies

### 3.1 Contributions

Reaction optimization and synthesis of substrates **3.19a**, **3.19b**, **3.19d**, **3.19f**, **3.19g-j**, **3.19l**, **3.19p**, **3.19r**, **3.19s**, **3.19w-z**, **3.21a**, and **3.21b** were performed by Russell Fritzscheier. Substrates **3.19c**, **3.19e**, **3.19k**, **3.19m-o**, **3.19q**, **3.19t**, **3.19u**, **3.19v**, and **3.21c-e** were synthesized by the author. Pargyline derivative **3.24** and oxaboroles **3.25a**, **3.25c**, and **3.25d** were prepared by the author. Oxaborole **3.25b** was prepared by Russell Fritzscheier. Deuterium labeling studies were performed by Russell Fritzscheier. DFT calculations were performed by Xueying Guo under the guidance of Prof. Zhenyang Lin at the Hong Kong University of Science and Technology. The final manuscript was prepared by Russell Fritzscheier, in collaboration with the author, Xueying Guo, and Prof. Zhenyang Lin. Prof. Webster Santos contributed to the preparation and editing of the final manuscript. This work has been published in the *Journal of Organic Chemistry* and is available online. Reprinted (adapted) with permission from (Fritzscheier, R.; Gates, A.; Xueying, G.; Zhenyang, L.; Santos, W. Transition Metal-Free Trans Hydroboration of Alkynoic Acid Derivatives: Experimental and Theoretical Studies *J. Org. Chem.* **2018**, *83*, 17, 10436-10444). Copyright (2018) American Chemical Society.

### 3.2 Abstract

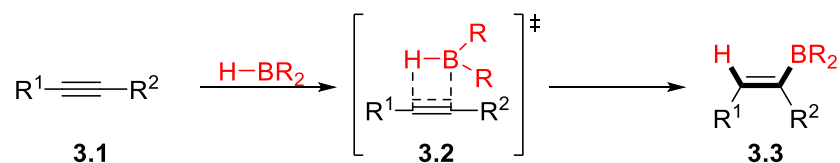
We report a phosphine-catalyzed *trans* hydroboration of alkynoate esters and amides. The reaction proceeds under mild conditions with exclusive (*E*) selectivity to afford (*E*)- $\beta$  borylacrylates and (*E*)- $\beta$  borylacrylamides in good to excellent yields. The reaction is tolerant of a variety of functional groups and allows efficient access to novel oxaboroles as well as a pargyline derivative (MAO inhibitor). Theoretical calculations suggest an internal hydride generates a phosphonium allenoxyborane followed by the formation of a key phosphonocyclobutene intermediate that collapses in a stereoselective, rate-limiting step.



### 3.3 Hydroboration of alkynes

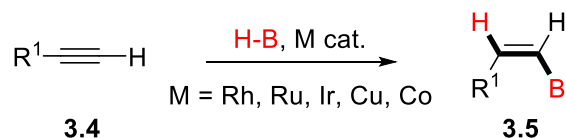
As described in Chapter 2, organoboron compounds are ubiquitous in organic chemistry due to the versatility of the C-B bond, as they efficiently undergo a wide variety of useful transformations, most notably the Suzuki-Miyaura cross-coupling reaction.<sup>1-6</sup> Alkenylboronates in particular are excellent substrates for such cross-coupling reactions.<sup>7</sup> Interest in organoboron compounds for medicinal applications highlights their significance not only as synthetic intermediates, but also as end products.<sup>8,9</sup> Therefore, development of novel borylation methods is warranted.

Synthesis of alkenylboronates is typically achieved through the hydroboration of alkynes; however, addition occurs almost exclusively in a *cis* fashion.<sup>10-12</sup> The concerted reaction proceeds through a four-membered transition state (3.2, Scheme 3.1).



**Scheme 3.1.** Hydroboration of alkynes resulting in *cis* alkenes.

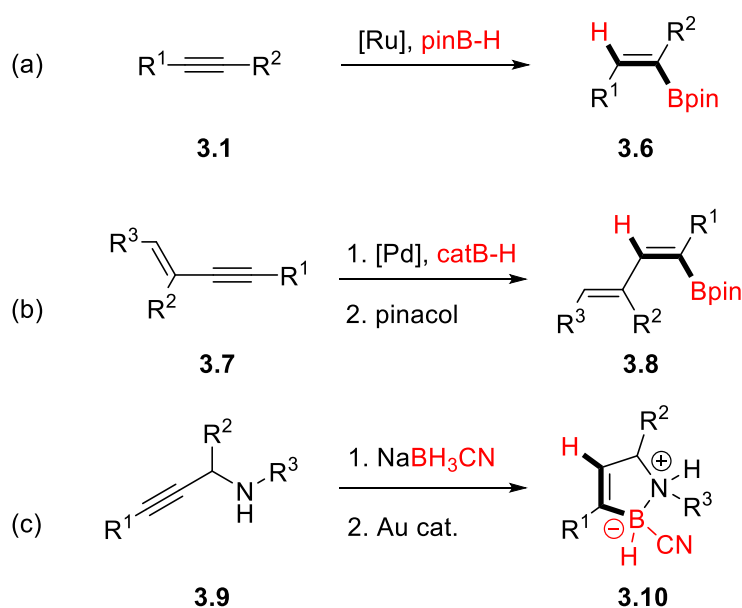
Overcoming classical *cis* addition has proven to be somewhat challenging. The *trans* hydroboration of terminal alkynes has seen varying degrees of success with examples reported using Rh,<sup>13</sup> Ru,<sup>14</sup> Ir,<sup>13</sup> Cu,<sup>15</sup> and Co<sup>16</sup> catalysts as well as one report of a transition metal-free borenium cation-mediated reaction (Scheme 3.2).<sup>17, 18</sup>



**Scheme 3.2.** *Trans* hydroboration of terminal alkynes.



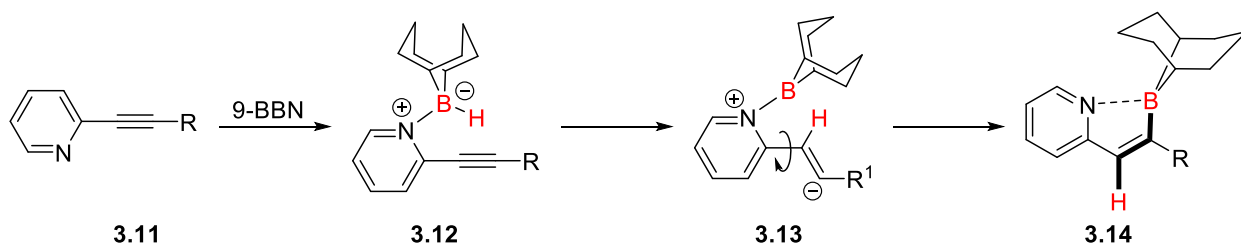
Examples of *trans* hydroboration of internal alkynes are even more limited. For example, Fürstner reported an elegant cationic Ru-catalyzed *trans* hydroboration of alkynes (Scheme 3.3a).<sup>19</sup> DFT studies suggested the formation of a key ruthenium metallacyclopropene intermediate in the mechanism.<sup>20</sup> Further, a stereoselective *trans* hydroboration of 1,3-enynes enabled by 1,4-azaborine-based phosphine-Pd complexed was demonstrated (Scheme 3.3b),<sup>21</sup> which was supported by DFT studies.<sup>22</sup> Finally, Au-catalyzed *trans* hydroboration of propargylamines to form cyclic aminoboranes has been described by Shi and co-workers (Scheme 3.3c).<sup>23</sup>



**Scheme 3.3.** Transition-metal-catalyzed *trans* hydroboration of internal alkynes.

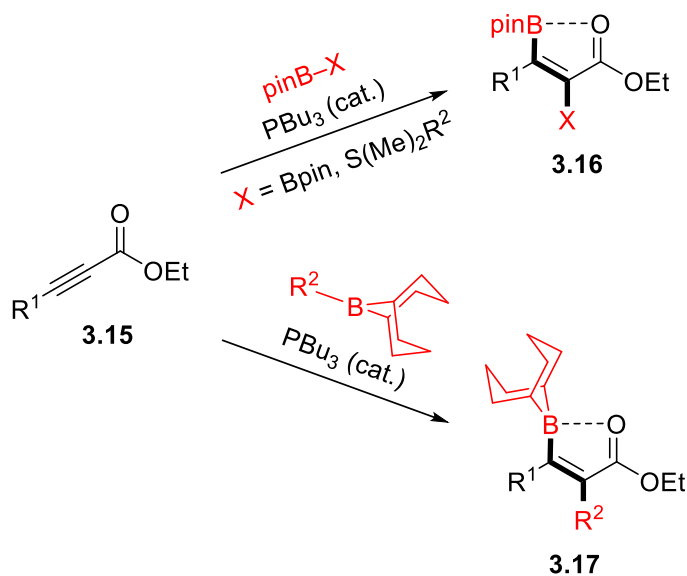
Unfortunately, transition-metal free *trans* hydroboration of internal alkynes examples are severely lacking. A few examples of transition metal-free *trans* diborations,<sup>24-26</sup> silaborations,<sup>24, 27</sup> and carboborations<sup>28-30</sup> of alkynes have been reported, but the corresponding hydroborations have remained elusive.<sup>31</sup> Interestingly, the *trans* hydroboration of internal alkynes can be effected using a pyridyl directing group (Scheme 3.4).<sup>32</sup> Theoretical calculations supports initial coordination of the pyridyl nitrogen on **3.11** to boron followed by a hydride migration. The corresponding vinyl

anion intermediate **3.13** promotes boryl transfer allowing formation of the lower energy *trans* product **3.14**.<sup>32</sup>



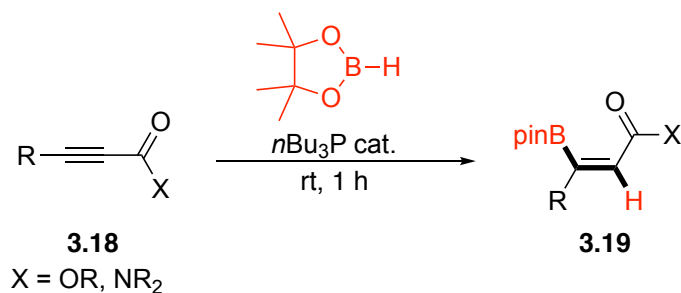
**Scheme 3.4.** Transition-metal-free *trans* hydroboration of an internal alkyne.

The scarcity of transition metal-free *trans* hydroborations and the limited substrate scope of known reactions demonstrates the necessity for new methods. Furthermore, new protocols that utilize commercially available reagents, such as pinacolborane, would be advantageous and desirable. Inspired by previous phosphine-catalyzed addition to alkynes (Scheme 3.5),<sup>24, 28, 29</sup> we hypothesized that phosphine may be able to catalyze the *trans* addition of pinacolborane to alkynoate esters (Scheme 3.6).



**Scheme 3.5.** Phosphine-catalyzed addition to alkynes.

Herein, we describe experimental and theoretical studies of the reaction employing pinacolborane and catalytic amounts of trialkylphosphine (Scheme 3.6). This atom efficient protocol proceeds with excellent regio- and stereoselectively in good to excellent yields under mild conditions either neat or in the presence of solvent.



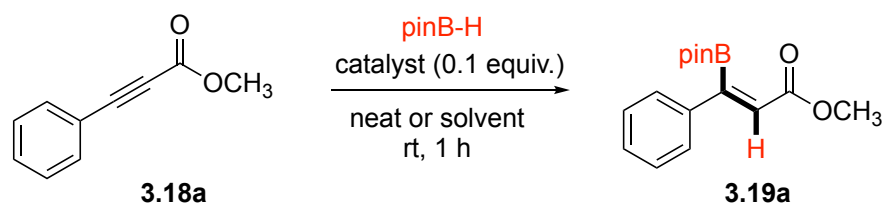
**Scheme 3.6.** This work: *trans* addition of pinacolborane to alkyneic acid derivatives.

### 3.4 Results and discussion

Upon initiating our studies, we were pleased to find that addition of pinacolborane and 10 mol % tri-*n*-butylphosphine to methyl 3-phenylpropiolate (**3.18a**) under neat conditions produced the corresponding (*E*)-borylcinnamate **3.19a** in excellent yield in an hour at room temperature (entry 1, Table 3.1). In the absence of phosphine catalyst, no reaction was observed.<sup>33</sup> In addition, we found that tricyclohexylphosphine and triethylphosphine catalyzed the hydroboration reaction as well (entries 3 and 4), albeit in lower yields. Unfortunately, triphenylphosphine was unable to mediate the reaction, and none of the desired product was observed (entry 5). Furthermore, no borylated material was observed with triethylphosphite or tri-*tert*-butylphosphine as the catalysts (entries 6 and 7). To investigate solvent effects, the reaction was performed in THF, acetonitrile, and toluene and minimal reduction in yield as determined (entries 8-10). In certain cases, solvent is useful in dissolving both the starting material and catalyst (*vide infra*). *N*-Heterocyclic carbenes (NHCs) were inefficient as catalysts (entries 11 and 12). Based on the catalyst screen, tri-*n*-butylphosphine was deemed as the optimal additive (entry 1). Confirmation of the (*E*)-

stereoselectivity was performed with 2D-NOESY experiments. In addition,  $^{11}\text{B}$  NMR studies showed a single peak at 30.1 ppm, suggesting the lack of internal coordination between boron and the carbonyl oxygen in contrast to amides (*vide infra*).

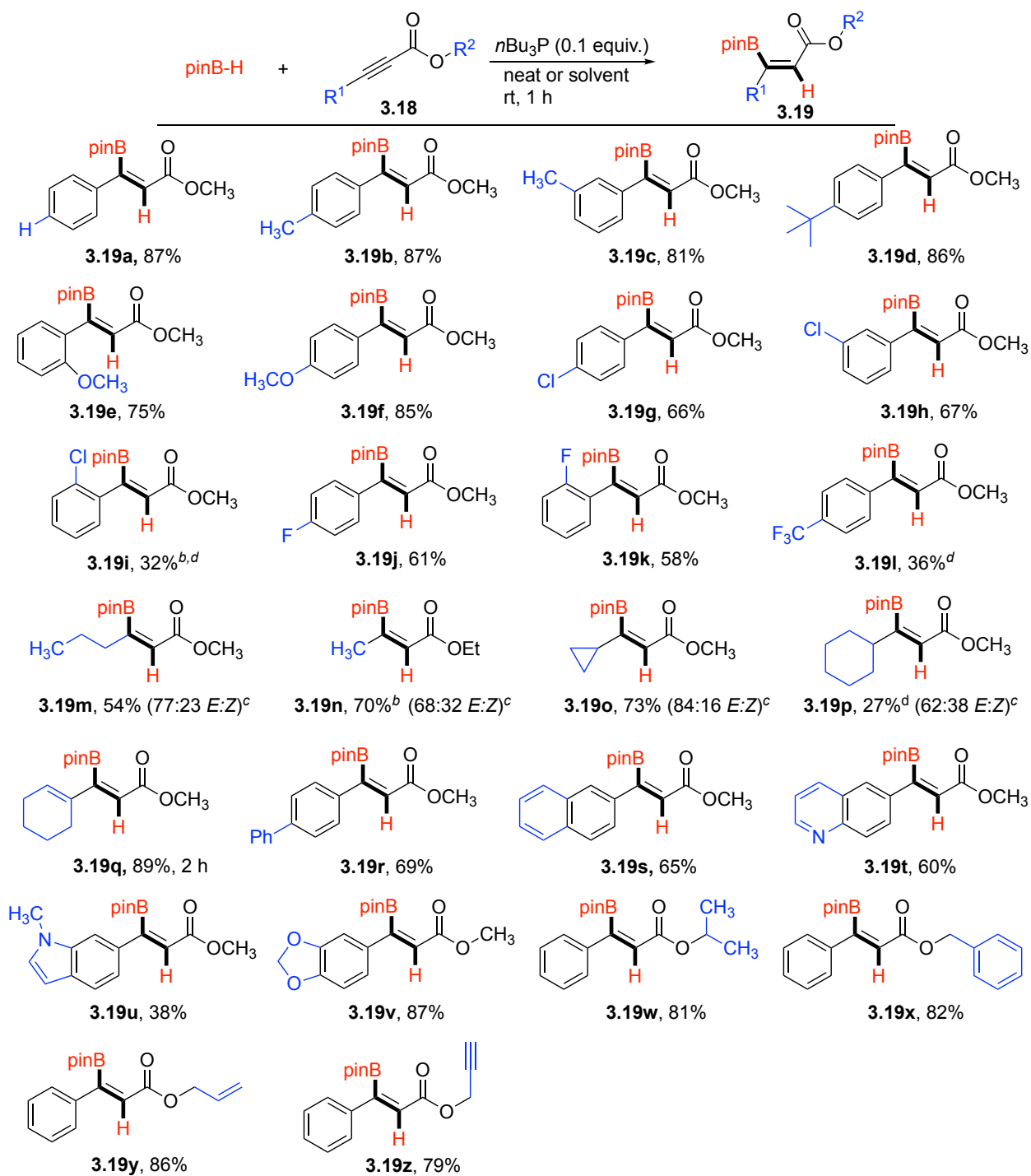
**Table 3.1.** Optimization of reaction conditions for hydroboration.<sup>a</sup>



entry	solvent	catalyst	% yield <sup>b</sup>
1	neat	PBu <sub>3</sub>	88 (87) <sup>c</sup>
2	neat	-	0
3	THF	PCy <sub>3</sub>	59
4	neat	PEt <sub>3</sub>	74
5	THF	PPh <sub>3</sub>	0
6	neat	P(OEt) <sub>3</sub>	trace
7	neat	P( <i>t</i> -Bu) <sub>3</sub>	0
8	THF	PBu <sub>3</sub>	86
9	MeCN	PBu <sub>3</sub>	80
10	toluene	PBu <sub>3</sub>	84
11	THF	IMes	0
12	THF	ICy	0

<sup>a</sup>General procedure: methyl 3-phenylpropiolate (0.34 mmol) and pinacolborane (0.37 mmol), followed by catalyst (0.034 mmol) at rt under nitrogen for 1 h. <sup>b</sup>NMR yields. <sup>c</sup>Isolated yield. IMes = 1,3-bis(2,4,6-trimethylphenyl)-imidazolium; ICy = 1,3-Dicyclohexylbenzimidazolium

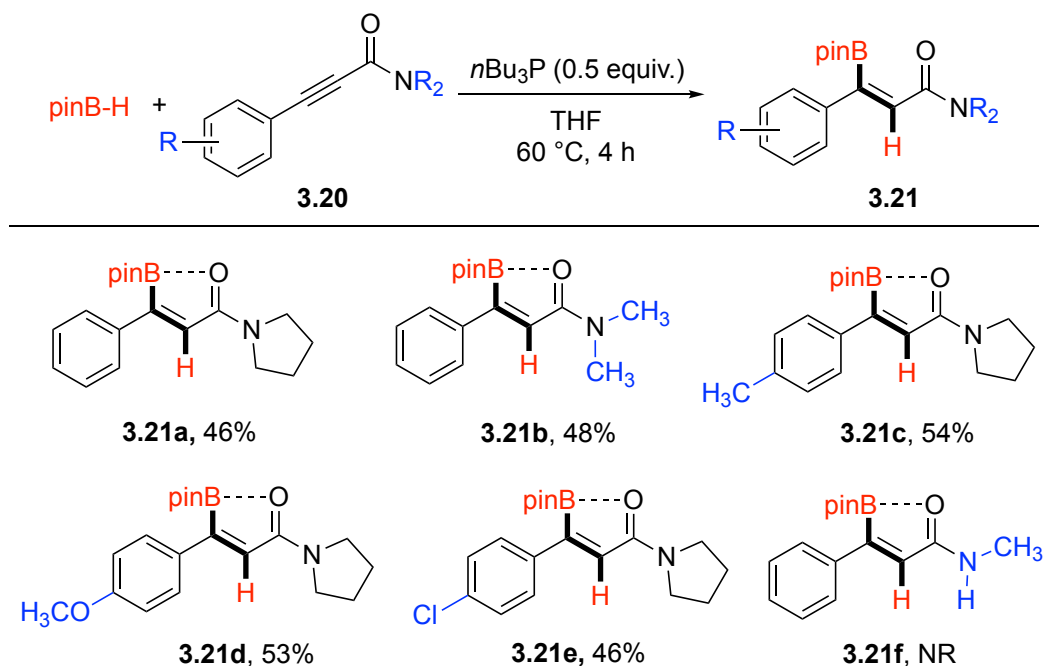
With optimized conditions (10 mol % tributylphosphine) in hand, we evaluated the substrate scope with a variety of alkynoate esters **3.18a-z** (Scheme 3.7). Alkyl substitutions on aryl rings were tolerated on various positions to afford products **3.19b-d** in excellent yields. Electron releasing substituents, such as a methoxy group, were well tolerated (**3.19e-f**). Furthermore, alkynoates substituted with electron withdrawing substituents on the phenyl ring, such as chlorine, fluorine and trifluoromethyl groups (**3.19g-l**), were also able to undergo reaction, albeit in slightly



**Scheme 3.7.** Substrate scope for hydroboration of alkynoates. <sup>a</sup>General procedure: alkyne (1 equiv.) and pinacolborane (1.1 equiv.) followed by PBU<sub>3</sub> (0.1 equiv.) at rt under nitrogen for 1 hour unless otherwise indicated. Isolated yields shown. <sup>b</sup>0.3 equiv. of PBU<sub>3</sub>. <sup>c</sup>Determined by GC. >99:1 *E:Z* selectivity unless stated otherwise. <sup>d</sup>Incomplete conversion.

reduced yields. In addition, 3-alkyl substituted propiolates were efficient substrates. Products bearing linear alkanes (**3.19m-n**) as well as cycloalkanes (**2.19o-q**) were afforded in good yields, although reduced stereoselectivity was observed in **3.19m-p**. Regioselective addition of Bpin to the  $\beta$  vs the  $\gamma$  carbon occurred in **3.19q**. Moreover, other aryl functional units served as good substrates. Biphenyl, naphthyl, quinolyl, indolyl and benzodioxolyl groups (**3.18r-v**) were transformed to the desired alkenylboronic ester products in up to 87% yield. Several attempts to hydroborate methyl propiolate were performed, but no reaction was observed. To investigate the effect of the ester moiety, isopropyl and benzyl propiolates were subjected to the reaction condition, which afforded **3.19w-x** in excellent yield. Notably, in the presence of competing alkene (**3.18y**) or alkyne (**3.18z**) substituents, chemoselective hydroboration proceeded with the internal alkyne in excellent yield.

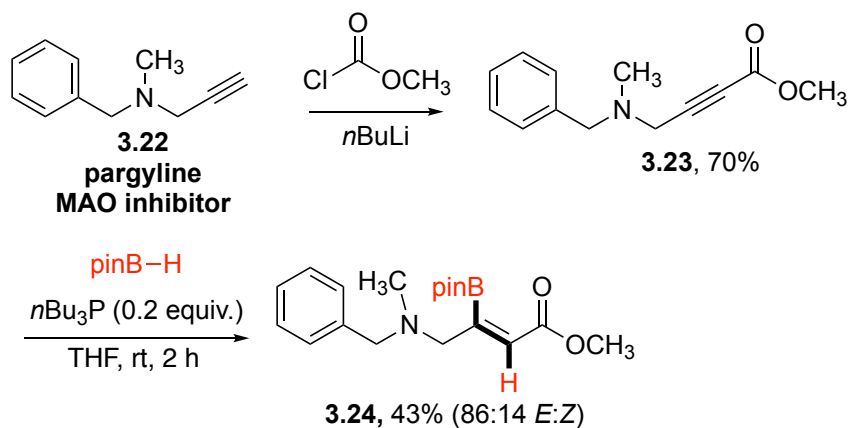
In addition to esters, we were pleased to discover that tertiary alkynamides were able to undergo hydroboration, though higher catalyst load and higher temperature were required (Scheme 3.8). For example, pyrrolidine (**3.20a**) and dimethylamine (**3.20b**) derivatives were hydroborated in good yield. Consistent with our previous studies,<sup>15c</sup> boron-oxygen coordination is suggested by the presence of a single peak at  $\sim 14$  ppm in the  $^{11}\text{B}$  NMR spectra, a chemical shift characteristic of quaternized neutral boron. Arylalkynamides **3.20c-e** bearing electron donating as well as electron withdrawing groups underwent the transformation in  $\sim 50\%$  yield. Finally, no hydroboration product was observed in the case of the corresponding *N*-methyl secondary amide derivative (**3.21f**).



**Scheme 3.8.** Substrate scope for hydroboration of alkynamides. <sup>a</sup>General procedure: alkynamide (1 equiv.) and pinacolborane (1.1 equiv.), followed by tri-*tert*-butylphosphine (0.5 equiv.) at 60 °C. Isolated yields shown. NR = no reaction.

### 3.5 Applications

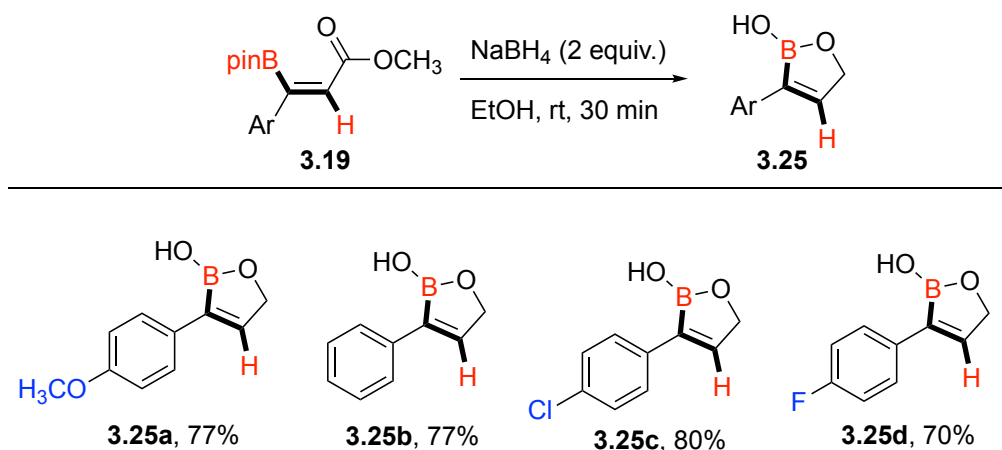
To demonstrate the utility of the developed reaction conditions, we applied the hydroboration reaction to the monoamine oxidase (MAO) inhibitor pargyline (**3.22**, Scheme 3.9).<sup>34</sup> Treatment of **3.22** with methylchloroformate and butyllithium afforded the requisite alkynamide



**Scheme 3.9.** Hydroboration of an MAO-inhibitor derivative.

**3.23.** We were pleased to find that the amine-bearing **3.23** was converted to the corresponding borylated pargyline derivative **3.24** in 43% yield.

Next, we sought to demonstrate the utility of these substrates to the synthesis of novel oxaboroles. Oxaboroles have recently gained much attention, largely due to the success of the FDA approved drugs Crisaborole (Eucrisa)<sup>35</sup> and Tavaborole (Kerydin).<sup>36</sup> Previous methods to synthesize 2(5H)-oxaboroles required propargyl alcohols, the products of which have non-H substitutions on the 5-position.<sup>25, 30, 37, 38</sup> We observed that the ester substrates underwent efficient reduction to the corresponding 4-monosubstituted 2(5H)-oxaboroles **3.25a–d** in excellent yields (Scheme 3.10). Reduction of (*E*)- $\beta$ -borylacrylate products represents an efficient route to previously elusive oxaborole structures, which may prove to have unique biological activity.



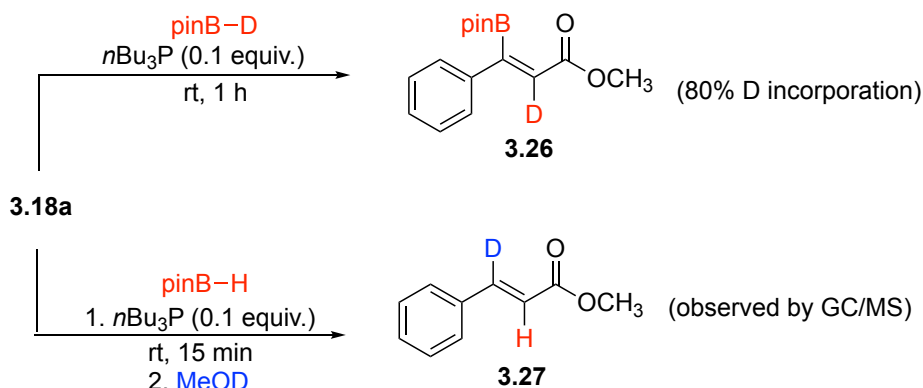
**Scheme 3.10.** Synthesis of 2-(5H)-oxaboroles <sup>a</sup>General procedure: borylacrylate **3.19** (1 equiv.) dissolved in EtOH followed by NaBH<sub>4</sub> (2 equiv.) at rt for 30 min. Isolated yields shown.

### 3.6 Mechanistic Studies

To gain insight into the mechanism of the *trans* hydroboration reaction, we performed deuterium labeling experiments (Scheme 3.11). Treatment of **3.18a** with deuteropinacolborane afforded deuterated product **3.26**, suggesting pinacolborane is the source of hydrogen. Interestingly, if the reaction is quenched in deuterated methanol prior to completion, we observed

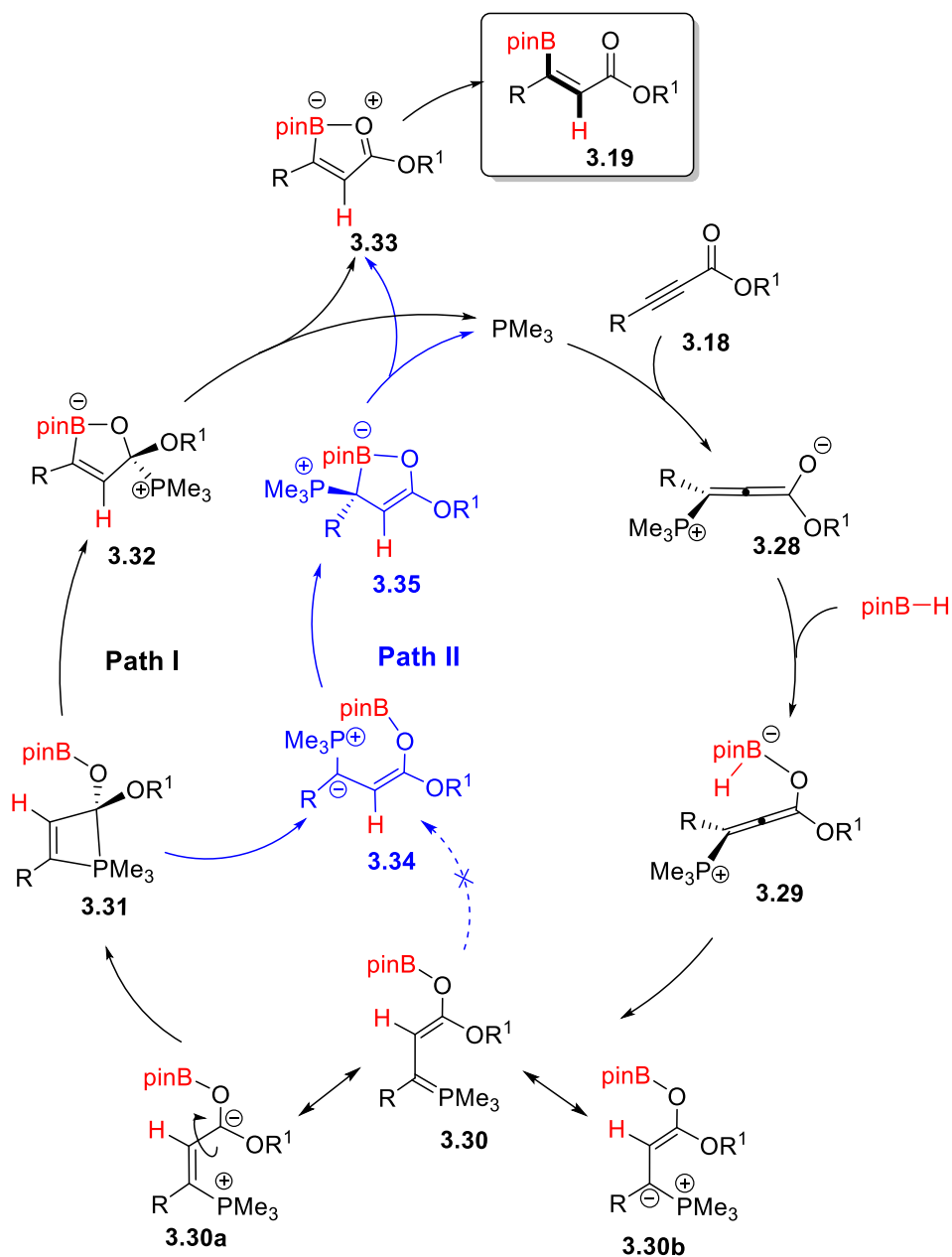


formation of deuterated methyl cinnamate **3.27** suggesting that **3.26** can also undergo deuterodeboration.



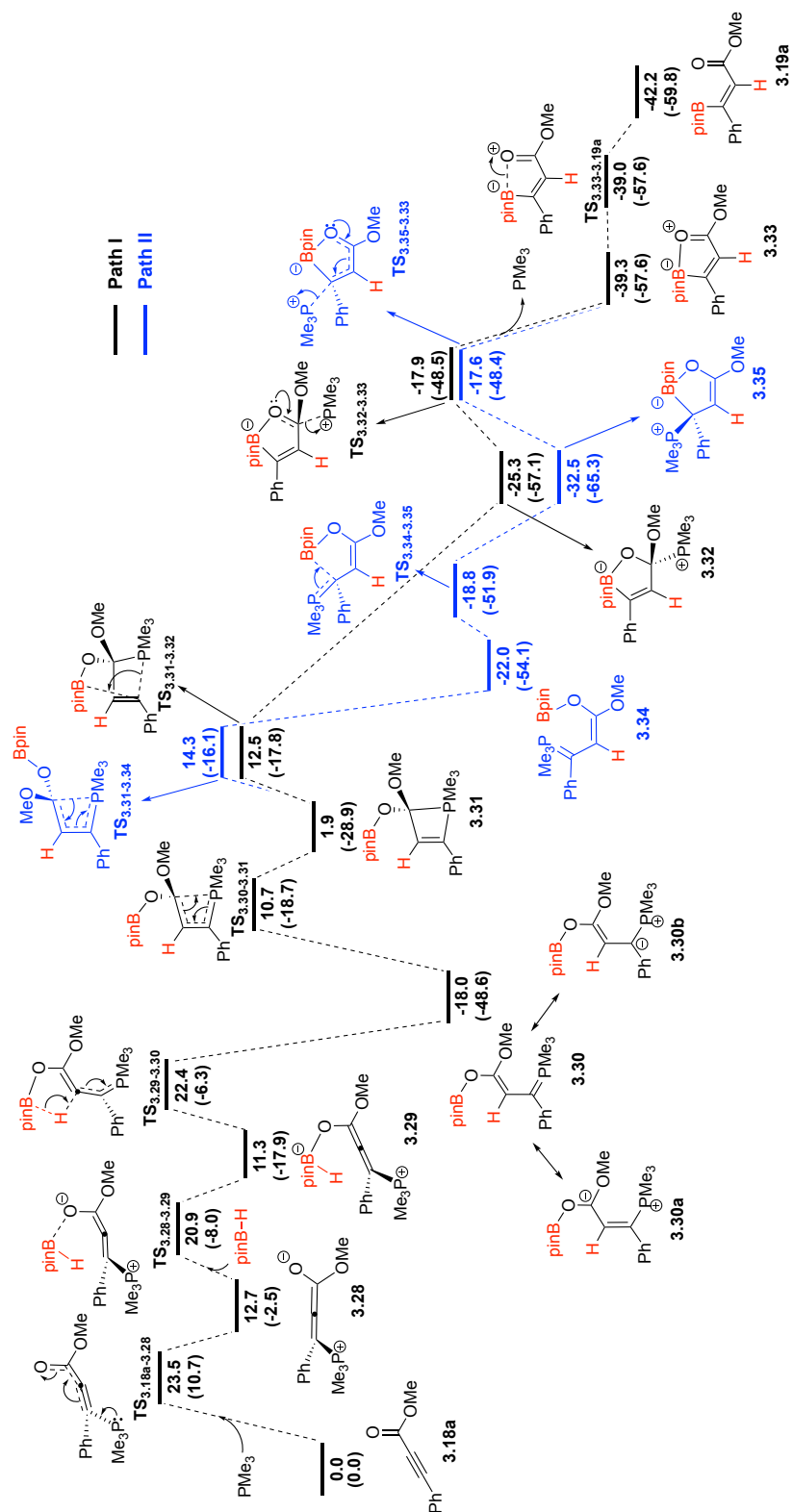
**Scheme 3.11.** Mechanistic studies.

To establish a complete catalytic cycle (Scheme 3.12), we also carried out density functional theory (DFT) calculations (Figure 3.1) (see Chapter 4, pg. 125). Figure 3.1 shows the energy profile calculated for the feasible reaction mechanism. In light of previous reports demonstrating  $\beta$ -addition of trialkylphosphines to acetylenic esters,<sup>39</sup> we surmised that the phosphine catalyst ( $\text{PMe}_3$  used for theoretical calculations) first nucleophilically attacks the  $\beta$ -carbon of the unsaturated ester **3.18** to form **3.28**, followed by addition of the Lewis acid pinacolborane to the terminal oxygen of **3.28** to give **3.29**. Hydride migration to the  $\alpha$ -carbon can proceed to generate intermediate **3.30**, which is supported by experimental deuteration studies (Scheme 3.11). **3.30** has a resonance structure **3.30a** with a single bond between the  $\alpha$ -carbon and the ester group that allows rotation along the single bond to facilitate a new phosphorous-carbon bond formation and achieve a four-membered ring phosphono-cyclobutene intermediate **3.31**. As the boron center in **3.31** is Lewis acidic, migration of the phosphorus-carbon bond to form a new boron- $\beta$ -carbon bond results in a high energy transition state to afford **3.32**. The release of  $\text{PMe}_3$



**Scheme 3.12.** Proposed catalytic cycles.

generates an internally coordinated intermediate **3.33**, which leads to the *trans* hydroboration product **3.19**. In another possibility, a resonance structure of **3.30** in **3.30b** can allow the attack of a negatively charged  $\beta$ -carbon to a Lewis acidic boron center to yield five-membered ring **3.34** (Scheme 3.12). However, to achieve this, the  $\pi$ -bond between  $\alpha$ -carbon and the ester group in **3.30b** must be broken through rotation to form the *trans*-intermediate **3.34**. Many attempts to



**Figure 3.1.** Energy profile calculated at B3LYP/6-31G\*\* for the proposed mechanism of *trans* hydroboration of methyl 3-phenylpropiolate. The solvation-corrected relative free energies and relative electronic energies (in parentheses) are given in kcal/mol.

locate the transition state of this rotation were not successful, and all attempted calculations led to transition state **TS<sub>C-D</sub>**, linking intermediates **3.30** and **3.31**.

A possible pathway that leads to **3.34** can occur through **3.31**. The cyclization affords **3.35** (Path II, marked in blue), which allows the release of  $\text{PMe}_3$  to generate **3.33**, a common intermediate with Path I. Our calculations indicate that Path II is less favorable than Path I (Figure 3.1). According to the energy profiles, the overall reaction free energy barrier of Path II (the energy difference between **3.30** and **TS<sub>3.31-3.34</sub>**) is 1.8 kcal/mol less favored than Path I, which is 30.5 kcal/mol (the energy difference between **3.30** and **TS<sub>3.31-3.32</sub>**). The rate-determining transition state corresponds to the ring expansion from a four-membered ring **3.31** towards a more stable five-membered ring **3.32** forming the  $\beta$ -carbon-boron bond. This is the step that also governs the stereoselectivity of the reaction.

### 3.7 Conclusions

In conclusion, we have developed a novel protocol for the hydroboration of alkynoate esters and amides under mild conditions. The organocatalytic reaction proceeds in a chemoselective fashion and leads to *trans* hydroborated derivatives that can be elaborated to a variety of products, including here-to-fore inaccessible 4-monosubstituted 2(5H)-oxaboroles. The detailed computational analysis of the proposed mechanism is in agreement with experiment. Current efforts are directed towards extending the method to borylations of primary and secondary alkynamides and their applications in biological systems.

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## Chapter 4. Experimental

### 4.1 General experimental methods

Unless otherwise noted, all reactions were performed under argon in flame- or oven-dried glassware. Dry acetonitrile and methanol used in Chapter 2 were purchased with Sure-Seal tops and used as received. All other solvents were dried using an Innovative Technology Pure Solv-MD solvent purification system. Bis(pinacolato)diboron and tetrahydroxydiboron were donated by AllyChem. Powdered molecular sieves (4 Å, <50 μm) were purchased from Acros Organics. All commercially available catalysts, substrates, and reagents were purchased and used as received. TLC analyses were performed using aluminum backed silica gel F<sub>254</sub> plates from SiliCycle Inc. Chromatography purification was performed using SiliaFlash P60 40-63 μm, 60 Å silica from SiliCycle Inc.

### 4.2 Instrumentation

<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, and <sup>11</sup>B NMR spectra were recorded using an Agilent MR-400 MHz, Varian Inova 400 MHz, or Bruker Avance II 500 MHz spectrometer. Spectra were internally referenced to CDCl<sub>3</sub> or TMS. Chemical shifts are reported in ppm. NMR data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, dq = doublet of quartets, br. = broad), coupling constants (Hz), and integration. Ratios of isomeric products were measured by integration of <sup>19</sup>F NMR signals. In Chapter 1, <sup>1</sup>H NMR yields were determined using 1,3,5-trimethoxybenzene as an internal standard, and ratios of isomeric products were determined through integration of the alkene or methyl protons. In Chapter 2, <sup>19</sup>F NMR yields were determined using 2-fluoro-4-iodoaniline as an internal standard, and isomeric ratios were determined through integration of the trifluoromethyl group. ESI mass spectra were acquired with

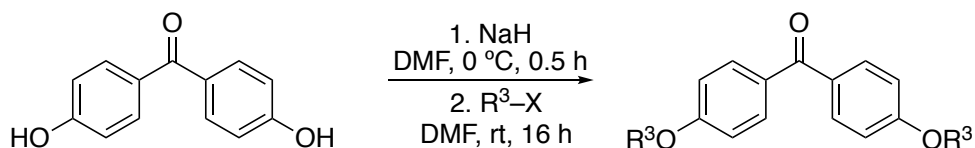
an Agilent 6220 LC-ESI-TOF or a Thermo Scientific Q-Exactive Orbitrap. ASAP-HRMS (Chapter 1) were acquired with a Micromass Ultima Q-TOF API. Spectral data for published compounds from Chapter 1 (DOI: 10.1055/s-0039-1690207) and Chapter 3 (DOI:10.1021/acs.joc.8b01493) can be found online. Spectral data for Chapter 2 can be found in the appendix.

### 4.3 Synthetic procedures and characterization of compounds for Chapter 1

Several ketones are commercially available and were used as received. Diaryl ketones were synthesized via the Williamson ether synthesis. Alpha-methylstyrene was commercially available and used as received. The rest of the styrenes were synthesized via the Wittig reaction. Allenes (**1.34a-l**, **1.36a-i**) were synthesized using the Doering-LaFlamme reaction as shown below.

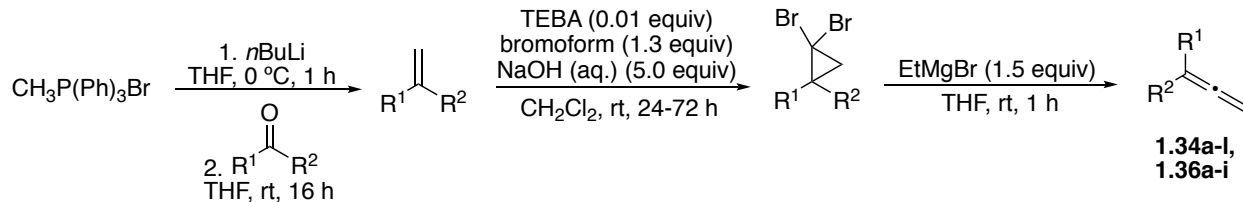
#### Example procedure for the synthesis of allenes:

##### *Synthesis of aryl ethers via Williamson ether synthesis*



Bis(4-hydroxyphenyl)methanone (1.0 g, 1.0 equiv., 4.6 mmol) was added to an oven-dried 50 mL round bottom flask equipped with a stir bar. Dry DMF (15 mL) was added and mixture was cooled to 0 °C. Sodium hydride (4.48 g, 4.00 equiv., 18.7 mmol) was slowly added (septum was removed to add the reagent and replaced) and the reaction was stirred at 0 °C. After 30 min, methyl iodide (870 μL, 3.0 equiv., 14 mmol) was added and the reaction was stirred overnight. After the reaction was complete, water (10 mL) was added and the reaction mixture was extracted with ethyl acetate (3 x 50 mL). The organic layer was washed with brine and dried over sodium sulfate. The solvent was removed in vacuo to give a yellow powder. The reaction was purified on silica (15% EtOAc in hexanes) to give the aryl ether as a white solid (937 mg, 3.87 mmol, 83%).

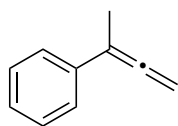
### Synthesis of allenes via the Doering-LaFlamme reaction.



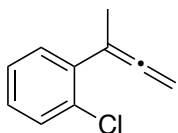
Methyltriphenylphosphonium bromide (1.65 g, 1.20 equiv., 4.61 mmol) was added to an oven-dried round bottom flask equipped with a stir bar. The flask was purged with argon, and dry THF (15 mL) was added. The suspension was cooled to  $0\text{ }^\circ\text{C}$  and 2.5 M  $n\text{BuLi}$  in hexanes (1.8 mL, 1.2 equiv., 4.6 mmol) was added dropwise. The reaction was stirred at  $0\text{ }^\circ\text{C}$  for 1 h. The ketone (930 mg, 1.0 equiv., 3.8 mmol) was added, the reaction was allowed to warm to room temperature, and was stirred overnight. When the reaction was complete, water (20 mL) was added. The aqueous layer was extracted with diethyl ether (3 x 20 mL). The organic layer was washed with brine and dried over sodium sulfate. Solvent was removed in vacuo and the crude reaction mixture was purified on silica (15% EtOAc in hexanes) affording the corresponding diaryl alkene as a white solid (320 mg, 1.33 mmol, 35%). The alkene intermediate (300 mg, 1.00 equiv., 1.25 mmol) was added to a 6 dram vial equipped with a stir bar, followed by dichl (4.0 mL), TEBA (3 mg, 0.01 equiv., 10  $\mu\text{mol}$ ), bromoform (0.14 mL, 1.3 equiv., 1.6 mmol), and a 50% w/w solution of aqueous sodium hydroxide (0.170 mL, 5.00 equiv., 6.24 mmol). The vial was purged with argon, capped, and sealed with parafilm. The biphasic solution stirred at room temperature for 48 h, at which point the reaction was diluted with 5 mL DI water. The aqueous phase was extracted with dichloromethane (2 x 10 mL) and dried over sodium sulfate. Solvent was removed under reduced pressure and the crude reaction mixture was purified on silica (10% EtOAc in hexanes) affording the dibromocyclopropyl intermediate as a white solid (304 mg, 0.740 mmol, 59%). The dibromocyclopropyl intermediate (218 mg, 1.00 equiv., 0.529 mmol) was added to a round bottom

flask, which was then purged with argon. THF (1.8mL) was added and the reaction was stirred at room temperature. A solution of EtMgBr (0.26mL, 1.5 equiv., 0.79 mmol, 3 M in diethyl ether) was added dropwise. The reaction was allowed to stir for 1 h, at which time water (2mL) was added slowly. The aqueous layer was extracted with diethyl ether (2 x 10 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The crude reaction mixture was purified via column chromatography (15% EtOAc in hexanes) to afford allene **1.36e** as a white solid (106 mg, 0.420 mmol, 79%).

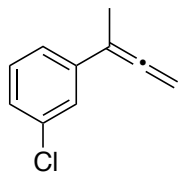
#### Characterization of allenes **1.34a-l**, **1.36a-i**.



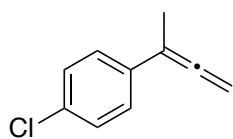
**buta-2,3-dien-2-ylbenzene (1.34a)**. Reaction Scale: 5.17 mmol, Yield: 501 mg (74%); colorless oil;  $R_f = 0.79$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (d,  $J = 8.5$  Hz, 2H), 7.35 (t,  $J = 7.7$  Hz, 2H), 7.23 (t,  $J = 7.3$  Hz, 1H), 5.05 (q,  $J = 3.2$  Hz, 2H), 2.13 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  matches reported literature values.<sup>1</sup>



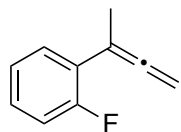
**1-(buta-2,3-dien-2-yl)-2-chlorobenzene (1.34b)**. Reaction Scale: 1.85 mmol, Yield: 226 mg (74%); pale yellow oil;  $R_f = 0.68$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.34 (m, 1H), 7.29 (dd,  $J = 7.5, 2.0$  Hz, 1H), 7.22 (td,  $J = 7.5, 1.6$  Hz, 1H), 7.17 (td,  $J = 7.6, 1.9$  Hz, 1H), 4.83 (q,  $J = 3.2$  Hz, 2H), 2.08 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>2</sup>



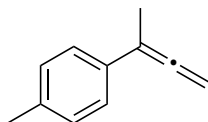
**1-(buta-2,3-dien-2-yl)-3-chlorobenzene (1.34c).** Reaction Scale: 1.85 mmol, Yield: 263 mg (86%); pale yellow liquid;  $R_f = 0.66$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.34 (m, 1H), 7.29 – 7.20 (m, 2H), 7.18 – 7.13 (m, 1H), 5.06 (q,  $J = 3.2$  Hz, 2H), 2.06 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  shifts match reported literature values.<sup>2</sup>



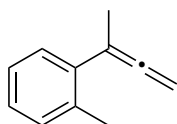
**1-(buta-2,3-dien-2-yl)-4-chlorobenzene (1.34d).** Reaction Scale: 660 mg, Yield: 276 mg (82%); white solid;  $R_f = 0.66$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 – 7.25 (m, 4H), 5.03 (q,  $J = 3.1$  Hz, 2H), 2.07 (t,  $J = 3.2, 0.5$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>2</sup>



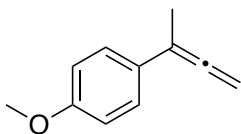
**1-(buta-2,3-dien-2-yl)-2-fluorobenzene (1.34e).** Reaction Scale: 2.03 mmol, Yield: 127 mg (66%); colorless liquid;  $R_f = 0.59$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (dt,  $J = 7.8, 1.8$  Hz, 1H), 7.23 – 7.16 (m, 1H), 7.09 (dt,  $J = 7.5, 1.3$  Hz, 1H), 7.02 (ddd,  $J = 11.4, 8.1, 1.3$  Hz, 1H), 4.90 (q,  $J = 3.2$  Hz, 2H), 2.12 (ddt,  $J = 3.2, 1.9, 0.4$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>3</sup>



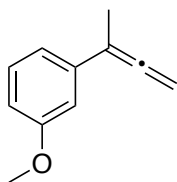
**1-(buta-2,3-dien-2-yl)-4-methylbenzene (1.34f).** Reaction Scale: 1.64 mmol, Yield: 0.170 g (71%); yellow oil;  $R_f = 0.52$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 (d,  $J = 8.2$  Hz, 2H), 7.14 (d,  $J = 8.0$  Hz, 2H), 5.01 (q,  $J = 3.1$  Hz, 2H), 2.34 (s, 3H), 2.09 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>4</sup>



**1-(buta-2,3-dien-2-yl)-2-methylbenzene (1.34g).** Reaction Scale: 1.1 mmol, Yield: 84 mg (52%); colorless liquid;  $R_f = 0.63$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 – 7.07 (m, 4H), 4.75 (q,  $J = 3.2$  Hz, 2H), 2.37 (s, 3H), 2.05 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>2</sup>

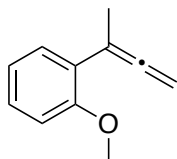


**1-(buta-2,3-dien-2-yl)-4-methoxybenzene (1.34h).** Reaction Scale: 1.87 mmol, Yield: 254 mg (85%); white solid;  $R_f = 0.18$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.29 (m, 2H), 6.92 – 6.85 (m, 2H), 5.00 (q,  $J = 3.2$  Hz, 2H), 3.81 (s, 3H), 2.07 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>2</sup>

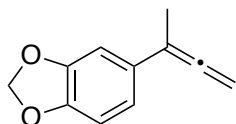


**1-(buta-2,3-dien-2-yl)-3-methoxybenzene (1.34i).** Reaction Scale: 1.87 mmol, Yield: 224 mg (75%); yellow liquid;  $R_f = 0.24$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.20 (m, 1H),

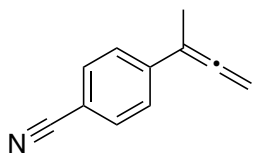
7.04 – 6.99 (m, 1H), 7.00 – 6.94 (m, 1H), 6.76 (dd,  $J = 8.0, 2.7$  Hz, 1H), 5.03 (q,  $J = 3.2$  Hz, 2H), 3.82 (s, 3H), 2.09 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H}$  NMR is consistent with literature values.<sup>2</sup>



**1-(buta-2,3-dien-2-yl)-2-methoxybenzene (1.34j).** Reaction Scale: 1.25 mmol, Yield: 58 mg (29%); colorless liquid;  $R_f = 0.34$  (hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 – 7.20 (m, 2H), 6.93 (td,  $J = 7.5, 1.1$  Hz, 1H), 6.90 – 6.86 (m, 1H), 4.79 (q,  $J = 3.1$  Hz, 2H), 3.84 (s, 3H), 2.09 (t,  $J = 3.2$  Hz, 3H).  $^1\text{H}$  NMR is consistent with literature values.<sup>2</sup>

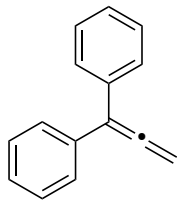


**5-(buta-2,3-dien-2-yl)benzo[d][1,3]dioxole (1.34k).** Reaction Scale: 1.20 mmol, Yield: 146 mg (70%); yellow oil;  $R_f = 0.33$  (hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.97 – 6.91 (m, 1H), 6.87 – 6.82 (m, 1H), 6.80 – 6.75 (m, 1H), 5.94 (s, 2H), 5.00 (q,  $J = 3.2$  Hz, 2H), 2.05 (t,  $J = 3.2$  Hz, 4H).  $^1\text{H}$  NMR matches reported literature values.<sup>2</sup>

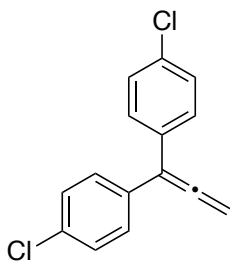


**4-(buta-2,3-dien-2-yl)benzonitrile (1.34l).** Reaction Scale: 1.3 mmol, Yield: 94 mg (48%); colorless oil;  $R_f = 0.35$  (10% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60 (d,  $J = 8.3$  Hz, 2H), 7.48 (d,  $J = 8.2$  Hz, 2H), 5.12 (q,  $J = 3.1$  Hz, 2H), 2.10 (t,  $J = 3.4$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  210.0, 142.1, 132.2, 126.3, 119.3, 109.9, 99.4, 78.1, 16.5. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{11}\text{H}_{10}\text{N}$ : 156.0808; Found: 156.0804.

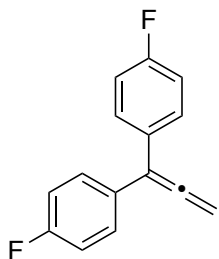




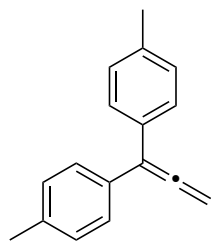
**propa-1,2-diene-1,1-diyl dibenzene (1.36a).** Reaction Scale: 0.994 mmol, Yield: 142 mg (74%); yellow oil;  $R_f = 0.58$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.26 (m, 10H), 5.27 (s, 2H).  $^1\text{H NMR}$  is consistent with literature values.<sup>1</sup>



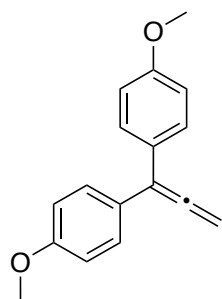
**4,4'-(propa-1,2-diene-1,1-diyl)bis(chlorobenzene) (1.36b).** Reaction Scale: 0.52 mmol, Yield: 38 mg (28%); white solid;  $R_f = 0.52$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 (d,  $J = 8.7$  Hz, 4H), 7.26 (d,  $J = 8.6$  Hz, 4H), 5.29 (s, 2H).  $^1\text{H NMR}$  is consistent with literature values.<sup>5</sup>



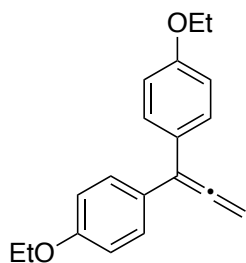
**4,4'-(propa-1,2-diene-1,1-diyl)bis(fluorobenzene) (1.36c).** Reaction Scale: 1.0 mmol, Yield: 160 mg (68%); white solid;  $R_f = 0.55$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.26 (m, 4H), 7.07 – 7.01 (m, 4H), 5.26 (s, 2H).  $^1\text{H NMR}$  is consistent with literature values.<sup>6</sup>



**4,4'-(propa-1,2-diene-1,1-diyl)bis(methylbenzene) (1.36d).** Reaction Scale: 1.05 mmol, Yield: 195 mg (84%); pale yellow solid;  $R_f = 0.39$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 (d,  $J = 8.2$  Hz, 4H), 7.15 (d,  $J = 7.9$  Hz, 4H), 5.22 (s, 2H), 2.36 (s, 6H).  $^1\text{H NMR}$  is consistent with literature values.<sup>5</sup>

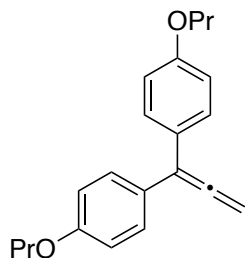


**4,4'-(propa-1,2-diene-1,1-diyl)bis(methoxybenzene) (1.36e).** Reaction Scale: 0.534 mmol, Yield: 106 mg (79%); white solid;  $R_f = 0.52$  (15% EtOAc in hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 (d,  $J = 8.9$  Hz, 4H), 6.89 (d,  $J = 8.9$  Hz, 4H), 5.22 (s, 2H), 3.82 (s, 6H).  $^1\text{H NMR}$  is consistent with literature values.<sup>7</sup>

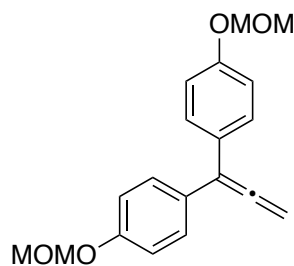


**4,4'-(propa-1,2-diene-1,1-diyl)bis(ethoxybenzene) (1.36f).** Reaction Scale: 0.795 mmol, Yield: 195 mg (88%); white solid; decomposed prior to melting;  $R_f = 0.22$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (d,  $J = 8.7$  Hz, 4H), 6.87 (d,  $J = 8.8$  Hz, 4H), 5.21 (s, 2H), 4.04 (q,  $J = 7.0$  Hz, 4H),

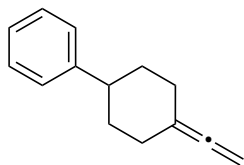
1.42 (t,  $J = 7.0$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  209.9, 158.7, 129.9, 129.0, 114.8, 108.7, 78.2, 63.9, 15.3. HRMS- +Mixed EIC:  $m/z$   $[\text{2M}^*]^+$  calcd for  $\text{C}_{38}\text{H}_{40}\text{O}_4$ : 560.2921; Found: 560.2907.



**4,4'-(propa-1,2-diene-1,1-diyl)bis(propoxybenzene) (1.36g).** Reaction Scale: 0.641 mmol, Yield: 152 mg (77%); white solid; decomposed prior to melting;  $R_f = 0.46$  (5% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 (d,  $J = 8.8$  Hz, 4H), 6.87 (d,  $J = 8.9$  Hz, 4H), 5.21 (s, 2H), 3.93 (t,  $J = 6.6$  Hz, 4H), 1.87 – 1.77 (m, 4H), 1.04 (t,  $J = 7.4$  Hz, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  209.6, 158.6, 129.6, 128.6, 114.5, 108.4, 77.8, 69.7, 22.8, 10.7. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{21}\text{H}_{25}\text{O}_2$ : 309.1849; Found: 309.1847.



**4,4'-(propa-1,2-diene-1,1-diyl)bis((methoxymethoxy)benzene) (1.36h).** Reaction Scale: 0.635 mmol, Yield: 136 mg (69%); viscous yellow oil;  $R_f = 0.36$  (10% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 (d,  $J = 8.8$  Hz, 4H), 7.02 (d,  $J = 8.9$  Hz, 4H), 5.22 (s, 2H), 5.19 (s, 4H), 3.49 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  209.7, 156.6, 130.0, 129.6, 116.3, 108.3, 94.6, 78.0, 56.2. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{21}\text{O}_4$ : 313.1434; Found: 313.1451.



**(4-vinylidenecyclohexyl)benzene (1.36i).** Reaction Scale: 0.38 mmol, Yield: 38 mg (55%); colorless oil;  $R_f = 0.34$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.26 (m, 2H), 7.23 – 7.16 (m, 3H), 4.65 – 4.53 (m, 2H), 2.58 (tt,  $J = 12.2, 3.4$  Hz, 1H), 2.43 (brd,  $J = 13.4$  Hz, 2H), 2.23 – 2.12 (m, 2H), 2.02 – 1.93 (m, 2H), 1.62 (qd,  $J = 12.8, 3.9$  Hz, 2H).  $^1\text{H NMR}$  is consistent with literature values.<sup>8</sup>

### **General Procedure for Optimization Reactions**

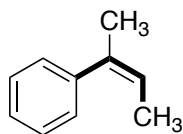
Diboron reagent and catalyst were weighed into a 1 dram vial containing a micro stir bar and fitted with a septum. After purging with argon, solvent was added, followed by buta-2,3-dien-2-ylbenzene (**1.34a**) (0.050 g, 1.0 equiv.) and water. The reaction was stirred at room temperature for 24 h. After 24 h, the reaction solution was diluted with dichloromethane (1.0 mL) and filtered through a pipette with a small plug of celite. The celite plug was rinsed thoroughly with dichloromethane. An internal standard, 1,3,5-trimethoxybenzene, was added and the solution was concentrated in vacuo.  $\text{CDCl}_3$  was added and the yield was determined by quantitative NMR.

### **General Procedure for Semireductions**

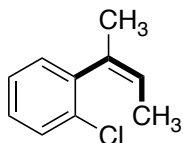
Tetrahydroxydiboron (35 mg, 1.0 equiv.) and Pd/C (41 mg, 0.050 equiv.) were weighed into a 1 dram vial containing a micro stir bar and fitted with a septum. After purging with argon, diethyl ether (1.0 mL) was added, followed by buta-2,3-dien-2-ylbenzene (**1.34a**) (0.050 g, 1.0 equiv.) and water (0.015 mL, 2.1 equiv.). The reaction was stirred at room temperature for 5 h. Upon completion, the reaction solution was diluted with diethyl ether (1.0 mL) and filtered through a pipette with a small plug of celite. The celite plug was rinsed thoroughly with diethyl ether. An

internal standard, 1,3,5-trimethoxybenzene, was added and the solution was concentrated in vacuo. CDCl<sub>3</sub> was added and the yield was determined by quantitative NMR.

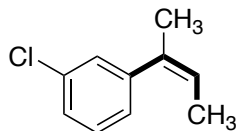
**Characterization of products 1.35a-l and 1.37a-i.** (\*Indicates minor isomer)



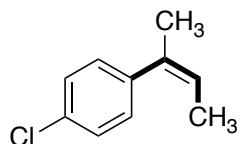
**but-2-en-2-ylbenzene (1.35a).** Reaction Scale: 0.384 mmol - NMR Yield: 68% *Z/E* = 86:14. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.38 – 7.15 (m, 5H, 5H\*), 5.85 (qq, *J* = 6.8, 1.4 Hz, 1H\*), 5.55 (qq, *J* = 6.9, 1.5 Hz, 1H), 2.04 – 2.01, (m, 3H, 3H\*), 1.79 (dq, *J* = 6.9, 1.1 Hz, 3H\*), 1.59 (dq, *J* = 6.9, 1.6 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>9</sup>



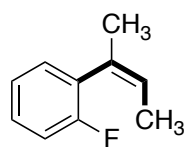
**1-(but-2-en-2-yl)-2-chlorobenzene (1.35b).** Reaction Scale: 0.304 mmol - NMR Yield: 69% *Z/E* = 91:9. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40 – 7.07 (m, 4H, 4H\*), 5.61 (qq, *J* = 6.7, 1.5 Hz, 1H), 5.47 (qq, *J* = 6.7, 1.4 Hz, 1H\*), 1.98 – 1.95 (m, 3H, 3H\*), 1.76 (dq, *J* = 6.8, 1.1 Hz, 3H\*), 1.39 (dq, *J* = 6.8, 1.6 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>9</sup>



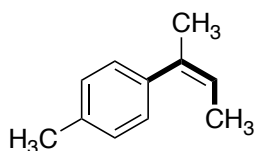
**1-(but-2-en-2-yl)-3-chlorobenzene (1.35c).** Reaction Scale: 0.298 mmol - NMR Yield: 67% *Z/E* = 88:12. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40 – 7.04 (m, 4H, 4H\*), 5.87 (qq, *J* = 6.8, 1.4 Hz, 1H\*), 5.58 (qq, *J* = 6.9, 1.5 Hz, 1H), 2.01 – 1.98 (m, 3H, 3H\*), 1.79 (dq, *J* = 6.8, 1.0 Hz, 3H\*), 1.58 (dq, *J* = 7.0, 1.6 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>9</sup>



**1-(but-2-en-2-yl)-4-chlorobenzene (1.35d).** Reaction Scale: 0.304 mmol - NMR Yield: 67% *Z/E* = 85:15. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.09 (m, 4H, 4H\*), 5.84 (qq, *J* = 6.9, 1.4 Hz, 1H\*), 5.57 (qq, *J* = 6.9, 1.5 Hz, 1H), 2.01 – 1.98 (m, 3H, 3H\*), 1.78 (dq, *J* = 6.9, 1.1 Hz, 3H\*), 1.58 (dq, *J* = 6.9, 1.6 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>9</sup>

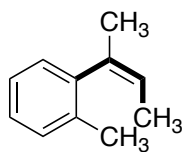


**1-(but-2-en-2-yl)-2-fluorobenzene (1.35e).** Reaction Scale: 0.310 mmol - NMR Yield: 61% *Z/E* = 86:14. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.27 – 6.96 (m, 4H, 4H\*), 5.68 (qq, *J* = 6.8, 1.5 Hz, 1H\*), 5.67 (qq, *J* = 6.8, 1.5 Hz, 1H), 2.02 – 2.01 (m, 3H, 3H\*), 1.79 (dq, *J* = 6.8, 1.2 Hz, 3H\*), 1.50 (dq, *J* = 6.8, 1.6, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 160.0 (d, *J* = 246.4 Hz), 159.7 (d, *J* = 245.3 Hz), 133.0 (d, *J* = 14.2 Hz), 132.2, 131.5, 130.6 (d, *J* = 4.7 Hz), 129.8 (d, *J* = 4.6 Hz), 129.3 (d, *J* = 16.9), 128.4 (d, *J* = 8.0 Hz), 128.0 (d, *J* = 8.3 Hz), 125.9 (d, *J* = 2.2 Hz), 124.3, 124.0 (d, *J* = 3.6 Hz), 123.9 (d, *J* = 3.5 Hz), 115.7 (d, *J* = 22.9 Hz), 115.7 (d, *J* = 22.6 Hz), 24.7 (d, *J* = 1.6 Hz), 16.8 (d, *J* = 3.8 Hz), 15.0 (d, *J* = 1.5 Hz), 14.2. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -115.5 – -115.4 (m), -115.6 – -115.7 (m\*). HRMS (ESI+): [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>10</sub>F: 150.0845; Found: 150.0797.

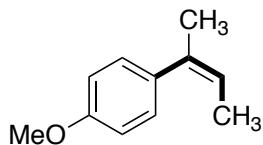


**1-(but-2-en-2-yl)-4-methylbenzene (1.35f).** Reaction Scale: 0.277 mmol - NMR Yield: 63% *Z/E* = 86:14. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.28 (d, *J* = 8.0 Hz, 2H\*), 7.19 – 7.15 (m, 2H), 7.12 (d, *J*

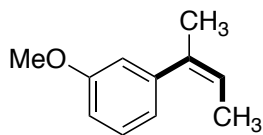
= 8.2 Hz, 2H, 2H\*), 5.85 (qq,  $J = 6.8, 1.4$  Hz, 1H\*), 5.56 (qq,  $J = 6.9, 1.5$  Hz, 1H), 2.37 (s, 3H), 2.34 (s, 3H\*), 2.05 – 2.02 (m, 3H, 3H\*), 1.81 (dq,  $J = 7.0, 1.1$  Hz, 3H\*), 1.63 (dq,  $J = 6.9, 1.6$  Hz, 3H).  $^1\text{H}$  NMR is consistent with literature values.<sup>10</sup>



**1-(but-2-en-2-yl)-2-methylbenzene (1.35g).** Reaction Scale: 0.173 mmol - NMR Yield: 58%  $Z/E = 91:9$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 – 7.08 (m, 4H), 7.02 – 6.98 (m, 4H\*), 5.54 (qq,  $J = 6.7, 1.5$  Hz, 1H), 5.36 (qq,  $J = 6.7, 1.5$  Hz, 1H\*), 2.26 (s, 3H\*), 2.20 (s, 3H), 1.94 – 1.91 (m, 3H), 1.91 – 1.89 (m, 3H\*), 1.76 (dq,  $J = 6.8, 1.1$  Hz, 3H\*), 1.35 (dq,  $J = 6.7, 1.6$  Hz, 3H).  $^1\text{H}$  NMR is consistent with literature values.<sup>11</sup>

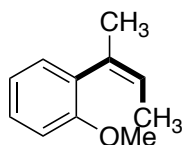


**1-(but-2-en-2-yl)-4-methoxybenzene (1.35h).** Reaction Scale: 0.312 mmol - NMR Yield: 63%  $Z/E = 85:15$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 (d,  $J = 8.9$  Hz, 2H\*), 7.14 (d,  $J = 8.8$  Hz, 2H), 6.89 (d,  $J = 8.8$  Hz, 2H), 6.84 (d,  $J = 8.8$  Hz, 2H\*), 5.78 (qq,  $J = 6.9, 1.4$  Hz, 1H\*), 5.53 (qq,  $J = 6.9, 1.5$  Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H\*), 2.03 – 2.00 (m, 3H, 3H\*), 1.78 (dq,  $J = 6.8, 1.0$  Hz, 3H\*), 1.61 (dq,  $J = 6.9, 1.5$  Hz, 3H).  $^1\text{H}$  NMR is consistent with literature values.<sup>18</sup>

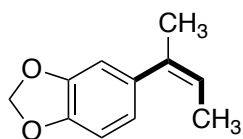


**1-(but-2-en-2-yl)-3-methoxybenzene (1.35i).** Reaction Scale: 0.312 mmol - NMR Yield: 57%  $Z/E = 86:14$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 – 7.17 (m, 1H, 1H\*), 6.80 – 6.72 (m, 3H, 3H\*),

5.86 (qq,  $J = 6.9, 1.4$  Hz, 1H\*), 5.54 (qq,  $J = 6.9, 1.5$  Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H\*), 2.03 – 1.97 (m, 3H, 3H\*), 1.78 (dq,  $J = 6.9, 1.1$  Hz, 3H\*), 1.60 (dq,  $J = 6.9, 1.6$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  159.5, 143.6, 136.9, 129.2, 121.9, 120.7, 114.0, 111.8, 55.3, 25.5, 15.0. HRMS (ESI+):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{11}\text{H}_{15}\text{O}$ : 163.1123; Found: 163.1130.

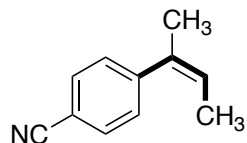


**1-(but-2-en-2-yl)-2-methoxybenzene (1.35j).** Reaction Scale: 0.156 mmol - NMR Yield: 72%  $Z/E = 88:12$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26 – 7.21 (m, 1H, 1H\*), 7.10 (dd,  $J = 7.4, 1.8$  Hz, 1H\*), 7.04 (dd,  $J = 7.4, 1.8$  Hz, 1H), 6.96 – 6.82 (m, 2H, 2H\*), 5.60 (qq,  $J = 6.7, 1.5$  Hz, 1H), 5.54 (qq,  $J = 6.7, 1.4$  Hz, 1H\*), 3.82 (s, 3H\*), 3.81 (s, 3H), 2.00 – 1.95 (m, 3H, 3H\*), 1.76 (dq,  $J = 6.8, 1.1$  Hz, 3H\*), 1.45 (dq,  $J = 6.7, 1.5$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 134.9, 131.0, 130.1, 128.0, 122.6, 120.6, 111.0, 55.6, 24.6, 14.9. HRMS (ESI+):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{11}\text{H}_{15}\text{O}$ : 163.1123; Found: 163.1128.

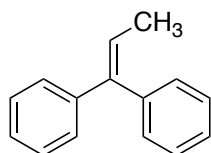


**5-(but-2-en-2-yl)benzo[d][1,3]dioxole (1.35k).** Reaction Scale: 0.287 mmol - NMR Yield: 65%  $Z/E = 86:14$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.93 – 6.63 (m, 3H, 3H\*), 5.93 (s, 2H), 5.91 (s, 2H\*), 5.75 (qq,  $J = 6.9, 1.4$  Hz, 1H\*), 5.51 (qq,  $J = 6.9, 1.5$  Hz, 1H), 2.00 – 1.95 (m, 3H, 3H\*), 1.76 (dq,  $J = 6.9, 1.1$  Hz, 3H\*), 1.59 (dq,  $J = 6.9, 1.6$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  147.4, 146.0, 136.5, 135.9, 121.7, 121.4, 108.8, 108.1, 101.0, 25.7, 15.1. HRMS (ESI+):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{11}\text{H}_{13}\text{O}_2$ : 177.0916; Found: 177.0924.

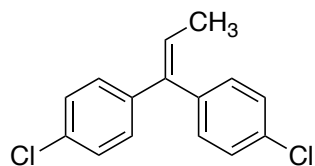




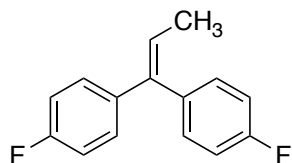
**4-(but-2-en-2-yl)benzonitrile (1.35I).** Reaction Scale: 0.161 mmol - NMR Yield: 39% *Z/E* = 81:19. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H\*), 7.44 (d, *J* = 8.4 Hz, 2H\*), 7.29 (d, *J* = 8.4 Hz, 2H), 5.99 (qq, *J* = 6.1, 1.2 Hz, 1H\*), 5.66 (qq, *J* = 6.8, 1.3 Hz, 1H), 2.04 – 2.01 (m, 3H, 3H\*), 1.83 (dq, *J* = 6.9, 1.1 Hz, 3H\*), 1.58 (dq, *J* = 7.0, 1.5 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 147.0, 135.4, 132.1, 129.0, 123.9, 119.2, 110.2, 25.0, 15.0. HRMS (ES<sup>+</sup>): [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>N: 158.0964; Found: 158.0982.



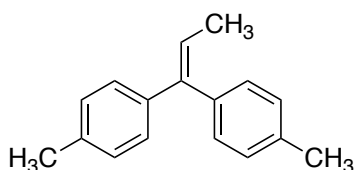
**prop-1-ene-1,1-diylidibenzene (1.37a).** Reaction Scale: 0.260 mmol - Yield: 43 mg (85%); colorless solid; R<sub>f</sub> = 0.39 (hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41 – 7.32 (m, 2H), 7.33 – 7.14 (m, 8H), 6.17 (q, *J* = 7.0 Hz, 1H), 1.76 (d, *J* = 7.0 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>12</sup>



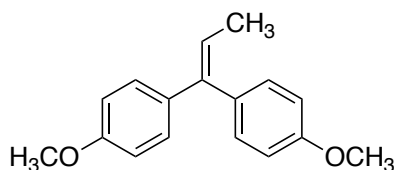
**4,4'-(prop-1-ene-1,1-diyl)bis(chlorobenzene) (1.37b).** Reaction Scale: 0.061 mmol - Yield: 14 mg (87%); colorless oil; R<sub>f</sub> = 0.52 (5% EtOAc in hexanes). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.15 – 7.08 (m, 4H), 6.16 (q, *J* = 7.1 Hz, 1H), 1.75 (d, *J* = 7.1 Hz, 3H). <sup>1</sup>H NMR is consistent with literature values.<sup>13</sup>



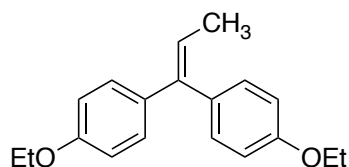
**4,4'-(prop-1-ene-1,1-diyl)bis(fluorobenzene) (1.37c).** Reaction Scale: 0.22 mmol - Yield: 43 mg (85%); colorless oil  $R_f = 0.36$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 – 7.10 (m, 4H), 7.11 – 7.04 (m, 2H), 7.00 – 6.91 (m, 2H), 6.11 (q,  $J = 7.0$  Hz, 1H), 1.76 (d,  $J = 7.0$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>14</sup>



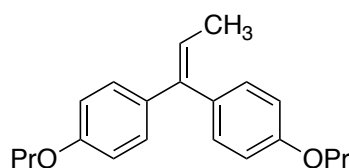
**4,4'-(prop-1-ene-1,1-diyl)bis(methylbenzene) (1.37d).** Reaction Scale: 0.23 mmol - Yield: 45 mg (88%); colorless oil;  $R_f = 0.40$  (hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 – 7.16 (m, 2H), 7.15 – 7.05 (m, 7H), 6.12 (q,  $J = 7.0$  Hz, 1H), 2.40 (s, 3H), 2.33 (s, 3H), 1.77 (d,  $J = 7.0$  Hz, 3H).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.3, 140.6, 137.2, 136.5, 136.5, 130.1, 128.9, 128.9, 127.3, 123.2, 21.4, 21.2, 15.8. HRMS (ES<sup>+</sup>):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{19}$ : 223.1487; Found: 223.1478.



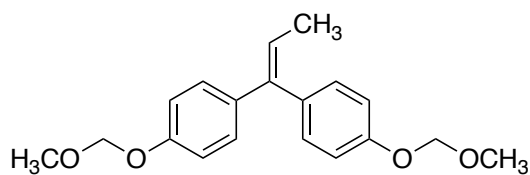
**4,4'-(prop-1-ene-1,1-diyl)bis(methoxybenzene) (1.37e).** Reaction Scale: 0.12 mmol - Yield: 23 mg (74%); white solid;  $R_f = 0.52$  (10% EtOAc in hexanes).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.14 (d,  $J = 8.9$  Hz, 2H), 7.10 (d,  $J = 8.8$  Hz, 2H), 6.90 (d,  $J = 8.8$  Hz, 2H), 6.79 (d,  $J = 8.9$  Hz, 2H), 6.02 (q,  $J = 7.0$  Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 1.75 (d,  $J = 7.0$  Hz, 3H).  $^1\text{H NMR}$  is consistent with literature values.<sup>15</sup>



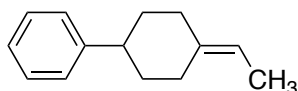
**4,4'-(prop-1-ene-1,1-diyl)bis(ethoxybenzene) (1.37f).** Reaction Scale: 0.18 mmol - Yield: 41 mg (81%); white solid; mp = 67-72 °C;  $R_f$  = 0.64 (10% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.13 (d,  $J$  = 8.9 Hz, 2H), 7.09 (d,  $J$  = 8.8 Hz, 2H), 6.89 (d,  $J$  = 8.8 Hz, 2H), 6.78 (d,  $J$  = 8.9 Hz, 2H), 6.02 (q,  $J$  = 7.0 Hz, 1H), 4.09 – 3.97 (m, 4H), 1.75 (d,  $J$  = 7.0 Hz, 3H), 1.46 – 1.37 (m, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.0, 157.9, 141.6, 136.1, 132.5, 131.3, 128.4, 122.1, 114.1, 114.1, 63.5, 63.5, 15.8, 15.1 15.0. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{23}\text{O}_2$ : 283.1693; Found: 283.1692.



**4,4'-(prop-1-ene-1,1-diyl)bis(propoxybenzene) (1.37g).** Reaction Scale: 0.094 mmol - Yield: 23 mg (78%); white solid; mp = 30-34 °C;  $R_f$  = 0.27 (5% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.12 (d,  $J$  = 8.9 Hz, 2H), 7.08 (d,  $J$  = 8.8 Hz, 2H), 6.89 (d,  $J$  = 8.8 Hz, 2H), 6.78 (d,  $J$  = 8.9 Hz, 2H), 6.01 (q,  $J$  = 7.0 Hz, 1H), 3.95 (t,  $J$  = 6.5 Hz, 2H), 3.90 (t,  $J$  = 6.6 Hz, 2H), 1.88 – 1.76 (m, 5H), 1.75 (d,  $J$  = 7.0 Hz, 3H), 1.07 (t,  $J$  = 7.4 Hz, 3H), 1.02 (t,  $J$  = 7.6 Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.2, 158.1, 141.6, 136.1, 132.5, 131.3, 128.5, 122.1, 114.1, 114.1, 69.6, 69.6, 22.8, 22.8, 15.9, 10.8, 10.7. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{21}\text{H}_{27}\text{O}_2$ : 311.2006; Found: 311.1984.



**4,4'-(prop-1-ene-1,1-diyl)bis((methoxymethoxy)benzene) (1.37h).** Reaction Scale: 0.14 mmol - Yield: 31 mg (68%); viscous colorless oil;  $R_f = 0.30$  (15% EtOAc in hexanes).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.15 (d,  $J = 8.9$  Hz, 2H), 7.10 (d,  $J = 8.9$  Hz, 2H), 7.04 (d,  $J = 8.9$  Hz, 2H), 6.93 (d,  $J = 8.9$  Hz, 2H), 6.05 (q,  $J = 7.0$  Hz, 1H), 5.21 (s, 2H), 5.16 (s, 2H), 3.52 (s, 3H), 3.48 (s, 3H), 1.76 (d,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 156.2, 141.4, 137.3, 133.8, 131.3, 128.5, 122.8, 115.9, 115.9, 94.6, 94.6, 56.2, 56.1, 15.8. HRMS- +Mixed EIC:  $m/z$   $[\text{M}+\text{Na}]^+$  calcd for  $\text{C}_{19}\text{H}_{22}\text{NaO}_4$ : 337.1410; Found: 337.1385.



**(4-ethylidenecyclohexyl)benzene (1.37i).** Reaction Scale: 0.27 mmol - NMR Yield: 63%.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.14 (m, 5H), 5.22 (qt,  $J = 6.7, 1.7$  Hz, 1H), 2.75 (brd,  $J = 13.4$  Hz, 1H), 2.67 (tt,  $J = 12.2, 3.5$  Hz, 1H), 2.30 (brd,  $J = 13.2$ , 1H), 2.18 (brt,  $J = 13.2$  Hz, 1H), 2.01 – 1.90 (m, 2H), 1.85 (brt,  $J = 13.5$  Hz, 1H), 1.61 (dt,  $J = 6.7, 1.7$  Hz, 3H), 1.57 – 1.40 (m, 2H).  $^1\text{H}$  NMR is consistent with literature values.<sup>16</sup>

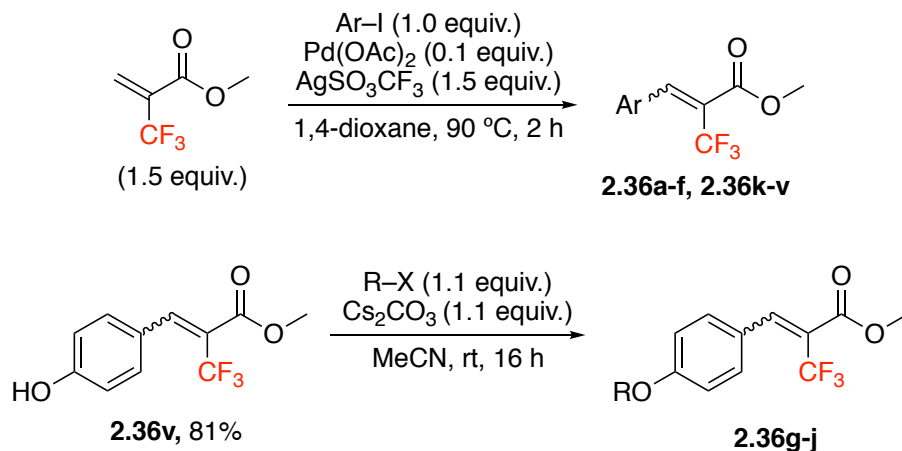
#### 4.4 Synthetic procedures and characterization of compounds for Chapter 2

##### General procedure for the synthesis of ester substrates 2.36a-u:

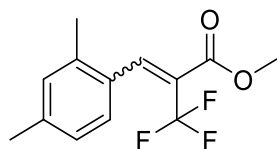
Silver trifluoromethane sulfonate (1.5 mmol, 1.5 equiv.) was added to a round bottom flask equipped with a stir bar. The reaction was purged with argon, and 1,4-dioxane (5.0 mL) was added. Methyl 2-(trifluoromethyl)acrylate (1.2 mmol, 1.2 equiv.) and aryl iodide (1.0 mmol, 1.0 equiv.) were added to the flask, and argon was bubbled through the reaction mixture for 5 minutes.

Palladium acetate (0.10 mmol, 0.10 equiv.) was added and the reaction was stirred at 90 °C for 2 h. The reaction was cooled to room temperature and celite was added. Solvent was removed *in vacuo*, and the crude reaction was purified via column chromatography (solid loading) to yield the corresponding esters **2.36a-f**, **2.36k-v**. Compounds **2.36a**, **2.36e**, **2.36f**, **2.36g**, **2.36m**, **2.36s**, **2.36u**, and **2.36v** are known.<sup>17</sup>

Cesium carbonate (1.1 equiv.) and **2.36v** (1.0 equiv.) were added to a round bottom flask containing a stir bar. The reaction was purged with argon, and dry acetonitrile (1.0 mL) and alkyl bromide or acetyl chloride were added (1.1 equiv.). The reaction was stirred overnight. Solvent was removed in *vacuo*, and the crude reaction was purified via column chromatography to yield the corresponding esters **2.36g-j**.

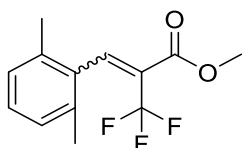


### Characterization of esters 2.36a-t.

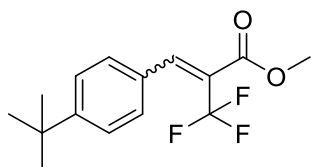


**Methyl 3-(2,4-dimethylphenyl)-2-(trifluoromethyl)acrylate (2.36b)**. Yellow liquid, 78% (201 mg, mixture of isomers *E/Z* 69/31). Purified on silica gel using dichloromethane:hexanes 2:3. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.19 (s, 1H, *Z*), 7.61 (s, 1H, *E*), 7.13 – 6.94 (m, 3H, *E* + 3H, *Z*), 3.90

(s, 3H, *Z*), 3.70 (s, 3H, *E*), 2.34 (s, 3H, *Z*), 2.33 (s, 3H, *E*), 2.30 (s, 3H, *E*), 2.28 (s, 3H, *Z*). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 163.9 (q, *J* = 1.8 Hz), 163.8 (q, *J* = 0.9 Hz), 148.6 (q, *J* = 3.0 Hz), 141.1 (q, *J* = 5.7 Hz), 140.4, 140.2, 136.9, 136.3, 131.3, 130.8, 129.6, 129.2, 128.7 (q, *J* = 3.3 Hz), 128.1, 126.7, 126.5, 123.6 (q, *J* = 31.2 Hz), 122.8 (q, *J* = 31.4 Hz), 122.3 (q, *J* = 273.0 Hz), 122.1 (q, *J* = 274.4 Hz), 52.9, 52.5, 21.4, 21.4, 20.0, 19.8. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -58.30 (s, *Z* isomer), -63.82 (d, *J* = 1.5 Hz, *E* isomer). HRMS: (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>O<sub>2</sub> 259.0940; Found 259.0940.

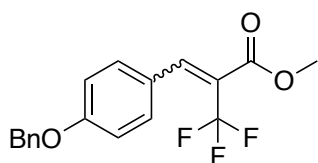


**Methyl 3-(2,6-dimethylphenyl)-2-(trifluoromethyl)acrylate (2.36c).** Colorless Liquid, 40% (104 mg, mixture of isomers *E/Z* 49/51). Purified on silica gel using dichloromethane:hexanes 2:3. <sup>1</sup>H NMR (400 MHz CDCl<sub>3</sub>) δ 8.15 (s, 1H, *Z*), 7.66 (s, 1H, *E*), 7.18 – 7.12 (m, 1H, *E* + 1H, *Z*), 7.07 – 7.02 (m, 2H, *E* + 2H, *Z*), 3.93 (s, 3H, *Z*), 3.61 (s, 3H, *E*), 2.19 – 2.18 (m, 6H, *E* + 6H, *Z*). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 163.1 (q, *J* = 1.3 Hz), 162.4 (q, *J* = 1.0 Hz), 149.1 (q, *J* = 3.3 Hz), 144.7 (q, *J* = 5.6 Hz), 134.6, 133.96 (q, *J* = 1.4 Hz), 132.9, 132.8, 128.4, 128.3, 127.5, 127.3, 126.5 (q, *J* = 30.6 Hz), 125.4 (q, *J* = 30.8 Hz), 121.96 (q, *J* = 273.3 Hz), 121.9 (q, *J* = 274.9 Hz), 53.0, 52.4, 20.3, 20.1. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -61.75 (s, *Z* isomer), -64.12 (d, *J* = 1.7 Hz, *E* isomer). HRMS: (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>14</sub>F<sub>3</sub>O<sub>2</sub> 259.0940; Found : 259.0945.

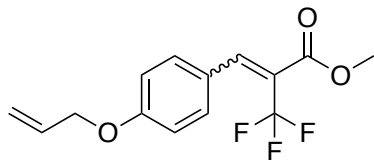


**Methyl 3-(4-(tert-butyl)phenyl)-2-(trifluoromethyl)acrylate (2.36d).** Colorless liquid, 87% (249 mg, mixture of isomers *E/Z* 70/30). Purified on silica gel using dichloromethane:hexanes 2:3.

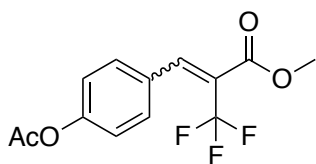
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (s, 1H, *Z*), 7.44 – 7.31 (m, 4H, *Z* + 5H, *E*), 3.89 (s, 3H, *Z*), 3.82 (s, 3H, *E*), 1.33 (s, 9H, *Z*), 1.32 (s, 9H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  164.3 (q,  $J = 2.1$  Hz), 164.2 (q,  $J = 1.0$  Hz), 154.3, 154.1, 148.7 (q,  $J = 2.9$  Hz), 140.4 (q,  $J = 5.7$  Hz), 129.9 (q,  $J = 2.6$  Hz), 129.6, 129.5 (br. s), 129.3, 125.8, 125.5, 122.4 (q,  $J = 273.0$  Hz), 122.1 (q,  $J = 274.1$  Hz), 122.1 (q,  $J = 31.4$  Hz), 121.4 (q,  $J = 32.3$  Hz), 52.9, 52.7, 35.1 (br. s), 31.3, 31.2.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.06 (s, *Z* isomer), -63.65 (d,  $J = 1.5$ , *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{18}\text{F}_3\text{O}_2$  287.1253; Found 287.1257.



**Methyl 3-(4-(benzyloxy)phenyl)-2-(trifluoromethyl)acrylate (2.36h).** Colorless oil, 53% (72 mg, mixture of isomers *E/Z* 80/20). Reaction Scale: 0.40 mmol Purified on silica gel with hexanes:EtOAc 9:1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (s, 1H, *Z*), 7.45 – 7.35 (m, 7H, *Z* + 7H, *E*), 7.34 (br. s, 1H, *E*), 7.02 – 6.96 (m, 2H, *Z* + 2H, *E*), 5.11 – 5.10 (m, 2H, *Z* + 2H, *E*), 3.89 (s, 3H, *Z*), 3.82 (s, 3H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  164.4 (q,  $J = 2.2$  Hz), 164.4 (q,  $J = 1.0$  Hz), 160.9, 160.8, 148.3 (q,  $J = 2.7$  Hz), 140.4 (q,  $J = 5.8$  Hz), 136.4, 132.4 (q,  $J = 2.7$  Hz), 131.7 (br. s), 128.8, 128.8, 128.4, 128.4, 127.6, 127.6, 124.9, 124.8, 122.6 (q,  $J = 272.8$  Hz), 122.3 (q,  $J = 273.9$  Hz), 120.5 (q,  $J = 31.2$  Hz), 119.8 (q,  $J = 32.4$  Hz), 115.1, 114.8, 70.2, 70.2, 52.8, 52.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.07 (s), -63.39 (d,  $J = 1.6$  Hz). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{16}\text{F}_3\text{O}_3$  337.0146; Found 337.0147.



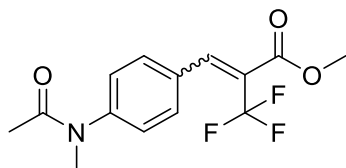
**Methyl 3-(4-(allyloxy)phenyl)-2-(trifluoromethyl)acrylate (2.36i).** Colorless oil, 88% (102 mg, mixture of isomers *E/Z* 81/19). Reaction Scale: 0.40 mmol. Purified on silica gel with hexanes:EtOAc 9:1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (s, 1H, *Z*), 7.41 (d,  $J = 8.7$  Hz, 2H, *Z*), 7.38 (d,  $J = 8.8$  Hz, 2H, *E*), 7.34 – 7.31 (m, 1H, *E*), 6.95 – 6.90 (m, 2H, *Z* + 2H, *E*), 6.09 – 5.98 (m, 1H, *Z* + 1H, *E*), 5.45 – 5.39 (m, 1H, *Z* + 1H, *E*), 5.33 – 5.29 (m, 1H, *Z* + 1H, *E*), 4.59 – 4.55 (m, 2H, *Z* + 2H, *E*), 3.88 (s, 3H, *Z*), 3.82 (s, 3H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  164.4 (q,  $J = 2.2$  Hz), 164.4 (q,  $J = 1.0$  Hz), 160.7, 160.7, 148.3 (q,  $J = 2.9$  Hz), 140.4 (q,  $J = 5.8$  Hz), 132.7, 132.4 (q,  $J = 2.8$  Hz), 131.7 (br s.), 124.8, 124.7, 122.6 (q,  $J = 272.8$  Hz), 122.3 (q,  $J = 273.9$  Hz), 120.4 (q,  $J = 31.2$  Hz), 119.7 (q,  $J = 32.4$  Hz), 118.3, 118.2, 114.9, 114.7, 69.0, 69.0, 52.8, 52.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.07 (s, *Z* isomer), -63.38 (d,  $J = 1.8$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{14}\text{F}_3\text{O}_3$  287.0890; Found 287.0889.



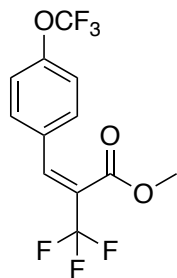
**Methyl 3-(4-acetoxyphenyl)-2-(trifluoromethyl)acrylate (2.36j).** Colorless semisolid, 88% (77 mg, mixture of isomers *E/Z* 76/24). Reaction Scale: 0.30 mmol. Purified on silica gel with hexanes/EtOAc 9:1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (s, 1H, *Z*), 7.44 – 7.39 (m, 2H, *Z* + 2H, *E*), 7.38 (s, 1H, *E*), 7.16 – 7.10 (m, 2H, *Z* + 2H, *E*), 3.88 (s, 3H, *Z*), 3.78 (s, 3H, *E*), 2.30 (s, 3H, *Z*), 2.30 (s, 3H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.0, 168.9, 163.7 (q,  $J = 2.1$  Hz), 163.6 (q,  $J = 0.9$  Hz), 152.3, 152.1, 147.4 (q,  $J = 3.0$  Hz), 139.5 (q,  $J = 5.8$  Hz), 130.9 (q,  $J = 2.6$  Hz), 130.6 (br. s.), 123.0, 129.8, 123.1 (q,  $J = 31.5$  Hz), 122.4 (q,  $J = 32.2$  Hz), 122.1 (q,  $J = 273.2$  Hz), 122.0,



121.8 (q,  $J = 274.3$  Hz), 121.7, 52.9, 52.7, 21.2 (br. s).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.06 (s, *Z* isomer), -63.86 (d,  $J = 1.8$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{13}\text{H}_{12}\text{F}_3\text{O}_4$  289.0682; Found 289.0688.

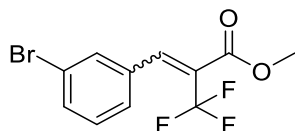


**Methyl 3-(4-(N-methylacetamido)phenyl)-2-(trifluoromethyl)acrylate (2.36k).** Yellow oil, 40% (114 mg, mixture of isomers *E/Z* 60/40 by  $^1\text{H}$  NMR). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (s, 1H, *Z*), 7.48 – 7.43 (m, 2H, *Z* + 2H, *E*), 7.42 – 7.40 (br. s, 1H, *E*), 7.26 – 7.22 (m, 2H, *Z* + 2H, *E*), 3.92 (s, 3H, *Z*), 3.83 (s, 3H, *E*), 3.30 (s, 3H, *Z*), 3.29 (s, 3H, *E*), 1.93 (br. s, 3H, *Z* + 3H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  170.3, 170.2, 163.6 (q,  $J = 1.9$  Hz), 163.5, 147.2, 146.2, 146.0, 139.6 (q,  $J = 5.8$  Hz), 130.8, 130.8, 130.7 (br. s), 127.2, 126.9, 123.8 (br. q,  $J = 31.7$  Hz), 123.2 (br. q,  $J = 32.7$  Hz), 122.0 (q,  $J = 273.3$  Hz), 121.8 (q,  $J = 274.4$  Hz), 53.0, 52.8, 37.1 (br. s), 22.5 (br. s).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.03 (s, *Z* isomer), -63.90 (d,  $J = 1.9$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{15}\text{F}_3\text{NO}_3$  302.0999; Found: 302.0980.

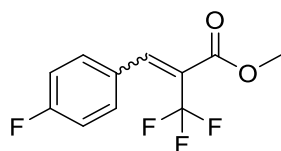


**Methyl (*E*)-3-(4-(trifluoromethoxy)phenyl)-2-(trifluoromethyl)acrylate (2.36l).** Pale yellow liquid, 70% (383 mg). Reaction Scale: 1.74 mmol. Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 (d,  $J = 8.8$  Hz, 2H), 7.40 (q,  $J$

= 1.8 Hz, 1H), 7.23 (d,  $J = 8.1$  Hz, 2H), 3.80 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.5 (q,  $J = 1.0$  Hz), 150.6 (q,  $J = 1.8$  Hz), 139.3 (q,  $J = 5.8$  Hz), 131.0, 130.8, 124.2 (q,  $J = 31.6$  Hz), 122.1 (q,  $J = 273.3$  Hz), 120.9, 120.5 (q,  $J = 258.3$  Hz), 52.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.77 (s, *Z* isomer), -64.01 (d,  $J = 1.6$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_9\text{F}_6\text{O}_3$  315.0450; Found 315.0466.

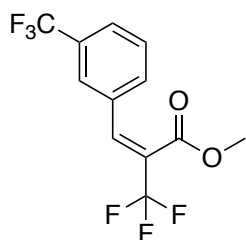


**Methyl 3-(3-bromophenyl)-2-(trifluoromethyl)acrylate (2.36n).** Pale Yellow liquid, 91% (272 mg, mixture of isomers *E/Z* 71/29). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (s, 1H, *Z*), 7.56 – 7.51 (m, 2H, *Z* + 2H, *E*), 7.38 – 7.35 (m, 1H, *E*), 7.33 – 7.25 (m, 2H, *Z* + 2H, *E*), 3.91 (s, 3H, *Z*), 3.80 (s, 3H, *E*).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.4 (q,  $J = 1.9$  Hz), 163.3 (q,  $J = 0.9$  Hz), 146.7 (q,  $J = 3.0$  Hz), 139.1 (q,  $J = 5.8$  Hz), 134.6, 134.4, 133.3, 133.0, 132.0, 131.8 (q,  $J = 2.3$  Hz), 130.2, 130.0, 127.6 (br. s), 127.6 (q,  $J = 2.6$ ), 124.8 (q,  $J = 31.7$  Hz), 123.9 (q,  $J = 32.2$  Hz), 122.7, 122.4, 121.9 (q,  $J = 273.4$  Hz), 121.7 (q,  $J = 274.6$  Hz), 53.1, 52.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.06 (s, *Z* isomer), -64.11 (d,  $J = 2.1$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{11}\text{H}_9\text{BrF}_3\text{O}_2$  308.9733; Found: 308.9730

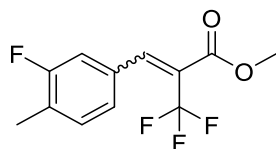


**Methyl 3-(4-fluorophenyl)-2-(trifluoromethyl)acrylate (2.36o).** Colorless liquid, 97% (253 mg, mixture of isomers *E/Z* 71/29). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (s, 1H, *Z*), 7.44 – 7.37 (m, 2H, *Z* + 2H, 1H, *E*), 7.13 – 7.05 (m, 2H, *Z* + 2H, *E*), 3.90 (s, 3H, *Z*), 3.80 (s, 3H, *E*).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.0 (d,  $J = 252.2$  Hz),

163.9 (d,  $J = 252.0$  Hz), 163.9 (q,  $J = 2.0$  Hz), 163.7 (q,  $J = 0.8$ ), 147.4 (q,  $J = 3.0$  Hz), 139.7 (q,  $J = 5.8$  Hz), 131.9 (dq,  $J = 8.6, 2.6$  Hz), 131.6 (d,  $J = 8.8$  Hz), 128.6 (d,  $J = 3.5$  Hz), 128.4 (d,  $J = 3.5$  Hz), 122.4 (qd,  $J = 32.2, 1.2$  Hz), 122.41 (qd,  $J = 31.6, 1.5$  Hz), 122.2 (q,  $J = 273.1$  Hz), 122.0 (q,  $J = 274.3$  Hz), 116.0 (d,  $J = 22.0$  Hz), 115.7 (d,  $J = 22.0$  Hz), 52.9, 52.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.10 (s, *Z* isomer), -63.85 (d,  $J = 1.8$  Hz, *E* isomer), -108.91 (ddd,  $J = 13.6, 8.4, 5.3$  Hz, *E* isomer), -109.24 (ddd,  $J = 13.7, 8.5, 5.3$  Hz, *Z* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M}+\text{NH}_4]^+$  calcd for  $\text{C}_{11}\text{H}_{12}\text{F}_4\text{NO}_2$  266.0799; Found : 266.0811.

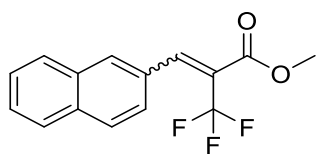


**Methyl (*E*)-2-(trifluoromethyl)-3-(3-(trifluoromethyl)phenyl)acrylate (2.36p).** Reaction scale – 1.85 mmol. Pale yellow liquid, 65% (358 mg). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67 (d,  $J = 7.2$  Hz, 1H), 7.64 (s, 1H), 7.58 – 7.51 (m, 2H), 7.47 (s, 1H), 3.78 (s, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  163.2, 139.3 (q,  $J = 5.8$  Hz), 133.2, 132.3, 131.3 (q,  $J = 32.8$  Hz), 129.3, 127.0 (q,  $J = 3.6$  Hz), 126.0 (q,  $J = 3.7$  Hz), 125.25 (q,  $J = 31.8$  Hz), 123.7 (q,  $J = 272.5$  Hz), 121.9 (q,  $J = 273.5$  Hz), 52.9.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.98 (s), -64.19 (d,  $J = 1.5$  Hz). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{12}\text{H}_8\text{F}_6\text{NaO}_2$  321.0321; Found 321.0327.

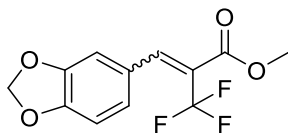


**Methyl 3-(3-fluoro-4-methylphenyl)-2-(trifluoromethyl)acrylate (2.36q).** Colorless liquid, 98% (258 mg, mixture of isomers *E/Z* 70/30). Purified on silica gel using dichloromethane:hexanes

2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (s, 1H, *Z*), 7.32 (s, 1H, *E*), 7.24 – 7.17 (m, 1H, *Z* + 1H, *E*), 7.10 – 7.04 (m, 2H, *Z* + 2H, *E*), 3.90 (s, 3H, *Z*), 3.81 (s, 3H, *E*), 2.32 – 2.29 (m, 3H, *Z* + 3H, *E*).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.8 (q,  $J = 2.0$  Hz), 163.8 – 163.7 (m), 162.4, 162.1, 159.9, 159.7, 147.2 (p,  $J = 2.9$  Hz), 139.3 (qd,  $J = 5.9, 2.4$  Hz), 131.8 (d,  $J = 5.5$  Hz), 131.8 (d,  $J = 8.2$  Hz), 131.6 (d,  $J = 8.2$  Hz), 131.5 (d,  $J = 5.4$  Hz), 128.0 (d,  $J = 17.3$  Hz), 127.7 (d,  $J = 17.2$  Hz), 123.5 (q,  $J = 31.6$  Hz), 123.0 (q,  $J = 32.2$  Hz), 122.2 (q,  $J = 273.2$  Hz), 122.0 (q,  $J = 274.2$ ), 116.1 (dq,  $J = 23.9, 2.6$  Hz), 115.6 (dd,  $J = 24.0, 0.7$  Hz), 53.0, 52.8, 14.7 (d,  $J = 3.4$  Hz), 14.73 (d,  $J = 3.4$  Hz).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.10 (s, *Z* isomer), -63.90 (d,  $J = 1.7$  Hz, *E* isomer), -116.41 (ddd,  $J = 10.3, 7.9, 2.4$  Hz, *E* isomer), -116.86 (ddd,  $J = 10.2, 7.8, 2.3$  Hz, *Z* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{11}\text{F}_4\text{O}_2$  263.0690; Found: 263.0685.



**Methyl 3-(naphthalen-2-yl)-2-(trifluoromethyl)acrylate (2.36r).** White semi-solid, 53% (150 mg, mixture of isomers *E/Z* 61/39). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.65 (s, 1H, *Z*), 8.11 (s, 1H, *E*), 7.96 – 7.77 (m, 3H, *Z* + 3H, *E*), 7.62 – 7.39 (m, 4H, *Z* + 4H, *E*), 3.96 (s, 3H, *Z*), 3.58 (s, 3H, *E*).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  163.6 (q,  $J = 1.7$  Hz), 163.5 – 163.4 (m), 147.7 (q,  $J = 3.0$  Hz), 140.7 (q,  $J = 5.7$  Hz), 133.4, 133.2, 130.9, 130.7, 130.5, 130.4, 130.4, 130.3, 128.9, 128.8, 127.2, 127.1, 126.7 – 126.6 (m), 126.6, 126.6, 126.4 (br. s), 125.9 (q,  $J = 31.2$  Hz), 125.2, 125.2, 124.5 (q,  $J = 31.6$  Hz), 124.4, 123.9, 122.1 (q,  $J = 273.3$  Hz), 122.0 (q,  $J = 274.4$  Hz), 53.0, 52.5.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -58.27 (s, *Z* isomer), -63.90 (d,  $J = 2.0$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{12}\text{F}_3\text{O}_2$  281.0784; Found: 281.0786.

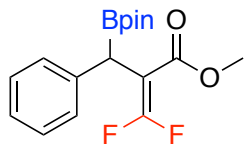


**Methyl 3-(benzo[d][1,3]dioxol-5-yl)-2-(trifluoromethyl)acrylate(2.36t).** Colorless liquid, 96% (264 mg, mixture of isomers *E/Z* 79/21). Purified on silica gel using dichloromethane:hexanes 2:3.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (s, 1H, *Z*), 7.28-7.26 (m, 1H, *E*), 7.00 – 6.88 (m, 2H, *Z* + 2H, *E*), 6.85 – 6.74 (m, 1H, *Z* + 1H, *E*), 6.03 (s, 2H, *Z*), 6.02 (s, 2H, *E*), 3.88 (s, 3H, *Z*), 3.83 (s, 3H, *E*).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.28 (q,  $J = 1.7$  Hz), 164.18 (q,  $J = 1.0$  Hz), 149.9, 149.9, 148.2, 148.2 (q,  $J = 2.8$  Hz), 148.0, 140.2 (q,  $J = 5.8$  Hz), 126.2 – 126.1 (m), 126.1, 125.9 – 125.8 (m), 122.5 (q,  $J = 272.9$  Hz), 122.2 (q,  $J = 274.0$  Hz), 121.1 (q,  $J = 32.1, 31.7$  Hz), 120.4 (q,  $J = 32.3$ ), 109.9 (q,  $J = 3.5$  Hz), 108.9, 108.6, 108.4, 101.9 (br. s) 52.8, 52.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -57.88 (*Z* isomer), -63.45 (d,  $J = 2.0$  Hz, *E* isomer). HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_9\text{F}_3\text{O}_4$  274.0447; Found: 274.0446

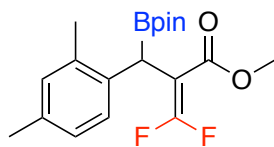
### **General procedure for the synthesis of borylated products 2.37a-u:**

Powdered 4 Å molecular sieves (0.050 g/0.20 mmol) were added to a 1 dram vial equipped with a stir bar. The vial was flame-dried and cooled under vacuum. To the vial was added copper iodide (0.1 equiv., 0.020 mmol), bis(pinacolato)diboron (1.5 equiv., 0.30 mmol), and sodium *tert*-butoxide (1.3 equiv., 0.26 mmol). The vial was capped with a septa and purged with argon. Dry acetonitrile (0.80 mL) was added, followed by the ester **2.36** (1.0 equiv., 0.20 mmol) and methanol (2.0 equiv., 0.40 mmol). The argon line was removed and the septum covered with parafilm. The reaction was stirred at room temperature for 16 h. Celite was added to the reaction mixture and the solvent removed *in vacuo*. The reaction mixture was purified via column chromatography (solid loading) to yield the corresponding borylated gem-difluoroalkenes **2.37**.

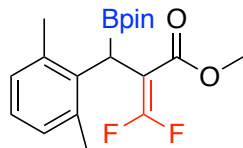
### Characterization of products 2.37a-t:



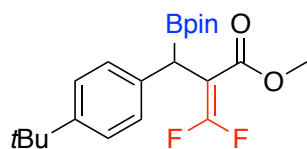
**Methyl 3,3-difluoro-2-(phenyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37a).** Colorless residue, 59% (40 mg). Purified on silica gel using dichloromethane/hexanes 1:3–1:0.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 – 7.23 (m, 4H), 7.21 – 7.14 (m, 1H), 3.76 (s, 3H), 3.41 (s, 1H), 1.28 (s, 6H), 1.24 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 13.0, 7.6$  Hz), 160.6 (dd,  $J = 311.5, 295.1$  Hz), 140.3 – 140.1 (m), 129.1, 128.4, 126.2, 91.3 (dd,  $J = 22.9, 6.4$  Hz), 84.2, 52.4, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.12 (d,  $J = 4.8$  Hz), -71.45 (d,  $J = 4.7$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{22}\text{BF}_2\text{O}_4$  339.1577; Found 339.1583.



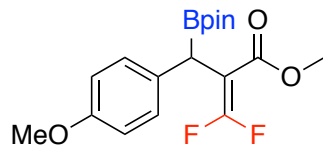
**Methyl 2-((2,4-dimethylphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37b).** Reaction Scale: 0.20 mmol – Colorless residue, 71% (52 mg). Reaction scale: 2.00 mmol – Off-white solid, 61% (445 mg). Purified on silica gel using dichloromethane:hexanes 1:3–1:0.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.01 (d,  $J = 7.8$  Hz, 1H), 6.97 – 6.90 (m, 2H), 3.78 (s, 3H), 3.55 (s, 1H), 2.28 (s, 3H), 2.27 (s, 3H), 1.26 (s, 6H), 1.24 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4 (dd,  $J = 13.2, 7.6$  Hz), 160.5 (dd,  $J = 311.1, 295.5$  Hz), 135.8, 135.4, 131.2, 127.8, 127.8, 126.8, 90.9 (dd,  $J = 22.9, 6.5$  Hz), 84.1, 52.5, 25.0, 24.7, 21.1, 20.0 (d,  $J = 1.0$  Hz).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.38 (d,  $J = 4.0$  Hz), -70.61 – -70.73 (m).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.6.  $\text{C}_{19}\text{H}_{26}\text{BF}_2\text{O}_4$  367.1890; Found 367.1888.



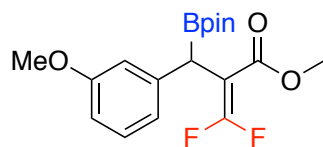
**Methyl 2-((2,6-dimethylphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37c).** Reaction scale 0.40 mmol. Colorless residue, 11% (16 mg). Purified on silica using EtOAc/hexanes 0:1 – 1:19).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.02 – 6.91 (m, 3H), 3.93 – 3.89 (m, 1H), 3.74 (s, 3H), 2.31 (s, 6H), 1.22 (s, 6H), 1.21 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4 (dd,  $J = 13.5, 7.0$  Hz), 159.1 (dd,  $J = 307.8, 298.2$  Hz), 137.2, 136.3, 128.6, 126.0, 90.0 (dd,  $J = 18.7, 7.8$  Hz), 84.0, 52.5, 24.9, 24.8, 21.3, 21.3.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.84 – -68.89 (m), -71.94 (d,  $J = 2.6$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.3. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{26}\text{BF}_2\text{O}_4$  367.1890; Found 367.1891.



**Methyl 2-((4-(*tert*-butyl)phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37d).** Colorless residue, 66% (52 mg). Purified on silica gel using dichloromethane/hexanes 1:3–1:0.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 – 7.25 (m, 2H), 7.24 – 7.20 (m, 2H), 3.75 (s, 3H), 3.39 (s, 1H), 1.29 (s, 15H), 1.25 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 13.0, 7.6$  Hz), 160.5 (dd,  $J = 311.1, 294.6$  Hz), 148.7, 136.9 (dd,  $J = 2.7, 1.9$  Hz), 128.9, 125.4, 91.5 (dd,  $J = 23.2, 6.0$  Hz), 84.1, 52.4, 34.5, 31.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.52 (d,  $J = 4.0$  Hz), -71.87 (d,  $J = 3.9$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{21}\text{H}_{30}\text{BF}_2\text{O}_4$  395.2204; Found 395.2231.

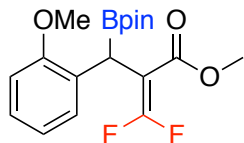


**Methyl 3,3-difluoro-2-((4-methoxyphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37e).** Colorless residue, 68% (50 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23 (d,  $J = 8.6$  Hz, 2H), 6.80 (d,  $J = 8.8$  Hz, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 3.35 (s, 1H), 1.28 (s, 6H), 1.25 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 13.0, 7.6$  Hz), 160.5 (dd,  $J = 311.3, 294.7$  Hz), 158.0, 132.30 – 132.17 (m), 130.3, 113.9, 91.7 (dd,  $J = 23.0, 5.8$  Hz), 84.2, 55.3, 52.4, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.52 (d,  $J = 3.7$  Hz), -72.08 (d,  $J = 3.5$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{24}\text{BF}_2\text{O}_5$  369.1683; Found 369.1684.

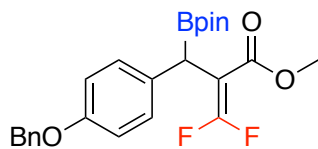


**Methyl 3,3-difluoro-2-((3-methoxyphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37f).** Colorless residue, 54% (40 mg). Purified on silica gel using dichloromethane/hexanes (1:1 – 1:0)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21 – 7.15 (m, 1H), 6.89 – 6.85 (m, 2H), 6.75 – 6.70 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.39 (s, 1H), 1.28 (s, 6H), 1.25 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 13.0, 7.6$  Hz), 160.6 (dd,  $J = 311.5, 295.1$  Hz), 159.5, 141.7 – 141.6 (m), 129.3, 121.5, 115.2, 111.4, 91.2 (dd,  $J = 22.9, 6.5$  Hz), 84.2, 55.2, 52.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.01 (d,  $J = 5.1$  Hz), -71.32 (d,  $J = 5.1$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{24}\text{BF}_2\text{O}_5$  369.1683; Found 369.1688.

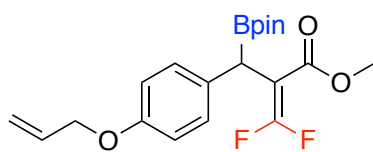




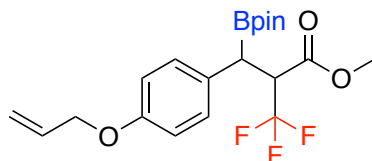
**Methyl 3,3-difluoro-2-((2-methoxyphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37g).** Colorless residue, 67% (49 mg). Purified on silica gel using dichloromethane/hexanes (1:1 – 1:0).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.19 – 7.11 (m, 2H), 6.87 (td,  $J = 7.5, 1.1$  Hz, 1H), 6.82 (dd,  $J = 8.1, 1.1$  Hz, 1H), 3.81 (s, 3H), 3.77 (s, 1H), 3.76 (s, 3H), 1.26 (s, 6H), 1.23 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.2 (dd,  $J_{\text{C-F}} = 13.1, 7.5$  Hz), 160.4 (dd,  $J_{\text{C-F}} = 310.4, 296.6$  Hz), 157.1, 128.5, 127.1, 120.5, 110.0, 89.7 (dd,  $J_{\text{C-F}} = 23.0, 6.8$  Hz), 55.3, 52.3, 25.0, 24.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.23 (d,  $J = 6.5$  Hz), -70.60 (d,  $J = 6.6$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{24}\text{BF}_2\text{O}_5$  369.1683; Found 369.1676.



**Methyl 2-((4-(benzyloxy)phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37h).** Colorless residue, 66% (58 mg). Purified on silica gel using ethyl acetate/hexanes 0:1 – 1:14.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 – 7.28 (m, 5H), 7.23 (d,  $J = 8.9$  Hz, 2H), 6.88 (d,  $J = 8.8$  Hz, 2H), 5.02 (s, 2H), 3.75 (s, 3H), 3.36 (s, 1H), 1.29 (s, 6H), 1.25 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0 (dd,  $J = 12.9, 7.7$  Hz), 160.3 (dd,  $J = 311.3, 294.5$  Hz), 157.2, 137.2, 132.4 – 132.3 (m), 130.2, 128.5, 127.9, 127.5, 114.6, 91.6 (dd,  $J = 23.2, 5.9$  Hz), 84.0, 69.9, 52.2, 24.8, 24.6.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.48 (d,  $J = 3.7$  Hz), -72.03 (d,  $J = 3.5$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{28}\text{BF}_2\text{O}_5$  445.1997; Found 445.2005.

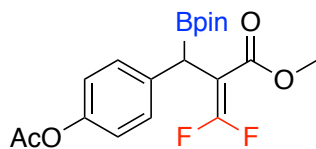


**2.37i**

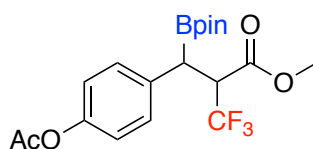


**2.38i**

**Methyl 2-((4-(allyloxy)phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37i).** Colorless residue, 72% (57 mg). Purified on silica gel using ethyl acetate/hexanes 0:1 – 1:14. Isolated with 10% **2.38i** impurity.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (d,  $J = 8.7$  Hz, 2H), 6.81 (d,  $J = 8.7$  Hz, 2H), 6.04 (ddt,  $J = 17.2, 10.6, 5.3$  Hz, 1H), 5.40 (dq,  $J = 17.3, 1.6$  Hz, 1H), 5.26 (dq,  $J = 10.5, 1.4$  Hz, 1H), 4.49 (dt,  $J = 5.3, 1.4$  Hz, 2H), 3.75 (s, 3H), 3.35 (s, 1H), 1.28 (s, 6H), 1.24 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 13.0, 7.6$  Hz), 160.5 (dd,  $J = 311.3, 294.6$  Hz), 157.1, 133.7, 132.4 - 132.3 (m), 130.3, 117.7, 114.7, 91.7 (dd,  $J = 23.0, 5.8$  Hz), 84.2, 68.9, 52.4, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.53 (d,  $J = 3.6$  Hz), -72.07 (d,  $J = 3.5$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{26}\text{BF}_2\text{O}_5$  395.1840; Found 395.1846.



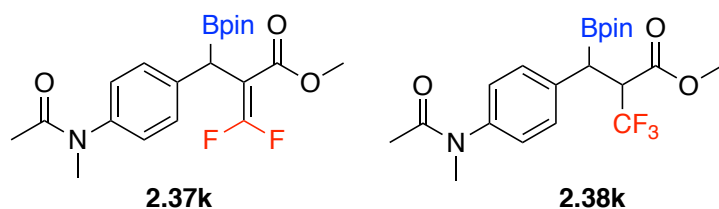
**2.37j**



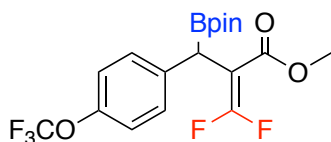
**2.38j**

**Methyl 2-((4-(acetoxy)phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37j).** Isolated sample contains 30% **2.38j**. Colorless residue, 25 mg (32%). Purified on silica using ethyl acetate:hexanes 0:1 – 1:10.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (d,  $J = 8.6$  Hz, 2H), 6.97 (d,  $J = 8.6$  Hz, 2H), 3.76 (s, 3H), 3.39 (s, 1H), 2.28 (s, 3H), 1.28 (s, 6H), 1.24 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.7, 166.0 (dd,  $J = 12.9, 7.6$  Hz), 160.6 (dd,  $J = 311.7, 295.0$  Hz), 149.1, 137.8 – 137.7 (m), 130.3, 121.2, 91.3 (dd,  $J = 22.9, 6.5$  Hz), 84.3, 52.5, 25.0, 24.8, 21.3.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.85 (d,  $J = 5.1$  Hz), -71.41 (d,  $J = 4.9$  Hz).  $^{11}\text{B}$  NMR

(128 MHz, CDCl<sub>3</sub>)  $\delta$  32.4. HRMS: (ESI)  $m/z$ : [M + Na]<sup>+</sup> calcd for C<sub>19</sub>H<sub>23</sub>BF<sub>2</sub>NaO<sub>6</sub> 419.1451; Found 419.1451.

