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Design, Synthesis and Suzuki-Miyaura Cross-Coupling Reactions of Potassium Organotrifluoroborates

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Abstract
The Suzuki–Miyaura cross-coupling reaction is one of the most efficient methods to form new carbon-carbon bonds, allowing a rapid increase in complexity among target molecules of interest. Among a variety of boron reagents utilized in Suzuki–Miyaura reactions, potassium organotrifluoroborates are of great interest because they have many advantages over other boron reagents. Organotrifluoroborates, which are tetracoordinate boron species, show better stability and reactivity, and they are much less prone to protodeboronation.

α-Chiral β-arylated carbonyl compounds are important substructures in organic chemistry, and their preparations, such as benzylations, asymmetric hydrogenations, and conjugate additions, have been studied. However, these methods have limitations in terms of selectivity and functional group tolerance. We developed a more direct method that could overcome the problems. Enantiomerically enriched potassium α-chiral β-trifluoroboratoamides were prepared, and the general conditions were found to couple successfully with various aryl and hetaryl chlorides to afford the corresponding α-chiral β-arylated carbonyl compounds. Moreover, the diastereoselectivities were greater than 95:5, and retained throughout the coupling reactions.

Aminomethyl moieties are readily encountered in biologically active compounds as well as in organic intermediates. Even though several synthetic methods have been reported, the means of preparation of these subunits are still limited. We developed a more efficient method to access aminomethyl substructures by preparation of air stable potassium Boc-protected primary and secondary aminomethyltrifluoroborates. The Suzuki–Miyaura cross-coupling reaction was investigated with these new aminomethylating boron reagents to provide the corresponding aminomethyl moieties. Aryl and hetaryl chlorides, mesylates, and sulfamates were proved to be effective electrophilic coupling partners under developed conditions. These methods provide a complementary way to access important building blocks that is more direct and general than currently available methods.

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DESIGN, SYNTHESIS AND SUZUKI–MIYAURA CROSS-COUPLING REACTIONS OF POTASSIUM ORGANOTRIFLUOROBORATES

Inji Shin

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DESIGN, SYNTHESIS AND SUZUKI–MIYAURA CROSS-COUPLING REACTIONS OF POTASSIUM ORGANOTRIFLUOROBORATES

Dedicated to

all my families,

especially

Wonsuk and Steve

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ABSTRACT

DESIGN, SYNTHESIS AND SUZUKI–MIYAURA CROSS-COUPLING REACTIONS OF POTASSIUM ORGANOTRIFLUOROBORATES

Inji Shin

Professor Gary A. Molander

The Suzuki–Miyaura cross-coupling reaction is one of the most efficient methods to form new carbon-carbon bonds, allowing a rapid increase in complexity among target molecules of interest. Among a variety of boron reagents utilized in Suzuki–Miyaura reactions, potassium organotrifluoroborates are of great interest because they have many advantages over other boron reagents. Organotrifluoroborates, which are tetracoordinate boron species, show better stability and reactivity, and they are much less prone to protodeboronation.

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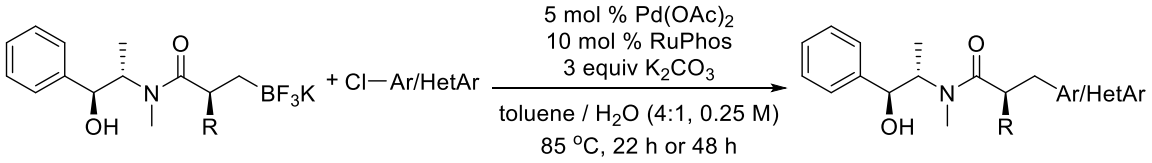
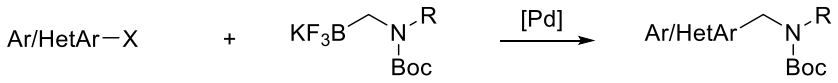
successfully with various aryl and hetaryl chlorides to afford the corresponding α-chiral β-arylated carbonyl compounds. Moreover, the diastereoselectivities were greater than 95:5, and retained throughout the coupling reactions.



R = Me, Et, *n*-Bu, *i*-Pr

dr > 95:5
yields: up to 82%

Aminomethyl moieties are readily encountered in biologically active compounds as well as in organic intermediates. Even though several synthetic methods have been reported, the means of preparation of these subunits are still limited. We developed a more efficient method to access aminomethyl substructures by preparation of air stable potassium Boc-protected primary and secondary aminomethyltrifluoroborates. The Suzuki–Miyaura cross-coupling reaction was investigated with these new aminomethylating boron reagents to provide the corresponding aminomethyl moieties. Aryl and hetaryl chlorides, mesylates, and sulfamates were proved to be effective electrophilic coupling partners under developed conditions. These methods provide a complementary way to access important building blocks that is more direct and general than currently available methods.



X = Cl, OMs, OSO_2NMe_2 R = H, alkyl

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List of Abbreviations

Ac	acetyl
aq.	aqueous
Ar	aryl
BOC	*t*-butoxycarbonyl
br	broad
CAM	cerium ammonium molybdate
CH_2Cl_2	methylene chloride
CI	chemical ionization
cod	1,5-cyclooctadiene
Cs_2CO_3	cesium carbonate
Cy	cyclohexyl
d	doublet
dan	1,8-naphtalenediaminatoborane
dba	dibenzylideneacetone
dd	doublet of doublets
δ	chemical shift in parts per million
DME	dimethoxyethane
dppf	1,1’-bis(diphenylphosphino)ferrocene
DMAP	4-(*N*,*N*-dimethylamino)pyridine
dr	diastereomeric ratio

ee	enantiomeric excess
Et	ethyl
Et_2O	diethyl ether
equiv	equivalent
ES	electrospray ionization
Et_3N	triethylamine
EtOAc	ethyl acetate
HetAr	heteroaryl
HMPA	hexamethylphosphoramide
H_2O	water
HRMS	high resolution mass spectrometry
Hz	hertz (s^{-1})
i-Pr	isopropyl
IR	infrared spectroscopy
J	coupling constant in Hertz
K_2CO_3	potassium carbonate
KHF_2	potassium hydrogen bifluoride
KHMDS	potassium hexamethyldisilazide
$KMnO_4$	potassium permanganate
KOH	potassium hydroxide
K_3PO_4	potassium phosphate
L	ligand

LDA	lithium diisopropylamide
m	multiplet
μ	micro
Me	methyl
MIDA	*N*-methyliminodiacetic acid
MeOH	methanol
$MgSO_4$	magnesium sulfate
mL	milliliter(s)
mmol	milimole(s)
mp	melting point
Ms	mesylate
NaH	sodium hydride
n-Bu	*n*-butyl
n-BuLi	*n*-butyllithium
NMR	nuclear magnetic resonance
n-PrOH	*n*-propanol
Nu:	nucleophile
Ph	phenyl
Pin	pinacol (2,3-dimethyl-2,3-butanediol)
ppm	parts per million
q	quartet
rt	room temperature

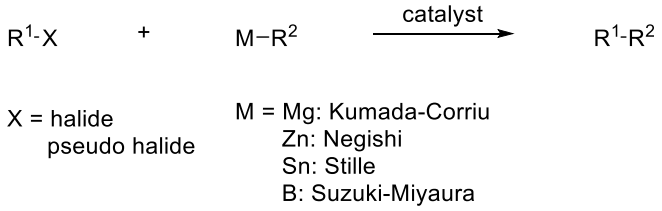
RuPhos	2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
s	singlet
SPhos	2-(dicyclohexylphosphino)-2′,6′-dimethoxybiphenyl
t	triplet
t-Bu	*tert*-butyl
t-BuOH	*tert*-butanol
Tf_2O	trifluoromethanesulfonic anhydride
THF	tetrahydrofuran
TLC	thin layer chromatography
Xc	chiral auxiliary
XPhos	2-(dicyclohexylphosphino)-2,4,6-triisopropylbiphenyl

Chapter 1. Suzuki–Miyaura Cross-Coupling Reactions and Potassium Organotrifluoroborates

1.1 Suzuki–Miyaura Cross-Coupling Reactions

Transition metal catalyzed cross-coupling reactions are one of the most powerful methods to prepare new carbon-carbon bonds.[1] Many metal catalyzed coupling reactions, such as Kumada-Corriu,[2] Negishi,[3] Stille,[4] and Suzuki–Miyaura reactions,[5] have been utilized to increase the complexity of molecular targets of interests (Equation 1.1).

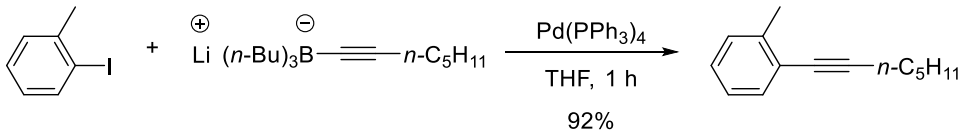
Equation 1.1 Transition Metal Catalyzed Cross-Coupling Reactions



Among them, the Suzuki–Miyaura cross-coupling reaction has been most widely used to construct carbon-carbon bonds because of the mild reaction conditions, lessened toxicity, and stability afforded by boron reagents compared to other coupling reactions.[6]

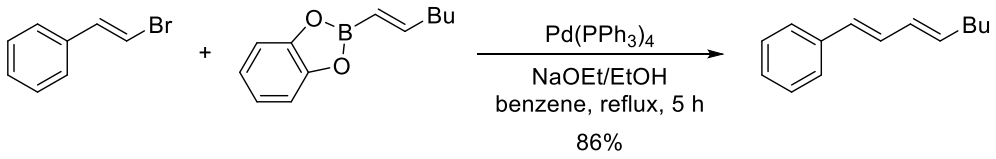
In 1978, the first example of a palladium catalyzed Suzuki–Miyaura cross-coupling was demonstrated using organoboron reagents with an aryl iodide by Negishi and coworkers (Equation 1.2).[7] In the presence of a $Pd(PPh_3)_4$ as the catalyst, an alkynylborate was successfully coupled with *o*-tolyl iodide to afford the desired product in 92% yield.

Equation 1.2



Later, Suzuki reported the palladium catalyzed coupling reaction with an alkenylboronate and alkenyl bromide (Equation 1.3).[8] Previously, alkenylborons were known to be inefficient coupling partners due to their low nucleophilicity.[9] However, the use of a tricoordinate organoboron species, instead of a tetracoordinate organoborate species, was demonstrated to overcome this problem. Thus, Suzuki and Miyaura revealed that the Suzuki–Miyaura cross-coupling reaction requires a base, unlike other organometallic reactions.[10] In the absence of a base, the reactions failed to form the desired products.

Equation 1.3



More recently, the Suzuki–Miyaura cross-coupling reaction is of great interest in both academia and industry. Even though Suzuki–Miyaura coupling reactions are efficient to form carbon-carbon bonds, many limitations exist in terms of efficiency and diversity. Therefore, many efforts have been made in this area to improve the reactions. Diverse

catalysts and ligands have been studied extensively by many research groups.[11] Particularly, Buchwald ligands, dialkyl biaryl phosphine ligands, are one class of effective ligands used widely to allow many difficult transformations in coupling reactions (Figure 1.1).[12]

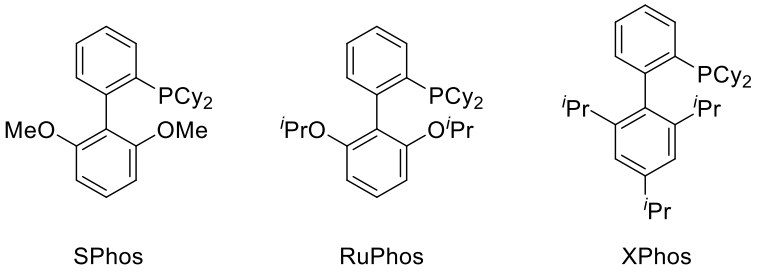


Figure 1.1 Examples of Buchwald Ligands

Moreover, the Buchwald group has developed preformed catalysts (Figure 1.2).[13] They show better reactivity, and the use of precatalysts have several advantages over traditional catalyst/ligand systems in terms of stability and activity. The coupling reactions can be more efficient because shorter reaction times, lower temperature, and lower catalyst loadings can be employed.

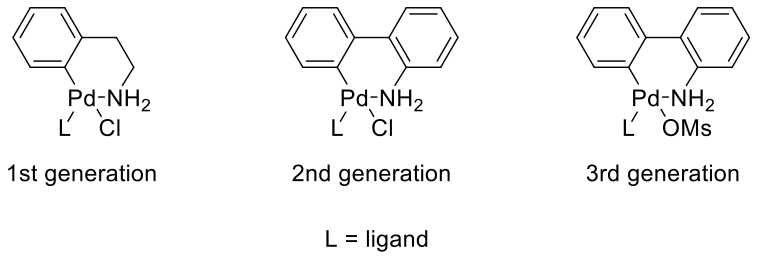
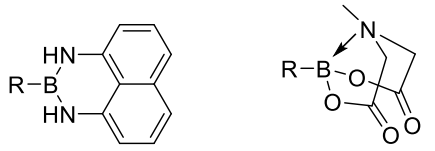


Figure 1.2 Examples of Buchwald Precatalysts

1.2. Potassium Organotrifluoroborates

Traditionally, boronic acids or trialkylboroane species are frequently used as the nucleophilic partners in Suzuki–Miyaura coupling reactions. Although these borane substrates have been employed effectively, the reactions are limited due to the instability to air and moisture and incompatibility to many reaction conditions.[14] Particularly, boronic acids exist as dimers or cyclic trimers rather than monomeric species, which are hard to purify. These organoboron species suffer from protodeboronation; therefore, excess boron reagents are required to complete the coupling reactions.[11a]

To overcome this limitation, several boronic acid surrogates, such as 1,8-naphthalenediaminatoborane [B(dan)][15] and *N*-methyliminodiacetic acid (MIDA),[16] have been reported (Figure 1.3). Even though these boron moieties have been proven to be effective as the nucleophilic partners in Suzuki–Miyaura cross-coupling reactions, additional synthetic steps, such as protection and deprotection, are required for their transformation in couplings.



