Development of Novel, Regioselective Borylation Protocols

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Abstract

Organoboron compounds are highly valued synthetic intermediates due to their diverse array of reactivity, which is often utilized in the synthesis of valuable organic molecules. For this reason, there is significant interest in the development of novel borylation protocols, especially those whose products are suitable for further synthetic transformations towards valuable classes of compounds. Research in organoboron synthesis has been geared heavily toward transition metal-catalyzed addition to double and triple bonds, though an increasing number of publications detail transition metal-free borylation techniques involving substrate-mediated activation of a diboron reagent. This dissertation describes the author's contributions to the development of both a transition metal-catalyzed diboration and a transition metal-free protoboration.

A transition metal-free diboration of alkynamides is described in Chapter 1 which uses the unsymmetrical, differentially protected diboron reagent, pinBBdan. The method installs both boron moieties in a regio- and stereoselective fashion. The products have synthetic value because they are shown to have chemoselectivity in downstream cross-coupling reactions; chemoselectivity is made possible by to the significant difference in Lewis acidity of the pinacol and diaminonapthalene-protected boron centers. This method allows for facile synthesis of tetrasubstituted alkenes with a set geometry about the double bond.

A protoboration of allenes employing a Cu(II) catalyst under aqueous and atmospheric conditions is described. Though Cu(I)-catalyzed allene protoboration is well-described in the

literature, this is the first report of an analogous Cu(II)-mediated process. The selectivity of the reaction is ligand-controlled, and moderate to good regioselectivities and yields can be achieved through use of a triphenylphosphine as ligand. The method is an environmentally friendly and facile means by which to borylate a challenging cumulated substrate.

Development of Novel, Regioselective Borylation Protocols

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General Audience Abstract

Organoboron compounds are valuable because of their ability to undergo a wide variety of chemical transformations, and they are often used as intermediates in the synthesis of challenging target molecules. In order for this reactivity to be exploited, methods must exist for the efficient synthesis of the desired boron-containing compound. This dissertation describes the author's contributions to the development of two new methods by which to synthesize organoboron products. The first method involves installation of two differently ligated boron moieties onto an alkynamide substrate to produce a single, uncommon *trans* isomer as product. A synthetic application of these diboration products is described. The second method involves installation of a single boron moiety into allenes. Though the same overall transformation has been achieved in the literature with use of highly air-sensitive catalysts and organic solvents, the described method entails use of air-stable $CuSO_4$ as catalyst and water as solvent. Therefore, the method is operationally simple and environmentally friendly relative to previously described methods.

Acknowledgements

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Chapter One: Substrate Assisted, Transition Metal-Free Diboration of Alkynamides with an Unsymmetrical Diboron Reagent

1.1 Contributions

A number of collaborators contributed to the following work. All alkynoic acids that were not commercially available were synthesized from terminal alkynes by Brett Rastatter or Dr. Yumin Dai. The synthesis of alkynamides from alknyoic acids was performed by both the author and Dr. Yumin Dai, the latter of whom synthesized the majority of alkynamides that were diborated in the publication. Optimization of reaction conditions for the alkynamides diboration are presented in Table 1.1 and were primarily run by Dr. Astha Verma, with the exception of entries 1-6, which were performed by the author. The diboration reactions in the substrate scope exploration were performed by the author (~70%) and Dr. Verma (~30%). DFT calculations were performed by members of the Yu group (Yinuo Yang and Dr. Haizhu Yu) from Anhui University as well as Dr. Fu Yao from the University of Science and Technology of China. The chemoselective cross-coupling reactions were exclusively performed by Dr. Yumin Dai. Dr. Webster Santos wrote the published manuscript[1], and the author did significant work in editing and reformatting the publication.

1.2 Abstract

A transition metal-free diboration of alkynamides with the unsymmetrical diboron reagent, pinBBdan, has been achieved with Bronsted-base activation, exclusively affording the *trans*-addition product. The reaction occurs regioselectively, installing the chemically inert Bdan moiety at the α-position exclusively. The reaction proceeds in good to excellent yields for a wide variety of substrates, including electron-rich or deficient aryl substituted alkynamides as well as a primary

and secondary alkynamides. We propose that the deprotonated alkynamide activates the B-B bond, leading to key boryl migration and cyclization steps. Mechanistic DFT studies are discussed as well as the application of the diboration products in chemoselective cross-coupling reactions.

1.3 Importance of Organoboron Compounds

Boron is a semi-metallic element with three valence electrons. Boron-containing compounds typically exist in either 1) sp^2-hybridized, three-coordinate, six-electron trigonal planar complex with an empty *p*-orbital or 2) sp^3-hybridized, four-coordinate, eight-electron tetrahedral complex bearing a formal negative charge on boron (Fig. 1.1). An sp^2-hybridized boron center typically acts as a Lewis acid, and reversible coordination at the vacant *p*-orbital of **1.1** generates the tetracoordinate borate complex **1.2**. *Organoboron* compounds are defined by the presence of at least one carbon-boron bond; activation of this C-B bond is a means toward greater elaboration of the organic portion of the molecule.[2-3] Organoboron compounds have also demonstrated use as final products in medicinal chemistry.[4-6]

The diverse reactivity of organoboron compounds is mechanistically initiated through nucleophilic coordination to the organoboron compound's sp^2 hybridized boron center. When connected to an sp^3-hybridized boron, the C-B bond lengthens with concomitant weakening of the bond and accumulation of partial negative charge on carbon. This in turn allows for carbon to act as a nucleophile. For example, this nucleophilic carbon may undergo facile transmetallation to a transition metal such as copper, palladium, or iridium. This has allowed organoboron compounds to be employed in a wide variety of cross-coupling reactions.[7-8] Several well-established methods

result in the construction of C-C bonds, the most important of which is Suzuki-Miyaura cross-coupling (SMC).[9-10]

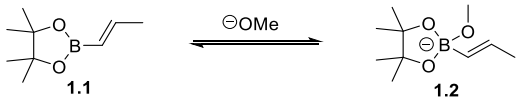


Figure 1.1 Reversible nucleophilic coordination to an organoboron compound.

Cross-Coupling Reactions:

Suzuki-Miyaura coupling (Fig. 1.2A) constructs C-C bonds through palladium(0)-catalyzed coupling of an aryl halide **1.19** and organoboron **1.3**. This coupling is achieved through the mechanistic cycle shown in Fig. 1.2B, and involves organohalide oxidative addition to form **1.7**, ligand exchange to form **1.10**, organoboron transmetallation to form **1.14**, and reductive elimination to form desired cross-coupled product **1.15**. Methods for Suzuki-type couplings have been extensively researched over the past few decades,[11-12] and the original methods have been extended significantly to include aryl chlorides[13] (which were previously inert to Suzuki's conditions) and aryl halides bearing a sterically-challenging *ortho* substituent.[14] Furthermore, developments such as aqueous SMC reactions and SMC reactions run *sans* ligands have been described and studied.[11] Finally, transition metal-catalysts other than palladium have been documented (*e.g.* copper[15-19], nickel,[20]). Some of these catalytic systems display complementary reactivity to Pd catalysts on the basis of subtle mechanistic differences from original Pd-catalysis; for instance, Cu-catalyzed SMCs proceed through organoboron transmetallation *prior to* halide oxidative addition,[18-19] thus avoiding side product formation when the aryl halide also functions as a Heck substrate.[19] Nickel catalysis can extend cross-coupling technology to include alkyl halides since formation of a metal-alkyl intermediate proceeds *via* generation of an alkyl radical

intermediate.[20] Even with these improvements, the original incarnation of SMC has found use in both industrial and academic settings.[21] For instance, it is a key step Merck's synthesis of Losartan, a direct product of synthetic intermediate **1.18**.[22]

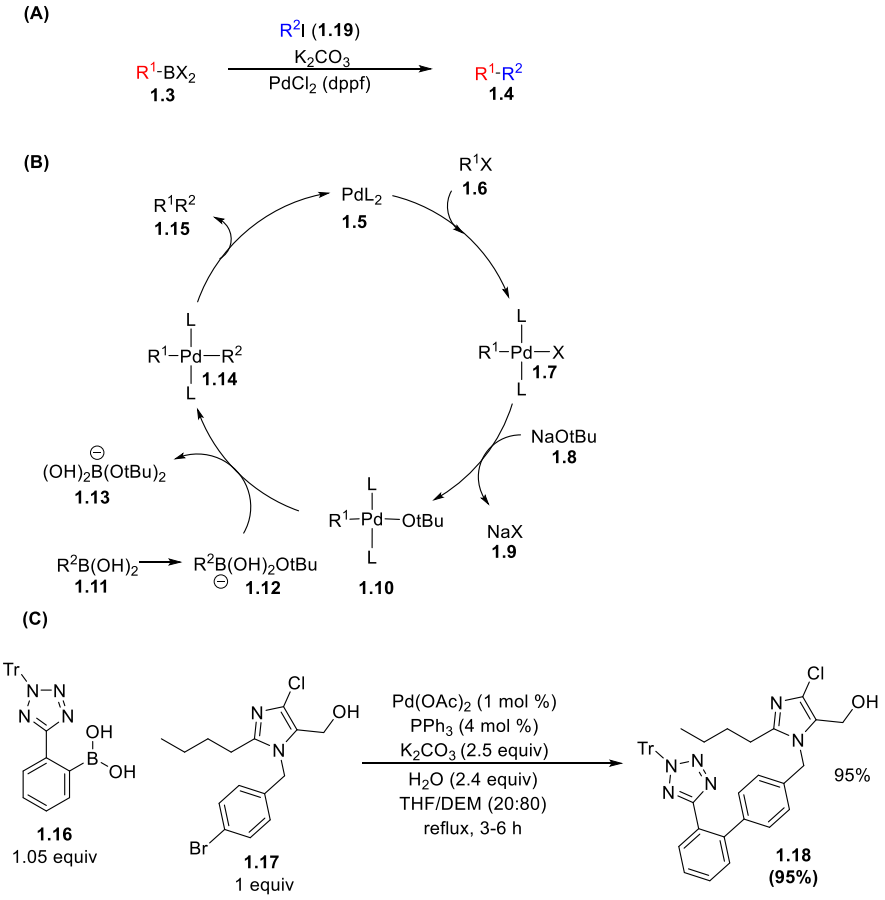


Figure 2..2 Suzuki-Miyaura cross-coupling. (A) Overall reaction (B) Catalytic cycle (C) Application in synthesis of Losartan.

Cross-coupling reactions of organoboron compounds are not limited to SMC (Fig 1.3). Modification of Suzuki's original conditions has allowed for facile generation of ketones (carbonylative coupling, **1.20** to **1.21**)[23] and esters (alkoxycarbonylation, **1.20** to **1.22**).[24] Carbonylative coupling results from carbon monoxide (added as a gas or produced *in situ*[25]) insertion into the oxidative addition intermediate along the SMC catalytic pathway (*vide supra*); continuation of the catalytic cycle furnishes a target ketone. If a Pd(II) catalyst, carbon monoxide,

alcohol, reoxidant, and organoboron compound are used, esters may be synthesized. Carbon-heteroatom linkages can be formed through copper(II)-catalyzed Chan-Lam coupling using an alcohol, thiol, or amine coupling partner (**1.20** to **1.23**).[8]

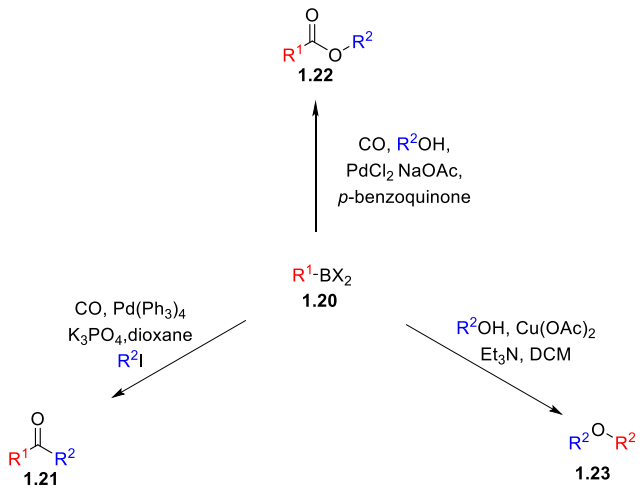


Figure 1.3 Carbonylative coupling, alkoxycarbonylation, and Chan-Lam coupling.

Oxidation and Matteson Homologation:

When nucleophilic activation of an organoboron compound occurs where the *nucleophile itself* has a leaving group, a boron-bound carbon may undergo migration with concomitant expulsion of the leaving group (Fig. 1.4). This is the mechanistic basis for Brown's oxidation reaction in which deprotonated H_2O_2 acts as a nucleophile with a hydroxyl leaving group (**1.24** to **1.25**). Another synthetically significant example of this mode of reactivity is Matteson homologation (**1.24** to **1.26**) during which lithium dichloromethanide acts as a nucleophile bearing two chloride leaving groups, thus allowing for two successive displacements.[26] Matteson

homologation can be done asymmetrically with use of a chiral auxiliary, and in either case the boron moiety is retained for further functionalization reactions.

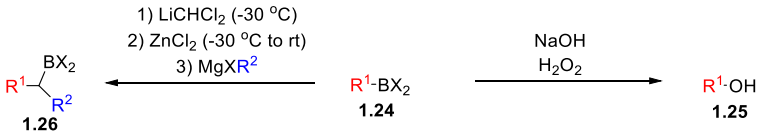
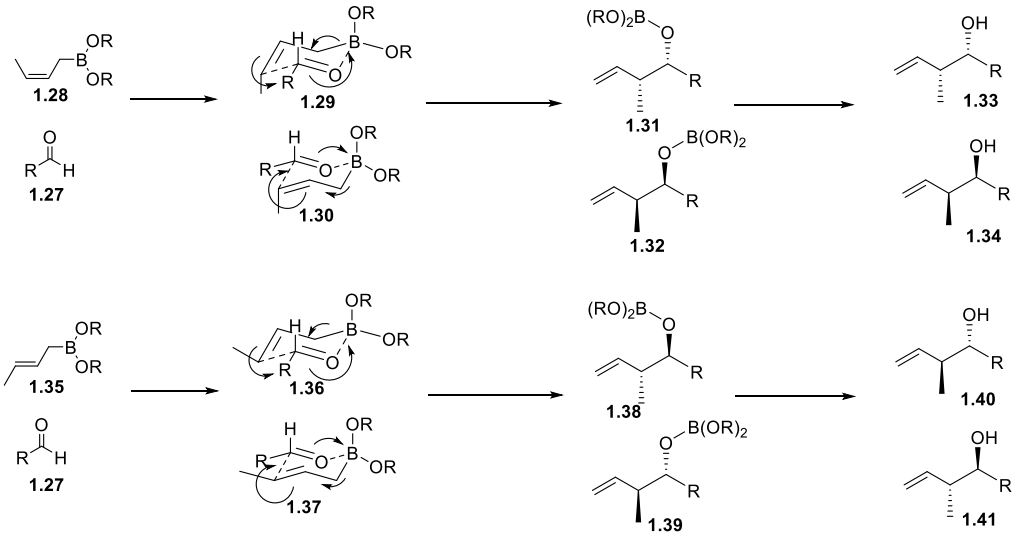


Figure 1.4 Brown's oxidation and Matteson homologation.

Crotylboration:

Another important reaction of organoboron compounds is the crotylboration reaction (Fig. 1.5). If a boron moiety is in an allylic position, attack from the γ-carbon to an aldehyde can occur through a six-membered transition state to diastereoselectively generate a borate (**1.31/1.32** or **1.38/1.39**). Hydrolysis of these borates results in the production of a synthetically valuable *syn* (**1.33/1.34**) or *anti* (**1.40/1.41**) homoallylic alcohol resulting from reaction with a *Z* or *E*- alkene, respectively. The diastereoselectivity is the result of a chair transition state which places the aldehyde "R" group in an equatorial position. Much effort has been applied to successfully extend this methodology to the asymmetric synthesis of homoallylic alcohols; asymmetric induction is achieved through use of chiral auxiliaries on boron.[27-29] Crotylboration reactions have been important in total syntheses; such as those involving construction of a macrocyclic backbone with chiral decorations.[30]



. Figure 1.5 Diastereoselective crotylboration reaction

1.4 Synthesis of Organoboron Compounds through Diboration

To exploit the diverse array of reactivity outlined above, an appropriate organoboron starting material must be synthesized whose structure will allow for elaboration to the target molecule of interest. To this end, there are numerous strategies to synthesize organoboron compounds; among them, hydroboration (Fig. 1.6A), protoboration (Fig. 1.6B), reaction of an organometallic reagent with a trialkyl boronate (Fig. 1.6C), and diboration reactions (Fig. 1.6D). Diboration reactions provide the advantage of simultaneously installing two functional groups for subsequent chemical transformations. If installation of a different moiety for each C-B bond is desired, the selectivity of the subsequent reactions must be carefully controlled through differential protection of each boron center or through substrate-controlled selectivity (*vide infra*).

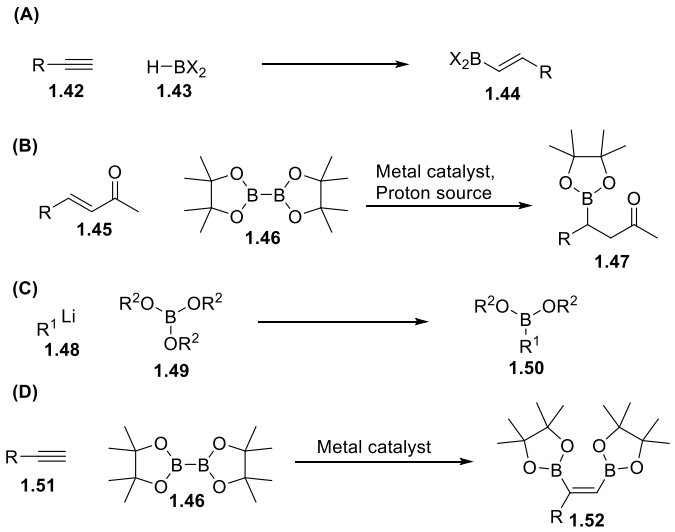


Figure 1.6 General routes to organoboron compounds. (A) Hydroboration (B) Protoboration (C) Attack of an organometallic reagent with a trialkyl borate (D) Vicinal diboration.

Diboration reactions have been successfully applied in addition reactions to alkynes, alkenes, imines, aldehydes, and ketones.[31] Furthermore, elegant diboration reactions which entail effective aryl substitutions have been described recently.[32] In this chapter, discussion of diboration reactions will be restricted to diboration reactions which result in diborated alkenes as products. Such products are among the most well-studied, and they are among the most amenable to further synthetic transformations.

The first diboration was reported in 1959 and employed reactive diboron compound B_2Cl_4.[33] This diboron reagent is reactive enough to add to an alkyne without use of a transition metal catalyst. However, both the reagent itself as well as its diboration products are too unstable for typical synthetic use. The majority of diboron reagents used in diboration reactions are significantly more stable than B_2Cl_4 and have ligands such as alkyl, alkoxy, or amine groups. While they display superior stability to B_2Cl_4, none are capable of adding directly to an alkyne without the help of a transition metal catalyst.

The first synthetically useful diboration was reported by Miyaura *et al*. and used $Pt(PPh_3)_4$ as a catalyst (Fig 1.7A).[34] This vicinal diboration employed bis(pinacolato)diboron (**1.54**) and produced exclusively *cis* diboration products (such as **1.55**). Since this seminal report, numerous platinum catalysts and conditions have been reported which achieve the diboration through a common mechanism. These include Pt(II) catalysts which form the active Pt(0) catalyst *in situ*. This mechanism is shown in Fig 1.7B. Oxidative addition of the diboron reagent to Pt(0) precatalyst **1.56** produces tetracoordinate platinum intermediate **1.57**; after ligand dissociation to form **1.58**, an alkene or alkyne (**1.59**) may then insert into the Pt-B bond to furnish intermediate **1.61**. Reductive elimination to regenerate active Pt(0) catalyst **1.63** furnishes the diboration product **1.62**. The *cis* geometry of the products can be easily rationalized through consideration of the four-membered transition state during the critical insertion step (**1.60** to **1.61**).

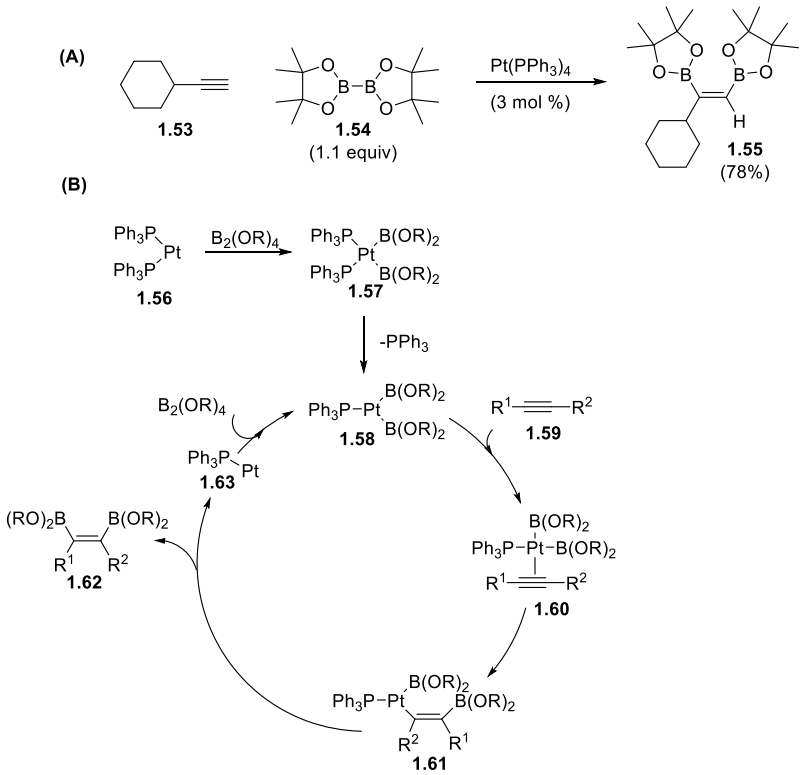


Figure 1.7 Miyaura's Pt-catalyzed diboration reaction. (A) Overall reaction (B) Catalytic cycle

Efforts have also been carried out to diborate with cheaper, more environmentally friends transition metal catalysts. Copper-catalyzed diborations of alkenes and alkynes have been described by Fernandez[35] and Yoshida[36], respectively. Yoshida *et al*. achieved diboration of internal alkynes using B_2pin_2, $Cu(OAc)_2$, and PCy_3 (Fig. 1.8). Alkynes bearing two aryl, two alkyl, or mixed substitutions perform well in this reaction. Interestingly, the authors found that substrates bearing one or more propargylic methoxy groups were partially substituted by a Bpin moiety, allowing access to tri- and tetra-borylated compounds. The reaction was thought to proceed through *in situ* generation of a boron-ligated copper intermediate **1.66**, alkyne insertion to form **1.68**, followed by transmetallation with another molecule of B_2pin_2 to regenerate **1.66** and furnish diboration product **1.70**.

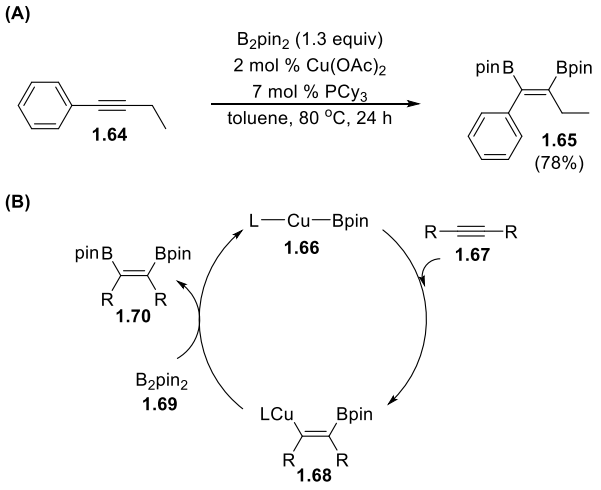


Figure 1.8 Copper-catalyzed diboration of alkynes. **(**A) Overall reaction (B) Proposed catalytic cycle

Nakamura *et al*.[37] demonstrated that iron-catalyzed diboration reactions are possible with use of $FeBr_2$, B_2pin_2, LiOMe, and OMeBpin additives (Fig. 1.9A). Furthermore, the authors demonstrated that organoferrate intermediates generated *in situ* could be readily trapped by alkyl bromides added in a 3-4 equivalent excess (and the absence of an OMeBpin electrophile), allowing

for synthesis of carboborated products such as **1.72**. This latter reaction was demonstrated on symmetrical alkynes, only. The mechanism proposed by the authors is shown in Fig. 1.9B. The active catalyst **1.74** was a methoxy-ligated iron species formed from transmetallation between $FeBr_2$ and LiOMe. Transmetallation of **1.74** and B_2pin_2 formed boron-ligated iron **1.75** after which alkene insertion resulted in organoferrate **1.77**. A final transmetallation with **1.78** (present in large quantities in the reaction as both an additive and product of the cycle) regenerated catalyst **1.74** as well as diboration product **1.79**. In the case of carboboration, **1.77** was trapped with an alkyl bromide, **1.80,** to form **1.82**.

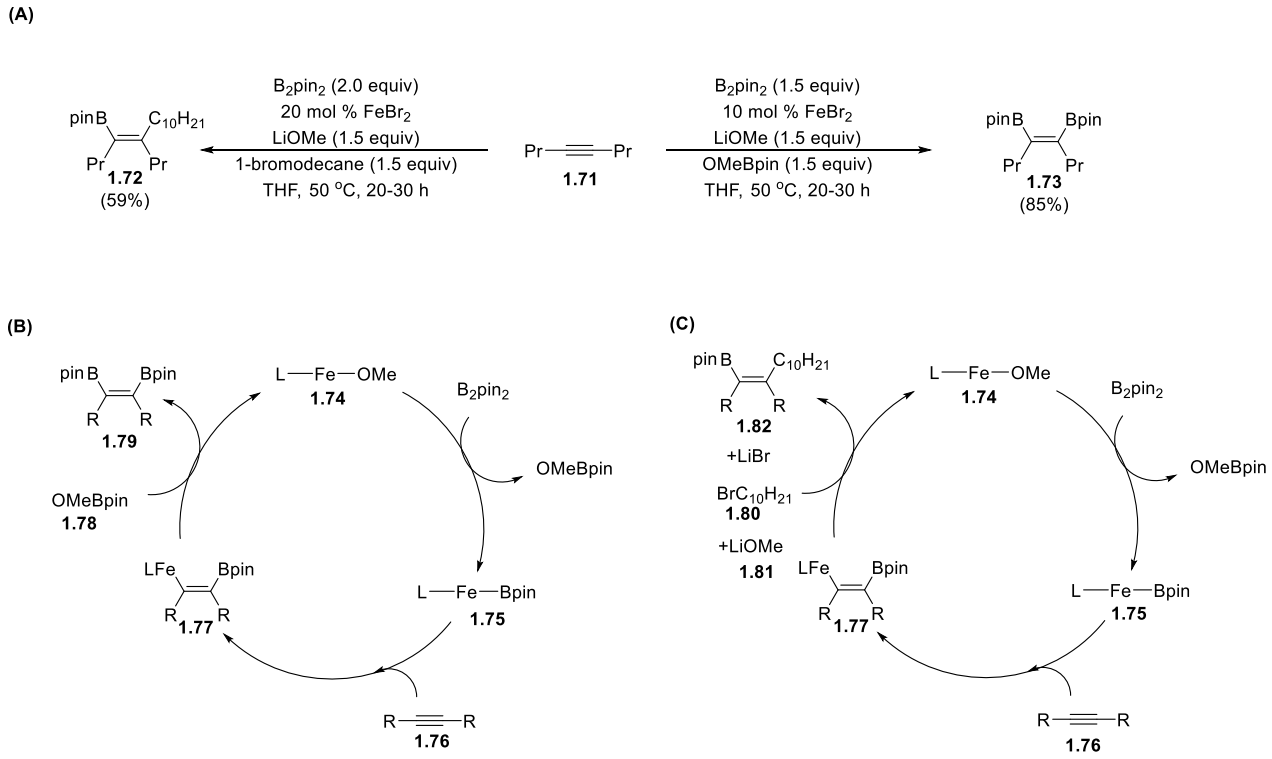


Figure 1.9 Iron-catalyzed diboration and carboboration (A) Overall reactions (B) Diboration catalytic cycle (C) Carboboration catalytic cycle.

As well-studied SMC coupling partners, these vicinal *cis* diboration products are suitable precursors to highly substituted alkenes. When an unsymmetrical alkyne is diborated, the chemoselectivity of the downstream reactions must be secured if different coupling partners are

desired for a given C-B bond. In the case of diborated terminal alkynes, it has been demonstrated that cross-coupling occurs with good selectivity for the terminal boron moiety (Fig. 1.10). For instance, Miyaura reported a successful coupling of 4-bromotoluene and diborated 1-hexyne (**1.85**) to form coupled product **1.87**, with only 7% yield of undesired doubly-coupled product **1.88**.[38]

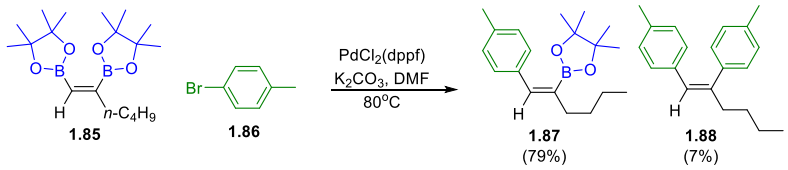


Figure 1.10 Chemoselective cross-coupling of a diborated terminal alkyne.

A novel diboration reaction of terminal alkynes which favors subsequent coupling at the *internal* carbon has been described by Suginome *et al.*[39]; this complementary reactivity is achieved through use of an unsymmetrical diboron reagent, pinBBdan (Fig. 1.11**,** **1.90**). The diaminonapthalene-ligated boron center acts as poor Lewis acid, largely due to significant electron donation from the adjacent nitrogen atoms; thus, it is resistant to the requisite nucleophilic coordination needed for transmetallation and cross-coupling to occur. Through use of either platinum or iridium catalysis, vicinal diboration with selective installation of Bdan at the terminal carbon was achieved in good yields and excellent selectivities. As such, cross-coupling of **1.91** with 4-bromotoluene (**1.92**) afforded coupling product **1.93** with reverse selectivity than that previously observed by Miyaura.

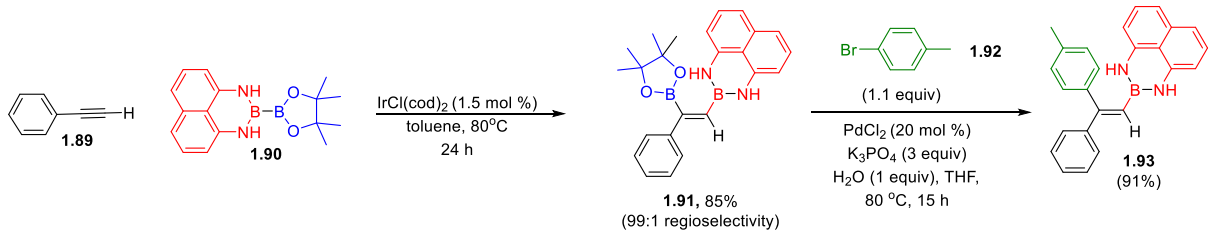


Figure 1.11 Diboration of a terminal alkyne with an unsymmetrical diboron reagent, and chemoselective cross-coupling at the internal C-B bond.

Internal alkynes pose a greater challenge for chemoselectivity in downstream cross-coupling reactions. When diborated with a symmetrical diboron reagent (*e.g.* B_2pin_2), there is typically nothing to bias selectivity toward one C-B bond or another. If diborated with pinBBdan, there is nothing to bias the regioselectivity of Bdan installation to one of the two available alkyne carbon atoms. However, some examples exist of vicinally diborated alkenes which exhibit chemoselectivity by virtue of steric or electronic effects.

Nishihara *et al.* [40] demonstrated one such chemoselective cross-coupling after diborating TMS-protected terminal alkynes (Fig. 1.12). When carefully optimized conditions along with $Pd(dppp)Cl_2$ as catalyst were used, selective cross-coupling occurred solely at the C-B geminal to the TMS moiety. For example, coupling of **1.94** with 4-iodoanisole (**1.95**) produced coupling product **1.96** solely at the position geminal to the phenyl group in 73 % yield. The authors suggest that the chemoselectivity of the cross-coupling resulted from the α-effect of silicon; this stabilizes the partial negative charge buildup inherent in transmetallation at the α-boron only. Interestingly, Nishihara *et al*. also silaborated (using pinB-$SiMe_2Ph$) Bpin-protected acetylene to produce a geminally diborated alkene, which retained the same selectivity pattern with the boron moieties geminal to one another. The authors demonstrated the utility of these latter diboration products through synthesizing challenging tetrasubstituted alkene **1.96** with defined stereochemistry about the C-C double bond.

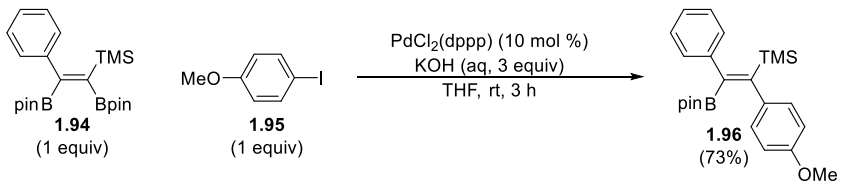


Figure 1.12 Chemoselective cross-coupling of a vicinally diborated alkyne.

In addition to vicinal diboration reactions, geminal diboration reactions have been reported. To produce a geminally diborated alkene, typically a monosubstituted or 1,1-disubstituted alkene is used as borylation substrate, with diboration occurring through an effective substitution of both alkene protons. However, such a transformation is synthetically challenging, as transition metal-mediated removal of alkene protons entails formation of metal-hydride intermediates capable of reducing the desired diborated alkene.

Despite this challenge, a rhodium-catalyzed geminal diboration of alkenes was described by Marder *et al.* in 2003.[41] Successful installation of bis(pinacolato)diboron or bis(neopentyl glycolato)diboron into monosubstituted alkenes or 1,1-disubstituted alkenes was achieved with use of *trans*-[Rh(Cl)(CO)(PPh_3)$_2$] as catalyst (Fig. 1.13). Notably, solvent choice was established as necessary for the suppression of hydrogenation products, especially in the case of a mono-substituted alkene (4-vinylanisole). The authors were unable to establish a strongly-supported mechanism, but suggested the mechanism may (in part) entail alkene insertion into Rh-B bonds followed by rapid β-hydride elimination.

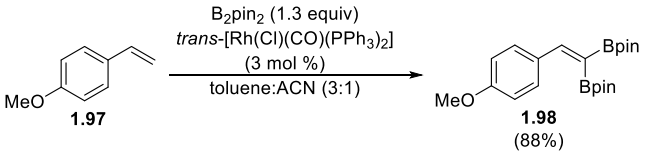


Figure 1.13 Rh-catalyzed geminal diboration.

A palladium-catalyzed geminal diboration of mono-substituted alkenes has also been reported by Iwasawa *et al* (Fig. 1.14).[42] The authors used $AlEt_3$ as additive and a PSip-pincer-ligated palladium (**1.103**), to effect the geminal diboration or rare *trans* diboration product, depending on substrate choice. Select examples are shown in Fig 1.14. The reaction was purported to proceed by two subsequent *in situ* formations of a Pd-B complex, alkene insertions into the Pd-B bond, and rapid β-hydride elimination. The *trans* selectivity was rationalized by positing a *syn* addition/β-hydride elimination to a *trans* monoborylated alkene.

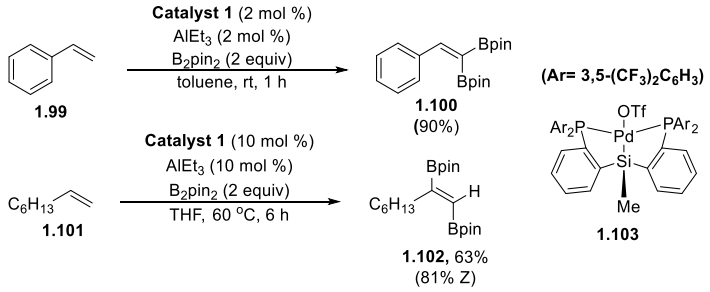


Figure 1.14 Pd-catalyzed geminal and *trans* diboration of alkenes.

Though the vast majority of diborations are transition metal-catalyzed, several effective diborations have been developed which proceed *sans* transition metal catalysts. Many of the most recent examples produce the uncommon *trans* diboration product and entail substrate-mediated activation of the diboron reagent, allowing for intramolecular attack at an unsaturation site to form C-B bonds.

The first of the transition metal-free vicinal diboration protocols was developed by Uchiyama and coworkers.[43] The authors disclosed diboration of propargylic alcohols (Fig 1.15). Mechanistically, the reaction was purported to proceed through deprotonation of the alcohol with *n*-butyllithium followed by coordination to the diboron reagent to form **1.108**. Installation of the uncoordinated Bpin moiety occurred through a five membered transition state, generating an

effective carbanion at the β position (**1.109**). This nucleophilic carbon was then capable of coordination to the second Bpin to furnish products **1.110**. The *trans* geometry of the products was ensured by the need for the C-Li bond to be positioned *cis* to the electrophilic portion of the intermediate. Hydrolysis of **1.110** furnished oxaborole products such as **1.111**. Experiments performed by Uchiyama and coworkers, as well as a DFT study, demonstrated that the lithium counterion was necessary to stabilize the reactive intermediates and transition states between them. Interestingly, exploration of the substrate scope revealed that a minimum of one α-substitution on the propargylic alcohol was required for reaction to occur. This was attributed to the Thorpe-Ingold effect. Overall, the reaction performs well for both arylpropargylic alcohols as well as alkylpropargylic alcohols, typically resulting in percent yields exceeding 70%.

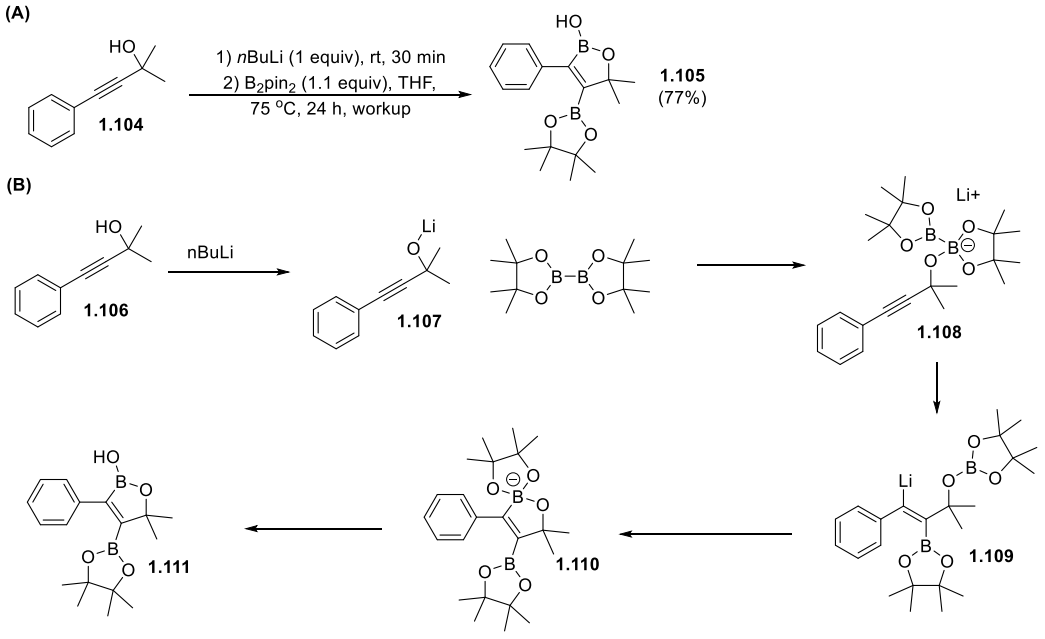


Figure 1.15 Transition metal-free diboration of propargylic alcohols. (A) Overall reaction (B) Reaction process.

A second example of transition metal-free vicinal *trans* diboration was described by Sawamura and coworkers (Fig. 1.16).[44] The authors used catalytic tributylphosphine to install

bis(pinacolato)diboron into alkynoic esters. The proposed mechanism entailed β-conjugate addition of the phosphine to the alkynoate (**1.113**) with concomitant attack on bis(pinacolato)diboron to form allenolate **1.114**. Intermediate **1.115** is produced *via* attack at the internal carbon through a five-membered transition state. Due to the delocalized nature of the alkene double bond, isomerization to **1.116** has a relatively low barrier to rotation. Attack of the ylide on the oxygen-bound boron generates intermediate **1.117**, which is then capable of expulsion of the active catalyst and formation of the desired *trans* diboration product **1.118**. They demonstrated that silaboration could occur through this process as well with installation of a silyl group at the α position and boron at the β position. Sawamura and coworkers demonstrated the applicability of their reaction to a variety of alkynoic esters bearing electron-rich and electron-deficient phenyl rings on the alkynoic ester triple bond as well as alkynoic esters bearing alkyl groups on the alkyne.

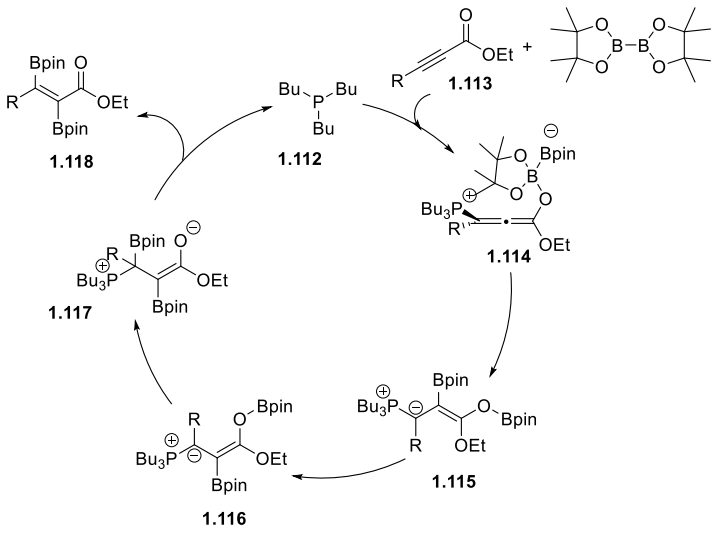


Figure 1.16 Sawamura's proposed mechanism for the *trans* diboration of alkynoic esters.

The diborated alkynoic esters are especially interesting diboration products in that they show chemoselective cross-coupling due to the electronic preference in transmetallation at the α-

Bpin (Fig. 1.17**, 1.122**). Reaction of the β-Bpin could then be achieved by increased reaction temperatures to furnish a tetrasubstituted alkene **1.124**. Sawamura elegantly demonstrated that these tandem cross-couplings in a formal synthesis of tamoxifen, an anti-breast cancer drug.

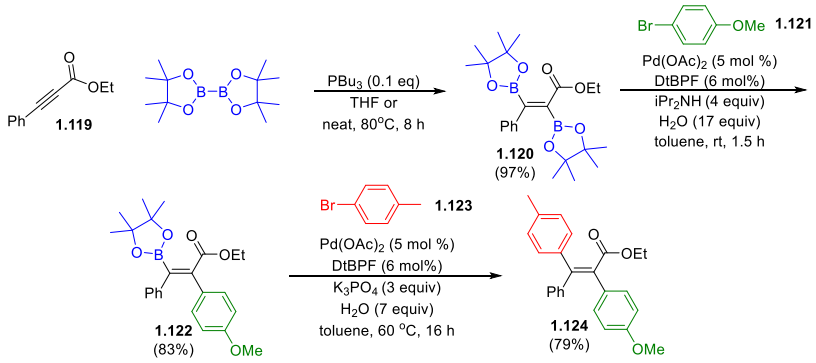


Figure 1.17 Chemoselective cross-coupling with *trans* diborated alkynoic esters.

Suginome *et al.*[45] reported a bipyridine-catalyzed *trans* diboration of acetylenedicarboxylates (Fig. 1.18A) which proceeds by a proposed mechanism similar to Sawamura *et al*, with bipyridine (**1.127**) in place of PBu_3 as the organocatalyst (Fig. 1.18B). Suginome's diboration proceeded with moderate to good yields and notably left other unsaturations unborylated.

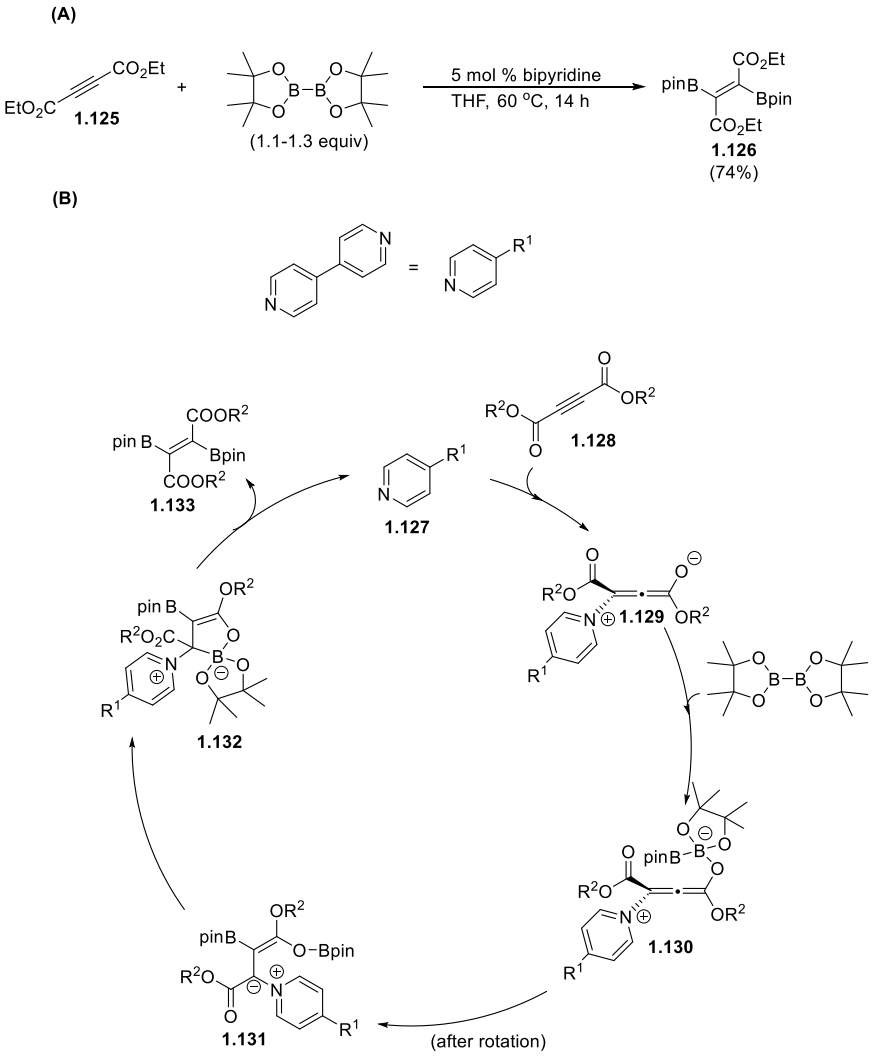


Figure 1.18 Suginome's *trans* diboration reaction. (A) Overall reaction (B) Proposed catalytic cycle.

A final example of *trans* vicinal diborations comes from Yamashita and coworkers[46] who reported the first transition metal-free diboration of terminal alkynes using the unsymmetrical diboron reagent pinBB(Mes)$_2$ (**1.136**) and 3 mol % *n*-BuLi (Fig. 1.19). Diboron reagent **1.136** had been shown to have unusually high Lewis acidity about the mesityl-ligated boron center. Steric contraints imposed by the ligands on each boron result in high overlap between the two vacant *p* orbitals, dramatically increasing Lewis acidity.[47] In the diboration reaction, deprotonated terminal alkyne first coordinates to the mesityl-ligated boron to form intermediate **1.137,** stabilized by the

lithium counterion. The Bpin moiety then migrates, generating intermediate **1.138**. Protonation of **1.138** with another molecule of terminal alkyne generates diboration product **1.139** and another molecule of **1.135** capable of undergoing the diboration. The high ratio of *trans* to *cis* diboration product were ascribed in part to the lithium coordination to intermediate **1.138,** though further mechanistic studies have not yet been reported to fully explain the stereoselectivity. The reaction was successfully applied to various phenylacetylenes and terminal alkynes with alkyl substitutions, the diboration products did not display any selectivity in subsequent cross-coupling reactions even with two differently ligated boron centers.

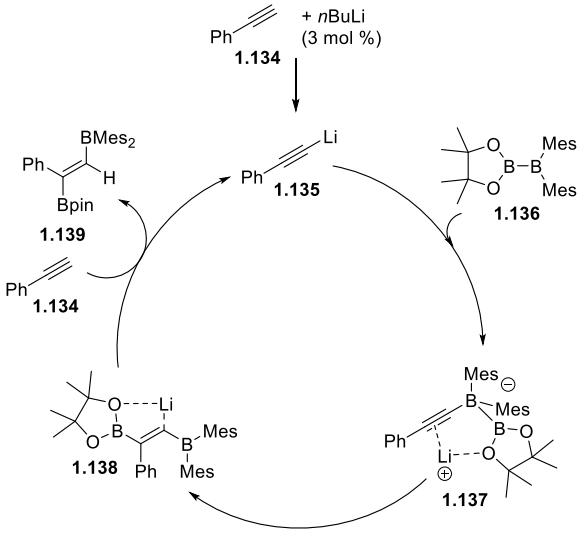


Figure 1.19 Catalytic cycle for the transition metal-free diboration reaction utilizing Mes_2BBpin.

In addition to transition metal-free vicinal diborations, transition metal-free routes to 1,1-diborylalkenes have been devised. Hiyama *et al*. used alkylidene-type carbenoids (*e.g.* **1.141**) to achieve geminal diboration (**1.142**, Fig. 1.20).[48-49] The diboration products were produced by nucleophilic attack on bis(pinacolato)diboron followed by a 1,2-migration with concomitant expulsion of bromine. The alkylidene starting materials could be produced *via* metal-halogen exchange of geminally dibrominated alkenes with *n*BuLi.

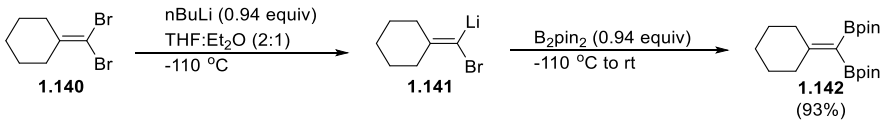


Figure 1.20 Hiyama's geminal diboration using alkylidene intermediates.

Sawamura *et al.*[50] described the LiO^{t}Bu-catalyzed geminal diboration of terminal alkynes bearing either an ester, amide, or azole group off the triple bond (Fig. 1.21). Deprotonation of the alkyne furnished a lithium acetylide capable of coordination to bis(pinacolato)diboron. A 1,2-migration of the tricoordinate boron center on the relatively electrophilic β-position followed by tautomerization furnished the desired 1,1-diborylalkenes.

