IRIDIUM CATALYZED C-H BORYLATION: IMPROVED SELECTIVITY BY ELECTROSTATIC AND HYDROGEN-BOND INTERACTIONS AND APPLICATIONS TO DEUTERATION AND LIGAND SYNTHESIS

By

Kristin Anne Gore

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ABSTRACT

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C-H bonds are pervasive in organic compounds, and methods for their functionalization are of particular interest. One method for functionalizing C-H bonds is through iridium catalyzed C-H borylation. The transformation of C-H bonds to C-B bonds opens up many synthetic routes, because of the versatility of the C-B bond.

In the first section, iridium-catalyzed deborylation is used to selectively deuterate aromatic substrates. This method is highly selective as deuterium is only incorporated where the Bpin had previously resided. It is also milder as it does not use harsher acidic conditions, which makes it more applicable to substatrates that may be sensitive to those conditions.

The next sections discuss methods for selective C-H borylations of enamines and phenols. The selective borylation reaction of enamines directed by a hydrogen-bonding interaction between the NH of the enamine and O of a boryl is discussed. This method allows of the selective C-H borylation of trans alkene C-H bonds with no borylation observed on the arene for styryl substrates.

Then, the traceless protection of phenols by HBpin for C-H borylation is discussed. The protection of the phenols by HBpin leads to electrostatic interactions between the bipyridine ligand of an iridium catalyst and the O-Bglycolate to direct the ortho-borylation. In cases where Bpin is used as the protecting group, phenols with a

substituent in the 4-position larger than fluorine generally had >99:1 ortho-selectivity. For phenols with substitution in the 2- or 3-positions or fluorine in the 4-position, Beg was used to increase stability of the transition states and therefore, the ortho-selectivity.

In the final section C-H borylation is used to functionalize 1,10-phenanthroline for to provide simple, high yielding routes to functionalized ligands using the versatility of the C-B bond.

To My Family

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KEY TO ABBREVIATIONS

Ac	Acetyl
Boc	tert-Butoxycarbonyl
B_2pin_2	Bis(pinacolato)diboron
bpy	Bipyridine
cat	catecholate
CHB	C-H borylation
CyH	Cyclohexane
cod	1,5-Cycloctadiene
coe	cyclooctene
Cp	Cyclopentadiene
DCM	Dichloromethane
DMG	Directed metalation group
D*o*M	Directed ortho-metalation
dtbpy	4,4'-ditertbutyl-2,2'bipyridine
EAS	Electrophilic aromatic substitution
equiv	equivalent
FG	functional group
GC-MS	Gas chromatography-mass spectrometry
HBpin	Pinacolborane
HRMS	High resolution mass spectrometry
Ind	Indenyl

LC-MS	Liquid chromatography-mass spectrometry
Mes	mesityl
MIDA	*N*-Methyliminodiacetic acid
mp	Melting point
MTBE	Methyl *tert*-butyl ether
NOE	Nuclear overhauser effect
NMR	Nuclear magnetic resonance
NPA	Natural population analysis
pin	pinacolate
rt	room temperature
SMAP	Silicon constrained monodentate phosphine
TBAF	Tetra-n-butylammonium fluoride
TFA	Trifluoroacetic acid
TIPS	Triisopropylsilyl
TLC	Thin layer chromatography
THF	Tetrahydrofuran
TON	Turnover number
TS	Transition state

CHAPTER 1

C-H Borylation of Arenes

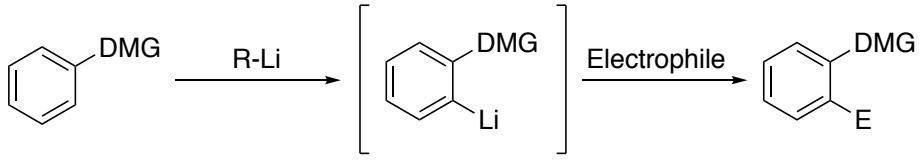
1.1 C-H Functionalization of Aromatic Compounds

C-H bonds are pervasive in organic compounds, and methods for their direct functionalization are of particular interest. These functionalized compounds have applications over a wide range of the chemical industry, including natural products, pharmaceuticals, and agrochemicals.[1]

Electrophilic Aromatic Substitution (EAS) was first reported in the early 19th century, and is one of the most popular methods for the functionalization of a C-H bond of an aromatic ring. In EAS, a hydrogen of an aromatic ring is substituted by a Lewis acid to afford a newly functionalized compound.

The regioselectivity for the products of EAS is governed by the number, types, and placement of functional groups on the substrate. Electron donating groups such as activating anilines, alkyls, and phenols, and deactivating halogens act as ortho/para directors. Electron withdrawing groups such as, carbonyls, cyano, and nitro act as meta directors.[2]

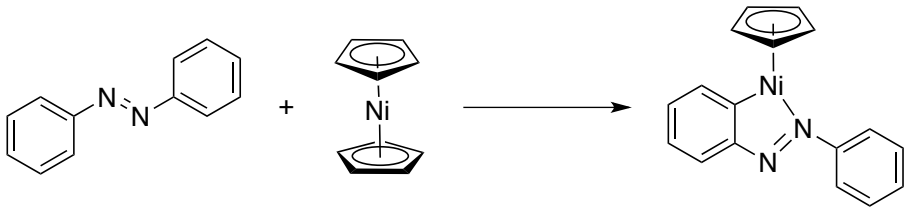
Scheme 1.1. Directed ortho-metalation



In 1934, Gilman and Young described the deprotonation of a benzene C-H bond ortho to the oxygen in dibenzofuran with lithium, and sodium. Subsequent carbonation afforded 4-dibenzofurancarboxylic acid.[3] This was the beginning of directed ortho-metalation (D*o*M) (Scheme 1.1), which has been able to overcome some of the limitations of EAS. The D*o*M reaction is the deprotonation of a site ortho to a heteroatom containing directed metalation group (DMG) such as an amide, tertiary amine, carbamate, or protected phenol. The concept of the DMG was first introduced by Wittig, Pockels, and Dröge in 1938.[4] The deprotonating agent is a strong base, usually an alkyllithium or lithium amide reagent, which leads to an ortho-lithiated intermediate. Upon treatment with an electrophile the substituted product is obtained.[5] While this method is very powerful there are some drawbacks including the need for cryogenic temperatures, a stoichiometric amount of base, and a narrow functional group tolerance.

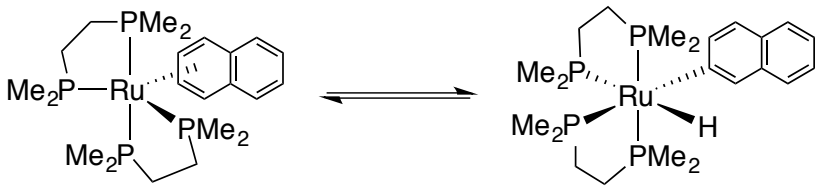
The earliest known example of a metal complex cleaving a C-H bond was reported by Chatt, Hart, and Watson in 1962. The attempted reduction of ruthenium and osmium complexes by sodium naphthalide to produce [$M(Me_2PCH_2CH_2PMe_2)_2$] resulted in the formation of a metal hydride.[6]

Scheme 1.2. C-H bond cleavage in azobenzene by Cp_2Ni



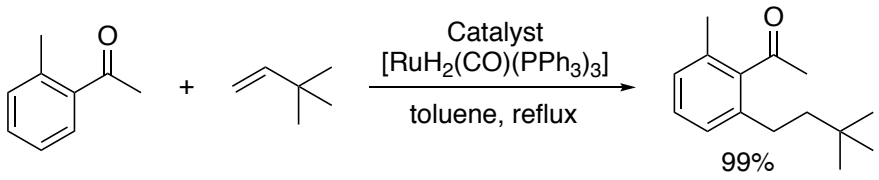
Soon after in 1963, the C-H bond cleavage in azobenzene by Cp_2Ni was reported by Kleiman and Dubeck (Scheme 1.2).[7] Two years later, in 1965, Chatt and Davidson reported the definitive first example of the oxidative addition of a C-H bond by a ruthenium complex resulting in the ruthenium hydride complex in equilibrium with the π-coordinated naphthalene ruthenium complex (**Scheme 1.3**).[8]

Scheme 1.3. Equilibrium between ruthenium complexes for the C-H activation of naphthalene



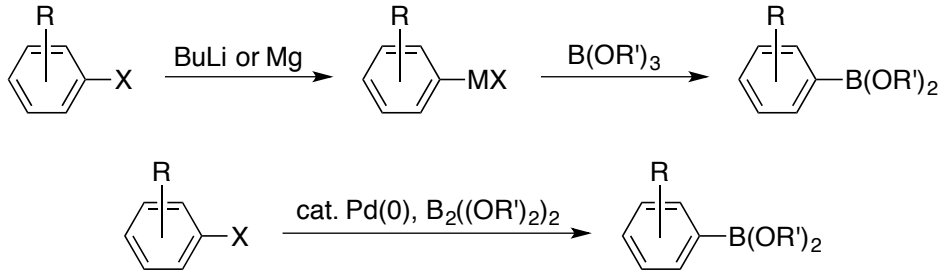
Since then, reactions where activated C-H bonds can be functionalized following activation have been found. One early example of this is the work reported by Murai and co-workers in 1993 where aryl ketones react with ethylene and vinylsilanes facilitated by $[RuH_2(CO)(PPh_3)_3]$ as the catalyst to produce an addition product of the C-H activation ortho to the ketone (Scheme 1.4).[9]

Scheme 1.4. Hydroarylation of arenes



Another area that has benefited from the advantages of C-H activation is the preparation of organic boron containing compounds. The synthesis of aryl and alkyl boronic acids and esters provides direct access to many subsequent synthetic processes.[10] The most notable is the Suzuki reaction, which is a Pd-catalyzed, C-C bond forming process that couples organoboron reagents and organic halide.[11] The Suzuki coupling can be performed under mild conditions, tolerates the presence of water and many functional groups, and results in nontoxic by-products.[12] For his discovery, Akira Suzuki was awarded the Nobel Prize in 2010.[13]

Scheme 1.5. Synthetic routes to aryl boronates



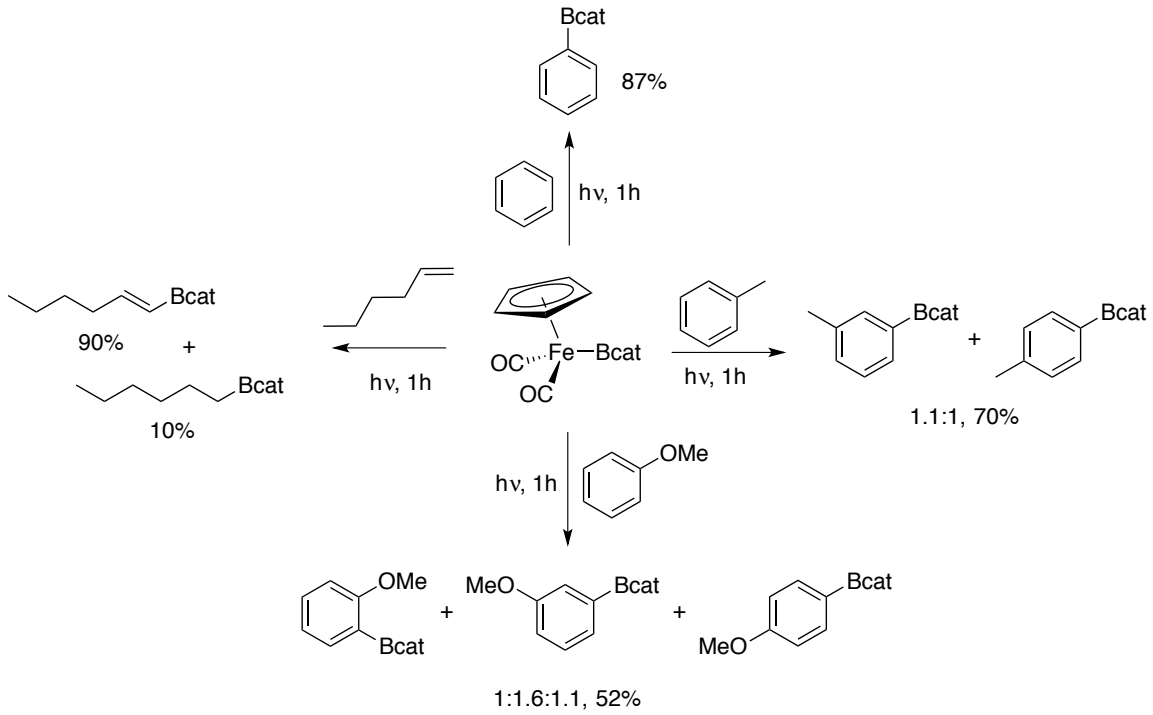
There are a few general strategies for synthesizing aryl and heteroaryl boronic acids and esters (Scheme 1.5). One involves converting the corresponding aryl or heteroaryl halide to a Grignard or organolithium intermediate (metal/ halogen exchange). This metalated species is then reacted with a trialkyl borate. After an acidic work up or the addition of a diol, the boronic acid or ester is obtained.[10] The previously discussed D*o*M method may also be employed.[14] Another method is a Pd-catalyzed cross-coupling from the aryl halide that by-passes the need for a Grignard or lithiation known as the Suzuki-Miyaura reaction.[15] This method exchanges the halide for a boronic ester or acid.

While these are useful synthetic methods, the need for cryogenic temperatures, stoichiometric amounts of base, and a low tolerance of functional groups are some of the drawbacks to the metal halogen exchange and D*o*M methods. A drawback to the Suzuki-Miyaura is that it will not be selective if there is more than one bromine, iodine, or triflate on the substrate. A more efficient and economical method could be one where C-H activation could be coupled with the formation of a C-B bond.

1.2 Discovery of C-H Activation/Borylation

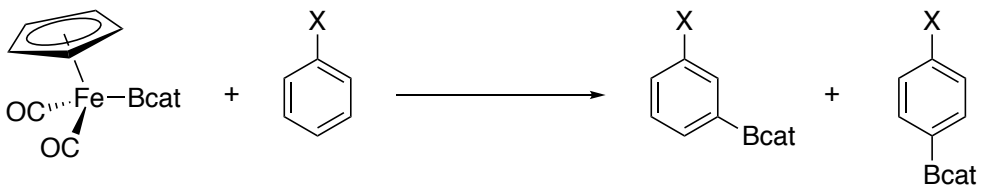
In 1995, the first stoichiometric C-H borylation (CHB) of arenes and alkenes by a defined metal-boryl complex resulting in free alkenyl and arylboronate esters in good yields was reported by Hartwig and co-workers (Scheme 1.6).[16]

Scheme 1.6. Stoichiometric borylations of arenes and alkenes by [$CpFe(CO)_2(Bcat)$]



The irradiation of [$CpFe(CO)_2(Bcat)$] in the presence of benzene resulted in PhBcat (80-90% yields). Furthermore, in a subsequent study the iron complex was found to yield meta- and para-substituted boronate esters from monosubstituted benzenes such as toluene and chlorobenzene, and a reaction with anisole resulted in a ortho-, meta-, para-borylated mixture of products in a 1.0:1.6:1.1 ratio (Table 1.1).[17]

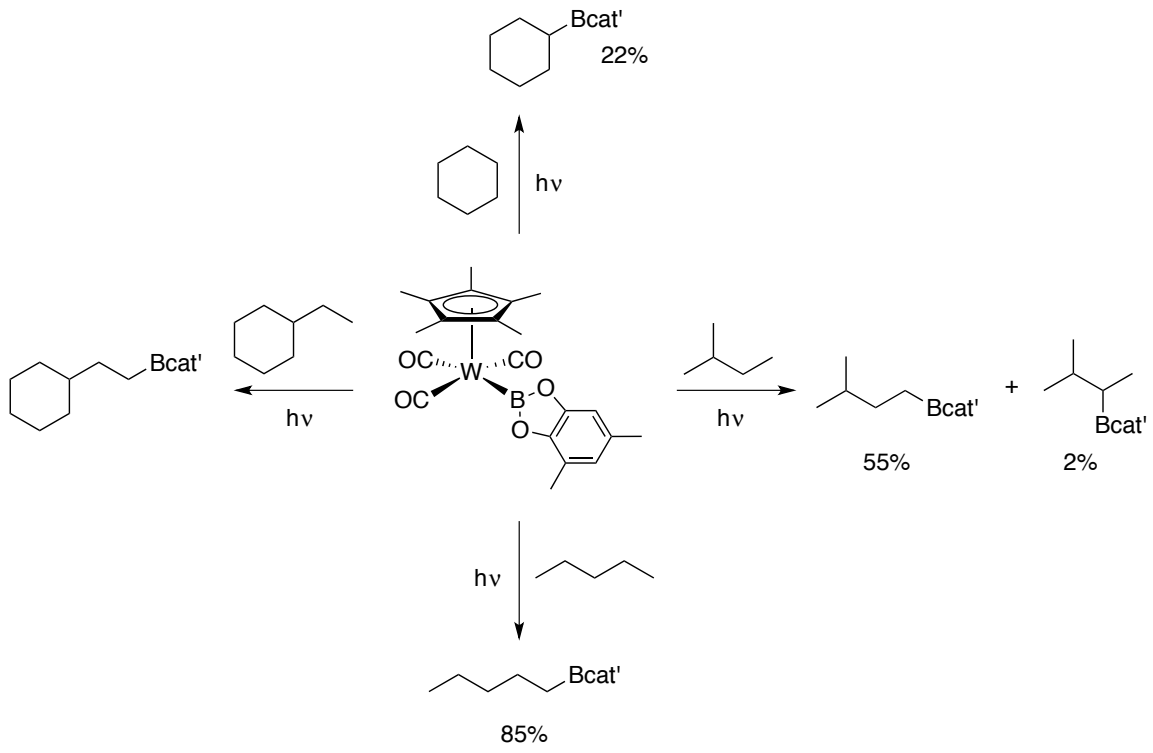
Table 1.1. Ratio of product isomers from reaction of $CpFe(CO)_2Bcat$ with C_6H_5X



	product isomer ratios		
X	*ortho*	*meta*	*para*
Me		1.1	1.0
OMe	1.0	1.6	1.1
Cl		1.5	1.0
CF_3		1.5	1.0
NMe_2		1.0	8.0

In 1997, the selective stoichiometric borylation of alkanes by [$Cp^*W(CO)_3Bcat'$] was reported (Scheme 1.7). It was found that both replacing and blocking the sp^2-hybridized C-H bonds in the ligands, and using a large excess of substrate, made activation of the alkanes possible. Furthermore, yields were increased by the use of tungsten instead of iron for the catalyst.[18]

Scheme 1.7. Stoichiometric borylation of alkanes by [Cp*W(CO)$_3$Bcat']

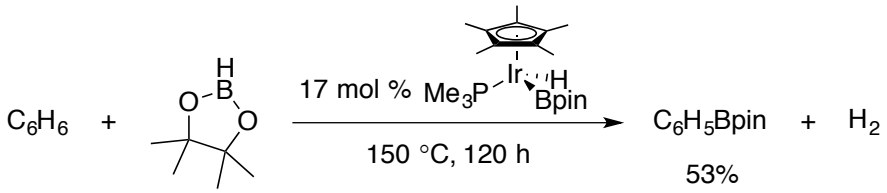


While these reactions showed that metal complexes could convert C-H bonds to C-B bonds, none of these reactions were catalytic. The regeneration of the boryl complex from the metal products in the previous examples required several synthetic steps. This prevented the reactions from being catalytic, as an active catalytic species could not be regenerated from the borylation reaction conditions.

In 1999, Smith and co-workers demonstrated the first catalytic C-H activation/borylation of arenes under thermal conditions (Scheme 1.8). The reaction was the borylation of benzene in the presence of HBpin and a catalytic amount of [Cp*IrH(PMe$_3$)(Bpin)].[19] Later that same year, Hartwig and co-workers also published

work describing the photocatalytic C-H activation/borylation of alkanes catalyzed by [Cp*Re(CO)$_3$] stabilized by an atmosphere of CO gas.[20]

Scheme 1.8. The first catalytic C-H activation/borylation of an arene

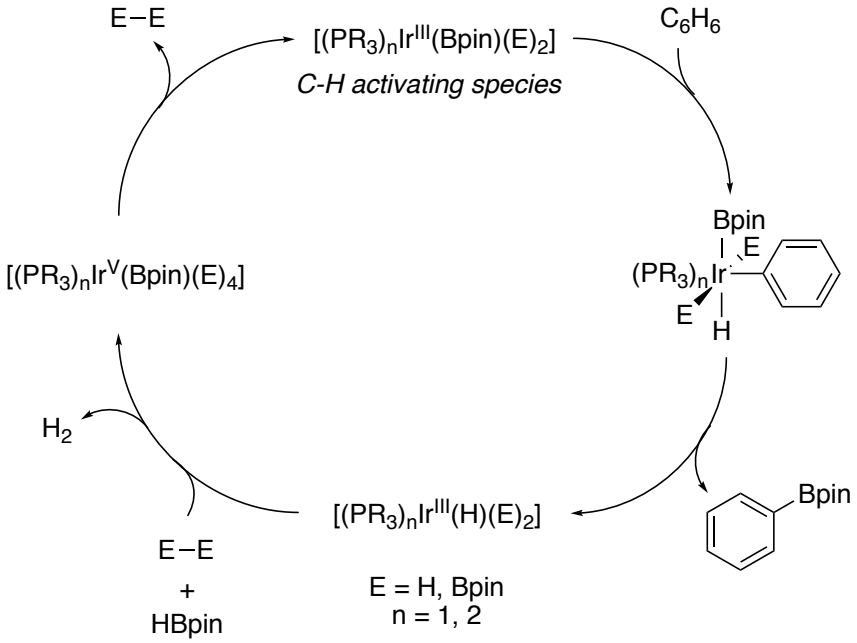


Subsequent studies by Smith and co-workers in 2002 led to new, more active catalysts using (Ind)Ir(cod) and chelating phosphorous ligands such as 1,2-bis(dimethyl)phosphinoethane), which was able to generate 4500 TON at 150 °C.[21] Around that same time, Hartwig also published work on a similar class of catalysts for C-H activation/borylation, which are generated in situ from an iridium dimer precatalyst ([Ir(cod)Cl]$_2$ or [Ir(cod)OMe]$_2$) and a nitrogen chelating ligand (4,4'-di-*tert*-butyl-2,2'-bipyridine).[22]

By studying the stoichiometric CHB reactions of [Ir(Bpin)(PMe$_3$)$_4$] and *fac*-[Ir(Bpin)$_3$(PMe$_3$)$_3$] with d_6-benzene and iodobenzene, Smith and co-workers attempted to determine whether Ir-catalyzed CHB operated via Ir$^{I/III}$ and/or Ir$^{III/V}$ catalytic cycles. Both complexes were indeed able to react with the benzene to afford PhBpin and the corresponding metal hydride species. However, the metal complexes reacted with iodobenzene differently. While, [Ir(Bpin)(PMe$_3$)$_4$] did react with iodobenzene, no PhIBpin was detected in the products. Whereas, the reaction with *fac*-[Ir(Bpin)$_3$(PMe$_3$)$_3$]

yielded *meta*- and *para*-$C_6H_4I(Bpin)$. While stoichiometric reactions cannot definitively exclude or support catalytic mechanisms, these reactions mirror the observations that catalytic CHBs of iodobenzene with an Ir^I precatalyst failed, whereas CHB with an Ir^{III} precatalyst gave a 77% yield of monoborylated C_6H_4IBpin isomers. These were the first experiments that were consistent with an operative $Ir^{III/V}$ catalytic cycle for Ir-catalyzed CHB.

Scheme 1.9. CHB catalytic cycle reported by Smith and Maleczka[21]



Subsequent studies by Hartwig and coworkers more firmly supported an $Ir^{III/V}$ mechanism. They isolated $[Ir(dtbpy)(coe)(Bpin)_3]$ and demonstrated it to be a precatalyst.[22] In 2003, Sakaki and co-workers published their computational analysis of the mechanism.[23] They were able to establish a proposed $Ir^{III/V}$ mechanism and resulting intermediates through their analysis. The barriers calculated for the proposed steps

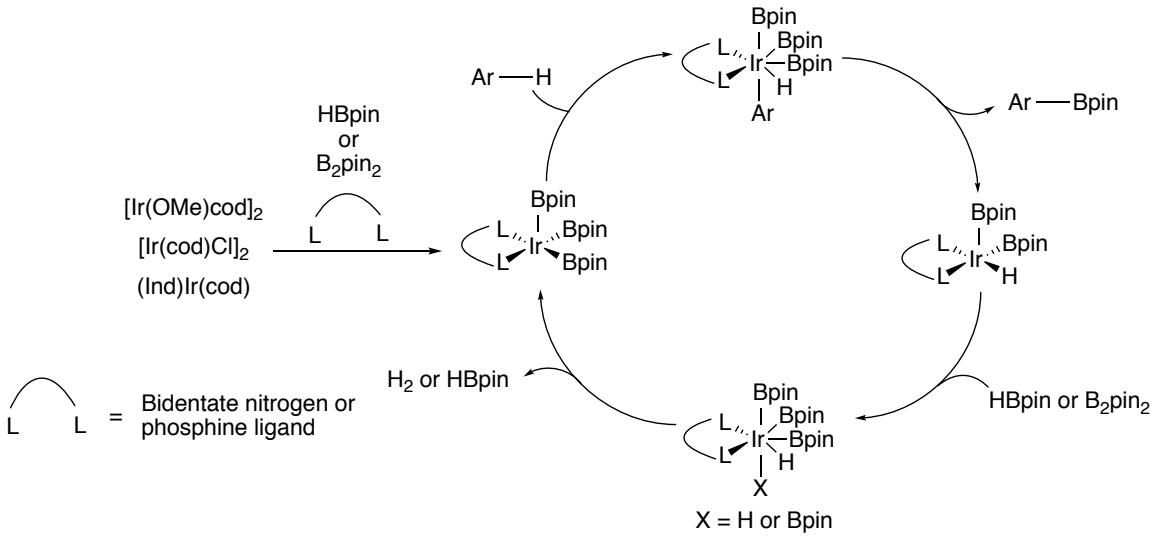
indicated that the turnover-limiting step was the C-H bond cleavage. They were also able to further elaborate on the support for the $Ir^{III/V}$ system proposed by Smith and co-workers in 2002.

In 2005 Hartwig and co-workers published an experimental study of the mechanism.[24] They were able to observe an Ir^{III} diboryl hydride intermediate, and they derived the rate law for the CHB reaction.

Additionally, the 16-electron active species [(dippe)Ir$(Bpin)_3$] was synthesized by Smith and co-workers and shown to facilitate the borylation of arenes and 2-methylthiophene.[25] They were able to establish that the steric influence of the chelating phosphine around the metal center influences the ability of the substrates to be activated. They also found that the calculated transition state for the diphosphine system is similar to that of the chelating nitrogen system calculated by Sakaki.[23]

The proposed catalytic cycle (Scheme 1.10) begins with the formation of the active catalyst from a precatalyst such as $[Ir(cod)Cl]_2$, $[Ir(cod)OMe]_2$, or (Ind)Ir(cod) with B_2pin_2 or HBpin, and a phosphorous or nitrogen donating chelating ligand. The active catalyst is an Ir^{III} species, which undergoes oxidative addition by an aryl substrate to afford an Ir^{V} species. Reductive elimination of ArBpin results in an Ir^{III} intermediate as an iridium-hydride. This complex then reacts with HBpin or B_2pin_2 in another oxidative addition step resulting in another Ir^{V} species. Reductive elimination of H_2 or HBpin results in the regeneration of the trisboryl $iridium^{III}$ active catalyst.

Scheme 1.10. Catalytic cycle for C-H activation/borylation

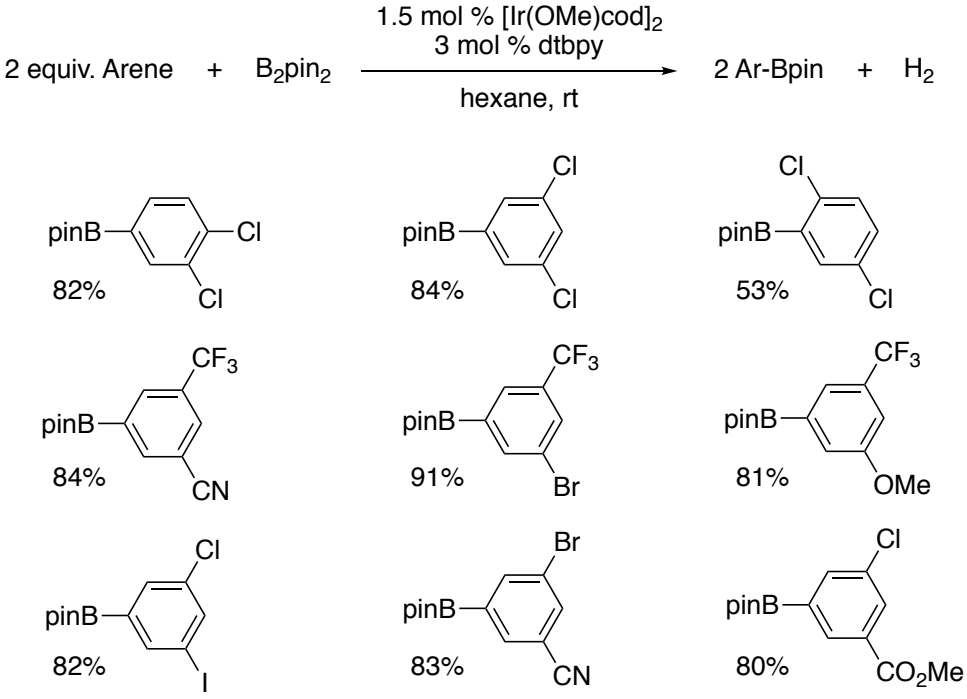


1.3. Selectivity of C-H Borylation

The CHB reaction is generally a regioselective reaction occurring at the least sterically hindered position of the arene. But electronic properties of the substrates can still effect the reactions as borylations of electron-poor arenes have been found to proceed faster than electron-rich arenes.[26]

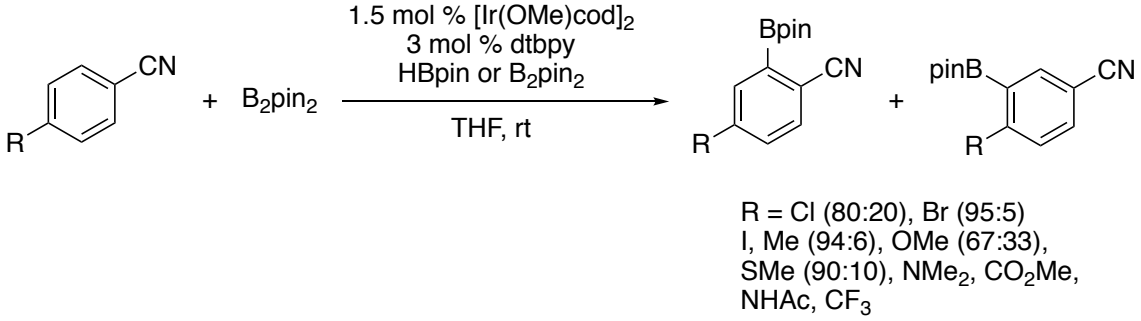
When the arene substrate has a 1,3-disubstitution pattern, the borylation will generally occur in the meta-position, while a borylation of a monosubstituted arene such as toluene will give a statistical distribution of meta- and para-borylated products.[26-27] But, because of the steric directed nature of the reaction, ortho-borylation to a functional group is not likely without other directing effects.

Scheme 1.11. Examples of products from iridium-catalyzed C-H borylation[28]



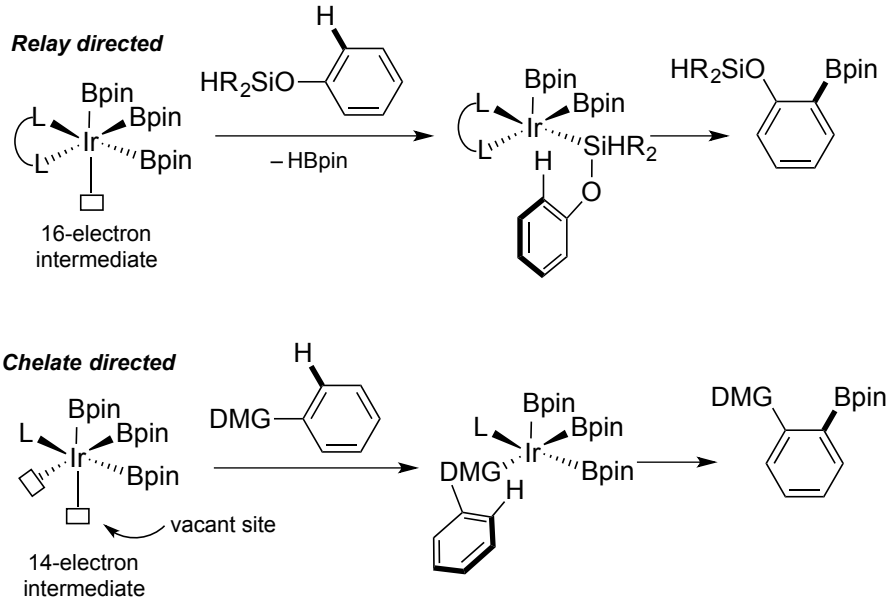
Borylations of 1,4-disubstituted arenes can give rise to ortho-borylated products. Symmetrically substituted substrates result 1,2,4-trisubstituted arenes, but if the 1,4-substituted substrates are not symmetrical, then a mixture of products is obtained. If the two functional groups differ from each other enough, then the selective reaction is possible. Smith and co-workers reported in 2005 the selective borylation ortho to cyano groups in 1,4-disubstituted benzonitriles (**Scheme 1.12**).[29] Because the cyano group is only slightly larger than a fluorine, borylation in the position next to that group was possible if the functional group para to it had the right electronic and steric properties.

Scheme 1.12. Iridium-catalyzed C-H borylation of benzonitriles



Although, the C-H activation/borylation reaction is generally controlled by sterics, there are other methods that afford directed borylation. One way to accomplish this is to use the substrate to affect the direction. For example, Hartwig and co-workers reported a silyl-directed iridium-catalyzed ortho-borylation of arenes.[30] The origin of the selectivity is thought to arise from reversible addition of a Si-H to the iridium center, which makes this directing effect known as relay directed interaction (Scheme 1.13). This interaction leads to activation of the C-H bond ortho to the functional group on the arene ring.

Scheme 1.13. Relay and chelate directed iridium-catalyzed C-H borylation



Another way to direct the CHB is by use of a ligand. There are examples of homogenous ligands and heterogeneous ligands that can facilitate a chelate directed CHB of esters and amides. In a chelate directed reaction the active catalyst species is a 14-electron complex that allows a directing group to interact with the iridium center and direct the C-H activation ortho to it. Sawamura and co-workers have reported a silica supported monophosphine system known as silica-SMAP,[31-34] which has a wide substrate scope. While this ligand is very active, the synthesis has many steps and is not trivial.[35]

Ishiyama and Miyaura and co-workers have also reported a monodentate phosphine ligand that leaves a vacant site on the metal center to facilitate the chelate directed CHB of esters.[36] More recently, Smith and Maleczka and co-workers reported the use of ligands with combination phosphorous or nitrogen donors with a silicon donor. The silicon acts as an X-type donor allowing chelate directed ortho-borylation to occur. The ligand synthesis is also straightforward and high yielding.[37]

Other chelate directed methods have been reported. Lassaletta reported the N-directed ortho-borylation of arylpyridines using a hemilabile diimine ligand.[38] Clark has also reported the ortho-borylation of benzylamines and phosphines. More methods for ortho-directed borylation will be discussed in Chapters 3 and 4.

More recently, methods for selective meta- and para-CHBs have been reported. As discussed earlier, the previously reported methods for meta-CHB arose from borylations of 1,3-disubstituted substrates. In 2015, Kanai and Kuninobu reported a meta-selective CHB where the regioselectivity is controlled by a hydrogen-bonding secondary reaction between a ligand and a substrate.[39] A urea moiety attached to an iridium-coordinated bipyridine ligand hydrogen bonds to the carbonyl of a substrate orienting it toward the metal center such that the meta C-H bond is activated.

In 2016, Chattopadhyay reported selective meta-CHB of amine-protected benzaldehydes.[40] The author theorized that the enhanced selectivity arose from the secondary interaction of the imine N atom and a boryl B attached to the iridium catalyst.

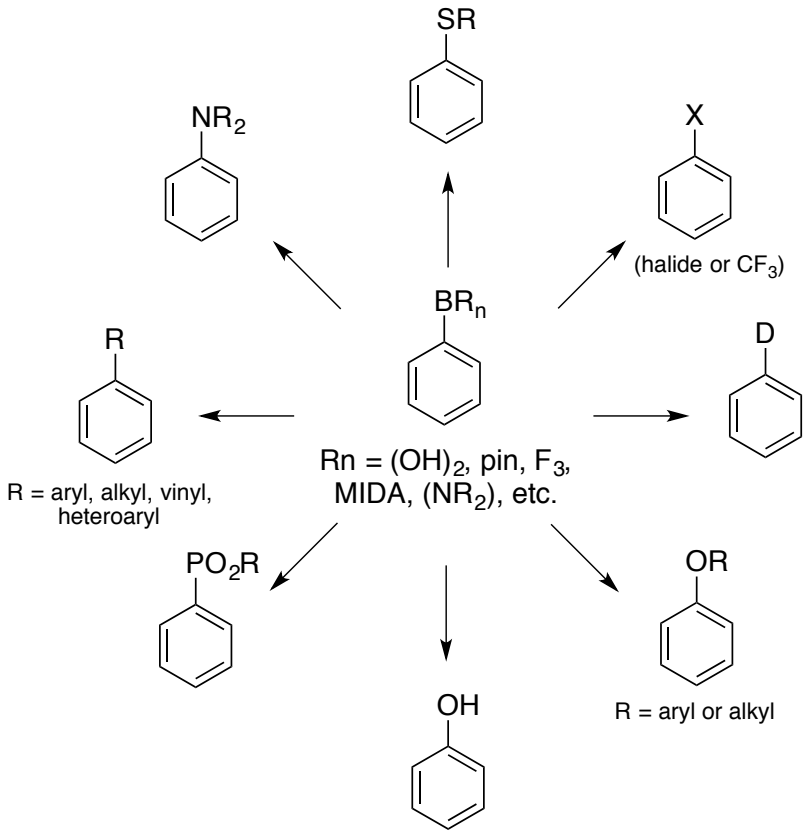
Another meta-directed method reported in 2016 was by Phillips. Their method used a noncovalent, ion-pair interaction between a cationic group on the substrate and an anionic group on the bipryidine ligand to influence the selectivity of the CHB.[41]

Itami and Segawa also reported in 2016, a para-selective CHB. The directing effect was achieved by using large, bulky groups on the phosphine ligands and the monosubstituted substrates to block the meta C-H activation.[42]

1.4 C-H Borylation in the Context of Other C-H Functionalizations

It has been previously discussed in this chapter that organoboron containing compounds are very useful to the Suzuki coupling reaction. However, there are other functional groups that can arise from the further functionalization of organoborons. Carbon-halide,[43] nitrogen,[44-45] oxygen,[46-47] and phosphorous[48] bonds can all be synthesized from organoboron compounds.

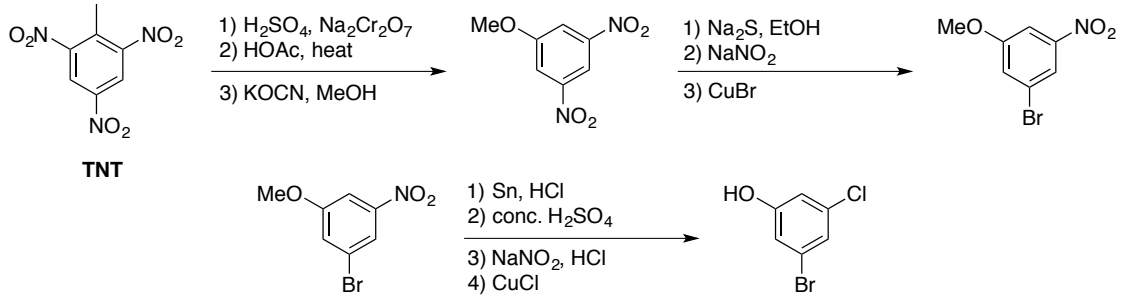
Scheme 1.14. Synthetic functionalizations of organoborons



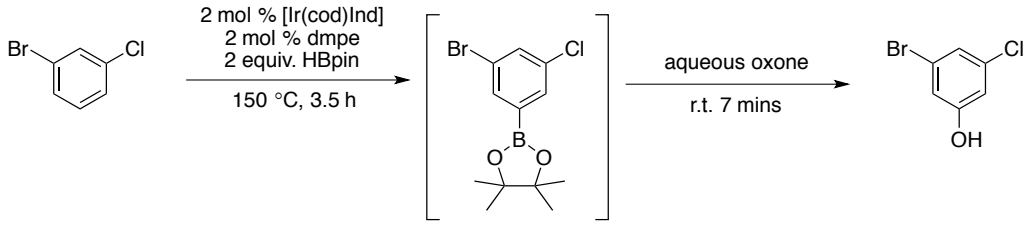
CHB/functionalization can be used to shorten many syntheses that were once long, multi-step processes with low yields. One of the best examples of this is the synthesis of 3-bromo-5-chlorophenol. Prior to the report of a two-step, one-pot synthesis by Smith and Maleczka in 2003,[47] the only known synthesis of this phenol was a ten-step process starting from TNT.[49]

Scheme 1.15. a) Synthesis of 3-bromo-5-chlorophenol from TNT **b)** Synthesis of 3-bromo-5-chlorophenol from 1-bromo-3-chloro-benzene

a) Hodgson and Wignall, 1926



b) Smith and Maleczka, 2003



CHAPTER 2

C-H Borylation/Deuteration of Arenes

2.1 Importance of Deuterated and Tritiated Arenes and Heterocyles and Methods for Their Synthesis

Deuterium and tritium labeled compounds are widely utilized as probes for pharmakinetics, reaction mechanisms, spectroscopy, and enzymology.[50] There have also been deuterium labeled molecules proposed as drug candidates.[51] While other isotopically labeled compounds also have some application in these fields, long synthetic routes and high cost to synthesize other compounds containing heavier isotopes make deuterium and tritium labeled molecules more desirable. This is because they can often be prepared in fewer steps from the proper precursor using D_2 gas or D_2O as the deuterium source.[52] In addition, some deuteration conditions may also be applied for the incorporation of tritium on organic molecules.[52] The most common methods for the incorporation of tritium into organic molecules are the reduction of a functional group by stoichiometric reagents to introduce C-^{3}H bonds or by catalytic methods for direct hydrogen isotope exchange (HIE).[53-55]

Indeed, Heys and co-workers have shown that organoiridium catalysts such as $[Ir(acetone)_2(H)_2(PPh_3)_2][BF_4]$ and $[Ir(cod)(PPh_3)_2][BF_4]$ are effective at labeling organic molecules with tritium gas. However, these methods are limited to substrates with aromatic functional groups that can coordinate to the metal center and the range of suitable solvents is narrow.[56-58]

Hesk and co-workers, in the mid-1990s, showed that Crabtree's Catalyst ([Ir(PCy_3)(py)(cod)][PF_6]) was effective at labeling acetanilides with deuterium.[59] Today, it is also employed as one of the most popular catalysts for tritium labeling of pharmaceuticals.[60] Again, it operates by an ortho exchange in the presence of a directing group. More recently, Chirik, Hesk, and co-workers have reported an iron catalyst bearing a saturated *N*-heterocyclic carbene ligand and two N_2 molecules ([(H_4-^{iPr}CNC)Fe(N_2)$_2$] where H_4-^{iPr}CNC = 2,6-(2,6-*i*Pr$_2$-C_6H_3-4,5-H_2-imidazol-2-ylidene)$_2$-C_5H_3N) as a catalyst for the labeling of drug molecules with both deuterium and tritium.[60] The selectivities of the catalyst are orthogonal to those accessed by the iridium catalysts (Figure 2.1).

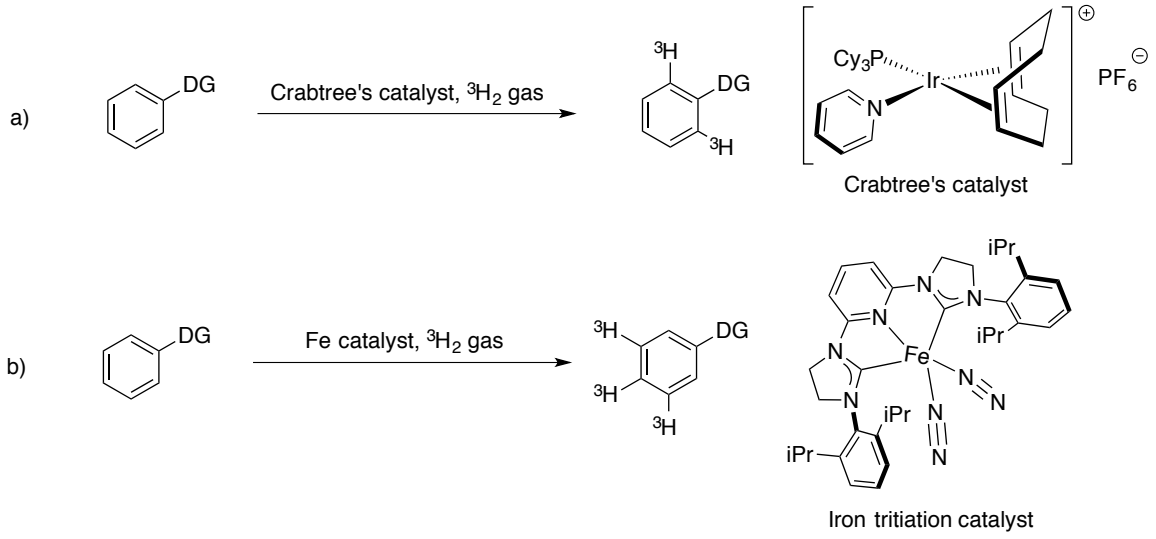


Figure 2.1. a) Reaction conditions and selectivity for tritiation with Crabtree's catalyst **b)** Reaction conditions and selectivity for tritiation with Chirik's iron catalyst

As the need and application for labeled compounds expands, so does the need for site selectivity in the labeling reaction. In the previously discussed methods, isotopic labeling generally occurs at multiple positions in the substrate, and it is not always

incorporated in the same quantity from position to position. Most reported methods that do not include a metal catalyst generally employ harsher conditions in the form of elevated temperature or strong acid/base conditions that may affect more sensitive functional groups, lead to incomplete deuteration, or poor regioselectivity.[52]

2.2 Selective Deuteration of Arenes Utilizing C-H Borylation/Deborylation

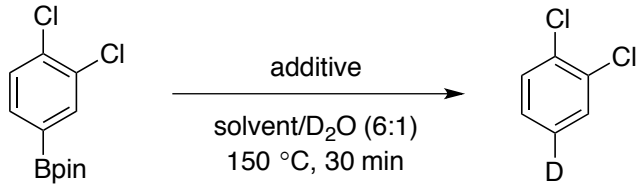
In the process of developing one-pot methods for iridium-catalyzed CHB and functionalization of organoboron intermediates,[61-63] we noticed a significant quantity of starting material present at the end of the second reaction, even when there had been no starting substrate observed at the end of the first reaction. This was an indication that the observed starting material arose from protolytic deborylation of the organoboronate intermediate.

Deborylation reactions of boronic acids and esters typically require long reaction times.[64] The reaction can be accelerated by more basic or acidic conditions or catalyzed by metals,[65-66] but often the conditions are quite harsh in aqueous media. The catalytic CHB of arenes is typically governed by sterics,[67] and heterocycles undergo CHB under mild conditions with high functional group tolerance.

Given, that these one-pot reactions still contained iridium and pure boronic esters do not typically deborylate in pure water, it was thought that the metal in the crude reaction mixture might be promoting the reaction. It was also theorized that this reaction could be utilized as a mild and selective isotopic labeling technique. Therefore, a study

was done by Feng Shi in Professor Maleczka's group to determine the optimal conditions for the deborylation reaction.[68]

Table 2.1. Catalyst screen for deuterodeborylation[a]



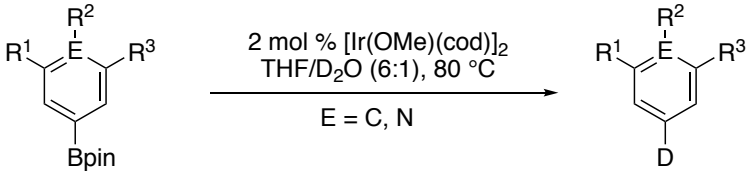
Entry	Additive[b]	Solvent	Conversion[c]
1	crude borylation mixture	THF	>99%
2	dmpe	THF	<1%
3	(Ind)Ir(cod)	THF	95%
4	(Ind)Ir(cod)	DME	97%
5	$[Ir(OMe)cod]_2$	THF	98%
6	$[Ir(PCy_3)(py)(cod)][PF_6]$	DME	>99%
7	$[IrCl_3(cod)_2]$	THF	33%
8	$IrCl_3 \bullet 3\ H_2O$	THF	<1%
9	$(C_6H_6)Ir(Bcat)_3$	THF	<1%
10	$(dtbpy)Ir(coe)(Bpin)_3$	DME	47%
11	none	THF	<1%

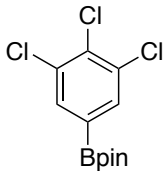
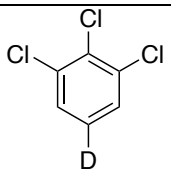
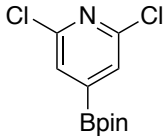
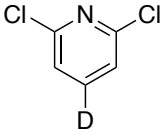
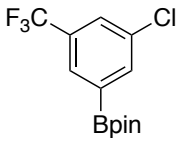
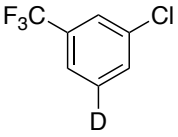
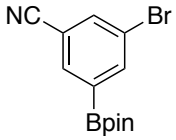
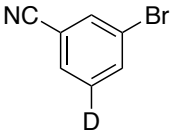
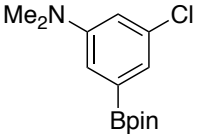
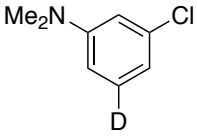
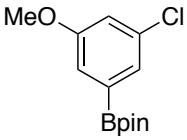
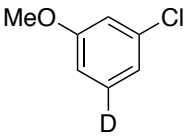
[a]All reactions were run in 1 mmol scale in 0.5 mL D_2O (~23 equiv) and 3-4 mL solvent, for 30 min. [b] 2 mol% Ir in every case. [c]GC area ratio calibrated with corresponding non-deuterated compound.

Iridium containing complexes were indeed able to promote the deuterodeborylation reaction (Table 2.1). (Ind)Ir(cod), $[Ir(OMe)cod]_2$, and $[Ir(PCy_3)(py)(cod)][PF_6]$ (Crabtree's Catalyst) were all effective at promoting the deborylation in the presence of D_2O. Furthermore, the ligand for the borylation step, 1,2-bis(dimethylphosphino)ethane (dmpe), as the only additive as well as a lack of additive failed to produce good deborylation, supporting that the iridium metal is necessary for the reaction.

Next, reaction conditions were explored that allowed for lower temperatures, which would be synthetically more appealing. It was found that the pure esters undergo selective deuterodeborylation at 80 °C with THF/D_2O (6:1) in the presence of 2 mol % of $[Ir(OMe)cod]_2$. A lower catalyst loading should result in longer reaction times, but the conversion and yield are effectively the same. GC analysis indicated full conversion to the desired deuterated product. Lower yields for **2.3b** and **2.4b** are due to loss of product upon isolation because of their volatility.

Table 2.2. Selective deuterodeborylations of arenes[a]



entry	arene	deuteration time	product	yield[b], %D[c]
1	 **2.1a**	2 h	 **2.1b**	80%, >98[d]
2	 **2.2a**	2 h	 **2.2b**	82%, 96
3	 **2.3a**	2 h	 **2.3b**	65%,[e] >98
4	 **2.4a**	2 h	 **2.4b**	60%, >98
5	 **2.5a**	4.5 h	 **2.5b**	74%, 96
6	 **2.6a**	3 h	 **2.6b**	74%, 93

[a]All reactions were run with 2 mmol of organoboronate. [b]Isolated yields. [c]Determined by integration of ^{13}C NMR spectra; see SI for details for calculation. [d]~4% 4-deuterated product was observed due to ~4% 4-borylated isomer in the starting material. [e]Owing to product volatility, solvent impurities were present.

Isotopic purity was determined by quantitative ^{13}C NMR spectroscopy using an inverse gated experiment, in which decoupling is on only during acquisition. The upfield triplet of the deuterated carbon was integrated against any residual protonated analogue, when it could be detected (Figure 2.2). Isotpoic purity was found to be generally high, and all were above 90%. The site of deuteration was also corroborated by ^{2}H NMR spectroscopy. Furthermore, the only position labeled on each substrate was the position where deborylation had occurred.

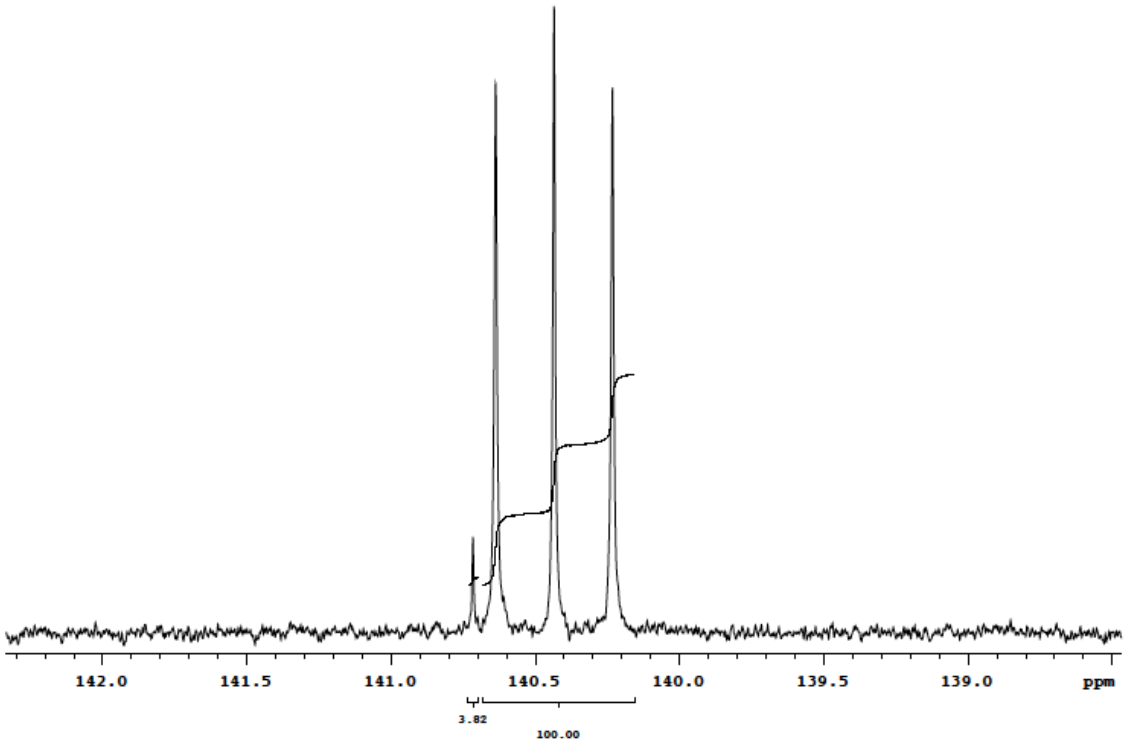
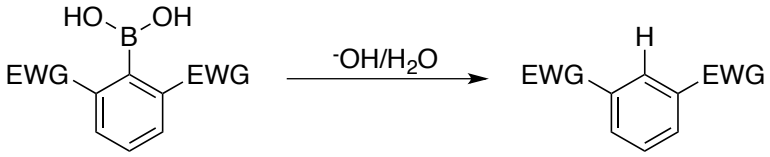


Figure 2.2. Representative ^{13}C NMR spectrum for deuterium incorporation for **2.2b**

We also addressed some other recently reported deborylation conditions in the context of our reaction scope. The first to be addressed were the conditions reported by Perrin and co-workers (Scheme 2.1).[69] Their method was a base promoted reaction that

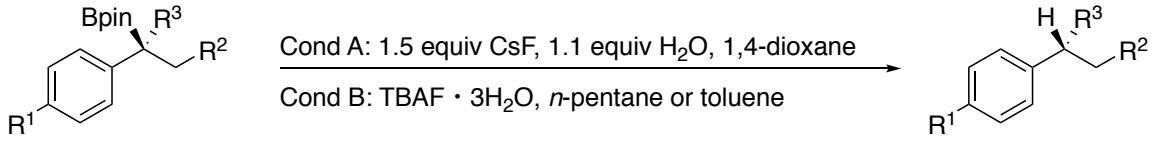
occurred at room temperature in the presence of KOH or KOD. However, there was a substrate dependence in that at least one electron withdrawing group was required in order for the reaction to occur. In most cases, that functional group was ortho to the boronic acid or ester. When these reaction conditions were applied to **2.2a**, no reaction was observed.

Scheme 2.1. Conditions for protiodeborylation by Perrin and co-workers[69]



Aggarwal and co-workers also published work that provided protiodeborylation of tertiary boronic esters with either CsF or TBAF (Scheme 2.2).[70] When the conditions using CsF were applied to **2.5a**, there was no reaction observed when it was monitored for 48 h. When the conditions using TBAF were applied to **2.5a**, trace conversion was observed for the reaction in toluene, but no change of the starting material was observed for the reaction in pentane.

Scheme 2.2. Conditions for protiodeborylation reported by Aggarwal and co-workers[70]

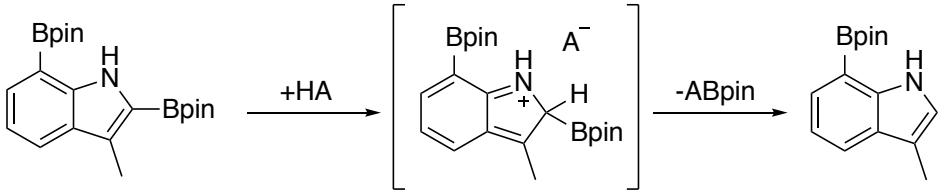


In a report by Movassaghi and co-workers[71] three different methods to deborylate and further functionalize C3-alkylindoles. The first (condition A), was to perform the

diborylation of 3-substituted indoles with 5 equiv of HBpin catalyzed by 2.5 mol% of $[Ir(OMe)cod]_2$ and 5 mol% of dtbpy in THF. After the borylation was complete the crude reaction mixture was then diluted with CH_2Cl_2 and trifluroacetic acid (TFA) is added at 0 °C. The reaction is then allowed to warm to room temperature for the deborylation affording the monoborylated product. The second set of conditions (condition B), was to diborylate *N*-2-(1H-Indol-3-yl)ethyl)-*N*,2,4,6-tetramethylbenzenesulfonamide under Ir-catalyzed conditions, purify it by flash chromatography, and then deborylate it with TFA in CH_2Cl_2. The third (condition C), was to diborylate with the Ir-catalyzed conditions, remove the volatiles under vacuum, and add a catalytic amount of $Pd(OAc)_2$. Acetic acid was added as the proton source for deborylation. For these conditions, both iridium and palladium were present.

This work directly impacted studies done by Venkata Kallepalli who showed that diborylated heterocycles including indoles and thiophenes could be selectively deborylated in the presences of an iridium catalyst and methanol.[72]

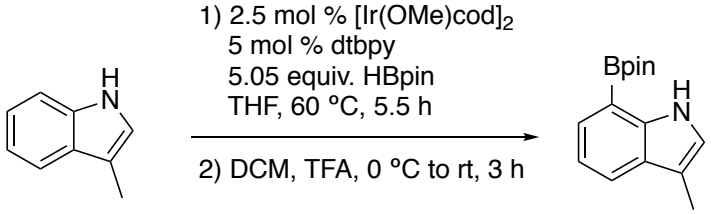
Scheme 2.3. Reaction mechanism for deborylation proposed by Movassaghi



However, the reaction mechanism proposed by Movassaghi gave no insights to the role of the metal (Scheme 2.3). Therefore, experiments were carried out to explore

that role. First, the synthesis of 7-borylated 3-methylindole was carried out according to the conditions described in their paper (Scheme 2.4). Similar results were obtained.

Scheme 2.4. One-pot diborylation/protiodeborylation conditions for 3-methylindole reported by Movassaghi and co-workers[71]

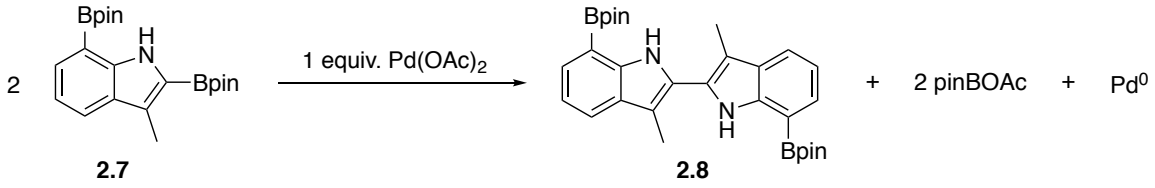


Next, a reaction was carried out where the protiodeborylation of 2,7-diborylated 3-methylindole was attempted without a metal in the presence of trifluoroacetic acid (TFA). After the same reaction time that condition A called for, an aliquot was removed from the reaction, and the volatiles were removed. ^{1}H NMR spectrum showed a complex mixture in the aromatic region.

Deborylations using acetic acid were carried out according to conditions C. One reaction used 2.5 mol% $[Ir(OMe)cod]_2$, and the other 5 mol% $Pd(OAc)_2$. After stirring for 8 hours at 30 °C, the reactions were analyzed by acquiring ^{1}H NMR of aliquots. Comparison of the integrals of the N-H resonance of the diborylated starting material and the monodeborylated product showed that the iridium-catalyzed reaction had proceeded to 75% conversion. A third species with an N-H resonance at δ 9.38 ppm was observed in the palladium-catalyzed reaction. This species increased when the palladium loading was increased. Attempts to separate this product from the other indole species were unsuccessful. However, in the ^{1}H NMR, the N-H resonance was similar to that of an

indole NH flanked by at least one Bpin group. Along with that, the other aromatic protons were similar to that of the diborylated indole. LC/MS also showed a molecular ion at m/z = 513.064. This mass is consistent with a homocoupled bisindole (Scheme 2.5). At 5 mol% loading of $Pd(OAc)_2$, deborylation with acetic acid at 30 °C for 8 h, the ratio of 7-borylated, 2,7-diborylated, and homocoupled bisindole species was 95:2:3 averaged over three runs. For the reactions where the crude diborylated indole is deborylated with catalytic palladium, only traces of **2.8** are observed.

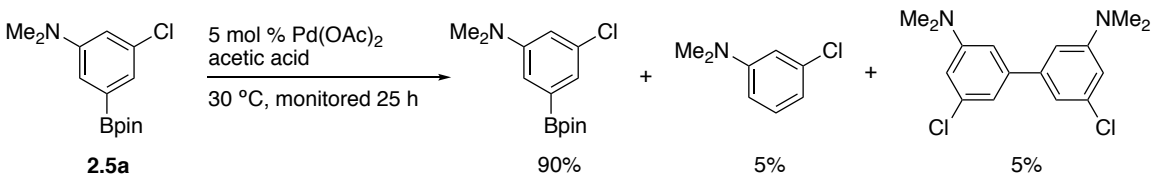
Scheme 2.5. Proposed homocoupling product



2.7 **2.8**

Furthermore, **2.5a** was subjected to deborylation conditions with 5 mol% $Pd(OAc)_2$ and acetic acid (**Scheme 2.6**). The reaction only produced 5% of the deborylated product, but it also produced 5% of a homocoupled product. This suggests that the first step in the deborylation reaction is a homocoupling reaction to generate Pd^0.

Scheme 2.6. Protiodeborylation of **2.5a** using Pd/AcOH

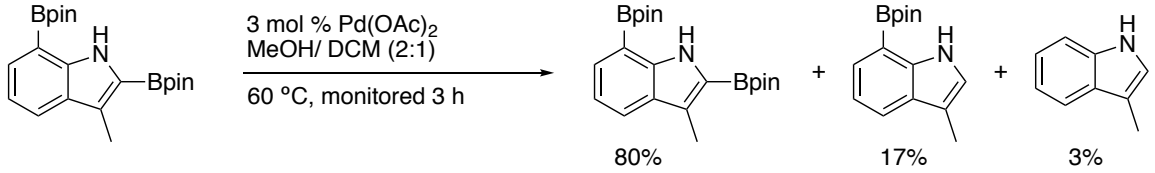


2.5a 90% 5% 5%

One further experiment completed the comparison of the Pd- and Ir-catalyzed deborylations. Deborylation of 2,7-diborylated 3-methylindole was carried out according

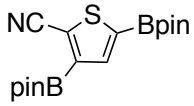
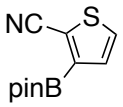
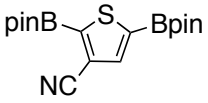
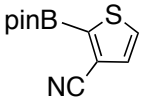
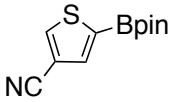
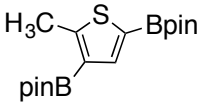
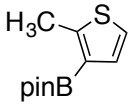
to the conditions found by Venkata Kallepalli where $Pd(OAc)_2$ was used as the catalyst in place of the $[Ir(OMe)cod]_2$ (Scheme 2.7). The reaction was monitored for 3 hours, and it was found that the reaction mixture contained 17% 7-borylated 3-methylindole and 3% 3-methylindole. The remaining 80% of the reaction was unreacted diborylated 3-methylindole. The greater performance of the iridium-catalyzed conditions makes them more favorable toward substrates that are sensitive to acidic environments.

Scheme 2.7. Deborylation of 2,7-diborylated 3-methylindole with $Pd(OAc)_2$ and MeOH/DCM



To complete the comparison of our deborylation conditions to the Movassaghi conditions, deborylations of thiophenes were carried out with $Pd(OAc)_2$ and in the presence of acetic acid or methanol.

Table 2.3. Palladium-catalyzed deborylation of thiophenes

Entry	Reactant	$Pd(OAc)_2$ loading, T, Solvent, Time	Product (% conversion)	
1	 **2.9**			
		5 mol %, 30 °C AcOH, 23 h	11%	
		3 mol %, 55 °C $MeOH/CH_2Cl_2$, 5.5 h	15%	
2[a]	 **2.10**			
		5 mol %, 30 °C AcOH, 23 h	8%	14%
		3 mol %, 55 °C $MeOH/CH_2Cl_2$, 5 h	7%	42%
3	 **2.11**			
		5 mol %, 30 °C AcOH, 23 h	59%	
		3 mol %, 55 °C $MeOH/CH_2Cl_2$, 5.5 h	39%	

[a]The diborylated thiophene rapidly deborylates to the 5-borylated product when washed with saturated $NaHCO_3$ solutions.

While the conversions were not quantitative, the deborylation with methanol and palladium generally had a higher conversion than that of acetic acid and palladium. Additionally, the deborylation for **2.10** was less selective than the iridium-catalyzed deborylation, which results in only one product. This is an added advantage of the iridium system as the deborylation reactions are both selective and progress to a high conversion.

2.3 Conclusions

We have shown that iridium-catalyzed deborylation can be used to selectively deuterate aromatic stubstrates with deuterium only being incorporated where the Bpin had previously resided. We have also shown that this labeling can be achieved under more mild conditions than those previously reported making this method applicable to substrates that might be sensitive to harsher conditions. Comparison of our method to other reported methods showed that there are advantages to both, but that our iridium system works well for a variety of substrates with mild, acid free conditions.

Chapter 3

Outer-Sphere Directed C-H Borylation of Enamines

3.1 Outer-Sphere Directed C-H Functionalizations

Typically "outer-sphere" refers to an electron transfer process. But, the term can also be used to define a directed functionalization where a ligand on a catalyst recognizes a functional group on a substrate. This molecular recognition can lead to higher selectivity for the reaction that is occurring. Outer-sphere has also been used to describe mechanisms for hydrogen transfer reactions and nucleophilic addition to π-allyl Pd compounds.[73-74]

Outer-sphere has also been used to describe C-H functionalization reactions (Figure 3.1).[75-79] When a metal is involved, the first step is the formation of a high oxidation state metal complex. The complex usually contains an activated ligand (metal-oxo, imido, or carbene species). Then, the activated ligand reacts with a C-H bond. There is either an insertion of the C-H bond or H-atom abstraction/radical rebound to afford the desired product.[75]

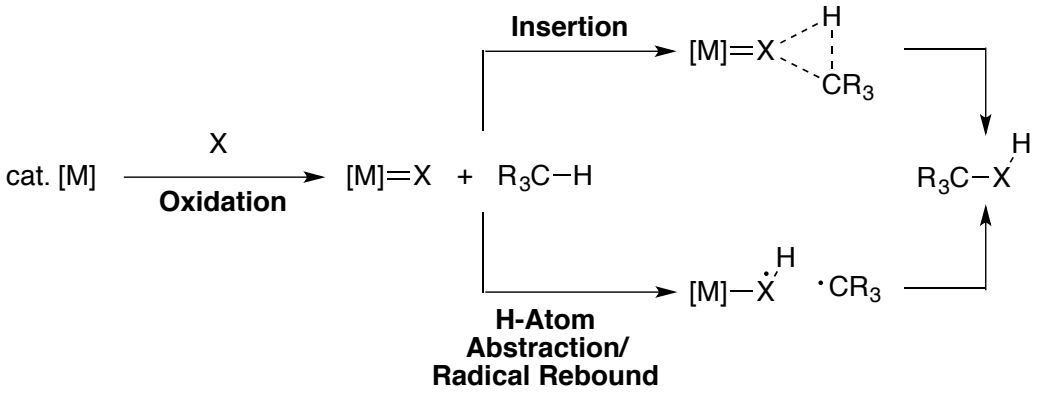


Figure 3.1. General reaction mechanism outer-sphere C-H functionalization

The most important thing to note is that the metal does not directly interact with the substrate. This follows the earlier definition where it was stated that the ligand on the metal recognizes the substrate. By saying that the reaction follows an "outer-sphere mechanism", we are saying that the reaction/functionalization/recognition is indirectly bound to the metal sphere or outside of it. If the reaction were to be called an "inner-sphere reaction" the reaction would take place directly bound to the metal.

3.2 Outer-Sphere Directed Borylation

The potential application for the use of outer-sphere direction for iridium-catalyzed borylation arose from a combined computational and experimental study.[80-81] Analysis of a variety of combinations of substrates and metal complexes supported the importance of the proton-transfer character in the C-H activation transition state.

There was a strong linear correlation between $\Delta G°$ and $\Delta G^{‡}$ for C-H activation and the natural population analysis (NPA) of the charge on the aryl group after the

activation. Figure 3.2 shows the correlation for the 5-membered heterocyclic intermediate subset.[82]

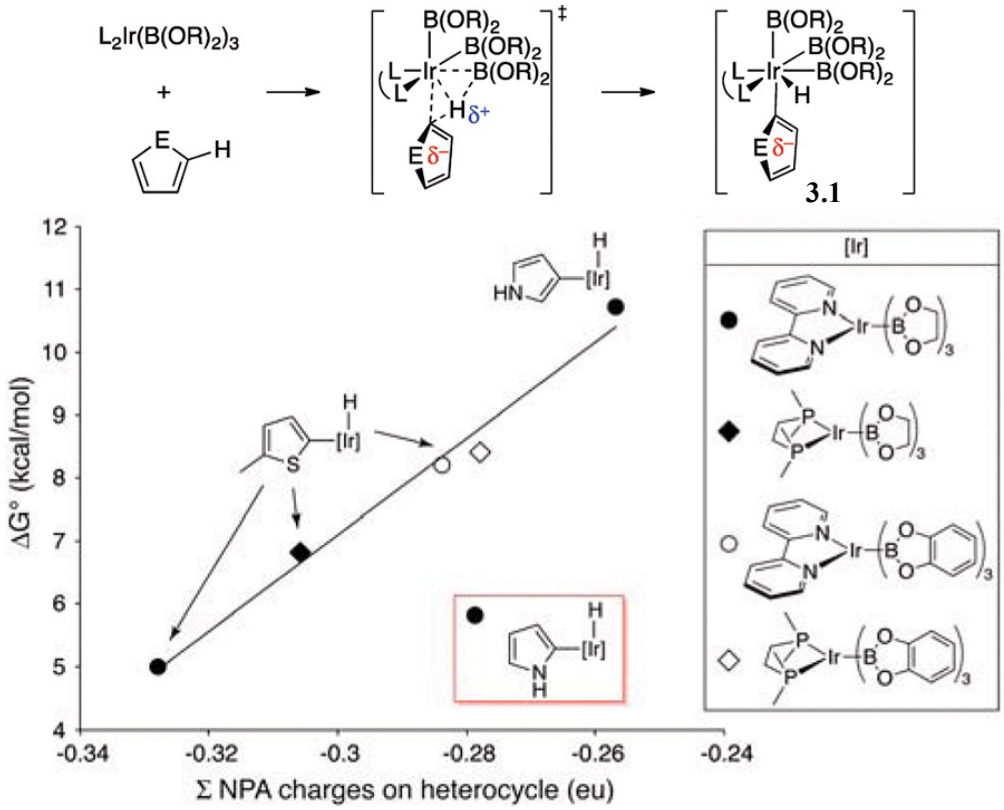


Figure 3.2. Calculated energies of intermediates vs. the total NPA charge on the C-H activated heterocycles Computational data excerpted from ref 80. Figure reprinted from ref. 82 Copyright 2012 American Chemical Society.

The charge/reactivity relationship was very predictive for most of the substrates. However, there was a deviation in the case of pyrrole. Borylation in the 2-position was found to be 2.3 kcal • mol^{-1} more favorable than predicted from a least-square fit of the other substrate/catalyst combination. Analysis of the calculated transition state and intermediate for the borylation of pyrrole in the 2-position indicated NHO interactions in both structures (Figure 3.3) where the N-H of the pyrrole is interacting with a Bpin oxygen.

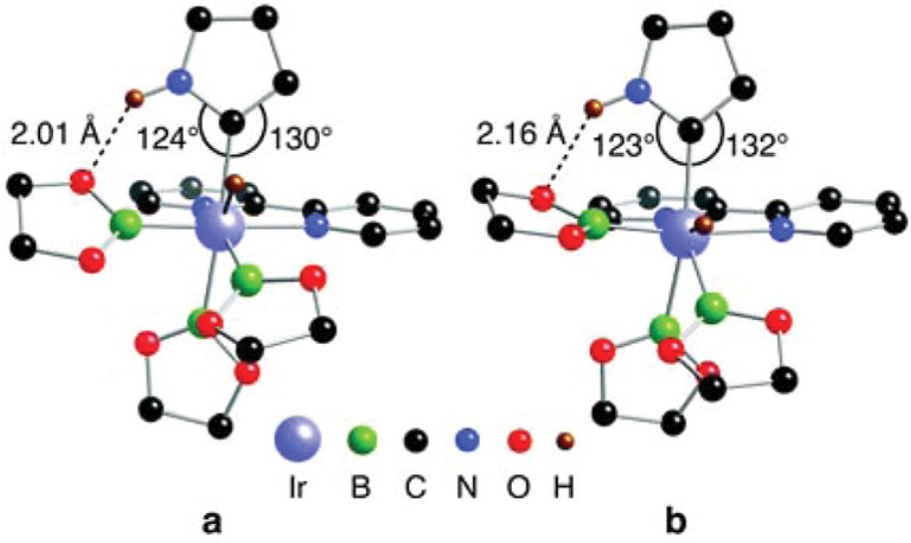


Figure 3.3. Lowest-energy M06/SDD(Ir)/6-31+G**(C H O N B) TS (a) and intermediate (b) for C–H activation of pyrrole at the 2-position by model complex Ir(bipy)(Beg)3 (eg = ethyleneglycolate). The NH–O distances and distortions for Ir–C–C and Ir–C–N angles indicate N–H–O hydrogen bonding. Figure reprinted from ref. 82 Copyright 2012 American Chemical Society.

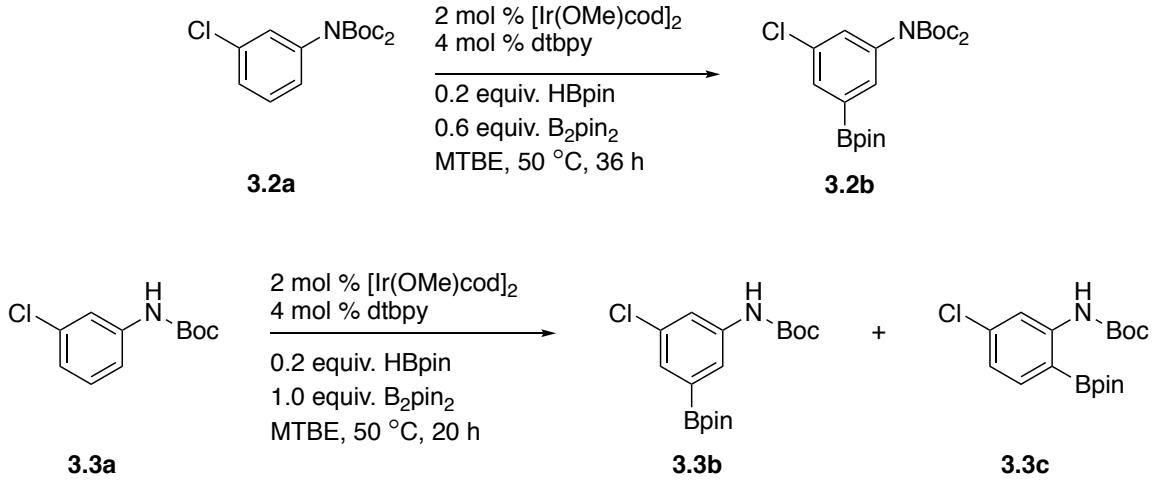
This interaction between the pyrrole NH and the oxygen of one of the Bpin bound to Ir, is an outer-sphere interaction. This likely accelerates the CHB of pyrrole, but it only reinforces the regioselectivity that is already preferred. Therefore, our group aimed to use similar interactions that could be applied to CHBs and result in complementary selectivity.

3.3 Outer-Sphere Directed Borylation of Boc-Protected Anilines

Preliminary studies showed that unprotected primary amines were hampered by poor conversion. Protecting groups such as triisopropylsilyl (TIPS) were shown to work well for the borylation of pyrrole, but are not practical due to their expense and the risk of hydrolysis.[83-84] *Tert*-butoxycarbonyl (Boc) protecting groups were found to be stable to borylation conditions.[84-86] Borylation of **3.2a** (Scheme 3.1) resulted in the meta-borylated

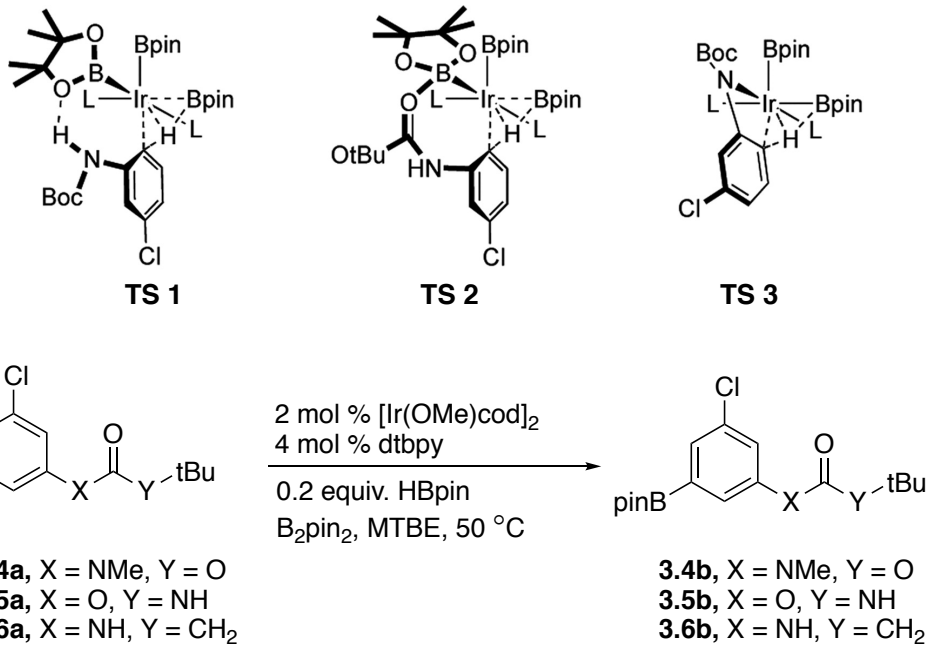
3.2b, which is the typical borylation pattern for 1,3-disubstituted arenes. However, when only one Boc group is used to protect the aniline group (**3.3a**), the selectivity changed to favor the formation of **3.3c** over **3.3b** by a 2:1 ratio.[82]

Scheme 3.1. Borylation of Boc-protected 3-chloroaniline



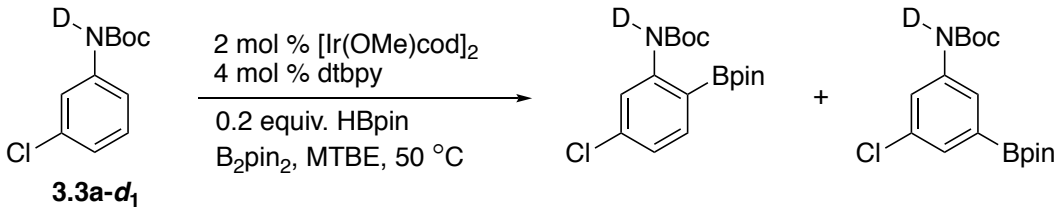
The authors theorized that there were 3 different transition states (TS) that this selectivity could originate from (Scheme 3.2). Substrates **3.4a**, **3.5a**, and **3.6a**. were chosen to probe the mechanism for the TS. For **3.4a**, **TS 1** and **3** are no possible because the H on the N has been replaced by a methyl. The CHB of **3.4a**, resulted in only the meta-isomer (**3.4b**). Substrate **3.5a** has the NH and O groups transposed from **3.3a**. This would affect the ring size of **TS 1** and **3** and therefore affect the selectivity of the CHB for them, but **TS 2** would not be as affected. The CHB borylation resulted in the meta-isomer again (**3.5b**), and therefore makes **TS 2** and unlikely participant in the CHB of **3.3a** in Scheme **3.1**. The CHB for **3.6a** was also meta-selective, which called the H-bonding mechanism of **TS 1** into question.

Scheme 3.2. Experiments to probe the mechanism for the CHB of **3.3a**



TS 1 and **3** were able to be distinguished from eachother by CHB of an *N*-deuterated substrate (**3.3a-*d*$_1$**) (Scheme 3.3). The product resulting from the CHB was still more than 95% *N*-deuterated. If the reaction were passing through **TS 3**, the amount of *N*-deuterated product would have been more greatly reduced, as it requires a cleavage of that N-D bond.

Scheme 3.3. Borylation of **3.3a-d_1**



2:1 ortho:meta
>95% N-D labelled product

These experiments were able to exclude **TS 2** and **3**, but provide no support for **TS 1**. It was theorized that an increase in the acidity of the N-H bond would affect the selectivity. But, borylations of substrates with more acidic N-H bonds (N-aryl triflamides) resulted in *N*-borylation. An experimental result that did provide support for the H-bonding mechanism was the observation that ortho-selectivity went up as the basicity of the dipyridyl ligands was increased (Figure 3.4). The authors proposed that the pinacolate oxygens in the complexes with more electronic-rich dipyridyl ligands were more basic, accounting for the increase in ortho-selectivity. This was the first case where dipyridyl electronic effects significantly affected regioselectivities.