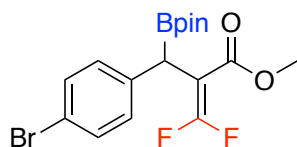


**Methyl 3,3-difluoro-2-((4-(N-methylacetamido)phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37k).** Isolated sample contains 20% **2.38k**. Colorless residue, 24 mg (29%). Purified using ethyl acetate:dichloromethane 0:1 – 1:10. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.33 (d,  $J$  = 8.2 Hz, 2H), 7.06 (d,  $J$  = 8.3 Hz, 2H), 3.79 (s, 3H), 3.43 (s, 1H), 3.24 (s, 3H), 1.88 (s, 3H), 1.30 (s, 6H), 1.26 (s, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  170.9, 166.0 (dd,  $J$  = 12.9, 7.7 Hz), 160.6 (dd,  $J$  = 311.8, 295.3 Hz), 142.5, 139.8 – 139.7 (m), 130.3, 126.9, 91.1 (dd,  $J$  = 22.9, 6.9 Hz), 84.3, 52.5, 37.2, 24.9, 24.7, 22.6. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  -67.53 (d,  $J$  = 5.3 Hz), -71.26 (d,  $J$  = 5.2 Hz). <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>)  $\delta$  32.3. [M + NH<sub>4</sub>]<sup>+</sup> calcd for C<sub>20</sub>H<sub>30</sub>BF<sub>2</sub>N<sub>2</sub>O<sub>5</sub> 427.2214; Found 427.2210.

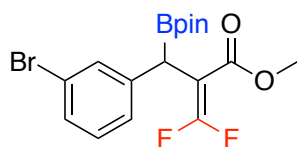


**Methyl 3,3-difluoro-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)(4-(trifluoromethoxy)phenyl)methyl)acrylate (2.37l).** Reaction scale: 0.4 mmol. Colorless residue, 39% (63 mg). Purified on silica gel using ethyl acetate/hexanes 0:1 – 1:25. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.34 – 7.28 (m, 2H), 7.12 – 7.07 (m, 2H), 3.77 (s, 3H), 3.40 (s, 1H), 1.29 (s, 6H), 1.25 (s, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  166.0 (dd,  $J$  = 12.9, 7.7 Hz), 160.6 (dd,  $J$  = 311.9, 295.2 Hz), 147.7, 138.9, 130.5, 120.9, 120.64 (q,  $J$  = 256.6 Hz), 91.2 (dd,  $J$  = 22.9, 6.9 Hz), 84.4, 52.6, 25.0, 24.8. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  -57.81, -67.59 (d,  $J$  = 5.3 Hz), -71.34 (d,  $J$  = 5.2 Hz).

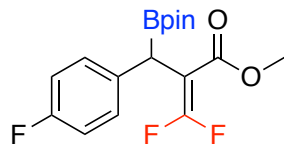
$^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.6. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{21}\text{BF}_5\text{O}_5$  423.11400; Found 423.1409.



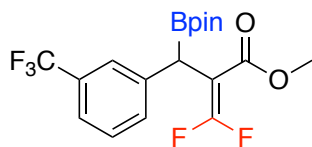
**Methyl 2-((4-bromophenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37m).** Reaction scale: 0.4 mmol. Colorless residue, 20% (34 mg). Purified on silica gel using ethyl acetate/hexanes 0:1 – 1:25.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 (d,  $J = 8.4$  Hz, 2H), 7.17 (d,  $J = 8.5$  Hz, 2H), 3.77 (s, 3H), 3.34 (s, 1H), 1.28 (s, 6H), 1.24 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0 (dd,  $J = 12.9, 7.5$  Hz), 160.6 (dd,  $J = 311.9, 295.2$  Hz), 139.3 – 139.2 (m), 131.5, 130.9, 91.0 (dd,  $J = 22.8, 6.8$  Hz), 84.4, 52.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.55 (d,  $J = 5.5$  Hz), -71.23 (d,  $J = 5.5$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.5. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{21}\text{BBrF}_2\text{O}_4$  417.0682; Found 417.0690.



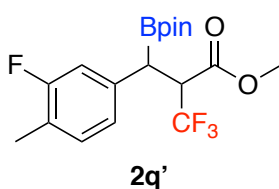
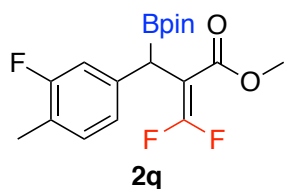
**Methyl 2-((3-bromophenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37n).** Reaction scale: 24% (20 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.39 (m, 1H), 7.31 (ddd,  $J = 7.9, 1.9, 1.0$  Hz, 1H), 7.23 (ddd,  $J = 8.3, 1.7, 1.1, 0.4$  Hz, 1H), 7.13 (t,  $J = 7.8$  Hz, 1H), 3.78 (s, 3H), 3.36 (s, 1H), 1.28 (s, 6H), 1.24 (s, 7H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0 (dd,  $J = 12.9, 7.6$  Hz), 160.7 (dd,  $J = 312.0, 295.5$  Hz), 142.6 – 142.5 (m), 132.1, 130.0, 129.4, 127.9, 122.5, 90.9 (dd,  $J = 22.8, 7.1$  Hz), 84.4, 52.6, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.29 (d,  $J = 6.2$  Hz), -70.82 (d,  $J = 6.2$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.5. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{NH}_4]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BBrF}_2\text{NO}_4$  434.0947; Found 434.0951.



**Methyl 3,3-difluoro-2-((4-fluorophenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37o).** Colorless viscous oil, 66%. (47 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29 – 7.23 (m, 2H), 6.98 – 6.90 (m, 2H), 3.76 (s, 3H), 3.37 (s, 1H), 1.28 (s, 6H), 1.25 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 12.6, 7.7$  Hz), 161.5 (d,  $J = 244.0$  Hz), 160.6 (dd,  $J = 311.6, 295.0$  Hz), 135.9 – 135.8 (m), 130.7 (dd,  $J = 8.1, 0.6$  Hz), 115.2 (d,  $J = 21.1$  Hz), 91.4 (dd,  $J = 22.5, 6.8$  Hz), 84.3, 52.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.98 (d,  $J = 4.6$  Hz), -71.68 (d,  $J = 4.5$  Hz), -117.44 (tt,  $J = 8.8, 5.4$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.6. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{21}\text{BF}_3\text{O}_4$  357.1483; Found 357.1500.

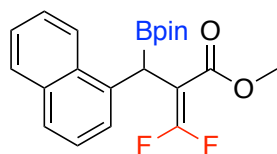


**Methyl 3,3-difluoro-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)(3-(trifluoromethyl)phenyl)methyl)acrylate (2.37p).** Crude NMR Yield: 13%.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.77 (d,  $J = 5.4$  Hz), -71.53 (d,  $J = 5.4$  Hz).

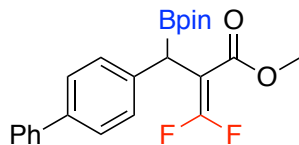


**Methyl 3,3-difluoro-2-((3-fluoro-4-methylphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37q).** Colorless residue, 49% (36 mg). Purified on silica gel using ethyl acetate:hexanes 0:1 – 1:14. Isolated with 5% **2q'**.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.05 (t,  $J = 8.0$  Hz, 1H), 7.00 – 6.91 (m, 2H), 3.77 (s, 3H), 3.36 (s, 1H), 2.21 (d,  $J = 1.9$  Hz, 3H), 1.28 (s, 6H),

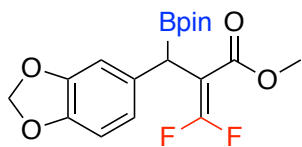
1.24 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0 (dd,  $J = 12.8, 7.7$  Hz), 162.2, 160.6 (dd,  $J = 311.7, 295.2$  Hz), 160.2, 139.8 – 139.7 (m), 131.2 (d,  $J = 5.5$  Hz), 124.4 (d,  $J = 3.1$  Hz), 122.5 (d,  $J = 17.2$  Hz), 115.7 (d,  $J = 22.7$  Hz), 91.1 (dd,  $J = 22.9, 6.7$  Hz), 84.3, 52.5, 25.0, 24.8, 14.3 (d,  $J = 3.4$  Hz).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.84 (d,  $J = 5.2$  Hz), -71.40 (d,  $J = 5.3$  Hz), -117.80 – -117.93 (m).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{23}\text{BF}_3\text{O}_4$  371.1636; Found 371.1641.



**Methyl 3,3-difluoro-2-(naphthalen-2-yl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)acrylate (2.37r).** Colorless residue, 39% (30 mg). Purified on silica gel using hexanes:EtOAc 19:1.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.99 (d,  $J = 8.2$  Hz, 1H), 7.86 – 7.82 (m, 1H), 7.70 (d,  $J = 8.1$  Hz, 1H), 7.53 – 7.44 (m, 2H), 7.43 – 7.36 (m, 1H), 7.33 (d,  $J = 7.2$  Hz, 1H), 4.22 (s, 1H), 3.80 (s, 3H), 1.26 (s, 6H), 1.21 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.4 (dd,  $J = 13.1, 7.4$  Hz), 160.45 (dd,  $J = 311.9, 297.4$  Hz), 136.1 – 136.0 (m), 134.0, 132.1, 129.0, 127.0, 125.8, 125.6, 125.5 (d,  $J = 1.1$  Hz), 125.4, 123.7 (d,  $J = 1.2$  Hz), 90.8 (dd,  $J = 22.2, 7.3$  Hz), 84.3, 52.6, 25.0, 24.7.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.44 (d,  $J = 5.0$  Hz), -70.01 (d,  $J = 5.0$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.9. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{21}\text{H}_{24}\text{BF}_2\text{O}_4$  389.1734; Found 389.1742.



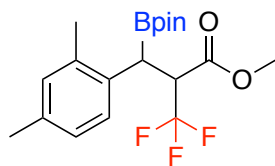
**Methyl 2-([1,1'-biphenyl]-4-yl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37s).** Colorless residue, 41% (34 mg). Purified on silica gel using hexanes:EtOAc 19:1.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 – 7.55 (m, 2H), 7.50 (d,  $J = 8.2$  Hz, 2H), 7.44 – 7.34 (m, 4H), 7.34 – 7.28 (m, 1H), 3.78 (s, 3H), 3.46 (s, 1H), 1.31 (s, 6H), 1.27 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 12.9, 7.7$  Hz), 160.6 (dd,  $J = 311.5, 294.9$  Hz), 141.2, 139.4 – 139.3 (m), 139.1, 129.6, 128.8, 127.2, 127.2, 127.1, 91.3 (dd,  $J = 22.9, 6.4$  Hz), 84.3, 52.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.91 (d,  $J = 4.9$  Hz), -71.40 (d,  $J = 4.8$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  33.0. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{26}\text{BF}_2\text{O}_4$  415.1891; Found 415.1896.



**Methyl 2-(benzo[*d*][1,3]dioxol-5-yl(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3-difluoroacrylate (2.37t).** Colorless residue, 67% (51 mg). Purified on silica gel using dichloromethane:hexanes 1:1–1:0.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.86 (d,  $J = 1.6$  Hz, 1H), 6.75 – 6.68 (m, 2H), 5.90 (q,  $J = 1.5$  Hz, 2H), 3.76 (s, 3H), 3.33 (s, 1H), 1.26 (d,  $J = 15.2$  Hz, 12H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1 (dd,  $J = 12.9, 7.6$  Hz), 160.6 (dd,  $J = 311.6, 294.8$  Hz), 147.5, 146.0, 134.0 – 133.9 (m), 122.2, 110.0, 108.2, 100.9, 91.7 (dd,  $J = 22.8, 6.1$  Hz), 84.2, 52.5, 25.0, 24.8.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -68.16 (d,  $J = 4.5$  Hz), -71.77 (d,  $J = 4.4$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.5. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{22}\text{BF}_2\text{O}_6$  383.1475; Found 383.1478.

### **Mechanistic Study - Procedure for the synthesis of borylated product 2.38b:**

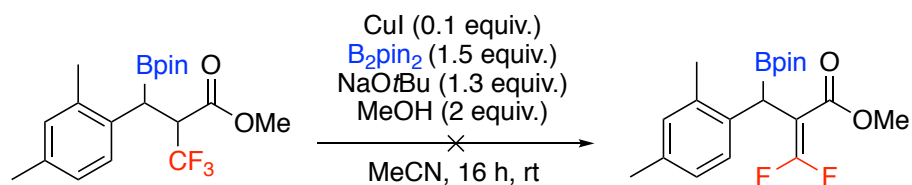
To a flame-dried 1 dram vial equipped with a stir bar was added copper iodide (0.1 equiv., 0.050 mmol), bis(pinacolato)diboron (1.5 equiv., 0.75 mmol), and sodium carbonate (1.3 equiv., 0.65 mmol). The vial was capped with a septa and purged with argon. Dry acetonitrile (2.0 mL) was added, followed by the ester **2.36b** (1.0 equiv., 0.50 mmol) and methanol (2.0 equiv., 1.0 mmol). The argon line was removed and the septum covered with parafilm. The reaction was stirred at room temperature for 16 h. Celite was added to the reaction mixture and the solvent removed *in vacuo*. The reaction mixture was purified via column chromatography (solid loading) to yield the corresponding borylated trifluoroalkene **2.38b**.



**Methyl 2-((2,4-dimethylphenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3,3,3-trifluoropropanoate (2.38b).** Colorless oil, 23% (44 mg). Purified on silica gel using dichloromethane:hexanes 1:4.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.07 (d,  $J = 7.8$  Hz, 1H), 6.93 – 6.91 (m, 1H), 6.91 – 6.87 (m, 1H), 3.92 (dq,  $J = 12.3, 7.8$  Hz, 1H), 3.40 (s, 3H), 3.20 (d,  $J = 12.4$  Hz, 1H), 2.34 (s, 3H), 2.23 (s, 3H), 1.14 (s, 6H), 1.10 (s, 6H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.7 (q,  $J = 3.2$  Hz), 136.8, 135.7, 132.1, 131.5, 127.6 (br. s), 126.7, 125.1 (q,  $J = 281.1$  Hz), 84.0, 52.5 (q,  $J = 26.4$  Hz), 52.3, 24.44, 24.43, 21.05, 20.18.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -67.22 (d,  $J = 7.7$  Hz).  $^{11}\text{B}$  NMR (128 MHz,  $\text{cdcl}_3$ )  $\delta$  32.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{27}\text{BF}_3\text{O}_4$  387.1952; Found 387.1953.



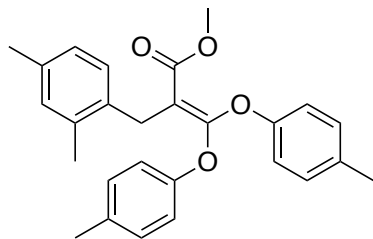
### Procedure for the mechanistic study:



To a flame-dried 1 dram vial equipped with a stir bar was added copper iodide (0.1 equiv., 0.020 mmol), powdered 4 Å molecular sieves (0.050 g/0.20 mmol), bis(pinacolato)diboron (1.5 equiv., 0.30 mmol), and sodium *tert*-butoxide (1.3 equiv., 0.26 mmol). The vial was capped with a septa and purged with argon. Dry acetonitrile (0.80 mL) was added, followed by the ester **2.38b** (1.0 equiv., 0.20 mmol) and methanol (2.0 equiv., 0.40 mmol). The argon line was removed and the septum covered with parafilm. The reaction was stirred at room temperature for 16 h. The reaction was filtered through a small pad of celite, rinsing with EtOAc, and the solvent removed *in vacuo*. The crude reaction mixture was dissolved in CDCl<sub>3</sub> and evaluated by <sup>19</sup>F NMR. Only starting material **2.38b** was observed.

### Procedure for the synthesis of 2.45:<sup>18</sup>

To a flame-dried 1 dram vial equipped with a stir bar was added **2.37b** (1.0 equiv., 0.10 mmol) and cesium carbonate (2.1 equiv., 0.21 mmol). The vial was capped with a septa and purged with argon. Dry THF (0.80 mL) was added, followed by 4-methylphenol (2.1 equiv., 0.21 mmol). The argon line was removed and the septum covered with parafilm. The reaction was stirred at 45 °C for 2 h. Solvent removed *in vacuo*. The reaction mixture was purified via column chromatography to yield **3**.

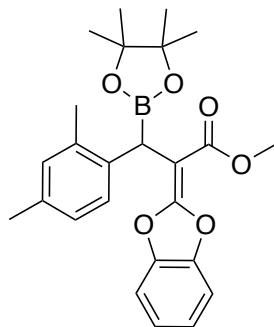


**Methyl 2-(2,4-dimethylbenzyl)-3,3-bis(*p*-tolylloxy)acrylate (2.45).** Colorless oil, 98% (41 mg).

Purified on silica gel using hexanes:EtOAc 19:1.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.18 (d,  $J = 7.5$  Hz, 1H), 7.03 – 6.93 (m, 6H), 6.81 (d,  $J = 8.5$  Hz, 2H), 6.74 (d,  $J = 8.5$  Hz, 2H), 3.74 (s, 2H), 3.61 (s, 3H), 2.32 (s, 3H), 2.28 (s, 3H), 2.26 (s, 3H), 2.26 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.7, 157.1, 152.7, 151.3, 136.2, 135.5, 135.1, 133.7, 133.2, 131.0, 129.9, 129.9, 127.8, 126.7, 118.2, 117.1, 102.1, 51.8, 29.4, 21.1, 20.8, 20.8, 19.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{27}\text{H}_{29}\text{O}_4$  417.2060; Found 417.2051.

**Procedure for the synthesis of 2.46:**

To a flame-dried 1 dram vial equipped with a stir bar was added **2.237b** (1.0 equiv., 0.10 mmol) and cesium carbonate (1.1 equiv., 0.11 mmol). The vial was capped with a septa and purged with argon. Dry THF was added, followed by catechol (1.1 equiv., 0.11 mmol). The argon line was removed and the septum covered with parafilm. The reaction was stirred at 45 °C for 2 h. Solvent removed *in vacuo*. The reaction mixture was purified via column chromatography to yield **2.46**.



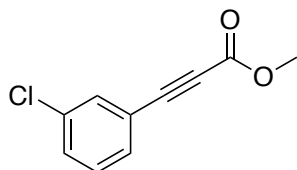
**Methyl 2-(benzo[*d*][1,3]dioxol-2-ylidene)-3-(2,4-dimethylphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (2.46).** Colorless oil, 30% (13 mg). Purified on silica gel using hexanes:EtOAc 19:1.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24 – 7.21 (m, 1H), 7.13 – 7.03 (m, 3H), 7.01 (d,  $J = 7.9$  Hz, 1H), 6.95 (s, 1H), 6.88 (d,  $J = 7.9$  Hz, 1H), 3.82 (s, 3H), 3.74 (s, 1H), 2.37 (s, 3H), 2.25 (s, 3H), 1.26 (s, 7H), 1.23 (s, 6H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  168.3, 165.9, 145.8, 144.2, 137.9, 135.5, 134.5, 130.8, 126.9, 126.8, 124.3, 124.2, 110.2, 109.8, 84.6, 83.7, 51.8, 25.2, 24.8, 21.1, 20.2.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{25}\text{H}_{30}\text{O}_6$  437.2134; Found 437.2122.

#### 4.5 Synthetic procedures and characterization of compounds for Chapter 3

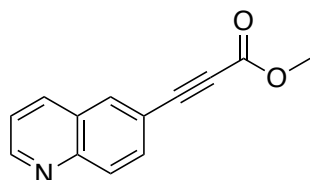
##### General Procedure for the synthesis of alkynoate ester substrates 3.18a – 3.18z.

Dry THF (20 mL) was added to the terminal acetylene (1 equiv, 5.0 mmol) in a round bottom flask equipped with a stir bar. The solution was cooled to  $-78$  °C (dry ice/acetone bath) and butyllithium (2.5M in hexanes, 5.0 mmol) was added dropwise and stirred. After 15 minutes methyl chloroformate (1 equiv, 5.0 mmol) was added dropwise to the mixture at  $-78$  °C and stirred for 2 hours. The reaction was then diluted with ethyl acetate, and water was added. The organic layer was washed with brine and dried over anhydrous sodium sulfate. Concentration *in vacuo* yielded a yellow oil which, upon purification by column chromatography (1:10, ethyl

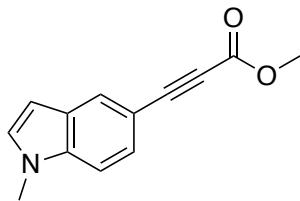
acetate:hexanes), yielded the corresponding ester. Esters **3.18a**,<sup>19</sup> **3.18b**,<sup>20</sup> **3.18c**,<sup>21</sup> **3.18d**,<sup>22</sup> **3.18e**,<sup>23</sup> **3.18f**,<sup>24</sup> **3.18g**,<sup>23</sup> **3.18i**,<sup>25</sup> **3.18j**,<sup>23</sup> **3.18k**,<sup>26</sup> **3.18l**,<sup>23</sup> **3.18m**,<sup>27</sup> **3.18o**,<sup>28</sup> **3.18p**,<sup>29</sup> **3.18q**,<sup>20</sup> **3.18r**,<sup>30</sup> **3.18s**,<sup>30</sup> **3.18v**,<sup>30</sup> **3.18w**,<sup>24</sup> **3.18x**,<sup>24</sup> **3.18y**,<sup>31</sup> **3.18z**,<sup>32</sup> and **3.23**<sup>33</sup> are known compounds. Compound **3.18n** was purchased commercially and used directly.



**Methyl 3-(3-chlorophenyl)propiolate (3.18h).** Clear oil, 67% (319 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.56 (t, *J* = 1.8 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.31 (t, *J* = 7.9 Hz, 1H), 3.84 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 154.2, 134.7, 132.8, 131.2, 131.1, 130.0, 121.4, 84.7, 81.2, 53.1. HRMS: (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>8</sub>ClO<sub>2</sub> 195.0207; Found 195.0203.



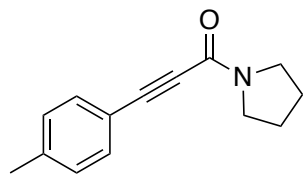
**Methyl 3-(quinolin-6-yl)propiolate (3.18t).** Light yellow solid, 35% (228 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.93 (s, 1H), 8.13 – 8.03 (m, 3H), 7.78 (s, 1H), 7.43 (s, 1H), 3.84 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 154.2, 152.1, 148.4, 136.0, 133.9, 131.9, 130.1, 127.6, 122.1, 117.7, 85.7, 81.1, 52.9, 52.9. HRMS: (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>10</sub>NO<sub>2</sub> 212.0706; Found 212.0717.



**Methyl 3-(1-methyl-1H-indol-5-yl)propiolate (3.18u).** Yellow oil, 74% (294 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (s, 1H), 7.42 (d,  $J = 8.5$  Hz, 1H), 7.28 (d,  $J = 8.5$  Hz, 1H), 7.09 (s, 1H), 6.49 (s, 1H), 3.82 (s, 3H), 3.79 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.2, 130.6, 128.4, 127.5, 126.4, 109.8, 109.8, 102.0, 89.9, 79.2, 52.8, 33.2. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{13}\text{H}_{12}\text{NO}_2$  214.0863; Found 214.0863.

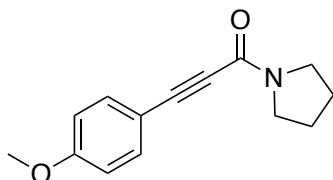
**General procedure for the synthesis of alkynamide substrates 3.20a – 3.20f.**

To a round bottom flask with stir bar was added the ester substrate (1 equiv, 3.0 mmol) followed by purging with  $\text{N}_2(\text{g})$ . Dry THF (20 mL) was then added followed by pyrrolidine (2 equiv, 6 mmol) and the mixture was allowed to stir at room temperature for 4 hours. The reaction mixture was diluted in ethyl acetate (20 mL) and water (20 mL). The organic layer was washed with brine, dried over sodium sulfate, and concentrated *in vacuo* to afford a yellow oil. The crude product was then subjected to silica chromatography (40% ethyl acetate in hexanes) to afford the product as a white solid. Alkynamides **3.20a**,<sup>34</sup> **3.20b**,<sup>35</sup> and **3.20f**<sup>36</sup> are known compounds.

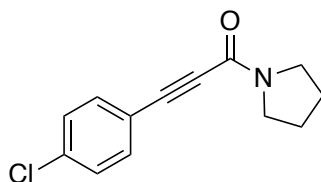


**1-(Pyrrolidin-1-yl)-3-(p-tolyl)prop-2-yn-1-one (3c).** White solid, 57% (350 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 (d,  $J = 8.1$  Hz, 2H), 7.15 (d,  $J = 7.9$  Hz, 2H), 3.72 (t,  $J = 6.8$  Hz, 2H), 3.52 (t,  $J = 7.0$  Hz, 2H), 2.36 (s, 3H), 2.00 – 1.90 (m, 4H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.0, 140.5,

132.5, 129.4, 117.6, 89.2, 82.4, 77.2, 48.3, 45.5, 25.5, 24.9, 21.8. HRMS: (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{14}H_{16}NO$  214.1226; Found 214.1214.



**3-(4-Methoxyphenyl)-1-(pyrrolidin-1-yl)prop-2-yn-1-one (3d).** White solid, 40% (360 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.48 (d,  $J = 9.0$  Hz, 2H), 6.86 (d,  $J = 9.0$  Hz, 2H), 3.82 (s, 3H), 3.72 (t,  $J = 6.8$  Hz, 2H), 3.52 (t,  $J = 7.0$  Hz, 2H), 2.00 – 1.89 (m, 4H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  161.0, 153.2, 134.3, 114.3, 112.6, 89.3, 82.1, 55.5, 48.3, 45.4, 25.5, 24.9. HRMS: (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{14}H_{16}NO_2$  230.1176; Found 230.1161.



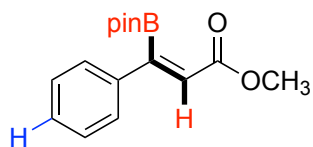
**3-(4-Chlorophenyl)-1-(pyrrolidin-1-yl)prop-2-yn-1-one (3e).** White solid, 48% (220 mg).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.46 (d,  $J = 8.8$  Hz, 2H), 7.33 (d,  $J = 8.8$  Hz, 2H), 3.71 (t,  $J = 6.8$  Hz, 2H), 3.53 (t,  $J = 7.0$  Hz, 2H), 1.95 (s, 4H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  152.6, 136.3, 133.7, 129.0, 119.2, 87.5, 83.6, 77.2, 48.3, 45.5, 25.5, 24.9. HRMS: (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{13}H_{13}ClNO$  234.0680; Found 234.0665.

### **General procedure for the hydroboration of alkynoate esters to form (*E*)- $\beta$ borylacrylates**

#### **3.19a – 3.19z.**

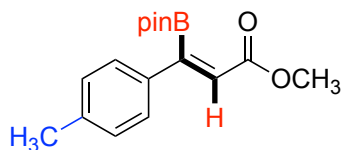
Alkynoate ester (0.34 mmol, 1.0 equiv.) was added to a flame dried 2-neck round bottom flask with a stir bar. The flask was then filled with  $N_{2(g)}$  by purging for 30 minutes. Solid esters were dissolved in 50  $\mu$ L dry THF, while oils were reacted neat. Pinacolborane (0.37 mmol, 1.1

equiv.) followed by tri-*n*-butylphosphine (0.034 mmol, 0.1 equiv.) were added to the vial at room temperature. The reaction was then allowed to stir at room temperature for 60 minutes. The reaction mixture was then directly loaded onto silica gel and purified by column chromatography (0-10% ethyl acetate in hexanes) to yield the product as a colorless oil.



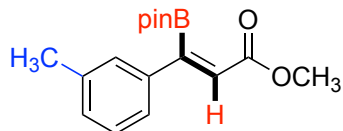
**Methyl (E)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19a).**

Colorless oil, 87% (85 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 – 7.46 (m, 2H), 7.42 – 7.32 (m, 3H), 6.44 (s, 1H), 3.79 (s, 3H), 1.42 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.5, 138.7, 129.3, 128.9, 127.3, 125.7, 84.5, 52.0, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.3. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{22}\text{BO}_4$  289.1609; Found 289.1588.



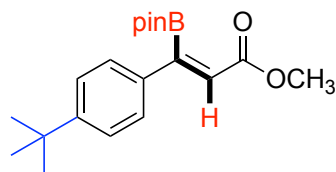
**Methyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(*p*-tolyl)acrylate (3.19b).**

Colorless oil, 87% (109 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 (d,  $J = 8.2$  Hz, 2H), 7.17 (d,  $J = 8.5$  Hz, 2H), 6.42 (s, 1H), 3.78 (s, 3H), 2.35 (s, 3H), 1.42 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 139.5, 135.9, 129.6, 127.2, 124.7, 84.5, 52.0, 25.2, 21.4;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.2. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BO}_4$  303.1765; Found 303.1770.



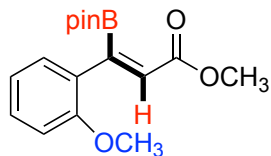
**Methyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(*m*-tolyl)acrylate (3.19c).**

Colorless oil, 81% (143 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 – 7.11 (m, 4H), 6.42 (s, 1H), 3.77 (s, 3H), 2.33 (s, 3H), 1.41 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.5, 138.6, 138.4, 130.0, 128.7, 127.9, 125.4, 124.3, 84.4, 51.9, 25.1, 21.5;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BO}_4$  303.1765; Found 303.1760.



**Methyl (E)-3-(4-(*tert*-butyl)phenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19d).**

Colorless oil, 86% (98 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 (d,  $J = 8.8$  Hz, 2H), 7.38 (d,  $J = 8.8$  Hz, 2H), 6.44 (s, 1H), 3.78 (s, 3H), 1.43 (s, 13H), 1.32 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.7, 152.6, 135.8, 127.1, 125.8, 124.7, 84.5, 52.0, 34.9, 31.4, 25.3;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{30}\text{BO}_4$  345.2237; Found 345.2239.

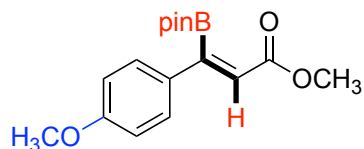


**Methyl (E)-3-(2-methoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19e).**

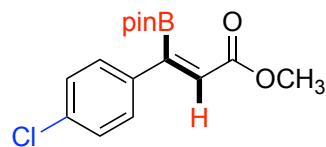
Colorless oil, 75% (75 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.27 (m, 2H), 6.94 (td,  $J = 7.5, 1.1$  Hz, 1H), 6.87 (dd,  $J = 8.2, 1.0$  Hz, 1H), 6.49 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 1.38 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 157.3, 130.4, 129.6, 129.3, 128.3, 121.2, 111.2,



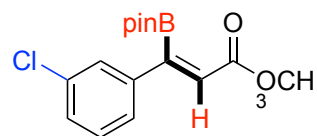
84.1, 55.6, 51.8, 25.3;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.2. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BO}_5$  319.1714; Found 319.1730.



**Methyl (E)-3-(4-methoxyphenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19f).** Colorless oil, 85% (92 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 (d,  $J = 8.7$  Hz, 2H), 6.88 (d,  $J = 8.8$  Hz, 2H), 6.38 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 1.42 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.8, 160.7, 131.1, 128.8, 123.4, 114.3, 84.5, 55.4, 51.9, 25.3.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BO}_5$  319.1714; Found 319.1727.

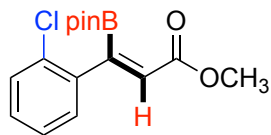


**Methyl (E)-3-(4-chlorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19g).** White solid, 66% (75 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (d, 2H), 7.33 (d, 2H), 6.40 (s, 1H), 3.79 (s, 3H), 1.40 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.3, 137.2, 135.3, 129.1, 128.5, 126.2, 84.7, 52.1, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.25. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{BClO}_4$ , 323.1219; Found 323.1205.

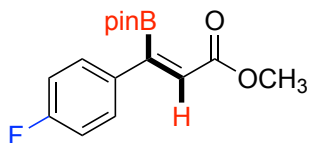


**Methyl (E)-3-(3-chlorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19h).** White solid, 67% (58 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (s, 1H), 7.40 – 7.32 (m, 1H), 7.35 – 7.24 (m, 3H), 6.40 (s, 1H), 3.78 (s, 3H), 1.40 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )

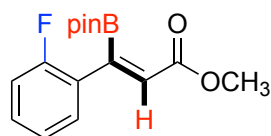
$\delta$  168.2, 140.5, 134.8, 130.1, 129.2, 127.3, 126.8, 125.3, 84.7, 52.2, 25.1;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.5. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{20}\text{BClNaO}_4$  345.1059; Found 345.1038.



**Methyl (E)-3-(2-chlorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19i).** White solid. 32% (30 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.20 (m, 4H), 6.38 (s, 1H), 3.79 (s, 3H), 1.35 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{cdcl}_3$ )  $\delta$  167.7, 138.6, 132.2, 131.1, 130.2, 129.9, 129.3, 126.9, 84.5, 52.1, 24.9;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  29.9. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{BClO}_4$  323.1216; Found 323.1195.

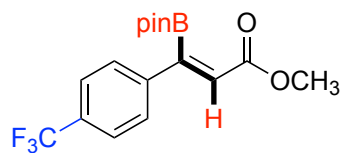


**Methyl (E)-3-(4-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19j).** Colorless oil, 61% (109 mg)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 – 7.42 (m, 2H), 7.03 (t,  $J = 8.7$  Hz, 2H), 6.37 (s, 1H), 3.77 (s, 3H), 1.40 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.4, 164.7, 162.2, 134.7, 129.1, 125.5, 115.9, 115.7, 84.5, 52.0, 25.1;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{21}\text{BFO}_4$  307.1514; Found 307.1521.

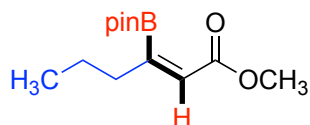


**Methyl (E)-3-(2-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19k).** Colorless oil, 58% (47 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (td,  $J = 7.8, 1.7$  Hz, 1H), 7.31 – 7.24 (m, 1H), 7.14 – 7.01 (m, 2H), 6.55 (s, 1H), 3.77 (s, 3H), 1.38 (s, 13H);  $^{13}\text{C}$  NMR (101

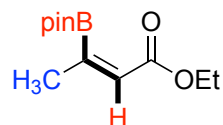
MHz, CDCl<sub>3</sub>) δ 168.1, 161.7, 159.2, 130.7, 130.7, 129.8, 129.8, 128.9, 128.9, 126.7, 126.6, 124.5, 124.4, 116.3, 116.1, 52.1, 25.2; <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>) δ 30.6. HRMS: (ESI) m/z: [M + H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>21</sub>BFO<sub>4</sub> 307.1514; Found 307.1518.



**Methyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)acrylate (3.19l).** Off-white solid, 36% (36 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (q, 4H), 6.45 (s, 1H), 3.81 (s, 3H), 1.41 (s, 13H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.1, 142.4, 131.1, 130.8, 127.9, 127.5, 125.8, 122.8, 110.2, 84.8, 52.3, 25.1; <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>) δ 30.5. HRMS: (ESI) m/z: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>21</sub>BF<sub>3</sub>O<sub>4</sub> 357.1483; Found 357.1490.

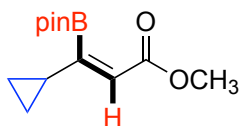


**Methyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-2-enoate (3.19m).** Colorless oil, 54% (99 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.98 (s, 1H), 3.69 (s, 3H), 2.28 – 2.18 (m, 2H), 1.49 (h, *J* = 7.4 Hz, 2H), 1.33 (s, 13H), 0.90 (t, *J* = 7.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.3, 125.7, 84.1, 51.7, 38.0, 25.0, 21.3, 14.0; <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>) δ 31.1. HRMS: (ESI) m/z: [M + H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>24</sub>BO<sub>4</sub> 255.1765; Found 255.1772.



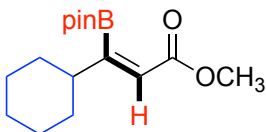
**Ethyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (3.19n).** Colorless oil, 70% (380 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.42 – 6.40 (q, 0.43H), 6.02 – 5.95 (m, 1H), 4.14

(m, 3H), 2.13 (s, 1H), 1.91 (s, 3H), 1.32 (s, 12H), 1.28 – 1.18 (m, 12H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 166.3, 130.7, 127.0, 84.2, 84.0, 60.5, 59.9, 24.9, 24.8, 21.2, 16.4, 14.4.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.6. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{12}\text{H}_{22}\text{BO}_4$  241.1608; Found 241.1622.



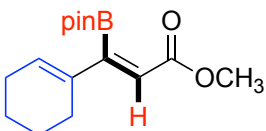
**Methyl (E)-3-cyclopropyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19o).**

Colorless oil, 73% (148 mg) (84:16).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.07 (s, 1H), 3.70 (s, 3H), 1.72 – 1.61 (m, 1H), 1.34 (s, 13H), 0.92 – 0.80 (m, 4H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.4, 123.3, 84.4, 51.7, 25.2, 18.1, 8.4;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{13}\text{H}_{22}\text{BO}_4$  253.1608; Found 253.1604.



**Methyl (E)-3-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19p).**

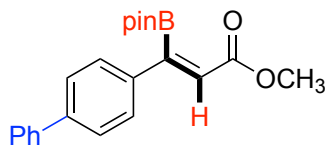
Colorless oil, 27% (30 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.98 (s, 1H), 3.70 (s, 3H), 2.23 – 2.13 (m, 1H), 1.82 – 1.72 (m, 4H), 1.73 – 1.60 (m, 2H), 1.36 (s, 13H), 1.31 – 1.08 (m, 7H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.7, 124.0, 84.1, 51.7, 44.8, 32.1, 26.4, 26.2, 25.2.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  31.1. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{16}\text{H}_{27}\text{BNaO}_4$  317.1898; Found 317.1879.



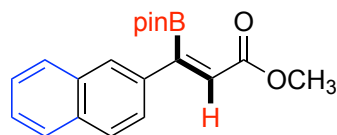
**Methyl (E)-3-(cyclohex-1-en-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19q).**

Colorless oil, 89% (109 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.12 (s, 1H), 5.99 (s, 1H),

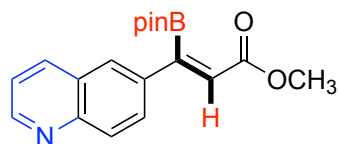
3.69 (s, 3H), 2.22 – 2.08 (m, 4H), 1.70 – 1.49 (m, 4H), 1.37 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.2, 137.6, 136.7, 120.3, 84.1, 51.6, 26.7, 25.4, 25.4, 22.4, 21.8;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.8. HRMS: (ESI)  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{26}\text{BO}_4$  293.1922; Found 293.1919.



**Methyl (E)-3-([1,1'-biphenyl]-4-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19r).** White solid, 69% (65 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64 – 7.54 (m, 6H), 7.45 (t,  $J = 7.9$  Hz, 2H), 7.40 – 7.31 (m, 1H), 6.50 (s, 1H), 3.81 (s, 3H), 1.45 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 142.1, 140.5, 137.7, 129.0, 127.8, 127.7, 127.6, 127.2, 125.5, 84.6, 52.1, 25.3;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{26}\text{BO}_4$  365.1919; Found 365.1947.

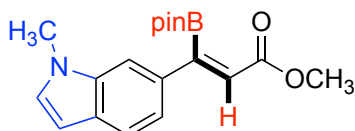


**Methyl (E)-3-(naphthalen-2-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19s).** White solid, 65% (46 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (s, 1H), 7.86 – 7.78 (m, 3H), 7.62 (dd,  $J = 8.6, 1.7$  Hz, 1H), 7.49 (dt,  $J = 6.2, 3.4$  Hz, 2H), 6.58 (s, 1H), 3.82 (s, 3H), 1.46 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 136.1, 133.7, 133.4, 128.6, 128.6, 127.8, 127.7, 126.9, 126.6, 125.8, 124.4, 84.6, 52.1, 25.25;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.5. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{24}\text{BO}_4$  339.1766; Found 339.1774.



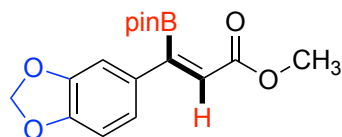
**Methyl (*E*)-3-(quinolin-6-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19t).**

White solid, 60% (68 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.91 (dd,  $J = 4.2, 1.7$  Hz, 1H), 8.13 (d,  $J = 1.3$  Hz, 1H), 8.08 (d,  $J = 8.8$  Hz, 1H), 7.93 (d,  $J = 2.0$  Hz, 1H), 7.85 (dd,  $J = 8.8, 2.1$  Hz, 1H), 7.41 (dd,  $J = 8.3, 4.2$  Hz, 1H), 6.58 (s, 1H), 3.82 (s, 3H), 1.45 (s, 13H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.4, 151.1, 148.6, 136.9, 136.6, 130.2, 128.2, 127.1, 126.9, 121.8, 84.8, 52.2, 25.2.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{23}\text{BNO}_4$  340.1718; Found 340.1730.



**Methyl (*E*)-3-(1-methyl-1*H*-indol-5-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19u).**

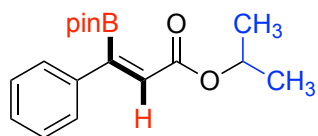
Off-white solid, 38% (60 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d,  $J = 1.7$  Hz, 1H), 7.41 (dd,  $J = 8.6, 1.7$  Hz, 1H), 7.29 (d,  $J = 8.6$  Hz, 2H), 7.05 (d,  $J = 3.1$  Hz, 1H), 6.49 (s, 1H), 6.47 (s, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 1.45 (s, 13H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.0, 137.4, 130.2, 129.8, 128.8, 123.1, 121.1, 120.7, 109.6, 102.0, 84.4, 51.9, 33.1, 25.3;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.9. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{25}\text{BNO}_4$  342.1871; Found 342.1872.



**Methyl (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19v).**

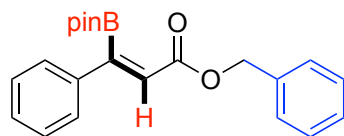
White solid, 87% (71 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.05 – 6.97 (m,

2H), 6.79 (dd,  $J = 7.8, 0.6$  Hz, 1H), 6.34 (s, 1H), 5.97 (s, 2H), 3.77 (s, 3H), 1.41 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.7, 148.8, 148.3, 132.8, 124.0, 122.2, 108.6, 107.0, 101.4, 84.5, 52.0, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{22}\text{BO}_6$  333.1507; Found 333.1524.



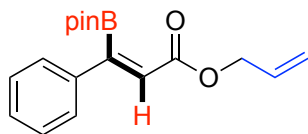
**Isopropyl (*E*)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19w).**

Colorless oil, 81% (94 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 – 7.45 (m, 2H), 7.40 – 7.27 (m, 3H), 6.41 (s, 1H), 5.11 (hept,  $J = 6.3$  Hz, 1H), 1.42 (s, 12H), 1.28 (d,  $J = 6.3$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 138.8, 129.1, 128.8, 127.3, 126.8, 84.4, 68.3, 25.2, 22.1;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.1. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{18}\text{H}_{25}\text{BNaO}_4$  339.1741; Found 339.1744.

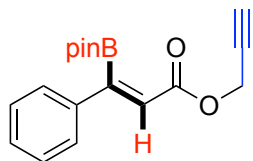


**Benzyl (*E*)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19x).**

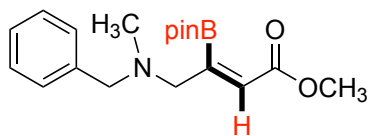
White solid, 82% (89 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 – 7.46 (m, 2H), 7.43 – 7.28 (m, 8H), 6.50 (s, 1H), 5.24 (s, 2H), 1.43 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.0, 138.7, 135.9, 129.3, 128.9, 128.7, 128.5, 128.4, 127.3, 125.8, 84.6, 66.8, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.6. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{26}\text{BO}_4$  365.1923; Found 365.1924.



**Allyl (*E*)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19y).** Colorless oil, 86% (78 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 – 7.46 (m, 2H), 7.41 – 7.31 (m, 3H), 6.47 (s, 1H), 6.04 – 5.89 (m, 1H), 5.36 (dq,  $J = 17.2, 1.6$  Hz, 1H), 5.25 (dq,  $J = 10.4, 1.3$  Hz, 1H), 4.70 (dt,  $J = 5.8, 1.5$  Hz, 2H), 1.42 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 138.7, 132.3, 129.3, 128.9, 127.3, 125.8, 118.6, 84.6, 65.6, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.4. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{24}\text{BO}_4$  315.1765; Found 315.1761.



**Prop-2-yn-1-yl (*E*)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.19z).** Colorless oil, 79% (103 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 – 7.45 (m, 2H), 7.41 – 7.32 (m, 3H), 6.48 (s, 1H), 4.81 (d,  $J = 2.5$  Hz, 2H), 2.49 (s, 1H), 1.42 (s, 14H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.1, 138.5, 129.5, 128.9, 127.3, 124.9, 84.7, 77.7, 75.2, 52.4, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.3. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{22}\text{BO}_4$  313.1609; Found 313.1619.



**Methyl (*E*)-4-(benzyl(methyl)amino)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enoate (3.24).** Purified as a mixture of *E*:*Z* isomers (86:14) by diluting crude oil in hexanes and extracting product with methanol. Colorless oil, 43% (34 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38

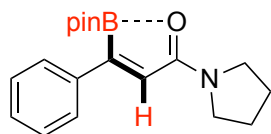


– 7.20 (m, 6H), 6.22 (s, 1H), 3.72 (s, 3H), 3.47 (s, 2H), 3.23 (s, 2H), 2.15 (s, 3H), 1.38 (s, 12H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 167.7, 138.9, 129.2, 128.2, 127.0, 126.3, 84.3, 62.9, 62.4, 51.7, 42.7, 25.0. <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>) δ 31.0. HRMS: (ESI) m/z: [M + K]<sup>+</sup> calcd for C<sub>19</sub>H<sub>28</sub>BKNO<sub>4</sub> 384.1746; Found 384.1775.

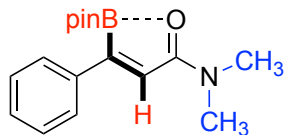
### **General procedure for the hydroboration of alkynamides to produce (*E*)-β borylacrylates**

#### **3.21a – 3.21e.**

Alkynamide (0.30 mmol, 1.0 equiv.) was added to a flame dried 2-neck round bottom flask with a stir bar. The flask was then filled with N<sub>2(g)</sub> by purging for 30 minutes. Dry THF was then added (0.5 mL). Pinacolborane (0.33 mmol, 1.1 equiv.) followed by tri-*n*-butylphosphine (0.15 mmol, 0.5 equiv.) were added to the vial at room temperature. The reaction was then allowed to stir at 60 °C for 4 hours. The reaction mixture was then directly loaded onto silica gel and purified by column chromatography (40% ethyl acetate in dichloromethane) to yield the product as a white solid.

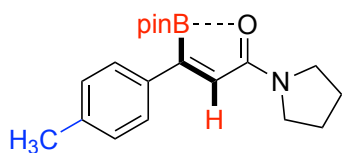


**(*E*)-3-Phenyl-1-(pyrrolidin-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-one (3.21a).** White solid, 46% (42 mg). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.72 – 7.65 (m, 2H), 7.38 – 7.27 (m, 3H), 6.35 (s, 1H), 3.71 (t, *J* = 6.9 Hz, 2H), 3.63 (t, *J* = 6.9 Hz, 2H), 2.08 – 1.88 (m, 4H), 1.26 (s, 12H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 171.3, 138.8, 128.9, 128.1, 127.9, 118.6, 80.5, 47.4, 47.1, 26.2, 25.6, 24.4. <sup>11</sup>B NMR (128 MHz, CDCl<sub>3</sub>) δ 14.0. HRMS: (ESI) m/z: [M + H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>27</sub>BNO<sub>3</sub> 328.2082; Found 328.2101.



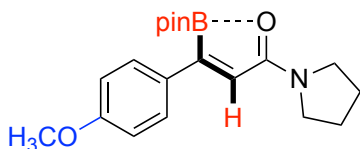
**(E)-N,N-Dimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide**

**(3.21b).** White solid, 48% (39 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 (d,  $J = 8.2$  Hz, 2H), 7.33 (q,  $J = 7.2, 6.4$  Hz, 3H), 6.50 (s, 1H), 3.18 (d,  $J = 4.0$  Hz, 6H), 1.28 (s, 13H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  173.4, 138.7, 129.0, 128.1, 127.8, 117.0, 77.2, 37.3, 26.1.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  13.7. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{Na}]^+$  calcd for  $\text{C}_{17}\text{H}_{24}\text{BNNaO}_3$  324.1730; Found 324.1745.



**(E)-1-(Pyrrolidin-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(p-tolyl)prop-2-en-1-one (3.21c).**

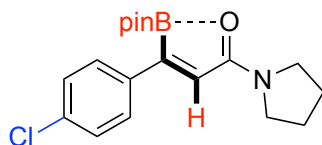
White solid, 54% (52 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60 (d,  $J = 8.1$  Hz, 2H), 7.13 (d,  $J = 7.9$  Hz, 2H), 6.32 (s, 1H), 3.68 (t,  $J = 6.9$  Hz, 2H), 3.60 (t,  $J = 6.9$  Hz, 2H), 2.33 (s, 3H), 2.06 – 1.85 (m, 5H), 1.26 (s, 12H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.3, 139.0, 135.8, 128.8, 127.9, 117.7, 80.4, 47.3, 47.0, 26.2, 25.5, 24.4, 21.5.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  14.0. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{29}\text{BNO}_3$  342.2239; Found 342.2256.



**(E)-3-(4-Methoxyphenyl)-1-(pyrrolidin-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-one (3.21d).**

White solid, 53% (41 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 (d,  $J = 8.9$  Hz, 2H), 6.87 (d,  $J = 8.9$  Hz, 2H), 6.31 (s, 1H), 3.82 (s, 3H), 3.71 (t,  $J = 6.9$  Hz, 2H), 3.62 (t,  $J = 6.9$  Hz, 2H), 2.08 – 1.88 (m, 4H), 1.29 (s, 13H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 160.7,

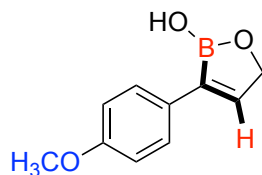
131.3, 129.8, 116.4, 113.6, 80.5, 55.4, 47.3, 47.1, 26.4, 25.6, 24.5.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  13.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{29}\text{BNO}_4$  358.2188; Found 358.2235.



**(E)-3-(4-Chlorophenyl)-1-(pyrrolidin-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-one (3.21e).** Purified by preparatory TLC (100% EtOAc). White solid, 46% (27 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.63 (d,  $J = 8.7$  Hz, 2H), 7.31 (d,  $J = 8.7$  Hz, 2H), 6.34 (s, 1H), 3.72 (t,  $J = 6.9$  Hz, 2H), 3.64 (t,  $J = 6.9$  Hz, 2H), 2.10 – 1.90 (m, 4H), 1.56 (s, 3H), 1.26 (s, 13H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.1, 137.2, 134.9, 129.3, 128.4, 118.8, 80.6, 47.5, 47.2, 26.2, 25.6, 24.5.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  13.8. HRMS: (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{26}\text{BCINO}_3$  362.1692; Found 362.1696.

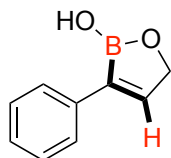
### **General procedure for the synthesis of oxaboroles 3.25a – 3.25d.**

To a round-bottom flask equipped with a stir bar was added hydroboration product (0.3 mmol, 1 equiv) and dissolved in ethanol (3 mL). Sodium borohydride (0.6 mmol, 2 equiv) was added and the mixture was allowed to stir for 30 minutes at room temperature. The mixture was concentrated *in vacuo* to afford an off-white solid, which was then purified *via* column chromatography to afford the final product as a white solid.

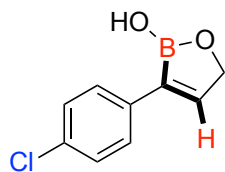


**3-(4-Methoxyphenyl)-1,2-oxaborol-2(5H)-ol (3.25a).** White solid, 77% (92 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 (d,  $J = 8.8$  Hz, 2H), 7.32 (s, 1H), 6.90 (d,  $J = 8.9$  Hz, 2H), 4.83 (s, 1H), 4.67

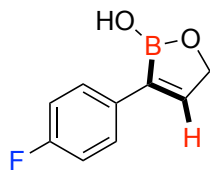
(s, 2H), 3.82 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  160.9, 159.2, 145.8, 128.1, 114.1, 71.8, 55.4.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  33.1. HRMS: (ESI)  $m/z$ :  $[\text{M} - \text{H}]^-$  calcd for  $\text{C}_{10}\text{H}_{10}\text{BO}_3$  189.0723; Found 189.0715.



**3-Phenyl-1,2-oxaborol-2(5H)-ol (3.25b).** White solid, 77% (45 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3-d$ )  $\delta$  7.65 (d,  $J = 8.4$  Hz, 2H), 7.43 – 7.32 (m, 3H), 7.30 – 7.23 (m, 1H), 6.45 (s, 1H), 4.71 (s, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  147.4, 135.9, 128.7, 127.6, 126.9, 71.8.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.6. HRMS: (ESI)  $m/z$ :  $[\text{M} - \text{H}]^-$  calcd for  $\text{C}_9\text{H}_8\text{BO}_2$  159.0623; Found 159.0597.



**3-(4-Chlorophenyl)-1,2-oxaborol-2(5H)-ol (3.25c).** White solid, 80% (89 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3-d$ )  $\delta$  7.58 (d,  $J = 8.3$  Hz, 2H), 7.43 (s, 1H), 7.32 (d,  $J = 8.5$  Hz, 2H), 4.85 (s, 1H), 4.68 (s, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  147.90, 134.28, 133.34, 128.83, 128.26, 105.30, 71.79.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.8. HRMS: (ESI)  $m/z$ :  $[\text{M} - \text{H}]^-$  calcd for  $\text{C}_9\text{H}_7\text{BClO}_2$  193.0223; Found 193.0229.

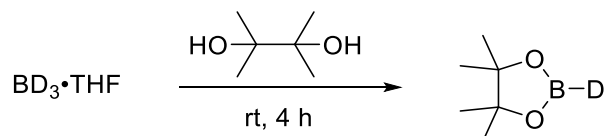


**3-(4-Fluorophenyl)-1,2-oxaborol-2(5H)-ol (3.25d).** White solid, 70% (40 mg).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 – 7.58 (m, 2H), 7.37 (s, 1H), 7.10 – 6.99 (m, 2H), 6.09 (d,  $J = 7.8$  Hz, 1H),

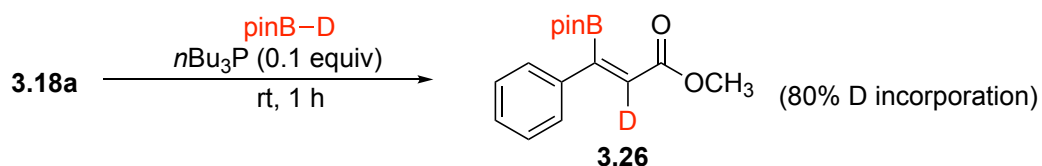
4.71 (s, 2H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  163.49, 161.04, 148.96, 146.76, 131.81, 128.38, 115.49, 115.27, 71.60.  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  32.9. HRMS: (ESI)  $m/z$ :  $[\text{M} - \text{H}]^-$  calcd for  $\text{C}_9\text{H}_7\text{BFO}_2$  177.0529; Found 177.0536.

### Deuterium Labeling Experiments

#### *Preparation of D-Bpin.*

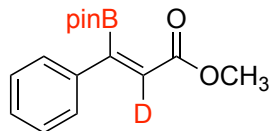


This procedure was adapted from the literature procedure.<sup>37</sup> A 2-neck round bottom flask with stir bar was placed under nitrogen *via* Schlenk technique.  $\text{BD}_3 \cdot \text{THF}$  1M in THF solution was added (2 mmol) and cooled to 0 °C. Pinacol was then added and the solution was allowed to warm to rt and stirred for 6 hours. The resulting solution was used directly with no further purification.



#### *Deuteroboration.*

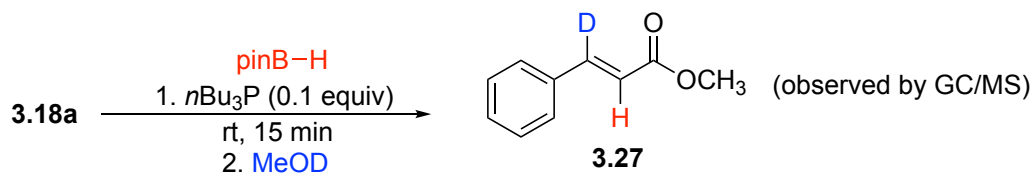
To a round-bottom flask with stir bar was added ester **3.18a** (1 mmol) and then placed under nitrogen *via* Schlenk technique. The solution of D-Bpin prepared above was then added (1 mmol), followed by tri-*n*-butylphosphine (0.1 mmol). The reaction was allowed to stir at room temperature for 50 minutes. The reaction mixture was then directly purified *via* silica chromatography (7% ethyl acetate in hexanes) to afford the product **3.26** as a colorless oil.



**methyl (E)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate-*d*** (3.26).

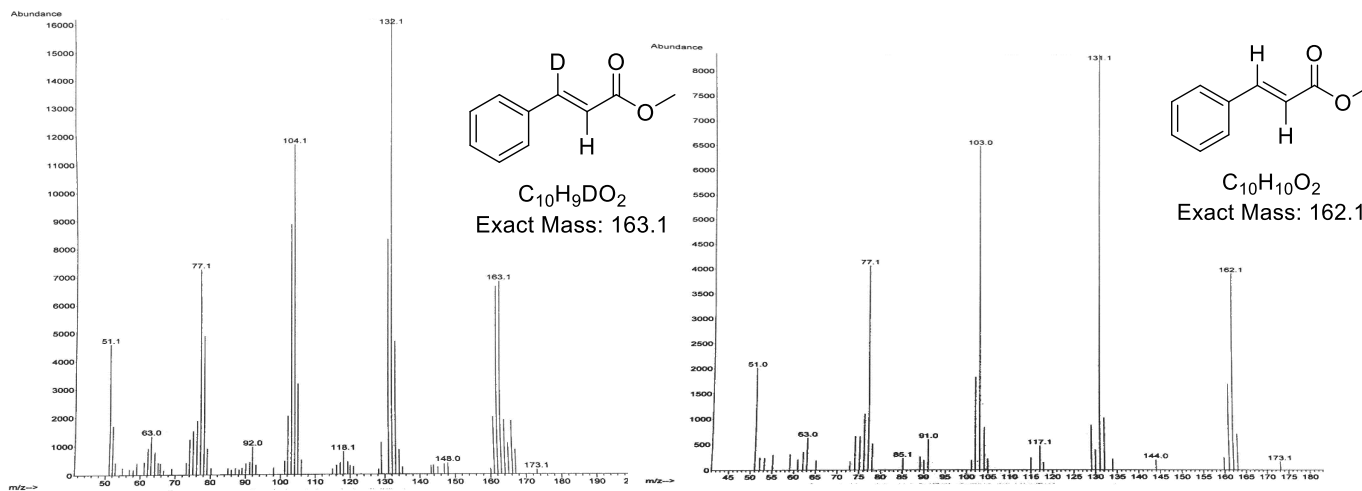
Colorless oil, 75%. 80% deuterium incorporation.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 – 7.46 (m, 2H), 7.40 – 7.31 (m, 3H), 6.44 (s, 0.19H), 3.79 (s, 3H), 1.42 (s, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.5, 138.7, 129.3, 128.9, 127.3, 125.7, 84.5, 52.0, 25.2;  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ )  $\delta$  30.3.

HRMS: (ESI)  $[\text{M}+\text{H}]^+$  calc. for  $\text{C}_{16}\text{H}_{21}\text{DBO}_4$ , 290.1671, observed, 290.1687.



### Hydroboration Quenching Experiment.

The hydroboration reaction (1 mmol scale) of **1a** was quenched after 10 minutes by the dropwise addition of either 1 mL MeOD or MeOH. GCMS analysis of the MeOH quenched mixture revealed the presence of methyl cinnamate (confirmed retention time with commercial *trans* methyl cinnamate). Quenching with MeOD revealed a compound with the same retention time, but a  $m/z$  corresponding to the deuterated methyl cinnamate.



**Figure S1:** MS identification of products from quenching experiment.

## **Computational Details**

All the calculations were performed with the Gaussian 09 program.<sup>38</sup> Geometry optimization was carried out using the DFT M06-2X functional.<sup>39</sup> In the DFT calculations, the 6-31G\*\* basis set was used for C, H, O, B while the Lanl2dz basis set<sup>40,41</sup> with polarization functions ( $\zeta_d = 0.387$ ) was used for P.<sup>42</sup> The SMD model<sup>43</sup> was employed to simulate the solvent effect with tetrahydrofuran as solvent and all the structures were optimized considering the solvation effect. Frequency calculations were made to make sure that all intermediates have no imaginary frequency and transition states each contain only one imaginary frequency. Intrinsic reaction coordinates (IRC)<sup>44,45</sup> were performed to ensure that a transition state did connect two relevant local minima. Cartesian coordinates and electronic energies for all the calculated structures.

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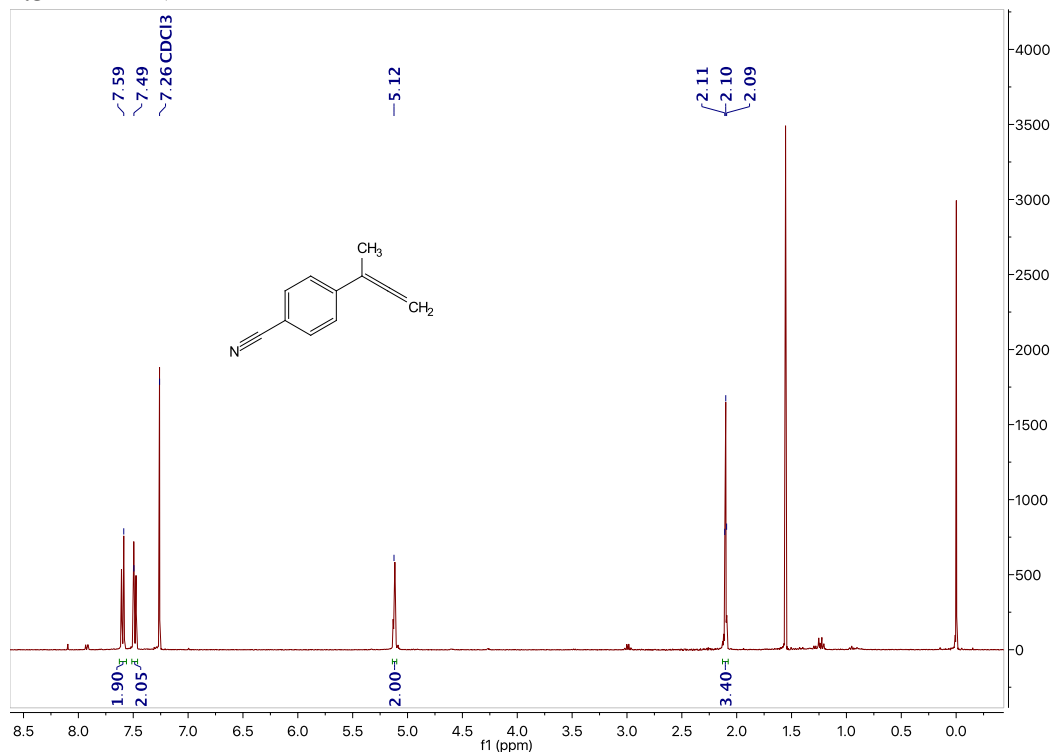
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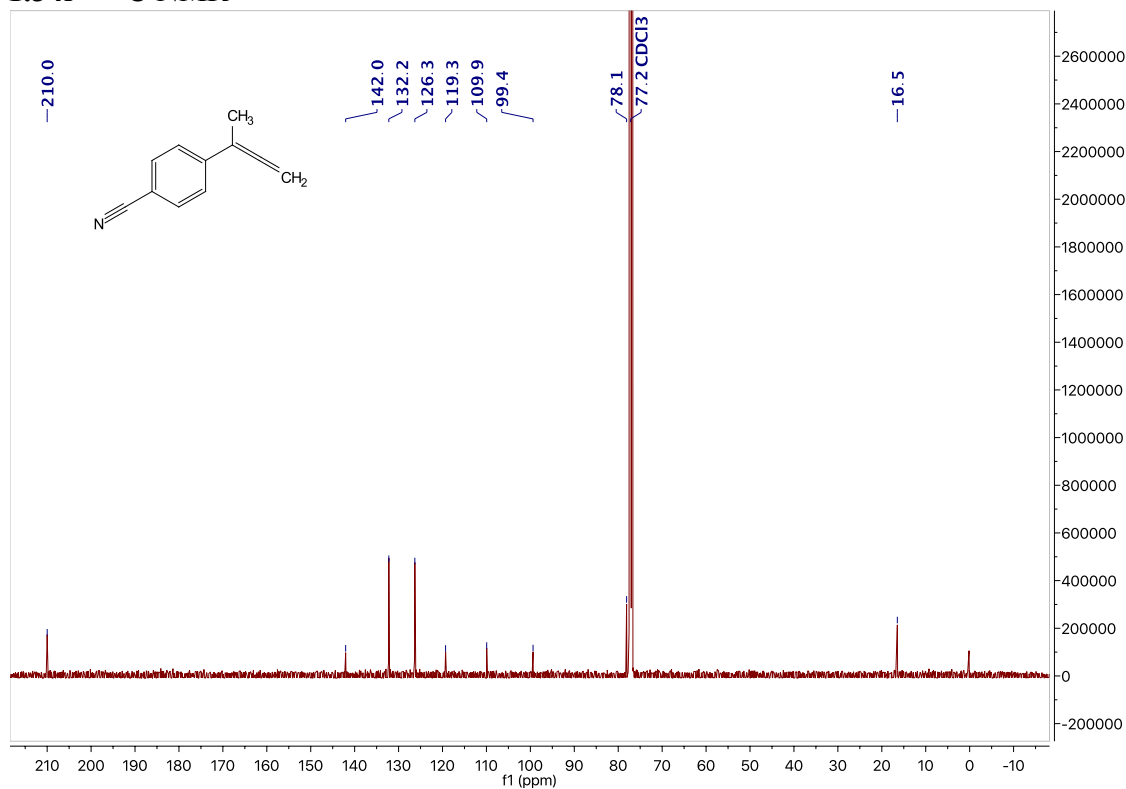
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## Appendix A

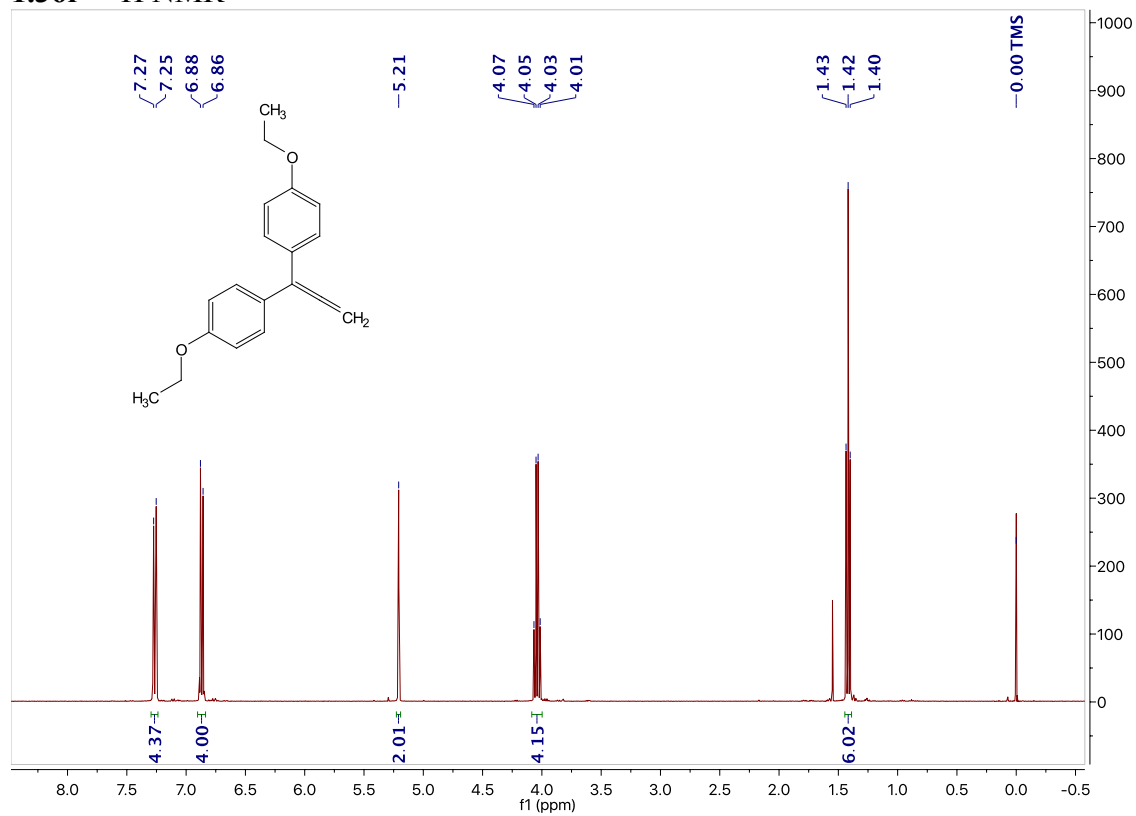
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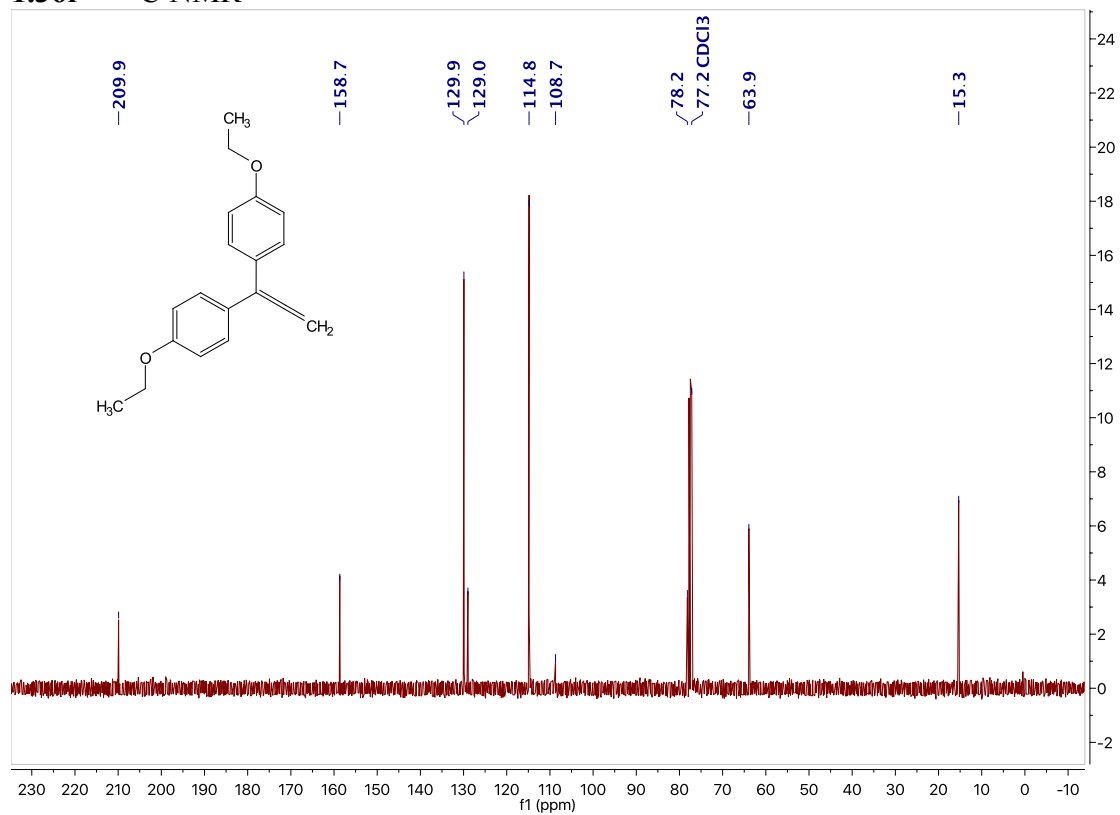
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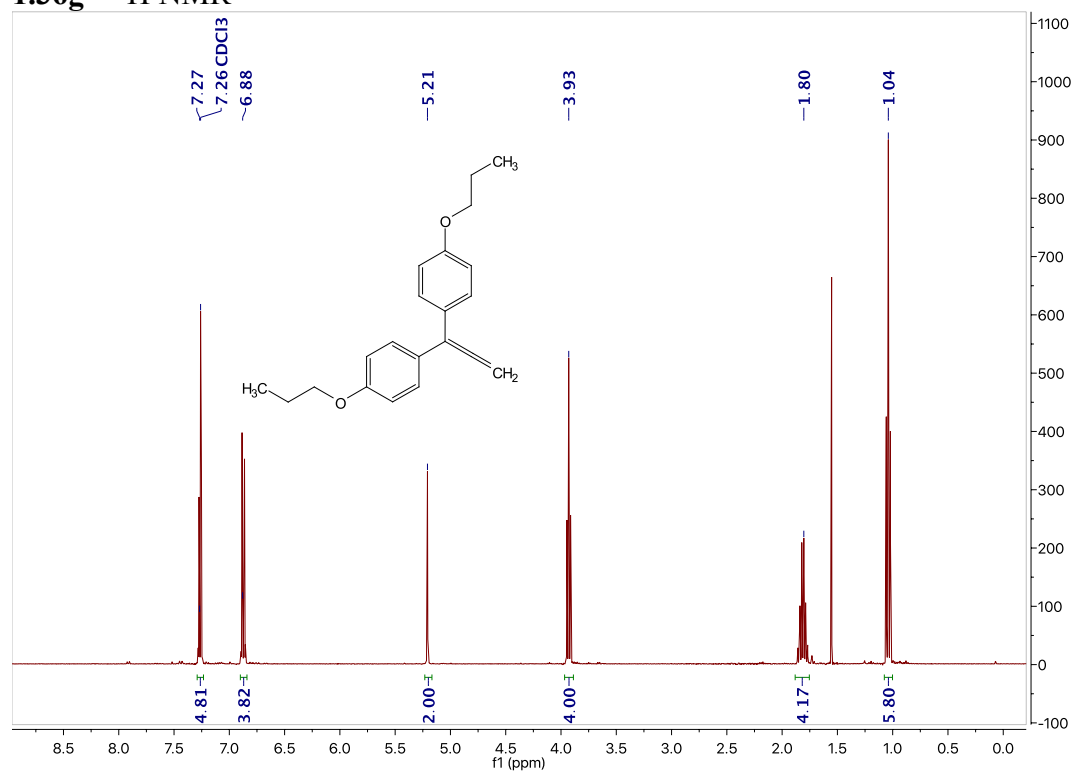
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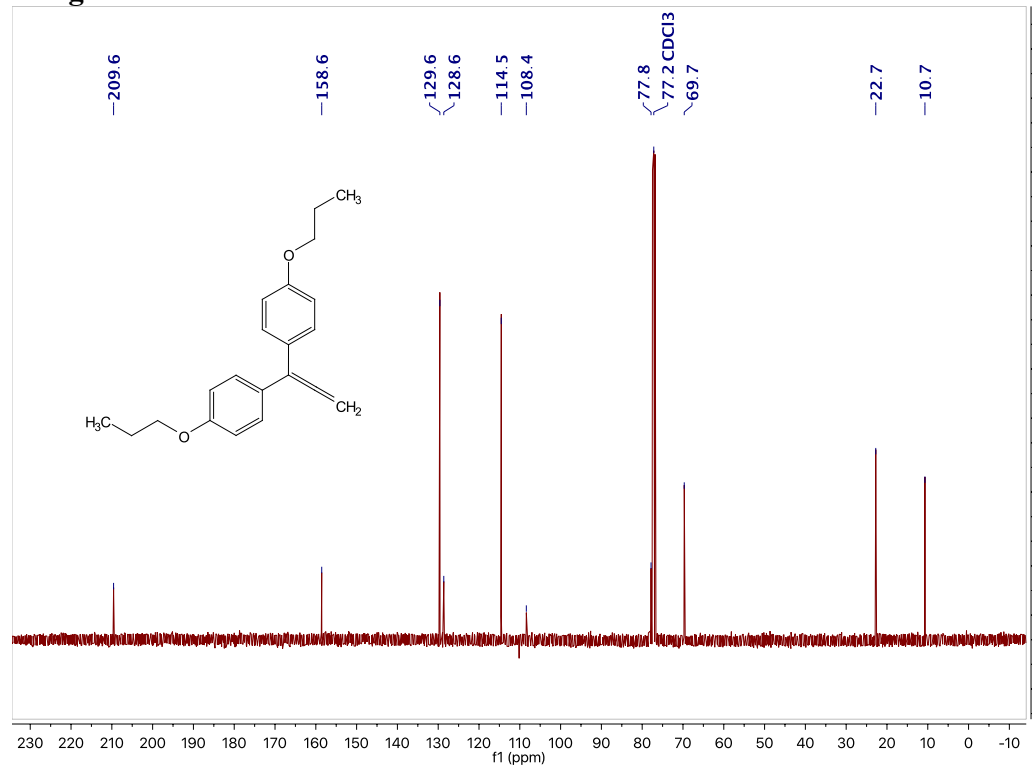
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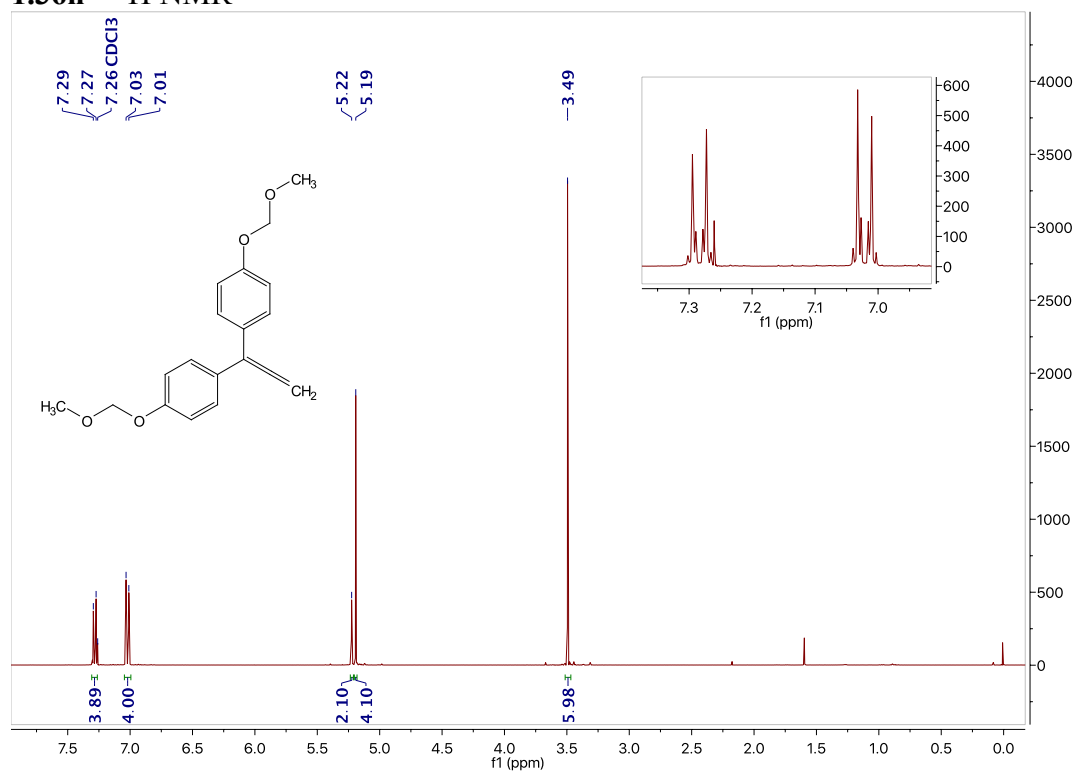


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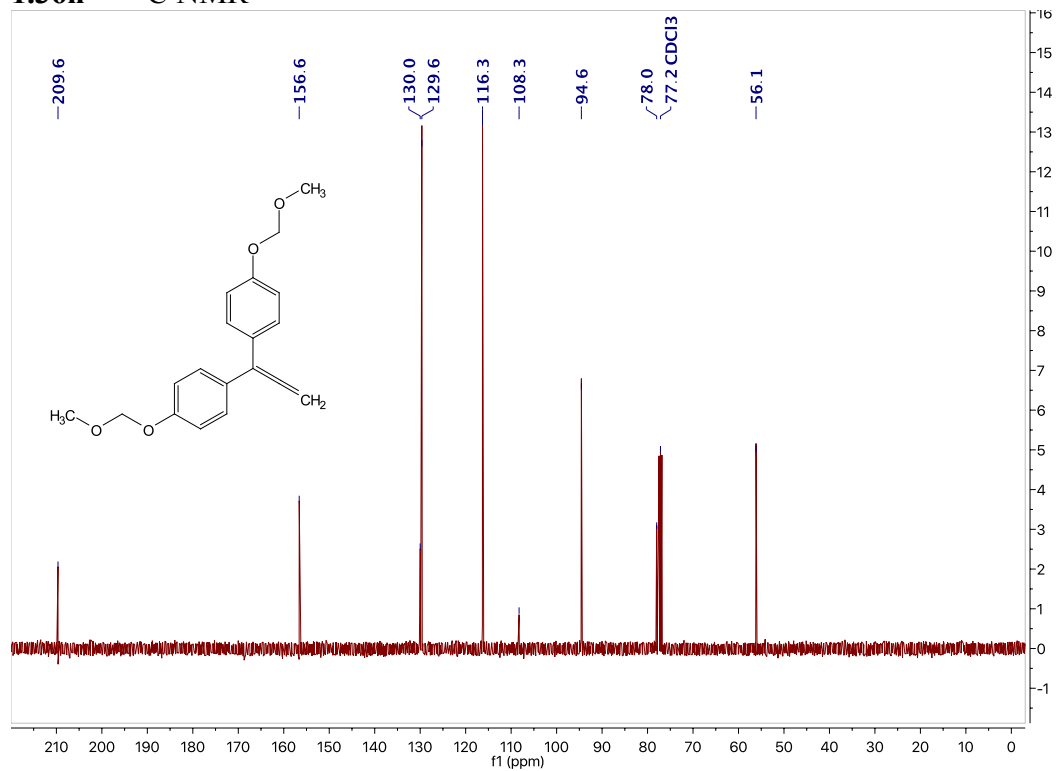




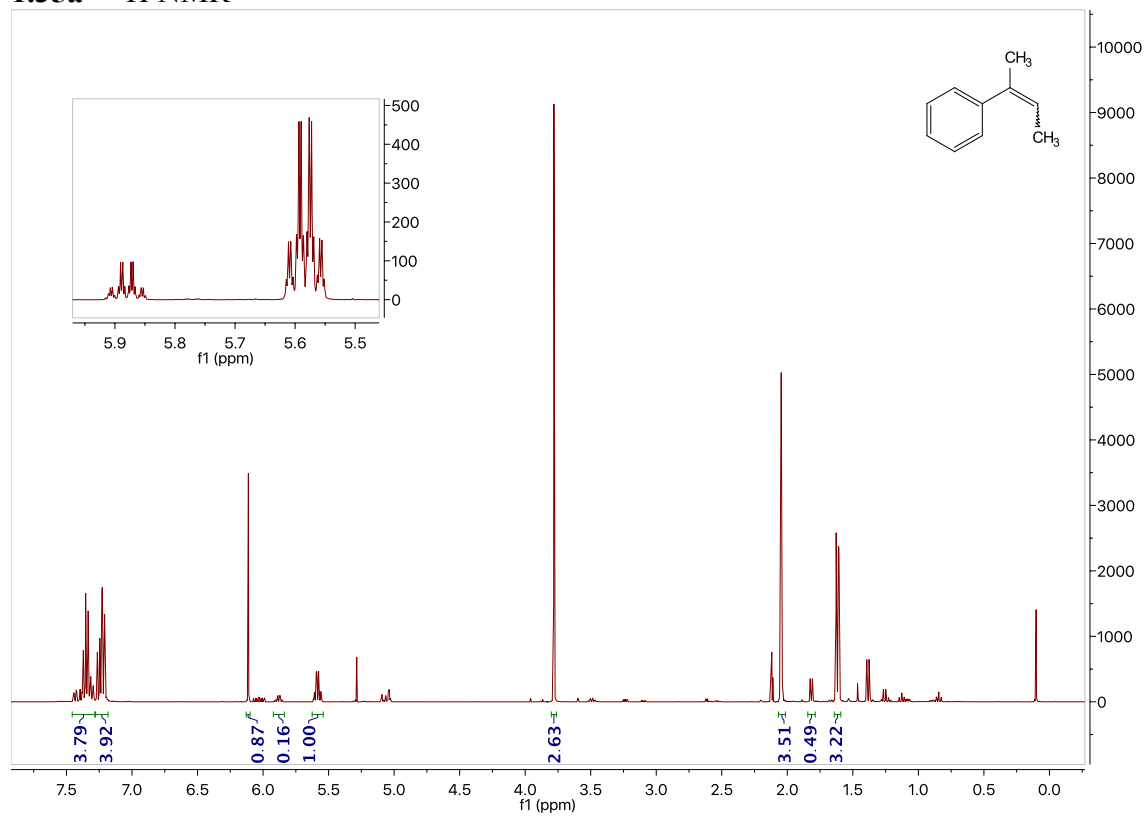
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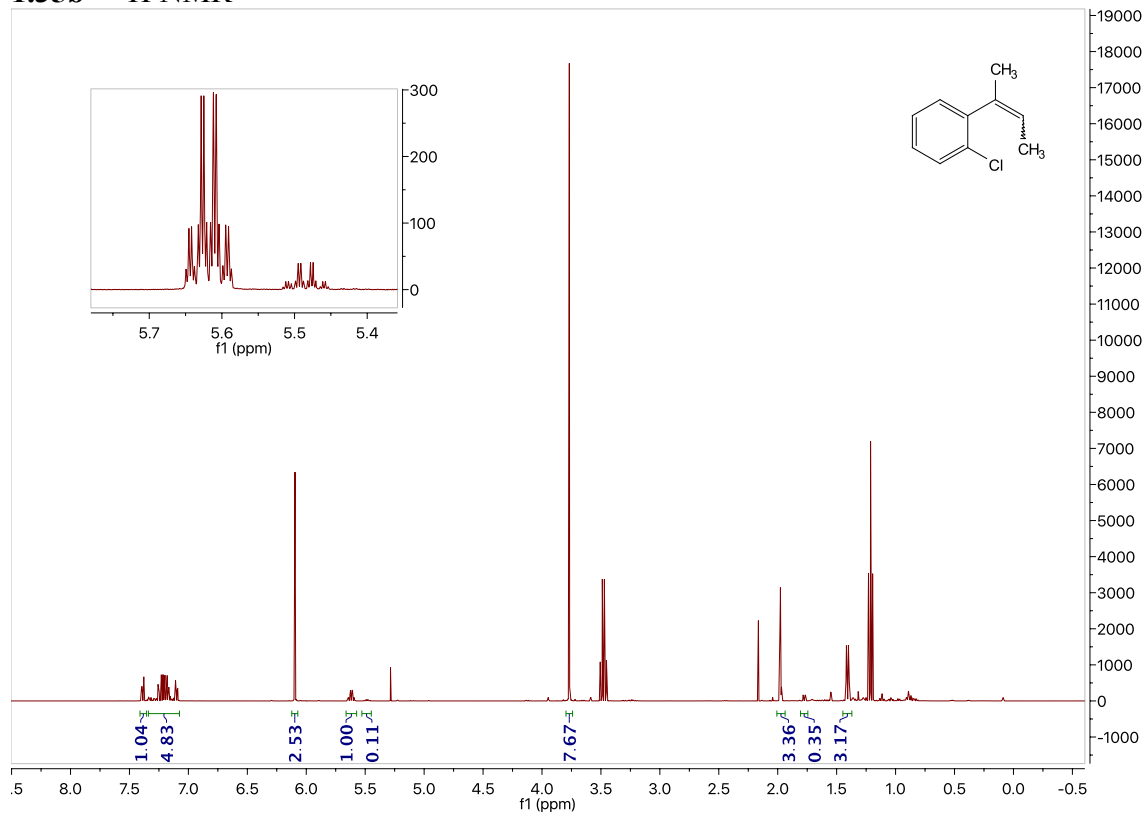
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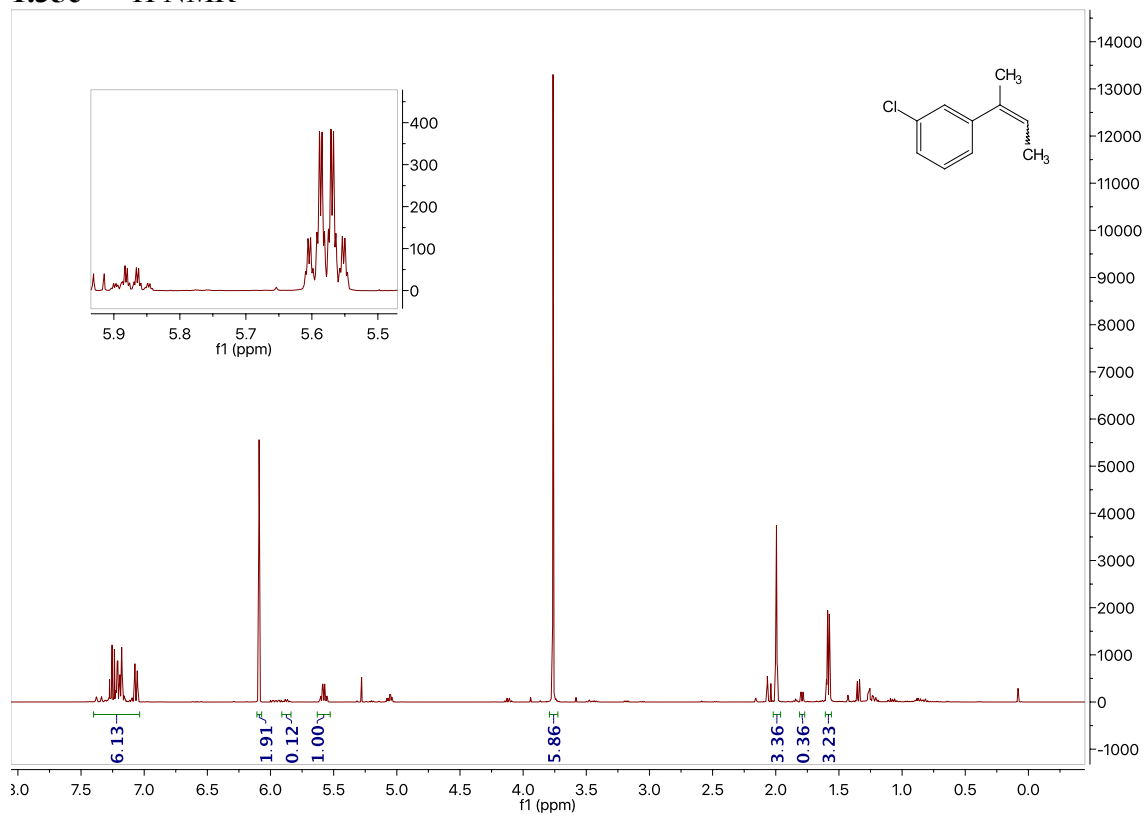
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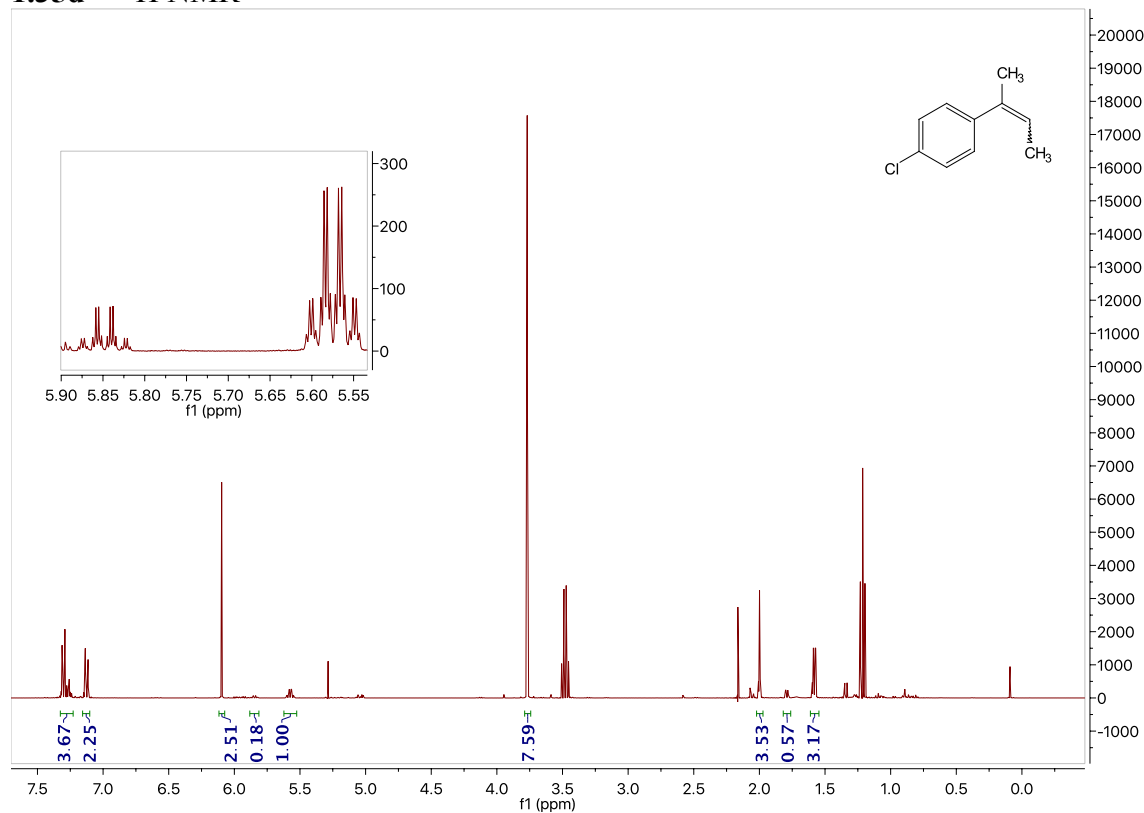
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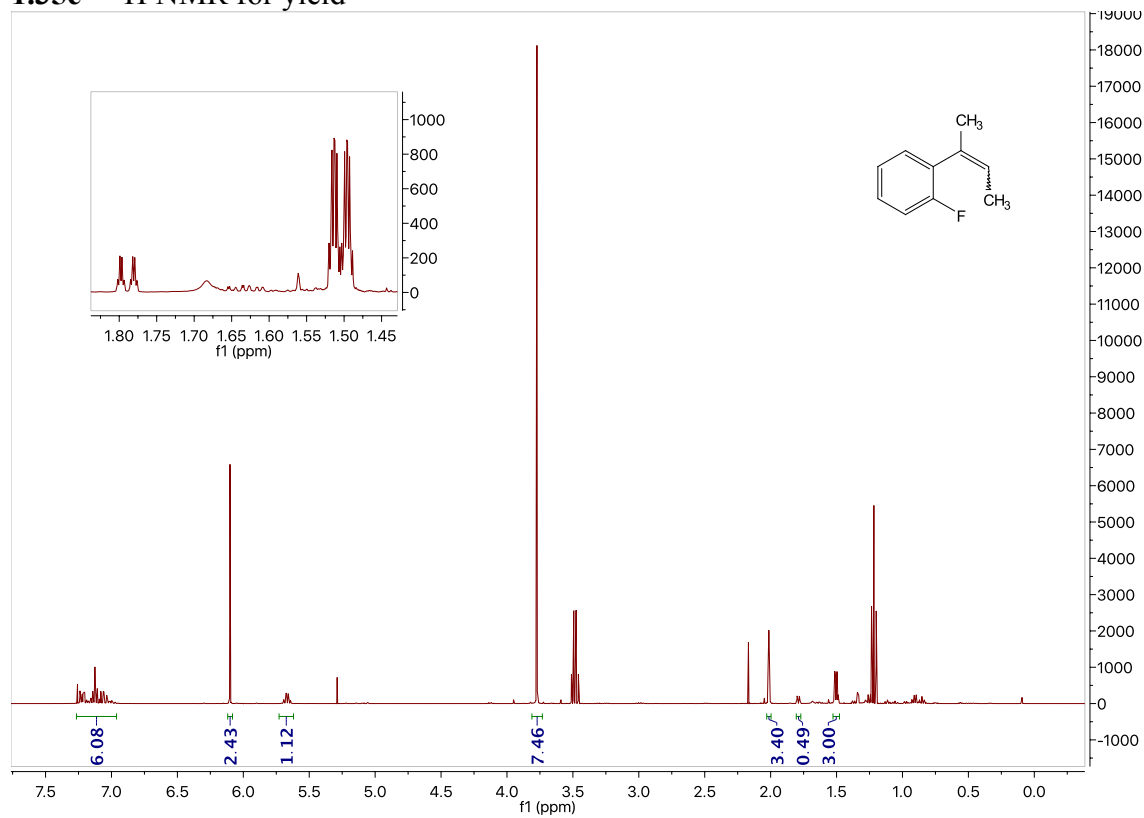
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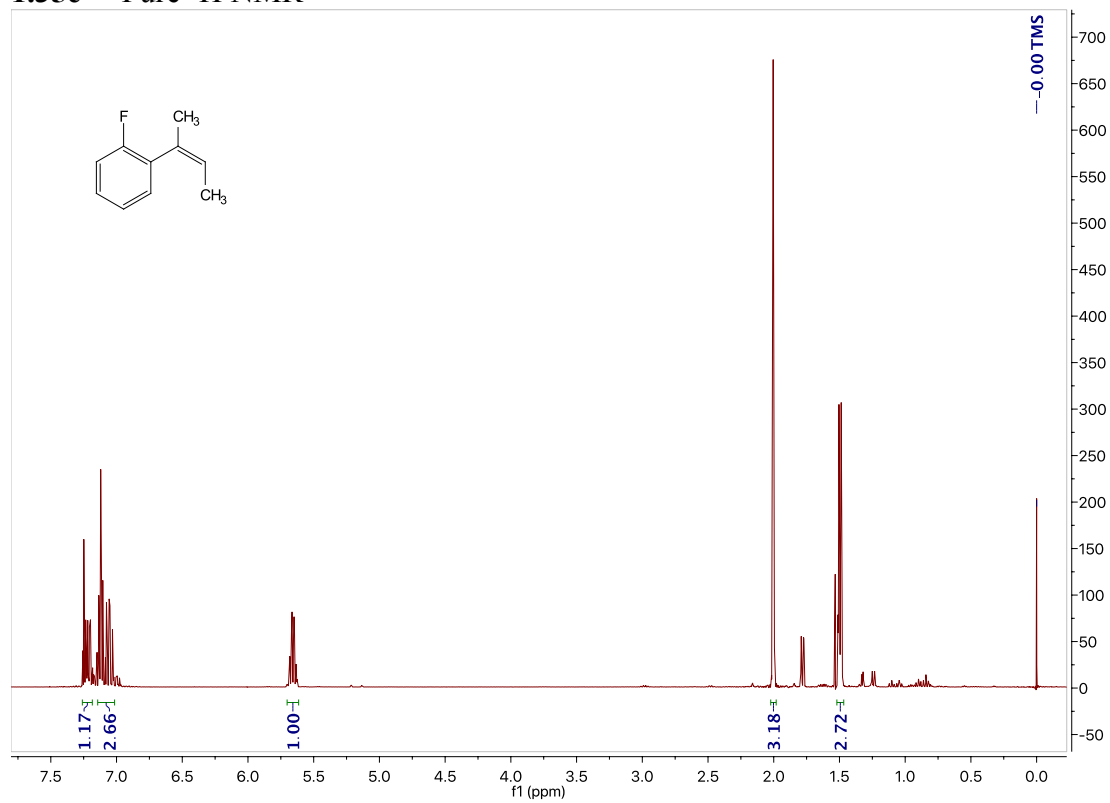
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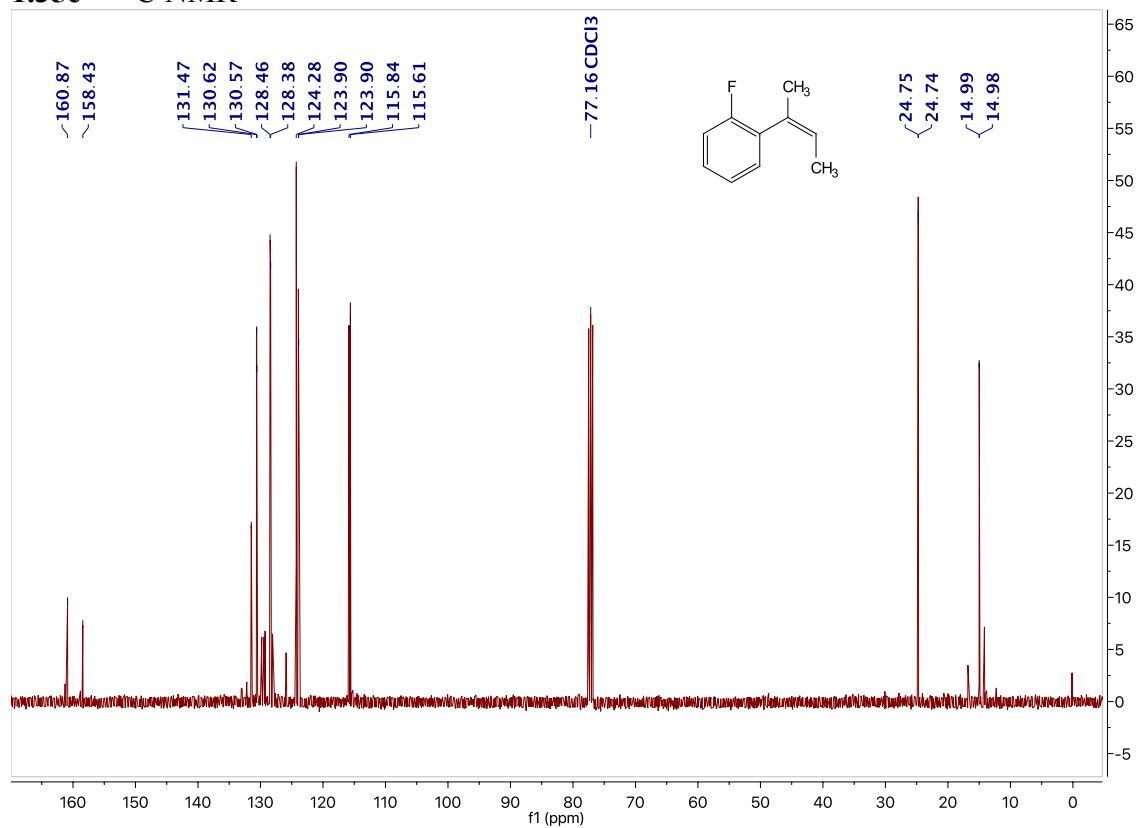
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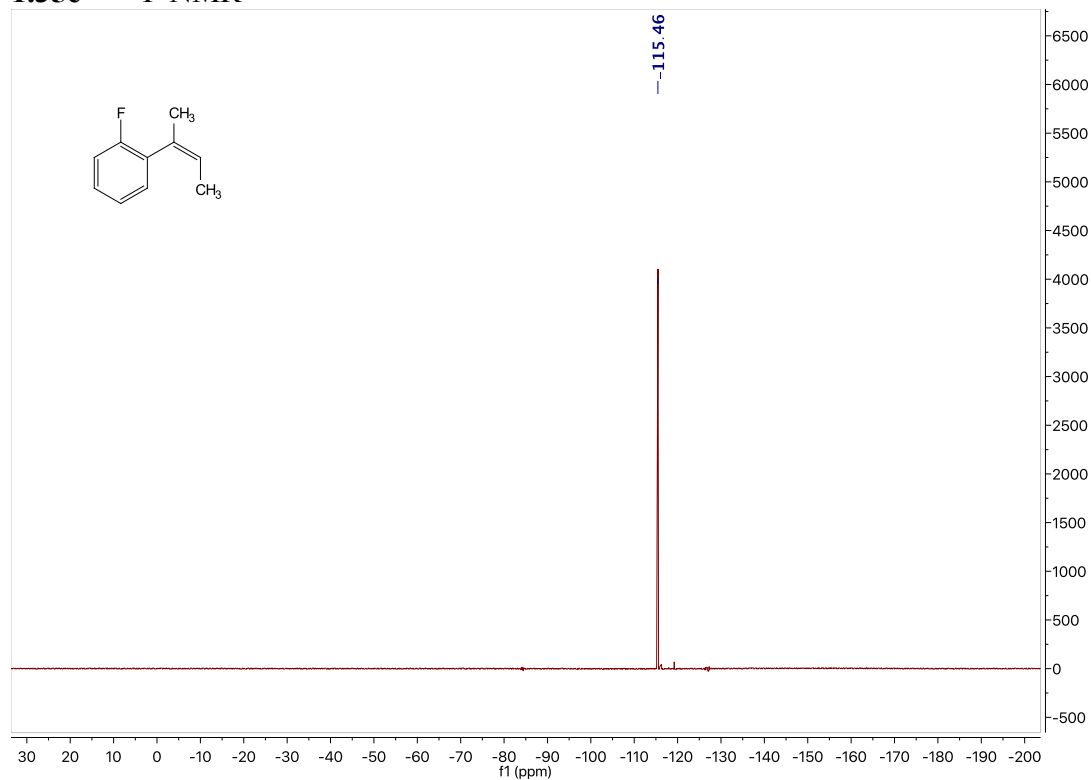
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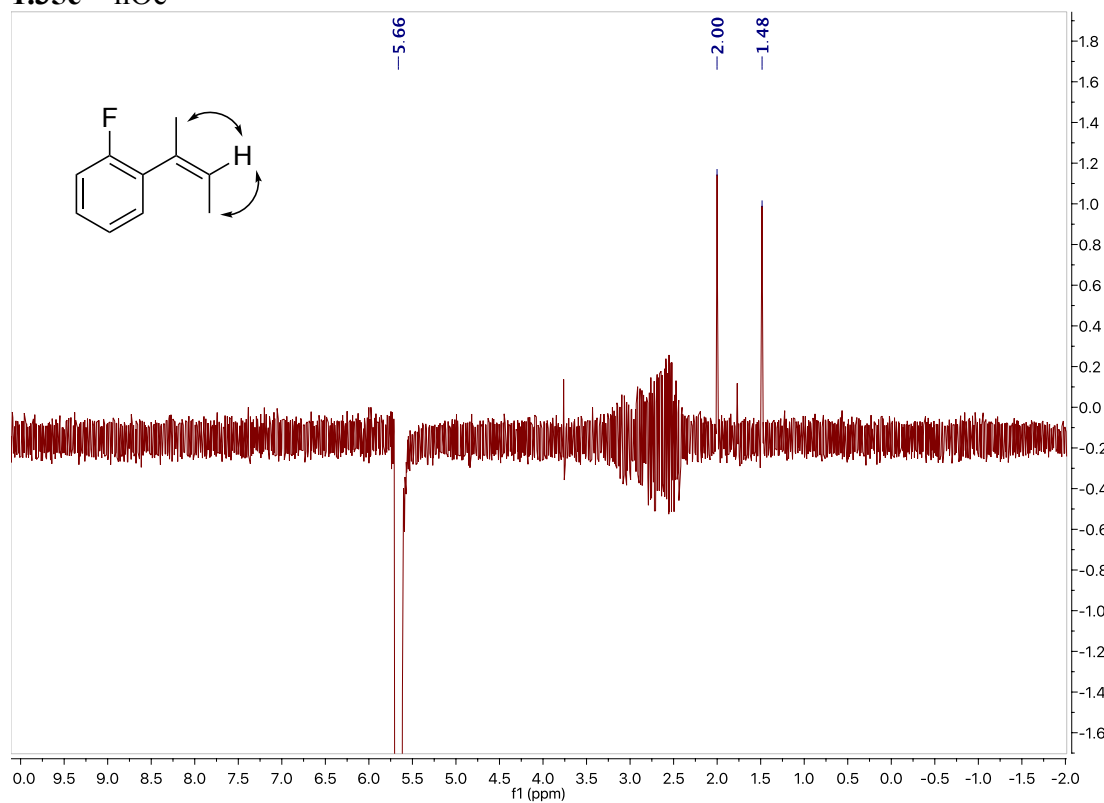
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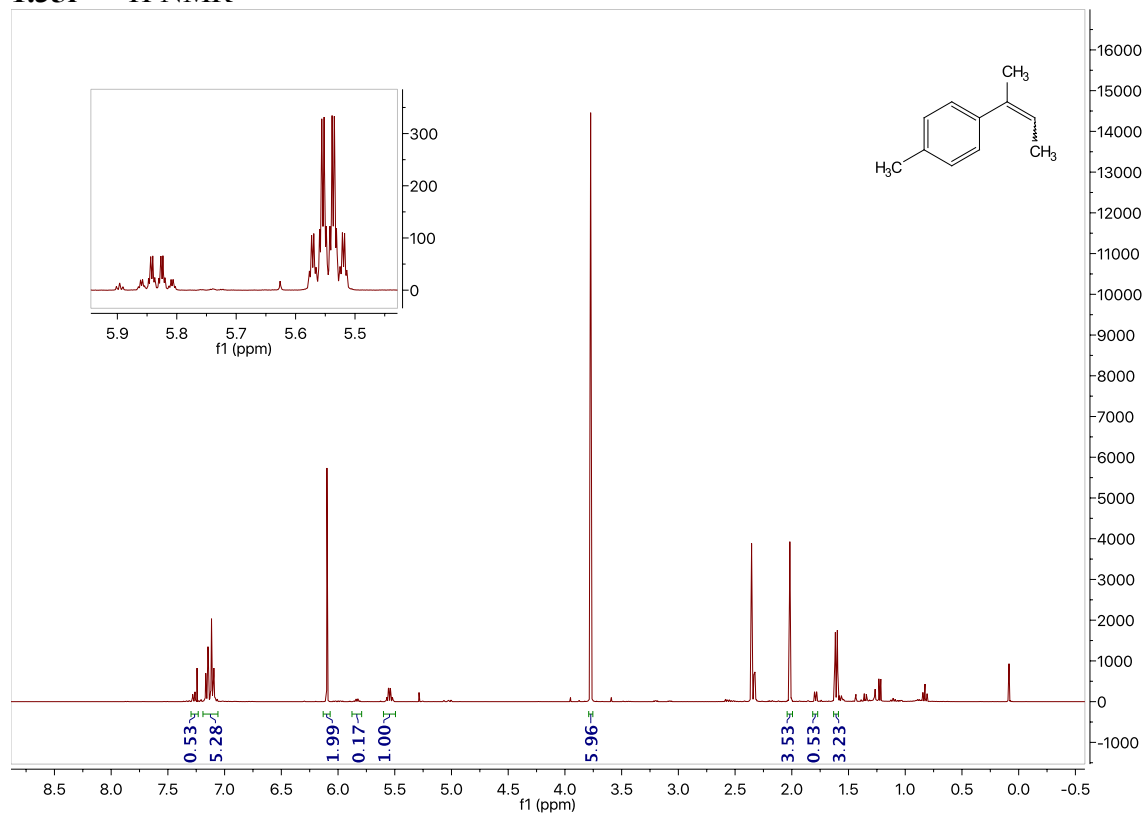
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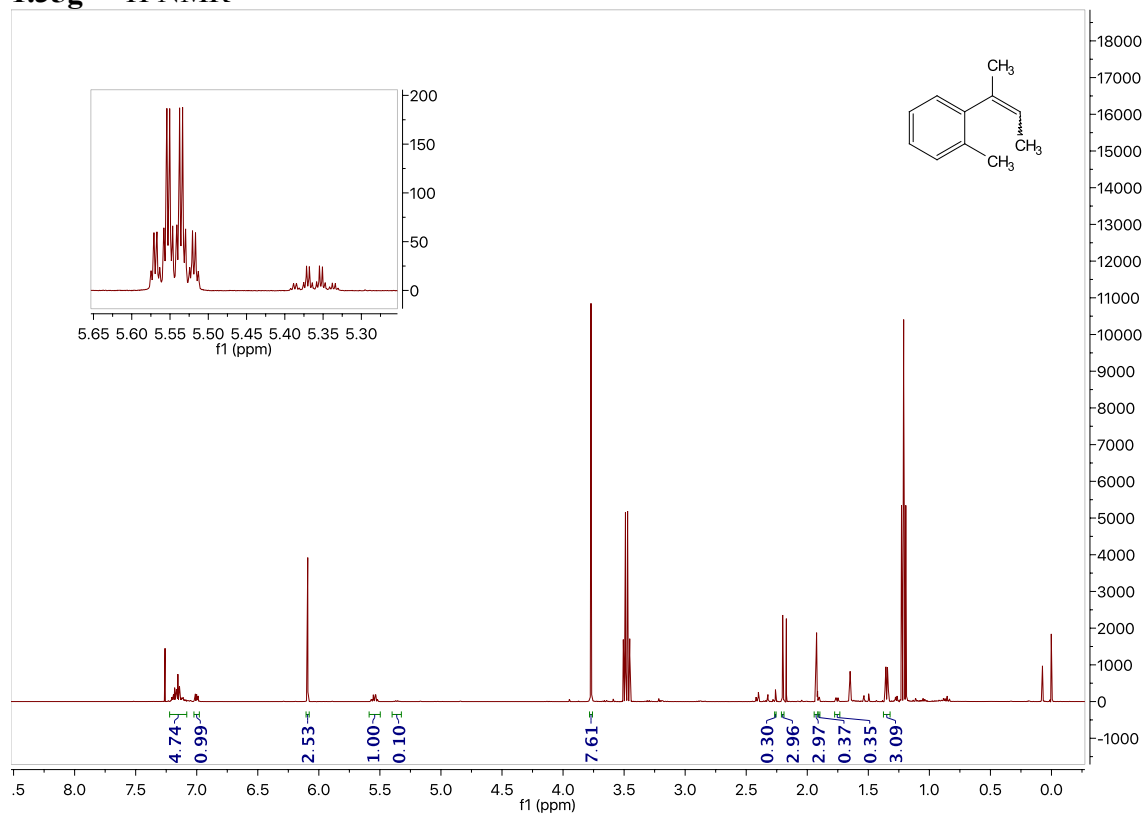
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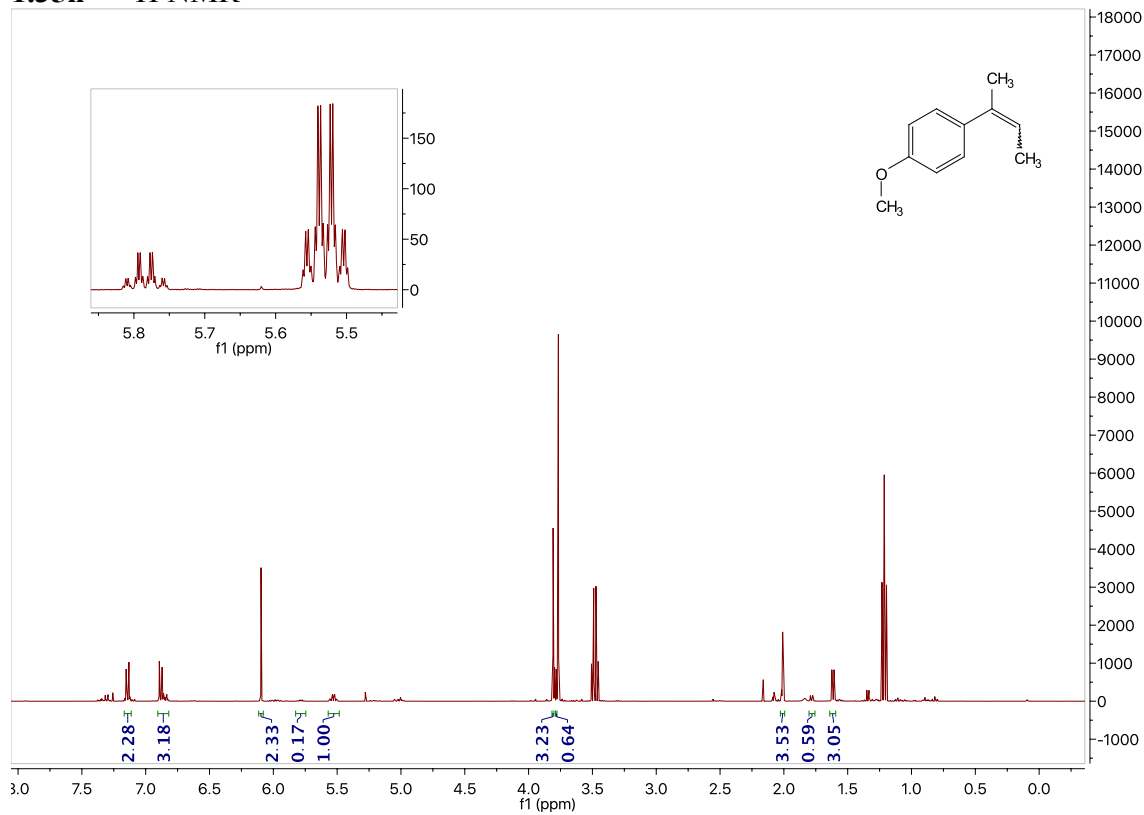
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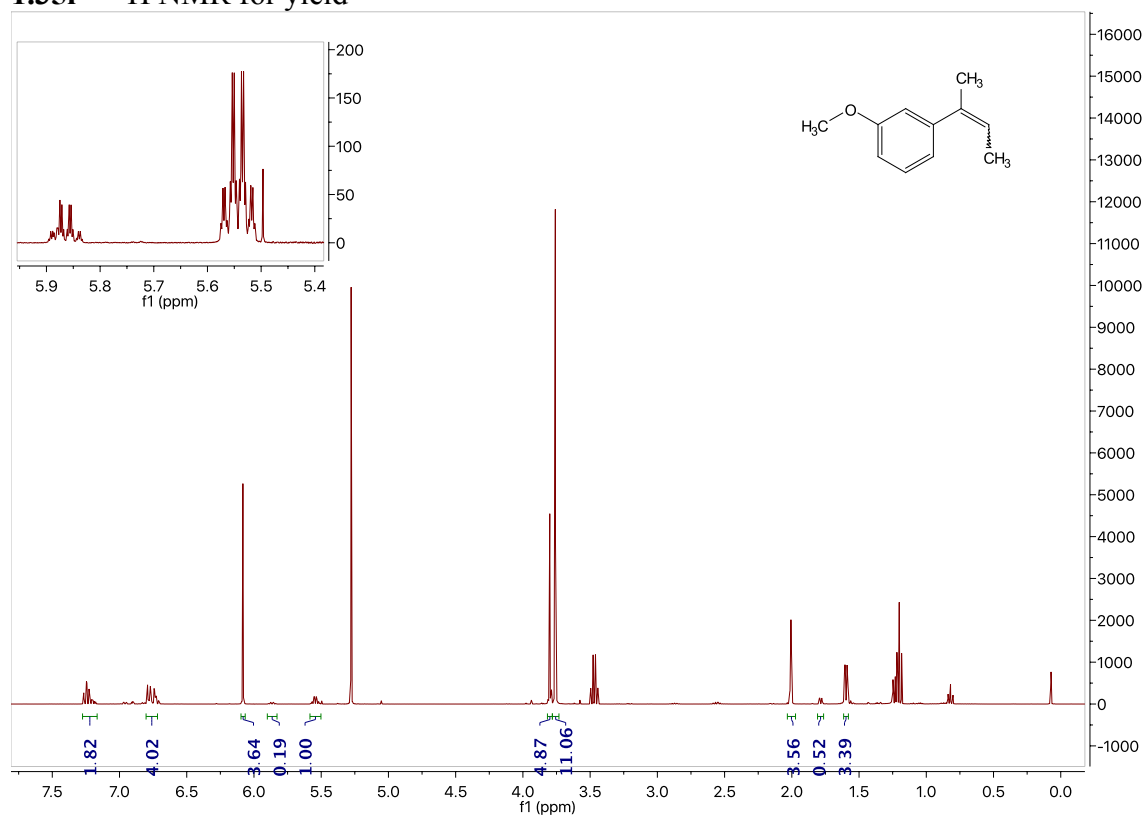
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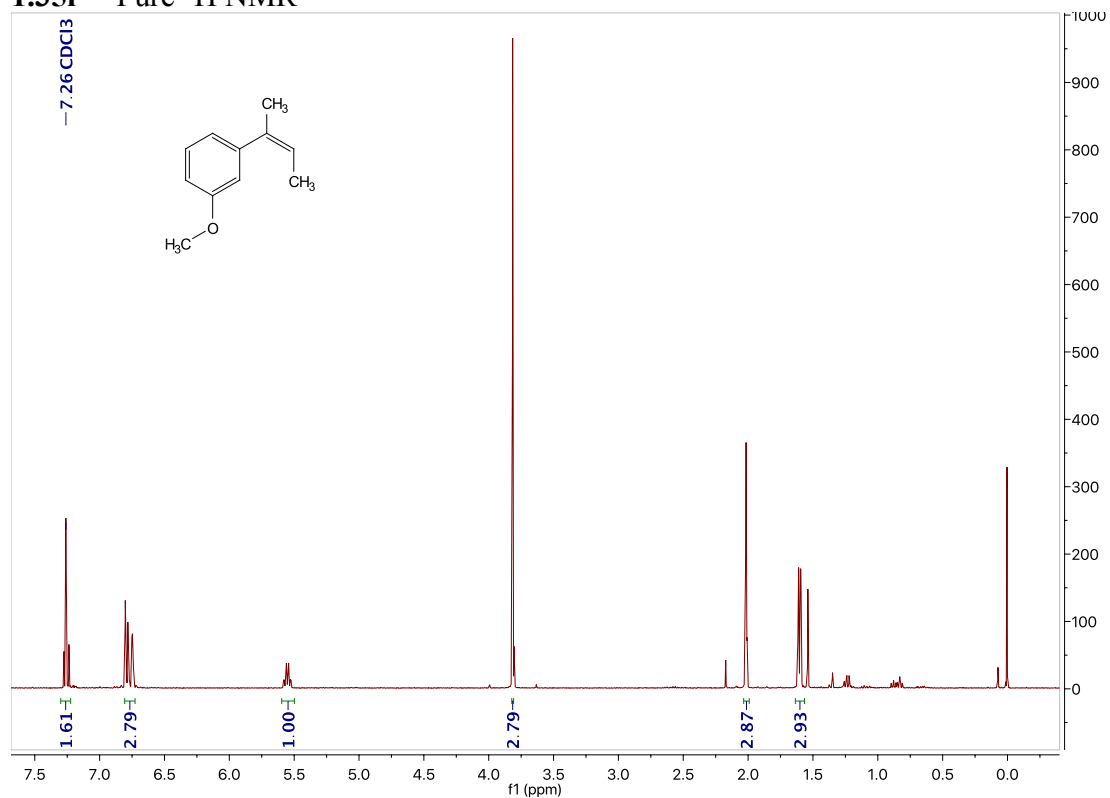
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### 1.35i – <sup>1</sup>H NMR for yield