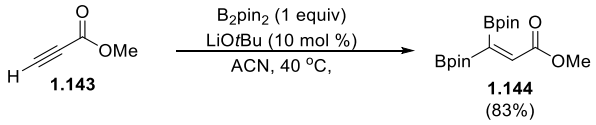


Figure 1.21 Lithium *tert* butoxide-catalyzed geminal diboration

The geminally diborated alkenes are of high synthetic interest because they display chemoselectivity in downstream cross-coupling reactions (Fig. 1.22).[51-52] In the case of Hiyama's products (Fig. 1.22A), cross-coupling of the position *cis* to an alkyl (or alkene) substituent will cross-couple first. The basis for this selectivity is poorly understood, but electronics likely play a more determinant role than steric effects, as evidenced by the retention of stereoselectivity in the presence of highly bulky alkyl groups (*ie tert*-butyl). In the case of Sawamura's product (Fig. 1.22B), [50] selectivities for the initial cross-coupling occur *trans* to the carbonyl group.

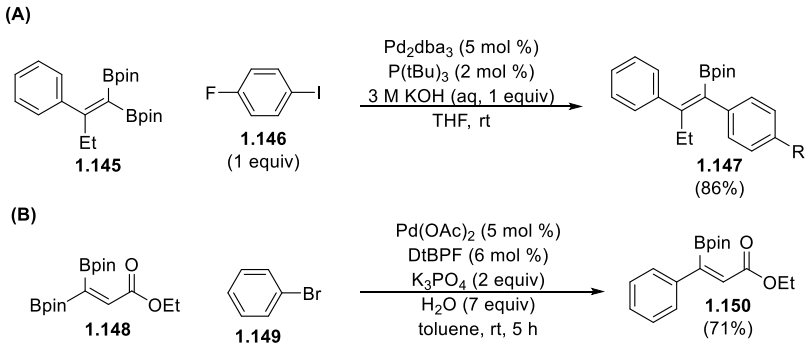


Figure 1.22 Chemoselective cross-coupling of geminally diborated alkenes. (A) Cross-coupling with Hiyama's products (B) Cross-coupling with Sawamura's products.

1.5 Project Motivation and Proposed Mechanism

Direct methods for alkynamide diboration *sans* transition metals had not been described, and the conditions of Sawamura *et al.* are unable to efficiently diborate these substrates due to the comparative lack of electropositivity at the β-carbon (*vide infra*). Furthermore, regio- and stereoselective installation of a *differentially protected* diboron reagent through such a method has not been described. Such a method would have synthetic value because the chemoselectivity of downstream reactions would be secured through protecting groups rather than substrate-dependent steric bulk or electronics. In order to address the shortcomings of the previously described methods and develop the relatively undeveloped field of transition metal-free diboration, alkynamides were diborated using the unsymmetrical diboron reagent, pinBBdan.

The proposed mechanism at the outset of the project is shown in Fig 1.23. Substrate-assisted activation of the diboron reagent would be achieved through coordination of a deprotonated alkynamide **1.152** to the pinacol-protected boron, forming intermediate **1.153**. Attack on the diaminonapthalene-ligated boron was considered unlikely due to its aforementioned lack of Lewis acidity. Installation of boron onto carbon would occur *via* successive five-membered transition states to furnish intermediates **1.156** and **1.157**, the latter of which furnishes diboration

product **1.158** (exclusively *trans*) after aqueous workup or exposure to silica. Attack *via* a six-membered transition state (**1.154**) was a possibility, but was considered to be kinetically less favored on the basis of Baldwin's rules. Furthermore, attack through a six-membered ring would likely generate a vinyl anion at the α-position, which would then face a challenging four-membered transition state in order to coordinate to Bpin. In such a case, the reaction might reverse and proceed through the five-membered transition states.

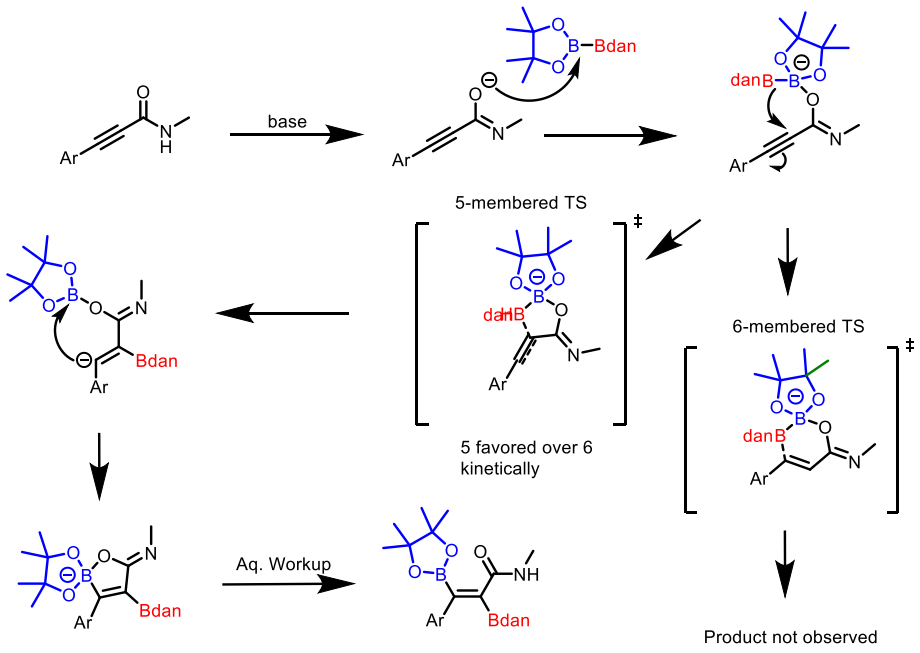
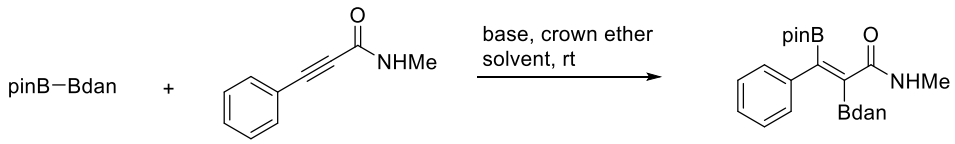


Figure 1.23 Proposed mechanism for the substrate-assisted diboration of alkynamides

1.6 Optimization of Reaction Conditions

Preliminary studies employing bases such as alkyllithium reagents and hydrides suggested that the desired product yields could be improved with the use of a chelating reagent as additive. There are two hypotheses to explain this. Firstly, coordination of the cation to the deprotonated amide's oxygen may attenuate its nucleophilicity such that rate of attack on the diboron reagent is diminished. Secondly, the putative vinyl anion may coordinate to the cation, which reduces its

ability to coordinate to the Bpin moiety. This is supported by experiments demonstrating that, without crown ether, more α-borylated product is contained in the product mixture. In these cases, it is hypothesized that the vinyl anion is unable to complete the intended reaction efficiently and instead reacts with adventitious water or labile protons from free pinBBdan. As such, appropriately sized crown ethers were employed in the optimization studies. The optimization table is shown in Table 1.1. Experiments employing weak bases produced either trace amounts of product or low yields (entries 1-7). Potassium *tert*-butoxide, while unable to quantitatively deprotonate an amide, gave a moderate yield of 54% (entry 8). Interestingly, lithium hydride and methyllithium failed to product diboration product in good yields (entries 9 and 10). However, sodium hydride and *n*-butyllithium produced 70% and 44% yields in toluene, respectively (entries 11 and 12). Testing both *n*-butyllithium and NaH in THF (entries 13 and 14, respectively) revealed the best conditions to be those employing NaH and 18-crown-6 in THF. Since solvent stabilization of the challenging vinyl anion-generating step might play a large role in reaction outcome, a short screen of solvents with various polarities was undertaken (entries 15-17). Though THF remained the best solvent for the *trans* diboration, the reaction was shown to work well in several other solvents. A control experiment using the best conditions *sans* crown ether demonstrated significant reduction in yield (entry 18). Lastly, an experiment run with a phosphine catalyst showed that Sawamura's catalyst system does not work on alkynamides (entry 19).



Entry	Base	Solvent	Crown Ether	Yield [%]
1	pyridine	THF	None	trace
2	DBU	THF	None	trace
3	TEA	THF	None	trace
4	NaOH	THF	15-crown-5	trace
5	NaOAc	THF	15-crown-5	trace
6[a]	$CsCO_3$	toluene	18-crown-6	16
7[a]	CsOH	toluene	18-crown-6	27
8[a]	KOtBu	THF	18-crown-6	54
9[a]	LiH	toluene	12-crown-4	14
10[a]	MeLi	toluene	12-crown-4	21
11[a]	BuLi	toluene	12-crown-4	44
12[a]	NaH	toluene	15-crown-5	70
13[a]	BuLi	THF	12-crown-4	71
14[a]	**NaH**	**THF**	**15-crown-5**	**81**
15[a]	NaH	1,4-dioxane	15-crown-5	74
16[a]	NaH	CPME	15-crown-5	50
17[a]	NaH	CH_3CN	15-crown-5	55
18[a]	NaH	THF	None	50
19[a]	PEt_3	THF	None	0

Table 1.1: Optimization table for the alkynamides diboration reaction. General procedure: Base (1 equiv), alkynamide (1 equiv), and crown ether (1 equiv) were added in THF (0.29M ,0 ^oC to rt) and stirred for 30 min. 1 (1.0 equiv) was added and the reaction was allowed to stir for 1 h. Yields were determined by ^1H NMR analysis of the crude reaction mixture after aqueous workup. [a] Performed by Dr. Astha Verma.

1.7 Determination of *trans* Geometry

The *trans* geometry of the products was established with an X-ray crystal structure, shown in Fig. 1.24, of the diboration product of *N*-methylphenylalkynamide. The crystal structure not only proves the predicted regio- and stereoselectivity of the reaction, but also reveals that there is coordination of the Bpin moiety by the amide oxygen.

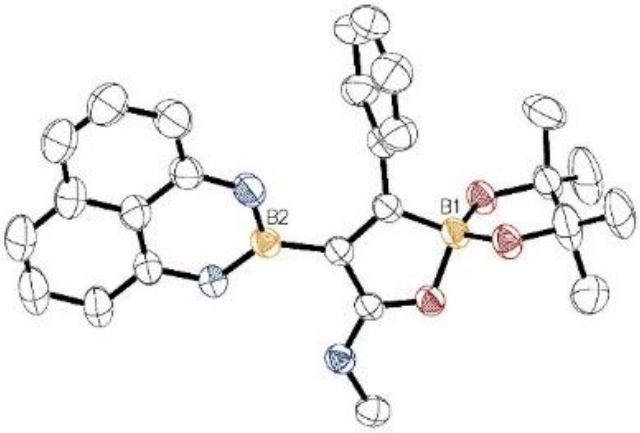


Figure 1.24 Crystal structure of diborated *N*-methylphenylalkynamide. The crystal structure is contained in the Cambridge Crystallographic Data Center: 1523026 and was elucidated by Dr. Carla Slebodnick and grown by Dr. Astha Verma.

This coordination is also shown in the ^{11}B NMR spectra of the products, as increasing sp^3 character of a boron center corresponds to an upfield shift of ^{11}B. Spectra for diborated alkynamides contain a shift corresponding to an sp^2 hybridized boron (~28 ppm) as well as a shift corresponding to a tetracoordinate boron (~14 ppm). A representative spectrum is shown in Fig. 1.25.

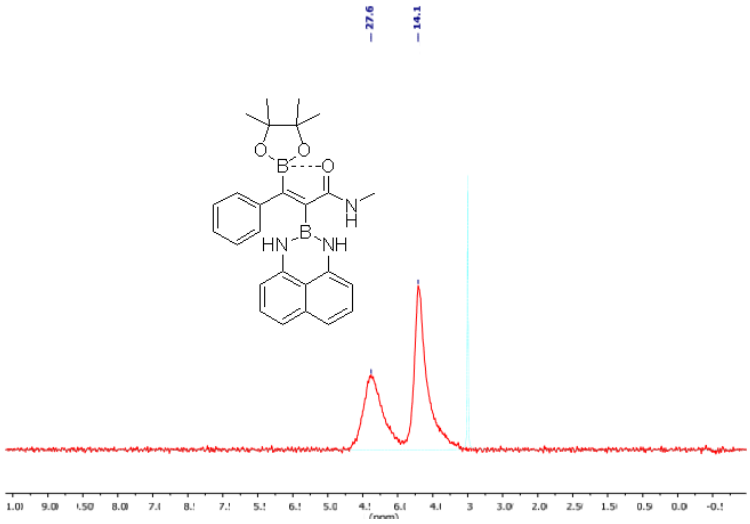


Figure 1.25 ^{11}B NMR spectrum of the diboration product for *N*-methylphenylalkynamide.

1.8 Substrate Synthesis and Substrate Scope

Because none of the alkynamides tested were commercially available, all were synthesized from an alkynoic acid produced *via* reaction of a commercially available alkyne with CO_2 and acidic workup. Only two alkynoic acid starting materials (phenylpropiolic acid and oct-2-ynoic acid) were available commercially.

Synthesis of the alkynamide substrates was easily achieved according to the following synthetic methods. Various *N*-methyl arylalkynamides were produced by conversion of the corresponding alknyoic acid to a pivalic anhydride *in situ* followed by substitution with methylamine solution (Fig. 1.26A).[53] When this method was applied with amines other than

methylamine, however, some pivalic amide byproduct (*e.g.* **1.165**) was formed which was challenging to remove.

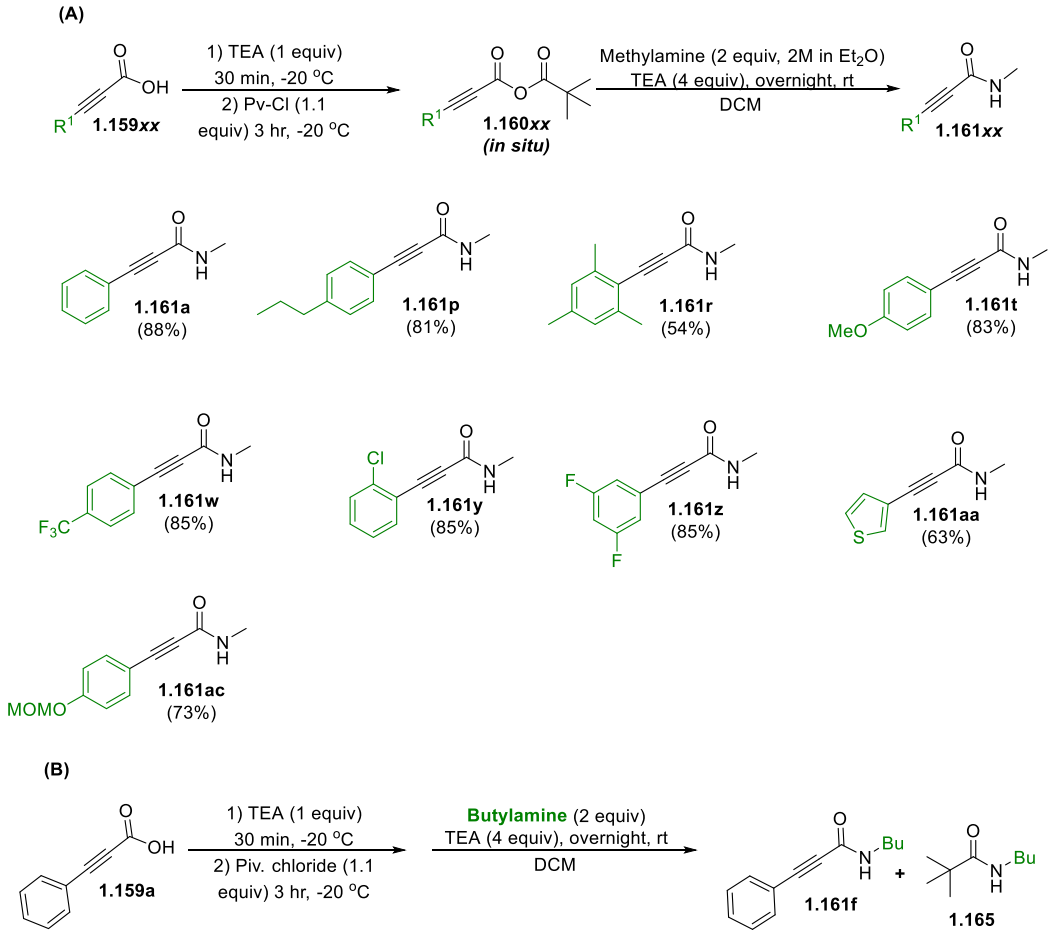


Figure 1.26 Synthesis of alkynamides through pivalic anhydride formation. (A) Overall reaction and substrates synthesized. (B) Side product formation with butylamine.

The remainder of the alkynamides were produced either through carbonyldiimidazole (CDI) mediated coupling of the alkynoic acid and amine (Fig 1.27A)[54] or N,N'-dicyclohexylcarbodiimide (DCC)-mediated coupling (Fig 1.27B).[55] From these two methods, several *N*-substituted alkynamides as well as novel *N*-methyl arylalkynamides were synthesized.

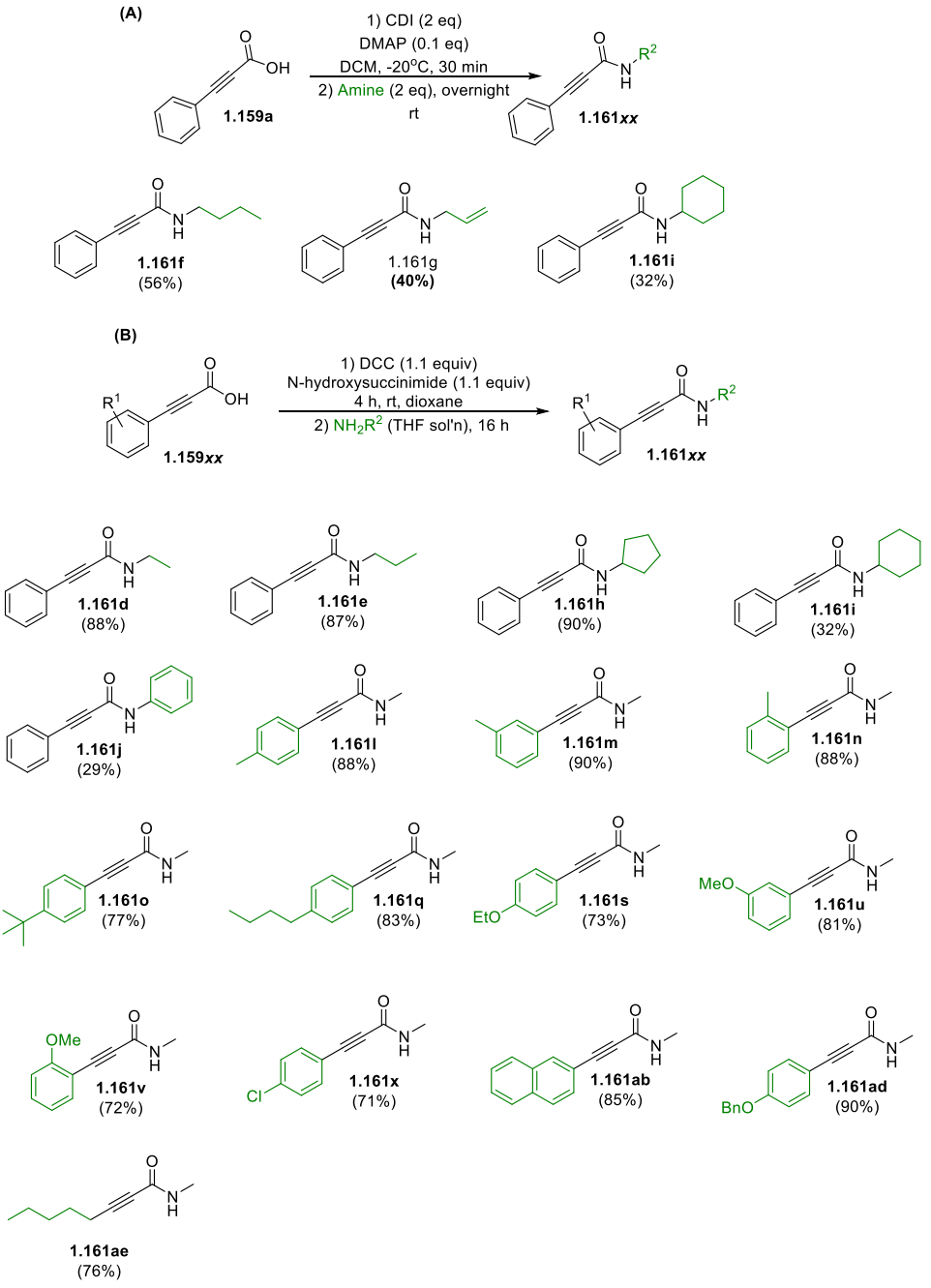


Figure 1.27 Synthesis of alkynamides through use of CDI (A) or DCC (B). All substrates in Fig. 1.27B, excluding **1.161ae**, were synthesized by Dr. Yumin Dai.

With alkynamides substrates in hand, studies aiming to elucidate the scope of the diboration reaction were pursued. Phenylalkynamides bearing various substitutions on the amide

nitrogen were first tested (Fig 1.28) and were compared with optimization product **1.171a**. A primary alkynamide underwent diboration in 57% yield (**1.171b**). A tertiary alkynamide failed to diborate (**1.171c**), consistent with the proposed mechanism requiring initial amide deprotonation. Alkynamides bearing straight-chain alkyl groups (**1.171d-f**) diborated with yields greater or equal to that of **1.171a**.

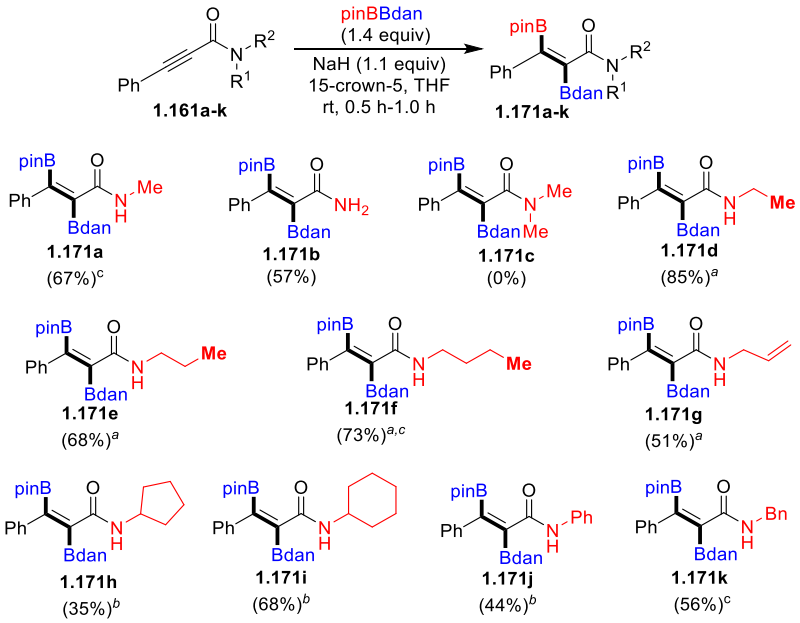


Figure 1.28 Diboration of *N*-substituted alkynamides. [a]2 equiv NaH/crown ether used. [b]4 equiv NaH/crown ether used, heated at 60 °C, 3 h. [c] Performed by Dr. Astha Verma.

Alkynamides bearing a secondary carbon α- to the amide nitrogen were more challenging diboration substrates. Both an *N*-cyclopentyl (**1.171h**) and *N*-cyclohexyl (**1.171i**) substitution required heating in a sealed vial (60°C) and extended reaction times (3 h) and furnished diboration products in 35% and 68% yield, respectively. It is hypothesized that these substrates attack the diboron reagent less efficiently due to steric bulk. An alkynamide bearing an *N*-phenyl substitution (**1.171j**) also required these comparatively harsh conditions, and its ability to act as a nucleophile

was likely attenuated by both electron delocalization into the phenyl ring as well as increased steric encumbrance in the vicinity of the attacking amide oxygen.

An allyl-subsituted alkynamide (**1.171g**) diborated in 51% yield with no evidence to suggest competing borylation of the alkene, demonstrating chemoselectivity for the triple bond. Finally, an *N*-benzyl substituted diboration product (**1.171k**) formed in 56% yield.

N-methyl alkynamides bearing substituted aryl rings were explored next in the context of the diboration reaction (Fig. 1.29). Steric encumbrance was well tolerated, and arylalkynamides bearing alkyl groups were efficiently diborated in good to excellent yields (**1.171l-r**), including those with *ortho* (**1.171n**) and *meta* (**1.171m**) methyl substitutions. Additionally, the sterically challenging mesityl group on the triple bond (**1.171r**) yielded 49% diboration product. The reduced yield may be due to the steric challenge in vinyl anion coordination to Bpin, thus allowing β-protonation to be competitive with the intended diboration process. Electron-rich substrates such as those bearing strongly electron-donating groups (**1.171s-v**), including methoxy groups at the *ortho* (**1.171v**) and *meta* (**1.171u**) position performed with roughly the same yield as the optimization substrate. Electron-deficient arylalkynamides bearing electron withdrawing groups at *para (***1.171w-x*)*, *ortho* (**1.171y**), and *meta* (**1.171z**) positions, were efficiently diborated in good yields. Alkynamides bearing groups such as thiophene and napthalene also underwent diboration in good yield (**1.171aa-ab**).

Because the proposed mechanism entailed formation of a vinyl anion, it was of interest to determine whether this intermediate was accessible without a phenyl ring to stabilize the transient buildup of negative charge on the β-carbon. As such, an alkyl-substituted alkynamide was

subjected to our conditions and afforded diboration product in 67% yield, demonstrating the ability of these substrates to undergo diboration *sans* stabilization afforded by conjugation (**1.171ae**).

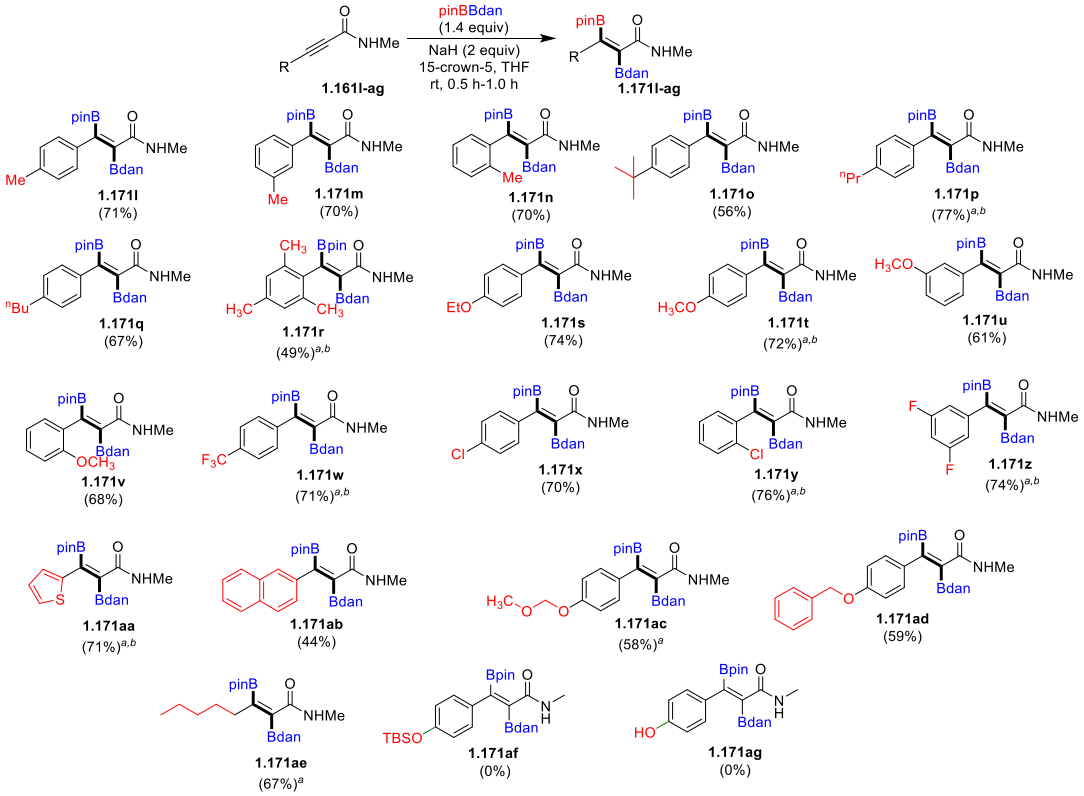


Figure 1.29 Substrate scope of *N*-methyl alkynamides. [a]1.1 equiv NaH/crown ether was used. [b] Performed by Dr. Astha Verma.

Finally, substrates with protecting groups were tested (**1.171ac-ad, 1.171af**). Those bearing benzyloxy (**1.171ad**) and methoxymethylether (**1.171ac**) groups at the *para* position performed in 59% and 58%, respectively. However, a TBS-protected *para* hydroxyl group was immediately deprotected with addition of NaH (**1.171af**). Furthermore, an unprotected hydroxyl group failed to undergo diboration, even with formation of the dianion *in situ*, employing two equivalents of *n*-BuLi (**1.171ag**).

1.9 DFT Studies

A DFT study was performed on the proposed reaction mechanism to check its plausibility and gain greater insight into the reaction mechanism. Calculations were performed by Yinuo Yang from Anhui University under the supervision of Dr. Fu Yao (University of Science and Technology of China) and Dr. Haizhu Yu (Anhui University). The calculations were done at the B3LYP level with 6-31+G(d) basis sets, and an implicit solvation model (THF, SMD model) was used to account for solvent. The results of the calculation are shown in Fig. 1.30.

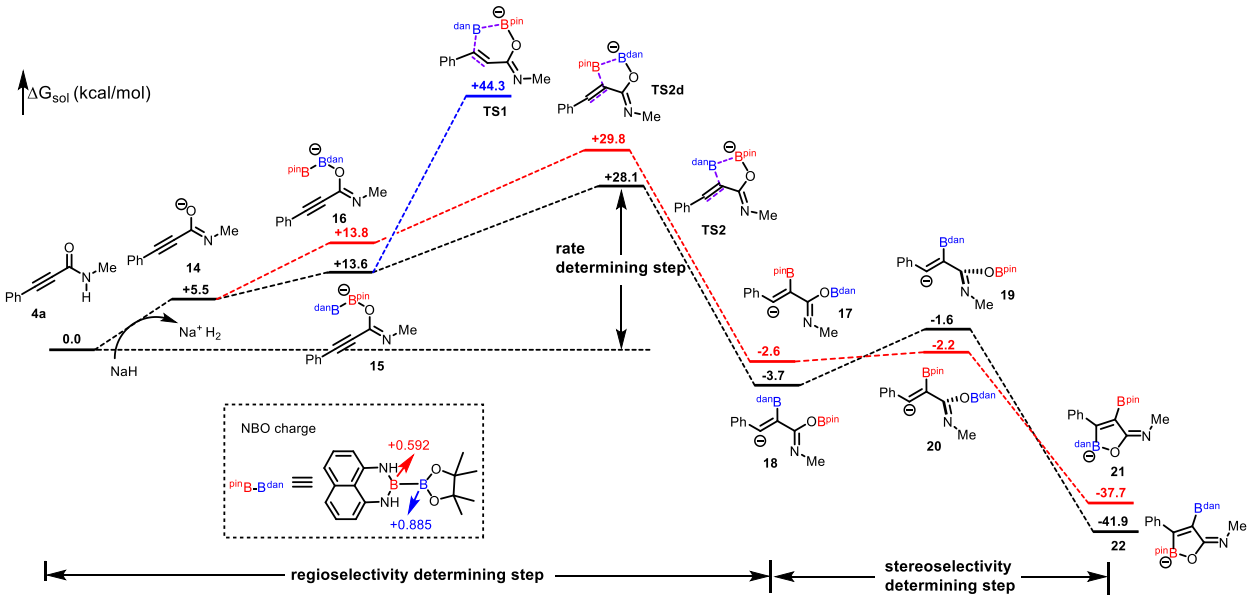


Figure 1.30 DFT calculations for the alkynamide diboration reaction at 298 K.

These calculations corroborate the proposed mechanism. Attack of the deprotonated alkynamide on Bdan (**14-16**) is kinetically less likely than attack on Bpin (**14-15**), and the resulting α-borylation with Bpin (**16-TS2d**) is also more kinetically challenging than the corresponding step in the proposed mechanism (**15-TS2**). Furthemore, α-borylation (by Bdan) through a six-membered transition state is less favored kinetically (**15-TS1**); thus, it can be concluded that the

α-selectivity of Bdan is governed by the kinetics of this step rather than an inability to proceed with the second borylation through a four-membered transition state.

Additionally, the electron density map (Fig. 1.31) of the highest occupied molecular orbital (HOMO) was mapped for an analog of the lowest-energy conformation of the vinylanion intermediate; the structure corresponds to the vinyl anion intermediate formed from diboration of an alkynoic acid with B_2pin_2. This suggests that there is only partial delocalization into the phenyl ring in the alkynamides diboration system, consistent with the perpendicular orientation of the phenyl ring's plane relative to that of the alkene. This may account for the minimal effects of phenyl substituents on reaction outcome.

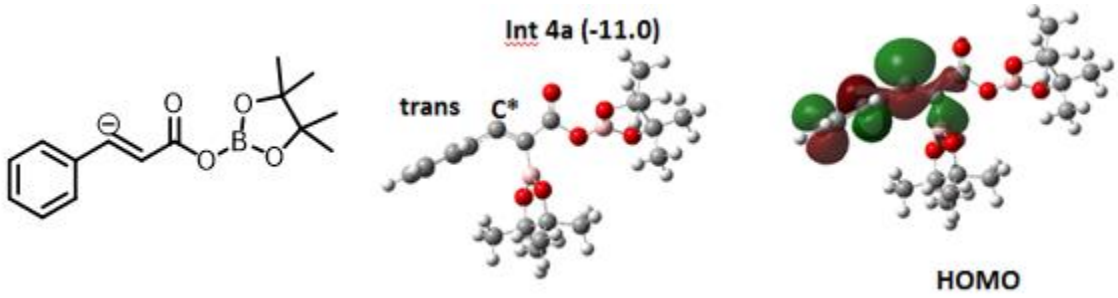


Figure 1.31 Electron density map of the HOMO of an analogous vinyl anion intermediate derived from alkynoic acid borylation with bis(pinacolato)diboron.

1.10 Applications: Chemoselective Cross-coupling

The ability of the diboration products to undergo chemoselective cross-coupling reactions was demonstrated through sequential cross-couplings (Fig 1.32). Reaction conditions were optimized such as to minimize degradation of the diboration products at elevated temperatures. Under microwave irradiation and using $Pd(PPh_3)_4$ as catalyst, 4-iodoanisole was first coupled to the β-position of alkynamide **1.171a** to furnish coupling product **1.175**. The diaminonapthalene moiety was deprotected under acidic conditions and reprotected with pinacol as described

previously in the literature[56] to form intermediate **1.176.** Finally, a coupling with aryl iodide **E** furnished tetrasubstituted alkene **1.177**.

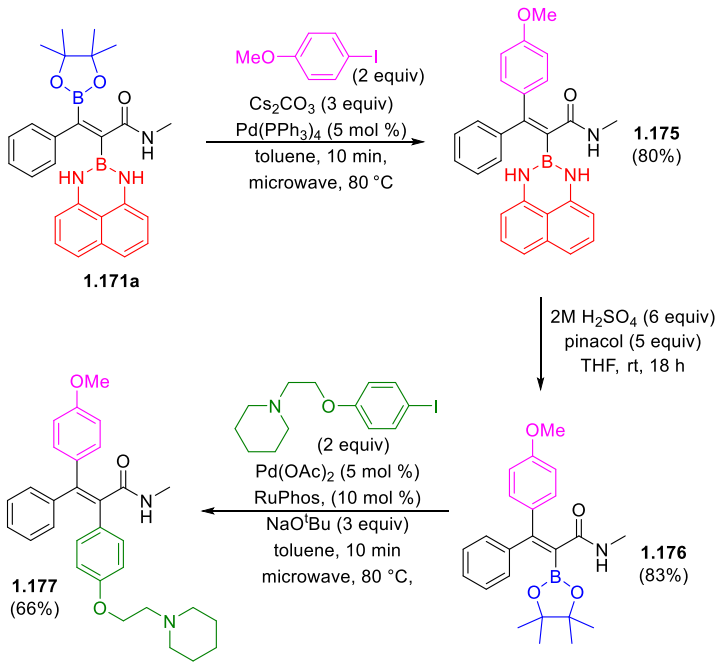


Figure 1.32. Chemoselective cross-coupling of the alkynamide diboration products. All reactions performed by Dr. Yumin Dai.

1.11 Conclusions

With this project, the authors have developed the first transition metal-free diboration of alkynamides.[1] The reaction occurs with complete stereoselectivity affording the *trans* diboration product bearing the Bdan moiety at the α-position. A wide substrate scope was demonstrated with examples of primary and secondary phenylalkynamides, alkylalkynamides, and heteroarylalkynamides. The products demonstrate chemoselectivity in downstream reactions by virtue of the differential protection of the boron moieties, which had not yet been demonstrated in a *trans* diboration or a transition metal-free diboration.

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Chapter Two: Copper(II)-catalyzed Protoboration of Allenes under Aqueous and Atmospheric Conditions

2.1 Contributions

The work in this section was performed solely by the author. Editing of the final manuscript was done by Dr. Webster Santos.

2.2 Abstract

The development of a novel Cu(II)-catalyzed protoboration of unactivated allenes under aqueous conditions is described. The regio- and stereochemistry of the products is ligand-controlled with use of 10 mol % triphenylphosphine additive allowing for the formal hydroboration of the internal alkene to afford product **2.2a** in moderate-to-good yields and selectivities. The reaction (Fig. 2.1) is tolerant of phenylallene derivatives as well as alkyl-substituted allenes.

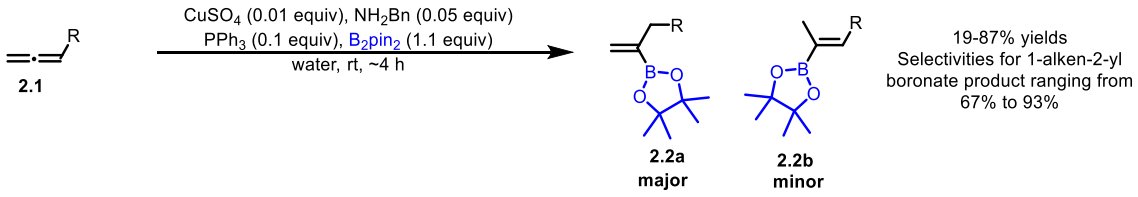


Figure 2.1 General scheme for the copper(II)-catalyzed protoboration.

2.3 Hydroboration Reactions

As discussed in Chapter 1, synthetically valuable organoboron products can be produced through both hydroboration and protoboration, both of which can be broadly defined as *formal hydroboration* reactions. *Bona fide* hydroborations utilize hydridic species, while protoboration reactions involve proton transfer by an organometallic intermediate.

Classical hydroboration reactions were first described by Brown *et al.* and involved addition of an organoborane reagent to an alkene or alkyne. Examples of common organoboranes are shown in Fig. 2.2A. As the reaction proceeds in a single concerted step with a four-membered transition state (Fig. 2.2B), hydroboration occurs *via syn* addition. Furthermore, boron is to varying degrees installed at the less substituted carbon. This regioselectivity can be rationalized in a few ways. Firstly, the B-H bond of the reactive intermediate is polarized such that boron bears a partial positive charge, and the buildup of partial negative charge required for nucleophilic attack on boron is best supported at the least substituted position. Consequently, the buildup of partial positive charge required for hydride attack is best supported at the more substituted position. Secondly, the comparative bulk of the boron center is better suited for installation at a sterically less encumbered position. As would be expected on the basis of these rationalizations, the regioselectivity of the hydroboration reaction increases with increasing steric bulk of the organoborane.

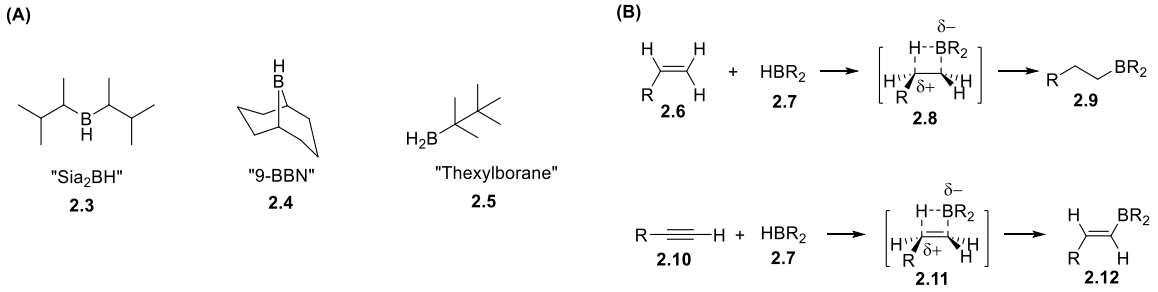


Figure 2.2 Common organoboranes (A) and general hydroboration scheme (B).

Some limitations of Brown-type hydroboration are worth consideration. Firstly, the reaction is limited to anti-Markovnikov addition, and requires a large steric/electronic difference between the two possible positions for C-B bond formation. Secondly, installation of boronic ester moieties by hydroboration requires comparatively harsh conditions.[1-3] This limitation is severe since boronic

esters are often reagents of choice in Suzuki-Miyaura cross-coupling reactions due to their stability and resistance to undesired homocoupling, oxidation, and protodeboronation.[4] Finally, certain classes of substrates do not borylate under classical hydroboration conditions; for instance, α,β-unsaturated ketones undergo O-borylation through a six-membered transition state and hydrolyze readily, resulting in a formal reduction[5] (Fig 2.3).

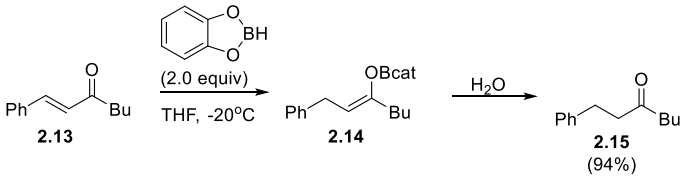


Figure 2.3 1,4-Conjugate reduction of α,β-unsaturated ester under hydroboration conditions.

Protoboration reactions have been developed for the formal hydroboration of unactivated alkynes/alkenes *via* transition metal catalysis (both anti-Markovnikov and Markovnikov addition). However, the largest subset of protoboration reactions involve β-borylation of alkenes with a highly electron-withdrawing group attached to the C-C double bond (*e.g.* α,β-unsaturated ketones). One of the first examples was a Pt-catalyzed β-boration of α,β-unsaturated ketones reported by Marder *et al.*[6] in 1997, and allowed for quantitative installation of B_2pin_2 or B_2cat_2 after 12 hours with heating, which after hydrolytic workup furnished the desired product (Fig. 2.4).

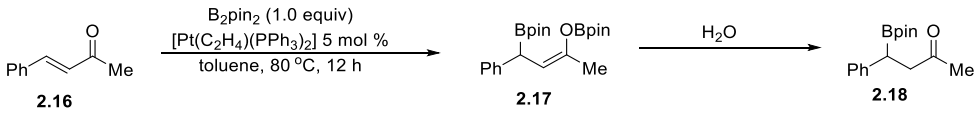


Figure 2.4 Pt-catalyzed β-borylation of α,β-unsaturated ketones.

In 2000, the first copper(I)-mediated β-borylation reactions of α,β-unsaturated ketones were independently reported by Hosomi[7] and Miyaura.[8] Hosomi *et al.* reported a Cu(I)-catalyzed

process, while Miyaura *et al*. reported a process employing stoichiometric amounts of CuCl. Furthermore, in 2006 Yun *et al*.[9] discovered that alcohol additives could significantly increase the rate of reaction of the β-borylation of α,β-unsaturated esters, nitriles, and phosphonates.

The general mechanistic scheme for a Cu(I)-catalyzed β-borylation is shown in Fig. 2.5. Transmetallation between a ligand-bound CuCl and KO*t*Bu furnishes a *tert*-butoxide-ligated copper species, which then is reactive enough to undergo transmetallation with bis(pinacolato)diboron to generate a boryl-copper intermediate (**2.21**). Alkene insertion occurs to generate organocopper species (**2.24**); the insertion is selective such that the partially negative copper-bound carbon is adjacent to the highly electron withdrawing group. Compound **2.24** then isomerizes to **2.25**, driven by the high bond strength of the Cu-O bond. In the presence of a proton source, protonation occurs directly to make **2.28** and product **2.27**. Another transmetallation of **2.28** will produce active catalyst **2.21** to complete the catalytic cycle. If a proton source is *not* added to the reaction mixture, then intermediate **2.25** will persist. This explains Miyaura's use of stoichiometric amounts of copper when borylating esters (*vide supra*). The exception is in the case of a copper enolate derived from aldehydes or ketones.[10-11] In those cases, metathesis of **2.25** with a molecule of B_2pin_2 will furnish active catalyst **2.21** and intermediate **2.26**, which upon hydrolysis furnishes intended product **2.27.**

Recently, copper(II)-catalyzed protoboration has been shown to be an alternative to some copper(I)-catalyzed boration protocols. These methods are facile and can be conducted open-to-air since copper is in its highest stable oxidation state. Furthermore, Cu(II)-catalysts are typically water soluble, allowing for more environmentally friendly borylation conditions compared to those run in organic solvents.

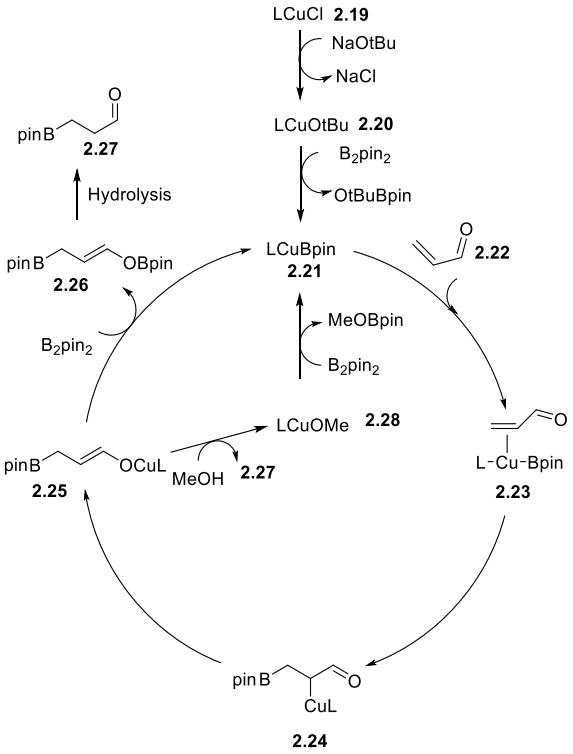


Figure 2.5 Copper-catalyzed β-borylation of an α,β-unsaturated aldehyde.

The first example of Cu(II)-catalyzed borylation in aqueous media was reported by Thorpe *et al.*[12] Activation of water by a 4-picoline additive allowed for hydroxyl coordination to boron in bis(pinacolato)diboron (Fig. 2.6A, **2.28**), which then could undergo transmetallation to Cu(II) to form boron-bound copper intermediate **2.30**. This species then reacts in a mechanistically similar manner to the copper(I)-boron complex described above. The ability of intermediate **2.30** to add to alkenes was demonstrated on α,β-unsaturated ketones (Fig. 2.6B).

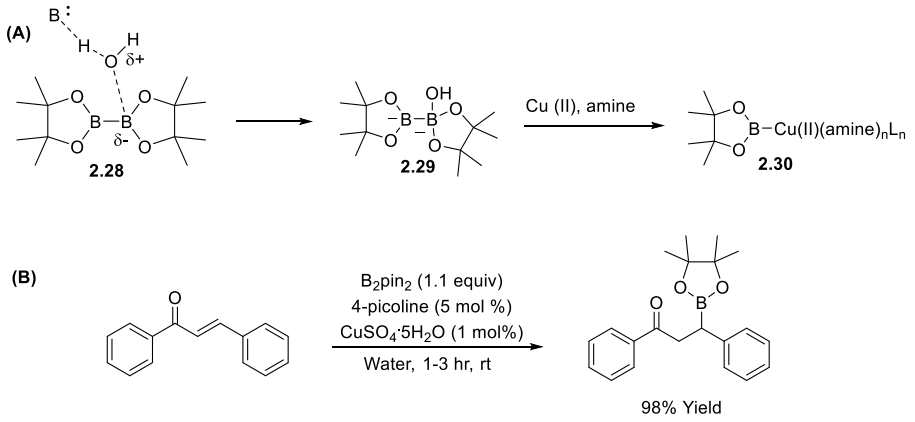


Figure 2.6 (A) Amine-assisted activation of bis(pinacolato)diboron by water to generate a Cu(II)-boron complex. (B) Example of Cu(II)-catalyzed protoboration of α,β-unsaturated ketones.

This basic method has been applied to a number of polarized double and triple bonds, including alkynoic esters and alkynamides,[13] and imines.[14-15] It has also been extended to asymmetric borylations.[16] However, the protocol has not been utilized for relatively unactivated C-C double or triple bonds; pursuing this variant of the reaction is the main focus of this project (*vide infra*).

2.4 Allene Hydroboration and Protoboration

Among the alkenes that may undergo formal hydroboration, allenes are a particularly challenging and versatile borylation substrate by virtue of the numerous isomers that can form (Fig. 2.7). There are six possible isomers (**2.32a-f**) for a monosubstituted allene.

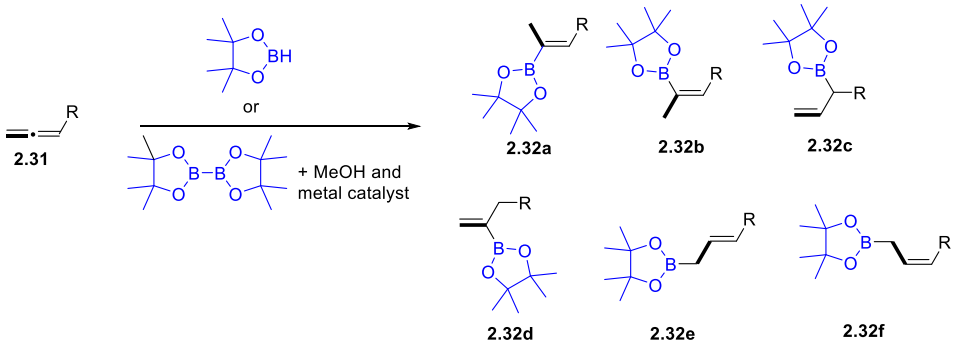


Figure 2.7 Possible isomers produced *via* formal hydroboration of a monosubstituted allene.

Classical hydroboration reactions have been applied to monosubstituted allenes.[1, 17-18] Brown utilized 9-BBN in a hydroboration to phenylallene; oxidation of the products furnished primarily allylic alcohols as shown in Fig. 2.8A. Thus, the selectivity of the borylation is likely dictated by the same factors as in a typical alkene, and boron is installed at the least sterically hindered carbon. The same selectivity was demonstrated with alcohol-ligated boranes; however, as in isolated alkenes, harsh conditions and long reaction times were required for the hydroboration to occur. In most cases the overall yields and selectivities were far inferior to those reported with 9-BBN hydroboration (Fig. 2.8B).

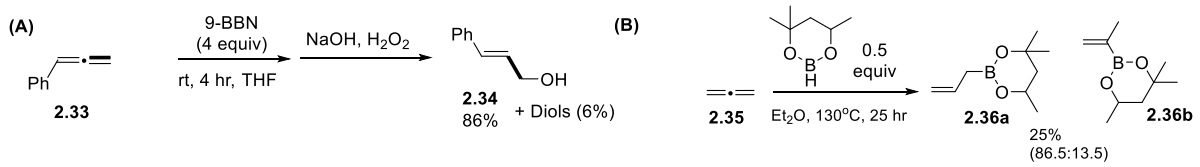


Figure 2.8 Classical hydroboration conditions applied to allenes.