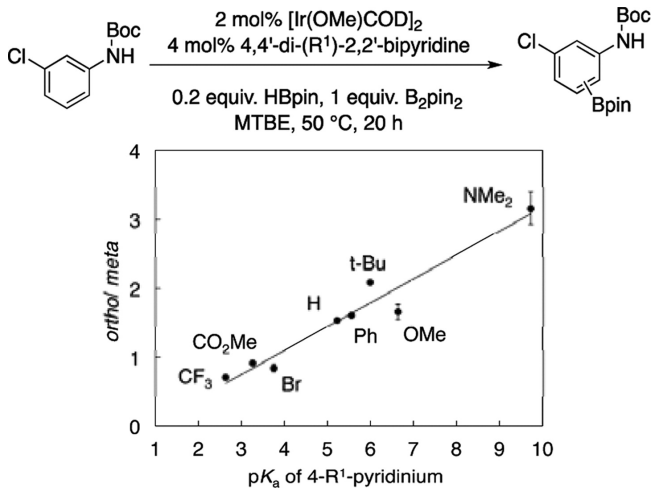
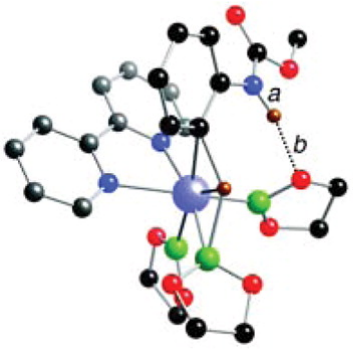


Figure 3.4. Plot of ortho/meta product ratios using 4,4'-di(R1)-2,2'-dipyridiyl catalysts vs pKa's of 4-R1-pyridium ions. Figure reprinted from ref. 82 Copyright 2012 American Chemical Society.

Theoretical calculations were able to determine the mechanism for the ortho direction. In M06/SDD(Ir)/6-31+G**(CHONB) calculations a series of TSs were located for the C-H activation of $PhNHCO_2Me$ by the model complex $(bpy)Ir(Beg)_3$. These calculations found ortho-CHB to be strongly favored, and the TS in Figure 3.5 shows a clear NH-O H-bond. The calculated TS also provided an explantion for the meta-selectivity in the CHB of **3.6a**. When the OCH_3 of the carbamate is replaced with an ethyl group and the Beg groups are replaced with Bpin groups, there is a tight steric interaction. The ortho transition structure is still favored enthalpically, but the restricted motion associated with the H-bond is disfavored entropically. Therefore, the selectivity is limited by entropy/enthalpy compensation.



a = 1.021 Å b = 1.897 Å

	o:m:p
$\Delta H^{\ddagger}$ (theory)	>99:<1:<1
$\Delta G^{\ddagger}$ (theory)	88:8:4
Experiment	90:5:5

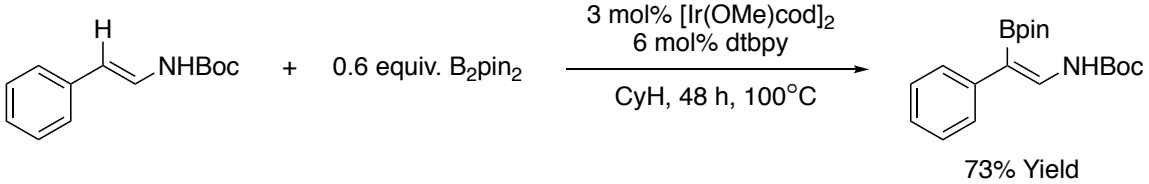
Figure 3.5. Lowest energy TS for the C-H activation of $PhNHCO_2Me$ by $(bpy)Ir(Beg)_3$. Figure reprinted from ref. 82 Copyright 2012 American Chemical Society.

The outer-sphere interaction could be used to further expand the substrate scope for the borylation on Boc-protected anilines. In the cases where a functional group larger than fluorine resides in the 4-position of the aniline, borylation is generally selective for ortho to the NH group. When the aniline is 3-substituted the selectivity is still favored ortho to NH, but meta-borylation is still observed.

3.4 Outer-Sphere Borylation of Enamines

The outer-sphere directed borylation of Boc-protected arylamines can be extended to the borylation of Boc-protected enamines (Scheme 3.4).

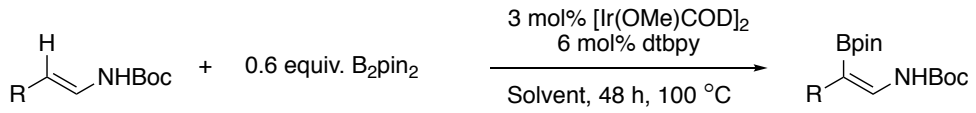
Scheme 3.4. Borylation of Boc-protected enamine

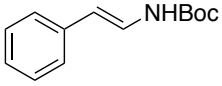
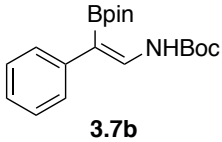
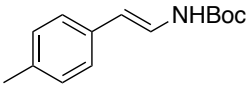
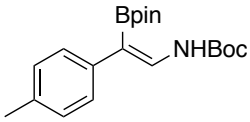
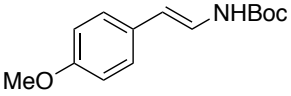
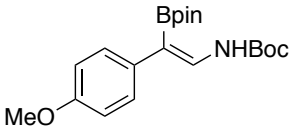
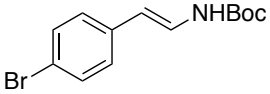
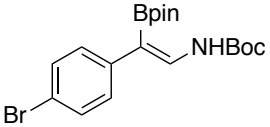
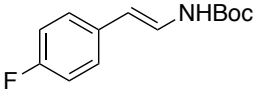
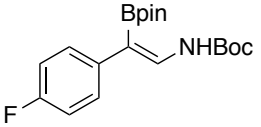
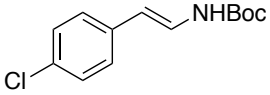
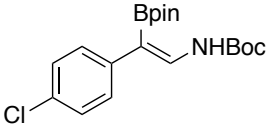
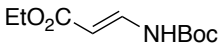
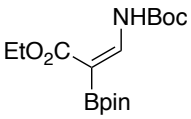
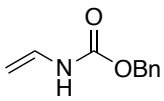
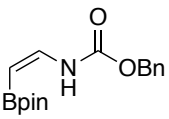


3.4a **3.4b**

Borylation of **3.4a** is selective for the vinyl C-H bond β to N in a ratio exceeding 99:1. Furthermore, the stereochemistry of the double bond remains intact and there is no evidence of phenyl CHB. With these promising results, we looked into if this chemistry could be expanded to include other Boc-protected enamines (Table 3.1).

Table 3.1. Borylation of Boc-protected enamines[a]



Entry	Enamine	Product	Yield[b,c]
1	 **3.7a**	 **3.7b**	n-Hex: (69%) CyH: 23%[d] (73%)
2	 **3.8a**	 **3.8b**	n-Hex: (72%) CyH: 33% (56%)
3	 **3.9a**	 **3.9b**	n-Hex: (62%) CyH: (66%)
4	 **3.10a**	 **3.10b**	n-Hex: (72%) CyH: (85%)
5	 **3.11a**	 **3.11b**	n-Hex: (60%) CyH: 20% (67%)
6	 **3.12a**	 **3.12a**	n-Hex: 57% CyH: 52%
7	 **3.13a**	 **3.13b**	n-Hex:15% CyH: 11%
8	 **3.14a**	 **3.14b**	n-Hex: -% CyH: 6% (12%)

[a]Reactions were 0.5 mmol scale of substrate. [b]Yields are isolated with respect to the substrate. [c]Yields in parentheses obtained by Buddhadeb Chattopadhyay. [d]Yield obtained from 9.1 mmol scale reaction

The aryl enamines (**3.7 – 3.12**) all showed generally good reactivity with high yields. Cyclohexane and *n*-hexane were found to be the best solvent for the reaction. However, **3.13**, and **3.14** showed a decrease in yield, and attempted borylations of **3.14a** in *n*-hexane were unsuccessful. In cases where the starting styryl enamine was synthesized from a mixture of *cis* and *trans* isomers, resulting in a mixed isomer substrate, the CHBs were unsuccessful.

It was initially believed that the borylation of **3.13a** had proceeded as expected and resulted in the retention of the trans olefin. However, upon obtaining crystal structure of **3.13b**, it was found that the olefin had isomerized (Figure 3.6).

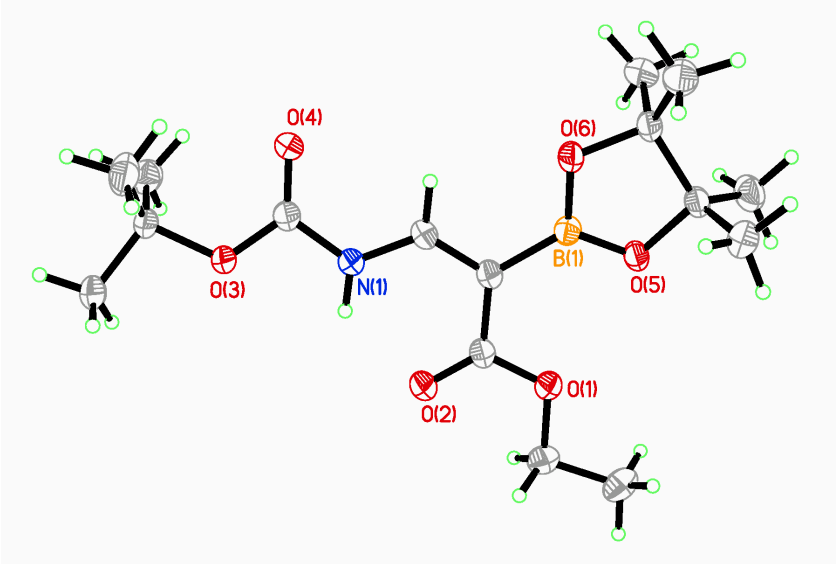


Figure 3.6. Crystal structure of **3.13b**. Thermal ellipsoids are shown at 50% probability.

Due to this observed isomerization of the borylated product, the original assignment of the synthesized starting enamine, **3.13a**, was called into question. ^{1}H NMR

showed that the coupling constant for the peaks corresponding to the vinylic protons to be 14 Hz, which supports the original assignment of a trans enamine. However, to confirm, a crystal structure was obtained to confirm the assignment (Figure 3.7).

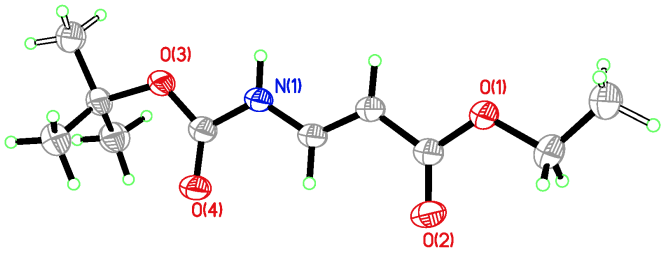


Figure 3.7. Crystal structure of **3.13a**. Thermal ellipsoids are shown at 50% probability

The structure of **3.13a** was confirmed to be a trans enamine by x-ray crystallography. Therefore, the isomerization is likely occurring during the borylation reaction. If that is true, that could also be the reason for the low yield of product. The alkene isomerization would lead to a loss of the hydrogen bond interaction of the NH of the enamine to the Bpin oxygen attached to iridium. This could result in a loss of reactivity for the substrate.

Indeed, when the reaction was run and aliquots taken for GCMS, a peak was observed to form within 2 hours of the reaction start time. This peak eluted 2.5 minutes before the peak for authentic **3.13a**. Also, by GCMS **3.13a** was fully consumed in that 2 h period. The mass corresponding to the new peak was *m/z* = 215, which was the same as that for **3.13a**. Therefore, it was concluded that **3.13a** is isomerizing under the borylation conditions leading to low borylation conversion. Furthermore, when **3.13a** was dissolved in cyclohexane and heated at 100 °C on its own, the same peak grew in corresponding to

an approximately 85% conversion of **3.13a** to the new peak over 2 hours. ^{1}H NMR of the mixture showed that the new GCMS peak likely corresponded to the *cis*-alkene of **3.13a** (**3.13c**).

The experiment was scaled up and repeated so that the two products could be separated from each other. Upon isolation and comparison of the ^{1}H NMR it became apparent that the new compound was indeed the *cis*-alkene.

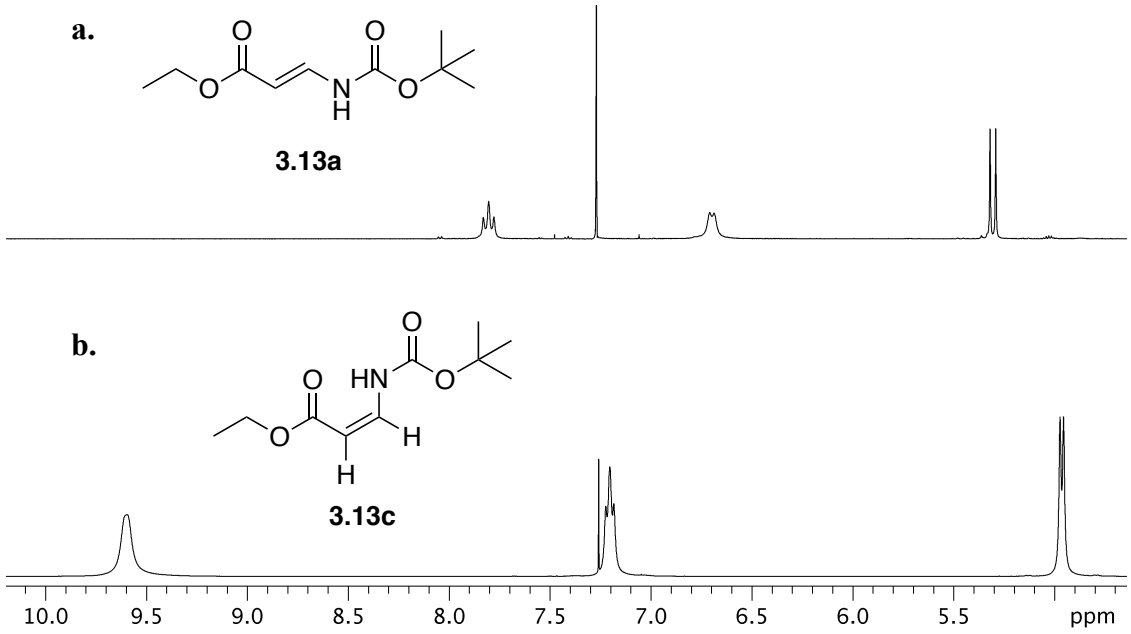


Figure 3.8. a) 500 MHz ^{1}H NMR of **3.13a**. **b)** 500 MHz ^{1}H NMR of **3.13c**.

Because **3.13c** is an oil, no crystal structure was able to be obtained for it. However, the ^{1}H NMR is informative. The peaks corresponding to the vinylic protons have very different coupling constants. For **3.13a**, as was previously mentioned, the doublet for the vinylic proton has a coupling constant of 14 Hz. This number is within the range that would be expected for a trans alkene. The coupling constant for the doublet for

3.13c (**Figure 3.8**b) is 8.9 Hz, which is well in line with what one would expect for a *cis*-alkene. Furthermore, the broad singlet of the NH in **Figure 3.8**b is further downfield than the peak in **Figure 3.8**a by approximately 3 ppm. This is likely because the NH of **3.13c** has the ability to form a hydrogen bond with the carbonyl oxygen of the ester; whereas that is not possible for **3.13a**. This is further support of the assignment.

Due to the results for **3.13a** and **3.13b**, it became important to confirm the geometry of the other substrates. **3.7b** and **3.12b** were evaluated to determine the geometry of the alkenes. At first, NOE was considered a favorable method, as the vinylic proton should show an NOE to the phenyl protons. However, initial studies showed no NOE in the molecule. This result neither confirms nor refutes the originally assigned geometry of the molecule. But, it does call it into question.

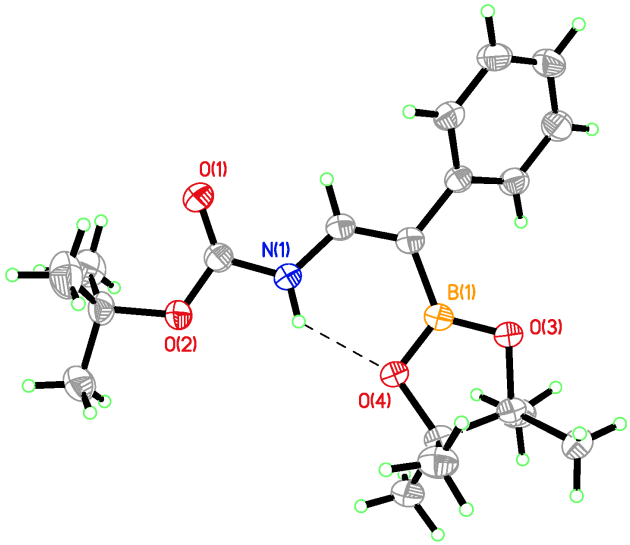


Figure 3.9. Crystal Structure of **3.7b**. Thermal ellipsoids are shown at 50% probability

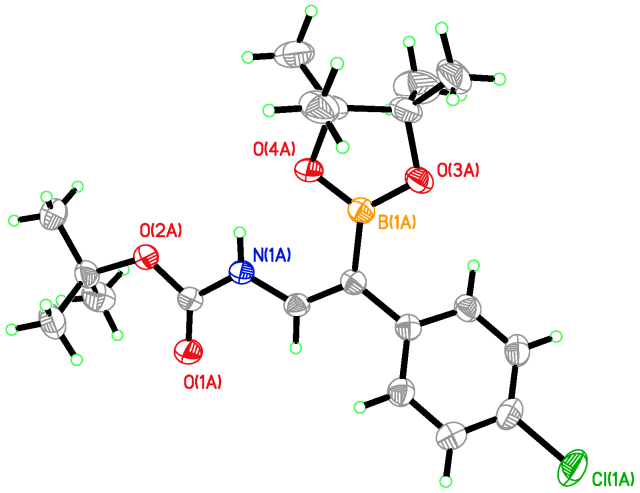


Figure 3.10. Crystal structure of **3.12b**. Thermal ellipsoids are shown at 50% probability

X-ray crystal structures confirmed that the geometry of **3.7a** and **3.12a** did remain *trans* throughout the borylation reaction to produce **3.7b** and **3.12b** respectively. Measurement of the distance through space between the vinylic proton and phenyl proton is 2.2 Å. So, the question was, what is happening in solution that resulted in a lack of NOE?

Looking back at the ^{1}H NMR of **3.7b**, it was noticed that there was a broadening in the peak corresponding to the vinylic proton that likely resulted from coupling to the NH proton. Therefore, this exchange resulted in an inability to read the NOE. Lowering the temperature of the NMR probe to -30 °C, slowed the exchange; resulting in a sharpening of the vinylic and NH proton peaks. Then, lengthening the relaxation delay and mixing time allowed the NOE interaction of the vinylic protons to the phenyl protons to be observed (Figure 3.9).

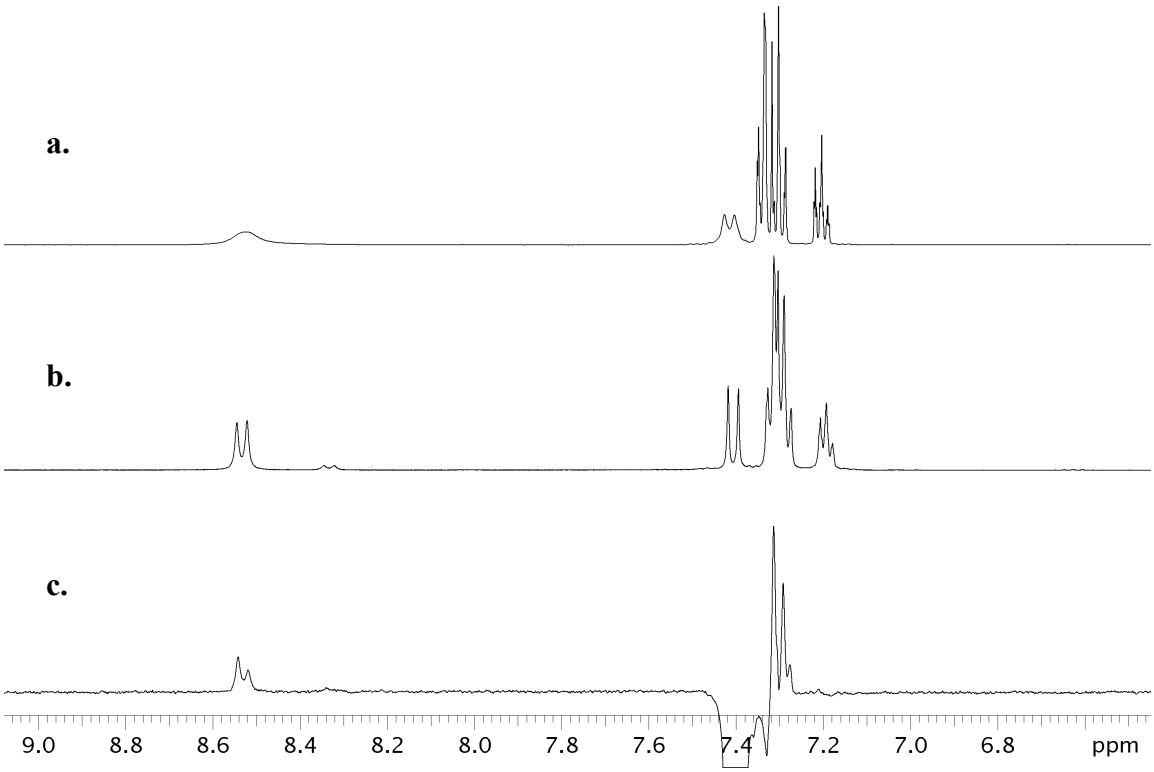


Figure 3.11. Low temperature NOE spectrum of **3.7b**. All spectra acquired on 500 MHz instrument in CD_3CN. **a)** Room temperature ^1H NMR of **3.7b**. **b)** ^1H NMR of **3.7b** at -30 °C. **c)** NOE at -30 °C of **3.7b** showing excitement of vinylic proton leading to response from phenyl protons.

Now that the stereochemistry of the styryl carbamate substrates is understood to remain trans through the borylation, we can return to the question of why **3.13a** does not retain the trans olefin in the reaction. As was previously discussed, the isomerization occurs in the borylation conditions and when the starting material is heated in solution. The fact that the *cis* enamine is observed in the borylation supports that the isomerization is occurring prior to borylation. In looking at the crystal structure, it can be observed that the isomerization results in a hydrogen bond from the amido hydrogen to the oxygen of the ester carbonyl (Figure 3.11). The hydrogen bond forms a 6-membered ring, and likely

creates the most stable structure for the enamine.[87] Therefore, the enamine remains locked in the *cis* form and does not revert back to the *trans* during the reaction.

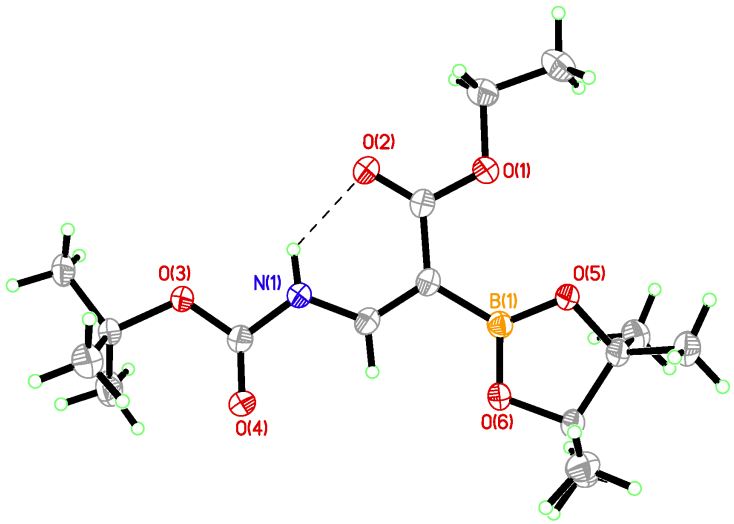
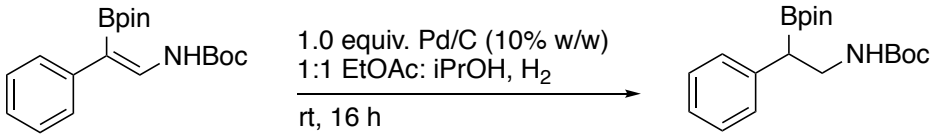


Figure 3.12. Crystal structure of **3.13b** depicting a hydrogen bond from N(1) to O(2). Thermal ellipsoids are shown at 50% probability

It was also found that the borylated enamines could be hydrogenated to obtain the sp^3 borylated compound (Scheme 3.5) in 96% yield. The reaction used Pd/C and the pressure of H_2 from a balloon to facilitate the reaction.

Scheme 3.5. Hydrogenation of **3.7b**



3.7b **3.15**

3.5 Conclusions

Outer-sphere borylation was applied to the functionalization of enamines. Styryl carbamates borylated exclusively on the olefin and no borylation was observed on the phenyl rings. They also retained their *trans* stereochemistry throughout the reaction. However, when the substrate contained a mixture of isomers, the CHBs were not successful. Furthermore, the isomerization of **3.13a** to **3.13c** removes the possibility for the outer-sphere directing effect between the NH and the O of a boryl ligand to occur. This in turn impacted the yield for the reaction. These borylated enamines are useful building block for further functionalization to more complex molecules.

CHAPTER 4

Electrostatically Directed C-H Borylation for ortho-Functionalization of Phenols

4.1 Overview of Electrostatically Directed Chemical Transformations

Electrostatic interactions play an important role in a variety of biological processes including protein stabilization.[88-89] Patterns and surface potentials have also provided a useful way to interpret biological and biochemical data. It can point to residues that may play vital functional roles.[89]

More recently there has been interest in utilizing electrostatic interactions for chemical transformations where the catalyst interacts electrostatically with a substrate. Breslow and co-workers reported in the 1990s a manganese catalyst that used cyclodextrins bound to the porphyrin ligand to bind olefins hydrophobically and perform selective epoxidations.[90] The catalyst was also found to hydroxylate unactivated saturated carbon bonds steroids.[91]

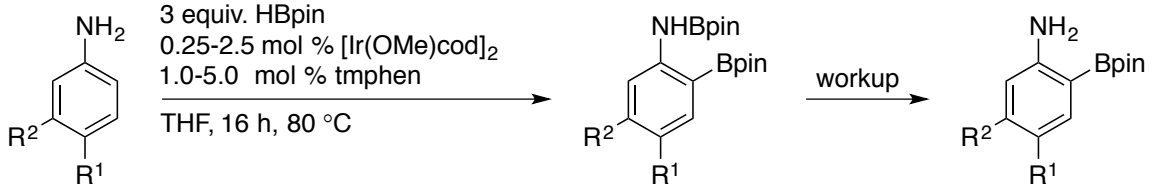
Bergman and Raymond utilized size differentiation by a host-guest ensemble to facilitate C-H activation.[92] This encapsulation of a cationic iridium species provides a method for mimicking active sites of metalloenyzmes. The assembly also provides specific shape and size selectivity towards substrates, which allows the substrate scope to be tuned depending on the encapsulated species.

Crabtree and Brudvig used molecular recognition through reversible hydrogen-bonding interactions between a di-μ-oxo dimanganese complex and the substrate to effect a oxygenation reaction of saturated C-H bonds in ibuprofen and (4-methylcyclohexyl) acetic acid.[93] The hydrogen-bonding interaction takes place between the carboxylic acid group of the catalyst and a carboxylic acid group on the substrate.

4.2 Traceless Protecting Groups for C-H Borylations

In Chapter 3, the outer-sphere directed borylation of Boc-protected anilines was examined. Upon further research, Sean Preshlock and Donald Plattner found that this same directing mechanism could be applied while utilizing *in-situ* protection and deprotection. This was achieved by the use of pinacolborane and the protecting group to afford a "traceless" protecting/directing group on the aniline. The result was the selective ortho-borylation of a number of anilines (Scheme 4.1).[94] The origins of the mechanism are still the outer-sphere direction observed for the Boc-protected anilines and enamines.

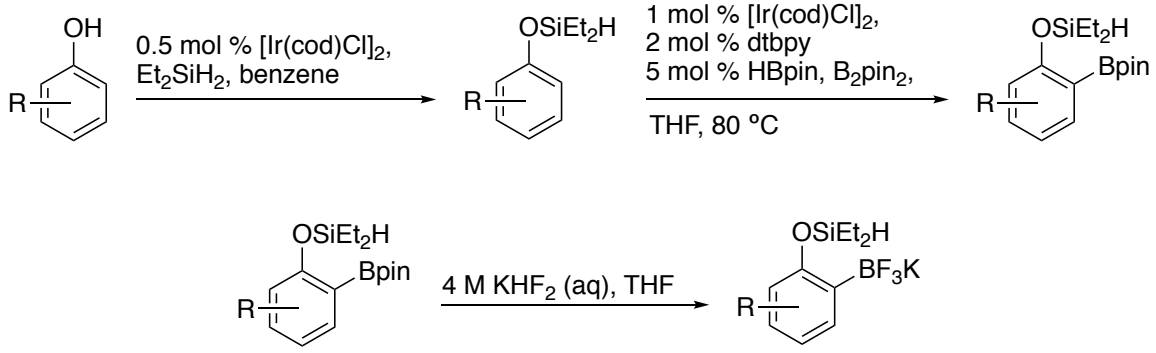
Scheme 4.1. Borylation of anilines with traceless protection using HBpin



This type of traceless protection could also be applied to heterocycles such as indole, pyrrole, azaindole, and pyrazole. This removed the protection/deprotection steps that lowered overall yield while still resulting in the desired borylated heterocycle.

Prior to this, Hartwig and co-workers reported the one-pot borylaton of phenols using in-situ silyl-protection (Scheme 4.2).[95] The selective ortho-borylation to the silyl ether are postulated to arise from the formation of a temporary Ir-Si bond, which leads to selective ortho C-H activation.

Scheme 4.2. Silyl-protected one-pot borylation of phenols reported by Hartwig and co-workers



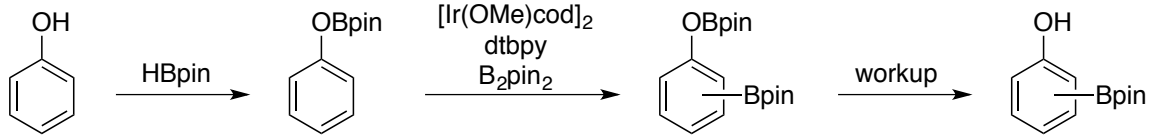
However, the scope of the reaction was limited, and protiodeborylation upon attempted isolation necessitated that the products be converted to potassium trifluoroborate salts. Thus, adding another step to the one-pot process.

4.3 Ortho-Borylation of Phenols using B_2pin_2

In the process of extending, our chemistry for traceless protection in borylation to phenols, we observed high selectivity for borylation of the C-H bond ortho to the O-H. When the borylation of phenol was examined with 2 equivalents of HBpin (Scheme 4.3), C_6H_5OBpin formed rapidly. Borylation of that intermediate with $[Ir(OMe)cod]_2$ and dtbpy as the precatalyst and ligand in the prescence of B_2pin_2 afforded a mixture of ortho,

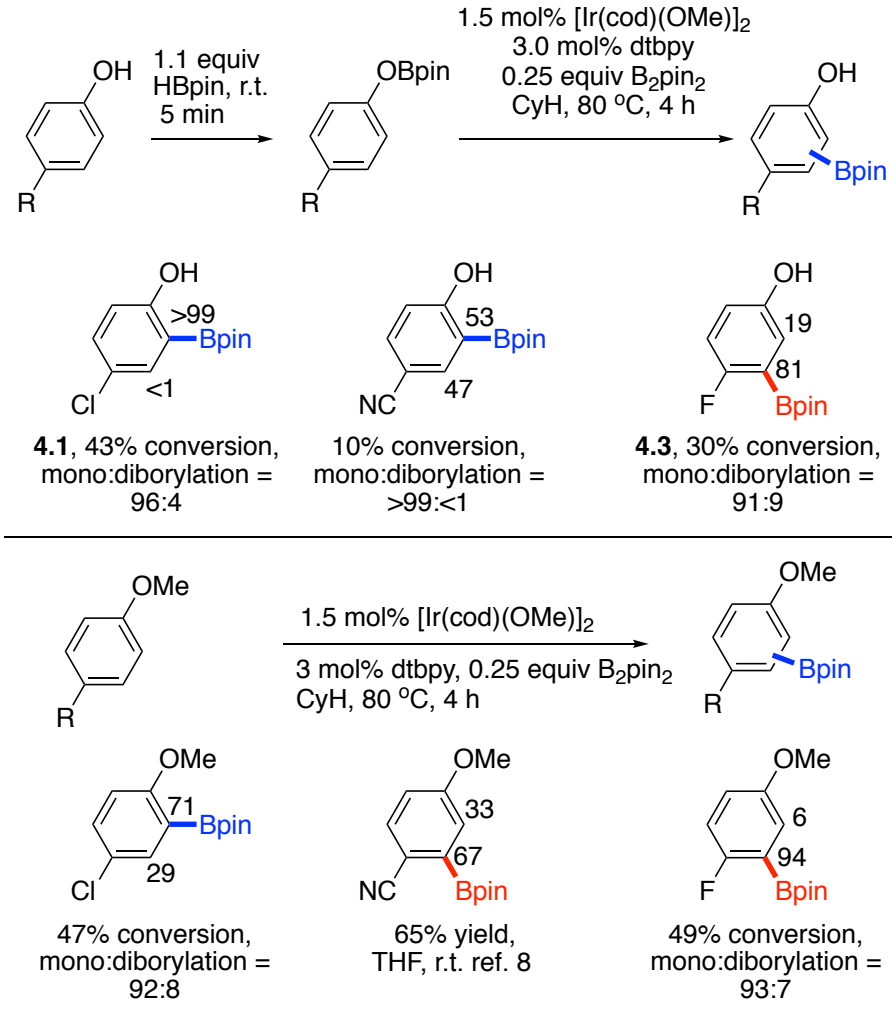
meta- and para-borylated phenol. A ratio of 15:85 (*o:m+p*) with respect to OH was observed. This amount of ortho-borylation was quite a bit higher than that observed for the borylation of anisole (*o:m+p* = 4:96) under identical conditions. The origins for the selectivity cannot arise from a hydrogen-bonding mechanism as in the borylation of Bpin protected anilines. Therefore, there is a different mechanism is at work to afford the ortho-borylation.

Scheme 4.3. Borylation of phenol with traceless protection



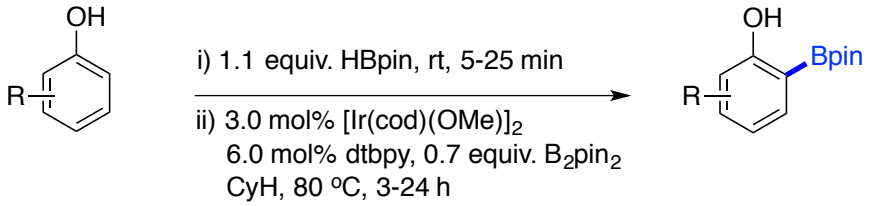
The tendency toward borylation ortho to OBpin was more apparent in the borylation of 4-substitututed phenols. These were also compared to the borylation of the corresponding anisole (Scheme 4.4). The series of 4-chloro, 4-cyano, and 4-fluoro provided a good series of substrates where the substituent deflects adjacent borylation in the order of Cl > CN >> F.

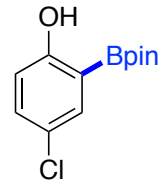
Scheme 4.4. C-H borylation of 4-substituted phenols and anisoles



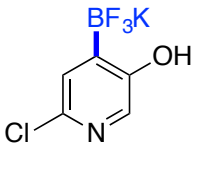
Selectivity for the borylation ortho to OBpin for 4-chlorophenol was very high. The selectivity dropped some with the removal of that OBpin for the 4-chloroanisole. The selectivity for borylation inverts for 4-cyanophenol versus 4-cyanoanisole. Then, in the borylation of 4-fluorophenol and anisole, both borylations favor borylation next to the fluorine. These results were encouraging and therefore, borylations of a range of phenols were performed. The results are shown in Table 4.1.

Table 4.1. ortho-Borylation of substituted phenols with B_2pin_2[a]

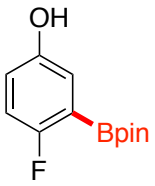




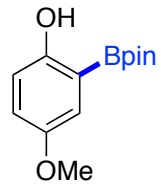
4.1, 74%[b]



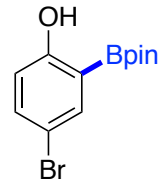
4.2, 87%[c]



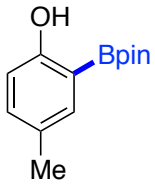
4.3
conversion: 100%[d]
o/m = 10/90



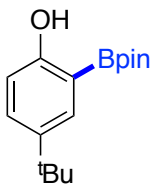
4.4, 58%



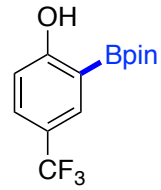
4.5 63%



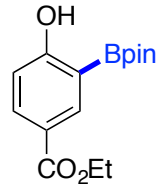
4.6, 85%



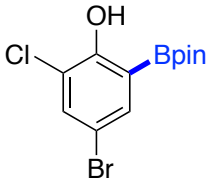
4.7, 84%



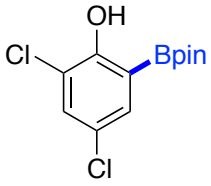
4.8, 65%



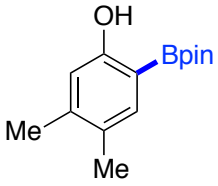
4.9, 51%



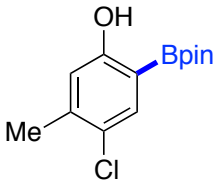
4.10, 75%



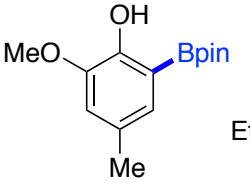
4.11, 49%



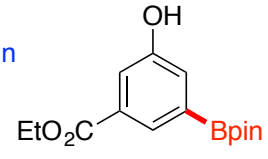
4.12, 68%



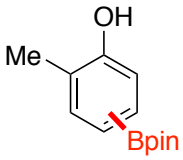
4.13, 68%



4.14, 66%



4.15
conversion: 100%[d]
o/m = 18/82



4.16
conversion: 100%[d]
o/m+p = 1/99

All yields reported except **4.1** and **4.2** isolated by Buddhadeb Chattopadhyay. [a]Yields are isolated. [b]Entry **4.1** was obtained in 74% yield on a 2 g scale using 1.5 mol% Ir-catalyst, 3.0 mol% dtbpy and 0.7 equiv B_2pin_2. [c]The Bpin product was converted to the BF_3K salt for isolation. [d]Conversion and isomer ratio based on GC-FID.

Yields for the isolated products range from very good to moderate. For the purposes of isolation, **4.2** needed to be converted to a BF_3K salt. The catalyst loading was also higher than that we normally employ. Therefore, a reaction was done to test the scalability of the reaction at a lower catalyst loading. Compound **4.1** was prepared from 2.0 g of 4-chlorophenol and 0.7 equivalents of B_2pin_2 using 1.5 mol% $[Ir(OMe)cod]_2$ and 3 mol% dtbpy. After purification 2.9 g (75% isolated yield) of **4.1** was obtained as a colorless oil.

Selectivity for the borylation ortho to OH was generally high and not affected by substitution in the 2-position of the phenol. However, substrates **4.3**, **4.4**, **4.15**, and **4.16** did not exhibit total ortho-selectivity. The degree of ortho-borylation (65:35 ortho/meta) for **4.4** was still high enough that the product could be isolated free of the meta-borylated product. The lack of higher amounts of ortho-borylation for **4.3**, **4.15**, and **4.16** leads to the conclusion that the substituent in the 4-position needs to at least be larger than a fluorine to ensure good selectivity.

The only product requiring transformation to facilitate isolation was **4.2**, which was isolated as the trifluoroborate salt. Once **4.2** had formed, it precipitated from the reaction mixture as a solid, which allowed for easy product recovery and high yield.

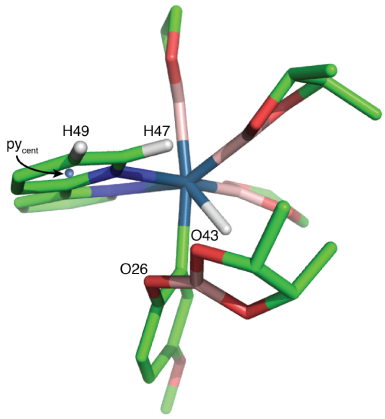
In the process described by Boebel and Hartwig discussed earlier, the isolation process necessitates the conversion of the boronic ester product to the trifluoroborate salt. Whereas, our method allows for direct access to the pinacol boronic ester product upon

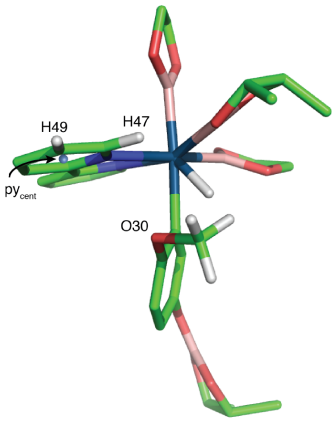
isolation. However, their method does allow for selective ortho to OH borylation when there is no substituent larger than fluorine in the 4-position.

Both our OBpin directed borylation and Hartwig's silane directed method have favorable features. But the mechanism that governs the Bpin directed method is different. Therefore, computational studies by Dr. Milton Smith and Dr. Daniel Singleton were used to investigate the origins of the selectivity.

Transition states for the CHB of OBpin-4-methoxyphenol were found in M06 calculations with an SDD basis set on Ir and a 6-31G* basis set on the other atoms. Two of the transition states are shown in Figure 4.1a. The structure for borylation ortho to OBpin is **TS3-OBpin'$_{anti}$**, and **TS3-OMe$_{anti}$** is the structure for borylation ortho to methoxy. The anti description refers to the arrangement of the methyl or Bpin' groups relative to the bpy ligand. Computational data showed that **TS3-OBpin'$_{anti}$** is enthalpically favored by 5.2 kcal•mol^{-1}. Because there is a steric interaction in **TS3-Opin'$_{anti}$** with the two pin' groups restricting motion, is entropically disfavored. However, it is still favored by 1.9 kcal•mol^{-1} in free energy. The enthalpic preference for **TS3-OBpin'$_{anti}$** was found to likely arise from an electrostatic interaction arising from the OBpin orienting toward the bpy pyridine ring.

a.

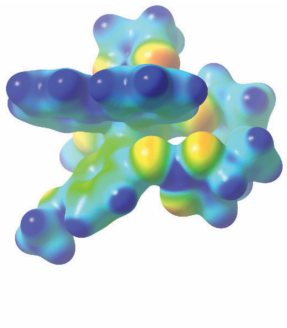




TS3-OBpin'$_{anti}$	**G_{rel} = 0 kcal·mol^{-1}**
Distances	NPA Charges
O43–H47 = 2.77 Å	H47, 0.27; H49, 0.26;
O43–H49 = 3.34 Å	O43, -0.78; O26, -0.76;
O26-py$_{cent}$ = 3.14 Å	py$_{cent}$, 0.12

TS3-OMe$_{anti}$	**G_{rel} = 1.8 kcal·mol^{-1}**
Distances	NPA Charges
O30–H47 = 2.85 Å	H47, 0.27; H49, 0.26;
O30–H49 = 4.13 Å	O30, -0.61;
O30–py$_{cent}$ = 3.45 Å	py$_{cent}$, 0.11

b.



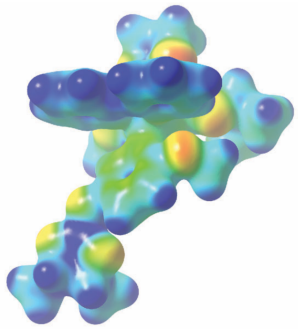


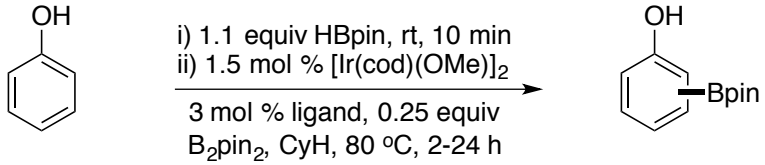
Figure 4.1. a) Lowest energy transition state structures for the borylation of OBpin-4-methoxyphenol (bpy)Ir(Beg)$_2$(Bpin') **b)** Calculated electrostatic potential surfaces for the borylation of OBpin-4-methoxyphenol with (bpy)Ir(Beg)$_2$(Bpin').

The NPA charges were calculated for the transition states to examine the role of the electrostatic interaction in the reaction. It was observed that the NPA charges for O1 and O2 in **TS3-OBpin'$_{anti}$** are more negative than O3 in **TS3-OMe$_{anti}$**. From the calculated electrostatic potential maps in Figure 4.1b, O1 is in the best position to make the most of the attraction to the positive charge of H1 and H2. A crude electrostatic model for **TS3-OBpin'$_{anti}$** was calculated; where the charge on the pyridine ring was estimated as a point charge at the center and the charge for OBeg corresponded to the

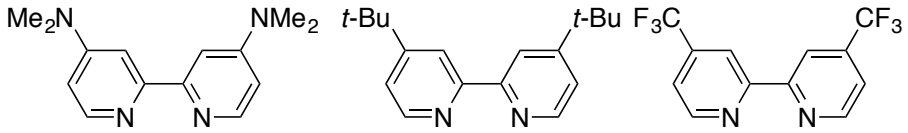
sum of the boron and surrounding oxygen atoms was placed on boron. For **TS3-OMe$_{anti}$**, the charge for the methoxy group was represented as the charge on oxygen. A stabilization of approximately 3 kcal•mol^{-1} was found for **TS3-OBpin'$_{anti}$**, which is enough for the selectivity observed.

Based on these computational results, alterations to the electronic character of the bipyridine ligand would alter the selectivity. A more electron rich ligand would shift the selectivity to favor more meta- and para-borylated products. A ligand that is more electron deficient would favor more ortho-borylated product formation. Exploiting this trend could allow for a method to improve the selectivity for substrates such as **4.3**. A screen of three bipyridine ligands was performed for the borylation of phenol (Scheme 4.5). Indeed, when there is an observed increasing selectivity for the ortho-borylated product as the ligand becomes more electron deficient. However, the greater selectivity comes at the cost of catalytic activity. Therefore, we searched for another method that would help improve the selectivity for substrates that had poor selectivity in Table 4.1.

Scheme 4.5. Ligand electronic effects on borylation regioselectivity



ligand	conversion	o:(m+p)
4.17	46%	6:94
4.18	49%	15:85
4.19	34%	35:65



4.17 **4.18** **4.19**

4.4 Ortho-Borylation of Phenols using B_2eg_2

The transition state structures in Figure 4.1a, showed considerable distortion for the arene geometries. Steric pressure from the Bpin' group push the arene away from the activating Beg group. The result is an elongation of the $H_{act} - B_{act}$ in **TS3-OBpin'$_{anti}$** compared to **TS3-OMe$_{anti}$**, which translates to a 23% decrease in the natural bond order between $H_{act} - B_{act}$.

Because Beg is the smallest glycolatoboryl ligand, a transition state with Beg ligands should decrease the distortion and allow for better transition state stabilization. The transition states for the borylation of OBeg-4-fluorophenol for ortho to fluorine (**TS5-F**) and ortho to oxygen (**TS5-OBeg$_{anti}$**) by (dtbpy)Ir(Beg)$_3$ were calculated. The geometries for the inner coordination spheres are nearly identical, indicating the reduced steric pressure restores the interaction **TS5-OBeg$_{anti}$**. Electrostatic interactions favor **TS5-**

OBeg$_{anti}$ over TS5-F by 1.5 kcal•mol-1, which favors borylation ortho to fluorine at a 93:7 ratio.

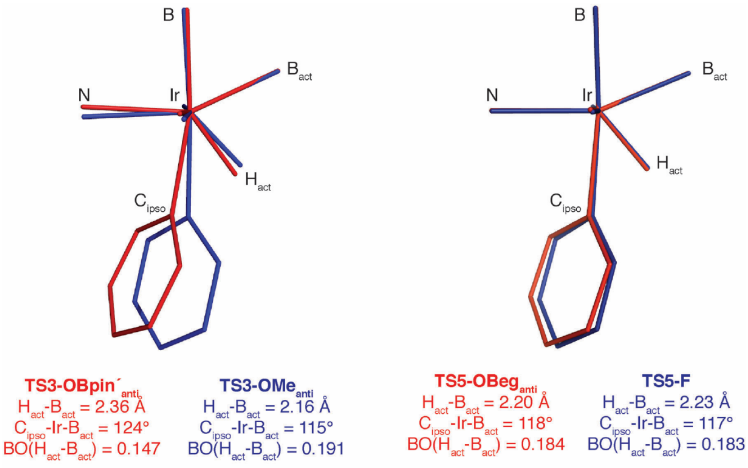
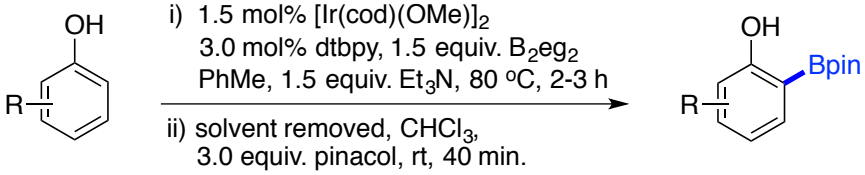
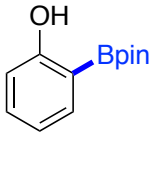


Figure 4.2. Calculated inner coordination spheres, selected metrical parameters, and natural bond orders for **TS3-OBpin´$_{anti}$** and **TS3-OMe$_{anti}$** (left) and **TS5-OBeg$_{anti}$** and **TS5-F** (right).

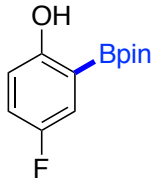
We tested the computational data by preparing B_2eg_2 from $B_2(OH)_4$ and ethylene glycol. Then, it was tested for borylation using the conditions shown in Table 4.2. As it turns out, the borylation with B_2eg_2 resulted in selective ortho to OH borylation for phenols that lacked a substitution larger than fluorine in the 4-position. For the substrates from Table 4.1 that showed a lack of ortho-selectivity (**4.3**, **4.15**, and **4.16**), only the ortho-borylated products (**4.21**, **4.22**, and **4.26**) were isolated from the reaction when the conditions with B_2eg_2 were applied. However, it is noted that diborylated side products were observed but were easily separated upon purification by chromatography.

Table 4.2. ortho-Borylation of substituted phenols with B_2eg_2

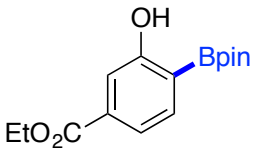




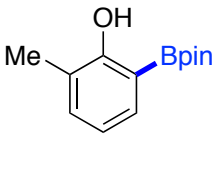
4.20, 65%[b]



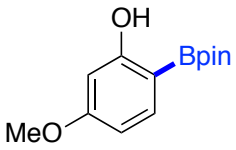
4.21, 50%[c]



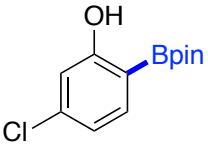
4.22, 56%



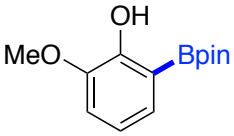
4.23, 73%



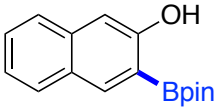
4.24, 80%[d]



4.25, 60%[e]



4.26, 73%



4.27, 67%

Yields reported isolated by Buddhadeb Chattopadhyay [a]Yields are isolated mono-borylated products. Diborylated products were not isolated. [b]Mono:*o,o'*-diborylation = 82:18. [c]B_2eg_2 used as 1.2 equiv, mono:*o,o'*-diborylation = 89:11. [d]Mono:*o,o'*-diborylation = 81:19. [e]Mono:*o,o'*-diborylation = 85:15.

Interestingly, the best solvent for this reaction was found to be toluene, and competing borylation was not observed. In addition, yields were improved by the addition of triethylamine. This result is attributed to the stabilization of HBeg, which is know to disproportionate into diborane and B_2eg_3, as HBeg•NEt_3.

4.5 Conclusions

Traceless protection of phenols lead to the ortho-directed CHB directed by electrostatic interactions between OBpin and a bpy ligand. The reactions which employ B_2pin_2 as the boron source are generally ortho-selective for most substrates with a group larger than fluorine in the 4-position. When B_2eg_2 is used the reaction becomes ortho-selective for those substrates with small groups in the 4-position due to better transition state stabilization.

Chapter 5

1,10-Phenanthroline Ligand Design Utilizing C-H Borylation

5.1 Functionalization of 1,10-Phenanthroline

1,10-Phenanthroline ligands are some of the most widely used chelating ligands in chemistry because of its advantageous structural and chemical properties.[96] They have been used in a wide variety of applications such as carbon-nitrogen coupling reactions,[97-99] fuel and solar cells,[100-103] and DNA binding probes.[104-105] They are also a versatile building block that can be functionalized at many positions with a wide variety of purposes.[106-109] and its properties can be tuned based on modification of its functional groups.

For C-H activation/borylation the combination of iridium catalyst with a chelating nitrogen donating ligand such as bipyridine has been most commonly employed.[110-111] But, lately there has been more interest in the use of 1,10-phenanthroline based ligands.[112-115] For one specific case, 3,4,7,8-tetramethyl-1,10-phenanthroline (tmphen) has been shown to outperform dtbpy. The constrained geometry of the ligand is thought to be a possible reason for this.[112]

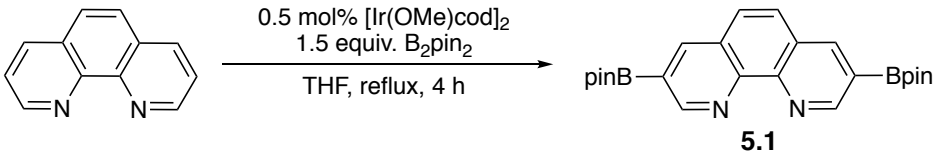
Even with their growing use in a wide variety of applications, many synthetic routes to functionalized 1,10-phenanthroline ligands remain long, low yielding, and poorly selective.[107-108] Our goal was to provide simple, high yielding routes to functionalized 1,10-phenanthroline ligands utilizing the versatility of the C-B bond. By

synthesizing the borylated 1,10-phenanthroline, a starting platform to obtain a wide range of more complex structures would be attainable from one isolatable intermediate.

5.2 Functionalization of 1,10-Phenanthroline via C-H Borylation

The diborylation of 1,10-phenanthroline (Scheme 5.1) was performed using $[Ir(OMe)cod]_2$ as the catalyst. No additional ligand was added to the reaction, as the substrate could serve as the ligand. Initially the reaction was performed at room temperature using 1.5 mol% of catalyst and 1.3 equivalents of B_2pin_2. However, after 21 hours, it did not reach full conversion (~80%). ^{1}H NMR showed possible mixture of mono- and di-borylated 1,10-phenanthroline. In refluxing conditions, with additional B_2pin_2, the reaction was able to run to full conversion. Stirring the crude reaction product suspended in hot heptane and filtering afforded **5.1** in 76% yield.

Scheme 5.1. Synthesis of 3,8-diborylated 1,10-phenanthroline



5.1

The diborylation was symmetric and was assigned based on the ^{1}H NMR (Figure 5.1). There were 4 symmetric structures that could have resulted from the reaction. A 2, 9-functionalized structure would likely show 2 doublets with ortho coupling constants (7-10 Hz) and 1 singlet. Borylation at the 4 and 7 positions would exhibit a similar spectrum to the 2,9-difunctionalized, but the peak corresponding to the proton adjacent to nitrogen would be further downfield. A 5,6-diborylated product would likely exhibit 2 doublets

and a doublet of doublets with both meta- and ortho-coupling constants. The peaks at δ 9.5 and 8.7 ppm are doublets displaying a small meta-coupling of 1.6 Hz. This means that the product is the 3,8-diborylated 1,10-phenanthroline.

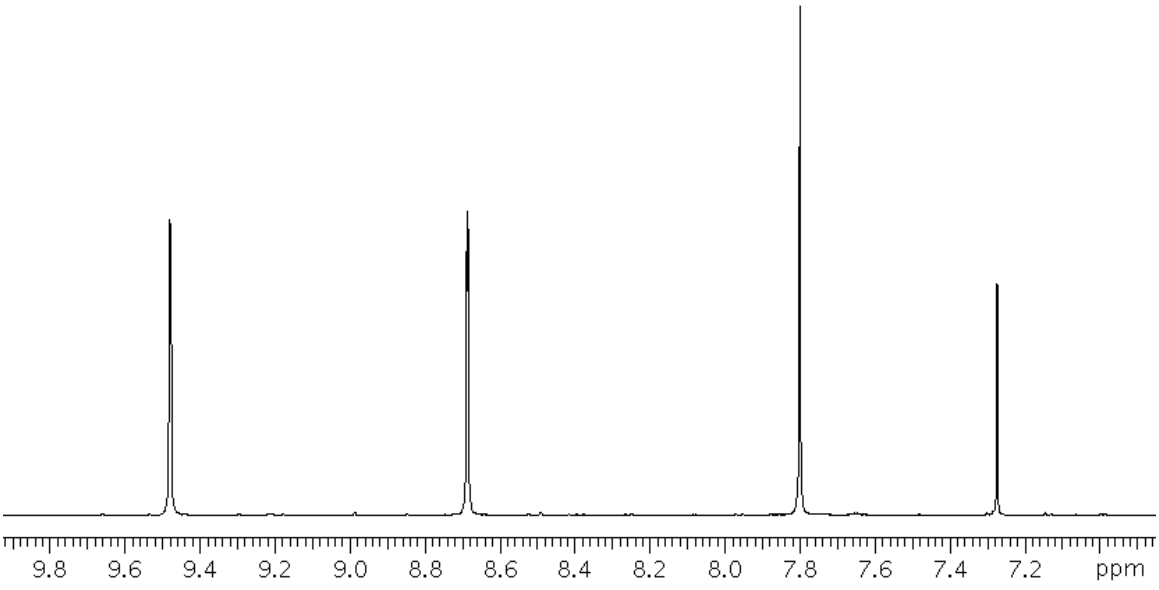


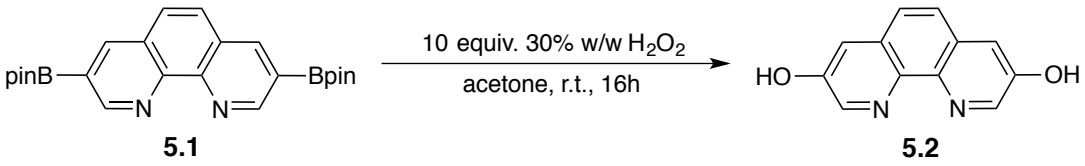
Figure 5.1. 500 MHz ^{1}H NMR of the aromatic region for **5.1** in $CDCl_3$

While the diborylated 1,10-phenanthroline is a valuable building block, we also wanted to make the monoborylated 1,10-phenanthroline. However, it was found that the diborylation occurs too quickly to stop. The diborylation is more facile than the monoborylation, and the monoborylated product is never observed.

5.3 Synthetic Transformations of Borylated 1,10-Phenanthroline

With **5.1** now in hand, we wanted to synthetically transform it. The first attempted reaction was the oxidation of the Bpin groups to produce the diol (Scheme 5.2).

Scheme 5.2. Synthesis of **5.2**

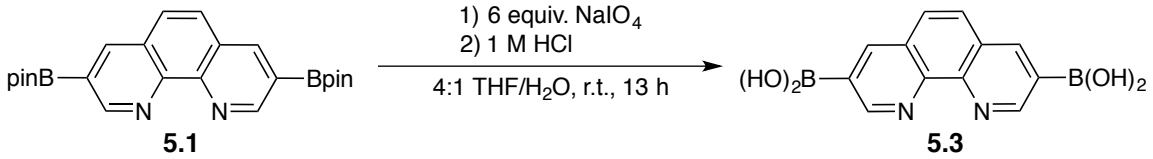


5.1 **5.2**

By stirring **5.1** in acetone in the presence of hydrogen peroxide, the diol, **5.2**, forms quantitatively in 16 h and precipitates from the reaction solution. To the best of our knowledge, this is only the second reported synthesis of **5.2**. The previously reported method required the synthesis of 3,8-dibromophenanthroline, then the substitution of the bromines to methoxy groups, followed by hydrolysis to afford **5.2**. The synthesis of 3,8-dibromophenanthroline also results in some over brominated product, which must be removed prior to the substitution step. CHB of the 1,10-phenanthroline gives only one product, as does the oxidation step.

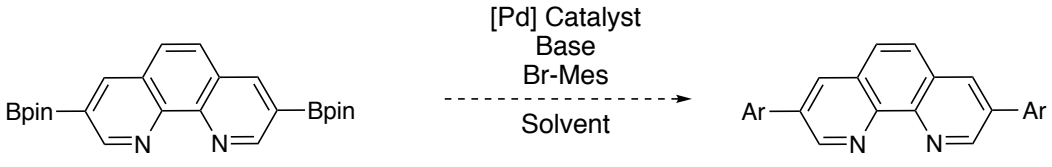
The other derivative that was synthesized was the diboronic acid (**5.3**) from **5.1** with sodium periodate (Scheme 5.3).[116] As with the synthesis of **5.2**, **5.3** precipitated from the reaction as it formed.

Scheme 5.3. Synthesis of **5.3**



The amination of **5.1** using the method reported by Morken was attempted,[117] but no product isolated from the reaction. However, the synthesis of boron-containing **5.1** and **5.3** should allow for further functionalization through coupling reactions, specifically Suzuki coupling. Reaction screens were done to determine favorable coupling conditions using different aryl halides as coupling partners. The results are shown in Table 5.1 and Table 5.2.

Table 5.1. Reaction conditions for attempted Suzuki cross-coupling of **5.1** with 2-bromomesitylene[a]



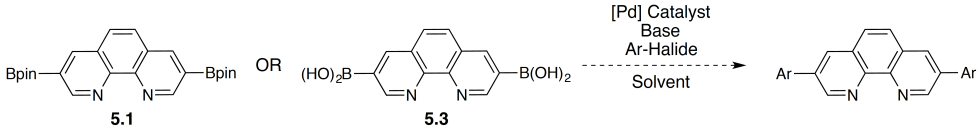
5.1

[(Pd(PCy$_3$)Cl)-2-aminobiphenyl] **1** [Pd(dppf)Cl$_2$] · CH$_2$Cl$_2$ **2** [Pd(PPh$_3$)$_4$] **3**

Entry	Catalyst (mol %)	Base	Temp. (°C)	Time (h)	Solvent	Result[a,b,c]
1	**1** (10)[d]	KOAc	100	24	CPME	No Change
2	**1** (10)	KOAc	100	24	DMA	No Change
3	**1** (10)	KOAc	100	24	DMF	No Change
4	**1** (10)	KOAc	100	24	Toluene	No Change
5	**1** (20)	K_3PO_4	100	24	CPME	Deborylation (36%)
6	**1** (20)	K_3PO_4	100	24	DMA	Deborylation
7	**1** (20)	K_3PO_4	100	24	Toluene	No Change
8	**2** (20)	K_3PO_4	100	24	CPME	Deborylation (30%)
9	**2** (20)	K_3PO_4	100	24	DMA	Deborylation
10	**2** (20)	K_3PO_4	100	24	Toluene	Deborylation (28%)
11	**3** (20)	K_3PO_4	100	18	Dioxane	Deborylation (61%)

[a]Reaction results were determined by ^{1}H NMR, GC/MS, and TLC [b]No Change = no change in borylated starting material observed. [c]When percentage not specified, full deborylation of the phenanthroline was observed.

Table 5.2. Reaction conditions for attempted Suzuki cross-coupling of **5.1** and **5.3** with aryl halides



5.1 5.3

Entry	Starting Material	Catalyst (mol%)	Aryl Halide[a]	Base	Temp. (°C)	Time (h)	Solvent	Result[b,c,d]
1	**5.1**	**1** (20)	I-Tol	K_3PO_4	100	24	CPME	No Change
2	**5.1**	**1** (20)	I-Tol	K_3PO_4	100	24	DMA	Deborylation & Trace Product
3	**5.1**	**1** (20)	I-Tol	K_3PO_4	100	24	Toluene	No Change
4	**5.1**	**2** (20)	I-Tol	K_3PO_4	100	48	CPME	No Change
5	**5.1**	**2** (20)	I-Tol	K_3PO_4	100	48	DMA	Deborylation & Trace Product
6	**5.1**	**2** (20)	I-Tol	K_3PO_4	100	48	Toluene	No Change
7	**5.1**	**3** (20)	I-Tol	K_3PO_4	100	48	Dioxane	Deborylation (39%)
8	**5.1**	**3** (2.5)	I-Tol	Na_2CO_3	100	24	Toluene & MeOH/H_2O (4:1)	Deborylation (64%)
9[e,f]	**5.1**	**3** (10)	I-Tol	$Ba(OH)_2$	100	18	DMF	No Change
10[f]	**5.1**	**3** (15)	Br-Tol	Na_2CO_3	80	18	THF/Tol/H_2O (7:7:3)	3.4% NMR yield of product
11	**5.3**	**3** (2.5)	I-Tol	Na_2CO_3	80	24	Toluene & MeOH/H_2O (4:1)	Deborylation
12	**5.3**	**3** (20)	I-Tol	K_2CO_3	80	12	THF/ H_2O (2:1)	No Product Formation[g]
13	**5.3**	**3** (20)	I-Tol	Cs_2CO_3	80	12	THF/ H_2O (2:1)	No Product Formation[g]
14	**5.3**	**2** (5)	I-Tol	Cs_2CO_3	105	48	CPME/H_2O (10:1)	Deborylation

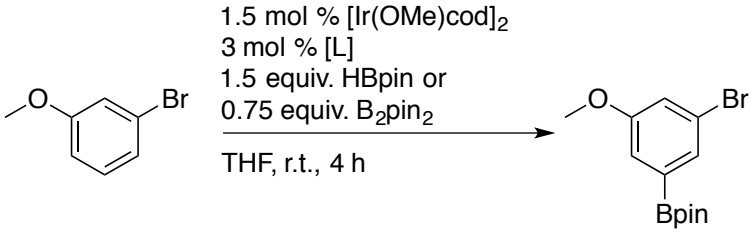
[a]I-Tol = 4-iodotoluene, Br-tol = 4-bromotoluene [b]Reaction results were determined by ^{1}H NMR, GC/MS, and TLC [c]No Change = no change in borylated starting material observed. [d]When percentage not specified, full deborylation of the phenanthroline was observed. [e]1.0 equivalent of CuCl added [f]Reactions were performed by Buddhadeb Chattopadhyay [g]GC/MS and ^{1}H NMR showed unreacted I-tol, but could not see the starting boronic acid or any phenanthroline by NMR.

The coupling was not as facile as expected. The reaction conditions in Table 5.1 either gave no reaction or resulted in deborylation. None of the desired product was observed.

For the reaction conditions in Table 5.2, the halide coupling partner was switched from bromo to iodo arene. However, many of these reaction conditions also showed no reaction or deborylation. Entries 2, 5 and 10 in Table 5.2 did show what we believe is a small amount of the desired product based on ^{1}H NMR. Attempts to optimize the conditions to produce more of the desired product and isolate it have thus far not been successful.

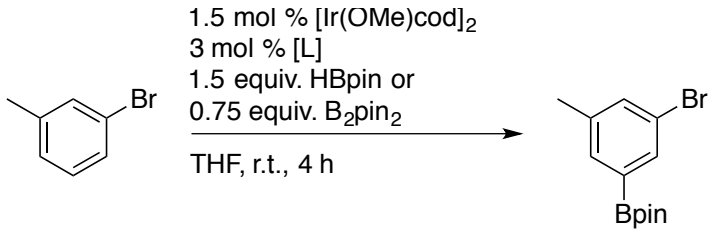
We next sought to see if **5.1** could perform as a ligand in the C-H activation/ borylation reaction. Three substrates were borylated comparing **5.1** and dtbpy as ligands with both B_2pin_2 and HBpin (Tables 5.3-5.5)

Table 5.3. Reaction screen using **5.1** as a ligand for the borylation of 3-bromoanisole



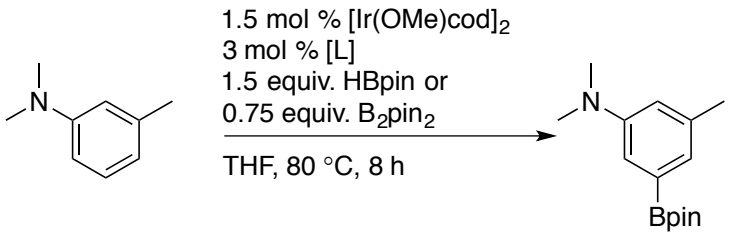
Entry	Borane	Ligand	Conversion (%)
1	B_2pin_2	**5.1**	82
2	B_2pin_2	dtbpy	95
3	HBpin	**5.1**	58
4	HBpin	dtbpy	66

Table 5.4. Reaction screen using **5.1** as a ligand for the borylation of 3-bromotoluene



Entry	Borane	Ligand	Conversion (%)
1	B_2pin_2	**5.1**	1
2	B_2pin_2	dtbpy	98
3	HBpin	**5.1**	3
4	HBpin	dtbpy	16

Table 5.5. Reaction screen using **5.1** as a ligand for the borylation of N,N-dimethyl-*m*-toluidine



Entry	Borane	Ligand	Conversion (%)
1	B_2pin_2	**5.1**	45
2	B_2pin_2	dtbpy	95
3	HBpin	**5.1**	100
4	HBpin	dtbpy	94

5.1 was indeed able to act as a ligand for the borylation reaction for 3-bromoanisole and *N*,*N*-dimethyl-*m*-toluidine. However, the reaction of 3-bromotoluene in the presence of **5.1** did not proceed past 3% conversion with HBpin over multiple trials. The fact that the borylation is able to reach completion at an elevated temperature (Table 5.5) could mean that the catalyst may be more thermally robust. It also leads to the possibility that due to how fast the borylation of 1,10-phenanthroline was observed to occur, that **5.1** is the actual ligand species in borylations where 1,10-phenanthroline is used.

5.4 Conclusions

1,10-Phenanthroline was functionalized utilizing C-H activation/borylation. The diborylated phenanthroline was also able to act as a borylation ligand, which leads to the possibility that 5.1 is the ligand species in borylation reactions using 1,10-phenanthroline. Attempts to utilize Suzuki coupling to further functionalize 1,10-phenanthroline have shown promise, but still require some optimization. These results could lead to more facile routes to an important class of ligands that would benefit more fields outside of C-H activation/borylation.

CHAPTER 6

EXPERIMENTAL

6.1 General Procedures and Methods

All commercially available chemicals were used as received unless otherwise indicated. Bis(pinacolato)diboron (B_2pin_2) and tetrahydroxydiboron ($B_2(OH)_4$) were generously supplied by BoroPharm, Inc., and pinacolborane (HBpin) was purchased from Anderson Chemical Company. Bis(η^4-1,5-cyclooctadiene)-di-μ-methoxy-diiridium(I) $[Ir(OMe)(cod)]_2$ was prepared per literature procedure.[118]

Cyclohexane (CyH), tetrahydrofuran (THF), *n*-hexane, toluene, and pentane were refluxed over sodium/benzophenone ketyl, distilled and degassed. Dichloromethane was obtained from a dry still packed with activated alumina and was degased prior to use. Methanol was obtained anhydrous from Sigma Aldrich and maintained under nitrogen or refluxed over Mg turnings and distilled.

Column chromatography was performed on Silia P-Flash silica gel. Thin layer chromatography was performed on 0.25 mm thick aluminum-backed silica gel plates and visualized with ultraviolet light (λ = 254 nm), iodine, alizarin, potassium permanganate, or phosphomolybdic acid. Sublimations were conducted with a water-cooled cold finger.

^{1}H, ^{2}H, ^{13}C, and ^{19}F NMR spectra were recorded on an Agilent DDR2 500 MHz NMR spectrometer or Varian 500 MHz NMR spectrometer running VNMRJ 3.2A. ^{11}B NMR spectra were recorded on an Agilent DDR2 500 MHz NMR spectrometer or a Varian 300 MHz NMR spectrometer running VNMRJ 3.2A. The boron bearing carbon atom was not observed due to quadrupolar relaxation. All coupling constants are apparent *J* values measured at the indicated field strengths in hertz (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, br = broad singlet, m = multiplet).

Crystal structures were obtained using a Bruker APEX-II CCD x-ray diffractometer. The crystals were kept at T = 173 K during data collection. Using Olex2, the structures were solved with the ShelXS structure solution program, using the Direct Methods solution method. The model was refined with version XL using Least Squares minimization.

GC-FID were measured on an Agilent 7890A GC using an Agilent J&W DB-1 low thermal mass column module 10 m x 0.18 mm x 0.20 μm.

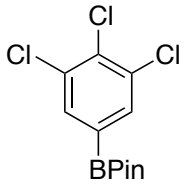
High-resolution mass spectra (HRMS) were obtained at the Michigan State University Mass Spectrometry Service Center using a Waters Xevo G2-XS UPLC/MS/MS (ESI+ or ESI-) or a Waters GCT Premier GC/time-of-flight MS (EI). Melting points were measured in a capillary melting point apparatus and are uncorrected.

6.2 Chapter 2

General Procedure for the Borylation of Arenes. In a glovebox, in an air-free flask, $[Ir(OMe)COD]_2$ (1 mol %), dtbpy (2 mol %), HBpin (1.8 equiv.), and the substrate (11 mmol) were combined neat or in cyclohexane. The flask was sealed, brought out of the dry box, and heated to a temperature depending on the substrate until GC/MS indicated a complete reaction. The reaction was pumped down to obtain the crude product, which was purified by column chromatography (DCM as eluent) to afford the pure product.

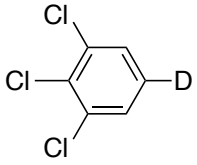
General Procedure for the Deuteration of Aryl Boronic Esters with D_2O. In the glovebox, in an air-free flask, $[Ir(OMe)cod]_2$ (2 mol %) and the aryl boronic ester (2 mmol) were combined in THF (3 mL). The flask was sealed and brought out of the box where it was charged with D_2O (0.5 mL). The flask was resealed and heated at 80°C until the reaction was judged to be complete by GC/MS. When the reaction was complete, it was poured into water and extracted with CH_2Cl_2, Et_2O, or pentane, dried over $MgSO_4$, filtered, and concentrated. Purification by Kugelrohr distillation, sublimation, or column chromatography afforded the pure product.

Synthesis of 5-Bpin-1,2,3-trichlorobenzene (2.1a)[119]



The reaction was carried out neat with 1,2,3-trichlorobenzene (11 mmol, 2.00 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 80 °C for 2 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.07 g, 91%) as a white solid. mp = 95 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (s, 2H), 1.34 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.4, 134.1, 133.9, 84.7, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.1. FT-IR (KBr): 2989, 2931, 1583, 1533, 1450, 1370, 1342, 1147, 1121, 965, 882, 847, 799, 703, 673, 555 cm^{-1}. HRMS (ESI-) m/z Calcd for $C_{12}H_{15}BCl_3O_3$ $[M+ OH]^-$ 323.0182, found 323.0185.

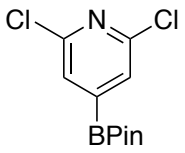
Synthesis of 1,2,3-Trichlorobenzene-5-*d* (2.1b)



The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-1,2,3-trichlorobenzene (2 mmol, 614 mg) and $[Ir(OMe)cod]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH (10:1 v/v). The product was extracted into CH_2Cl_2, dried over $MgSO_4$, filtered, and concentrated. The crude

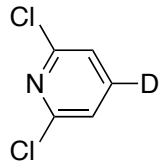
product was purified by passing it through a short silica column ($CHCl_3$) to afford the deuterated compound as a white solid (292 mg, 80%). mp = 53 °C. Approximately 3-4 % of the isolated deuterium compound was 1,2,3-trichlorobenzene-4-*d* as determined by ^{1}H NMR and confirmed by ^{2}H NMR. Due to spectral overlap, deconvolution of the spectra was necessary to extract accurate integration. There was also approximately 3-4 % of 4-Bpin-1,2,3-trichlorobenzene observed in the isolated borylated starting material. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (apparent t, $J_{H\text{-}D}$ = 1.0 Hz, 2H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.18. ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.3 (t, $^3J_{C\text{-}D}$ = 1.76 Hz), 131.5, 128.6, 127.2 (t, $J_{C\text{-}D}$ = 25 Hz). LRMS (EI): *m/z* 181 (M^+). HRMS (EI): *m/z* calculated for $[C_6H_2DCl_3]^+$ 180.9363, found 180.9365. Percent D incorporation (based on quantitative ^{13}C NMR): >98.1%.

Synthesis of 4-Bpin-2,6-dichloropyridine (2.2a)



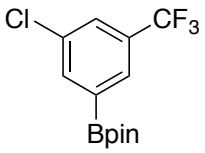
The reaction was carried out in cyclohexane (20 mL) with 2,6-dichloropyridine (11 mmol, 1.63 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 80 °C for 1 h. The crude product was purified as outlined in the general procedure to afford the pure product (2.65 g, 88%) as a white solid. mp = 115 °C. The NMR spectra were in accordance with the literature.[120]

Synthesis of 2,6-dichloropyridine-4-*d* (2.2b)



The deuteration was carried out in THF and D_2O as outlined in the general procedure with 4-Bpin-2,6-dichloropyridine (2 mmol, 496 mg) and $[Ir(OMe)cod]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water, and the product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by sublimation (0.08 mm Hg/ 45 °C) to afford the deuterated compound as a white solid (244 mg, 82%). mp = 86 °C. ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.36 (t. $J_{H\text{-}D}$ = 1.0 Hz, 2H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.61. ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.6 (t, $^3J_{C\text{-}D}$ = 1.71 Hz), 140.4 (t, $J_{C\text{-}D}$ = 25 Hz), 122.8. LRMS (EI): *m/z* 148 (M^+). HRMS (ESI+): *m/z* calculated for $[C_5H_3DCl_2N]^+$ 148.9783, found 148.9792. Percent D incorporation (based on quantitative ^{13}C NMR): 96.3%.

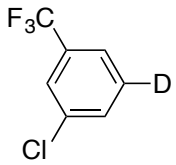
Synthesis of 5-Bpin-3-chlorobenzotrifluoride (2.3a)



The reaction was carried out neat with 3-chlorobenzotrifluoride (11 mmol, 1.98 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 80 °C for 1 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.10

g, 92%) as a clear, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.90 (s, 1H), 7.65 (s, 1H), 1.33 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.9, 136.9, 134.5, 131.7 (q, $^{2}J_{C\text{-}F}$ = 33 Hz), 129.4 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 127.9 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz), 123.4 (q, $^{1}J_{C\text{-}F}$ = 272 Hz), 84.6, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.1. FT-IR (KBr): 2982, 2933, 2873, 1611, 1367, 1296, 1172, 1140, 965, 887, 847, 823, 724, 706, 685 cm^{-1}. HRMS (ESI) m/z Calcd for $C_{13}H_{16}BClF_3O_3$ [M+ $^{-}$OH]$^{-}$ 323.0836, found 323.0835.

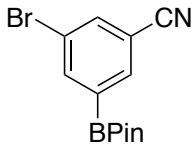
Synthesis of 3-Chlorobenzotrifluoride-5-*d* (2.3b)



The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chlorobenzotrifluoride (2 mmol, 615 mg) and $[Ir(OMe)cod]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by passing it through a short silica column ($CHCl_3$) to afford the deuterated compound as a clear oil (236 mg, 65%). THF (2.2 mg) and Et_2O (not quantifiable) were observed in the ^{13}C NMR and ^{1}H NMR spectra respectively. But, owing to the volatility of the compound, it could not be removed, because of the risk of loss of the product. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (br s, 1H), 7.51 (d, J = 7.2 Hz, 2H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.42. ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.9 (t, $^{3}J_{C\text{-}D}$ = 1.7 Hz), 132.3 (dq, $^{2}J_{C\text{-}F}$ = 33 Hz, $^{3}J_{C\text{-}D}$ = 1.3 Hz), 131.9 (q, $^{4}J_{C\text{-}F}$ = 1.2 Hz), 129.9 (t, $^{3}J_{C\text{-}D}$ = 25 Hz), 125.7 (q, $^{3}J_{C\text{-}F}$ = 4 Hz),

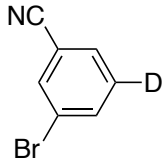
123.33 (q, $^{1}J_{C\text{-}F}$ = 272.5 Hz), 123.32 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz). LRMS (EI): *m/z* 181 (M^{+}). Percent D incorporation (based on quantitative ^{13}C NMR): 98.1%.

Synthesis of 5-Bpin-3-bromobenzonitrile (2.4a)



The reaction was carried out neat with 3-bromobenzonitrile (11 mmol, 2.00 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 50 °C for 2.5 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.04 g, 90%) as a white solid; mp = 84 °C. The NMR spectra were in accordance with the literature.[121]

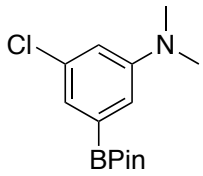
Synthesis of 3-Bromobenzonitrile-5-*d* (2.4b)



The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-bromobenzonitrile (2 mmol, 616 mg) and $[Ir(OMe)cod]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into CH_2Cl_2, dried over $MgSO_4$, and concentrated. The crude product was purified by sublimation (0.15 mm Hg/ 50 °C) to afford the deuterated compound as a white solid

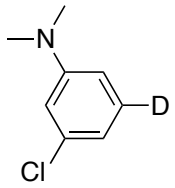
(219 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (t. J = 1.8 Hz, 1H), 7.71 (br, 1H), 7.57 (br, 1H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.38. ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.0, 134.7, 130.6, 130.3 (t, $J_{C\text{-}D}$ = 25 Hz), 122.9 (t, $^{3}J_{C\text{-}D}$ = 1.5 Hz), 114.2 (t, $^{3}J_{C\text{-}D}$ = 1.4 Hz). LRMS (EI): *m/z* 182 (M^+). HRMS (EI): *m/z* calculated for $[C_7H_3DBrN]^+$ 181.9596, found 181.9590. Percent D incorporation (based on quantitative ^{13}C NMR): >98.1%.

Synthesis of 5-Bpin-3-chloro-N,N-dimethylaniline (2.5a)



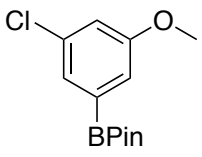
The reaction was carried out neat with 3-chloro-N,N-dimethylaniline (11 mmol, 1.71 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 80 °C for 16 h. The crude product was purified as outlined in the general procedure to afford the pure product (2.44 g, 79%) as a white solid. mp = 129 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (app s, 1H), 7.02 (d, 1H, J = 2.49 Hz) 6.77 (app t, 1H, J = 2.21 Hz), 2.97 (s, 6 H), 1.31 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.1, 134.8, 122.1, 116.5, 114.9, 83.9, 40.5, 24.9. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.52. FT-IR (KBr): 2974, 2926, 2809, 1601, 1562, 1432, 1372, 1325, 1304, 1152, 1110, 997, 964, 876, 847, 813, 703 cm^{-1}. HRMS (ESI) *m/z* Calcd for $C_{14}H_{21}BClNO_2H$ $[M+H]^+$ 282.1435, found 282.1447.

Synthesis of 3-Chloro-N,N-dimethylaniline-5-*d* (2.5b)



The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chloro-N,N-dimethylaniline (2 mmol, 563 mg) and $[Ir(OMe)cod]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 4.5 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by Kugelrohr distillation (20 mm Hg/ 120 °C) to afford the deuterated compound as a clear, colorless oil (231 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.67 – 6.65 (m, 2H), 6.56 (br s, 1H), 2.93 (s, 6 H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.14. ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 134.9 (t, $^3J_{C\text{-}D}$ = 1.8 Hz), 129.7 (t, $J_{C\text{-}D}$ = 25 Hz), 116.0, 112.2, 110.4, 40.3. LRMS (EI): *m/z* $[M\text{-}H]^+$ 155. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_8H_{10}DClN]^+$ 157.0643, found 157.0645. Percent D incorporation (based on quantitative ^{13}C NMR): 95.9%

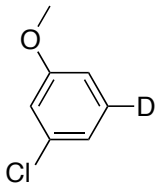
Synthesis of 5-Bpin-3-chloroanisole (2.6a)



The reaction was carried out neat with 3-chloro-N,N-dimethylaniline (11 mmol, 1.56 g), $[Ir(OMe)cod]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBpin (19.8 mmol, 2.5 g). The reaction mixture was stirred at 80 °C for 16 h.