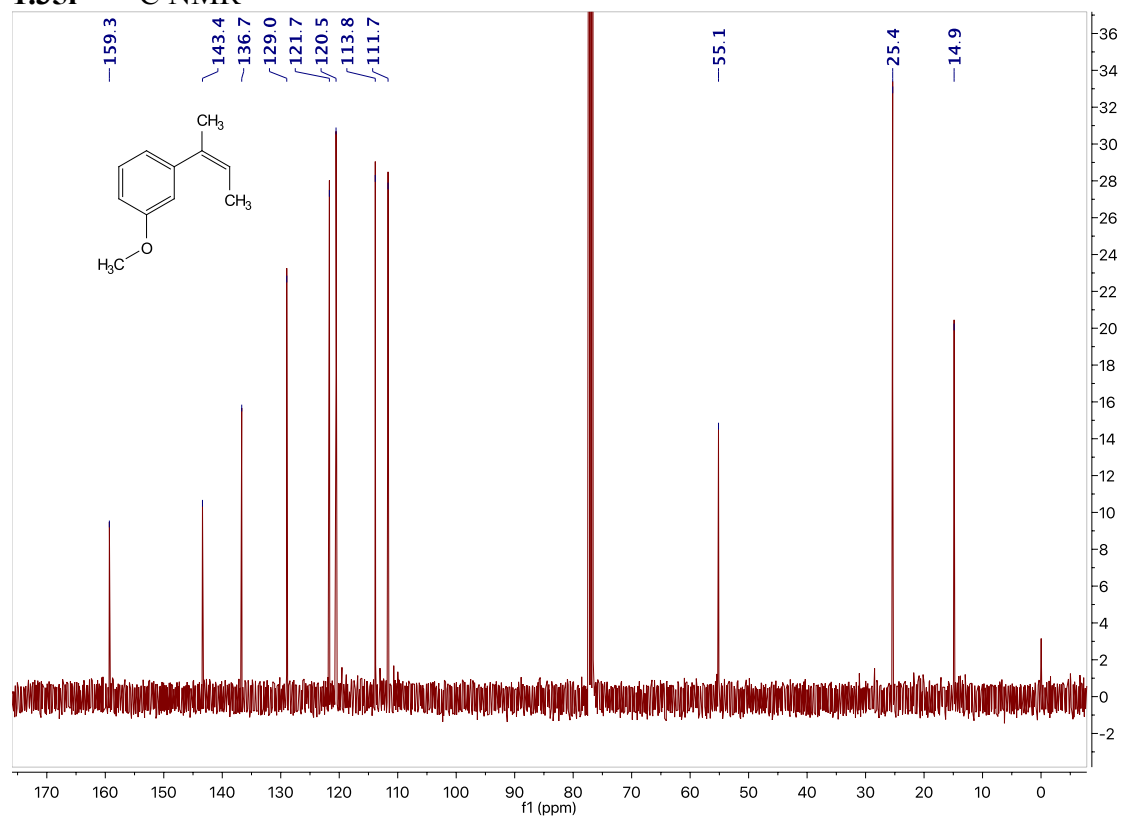


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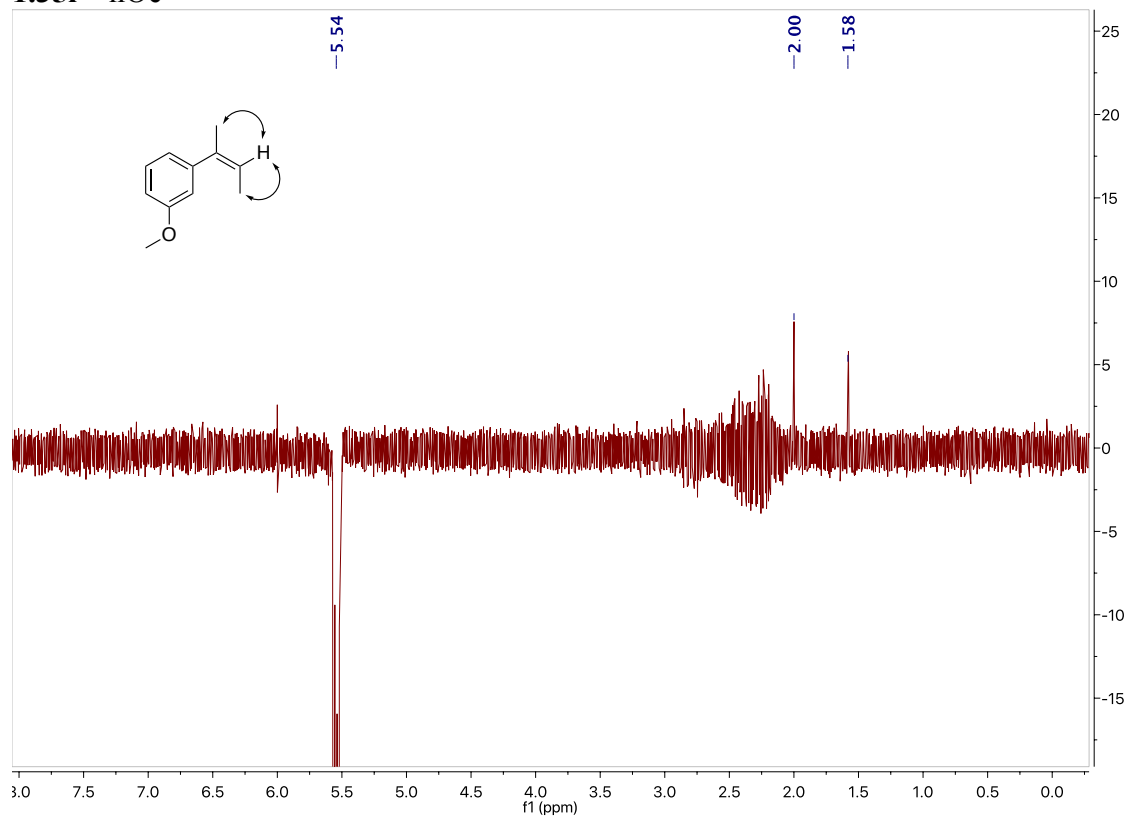




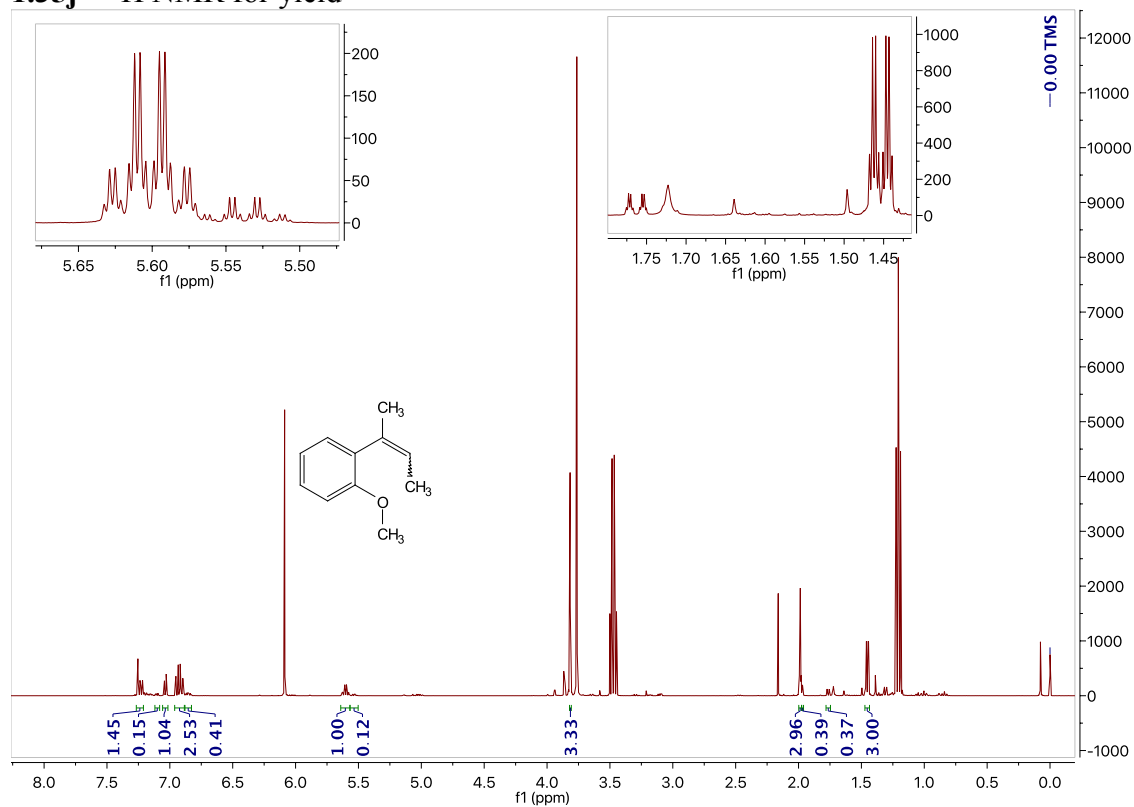
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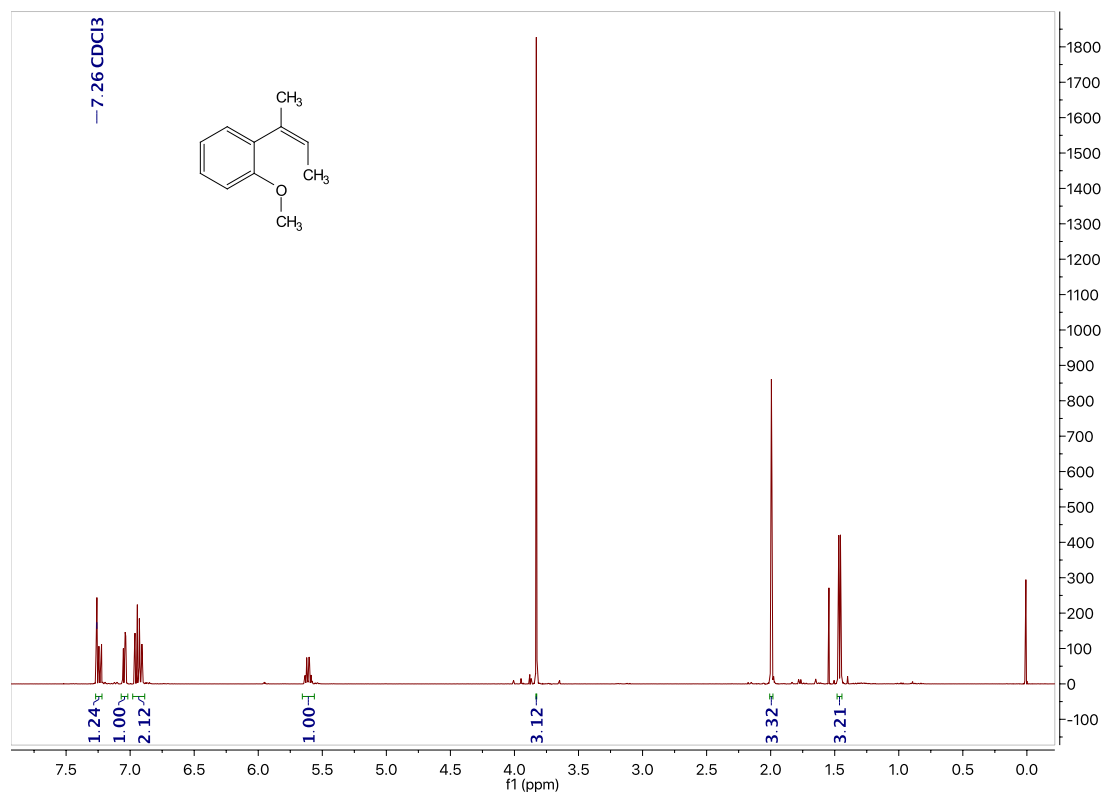
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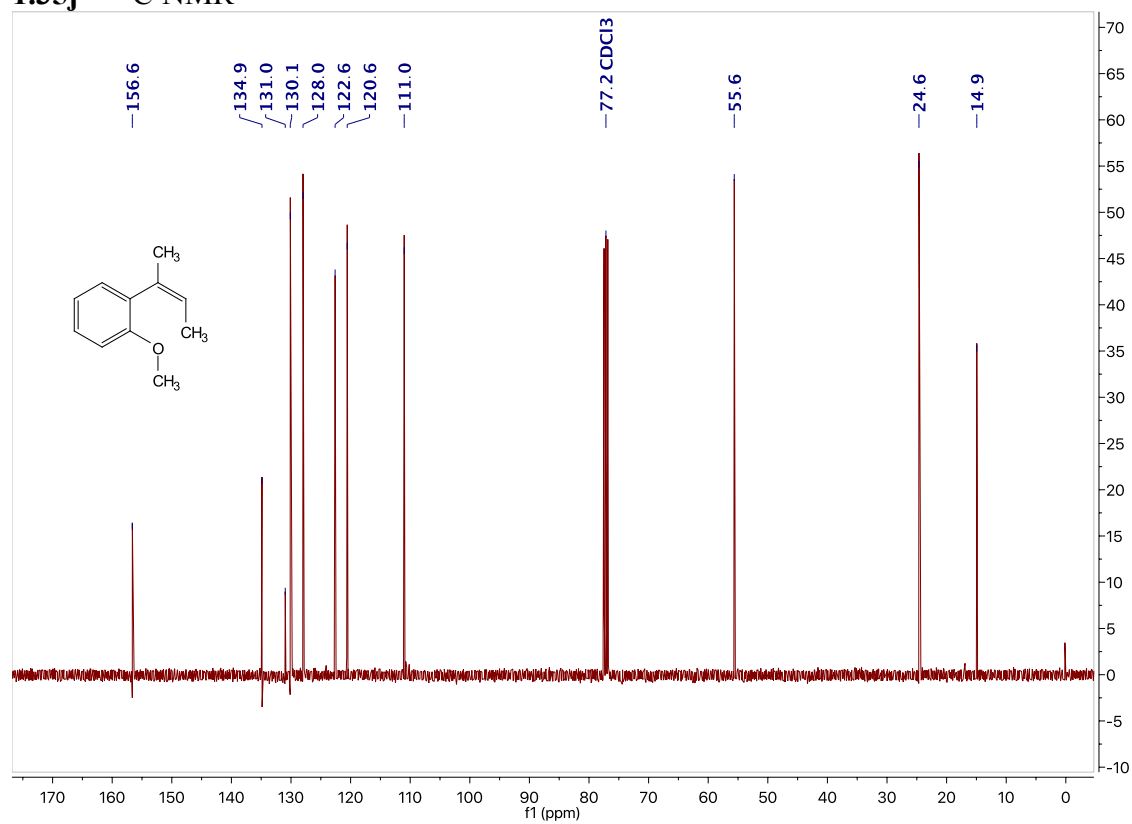
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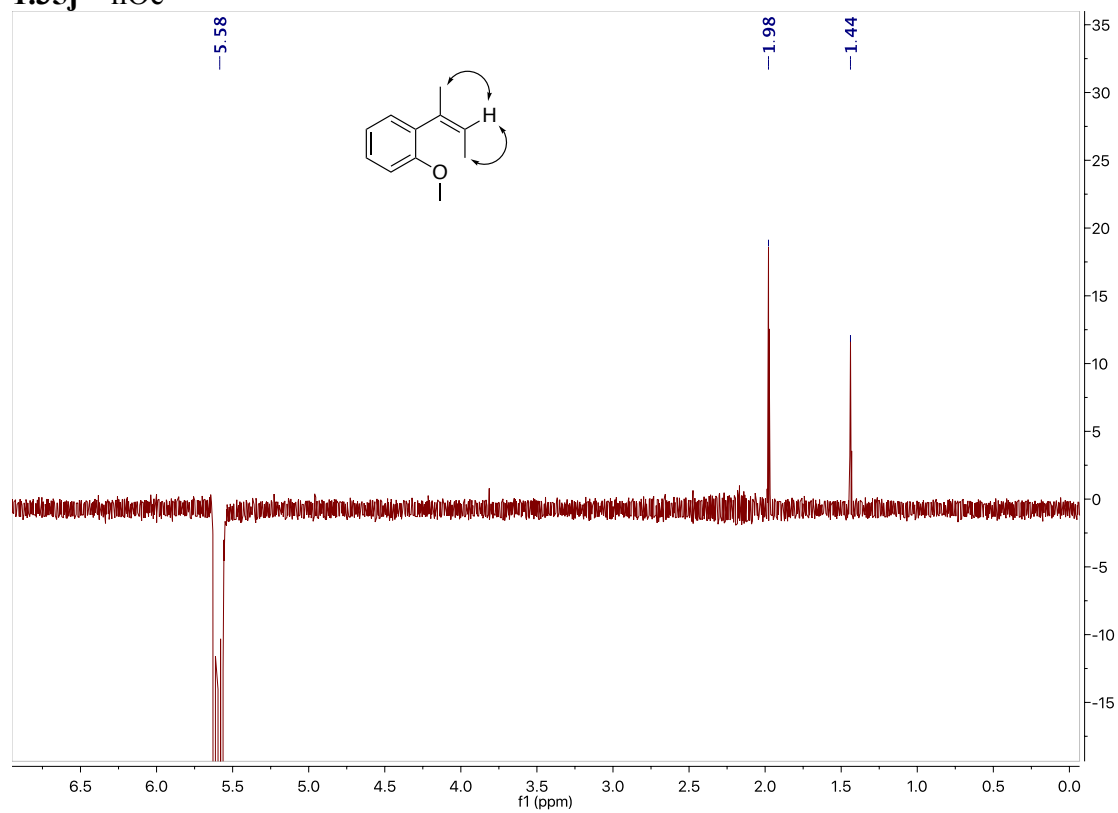
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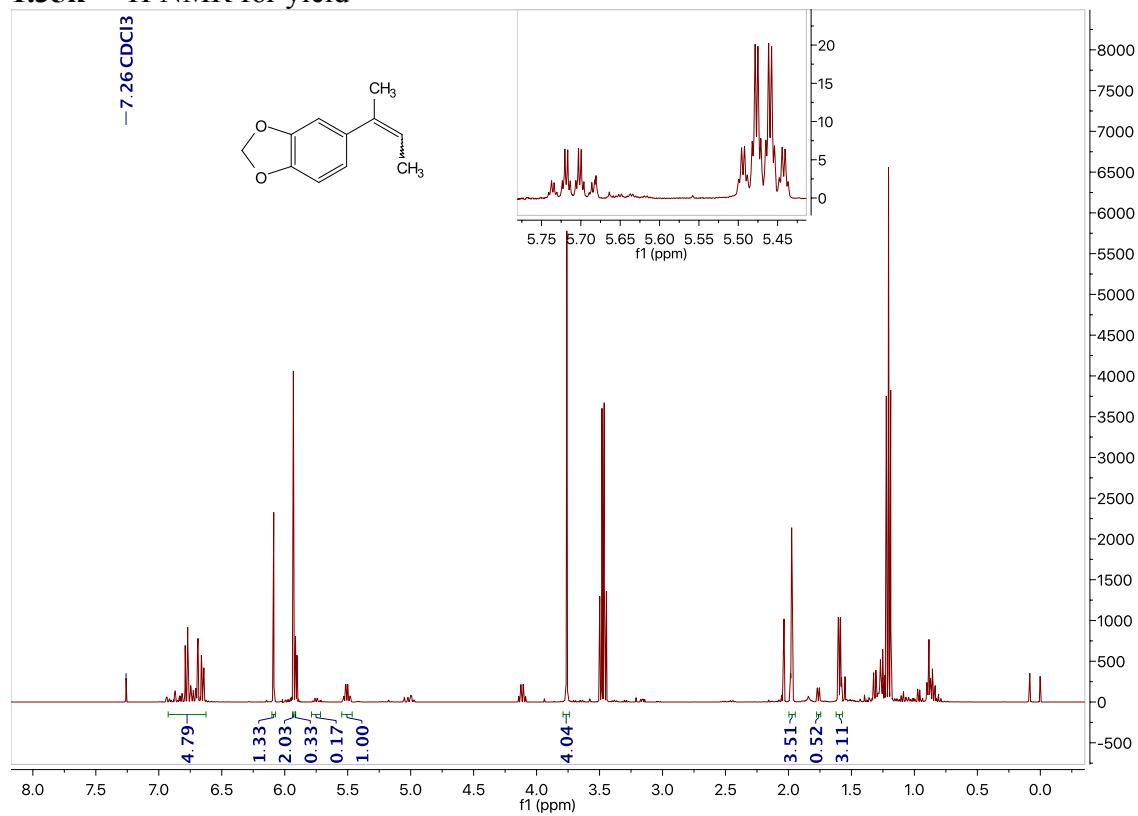
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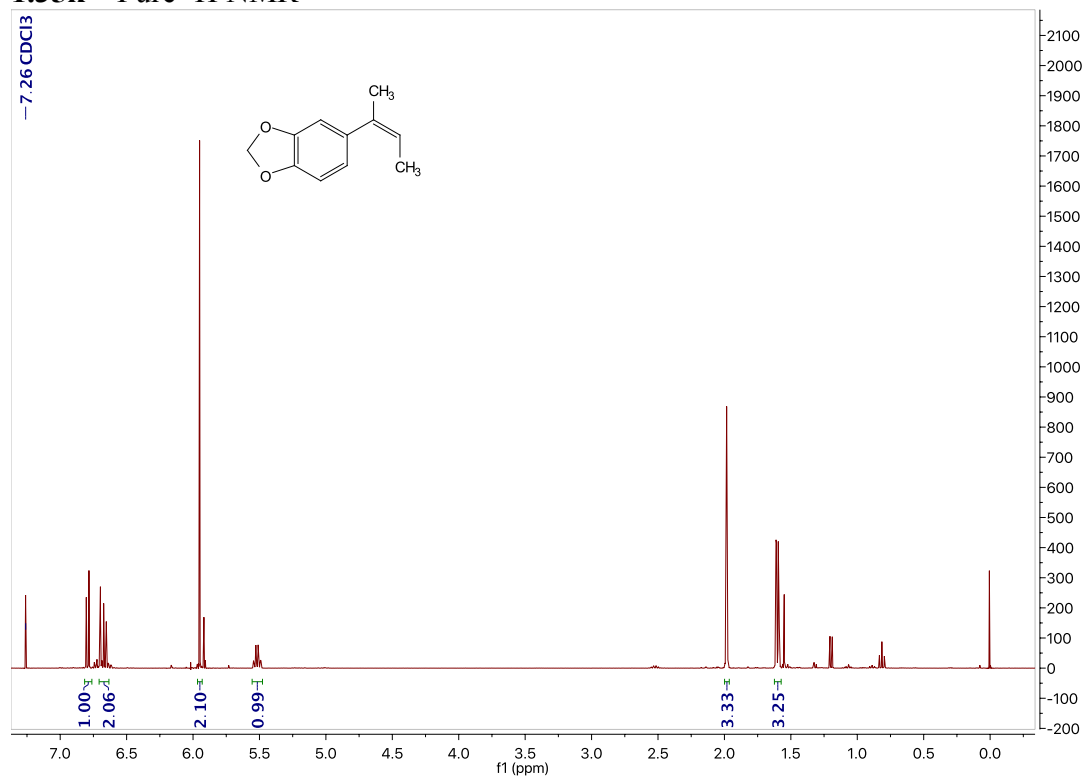
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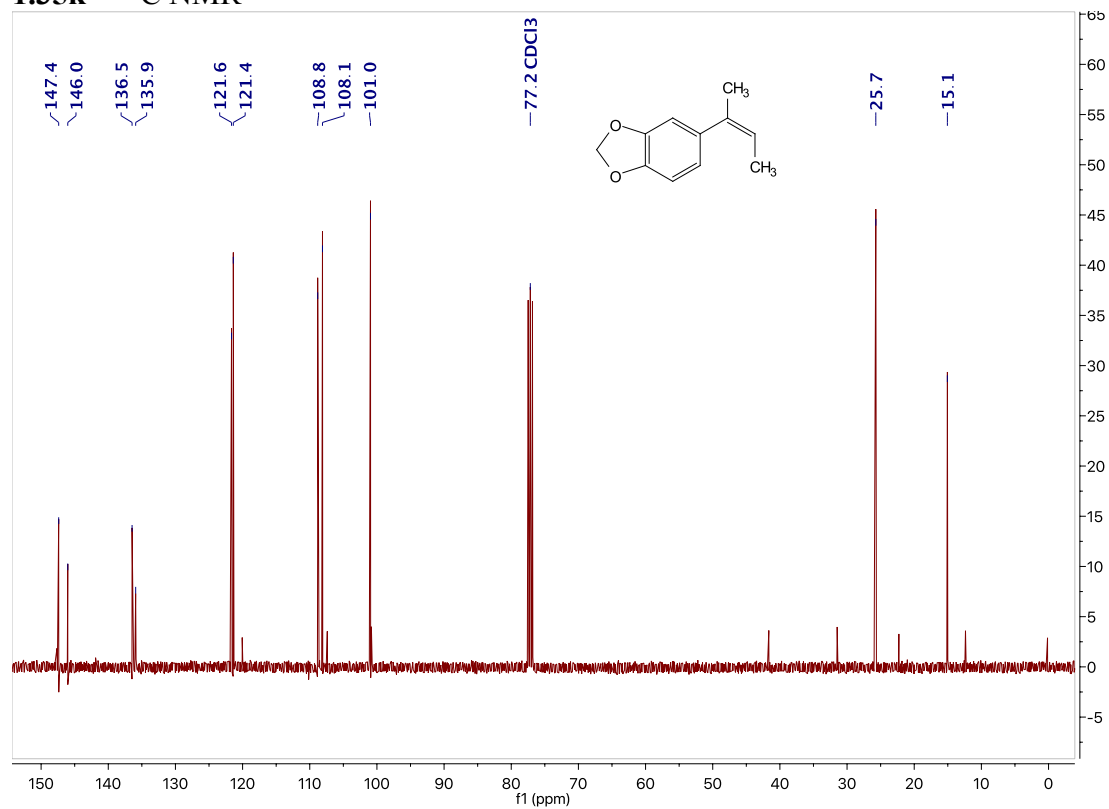
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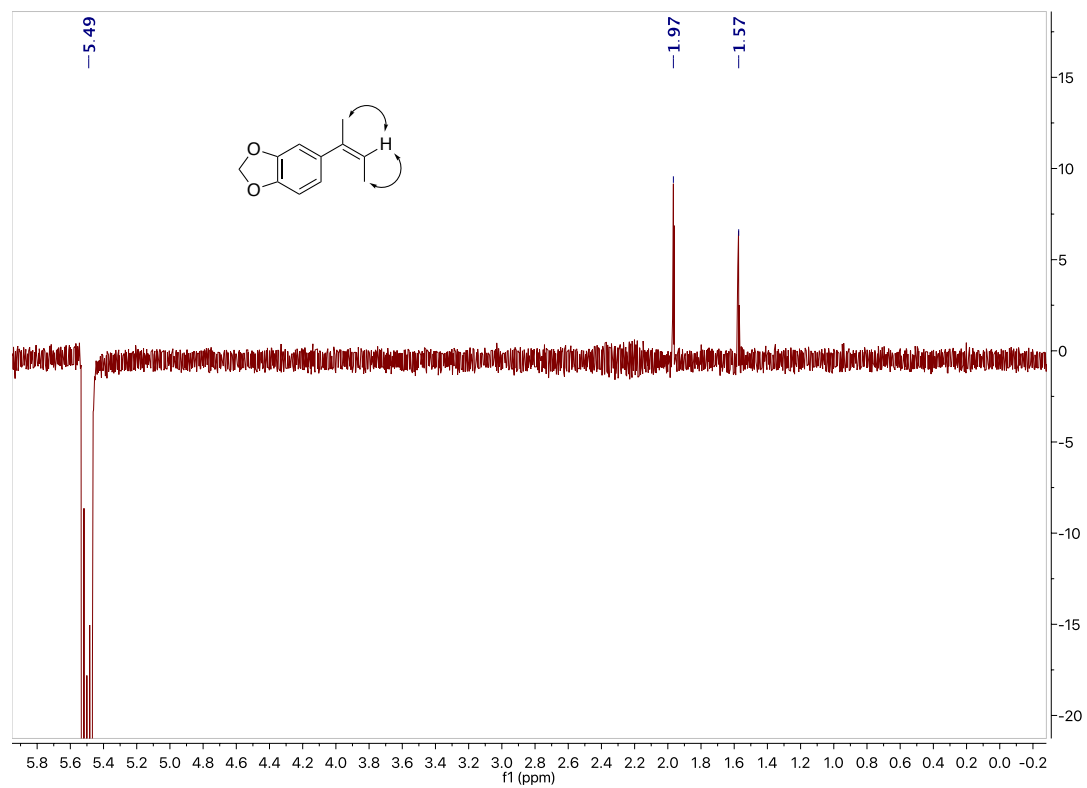
### 1.35k – Pure <sup>1</sup>H NMR