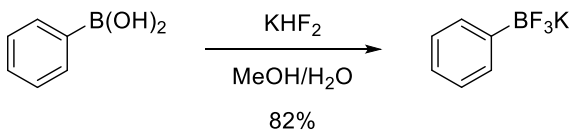
RB(dan) MIDA boronate

Figure 1.3 RB(dan) and MIDA Boronate

More recently, tetracoordinate boronate salts, potassium organotrifluoroborates, have been considered one of the most effective organoboron species in terms of stability and reactivity.[17]

Chambers and coworkers reported the first synthesis of a potassium organotrifluoroborate in 1960.[18] However, the method was not general to prepare organotrifluoroborates. In 1995, Vedejs and coworkers demonstrated a simple preparative method for the synthesis of potassium organotrifluoroborate using inexpensive potassium hydrogen fluoride (KHF_2) with the corresponding boronic acids (Equation 1.4).[19] These methods are widely used to prepare a large range of potassium organotrifluoroborates.

Equation 1.4

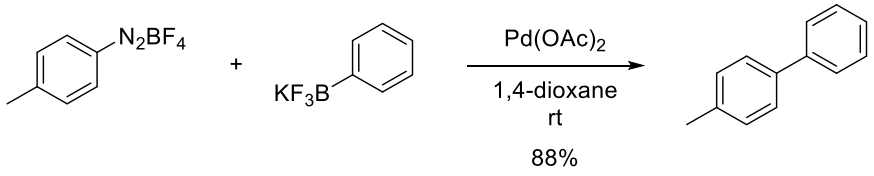


In most cases, potassium organotrifluoroborates are crystalline solids or powders, and show indefinite air and moisture stability. Moreover, many organic transformations, such as oxidations,[20] Wittig reactions,[21] reductive aminations,[22] Cu-catalyzed carbon-nitrogen bond formations,[23] selective cross-coupling reactions,[24] and 1,3-dipolar cycloadditions,[25] have been studied in the presence of these salts, and organotrifluroborates remained intact throughout the reactions.

1.3 Use of Potassium Organotrifluoroborates in the Suzuki–Miyaura Reaction

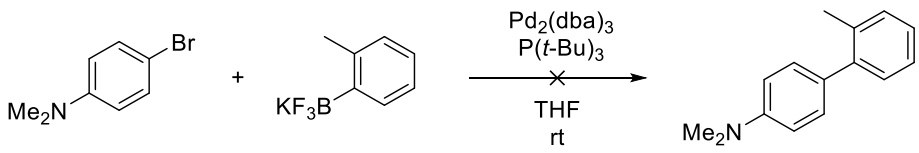
One of the most important studies toward organotrifluoroborates is their use in the Suzuki–Miyaura cross-coupling reaction as the nucleophilic coupling partners. In 1997, Genet and coworkers reported the first palladium catalyzed cross-coupling reactions with potassium organotrifluoroborates and aryldiazonium tetrafluoroborate salts to provide the desired product (Equation 1.5).[26] A few years later, Xia and Chen described the coupling reactions of organotrifluoroborates with diaryliodonium salts.[27] In both cases, a base and a ligand were not required to obtain the product.

Equation 1.5



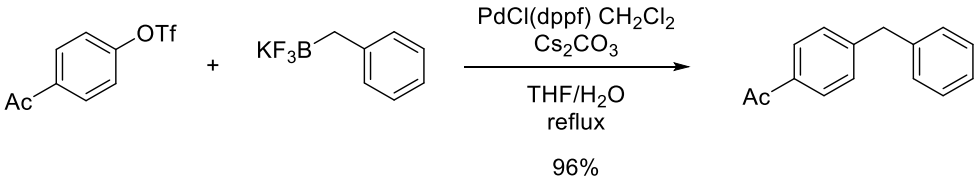
In 2000, Fu and coworkers failed to obtain the desired cross-coupled product by reacting potassium *o*-tolyltrifluoroborate with an aryl bromide in the absence of a base (Equation 1.6).[28]

Equation 1.6



In 2001, the Molander group demonstrated that the cross-doupling reactions of potassium alkyltrifluoroborates with triflates as the electrophilic partners to provide the product effectively (Equation 1.7).[29] Since this report, the Suzuki–Miyaura cross-coupling reaction with potassium organotrifluoroborates has been widely investigated. Particularly, the Molander group has contributed extensively to this area.[30]

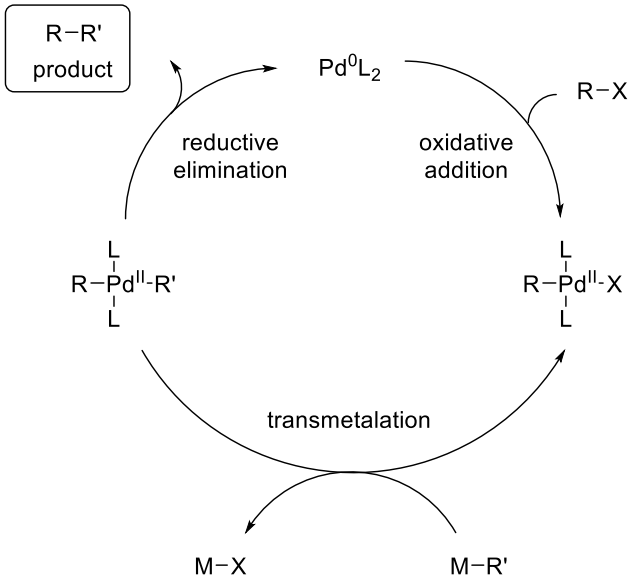
Equation 1.7



1.4 Mechanism of Suzuki–Miyaura Reactions with Organotrifluoroborates

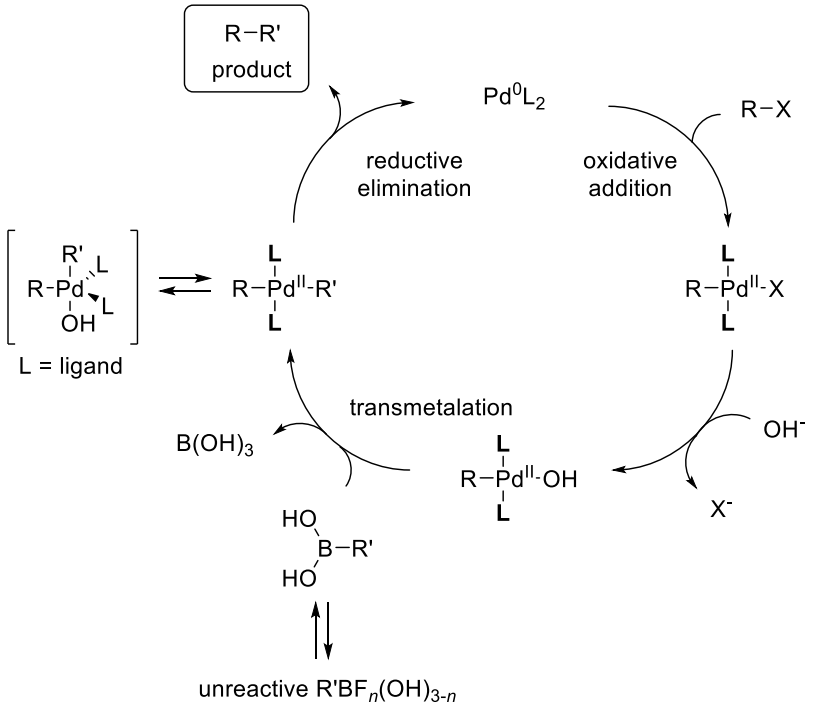
The general mechanism of metal catalyzed cross-coupling reactions include three steps: oxidative addition, transmetalation, and reductive elimination, to provide the corresponding product with a new carbon-carbon bond (Scheme 1.1).[1] The oxidative addition of a halide or pseudohalide to a Pd(0) complex to generate RPd(II)X intermediate is followed by transmetalation with an organometallic species to give RPd(II)R' complex. Finally, the corresponding coupled product is formed by reductive elimination, and the active Pd(0) complex is regenerated.

Scheme 1.1 General Mechanism of Transition Metal Catalyzed Cross-Coupling Reactions



In the case of the Suzuki–Miyaura cross-coupling reaction, a base is required to afford the desired product. In fact, the base, such as hydroxide or carbonate, plays an important role in the catalytic cycle.[31] Hydroxide ions form RPd(II)(OH), which is the key intermediate for the transmetalation with the organoboron species (Scheme 1.2). Moreover, hydroxide ions promote the reductive elimination via a five-coordinate Pd species.[31a]

Scheme 1.2 Catalytic Cycle of the Suzuki–Miyaura Cross-Coupling Reaction



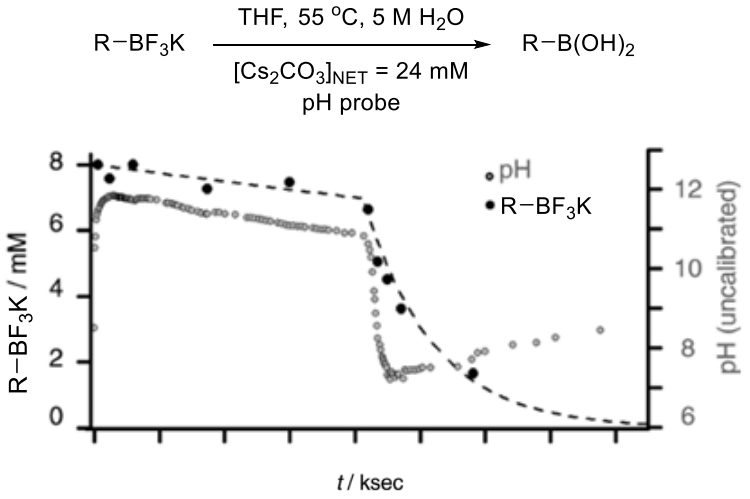
The Suzuki–Miyaura reaction with potassium organotrifluoroborates requires steps to generate the active organoboron species, a boronic acid, for the transmetalation. Several studies have demonstrated that RBF_3^- or boronates are unreactive in the catalytic cycle, and require the use of a base to generate the corresponding boronic acids from unreactive boronates.[29,31,32] In the presence of a base, such as hydroxide, RBF_3^- is in equilibrium with $RBF_n(OH)_{3-n}^-$ and the corresponding boronic acids (Equation 1.8).

Equation 1.8

$$\ominus \quad \ominus \quad \ominus \quad \ominus$$
$$RBF_3 \xrightleftharpoons{H_2O\ /\ base} RBF_2OH \xrightleftharpoons{H_2O\ /\ base} RBF(OH)_2 \xrightleftharpoons{H_2O\ /\ base} RB(OH)_3 \xrightleftharpoons{H_2O\ /\ base} RB(OH)_2$$

In 2012, Lloyd-Jones and coworkers demonstrated an acid-base paradox in Suzuki–Miyaura cross-coupling reactions of organotrifluoroborates.[33] Even though the Suzuki–Miyaura reaction requires a base, which makes the reaction media basic, acidity is important for the hydrolysis of organotrifluoroborates. Initially, the basic aqueous media suppresses the hydrolysis of organotrifluoroborates. Slowly generated HF/KHF_2 lowers the pH of the organic layer, increasing the rate of the hydrolysis to the active boronic acid reagents (Scheme 1.3). Moreover, the vessel shape, material size, and stirring rate are important for effective hydrolysis under heterogeneous reaction conditions.

Scheme 1.3 Hydrolysis of Organotrifluoroborates under Basic Heterogeneous Conditions



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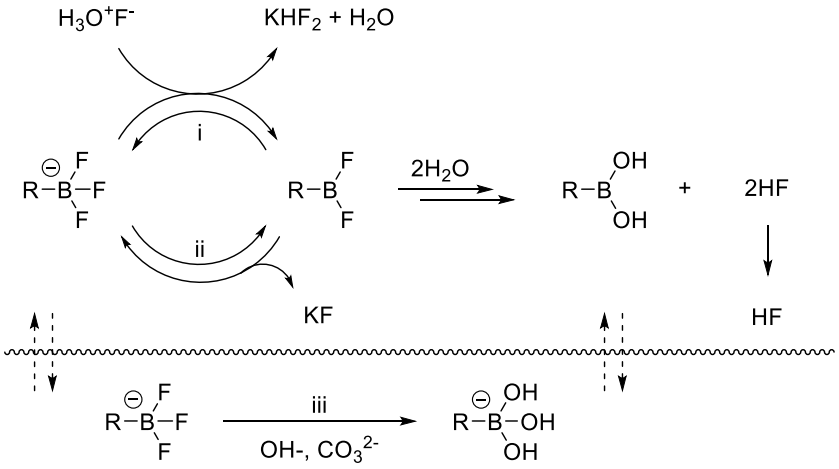
Potassium organotrifluoroborates can be categorized into three groups depending on the nature of trifluoroborates (Scheme 1.4). The first group undergoes slow hydrolysis by the acid-catalyzed pathway i. This group includes simple aryl and benzyl trifluoroborates. The second group undergoes into rapid hydrolysis by direct equilibrium dissociation pathway ii. In this case, the R group, such as cycloalkyl or electron-rich aryl, is able to stabilize the boron species by π-overlap or hyperconjugation. Pathway iii represents a group of alkynyl or electron-poor aryltrifluoroborates that are hydrolyzed very slowly.

Scheme 1.4 Hydrolysis Pathways Depending on the Nature of Organotrifluoroborates



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In 2012, Amatore and Jutand reported the important role of fluoride ions in coupling reactions of organotrifluoroborates.[34] Similar to hydroxide ions, fluoride ions are

able to facilitate the catalytic cycle by the formation of an RPd(II)F complex, which allows transmetalation with boronic acids, and also promotes the reductive elimination via five-coordinate intermediate with fluoride ion (Figure 1.4).