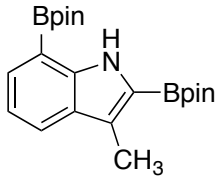
The crude product was purified as outlined in the general procedure to afford the pure product (2.24 g, 76%) as a clear, colorless oil. The NMR spectra were in accordance with the literature.[122]

Synthesis of 3-Chloroanisole-5-*d* (2.6b)



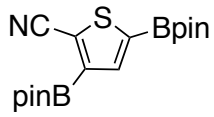
The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chloroanisole (5 mmol, 1.34 g), $[Ir(OMe)cod]_2$ (2 mol %, 0.1 mmol, 66.4 mg), and D_2O (1.25 mL). The reaction was heated at 80 °C for 3 h. When the reaction was complete, it was poured into water. The product was extracted into pentane, dried over $MgSO_4$, and concentrated. The crude product was purified by Kugelrohr distillation (25 mm Hg/ 90 °C) to afford the deuterated compound as a clear, colorless oil (212 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.91 (br, 1H), 6.88 (t, J = 1.9 Hz, 1H), 6.77 (br, 1H), 3.78 (s, 3H). ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.20. ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 134.9 (t, $^3J_{C\text{-}D}$ = 1.8 Hz), 129.9 (t, $J_{C\text{-}D}$ = 25 Hz), 120.7, 114.3, 112.4, 55.4. LRMS (EI): *m/z* 143 (M^+). HRMS (EI): *m/z* calculated for $[C_7H_6DClO]^+$ 143.0248, found 143.0245. Percent D incorporation (based on quantitative ^{13}C NMR): 93.0%.

Synthesis of 2,7-bis(Bpin)-3-methylindole (2.7)



In the glovebox, a 15 mL pressure tube was charged with [Ir(OMe)cod]2 (2 mol %, 0.06 mmol, 40 mg) in THF. HBpin (6 mol %, 0.18 mmol, 52 μL) was added and the solution was stirred a few minutes. Next, dtbpy (4 mol %, 0.12 mmol, 32 mg), B_2pin_2 (4.8 mmol, 1.219 g), and 3-methylindole (3 mmol, 393.5 mg) were added to the pressure tube with THF (4 mL). The pressure tube was sealed and the reaction was heated at 60 °C for 22 h. The reaction was cooled, and the solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography (5% ethyl acetate/ 95% hexanes) to afford the pure product as a white solid (701 mg, 61%). mp = 128 °C ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.08 (br, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 2.55 (s, 3H), 1.41 (s, 12 H), 1.38 (s, 12 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.9, 131.2, 127.9, 124.2, 123.3, 118.4, 83.7, 83.5, 25.0, 24.9, 10.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.2. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{21}H_{32}B_2NO_4]^+$ 384.2517, found 384.2512.

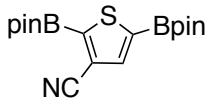
Synthesis of 3,5-diborylated-2-cyanothiophene (2.9)



In the glovebox, a 50 mL Schlenk flask was charged with $[Ir(OMe)cod]_2$ (1 mol %, 0.05 mmol, 33.2 mg) and HBpin (20 mmol, 2.55 g) in THF, and the mixture was

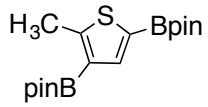
stirred for a few minutes. Then, dtbpy (2 mol %, 0.01 mmol, 26.8 mg) was added, followed by 2-cyanothiophene (5 mmol, 456.6 μL). The reaction was sealed and brought out of the glovebox where it was stirred at room temperature overnight. After that time, the reaction had not reached completion, so the temperature was raised to 60 °C for a few hours. The total stirring time was 24 h. The reaction was then cooled, and all volatiles where removed. The crude product was purified by column chromatography (10% EtOAc/ 90% hexanes) to afford the pure product as a white solid (1.44 g, 80 %). The NMR spectra were in accordance with the literature.[123]

Synthesis of 2,5-diborylated-3-cyanothiophene (2.10)



In the glovebox, a 20 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.075 mmol, 49.8 mg) and HBpin (12.5 mmol, 1.6 g) in pentane (4 mL), and the mixture was stirred for a few minutes. Then, dtbpy (3 mol%, 0.15 mmol, 40.2 mg) was added, followed by 3-cyanothiophene (5 mmol, 545 mg). The reaction was sealed and allowed to stir at room temperature for 6 hours. The volatiles were then removed under reduced pressure, and the crude product was purified by passing it through a plug of silica with dichloromethane to afford a white solid (755 mg, 42%). The NMR spectra were in accordance with the literature.[123]

Synthesis of 3,5-diborylated-2-methylthiophene (2.11)



In the glovebox, a 50 mL Schlenk flash was charged with $[Ir(OMe)cod]_2$ (1.5 mol %, 0.075 mmol, 49.8 mg) and B_2pin_2 (12.5 mmol, 3.2 g) in THF (15 mL) and stirred for a few minutes. Then, dtbpy (3 mol%, 0.15 mmol, 40.2 mg) was added, followed by 2-methylthiophene (5 mmol, 474 μL). The reaction was sealed and brought out of the glovebox. It was stirred at 60 °C overnight. The volatiles were then removed under reduced pressure, and the crude product was purified by passing it through a plug of silica with dichloromethane to afford the product as a white solid (1.47 g, 84 %). mp = 136 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (s, 1H), 2.72 (s, 3H), 1.32 (s, 12H), 1.31 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7, 144.9, 83.8, 83.2, 24.9, 24.8, 15.9. ^{11}B NMR (160 MHz, $CDCl_3$): δ 28.9. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{17}H_{29}B_2O_4S]^+$ 351.1973, found 351.1969.

Determination of Deuterium Incorporation by Quantitative ^{13}C NMR:

The data was collected on a Varian 500 MHz superconducting NMR-Spectrometer operating at 499.955 MHz with a Dell Precision 870 and running CentOS 5.5 with VnmrJ 3.2A. Each sample was prepared as 0.671 M in $CDCl_3$ (5.17e-4 mol in 770 μL). In order to ensure that the ^{13}C experiments were quantitative, the longest T_1 was estimated using an inversion recovery experiment. The experiment was run using 1,2,3-trichlorobenzene-5-*d* with the delay set to give a null signal for the carbon with the

longest T_1. 1.41 times that delay value gave the longest T_1. This gave an approximate T_1 of 41 s.

The percentage of deuterium incorporation was determined by quantitative ^{13}C NMR using an inverse gated experiment, in which decoupling is only on during acquisition. All experiments were run with 292 scans using and a three-minute recycle delay (approximately 5 x T_1). Exponential multiplication with a line broadening factor of 0.5 Hz was used for all experiments. The number of scans used was such that a signal to noise ratio around the peak of interest was 100:1, and the digital resolution was set to give at least 5 points above the half height of the peak.

The percentage of deuterium incorporation was determined from the ^{13}C spectra by integration of the peaks corresponding to the C-D and the C-H impurity. Calculating the percentage from the integrals of the peaks of interest gave the percentage of deuterium incorporation.

Protiodeborylation of 5-Bpin-3-chloro-N,N-dimethylaniline using CsF.[124]

Using the reaction conditions reported by Aggarwal and co-workers 5-Bpin-3-chloro-N,N-dimethylaniline (1 mmol, 281 mg), CsF (1.5 mmol, 228 mg), and water (1.1 mmol, 20 mL) were combined in dry 1,4-dioxane (10 mL) in an air-free flask under N_2. The reaction was sealed and stirred at 45°C for 48 h. The reaction was monitored by GC/MS. No reaction was observed, and the starting material was left unchanged.

Protiodeborylation of 5-Bpin-3-chloro-N,N-dimethylaniline using TBAF.[124]

Using the reaction conditions reported by Aggarwal and co-workers, 2 reactions were set up using 5-Bpin-3-chloro-N,N-dimethylaniline (0.25 mmol, 70 mg), TBAF•$3H_2O$ (0.375 mmol, 118 mg) and either pentane (2.5 mL) or toluene (2.5 mL) as the solvent in an air-free flask under N_2. The reactions stirred at 45°C for 24 h. GC/FID showed trace conversion for the reaction in toluene, but no reaction for the one in pentane. The temperature was then increased to 60°C, and the reaction mixture was stirred an additional 24 h. GC/FID and GC/MS showed no change.

Base-promoted Protiodeborylation of 4-Bpin-2,6-dichloropyridine.[125]

Using the reaction conditions reported by Perrin and co-workers, 4-Bpin-2,6-dichloropyridine (0.1 mmol, 27.4 mg) was dissolved in THF (5 mL). A basic solution of KOH (200 mM, 5 mL) was added, and the reaction mixture was stirred at room temperature for 24 h. The reaction was monitored by GC/FID, but no reaction was observed. The starting material was left unchanged.

Protiodeborylation of 2,7-bis(Bpin)-3-methylindole using trifluoroacetic acid (no catalyst).[126]

Under an N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.297 mmol, 113.8 mg). Dry dichloromethane (2 mL) was added via syringe, and the solution was cooled in an ice bath to 0°C. Trifluoroacetic acid (3 mL)

was added dropwise to the cooled solution. Upon completion of the trifluoroacetic acid addition, the reaction mixture was stirred at 0°C for a further ten minutes. Then, the ice bath was removed, and the reaction was allowed to stir at room temperature. After three hours, the reaction was diluted with dichloromethane (50 mL) and washed with saturated sodium bicarbonate solution (2 x 25 mL). The organic layer was dried over $MgSO_4$, filtered, and the solution was concentrated. ^1H NMR was acquired of the resulting orange/brown oil. At least four products were observed in the spectrum. They are proposed to be 3-methylindole, 7-Bpin-3-methylindole, 2-Bpin-3-methylindole, and 2,7-bis(Bpin)-3-methylindole. However, there are an additional four species with apparent NH peaks that could not be identified.

Protiodeborylation of 4-Bpin-2,6-dichloropyridine using trifluoroacetic acid (no catalyst).[126]

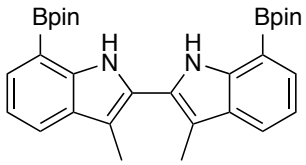
Under an N_2 atmosphere, a 10 mL Schlenk flask was charged with 4-Bpin-2,6-dichloropyridine (0.297 mmol, 82.5 mg). It was dissolved in dry dichloromethane and cooled in an ice bath to 0°C. Trifluoroacetic acid was added via syringe slowly over a few minutes. Once all of the TFA had been added, the reaction was allowed to stir an additional 10 minutes at 0°C. Then, the ice bath was removed and the reaction was allowed to come to room temperature. It was monitored by ^1H NMR for 18 h, but no reaction was observed. The starting material was left unchanged.

One-Pot Borylation/Deborylation of 3-methylindole using acetic acid (no palladium).[126]

Under an N_2 atmosphere in a glovebox, an air-free flask was charged with 3-methylindole (1.53 mmol, 201 mg), $[Ir(OMe)cod]_2$ (2.5 mol %, 38.3 μmol, 25.4 mg), and 4,4'-di-*tert*-butyl-bipyridine (5 mol %, 76.6 μmol, 25.4 mg). They were dissolved in THF (11 mL), and the HBpin (7.66 mmol, 0.970 g) was added in a single portion. The flask was sealed and brought out of the glovebox. The reaction mixture was heated at 60 °C for 9 h. Then, the reaction mixture was cooled to room temperature, and the volatiles were removed under reduced pressure. The red/brown residue was then dissolved in acetic acid (4.0 mL), and the reaction mixture was stirred at 30°C. After 11 h, the reaction was determined to be complete, so it was filtered through celite using ethyl acetate (150 mL), and the filtrate was washed with saturated sodium bicarbonate solution (200 mL). The organic layer was then dried over $MgSO_4$ and concentrated. The resulting residue was purified by column chromatography (10 % EtOAc/ 90 % hexanes) to afford the 7-Bpin-3-methylindole as a white solid (0.800 mmol, 205.8 mg, 52.3 %)

Protodeboylation of 2,7-bis(Bpin)-3-methylindole using Pd/AcOH.[126]

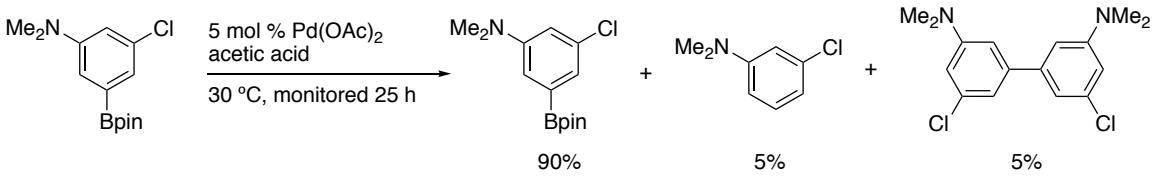
Under an N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (1 mmol, 383 mg) and $Pd(OAc)_2$ (5 mol %, 0.05 mmol, 11.2 mg). The flask was sealed, and acetic acid (2.6 mL) was added via syringe. The reaction mixture was stirred at 30°C. After 8 h the reaction was filtered through celite using ethyl acetate (100 mL), and then it was washed with saturated sodium bicarbonate (150 mL). The organic layer was dried over $MgSO_4$ and concentrated to afford a dark brown oil. ^1H NMR showed that there was a second product resulting from the reaction. However, not all of the peaks from this product could be resolved from the deborylation product. Attempts to separate the 7-Bpin-3-methylindole product from the unknown product by column chromatography were unsuccessful. When the amount of palladium was increased to 20 mol %, the amount of the unknown that was observed doubled. An LC/MS (ES+) acquired of this mixture of products showed two masses. The first mass was m/z 257.976 $[M+H]^+$ for the 7-Bpin-3-methylindole. The second mass was m/z 513.064 $[M+H]^+$ for the unknown, which we propose is a coupling product between two of the 2,7-bis(Bpin)-3-methylindole catalyzed by the palladium in the reaction (shown below). The ratio of products in the ^1H NMR for the 7-borylated, 2,7-diborylated, to homocoupled product was 95:2:3.



Protodeboylation of 2,7-bis(Bpin)-3-methylindole using Ir/AcOH.[126]

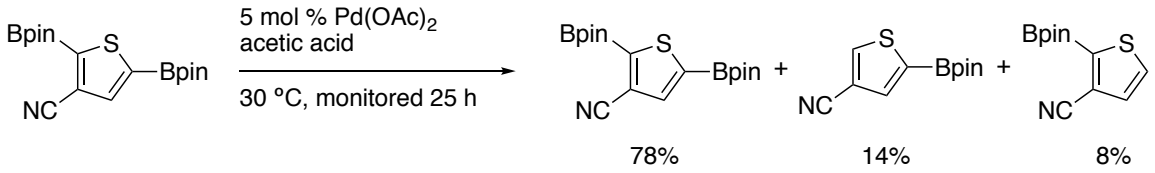
Under an N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.297 mmol, 113.8 mg) and $[Ir(OMe)cod]_2$ (2.5 mol %, 7.5 μmol, 5 mg). The flask was sealed, and acetic acid (776 μL) was added via syringe. The reaction mixture was stirred at 30°C for 8 h. ^{1}H NMR of the reaction mixture showed that the deborylation reaction was approximately 75% complete.

Protiodeborylation of 5-Bpin-3-chloro-N,N-dimethylaniline using Pd/AcOH.[126]



Under an N_2 atmosphere, a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-N,N-dimethylaniline (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe and the reaction was allowed to stir at 30°C for 25 h. The reaction was monitored by ^{1}H NMR and GC-FID by removing an aliquot from the reaction, diluting it with ethyl acetate, and washing with a saturated sodium bicarbonate solution. The organic layer was separated and concentrated. ^{1}H NMR and GC-FID were acquired of the residue. The spectrum showed 5% deborylation of the starting material and 5% of a coupling product shown in the scheme above.

Protiodeborylation of 2,5-bis(Bpin)-3-cyanothiophene using Pd/AcOH.[126]



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 2,5-bis(Bpin)-3-cyanothiophene (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe and the reaction was allowed to stir at 30°C for 25 h. The reaction was monitored by 1H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to aquire the spectrum directly. 22 % deborylation was observed over 25 h. However, the reaction was not exclusively selective. ^{1}H NMR integrals showed approximately 14 % for the 5-borylated product and 8 % for the 2-borylated product.

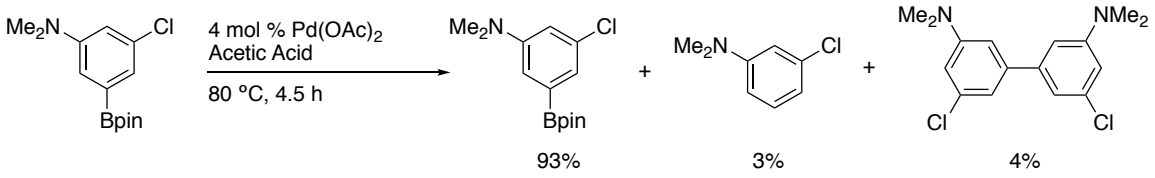
Protiodeborylation of 3,5-bis(Bpin)-2-cyanothiophene using Pd/AcOH.[126]

Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-cyanothiophene (0.5 mmol, 180.5 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe and the reaction was allowed to stir at 30°C for 23 h. The reaction was monitored by ^{1}H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to aquire the spectrum directly. Deborylation (11%) was observed over 23 h.

Protiodeborylation of 3,5-bis(Bpin)-2-methylthiophene using Pd/AcOH.[126]

Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-methylthiophene (0.5 mmol, 175 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe and the reaction was allowed to stir at 30°C for 23 h. The reaction was monitored by ^1H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to aquire the spectrum directly. Deborylation (59%) was observed over 23 h.

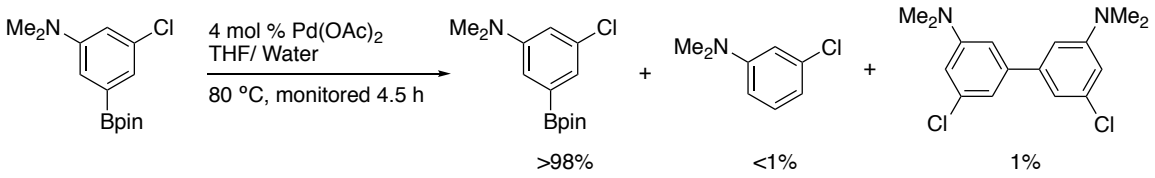
Protiodeborylation of 5-Bpin-3-chloro-N,N-dimethylaniline using Pd/AcOH. (elevated temp-erature)[126]



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-N,N-dimethylaniline (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (4 mol %, 0.02 mmol, 4.5 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 80°C for 4.5 hours. The reaction was cooled and filtered through celite with ethyl acetate (50 mL). Then, it was washed with saturated $NaHCO_3$ (50 mL), and dried with $MgSO_4$. The solvent was removed under reduced pressure, and ^1H NMR was acquired of

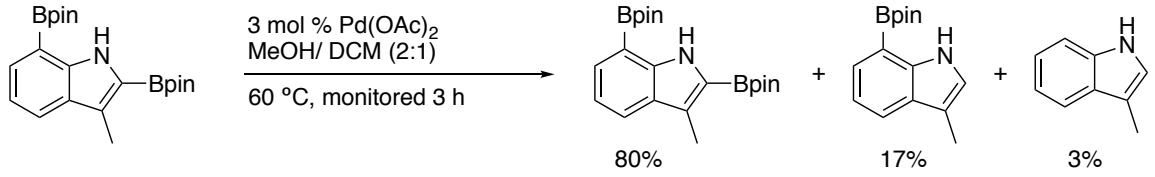
the crude reaction material. Deborylation (3%) of the starting material was observed along with 4% of a coupling product shown in the scheme above.

Protiodeborylation of 5-Bpin-3-chloro-N,N-dimethylaniline using Palladium and THF/ Water.



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-N,N-dimethylaniline (0.25 mmol, 70 mg) and $Pd(OAc)_2$ (4 mol %, 0.01 mmol, 2.2 mg) in THF (750 μL). Degased DI water (125 μL) was added via syringe, and the reaction was allowed to stir at 80°C for 4.5 hours. GC-FID was acquired of the reaction and it showed <1% deborylation of the starting material, and 1% for the coupling product.

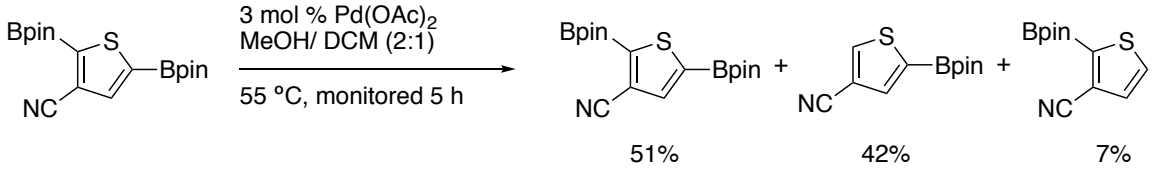
Protiodeborylation of 2,7-bis(Bpin)-3-methylindole using Palladium and DCM/MeOH.



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.25 mmol, 95.7 mg) and $Pd(OAc)_2$ (3 mol %, 0.0075 mmol, 1.7 mg) in dichloromethane (0.5 mL). Dry, degased methanol (1.0 mL) was added and the reaction mixture was stirred at 60°C. It was monitored for 3 h. After 50 minutes 17% deborylation

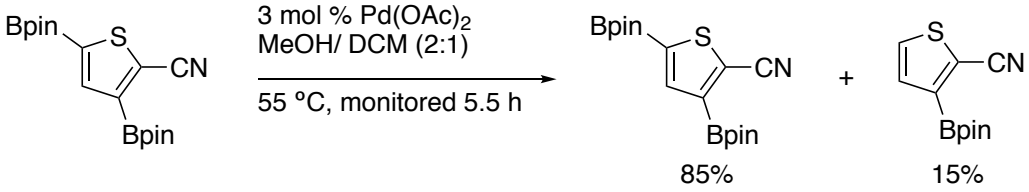
to the 7-Bpin-3-methylindole was observed along with 3% to the 3-methylindole, but no further reaction happened.

Protiodeborylation of 2,5-bis(Bpin)-3-cyanothiophene using Palladium and DCM/MeOH.



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 2,5-bis(Bpin)-3-cyanothiophene (0.25 mmol, 90.5 mg) and $Pd(OAc)_2$ (3 mol %, 0.0075 mmol, 1.7 mg) in DCM (0.5 mL). Dry, degased methanol (1.0 mL) was added via syringe and the reaction was allowed to stir at 55°C for 5 h. At that time, 42% deborylation to the 5-Bpin-3-cyanothionphene was observed along with 7% to the 2-Bpin-3-cyanothiophene.

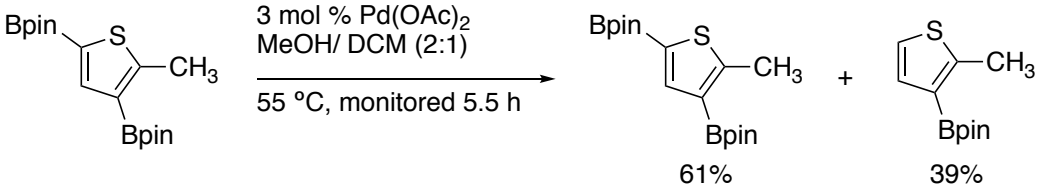
Protiodeborylation of 3,5-bis(Bpin)-2-cyanothiophene using Palladium and DCM/MeOH.



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-cyanothiophene (0.5 mmol, 180.5 mg) and $Pd(OAc)_2$ (3 mol %, 0.015 mmol, 3.4 mg) in DCM (0.8 mL). Dry, degased methanol (1.7 mL) was added via syringe and the

reaction was allowed to stir at 55°C for 5.5 h. At that time, 15% deborylation to the 3-Bpin-2-cyanothionphene was observed.

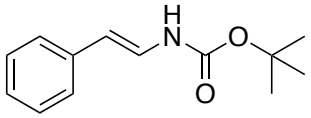
Protiodeborylation of 3,5-bis(Bpin)-2-methylthiophene using Palladium and DCM/MeOH.



Under an N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-methylthiophene (0.5 mmol, 175 mg) and $Pd(OAc)_2$ (3 mol %, 0.015 mmol, 3.4 mg) in DCM (0.8 mL). Dry, degased methanol (1.7 mL) was added via syringe and the reaction was allowed to stir at 55 °C for 5 h. At that time, 39% deborylation to the 3-Bpin-3-methylthionphene was observed.

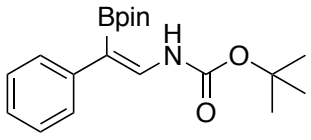
6.3 Chapter 3

Synthesis of *tert*-butyl (*E*)-styrylcarbamate (3.7a)



Sodium azide (48.0 mmol, 3.12 g) was dissolved in water (40 mL) and the solution was cooled to 0 °C. To this mixture a solution of cinnamoyl chloride (40.0 mmol, 6.68 g) and tetrabutylammonium iodide (2.0 mmol, 740 mg) in toluene (40 mL) was added dropwise. This biphasic reaction was allowed to stir at 0 °C 5 hours, then room temperature for 20 minutes. The toluene layer was separated and washed with saturated Na_2CO_3 (3 x 30 mL) resulting in a colorless solution. Then, it was washed with brine and dried over $MgSO_4$. The toluene solution was slowly added to a preheated mixture of *tert*-butanol (0.418 mol, 40 mL), pyridine (2.5 mmol, 200 μL), and hydroquinone (2.0 mmol, 220 mg) at 100 °C. The reaction mixture was refluxed for 1 hour. The toluene and excess *tert*-butanol were removed under reduced pressure. The crude product was washed with hexanes and isolated by filtration to afford a white solid (21.4 mmol, 53.4%). The NMR spectra were in accordance with the literature.[127]

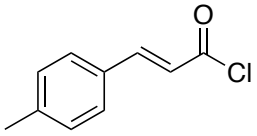
Borlyation of *tert*-butyl (*E*)-styrylcarbamate (gram scale) (3.7b)



In the glovebox, a pressure tube (50 mL) was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.274 mmol, 182 mg) and B_2pin_2 (5.47 mmol, 1.39 g) in cyclohexane (20 mL). The

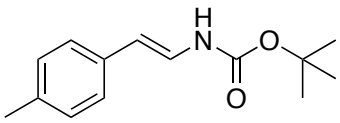
dtbpy (6 mol %, 0.542 mmol, 146 mg) and *tert*-butyl (*E*)-styrylcarbamate (9.12 mmol, 2.0 g) were added and the pressure tube was sealed and brought out of the glovebox. The reaction was heated at 100 °C for 48 h. The volatiles were removed and the crude product was purified by column chromatography (8% EtOAc/ 90% hexanes) to afford the product as a white solid (732 mg, 23 %). The NMR spectra were in accordance with the literature.[128]

Synthesis of (*E*)-3-(*p*-tolyl)acryloyl chloride



(*E*)-3-(*p*-Tolyl)acrylic acid (6.2 mmol, 1.0 g) was dissolved in dry dichloromethane (30 mL) under N_2, and a few drops of N,N-dimethylformamide were added. The solution was cooled to 0 °C, and oxalyl chloride (12.4 mmol, 1.06 mL) was added dropwise via syringe. Once all of the oxalyl chloride was added, the reaction was allowed to stir a further ten minutes at 0 °C. Then, it was stirred at room temperature for 2 hours. The volatiles were removed under reduced pressure, and the crude product was used without further purification.

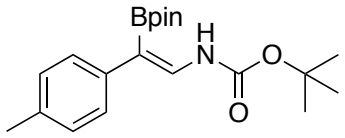
Synthesis of *tert*-butyl (*E*)-(4-methylstyryl)carbamate (3.8a)



A 50 mL round bottom flask was charged with sodium azide (18.6 mmol, 1.2 g) in acetone (12.5 mmol) and the solution was cooled to 0 °C. (*E*)-3-(*p*-Tolyl)acryloyl

chloride (6.2 mmol, 1.11 g) was added, and the reaction mixture was stirred for 5 minutes at 0 °C; then room temperature for 2 hours. The reaction mixture was filtered and the volatiles were removed under reduced pressure. The crude azide was dissolved in toluene (12.5 mL) and slowly added to a solution of tert-butanol (98.2 mmol, 9.4 mL), hydroquinone (0.313 mmol, 34.4 mg), and pyridine (0.313 mmol, 30 μL) preheated at 100 °C. After 1 hour the reaction mixture was cooled and the volatiles were removed under reduced pressure. The crude product was washed with hexanes to afford the pure product as a white solid (524 mg, 36%). mp = 99 °C. ^{1}H NMR (500 MHz, CD_3CN): δ 7.53 (br, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 12.6 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.01 (d, *J* = 14.7 Hz, 1H), 2.31 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.7, 135.8, 133.7, 129.3, 125.1, 123.5, 109.8, 80.8, 28.3, 21.1. HRMS (ESI+): *m/z* calculated for $[M-H]^-$ $[C_{14}H_{18}NO_2]^-$ 232.1338, found 232.1331.

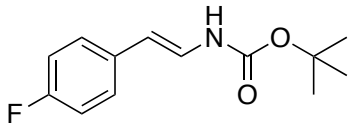
Borylation of *tert*-butyl (*E*)-(4-methylstyryl)carbamate (3.8b)



In the glovebox, a 5 mL conical vial was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.015 mmol, 10 mg), dtbpy (6 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.3 mmol, 76.2 mg), and *tert*-butyl (*E*)-(4-chlorostyryl)carbamate (0.5 mmol, 117 mg) as solids. Cyclohexane (3 mL) was added to the vial and the reaction was sealed. The vial was brought out of the glovebox and the reaction mixture was heated at 100 °C for 48 h. The volatiles were removed under reduced pressure and the crude reaction was purified by column chromatography (2% ethyl acetate/ 98% hexanes) to afford the product as a white solid

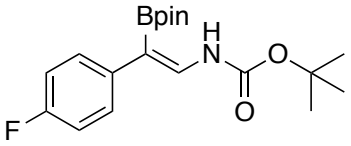
(59.4 mg, 33 %); mp = 137 °C. ^{1}H NMR (500 MHz, CD_3CN): δ 8.50 (br, 1H), 7.40 (d, *J* = 11.4 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 2.34 (s, 3H), 1.54 (s, 12H), 1.36 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 140.4, 138.3, 135.2, 128.7, 127.7, 83.8, 80.8, 27.4, 24.1, 20.0. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.1. HRMS (ESI-): *m/z* calculated for $[M-H]^-$ $[C_{20}H_{29}BNO_4]^-$ 358.2193, found 358.2196.

Synthesis of *tert*-butyl (*E*)-(4-fluorostyryl)carbamate (3.11a)



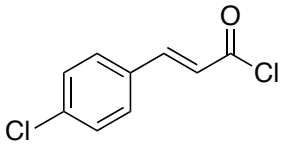
(*E*)-3-(4-Fluorophenyl)acryloyl chloride (2.7 mmol, 500 mg) was added to a solution of sodium azide (8 mmol, 525 mg) in acetone (7.5 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 5 minutes then room temperature for 2 hours. The reaction mixture was filtered and concentrated under reduced pressure. The crude azide was dissolved in toluene (10 mL) and slowly added to a solution of tert-butanol (7.5 mL), hydroquinone (0.25 mmol, 28 mg), and pyridine (0.25 mmol, 24 μL) preheated at 100 °C. The reaction mixture was stirred for 1 hour and then it was filtered. The reaction mixture was concentrated and the crude product was washed with hexanes to afford the pure product as a white solid (435 mg, 68%). mp = 127 °C. ^{1}H NMR (500 MHz, CD_3CN): δ 7.57 (br, 1H), 7.34 (dd, *J* = 8.8, 5.7 Hz, 2H), 7.14 (t, *J* = 12.6 Hz, 1H), 7.04 (t, *J* = 8.8 Hz, 2H), 6.03 (d, J = 14.9 Hz , 1H) 1.49 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4 (d, $^{1}J_{C\text{-}F}$ = 245), 152.7, 132.7 (d, $^{4}J_{C\text{-}F}$ = 3.6), 126.5 (d, $^{3}J_{C\text{-}F}$ = 8.0), 124.1, 115.5 (d, $^{2}J_{C\text{-}F}$ = 21.8), 108.7, 81.0, 28.3. ^{19}F NMR (470 MHz, CD_3CN): δ -118.7 – -118.8 (m). HRMS (ESI-): *m/z* calculated for $[M-H]^-$ $[C_{13}H_{15}FNO_2]^-$ 236.1087, found 236.1079.

Borylation of *tert*-butyl (*E*)-(4-fluorostyryl)carbamate (3.11b)



In the glovebox, a 5 mL conical vial was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.015 mmol, 10 mg), dtbpy (6 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.3 mmol, 76.2 mg), and *tert*-butyl *tert*-butyl (*E*)-(4-fluorostyryl)carbamate (0.5 mmol, 119 mg) as solid. Cyclohexane (3 mL) was added to the vial and the reaction was sealed. The vial was brought out of the glovebox and the reaction mixture was heated at 100 °C for 48 h. The volatiles were removed under reduced pressure and the crude reaction mixture was purified by column chromatography (6% ethyl acetate/ 94% hexanes) to afford the product as a white solid (36.1 mg, 20%). mp = 111 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (br, 1H), 7.49 (d, J = 11.5 Hz 1H), 7.33 (t, J = 7.6 Hz, 2H), 6.98 (t, J = 8.3 Hz, 2H), 1.55 (s, 9H), 1.36 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4 (d, $^1J_{C\text{-}F}$ = 243 Hz), 152.8, 141.5, 137.1, 129.0 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 114.9 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 83.7, 80.9, 28.3, 24.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ -118.4 (s). ^{11}B NMR (96 MHz, $CDCl_3$): δ 30.2. HRMS (ESI-): *m/z* calculated for $[M\text{-}H]^-$ $[C_{19}H_{26}BFNO_4]^-$ 362.1939, found 362.1935

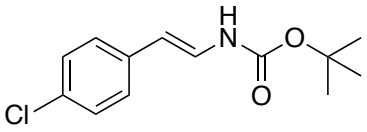
Synthesis of (*E*)-3-(4-chlorophenyl)acryloyl chloride



(*E*)-3-(4-Chlorophenyl)acrylic acid (15.0 mmol, 2.74 g) was dissolved in dry dichloromethane (35 mL) under N_2, and a few drops of N,N-dimethylformamide were added. The solution was cooled to 0 °C, and oxalyl chloride was added dropwise via

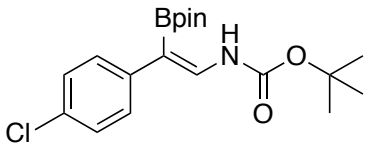
syringe (19.5 mmol, 1.67 mL). Once all of the oxalyl chloride was added, the reaction was allowed to stir a further ten minutes at 0 °C. Then, it was stirred at room temperature overnight. The volatiles were removed under reduced pressure, and the product was used without further purification.

Preparation of *tert*-butyl (*E*)-(4-chlorostyryl)carbamate (3.12a)



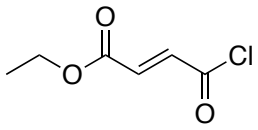
Sodium azide (18.0 mmol, 1.17 g) was dissolved in water (15 mL) and the solution was cooled to 0 °C. To this a solution of (*E*)-3-(4-chlorophenyl)acryloyl chloride (15 mmol, 3.0 g) and tetrabutylammonium iodide (0.75 mmol, 277 mg) in toluene (15 mL) was added dropwise. This biphasic reaction was allowed to stir at 0 °C 5 hours, then room temperature for 20 minutes. The toluene layer was separated and washed with saturated Na_2CO_3 (6 x 30 mL) resulting in a colorless solution. Then, it was washed with brine and dried over $MgSO_4$. The toluene solution was slowly added to a preheated mixture of *tert*-butanol (0.157 mol, 15 mL), pyridine (0.93 mmol, 208 μL), and hydroquinone (0.75 mmol, 82.6 mg) at 100 °C. The reaction mixture was refluxed for 1 hour. The toluene and excess *tert*-butanol were removed under reduced pressure, and the crude product was washed with hexanes and dried to afford a white solid (8.39 mmol, 53.4%). mp = 136 °C. ^{1}H NMR (500 MHz, CD_3CN): δ 7.61 (br, 1H), 7.33 – 7.27 (m, 4H), 7.21 (dd, *J* = 14.5, 11.2 Hz, 1H), 6.01 (d, *J* = 14.8 Hz, 1H) 1.49 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.7, 135.2, 131.4, 128.7, 126.3, 124.9, 108.5, 81.1, 28.3. HRMS (ESI+): *m/z* calculated for $[M+Na]^+$ $[C_{13}H_{16}ClNO_2Na]^+$ 276.0767, found 276.0775.

Borylation of *tert*-butyl (*E*)-(4-chlorostyryl)carbamate (3.12b)



In the glovebox, a 5 mL conical vial was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.015 mmol, 10 mg), dtbpy (6 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.3 mmol, 76.2 mg), and *tert*-butyl (*E*)-(4-chlorostyryl)carbamate (0.5 mmol, 127 mg) as solid. Cyclohexane or *n*-hexane (3 mL) was added to the vial and the reaction was sealed. The vial was brought out of the glovebox and the reaction mixture was heated at 100 °C for 48 h. The volatiles were removed under reduced pressure and the crude reaction was purified by column chromatography (dichloromethane) to afford the product as a white solid (CyH: 99.6 mg, 52 %; *n*-Hex: 108 mg, 57%). mp = 100 °C. ^{1}H NMR (500 MHz, CD_3CN): δ 8.54 (br, 1H), 7.46 (d, J = 12.2 Hz, 1H), 7.38 – 7.30 (m, 4H), 1.54 (s, 12H), 1.37 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.7, 141.8, 139.6, 131.3, 128.9, 128.2, 83.8, 81.0, 28.2, 24.9. ^{11}B NMR (160 MHz, $CDCl_3$): δ 29.7. HRMS (ESI-): *m/z* calculated for $[M-H]^-$ $[C_{19}H_{26}BClNO_4]^-$ 378.1643, found 378.1618.

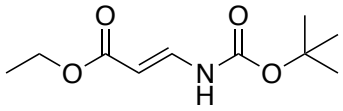
Preparation of ethyl (*E*)-4-chloro-4-oxobut-2-enoate



(*E*)-4-ethoxy-4-oxobut-2-enoic acid (20 mmol, 2.88 g) was dissolved in dry dichloromethane (20 mL) under N_2, and a few drops of N,N-dimethylformamide were added. The solution was cooled to 0 °C, and oxalyl chloride (50.0 mmol, 4.3 mL) was added dropwise via syringe. Once all of the oxalyl chloride was added, the reaction

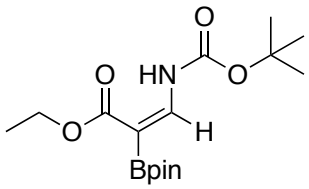
mixture was allowed to stir a further ten minutes at 0 °C. Then, it was stirred at room temperature for 2 hours. The volatiles were then removed under reduced pressure, and the product was used without further purification.

Preparation of ethyl (*E*)-3-((*tert*-butoxycarbonyl)amino)acrylate (3.13a)



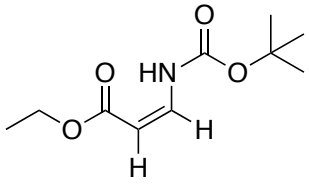
Sodium azide (24.0 mmol, 1.56 g) was dissolved in water (20 mL) and the solution was cooled to 0 °C. To this a solution of ethyl (E)-4-chloro-4-oxobut-2-enoate (20 mmol, 3.24 g) and tetrabutylammonium iodide (1.0 mmol, 369 mg) in toluene (20 mL) was added dropwise. This biphasic reaction was allowed to stir at 0 °C 5 hours, then room temperature for 20 minutes. The toluene layer was separated and washed with saturated Na_2CO_3 (5 x 30 mL) resulting in a colorless solution. Then, it was washed with brine and dried over $MgSO_4$. The toluene solution was slowly added to a preheated mixture of tert-butanol (0.209 mol, 20 mL), pyridine (1.2 mmol, 277 μL), and hydroquinone (1.0 mmol, 110 mg) at 100 °C under N_2. The reaction mixture was refluxed for 30 minutes. The toluene and excess *tert*-butanol were removed under reduced pressure, and the crude product was washed with hexanes and dried to afford a white solid (12.0 mmol, 60.0%); mp = 107 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (t, *J* = 13.1 Hz, 1H), 6.70 (d, *J* = 12.0 Hz, 1H), 5.30 (d, *J* = 14.1 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.50 (s, 9H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 151.6, 139.7, 98.9, 82.4, 59.9, 28.0, 14.3. HRMS (ESI-): *m/z* calculated for $[M-H]^-$ $[C_{10}H_{16}NO_4]^-$ 214.1075, found 214.1079.

Borylation of ethyl (*E*)-3-((*tert*-butoxycarbonyl)amino)acrylate (3.13b)



In the glovebox, a 5 mL conical vial was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.015 mmol, 10 mg), dtbpy (6 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.3 mmol, 76.2 mg), and *tert*-butyl (*E*)-(4-chlorostyryl)carbamate (0.5 mmol, 107 mg) as solids. Cyclohexane or *n*-hexane (3 mL) was added to the vial and the reaction was sealed. The vial was brought out of the glovebox and the reaction mixture was heated at 100 °C for 48 h. The volatiles were removed under reduced pressure and the crude reaction was purified by column chromatography (8% EtOAc/ 92% hexanes) to afford the product as a white solid (CyH: 19.3 mg, 11.3 %; *n*-Hex: 24.6 mg, 14.5%). mp = 102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.23 (d, J = 12.2 Hz, 1H), 7.88 (d, J = 12.1 Hz, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.50 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H), 1.27 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ170.9, 151.9, 150.9, 83.2, 82.2, 60.0, 28.0, 24.7, 14.1. ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.2. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{16}H_{28}BNO_4Na]^+$ 364.1907, found 364.1919.

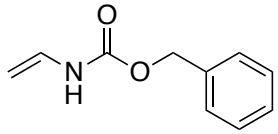
Synthesis of ethyl (*Z*)-3-((*tert*-butoxycarbonyl)amino)acrylate (3.13c)



(*E*)-3-((*tert*-Butoxycarbonyl)amino)acrylate (220 mg, 1.02 mmol) was dissolved in cyclohexane (4 mL) in a 5 mL vial. It was heated at 100 °C for 48 h. GC-FID showed

41% conversion to the isomerized product. The solvent was removed and the pure product was isolated by column chromatography (8% EtOAc/ 92% hexanes) to afford a colorless oil (52 mg, 24%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.60 (br, 1H), 7.20 (t, J = 9.5, 1H), 4.96 (d, J = 8.9 Hz, 1H), 4.13 (q, J = 7.2 Hz, 2H), 1.46 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1, 152.2, 140.3, 93.8, 81.8, 59.8, 28.0, 14.2. HRMS (ESI-): *m/z* calculated for $[M-H]^-$ $[C_{10}H_{16}NO_4]^-$ 214.1079, found 214.1079.

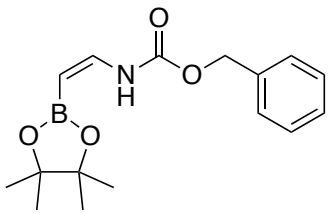
Synthesis of benzyl vinylcarbamate (3.14a)



Sodium azide (58.5 mmol, 3.8 g) was dissolved in water (50 mL) and cooled to 0 °C. To this a solution of acryloyl chloride (50 mmol, 4.06 mL) in toluene (50 mL) was added dropwise. This biphasic reaction was allowed to stir at 0 °C 5 hours. The toluene layer then was separated and washed with saturated Na_2CO_3 and then water. Then, it was dried over $MgSO_4$. The toluene solution was slowly added to a preheated mixture of benzyl alcohol (60 mmol, 6.2 mL), pyridine (25 mmol, 2.0 mL), and hydroquinone (2.75 mmol, 305 mg) at 110 °C under N_2. The mixture was refluxed for 30 minutes. The toluene and excess benzyl alcohol were removed under reduced pressure, and the product was purified by Kugelrohr distillation to afford the product as a low melting colorless crystalline solid (4.07 g, 46%). mp = 42 °C. ^{1}H NMR (500 MHz, CD_3CN) δ 7.77 (br, 1H), 7.45 – 7.34 (m, 5H), 6.71 (ddd, J = 15.9, 10.7, 8.9 Hz, 1H), 5.16 (s, 2H), 4.63 (d, J = 15.2 Hz, 1H), 4.29 (d, J = 8.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 136.8, 130.4,

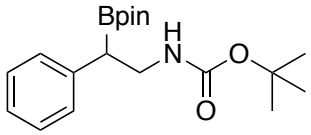
128.6, 128.1, 127.9, 117.4, 92.8, 66.5. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{10}H_{12}NO_2]^+$ 178.0868, found 178.0863.

Borylation of benzyl vinylcarbamate (3.14b)



In the glovebox, a 5 mL conical vial was charged with $[Ir(OMe)cod]_2$ (3 mol %, 0.015 mmol, 10 mg), dtbpy (6 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.3 mmol, 76.2 mg), and *tert*-butyl benzyl vinylcarbamate (0.5 mmol, 88.6 mg) as solids. Cyclohexane (3 mL) was added to the vial and the reaction was sealed. The vial was brought out of the glovebox and the reaction mixture was heated at 100 °C for 48 h. The volatiles were removed under reduced pressure and the crude reaction mixture was purified by column chromatography (8% EtOAc/ 92% hexanes) to afford the product as a colorless oil (CyH: 9.1 mg, 6%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (br, 1H), 7.45 – 7.31 (m, 6H), 5.22 (s, 2H), 4.48 (d, *J* = 10.8 Hz, 1H), 1.30 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.7, 143.2, 136.0, 128.6, 128.4, 128.3, 83.4, 67.3, 24.8. ^{11}B NMR (160 MHz, $CDCl_3$): δ 29.6. HRMS (ESI+): *m/z* calculated for $[M+Na]^+$ $[C_{16}H_{22}BNO_4Na]^+$ 326.1543, found 326.1545.

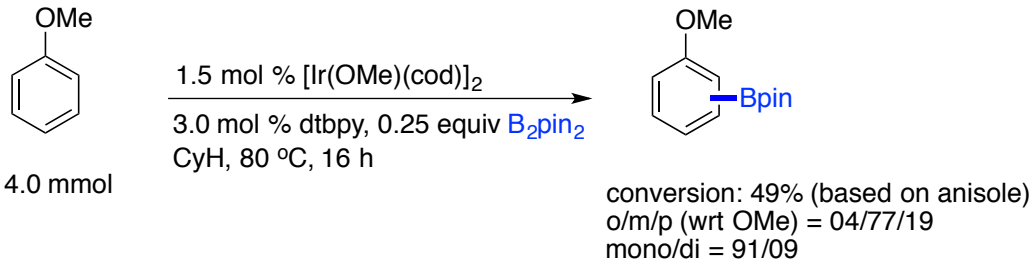
Synthesis of borylated *tert*-butyl phenethylcarbamate (3.15)



Borylated *tert*-butyl (*E*)-styrylcarbamate (**3.4b**) (0.724 mmol, 250 mg) and Pd/C (10% w/w, 0.724 mmol, 77 mg) were combined as solids in a 100 mL round bottom flask. The flask was stoppered, placed under vacuum, and back filled with N_2 three times. Then, dry ispropanol (9 mL) and ethyl acetate (9 mL) were added via syringe. The reaction mixture was further degased with a long needle for 5 minutes. Then, a balloon filled with H_2 gas was fixed to the reaction. It was allowed to stir for 16 h at room temperature. The reaction was then filtered through celite and the volatiles were removed to afford the product as a colorless oil (240 mg, 96%). ^{1}H NMR (500 MHz, CD_3CN) δ 7.35 – 7.28 (m, 2H), 7.23 – 7.18 (m, 3H), 5.12 (br, 1H), 3.52 – 3.43 (m, 1H), 3.36 – 3.26 (m, 1H), 2.59 (t, J = 8.1 Hz, 1H), 1.39 (s, 9H), 1.24 (s, 6H), 1.22 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 140.2, 128.8, 128.6, 125.9, 83.6, 78.9, 43.0, 28.4, 24.7, 24.6. ^{11}B NMR (160 MHz, $CDCl_3$): δ 32.6. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{19}H_{31}BNO_4]^+$ 348.2346, found 348.2342.

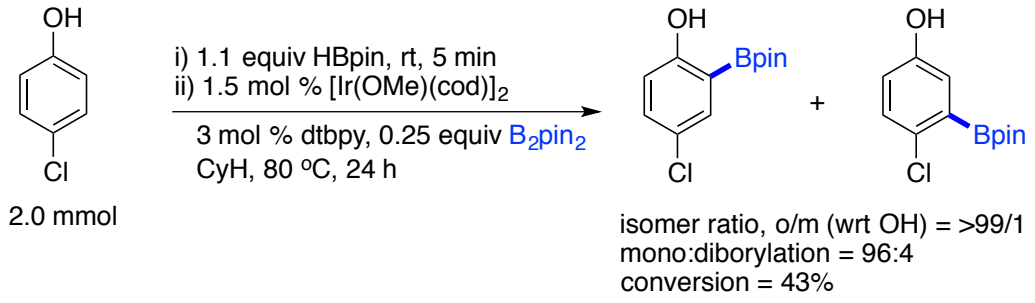
6.4 Chapter 4

Borylation of Anisole:



The reaction was conducted using a modified version of a previously reported procedure.[129] In a glovebox, a 5 mL conical vial was charged with anisole (435 μL, 4.0 mmol), $[Ir(OMe)(cod)]_2$ (10.0 mg, 1.5 mol %, 0.015 mmol), dtbpy (8.0 mg, 3 mol %, 0.03 mmol), B_2Pin_2 (254.0 mg, 1.0 mmol, 0.25 equiv), and dry cyclohexane (3 mL). The vial was sealed and placed in a preheated aluminum block at 80°C for 16 h. The volatiles were then removed on the rotary evaporator, and the conversion and isomer ratios were determined by GC/FID. The results are shown in the scheme.

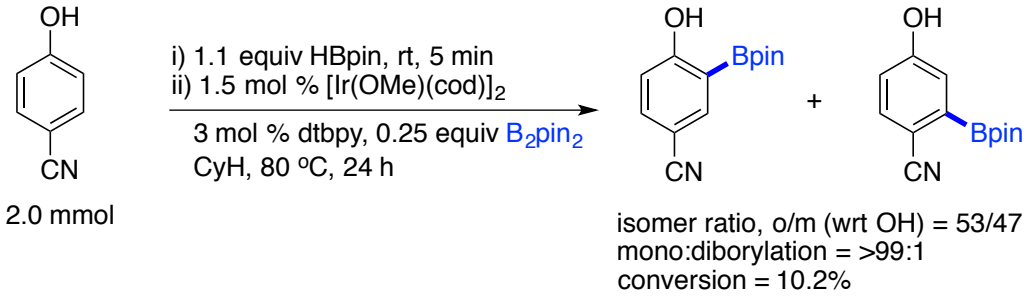
Borylation of 4-Chlorophenol with limiting B_2Pin_2 (1a)



In a glovebox, a 5 mL conical vial was charged with 4-chlorophenol (257.1 mg, 2.0 mmol) and pinacolborane (319.36 μL, 1.1 equiv) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (10.0 mg, 1.5 mol %, 0.015 mmol), dtbpy

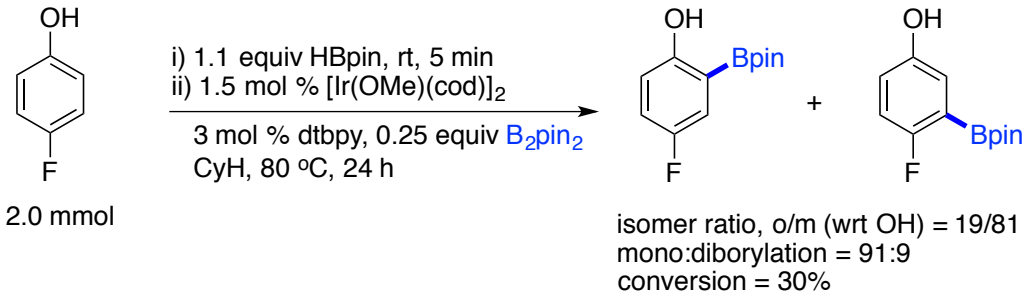
(8.0 mg, 3.0 mol %, 0.03 mmol), and B_2pin_2 (127.0 mg, 0.25 equiv) was charged. Dry cyclohexane (3 mL, 0.33 M) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into pre-heated aluminum block at 80 °C. The reaction mixture was stirred for 4 h. The borylation results are shown in the scheme above and the results are based on GC and ^{1}H NMR data of the crude material.

Borylation of 4-Cyanophenol with limiting B_2Pin_2 (1b)



In a glovebox, a 5 mL conical vial was charged with 4-cyanophenol (238.2 mg, 2.0 mmol) and pinacolborane (319.36 μL, 1.1 equiv) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (10.0 mg, 1.5 mol %, 0.015 mmol), dtbpy (8.0 mg, 3.0 mol %, 0.03 mmol), and B_2pin_2 (127.0 mg, 0.25 equiv) was charged. Dry cyclohexane (3 mL, 0.33 M) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into pre-heated aluminum block at 80 °C. The reaction mixture was stirred for 4 h. The borylation results are shown in the scheme and the results are based on the ^{1}H NMR data of the crude material.

Borylation of 4-Fluorophenol with limiting B_2Pin_2 (1c)

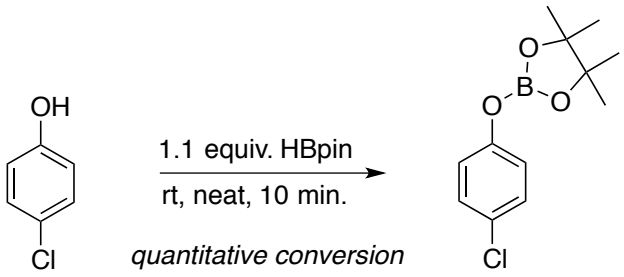


In a glovebox, a 5 mL conical vial was charged with 4-fluorophenol (224.0 mg, 2.0 mmol) and pinacolborane (319.36 μL, 1.1 equiv) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (10.0 mg, 1.5 mol %, 0.015 mmol), dtbpy (8.0 mg, 3.0 mol %, 0.03 mmol), and B_2pin_2 (127.0 mg, 0.25 equiv) was charged. Dry cyclohexane (3 mL, 0.33 M) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into pre-heated aluminum block at 80 ^oC. The reaction mixture was stirred for 4 h. The borylation results are shown in the scheme and the results are based on GC data of the crude material.

General Procedure for the Synthesis of Intermediate Pinacolborane (Bpin) Protected Phenols:

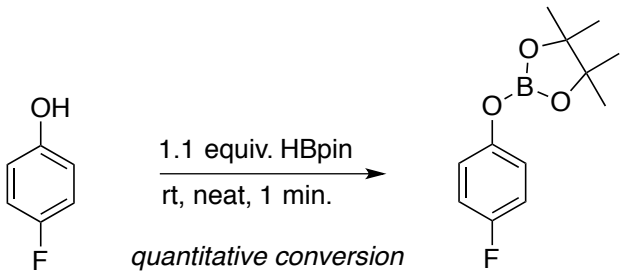
In a glovebox, under a N_2 atmosphere phenols (0.5 mmol) and HBpin (0.55 mmol) were charged in a 2 mL vial, and stirred at room temperature until a solid formed or for 30 minutes. The product was characterized by ^1H, ^{13}C, and ^{11}B NMR in air-free, screw cap NMR tubes.

Preparation of 2-(4-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



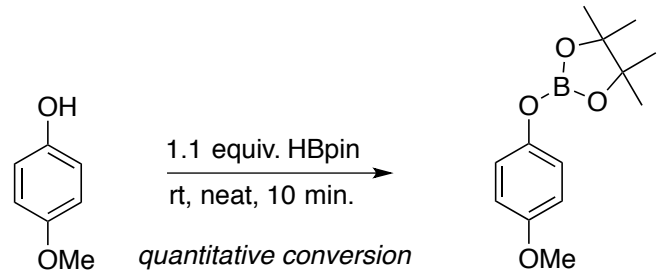
The Bpin protected 4-chlorophenol was prepared as described in the general procedure using 4-chlorophenol (0.5 mmol, 64 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 - 7.19 (m, 2H), 7.03 – 6.99 (m, 2H), 1.30 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.0, 129.2, 128.1, 120.8, 83.7, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 2-(4-fluorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



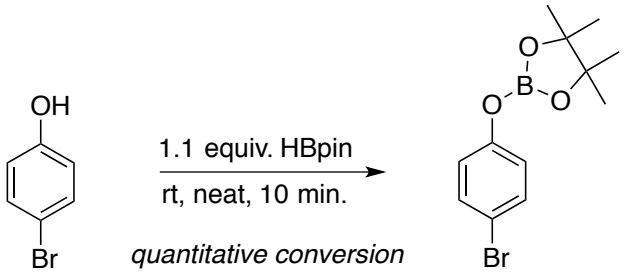
The Bpin protected 4-fluorophenol was prepared as described in the general procedure using 4-fluorophenol (0.5 mmol, 56 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.03 – 7.00 (m, 2H), 6.95 – 6.90 (m, 2H), 1.30 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.5, 157.6, 149.2 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz), 120.6 (d, $^{4}J_{C\text{-}F}$ = 8.6 Hz), 115.7 (d, $^{4}J_{C\text{-}F}$ = 23.4 Hz), 83.6, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -121.1 (td, J = 13.3, 8.3, 4.9 Hz).

Preparation of 2-(4-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



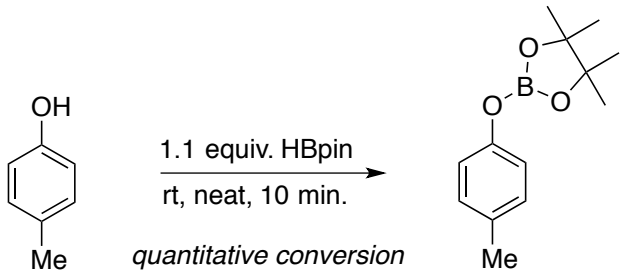
The Bpin protected 4-methoxyphenol was prepared as described in the general procedure using 4-methoxyphenol (0.5 mmol, 54 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.01 – 6.97 (m, 2H), 6.80 – 6.76 (m, 2H), 3.74 (s, 3H), 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.3, 147.3, 120.1, 114.3, 83.5, 55.6, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 2-(4-bromophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The Bpin protected 4-bromophenol was prepared as described in the general procedure using 4-bromophenol (0.5 mmol, 87 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.33 (m, 2H), 6.97 – 6.95 (m, 2H), 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.6, 132.2, 121.4, 115.7, 83.8, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

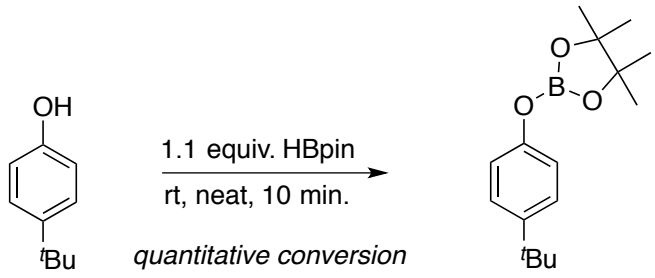
Preparation 4,4,5,5-tetramethyl-2-(p-tolyloxy)-1,3,2-dioxaborolane:



The Bpin protected *p*-cresol was prepared as described in the general procedure using the *p*-cresol (0.5 mmol, 54 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07 – 7.03 (m, 2H), 6.97 – 6.93 (m, 2H), 2.27 (s, 3H) 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.2, 132.4, 129.8, 119.2, 83.5, 24.6, 20.7

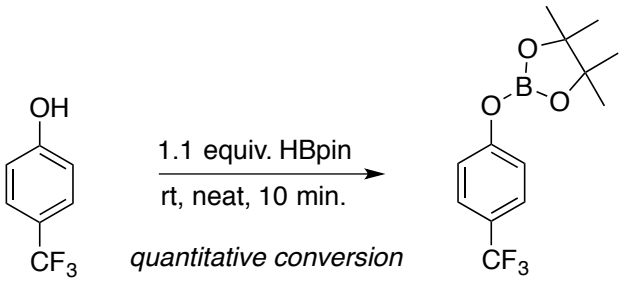
^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 2-(4-(tert-butyl)phenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



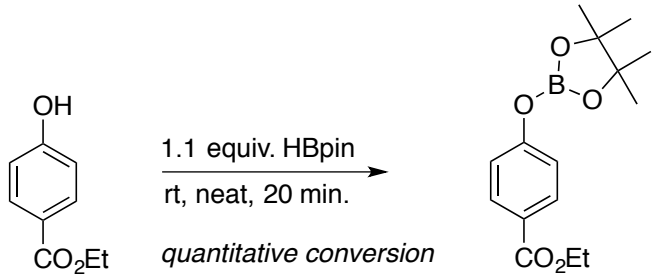
The Bpin protected 4-tertbutylphenol was prepared as described in the general procedure using 4-tertbutylphenol (0.5 mmol, 75 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.25 (m, 2H), 7.01 – 6.98 (m, 2H), 1.30 (s, 12H), 1.30 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.0, 145.6, 126.1, 118.8, 114.7, 83.5, 34.2, 31.5, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (br s).

Preparation of 4,4,5,5-tetramethyl-2-(4-(trifluoromethyl)phenoxy)-1,3,2-dioxaborolane:



The Bpin protected 4-trifluorophenol was prepared as described in the general procedure using 4-trifluorophenol (0.5 mmol, 81 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 1.34 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0, 126.8 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz), 125.3 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 124.2, (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 119.8, 83.9, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

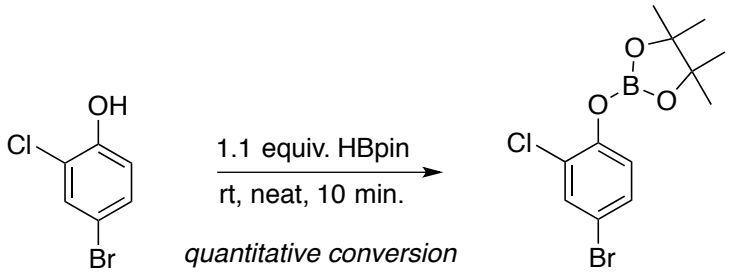
Preparation of ethyl 4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate:



The Bpin protected ethyl 4-hydroxybenzoate was prepared as described in the general procedure using ethyl 4-hydroxybenzoate (0.5 mmol, 83 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 – 7.94 (m, 2H), 7.14 – 7.10 (m, 2H), 4.32 (qd, J = 7.1, 7.1, 4.9, 2.2 Hz, 2H), 1.35 (ddd, J = 7.2, 4.7, 2.5 Hz, 3H), 1.30 (s, 12H).

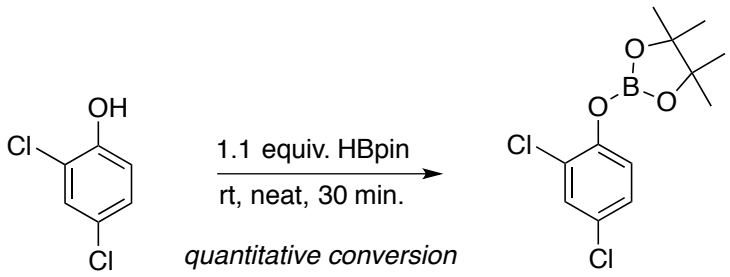
^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 157.2, 131.3, 125.4, 119.4, 83.9, 60.7, 24.6, 14.3. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (br s).

Preparation of 2-(4-bromo-2-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The Bpin protected 4-bromo-2-chlorophenol was prepared as described in the general procedure using 4-bromo-2-chlorophenol (0.5 mmol, 104 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, J = 2.4 Hz, 1H), 7.31 (dd, J = 8.6, 2.5 Hz, 1H), 7.07 (d, J = 8.6 Hz, 1H), 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.9, 132.7, 130.7, 126.4, 122.6, 115.9, 84.2, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.6 (s).

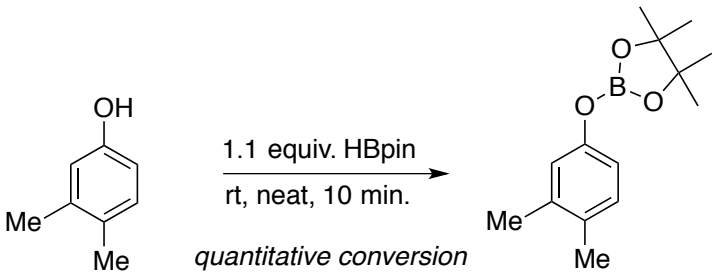
Preparation of 2-(2,4-dichlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The Bpin protected 2,4-dichlorophenol was prepared as described in the general procedure using 2,4-dichlorophenol (0.5 mmol, 81.5 mg) and HBpin (0.55 mmol, 80 μL).

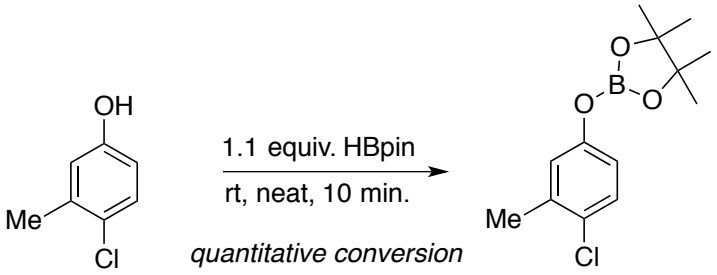
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.5, 129.8, 127.8, 126.0, 122.1, 117.1, 84.2, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.6 (s).

Preparation of 2-(3,4-dimethylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



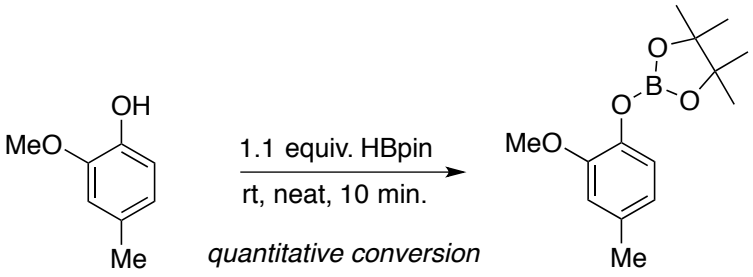
The Bpin protected 3,4-dimethylphenol was prepared as described in the general procedure using 3,4-dimethylphenol (0.5 mmol, 61 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.03 (d, *J* = 8.3 Hz, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 6.84 (dd, *J* = 8.2, 2.6 Hz, 1H), 2.21 (s, 3H), 2.17 (s, 3H), 1.29 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.4, 137.6, 131.2, 130.2, 120.7, 116.6, 83.4, 24.6, 19.9, 19.0. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.8 (s).

Preparation of 2-(4-chloro-3-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The Bpin protected 4-chloro-3-methylphenol was prepared as described in the general procedure using 4-chloro-3-methylphenol (0.5 mmol, 71 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, J = 8.6 Hz, 1H), 6.93 (d, J = 3.0 Hz, 1H), 6.85 (dd, J = 8.7, 3.1 Hz, 1H), 2.31 (s, 3H), 1.30 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.9, 136.9, 129.5, 128.4, 121.9, 118.3, 83.7, 24.6, 20.2. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

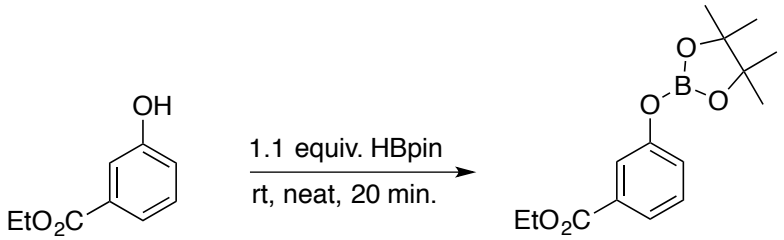
Preparation of 2-(2-methoxy-4-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The Bpin protected 2-methoxy-4-methylphenol was prepared as described in the general procedure using 2-methoxy-4-methylphenol (0.5 mmol, 69 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (d, J = 8.1 Hz, 1H), 6.72 (s, 1H), 6.67 (d, 1H, J = 8.2 Hz), 3.83 (s, 3H), 2.31 (s, 3H), 1.30 (s, 12H). ^{13}C NMR (125 MHz,

$CDCl_3$): δ 149.7, 140.7, 133.5, 121.1, 120.1, 113.0, 83.4, 55.6, 24.5, 21.3. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.9 (s).

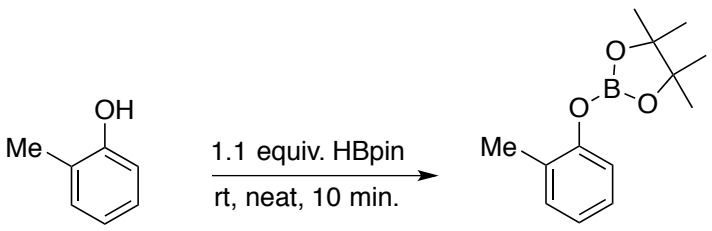
Preparation of ethyl 3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate:



quantitative conversion

The Bpin protected ethyl 3-hydroxybenzoate was prepared as described in the general procedure using ethyl 3-hydroxybenzoate (0.5 mmol, 83 mg) and HBpin (0.55 mmol, 80 μL). ^1H NMR (500 MHz, $CDCl_3$): δ 7.77 – 7.74 (m, 2H), 7.35 (t, J = 8.0 Hz, 1H), 7.30 – 7.27 (m, 1H), 4.37 (q, J = 7.0 Hz, 2H), 1.39 (t, J = 7.0 Hz, 3H), 1.33 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 153.4, 131.8, 129.2, 124.3, 124.1, 120.7, 83.8, 61.0, 24.6, 14.3. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 4,4,5,5-tetramethyl-2-(o-tolyloxy)-1,3,2-dioxaborolane:

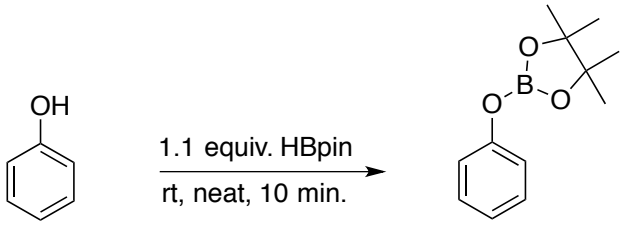


quantitative conversion

The Bpin protected *o*-cresol was prepared as described in the general procedure using *o*-cresol (0.5 mmol, 54 mg) and HBpin (0.55 mmol, 80 μL). ^1H NMR (500 MHz, $CDCl_3$): δ 7.18 – 7.12 (m, 2H), 7.09 – 7.08 (m, 1H), 6.99 (ddd, J = 7.3, 7.3, 1.2 Hz, 1H),

2.25 (s, 3H), 1.33 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.9, 130.9, 128.4, 126.7, 123.3, 119.4, 83.5, 24.6, 16.4. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

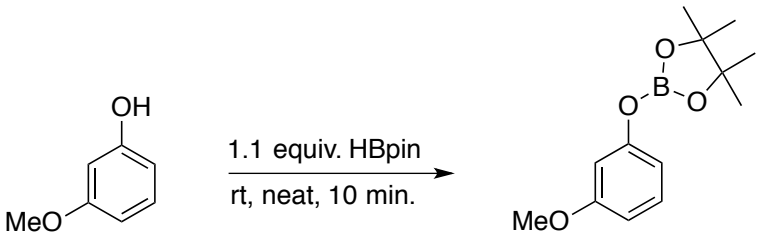
Preparation of 4,4,5,5-tetramethyl-2-phenoxy-1,3,2-dioxaborolane:



quantitative conversion

The Bpin protected phenol was prepared as described in the general procedure using phenol (0.5 mmol, 47 mg) and HBpin (0.55 mmol, 80 μL) and stirring for ten minutes. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (t, *J* = 7.7 Hz, 2H) , 7.11 (d, *J* = 7.9 Hz, 2H), 7.06 (t, *J* = 7.0 Hz, 1H), 1.33 (s, 12H).^{13}C NMR (125 MHz, $CDCl_3$): δ 153.4, 129.3, 123.1, 119.5, 83.5, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 2-(3-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



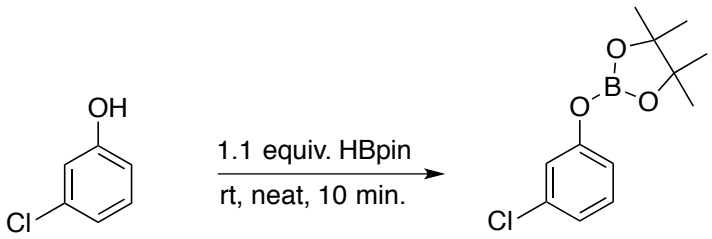
quantitative conversion

The Bpin protected 3-methoxyphenol was prepared as described in the general procedure using 3-methoxyphenol (0.5 mmol, 62 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (t, *J* = 8.2 Hz), 6.72 (ddd, *J* = 8.0, 2.3, 0.87 Hz, 1H), 6.68 (t, *J* = 2.3 Hz, 1H), 6.63 (ddd, *J* = 8.3, 2.4, 0.87 Hz, 1H), 3.76 (s, 3H), 1.30 (s, 12H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 154.5, 129.7, 111.9, 108.6, 105.9, 83.6, 55.3, 24.6.

^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

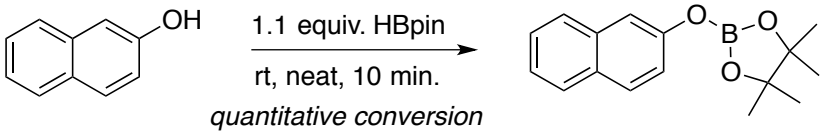
Preparation of 2-(3-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



quantitative conversion

The Bpin protected 3-chlorophenol was prepared as described in the general procedure using 3-chlorophenol (0.5 mmol, 64.3 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (t, *J* = 8.2 Hz, 1H), 7.10 (t, *J* =2.4 Hz, 1H), 7.02 (ddd, *J* = 7.8, 3.0, 1.0 Hz, 1H), 6.97 (ddd, *J* = 8.3 Hz, 3.0 Hz, 1.0 Hz, 1H), 1.30 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 154.1, 134.4, 130.0, 123.4, 120.1, 117.9, 83.8, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.7 (s).

Preparation of 4,4,5,5-tetramethyl-2-(naphthalen-2-yloxy)-1,3,2-dioxaborolane:

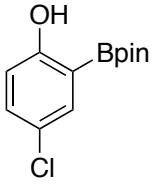


quantitative conversion

The Bpin protected 2-naphthol was prepared as described in the general procedure using 2-naphthol (0.5 mmol, 72 mg) and HBpin (0.55 mmol, 80 μL). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 – 7.73 (m, 3H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.42 (ddd, *J* = 8.1, 5.9, 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.2, 6.0, 1.4 Hz, 1H), 7.26 (dd, *J* = 8.8, 2.5 Hz, 1H), 1.33 (s, 12H).

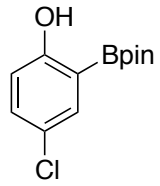
^{13}C NMR (125 MHz, $CDCl_3$): δ 151.3, 134.2, 130.1, 129.3, 127.6, 127.2, 126.3, 124.5, 120.7, 115.2, 83.7, 24.6. ^{11}B NMR (176, MHz, $CDCl_3$): δ 21.9 (s).

Borylation of 4-Chlorophenol with B_2pin_2 (4.1):



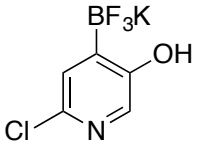
In a glovebox, a 5 mL conical vial was charged with 4-chlorophenol (128.56 mg, 1.0 mmol) and pinacolborane (159.68 μL, 1.1 equiv) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (20.0 mg, 3.0 mol %, 0.03 mmol), dtbpy (16.0 mg, 6.0 mol %, 0.06 mmol), and B_2pin_2 (254.0 mg, 1.0 equiv) was charged. Dry cyclohexane (3 mL, 0.33 M) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into pre-heated aluminum block at 80 ^oC. The reaction mixture was stirred for 3 h. After completion (judged by GC), the cyclohexane was removed under reduced pressure and chromatographic separation with silica gel (chloroform as eluent) afforded the ortho-borylated product as a white solid (203 mg, 80%). The NMR data were in accordance with the literature.[130]

Large Scale (Gram) Borylation of 4-Chlorophenol (4.1):



In a glovebox, a 100 mL air free flask was charged with 4-chlorophenol (2.0 g, 15.5 mmol) and HBpin (2.18 g, 17.05 mmol). After stirring for 5 minutes, a solid had formed. Then, $[Ir(OMe)cod]_2$ (150.0 mg, 1.5 mol %, 0.226 mmol), dtbpy (125.0 mg, 3 mol %, 0.465 mmol), B_2Pin_2 (2.75 g, 10.85 mmol), and dry cyclohexane (25 mL) were added. The flask was sealed and heated at 80°C. After 3 h, the reaction was complete (judged by GC/FID), and the volatiles were removed under reduced pressure. Purification by column chromatography with chloroform as the eluent afforded 2.92 g of the pure ortho-borylated product (74%) as a white solid.

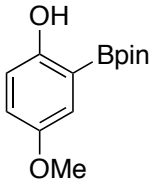
Borylation of 2-Chloro-5-hydroxypyridine with B_2pin_2 (4.2):



In a glovebox, a 5 mL conical vial was charged with 2-chloro-5-hydroxypyridine (129.0 mg, 1.0 mmol) and pinacolborane (159.68 μL, 1.1 equiv) in THF (1.5 mL) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (10.0 mg, 1.5 mol %, 0.015 mmol), dtbpy (8.0 mg, 3.0 mol %, 0.03 mmol), and B_2pin_2 (127.0 mg, 0.5 equiv) was charged. Additional THF (1.5 mL) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into a pre-heated aluminum block at 80 ^oC. The reaction mixture was stirred for 5 hours. The reaction mixture was then cooled to

room temperature and transferred to a round bottom flask. The reaction mixture was washed in the flask with additional THF (3 mL). The solution was cooled to 0 ^{o}C and degased with N_2 for 5 minutes. Then, KHF_2 (2.2 mL, 8.8 mmol, 4.0 M in H_2O) was added via syringe dropwise. The reaction mixture was allowed to stir at 0 ^{o}C for 10 minutes, then the ice bath was removed and the reaction mixture warmed to room temperature. After stirring at room temperature for 16 h, the reaction mixture was filtered, and the recovered solid washed with THF to afford the organotrifluoroborate product as a white solid (205 mg, 87%). mp = 226 – 230 ^{o}C dec. ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 7.65 (s, 1H), 7.47 (q, 1H, J = 11.4 Hz), 7.15 (br, 1H). ^{13}C NMR (125 MHz, $(CD_3)_2SO$): δ_C 156.18, 140.18, 135.58, 127.59 (q, 1.88 Hz). ^{11}B NMR (160 MHz, $(CD_3)_2CO$): δ 2.65 (q, J = 51.5 Hz). HRMS (ESI-): *m/z* calculated for $[M-K]^-$ $C_5H_3BClF_3NO$ $[M-K]^-$ 195.9955, found 195.9948

Borylation of 4-methoxyphenol with B_2pin_2 (4.4):

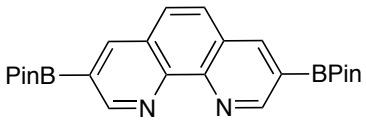


In a glovebox, a 5 mL conical vial was charged with 4-methoxyphenol (124.14 mg, 1.0 mmol) and pinacolborane (159.68 μL, 1.1 equiv) and stirred for 5 min at room temperature. To this mixture, $[Ir(OMe)(cod)]_2$ (20.0 mg, 3.0 mol %, 0.03 mmol), dtbpy (16.0 mg, 6.0 mol %, 0.06 mmol), and B_2pin_2 (177.8 mg, 0.7 equiv) was charged. Dry cyclohexane (3 mL, 0.33 M) was added under an inert atmosphere. The vial was capped with a teflon pressure cap and placed into pre-heated aluminum block at 80 ^{o}C. The

reaction mixture was stirred for 24 h. After completion (judged by GC), the ratio of ortho/meta (wrt OH) borylated product was found to be 65/35. The cyclohexane was removed under reduced pressure and chromatographic separation with silica gel (chloroform as eluent) gave 144.0 mg of the ortho-borylated product (58%) as a colorless oil. The spectra were in accordance with the literature.[130]

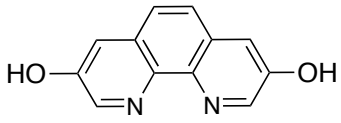
6.5 Chapter 5

3,8-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,10-phenanthroline (5.1)



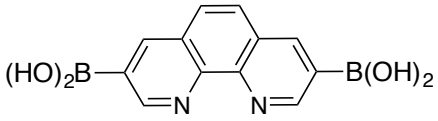
In the glovebox, a 500 mL Schlenk flask was charged with $[Ir(OMe)cod]_2$ (66.4 mg, 0.1 mmol, 0.5 mol %) in THF (50 mL). B_2Pin_2 (7.6 g, 30 mmol) was dissolved in THF (100 mL), added to the solution, and stirred for 5 minutes. Then, 1,10-phenanthroline (3.6 g, 20 mmol) was added as a solution in THF (100 mL). The Schlenk flask was sealed with a septum, and brought out of the glovebox. The septum was replaced with a reflux condenser under N_2, and the reaction was heated to reflux at 85°C for 4.5 hours. The volatiles were removed under vacuum, to afford the crude product. Dry heptane (35 mL) was added, and the mixture was heated to 85 °C and stirred until a fine powder was observed in the flask (approximately 1 hr). The solution was filtered hot, washed with hot heptane (10 mL), and dried under vacuum to afford the product as a tan powder (6.52 g, 15.1 mmol, 76%). mp = 260 °C (dec). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (s, 24H), 7.77 (s, 2H), 8.65 (d, 2H, J = 1.5 Hz), 9.45 (d, 2H, J = 1.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$,) δ 24.8, 84.3, 126.5, 128.3, 143.4, 147.5, 154.9; ^{11}B NMR (96.18 MHz, $CDCl_3$) δ 30.9; HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $C_{24}H_{31}B_2N_2O_4$ 433.2470, found 433.2484.

Synthesis of 1,10-Phenanthroline-3,8-diol (5.2)



3,8-Diborylated 1,10-phenanthroline (0.2 mmol, 101 mg) was dissolved in acetone (15 mL) in a 50 mL round bottom flask. H_2O_2 (30 w/w%, 0.231 mmol, 0.230 mL) was added, and the reaction flask was sealed with a stopper. It was stirred at room temperature for 14 hours. The reaction was then filtered and the solid was washed with acetone to afford the product as a tan colored powder (0.24 mmol, 50 mg, 100%). mp > 260 °C. ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ 10.30 (s, 2H), 7.59 (d, 2H, J = 2.9 Hz), 7.74 (s, 2H), 8.62 (d, 2H, J = 2.4 Hz). ^{13}C NMR (125 MHz, $(CD_3)_2SO$) δ 117.5, 126.5, 128.0, 139.4, 141.2, 152.0. HRMS (ESI+): *m/z* calculated for $[M+H]^+$ $[C_{12}H_9N_2O_2]^+$ 213.0664, found 213.0659.