Transition metal-catalyzed hydroboration and protoboration reactions of allenes have also been described, which produce complementary products to classical hydroboration. The selectivities of these reactions are highly dependent on ligand choice in the catalytic system. The seminal report of transition metal-catalyzed hydroboration entailed use of Pt(0) catalysts, pinacolborane, and either a 1,1-disubstituted allene or a monosubstituted allene (Fig. 2.9).[19] Interestingly, the selectivities for either 1-alken-2-yl boronate product **2.38b** or (*Z*)-2-alken-2-yl boronate product **2.38c** could be attained through use of tris-*tert*butylphosphine and tris(trimethoxyphenyl)phosphine, respectively.

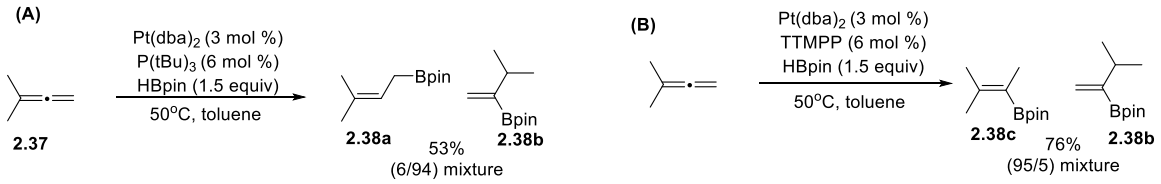


Figure 2.9 Pt-catalyzed hydroboration of 3-methylbuta-1,2-diene using (A) bulky $P(tBu)_3$ or (B) compact TTMPP.

A copper-catalyzed hydroboration was reported by Semba that used HBpin to achieve *E*-allylboron products.[20] The conditions were shown to be applicable to alkyl-substituted allenes, phenylallene derivatives, and a single 1,3-disubstituted allene producing yields >52% and selectivities for allylboron products in excess of 89%. The mechanism is shown in Fig 2.10. Coordination of base to HBpin allows for transmetallation to generate a copper hydridic species **2.41**. Insertion of allene (**2.42**) into the Cu-H bond occurs to position copper on the least substituted and least hindered position to generate a *Z* allylcopper species (**2.43**), which isomerizes to the *E* isomer (**2.44**). Sigma bond metathesis with another molecule of HBpin regenerates the active CuH catalyst **2.41** and producse borylated product **2.46**.

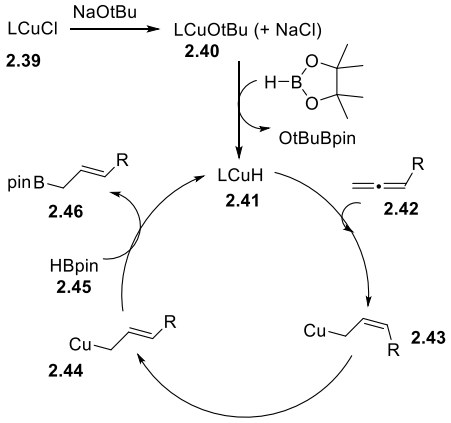


Figure 2.10 Catalytic cycle for Semba's allene hydroboration.

The state-of-the-art methods for monosubstituted allene *protoboration* involve copper(I) catalysis, diboron reagents, and a proton source such as methanol (Fig. 2.11). As in the platinum-

catalyzed hydroboration, selectivity for either the internal or external double bond was determined by ligand choice. Ma and coworkers reported phosphine-controlled selectivity under copper(I)-catalyzed conditions, with bulky bidentate BIPHEP and compact, highly electron-donating [$P(C_6H_4OMe\text{-}p)_3$ furnishing **2.48a** and **2.48b,** respectively.[21] Recently, Hoveyda and coworkers employed the same strategy but with N-heterocyclic carbenes formed from *in situ* deprotonation of the corresponding imidazolium salt precursors.[22] A compact dimethylimidazolium-derived NHC (**2.53**) or a bulky 1,3-bis(2,6-diisopropylphenyl)imidazolium-derived NHC (**2.52**, "IPr") furnished **2.50b** and **2.50a,** respectively. Both sets of conditions could be successfully applied to either phenylallene derivatives or alkyl-substituted allenes with selectivities typically exceeding 93% for the desired isomer.

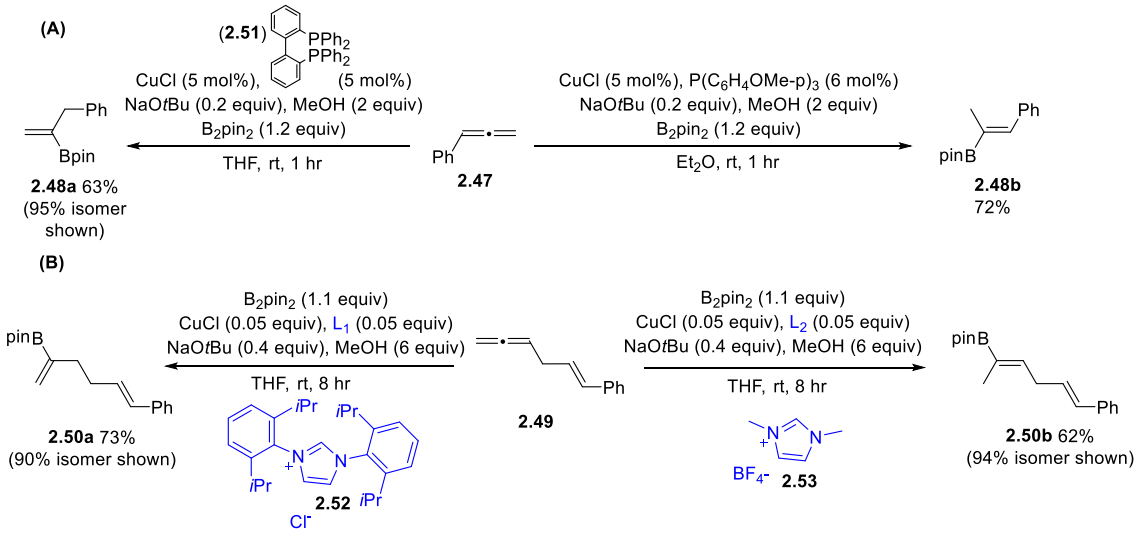


Figure 2.11 Copper(I)-catalyzed protoboration of allenes, using (A) phosphine ligands or (B) N-heterocyclic carbine ligands.

The mechanistic basis for this ligand control was investigated by Hoveyda and corroborated by a DFT study (Fig. 2.12). Formation of boron-copper species **2.56** occurs through a transmetallation between *in situ* generated Cu*O*t*B*u and B_2pin_2. The allene is then capable of inserting into the Cu-B bond to furnish one of two possible allylcopper species (**2.58a** or **2.58b**).

Intermediate **2.58a** is favored both thermodynamically and kinetically due to stabilization of the partial negative charge inherent in a Cu-C bond at a terminal carbon as well as decreased steric interactions between Cu and the R group. Intermediates **2.58a** and **2.58b** can interconvert through a four-membered, copper-containing transition state. Isomerization is minimized when a bulky ligand is attached to copper. Thus, when a large ligand is used, intermediate **2.58a** forms, and gamma protonation (*via* chair-like transition state **2.59a**) produces product **2.60a**. When a small ligand is used, isomerization to **2.58b** occurs (with equilibrium still favoring **2.58a**). However, **2.58b** is significantly more reactive, thus favoring formation of **2.60b**. This is an example of the Curtin-Hammett principle. (*Z*)-selectivity is observed because chair **2.59b** is the lowest energy transition state during the gamma protonation; the "R" and "Bpin" groups are both in the axial position to minimize steric strain, and there are no diaxial interactions that destabilize formation of this transition state.

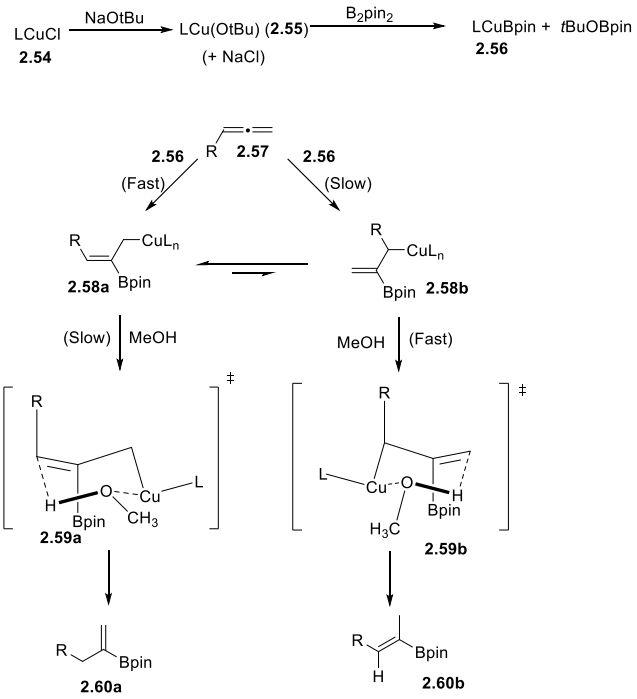


Figure 2.12 Mechanism for Cu(I)-catalyzed protoboration of allenes.

2.5 Project Motivation and Optimization of Reaction Conditions

It is of interest to extend the methods for allene borylation to include Cu(II) catalysis in water. Such a method would entail use of more environmentally friendly conditions, and it would be operationally more simple than the current, highly air-sensitive Cu(I)-catalyzed protocols. Such a project constitutes a significant challenge in terms of selectivity since the solvent itself has the ability to disrupt the equilibrium of product-determining intermediates (*vide supra*).

In the first report of Cu(II)-catalyzed protoboration of α,β-unsaturated ketones by Thorpe *et al*., a wide variety of bases were tested and found to effect the β-borylation in excellent yields. Among the many bases tested, 4-picoline was the most effective. Thus, in the allene protoboration reaction, base choice was the first parameter varied and experiments were begun using 4-picoline.

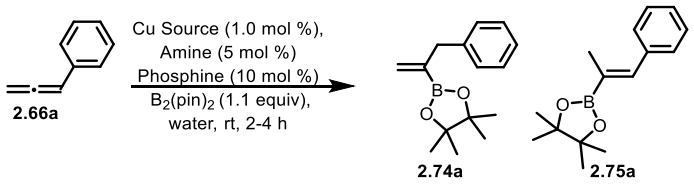
Phenylallene (**2.66a**) was selected as the optimization substrate. The conditions initially selected involved addition of 1.5 equiv bis(pinacolato)diboron, 5 mol % 4-picoline, and 1 mol % copper(II) sulfate (entry 1, Table 2.1). Unfortunately, while quite effective for the borylation of α,β-unsaturated ketones, these conditions were found to be unsuitable for the borylation of phenylallene. A 10% yield of combined isomers **2.74a** and **2.75a** was observed with selectivity favoring the latter (66:34). Screening several other bases including proton sponge, NaOAc, DMAP, and benzylamine (entries 2-5) did little to improve the yield or selectivity; the highest yield was afforded by benzylamine (entry 5, 24% with 65% **2.75a**).

Gratifyingly, the addition of 10 mol% tricyclohexylphosphine dramatically increased yield and selectivity (entry 6, 65% combined isomers, 77% selectivity for **2.75a**). Inspired by the copper-catalyzed, surfactant-mediated silylation reported by Lipshutz et al.[23], we used an aqueous solution of 1% TPS-750-M as solvent; however, yields were reduced to 49% combined yields (entry 7). To

ensure the reaction was not phosphine-catalyzed, a control reaction *sans* copper was run, which produced no product (entry 8). Finally, a reaction using PCy_3 without benzylamine was run (entry 9). Though the performance of this reaction was comparable to that in which benzylamine was present, it displayed a relatively long induction time. Thus, benzylamine was retained in the subsequent optimization experiments.

Gas chromatography experiments determined that an over-borylation product was present in the product mixture. To prevent significant formation of this byproduct, the number of equivalents of bis(pinacolato)diboron was lowered to 1.1 equiv, which reduced its formation significantly. Next, several ligands were tested to determine if the yield or selectivity could be improved. Surprisingly, the bulky bidentate DPEphos ligand produced the poorest selectivity with approximately a 50/50 mixture of isomers (entry 10). In contrast, SPhos (entry 11) and PPh_3 (entry 12) both selected for **2.74a** (~80%) and their use resulted in relatively high yields (~60%). Tricyclohexylphosphine (with 1.1 equiv B_2pin_2) was finally tried and furnished the opposite selectivity (entry 13, 69% **2.75a,** combined 63% yield).

Several attempts to improve the selectivity and yield through use of a cosolvent were performed. It was hypothesized that addition of toluene would 1) increase solubility of phenylallene and bis(pinacolato)diboron (both of which are sparingly soluble in water) and 2) reduce the amount of water in the vicinity of the insertion intermediate, thus allowing for isomerization of intermediates and improvement of the selectivity. Unfortunately, neither conditions with high (80%) or low (20%) toluene content improved the reaction outcome to favor **2.74a** (*e.g.* use of PPh_3) or **2.75a** (*e.g.* use of PCy_3) (entries 18-21).



Entry	Base	Cu Source	Ligand	% Yield[b] (2.74/2.75)
1[a]	4-picoline	$CuSO_4$	None	10 (34:66)
2[a]	proton sponge	$CuSO_4$	None	13 (40:60)
3[a]	DMAP	$CuSO_4$	None	9 (30:70)
4[a]	NaOAc	$CuSO_4$	None	16 (38:62)
5[a]	NH_2Bn	$CuSO_4$	None	24 (35:65)
6[a]	NH_2Bn	$CuSO_4$	PCy_3	65 (23:77)
7[a,c]	NH_2Bn	$CuSO_4$	PCy_3	49 (21:79)
8[a]	NH_2Bn	None	PCy_3	0
9[a]	None	$CuSO_4$	PCy_3	68 (33:67)
10	NH_2Bn	$CuSO_4$	DPEPhos	52 (46:54)
11	NH_2Bn	$CuSO_4$	Sphos	63 (81:19)
12	**NH_2Bn**	**$CuSO_4$**	**PPh_3**	**61 (84:16)**
13	NH_2Bn	$CuSO_4$	PCy_3	63 (31:69)
14	NH_2Bn	$Cu(acac)_2$	PPh_3	60 (85:15)
15	NH_2Bn	$Cu(BF_4)_2$	PPh_3	53 (77:23)
16[f]	NH_2Bn	$C_{10}H_6CuN_4O_4$	PPh_3	32 (81:19)
17	NH_2Bn	$Cu(OH)_2$	PPh_3	19 (76:24)
18[d]	NH_2Bn	$CuSO_4$	PPh_3	50 (74:26)
19[d]	NH_2Bn	$CuSO_4$	PCy_3	57 (27:73)
20[e]	NH_2Bn	$CuSO_4$	PCy_3	52 (30:70)
21[e]	NH_2Bn	$CuSO_4$	PPh_3	36 (64:36)

Table 2.1 Optimization experiments for the Cu(II)-catalyzed allene protoboration reaction. [a]1.5 equiv B_2pin_2 used [b] Yields determined by NMR with TMS internal standard. [c]1% TPS-750-M surfactant [d]20 % toluene used as cosolvent [e]80 % toluene used as cosolvent. [f] Cu(II) 2-pyrazinecarboxylate.

Our focus was then concentrated to the formation of **2.74a**. It was hypothesized that the use of a protic solvent (*i.e.* water) would severely reduce isomerization between the two insertion

intermediates, as a super-stoichiometric amount of proton source would cause the protonation step to rapidly outcompete the isomerization step. Thus, selection for 2-alken-2-yl boronate product would be extremely challenging since formation of the appropriate intermediate *directly* from Cu-B addition to the allene is both thermodynamically and kinetically unfavorable (relative to the intermediate which forms 1-alken-2-yl boronate product, *vide infra*).

Lastly, several copper(II) catalysts were screened (entries 14-17). While copper(II) pyrazinecarboxylate and copper(II) hydroxide produced low yields, Cu(II) acetylacetoneate and $Cu(BF_4)$ performed about as well as $CuSO_4$. Thus, the overall optimized conditions were determined to be those shown in entry 12.

2.6 Synthesis of Allene Substrates

Among the allenes tested, only cyclohexylallene (**2.66m)** was commercially available. Therefore, a set of allenes were synthesized following well-established methods. Phenylallene derivatives were synthesized through a Doering-Laflamme allene synthesis.[24] Commercially available styrenes were treated with bromoform, aqueous NaOH (25 M), and a phase transfer catalyst (triethylbenzylammonium chloride) to give dibromocyclopropane products **2.65a-l** through α-elimination of bromoform and addition to the alkene portion of styrene. Products were furnished in moderate to excellent yields, and the dibromocyclopropanes in Fig 2.13 comprise those made for this project.

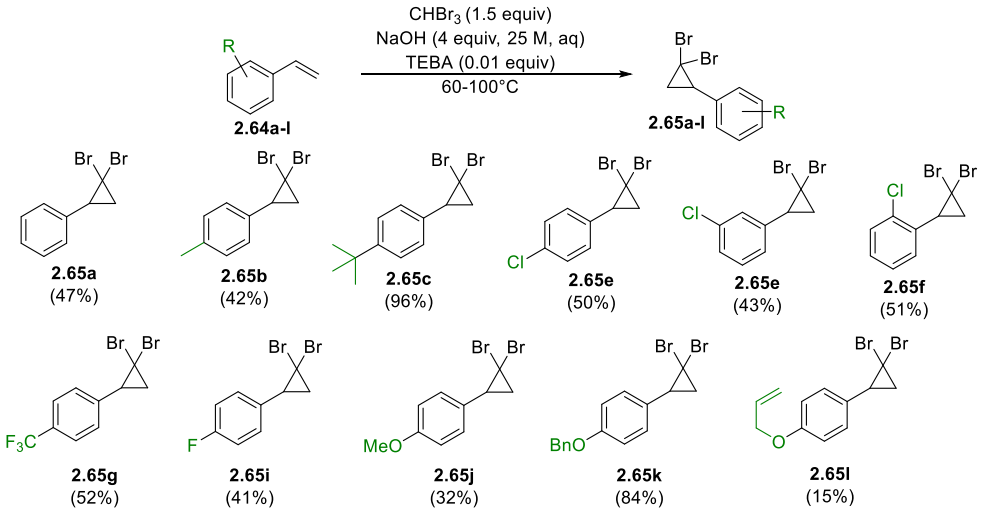


Figure 2.13 Synthesis of dibromocyclopropane precursors **2.65a-l**.

Next, dibromocyclopropanes **2.65a-l** were treated with ethylmagnesium bromide to effect conversion (through metal halogen exchange) to a carbenoid intermediate, which readily collapses to a monosubstituted allene. This reaction afforded allenes **2.66a-l** in moderate to good yields. Allenes produced *via* this method are shown in Fig 2.14.

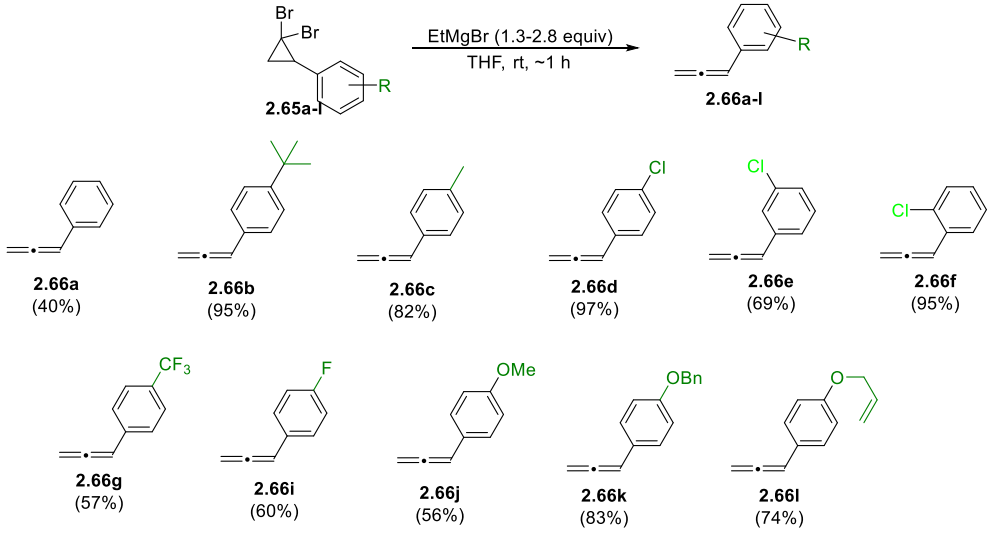


Figure 2.14 Phenylallene derivatives synthesized.

For styrenes **2.64k** and **2.64l**, the corresponding styrene was prepared through saponification of **2.67** followed by Williamson ether synthesis of **2.68** with either allyl bromide or benzyl bromide (Fig 2.15).

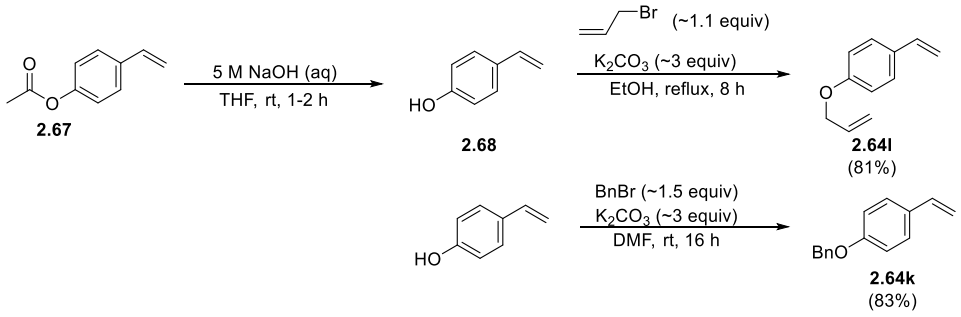


Figure 2.15 Styrenes synthesized for use in the Doering Laflamme synthesis.

Alkyl-substituted allenes are typically challenging to synthesize through Doering-Laflamme synthesis as their dibromocyclopropane precursors do not efficiently convert to allenes. Thus, an alternative procedure developed by Ma and coworkers[25] was used to produce alkyl-substituted allenes of interest (Fig. 2.16A). The procedure entails a one-pot, copper catalyzed Mannich reaction[26] followed by a copper-mediated hydride transfer from dicyclohexylamine to furnish the allene (Fig 2.16B). In this manner, allenes **2.66n-r** were produced in 15-94% yields.

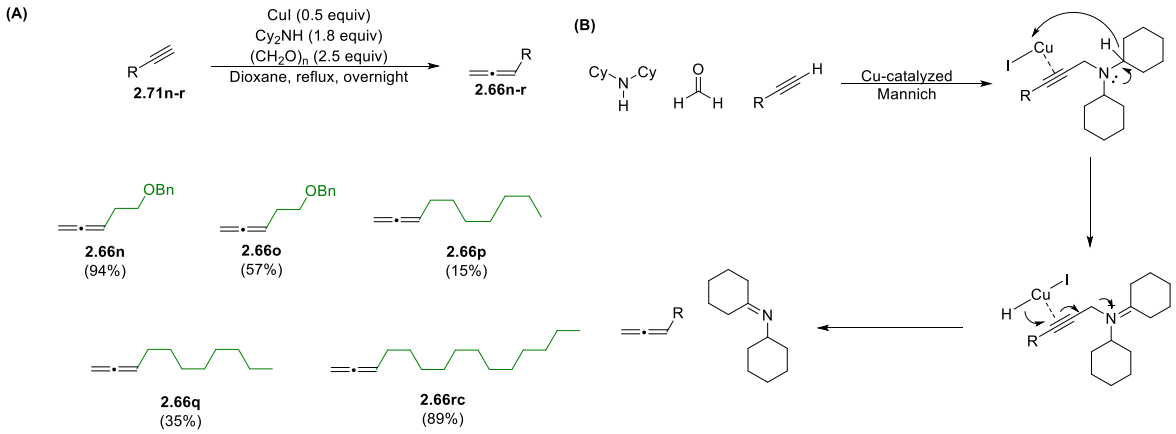


Figure 2.16 (A)Synthesis of allenes **2.66n-r**. (B) Mechanism for the allene synthesis.

2.7 Substrate Scope of the Allene Protoboration

With optimized conditions and a variety of allenes in hand, exploration of the substrate scope was performed (Fig. 2.17). Phenylallene derivatives bearing a *p*-methyl or *p*-*t*Bu resulted in ~9:1 selectivity in 67% (**2.74b**) and 47% yields (**2.74c**), respectively. When derivatives bore electron-withdrawing groups, such as *ortho*, *meta*, or *para* chloro substituents, borylation proceeded in ~9:1 selectivity with high yields (**2.74d-f**). When a *p*-F substituted phenylallene derivative was borylated, both isolated yield and selectivity were reduced somewhat (**2.74i**). A trifluoromethyl-substituted phenylallene derivative showed excellent selectivity (**2.74g**) and poor yield, despite complete consumption of starting allene.

Interestingly, phenylallene derivatives bearing electron-donating groups showed a marked reduction in selectivity for terminal reduction product. A derivative with a *p*-OMe group borylated in 46% yield (**2.74j**) but showed only 67% selectivity for intended product. Both the allyloxy (**2.74l**) and benzyloxy-protected (**2.74k**) derivatives demonstrated protecting group stability under the reaction conditions, but selectivities for internal hydroboration product were 75% and 67% respectively. In the case of the benzyloxy-protected derivative (**2.74k**), the solid starting material was unable to undergo the reaction under standard conditions. This was likely due to inability to partially solubilize in water. This problem was solved through use of 1% surfactant, affording the desired product in 37% yield.

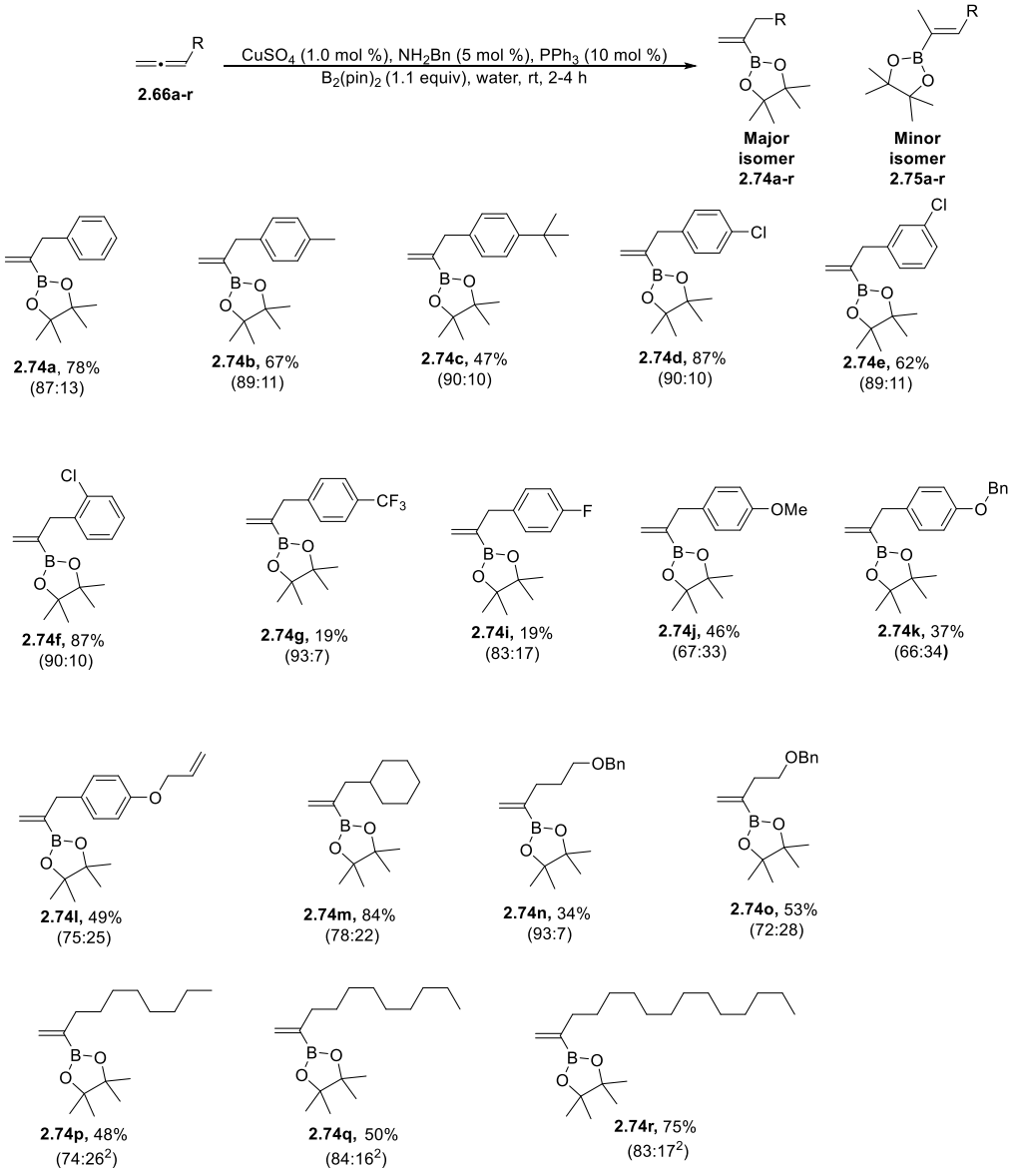


Figure 2.17 Substrate scope of the copper (II)-catalyzed protoboration. [1]1% TPS-750-M used. [2] Toluene/water (20:80) mixture used in the reaction.

To further investigate the scope of the reaction, alkyl substituted allenes were investigated. We were interested in determining whether stabilization by an aryl group of partial negative charge was necessary for the reaction to proceed. Fortunately, several alkyl-substituted allenes were borylated in moderate yields and regioselectivites (**2.74m-r**). Some straight-chain allenes (nonyne-derived, decyne-derived, and tetradecyne-derived allenes) were unable to borylate under standard

conditions. This was most likely due to inability of the highly nonpolar substrates to dissolve in water. Thus, 20% toluene was added as cosolvent, which furnished the products in reasonable to good yields and selectivities (**2.74p-r**).

2.8 Proposed Mechanism

The proposed mechanism for the selective internal protoboration of allenes is shown in Fig 2.18. In contrast to previously-reported systems, the proton source is most likely the *solvent itself* rather than an additive, as solvent molecules vastly outnumber other protic species in the reaction mixture. In contrast, previous Cu(I)-catalyzed allene protoborations employ 2-6 equivalents of methanol as the proton source.[21-22] As such, we hypothesize that there is reduced time for equilibration between the two insertion intermediates due to a rapid and competitive γ-protonation. Rather than selectivity being due to the reactivity of the **2.81a** or **2.81b**, the product distribution would then reflect the relative rates of insertion product formation.

In the mechanism, amine-assisted activation of water is proposed to allow for hydroxyl coordination to a molecule of bis(pinacolato)diboron to form **2.76**. This intermediate then undergoes transmetallation with copper(II) to form **2.78**, which coordinates to one of the unsaturation sites present in the allene reactant through an η-2 bond; either **2.80a** or **2.80b** is formed. The former forms preferentially due to minimization of steric interactions and the increased stabilization of the partial negative charge at the terminal carbon. Insertion then forms intermediate **2.81a** or **2.81b**. In contrast to the previously reported allene protoborations, isomerization between **2.81a** and **2.81b** is likely outcompeted by γ-protonation by the solvent, water. Thus, **2.81a** and **2.81b** convert to **2.82a** or **2.82b** respectively with regeneration of the copper catalyst **2.78**. Because the reaction yields increased significantly in the presence of

phosphine ligands (entries 6-21 vs. entries 1-5), we hypothesize that a phosphine-coordinated Cu(II)-Bpin species is most suitable for addition to an unpolarized C-C bond.

As noted above, phenylallene derivatives bearing electron-donating groups exhibited markedly less selectivity for internal hydroboration product **2.82a**. It is hypothesized that in these cases formation of **2.80b** is competitive with formation of **2.80a** due to the relatively electron rich allylic double bond; immediate and irreversible conversion of **2.80b** to **2.81b** results in increased formation of (*Z*)-2-alken-2-yl boronate product **2.82b**.

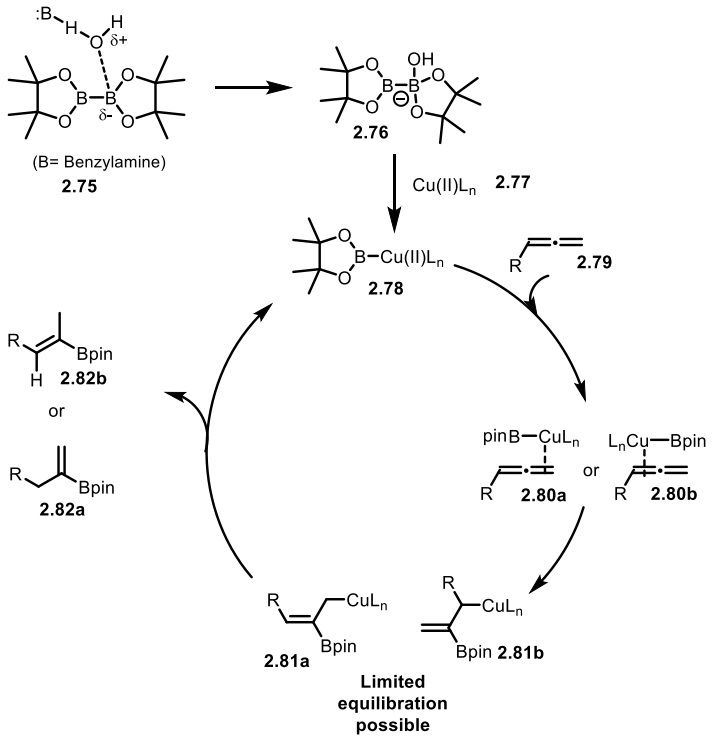


Figure 2.18 Proposed mechanism for the Cu(II)-catalyzed protoboration reaction.

2.9 Conclusions

This project constitutes the first Cu(II)-catalyzed borylation of allenes, and the first borylation of allenes using water as solvent. The selectivity is ligand-controlled but the effect of ligand on

reaction selectivity is poorly understood. The bulky DPEPhos ligand produced ~50/50 selectivity, and the relatively compact triphenylphosphine ligand produced among the highest selectivities for 1-alken-2-yl boronate product. The method provides a facile route to 1-alken-2-yl boronate products from allenes *via* selective protoboration of the internal double bond.

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Chapter Three: Experimental

3.1 General Methods

With the exception of the copper(II)-catalyzed allene borylation reactions, all reactions were performed under a nitrogen or argon atmosphere. Tetrahydrofuran, dichloromethane, dimethylformamide, and acetonitrile were obtained from an Innovative Technology Pure Solv-MD system. For the diboration experiments in Chapter 1, tetrahydrofuran was degassed by freeze-pump-thawing three times prior to use in the reaction. To ensure trace amounts of undesired transition metals were not present in the solvent for the allene borylation (Chapter 2) experiments, a Barnstead Easypure Uv Compact Ultrapure Water System was used to obtain water for all borylation experiments and in preparation of the $CuSO_4$ solutions.

Most commercially available reagents were used without further purification. However, crown ethers used in the optimization and substrate scope sections of Chapter 1 were distilled prior to use in the diboration reactions. Bis(pinacolato)diboron was purchased from Boron Molecular or donated by AllyChem. The unsymmetrical diboron reagent pinBBdan was synthesized as previously described in the literature.[1]

Reactions were monitored through TLC analysis or GC analysis. TLC analyses were performed with EMD silica gel 60 F_{254} plates. Spots were visualized under UV light (254 nm or 365 nm) and with permanganate stain. NMR yields were taken in deuterated chloroform purchased with 0.05% v/v tetramethylsilane internal standard.

3.2 Instrumentation

NMR spectra were obtained on Bruker 500 MHz spectrometer at 500 (^{1}H) and 125 (^{13}C) MHz or Unity-plus 400 at 400 (^{1}H) and 100 (^{13}C) MHz. Chemical shifts for proton and carbon spectra are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm for ^{1}H spectra and 77.16 ppm for ^{13}C spectra). The shift for boron-bound carbon atoms in the ^{13}C are typically not observed due to quadrupolar relaxation. Chemical shifts for ^{11}B spectra, which were taken in a quartz NMR tube, are reported in ppm with boron trifluoride diethyl etherate as an external standard ($BF_3O(C_2H_5)_2$: 0 ppm). Data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, qt = quartet of triplets, tt = triplet of triplets, br = broad), coupling constants (Hz), and integration. High-resolution ESI mass spectra were obtained on an Agilent 6220 accurate mass TOF LC/MS, while low-resolution ESI mass spectra were obtained on an Agilent 7890B GC System with an Agilent 5977A MSD. GC samples were injected with a 7963 Agilent autosampler system.

3.3 Synthetic Procedures and Characterization Data for Novel Compounds in Chapter One:

General Procedure 1A for the Synthesis of Alkynoic acids from Terminal Alkynes:

A 0.24 M solution of terminal alkyne was prepared in dry THF and cooled to -78 °C. Then *n*-butyllithium was added and stirring was begun for 30 min. The mixture was warmed to 0 °C, and a CO_2 balloon was bubbled through the mixture with stirring for an additional 30 minutes. Upon completion, the reaction was quenched with 1 M HCl, diluted with deionized water, and extracted with EtOAc. The organic layers were washed with water and brine and dried over sodium

sulfate. After concentration *in vacuo*, the residue was purified on silica (40% EtOAc in hexanes with 1% acetic acid additive), furnishing the alkynoic acid as a white solid.

General Procedure 1B for the Synthesis of Alkynamides from Alkynoic Acids using DCC:

A solution containing alkynoic acid, N-hydroxysuccinimide (1.1 equiv), and DCC (1.1 equiv) was prepared in 1,4-dioxane and stirred for 4 h at rt. A methylamine solution (2M in THF, 1.5 equiv) was added dropwise, and stirring was continued for 16 h. A precipitate formed and was filtered off, and the supernatant was concentrated *in vacuo.* The residue was purified on silica (40% EtOAc in hexanes) to afford the alkynamides products.

General Procedure 1C for the Synthesis of Alkynamides from Alkynoic Acids using Pivaloyl Chloride:

A solution of triethylamine (1.1 equiv) and alkynoic acid (0.75 M in CH_2Cl_2) was stirred at -20 ^oC for 30 minutes. Pivaloyl chloride (1.1 equiv) was added and stirring was continued at -20 ^oC for 3 h. A solution of triethylamine (3 M, 4 equiv) was prepared in CH_2Cl_2 and stirred for at -20 ^oC after which methylamine was added (2M in diethyl ether, 2 equiv). Stirring was continued for 30 minutes, and then the methylamine solution was cannulated into the pivaloyl chloride-containing solution. The reaction was warmed to room temperature and allowed to stir overnight (16 h). Upon completion, the reaction was quenched with water and extracted x3 with CH_2Cl_2. The combined organic layers were washed with water and 10% aqueous NaOH solution, then dried over sodium sulfate. The organic solvents were removed *in vacuo* and the residue was purified by flash chromatography (0-40% linear gradient of EtOAc in hexanes) to yield the final alkynamide product.

General Procedure 1D for the Synthesis of Alkynamides from Alkynoic Acids using CDI:

A solution of alkynoic acid, CDI (2 equiv) and DMAP (0.1 equiv) was prepared in dichloromethane and cooled to 0 ^{o}C. Stirring was maintained for 30 min after which amine was added (2 equiv). The reaction was warmed to rt and allowed to stir overnight. Upon completion, the reaction was washed with 0.5 M HCl, dried over sodium sulfate, and purified on silica (0-40% EtOAc in hexanes) to furnish the alkynamides.

General Procedure 1E for the Synthesis of Diboration Products from Alkynamides (1.171a-ag):

The alkynamides was dissolved in THF at 0 ^{o}C. Sodium hydride (1-4 equiv) and 15-crown-5 (1 equiv relative to NaH) was added, and the resulting mixture was allowed to stir at 0 ^{o}C for 30 min. The mixture was warmed to rt and pinBBdan (1.4 equiv) was added. The reaction mixture was stirred for 1 h (unless otherwise noted), and upon completion, the THF was removed *in vacuo*. The residue was purified by flash chromatography (0-40% EtOAc in DCM) to furnish the diboration products.

General Procedure 1F for the Synthesis of Cross-Coupled Product 1.175:

Tetrakis(triphenylphosphine) palladium (0) (5 mol %), **1.171a**, $CsCO_3$ (3 equiv), and 4-iodoanisole (2 equiv) were put in a 15 mL microwave tube and purged with argon. After addition of toluene, the mixture was heated at 80 ^{o}C for 10 minutes in a CEM Discover microwave reactor. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography (30% EtOAc in hexanes) to afford product **1.175**.

General Procedure 1G for the Bdan Deprotection/Bpin Reprotection of 1.175 to form 1.176:

Product **1.175** was dissolved in THF, and 2 M sulfuric acid (6 equiv) as well as pinacol (5 equiv) was added. The mixture was stirred at rt for 18 h, diluted with water, and extracted with

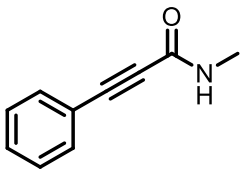
EtOAc. The combined organic layers were dried over sodium sulfate, concentrated under vacuum, and purified by flash chromatography (40% EtOAc in hexanes) to furnish **1.176**.

General Procedure 1H for Coupling of 1.176 to form 1.177:

Product **1.176,** sodium *tert*-butoxide (3 equiv), $Pd(OAc)_2$ (5 mol %), RuPhos (10 mol %), and 1-(4iodophenethyl)piperidine (2 equiv) were added to a 15 mL microwave tube and purged with Ar. A toluene/water mixture (10:1) was added, and the mixture was heated and stirred in a CEM Discover microwave reactor at 80 ºC for 10 min. The mixture was concentrated *in vacuo* and the residue was purified by flash chromatography (10% MeOH in DCM) to afford **1.177**.

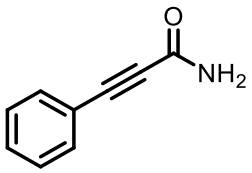
Characterization data for alkynamides 1.161a-1.161ae:

***N*-methyl-3-phenylpropiolamide (1.161a):**



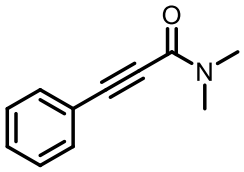
Synthesized by **General Procedure 1C** in 88%% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[2]

3-phenylpropiolamide (1.161b):



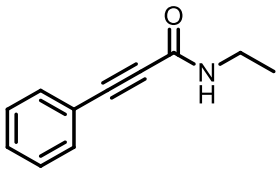
Synthesized by conversion of methyl 3-phenylpropiolate to product. The ester was stirred at room temperature for 6h in methanol with 100 equiv. ammonium hydroxide to furnish the amide in 83% yield. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[3]

***N,N*-dimethyl-3-phenylpropiolamide (1.161c):**



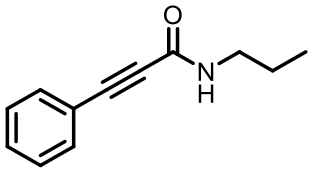
Synthesized by **General Procedure 1B** in 16% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[4]

***N*-ethyl-3-phenylpropiolamide (1.161d):**



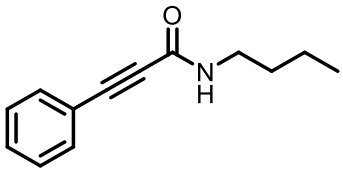
Synthesized by **General Procedure 1B** in 88% yield as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 2H), 7.45 – 7.31 (m, 3H), 5.96 (s, 1H), 5.77* (s, 1H), 3.60 – 3.48* (m, 2H), 3.40 (qd, *J* = 7.2, 5.7 Hz, 2H), 1.29 – 1.26* (m, 3H), 1.21 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.31, 132.54*, 132.47, 130.26*, 130.01, 128.56*, 128.51, 120.27, 84.39, 83.10*, 38.30*, 34.89, 16.02*, 14.62. HRMS data is consistent with the literature.[5]

3-phenyl-*N*-propylpropiolamide (1.161e):



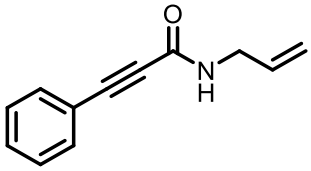
Synthesized by **General Procedure 1B** in 88% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature. [6]

***N*-butyl-3-phenylpropiolamide (1.161f):**



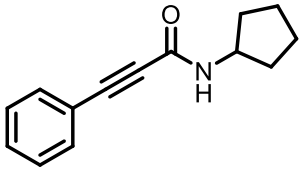
Synthesized by **General Procedure 1D** in 56% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[7]

***N*-allyl-3-phenylpropiolamide (1.161g):**



Synthesized by **General Procedure 1D** in 40% yield as a yellow oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[8]

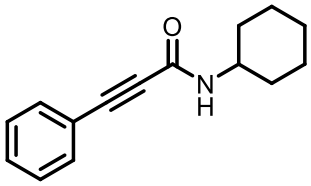
***N*-cyclopentyl-3-phenylpropiolamide (1.161h):**



Synthesized by **General Procedure 1B** in 90% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.56-7.53 (m, 2H), 7.52 – 7.50 (m, 2H), 7.41 – 7.37 (m, 1H), 7.35 – 7.32 (m, 2H), 6.05 (brs, 1H), *5.98 (brs, 1H), 4.29 (m, 1H), 2.01 (m, 2H), 1.70 (dd, J = 9.8, 5.7 Hz, 2H), 1.61

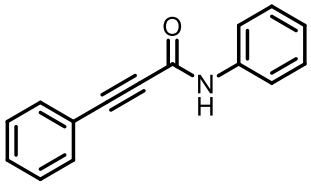
(m, 2H), 1.47 (dd, J = 13.6, 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ *155.8, 153.0, *132.6, 132.4, *130.3, 129.9, *128.7, 128.5, 120.3, 84.2, 83.3, *55.2, 51.7, *34.0, 33.0, 23.7. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{14}H_{16}NO$, 214.1226, observed, 214.1230.

***N*-cyclohexyl-3-phenylpropiolamide (1.161i):**



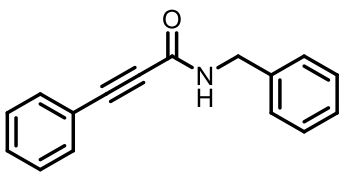
Synthesized by **General Procedure 1D** in 32% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[9]

***N*,3-diphenylpropiolamide (1.161j):**



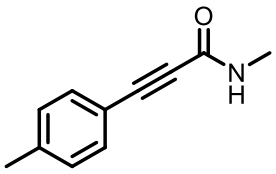
Synthesized by **General Procedure 1B** in 29% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[10]

***N*-benzyl-3-phenylpropiolamide (1.161k):**



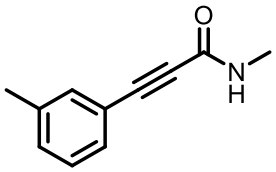
Synthesized by **General Procedure 1B** in 29% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[11]

N-methyl-3-(p-tolyl)propiolamide (1.161l):



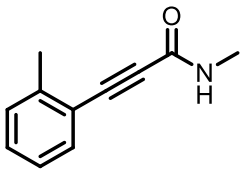
Synthesized by **General Procedure 1B** in 88% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.45 (d, J = 7.9 Hz, 2H), 7.41 (d, J = 8.0, 2H), 7.15 (d, J = 8.0 Hz, 2H), 5.96 (brs, 1H), *5.72 (brs, 1H), *3.11 (d, J = 5.2 Hz, 3H), 2.91 (d, J= 5.0 Hz, 3H), *2.38 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 140.5, *132.5, 132.4, *129.4, 129.3, 117.1, 85.0, 82.5, 26.6, 21.6. HRMS: (ESI) $[M+H]^+$ calcd. For $C_{11}H_{12}NO$, 174.0913, observed, 174.0924.

***N*-methyl-3-(m-tolyl)propiolamide (1.161m):**



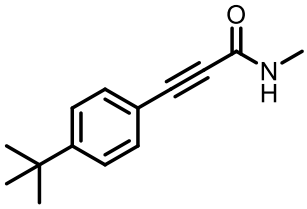
Synthesized by **General Procedure 1B** in 90% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.37-7.35 (m, 1H), 7.34 – 7.32 (m, 1H), 7.31 – 7.30 (m, 1H), 7.25 – 7.23 (m, 1H), 7.23 – 7.21 (m, 1H), 6.02 (brs, 1H), *5.79 (brs, 1H), *3.11 (d, J = 5.2 Hz, 3H), 2.91 (d, J = 5.0 Hz, 3H), *2.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 138.3, *133.1, 133.0, *131.3, 130.9, *129.7, 129.6, *128.5, 128.4, 120.0, 84.8, 82.6, 26.6, 21.2. HRMS: (ESI) $[M+H]^+$ calcd for $C_{11}H_{12}NO$, 174.0913, observed, 174.0923.

***N*-methyl-3-(o-tolyl)propiolamide (1.161n):**



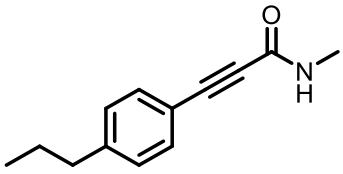
Synthesized by **General Procedure 1B** in 88% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[12]

3-(4-(tert-butyl)phenyl)-N-methylpropiolamide (1.161o):



Synthesized by **General Procedure 1B** in 77% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 5.98 (brs, 1H), 2.92 (d, J = 5.1 Hz, 3H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 132.3, 125.5, 117.1, 84.9, 82.5, 34.9, 31.0, 26.6. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{14}H_{18}NO$, 216.1383, observed, 216.1386.

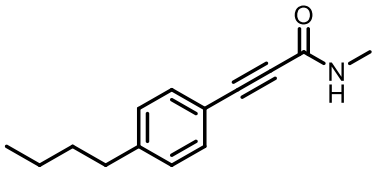
N-methyl-3-(4-propylphenyl)propiolamide (1.161p):



Synthesized by **General Procedure 1C** in 81% yield as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.48 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), *7.19 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 5.89 (brs, 1H), *5.59 (brs, 1H), *3.12 (d, J = 5.2 Hz, 3H), 2.92 (d, J = 5.0 Hz, 3H),

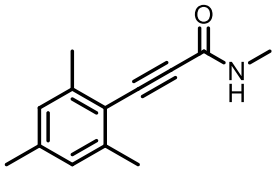
2.59 (t, J = 7.6 Hz, 2H), 1.63 (qt, J = 7.6, 7.3 Hz, 2H), 0.93 (t, J = 7.3, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 145.4, *132.7, 132.6, *128.9, 128.8, 117.5, 85.2, 82.7, 38.2, 26.8, 24.3, 13.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{13}H_{16}NO$, 202.1126, observed, 202.1126.

^{3}-(4-butylphenyl)-N-methylpropiolamide (1.161q):



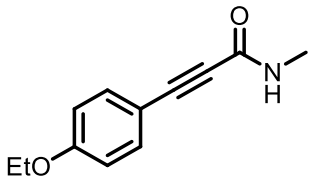
Synthesized by **General Procedure 1B** in 83% yield as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.48 (d, J =8.3 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 8.2 Hz, 2H), 5.94 (brs, 1H), *5.68 (brs, 1H), *3.11 (d, J = 5.2 Hz, 3H), 2.91 (d, J = 5.0 Hz, 3H), 2.61 (t, J = 7.7 Hz, 2H), 1.62 – 1.54 (m, 2H), 1.38 – 1.29 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 145.6, *132.7, 132.6, *128.8, 128.8, 117.4, 85.2, 82.7, 35.8, *34.1, 33.4, 26.8, *25.8, *25.1, 22.4, 14.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{14}H_{18}NO$, 216.1383, observed, 216.1390.

