Select Reactions of Organoboranes and Organostannanes

A Dissertation Presented for

the Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

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August 2012

DEDICATION

I dedicate this work to Lisa, Preston, and Clarissa Blevins.

ACKNOWLEDGEMENTS

I would like to thank Dr. George Kabalka for giving me the opportunity to do research in the Boron group, and for providing me with financial support. Thanks to Dr. Min-Liang Yao for your help and advice in my research. Also, I would like to acknowledge Dr. Michael Quinn, Vitale Coltuclu, and Dr. Li Yong for kindly offering their assistance whenever I needed it.

To my wife and children, Lisa, Clarissa, and Preston, thank you all for your support and encouragement. You all are such a blessing in my life. Also, I would like to thank Ronald and Judy Hensley for their friendship, support, and prayers during the last two years, and most of all I would like to thank God for my loving family.

ABSTRACT

Potassium aryl- and alkenyltrifluoroborates and tributyl(aryl)stannanes were found to undergo halodemetallation using trihalide salts, $Y(X_3)$, where X=Br or I; Y=Cs or pyridinium. The hydrolysis of organotrifluoroborates was observed to be promoted by iron(III) chloride, zinc dust, and zinc oxide.

A variety of potassium aryltrifluoroborates and an alkenyltrifluoroborate were found to undergo bromodeboronation at room temperature in a (1:1) THF/water solution in 30-40 minutes using pyridinium tribromide, providing good yields of aryl and vinyl bromides. Activated arenes underwent dibromination, but this was reduced by adding potassium bromide to the reaction.

Potassium aryltrifluoroborates and an alkenyltrifluoroborate were observed to undergo iododeboronation in a (1:2) DMF/water solution at 80 degrees Celsius using cesium triiodide. Activated aryl substrates provide the highest yields of the aryl iodide products. Aryltrifluoroborates with electron withdrawing substituents provided low product yields. Potassium pyridinyl-4-trifluoroborate did not undergo iododeboronation. Unsubstituted aryltrifluoroborates provided modest product yields.

A route to (*Z*)-1,2-dibromoalkenes via the bromodeboronation of stereo-defined potassium alkenylditrifluoroborates using tetrabutylammonium tribromide was investigated. The reaction was found to produce good product yields with very high *(Z)* stereoselectivity from functionally unsubstituted potassium alkenylditrifluoroborates, but functionalized alkenylditrifluoroborates could not be obtained due to the lack of reactivity of the functionalized alkyne precursors in the diborylation reaction required for their synthesis.

Iron(III) chloride, zinc dust, and zinc oxide were found to promote the efficient hydrolysis of potassium organotrifuoroborates in a (1:1) THF/water solution. Excellent yields of the corresponding alkyl-, aryl-, and alkenylboronic acids were obtained in most cases. The hydrolysis reactions are thought to occur due the formation of insoluble fluoride salts.

Iron(III) chloride/sodium iodide was found to be an effective combination to carry out iododeboronation reactions of potassium aryl- and alkenyltrifluoroborates in dry acetonitrile at 80 degrees Celsius in about 19 hours. Good yields of the corresponding iodide products were obtained in most trials.

Iron(III) chloride/sodium iodide was also found to be an effective combination to carry out iododestannation reactions of a variety of tributyl(aryl)stannanes at room temperature in a (1:1) THF/water solution. The reactions generally require 40-60 minutes providing excellent yields of the aryl iodide products in most cases.

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List of Abbreviations

µm	Micrometer
CC	Cubic Centimeter
Chloramine-T	N-chlorotosylamide
DART	Direct analysis in real time
DCM	Dichloromethane
DCME	α,α-Dichloromethyl methyl ether
DMF	N,N-dimethylformamide
DMSO	Dimethylsulfoxide
GC/MS	Gas chromatography/mass spectroscopy
i-Propyl	Isopropyl
MeOH	Methanol
M/Z	Mass to charge ratio
mL	Milliliter
Mol	Mole
NCS	N-chlorosuccinimide
NMR	Nuclear magnetic resonance
NOESY	Nuclear overhauser effect spectroscopy
OAc	Acetate
S_E2	Bimolecular electrophilic substitution
Selectfluor®	1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo-[2.2.2]octane bis(tetrafluoroborate)
S_N2	Bimolecular nucleophilic substitution
TBATB	Tetrabutylammonium tribromide
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Tetramethylsilane
TOF	Time of flight

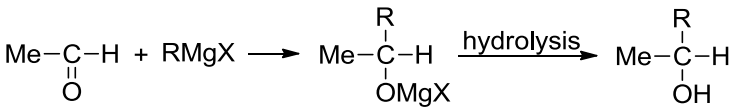
CHAPTER I
SIGNIFIGANCE OF ARYL HALIDES AND ALKENYL HALIDES IN ORGANIC CHEMISTRY

1.1 Aryl Halides and Vinyl Halides in the Formation of Organomagnesium and Organolithium Reagents

Aryl halide functionality occurs in many natural products, and it is also a key synthetic building block for constructing carbon-carbon and carbon-heteroatom bonds. Marine natural products, Streptomyces bacteria, and fungi are sources of naturally occurring organohalides and many of these compounds exhibit biological activity. Some of the demonstrated pharmacological activities of organohalogen compounds include anticancer, anti-inflammatory, antiviral, and antitubercular activity.[1]

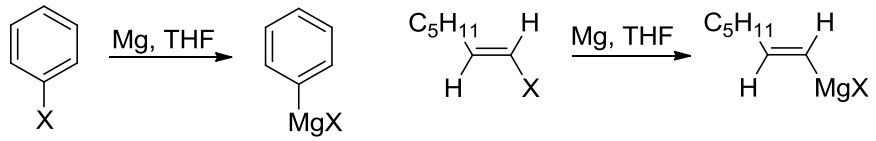
Organometallic reagents are vital to organic synthesis and are frequently formed from organohalides. The Grignard reaction is one of the most useful carbon-carbon bond forming reactions available, and is used to produce primary, secondary, and tertiary alcohols. In the Grignard reaction, an alkyl, aryl, or vinyl group in the Grignard reagent undergoes a nucleophilic 1,2-addition to an aldehyde or ketone to produce an alcohol, Scheme 1.1. [2]

Scheme 1.1 Nucleophilic Addition of Grignard Reagent to a Carbonyl.



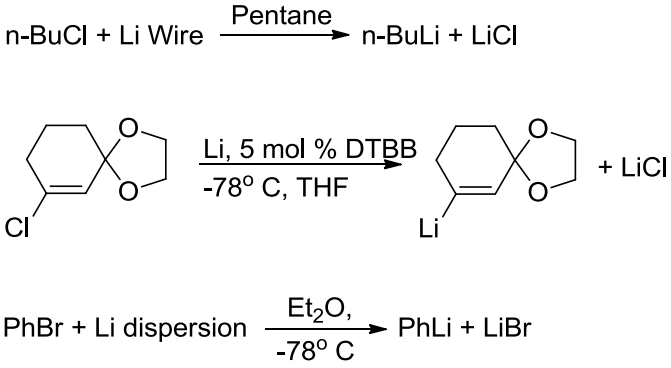
Aryl and vinyl Grignard reagents are generally formed from the corresponding aryl or vinyl bromides and iodides in THF as the solvent, Scheme 1.2.[3]

Scheme 1.2 The Formation of Aryl and Alkenyl Grignard Reagents. X=I, Br, Cl.



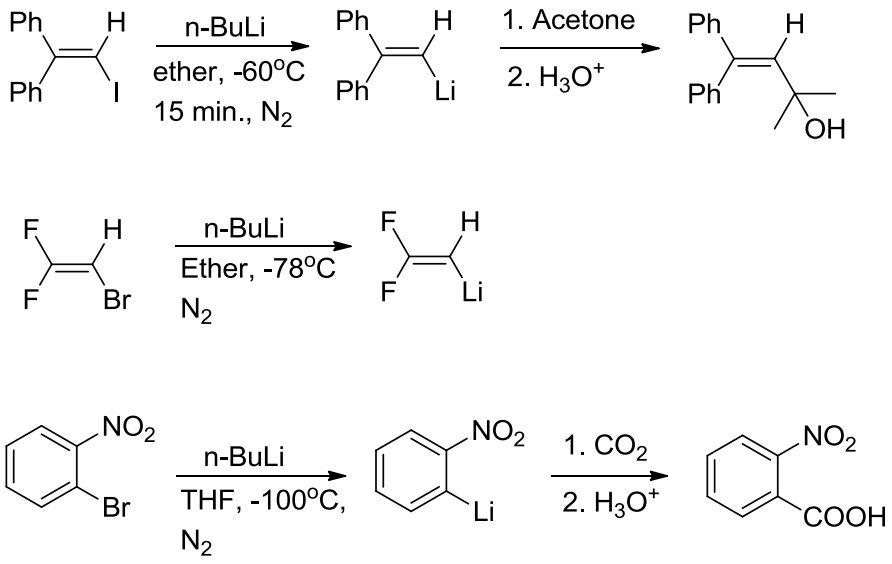
Aryl and vinyllithium reagents are also important nucleophilic organometallic reagents that have similar reactivity to Grignard reagents. Aryl, vinyl, and alkyl organolithiums can be prepared from the corresponding bromides or chlorides using lithium metal, Scheme 1.3.[4,5,6]

Scheme 1.3 The Formation of Organolithium Reagents from Organohalides and Lithium Metal.



Aryl and vinyl lithium reagents may also be prepared by a lithium-halogen exchange reaction. In a lithium halogen exchange reaction, an aryl or vinyl halide undergoes an exchange of the halogen atom with the lithium atom of an alkyl lithium species to form an alkyl halide and a less basic C_{sp}^2-Li species, Scheme 1.4.[7, 8,9]

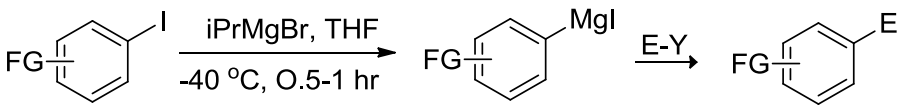
Scheme 1.4 Lithium-Halogen Exchange Reaction and Addition to Carbonyls.



1.2 Organometallic Reagents Derived from Organomagnesium and Organolithium Reagents

Although Grignard and organolithium reagents may be easily synthesized from organohalides, their high reactivity limits many applications in organic synthesis. They may act as bases, undergo competing nucleophilic addition to other functional groups, or in the case of S_N2 reactions with alkyl halides undergo a competing radical side reaction.[10,11] These reactivity and selectivity issues can be partially avoided by use of an iodine-magnesium exchange protocol. In this protocol, an aryl iodide containing a functionality not normally compatible with formation of a Grignard reagent undergoes iodine-magnesium exchange with isopropyl magnesium bromide and then undergoes a nucleophilic reaction with an electrophile, Scheme 1.5.[10]

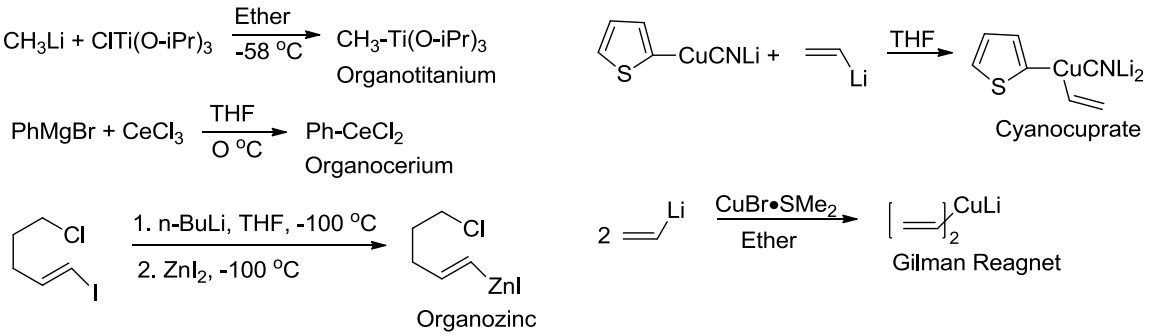
Scheme 1.5 The Generation and Reaction of Functionalized Grignard Reagents by Iodine-Magnesium Exchange.



FG= Br, CON_2, CN, CO_2Et, CO_2t-Bu
E-Y= Aldehyde, Allyl bromide

In an effort to develop improved selectivity and functional group tolerance, new nucleophilic organometallic reagents have been developed through the use of transmetallation reactions of organolithium and Grignard reagents, Scheme 1.6, Table 1.1.[12]

Scheme 1.6 Formation of Various Organometallic Reagents by Transmetallation.



Organotitanium reagents are less reactive and less basic than Grignard reagents and organolithium reagents, and as a result they exhibit higher selectivity in reactions where the substrate contains more than one carbonyl functionality or an α,β-unsaturated carbonyl, Table 1.1.

Organocerium reagents are signifigantly less basic than organomagnesiums and organolithiums and are selective for 1,2-additon. Phenylcerium chloride selectively adds to cyclopent-3-one and benzylidene acetone, Figure 1.1.[13]

Vinyl- or aryl-zinc reagents react with tosyl cyanide to produce aryl or vinyl cyanides in good yields rather than imine products, Scheme 1.7.[14]

Scheme 1.7 Generation and Reaction of (E)-(5-Chloropent-1-en-1-yl)zinc(II) iodide and Benzo[d]thiazol-2-ylzinc(II) Iodide with Tosyl Cyanide.

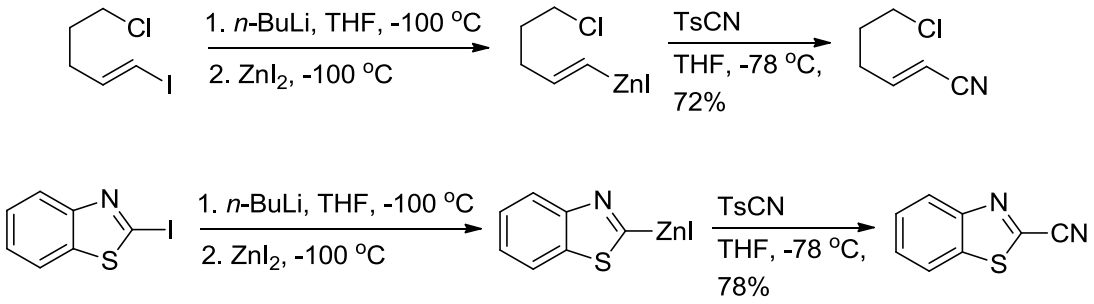
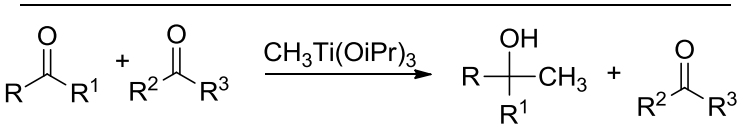
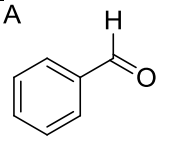
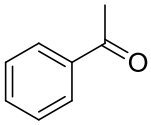
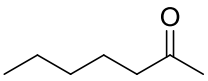
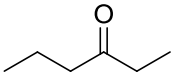
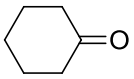
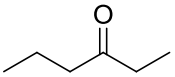
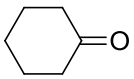
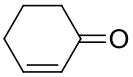


Table 1.1 Selectivity of Organotitanium Reagents in 1,2-Additions. Adapted from: Seebach, D. Modern Synthetic Methods, Wiley: Chichester, UK, **1983**, Vol. 3, pp 217. Zweifel, George S.; Nantz, Michael H. Modern Organic Synthesis: An Introduction; Freeman: New York, **2007**.



A	B	C	(unreacted)
Most Reactive A		Less Reactive B	Selectivity (%) C
			99.9
			92
			97
			94

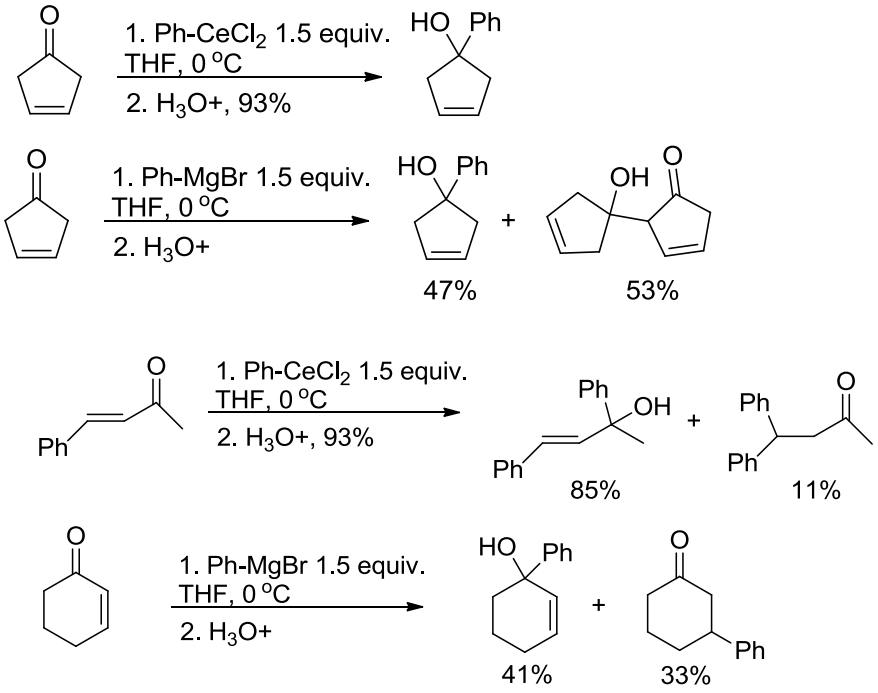
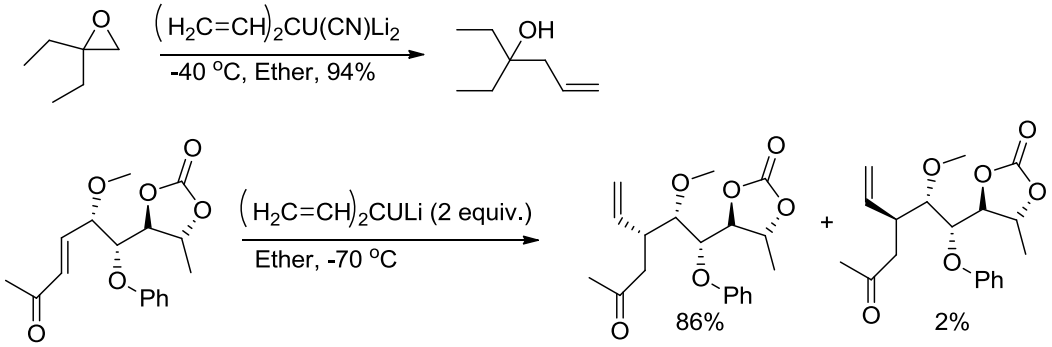


Figure 1.1 Comparison of Selectivity of Grignard and Organocerium Reagents. Adapted form: *J. Am. Chem. Soc.* **1989**, *111,* 4392.

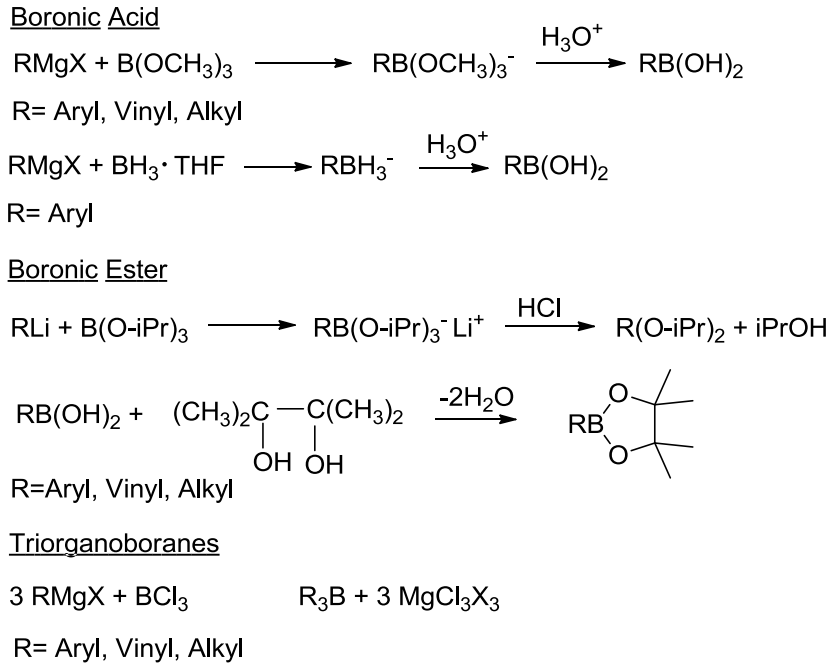
Organocopper reagents also react differently than organomagnesium and organolithium reagents. Organocopper reagents are better at displacing leaving groups in S_N2 reactions, react by conjugate addition selectively over 1,2-addition with α,β-unsaturated systems, and selectively open expoxides to form alcohols by displacing oxygen at the less hindered carbon, Scheme 1.8.[6,15,16]

Scheme 1.8 Vinyl Cyanocuprate and Vinyl Homocuprate (Gilman Reagent) Exhibit High Regioselectivity and Chemoselectivity.



Aryl-, vinyl-, and alkylboronic acids, boronic esters, and triorganoboranes may be synthesized via transmetallation to boron from organomagnesium or organolithium reagents. Arylboronic acids may also be synthesized by the addition of an aryl Grignard reagent to borane followed by an acid workup. Esterification of a boronic acid with a diol produces a cyclic boronic ester, Scheme 1.9.[17,18]

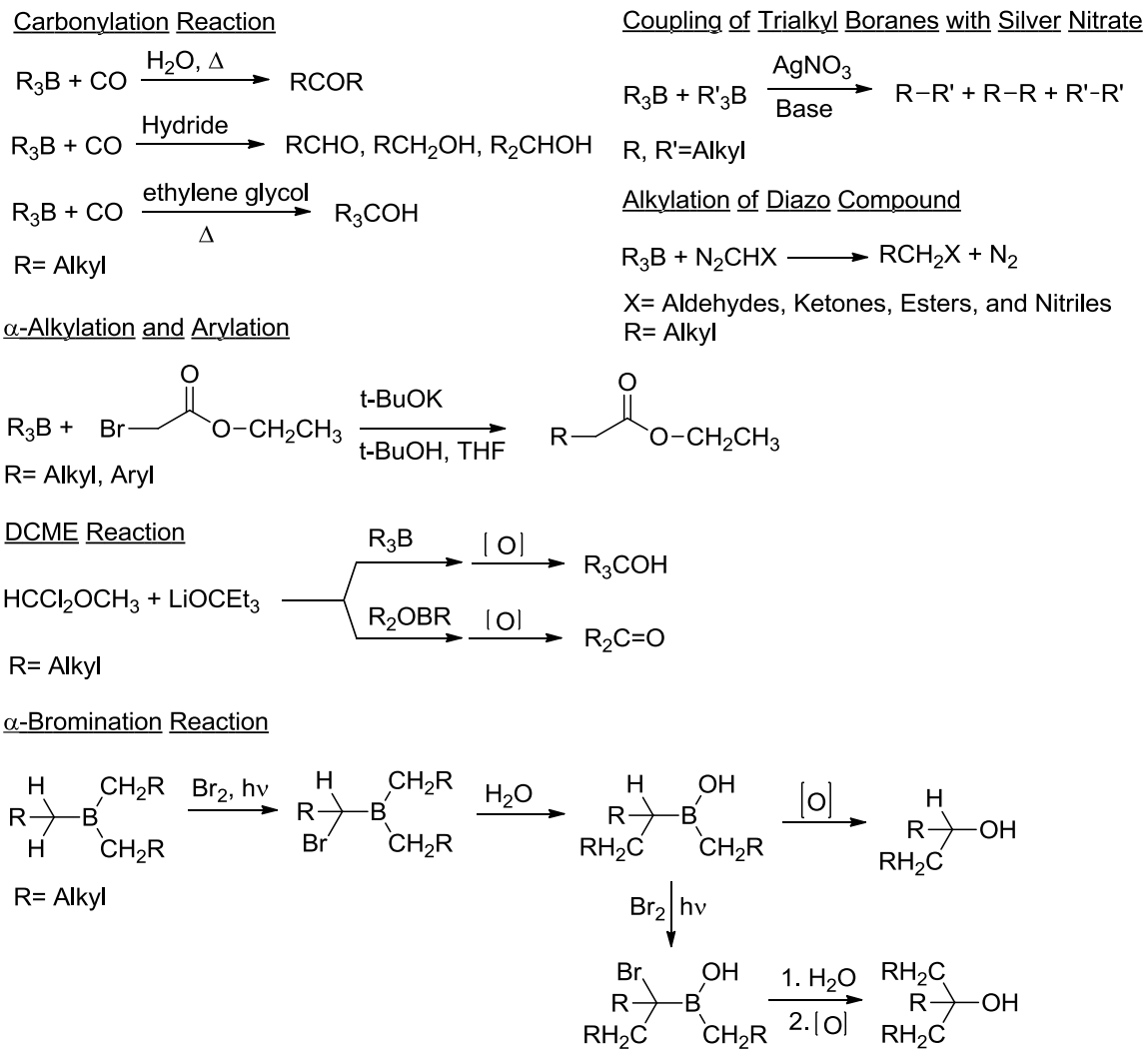
Scheme 1.9 Formation of Boronic Acids, Boronic Esters, and Triorganoboranes from Organomagnesiums and Organolithiums.



Organoboron compounds are versatile reagents that are widely used in organic synthesis. Their demonstrated applications include carbon-carbon bond formation, carbon-oxygen bond formation, carbon-nitrogen bond formation, and carbon-halogen bond formation (palladium catalyzed coupling reactions of aryl and vinyl organoboranes will be discussed in the next section, and halogenation reactions will be discussed in later chapters). Some carbon-carbon bond forming reactions of organoboranes include a carbonylation reaction,[19] coupling of trialkylboranes using silver nitrate,[20] alkylation of diazo compounds,[21] *alpha* alkylation and arylation of bromoesters, bromoketones, and bromosulfonyl

compounds,[22] production of ketones or tertiary alcohols by a DCME reaction,[23] and production of secondary and tertiary alcohols by the *alpha* bromination reaction, Scheme 1.10.[24]

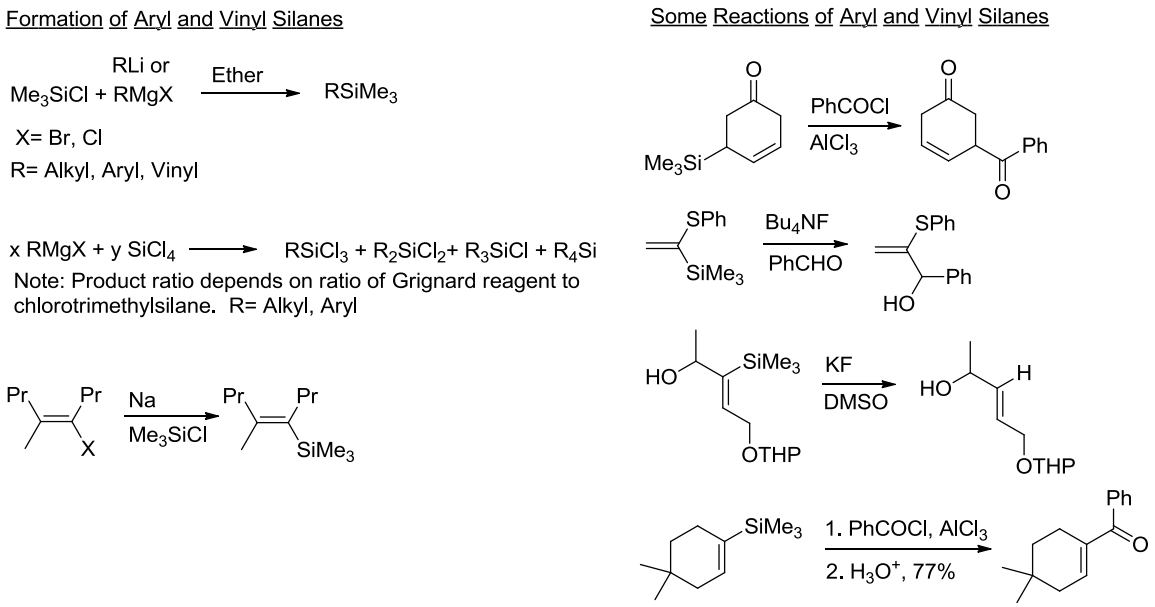
Scheme 1.10 Carbon-Carbon Forming Reactions of Organoboranes.



Trialkyl(aryl)- and trialkyl(vinyl)silanes may be synthesized from aryl Grignards or aryllithium reagents in an S_N2 reaction with a trialkyl(halo)silane. Vinyl silanes may also be produced from vinyl halides by an *in-situ* reaction between sodium metal with a vinyl halide followed by the reaction of the vinyl sodium species with

a trialkyl(halo)silane. Also, aryltrichlorosilanes, aryldichlorosilanes, arylchlorosilanes, and tetraarylsilanes be generated by the reaction of aryl Grignard reagents with silicon tetrachloride. Some of the reactions of aryl- and vinylsilanes include nucleophilic 1,2-addition to carbonyls, dehydrosilylaton, and synthesis of α,β-unsaturated ketones, Scheme 1.11.[25,26]

Scheme 1.11 Formation and Reactions of Aryl- and Trialky(vinyl)silanes.



Like organosilanes, aryl-, vinyl-, and alkyltin compounds may be prepared by reaction of organolithium and Grignard reagents with tin(IV) chloride or trialkyl tin halides. Also, reaction of a vinyl halide with sodium metal to generate vinylsodium and subsequent reaction with tin(IV) chloride generates the tetraorganotin species. The main use of aryl and vinyl tin reagents in organic synthesis is in the Stille coupling reaction (the Stille coupling will discussed in the next section).[27]

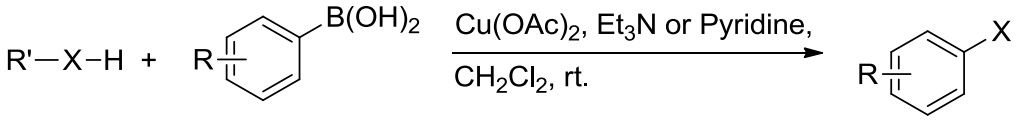
1.3 Palladium Catalyzed Coupling Reactions That Utilize Aryl and Vinyl Halides

One of the most versatile reactions that utilize organoboranes for carbon-carbon bond formation is the Suzuki coupling reaction. The Suzuki reaction has been used to couple aryl halides and vinyl halides with boronic acids, esters, and potassium trifluoroborates. A solventless Suzuki coupling reaction has previously been developed by the Kabalka group that uses 5 mole% palladium powder on KF/Al_2O_3 and microwave irradiation to efficiently couple aryl- and vinylboronic acids with aryl or vinyl bromides and iodides, Figure 1.2.[28,29,30]

A variety of palladium catalyzed coupling reactions have been developed and most of them utilize aryl and vinyl halides. These reactions occur under mild conditions that tolerate sensitive functional groups.

Chan and co-workers developed a method of N- and O- arylations using phenylboronic acids and cupric acetate. The method was found to be effective for phenols, amines, anilines, amides, imides, ureas, carbamates, and sulfonamides producing good yields in most cases, Scheme 1.12.[31]

Scheme 1.12 N- and O- Arylations with Phenylboronic Acids.

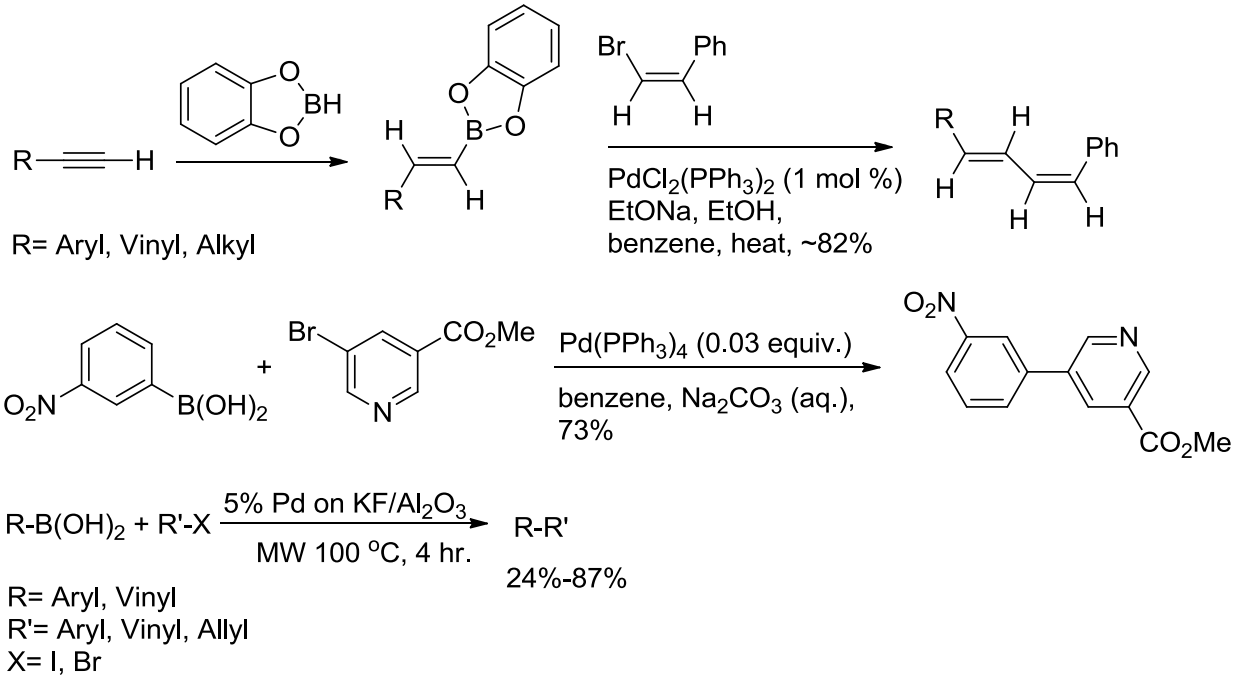


When X= N, (R'= Alkyl, Aryl)
When X= O, (R'= Aryl)
R= Me, H, F, OMe, Cl

4%-96%

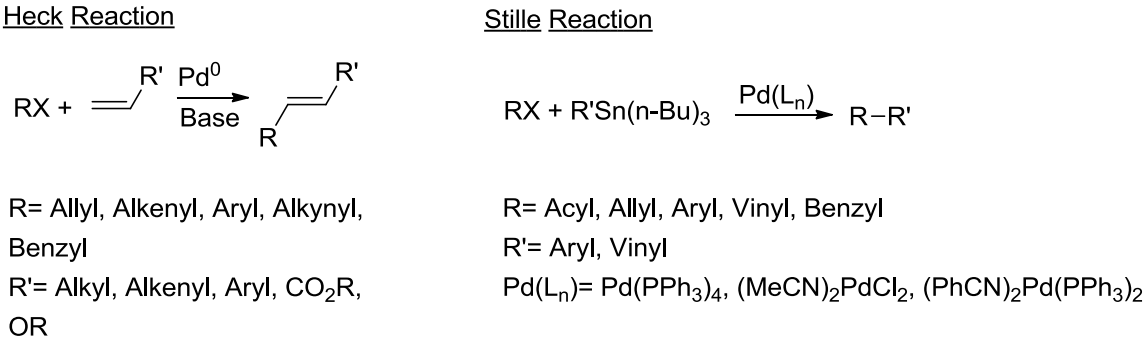
In addition to the Suzuki coupling, other palladium catalyzed coupling reactions that utilize aryl halides, vinyl halides, or pseudo-halides are important in organic synthesis. These include the Heck reaction to couple aryl and alkenyl halides with alkenes, the Negishi reaction to couple organozinc, organo-aluminum, and organozirconium compounds with vinyl, aryl, and alkynyl halides.

Figure 1.2 The Suzuki Reaction Allows the Coupling of Aryl, Alkyl, and Vinyl Halides with Aryl- and Vinylboronic Acids and Esters.

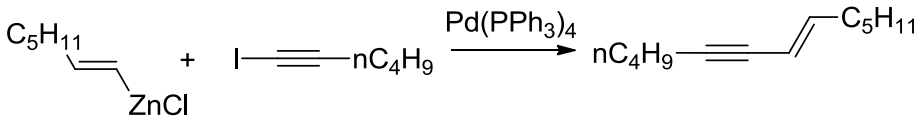


the Sonogashira reaction to couple terminal alkynes with aryl halides, and the Stille coupling to couple aryl and vinyl halides with aryl or vinyl tin reagents Scheme 1.13.[32-35]

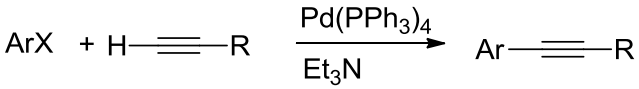
Scheme 1.13 Palladium Catalyzed Coupling Reactions.



Negishi Reaction



Sonogashira Reaction

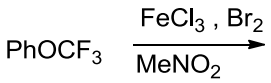


X= Cl, Br, I, OTf

1.4 Methods for Synthesizing Aryl Halides

One of the most important methods for synthesizing aryl halides is electrophilic aromatic substitution using halogens. The electronic nature of the aryl ring determines the substitution pattern obtained. Electron withdrawing substituents are *meta* directors for the incoming halogen due to a lower energy of activation for the formation of the arenium ion formed by attack at the *meta* ring position. Electron donating substituents are *ortho* and *para* directors due to a lower energy of activation for the formation of the arenium ion by electrophilic attack at the *ortho* and *para* ring positions. Usually mixtures of products are obtained and these may be difficult to separate. Activated aryl rings bearing electron donating substituents may also undergo multiple halogenations. Both chlorination and bromination may be carried out using iron or iron(III) chloride as catalyst, but direct iodination of an aryl ring is more difficult due to the lower electrophilicity of iodine and the reversibility of the reaction. A major drawback to electrophilic aromatic substitution is the fact that products with substitution patterns that differ from what is favored by the electronic nature of the substrate can be difficult to synthesize, Scheme 1.14.[36]

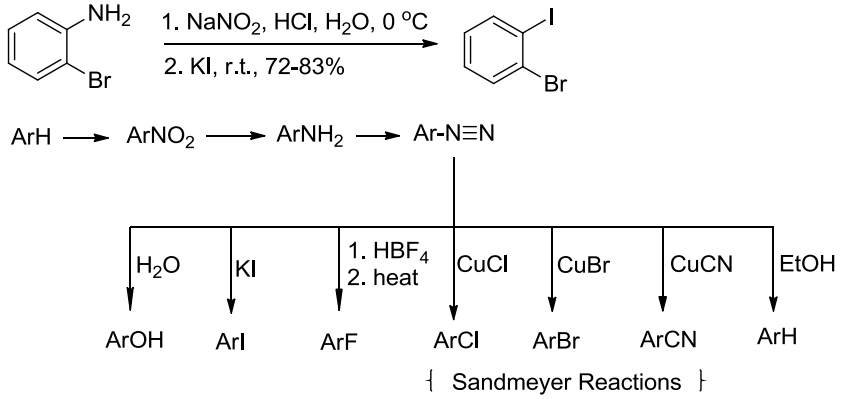
Scheme 1.14 Electrophilic Halogenation of Trifluoromethoxybenzene.



Substrate	Electrophile	% Isomer Distribution Ortho	Meta	Para
CF_3Ph	Br_2	12.5		87.5
	Cl_2	22.9	6	71.1

Schieman and Sandmeyer reactions allow the regiospecific preparation of aryl iodides, chlorides, bromides. Also, these reactions allow for the generation of substitution patterns not available by electrophilic aromatic substitution. In these reactions, an aryl amine undergoes diazotization to form an aryl diazo intermediate that loses nitrogen to form an aryl cation that can react with water, cyanide, iodide, chloride, bromide, or fluoride to regiospecifically incorporate the new substituent onto the aryl ring, Scheme 1.15.[38]

Scheme 1.15 Synthesis of Substituted Arenes by the Decomposition of Aryl Azides.



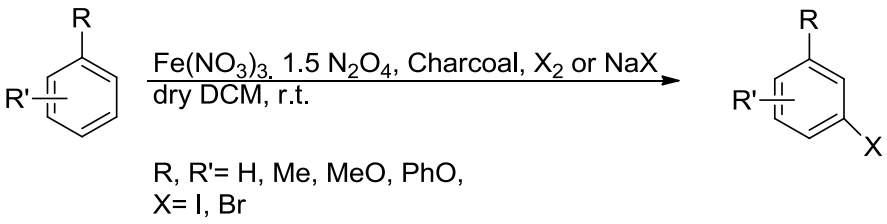
To increase the reactivity of iodine in electrophilic aromatic substitution reactions, several approaches have been taken. One approach is to oxidize the iodine to a more electrophilic species such as hypoiodate or hypoiodic acid, another approach is to coordinate the iodine molecule with a lewis acid to polarize the molecule, or through the use of the interhalogen iodine monochloride. These reactions generally require harsh conditions that limit their

applications for arenes with sensitive functional groups because; these methods may utilize HNO_3/H_2SO_4, HIO_4 or HIO_4/H_2SO_4, $KMnO_4/H_2SO_4$, CrO_3/I_2 in acid, vanadium salts/CF_3SO_3H, $Pb(OAc)_4$/ AcOH, and NIS/CF_3CO_2H. One reported method uses $ICl/Ag_2SO_4/H_2SO_4$.[37,38]

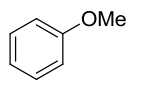
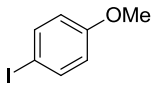
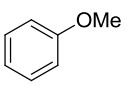
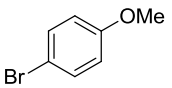
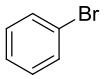
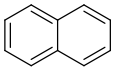
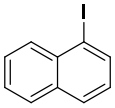
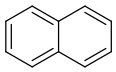
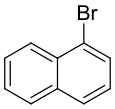
The Kabalka group previously developed an electrophilic aromatic substitution method that utilized dehydrated alumina either in solution phase or solid phase. The dehydrated alumina surface with exposed Al^{3+} sites can coordinate iodine to polarize the molecule increasing electrophilicity, in addition the iodine can react with O^{2-} ions on the surface to produce hypoiodite or hypoiodic acid. The most reactive substrates were anisole, N,N-dimethylaniline, and azulene which produced useful yields of aryl iodides.[39] An iron(III) nitrate, dinitrogen tetroxide, charcoal system has been developed for halogenation arenes using iodine or bromine. Also, either sodium iodide or sodium bromide may be employed, but the reaction iodinates most effectively using iodine. As expected, activated substrates produce the best yields. Benzene is iodinated in 74% yield, toluene is iodinated to produce a mixture of *ortho* and *para* products in 94% yield, and naphthalene is iodinated in 50% yield.

Bromination was also carried out on activated and unactivated aryl substrates with both bromine and sodium bromide. High yields and high selectivity were obtained with most of the substrates. Highly activated 2,4-dimethoxy benzene was monobrominated in 91% and 93% yield. 1-Methoxynaphthalene was monobrominated in 85% and 87% yield. Benzene was brominated in 80% and 85% yield. Bromination of toluene produced a mixture of *ortho* and *para* brominated products, Scheme 1.16 and1.17.[39]

Scheme 1.16 Iodination of Activated and Unactivated Arenes.

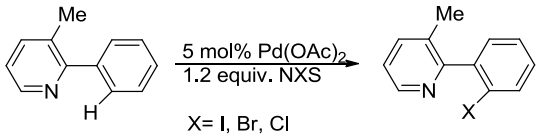


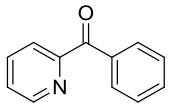
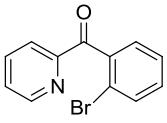
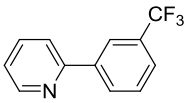
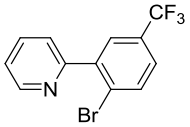
Scheme 1.17 Bromination of Activated and Unactivated Arenes. Adapted from: *Tet. Lett.* **2003**, *44*, 8781.

Substrate	Product	X_2 Yield(%)	NaX Yield(%)	Substrate	Product	X_2 Yield(%)	NaX Yield(%)
		96	94			95	94
		74	0			85	80
		50	0			89	70

A palladium(II) acetate catalyzed, ligand directed, carbon-hydrogen bond activation of arenes leads to regioselective iodination, bromination, and chlorination of various substituted arenes using N-iodosuccinimide, N-bromosuccinimide, or N-chlorosuccinimide as the halogen source. Halogenations were accomplished at ring locations not favored by the electronic nature of the substrate, entries 7 and 8. Moderate to good yields of aryl halides were obtained, Scheme 1.18.[40]

Scheme 1.18 Ligand Directed $Pd(OAc)_2$ Catalyzed Halogenation of Arenes. Adapted from: *Org. Lett.* **2006**, *8:12*, 2523.



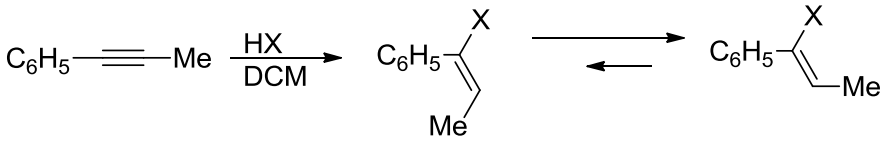
Substrate:	Product:	Yield(%)
		56
		63

Halodemetallation with bromine, iodine or other halogen sources to produce aryl bromides and iodides is a general reaction of organometallic compounds. These types of reactions will be discussed in the next section.

1.5 Methods for Synthesizing Vinyl Halides

Vinyl iodides, bromides, and chlorides may be produced from an alkyne using hydroiodic, hydrobromic, or hydrochloric acid. Addition of the acid to the triple bond occurs following Markovnikov's rule. Addition of hydrogen bromide in the presence of peroxides occurs by a radical mechanism and produces the anti-Markovnikov product. Addition of silica or alumina has been shown to increase both the reaction rate and product yield. Phosphorous tribromide, oxalyl chloride, and acetyl iodide were also found to be effective in generating hydrogen halides in the presence of silica or alumina, Scheme 1.19.[41]

Scheme 1.19 Hydrohalogenation of Alkynes. Adapted from: *J. Am. Chem. Soc.* **1990**, *112*, 7433.



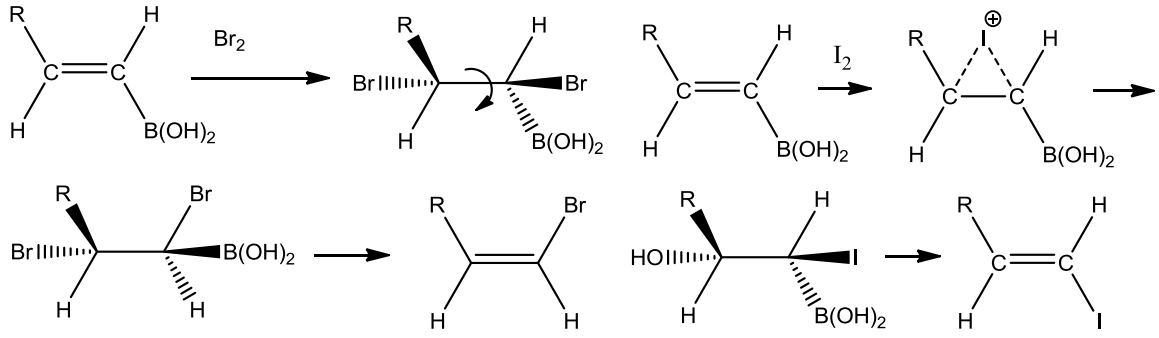
Conditions:	%Yield	%Yield
HCl, 1h	0	0
HCl, SiO_2, 1h	39	11
$(COCl)_2$, Al_2O_3, 0.3h	85	14
3h	3	96
HBr, 3h	29	8
HBr, Al_2O_3, 3h	14	79
PBr_3, Al_2O_3, 3h	82	10
PBr_3(excess), Al_2O_3, 3h	4	80
HI, 24h	74	19
AcI, Al_2O_3, 0.3h	92	6

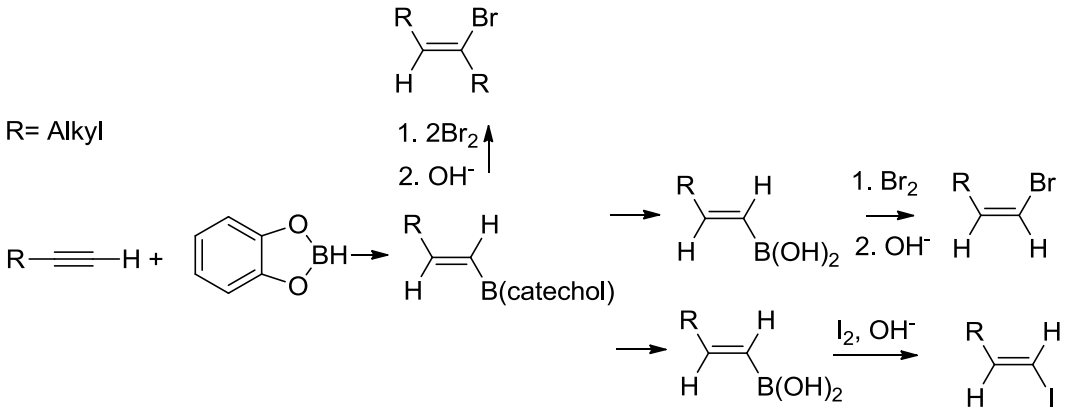
(*E*)-1,2-Dibromo alkenes may be generated by allowing alkynes to react with bromine or chlorine. Iodine on alumina will add hydrogen iodide to terminal alkynes to form 2-iodoalkenes. The Kabalka group has reported the bromination of alkynes to produce (*E*)-1,2-dibromoalkenes using sodium perborate/sodium bromide in acetic acid. The dibromoalkenes were produced in very good yields. Also, Kabalka and coworkers reported the stereospecific addition of iodine to

alkynes on dehydrated alumina to form (*E*)-1,2-iodoalkenes. Various terminal alkynes produced the (*E*)-1,2-diiodoalkenes in very good yields, and an internal alkyne (dimethylacetylene dicarboxylate) produced corresponding (*E*)-1,2-diiodoalkene in 50% yield.[40,42]

Various methods have been developed to selectively produce *Z* and *E* vinyl bromides and iodides from alkynes. (*Z*)-Vinyl bromides or (*E*)-vinyl iodides are produced when a terminal alkynes undergo hydroboration with catecholborane followed by halogenation. Aqueous acidic workup will convert the hydroboration intermediate into a boronic acid. Reaction of the boronic acid with either bromine or iodine in basic aqueous or methanolic solution stereospecifically produces the vinyl halide. Bromination of the vinylboronic acid produces the (*Z*)-vinyl halide and reaction with iodine produces the (*E*)-vinyl halide. Bromination produces the (*Z*)-vinyl bromide because after the addition of bromine to the double bond, there is a base-induced *trans* elimination of boric acid and bromine. Iodination of the vinylboronic acid intermediate produces the (*E*)-vinyl iodide via a *cis* elimination of tetrahydroxyborate. Hydroboration of internal alkynes followed by bromination of the corresponding vinyl boronic acid produces (Z)-vinyl halides. Reaction of the (*E*)-vinyl boronic acid intermediate with chlorine in methylene chloride produces the (*Z*)-vinyl chloride, Scheme 1.20.[43]

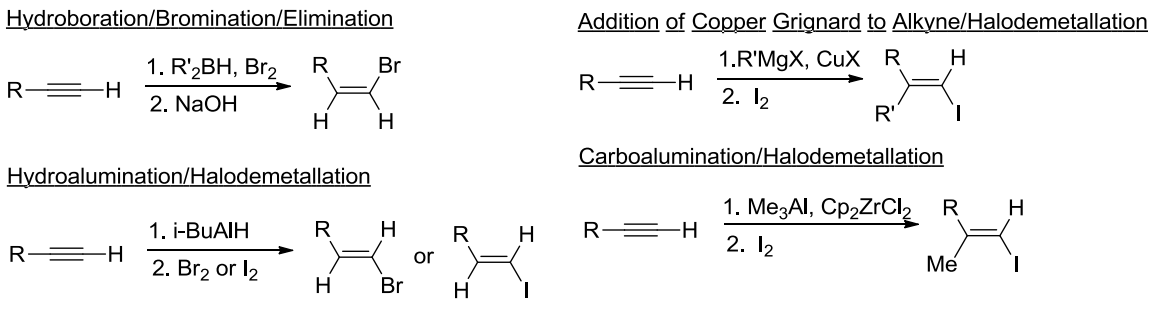
Scheme 1.20 Reactions of Vinylboronic Acids with Iodine and Bromine. Adapted from: *J. Am. Chem. Soc.* **1973**, *95:19*, 6456., *Tet. Lett.* **1985**, *26:3*, 279.

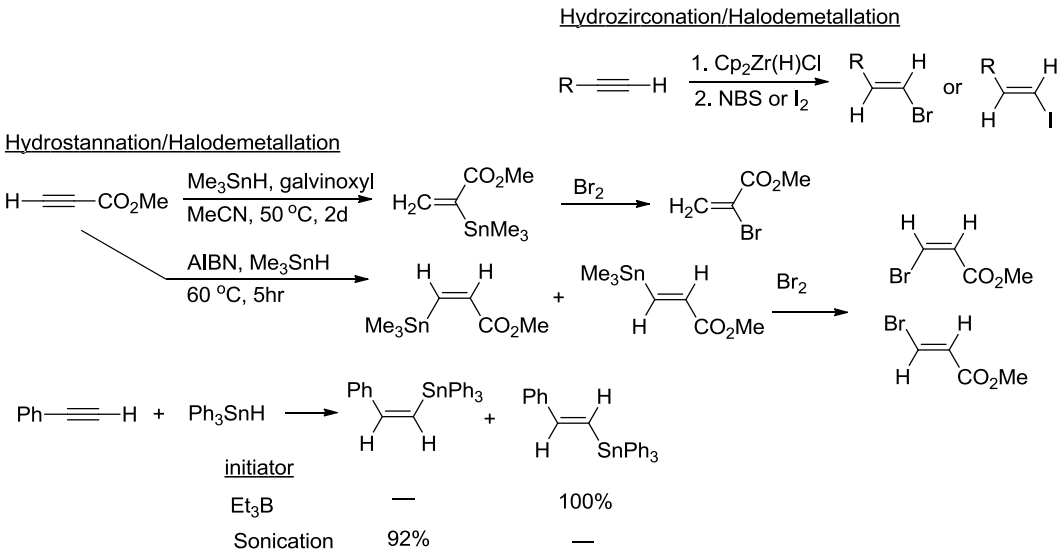




Other methods of synthesizing stereodefined vinyl halides are the hydroalumination, hydrozirconation, and reactions of terminal alkynes with bromine, iodine, or N-bromosuccinimide to produce (*E*)-vinyl halides. Carbometallation of a terminal alkyne with a Grignard/copper(I) halide or trimethylaluminum followed by reaction with iodine produces (*Z*)-vinyl iodides or (*E*)-vinyl iodides respectively. The hydrostannation of alkynes also provides a versatile way of preparing vinyl halides. The hydrostannation of polar alkynes occurs by either a hererolytic mechanism or a homolytic mechanism depending upon the reaction conditions. Nonpolar alkynes react by the homolytic mechanism and either the (*Z*)-vinylstannane or (*E*)-vinylstannane can be selected depending upon the reaction conditions, Scheme 1.21.[29,44-47]

Scheme 1.21 Synthesis of (*Z*) and (*E*)-Vinyl bromides. Adapted from: *J. Am. Chem. Soc.* **1975**, *97*, 679., *J. Am. Chem. Soc.* **1975**, *97*, 679., *Synthesis* **1981**, 841., *Synthesis* **1979**, 501., Davies, Alwyn G. Organotin Chemistry; VCH: New York, **1997**.

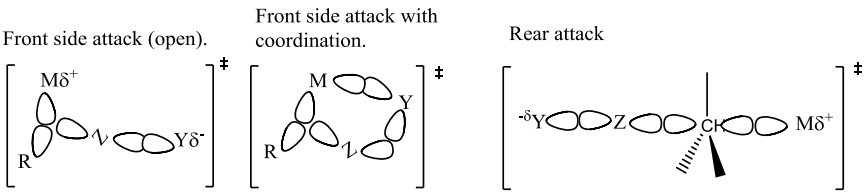




Halodemetallation of organometallic reagents is thought to occur by a S_E2 mechanism. In the S_E2 (electrophilic bimolecular substitution) mechanism, attack on the carbon-metal bond by an electrophile may occur from the front side or from the rear. In alkyl carbon-metal bonds, front side attack leads to retention of stereochemistry, and backside attack leads to inversion. In S_E2 reactions involving Sp^2 carbon-metal bonds front side attack is thought to occur. Two possible transition states are proposed for the front attack by the electrophile in the S_E2 mechanism. In the S_E2 open mechanism, the electrophile attacks the carbon-metal bond without coordination by its anionic side ($Y^{\delta-}$) to the metal. In the cyclic S_E2 transition state, the anionic end of the electrophile ($Y^{\delta-}$) coordinates the metal either prior to the electrophilic attack of the carbon-metal bond or simultaneously with the electrophilic attack of the carbon metal bond. Substitution occurs with retention of stereochemistry in vinylstannanes, Scheme 1.22.[29,48]

Scheme 1.22 Proposed Transition States for the S_E2 Reaction.

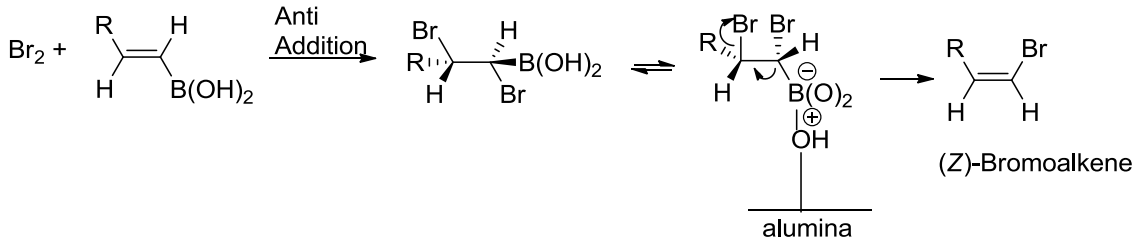
Adapted from: *Acc. Chem. Res.* **1983**, *16*, 177.

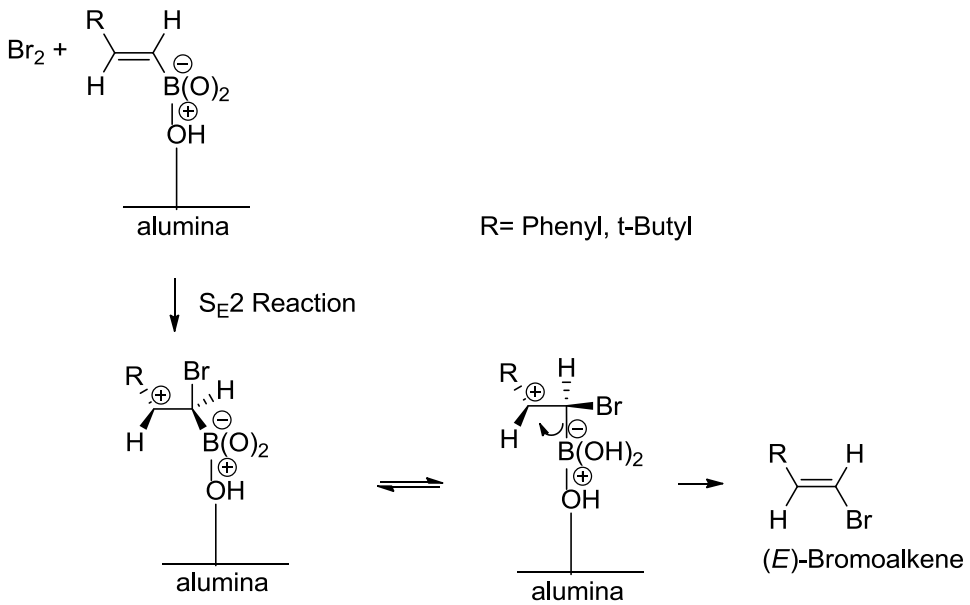


1.6 Halodemetallations of Aryl- and Vinylboranes

The synthesis of vinyl iodides and bromides on unactivated alumina from (*E*)-1-alkenylboronic acids was developed by the Kabalka group. In the case of iodinations, straight chain (*E*)-1-alkenylboronic acids produce mixtures of the (*E*) and (*Z*)-alkenyl iodides, in about equal quantities. (*E*)-1-Alkenylboronic acids bearing a phenyl substituent produce only the (*E*)-alkenyl iodides. To explain these results, it was postulated that the boronic acids were iodinated by three different mechanisms. The straight chain substrates not bound to the alumina surface react by iodination of the alkene to form a diiodinated boronic acid followed by complexation to the surface hydroxyl groups of the alumina, and then the *trans* elimination of boric acid and iodide to produce the (*Z*)-1-alkenyl iodide. The unbound substrate bearing a phenyl substituent reacts by iodination of the alkene to form a diodinatedboronic acid. Then complexation to the surface hydroxyl groups of the alumina, followed by the *syn* elimination, due to steric constraints, of boric acid and iodide to produces the (*E*)-1-alkenyl iodide. The (*E*)-1-alkenyl boronic acid that bound to the alumina surface prior to iodination forms a borate species and the borate species reacts by a front S_E2 mechanism to produce the (*E*)-1-alkenyl iodide.[49] The brominations of straight chain 1-alkenylboronic acids on alumina produces moderate yields of the 1-akenyl bromides as (*E*) and (*Z*) mixtures, but differed in the ratio of *E/Z* produced. A 1:3 ratio of E/Z was observed. Brominations of (*E*)-1-alkenylboronic acids with a phenyl substitiuent produces mostly the *Z*-isomer by the previously mentioned *syn* elimination, Scheme 1.23.[50]

Scheme 1.23 Mechanisms of Halogenation of 1-Alkenylboronic Acids.



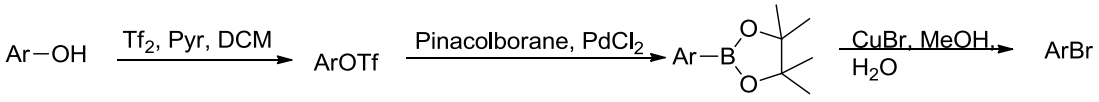


Adapted from: *J. Organomet. Chem.* ***1995****, 487, 35.*

A solution phase iodination of 1-alkenyl pinacolboronate esters has been developed using iodine monochloride and sodium methoxide as the base. Good to excellent *E/Z* stereoselectivity was observed by changing the order of addition of the halogen and base. Yields of 1-iodo-1-alkenes ranged from 43%-88%.[51]

The Kabalka group developed a mild method of converting phenols to aryl halides using copper(II) bromide. The phenol undergoes triflation and palladium chloride catalyzed coupling with pinacolborane to form the aryl pinacol boronic ester intermediate that is then reacted with copper(II) bromide form the aryl bromide, Scheme 1.24.[52]

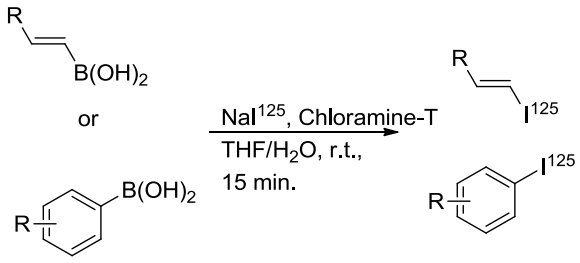
Scheme 1.24 Conversion of Phenol to Aryl Iodide.



Substrate	Product Yield(%)	Substrate	Product Yield(%)
PhOH	38	2-naphthol	88
p-t-Bu-Ph-OH	81	m-chlorophenol	12

Kabalka and coworkers also developed an iododeboronation procedure using alkyl boranes that utilized sodium iodide and chloramine-T. The chloramine-T oxidizes the iodide to either iodine monochloride or a hydrated iodonium ion. Either of these is a source of electrophilic I^+ that will affect the iododeboronation by an S_E2 mechanism to form the alkyl iodides. Excellent yields were obtained in most cases. This methodology was next applied to the iodine^{125} labeling of aryl- and vinylboronic acids. The reaction is very mild, occurring at room temperature in THF and water in 15 minutes with no added base. Arylboronic acids produce excellent radiochemical yields ranging from 74%-91%. Vinylboronic acids produce lower radiochemical yields ranging from 41%-77%, Scheme 1.25.[52]

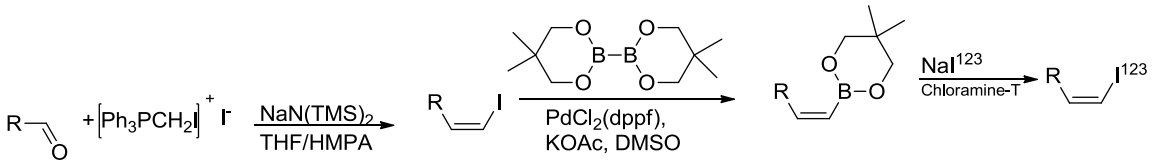
Scheme 1.25 Radiolabelling of Aryl- and Vinylboronic Acids with I^{125}.



Substrate	Yield(%)
$PhB(OH)_2$	91
p-Br-$PhB(OH)_2$	78
p-Me-$PhB(OH)_2$	86
(*E*)-*n*-PrCH=CH$B(OH)_2$	77
(*Z*)-*n*-HeptylCH=C($B(OH)_2$, *n*-Heptyl-CO_2Me)	41

Kabalka and coworkers reported a fast, high radiochemical yield synthesis of iodine-123 labeled (*Z*)-vinyl iodides from (*Z*)-vinylboronates. The boronate precursors were synthesized from the corresponding aldehydes. Olefination of the aldehydes was carried out using iodomethyltriphenylphos-phonium iodide and sodium hexamethyldisilizane in a THF/HMPA mixture at room temperature which yielded the (*Z*)-vinyl iodides. Coupling of the iodides with bis(neopentylglycato)diboron using $PdCl_2$(dppf) and potassium carbonate in DMSO furnished the (*Z*)-alkenyl boronates. No-carrier-added radioiodinations were carried out using sodium iodide-123 with chloramine-T as an oxidant with a reaction time of 5 minutes. Excellent radiochemical yields were observed with all substrates, Scheme 1.26.[53]

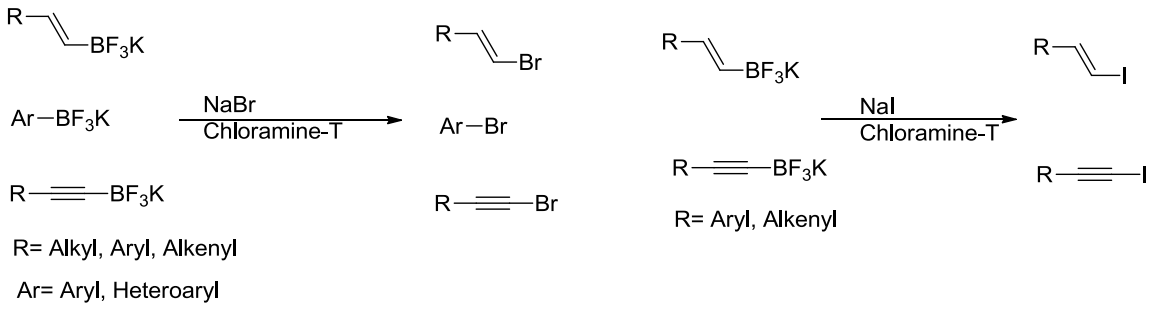
Scheme 1.26 Synthesis of I^{123} Labeled (*Z*)-Vinyl Iodides.

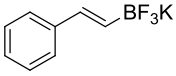
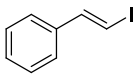
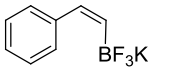
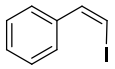
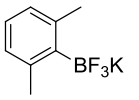
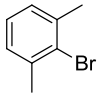
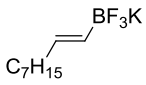
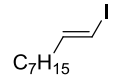
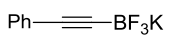
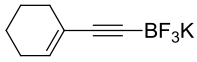
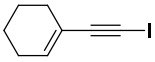
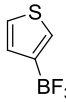
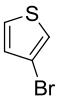
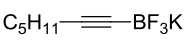
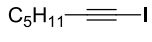
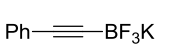
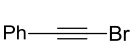
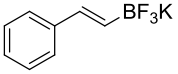
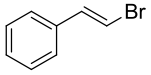
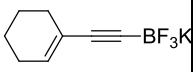
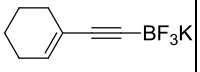
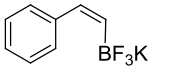
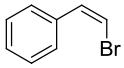
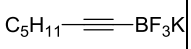
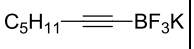
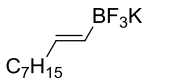
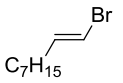


R=	Yield(%)	R=	Yield(%)
Phenyl	78	4-MeO-phenyl	67
Cyclohexyl	83	3-Cl-phenyl	82
2-napthyl	77	propyl	70

Also, it was discovered that potassium aryl-, vinyl-, and alkynyltrifluoroborate salts are readily brominated and iodinated in THF and water with chloramine-T and sodium iodide or sodium bromide. The reactions occurred very rapidly at room temperature producing very good yields of aryl, vinyl, and alkynyl bromides and iodides. The bromination of vinyltrifluoroborates and aryltrifluoroborates required a catalytic amount of trifluoroacetic acid. The iodinations of a variety of substrates consistently produced better yields than observed with the bromination reactions. Vinyl substrates were halogenated with retention of stereochemistry, Scheme 1.27.[54]

Scheme 1.27 Sodium Halide/Chloramine-T Halodemetallations of Organotrifluoroborates. Adapted from: *Organometallics* **2004**, *23*, 4519., *Tet. Lett.* **2004**, 1417.

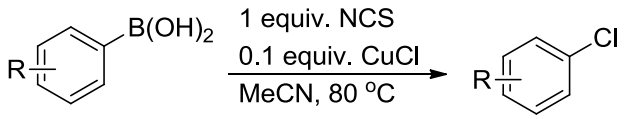


Substrate	Time(min)	Yield(%)	Product	Substrate	Time(min)	Yield(%)	Product
Ph-BF_3K	10	76	Ph-Br		10	95	
p-MeO-Ph-BF_3K	10	87	*p*-MeO-Ph-Br		10	92	
o-Tolyl-BF_3K	10	72	*o*-Tolyl-Br				
	15	83			10	91	
p-Cl-Ph-BF_3K	15	78	*p*-Cl-Ph-Br		20	96	
1-naphthyl-BF_3K	10	86	1-naphthyl-Br		20	94	
	10	65			20	95	
	20	87			10	92	
	20	78			10	89	
	20	79			10	72	

The efficient halodemetallation of potassium organotrifluoroborates in the presence of ammonium bromide-76 and peracetic acid as the oxidant was applied in the no-carrier added bromine-76 labeling of alkenyl- and alkynyl-trifluoroborate salts. Good radiochemical yields ranging form 64%-85% were observed in most cases with a variety of substituted alkenes and alkynes.[55]

Hynes and Wu reported a very efficient copper(I)-catalyzed chloro-deboronation of functionalized arylboronic acids. It was postulated that the reaction proceeds by the oxidative addition of NCS to the copper(I) chloride at the nitrogen-chlorine bond followed by decoordination of succinimide the oxidative addition of an arylboronic acid to the copper(I) intermediate. Reductive elimination of the aryl chloride regenerates the active catalyst. A 0.1 equivalent catalyst loading was used and excellent product yields were observed, Scheme 1.28.[56]

Scheme 1.28 Copper(I) Catalyzed Chlorination of Arylboronic Acids.



Products	Time(h)	Yield(%)	Products	Time(h)	Yield(%)
m-Cl-Ph-NO_2	12	98	*o*-Cl-Ph-CN	18	98
m-Cl-Ph-Ph	20	98	*p*-Cl-Ph-CF_3	18	98
m-Cl-Ph-NHAc	18	96	*p*-Cl-Ph-Ac	18	93
o-Cl-Ph-OMe	24	79	*o*-Cl-Ph-Ph	18	83

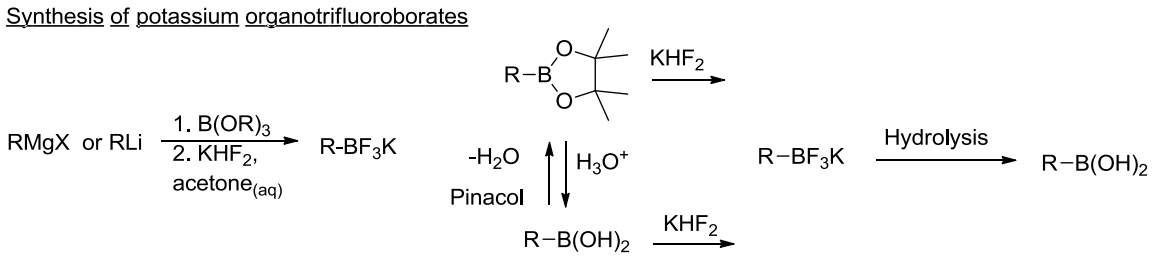
1.7 Recent Advances By the Kabalka Group in the Halodemetallation Reactions of Organoboranes

The Kabalka group has done much work in developing efficient radiohalogenation reactions for syntheses of radiopharmaceuticals utilizing organoboron chemistry. Organoboron compounds are well suited for this purpose due to their low toxicity. Organoboron reagents are more available than ever before to due the development of palladium-catalyzed borylation of aryltriflates, tosylates, and halides, and the iridium-catalyzed direct borylation of arenes by carbon-hydrogen bond activation. Direct borylation of arenes allows the preparation of boronic esters from variety of substituted arenes, and some of these borylated arenes can be utilized to produce aryl halides via halodeboronation reactions that have substitution patterns not favored by electrophilic aromatic substitution.[57] In addition to this, through the development of potassium organotrifluoroborate chemistry, it has been demonstrated that potassium organotrifluoroborates are valuable in synthesis because of the ability of the potassium trifluoroborate substituent to survive many reaction conditions. Potassium organotrifluoroborates are easily converted to boronic acids, and they often serve as a protecting group for the more sensitive boronic acid functionality. Organotrifluoroborates also may be used directly in the Suzuki reaction. In this

case the reactive species is the boronic acid that is produced *in-situ* by hydrolysis during the reaction. Also, potassium aryltrifluoroborate salts undergo coupling with aryldiazonium salts. Kabalka and coworkers developed a microwave enhanced, ligand-free, and base-free cross-coupling of potassium aryltrifluoroborate salts with aryl triflates. A variety of functionally substituted potassium aryltrifluoroborates and functionally substituted aryl triflates were coupled in 15 minutes using 1.5 mol% $Pd(OAc)_2$ and microwave irradiation. Excellent yields of the biaryl products were obtained in most cases.

Boronic acids and esters are easily converted to potassium organotrifluoroborate salts by stirring at room temperature in an acetone/water solution of potassium hydrogen fluoride, Scheme 1.29. [58]

Scheme 1.29 Synthesis and Interconversions of Potassium Organotrifluoroborates.

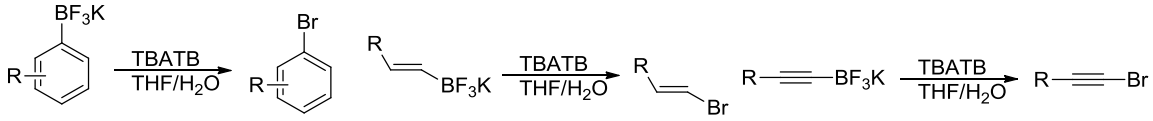


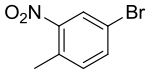
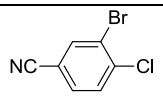
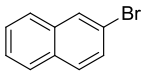
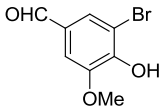
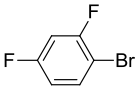
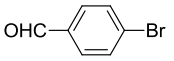
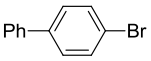
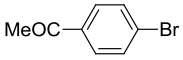
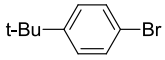
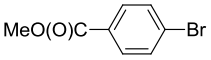
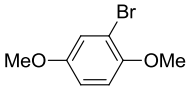
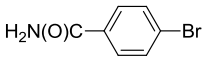
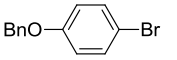
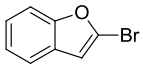
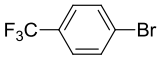
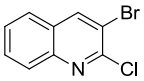
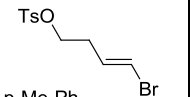
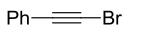
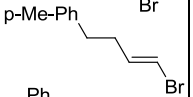
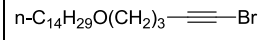
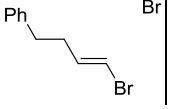
The deprotection of potassium organotrifluoroborates has been carried out in a variety of ways that will be discussed in a later chapter.

The Kabalka group recently developed a chemoselective bromodeboronation of potassium organotrifluoroborates using tetrabutylammonium tribromide and applied it in the synthesis of (*Z*)-1,2-dibromoalkenes and a variety of aryl bromides, heteroaryl bromides, alkenyl bromides, and alkynyl bromides. Tetrabutylammonium tribromide was found to be an effective bromodeboronation reagent for a wide range of functionally substituted potassium aryltrifluoroborates. *o*-Nitrotolyl-*p*-trifluoroborate was found to undergo bromodeboronation in 40 minutes at room temperature. This is in sharp contrast to the results of the

bromodeboronation reaction observed using a chloramine-T and sodium bromide system which produced only a trace of the aryl bromide after 24 hours at reflux. Most aryltrifluoroborates underwent bromodeboronation in twenty minutes at room temperature in a 1:1 THF/water mixture, and the ionic nature of the reactants simplified the product purification process. (*E*)-Alkenyl trifluoroborates were brominated with retention of stereochemistry, Scheme 1.30.[59]

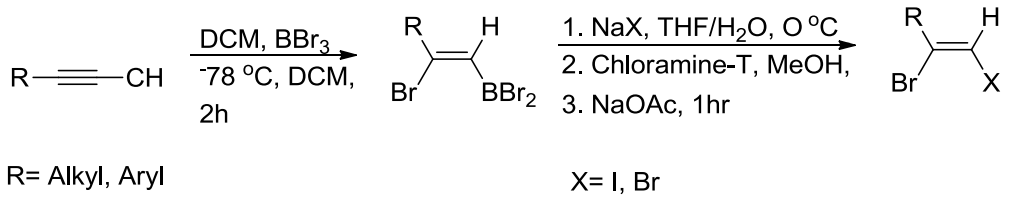
Scheme 1.30, Bromodeboronation Reactions of Aryl-, Alkenyl-, and Alkynyltrifluoroborates.



Product	Temp(°C)/Time	Yield(%)	Product	Temp(°C) /Time	Yield(%)
	rt/40 min	68		60/2 h	74
	rt/20 min	99		rt/40 min	94
	rt/20 min	67		60/2 h rt/12 h	77 75
	rt/20 min	94		60/2 h	73
	rt/20 min	86		60/ 2 h rt/12 h	76 81
	rt/20 min	72		rt/20 min	79
	rt/20 min	92		rt/20 min	88
	60/2 h	83		rt/12 h	91
	20/rt	91		rt/20	96
	20/rt	85		rt/20	99
	20/rt	71			

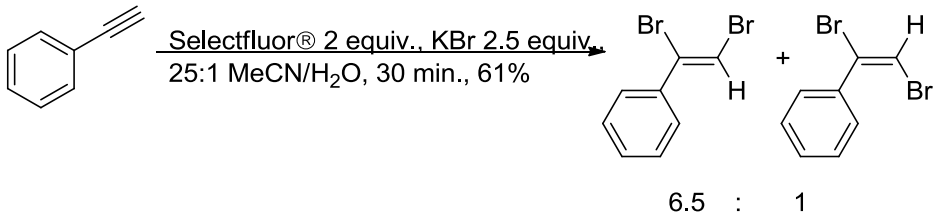
The synthesis of (*Z*)-1,2-dibromoalkenes is thermodynamically disfavored and presents a challenge in organic synthesis. Suzuki and coworkers developed a method in which the bromoboration of 1-alkynes with tribromoborane followed by halodeboronation with iodine chloride or bromine chloride afforded the (*Z*)-1,2-dibromo-1-alkenes in moderate to good yields with very good isomeric purity in most cases, Scheme 1.31.[60]

Scheme 1.31 Synthesis of (*Z*)-1,2-Dihalo-1-alkenes.



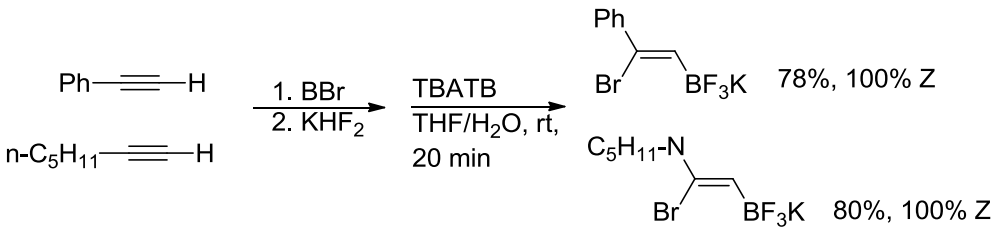
Shreeve and coworkers reported a method of producing (*Z*)-1,2-dibromo-styrene from phenyl acetylene. Phenyl acetylene was reacted with Selectfluor® and potassium bromide to produce a 6.5 to 1 mixture of *Z* and *E* styrene products in 61% overall yield, Scheme 1.32.[61]

Scheme 1.32 Synthesis of (*Z*)-1,2-Dibromo-1-phenylethylene Using Selectfluor®.



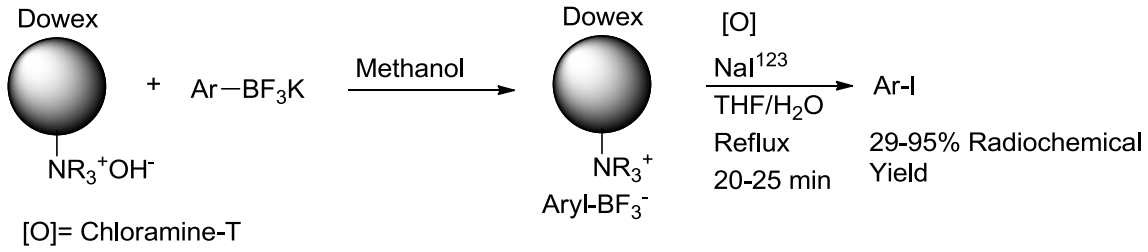
Kabalka and coworkers devised a two step route to obtain (*Z*)-1,2-dibromo-1-alkenes from terminal alkynes. In step one, a terminal alkyne is subjected to halobromination to form a potassium (*Z*)-1-bromo-vinyl-2-trifluoroborate. Halodebromination with TBATB stereospecifically yields the (*Z*)-1,2-dibromo-1-alkene in good yields, Scheme 1.33.[63]

Scheme 1.33 Synthesis of (*Z*)-1,2-Dibromo-1-alkenes from (*Z*)-2-Bromoakenyl-1-trifluoroborates Using TBATB.



The Kabalka group recently developed a no-carrier-added radioiodination of polymer supported ayrl- and alkenyltrifluroborates. Dowex-supported organotrifluoroborates were made by ion exchange of the Dowex resin with potassium organotrifluoroborates. This formed a tetraalkylammonium organotrifluoroborate. Reaction of Dowex supported organotrifluoroborates with sodium iodide-123 in a one-to-one THF/H_2O solution at reflux for 20-25 minutes yielded the iodine-123 labeled products good radiochemical yields. The main advantage of the protocol is the ease of purification due to the polymer-supported reagent, scheme 1.34.[62]

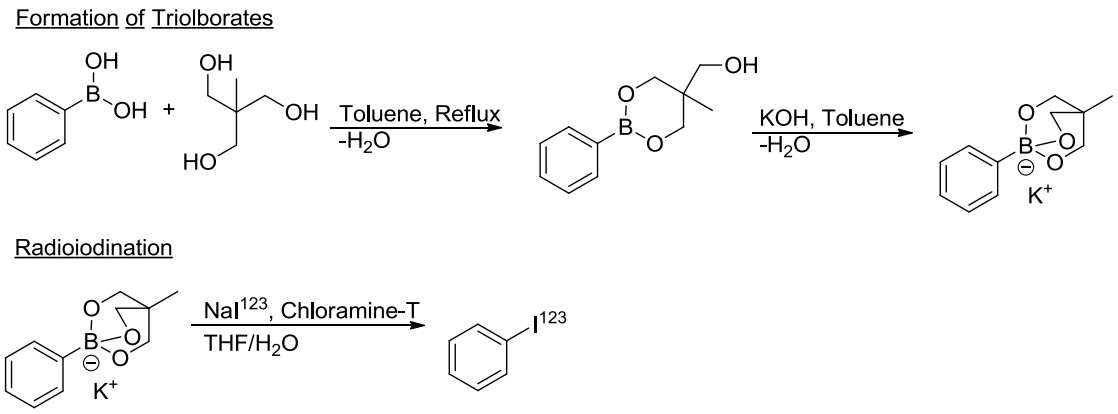
Scheme 1.34 Radioiodination Using Dowex-Supported Organotrifluoroborates.

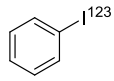
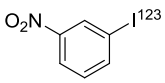
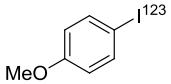
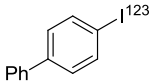
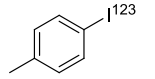
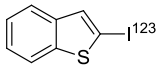
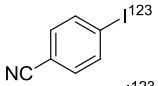
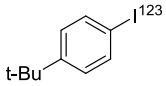
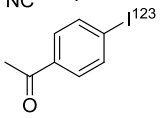
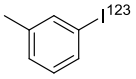


The Kabalka group also recently investigated the feasibility of radioiodinations of potassium triolborates. Potassium organotriolborates are formed from organoboronic acids and 2-(hydroxymethyl)-2-methylpropane-1,3-diol. Refluxing these reagents in toluene forms an intermediate organoboronic ester, which then is allowed to react with potassium hydroxide to form the potassium organotriolborate salt. Radioiodinations were carried out using chloramine-T as

the oxidant and sodium iodide-123. A variety of aryl- and heteroaryltriolborates underwent radioidination at room temperature or at 50 °C to produce the aryl iodides in excellent radiochemical yields, Scheme 1.35.[63]

Scheme 1.35 Radioiodination of Potassium Aryltriolborates.