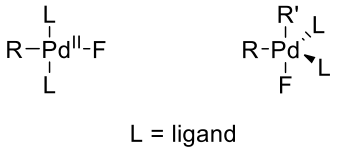

Figure 1.4 Important Intermediates with Fluoride Ions

1.5 Conclusions

The Suzuki–Miyaura cross-coupling reaction has proven to be one of the most effective coupling reactions among the many transition metal catalyzed reactions. Because of the mild reaction conditions and the commercial availability of organoboron species, the reactions have been widely utilized to construct new carbon-carbon bonds. Many optimizations, such as improvements in ligands and catalysts, have been made to facilitate the Suzuki–Miyaura reaction.

Recently, potassium organotrifluoroborates have been employed in coupling reactions, rather than traditional trivalent organoboron species. Organotrifluoroborates are prepared from inexpensive KHF_2 and the corresponding organoboron reagent, and they have shown enhanced stability to air and moisture. Therefore, they are easier to handle and store compared to other organoboranes.

Unlike other metal catalyzed cross-coupling reactions, a base is crucial in the Suzuki–Miyaura cross-coupling reaction. More recently, mechanistic studies on the

Suzuki–Miyaura reaction of potassium organotrifluoroborates have been reported by several research groups. Hydroxide and fluoride ions play an important role in the catalytic cycles to generate the important transmetalating intermediate. Moreover, they facilitate the reductive elimination via formation of five-coordinate complexes.

Additionally, acid catalysis is required to release the active boronic acid reagents from unreactive organotrifluoroborates. Even though Suzuki–Miyaura coupling reactions are under heterogeneous basic conditions, the organic phase becomes acidic over the time, which hydrolyzes the organotrifluoroborates efficiently.

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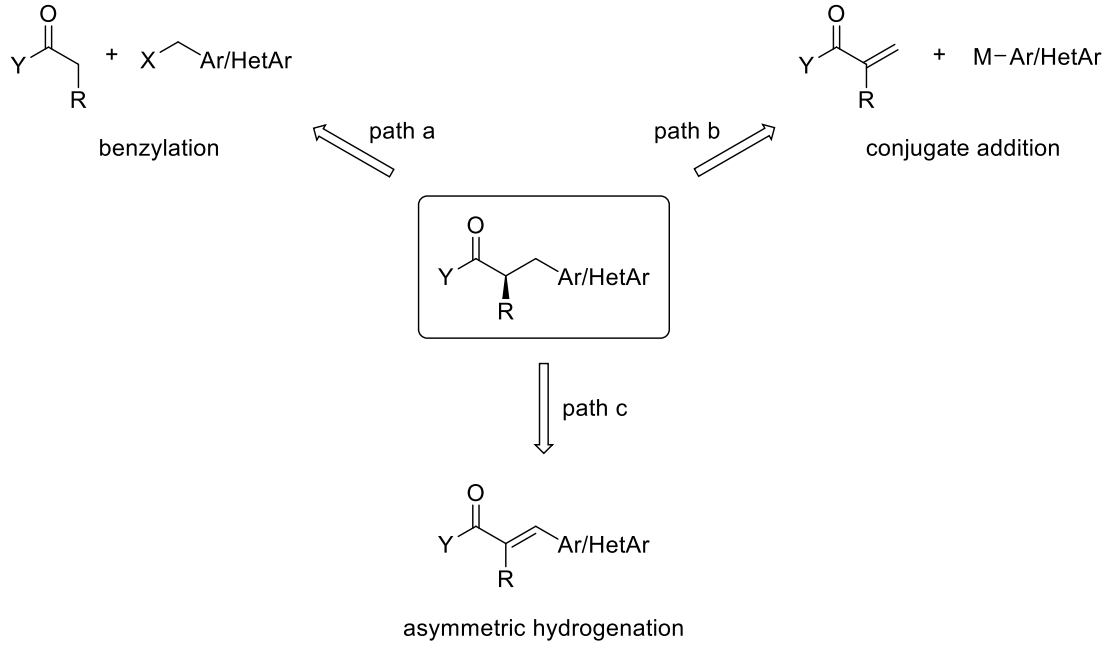
Chapter 2. Enantiomerically Enriched Potassium β-Trifluoroboratoamides

2.1 Preparation of α-Chiral β-Arylated Carbonyl Compounds

α-Chiral β-arylated carbonyls are encounted in many organic compoudns. They are one of the important substructures in synthetic organic chemistry. Several synthetic pathways have been reported to install these target substructures. The common approaches to these moieties are benzylation of enolates,[1] conjugate additions of arylmetallics to α,β-unsaturated carbonyl precusors,[2] and catalytic asymmetric hydrogenation of α-substituted α,β-unsaturated carbonyl substrates (Scheme 2.1).[3]

Scheme 2.1 Strategies for the Synthesis of α-Chiral β-Arylated Carbonyl Compounds



The benzylation approach is one of the highly attractive pathways because many chiral auxiliaries are readily available (Scheme 2.1, path a).[1] However, only limited numbers of benzylic halide precursors are commercially available. Another drawback is the control of the chemoselectivity throughout the alkylation steps.

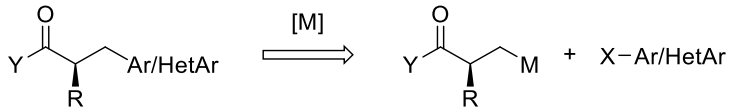
An alternative route is a 1,4-conjugate addition of arylmetallic reagents to α,β-unsaturated carbonyl compounds (Scheme 2.1, path b).[2] After the addition, the corresponding enolate requires to protonate enantioselectively to provide the target β-arylated carbonyl compounds. However, this method is highly substrate dependent and lack of efficacy.[4]

Another way to prepare the β-arylated carbonyl substructure is transition metal catalyzed asymmetric hydrogenation of α-substituted α,β-unsaturated carbonyls (Scheme 2.1, path c).[3] Similar to the protonation process, enantioselective hydrogenation of carbon-carbon double bonds is important. Therefore, access to a stereodefinded trisubstituted alkene substrate is required.

2.2. Transition Metal Catalyzed Reactions of β-Metallohomoenolates

A more direct and efficient way to build α-chiral β-arylated carbonyl compounds is the transition metal catalyzed cross-coupling reactions of α-chiral β-metallo carbonyl reagents with aryl and hetaryl halides (Scheme 2.2).

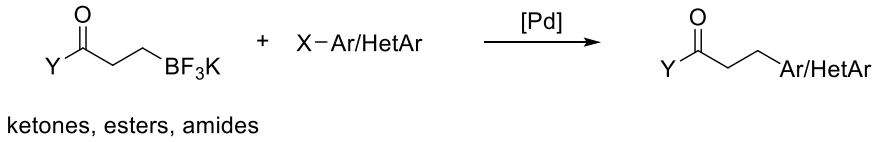
Scheme 2.2 Cross-Coupling of β-Metallo Carbonyl Compounds



β-Metallo carbonyl species or metallohomoenolates possessing 'umpolung' reactivity have been demonstrated in synthetic chemistry. Zinc,[5] titanium,[6] silicon,[7] tin,[8] and boron homoenolates[9] have been prepared by different synthetic strategies. However, only a few reports exist that demonstrate the coupling of previously prepared metallohomoenolates as the nucleophilic partners to provide the target β-arylated carbonyl substructures.

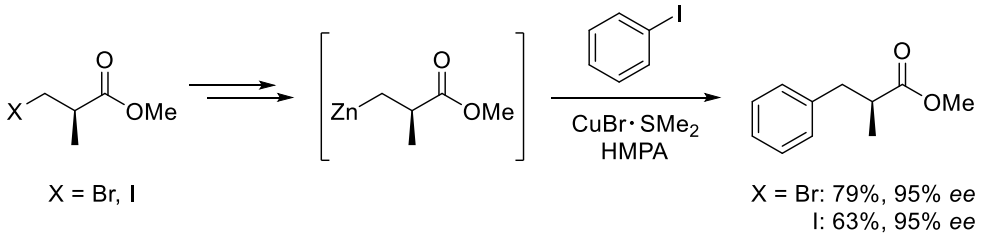
More recently, the preparation and Suzuki–Miyaura cross-coupling reactions of β-trifluoroborato ketones, esters, and amides have been described by the Molander group (Scheme 2.3).[10] These β-trifluoroborato carbonyl reagents proved to be efficient to install the β-arylated carbonyl compounds through coupling with various aryl and hetaryl halides. Particularly, aryl and hetaryl halides are more readily available compared to the benzyl halides required for the benzylation pathway. Moreover, the Suzuki–Miyaura reaction have proven to be efficient because it shows better functional group tolerance and minimal toxicity.[11] Even though these β-trifluoroborato carbonyl substances have been studied, α-chiral β-trifluoroborato carbonyl substances have not been investigated.

Scheme 2.3 Study of β-Trifluoroborato Carbonyl Reagents



α-Chiral β-arylated carbonyl compounds have previously been prepared with organozinc homoenolates through Negishi cross-coupling reactions (Sheme 2.4). [12] Enantiomerically enriched α-chiral organozinc coupling partners have proven to be the effective coupling partners to build the target substructures. However, organozinc homoenolates are known to be unstable to moisture and air. Therefore, zinc reagents must be prepared *in situ* and also handled under an inert atmosphere. Moreover, sensitive functional groups may not be compatible with zinc species because they exhibit reactivity with various electrophiles.[13]

Scheme 2.4 α-Chiral Organozinc Homoenolates in Negishi Cross-Coupling Reactions

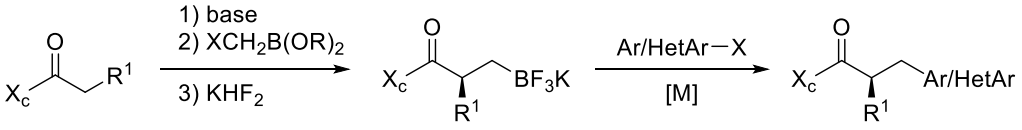


2.3 Results and Discussion

To expand the study of previous work on β-trifluoroboratoamides, we envisioned the synthesis and the Suzuki–Miyaura reaction of α-chiral β-trifluoroboratoamides using

chiral auxiliaries. This development would be a useful asymmetric synthetic pathway for the preparation of α-chiral β-arylated carbonyl compounds. To the best of our knowledge, this type of chiral boron reagent has not been prepared or applied in couplings (Scheme 2.5).

Scheme 2.5 Strategy for the Synthesis and the Suzuki–Miyaura Reaction of α-Chiral β-Trifluoroboratoamides



X_c = chiral auxiliary
R^1 = alkyl

However, one of the concerns is retention of the stereocenter under the aqueous basic conditions at high temperature required for the organotrifluoroborate couplings. Only a few examples have been reported with the application of boron containing substances with a stereocenter in Suzuki–Miyaura coupling reactions;[14] however, these examples do not involve α-chiral β-arylated carbonyl boron reagents.

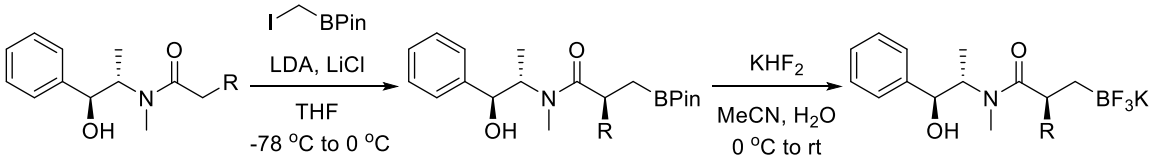
2.3.1 Synthesis of Enantiomerically Enriched Potassium β-Trifluoroboratoamides

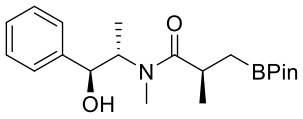
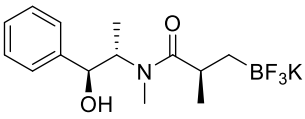
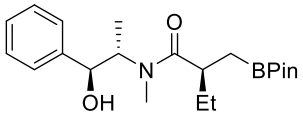
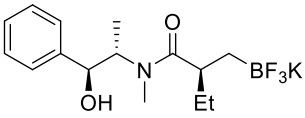
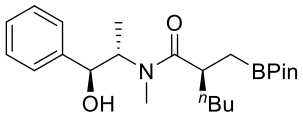
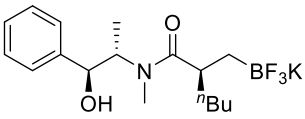
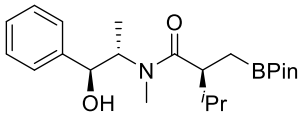
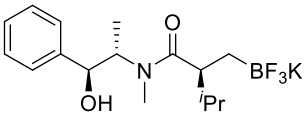
First, we employed several chiral auxiliaries, such as Evans oxazolidinone, Oppolzer's sultam, and Meyers' pseudoephedrine, to prepare α-chiral β-trifluoroboratoamides. Even though we could prepare α-chiral β-trifluoroboratoamides using all of the auxiliaries, later, we found that Evans oxazolidinones and the Oppolzer's

sultam derivatives were inefficient due to cleavage of auxiliaries during the cross-coupling reactions.

Based on the Matteson's enolate chemistry with chiral α-halo boronic esters[15] and Meyers pseudoephedrine study, [16] enantiomerically enriched α-chiral β-trifluoroboratoamides using (1*S*, 1*S*)-(+)-pseudoephedrine as the chiral auxiliary were successfully prepared through a two-step synthesis (Table 2.1). First, the steregenic center was installed via alkylation of the enolate using iodomethylpinacolboronate. The alkylated α-chiral β-pinacolboronates were obtained in good to excellent yields. The diastereomeric ratios of these intermediates were greater than 95:5 by ^{1}H NMR. Addition of KHF_2 to the solution of pinacolboronates provided the desired enantiomerically enriched α-chiral β-trifluoroboratoamides in moderate to excellent isolated yields. Successfully prepared β-trifluoroboratoamides were white solids, which were air stable and could be stored on the bench without decomposition or epimerization.