3-mesityl-*N*-methylpropiolamide (1.161r):



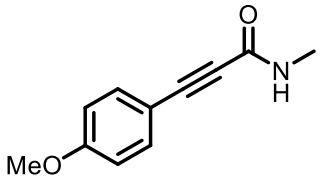
Synthesized by **General Procedure 1C** in 54% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *6.90 (s, 2H), 6.87 (s, 2H), 5.84 (s, 1H), *5.59 (s, 1H), *3.14 (d, J= 5.2 Hz, 3H), 2.93 (d, J= 5.0 Hz, 3H), *2.45 (s, 6H), 2.41 (s, 6H), *2.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 141.7, 139.9, 128.0, 117.2, 90.6, 83.0, 26.8, 21.6, 21.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{13}H_{16}NO$, 202.1226, observed, 202.1243.

3-(4-ethoxyphenyl)-*N*-methylpropiolamide (1.161s):



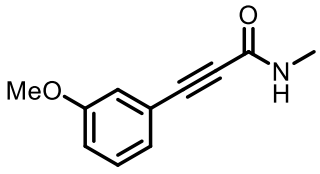
Synthesized by **General Procedure 1B** in 73% yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.50 (d, J = 7.7 Hz, 2H), 7.44 (d, J = 7.7 Hz, 2H), *6.86 (d, J = 7.7 Hz, 2H), 6.84 (d, J = 7.7 Hz, 2H), 5.95 (brs, 1H), *5.68 (brs, 1H), 4.04 (q, J = 7.0 Hz, 2H), *3.10 (d, J = 5.2 Hz, 3H), 2.91 (d, J = 5.1 Hz, 3H), *1.42 (d, J = 7.0 Hz, 3H), 1.41 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 154.6, *134.5, 134.4, *114.8, 114.8, 112.0, 85.4, 82.3, 63.8, 26.8, 14.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{12}H_{14}NO_2$, 204.1019, observed, 204.1036.

3-(4-methoxyphenyl)-N-methylpropiolamide (1.161t):



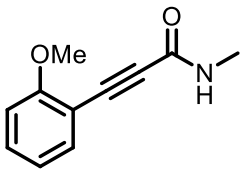
Synthesized by **General Procedure 1C** in 83% yield as a white solid. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[12]

3-(3-methoxyphenyl)-*N*-methylpropiolamide (1.161u):



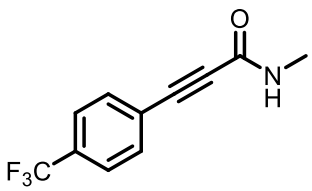
Synthesized by **General Procedure 1B** as a light yellow solid in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, J = 7.7 Hz, 1H), *7.16 (ddd, J = 7.6, 1.4, 1.0 Hz, 1H), 7.11 (ddd, J = 7.7, 1.4, 1.0 Hz, 1H), *7.09 (dd, J = 2.6, 1.4, 1H), 7.05 (dd, J = 2.6, 1.4 Hz, 1H), *7.00 (dd, J = 2.6, 1.0 Hz, 1H), 6.96 (ddd, J = 7.7, 2.6, 1.4 Hz, 1H), 5.93 (brs, 1H), *5.67 (brs, 1H), *3.82 (s, 3H), 3.80 (s, 3H), *3.13 (d, J =5.2 Hz, 3H), 2.92 (d, J = 5.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 156.8, 129.8, 125.1, 121.3, 117.3, 116.9, 84.7, 82.8, 55.5, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{11}H_{12}NO_2$, 190.0863, observed,190.0876.3

-(2-methoxyphenyl)-*N*-methylpropiolamide (1.161v):



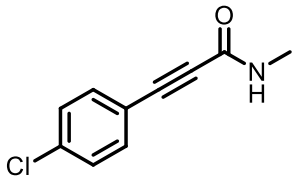
Synthesized by **General Procedure 1B** as a white solid in 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.52 (dd, J = 7.7, 1.7 Hz, 1H), 7.48 (dd, J = 7.7, 1.7, 1H), *7.40 (td, J = 8.4, 1.7 Hz, 1H),7.37 (td, J = 8.4,1.7 Hz, 1H), 6.92 (td, J = 7.7, 1.7, 1H), 6.88 (d, J = 8.4, 1H), 6.00 (brs, 1H), *5.69 (brs, 1H), *3.89 (s, 3H), 3.88, (s, 3H), *3.15 (d, J = 5.2 Hz, 3H), 2.91 (d, J = 5.0, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 154.4, 134.7, *134.6, *132.1, 131.8, 120.7, 110.8, 109.6, 87.0, 81.6, 55.9, 26.7. HRMS: (ESI) $[M+H]^+$ calcd for $C_{11}H_{12}NO_2$, 190.0863, observed, 190.0875.

***N*-methyl-3-(4-(trifluoromethyl)phenyl)propiolamide (1.161w):**



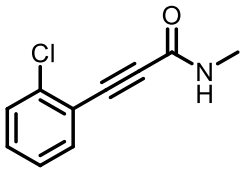
Synthesized by **General Procedure 1C** as a white solid in 85% yield. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[12]

3-(4-chlorophenyl)-*N*-methylpropiolamide (1.161x):



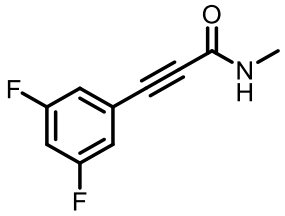
Synthesized by **General Procedure 1B** as a white solid in 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.50 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), *7.36 (d, J = 8.7 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H), 6.00 (brs, 1H), *5.66 (brs, 1H), *3.12 (d, J = 5.2 Hz, 3H), 2.91 (d, J = 5.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 136.5, *133.9, 133.8, *129.2, 129.1, 118.8, 83.9, 83.5, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{10}H_9NOCl$, 194.0367, observed,194.0372.

3-(2-chlorophenyl)-*N*-methylpropiolamide (1.161y):



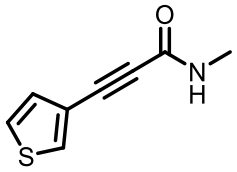
Synthesized by **General Procedure 1C** as a white solid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.60 (dd, J = 7.7, 1.7 Hz, 1H), 7.51 (dd, J = 7.7, 1.7 Hz, 1H), *7.41 (dd, J = 7.7,1.3Hz, 1H), 7.37 (dd, J = 7.7, 1.3 Hz, 1H), *7.34 (m, 1H), 7.30 (td, J = 7.7, 1.7 Hz, 1H), *7.24 (m, 1H), 7.20 (td, J = 7.7, 1.3 Hz, 1H), 6.41 (brs, 1H), *6.01 (brs, 1H), *3.13 (d, J = 5.2 Hz, 3H), 2.90 (d, J = 5.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 136.9, *134.8, 134.4, *131.5 131.2, *129.6, 129.6, *126.9, 126.8, 120.6, 87.5, 81.0, *30.0 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{10}H_9NOCl$, 194.0367, observed, 194.0385.

3-(3,5-difluorophenyl)-*N*-methylpropiolamide (1.161z):



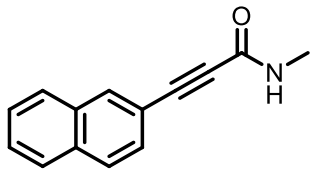
Synthesized by **General Procedure 1C** as a white solid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.10-7.04 (m, 2H), 7.03 (ddd, J = 6.1, 2.3, 1.4 Hz, 2H), *6.93 (t, J = 2.3 Hz, 1H), 6.88 (tt, J = 8.8, 2.3 Hz, 1H), 6.03 (brs, 1H), *5.76 (brs, 1H), *3.11 (d, J = 5.2 Hz, 3H), 2.93 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (dd, J = 250, 13.0 Hz), 153.4, 123.0, 115.5 (dd, J = 20, 8 Hz), 106.5 (d, J = 25 Hz), 84.3, 81.8, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{10}H_8NOF_2$, 196.0568, observed, 196.0576.

***N*-methyl-3-(thiophen-3-yl)propiolamide (1.161aa):**



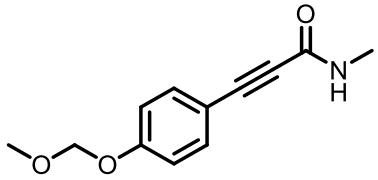
Synthesized by **General Procedure 1C** as a white solid in 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.70 (dd, J =2.9, 1.0 Hz, 1H), 7.64 (dd, J = 3.0, 1.0 Hz, 1H), *7.33 (dd, J = 5.0, 3.0 Hz, 1H), 7.30 (dd, J = 5.0, 3.0 Hz, 1H), *7.21 (dd, J =5.0, 1.0 Hz, 1H), 7.17 (dd, J = 5.0, 1.0 Hz, 1H), 5.98 (brs, 1H), *5.72 (brs, 1H), *3.10 (d, J =5.2 Hz, 3H), 2.91 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, *132.7, 132.3, 130.0, *126.2, 126.0, 119.5, 83.0, 80.1, *29.9, 26.7. HRMS: (ESI) $[M+H]^+$ calcd. for C_8H_8NOS, 166.0321, observed, 166.0334.

***N*-methyl-3-(naphthalen-2-yl)propiolamide (1.161ab):**



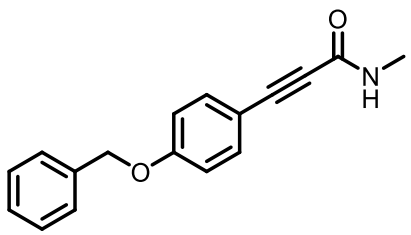
Synthesized by **General Procedure 1B** as a white solid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *8.13 (brs, 1H), 8.08 (brs, 1H), 7.84 – 7.80 (m, 3H), 7.56 – 7.50 (m, 3H), 5.96 (brs, 1H), *5.67 (brs, 1H), *3.18 (d, J = 5.1 Hz, 3H), 2.95 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 133.7, 133.5, 132.8, 128.4, 128.3, 128.2, 128.0, 127.8, 127.0, 117.6, 85.2, 83.3, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{14}H_{12}NO$, 210.0913, observed, 210.0930.

3-(4-(methoxymethoxy)phenyl)-*N*- methylpropiolamide (1.161ac):



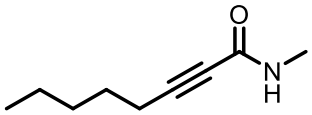
Synthesized by **General Procedure 1C** as a white solid in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.51 (d, J = 8.9 Hz, 2H), 7.46 (d, J = 8.9 Hz, 2H), *7.03 (d, J = 8.9 Hz, 2H), 7.00 (d, J = 8.9 Hz, 2H),5.89 (brs, 1H), *5.69 (brs, 1H), *5.20 (s, 1H), 5.19 (s, 1H), *3.48 (s, 3H), 3.47 (s, 3H), *3.11 (d, J = 5.1 Hz, 3H), 2.91 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7,154.4, *134.5, 134.3, *116.5, 116.4, 113.4, 94.3, 85.0, 82.4, 56.4, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{12}H_{14}NO_3$, 220.0968, observed, 220.0966.

3-(4-(benzyloxy)phenyl)-*N*-methylpropiolamide (1.161ad)



Synthesized by **General Procedure 1B** as a white solid in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ *7.51 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 8.9 Hz, 2H), 7.41 – 7.39 (m, 5H), *6.96 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 5.89 (brs, 1H), *5.62 (brs, 1H), *5.09 (s, 2H), 5.08 (s, 2H), *3.11 (d, J = 5.0 Hz, 3H), 2.91 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 154.5, 136.4, *134.6, 134.4, 128.8, *128.4, 128.4, 127.6, *115.3, 115.2, 112.5, 85.2, 82.4, 70.2, 26.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{17}H_{16}NO_2$, 266.1176, observed, 266.1187.

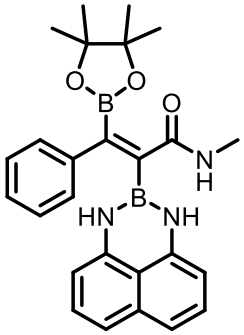
N-methyloct-2-ynamide (1.161ae):



Synthesized by **General Procedure 1B** as a yellow oil in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (brs, 1H), *3.01 (d, J = 5.0 Hz, 3H), 2.84 (d, J = 5.0 Hz, 3H), *2.37 (t, J = 7.2 Hz, 2H), 2.27 (t, J = 7.2 Hz, 2H), *1.60 (dt, J = 14.5, 6.9 Hz, 2H), 1.54 (dt, J = 14.5, 6.9 Hz, 2H), *1.38 (m, 4H), *1.34 (m, 4H), *0.90 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 87.5, 75.6, *34.1, 31.1, 27.6, 26.6, *25.8, *25.1, 22.3, *19.0, 18.7, 14.0 HRMS: (ESI) $[M+H]^+$ calcd. for $C_9H_{16}NO$, 154.1126, observed, 154.1128.

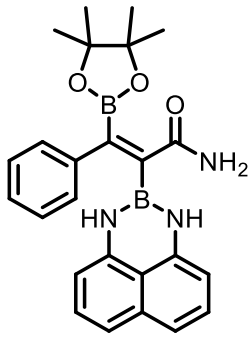
<u>Characterization Data for Diborated Alkynamides 1.171a-1.171ae:</u>

(*E*)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171a):



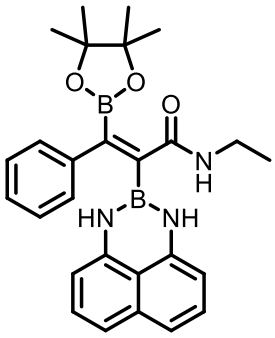
Synthesized by **General Procedure 1E** as a yellow solid in 67% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H), 7.33 – 7.23 (m, 3H), 7.11 – 6.98 (m, 4H), 6.49 (q, J = 5.0 Hz, 1H), 6.14 (dd, J = 6.3, 2.0 Hz, 2H), 5.54 (s, 2H), 3.13 (d, J = 5.0 Hz, 3H), 1.25 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 140.0, 139.4, 136.2, 128.7, 128.2, 127.9, 127.6, 120.0, 118.7, 106.7, 80.8, 28.9, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.6, 14.1. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{26}H_{30}B_2N_3O_3$, 454.2468, observed, 454.2463.

(*E*)-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)acrylamide (1.171b):



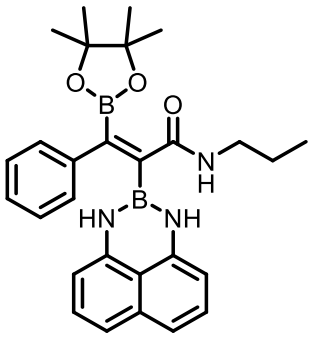
Synthesized by **General Procedure 1E** as a yellow solid in 57% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 2H), 7.30 – 7.23 (m, 3H), 7.07 – 6.99 (m, 4H), 6.22 (t, J = 4.2 Hz, 2H), 5.74 (s, 2H), 2.21 (s, 2H), 1.24 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 140.1, 139.0, 136.2, 129.1, 128.3, 127.9, 127.7, 120.0, 118.6, 106.8, 81.1, 25.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.6, 15.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{25}H_{28}B_2N_3O_3$, 440.2311, observed 440.2292.

(*E*)-*N*-ethyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171d):



Synthesized by **General Procedure 1E** as a yellow solid in 85% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 7.6, 1.9 Hz, 2H), 7.30 – 7.24 (m, 3H), 7.10 – 7.04 (m, 4H), 6.29 (brs, 1H), 6.24 (dd, J = 6.6, 1.7 Hz, 2H), 5.54 (s, 2H), 3.59 (q, J = 7.3 Hz, 2H), 1.29 (t, J = 7.3 Hz, 3H), 1.23 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 140.0, 139.4, 136.2, 128.6, 128.1, 127.9, 127.7, 120.0, 118.8, 106.8, 80.7, 37.4, 26.0, 14.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.5, 13.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_3$, 468.2624, observed, 468.2625.

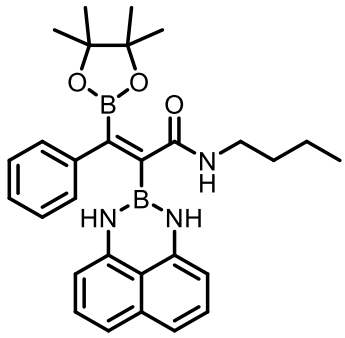
(*E*)-*N*-propyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171e):



Synthesized by **General Procedure 1E** as a yellow solid in 68% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 6.7 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.08 – 7.04 (m, 4H), 6.31 (brs, 1H), 6.22 (dd, J = 6.8, 1.5 Hz, 2H), 5.50

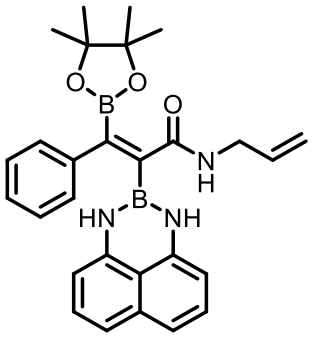
(s, 2H), 3.50 (q, J = 6.5 Hz, 2H), 1.67 (q, J = 7.3 Hz, 3H), 1.24 (s, 12H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 140.0, 139.4, 136.2, 128.6, 128.1, 127.9, 127.7, 119.9, 118.7, 106.8, 80.7, 44.1, 26.0, 22.5, 11.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.9, 13.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{28}H_{34}B_2N_3O_3$, 482.2781, observed, 482.2765.

(*E*)-*N*-*n*-butyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171f):



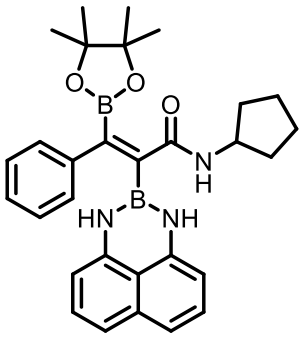
Synthesized by **General Procedure 1E** as a yellow solid in 73% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 6.7 Hz, 2H), 7.31 – 7.28 (m, 3H), 7.10 – 7.05 (m, 4H), 6.27 (brs, 1H), 6.22 (d, J = 6.7 Hz, 2H), 5.48 (s, 2H), 3.54 (q, J = 6.9 Hz, 2H), 1.66 – 1.61(m, 2H), 1.38 (h, J = 7.3 Hz, 2H), 1.24 (s, 12H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 140.0, 139.4, 136.2, 128.6, 128.1, 127.9, 127.7, 119.9, 118.8, 106.8, 80.7, 42.2, 31.2, 26.0, 20.1, 13.8. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.1, 13.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{29}H_{36}B_2N_3O_3$, 496.2937, observed, 496.2949.

(*E*)-*N*-allyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171g):



Synthesized by **General Procedure 1E** as a yellow solid in 51% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.1, 1.4 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.10 – 7.04 (m, 4H), 6.35 (brs, 1H), 6.22 (dd, J = 6.8, 1.5 Hz, 2H), 5.88 (ddt, J = 16.6, 10.1, 6.1 Hz, 1H), 5.51 (s, 2H), 5.28 (m, 2H), 4.16 (t, J = 6.0 Hz, 2H), 1.24 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 139.9, 139.3, 136.2, 131.8, 128.8, 128.1, 127.9, 127.7, 119.9, 119.5 118.8, 106.8, 80.8, 44.8, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.1, 14.3. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{28}H_{32}B_2N_3O_3$, 480.2624, observed, 480.2619.

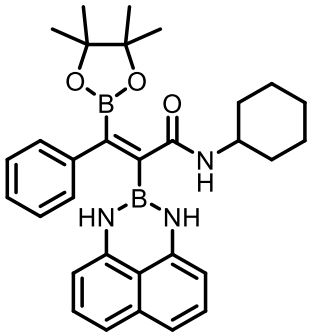
(*E*)-*N*-cyclopentyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-phenyl-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171h):



Synthesized by **General Procedure 1E** as a brown solid in 35% yield. Four equiv. NaH/15-crown-5 used. Reaction run at 60 ºC after addition of diboron reagent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, J = 8.1, 1.4 Hz, 2H), 7.33 – 7.22 (m, 3H), 7.12 – 7.02 (m,

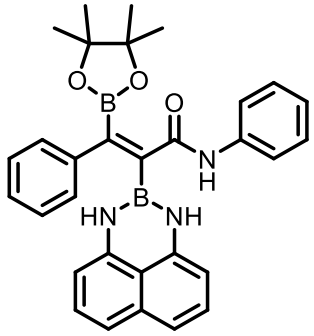
4H), 6.22 (dd, J = 6.8, 1.4 Hz, 2H), 6.17 (d, J = 7.5 Hz, 1H), 5.51 (s, 2H), 4.41 (h, J = 7.2 Hz, 1H), 2.12 (tt, J = 12.1, 5.5 Hz, 2H), 1.77 – 1.59 (m, 4H), 1.52 (dq, J = 14.0, 7.5, 7.1 Hz, 2H), 1.24 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 140.1, 139.4, 136.2, 128.5, 128.0, 127.8, 127.7, 120.0, 118.7, 106.8, 80.7, 54.2, 33.1, 30.5, 29.8, 26.0, 23.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.7,14.1. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{30}H_{36}B_2N_3O_3$, 508.2948, observed, 508.2953.

(*E*)-*N*-cyclohexyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171i):



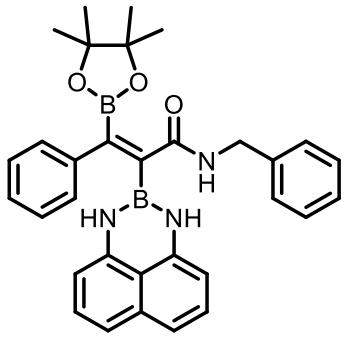
Synthesized by **General Procedure 1E** as a yellow solid in 68% yield. Four equiv. NaH/15-crown-5 used. Reaction run at 60 ºC after addition of diboron reagent. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.1, 1.4 Hz, 2H), 7.29 – 7.20 (m, 3H), 7.10 – 7.02 (m, 4H), 6.24 (dd, J = 6.8, 1.2 Hz, 2H), 6.10 (d, J = 8.1 Hz, 1H), 5.53 (s, 2H), 4.04 – 3.90 (m, 1H), 2.07 – 1.98 (m, 2H), 1.79 – 1.67 (m, 2H), 1.63 (dt, J = 13.1, 3.8 Hz, 1H), 1.47 – 1.23 (m, 5H), 1.21 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 140.1, 139.4, 136.2, 128.5, 128.0, 127.9, 127.7, 120.0, 118.7, 106.8, 80.7, 51.8, 32.7, 25.9, 25.3, 24.7. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.4, 13.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{31}H_{38}B_2N_3O_3$, 522.3094, observed,522.3100.

(*E*)-*N*-phenyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171j):



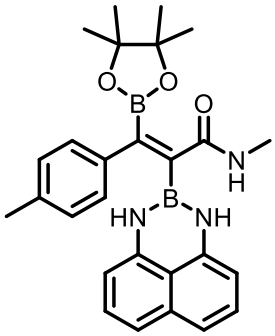
Synthesized by **General Procedure 1E** as a yellow solid in 44% yield. Two equiv. NaH/15-crown-5 used. Reaction run at 60 °C after addition of diboron reagent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.67 (d, J = 7.5 Hz, 2H), 7.58 (d, J = 7.5 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.32 (m, 3H), 7.24 (m, 1H), 7.13 – 7.10 (m, 4H), 6.28 (d, J = 6.3 Hz, 2H), 5.64 (m, 2H), 1.28 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 139.9, 139.1, 136.3, 135.8, 129.4, 129.1, 128.2, 128.1, 127.7, 126.7, 121.5, 120.1, 119.0, 107.0, 81.2, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.1, 15.7. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{31}H_{32}B_2N_3O_3$, 516.2624, observed, 516.2608.

(*E*)-*N*-benzyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171k):



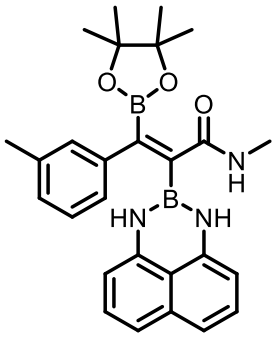
Synthesized by **General Procedure 1E** as a yellow solid in 56% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 6.8 Hz, 2H), 7.38 – 7.28 (m, 8H), 7.07 – 7.02 (m, 4H), 6.56 (brs, 1H), 6.19 (d, J = 6.8 Hz, 2H), 5.52 (s, 2H), 4.71 (d, J = 5.7 Hz, 2H), 1.26 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 143.0, 139.6, 136.2, 130.1, 127.9 , 127.7 , 125.1, 123.2, 120.0, 119.0, 106.9, 80.9, 29.0, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.1, 14.5. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{32}H_{34}B_2N_3O_3$, 530.2781, observed, 530.2789.

(*E*)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)-3-(*p*-tolyl)acrylamide (1.171l):



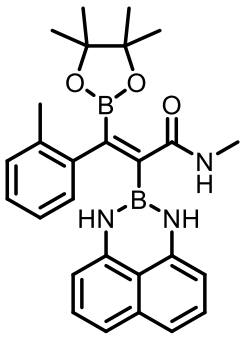
Synthesized by **General Procedure 1E** as a yellow solid in 71% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 7.08 – 7.03 (m, 4H), 6.38 (brs, 1H), 6.16 (dd, J = 7.0, 0.9 Hz, 2H), 5.52 (brs, 2H), 3.12 (d, J = 5.0 Hz, 3H), 2.30 (s, 3H), 1.26 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 140.0, 138.9, 136.3, 136.2, 128.9, 128.3, 127.6, 119.9, 118.6, 106.7, 80.7, 28.8, 26.2, 21.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.5, 14.4. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_3$, 468.2624, observed, 468.2608.

(*E*)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)-3-(*m*-tolyl)acrylamide (1.17m):



Synthesized by **General Procedure 1E** as a yellow solid in 70% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H) 7.08 – 7.01 (m, 5H), 6.38 (brs, 1H), 6.18 (d, J = 7.0 Hz, 2H), 5.52 (brs, 2H), 3.13 (d, J = 5.0 Hz, 3H), 2.28 (s, 3H), 1.25 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 140.0, 139.2, 137.5, 136.2, 129.5, 128.9, 128.1, 127.6, 124.8, 119.9, 118.7, 106.7, 80.8, 28.9, 26.1, 21.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.5, 14.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_3$, 468.2624, observed, 468.2616.

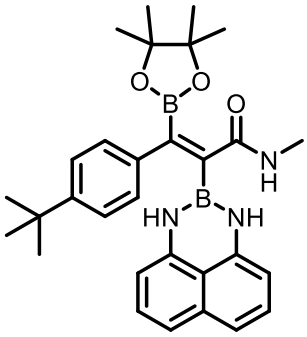
(*E*)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)-3-(*o*-tolyl)acrylamide (1.171n):



Synthesized by **General Procedure 1E** as a yellow solid in 70% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.08 (m, 4H), 6.99 – 7.05 (m, 4H), 6.49 (brs, 1H), 6.12 (dd, J = 7.0, 0.9 Hz, 2H), 5.30 (brs, 2H), 3.17 (d, J = 4.9 Hz, 3H), 2.30 (s, 3H), 1.07 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 140.5, 139.9, 136.2, 133.0, 129.9, 127.6, 126.7,

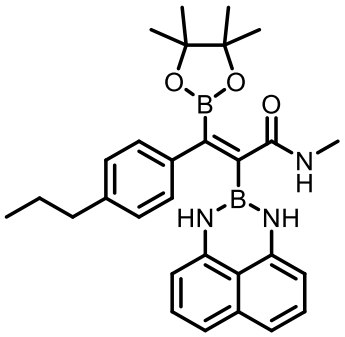
125.2, 125.0, 119.8, 118.7, 106.7, 80.6, 29.0, 25.2, 20.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 26.6, 13.7. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_3$, 468.2624, observed, 468.2613.

(*E*)-3-(4-(tert-butyl)phenyl)-N-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3- (4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171o):



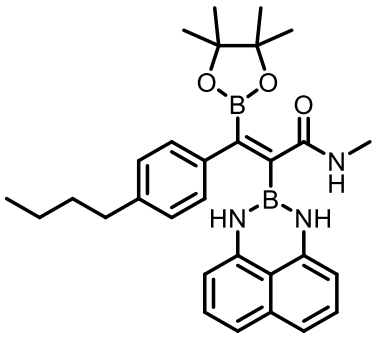
Synthesized by **General Procedure 1E** as a yellow solid in 56% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4Hz, 2H), 7.07 – 7.02 (m, 4H), 6.46 (d, J = 5.3 Hz, 1H), 6.13 (dd, J = 5.8, 2.6 Hz, 2H), 5.60 (s, 2H), 3.11 (d, J = 4.9 Hz, 3H), 1.27 (s, 9H), 1.26 (s, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.0, 152.1, 140.2, 136.3, 136.1, 128.2, 127.7, 125.1, 120.0, 118.5, 106.7, 80.9, 34.8, 31.4, 28.9, 26.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.1, 14.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{30}H_{38}B_2N_3O_3$, 510.3094, observed, 510.3083.

(*E*)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4-propylphenyl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171p):



Synthesized by **General Procedure 1E** as a yellow solid in 77% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 7.06 – 6.99 (m, 4H), 6.47 (q, J = 4.6 Hz, 1H), 6.09 (dd, J = 5.6, 2.7 Hz, 2H), 5.52 (s, 2H), 3.13 (d, J = 5.0 Hz, 3H), 2.53 (t, J = 7.7 Hz, 2H), 1.59 (h, J = 7.4 Hz, 2H), 1.27 (s, 12H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 143.8, 140.1, 136.5, 136.2, 128.3, 128.3, 127.6, 119.9, 118.5, 106.7, 80.7, 38.0, 28.9, 26.2, 24.4, 14.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.2, 14.3. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{29}H_{36}B_2N_3O_3$, 496.2937, observed, 496.2936.

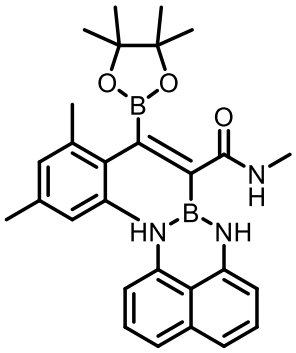
(*E*)-3-(4-butylphenyl)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171q):



Synthesized by **General Procedure 1E** as a yellow solid in 67% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2H), 7.05 – 7.02 (m, 6H), 6.47 (brs, 1H), 6.16 (t, J = 4.1 Hz, 2H), 5.72 (brs, 2H), 3.12 (d, J = 5.0

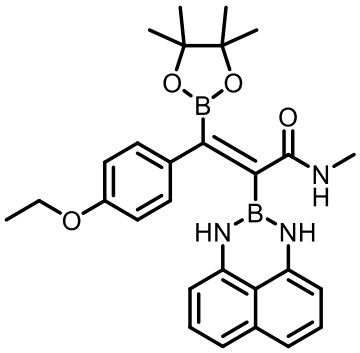
Hz, 3H), 2.52 (t, J = 7.7 Hz, 2H), 1.53 (tt, J = 7.7 Hz, 7.7 Hz, 2H), 1.30 (h, J = 7.4 Hz, 2H), 1.07 (s, 12H), 0.89 (t, J = 7.4 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 143.9, 140.2, 136.4, 136.2, 128.2, 128.2, 127.6, 120.0, 118.5, 106.7, 80.9, 35.7, 33.5, 28.9, 26.0, 22.5, 14.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.4, 14.2. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{30}H_{38}B_2N_3O_3$, 510.3094, observed, 510.3085.

(*E*)-3-mesityl-*N*-methyl-2-(1*H*-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171r):



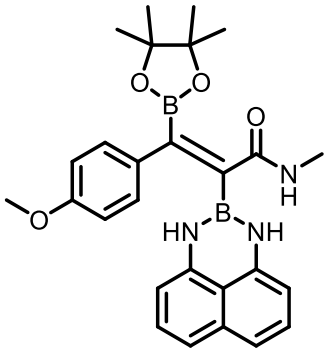
Synthesized by **General Procedure 1E** as a yellow solid in 49% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 – 6.99 (m, 4H), 6.80 (s, 2H), 6.51 (brs, 1H), 6.10 (d, J = 6.7 Hz, 2H), 5.33 (brs, 2H), 3.18 (d, J = 4.9 Hz, 3H), 2.25 (s, 3H), 2.22 (s, 6H), 1.06 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 140.0, 137.1, 136.1, 135.5, 132.3, 127.9, 127.5, 119.8, 118.5, 106.6, 80.5, 28.9, 25.0, 21.1, 20.6. ^{11}B NMR (128 MHz, $CDCl_3$) δ 26.4, 14.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{29}H_{36}B_2N_3O_3$, 496.2937, observed, 496.2971.

(*E*)-3-(4-ethoxyphenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171s):



Synthesized by **General Procedure 1E** as a yellow solid in 74% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.7 Hz, 2H), 7.03 – 7.01 (m, 4H), 6.68 (d, J = 8.7 Hz, 2H), 6.41 (brs, 1H), 6.24 (dd, J = 5.9, 2.4 Hz, 2H), 5.87 (s, 2H), 3.88 (q, J = 7.0 Hz, 2H), 3.11 (d, J = 5.0 Hz, 3H), 1.33 (t, J = 7.0 Hz, 3H), 1.24 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 159.9, 140.3, 136.3, 131.4, 130.2, 127.7, 120.1, 118.5, 114.0, 106.8, 81.0, 63.4, 28.8, 26.0, 14.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.2, 13.2. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{28}H_{34}B_2N_3O_4$, 498.2730, observed, 498.2730.

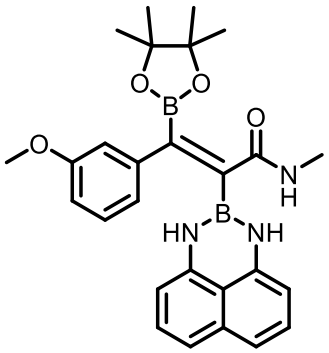
(*E*)-3-(4-methoxyphenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171t):



Synthesized by **General Procedure 1E** as a yellow solid in 72% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.8 Hz, 2H), 7.11 – 7.01 (m, 4H), 6.83 (d, J = 8.8 Hz, 2H), 6.34 (q, J = 4.7 Hz, 1H), 6.18 (dd, J = 6.7, 1.3

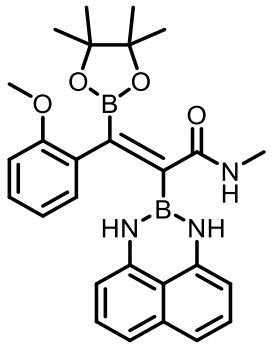
Hz, 2H), 5.54 (s, 2H), 3.77 (s, 3H), 3.12 (d, J = 5.0 Hz, 3H), 1.28 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 160.5, 140.1, 136.2, 131.6, 130.3, 127.6, 119.9, 118.7, 113.6, 106.8, 80.7, 55.3, 28.8, 26.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.8, 14.3. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_4$, 484.2573, observed, 484.2598.

(*E*)-3-(3-methoxyphenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171u):



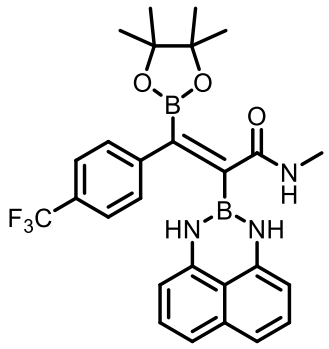
Synthesized by **General Procedure 1E** as a yellow solid in 61% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 1H), 7.18 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.08 – 7.03 (m, 4H), 6.81 (dd, J = 7.7, 2.2 Hz, 1H), 6.37 (brs, 1H), 6.20 (dd, J = 6.7, 1.3 Hz, 2H), 5.51 (s, 2H), 3.74 (s, 3H), 3.13 (d, J = 5.0 Hz, 3H), 1.25 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 159.2, 140.7, 139.9, 136.2, 129.2, 127.6, 120.2, 119.9, 118.7, 115.2, 112.5, 106.7, 80.8, 55.2, 28.9, 26.1. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.2, 14.2. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_4$, 484.2573, observed, 484.2561.

(*E*)-3-(2-methoxyphenyl)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171v):



Synthesized by **General Procedure 1E** as a yellow solid in 68% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (dd, J = 7.6, 1.7 Hz, 1H), 7.22 (td, J = 7.6, 1.7 Hz, 1H),7.09 – 7.05 (m, 2H), 6.97 – 7.02 (m, 3H), 6.79 (d, J = 8.2 Hz, 1H),6.39 (brs, 1H), 6.23 (d, J = 7.2 Hz, 2H), 5.54 (brs, 2H), 3.59 (s, 3H), 3.13 (d, J = 5.0 Hz, 3H), 1.22 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 155.3, 140.6, 136.3, 130.4, 129.5, 128.3, 127.6, 120.4, 119.7, 118.0, 111.3, 106.3, 80.6, 55.3, 28.8, 25.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.0, 13.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{32}B_2N_3O_4$, 484.2573, observed, 484.2561.

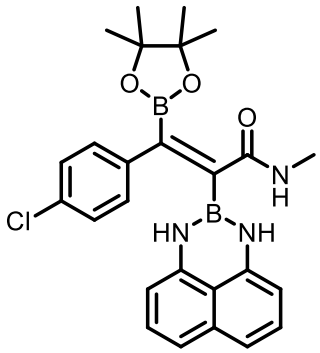
(*E*)-*N*-methyl-2-(1*H*-naphtho[1,8-de][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)acrylamide (1.171w):



Synthesized by **General Procedure 1E** as a yellow solid in 71% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 8.1 Hz,

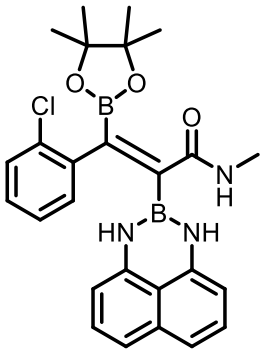
2H), 7.10 – 7.07 (m, 4H), 6.46 (brs, 1H), 6.21 (d, J = 7.7 Hz, 2H), 5.47 (s, 2H), 3.15 (d, J = 5.0 Hz, 3H), 1.23 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 143.0, 139.6, 136.2, 130.2 (q, J = 3.6 Hz), 127.9, 127.7, 125.1 (q, J = 3.6 Hz), 124.3 (q, J = 272 Hz), 119.9, 119.1, 106.8, 80.9, 29.0, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.0, 14.0. HRMS: (ESI) $[2M+K]^+$ calcd. for $C_{54}H_{56}B_4F_6KN_6O_6$, 1081.4201, observed, 1081.4246.

(*E*)-3-(4-chlorophenyl)-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171x):



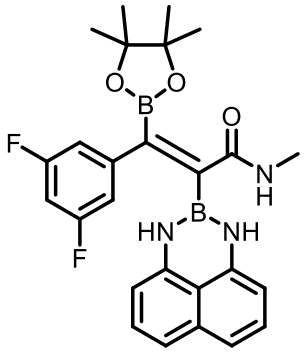
Synthesized by **General Procedure 1E** as a yellow solid in 70% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.26 (d, 8.4 Hz 2H), 7.11 – 7.04 (m, 4H), 6.42 (d, J = 4.6 Hz, 1H), 6.22 (dd, J = 6.5, 1.4 Hz, 2H), 5.52 (s, 2H), 3.13 (d, J = 5.0 Hz, 3H), 1.24 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 139.8, 137.7, 136.2, 134.7, 129.4, 128.4, 127.7, 120.0, 118.9, 106.9, 80.9, 28.9, 26.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.5, 14.2. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{26}H_{29}B_2ClN_3O_3$, 488.2088, observed, 488.2079.

(*E*)-3-(2-chlorophenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171y):



Synthesized by **General Procedure 1E** as a yellow solid in 76% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 8.0 Hz, 1H), 7.30 (dd, J = 7.7, 1.7 Hz, 1H), 7.23 (td, J = 7.5, 1.2 Hz, 1H), 7.14 (td, J = 7.7, 1.8 Hz, 1H), 7.09 – 6.98 (m, 4H), 6.48 (q, J = 6.0 Hz, 1H), 6.21 (d, J = 7.1 Hz, 2H), 5.56 (s, 2H), 3.17 (d, J = 5.0 Hz, 3H), 1.09 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 139.9, 139.4, 136.2, 129.7, 129.3, 128.0, 127.6, 126.2, 120.0, 118.7, 106.7, 80.6, 29.0, 25.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.4, 14.5. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{26}H_{29}B_2ClN_3O_3$, 488.2078, observed,488.2075.

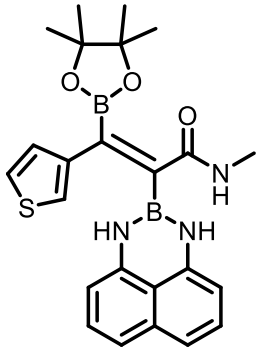
(*E*)-3-(3,5-difluorophenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171z):



Synthesized by **General Procedure 1E** as a yellow solid in 74% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 – 7.01 (m, 6H), 6.70 (tt, J = 8.8, 2.1 Hz, 1H), 6.42 (q, J = 6.0 Hz, 1H), 6.26 (dd, J = 6.7, 1.7 Hz, 2H), 5.50 (s, 2H), 3.14 (d, J = 5.0

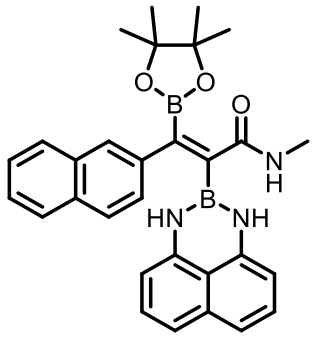
Hz, 3H), 1.23 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 162.7 (dd, J = 249, 12.9 Hz), 142.7 (J = 9.7 Hz), 139.6, 136.2, 127.7, 120.0, 119.1, 110.3 (dd, J = 20, 8 Hz), 106.9, 103.6 (d, J = 25.4 Hz), 81.0, 29.0, 25.9. ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.6, 13.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{26}H_{28}F_2B_2N_3O_3$, 490.2279, observed, 490.2288.

(*E*)-*N*-methyl-2-(1*H*-naphtho[1,8-*de*][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5 tetramethyl-1,3,2- dioxaborolan-2-yl)-3-(thiophen-2-yl)acrylamide (1.71aa):



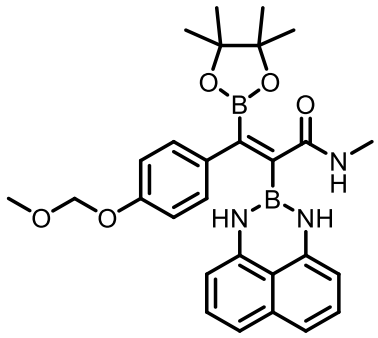
Synthesized by **General Procedure 1E** as a yellow solid in 71% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 2.9 Hz, 1H), 7.40 (d, J = 5.0 Hz, 1H), 7.20 (dd, J = 5.0, 2.9 Hz, 1H), 7.12 – 7.02 (m, 4H), 6.37 (q, J = 5.0 Hz, 1H), 6.19 (dd, J = 6.7, 1.7 Hz, 2H), 5.62 (s, 2H), 3.12 (d, J = 5.0 Hz, 3H), 1.31 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 140.1, 140.0, 136.3, 128.0, 127.8, 127.7, 125.5, 120.0, 118.8, 106.8, 80.8, 28.9, 26.5. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.5, 14.5. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{24}H_{28}B_2N_3O_3S$, 460.2032, observed, 460.2035.

(*E*)-*N*-methyl-3-(naphthalen-2-yl)-2-(1*H*-naphtho[1,8-de][1,3,2]diazaborinin-2(3*H*)-yl)-3-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171ab):



Synthesized by **General Procedure 1E** as a yellow solid in 44% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.82 (m, 1H), 7.77 (m, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.44 (m, 2H), 7.04 – 7.03 (m, 4H), 6.41 (brs, 1H), 6.16 (t, J = 4.1 Hz, 2H), 5.55 (brs, 2H), 3.16 (d, J = 5.0 Hz, 3H), 1.28 (s, 12H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 139.9, 136.7, 136.2, 133.5, 133.1, 128.8, 128.0, 127.8, 127.7, 127.6, 126.5, 126.2, 126.1, 120.0, 118.8, 106.8, 80.9, 28.9, 26.2. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.0, 14.3. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{30}H_{32}B_2N_3O_3$, 504.2624, observed, 504.2626.

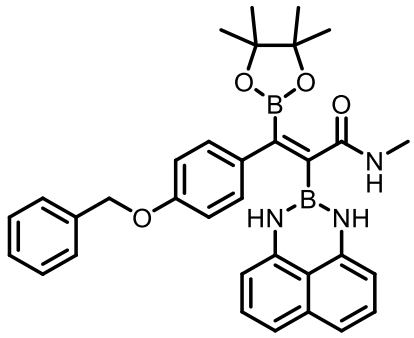
(*E*)-3-(4-(methoxymethoxy)phenyl)-N-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171ac):



Synthesized by **General Procedure 1E** as a yellow solid in 58% yield. One equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.7 Hz, 2H), 7.09 – 7.03 (m, 4H), 6.91 (d, J = 8.7 Hz, 2H), 6.34 (d, J = 4.7 Hz, 1H), 6.20 (dd, J = 6.6, 1.5

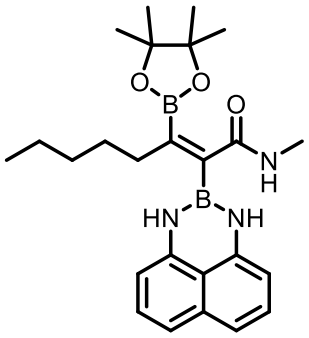
Hz, 2H), 5.60 (brs, 2H), 5.11 (s, 2H), 3.43 (s, 3H), 3.09 (d, J = 5.0 Hz, 3H), 1.25 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 158.2, 140.1, 136.2, 132.7, 130.1, 127.6, 120.0, 118.6, 115.8, 106.7, 94.4, 80.8, 56.2, 26.2, 25.0. ^{11}B NMR (128 MHz, $CDCl_3$) δ28.3, 14.1. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{28}H_{34}B_2N_3O_5$, 514.2679, observed, 514.2691.

(*E*)-3-(4-(benzyloxy)phenyl)-*N*-methyl-2-(1*H*-naphtho[1,8-de][1,3,2]diazaborinin-2(3*H*)-yl)-3- (4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylamide (1.171ad):



Synthesized by **General Procedure 1E** as a yellow solid in 59% yield. Two equiv. NaH/15-crown-5 used. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.7 Hz, 2H), 7.40 – 7.31 (m, 5H), 7.10 – 7.05 (m, 4H), 6.90 (d, J = 8.7 Hz, 2H), 6.50 (brs, 1H), 6.20 (dd, J = 5.9, 2.2 Hz, 2H), 5.55 (brs, 2H), 5.02 (s, 2H), 3.11 (d, J = 5.0 Hz, 3H), 1.28 (s, 12H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 159.7, 140.0, 136.9, 136.2, 131.9, 130.2, 128.7, 128.1, 127.7, 120.0, 118.7, 114.5, 106.8, 80.8, 70.0, 28.8, 26.3. ^{11}B NMR (128 MHz, $CDCl_3$) δ 28.0, 14.2. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{33}H_{36}B_2N_3O_4$, 560.2886, observed, 560.2892.

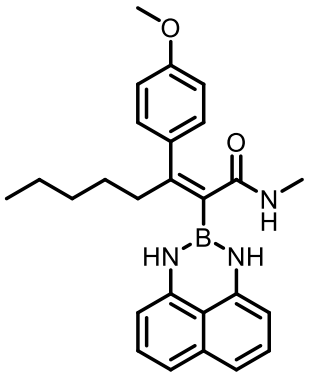
***(E)*-*N*-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)-3-(4,4,5,5tetramethyl-1,3,2-dioxaborolan-2-yl)oct-2-enamide (1.171ae):**



Synthesized by **General Procedure 1E** as a white solid in 67% yield. Two equiv NaH/15-crown-5 used. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, J = 7.7 Hz, 2H), 7.08 (d, J = 8.2 Hz, 2H), 6.33 (d, J = 7.1 Hz, 2H), 6.09 (m, 1H), 5.60 (brs, 2H), 3.06 (d, J = 5.0 Hz, 3H), 2.49 (m, 2H), 1.63 (p, J = 6.9 Hz, 2H), 1.30 (m, 4H), 1.27 (s, 12H), 0.86 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 140.1, 136.3, 127.7, 120.0, 118.8, 106.7, 80.5, 33.4, 32.6, *32.1, 29.8, *29.5, 28.6, 25.7, *25.0, *22.8, 22.6, *14.3, 14.1; ^{11}B NMR (128 MHz, $CDCl_3$) δ 27.8, 14.0. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{25}H_{36}B_2N_3O_3$, 448.2937, observed, 448.2976.

Characterization Data for Cross-coupling Products 1.175-1.177:

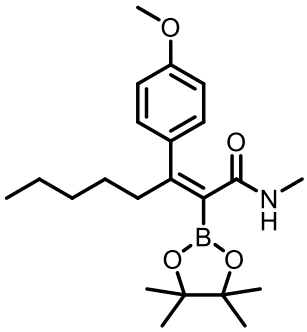
***(Z)*-3-(4-methoxyphenyl)-N-methyl-2-(1H-naphtho[1,8-de][1,3,2]diazaborinin-2(3H)-yl)3-phenylacrylamide (1.175):**



Synthesized by **General Procedure 1F** in 80% yield as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (m, 3H), 7.30 (m, 2H), 7.24 (d, J = 8.8 Hz, 2H), 6.99 (m, 2H), 6.91 (d, J = 8.0 Hz,

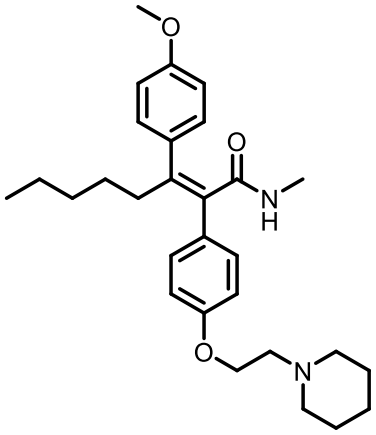
2H), 6.84 (d, J = 8.8 Hz, 2H), 5.97 (d, J = 7.0 Hz, 2H), 5.55 (brs, 2H), 5.35 (q, J = 4.5 Hz, 1H), 3.81 (s, 3H), 2.68 (d, J = 5.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 159.9, 155.1, 142.1, 141.0, 136.2, 133.7, 130.3, 129.1, 128.7, 128.6, 127.6, 119.7, 117.4, 113.8, 106.0, 55.4, 26.8; ^{11}B NMR (128 MHz, $CDCl_3$) δ 26.9. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{27}H_{25}BN_3O_2$, 434.2034, observed, 434.2076.

***(Z)*-3-(4-methoxyphenyl)-N-methyl-3-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2yl)acrylamide (1.176):**



Synthesized by **General Procedure 1G** in 83% yield as a light yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 3H), 7.20 (m, 2H), 7.16 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 5.19 (m, 1H), 3.80 (s, 3H), 2.61 (d, J = 5.0 Hz, 3H), 1.13 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 159.9, 155.3, 143.0, 133.2, 131.0, 129.7, 128.5, 128.1, 113.6, 84.0, 55.4, 26.5, 24.6; ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.3. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{23}H_{29}BNO_4$, 394.2184, observed, 394.2232.