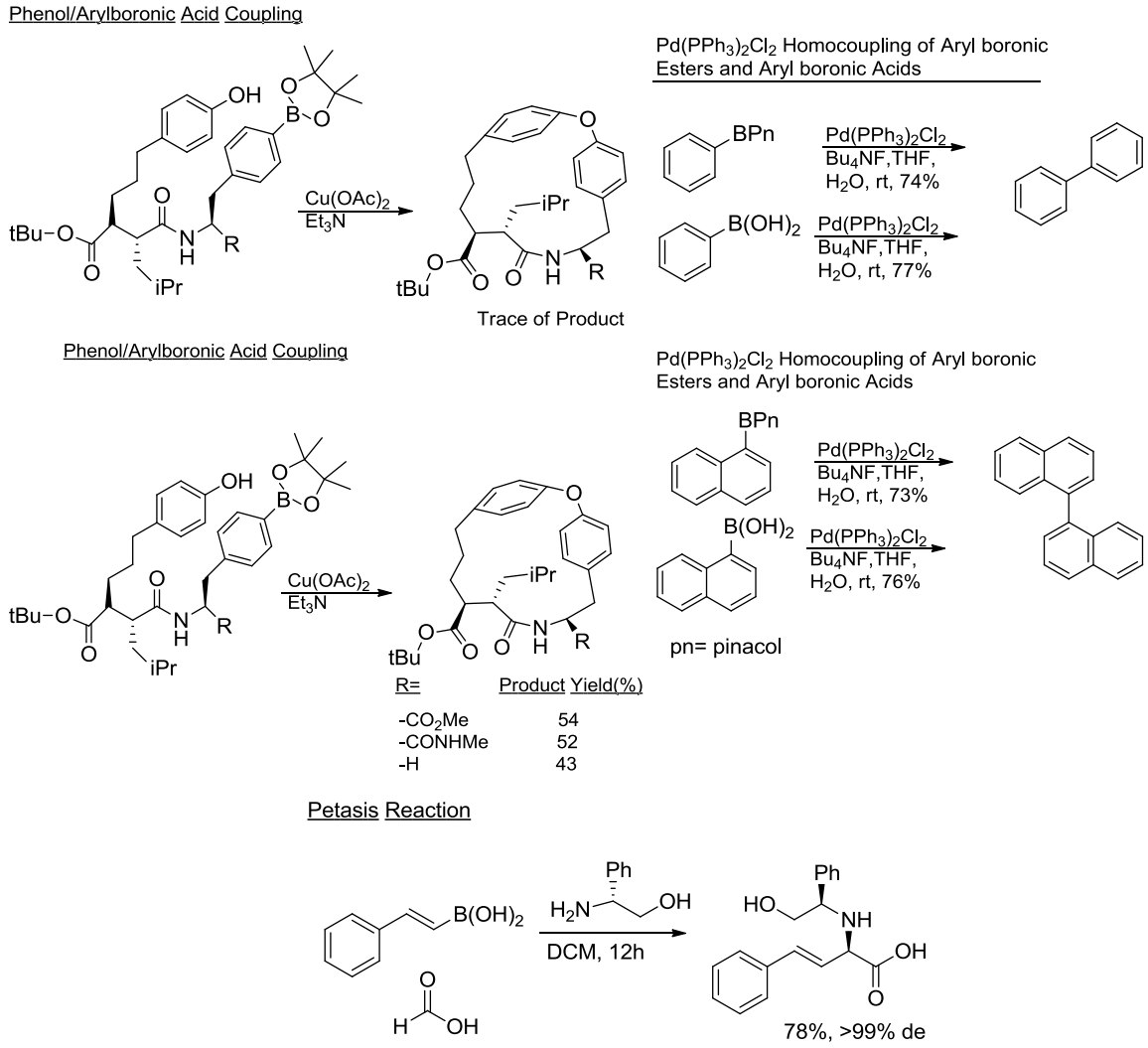
Products	Time(min)/Temp(°C)	Yield(%)	Products	Time(min)/Temp(°C)	Yield(%)
	20/rt	75		90/50	52
	20/rt	89		20/rt	80
	20/rt	85		20/rt	72
	30/50	68		20/rt	86
	30/50	64		20/rt	80

1.8 The Hydrolysis of Potassium Organotrifluroborates

Organoboronic acids, organoboronic esters, and organotrifluoroborates are interconvertible (see Scheme 1.29). In most applications, reactivity of organoboronic esters and organotrifuoroborates is comparable to or superior to that of organoboronic acids, but there are instances where use of organoboronic

acids is desirable. For example, the Petasis reaction, carbon heteroatom couplings, and oxidative homocoupling reactions are more efficient using organoboronic acids, Scheme 1.36.[64]

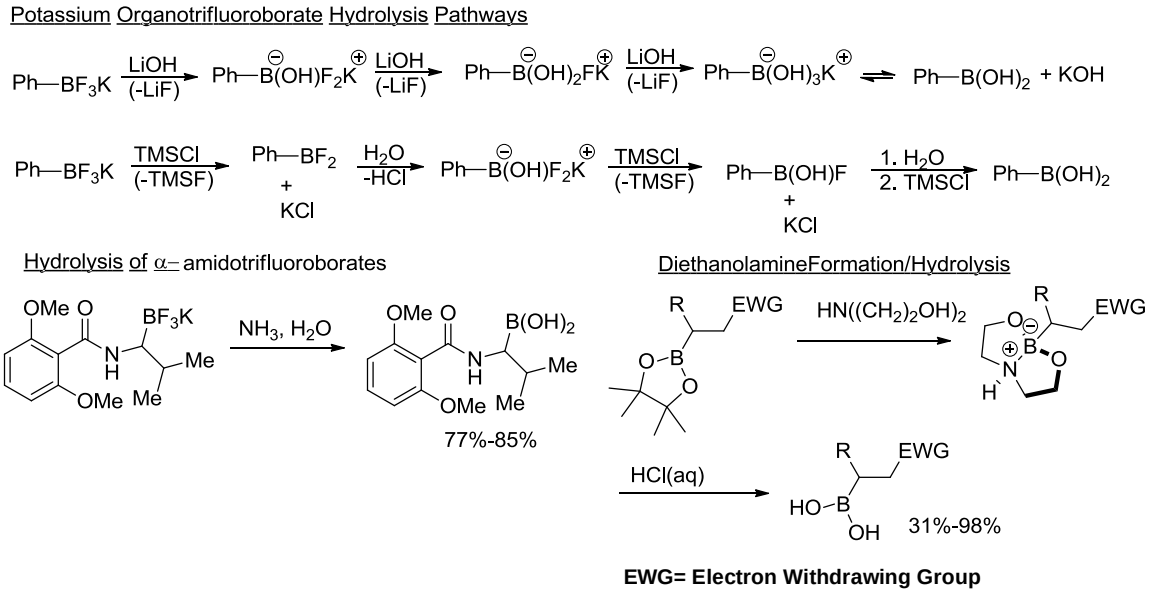
Scheme 1.36 The Advantage of Boronic Acids Over Boronic Esters in Certain Reactions.



The efficient conversion of organoboronic esters to organoboronic acids is an important goal in synthetic organic chemistry. Organoboronic acids have been used as biological inhibitors and sensors.[65] Pinanediol esters of boronic acids are important organoboronic acid protecting groups used for chiral induction, but

their removal can be problematic. Reported methods of conversion of organoboronic esters to organoboronic acids include acidic hydrolysis, reduction, reaction with boron trichloride, transesterification with phenyboronic acid, and oxidative cleavage with sodium periodate, Scheme 1.37.

Scheme 1.37 Methods of Conversion of Boronic Esters to Boronic Acids.

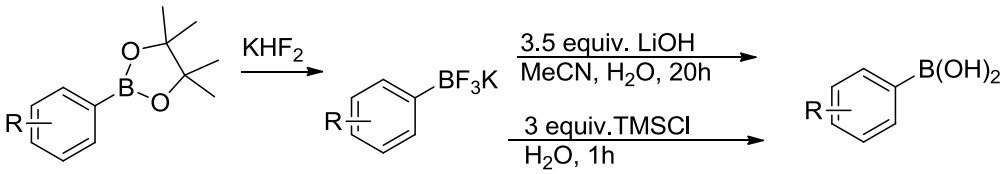


The mildest of these methods is the transesterification method, but it is carried out in a biphasic system that relies on solubility differences in the starting ester (aqueous phase) and the phenylboronic pinanediol ester (organic phase), and for this reason may not be applicable in all situations. In addition to this, other problems with the transesterification procedure are incomplete reaction and difficulties in separating the desired boronic acid product from the excess phenylboronic acid used as the coupling partner. Acidic hydrolysis does not occur with all boronic esters, and the use of oxidative cleavage, reduction, or boron trichloride is not compatible with a variety of functionalities.[66-68] Polymer-supported organoboronic acids have been tested as transesterification partners for the conversion of organoboronic esters to the corresponding organoboronic

acids with good success, but these polymer supported organoboronic acids are not currently commercially available.

In an effort to overcome these difficulties in the deprotection and conversion of organoboronic esters to organoboronic acids, two step procedures have been developed. One approach is to convert the organoboronic ester to a diethanolamine-protected boronic ester which then undergoes basic or acidic hydrolysis to yield the organoboronic acid. In another method, the organoboronic ester is converted to an organotrifluoroborate in the first step using potassium hydrogen difluoride, and in the second step, basic hydrolysis of the organotrifluoroborate using lithium hydroxide in aqueous acetonitrile or reaction with the fluorophile trimethylsilylchloride in water yields the corresponding organoboronic acid. A modification of this procedure has been applied in the conversion of pinanediol and pinacol-boronate esters bearing *α*-amido substituents to the corresponding organoboronic acids that uses aqueous ammonia to hydrolyze an intramolecular *α*-amido carbonyl coordinated difluoroborane intermediate that is produced when these type of organotrifluoroborates undergo hydrolysis, Scheme 1.37 and 1.38.[68,69]

Scheme 1.38 Hydrolysis of Organotrifluoroborates.

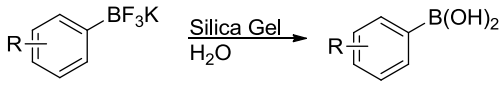


R=	Yield(%) LiOH	Yield(%) TMSCl	R=	Yield(%) LiOH	Yield(%) TMSCl
H	100	-	2-OTs	100	100
2-Me	71	100	2-CHO	100	100
4-Me	85	-	2-Cl	75	100
2-OH	0	90	4-F	100	-
2-OMe	49	70	4-Br, 3-NHCbz	-	93
4-OMe	95	-	4-Br, 3-CO_2Me	-	100

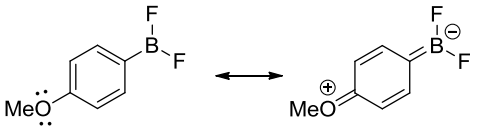
The hydrolysis of organotrifluoroborates is thought to occur through the stepwise loss of fluoride ions as an insoluble salt or through removal by silicon, Scheme 1.37.

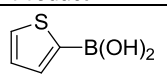
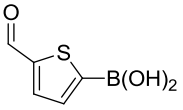
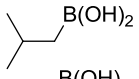
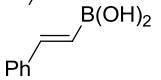
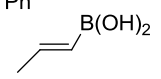
Molander and coworkers reported the use of slica gel as an effective fluorophile to affect the hydrolysis of potassium organotrifluoroborates in water. Stirring various potassium alkyl-, alkenyl-, aryl-, and heteroaryltrifluoroborates in water at room temperature resulted in conversion to the corresponding boronic acids. The reaction time ranged from one hour for organotrifluoroborates with electron donating substituents to 24 hours for organotrifluoroborates with electron withdrawing substituents such as a nitro group. Organotrifluoroborates with electron donating substituents hydrolyze faster because of resonance stabilization of the organodifluoroborane hydrolysis intermediate, Scheme 1.39.[70]

Scheme 1.39 Hydrolysis of Potassium Organotrifluoroborates with Silica Gel.



Difluoroborane Intermediate with Electron Donating Group

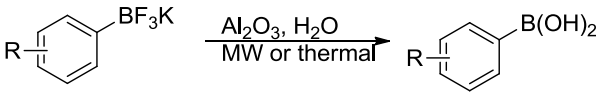


R=	Time(h)	Yield(%)	R=	Time(h)	Yield(%)	Product	Time(h)	Yield(%)
p-MeO	1	86	*o*-CHO	24	64		3	81
m-MeO	3	83	*p*-CHO	24	88			
o-MeO	1	67	*p*-CN	24	66		24	73
p-Me	1	76	*o*-NO_2	24	86			
o-Me	1	67	*p*-F	4	80		1	73
2-naphthyl	1	63	*p*-Cl	1	60		1	63
phenyl	4	65	*p*-Br	1	71		1	81

A rapid method of hydrolysis of organotrifluoroborates into the corresponding boronic acids was recently developed in our lab by Kabalka and Coltuclu. In this method, a potassium organotrifluoroborate is hydrolyzed in 15 minutes at 70 $^{\circ}$C in

the presence of alumina. Heating occurred either thermally or by microwave irradiation. Yields of boronic acids were higher with microwave heating, Scheme 1.40.[71]

Scheme 1.40 Hydrolysis of Potassium Organotrifluoroborates in the Presence of Alumina.



R=	MW Yield(%)	Thermal Yield(%)	R=	MW Yield(%)	Thermal Yield(%)
p-Me	90	88	p-CHO	92	89
p-F	94	90	p-MeCO	95	91
p-OMe	93	92	p-CF_3	85	82
2,6-dimethoxy	87	84	PhBF_3K	92	89
BF_3K Ph	91	89			

Chapter 2

Bromodeboronation of Potassium Aryl- and Alkenyltrifluoroborates Using Pyridinium Tribromide

2.1 Introduction

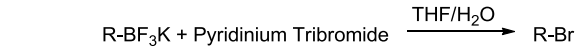
As noted in Chapter 1, the Kabalka group recently reported, for the first time, that tetrabutylammonium tribromide (TBATB) is an effective reagent for boromodeboronation reactions.[63] In a continuation of our efforts to investigate bromodeboronations of potassium aryl- and alkenyltrifluoroborates using tribromide ion, a study of the effectiveness of pyridinium tribromide as a bromodeboronation reagent was undertaken. Pyridinium tribromide is a commercially available reagent that is a crystalline solid. It has a reddish/orange color and a pungent odor. A variety of functionally substituted potassium aryltrifluroborates, an alkenyltrifluoroborate, and a heteroaryltrifluoroborate were investigated.

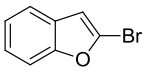
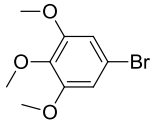
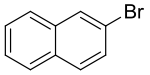
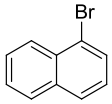
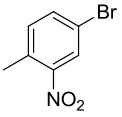
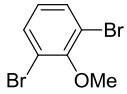
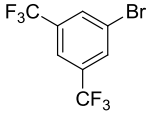
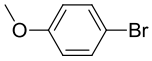
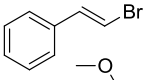
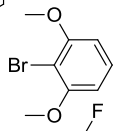
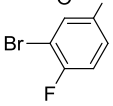
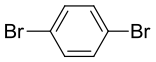
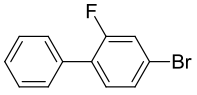
2.2 Results and Discussion

Based on the conditions established for the bromodeboronation of aryl- and alkenyltrifluorobortes using TBATB, the initial conditions for evaluating pyridinium tribromide's effectiveness in bromodeboronation reactions were a one-to-one THF/H_2O solvent system at room temperature and one equivalent of pyridinium tribromide. These conditions worked well for unfunctionalized aryltrifluoroborates such as potassium (*E*)-1-phenylethylene-2-trifluoroborate, potassium *p*-bromophenyltrifluoroborate, and potassium 2-fluorobiphenyl-4-trifluoroborate (Products 3, 4, 9, 12 and 13), Scheme 2.1. These substrates produced good yields of the products in 20-40 minutes, but aryltrifluoroborates with electron withdrawing substituents such as a nitro group or two fluoride groups required heating to 45 $^{\circ}$C and 70 $^{\circ}$C respectively and a 40 minute reaction time. Decreased yields of the corresponding aryl bromides were produced (Products 5 and 11). Potassium 3,5-ditrifluromethylphenyltrifluoroborate was

unreactive even at reflux (Product 7). Potassium benzofuranyl-2-trifluoroborate produced only trace of the desired product due to its propensity to polymerize (Product 1), Scheme 2.1.[72]

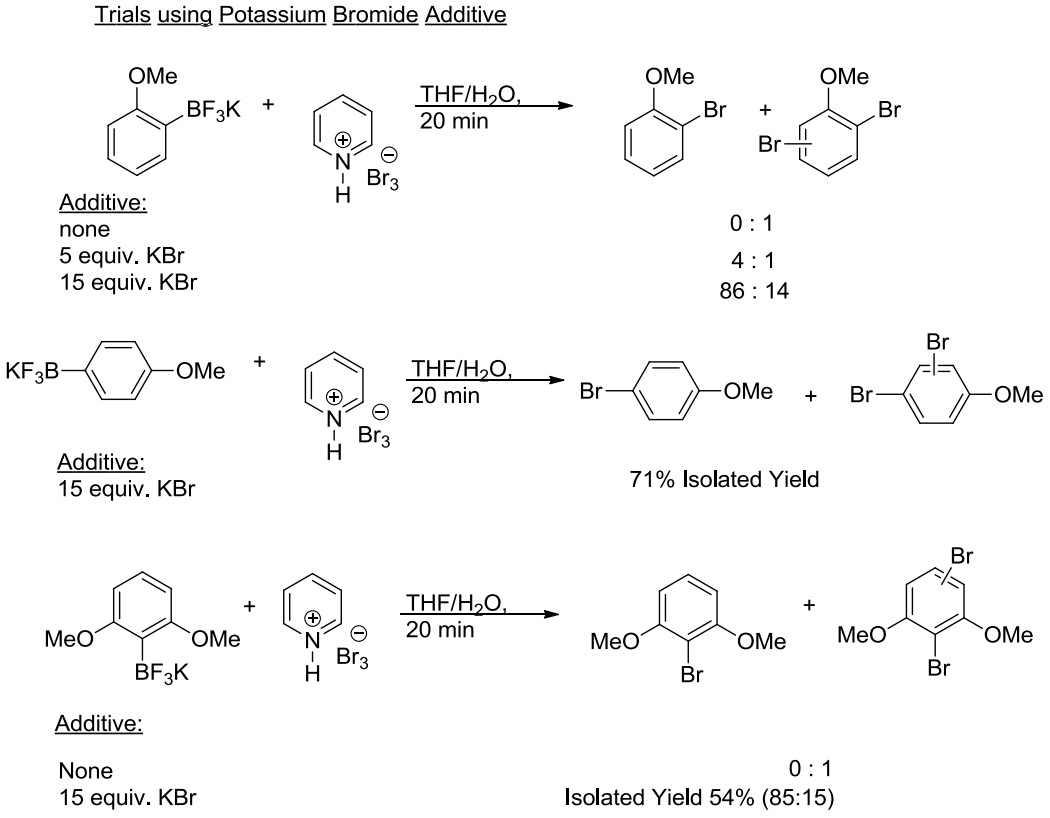
Scheme 2.1 Bromodeboronation of Potassium Organotriflouroborates Using Pyridinium Tribromide.[72]

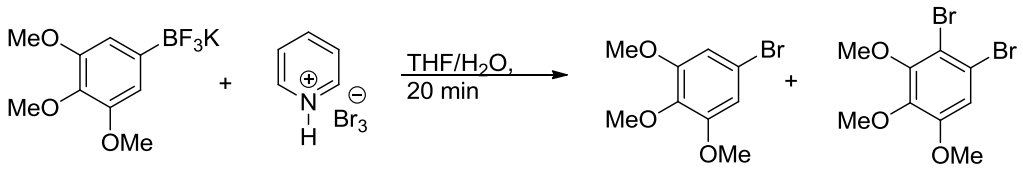


Product		Temp. (°C)	Time (min.)	Yield (%)
1		25	30	6
2		25	30	0
3		25	30	90
4		25	30	90
5		45	40	51
6		25	30	39
7		Reflux	40	0
8		25	30	71
9		25	30	91
10		25	30	54
11		Reflux	40	56
12		25	30	99
13		25	40	74

Aryltrifluoroborates with electron donating groups such as potassium 2-methoxyphenyltrifluoroborate underwent dibromination using the standard reaction conditions producing only the dibrominated product, (Product 6; Figure 2.1, page 43). This result is unexpected since activated aryltrifluroborates produce good yields of the monobrominated products using TBATB. In an attempt to suppress dibromination of activated aryltrifluoroborates bearing one, two, or three methoxy substituents, potassium bromide was added to the reaction solution. The hypothesis was that dibromination occurs because a small amount of bromine is formed in equilibrium with bromide ion during the reaction. Adding a large excess of potassium bromide should reduce the concentration of bromine in the reaction solution, and therefore, prevent or reduce the amount of dibromination, Scheme 2.2.

Scheme 2.2 Effect of KBr Additive on the Halodemetallation of Activated Substrates.





Additive:		
None	0 : 1	
15 equiv KBr	0 : 1	

As shown in Scheme 2.2, in the absence of potassium bromide, only dibrominated products formed during the bromination of 2-methoxyphenyltrifluoroborate (Figure 2.1, page 43). Halodemetallation occurred at the boron-carbon bond and an electrophilic aromatic substitution reaction also occurred yielding the dibrominated products. Addition of five equivalents of potassium bromide to the reaction of 2-methoxyphenyltrifluroborate resulted in a 4:1 ratio of the desired monobrominated product to the dibrominated product as determined by peak areas in GC analysis of an extract of the reaction (Figures 2.2 and 2.3). Addition of 15 equivalents of potassium bromide resulted in an 86:14 ratio of monobrominated product to dibrominated product as determined by the peak area ratios in a GC analysis of an extract of the reaction (Figures 2.4 and 2.5). Using 15 equivalents of potassium bromide in the reaction of potassium *p*-methoxyphenyltrifluoroborate successfully suppressed dibromination enough to generate a 71% isolated yield of the desired monobrominated product (Product 8). Attempts to suppress the dibromination of the even more reactive potassium 2,6-dimethoxyphenyltrifluoroborate using 15 equivalents of potassium bromide yielded approximately the same result as was observed for the monomethoxy substrate as determined by the GC analysis of the product mixture. The peak areas observed were 85% monobrominated: 15% dibrominated, but the monobrominated product was isolated in only 54% yield (Product 10; Figures 2.6 and 2.7). All attempts to obtain the monobrominated product from the highly activated 3,4,5-trimethoxyphenyltrifluoroborate were unsuccessful (Figures 2.8 and 2.9), Scheme 2.2.

2.3 Conclusion

Pyridinium tribromide was evaluated as a reagent for bromodeboronation reactions of aryl-, alkenyl-, and heteroaryltrifluoroborates. Substrates with electron withdrawing groups were less reactive requiring additional reaction times or elevated temperatures. Reagents containing electron neutral substituents underwent bromodeboronation to produce good yields of the corresponding aryl bromide products, but aryltrifluoroborates with activating methoxy substituents exhibited unexpected dibromination. Addition of potassium bromide suppressed the dibromination of methoxyphenyltrifluoroborate and dimethoxyphenyl-trifluoroborate producing useful quantities of the aryl bromides. In general, pyridinium tribromide proved to be less effective in bromodeboronations of potassium organotrifluoroborates than TBATB. Perhaps, the pyridinium ion's acidity contributed to the different reactivity, hydrogen bonding of the pyridinium nitrogen proton with the fluoride groups of the trifluroborates, and *pi-pi* stacking of pyridinium with the aryl rings of the substrates may also play a role.

The work presented in this chapter was carried out by the author, and the majority of this work has been published in the following publication:
Yao, M.; Kabalka, G. W.; Blevins D. W.; Reddy, M. S.; Yong, L. Halodeboronation of Organotrifluoroborates Using Tetrabutylammonium Tribromide or Cesium Triiodide. *Tetrahedron* **2012**, *68*, 3738.

2.4 Experimental

Reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE). ^{1}H NMR and ^{13}C NMR spectra were recorded at (250.13 or 300) and (62.89 or 75) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. Gas Chromatography/Mass Spectroscopy studies were carried out using a Hewlett Packard: HP 6890 series GC System with 5973

Mass Selective Detector; Column: Agilent 19091S-433E, 30.0mm X 0.25mm X 0.25 μm; Gas (He) flow rate: 0.8 mL/min; Initial temperature: 90 ˚C; Ramp temperature rate: 10 ˚C/min to maximum 240 ˚C. Melting points were obtained by using a Mel-Temp melting point apparatus with a mercury thermometer.

2.5 Typical Reaction Procedure for Bomodeboronations

The trifluoroborate (1.0 mmol) was dissolved in a (1:1) mixture of tetrahydrofuran and water (10 mL). Pyridinium tribromide (1.0 mmol) was added to this solution. The mixture was stirred for the appropriate time and temperature (scheme 2.2) and then diluted with 10 mL of ether. The aqueous layer was extracted twice with ether (5 mL) and the combined organic phase was dried over anhydrous Na_2SO_4. After evaporation of the solvent the residue was purified by silica gel column chromatography with hexanes, ethyl acetate, diethyl ether, or an appropriate mixture of these as determined by TLC.

2.6 Characterization of Compounds

(NMR spectra in appendix)

2-Bromobenzofuran (1).[73] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43-7.39 (m, 2H), 7.21-7.17 (m, 2H), 6.62 (d, J = 2.4 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 155.7, 128.6, 128.1, 124.1, 123.3, 120.0, 110.8, 108.2.

2-Bromonaphthalene (3).[74] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.94 (s, 2H), 7.73-7.61 (m, 3H), 7.51-7.41 (m, 3H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 134.4, 131.7, 129.8, 129.5, 129.1, 127.8, 126.9, 126.8, 126.2, 119.7.

1-Bromonaphthalene (4).[75] ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.15-8.23 (d, J=10 Hz, 1H), 7.65-7.75 (t, J=7.5 Hz, 3H), 7.39-7.55 (m, J=7.5 Hz, 2H), 7.16-7.24 (t, J=7.5 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 134.7, 132.1, 130.0, 128.4, 128.0, 127.4, 127.2, 126.7, 126.2, 122.9.

4-Bromo-2-nitrotoluene (5).[59] ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.07-8.16 (s, 1H), 7.55-7.67 (d, J=7.5 Hz, 1H), 7.19-7.26 (d, J=7.5 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 136.1, 134.3, 132.7, 127.7, 120.1, 119.8, 20.2.

1-Bromo-4-methoxybenzene (8).[76] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (d, J =9.3 Hz, 2H), 6.79 (d, J = 9.3 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 132.2, 115.7, 112.5.

***trans*-2-(Phenyl)vinylbromide** (9).[77] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.32-7.27 (m, 5H), 7.10 (d, J = 14.0 Hz, 1H), 6.75 (d, J = 14.0 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 137.1, 135.8, 128.7, 128.2, 126.0, 106.4.

2-Bromo-1,3-dimethoxybenzene (10).[78] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21 (t, J =9.0 Hz, 1H), 6.56 (d, J = 9.0 Hz), 3.87 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.9, 128.3, 104.3, 100.5, 56.3.

1-Bromo-2,4-difluorobenzene (11).[79] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.55-7.46 (m, 1H), 6.93-6.80 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 133.9, 112.9, 112.8, 105.2, 104.7.

1,4-Dibromobenzene (12).[54] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.3, 121.2.

4-Bromo-2-fluorobiphenyl (13).[80] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.53 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 134.9, 131.9, 131.8, 129.0, 128.2, 127.9, 127.8, 121.5, 121.4, 119.8.

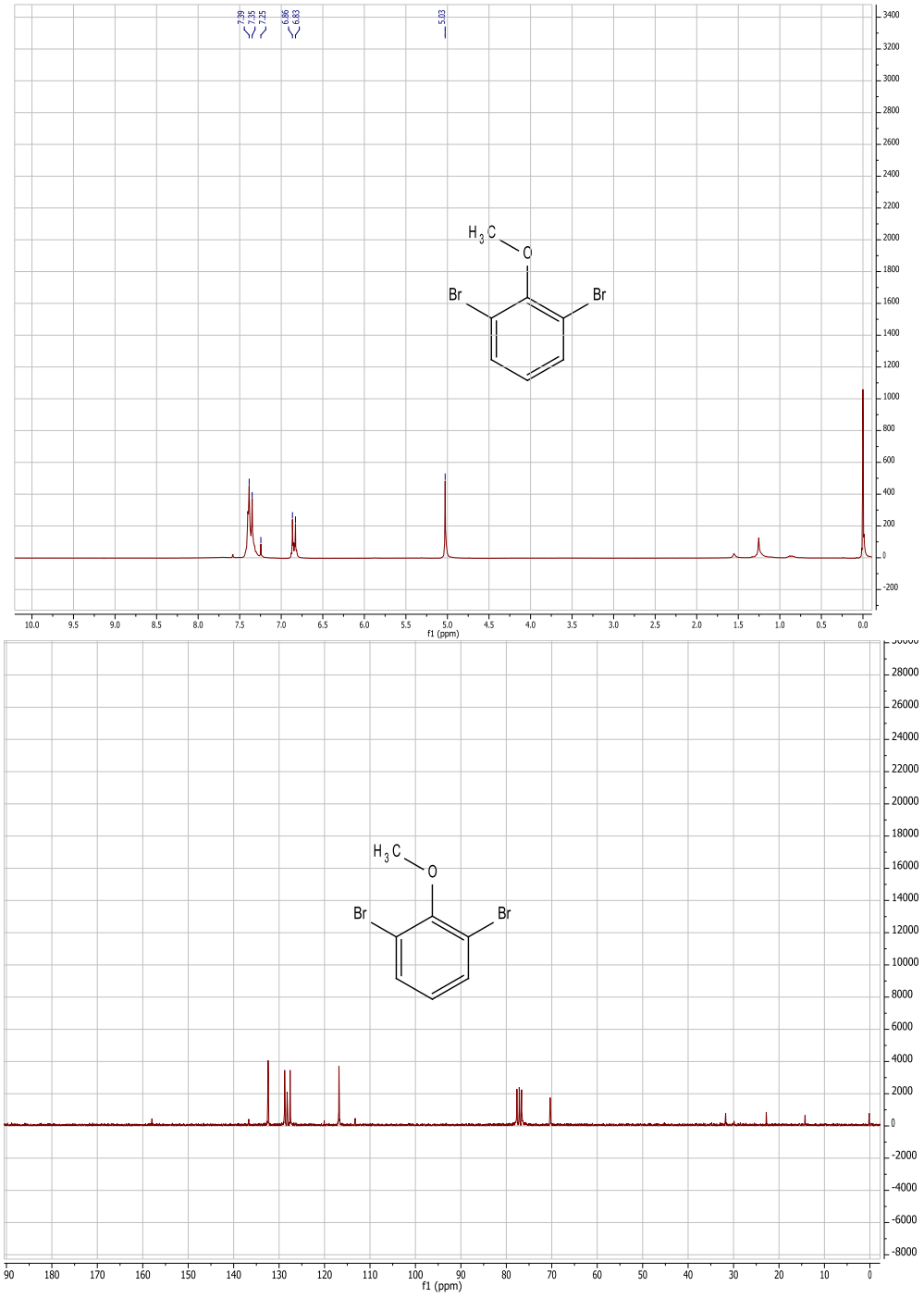


Figure 2.1 ^{1}H and ^{13}C NMR of the Isolated Dibromoanisole Product of the Reaction of Potassium 2-Methoxyphenyltrifluoroborate with Pyridinium Tribromide with no KBr Added. The product has some impurities. Expected melting point: 198 °C; Observed: 189-193 °C, *Journal of the University of Bombay, Science: Physical Sciences, Mathematics, Biological Sciences and Medicine* **1935**, *4*, 94.

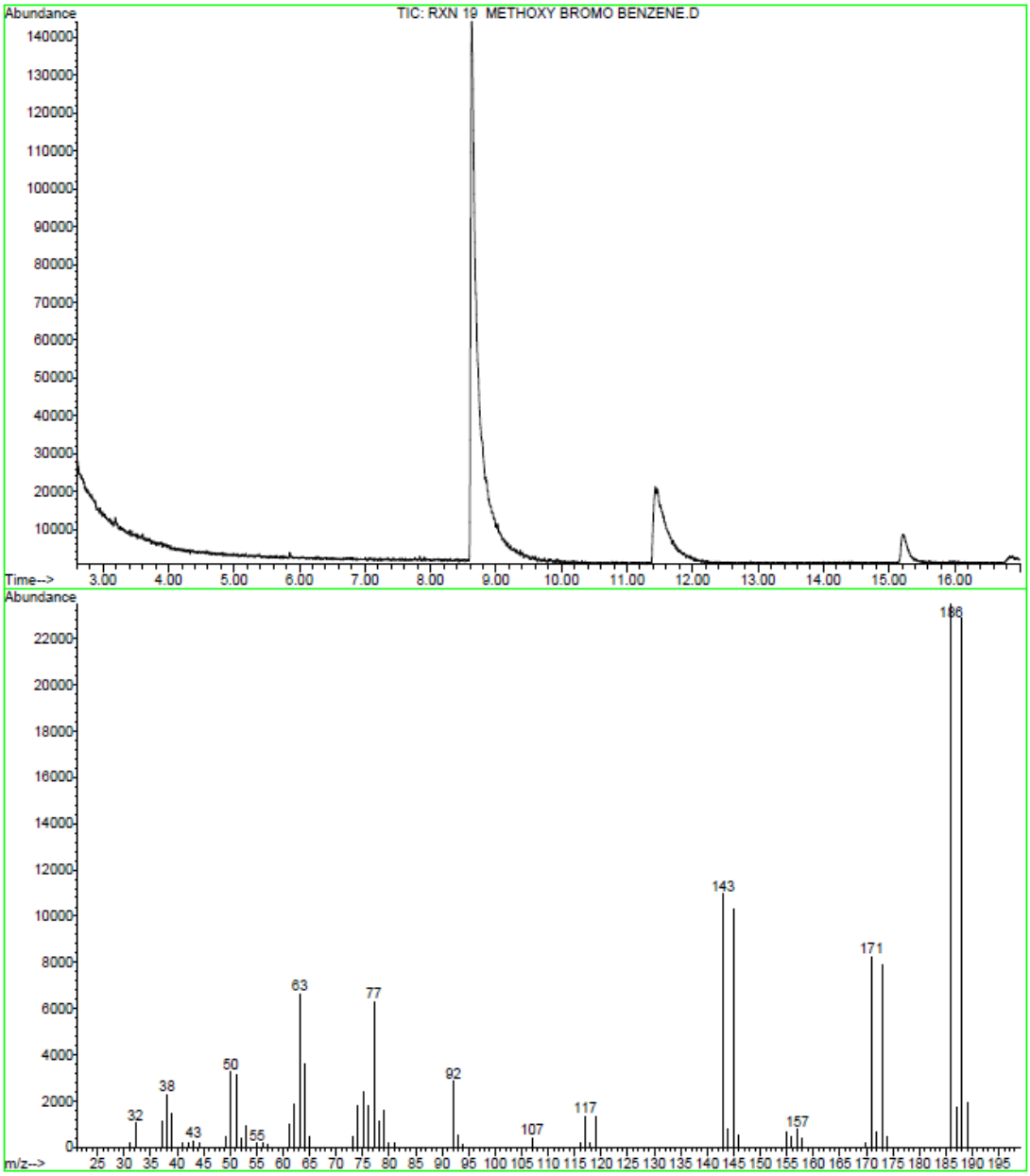


Figure 2.2 Bromodeboronation of Potassium 2-Methoxyphenyltrifluoroborate with 5 Equivalents of KBr Added. Mass spectrum of peak at 8.64 min (*o*-bromomethoxybenzene).

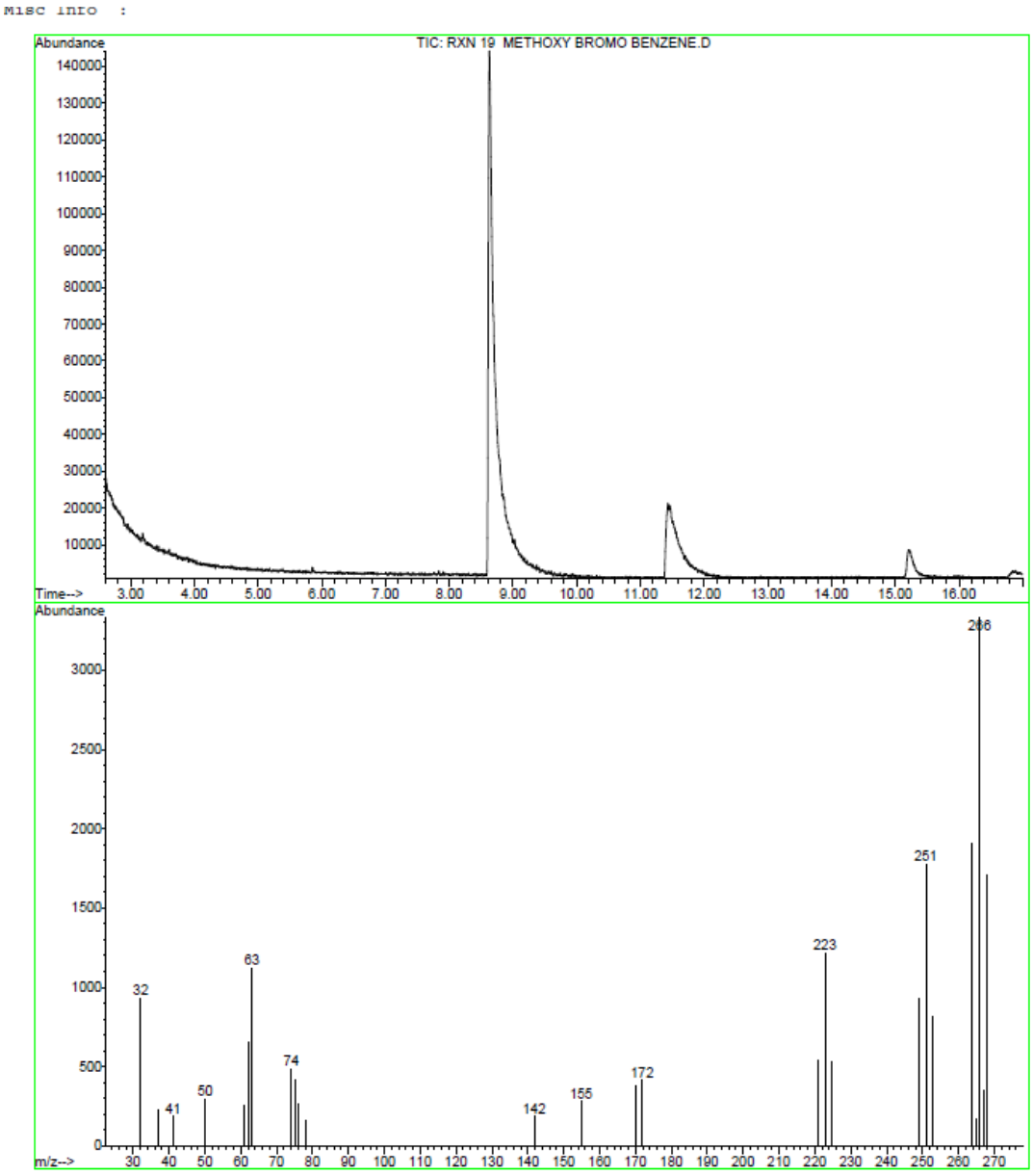


Figure 2.3 Bromodeboronation of Potassium 2-Methoxyphenyltrifluoroborate with 5 Equivalents of KBr Added. Mass spectrum of peak at 11.44 min (dibromomethoxybenzene).

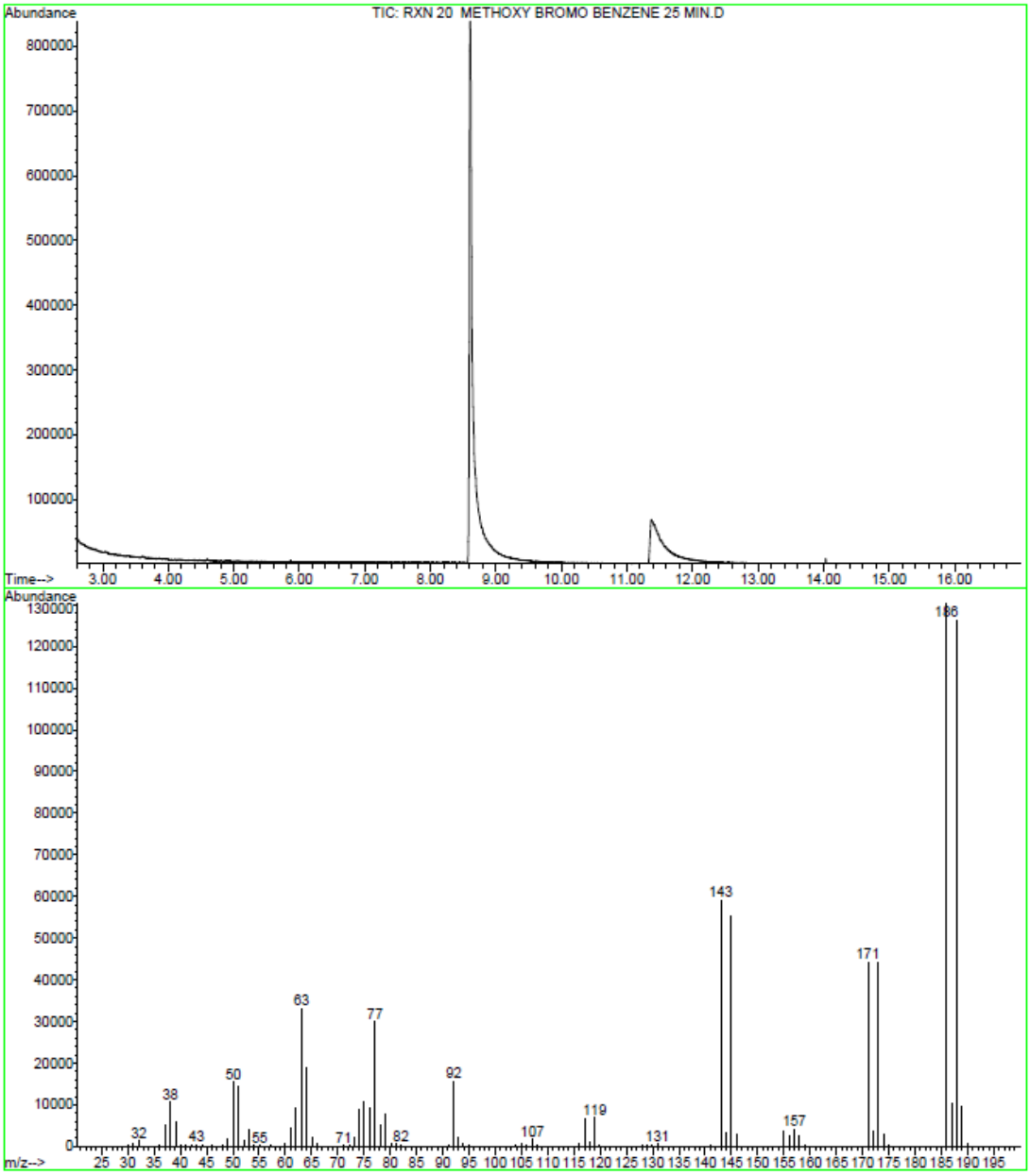


Figure 2.4 Bromodeboronation of Potassium 2-Methoxyphenyltrifluoroborate with 15 Equivalents of KBr Added. Mass spectrum of peak at 8.61 min.

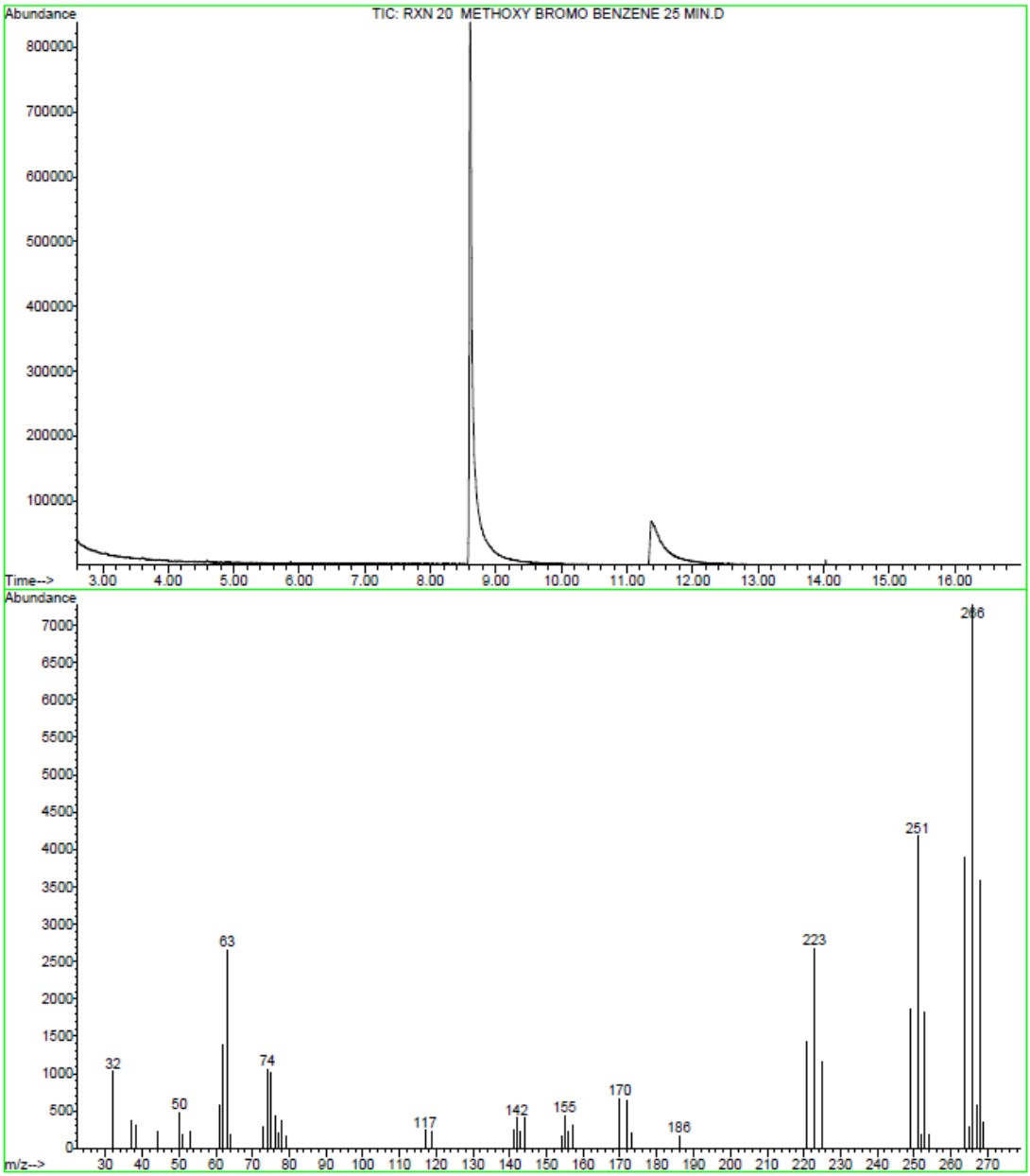


Figure 2.5 Bromodeboronation of Potassium 2-Methoxyphenyltrifluoroborate with 15 Equivalents of KBr Added. Mass spectrum of peak at 11.38 min.

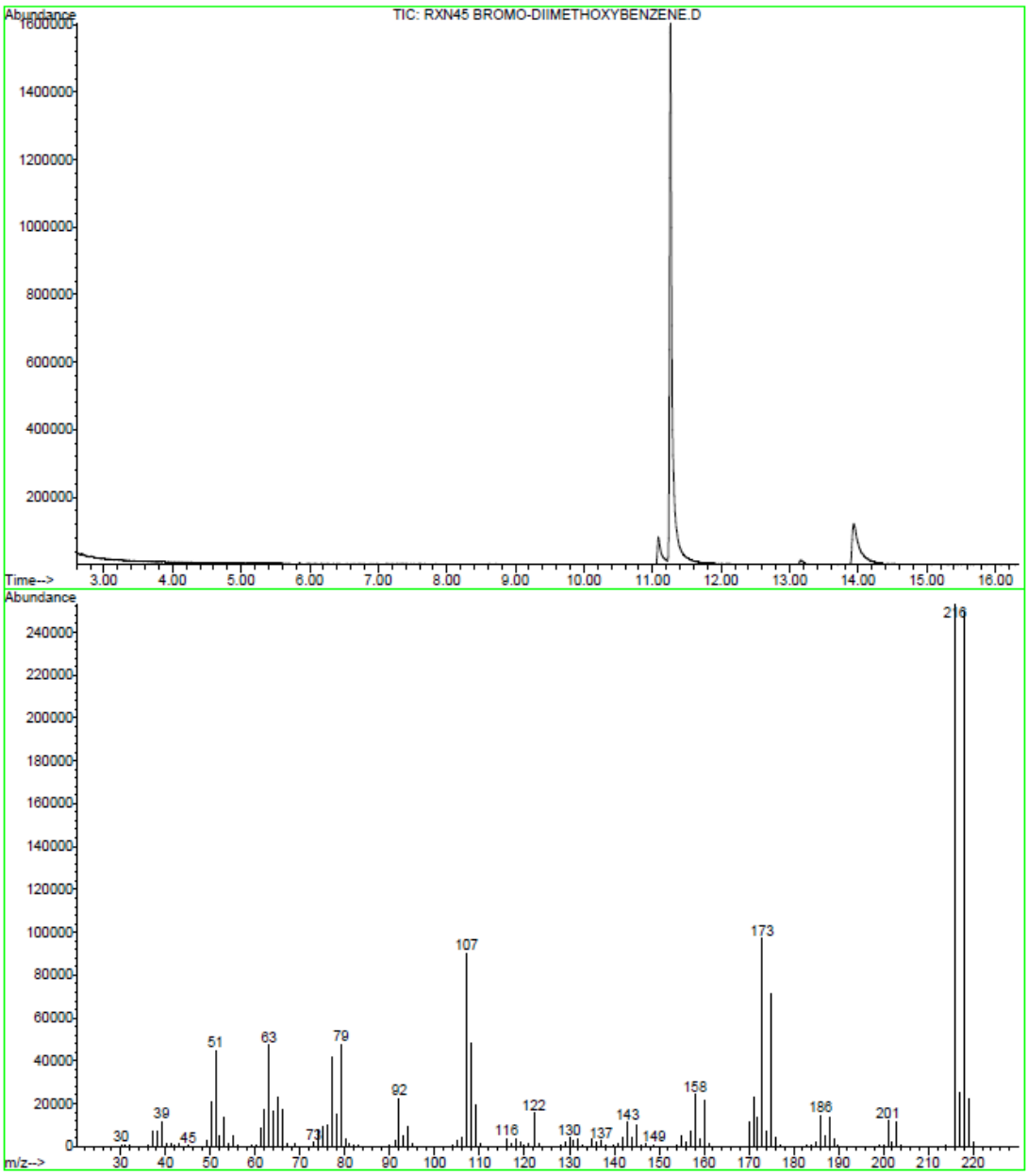


Figure 2.6 Bromodeboronation of Potassium 2,6-Dimethoxyphenyl-trifluoroborate with 15 Equivalents of KBr Added. Mass spectrum of peak at 11.26 min (2-bromo-1,3-dimethoxybenzene).

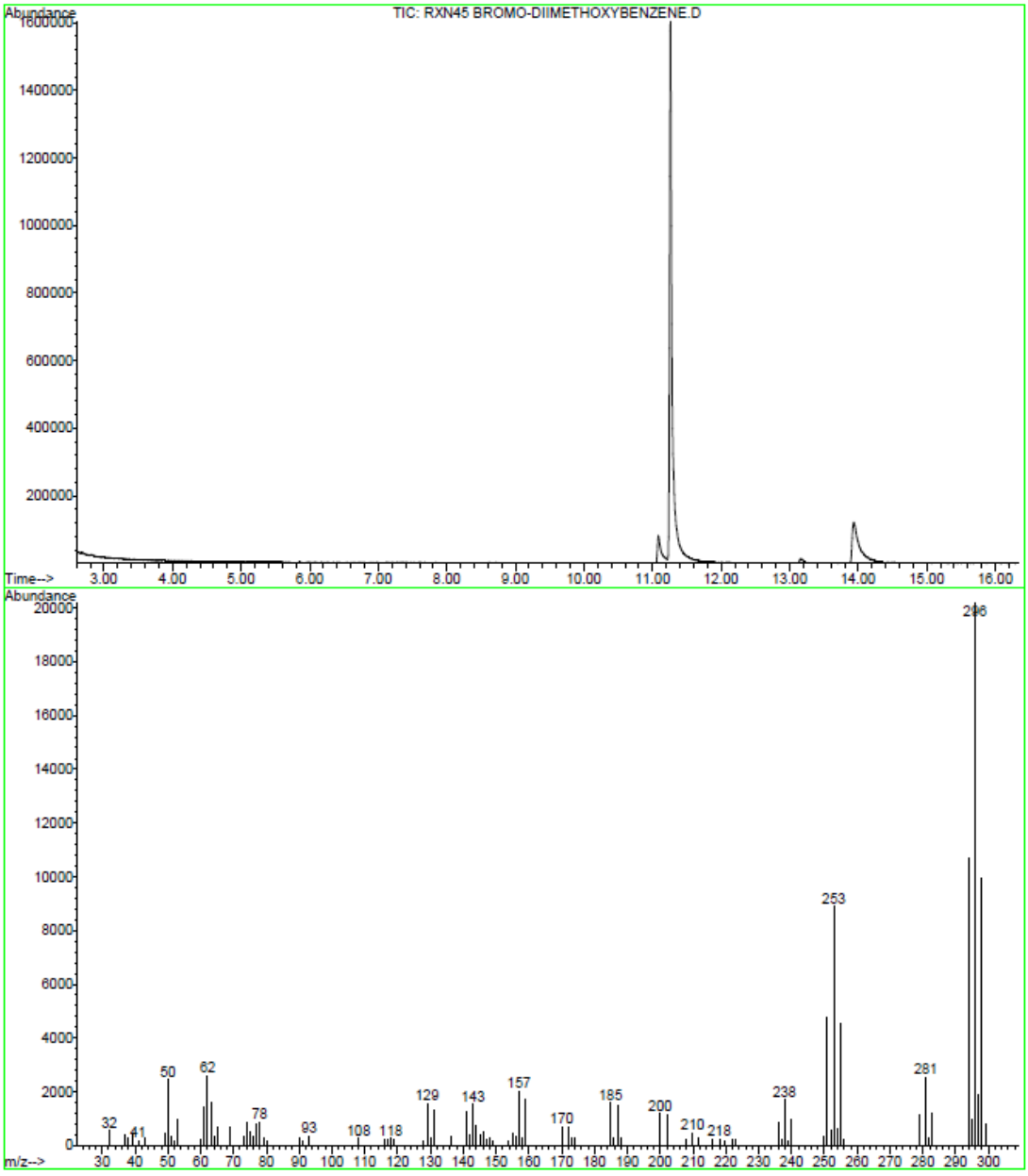


Figure 2.7 Bromodeboronation of Potassium 2,6-Dimethoxyphenyl-trifluoroborate with 15 Equivalents of KBr Added. Mass spectrum of peak at 13.94 min (dibromodimethoxybenzene).

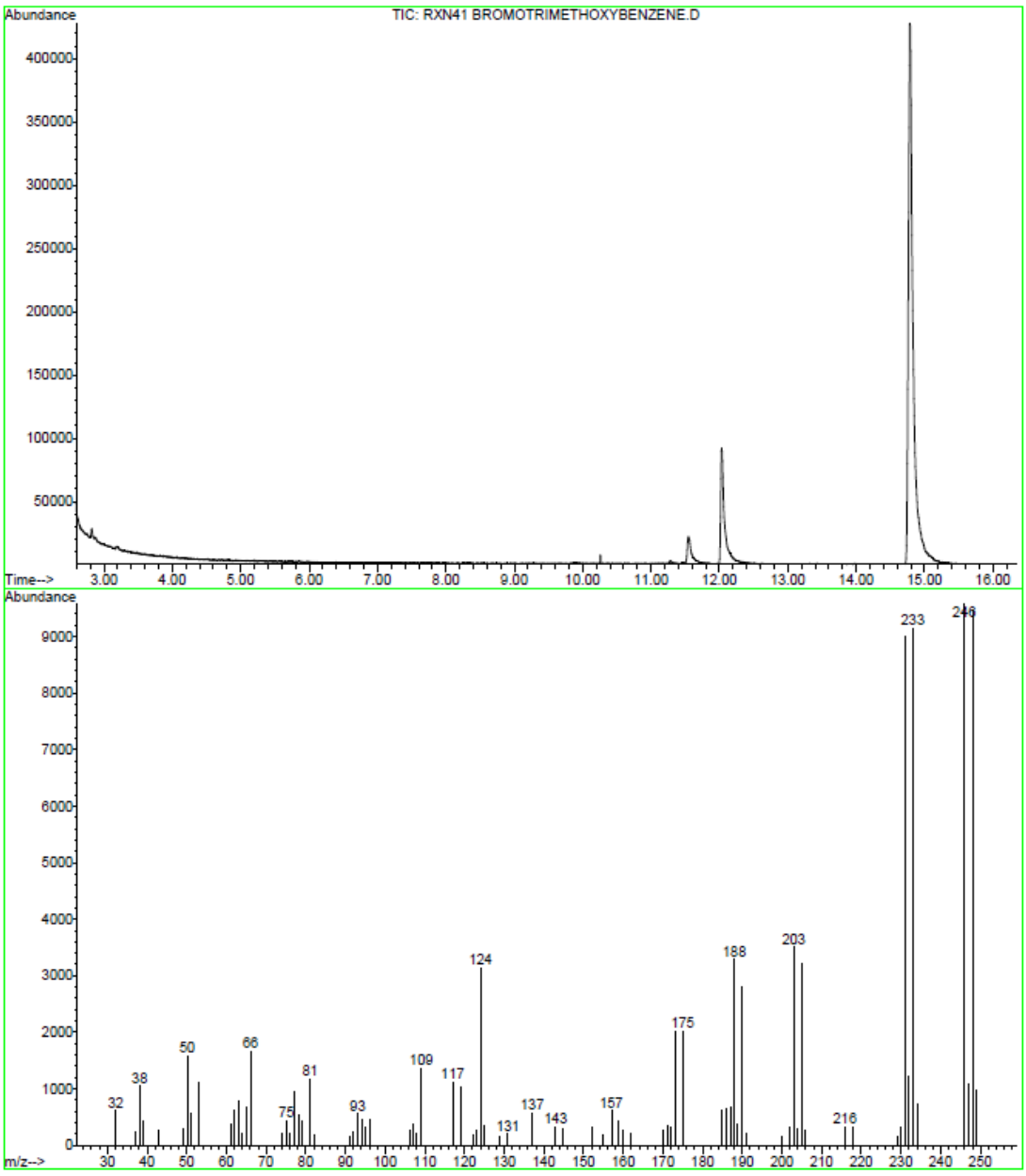


Figure 2.8 Bromodeboronation of Potassium 3,4,5-Trimethoxypenyl-trifluoroborate with 15 equivalents of KBr Added. Mass Spectrum of peak at 12.03 min (1-bromo-3,4,5-trimethoxybenzene).

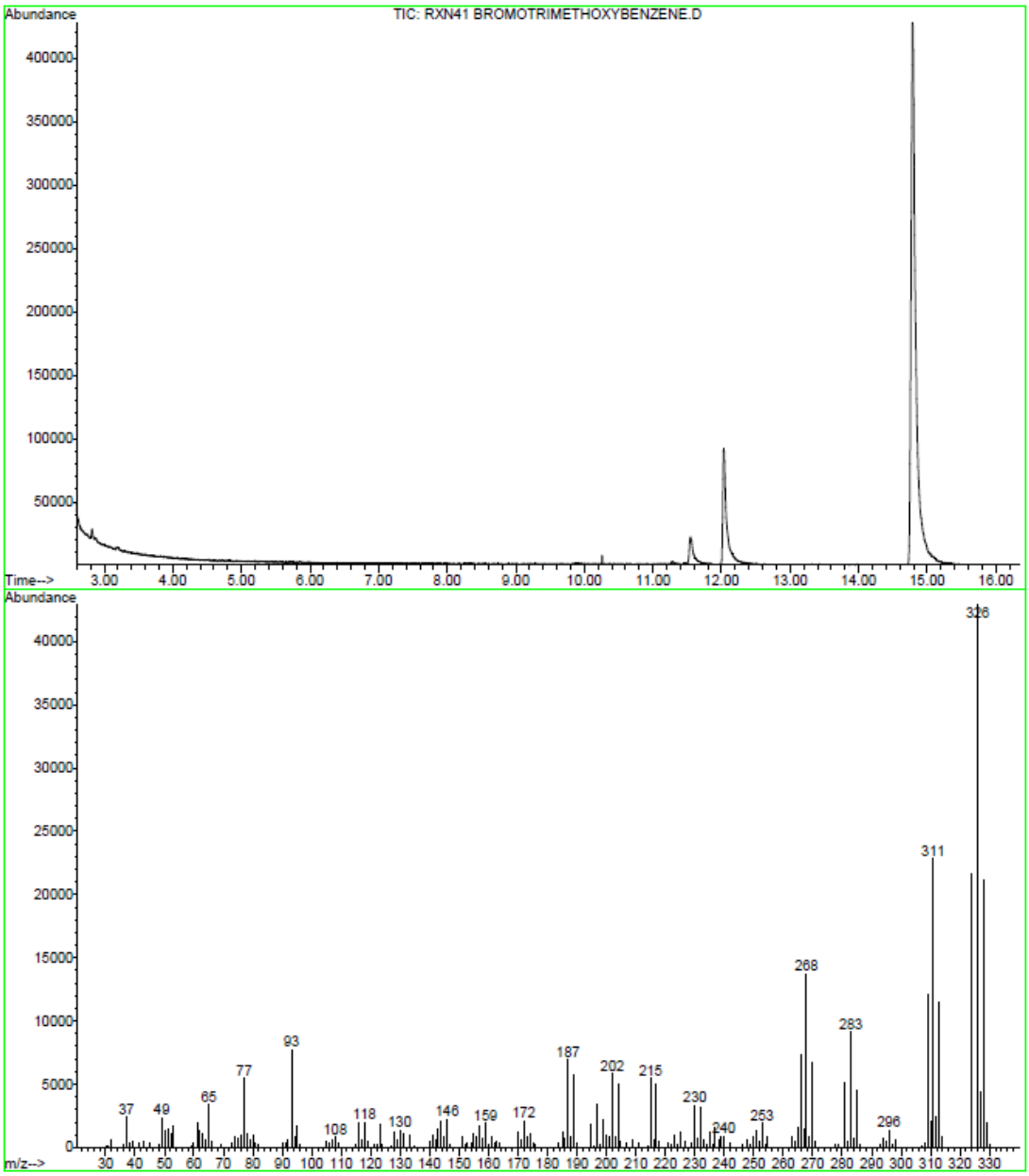


Figure 2.9 Bromodeboronation of Potassium 3,4,5-Trimethoxypenyl-trifluoroborate with 15 equivalents of KBr Added. Mass Spectrum of peak at 14.79 min (dibromotrimethoxybenzene).

CHAPTER 3
IODODEBORONATION OF POTASSIUM ARYL- AND ALKENYLTRIFLUOROBORATES USING CESIUM TRIIODIDE

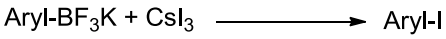
3.1 Introduction

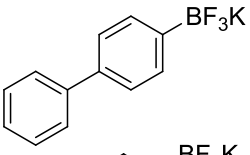
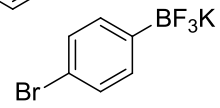
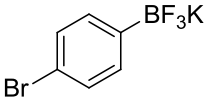
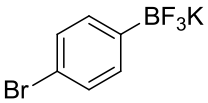
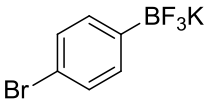
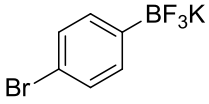
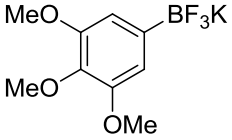
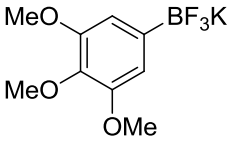
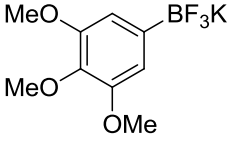
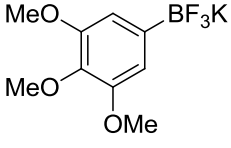
Iodine is the least reactive of the halogens in electrophilic aromatic substitution reactions. As noted in Chapter 1, iododeboronation of organotrifluoroborates using sodium iodide and chloramine-T provides an efficient way to regioselectively produce an aryl or vinyl iodide in good yields and a variety of functional groups are tolerant of the mild reaction conditions. In an effort to determine if the triiodide anion is a useful iododeboronation reagent for aryl- and alkenyltrifluoroborates, an investigation was conducted using cesium triiodide. Cesium triiodide is a commercially available, grayish-purple salt that has no detectable odor. Initially, the same reaction conditions were tried that were used with TBATB and pyridinium tribromide, but due to the lower reactivity of cesium triiodide, new reaction conditions were developed.

3.2 Results and Discussion

The initial investigation into the use of cesium triiodide as an iododeboronation reagent for use with organotrifluoroborates began with potassium biphenyl-4-trifluoroborate. The reaction conditions chosen were a one-to-one THF/water solvent system, room temperature, and 1 equivalent of cesium triiodide salt. Since cesium triiodide forms a purple solution and 1 equivalent was used, dissipation of the dark purple color should indicate completion of the reaction. The reaction was allowed to proceed for 5.5 hours. Isolation of the product by extraction into hexanes and column chromatography gave a 26% yield of 4-iodobiphenyl as a white solid with a melting point of 108-110 $^{\circ}$C (Trial 1, Scheme 3.1). In the second trial, potassium *p*-bromophenyltrifluoroborate was used and, in an effort to increase the reaction

Scheme 3.1 Optimization of Iododeboronation Using CsI_3.



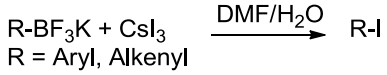
Trial	Substrate	Solvent	Temperature(°C)	Time(h)	Yield(%)
1		THF/H_2O	rt	5.5	26
2		THF/H_2O	45	66	8
3		Isoproanol	45	72	Trace
4		1 H_2O/ 2 DMSO	rt	24	62
5		1 H_2O/ 2 DMF	rt	10	67
6		1 H_2O/ 2 DMF	80	5	94
7		1 H_2O/ 2 DMF	rt	6	25
8		1 H_2O/ 2 DMF	45	8.5	48
9		1 H_2O/ 2 DMF	60	8.5	58
10		1 H_2O/ 2 DMF	80	3	83

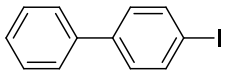
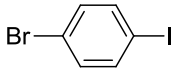
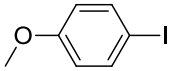
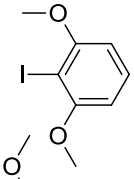
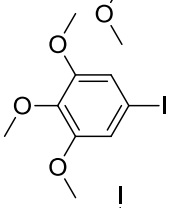
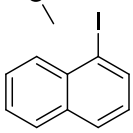
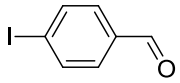
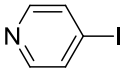
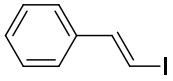
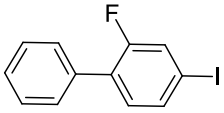
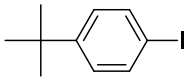
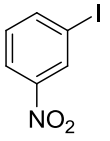
rate, the reaction was heated to 45 °C. The reaction was allowed to proceed for 66 hours, at which time the reaction solution remained a dark purple color. Isolation of the product by extraction into hexanes and column chromatography resulted in an 8% isolated yield of *p*-bromoiodobenzene, a white solid with a melting point of 87.8-90 °C (Trial 2). In an effort to increase the reaction yield and rate, isopropanol was used as the solvent in the third trial. After allowing the reaction to proceed for 72 hours at 45 °C only a trace of the *p*-bromoiodobenzene product was isolated (Trial 3). In the fourth trial, a one-to-two water/DMSO solvent system was chosen. The reaction was allowed to proceed for 24.5 hours at room temperature, at this time the reaction color was significantly lighter in color, and the *p*-bromoiodobenzene product was isolated by extraction into hexanes and column chromatography in 62% yield (Trial 4). The fifth trial was conducted using a one-to-two water/DMF solvent system. The reaction was allowed to proceed for 10 hours at room temperature, and the *p*-bromoiodobenzene product was isolated in 67% yield (Trial 5). Since the DMF/water solvent solution produced the best yield in Trial 6, the temperature was increased to 80 °C and the reaction was complete in 5 hours as judged by the dissipation of the dark purple color of cesium triodide. The *p*-bromoiodobenzene product was isolated by column chromatography and a 94% yield was obtained. In an effort to ascertain the reactivity of potassium aryltrifluoroborates with cesium triiodide, Trial 7 was conducted with potassium 3,4,5-trimethoxyphenyltrifluoroborate in a two-to-one DMF/water solution at room temperature. The reaction was allowed to proceed for six hours. Isolation of the product by extraction into a ten-to-one hexanes/ethyl acetate, followed by drying over anhydrous magnesium sulfate, gave a 25% yield of 5-iodo-1,2,3-trimethoxybenzene, a white solid with a melting point of 87-89 °C, (Trial 7). This result was surprising since it was expected that the activated benzene ring of potassium 3,4,5-trimethoxyphenyltrifluoroborate would be more reactive than the biphenyltrifluoroborate substrate used in Trial 1. In Trials 8-10, the temperature was slowly increased in increments to 45 °C, 60 °C, and 80 °C (Trials 8-10). Trial

10 was conducted at 80 ^{o}C for 3 hours at which point the dark color had dissipated. Isolation of the product by extraction into a ten-to-one hexanes/ethyl acetate mixture and then column chromatograpy, yielded 83% of 5-iodo-1,2,3-trimethoxybenzene (Trial 10).

After analysis of the trial results, it was determined that the highest yields were obtained at 80 $^{\circ}$C in a one-to-two water/DMF solution. Using these reaction conditions, a number of potassium aryltrifluoroborates and an alkenyl-trifluoroborate were evaluated. In general, the iododeboronations of aryl- and alkenyltrifluorobrates using cesium triiodide gave lower yields of the corresponding aryl halides when compared to the bromodeboronation reactions using TBATB and pyridinium tribromide.[72] Electron neutral potassium aryltrifluoroborates underwent iododeboronation to produce lower product yields than expected since this type of substrate produced some the best product yields with TBATB and pyridinium tribromide (Products 13, 18, and 23, Scheme 3.2, page 56). The product yields with these substrates ranged from 45%-65%. Aryl substrates with activating methoxy groups produced the highest yields of aryl iodides (Products 15-17). The yields observed for these activated substrates ranged from 83%-99%. In contrast to the bromodeboronation reactions using pyridinium tribromide, no diiodinated products were observed with these activated substrates. Potassium aryltrifluoroborates bearing electron withdrawing substituents produced poor yields of the corresponding aryl iodides (Products 19, 22, and 24). Yields produced with these substrates ranged from 6% to 16%. Potassium pyridine-4-trifluoroborate did not undergo iododeboronation under the reaction conditions used (Product 20). Potassium (*E)*-(1-phenyl)vinyl-2-trifluoroborate underwent iododeboronation to produce the corresponding vinyliodide in 81% yield with retention of stereochemistry (Product 21).

Scheme 3.2 Results of the Iododeboronation of Aryl- and Alkenyltrifluoroborates Using Cesium Triiodide.



Product		Temperature(°C)	Time(h)	Yield(%)
13		80	6	45
14		80	5	94
15		25	6	98
16		80	3.33	99
17		80	3	83
18		80	3	65,65
19		80	9	6
20		80	10	0
21		80	3.5	81
22		80	8	16
23		80	6	46
24		80	8	14

One of the reasons for the poor yields produced by some substrates was determined to be, in part, due to hydrolysis of the potassium organotrifluoroborates to the corresponding organoboronic acids at the elevated reaction temperatures. Arylboronic acids do not undergo iodination with cesium triiodide under the reaction conditions used. Adding sodium fluoride or potassium hydrogen fluoride in attempt to prevent hydrolysis and increase product yields resulted in decreased product yields.

3.3 Conclusions

Cesium triiodide is an effective iododeboronation reagent for activated aryltrifluoroborates, and aryltrifluoroborates bearing a bromine substituent. Excellent yields of aryl iodides were observed with these substrates. Electronically neutral aryltrifluoroborates produce only moderate yields of the aryl iodides due to a competing hydrolysis of the organotrifluoroborate to the corresponding boronic acid. Vinyltrifluoroborates undergo reaction to produce the vinyl iodides in good yields with retention of stereochemistry. Aryltrifluoroborates with electron withdrawing substituents are essentially unreactive toward iododeboronation under the conditions used. Heteroaryltrifluoroborates also are unreactive.

The work presented in this chapter was carried out by the author, and the majority of this work has been published in the following publication:

Yao, M.; Kabalka, G. W.; Blevins D. W.; Reddy, M. S.; Yong, L. Halodeboronation of Organotrifluoroborates Using Tetrabutylammonium Tribromide or Cesium Triiodide. *Tetrahedron* **2012**, *68*, 3738.

3.4 Experimental

Reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE). ^{1}H-NMR and ^{13}C-NMR spectra were

recorded at (250 or 300) and (62.89 or 75) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. Gas chromatography/mass spectroscopy studies were carried out using a Hewlett Packard: HP 6890 series GC System with 5973 Mass Selective Detector; Column: Agilent 19091S-433E, 30.0mm X 0.25mm X 0.25 μm; Gas (He) flow rate: 0.8 mL/min; Initial temperature: 90 ˚C; Ramp temperature rate: 10 ˚C/min to maximum 240 ˚C. Melting points were obtained by using a Mel-Temp melting point apparatus with a mercury thermometer.

3.5 Typical Procedure for Iododeboronation Reactions

The potassium organotrifluoroborate (1.0 mmol) was added to a small round bottomed flask. Water (1 mL) and of DMF (2 mL) were then added. Cesium triiodide was added (1.0 mmol) and a rubber septum was place onto the round bottomed flask. The reaction was heated to 80 $^{\circ}$C in an oil bath until the dark color of the cesium triiodide dissipated. The reaction solution was placed directly onto a silica gel column and eluted with hexanes or an appropriate mixture of ethyl acetate and hexanes as determined by TLC. Solvent was removed under reduced pressure.

3.6 Characterization of Compounds

(NMR Spectra are in Appendix)

4-Iodobiphenyl (13).[81] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.81 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.8, 140.1, 137.9, 129.1, 129.0, 127.8, 127.0, 93.2. Melting point: 108-110 $^{\circ}$C.

1-Bromo-4-iodobenzene (14).[82] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, J = 10.5 Hz, 2H), 7.23 (d, J = 10.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.2, 133.6, 120.1, 92.2. Melting point: 88-90 $^{\circ}$C.

1-Iodo-4-methoxybenzene (15).[83] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.55 (d, J = 9.0 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 159.6, 138.3, 116.5, 82.8, 55.4. Melting point: 50-52 °C.

1-Iodo-2,6-dimethoxybenzene (16).[84] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.26 (t, J = 8.3 Hz, 1H), 6.51 (d, J = 8.3 Hz, 2H), 3.89 (s, 6H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 137.1, 135.8, 128.7, 128.2, 126.0, 106.4. Melting point: 100-102 °C.

1-Iodo-3,4,5-trimethoxybenzene (17).[85] ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.89 (s, 2H), 3.82-3.84 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 154.1, 115.2, 86.2, 61.0, 56.5. Melting point: 87-89 °C.

1-Iodonaphthalene (18).[83] ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.05-8.09 (m, 2H), 7.72-7.82 (m, 2H), 7.45-7.59 (m, 2H), 7.11-7.22 (m, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 137.6, 134.5, 134.3, 132,3, 129.1, 128.7, 127.8, 127.0, 126.9, 99.7.

4-Iodobenzaldehyde (19).[86] ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.96 (s, 1H), 7.94 (d, J=8.5 Hz, 2H), 7.59 (d, 8.52 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.6, 138.5, 135.6, 130.9, 121.0.

***trans*-2-(Phenyl)vinyliodide** (21).[87] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43 (d, J = 14.8 Hz, 2H), 7.28-7.32 (m, 5H), 6.83 (d, J = 14.8 Hz, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 144.6, 137.4, 128.5, 128.1, 125.8, 76.9.

2-Fluoro-4-iodo-1,1'-biphenyl (22).[86] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32-7.60 (m, J=9 Hz, 7H), 7.10-7.19 (t, J=9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.9, 157.5, 134.8, 133.6, 132.0, 128.8, 128.5, 128.0, 125.4, 91.9.

1-Iodo-4-tert-butylbenzene (23).[88] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 6 Hz, 2H), 7.13 (d, J = 6 Hz, 2H), 1.29 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.0, 137.2, 127.7, 90.8, 34.7, 31.3.

1-Iodo-3-nitrobenzene (24).[89] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.19-8.23 (m, 1H), 8.02-8.05 (m, 1H), 7.27-7.32 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.6, 143.6, 132.6, 130.8, 122.9, 93.6. Melting point: 34-36 °C.

THE SYNTHESIS OF (*Z*)-1,2-DIBROMOALKENES FROM STEREODEFINED POTASSIUM ALKENYL DITRIFLUOROBORATES

4.1 Introduction

As discussed previously in Section 1.7, we recently reported the synthesis of (*Z*)-1,2-dibromoalkenes from terminal alkynes. Bromoboration of a terminal alkyne using boron tribromide followed by conversion of the bromoboration intermediate into an (*Z*)-1-bromoalkenyltrifluoroborate by reaction with potassium hydrogen difluoride followed by bromodeboronation with TBATB yields a (*Z*)-1,2-dibromoalkene. The method is only applicable to terminal alkynes. In an effort to develop a route to (*Z*)-1,2-dibromoalkenes from internal alkynes, the platinum catalyzed diboration of alkynes was applied to internal alkynes to create (*Z*)-1,2-bis(boryl)alkenes. The (*Z*)-1,2-bis(boryl)alkenes are produced with very high *syn* selectivity.[90] Conversion of (*Z*)-1,2-bis(boryl)alkenes into the corresponding stereodefined (*Z*)-1,2-bis(trifluoroboryl)alkenes by reaction with potassium hydrogen fluoride followed by bromodeboronation using TBATB was found to yield the (*Z*)-1,2-dibromoalkene products.

4.2 Results and Discussion

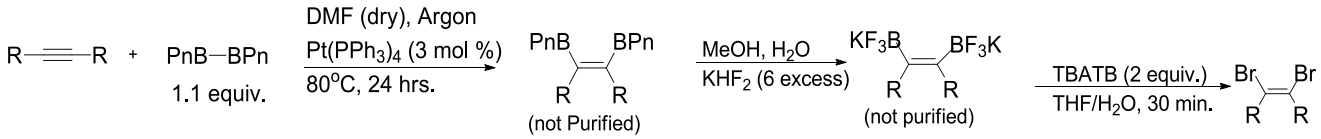
The reaction sequence used to synthesize (*Z*)-1,2-dibromoalkenes from alkynes begins with the tetrakistriphenylphosphine platinum(0) catalyzed diborylaton of alkynes using pinacoldiborane. This reaction is carried out in dry DMF under an argon atmosphere at 80 $^{\circ}$C for 24 hours. A 3 mol% catalyst loading is required and the reactions typically yield 79-86% of the (*Z*)-1,2-bis(boryl)alkene. The (*Z*)-1,2-bis(boryl)alkene is not purified. Instead the DMF is removed from the reaction mixture using a high vacuum pump. Then, six equivalents of aqueous potassium hydrogen fluoride are added in methanol to convert the (*Z*)-1,2-bis(boryl)alkene into a (*Z*)-1,2-alkenylditrifluoroborate. This

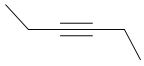
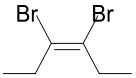
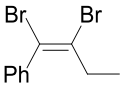
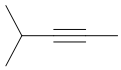
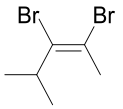
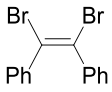
solid product is filtered and washed with ether. Next, this crude product is reacted with TBATB at room temperature in a one-to-one THF/water solution to produce the (*Z*)-1,2-dibromoalkene. Products are purified by column chromatography.

In the first trial, 3-hexyne was converted into (*Z*)-3,4-dibromohex-3-ene, a colorless liquid, in 60% overall yield, (Product 25). The second substrate utilized for the reaction sequence was 4-methyl-2-pentyne. The first trial with this substrate produced only a 15% yield of (*Z*)-2,3-dibromo-4-methylpent-2-ene. Four additional trials with this substrate were carried out with the following yields of final product: 23%, 40%, 15%, and 33%. It was decided to isolate the bis(boryl)alkene from the diboration reaction to determine if it was produced in the expected yield. In the sixth trial, the bis(boryl)alkene was isolated by vacuum distillation in 80% yield as a waxy solid with an observed melting point of 89-91 $^{\circ}$C. The ^{1}H NMR was consistent with the expected product (Figure 4.1). Conversion of this isolated (*Z*)-diborylalkene to the corresponding potassium (*Z*)-1,2-bis(boryl)alkenyltrifluoroborate, and then reaction with TBATB, produced only a 9% isolated yield of the desired (*Z*)-1,2-dibromoalkene product. It was hypothesized, that peroxides may have formed in the THF prior to the reaction, and that a radical reaction may have occurred. GC/MS analysis of an extract of the reaction mixture showed a monobrominated product (m/z=162), multiple dibrominated products (m/z= 242), two tribrominated products (m/z=320), and several other product peaks. An iodide/starch test of the THF used showed that peroxides were present. To test whether peroxide formation in the THF was the reason for the poor yields, freshly distilled THF was used in the next trial for the bromodeboronation reaction with this substrate, and the final product, (*Z*)-2,3-dibromo-4-methylpent-2-ene, was isolated in 62.4% yield as a colorless liquid (Product 26). A NOESY NMR experiment was performed to verify the (*Z*) stereochemistry and a cross peak was observed for the single hydrogen of the *i*-propyl group and the methyl group on the opposite carbon of the carbon-carbon double bond. (Figure 4.2). In the next trial, 1-phenyl-1-butyne was used and an

overall yield of 64%, over 3 steps, was obtained of (*Z*)-1,2-dibromo-1-phenylbut-1-ene, a colorless liquid (Product 27). In the fourth trial, diphenylacetylene was utilized and an 80% yield of (*Z*)-(1,2-dibromo)stilbene, a faintly yellow solid with a melting point of 66-68 °C, was obtained (Product 28). Due to a discrepancy between the Carbon-13 NMR in the literature reference for compound 28 and the Carbon-13 NMR obtained with this compound, an X-ray diffraction analysis of this compound was conducted, and the results show that the desired (*Z*)-(1,2-dibromo)stilbene was produced (see Appendix), Scheme 4.1.

Scheme 4.1 Synthesis of (*Z*)-1,2-Dibromoalkenes.

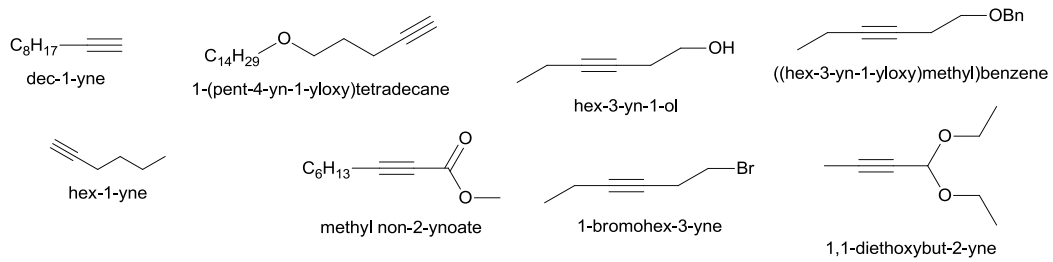


Substrate	Product	Yield (%)	Substrate	Product	Yield (%)
	25 	60	Ph—≡—	27 	64
	26 	62	Ph—≡—Ph	28 	80

To further test the utility of this methodology to obtain (*Z*)-1,2-dibromoalkenes from alkynes, 1-hexyne and 1-decyne were utilized. The expected (*Z*)-1,2-dibromoalkene products were only formed in trace amounts along with other inseparable products. After several trials, it was determined that this methodology is not applicable to terminal alkynes. Next, several functionalized internal alkynes were evaluated using this methodology. 1-(Pent-4-yn-1-yloxy)tetradecane, methyl non-2-ynoate, hex-3-yn-1-ol, 1-bromohex-3-yne, ((hex-3-yn-1-yloxy)methyl)benzene, and 1,1-diethoxybut-2-yne were all used in an attempt to synthesize the corresponding (*Z*)-1,2-dibromoalkene products, but

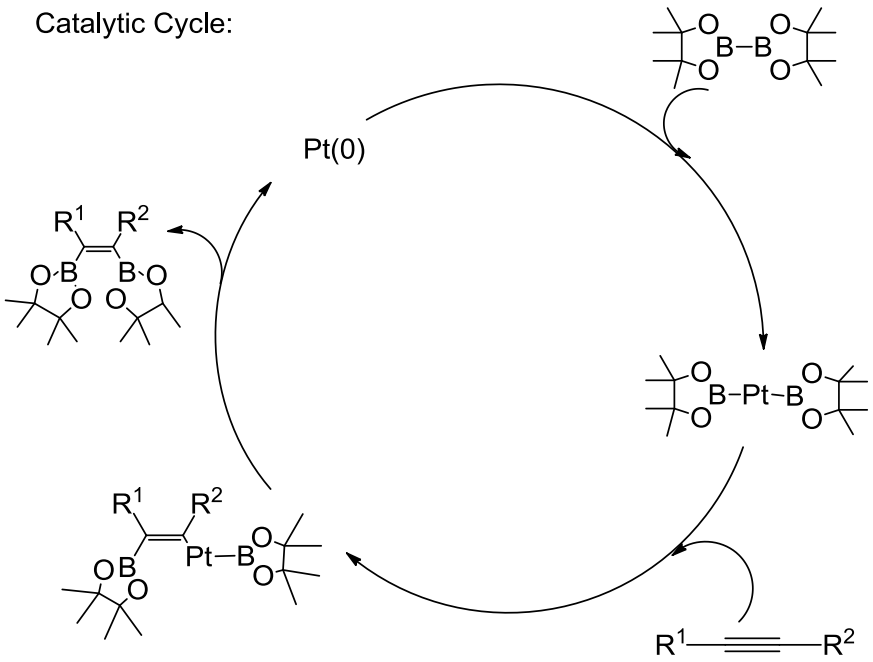
the expected products were only produced in trace amounts. It was determined that, the diboration step in these reactions did not produce the expected (*Z*)-1,2-bis(boryl)alkene in any significant amount, Scheme 4.2.

Scheme 4.2 Substrates that did not Successfully Udergo the Diborylation/Bromodedoronation Sequence.



To explain the observed results, it was hypothesized that the functionalized alkynes must form complexes with the tetrakistriphenylphosphine platinum(0) catalyst that disrupt the diboration catalytic cycle, Scheme 4.3.

Scheme 4.3 Catalytic Cycle of the Diborylation of Alkynes. Adapted from: *J. Am. Chem. Soc.* **1993**, *115*, 11018.



The diboration catalytic cycle is thought to proceed by the oxidative addition of pinacoldiborane to the platinum(0) complex followed by stereospecific insertion of the alkyne into the boron-platinum bond, and reductive elimination of the stereodefined bis(boryl)alkene.

4.3 Conclusions

A route to (*Z*)-1,2-dibromoalkenes from stereodefined (*Z*)-1,2-alkenylditrifluoroborates was successfully evaluated and found to be applicable to unfunctionalized internal alkynes. This methodology, in combination with our previously reported route to (*Z*)-1,2-dibromo-1-alkenes, allows the efficient stereospecific synthesis of a variety of (*Z*)-1,2-dibromoalkenes in good yields.

The work presented in this chapter was carried out by the author, and this work has been published in the following publication:

Yao, M.; Kabalka, G. W.; Blevins D. W.; Reddy, M. S.; Yong, L. Halodeboronation of Organotrifluoroborates Using Tetrabutylammonium Tribromide or Cesium Triiodide. *Tetrahedron* **2012**, *68*, 3738.

4.4 Experimental

Reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE). ^{1}H-NMR and ^{13}C-NMR spectra were recorded at (250, 300, or 500) and (62.89, 75, or 125) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. Gas chromatography/mass spectroscopy studies were carried out using a Hewlett Packard: HP 6890 series GC System with 5973 Mass Selective Detector; Column: Agilent 19091S-433E, 30.0mm X 0.25mm X 0.25 μm; Gas (He) flow rate: 0.8 mL/min; Initial temperature: 90 ˚C; Ramp temperature rate: 10 ˚C/min to maximum 240 ˚C. Melting points were obtained by using a Mel-Temp melting

point apparatus with a mercury thermometer. An APEX II CCD detector, radiation safety enclosure system, and a SMART APEX II 3-axis system incorporating a fixed-chi stage with a chi angle of approximately 54°, a phi drive with 360° rotation, and a freely rotating omega, with a Mo radiation source were used in the detection of X-Ray crystal data. SHELXTL based refinement software was used for analysis. High Resolution Mass Spectrometry was performed using a JEOL AccuTOF™ DART Mass Spectrometer.