Table 2.1 Synthesis of α-Chiral β-Trifluoroboratoamides

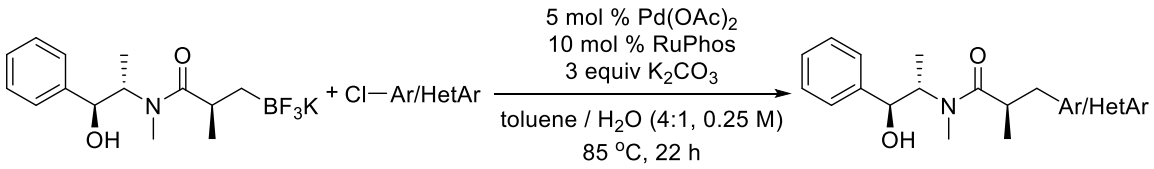


entry	pinacol boronate	isolated yield(%)	trifluoroboratoamide	isolated yield(%)
1		95		90
2		99		72
3		69		83
4		83		51

2.3.2 Suzuki–Miyaura Cross-Coupling Reaction with Aryl and Hetaryl Chlorides

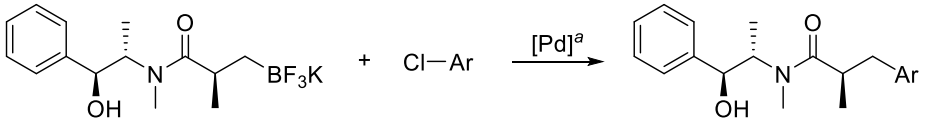
With these enantiomerically enriched β-trifluoroboratoamides in hand, their utility as the nucleophilic coupling partners in Suzuki–Miyaura coupling reactions was investigated. The optimization process was conducted with the α-methyl substituted β-trifluoroboratoamide and chlorobenzene. Several ligands, bases, solvents, and times were screened, and the combination of 5 mol % of $Pd(OAc)_2$, 10 mol % of RuPhos and 3 equiv of K_2CO_3 in a mixture of toluene / H_2O (4:1, 0.25 M) at 85 °C for 22 h emerged as the best conditions (Equation 2.1).

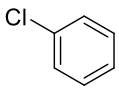
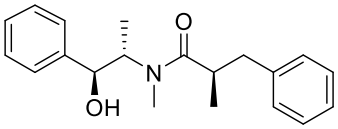
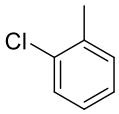
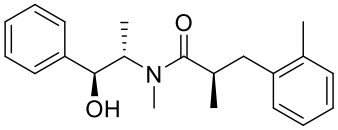
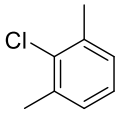
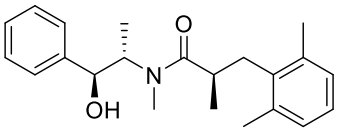
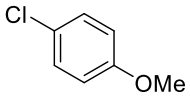
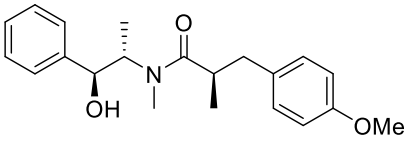
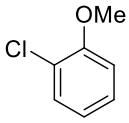
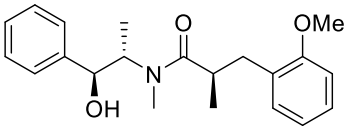
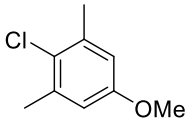
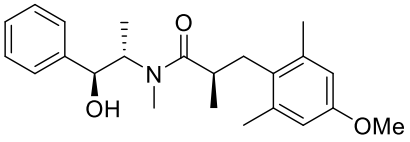
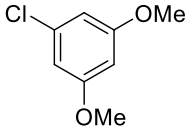
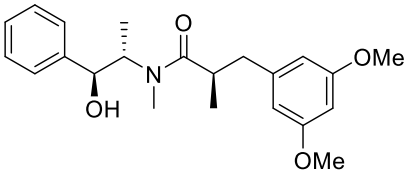
Equation 2.1 Optimization of Cross-Coupling Reactions with α-Chiral β-Trifluoroboratoamide



To investigate the scope of the electrophiles, various electron-neutral and electron-donating aryl chlorides were employed in cross-couplings using the optimized conditions (Table 2.2). All of the electrophiles successfully provided the desired products in moderate to good yields. Substrates with methyl substituents at the *ortho* position provided the expected products in lower yields (Table 2.2, entries 2, 3 and 6). In the case of 4-chloroanisole as the electrophilic coupling partner, SPhos was used instead of RuPhos to obtain a better result (Table 2.2, entry 4). The electrophiles with electron-rich substituents on the *ortho, meta*, and *para* positions gave the corresponding products in moderate yields (Table 2.2, entries 4–7). Interestingly, the substrate containing more electron-donating substituents provided the desired product in the better yield compared to substrates processing only one electron-rich substituent (Table 2.2, entry 7), even though the electron-rich electrophiles are known to be inefficient coupling partners in Suzuki–Miyaura coupling reactions.[17]

Table 2.2 Cross-Coupling of α-Chiral β-Trifluoroboratoamide with Various Aryl Chlorides

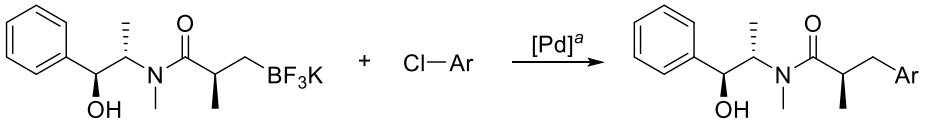


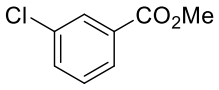
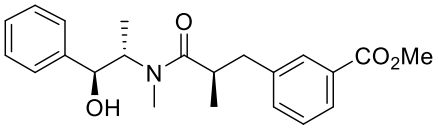
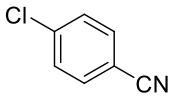
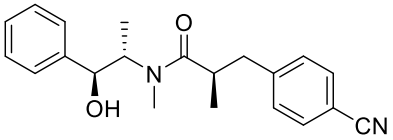
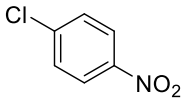
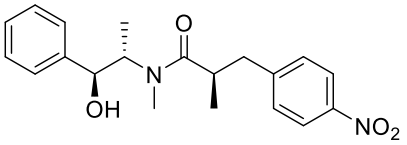
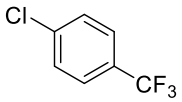
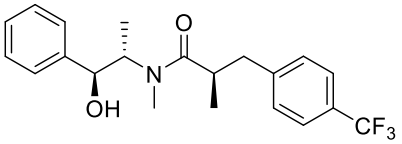
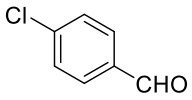
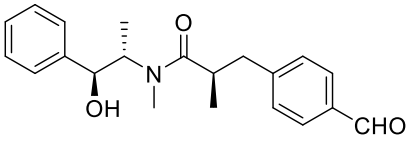
entry	Cl—Ar	product	isolated yield(%)
1			70
2			40
3			38
4			51[b]
5			55
6			41
7			62

[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroboratoamide, 5 mol % $Pd(OAc)_2$, 10 mol % RuPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] SPhos.

Next, electrophiles containing an electron-withdrawing group on the aryl ring were studied using the same set of conditions (Table 2.3). The desired products were obtained in moderate to good yields. In general, electron-poor substrates showed relatively better results compared to electron-neutral and electron-rich coupling partners. Several functional groups, such as esters, nitriles, nitro groups, and aldehydes were compatible throughout the coupling reactions. It should be noted that these functional groups would not be tolerated with enolate alkylation method to prepare the target structure. In the case of the electrophile with a nitrile moiety on the aryl ring, SPhos was found to be more efficient than RuPhos to give a better yield (Table 2.3, entry 2). Unfortunately, *p*-trifluoromethylphenyl chloride as an electrophile provided the expected product in low yield, 43% (Table 2.3, entry 4).

Table 2.3 Cross-Coupling of α-Chiral β-Trifluoroboratoamide with Various Aryl Chlorides



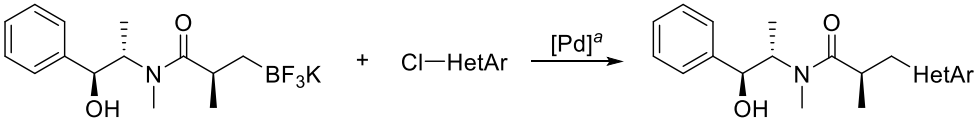
entry	Cl—Ar	product	isolated yield(%)
1			57
2			75[b]
3			75
4			43
5			82

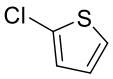
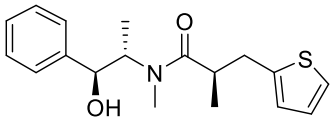
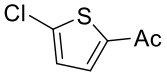
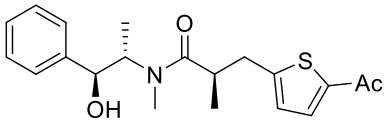
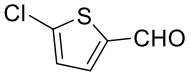
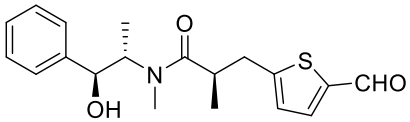
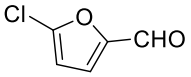
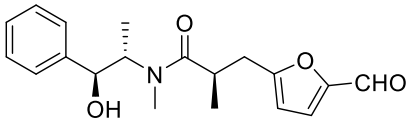
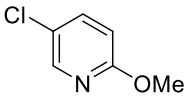
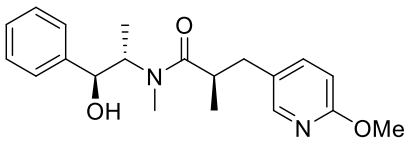
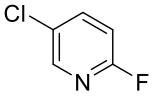
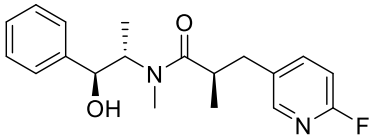
[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroboratoamide, 5 mol % $Pd(OAc)_2$, 10 mol % RuPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] SPhos.

To expand the scope of electrophiles, hetaryl chlorides were tested as the coupling partners employing the developed reaction conditions (Table 2.4). Various hetaryl chlorides, such as thiophenes, furans and pyridines, proved to be efficient coupling counterparts to provide the desired products in moderate to good yields, up to 80% isolated yield. Again, sensitive functional groups, such as esters and aldehydes, were tolerated

under coupling reactions. Interestingly, pyridine with an electron-poor substituent afforded the corresponding product in a higher yield compared to electron-rich pyridine derivative (Table 2.4, entries 5 and 6).

Table 2.4 Cross-Coupling of α-Chiral β-Trifluoroboratoamide with Various Hetaryl Chlorides

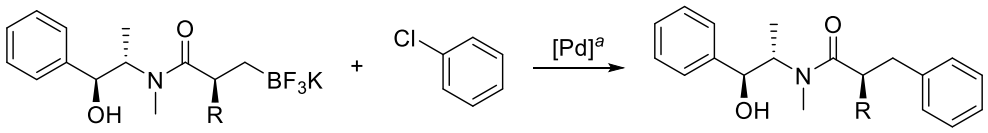


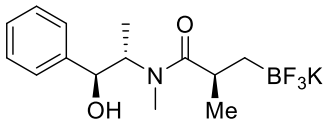
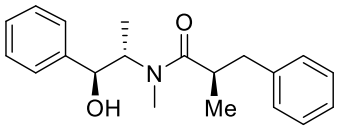
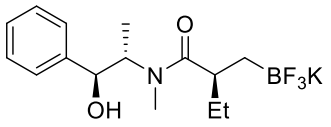
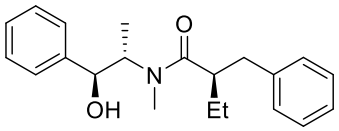
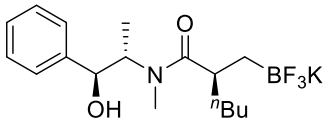
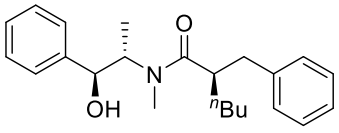
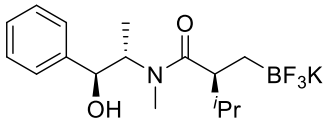
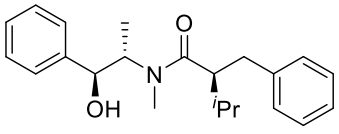
entry	Cl—HetAr	product	isolated yield(%)
1			53
2			73
3			60
4			69
5			55
6			80

[a] Reaction conditions: 1.0 equiv of hetaryl chloride, 1.05 equiv of trifluoroboratoamide, 5 mol % $Pd(OAc)_2$, 10 mol % RuPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 ^oC, 22 h.

Then, various potassium β-trifluoroboratoamides were tested in the Suzuki–Miyaura cross-coupling reaction as the nucleophilic coupling partners (Table 2.5). Different substituents α to the carbonyl affected the yields depending on the steric hindrance. Substrates with methyl and ethyl α to the carbonyl provided the desired products in good yields (Table 2.5, entries 1 and 2). However, the isolated yields were dramatically dropped with more sterically demanding substrates, such as *n*-butyl and isopropyl groups, and also longer reaction times were required for the reaction to go to completion (Table 2.5, entries 3 and 4).