***(Z)*-3-(4-methoxyphenyl)-N-methyl-3-phenyl-2-(4-(2-(piperidin-1yl)ethoxy)phenyl)acrylamide (1.177):**



Synthesized by **General Procedure 1H** in 66% yield as a light yellow solid. ^{1}H NMR (500 MHz, CDCl3) δ 7.21 (d, J = 8.8 Hz, 2H), 7.14 (m, 3H), 7.07 (d, J = 8.2 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.98 (m, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.66 (d, J = 8.8 Hz, 2H), 5.50 (q, J = 4.8 Hz, 1H), 4.10 (t, J = 5.7 Hz, 2H), 3.81 (s, 3H), 2.83 (t, J = 5.7 Hz, 2H), 2.68 (d, J = 5.0 Hz, 3H), 2.61 (brs, 4H), 1.67 (m, 4H), 1.48 (brs, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 159.4, 157.7, 142.3, 141.7, 136.0, 134.7, 131.5, 131.1, 131.0, 130.7, 128.0, 127.4, 114.4, 113.7, 65.4, 57.7, 55.4, 55.0, 26.8, 24.8, 22.8. HRMS: (ESI) $[M+H]^+$ calcd. for $C_{30}H_{35}N_2O_3$, 471.2647, observed, 471.2642.

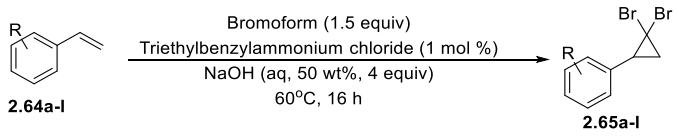
3.4 Synthetic Procedures and Characterization Data for Novel Compounds in Chapter Two:

General Procedure 2A for the Synthesis of Dibromocyclopropane precursors 2.65a-l:

Styrene (1.0 equiv, bromoform (1.5 equiv), and triethylbenzylammonium chloride (0.01 equiv) were added to a 25 mL round bottomed flask equipped with a stir bar. The flask was attached to a reflux condenser under nitrogen and heated to 60 ^{o}C with stirring. An aqueous solution of NaOH (50 wt %, 4 equiv) was added semi-dropwise to the solution such that the

temperature of the reaction was maintained. After addition of this solution, a dark purple and highly viscous reaction mixture was observedd. The mixture was allowed to stir overnight (16 h).

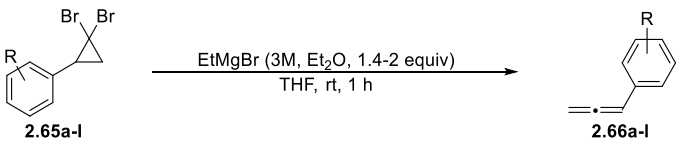
The product mixture was quenched with water and extracted thrice with chloroform. The combined organic layers were dried over sodium sulfate and filtered. After removal of the solvent *in vacuo*, the remaining residue was purified by either flash chromatography (100% hexane) or Kugel rohr distillation to furnish the products as viscous oils.



General Procedure 2B for the Synthesis of Phenylallene Derivatives (2.66a-l) from Dibromocyclopropane precursors 2.65a-l:

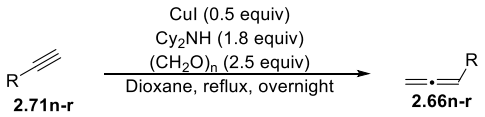
The dibromocylopropane precursor was dissolved in THF (0.5 M) and stirred under nitrogen. A solution of EtMgBr (3 M in diethyl ether, 1.4-2 equiv) was added dropwise to the solution, which turned from clear to yellow. After completion of Grignard addition, the solution was allowed to stir until all dibromocyclopropane was consumed as monitored by TLC.

The reaction mixture was then quenched with water (added dropwise) and extracted with hexanes or petroleum ether thrice. The combined organic layers were dried over sodium sulfate, filtered, and removed *in vacuo* to furnish a yellow residue. This residue was then purified by a silica plug (eluting with hexanes) or flash column (again, eluting with hexanes) to furnish the pure allene.



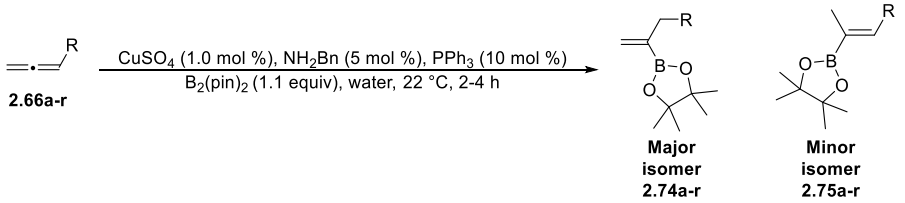
General Procedure 2C for the Synthesis of Allenes 2.66n-r from Terminal Alkynes:

Paraformaldehyde (2.5 equiv), copper (I) iodide (0.5 equiv), dioxane, alkyne **2.71n-r** (1 equiv), and dicyclohexylamine (1.8 equiv) were added to a round bottom flask equipped with a stirbar and attached to a reflux condenser under nitrogen. The mixture was stirred overnight (16 h) at reflux during which time a dark solution formed. Deionized water was then added to the reaction mixture, and the mixture was extracted thrice with diethyl ether, dried over sodium sulfate, and filtered. The ether was removed *in vacuo* and the resulting residue was purified by flash chromatography (eluting with hexanes) to furnish the allene products as clear, viscous oils.



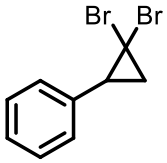
General Procedure 2D for the Synthesis of Protoborated Allene Products 2.74/2.75a-r:

Reactions were run in a 2 DR vial equipped with a small stir bar. The vial was charged with allene (1 equiv), bis(pinacoloto)diboron (1.1 equiv), benzylamine (5 mol %), and triphenylphosphine (10 mol%). Ultrapure water and a 2.6 mg/mL $CuSO_4$ solution were added in equal amounts such that 1 mol % $CuSO_4$ was dispensed into the reaction mixture. Immediately upon addition of copper solution, the mixture turned black. The reaction was stirred and monitored by TLC/GC until all starting material was consumed. The reaction was quenched with chloroform, and the water layer was extracted thrice with chloroform. Upon removal of chloroform *in vacuo*, the resulting yellow residue was purified by flash chromatography (0-4% EtOAc in hexanes) to yield borylation products as off-yellow oils.



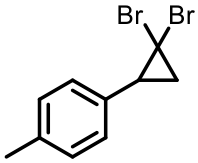
Characterization Data for Dibromocyclopropanes 2.65a-l:

(2,2-dibromocyclopropyl)benzene (2.65a)



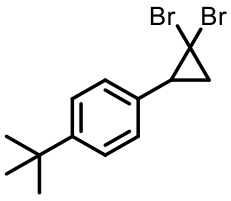
Synthesized by General Procedure 2A in 47% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[13]

1-(2,2-dibromocyclopropyl)-4-methylbenzene (2.65b)



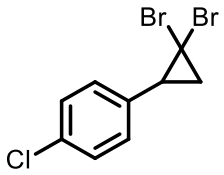
Synthesized by General Procedure 2A in 42% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[13]

1-(tert-butyl)-4-(2,2-dibromocyclopropyl)benzene (2.65c)



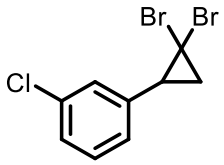
Synthesized by General Procedure 2A in 96% yield; isolated as a clear oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 2H), 7.22 – 7.14 (m, 2H), 2.93 (ddd, *J* = 10.5, 8.3, 0.8 Hz, 1H), 2.12 (dd, *J* = 10.6, 7.7 Hz, 1H), 1.99 (dd, *J* = 8.3, 7.7 Hz, 1H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.69, 133.07, 128.65, 125.33, 35.74, 34.73, 31.47, 29.04, 27.51.

1-chloro-4-(2,2-dibromocyclopropyl)benzene (2.65d)



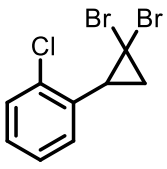
Synthesized by General Procedure 2A in 50% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[13]

1-chloro-3-(2,2-dibromocyclopropyl)benzene (2.65e)



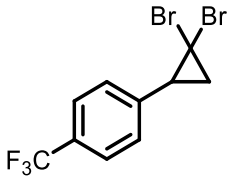
Synthesized by General Procedure 2A in 43% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-chloro-2-(2,2-dibromocyclopropyl)benzene (2.65f)



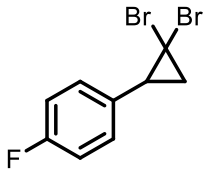
Synthesized by General Procedure 2A in 51% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-(2,2-dibromocyclopropyl)-4-(trifluoromethyl)benzene (2.65g)



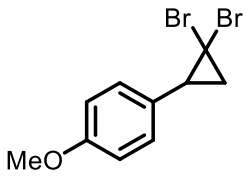
Synthesized by General Procedure 2A in 52% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-(2,2-dibromocyclopropyl)-4-fluorobenzene (2.65i)



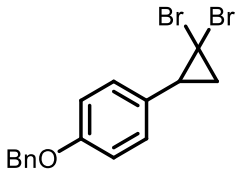
Synthesized by General Procedure 2A in 41% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-(2,2-dibromocyclopropyl)-4-methoxybenzene (2.65j)



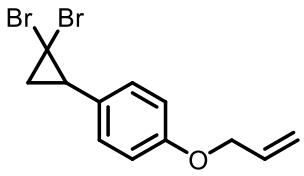
Synthesized by General Procedure 2A in 32% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-(benzyloxy)-4-(2,2-dibromocyclopropyl)benzene (2.65k)



Synthesized by General Procedure 2A in 84% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[15]

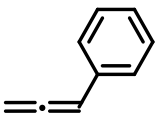
1-(allyloxy)-4-(2,2-dibromocyclopropyl)benzene (2.65l):



Synthesized by General Procedure 2A in 15% yield; isolated as a clear liquid. Product contains ethyl acetate impurities as was taken forward crude in General Procedure 2B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.11 (m, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.12 – 5.94 (m, 1H), 5.40 (ddd, *J* = 17.2, 1.6, 0.5 Hz, 1H), 5.27 (dqd, *J* = 10.5, 1.4, 0.5 Hz, 1H), 4.52 (dt, *J* = 5.3, 1.5 Hz, 2H), 2.92 – 2.77 (m, 1H), 2.12 – 2.05 (m, 1H), 1.93 (dd, *J* = 8.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.21, 133.30, 130.21, 130.11, 128.48, 117.91, 114.60, 68.97, 35.46, 29.35, 27.45.

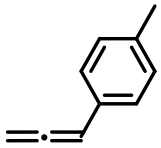
<u>Characterization Data for Allenes 2.66a-r:</u>

Propa-1,2-dien-1-ylbenzene (2.66a):



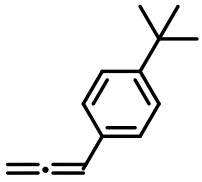
Synthesized by **General Procedure 2B** in 40% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[16]

1-methyl-4-(propa-1,2-dien-1-yl)benzene (2.66b):



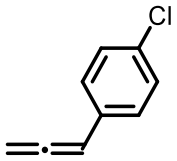
Synthesized by **General Procedure 2B** in 82% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[16]

1-(tert-butyl)-4-(propa-1,2-dien-1-yl)benzene (2.66c):



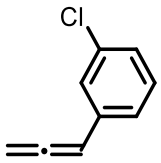
Synthesized by **General Procedure 2B** in 95% yield. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[17]

1-chloro-4-(propa-1,2-dien-1-yl)benzene (2.66d):



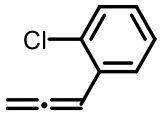
Synthesized by **General Procedure 2B** in 97% yield as a clear oil. 2B in 82% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[16]

1-chloro-3-(propa-1,2-dien-1-yl)benzene (2.66e):



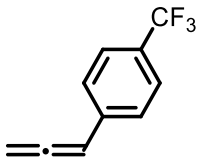
Synthesized by **General Procedure 2B** in 69% yield, obtained as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-chloro-2-(propa-1,2-dien-1-yl)benzene (2.66f):



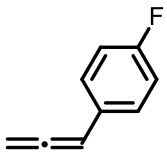
Synthesized by **General Procedure 2B** in 95 % yield, obtained as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-(propa-1,2-dien-1-yl)-4-(trifluoromethyl)benzene (2.66g):



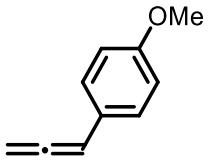
Synthesized by **General Procedure 2B** in 57% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[14]

1-fluoro-4-(propa-1,2-dien-1-yl)benzene (2.66i):



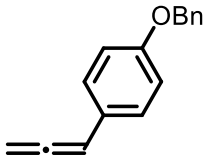
Synthesized by **General Procedure 2B** in 60% yield; isolated as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[16]

1-methoxy-4-(propa-1,2-dien-1-yl)benzene (2.66j):



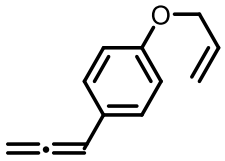
Synthesized by **General Procedure 2B**; isolated in 56% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[18]

1-(benzyloxy)-4-(propa-1,2-dien-1-yl)benzene (2.66k):



Synthesized by **General Procedure 2B**, isolated as a clear oil in 83% yield. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[15]

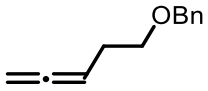
1-(allyloxy)-4-(propa-1,2-dien-1-yl)benzene (2.66l):



Synthesized by **General Procedure 2B**, isolated in 74% yield as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 2H), 6.93 – 6.82 (m, 2H), 6.12 (t, *J* = 6.8 Hz, 1H), 6.05 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 5.41 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.29 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.12 (dd, *J* = 6.8, 0.6 Hz, 2H), 4.53 (dt, *J* = 5.3, 1.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.51, 157.83,

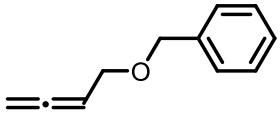
133.37, 127.87, 126.43, 117.85, 115.12, 93.48, 78.92, 69.00. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{20}BClO_2$ 172.09, observed 172.1.

((penta-3,4-dien-1-yloxy)methyl)benzene (2.66n):



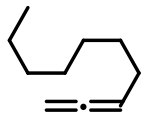
Synthesized by **General Procedure 2C** in 94% yield; isolated as a yellow oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[19]

((buta-2,3-dien-1-yloxy)methyl)benzene (2.66o):



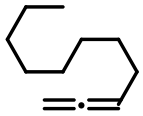
Synthesized by **General Procedure 2C**; isolated as a dark oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[20]

Deca-1,2-diene (2.66p):



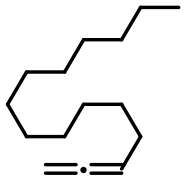
Synthesized by **General Procedure 2C**; isolated in 15% yield as a clear oil. The terminal protons on the allene display a doublet of triplets due to both ^{4}J coupling and ^{5}J (homoallenic) coupling, the latter of which has been readily established in the literature for allene ^{1}H spectra.[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (p, J = 6.8 Hz, 1H), 4.65 (dt, J = 6.6, 3.2 Hz, 2H), 1.99 (ddt, J = 10.9, 6.7, 3.4 Hz, 2H), 1.47 – 1.18 (m, 10H), 0.98 – 0.81 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.60, 90.27, 74.66, 32.00, 29.30, 29.27, 29.21, 28.43, 22.81, 14.26.

Undeca-1,2-diene (2.66q):



Synthesized by **General Procedure 2C**; isolated in 35% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[22]

Pentadeca-1,2-diene (2.66r):

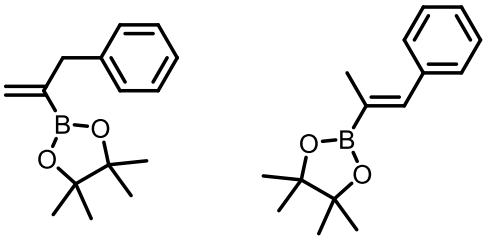


Synthesized by **General Procedure 2C**; isolated in 89% yield as a clear oil. ^{1}H and ^{13}C NMR spectra are consistent with the literature.[23]

Characterization of Protoboration Products 2.74/2.75a-r:

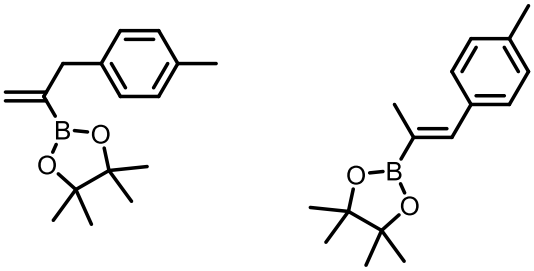
Isolated peaks in the ^{1}H and ^{13}C spectra corresponding solely to the minor isomer are labelled with an asterisk. In some instances, the highest quality spectrum was obtained after repurification of the borylation products. Because products **2.74a-r** degrade more rapidly than **2.75a-r**, the isomeric ratios in those spectra do not reflect the initial isomeric ratios, and a second ^{1}H spectrum is given in these cases to show the true ratios.

4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane (2.74a) and (Z)-4,4,5,5-tetramethyl-2-(1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane (2.75a):



Isolated as an off yellow oil, 78% yield, 87:13 isomeric ratio **2.74a** to **2.75a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.04** (m, 5H), 5.76 (d, *J* = 2.8 Hz, 1H), 5.45 (s, 1H), 3.41 (s, 2H), 1.92* (d, *J* = 1.4 Hz, 3H), 1.23* (s, 12H), 1.13 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.49*, 140.80, 129.94, 129.53*, 129.31, 129.26*, 128.20, 128.15*, 127.21*, 125.80, 83.63*, 83.60, 41.50, 24.99*, 24.81, 16.04*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.09. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{21}BO_2$ 244.16, observed 244.1.

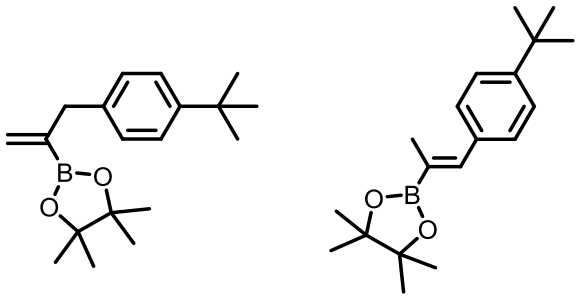
4,4,5,5-tetramethyl-2-(3-(p-tolyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (2.74b) and (Z)-4,4,5,5-tetramethyl-2-(1-(p-tolyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (2.75b):



Isolated as an off yellow oil, 67% yield, 89:11 isomeric ratio of **2.74b** to **2.75b.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31* (d, *J* = 7.9 Hz, 2H), 7.23* (s, 1H), 7.17* (d, *J* = 7.8 Hz, 2H), 7.12 – 7.05 (m, 4H), 5.85 – 5.79 (m, 1H), 5.52 (s, 1H), 3.45 (s, 3H), 2.36* (s, 3H), 2.32 (s, 3H), 2.01* (s, 3H), 1.33* (s, 12H), 1.24 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.49*, 137.72, 137.03*, 135.30*, 135.15, 129.75, 129.57*, 129.13, 128.92, 128.89*, 83.58, 83.56*, 40.98, 25.00*, 24.85, 21.38*,

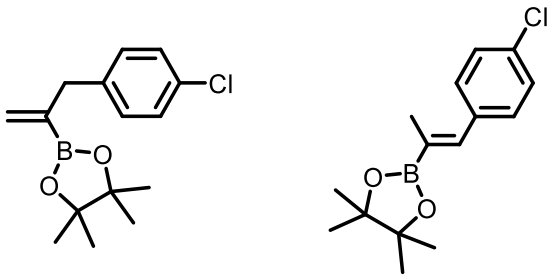
21.14, 16.06*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.16. LRMS: (EI) $[M]^{+\cdot}$ $C_{16}H_{23}BO_2$ 258.18, observed 258.3.

2-(3-(4-(tert-butyl)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74c) and (Z)-2-(1-(4-(tert-butyl)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75c):



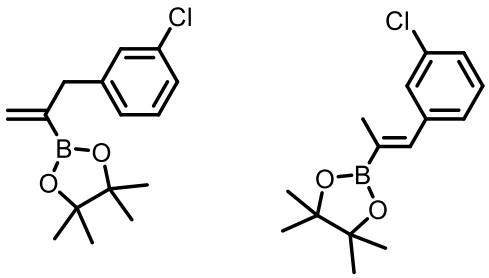
Isolated as off yellow oil, 47% yield, 90:10 isomeric ratio of **2.74c** to **2.75c**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33* (q, *J* = 8.6 Hz, 4H), 7.24 (d, *J* = 4.2 Hz, 2H), 7.18* (s, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.79 (s, 1H), 5.49 (s, 1H), 3.42 (s, 2H), 1.98* (s, 3H), 1.30* (s, 9H), 1.29* (s, 12H), 1.27 (s, 9H), 1.19 (s, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.21*, 148.55, 142.37*, 137.73, 129.76, 129.41*, 128.91, 125.12, 83.60, 40.88, 34.73*, 34.46, 31.57, 31.44*, 25.00*, 24.83, 16.15*.^{11}B NMR (128 MHz, $CDCl_3$) δ 30.07. LRMS: (EI) $[M]^{+\cdot}$ $C_{19}H_{29}BO_2$ 300.23, observed 300.3.

2-(3-(4-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74d) and (Z)-2-(1-(4-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75d):



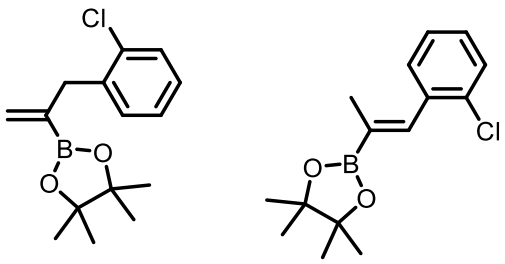
Isolated as yellow oil, 87% yield, 90:10 isomeric ratio **2.74d** to **2.75d**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31* (s, 4H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.17* (s, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 5.83 (s, 1H), 5.53 (s, 1H), 3.43 (s, 2H), 1.96* (s, 3H), 1.31 (s, 12H), 1.21 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.13*, 139.39, 131.60, 130.80*, 130.61, 130.31, 128.40*, 128.31, 83.73, 40.96, 25.01*, 24.85, 16.01*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.92. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{20}BClO_2$ 278.12, observed 278.1.

2-(3-(3-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74e) and (Z)-2-(1-(4-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75e):



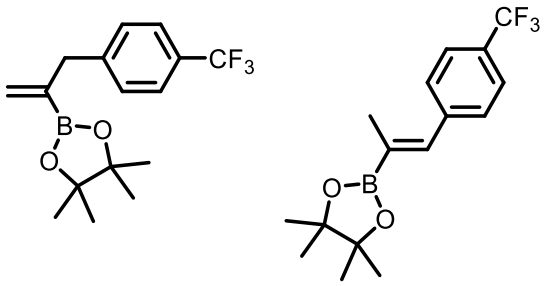
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 – 6.96 (m, 4H), 5.77 (d, *J* = 2.3 Hz, 1H), 5.48 (s, 1H), 3.36 (s, 2H), 1.92 – 1.86* (m, 3H), 1.23* (s, 12H), 1.13 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.03, 140.91*, 133.97, 130.50, 129.44, 129.35, 127.61*, 127.40, 127.22*, 126.00, 83.74, 41.35, 24.99*, 24.82, 16.0*.

2-(3-(2-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74f) and (Z)-2-(1-(2-chlorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75f):



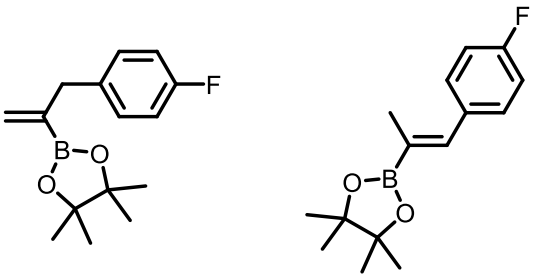
Isolated as yellow oil, 87% yield, 90:10 isomeric ratio **2.74f** to **2.75f.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.12** (m, 4H), 5.92 (s, 1H), 5.47 (s, 1H), 3.62 (s, 2H), 1.89* (s, 3H), 1.35 (s, 12H), 1.27 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.43*, 138.41, 136.22*, 134.53, 133.74*, 131.26, 130.79*, 130.70, 129.48*, 129.41, 128.42*, 127.39, 126.55, 126.11*, 83.68, 38.23, 24.99*, 24.85, 15.97*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.05. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{20}BClO_2$ 278.12, observed 278.1.

4,4,5,5-tetramethyl-2-(3-(4-(trifluoromethyl)phenyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (2.74g) and (Z)-4,4,5,5-tetramethyl-2-(1-(4-(trifluoromethyl)phenyl)prop-1-en-2-yl)-1,3,2-dioxaborolane (2.75g)



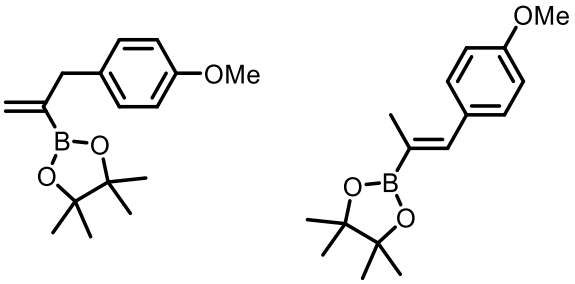
Isolated as a yellow oil, 19% yield, 93:7 isomeric ratio **2.74g** to **2.75g**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 5.80 (d, *J* = 3.0 Hz, 1H), 5.48 (d, *J* = 3.4 Hz, 1H), 3.45 (s, 2H), 1.90* (d, *J* = 1.9 Hz, 3H), 1.24* (s, 12H), 1.13 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.94, 129.65, 128.33, 127.05 (q, *J* = 32.2 Hz), 124.49 (q, *J* = 271.7 Hz), 123.96 (q, *J* = 3.8 Hz), 82.62, 40.22, 28.68, 23.64. ^{11}B NMR (128 MHz, $CDCl_3$) δ 29.80.

2-(3-(4-fluorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74i) and (Z)-2-(1-(4-fluorophenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75i):



Isolated as a yellow oil, 19% isolated yield, 50% NMR yield, 83:17 isomeric ratio **2.74i** to **2.75i**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.31* (m, 2H), 7.18* (s, 1H), 7.17 – 7.12 (m, 2H), 7.03* (t, *J* = 8.6 Hz, 2H), 6.94 (t, *J* = 8.6 Hz, 2H), 5.82 (s, 1H), 5.53 (s, 1H), 3.44 (s, 2H), 1.97* (s, 3H), 1.31* (s, 12H), 1.20 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.45 (d, *J* = 243.0 Hz), 141.30, 136.48 (d, *J* = 3.0 Hz), 131.21* (d, *J* = 8.1 Hz), 130.60 (d, *J* = 7.7 Hz), 129.98, 114.91 (d, *J* = 20.9 Hz), 100.15*, 83.69, 40.84, 25.01*, 24.83, 15.93*.^{11}B NMR (128 MHz, $CDCl_3$) δ 29.98. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{20}BFO_2$ 262.15, observed 262.3.

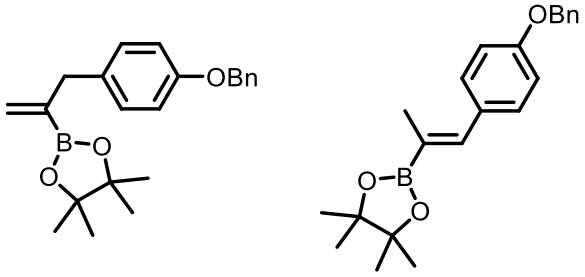
2-(3-(4-methoxyphenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74j) and (Z)-2-(1-(4-methoxyphenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75j:



Isolated as an off yellow oil, 46% yield, 67:33 isomeric ratio **2.74j** to **2.75j**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32* (m, 2H), 7.18* (d, *J* = 1.8 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.92 – 6.85* (m, 2H), 6.85 – 6.77 (m, 2H), 5.81 (dt, *J* = 3.3, 1.2 Hz, 1H), 5.51 (dt, *J* = 3.4, 1.6 Hz, 1H), 3.82* (s, 3H), 3.78 (s, 3H), 3.42 (d, *J* = 1.4 Hz, 2H), 2.00* (d, *J* = 1.7 Hz, 3H), 1.31* (s, 12H), 1.21 (s, 12H).

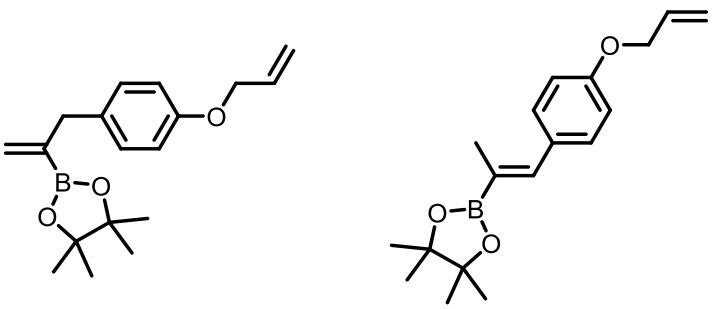
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.78*, 157.85, 142.09*, 132.89, 131.07*, 130.88, 130.18*, 129.57, 113.65, 113.60*, 83.60, 83.54*, 55.37, 55.35*, 40.61, 24.99*, 24.84, 16.07*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.21. LRMS: (EI) $[M]^{+\cdot}$ $C_{16}H_{23}BO_3$ 274.17, observed 274.3.

2-(3-(4-(benzyloxy)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74k) and (Z)-2-(1-(3-(benzyloxy)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75k):



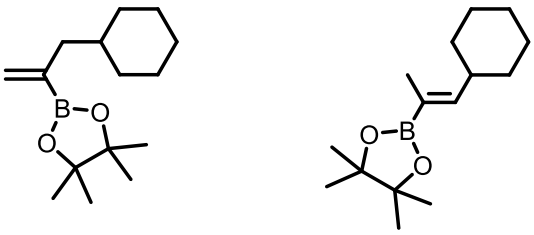
White solid, 37%, 66:34 isomeric ratio **2.74k** to **2.75k**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.30** (m, 5H from **2.74k** and 7H from **2.75k**), 7.20* (s, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.97* (d, *J* = 8.1 Hz, 0H), 6.90 (d, *J* = 7.8 Hz, 2H), 5.82 (s, 1H), 5.53 (s, 1H), 5.08* (s, 2H), 5.05* (s, 2H), 3.44 (s, 2H), 2.02* (s, 3H), 1.32* (s, 12H), 1.22 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.03*, 157.09, 142.04*, 137.42, 137.07*, 133.22, 131.14*, 131.10*, 130.22, 129.60, 128.74*, 128.67, 128.13*, 127.98, 127.65*, 127.61, 114.67, 114.52*, 83.61, 83.56*, 70.16, 70.11*, 40.67, 25.00*, 24.84, 16.10*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.13. LRMS: (EI) $[M]^{+\cdot}$ $C_{22}H_{27}BO_3$ 350.21, observed 350.3.

2-(3-(4-(allyloxy)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74l) and (Z)-2-(1-(4-(allyloxy)phenyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75l):



Isolated as an off yellow oil, 49% yield, 75:25 isomeric ratio. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35* (d, *J* = 8.6 Hz, 2H), 7.17* (s, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.89* (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.06** (ddq, *J* = 15.7, 10.3, 5.0 Hz, 1H), 5.81 – 5.79 (m, 1H), 5.51 (s, 1H), 5.41** (dd, *J* = 17.2, 10.3 Hz, 1H), 5.28** (t, *J* = 11.6 Hz, 1H), 4.55* (d, *J* = 5.2 Hz, 2H), 4.51 (d, *J* = 5.2 Hz, 2H), 3.41 (s, 2H), 1.99* (s, 3H), 1.31* (s, 12H), 1.21 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.69*, 156.75, 141.91*, 133.56, 133.25, 133.00, 130.90*, 130.02, 129.38, 117.67*, 117.40, 114.43, 114.27*, 83.44, 83.39*, 68.86, 68.77*, 40.53, 24.84*, 24.69, 15.91*. ^{11}B NMR (128 MHz, $cdcl_3$) δ 30.02. HRMS: (ESI) $[M+H]^+$ $C_{18}H_{25}BO_3$ 301.20, observed 301.1968.

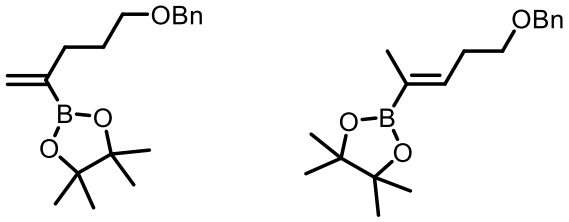
2-(3-cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74m) and (Z)-2-(1-cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75m):



Isolated as a yellow oil, 84% yield, 78:22 isomeric ratio **2.74m** to **2.75m**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.11* (d, *J* = 8.7 Hz, 1H), 5.81 – 5.70 (m, 1H), 5.53 (s, 1H), 2.43 – 2.26* (m, 1H), 2.03 (d, *J* = 6.8 Hz, 2H), 1.74-1.58 (m, 6H), 1.25 (s, 12H), 1.22-1.05 (m, 3H), 0.84 (q, *J* = 11.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.89*, 130.01, 83.38, 83.14*, 43.44, 37.84, 37.66*, 33.33,

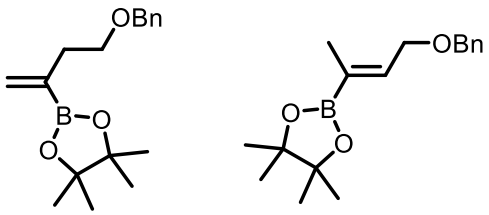
32.39*, 26.81, 26.55, 26.26*, 26.11*, 24.95*, 24.84, 14.01*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.16. LRMS: (EI) $[M]^{+\cdot}$ $C_{15}H_{27}BO_2$ 250.21, observed 250.3.

2-(5-(benzyloxy)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74n) and (Z)-2-(5-(benzyloxy)pent-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75n):



Isolated as a yellow oil, 34%, 93:7 isomeric ratio **2.74n** to **2.75n**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 5H), 6.38 – 6.28* (m, 1H), 5.79 (d, *J* = 3.3 Hz, 1H), 5.64 – 5.60 (m, 1H), 4.53* (s, 2H), 4.50 (s, 2H), 3.54 (t, *J* = 7.2 Hz, 2H), 3.48 (t, *J* = 6.7 Hz, 2H), 2.48* (q, *J* = 7.0 Hz, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 1.77 (dt, *J* = 14.1, 6.8 Hz, 2H), 1.71* (s, 3H), 1.26 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.87*, 138.83, 138.59*, 129.47, 128.46*, 128.43, 127.78, 127.63, 127.56*, 83.46, 83.29, 72.98*, 72.91, 70.16, 69.30*, 31.99, 29.51*, 29.26, 24.93*, 24.88, 14.19*. LRMS: (EI) $[M]^{+\cdot}$ Calculated for $C_{18}H_{27}BO_3$ 302.21, observed 302.3.

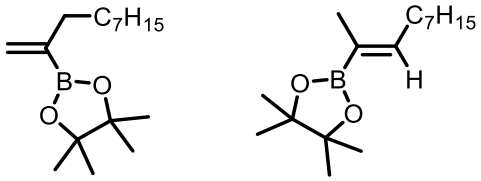
2-(4-(benzyloxy)but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74o)and (Z)-2-(4-(benzyloxy)but-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75o):



Isolated as a yellow oil, 53%, 72:18 isomeric ratio **2.74o** to **2.75o**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 5H), 6.48* (tq, *J* = 5.8, 1.7 Hz, 1H), 5.85 (dt, *J* = 3.5, 0.9 Hz, 1H), 5.70 (dt, *J* =

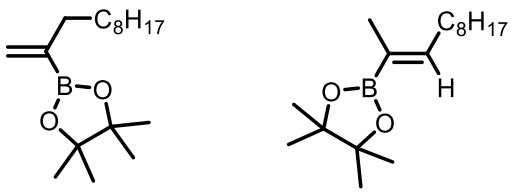
3.3, 1.4 Hz, 1H), 4.53* (s, 2H), 4.52 (s, 2H), 4.17 (dq, *J* = 5.8, 1.1 Hz, 2H), 3.56 (t, *J* = 7.0 Hz, 2H), 2.49 (tt, *J* = 7.0, 1.1 Hz, 3H), 1.69* (dd, *J* = 1.8, 0.9 Hz, 3H), 1.26* (s, 12H), 1.24 (s, 12H). ^{13}C NMR (101 MHz, cdcl$_3$) δ 141.91*, 138.83, 131.17, 128.47*, 128.40, 127.85*, 127.76, 127.67*, 127.50, 83.52, 72.82, 72.61*, 70.09, 67.13*, 35.87, 24.93*, 24.86, 14.45*. LRMS: (EI) $[M]^{+\cdot}$ Calcd. for $C_{17}H_{25}BO_3$ 288.19, observed 288.3.

2-(dec-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.74p) and (Z)-2-(dec-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.75p):



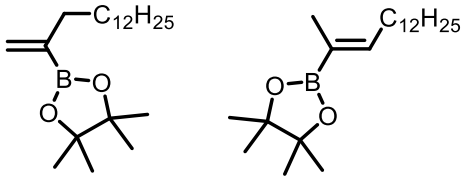
Isolated as a yellow oil, 48%. Isomeric ratio **2.74p** to **2.75p** is 74:26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.31* (t, *J* = 5.9 Hz, 1H), 5.83 – 5.68 (m, 1H), 5.58 (s, 1H), 2.12 (q, *J* = 7.3 Hz, 2H), 1.66* (s, 3H), 1.26 (s, 24H), 0.87 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.84*, 128.77, 83.39, 83.16*, 35.51, 32.06, 31.99*, 29.85*, 29.67, 29.64, 29.43, 29.37, 29.01*, 28.85*, 24.95*, 24.88, 22.84, 14.24, 13.98*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.16. LRMS: (EI) $[M]^{+\cdot}$ $C_{16}H_{31}BO_2$ 266.24, observed 266.3.

4,4,5,5-tetramethyl-2-(undec-1-en-2-yl)-1,3,2-dioxaborolane (2.74q) and (Z)-4,4,5,5-tetramethyl-2-(undec-2-en-2-yl)-1,3,2-dioxaborolane (2.75q):



Isolated as a yellow oil, 50% yield, 84:16 isomeric ratio **2.74q** to **2.75q**. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.31* (t, *J* = 6.0 Hz, 1H), 5.74 (s, 1H), 5.57 (s, 1H), 2.12 (t, *J* = 7.4 Hz, 2H), 1.66* (s, 3H), 1.43-1.20 (m, 26H), 0.87 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.83*, 128.76, 83.37, 83.15*, 35.50, 32.08, 29.85*, 29.73, 29.72, 29.68*, 29.65*, 29.49, 29.43, 29.38, 29.01*, 28.85*, 24.94*, 24.88, 22.83, 14.24, 13.97*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.13. LRMS: (EI) $[M]^{+\cdot}$ Calculated for $C_{17}H_{33}BO_2$ 280.26, observed 280.4.

4,4,5,5-tetramethyl-2-(pentadec-1-en-2-yl)-1,3,2-dioxaborolane (2.74r) and (Z)-4,4,5,5-tetramethyl-2-(pentadec-2-en-2-yl)-1,3,2-dioxaborolane (2.75r):



Yellow oil, 75% yield, 83:17 isomeric ratio **2.74r** to **2.75 r**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.32* (d, *J* = 6.4 Hz, 1H), 5.74 (s, 1H), 5.57 (s, 1H), 2.12 (t, *J* = 7.4 Hz, 2H), 1.66* (s, 3H), 1.44 – 1.16 (m, 34H), 0.87 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.82*, 128.77, 83.36, 83.13*, 35.51, 32.08, 29.86, 29.82, 29.79, 29.73, 29.52, 29.44, 29.39, 29.02, 28.85, 24.94*, 24.88, 22.84, 14.24, 13.96*. ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.15. LRMS: (EI) $[M]^{+\cdot}$ Calculated for $C_{21}H_{41}BO_2$ 336.32, observed 336.4.