4.5 General Procedure for the Synthesis of (*Z*)-1,2-Dibromoalkenes

Representative procedure for the preparation of (Z)-1,2-dibromoalkenes from alkynes through (*Z*)-1,2-alkenylditrifluoroborate *intermediates:* To a solution of bis(pinacolato)-diboron (279 mg, 1.1 mmol) in dry DMF (1.6 mL)/ degassed by bubbling argon through the solution for 5 min. Tetrakis(triphenylphosphine)platinum (37 mg, 3.0 mol%) and alkyne (1.0 mmol) were added sequentially. The reaction mixture was stirred at 80 ^{o}C and the reaction was monitored by TLC and typically required 24 hours. The solvent was removed under vacuum and the residue was dissolved in a minimum amount of MeOH. To the resultant solution, aqueous KHF_2 (468 mg, 6.0 mmol) was added and the reaction stirred at room temperature for 30 min. The solid potassium (Z)-1,2-alkenylditrifluoroborate was filtered and washed with Et_2O. The crude organotrifluoroborate was then subjected to bromodeboronation using tetrabutylammonium tribromide (2.0 mmol) under typical reaction conditions for bromodeboronation of organotrifluoroborates using TBATB (see chapter 2). Potassium bisulfite was added to remove any remaing tribromide. Then extraction into hexanes and column chromatography yielded the pure isolated products.

4.6 Characterization of Compounds

(NMR Spectra in Appendix)

(*Z*)-3,4-Dibromohex-3-ene (25). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.57 (q, J=4.5 Hz, 4H), 1.15 (t, J=4.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 128.2, 31.7, 13.8. Anal. Calcd. For $C_6H_{10}Br_2$: C, 29.78; H, 4.17; Br, 66.05. Found: C, 29.52; H, 3.95; Br, 66.34. HRMS for $C_6H_{11}Br_2$ (MH^+): 240.9228. Found: 240.9235.

(*Z*)-2,3-Dibromo-4-methylpent-2-ene (26).[72] Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): 2.93 (septet, J=6.0 Hz, 1H), 2.40 (s, 3H), 1.08 (d, J=6.0 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl^3$): δ 135.4,119.4, 34.0, 25.6, 22.1. HRMS for $C_6H_{11}Br_2$ (MH^+): 240.9228. Found: 240.9217.

(*Z*)-(1,2-Dibromobut-1-en-1-yl)benzene (27).[91] Colorless liquid. ^{1}H NMR (250 MHz, $CDCl_3$): d 7.34 (m, 5H), 2.42 (q, J=7.5 Hz, 2H),1.11 (t, J=7.5 Hz, 3H). ^{13}C NMR (62.5 MHz, $CDCl_3$): d 139.6, 132.3, 128.8, 128.7, 128.6, 122.1, 32.6, 14.1. HRMS for $C_{10}H_{11}Br_2$(MH^+): 288.9228. Found: 288.9220.

(*Z*)-(1,2-Dibromo)stilbene (28).[92] White solid: m.p. 66-68 ºC. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.13e7.21 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.6, 130.0, 128.5, 128.2, 125.8. HRMS for $C_{14}H_{10}Br_2$ (M^+): 335.9149. Found: 335.9157.

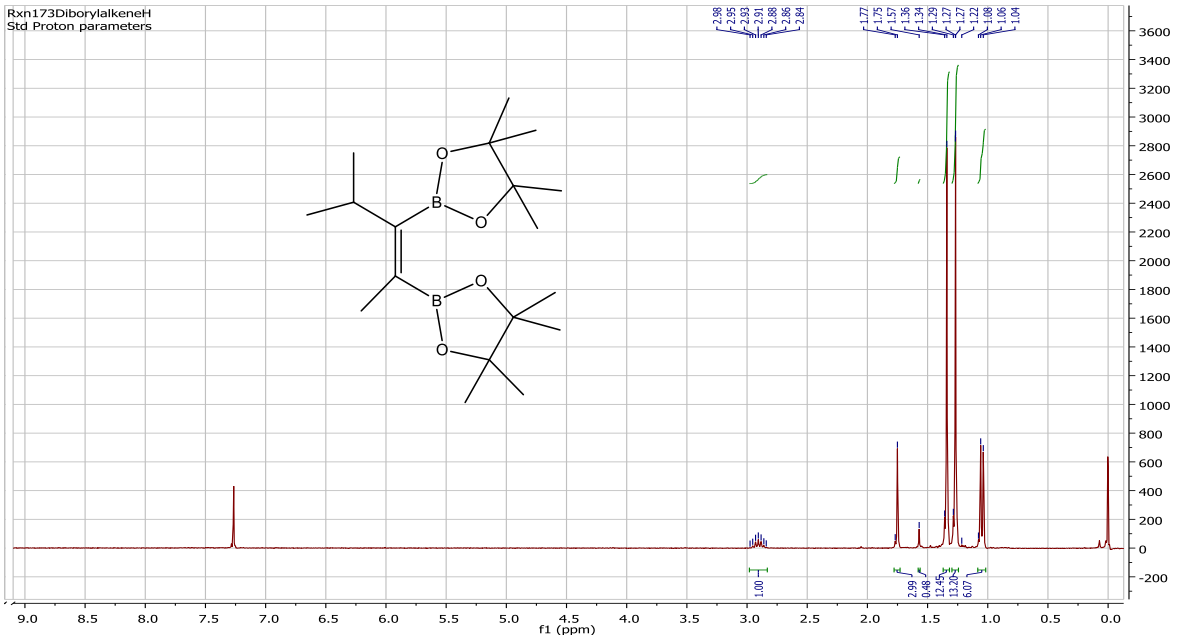


Figure 4.1 ^{1}H-NMR of (Z)-2,2'-(4-Methylpent-2-ene-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane).

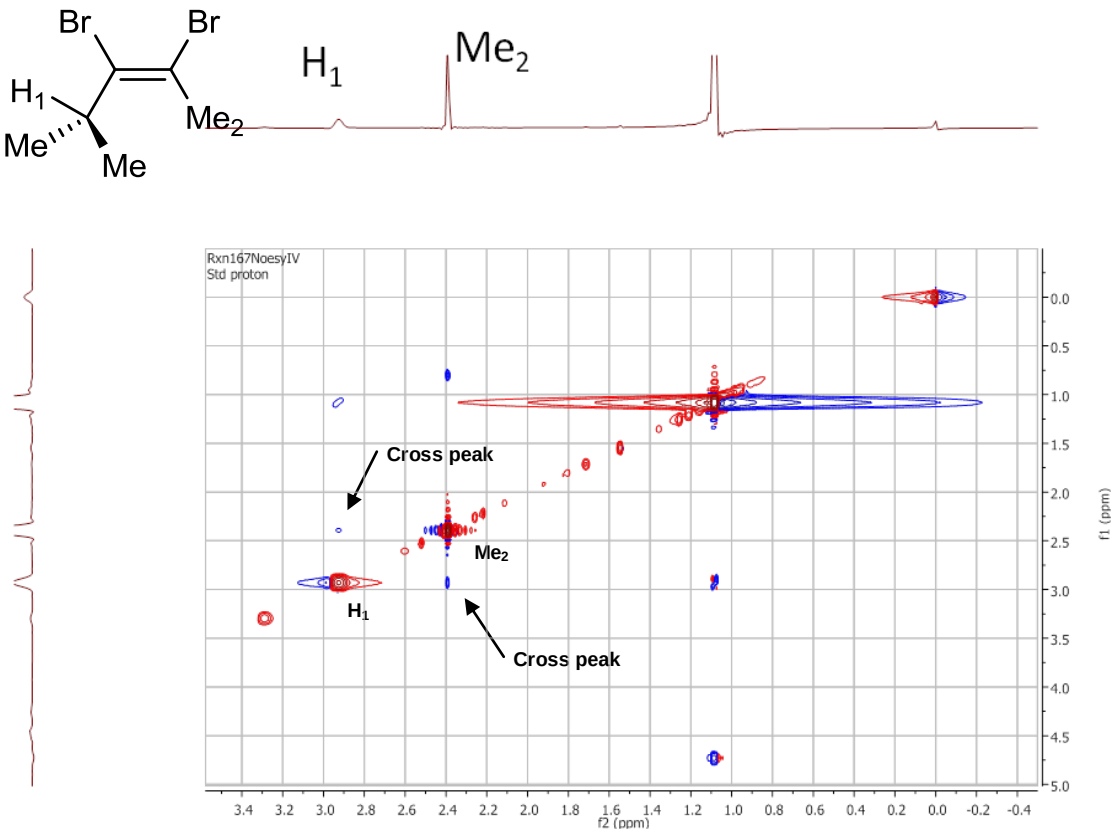


Figure 4.2 500 MHz NOESY Spectrum of Product 26.

CHAPTER 5
IRON(III) CHLORIDE PROMOTED HYDROLYSIS OF POTASSIUM ORGANOTRIFLUOROBORATES

5.1 Introduction

In Chapter 1, the hydrolysis of potassium organotrifuoroborates was discussed in detail. Potassium organotrifluoroborates are stable salts that can undergo many reactions, and they can also serve as protecting groups for organoboronic acids. While several methods are reported to convert organotrifluoroborates to the corresponding organoboronic acids, these methods rely on the use of reactive fluorophiles such as silicon tetrachloride or trimethylsilyl chloride. Bases such as lithium hydroxide and sodium carbonate also have been employed but are inefficient and have a limited scope. Silica gel has been shown to be effective in the hydrolysis of organotrifluoroborates, and is tolerant of a wide range of functionally substituted aryl-, alkenyl-, heteroaryl-, and alkyltrifluoroborates, but the hydrolysis of organotrifluoroborates with electron withdrawing substituents requires long reaction times (up to 24 hours) and some substrates produce only moderate yields of the corresponding organoboronic acids. Alumina was shown by our group to hydrolyze organotrifluoroborates rapidly at 70 $^{\circ}$C with microwave or thermal heating in fifteen minutes.

Recently we discovered that iron(III) chloride efficiently promotes the hydrolysis of a variety of organotrifluoroborates at room temperature.[93] Also, in a preliminary investigation, it was discovered that zinc powder and zinc oxide will promote the hydrolysis of potassium organotrifluoroborates.

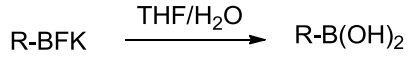
5.2 Results and Discussion

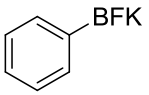
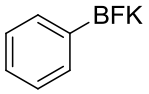
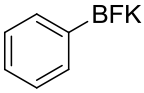
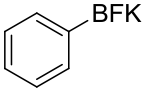
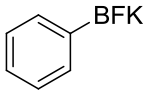
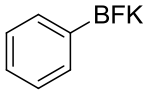
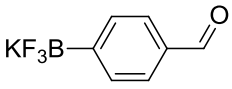
For the preliminary investigation of the iron(III) chloride promoted hydrolysis of organotrifluoroborates, a one-to-one THF/water solution (3 mL per mmol of organotrifluoroborate) was used as the solvent. Potassium phenyltrifluoroborate

was chosen for the reaction optimization trials. In the first trial, 1 equivalent of iron(III) chloride and potassium phenytrifluoroborate (1 mmol) was used. A reaction time of 20 minutes was chosen, and then the product was extracted into ethyl acetate; the organic layer was dried over anhydrous magnesium sulfate. Removal of the solvent using a rotary evaporator yielded 80 mg (66% yield) of phenylboronic acid (Trial 1). For Trial 2, the reaction was repeated on a 2 mmol scale, and the reaction time was increased to 30 minutes to determine if more time would result in an increased product yield. Extraction of the product, drying the organic layer, and solvent removal produced a 64% yield of phenyboronic acid (Trial 2). In Trial 3, phenyltrifluoroborate (2 mmol) was used and the amount of iron(III) chloride was increased to 1.1 equivalents. After a 30 minute reaction time, the product was extracted into ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed to yield 192 mg (70% yield) of phenylboronic acid (Trial 3). Trial 4 was conducted using the same conditions as in Trial 3, except that the reaction time was increased to 45 minutes to determine if the yield would increase. After 45 minutes, the product was extracted into ethyl acetate, the organic layer was dried, and the solvent removed to yield 171 mg (66% yield) of phenylboronic acid (Trial 4). Trial 5 was carried out as in Trial 4, except a one hour reaction time was allowed. At one hour, the product was extracted into ethyl acetate and the solvent removed, to yield 166 mg (68%) yield of phenyl boronic acid (Trial 5). In Trial 6, the isolation method was changed to filtration through alumina to determine if an increased product yield could be obtained. The reaction was carried out on a one mmol scale. Based on the data of the previous trials, a 30 minute reaction time was allowed. At this time, the reaction solution was placed into a small glass column with 8 cc of neutral alumina. The product was eluted using a two-to-one ethyl acetate/hexanes solution. After solvent removal, 105 mg (86%) of phenylboronic acid was obtained (Trial 6). A test reaction using potassium *p*-formylphenyltrifluoroborate without iron(III) chloride followed by alumina filtration gave 5% conversion to the boronic acid (Trial 9). Based on the data, the

standard method used to hydrolyze organotrifluoroborates, using iron(III) chloride is a one-to-one THF/water solution (3 mL per mmol of organotrifluoroborate), 1.1 equivalents of iron(III) chloride, and a 30 minute reaction time followed by filtration through 8 cc of neutral alumina using two-to-one ethyl acetate/hexanes.

Scheme 5.1 Optimization of the $FeCl_3$ Promoted Hydrolysis of Organotrifluoroborates.



Trial	Substrate	Time(min)	$FeCl_3$	Isolation Method	Yied(%)
1		20	1 equiv.	Extraction	66
2		30	1 equiv.	Extraction	64
3		30	1.1 equiv.	Extraction	70
4		45	1.1 equiv.	Extraction	66
5		60	1.1 equiv.	Extraction	68
6		30	1.1 equiv.	8 mL Alumina Filter	86
7		30	———	8 mL Alumina Filter	9

Next, a range of aryl-, alkyl-, and alkenyltrifluoroborates were hydrolyzed using the standard method. Unsubstituted potassium aryltrifluoroborates such as phenyltrifluoroborate and 2-napthyltrifluoroborate underwent hydrolysis in 30 minutes to give excellent yields of the corresponding boronic acids (Products 35

and 36). Potassium *o*-tolyltrifluoroborate underwent hydrolysis in 30 minutes to give a 92% yield of the organoboronic acid, but potassium 2,6-dimethylphenyltrifluoroborate required only 25 minutes to attain the maximum yield of the organoboronic acid (70%). Allowing 30 minutes for this substrate resulted in a decreased yield of 65% (Products 37 and 38). Potassium *o*-bromophenyltrifluroborate hydrolyzed in 30 minutes to produce a 91% yield of the organoboronic acid (Product 33).

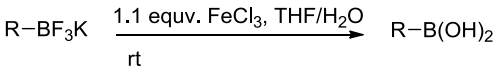
Potassium *p*-methoxyphenyltrifluoroborate was hydrolyzed in 30 minutes to yield 81% of the boronic acid (Product 34). Potassium arytrifluoroborates with electron withdrawing substituents required longer reaction times to achieve complete hydrolysis and unexpectedly, these substrates produced the best yields of organoboronic acids. Previously reported methods have shown that these substrates produced yields that were often lower than unsubstituted arytrifluoroborates and arytrifluoroborates with electron donating substituents. Potassium *o*-nitrotolyl-*p*-trifluoroborate hydrolyzed in 60 minutes and produced a 98% yield of the corresponding organoboronic acid. The silica gel hydrolysis method reported by Molander and coworkers required 24 hours and produced an 86% yield with this substrate (Product 29). Similarly, *p*-formylphenyltrifluoroborate hydrolyzed in sixty minutes to produce a 97% yield of the organoboronic acid (Product 30). The silica gel hydrolysis of this substrate produced only an 88% yield after 24 hours. 2,6-Difluorophenyltrifluoroborate hydrolyzed in one hour to produce a 94% yield of the organoboronic acid (Product 31). Potassium 2,5-ditrifluoromethylphenyltrifluoroborate was unreactive toward hydrolysis at room temperature. After 24 hours at room temperature, only a trace of the boronic acid could be detected by ^{11}B NMR. At this point, the reaction temperature was increased to 75 $^{\circ}$C and after 7 hours a 98% conversion was achieved (Product 32). Potassium 3-acetylphenyltrifluoroborate hydrolyzed in 30 minutes to give a 96% yield of the boronic acid (Product 74). Potassium alkenyltrifluoroborates were also found to undergo hydrolysis with retention of stereochemistry. Potassium (*E)*-1-chloro-1-

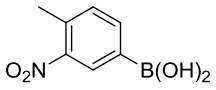
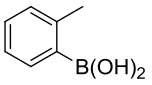
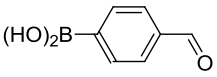
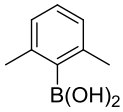
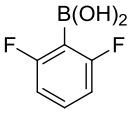
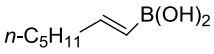
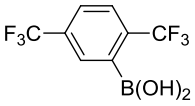
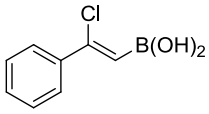
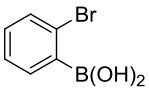
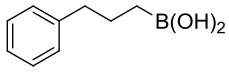
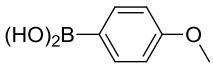
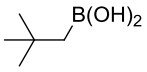
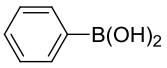
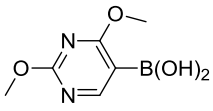
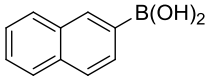
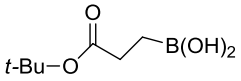
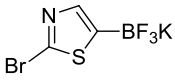
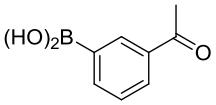
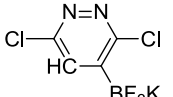
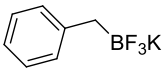
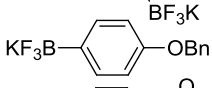
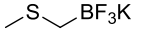
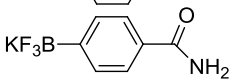
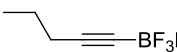
phenylethene-2-trifluoroborate and potassium (*E*)-1-heptene-1-trifluoroborate underwent hydrolysis in 30 minutes to yield the corresponding organoboronic acids in 85% and 87% yields respectively (Products 39 and 40). Alkyltrifluoroborates were also hydrolyzed effectively using this methodology. Potassium 1-phenylpropyl-3-trifluoroborate and potassium 2,2-dimethylpropyl-1-trifluoroborate hydrolyzed in 30 and 25 minutes respectively to give excellent yields of the corresponding organoboronic acids (Products 41 and 42). Allowing 30 minutes for the hydrolysis of potassium 2,2-dimethylpropyl-3-trifluoroborate produced a lower product yield (72%) due to protonolysis of the carbon-boron bond. Potassium *t*-butylpropanoate-3-trifluoroborate was hydrolyzed in 30 minutes to give a 97% yield of the organoboronic acid (Product 73). Potassium (2,6-dimethoxypyrimidin-4-yl)trifluoroborate underwent hydrolysis in one hour to give the corresponding organoboronic acid in 80% yield (Product 43). Potassium (4-(benzyloxy)phenyl)trifluoroborate and potassium (4-carbamoylphenyl)-trifluoroborate produced low yields of the corresponding organoboronic aicds due to significant protonolysis. Attempts to hydrolyze potassium (3,6-dichloropyridazin-4-yl)trifluoroborate failed to produce any boronic acid. Potassium 1-hexyne-1-trifluoroborate, potassium benzyltrifluoroborate, potassium ((methylthio)methyl)trifluoroborate, and potassium (4-bromothiazol-2-yl)trifluoroborate did not hydrolyze, instead each underwent protonolysis of the carbon-boron bond, Scheme 5.2.

As shown in Scheme 5.2, the iron(III) chloride-promoted hydrolysis of potassium orgaonotrifluoroborates is very efficient for a broad range of organotrifluoroborates. For all organotrifluoroborates investigated, iron(III) chloride-promoted hydrolysis was more effective than previously reported methods. A detailed mechanistic study has not been carried out, but it is thought that the iron(III) cation promotes the hydrolysis of organotrifluoroborates because the resulting iron(III) fluoride has a large lattice enthalpy (5,870 Kj/mol) and low solubility in the THF/water solution used.[94] These are the same factors thought

to govern the lithium hydroxide and alumina mediated hydrolyses of organotrifluoroborates.

Scheme 5.2 $FeCl_3$ Promoted Hydrolysis of Organotrifluoroborates.



Product		Time (min)	Yield (%)	Product		Time (min)	Yield (%)
29		60	98	37		30	92
30		60	97	38		25,30	70,65
31		60	94	39		30	87
32		7 hrs Reflux	98	40		30	85
33		30	91	41		30	98
34		30	81	42		25,30	86,72
35		30	86	43		60	80
36		30	94	73		30	97
		Protonolysis		74		30	96
		No hydrolysis				Protonolysis	
		Protonolysis				Protonolysis	
		Protonolysis				Protonolysis	

5.3 Other Investigations

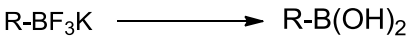
Zinc proved to be effective in hydrolyzing organotrifluoroborates. Stirring zinc powder (or zinc oxide) in water with a potassium organotrifluoroborate salt generates the corresponding organoboronic acid in a few hours. In the first trial, (0.5 mmol) of potassium 1-napthyltrifluoroborate was used with 4 equivalents of zinc powder in 2 mL of water. The reaction was stirred at room temperature for two hours. The solution was then filtered, extracted into ethyl acetate, and the organic layer dried over anhydrous magnesium sulfate. The solvent was removed to give a 70% yield of 1-napthylboronic acid (Trial 1). Conversion was confirmed by ^{11}B NMR. In an effort to evaluate the scope of the zinc-promoted hydrolysis, additional trials were conducted using zinc metal and two trials were carried out using zinc oxide. In the second trial with zinc metal, 2,6-dimethoxyphenyltrifluoroborate (0.5 mmol) was hydrolyzed using 3 equivalents of zinc powder in 2 mL of water at room temperature. The reaction was allowed to proceed for two hours and then filtered. The product was extracted into diethyl ether and dried over anhydrous magnesium sulfate. After solvent removal, a 74% yield of 2,6-dimethoxyphenylboronic acid was obtained (Trial 2). Next, two trials were conducted using both zinc dust and zinc oxide and potassium 2-napthyltrifluoroborate in 3 mL of a one-to-one THF/water solution. After 2 hours, the products of each reaction were extracted into diethyl ether. After drying the organic layer over anhydrous sodium sulfate and solvent removal, yields of 66% and 68% respectively of 2-napthylboronic acid were obtained (Trial 3). Allowing 3 hours for the hydrolysis of potassium 2-napthyltrifluoroborate increased the yields of both the zinc-promoted hydrolysis and the zinc oxide-promoted hydrolysis to 94% and 98% respectively. In the next hydrolysis trial using zinc powder, 1 mmol of potassium 2,2-dimethylpropyl-1-trifluoroborate, 3 mL of one-to-one THF/water, and 3 equivalents of zinc powder were used. The reaction was monitored by ^{11}B NMR and was complete at 2.5 hours (nearly complete conversion was observed at 1.75 hours (Figure 5.1, page 85) with no protonolysis of the carbon-boron bond. Filtration through a small amount of silica

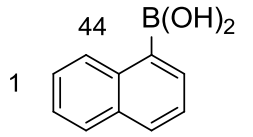
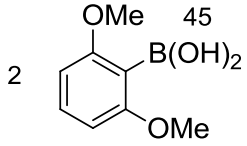
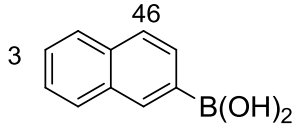
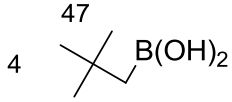
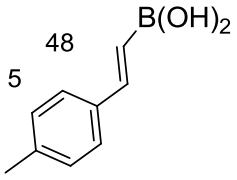
using a one-to-one hexanes ethyl acetate mixture yielded the boronic acid in 95% yield (Trial 4). In Trial 5, 1 mmol of potassium (*E*)-(4-methylstyryl)trifluoroborate, 3 equivalents of zinc powder, and 3 mL of one-to-one THF/water were used. After stirring at room temperature for 1.75 hours, ^{11}B NMR showed essentially complete conversion to the organoboronic acid with some boric acid formation due to protonolysis of the carbon-boron bond (Figure 5.2, page 86). Filtration through silica followed by solvent removal yielded 75% of (*E*)-(4-methylstyryl)boronic acid. Next, potassium 3-acetylphenyltrifluoroborate was hydrolyzed using 3 equivalents of zinc powder and 3 mL of THF/water. The reaction was monitored by ^{11}B NMR and was determined to be about 25% complete at 1 hour and 80% complete in 4 hours; after reaction for 5.5 hours filtration through silica gel and solvent removal yielded 3-acetylphenylboronic acid in 77% yield (Trial 6), (Figures 5.3 and 5.4, pages 86 and 87). In the seventh trial with zinc powder, 1 mmol of potassium (4-(benzyloxy)phenyl)trifluoroborate, 3 mL THF/water, and 3 equivalents of zinc powder were used. ^{11}B NMR data obtained at two hours of reaction time showed approximately 50% conversion to the organoboronic acid. The reaction was filtered through silica at 4 hours. After solvent removal, a 93% yield of (4-(benzyloxy)phenyl)boronic acid was obtained. Complete conversion was confirmed by ^{11}B NMR (Figure 5.5, page 87).

In an effort to determine if zinc hydrolysis was applicable to substrates that underwent protonolysis using iron(III) chloride, potassium benzyltrifluoroborate and potassium (4-bromothiazol-2-yl)trifluoroborate were used in hydrolysis trials with 3 equivalents of zinc powder. No hydrolysis to the corresponding boronic acids occurred with these substrates. ^{11}B NMR showed only boric acid (Trials 8 and 9), (Figures 5.6 and 5.7, pages 88 and 89). Next, a trial using 1 mmol of potassium 3-nitrophenyltrifluoroborate, 3 equivalents of zinc powder, and THF/water was carried out. ^{11}B NMR of an aliquot of the reaction mixture at 2 hours revealed that no boronic acid or boric acid had formed. In an attempt to promote the hydrolysis, the reaction was heated at 47 $^{\circ}$C for 8.5 hours at this time

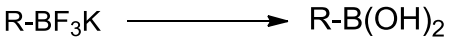
a ^{11}B NMR showed approximately 50% conversion into an approximately equal mixture of the organoboronic acid and boric acid (Figure 5.8, page 89). Attempts to isolate the 3-nitrophenylboronic acid, after 12 hours of reaction time, resulted in only a trace of the organoboronic acid and a mixture of degradation products (Trial 10), Scheme 5.3.

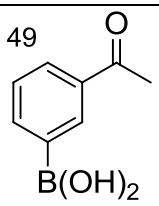
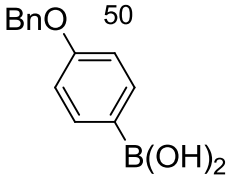
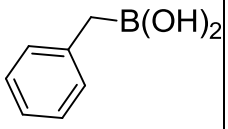
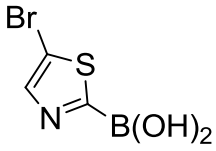
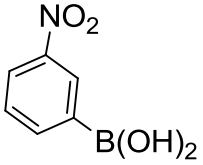
Scheme 5.3 Zinc-Promoted Hydrolysis of Organotrifluoroborates.



Trial	Product	Solvent	Zinc Type	Time(hr)	Yield(%)
1	 44	H_2O	Zn^0	2	70
2	 45	H_2O	Zn^0	2	74
3	 46	THF/ H_2O	ZnO Zn^0	2, 3 2, 3	68, 98 66, 94
4	 47	H_2O	Zn^0	2.5	95
5	 48	THF/ H_2O	Zn^0	2	75

Scheme 5.3 (Continued)

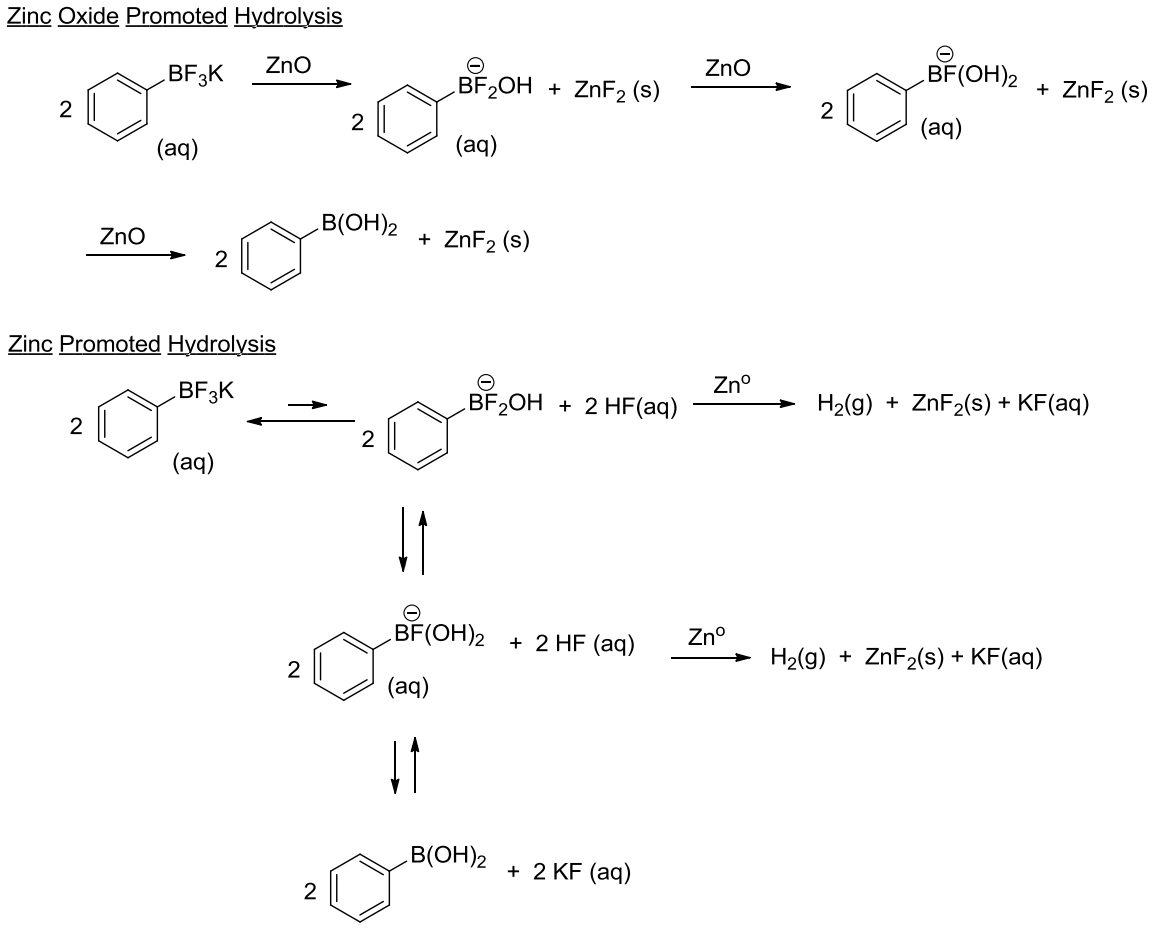


Trial	Product	Solvent	Zinc Type	Time(hr)	Yield(%)
6	49 	THF/ H_2O	Zn^0	5.5	77
7		THF/ H_2O	Zn^0	4	93
8		THF/ H_2O	Zn^0	Protonolysis	
9		THF/ H_2O	Zn^0	Protonolysis	
10		THF/ H_2O	Zn^0	Protonolysis	

A hypothesis to explain the results observed in the zinc metal-promoted hydrolysis of organotrifluoroborates is that hydrogen fluoride is generated during the hydrolysis and reacts with the zinc metal to produce hydrogen gas and zinc fluoride. Zinc fluoride solubility in water is 1.55g/100 mL but, in a one-to-one THF/water solution, is presumably lower. Potassium organotrifluoroborates in water produce an acidic solution with a pH of around 5, due to a process in which hydrogen fluoride is in equilibrium with a hydroxyorganodifluoroborane

intermediate.[58] A hypothesis to explain the results observed in the zinc oxide promoted hydrolysis of organotrifluoroborates is that hydrogen fluoride forms in solution and reacts with a very small concentration of zinc oxide in solution or at the solid zinc oxide surface to form zinc fluoride, Scheme 5.4.

Scheme 5.4 Proposed Pathways for the Zinc Metal and Zinc Oxide Promoted Hydrolysis of Potassium Organotrifluoroborates.



In an attempt to hydrolyze substrates that underwent protonolysis using iron(III) chloride and zinc powder, sodium sulfide (in a one-to-one THF/water mixture) was investigated. Potassium 2,2-methylpropyl-1-trifluoroborate was found to undergo complete hydrolysis in 4.5 hours, as determined by ^{11}B NMR, in the presence of 1.2 equivalents of sodium sulfide nonahydrate. Extraction into

ethyl acetate/ drying over anhydrous sodium sulfate, and solvent removal gave a 74% yield of 2,2-methylpropyl-1-boronic acid. Potassium benzyltrifluoroborate and potassium (1-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)trifluoroborate underwent complete protonolysis and partial protonolysis, with no boronic acid formed, at 2 hours respectively. Potassium 3-nitrophenyltrifluoroborate was unchanged after two hours under these reaction conditons.

5.4 Conclusions

Iron(III) chloride was found to efficiently promote the hydrolysis of a range of organotrifluoroborates in a more efficient manner than previously reported methods. Simply placing the reaction solution onto 8 cc of neutral alumina and eluting using a two-to-one ethyl acetate/hexanes mixture gives the pure organoboronic acid product in excellent yield in most cases.

In a related investigation, zinc powder and zinc oxide were both found to efficiently promote hydrolysis of organotrifluoroborates. Good yields of organoboronic acids were observed in most cases. It is believed that the hydrolysis forms hydrogen fluoride; in the case of zinc dust, hydrogen fluoride is thought to react with zinc metal to produce zinc fluoride, a salt with very low solubility in a one-to-one THF/water solution. In the case of zinc oxide, reaction of hydrogen fluoride with zinc oxide also produces zinc fluoride. Sodium sulfide may also be an effective reagent to promote organotrifluoroborate hydrolysis.

The work presented in this chapter was carried out by the author, and the majority of this work has been published or has been accepted for publication in the following journals:

Blevins, D. W.; Yao, M. L.; Yong, L.; Kabalka, G. W. Iron Trichloride Promoted Hydrolysis of Potassium Organotrifluoroborates. *Tet. Lett.* **2011**, *52,* 6534.

Accepted for publication:

Blevins, David W.; Yao, Min-Liang; Yong, Li; Kabalka, George W. Hydrolysis of

potassium organotrifluoroborates using iron trichloride or zinc dust. *ARKIVOC* **2012**.

5.5 Experimental

Reagents were used as received. Filtration was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany) or neutral absorption alumina from Fischer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at (250.13, 300) and (62.89 and 75) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. ^{11}B NMR spectra were recorded at 128.39 MHz.

5.6 Typical Procedures

Representative procedure for the iron(III) chloride promoted hydrolysis of potassium organotrifluoroborates: potassium phenyltrifluoroborate (184 mg, 1.00 mmol) was added to a solution of iron trichloride (185 mg, 1.10 mmol) in 3 mL of 1:1 THF/water. The mixture was stirred at room temperature for 30 min. The reaction mixture was then placed directly into a small glass column containing 8 cc of neutral absorption alumina. The alumina was then washed with a mixture of ethyl acetate/hexanes (2:1) to obtain pure phenylboronic acid (Product 35) (105 mg, 86%). The boronic acid products may also be isolated by extraction techniques.

Representative procedure for the zinc-promoted hydrolysis of potassium organotrifluoroborates: potassium 2,2-dimethylpropyl-3-trifluoroborate 178 mg (1.00 mmol) was placed in a 10 mL round bottomed flask along with 3 equiv. (196 mg) of zinc dust. A THF/H_2O solution was added (3 mL, 1:1 vol.). A small stir bar was added and a rubber septum was used to stopper the flask. The reaction was stirred for 2.5 hours, at which time ^{11}B NMR indicated complete conversion. The reaction mixture was placed directly into a small glass column containing 15 cc of silica gel. The silica was washed with a 1:1 ethyl acetate/hexanes mixture to yield, after solvent removal, 110 mg (95% yield) of a

white waxy solid 2,2-dimethylpropylboronic acid. Note: extraction may also be used to obtain the product.

5.7 Characterization of Compounds

(NMR Spectra are in Appendix)

***o*-Nitrotolyl-*p*-boronic acid** (29). ^{1}H NMR (300 MHz, $CDCl_3$, Acetone D_6): δ 8.03-8.51 (d, J=7.5 Hz, 1H), 7.52 (s,1H), 7.46-7.49 (d, J=7.5 Hz), 2.57 (s, 3H). ^{11}B NMR (128 MHz, $CDCl_3$, Acetone D_6): 28.24 ppm (s).

***p*-Formylphenylboronic acid** (30).[70] ^{1}H NMR (300 MHz, DMSO D_6): δ 10.36 (s, 1H), 8.34-8.37 (d, J=7.5 Hz, 2H), 8.05-8.09 (d, J=7.5 Hz, 2H), 4.91 (s, 3H). ^{11}B NMR (128 MHz, DMSO D_6): 30.25 ppm (s).

2,6-Difluorophenylboronic acid (31).[96] ^{1}H NMR (300 MHz, $CDCl_3$, Acetone D_6): δ 7.76 (s, 2H), 7.36-7.77 (m, 1H), 6.88-6.94 (m, 2H). ^{11}B NMR (128 MHz, Acetone D_6): 27.9 ppm (s).

2,5-Ditrifluoromethylphenylboronic acid (32). ^{11}B NMR (128 MHz, THF/H_2O, D_2O): δ 29.63 (S).

***o*-Bromophenylboronic acid** (33).[96] ^{1}H NMR (300 MHz, DMSO D_6): δ 8.25 (b,1.63H), 7.51-7.53 (d, J=7.8 Hz, 1H), 7.23-7.35 (m, J=7.2 Hz, 8.7 Hz, 3H). ^{11}B NMR (128 MHz, DMSO D_6): 29.9 ppm (s).

***p*-Methoxyphenylboronic acid** (34).[70] ^{1}H NMR (300 MHz, $DMSO_6$): δ 7.66-7.69 (d, J=9 Hz, 2H), 6.85-6.87 (d, 9 Hz), 3.70 (s, 3H). ^{11}B NMR (128 MHz, DMSO D_6): 29.9 ppm (s).

Phenylboronic acid (35).[70] ^{1}H NMR (300 MHz, DMSO D_6): δ 7.86-7.93 (d, J=3 Hz, 2H), 7.33-7.41 (m, J=3.6 Hz, 3H). ^{11}B NMR (128 MHz, DMSO D_6): 30.1 ppm (s).

2-Naphthylboronic acid (36).[70] ^{1}H NMR (300 MHz, $CDCl_3$, DMSO D_6, Acetone D_6): δ 8.43 (s, 1H), 7.78-7.98 (m, J=8 Hz, 6H), 7.45-7.53 (m, J=5.4 Hz, 1H). ^{11}B NMR (128 MHz, DMSO D_6, Acetone D_6): 28.0 ppm (s).

***o*-Tolylboronic acid** (37).[70] ^{1}H NMR (300 MHz, $DMSO_6$): δ 7.52-7.57 (d, J=9 Hz, 1H), 7.31-7.38 (t, J=9 Hz, 1H), 7.20-7.26 (m, J=9 Hz). ^{11}B NMR (128 MHz, $DMSO_6$): δ 30.13 (s).

2,6-Dimethylphenylboronic acid (38).[70] ^{1}H NMR (300 MHz, Acetone D_6): δ 7.22 (s, 2H), 7.00-7.26 (t, J=6.9 Hz, 1H), 6.86-6.90 (d, J=6.9 Hz, 2H), 2.23 (s, 6H). ^{11}B NMR (128 MHz, Acetone D_6): δ 30.17 (s).

(*E*)-1-Heptene-1-boronic acid (39).[97] ^{1}H NMR (300 MHz, Acetone D_6): δ 6.65 (s, 2H), 6.50-6.62 (dt, J= 18 Hz, J=6 Hz, 1H)), 5.37-5.47 (d, J=18 Hz, 1H), 2.10-2.26 (m, J=9 Hz, 2H), 1.37-1.51 (m, J=6 Hz, 2H), 1.31-1.51 (m, J=6 Hz, 2H), 1.31 (m, 5H), 0.88 (m, J=6 Hz, 3H). ^{11}B NMR (128 MHz, Acetone D_6): δ 30.06 (s).

(*E*)-1-Chloro-1-phenylethenyl-1-boronic acid (40). ^{1}H NMR (300 MHz, DMSO D_6): δ 7.72-7.59 (s, 2H), 7.31-7.47 (s, 3H), 6.30-6.38 (s, 1H). ^{11}B NMR (128 MHz, DMSO D_6): δ 29.34 (s).

1-Phenylpropyl-3-boronic acid (41). ^{1}H NMR (300 MHz, Acetone D_6): δ 7.11-7.29 (m,J=9 Hz, 4H), 6.75 (s, 2H), 2.56-2.65 (t, J=9 Hz, 2H), 1.69-1.81 (p, J=9 Hz, 2H), 0.76-0.84 (t, J=9 Hz, 2H). ^{11}B NMR (128 MHz, Acetone D_6): δ 31.30 (s).

2,2-Dimethylpropyl-1-boronic acid (42). ^{1}H NMR (300 MHz, DMSO D_6): δ 0.90-0.96 (s, 9H), 0.60-0.64 (s, 2H). ^{11}B NMR (128 MHz, DMSO D_6): δ 30.99 (s).

(2,4-Dimethoxypyrimidin-5-yl)boronic acid (43).[70] ^{1}H NMR (300 MHz, DMSO D_6): δ 8.41 (s, 1H), 7.84 (s, 2H), 3.89 (s, 6H). ^{11}B NMR (128 MHz, DMSO D_6): δ 27.92 (s).

(*E*)-(4-Methylstyryl)boronic acid (48).[98] ^{1}H NMR (300 MHz, $CDCl_3$, DMSO D_6): δ 7.35-7.40 (d, J=8 Hz, 2H), 7.23-7.31 (d, J=18.6 Hz, 2H), 7.11-7.17 (d, J=8.1 Hz, 2H), 6.06-6.14 (d, J=18.3 Hz, 1H), 2.30-2.33 (s, 3H). ^{11}B NMR (128 MHz, THF/H_2O/D_2O): δ 28.41 (s).

3-Acetylphenylboronic acid (49, 74). ^{1}H NMR (300 MHz, DMSO D_6): δ 8.30-8.37 (s, 1H), 7.91-8.00 (t, J=7.2 Hz, 2H), 7.43-7.52 (t, J=7.5 Hz, 1H), 4.03-4.06 (s, 2H), 2.25-2.57 (s, 3H). ^{11}B NMR (128 MHz, DMSO D_6): δ 27.51 (s).

(4-(Benzyloxy)phenyl)boronic acid (50).[99] ^{1}H NMR (300 MHz, DMSO D_6): δ 7.73-7.77 (d, J=8.4 Hz, 2H), 7.27-7.46 (m, J=7Hz, 7.93H), 6.91-6.95 (d, J=8.4 Hz, 2H), 5.07-5.09 (s, 2H). ^{11}B NMR (128 MHz, DMSO D_6): δ 29.28 (s).

(3-(*tert*-Butoxy)-3-oxopropyl)boronic acid (73). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.260-2.38 (t, J=7.5 Hz, 2H), 1.32-1.43 (s, 9H), 0.857-0.99 (t, J=7.5 Hz, 2H) ^{11}B NMR (128 MHz, $CDCl_3$): δ 31.0 (s).

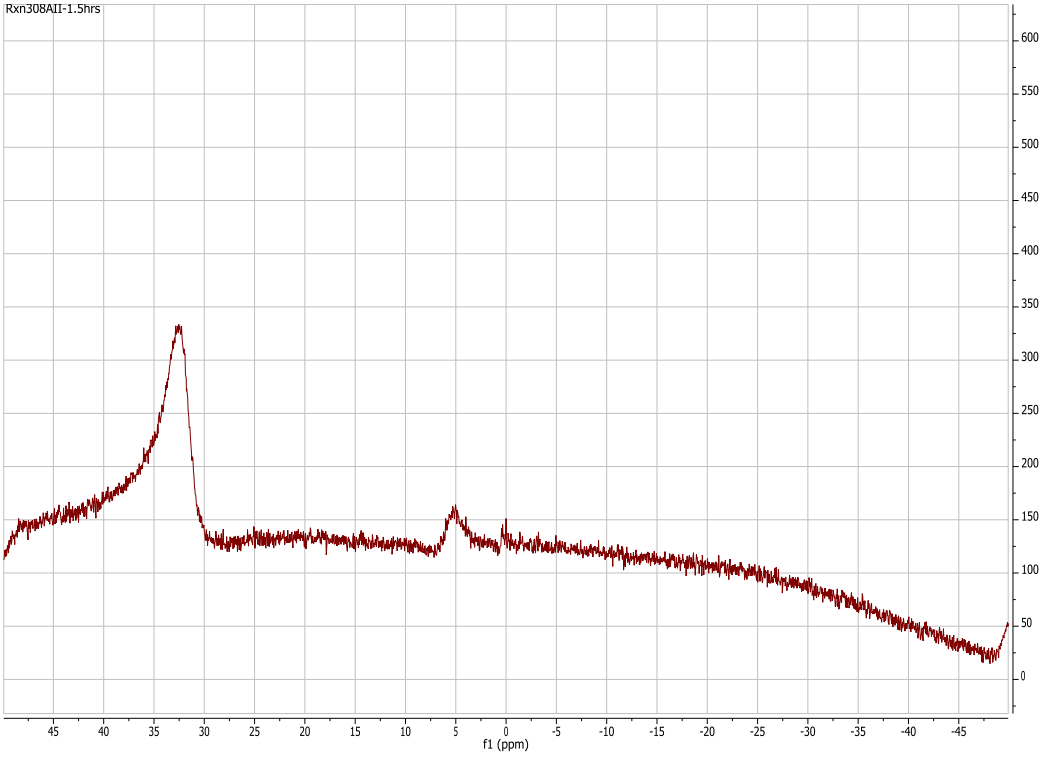


Figure 5.1 ^{11}B NMR of the Progress of the Hydrolysis of 2,2-Dimethylpropyl-1-trifluoroborate at 1.5 Hours as Determined by ^{11}B NMR. The organotrifluoroborate is almost completely hydrolyzed to the oranoboronic acid.

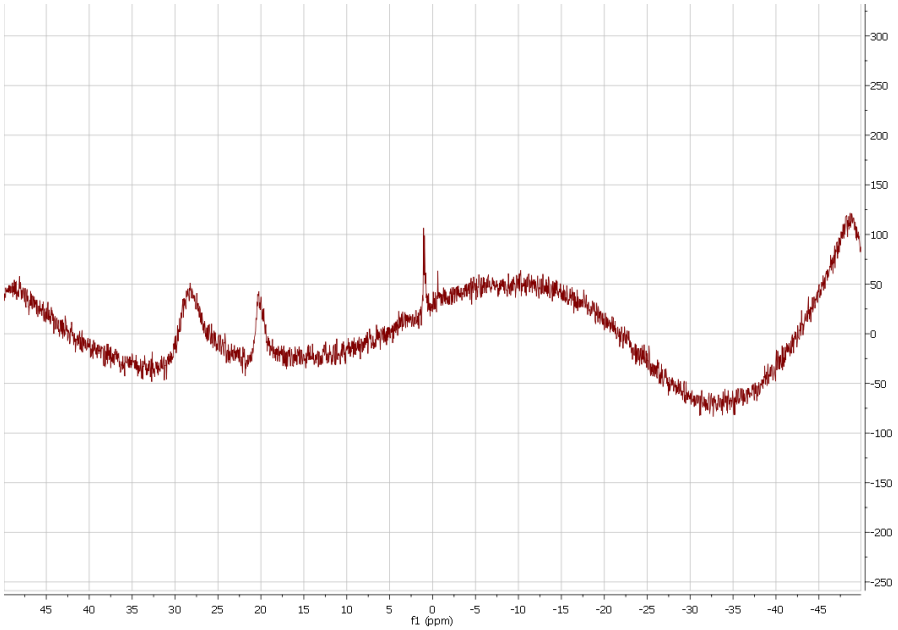


Figure 5.2 ^{11}B NMR of the Zinc-Promoted Hydrolysis of Potassium (*E*)-(4-Methylstyryl)trifluoroborate at 1.75 Hours.

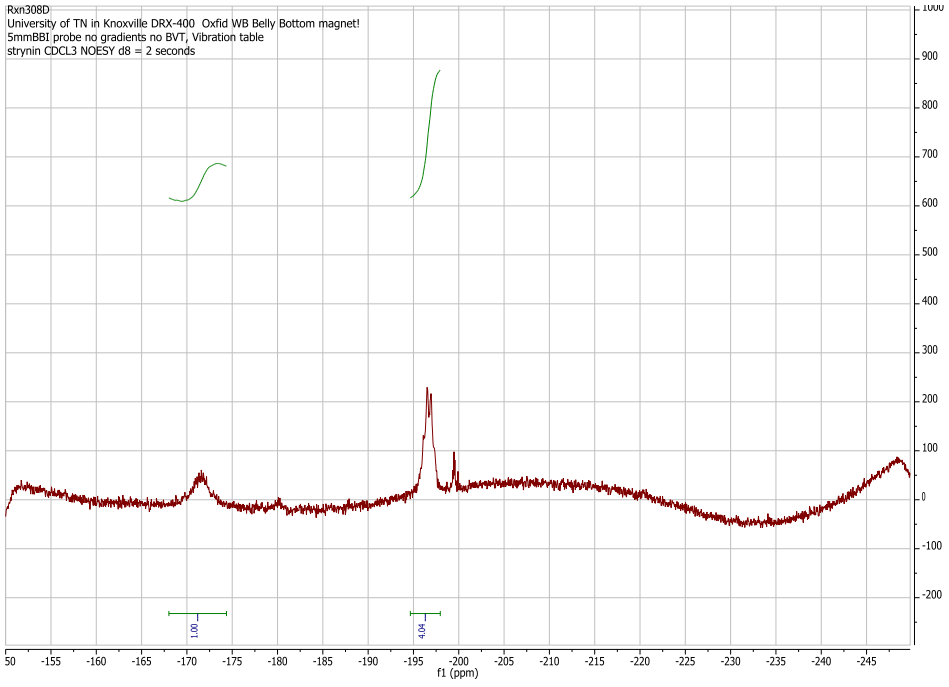


Figure 5.3 ^{11}B NMR of the Zinc-promoted Hydrolysis of Potassium 3-Acetylphenyltrifluoroborate at 1 Hour. Organoboronic acid at -172 ppm is actually at 30 ppm relative to boric acid and the organotrifluoroborate peak at -197 ppm is at 3.5 ppm relative to boric acid.

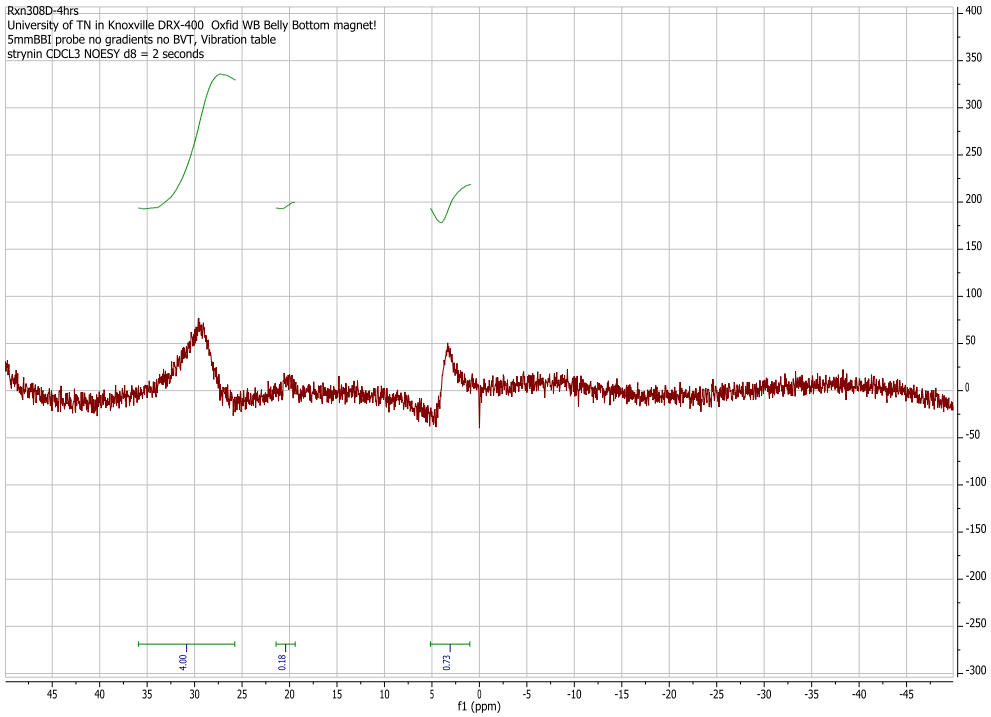


Figure 5.4 ^{11}B NMR of the Zinc Hydrolysis of Potassium 3-Acetylphenyltrifluoroborate at 4 Hours.

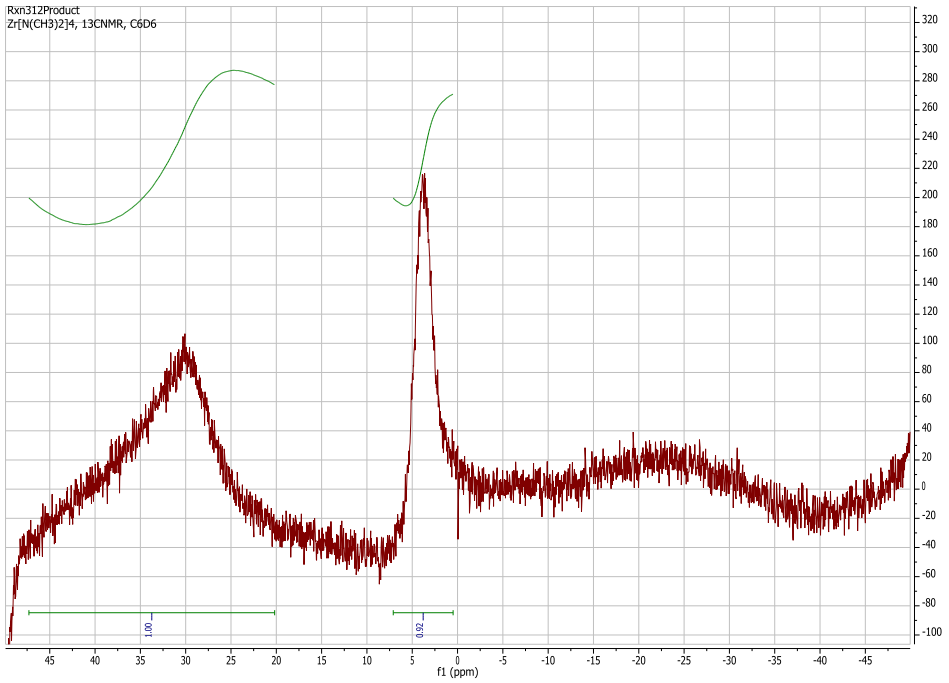


Figure 5.5 ^{11}B NMR of the Zinc-Promoted Hydrolysis of Potassium (4-(Benzyloxy)phenyl)trifluoroborate at 2 Hours.

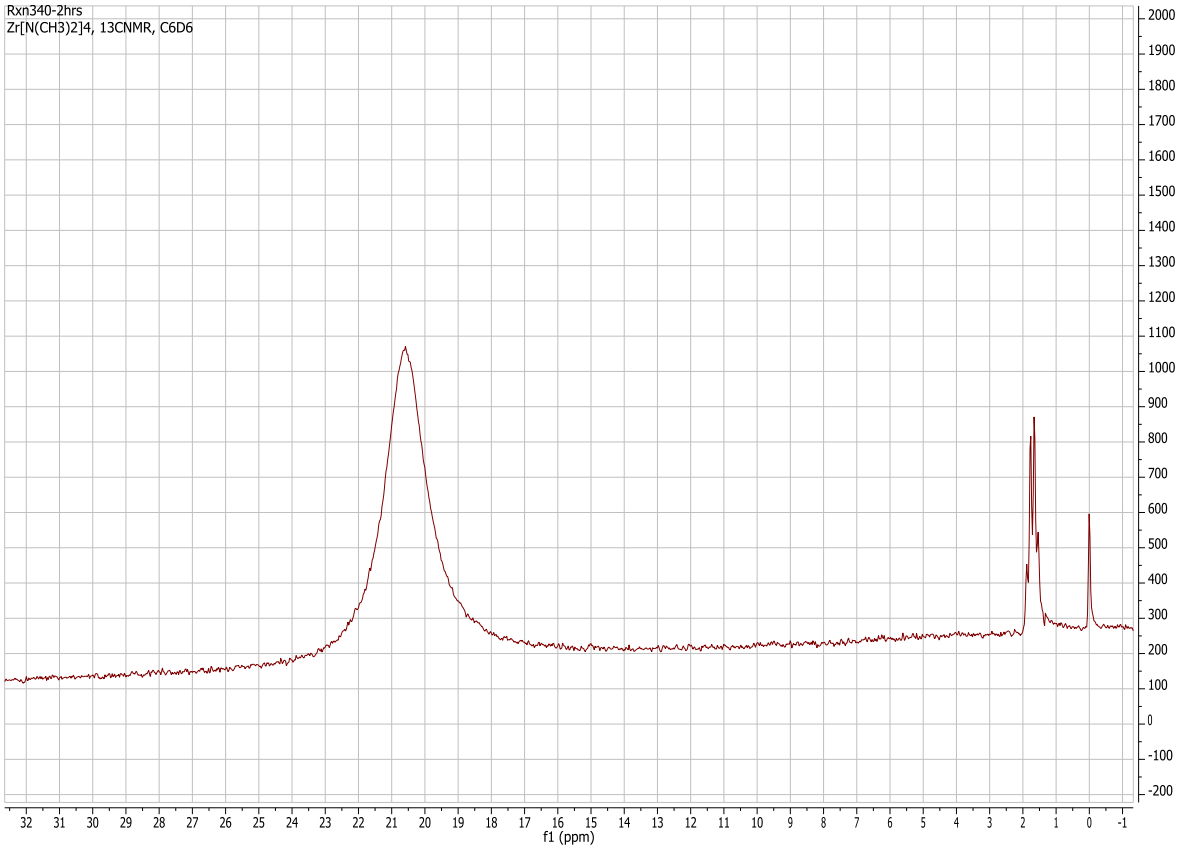


Figure 5.6 ^{11}B NMR of the Zinc-Promoted Hydrolysis of Potassium Benzyltrifluoroborate at 2 Hours.

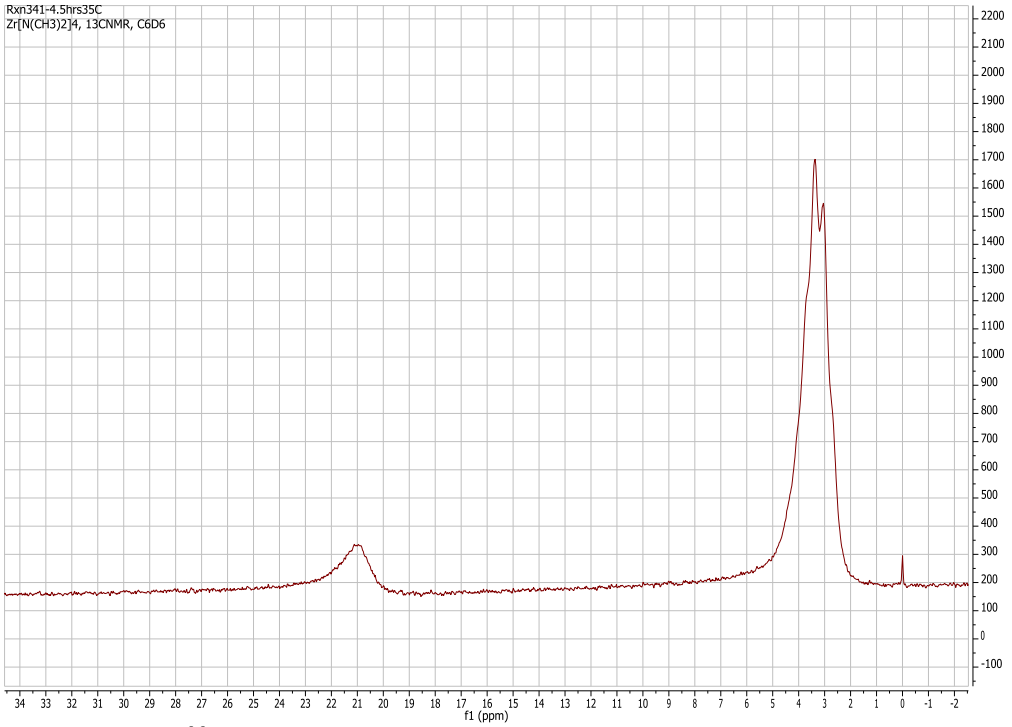


Figure 5.7 ^{11}B NMR of the Zinc-Promoted Hydrolysis of Potassium (4-Bromothiazol-2-yl)trifluoroborate at 4 Hours.

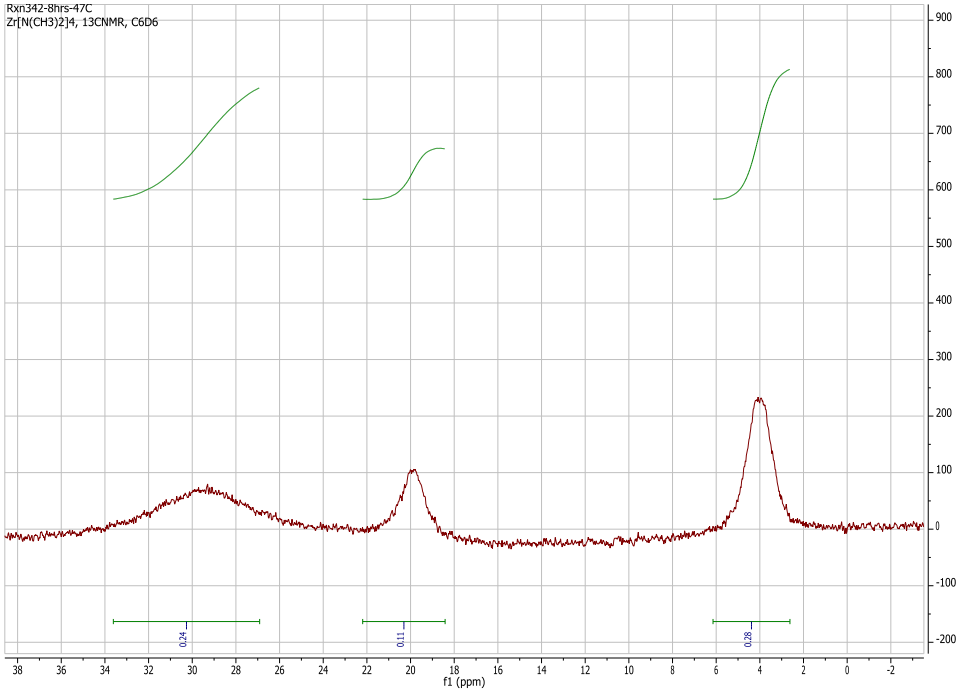


Figure 5.8 ^{11}B NMR of the Zinc-Promoted Hydrolysis of Potassium *m*-Nitrophenyltrifluoroborate.

CHAPTER 6
IODODEBORONATION OF POTASSIUM ARYL- AND ALKENYLTRIFLUOROBORATES WITH IRON(III) CHLORIDE AND SODIUM IODIDE

6.1 Introduction

Iron(III) chloride and sodium iodide can be used as an iodine source in iododeboronation reactions of potassium aryl- and alkenyltrifluoroborates. The reactions produce good yields of iodides in most cases. The reaction was recently applied to a radiiodination of Iodine-123-labeled Baclofen and Refecoxib.

6.2 Results and Discussion

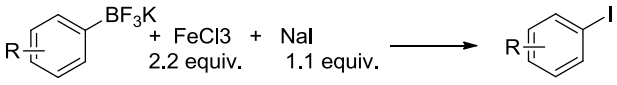
Iron(III) chloride rapidly oxidizes iodide ion in a one-to-one THF/water solution to produce iodine, diiodine chloride, and iodine chloride. In the initial investigation of iododeboronation reactions using iron(III) chloride and sodium iodide, potassium phenyltrifluoroborate, potassium biphenyl-4-trifluoroborate, and potassium 2-napthyltrifluoroborate were the substrates used. In Trial 1 (Scheme 6.1), the solvent dichloromethane (DCM), 2.2 equivalents of oven dried iron(III) chloride, and 1.1 equivalents of oven dried sodium iodide were used. The reaction was conducted at room temperature for 19 hours under an argon atmosphere. No iododeboronation occurred (Trial 1). In Trial 2, THF was substituted for DCM. The reaction was allowed to proceed for 16 hours, and no product was formed (Trial 2). DMF and room temperature were used in the next trial. The reaction was allowed to stir for 16 hours and none of the desired product was produced (Trial 3). It was thought that tetrabutylammonium 4-biphenyltrifluoroborate might be more reactive than potassium phenyltrifluoroborate under the anhydrous conditions used, since it is more soluble in organic solvents. A reaction in THF at room temperature for 16 hours produced no iododeboronaton product (Trial 4). In the next trial, the temperature

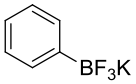
was raised to 45 °C and after a 6.5 hour reaction time the reaction was filtered through silica and a 12.6% yield of 4-iodobiphenyl was obtained (Trial 5). In the next trial with this substrate, the temperature was increased to 60 ºC, and the solvent was changed to dry acetonitrile at 5.5 hours the reaction was filtered through silica to obtain a 35% yield of 4-iodobiphenyl (Trial 6). Then, potassium 4-biphenyltrifluoroborate was allowed to react in dry acetonitrile at 80 °C and, at 19 hrs, the reaction was complete. Filtration through silica produced a 90% yield of 4-iodobiphenyl (Trial 7).

To determine if boronic esters would also undergo iododeboronation using iron(III) chloride/sodium iodide, two trials were carried out using 2-napthylpinacolboronic ester. First, 2-napthylpinacolboronic was reacted in a one-to-one THF/water solution at room temperature for 19 hours. No reaction occurred (Trial 8). Next, the temperature was increased to 120 °C; no product could be detected by TLC after 3 hours.

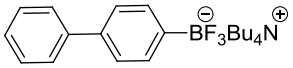
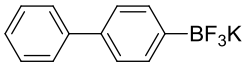
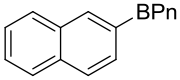
Based on these results, the conditions chosen for the iododeboronation of potassium organotrifluoroborates using iron(III) chloride/sodium iodide are 1 equivalent of potassium organotrifluoroborate, 2.2 equivalents of oven dried iron(III) chloride, 1.1 equivalents of oven dried sodium iodide, 12 mL of dry acetonitrile per mmol of organotrifluoroborate, an argon atmosphere, and 19 hrs at 80 °C, Scheme 6.1.

Scheme 6.1 Optimization of Iododeboronation of Organotrifluoroborates.



Trial	Substrate	Solvent	Temperature (°C)	Time (Hours)	Yield (%)
1		DCM	rt	19	No Reaction
2		THF	rt	16	No Reaction
3		DMF	rt	16	Trace of Product

Scheme 6.1 (Continued)

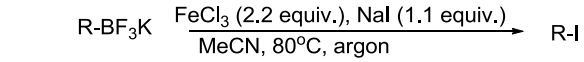
Trial	Substrate	Solvent	Temperature (°C)	Time (Hours)	Yield (%)
4		THF	rt	16	No Reaction
5		THF	45	6.5	12
6		MeCN	60	5.5	35
7		MeCN	80	19	90
8		THF/H_2O	rt	19	No Reaction
9		THF/H_2O	120	1.5	No Reaction

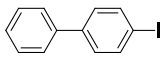
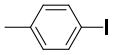
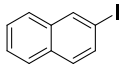
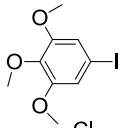
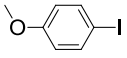
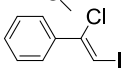
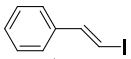
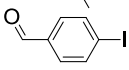
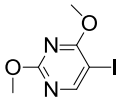
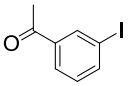
Pn= Pinacol

The iododeboronation of a variety of aryl- and alkenyltrifluoroborates was carried out using iron(III) chloride/sodium iodide. Since iron(III) chloride rapidly hydrolyzes organotrifluoroborates in the presence of water anhydrous conditions were used. Unsubstituted aryltrifluoroborates produced good yields of the corresponding aryl iodides. Potassium 4-biphenyltrifluoroborate and potassium 2-napthyltrifluoroborate yielded 90% and 72% of the corresponding aryl iodides, respectively (Products 51 and 52). Aryltrifluoroborates with alkyl substituents produced good to moderate yields of aryl iodides. Potassium 2,6-dimethylphenyltrifluoroborate, potassium *o*-tolyltrifluoroborate, and potassium *p*-tolyltrifluoroborate produce 76%, 87%, and 55% yields of aryl iodides respectively (Products 54, 58, and 59). Aryltrifluoroborates with electron donating methoxy groups also produced good to moderate yields of aryl iodides. *p*-Methoxyphenyltrifluoroborate and 3,4,5-trimethoxyphenyltrifluoroborate generated 85% and 75% of the corresponding aryl iodides respectively. Potassium 3,4,5-trimethoxyphenyltrifluoroborate produced the highest yield (75%) at 70 ºC. At 80 ºC, a mixture of products was isolated, but no diiodination was observed (Figure 6.1) (Products 53 and 60). Potassium aryltrifluoroborates with electron withdrawing substituents generally required longer reaction times and produced lower yields of corresponding aryl iodides. Potassium *p*-acetylphenyltrifluoroborate, potassium *p*-formylphenyltrifluoroborate, and

potassium 2,6-difluorophenyltrifluoroborate produced 72% (25 hours), 41% (20 hours), and 68% yields respectively of aryl iodides (Products 55, 56, and 57). As observed in bromodeboronation with pyridinium tribromide, an aryltrifluoroborate with a bromine substituent reacts well in halodeboronation reactions. Potassium *o*-bromophenyltrifluoroborate produced an 80% yield of 1-iodo-2-bromobenzene (Product 64). A heteroaryl substrate with two methoxy substituents did not react well under the conditions used. Potassium 2,4-dimethoxypyrimidine-5-trifluoroborate produced a 29% yield of 5-iodo-2,4-dimethoxypyrimidine; reaction of this substrate at 80 ºC produced a 13% yield of the aryl iodide (Product 63). Potassium alkenyltrifluoroborates were found to undergo iododeboronation with retention of stereochemistry. Potassium (*E*)-1-phenylvinyl-2-trifluoroborate and potassium (Z)-1-chloro-1-phenylvinyl-2-trifouoroborate underwent iododeboronation to yield 62% and 47% yields of the corresponding aryl idodies respectively (Products 62 and 61), Scheme 6.2.

Scheme 6.2 Iododeboronation Using Iron(III) Chloride/NaI.



Product		Time (Hrs)	Yield (%)	Product		Time (Hrs.)	Yield (%)
51		19	90	59		19	55
52		19	72	60		19 (70°C)	75
53		19	85				
				61		20,24	47,42
54		19	76				
				62		19	62
55		20	41				
				63		19,10 (70°C)	13,29,
56		25	72				
				64		19	80
57		19	68				
58		19	87				

6.3 Conclusions

A method was developed to carry out iododeboronations of potassium organotrifluoroborates. The method was evaluated employing a range of potassium organotrifluoroborates. Aryltrifluoroborates with electron donating substituents and unsubstituted aryltrifluoroborates were found to provide the best yields of the iodinated products.

The work presented in this chapter was carried out by the author. The majority of this work was presented at the Boron Americas XIII conference in a presentation titled "Iododemetallation of Organotrifluoroborate and Organotin Reagents Using a $FeCl_3$-NaI System."

6.4 Experimental

Reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE). ^{1}H NMR and ^{13}C NMR spectra were recorded at (250 or 300) and (62.89 or 75) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. Gas Chromatography/Mass Spectroscopy studies were carried out using a Hewlett Packard: HP 6890 series GC System with 5973 Mass Selective Detector; Column: Agilent 19091S-433E, 30.0mm X 0.25mm X 0.25 μm; Gas (He) flow rate: 0.8 mL/min; Initial temperature: 90 ˚C; Ramp temperature rate: 10 ˚C/min to maximum 240 ˚C. Melting points were obtained by using a Mel-Temp melting point apparatus with a mercury thermometer.

6.5 Typical Procedure

Iododeboronation using the $FeCl_3$/NaI procedure: Iron(III) chloride (2.2 equivalents) is placed in a 25 mL round bottomed flask with a stir bar. The flask is placed in an oven for 3 hours at 140 ˚C. Sodium iodide (1.1 equivalents) is placed in another small round bottomed flask and put into an oven for 3 hours at

140 °C. After 3 hours, the round bottomed flasks containing the above reagents are removed from the oven, covered with septa, and flushed with dry argon until cool. A potassium organotrifluoroborate (1.0 equiv.) is then quickly added the to the round bottomed flask containing the iron(III) chloride, and the sodium iodide is then quickly added. The round bottomed flask is then attached to a reflux condenser, the system flushed with argon, and an argon balloon is then attached. Dry acetonitrile (12 mL/mmol) is added via a cannula, and the reaction heated in a sand bath at 80 °C for 19 hours. The reaction is then allowed to cool, removed from the condenser, and any remaining halogen is neutralized by adding small amount of potassium bisulfite and about 1 mL of water. Purification is accomplished by placing the reaction solution directly into a silica gel column and eluting with an appropriate solvent. Removal of solvent from the eluent under vacuum yields the pure product.

6.6 Characterization of Compounds

(NMR Spectra are in Appendix)

2-Iodonapthalene (52).[81] ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.24-8.28 (s, 1H), 7.68-7.85 (m, J=3.75 Hz, 4H), 7.45-7.57 (m, J=4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.6, 135.0, 134.3, 132.1, 129.5, 127.8, 126.8, 126.7, 126.4, 91.6.

2-Iodo-1,3-dimethylbenzene (54).[72] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06-7.12 (t, J=7.5 Hz, 1H), 6.98-7.04 (d, J=7.2 Hz, 2H), 2.45 (s, 6H). ^{13}C NMR (75 MHz,$CDCl_3$): δ 142.1, 127.7, 127.0, 108.6, 29.9.

***p*-Iodobenzaldehyde** (55).[83] ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.94 (s, 1H), 7.87-7.93 (d, J=6 Hz, 1H), 7.55-7.61 (d, J=6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.5, 138.5, 135.6, 130.9, 103.0.

1-(3-Iodophenyl)ethanone (56).[101] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.74-7.90 (t, J=6.5 Hz, 2H), 7.06-7.18 (t, J=6.5 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.6, 141.9, 138.8, 137.3, 130.4, 127.5, 94.5, 26.6.

1,3-Difluoro-2-iodobenzene (57).[102] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24-7.35 (m, J=9 Hz, J=3 Hz, 1H), 6.83-6.92 (m, J=6 Hz, J=9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.4, 161.2, 130.7, 111.5.

1-Iodo-2-methylbenzene (58).[83] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68-7.73 (d, J=9 Hz, 1H), 7.11-7.15 (d, J=6 Hz, 2H), 6.71-6.80 (m, J=3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.4, 139.0, 129.9, 128.3, 127.5, 101.3, 28.3.

***p*-Iodotoluene** (59).[83] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.58 (d, J=9 Hz, 2H), 6.88-6.94 (d, J=9 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.5, 137.3, 131.3, 90.4, 21.3.

(*Z*)-(1-Chloro-2-iodovinyl)benzene (61).[103] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.56 (m, J=3 Hz, 2H), 7.33-7.36 (m. J=3 Hz, 3H), 7.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.2, 137.3, 132.2, 129.5, 128.7, 127.0, 78.5.

5-Iodo-2,4-dimethoxypyrimidine (63).[104] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (s, 1H), 4.03 (s, 3H), 3.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 165.6, 164.9, 105.2, 55.4, 55.3.

1-Iodo-2-bromobenzene (64).[105] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83-7.90 (d, J=9 Hz, 1H) 7.60-7.66 (d, J=9 Hz, 1H), 7.16-7.24 (t, J=9 Hz, 1H), 6.95-7.04 (t, J=9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.4, 132.9, 129.8, 129.6, 128.5, 101.3.

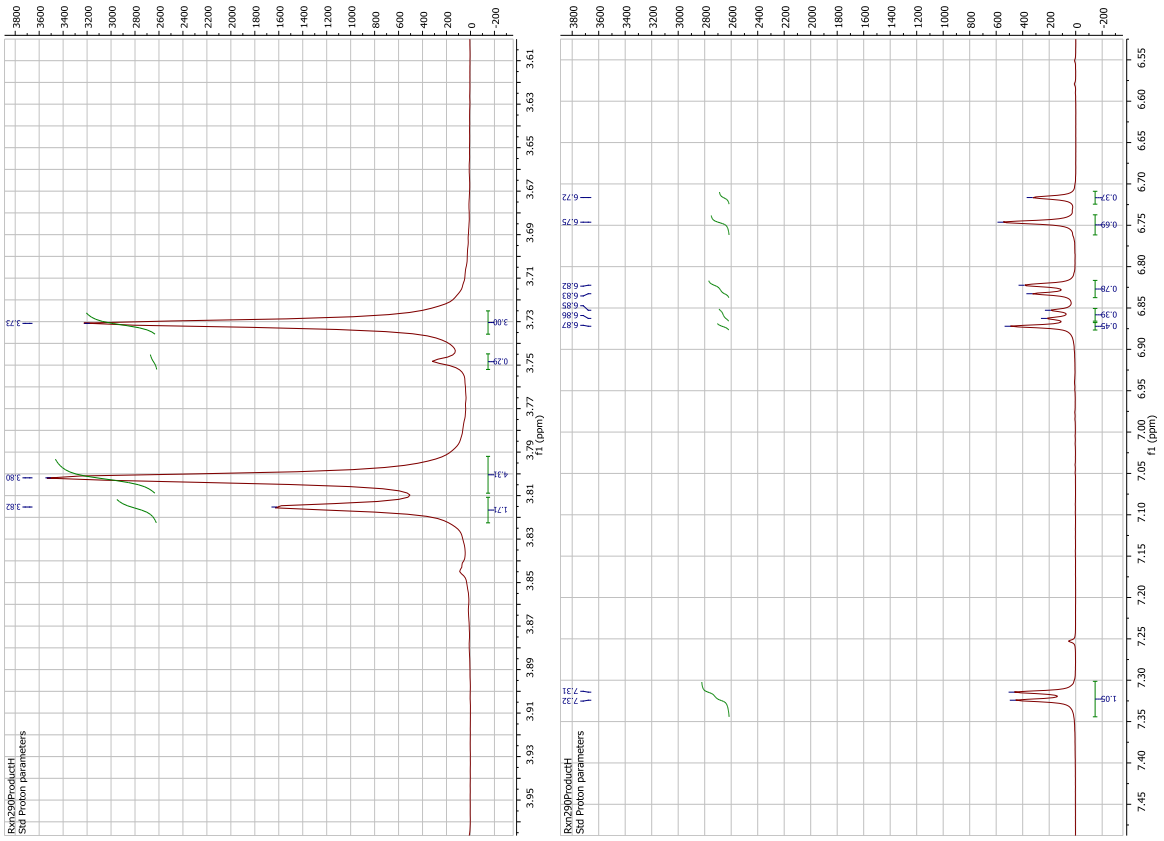


Figure 6.1 ^{1}H NMR of Mixture of Products Isolated from the Iododeboronation of 3,4,5-Trimethoxyphenyltrifluoroborate at 80 ºC.

CHAPTER 7
IODODEBORONATION OF TRIBUTYL(ARYL)STANNANES

7.1 Introduction

The iron(III) chloride/sodium iodide reaction system was utilized in the iododestannation of tributyl(aryl)stannanes. The iododestannation reactions were found to occur at room temperature in a one-to-one THF/water solution in 40-60 minutes for most substrates, and generally gave excellent yields of aryl iodides. The main concern with the methodology is the toxicity of the organotin reagents, and the organotin halide reaction by-products. All work was carried out in a fume hood, and gloves were worn at all times.

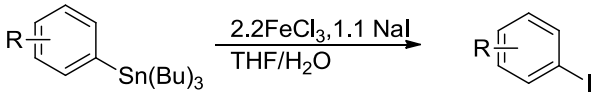
7.2 Results and Discussion

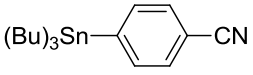
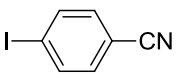
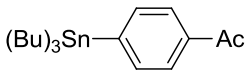
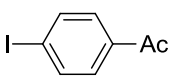
In the initial investigation, the conditions utilized in bromodeboronations using TBATB and pyridinium tribromide were used and found to provide good product yields. The initial reaction conditions used were 4 mL of a one-to-one THF/water solution/1 mmol of tributyl(aryl)stannane, room temperature, 2.2 equivalents of iron(III) chloride, and 1.1 equivalents of sodium iodide. The reactions were monitored by TLC and required 40-60 minutes to go to completion, except for one example that required heating for 1.5 hours.

A series of tributyl(aryl)stannanes were synthesized from established procedures and the spectral data for the synthesized compounds matched the literature references.[95] The first iododestannation reaction was carried out using 4-(tributylstannyl)benzonitrile. The reaction required 60 minutes to go to completion. To purify the product and remove the tributyltin chloride produced during the reaction, column chromatography, using silica gel mixed with 15 weight % of finely ground potassium carbonate, was carried out and this yielded the pure *p*-iodobenzonitrile in 93% yield (Product 65). 1-(4-(Tributylstannyl)phenyl)ethanone was reacted next, and required 50 minutes to

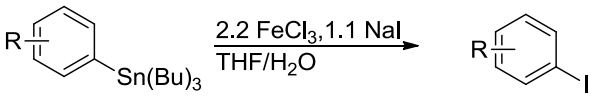
react completely and after purification using column chromatography produced a 96% yield of 1-(4-iodophenyl)ethanone (Product 66). Tributyl(4-methoxyphenyl)stannane underwent iododeboronation in 40 minutes to yield 1-iodo-2-methoxybenzene in 92% yield (Product 67). As with halodeboronation reactions, it was observed that tributyl(aryl)stannanes with electron donating substituents were more reactive in iododestannation reactions. Next, tributyl(phenyl)stannane underwent iododestannation in 40 minutes to yield, after purification, 92% yield of iodobenzene (Product 68). Tributyl(*o*-nitrophenyl)stannane underwent iododeboronation in 90 minutes at 70 °C to produce a yield 78% of 1-iodo-2-nitrobenzene (Product 69). No product was produced at room temperature with this substrate after 1 hour of reaction. 3-(4-(Methylsulfonyl)phenyl)-2-(4-(tributylstannyl)phenyl)-cyclopent-2-enone underwent iododestannation in 50 minutes to produce 2-(4-iodophenyl)-3-(4-(methylsulfonyl)phenyl)cyclopent-2-enone (iodinated Vioxx®) in 87% yield (Product 70). Tributyl(*p*-formylphenyl)stannane was reacted in 50 minutes, but the isolated yield of 4-iodobenzaldehyde was only 21%. Although no carboxylic acid was observed in the ^{1}H NMR it is hypothesized that the aldehyde group was partially oxidized during the reaction in the conditions used (Product 71). Tributyl(*p*-chlorophenyl)stannane was iodinated in 90% yield in 50 minutes (Product 72), Scheme 7.1.

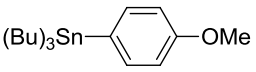
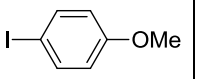
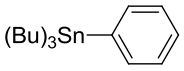
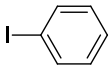
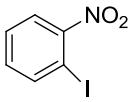
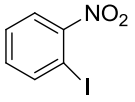
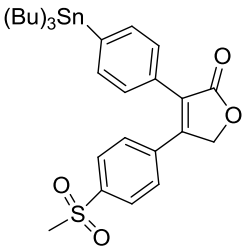
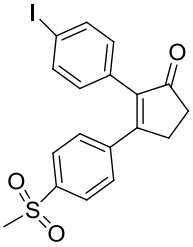
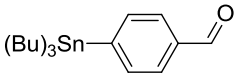
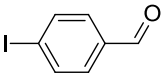
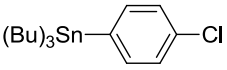
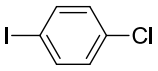
Scheme 7.1 Iododestannation of Tributyl(aryl)stannanes.



Reactant	Time (min.)	Yield (%)	Product	number
	60	93		65
	50	96		66

Scheme 7.1 (Continued)



Reactant	Time (min.)	Yield (%)	Product	number
	40	92		67
	40	92		68
	90	78		69
	50	87		70
	50	21		71
	50	90		72

7.3 Conclusions

The Iron(III) chloride/sodium iodide reaction system proved to be very effective in the iododestannation reactions of tributyl(aryl)stannanes. As with halodeboronations, electron donating substituents decrease reaction times, and electron withdrawing substituents require longer reaction times and/or heating. In general, excellent yields of aryl iodides were obtained. The aldehyde functionality does not appear to tolerate the reactions conditions most likely undergoing oxidation. A nitro group, a lactone ring, and a methylsulfonyl group were observed to survive the reaction conditions.

The work presented in this chapter was carried out by the author. The majority of this work was presented at the Boron Americas XIII conference in a presentation titled “Iododemetallation of Organotrifluoroborate and Organotin Reagents Using a $FeCl_3$-NaI System.”

7.4 Experimental

Reagents were used as received. Column chromatography was performed using silica gel (60 Å, 230–400 mesh, ICN Biomedicals GmbH, Eschwege, Germany). Analytical thin-layer chromatography was performed using 250 μm silica plates (Analtech, Inc., Newark, DE). ^{1}H NMR and ^{13}C NMR spectra were recorded at (250.13, 300, and 500) and (62.89 or 75) MHz, respectively. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra were referenced to the residual protons of the deuterated solvents or to TMS. Gas Chromatography/Mass Spectroscopy studies were carried out using a Hewlett Packard: HP 6890 series GC System with 5973 Mass Selective Detector; Column: Agilent 19091S-433E, 30.0mm X 0.25mm X 0.25 μm; Gas (He) flow rate: 0.8 mL/min; Initial temperature: 90 ˚C; Ramp temperature rate: 10 ˚C/min to maximum 240 ˚C. Melting points were obtained by using a Mel-Temp melting point apparatus with a mercury thermometer. High Resolution Mass Spectrometry was performed using a JEOL AccuTOF™ DART Mass Spectrometer.

7.5 Typical Procedure

In a fume hood, tributyl(aryl)stannane (1 equivalent) was added to a 25 mL round bottomed flask containing a small stir bar. Iron(III) chloride (2.2 equivalents) and sodium iodide (1.1 equivalents) were added. The round bottomed flask was sealed with a rubber septum and stirred at room temperature for the appropriate time. After the reaction was complete, a small amount of potassium bisulfite was added to remove any remaining halogen. Removal of tributyltin chloride was accomplished by using a combination of silica gel and (15

weight%) finely ground potassium carbonate.[110] Column chromatography using this mixture gave the purified products, after solvent removal under vacuum.

7.6 Characterization of Compounds

(NMR Spectra are in Appendix)

4-Iodobenzonitrile (65).[95] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.82-7.88 (d, J=8 Hz, 2H), 7.33-7.41 (d, J=8 Hz, 2H), ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 138.6, 133.3, 118.4, 111.8, 100.5.

1-(4-Iodophenyl)ethanone (66).[106] ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.76-7.83 (d, J=8 Hz, 2H), 7.60-7.66 (d, J=8 Hz, 2H), 2.51-2.58 (s, 3H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 197.3, 138.1, 136.4, 129.8, 101.2, 26.6.

1-Iodo-4-methoxybenzene (67).[83] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, J = 9.0 Hz, 2H), 6.68 (d, J = 9.0 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 138.3, 116.5, 82.8, 55.4. Melting point: 50-52 °C.