Table 2.5 Cross-Coupling of Various α-Chiral β-Trifluoroboratoamides with Chlorobenzene



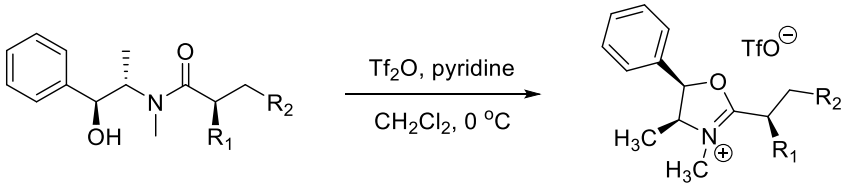
entry	trifluoroboratoamide	product	isolated yield(%)
1			70
2			70
3			47[b]
4			30[b]

[a] Reaction conditions: 1.0 equiv of chlorobenzene, 1.05 equiv of trifluoroboratoamide, 5 mol % $Pd(OAc)_2$, 10 mol % RuPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] 48 h.

2.3.3 Diastereoselectivity of the Suzuki–Miyaura Reaction

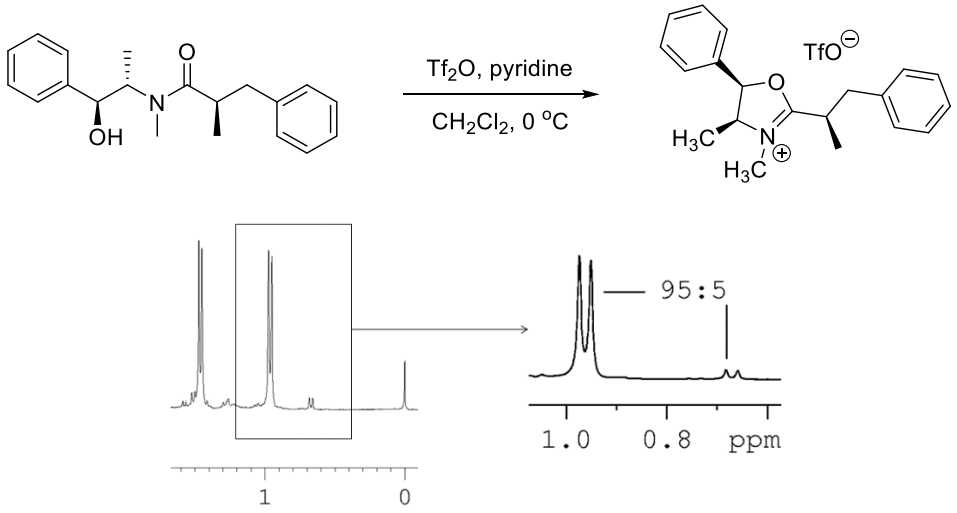
After the cross-coupling reactions, the diastereomeric ratios of the coupled products needed to be determined. The method developed by Meyers using triflic anhydride and pyridine to form cyclic oxazolium triflates from pseudoephedrine derivatives was employed to determine the degree of stereoretention (Equation 2.2). [18] The diastereoselectivities were easily detectable by ^{1}H NMR chemical shifts with the methyl substituent at the α stereocenter.

Equation 2.2 Determining the Diastereomeric Ratios by the Meyers Method



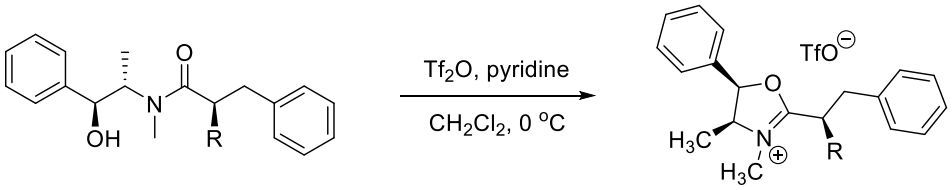
We applied this method to the final products to determine the diastereomeric ratios after the coupling reactions. Most of the products were tested and gave diastereomeric ratios greater than 95:5. Unfortunately, some of substrates, such as the compounds prossessing sensitive functional groups and hetayl derivatives, were incompatible with triflic acid, and their diastereoselectivities could not be determined in this manner. The stereochemistry of the major diastereomer was determined by comparison to the known compound (Figure 2.1).

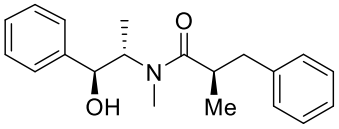
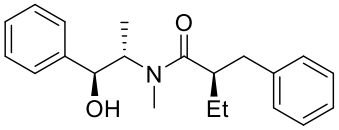
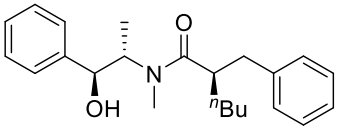
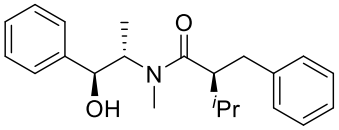
Figure 2.1 Study of Diastereomeric Ratio



Particularly, the diastereoselectivities gave different results depending on the substituents α to the carbonyl (Table 2.6). More sterically hindered substrates gave slightly better diastereomeric ratios (Table 2.6, entries 3 and 4). Finally, we concluded that the diastereoselectivities were retained throughout the coupling reactions.

Table 2.6. Determining the Diastereomeric Ratio of the Coupled Products



entry	substrate	dr
1		95:5
2		97:3
3		98:2
4		98:2

2.4 Conclusions

Enantiomerically enriched potassium α-chiral β-trifluoroboratoamides were successfully prepared using pseudoephedrine as a chiral auxiliary employing Matteson's chemistry. These β-trifluoroboratoamides were air stable white solids and could be stored on the bench without loss of stereochemistry. Subsequently, palladium catalyzed Suzuki–Miyaura cross-coupling reactions were investigated with the β-trifluoroboratoamides. All of them proved to be efficient nucleophilic coupling partners with various aryl and hetaryl chlorides. This development provides a complementary approach to previous reports to build the target structures. Use of the β-trifluoroboratoamides, which afford an umpolung

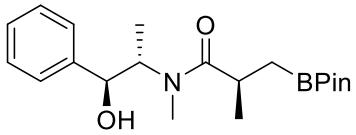
pathway, proved superior to other routes, such as alkylation, conjugate addition/enantioselective protonation, and asymmetric hydrogenation, in terms of availability of reagents and compatibility of functional groups. Moreover, the diastereoselectivities were greater than 95:5 in all cases, and the stereochemistry was preserved under the aqueous basic conditions of cross-couplings.

2.5 Experimental

General.

$Pd(OAc)_2$, RuPhos, SPhos and K_2CO_3 were used as received. All halides were used as received. Lithium chloride was dried under vacuum at 150 °C for 24 h prior to use. Toluene was distilled from sodium/benzophenone prior to use. H_2O was degassed prior to use. Melting points (°C) are uncorrected. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at 500.39, 125.75, and 470.55 MHz, respectively. ^{19}F NMR chemical shifts were referenced to external $CFCl_3$ (0.0 ppm). ^{11}B NMR spectra at 128.4 MHz were obtained on a spectrometer equipped with the appropriate decoupling accessories. All ^{11}B NMR chemical shifts were referenced to external $BF_3{\bullet}OEt_2$ (0.0 ppm) with a negative sign indicating an upfield shift. Analytical thin layer chromatography (TLC) was performed on TLC silica gel plates (250 μm) precoated with a fluorescent indicator. Standard flash chromatography procedures[19] were followed using 32–63 μm silica gel. Visualization was effected with ultraviolet light, cerium ammonium molybdate (CAM), and $KMnO_4$.

General Procedure for the Alkylation Reaction.

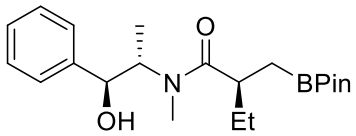


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanamide.

A flame-dried round bottom flask was charged with LiCl (1.1 g, 27.1 mmol, 6.0 equiv), *i*-Pr_2NH (1.5 mL, 10.6 mmol, 2.4 equiv), and THF (13 mL). The solution was cooled to –78 °C, and added to a solution of *n*-BuLi in hexanes (2.5 M, 4.4 mL, 9.5 mmol, 2.1 equiv). The resulting mixture was briefly warmed to 0 °C and cooled to –78 °C again. A cooled solution of amide (1.0 g, 4.5 mmol, 1.0 equiv) in THF (15 mL) was added to the reaction flask. The mixture was stirred at –78 °C for 1 h at 0 °C for 15 min, and at rt for 5 min and then cooled to 0 °C. Iodomethylpinacolboronate (1.8 g, 6.75 mmol, 1.5 equiv) was added to reaction mixture and stirred at 0 °C for 30 min, and then the reaction was quenched by the addition of saturated aq. NH_4Cl solution (10 mL). The mixture was extracted with EtOAc (2 ×30 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexanes:EtOAc = 1:1) to afford the product (1.4 g, 3.9 mmol) as a colorless oil in 86% isolated yield.

$[\alpha]^{20}_D$ +60.8 (c 1.20, $CHCl_3$); ^{1}H NMR (1.2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.39–7.06 (m, 5H), 4.72 (br, 1H), 4.42 (d, *J* = 9.0 Hz, 1H), 4.14* (d, *J* = 1.5 Hz, 1H), 4.12–4.02* (m, 1H), 4.02–3.94 (m, 1H), 3.34–3.27 (m, 1H), 2.77 (s, 3H), 2.69–2.63* (m, 1H), 2.37* (s, 3H), 1.71 (dd, *J* = 16.0, 10.0 Hz, 1H), 1.25 (dd, 1H, *J*

= 15.5, 7.0 Hz, 1H), 1.14* (s, 12H), 1.12–1.11 (m, 15H), 1.03 (d, 3H, *J* = 7.0 Hz, 3H), 0.60* (d, 3H, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) 179.7*, 178.8 128.8, 142.5*, 141.1, 128.6, 128.3*, 128.1*, 127.5*, 127.1, 126.6, 83.2*, 82.9, 76.2*, 75.5, 58.8, 33.1*, 32.3, 26.9, 25.9, 24.7*, 24.5, 20.3, 19.4*, 15.8, 14.2*; ^{11}B NMR (128.4 MHz, C_6D_6) δ 31.8; IR (neat) 3369, 2976, 1617 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{32}BNO_4Na$ $[M+Na]^+$ 383.2322, found 383.2314.

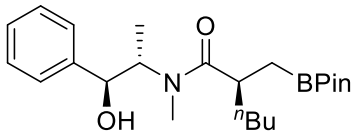


(*S*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*-methyl-2-{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}butanamide.

The reaction was carried out with the corresponding amide (4.1 g, 17.4 mmol, 1.0 equiv) according to the general alkylation procedure to obtain the product (6.5 g, 17.2 mmol) as a colorless oil in 99% yield.

$[\alpha]^{20}_D$ +72.0 (c 1.54, $CHCl_3$); ^{1}H NMR (1:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.39 (t, *J* = 8.0 Hz, 2H), 7.22–7.06 (m, 3H), 4.80–4.74 (m, 1H), 4.71* (br, 1H), 4.42 (d, *J* = 9.0 Hz, 1H), 4.11–4.02 (m, 1H), 3.27–3.18* (m, 1H), 2.80 (s, 3H), 2.62–2.53 (m, 1H), 2.45* (s, 3H), 1.84–1.73 (m, 1H), 1.70–1.62* (dd, *J* = 16.0, 10.0 Hz, 1H), 1.61–1.40 (m, 2H), 1.32–1.25 (m, 1H), 1.13* (d, *J* = 10.5 Hz, 12H), 1.10 (s, 12H), 1.08 (d, *J* = 7.0 Hz, 3H), 0.86* (t, *J* = 7.5 Hz, 3H), 0.81 (t, *J* = 7.5 Hz, 3H), 0.64* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ179.2*, 178.2, 142.6*, 141.2, 128.7, 128.4, 128.2*, 127.7*, 127.2, 126.8*, 83.5, 83.1*, 78.4*, 75.7, 59.0, 39.7*, 38.8, 28.0, 27.7*, 26.9,

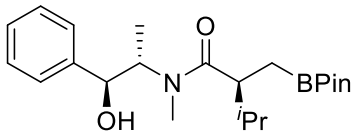
25.0, 24.8*, 24.6, 16.1, 14.5*, 11.9*, 11.9; ^{11}B NMR (128.4 MHz, C_6D_6) δ 31.9; IR (neat) 3435, 1638 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{35}NO_4$ $[M+H]^+$ 376.2659, found 376.2653.



(*S*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*-methyl-2-{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}hexanamide.

The reaction was carried out with the corresponding amide (1.1 g, 4.18 mmol, 1.0 equiv) according to the general alkylation procedure to obtain the product (1.4 g, 3.47 mmol) as a colorless oil in 83% yield.

$[\alpha]^{20}_D$ +61.8 (c 1.23, $CHCl_3$); ^{1}H NMR (1:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.39 (dd, *J* = 7.0, 5.0 Hz, 2H), 7.22–7.07 (m, 3H), 4.77* (s, 1H), 4.46 (d, *J* = 9.0 Hz, 1H), 4.36 (s, 1H), 4.18–4.08 (m, 1H), 3.36–3.28* (m, 1H), 2.82 (s, 3H), 2.72–2.63 (m, 1H), 2.51* (s, 3H), 1.82–1.73* (m, 1H), 1.65 (dd, *J* = 16.0, 10.0 Hz, 1H), 1.60–1.43 (m, 2H), 1.32–1.17 (m, 5H), 1.14* (d, *J* = 10.0 Hz, 12H), 1.11 (s, 12H), 0.87* (t, *J* = 7.0 Hz, 3H), 0.76 (t, *J* = 7.0 Hz, 3H), 1.37 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 179.4*, 178.4, 142.7*, 141.3, 128.7, 128.4, 128.3*, 127.7*, 127.3, 126.8*, 83.5, 83.2*, 76.5*, 75.8, 59.0, 38.2*, 37.1, 34.7, 34.5*, 29.7*, 29.4, 26.9, 25.0, 24.8*, 24.6, 22.9*, 22.7, 16.1, 14.5*, 14.1*, 14.0; ^{11}B NMR (128.4 MHz, C_6D_6) δ 31.7; IR (neat) 3436, 1634 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{39}NO_4B$ $[M+H]^+$ 404.2972, found 404.2984.