Synthesis of (1,10-Phenanthroline-3,8-diyl)diboronic acid (5.3)



3,8-Diborylated 1,10-phenanthroline (2.31 mmol, 1.0 g) was dissolved in THF (40 mL) in a 100 mL round bottom flask wrapped in aluminum foil. A slurry of $NaIO_4$ (13.85 mmol, 3.0 g) in water (10 mL) was added, and the reaction mixture was stirred for ten minutes. During this time a solid began to precipitate from the solution. HCl (1.0 M, 9 mmol, 9 mL) was added, and the solid dissolved. The reaction mixture was stirred at room temperature for 13 hours. The product precipitated from the reaction as a cream colored solid that was isolated by filtration. It is sparingly soluble in organic solvents. ^{1}H

NMR was acquired in both methanol and dimethylsulfoxide. The product is more soluble in the methanol, however, the –OH peaks are not visible. DMSO shows all peaks. mp = 200°C (dec). ^{1}H NMR (500 MHz, $(CD_3)_2SO$) δ 9.37 (s, 2H), 8.80 (s, 2H), 8.62 (s, 4H), 7.97 (s, 2H). ^{1}H NMR (500 MHz, CD_3OD) δ 9.25 (s, 2H), 8.99 (s, 2H), 8.12 (s, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ 151.0, 145.8, 138.5, 128.9, 126.9. ^{11}B NMR (160 MHz, CD_3OD): δ 17.6. HRMS (ESI+): *m/z* calculated for $[M+Na]^+$ $[C_{12}H_{10}B_2N_2O_4Na]^+$ 291.0724, found 213.0714.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 1)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (14.7 mg, 0.025 mmol, 10 mol%), potassium acetate (147 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). CPME (4 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 2)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (14.7 mg, 0.025 mmol, 10 mol%), potassium acetate (147 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). DMA (4 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C

and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 3)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (14.7 mg, 0.025 mmol, 10 mol%), potassium acetate (147 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). DMF (4 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 4)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (14.7 mg, 0.025 mmol, 10 mol%), potassium acetate (147 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). Toluene (4 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 5)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). CPME (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation (36%) of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 6)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). DMA (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed complete deborylation of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 7)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20

mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). Toluene (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 8)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). CPME (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed complete deborylation (30%) of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 9)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). DMA (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and

stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed complete deborylation of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 10)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). Toluene (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation (61%) of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 2-Bromomesitylene (Table 5.1, Entry 11)

In a glovebox, under an atmosphere of N_2, a 25 mL air-free flask was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PPh_3)$_4$] (57.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 2-bromomesitylene (119 mg, 0.6 mmol). Dioxane (2 mL) was added to the mixture and the flask was sealed. The reaction mixture was heated at 100 °C and stirred for 48 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation (61%) of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 1)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). CPME (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 2)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). DMA (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation of the borylated starting material and trace conversion to the desired product.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 3)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PCy_3)Cl)-2-aminobiphenyl] (29.5 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6

mmol). Toluene (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 4)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). CPME (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 48 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 5)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). DMA (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 48 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation of the borylated starting material and trace conversion to the desired product.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 6)

In a glovebox, under an atmosphere of N_2, a 5 mL conical vial was charged with **5.1** (108 mg, 0.25 mmol), [Pd(dppf)Cl_2]•CH_2Cl_2 (40.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). Toluene (2 mL) was added to the mixture and the vial was sealed and brought out of the glovebox. The reaction mixture was heated in an aluminum heating block at 100 °C and stirred for 48 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed no change in the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 7)

In a glovebox, under an atmosphere of N_2, a 25 mL air-free flask was charged with **5.1** (108 mg, 0.25 mmol), [Pd(PPh_3)$_4$] (57.8 mg, 0.050 mmol, 20 mol%), potassium phosphate (318 mg, 1.5 mmol), and 4-iodotoluene (131 mg, 0.6 mmol). Dioxane (2 mL) was added to the mixture and the flask was sealed. The reaction mixture was heated at 100 °C and stirred for 48 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation (39%) of the borylated starting material.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 8)

Under an atmosphere of N_2, a 50 mL Schlenk flask was charged with **5.1** (750 mg, 1.73 mmol) and [Pd(PPh_3)$_4$] (50 mg, 0.043 mmol, 2.5 mol%) in toluene (10 mL). Another flask was charged with sodium carbonate (730 mg, 6.9 mmol) and 4-iodotoluene (829 mg, 3.8 mmol) in H_2O/MeOH (4:1 v/v, 10 mL). The H_2O/MeOH mixture was cannula

transferred to the toluene mixture. The reaction mixture was refluxed at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed deborylation (64%) of the borylated starting material.

Attempted Suzuki Coupling of 5.3 with 4-Iodotoluene (Table 5.2, Entry 11)

Under an atmosphere of N_2, a 50 mL Schlenk flask was charged with **5.3** (750 mg, 2.8 mmol) and [$Pd(PPh_3)_4$] (81 mg, 0.07 mmol, 2.5 mol%) in toluene (10 mL). Another flask was charged with sodium carbonate (1.18 g, 11.2 mmol) and 4-iodotoluene (1.34 g, 6.16 mmol) in H_2O/MeOH (4:1 v/v, 10 mL). The H_2O/MeOH mixture was cannula transferred to the toluene mixture. The reaction mixture was refluxed at 100 °C and stirred for 24 hours. The volatiles were removed under reduced pressure. ^{1}H NMR of the crude reaction mixture showed full deborylation of the borylated starting material

Attempted Suzuki Coupling of 5.3 with 4-Iodotoluene (Table 5.2, Entry 12)

Under an atmosphere of N_2, a 25 mL Schlenk flask was charged with **5.3** (100 mg, 0.373 mmol), [$Pd(PPh_3)_4$] (86 mg, 0.074 mmol, 20 mol%), potassium carbonate (309 mg, 2.2 mmol) and 4-iodotoluene (163 mg, 0.746 mmol). THF/H_2O (2:1 v/v, 6 mL) was added to the mixture and the reaction mixture was refluxed at 80 °C and stirred for 12 hours. The reaction was extracted with Et_2O (2x20 mL), dried over $MgSO_4$, and filtered. The volatiles were removed under reduced pressure. GC/MS and ^{1}H NMR showed unreacted I-tol, but no starting boronic acid or any phenanthroline was observed by NMR.

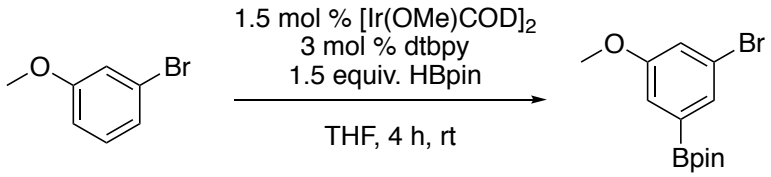
Attempted Suzuki Coupling of 5.3 with 4-Iodotoluene (Table 5.2, Entry 13)

Under an atmosphere of N_2, a 25 mL Schlenk flask was charged with **5.3** (100 mg, 0.373 mmol), [$Pd(PPh_3)_4$] (86 mg, 0.074 mmol, 20 mol%), cesium carbonate (729 mg, 2.2 mmol) and 4-iodotoluene (163 mg, 0.746 mmol). THF/H_2O (2:1 v/v, 6 mL) was added to the mixture and the reaction mixture was refluxed at 80 °C and stirred for 12 hours. The reaction was extracted with Et_2O (2x20 mL), dried over $MgSO_4$, and filtered. The volatiles were removed under reduced pressure. GC/MS and ^1H NMR showed unreacted I-tol, but no starting boronic acid or any phenanthroline was observed by NMR.

Attempted Suzuki Coupling of 5.1 with 4-Iodotoluene (Table 5.2, Entry 14)

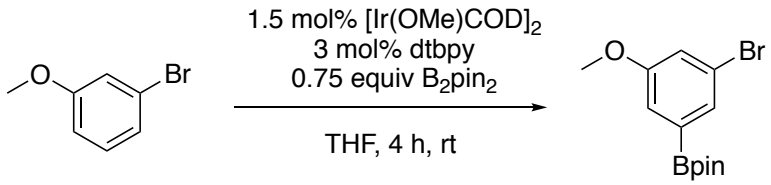
A 25 mL air-free flask was charged with **5.1** (108 mg, 0.25 mmol), [$Pd(dppf)Cl_2$]•CH_2Cl_2 (10 mg, 0.0125 mmol, 5 mol%), cesium carbonate (244 mg, 0.75 mmol), and 4-iodotoluene (131 mg, 0.6 mmol) under an atmosphere of N_2. CPME/H_2O (10:1v/v, 5 mL) was added to the mixture and the flask was sealed. The reaction mixture was heated at 105 °C and stirred for 48 hours. The reaction was extracted into DCM (2 x 10 mL), dried over $MgSO_4$, and filtered. The volatiles were removed under reduced pressure. ^1H NMR of the crude reaction mixture showed full deborylation of the borylated starting material.

Borylation of 3-bromoanisole with dtbpy as ligand (HBpin)



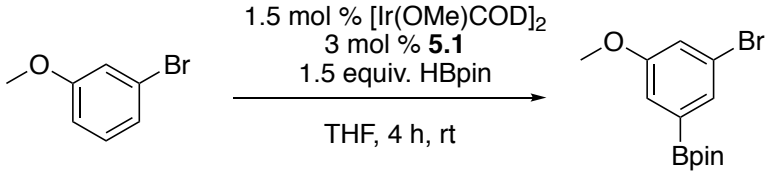
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), HBpin (1.5 mmol, 192 mg), and 3-bromoanisole (1 mmol, 127 μL) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (66%).

Borylation of 3-bromoanisole with dtbpy as ligand (B_2pin_2)



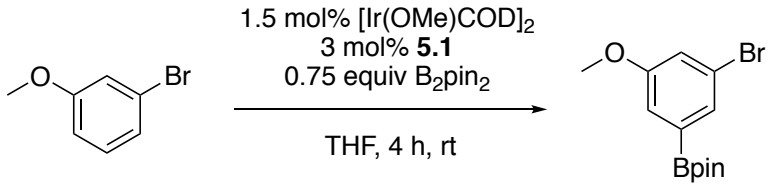
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.75 mmol, 191 mg), and 3-bromoanisole (1 mmol, 127 μL) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (95%).

Borylation of 3-bromoanisole with 5.1 as ligand (HBpin)



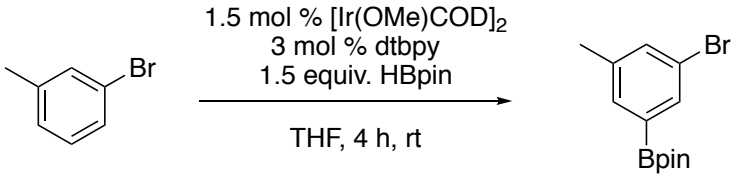
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), HBpin (1.5 mmol, 192 mg), and 3-bromoanisole (1 mmol, 127 μL) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (58%).

Borylation of 3-bromoanisole with 5.1 as ligand (B_2pin_2)



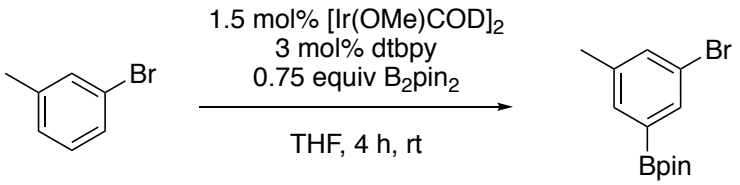
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), B_2pin_2 (0.75 mmol, 191 mg), and 3-bromoanisole (1 mmol, 127 μL) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (82%).

Borylation of 3-bromotoluene with dtbpy as ligand (HBpin)



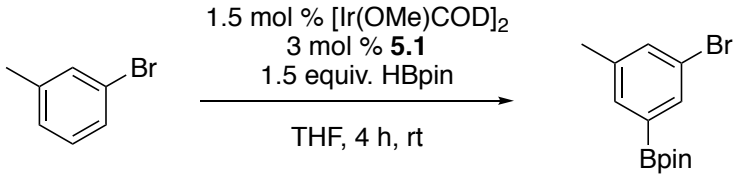
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), HBpin (1.5 mmol, 192 mg), and 3-bromotoluene (1 mmol, 171 mg) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^1H NMR using dibromoethane as an internal standard (16%).

Borylation of 3-bromotoluene with dtbpy as ligand (B_2pin_2)



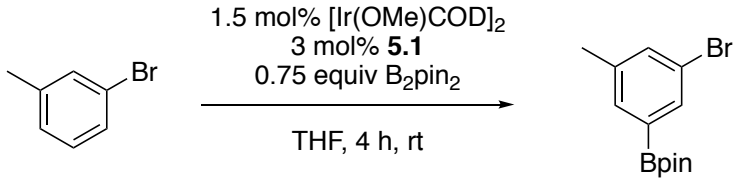
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.75 mmol, 191 mg), and 3-bromotoluene (1 mmol, 171 mg) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^1H NMR using dibromoethane as an internal standard (98%).

Borylation of 3-bromotoluene with 5.1 as ligand (HBpin)



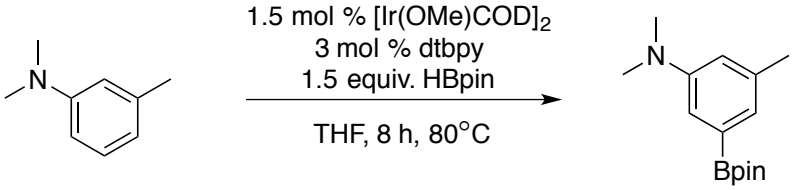
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), HBpin (1.5 mmol, 192 mg), and 3-bromotoluene (1 mmol, 171 mg) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (3%).

Borylation of 3-bromotoluene with 5.1 as ligand (B_2pin_2)



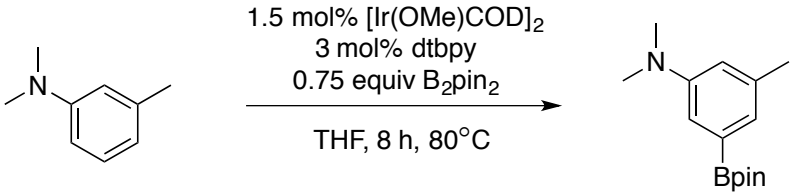
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), B_2pin_2 (0.75 mmol, 191 mg), and 3-bromotoluene (1 mmol, 171 mg) in THF (3 mL). The reaction mixture was stirred at room temperature for 4 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (1%).

Borylation of N,N-dimethyl-*m*-toluidine with dtbpy as ligand (HBpin)



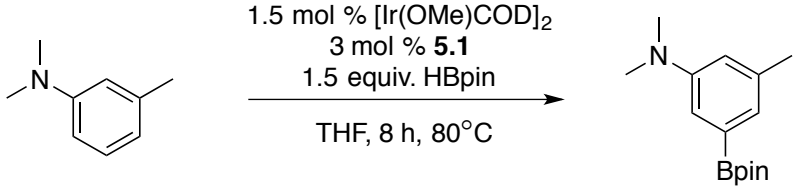
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), HBpin (1.5 mmol, 192 mg), and N,N-dimethyl-*m*-toluidine (1 mmol, 145 μL) in THF (3 mL). The reaction mixture was stirred at 80 °C for 8 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (14%).

Borylation of N,N-dimethyl-*m*-toluidine with dtbpy as ligand (B_2pin_2)



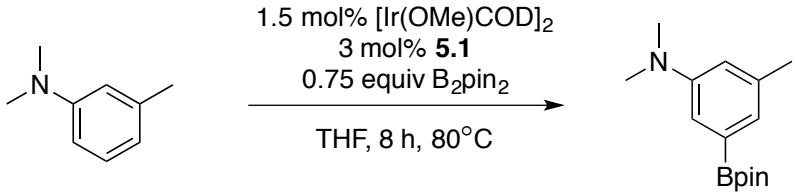
In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), dtbpy (3 mol %, 0.03 mmol, 8 mg), B_2pin_2 (0.75 mmol, 191 mg), and N,N-dimethyl-*m*-toluidine (1 mmol, 145 μL) in THF (3 mL). The reaction mixture was stirred at 80 °C for 8 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (45%).

Borylation of N,N-dimethyl-*m*-toluidine with 5.1 as ligand (HBpin)



In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), HBpin (1.5 mmol, 192 mg), and N,N-dimethyl-*m*-toluidine (1 mmol, 145 μL) in THF (3 mL). The reaction mixture was stirred at 80 °C for 8 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (94%).

Borylation of N,N-dimethyl-*m*-toluidine with 5.1 as ligand (B_2pin_2)



In the glovebox a 5 mL vial was charged with $[Ir(OMe)cod]_2$ (1.5 mol%, 0.015 mmol, 10 mg), **5.1** (3 mol %, 0.03 mmol, 13 mg), B_2pin_2 (0.75 mmol, 191 mg), and N,N-dimethyl-*m*-toluidine (1 mmol, 145 μL) in THF (3 mL). The reaction mixture was stirred at 80 °C for 8 hours. Reaction conversion was determined by ^{1}H NMR using dibromoethane as an internal standard (100%).