Iodobenzene (68).[107] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-7.71 (d, J=8.4 Hz, 2H), 7.28-7.34 (t, J=8 Hz, 1H), 7.05-7.12 (t, J=8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.5, 130.3, 127.6, 94.5.

1-Iodo-2-nitrobenzene (69).[108] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93-7.98 (d, J=8 Hz), 7.74-7.80 (d, J=8 Hz, 1H, 7.38-7.45 (t, J=8 Hz,1H), 7.16-7.23 (t, J=8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.0, 142.0, 133.5, 129.2, 125.5, 86.3.

4-(4-(Methylsulfonyl)phenyl)-3-(4-(tributylstannyl)phenyl)furan-2(5H)-one (70). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90-7.94 (d, J=4.8 Hz, 2H), 7.52-7.56 (d, J=4.8 Hz, 2H), 7.48-7.51 (d, J=4.8 Hz, 2H), 7.31-7.35 (d, J=4.8 Hz, 2H), 5.19 (s, 2H), 3.08 (s, 3H), 1.52-1.58 (t, J=4.5 Hz, 6H), 1.30-1.37 (q, J=4.5 Hz, 6H), 1.06-1.10 (t, J=4.5 Hz, 6H), 0.86-0.93 (t, J=4.5 Hz, 10H). ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 172.7, 153.0, 144.8, 136.9, 136.4, 129.1, 128.5, 128.2, 128.1, 70.4, 44.3, 29.1, 27.3, 13.7, 9.7. HRMS for $C_{29}H_{40}O_4SSn$ estimated MH^+: 605.17518 found: 605.17406.

2-(4-Iodophenyl)-3-(4-(methylsulfonyl)phenyl)cyclopent-2-enone (70). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93-7.98 (d, J=4.8 Hz, 2H), 7.72-7.77 (d, J=4.8 Hz,

2H), 7.49-7.54 (d, J=4.8 Hz, 2H), 7.12-7.18 (d, J=4.8 Hz, 2H), 5.15-5.20 (s, 2H), 3.06-3.11 (s, 3H). ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 172.2, 154.1, 142.4, 138.4, 136.1, 131.0, 128.7, 128.6, 128.4, 128.2, 96.1, 70.6, 44.3. HRMS for $C_{17}H_{13}IO_4S$ Estimated MH^+: 440.96575, Found: 440.96513.

***p*-Iodobenzaldehyde** (71).[83] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89-7.95 (d, J=8.7 Hz, 2H), 7.57-7.63 (d, J=8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.54, 138.6, 135.7, 130.9, 103.0.

1-Iodo-4-chlorobenzene (72).[109] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-7.63, (d, J=6.9 Hz, 2H), 7.04-7.11 (d, J=6.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.8, 134.3, 130.6, 91.3.

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APPENDIX

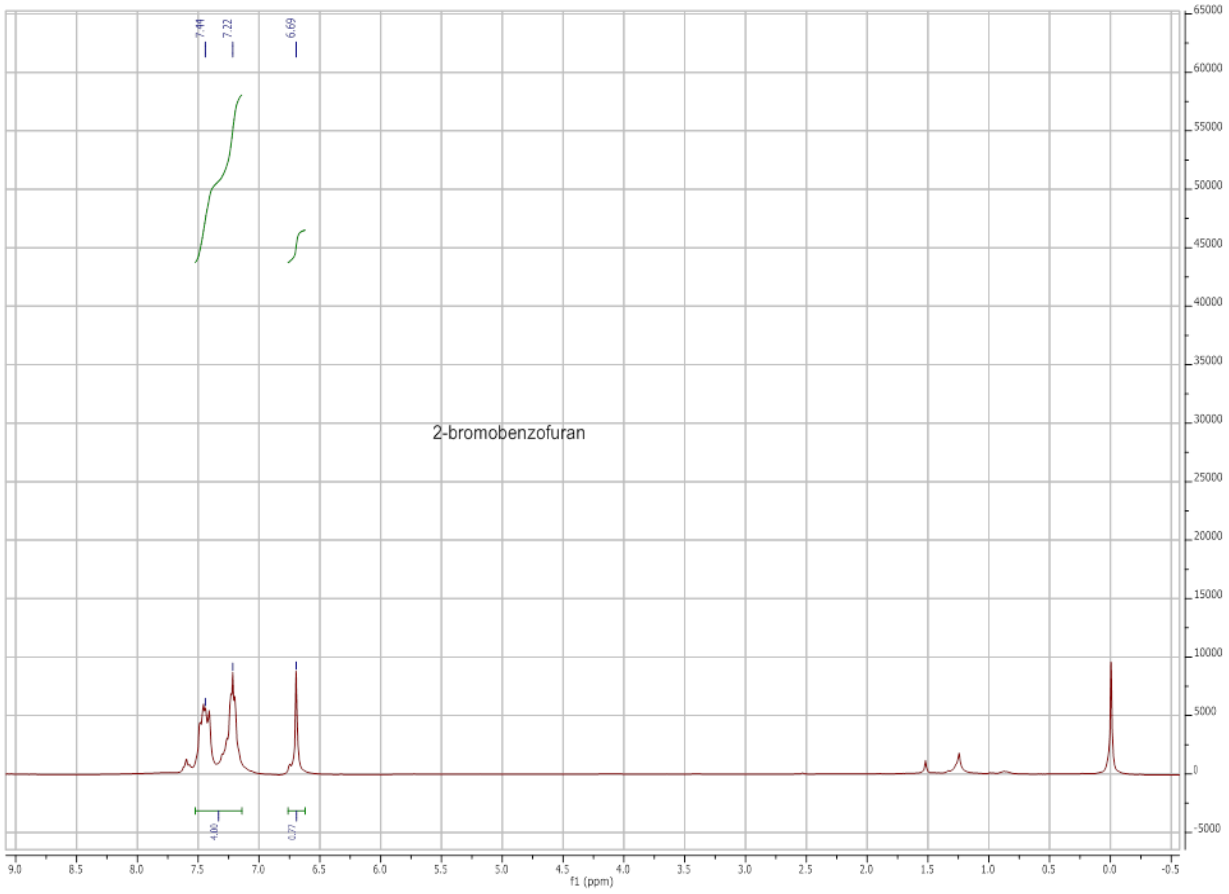


Figure A-1 ^{1}H NMR of 2-Bromobenzofuran.

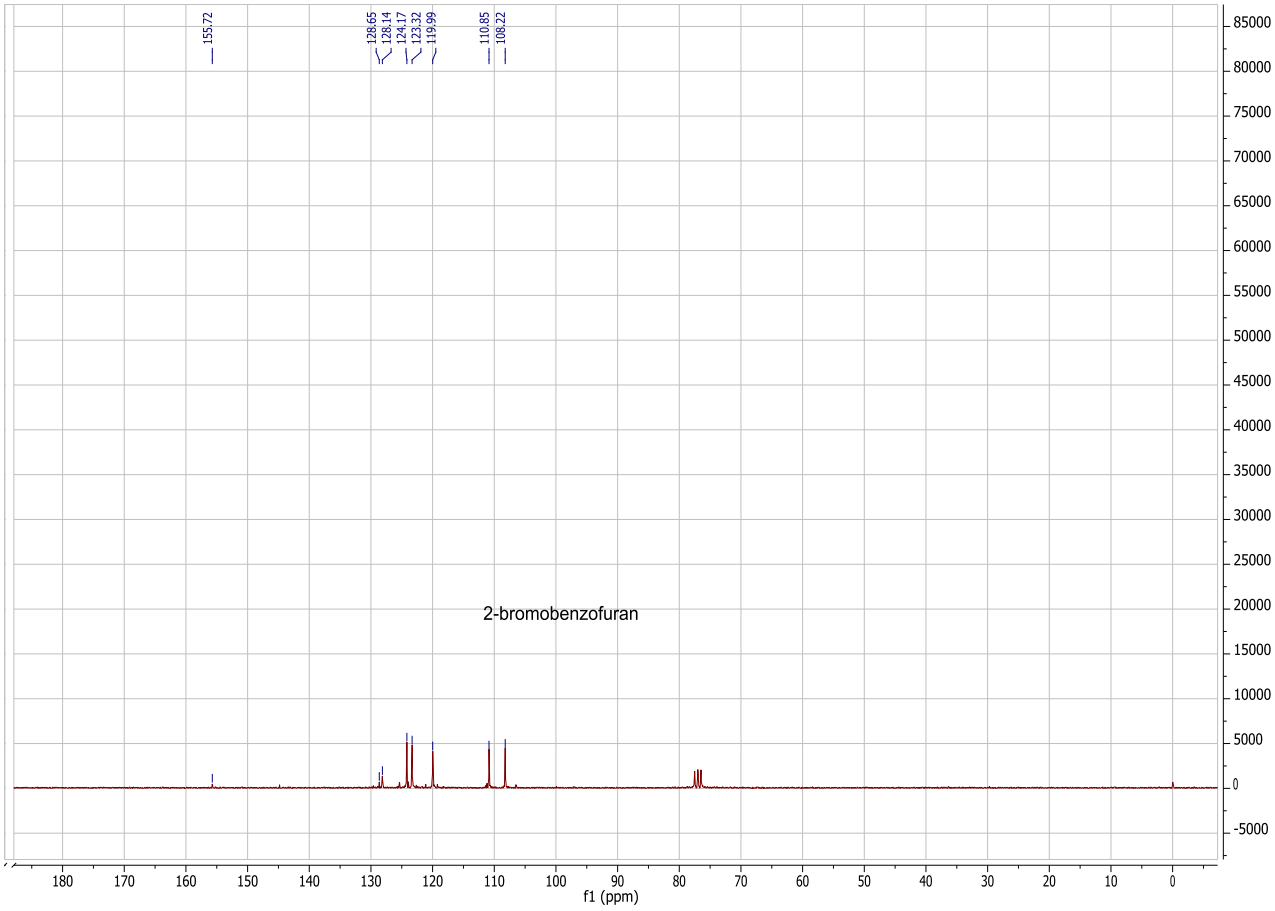


Figure A-2 ^{13}C NMR of 2-Bromobenzofuran.

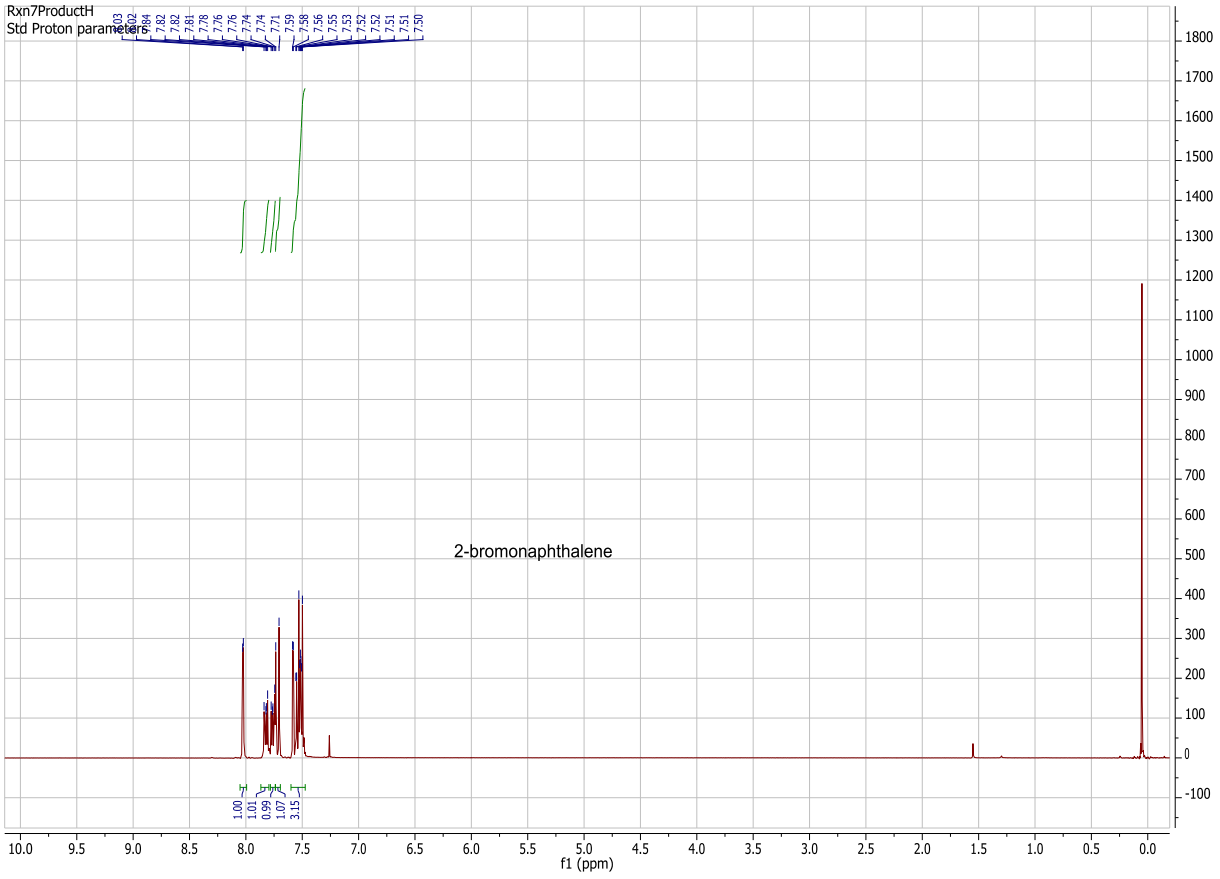


Figure A-3 ^{1}H NMR of 2-Bromonaphthalene.

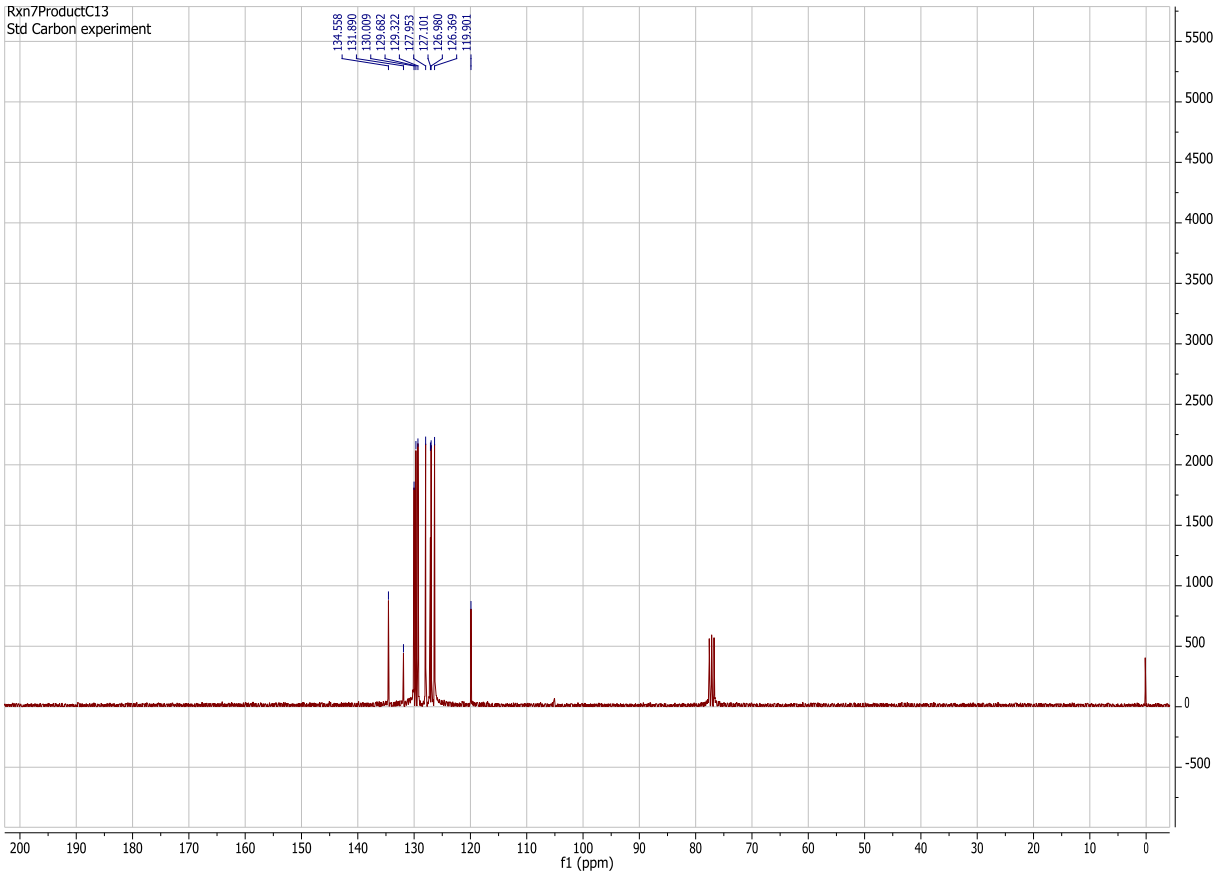


Figure A-4 ^{13}C NMR of 2-Bromonaphthalene.

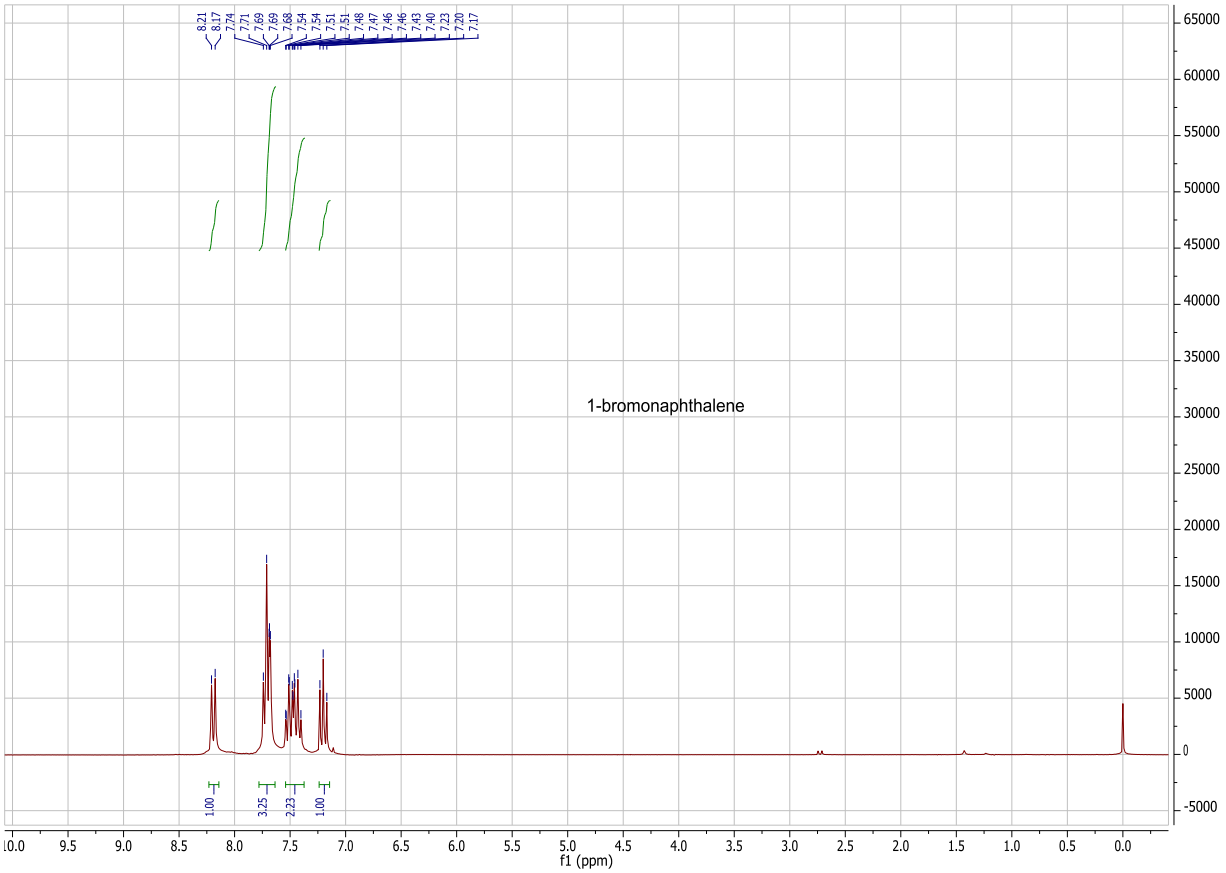


Figure A-5 ^{1}H NMR of 1-Bromonaphthalene.

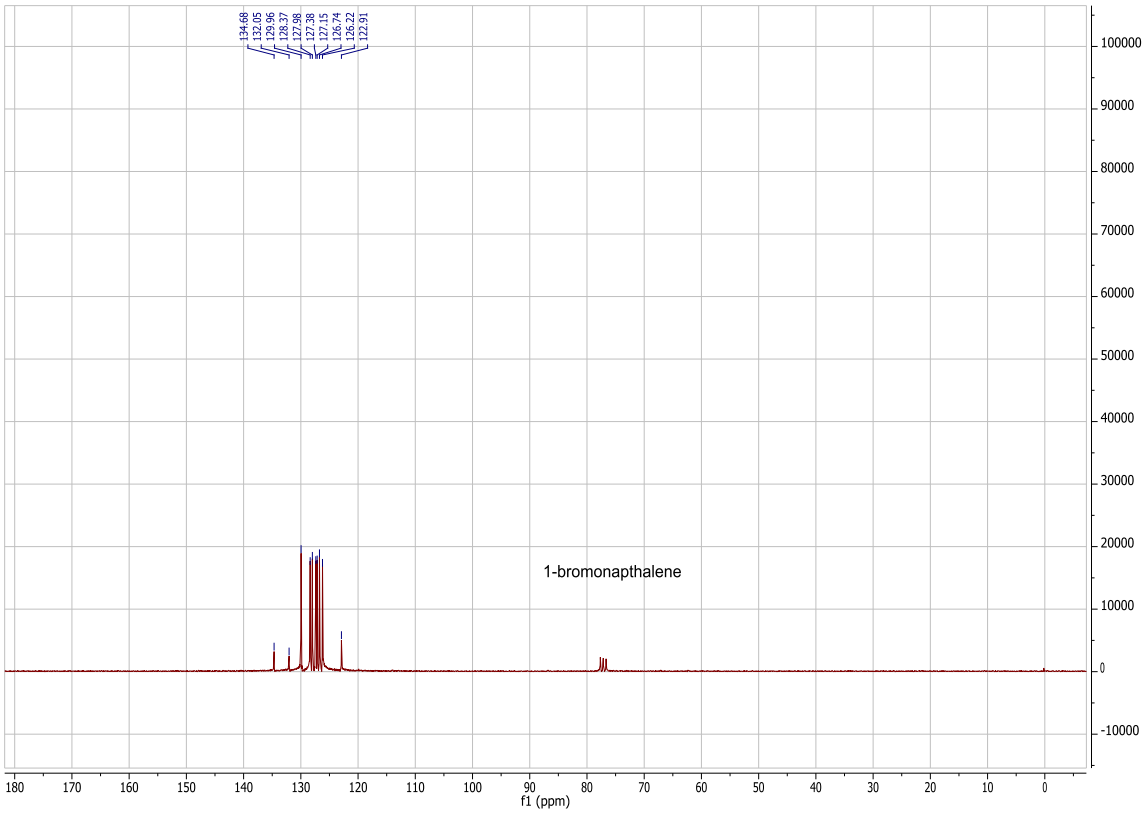


Figure A-6 ^{13}C NMR of 1-Bromonaphthalene.

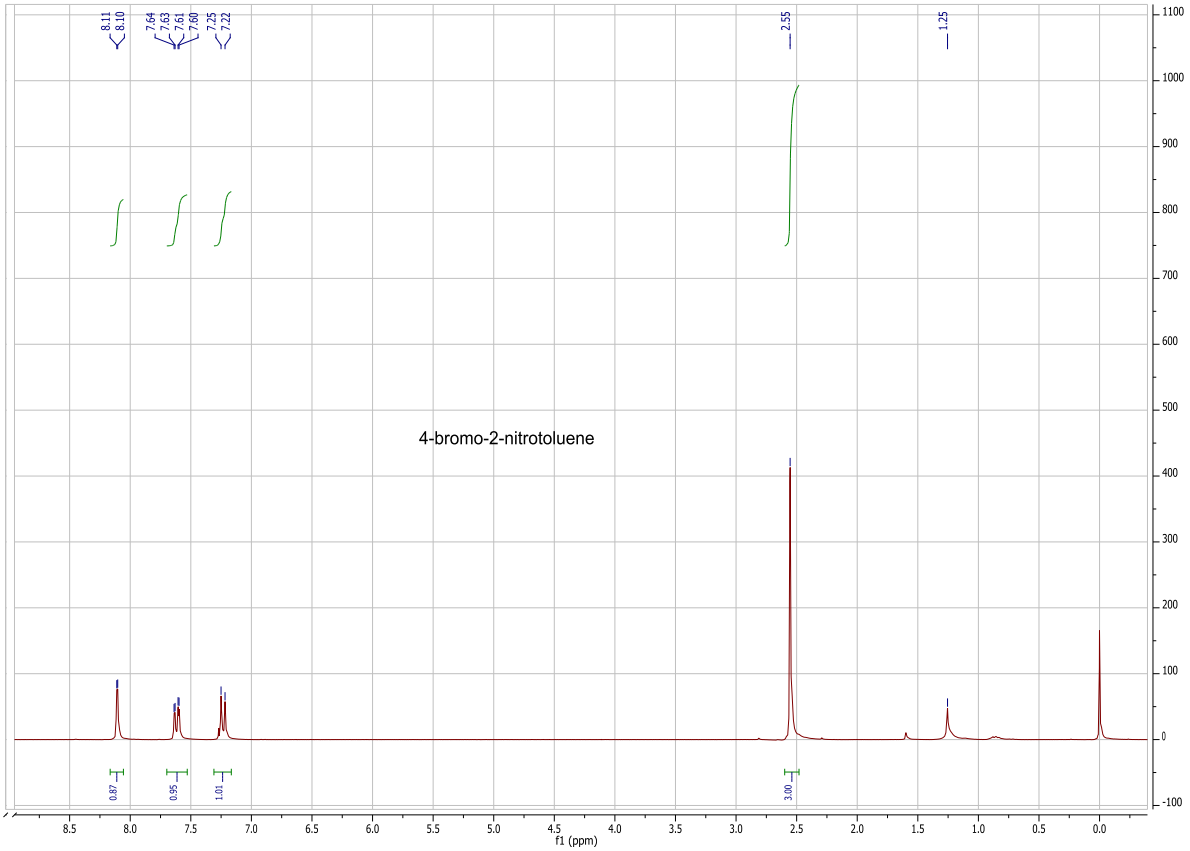


Figure A-7 ^{1}H NMR of 4-Bromo-2-nitrotoluene.

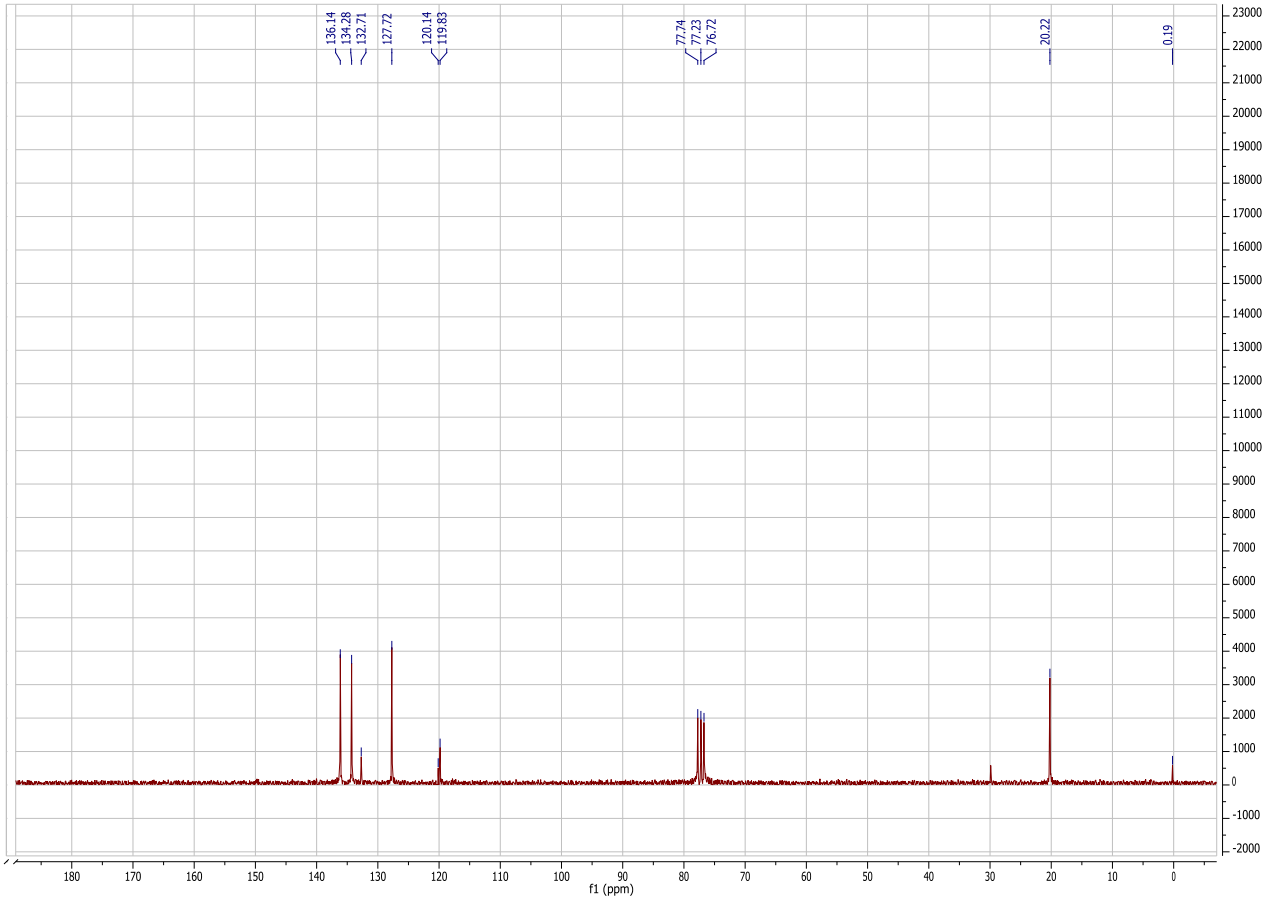


Figure A-8 ^{13}C NMR of 4-Bromo-2-nitrotoluene.

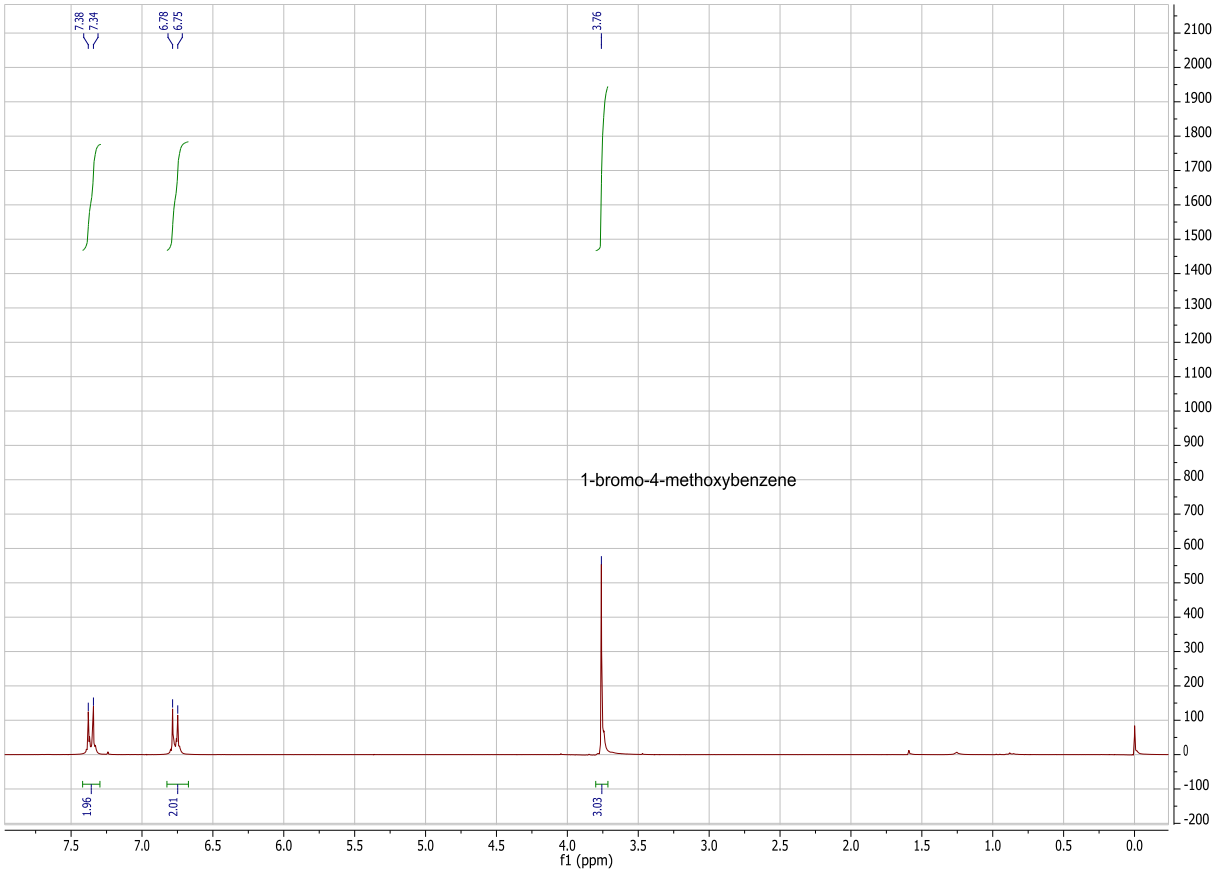


Figure A-9 ^{1}H NMR of 1-Bromo-4-methoxybenzene.

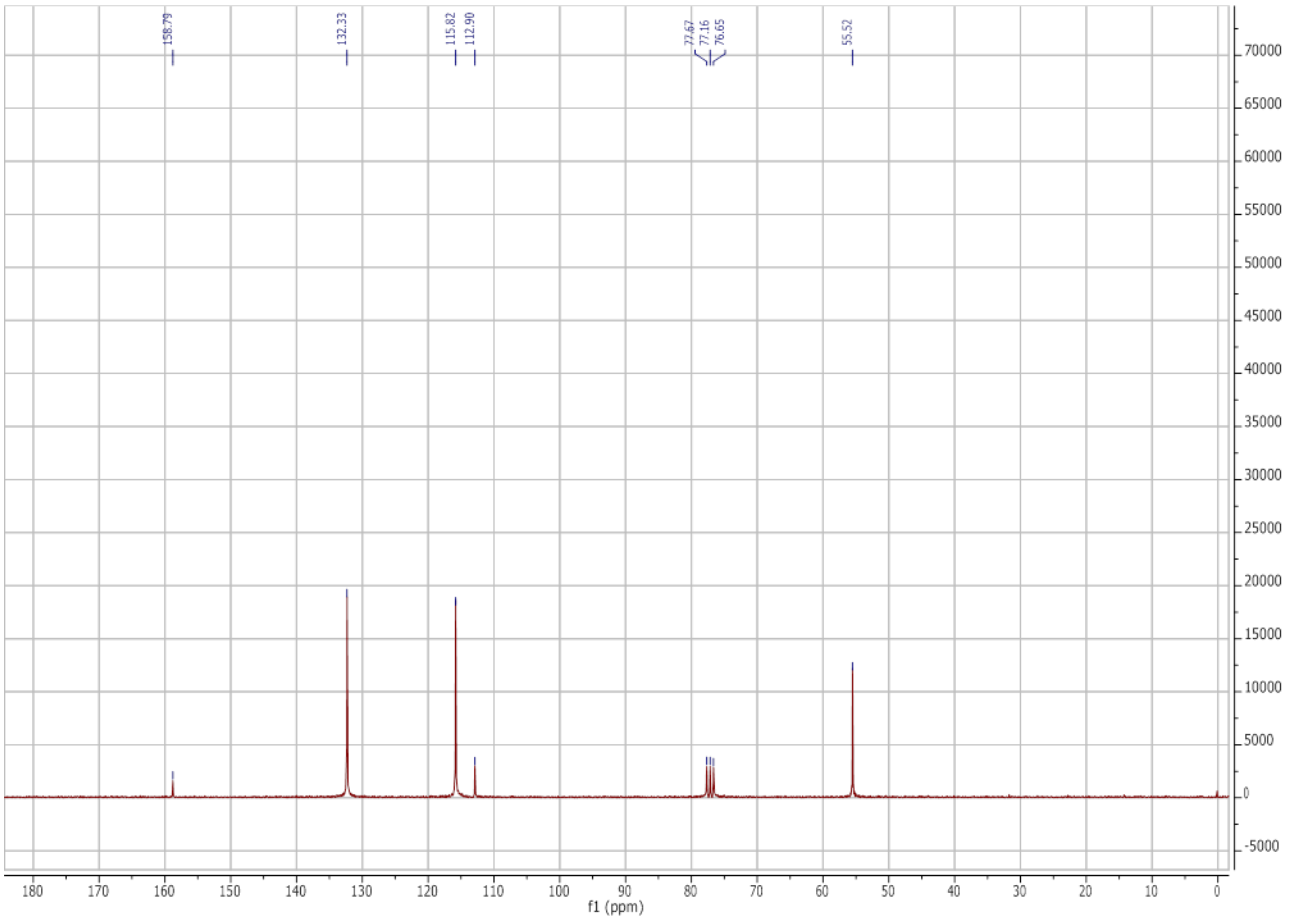


Figure A-10 ^{13}C NMR of 1-Bromo-4-methoxybenzene.

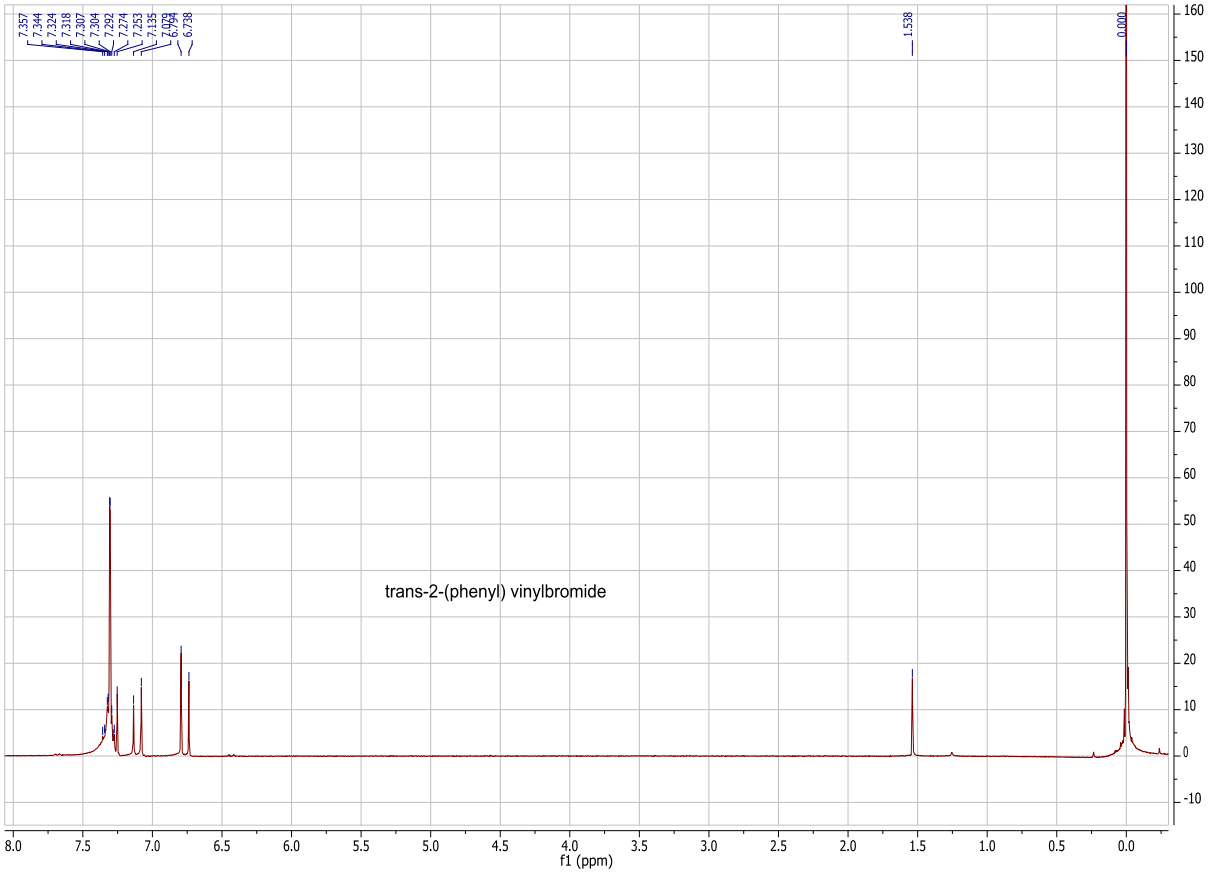


Figure A-11 ^{1}H NMR of *trans*-2-(Phenyl)vinylbromide.

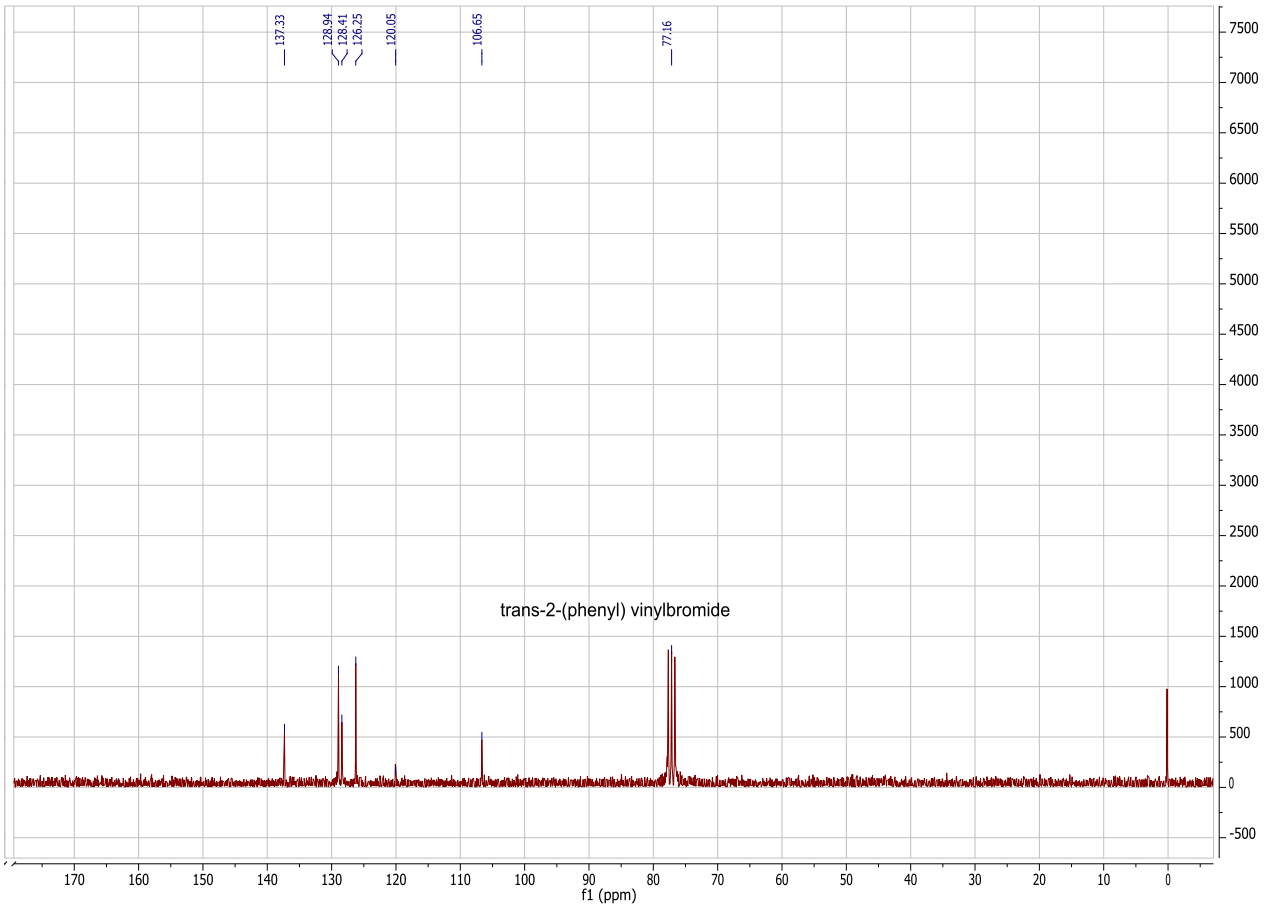


Figure A-12 ^{13}C NMR of *trans*-2-(Phenyl)vinylbromide.

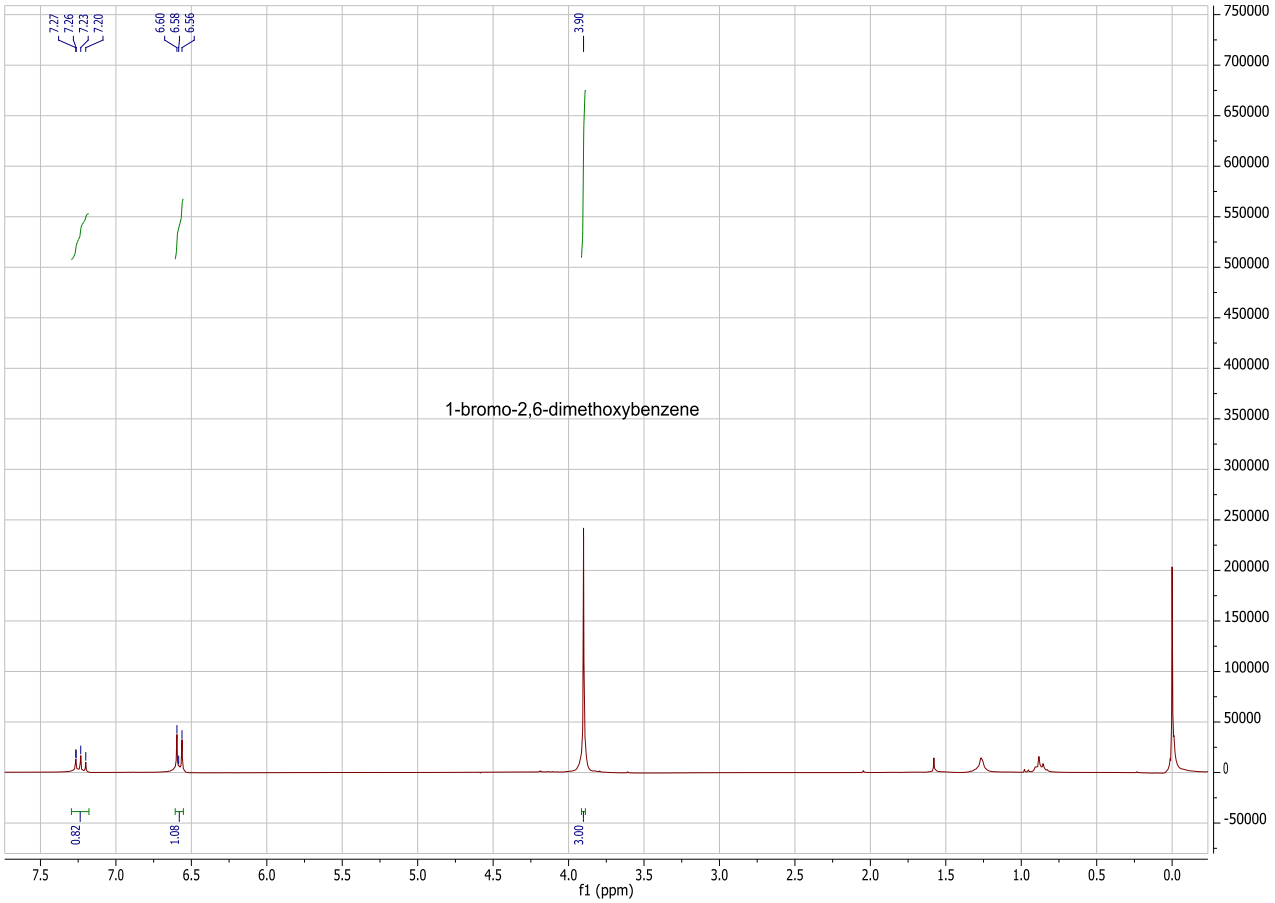


Figure A-13 ^{1}H NMR of 2-Bromo-1,3-dimethoxybenzene.

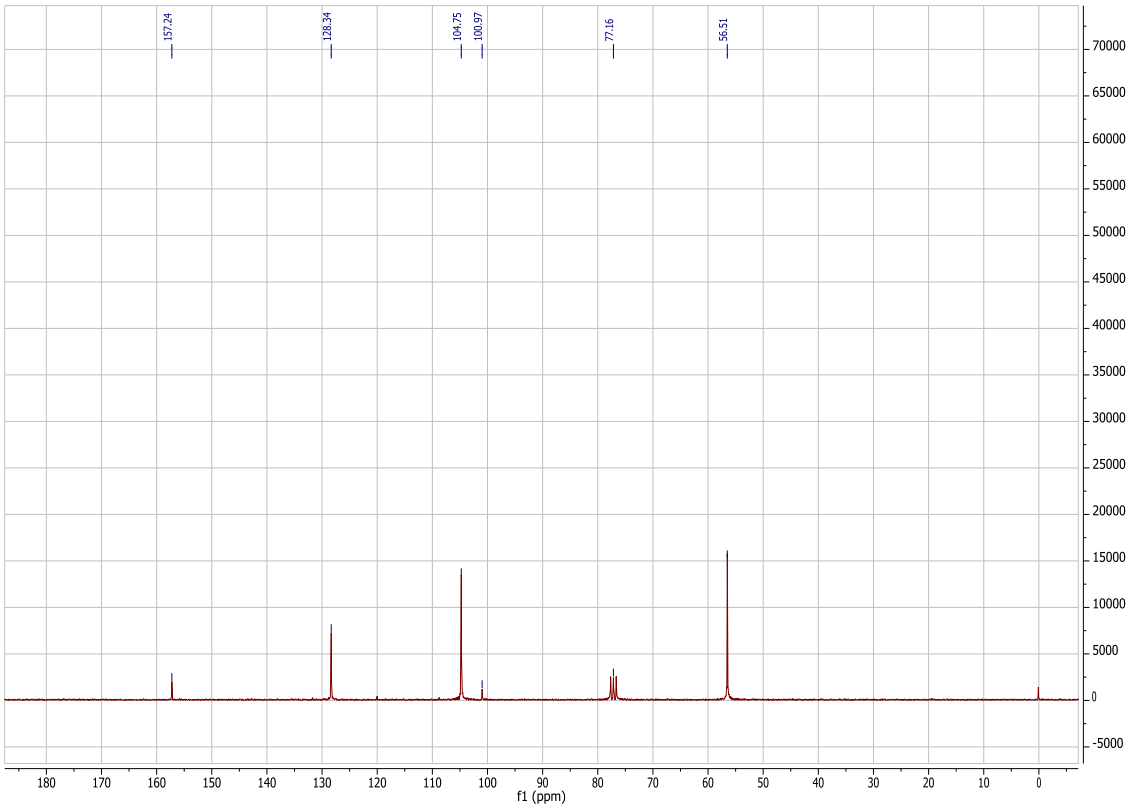


Figure A-14 ^{13}C NMR of 2-Bromo-1,3-dimethoxybenzene.

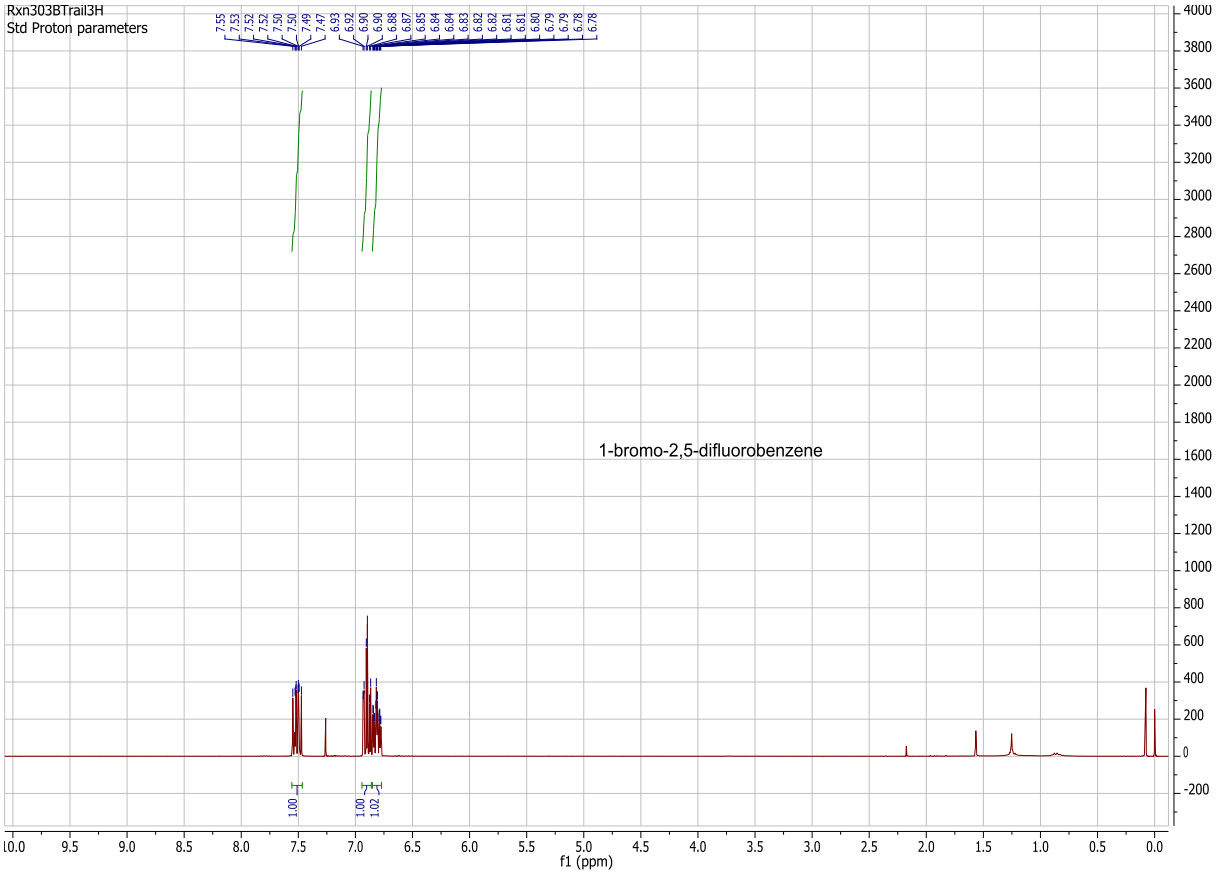


Figure A-15 ^{1}H NMR 1-Bromo-2,4-difluorobenzene.

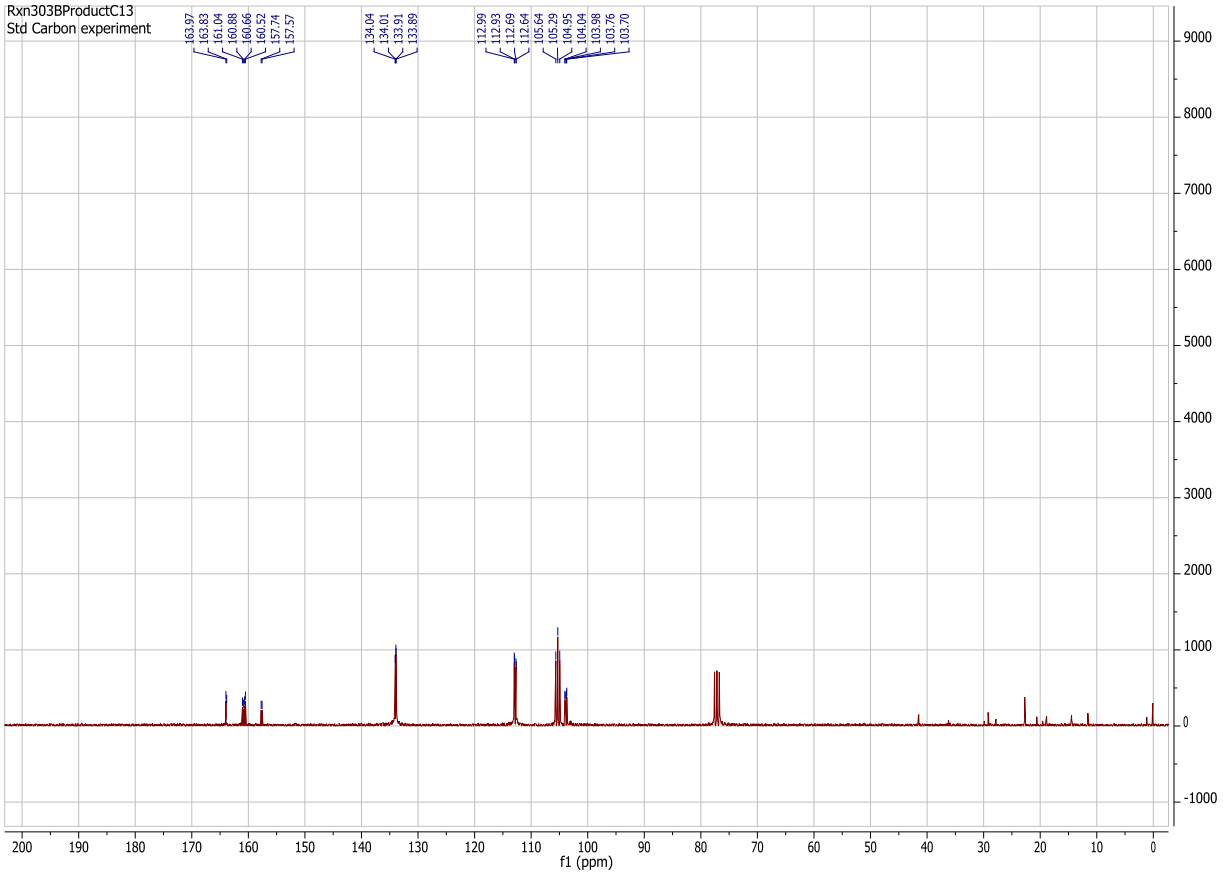


Figure A-16 ^{13}C NMR 1-Bromo-2,4-difluorobenzene.

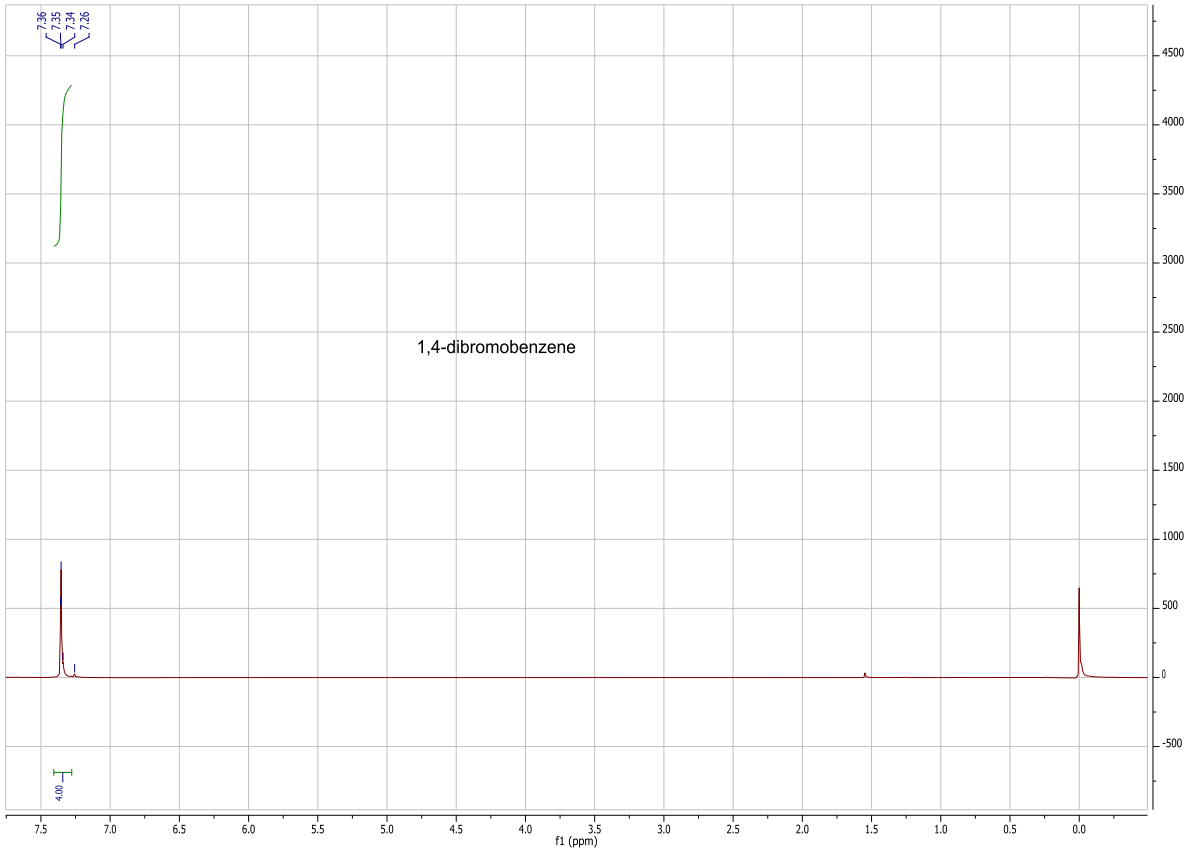


Figure A-17 ^{1}H NMR 1,4-Dibromobenzene.

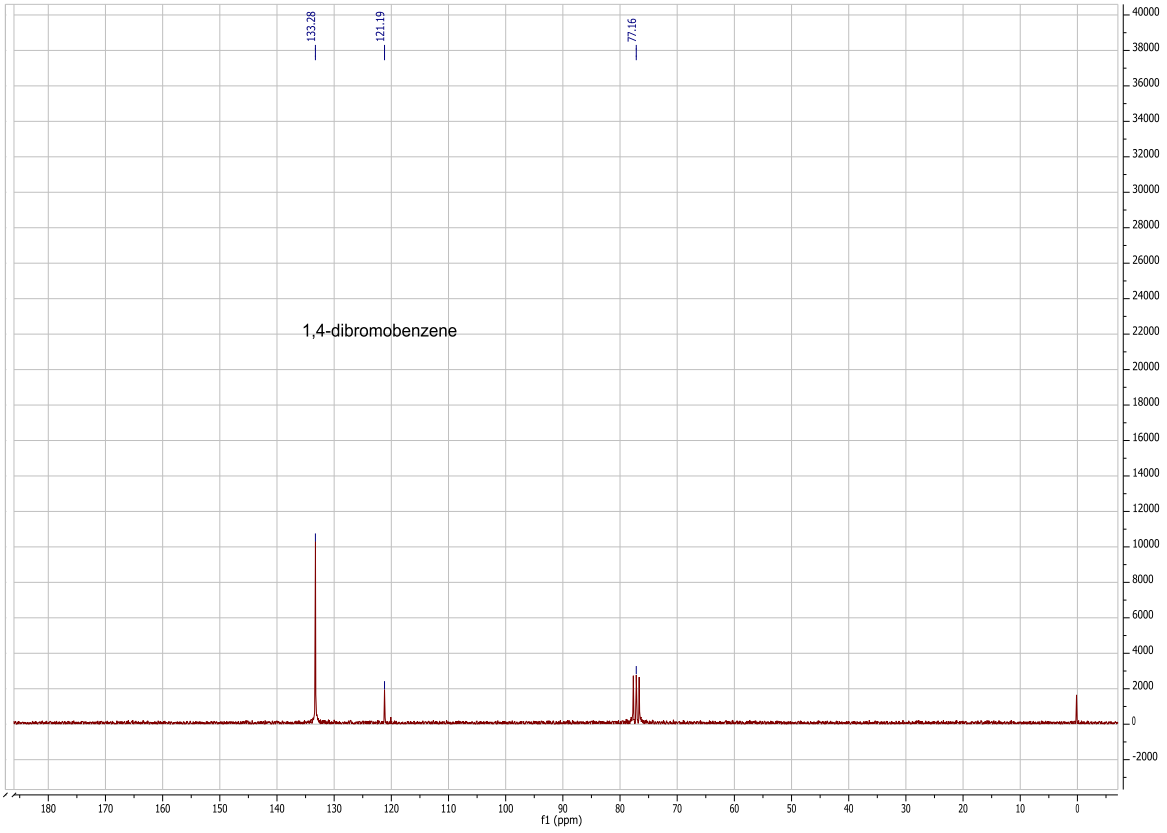


Figure A-18 ^{13}C NMR of 1,4-Dibromobenzene.

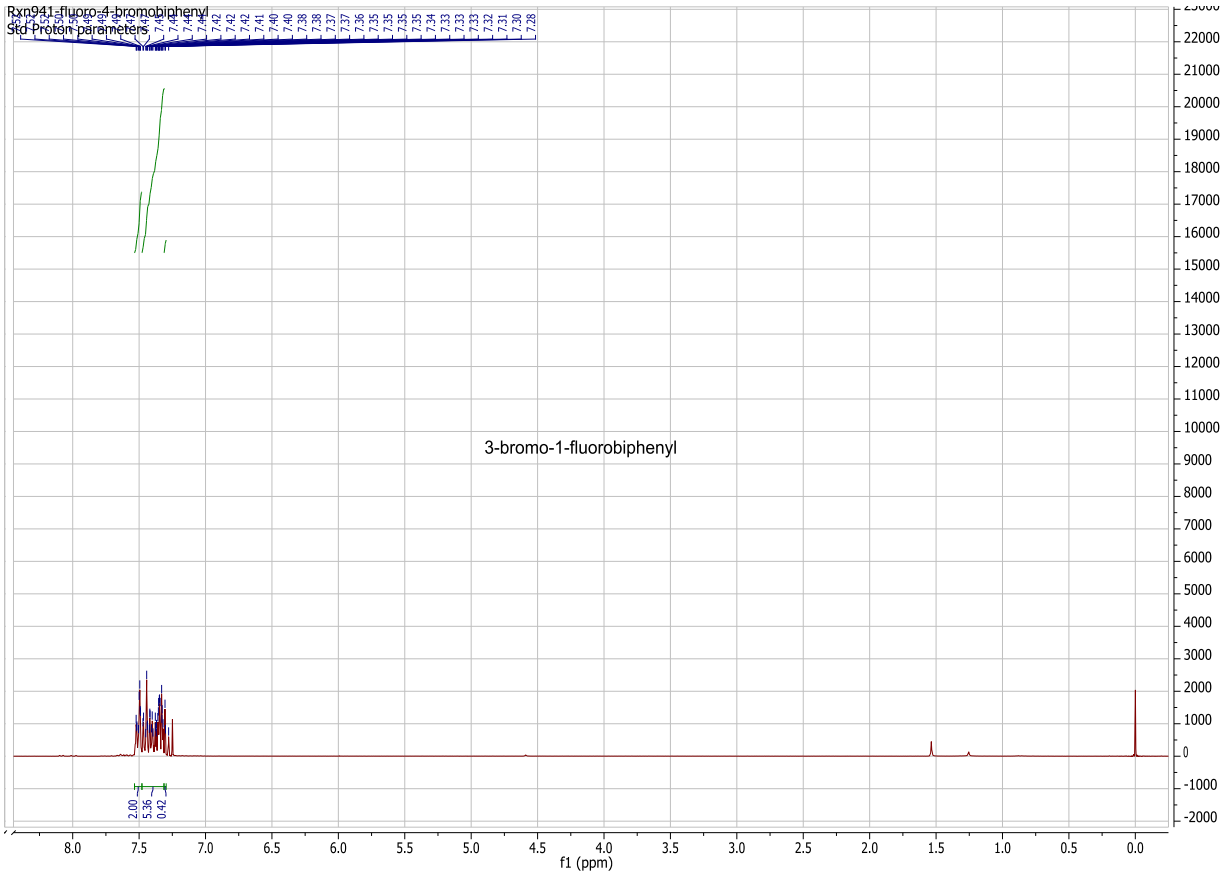


Figure A-19 ^{1}H NMR 4-Bromo-2-fluorobiphenyl.

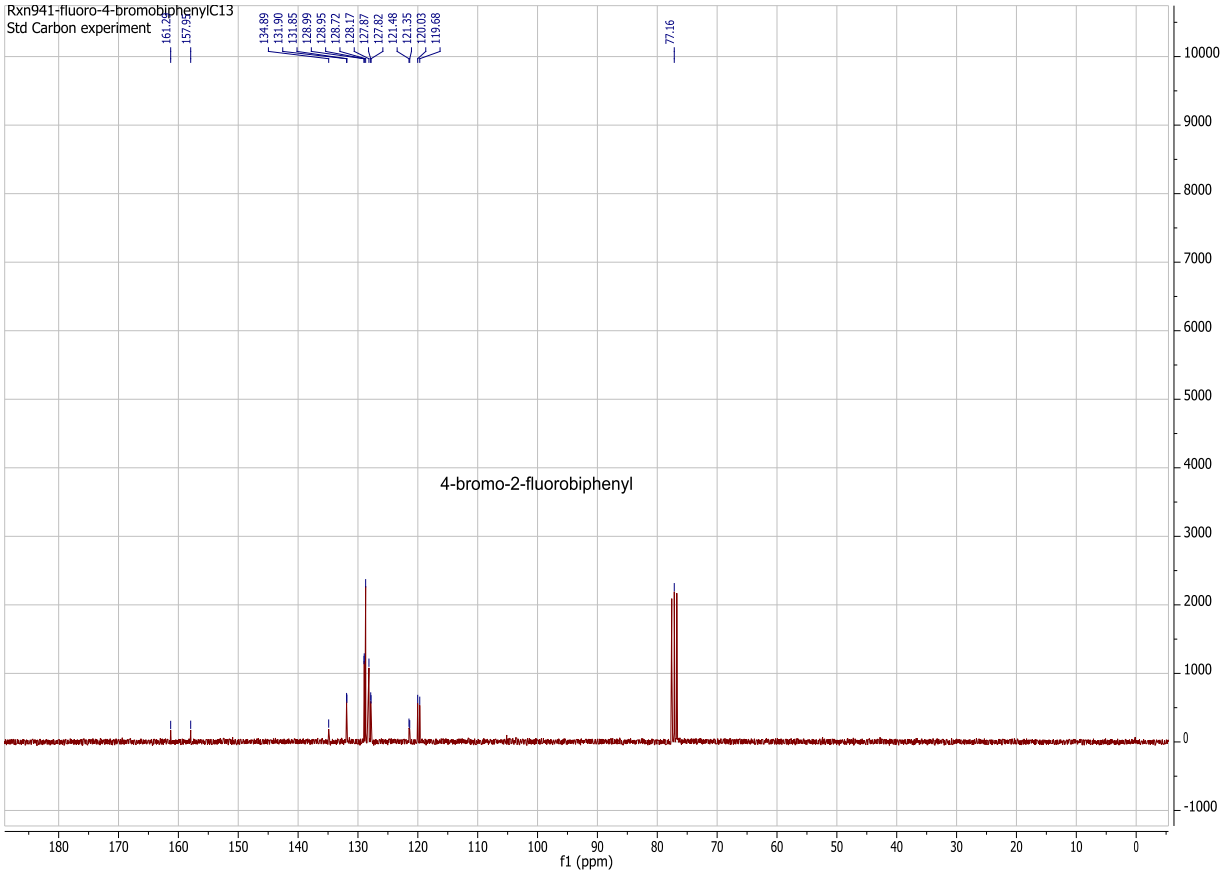


Figure A-20 ^{13}C NMR 4-Bromo-2-fluorobiphenyl.

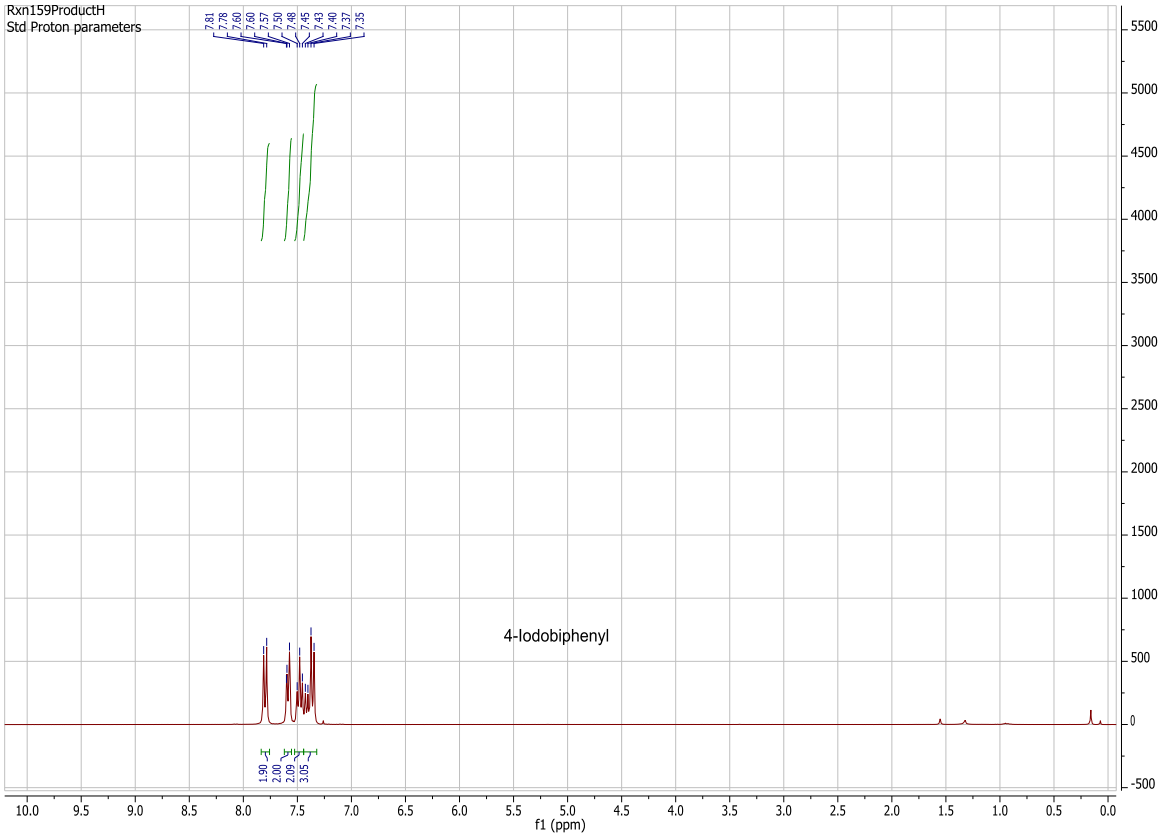


Figure A-21 ^{1}H NMR of 4-Iodobiphenyl.

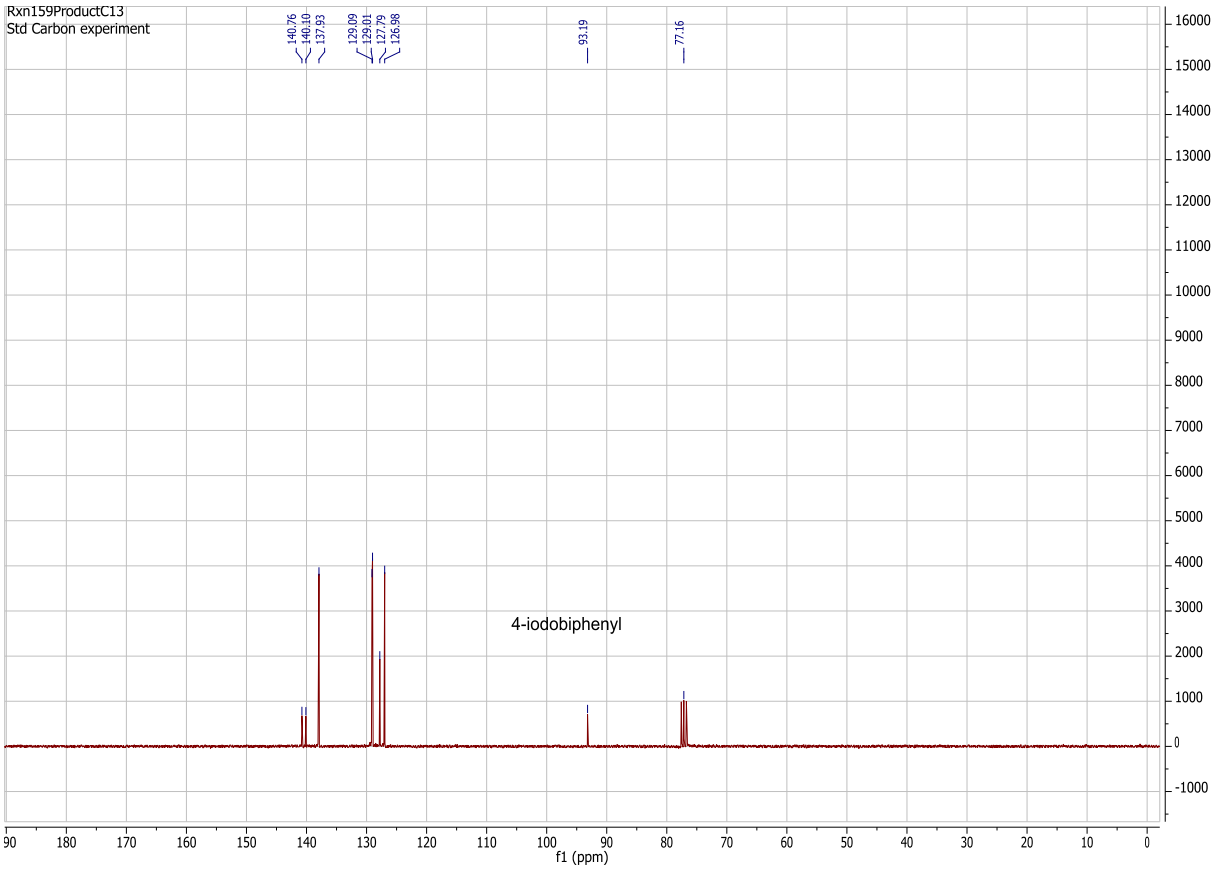


Figure A-22 ^{13}C NMR of 4-Iodobiphenyl.

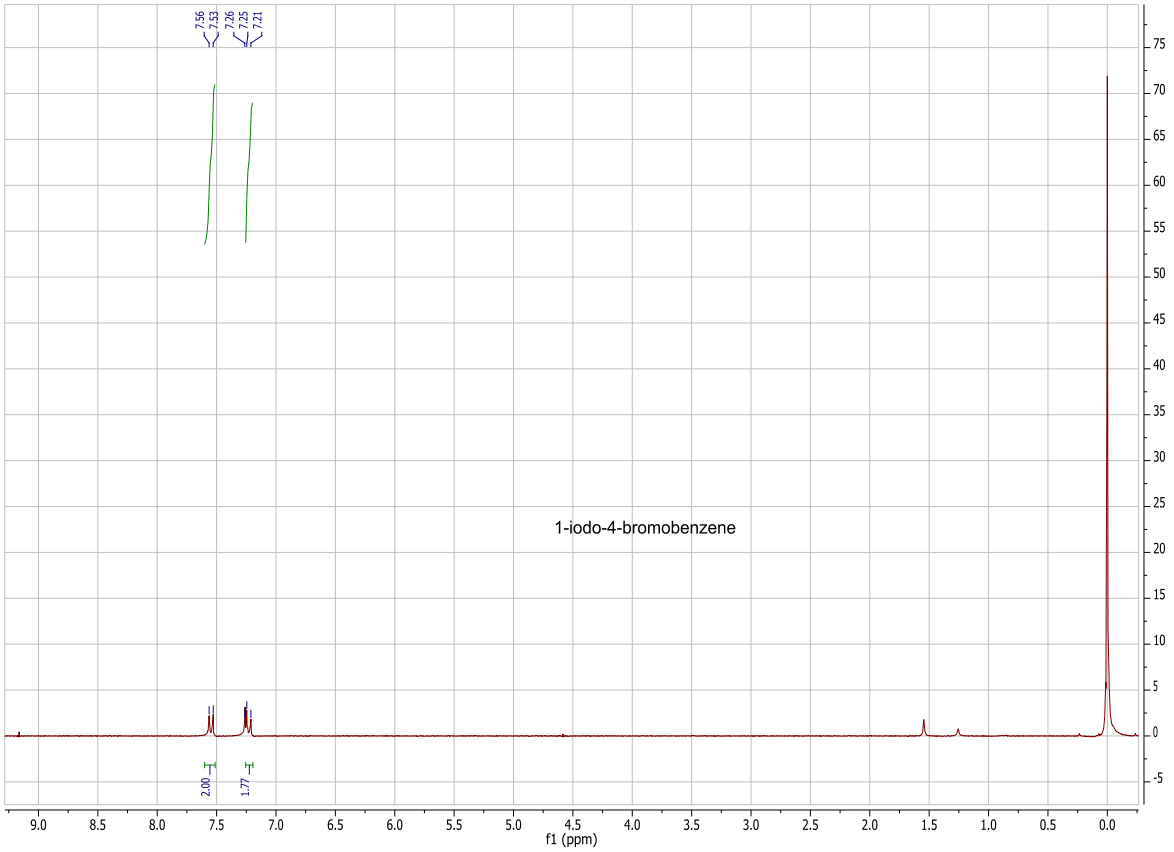


Figure A-23 ^{1}H NMR of 1-Iodo-4-bromobenzene.

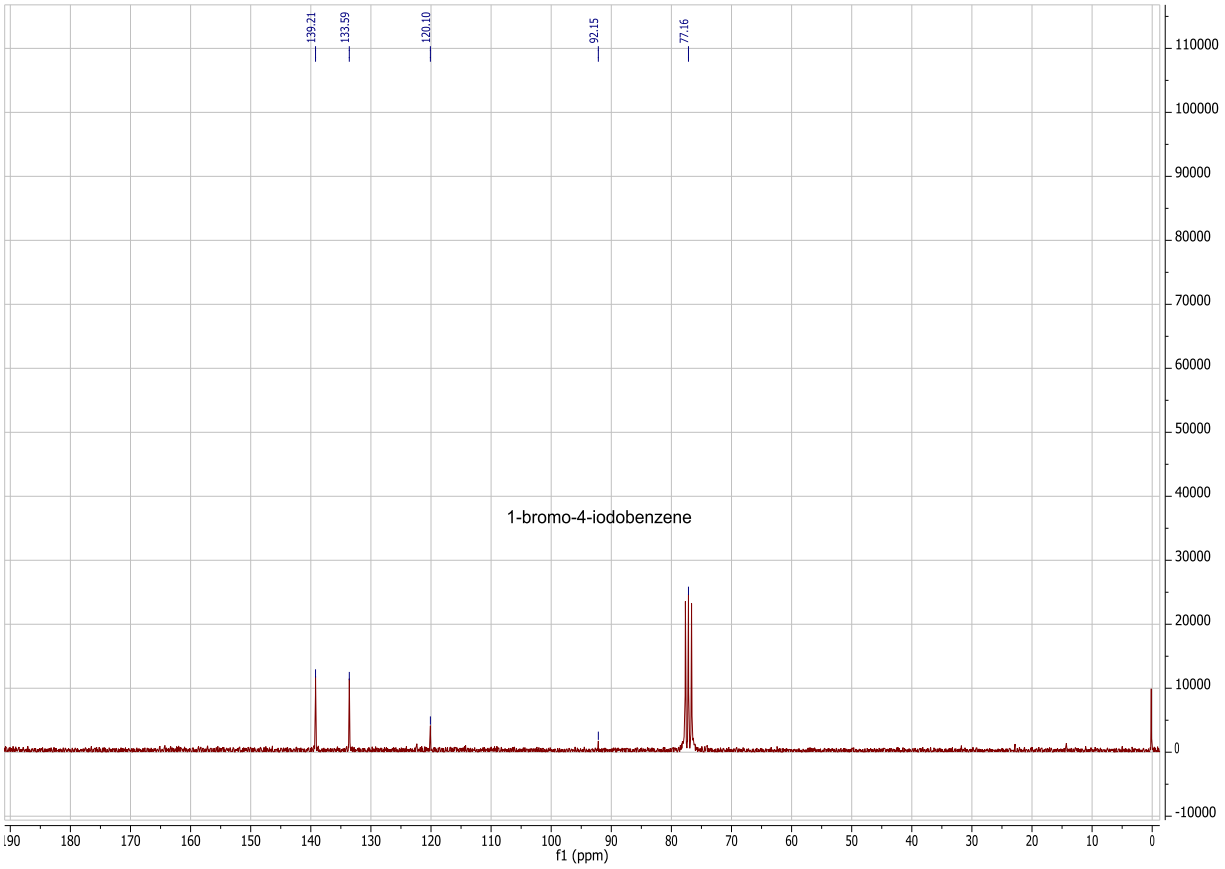


Figure A-24 ^{13}C NMR of 1-Iodo-4-bromobenzene.

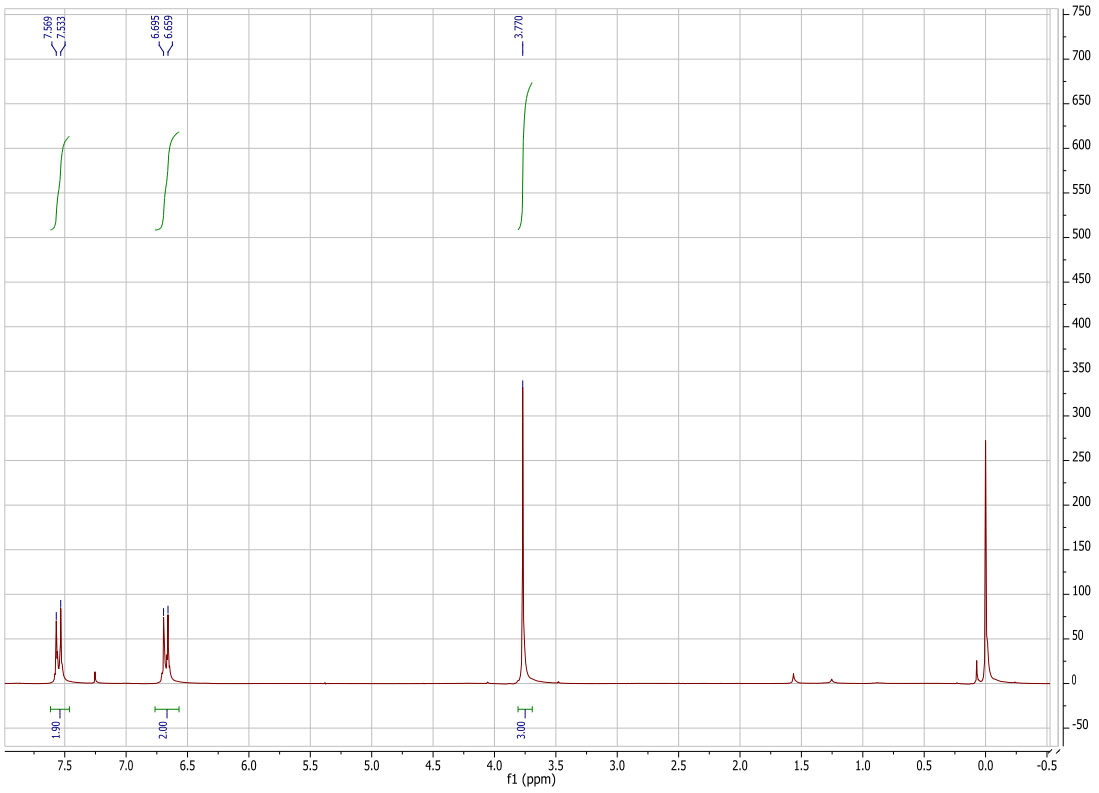


Figure A-25 ^{1}H NMR 1-Iodo-4-methoxybenzene.