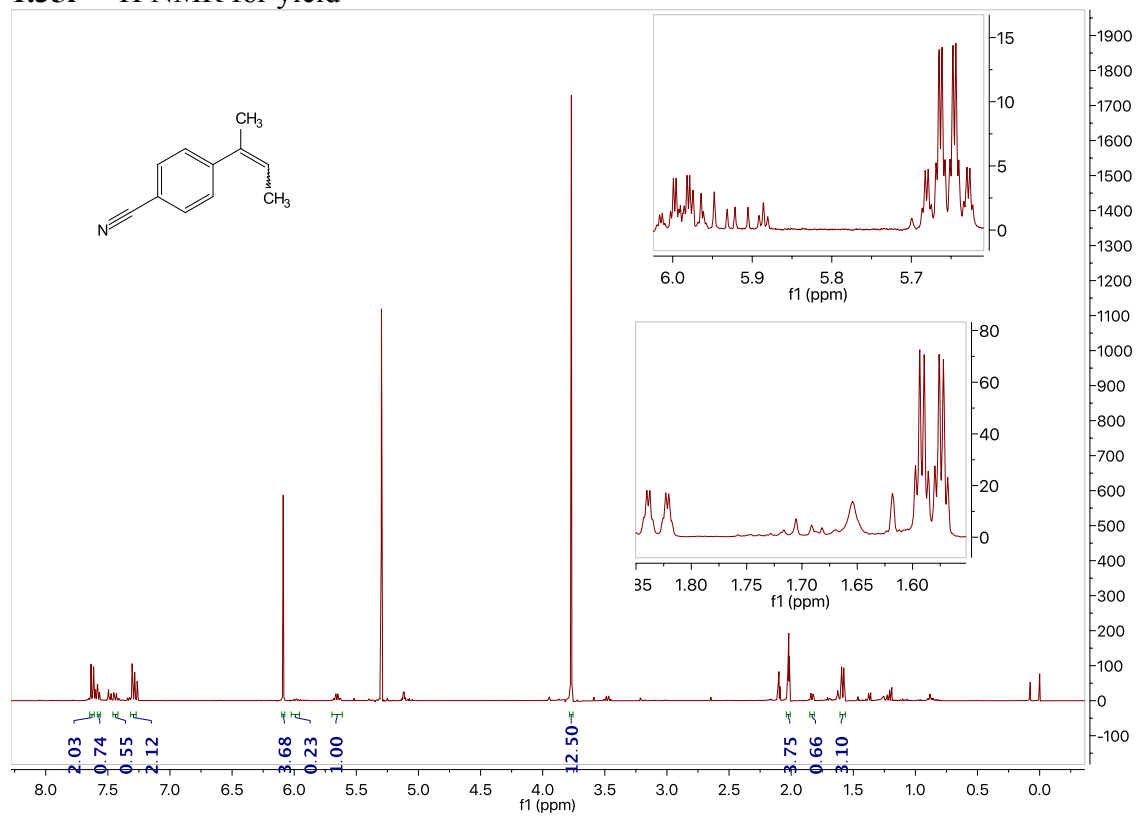
### 1.35k – <sup>13</sup>C NMR



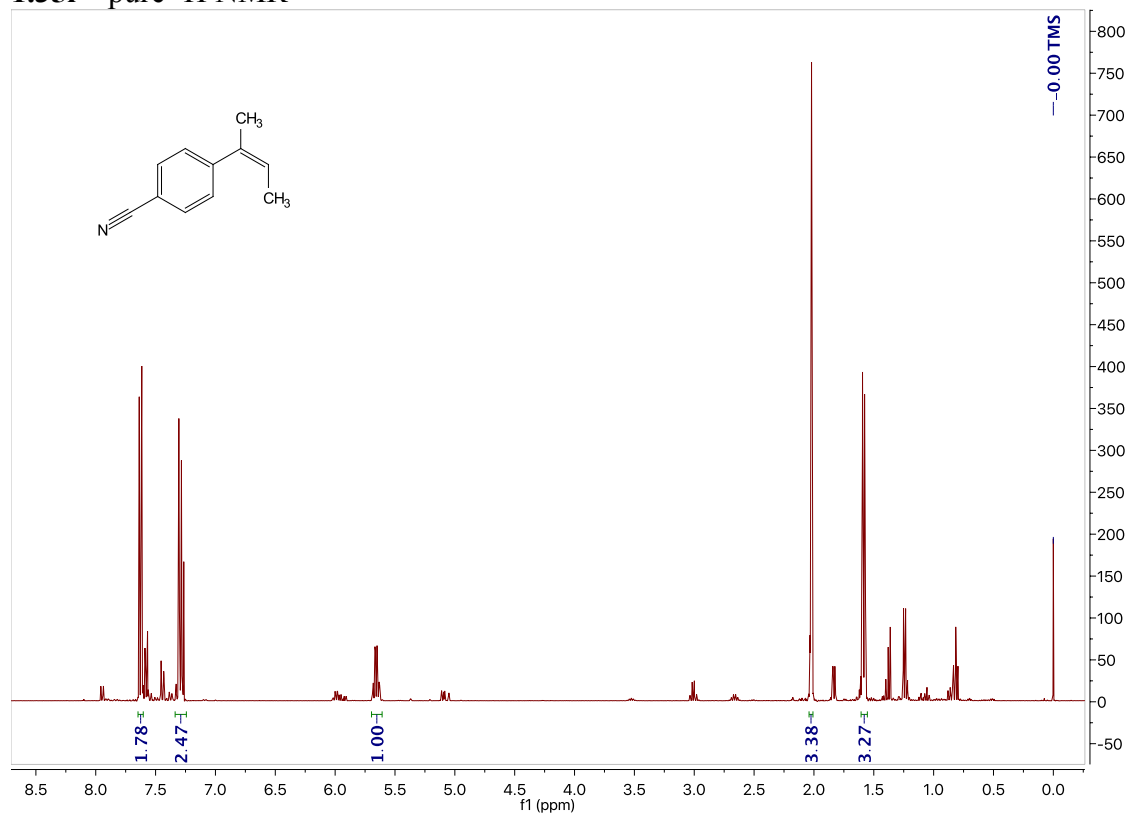
### 1.35k – nOe



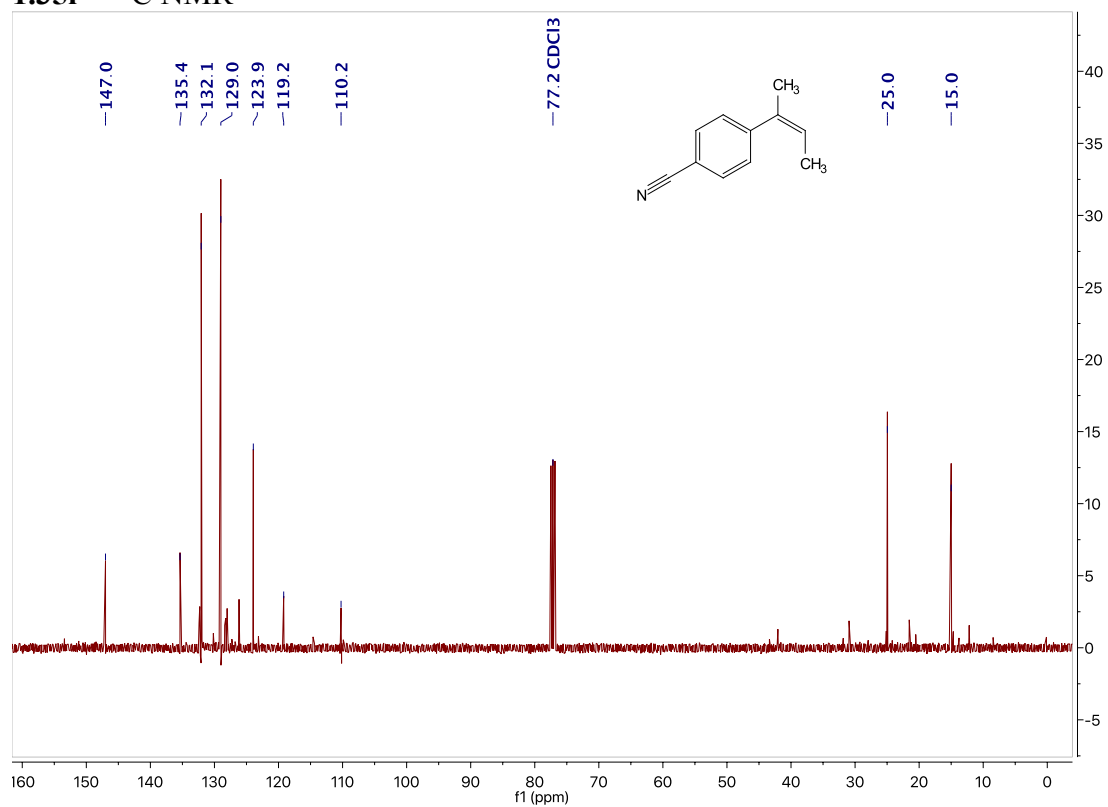
### 1.35I – <sup>1</sup>H NMR for yield



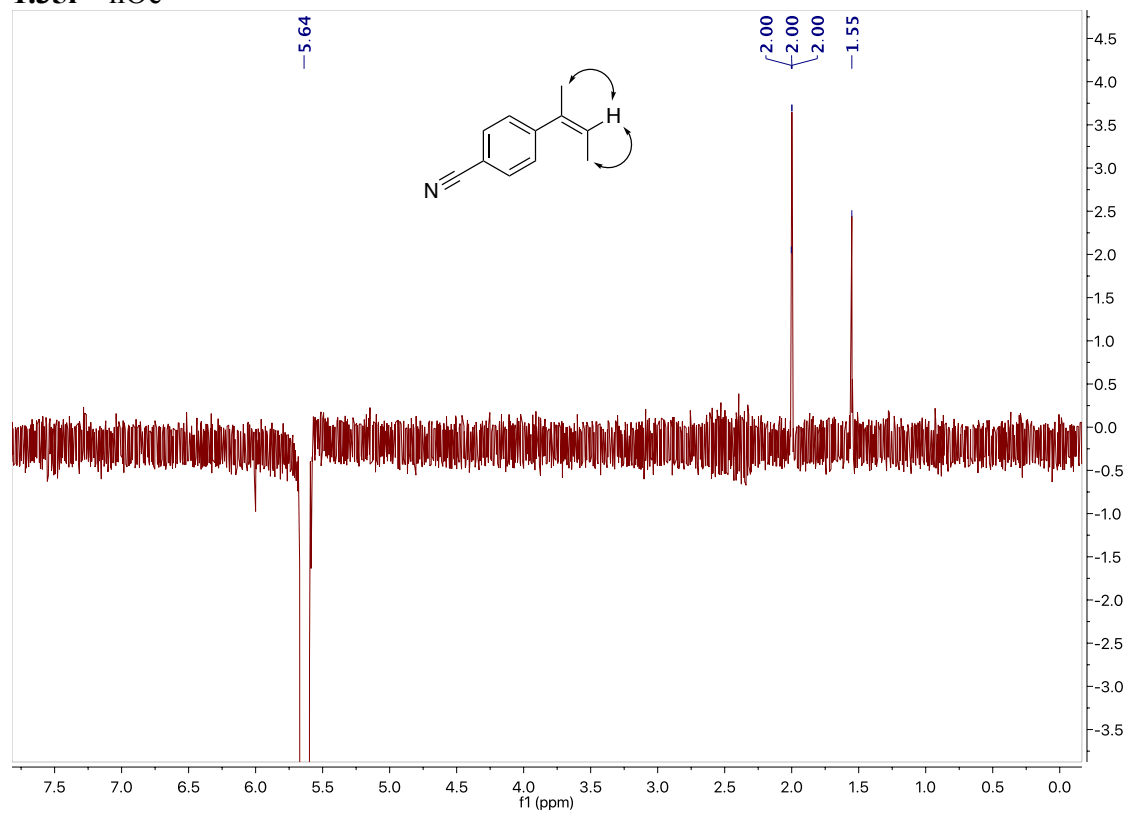
### 1.35I – pure <sup>1</sup>H NMR



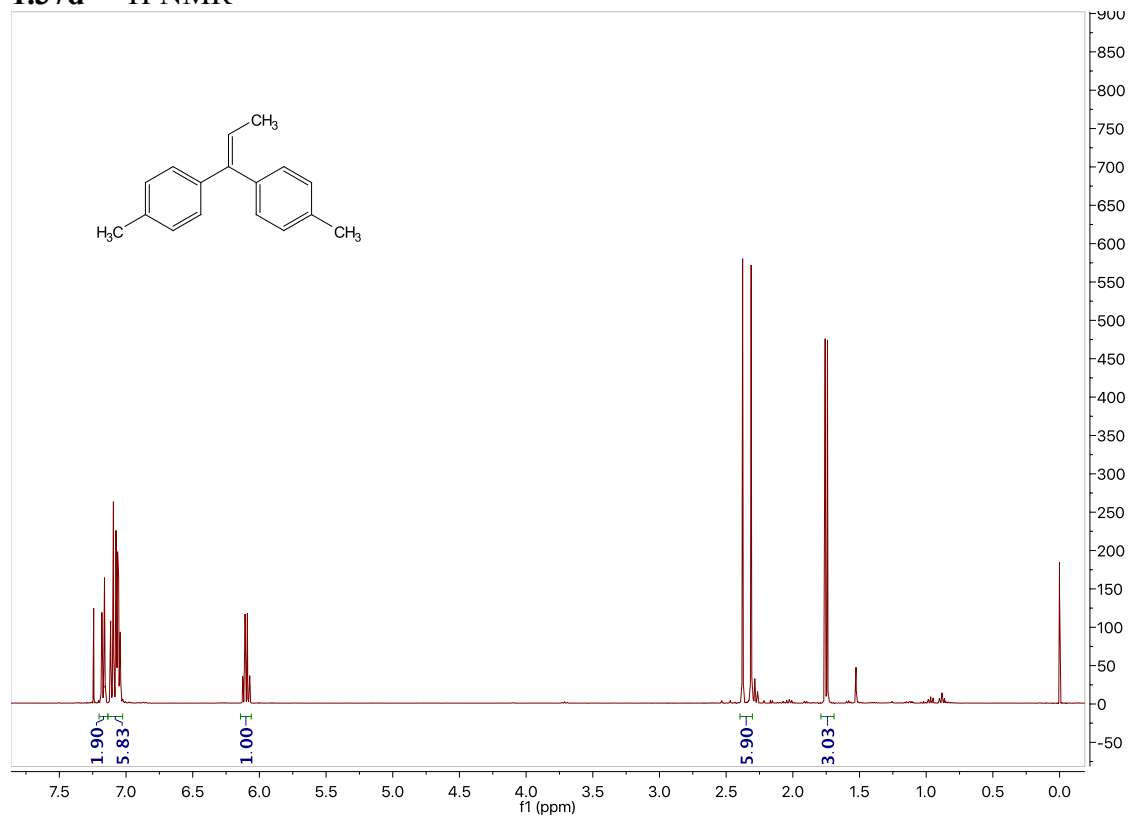
### 1.351 – $^{13}\text{C}$ NMR



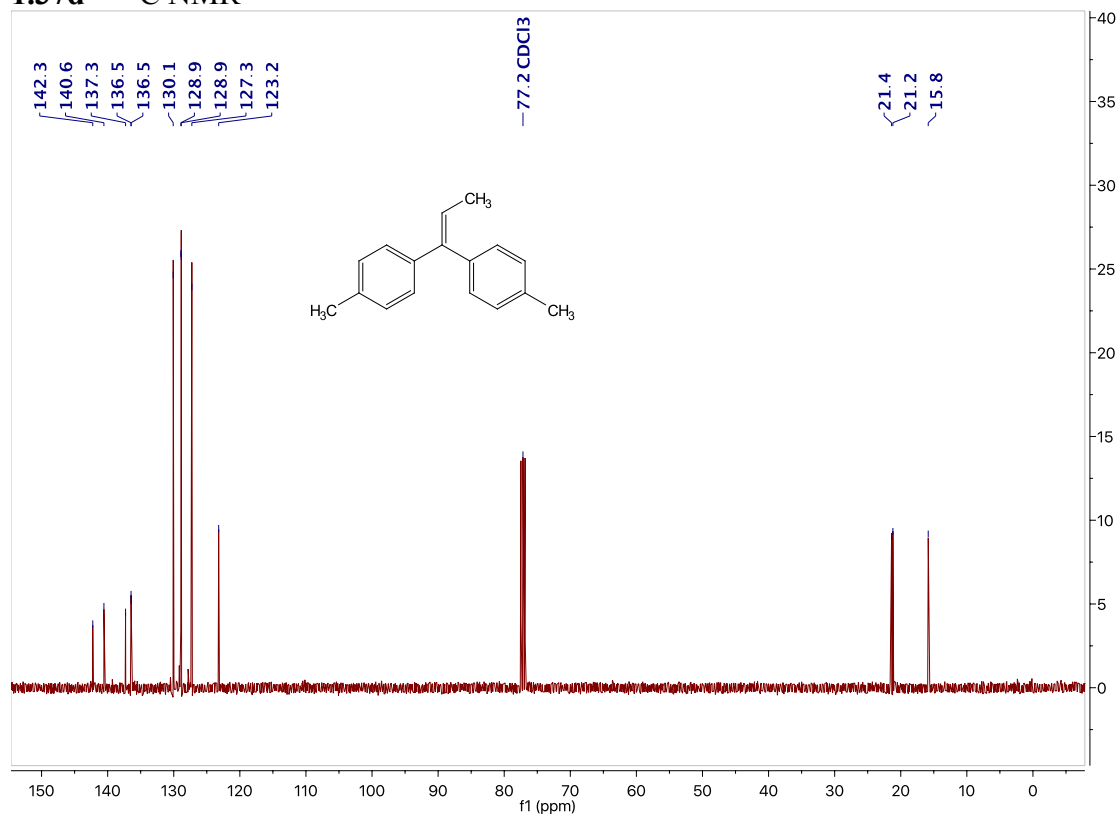
### 1.351 – nOe



### 1.37d – <sup>1</sup>H NMR

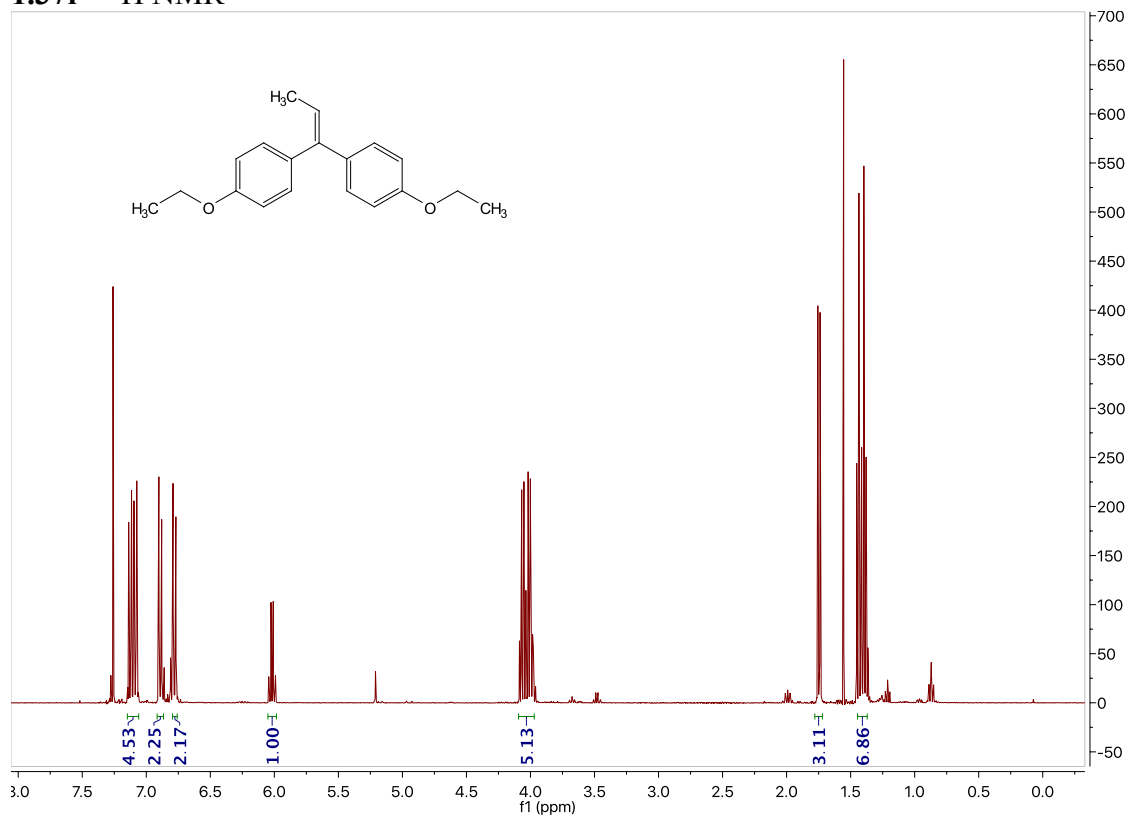


### 1.37d – <sup>13</sup>C NMR

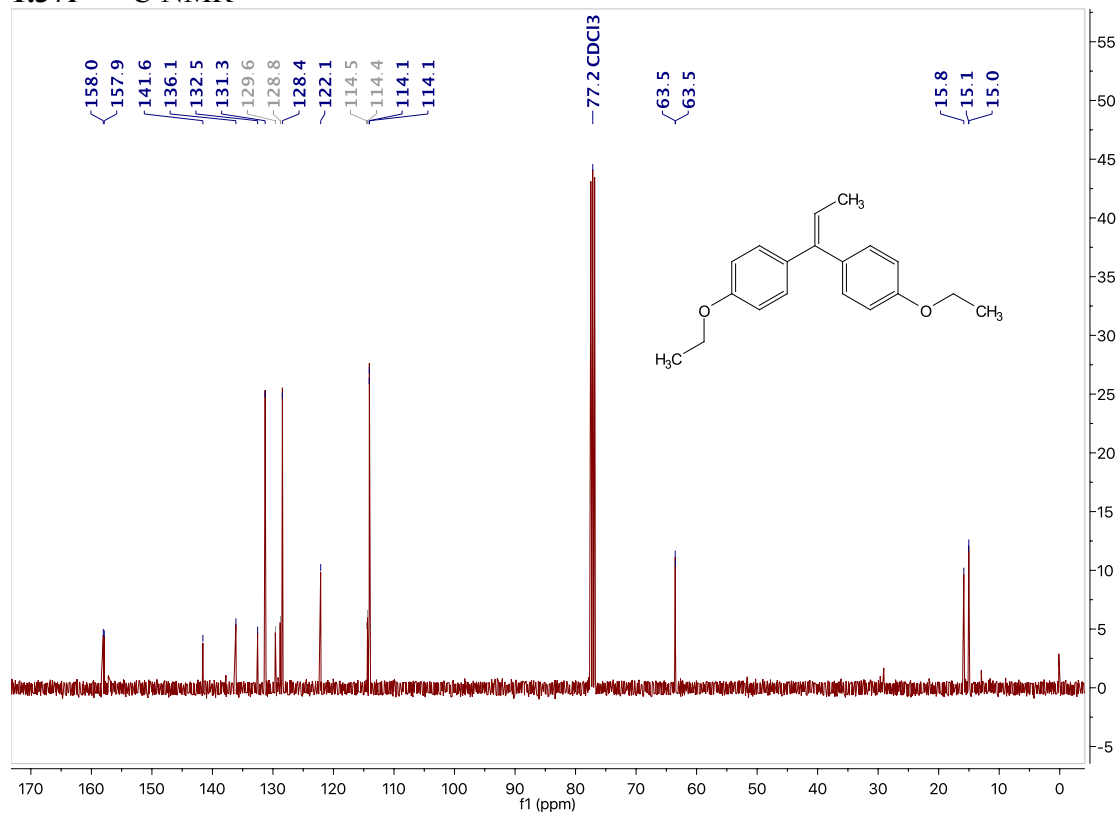




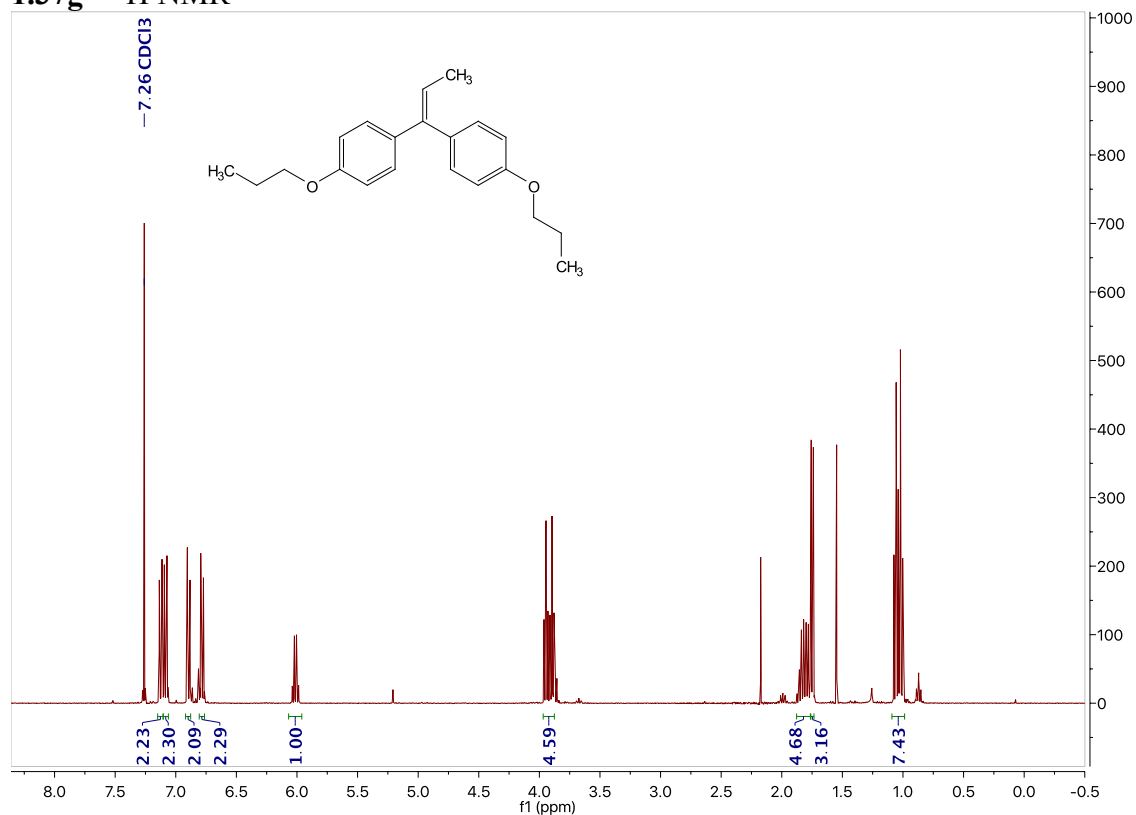
1.37f – <sup>1</sup>H NMR



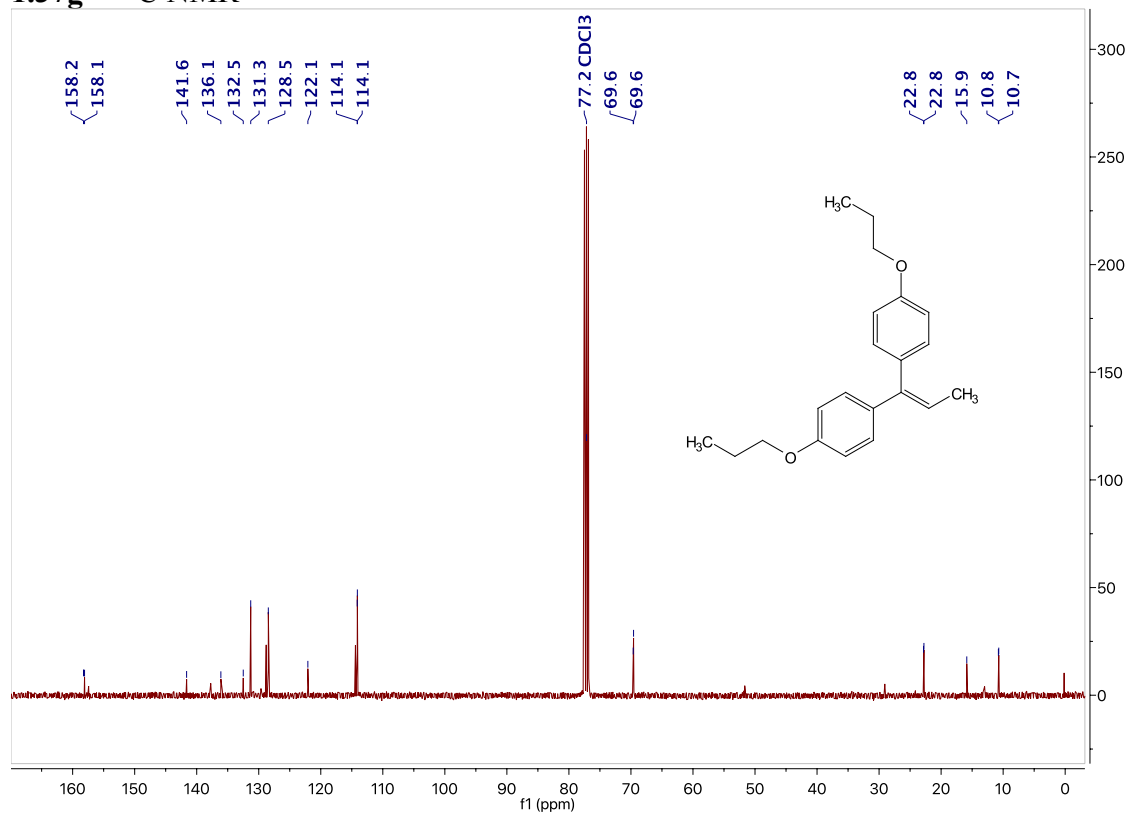
1.37f – <sup>13</sup>C NMR



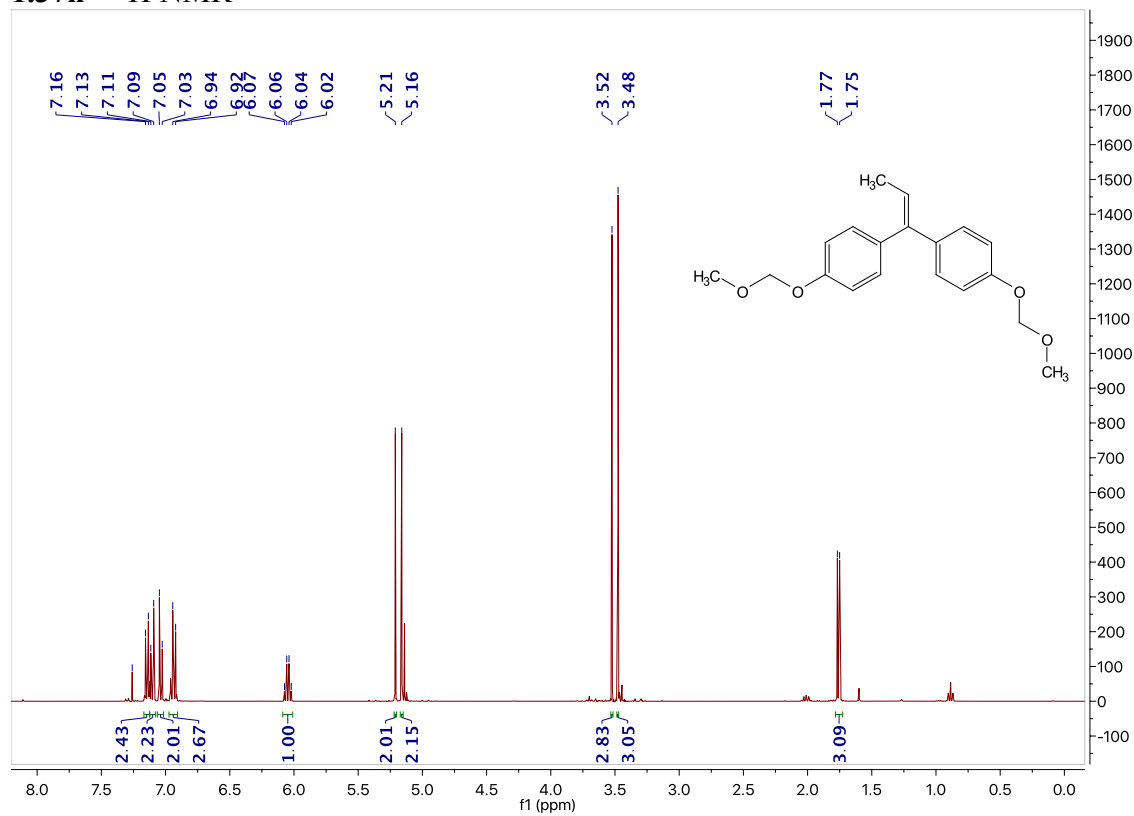
### 1.37g – <sup>1</sup>H NMR



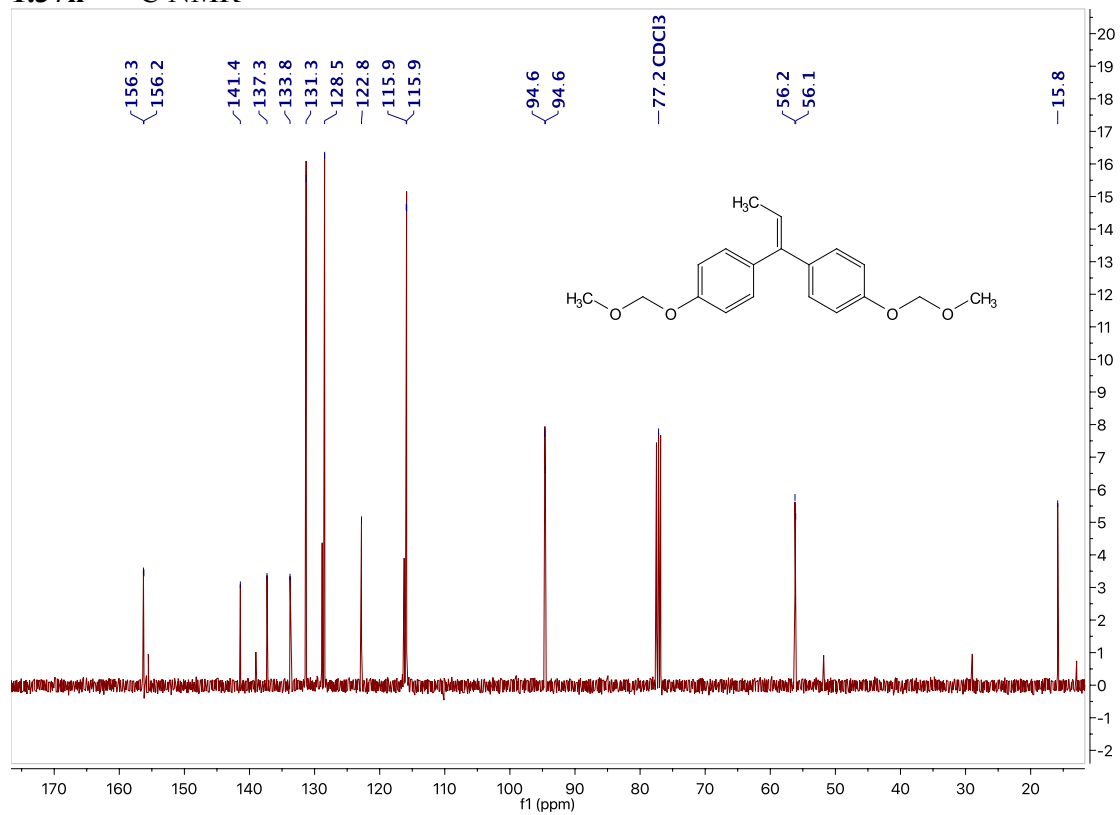
### 1.37g – <sup>13</sup>C NMR



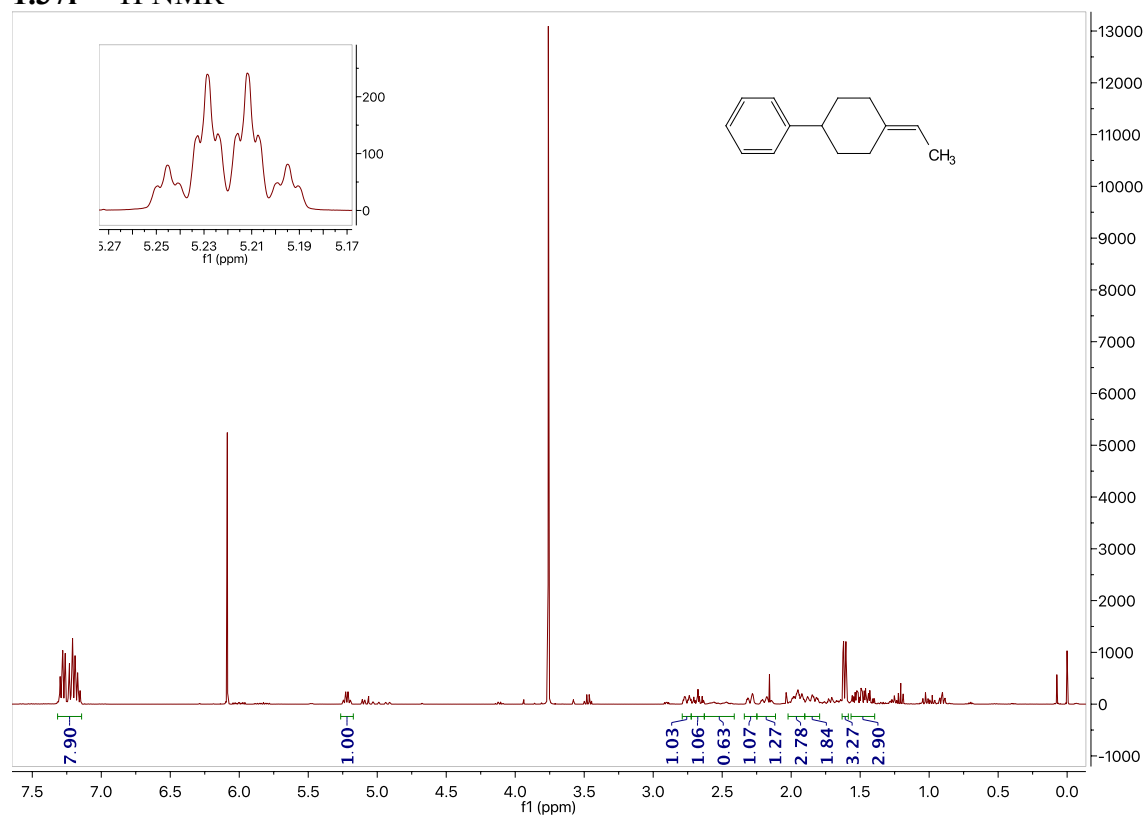
1.37h – <sup>1</sup>H NMR



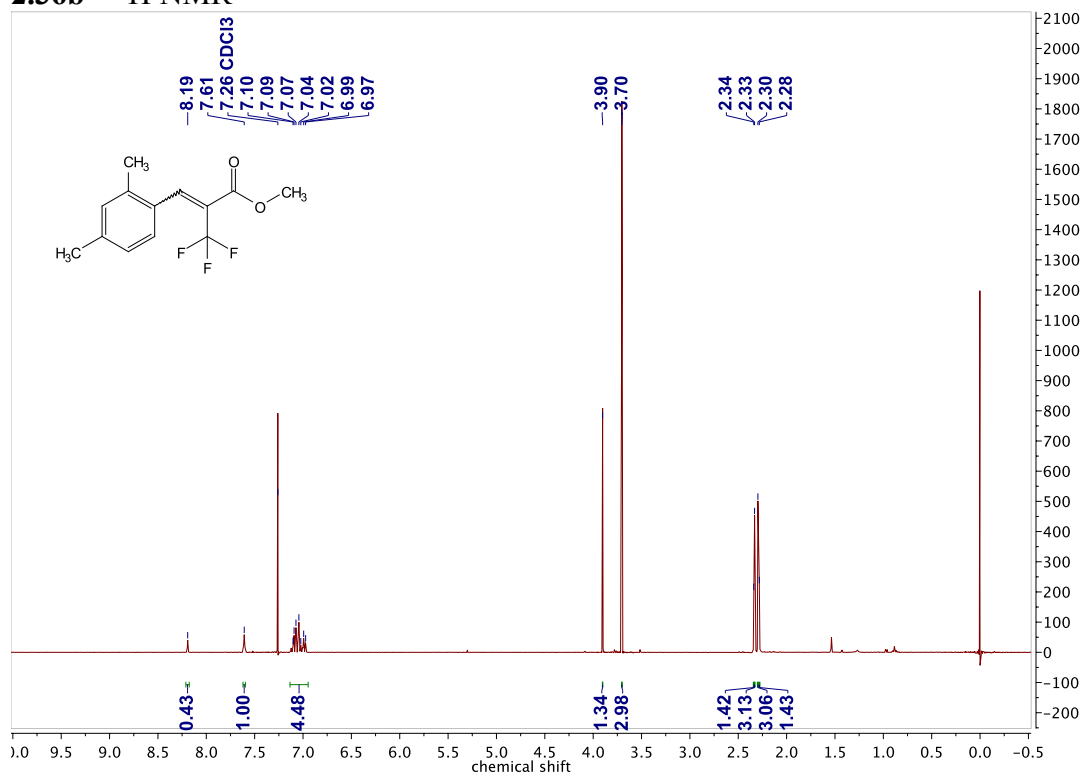
1.37h – <sup>13</sup>C NMR



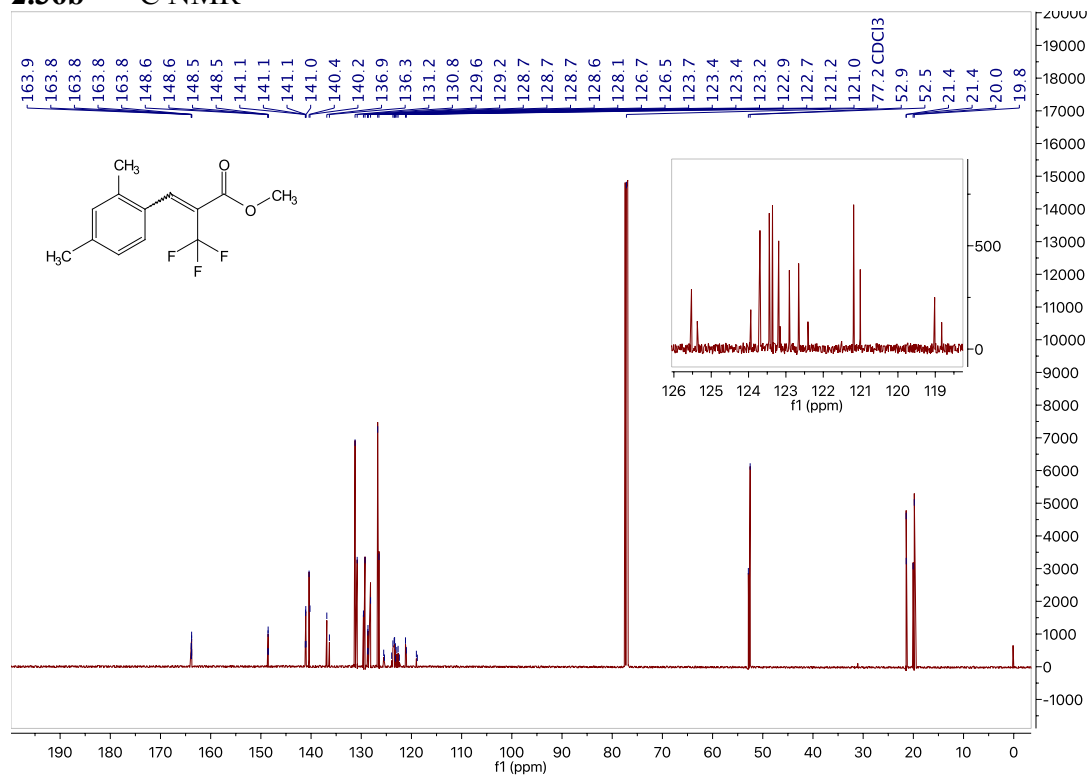
### 1.37i – $^1\text{H}$ NMR



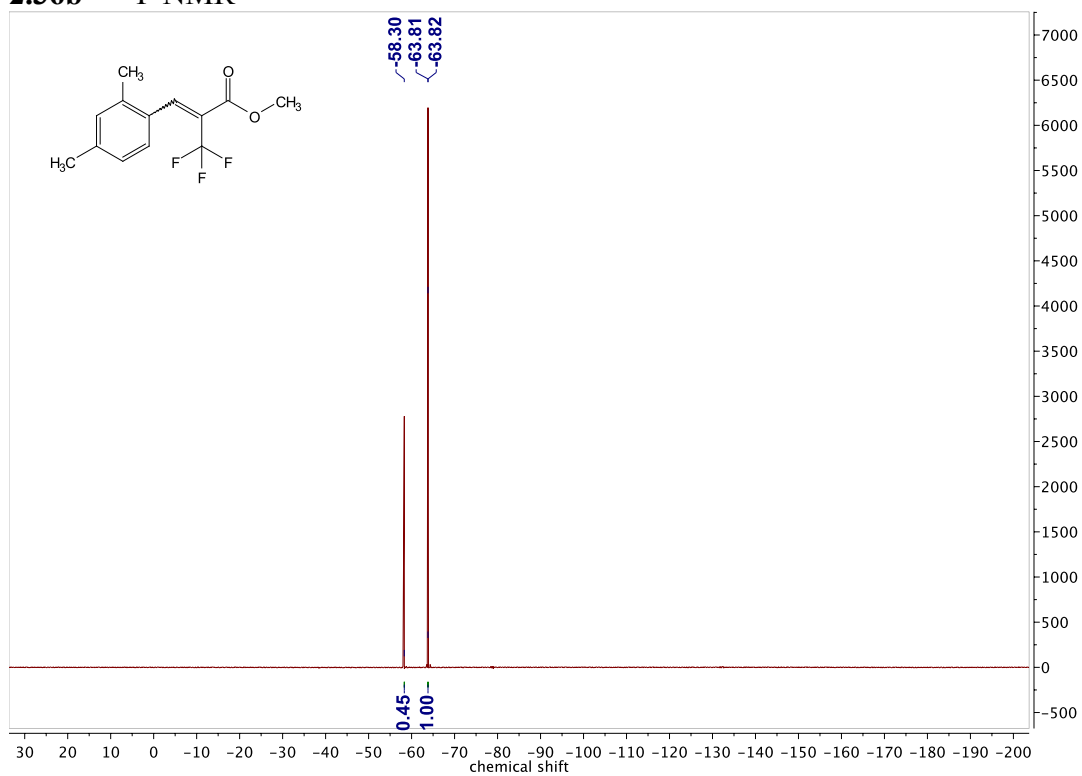
2.36b – <sup>1</sup>H NMR



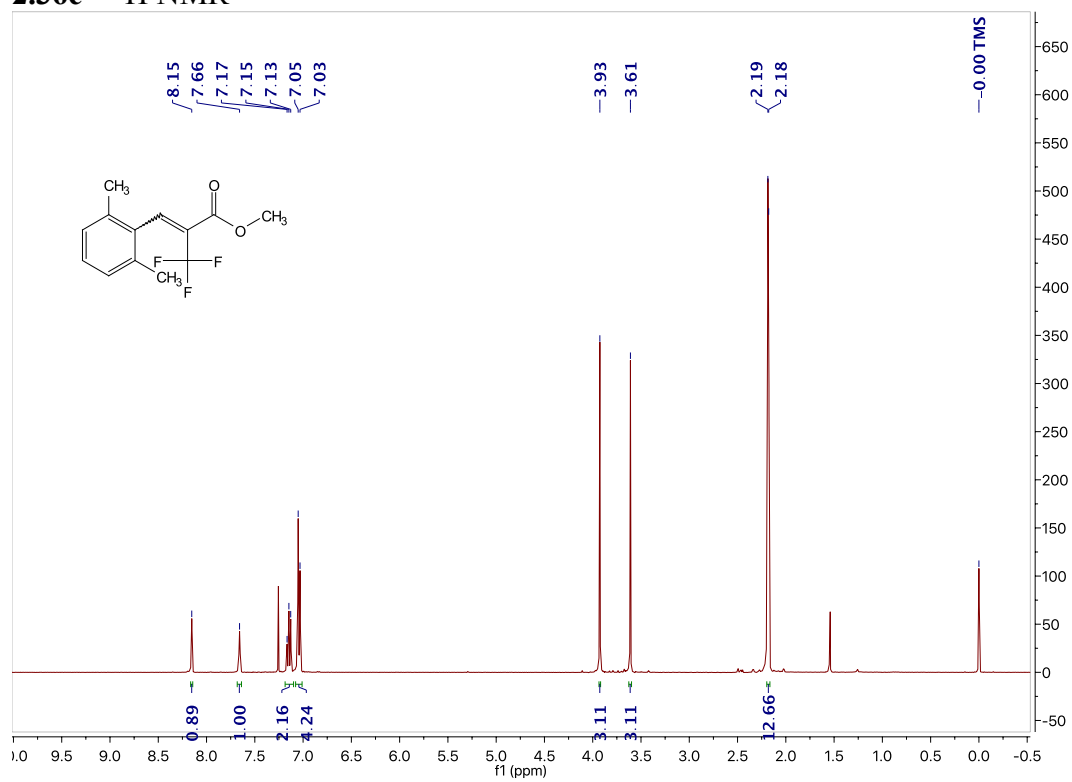
2.36b – <sup>13</sup>C NMR



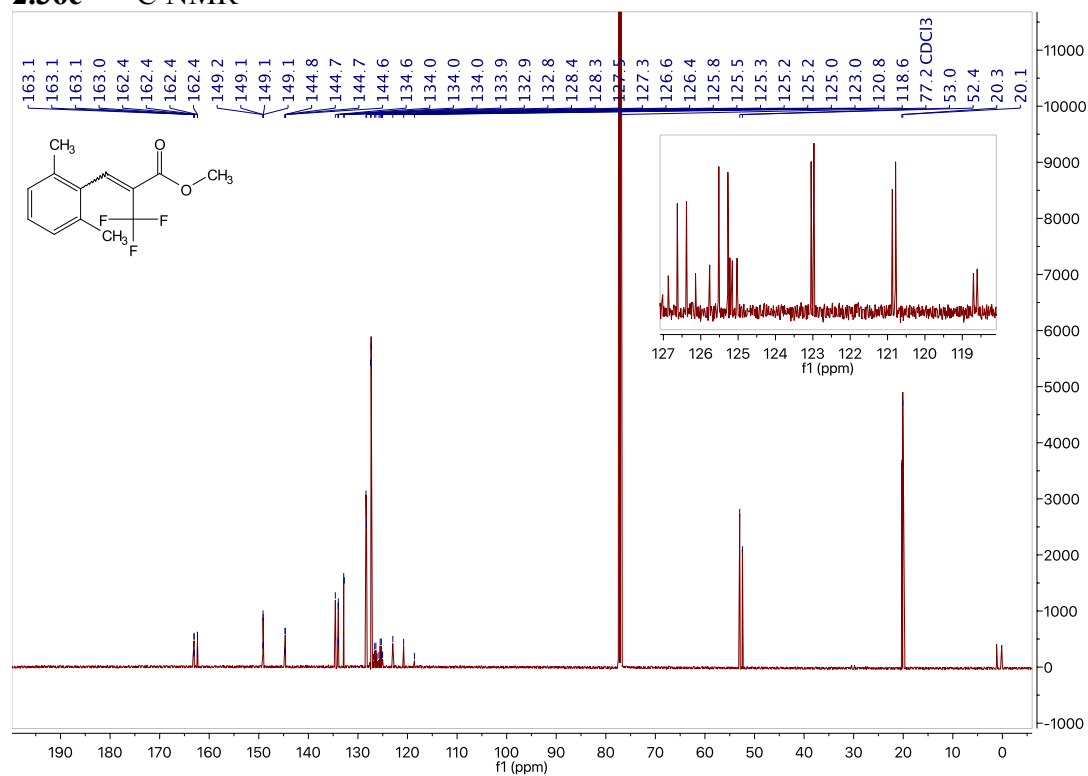
### 2.36b – <sup>19</sup>F NMR



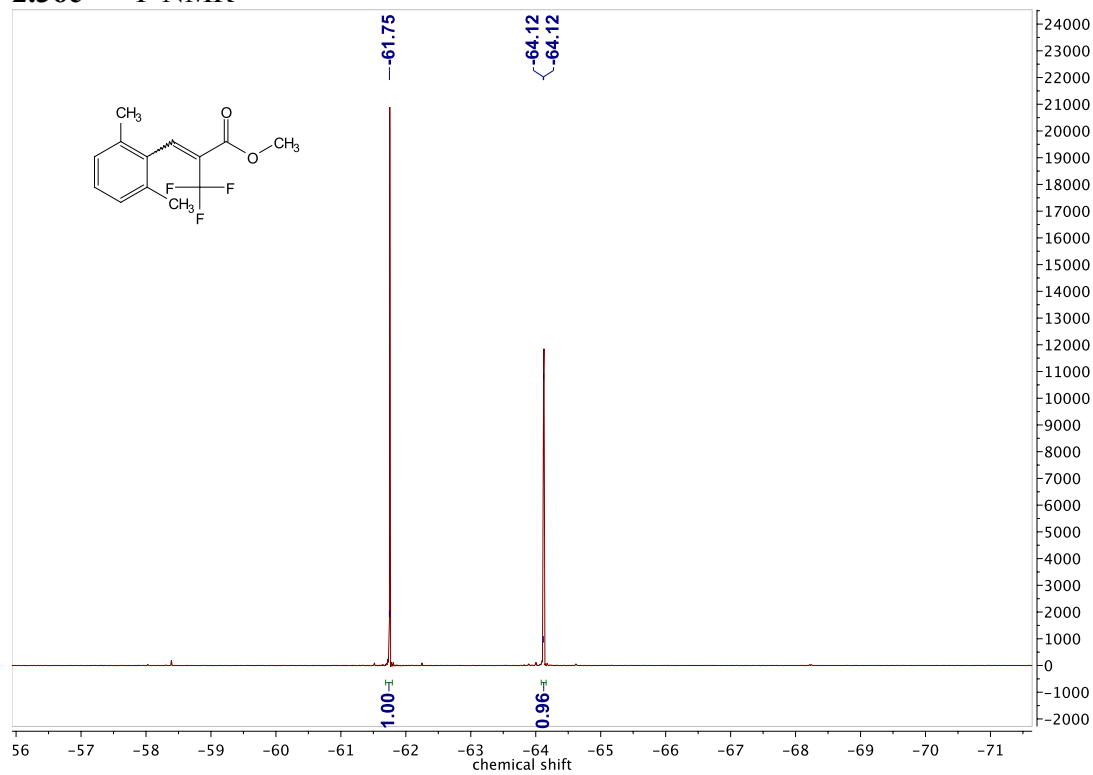
### 2.36c – <sup>1</sup>H NMR



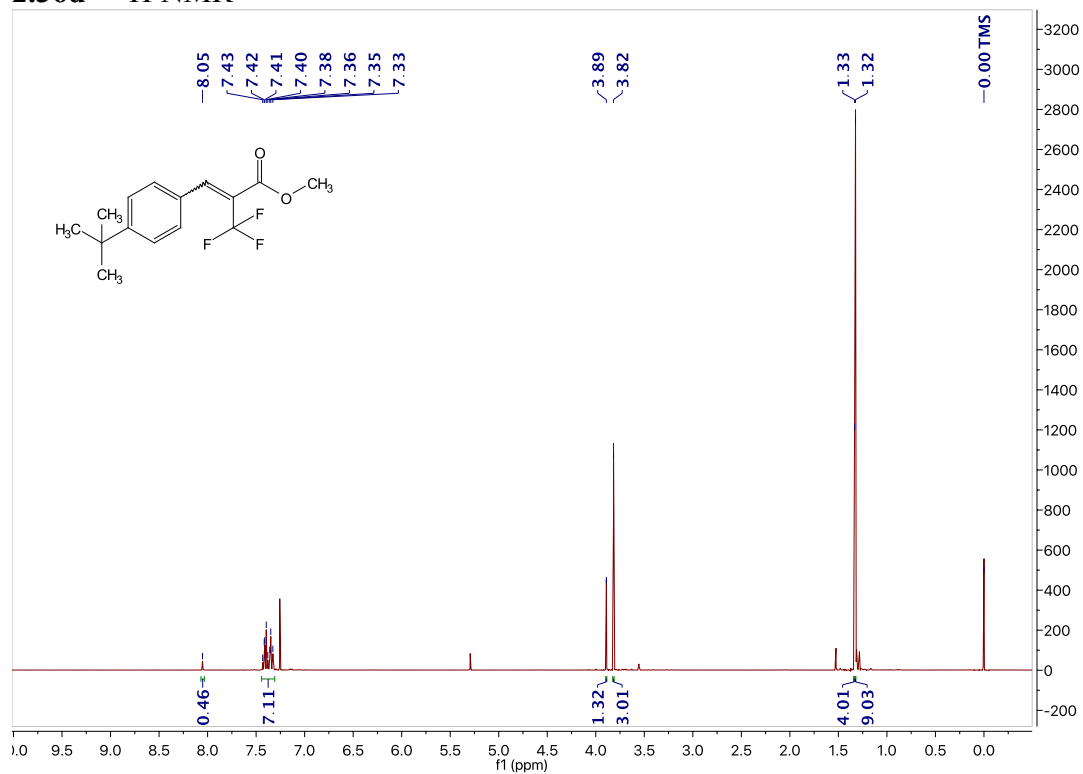
### 2.36c – <sup>13</sup>C NMR



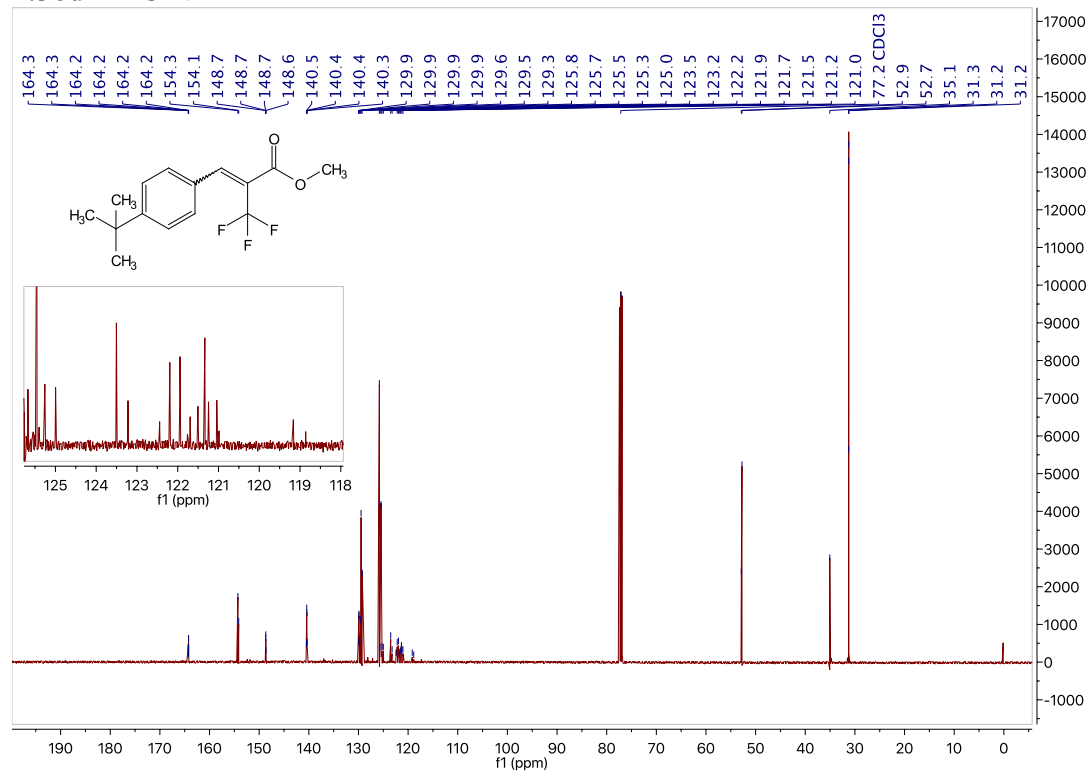
### 2.36c – <sup>19</sup>F NMR



## 2.36d – <sup>1</sup>H NMR

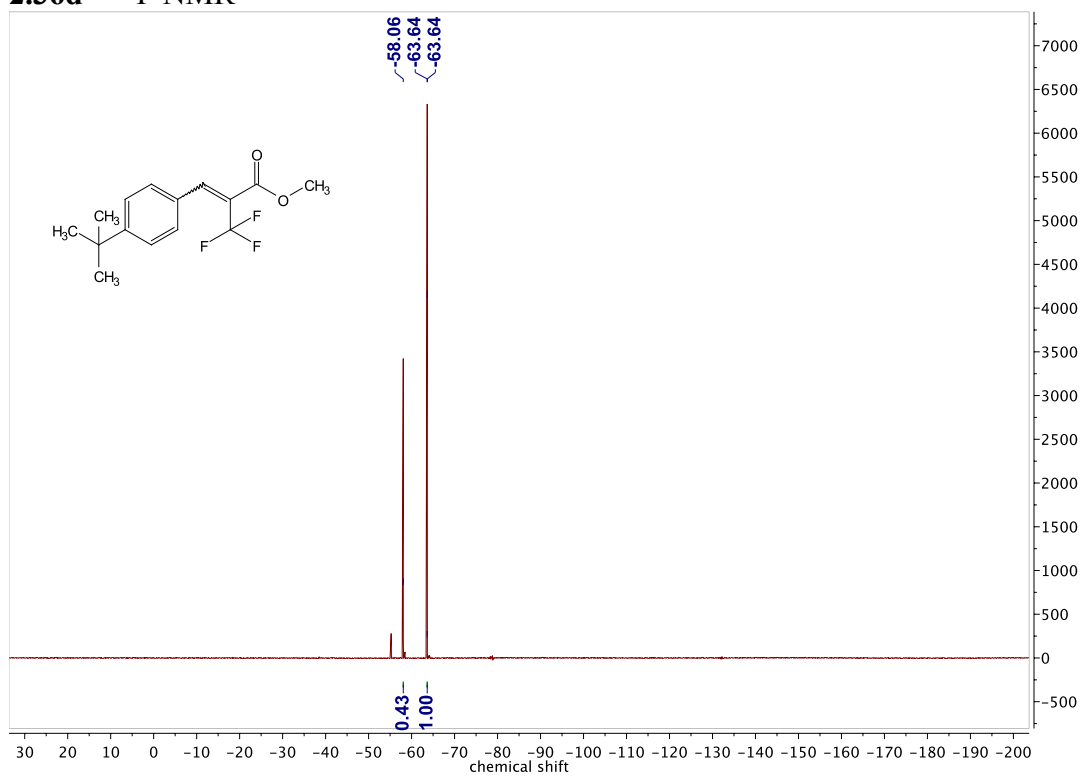


## 2.36d – <sup>13</sup>C NMR

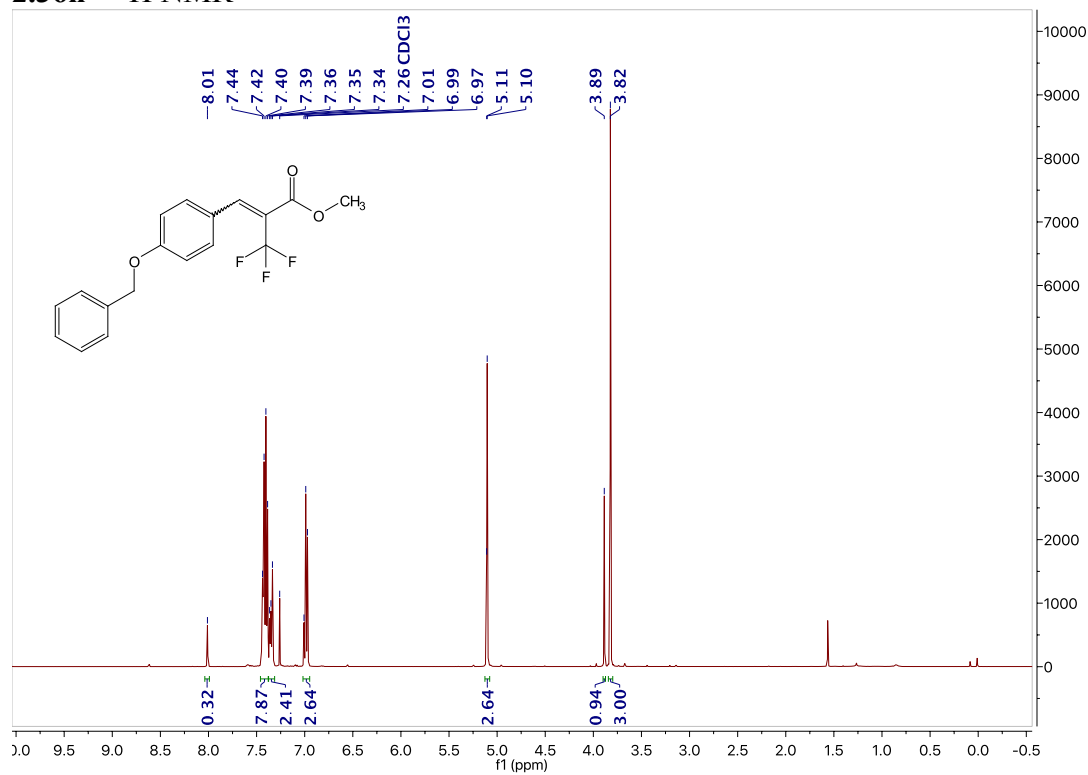




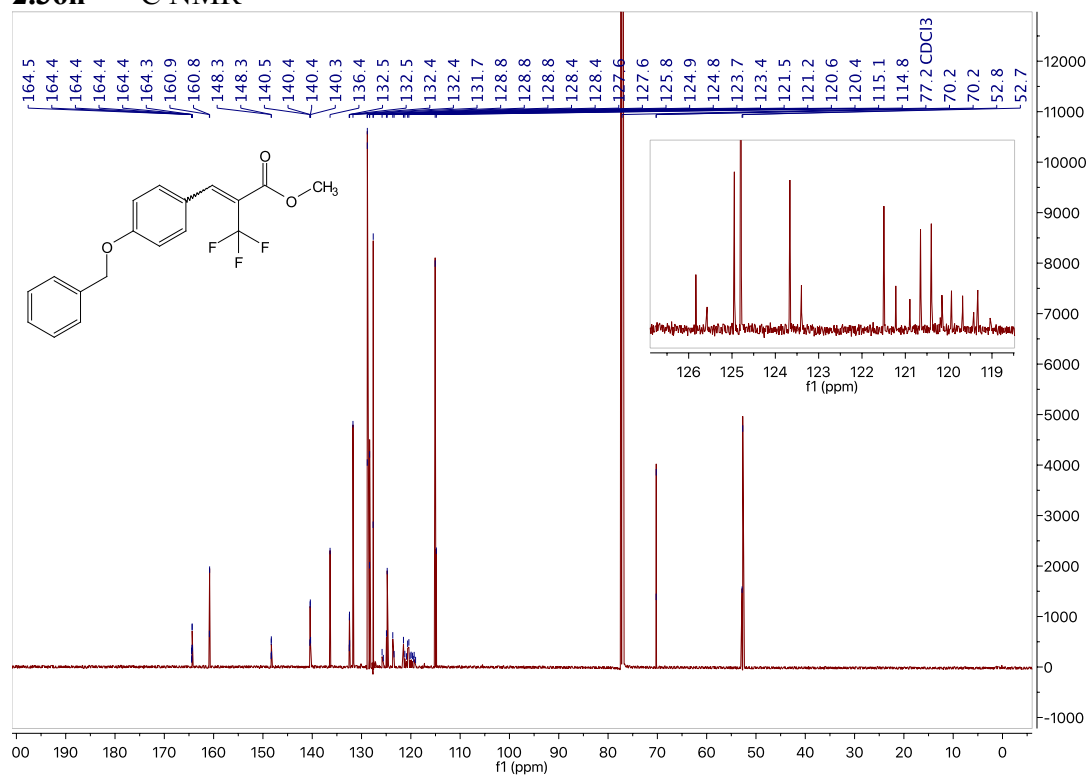
### 2.36d – <sup>19</sup>F NMR



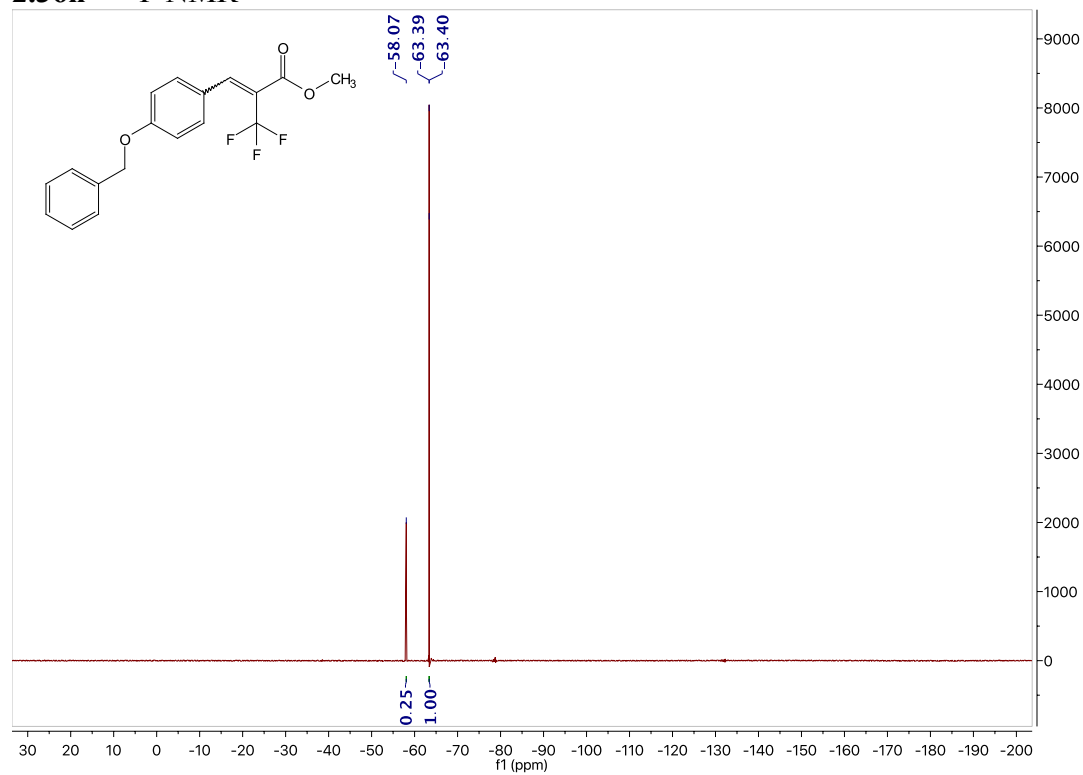
### 2.36h – <sup>1</sup>H NMR



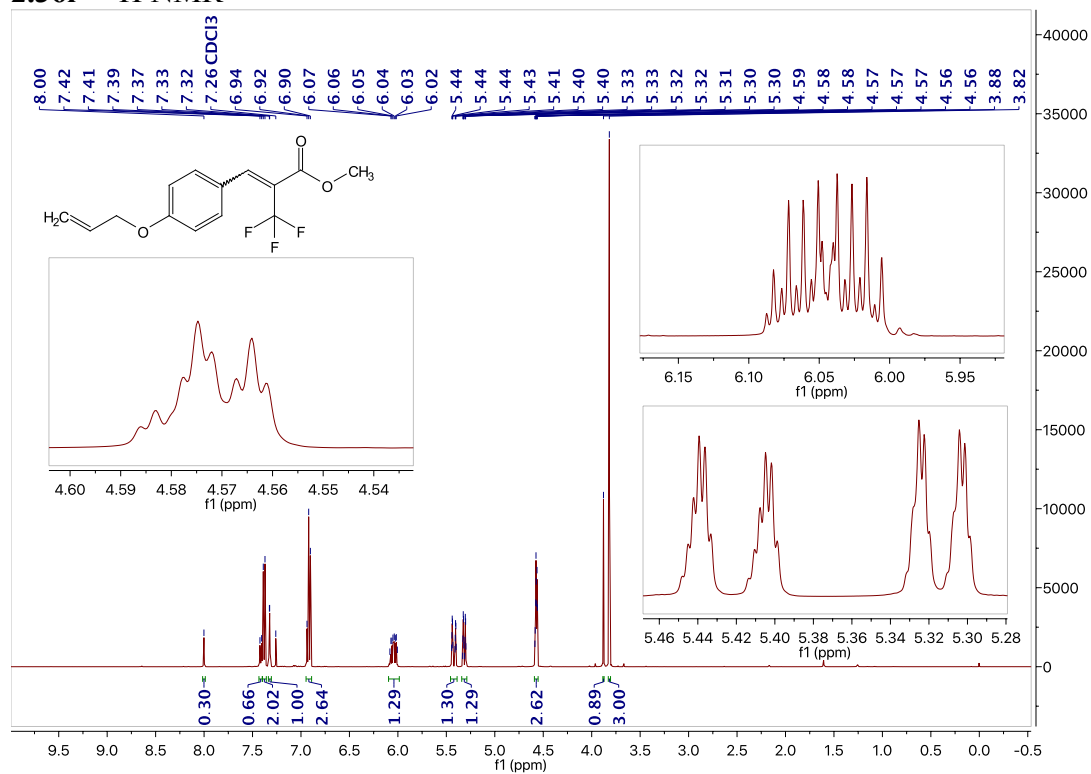
2.36h – <sup>13</sup>C NMR



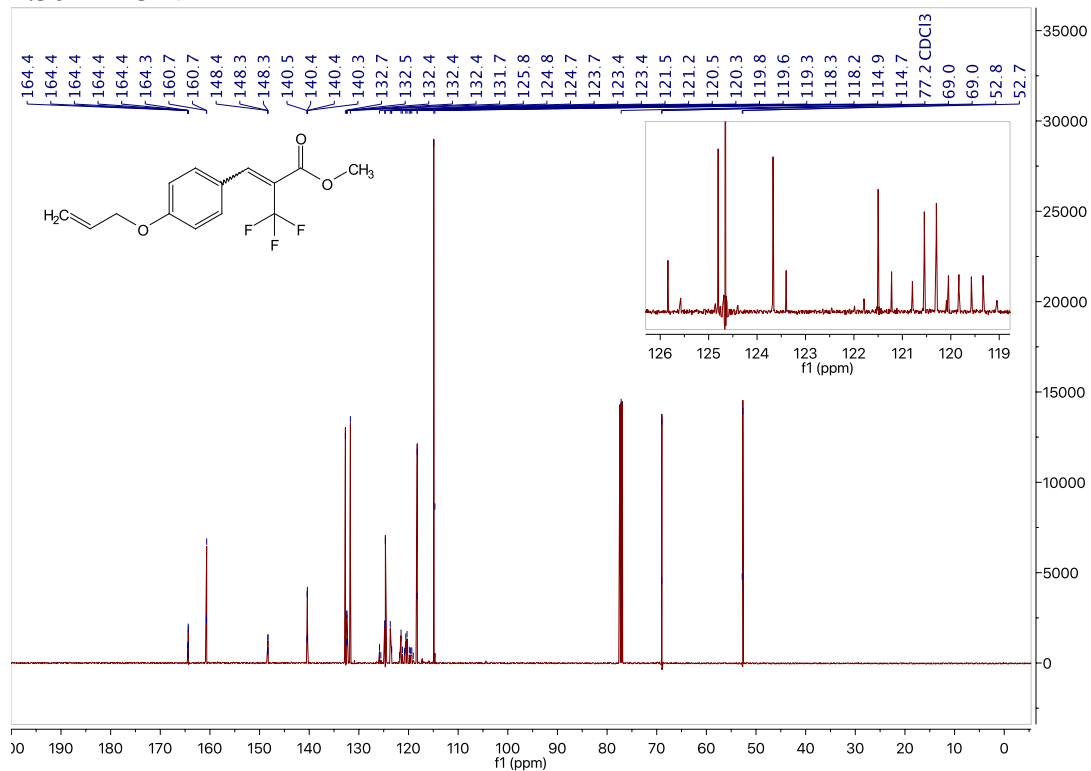
2.36h – <sup>19</sup>F NMR



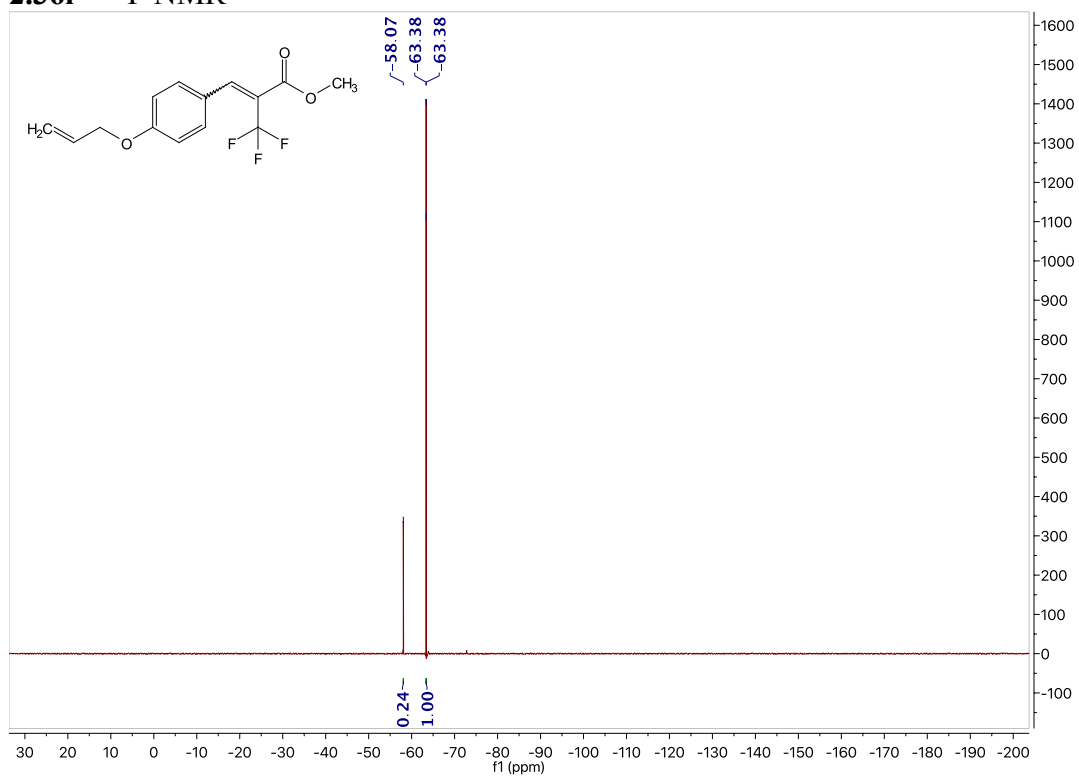
### 2.36i – <sup>1</sup>H NMR



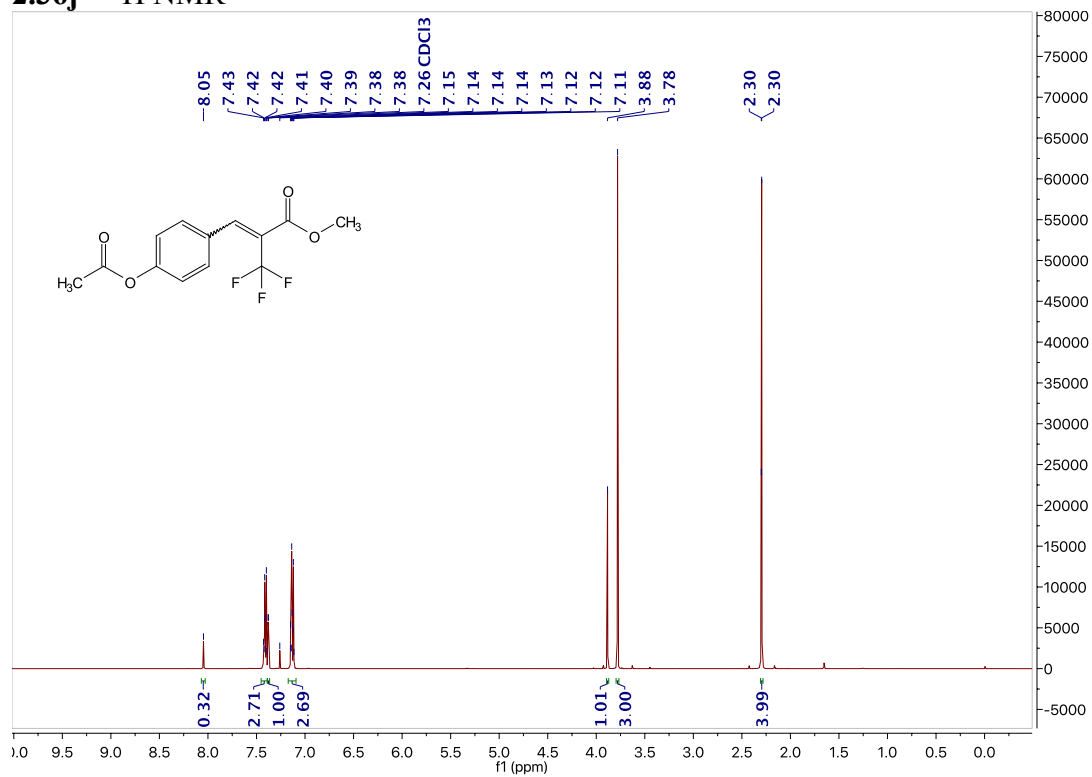
### 2.36i – <sup>13</sup>C NMR



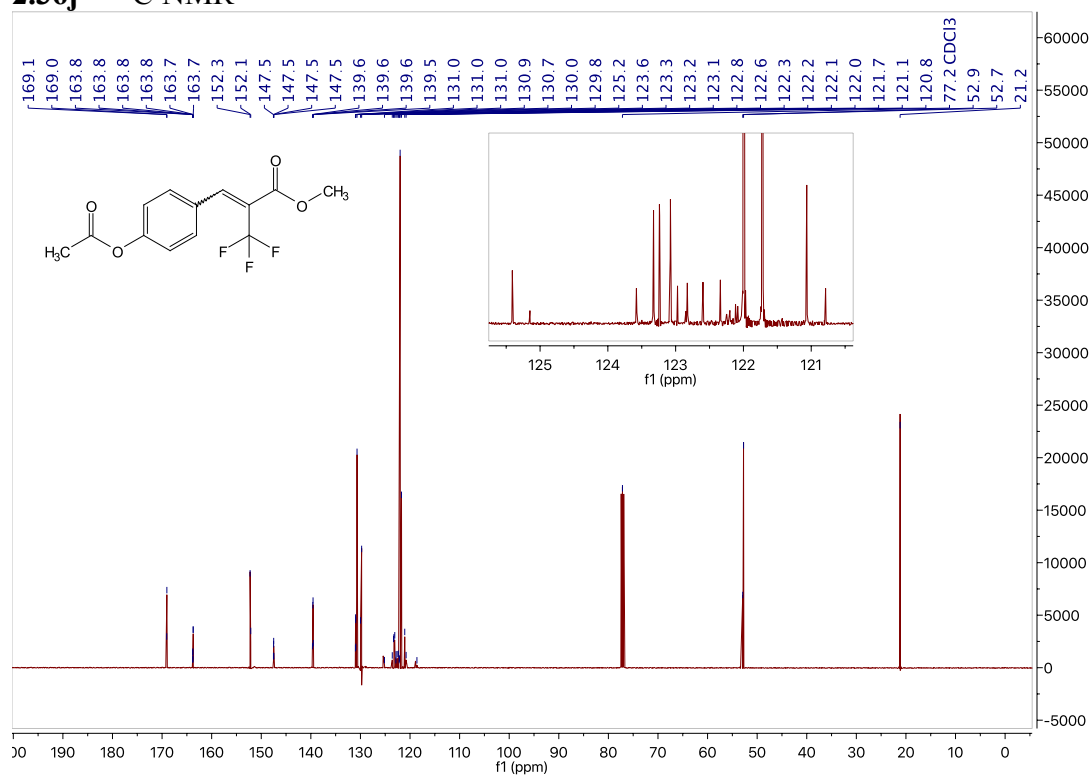
### 2.36i – <sup>19</sup>F NMR



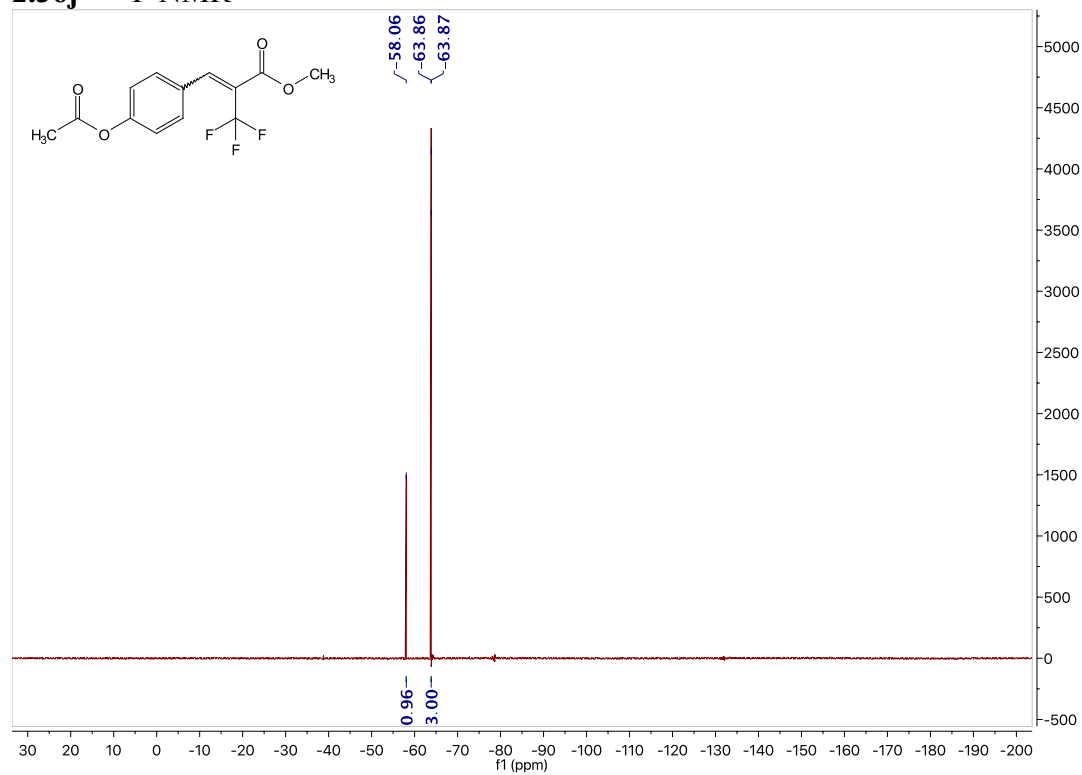
### 2.36j – <sup>1</sup>H NMR



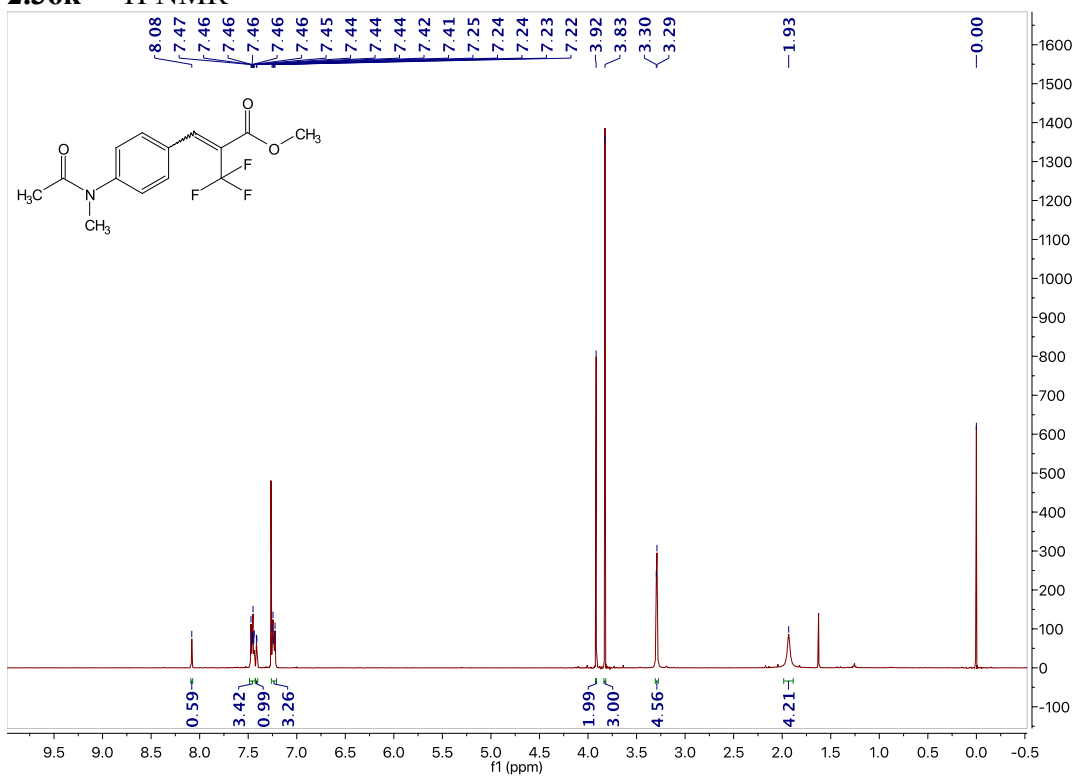
### 2.36j – <sup>13</sup>C NMR



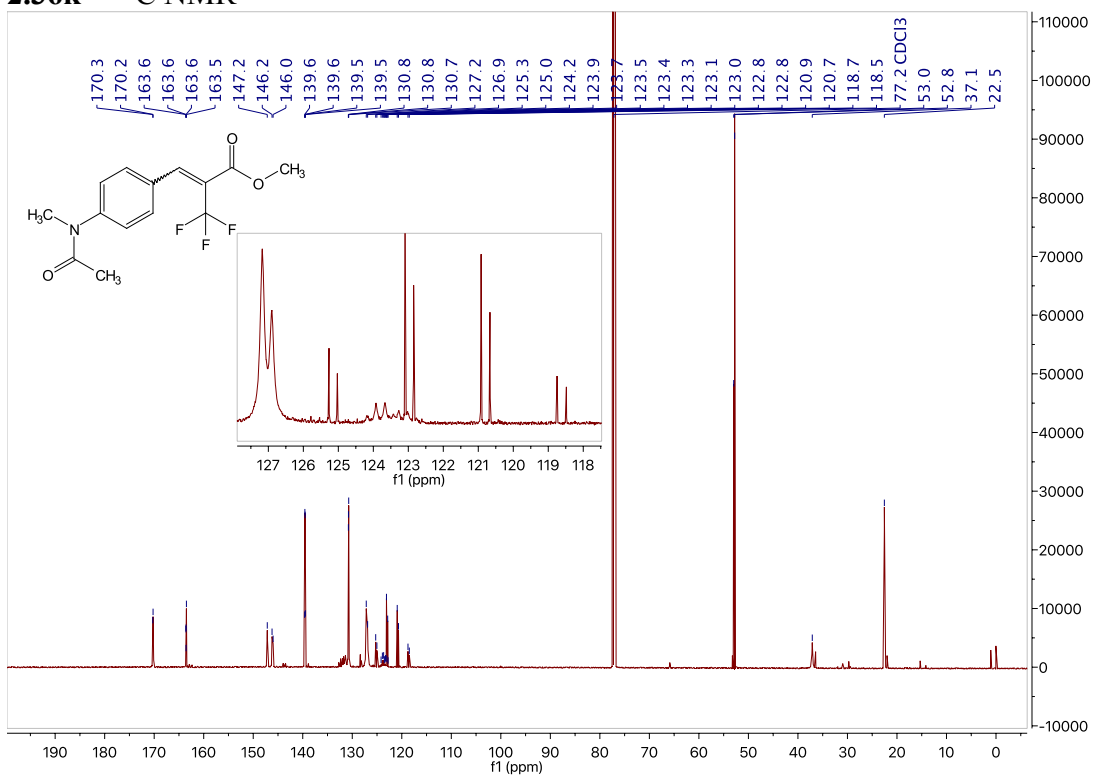
### 2.36j – <sup>19</sup>F NMR



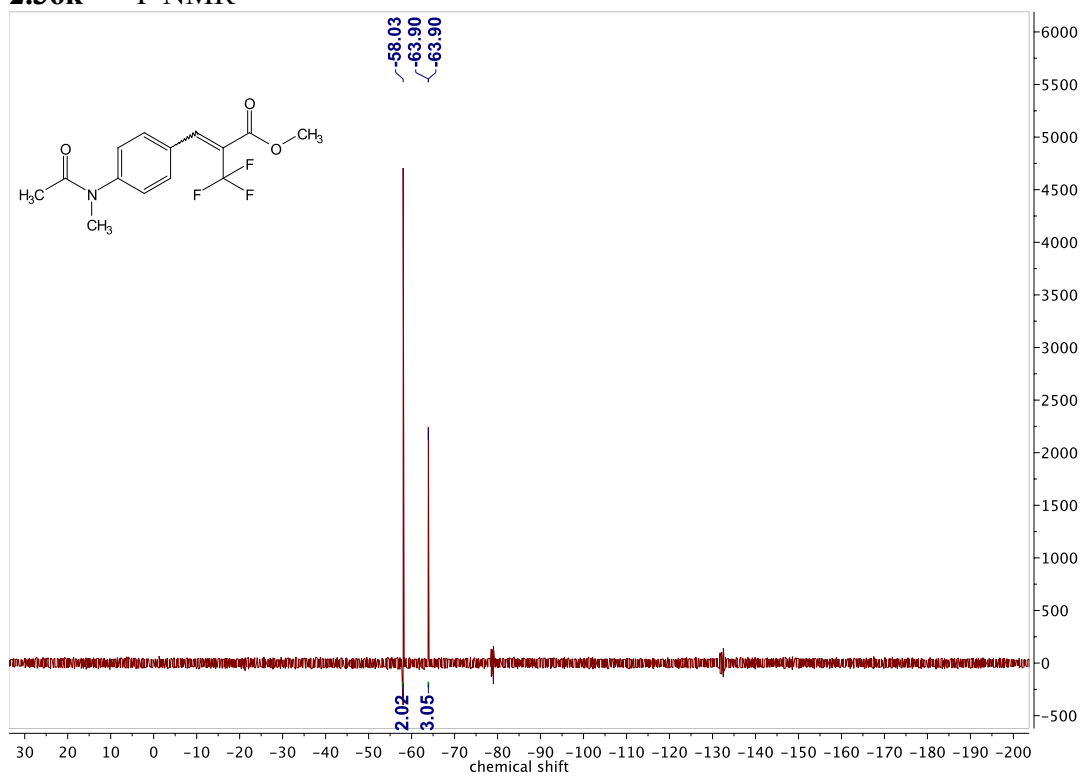
2.36k – <sup>1</sup>H NMR



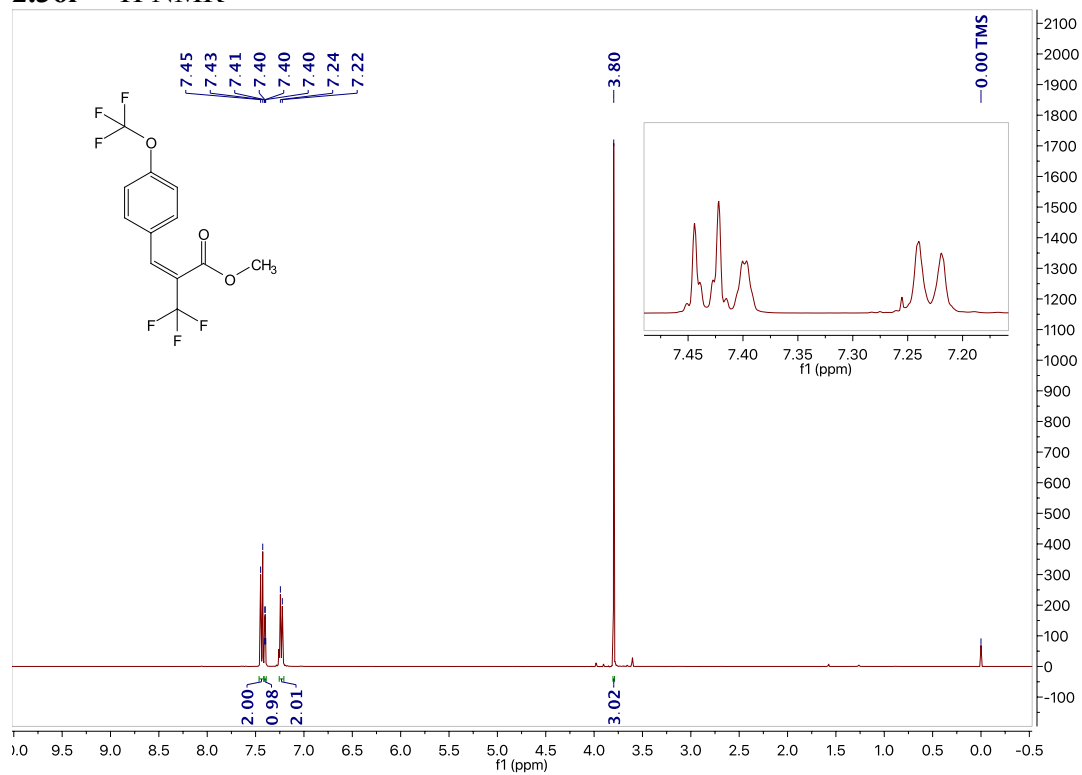
2.36k – <sup>13</sup>C NMR



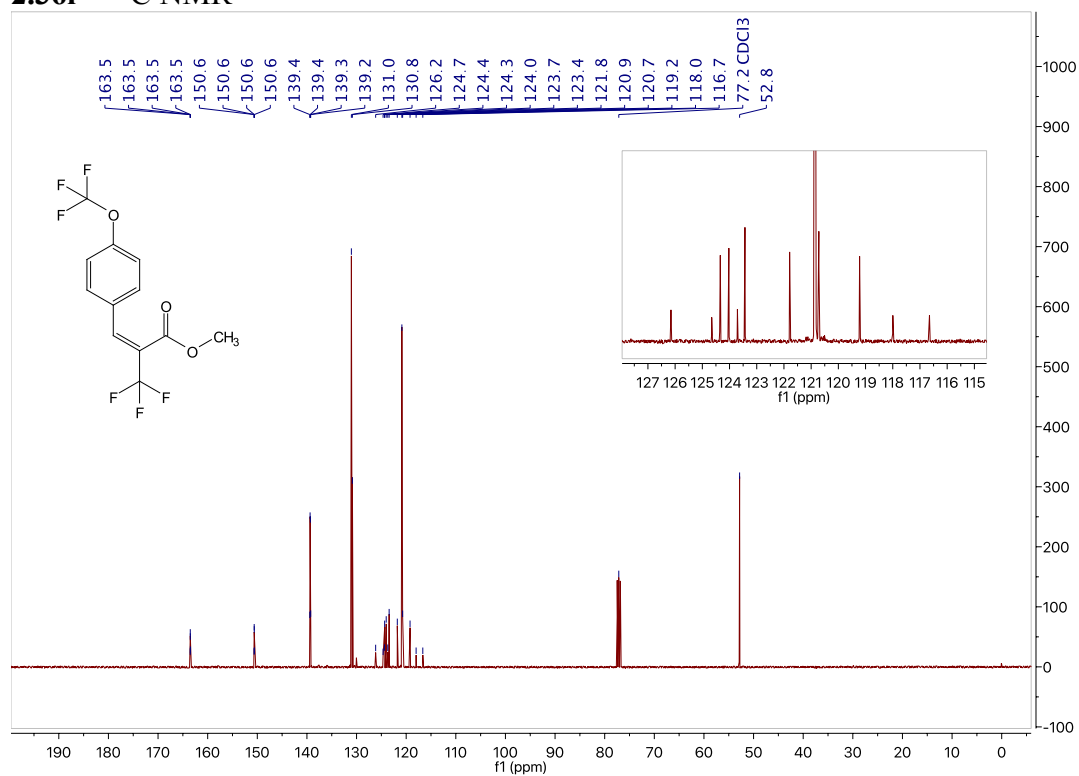
### 2.36k – <sup>19</sup>F NMR



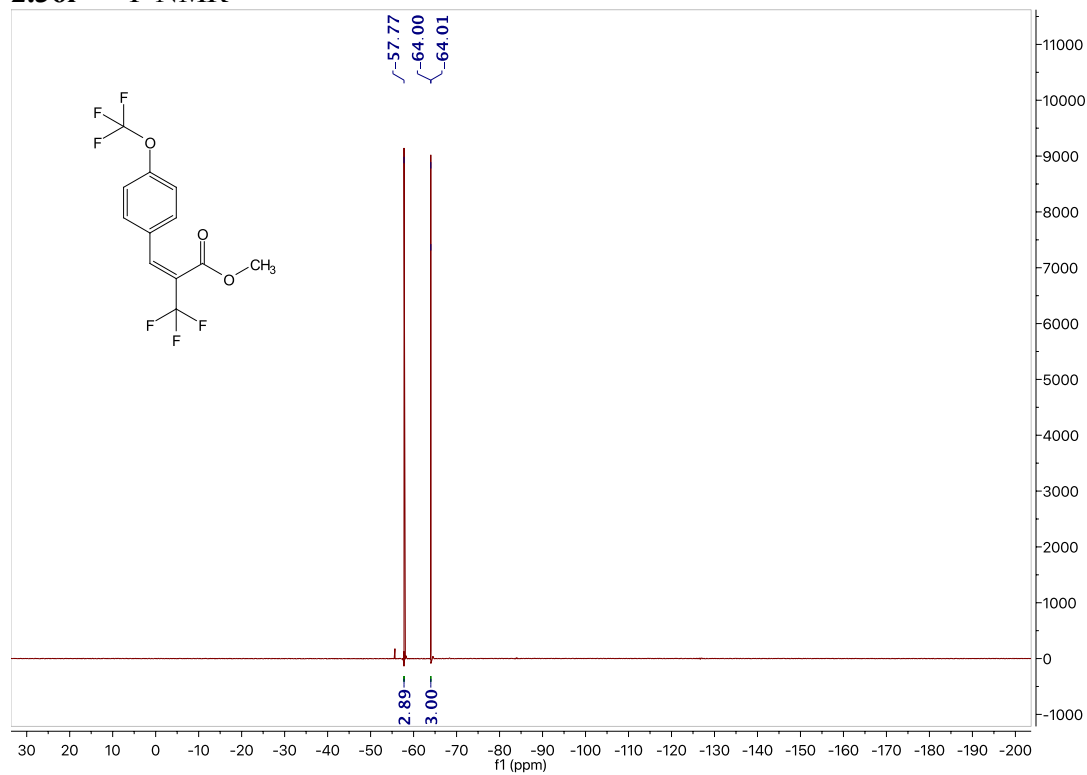
### 2.36l – <sup>1</sup>H NMR



### 2.361 – <sup>13</sup>C NMR

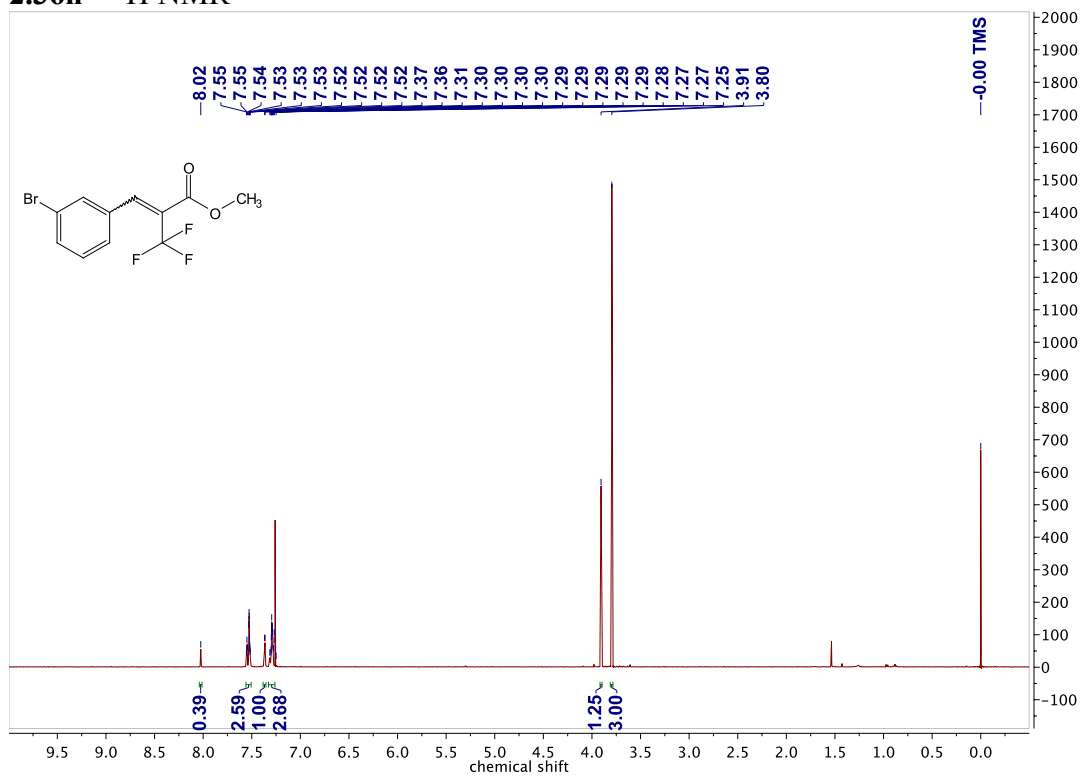


### 2.361 – <sup>19</sup>F NMR

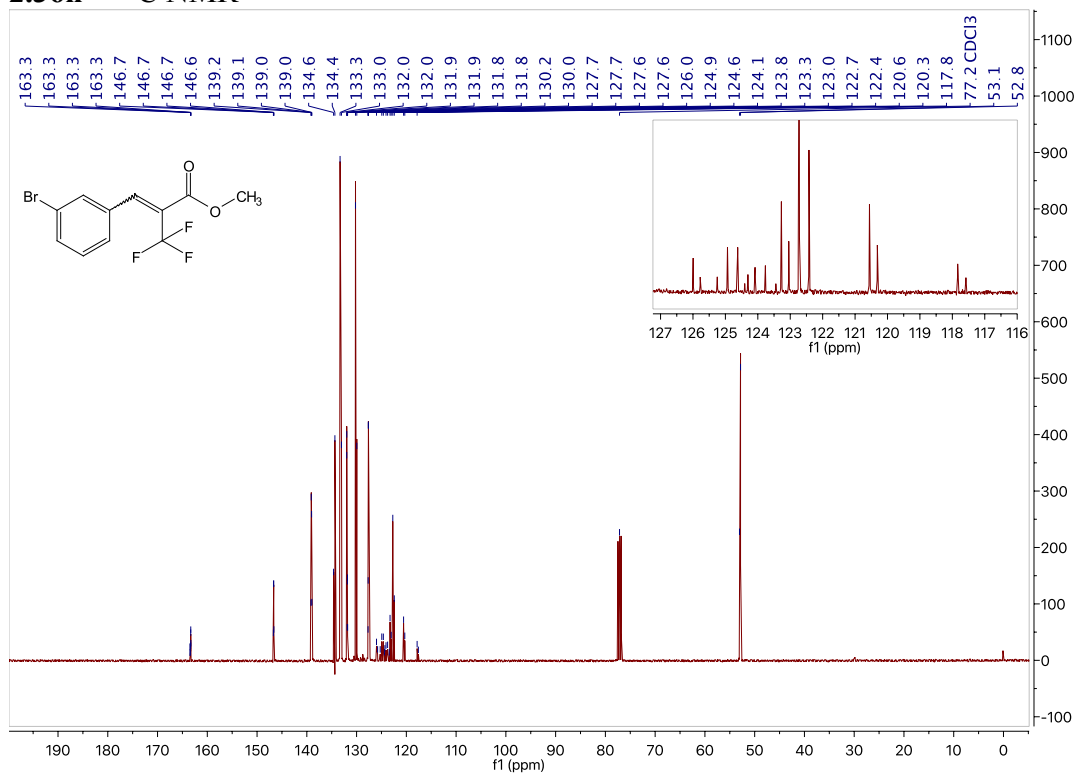




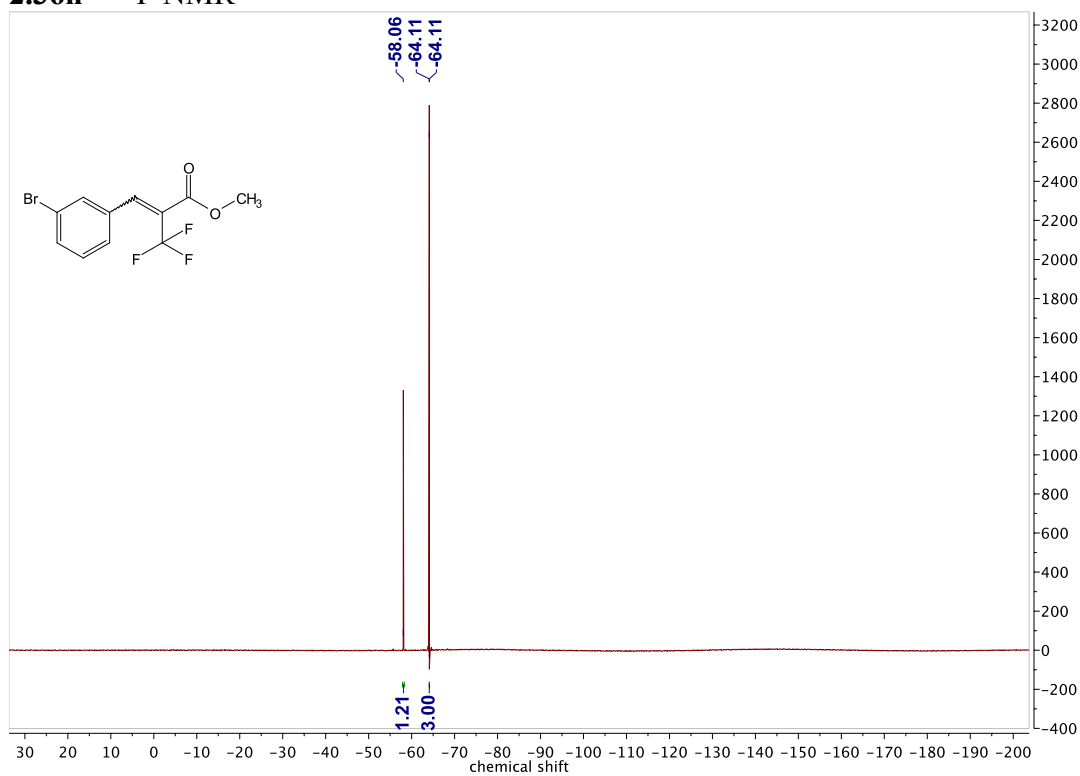
### 2.36n – <sup>1</sup>H NMR



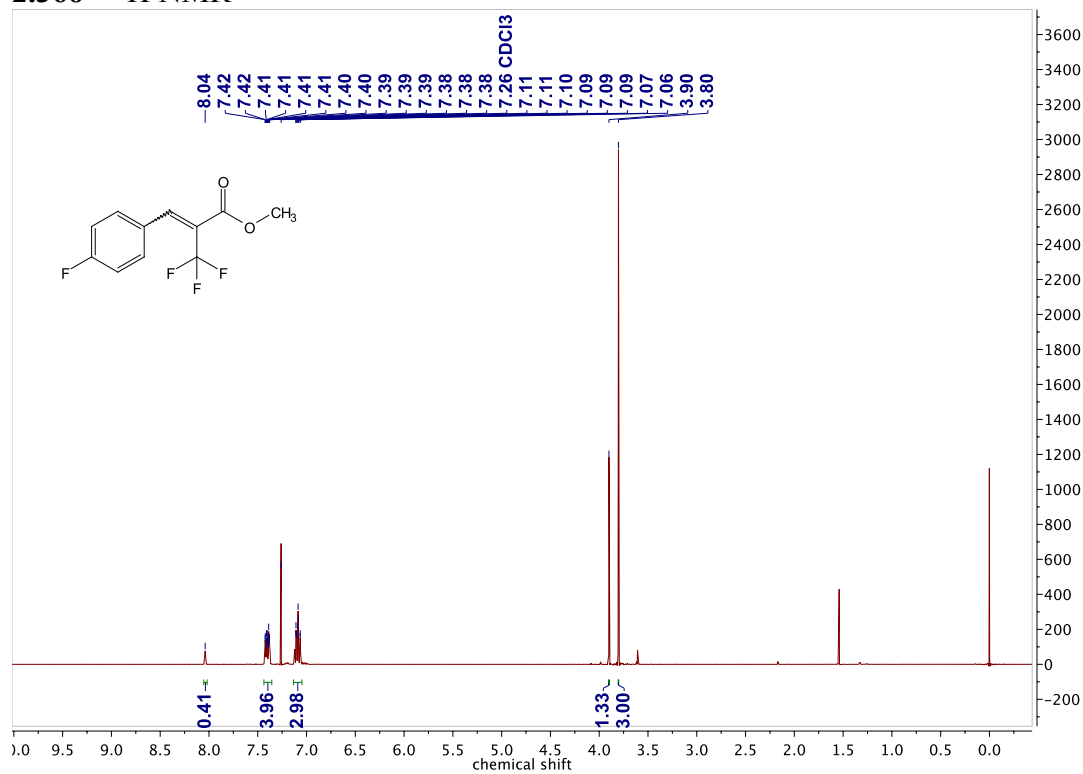
### 2.36n – <sup>13</sup>C NMR



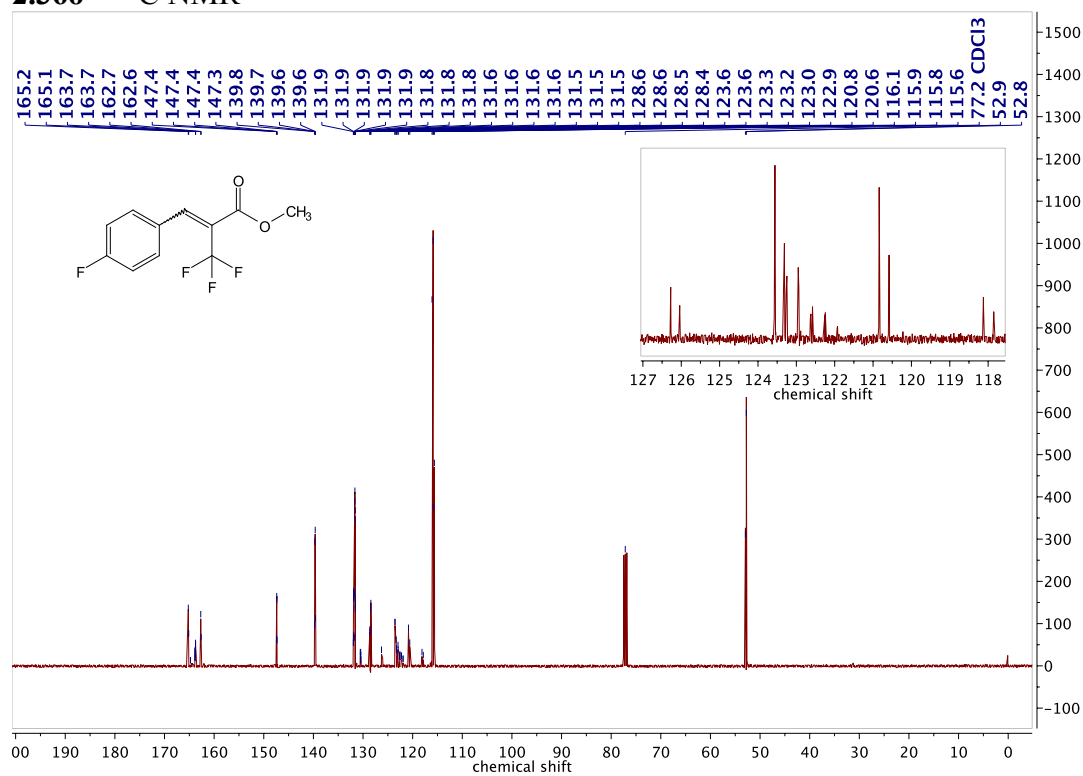
### 2.36n – <sup>19</sup>F NMR



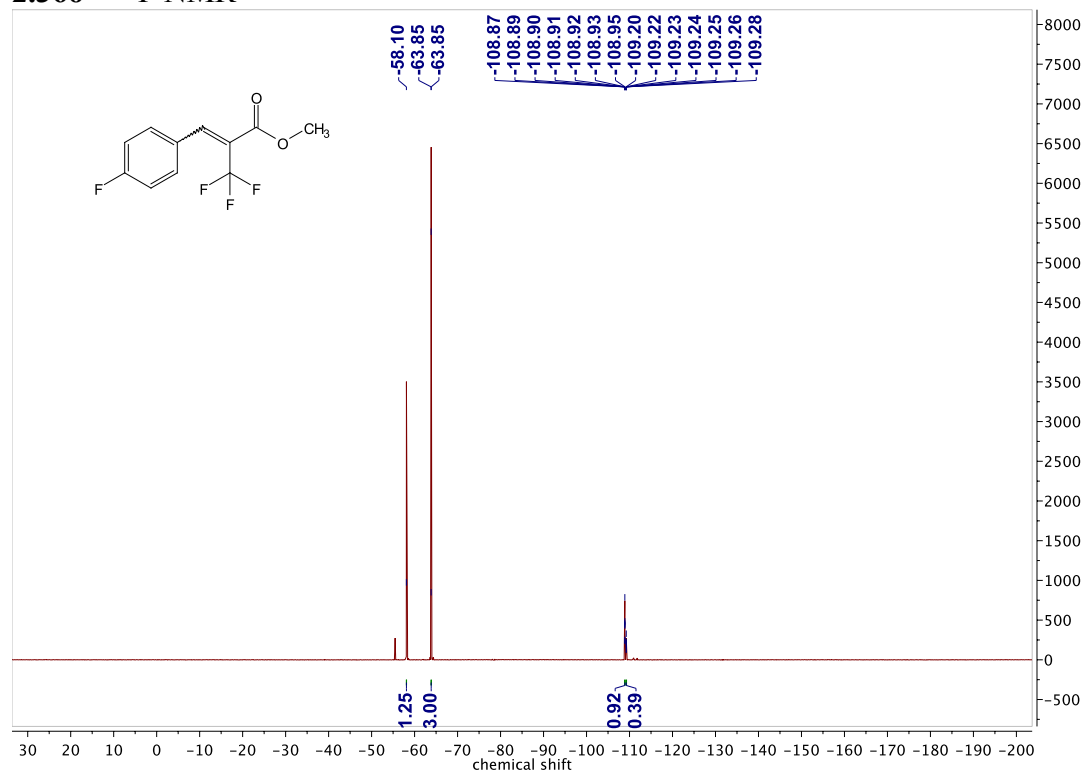
### 2.36o – <sup>1</sup>H NMR



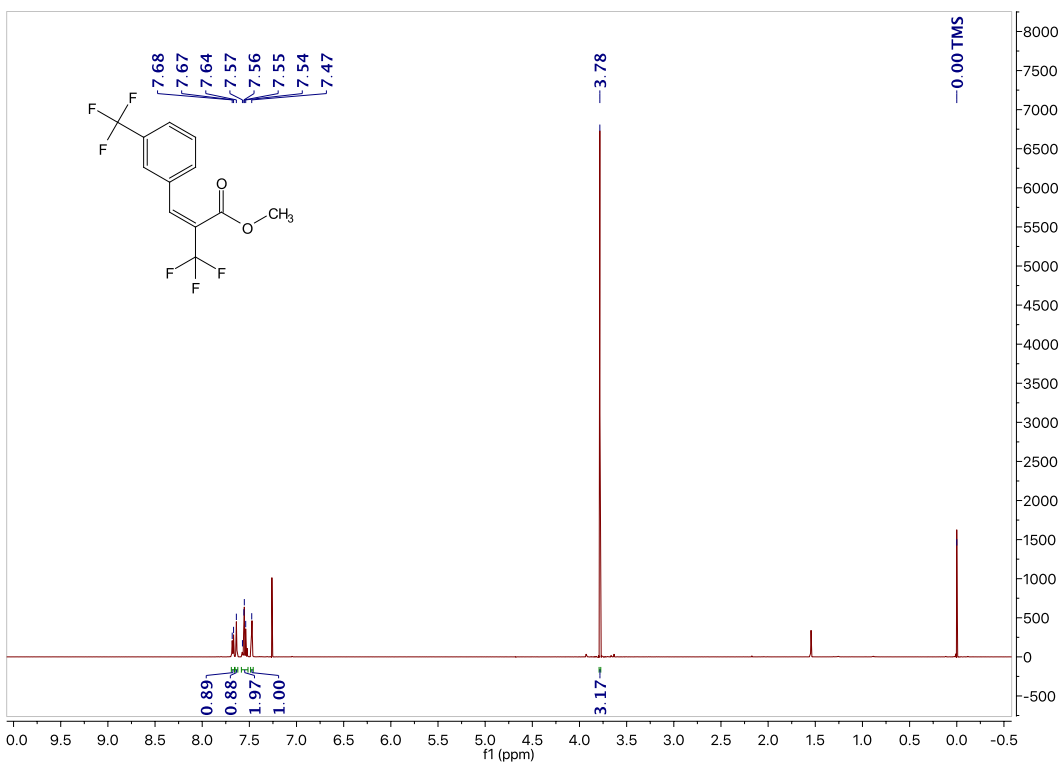
### 2.360 – <sup>13</sup>C NMR



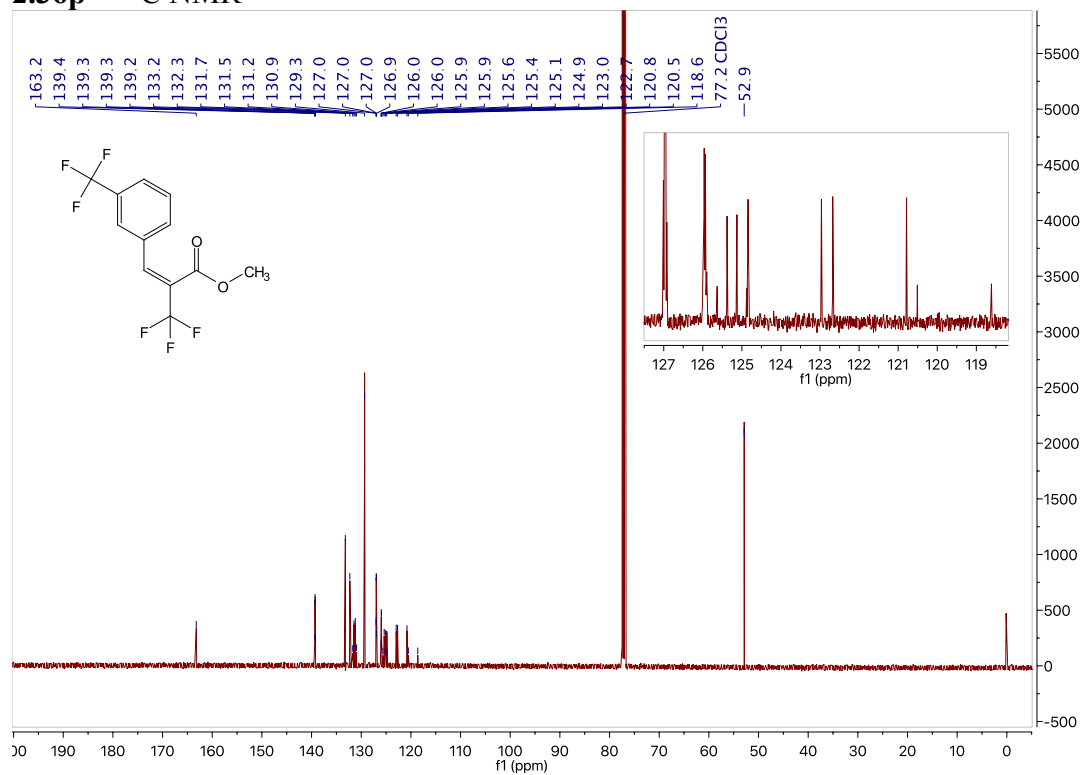
### 2.360 – <sup>19</sup>F NMR



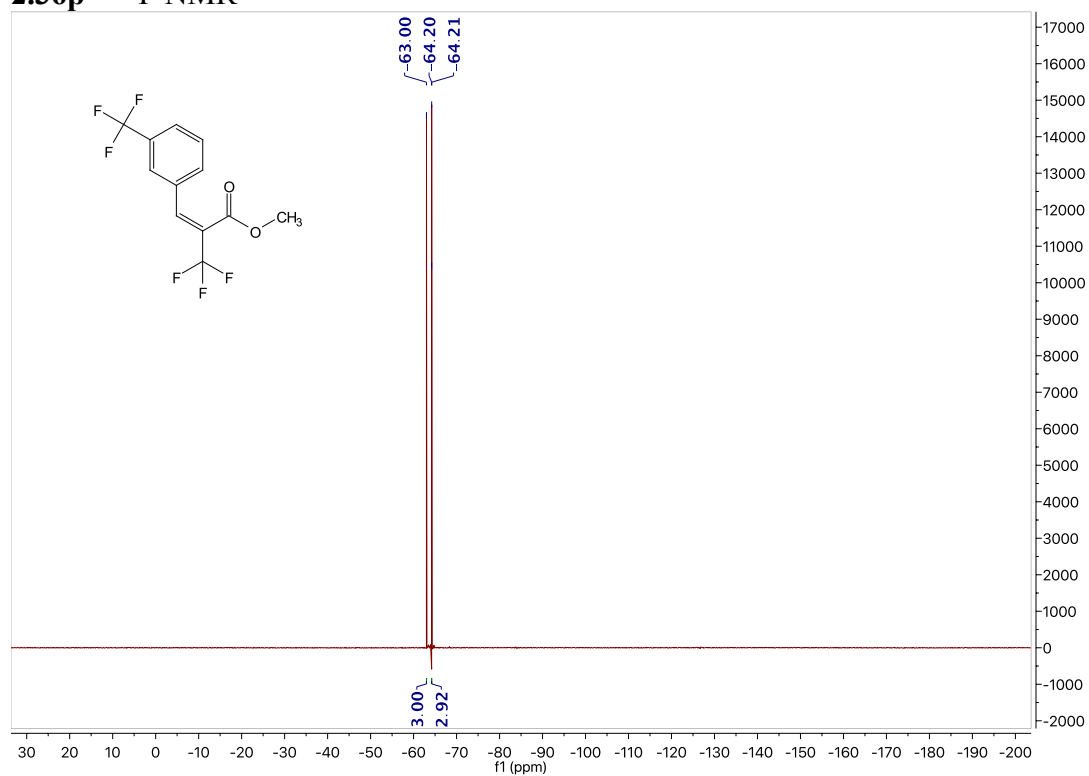
### 2.36p – <sup>1</sup>H NMR



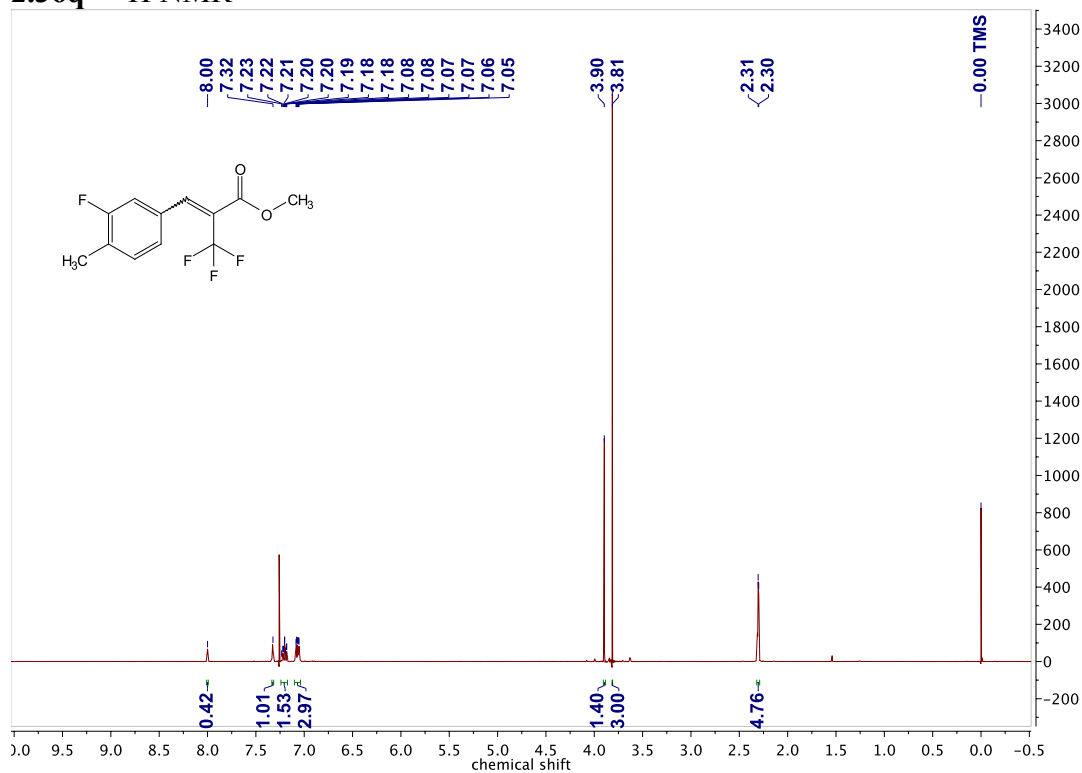