APPENDICES

APPENDIX A

NMR Spectra

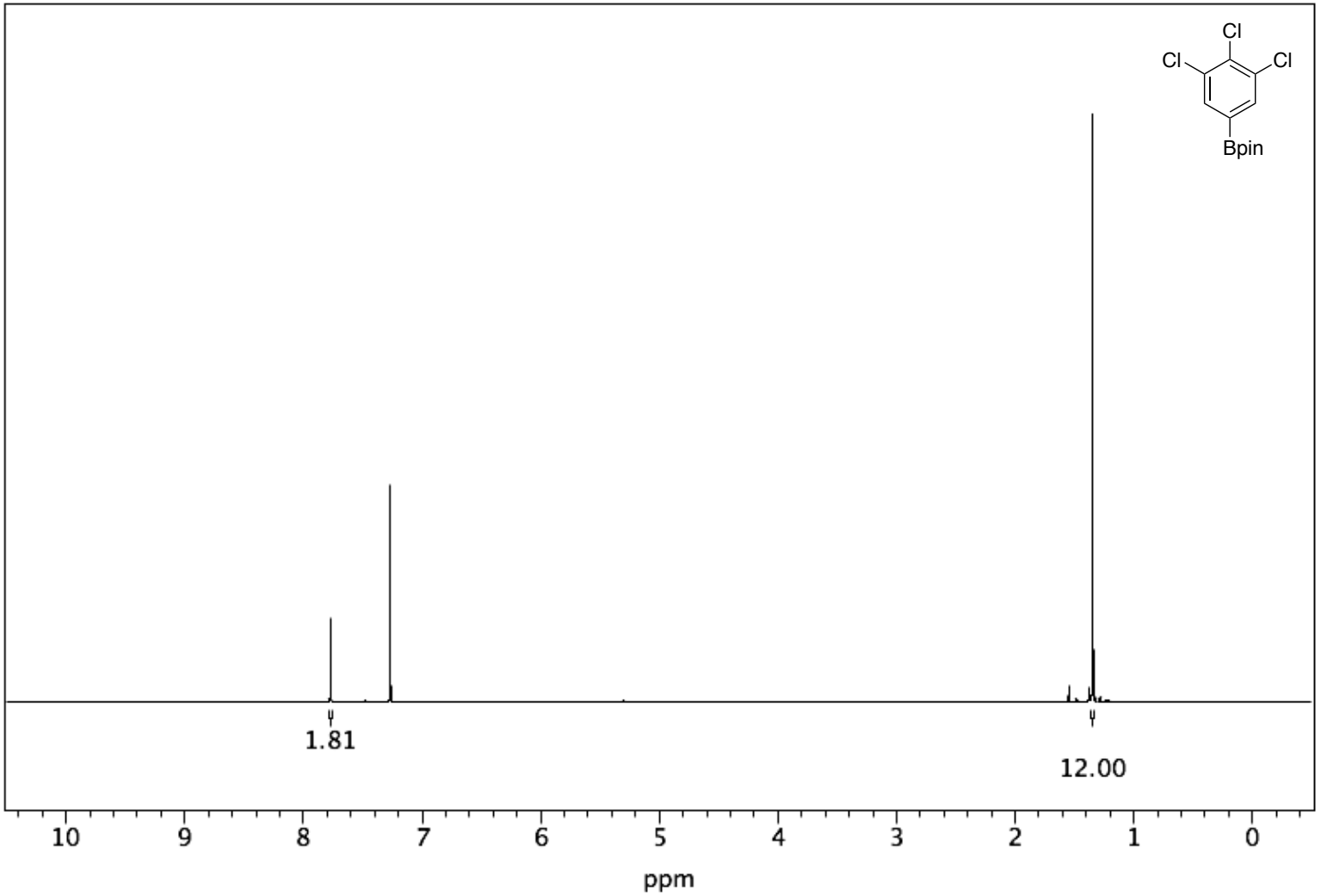


Figure A1. 500 MHz ^{1}H NMR of **2.1a** in $CDCl_3$

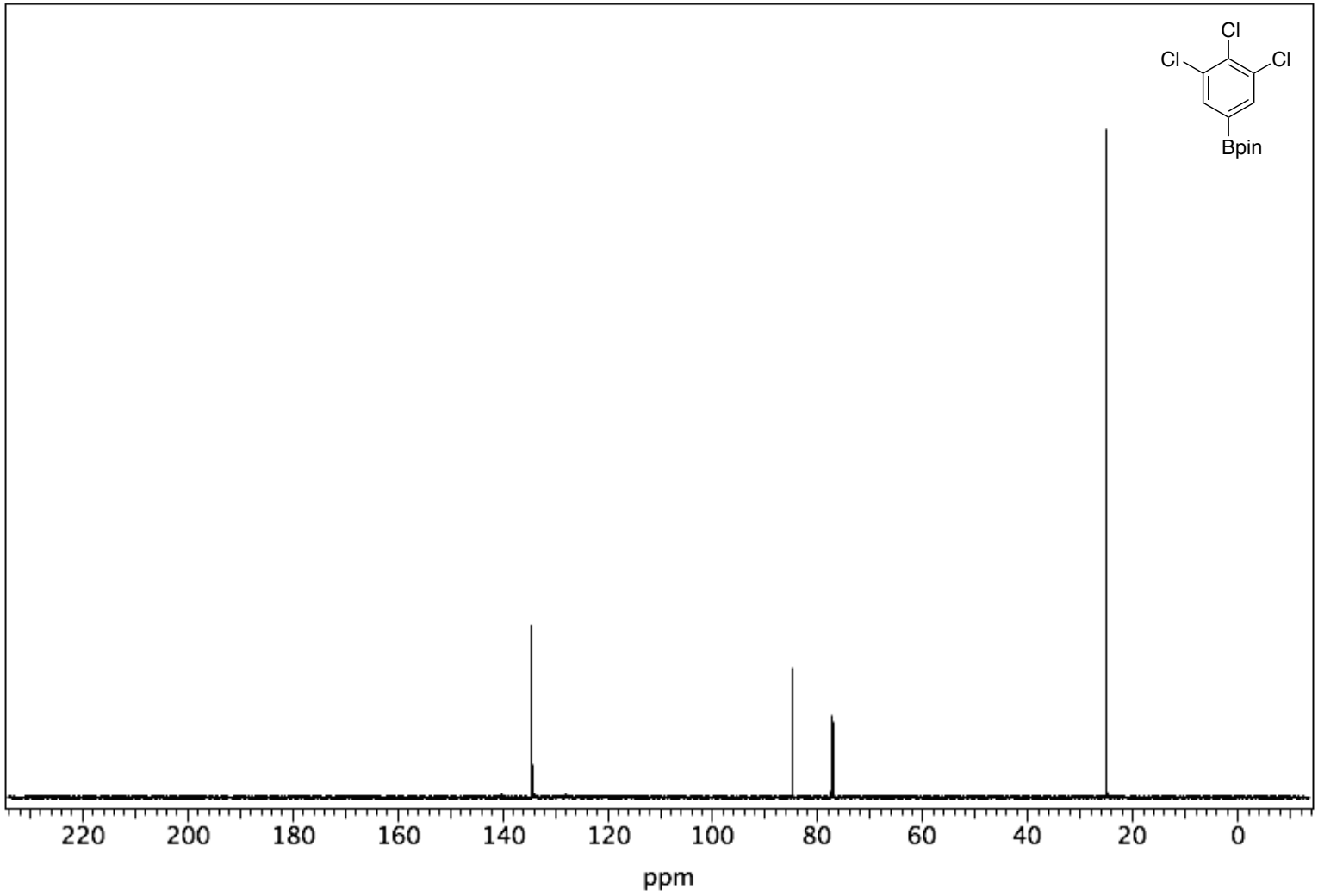


Figure A2. 125 MHz ^{13}C NMR of **2.1a** in $CDCl_3$

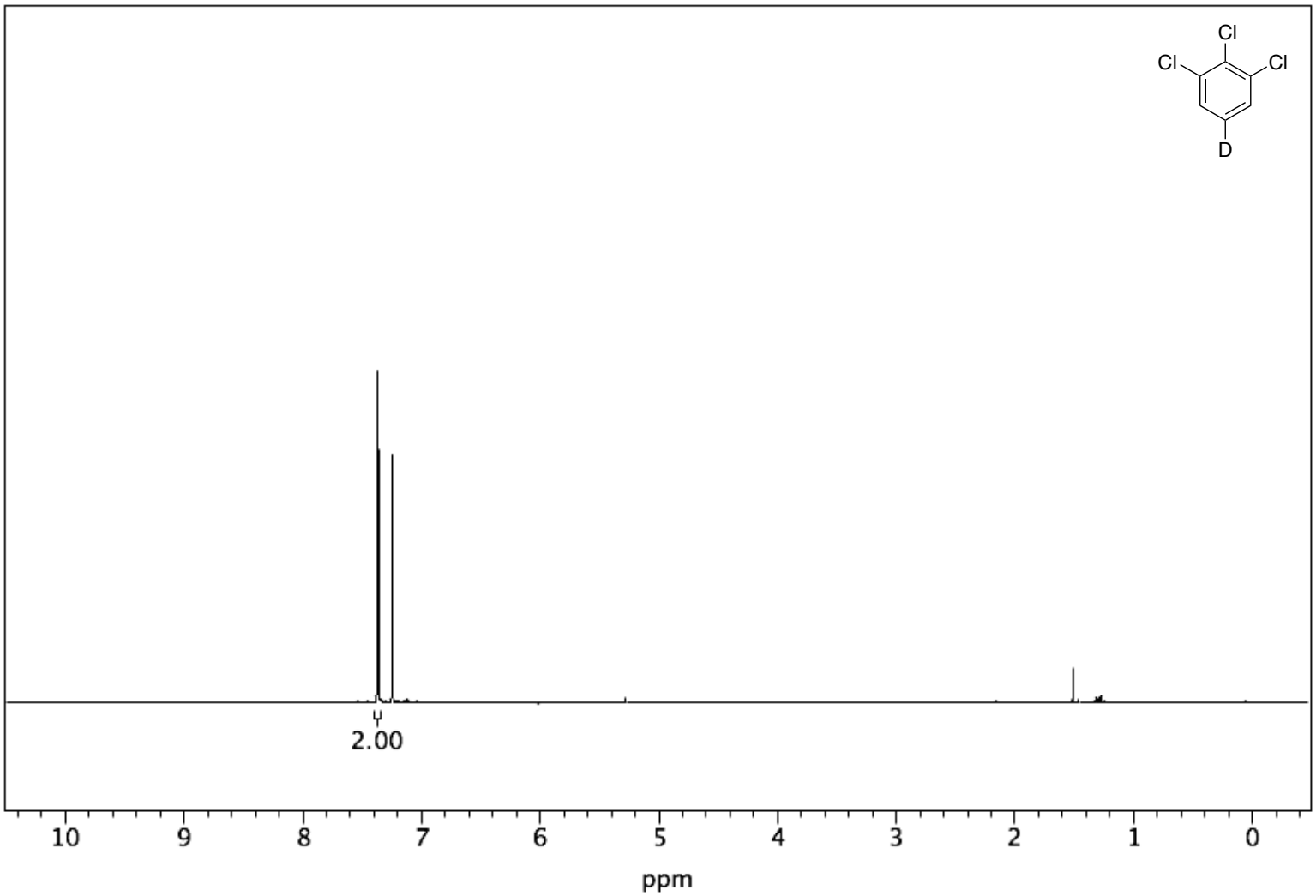


Figure A3. 500 MHz ^{1}H NMR of **2.1b** in $CDCl_3$

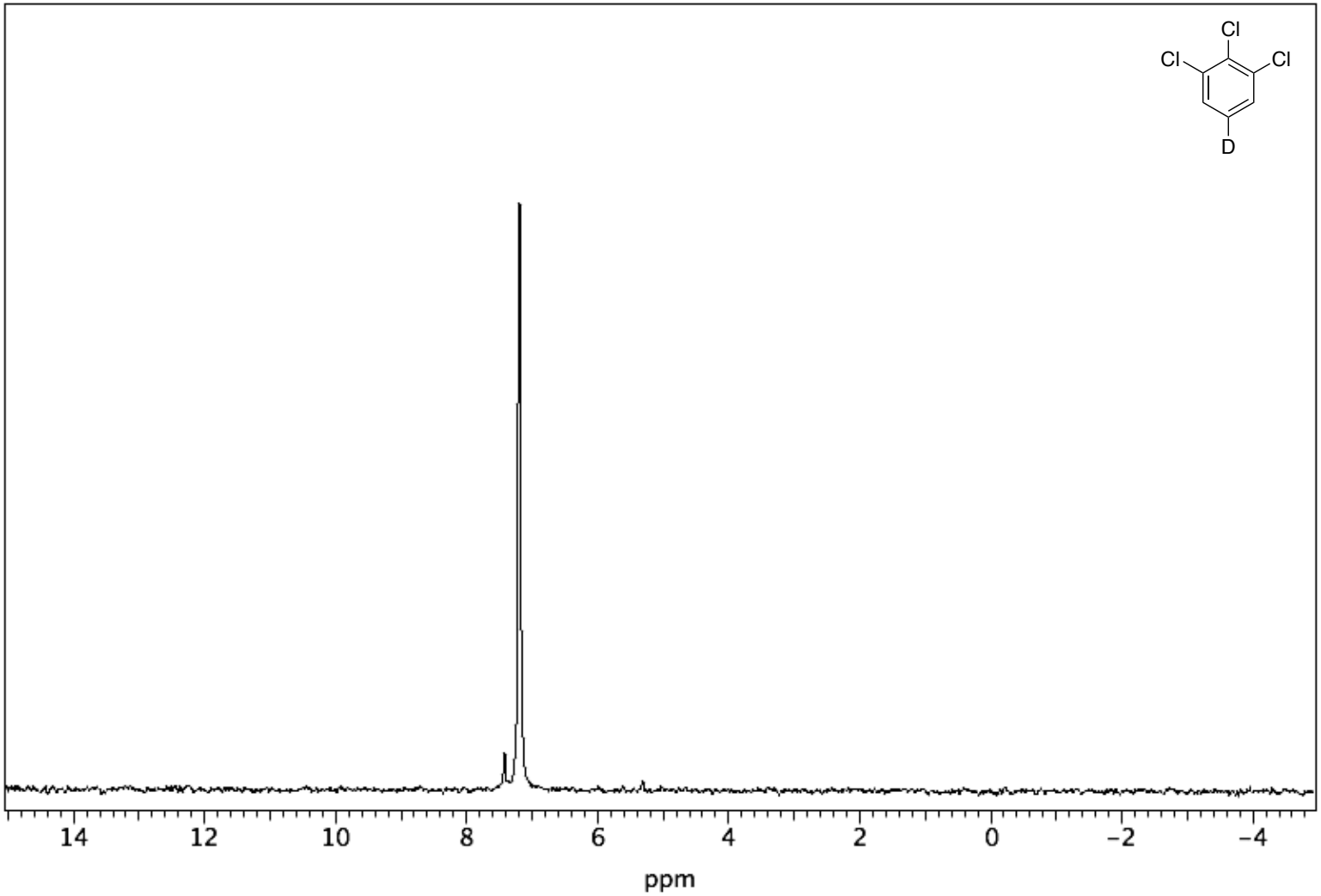


Figure A4. 76.75 MHz ^{2}H NMR of **2.1b** in CH_2Cl_2

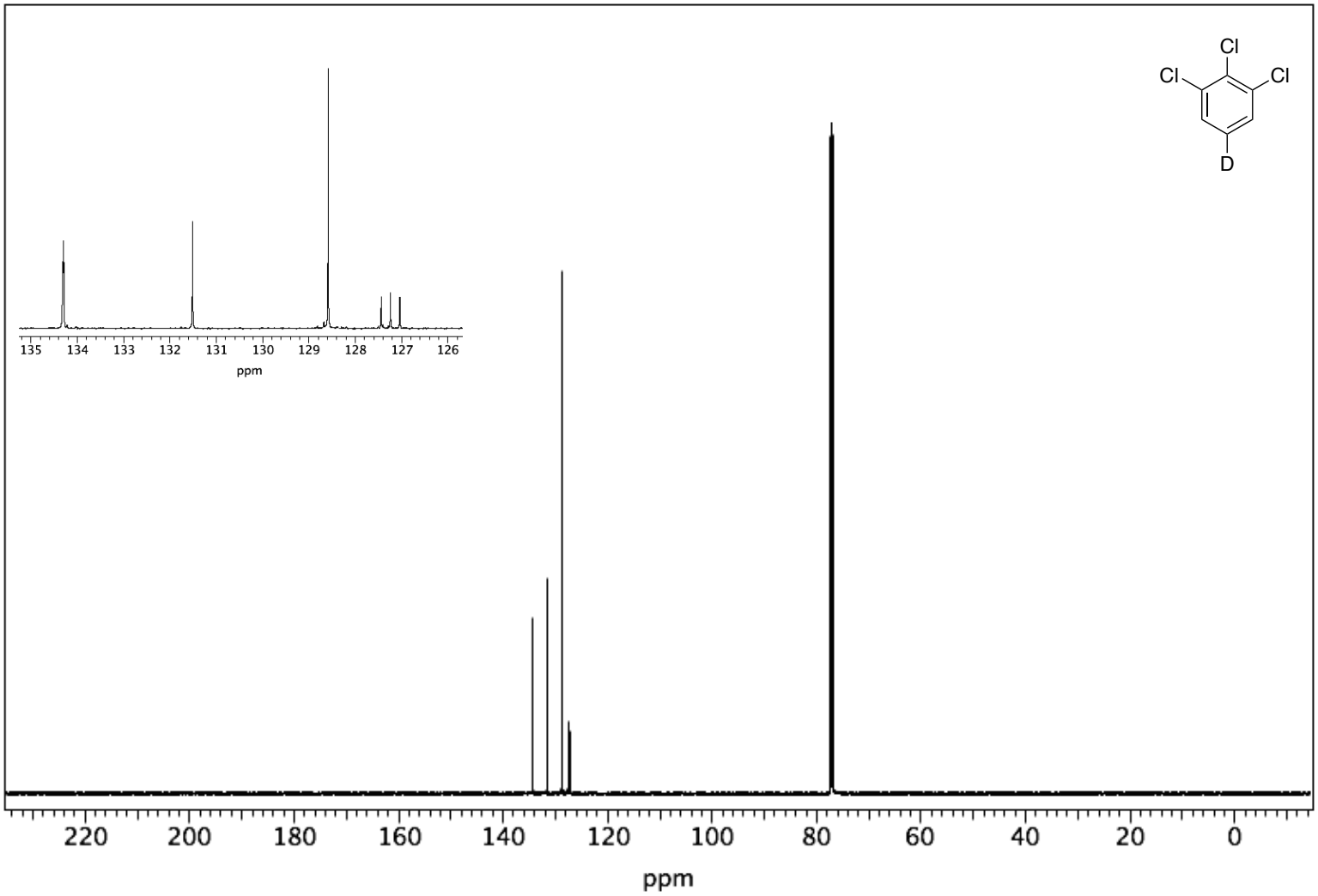


Figure A5. 125 MHz ^{13}C NMR of **2.1b** in $CDCl_3$

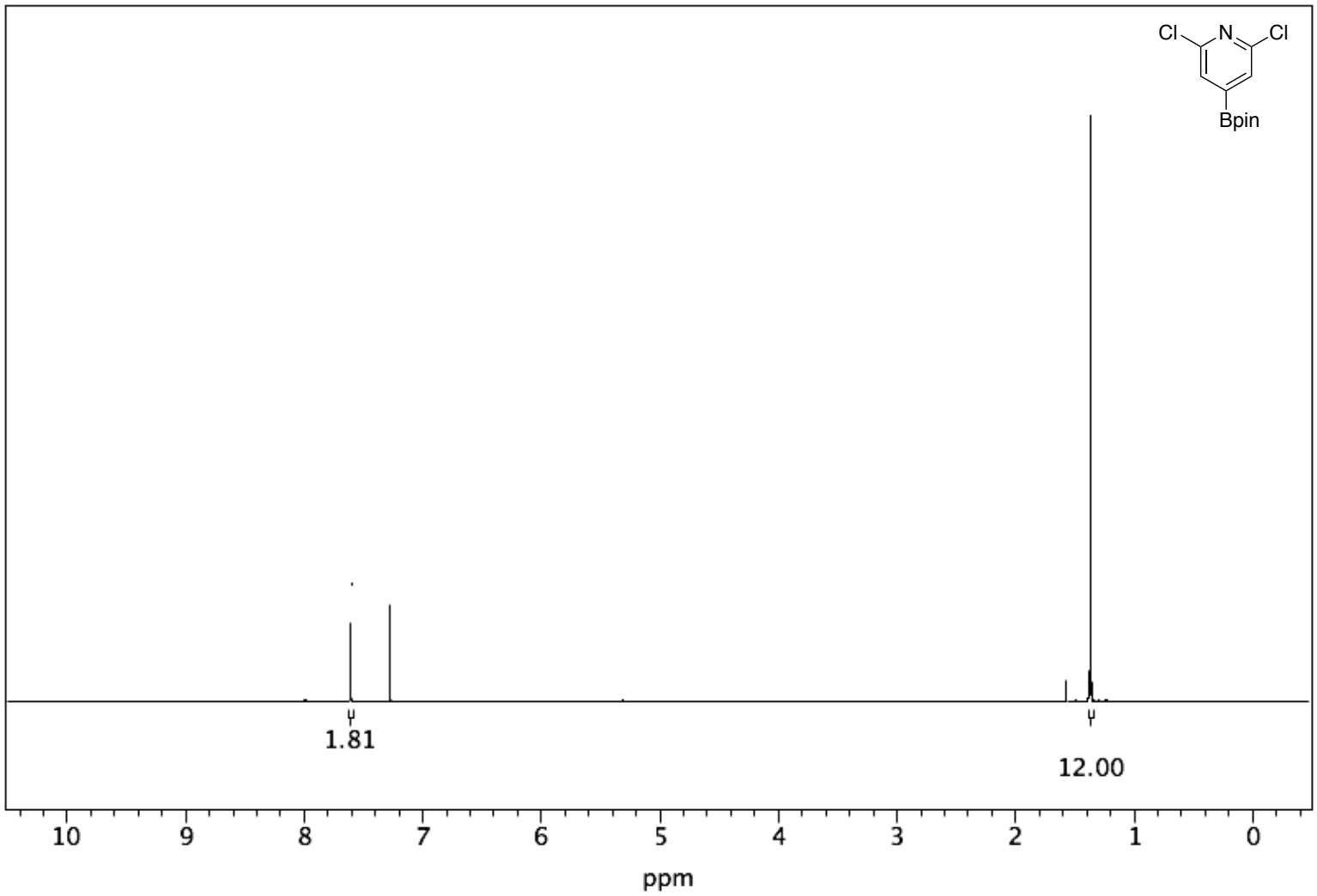


Figure A6. 500 MHz ^{1}H NMR of **2.2a** in $CDCl_3$

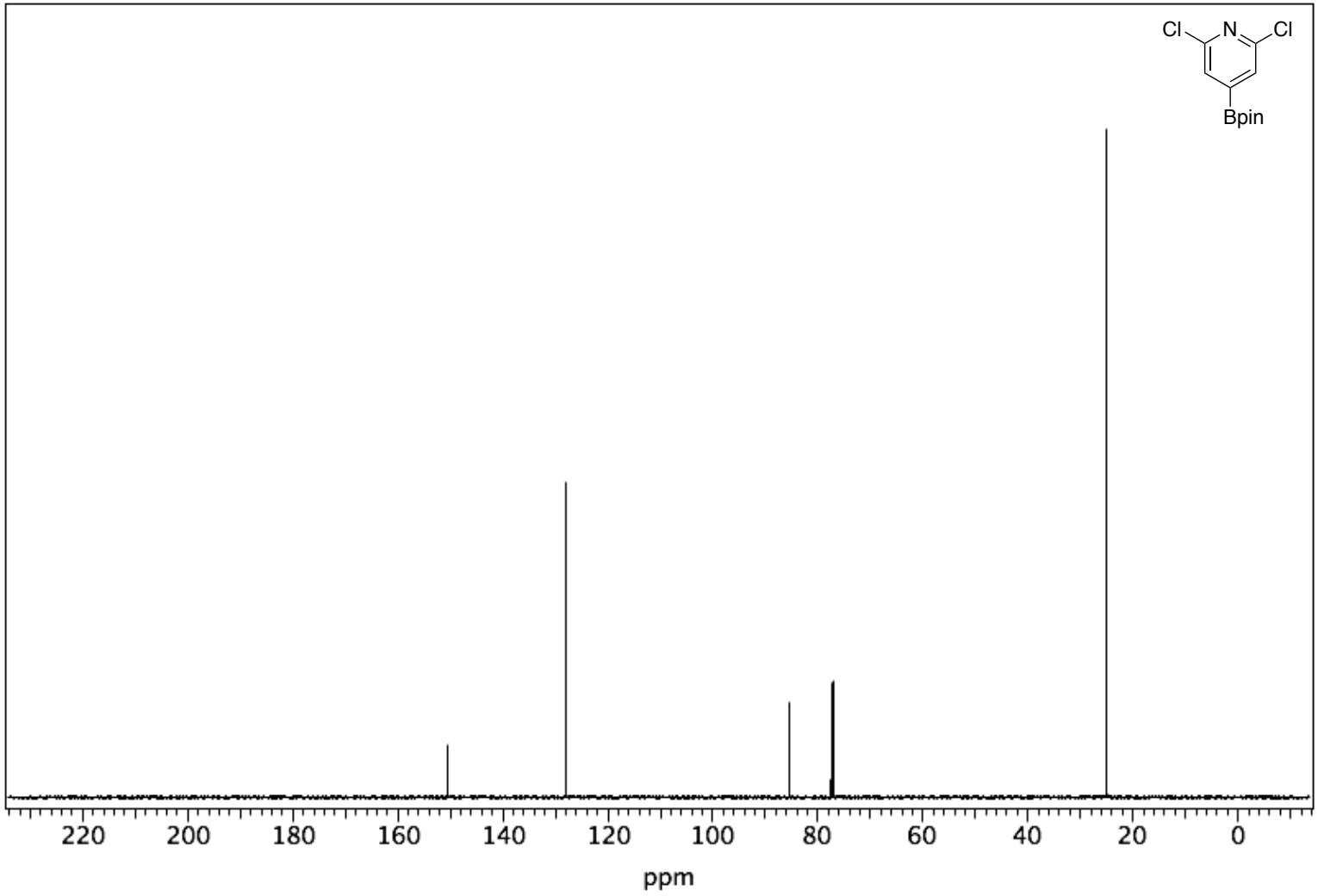


Figure A7. 125 MHz ^{12}C NMR of **2.2a** in $CDCl_3$

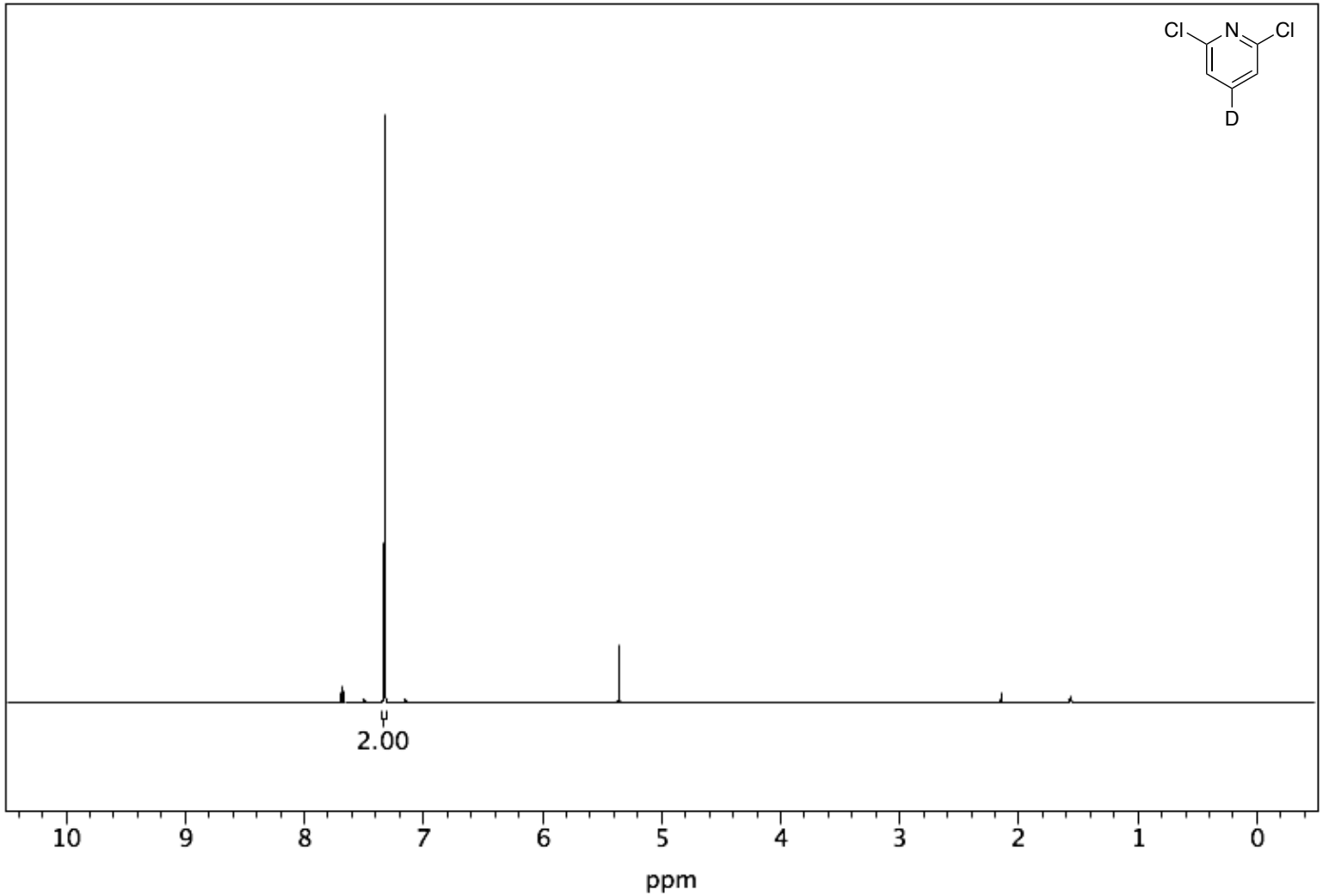


Figure A8. 500 MHz ^{1}H NMR of **2.2b** in $CDCl_3$

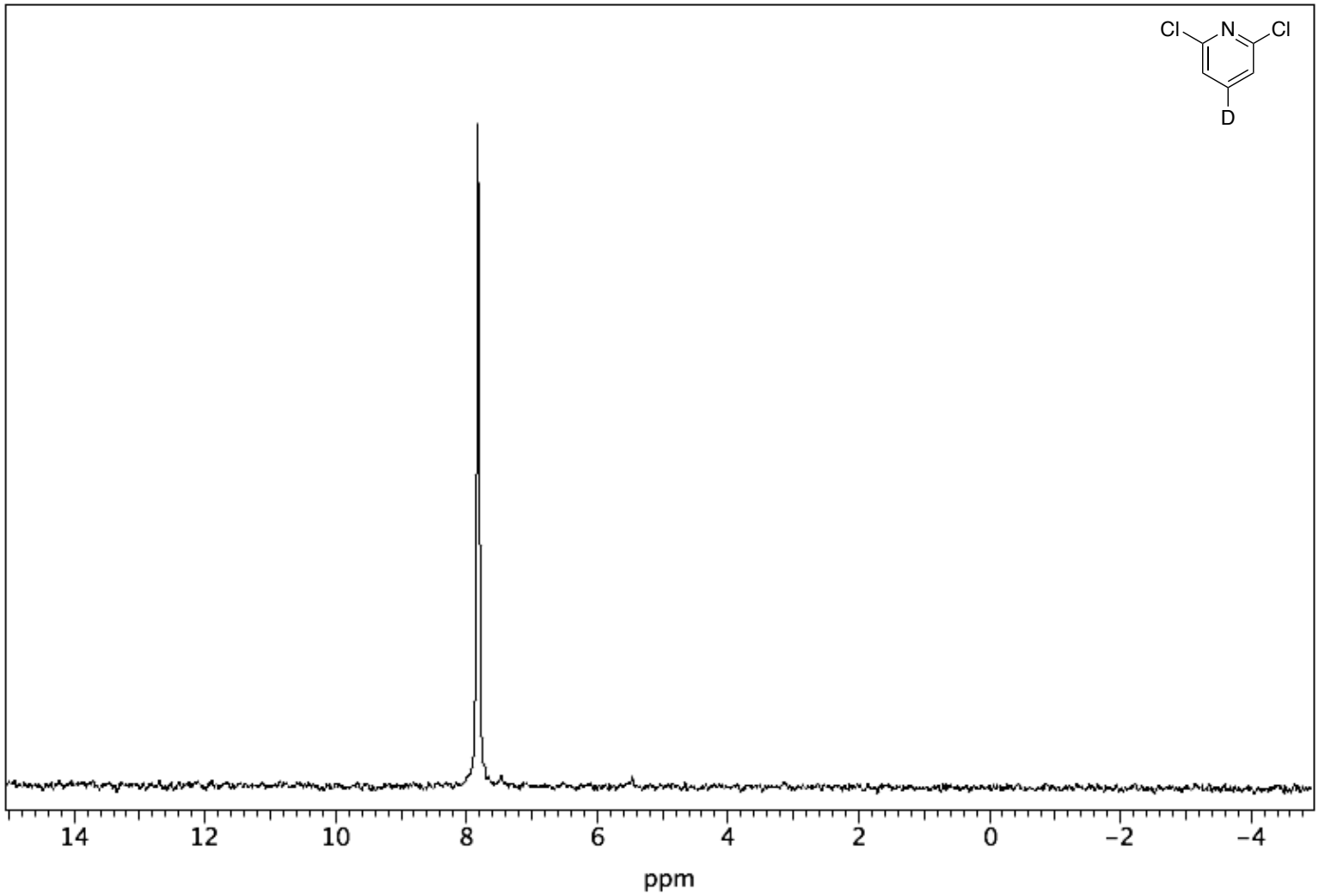


Figure A9. 76.75 MHz ^{2}H NMR of **2.2b** in CH_2Cl_2

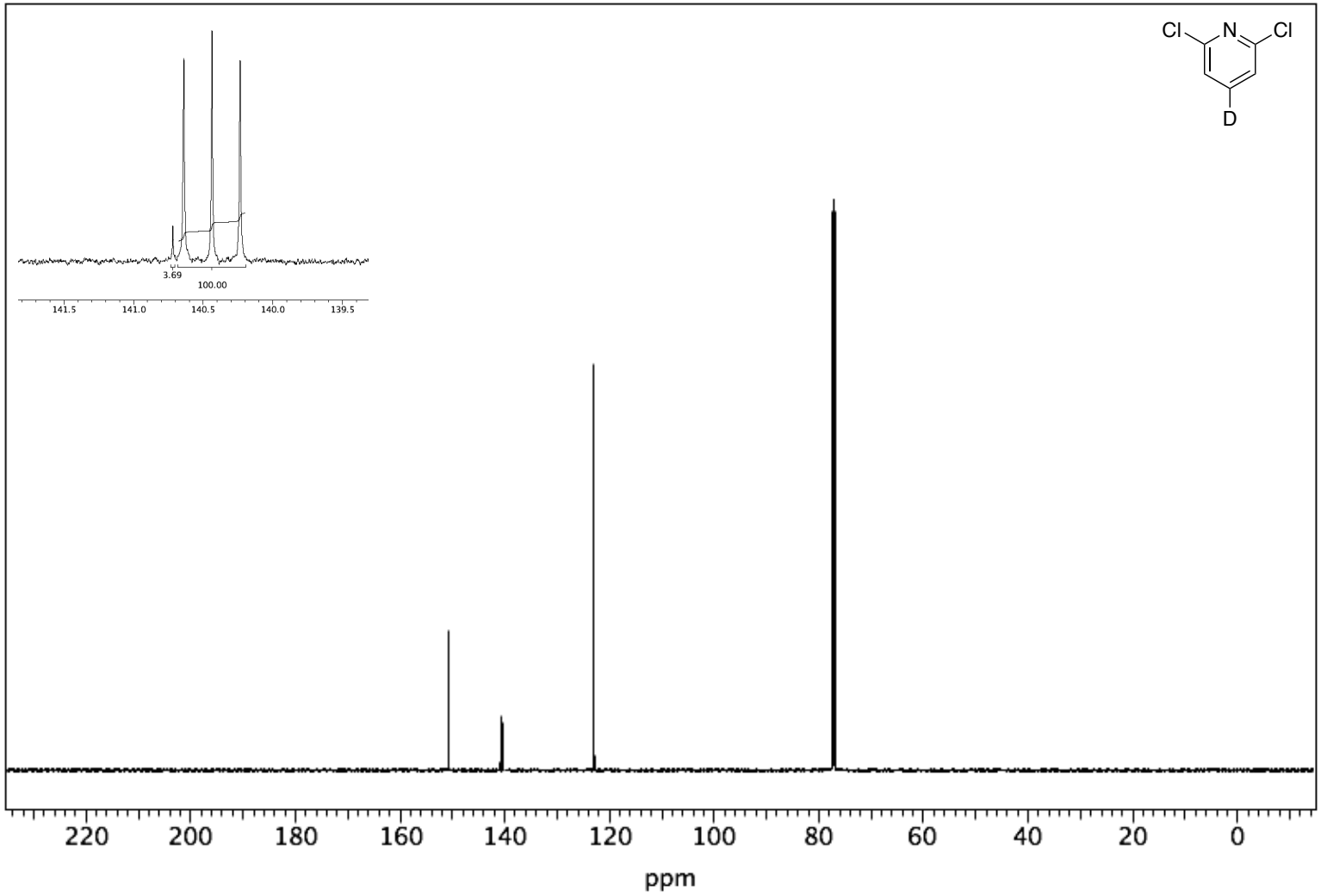


Figure A10. 125 MHz ^{13}C NMR of **2.2b** in $CDCl_3$

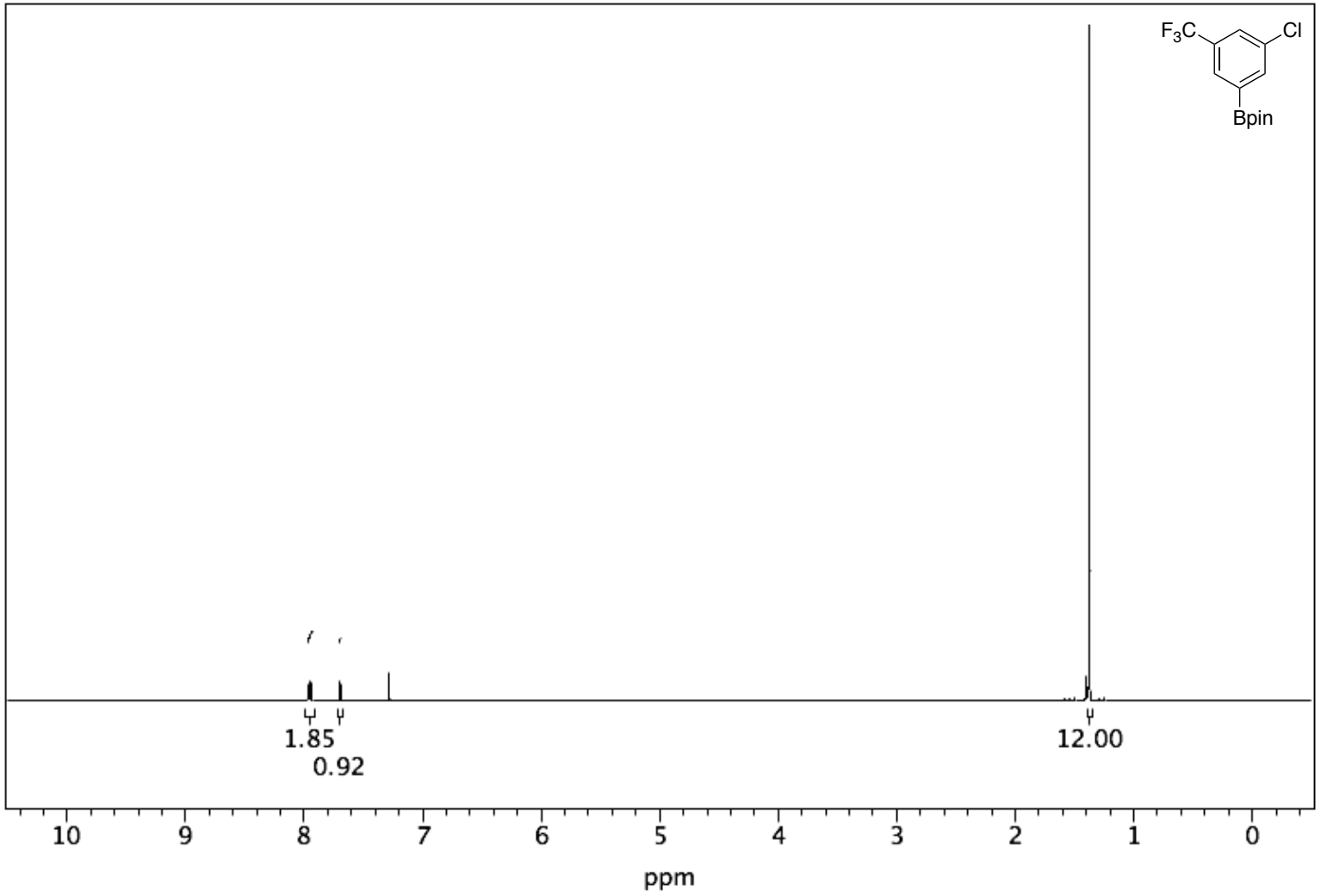


Figure A11. 500 MHz ^{1}H NMR of **2.3a** in $CDCl_3$

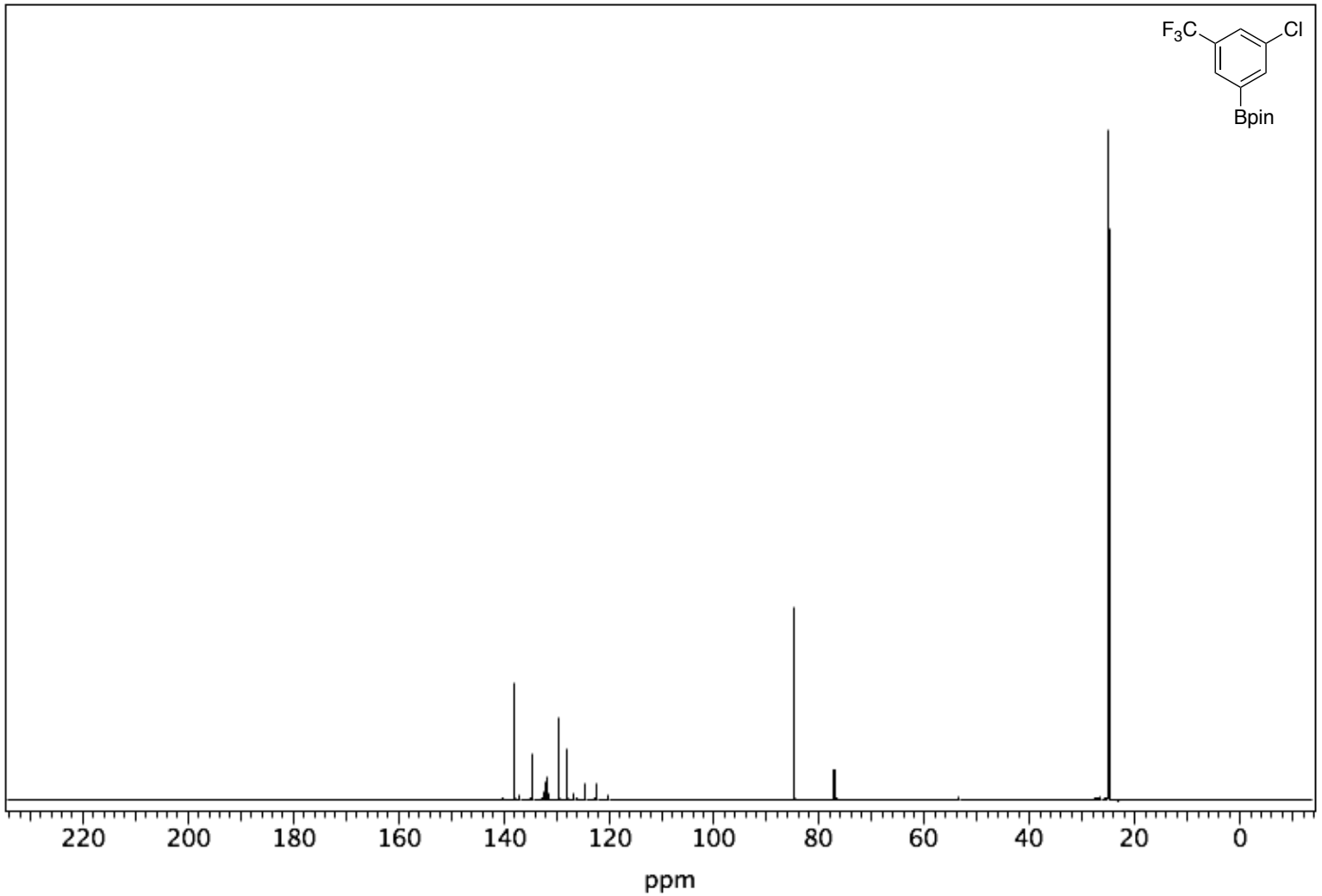


Figure A12. 125 MHz ^{13}C NMR of **2.3a** in $CDCl_3$

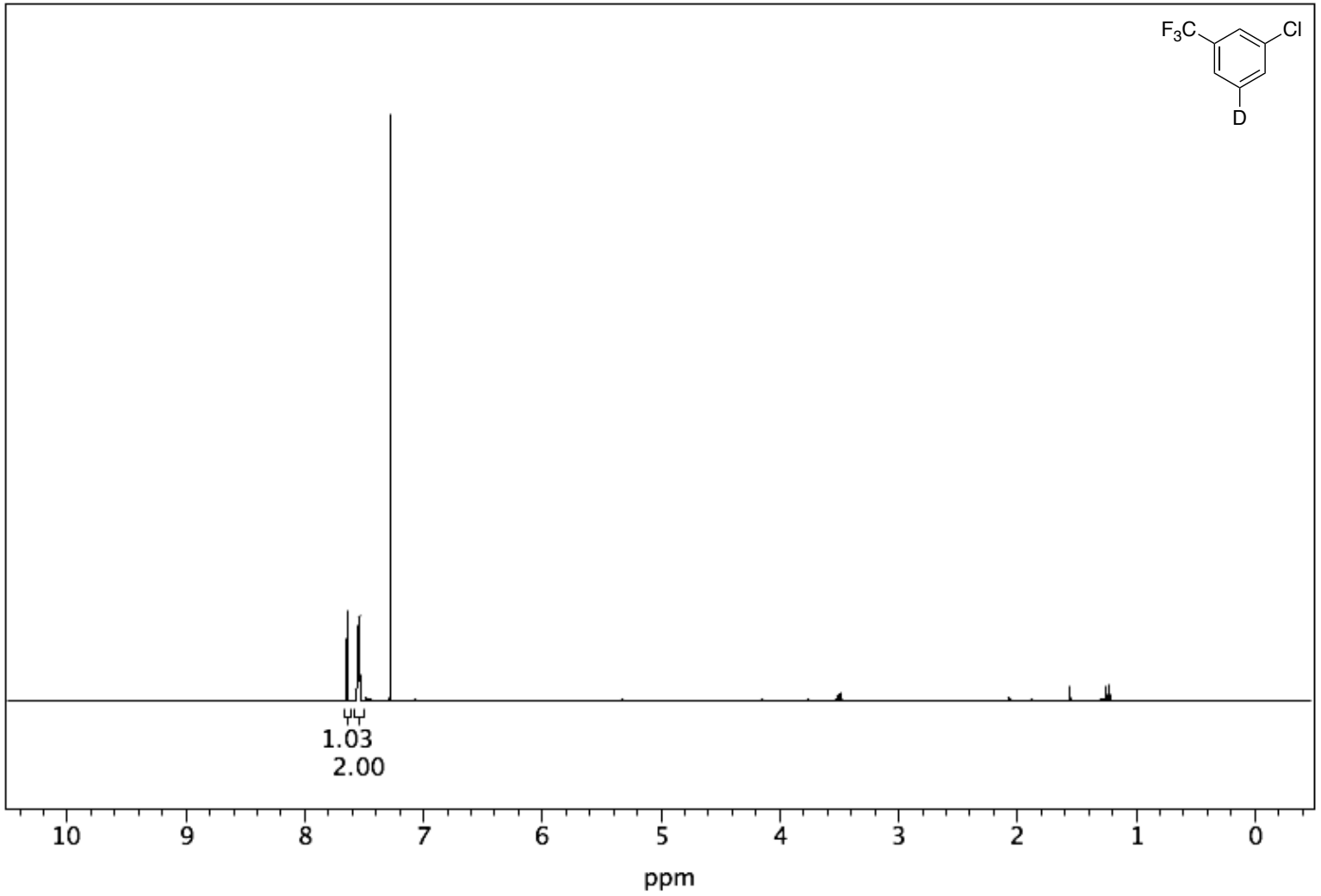


Figure A13. 500 MHz ^{1}H NMR of **2.3b** in $CDCl_3$

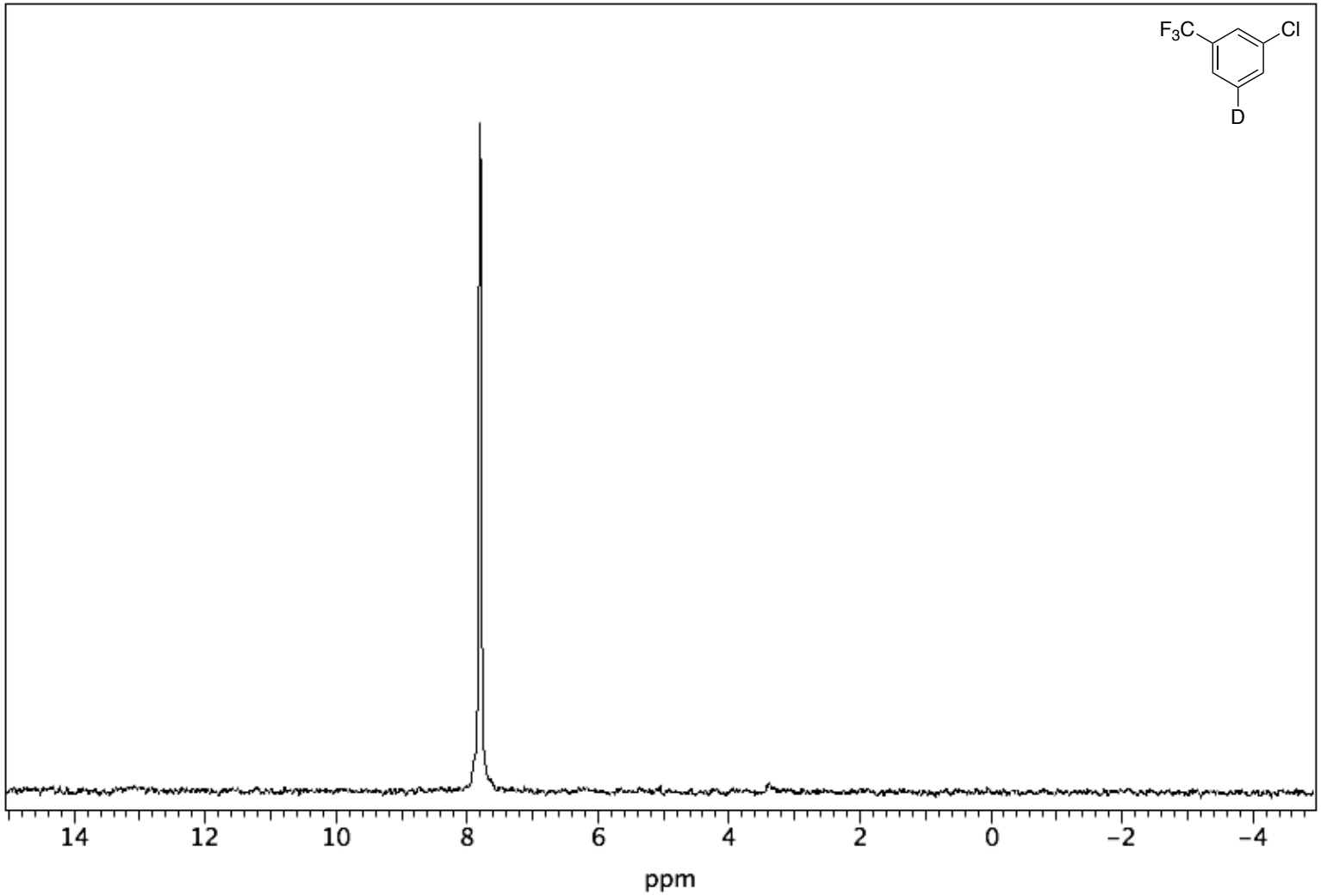


Figure A14. 76.75 MHz ^{1}H NMR of **2.3b** in CH_2Cl_2

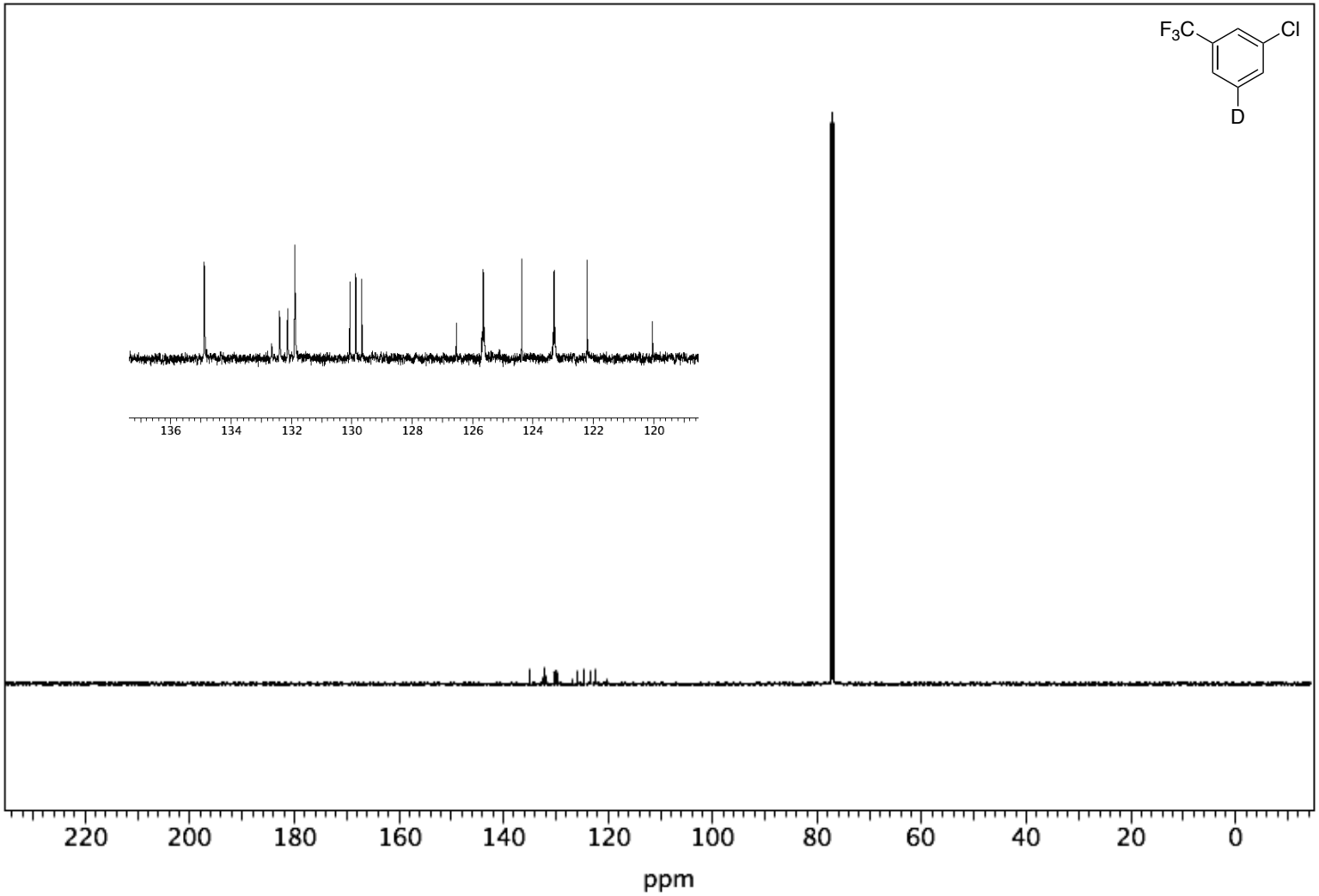


Figure A15. 125 MHz ^{13}C NMR of **2.3b** in $CDCl_3$

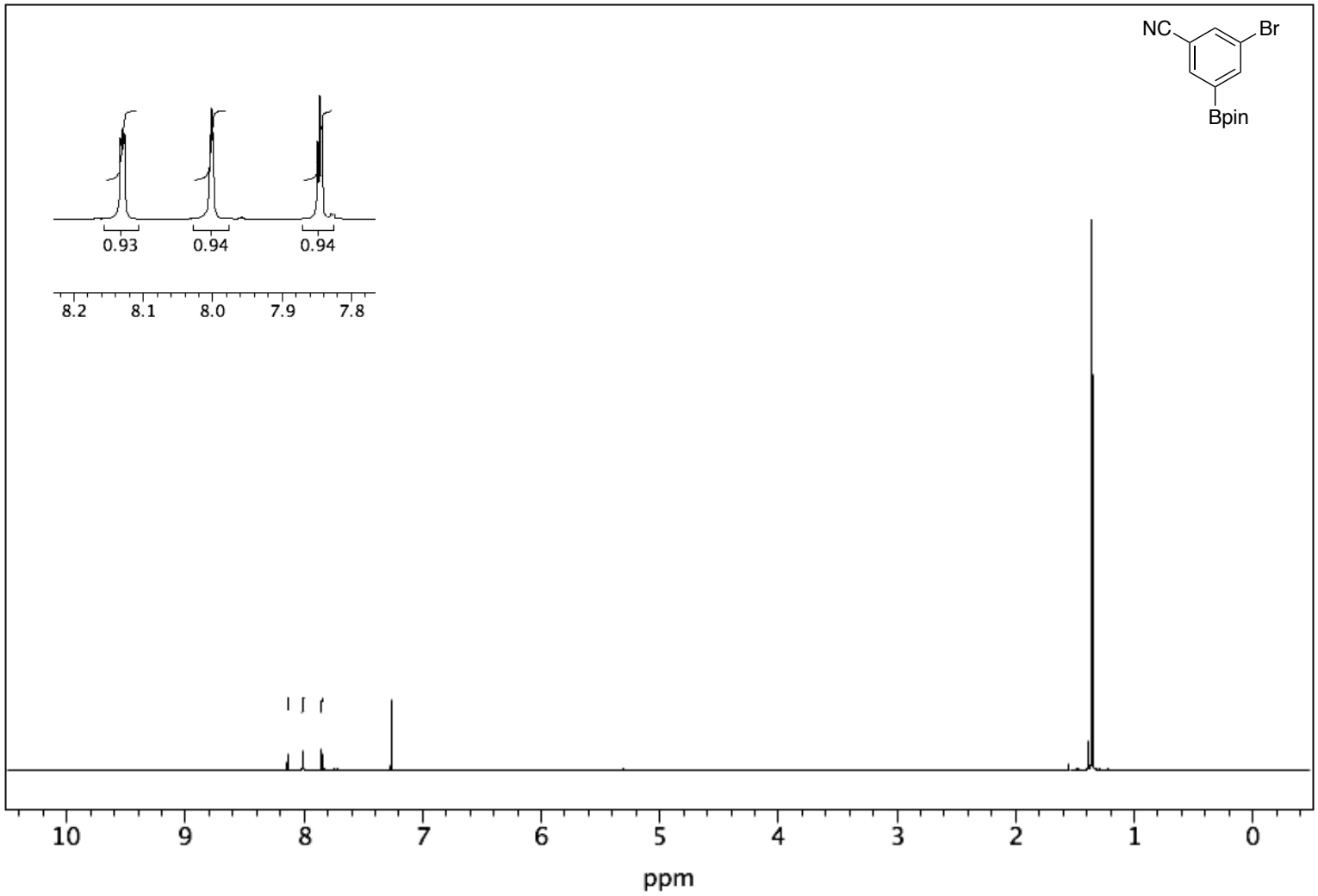


Figure A16. 500 MHz ^{1}H NMR of **2.4a** in $CDCl_3$

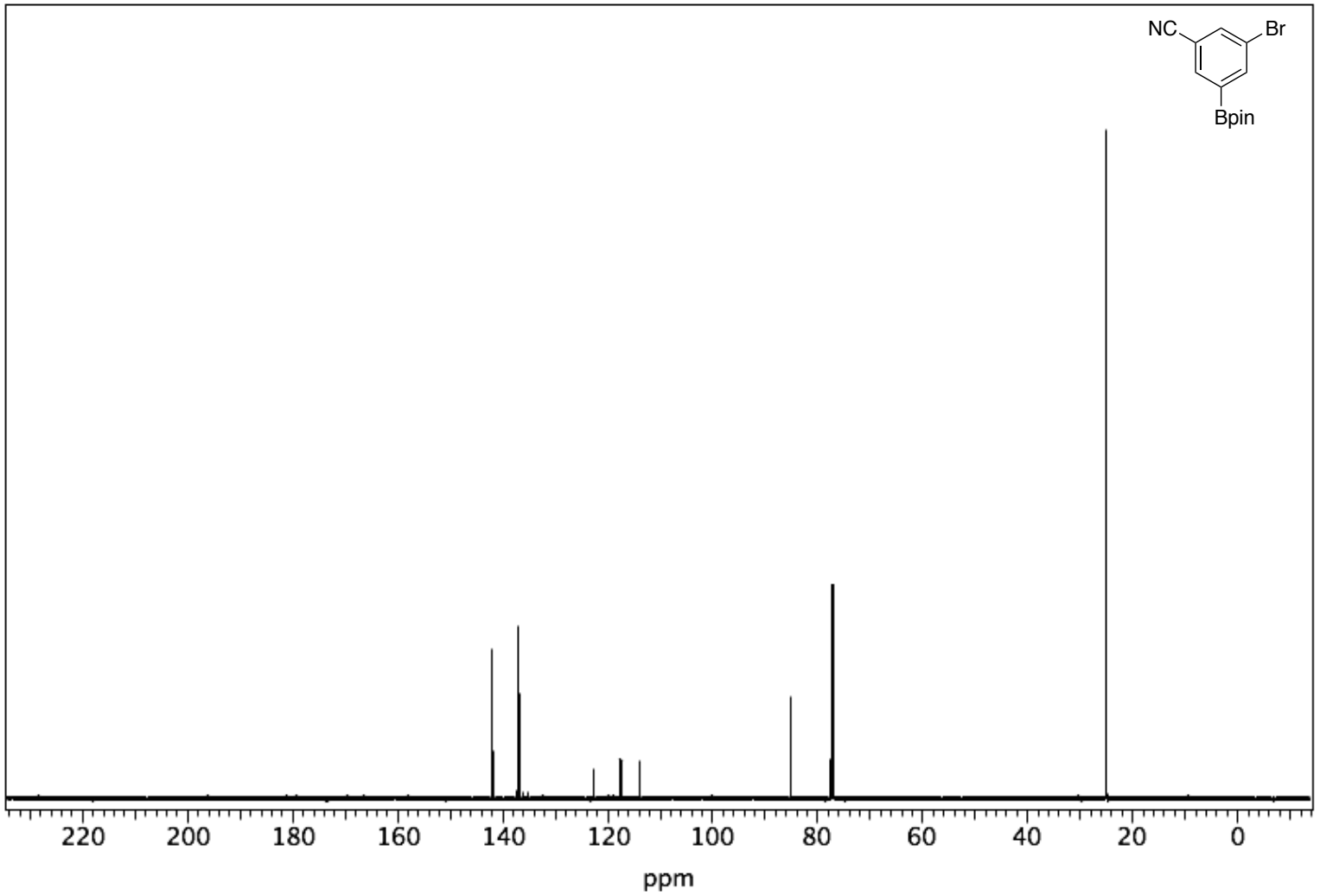


Figure A17. 125 MHz ^{13}C NMR of **2.4a** in $CDCl_3$

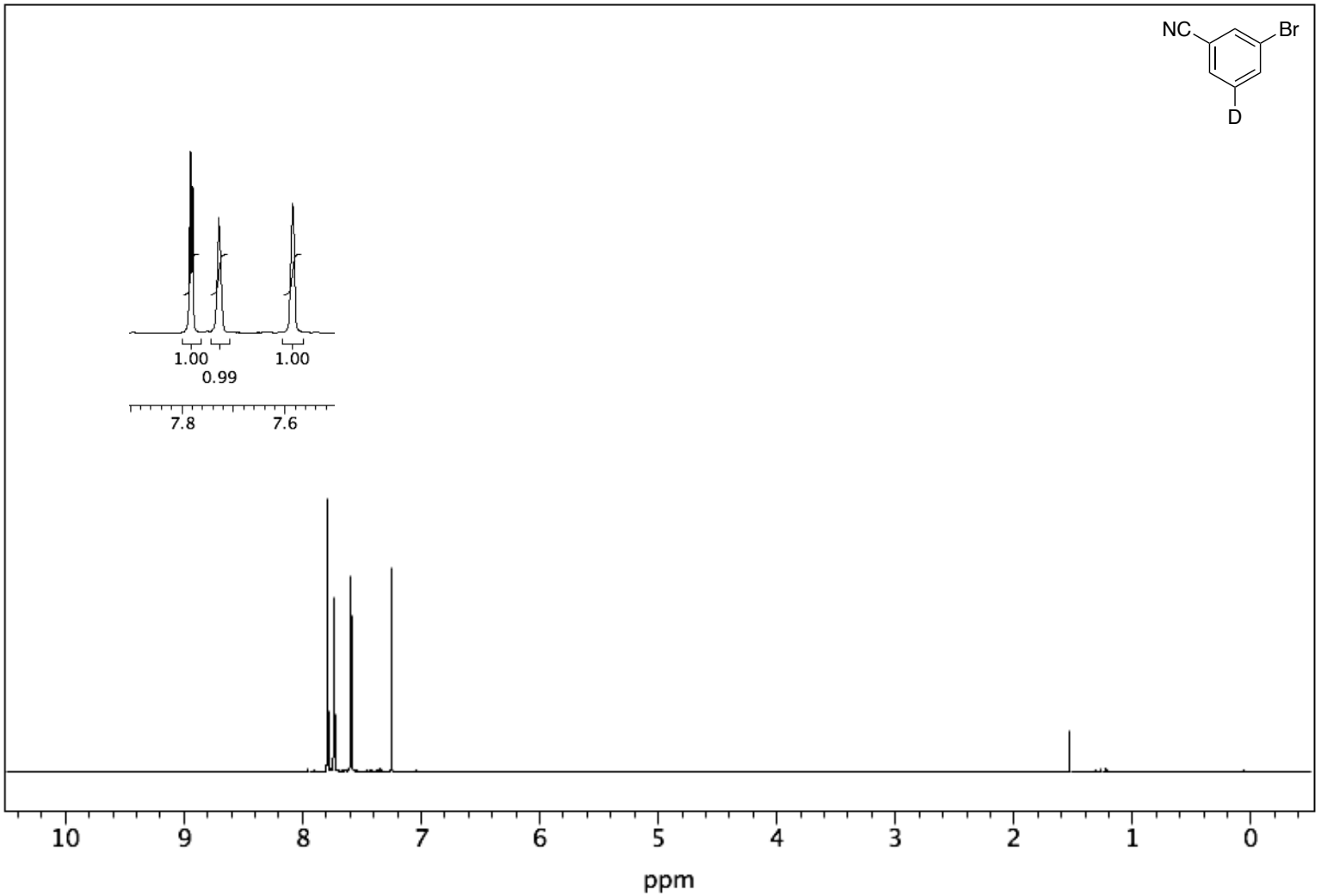


Figure A18. 500 MHz ^{1}H NMR of **2.4b** in $CDCl_3$

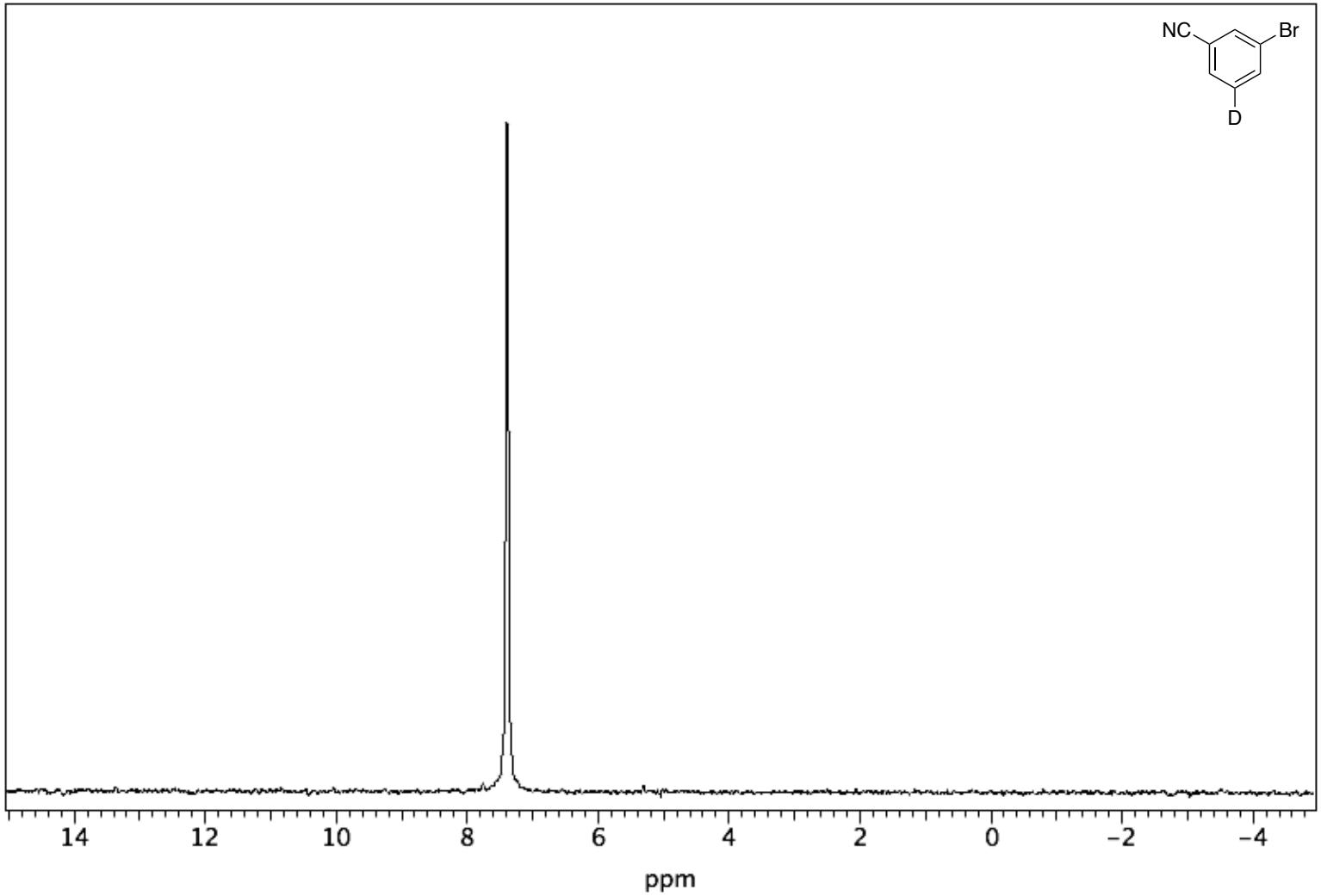


Figure A19. 76.75 MHz ^{2}H NMR of **2.4b** in CH_2Cl_2

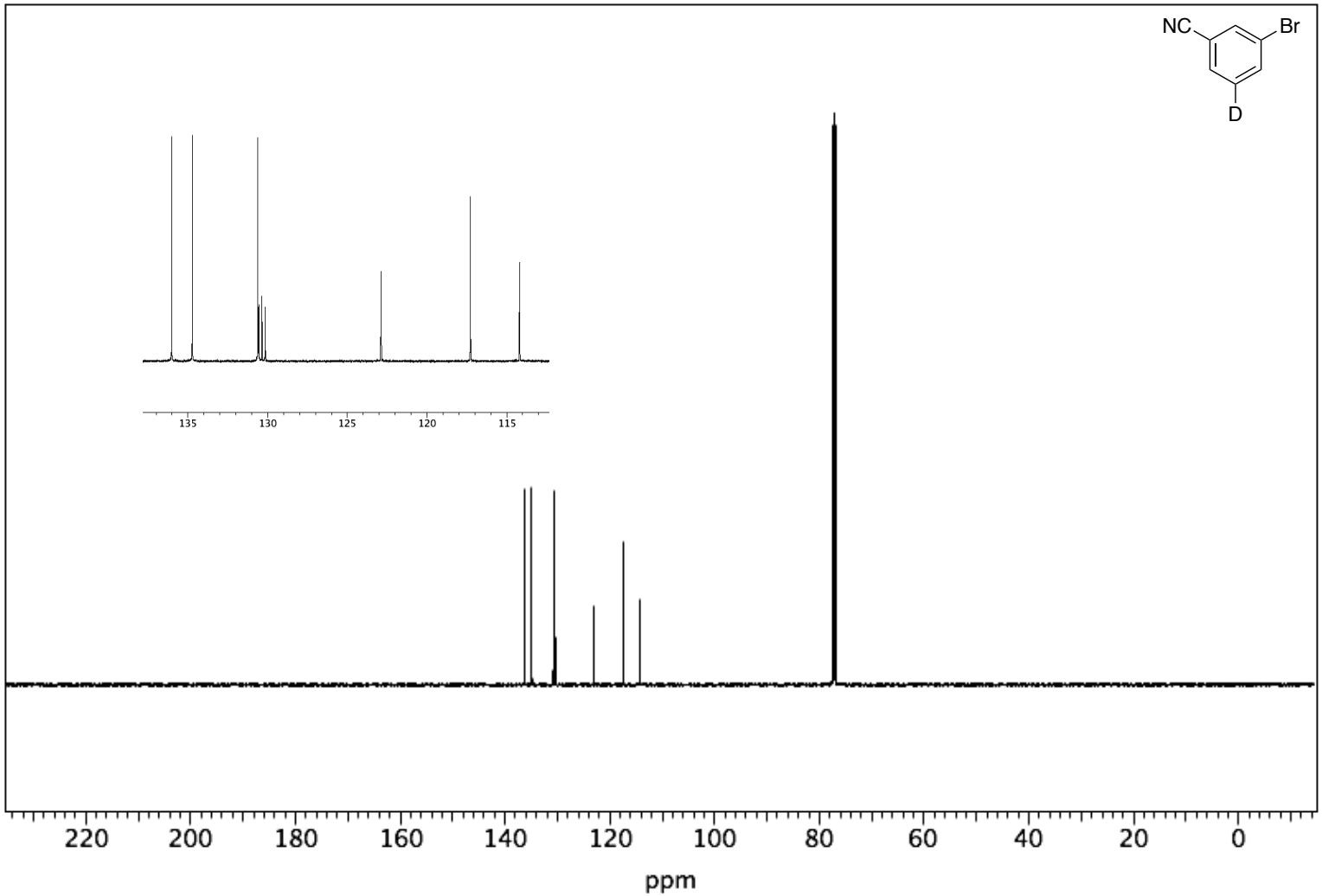


Figure A20. 125 MHz ^{13}C NMR of **2.4b** in $CDCl_3$

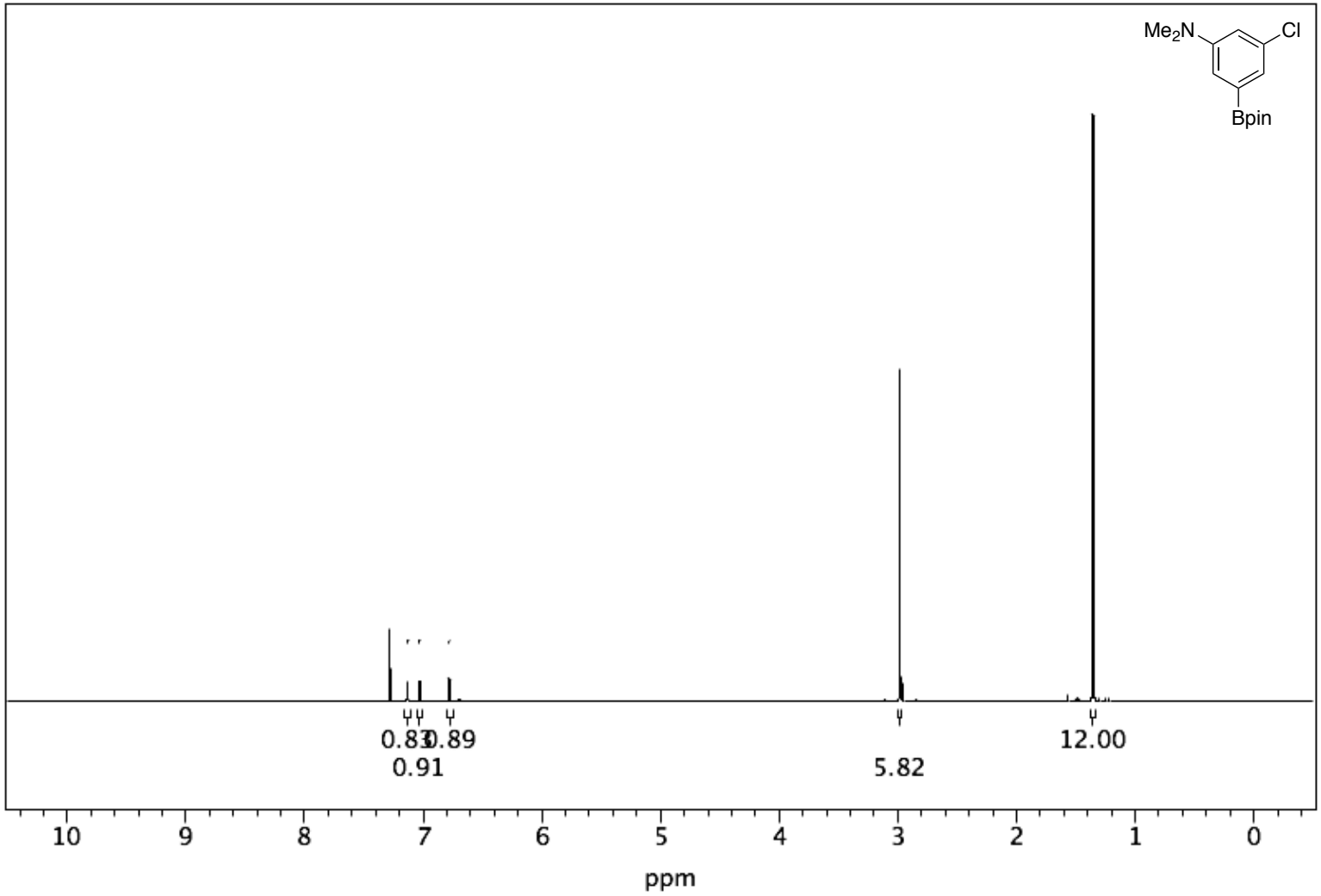


Figure A21. 500 MHz ^{1}H NMR of **2.5a** in $CDCl_3$

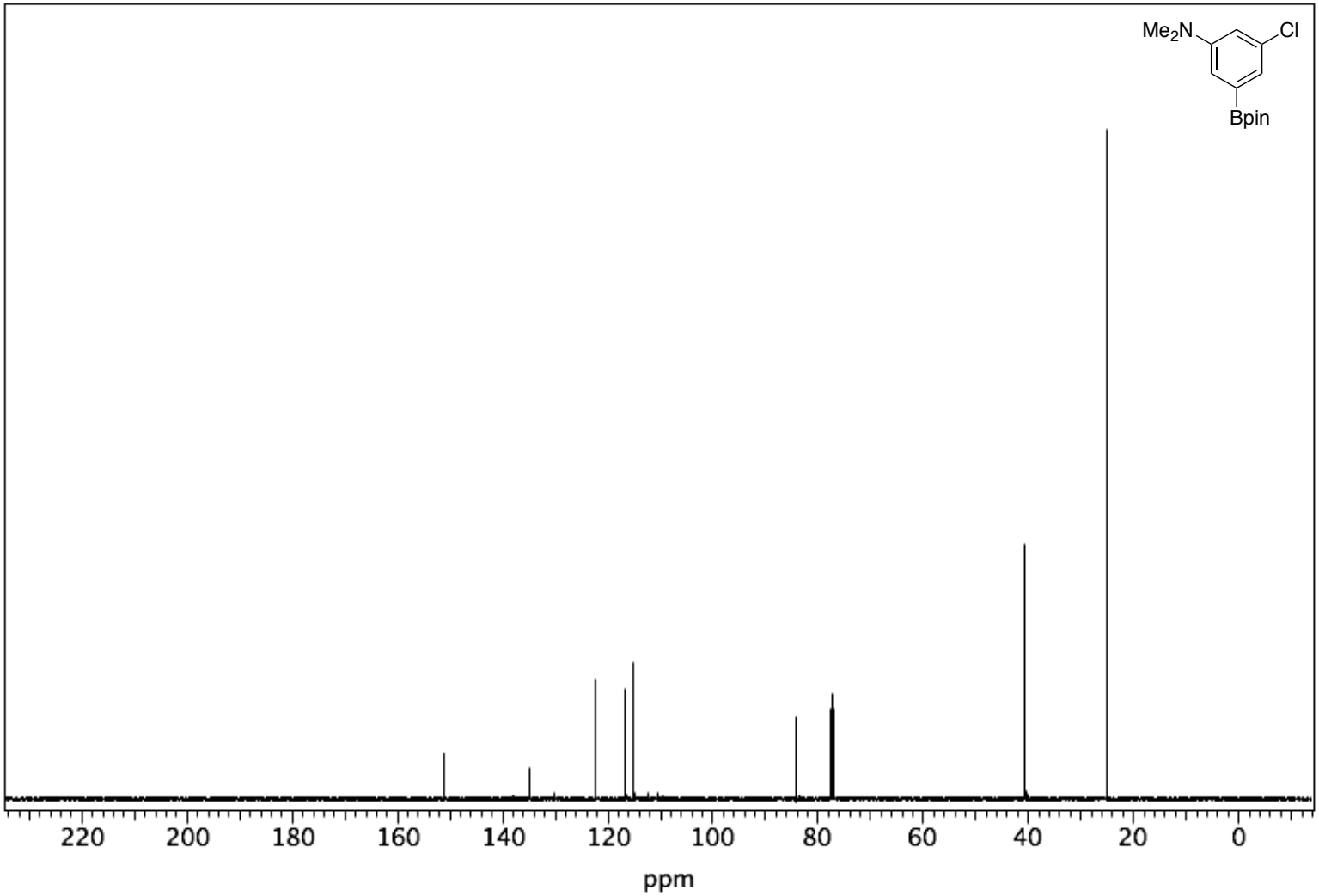


Figure A22. 125 MHz ^{13}C NMR of **2.5a** in $CDCl_3$

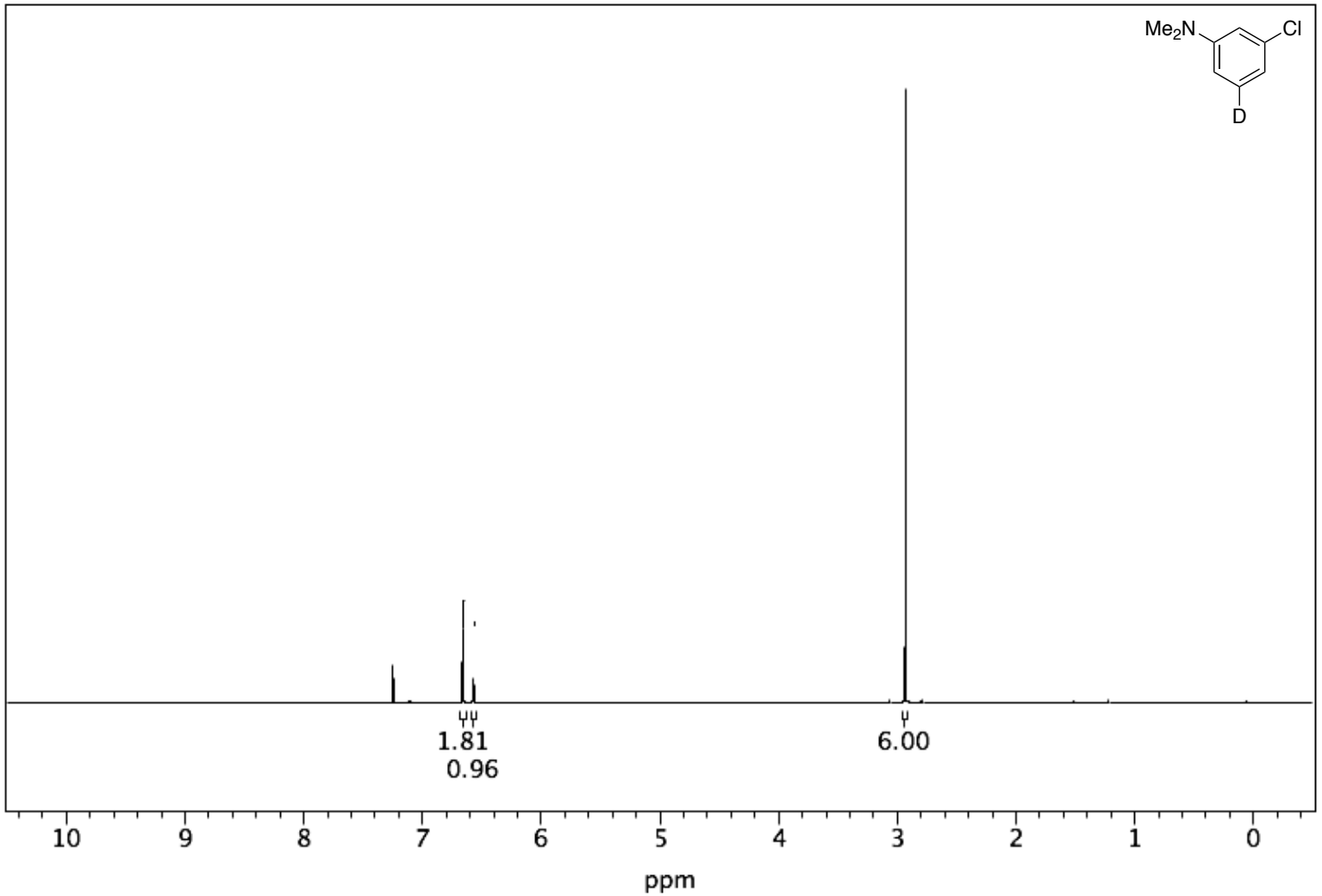


Figure A23. 500 MHz ^{1}H NMR of **2.5b** in $CDCl_3$

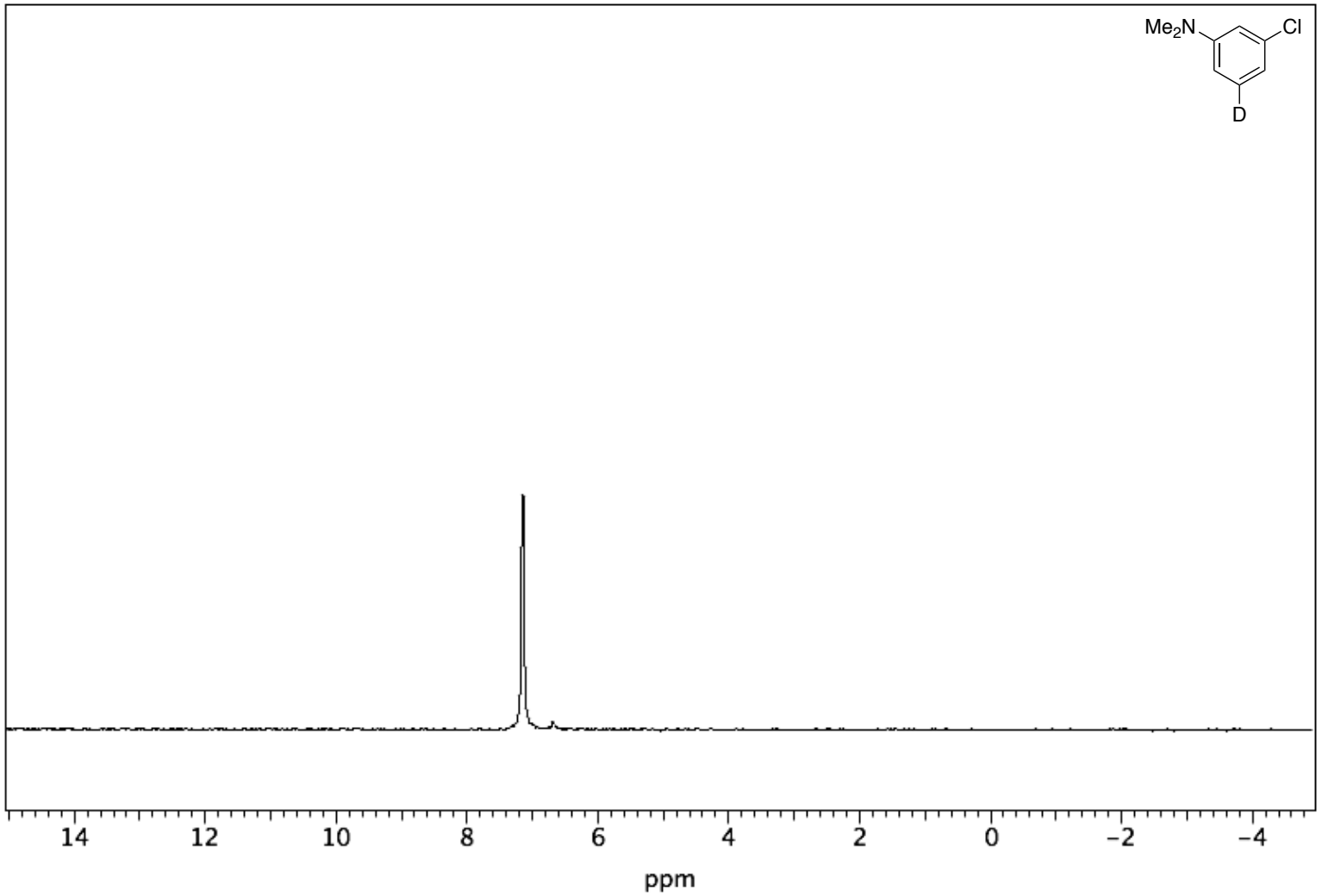


Figure A24. 76.75 MHz ^{2}H NMR of **2.5b** in CH_2Cl_2

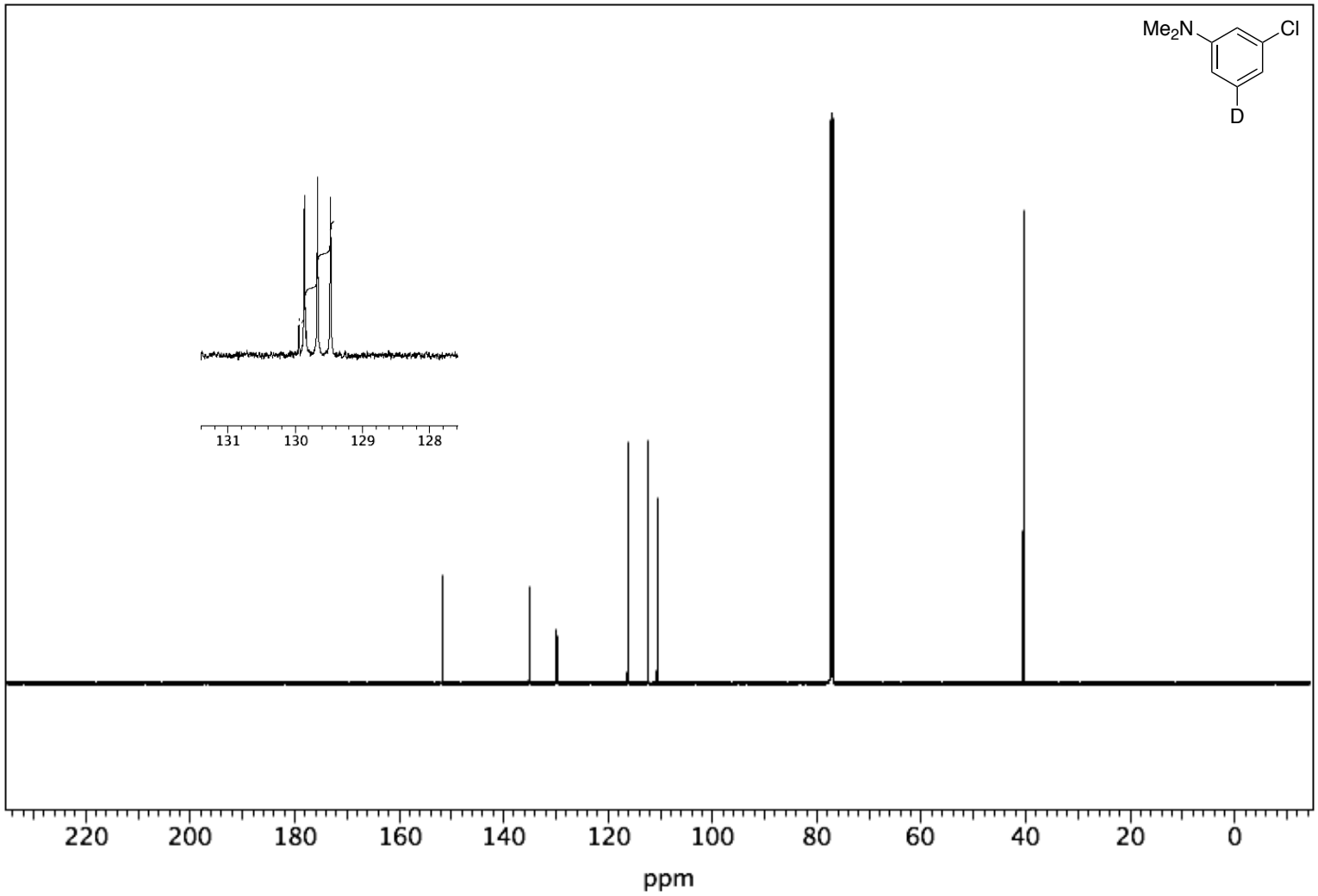


Figure A25. 125 MHz ^{13}C NMR of **2.5b** in $CDCl_3$

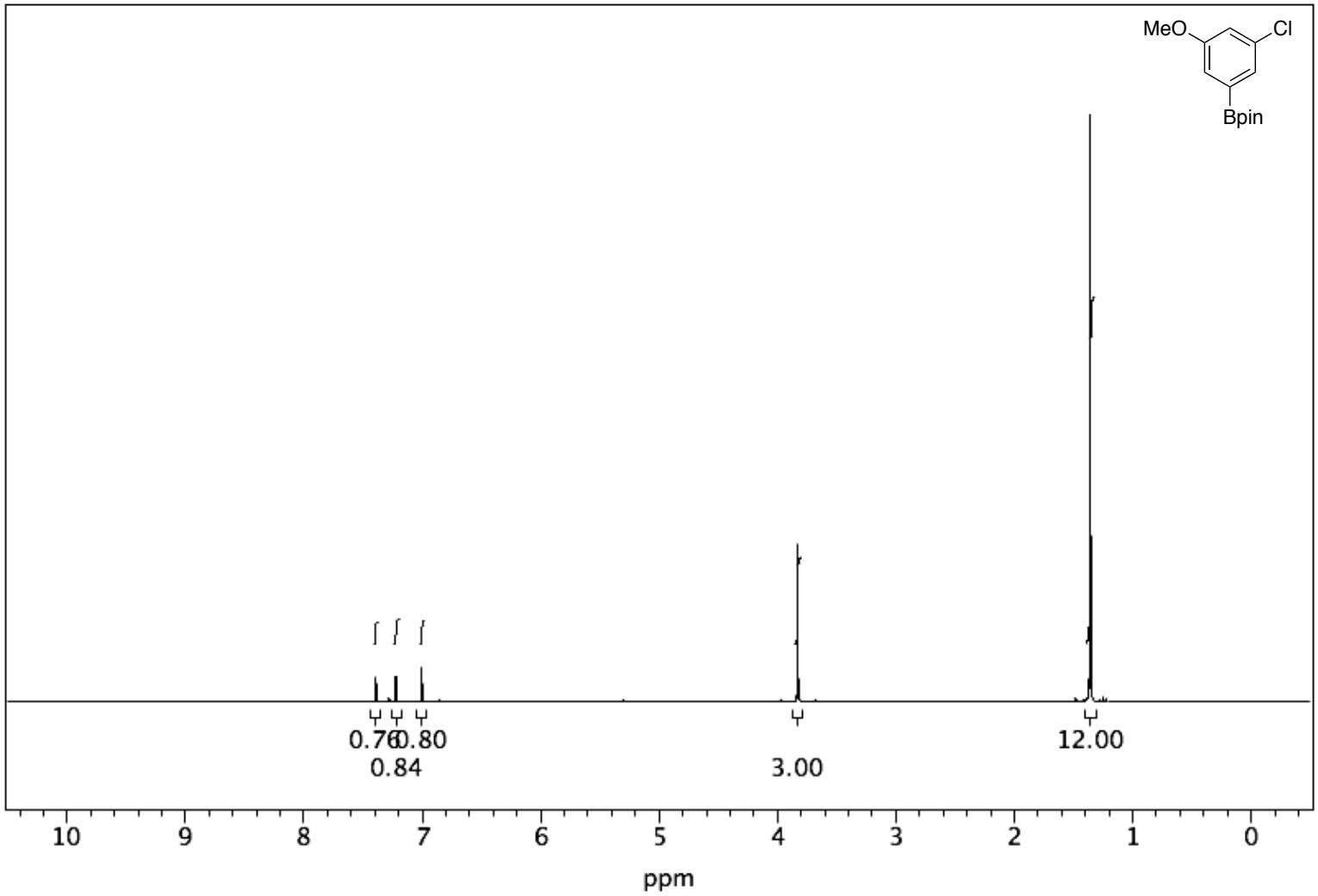


Figure A26. 500 MHz ^{1}H NMR of **2.6a** in $CDCl_3$

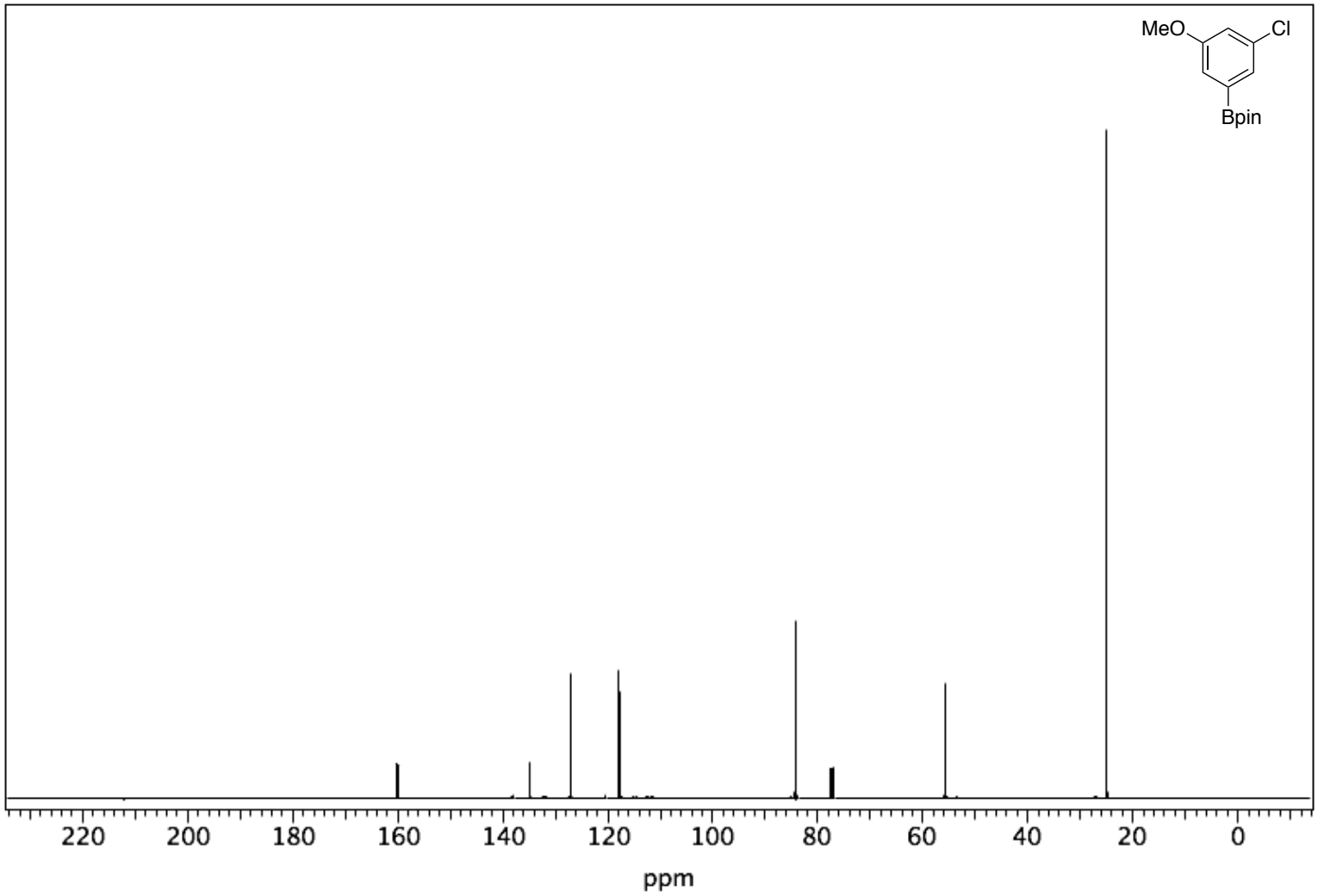


Figure A27. 125 MHz ^{13}C NMR of **2.6a** in $CDCl_3$

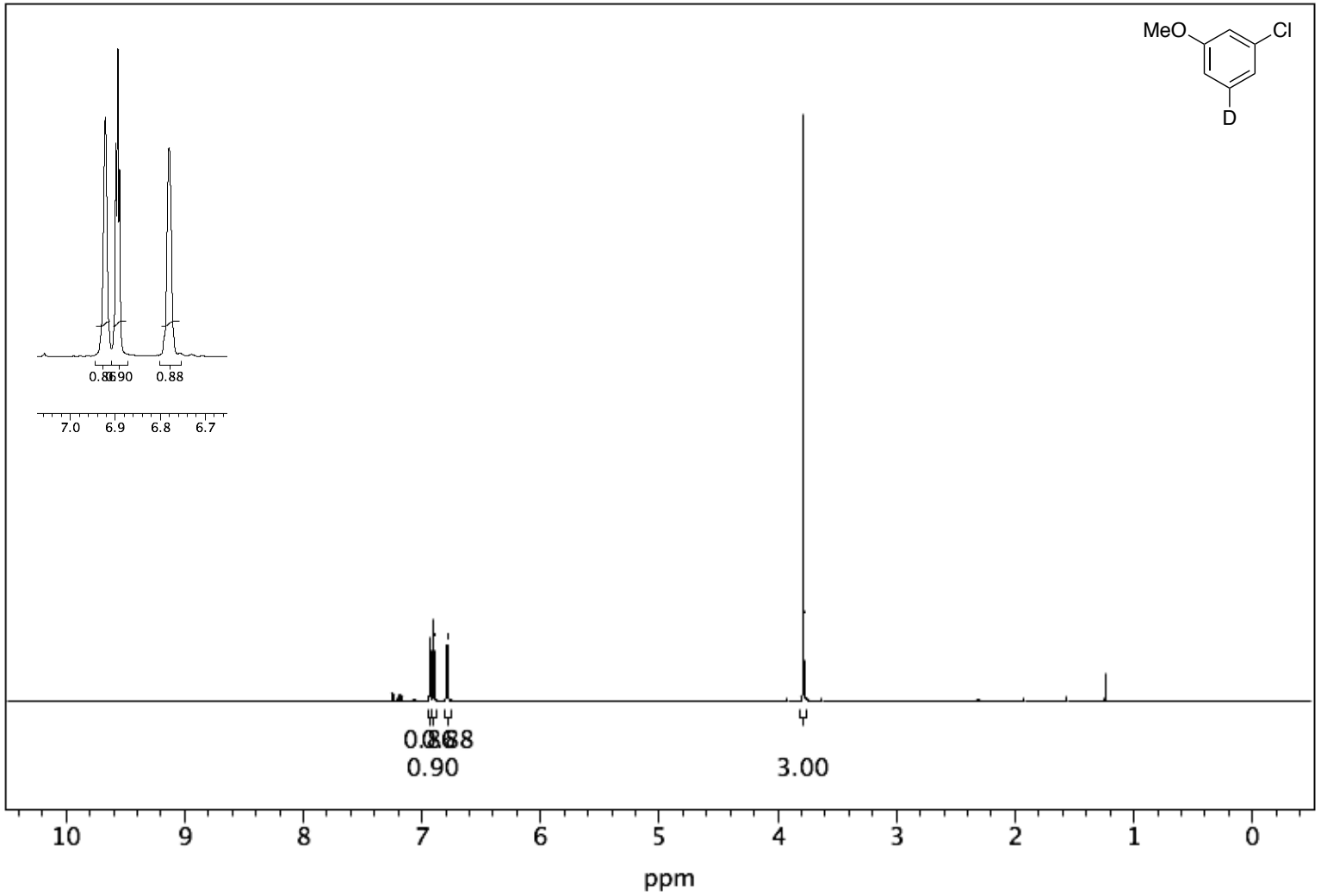


Figure A28. 500 MHz ^{1}H NMR of **2.6b** in $CDCl_3$

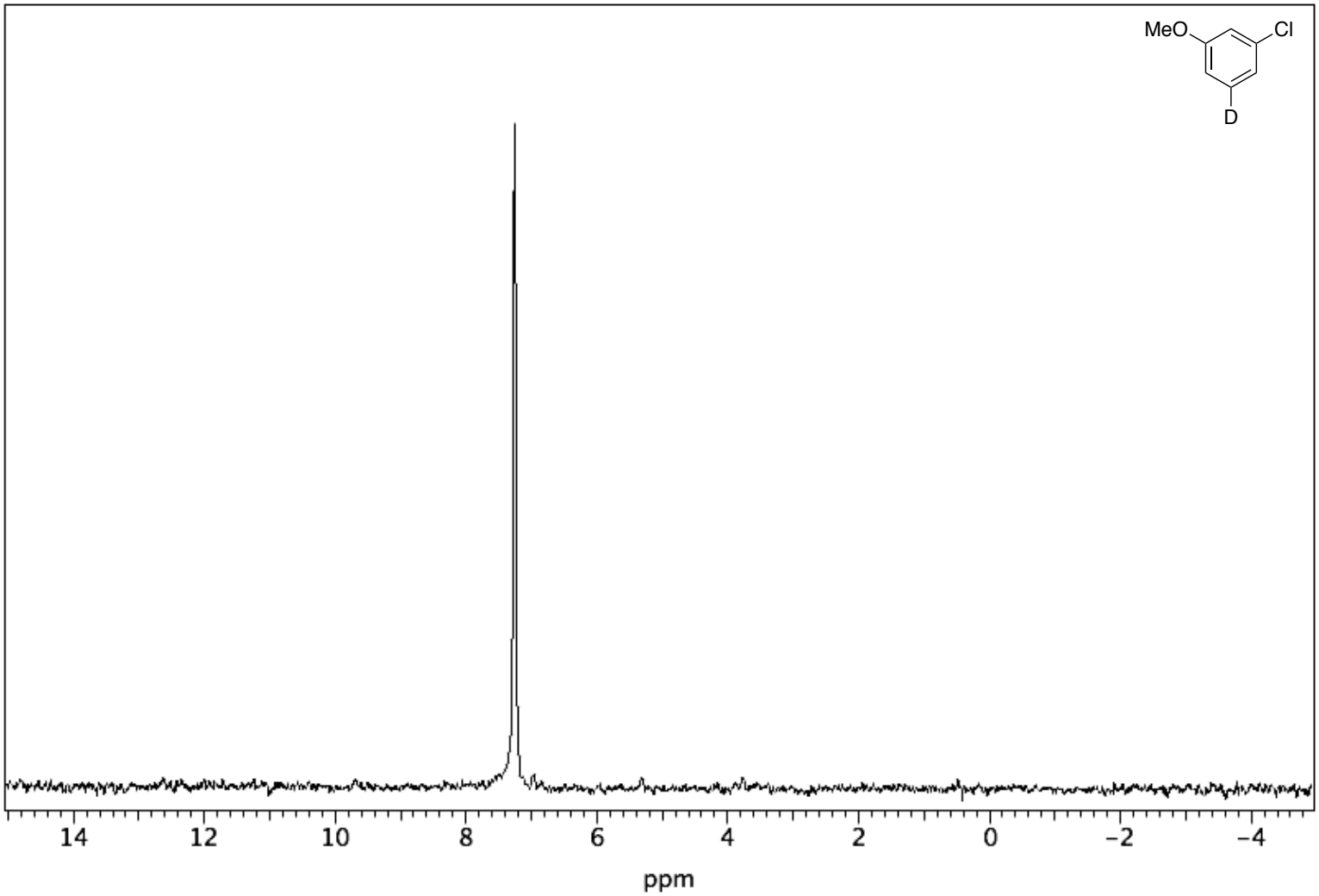


Figure A29. 76.75 MHz ^{2}H NMR of **2.6b** in CH_2Cl_2

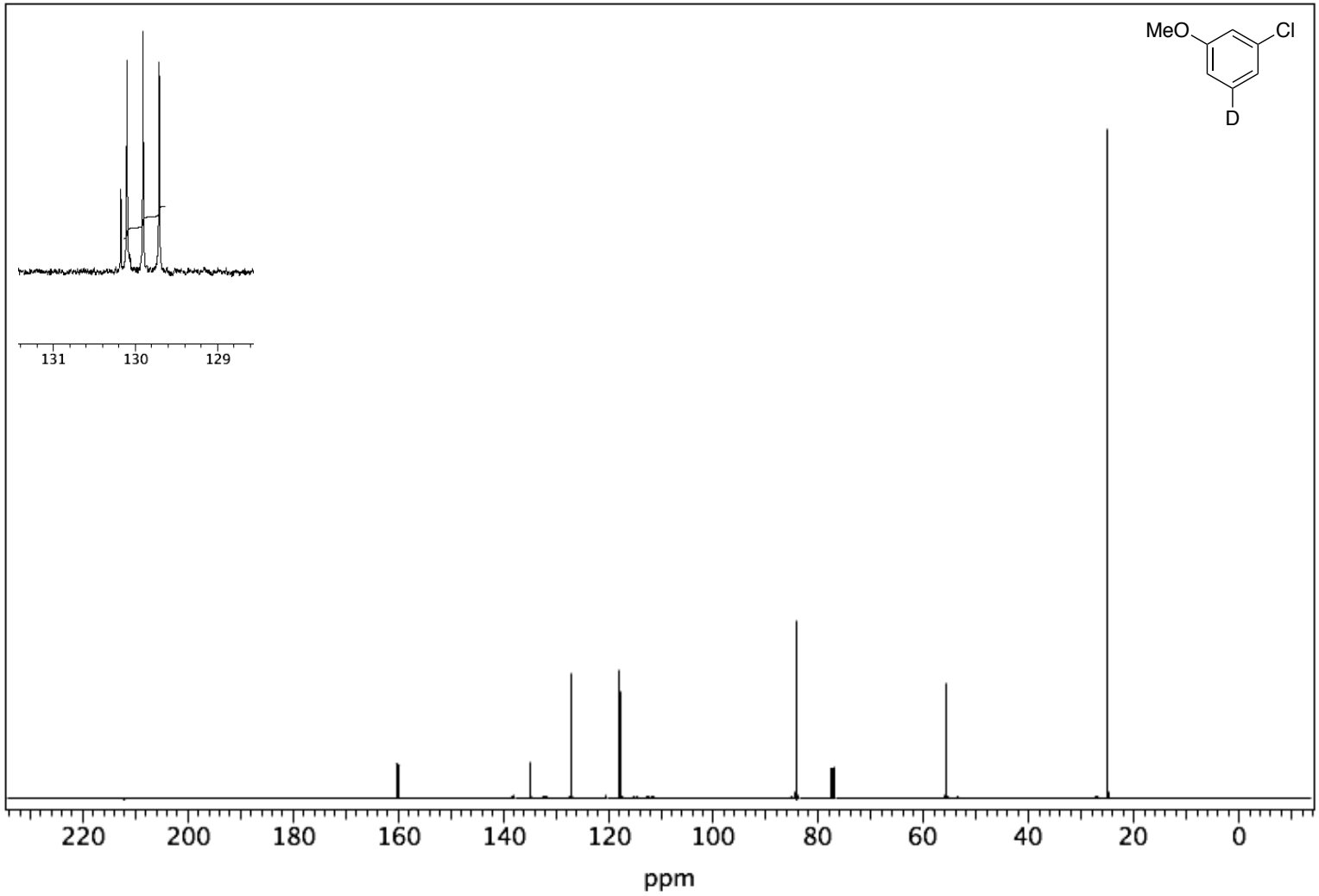


Figure A30. 125 MHz ^{13}C NMR of **2.6b** in $CDCl_3$

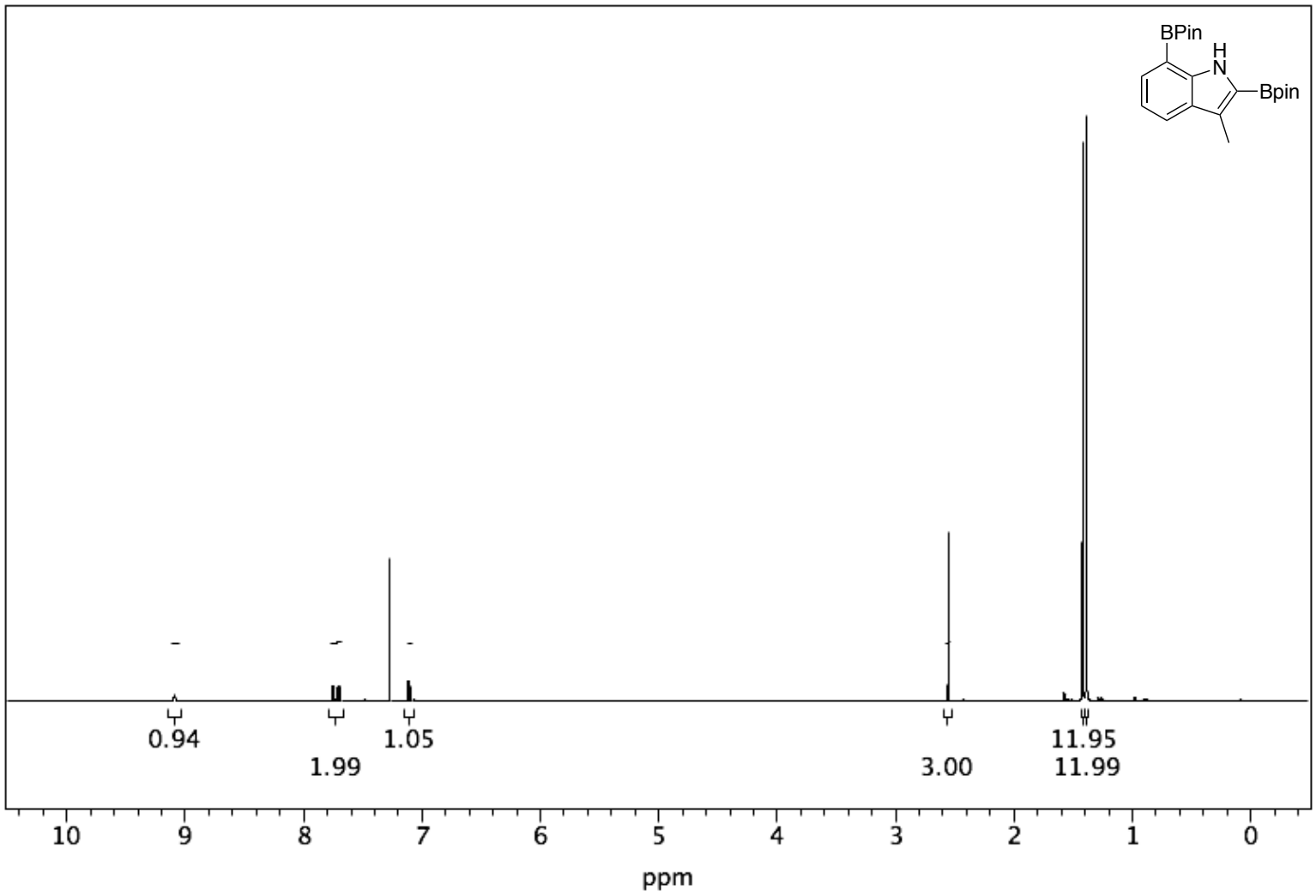


Figure A31. 500 MHz ^{1}H NMR of **2.7** in $CDCl_3$

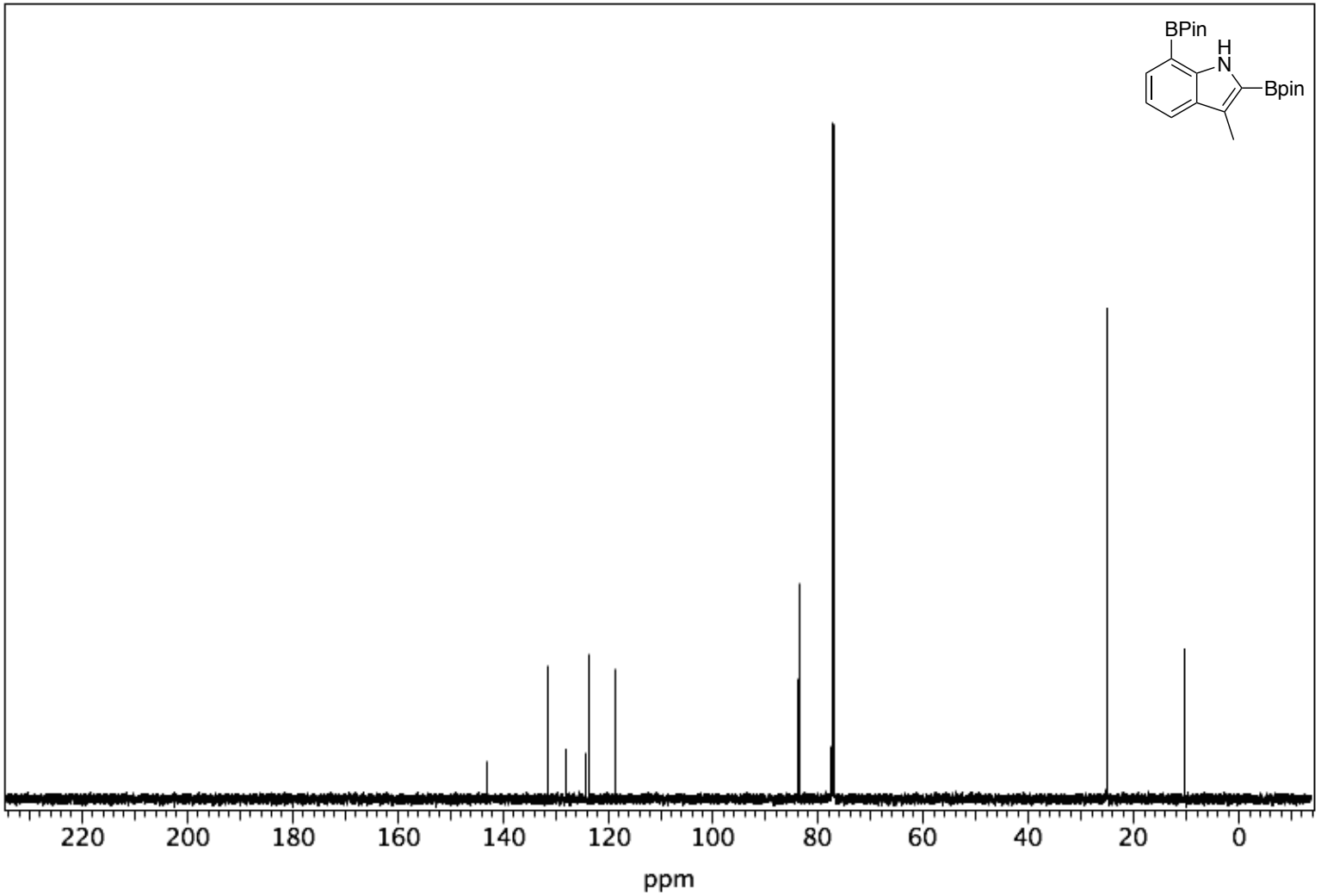


Figure A32. 125 MHz ^{13}C NMR of **2.7** in $CDCl_3$