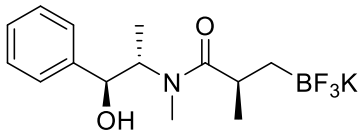


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,3-dimethyl-2-{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}butanamide.

The reaction was carried out with the corresponding amide (1.4 g, 5.62 mmol, 1 equiv) according to the general alkylation procedure to obtain the product (1.5 g, 3.85 mmol) as a colorless oil in 69% yield.

$[\alpha]^{20}_{D}$ +73.5 (c 2.04, $CHCl_3$); ^{1}H NMR (1:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.40 (dd, *J* = 15.0, 7.5 Hz, 2H), 7.23–7.07 (m, 3H), 4.83–4.78* (m, 1H), 4.76* (s, 1H), 4.47 (d, *J* = 8.0 Hz, 2H), 4.18–4.08 (m, 1H), 3.25–3.19* (m, 1H), 2.80 (s, 3H), 2.56* (s, 3H), 2.55–2.47 (m, 1H), 2.08–1.99* (m, 1H), 1.89–1.78 (m, 1H), 1.70–1.61* (m, 1H), 1.35* (dd, *J* = 16.0, 9.0 Hz, 1H), 1.12* (d, *J* = 14.0 Hz, 12H), 1.10 (s, 12H), 1.00 (ddd, *J* = 21.0, 16.5, 5.0 Hz, 2H), 0.89 (dd, *J* = 11.5, 6.5 Hz, 6H), 0.83 (d, *J* = 7.0 Hz, 3H), 0.66* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ178.8*, 177.6, 142.6*, 141.2, 128.7, 128.3, 128.1*, 127.6*, 127.2, 126.8*, 83.5, 83.1*, 76.4*, 75.7, 59.1, 44.4*, 43.0, 31.7, 31.5*, 26.8*, 24.9, 24.7*, 24.5, 21.5, 21.1*, 19.0*, 18.5, 16.2, 14.3*; ^{11}B NMR (128.4 MHz, C_6D_6) δ 32.3; IR (neat) 3435, 1620 cm^{-1}; HRMS (ES+) calcd. for $C_{22}H_{37}NO_4B$ $[M+H]^+$ 390.2816, found 390.2797.

General Procedure for the Preparation of Enantiomerically Enriched Potassium α-Chiral β-Trifluoroboratoamides.

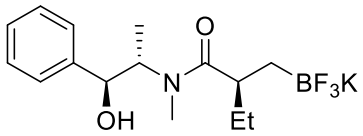


Potassium (*R*)-3-(Trifluoroborato)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

The corresponding boronate ester (4.4 g, 12.2 mmol, 1.0 equiv) was dissolved in MeCN (24 mL) and cooled to 0 °C. KHF_2 (2.9 g, 36.5 mmol, 3.0 equiv) in H_2O (8 mL) was added. The reaction mixture was stirred for 20 min at 0 °C. The solution was concentrated in vacuo and then dried in vacuo overnight. The crude mixture was extracted with acetone (2 × 20 mL), and the extracts were combined and concentrated. Et_2O (30 mL) was added to precipitate the product. The product (3.7 g, 11.0 mmol) was filtered and dried in vacuo and obtained as a white solid in 90% isolated yield.

$[\alpha]^{20}_D$ +48.2 (c 1.42, MeOH); mp: 124–129 °C; ^{1}H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, with less than 5% of pinacol, 500 MHz, DMSO-d_6) δ 7.47–7.19 (m, 5H), 5.31–5.18 (m, 1H), 5.07–4.99* (m, 1H), 4.68–4.54 (m, 1H), 4.54–4.45 (m, 1H), 4.25–4.15* (m, 1H), 2.82 (s, 3H), 2.70* (s, 3H), 2.59–2.51 (m, 1H), 0.94* (d, J = 6.0 Hz, 3H), 0.88 (d, J = 6.5 Hz, 3H), 0.79 (d, J = 6.5 Hz, 3H), 0.68–0.65* (m, 1H), 0.23–0.12 (m, 1H), 0.07– –0.11 (m, 1H); ^{13}C NMR (125.6 MHz, DMSO-d_6) δ 179.5, 179.4*, 143.9, 143.8*, 128.0*, 127.8, 127.5*, 127.3*, 127.0, 126.9, 74.2, 74.0, 73.5*, 56.2, 32.3, 32.0*, 29.5*, 26.0*, 25.0, 20.0*, 18.9, 15.4*, 13.9; ^{19}F NMR (470.8 MHz, DMSO-d_6) δ –135.2*,

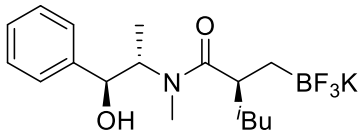
–136.1; ^{11}B NMR (128.4 MHz, DMSO-d_6) δ 3.92; IR (KBr) 3505, 2970, 1615 cm^{-1}; HRMS (ES-) calcd. for $C_{15}H_{22}BNO_2F_3$ $[M–K]^-$ 302.1539, found 302.1547.



Potassium (*S*)-2-{(Trifluoroborato)methyl}-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*-methylbutanamide.

The reaction was carried out with the corresponding boronate ester (6.1 g, 16.3 mmol, 1.0 equiv) according to the general procedure for the preparation of enantiomerically enriched potassium α-chiral β-trifluoroboratoamides to obtain the product (4.2 g, 11.8 mmol) as a white solid in 72% yield.

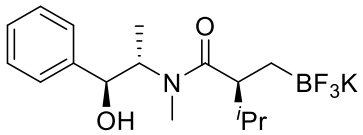
$[\alpha]^{20}_D$ +52.3 (c 1.21, MeOH); mp: 185–186 °C; ^{1}H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, DMSO-d_6) δ 7.63–7.29 (m, 5H), 5.36 (s, 1H), 5.03* (s, 1H), 4.76 (br, 1H), 4.70–4.68 (m, 1H), 4.62–4.58* (m, 1H), 4.39–4.38* (m, 1H), 2.95 (s, 3H), 2.86* (s, 3H), 2.65–2.57 (m, 1H), 1.67–1.55* (m, 2H), 1.55–1.44 (m, 2H), 0.99 (d, J = 6.5 Hz, 3H), 0.92* (d, J = 6.0 Hz, 3H), 0.77* (t, J = 7.0 Hz, 3H), 0.70 (t, J = 7.0 Hz, 3H), 0.65–0.58* (m, 1H), 0.30–0.18 (m, 1H), 0.18–0,07 (m, 1H); ^{13}C NMR (125.6 MHz, DMSO-d_6) δ 178.7, 178.5*, 143.9, 143.8*, 128.0, 127.8, 127.5*, 127.3*, 126.8*, 126.7, 74.4*, 74.1, 56.2, 53.5*, 40.1, 30.2, 27.9, 26.8, 25.9*, 15.5*, 13.9, 12.9*, 12.7; ^{19}F NMR (470.8 MHz, DMSO-d_6) δ –134.9*, –136.0; ^{11}B NMR (128.4 MHz, DMSO-d_6) δ 4.5; IR (KBr) 3504, 2968, 1611 cm^{-1}; HRMS (ES-) calcd. for $C_{15}H_{22}BNO_2F_3$ $[M–K]^-$ 316.1696, found 316.1707.



Potassium (*S*)-2-{(Trifluoroboryl)methyl}-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*-methylhexanamide.

The reaction was carried out with the corresponding boronate ester (1.2 g, 3.00 mmol, 1.0 equiv) according to the general procedure for the preparation of enantiomerically enriched potassium α-chiral β-trifluoroboratoamides to obtain the product (590 mg, 1.54 mmol) as a white solid in 61% yield.

$[\alpha]^{20}_{D}$ +44.9 (c 1.02, MeOH); mp: 64–68 °C; ^{1}H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, with less than 5% of pinacol, 500 MHz, DMSO-d_6) δ 7.56–7.24 (m, 5H), 5.32 (s, 1H), 5.01–4.94* (m, 1H), 4.76–4.66 (m, 1H), 4.66–4.59 (m, 1H), 4.57–4.49* (m, 1H), 4.37–4.28* (m, 1H), 2.88 (s, 3H), 2.80* (s, 3H), 2.67–2.59* (m, 1H), 2.57 (s, 1H), 1.62–1.37 (m, 2H), 1.36–1.17 (m, 2H), 1.11–0.97 (m, 2H), 0.95 (d, J = 6.5 Hz, 3H), 0.87 (dd, J = 14.0, 7.5 Hz, 3H), 0.65–0.53* (m, 1H), 0.23–0.11 (m, 1H), 0.11–0.00 (m, 1H); ^{13}C NMR (125.6 MHz, DMSO-d_6) δ 178.9, 178.7*, 143.9, 128.0, 127.7, 127.5*, 127.3*, 126.8*, 126.7, 74.5, 74.2, 73.6*, 56.3, 38.0, 34.8*, 33.8, 30.4*, 29.9, 26.0*, 25.0, 22.6, 15.5*, 14.1, 14.0*, 13.9; ^{19}F NMR (470.8 MHz, DMSO-d_6) δ –134.9*, –136.0; ^{11}B NMR (128.4 MHz, DMSO-d_6) δ 4.19; IR (KBr) 3400, 2931, 1611 cm^{-1}; HRMS (ES-) calcd. for $C_{17}H_{26}BNO_2F_3$ $[M–K]^-$ 344.2009, found 344.2017.



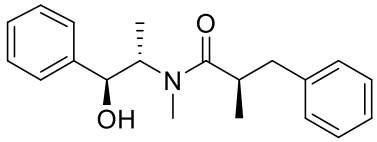
Potassium (*S*)-2-{(Trifluoroboryl)methyl}-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,3-dimethylbutanamide.

The reaction was carried out with the corresponding boronate ester (1.3 g, 3.44 mmol, 1.0 equiv) according to the general procedure for the preparation of enantiomerically enriched potassium α-chiral β-trifluoroboratoamides to obtain the product (1.1 g, 2.98 mmol) as a white solid in 83% yield.

$[\alpha]^{20}_{D}$ +49.6 (c 1.21, MeOH); mp: 70–75 °C; ^{1}H NMR (3:2 rotamer ratio, asterisk denotes minor rotamer peaks, with less than 5% of pinacol, 500 MHz, DMSO-d_6) δ 7.51–7.18 (m, 5H), 5.01 (s, 1H), 4.74–4.64* (m, 1H), 4.61–4.48 (m, 2H), 4.45–4.38* (m, 1H), 4.32–4.24* (m, 1H), 2.85 (s, 3H), 2.71* (s, 3H), 2.28–2.24* (m, 1H), 2.24–2.17 (m, 1H), 1.64–1.54* (m, 1H), 1.54–1.45 (m, 1H), 0.82 (ddd, *J* = 29.0, 14.0, 7.5 Hz, 6H), 0.70* (d, *J* = 6.5 Hz, 3H), 0.64 (d, *J* = 7.0 Hz, 3H), 0.34–0.26 (m, 1H), 0.22–0.06 (m, 1H); ^{13}C NMR (125.6 MHz, DMSO-d_6) δ 178.5, 178.3*, 144.0*, 143.9, 127.9, 127.7, 127.5*, 127.2*, 126.8, 74.9*, 74.2, 56.5, 44.7, 44.4*, 33.2*, 32.4, 26.0, 24.9*, 21.5*, 21.0, 20.6*, 20.5, 15.4*, 13.7; ^{19}F NMR (470.8 MHz, DMSO-d_6) δ –134.3*, –135.9; ^{11}B NMR (128.4 MHz, DMSO-d_6) δ 3.58; IR (KBr) 3512, 2964, 1611 cm^{-1}; HRMS (ES-) calcd. for $C_{16}H_{24}BNO_2F_3$ $[M–K]^-$ 330.1852, found 330.1855.

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction.

A sealed tube was charged with chiral potassium α-chiral β-trifluoroboratoamides (90 mg, 0.263 mmol, 1.05 equiv), an aryl or hetaryl chloride (0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (3 mg, 0.013 mmol, 0.05 equiv), RuPhos ligand (0.03 mmol, 0.1 equiv) and K_2CO_3 (104 mg, 0.75 mmol, 3.0 equiv). The mixture was then was purged 3 times with N_2. (Liquid electrophiles were added last, after purging with N_2). Toluene / H_2O (4:1, 0.8 mL/0.2 mL) was then added to the reaction tube. The reaction mixture was stirred for 22 h at 85 °C and then cooled to rt. A solution of pH 7 buffer (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$) and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.



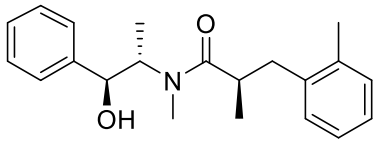
(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-phenylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (54 mg, 0.18 mmol) was obtained as a white solid in 70% yield after column chromatography (hexanes/EtOAc = 2:1).

^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.33–6.98 (m, 10H), 4.70 (br, 1H), 4.57–4.36 (m, 2H), 4.22* (dd, *J* = 8.0, 3.0 Hz, 1H), 3.96–3.87* (m, 1H), 3.39* (dd, *J* = 13.5, 6.0 Hz, 1H), 3.01 (dd, *J* = 13.0, 8.0 Hz), 2.80* (s, 3H),

2.65–2.55 (m, 1H), 2.39 (dd, *J* = 13.5, 6.5 Hz, 1H), 2.15 (s, 3H), 1.06* (d, *J* = 6.5 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.0 Hz, 3H), 0.68* (d, *J* = 7.0 Hz, 3H).