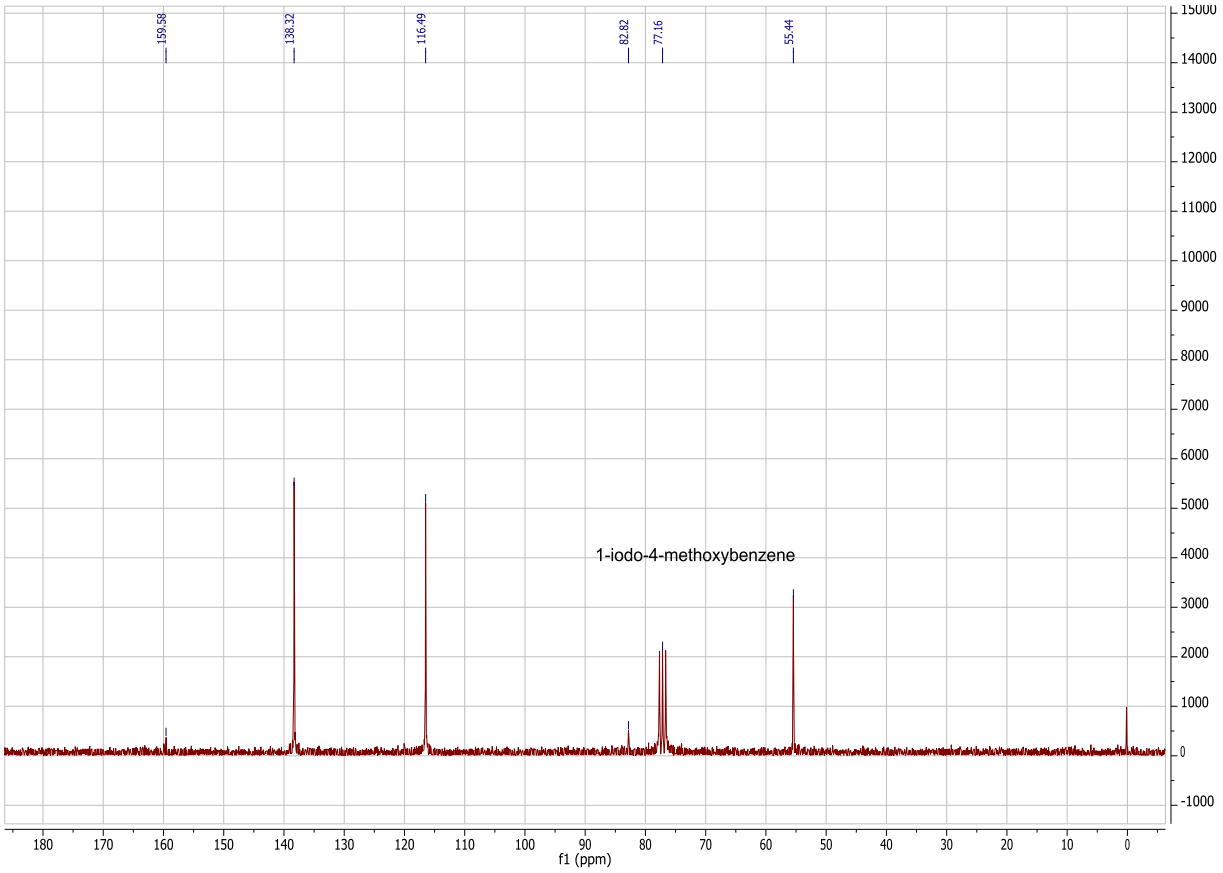


Figure A-26 ^{13}C NMR of 1-Iodo-4-methoxybenzene.

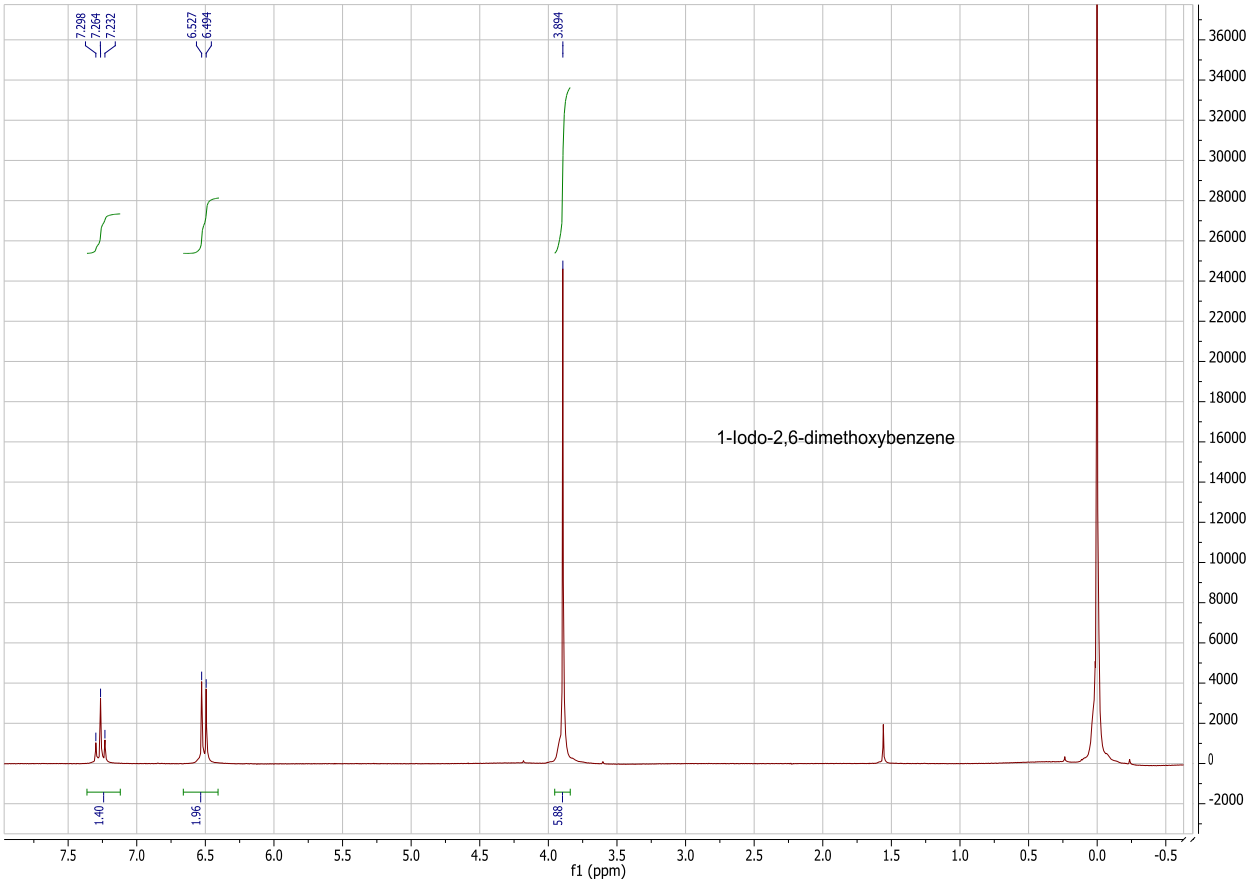


Figure A-27 ^{1}H NMR of 1-Iodo-2,6-dimethoxybenzene.

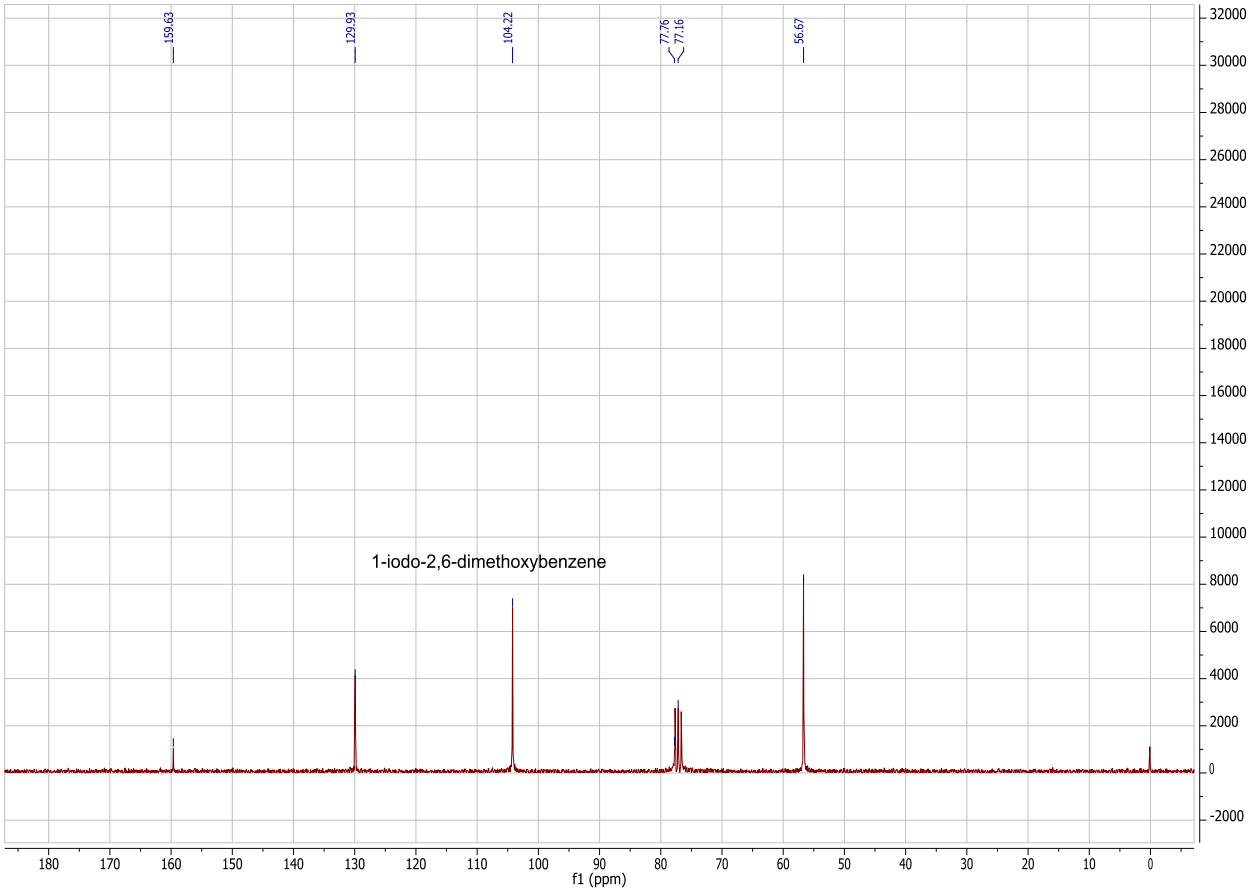


Figure A-28 ^{13}C NMR of 1-Iodo-2,6-dimethoxybenzene.

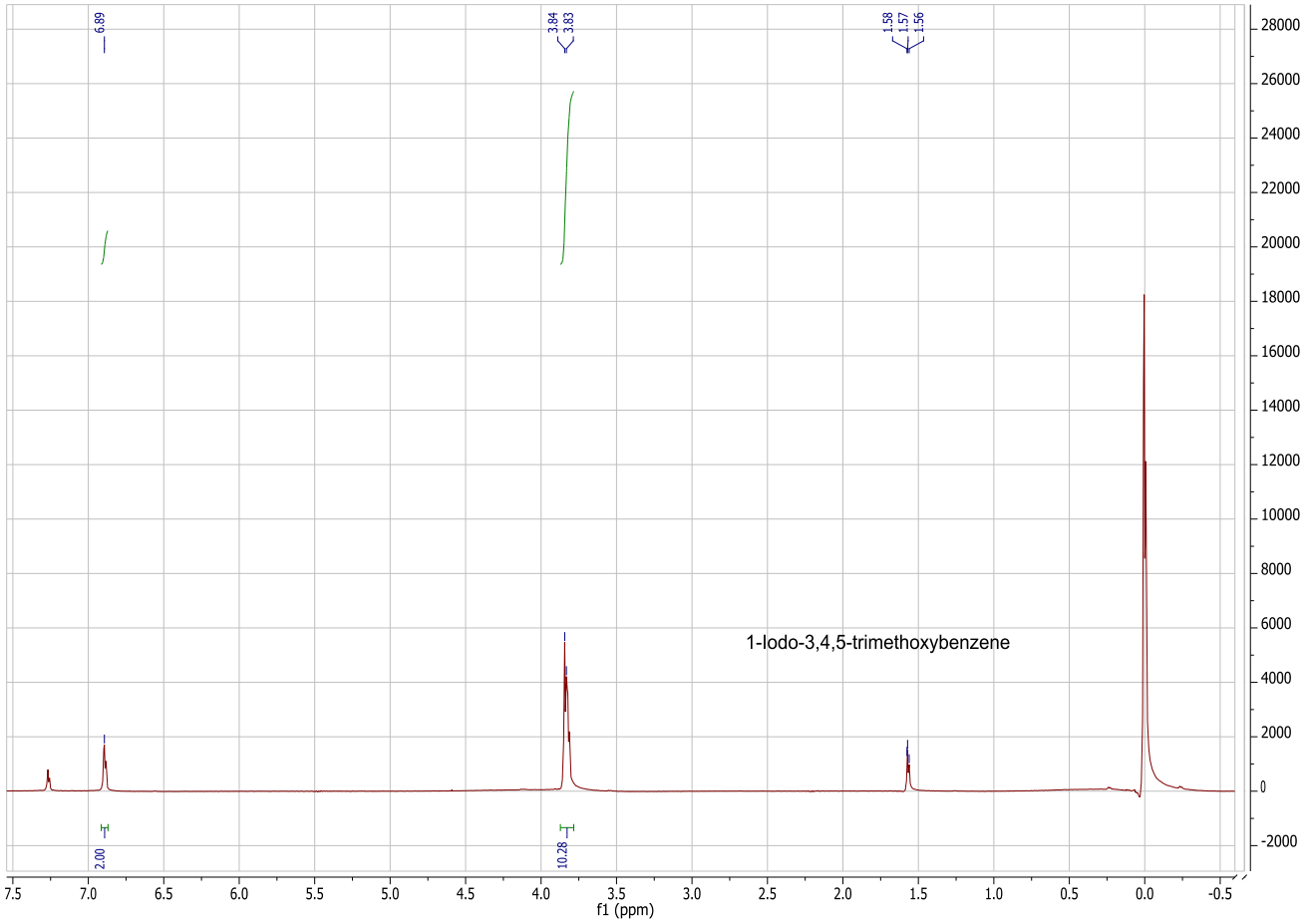


Figure A-29 ^{1}H NMR of 1-Iodo-3,4,5-trimethoxybenzene.

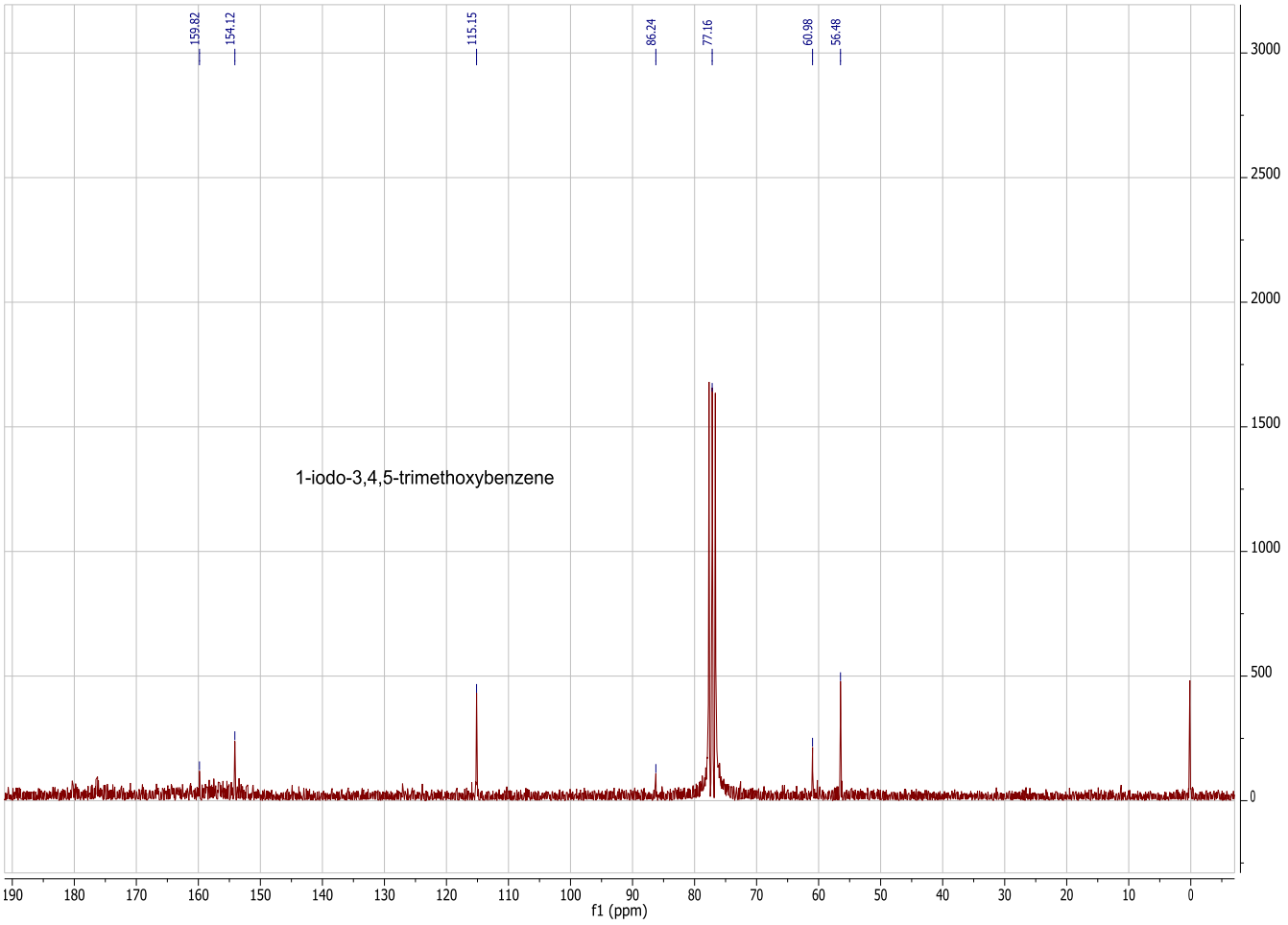


Figure A-30 ^{13}C NMR of 1-Iodo-3,4,5-trimethoxybenzene.

.

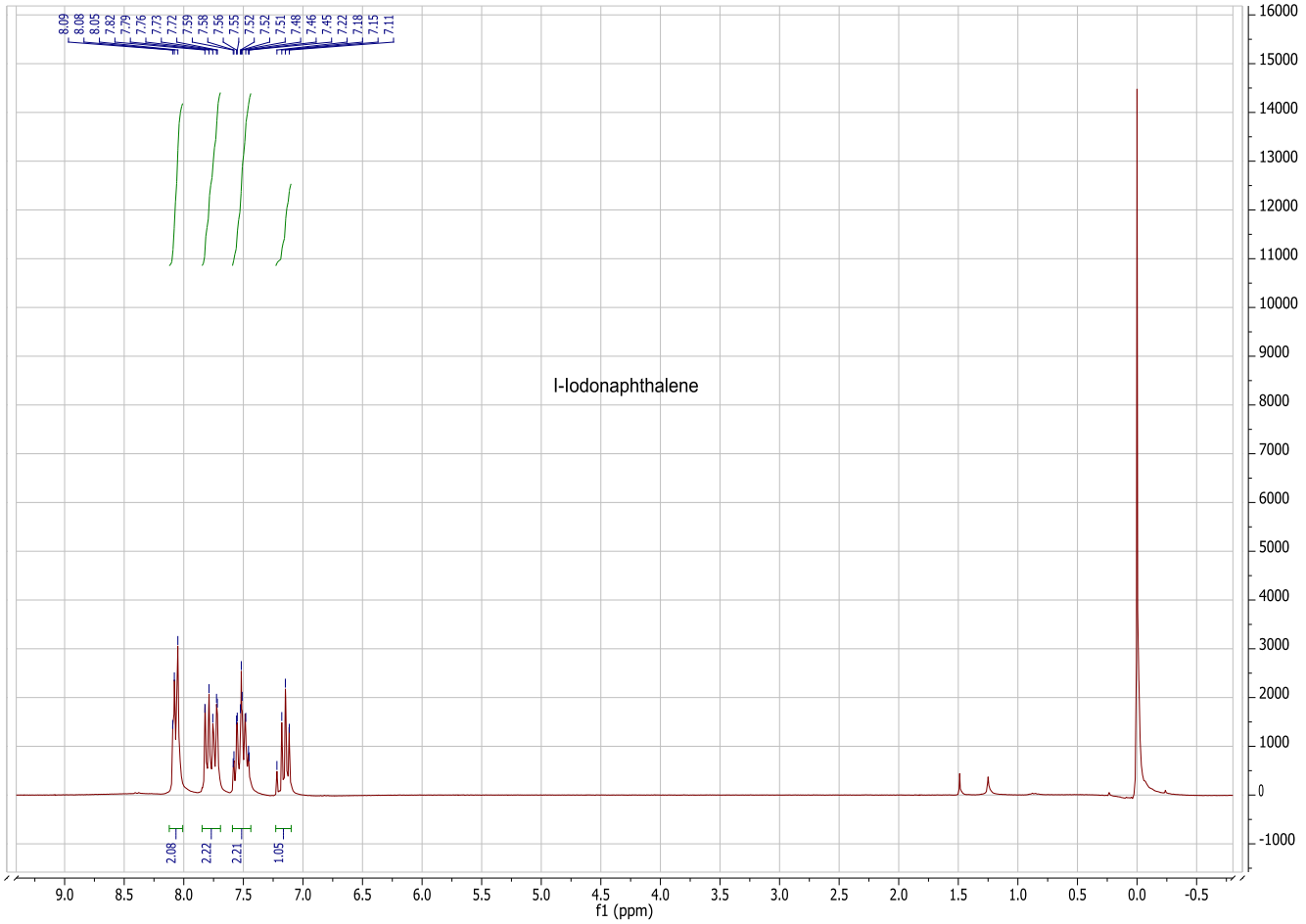


Figure A-31 ^{1}H NMR of 1-Iodonaphthalene.

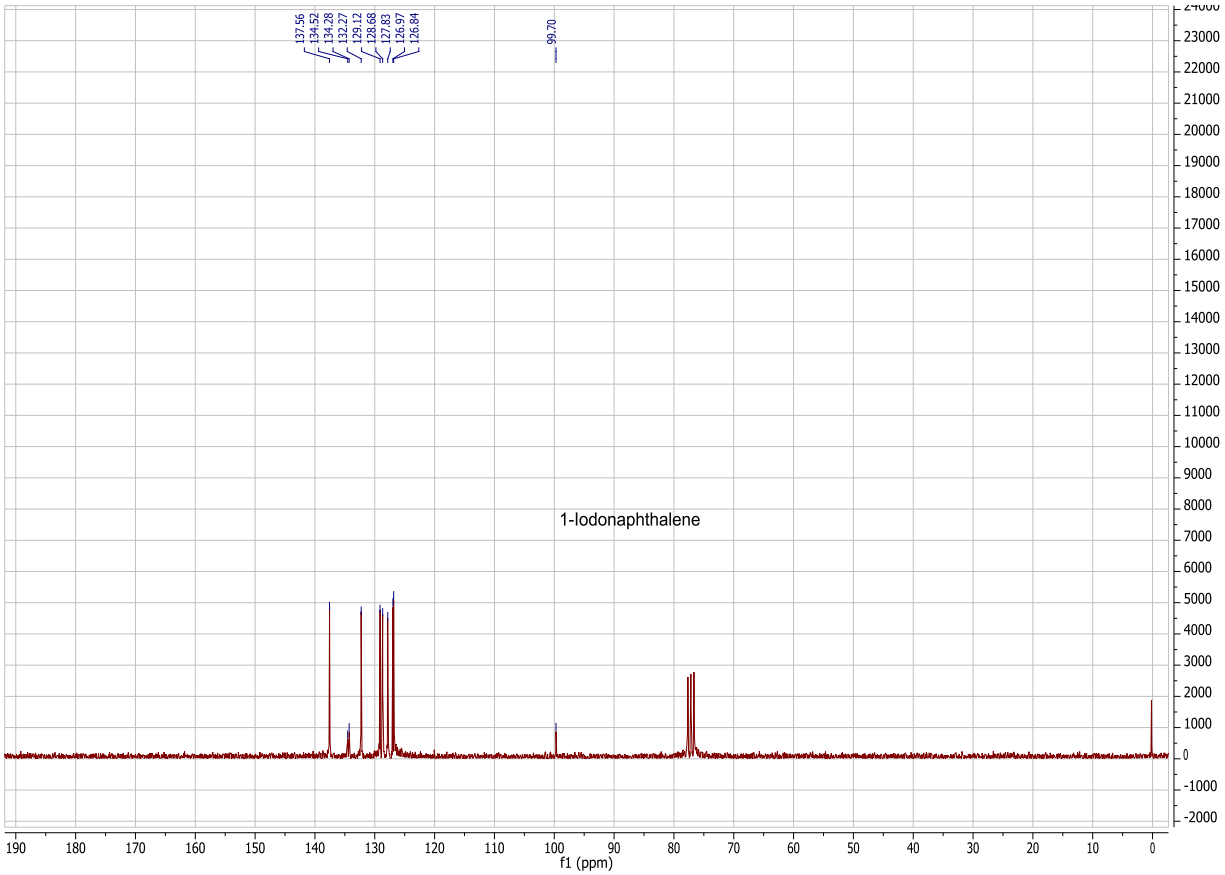


Figure A-32 ^{13}C NMR of 1-Iodonaphthalene.

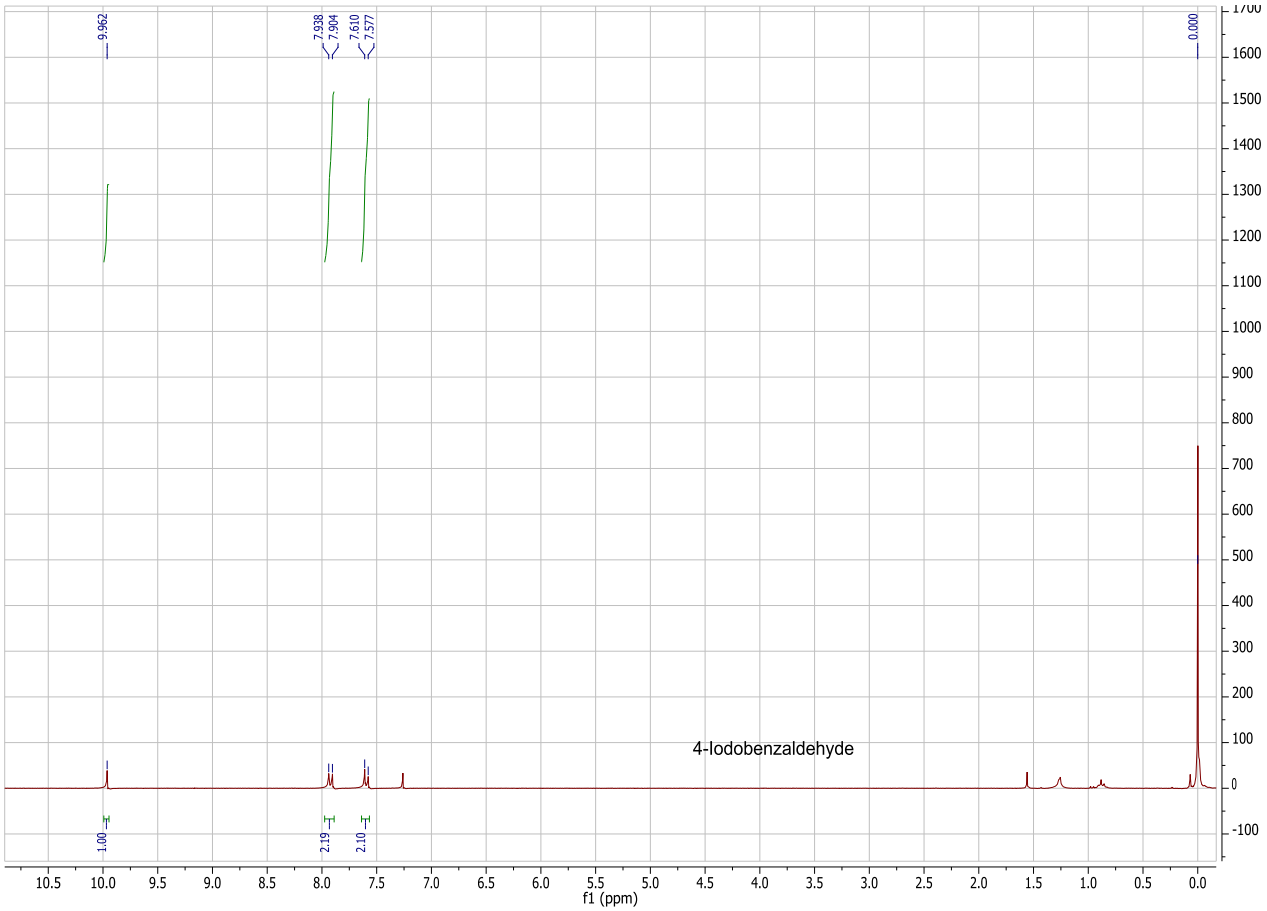


Figure A-33 ^{1}H NMR of 4-Iodobenzaldehyde.

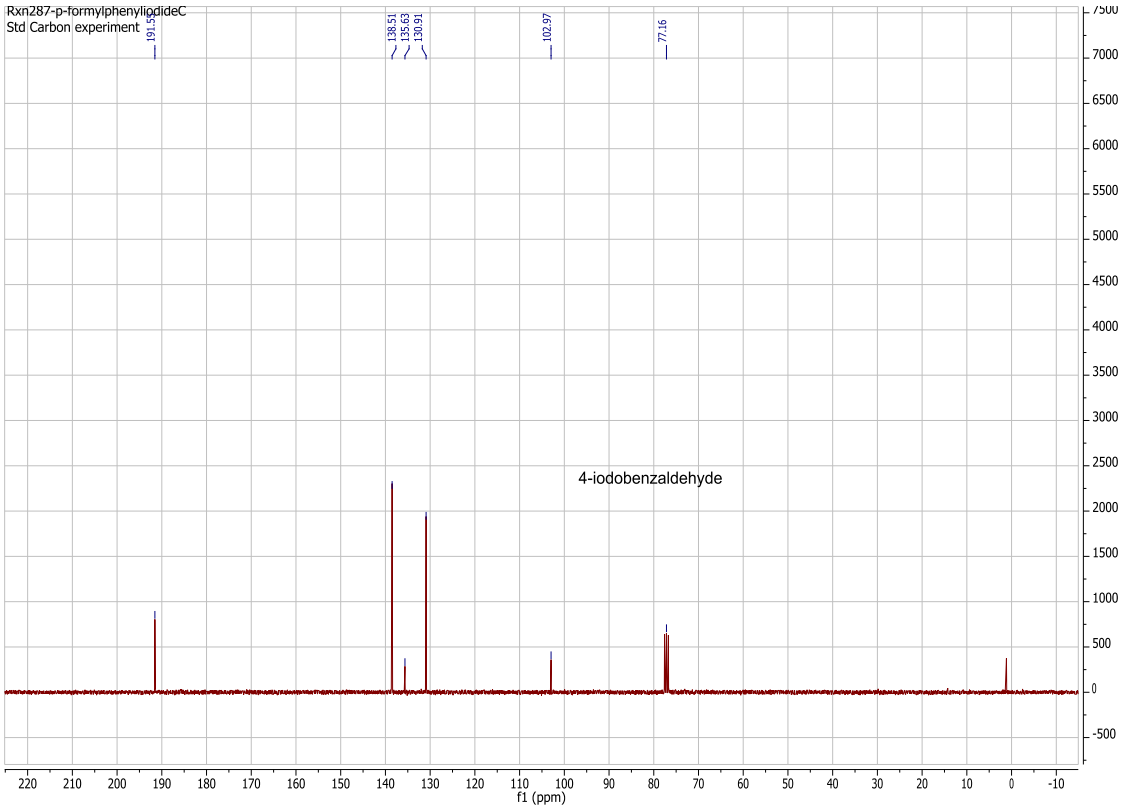


Figure A-34 ^{13}C NMR of 4-Iodobenzaldehyde.

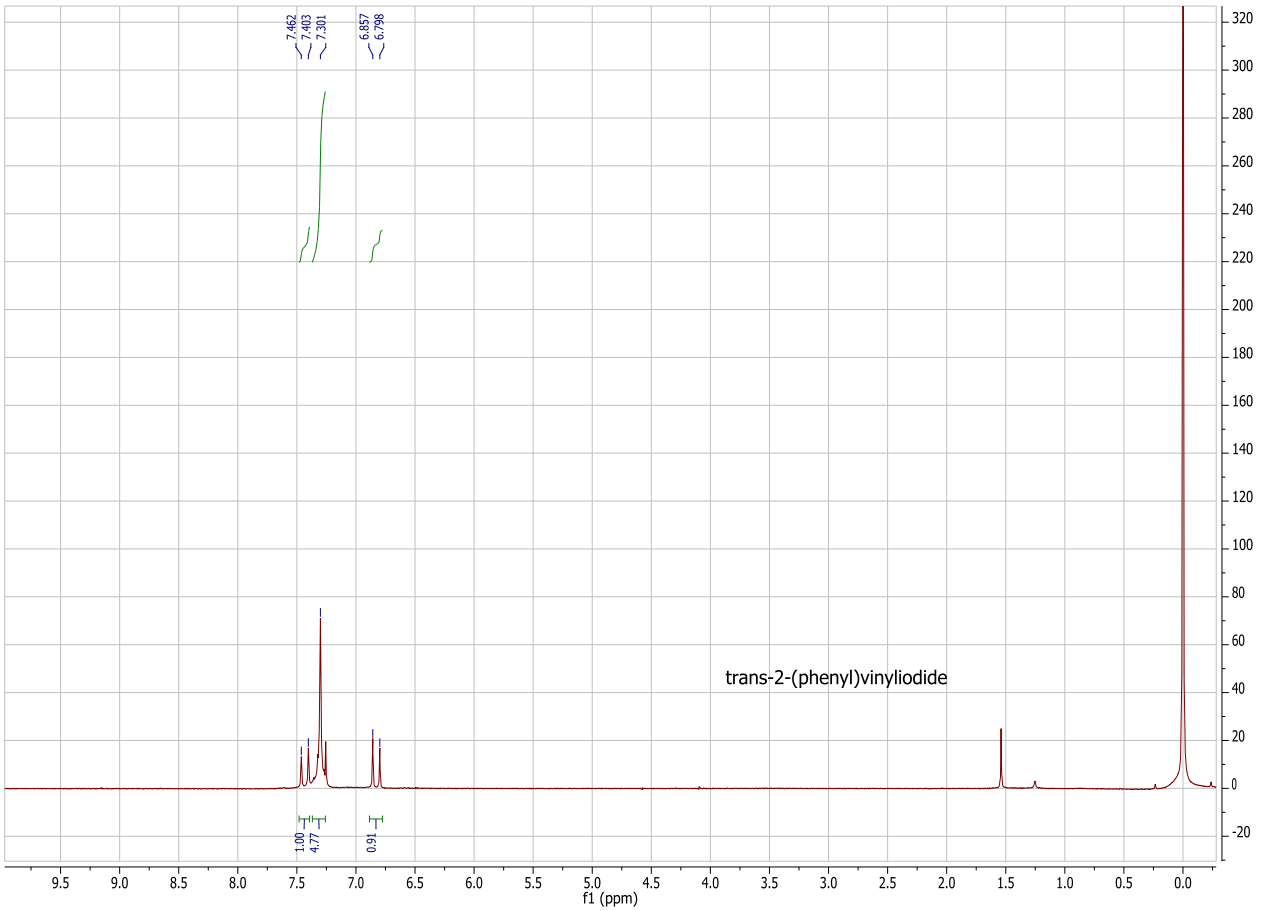


Figure A-35 ^{1}H NMR of *trans*-2-(Phenyl)vinyliodide.

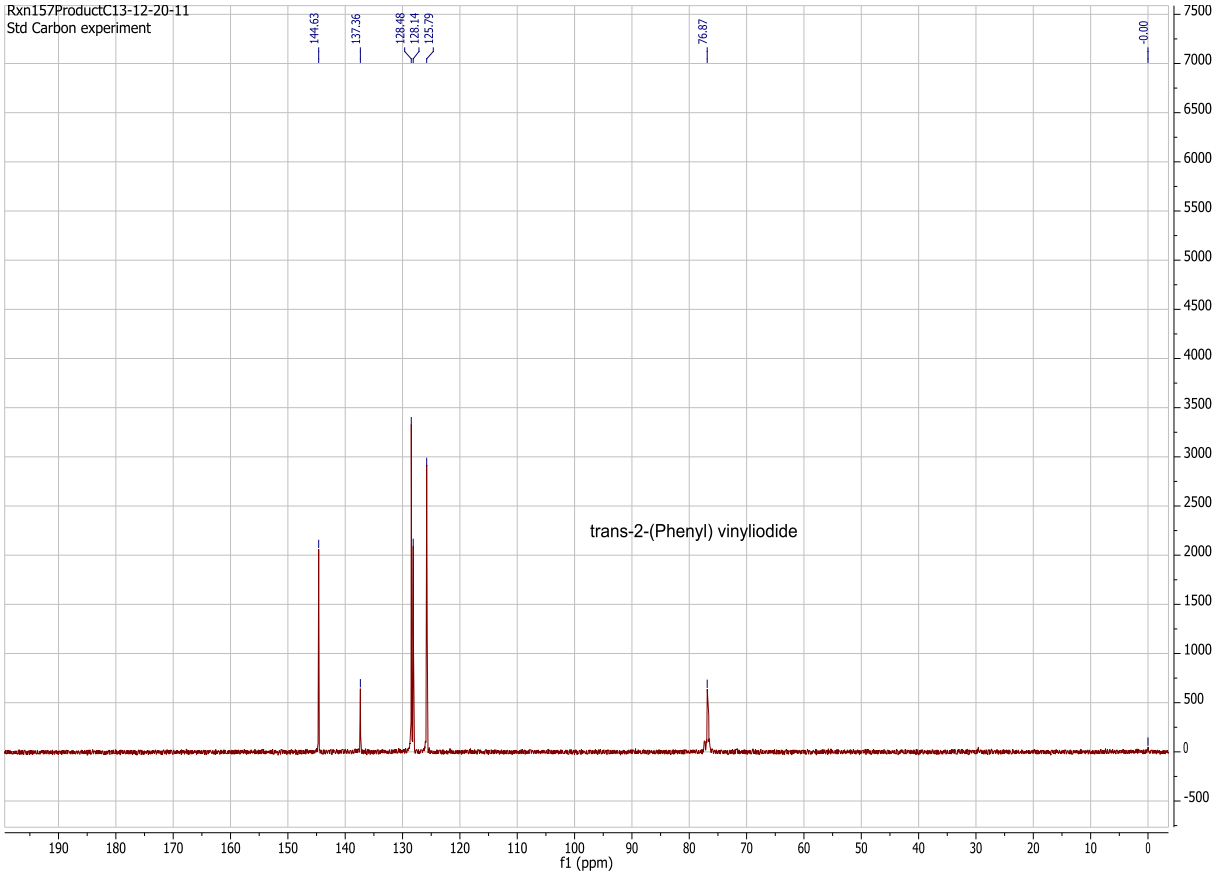


Figure A-36 ^{13}C NMR of *trans*-2-(Phenyl)vinyliodide.

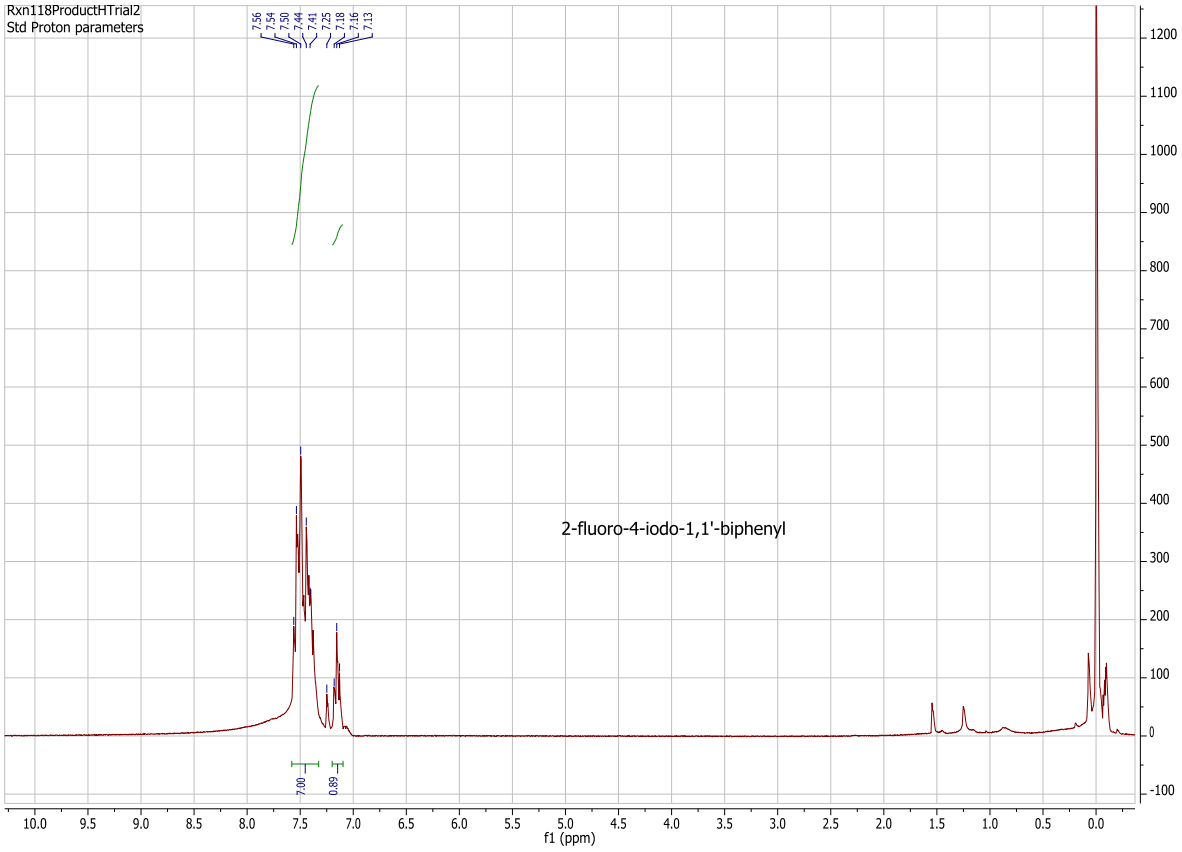


Figure A-37 ^{1}H NMR of 2-Fluoro-4-iodo-1,1'-biphenyl.

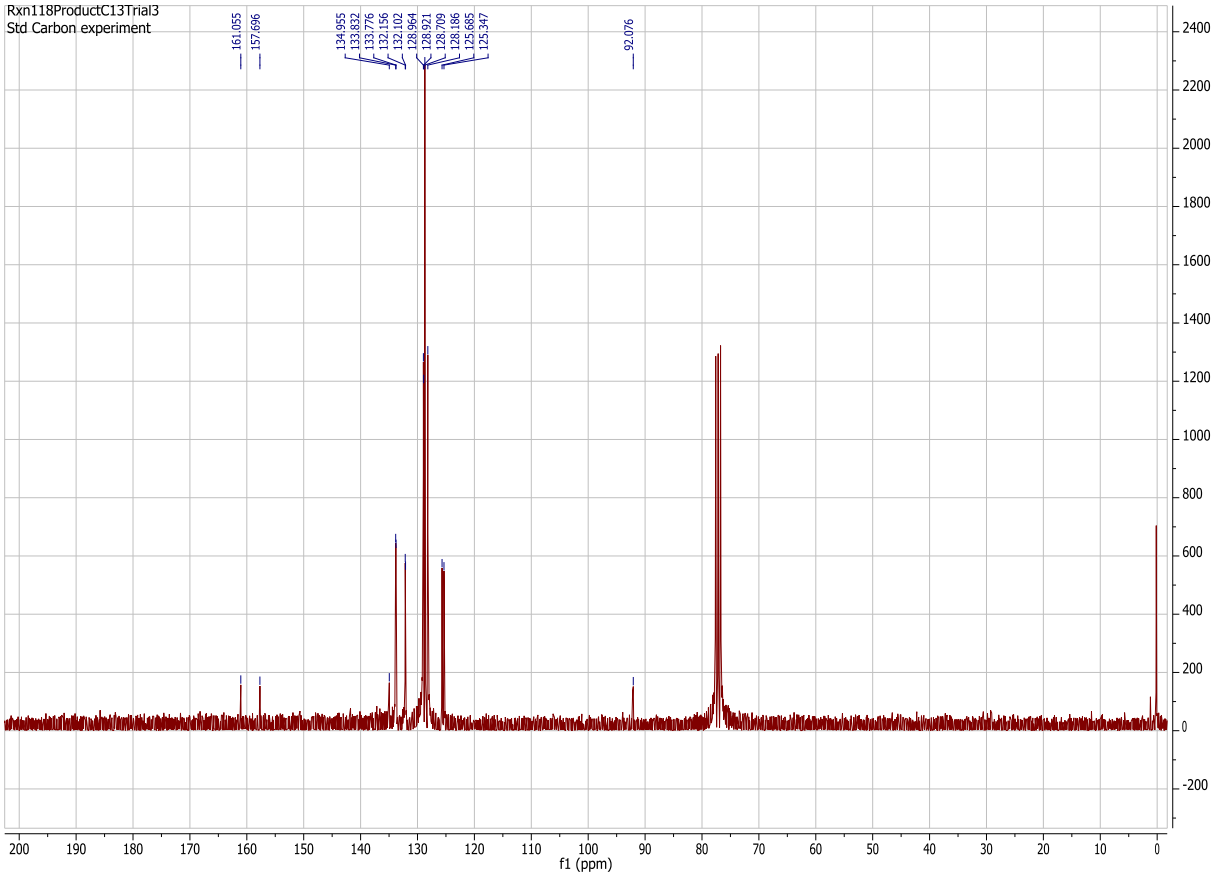


Figure A-38 ^{13}C NMR of 2-Fluoro-4-iodo-1,1'-biphenyl.

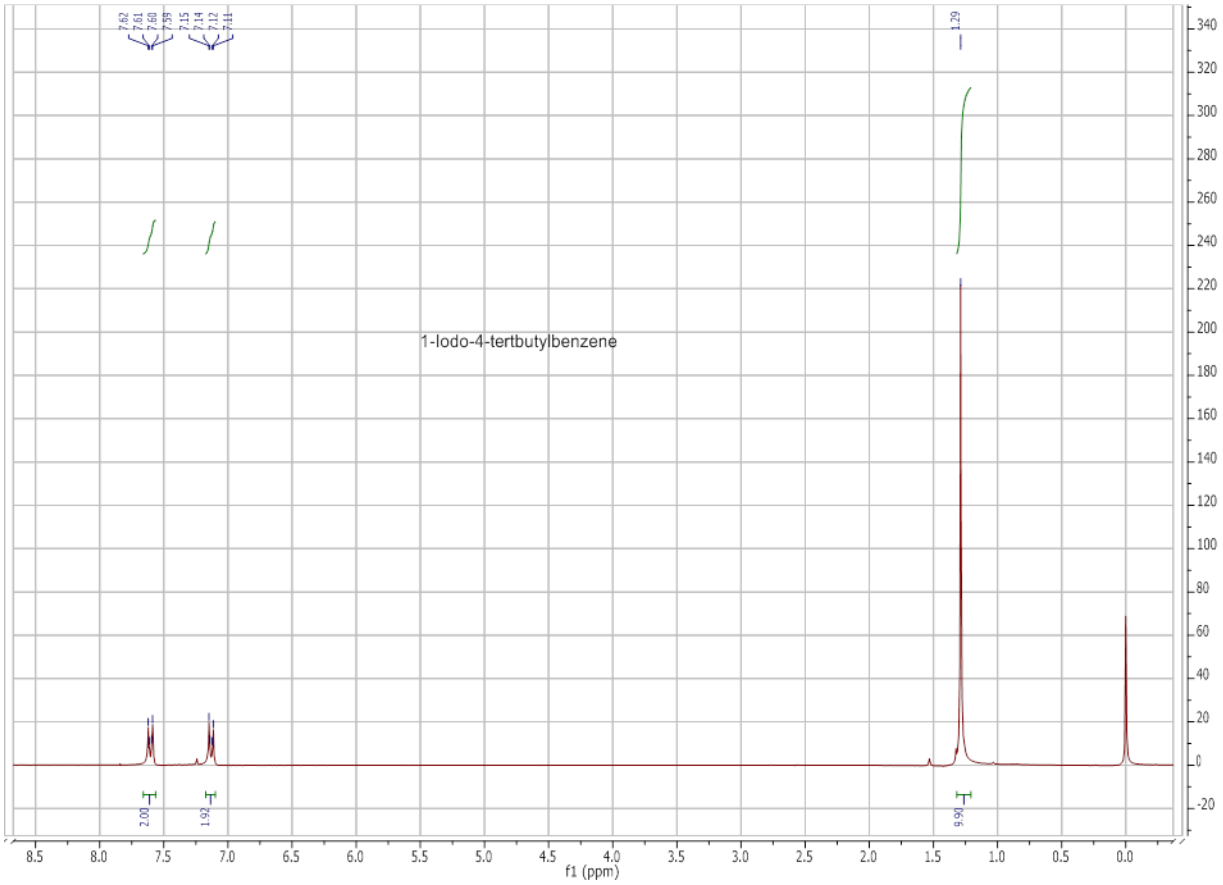


Figure A-39 ^{1}H NMR of 1-Iodo-4-*tert*-butylbenzene.

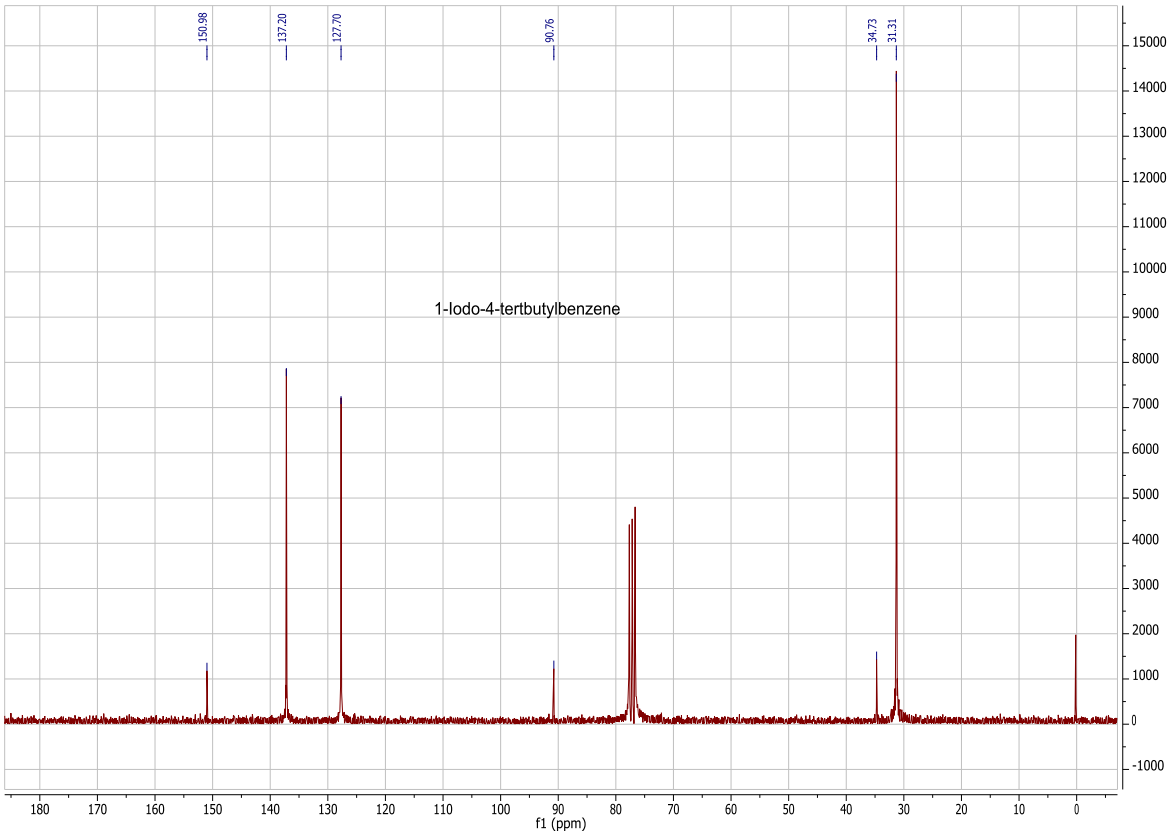


Figure A-40 ^{13}C NMR of 1-Iodo-4-*tert*-butylbenzene.

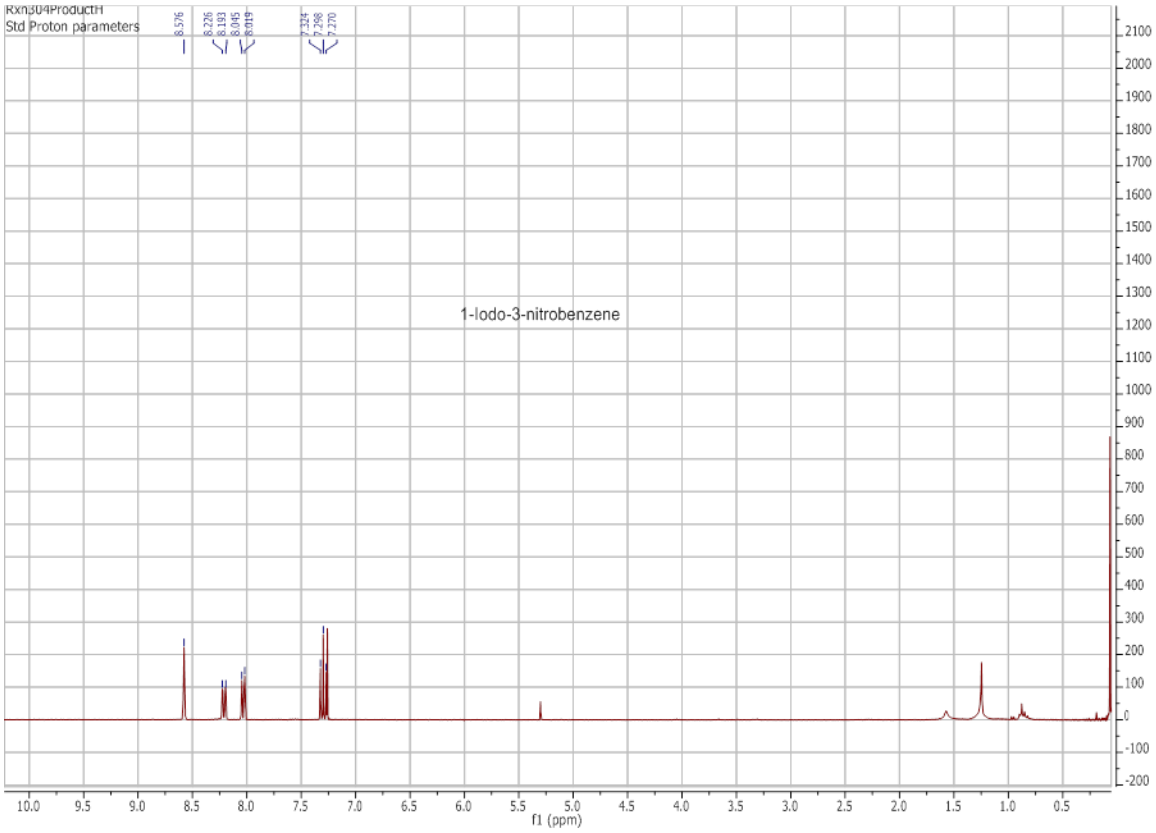


Figure A-41 ^{1}H NMR of 1-Iodo-3-nitrobenzene.

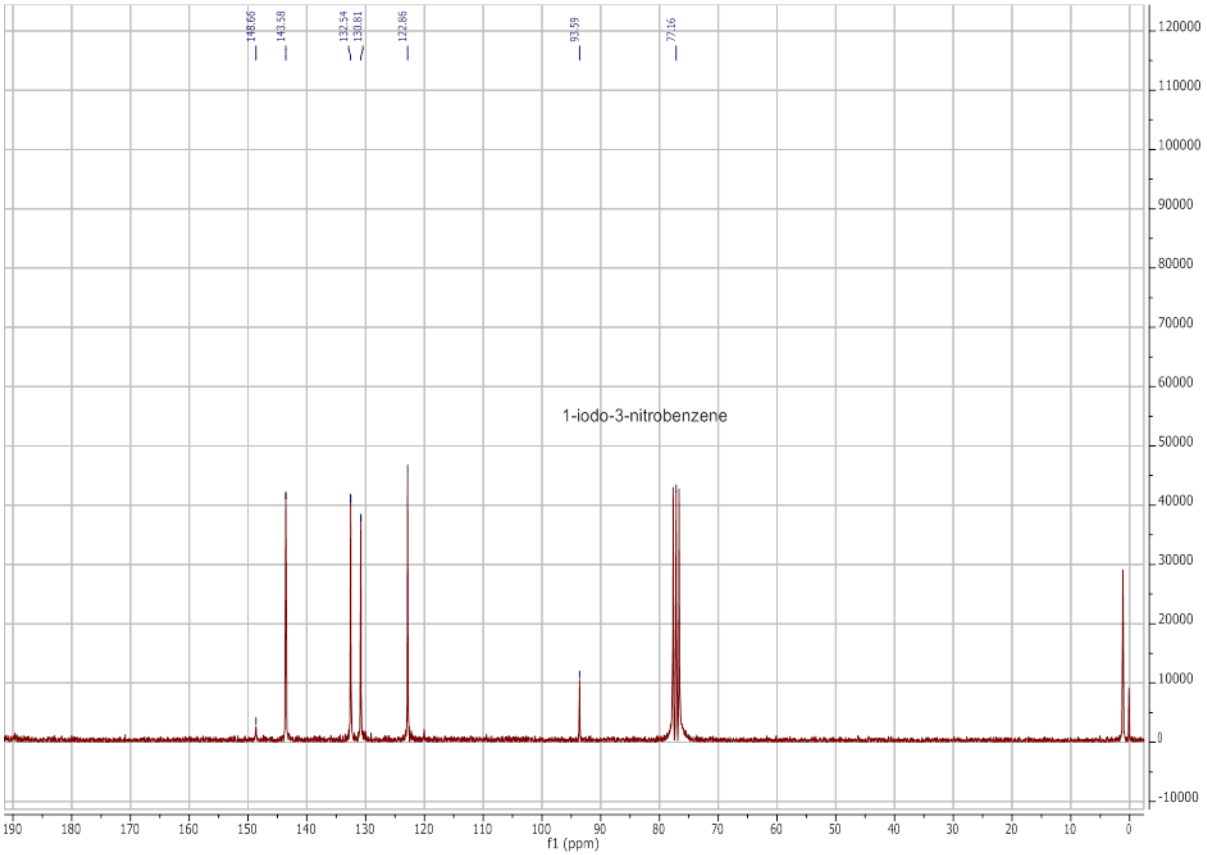


Figure A-42 ^{13}C NMR of 1-Iodo-3-nitrobenzene.

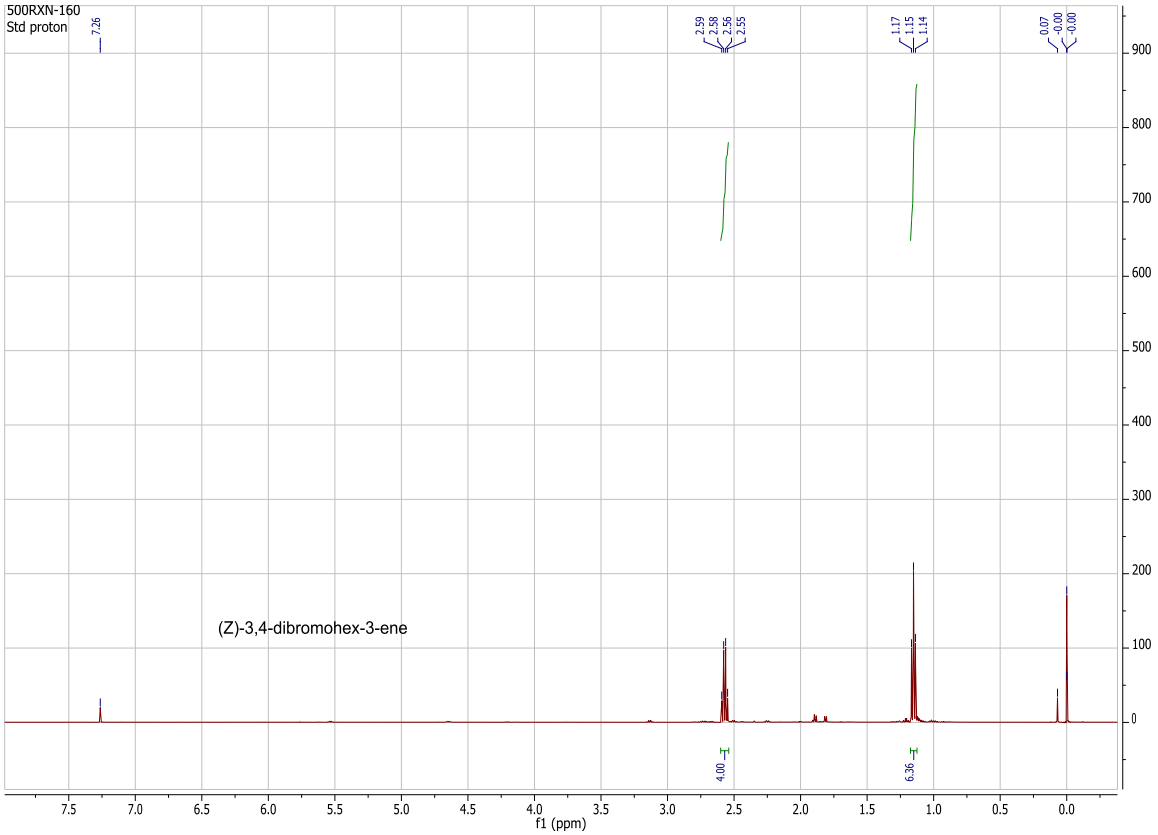


Figure A-43 ^{1}H NMR of (*Z*)-3,4-Dibromohex-3-ene.

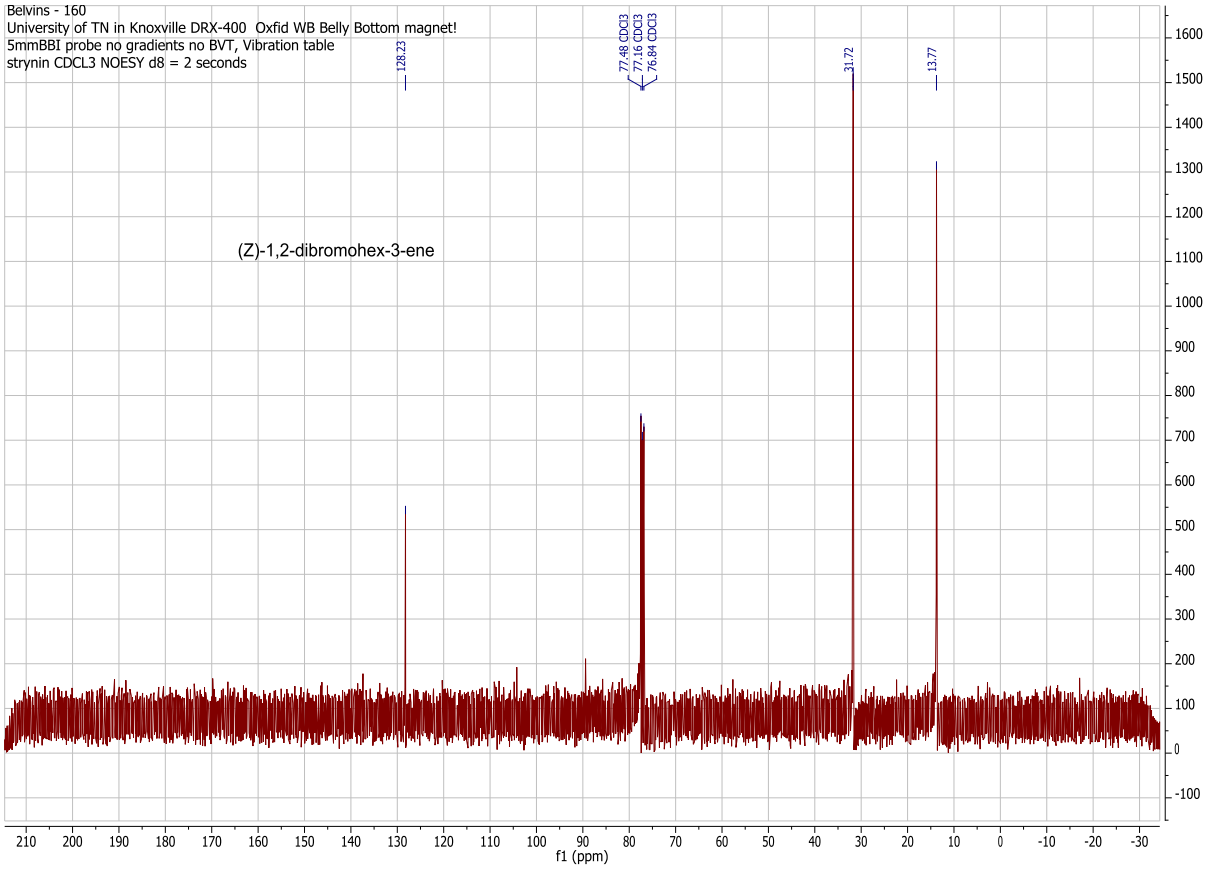


Figure A-44 ^{13}C NMR of (*Z*)-3,4-Dibromohex-3-ene.

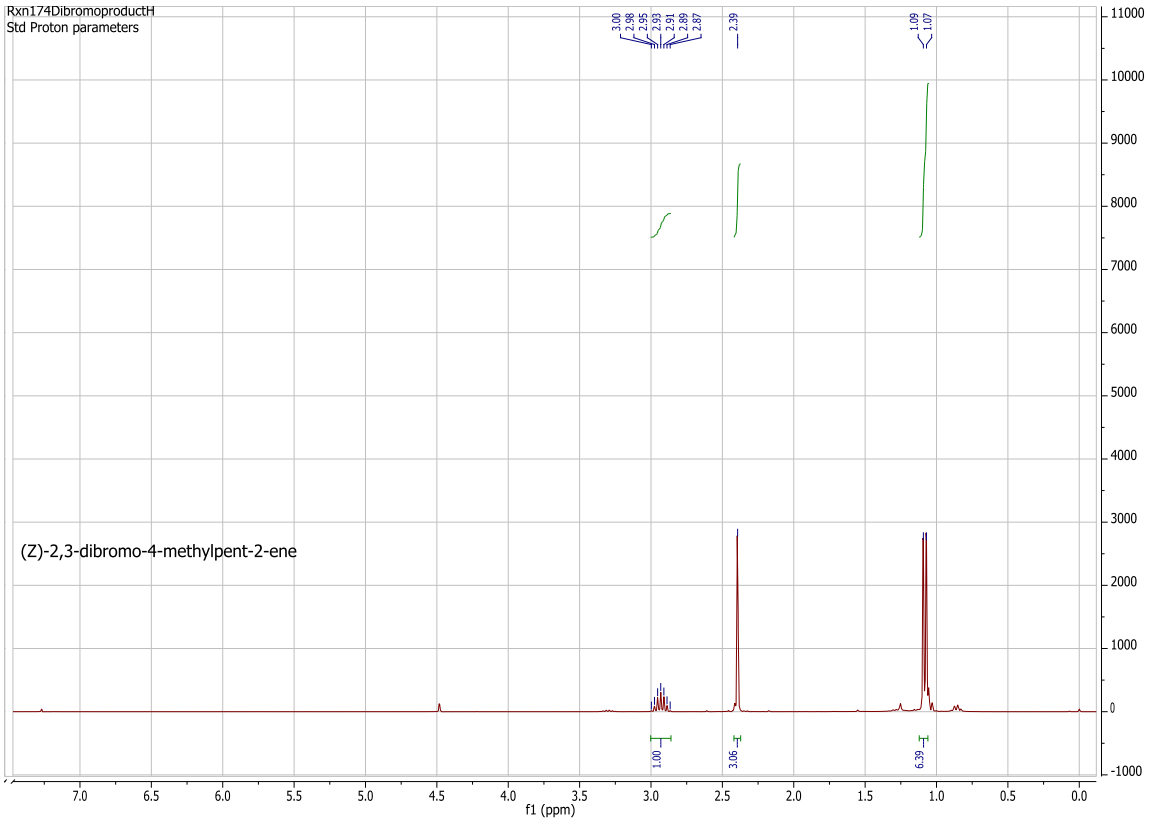


Figure A-45 ^{1}H NMR of (*Z*)-2,3-Dibromo-4-methylpent-2-ene.

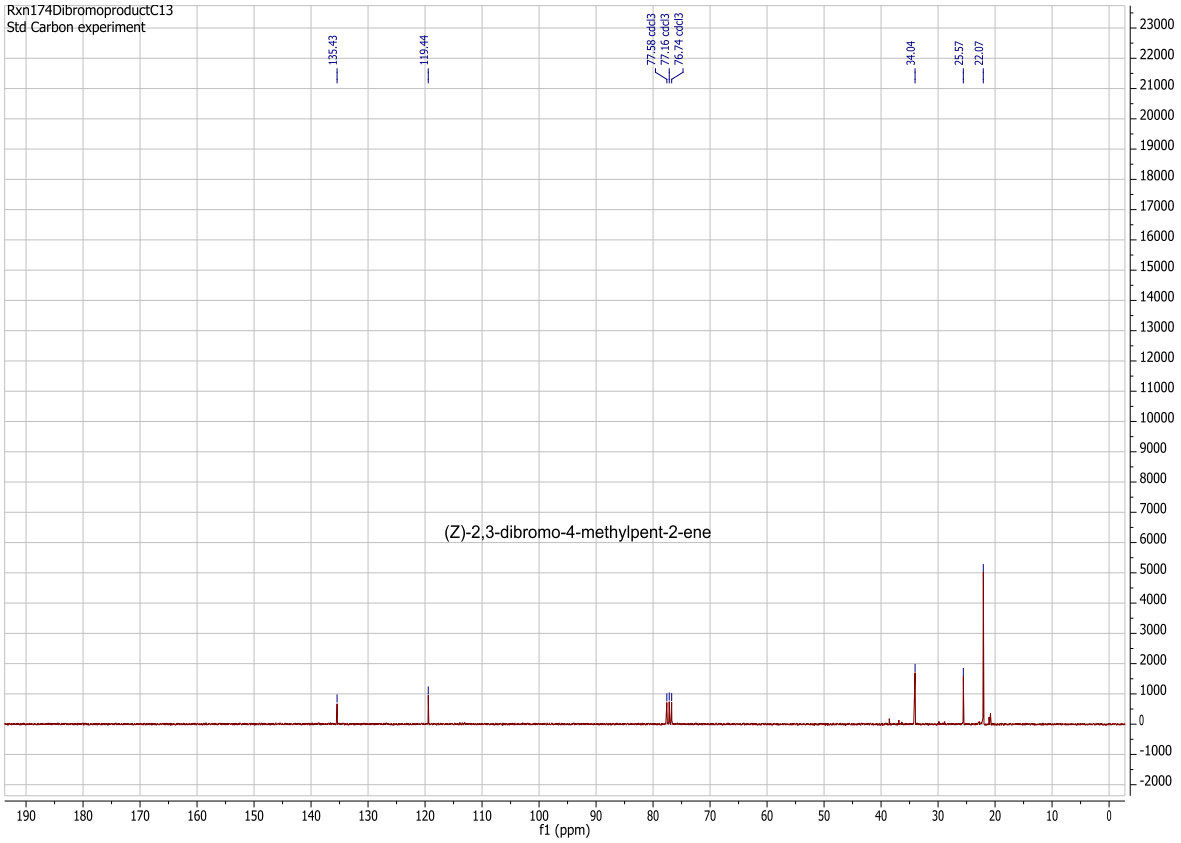


Figure A-46 ^{13}C NMR of (*Z*)-2,3-Dibromo-4-methylpent-2-ene.

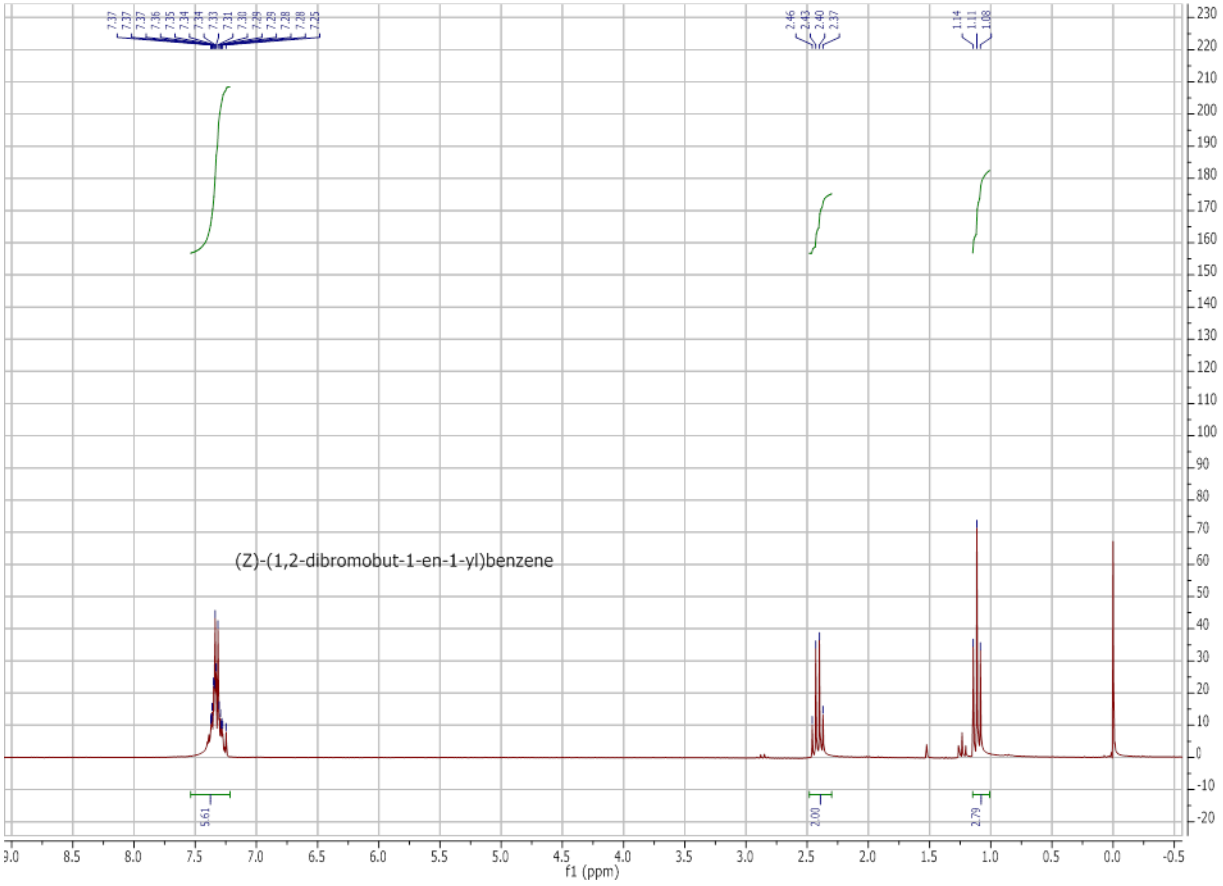


Figure A-47 ^{1}H NMR of (*Z*)-(1,2-Dibromobut-1-en-1-yl)benzene.

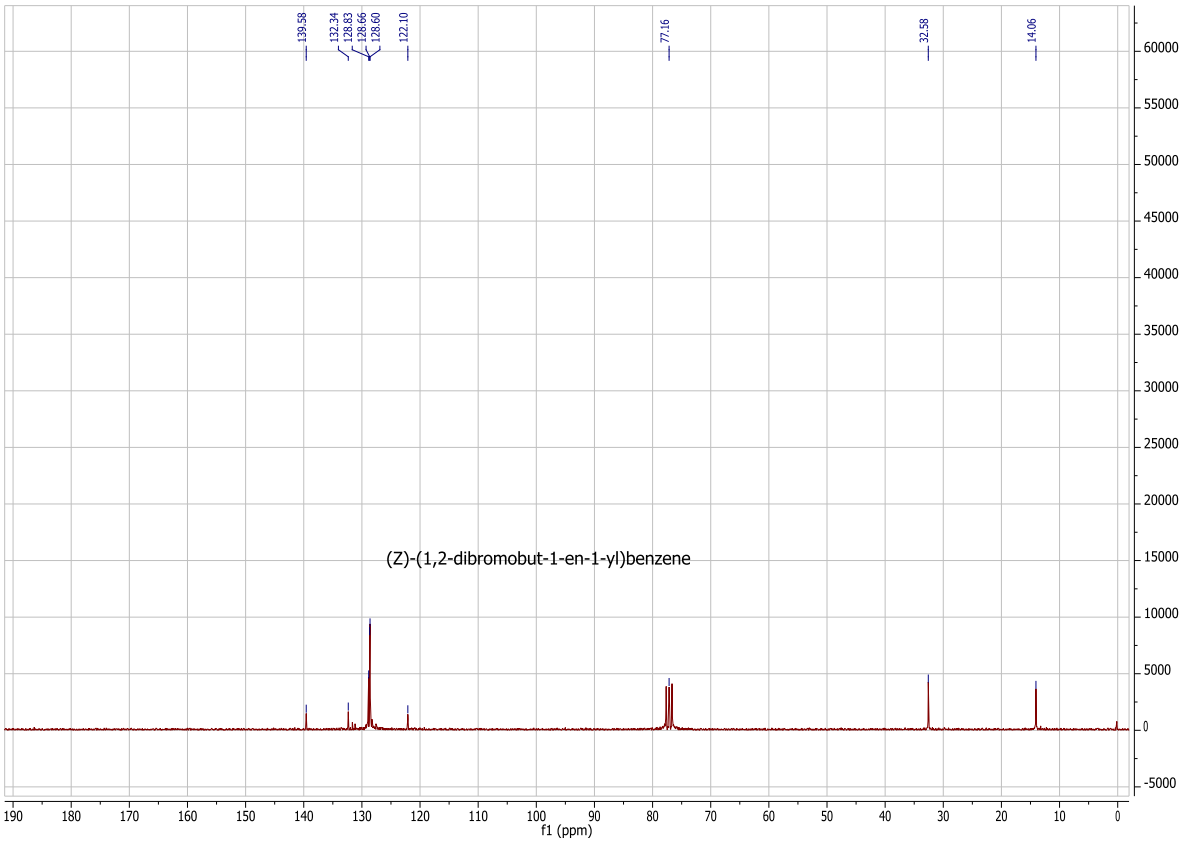


Figure A-48 ^{13}C NMR of (*Z*)-(1,2-Dibromobut-1-en-1-yl)benzene.

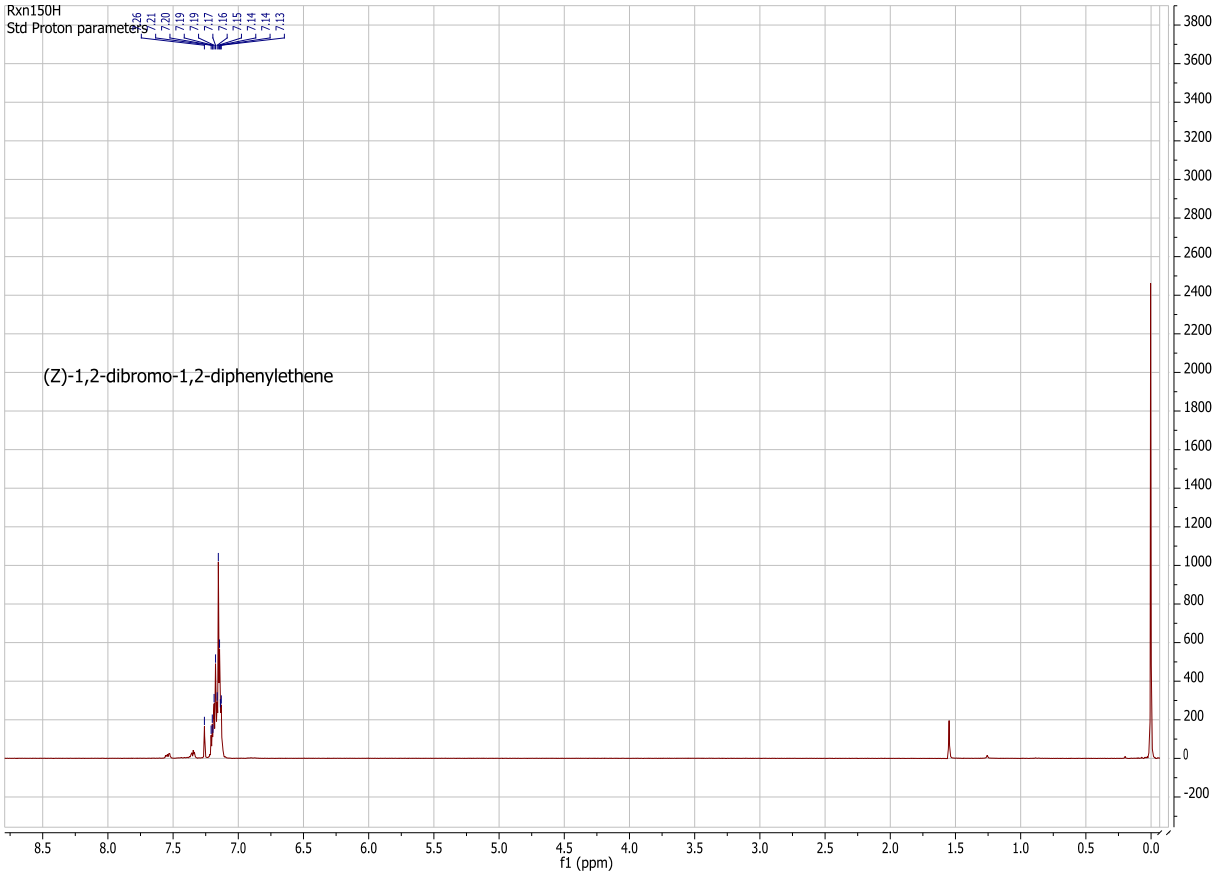


Figure A-49 ^{1}H NMR of (*Z*)-1,2-Dibromo-1,2-diphenylethene.

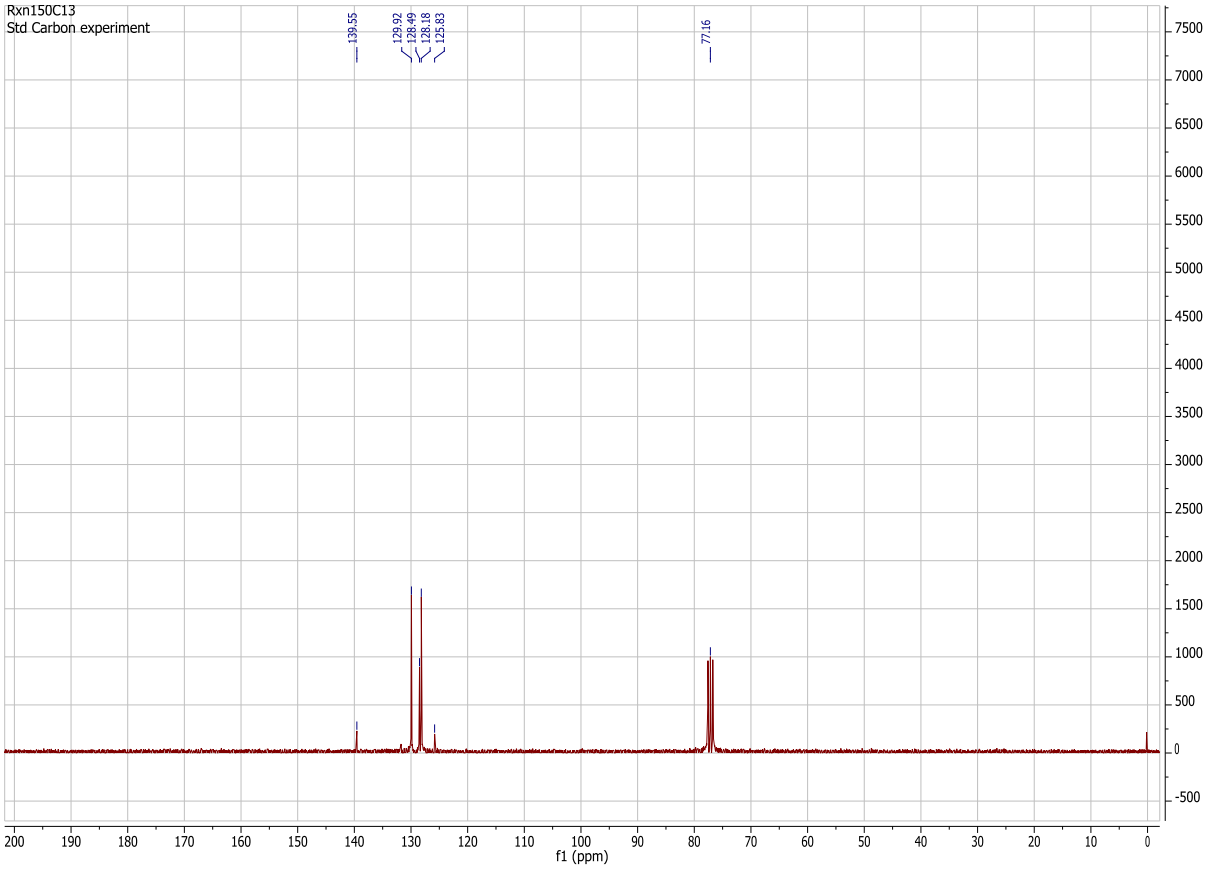
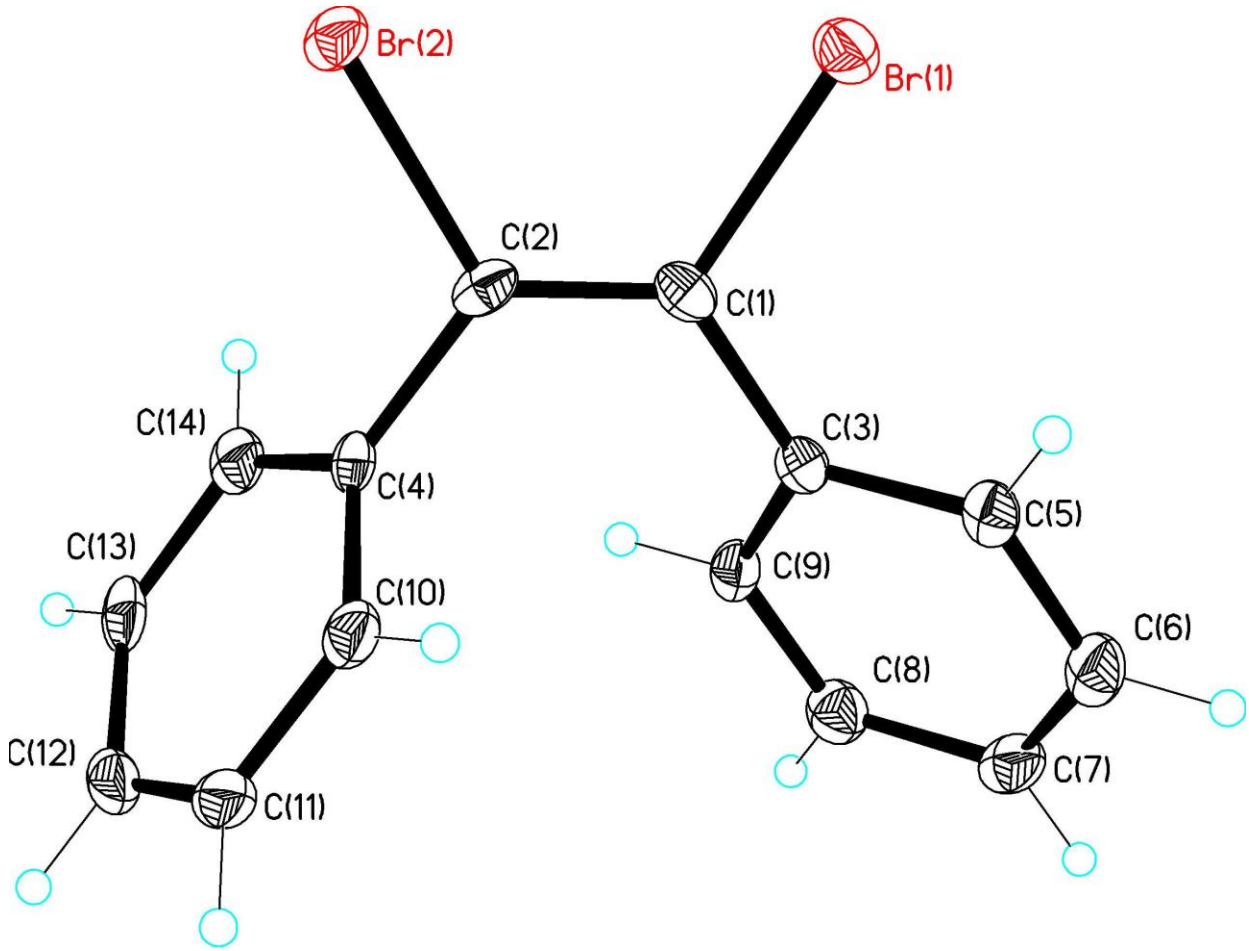


Figure A-50 ^{13}C NMR of (*Z*)-1,2-Dibromo-1,2-diphenylethene.