### 2.36p – <sup>13</sup>C NMR



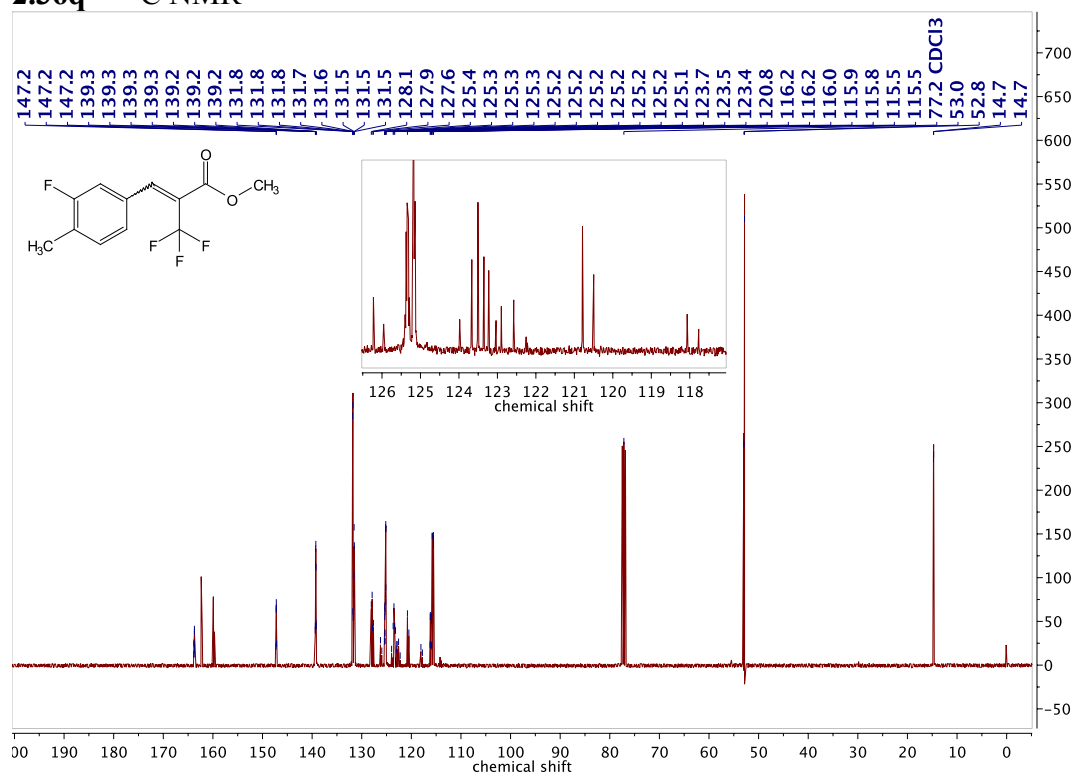
### 2.36p – $^{19}\text{F}$ NMR



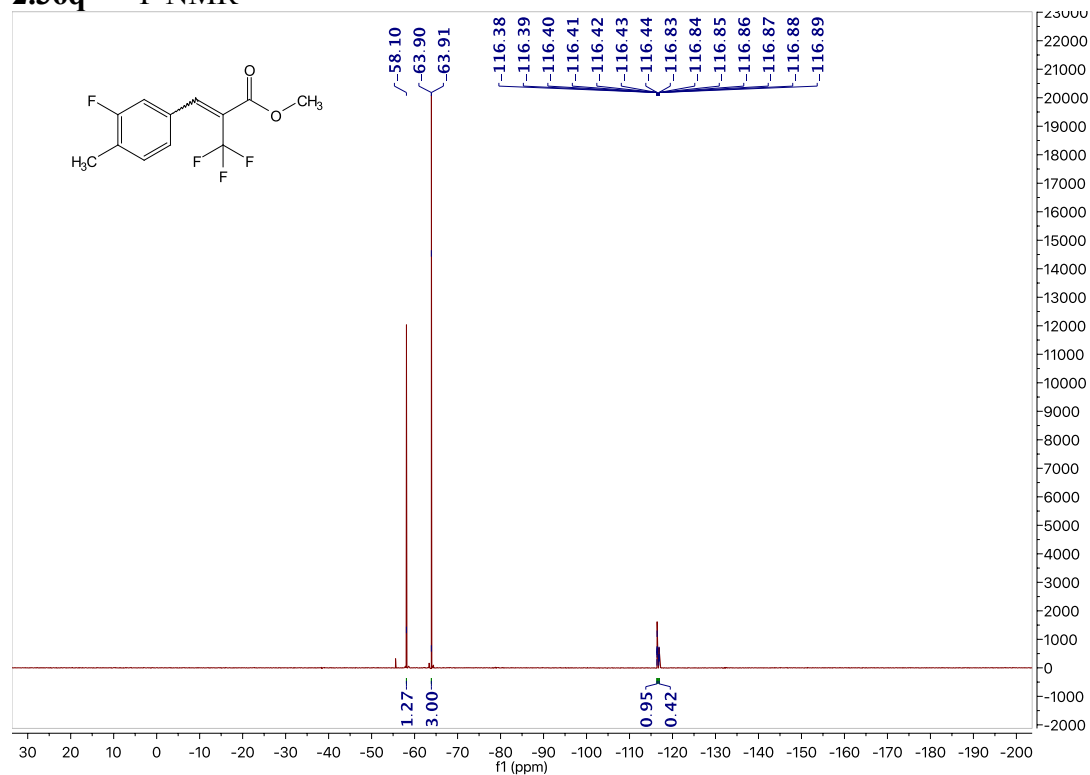
### 2.36q – $^1\text{H}$ NMR



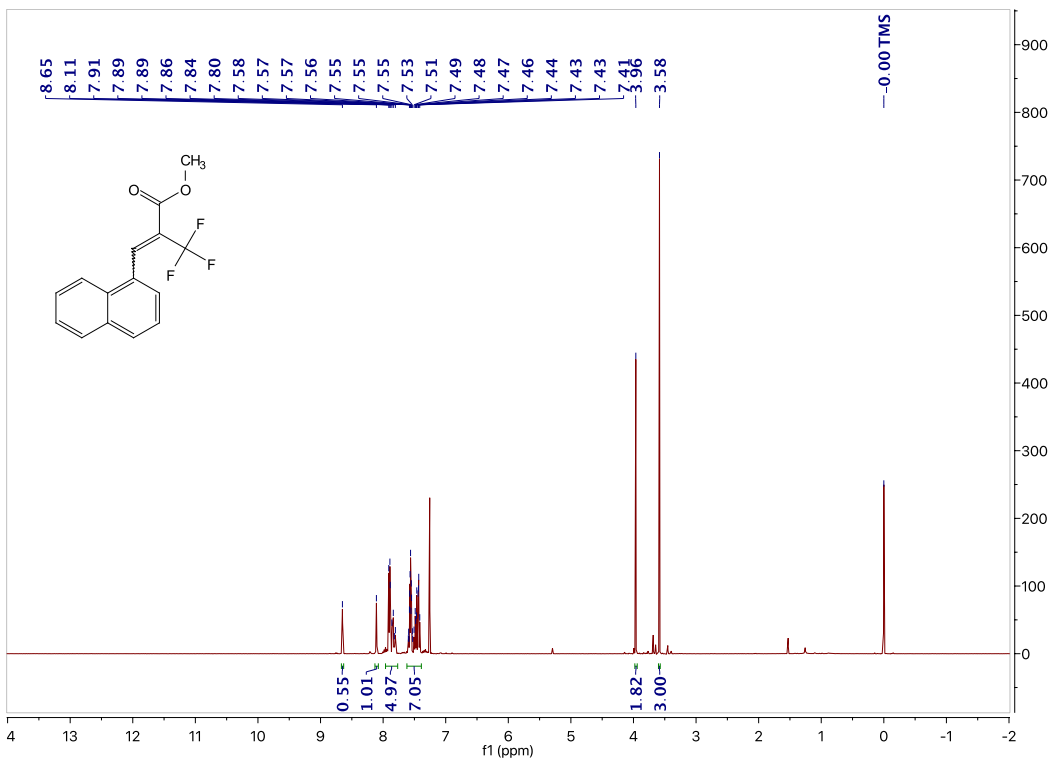
### 2.36q – <sup>13</sup>C NMR



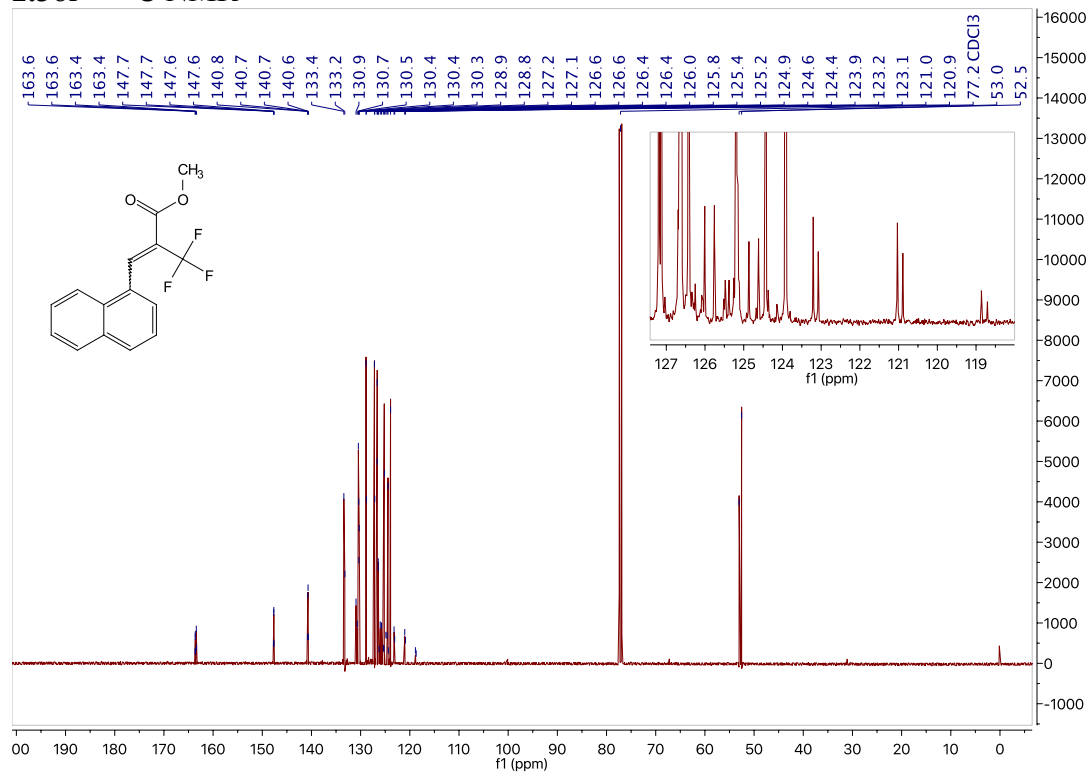
### 2.36q – <sup>19</sup>F NMR



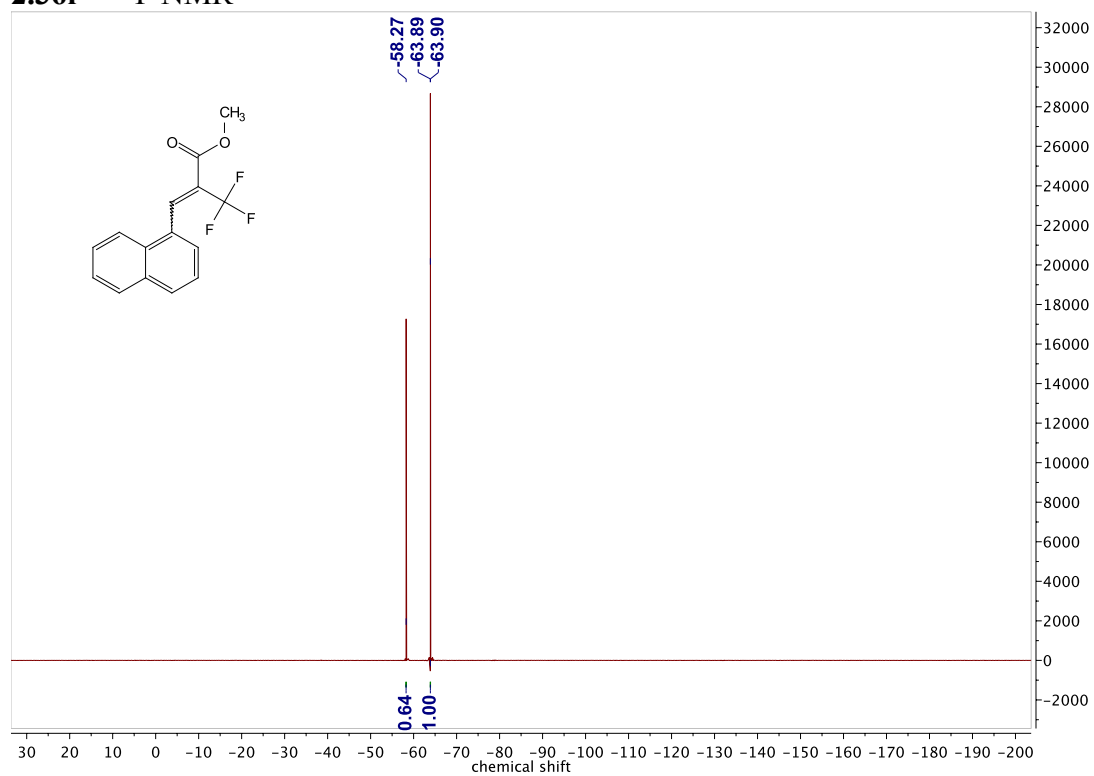
2.36r – <sup>1</sup>H NMR



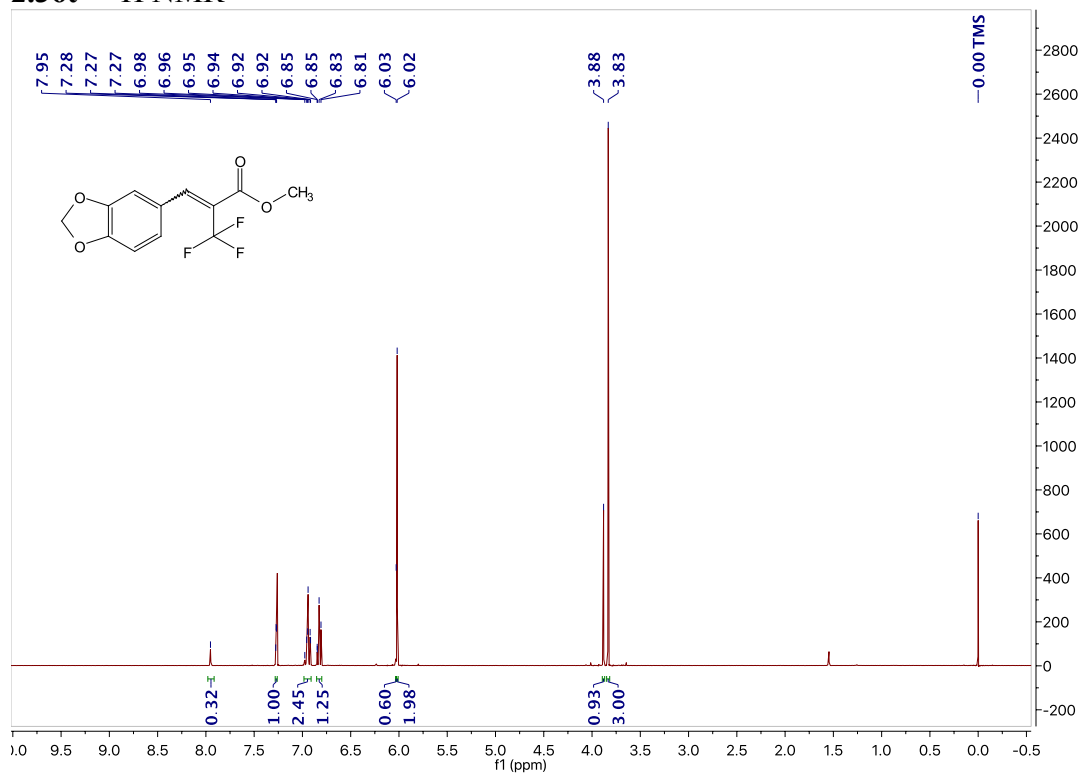
2.36r – <sup>13</sup>C NMR



### 2.36r – <sup>19</sup>F NMR

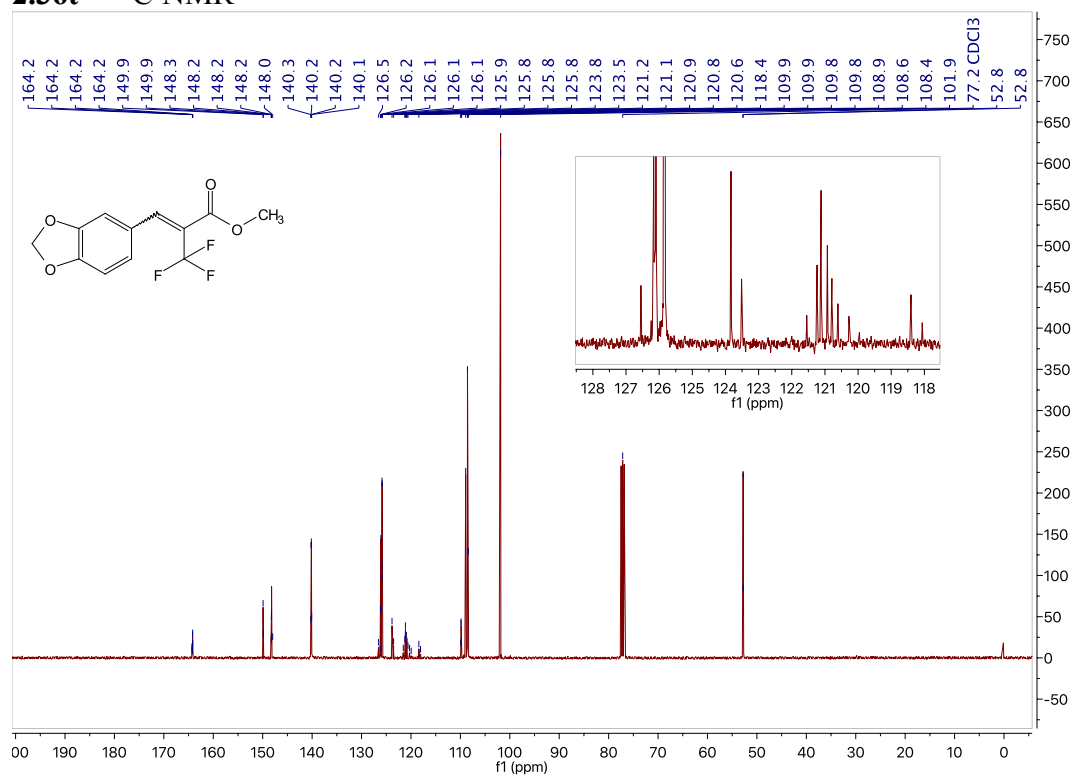


### 2.36t – <sup>1</sup>H NMR

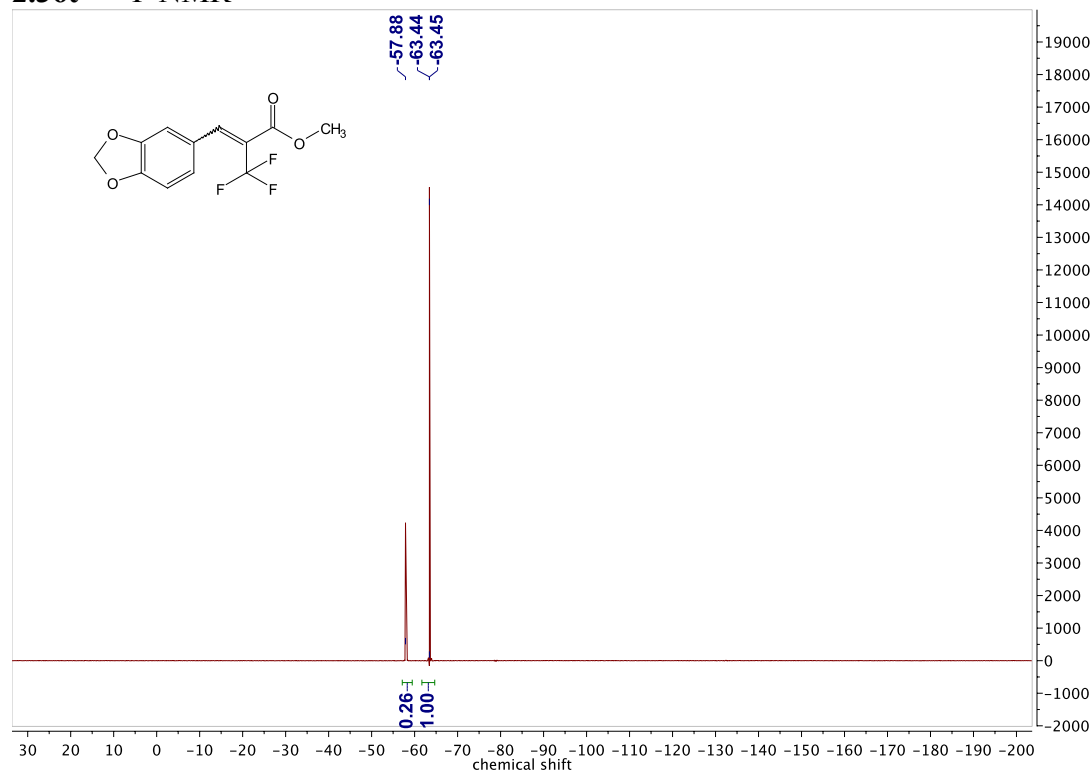




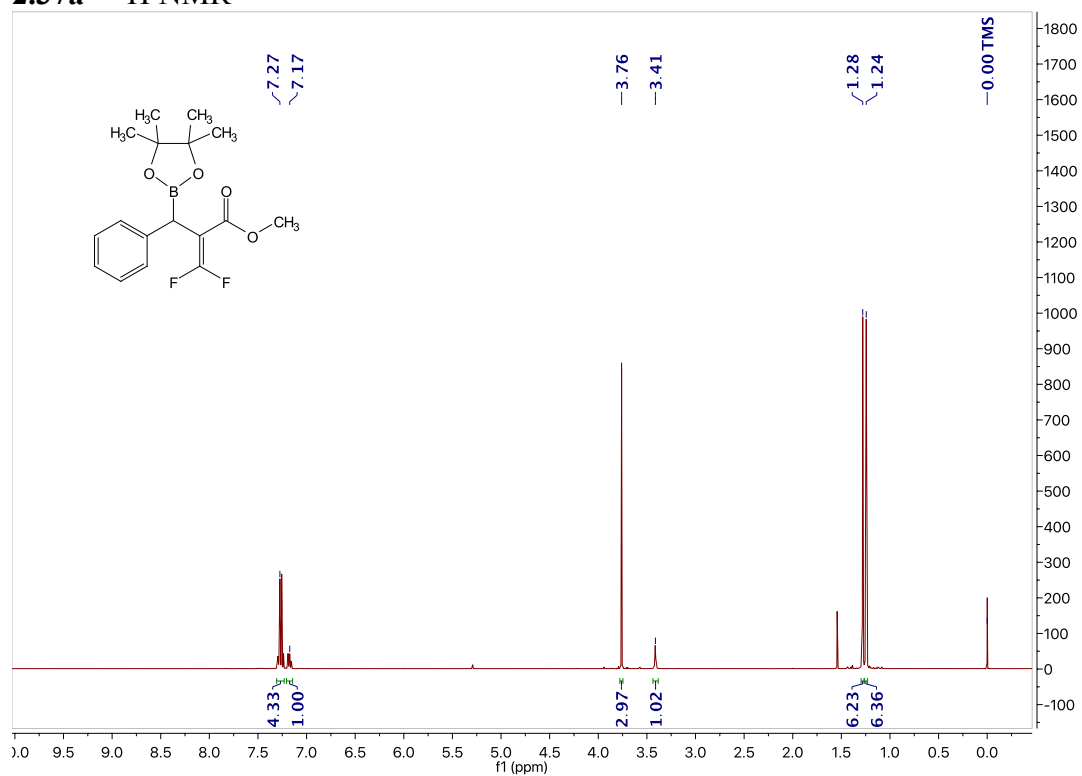
### 2.36t – <sup>13</sup>C NMR



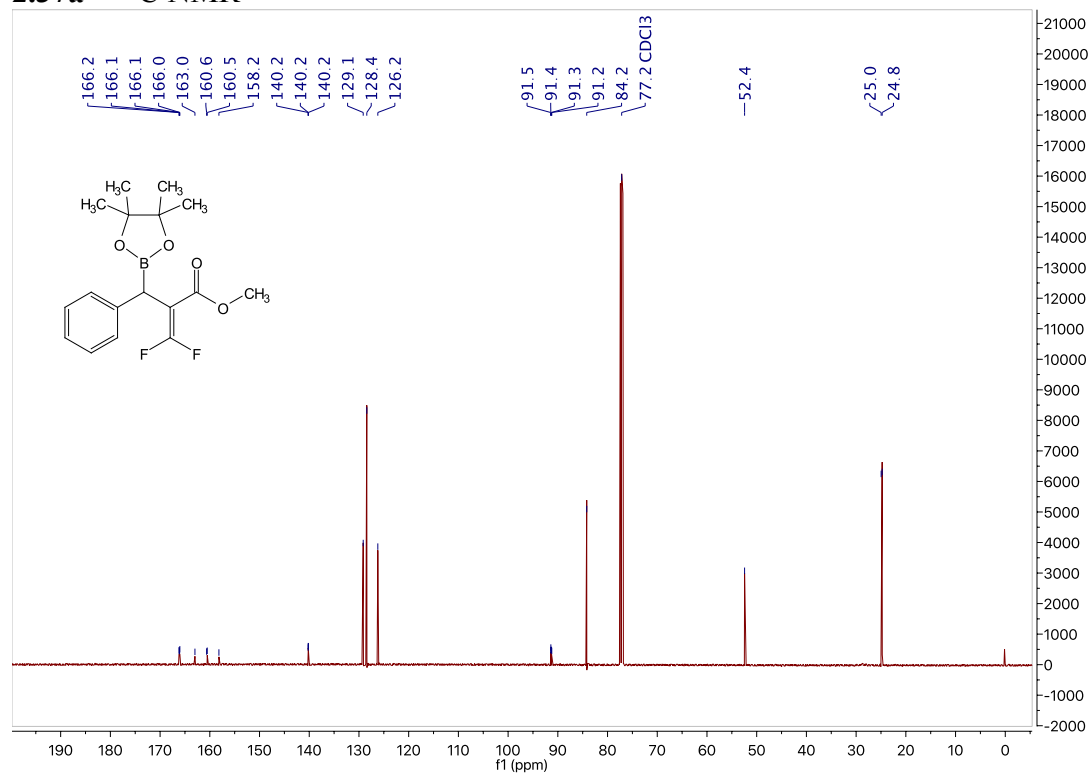
### 2.36t – <sup>19</sup>F NMR



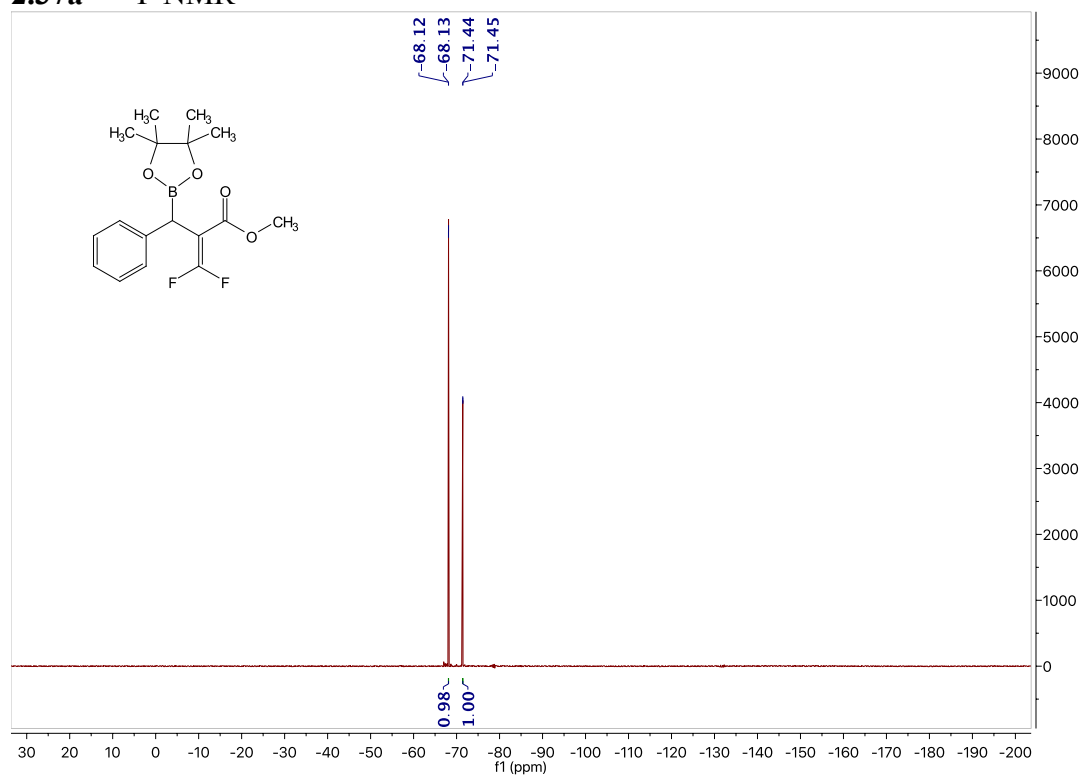
2.37a – <sup>1</sup>H NMR



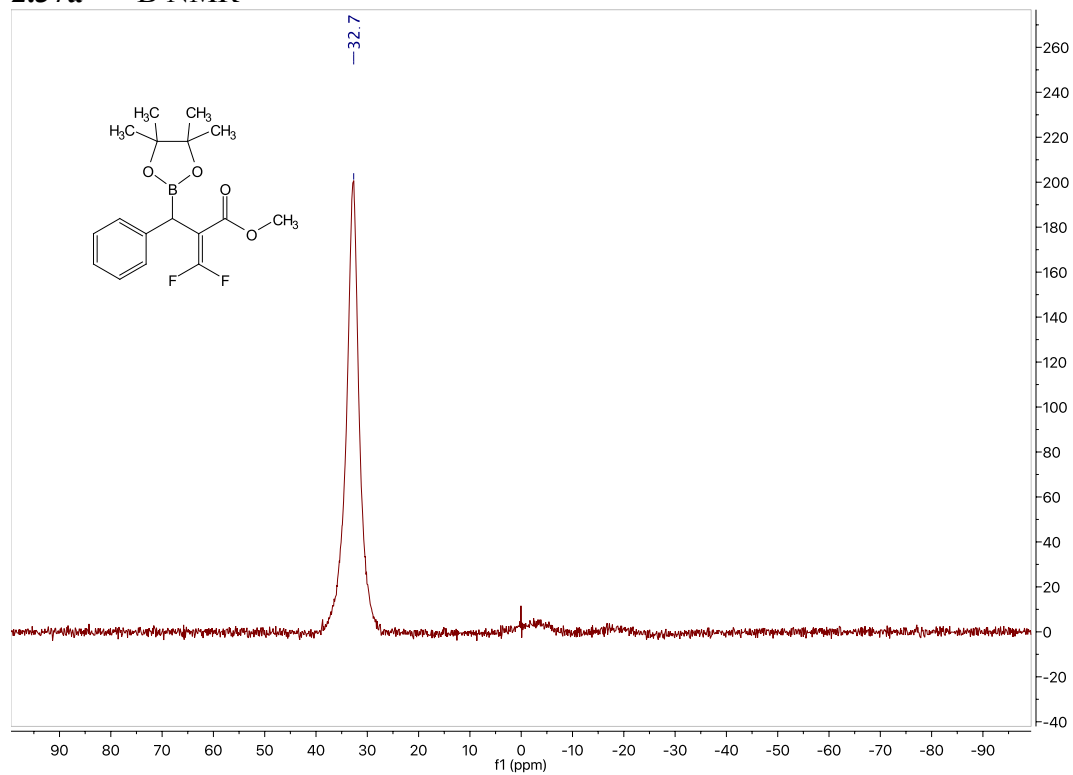
2.37a – <sup>13</sup>C NMR



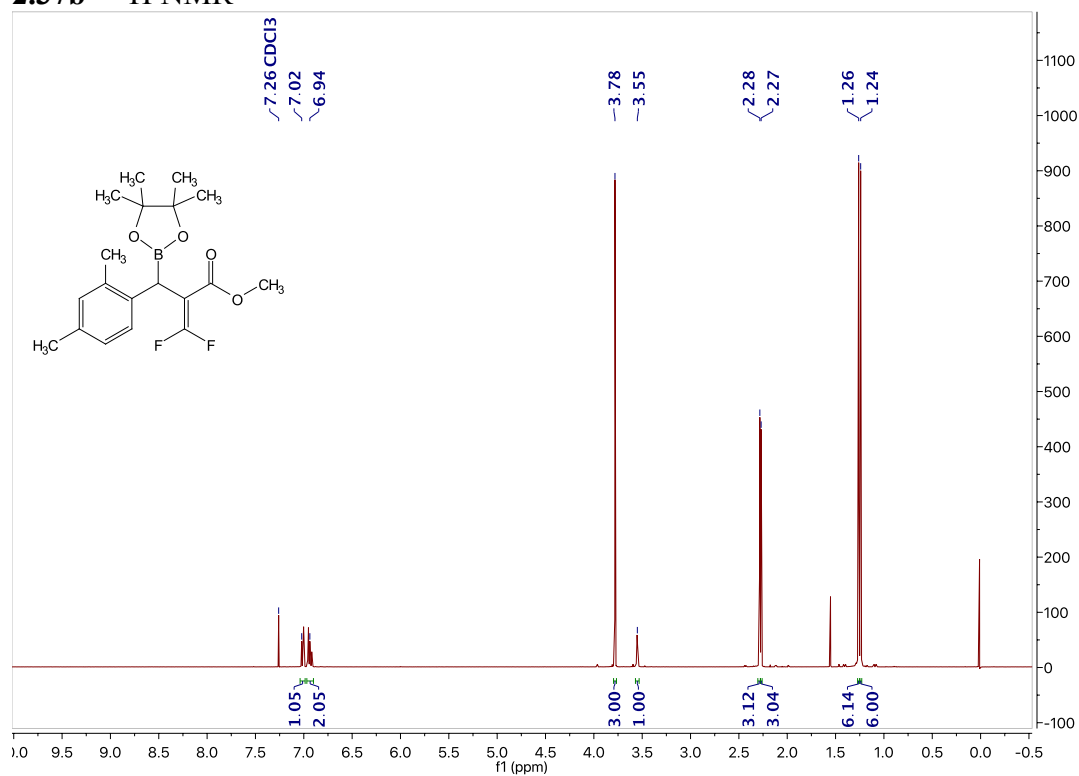
### 2.37a – $^{19}\text{F}$ NMR



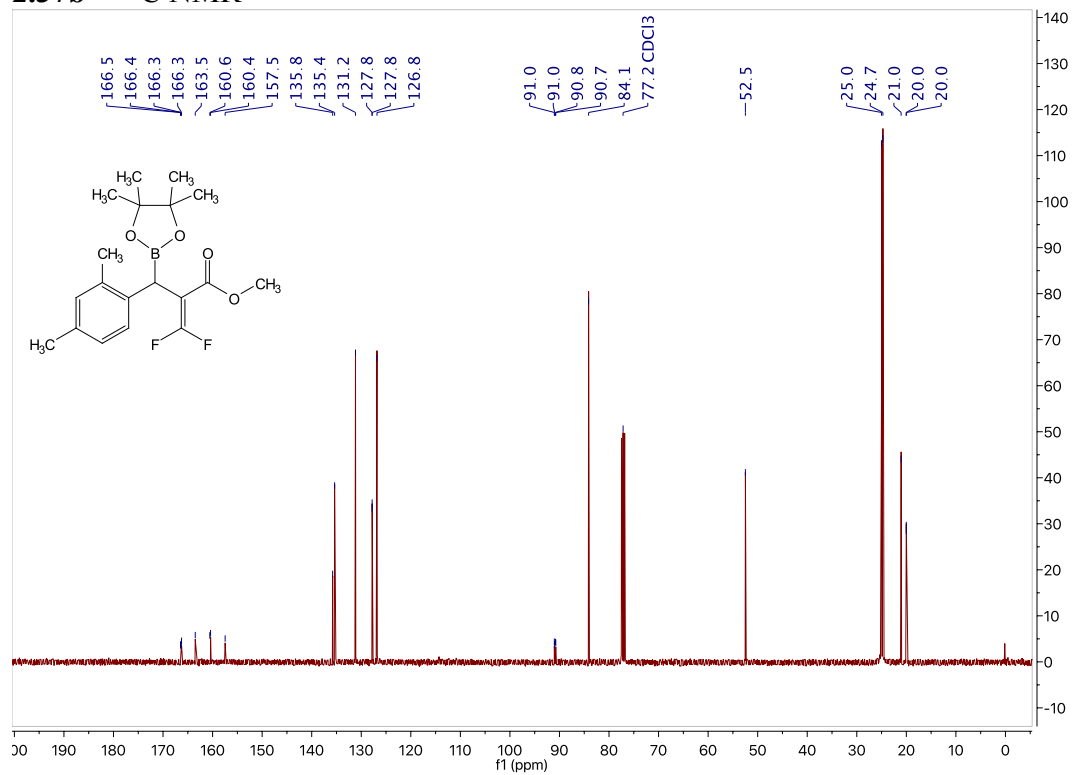
### 2.37a – $^{11}\text{B}$ NMR



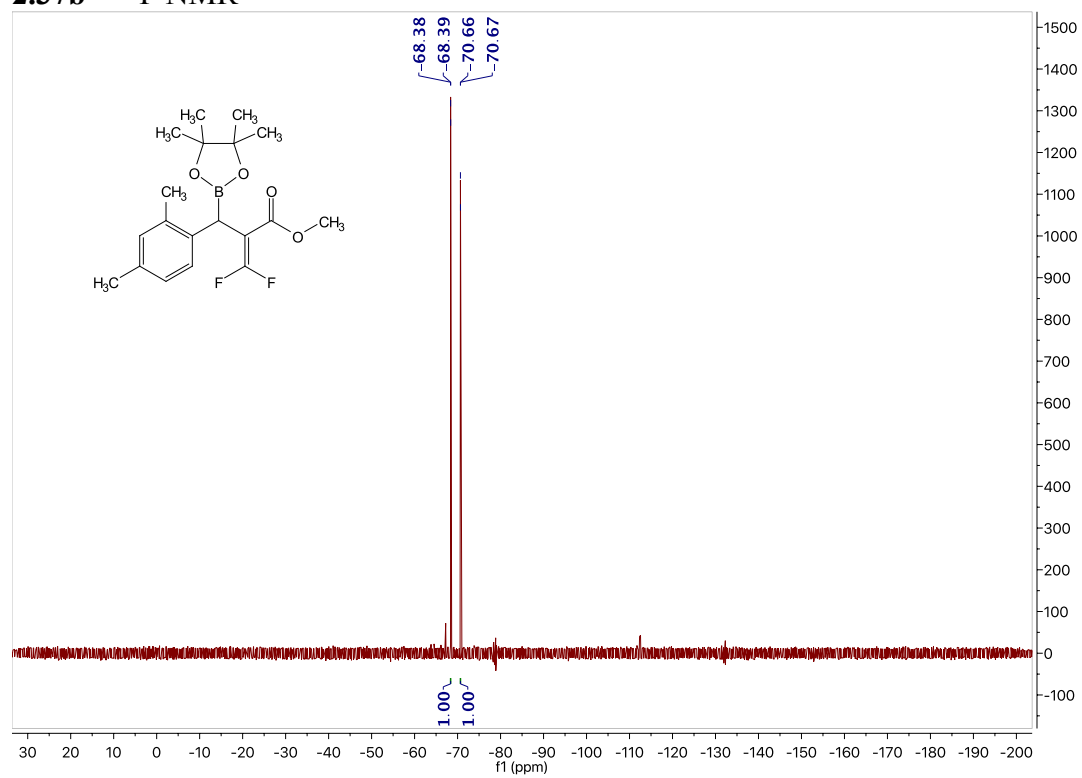
### 2.37b – <sup>1</sup>H NMR



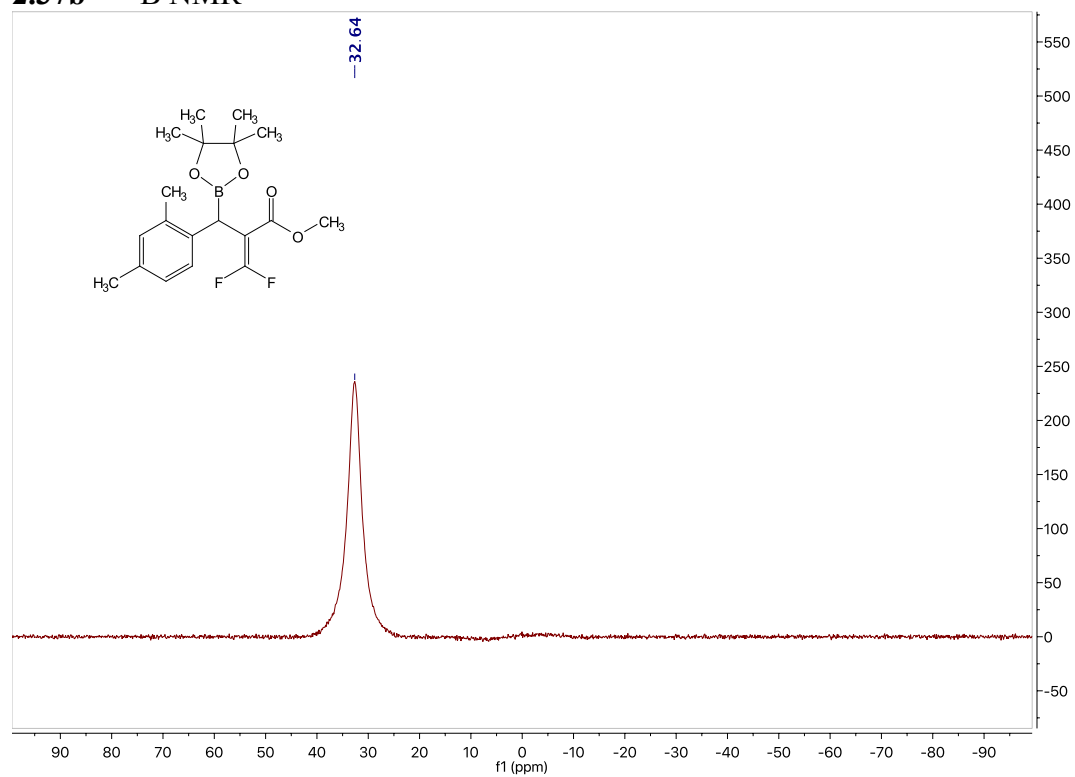
### 2.37b – <sup>13</sup>C NMR



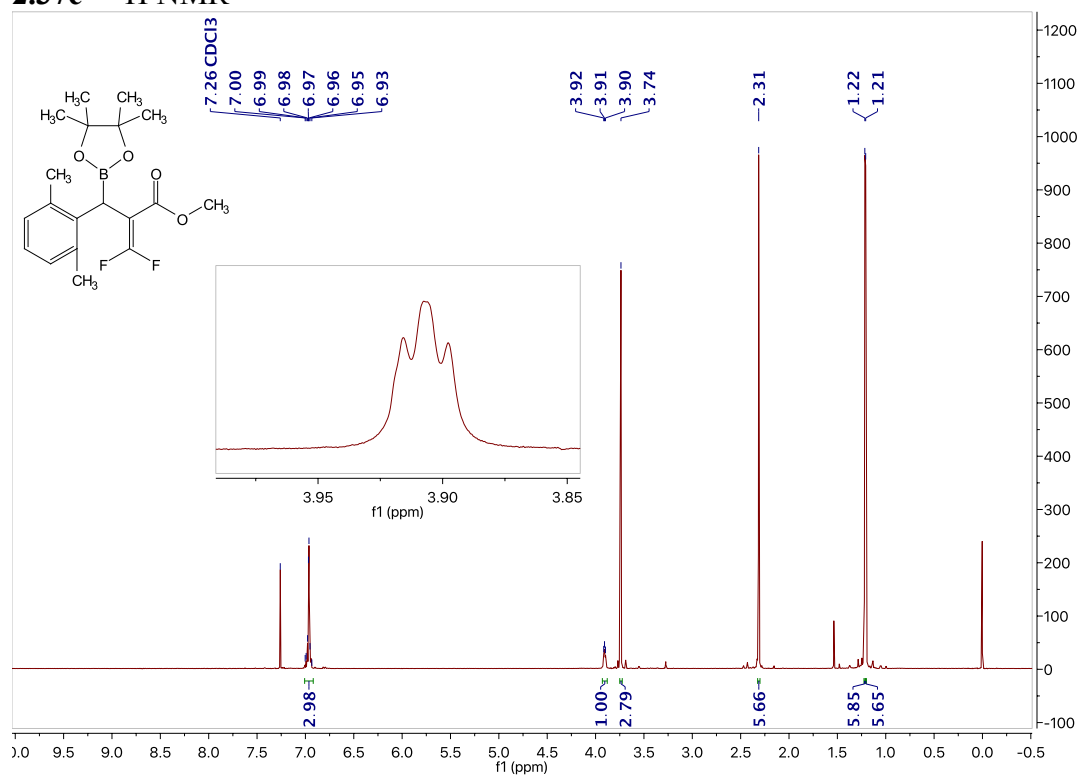
### 2.37b – $^{19}\text{F}$ NMR



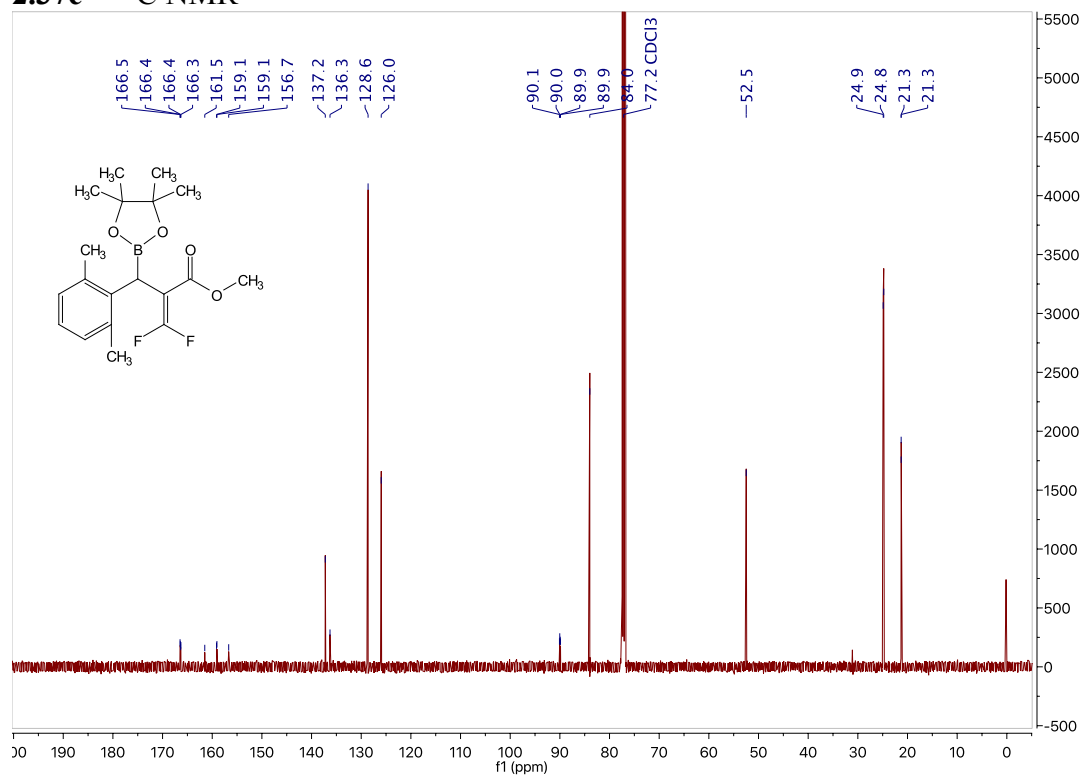
### 2.37b – $^{11}\text{B}$ NMR



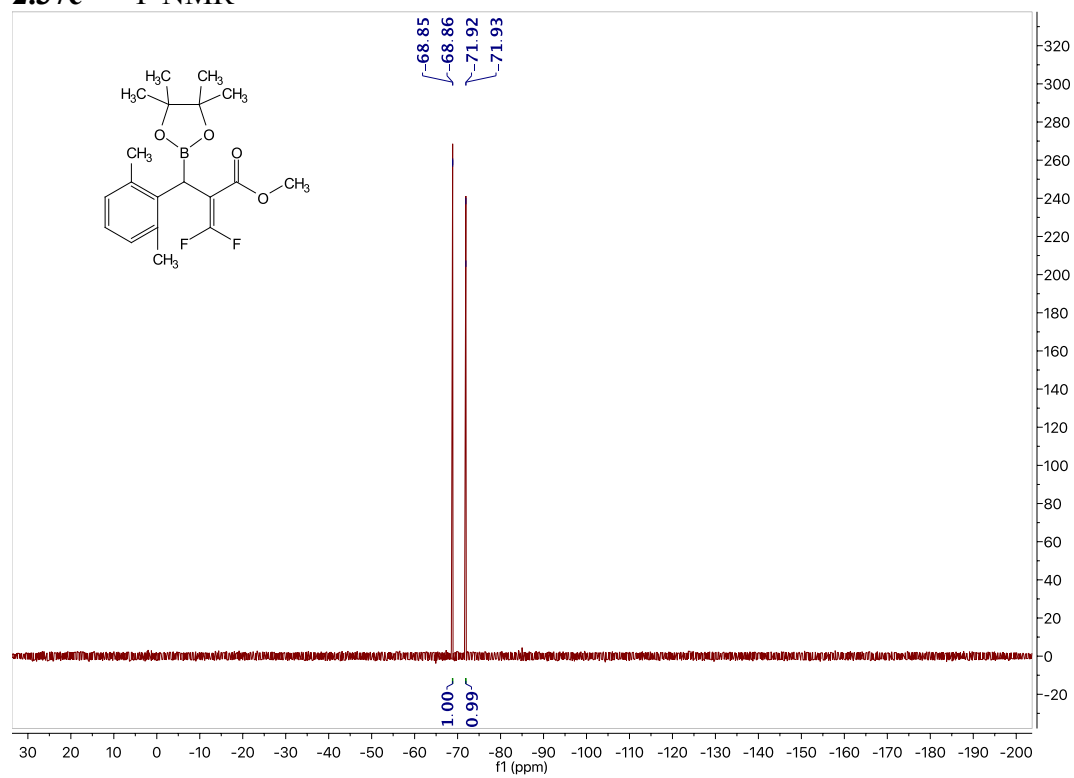
### 2.37c – <sup>1</sup>H NMR



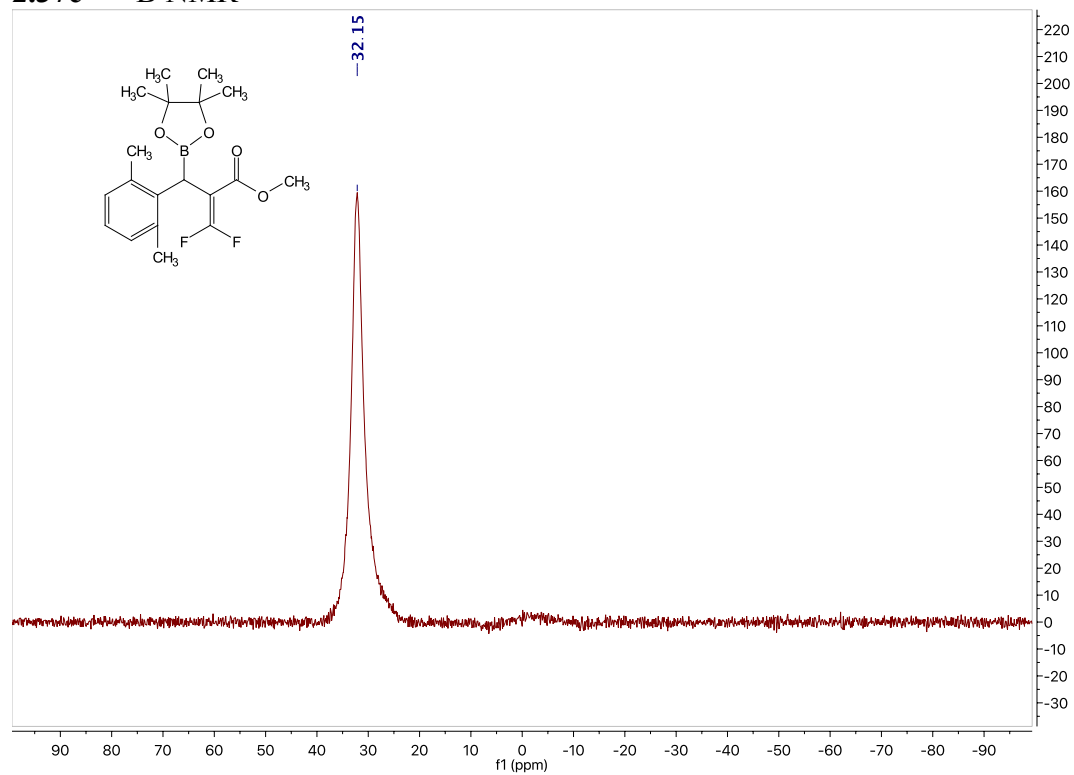
### 2.37c – <sup>13</sup>C NMR



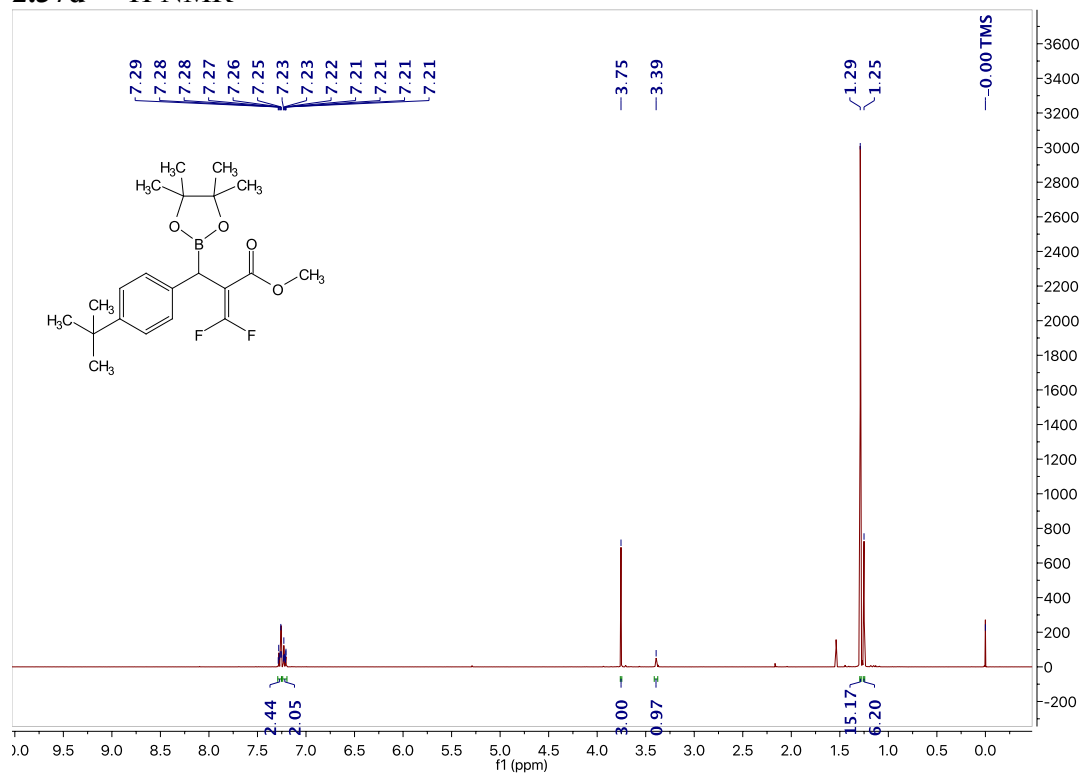
### 2.37c – <sup>19</sup>F NMR



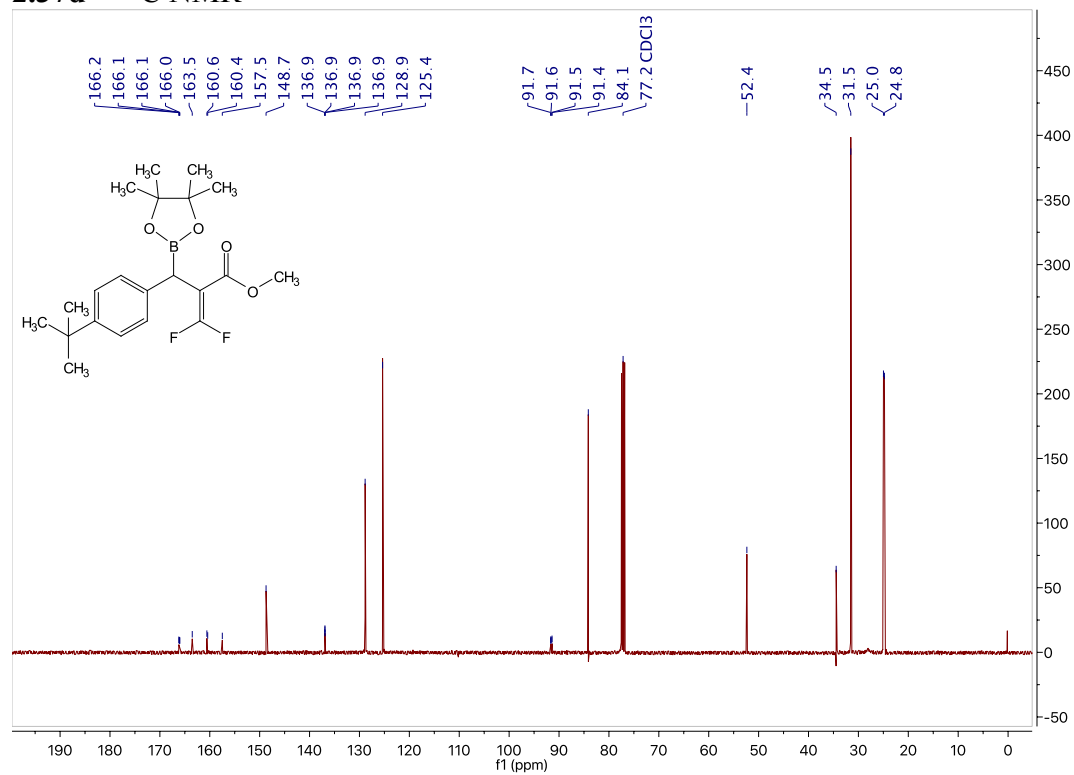
### 2.37c – <sup>11</sup>B NMR



### 2.37d – <sup>1</sup>H NMR

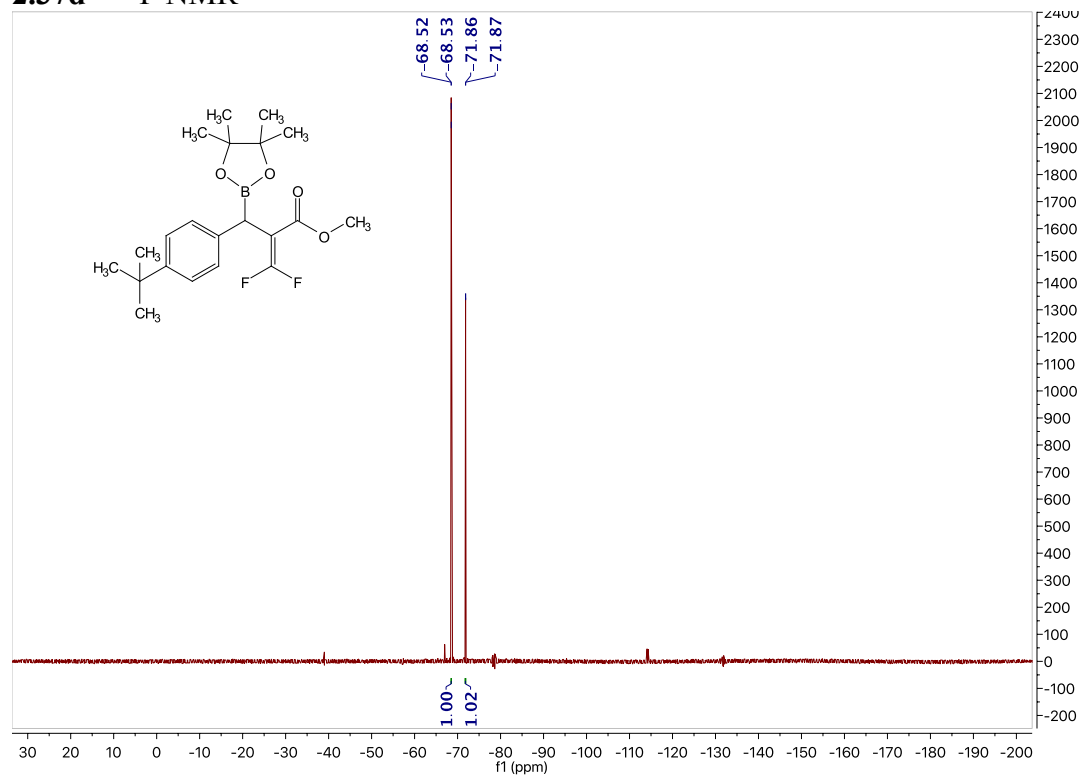


### 2.37d – <sup>13</sup>C NMR

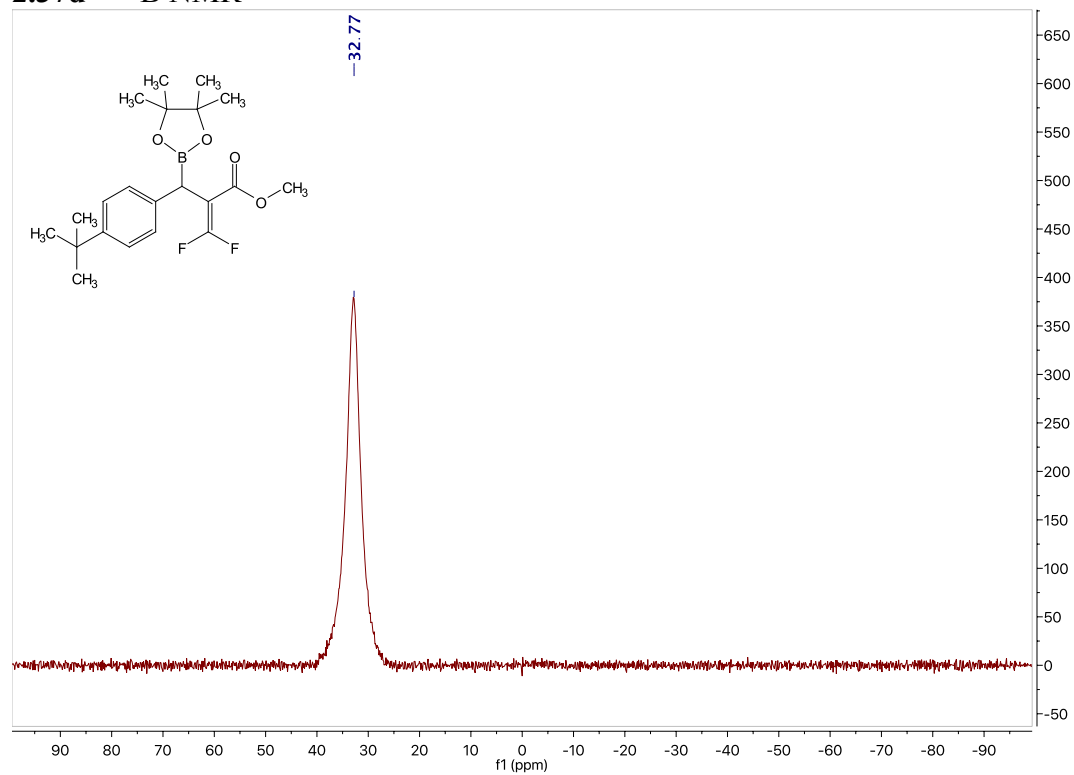




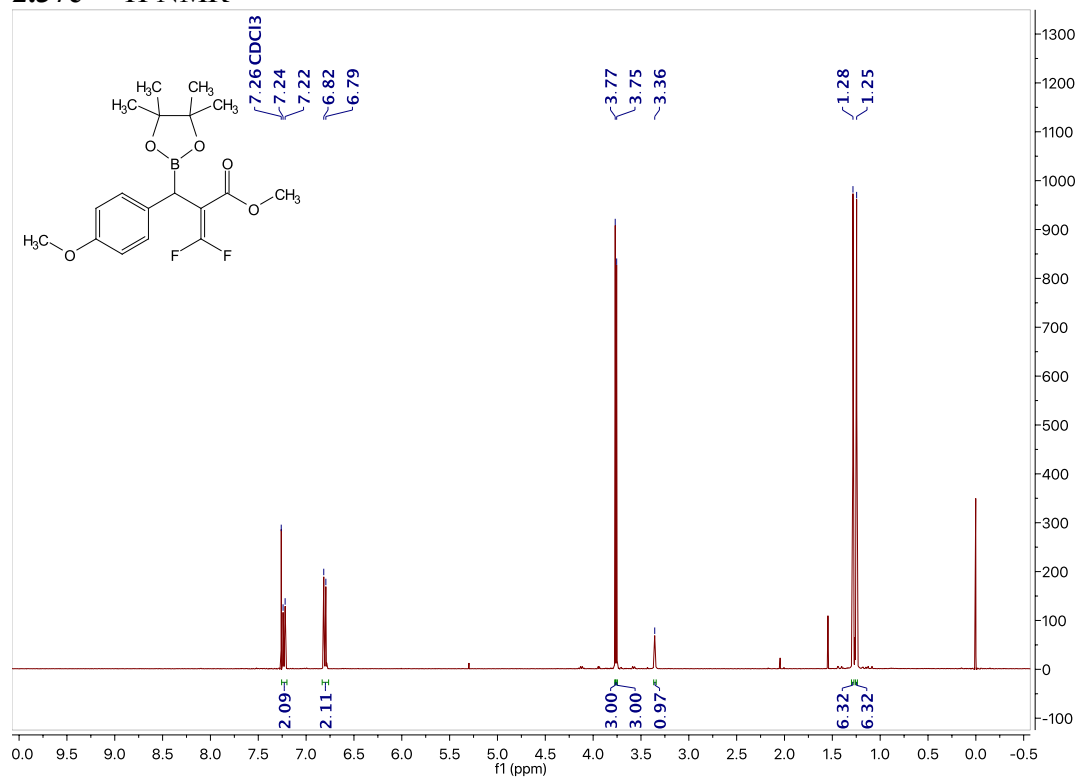
### 2.37d – $^{19}\text{F}$ NMR



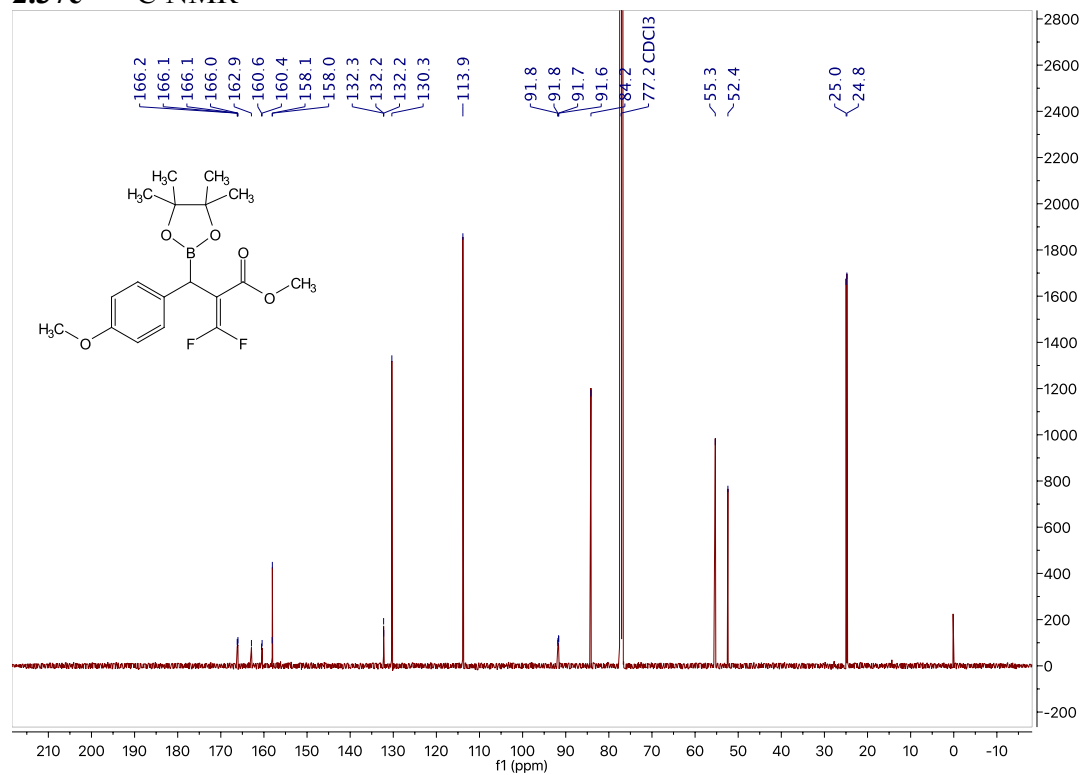
### 2.37d – $^{11}\text{B}$ NMR



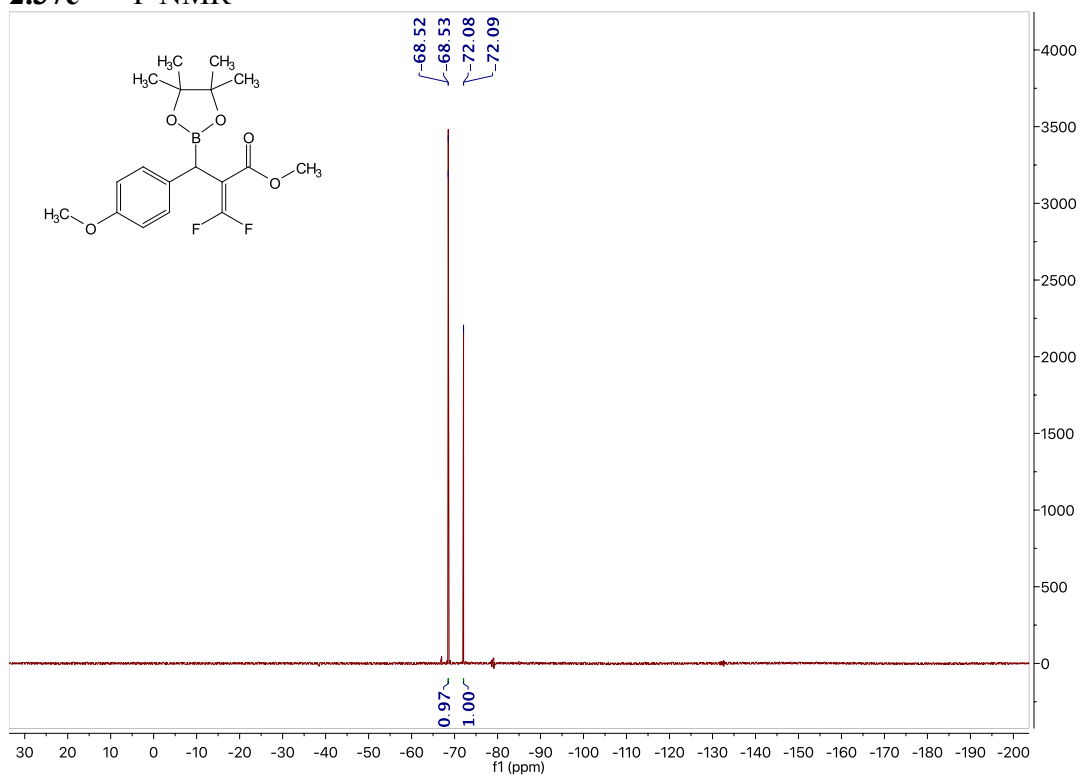
2.37e – <sup>1</sup>H NMR



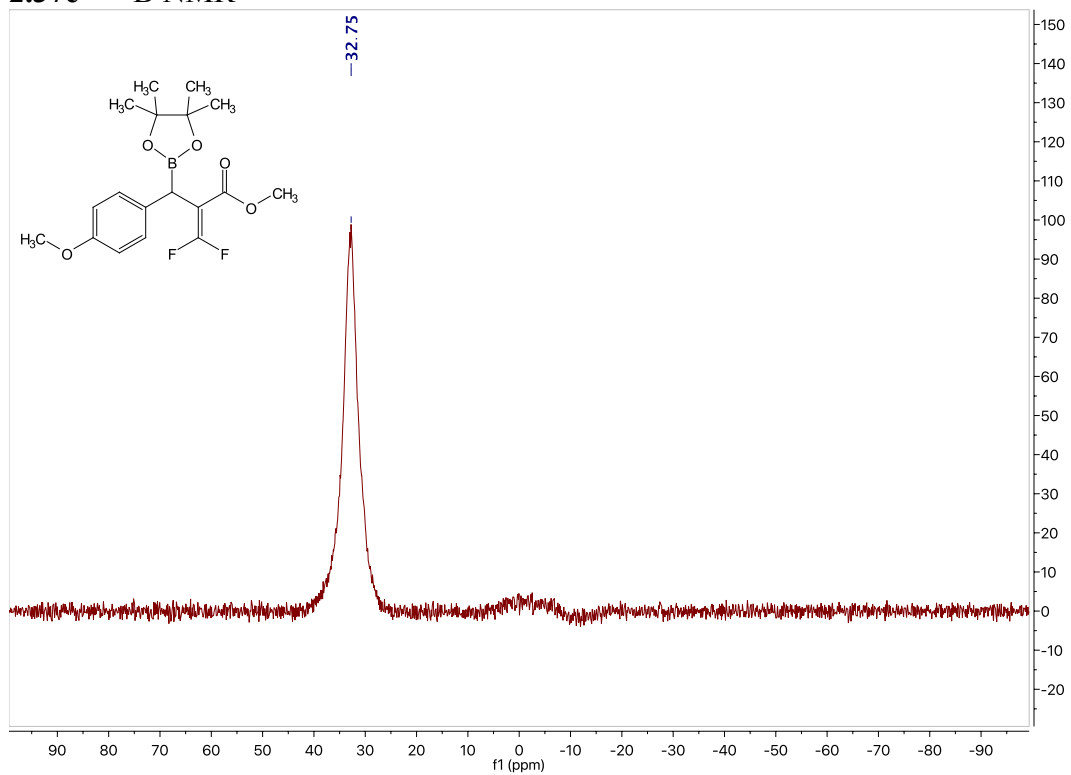
2.37e – <sup>13</sup>C NMR



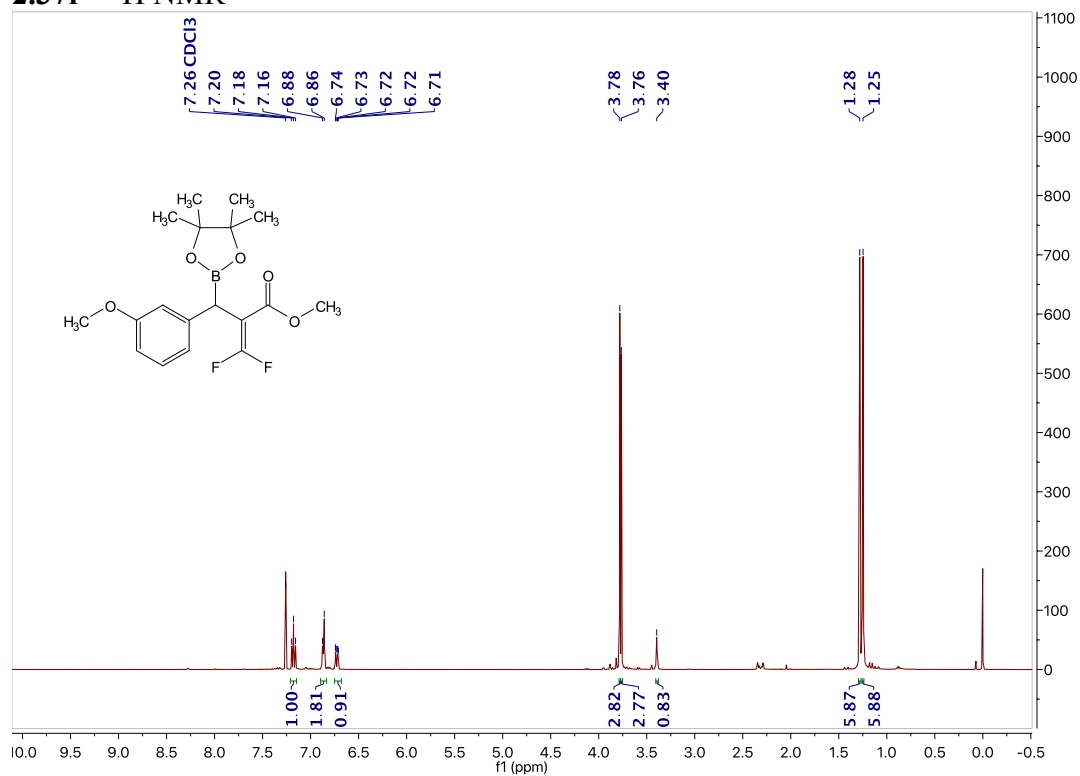
### 2.37e – <sup>19</sup>F NMR



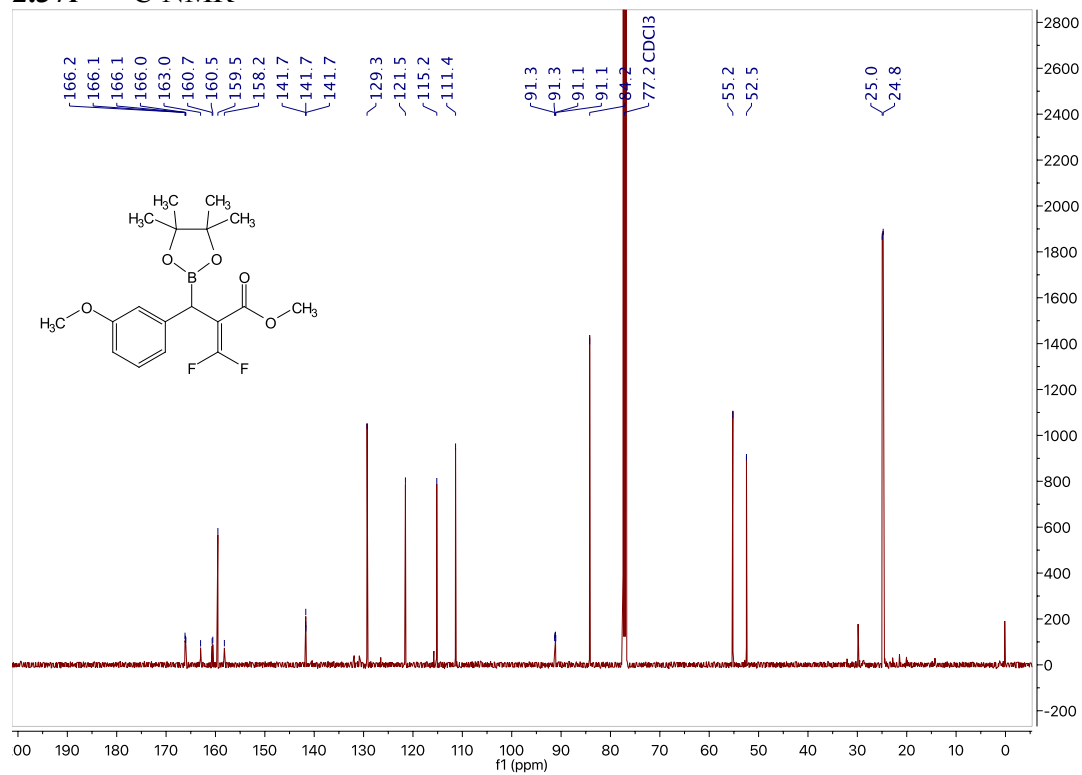
### 2.37e – <sup>11</sup>B NMR



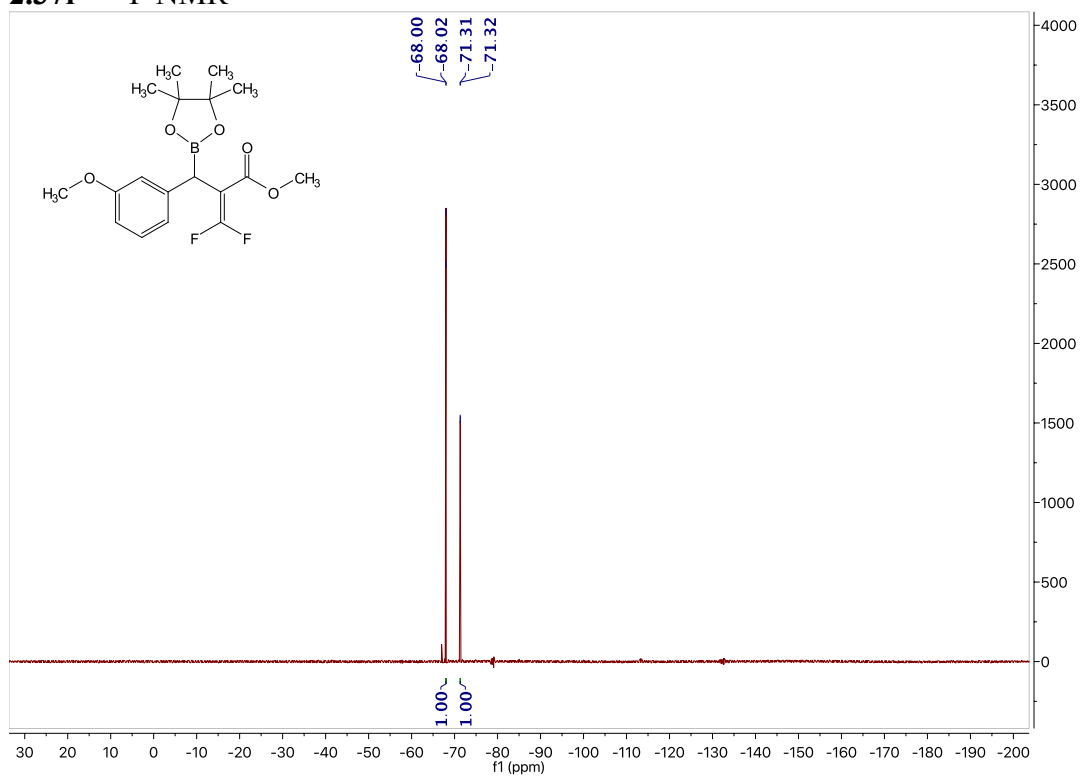
### 2.37f – <sup>1</sup>H NMR



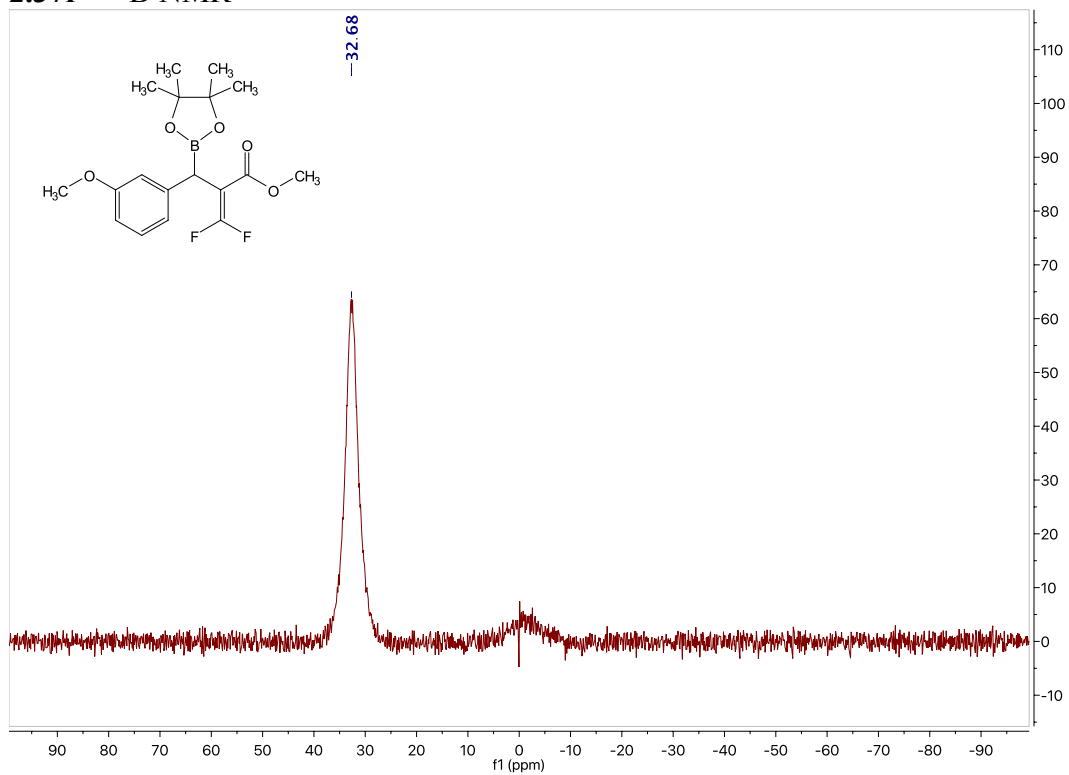
### 2.37f – <sup>13</sup>C NMR



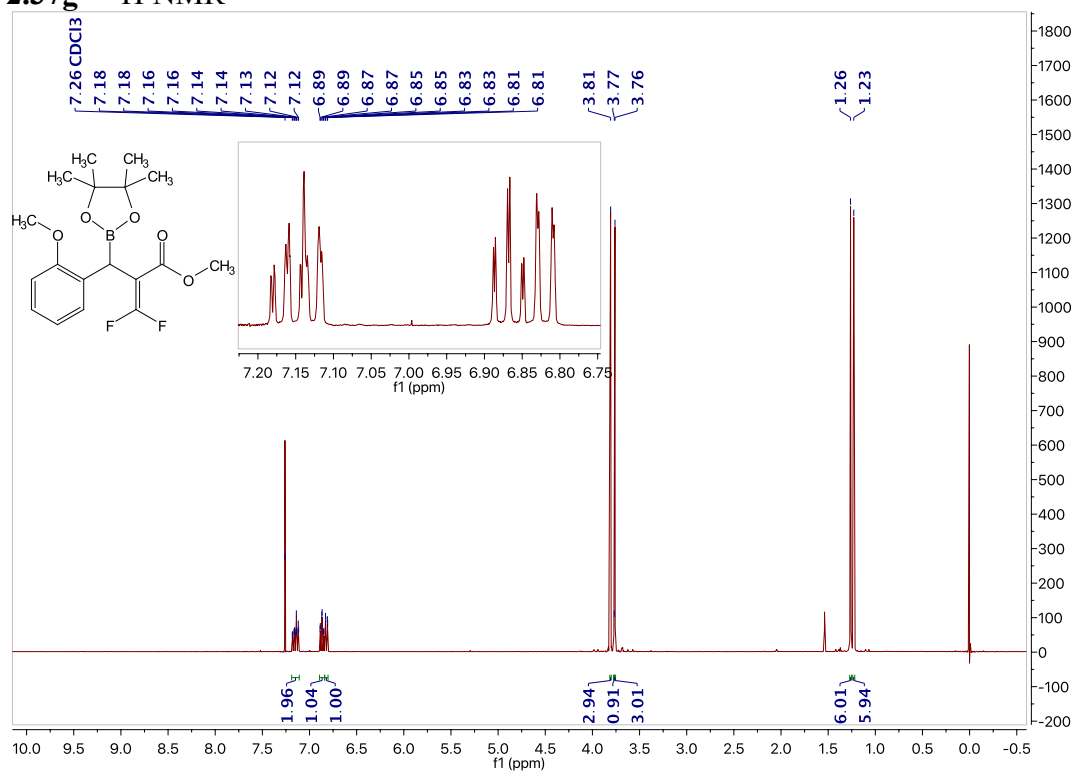
### 2.37f – <sup>19</sup>F NMR



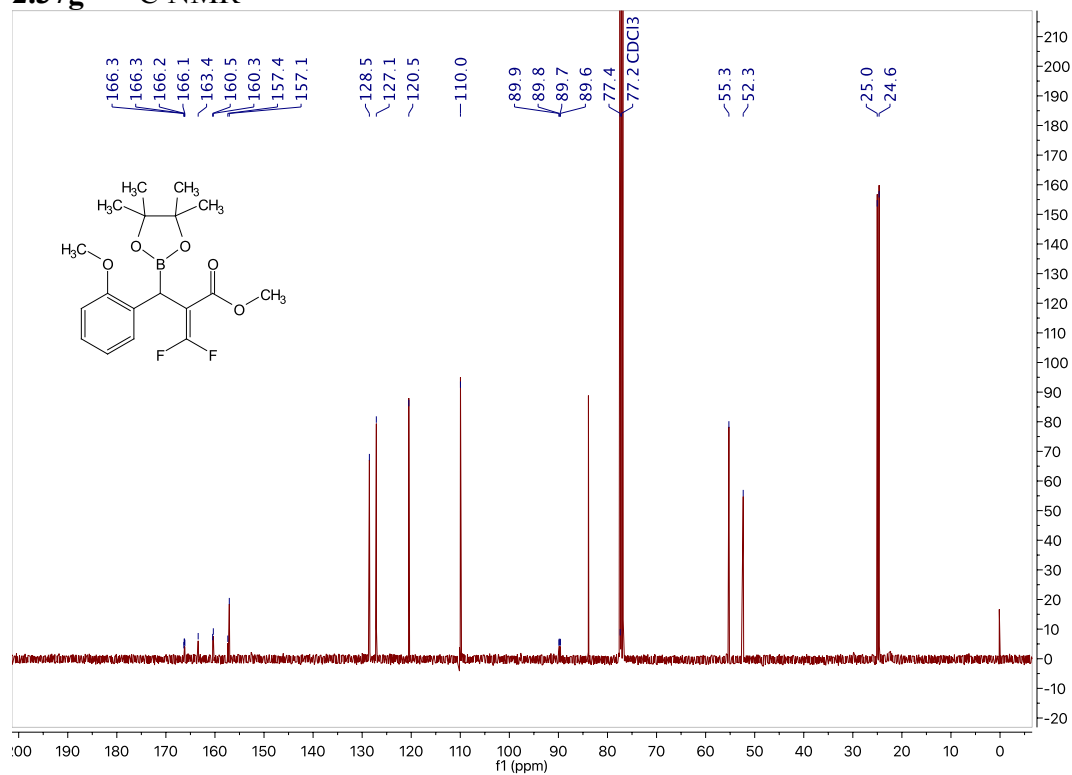
### 2.37f – <sup>11</sup>B NMR



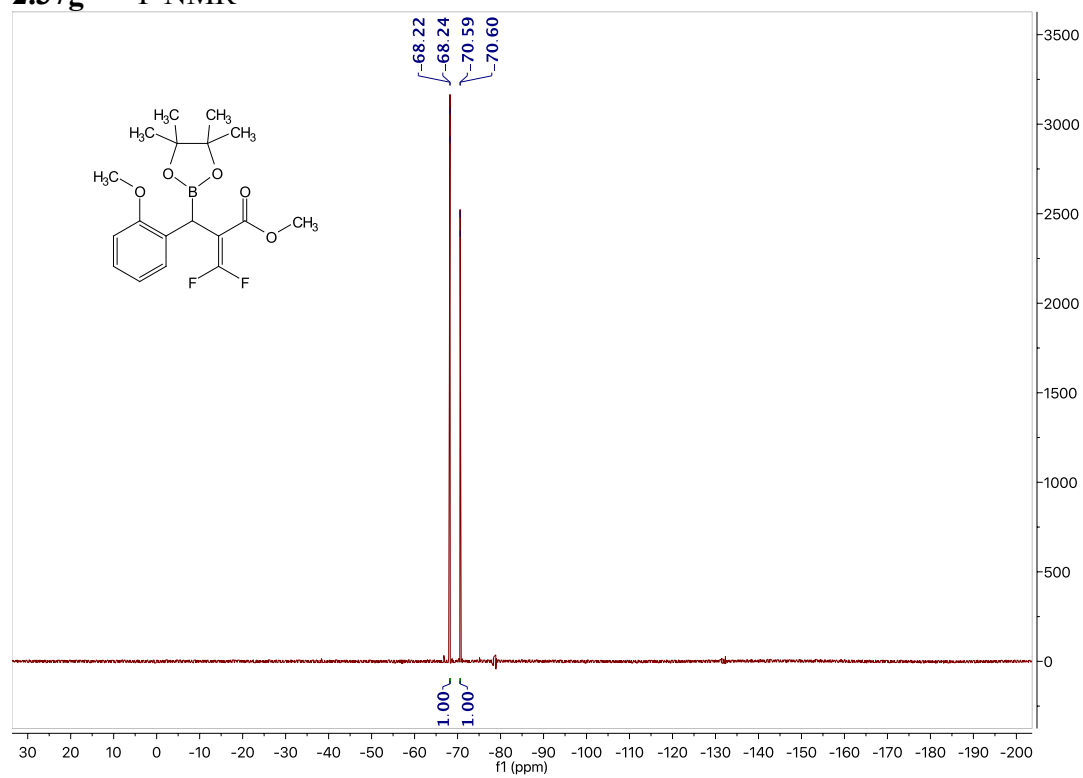
### 2.37g – <sup>1</sup>H NMR



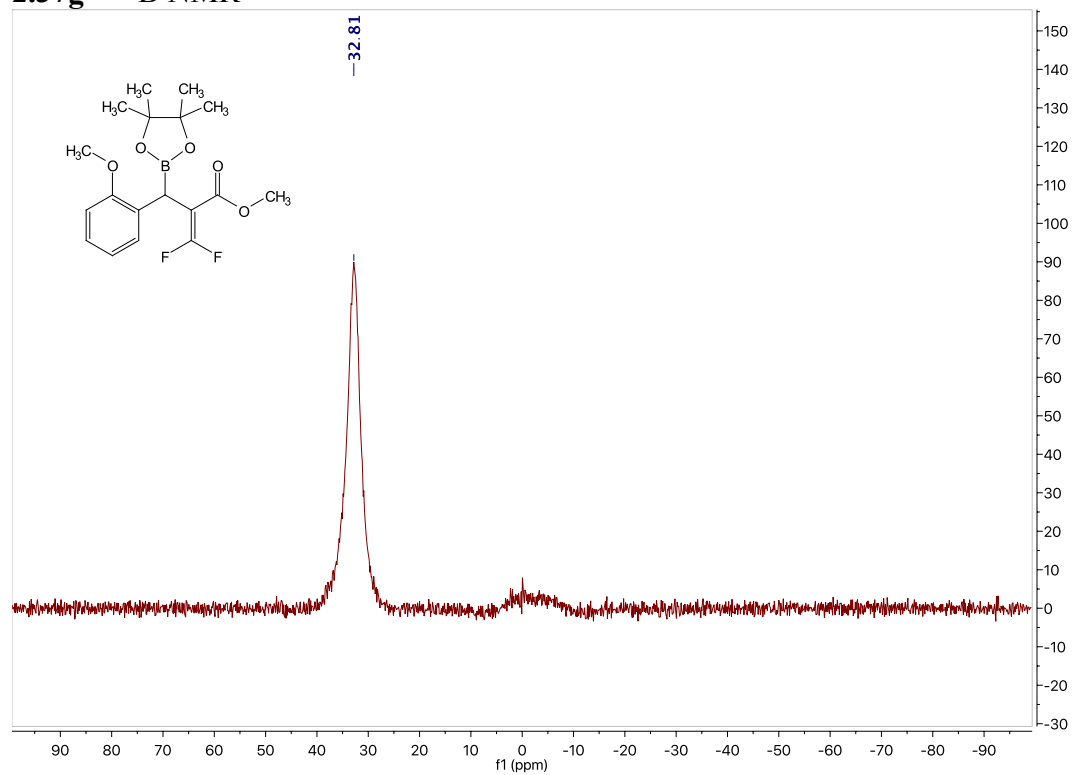
### 2.37g – <sup>13</sup>C NMR



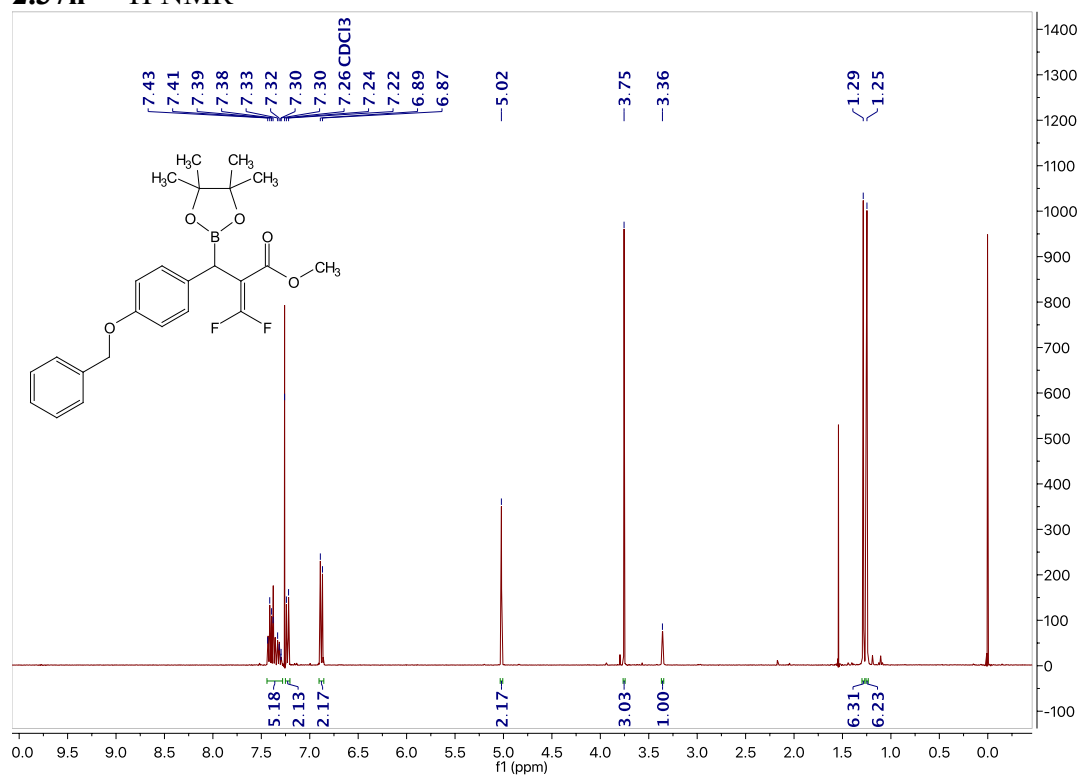
### 2.37g – $^{19}\text{F}$ NMR



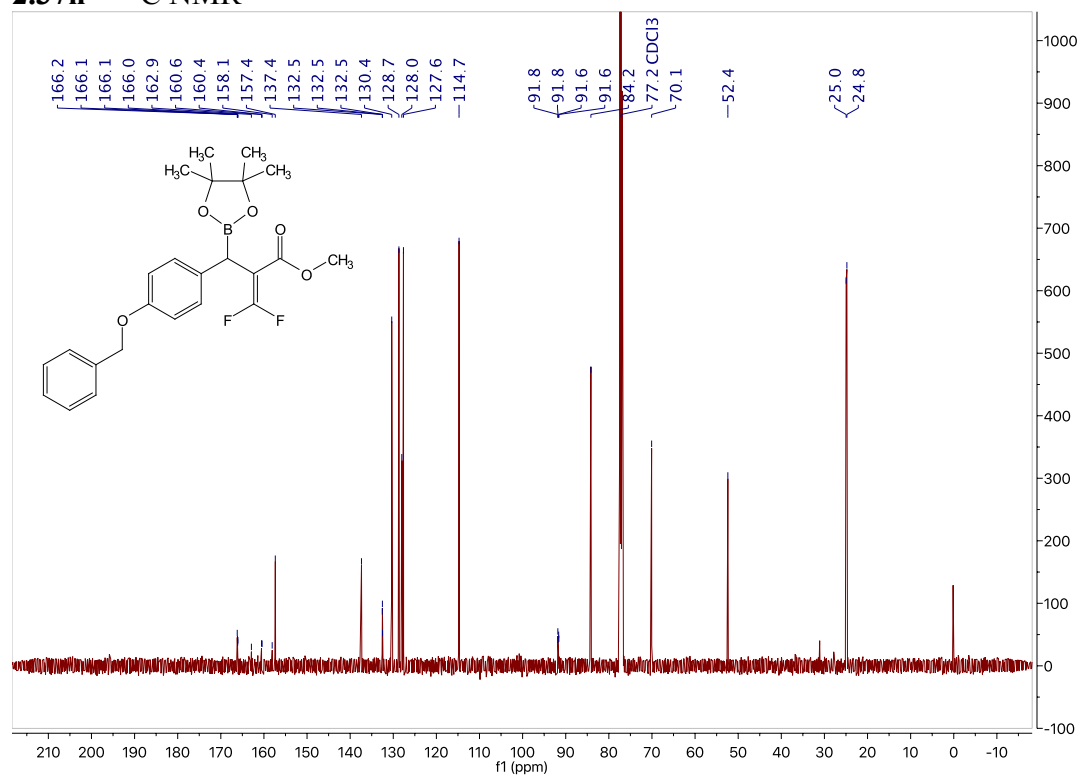
### 2.37g – $^{11}\text{B}$ NMR



### 2.37h – <sup>1</sup>H NMR

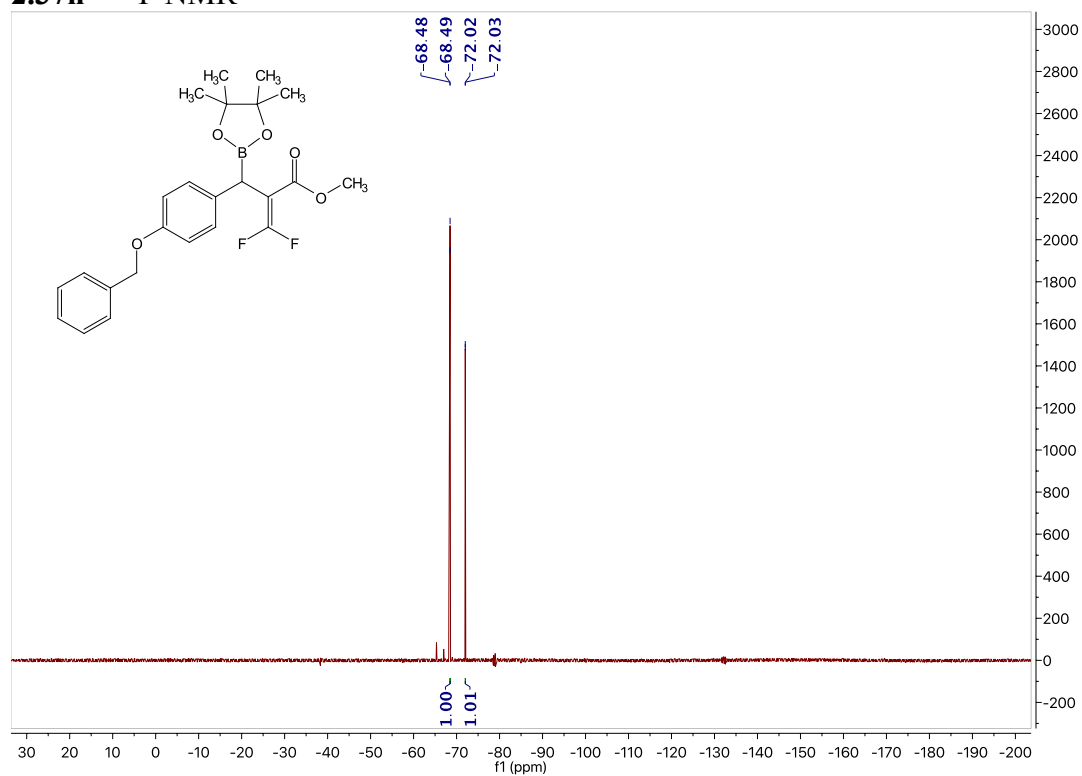


### 2.37h – <sup>13</sup>C NMR

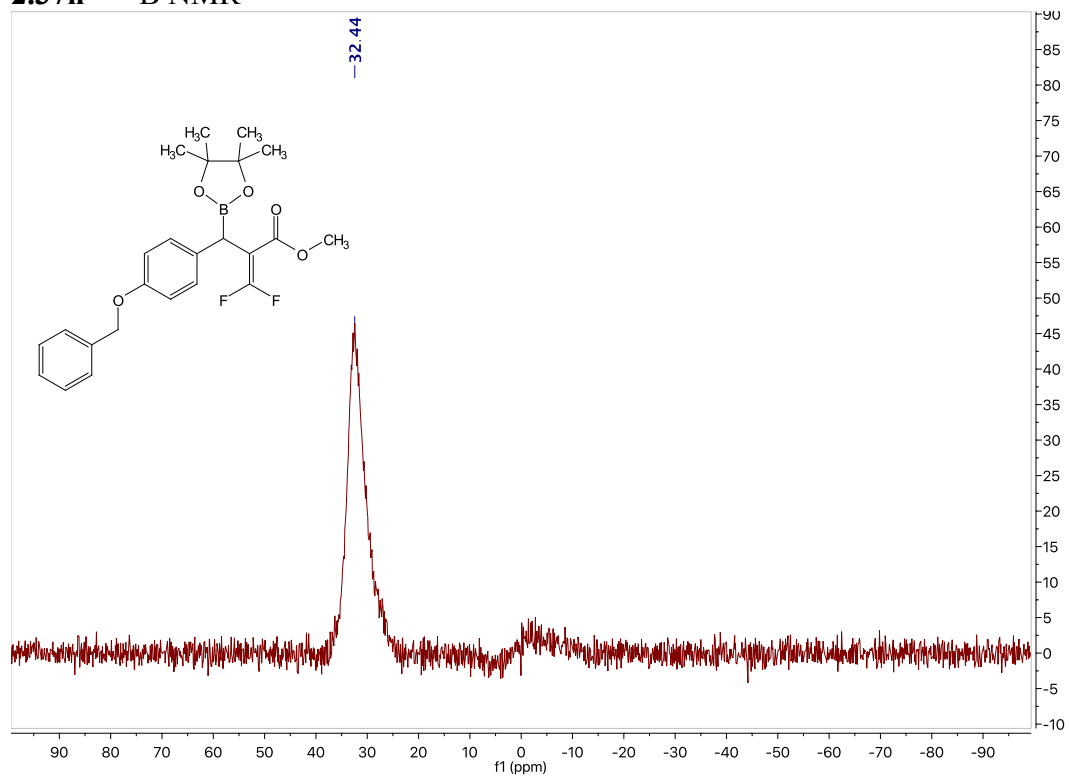




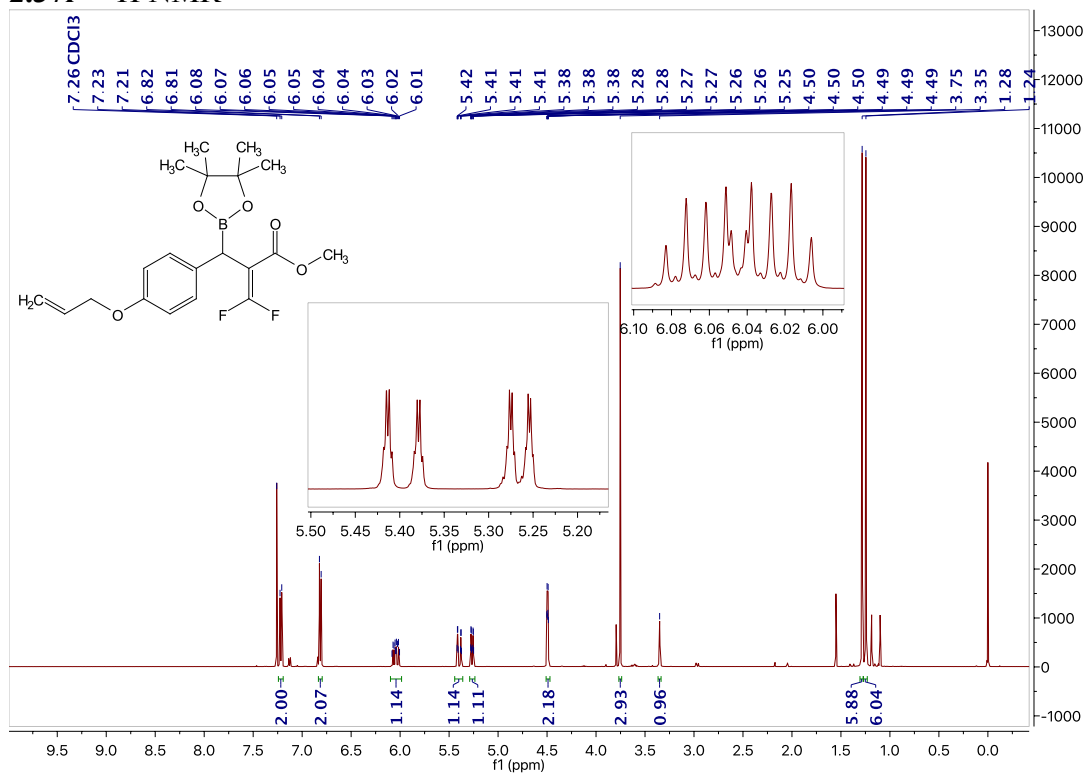
### 2.37h – $^{19}\text{F}$ NMR



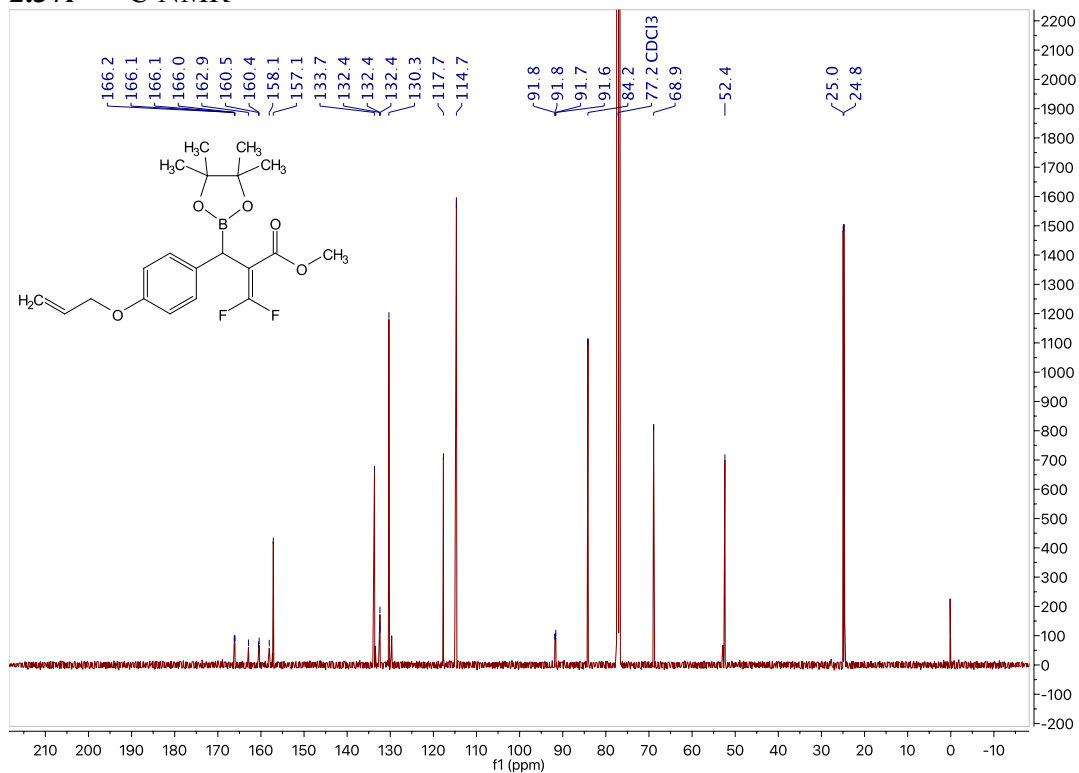
### 2.37h – $^{11}\text{B}$ NMR



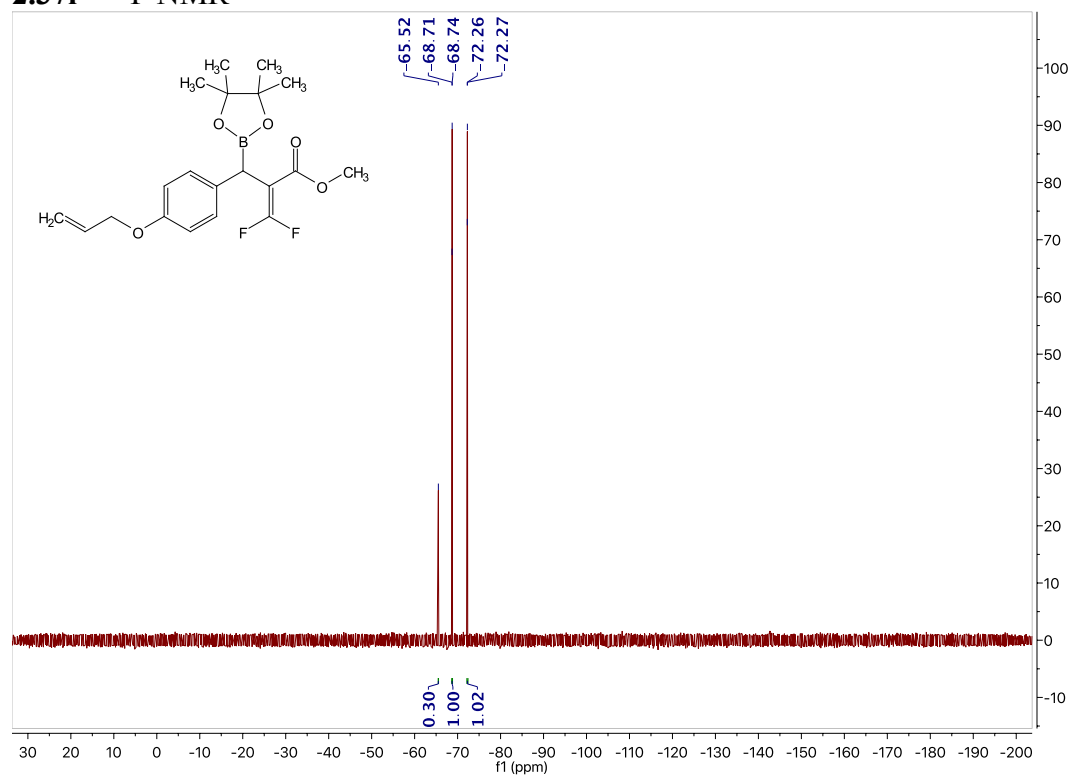
### 2.37i – <sup>1</sup>H NMR



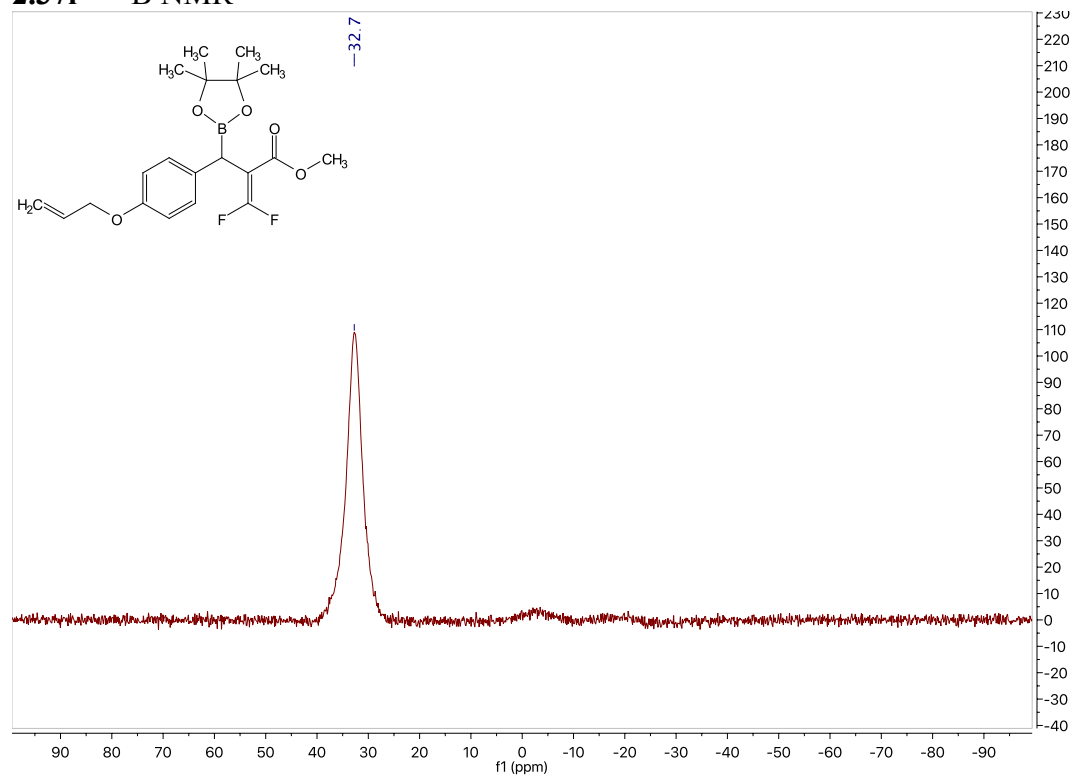
### 2.37i – <sup>13</sup>C NMR



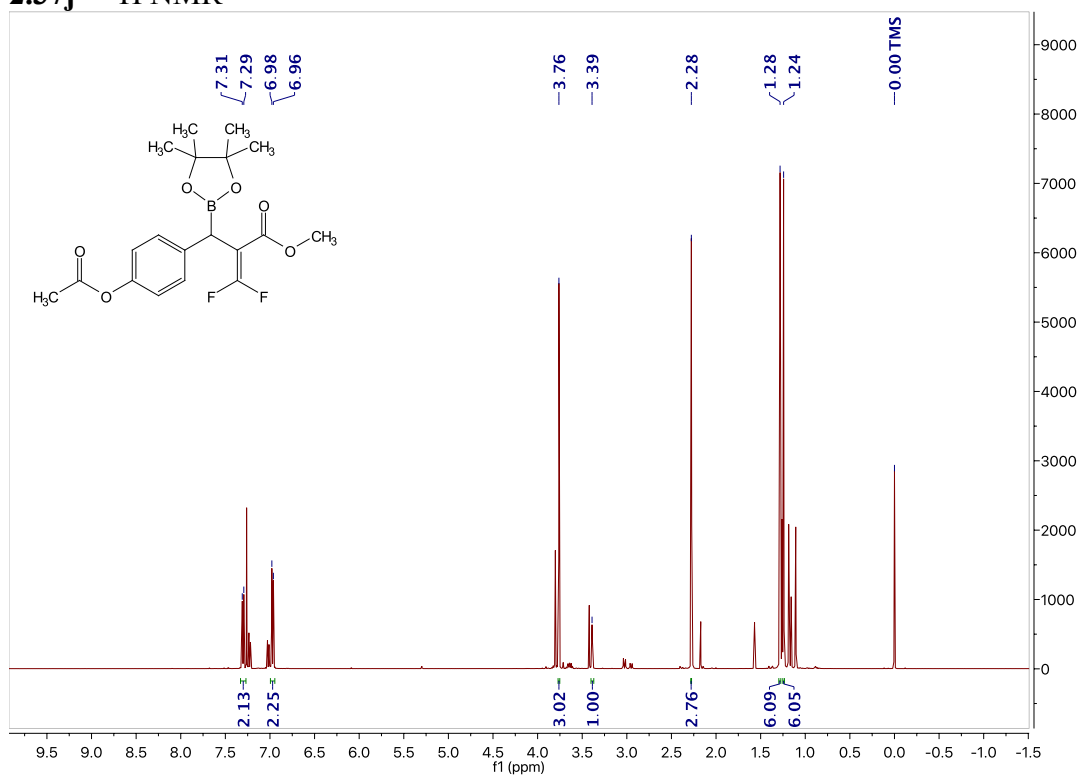
### 2.37i – <sup>19</sup>F NMR



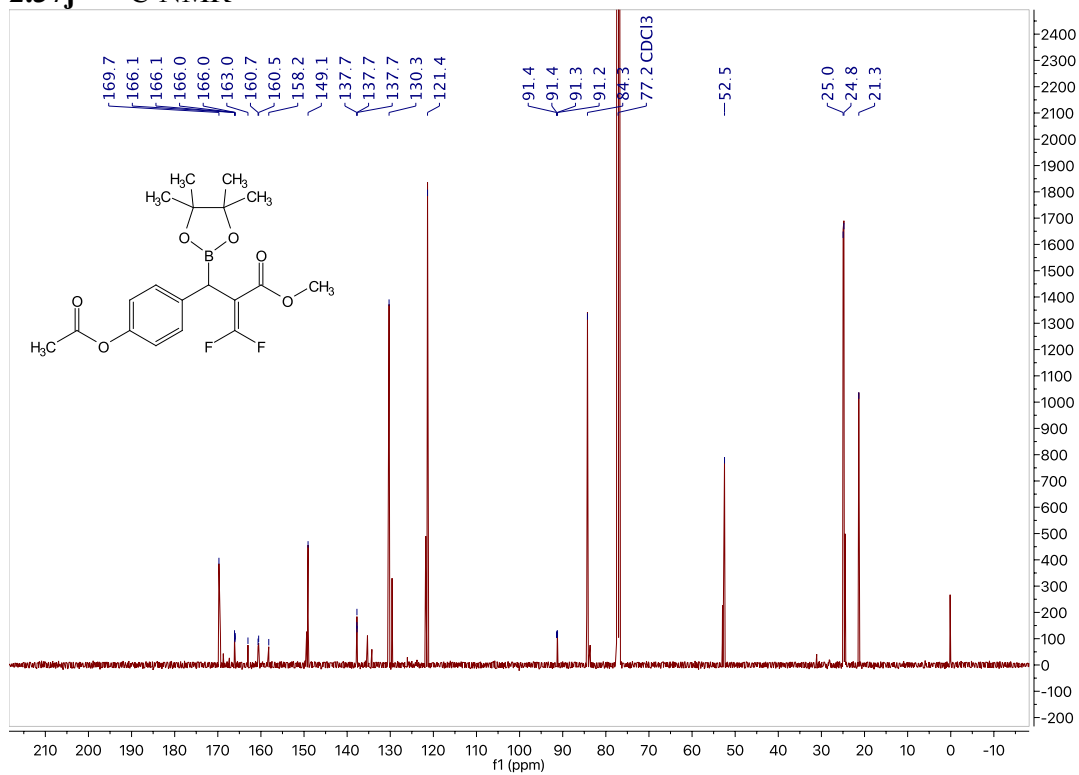