3.4 References

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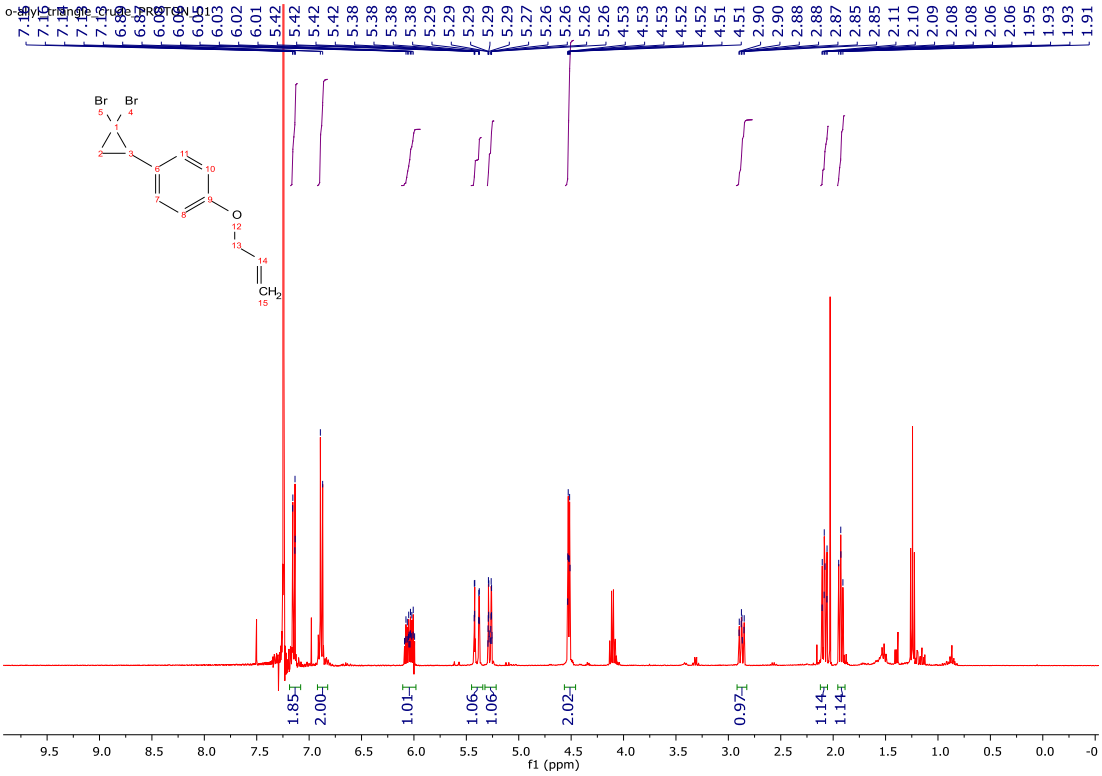
Appendix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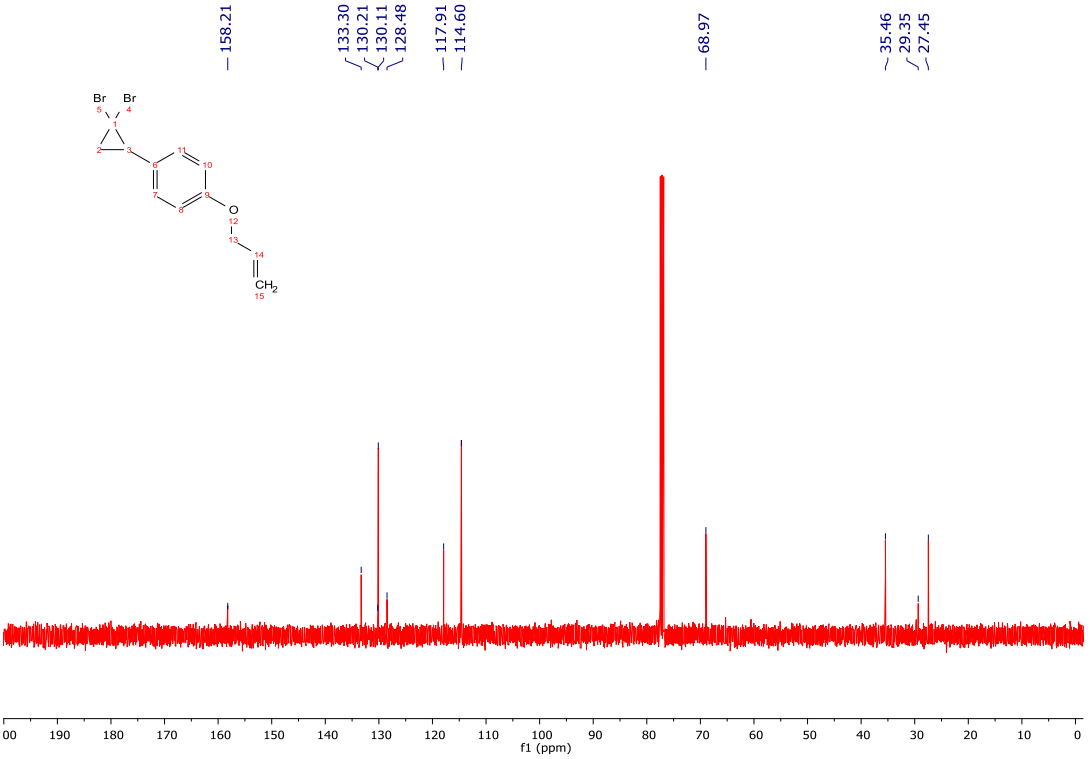
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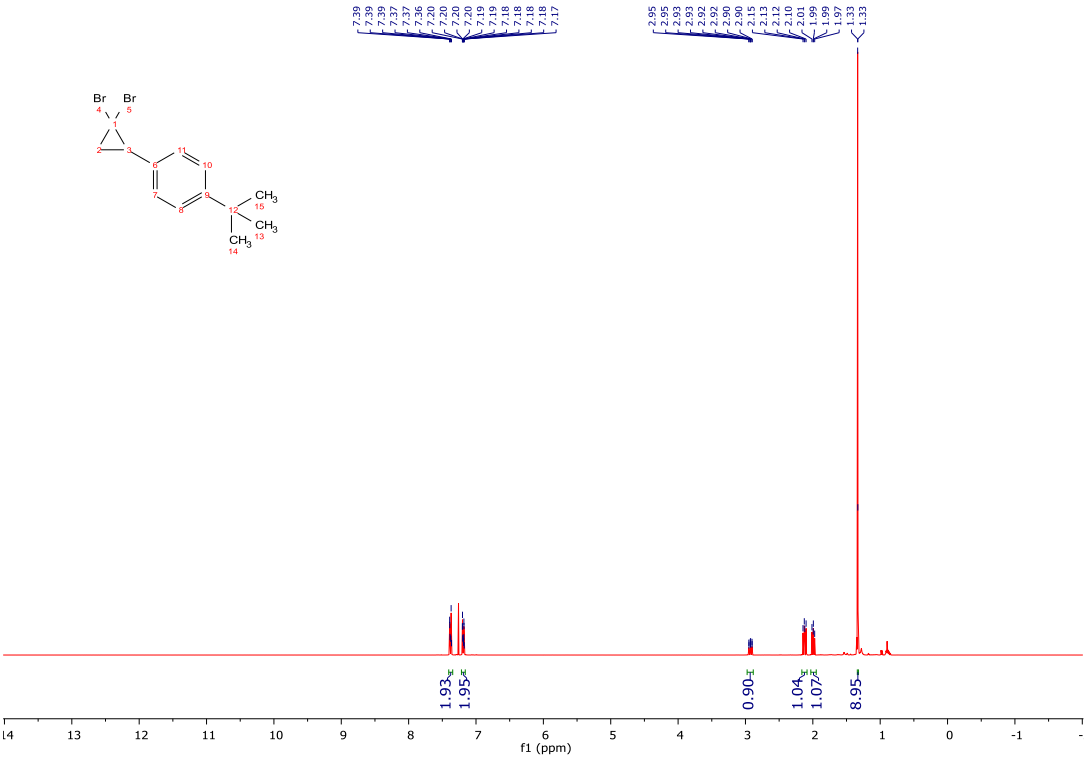
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7.17
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2.95
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2.92
2.92
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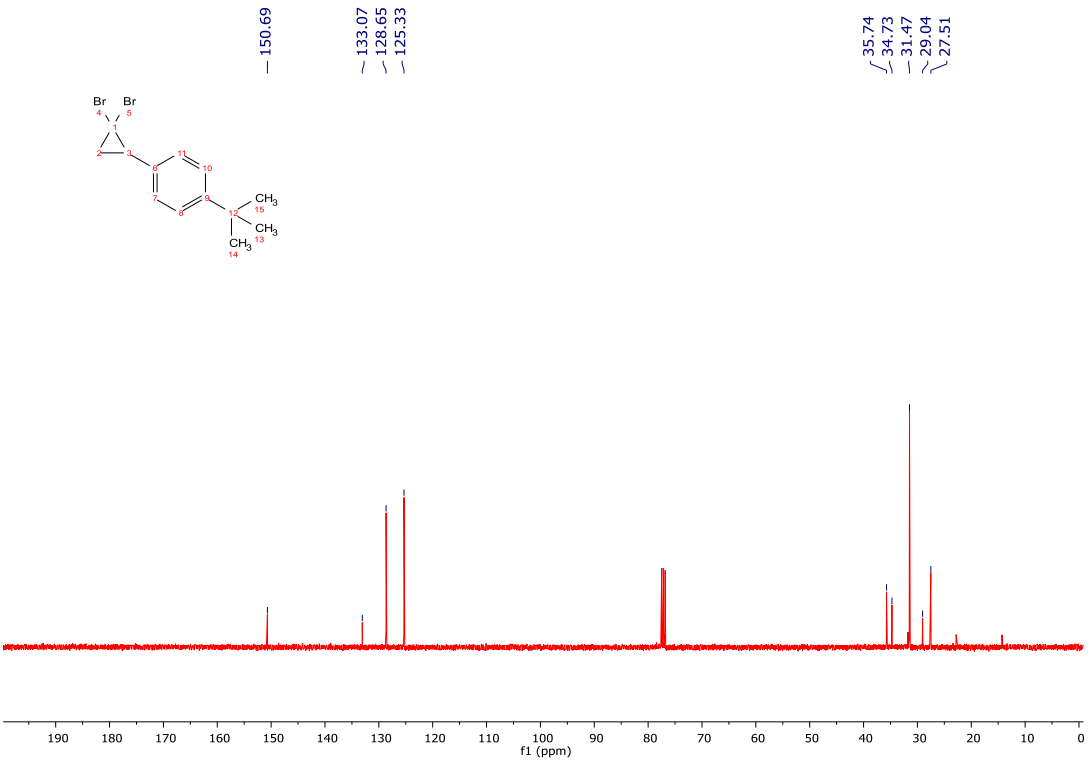
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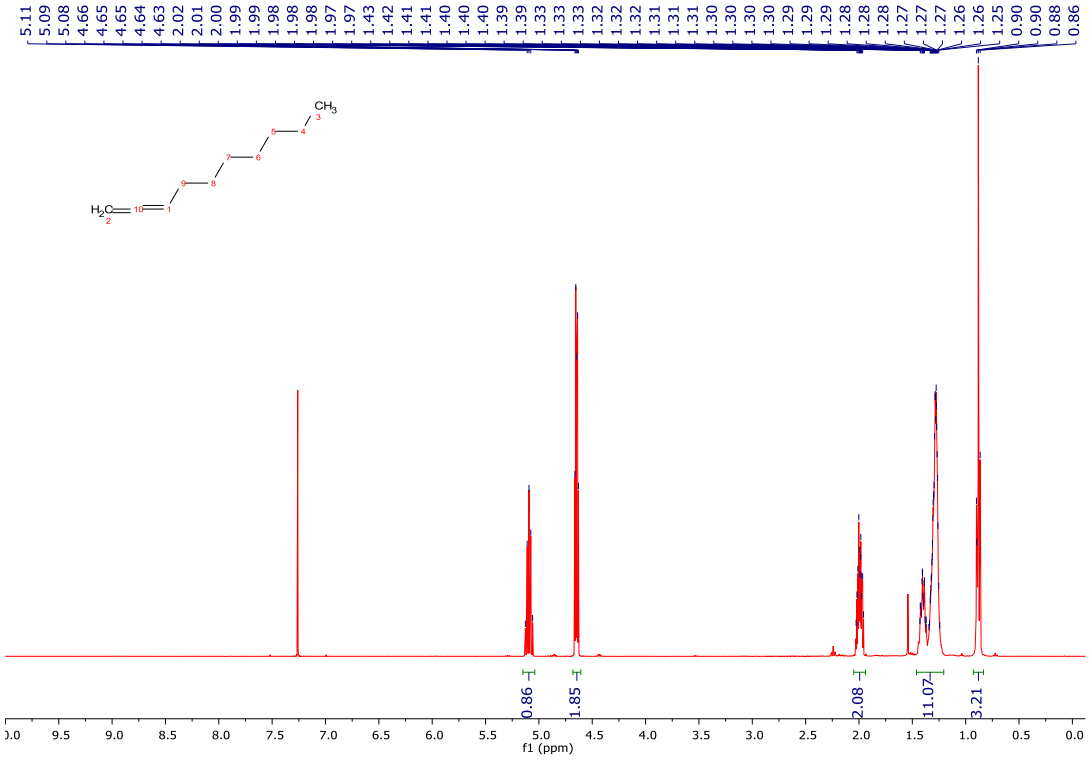
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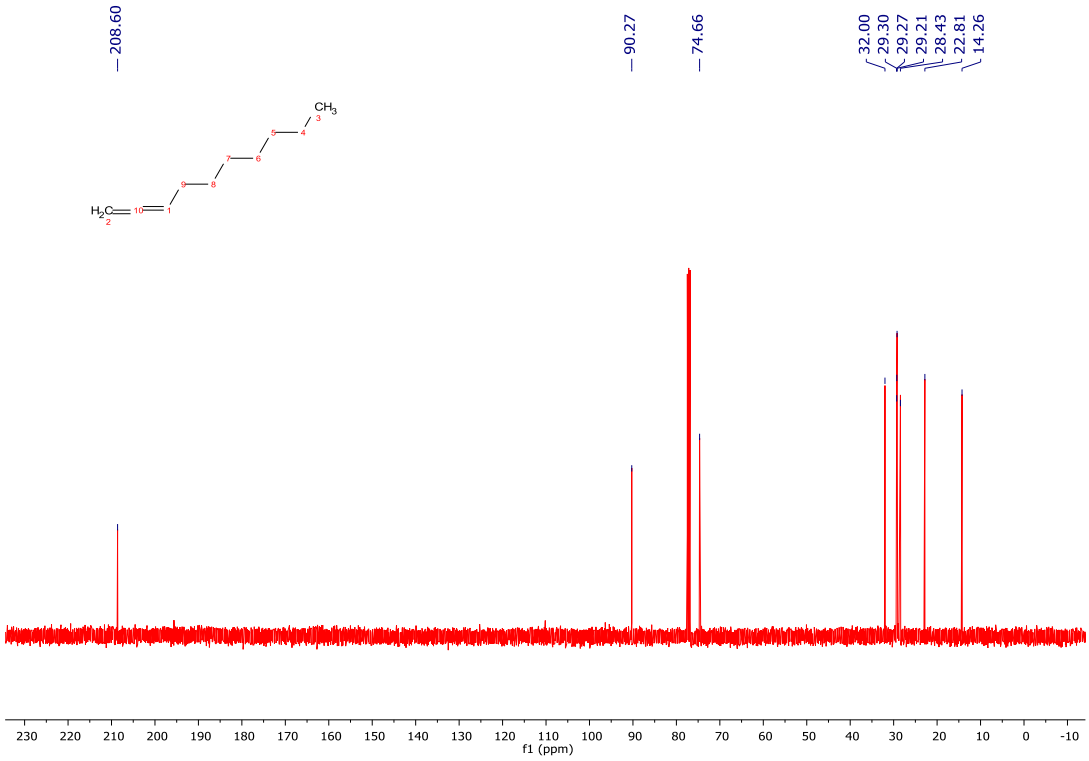
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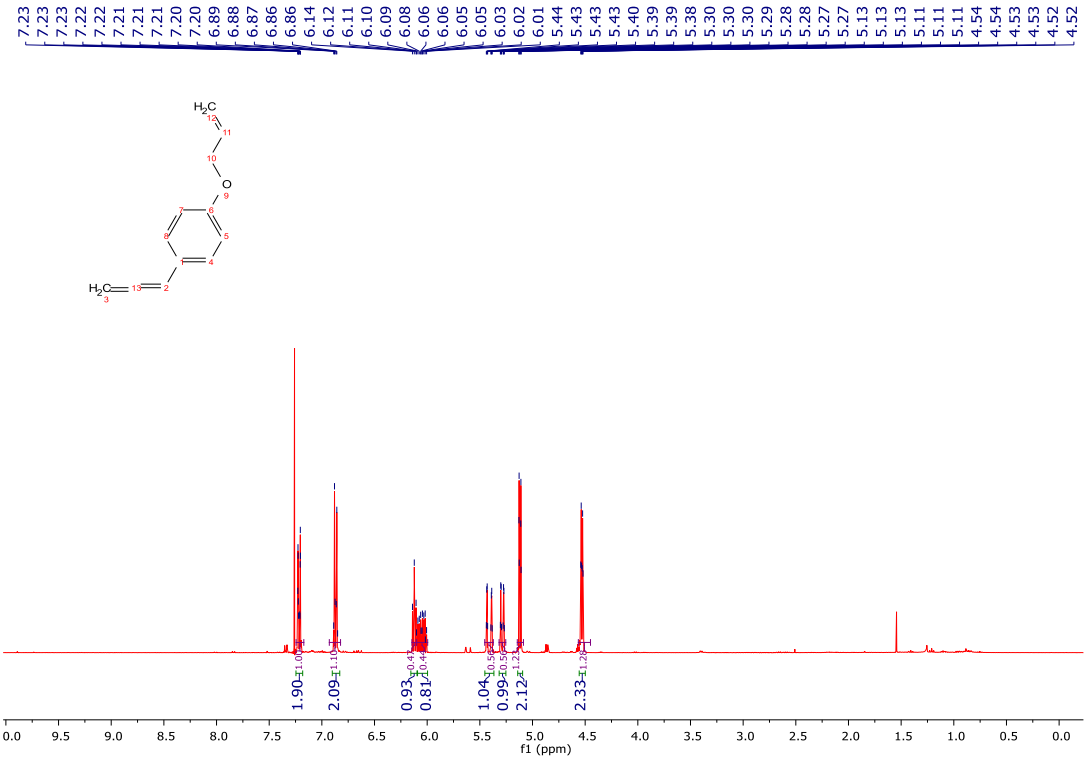
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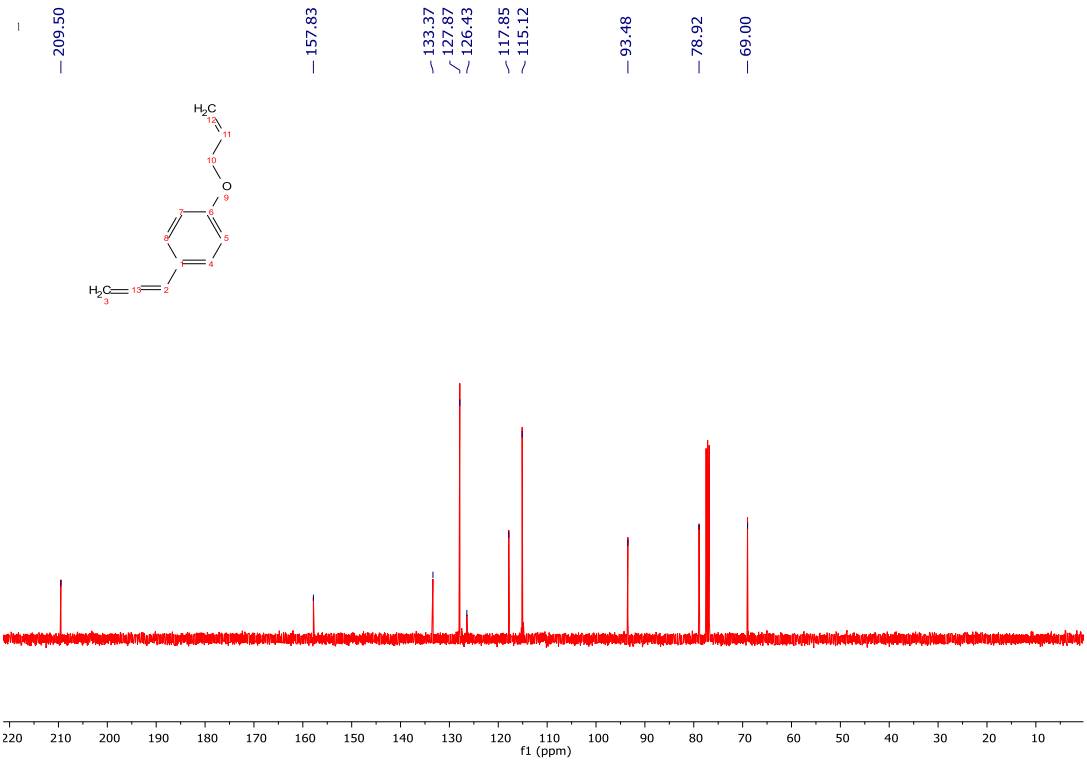
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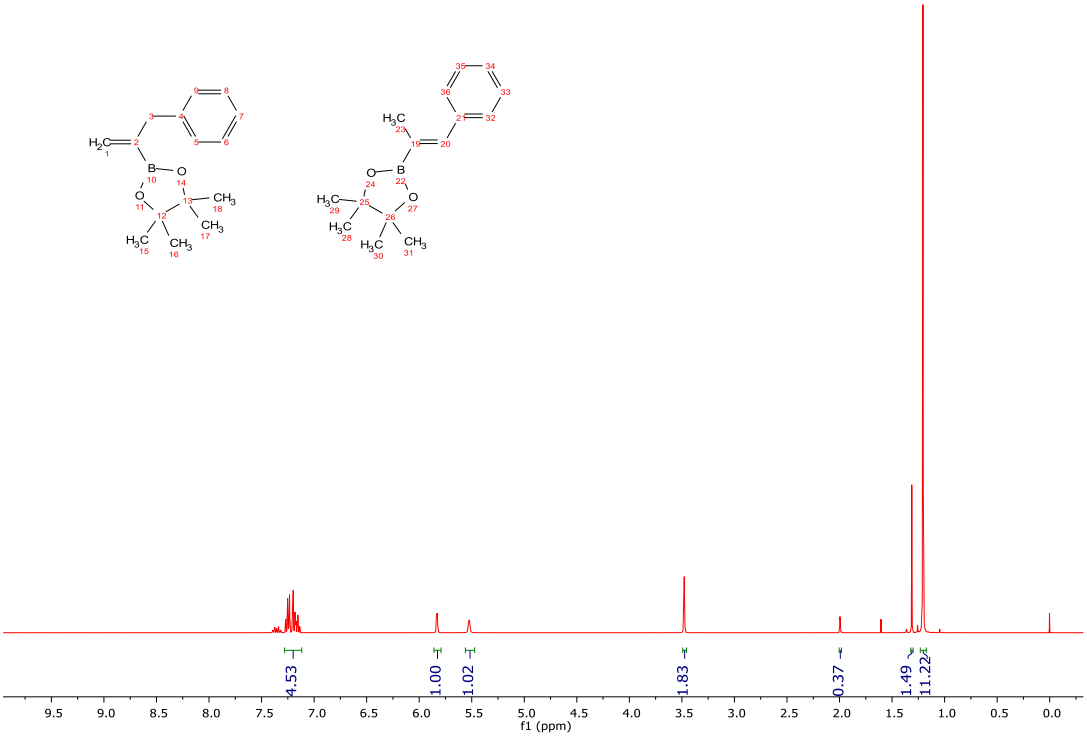
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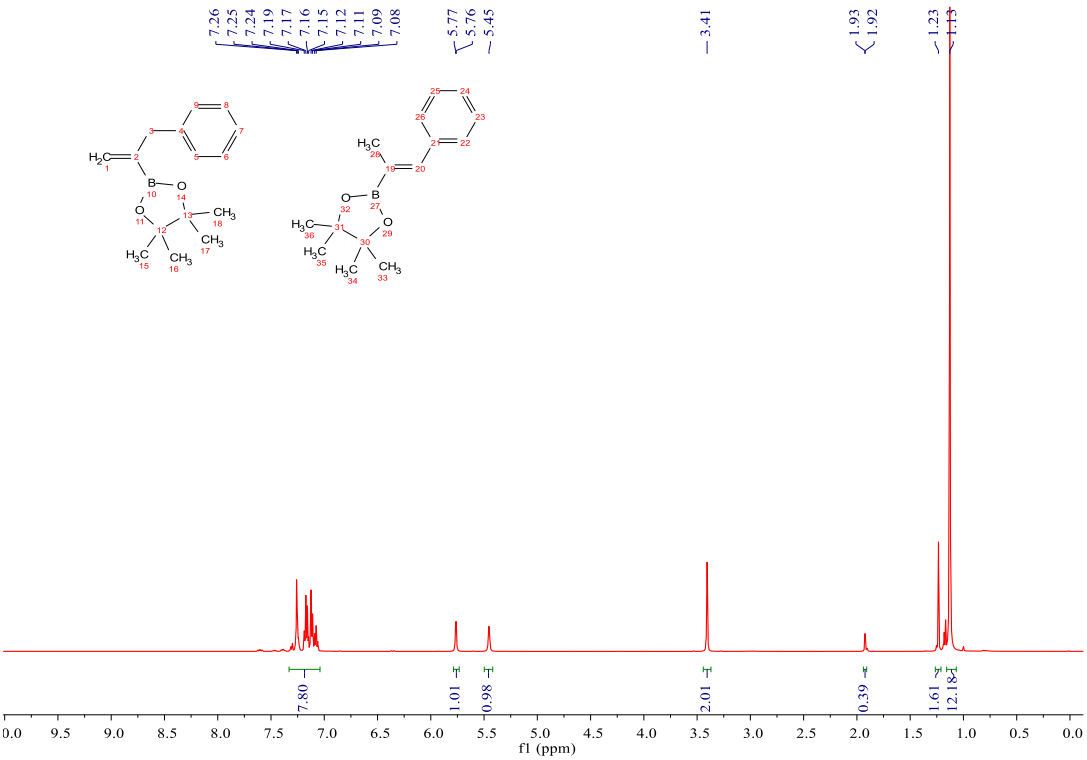
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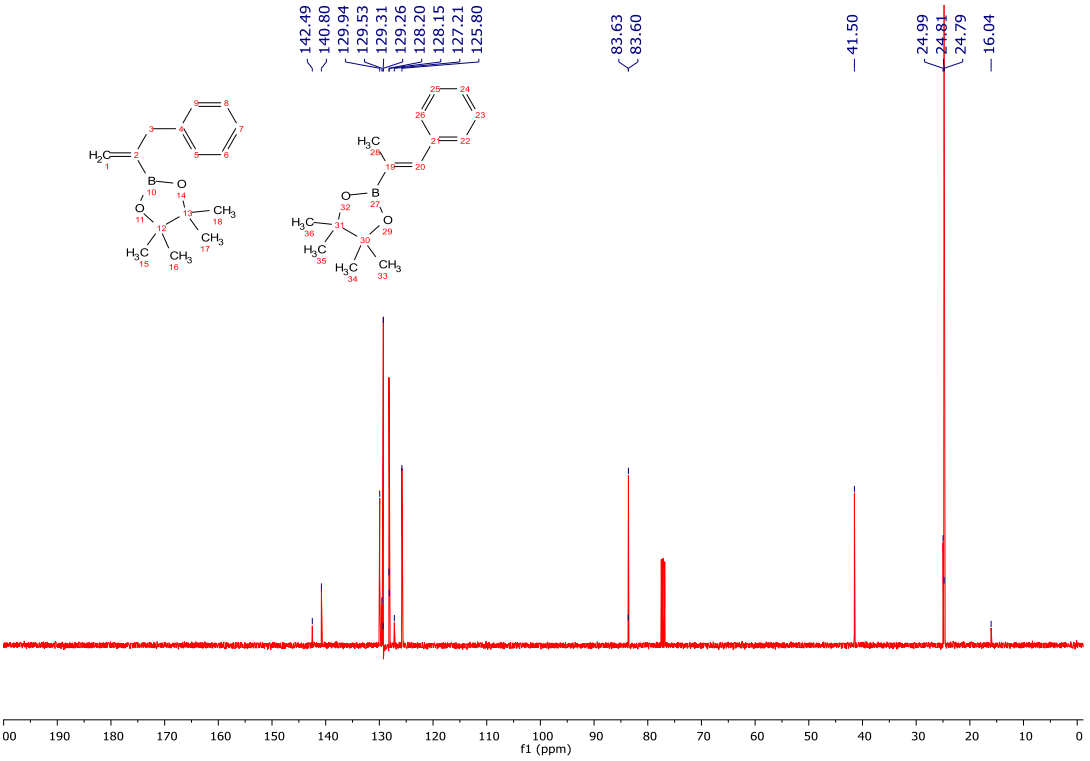
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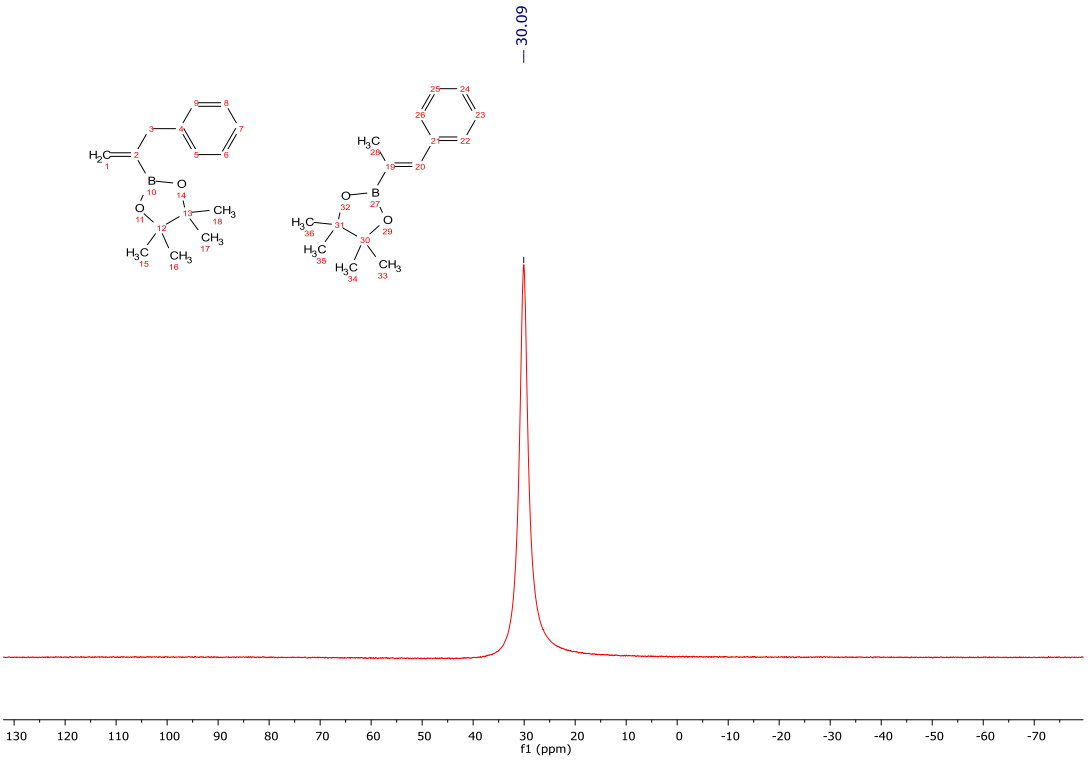
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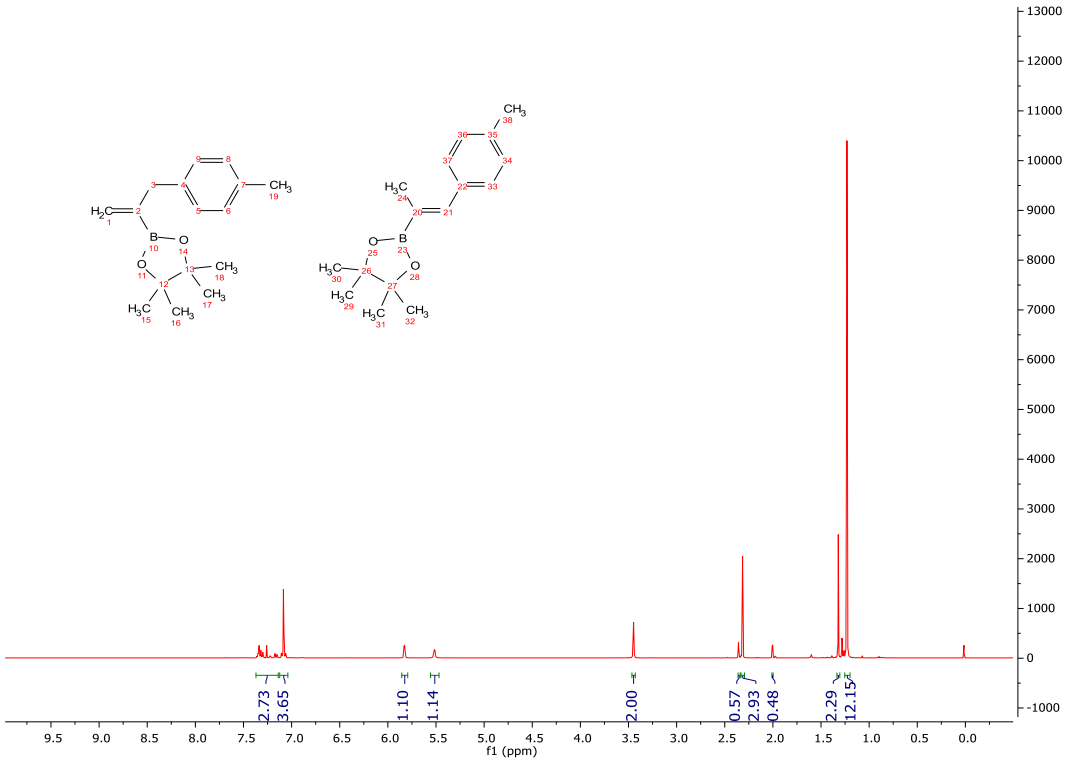
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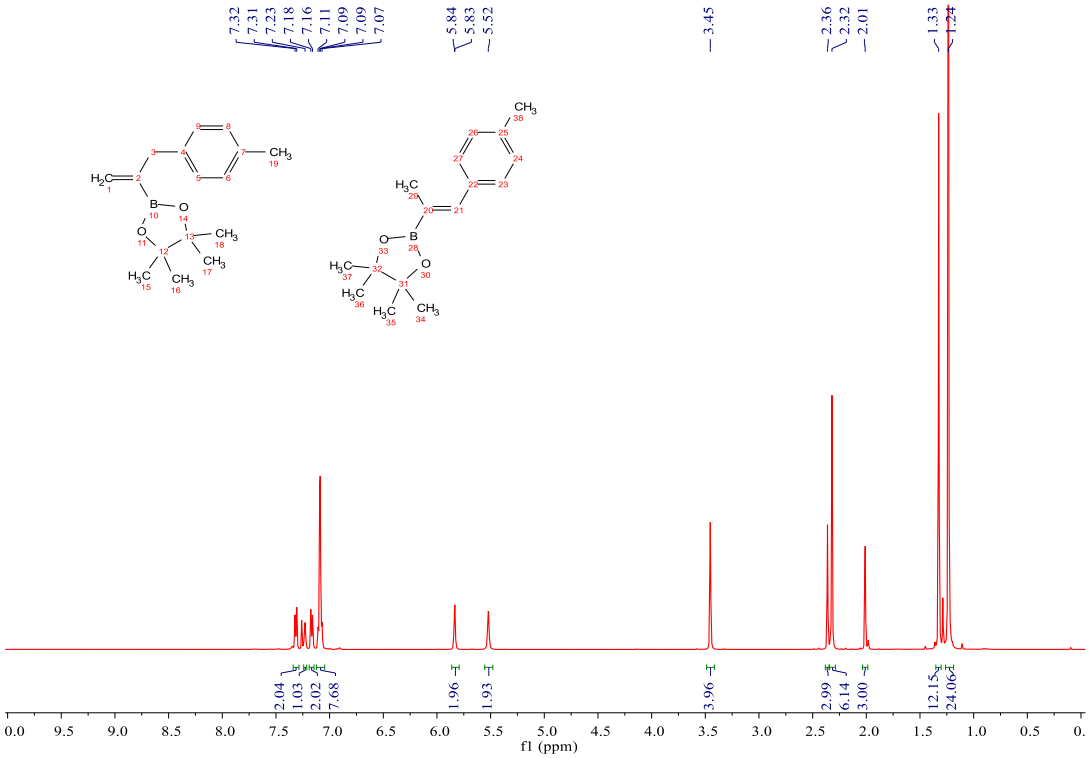
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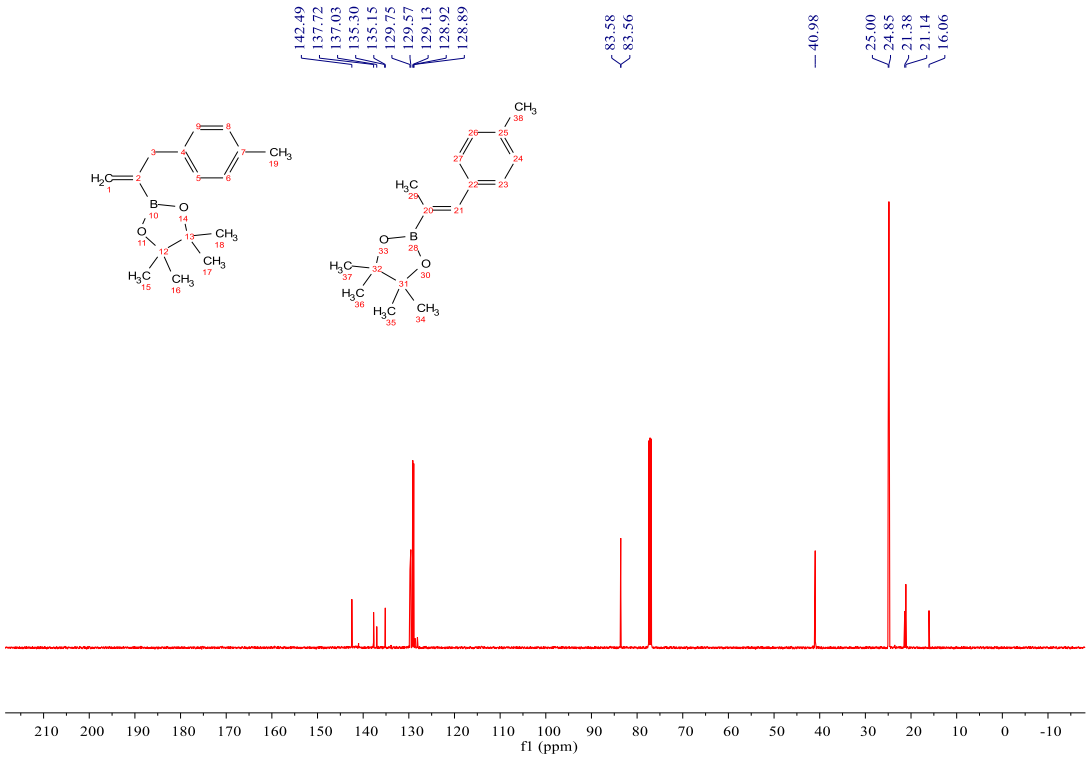
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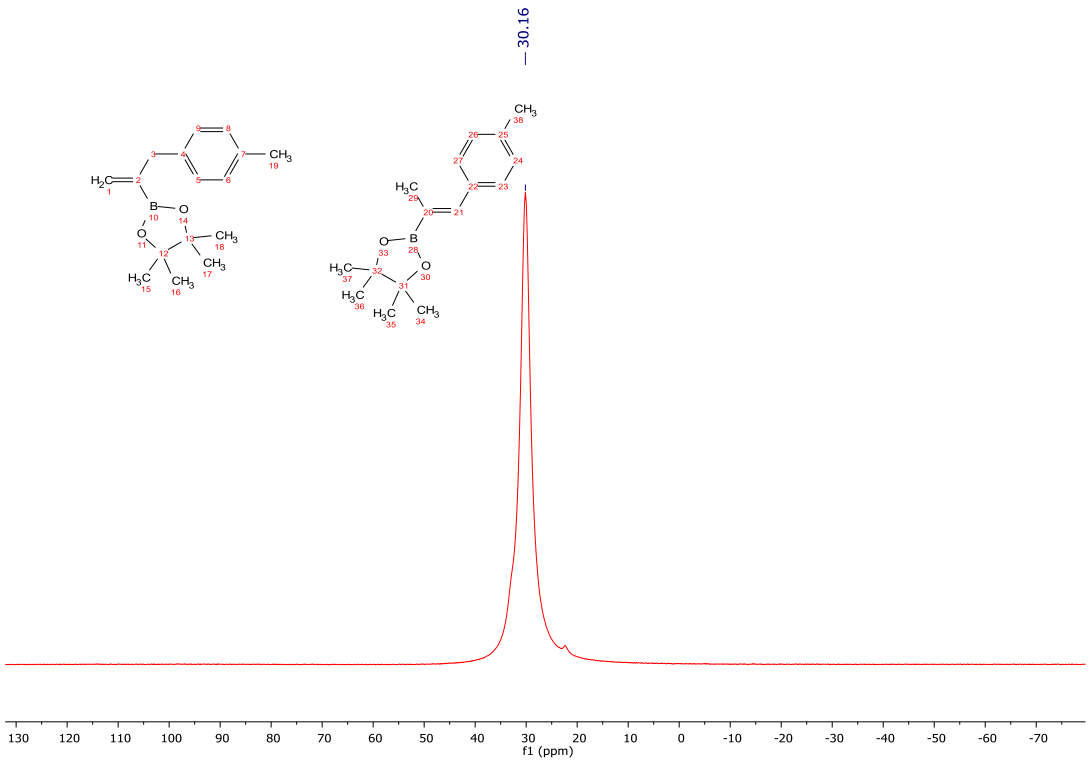
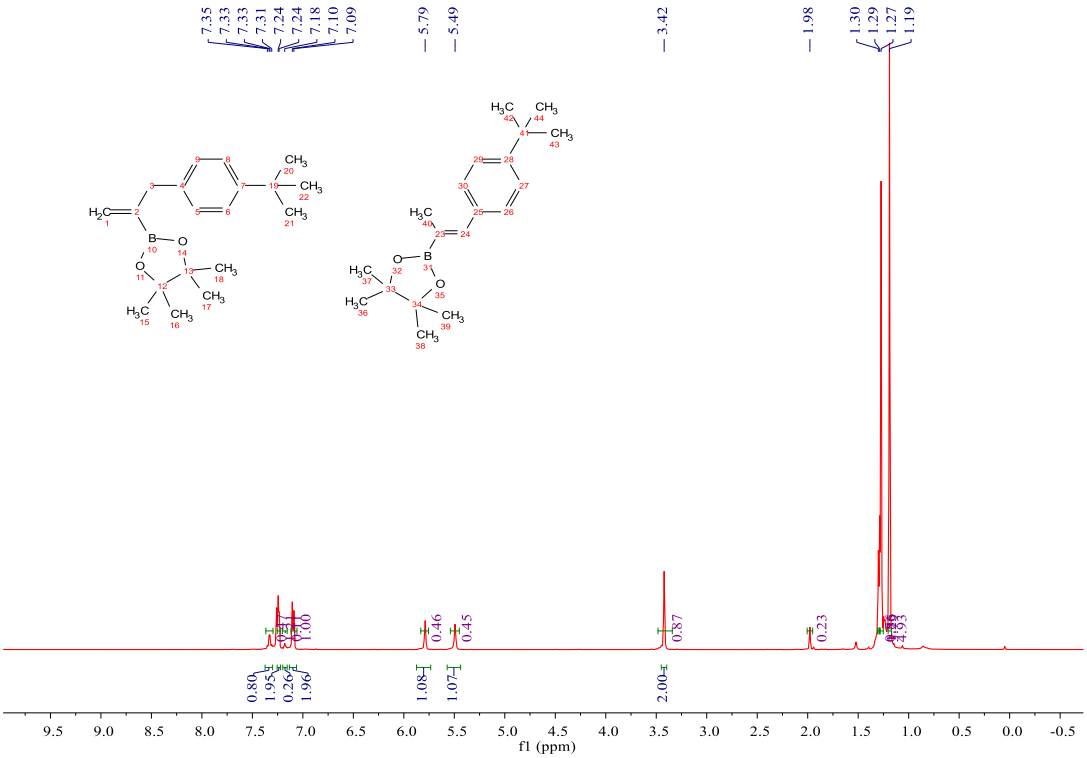
f1 (ppm)


30.16
f1 (ppm)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7.33
7.31
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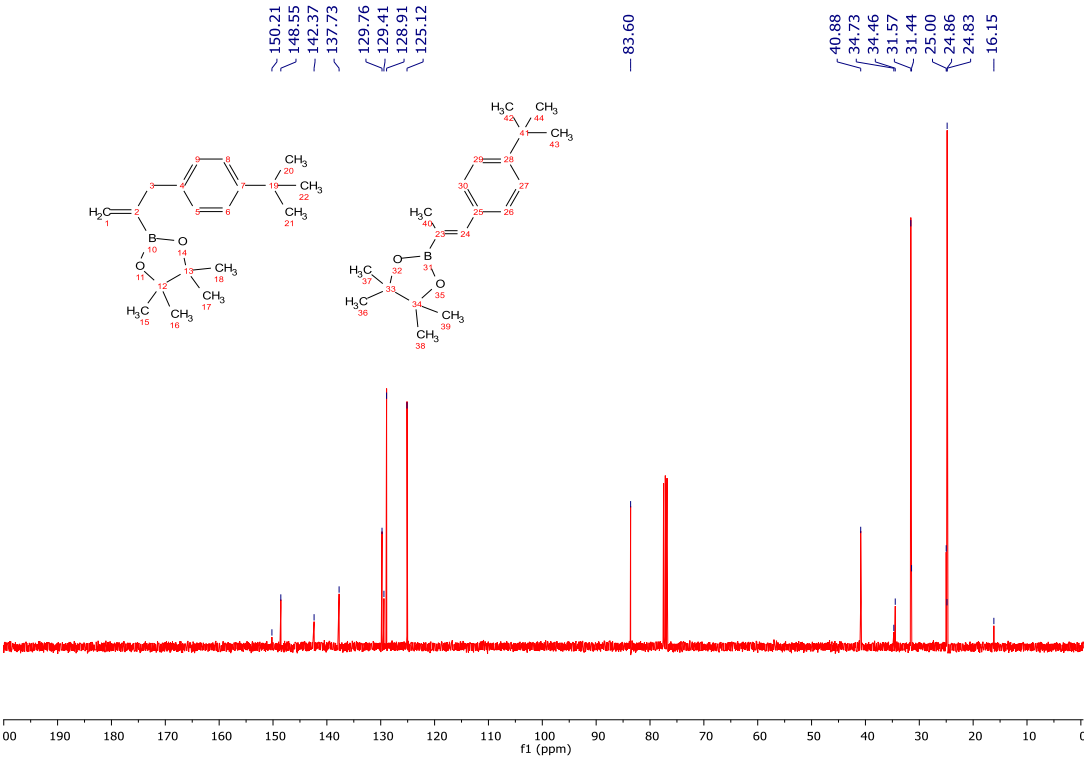
7.24
7.18
7.10
7.09
5.79
5.49
3.42
1.98
1.30
1.29
1.27
1.19
0.80
1.95
0.26
1.96
1.08
1.07
2.00
0.23
0.87
0.46
0.45
f1 (ppm)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148.55
142.37
137.73
129.76
129.41
128.91
125.12
83.60
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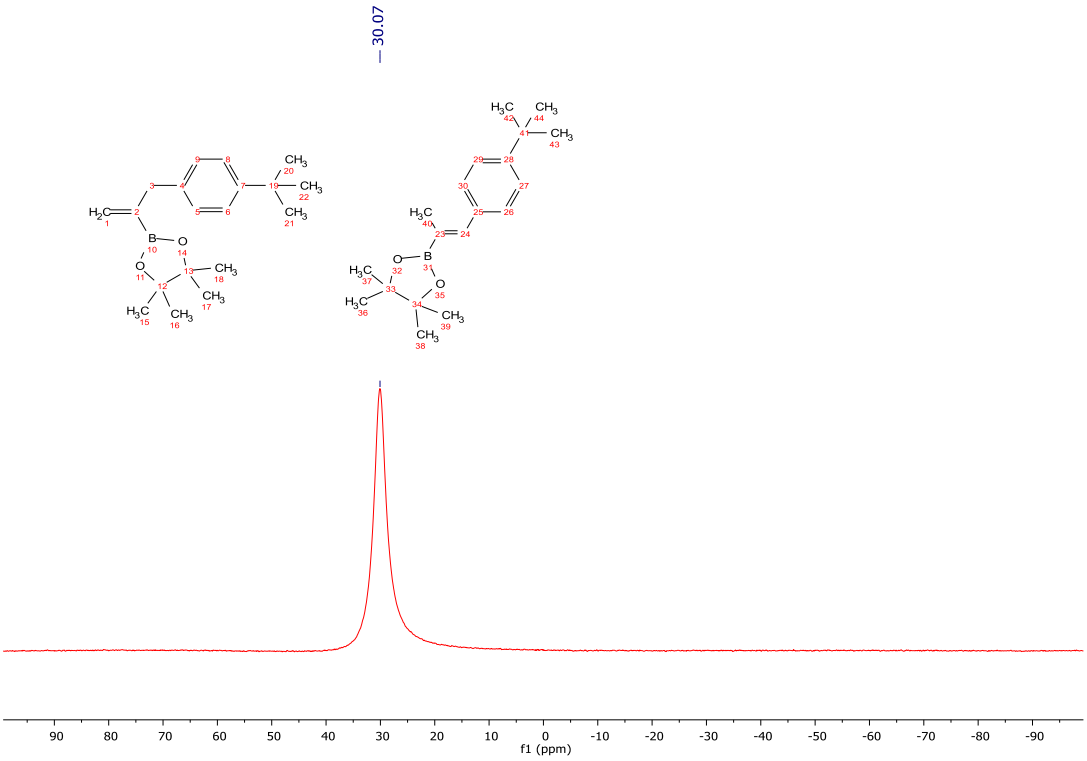
34.73
34.46
31.57
31.44
25.00
24.86
24.83
16.15
f1 (ppm)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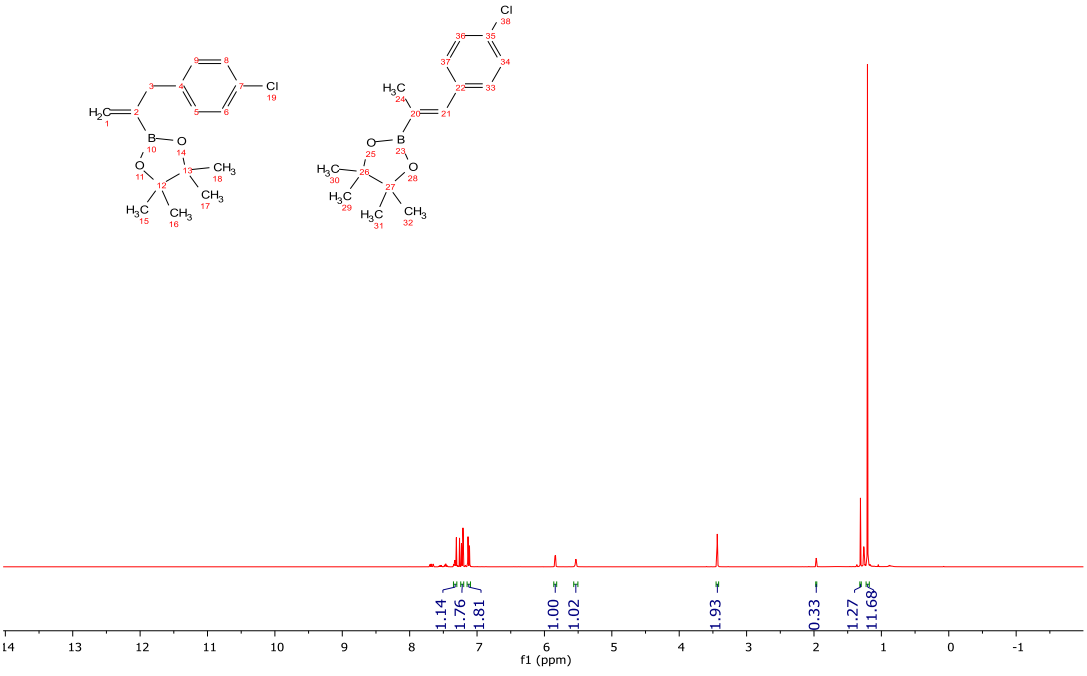
f1 (ppm)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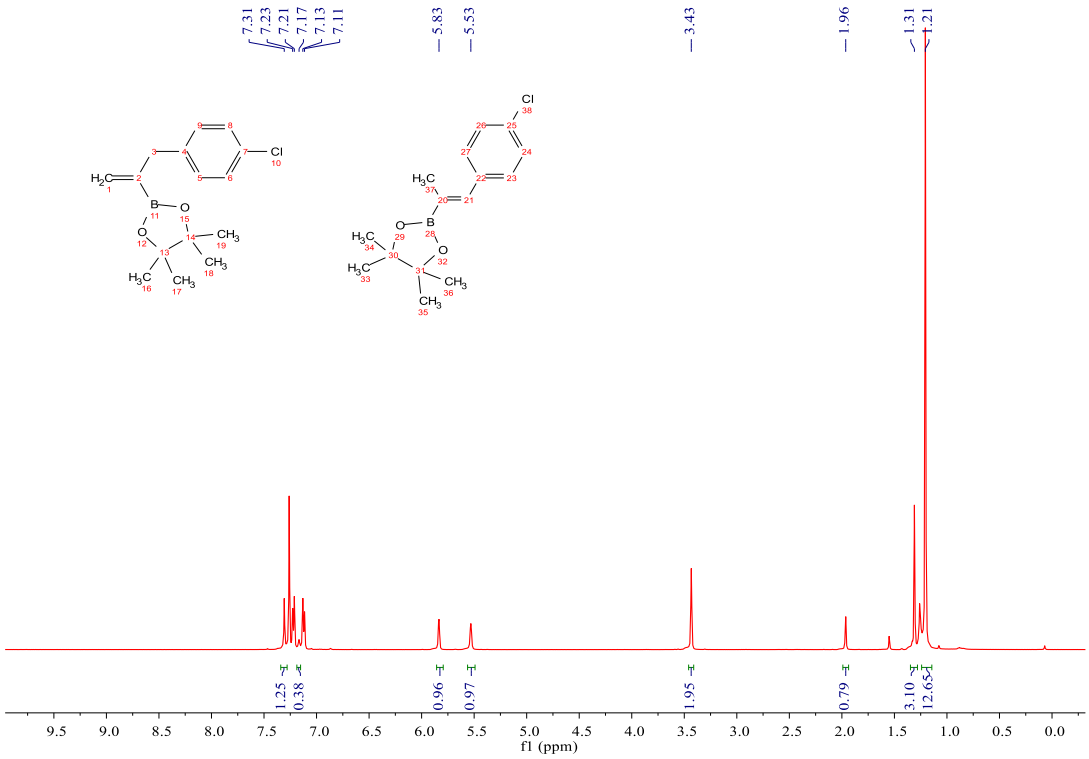
1.81
1.00
1.02
1.93
0.33
1.27
11.68
f1 (ppm)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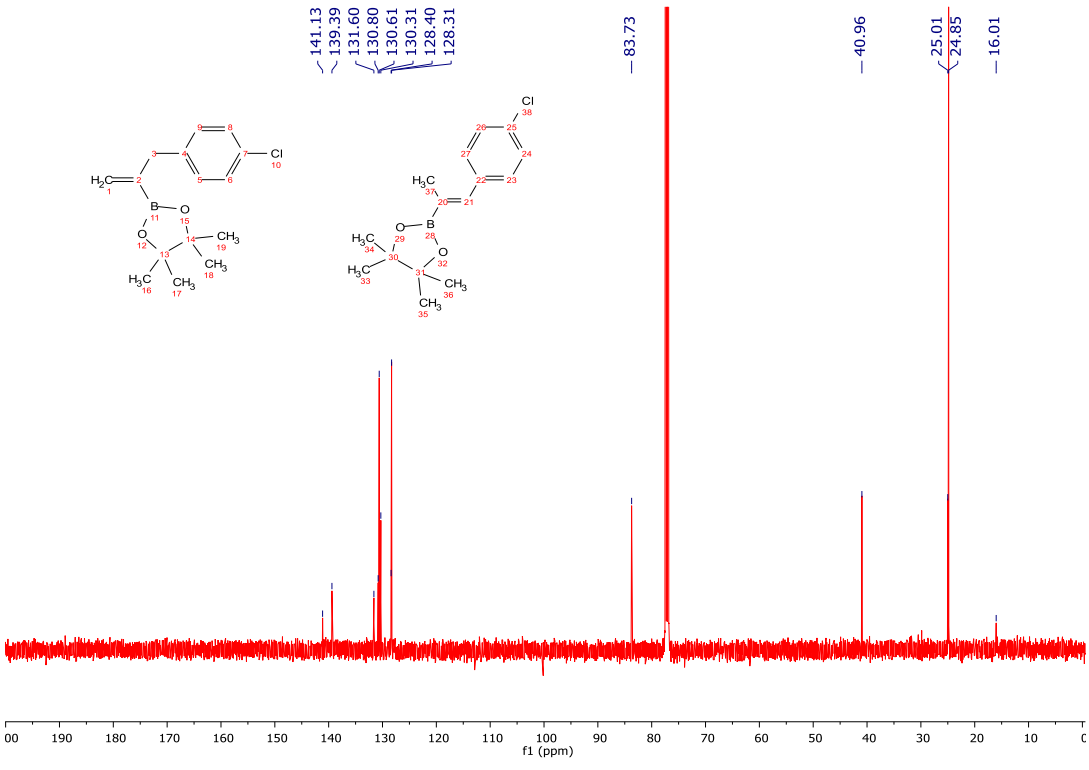
7.23
7.21
7.17
7.13
7.11
5.83
5.53
3.43
1.96
1.31
1.21
1.25
0.38
0.96
0.97
1.95
0.79
3.10
12.65
f1 (ppm)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139.39
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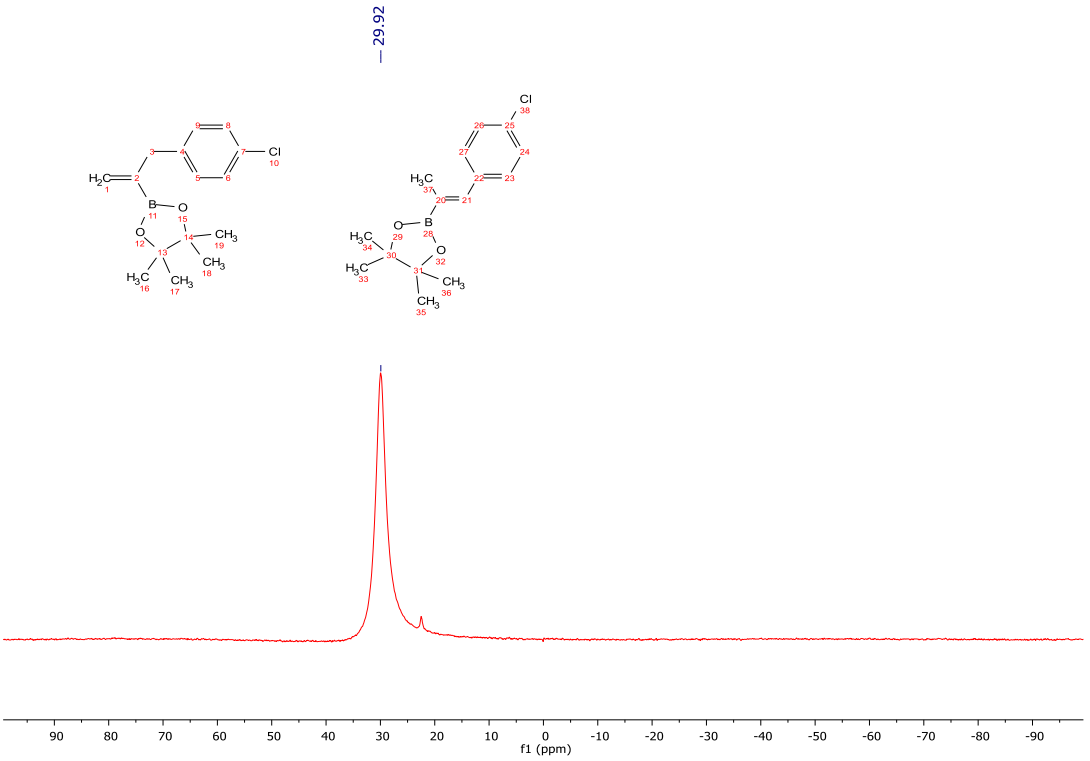
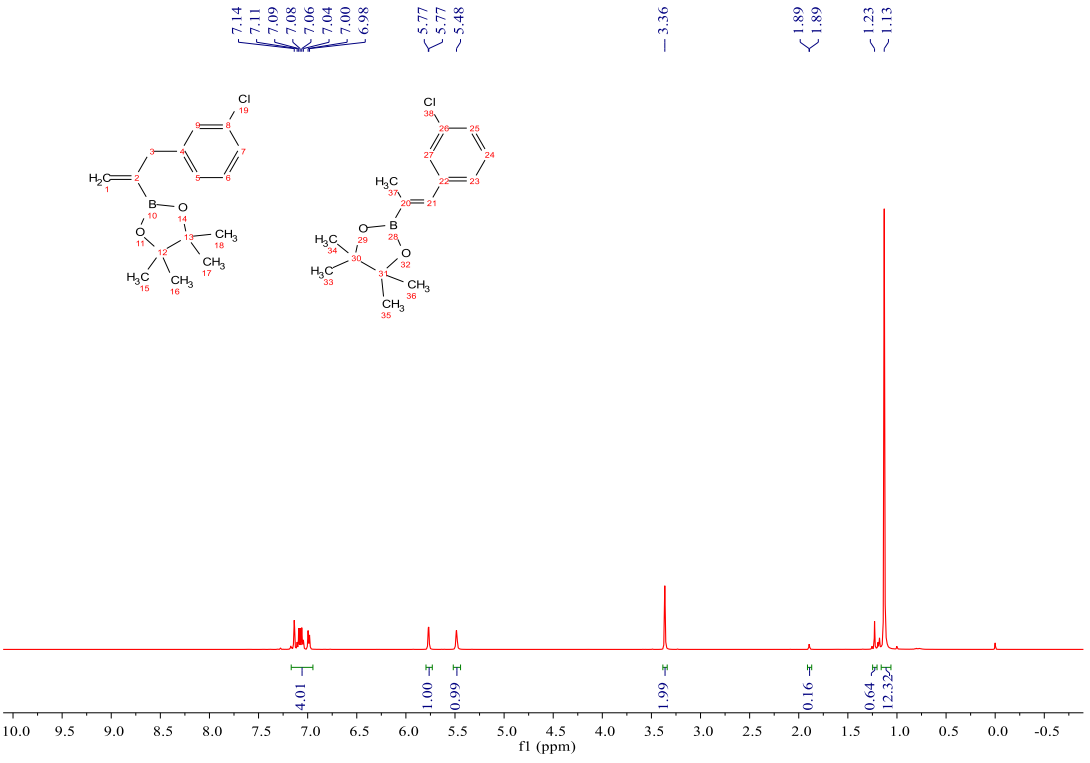
130.31
128.40
128.31
83.73
40.96
25.01
24.85
16.01
f1 (ppm)