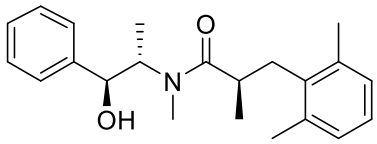
Data is consistent with that reported in the literature.[16b]



(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-(*o*-tolyl}propanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (33 mg, 0.1 mmol) was obtained as a colorless oil in 40% yield.

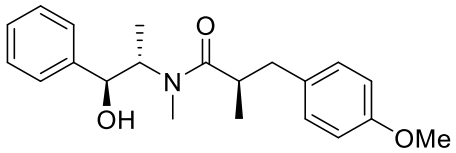
$[\alpha]^{20}_{D}$ +10.6 (c 1.60, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.38–6.91 (m, 9H), 4.85 (br, 1H), 4.60 (br, 1H), 4.53 (d, *J* = 6.5 Hz, 1H), 4.33* (d, *J* = 8.5 Hz, 1H), 4.00–3.92* (m, 1H), 3.80* (br, 1H), 3.39* (dd, *J* = 13.5, 5.5 Hz, 1H), 3.32–3.24* (m, 1H), 3.00 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.94* (dd, *J* = 13.5, 8.5 Hz, 1H), 2.82* (s, 3H), 2.74–2.70 (m, 1H), 2.59 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.38* (s, 3H), 2.20 (s, 3H), 2.14 (s, 3H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.72* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 178.5, 177.4*, 142.5, 141.3*, 138.6*, 138.1, 136.5*, 136.1, 130.4*, 130.3, 130.1*, 129.7, 128.7*, 128.4, 127.6, 126.9*, 126.5, 126.4, 126.4*, 125.9 76.5, 75.1*, 58.3, 37.5, 37.2, 37.1*, 36.6*, 32.2, 27.1*, 19.6*, 19.5, 17.9*, 17.7, 15.6*, 14.3; IR (neat) 3370, 2972, 2933, 1618 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{28}NO_2$ $[M+H]^+$ 326.2120, found 326.2115.



(*R*)-3-(2,6-Dimethylphenyl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (32 mg, 0.09 mmol) was obtained as a colorless oil in 38% yield.

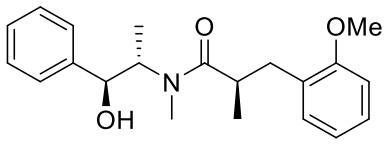
$[\alpha]^{20}_{D}$ –10.1 (c 1.05, $CHCl_3$); ^{1}H NMR (5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.32–6.84 (m, 8H), 4.59 (br, 1H), 4.43 (d, *J* = 7.5 Hz, 1H), 4.16* (d, *J* = 9.0 Hz, 1H), 3.87–3.78* (m, 1H), 3.39–3.25* (m, 2H), 3.19–3.10* (m, 1H), 3.03 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.82–2.72 (m, 1H), 2.78* (s, 3H), 2.68 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.42* (s, 6H), 2.18 (s, 6H), 2.06 (s, 3H), 1.08 (d, *J* = 6.5 Hz, 3H), 1.07* (d, *J* = 6.5 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 3H), 0.60* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 179.2, 142.5, 137.4*, 137.0, 136.8, 128.8*, 128.5*, 128.5, 128.4, 127.8, 127.0*, 126.6, 126.3, 76.7, 58.5, 36.2, 35.8*, 34.0, 33.4*, 29.8, 27.0*, 20.6*, 20.5, 17.8, 15.8*, 14.4; IR (neat) 3369, 2929, 1617 cm^{-1}; HRMS (ES+) calcd. for $C_{22}H_{30}NO_2$ $[M+H]^+$ 340.2277, found 340.2275.



(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-3-(4-methoxyphenyl)-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, SPhos instead of RuPhos, the product (44 mg, 0.13 mmol) was obtained as a colorless oil in 51% yield.

$[\alpha]^{20}_D$ +18.1 (c 1.38, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.37–6.71 (m, 9H), 4.96 (br, 1H), 4.60 (br, 1H), 4.53 (d, *J* = 7.5 Hz, 1H), 4.41* (d, *J* = 8.0 Hz, 1H), 4.04–3.97* (m, 1H), 3.35* (s, 3H), 3.33 (s, 3H), 3.16–3.09* (m, 1H), 2.97 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.84* (s, 3H), 2.97* (dd, *J* = 13.5, 9.0 Hz, 1H), 2.68–2.60 (m, 1H), 2.47 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.26 (s, 3H), 1.07* (d, *J* = 6.5 Hz, 3H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.76* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ178.3, 177.3*, 158.1, 158.0*, 142.4, 141.5*, 132.6*, 132.1, 130.2*, 129.9, 128.6*, 128.3, 128.2*, 127.6, 127.0*, 126.5, 113.8*, 113.7, 76.4, 75.3*, 58.0, 55.2, 39.5, 39.1, 38.2*, 32.2, 27.3*, 24.8*, 17.5*, 17.4, 15.5*, 14.3; IR (neat) 3377, 2971, 1614 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{28}NO_3$ $[M+H]^+$ 342.2069, found 342.2065.

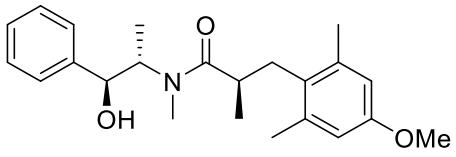


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-3-(2-methoxyphenyl)-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (47 mg, 0.14 mmol) was obtained as a colorless oil in 55% yield.

$[\alpha]^{20}_D$ 2.6 (c 1.50, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.36–7.00 (m, 7H), 6.86* (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.0 Hz, 1H), 6.60* (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 5.00 (br, 1H), 4.58–4.52 (m,

1H), 4.46–4.37 (m, 1H), 4.31* (d, *J* = 7.5 Hz, 1H), 4.20–4.12* (m, 1H), 3.56* (dd, *J* = 13.0, 6.0 Hz, 1H), 3.42* (s, 3H), 3.28 (s, 3H), 3.05–2.95 (m, 2H) (m, 1H), 2.84–2.75 (m, 1H), 2.78* (s, 3H), 2.34 (s, 3H), 1.12 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.69* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 179.0, 177.7*, 157.6*, 157.5, 142.6, 141.3*, 131.6*, 131.3, 128.6, 128.0*, 127.7, 127.5, 127.2*, 126.5, 120.4, 110.3*, 110.1, 76.5, 75.2*, 58.9*, 58.1, 55.3*, 55.2, 36.1, 35.5, 35.4*, 32.7, 26.8*, 17.7*, 17.1, 15.4*, 14.4; IR (neat) 3370, 2970, 1616 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{28}NO_3$ $[M+H]^+$ 342.2069, found 342.2075.

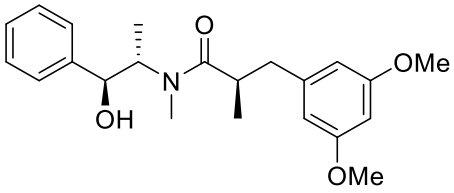


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-3-(4-methoxy-2,6-dimethylphenyl)-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (38 mg, 0.10 mmol) was obtained as a colorless oil in 41% yield.

$[\alpha]^{20}_D$ +0.6 (c 0.69, $CHCl_3$); ^{1}H NMR (3.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ7.33 (d, *J* = 7.5 Hz, 2H), 7.22–7.04 (m, 3H), 6.70* (s, 2H), 6.57 (s, 2H), 4.66 (br, 2H), 4.48 (br, 1H), 4.28* (d, *J* = 9.0 Hz, 1H), 3.93–3.85* (m, 1H), 3.49–3.42* (m, 1H), 3.40* (s, 3H), 3.37 (s, 3H), 3.34–3.27* (m, 2H), 3.00 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.85* (s, 3H), 2.81–2.74 (m, 1H), 2.65 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.42* (s, 6H), 2.18 (s, 6H), 2.13 (s, 3H), 1.13 (d, *J* = 6.5 Hz, 3H), 1.10* (d, *J* = 6.5 Hz, 1H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.65* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 179.1, 177.9*, 157.5,

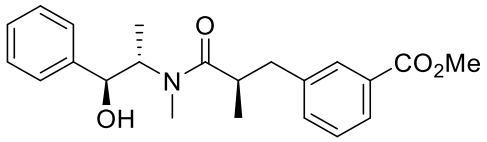
142.5, 141.4*, 138.7*, 138.2, 129.5, 129.0*, 128.7*, 128.4, 127.7, 126.9*, 126.6, 113.7*, 113.6, 76.6, 75.1*, 58.4, 57.6*, 55.1, 36.4, 36.0*, 33.4, 32.5*, 31.7, 27.0*, 20.9*, 20.7, 17.8*, 17.7, 15.7*, 14.4; IR (neat) 3381, 2966, 1616 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{31}NO_3Na$ $[M+Na]^+$ 392.2202, found 392.2199.



(*R*)-3-(3,5-Dimethoxyphenyl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (57 mg, 0.15 mmol) was obtained as a colorless oil in 62% yield.

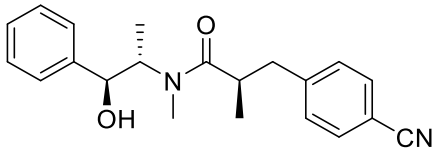
$[\alpha]^{20}_D$ +26.4 (c 2.25, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.40–6.34 (m, 8H), 4.60–4.48 (m, 1H), 4.50 (d, *J* = 7.0 Hz, 1H), 4.28* (d, *J* = 8.5 Hz, 1H), 4.01–3.90* (m, 1H), 3.43* (s, 6H), 3.36 (s, 6H), 3.21–3.12* (m, 1H), 3.04 (dd, *J* = 13.0, 8.5 Hz, 1H), 2.82* (s, 3H), 2.75–2.64 (m, 1H), 2.51 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.24 (s, 3H), 1.14* (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.79 (d, *J* = 6.0 Hz, 3H), 0.71* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 178.4, 177.2*, 160.9*, 160.8, 142.5, 142.5, 141.5*, 128.7*, 128.4, 127.7, 127.3*, 127.0*, 126.6, 107.3*, 107.2, 98.4*, 98.2, 77.4, 76.6, 75.5*, 58.2*, 55.4, 40.7, 40.5*, 38.8, 38.0*, 27.3*, 25.0, 17.9*, 17.6, 15.6*, 14.5; IR (neat) 3370, 2971, 2930, 1607 cm^{-1}; HRMS (ES+) calcd. for $C_{22}H_{29}NO_4Na$ $[M+Na]^+$ 394.1994, found 394.1993.



Methyl 3-[(*R*)-3-[{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}(methyl)amino]-2-methyl-3-oxopropyl]benzoate.

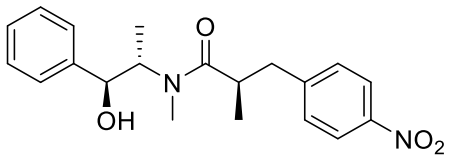
According to the general procedure for Suzuki–Miyaura cross-coupling, the product (53 mg, 0.14 mmol) was obtained as a colorless oil in 57% yield.

$[\alpha]^{20}_{D}$ +13.6 (c 2.06, $CHCl_3$); ^{1}H NMR (2.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 8.24–6.97 (m, 9H), 4.69 (br, 1H), 4.61 (br, 1H), 4.50 (d, *J* = 7.0 Hz, 1H), 4.36* (d, *J* = 7.5 Hz, 1H), 3.98* (br, 1H), 3.96–3.89* (m, 1H), 3.53* (s, 3H), 3.50 (s, 3H), 3.28* (dd, *J* = 13.5 Hz, 5.5 Hz, 1H), 3.11–3.02* (m, 1H), 2.99 (dd, *J* = 13.0 Hz, 8.5 Hz, 1H), 2.84* (s, 3H), 2.79–2.71* (m, 1H), 2.64-2.55 (m, 1H), 2.44 (dd, *J* = 13.5 Hz, 5.5 Hz, 1H), 2.22 (s, 3H) 0.96 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.75* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.5, 176.8*, 167.3*, 167.1, 142.3, 141.7*, 140.9*, 140.4, 130.3*, 133.8, 130.1, 129.8, 128.6*, 128.4, 128.2, 128.2*, 128.0*, 127.8*, 127.5, 127,5, 127.3*, 126.8*, 126.4, 76.2, 75.3, 57.9, 57.4*, 52.0, 39.9, 39.4*, 38.6, 37.5*, 31.9, 27.4*, 17.4, 15.6*, 14.2; IR (neat) 3401, 2974, 1720, 1618 cm^{-1}; HRMS (ES+) calcd. for $C_{22}H_{27}NO_4Na$ $[M+Na]^+$ 392.1838, found 392.1838.



(*R*)-3-(4-Cyanophenyl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

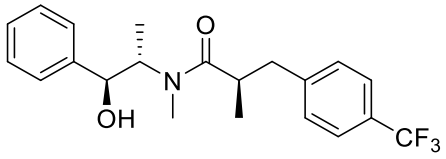
According to the general procedure for Suzuki–Miyaura cross-coupling, SPhos instead of RuPhos, the product (63 mg, 0.19 mmol) was obtained as a white solid in 75% yield. $[\alpha]^{20}_{D}$ +27.8 (c 1.29, $CHCl_3$); mp: 140–142 °C; ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.35–6.76 (m, 9H), 4.53 (d, *J* = 6.5 Hz, 1H), 4.48 (br, 1H), 4.23* (d, *J* = 8.0 Hz, 1H), 3.93–3.85* (m, 1H), 3.29* (dd, *J* = 13.5, 7.0 Hz, 1H), 3.14–3.05* (m, 1H), 2.93 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.84* (s, 3H), 2.64* (dd, *J* = 13.5, 6.5 Hz, 1H), 2.52–2.43 (m, 1H), 2.33 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.22 (s, 3H), 1.02* (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.77* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.0, 176.2*, 146.5*, 145.9, 142.2, 141.5*, 132.1, 132.0*, 130.1*, 129.9, 128.7*, 128.3, 127.7, 126.8*, 126.4, 119.2*, 119.0, 110.1, 109.7*, 76.2, 75.2*, 57.9, 40.1, 39.8*, 38.5, 37.4*, 32.2, 27.4*, 17.7*, 17.6, 15.6*, 14.3; IR (neat) 3430, 1622 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{25}N_2O_2$ $[M+H]^+$ 337.1916, found 337.1931.