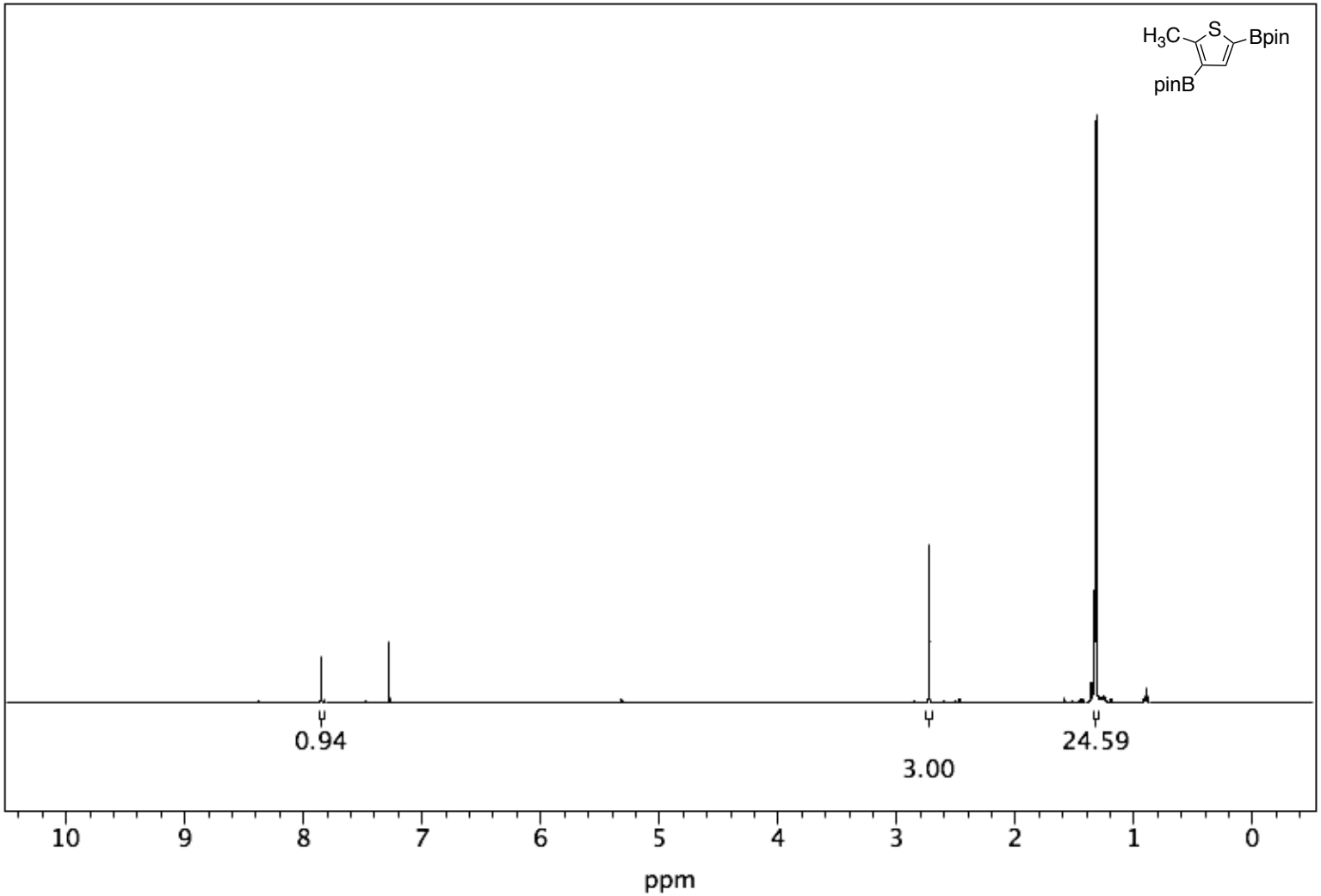


Figure A33. 500 MHz ^{1}H NMR of **2.11** in $CDCl_3$

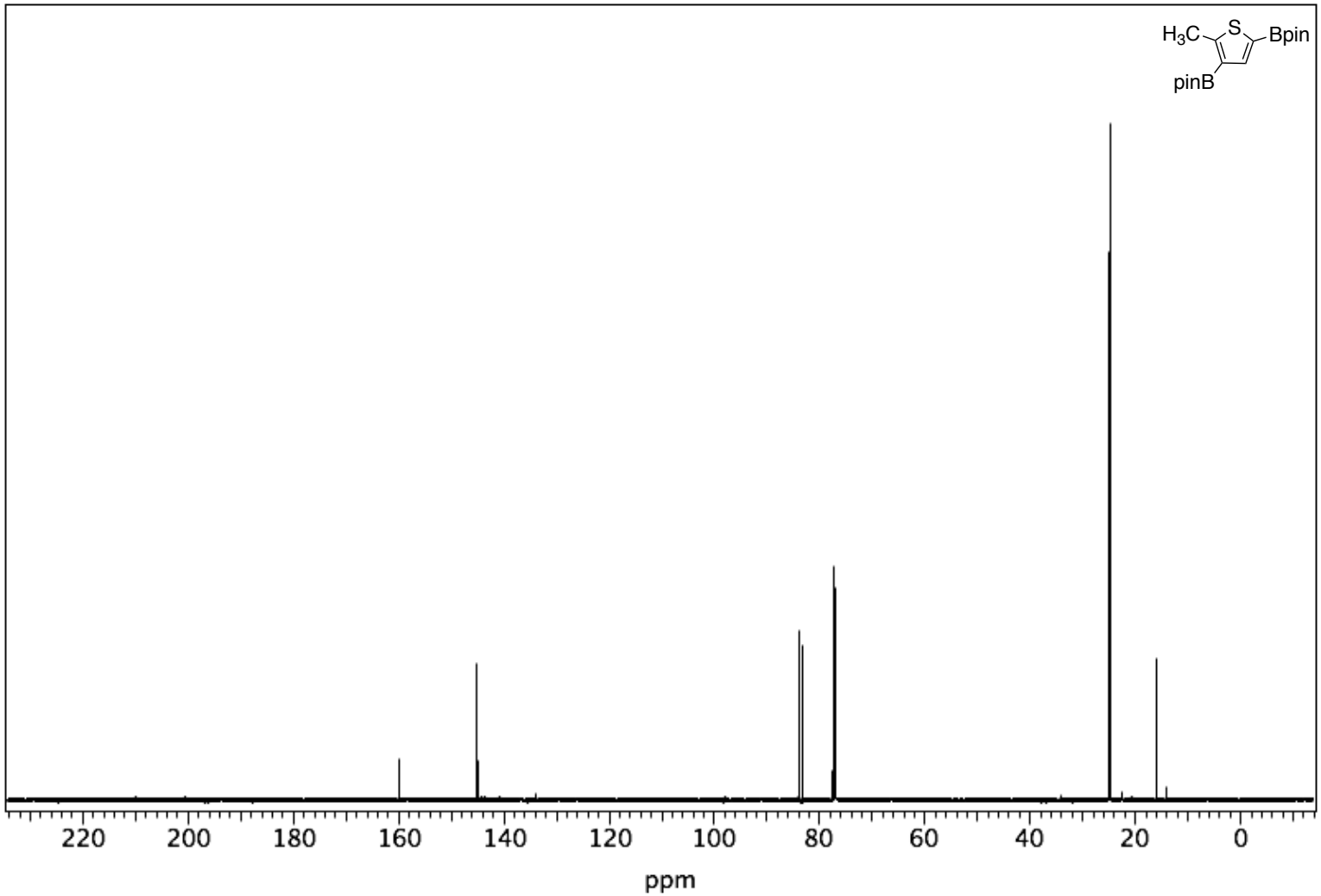


Figure A34. 125 MHz ^{13}C NMR of **2.11** in $CDCl_3$

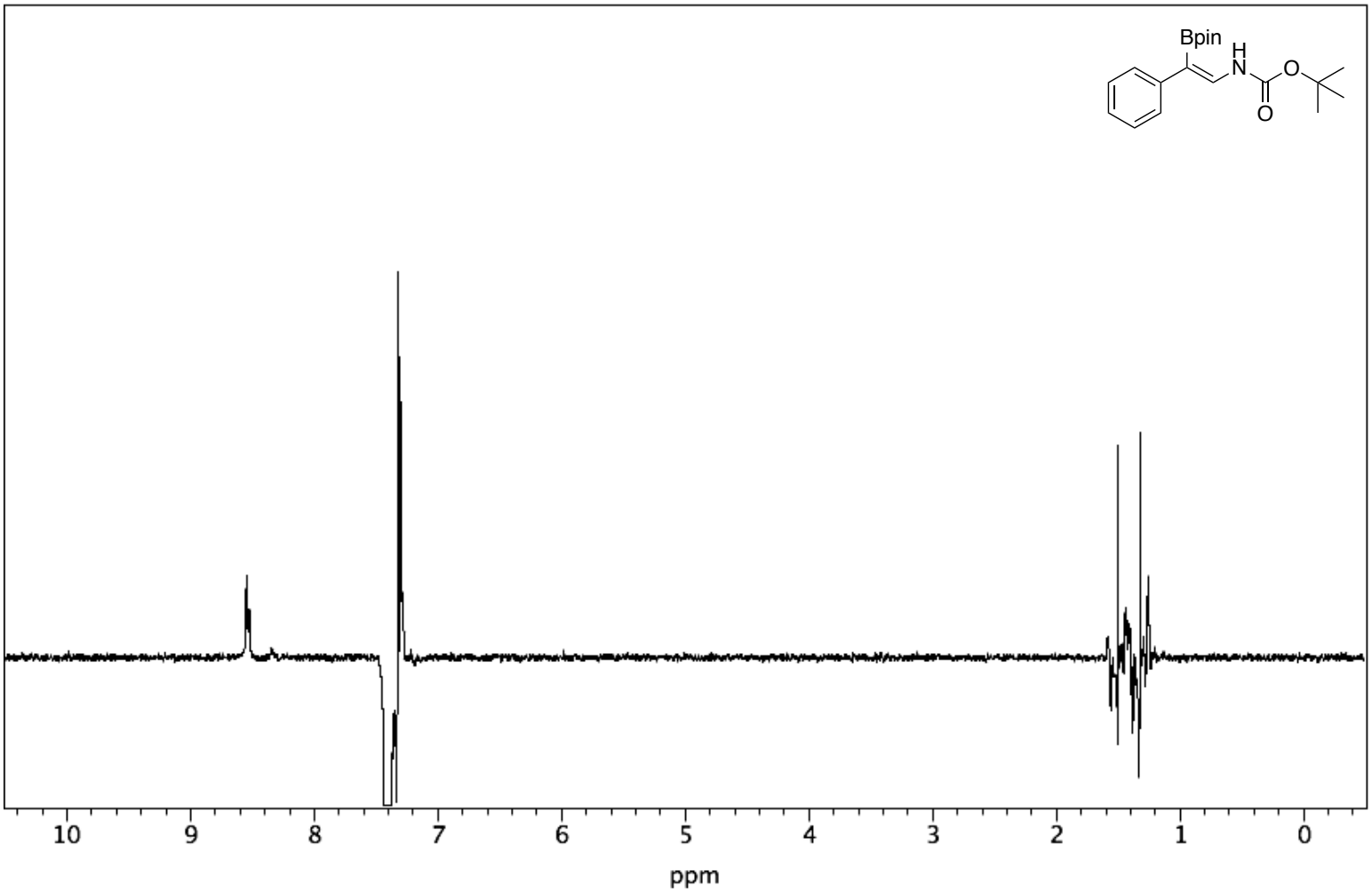


Figure A35. 500 MHz ^{1}H 1D NOE of **3.7b** in CD_3CN

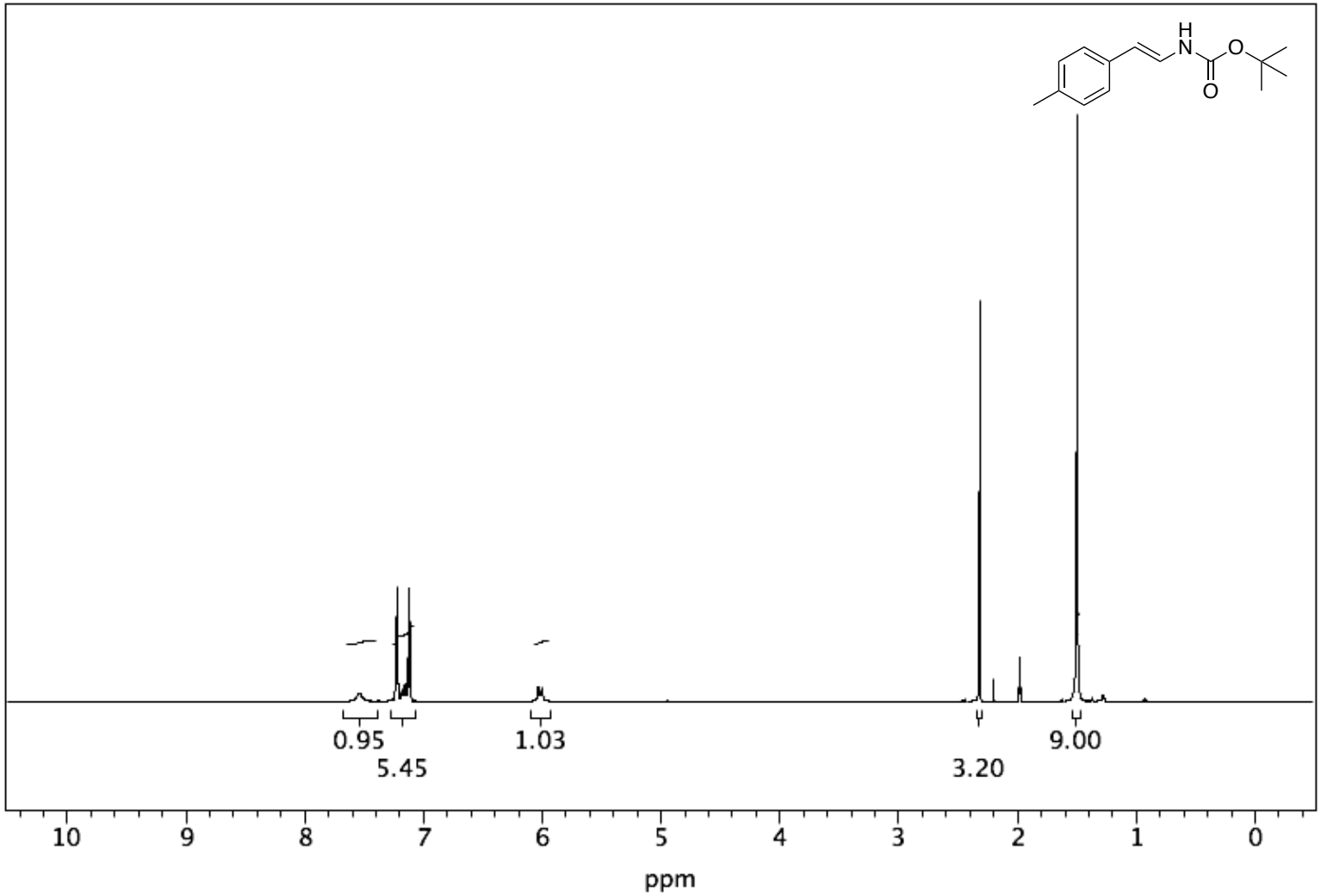


Figure A36. 500 MHz ^{1}H NMR of **3.8a** in $CDCl_3$

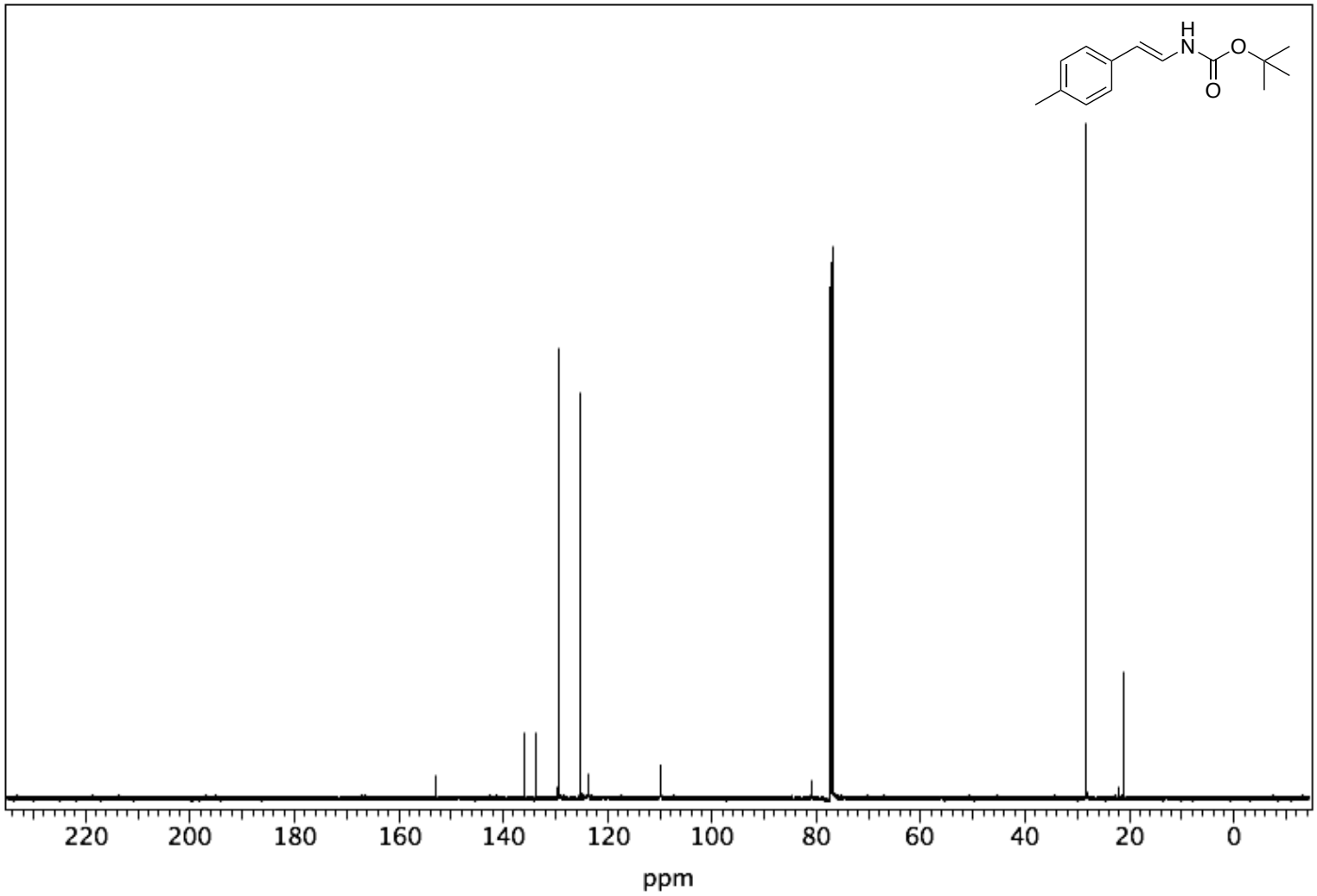


Figure A37. 125 MHz ^{13}C NMR of **3.8a** in $CDCl_3$

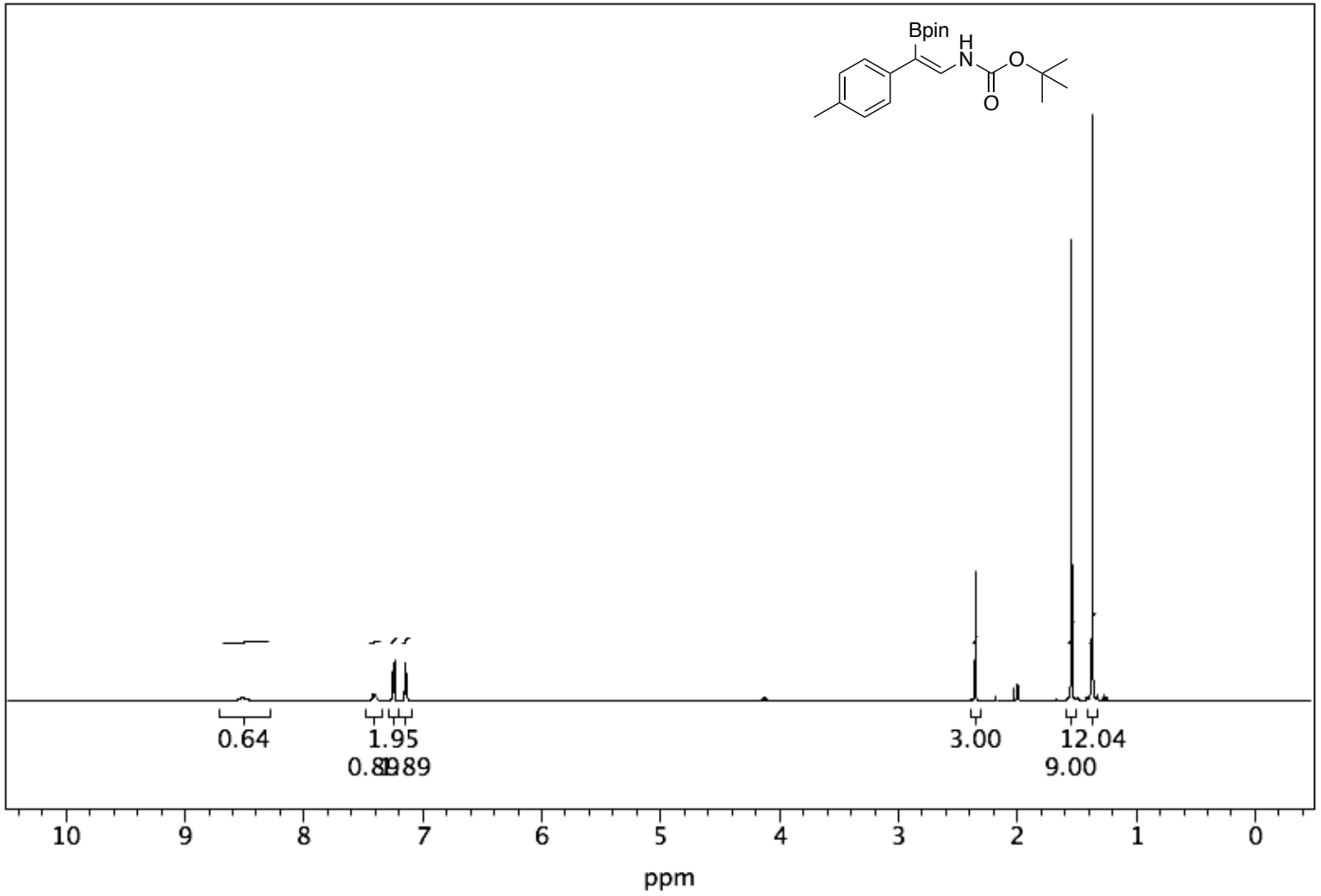


Figure A38. 500 MHz ^{1}H NMR of **3.8b** in CD_3CN

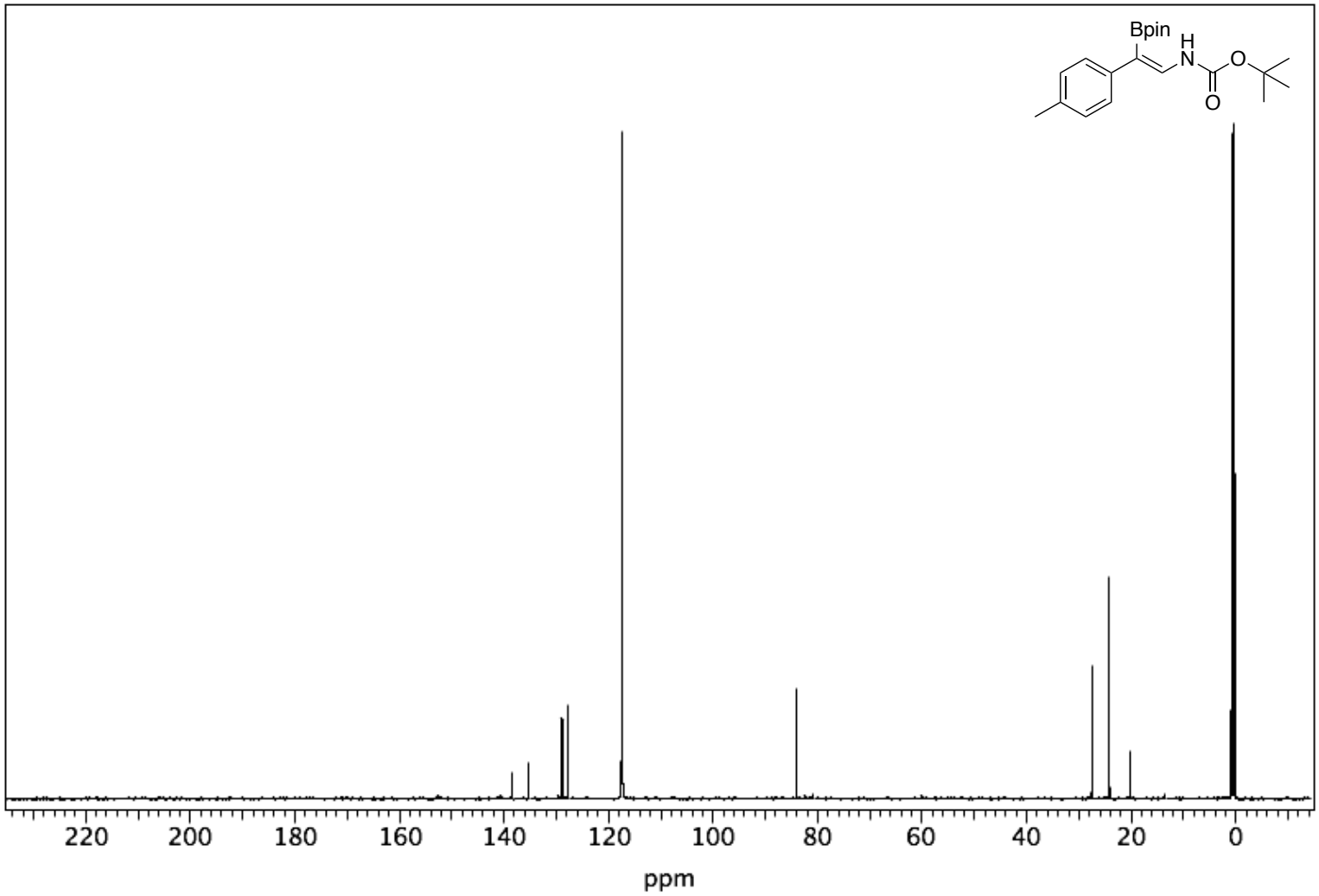


Figure A39. 125 MHz ^{13}C NMR of **3.8b** in CD_3CN

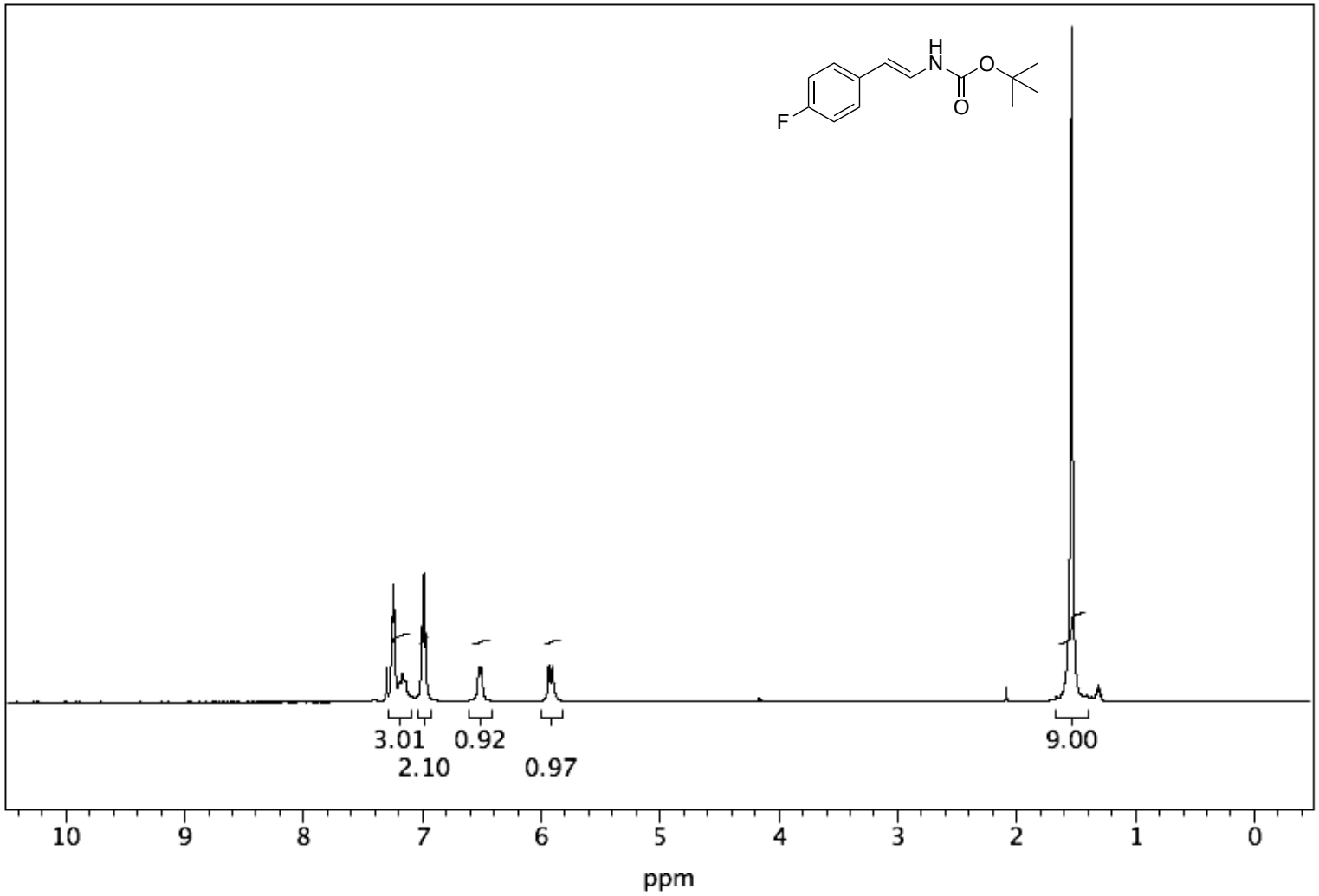


Figure A40. 500 MHz ^{1}H NMR of **3.11a** in $CDCl_3$

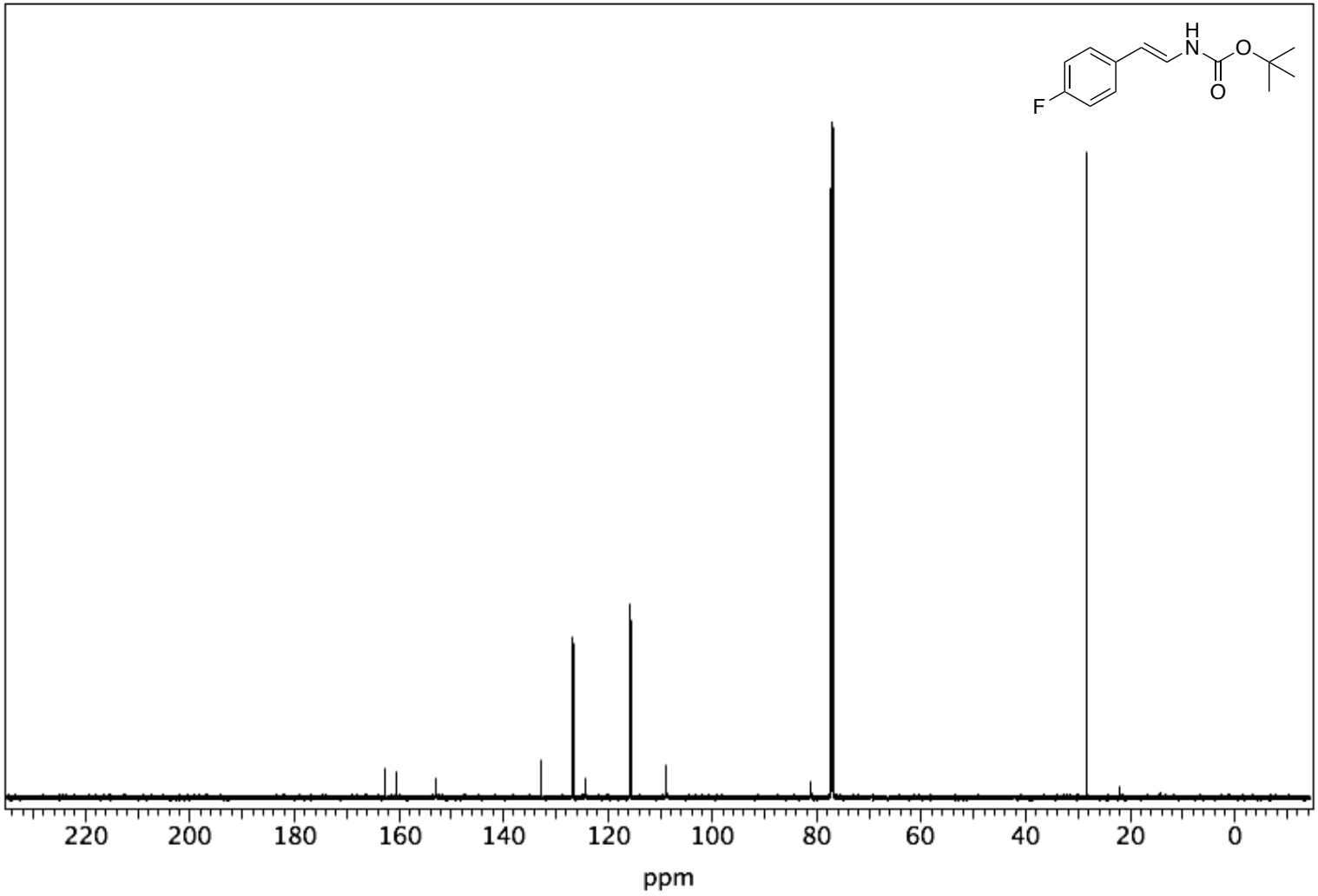


Figure A41. 125 MHz ^{13}C NMR of **3.11a** in $CDCl_3$

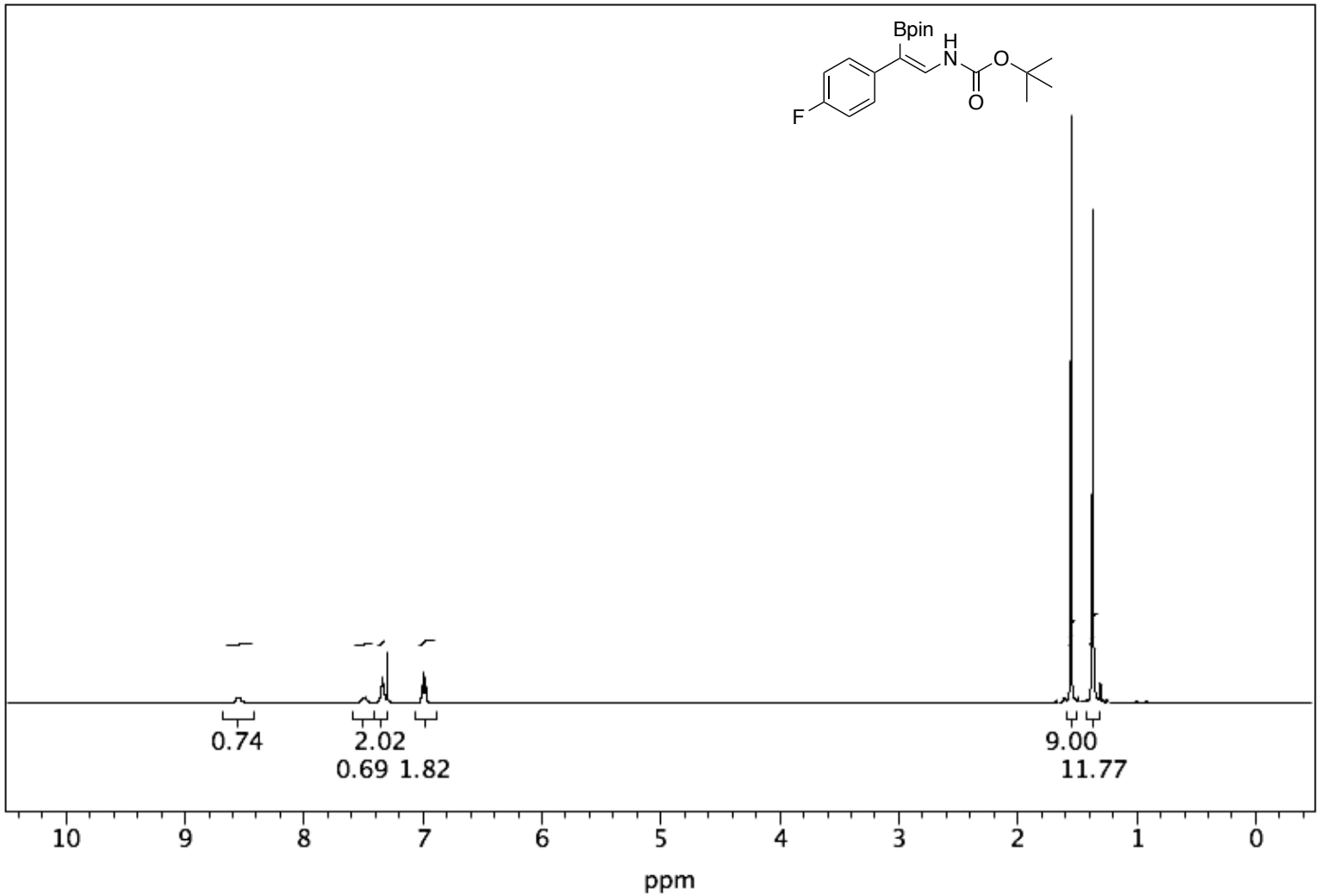


Figure A42. 500 MHz ^{1}H NMR of **3.11b** in $CDCl_3$

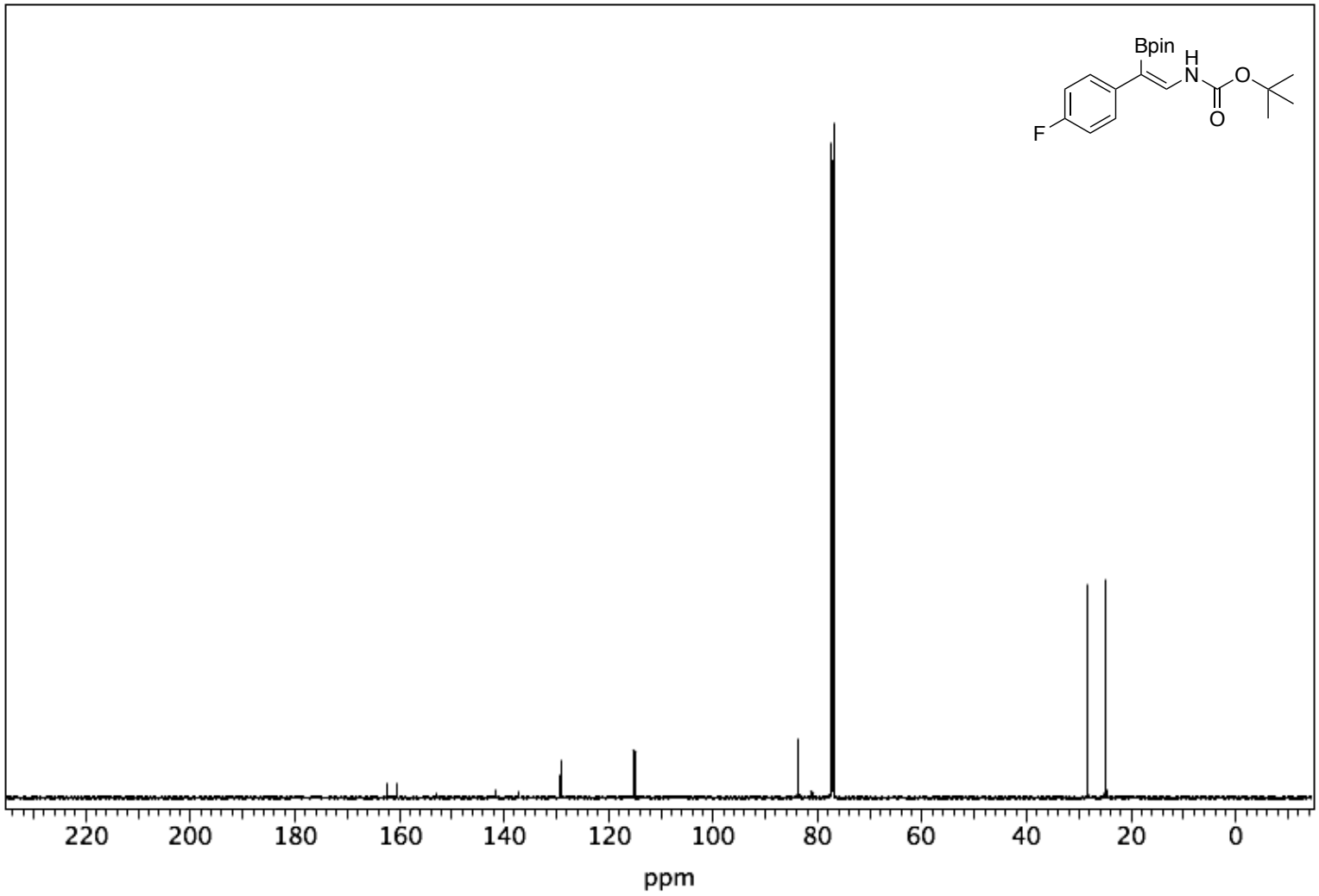


Figure A43. 125 MHz ^{13}C NMR of **3.11b** in $CDCl_3$

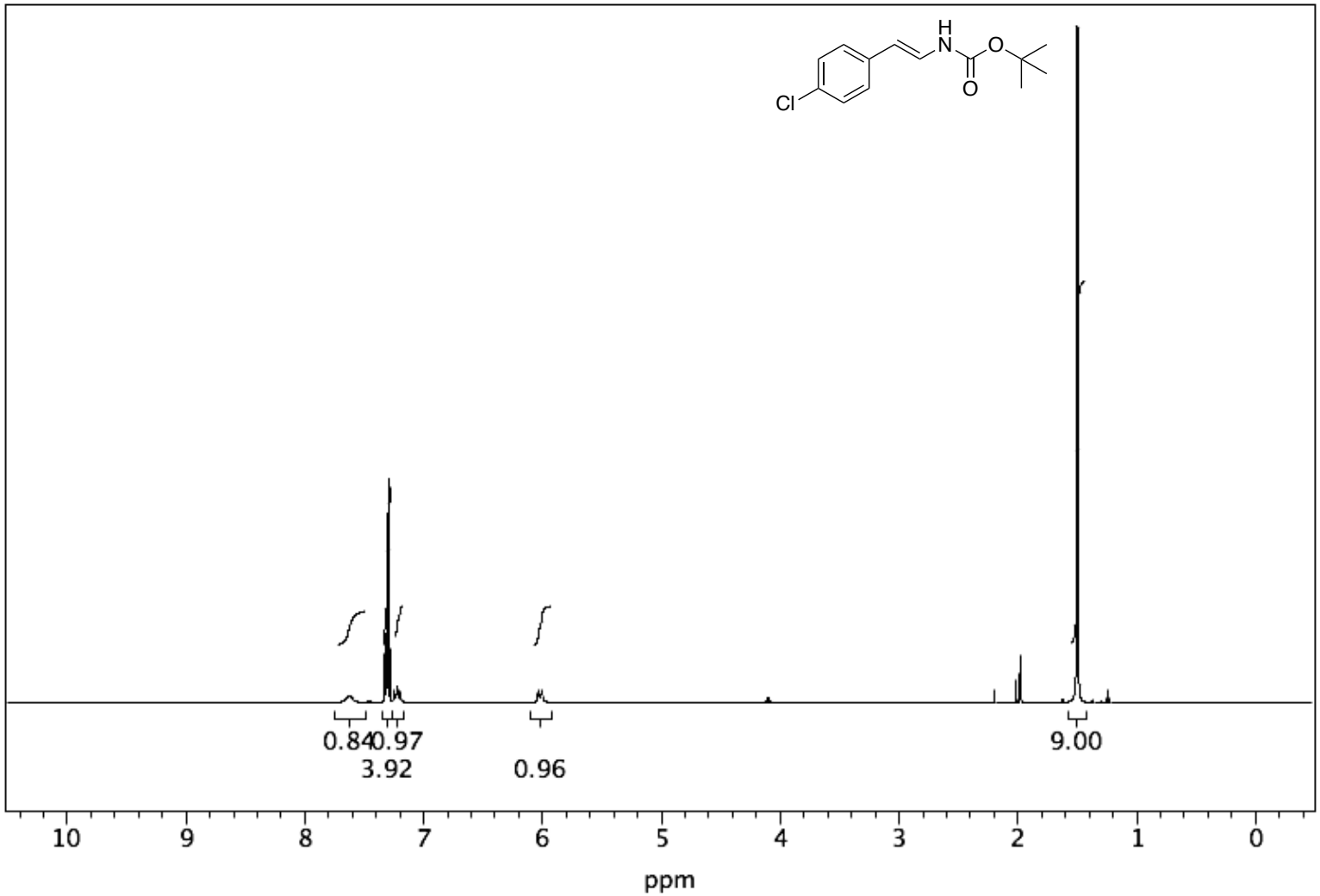


Figure A44. 500 MHz ^{1}H NMR of **3.12a** in CD_3CN

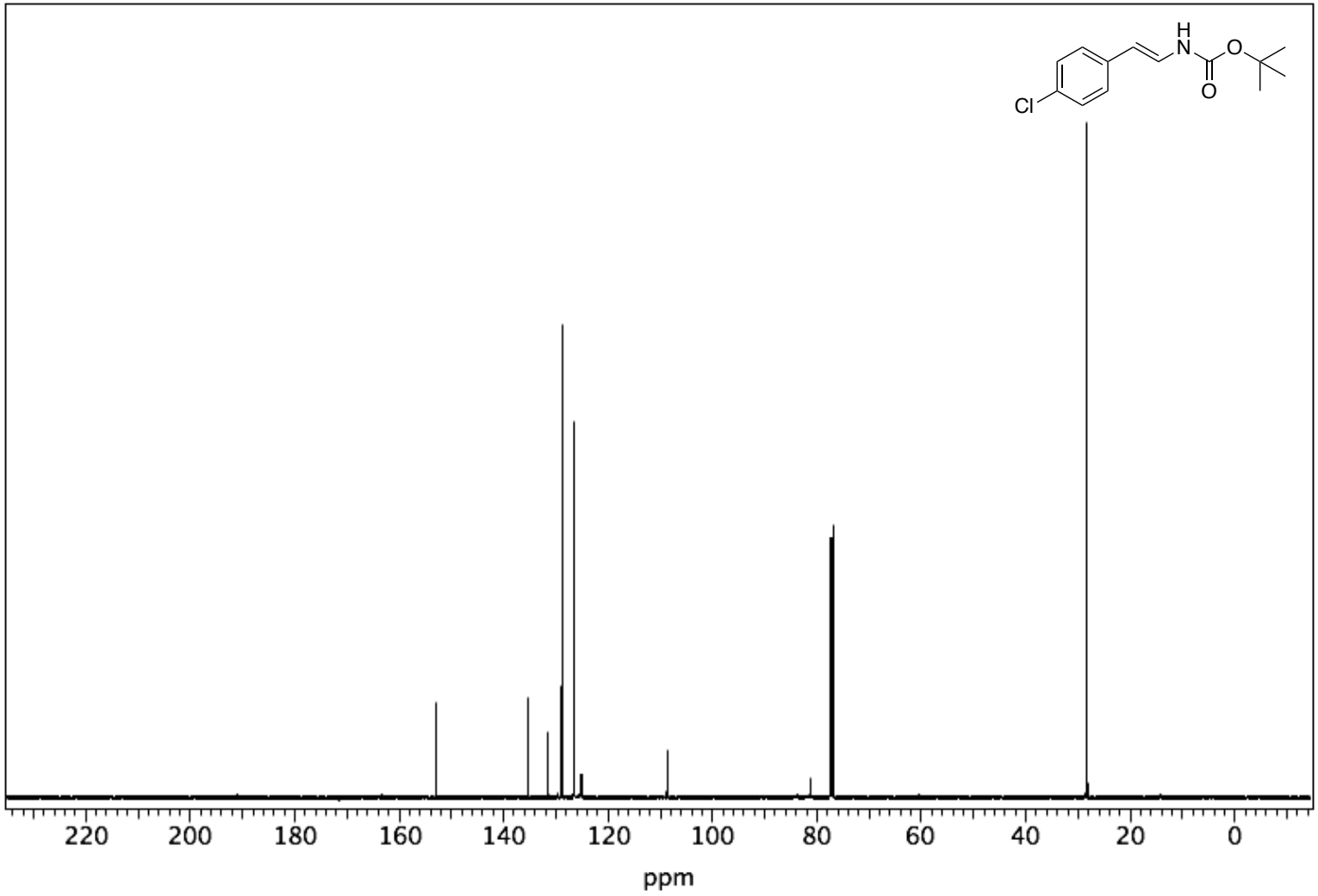


Figure A45. 125 MHz ^{13}C NMR of **3.12a** in $CDCl_3$

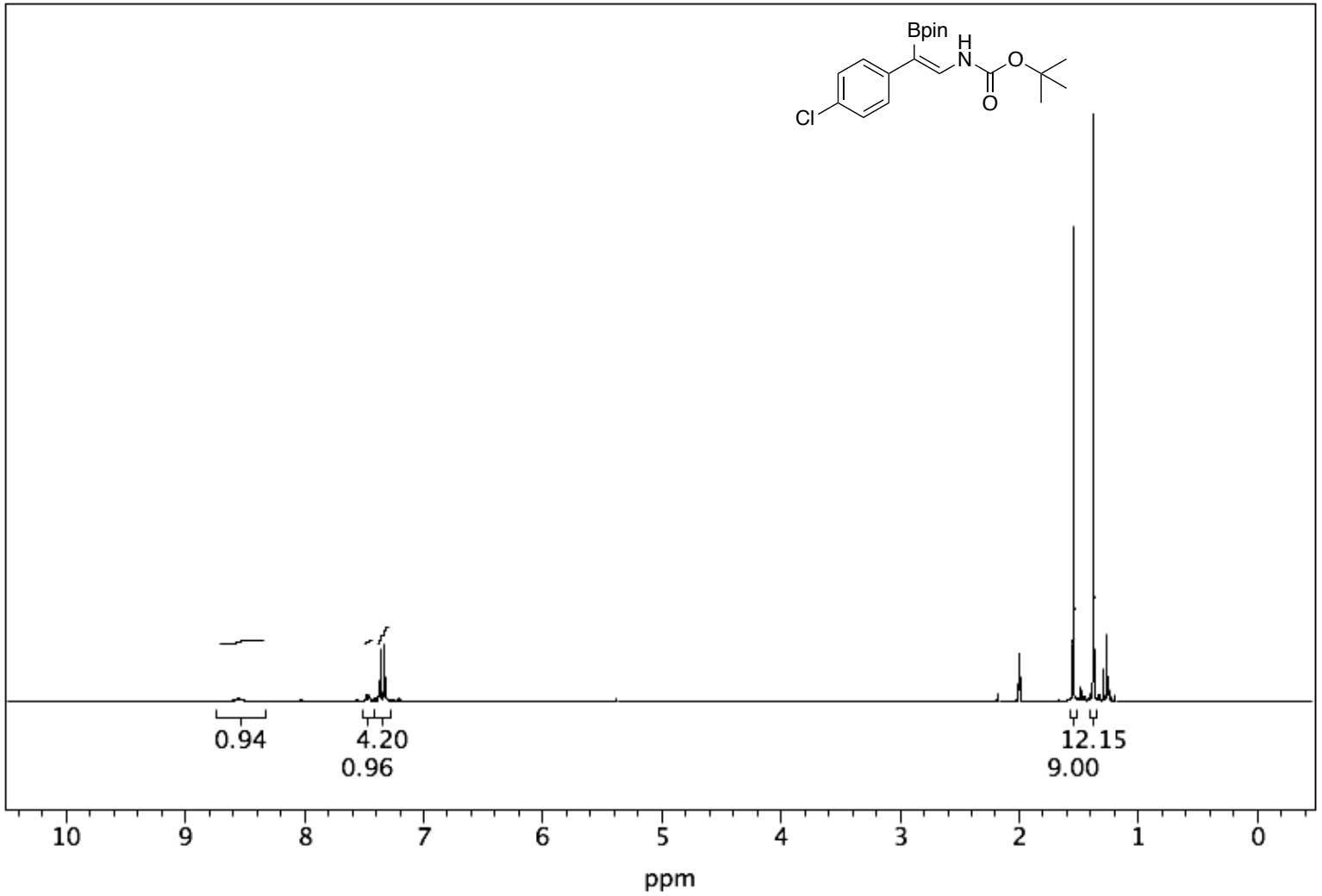


Figure A46. 500 MHz ^{1}H NMR of **3.12b** in CD_3CN

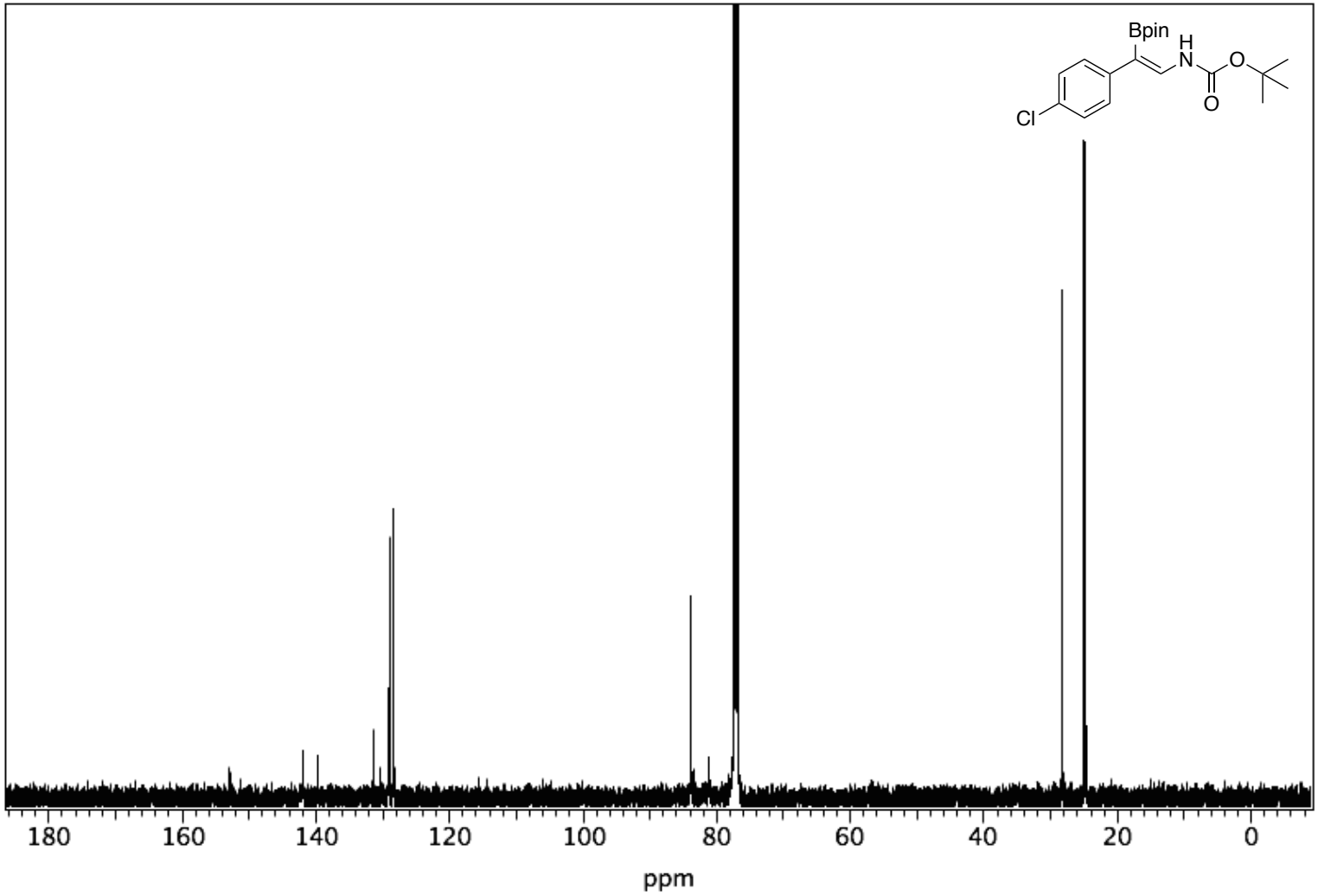


Figure A47. 125 MHz ^{13}C NMR of **3.12b** in $CDCl_3$

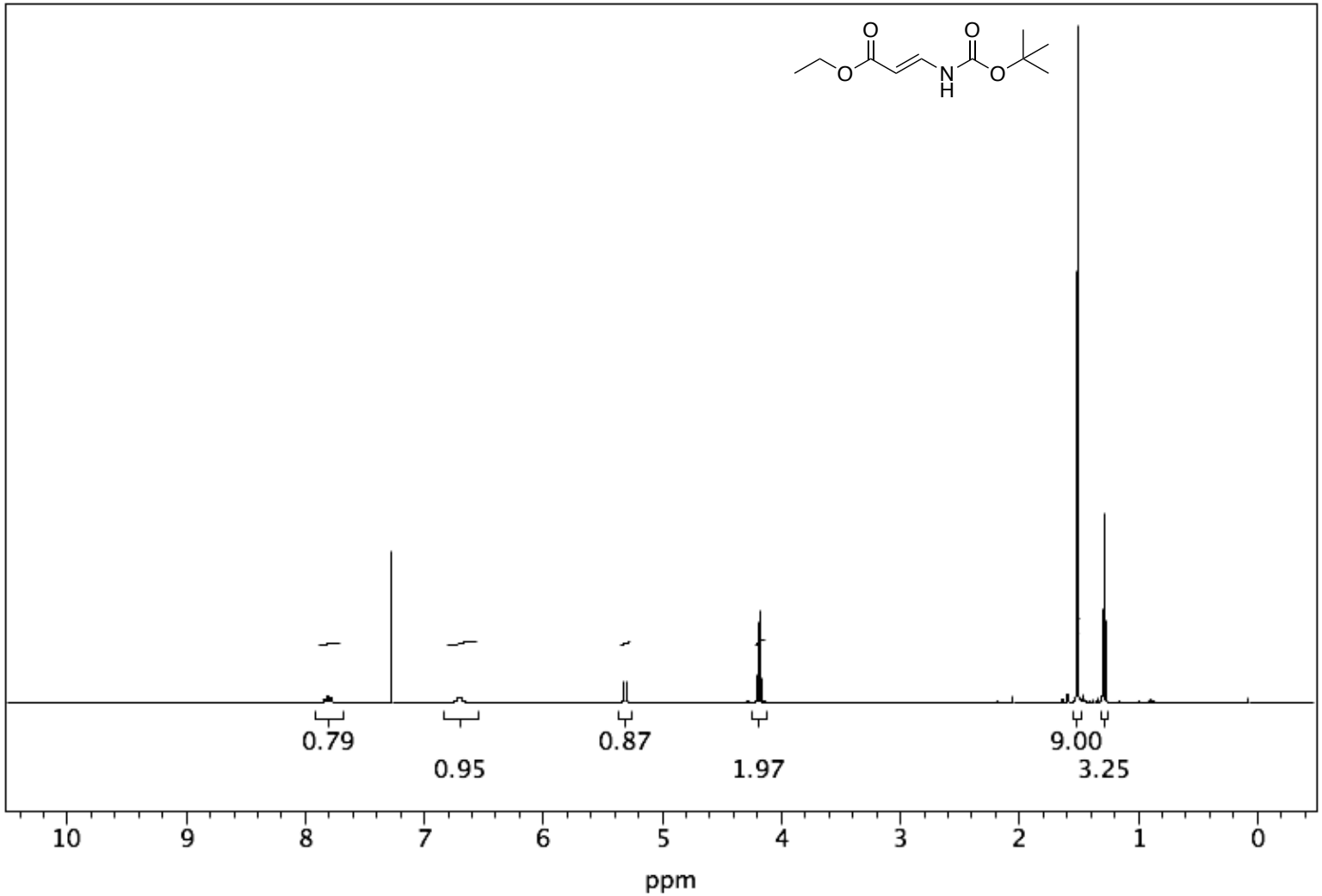


Figure A48. 500 MHz ^{1}H NMR of **3.13a** in $CDCl_3$

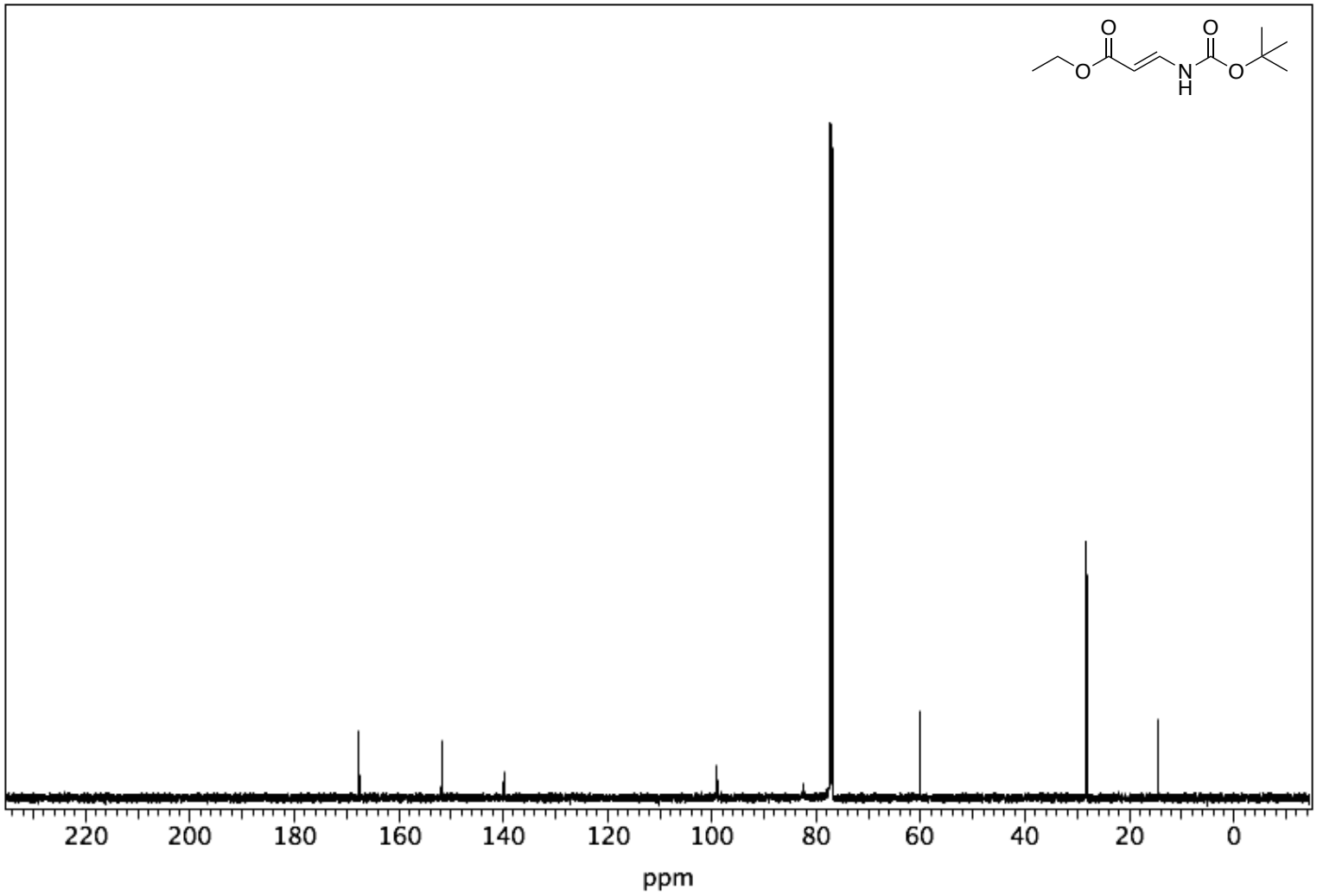


Figure A49. 125 MHz ^{13}C NMR of **3.13a** in $CDCl_3$

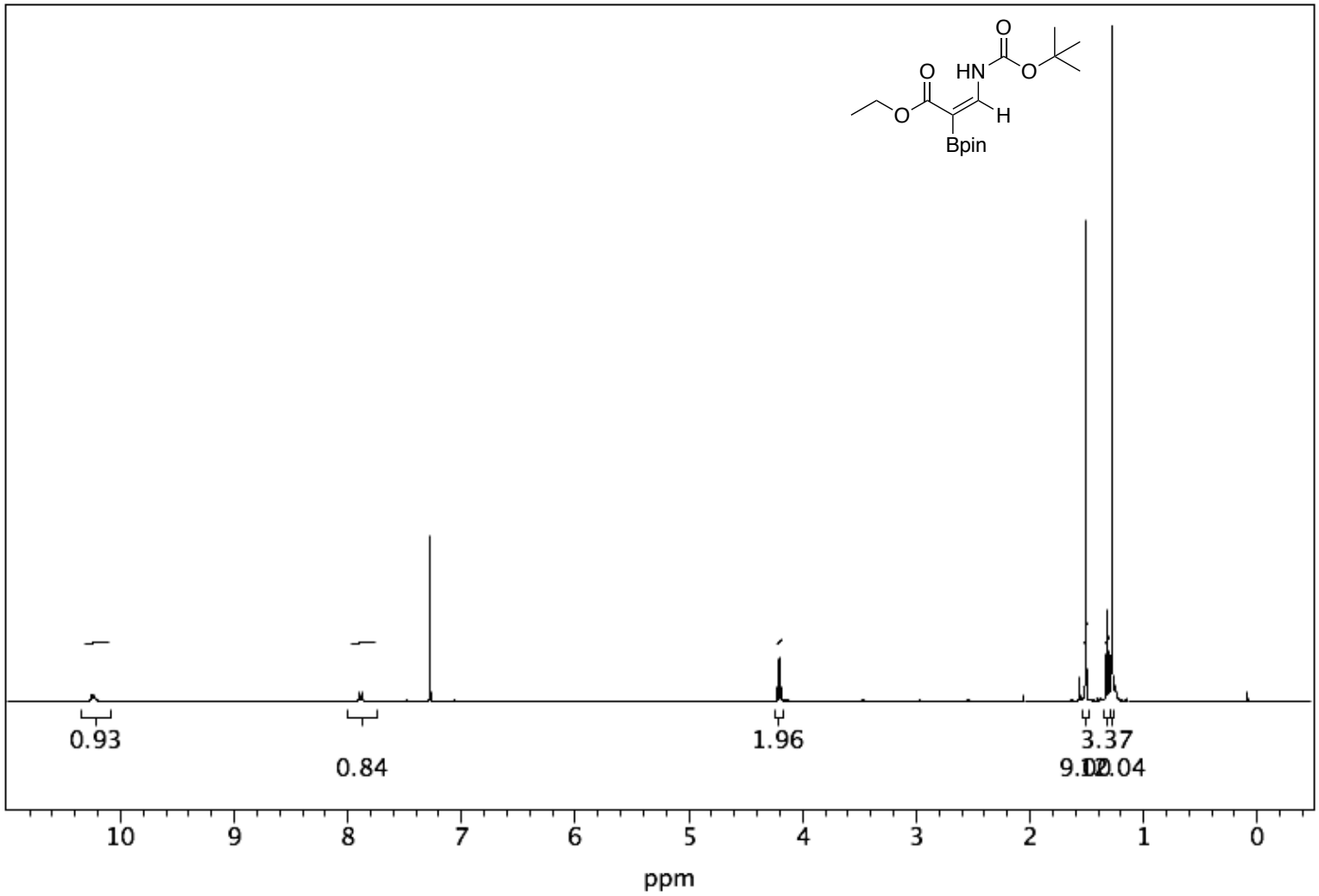


Figure A50. 500 MHz ^{1}H NMR of **3.13b** in $CDCl_3$

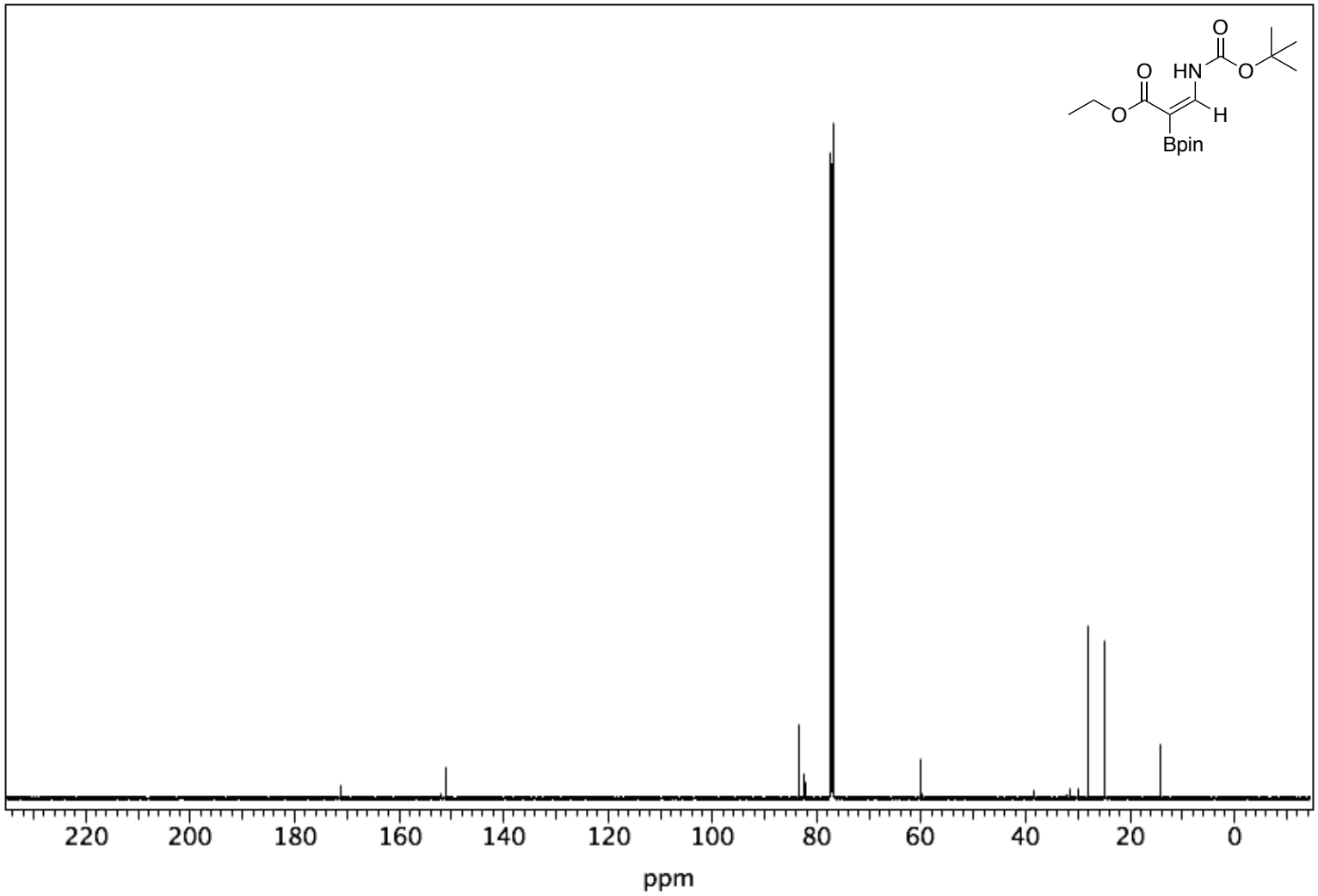


Figure A51. 125 MHz ^{13}C NMR of **3.13b** in $CDCl_3$

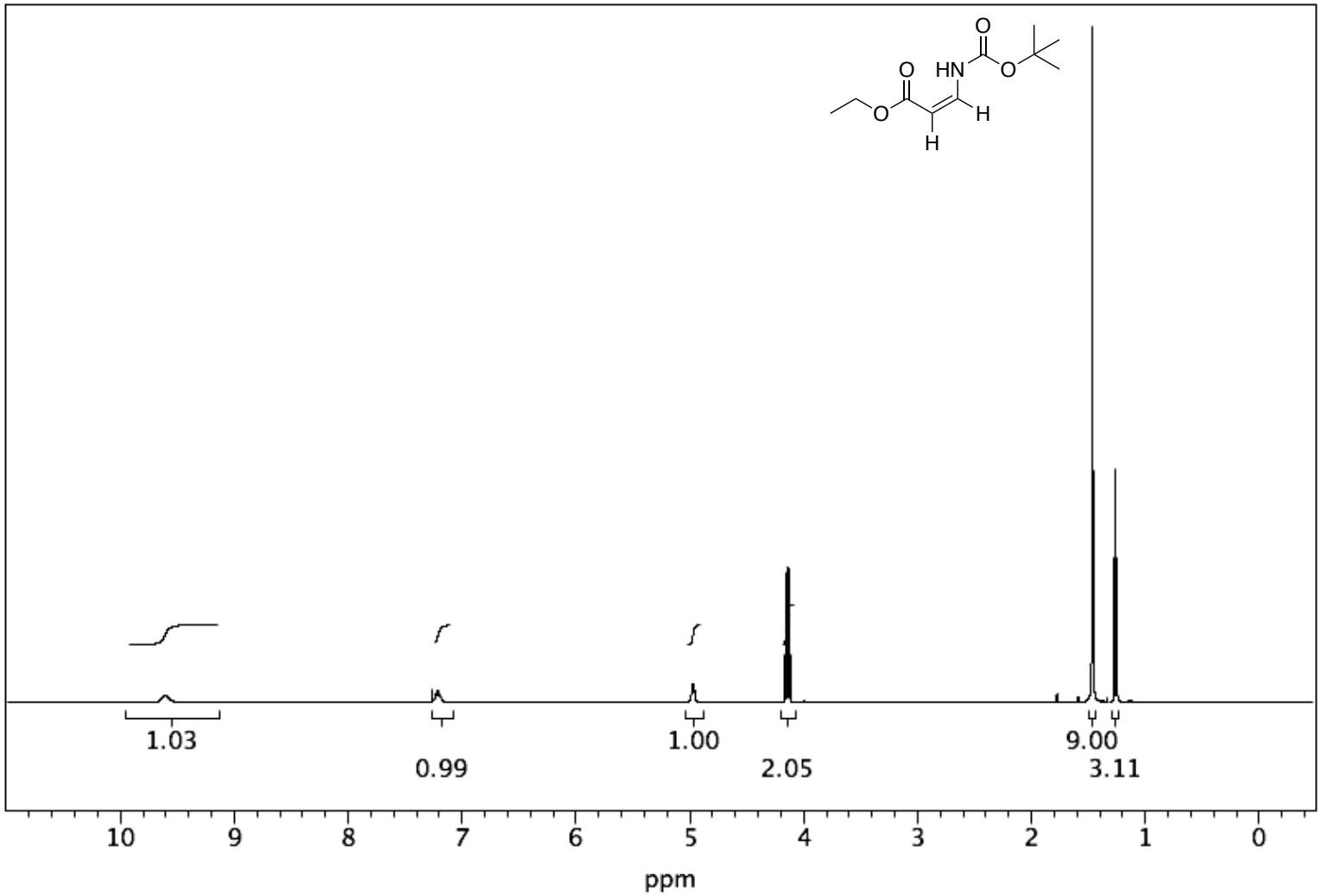


Figure A52. 500 MHz ^{1}H NMR of **3.13c** in $CDCl_3$

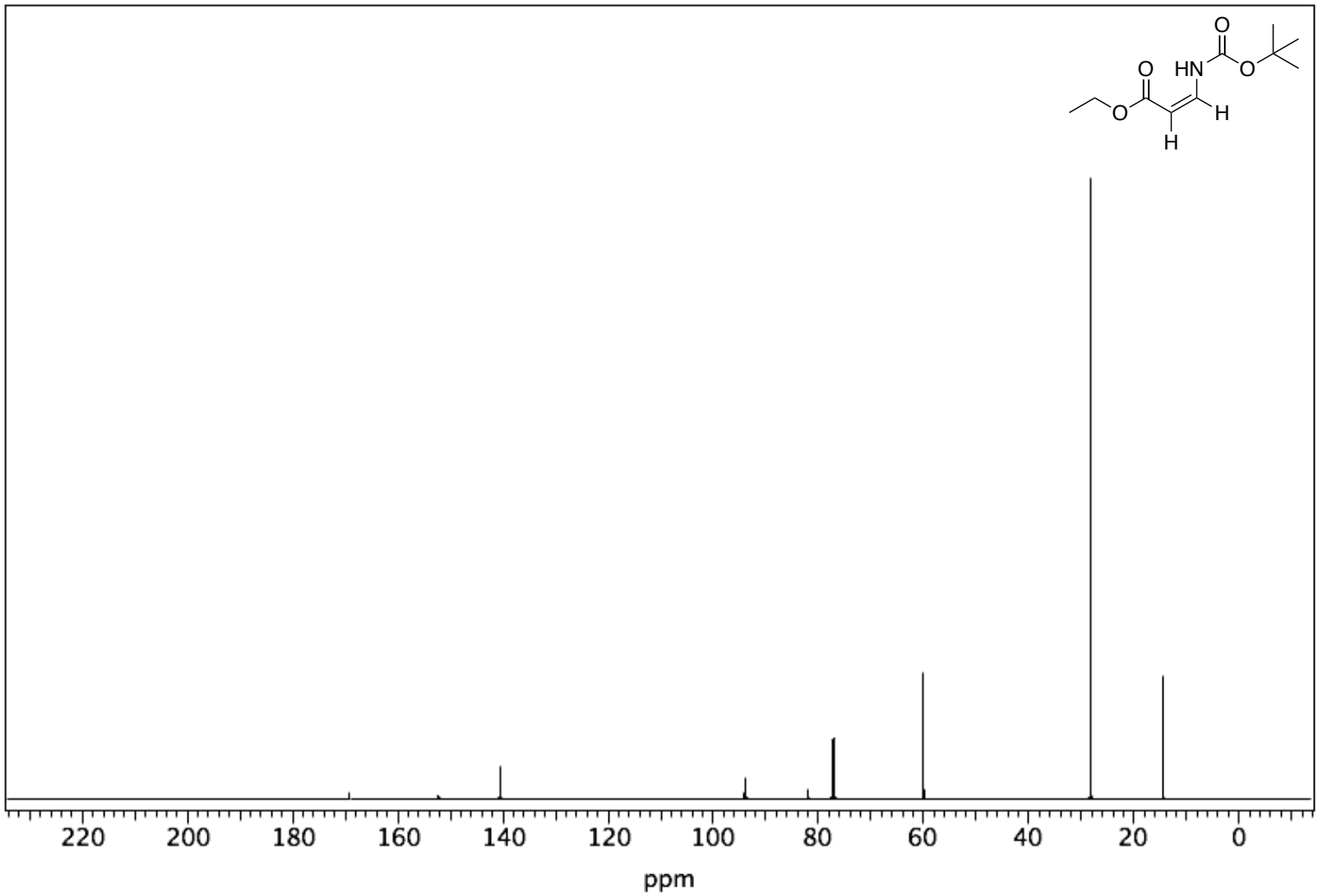


Figure A36. 125 MHz ^{13}C NMR of **3.13c** in $CDCl_3$

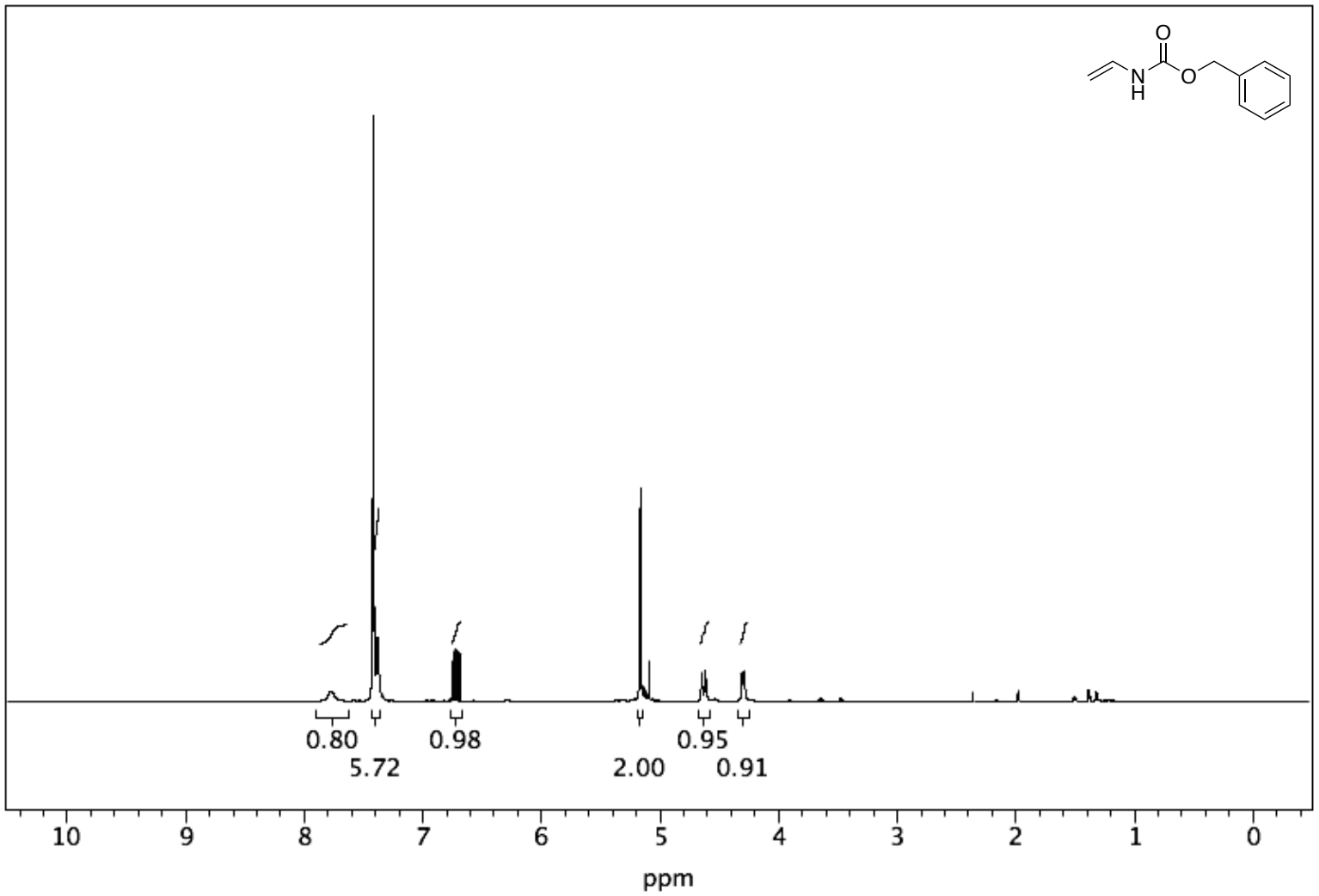


Figure A54. 500 MHz ^{1}H NMR of **3.14a** in $CDCl_3$

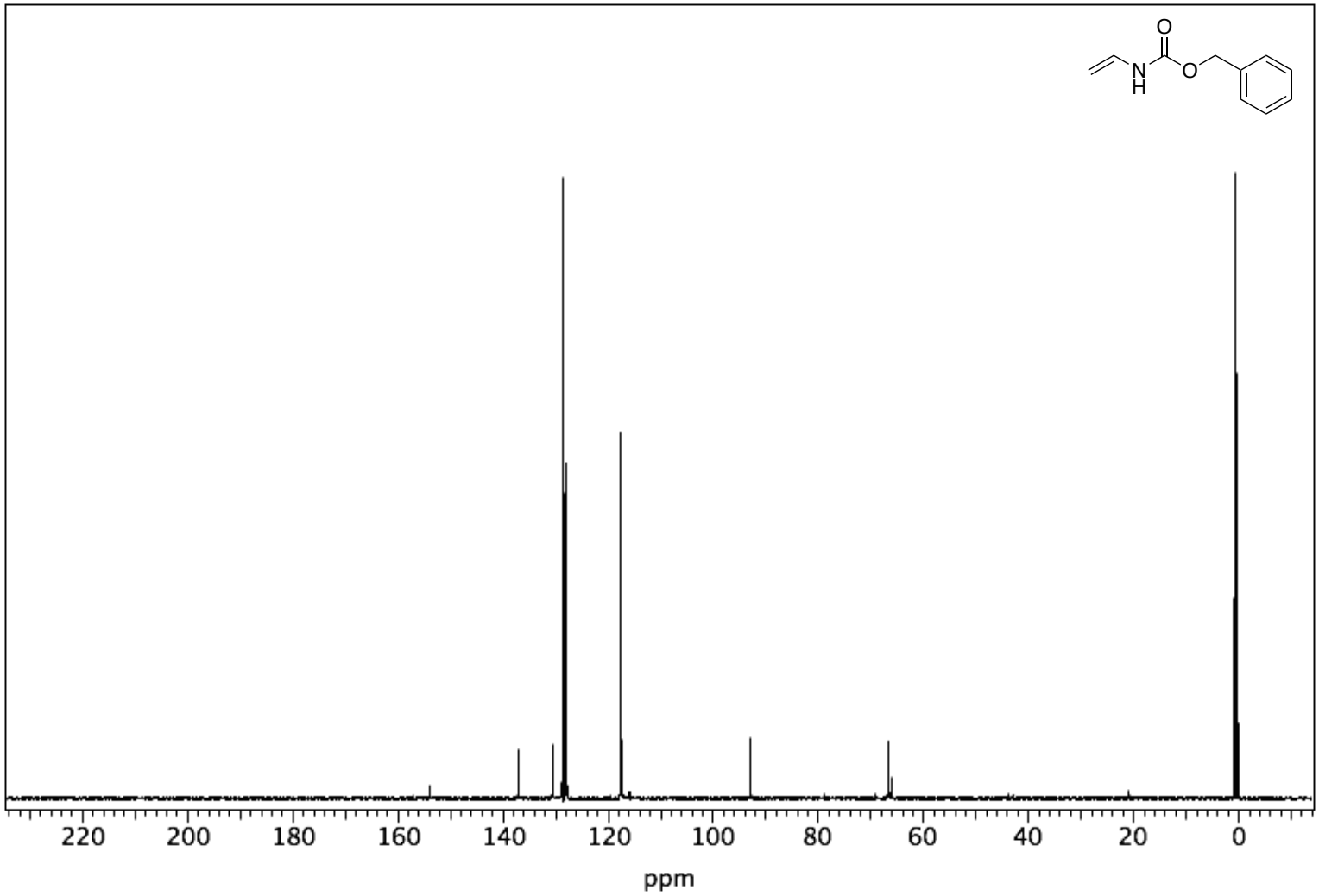


Figure A55. 125 MHz ^{13}C NMR of **3.14a** in CD_3CN

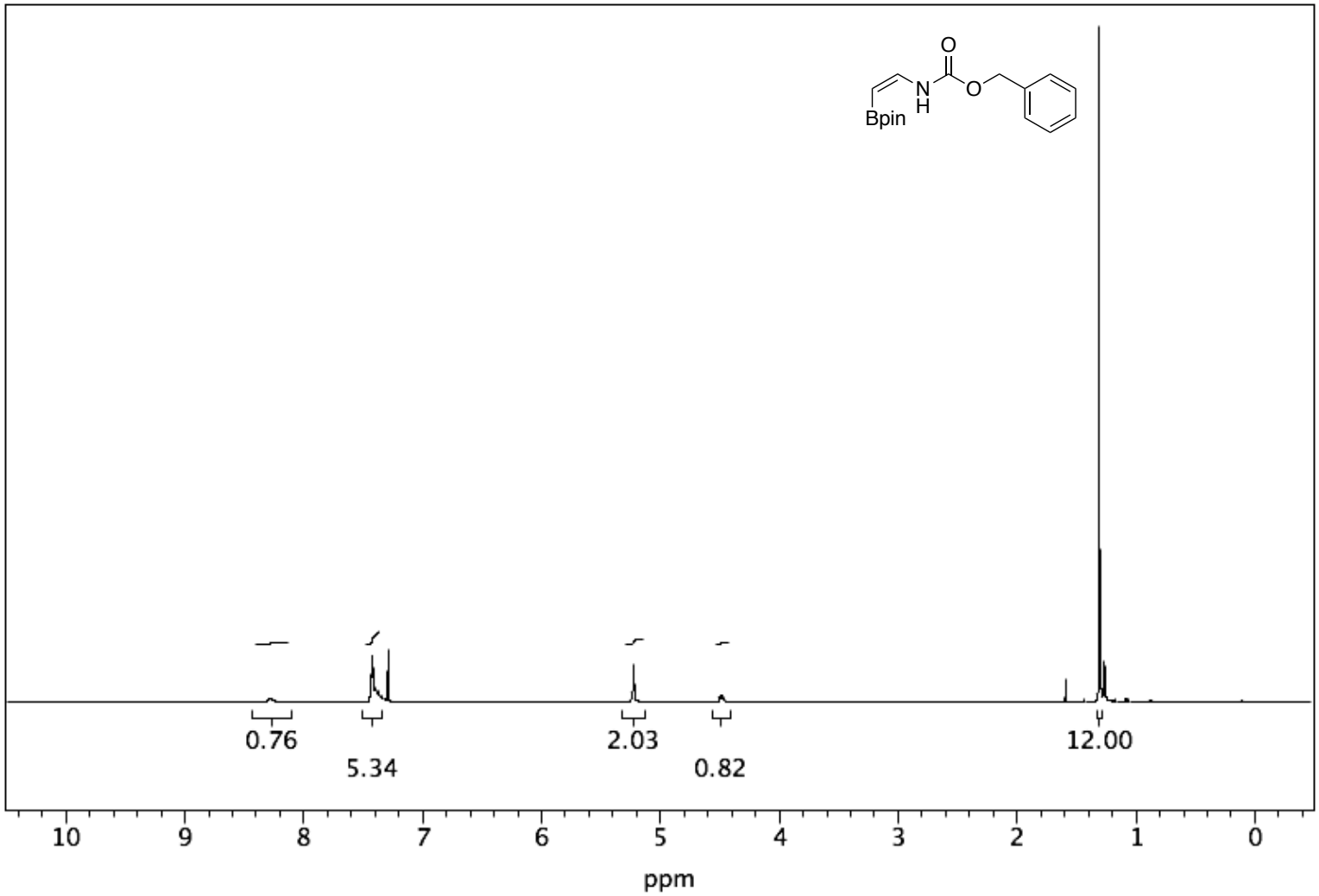


Figure A56. 500 MHz ^{1}H NMR of **3.14b** in $CDCl_3$

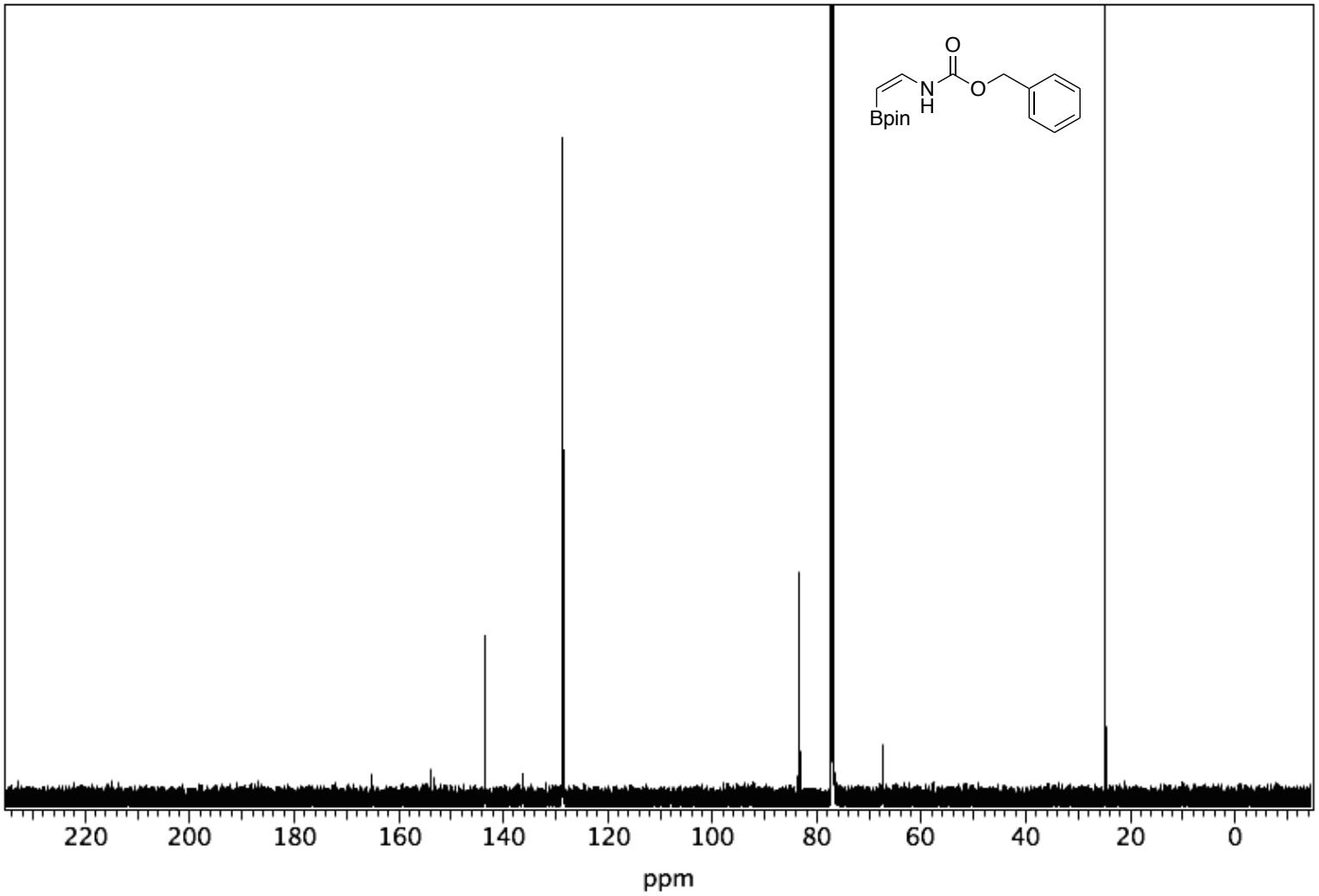


Figure A57. 125 MHz ^{13}C NMR of **3.14b** in $CDCl_3$

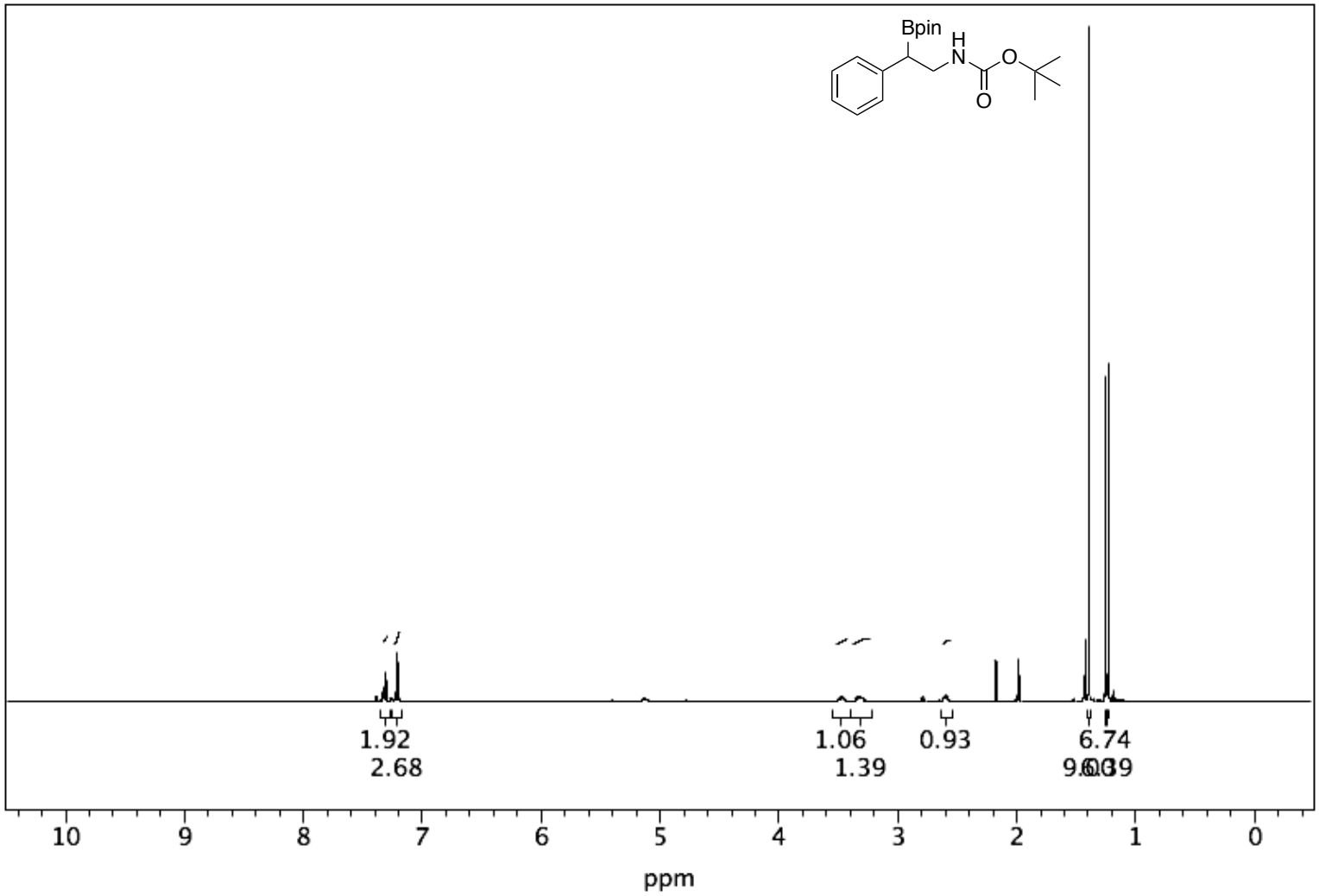


Figure A58. 500 MHz ^{1}H NMR of **3.15** in CD_3CN

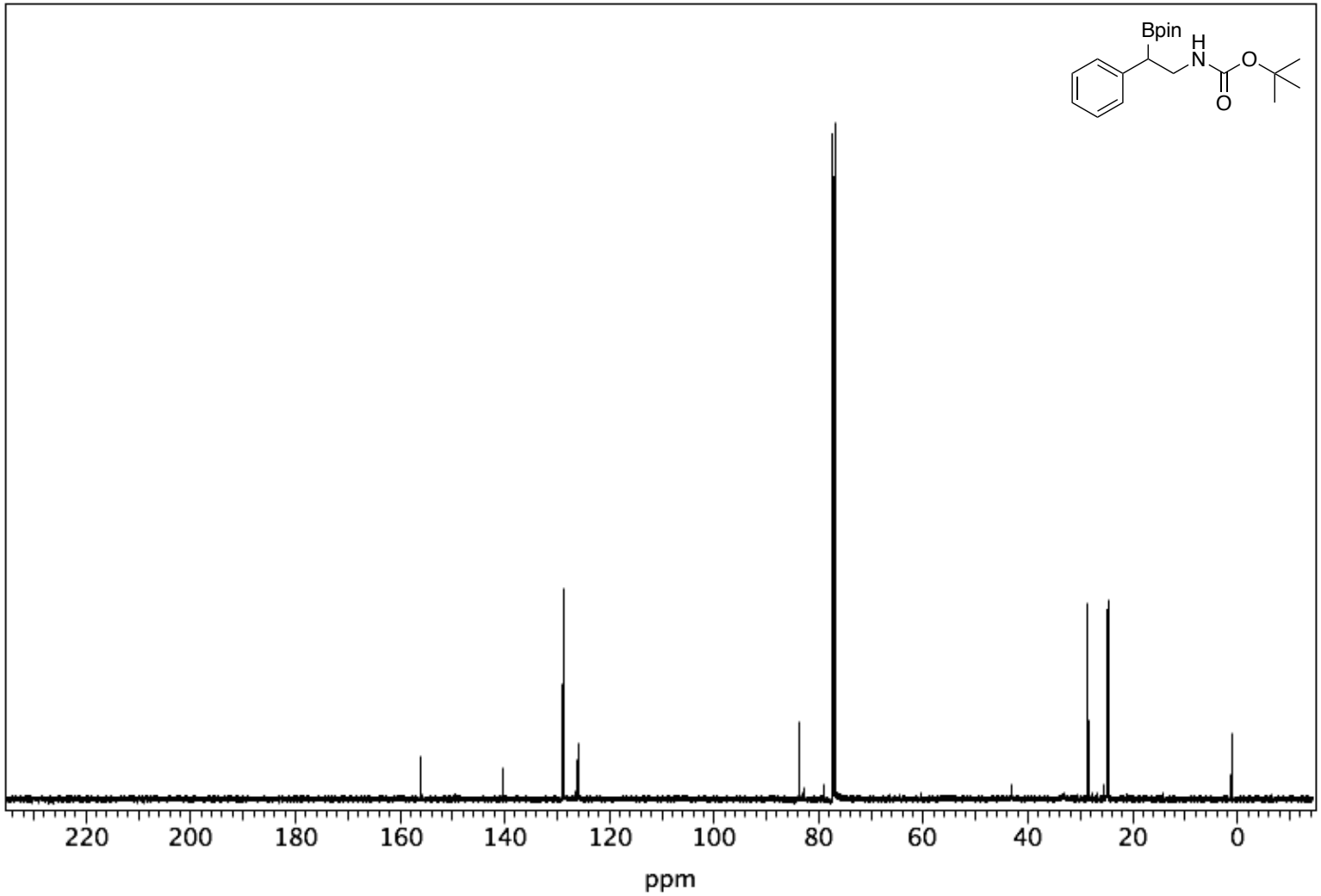


Figure A59. 125 MHz ^{13}C NMR of **3.15** in $CDCl_3$

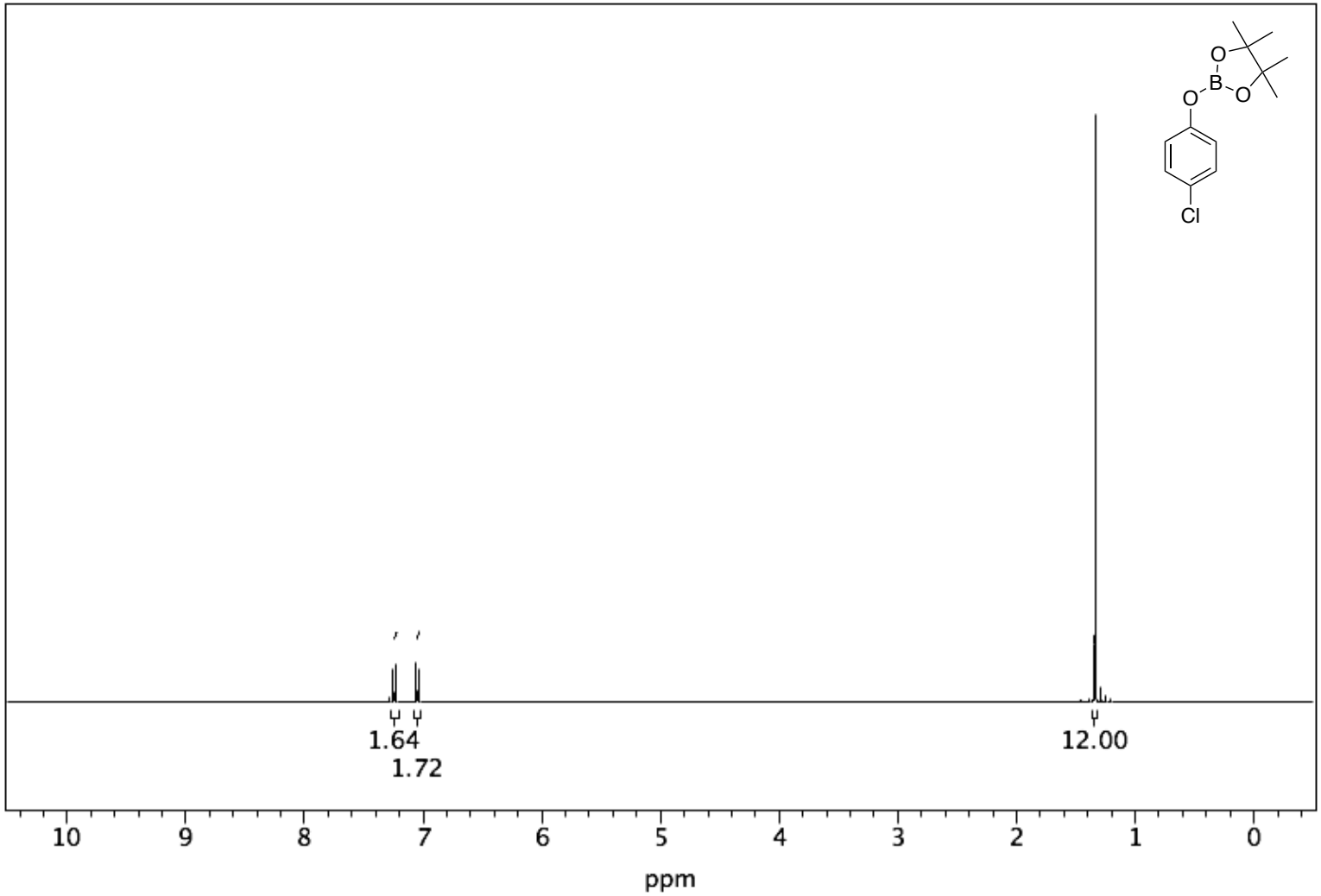


Figure A60. 500 MHz ^{1}H NMRNMR of 2-(4-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

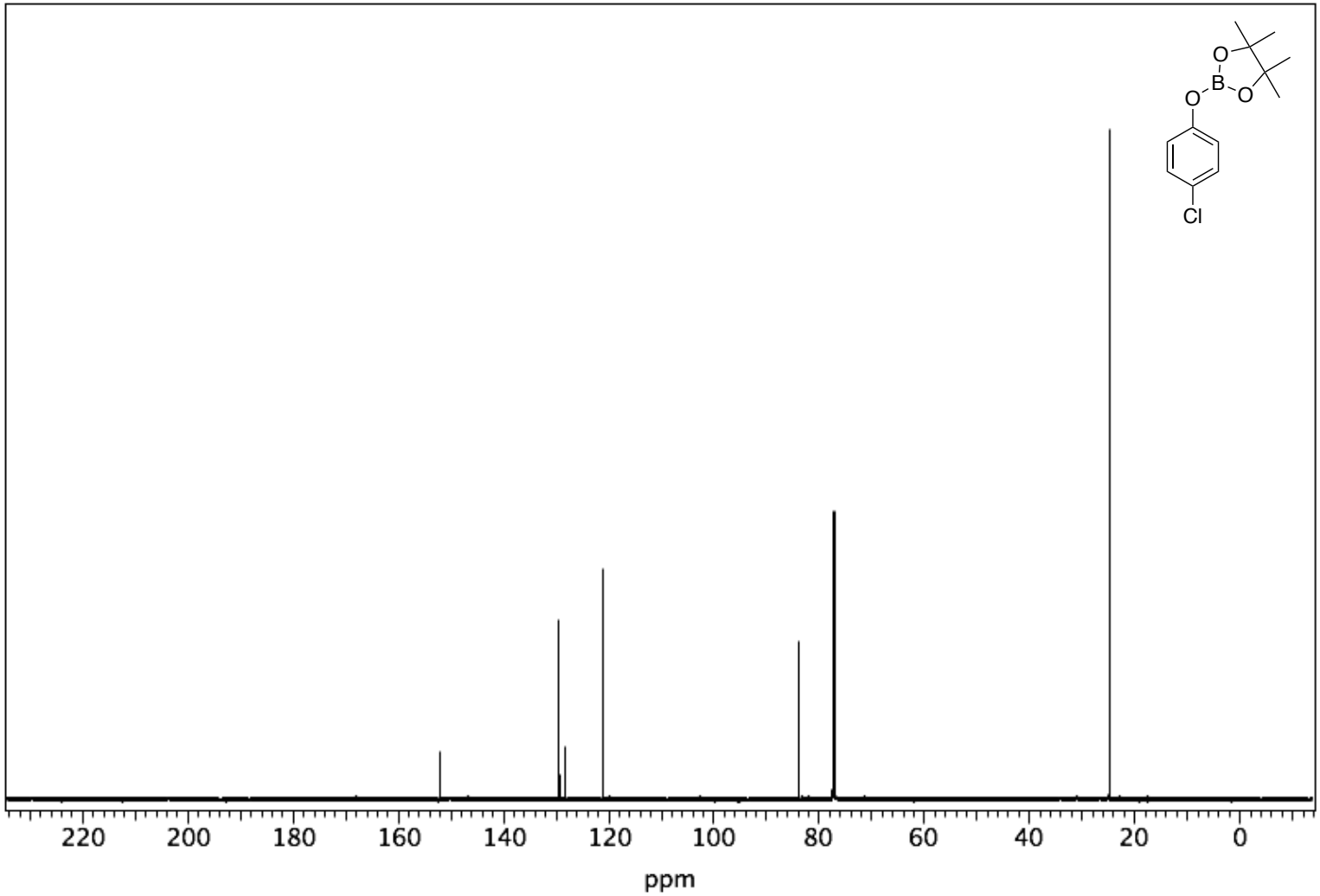


Figure A61. 125 MHz ^{13}C NMR of 2-(4-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

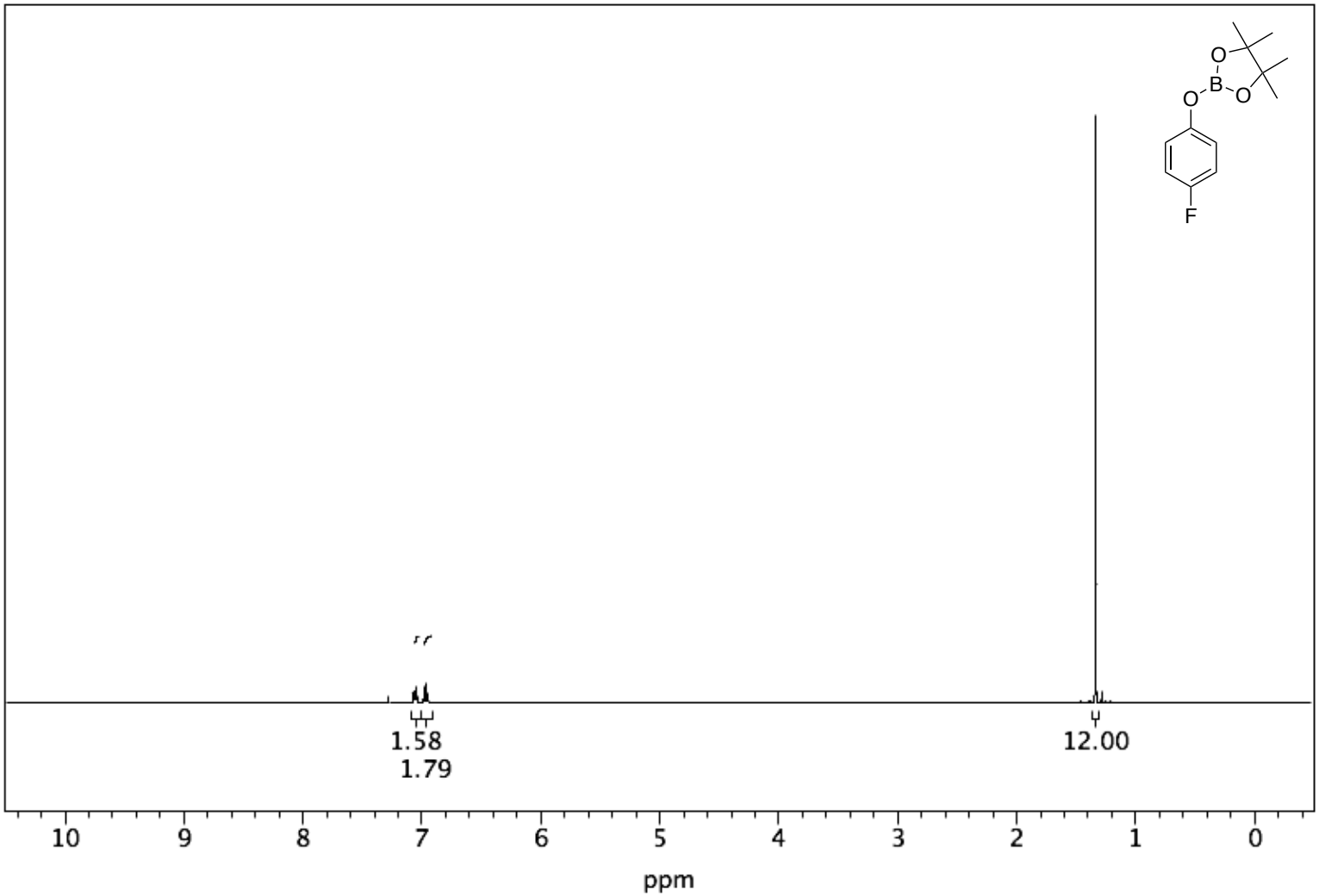


Figure A62. 500 MHz ^{1}H NMR of 2-(4-fluorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

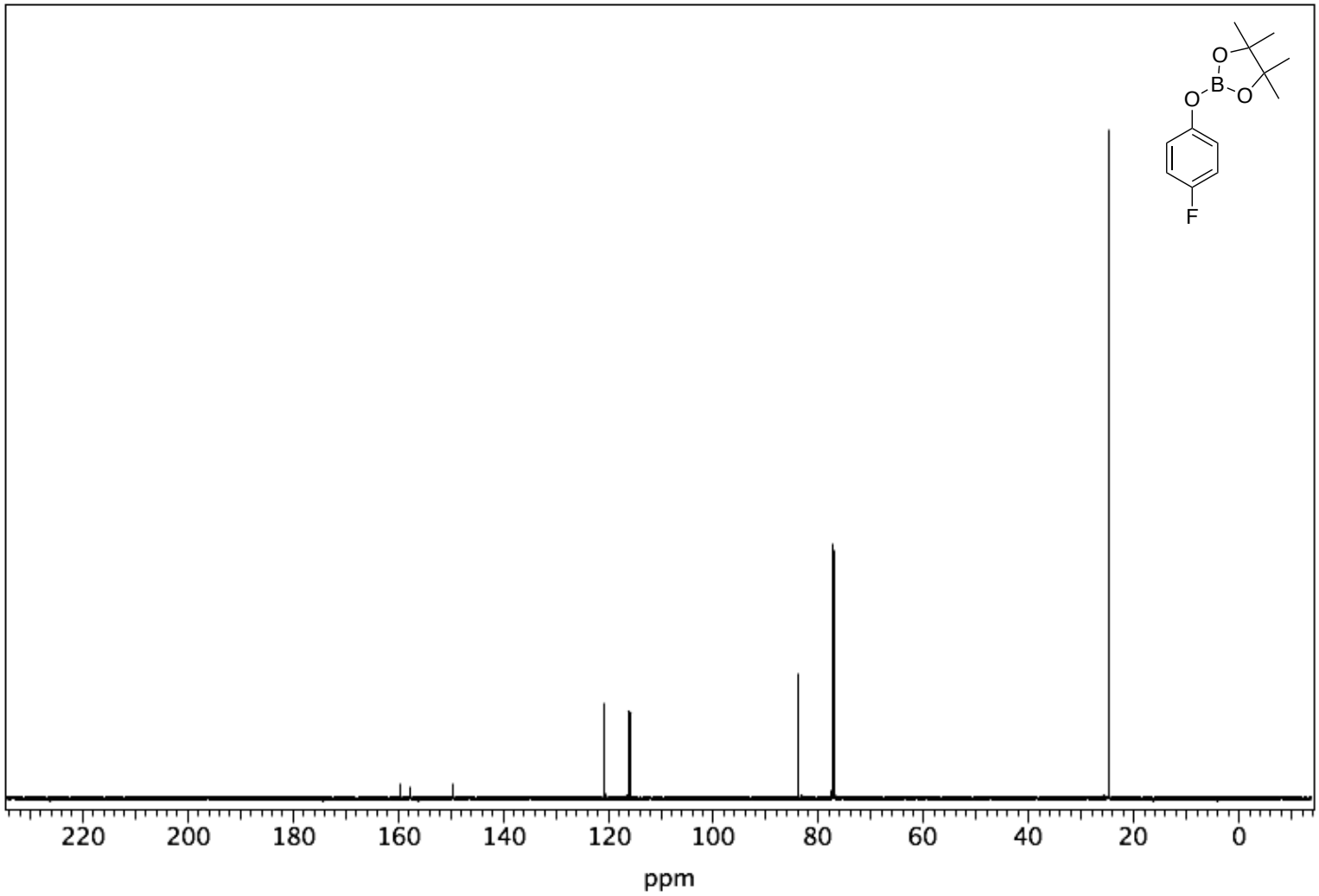


Figure A63. 125 MHz ^{13}C NMR of 2-(4-fluorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