29.92
f1 (ppm)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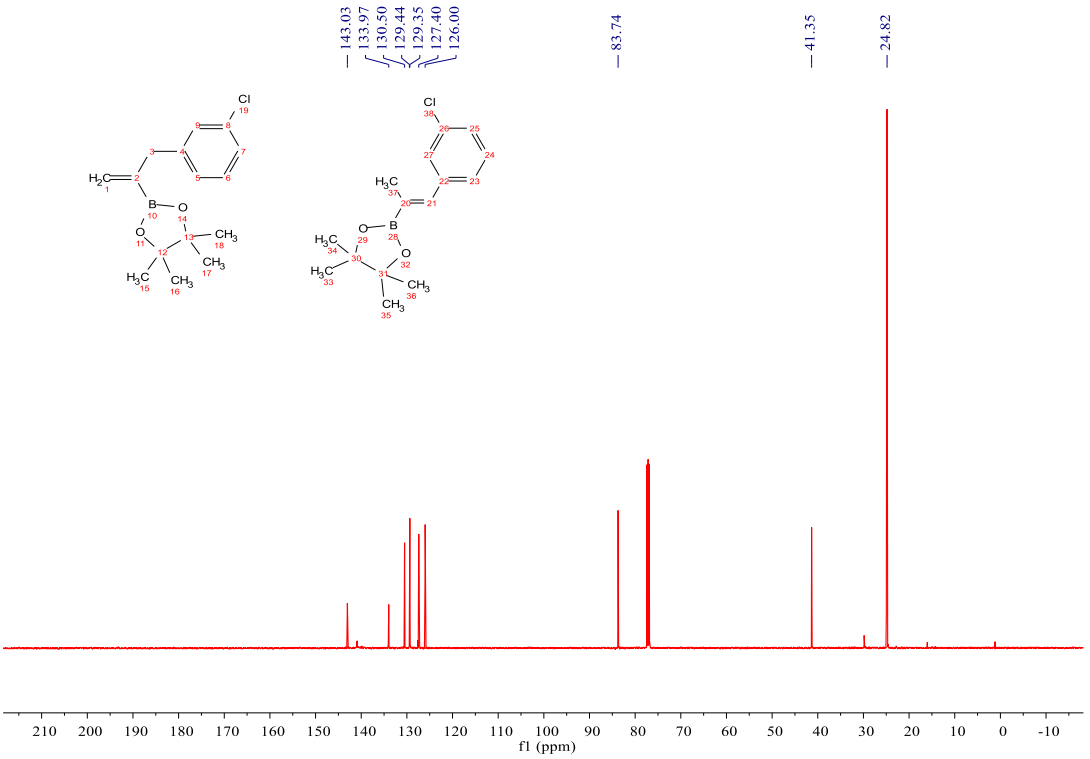
7.08
7.06
7.04
7.00
6.98
5.77
5.77
5.48
3.36
1.89
1.89
1.23
1.13
4.01
1.00
0.99
1.99
0.16
0.64
12.32
f1 (ppm)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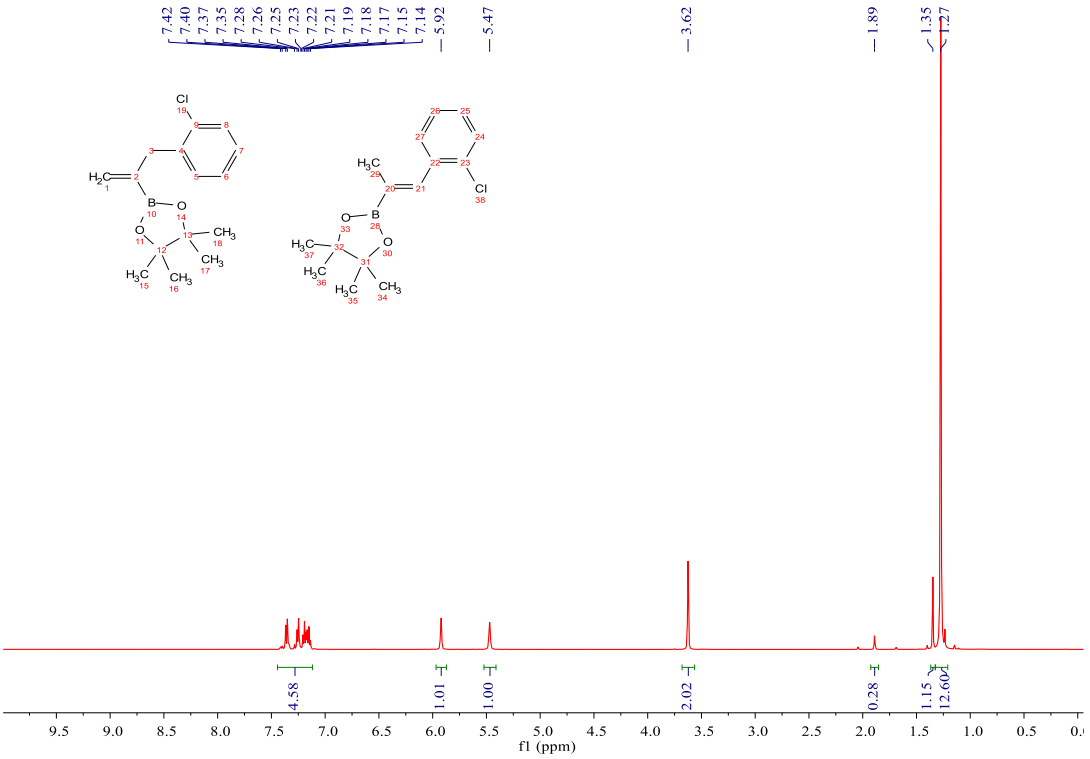
133.97
130.50
129.44
129.35
127.40
126.00
83.74
41.35
24.82
Cl
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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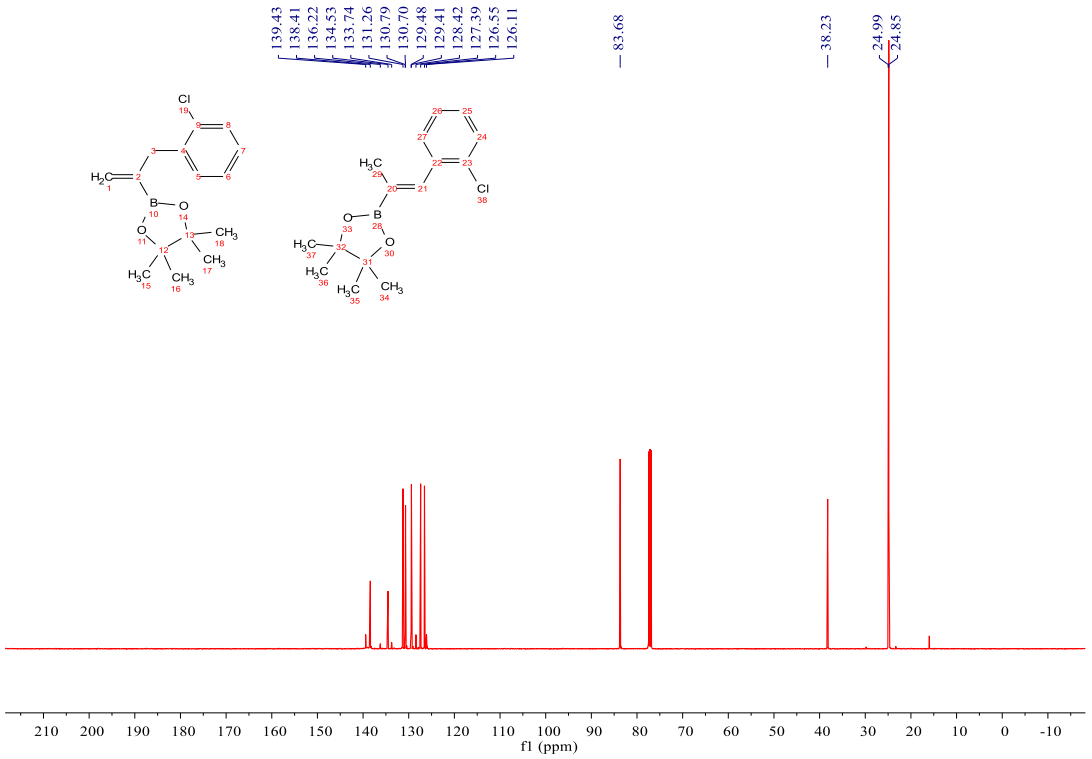
7.26
7.25
7.23
7.22
7.21
7.19
7.18
7.17
7.15
7.14
5.92
5.47
3.62
1.89
1.35
1.27
Cl
Cl
4.58
1.01
1.00
2.02
0.28
1.15
12.60
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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138.41
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131.26
130.79
130.70
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129.41
128.42
127.39
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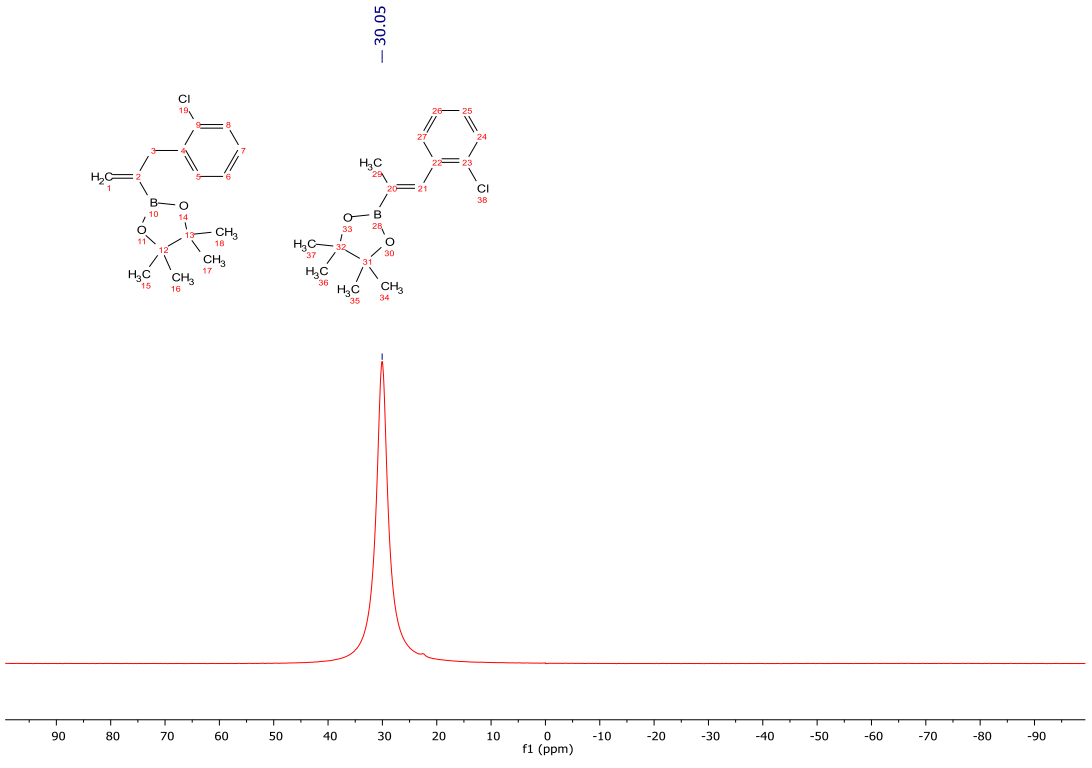
126.11
83.68
38.23
24.99
24.85
f1 (ppm)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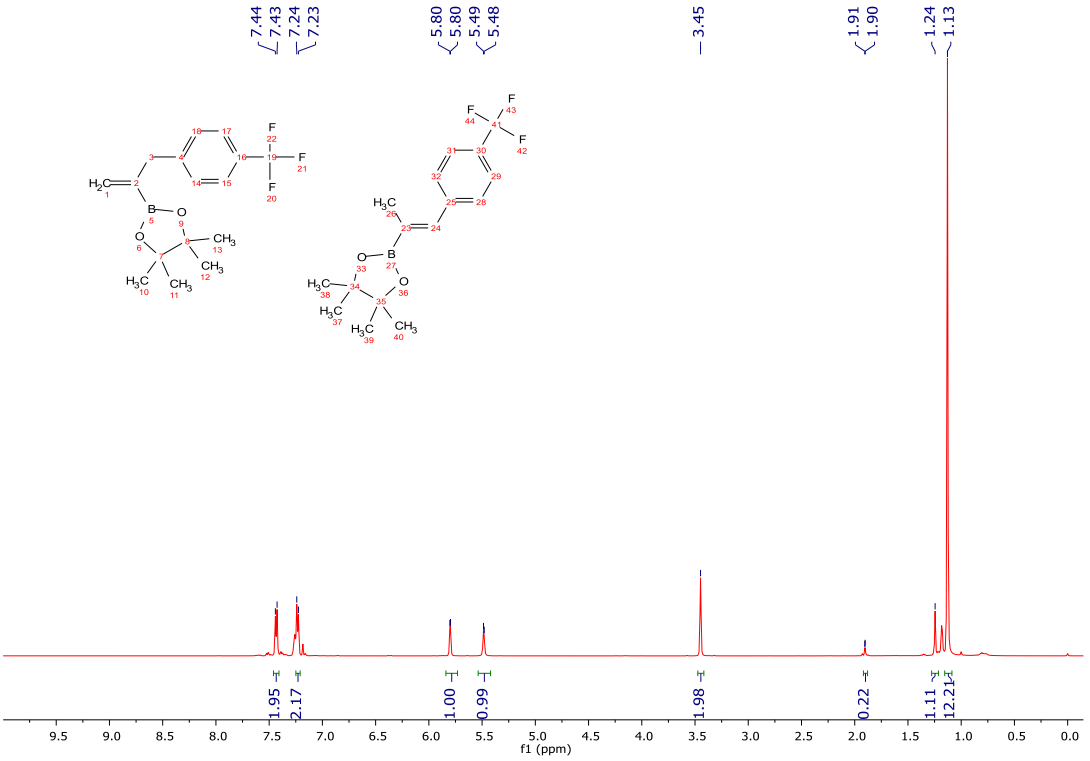
f1 (ppm)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7.43
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7.23
5.80
5.80
5.49
5.48
3.45
1.91
1.90
1.24
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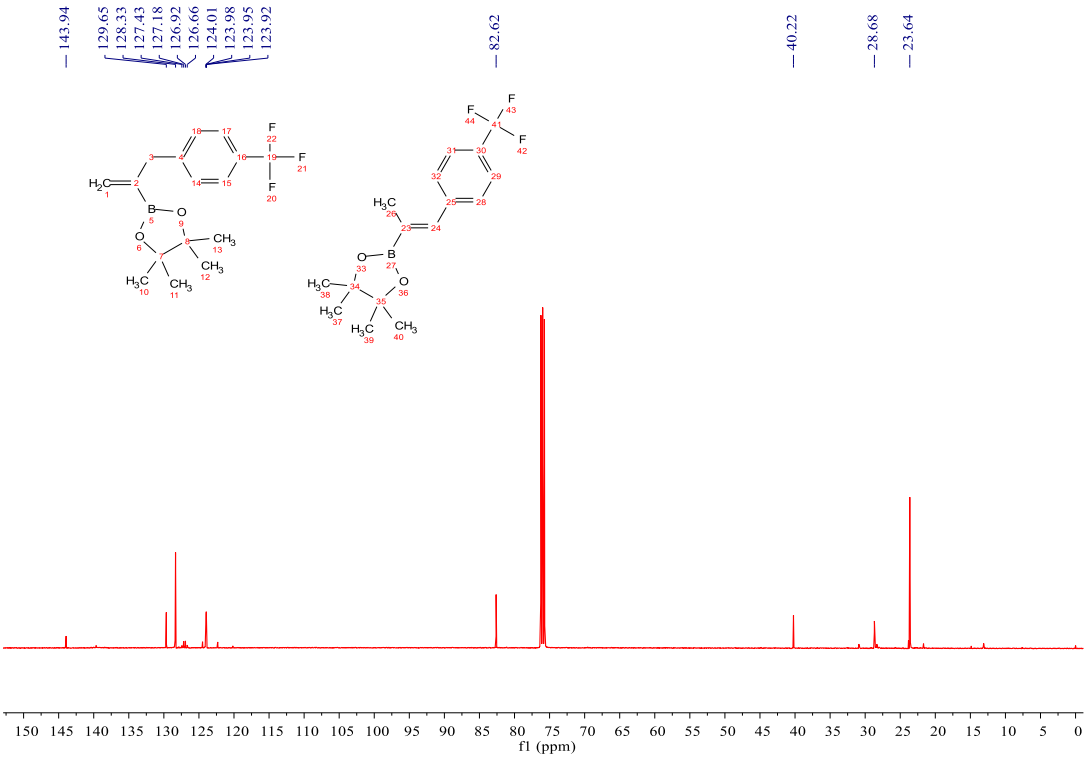
1.95
2.17
1.00
0.99
1.98
0.22
1.11
12.21
f1 (ppm)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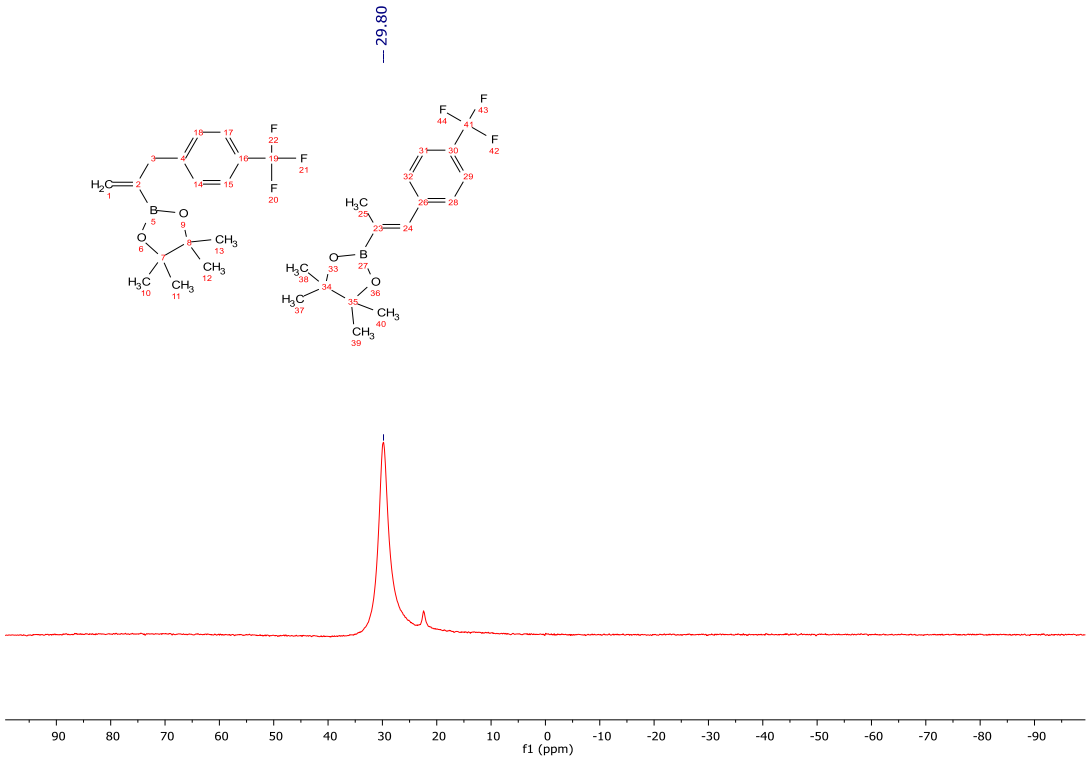
129.65
128.33
127.43
127.18
126.92
126.66
124.01
123.98
123.95
123.92
82.62
40.22
28.68
23.64
f1 (ppm)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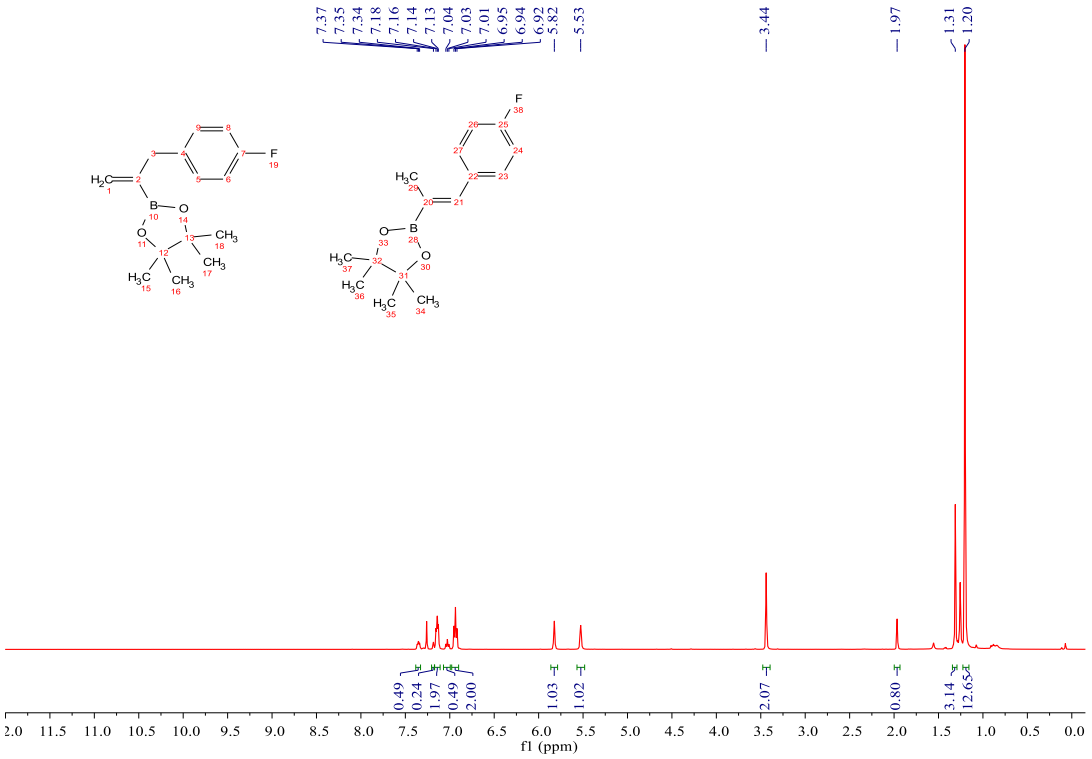
f1 (ppm)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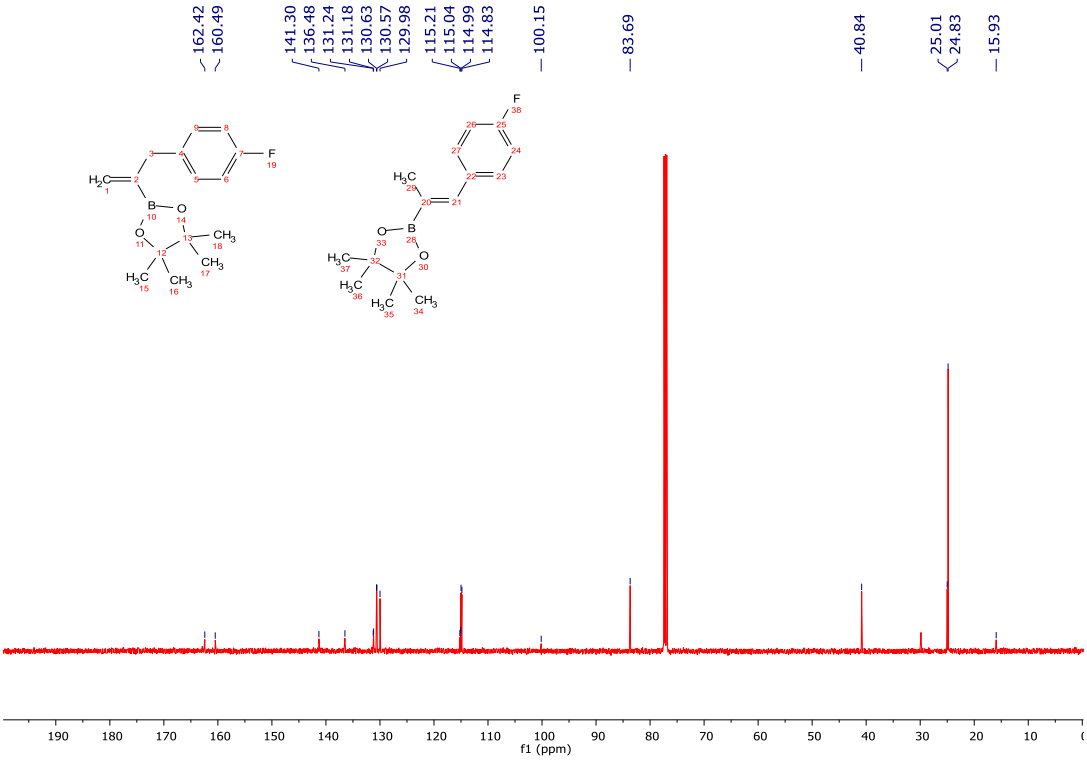
7.34
7.18
7.16
7.14
7.13
7.04
7.03
7.01
6.95
6.94
6.92
5.82
5.53
3.44
1.97
1.31
1.20
0.49
0.24
1.97
0.49
2.00
1.03
1.02
2.07
0.80
3.14
12.65
f1 (ppm)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160.49
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131.24
131.18
130.63
130.57
129.98
115.21
115.04
114.99
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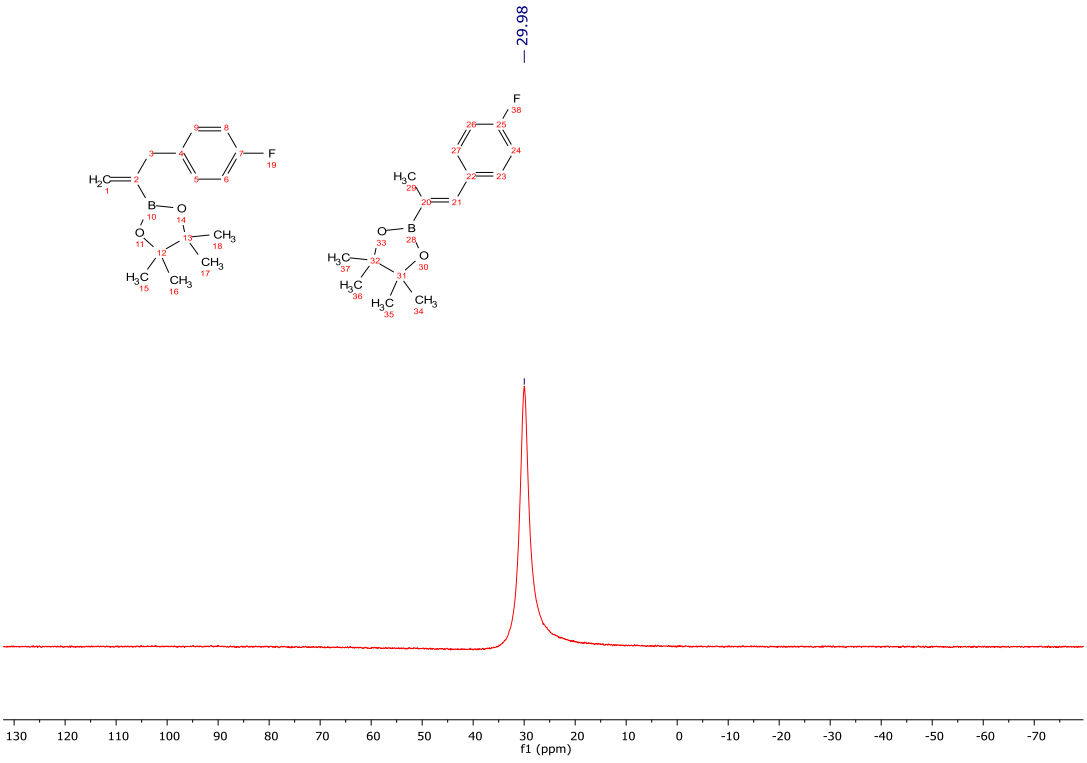
40.84
25.01
24.83
15.93
f1 (ppm)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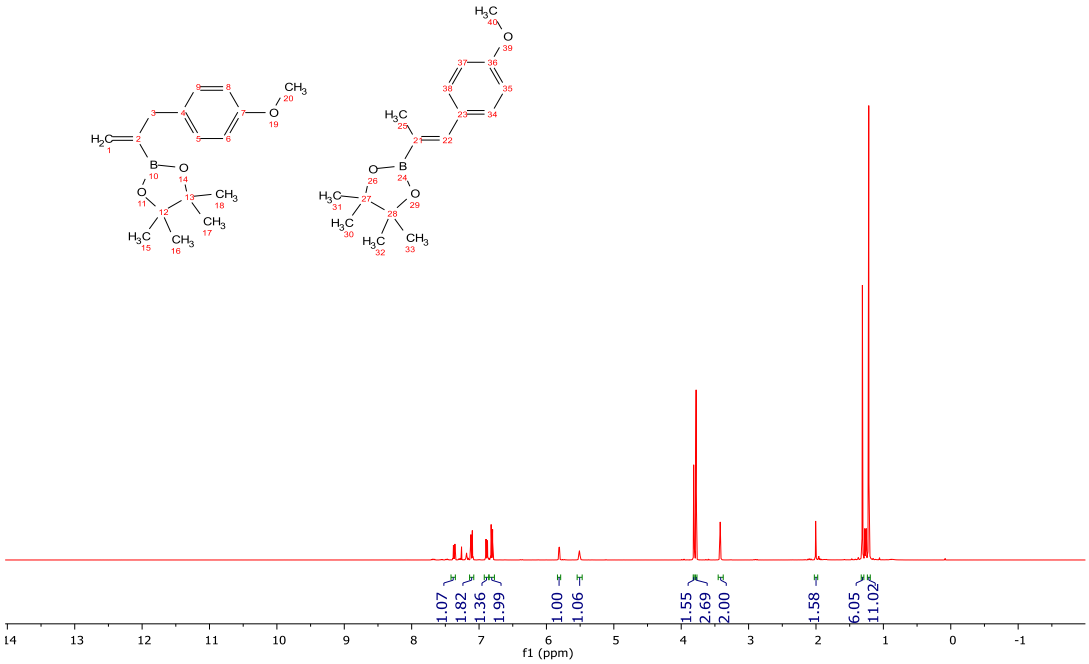
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1.82
1.36
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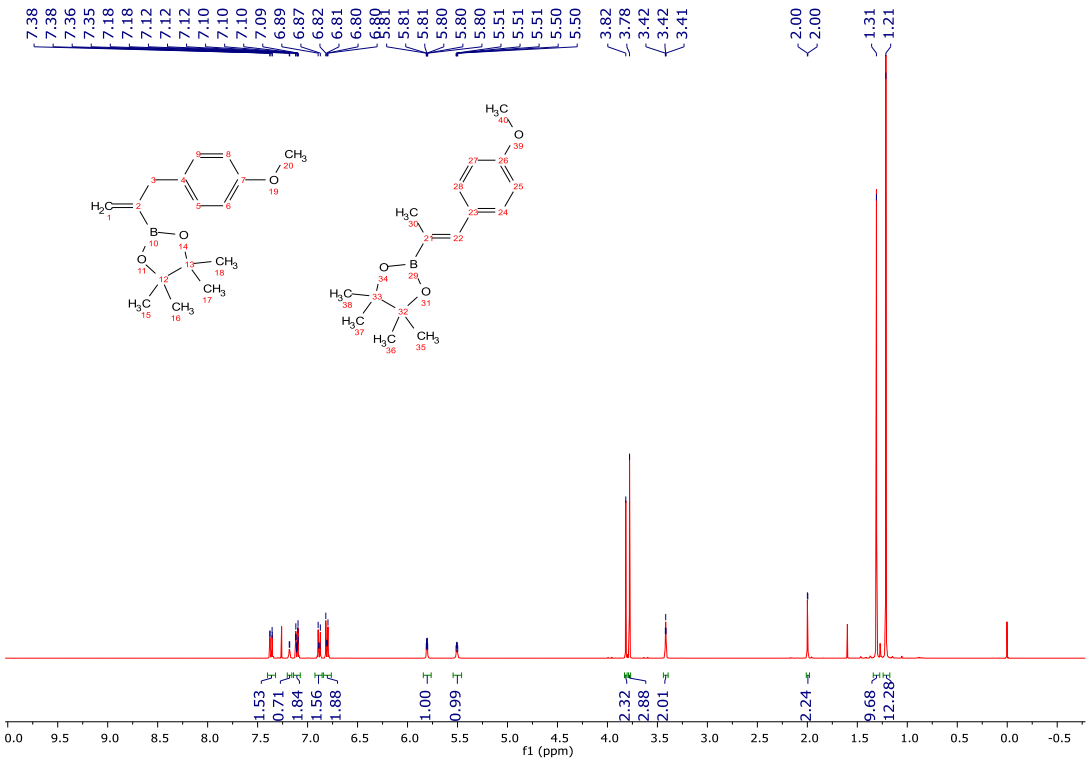
1.00
1.06
1.55
2.69
2.00
1.58
6.05
11.02
f1 (ppm)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7.10
7.10
7.10
7.09
6.89
6.87
6.82
6.81
6.80
5.81
5.81
5.80
5.80
5.80
5.51
5.51
5.51
5.50
5.50
3.82
3.78
3.42
3.42
3.41
2.00
2.00
1.31
1.21
1.53
0.71
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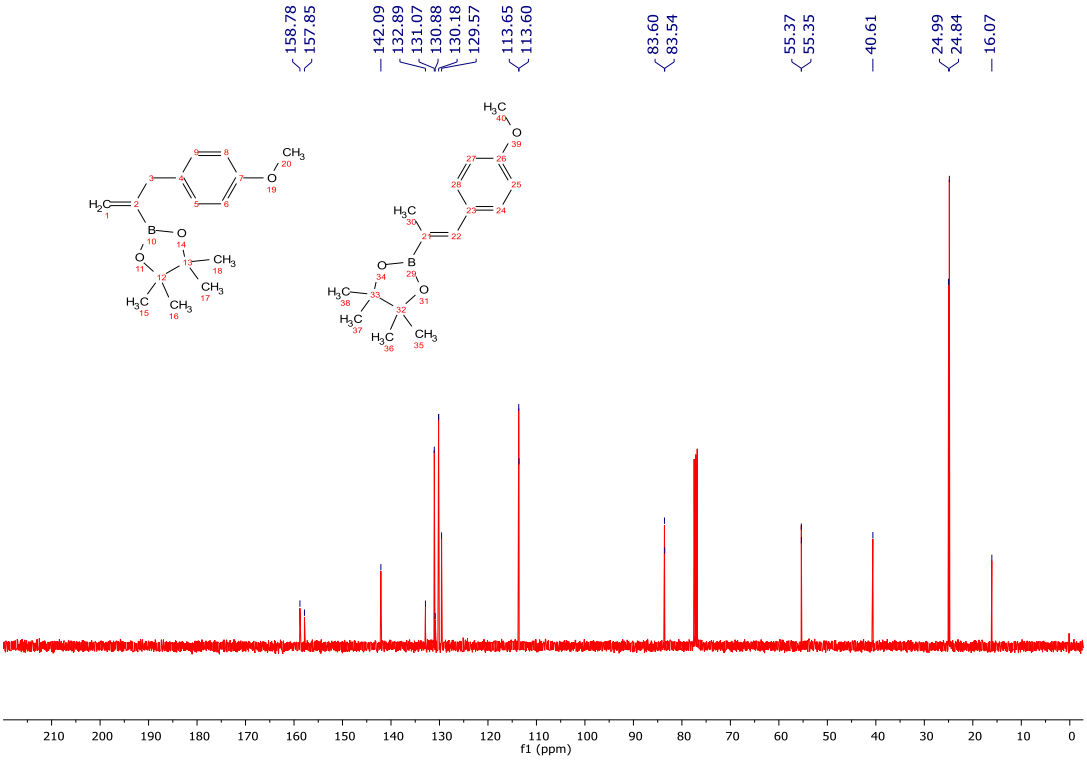
1.00
0.99
2.32
2.88
2.01
2.24
9.68
12.28
f1 (ppm)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130.88
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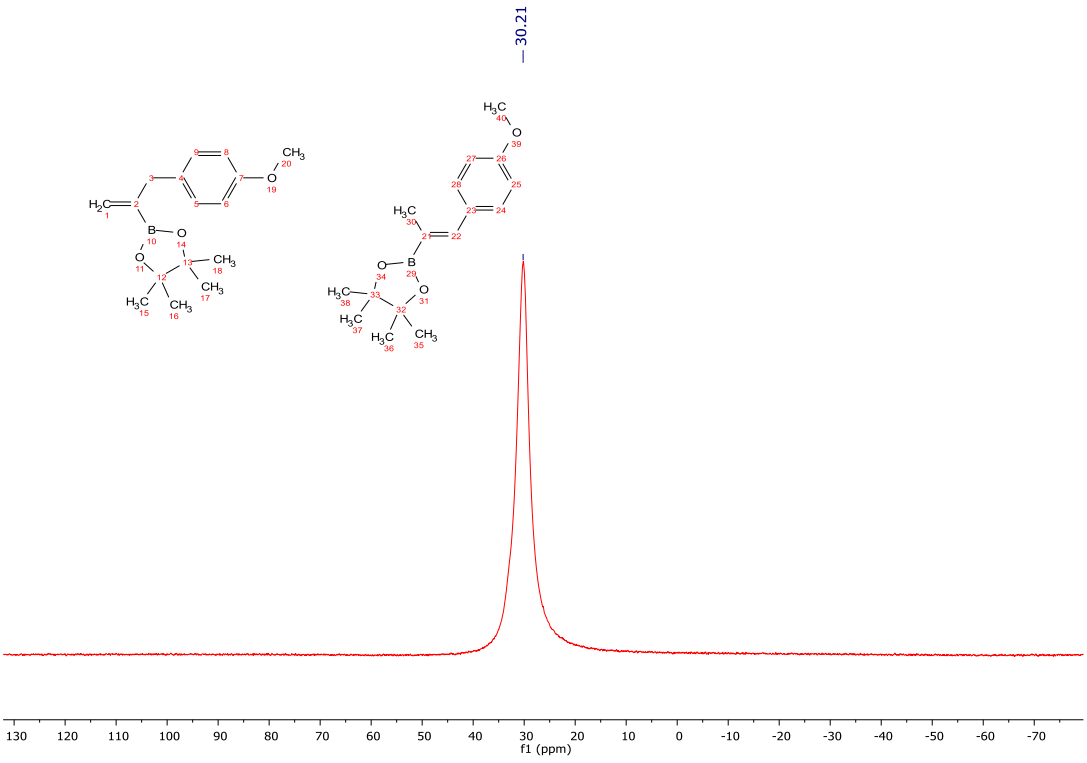
55.35
40.61
24.99
24.84
16.07
f1 (ppm)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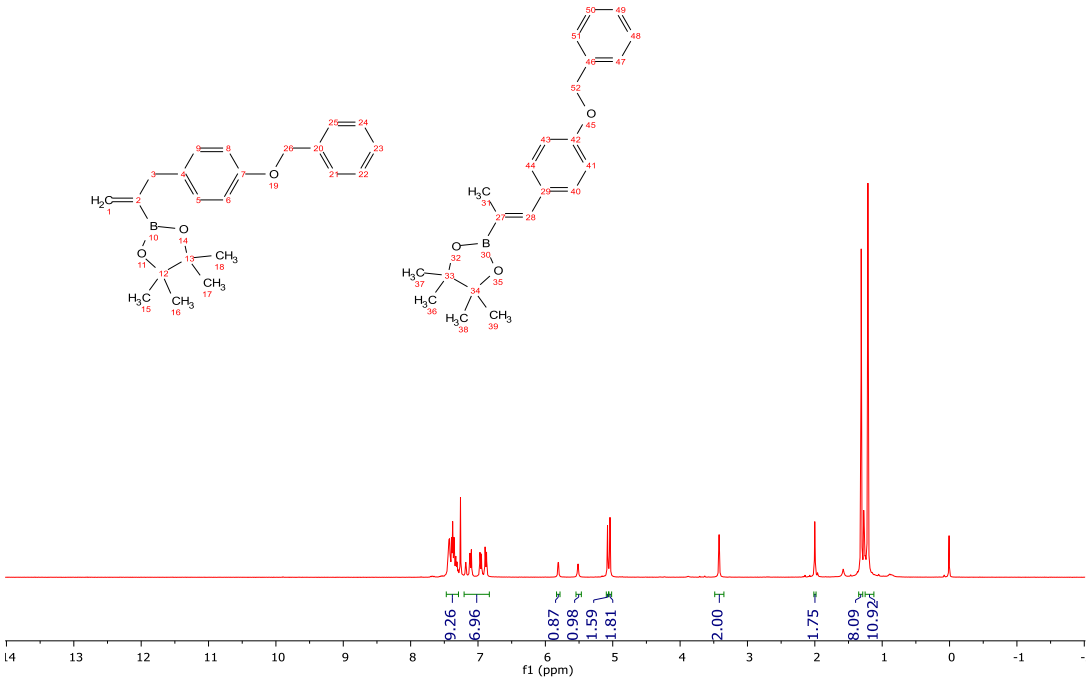
f1 (ppm)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1.75
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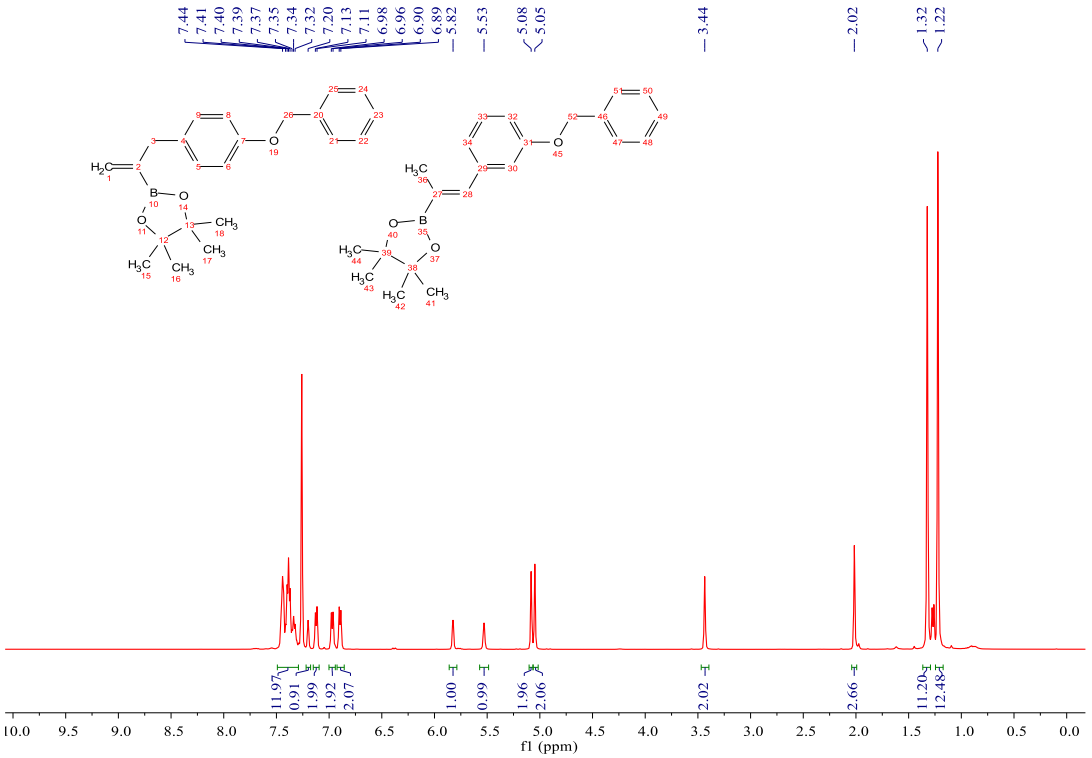
10.92
f1 (ppm)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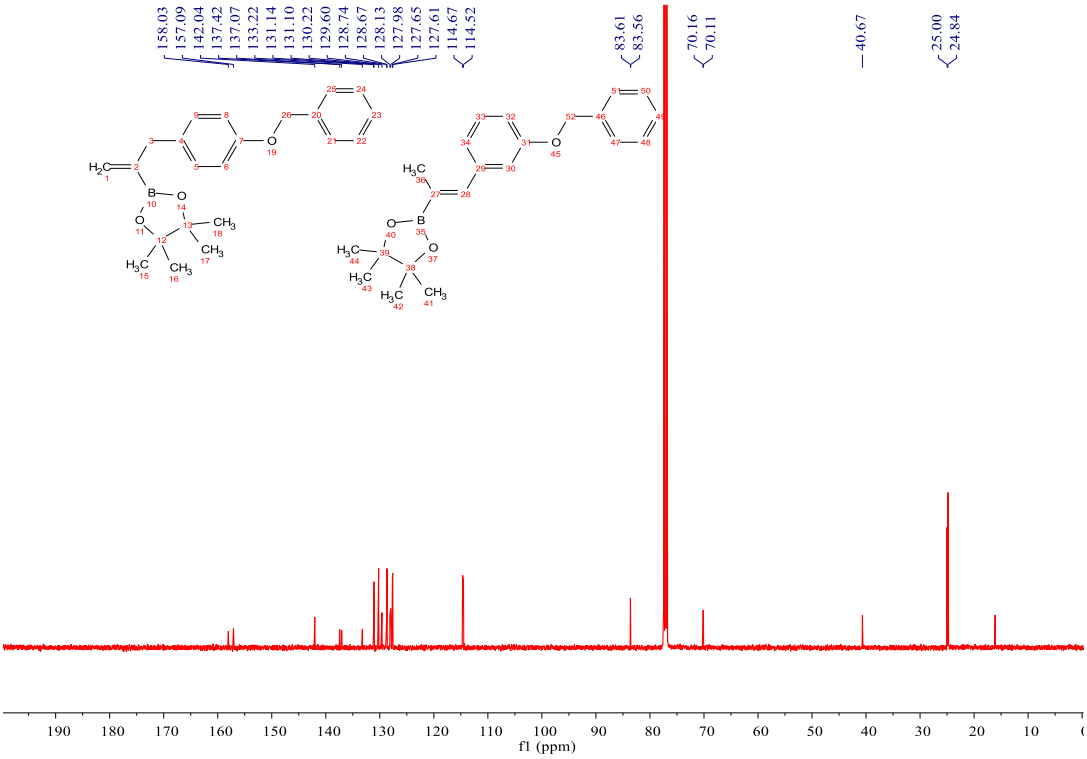
7.34
7.32
7.20
7.13
7.11
6.98
6.96
6.90
6.89
5.82
5.53
5.08
5.05
3.44
2.02
1.32
1.22
11.97
0.91
1.99
1.92
2.07
1.00
0.99
1.96
2.06
2.02
2.66
11.20
12.48
f1 (ppm)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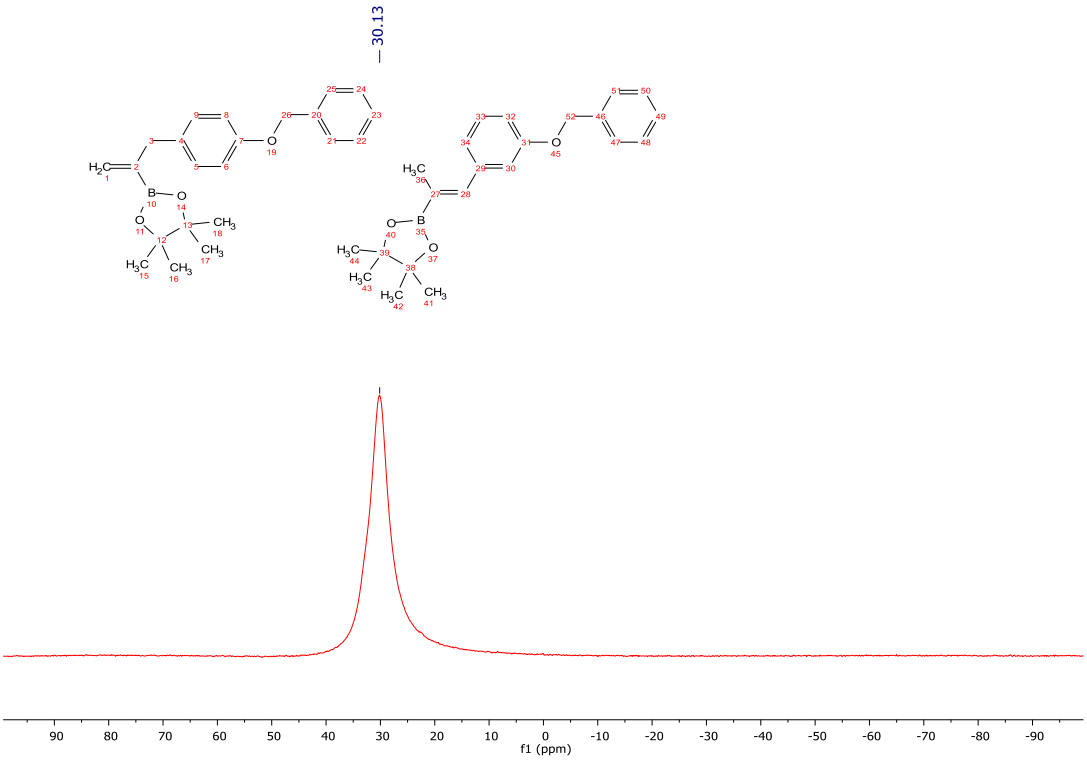
137.07
133.22
131.14
131.10
130.22
129.60
128.74
128.67
128.13
127.98
127.65
127.61
114.67
114.52
83.61
83.56
70.16
70.11
40.67
25.00
24.84
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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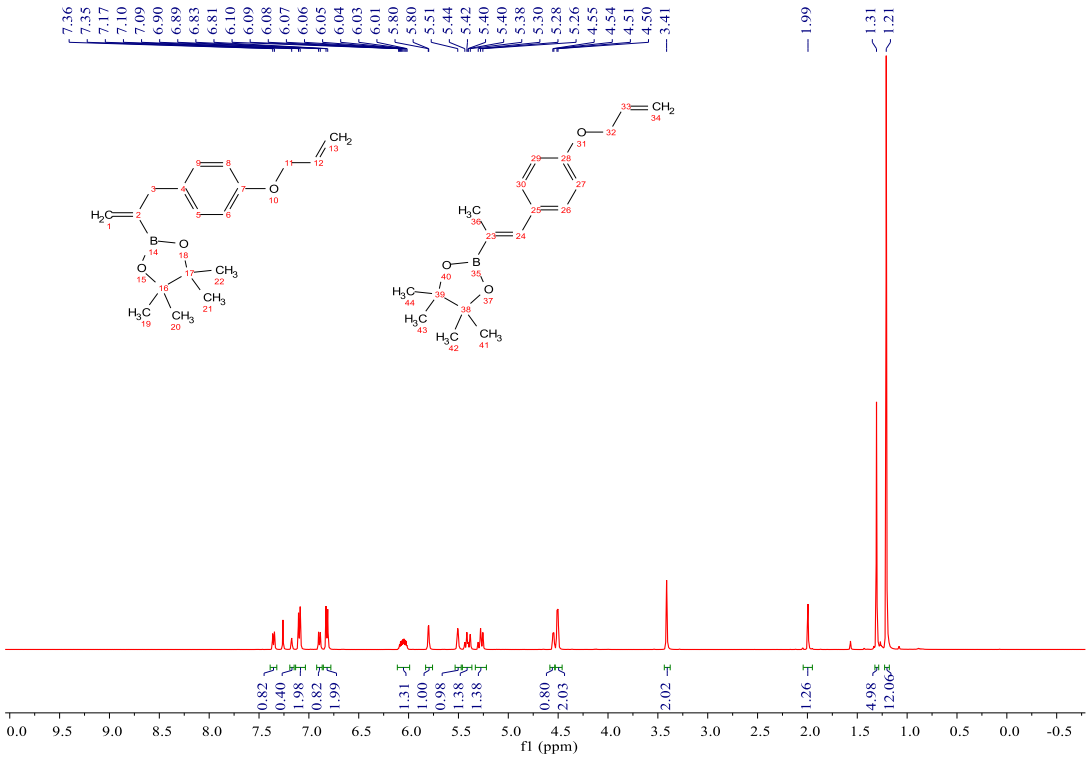
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90
f1 (ppm)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6.08
6.07
6.06
6.05
6.04
6.03
6.01
5.80
5.80
5.51
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5.42
5.40
5.40
5.38
5.30
5.28
5.26
4.55
4.54
4.51
4.50
3.41
1.99
1.31
1.21
0.82
0.40
1.98
0.82
1.99
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1.38
0.80
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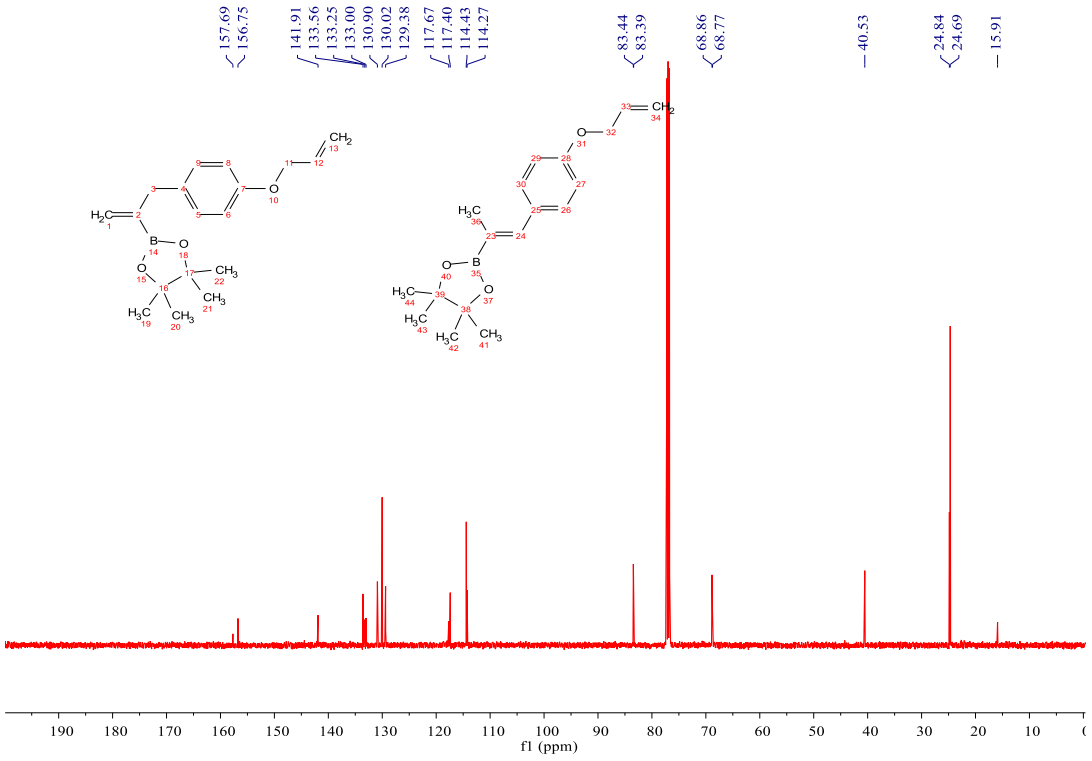
2.02
1.26
4.98
12.06
f1 (ppm)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117.67
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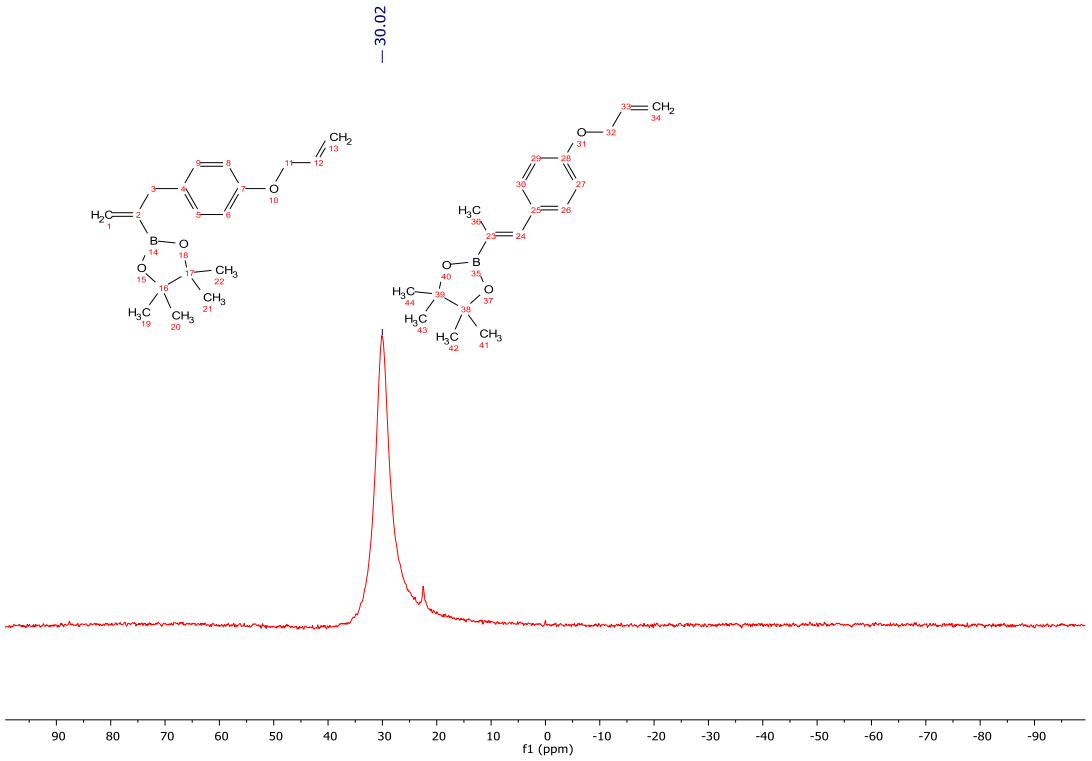
83.39
68.86
68.77
40.53
24.84
24.69
15.91
f1 (ppm)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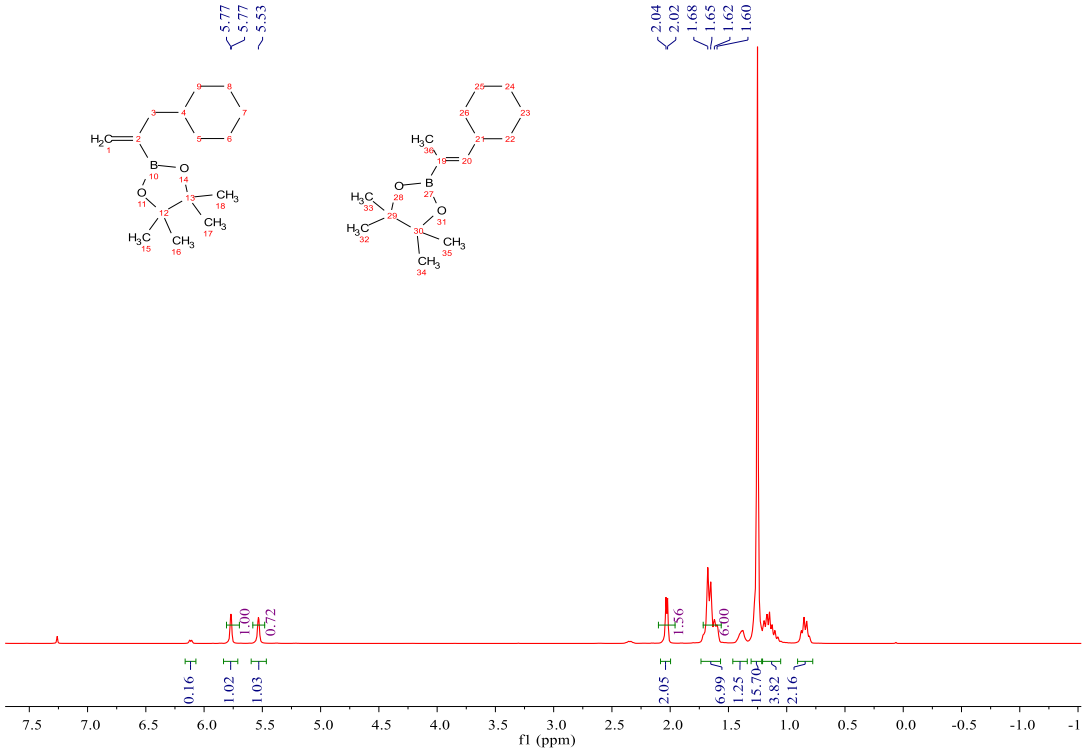
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1.68
1.65
1.62
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1.00
0.72
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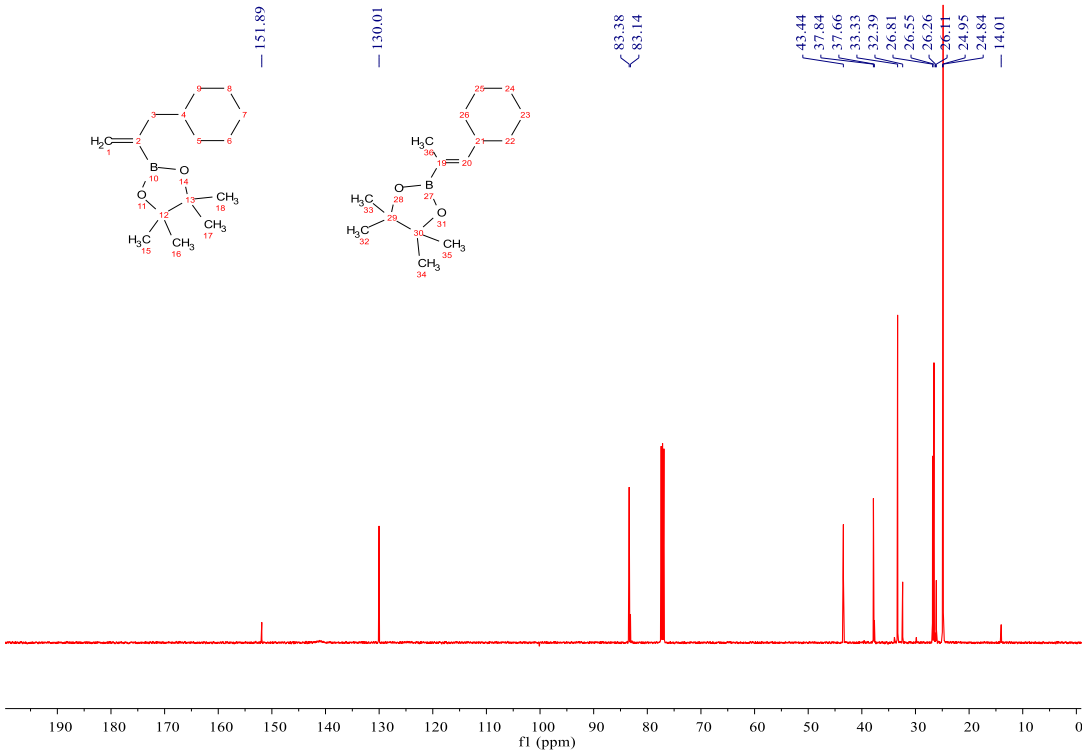
1.02
1.03
2.05
6.99
1.25
15.70
3.82
2.16
f1 (ppm)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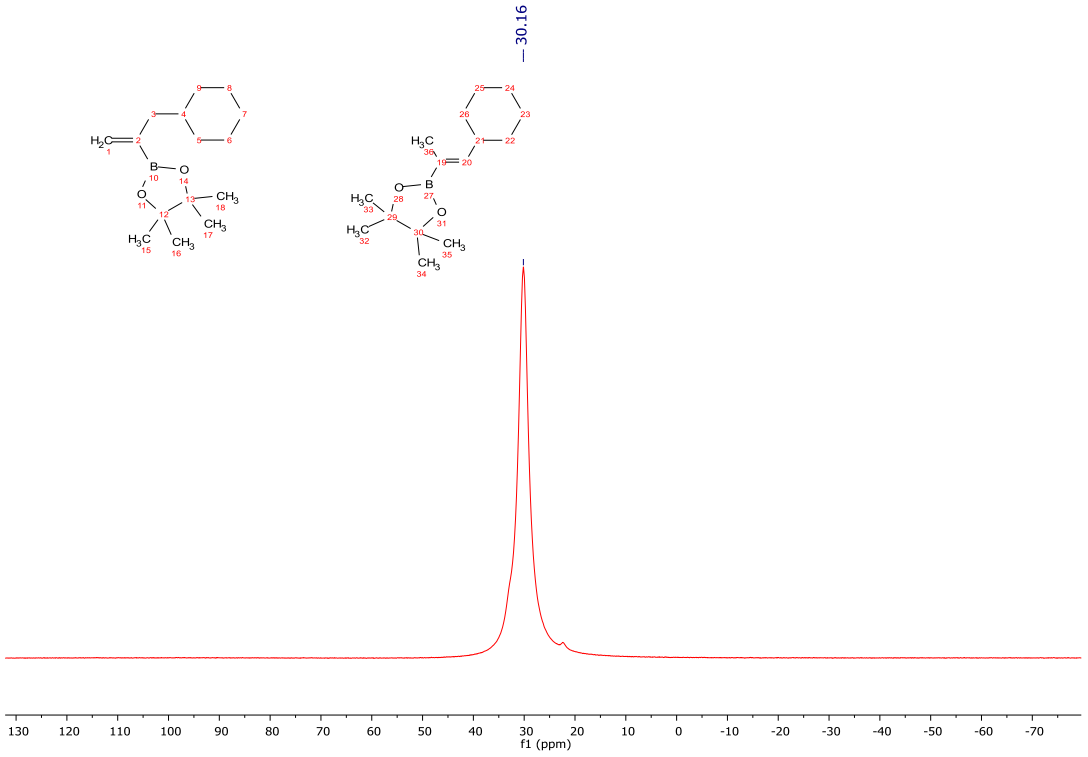
26.81
26.55
26.26
26.11
24.95
24.84
14.01
f1 (ppm)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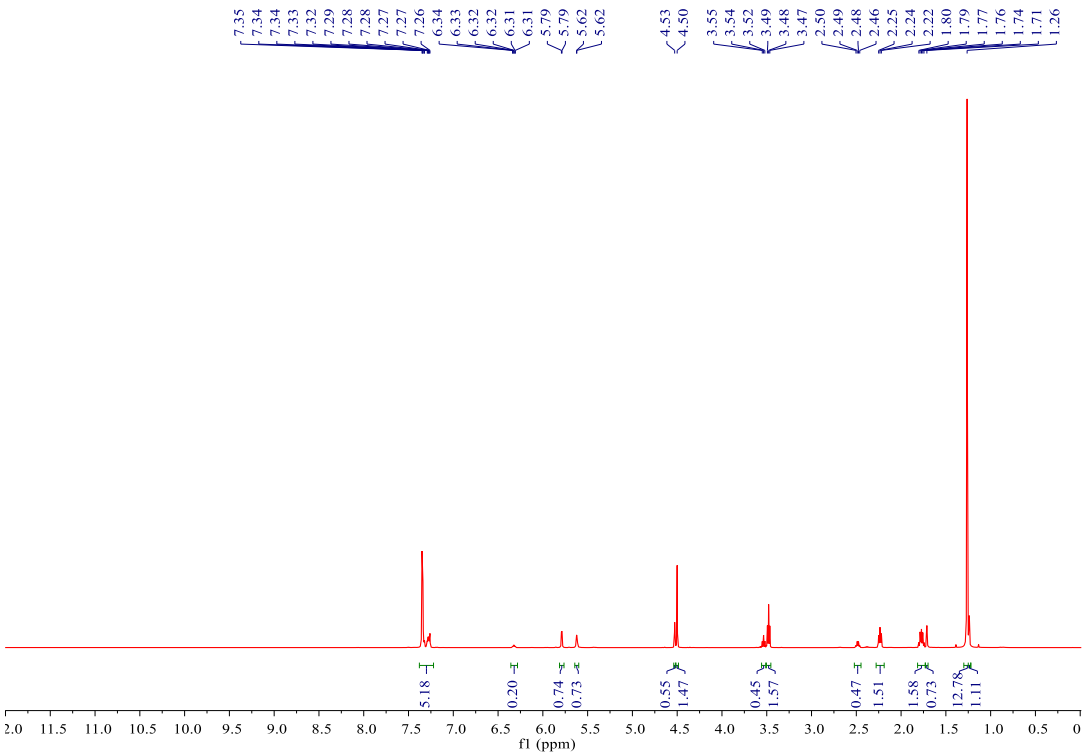
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2.46
2.25
2.24
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1.79
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1.76
1.74
1.71
1.26
5.18
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0.74
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0.45
1.57
0.47
1.51
1.58
0.73
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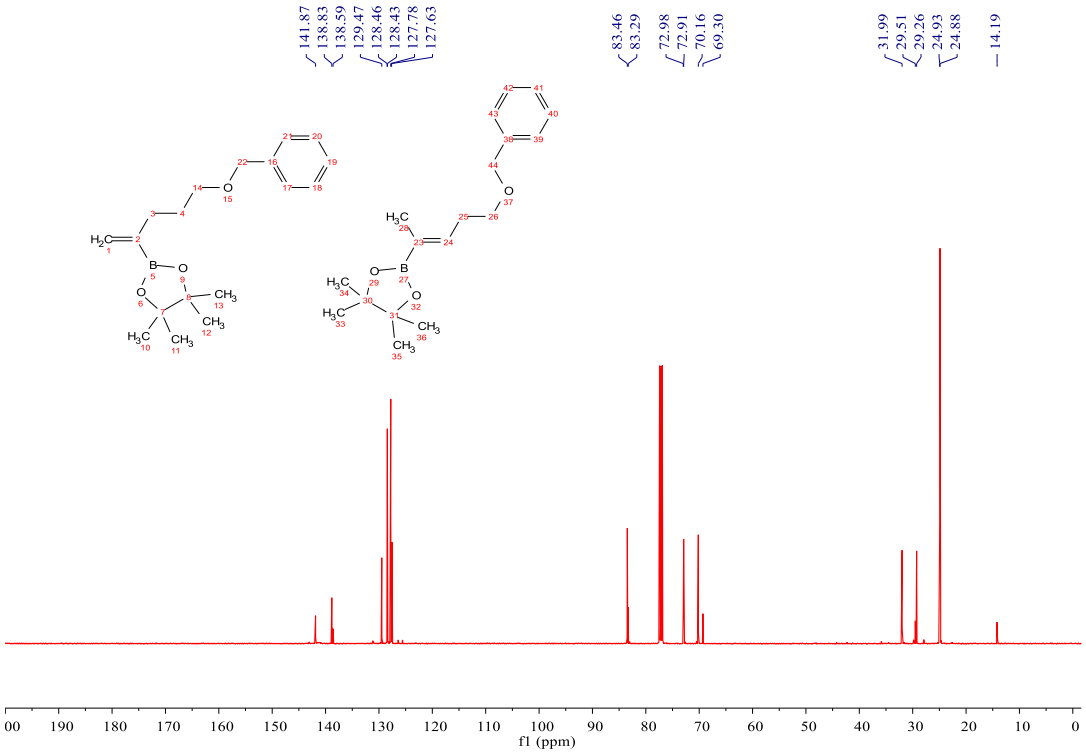
1.11
f1 (ppm)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72.98
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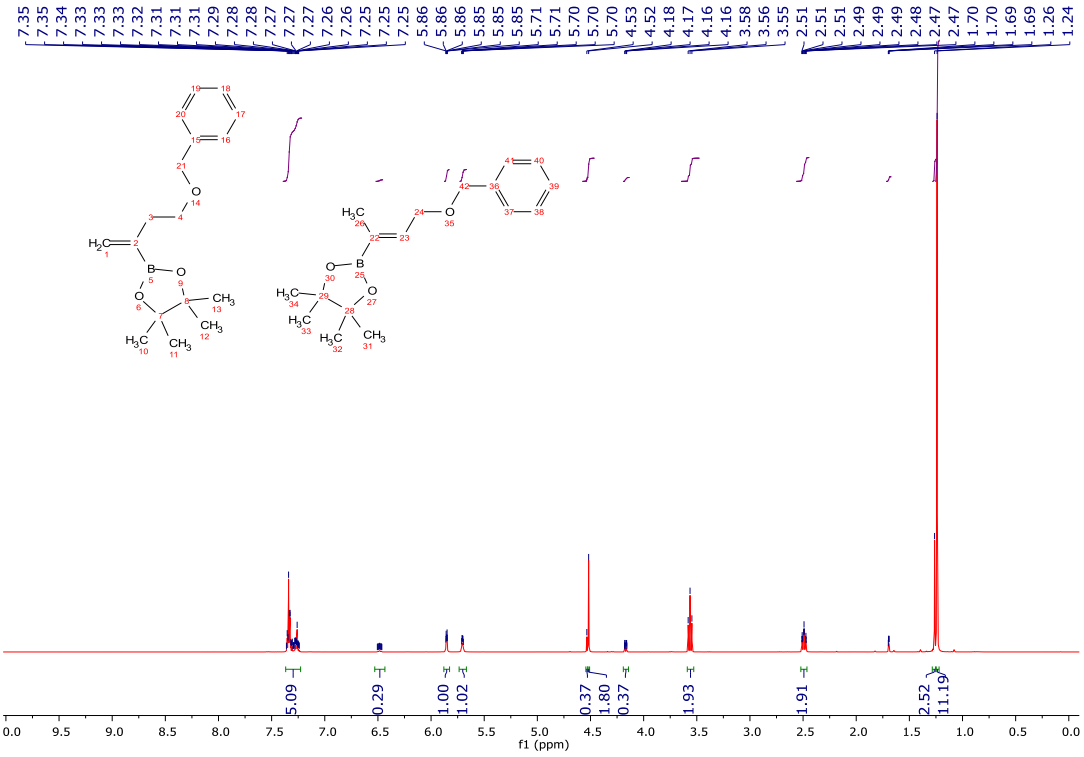
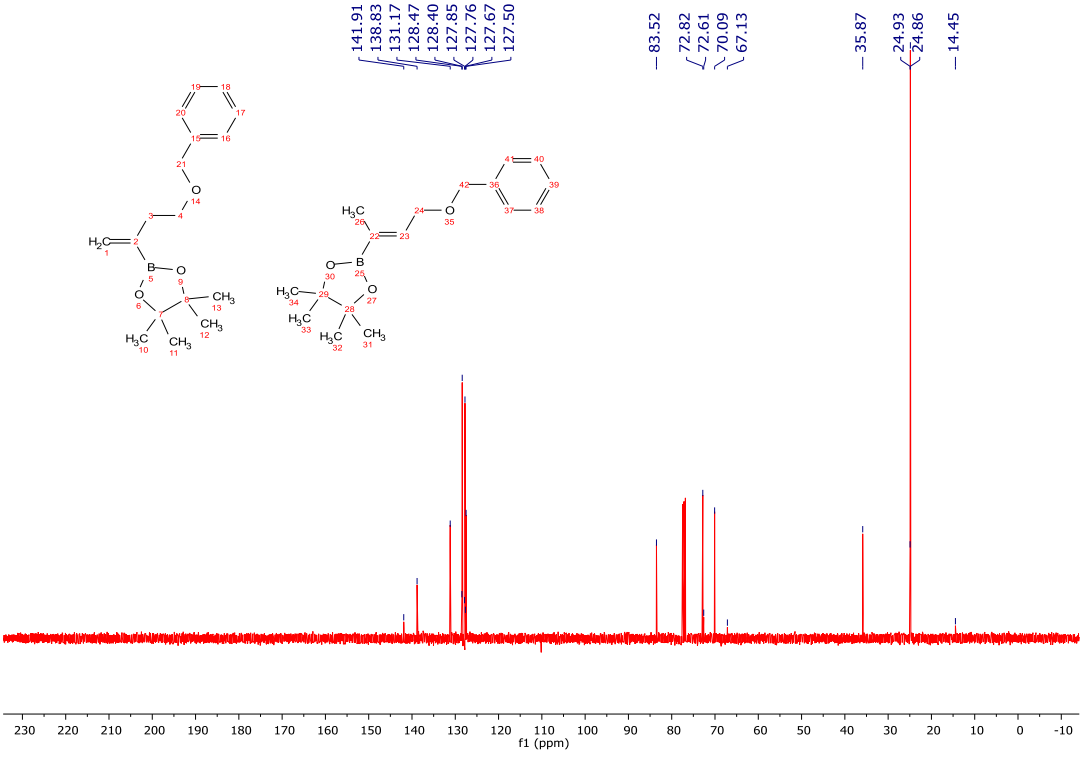
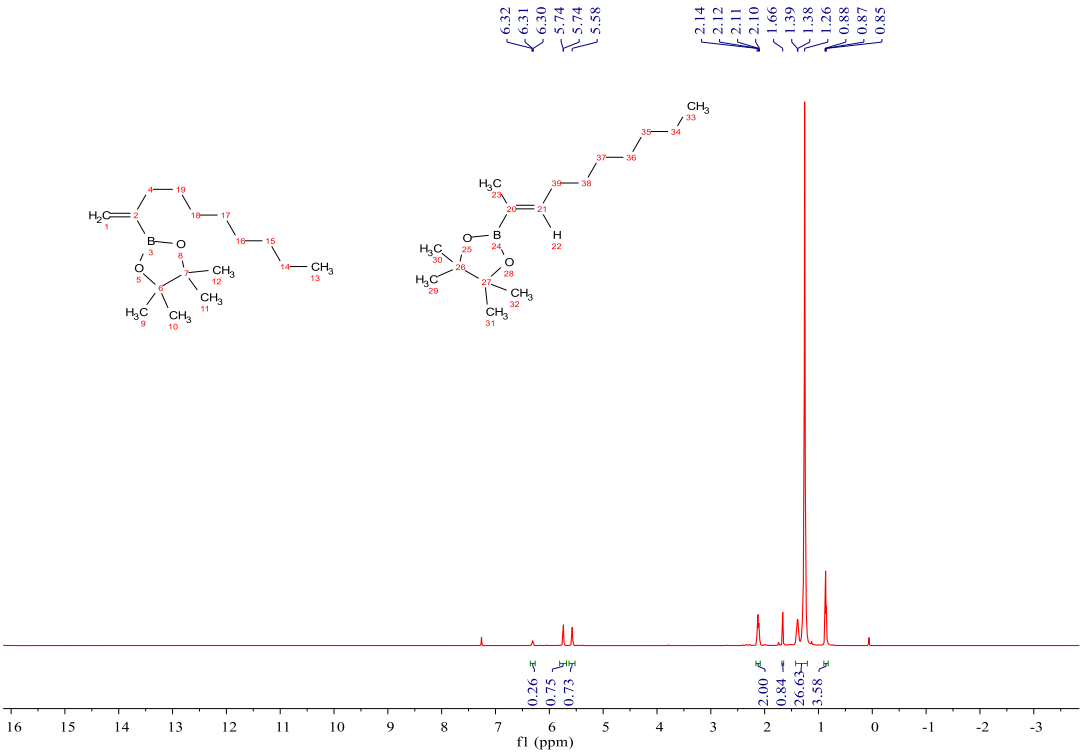
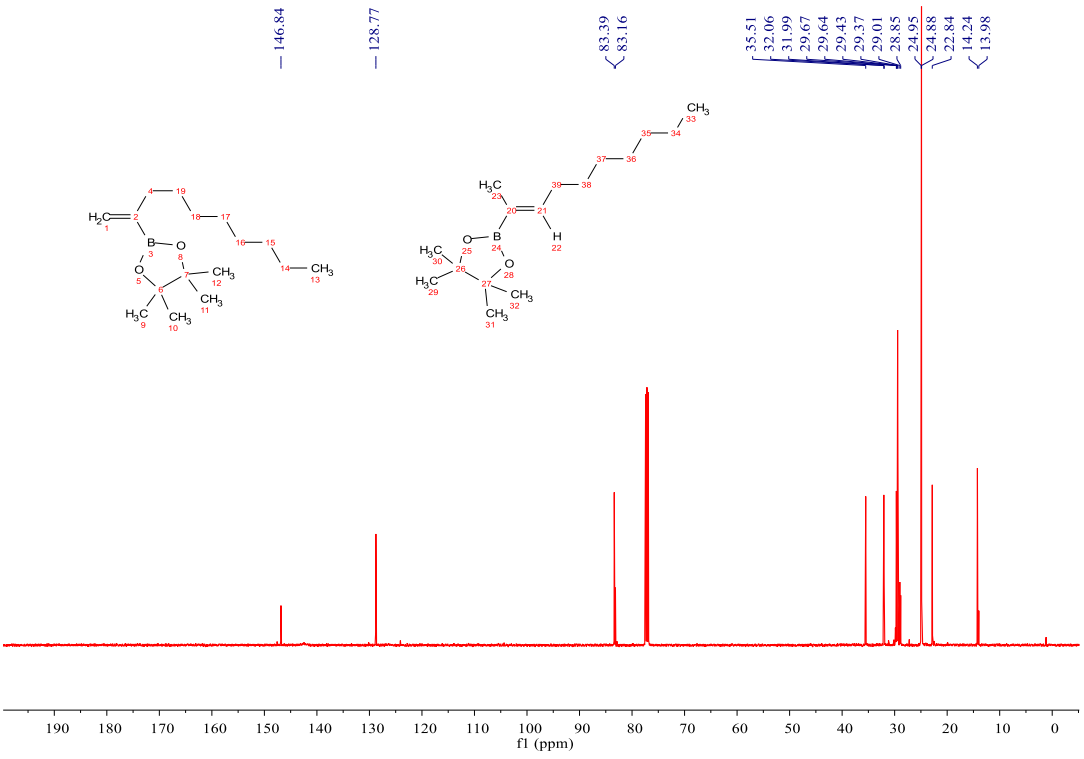
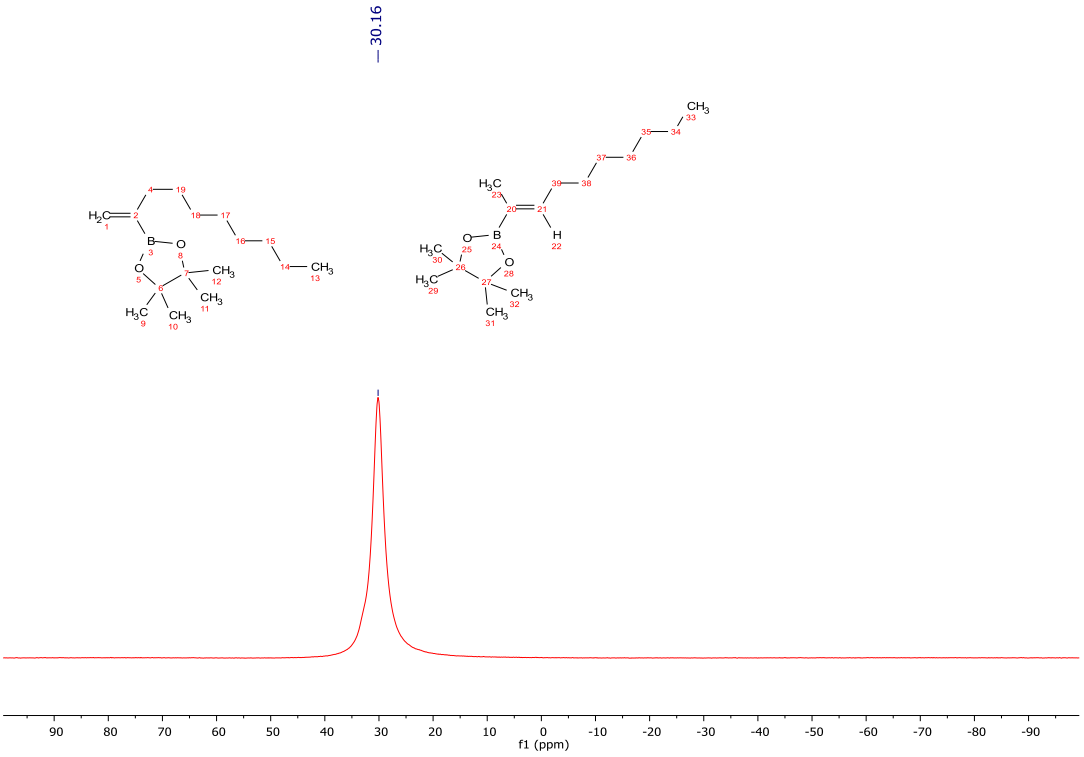
69.30
31.99
29.51
29.26
24.93
24.88
14.19
f1 (ppm)