ORTEP drawing of (*Z*)-dibromodiphenylalkene showing 50% probability of the thermal ellipsoid.

Figure A-51 X-Ray Diffraction data for (*Z*)-(1,2-dibromo)stilbene. Supplemental data tables follow.

Table A-1 Crystal data and structure refinement for (Z)-dibromodiphenylalkene.

Identification code	yml-2012	
Empirical formula	C14 H10 Br2	
Formula weight	338.04	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	p 21/n	
Unit cell dimensions	a = 5.8014(7) Å	α= 90°.
	b = 12.4876(13) Å	β= 92.819(5)°.
	c = 16.8978(19) Å	γ = 90°.
Volume	1222.7(2) $Å^3$	
Z	4	
Density (calculated)	1.836 Mg/m^3	
Absorption coefficient	6.598 mm^{-1}	
F(000)	656	
Crystal size	0.12 x 0.10 x 0.05 mm^3	
Theta range for data collection	2.03 to 27.30°.	
Index ranges	-7<=h<=7, -15<=k<=16, -21<=l<=21	
Reflections collected	12980	
Independent reflections	2733 [R(int) = 0.0543]	
Completeness to theta = 27.30°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7338 and 0.5049	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2733 / 0 / 146	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0338, wR2 = 0.0756	
R indices (all data)	R1 = 0.0483, wR2 = 0.0813	
Largest diff. peak and hole	0.903 and -0.756 $e.Å^{-3}$	

Table A-2 Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103) for Yml-2012. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br(1)	1248(1)	502(1)	3605(1)	21(1)
Br(2)	4369(1)	2556(1)	3007(1)	20(1)
C(1)	763(5)	1089(2)	2567(2)	16(1)
C(2)	1998(5)	1925(2)	2333(2)	16(1)
C(3)	-991(5)	503(2)	2066(2)	15(1)
C(4)	1716(5)	2455(2)	1550(2)	16(1)
C(6)	-4667(6)	-406(3)	1914(2)	22(1)
C(5)	-3045(5)	156(2)	2378(2)	16(1)
C(8)	-2179(6)	-321(3)	820(2)	22(1)
C(7)	-4227(6)	-656(3)	1133(2)	23(1)
C(9)	-580(5)	246(2)	1278(2)	18(1)
C(14)	3465(6)	2421(2)	1015(2)	20(1)
C(10)	-324(5)	3010(3)	1350(2)	19(1)
C(12)	1145(6)	3471(3)	87(2)	23(1)
C(11)	-584(6)	3516(3)	616(2)	22(1)
C(13)	3174(6)	2919(3)	283(2)	21(1)

Table A-3 Bond lengths [Å] and angles [°] for Yml-2012.

Br(1)-C(1)	1.909(3)
Br(2)-C(2)	1.912(3)
C(1)-C(2)	1.337(4)
C(1)-C(3)	1.484(4)
C(2)-C(4)	1.482(4)
C(3)-C(5)	1.396(4)
C(3)-C(9)	1.401(4)
C(4)-C(14)	1.392(5)
C(4)-C(10)	1.398(4)
C(6)-C(5)	1.385(4)
C(6)-C(7)	1.393(5)
C(6)-H(6)	0.9500
C(5)-H(5)	0.9500
C(8)-C(9)	1.375(4)
C(8)-C(7)	1.389(5)
C(8)-H(8)	0.9500
C(7)-H(7)	0.9500
C(9)-H(9)	0.9500
C(14)-C(13)	1.387(5)
C(14)-H(14)	0.9500
C(10)-C(11)	1.394(5)
C(10)-H(10)	0.9500
C(12)-C(11)	1.377(5)
C(12)-C(13)	1.390(5)
C(12)-H(12)	0.9500
C(11)-H(11)	0.9500
C(13)-H(13)	0.9500
C(2)-C(1)-C(3)	125.4(3)
C(2)-C(1)-Br(1)	120.9(2)
C(3)-C(1)-Br(1)	113.7(2)
C(1)-C(2)-C(4)	125.1(3)

Table A-3 (Continued)

C(1)-C(2)-Br(2)	121.8(2)
C(4)-C(2)-Br(2)	113.1(2)
C(5)-C(3)-C(9)	118.5(3)
C(5)-C(3)-C(1)	120.8(3)
C(9)-C(3)-C(1)	120.7(3)
C(14)-C(4)-C(10)	119.6(3)
C(14)-C(4)-C(2)	120.9(3)
C(10)-C(4)-C(2)	119.5(3)
C(5)-C(6)-C(7)	119.9(3)
C(5)-C(6)-H(6)	120.0
C(7)-C(6)-H(6)	120.0
C(6)-C(5)-C(3)	120.8(3)
C(6)-C(5)-H(5)	119.6
C(3)-C(5)-H(5)	119.6
C(9)-C(8)-C(7)	120.5(3)
C(9)-C(8)-H(8)	119.8
C(7)-C(8)-H(8)	119.8
C(8)-C(7)-C(6)	119.6(3)
C(8)-C(7)-H(7)	120.2
C(6)-C(7)-H(7)	120.2
C(8)-C(9)-C(3)	120.8(3)
C(8)-C(9)-H(9)	119.6
C(3)-C(9)-H(9)	119.6
C(13)-C(14)-C(4)	120.3(3)
C(13)-C(14)-H(14)	119.9
C(4)-C(14)-H(14)	119.9
C(11)-C(10)-C(4)	119.5(3)
C(11)-C(10)-H(10)	120.2
C(4)-C(10)-H(10)	120.2
C(11)-C(12)-C(13)	120.0(3)
C(11)-C(12)-H(12)	120.0
C(13)-C(12)-H(12)	120.0

Table A-3 (Continued)

C(12)-C(11)-C(10)	120.6(3)
C(12)-C(11)-H(11)	119.7
C(10)-C(11)-H(11)	119.7
C(14)-C(13)-C(12)	120.0(3)
C(14)-C(13)-H(13)	120.0
C(12)-C(13)-H(13)	120.0

Symmetry transformations used to generate equivalent atoms:

Table A-4 Anisotropic displacement parameters (Å2x 103) for Yml-2012. The anisotropic displacement factor exponent takes the form: -2□2[h2 a*2U11 + ... + 2 h k a* b* U12]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	25(1)	18(1)	19(1)	3(1)	-1(1)	-1(1)
Br(2)	20(1)	12(1)	26(1)	-1(1)	-5(1)	-1(1)
C(1)	19(2)	14(2)	16(2)	2(1)	2(1)	4(1)
C(2)	13(2)	12(2)	22(2)	-5(1)	-4(1)	2(1)
C(3)	18(2)	7(2)	21(2)	2(1)	-2(1)	1(1)
C(4)	19(2)	8(2)	21(2)	0(1)	-2(1)	-5(1)
C(6)	19(2)	14(2)	34(2)	4(1)	2(1)	0(1)
C(5)	18(2)	9(2)	22(2)	1(1)	2(1)	2(1)
C(8)	26(2)	20(2)	21(2)	0(1)	0(1)	-2(1)
C(7)	22(2)	15(2)	30(2)	0(1)	-7(1)	-2(1)
C(9)	18(2)	16(2)	20(2)	1(1)	2(1)	-4(1)
C(14)	21(2)	10(2)	28(2)	-1(1)	-1(1)	-1(1)
C(10)	17(2)	14(2)	25(2)	-1(1)	-1(1)	-4(1)
C(12)	33(2)	16(2)	20(2)	3(1)	-6(1)	-9(1)
C(11)	22(2)	14(2)	29(2)	1(1)	-9(1)	-2(1)
C(13)	29(2)	13(2)	23(2)	-3(1)	5(1)	-9(1)

Table A-5 Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3) for Yml-2012.

	x	y	z	U(eq)
H(6)	-6077	-621	2129	27
H(5)	-3334	307	2915	20
H(8)	-1880	-485	286	27
H(7)	-5322	-1053	815	27
H(9)	820	465	1058	22
H(14)	4864	2055	1152	24
H(10)	-1523	3043	1712	23
H(12)	951	3817	-412	28
H(11)	-1967	3895	479	27
H(13)	4361	2882	-84	26

Table A-6 Torsion angles [°] for Yml-2012.

C(3)-C(1)-C(2)-C(4)	4.2(5)
Br(1)-C(1)-C(2)-C(4)	-178.4(2)
C(3)-C(1)-C(2)-Br(2)	-175.6(2)
Br(1)-C(1)-C(2)-Br(2)	1.8(4)
C(2)-C(1)-C(3)-C(5)	-140.2(3)
Br(1)-C(1)-C(3)-C(5)	42.3(3)
C(2)-C(1)-C(3)-C(9)	42.7(4)
Br(1)-C(1)-C(3)-C(9)	-134.9(2)
C(1)-C(2)-C(4)-C(14)	-114.4(4)
Br(2)-C(2)-C(4)-C(14)	65.3(3)
C(1)-C(2)-C(4)-C(10)	66.5(4)
Br(2)-C(2)-C(4)-C(10)	-113.7(3)
C(7)-C(6)-C(5)-C(3)	1.8(5)
C(9)-C(3)-C(5)-C(6)	-1.7(4)
C(1)-C(3)-C(5)-C(6)	-178.9(3)
C(9)-C(8)-C(7)-C(6)	0.5(5)
C(5)-C(6)-C(7)-C(8)	-1.2(5)
C(7)-C(8)-C(9)-C(3)	-0.5(5)
C(5)-C(3)-C(9)-C(8)	1.0(4)
C(1)-C(3)-C(9)-C(8)	178.3(3)
C(10)-C(4)-C(14)-C(13)	-1.1(4)
C(2)-C(4)-C(14)-C(13)	179.9(3)
C(14)-C(4)-C(10)-C(11)	0.5(4)
C(2)-C(4)-C(10)-C(11)	179.5(3)
C(13)-C(12)-C(11)-C(10)	-0.1(5)
C(4)-C(10)-C(11)-C(12)	0.1(5)
C(4)-C(14)-C(13)-C(12)	1.2(5)
C(11)-C(12)-C(13)-C(14)	-0.6(5)

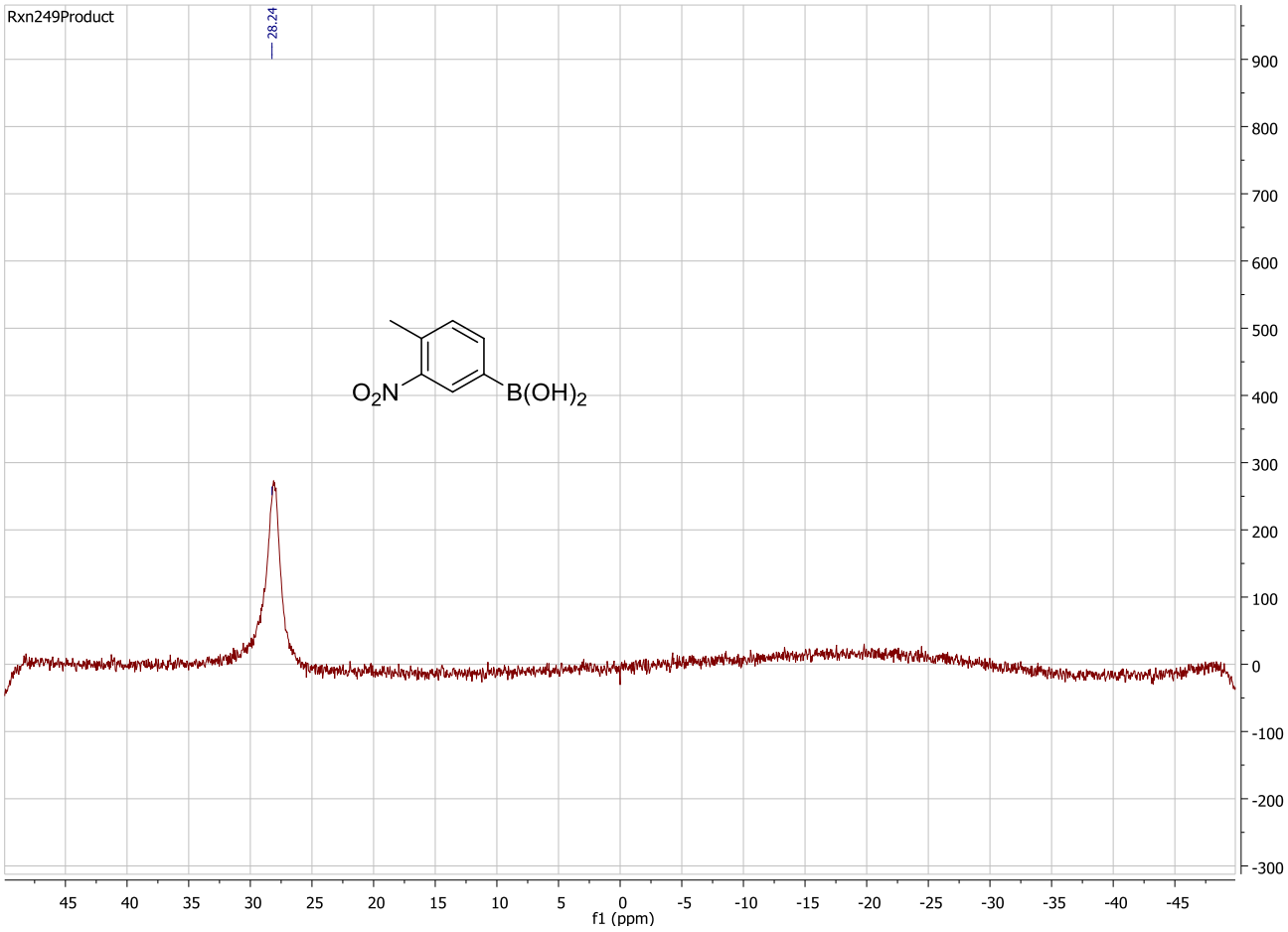


Figure A-52 ^{11}B NMR of *o*-Nitrotolyl-*p*-boronic Acid.

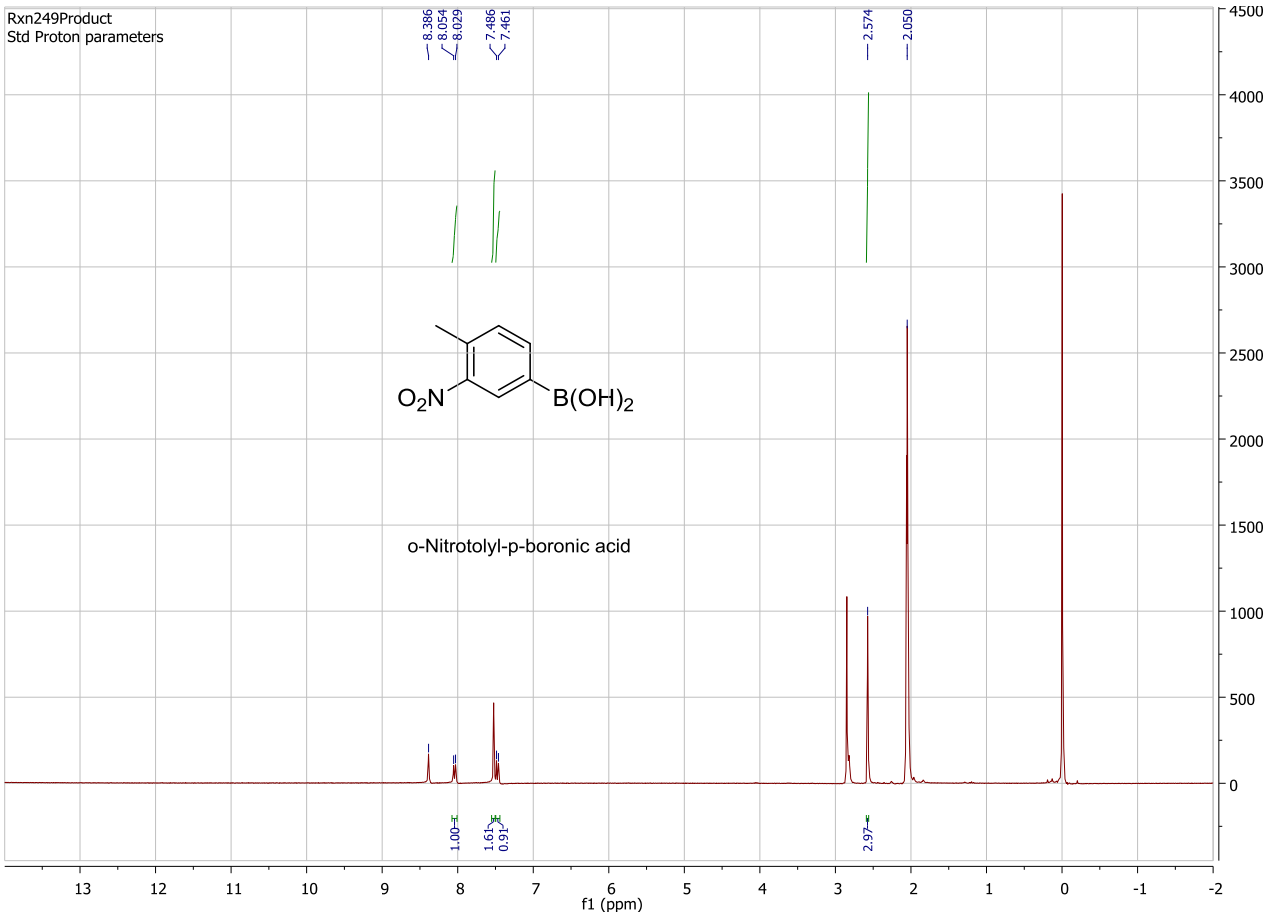


Figure A-53 ^{1}H NMR of *o*-Nitrotolyl-*p*-boronic Acid.

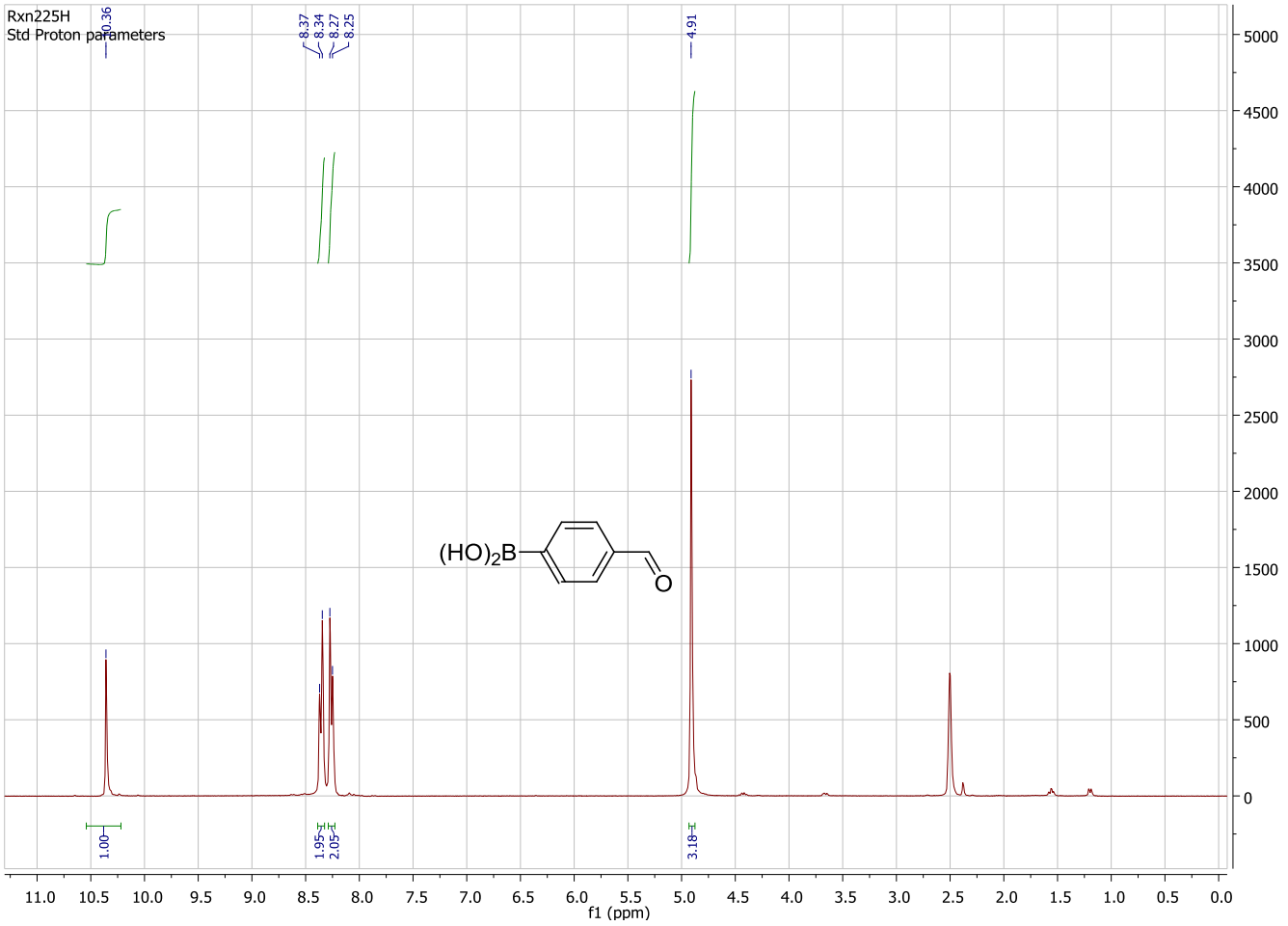


Figure A-54 ^{1}H NMR of *p*-Formylphenylboronic Acid.

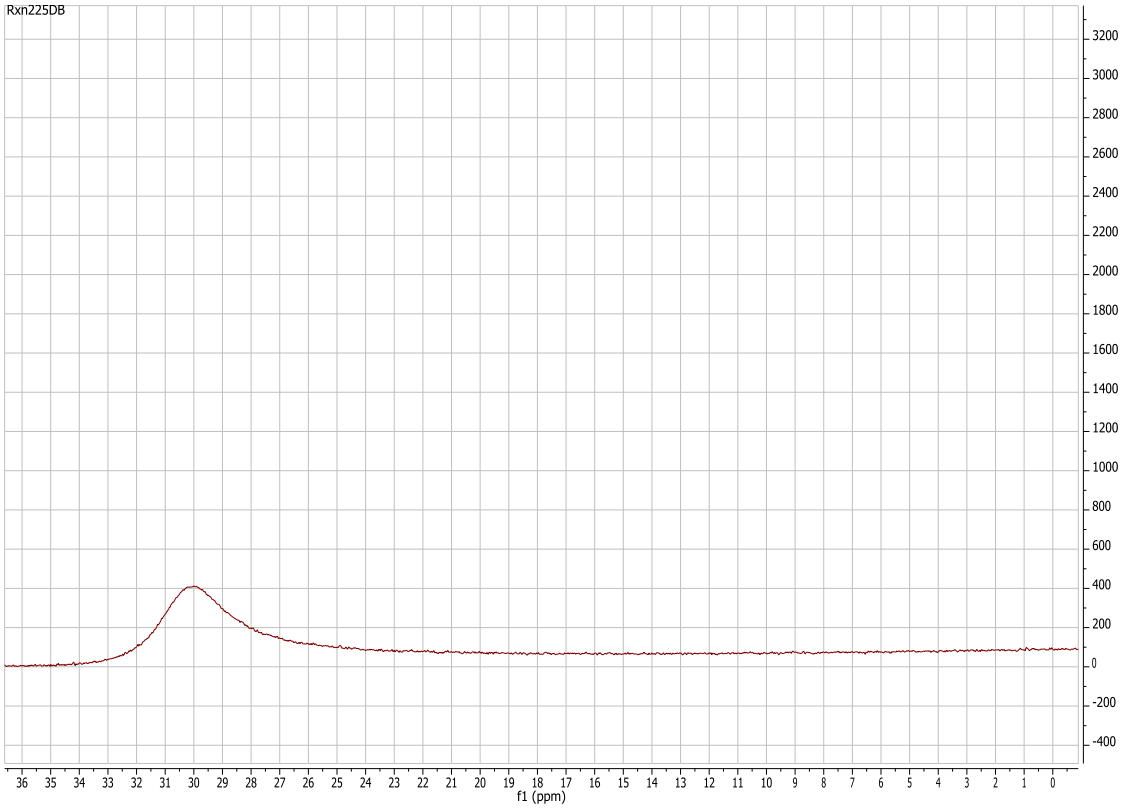


Figure A-55 11B NMR of *p*-Formylphenylboronic Acid.

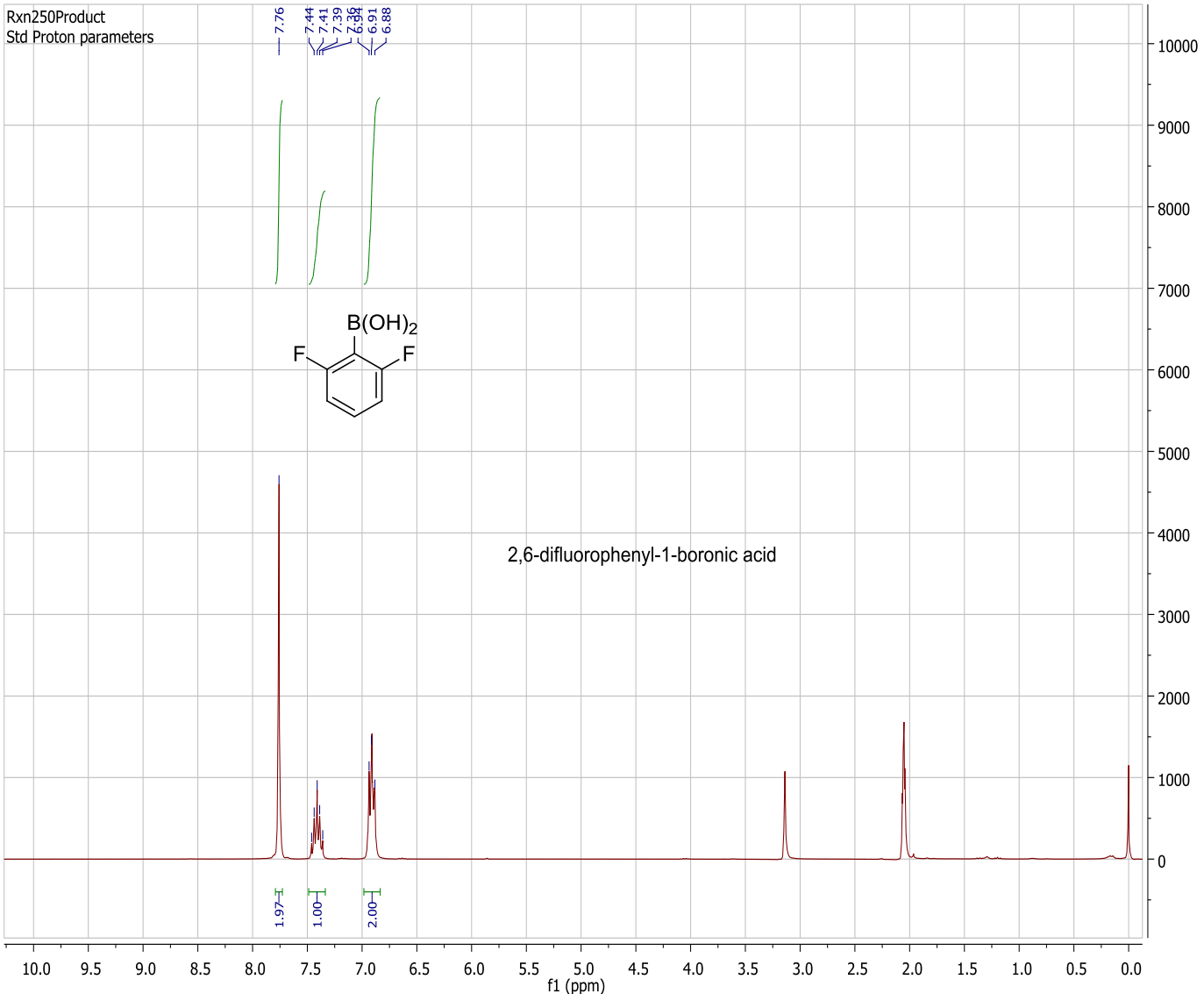


Figure A-56 ^{1}H NMR of 2,6-Difluorophenylboronic Acid.

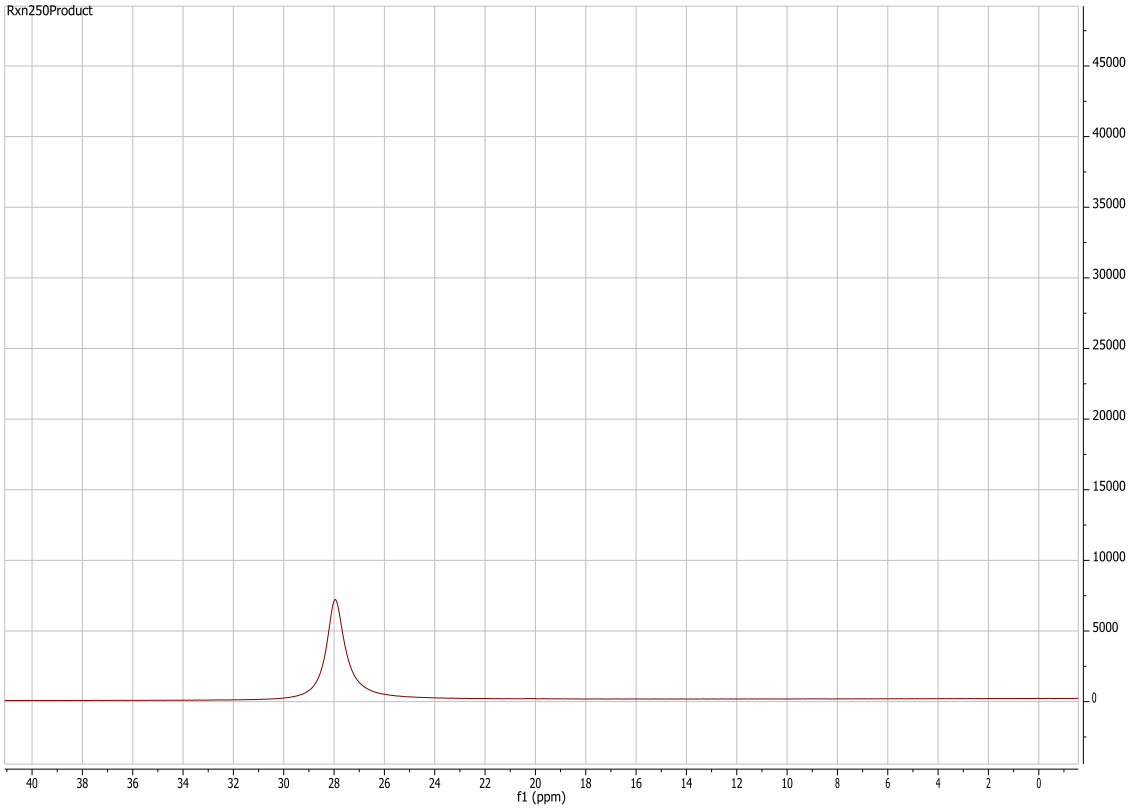


Figure A-57 ^{11}B NMR of 2,6-Difluorophenylboronic Acid.

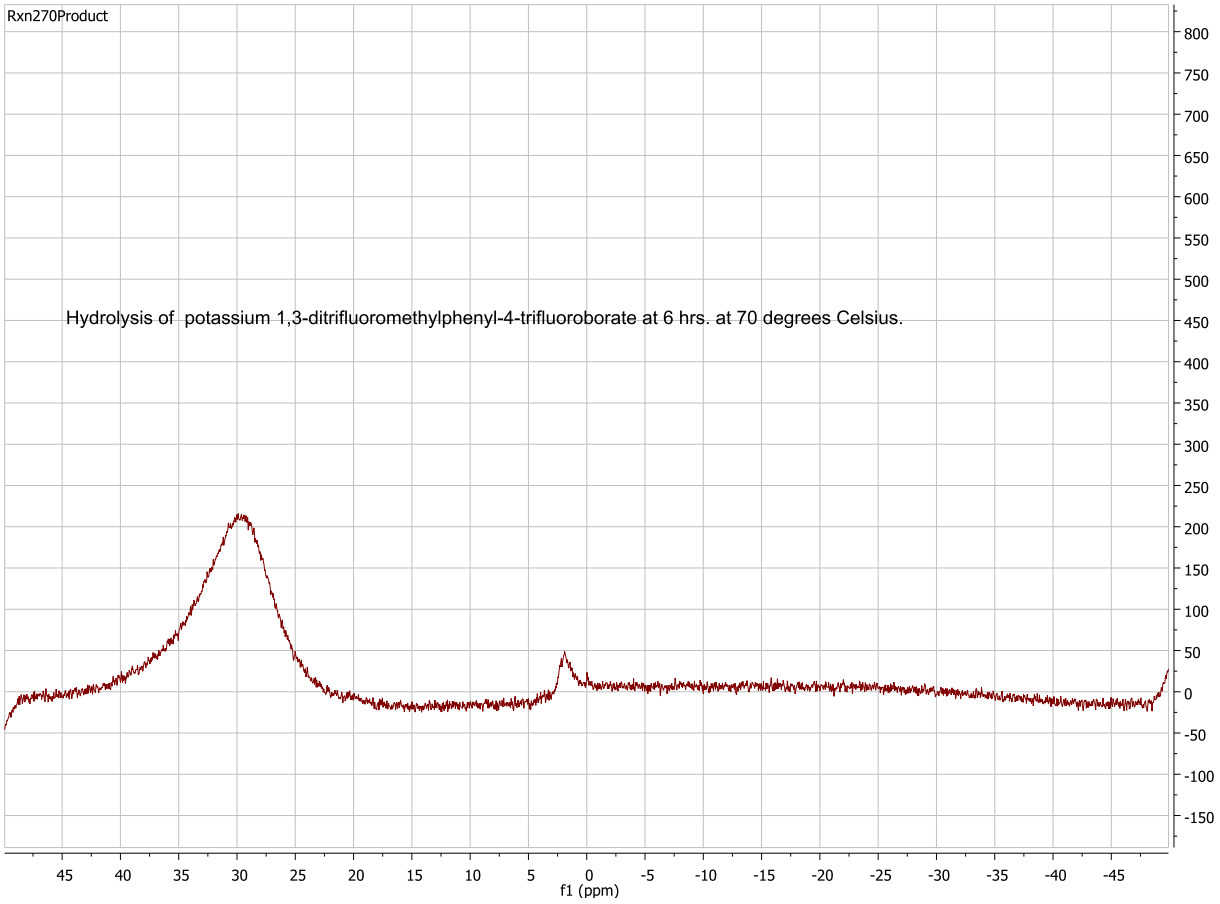


Figure A-58 ^{11}B NMR of (2,3-bis(Trifluoromethyl)phenyl)boronic Acid at 6 Hours of Reaction Time.

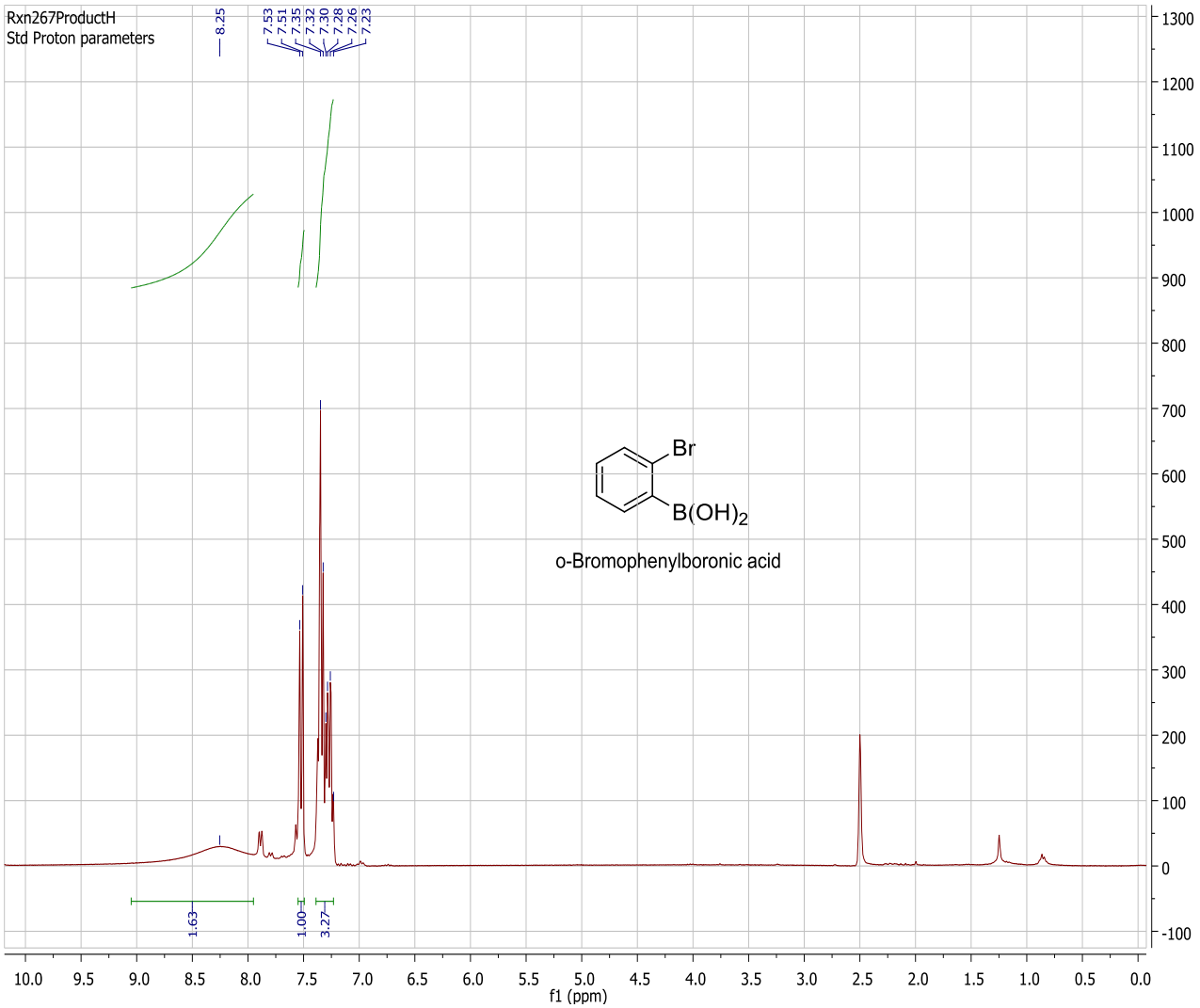


Figure A-59 ^{1}H NMR of *o*-Bromophenylboronic Acid.

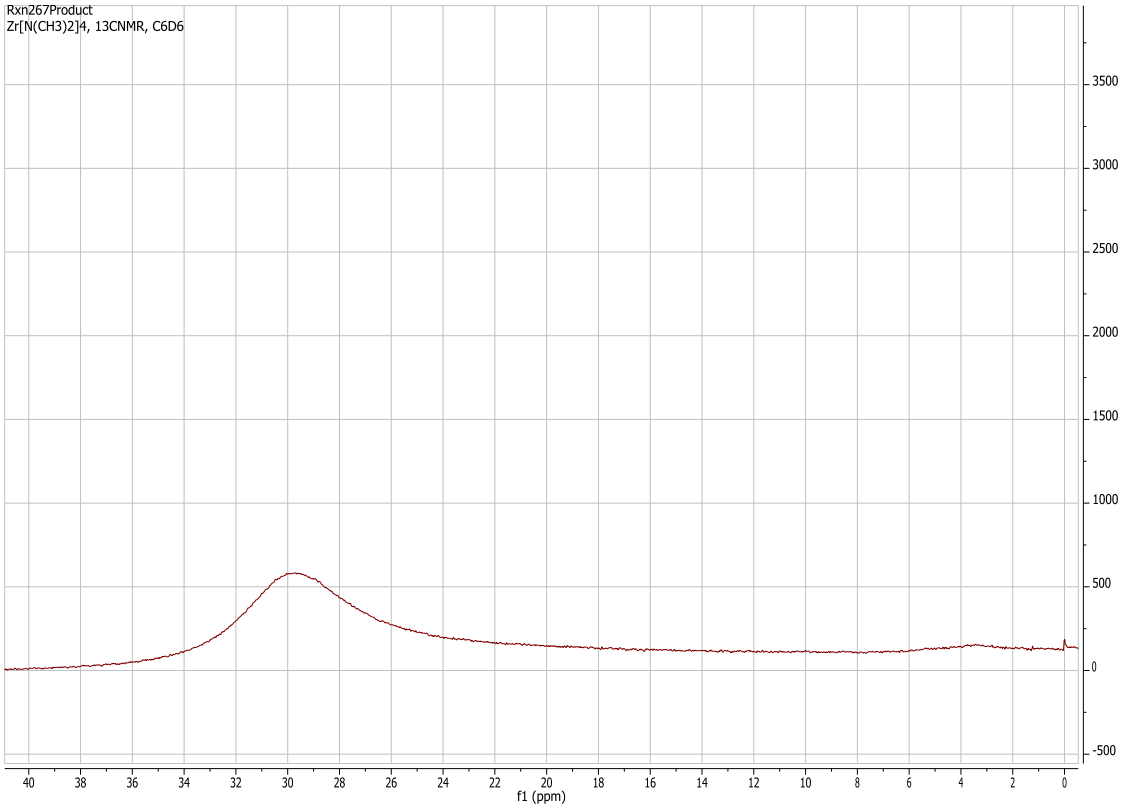


Figure A-60 ^{11}B NMR of *o*-Bromophenylboronic Acid.

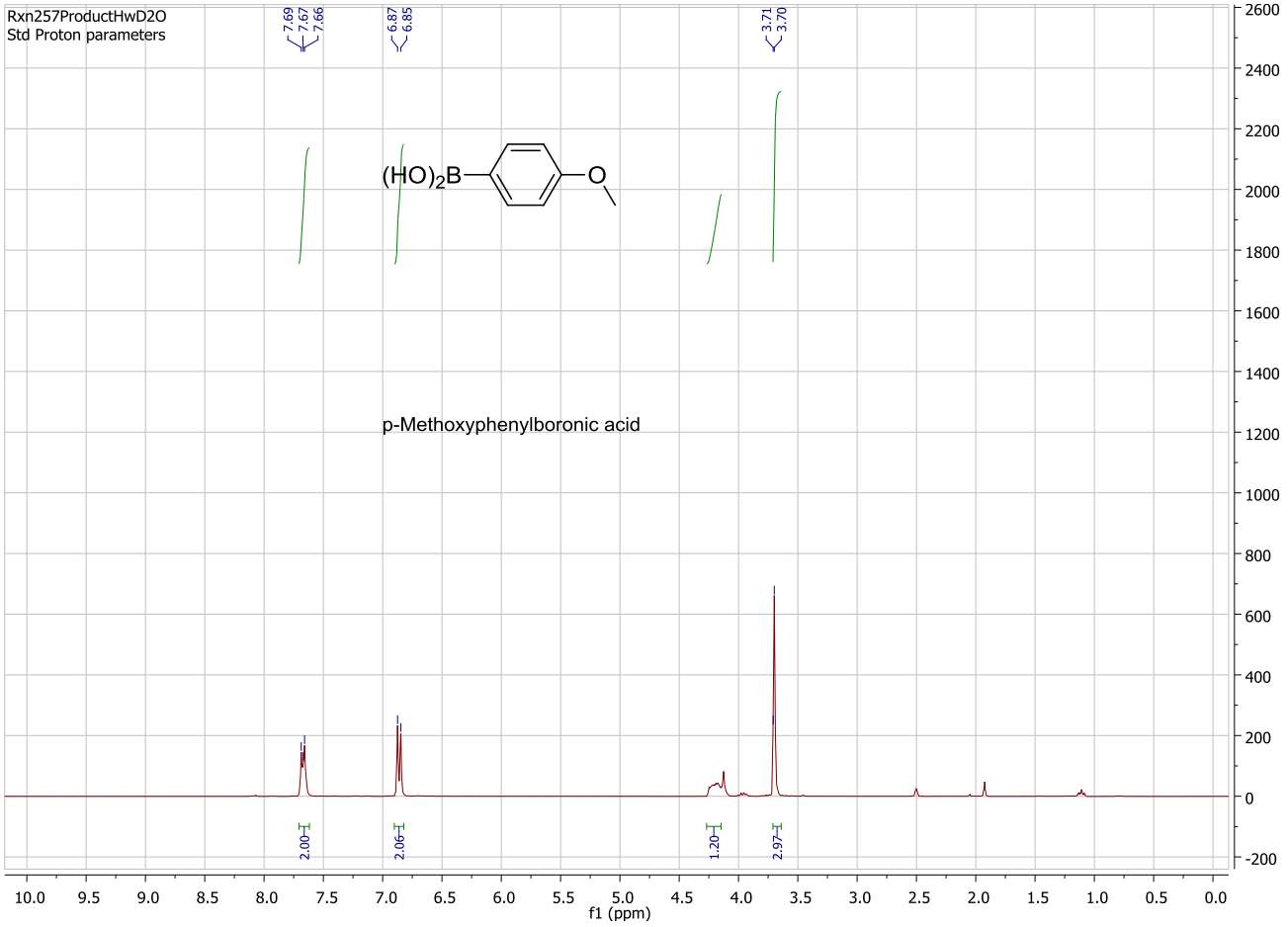


Figure A-61 ^{1}H NMR of *p*-Methoxyphenylboronic Acid.

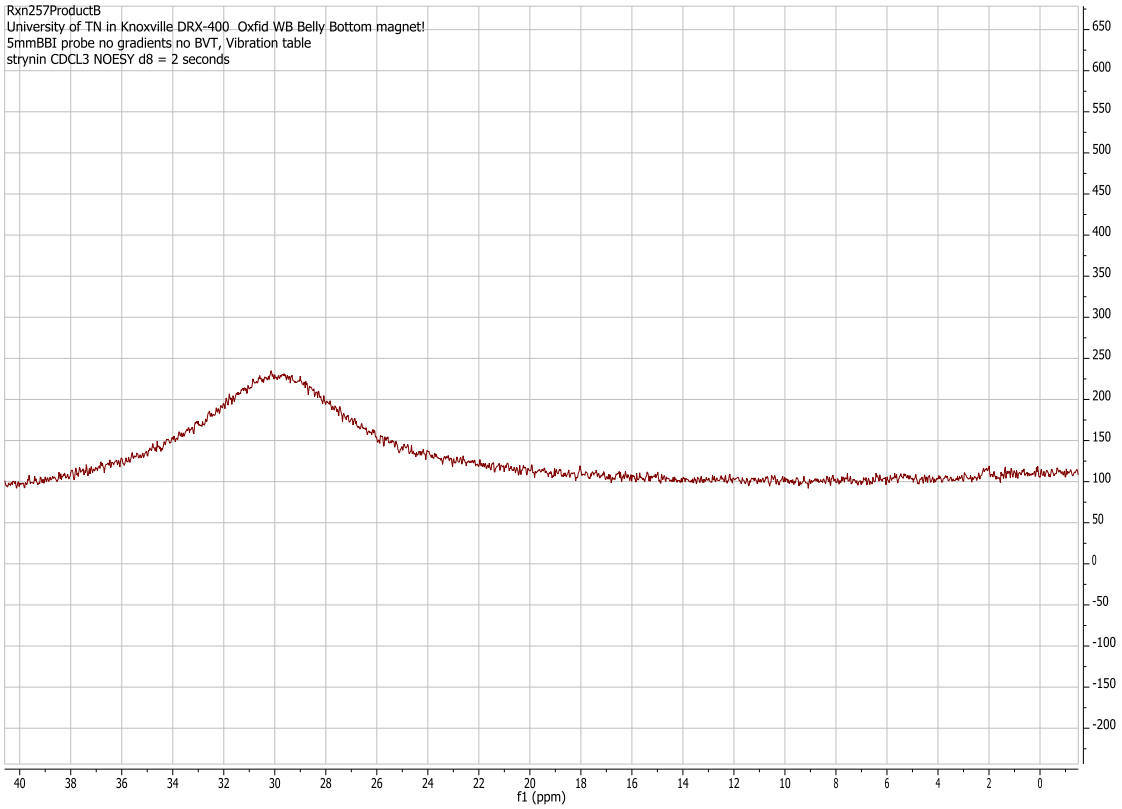


Figure A-62 ^{11}B NMR of *p*-Methoxyphenylboronic Acid.

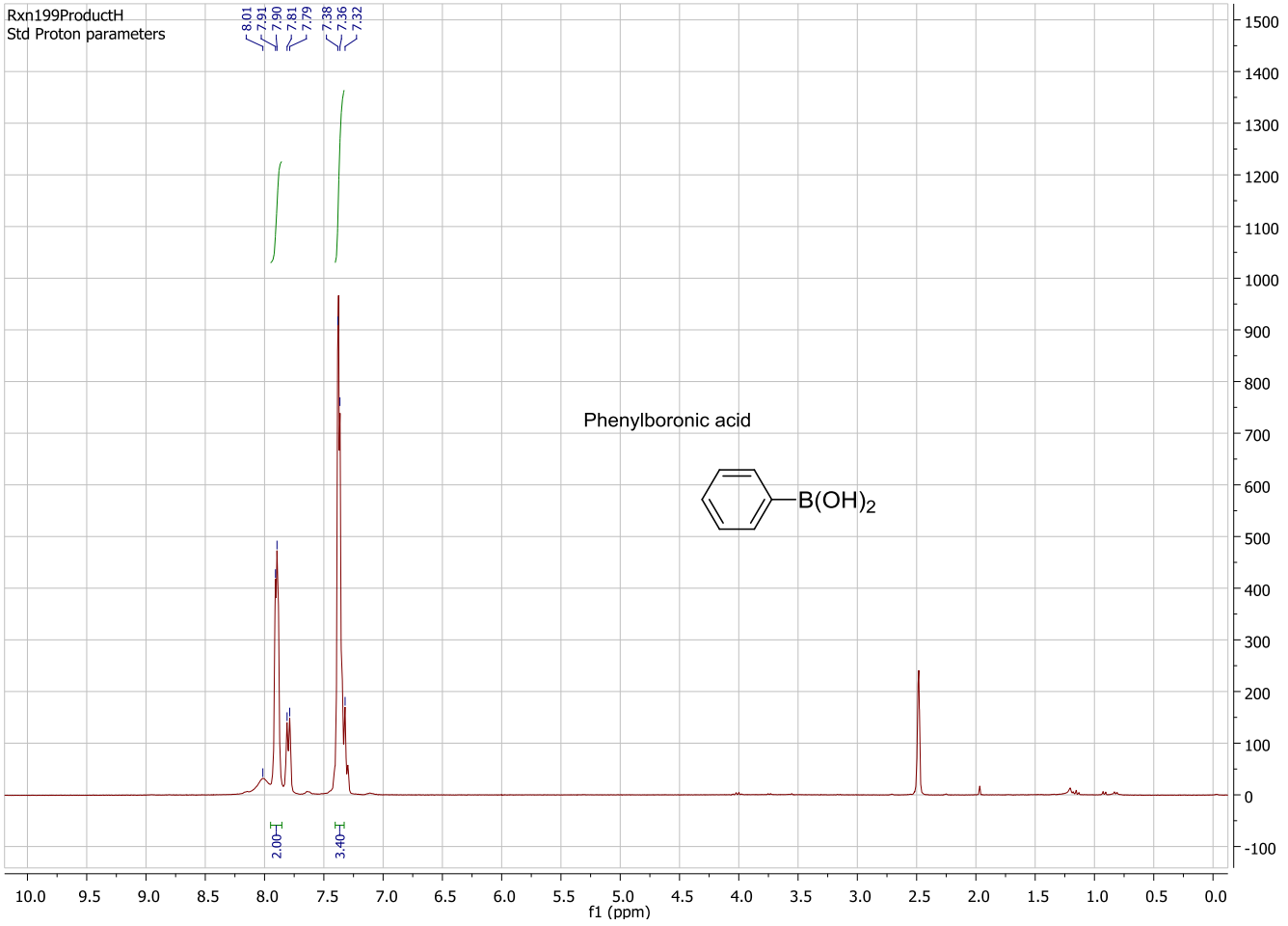


Figure A-63 ^{1}H NMR of Phenylboronic Acid.

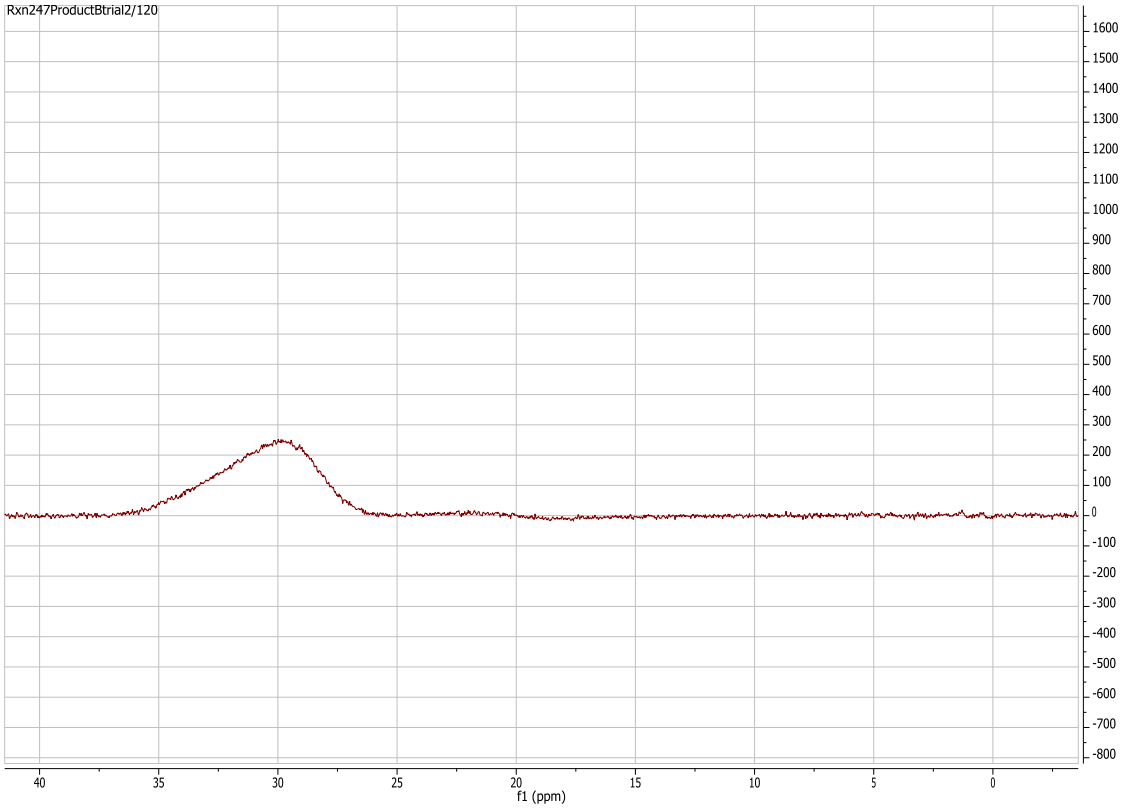


Figure A-64 ^{11}B NMR of Phenylboronic Acid.

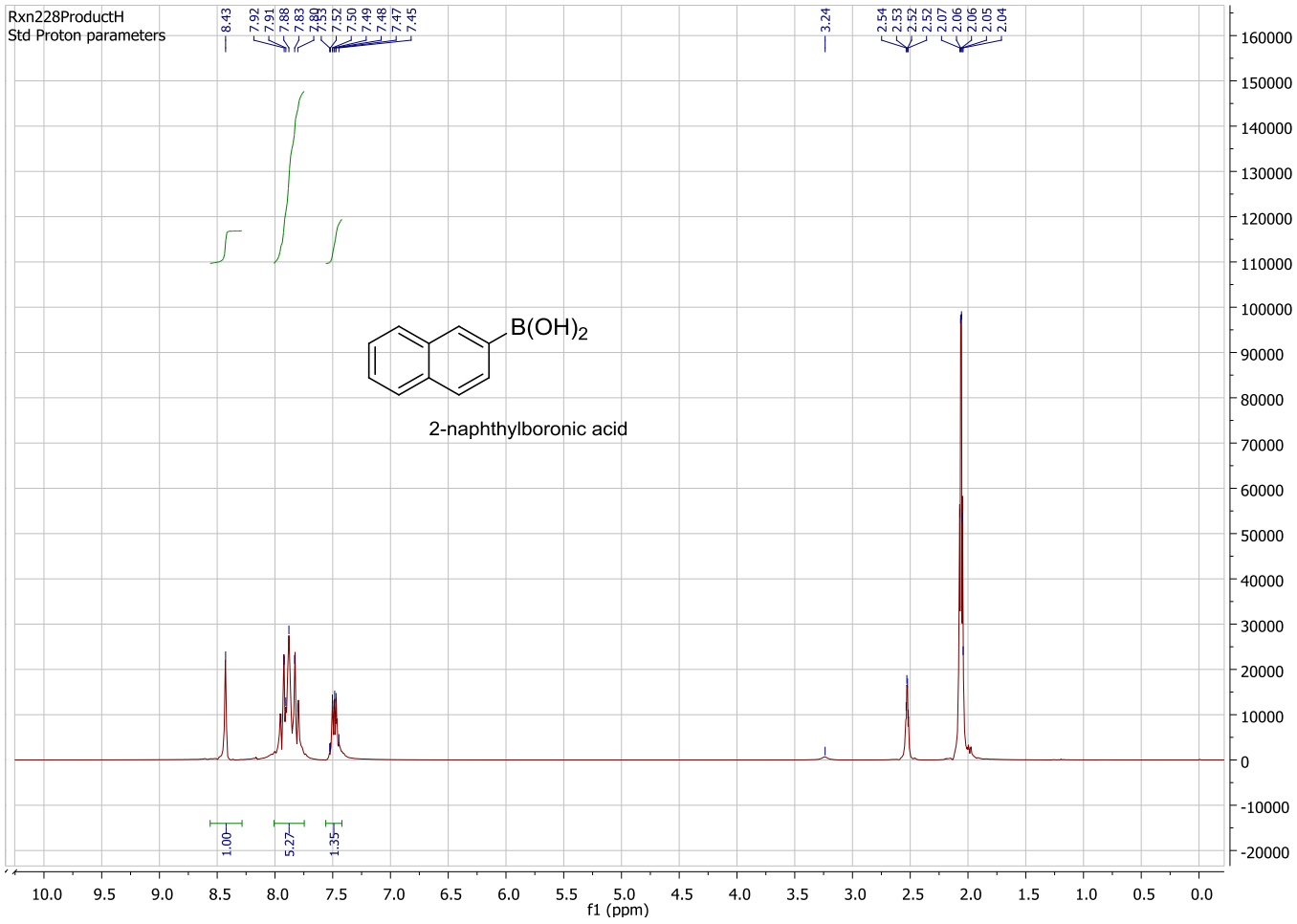


Figure A-65 ^{1}H NMR of 2-Naphthylboronic Acid.

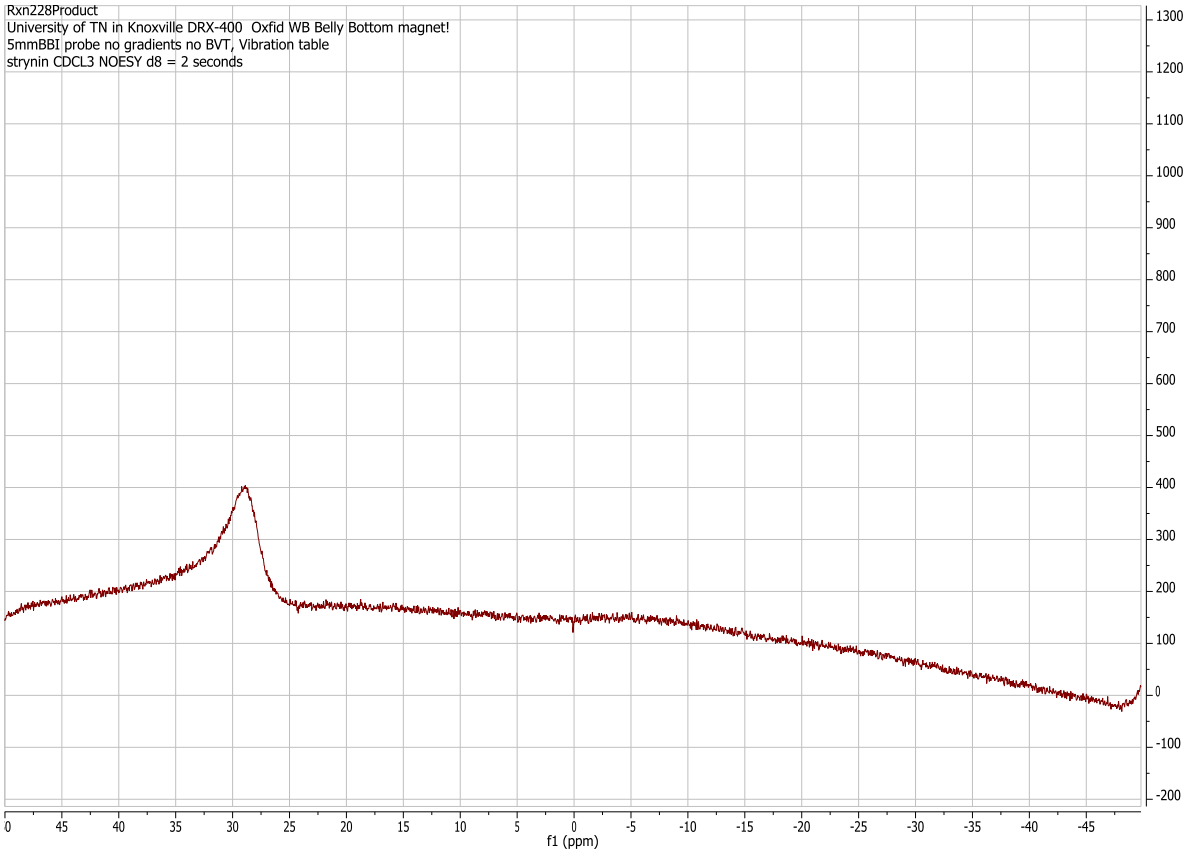


Figure A-66 ^{11}B NMR of 2-Naphthylboronic Acid.

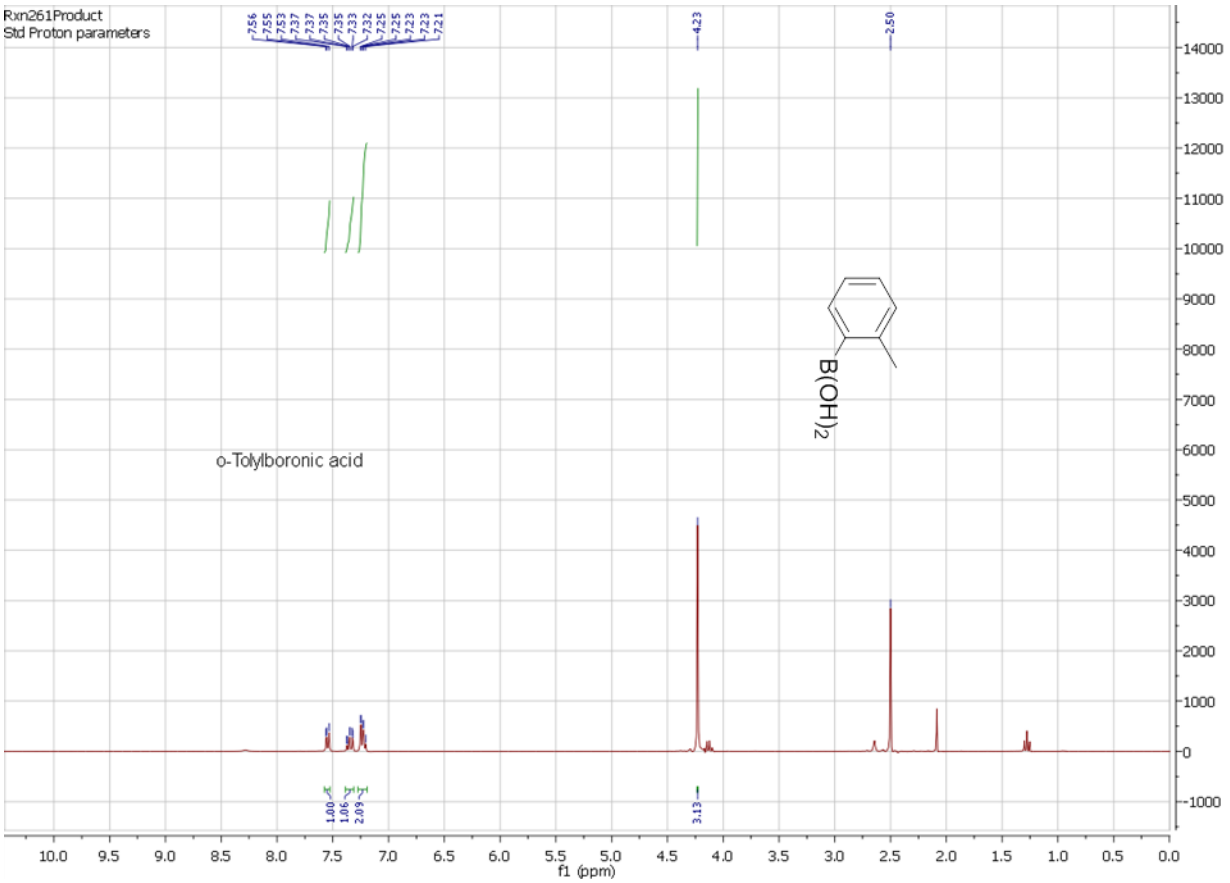


Figure A-67 ^{1}H NMR of *o*-Tolylboronic Acid.

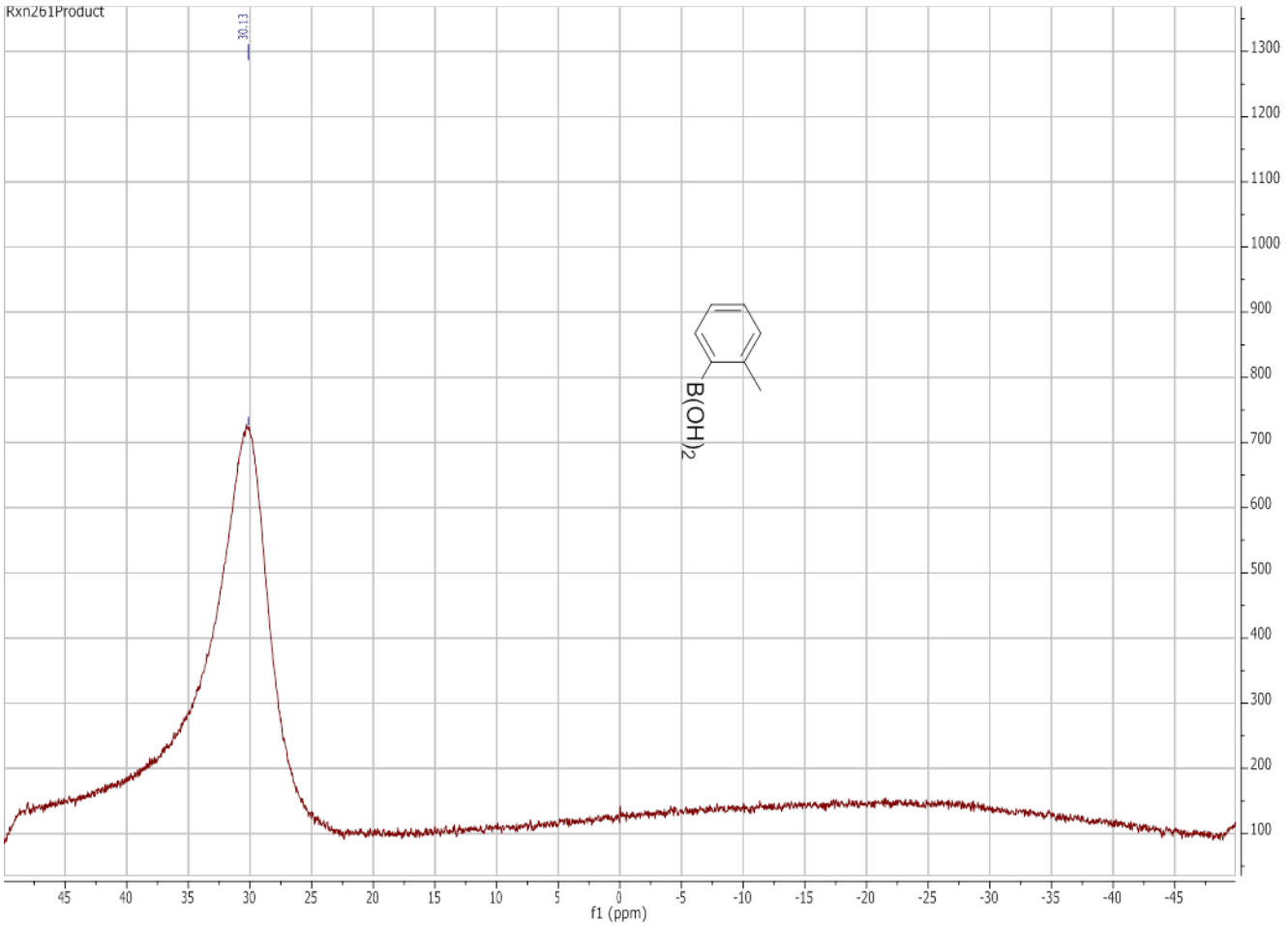


Figure A-68 ^{11}B NMR of *o*-Tolylboronic Acid.

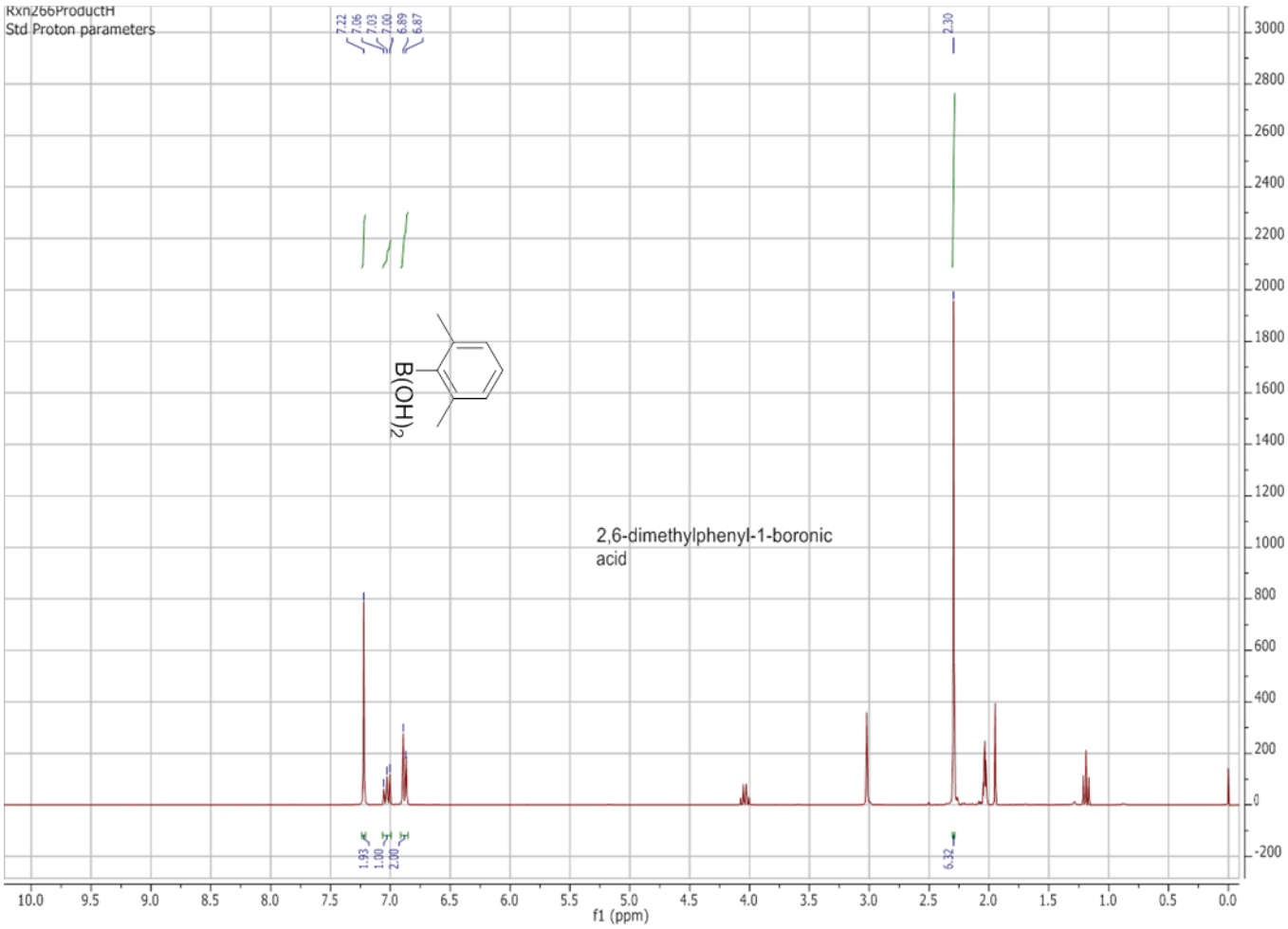


Figure A-69 ^{1}H NMR of 2,6-Dimethylphenylboronic Acid.

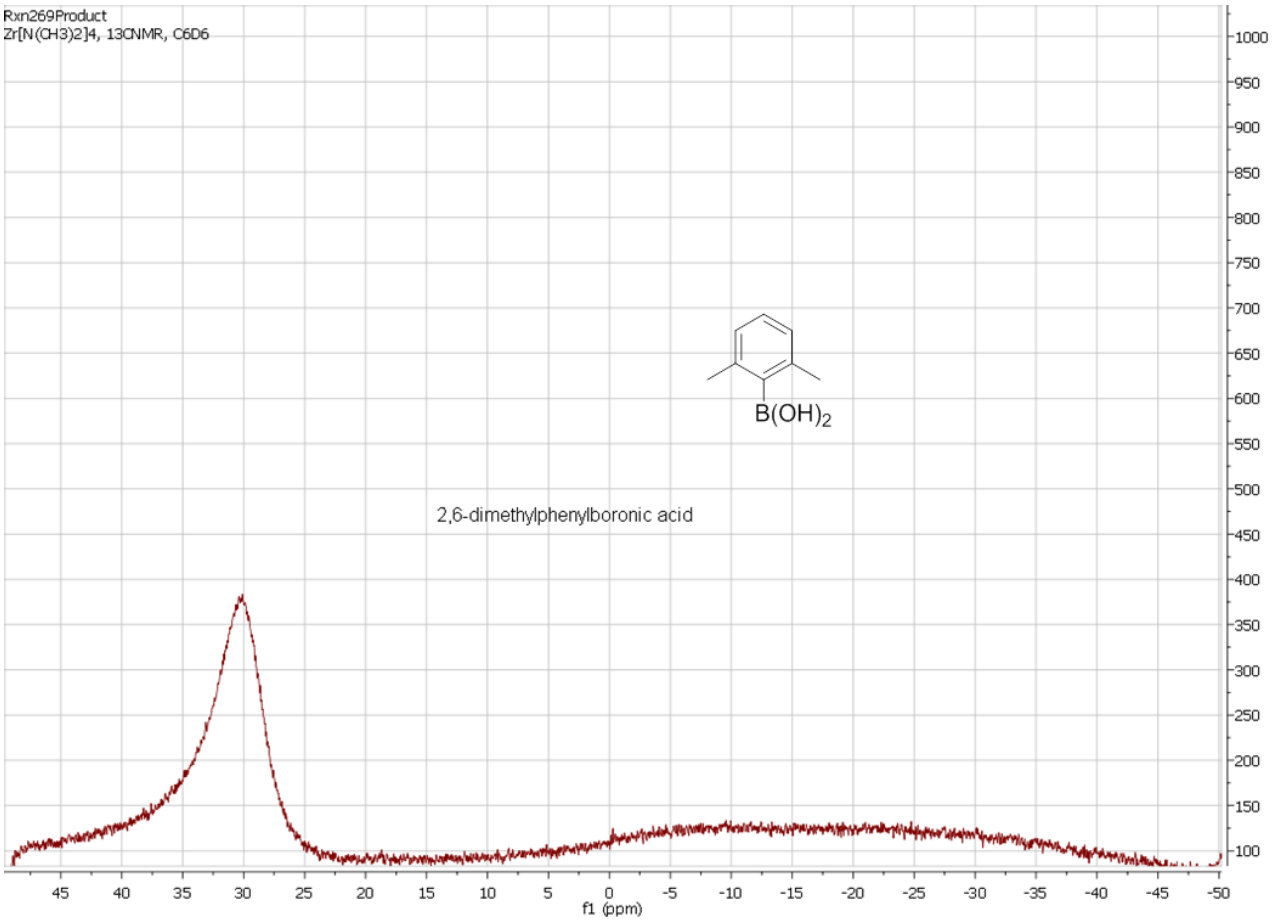


Figure A-70 ^{11}B NMR of 2,6-Dimethylphenylboronic Acid.

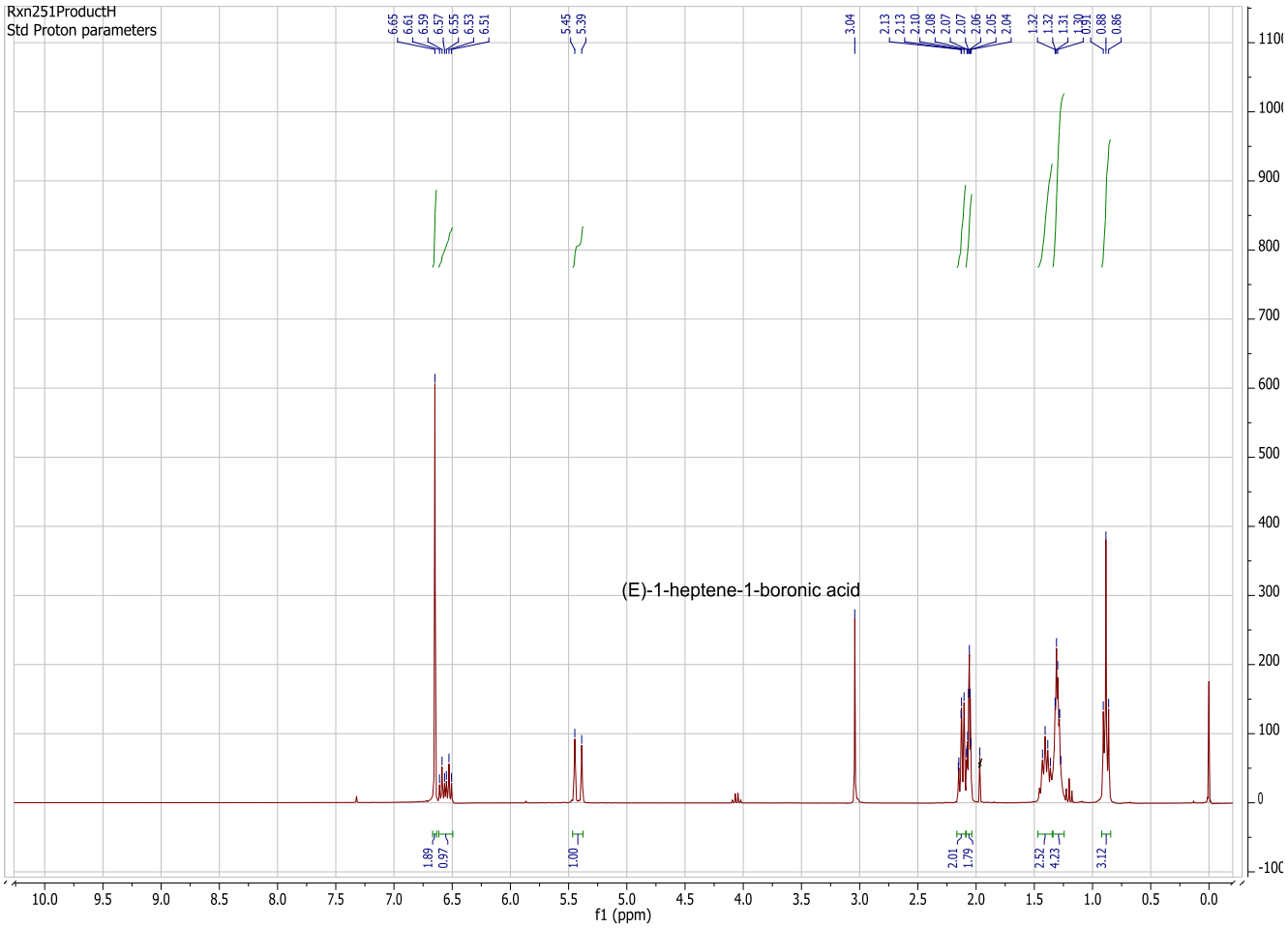


Figure A-71 ^{1}H NMR of (*E*)-1-Heptene-1-boronic Acid.

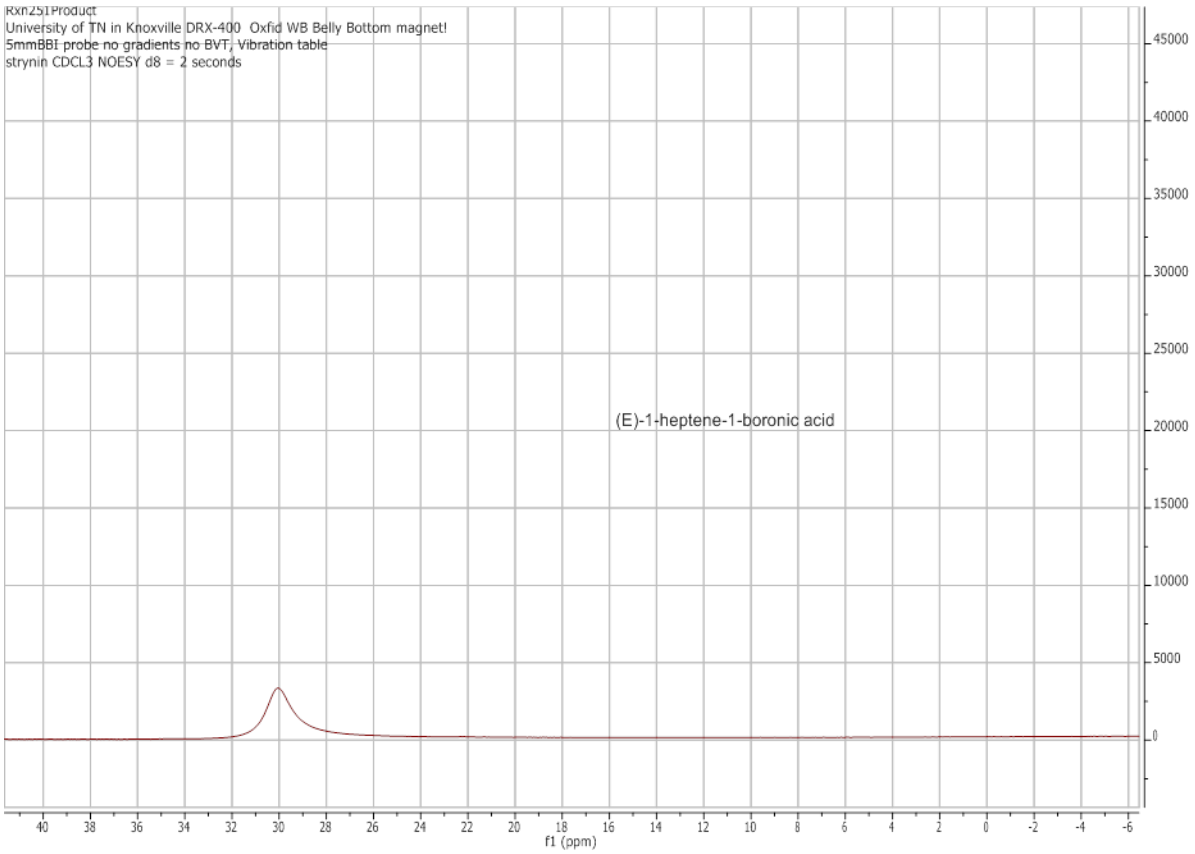


Figure A-72 ^{11}B NMR of (*E*)-1-Heptene-1-boronic Acid.

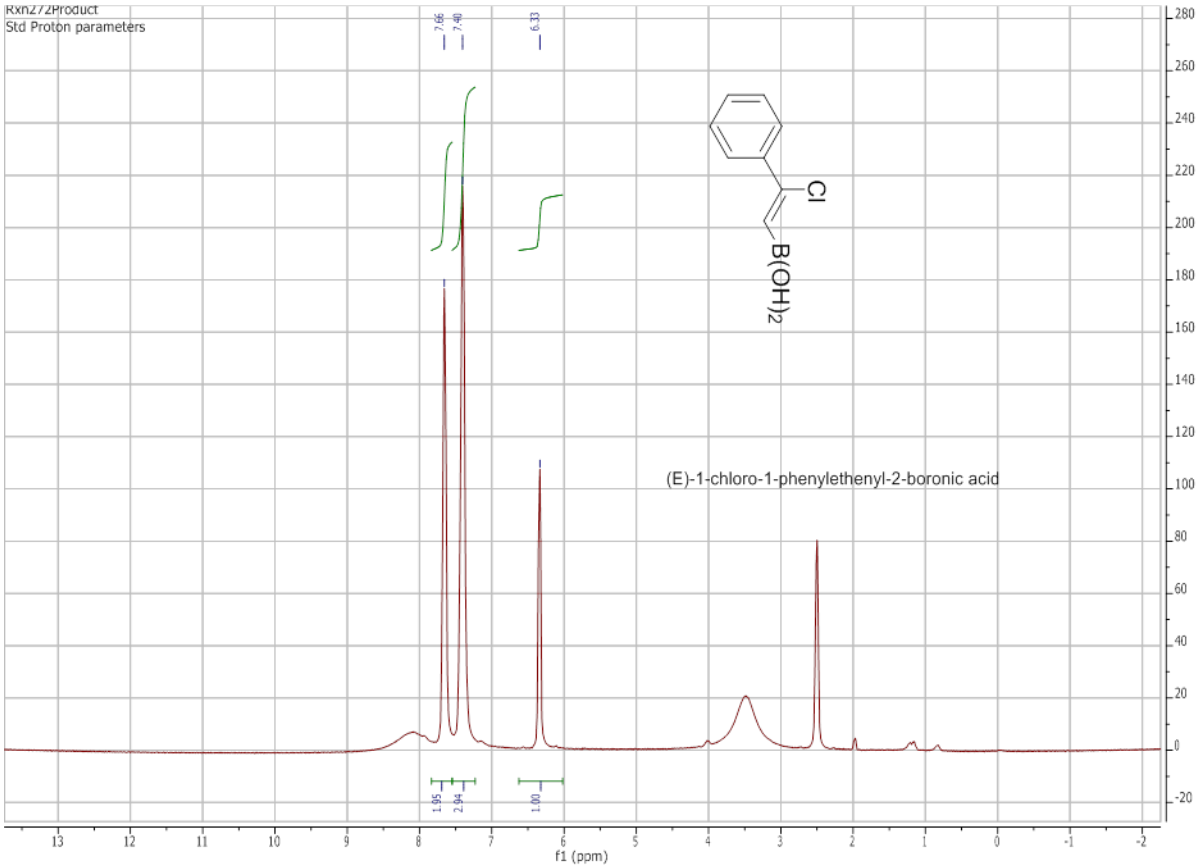


Figure A-73 ^{1}H NMR of (*E*)-1-Chloro-1-phenylethenyl-1-boronic Acid.