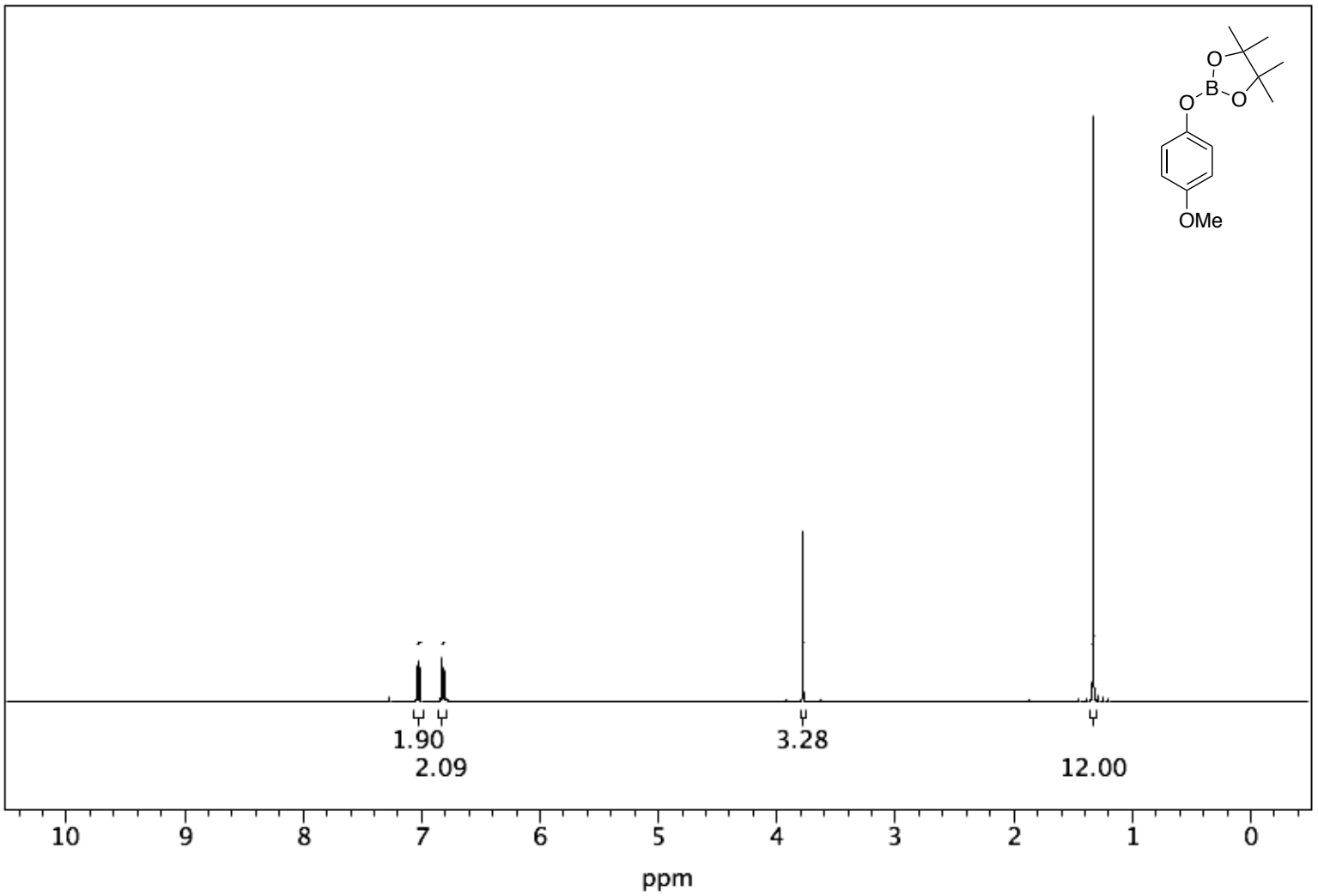


Figure A64. 500 MHz ^{1}H NMR of 2-(4-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

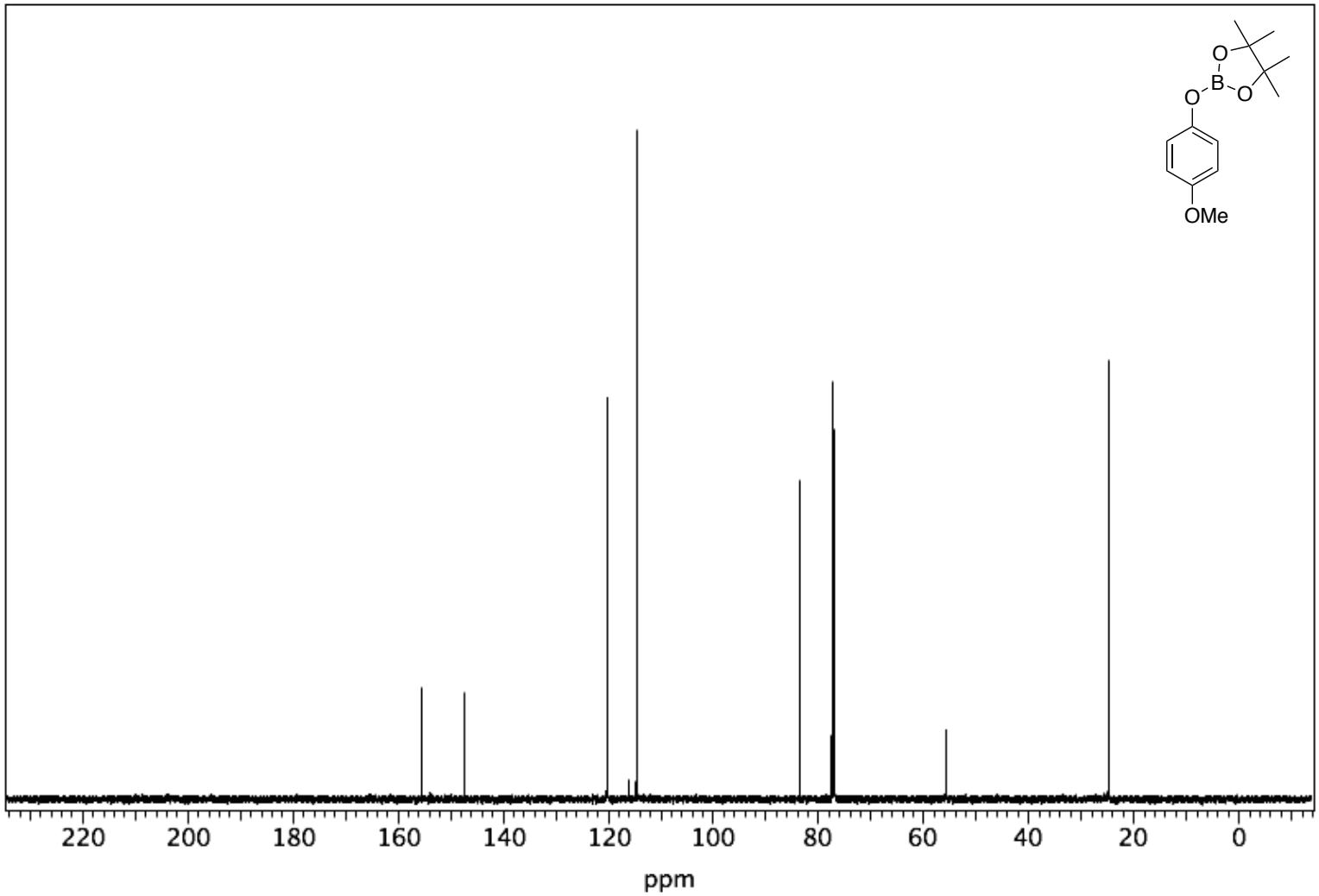


Figure A65. 125 MHz ^{13}C NMR of 2-(4-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

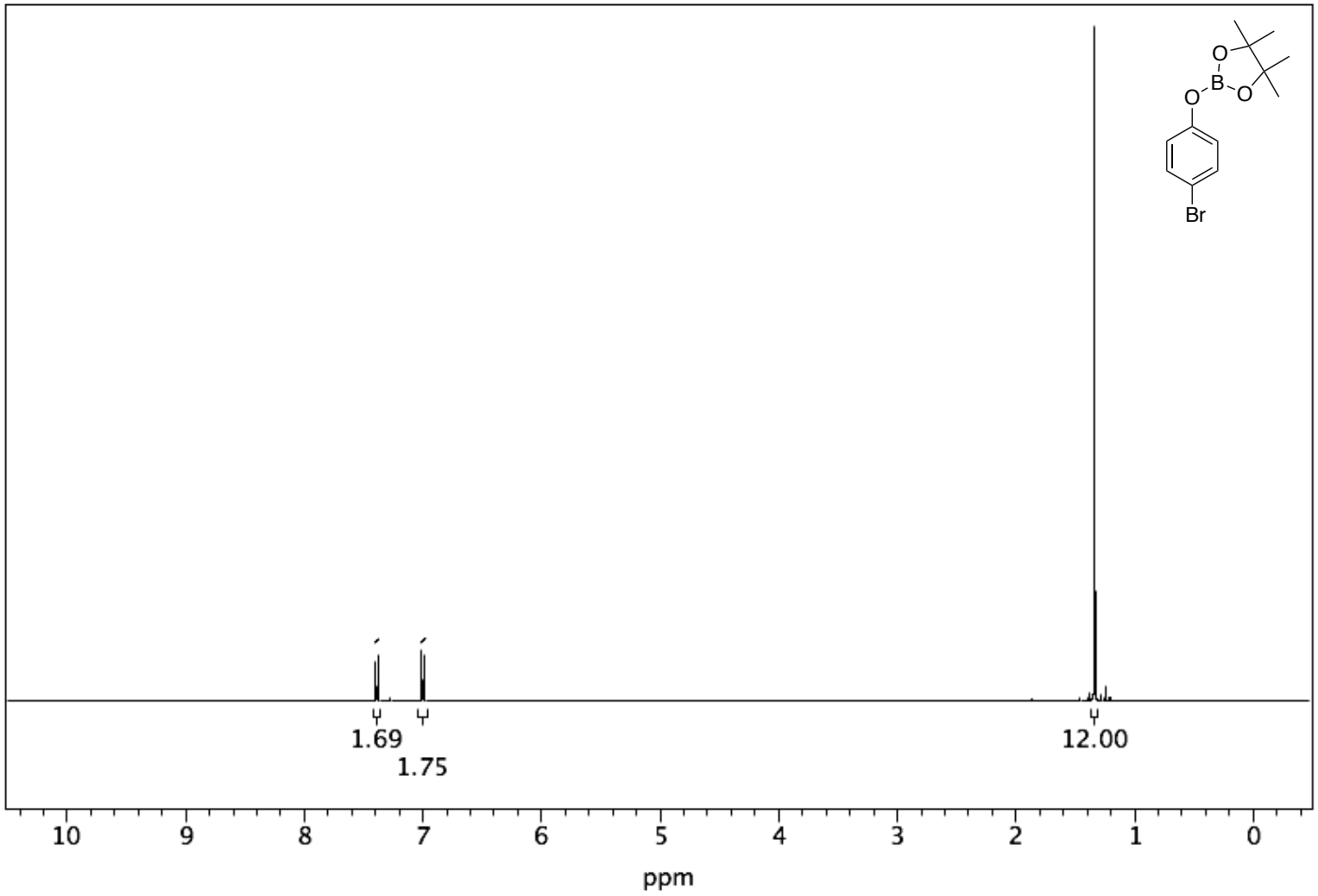


Figure A66. 500 MHz ^{1}H NMR of 2-(4-bromophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

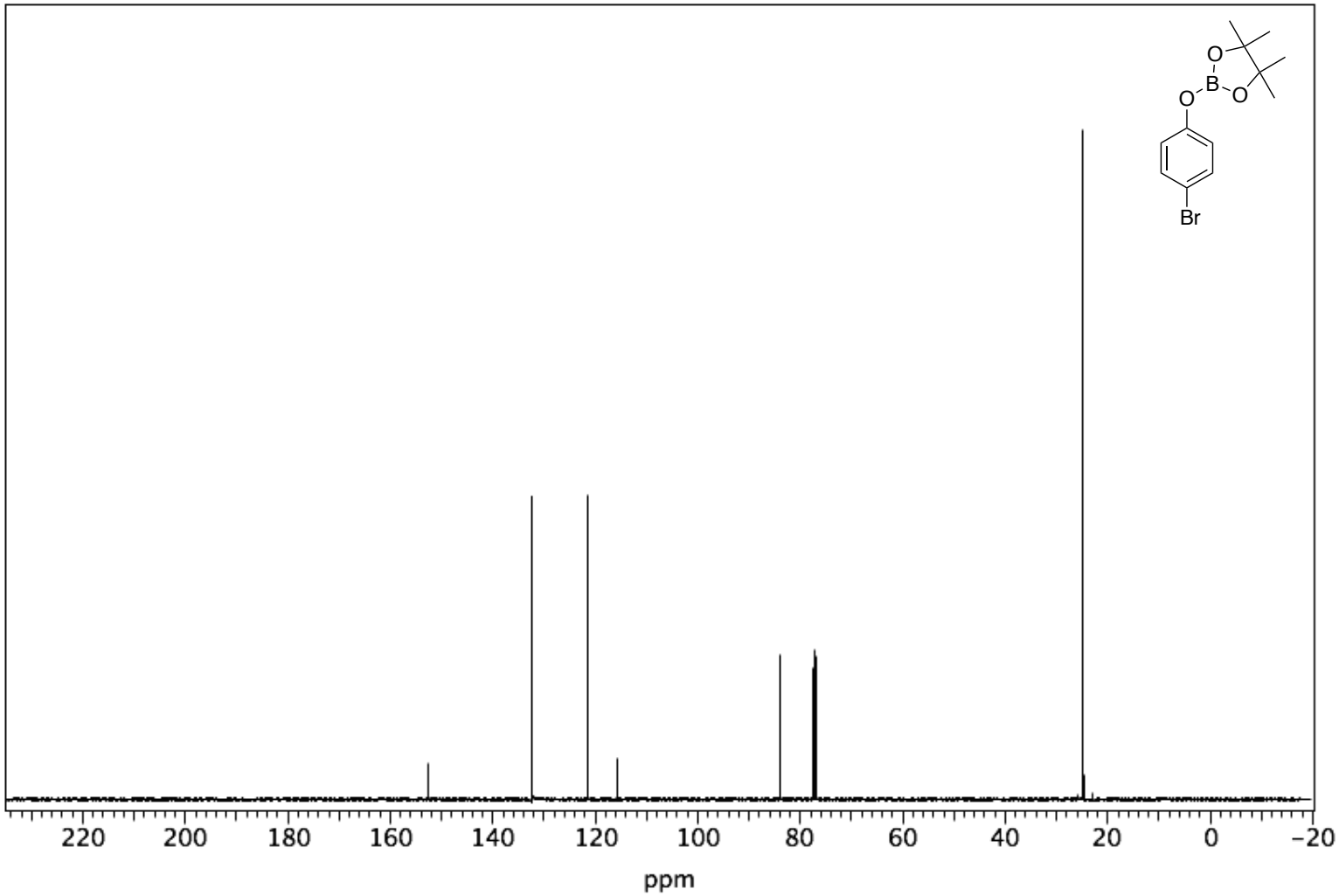


Figure A67. 125 MHz ^{1}C NMR of 2-(4-bromophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

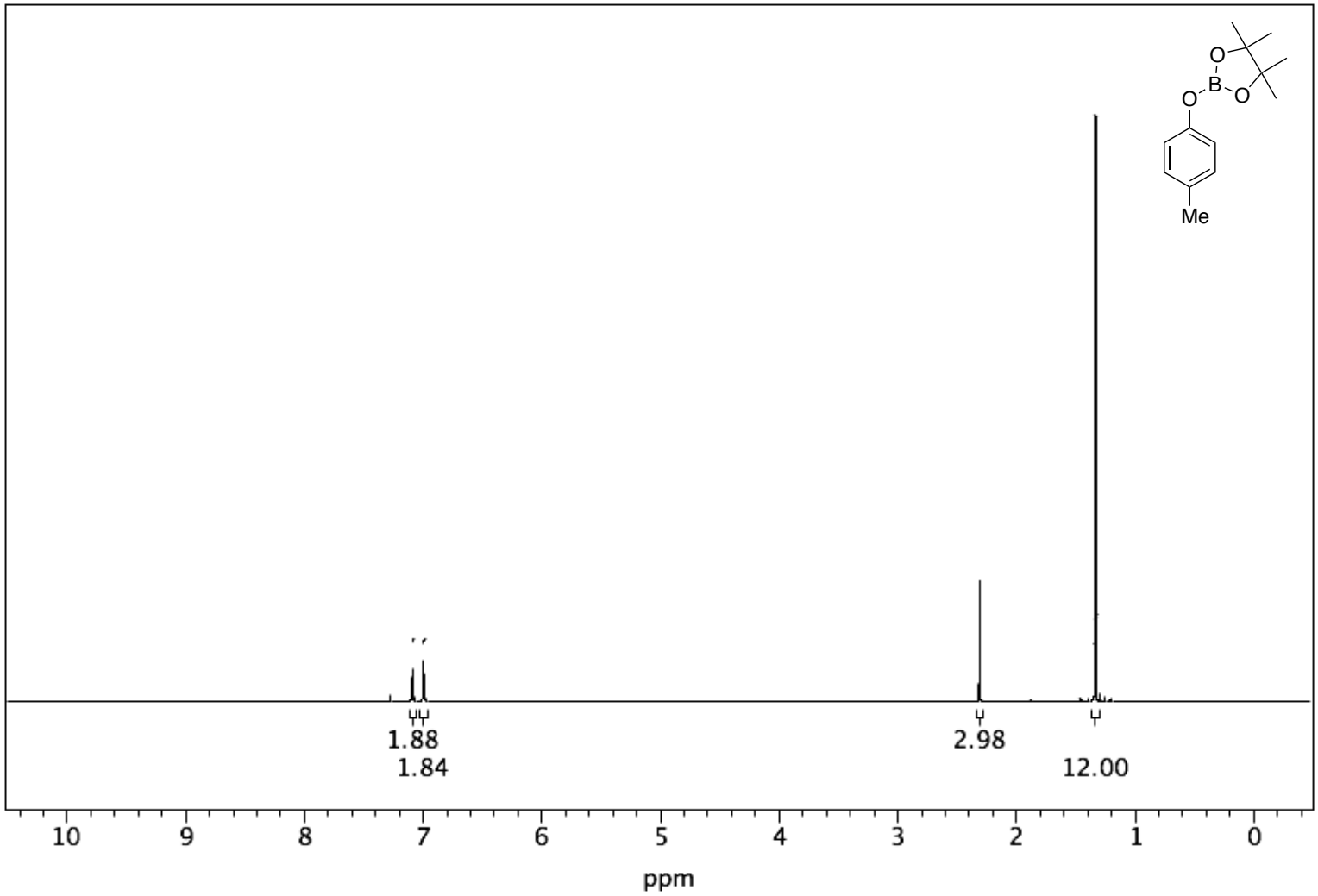


Figure A68. 500 MHz ^{1}H NMR of 4,4,5,5-tetramethyl-2-(p-tolyloxy)-1,3,2-dioxaborolane in $CDCl_3$

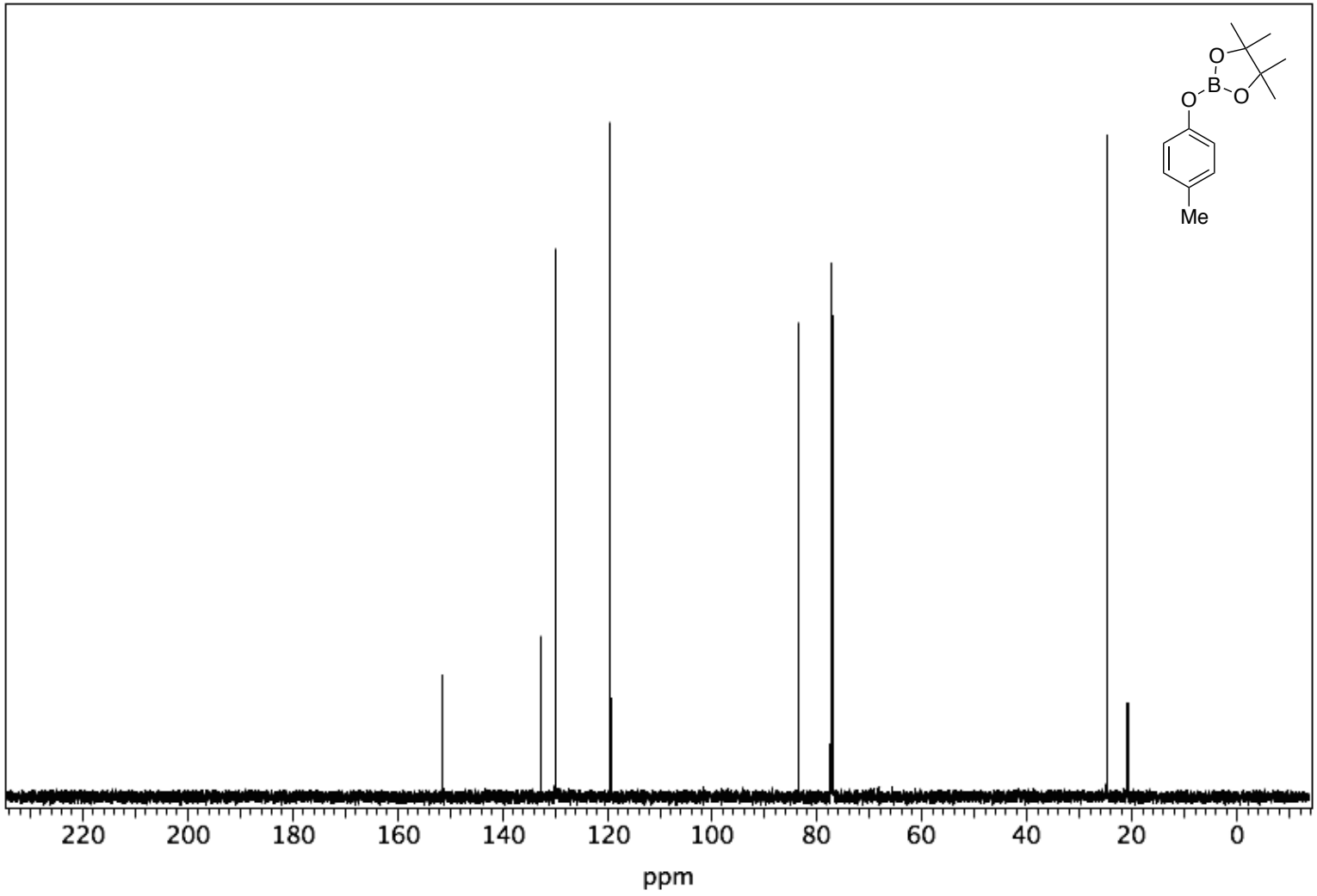


Figure A69. 125 MHz ^{13}C NMR of 4,4,5,5-tetramethyl-2-(p-tolyloxy)-1,3,2-dioxaborolane in $CDCl_3$

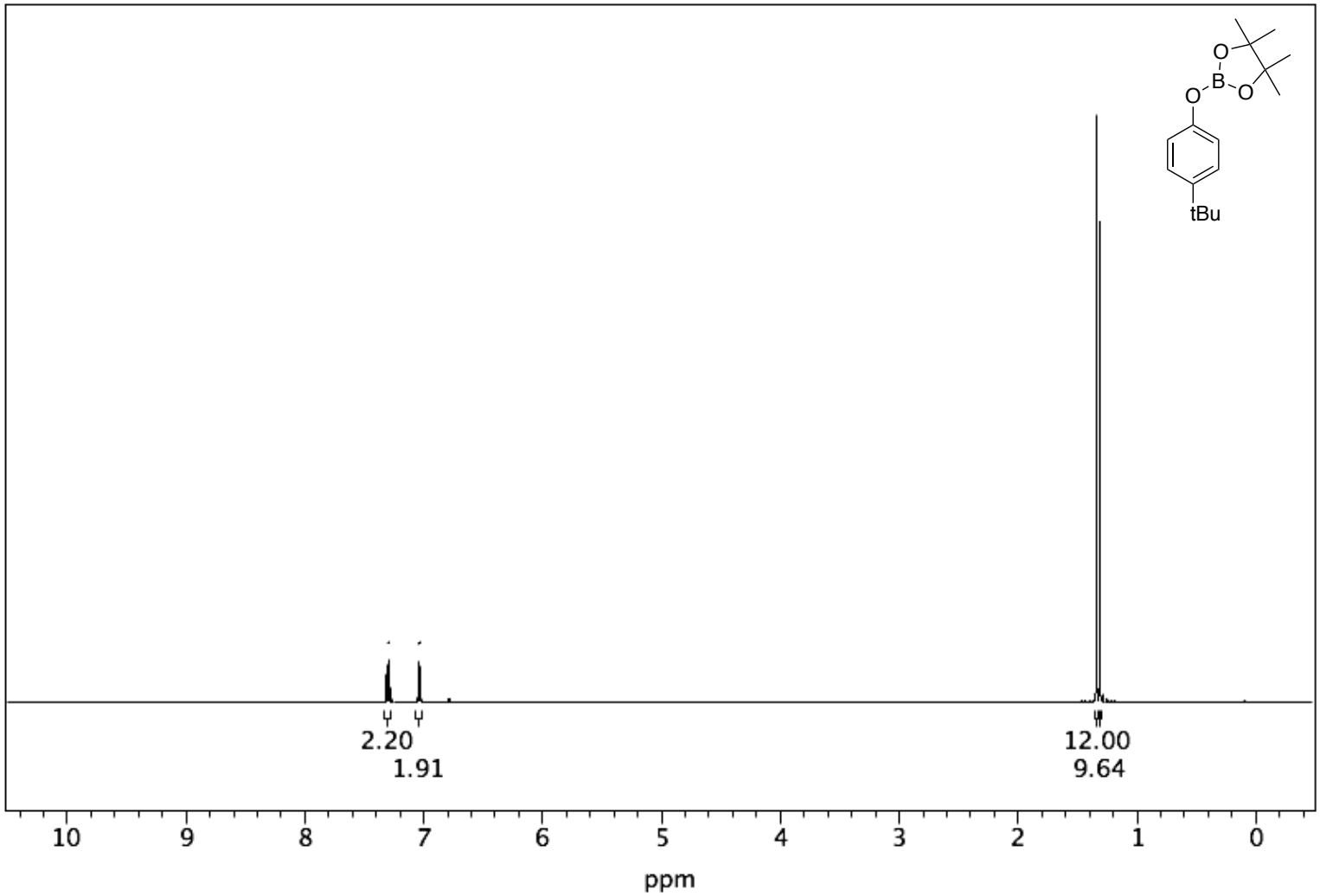


Figure A70. 500 MHz ^{1}H NMR of 2-(4-(tert-butyl)phenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

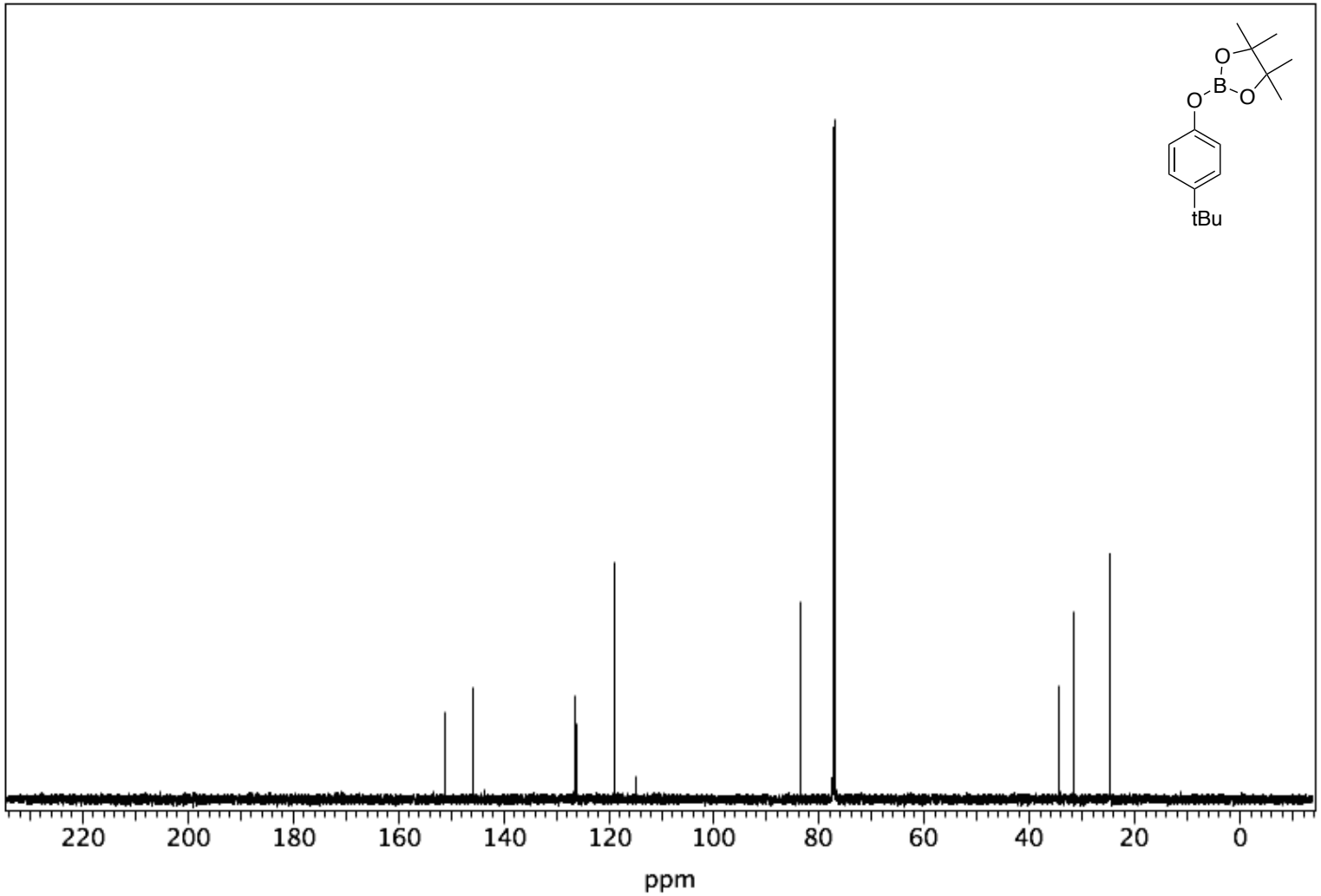


Figure A71. 125 MHz ^{13}C NMR of 2-(4-(tert-butyl)phenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

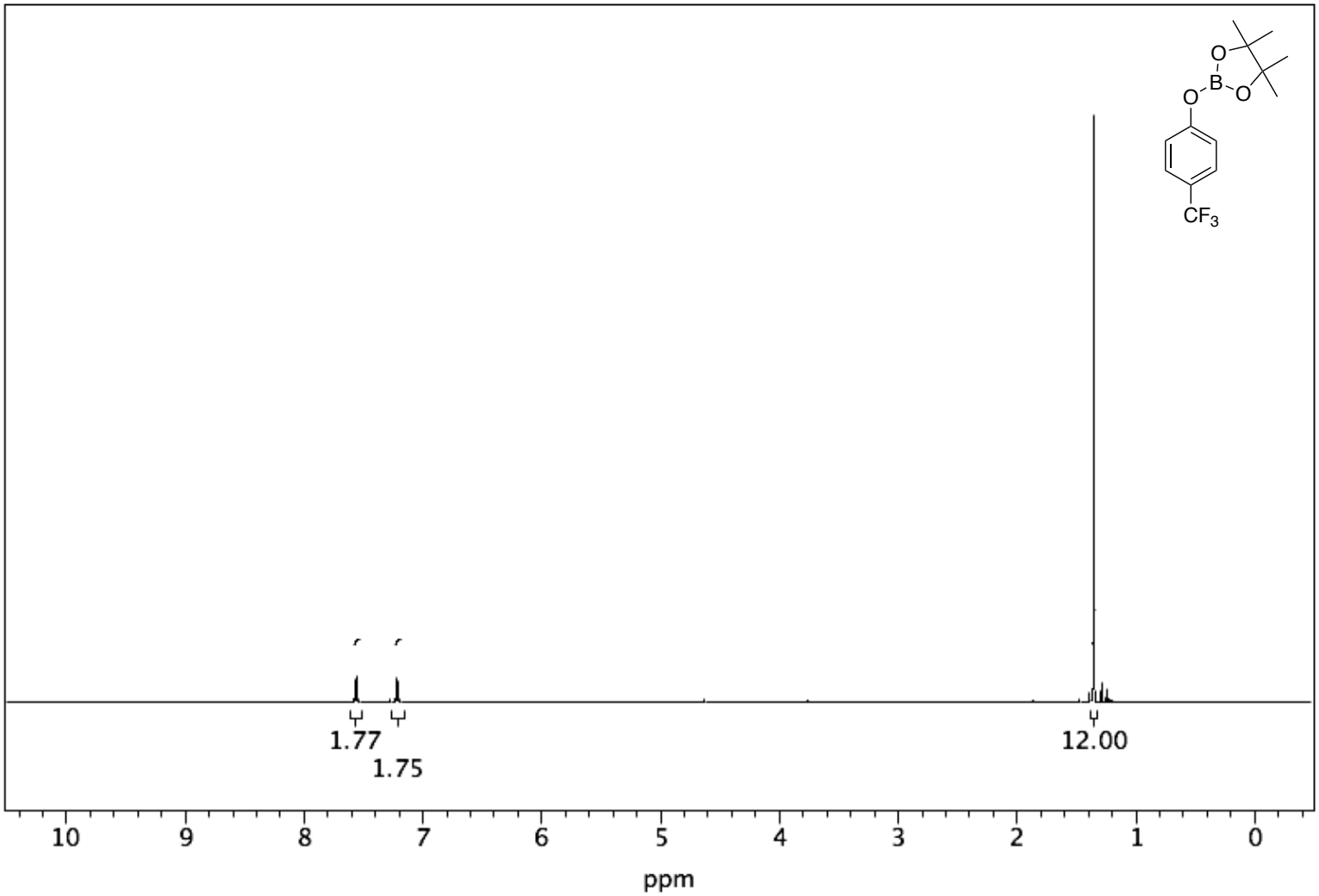


Figure A72. 500 MHz ^{1}H NMR of 4,4,5,5-tetramethyl-2-(4-(trifluoromethyl)phenoxy)-1,3,2-dioxaborolane in $CDCl_3$

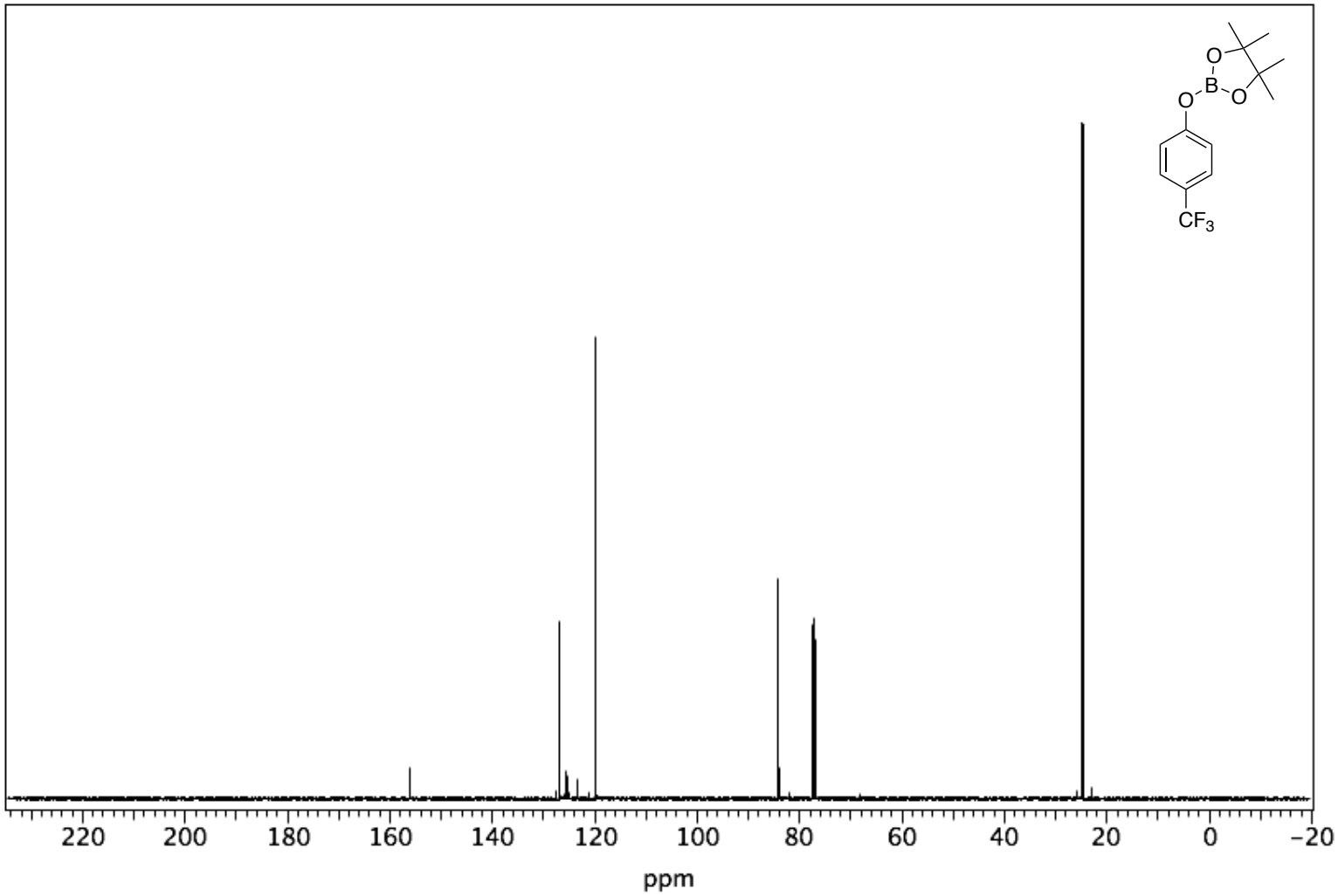


Figure A73. 125 MHz ^{13}C NMR of 4,4,5,5-tetramethyl-2-(4-(trifluoromethyl)phenoxy)-1,3,2-dioxaborolane in $CDCl_3$

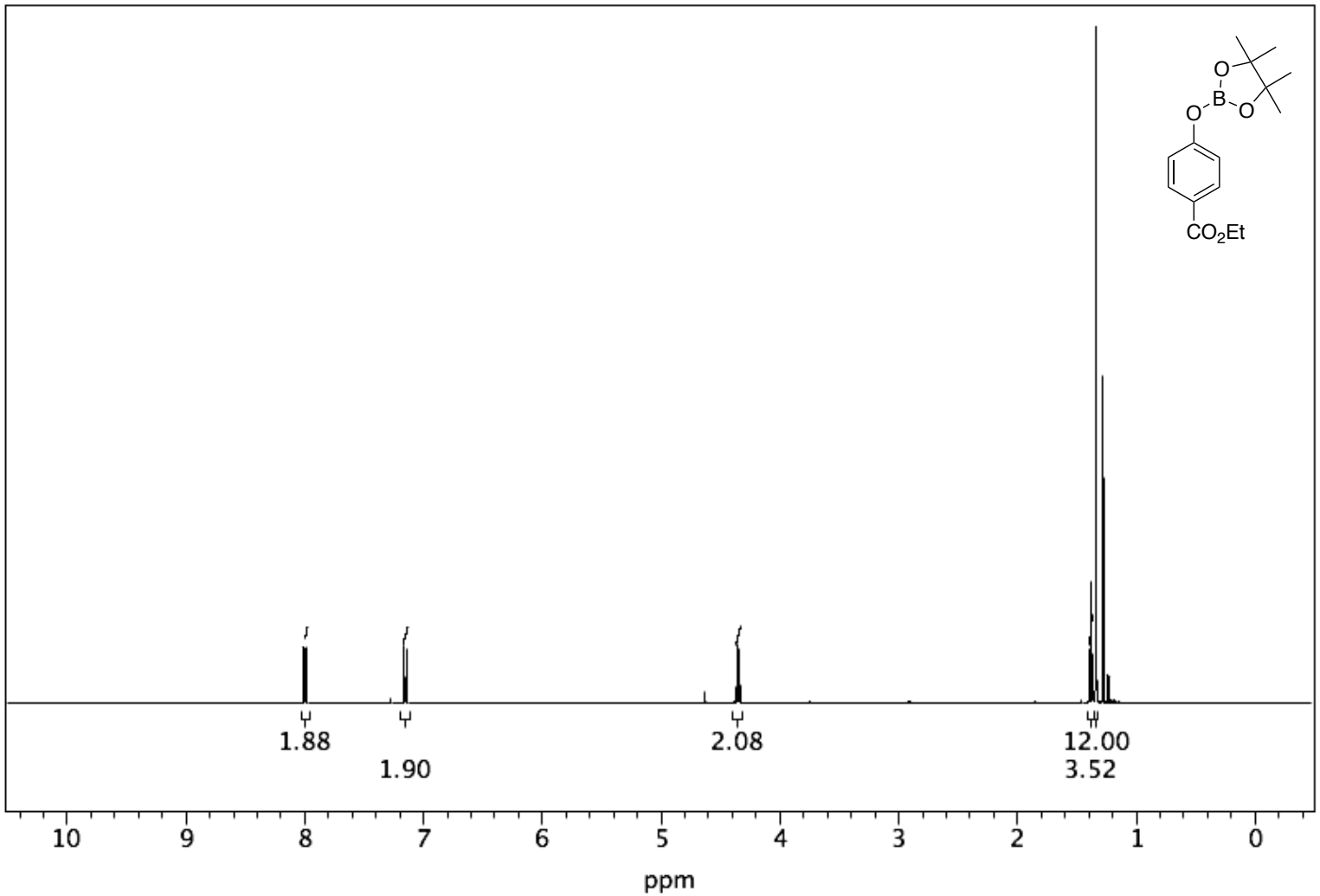


Figure A74. 500 MHz ^{1}H NMR of ethyl 4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate in $CDCl_3$

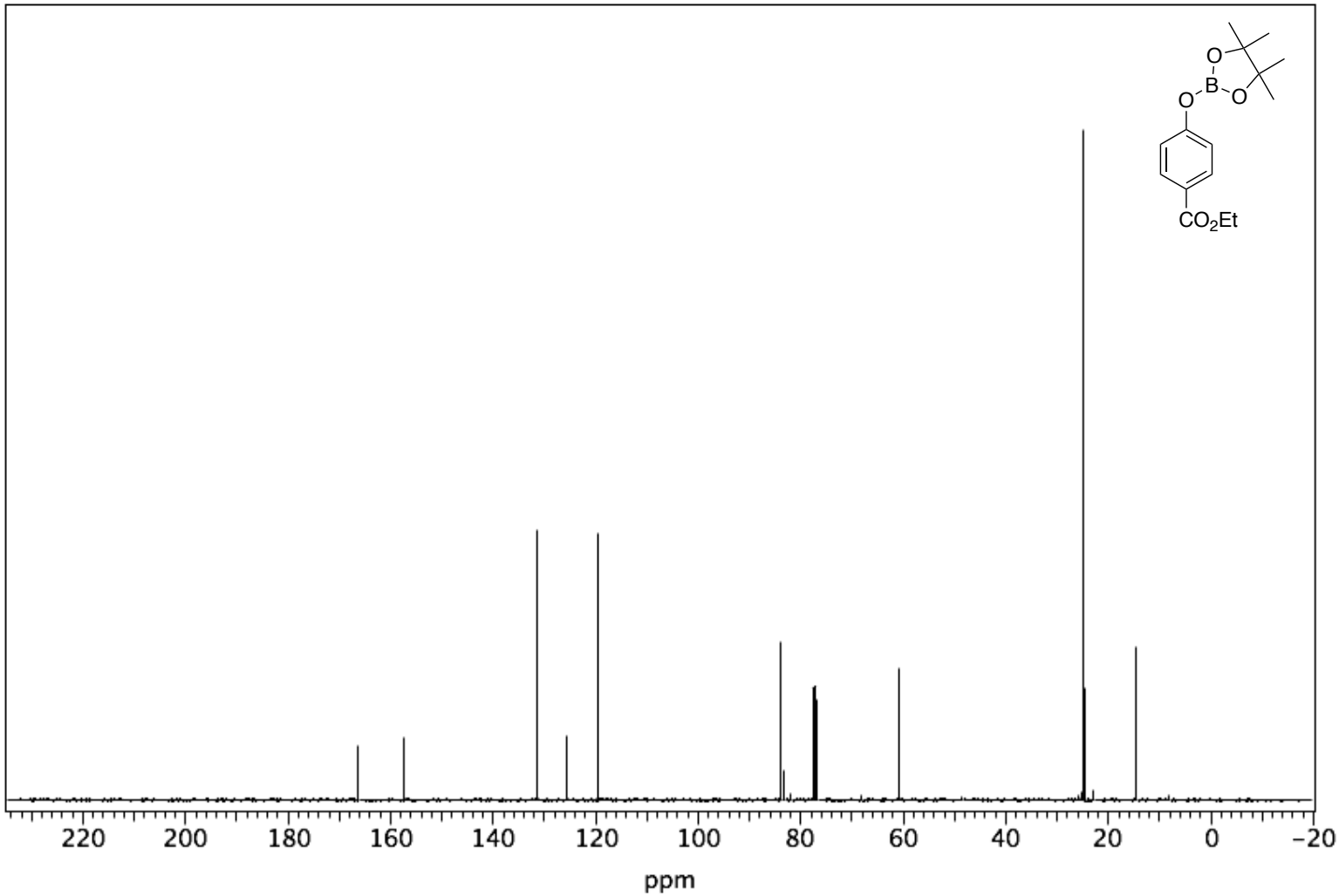


Figure A75. 125 MHz ^{13}C NMR of ethyl 4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate in $CDCl_3$

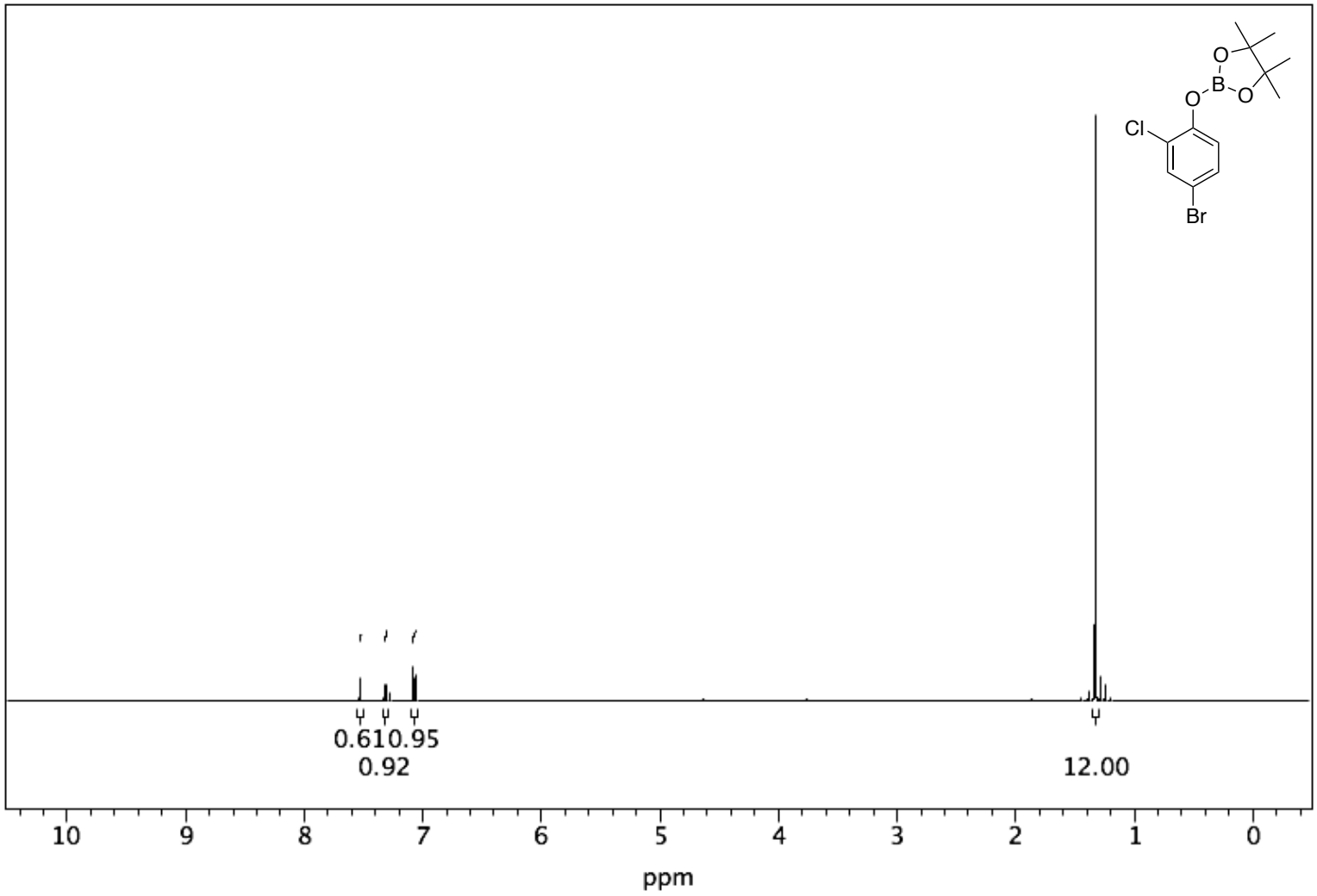


Figure A76. 500 MHz ^{1}H NMR of 2-(4-bromo-2-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

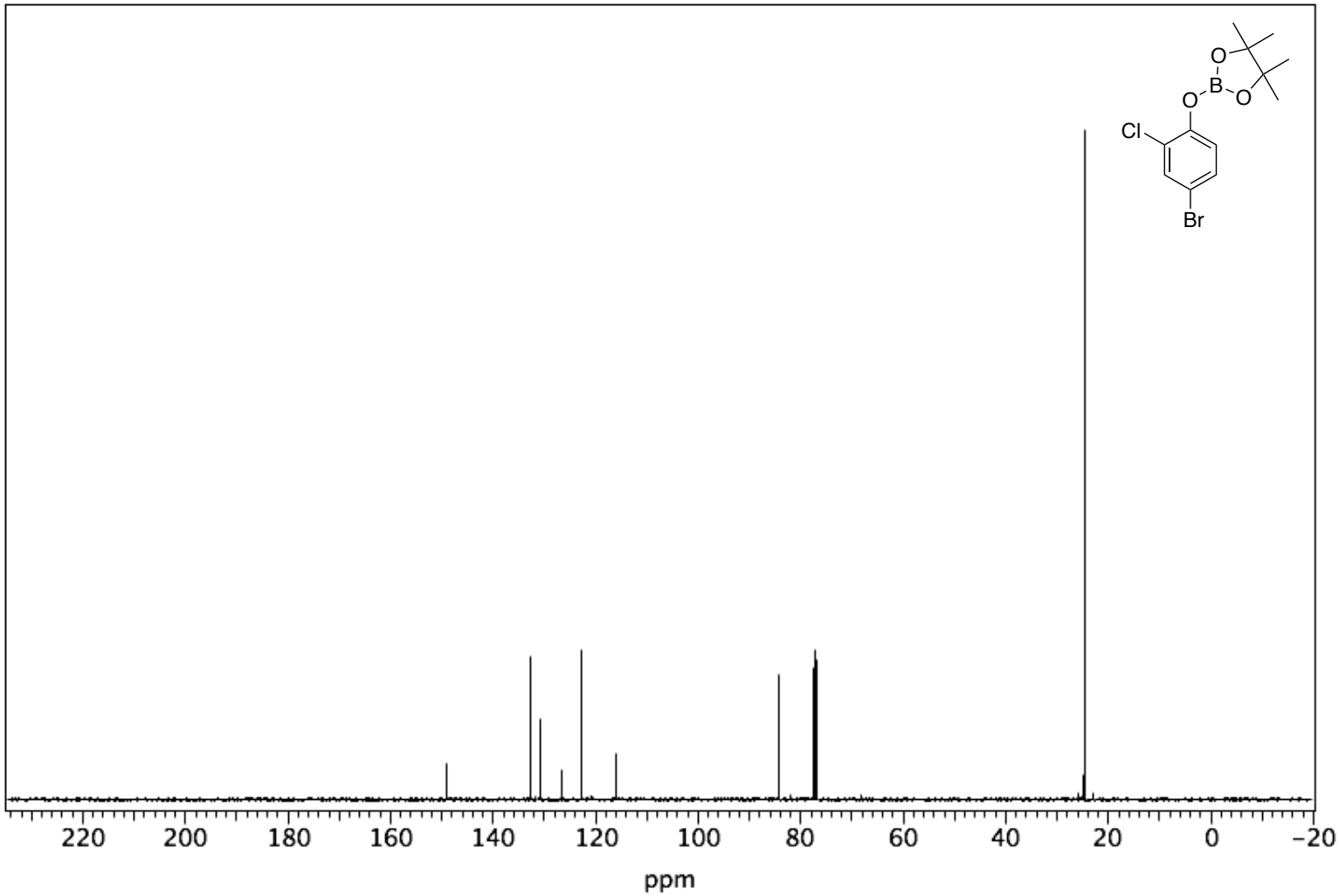


Figure A77. 125 MHz ^{13}C NMR of 2-(4-bromo-2-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

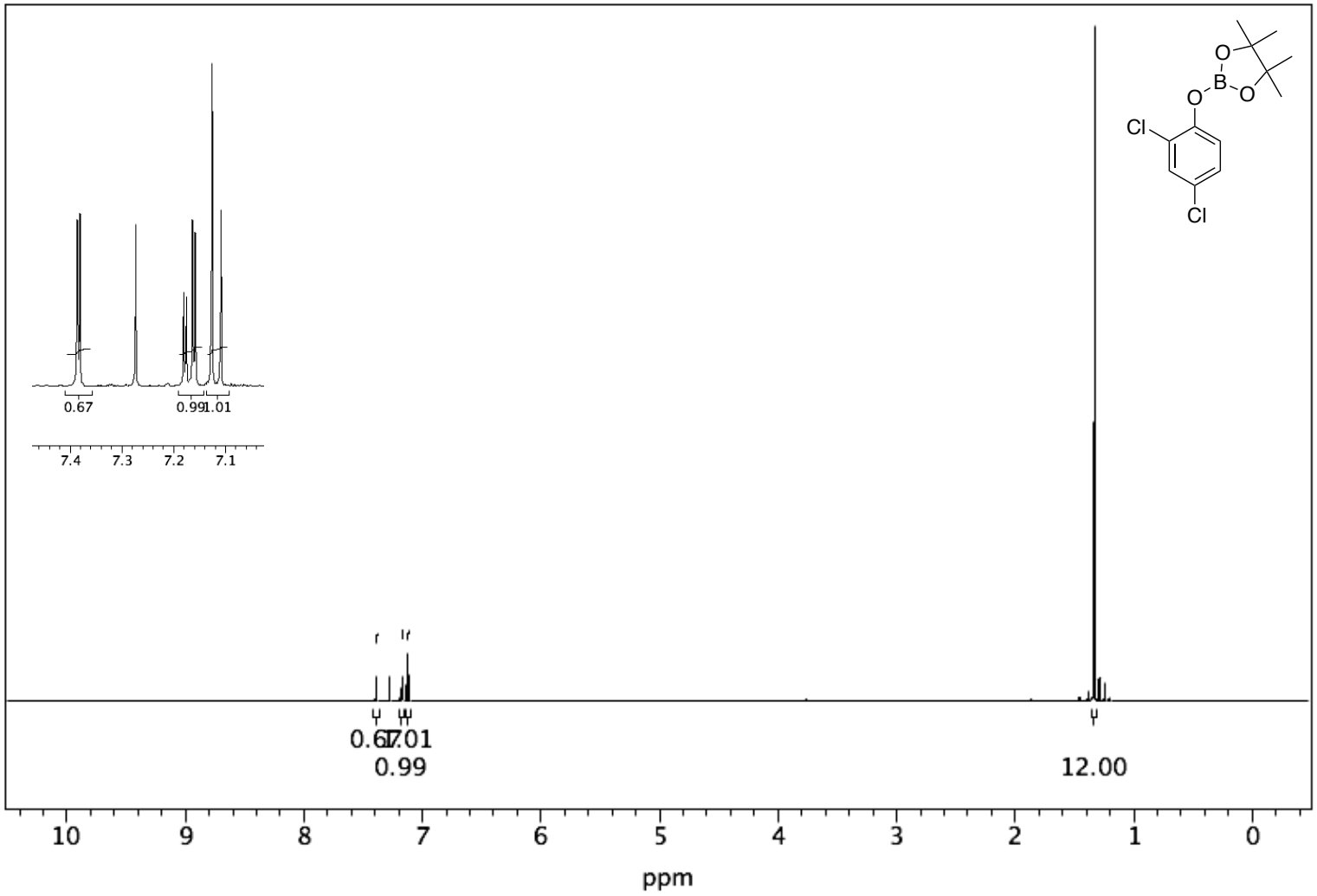


Figure A78. 500 MHz ^{1}H NMR of 2-(2,4-dichlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

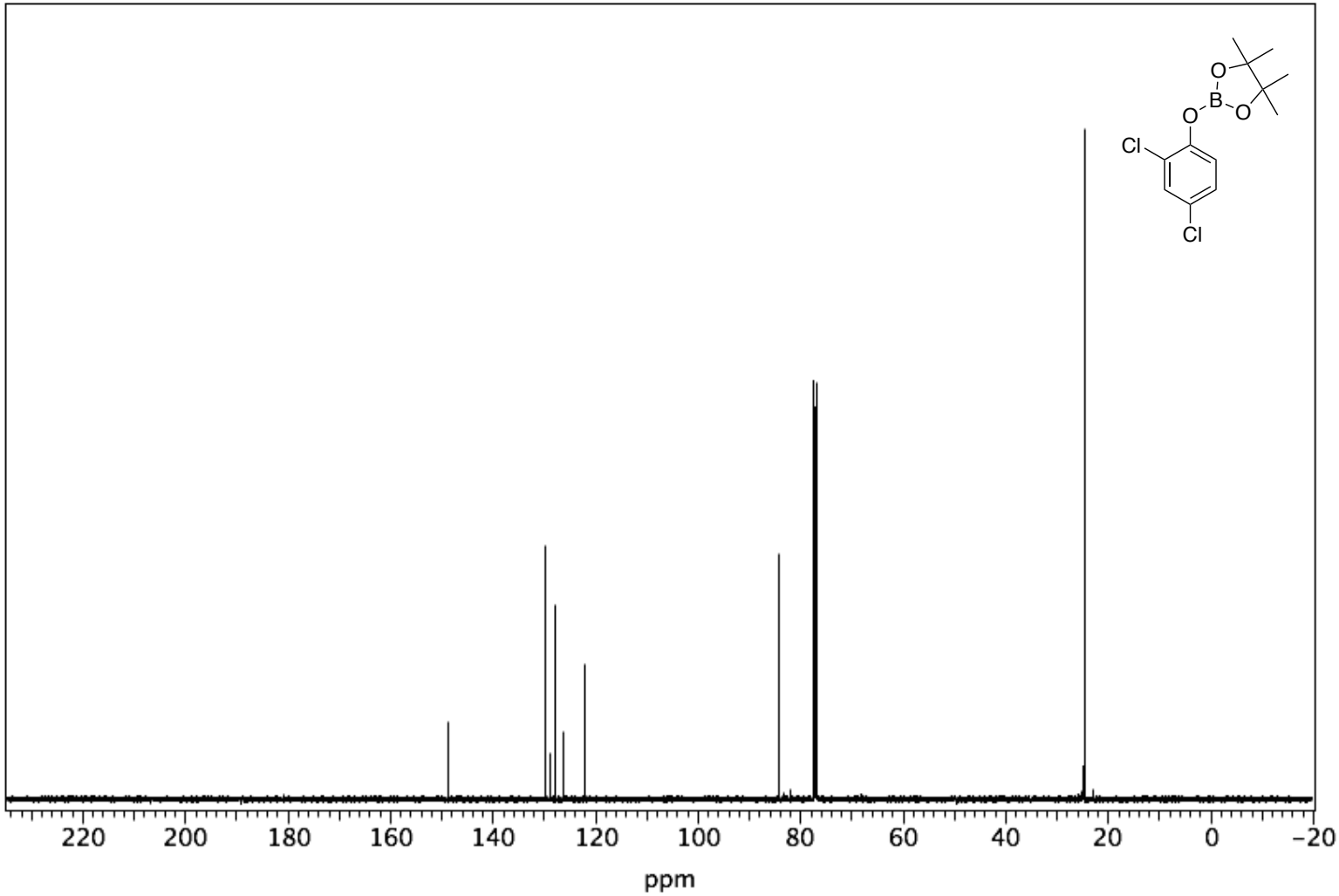


Figure A79. 125 MHz ^{13}C NMR of 2-(2,4-dichlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

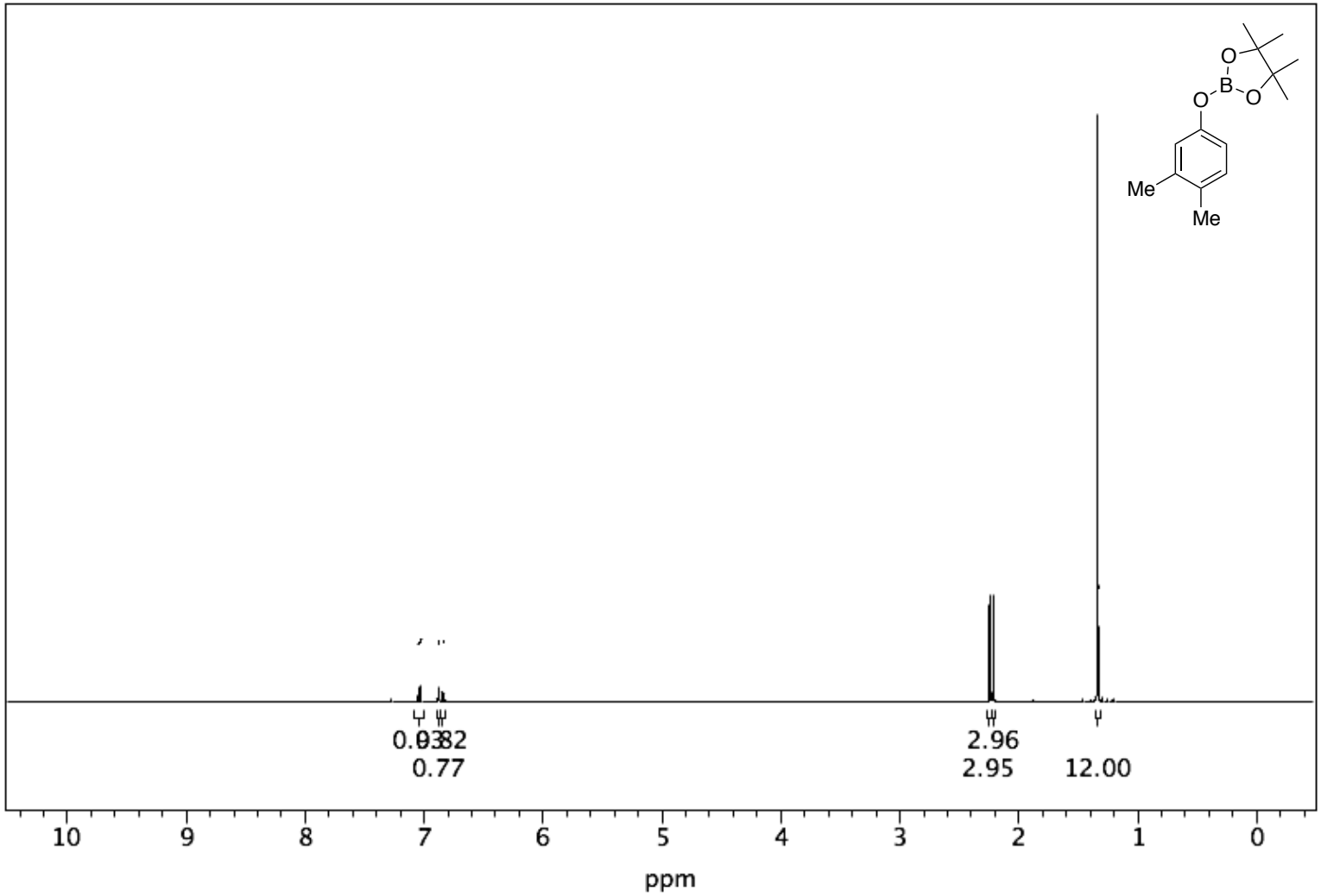


Figure A80. 500 MHZ ^{1}H NMR of 2-(3,4-dimethylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

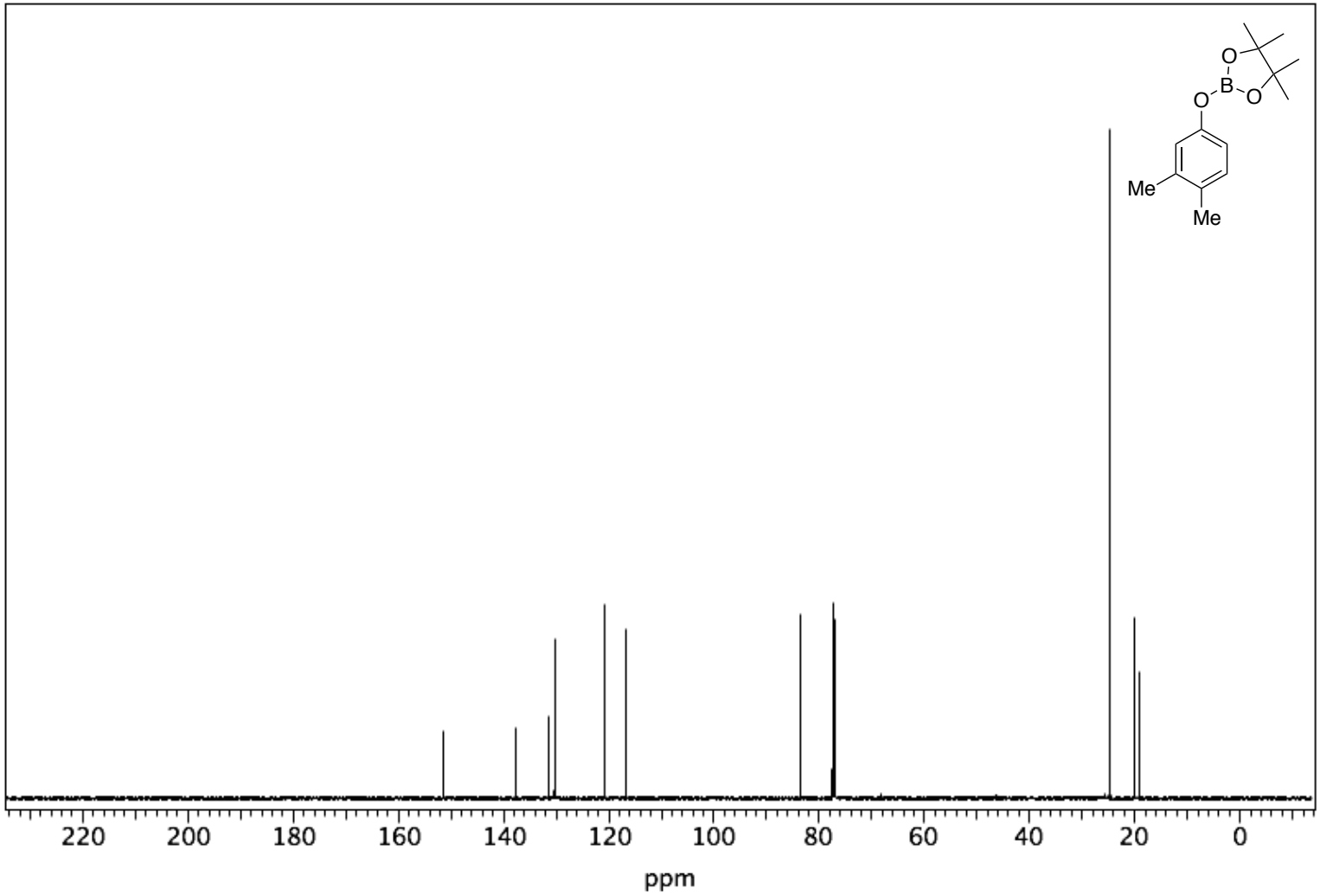


Figure A81. 125 MHZ ^{13}C NMR of 2-(3,4-dimethylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

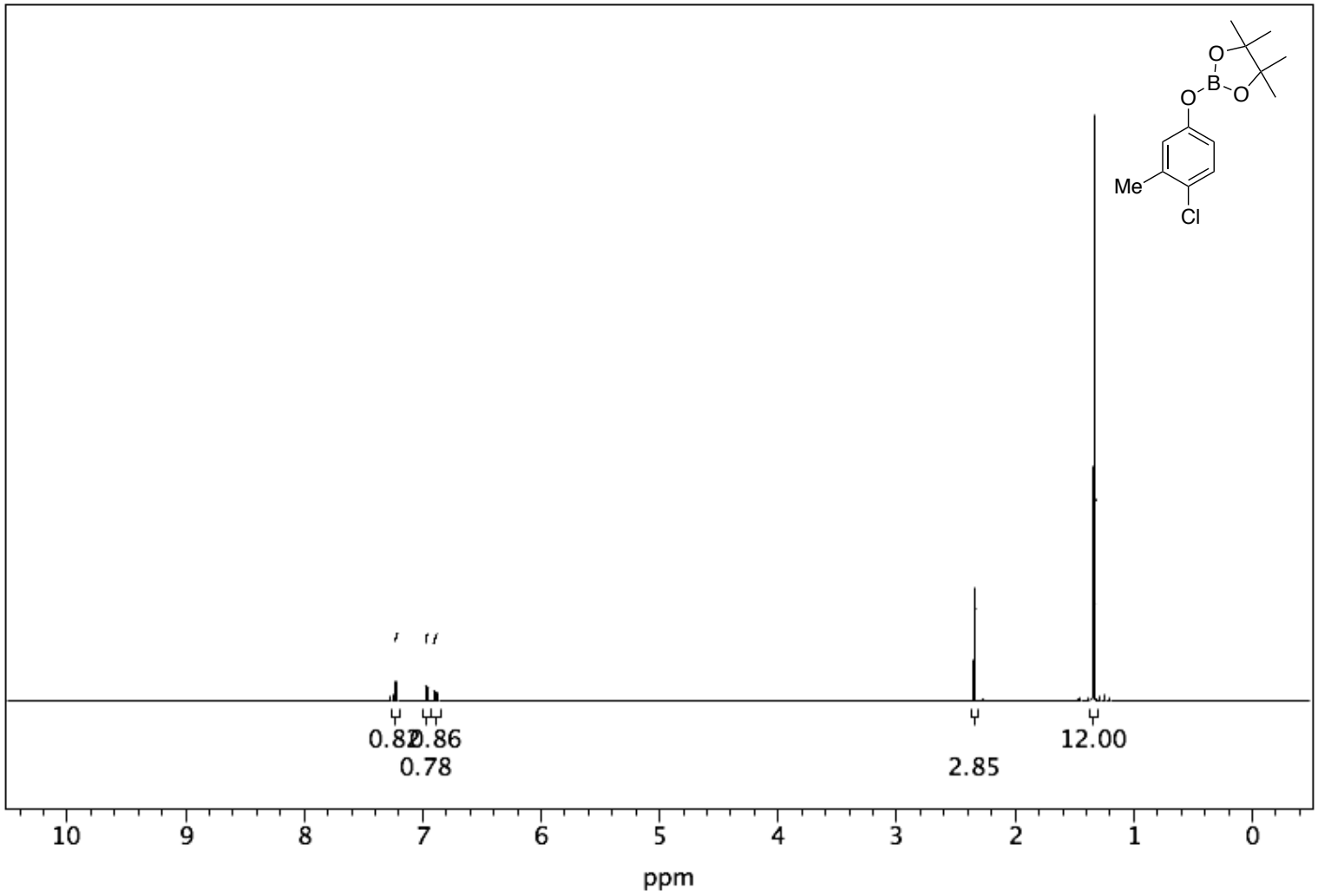


Figure A82. 500 MHz ^{1}H NMR of 2-(4-chloro-3-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

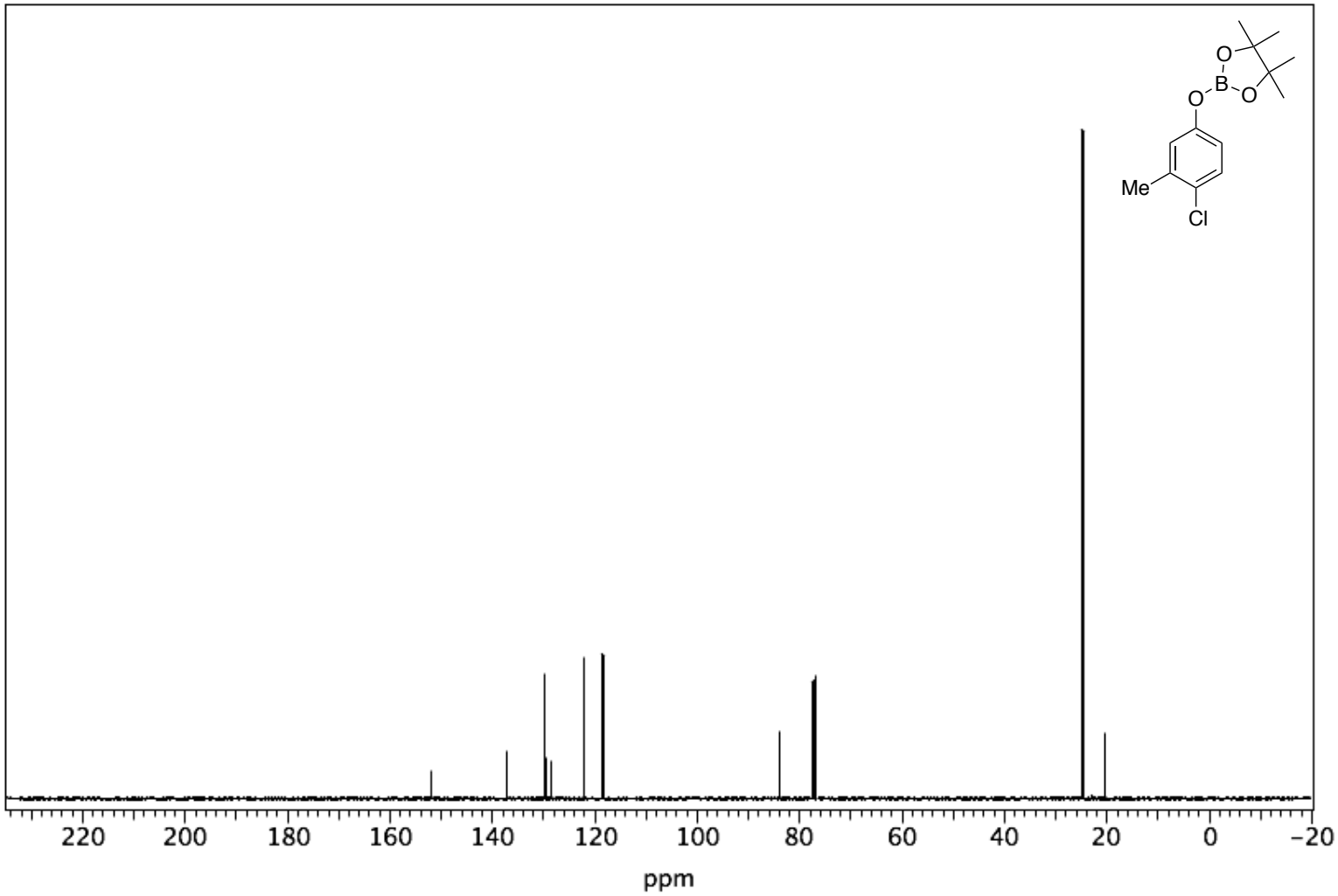


Figure A83. 125 MHz ^{13}C NMR of 2-(4-chloro-3-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

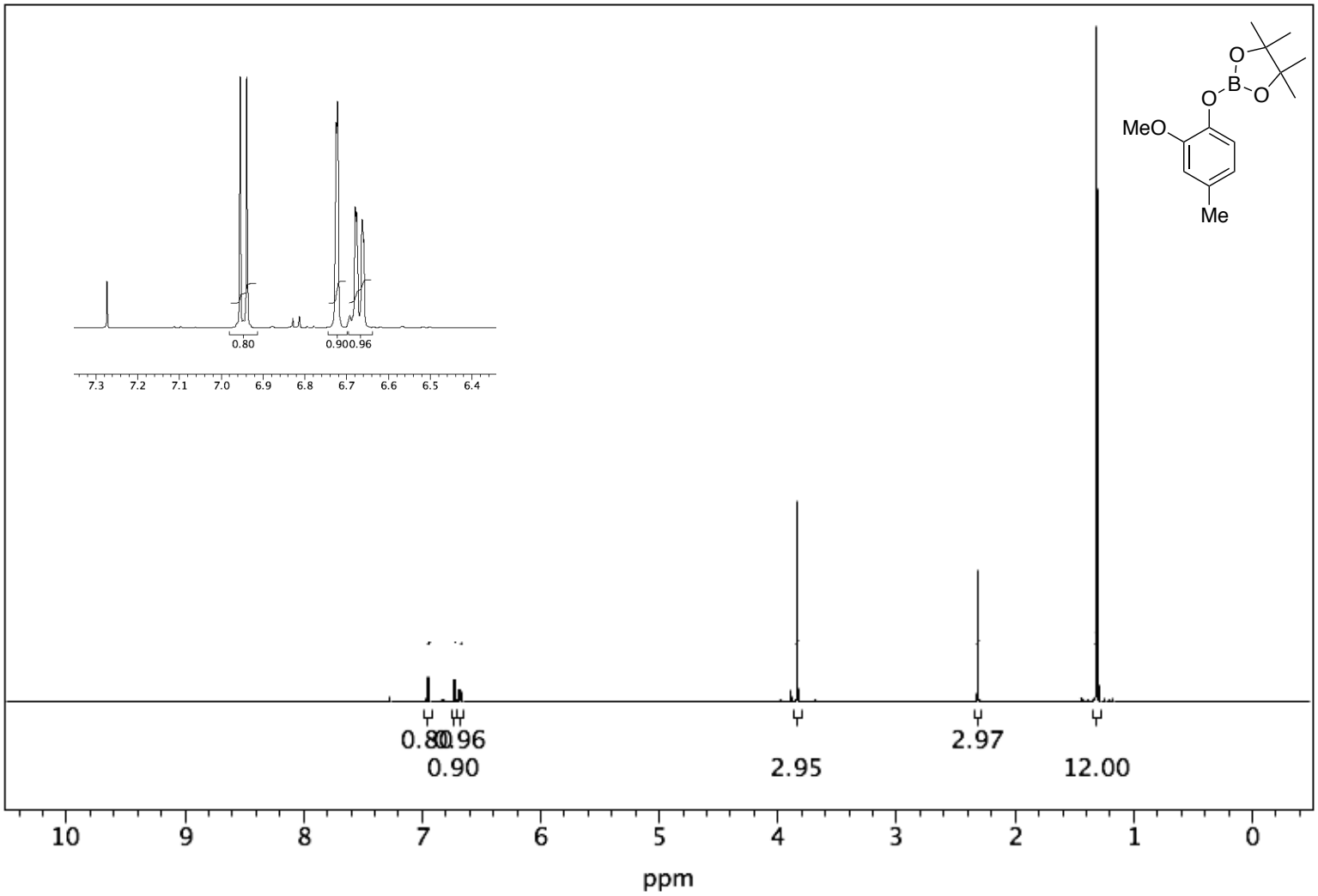


Figure A84. 500 MHz ^{1}H NMR of 2-(2-methoxy-4-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

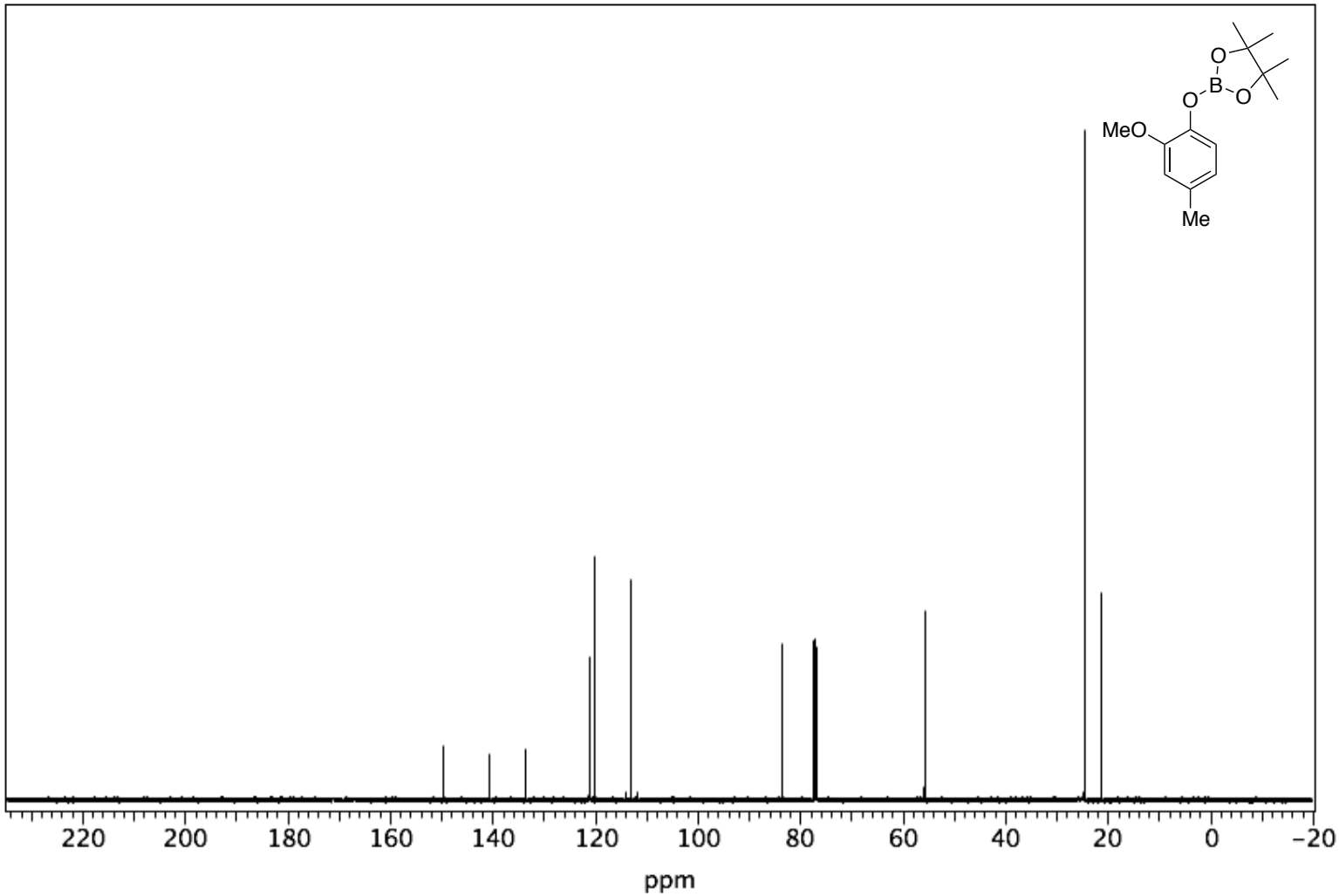


Figure A85. 125 MHz ^{13}C NMR of 2-(2-methoxy-4-methylphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