### 2.37i – <sup>11</sup>B NMR



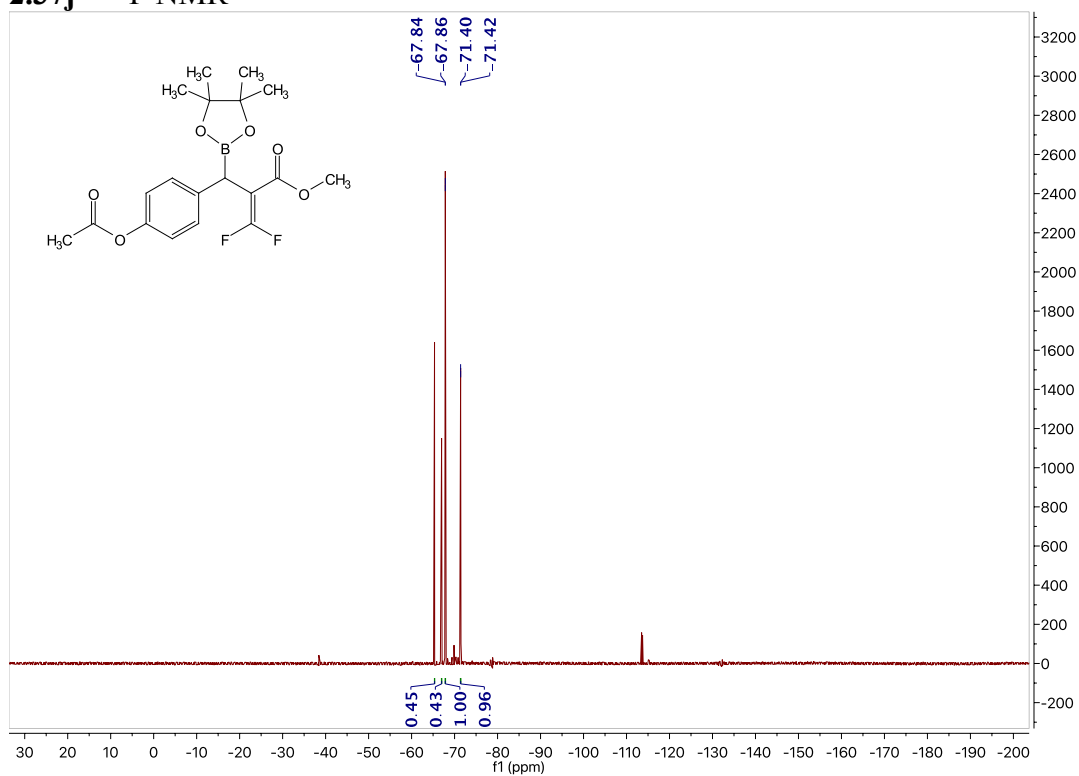
### 2.37j – <sup>1</sup>H NMR



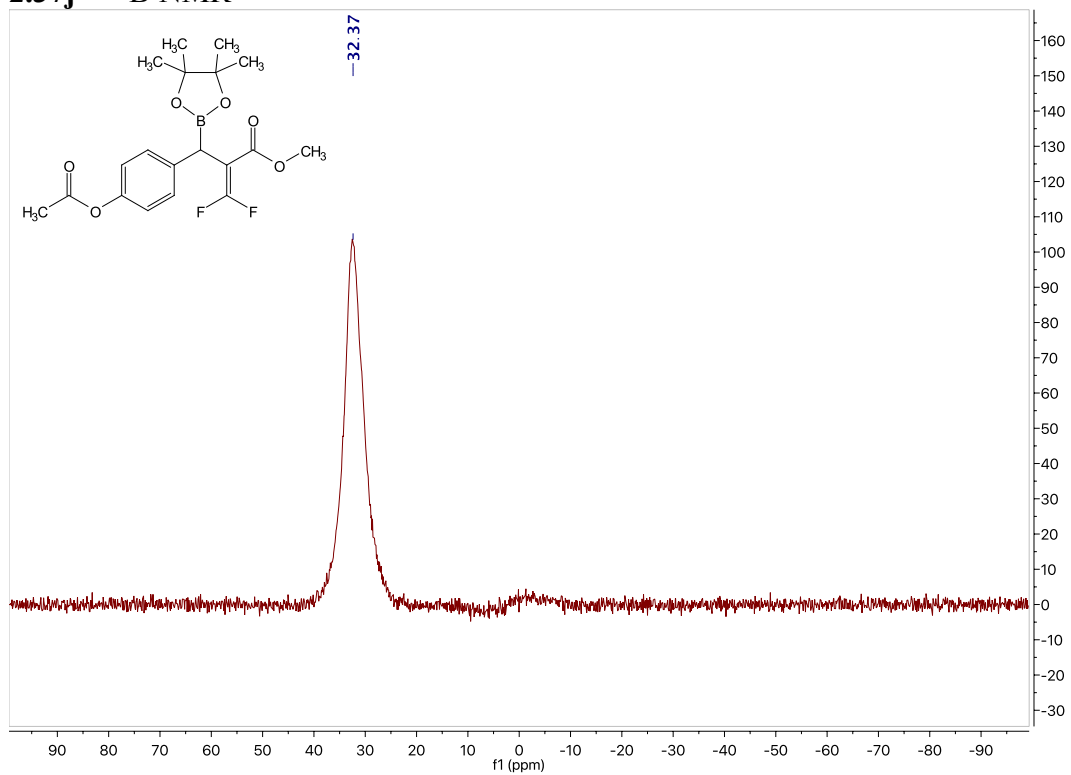
### 2.37j – <sup>13</sup>C NMR



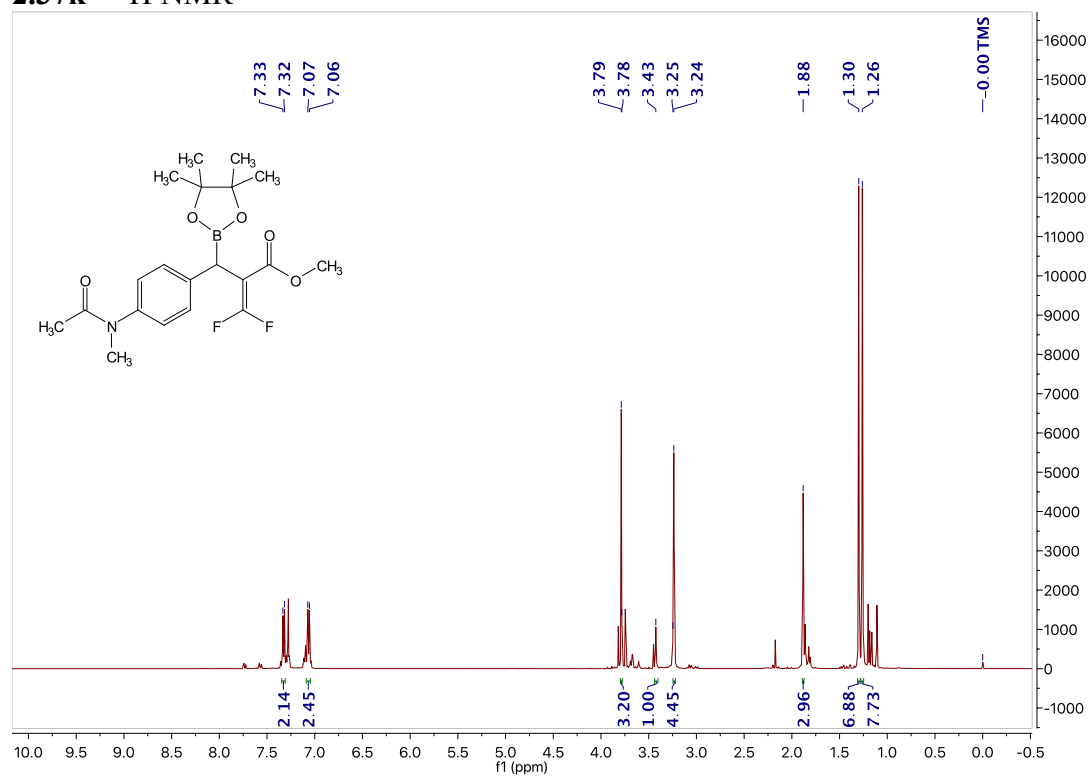
### 2.37j – <sup>19</sup>F NMR



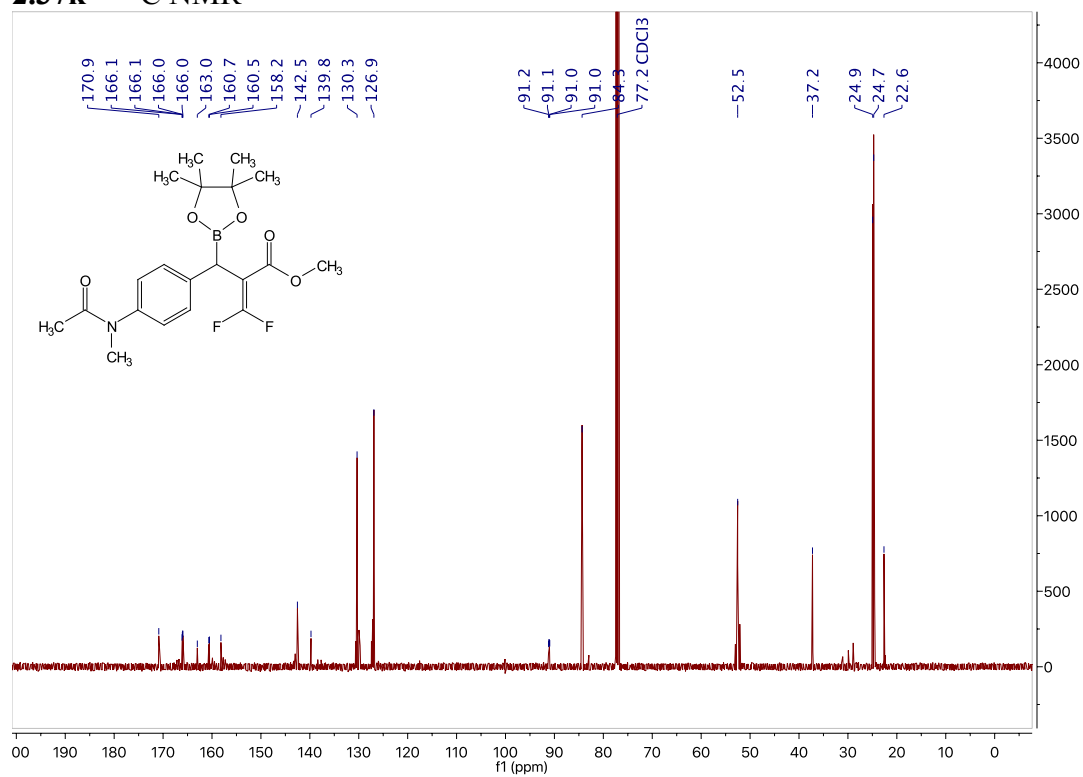
### 2.37j – <sup>11</sup>B NMR



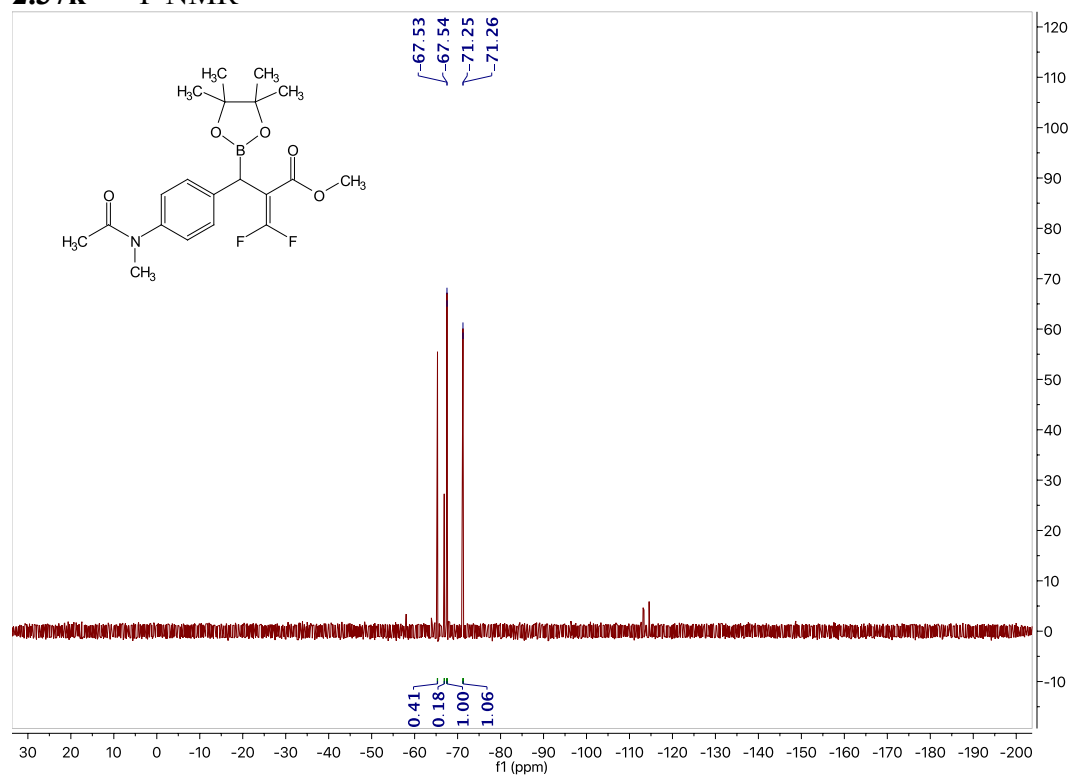
### 2.37k – <sup>1</sup>H NMR



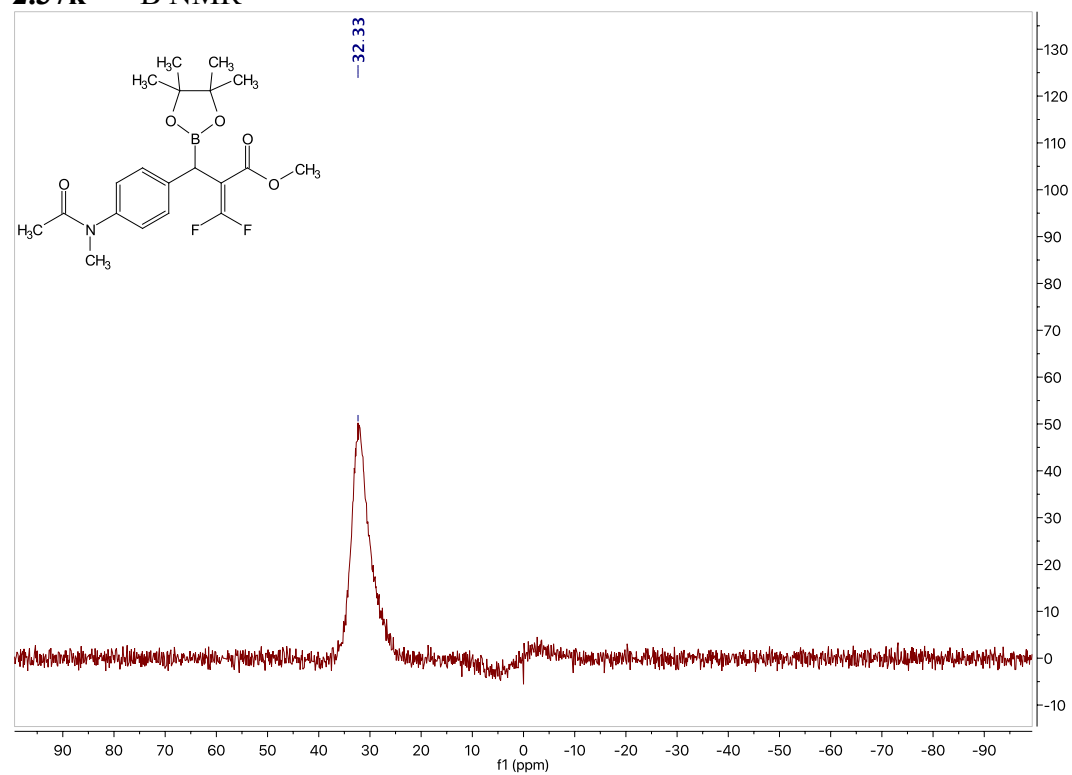
### 2.37k – <sup>13</sup>C NMR



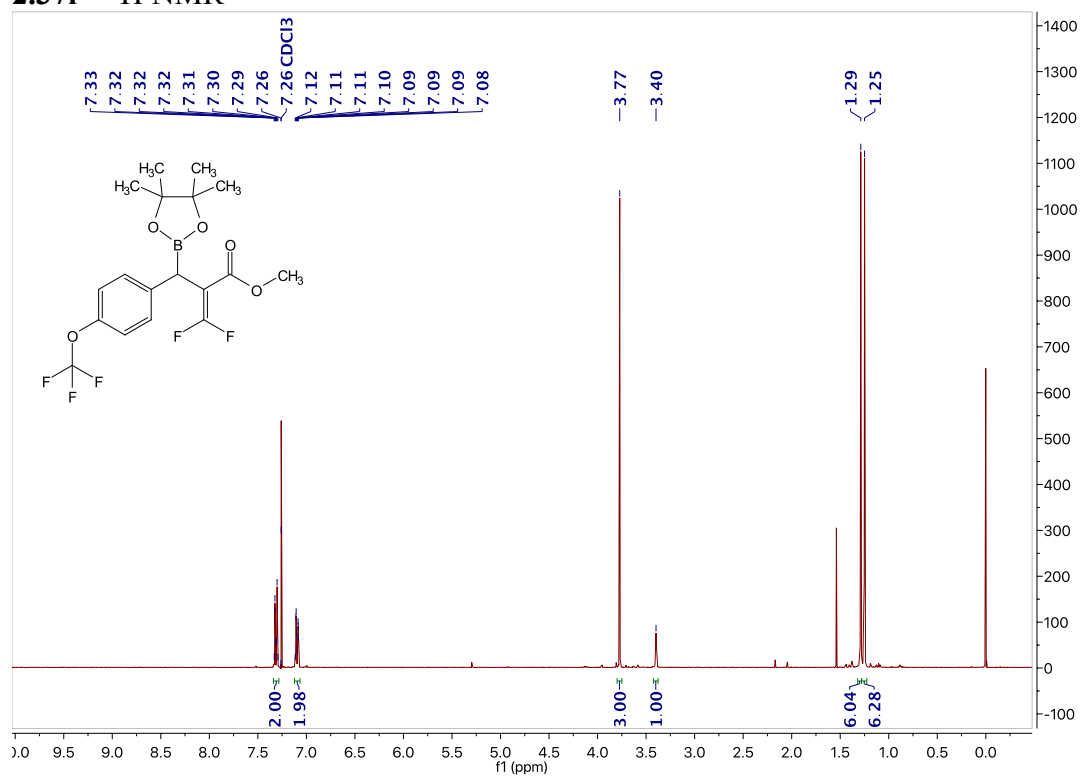
### 2.37k – $^{19}\text{F}$ NMR



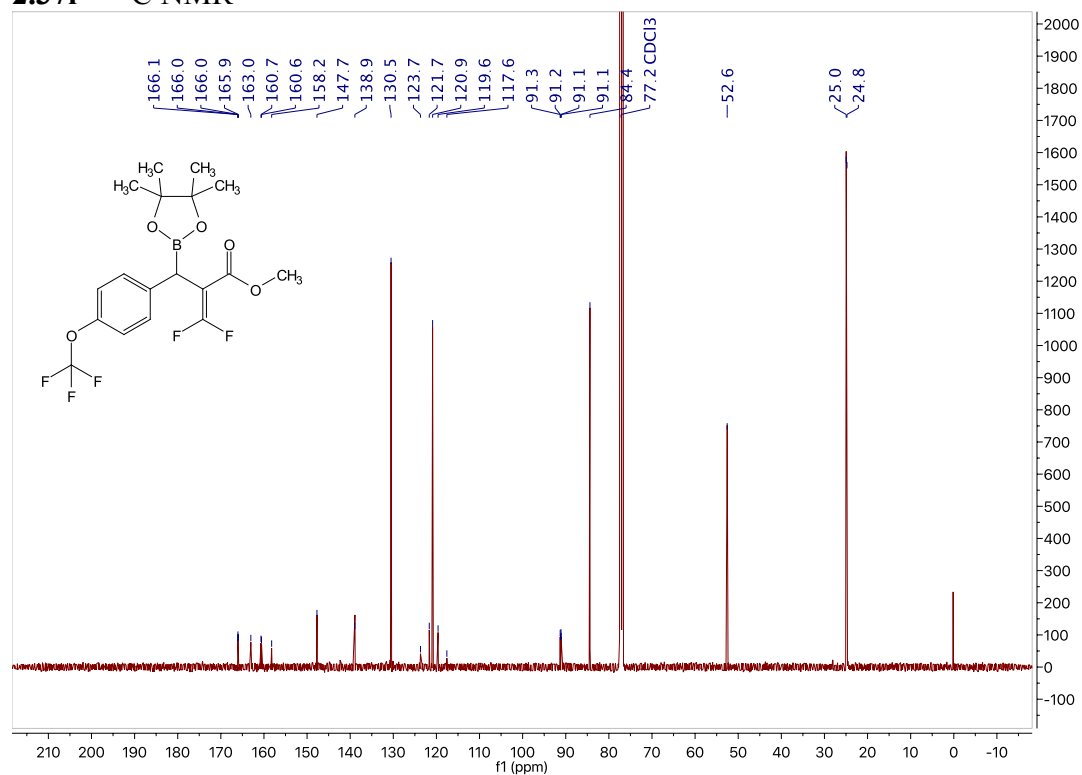
### 2.37k – $^{11}\text{B}$ NMR



## 2.371 – <sup>1</sup>H NMR

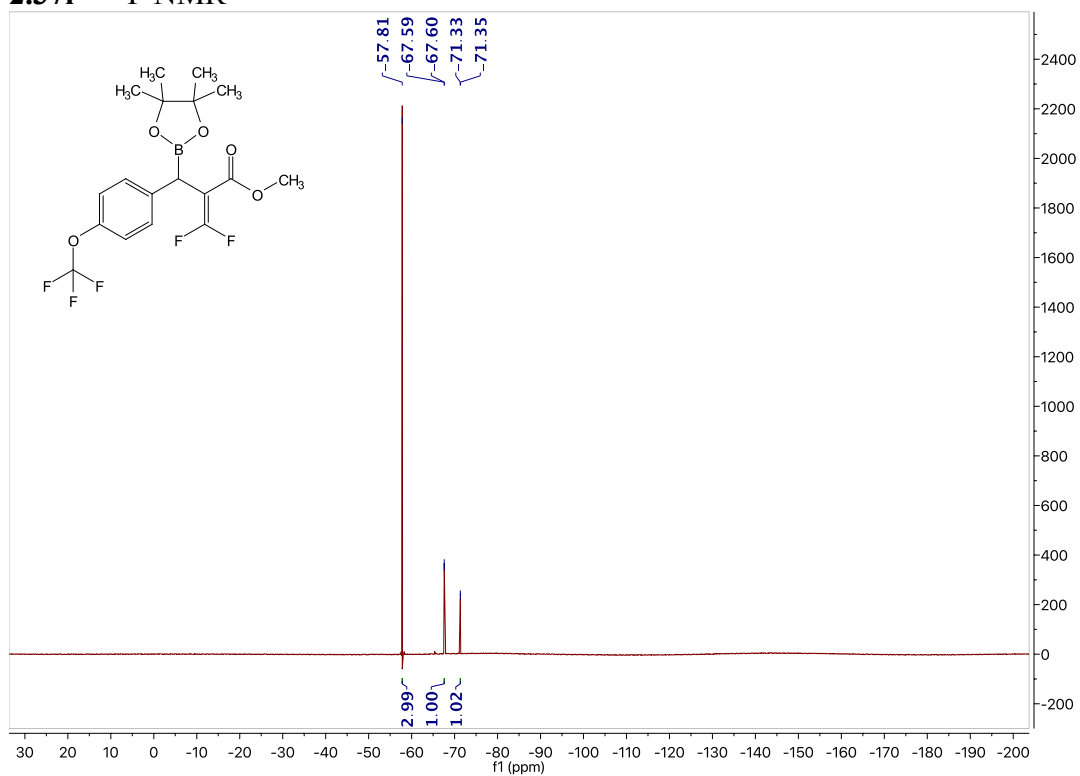


## 2.371 – <sup>13</sup>C NMR

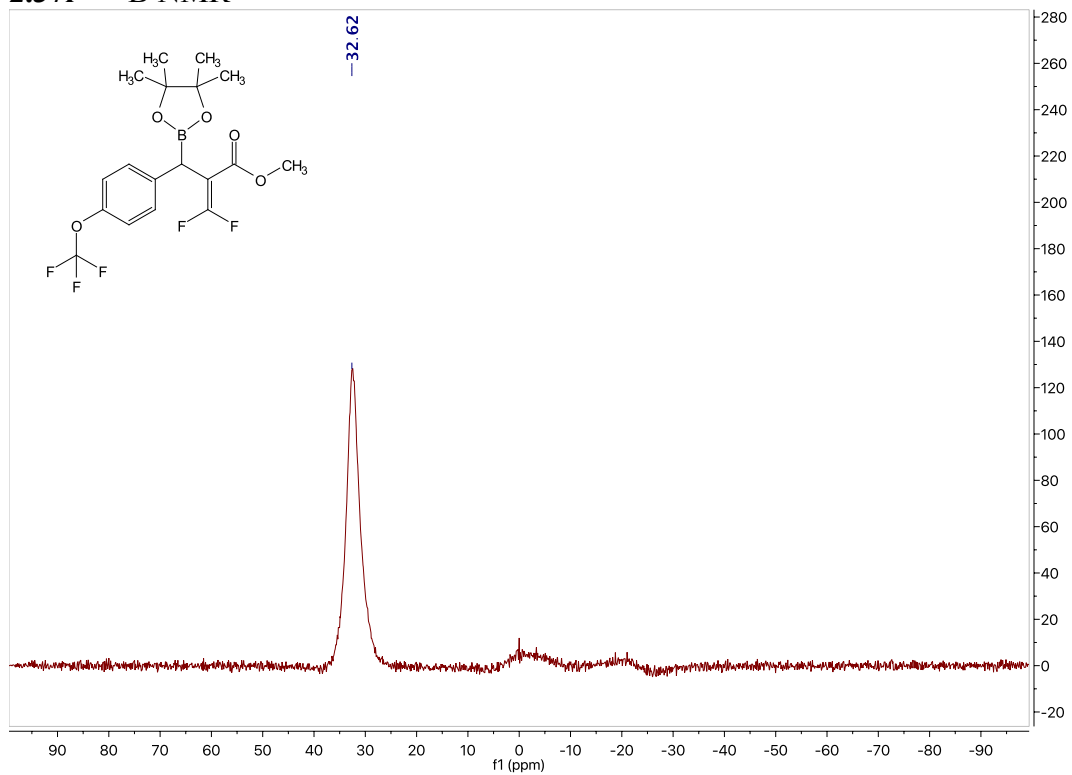




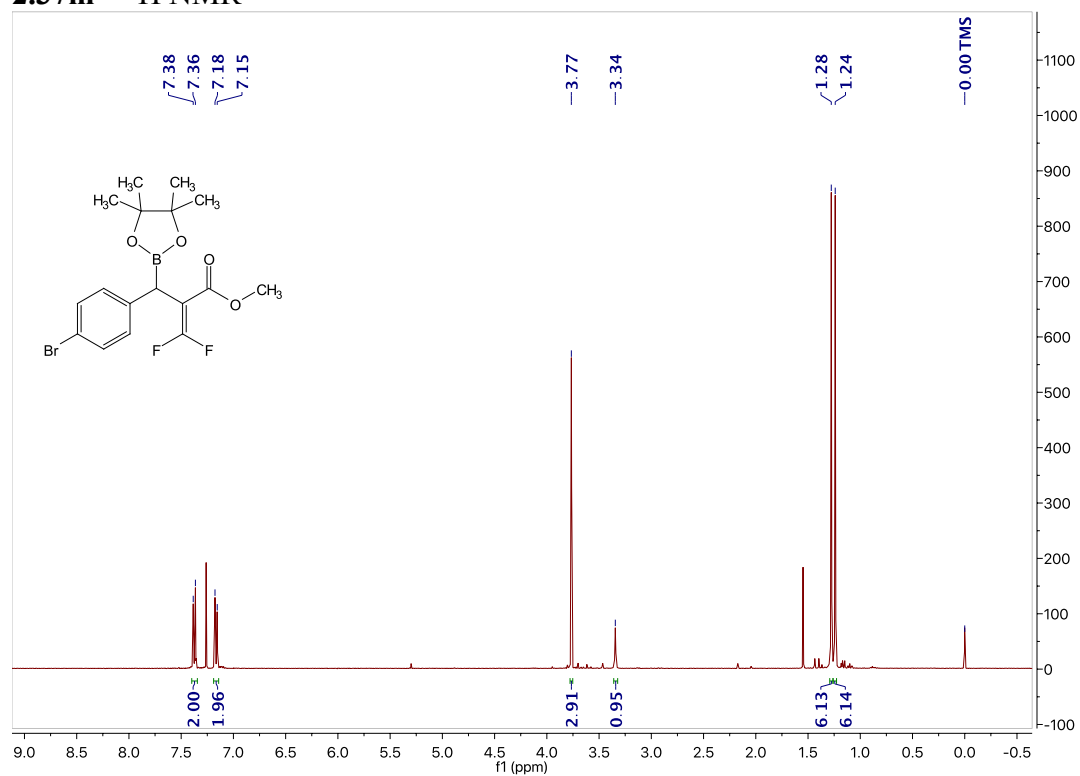
### 2.371 – <sup>19</sup>F NMR



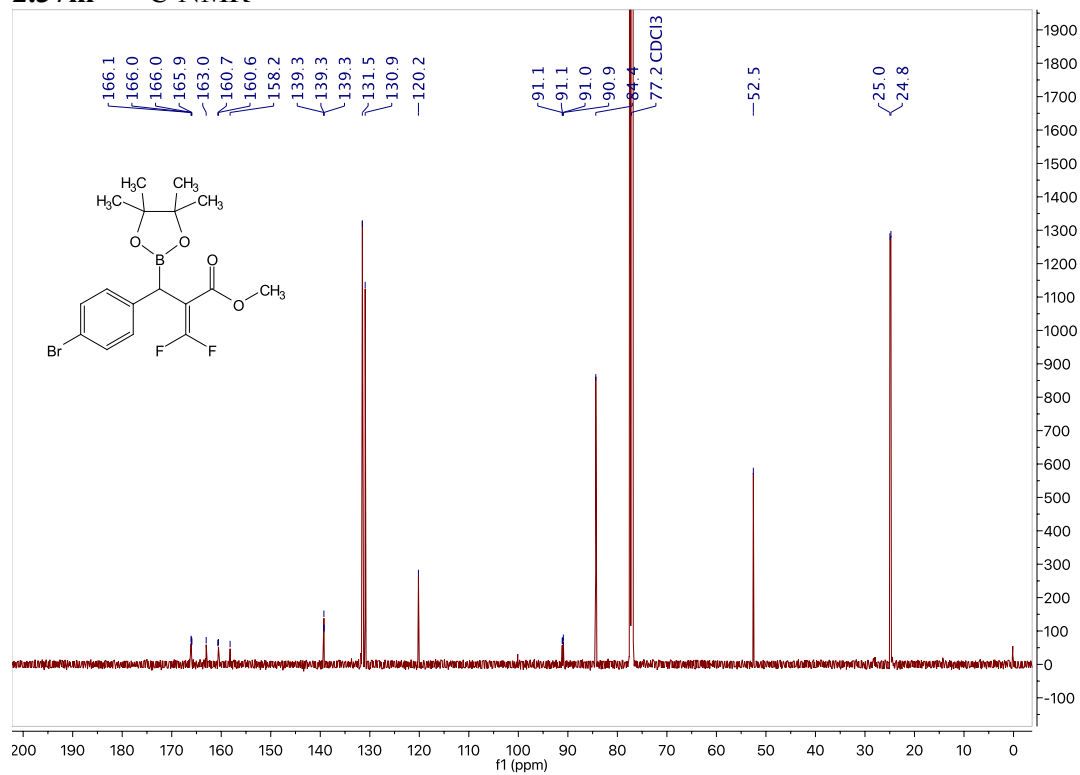
### 2.371 – <sup>11</sup>B NMR



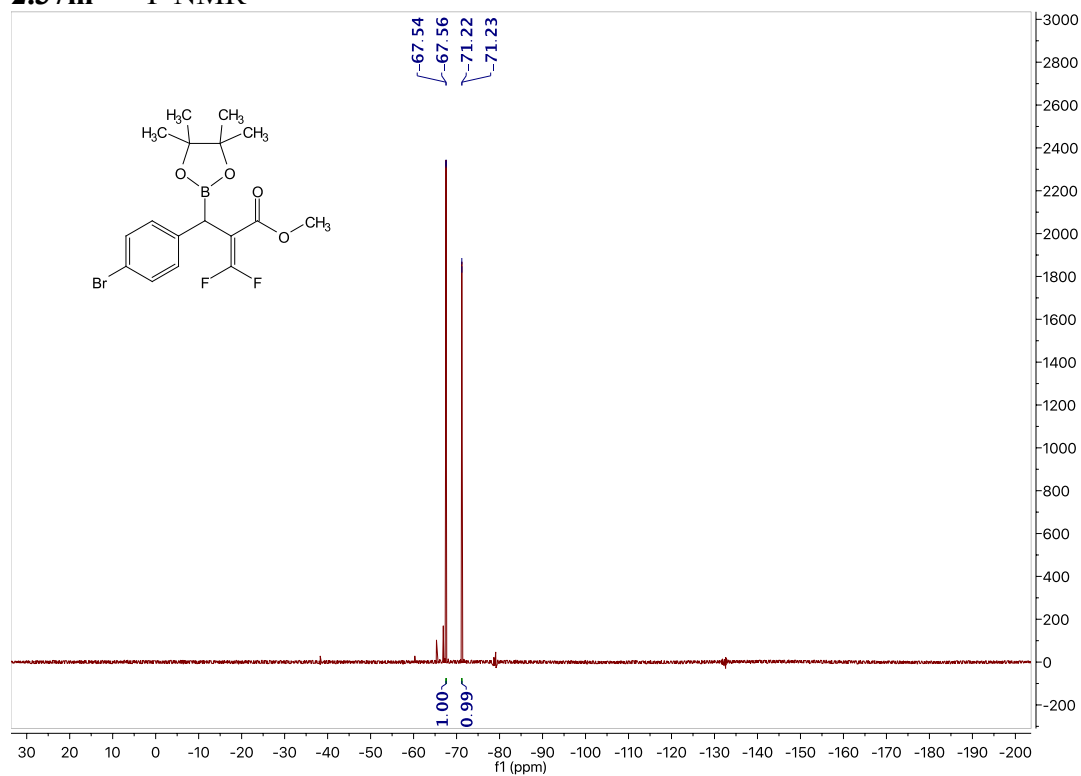
### 2.37m – <sup>1</sup>H NMR



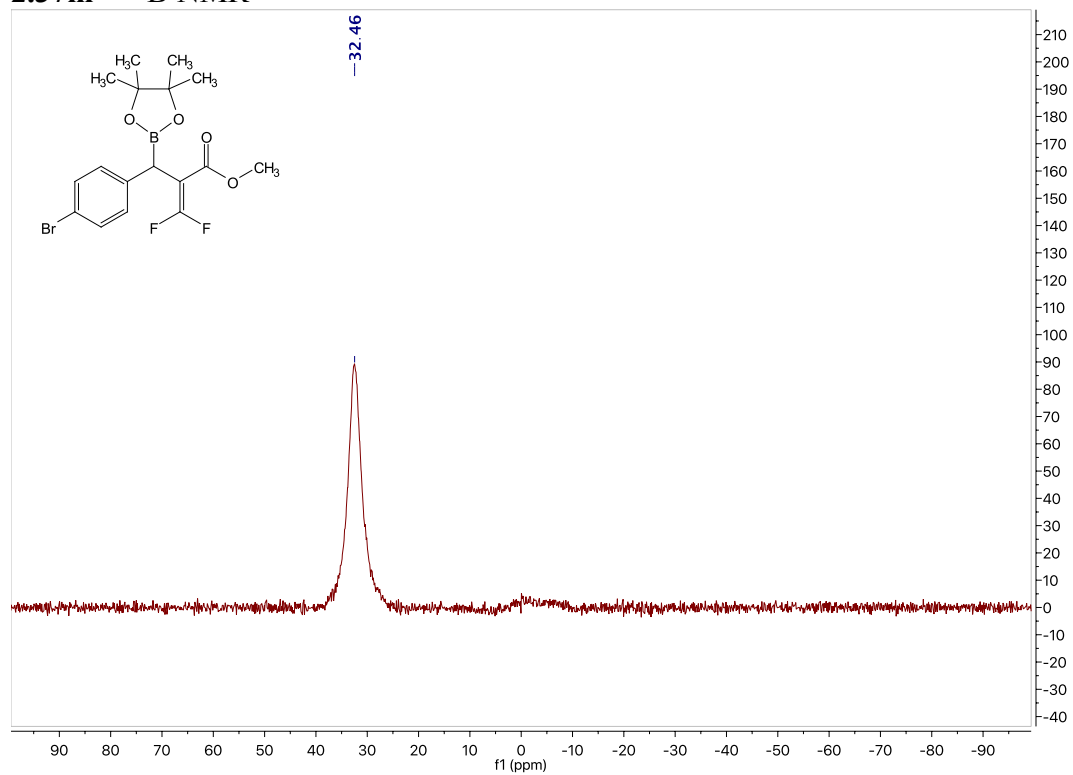
### 2.37m – <sup>13</sup>C NMR



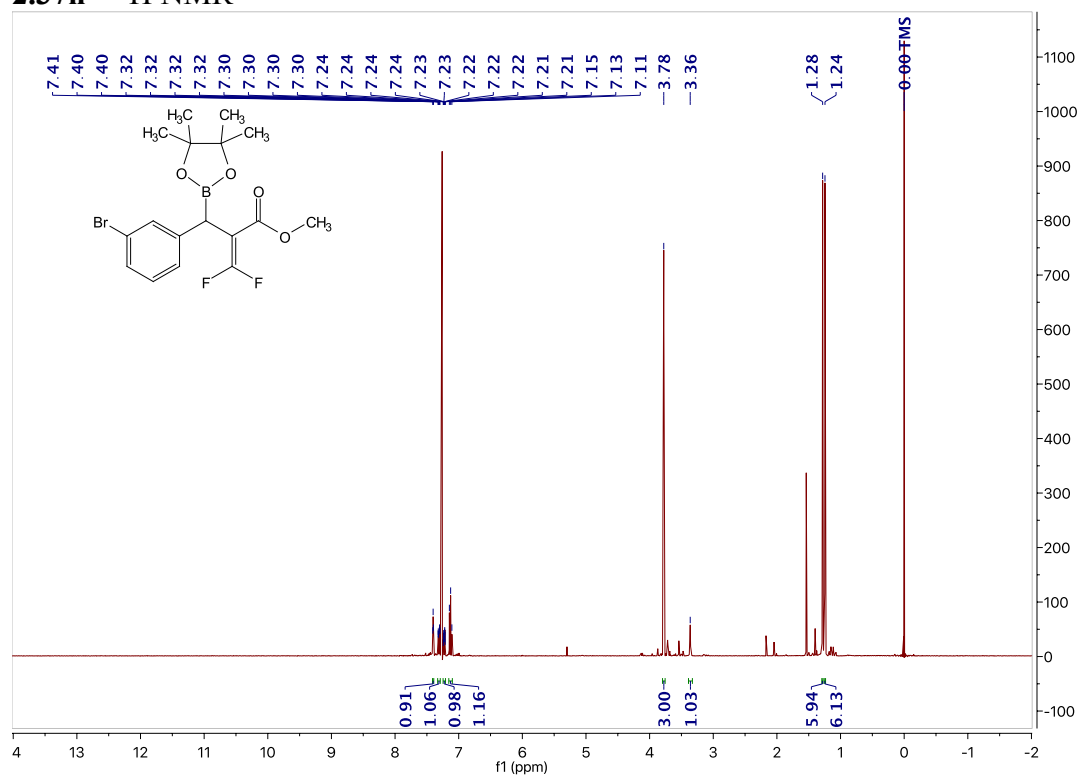
### 2.37m – $^{19}\text{F}$ NMR



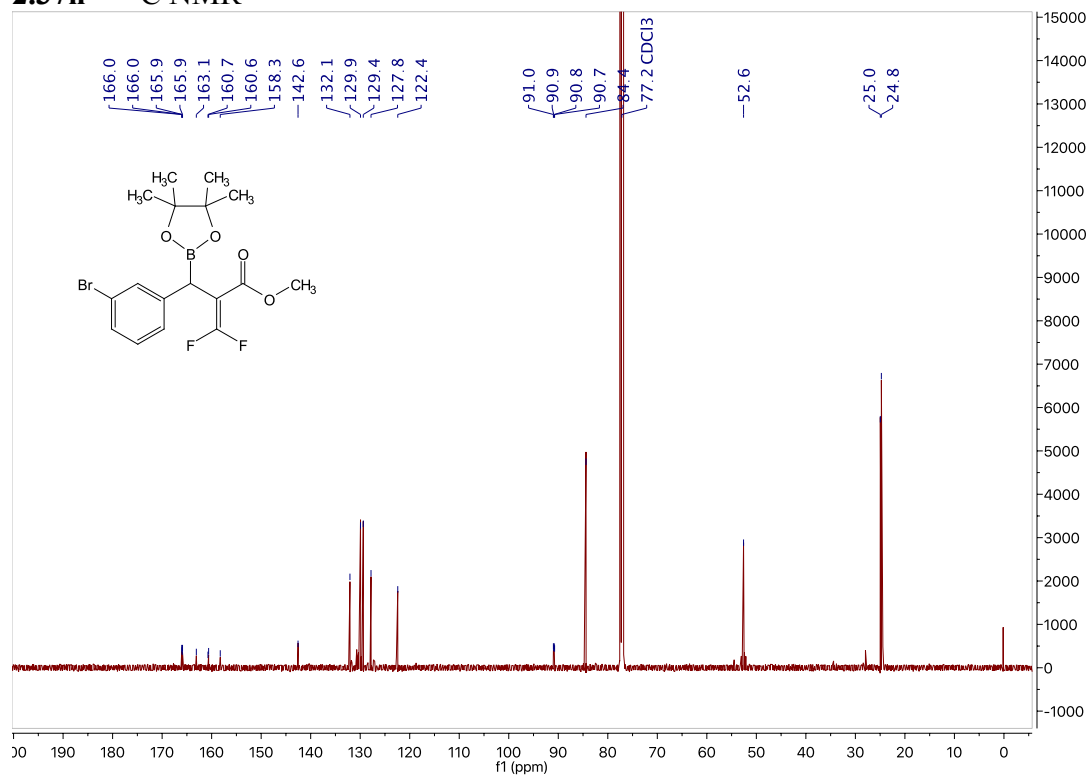
### 2.37m – $^{11}\text{B}$ NMR



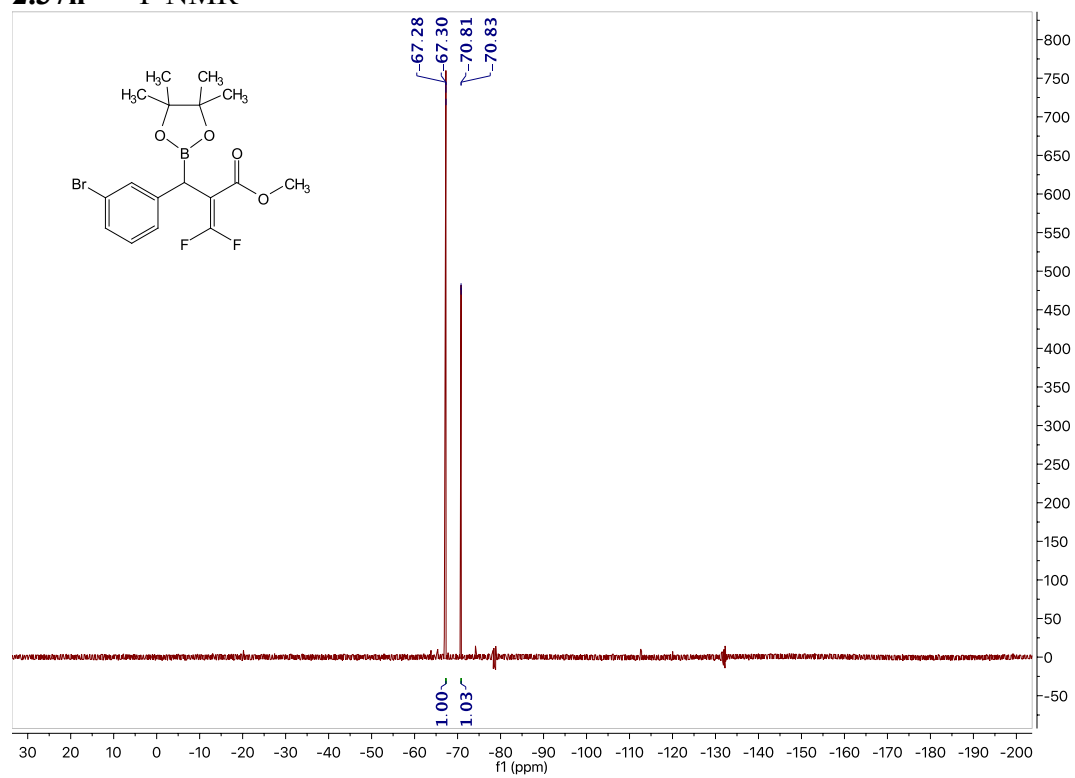
### 2.37n – <sup>1</sup>H NMR



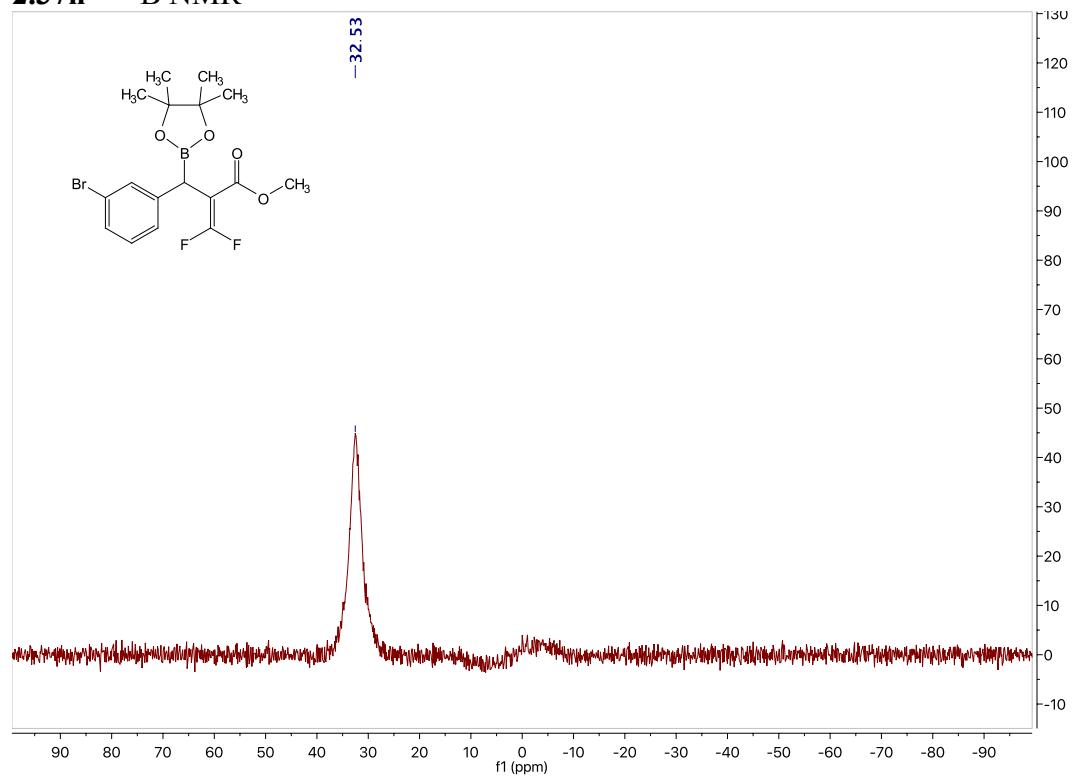
### 2.37n – <sup>13</sup>C NMR



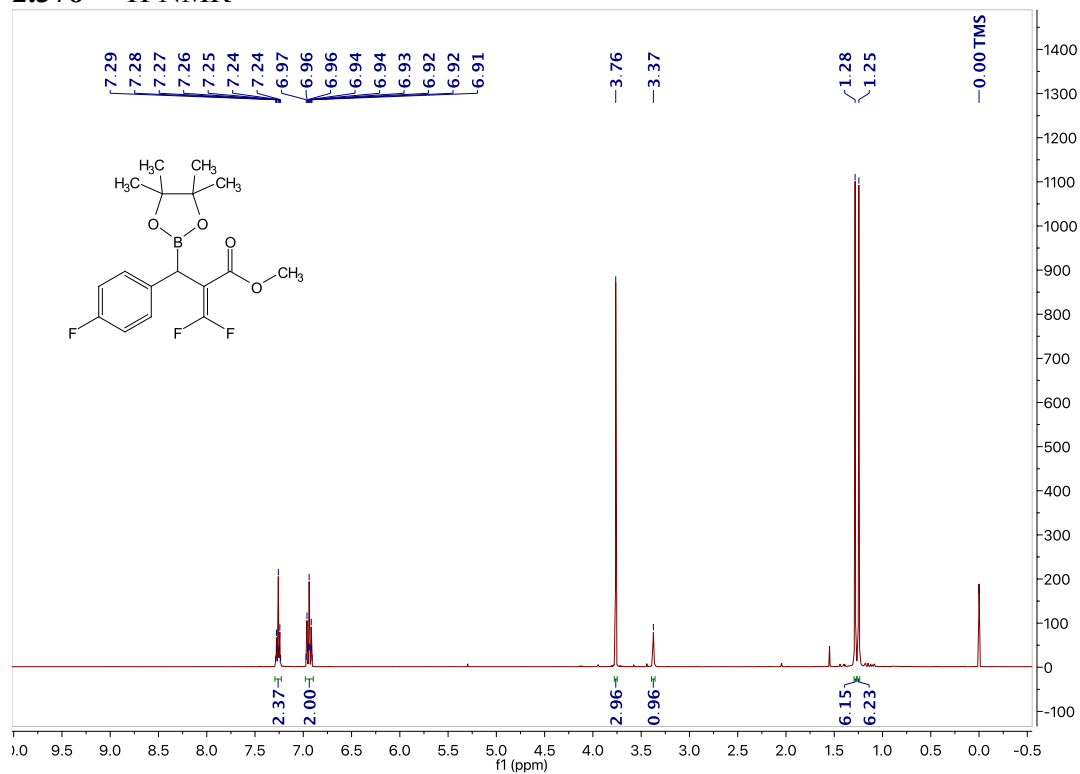
### 2.37n – $^{19}\text{F}$ NMR



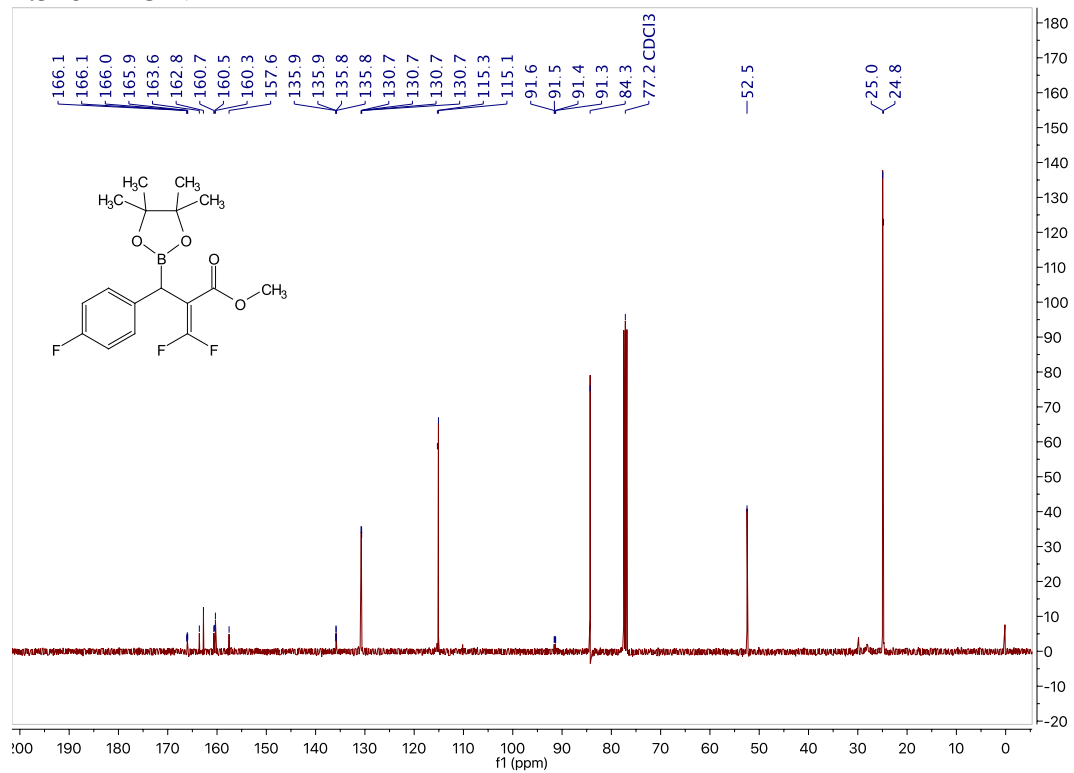
### 2.37n – $^{11}\text{B}$ NMR



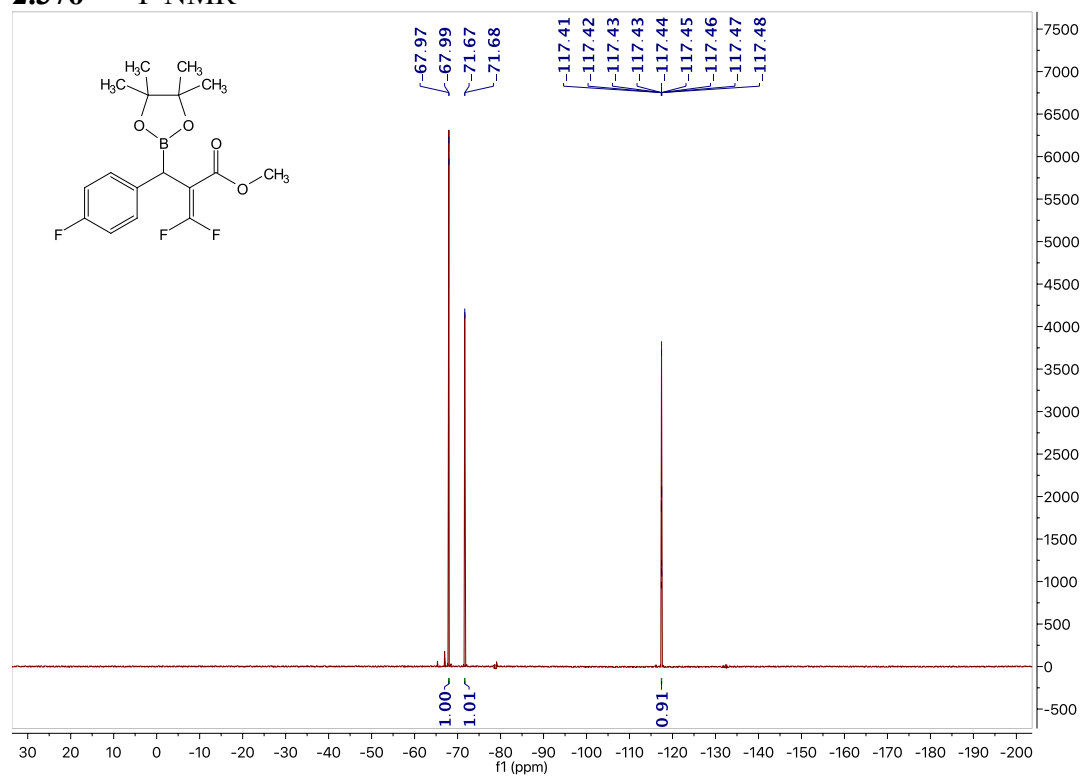
### 2.37o – <sup>1</sup>H NMR



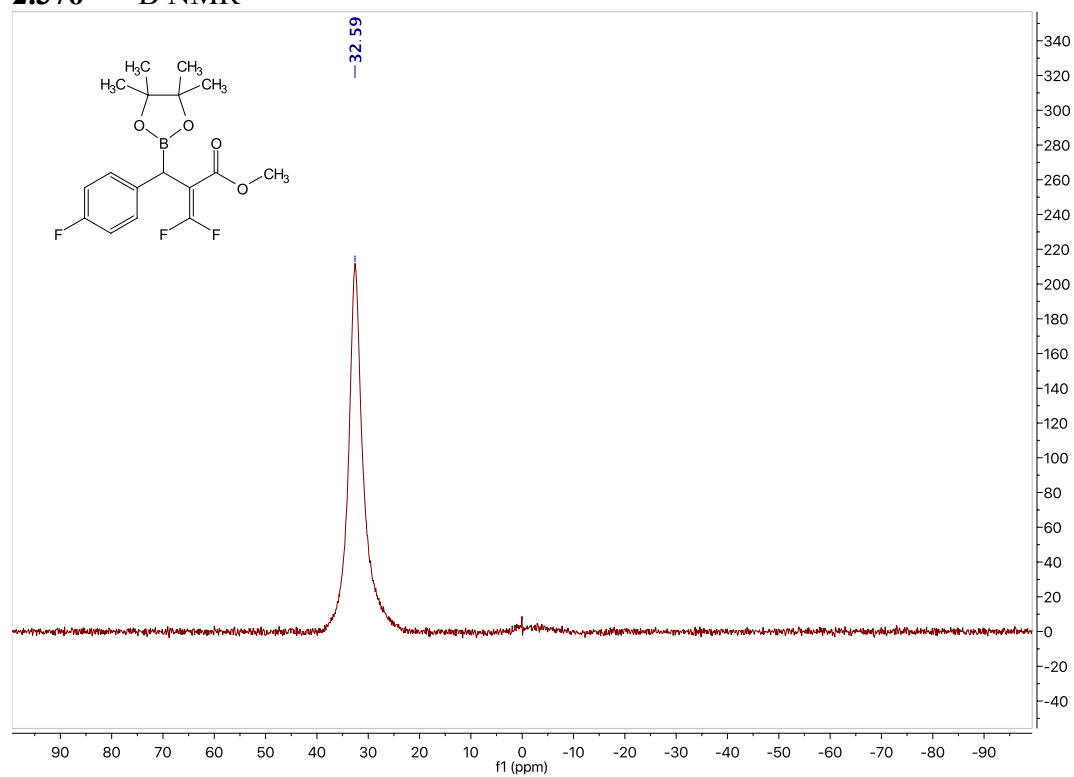
### 2.37o – <sup>13</sup>C NMR



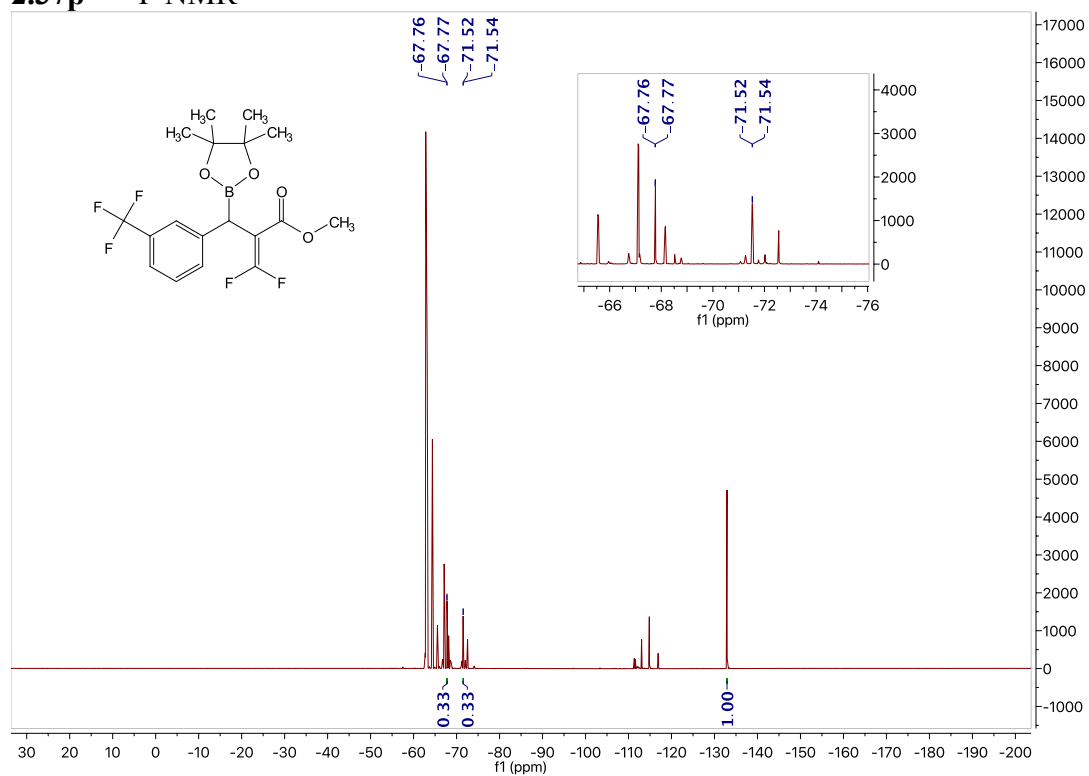
### 2.37o – <sup>19</sup>F NMR



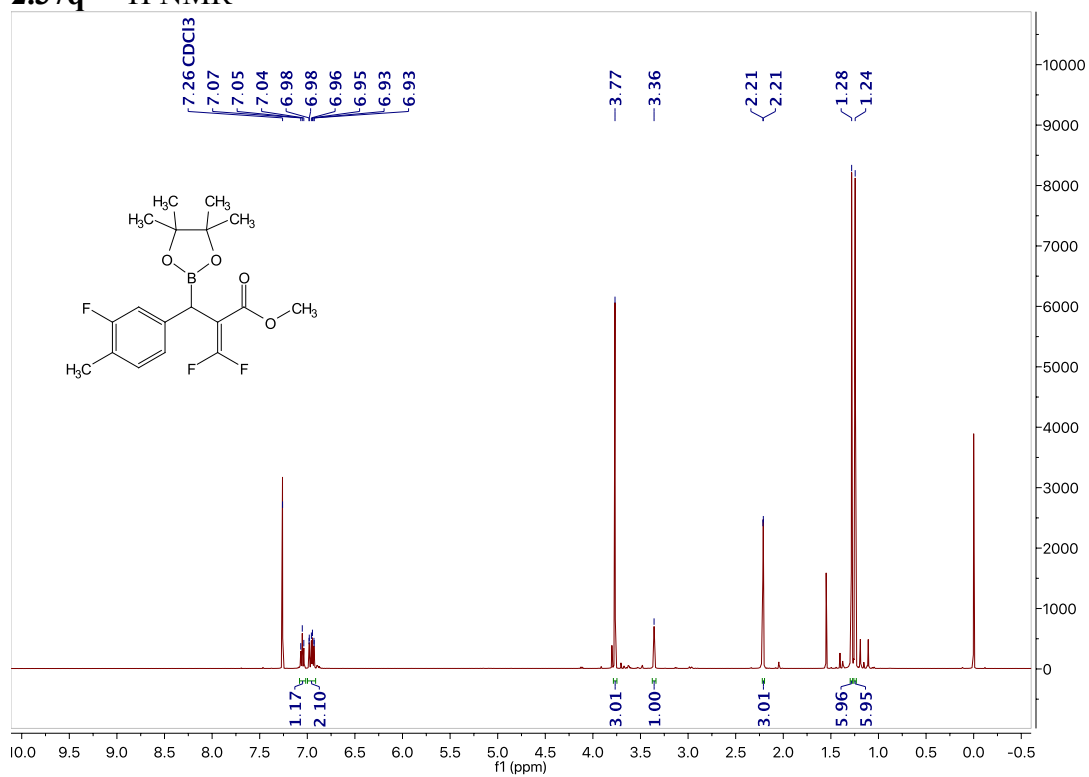
### 2.37o – <sup>11</sup>B NMR



### 2.37p – $^{19}\text{F}$ NMR

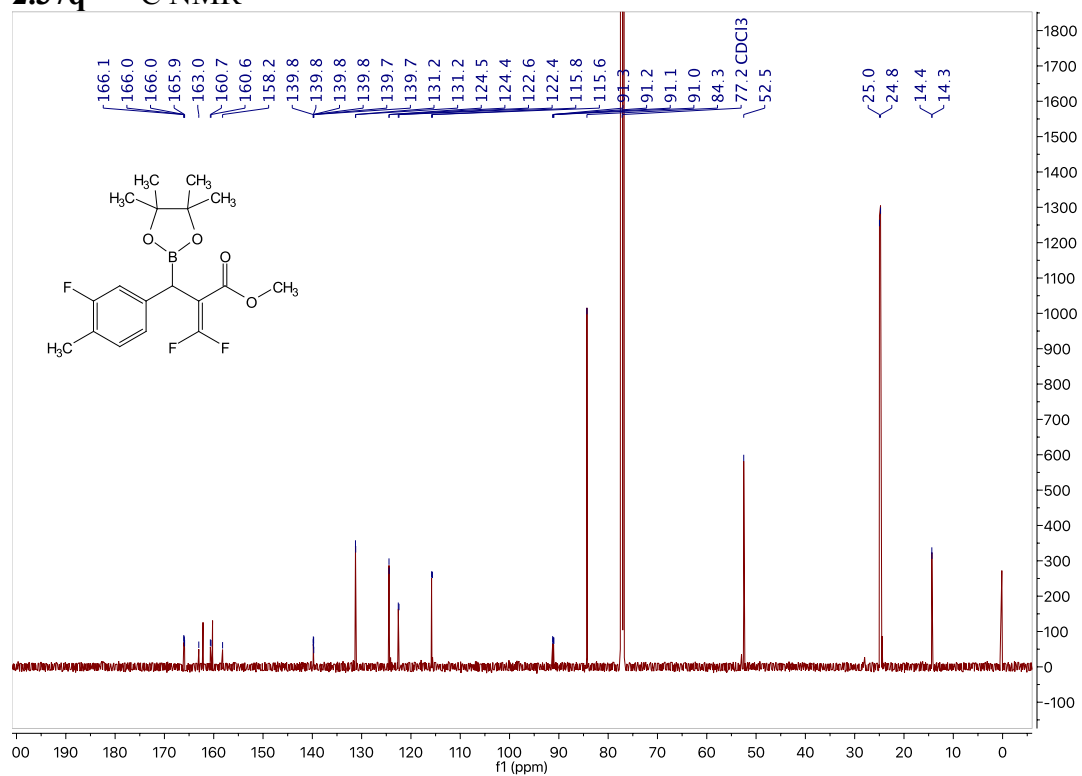


### 2.37q – $^1\text{H}$ NMR

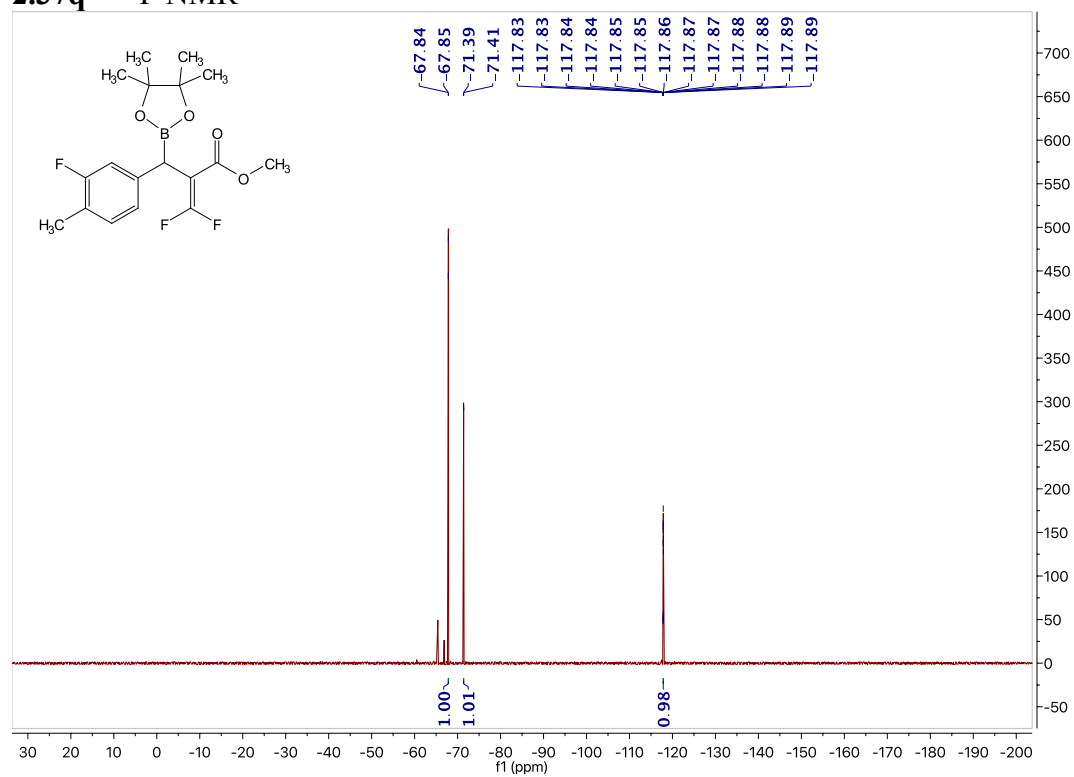




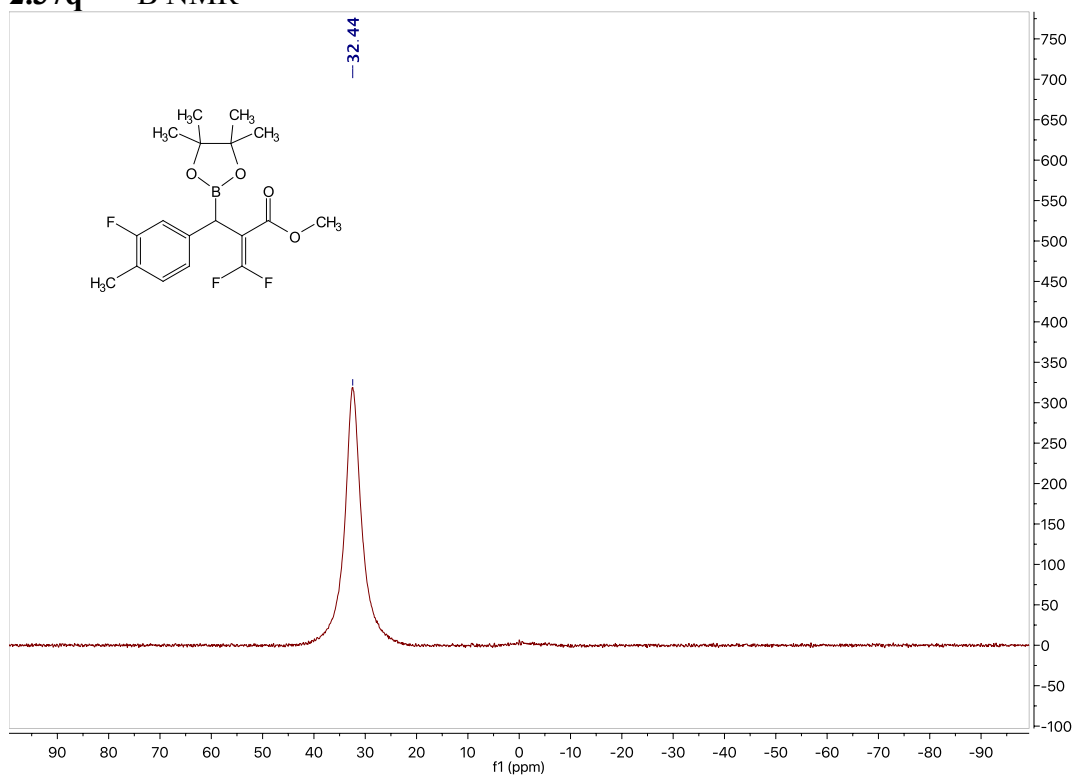
### 2.37q – <sup>13</sup>C NMR



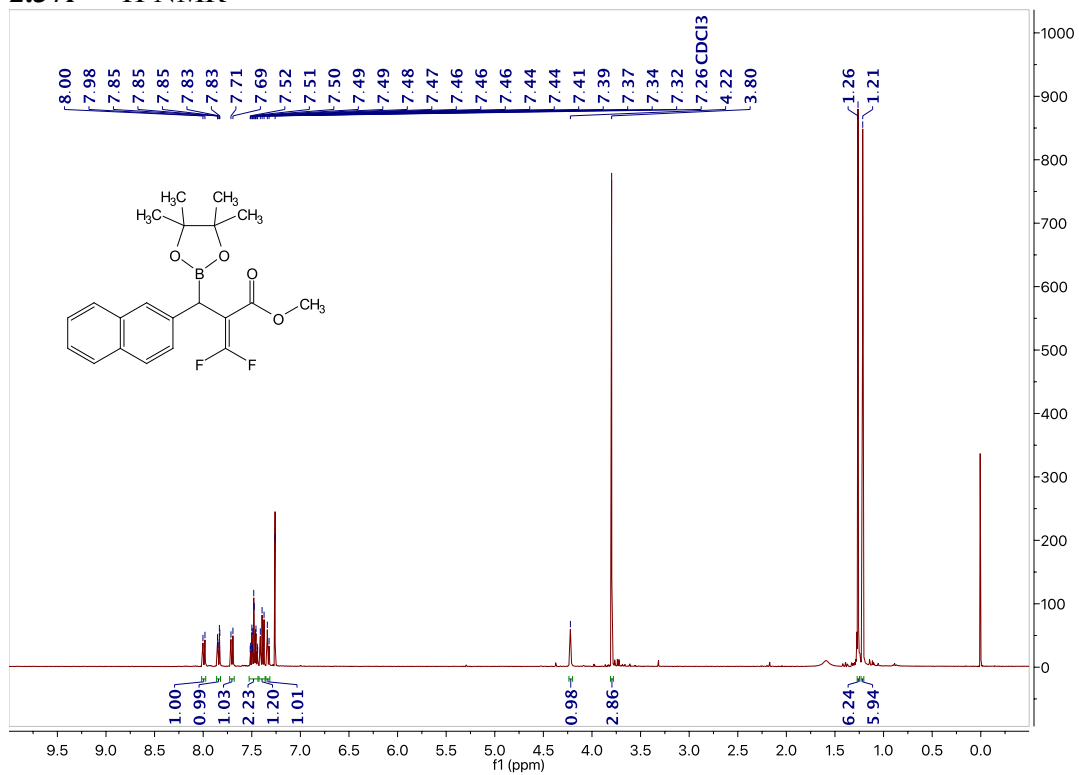
### 2.37q – <sup>19</sup>F NMR



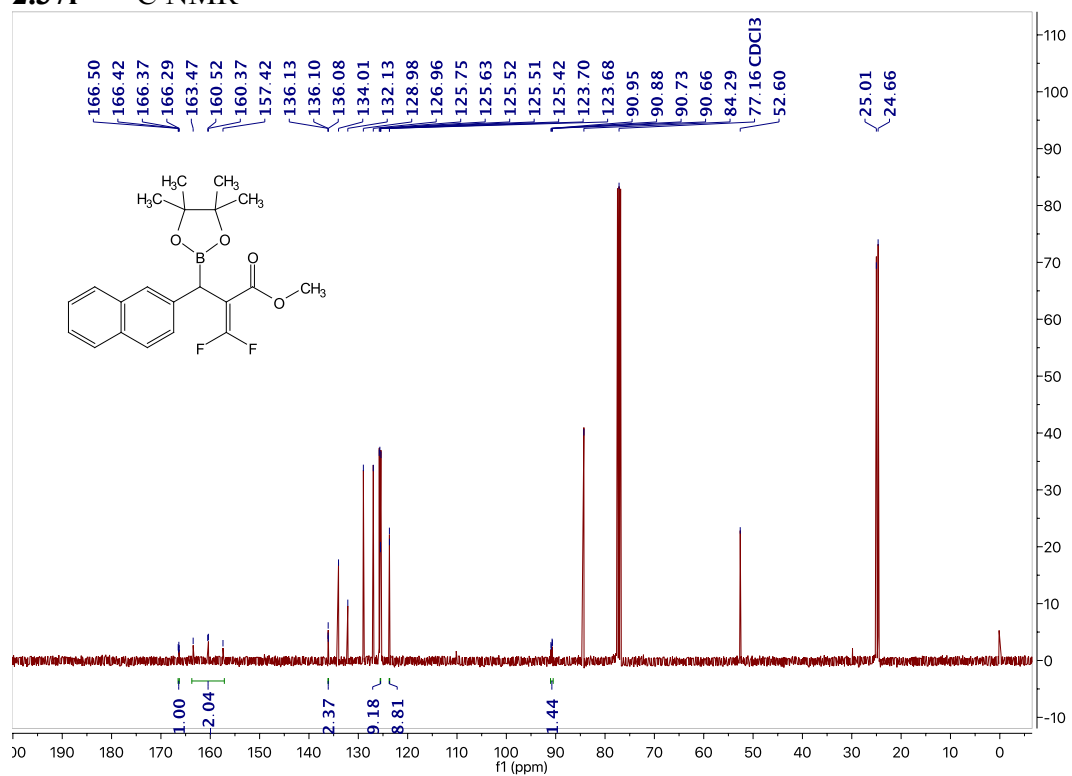
2.37q –  $^{11}\text{B}$  NMR



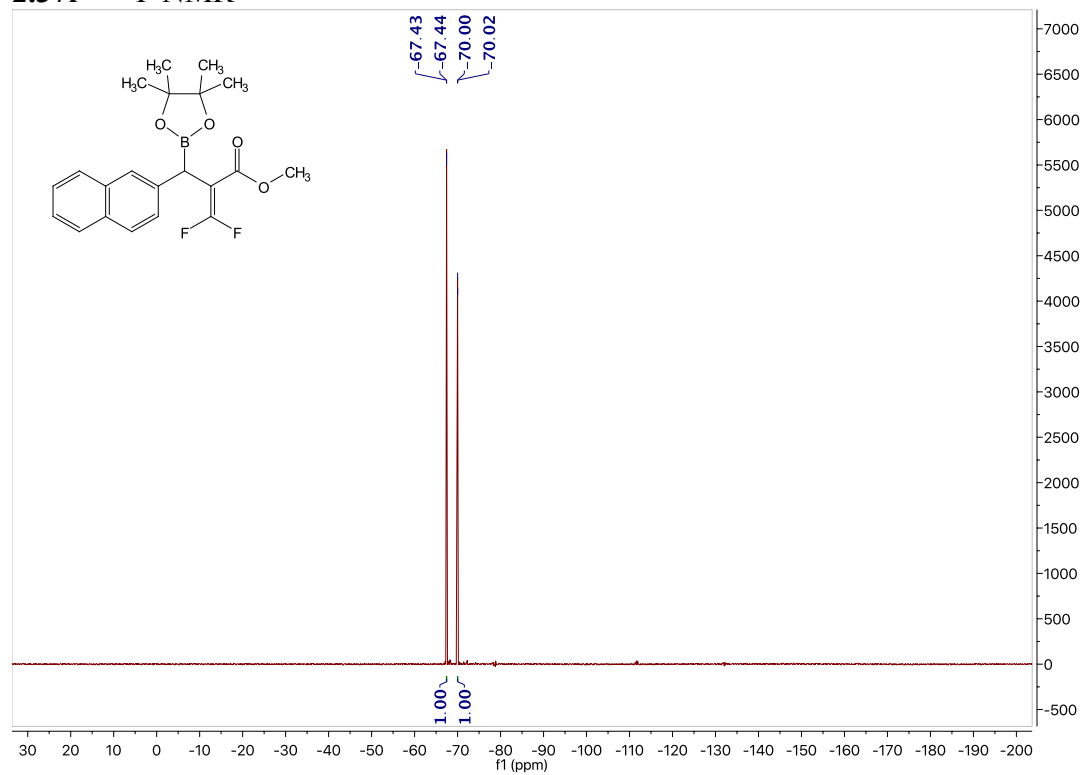
2.37r –  $^1\text{H}$  NMR



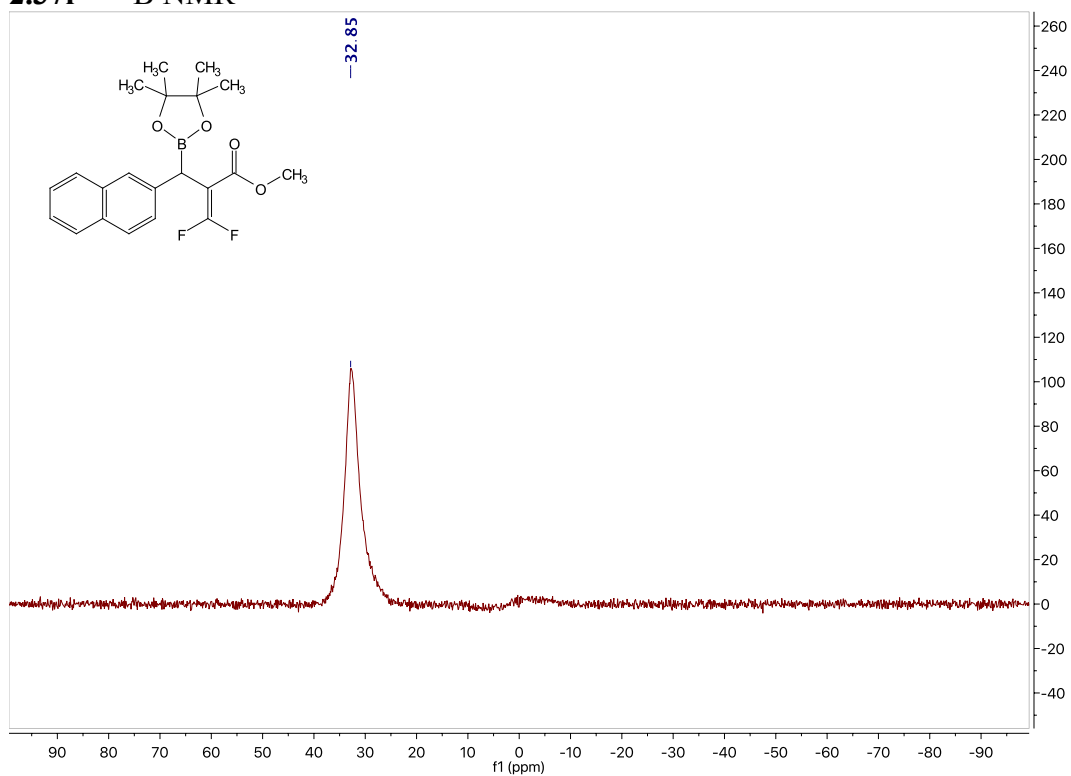
2.37r – <sup>13</sup>C NMR



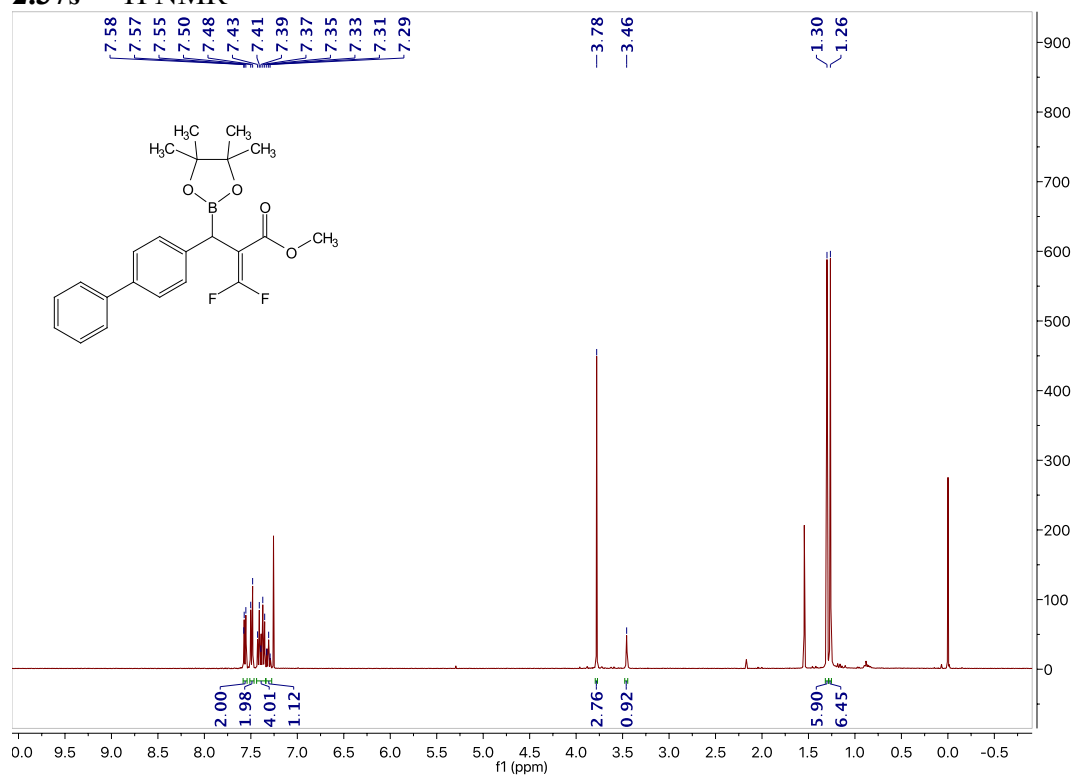
2.37r – <sup>19</sup>F NMR



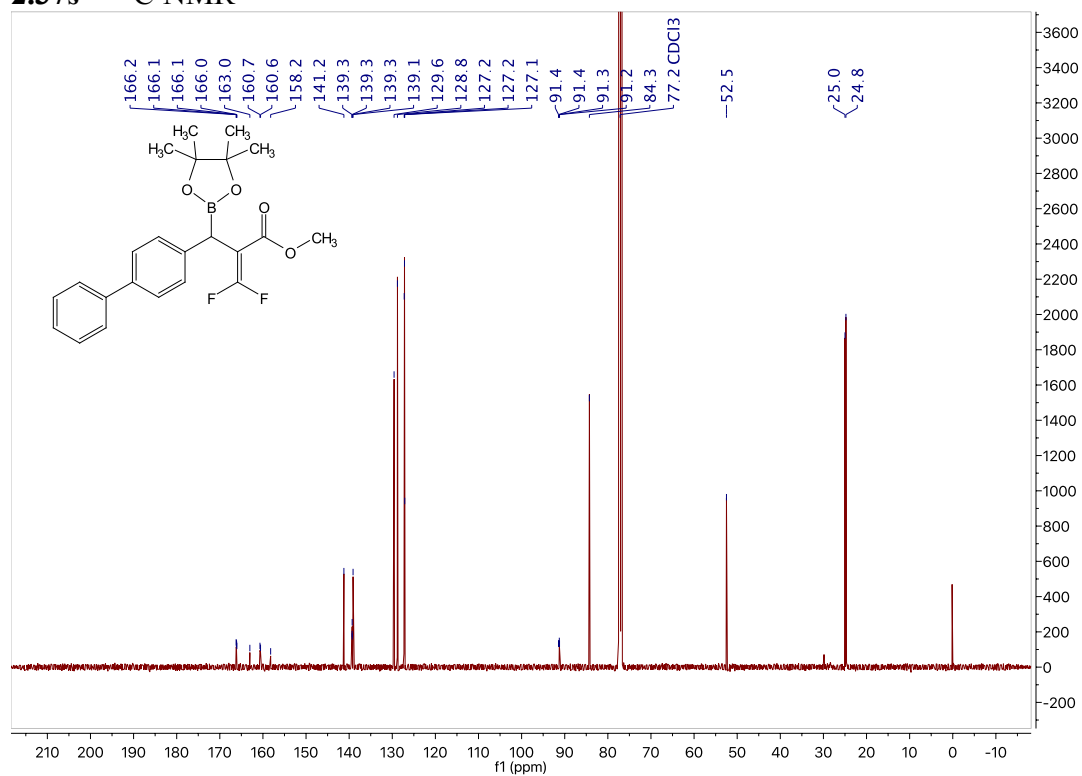
2.37r – <sup>11</sup>B NMR



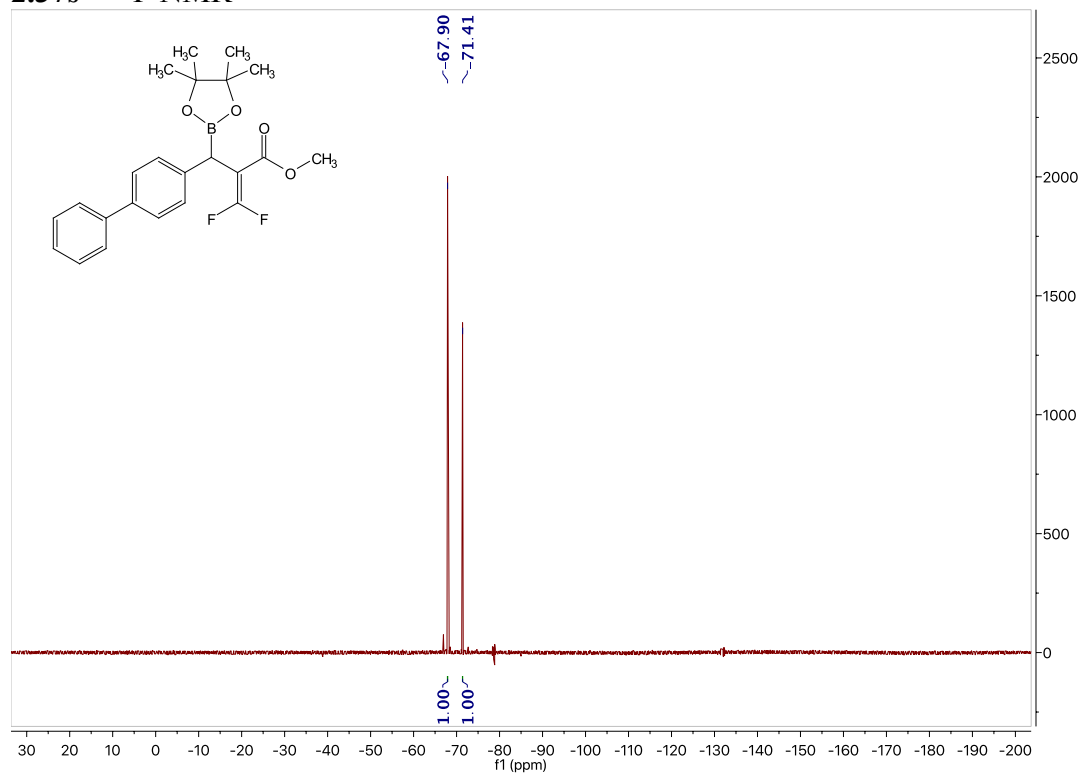
2.37s – <sup>1</sup>H NMR



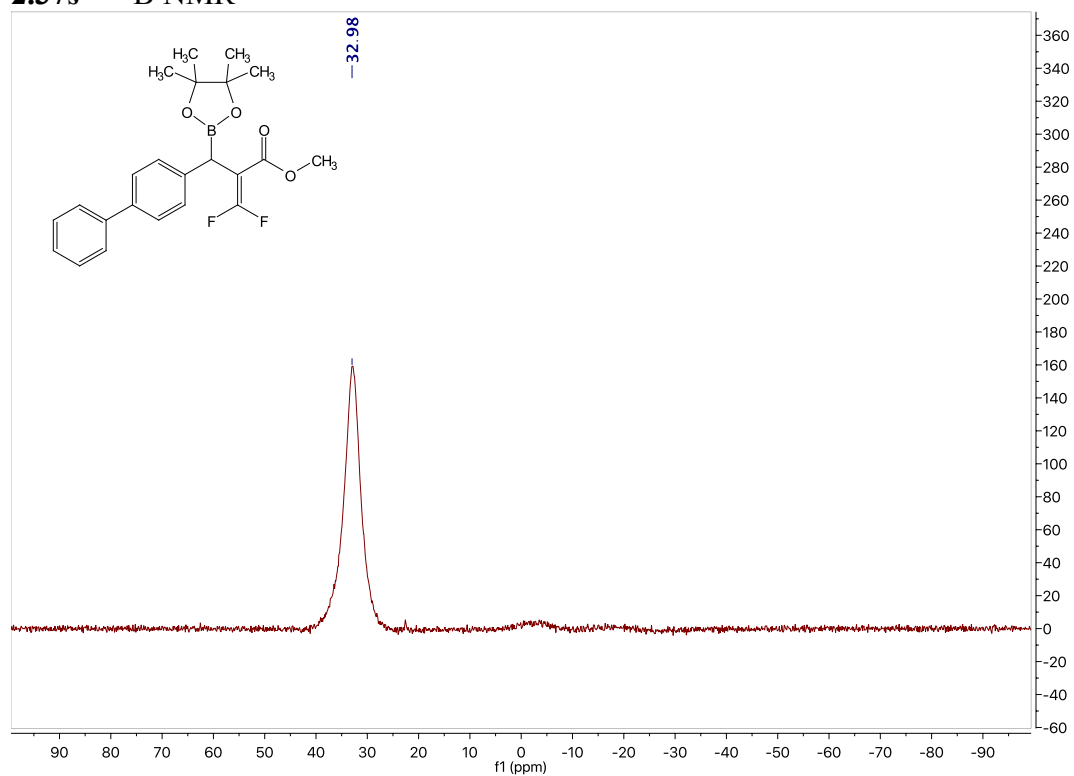
2.37s – <sup>13</sup>C NMR



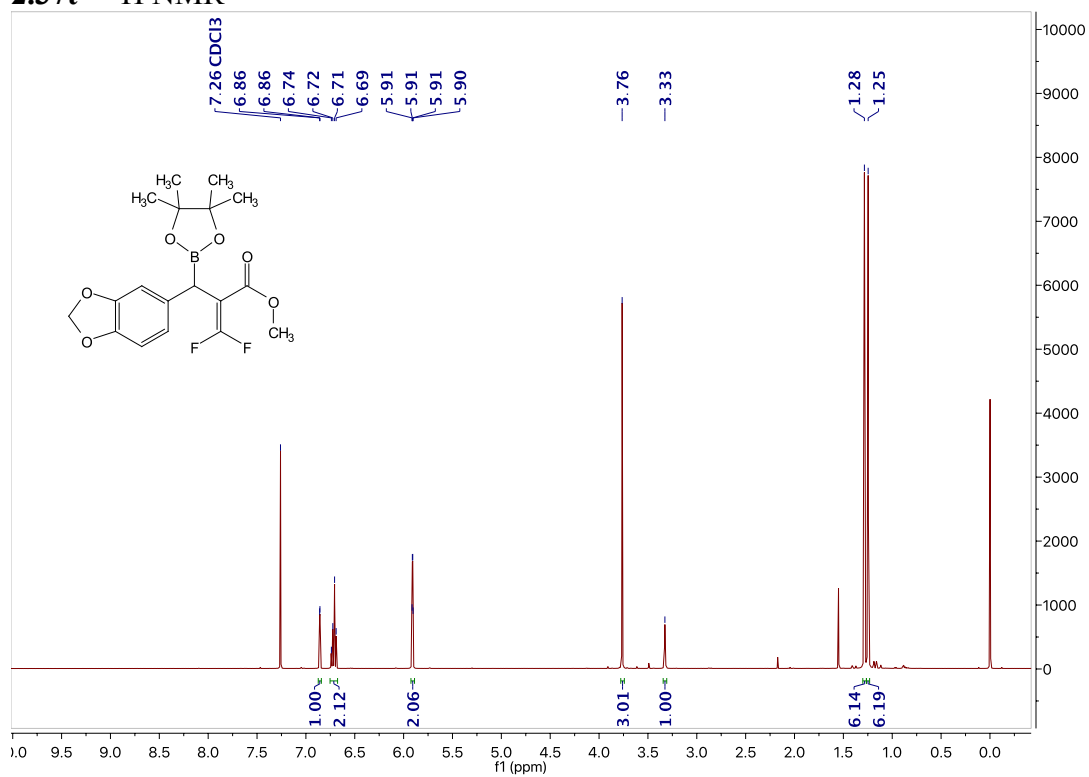
2.37s – <sup>19</sup>F NMR



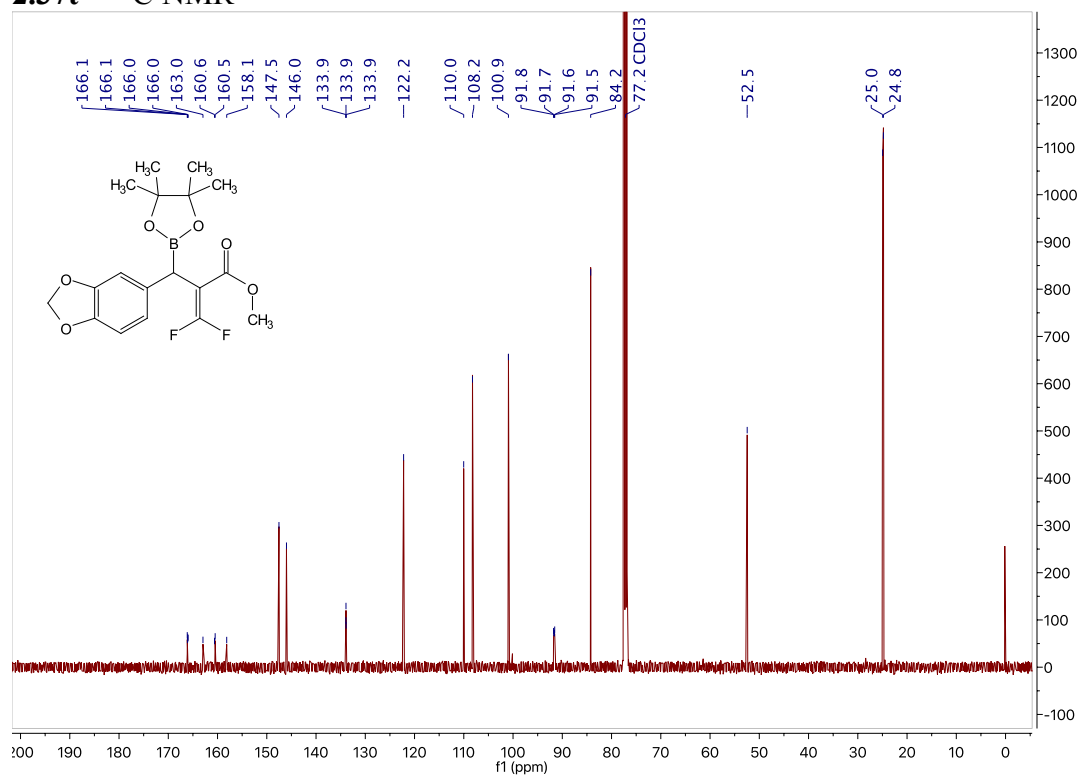
### 2.37s – <sup>11</sup>B NMR



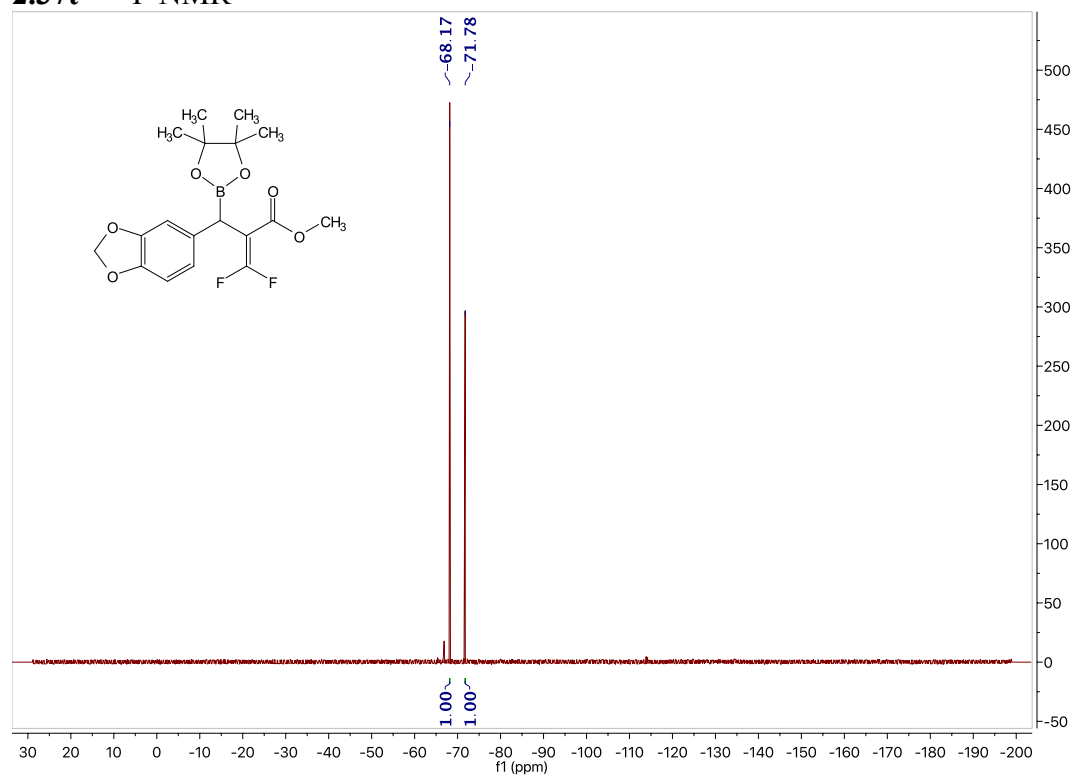
### 2.37t – <sup>1</sup>H NMR



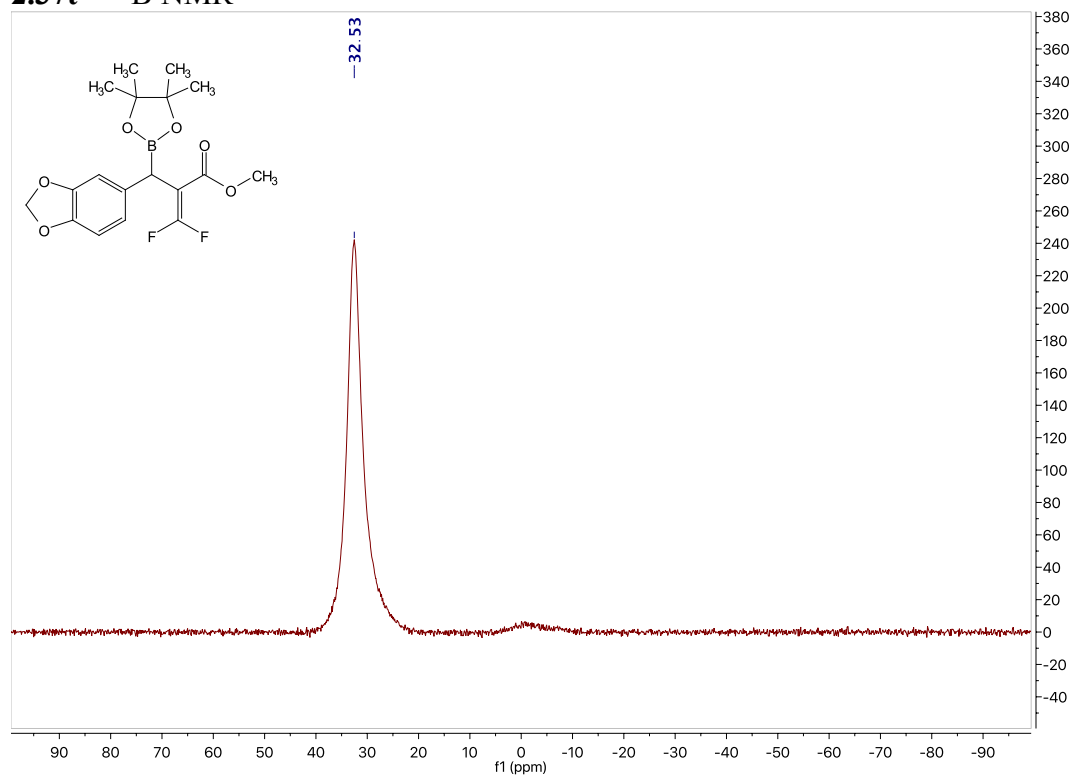
2.37t – <sup>13</sup>C NMR



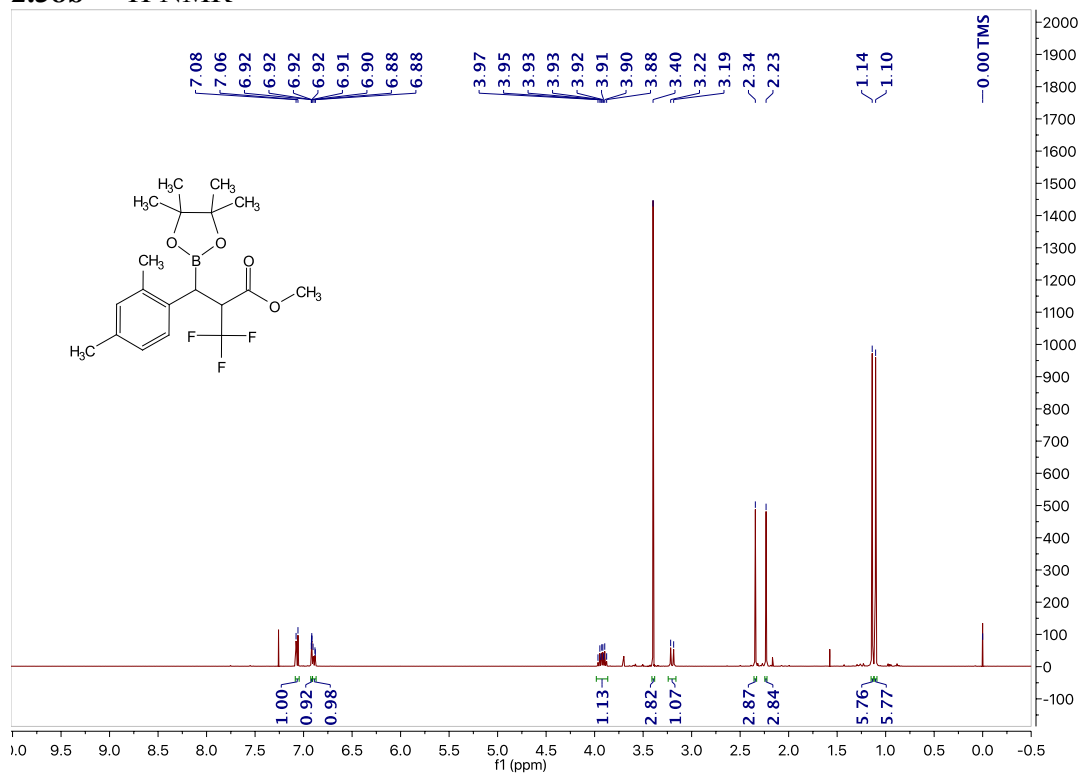
2.37t – <sup>19</sup>F NMR



### 2.37t – <sup>11</sup>B NMR

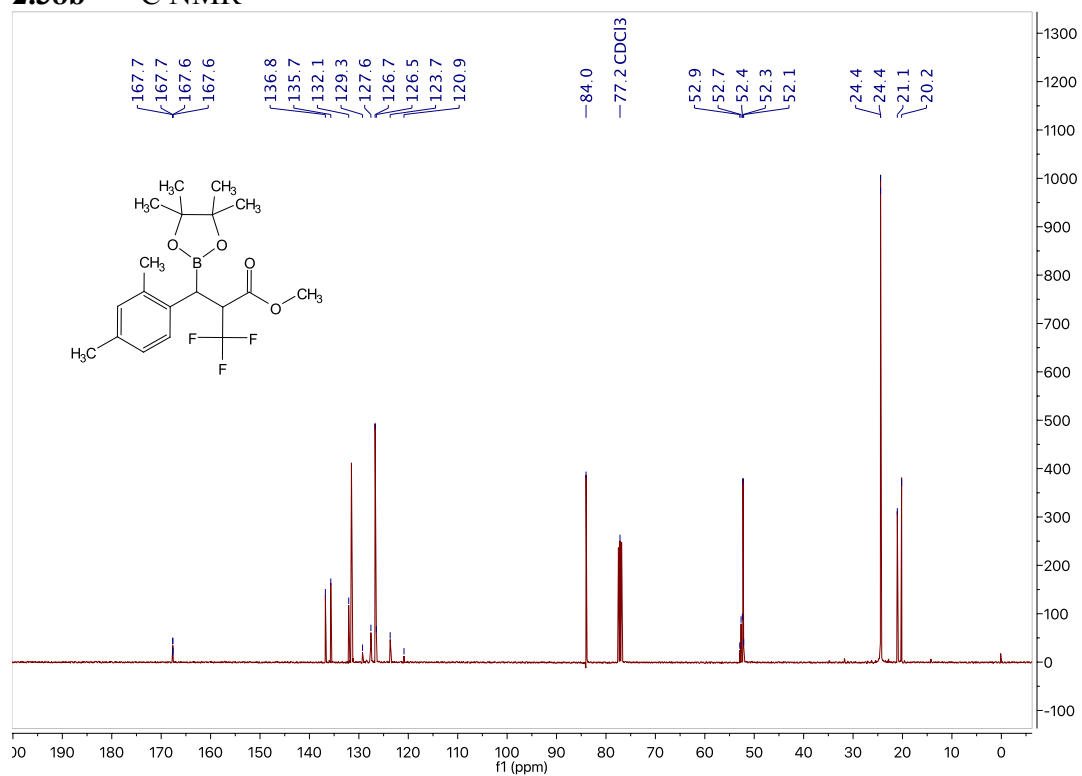


### 2.38b – <sup>1</sup>H NMR

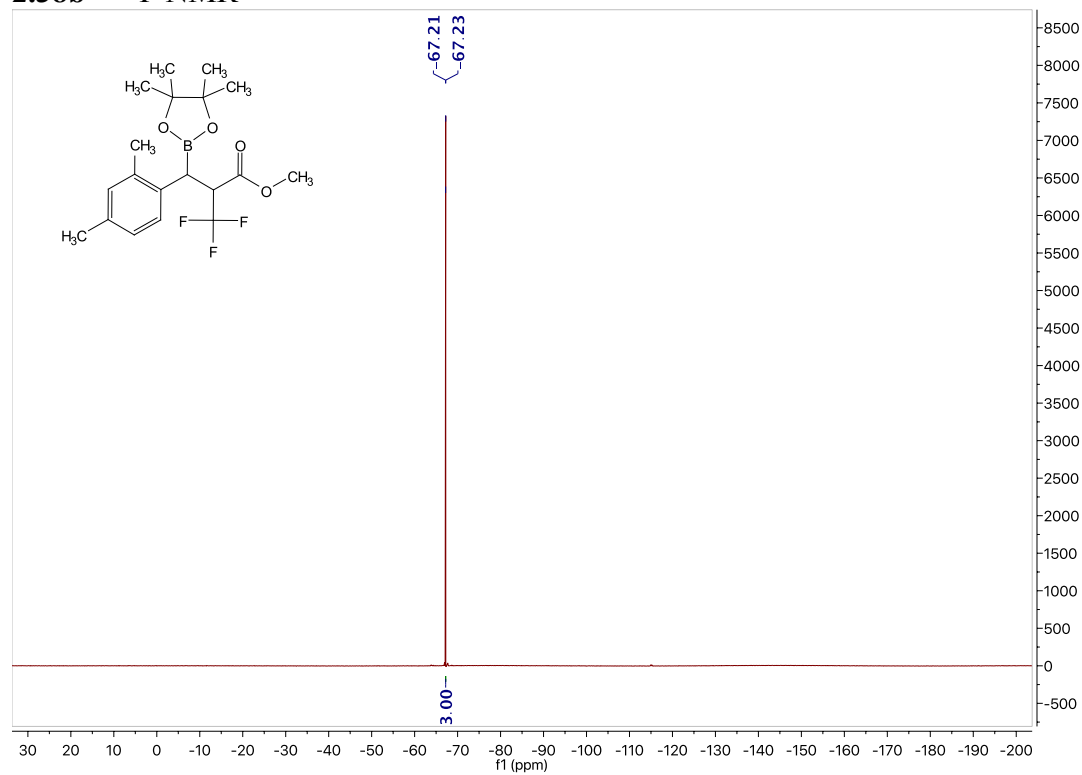




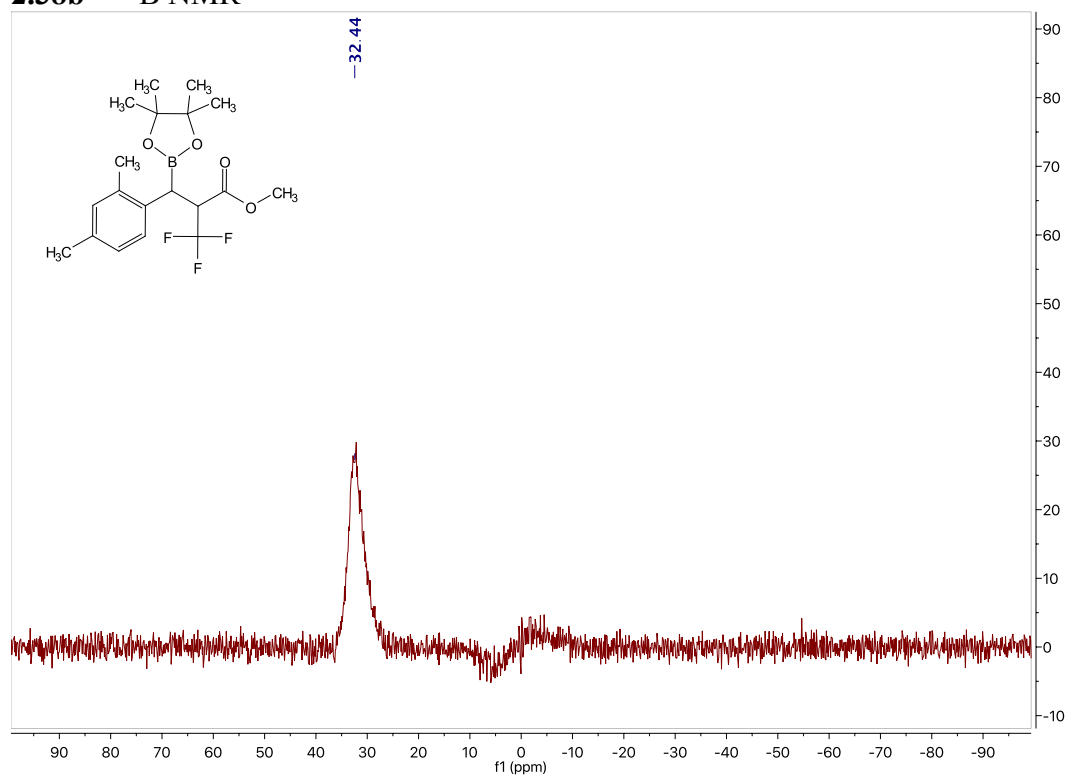
### 2.38b – <sup>13</sup>C NMR



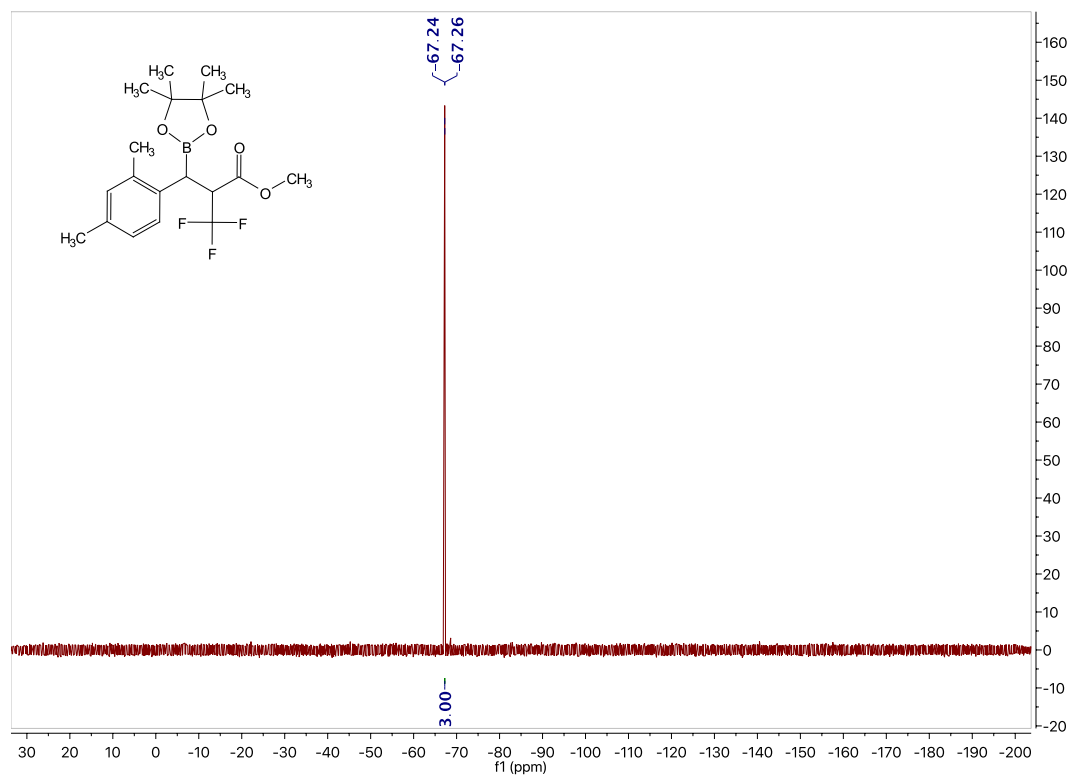
### 2.38b – <sup>19</sup>F NMR



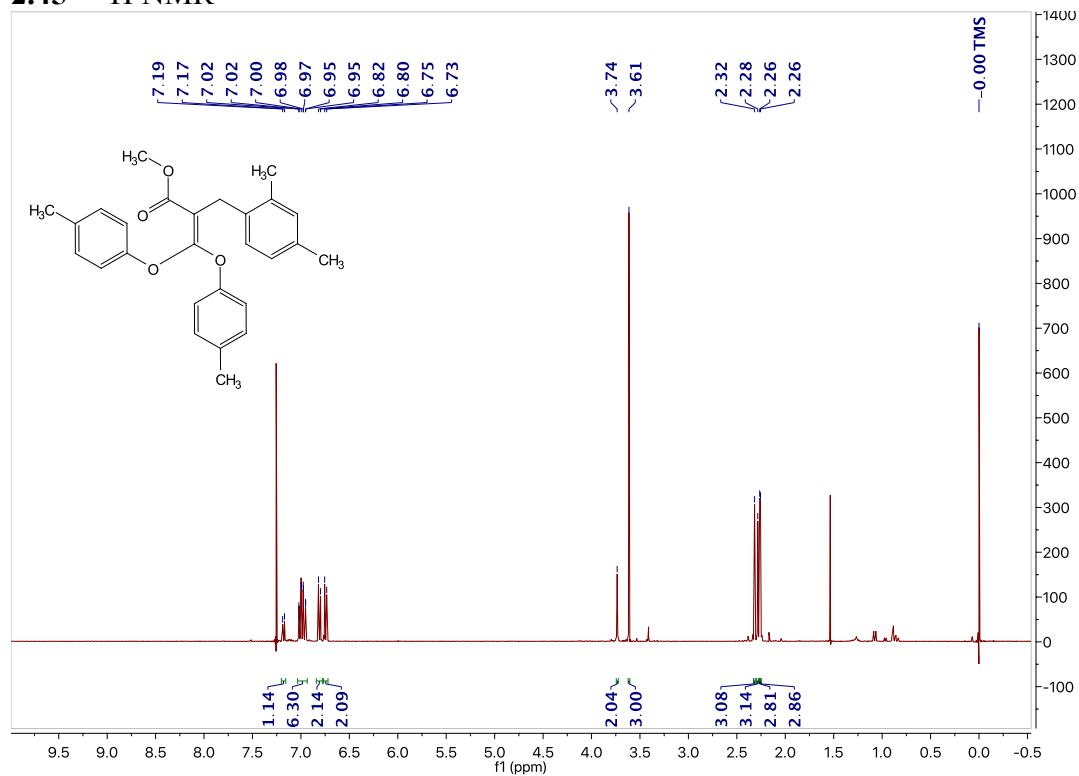
## 2.38b – $^{11}\text{B}$ NMR



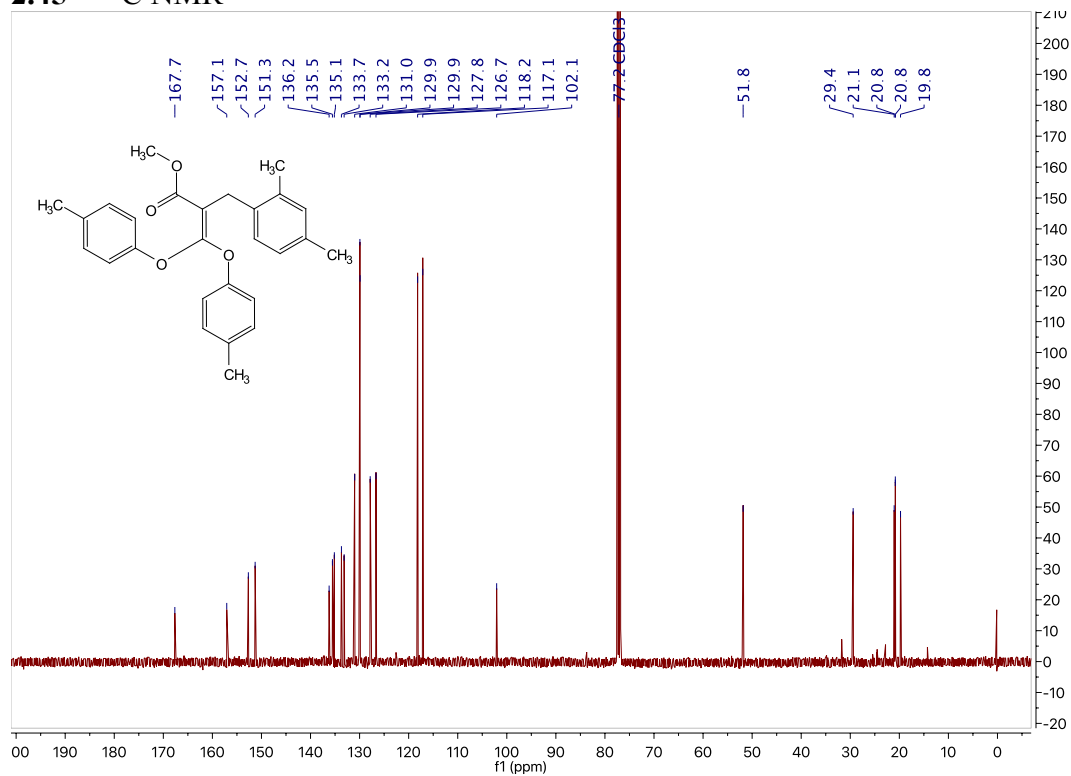
## Mechanistic Study – Crude $^{19}\text{F}$ NMR