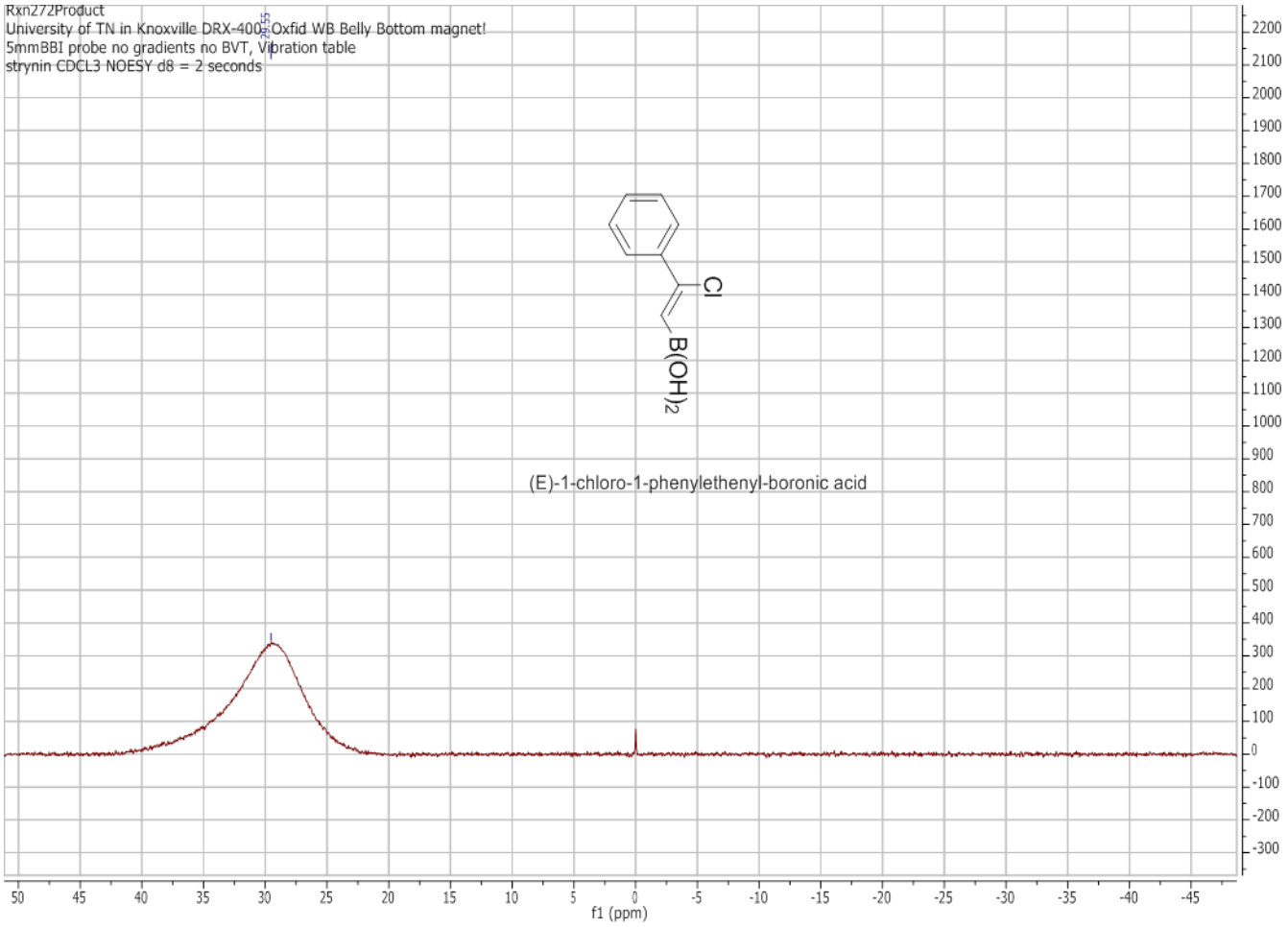


Figure A-74 ^{11}B NMR of (*E*)-1-Chloro-1-phenylethenyl-1-boronic Acid.

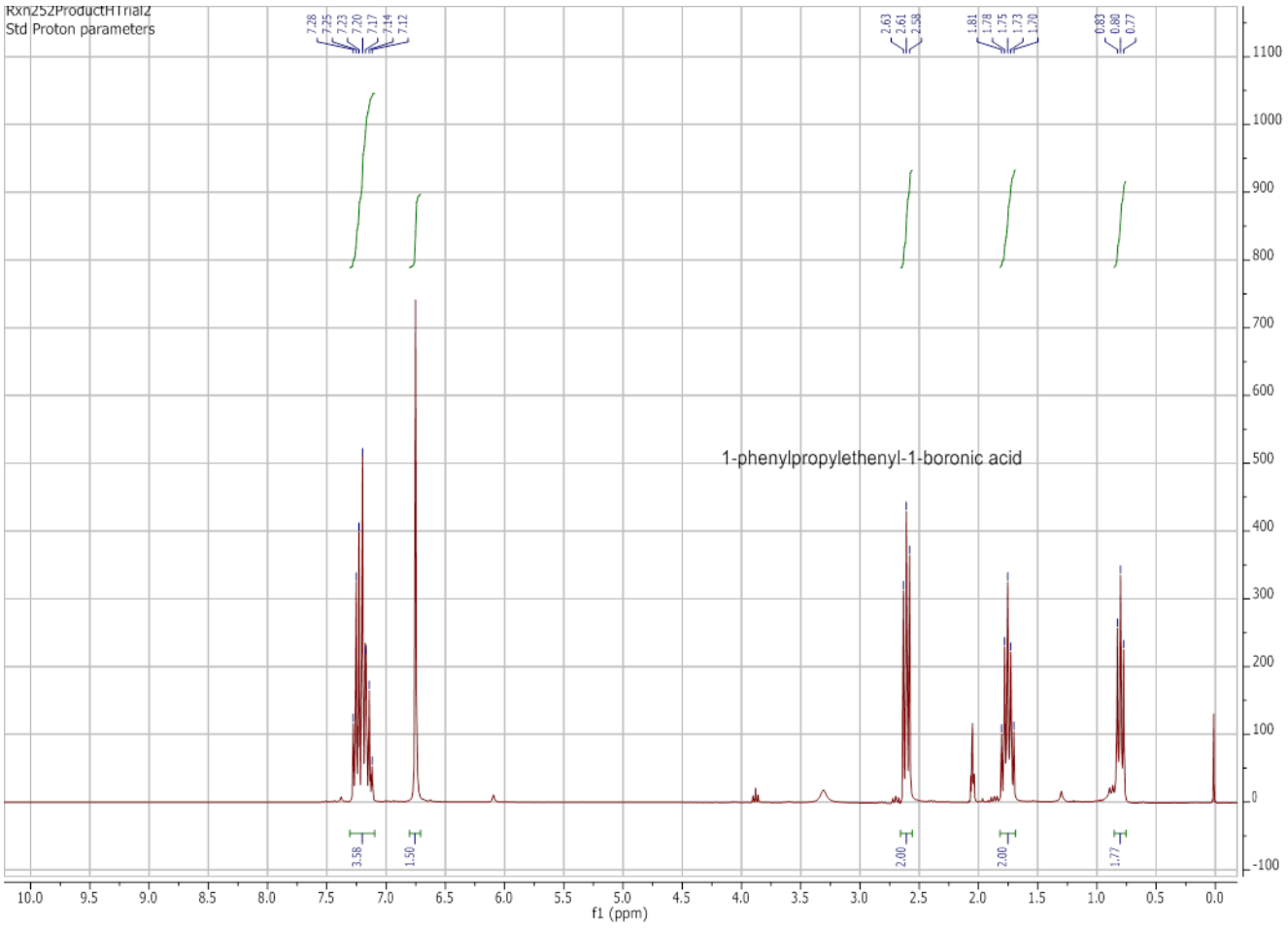


Figure A-75 ^{1}H NMR of 1-Phenylpropyl-3-boronic Acid.

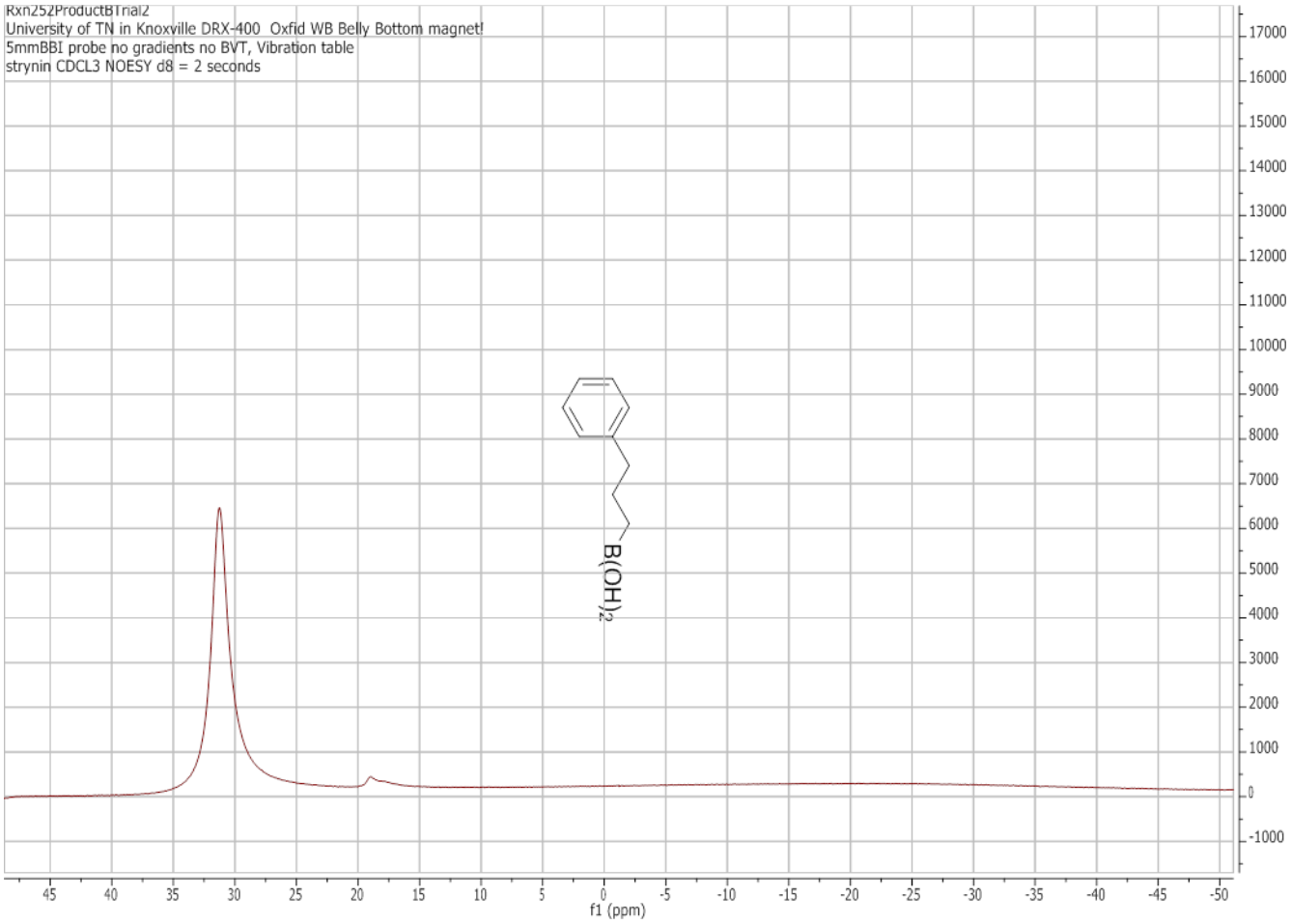


Figure A-76 ^{11}B NMR of 1-Phenylpropyl-3-boronic Acid.

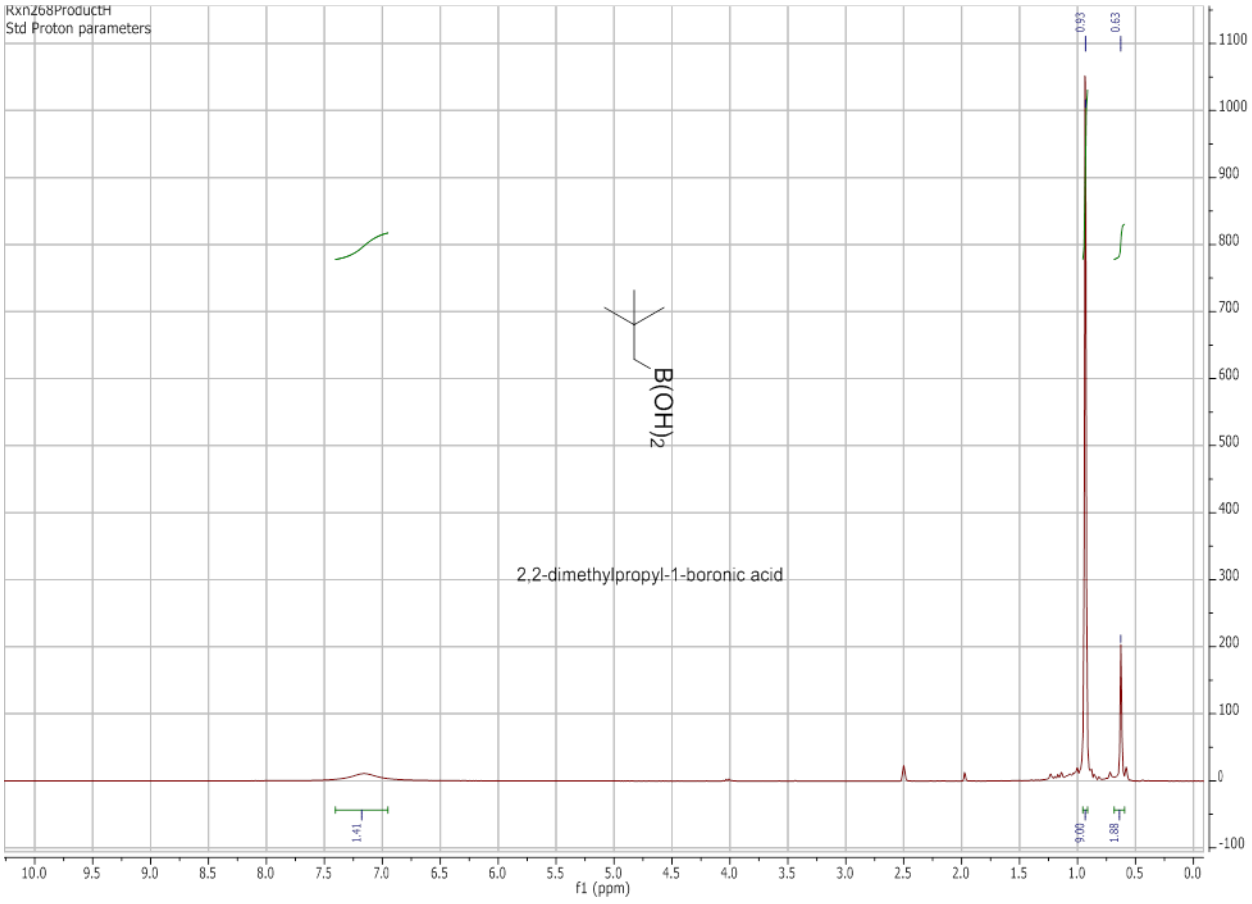


Figure A-77 ^{1}H NMR of 2,2-Dimethylpropyl-1-boronic Acid.

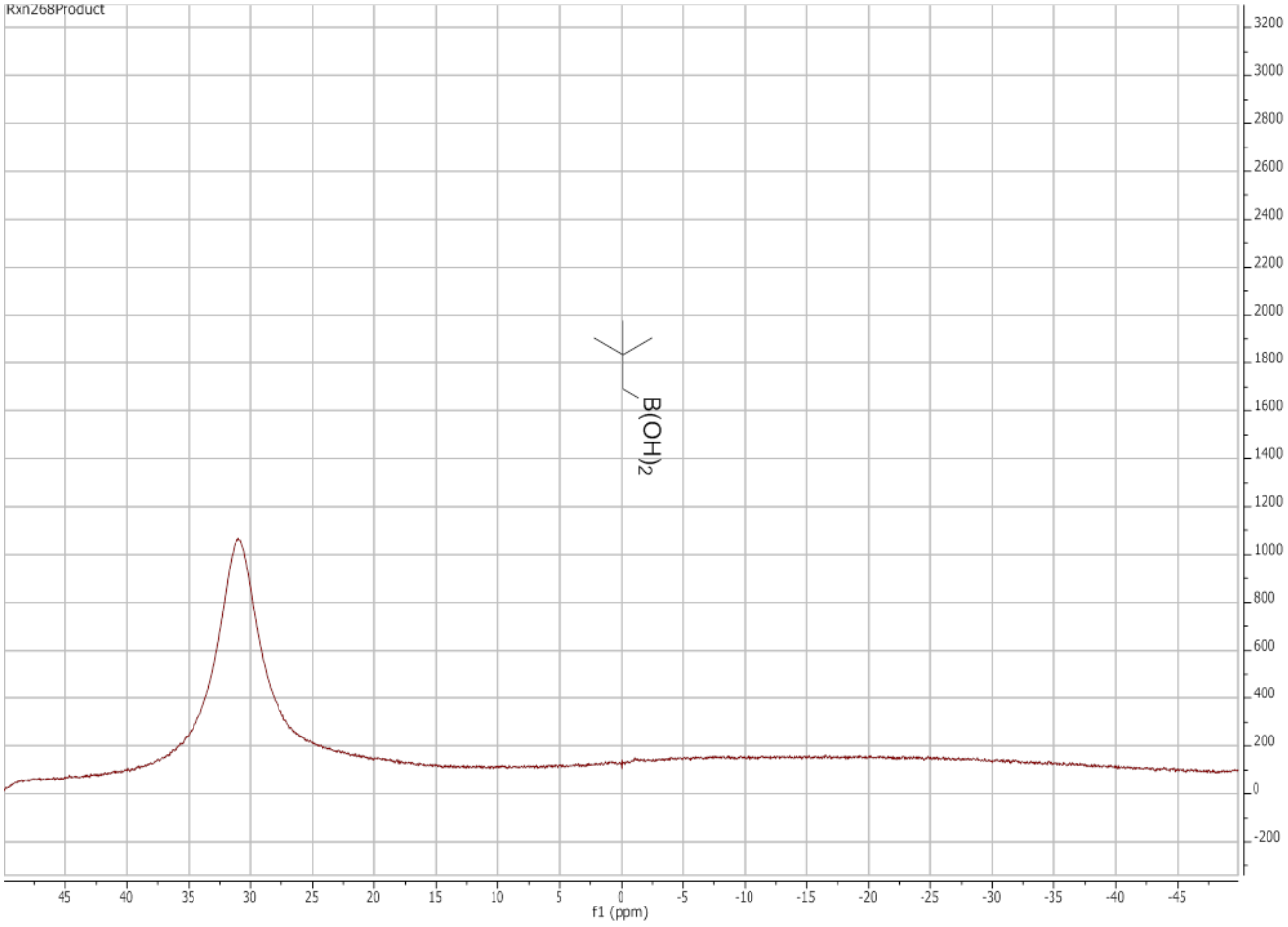


Figure A-78 ^{11}B NMR of 2,2-Dimethylpropyl-1-boronic Acid.

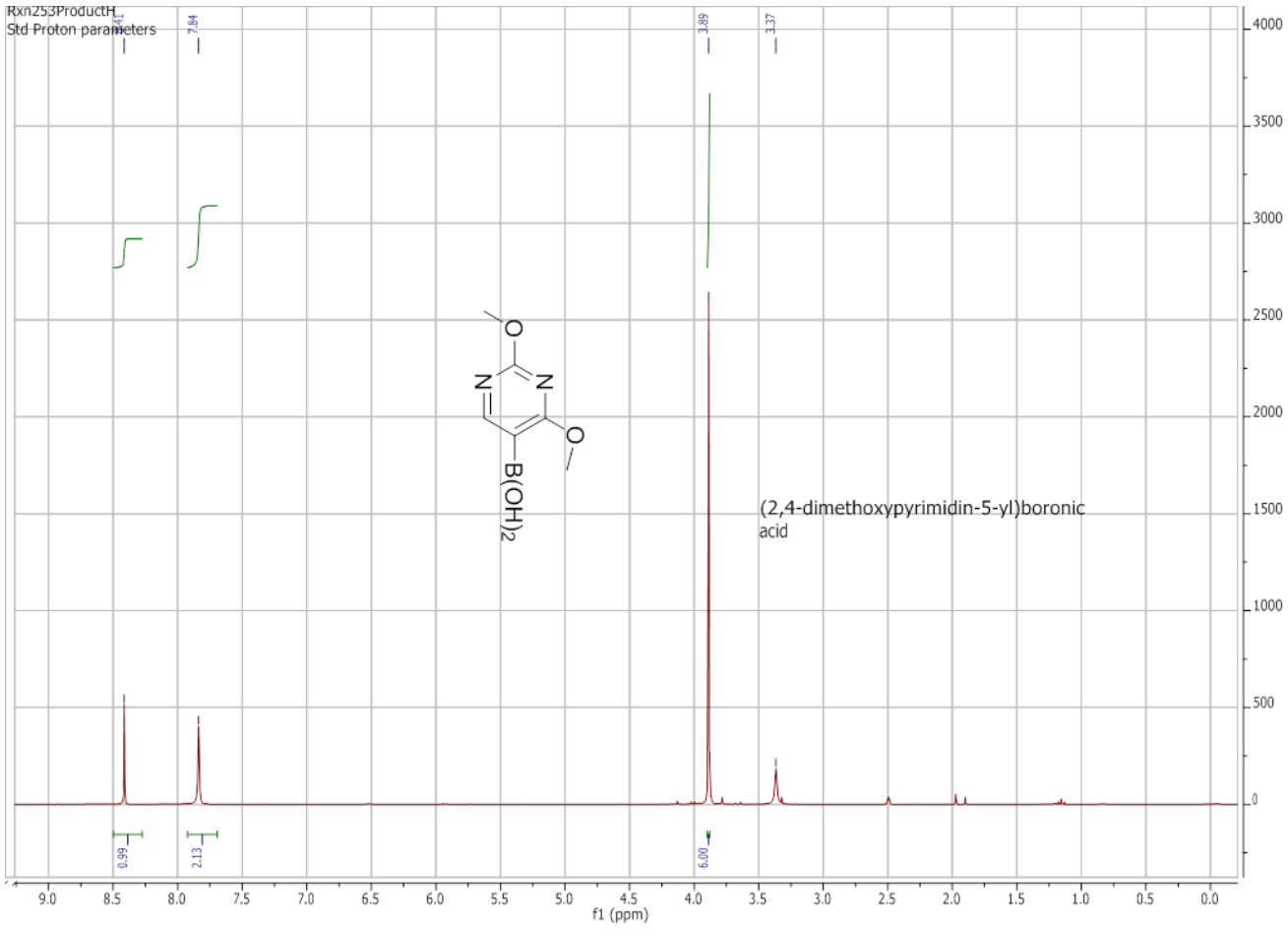


Figure A-79 ^{1}H NMR of (2,4-Dimethoxypyrimidin-5-yl)boronic Acid.

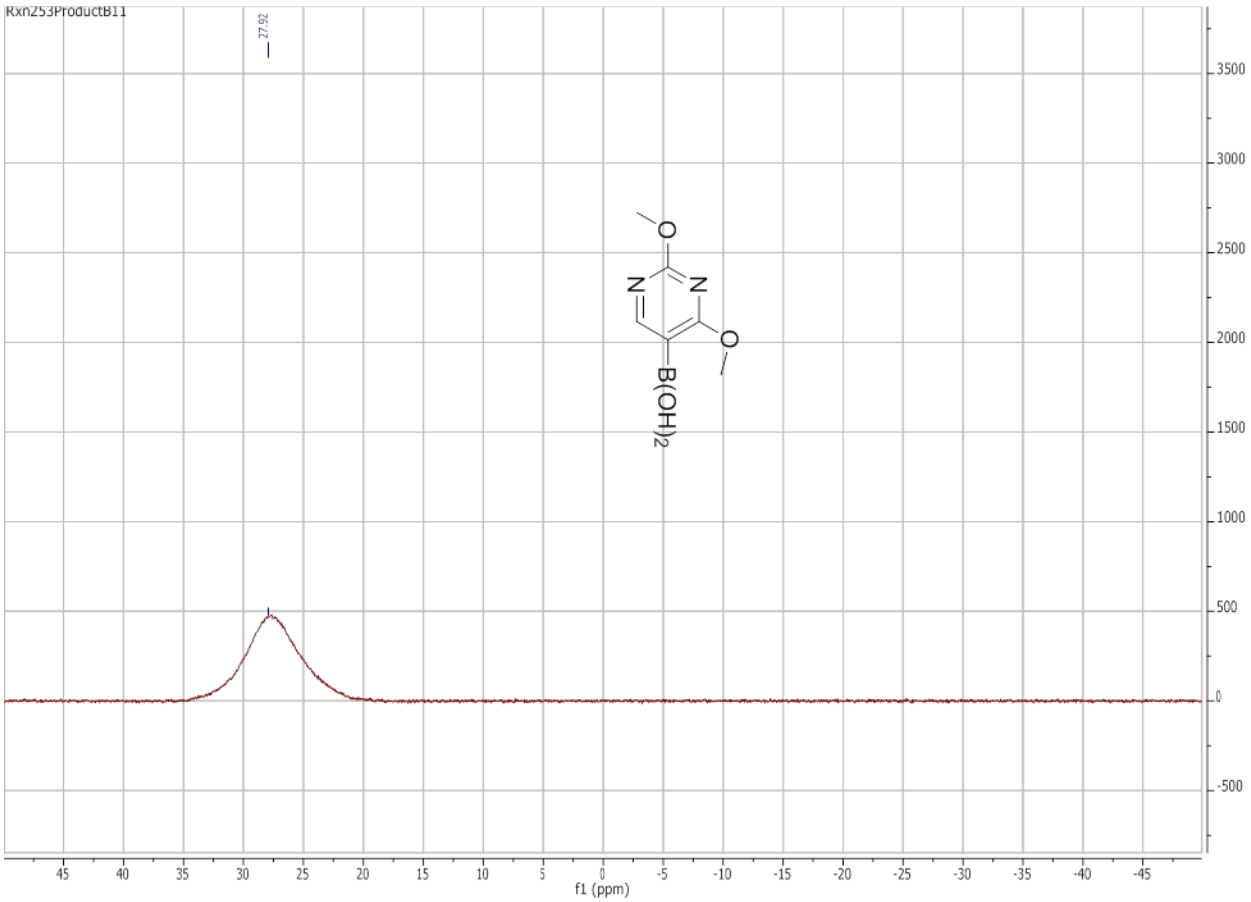


Figure A-80 ^{11}B NMR of (2,4-Dimethoxypyrimidin-5-yl)boronic Acid.

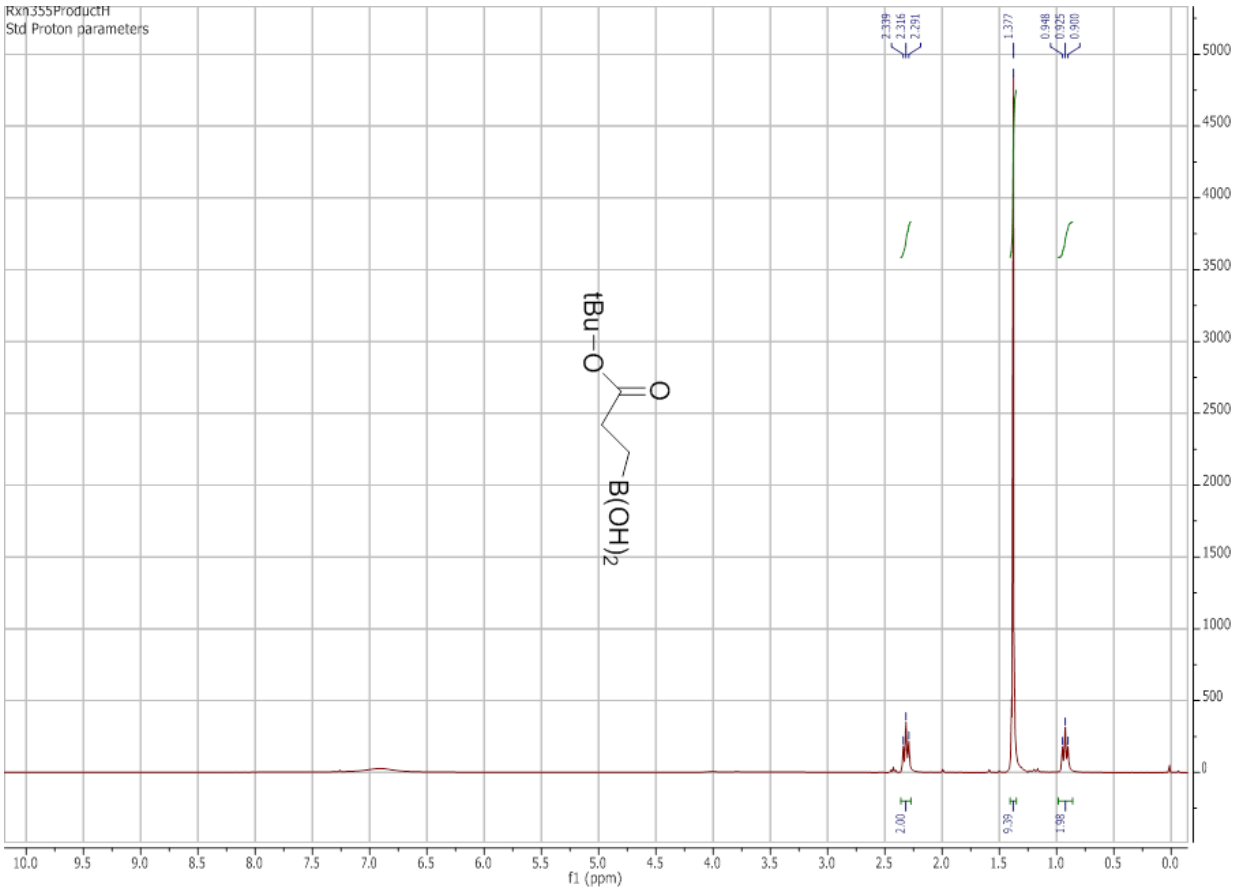


Figure A-81 ^{1}H NMR of (3-(*tert*-Butoxy)-3-oxopropyl)boronic Acid.

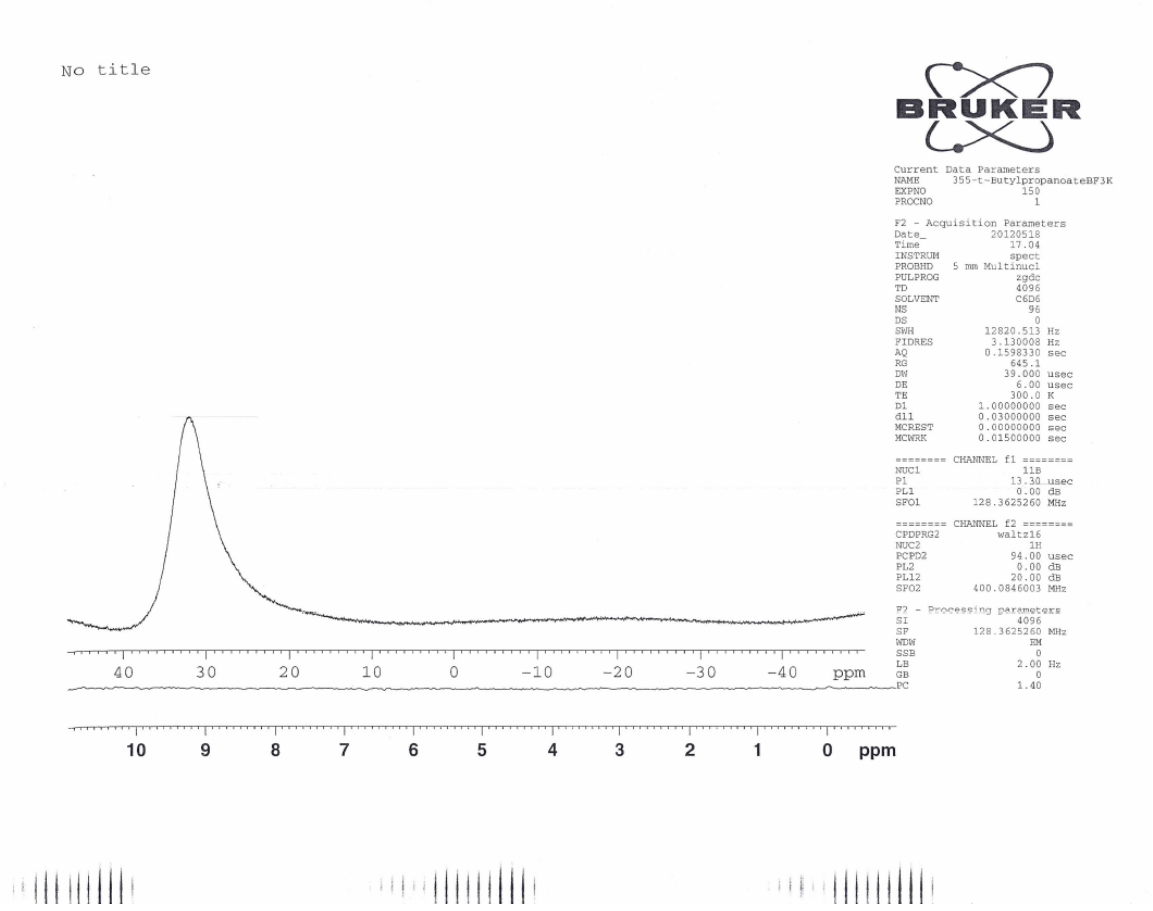


Figure A-82 ^{11}B NMR of (3-(*tert*-Butoxy)-3-oxopropyl)boronic Acid.

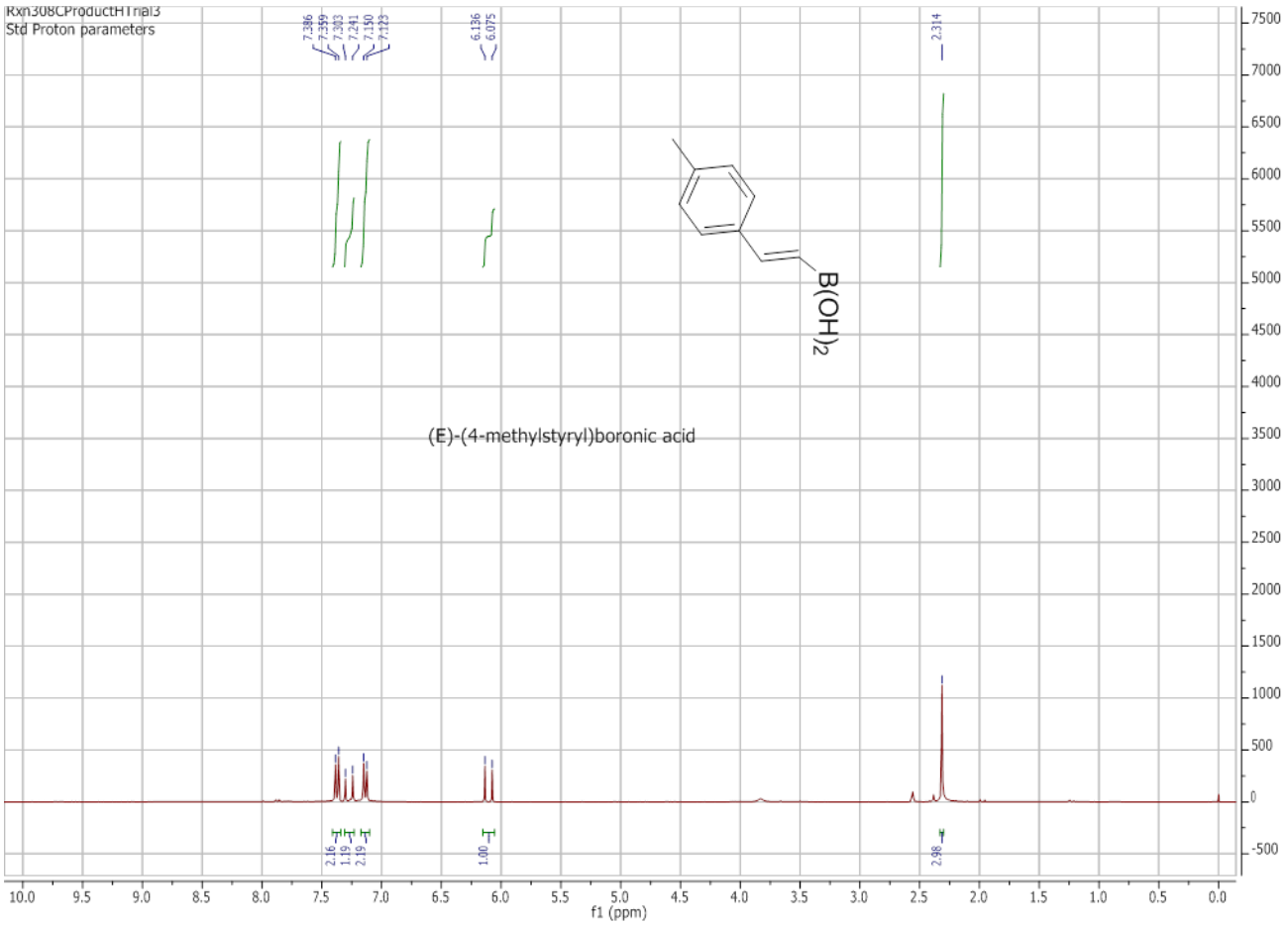


Figure A-83 ^{1}H NMR of (*E*)-(4-Methylstyryl)boronic Acid.

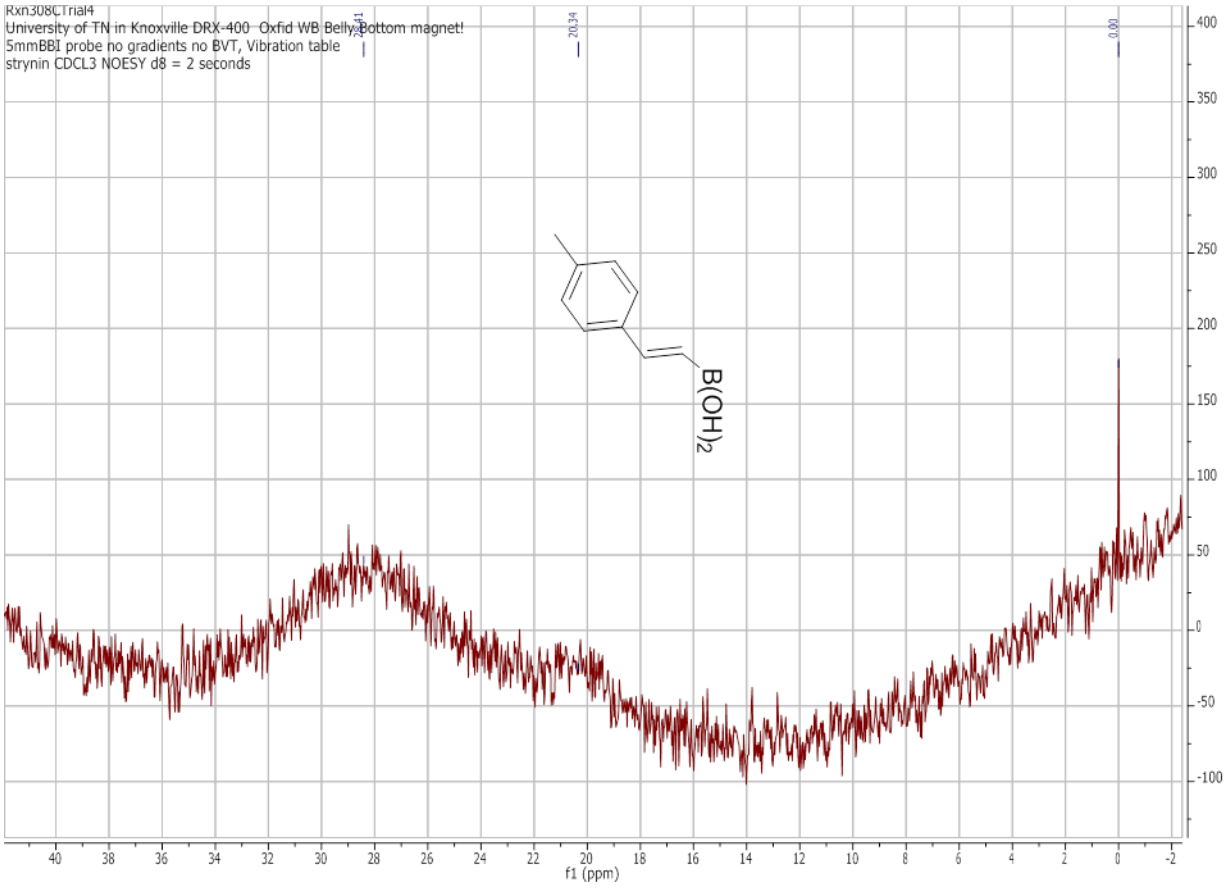


Figure A-84 ^{11}B NMR of (*E*)-(4-Methylstyryl)boronic Acid.

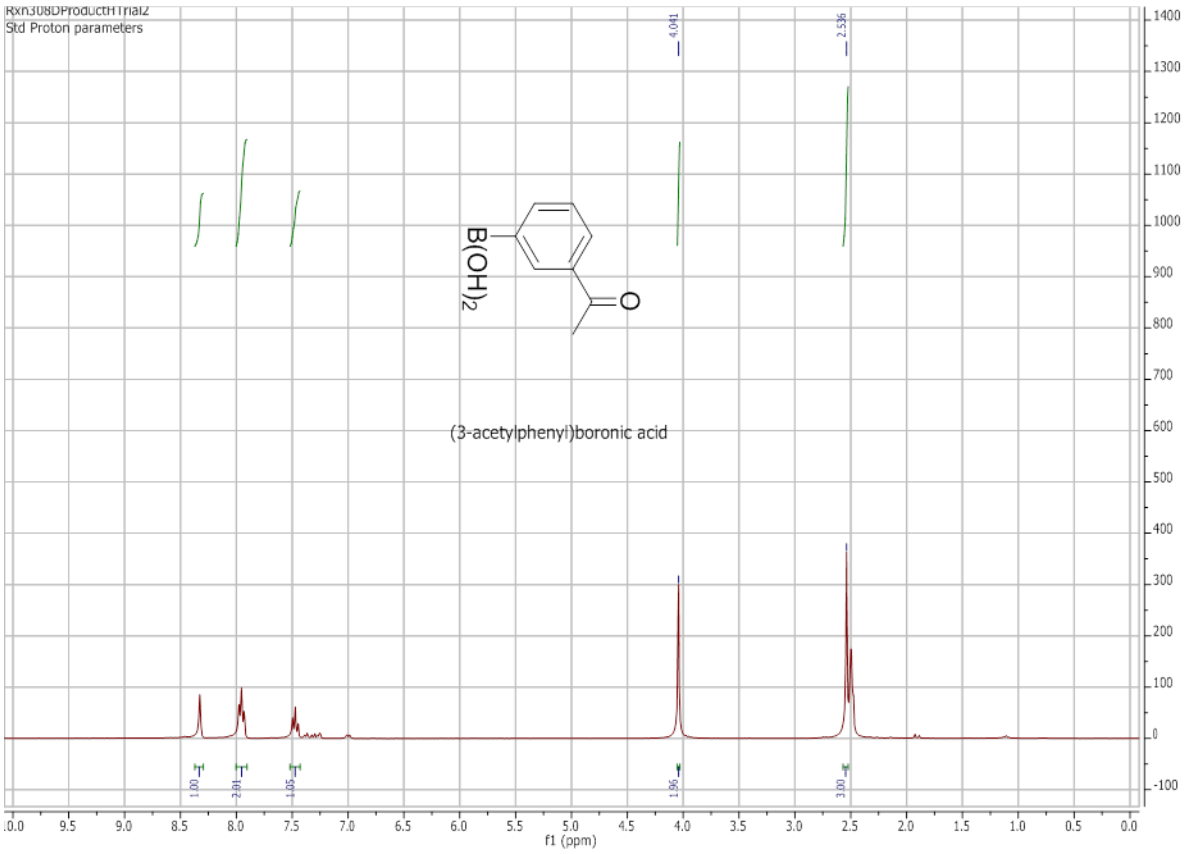


Figure A-85 ^{1}H NMR of 3-Acetylphenylboronic Acid.

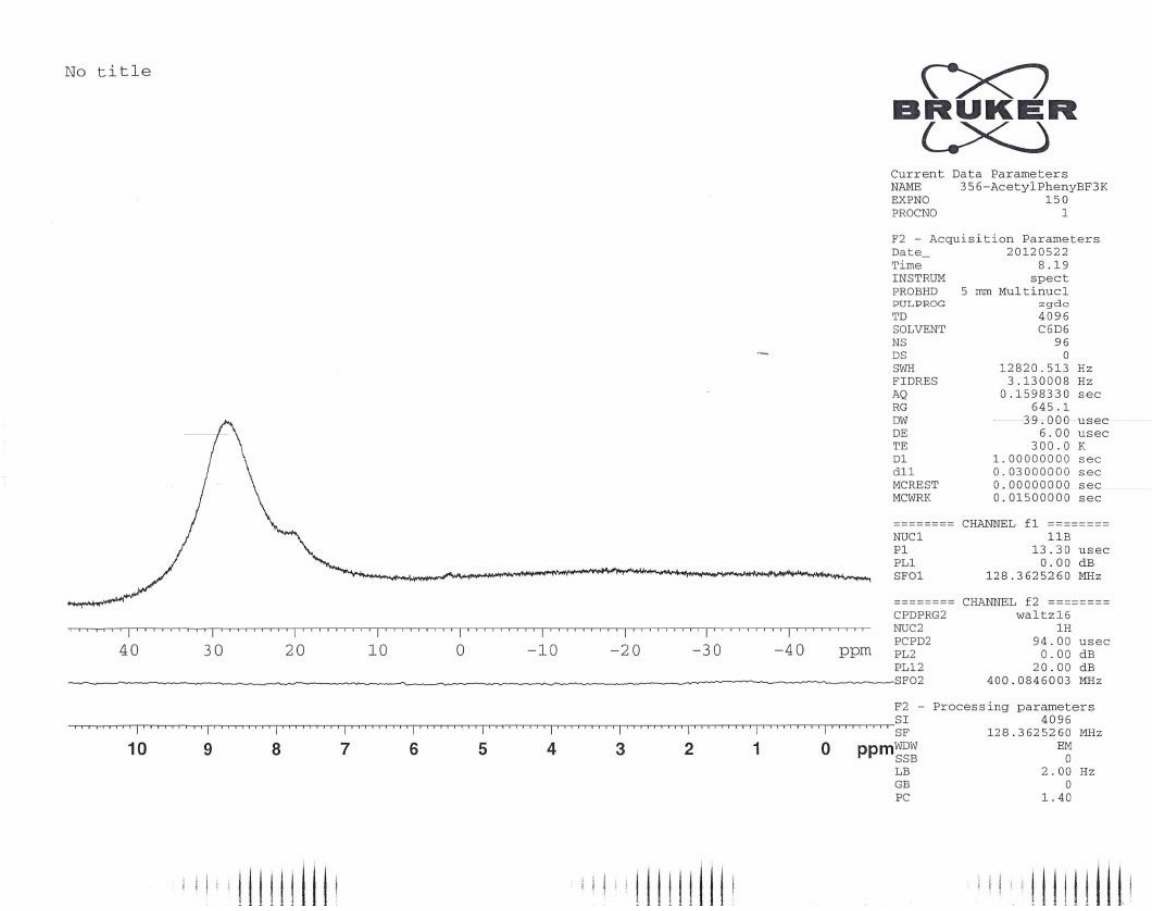


Figure A-86 ^{11}B NMR of 3-Acetylphenylboronic Acid.

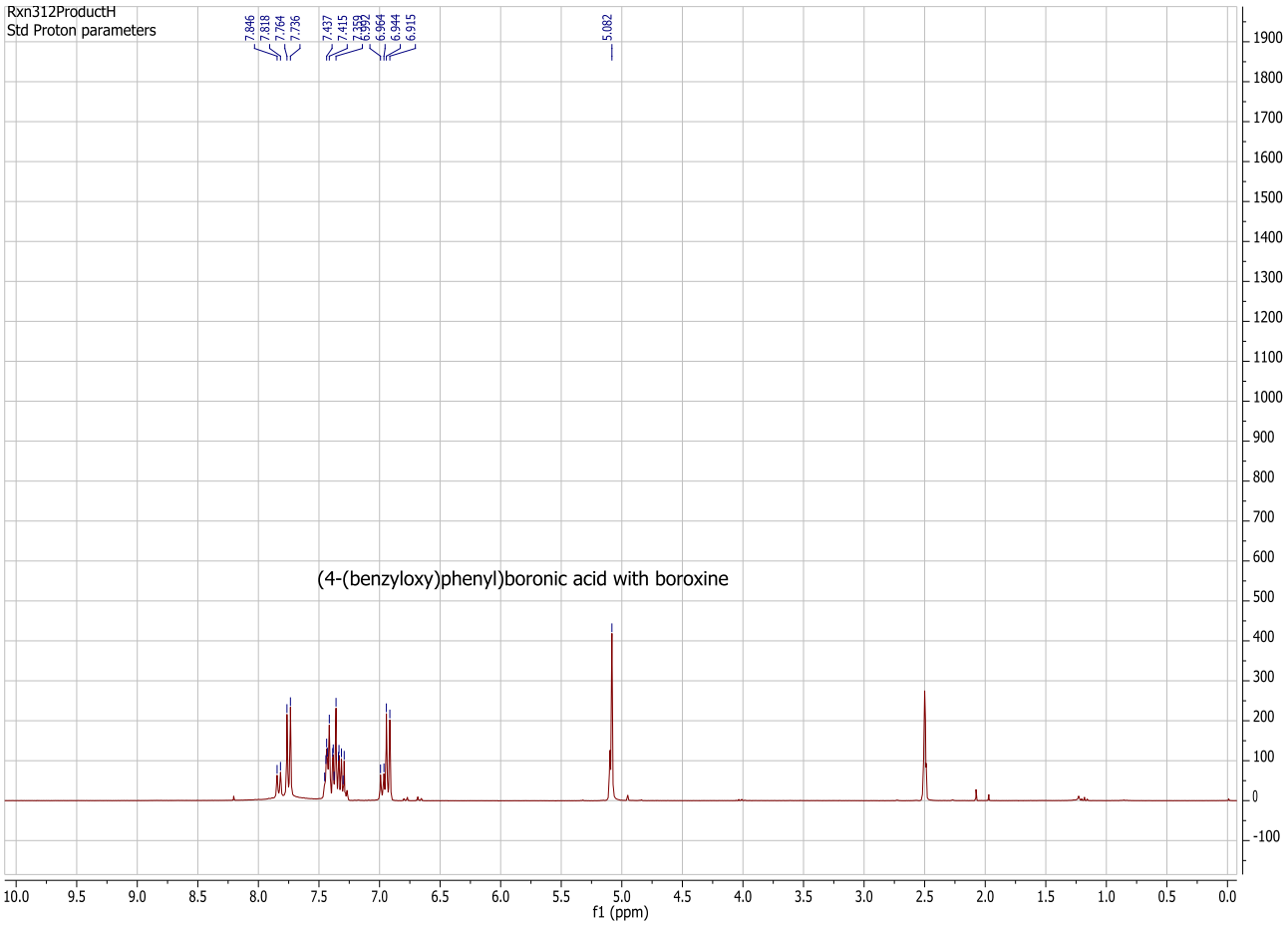


Figure A-87 ^{1}H NMR of (4-(Benzyloxy)phenyl)boronic Acid.

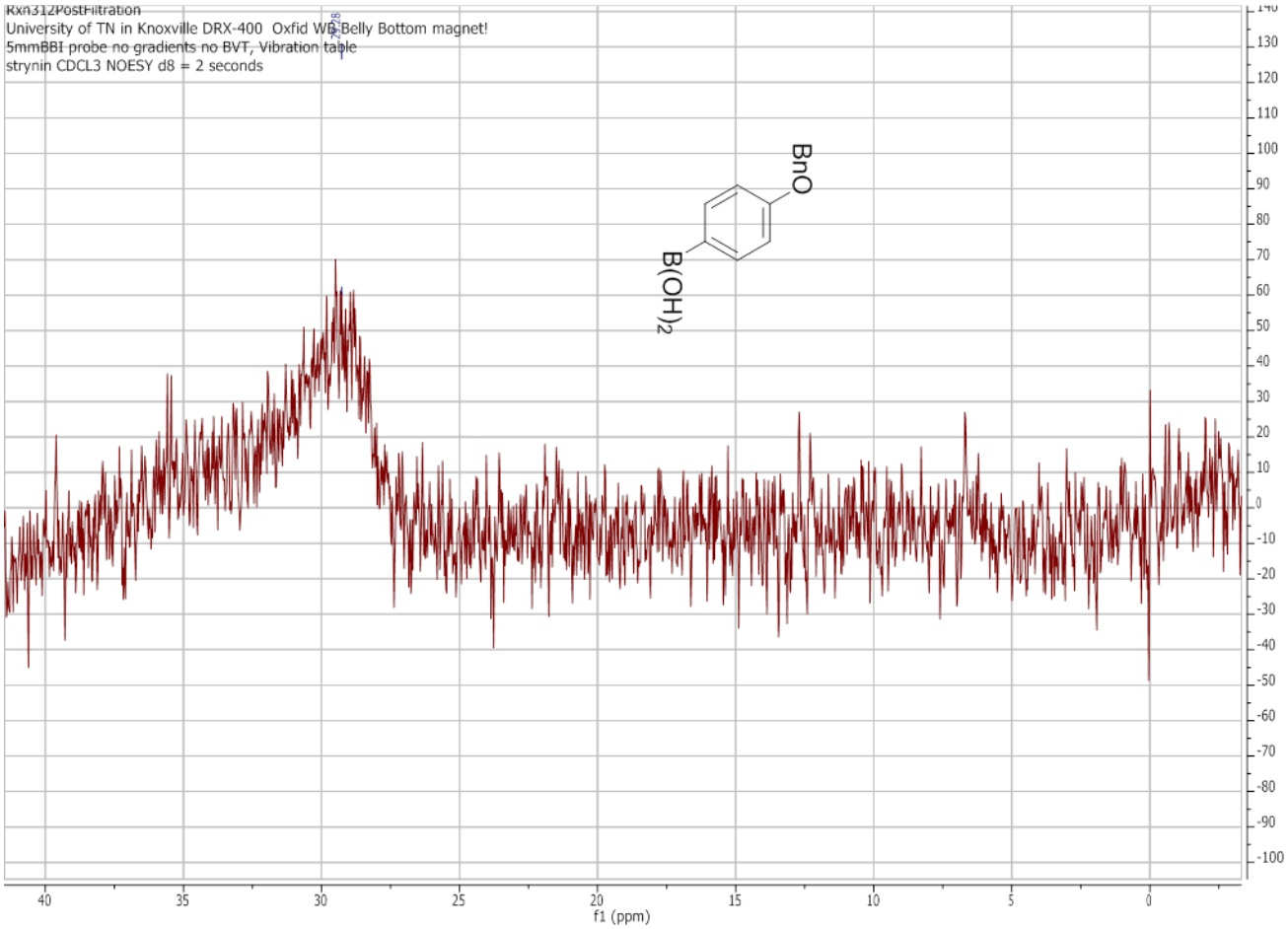


Figure A-88 ^{11}B NMR of (4-(Benzyloxy)phenyl)boronic Acid.

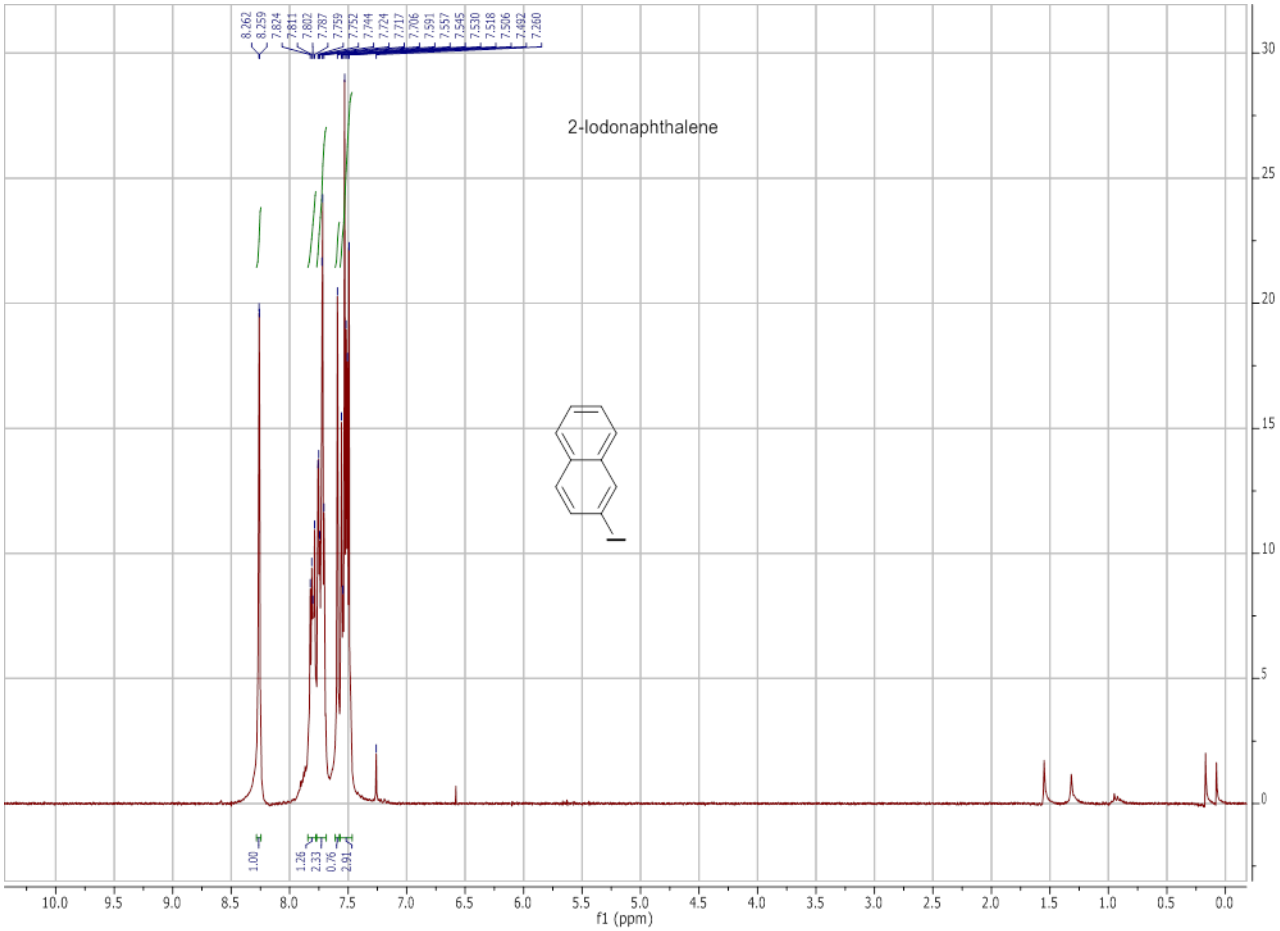


Figure A-89 ^{1}H NMR of 2-Iodonapthalene.

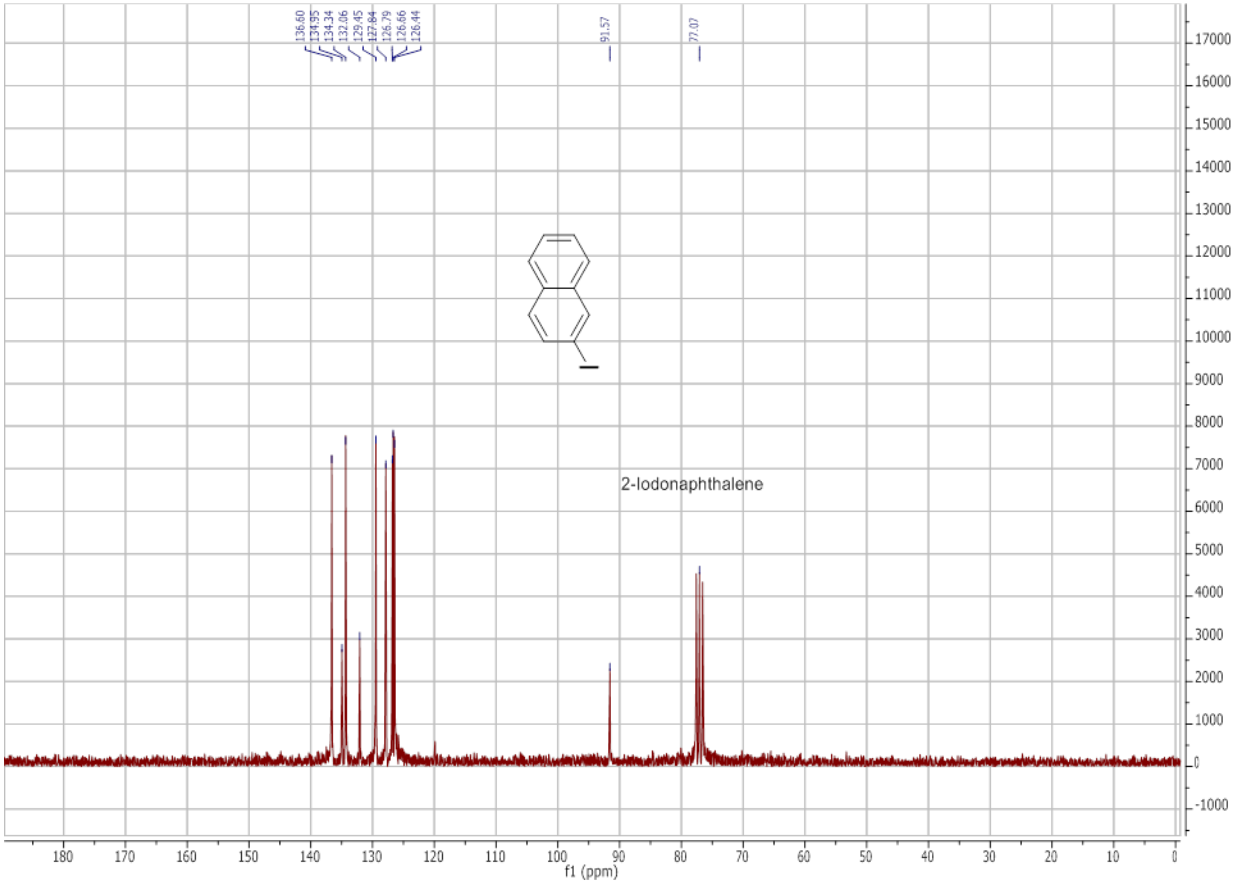


Figure A-90 ^{13}C NMR of 2-Iodonapthalene.

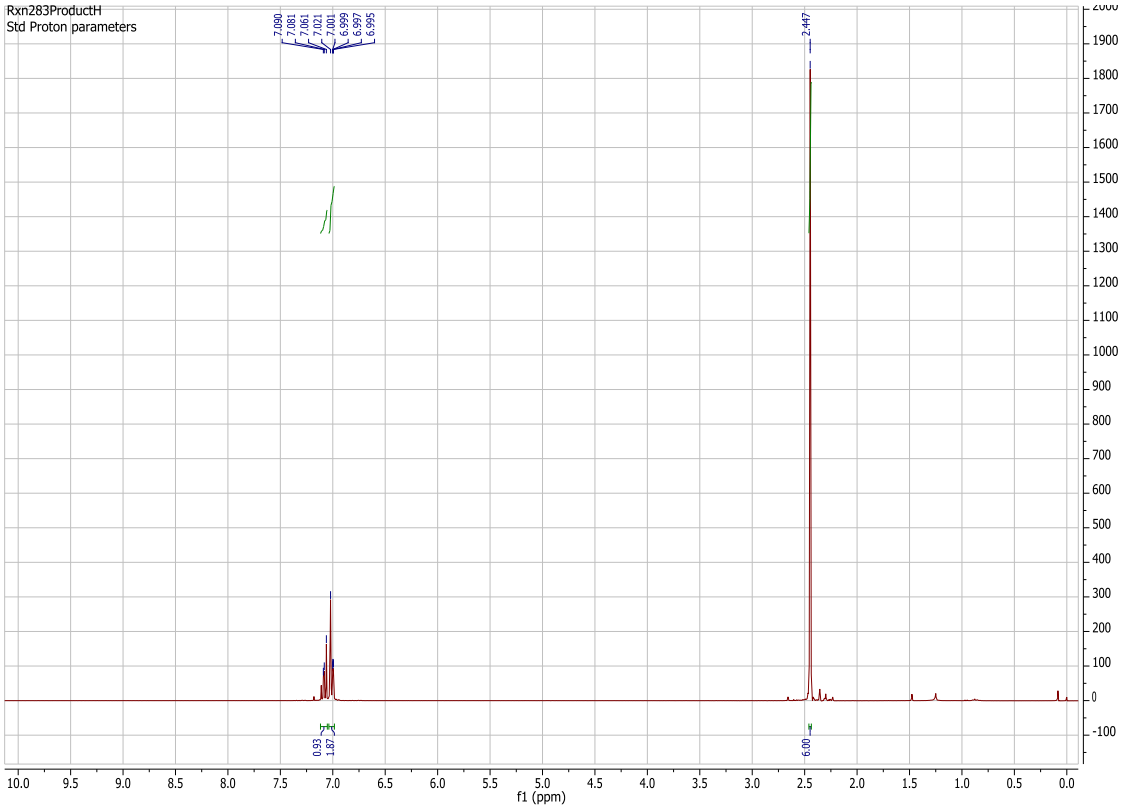


Figure A-91 ^{1}H NMR of 2-Iodo-1,3-dimethylbenzene.

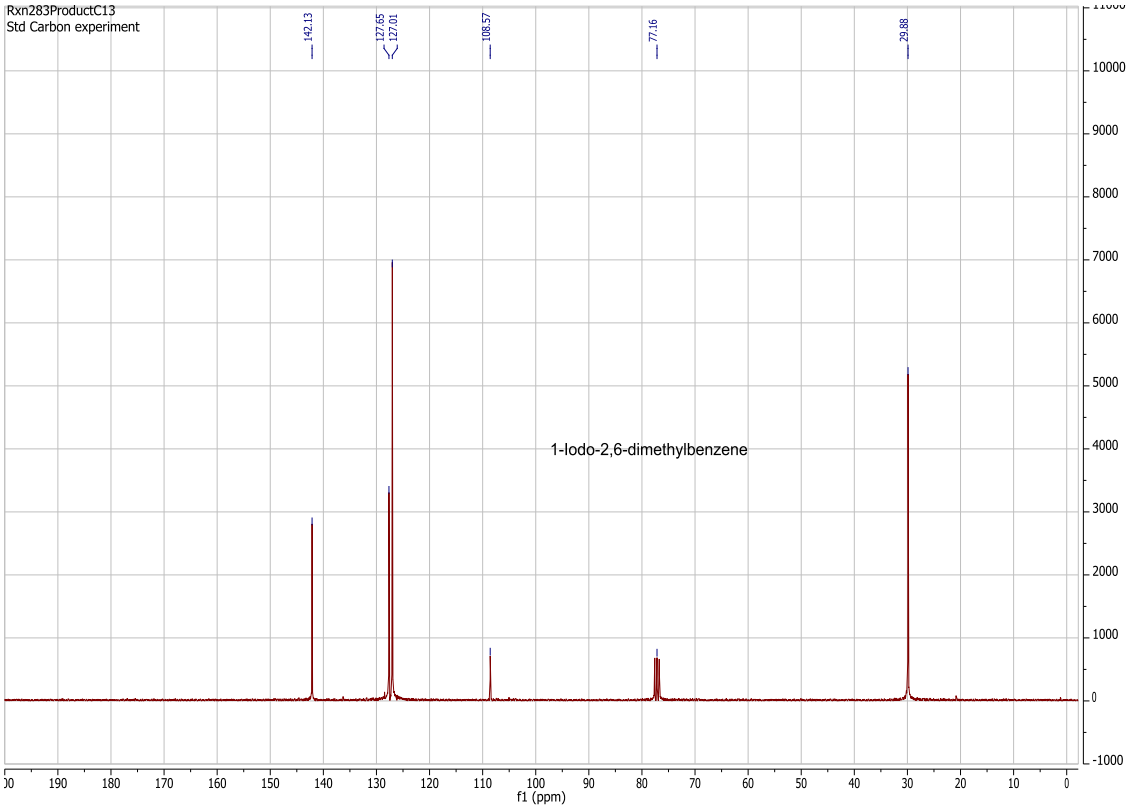


Figure A-92 ^{13}C NMR of 2-Iodo-1,3-dimethylbenzene.

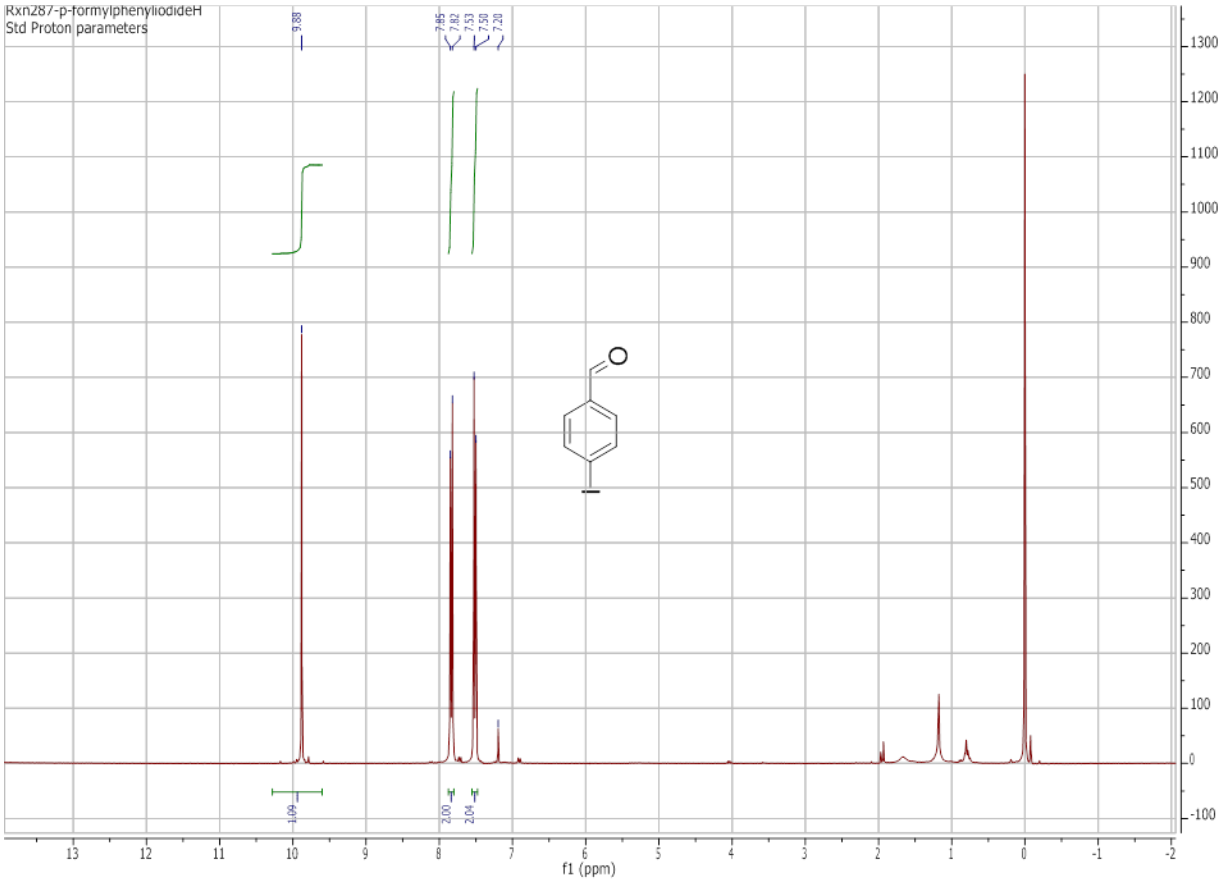


Figure A-93 ^{1}H NMR of *p*-Iodobenzaldehyde.

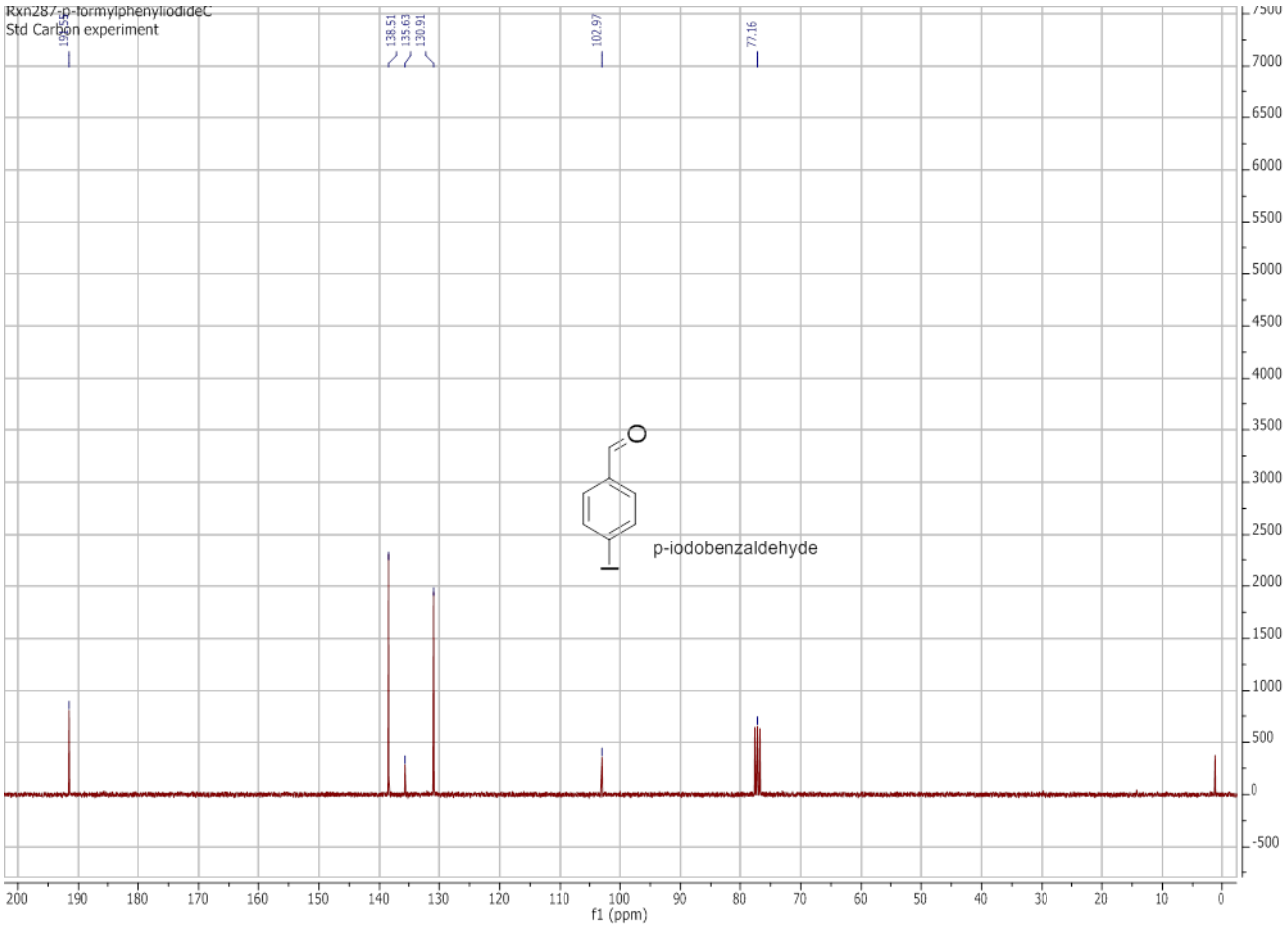


Figure A-94 ^{13}C NMR of *p*-Iodobenzaldehyde.

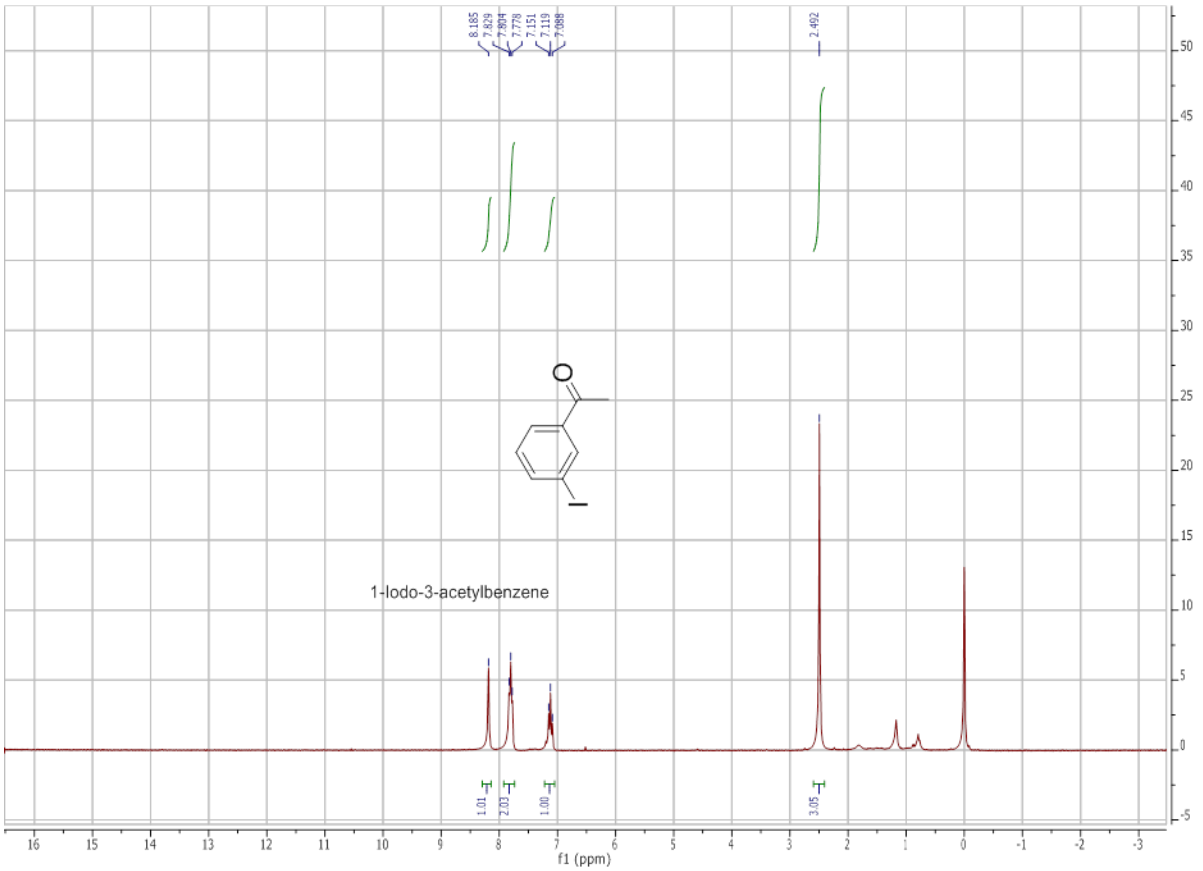


Figure A-95 ^{1}H NMR of 1-(3-Iodophenyl)ethanone.

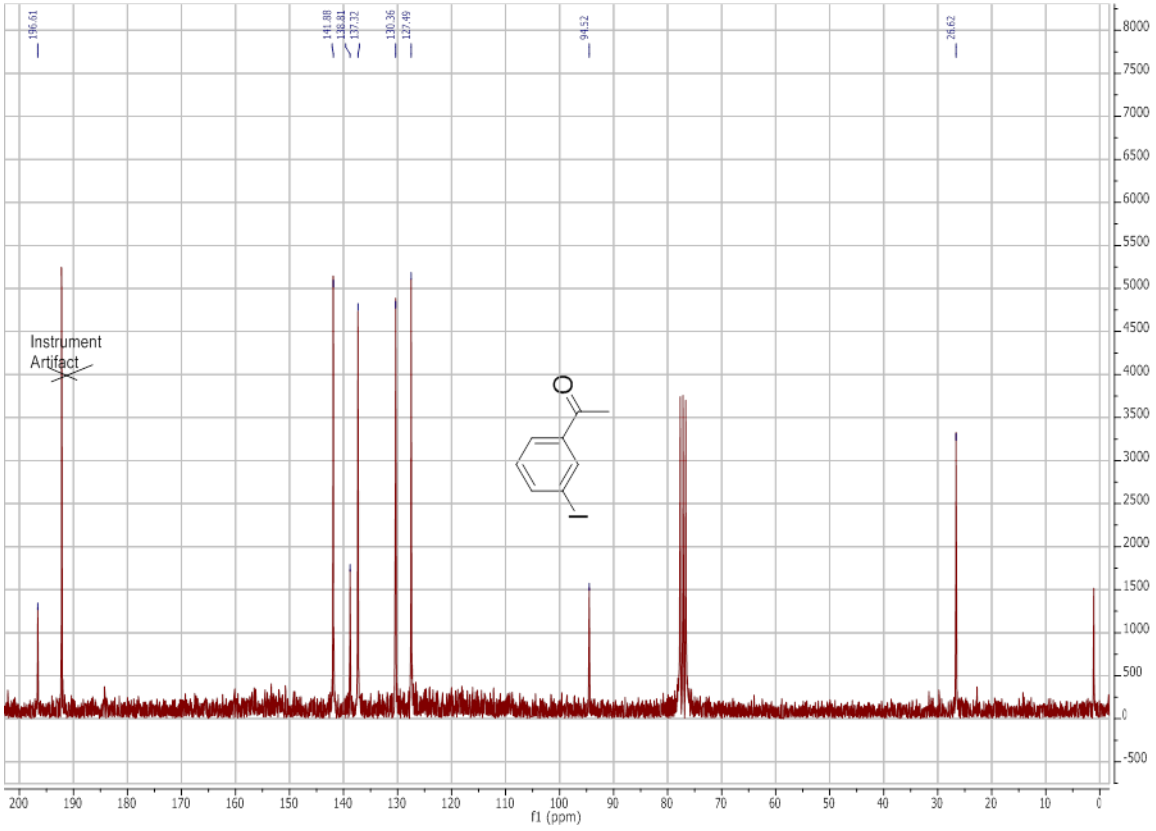


Figure A-96 ^{13}C NMR of 1-(3-Iodophenyl)ethanone.

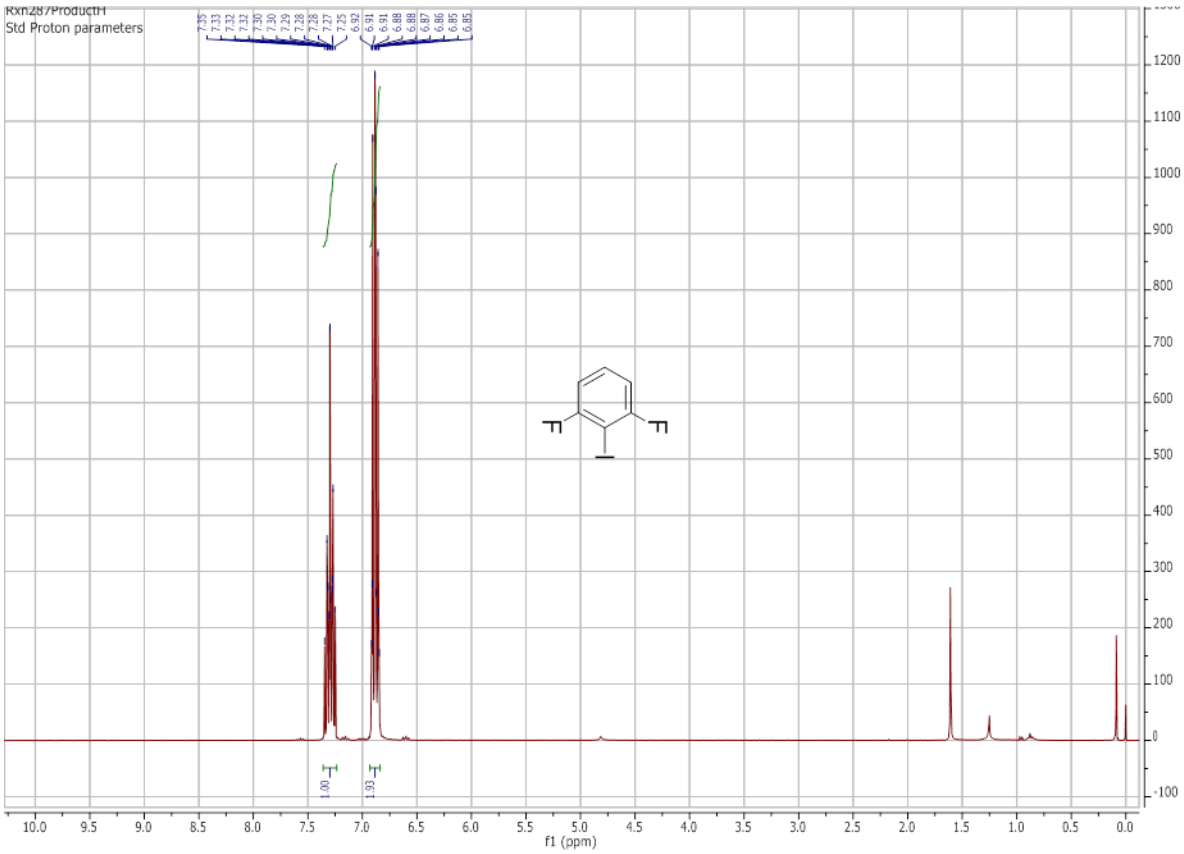


Figure A-97 ^{1}H NMR of 1,3-Difluoro-2-iodobenzene.