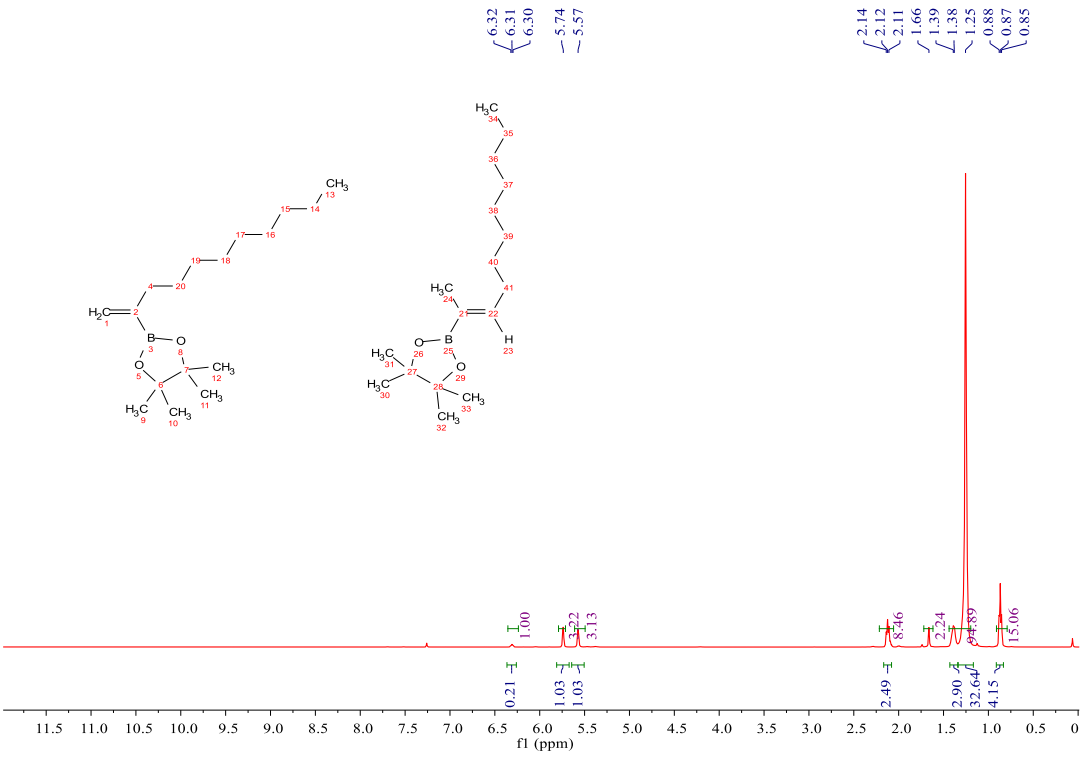

7.35 7.35 7.34 7.33 7.33 7.33 7.32 7.31 7.31 7.31 7.29 7.28 7.28 7.27 7.27 7.27 7.26 7.26 7.25 7.25 7.25
5.86 5.86 5.86 5.85 5.85 5.85 5.71 5.71 5.70 5.70 5.70 4.53 4.52 4.18 4.17 4.16 4.16 3.58 3.56 3.55
2.51 2.51 2.51 2.49 2.49 2.49 2.48 2.47 2.47 1.70 1.70 1.69 1.69 1.26 1.24
5.09 0.29 1.00 1.02 0.37 1.80 0.37 1.93 1.91 2.52 11.19
f1 (ppm)

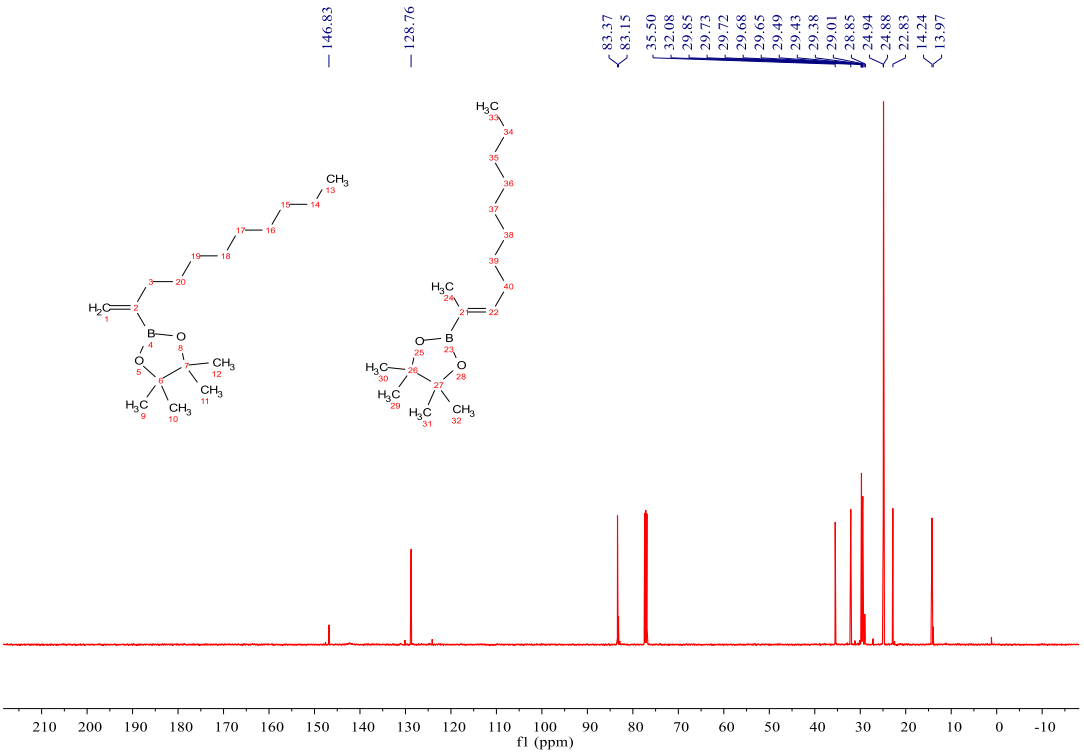

141.91 138.83 131.17 128.47 128.40 127.85 127.76 127.67 127.50
83.52 72.82 72.61 70.09 67.13
35.87 24.93 24.86 14.45
f1 (ppm)

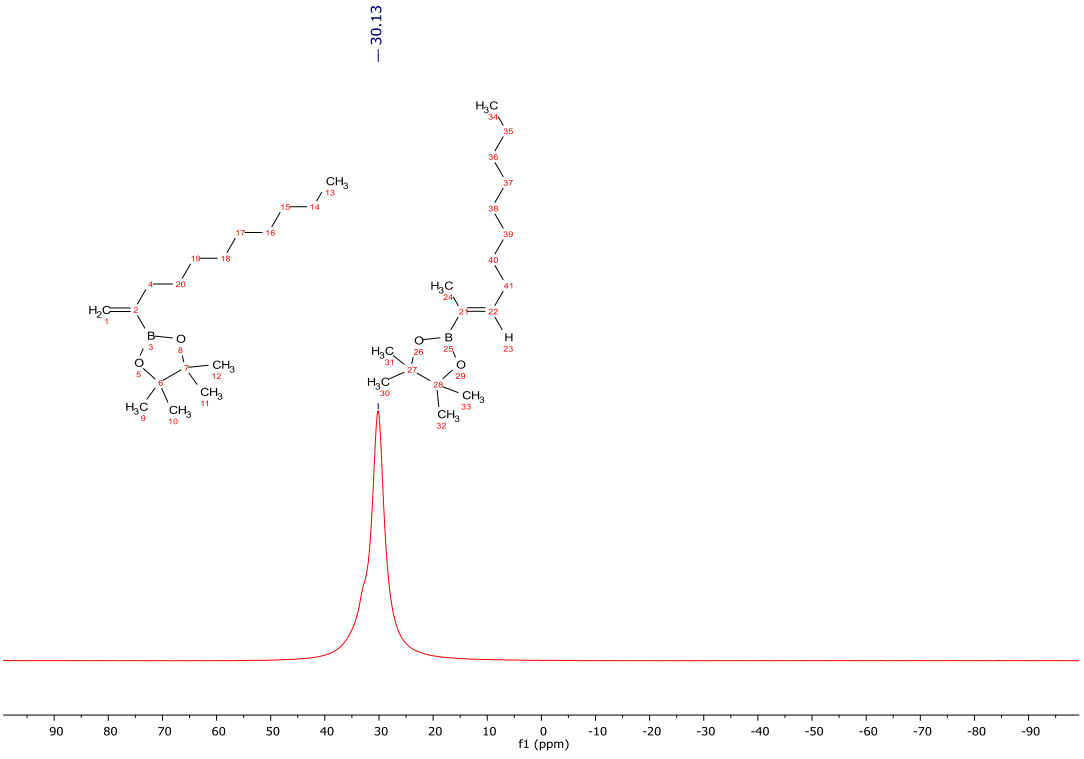

6.32
6.31
6.30
5.74
5.74
5.58
2.14
2.12
2.11
2.10
1.66
1.39
1.38
1.26
0.88
0.87
0.85
0.26
0.75
0.73
2.00
0.84
26.63
3.58
f1 (ppm)

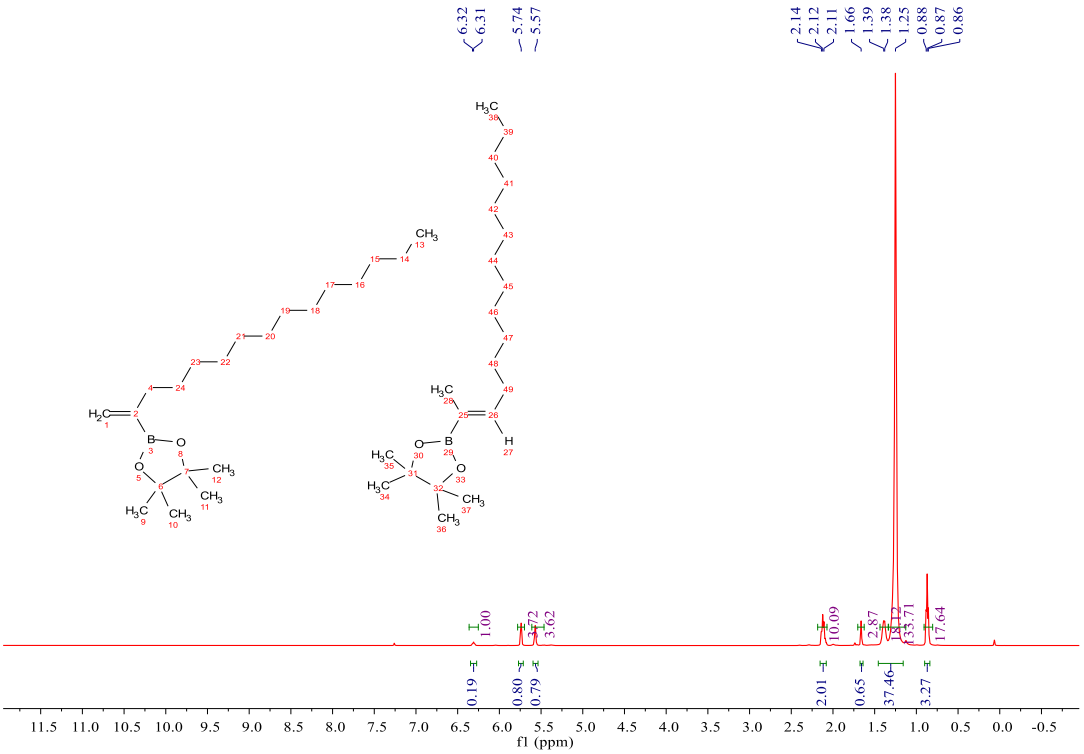

146.84
128.77
83.39
83.16
35.51
32.06
31.99
29.67
29.64
29.43
29.37
29.01
28.85
24.95
24.88
22.84
14.24
13.98
f1 (ppm)

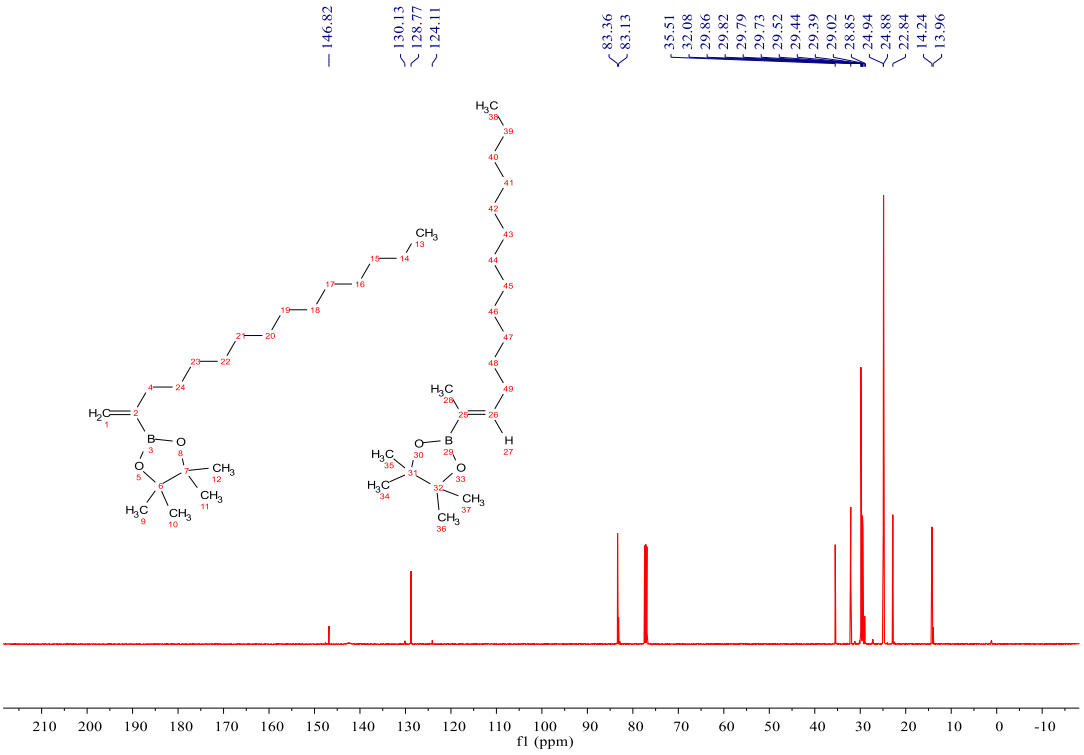

30.16
f1 (ppm)

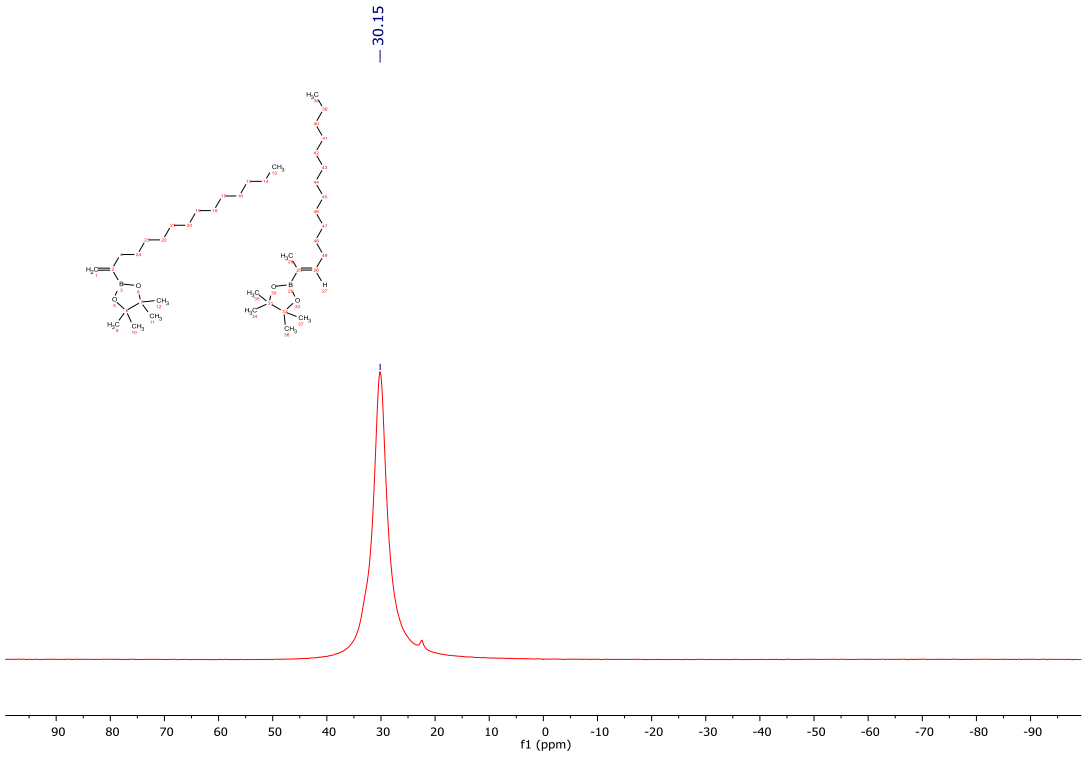

6.32
6.31
6.30
5.74
5.57
2.14
2.12
2.11
1.66
1.39
1.38
1.25
0.88
0.87
0.85
1.00
3.22
3.13
8.46
2.24
4.89
15.06
0.21
1.03
1.03
2.49
2.90
32.64
4.15
f1 (ppm)


146.83
128.76
83.37
83.15
35.50
32.08
29.85
29.73
29.72
29.68
29.65
29.49
29.43
29.38
29.01
28.85
24.94
24.88
22.83
14.24
13.97
f1 (ppm)


30.13
f1 (ppm)


6.32
6.31
5.74
5.57
2.14
2.12
2.11
1.66
1.39
1.38
1.25
0.88
0.87
0.86
1.00
3.72
3.62
10.09
2.87
18.12
33.71
17.64
0.19
0.80
0.79
2.01
0.65
37.46
3.27
f1 (ppm)


146.82
130.13
128.77
124.11
83.36
83.13
35.51
32.08
29.86
29.82
29.79
29.73
29.52
29.44
29.39
29.02
28.85
24.94
24.88
22.84
14.24
13.96
f1 (ppm)


30.15
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
f1 (ppm)