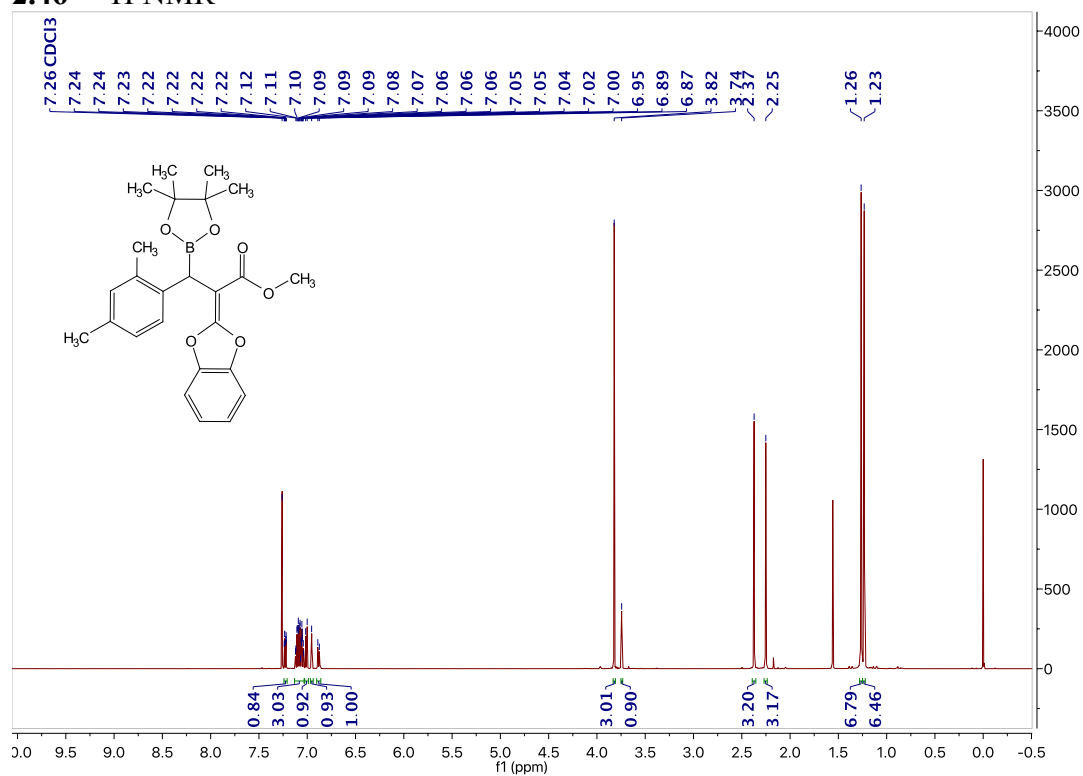
## 2.45 – <sup>1</sup>H NMR



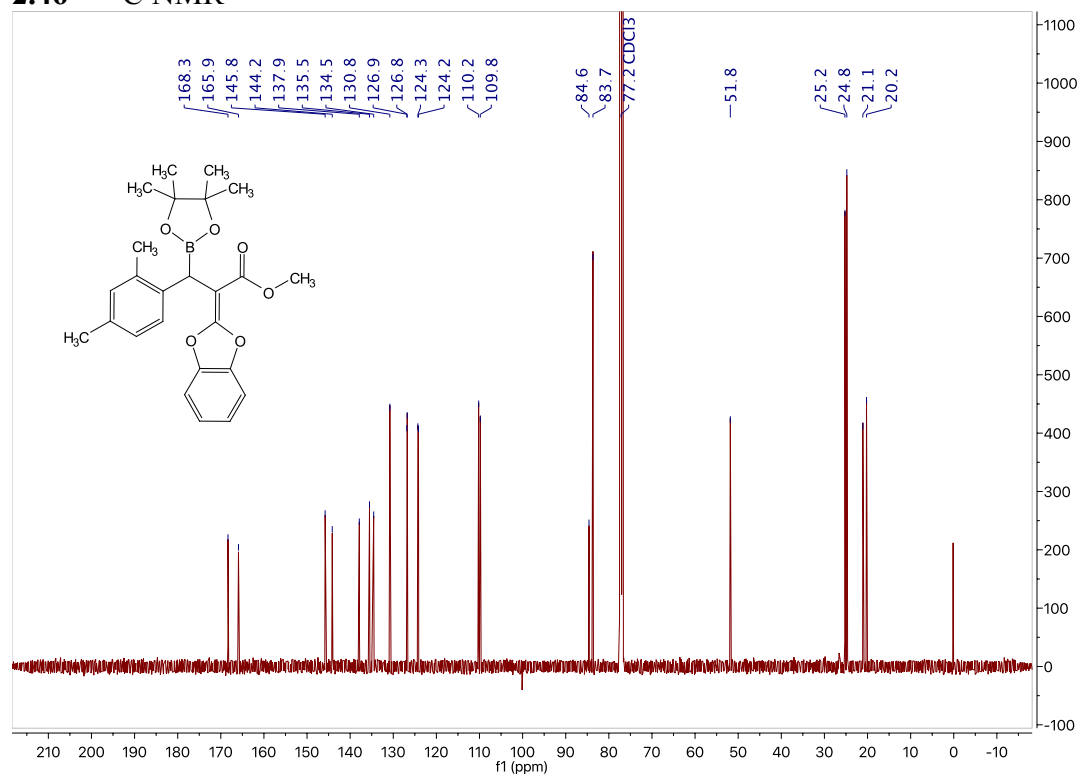
## 2.45 – <sup>13</sup>C NMR



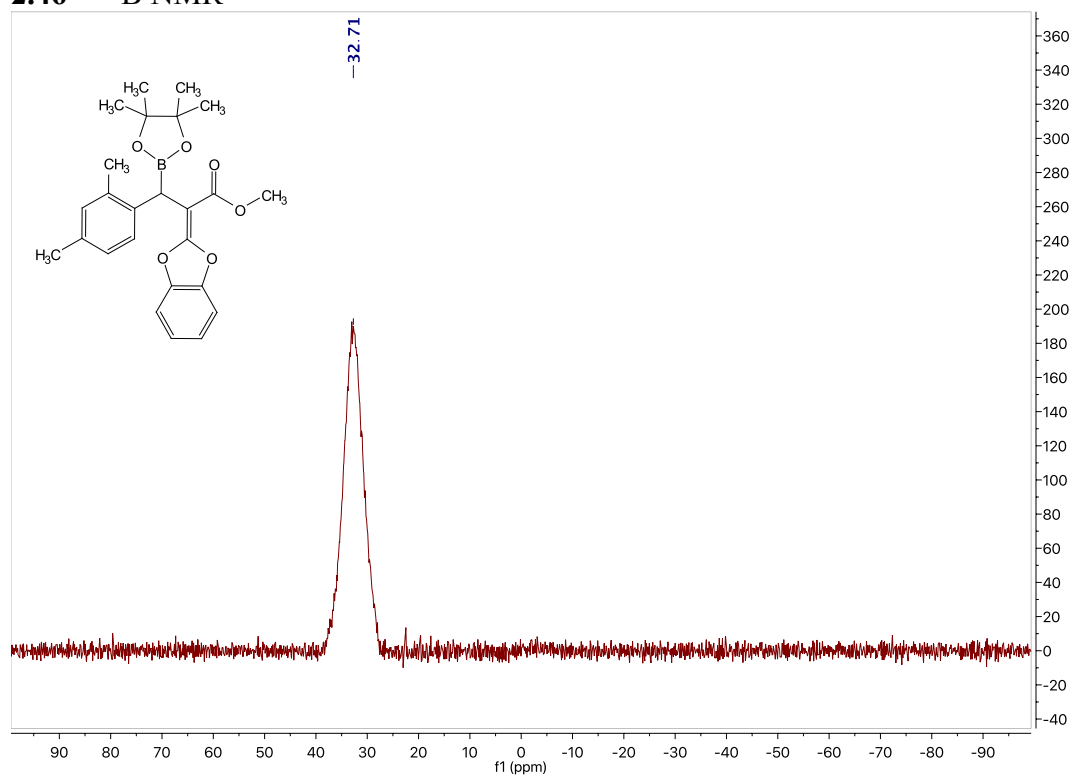
## 2.46 – <sup>1</sup>H NMR



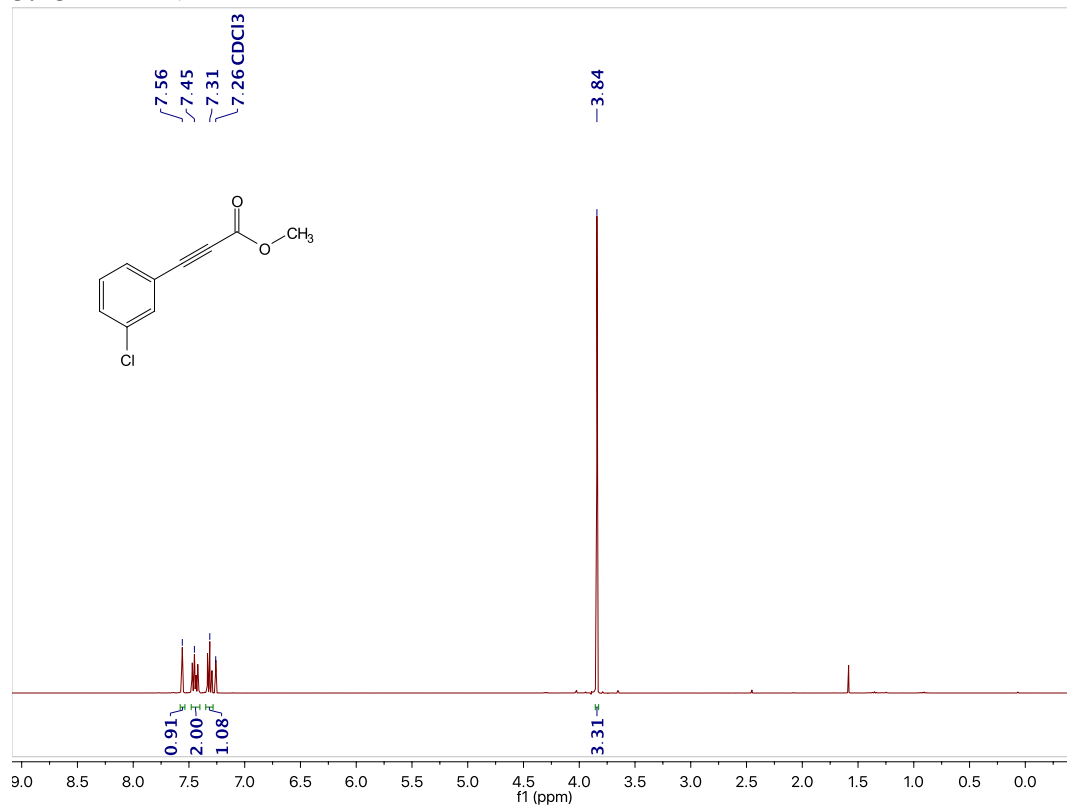
## 2.46 – <sup>13</sup>C NMR



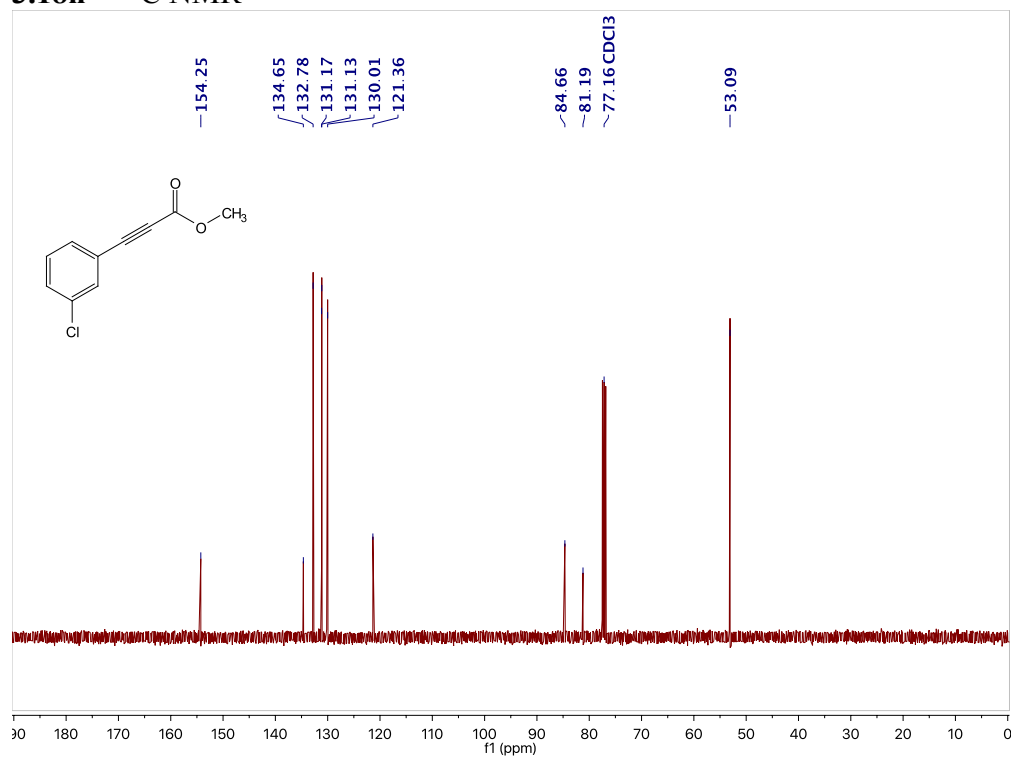
## 2.46 – $^{11}\text{B}$ NMR



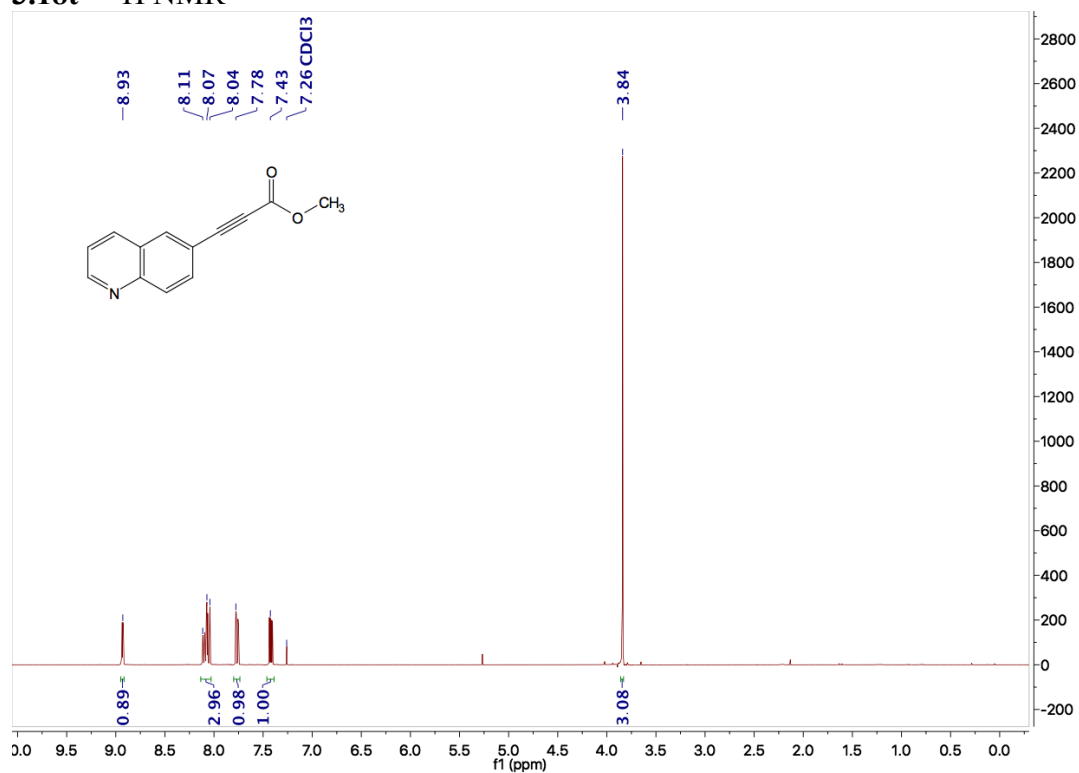
### 3.18h – <sup>1</sup>H NMR



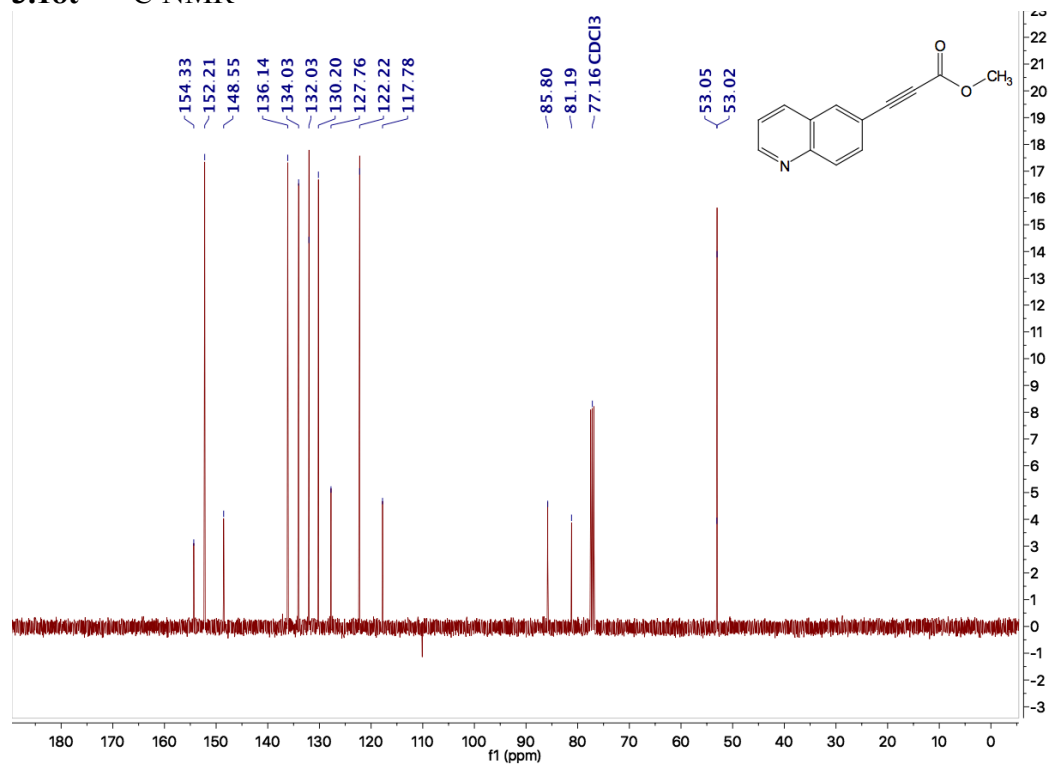
### 3.18h – <sup>13</sup>C NMR



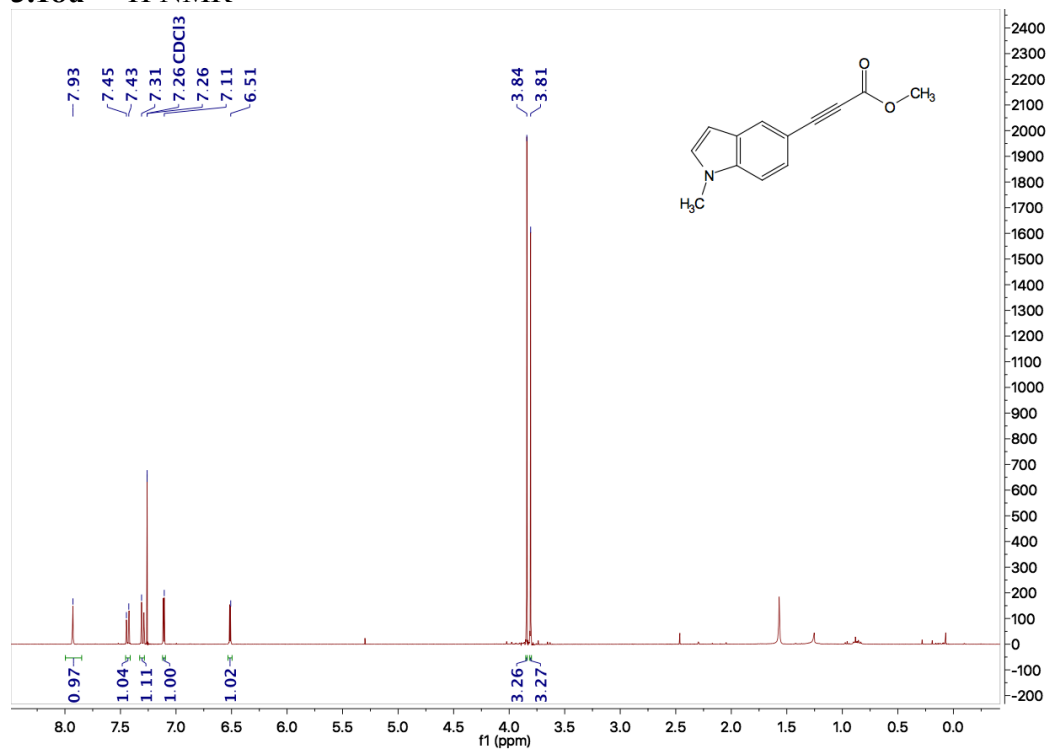
### 3.18t – <sup>1</sup>H NMR



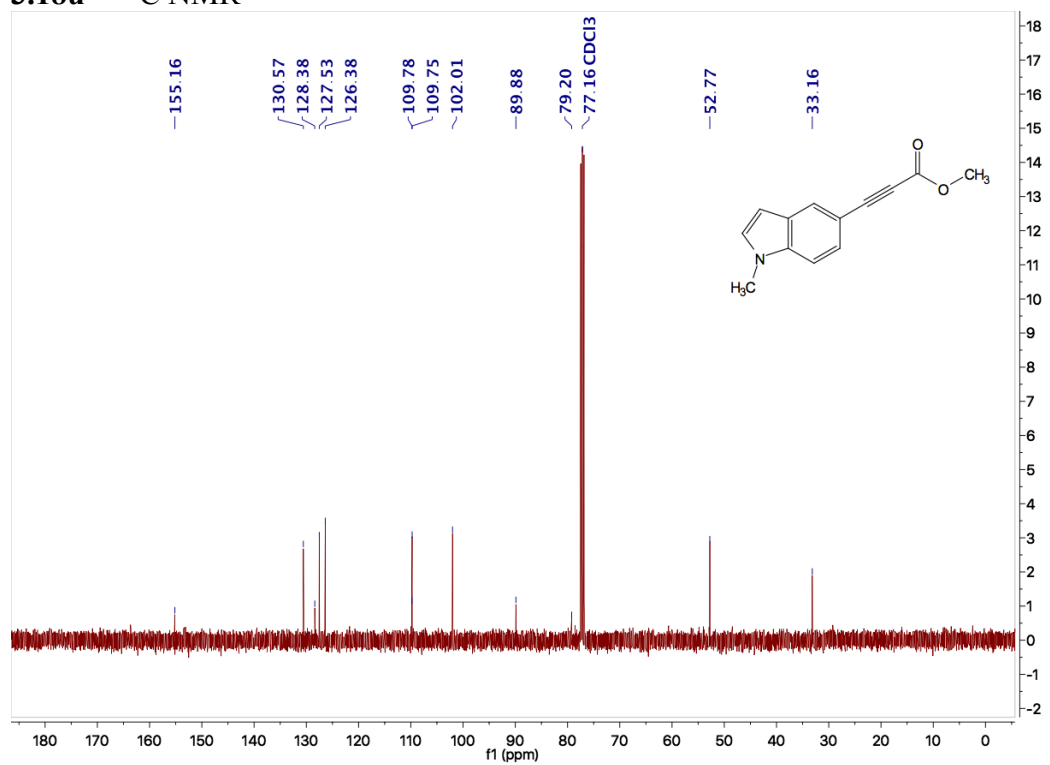
### 3.18t – <sup>13</sup>C NMR



### 3.18u – <sup>1</sup>H NMR

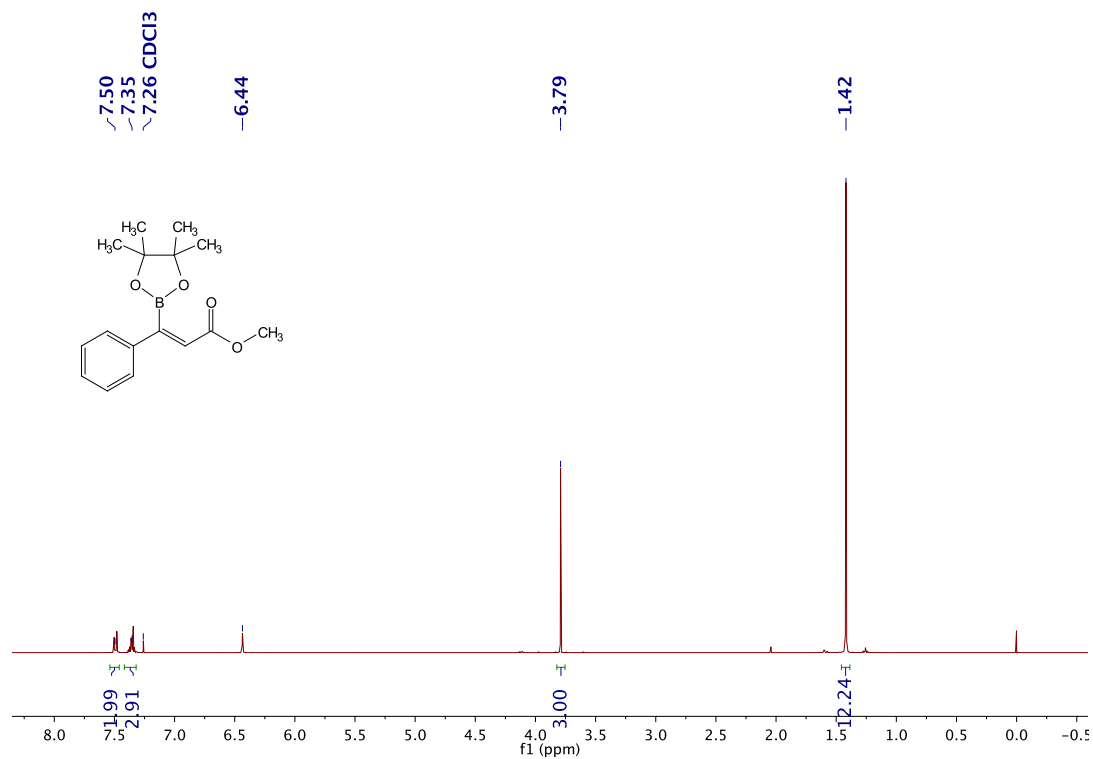


### 3.18u – <sup>13</sup>C NMR

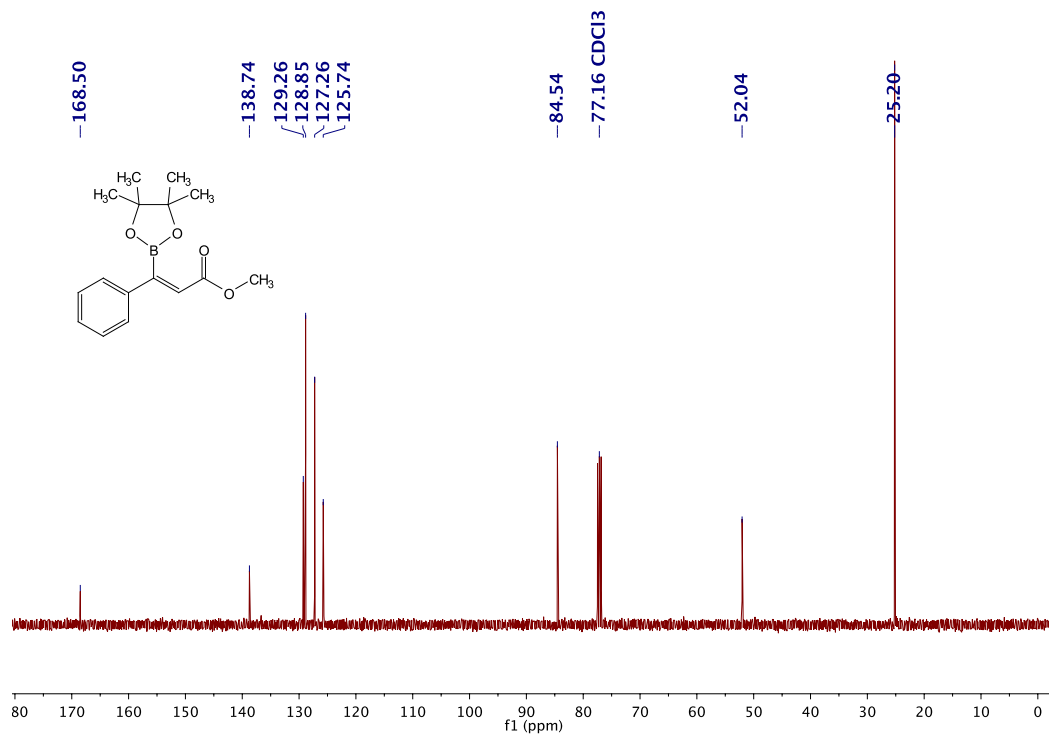




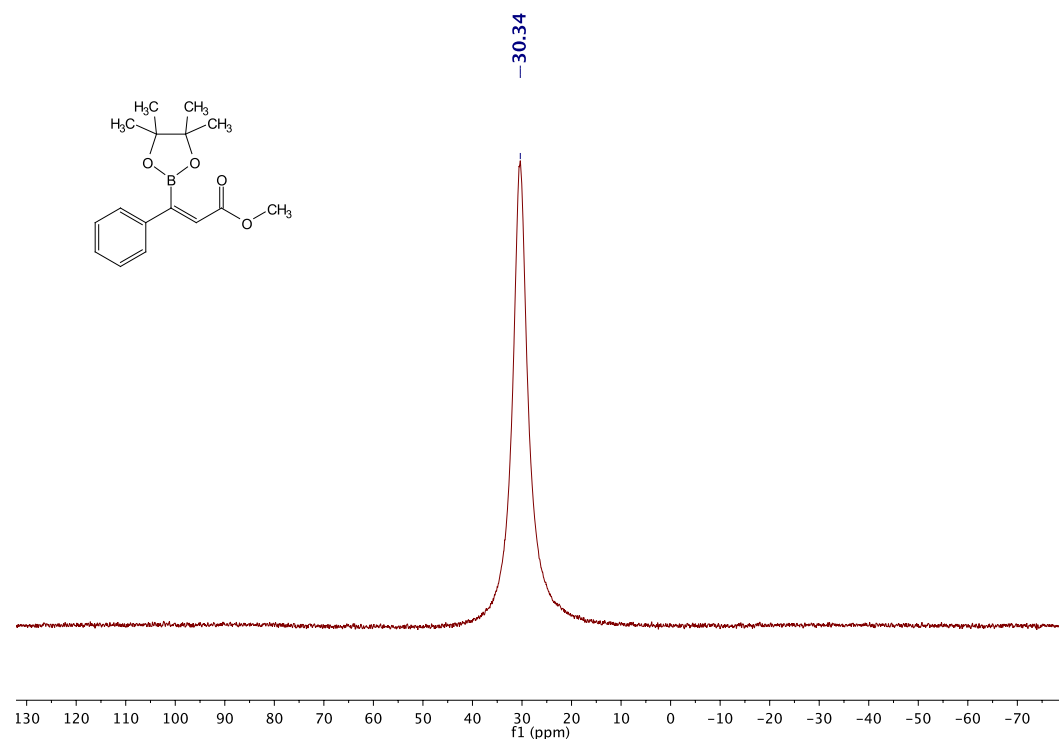
### 3.19a – <sup>1</sup>H NMR



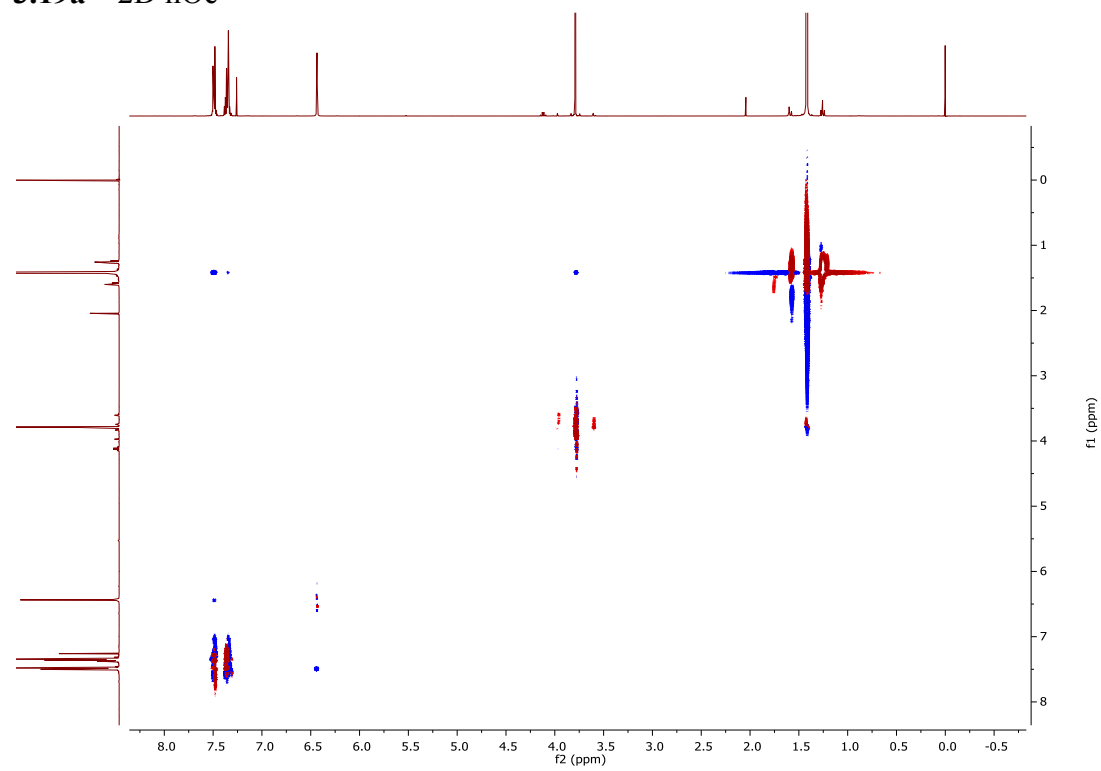
### 3.19a – <sup>13</sup>C NMR



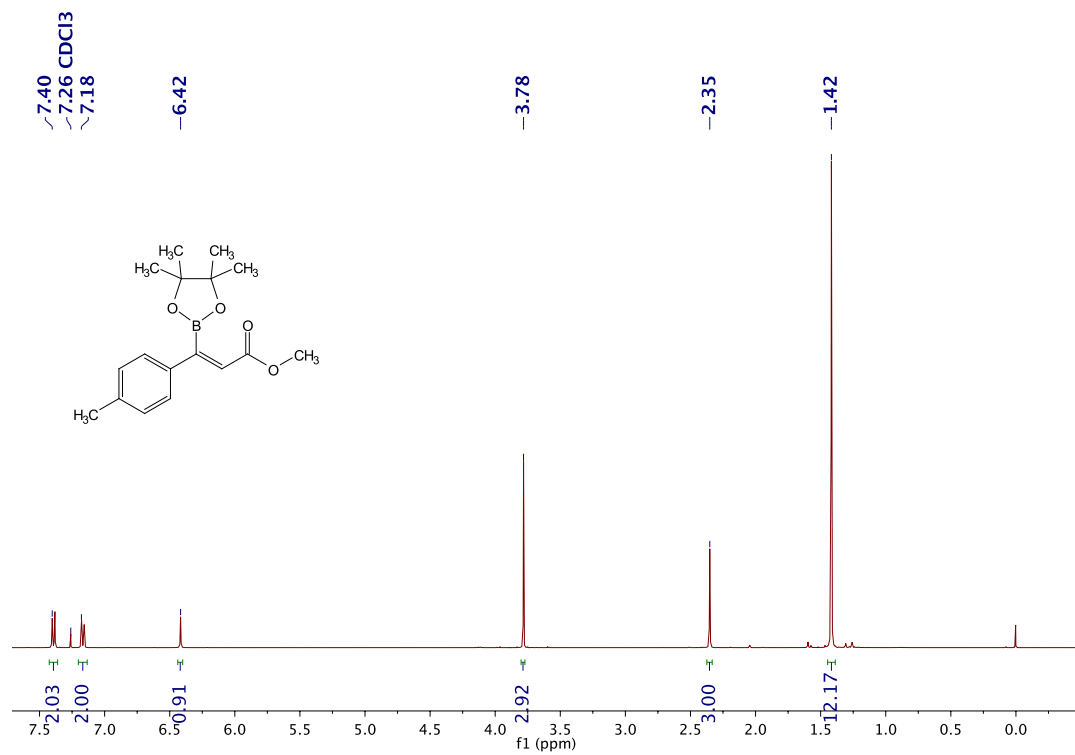
### 3.19a – $^{11}\text{B}$ NMR



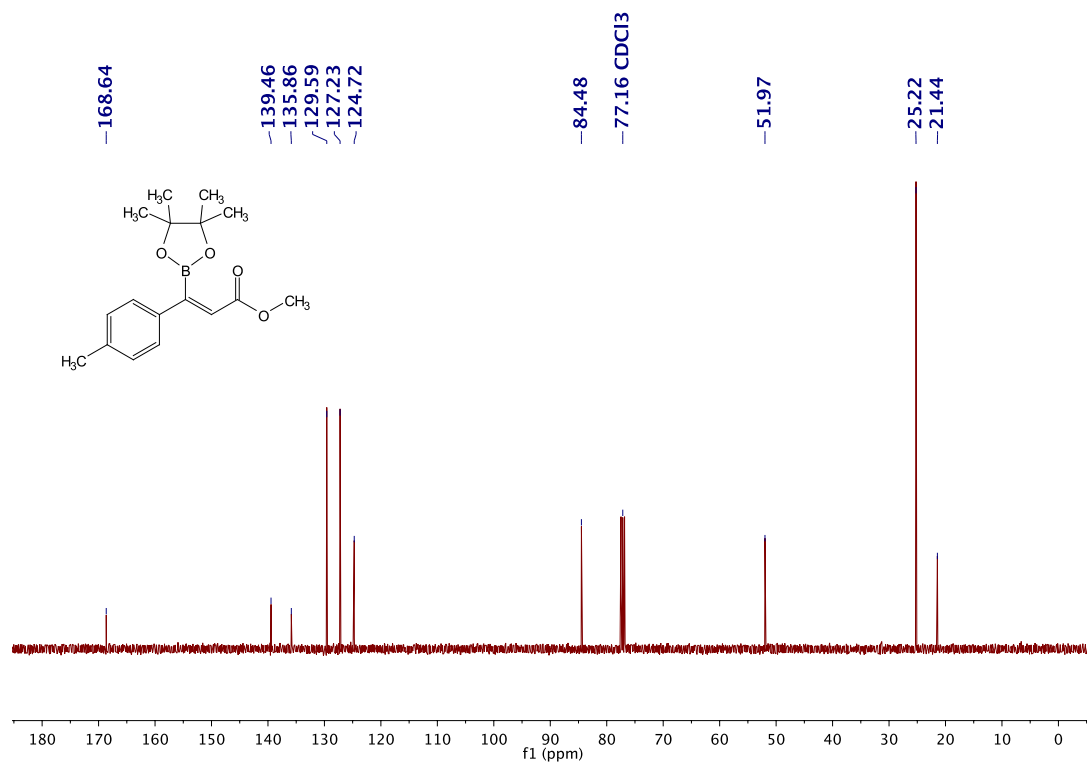
### 3.19a – 2D nOe



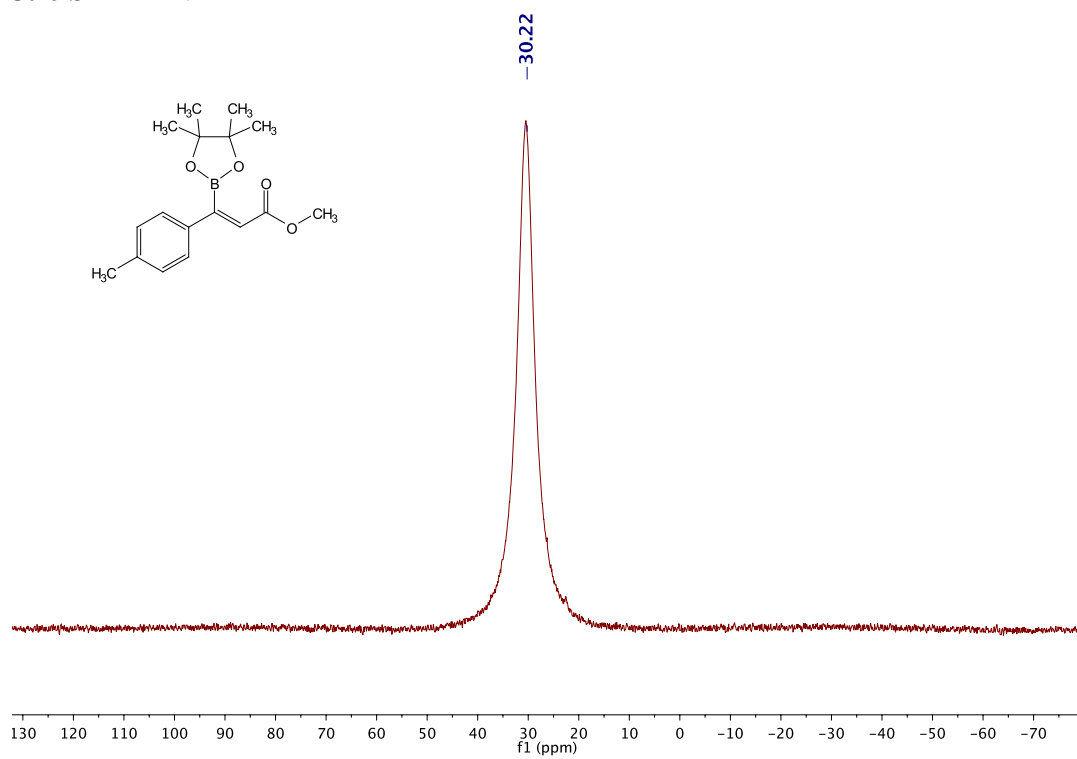
### 3.19b – <sup>1</sup>H NMR



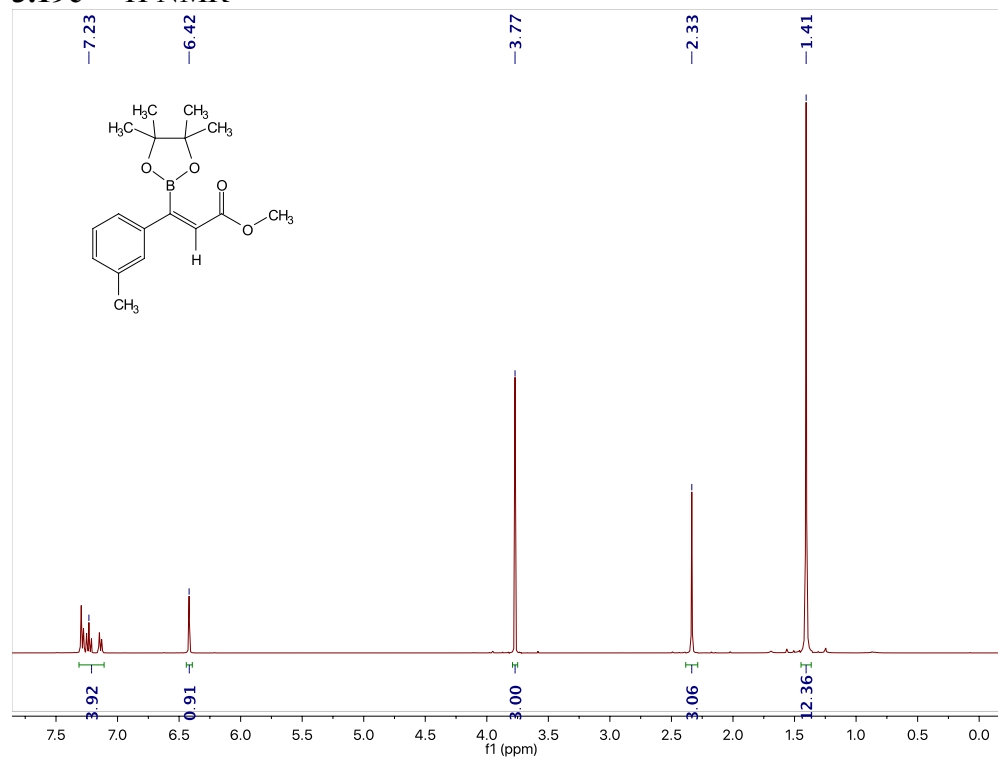
### 3.19b – <sup>13</sup>C NMR



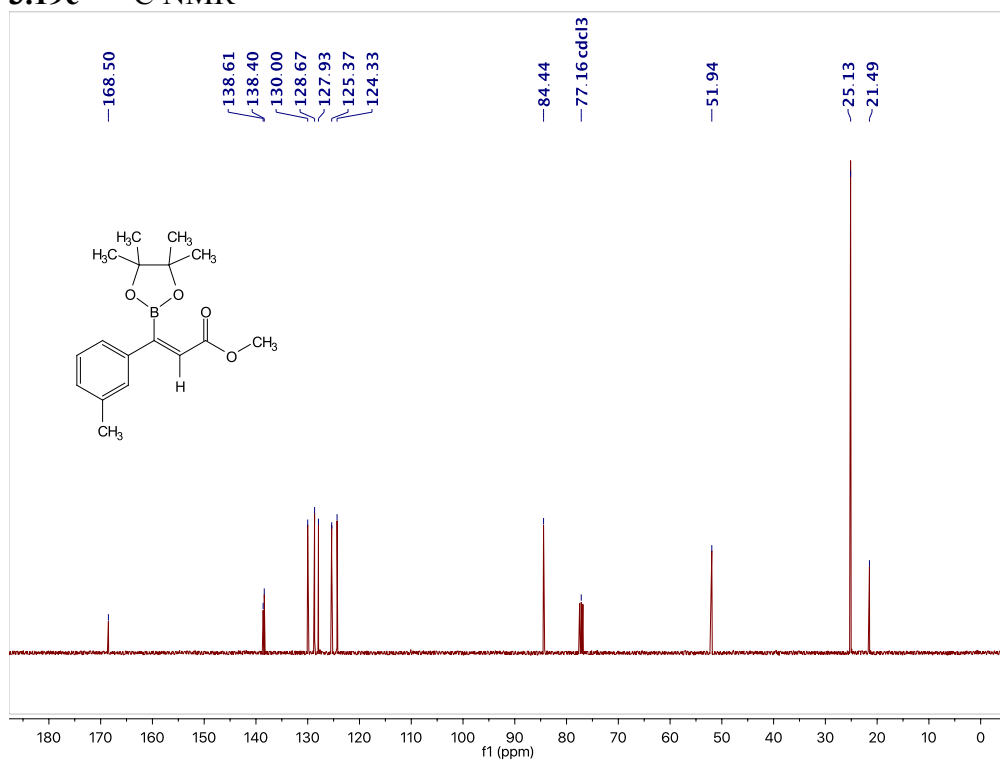
### 3.19b – $^{11}\text{B}$ NMR



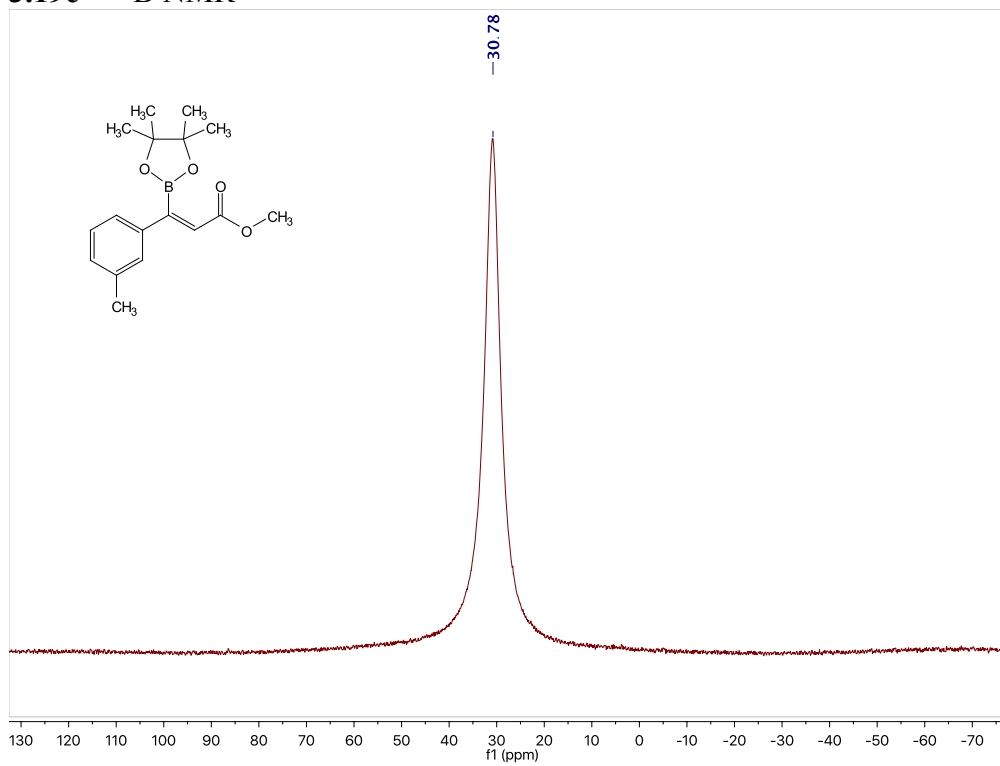
### 3.19c – $^1\text{H}$ NMR



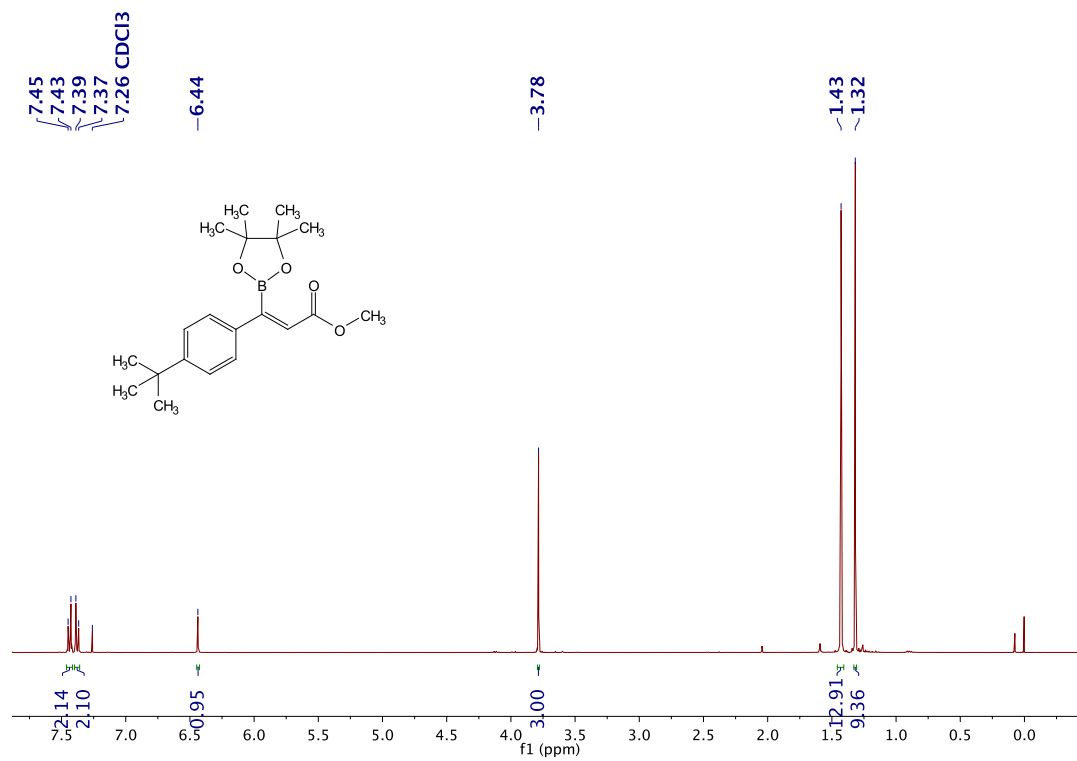
### 3.19c – $^{13}\text{C}$ NMR



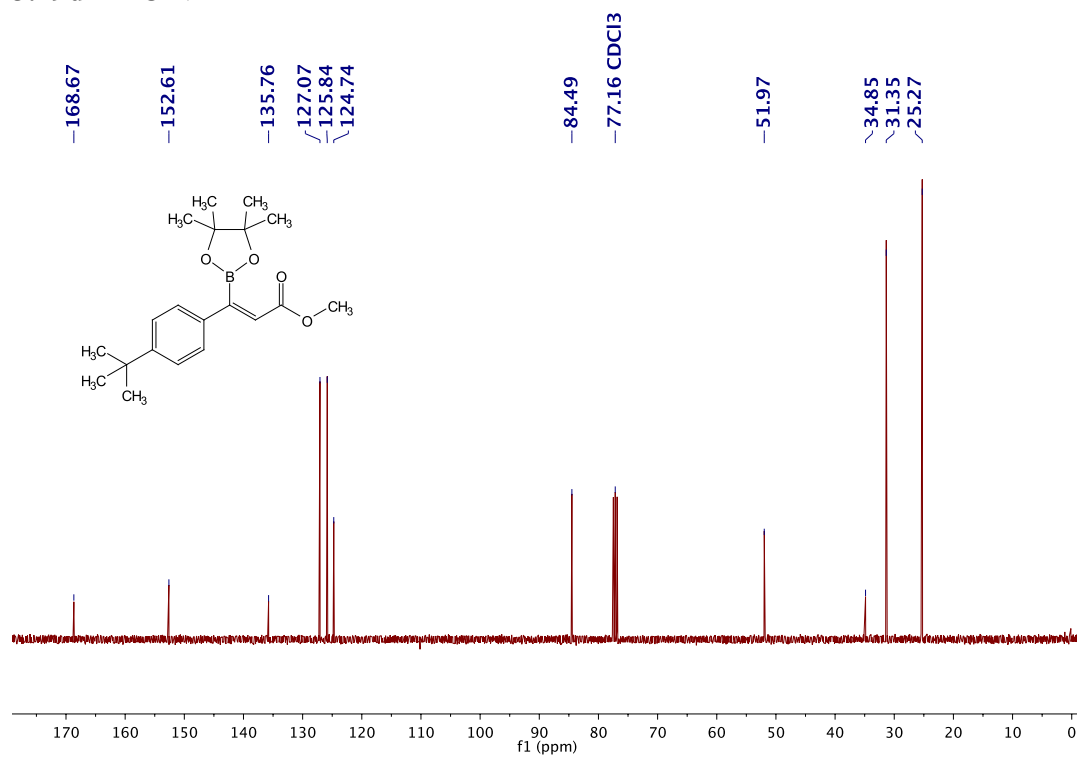
### 3.19c – $^{11}\text{B}$ NMR



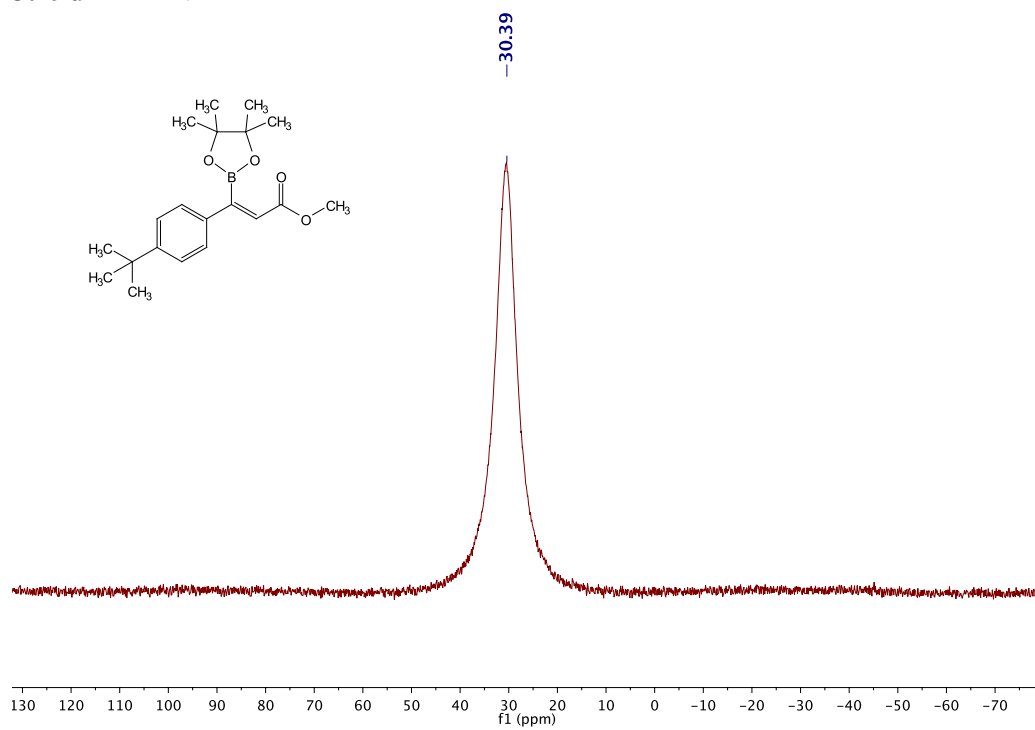
### 3.19d – <sup>1</sup>H NMR



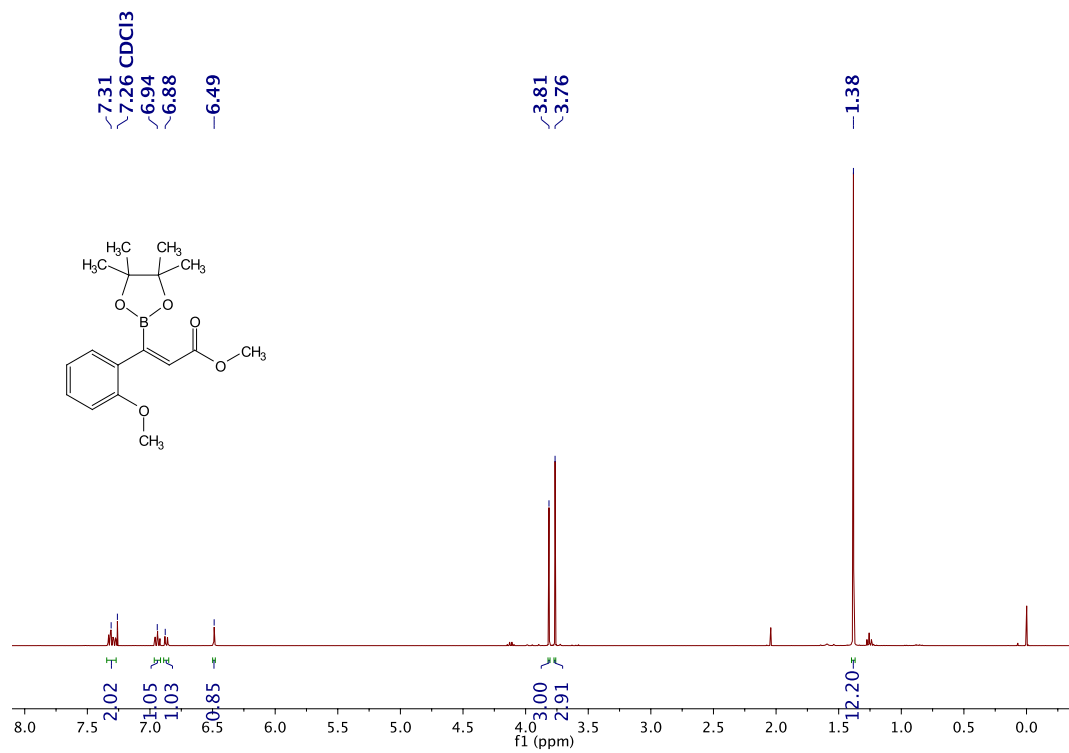
### 3.19d – <sup>13</sup>C NMR



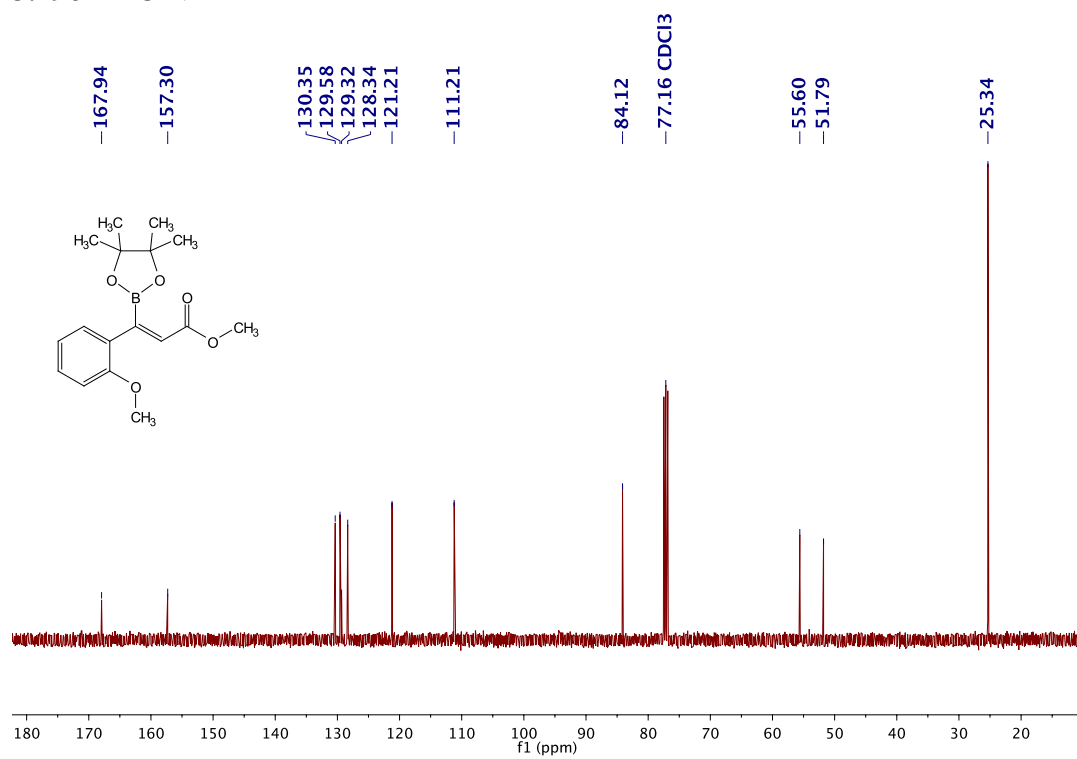
### 3.19d – $^{11}\text{B}$ NMR



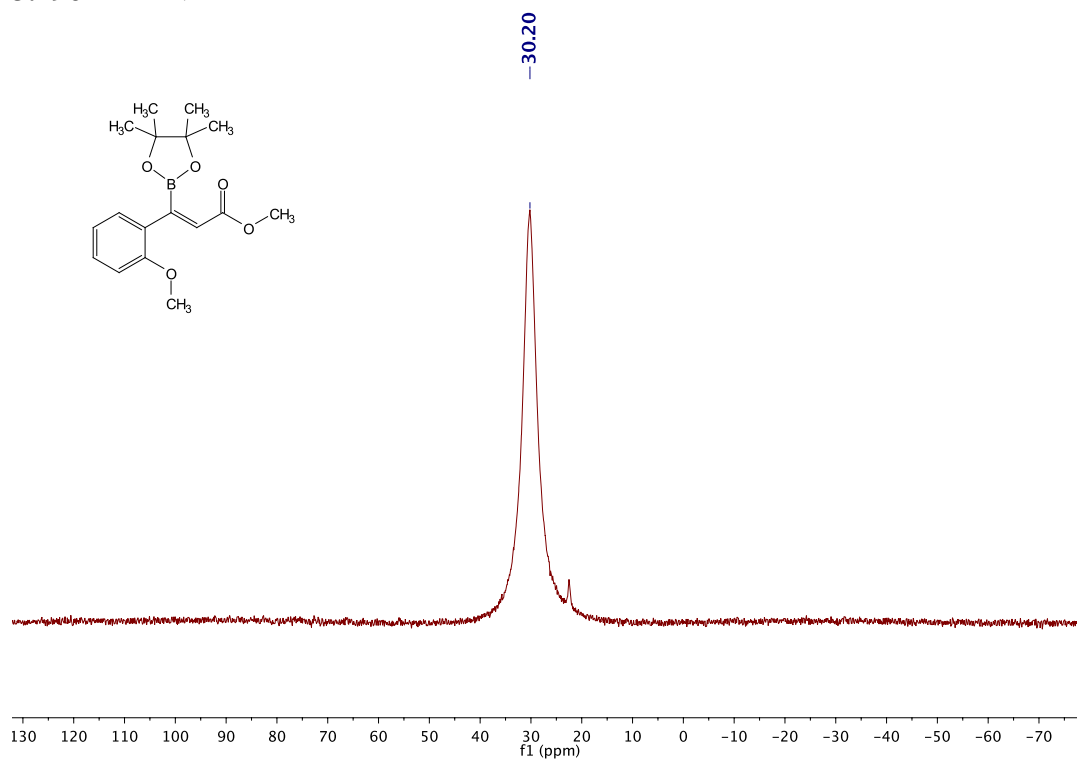
### 3.19e – $^1\text{H}$ NMR



### 3.19e – <sup>13</sup>C NMR

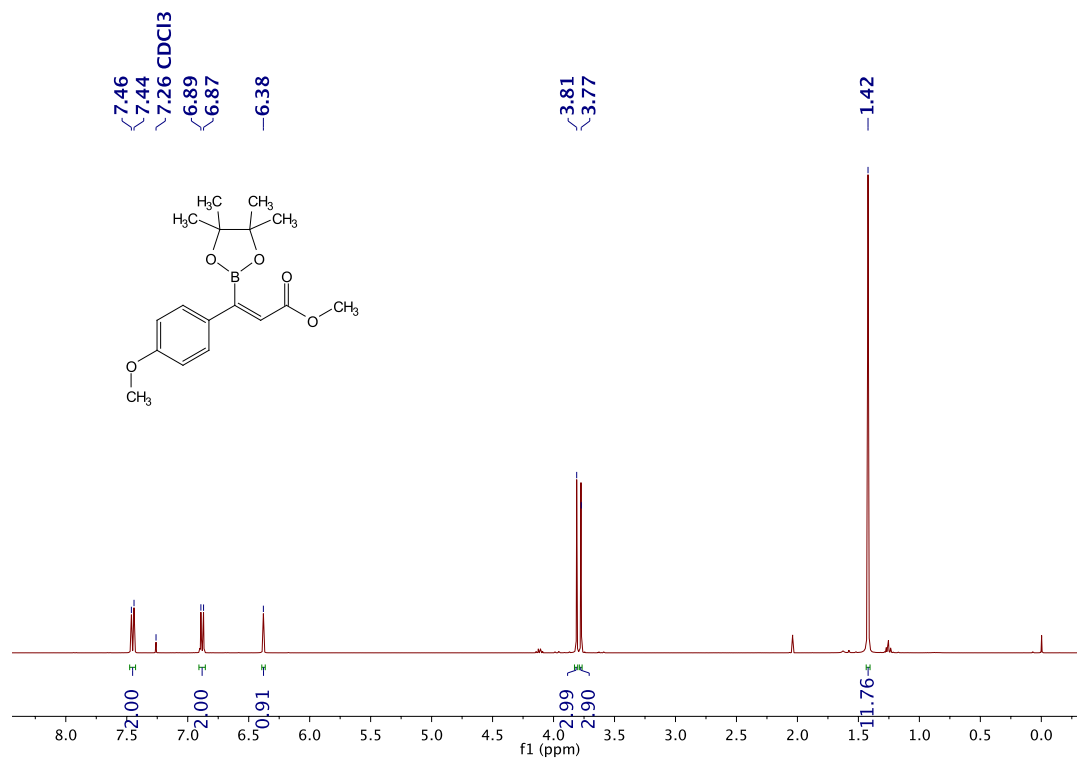


### 3.19e – <sup>11</sup>B NMR

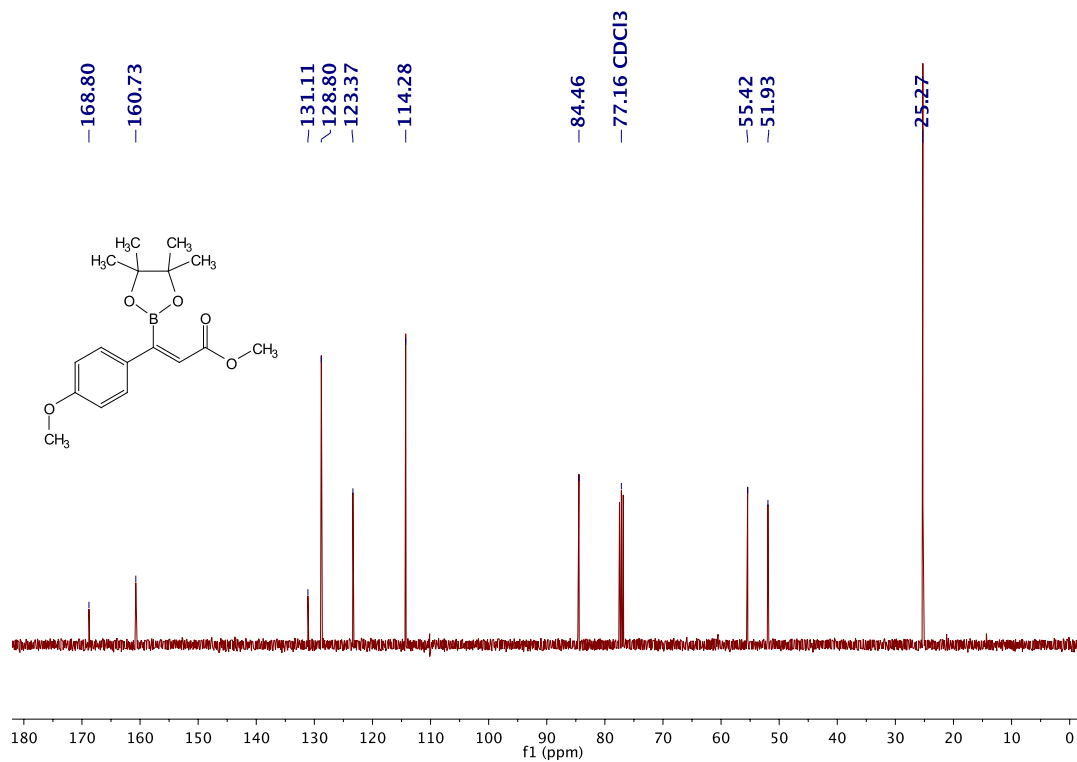




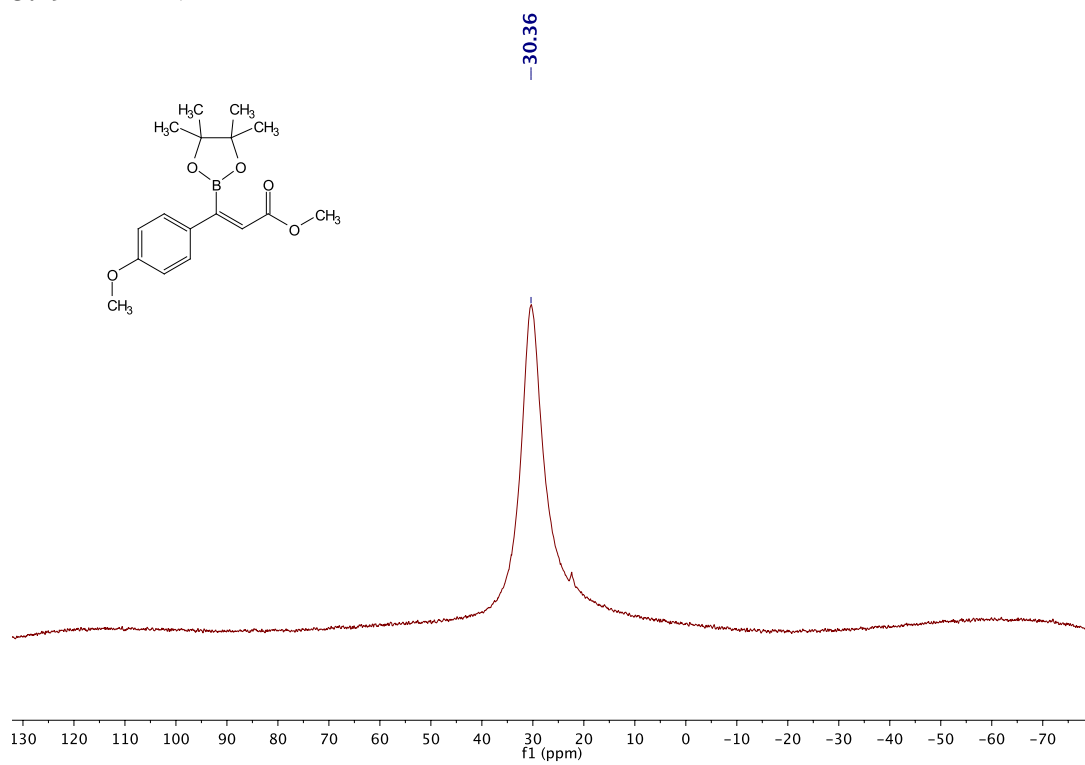
### 3.19f – $^1\text{H}$ NMR



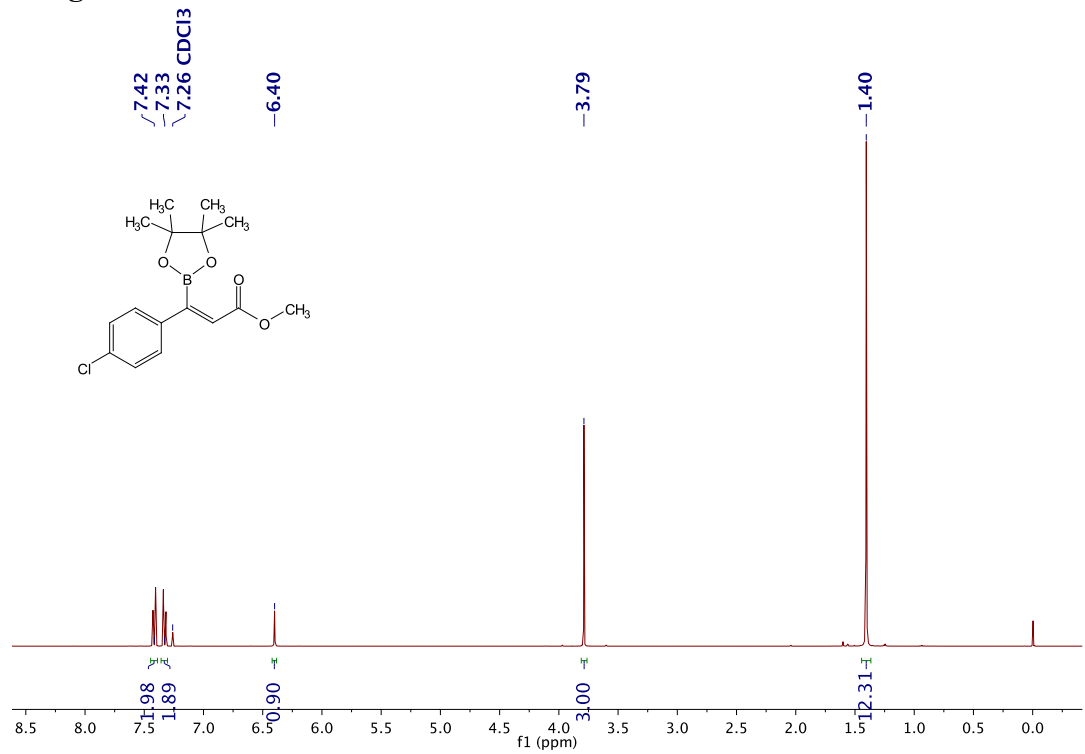
### 3.19f – $^{13}\text{C}$ NMR



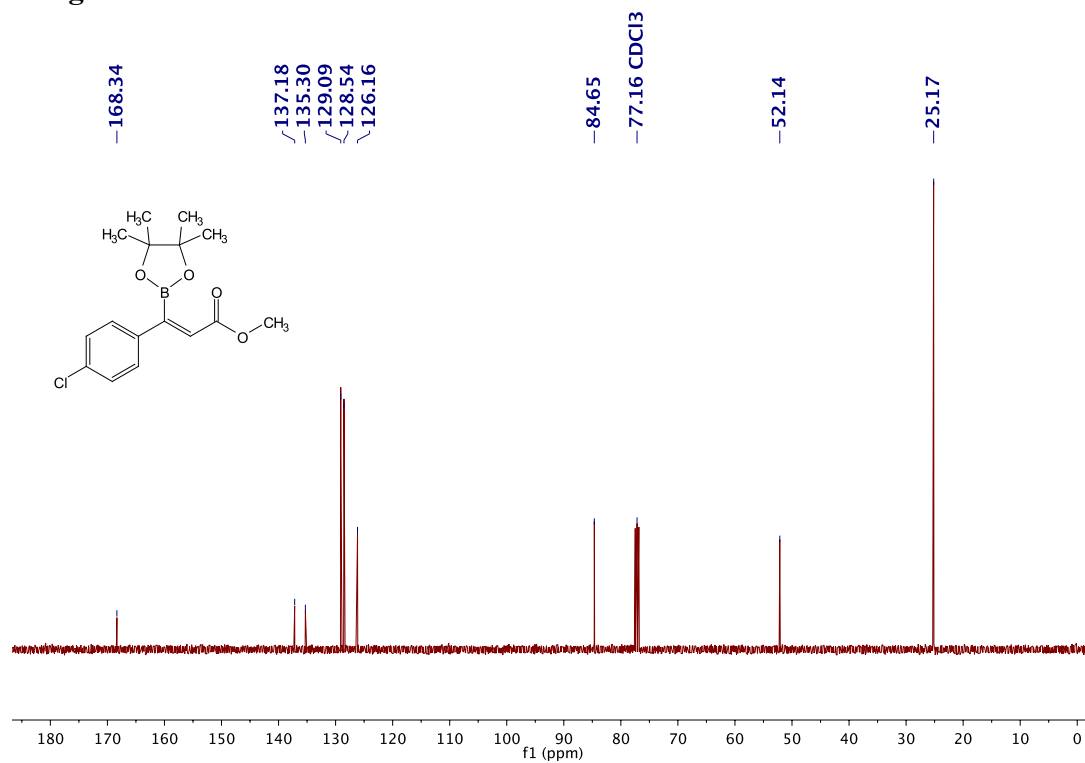
### 3.19f – $^{11}\text{B}$ NMR



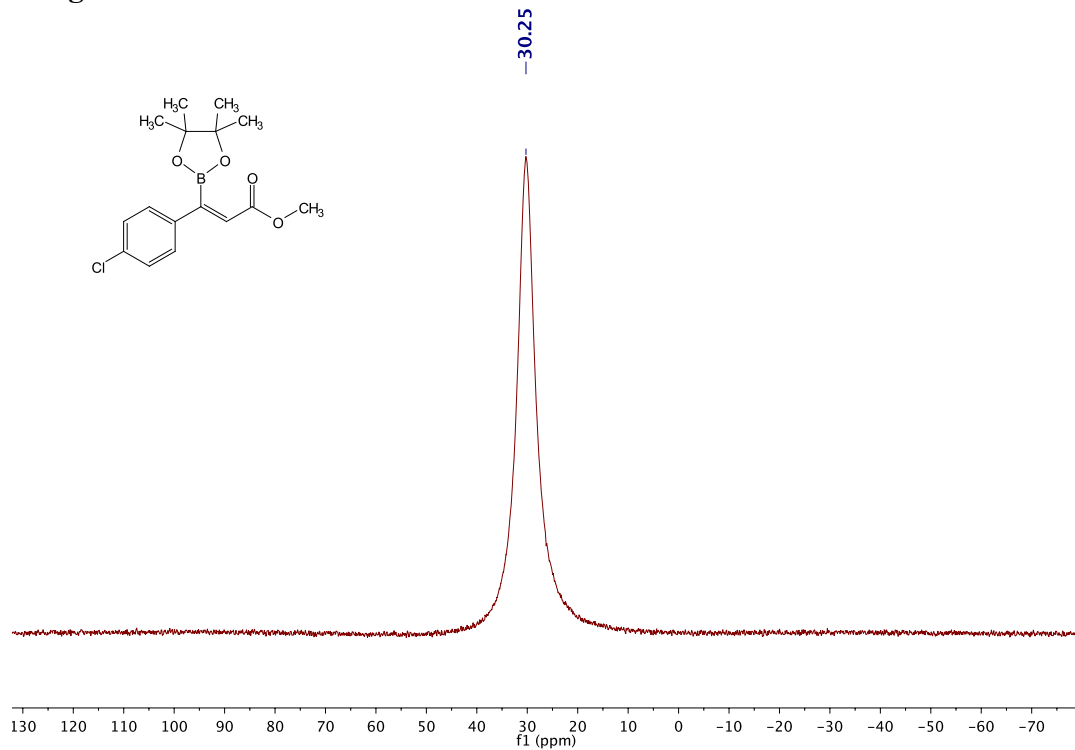
### 3.19g – $^1\text{H}$ NMR



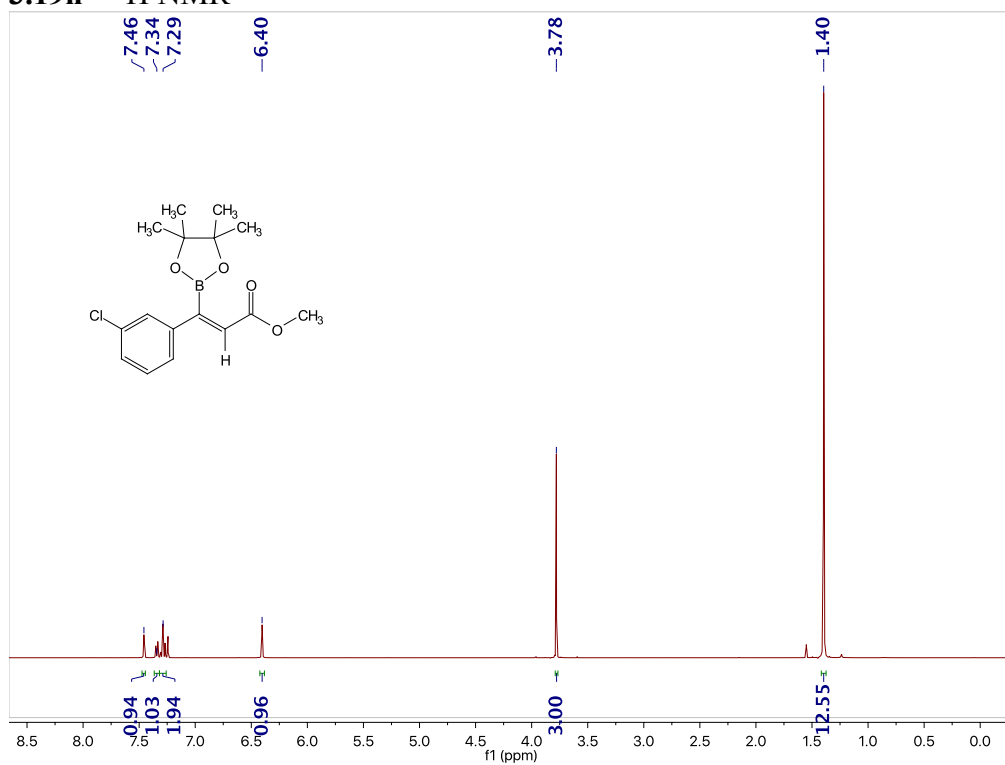
### 3.19g – $^{13}\text{C}$ NMR



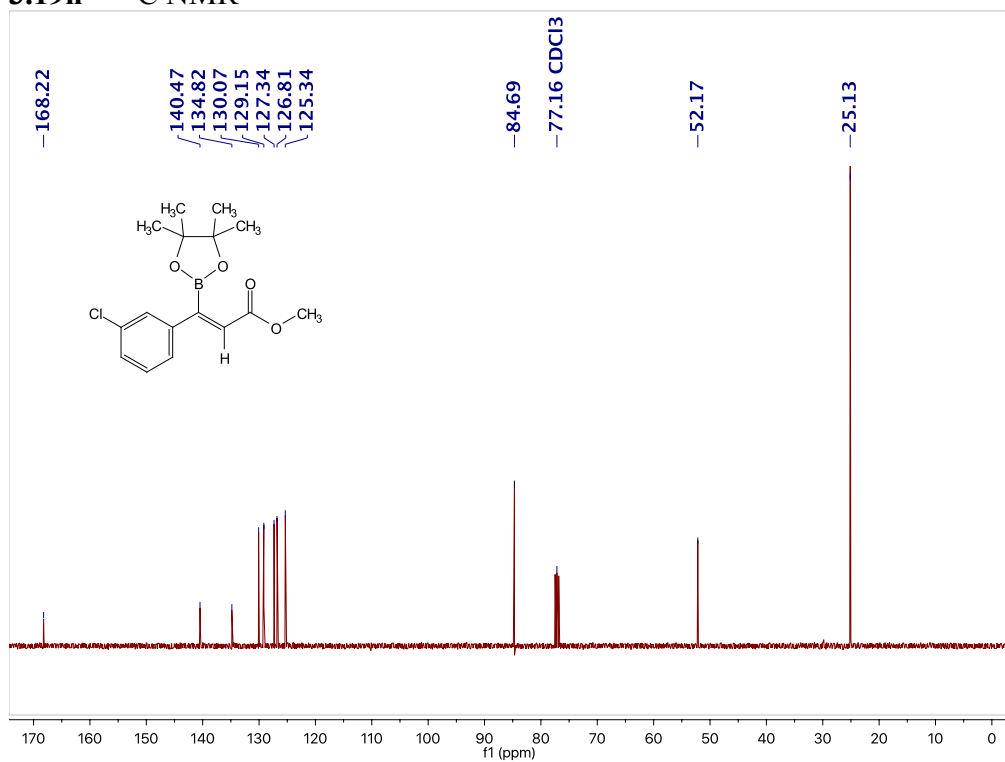
### 3.19g – $^{11}\text{B}$ NMR



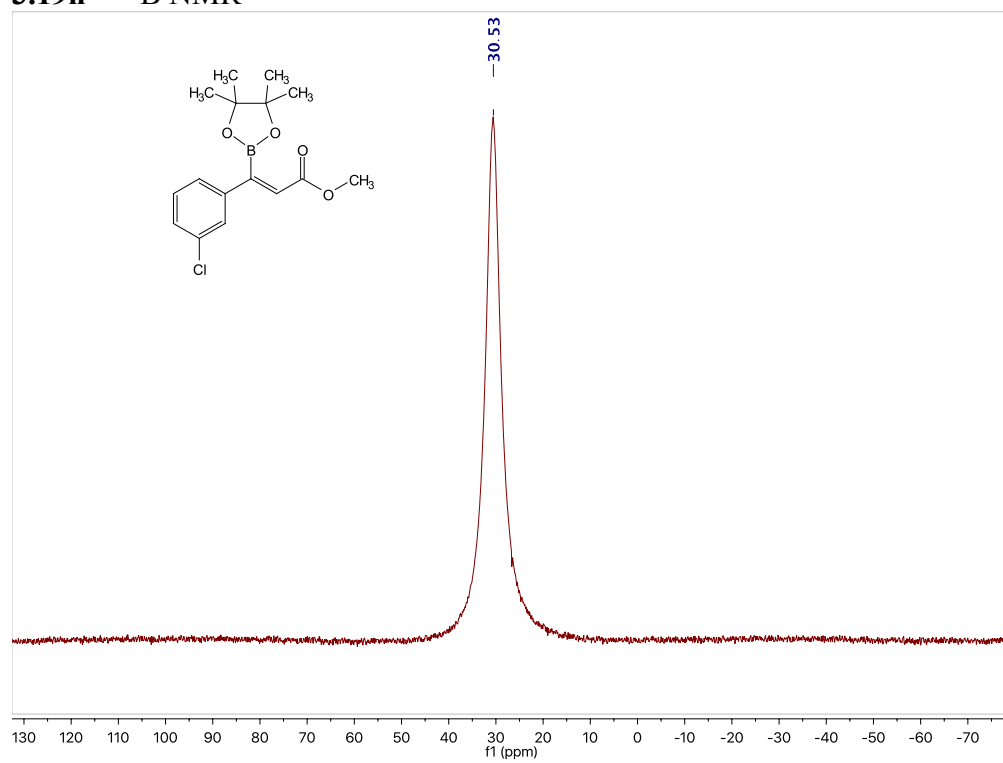
### 3.19h – <sup>1</sup>H NMR



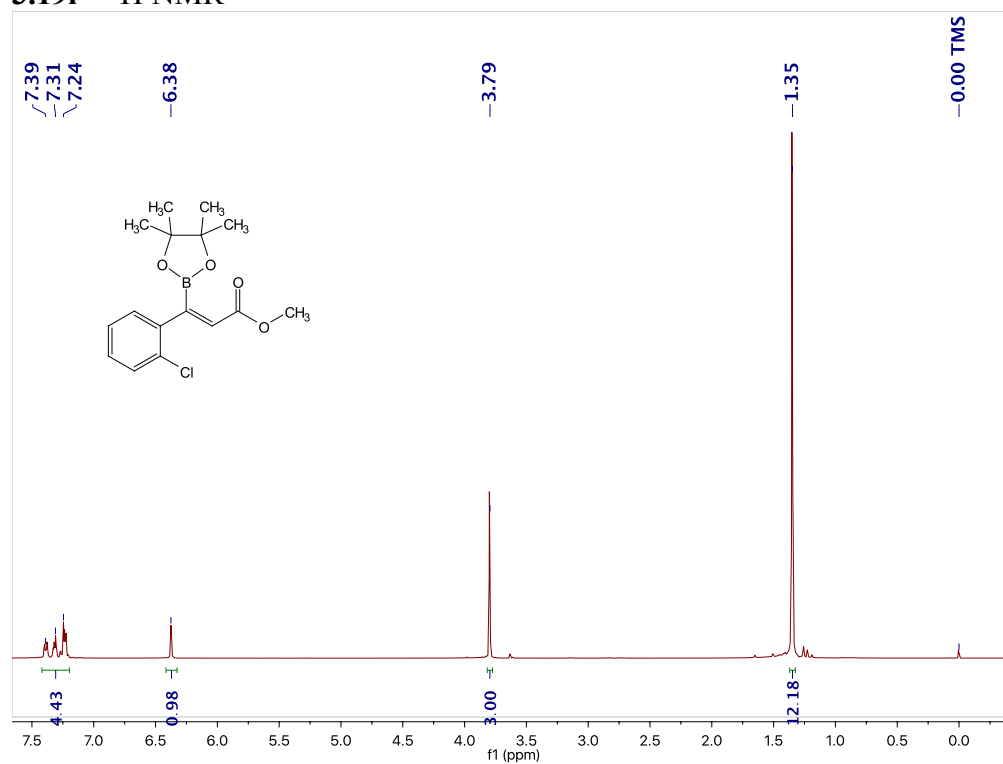
### 3.19h – <sup>13</sup>C NMR



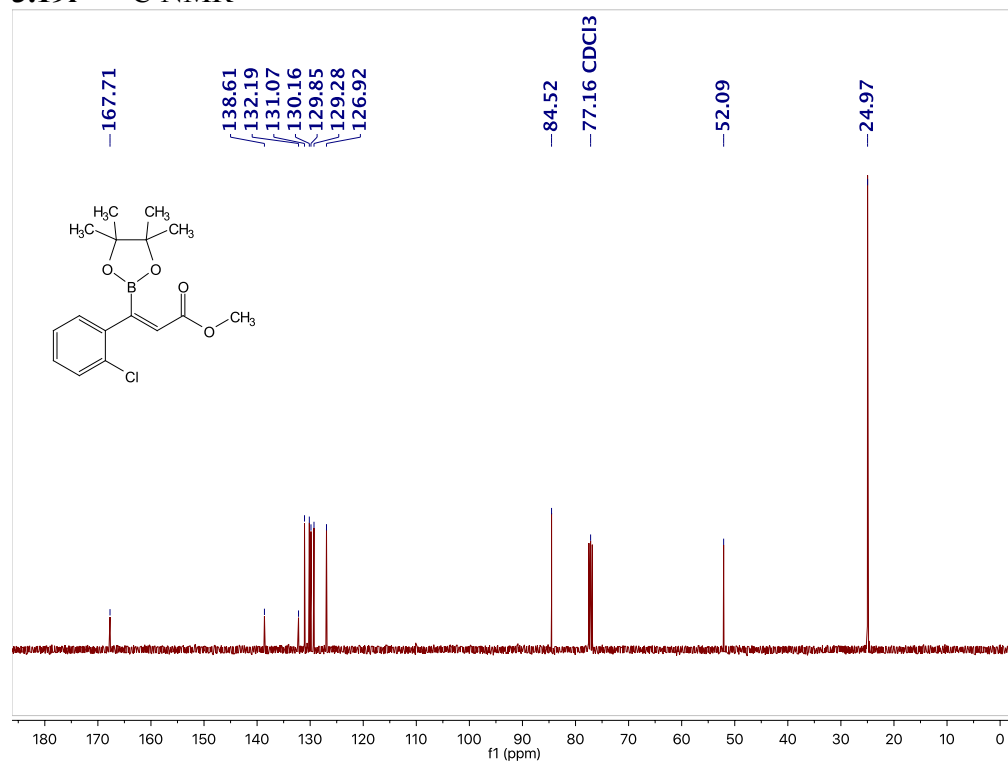
### 3.19h – $^{11}\text{B}$ NMR



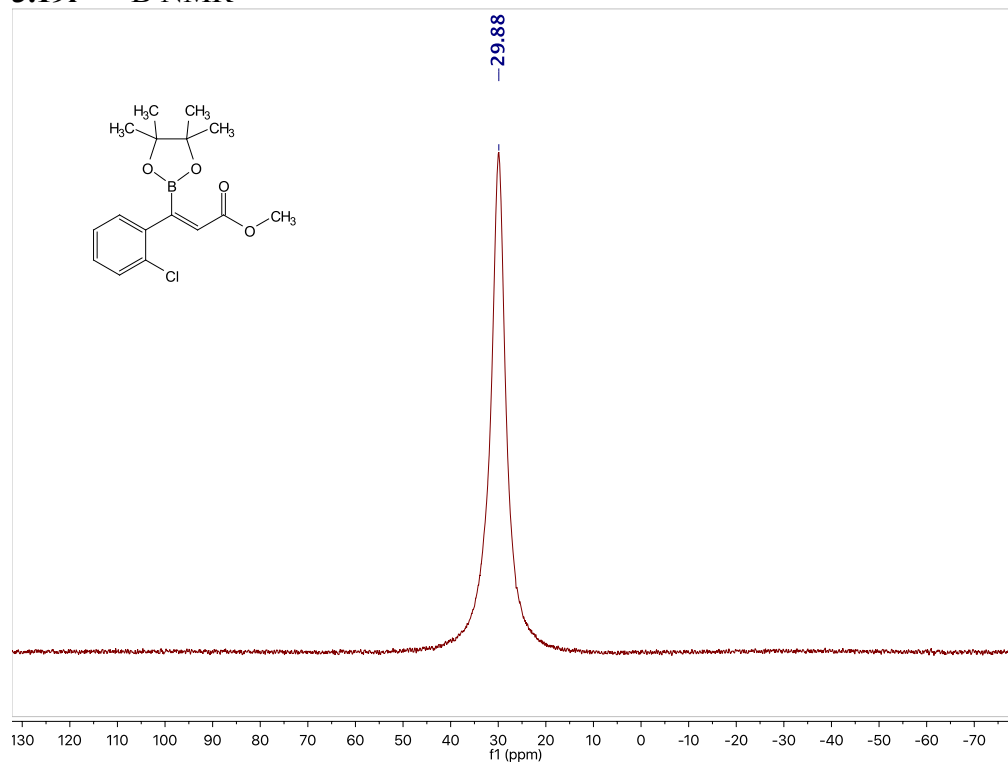
### 3.19i – $^1\text{H}$ NMR



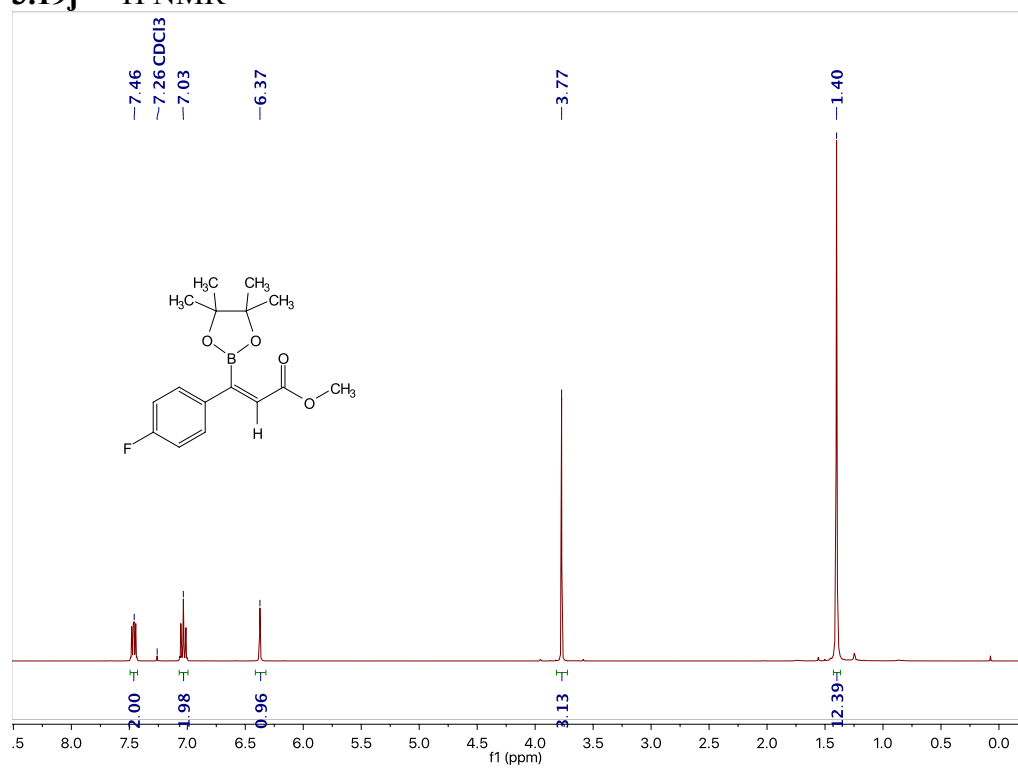
### 3.19i – $^{13}\text{C}$ NMR



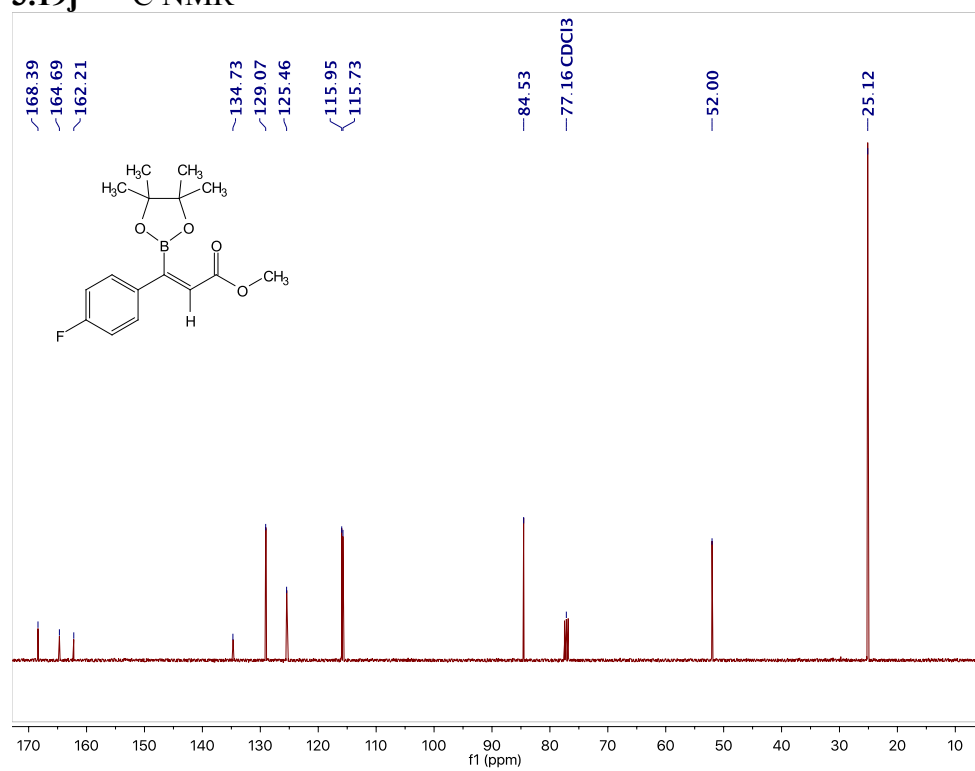
### 3.19i – $^{11}\text{B}$ NMR



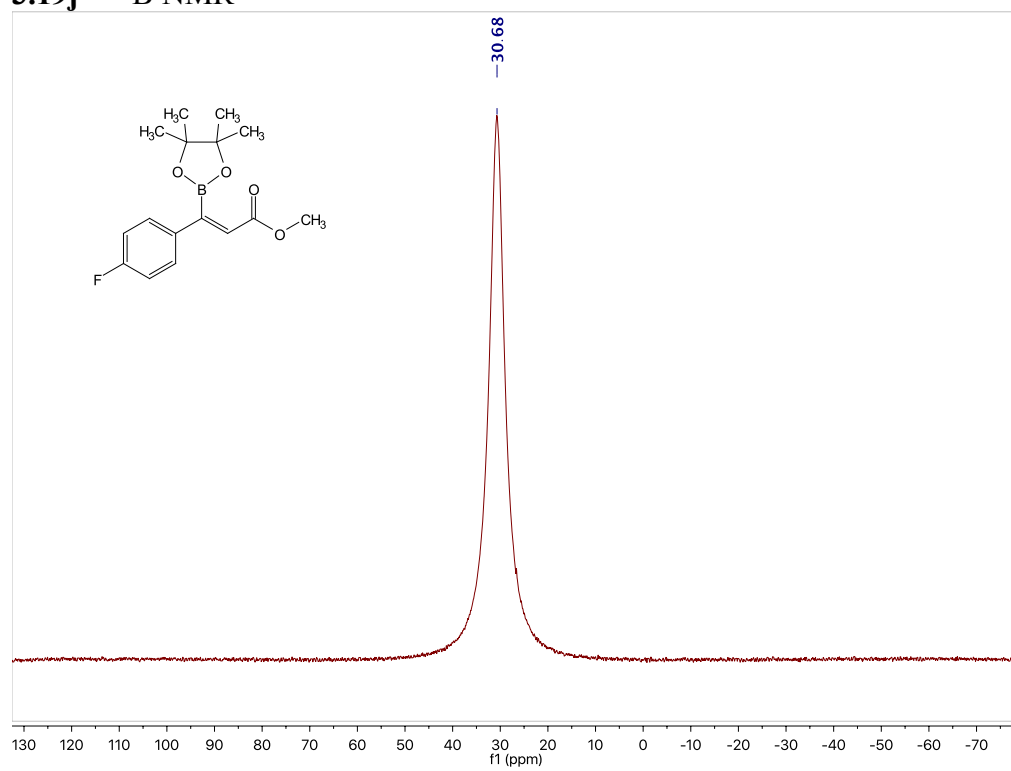
### 3.19j – $^1\text{H}$ NMR



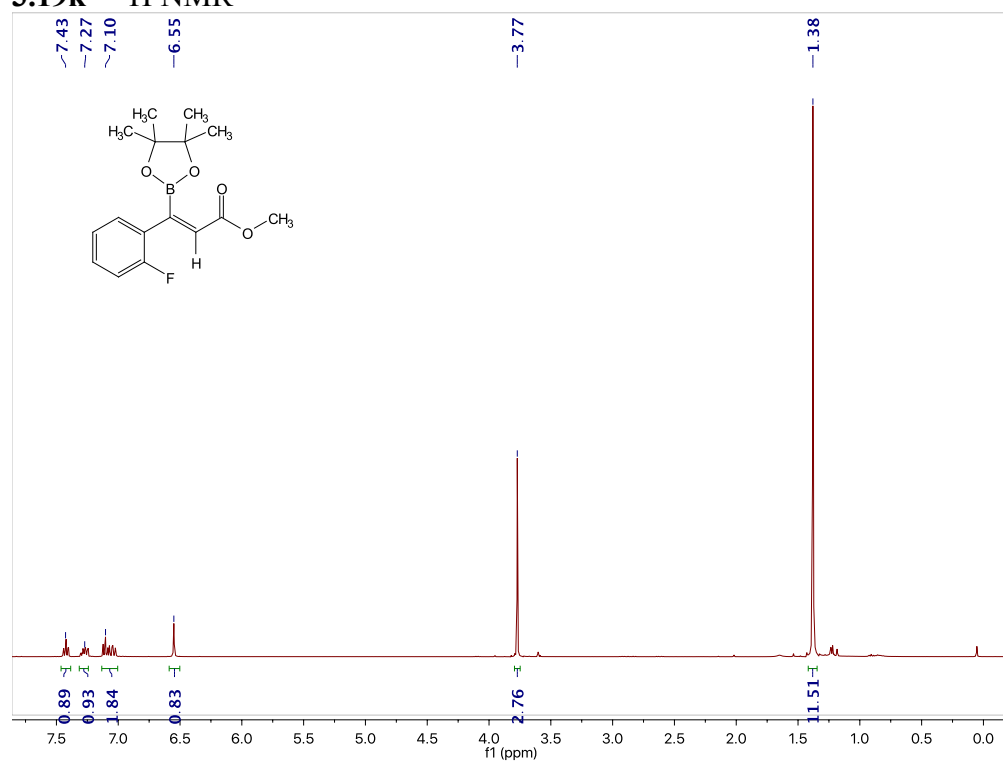
### 3.19j – $^{13}\text{C}$ NMR



### 3.19j – $^{11}\text{B}$ NMR

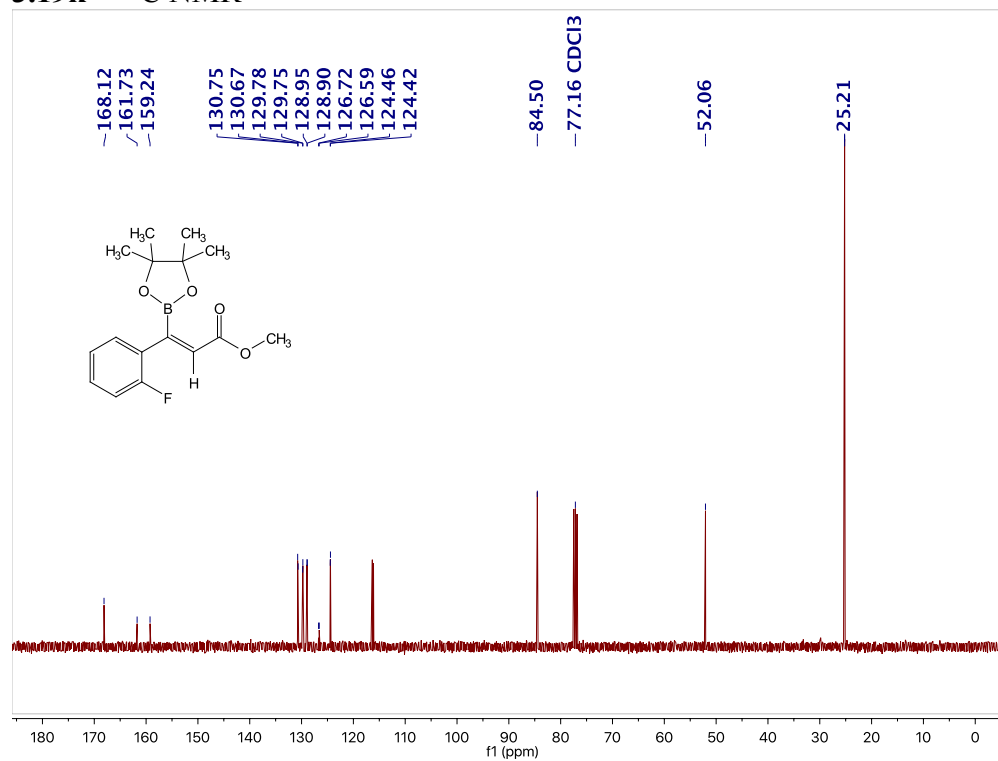


### 3.19k – $^1\text{H}$ NMR

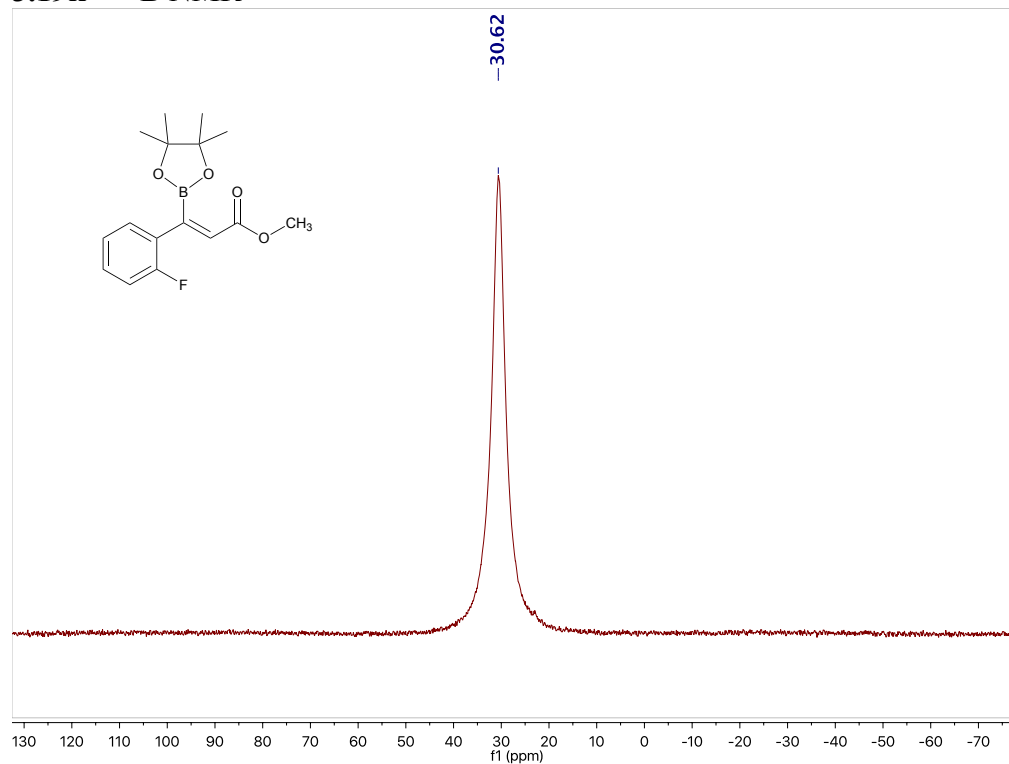




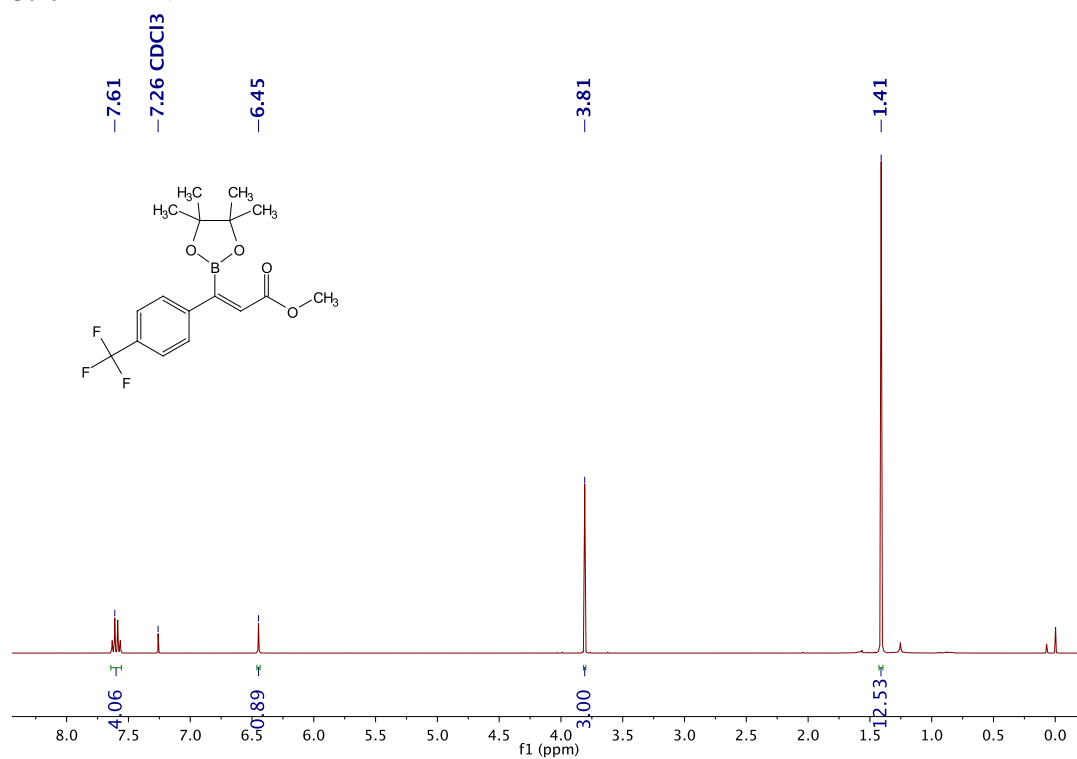
### 3.19k – $^{13}\text{C}$ NMR



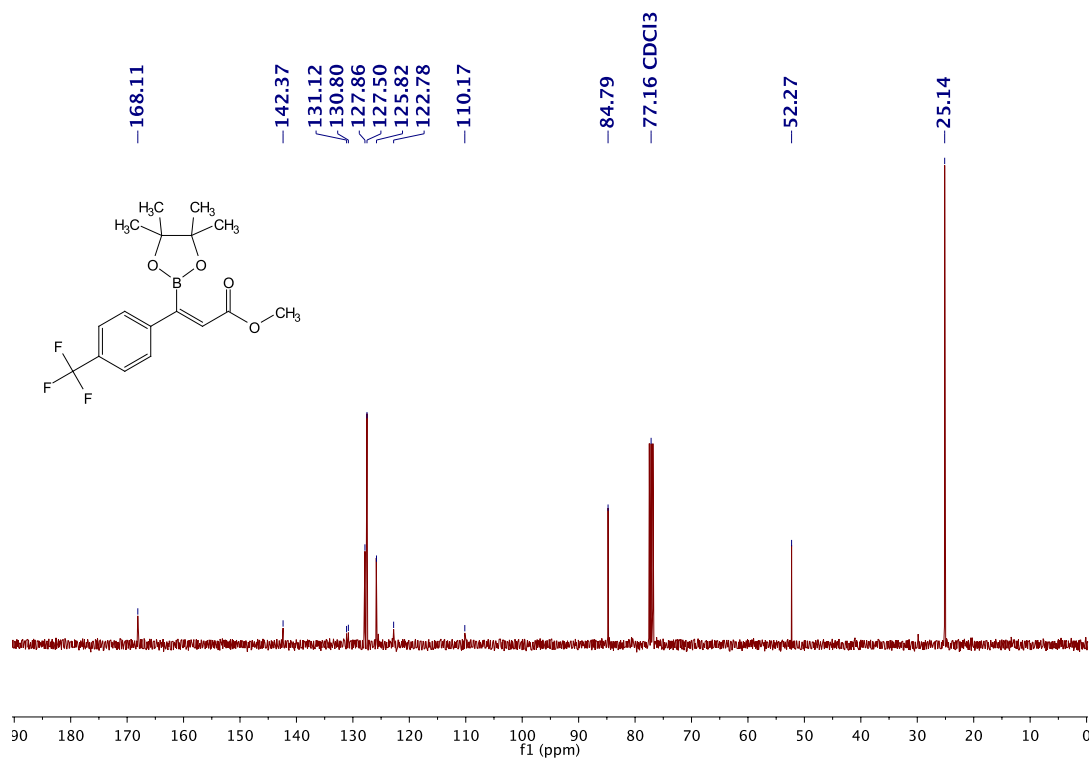
### 3.19k – $^{11}\text{B}$ NMR



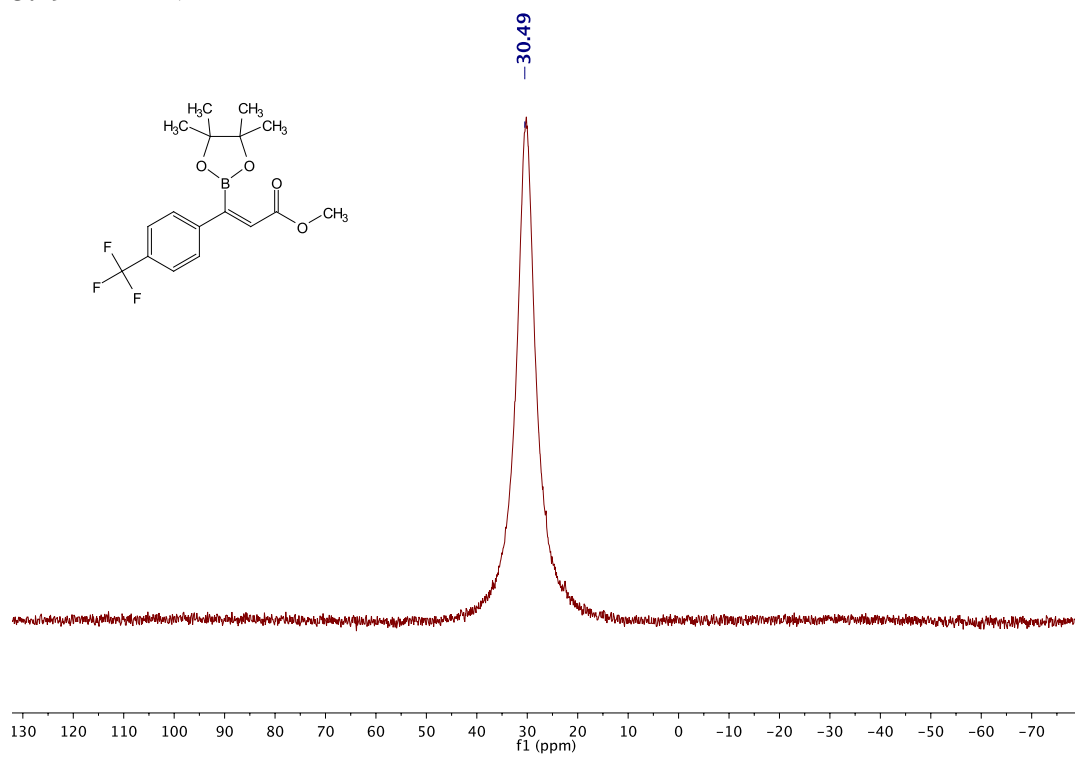
### 3.191 – $^1\text{H}$ NMR



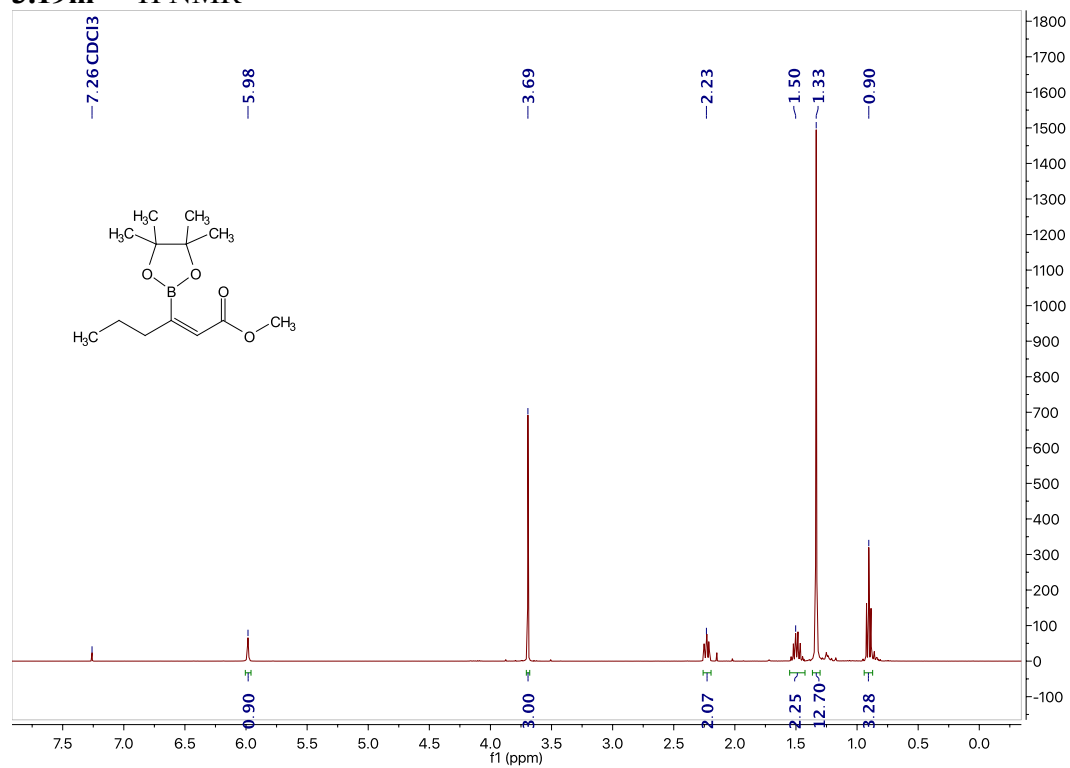
### 3.191 – $^{13}\text{C}$ NMR



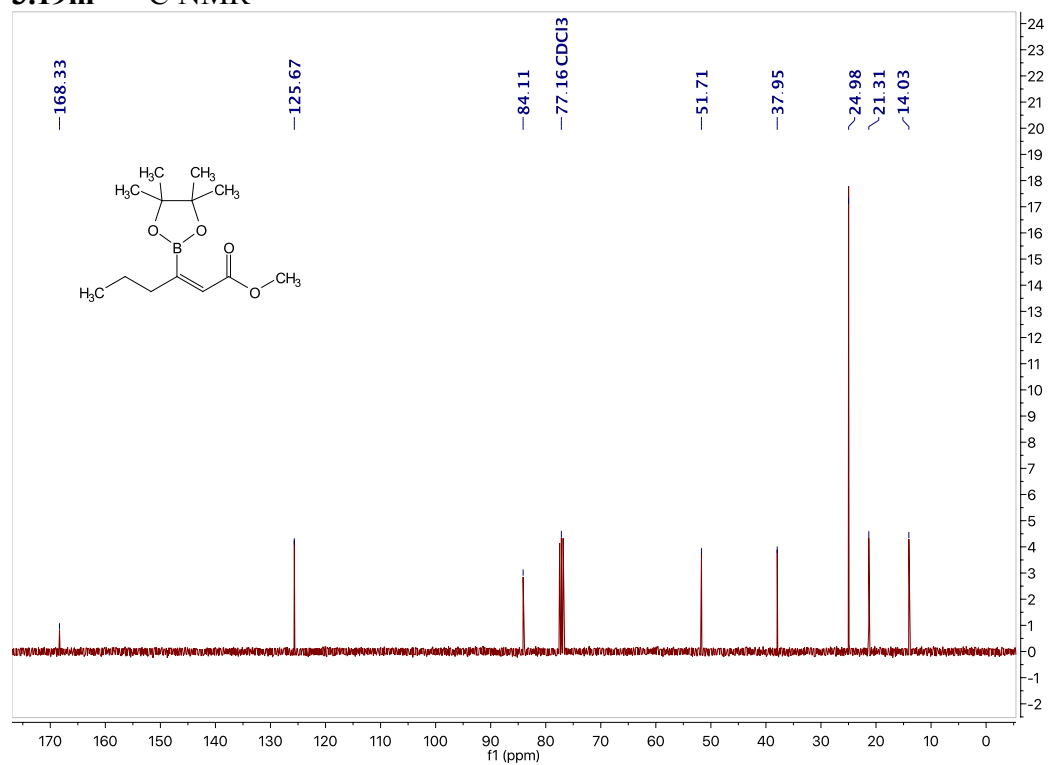
### 3.19l – $^{11}\text{B}$ NMR



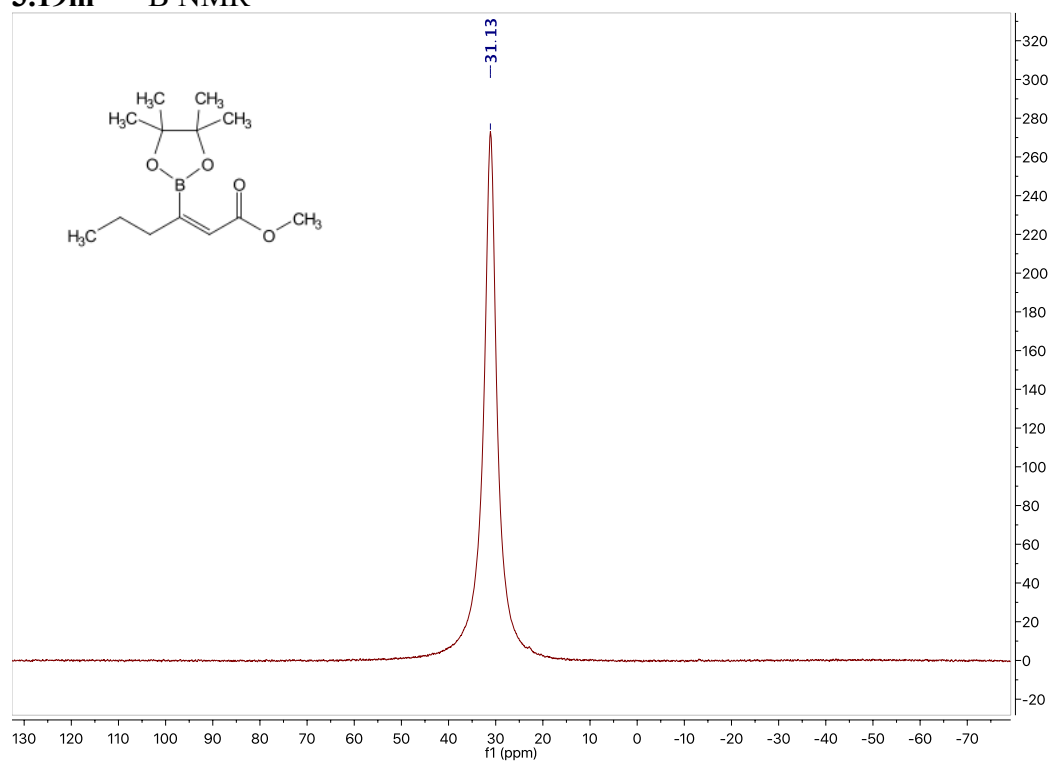
### 3.19m – $^1\text{H}$ NMR



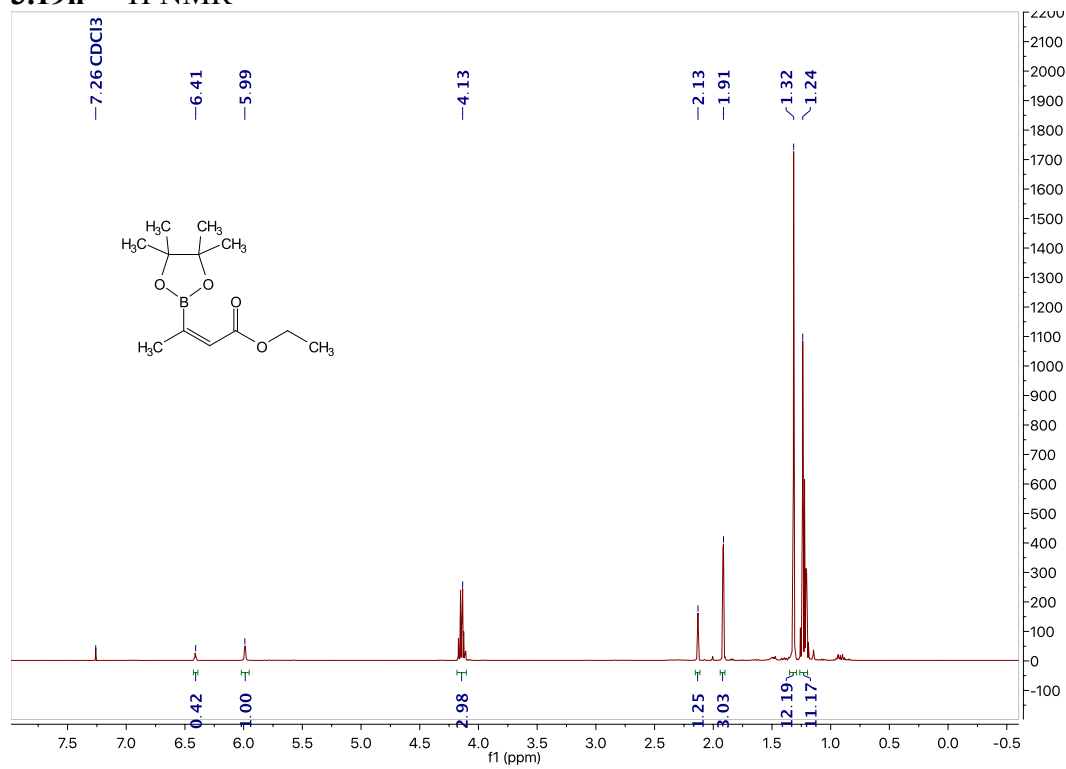
### 3.19m – $^{13}\text{C}$ NMR



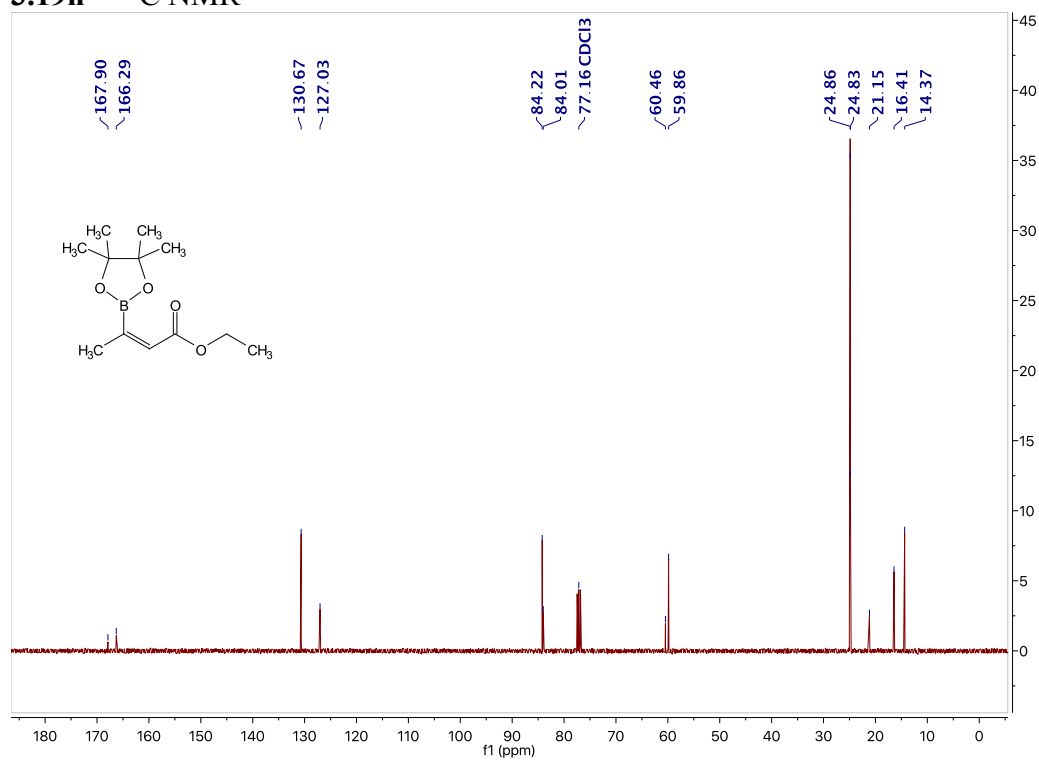
### 3.19m – $^{11}\text{B}$ NMR



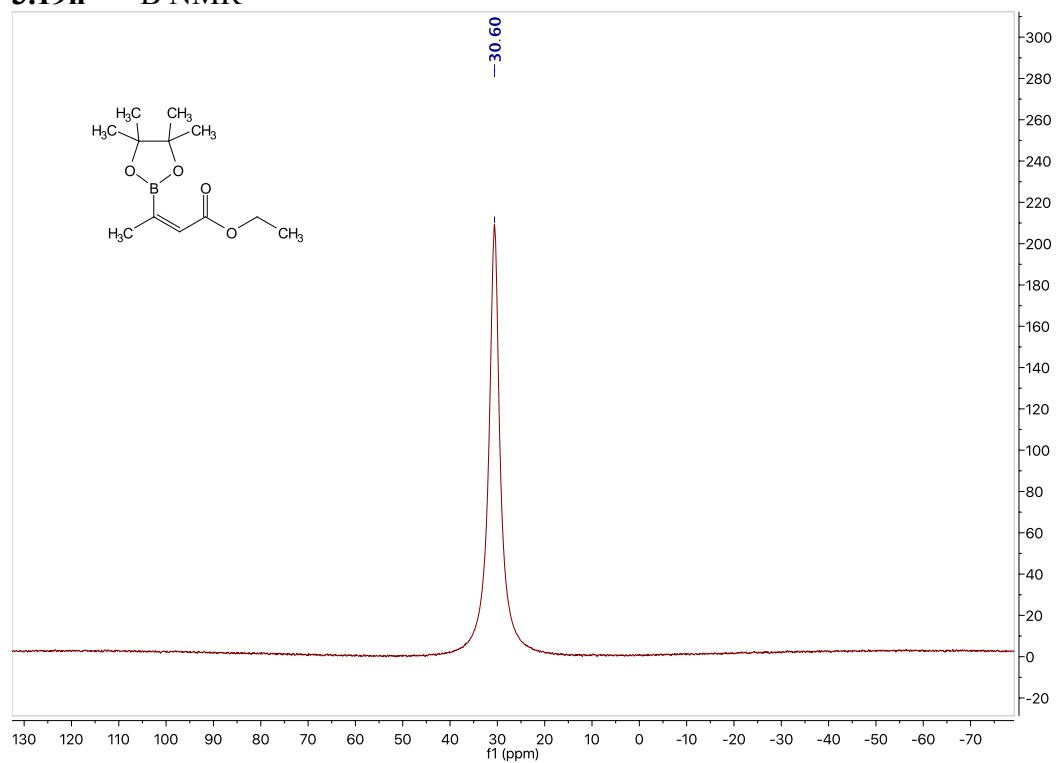
### 3.19n – <sup>1</sup>H NMR



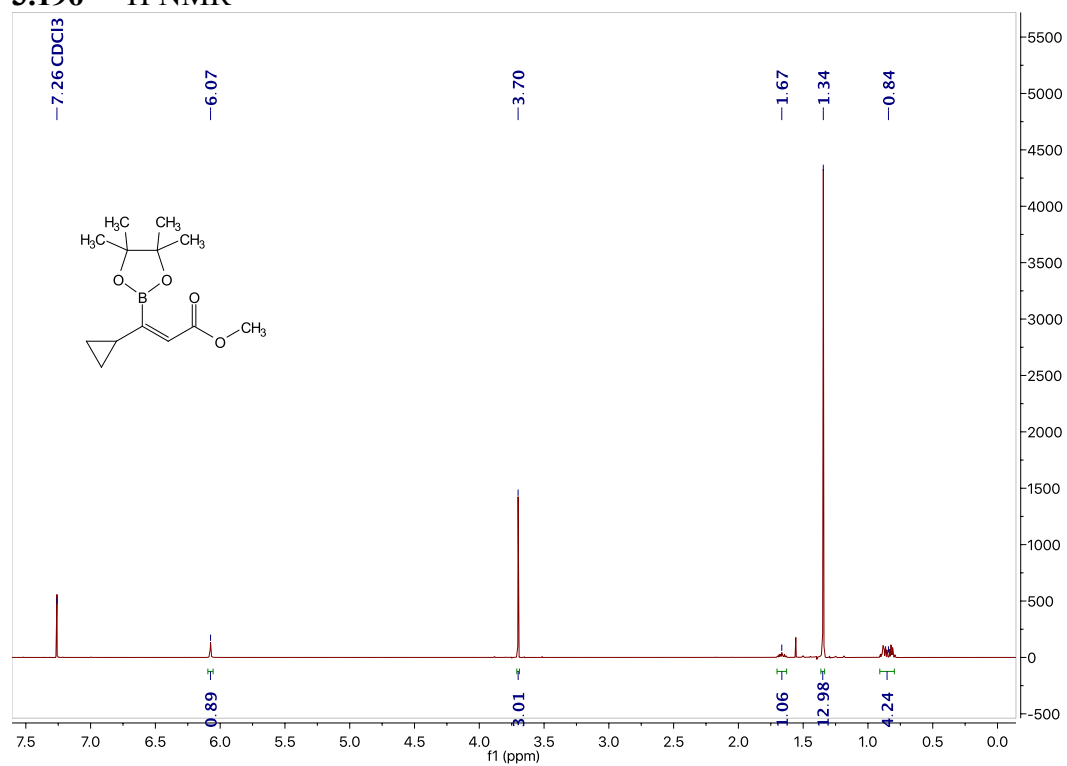
### 3.19n – <sup>13</sup>C NMR



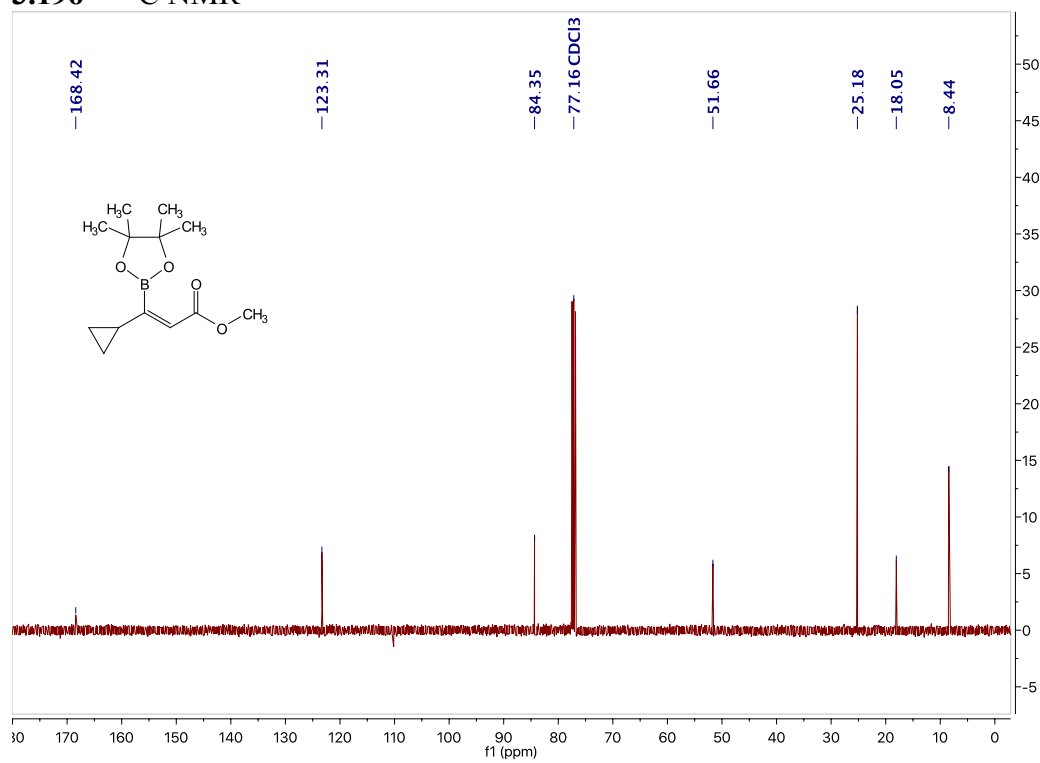
### 3.19n – $^{11}\text{B}$ NMR



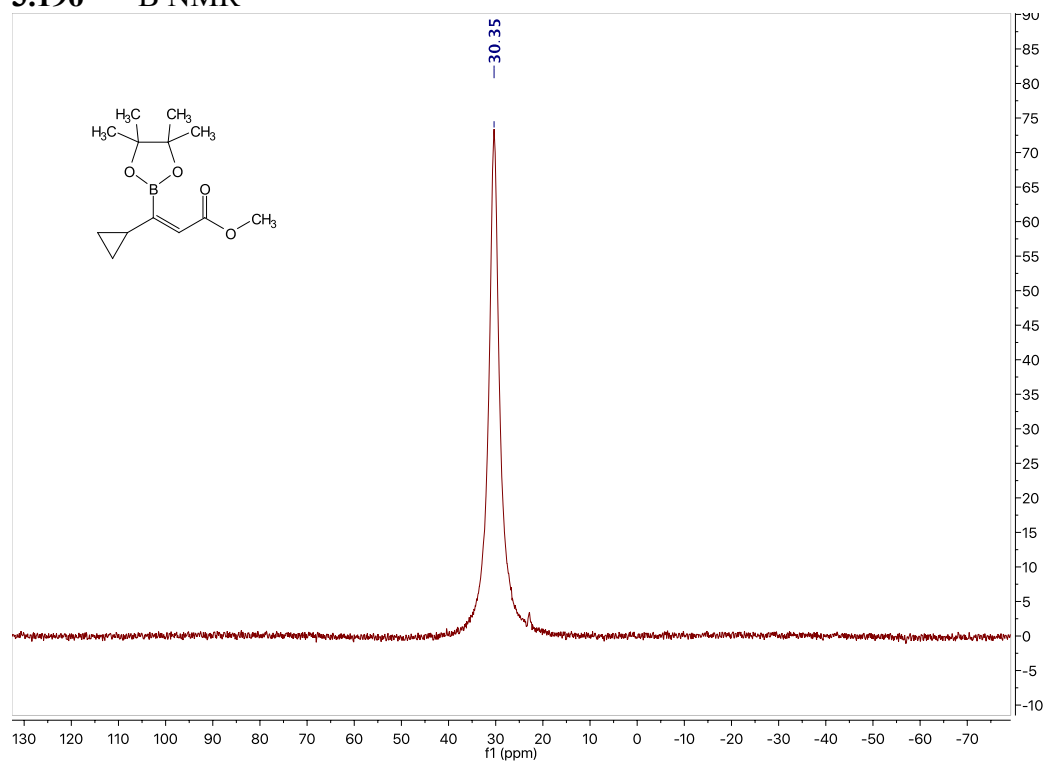
### 3.19o – $^1\text{H}$ NMR



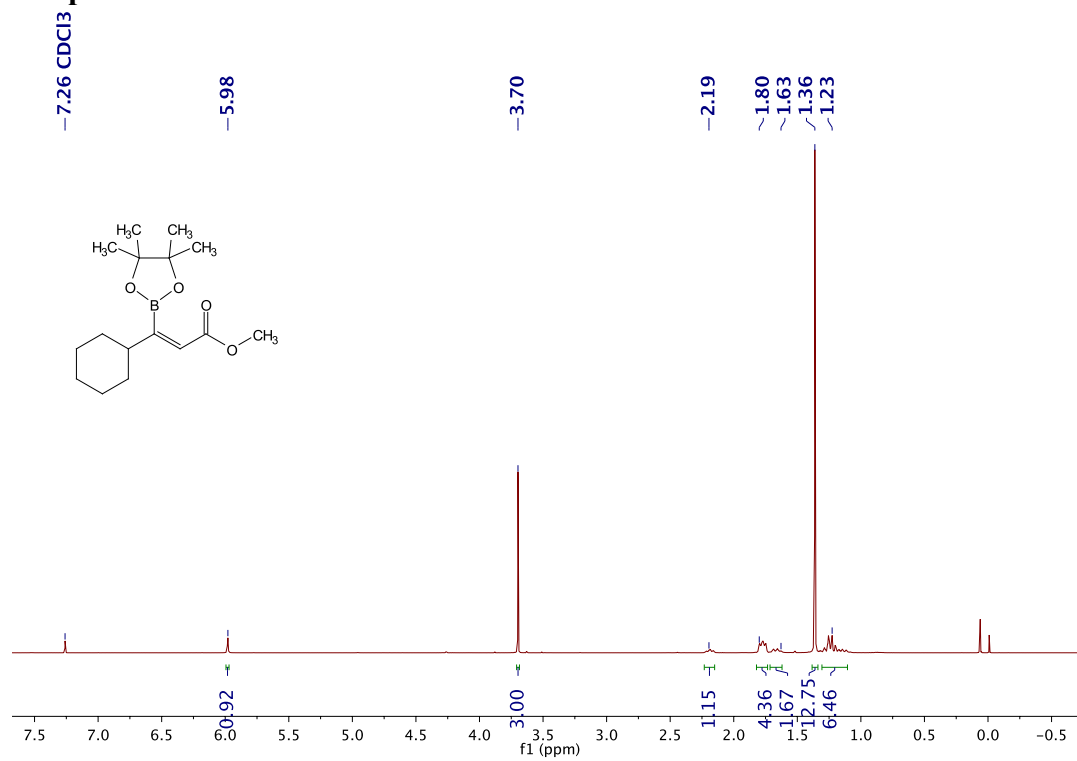
### 3.19o – $^{13}\text{C}$ NMR



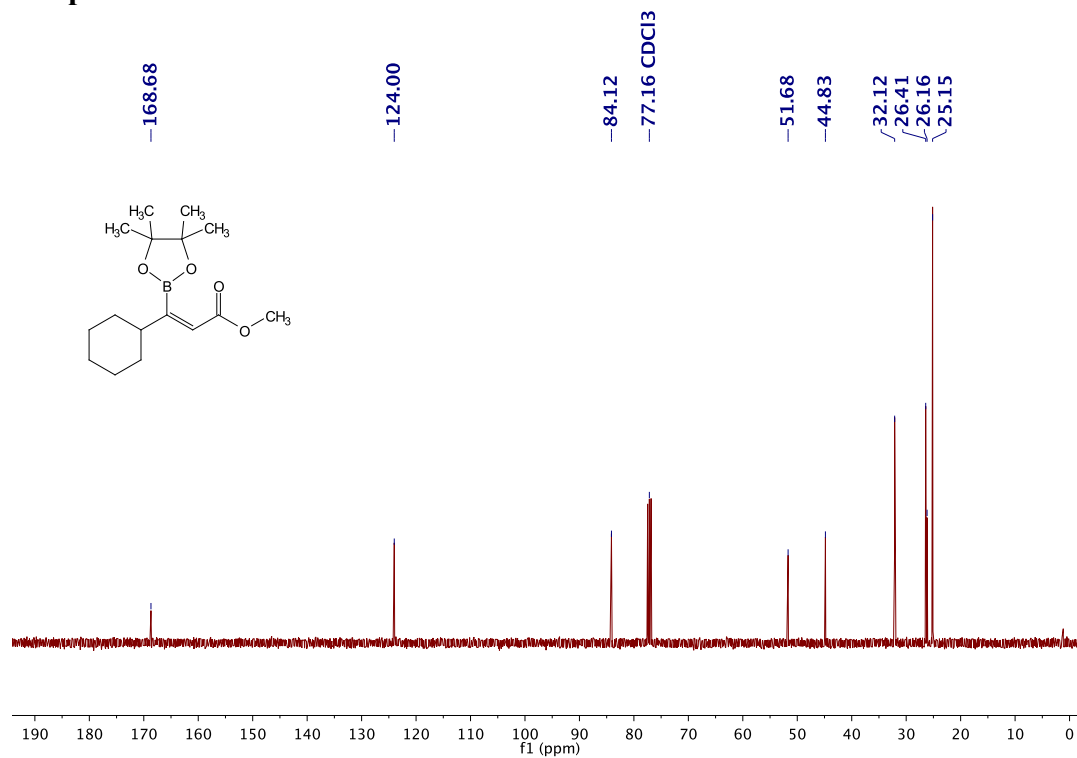
### 3.19o – $^{11}\text{B}$ NMR



### 3.19p – <sup>1</sup>H NMR

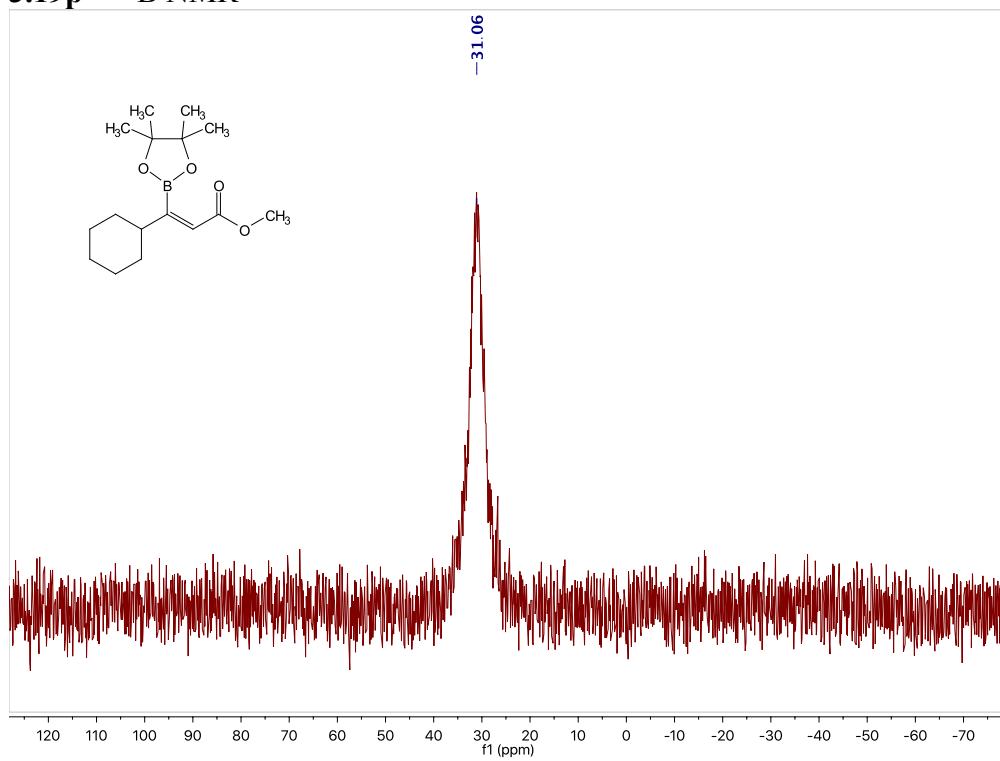


### 3.19p – <sup>13</sup>C NMR

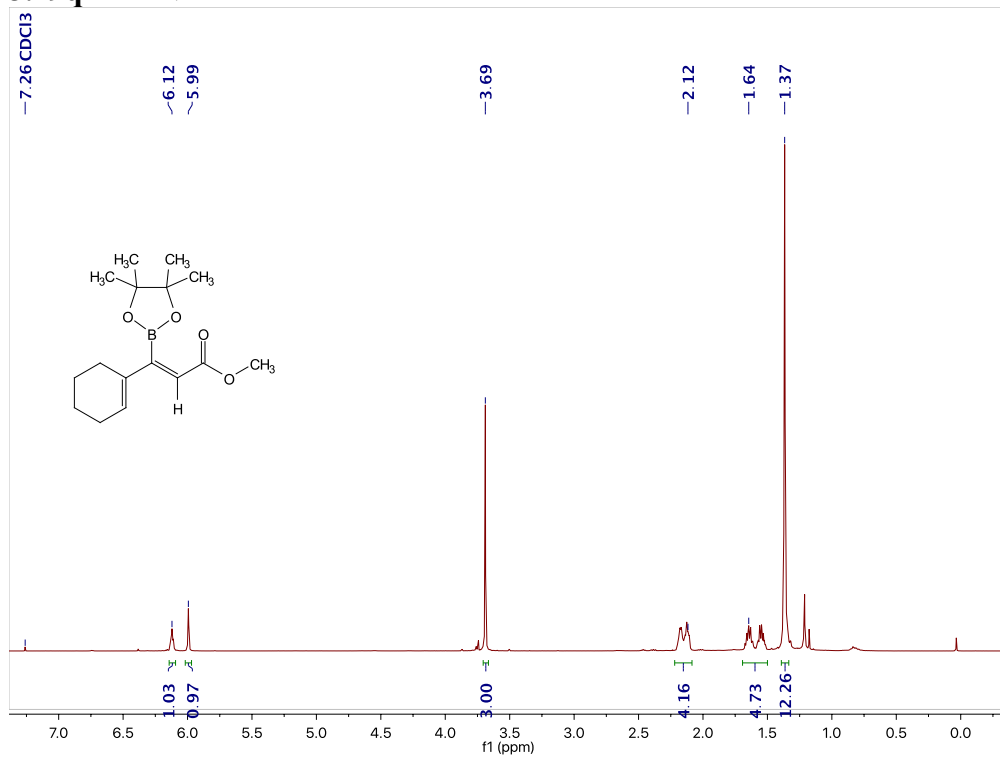




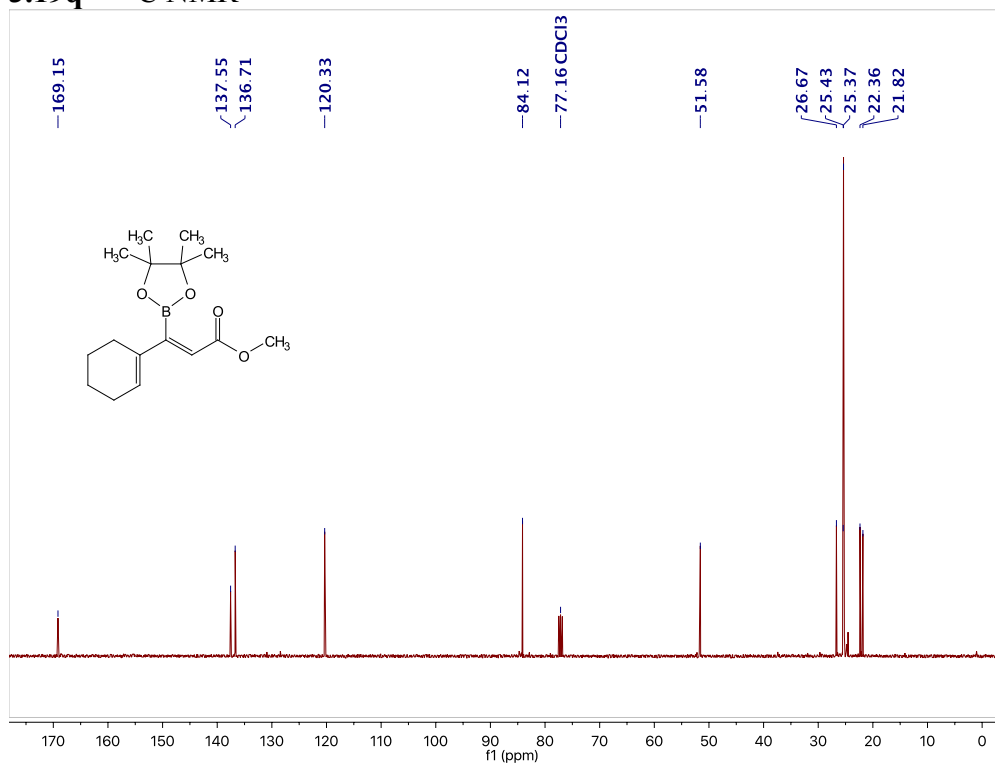
### 3.19p – $^{11}\text{B}$ NMR



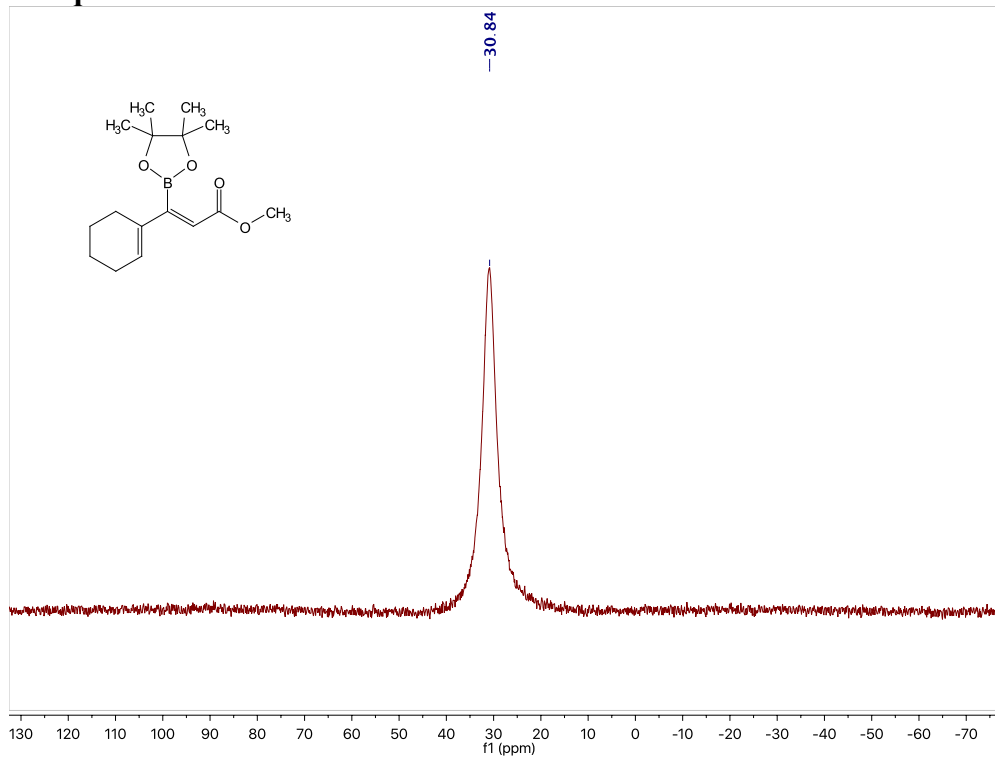
### 3.19q – $^1\text{H}$ NMR



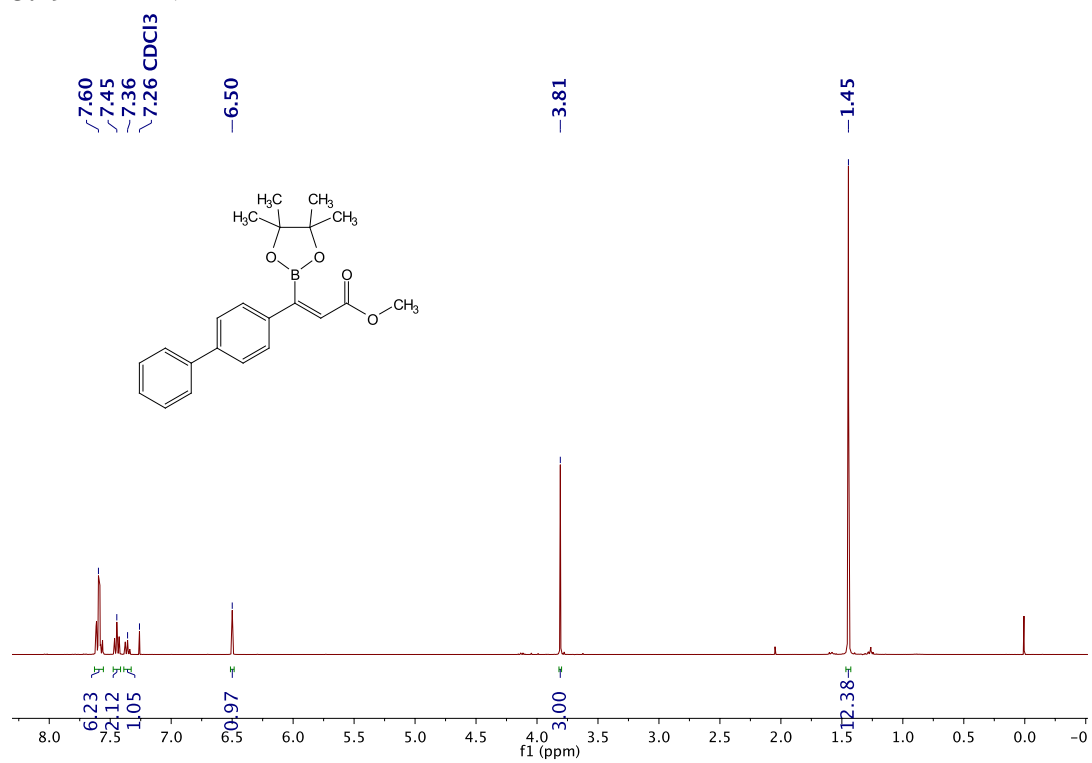
### 3.19q – $^{13}\text{C}$ NMR



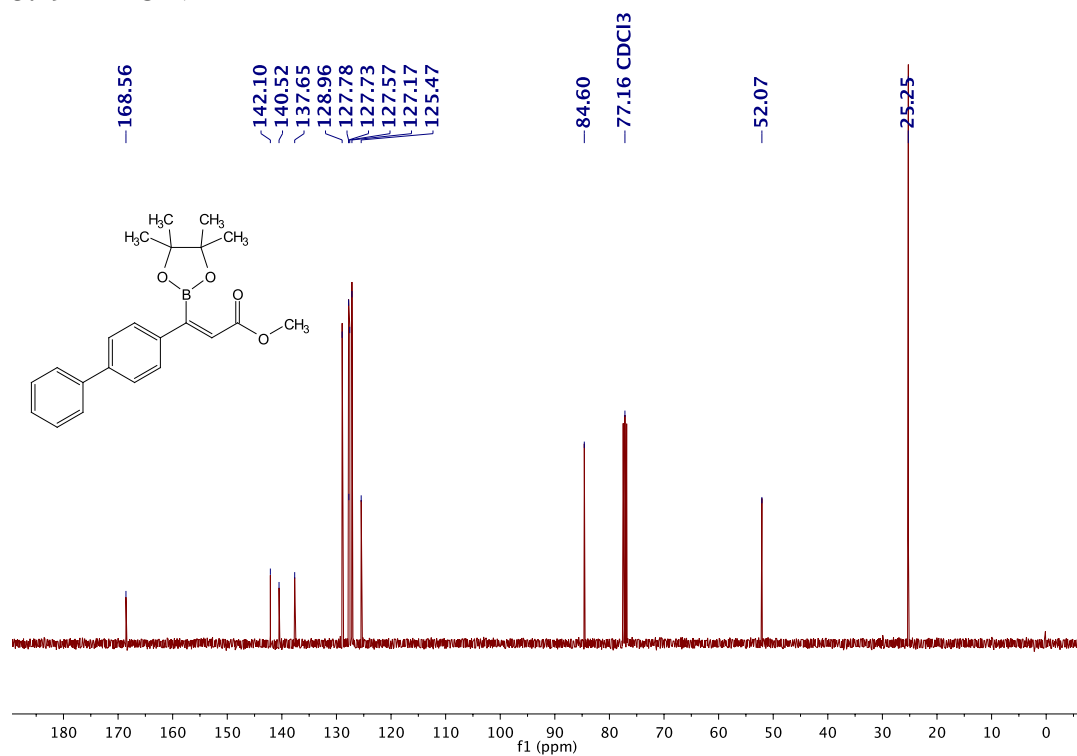
### 3.19q – $^{11}\text{B}$ NMR



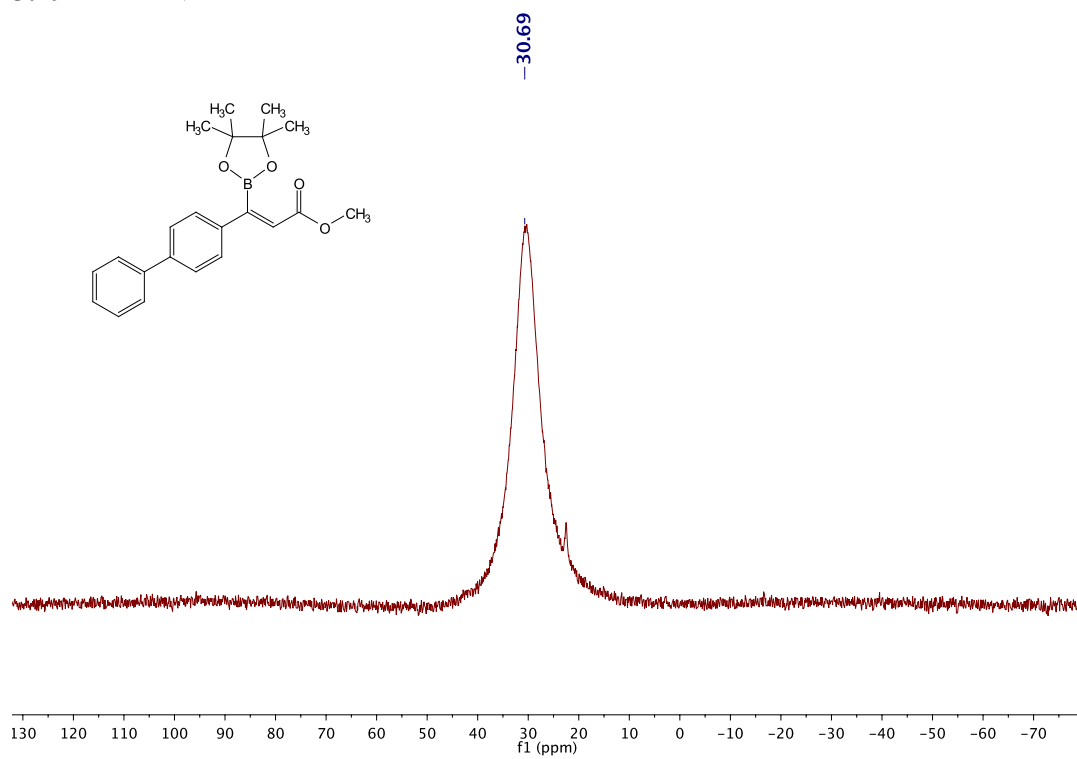
### 3.19r – <sup>1</sup>H NMR



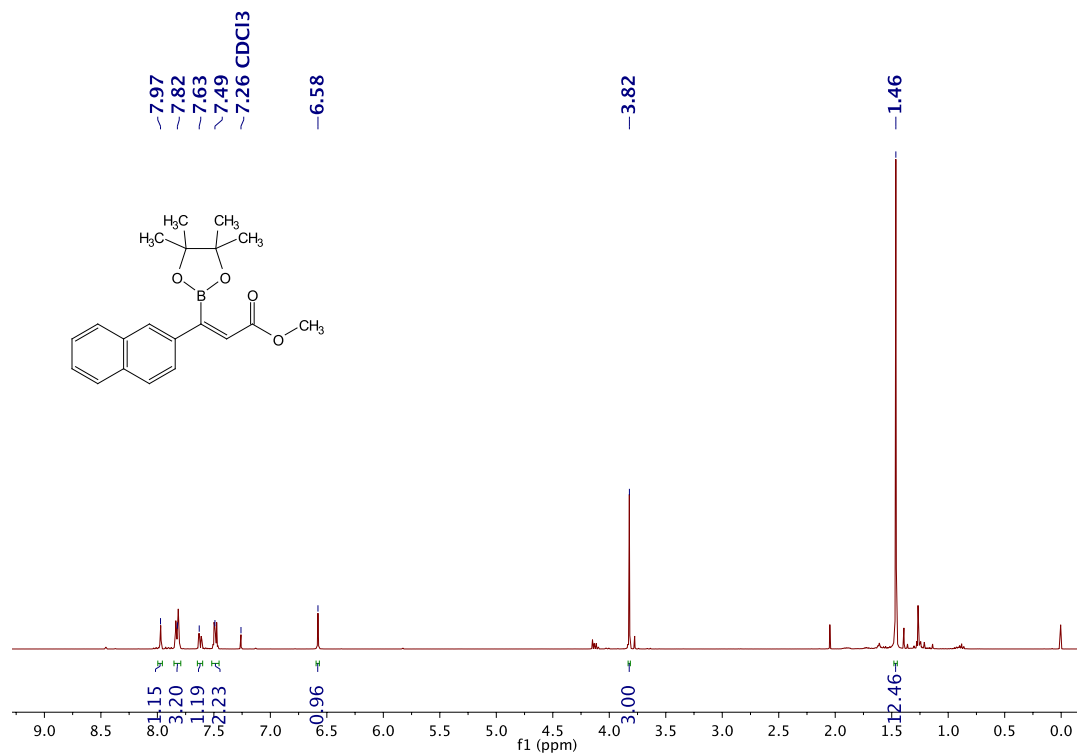