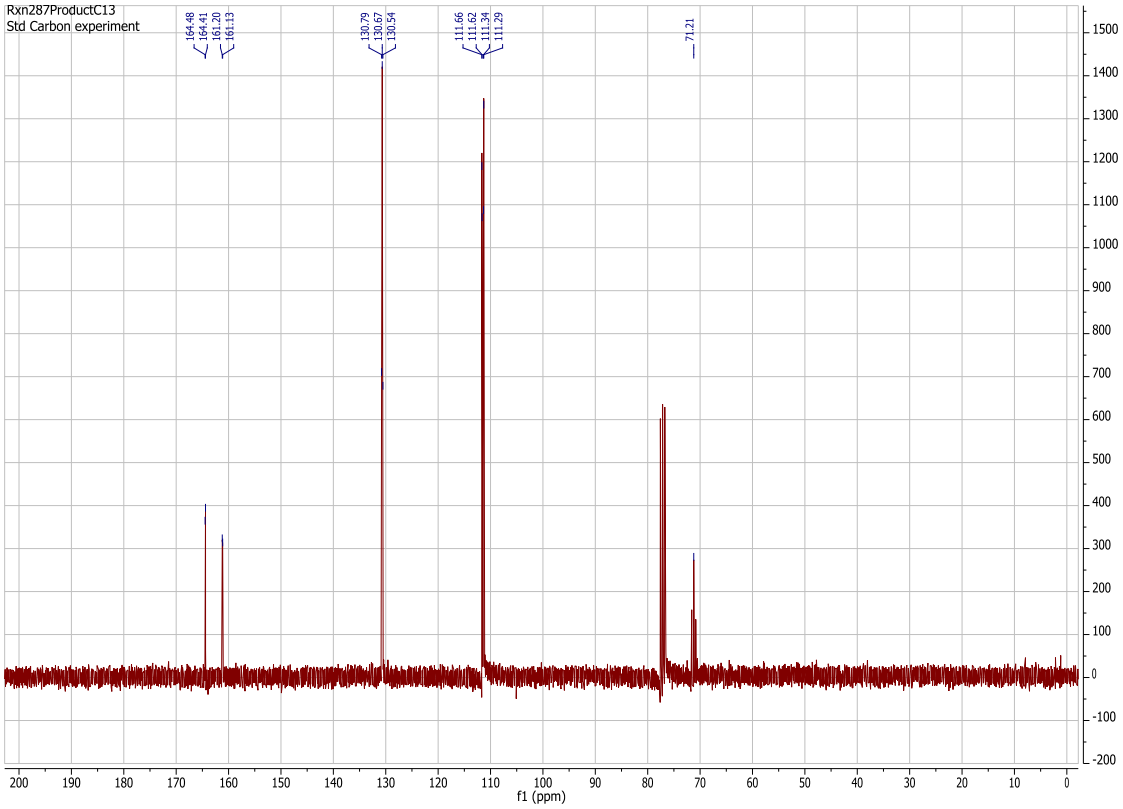


Figure A-98 ^{13}C NMR of 1,3-Difluoro-2-iodobenzene.

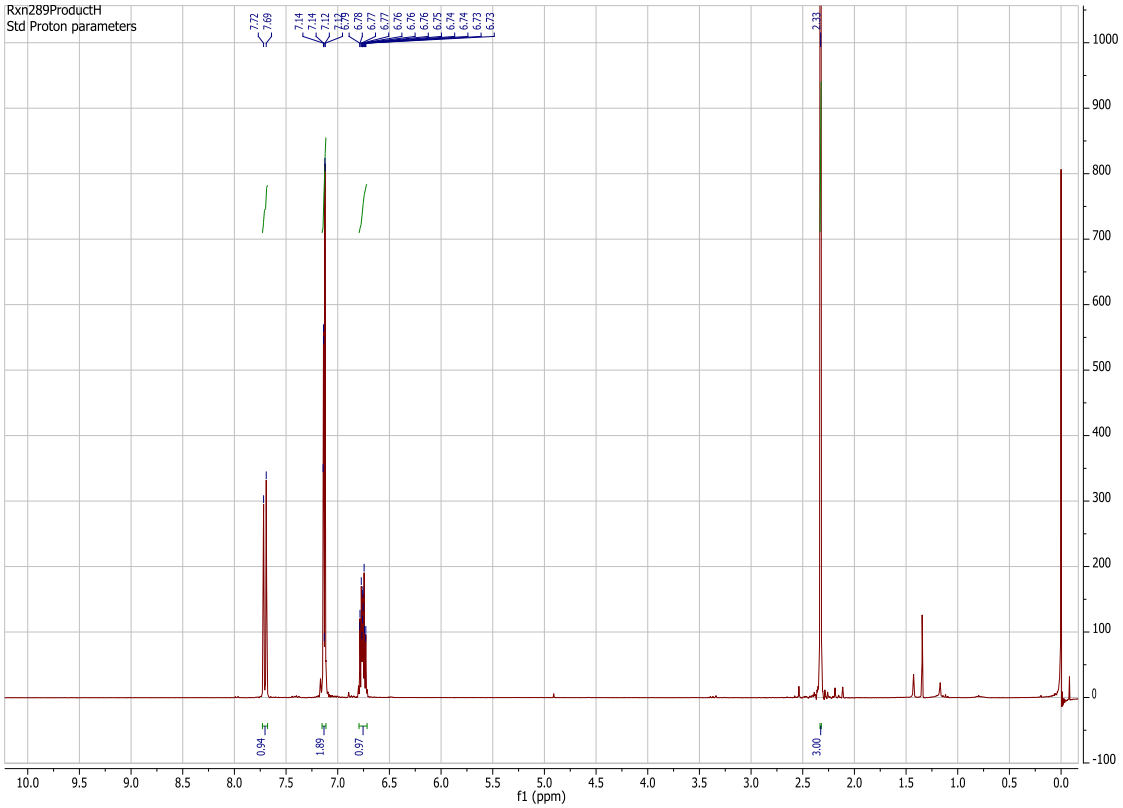


Figure A-99 ^{1}H NMR of 1-Iodo-2-methylbenzene.

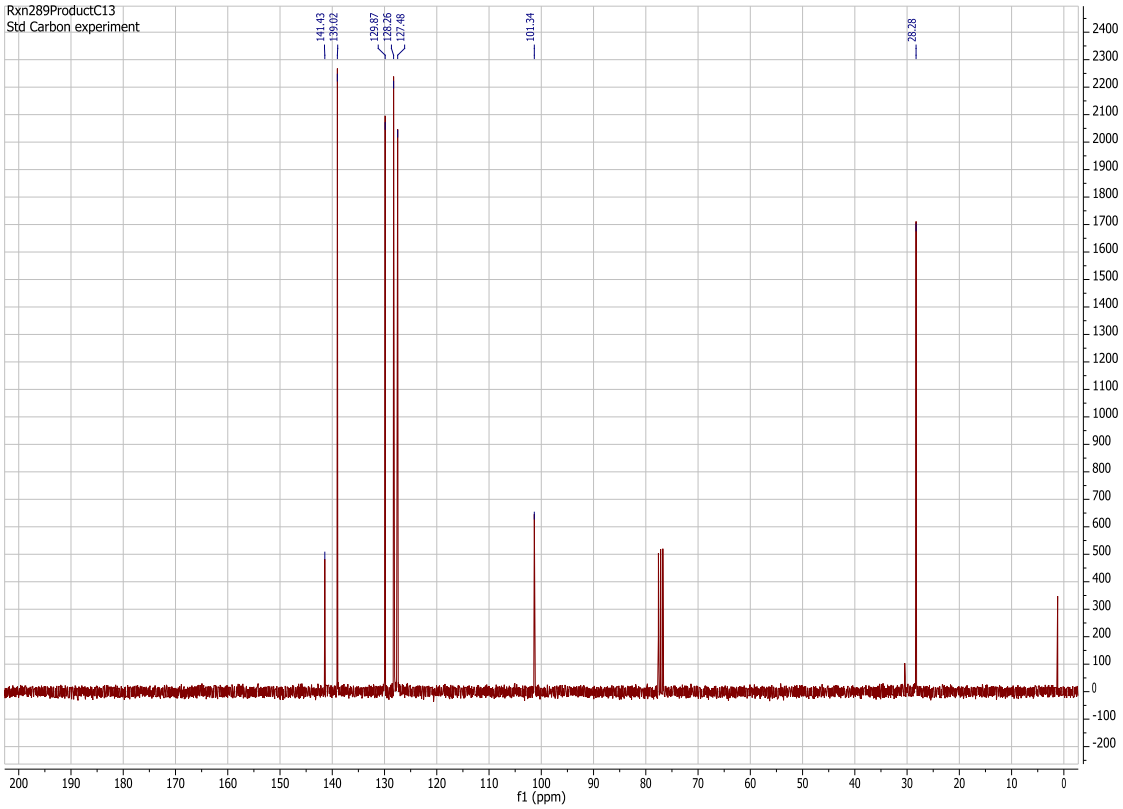


Figure A-100 ^{13}C NMR of 1-Iodo-2-methylbenzene.

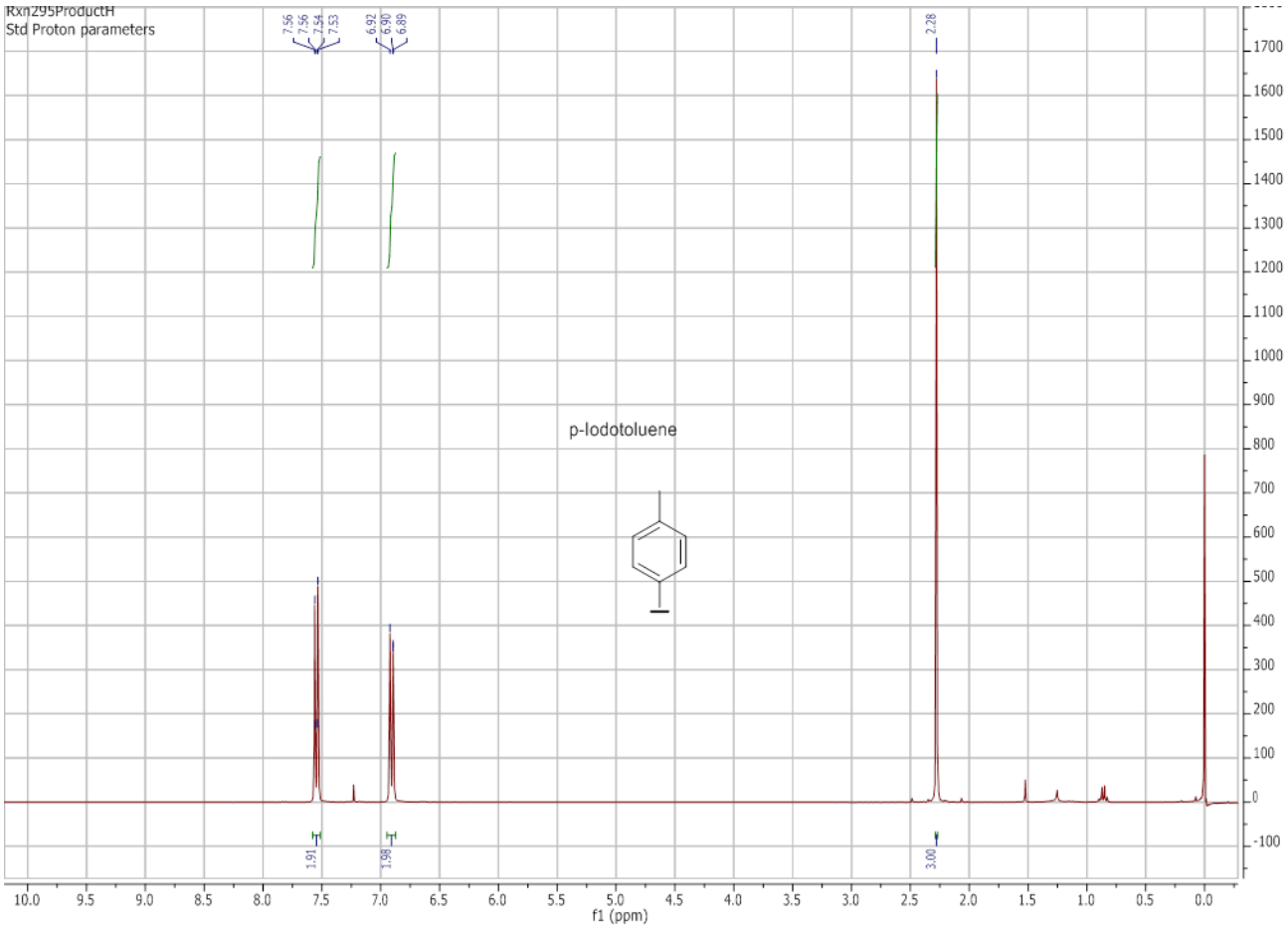


Figure A-101 ^{1}H NMR of *p*-Iodotoluene.

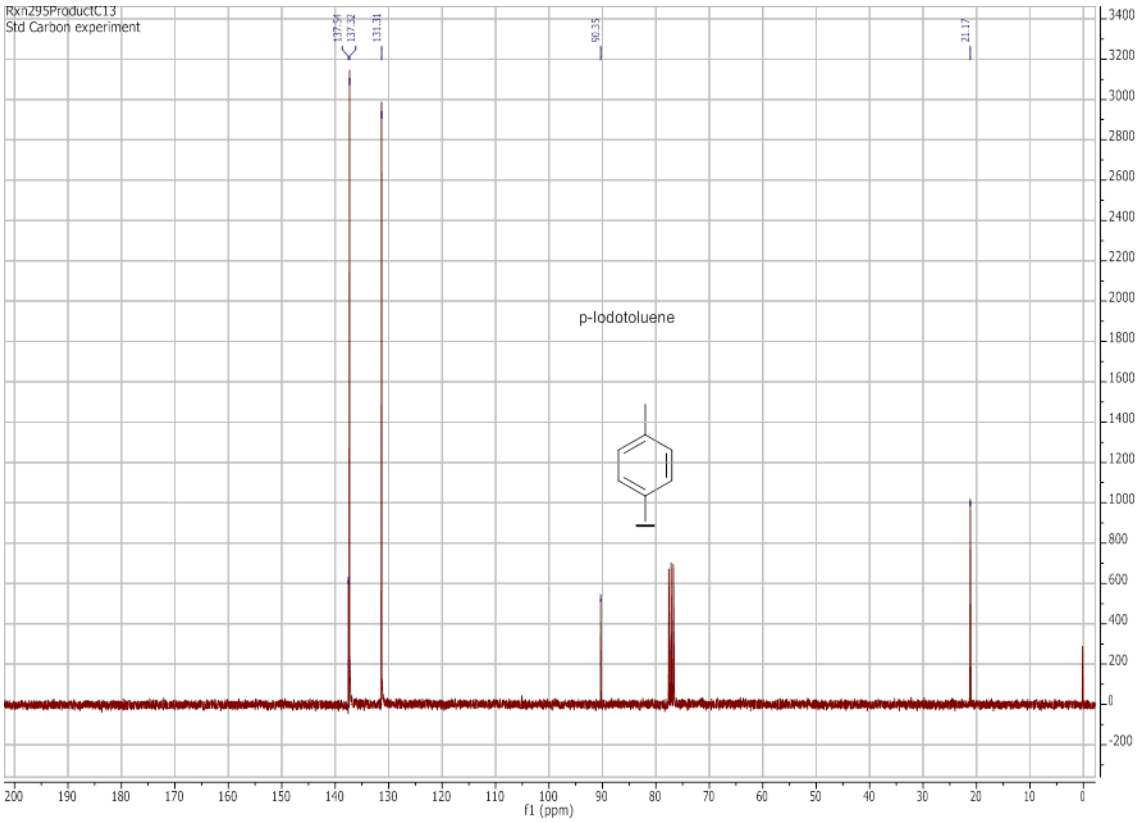


Figure A-102 ^{13}C NMR of *p*-Iodotoluene.

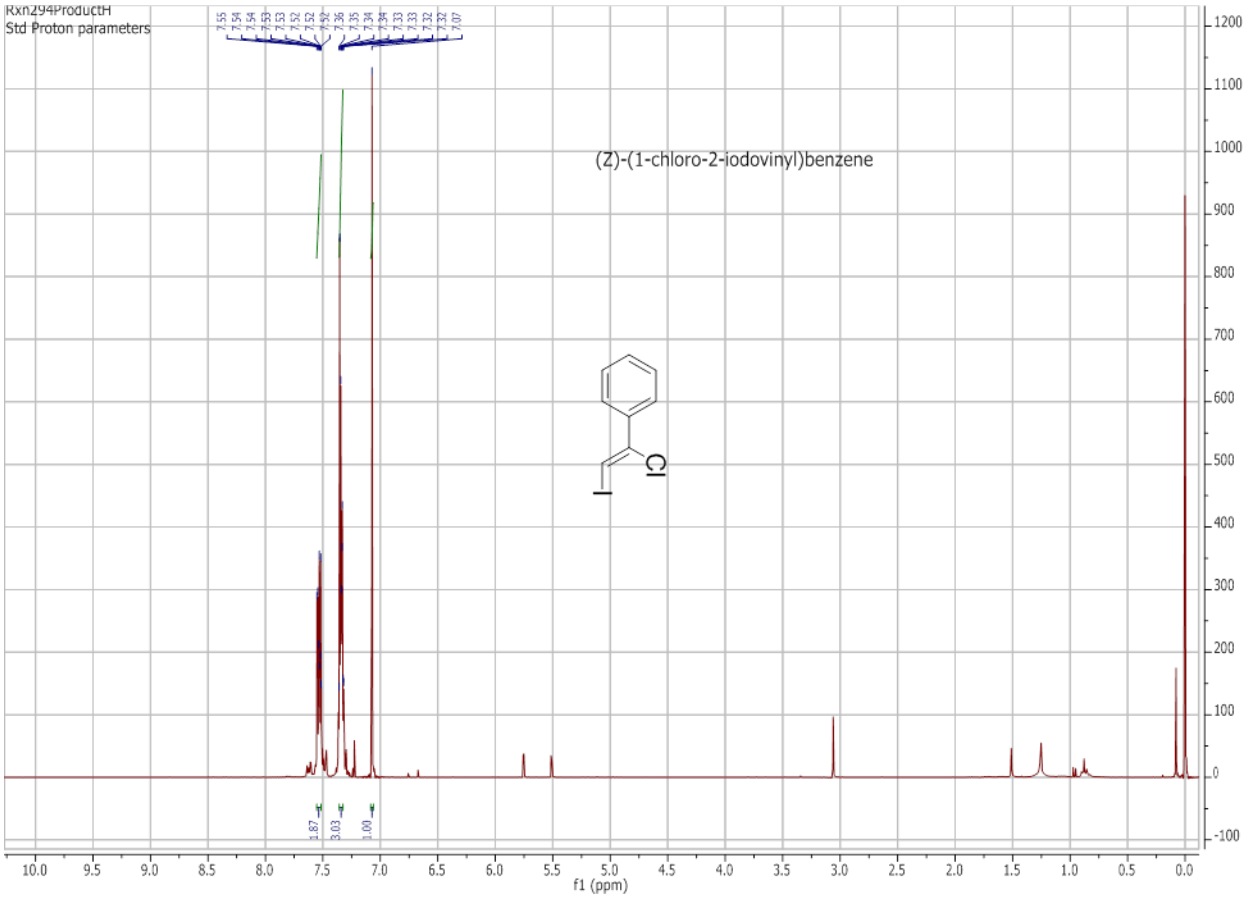


Figure A-103 ^{1}H NMR of (*Z*)-(1-Chloro-2-iodovinyl)benzene.

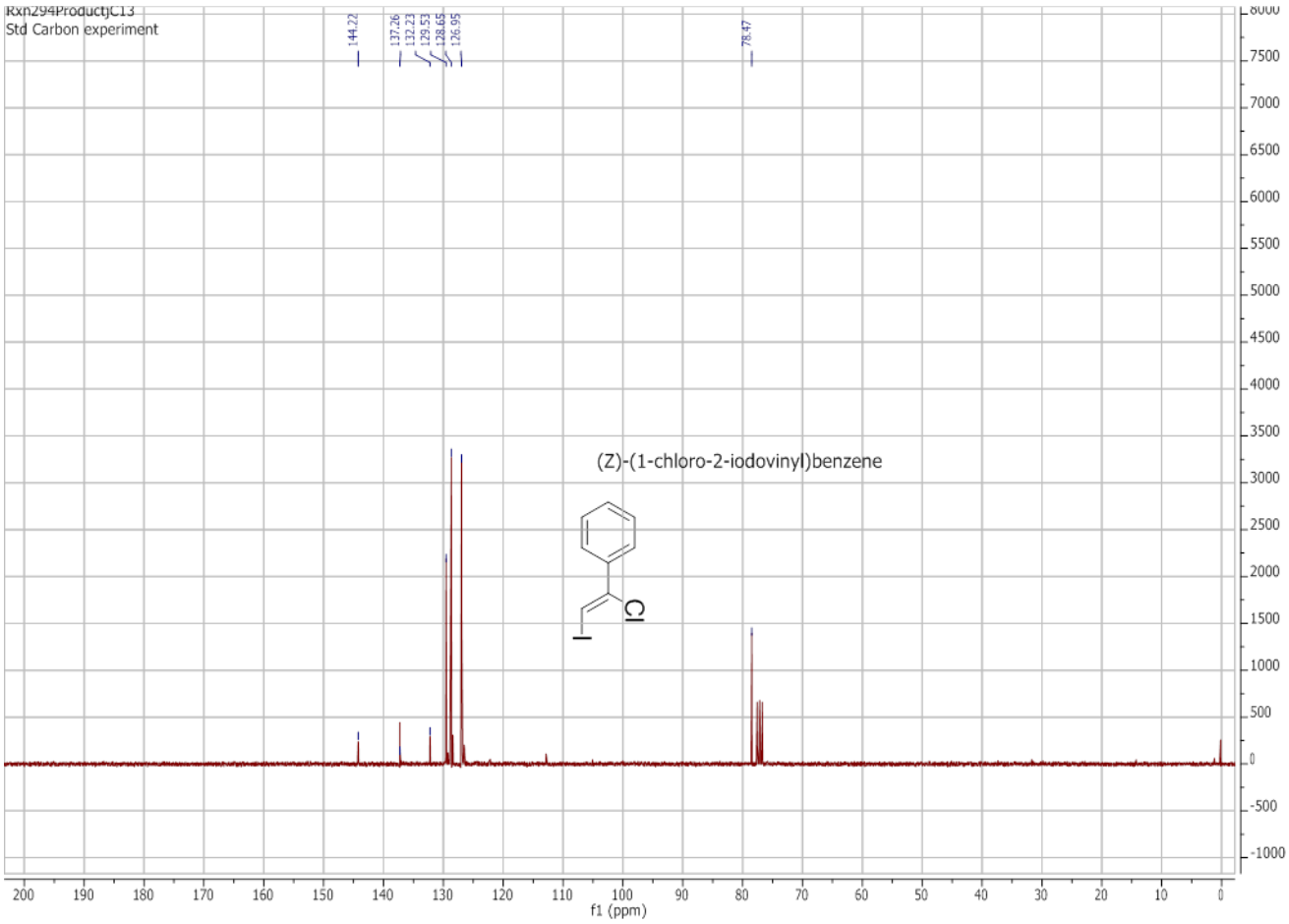


Figure A-104 ^{13}C NMR of (*Z*)-(1-Chloro-2-iodovinyl)benzene.

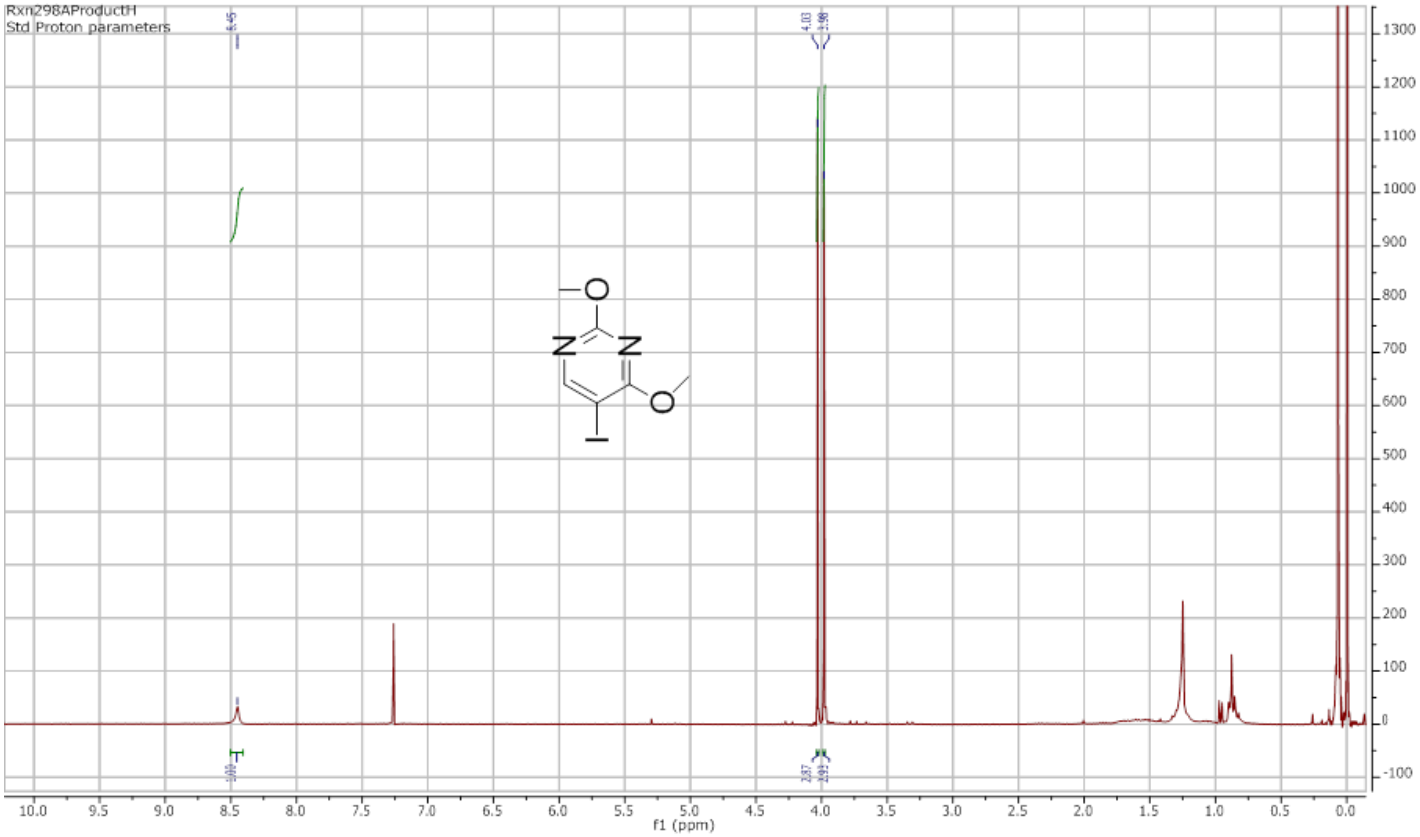


Figure A-105 ^{1}H NMR of 5-Iodo-2,4-dimethoxypyrimidine.

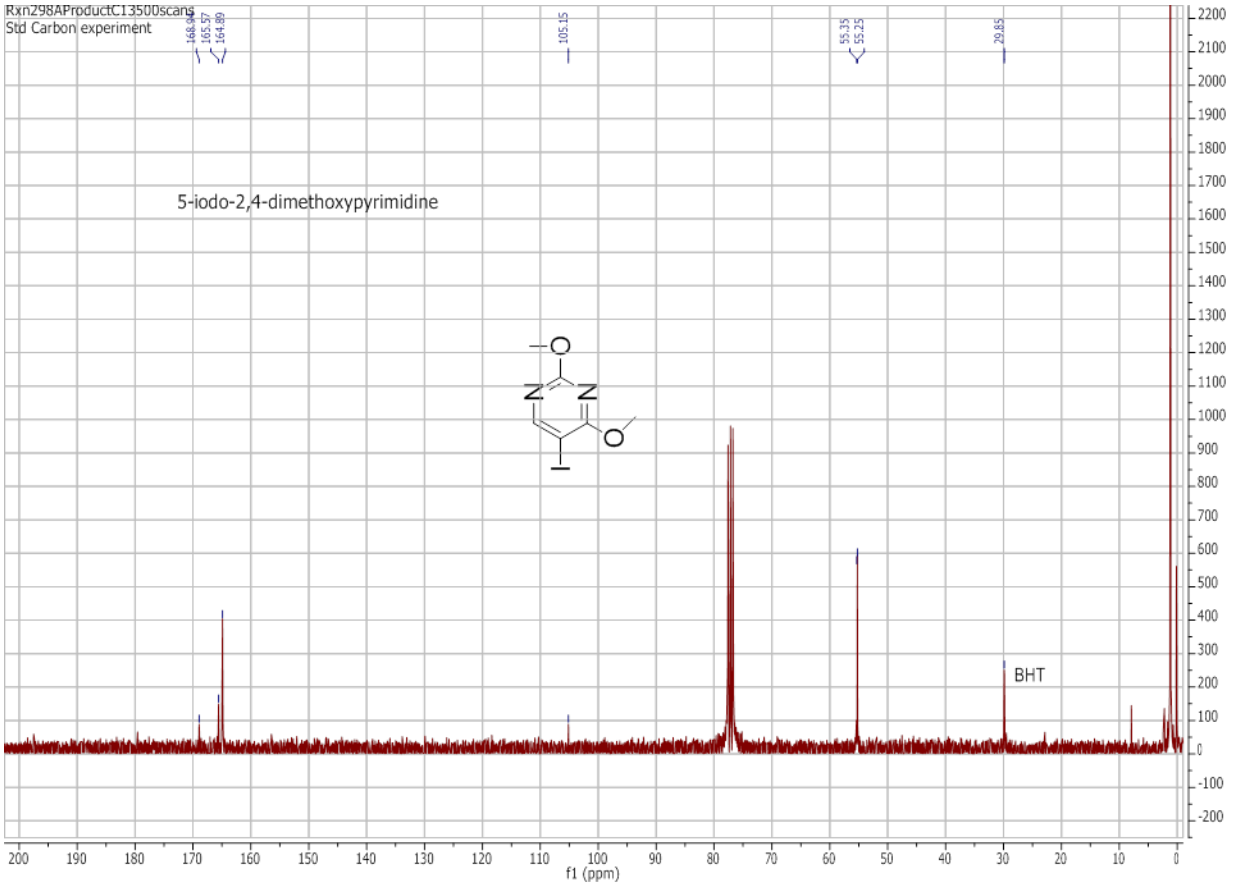


Figure A-106 ^{13}C NMR of 5-Iodo-2,4-dimethoxypyrimidine.

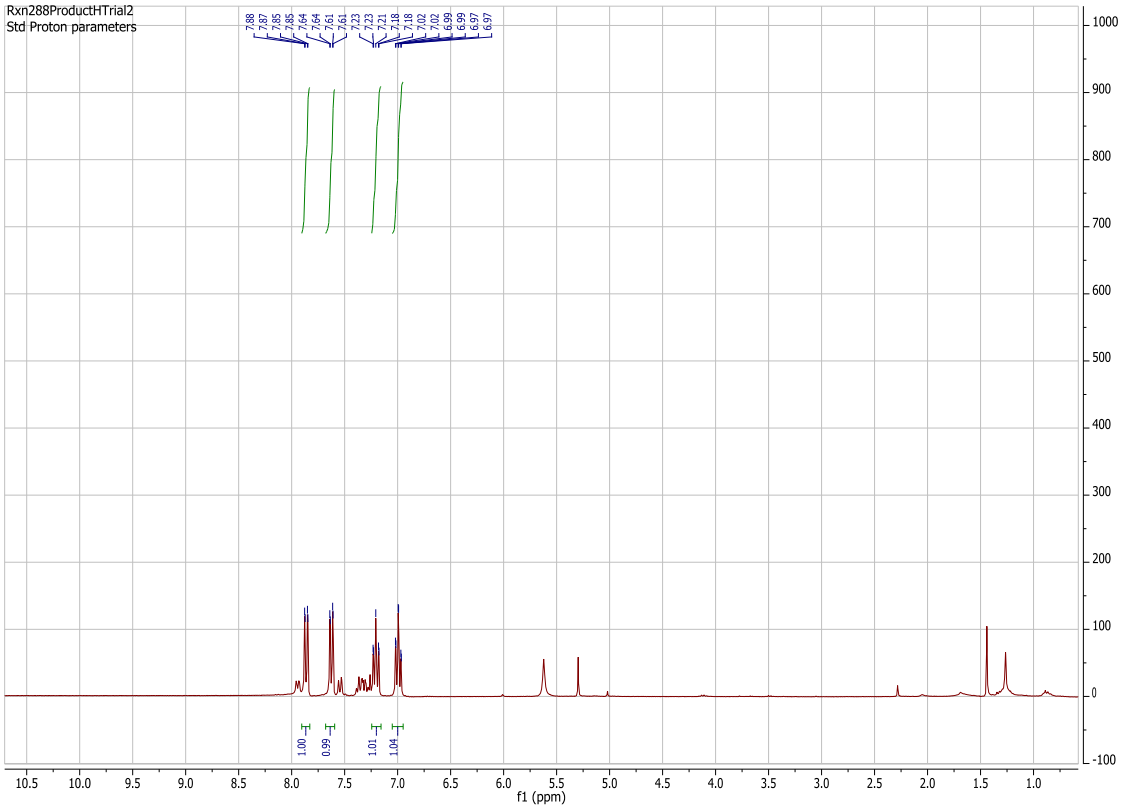


Figure A-107 ^{1}H NMR of 1-Iodo-2-bromobenzene.

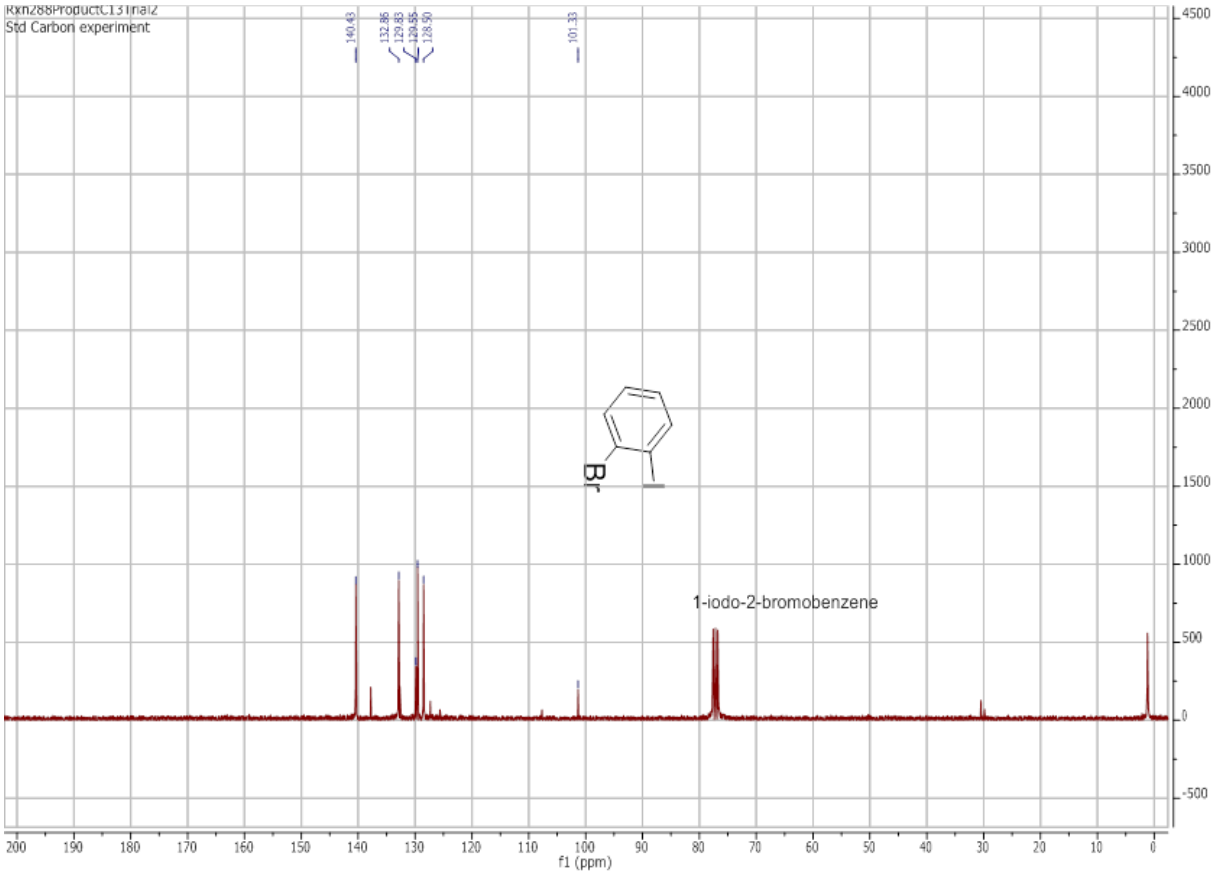


Figure A-108 ^{13}C NMR of 1-Iodo-2-bromobenzene.

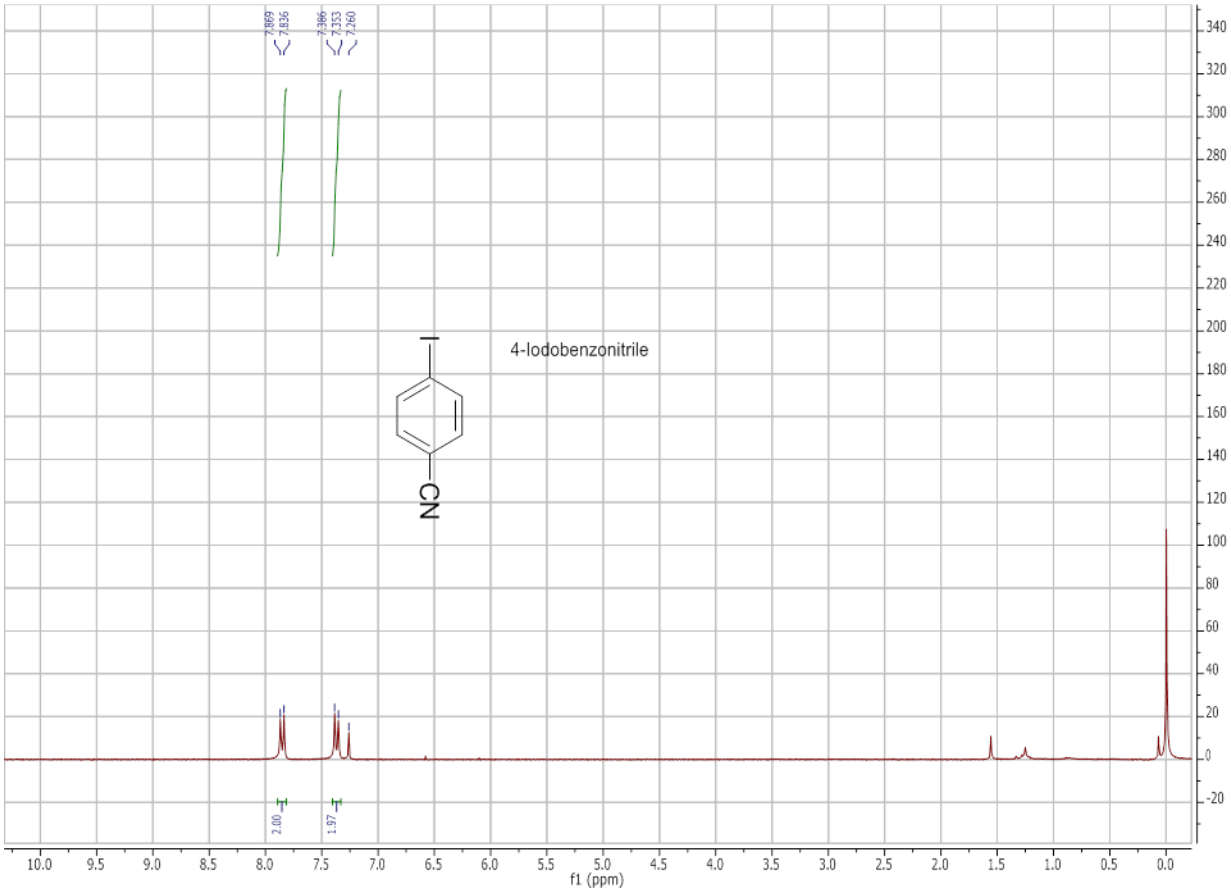


Figure A-109 ^{1}H NMR of 4-Iodobenzonitrile.

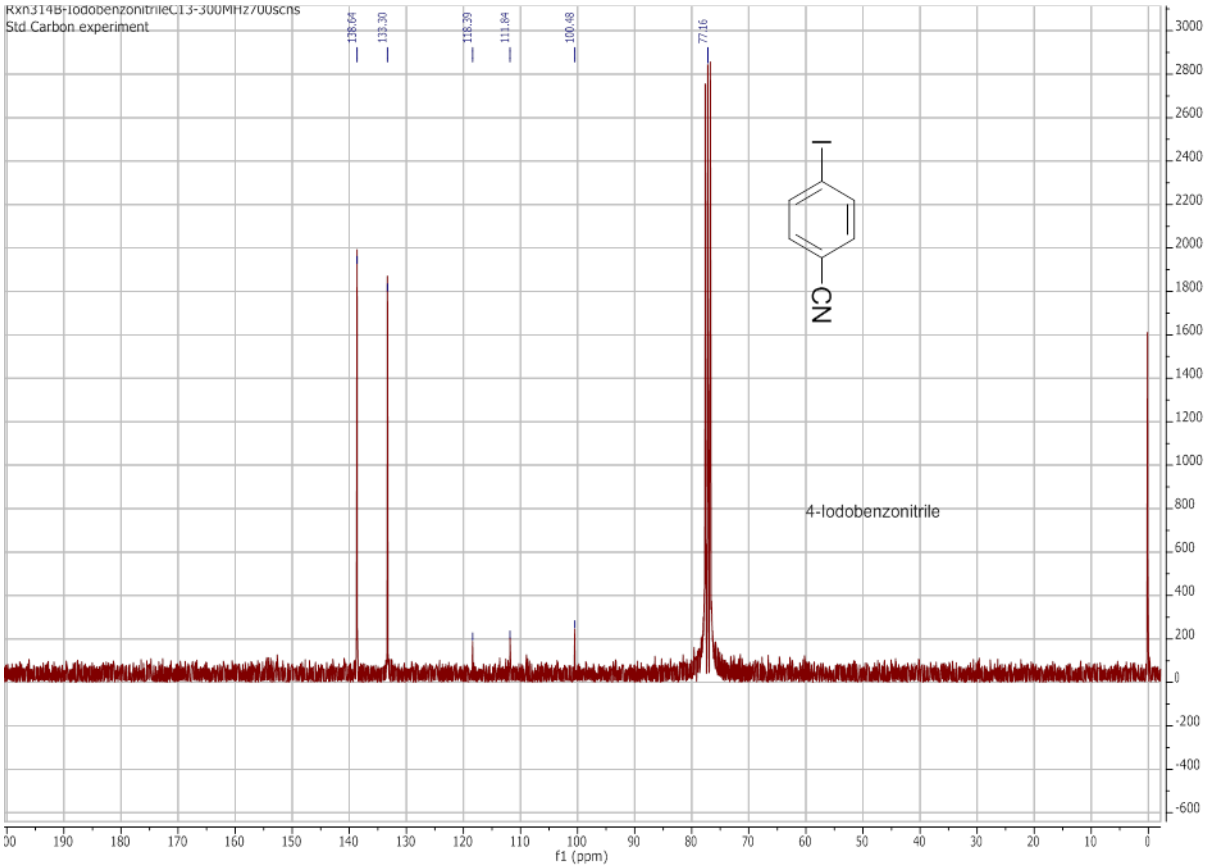


Figure A-110 ^{13}C NMR of 4-Iodobenzonitrile.

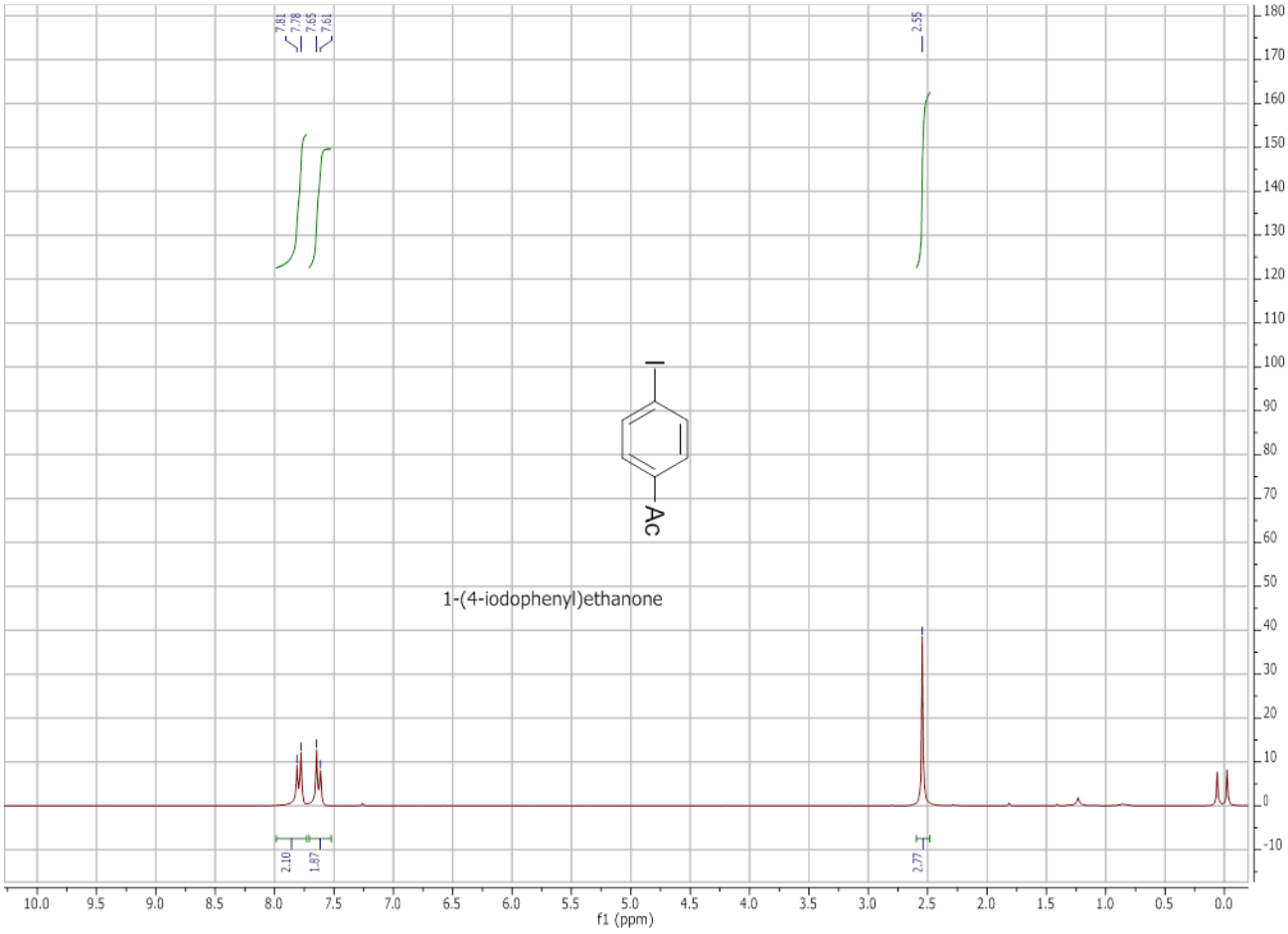


Figure A-111 ^{1}H NMR of 1-(4-Iodophenyl)ethanone.

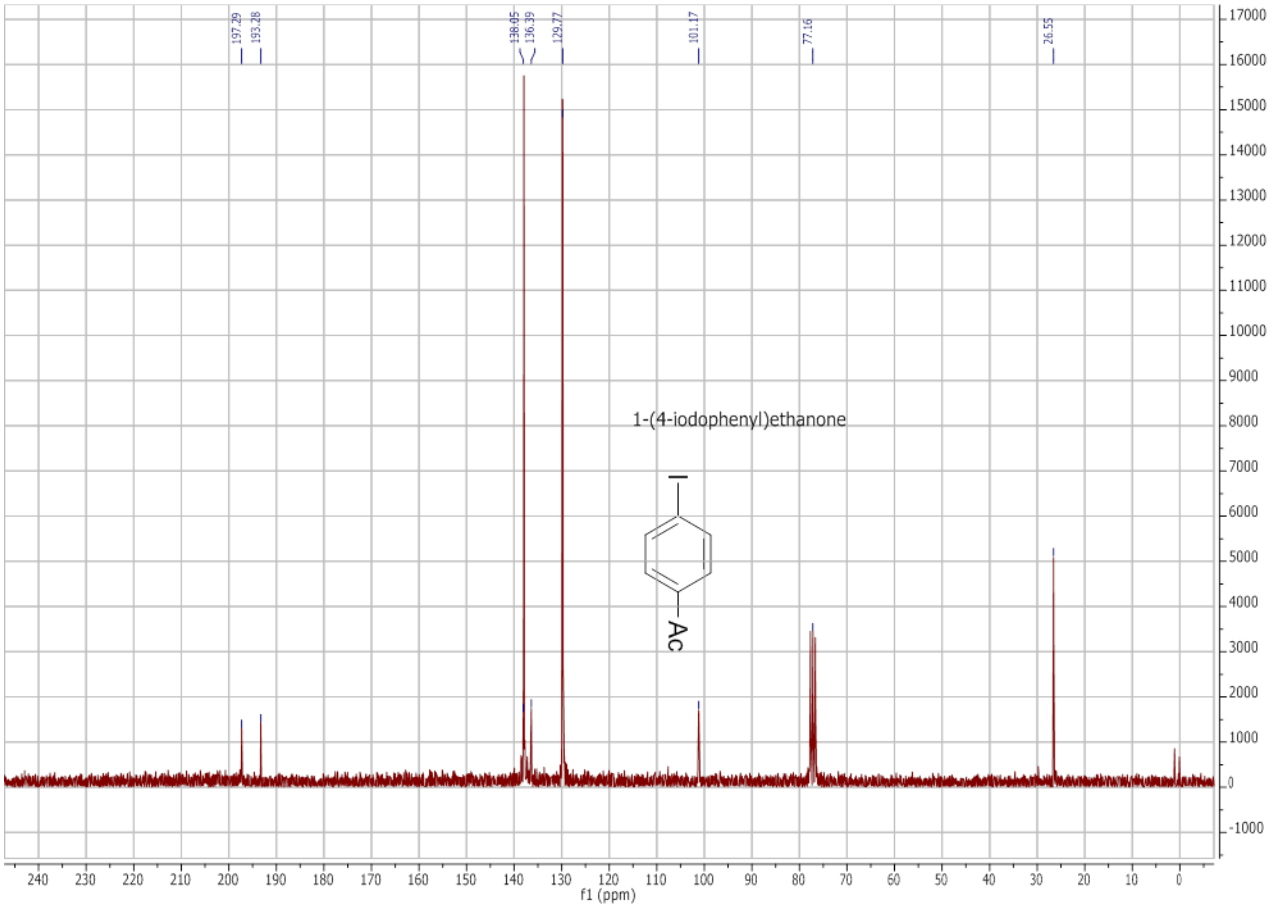


Figure A-112 ^{13}C NMR of 1-(4-Iodophenyl)ethanone.

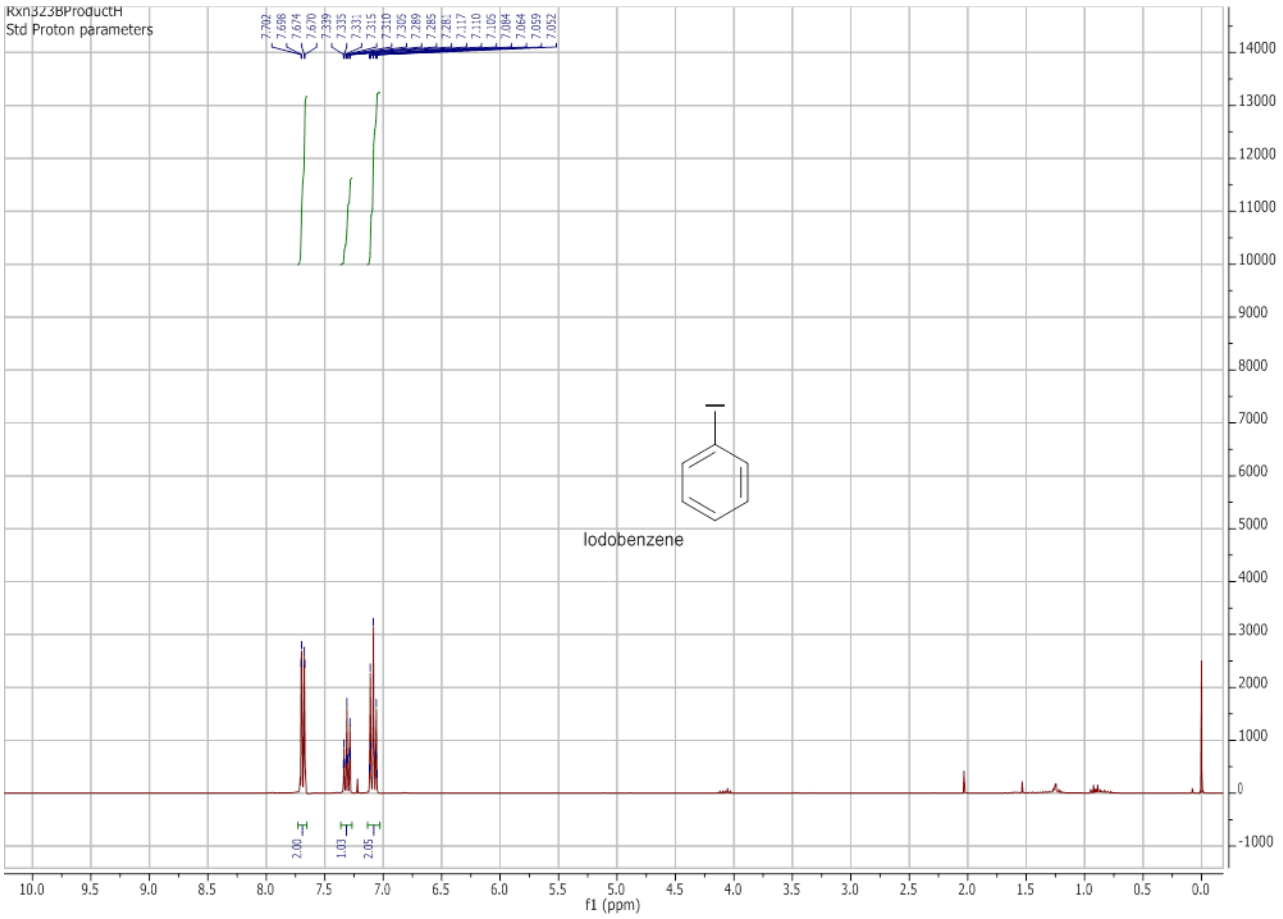


Figure A-113 ^{1}H NMR of Iodobenzene.

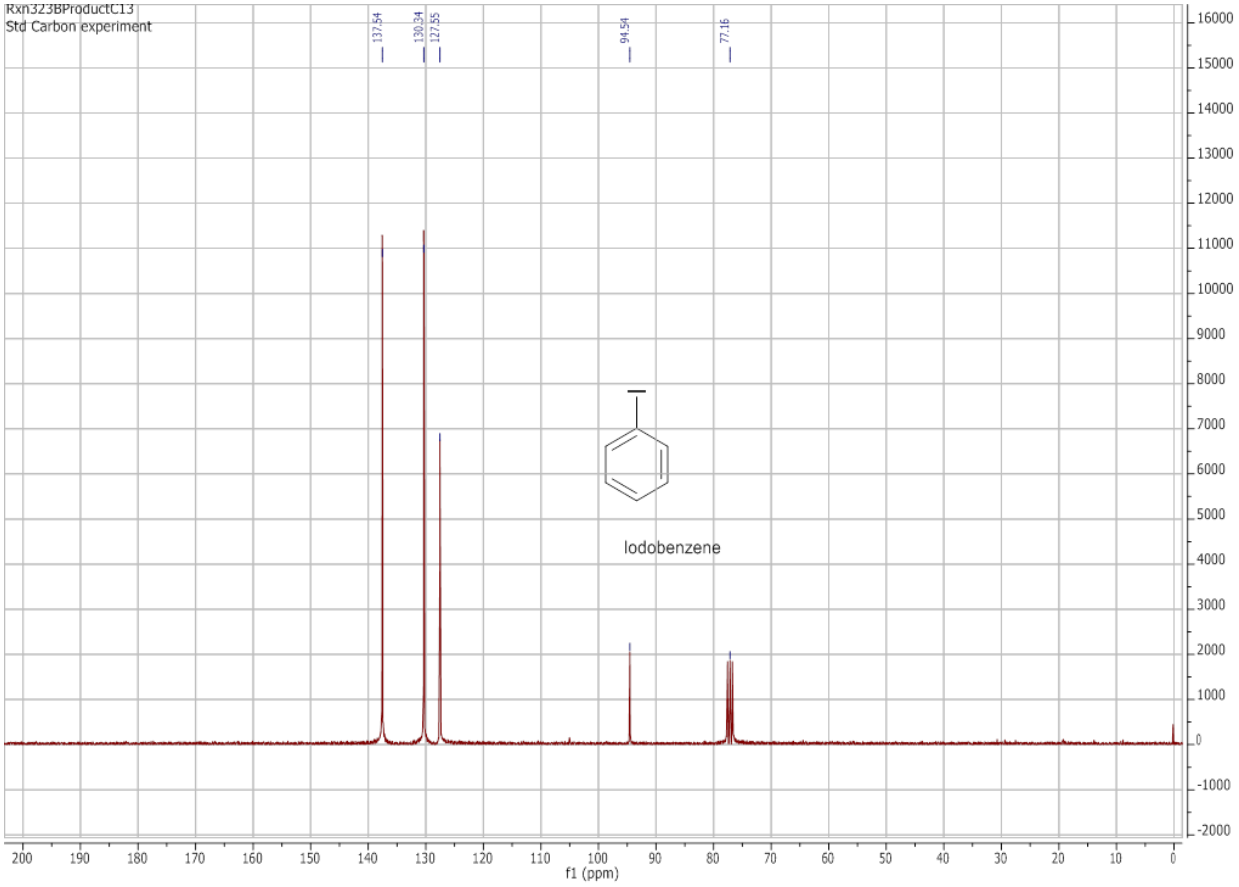


Figure A-114 ^{13}C NMR of Iodobenzene.

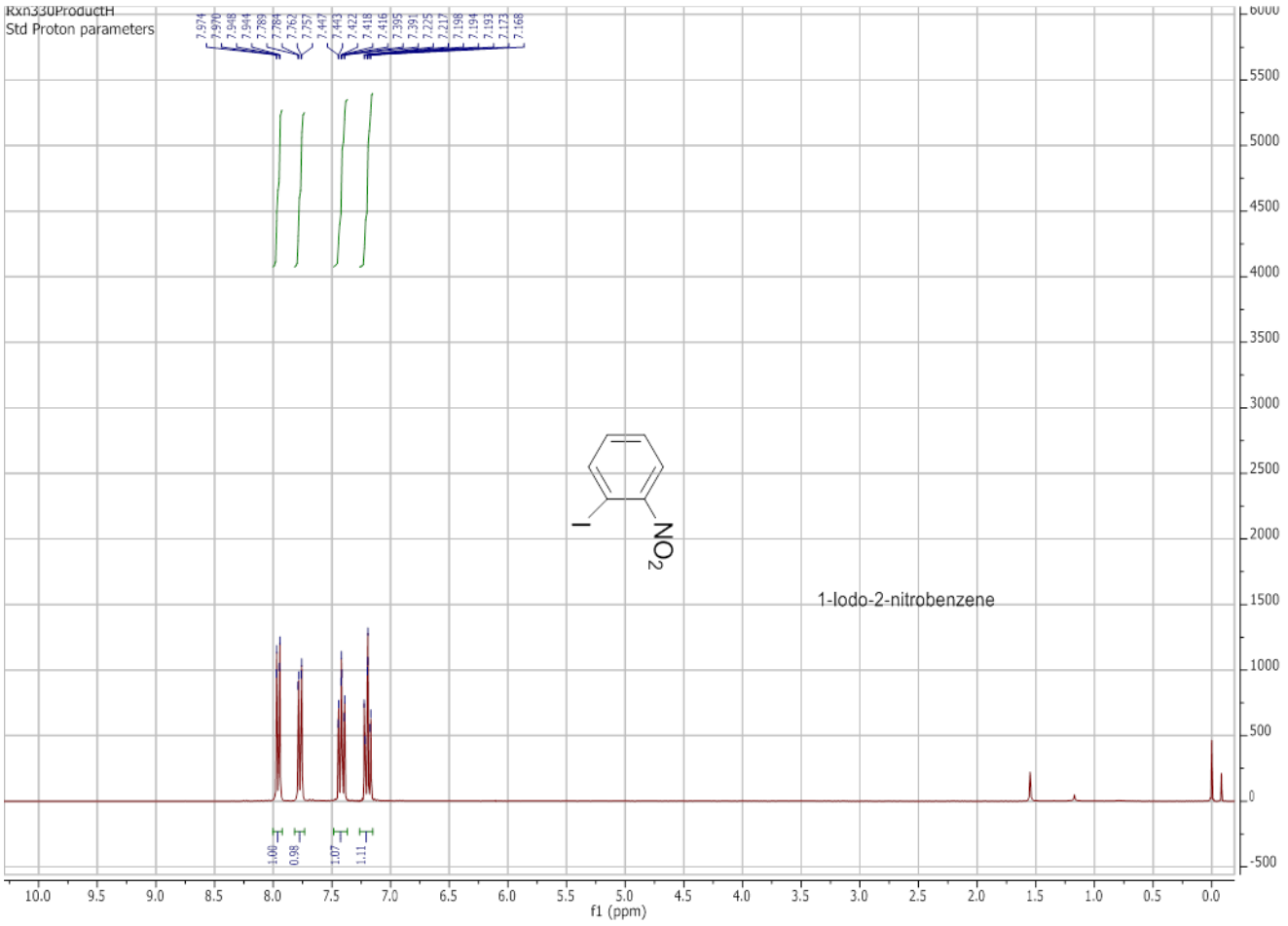


Figure A-115 ^{1}H NMR of 1-Iodo-2-nitrobenzene.

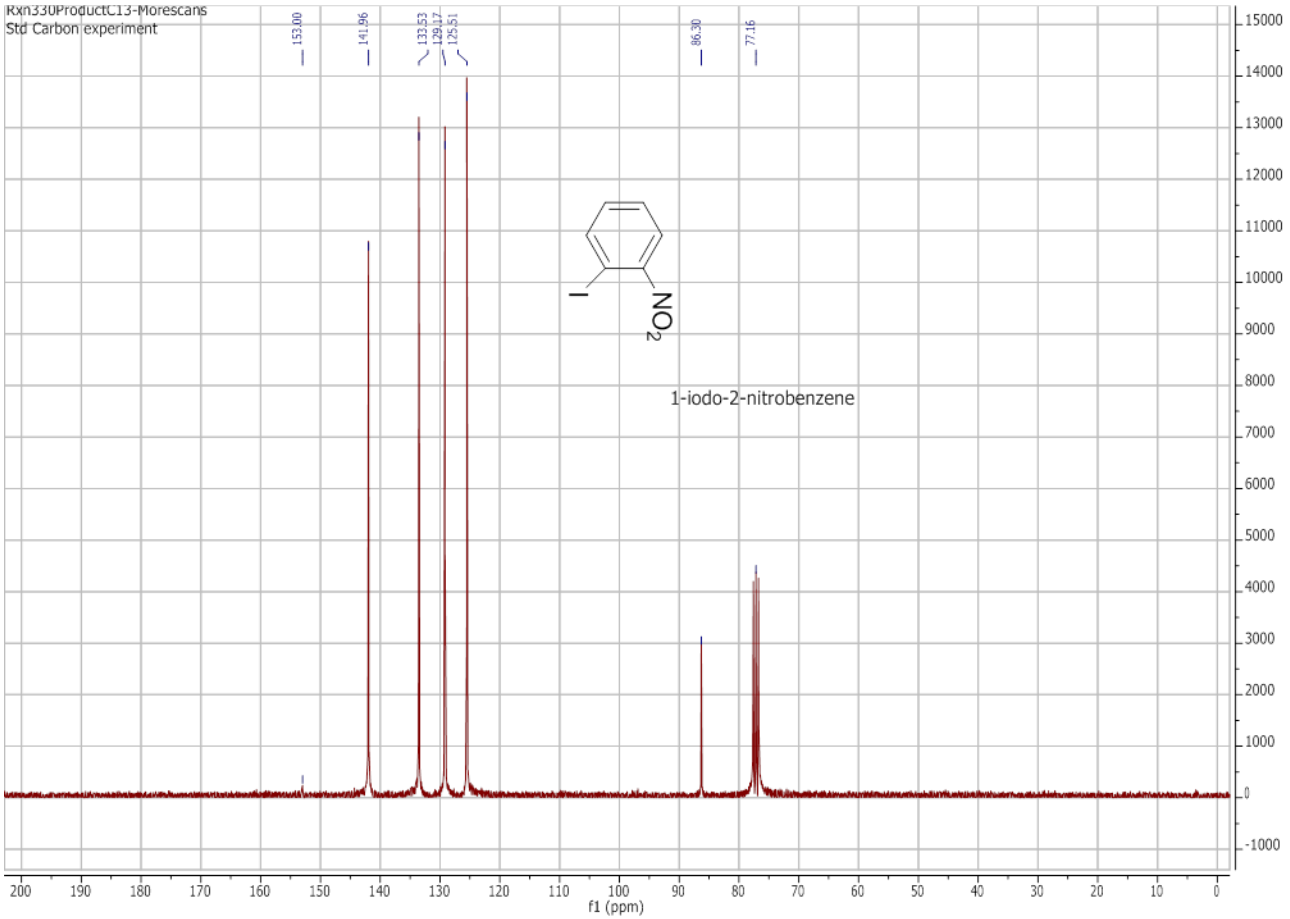


Figure A-116 ^{13}C NMR of 1-Iodo-2-nitrobenzene.

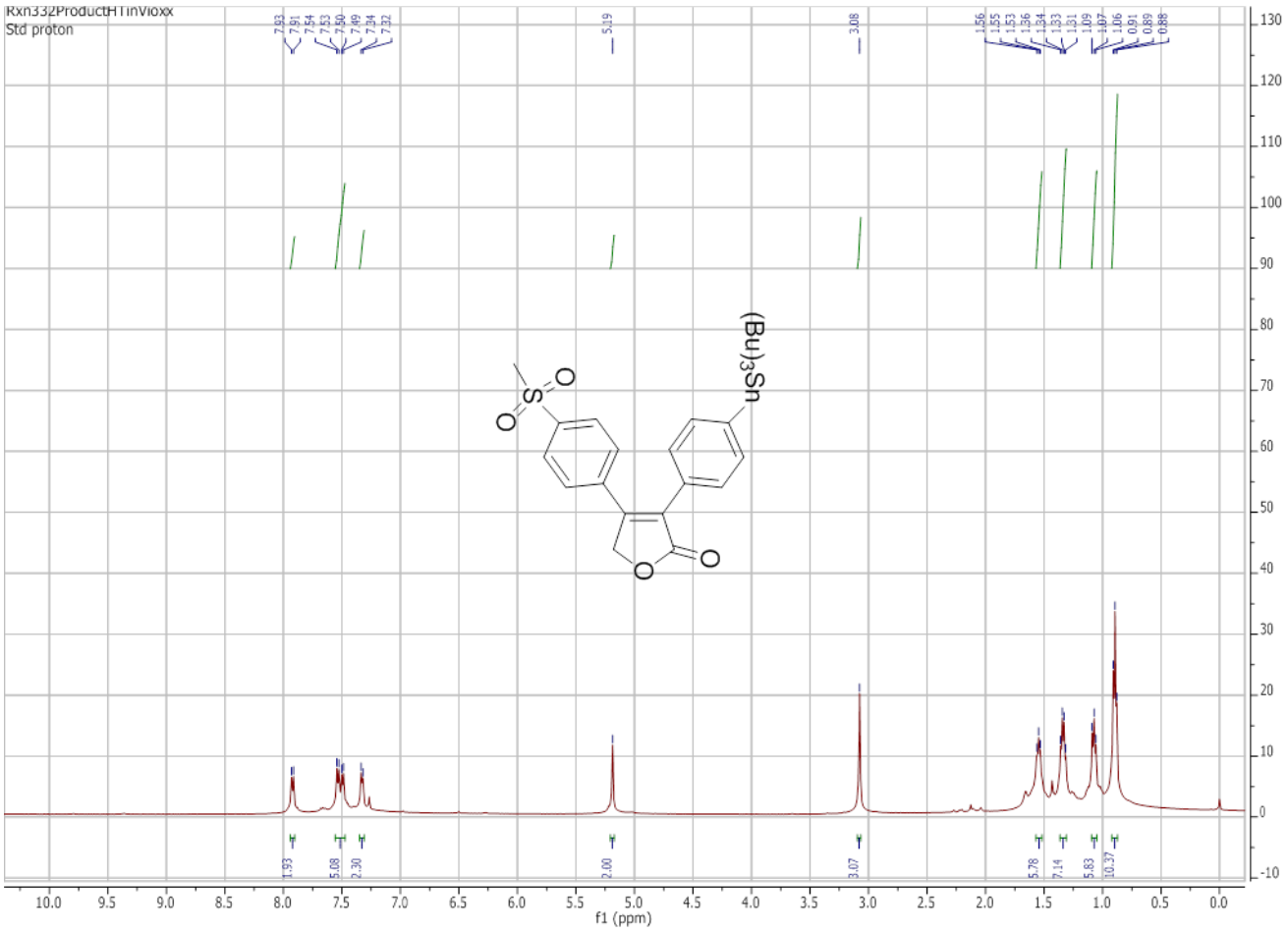


Figure A-117 ^{1}H NMR of 4-(4-(Methylsulfonyl)phenyl)-3-(4-(tributylstannyl)phenyl)furan-2(5H)-one.

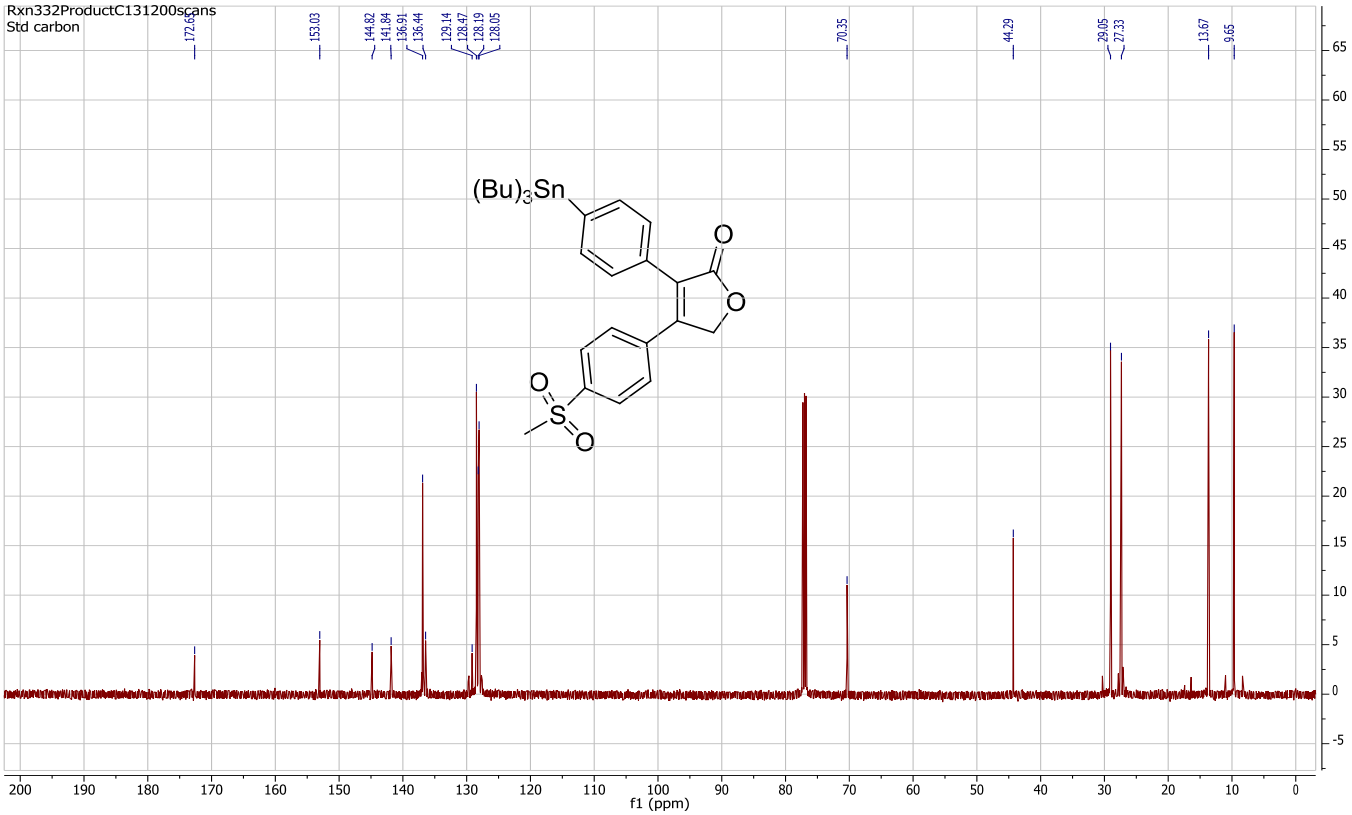


Figure A-118 ^{13}C NMR of 4-(4-(Methylsulfonyl)phenyl)-3-(4-(tributylstannyl)phenyl)furan-2(5H)-one.

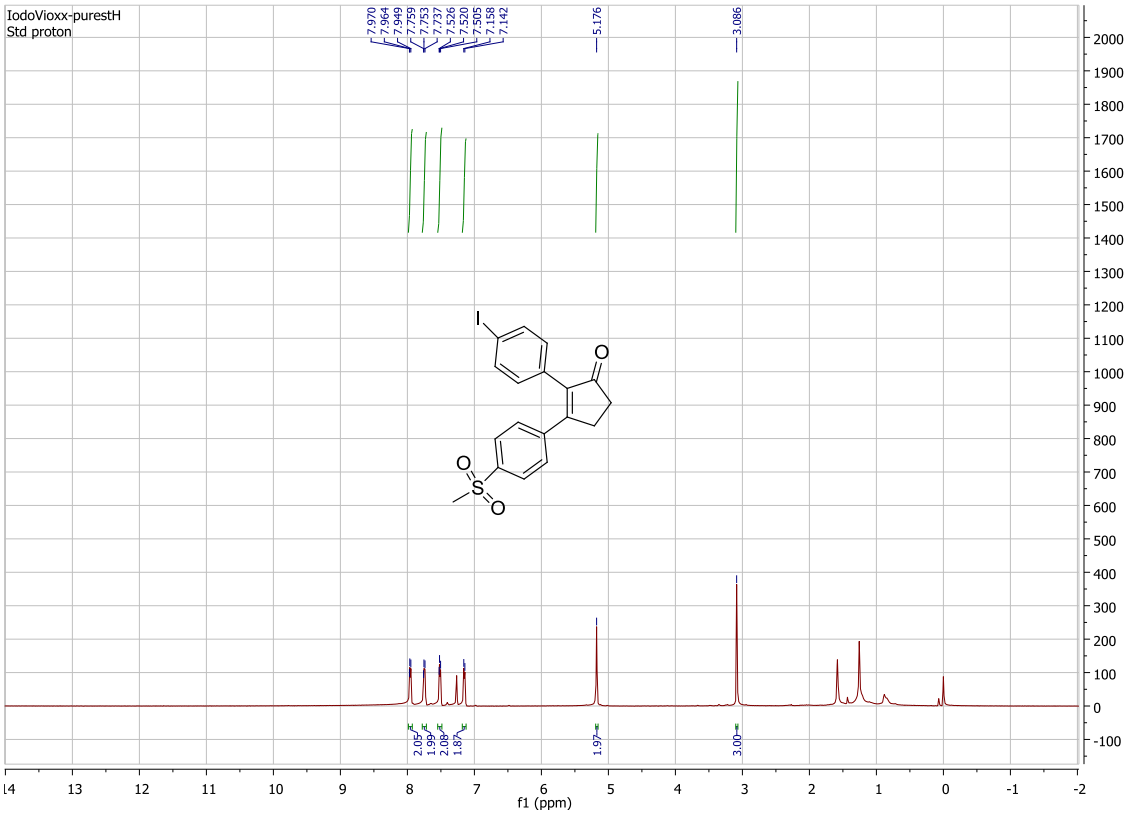


Figure A-119 ^{1}H NMR of 2-(4-Iodophenyl)-3-(4-(methylsulfonyl)phenyl)cyclopent-2-enone.

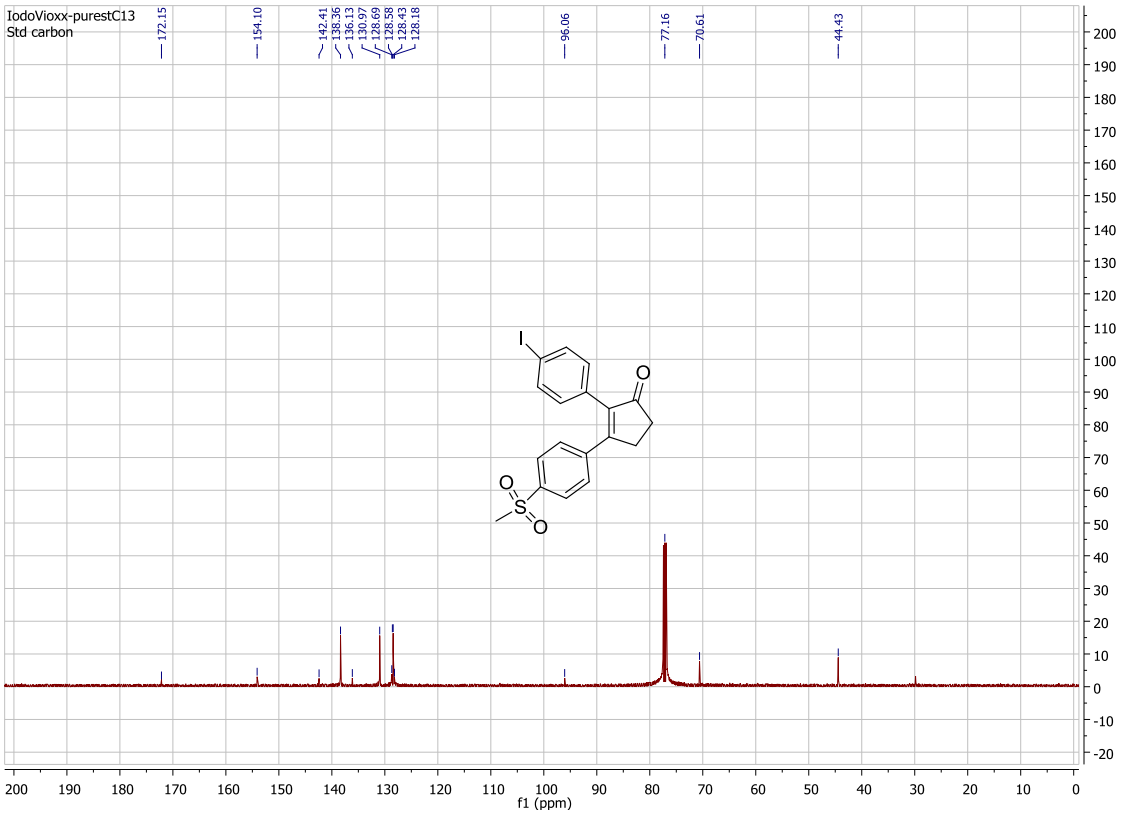


Figure A-120 ^{13}C NMR of 2-(4-Iodophenyl)-3-(4-(methylsulfonyl)phenyl)cyclopent-2-enone.

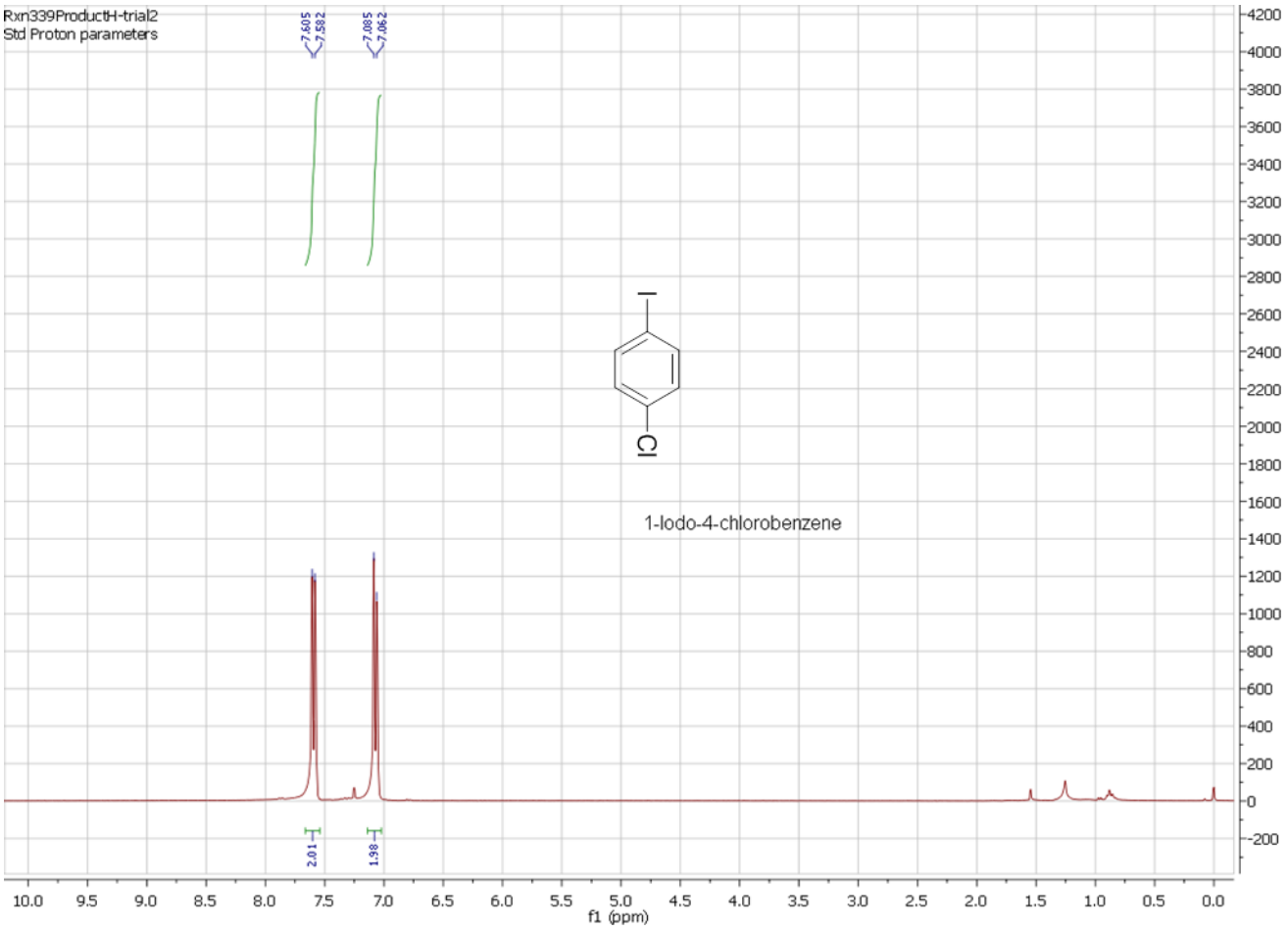


Figure A-121 ^{1}H NMR of 1-Iodo-4-chlorobenzene.

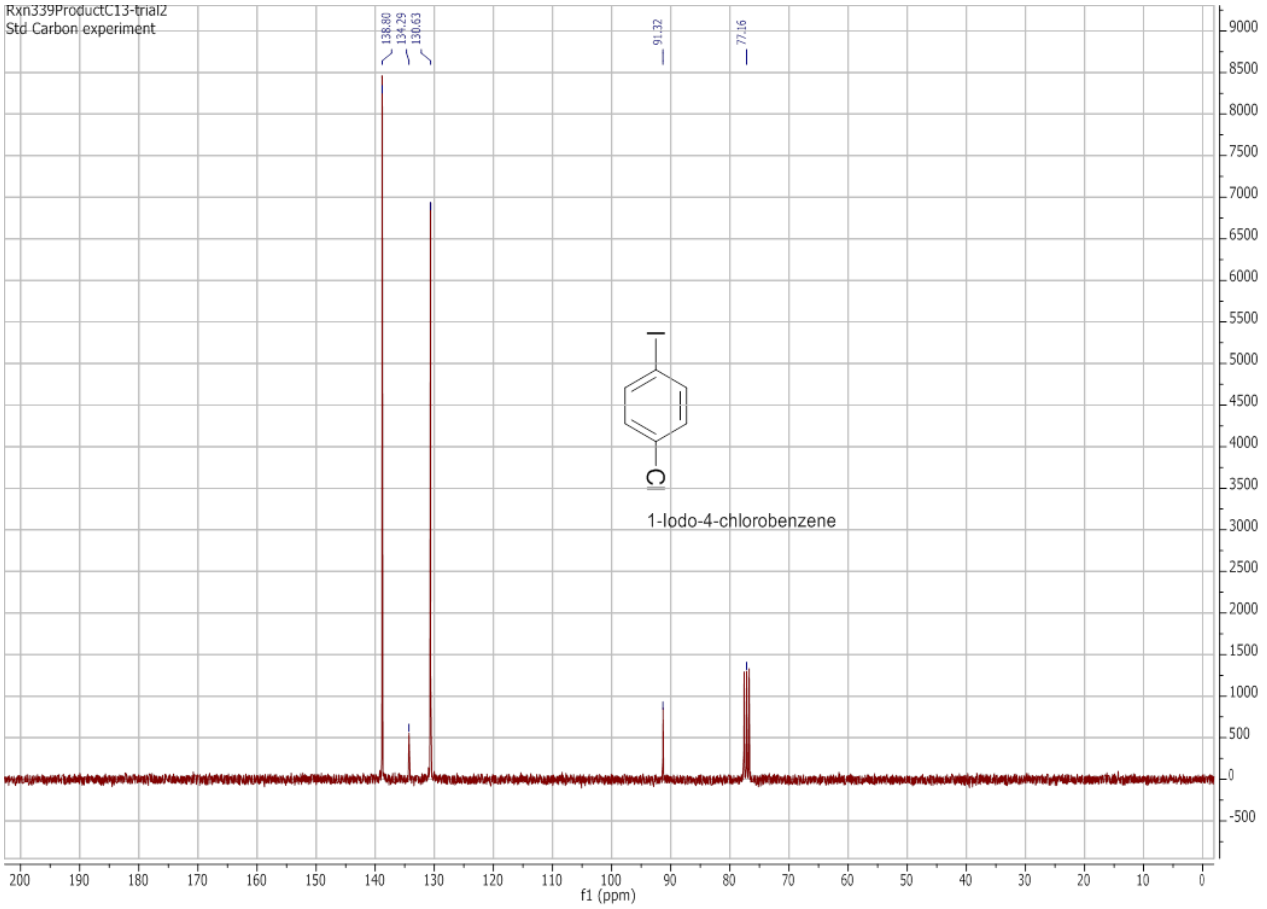


Figure A-122 ^{13}C NMR of 1-Iodo-4-chlorobenzene.

Vita

David W. Blevins was born in Prince William County, Virginia on December 2, 1968 to Lloyd and Mary Blevins. He grew up in Dickenson County Virginia. He graduated from Clintwood High School in Clintwood, Virginia in 1987. In 1989, he graduated from Mountain Empire Community College in Big Stone Gap, Virginia with an Associate Degree in drafting and design. He met Lisa Leona Church in 1987, and they were married on November 4, 1989. Their son, Preston Lloyd Blevins, was born on October 25, 1990. Their daughter, Clarissa Leona Blevins, was born on November 21, 1993. He graduated from The University of Virginia's College at Wise in Wise, Virginia in December of 2003 with a Bachelor of Arts degree in chemistry with a minor in biology. He began graduate studies at the University of Tennessee, Knoxville in August 2004 in the chemistry department, but had to return home help his wife who was injured in an automobile accident. In August 2008, he resumed graduate studies at the University of Tennessee, Knoxville.