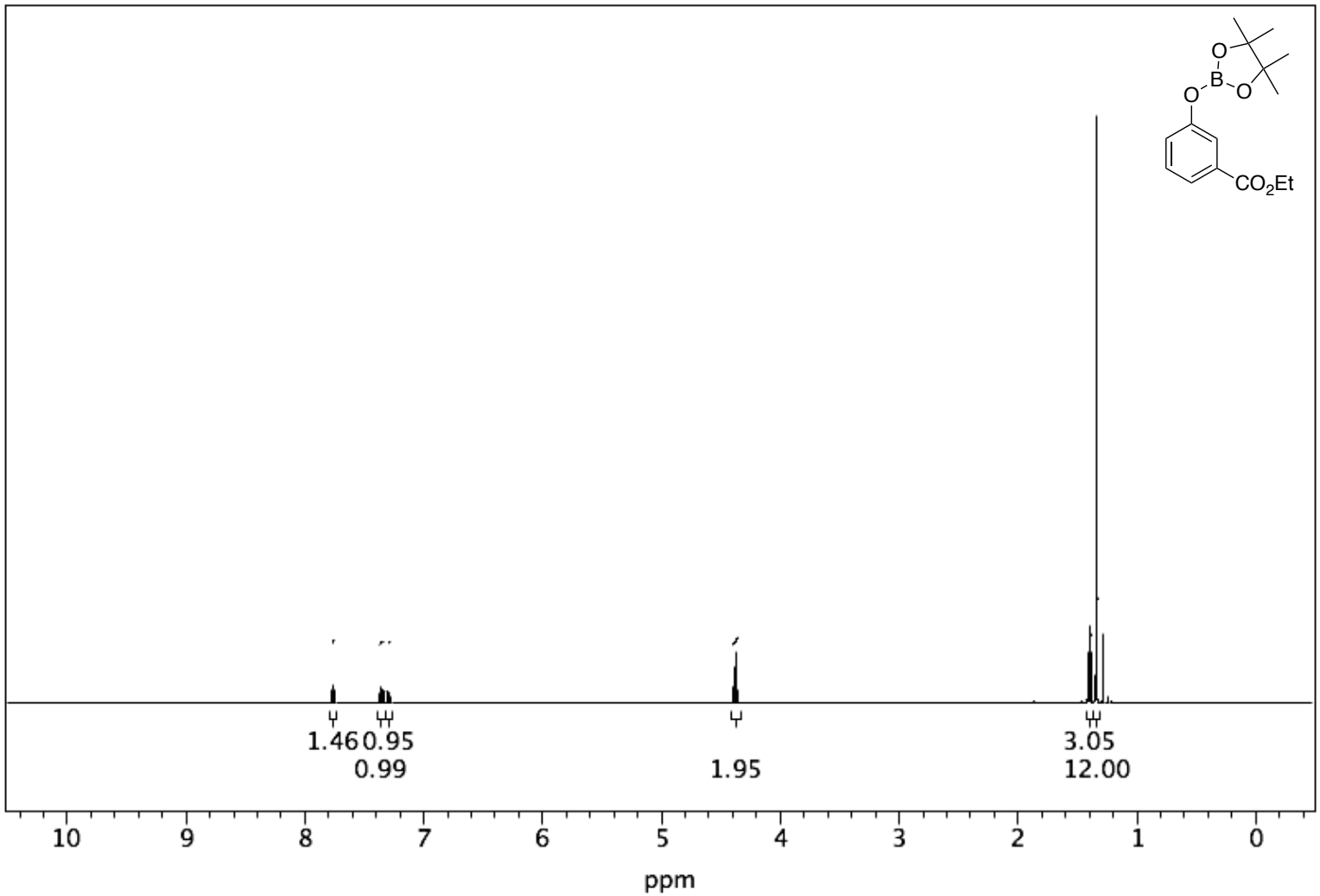


Figure A86. 500 MHZ ^{1}H NMR of ethyl 3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate in $CDCl_3$

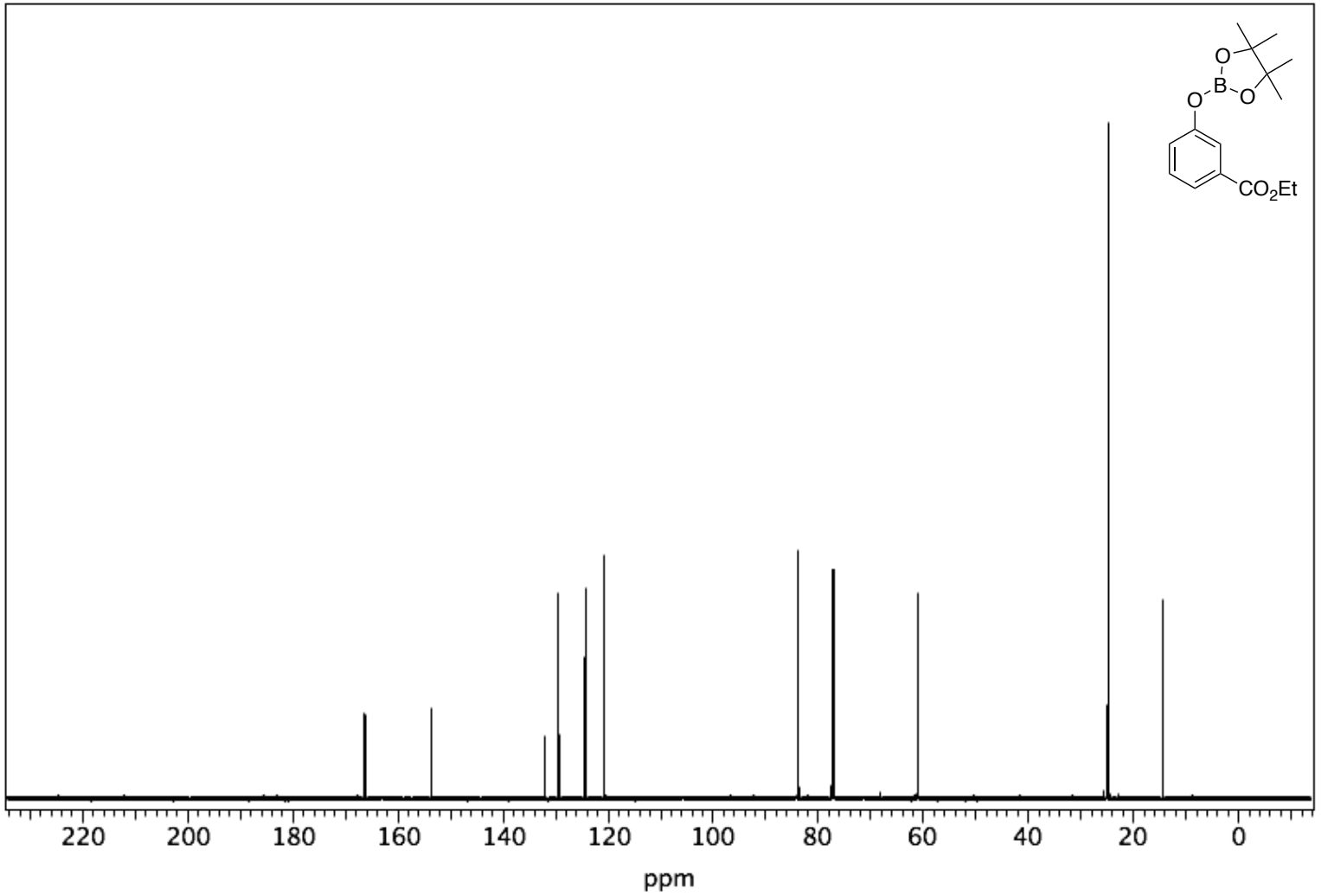


Figure A87. 125 MHZ ^{13}C NMR of ethyl 3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oxy)benzoate in $CDCl_3$

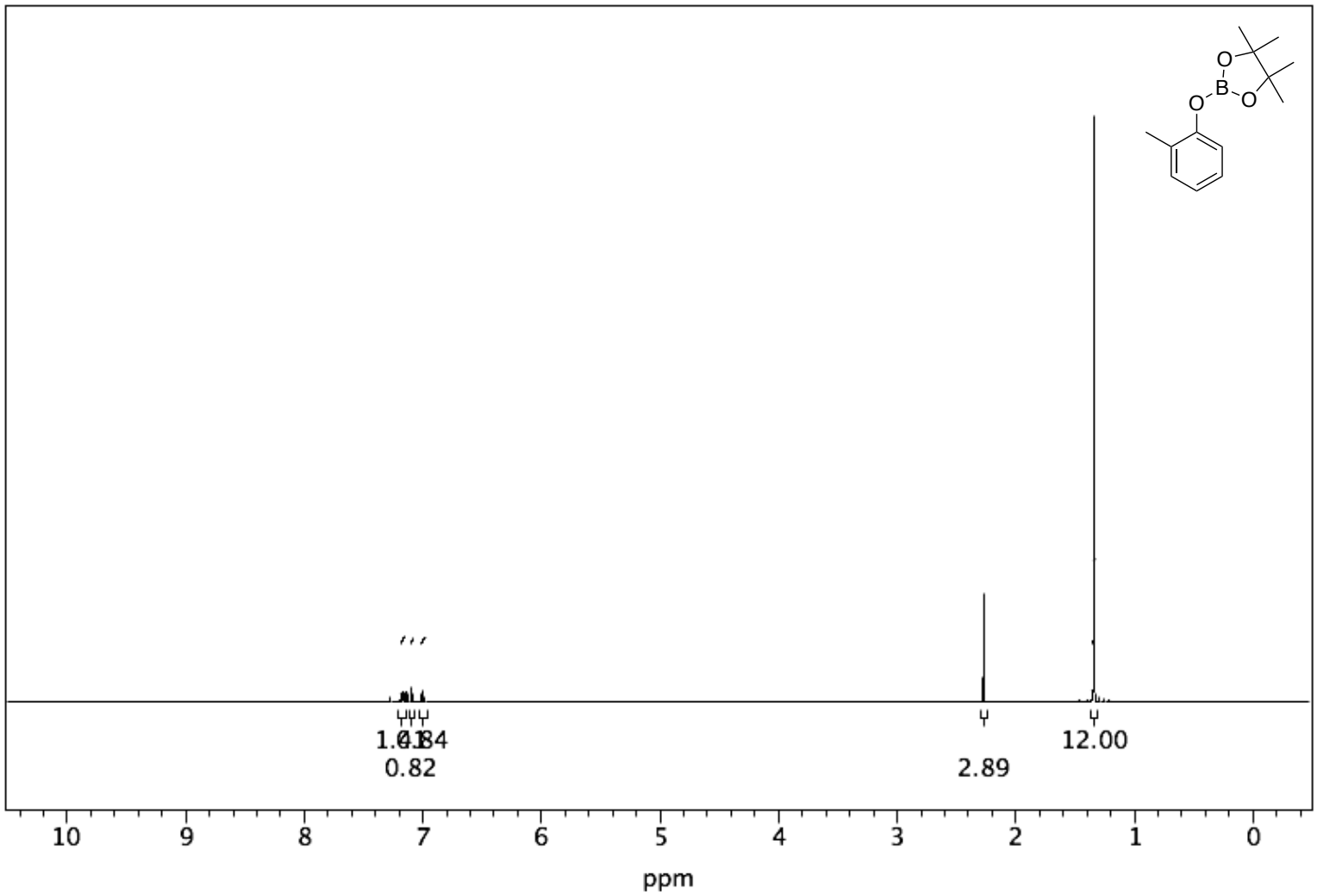


Figure A88. 500 MHz ^{1}H NMR of 4,4,5,5-tetramethyl-2-(o-tolyloxy)-1,3,2-dioxaborolane in $CDCl_3$

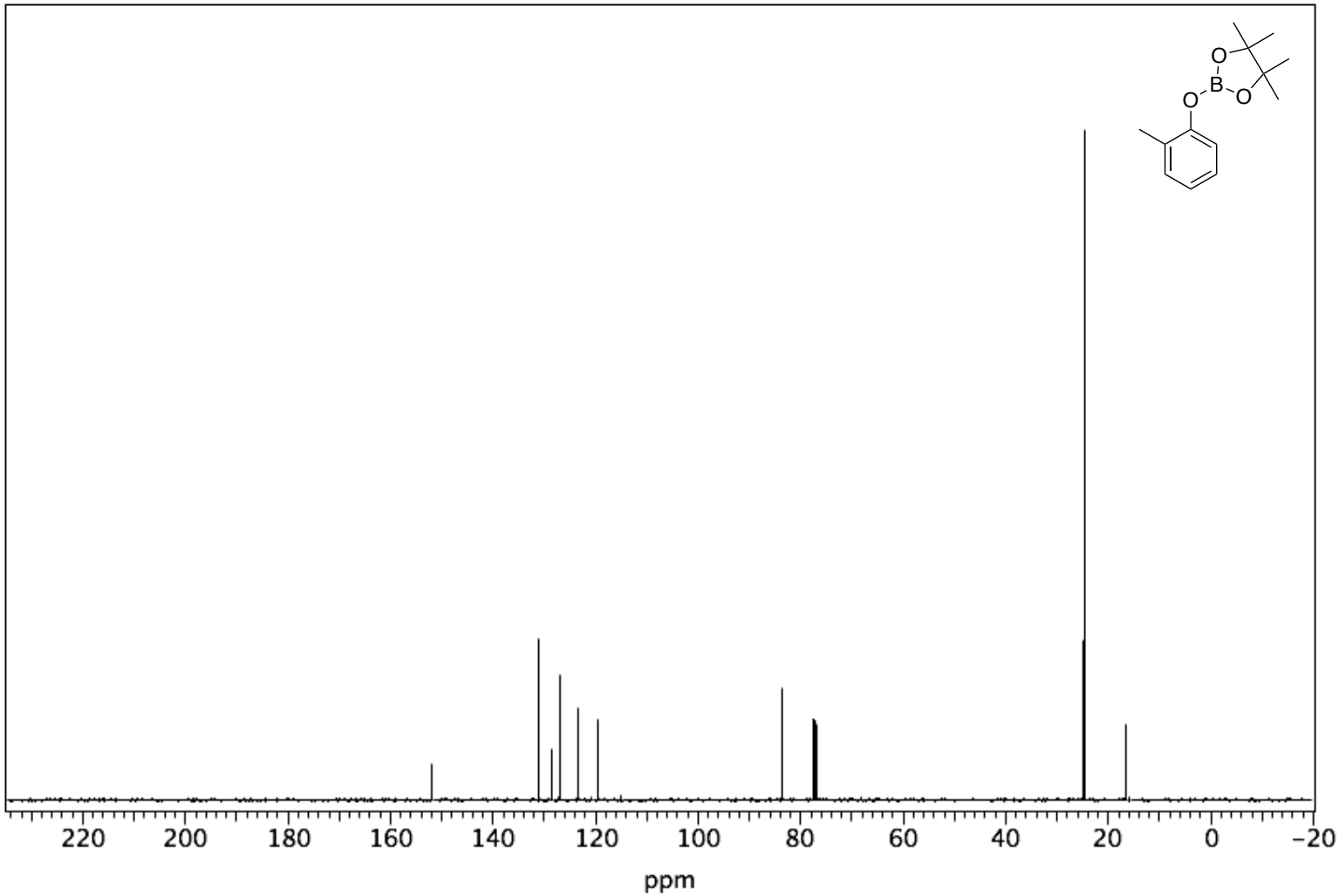


Figure A89. 125 MHz ^{13}C NMR of 4,4,5,5-tetramethyl-2-(o-tolyloxy)-1,3,2-dioxaborolane in $CDCl_3$

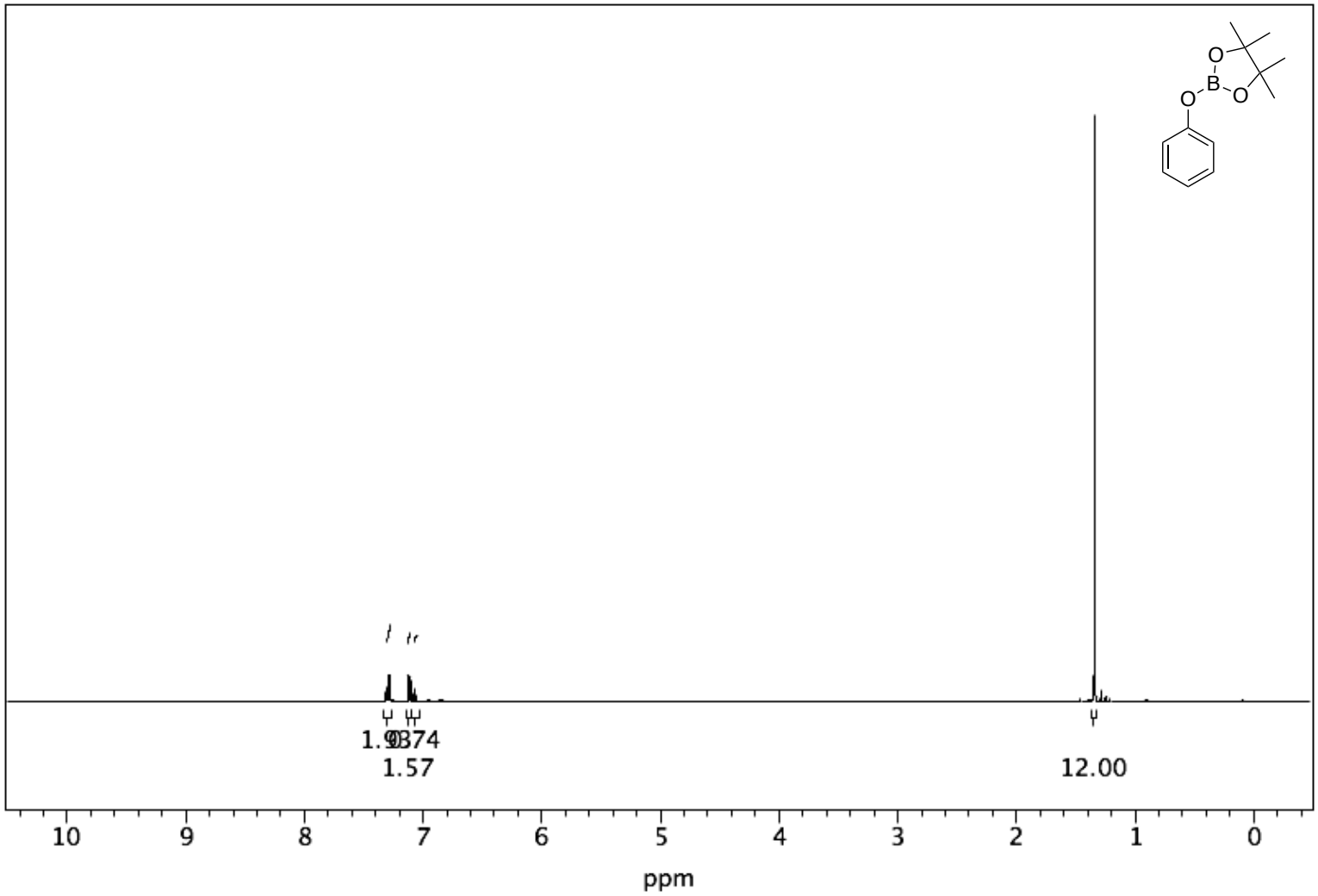


Figure A90. 500 MHz ^{1}H NMR of 4,4,5,5-tetramethyl-2-phenoxy-1,3,2-dioxaborolane in $CDCl_3$

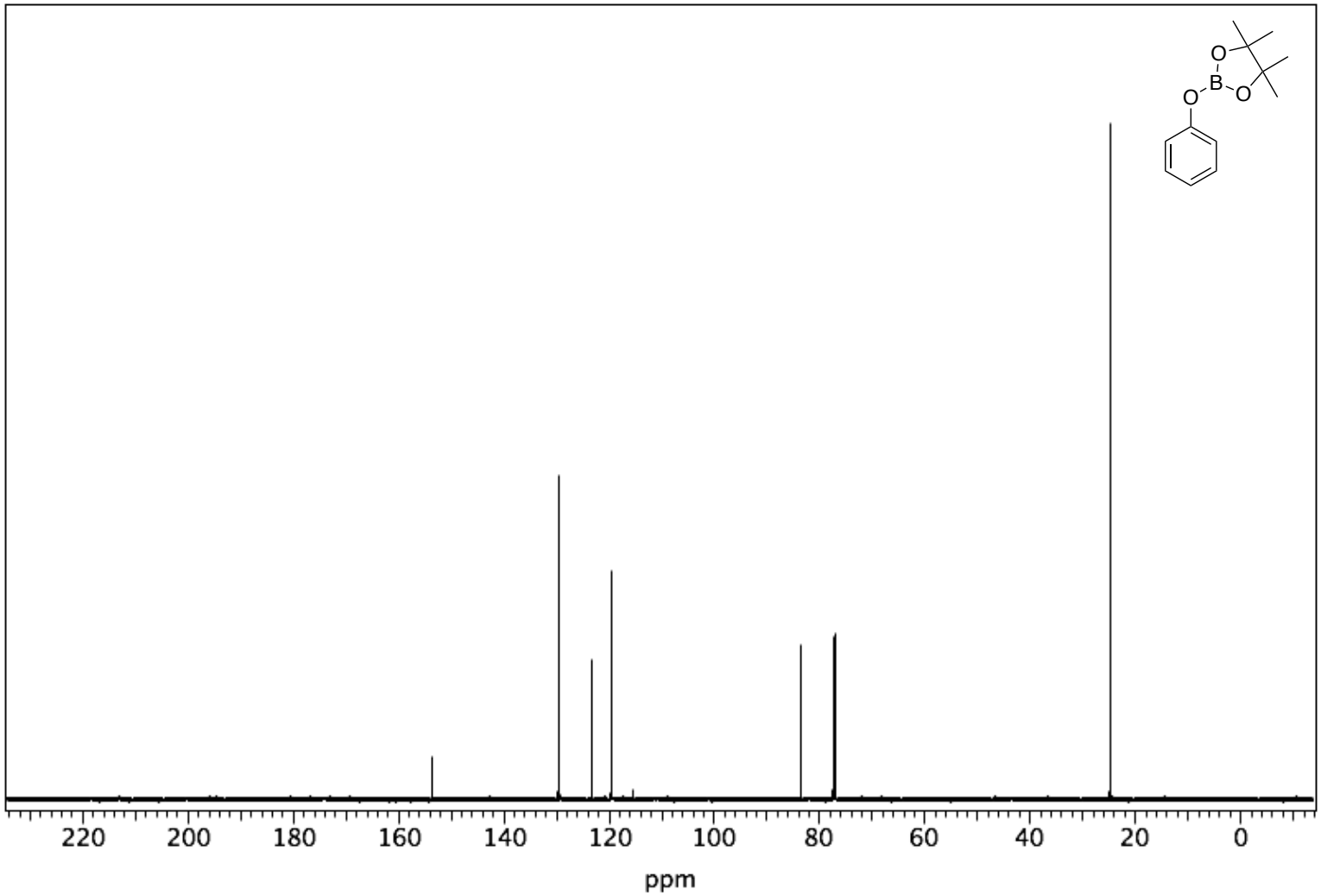


Figure A91. 125 MHz ^{13}C NMR of 4,4,5,5-tetramethyl-2-phenoxy-1,3,2-dioxaborolane in $CDCl_3$

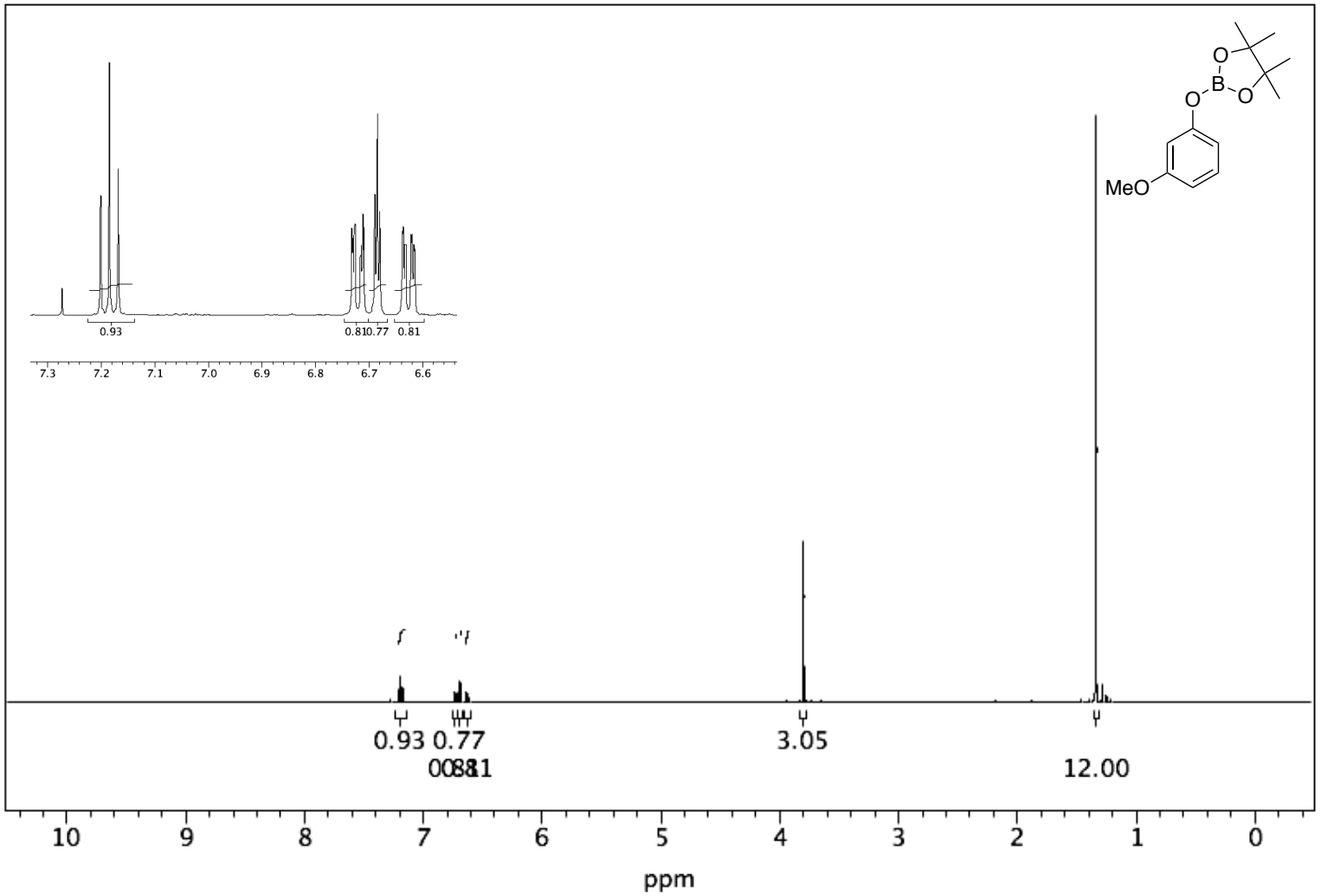


Figure A92. 500 MHz ^{1}H NMR of 2-(3-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

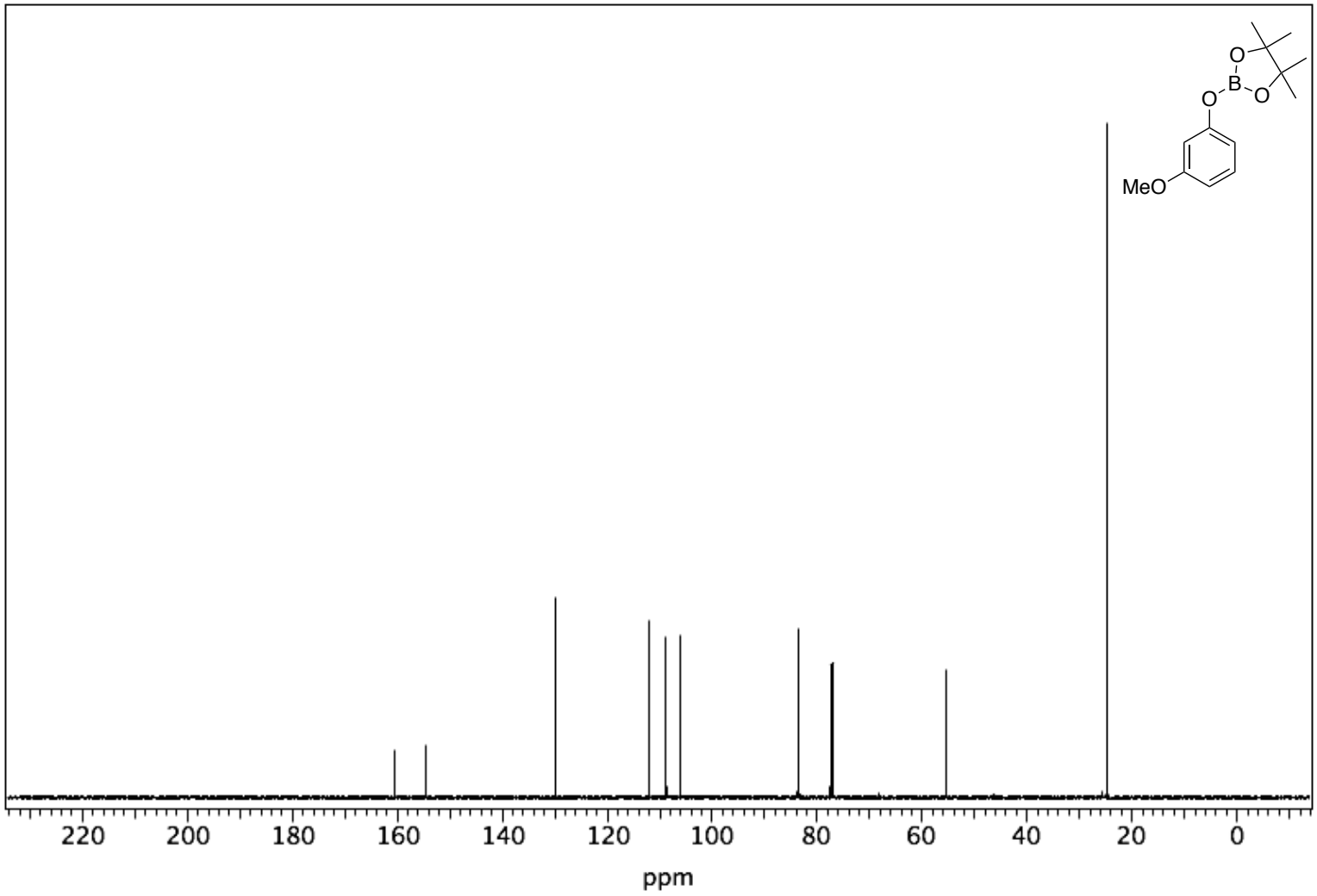


Figure A93. 125 MHz ^{13}C NMR of 2-(3-methoxyphenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

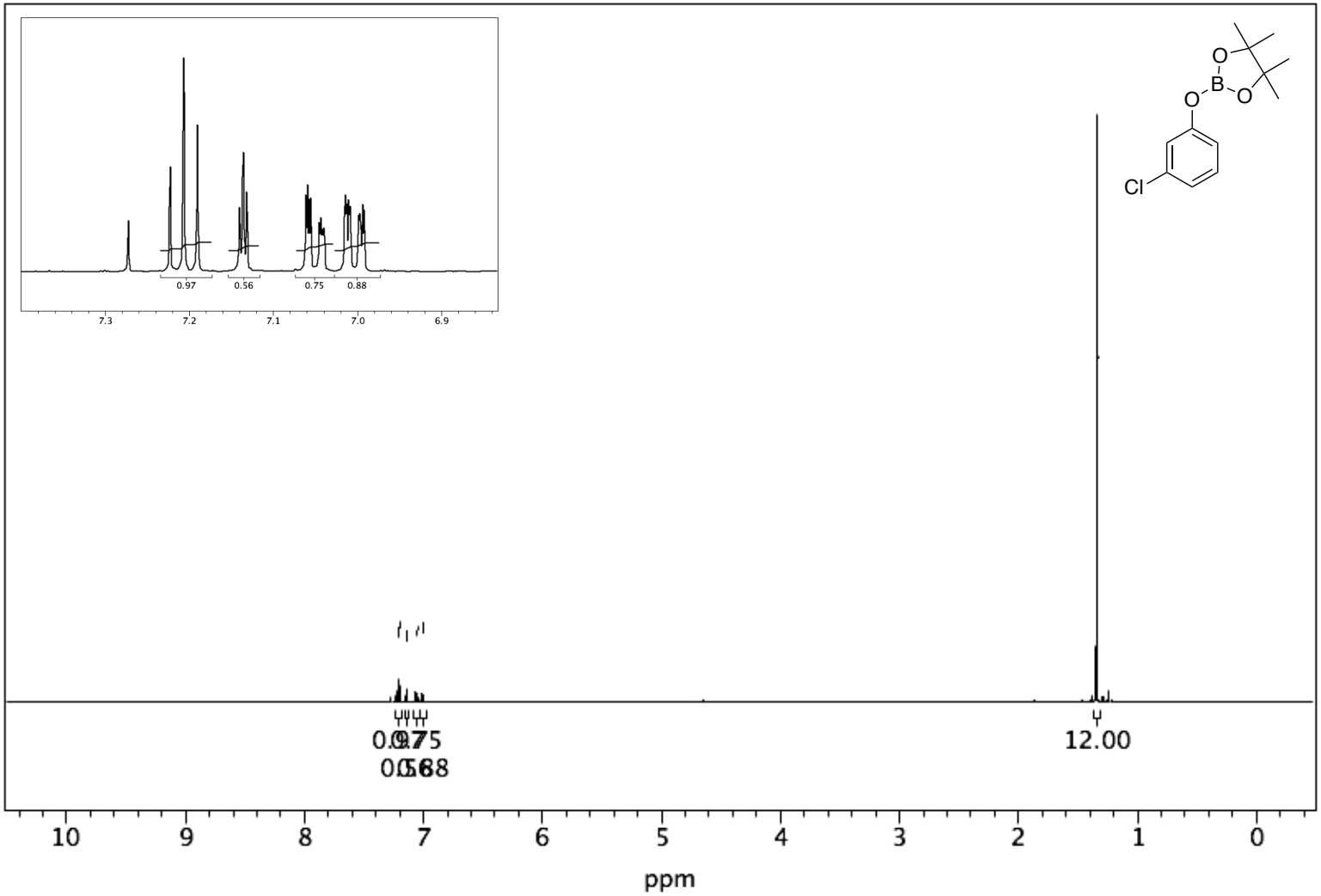


Figure A94. 500 MHz ^{1}H NMR of 2-(3-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

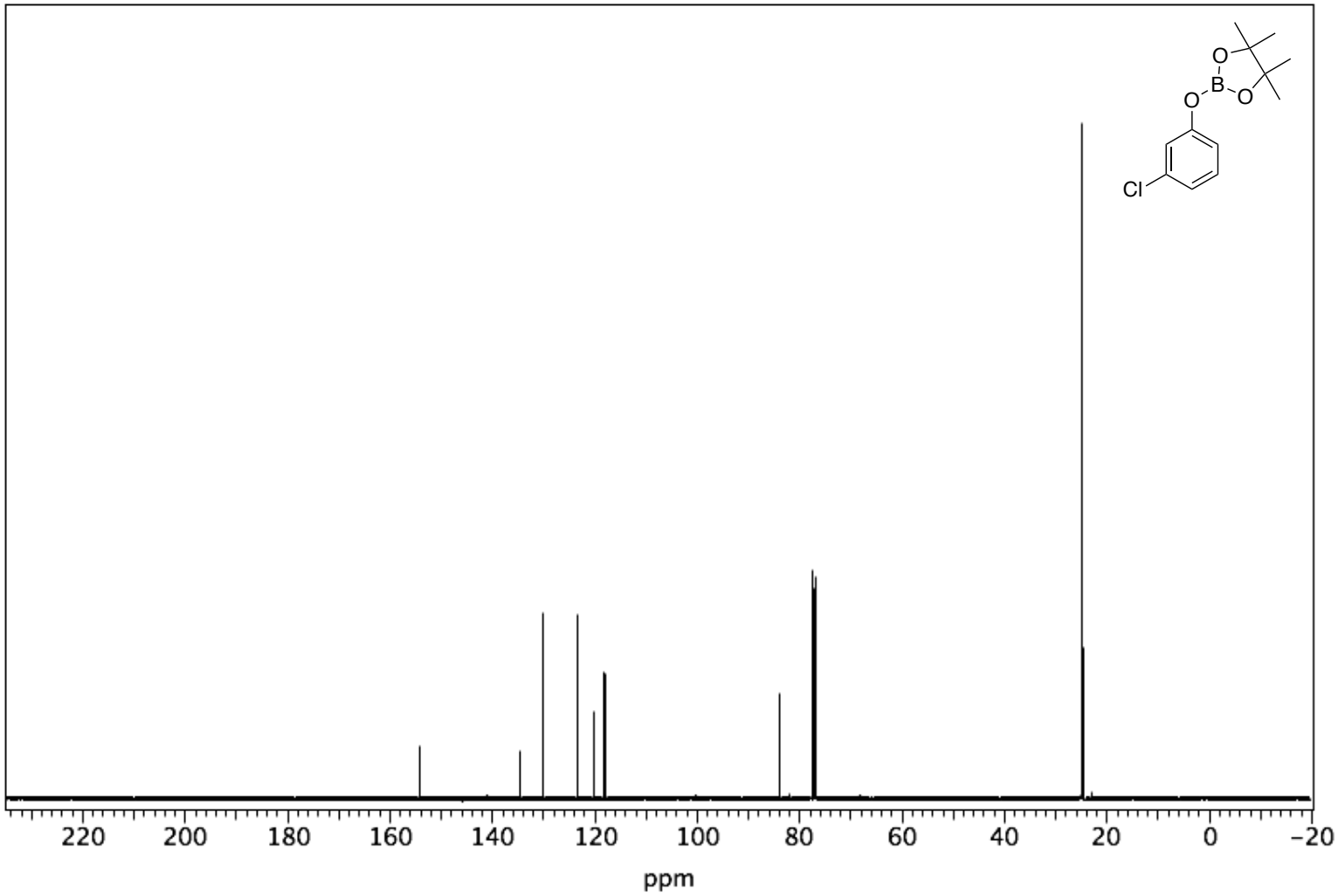


Figure A95. 125 MHz ^{13}C NMR of 2-(3-chlorophenoxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in $CDCl_3$

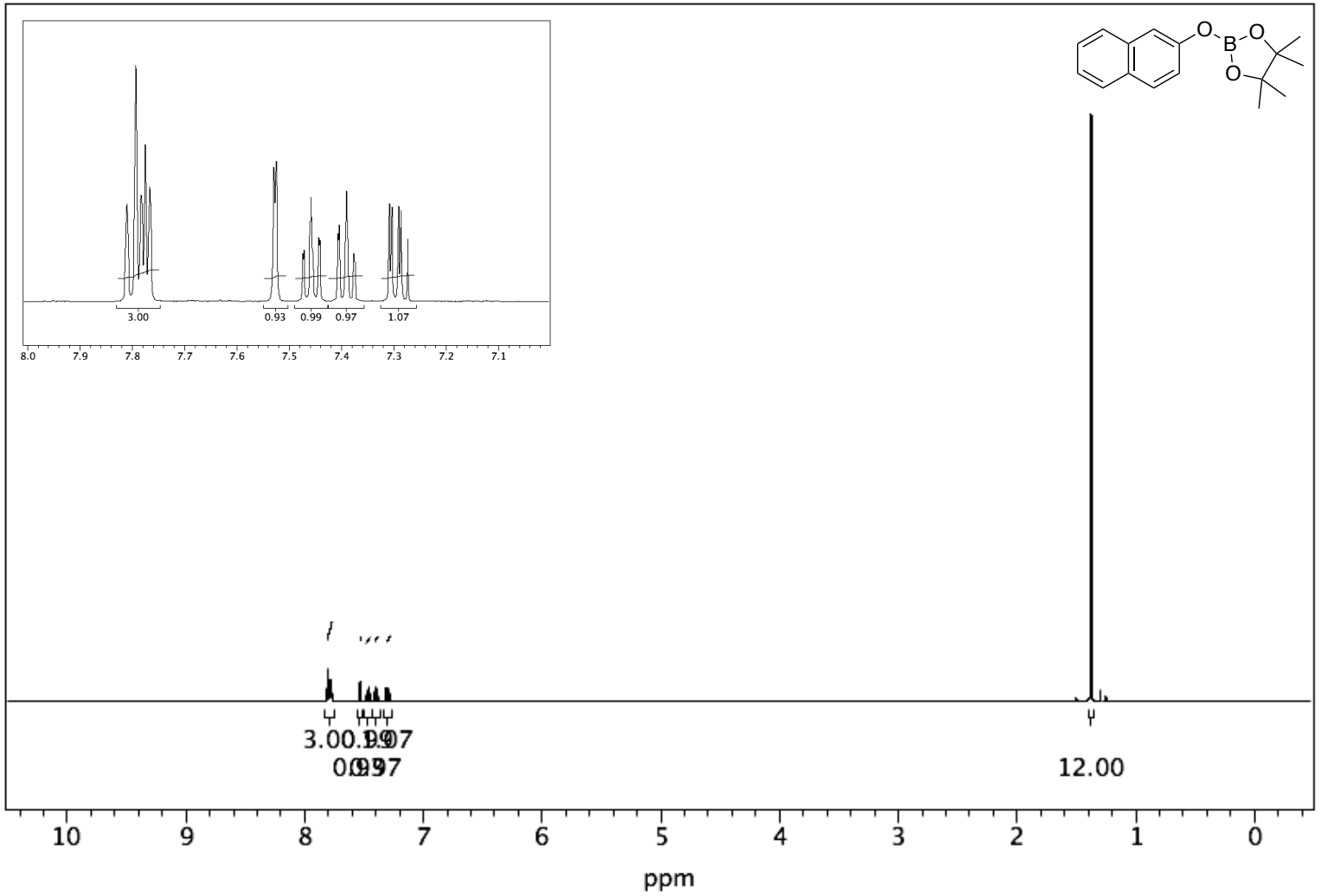


Figure A96. 500 MHz ^{1}H NMR of 4,4,5,5-tetramethyl-2-(naphthalen-2-yloxy)-1,3,2-dioxaborolane in $CDCl_3$

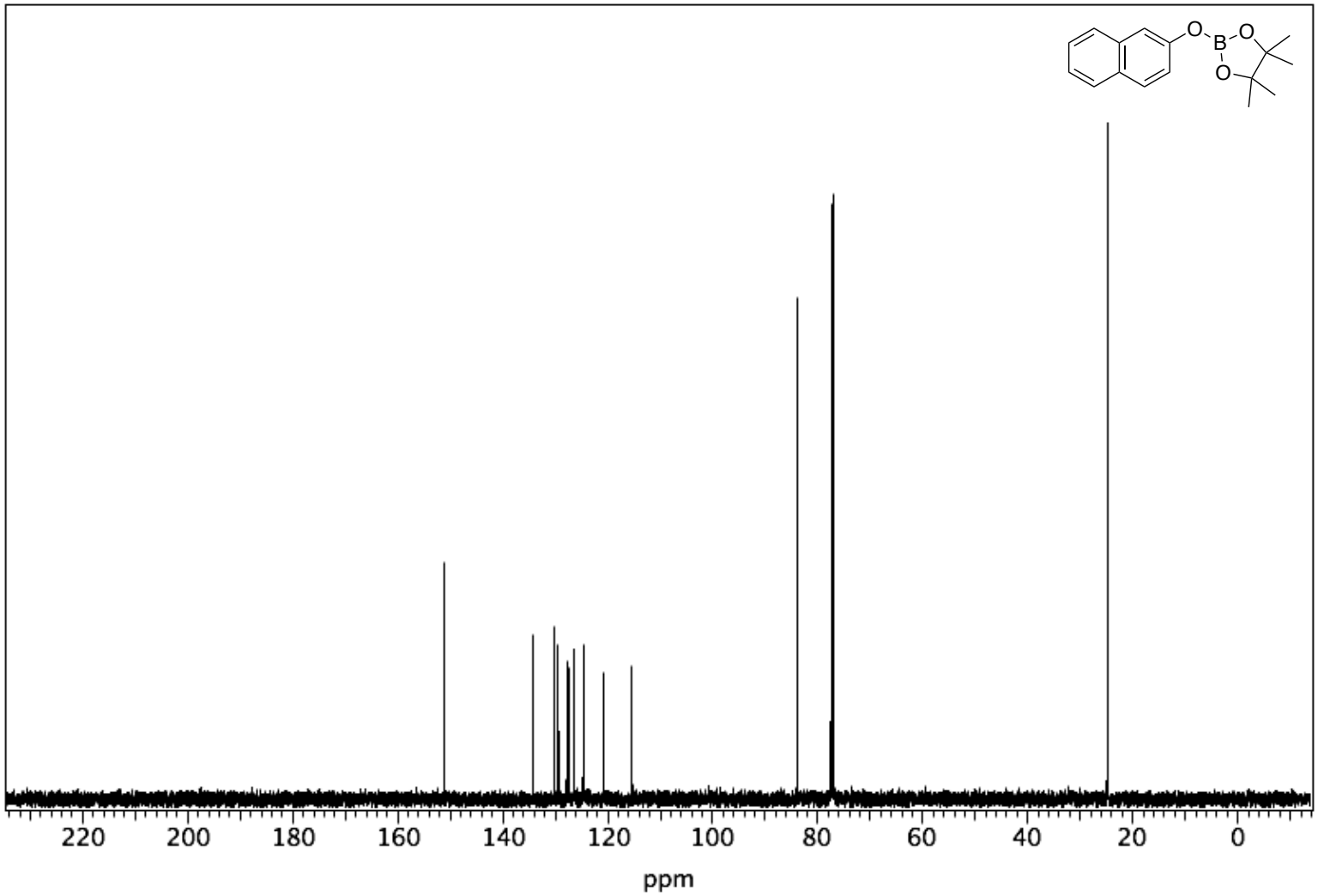


Figure A97. 125 MHz ^{13}C NMR of 4,4,5,5-tetramethyl-2-(naphthalen-2-yloxy)-1,3,2-dioxaborolane in $CDCl_3$

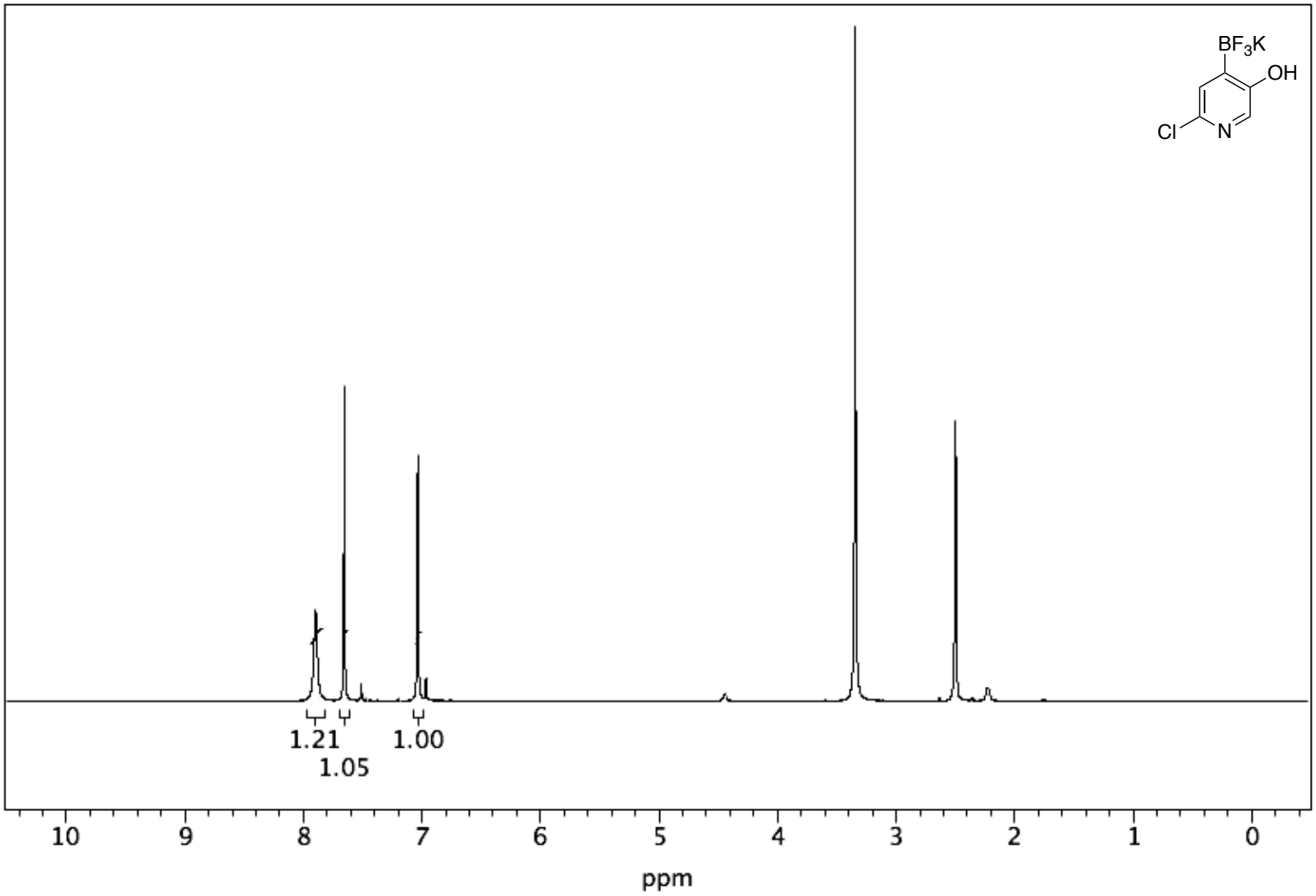


Figure A98. 500 MHz ^{1}H NMR of **4.2** in $(CD_3)_2SO$

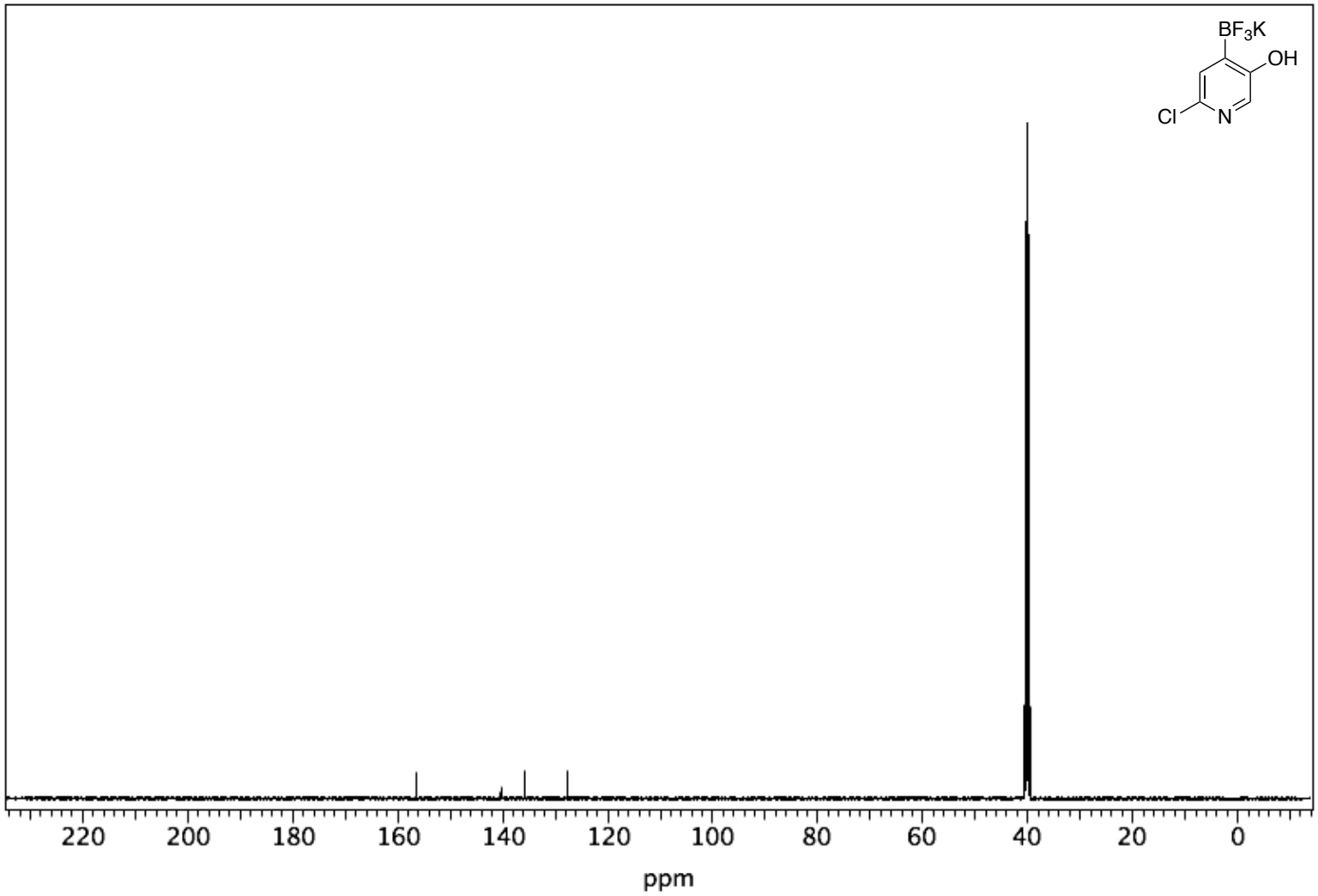


Figure A99. 125 MHz ^{13}C NMR of **4.2** in $(CD_3)_2SO$

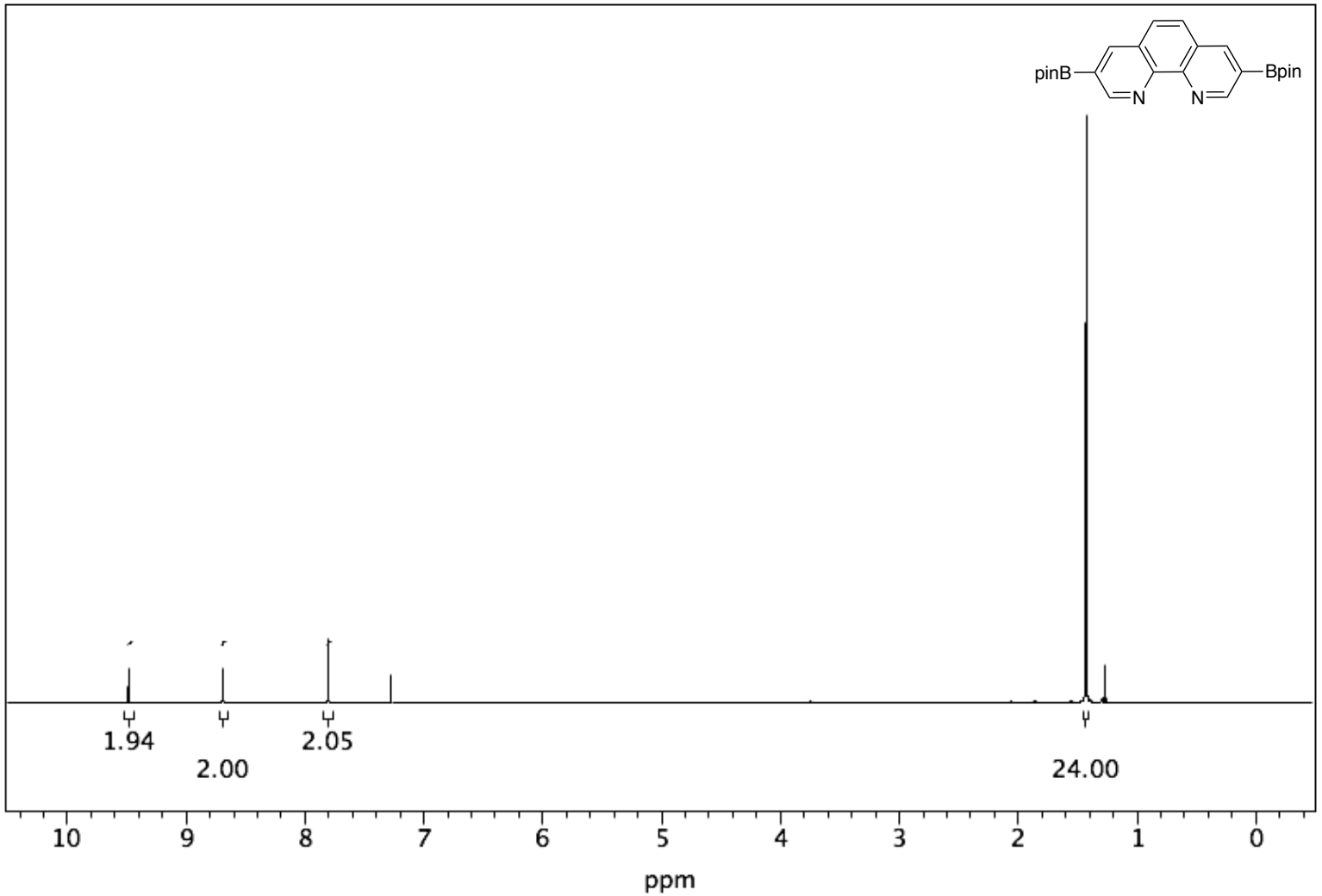


Figure A100. 500 MHz ^{1}H NMR of **5.1** in $CDCl_3$

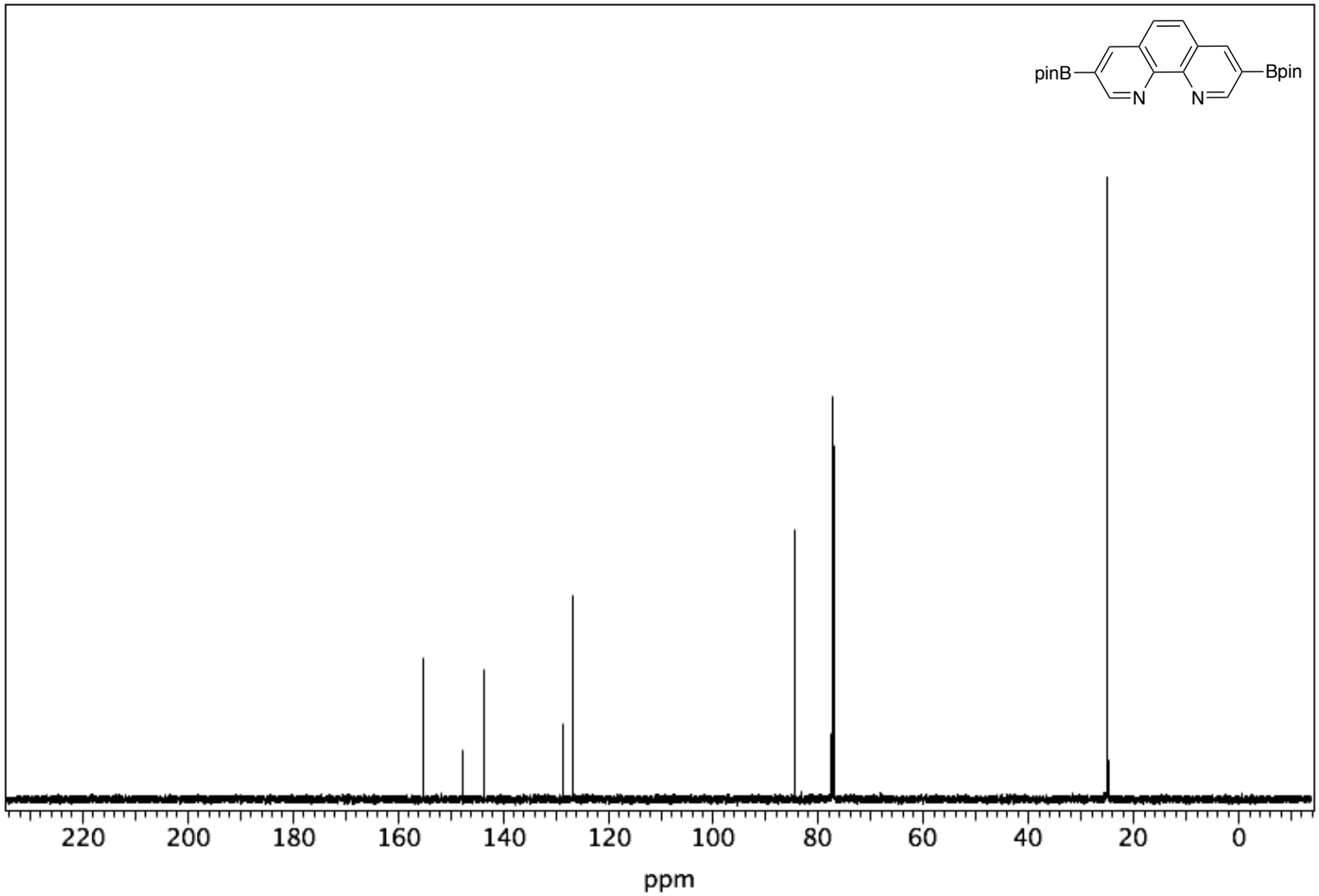


Figure A101. 125 MHz ^{13}C NMR of **5.1** in $CDCl_3$

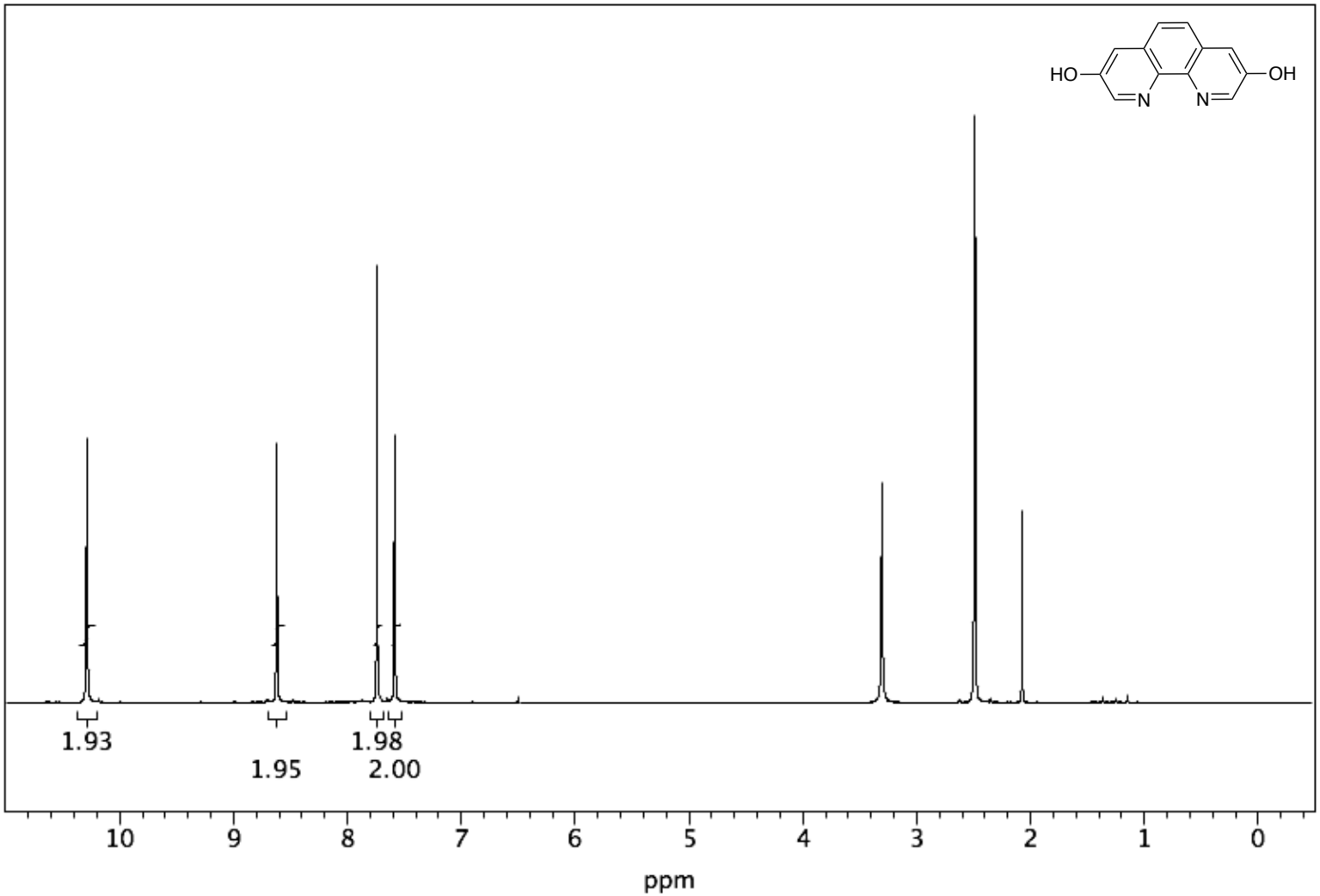


Figure A102. 500 MHz ^{1}H NMR **of 5.2** in $(CD_3)_2SO$

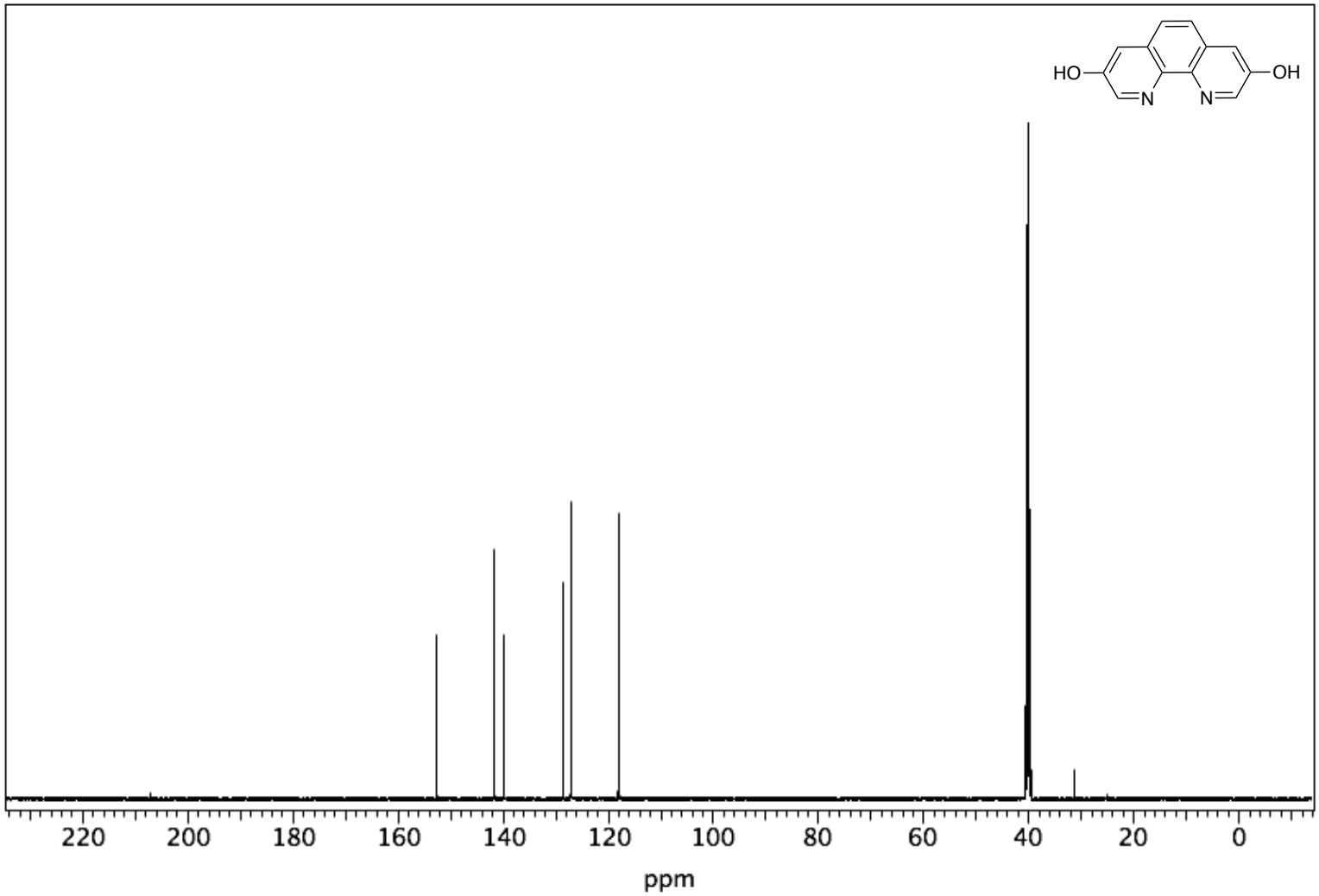


Figure A103. 125 MHz ^{13}C NMR of **5.2** in $(CD_3)_2SO$

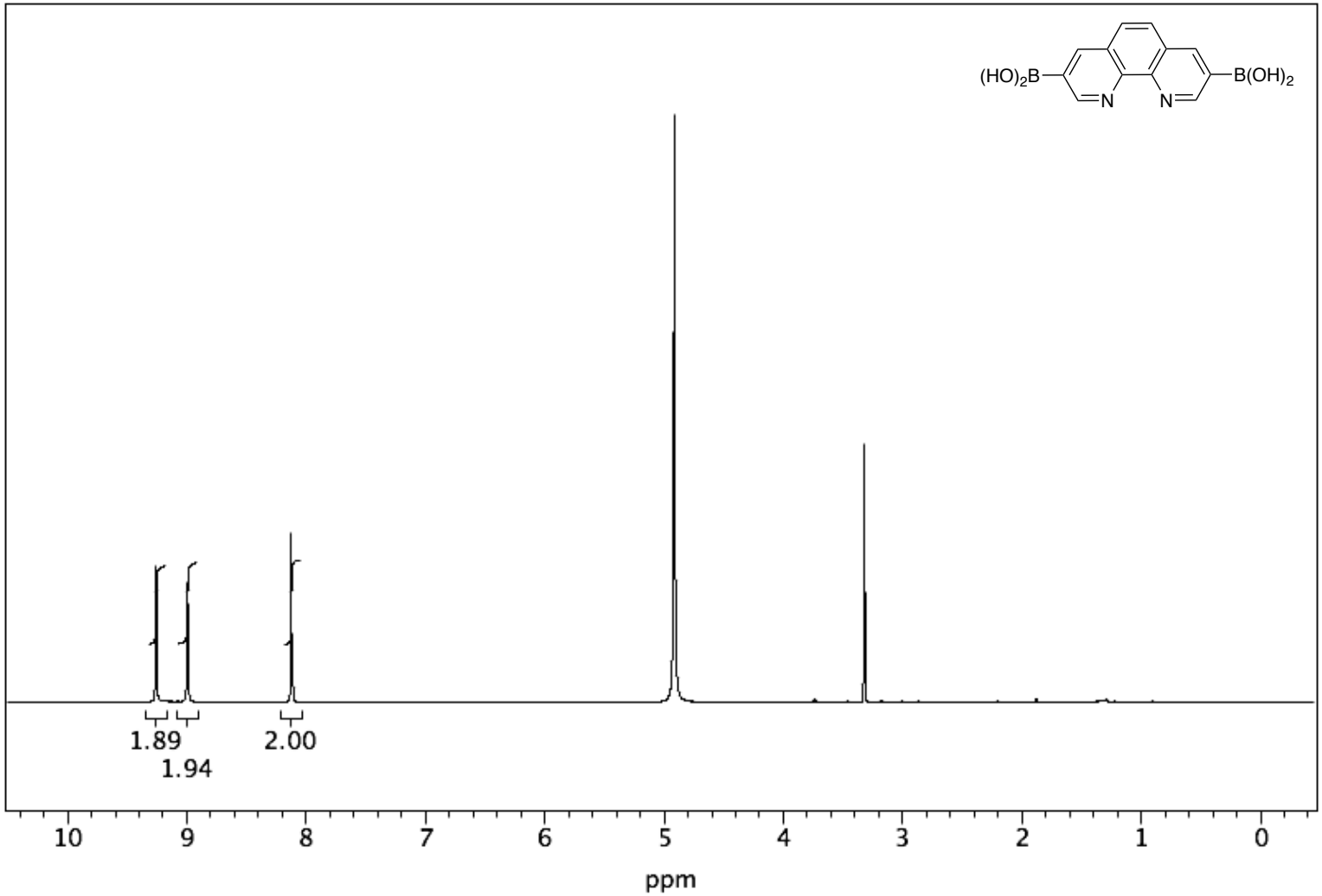


Figure A104. 500 MHz ^{1}H NMR of **5.3** in CD_3OD

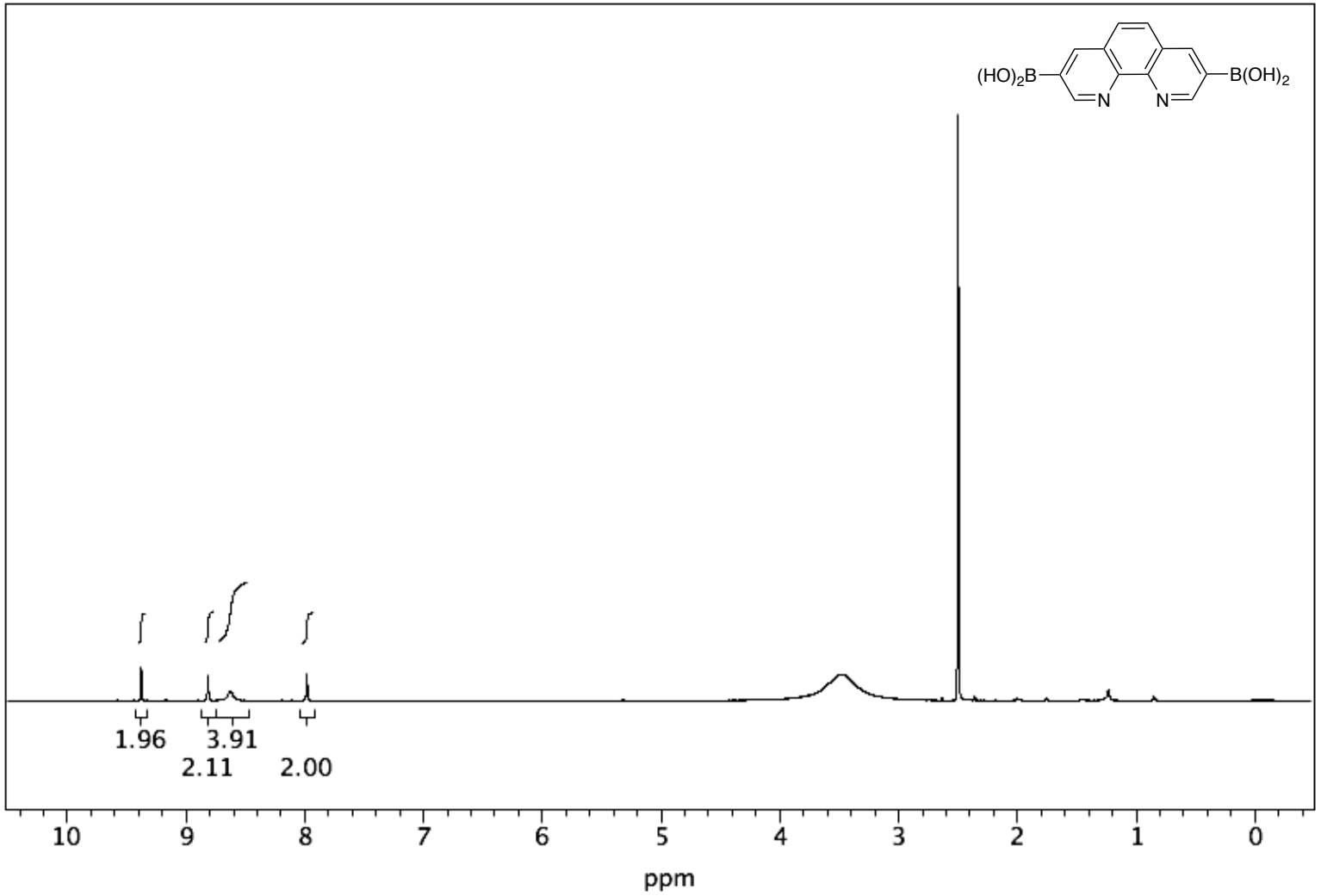


Figure A105. 500 MHz ^{1}H NMR of **5.3** in $(CD_3)_2SO$

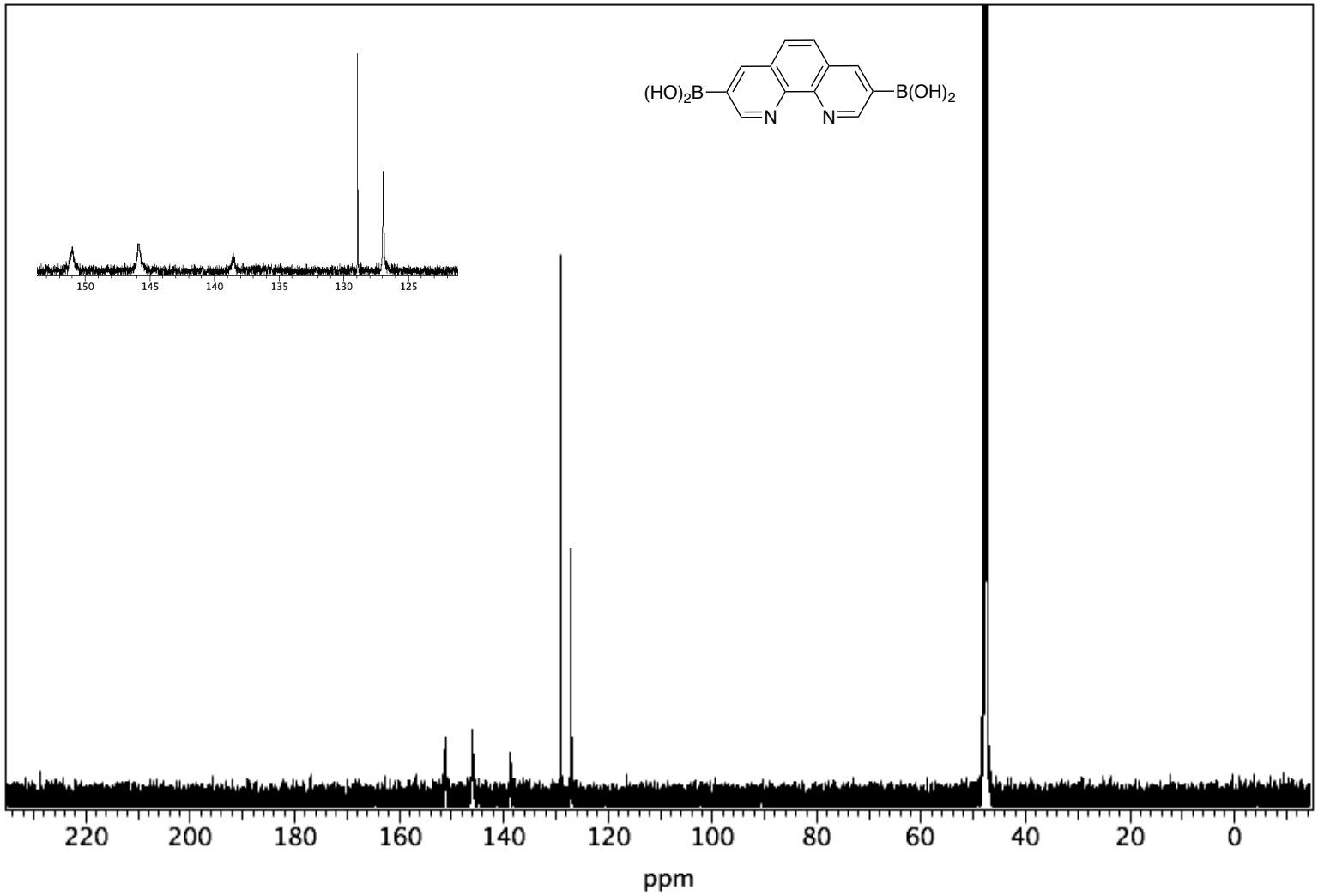


Figure A106. 125 MHz ^{13}C NMR of **5.3** in $(CD_3)_2SO$

APPENDIX B

Crystal Structure Data

Table B1. Crystal structure data for **3.7b**

Compound	**kg94-2_a**
Formula	$C_{19}H_{28}BNO_4$
$D_{calc.}$/ g cm^{-3}	1.155
μ/mm^{-1}	0.079
Formula Weight	345.23
Colour	colourless
Shape	block
Size/mm^3	0.50×0.33×0.29
T/K	173(2)
Crystal System	monoclinic
Space Group	$P2_1/c$
a/Å	18.391(3)
b/Å	9.8048(14)
c/Å	11.2796(16)
α/°	90
β/°	102.656(2)
γ/°	90
V/Å^3	1984.5(5)
Z	4
Z'	1
Wavelength/Å	0.710730
Radiation type	MoK_α
Θ_{min}/°	2.270
Θ_{max}/°	28.699
Measured Refl.	18771
Independent Refl.	4744
Reflections Used	3189
R_{int}	0.0429
Parameters	233
Restraints	0
Largest Peak	0.227
Deepest Hole	-0.188
GooF	1.034
wR_2 (all data)	0.1325
wR_2	0.1144
R_1 (all data)	0.0770
R_1	0.0482

Table B2. Crystal Structure Data for **3.12b**

Compound	**KG100-2_a**
Formula	$C_{19}H_{27}BClNO_4$
$D_{calc.}$/ g cm^{-3}	1.197
μ/mm^{-1}	1.784
Formula Weight	379.67
Colour	colourless
Shape	needle
Size/mm^3	0.53×0.31×0.11
T/K	173(2)
Crystal System	triclinic
Space Group	P-1
a/Å	8.91430(10)
b/Å	11.8263(2)
c/Å	21.1768(3)
α/°	89.5970(10)
β/°	81.2910(10)
γ/°	72.8310(10)
V/Å^3	2106.77(5)
Z	4
Z'	2
Wavelength/Å	1.541838
Radiation type	CuK_α
Θ_{min}/°	2.112
Θ_{max}/°	72.147
Measured Refl.	32912
Independent Refl.	7973
Reflections Used	5841
R_{int}	0.0641
Parameters	483
Restraints	0
Largest Peak	0.305
Deepest Hole	-0.322
GooF	1.023
wR_2 (all data)	0.1229
wR_2	0.1102
R_1 (all data)	0.0648
R_1	0.0442

Table B3. Crystal Structure Data for **3.13a**

Compound	**KG81-1**
Formula	$C_{10}H_{17}NO_4$
$D_{calc.}$/ g cm^{-3}	1.194
μ/mm^{-1}	0.768
Formula Weight	215.24
Colour	colourless
Shape	block
Size/mm^3	0.23×0.17×0.09
T/K	173(2)
Crystal System	orthorhombic
Hooft Parameter	0.0(10)
Space Group	Pnma
a/Å	9.9483(4)
b/Å	7.9043(4)
c/Å	15.2317(5)
α/°	90
β/°	90
γ/°	90
V/Å^3	1197.73(9)
Z	4
Z'	0.5
Wavelength/Å	1.541838
Radiation type	CuK_α
Θ_{min}/°	5.311
Θ_{max}/°	72.112
Measured Refl.	6240
Independent Refl.	1260
Reflections Used	918
R_{int}	0.0530
Parameters	91
Restraints	0
Largest Peak	0.265
Deepest Hole	-0.175
GooF	1.030
wR_2 (all data)	0.1418
wR_2	0.1256
R_1 (all data)	0.0719
R_1	0.0497

Table B4. Crystal Structure Data for **3.13b**

Compound	**KG83-1**
Formula	$C_{16}H_{28}BNO_6$
$D_{calc.}$/ g cm^{-3}	1.208
μ/mm^{-1}	0.745
Formula Weight	341.20
Colour	colourless
Shape	needle
Size/mm^3	0.49×0.12×0.06
T/K	173(2)
Crystal System	orthorhombic
Flack Parameter	0.28(17)
Hooft Parameter	0.34(16)
Space Group	$P2_12_12_1$
a/Å	6.6625(3)
b/Å	14.0154(6)
c/Å	20.0938(8)
α/°	90
β/°	90
γ/°	90
V/Å^3	1876.31(14)
Z	4
Z'	1
Wavelength/Å	1.541838
Radiation type	CuK_α
Θ_{min}/°	3.845
Θ_{max}/°	71.839
Measured Refl.	11491
Independent Refl.	3494
Reflections Used	2840
R_{int}	0.0580
Parameters	229
Restraints	0
Largest Peak	0.242
Deepest Hole	-0.242
GooF	1.019
wR_2 (all data)	0.1177
wR_2	0.1093
R_1 (all data)	0.0622
R_1	0.0470

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