### 3.19r – <sup>13</sup>C NMR



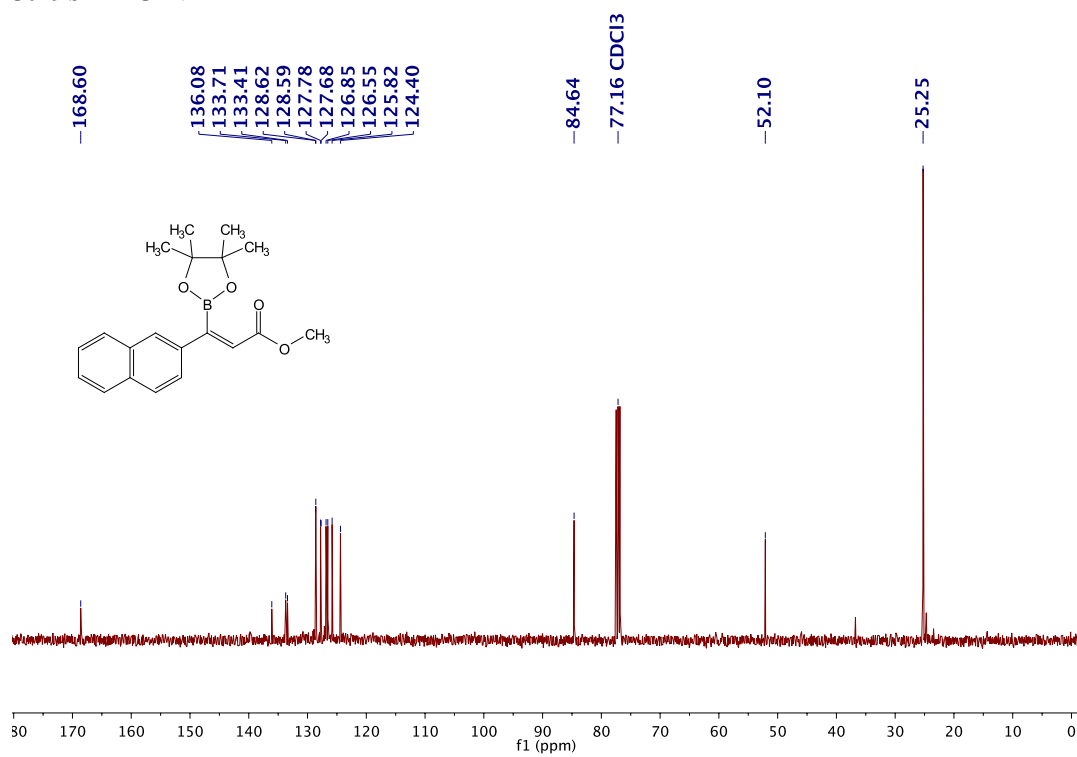
### 3.19r – $^{11}\text{B}$ NMR



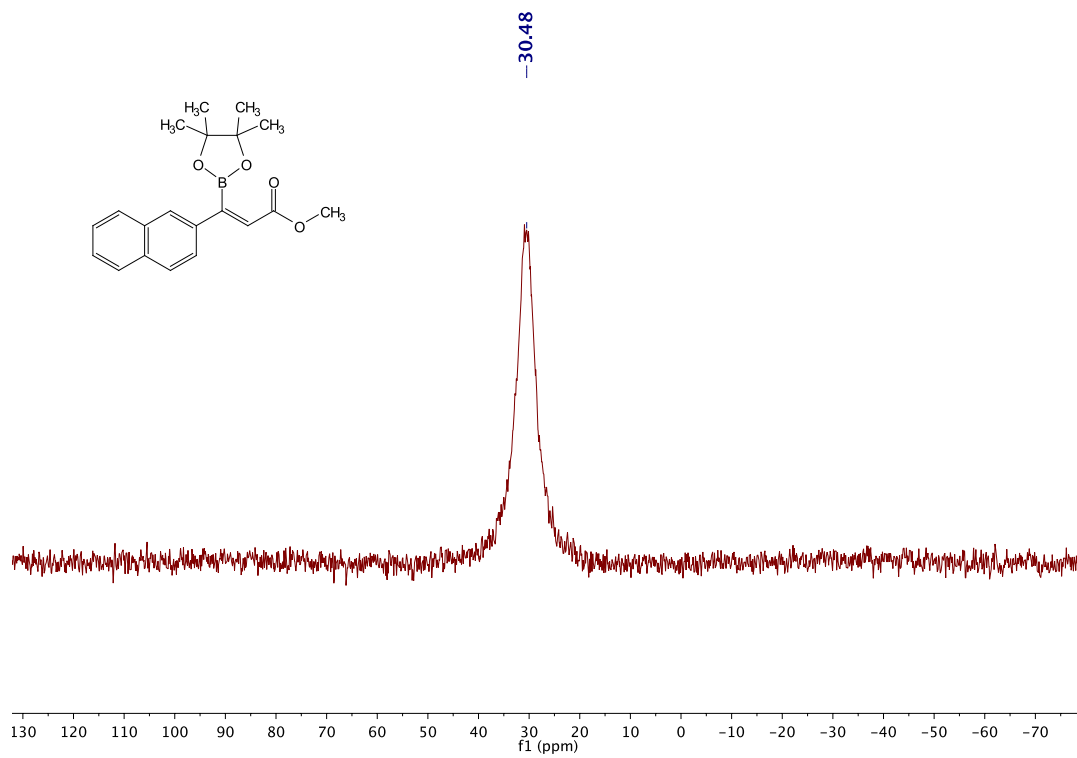
### 3.19s – $^1\text{H}$ NMR



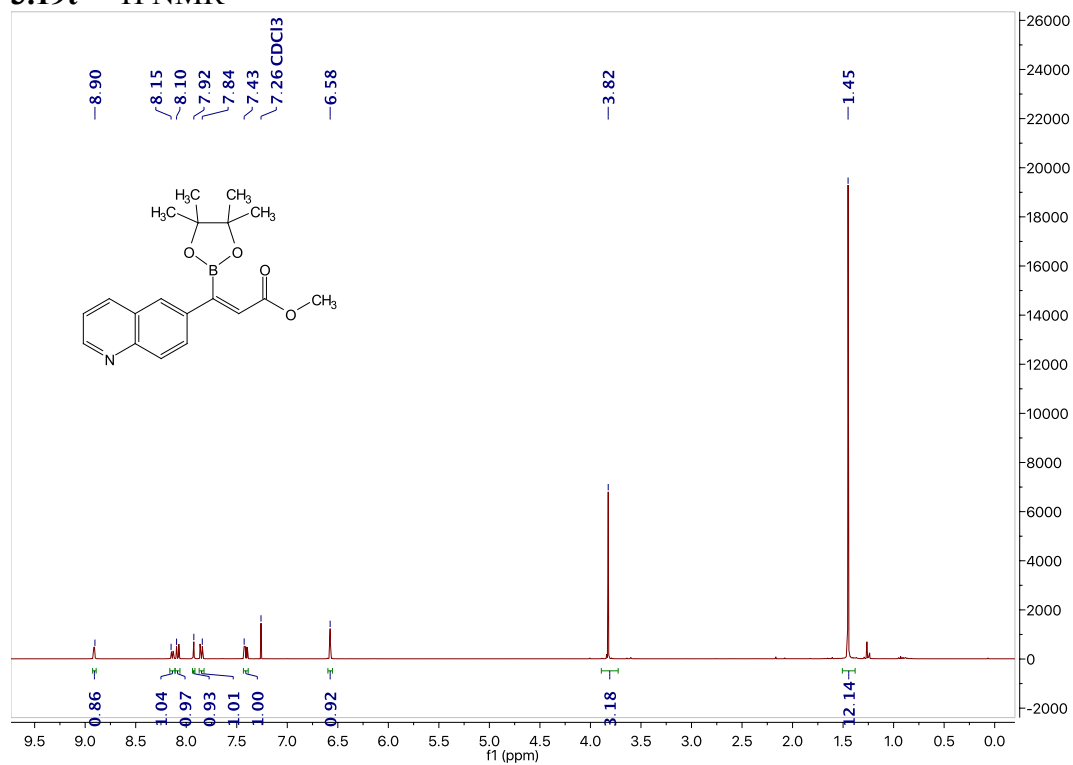
### 3.19s – $^{13}\text{C}$ NMR



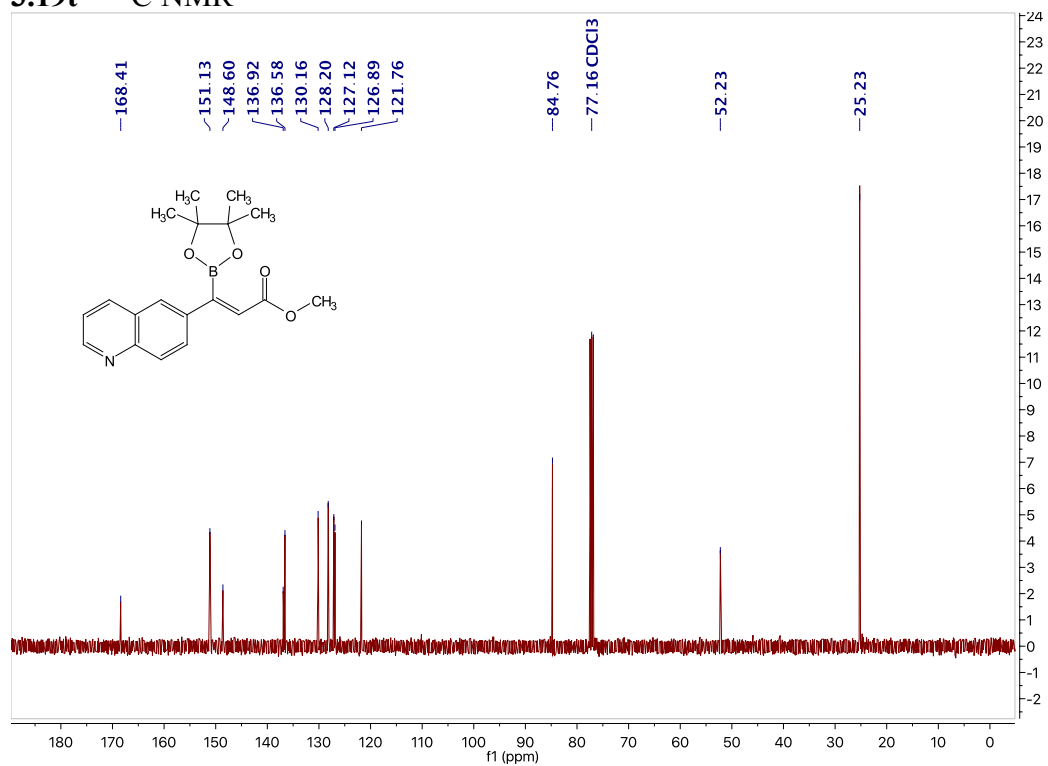
### 3.19s – $^{11}\text{B}$ NMR



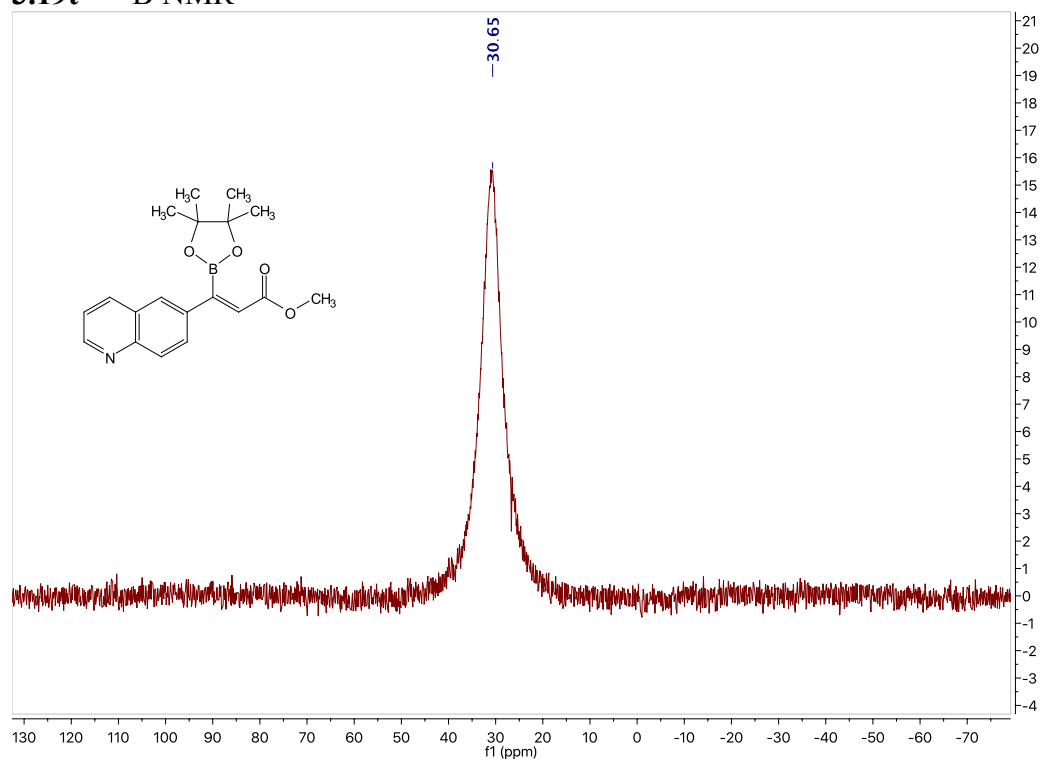
### 3.19t – <sup>1</sup>H NMR



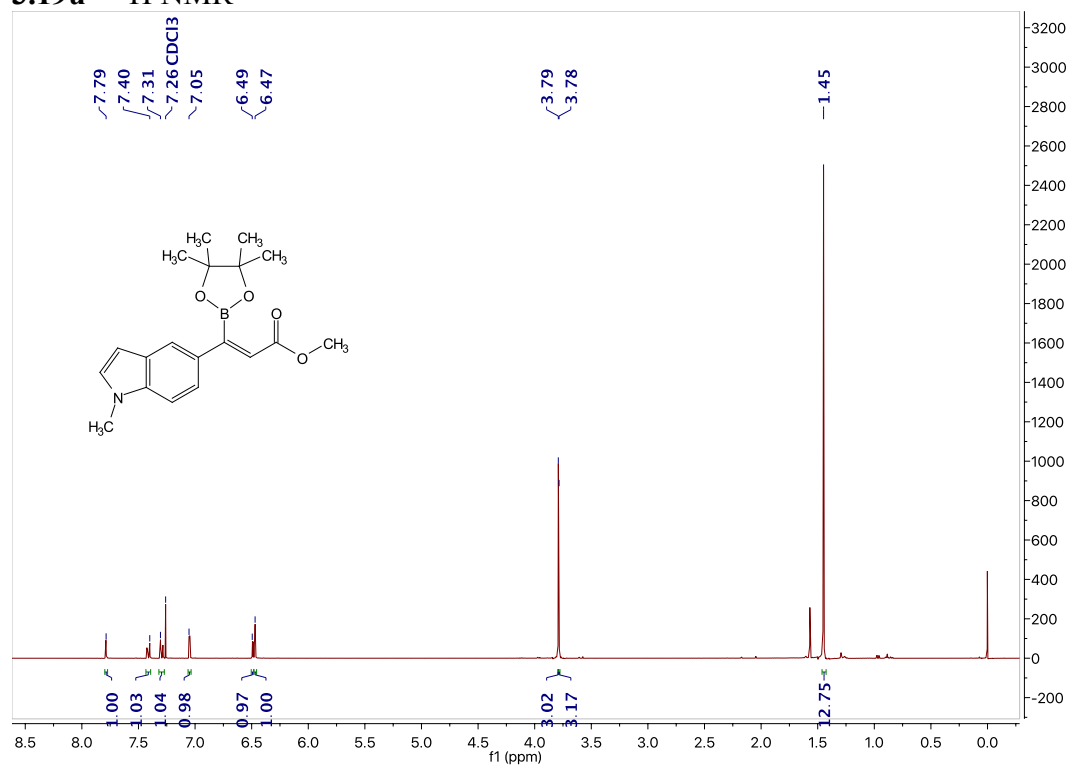
### 3.19t – <sup>13</sup>C NMR



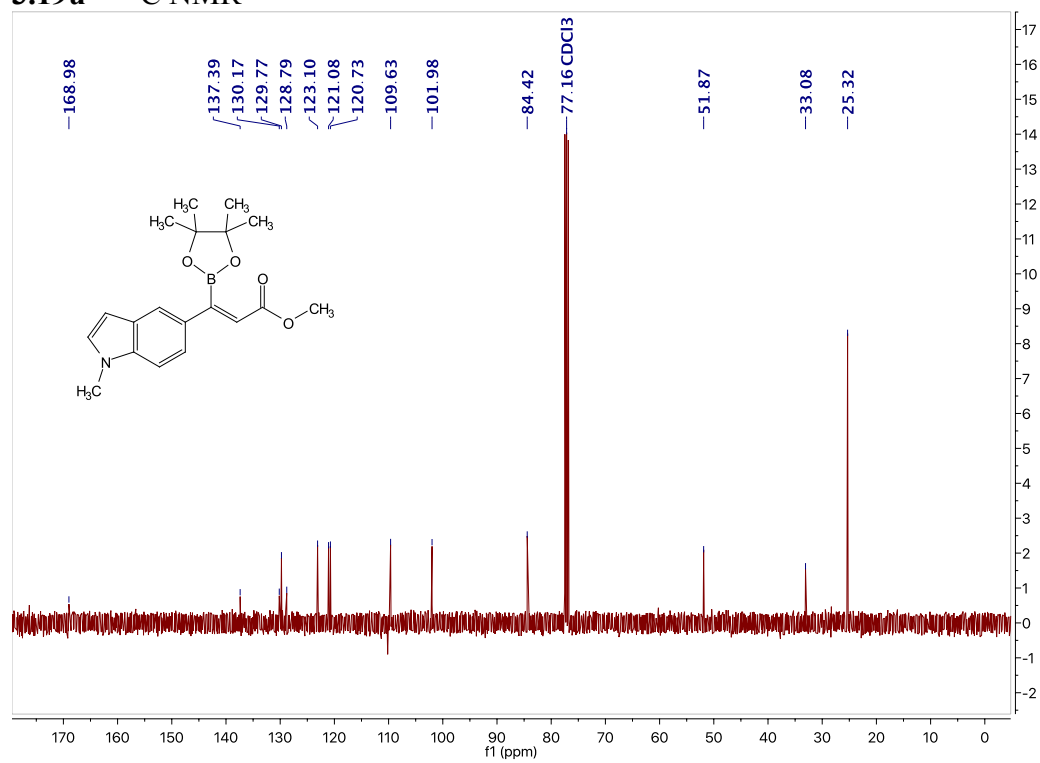
### 3.19t – $^{11}\text{B}$ NMR



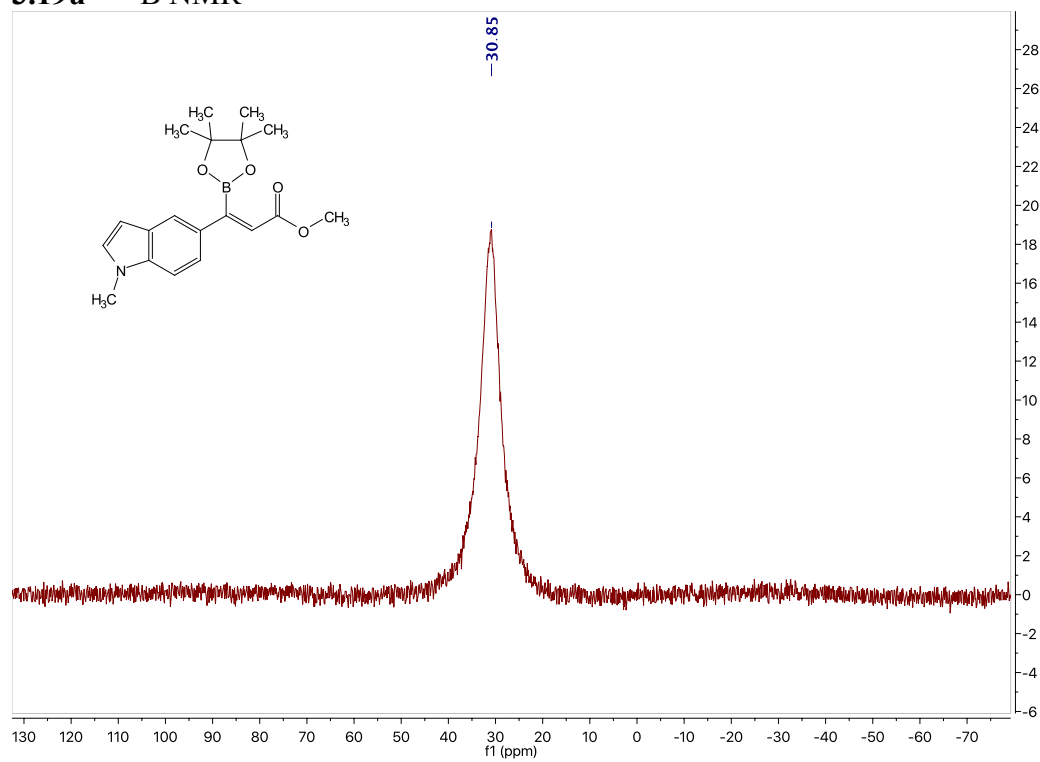
### 3.19u – $^1\text{H}$ NMR



### 3.19u – <sup>13</sup>C NMR

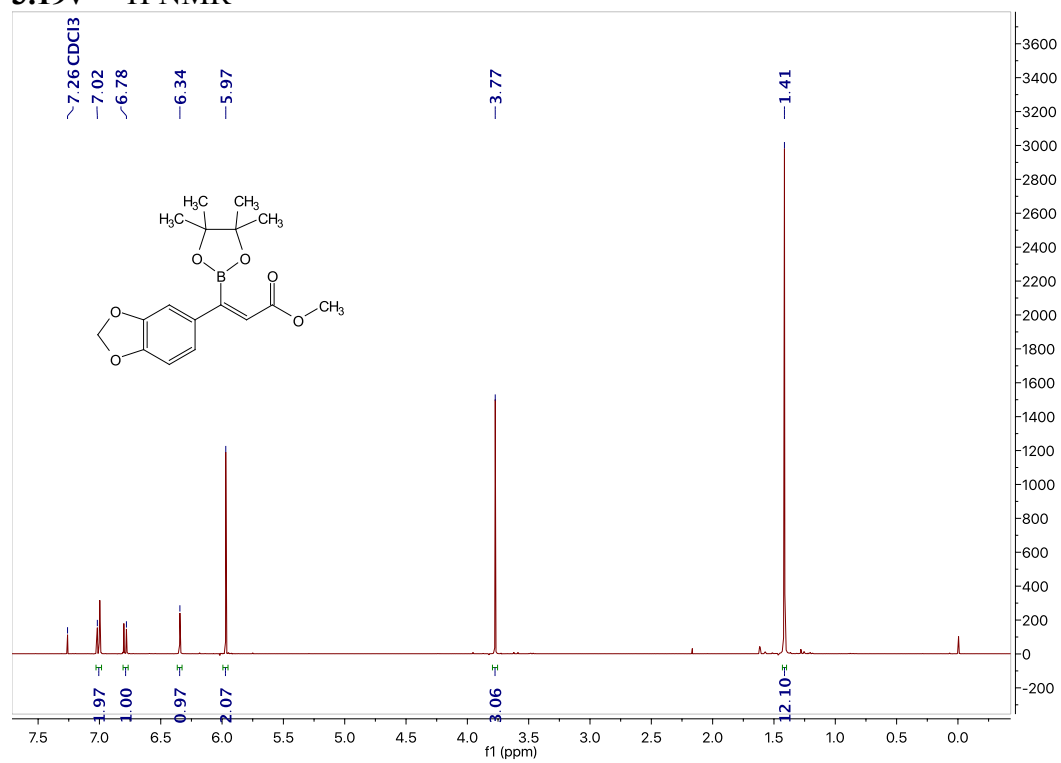


### 3.19u – <sup>11</sup>B NMR

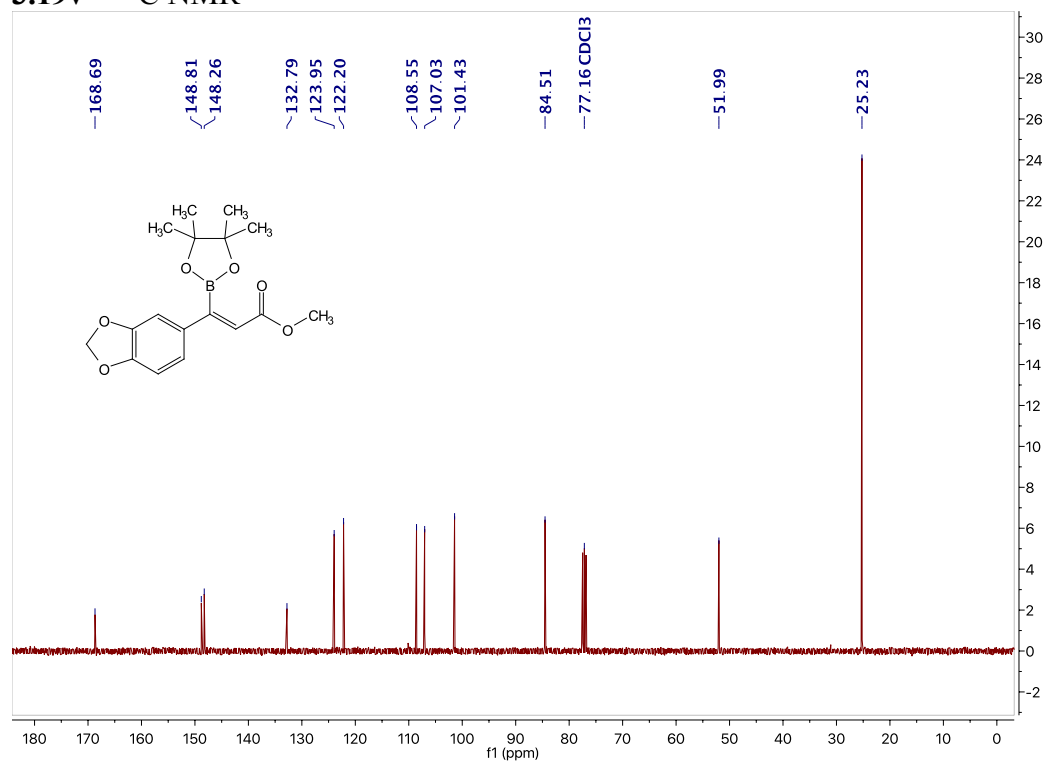




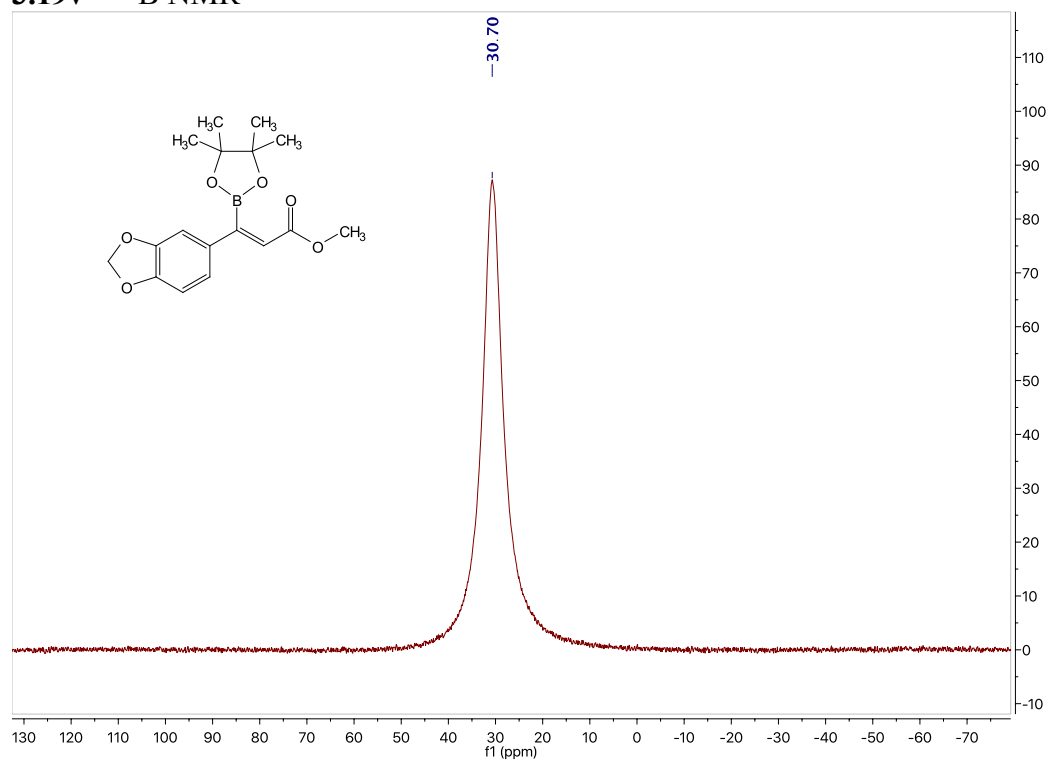
### 3.19v – <sup>1</sup>H NMR



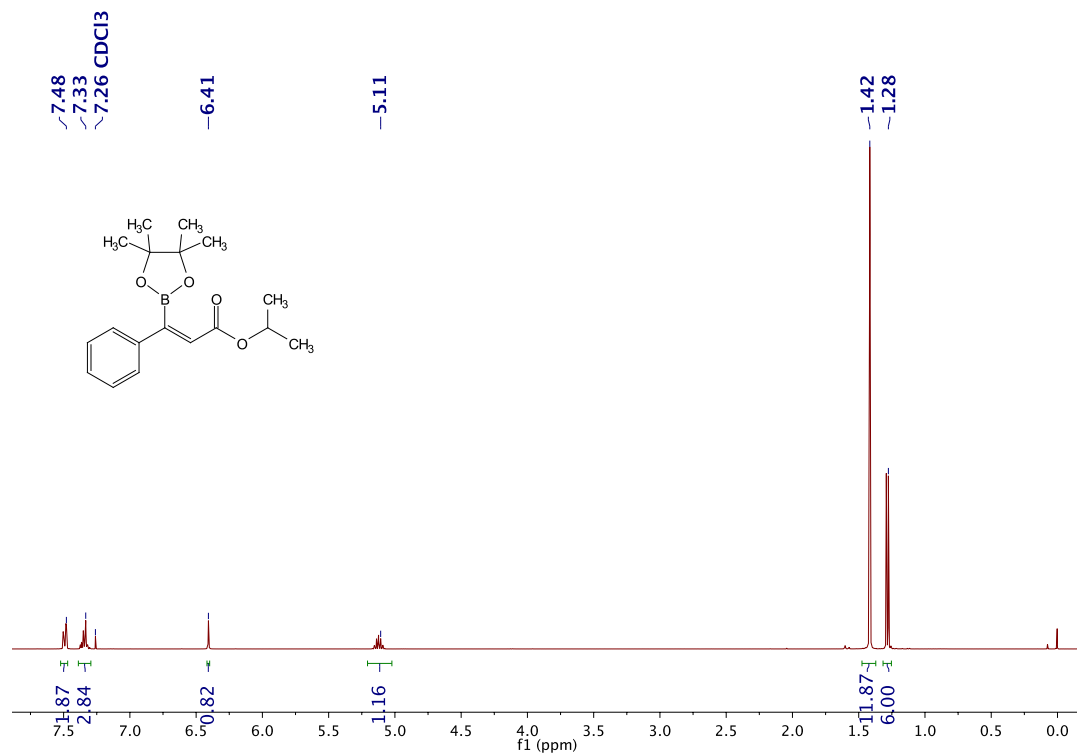
### 3.19v – <sup>13</sup>C NMR



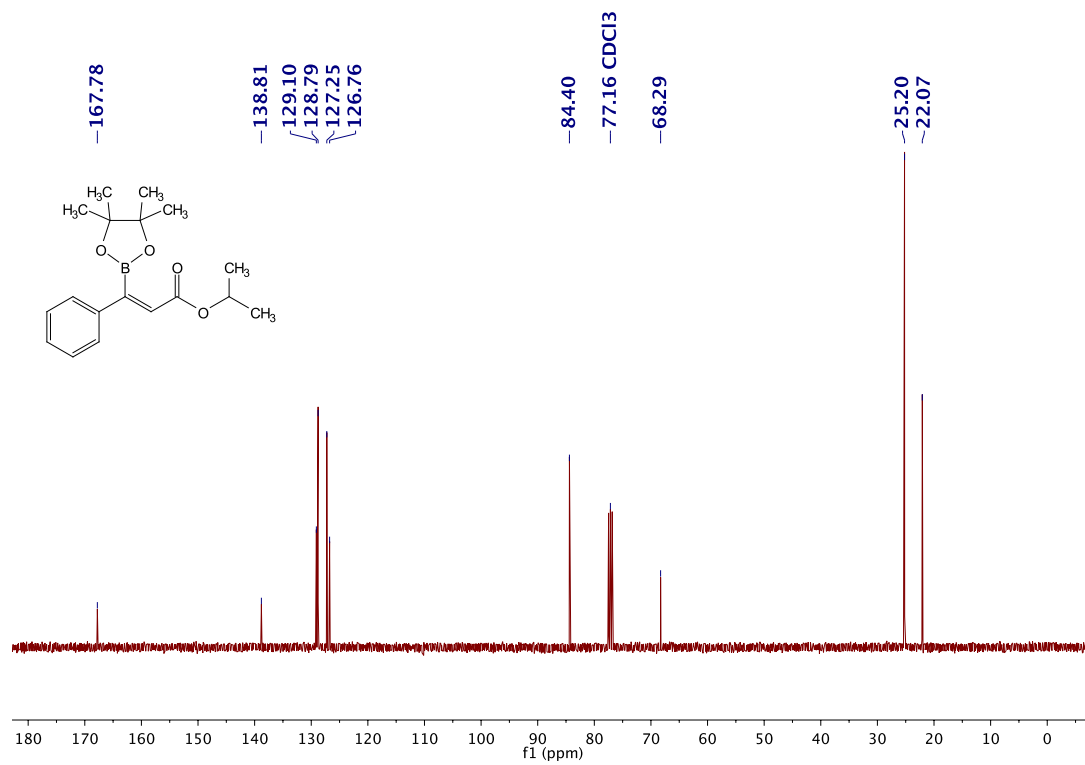
### 3.19v – $^{11}\text{B}$ NMR



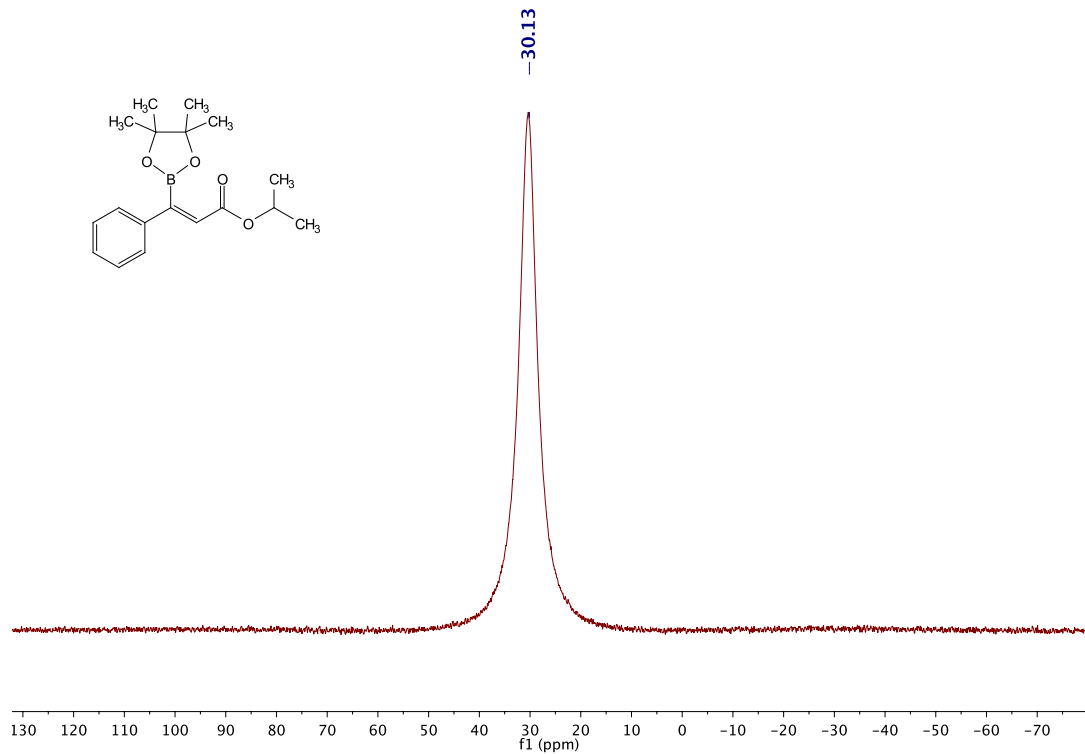
### 3.19w – $^1\text{H}$ NMR



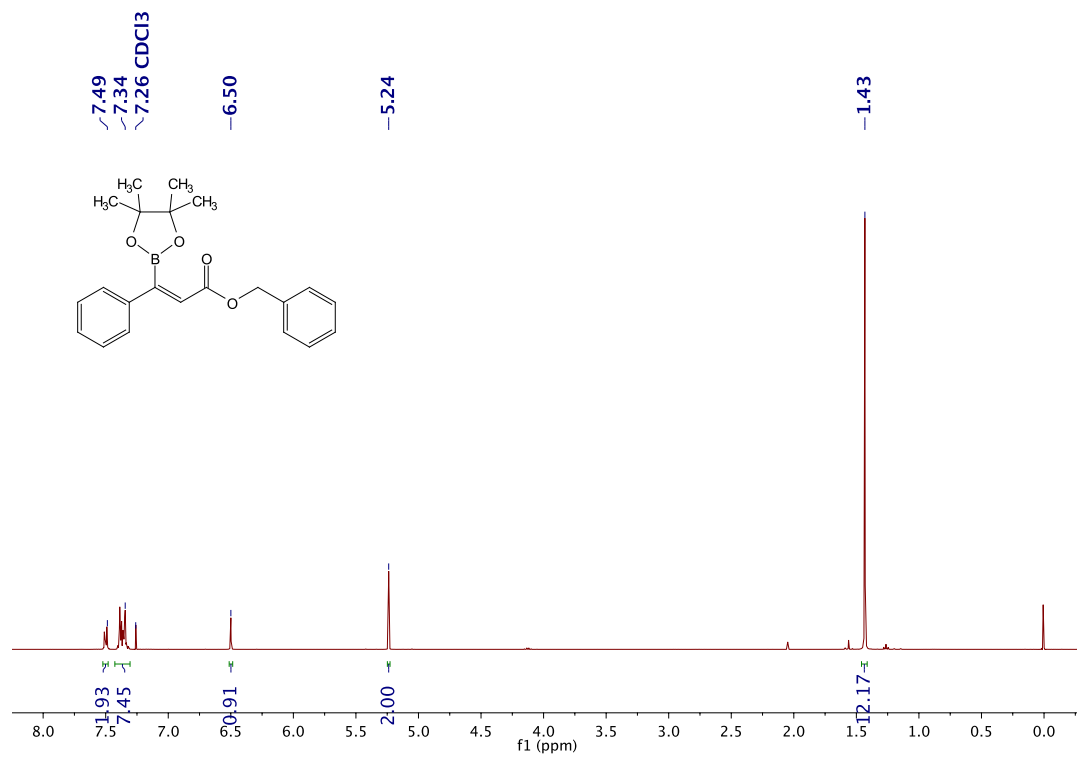
### 3.19w – $^{13}\text{C}$ NMR



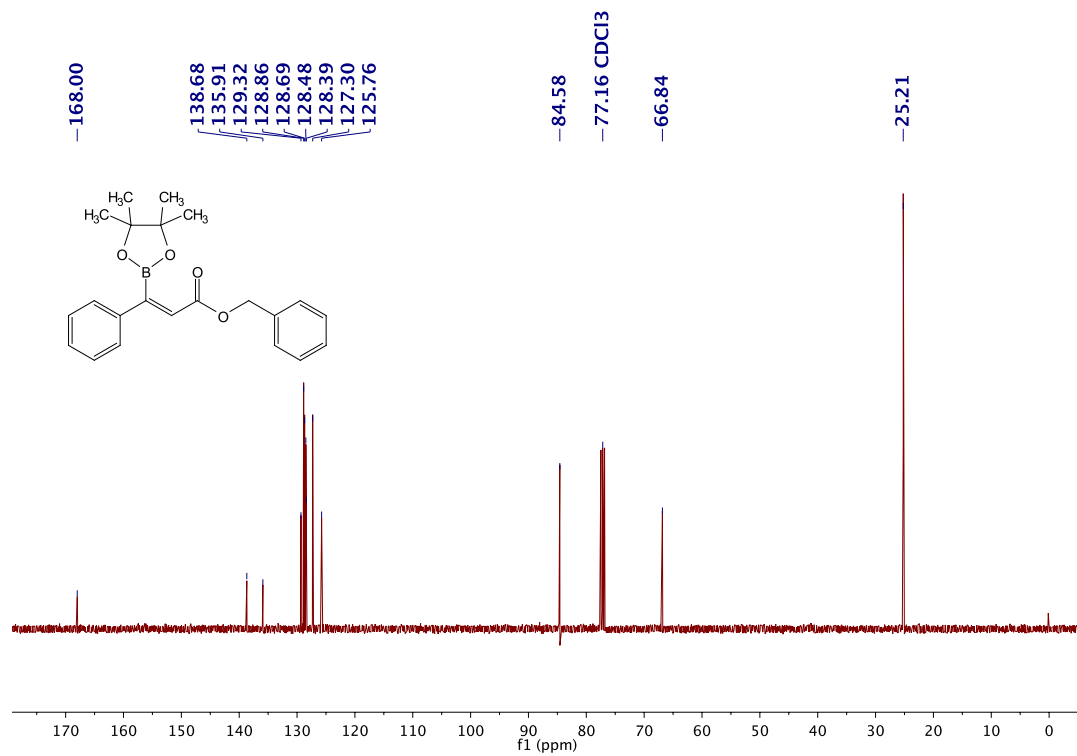
### 3.19w – $^{11}\text{B}$ NMR



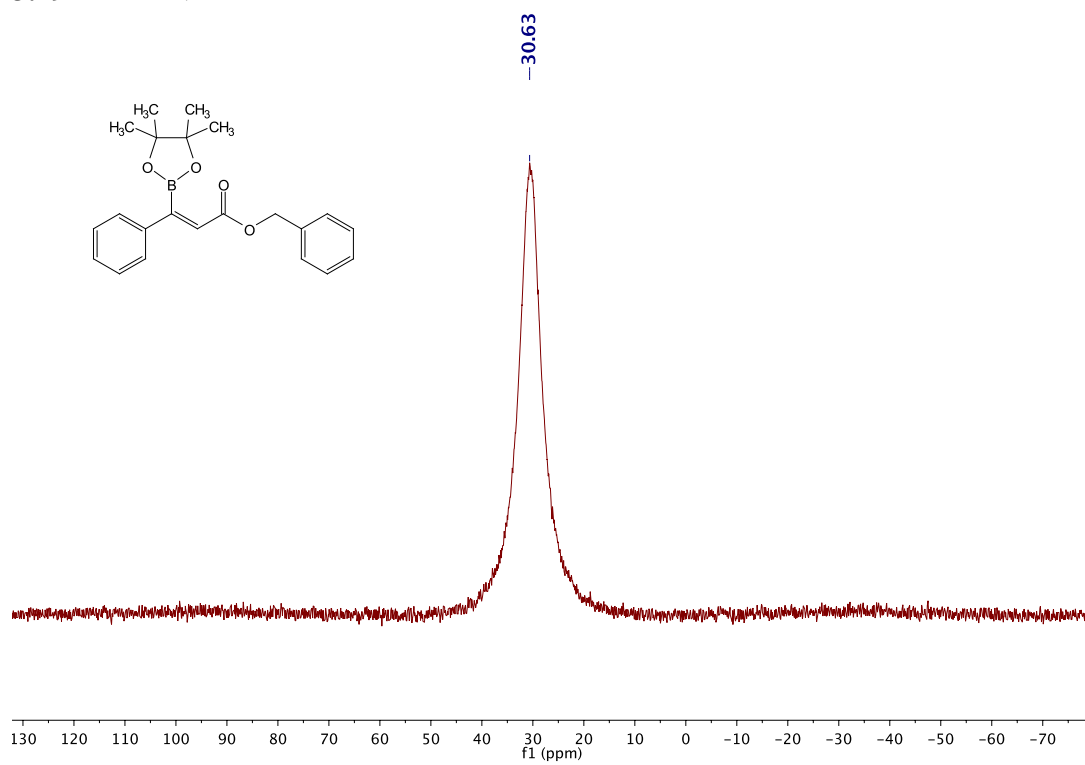
### 3.19x – <sup>1</sup>H NMR



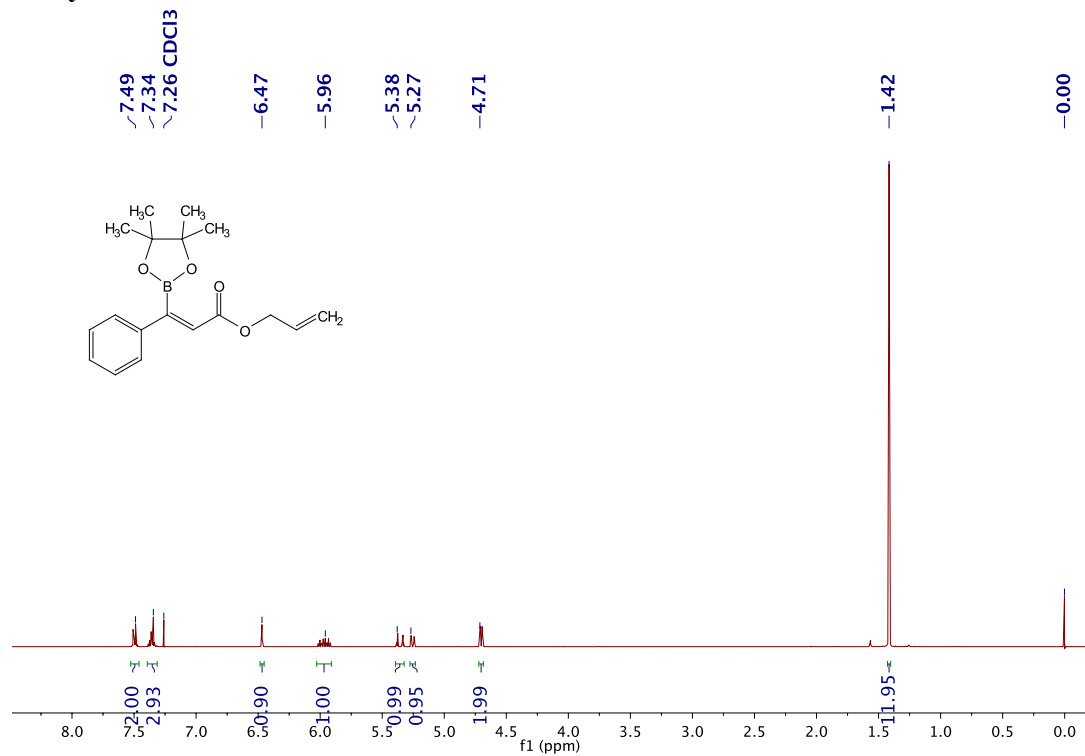
### 3.19x – <sup>13</sup>C NMR



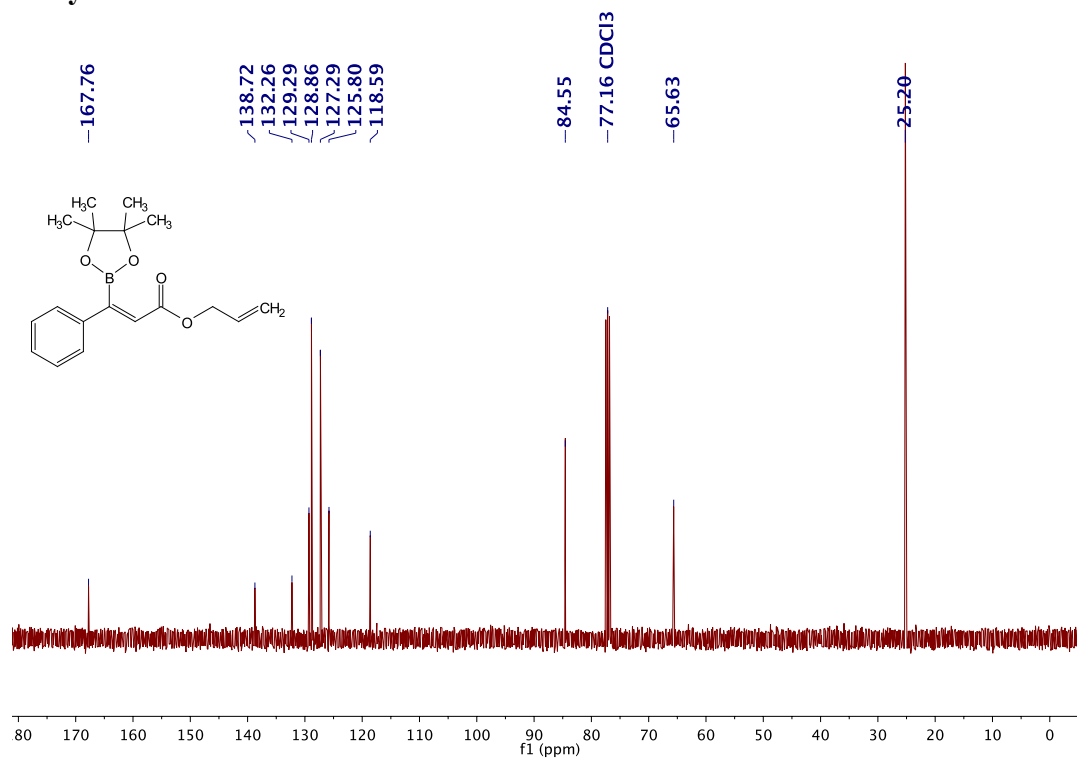
### 3.19x – $^{11}\text{B}$ NMR



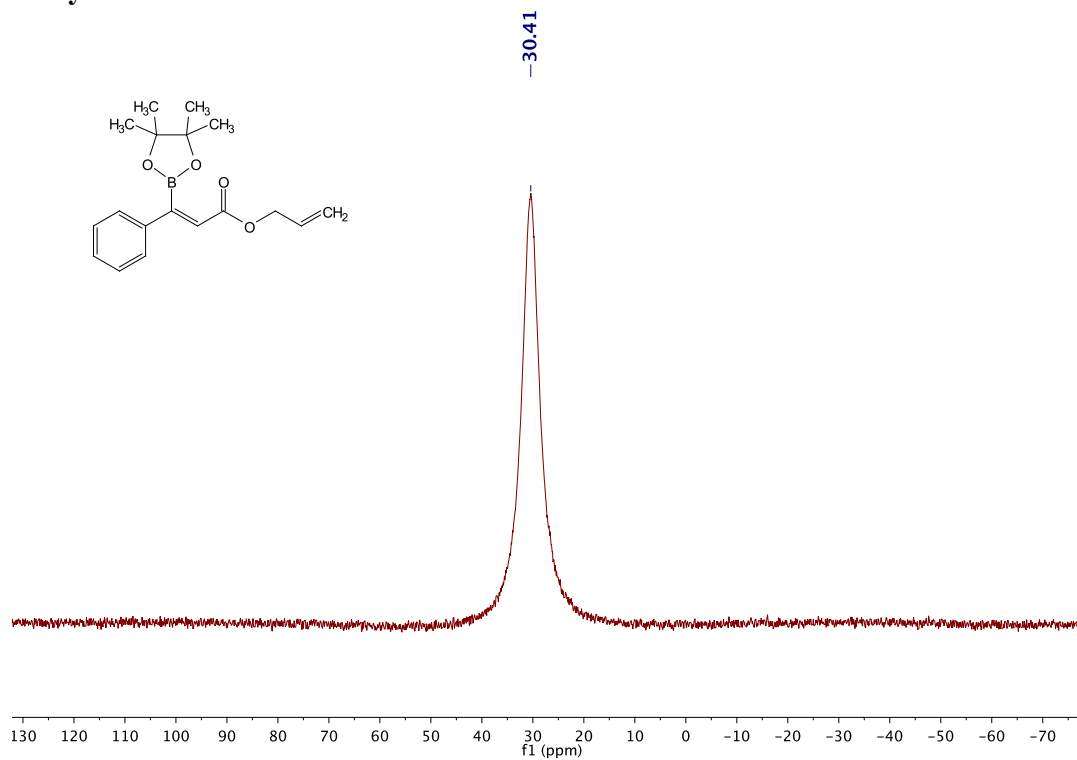
### 3.19y – $^1\text{H}$ NMR



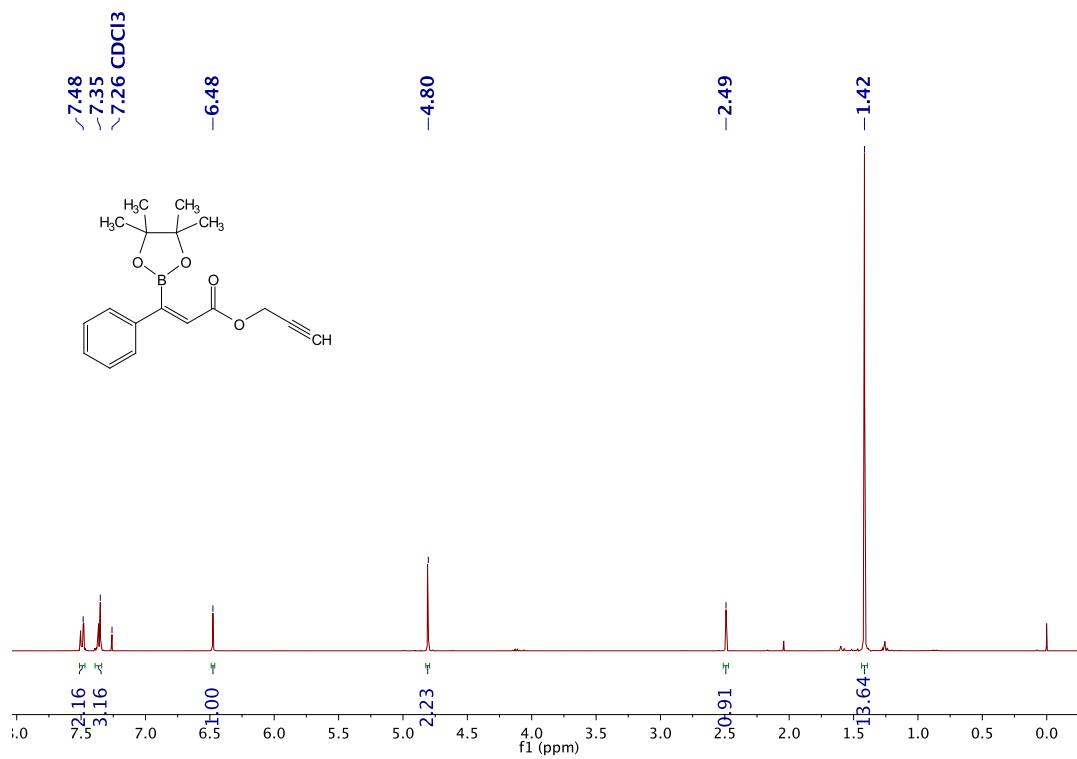
### 3.19y – $^{13}\text{C}$ NMR



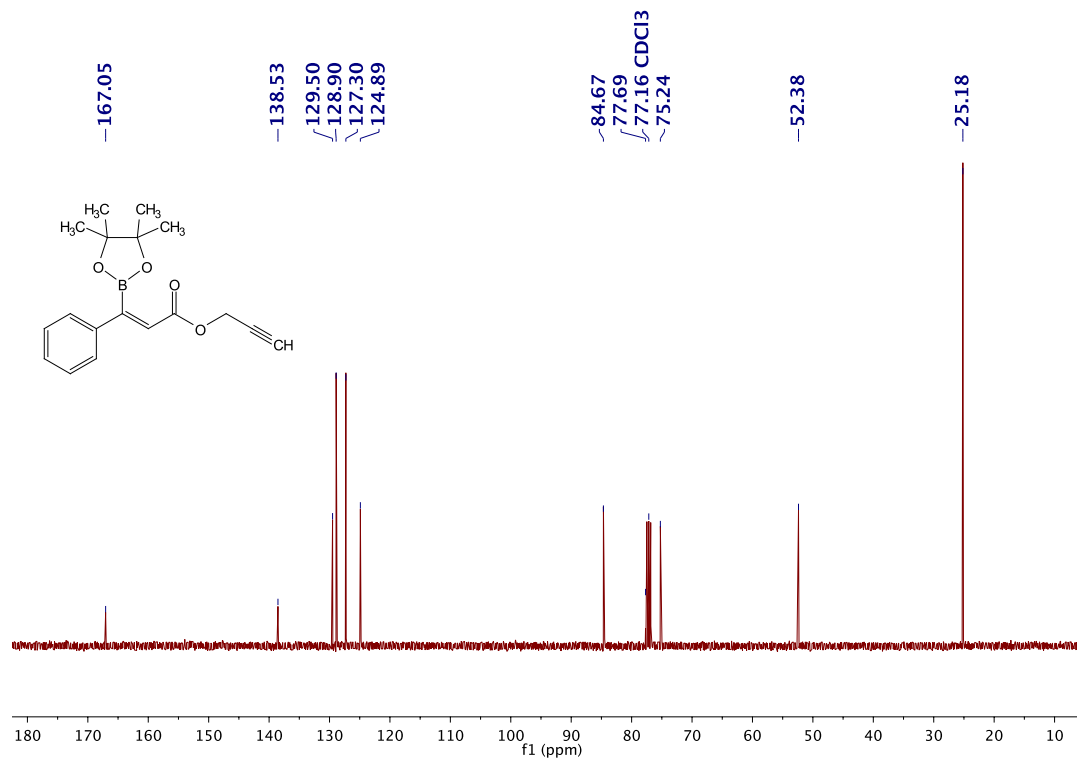
### 3.19y – $^{11}\text{B}$ NMR



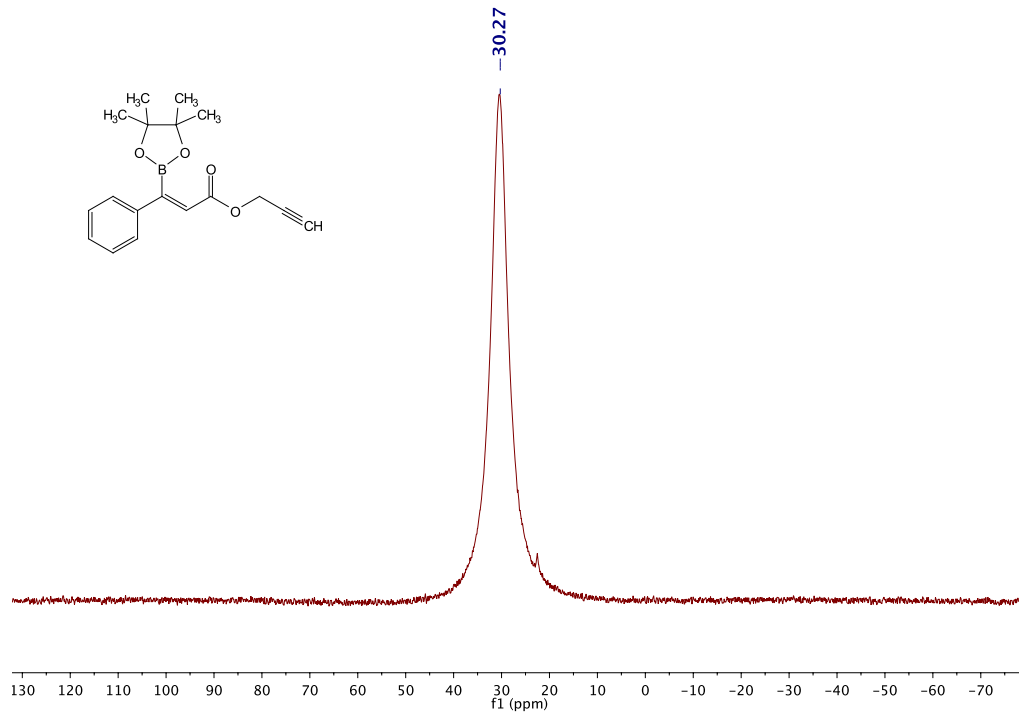
### 3.19z – <sup>1</sup>H NMR



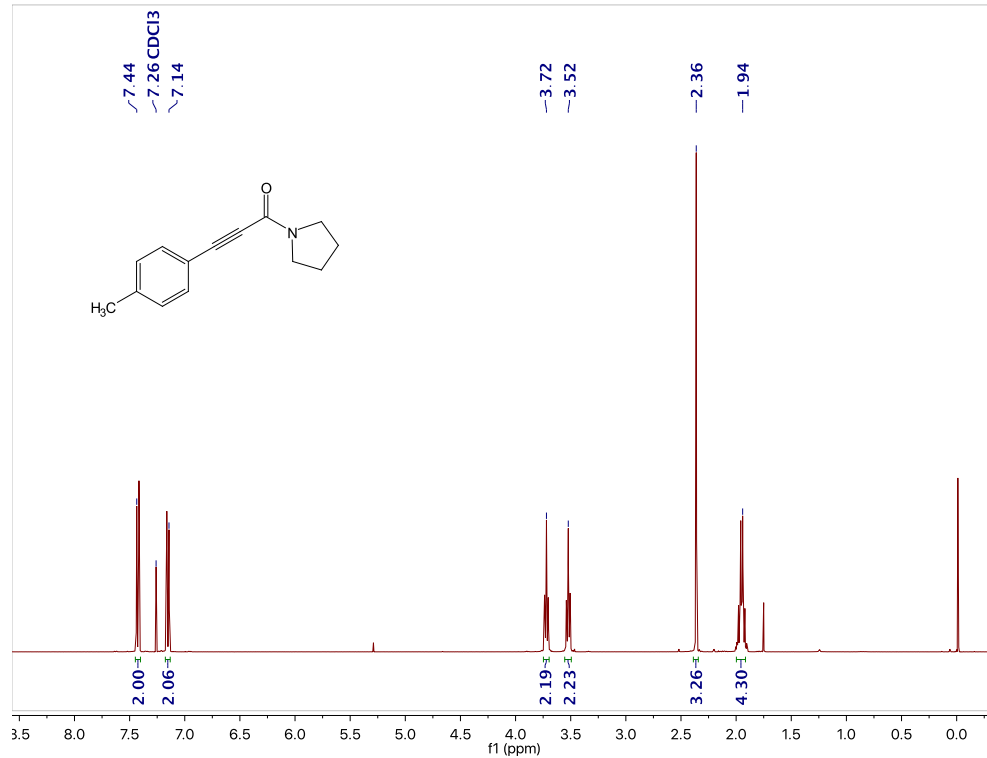
### 3.19z – <sup>13</sup>C NMR



### 3.19z – $^{11}\text{B}$ NMR

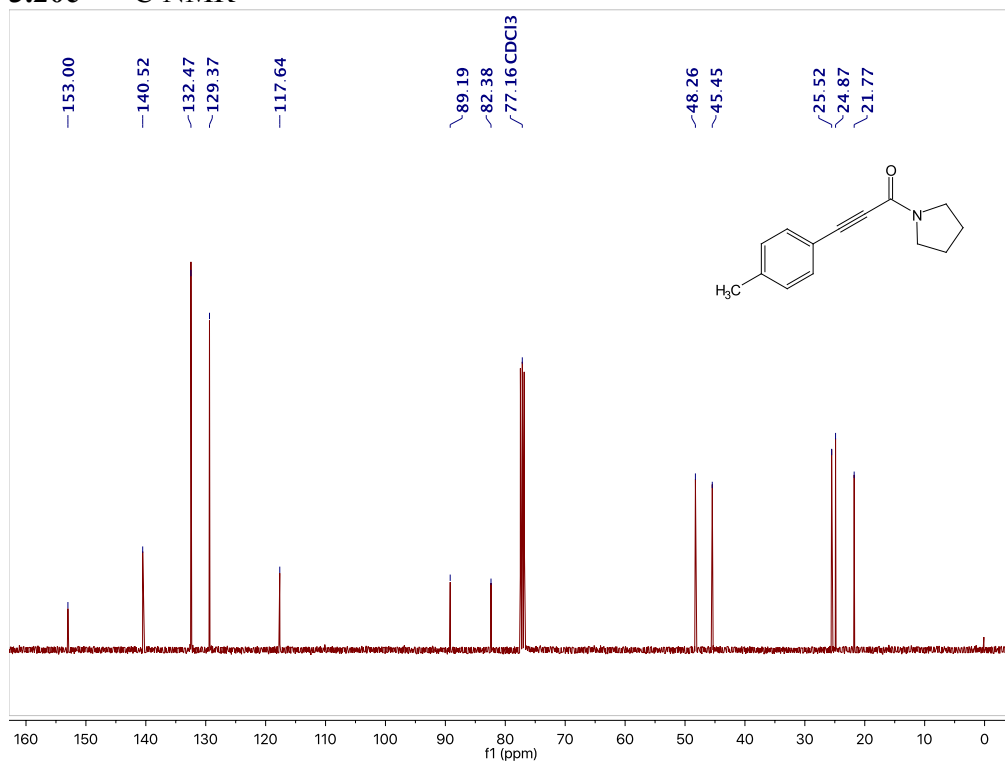


### 3.20c – $^1\text{H}$ NMR

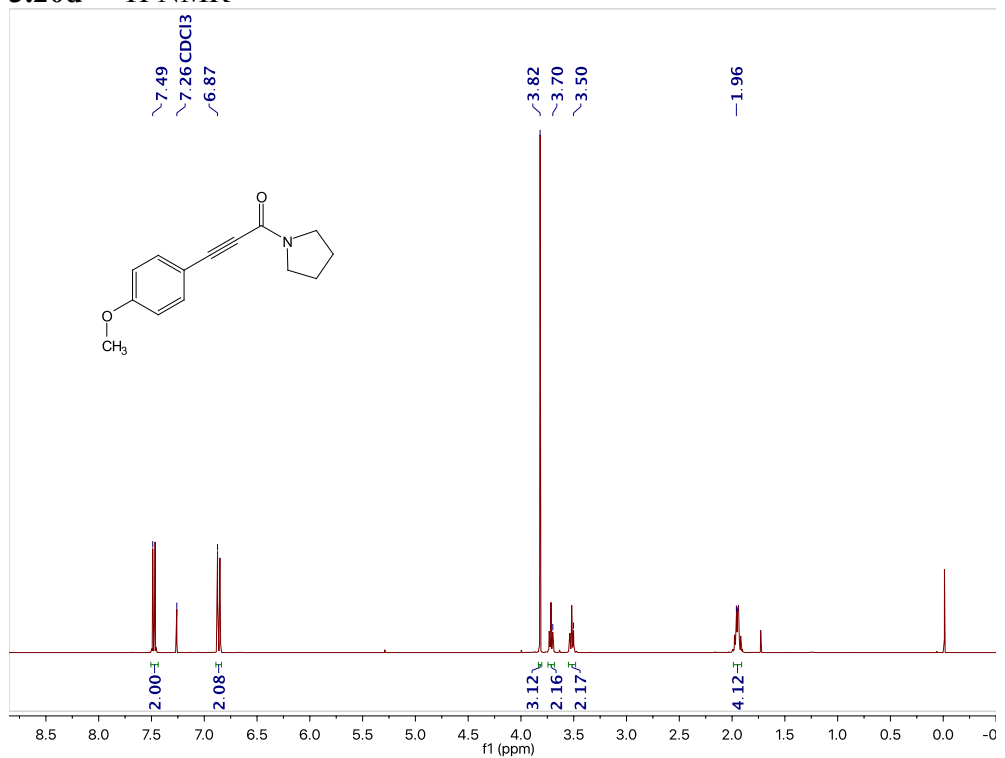




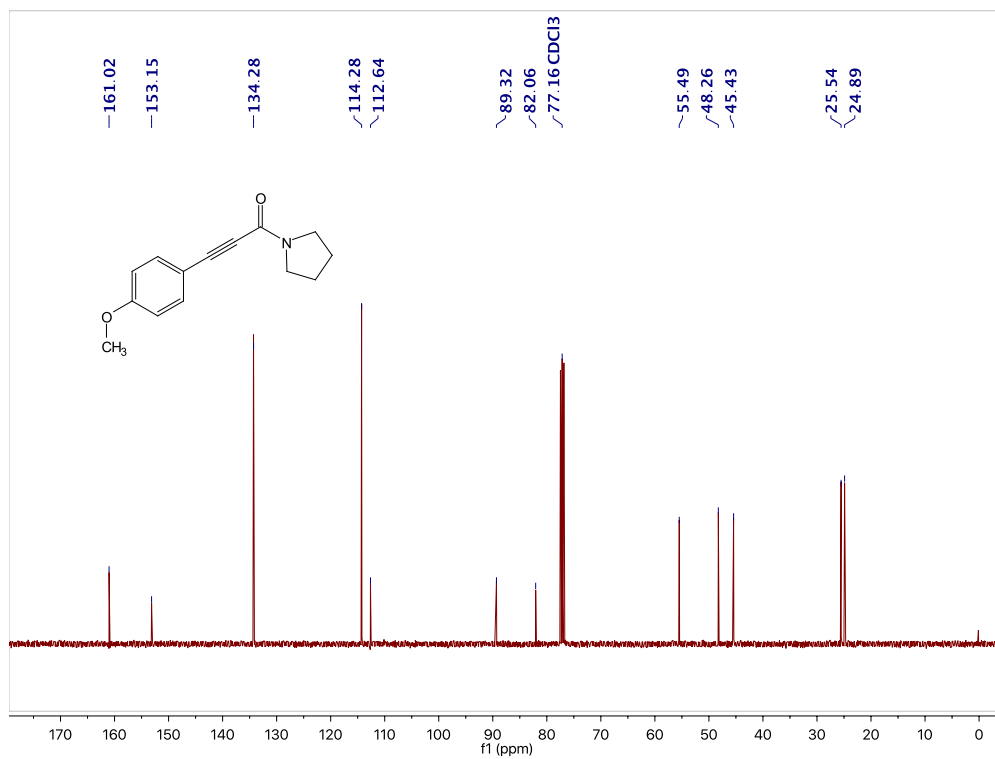
### 3.20c – $^{13}\text{C}$ NMR



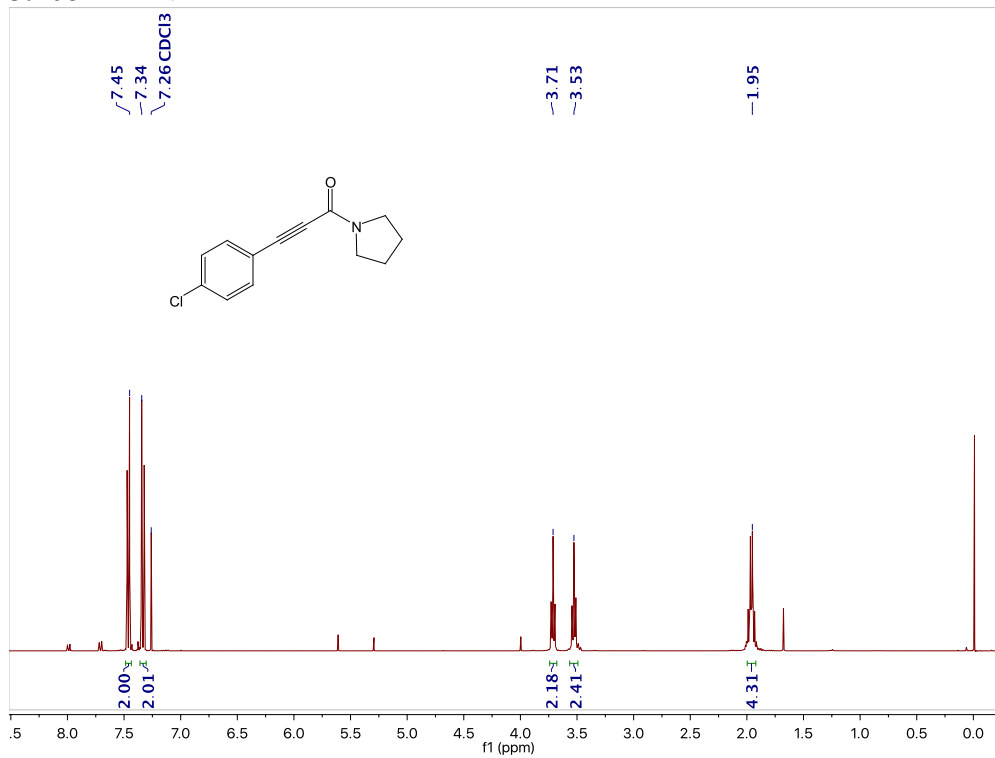
### 3.20d – $^1\text{H}$ NMR



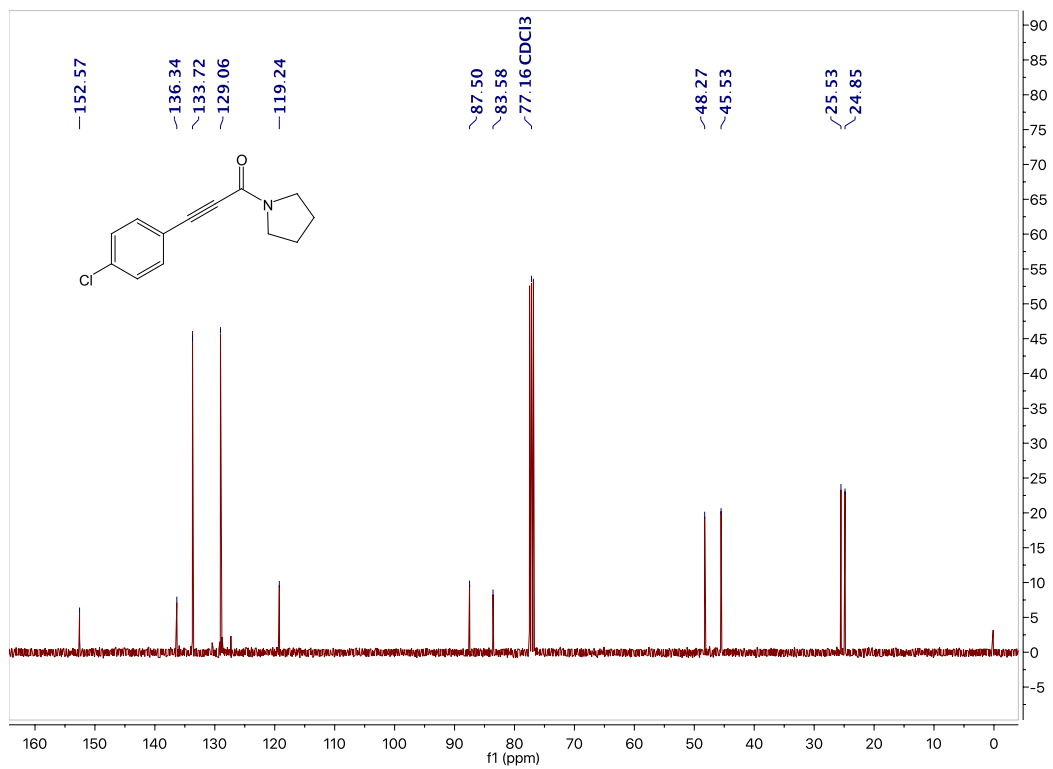
### 3.20d – $^{13}\text{C}$ NMR



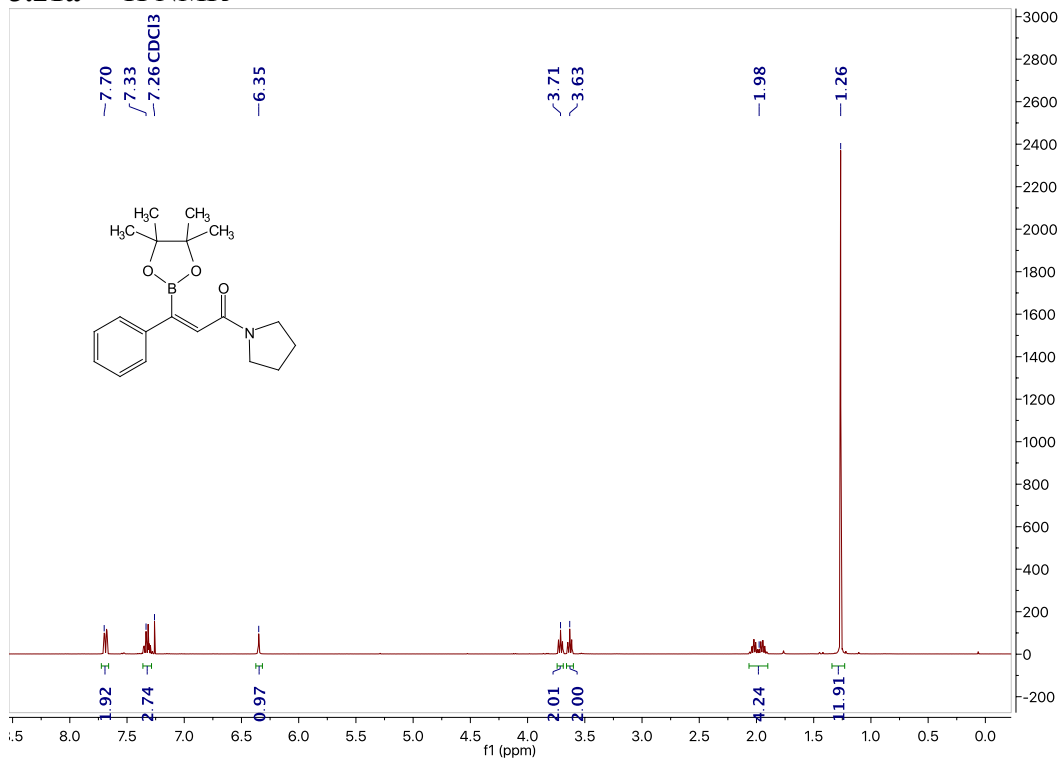
### 3.20e – $^1\text{H}$ NMR



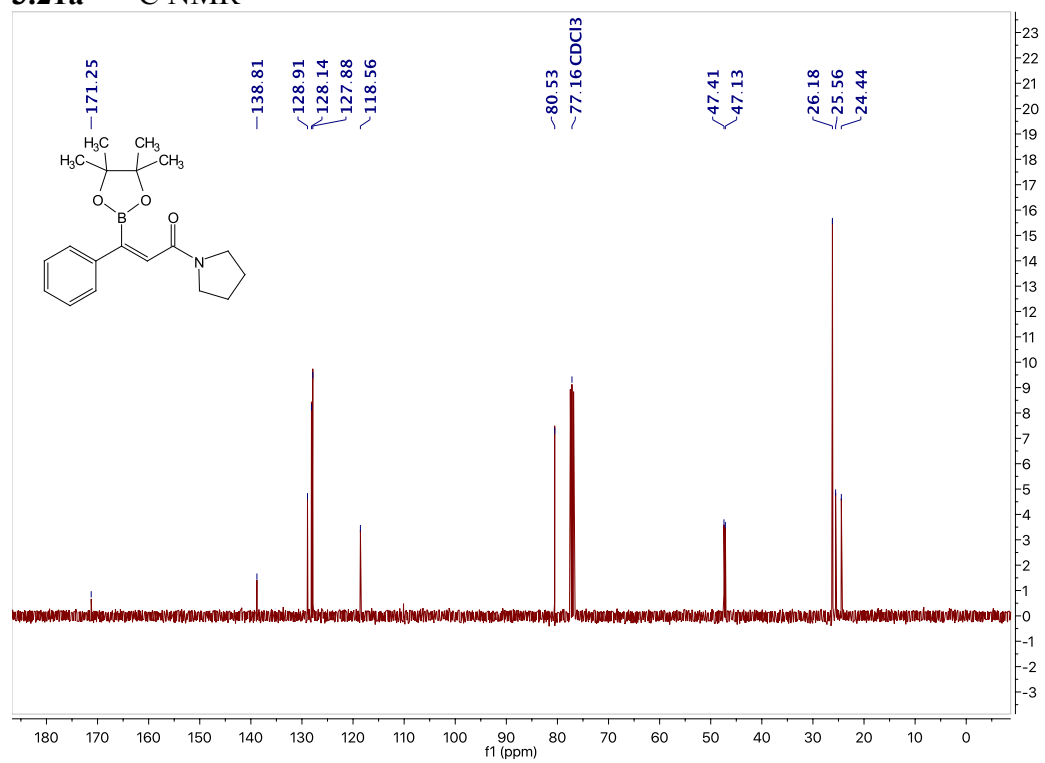
### 3.20e – $^{13}\text{C}$ NMR



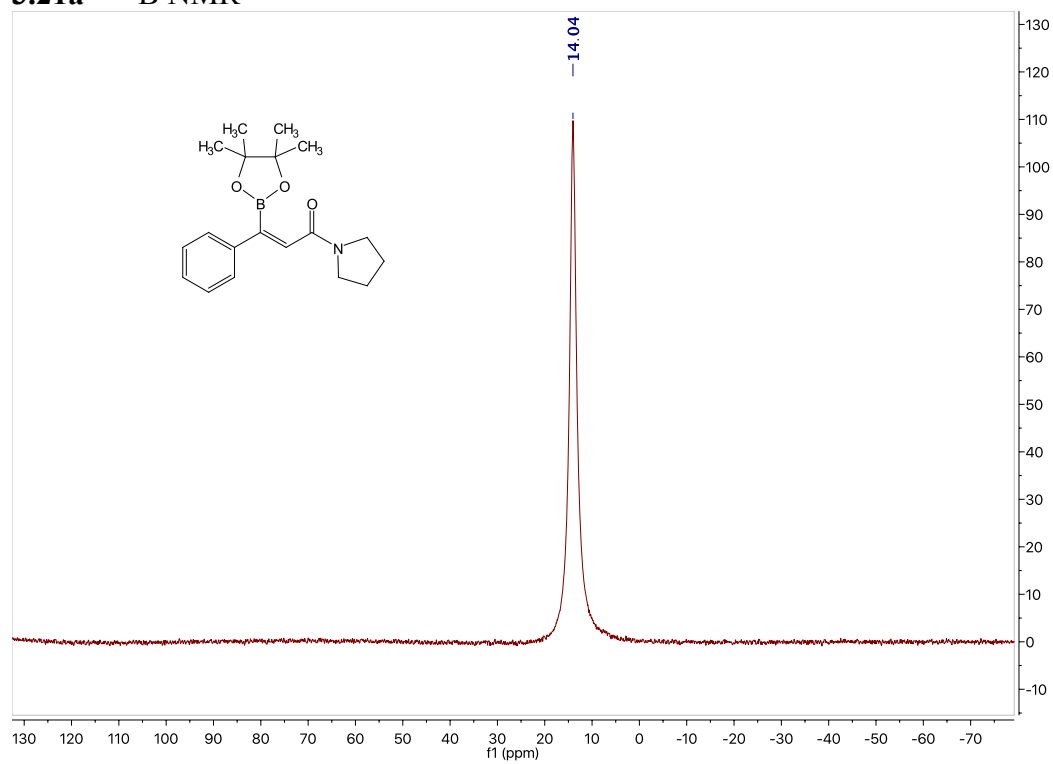
### 3.21a – $^1\text{H}$ NMR



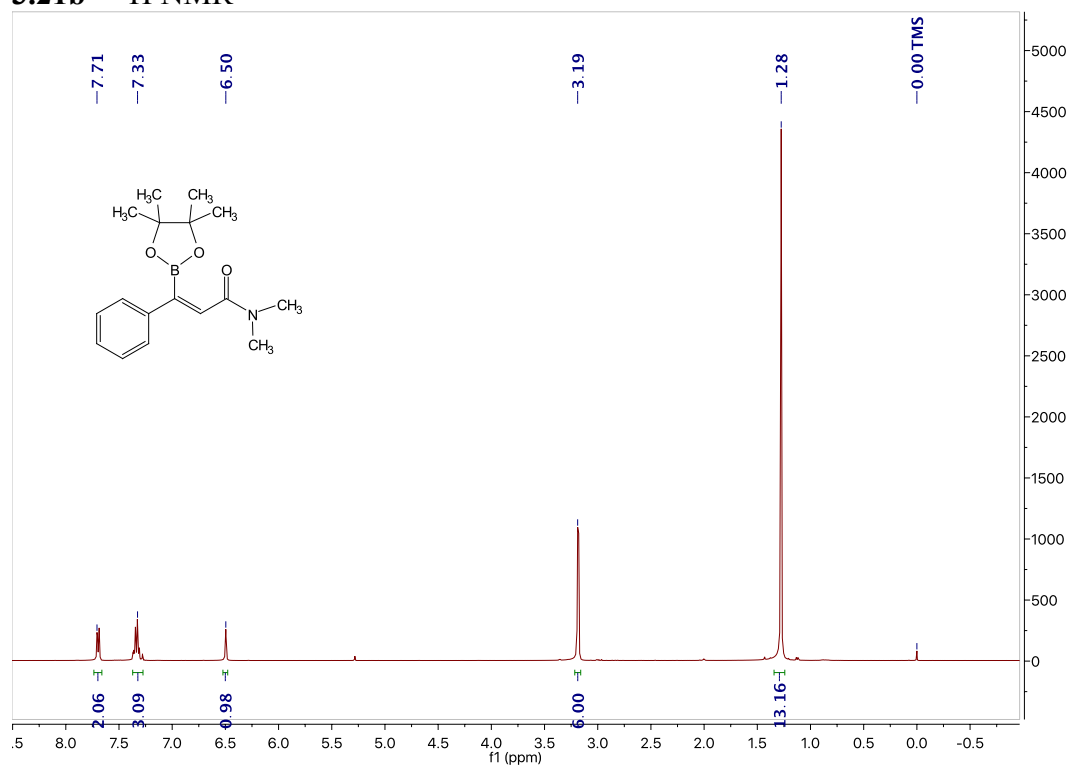
### 3.21a – $^{13}\text{C}$ NMR



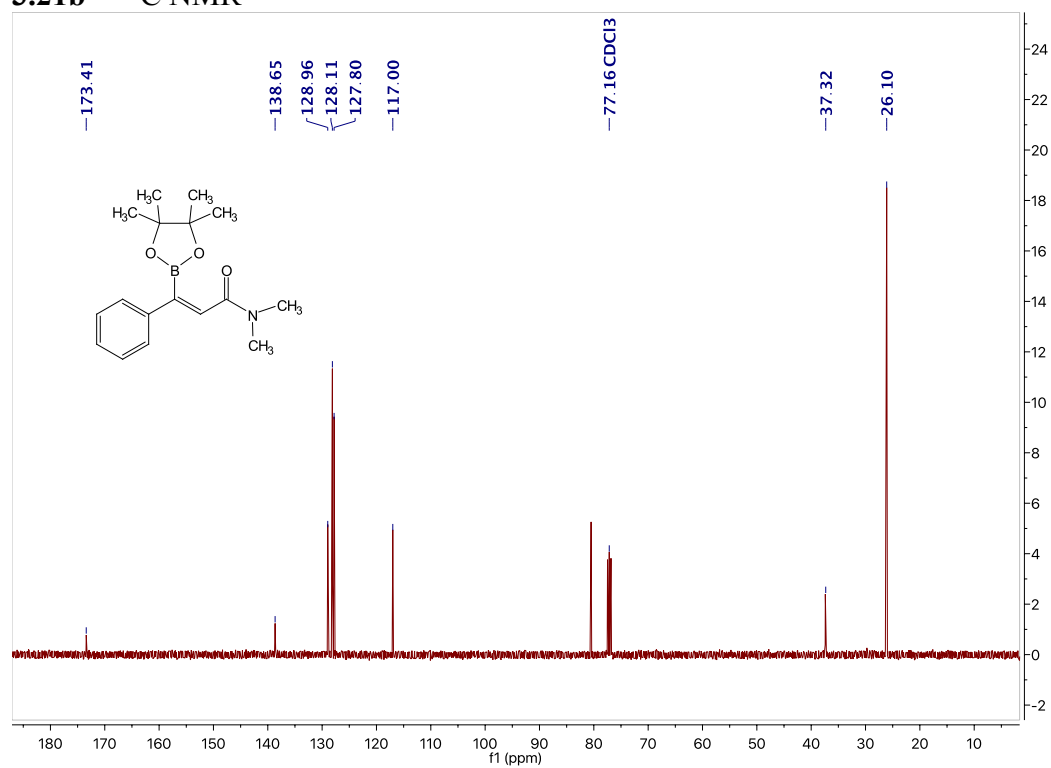
### 3.21a – $^{11}\text{B}$ NMR



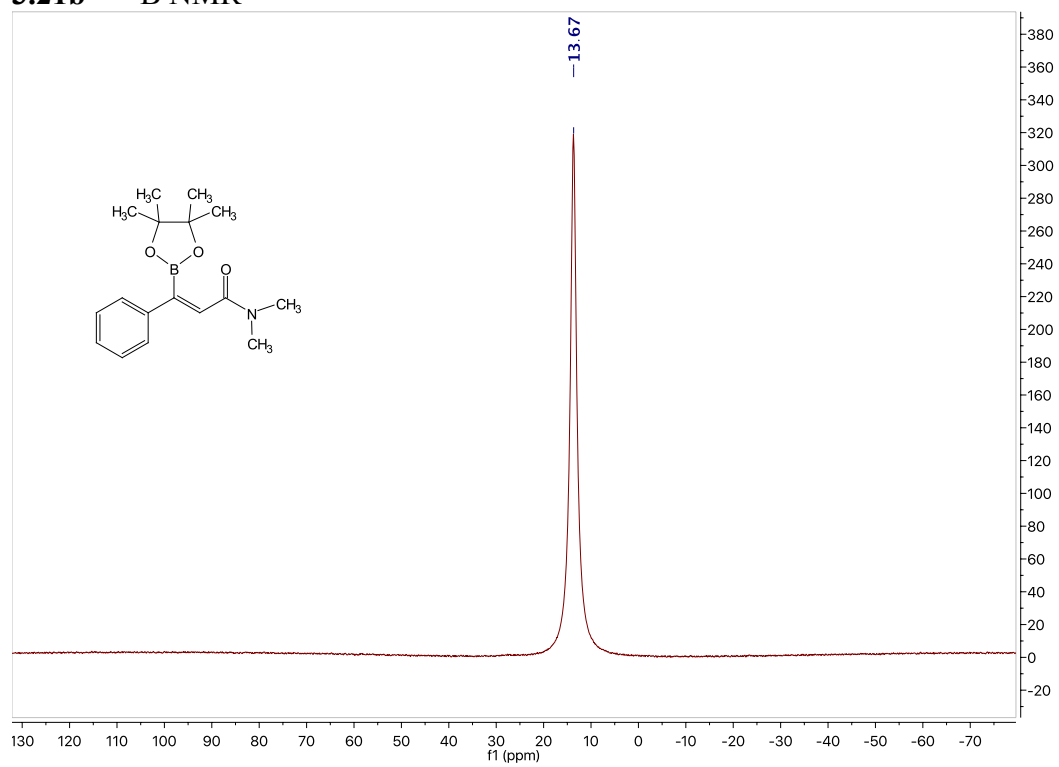
### 3.21b – <sup>1</sup>H NMR



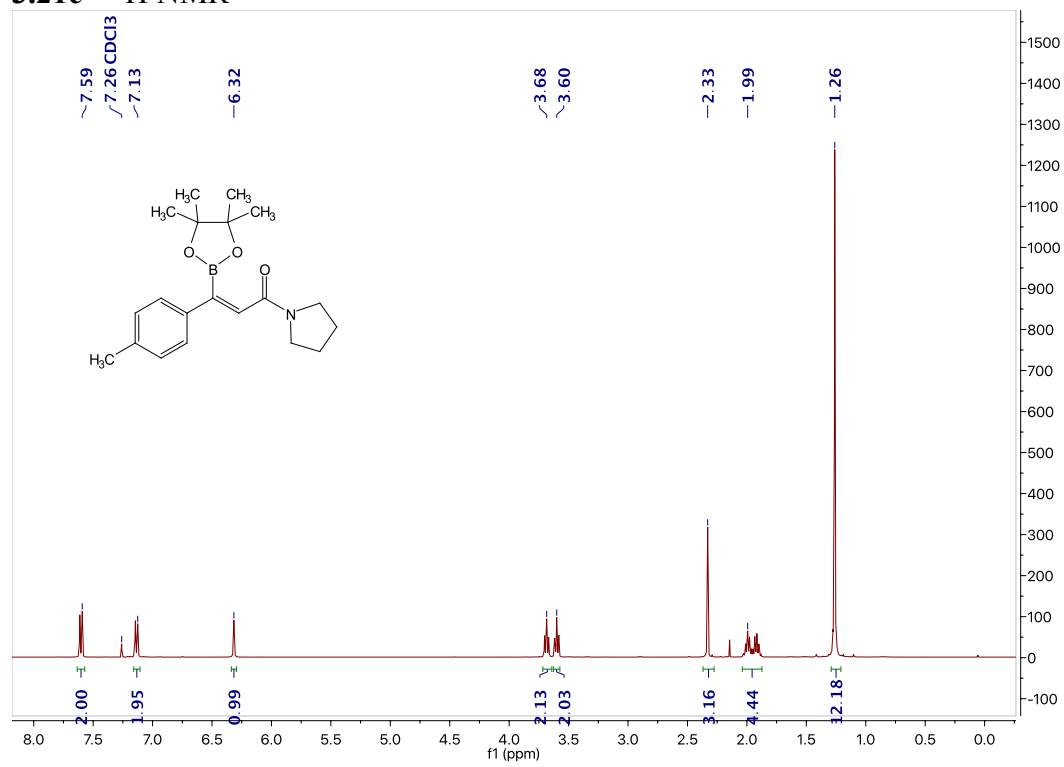
### 3.21b – <sup>13</sup>C NMR



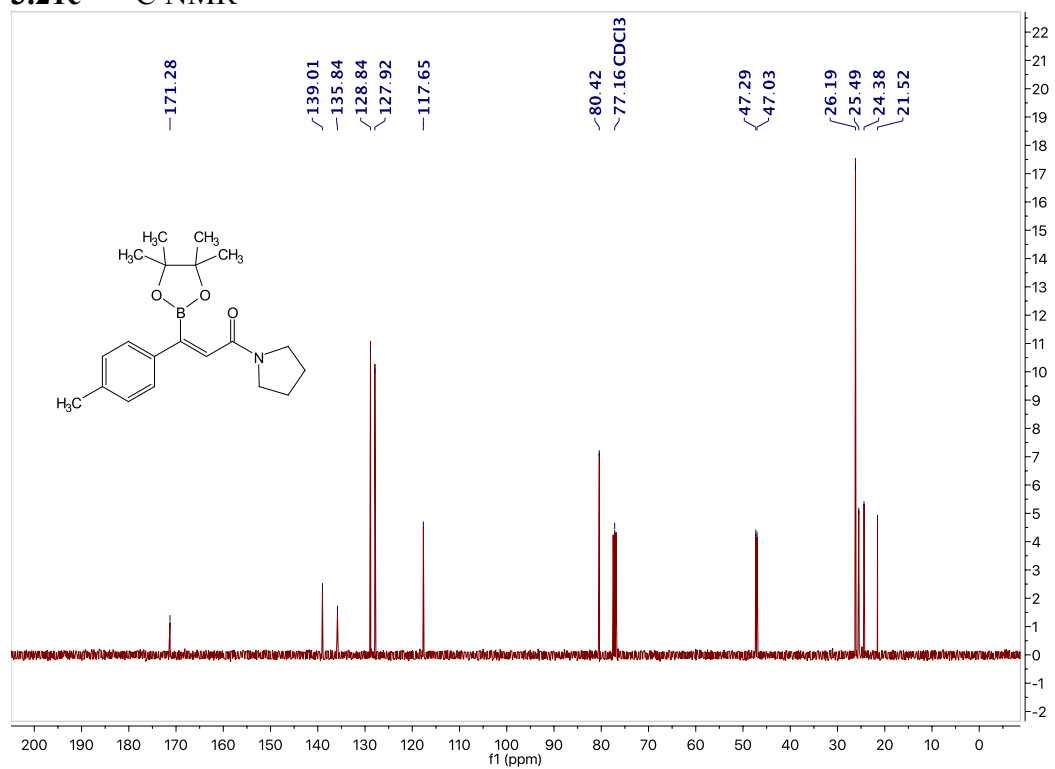
### 3.21b – $^{11}\text{B}$ NMR



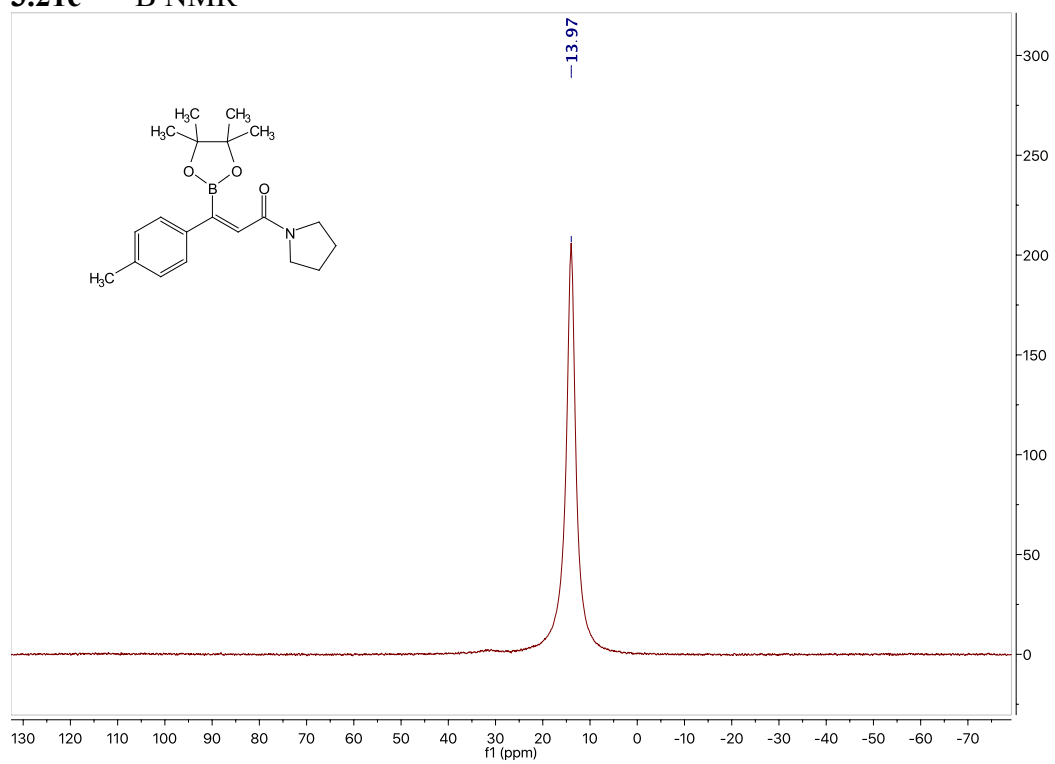
### 3.21c – $^1\text{H}$ NMR



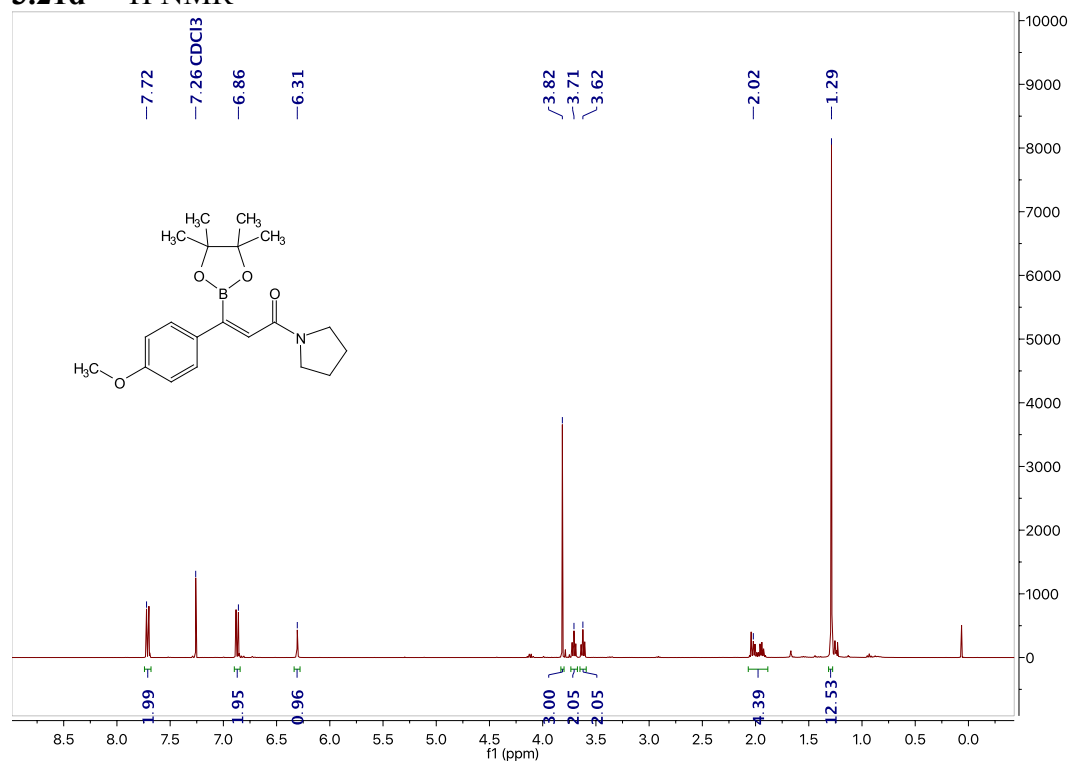
### 3.21c – <sup>13</sup>C NMR



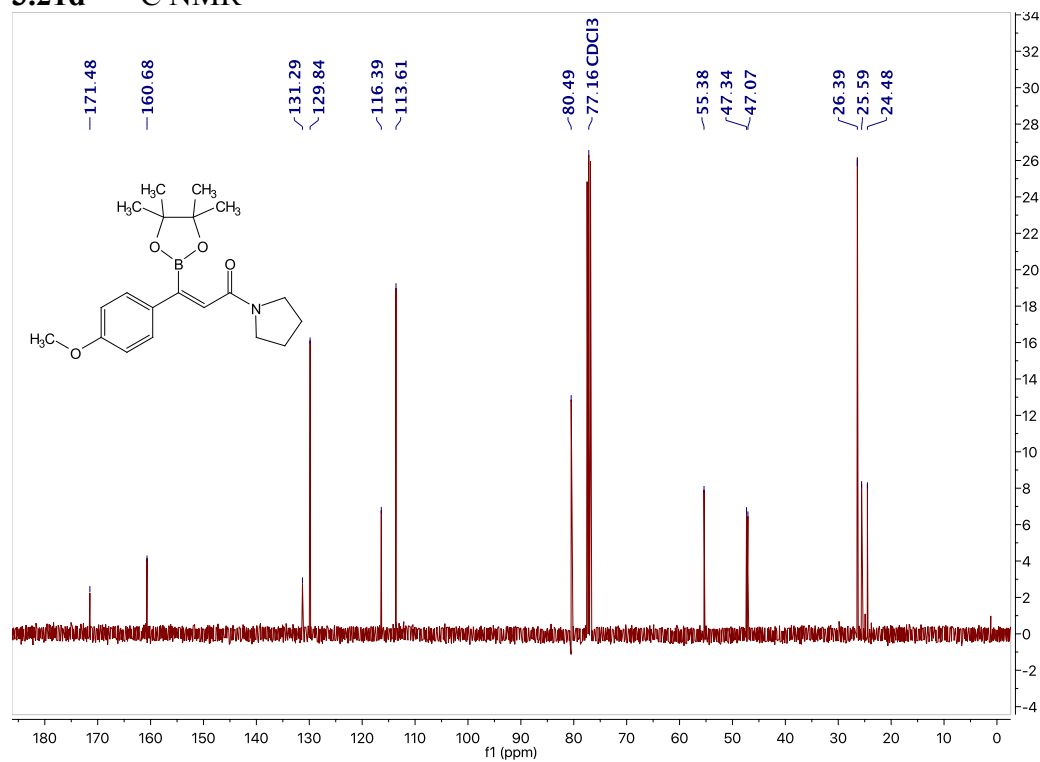
### 3.21c – <sup>11</sup>B NMR



### 3.21d – <sup>1</sup>H NMR

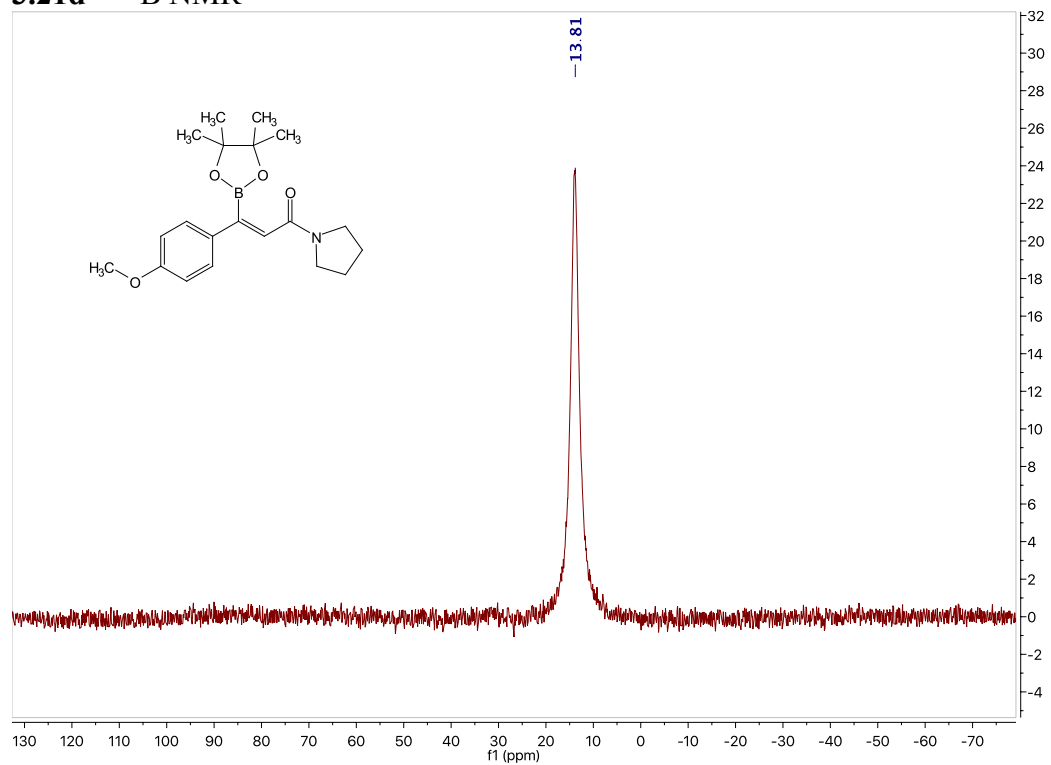


### 3.21d – <sup>13</sup>C NMR

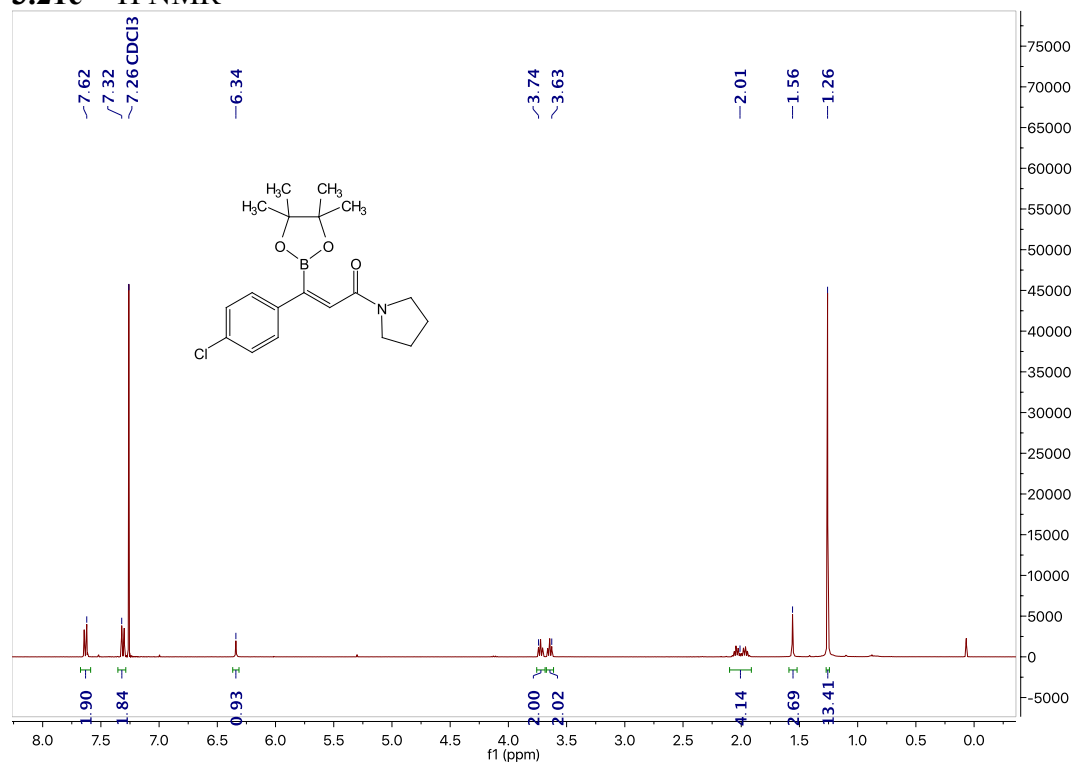




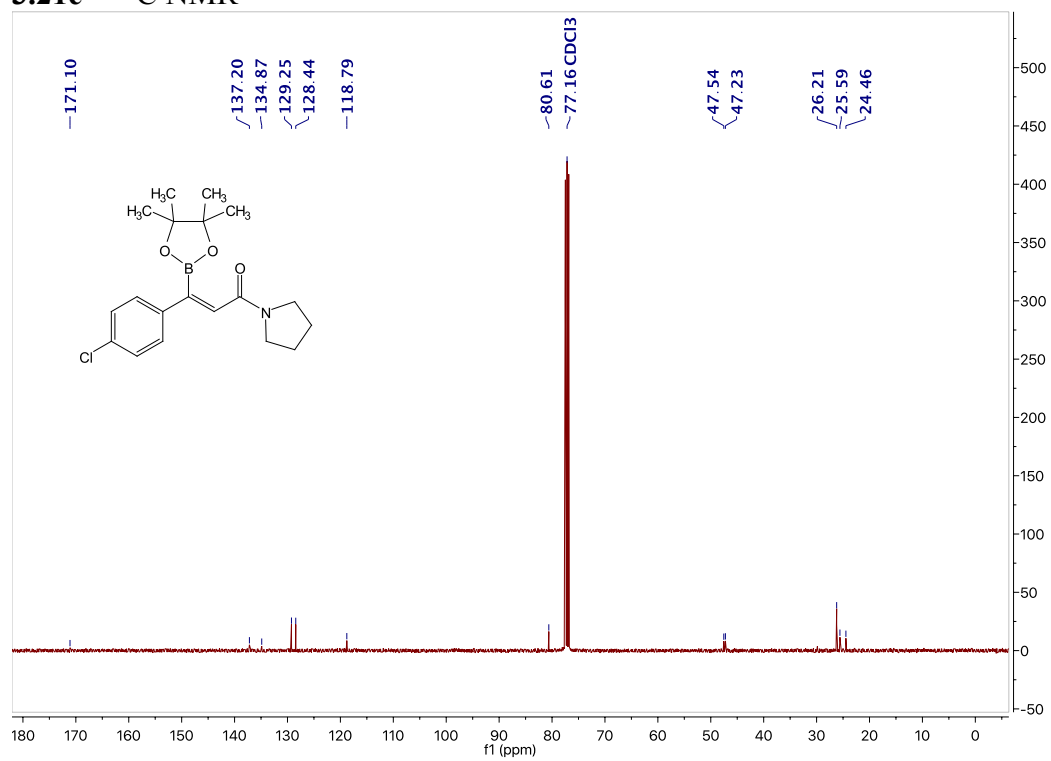
### 3.21d – $^{11}\text{B}$ NMR



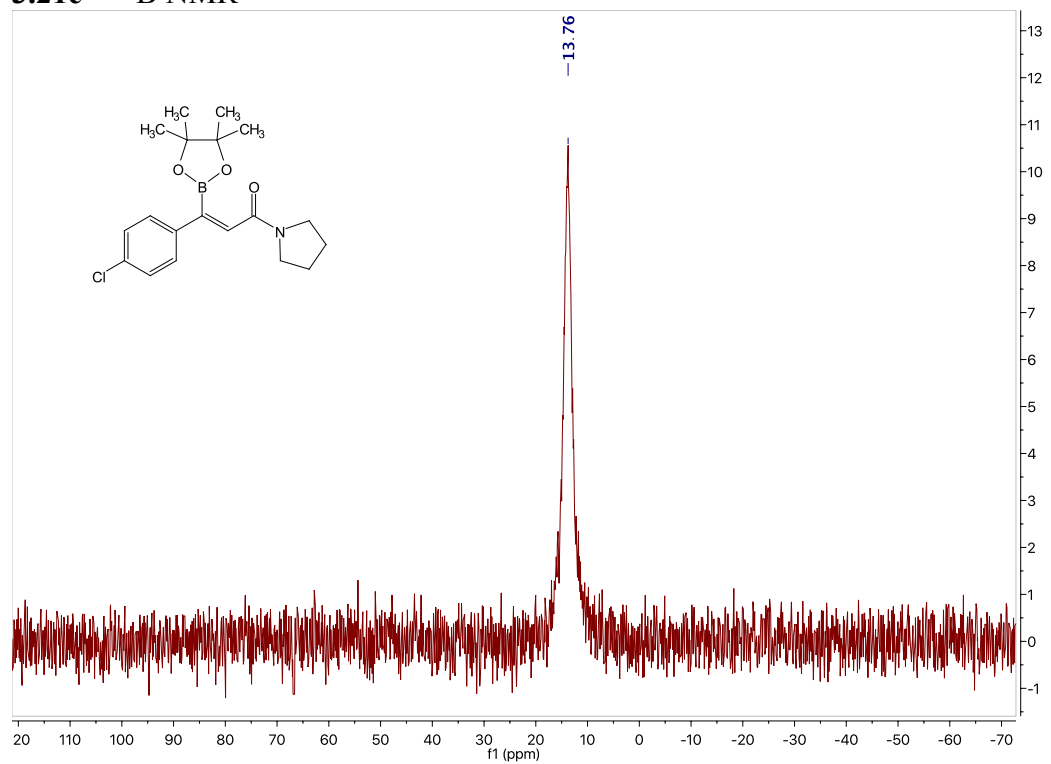
### 3.21e – $^1\text{H}$ NMR



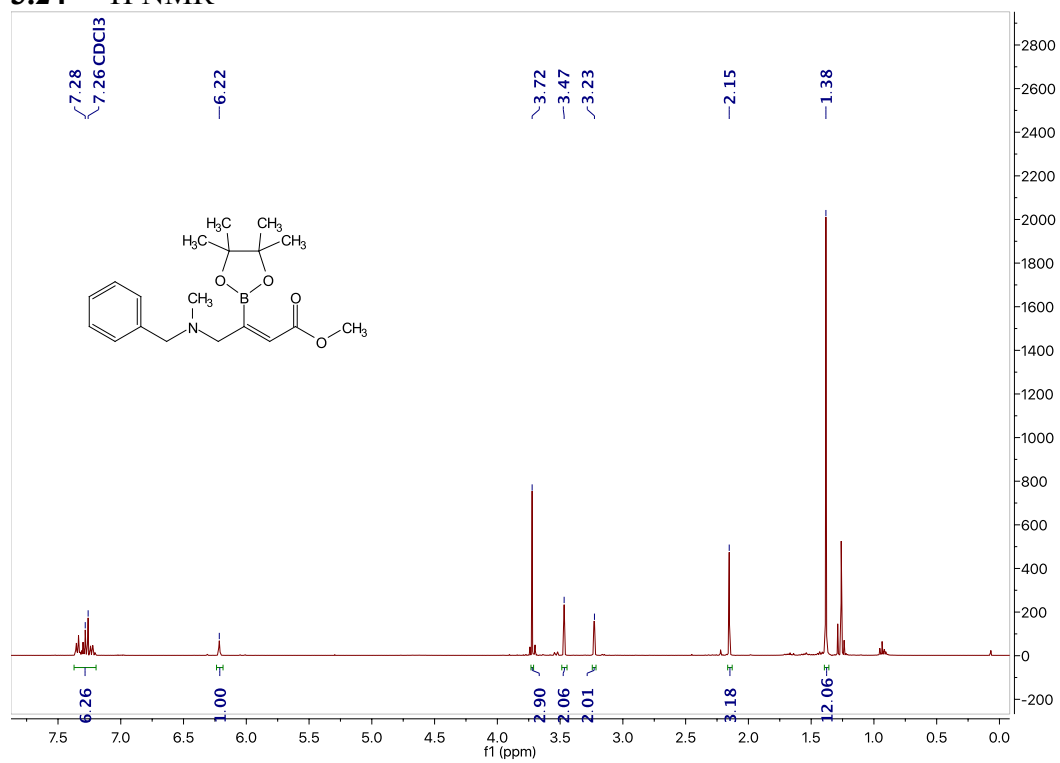
### 3.21e – $^{13}\text{C}$ NMR



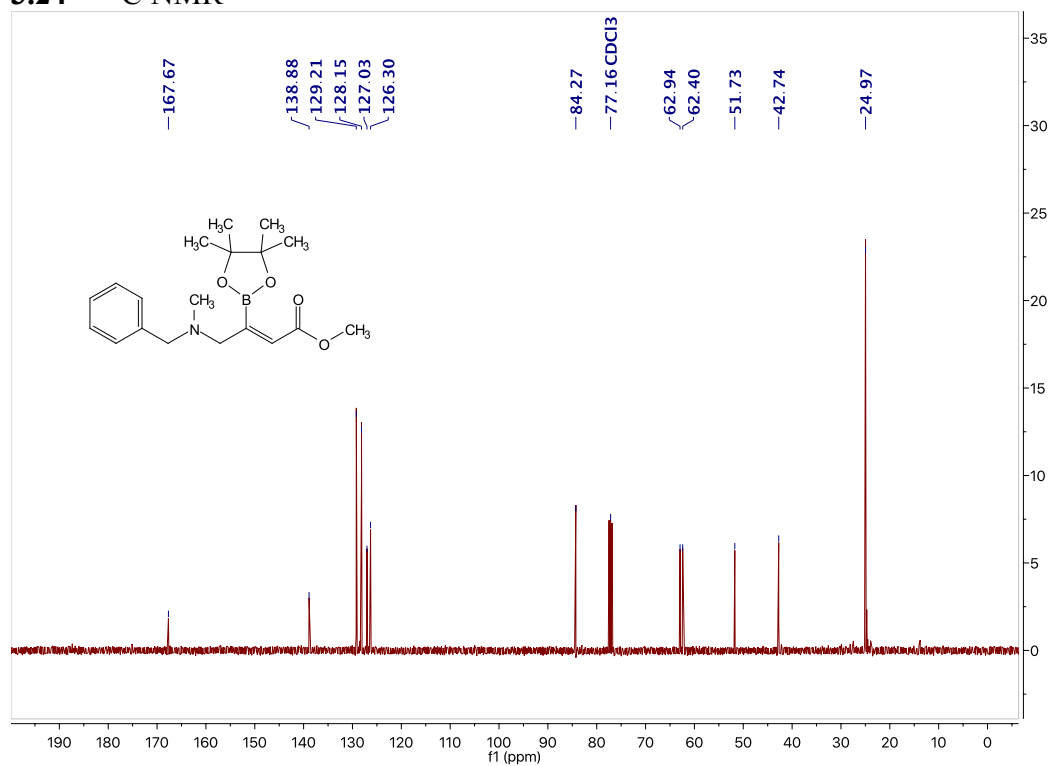
### 3.21e – $^{11}\text{B}$ NMR



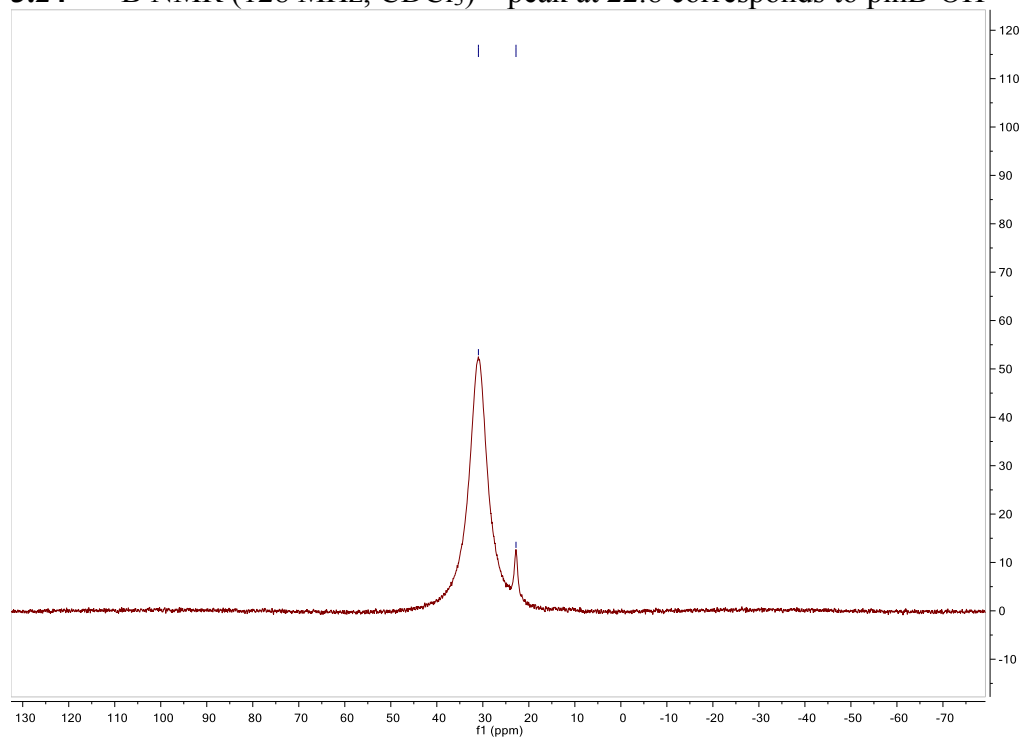
### 3.24 – $^1\text{H}$ NMR



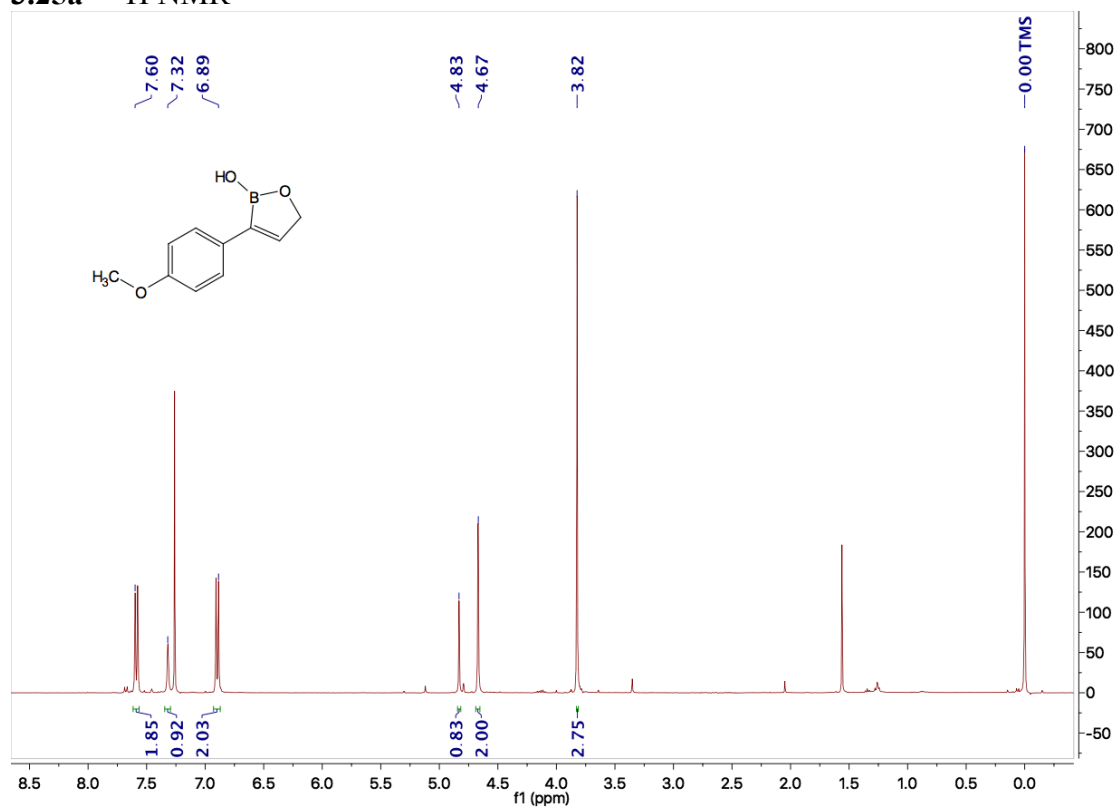
### 3.24 – $^{13}\text{C}$ NMR



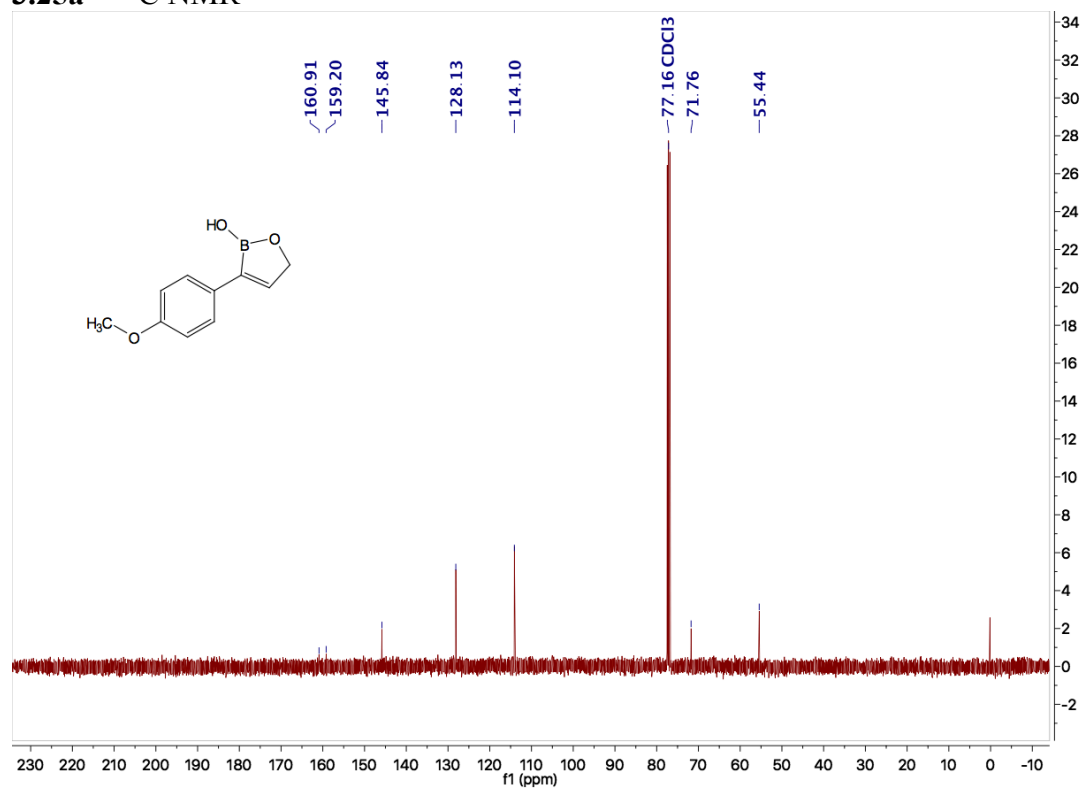
3.24 –  $^{11}\text{B}$  NMR (128 MHz,  $\text{CDCl}_3$ ) \* peak at 22.8 corresponds to pinB-OH



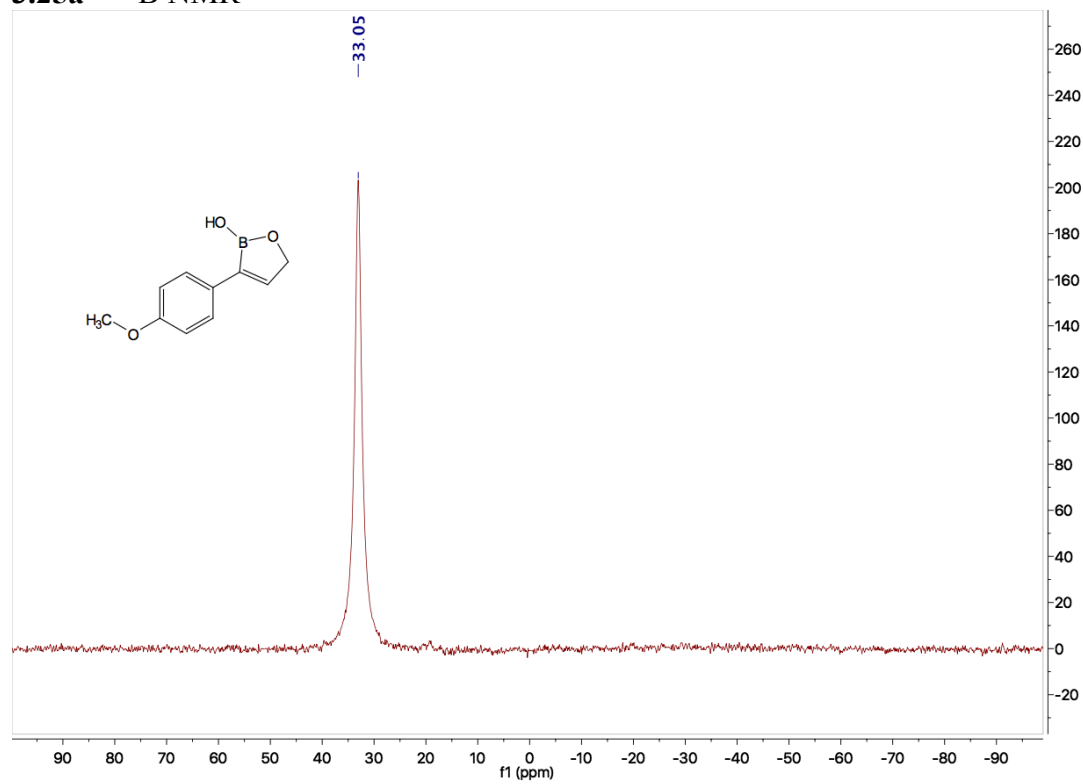
3.25a –  $^1\text{H}$  NMR



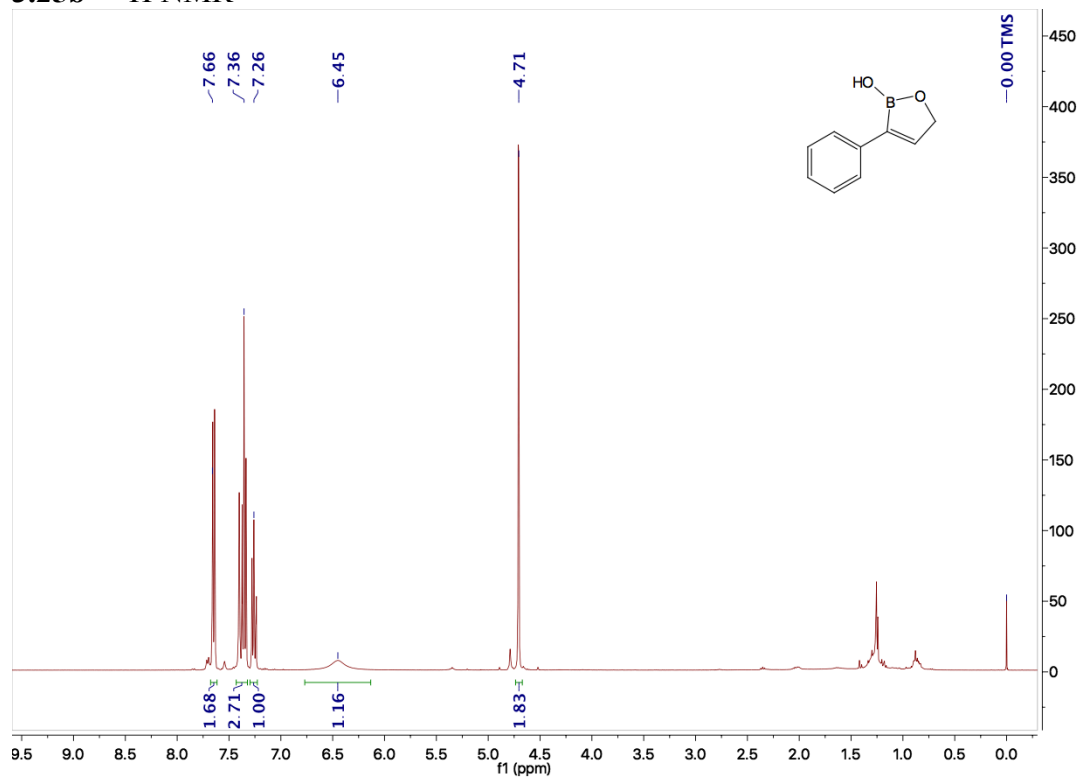
### 3.25a – $^{13}\text{C}$ NMR



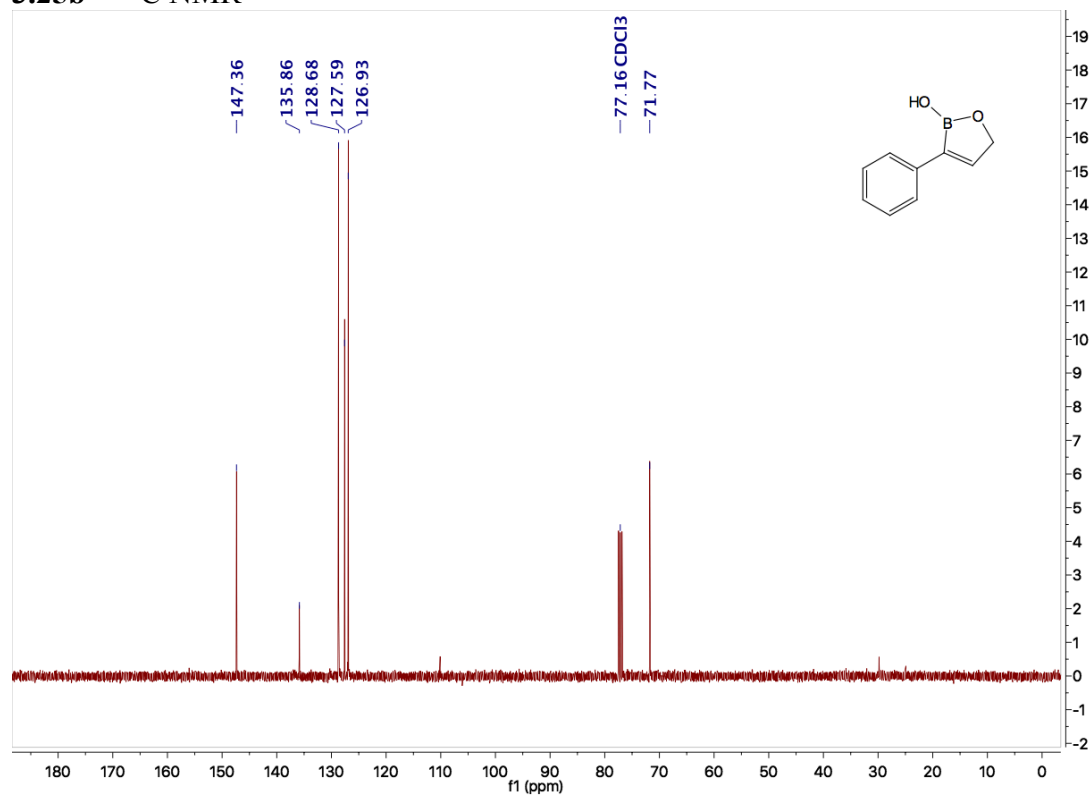
### 3.25a – $^{11}\text{B}$ NMR



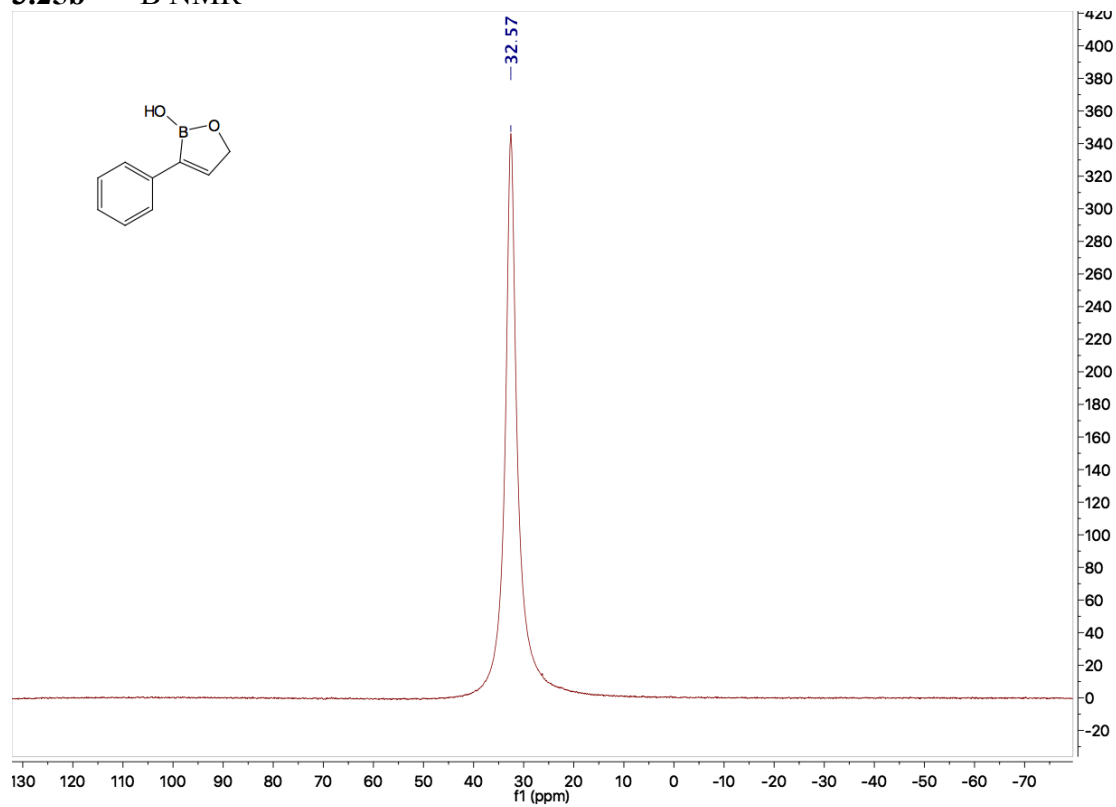
### 3.25b – $^1\text{H}$ NMR



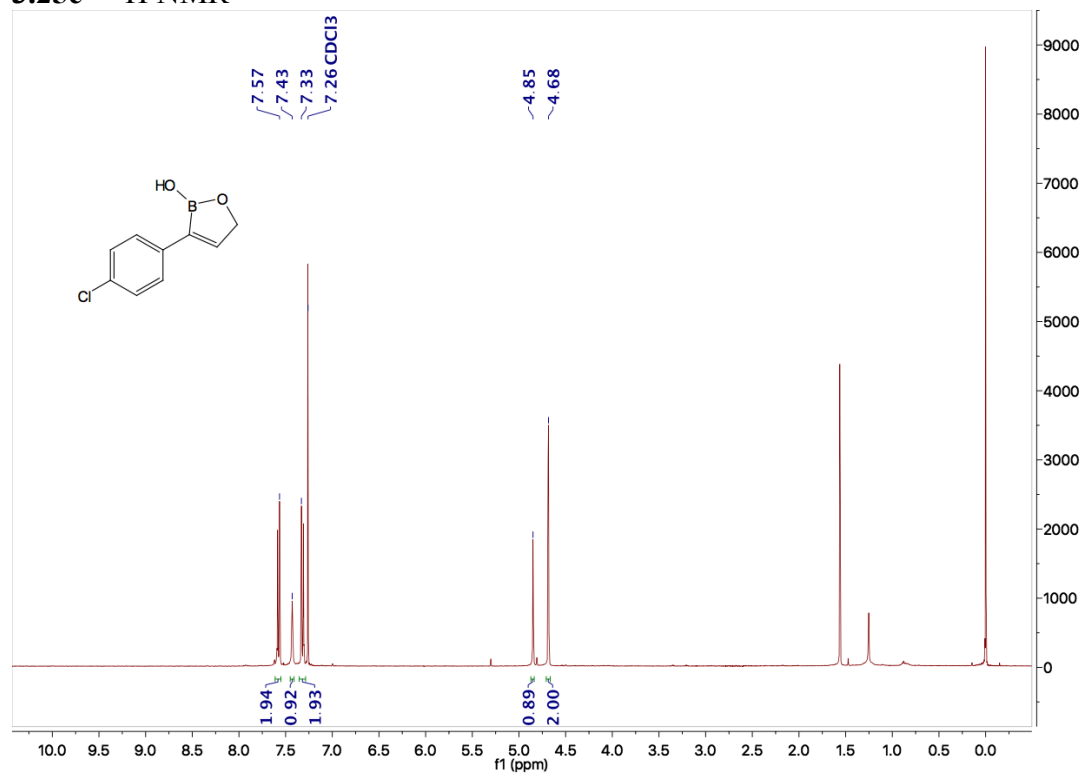
### 3.25b – $^{13}\text{C}$ NMR



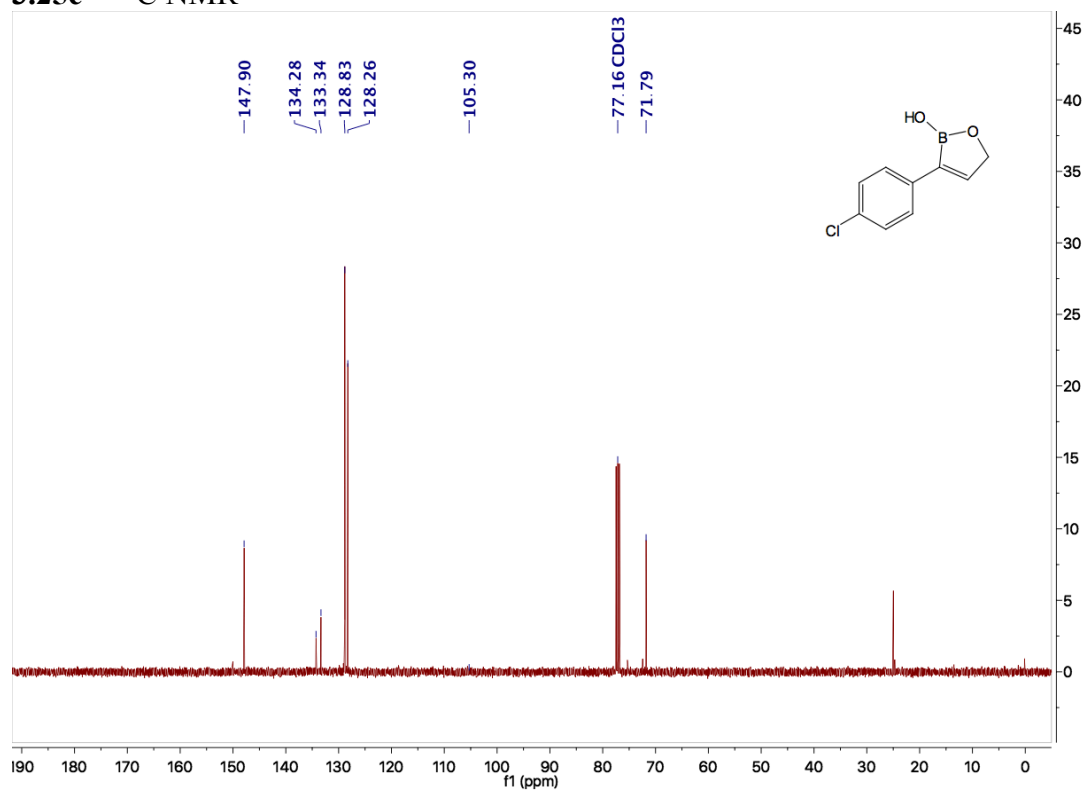
### 3.25b – $^{11}\text{B}$ NMR



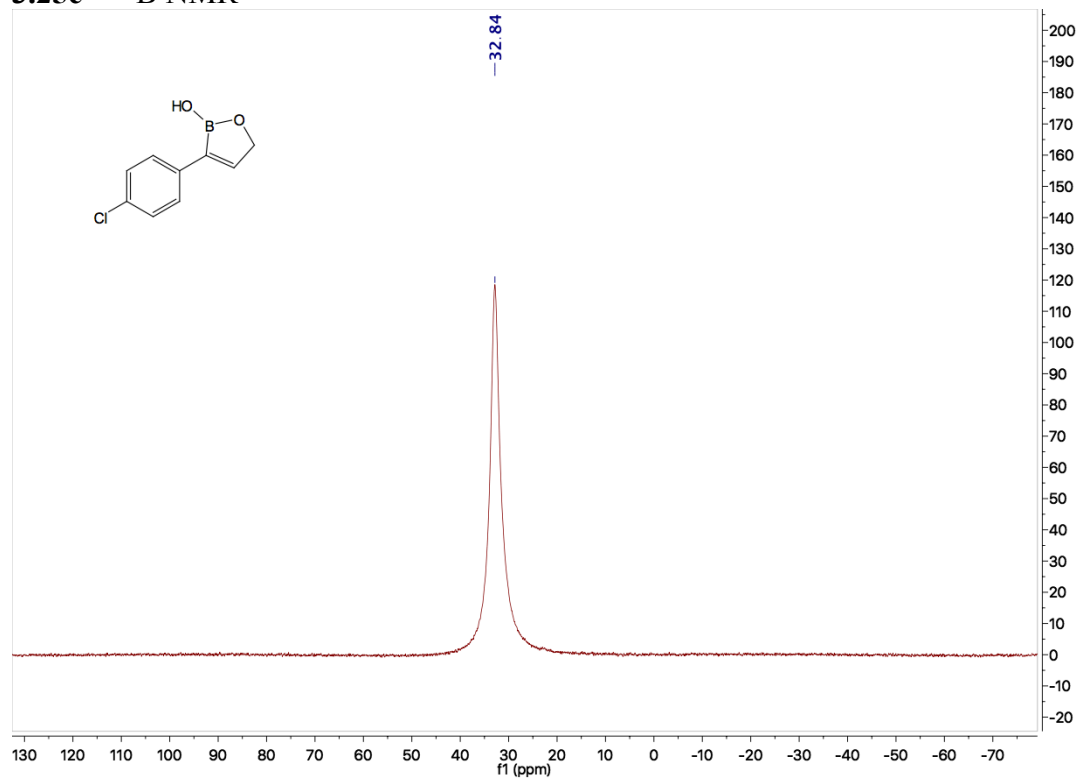
### 3.25c – $^1\text{H}$ NMR



### 3.25c – $^{13}\text{C}$ NMR

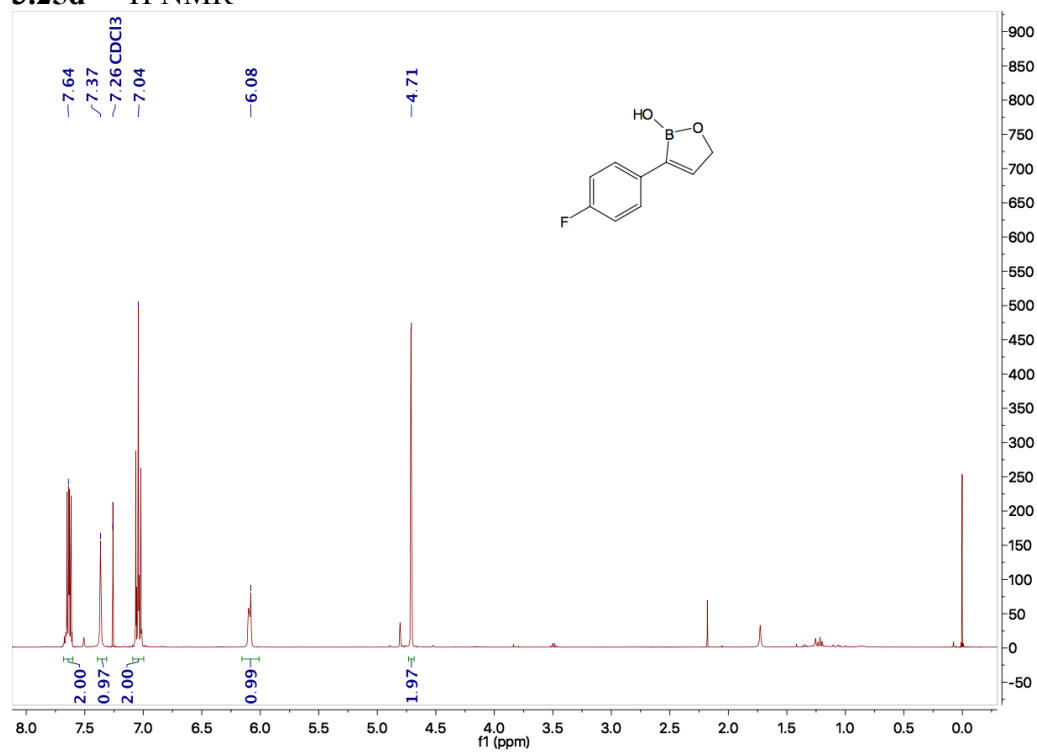


### 3.25c – $^{11}\text{B}$ NMR

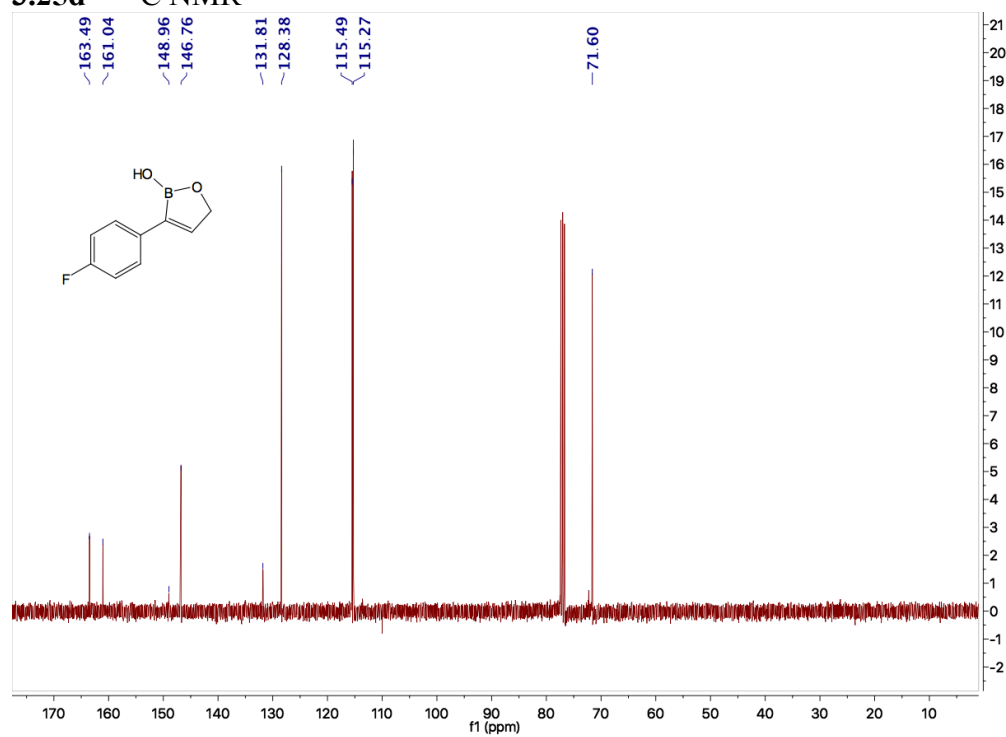




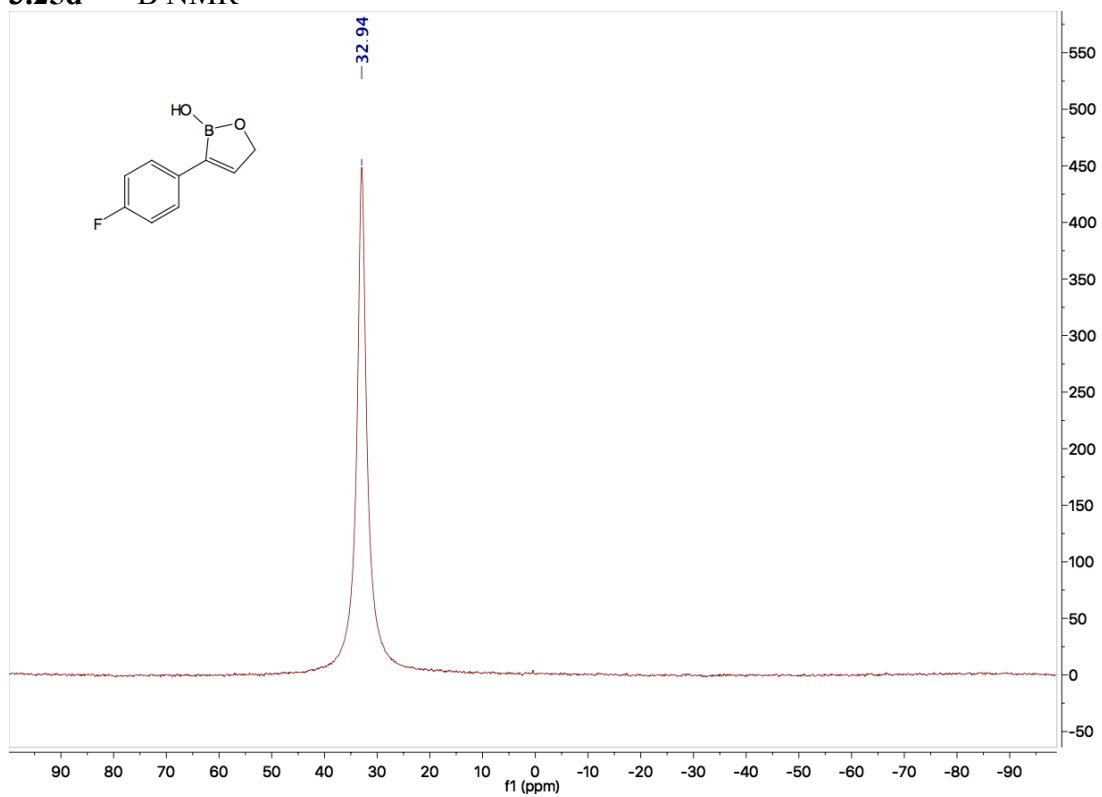
### 3.25d – <sup>1</sup>H NMR



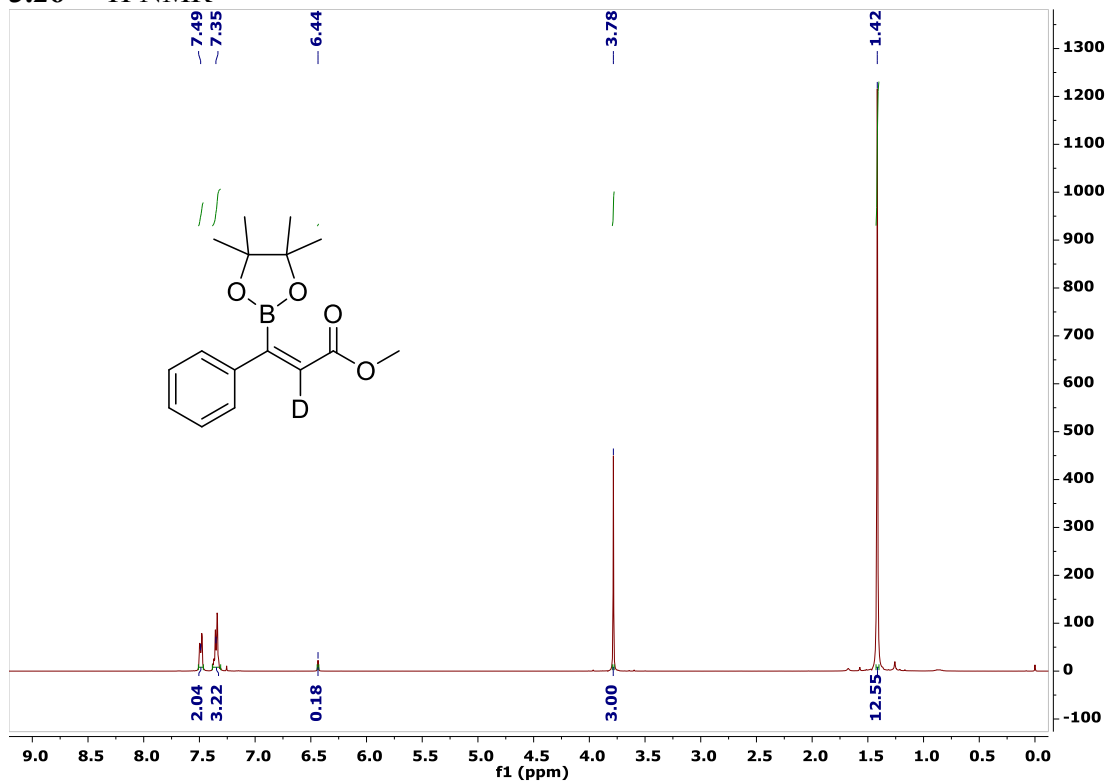
### 3.25d – <sup>13</sup>C NMR



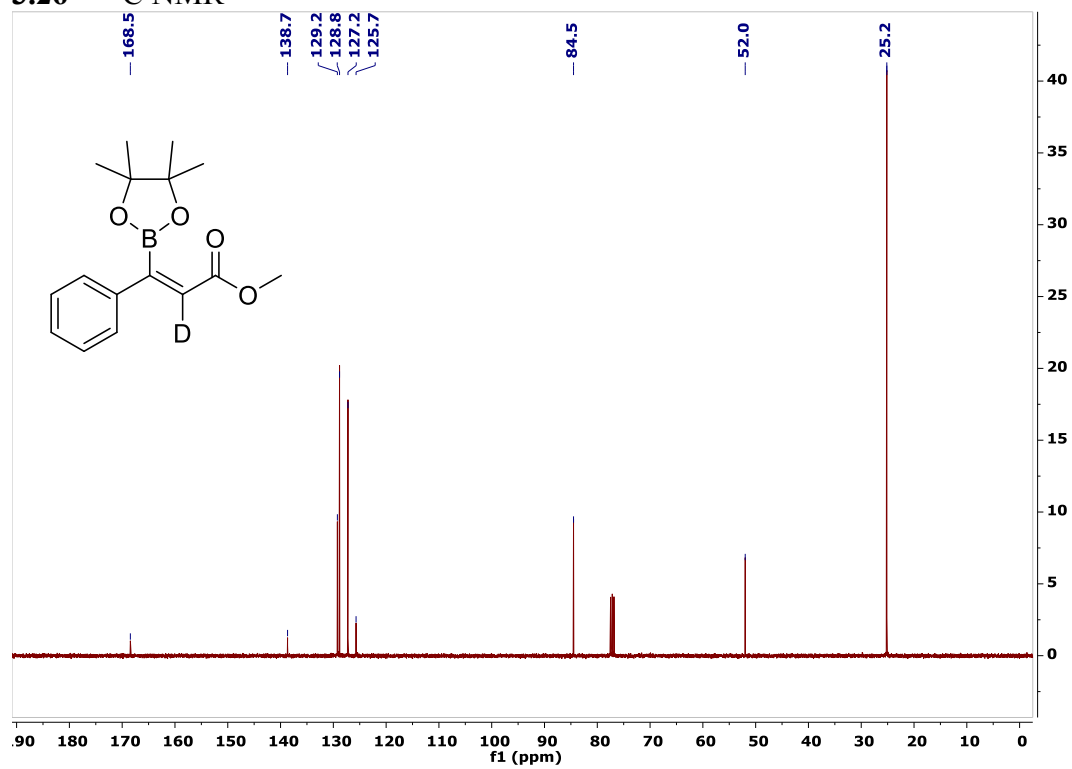
### 3.25d – $^{11}\text{B}$ NMR



### 3.26 – $^1\text{H}$ NMR



### 3.26 – $^{13}\text{C}$ NMR



### 3.26 – $^{11}\text{B}$ NMR