(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-(4-nitrophenyl)propanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (67 mg, 0.19 mmol) was obtained as a yellow solid in 75% yield.

$[\alpha]^{20}_D$ +40.0 (c 1.01, $CHCl_3$); mp: 161–164 °C; ^{1}H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.93* (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.30–7.03 (m, 5H), 6.73 (d, *J* = 8.0 Hz, 2H), 4.43 (br, 2H), 4.14* (d, 8.0 Hz, 1H), 3.87–3.68* (m, 1H), 3.22* (dd, *J* = 13.5, 7.5 Hz, 1H), 3.09–3.00* (m, 1H), 2.96 (br, 1H), 2.86 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.74* (s, 3H), 2.56* (dd, *J* = 13.5, 6.5 Hz, 1H), 2.47–2.35 (m, 1H), 2.26 (dd, *J* = 13.5, 5.5 Hz, 1H), 2.15 (s, 3H), 0.93* (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.80 (d, *J* = 5.0 Hz, 3H), 0.68* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.1, 176.2*, 148.7*, 148.2, 146.7, 146.5*, 142.3, 130.1*, 129.9, 128.9*, 128.6*, 128.5, 127.8, 126.9*, 126.4, 123.7, 123.5*, 76.4, 75.4*, 58.0, 39.9, 39.7*, 38.7, 37.6*, 32.4, 27.4*, 18.0*, 17.8, 15.7*, 14.5; IR (neat) 3370, 2976, 2932, 1619, 1517, 1346 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{25}N_2O_4$ $[M+H]^+$ 357.1814, found 357.1823.

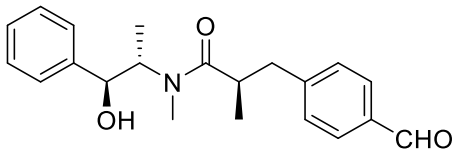


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-{4-(trifluoromethyl)phenyl}propanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (41 mg, 0.11 mmol) was obtained as a white solid in 43% yield.

$[\alpha]^{20}_D$ +11.0 (c 1.10, $CHCl_3$); mp: 118–120 °C; ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.42–6.85 (m, 9H), 4.63 (br, 1H), 4.55–4.40 (m, 1H), 4.45 (s, 1H), 4.27* (d, 8.0 Hz, 1H), 3.94–3.84* (m, 1H), 3.67* (s, 1H), 3.09–3.00* (m, 1H), 2.90 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.79* (s, 3H), 2.67* (dd, *J* = 13.5, 7.5 Hz,

1H), 2.52–2.41 (m, 1H), 2.34 (dd, *J* = 13.0, 6.0 Hz, 1H), 2.16 (s, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 5.5 Hz, 3H), 0.73* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.4, 176.6*, 144.9*, 144.3, 142.3, 141.7*, 129.6, 129.4*, 129.3, 128.7, 128.4*, 128.3, 127.6, 126.9*, 126.4, 125.2 (q, *J* = 3.8 Hz), 123.3*, 76.2, 75.4*, 57.9, 39.9, 39.5*, 38.6, 37.5*, 32.1, 27.5*, 17.5, 17.5*, 15.5*, 14.2; IR (neat) 3380, 2976, 1619, 1326 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{24}NO_2Na$ $[M+Na]^+$ 402.1657, found 402.1649.

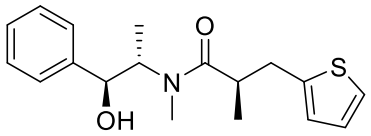


(*R*)-3-(4-Formylphenyl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (70 mg, 0.21 mmol) was obtained as a colorless oil in 82% yield.

$[\alpha]^{20}_D$ +35.7 (c 1.71, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 9.71* (s, 1H), 9.70 (s, 1H), 7.64–7.06 (m, 9H), 4.55–4.34 (br, 3H), 4.22* (d, *J* = 8.0 Hz, 1H), 3.93–3.84* (m, 1H), 3.31* (dd, *J* = 13.5, 6.5 Hz, 1H), 3.16–3.07* (m, 1H), 2.95 (dd, *J* = 13.0, 8.5 Hz, 1H), 2.78* (s, 3H), 2.70* (dd, *J* = 13.5, 7.5 Hz, 1H), 2.56–2.45 (m, 1H), 2.38 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.16 (s, 3H), 0.98* (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 5.5 Hz, 3H), 0.70* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 192.2, 192.0*, 177.5, 176.6*, 148.3*, 147.6, 142.3, 141.4*, 134.89*, 134.9, 130.0*, 130.0*, 129.9, 129.8, 128.8*, 128.4, 128.3*, 127.8, 126.9*, 126.5, 76.4,

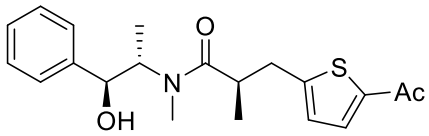
75.4*, 58.1, 40.4, 40.0*, 38.7, 37.7*, 27.4, 17.8*, 17.7, 15.7*, 14.4; IR (neat) 3401, 1607 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{25}NO_3Na$ $[M+Na]^+$ 362.1732, found 362.1740.



(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethyl-3-(thiophen-2-yl)propanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (42 mg, 0.13 mmol) was obtained as a white solid in 53% yield.

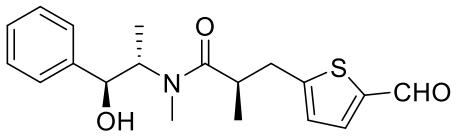
$[\alpha]^{20}_D$ +25.6 (c 0.80, $CHCl_3$); mp: 100–103 °C; ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.34–6.64 (m, 8H), 4.48 (s, 2H), 4.22* (d, *J* = 8.0 Hz, 1H), 3.95–3.86* (m, 1H), 4.00* (dd, *J* = 14.5, 6.0 Hz, 1H), 3.26 (dd, *J* = 13.5, 7.5 Hz, 1H), 3.17–3.07* (m, 1H), 3.04–2.95* (m, 1H), 2.79* (s, 3H), 2.71–2.57 (m, 2H), 2.24 (s, 3H), 1.33* (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.0 Hz, 3H), 0.68* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.8, 176.8*, 143.1*, 142.6, 142.4, 141.2*, 128.8*, 128.4, 127.7, 127.0*, 127.0*, 126.9, 126.6, 125.8*, 125.6, 123.7*, 123.6, 76.7, 75.5*, 58.2, 39.6, 38.8*, 34.2, 34.1*, 32.5, 27.4*, 17.7*, 17.5, 15.6*, 14.4 ; IR (neat) 3429, 1634 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{23}NO_2SNa$ $[M+Na]^+$ 340.1347, found 340.1333.



(*R*)-3-(5-Acetylthiophen-2-yl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (66 mg, 0.18 mmol) was obtained as a yellow oil in 73% yield.

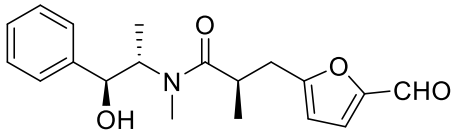
$[\alpha]^{20}_{D}$ +47.3 (c 1.04, $CHCl_3$); ^{1}H NMR (2.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.39–6.97 (m, 6 H), 6.69* (d, *J* = 3.5 Hz, 1H), 6.56 (d, *J* = 3.5 Hz, 1H), 4.46 (s, 2H), 4.30 (br, 1H), 4.22* (d, *J* = 8.5 Hz, 1H), 3.91–3.82* (m, 1H), 3.37* (dd, *J* = 14.5, 6.5 Hz, 1H), 3.19 (dd, *J* = 13.5, 8.0 Hz, 1H), 3.12–3.03* (m, 1H), 2.88* (dd, *J* = 14.5, 8.0 Hz, 1H), 2.80* (s, 3H), 2.61–2.51 (m, 1H), 2.50 (dd, *J* = 14.0, 5.5 Hz, 1H), 2.25 (s, 3H), 2.07* (s, 3H), 2.05 (s, 3H), 1.00* (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.71* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 190.7*, 190.6, 177.1, 176.2*, 153.4*, 152.8, 142.8, 142.7*, 142.3, 141.3*, 133.0*, 132.9, 128.9*, 128.5*, 128.5, 127.8, 127.3*, 127.2, 126.9*, 126.5, 76.5, 75.6*, 58.1, 39.3, 38.4*, 34.8, 34.7*, 43.4, 27.6*, 26.6, 25.0*, 17.7*, 17.6, 15.7*, 14.5 ;IR (neat) 3401, 2974, 2935, 1656, 1620 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{25}NO_3SNa$ $[M+Na]^+$ 382.1453, found 382.1436.



(*R*)-3-(5-Formylthiophen-2-yl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (52 mg, 0.15 mmol) was obtained as a light yellow oil in 60% yield.

$[\alpha]^{20}_D$ +8.6 (c 1.74, $CHCl_3$); ^1H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 9.53* (s, 1H), 9.50 (s, 1H), 7.40–7.04 (m, 5H), 7.01* (d, *J* = 3.0 Hz, 1H), 6.92 (d, *J* = 3.5 Hz, 1H), 6.69* (d, *J* = 3.0 Hz, 1H), 6.92 (d, *J* = 3.0 Hz, 1H), 4.51 (br, 1H), 4.48–4.42 (m, 1H), 4.30 (br, 1H), 4.25* (d, *J* = 7.5 Hz, 1H), 3.88–3.79* (m, 1H), 3.45* (br, 1H), 3.32* (dd, *J* = 145, 6.5 Hz, 1H), 3.15 (dd, *J* = 14.0, 8.5 Hz, 1H), 3.08–2.99* (m, 1H), 2.89–2.78* (m, 1H), 2.81* (s, 3H), 2.55–2.47 (m, 1H), 2.44 (dd, *J* = 14.5, 5.5 Hz, 1H), 2.25 (s, 3H), 0.94* (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.0 Hz, 6H), 0.73* (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 182.8*, 182.8, 176.7, 175.9*, 155.2*, 154.6, 142.3, 141.5, 137.1*, 137.0, 128.8*, 128.4, 127.8, 127.5*, 127.4, 126.8*, 126.5, 76.4, 75.5*, 58.0, 39.2, 38.2*, 34.9, 34.8*, 27.6*, 25.0, 17.7*, 17.6, 15.7*, 14.4 ; IR (neat) 3411, 1661, 1620 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{24}NO_3S$ $[M+H]^+$ 346.1477, found 346.1486.

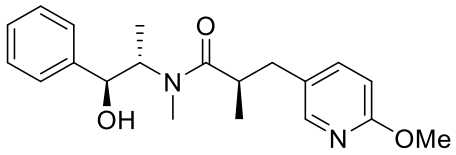


(*R*)-3-(5-Formylfuran-2-yl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (57 mg, 0.17 mmol) was obtained as a yellow oil in 69% yield.

$[\alpha]^{20}_D$ +21.5 (c 1.43, $CHCl_3$); ^1H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 9.82* (s, 1H), 9.25 (s, 1H), 7.39–7.02 (m, 5H), 6.60* (s, 1H), 6.53 (d, *J* = 3.0 Hz, 1H), 6.01* (d, *J* = 3.5 Hz, 1H), 5.81 (d, *J* = 3.0 Hz, 1H), 4.49 (br, 3H), 4.32* (d, *J* = 8.5 Hz, 1H), 3.99–3.89* (m, 1H), 3.32–3.21 (m, 1H), 2.92 (dd, *J* = 14.5, 8.5

Hz, 1H), 2.80* (s, 3H), 2.77–2.70* (m, 1H), 2.64* (dd, *J* = 14.0, 6.5 Hz, 1H), 2.41 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.31 (s, 3H), 0.94* (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.70* (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 176.9*, 176.8, 176.7, 175.9*, 162.2*, 161.5, 152.0, 151.8*, 142.3, 141.5*, 128.8, 128.4, 128.3*, 127.7*, 127.6*, 126.9, 126.4, 126.3*, 110.3, 110.0*, 76.2, 75.3*, 58.2, 35.6, 34.8*, 32.5, 27.3, 18.0*, 17.4, 15.7*, 14.3; IR (neat) 3412, 1636 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{23}NO_4Na$ $[M+Na]^+$ 352.1525, found 352.1510.

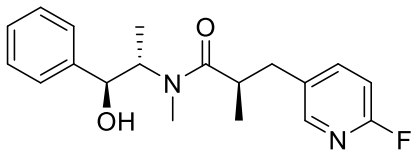


(*R*)-*N*-{(1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl}-3-(6-methoxypyridin-3-yl)-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (47 mg, 0.14 mmol) was obtained as a light yellow oil in 55% yield.

$[\alpha]^{20}_D$ +26.3 (c 1.70, $CHCl_3$); ^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 8.23* (d, *J* = 2.0 Hz, 1H), 8.03 (d, *J* = 2.5 Hz, 1H), 7.40–7.03 (m, 6H), 6.67* (d, *J* = 8.5 Hz, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 4.69 (br, 1H), 4.75–4.50 (m, 1H), 4.48 (d, *J* = 7.0 Hz, 1H), 4.27* (d, 1H, *J* = 8.0 Hz, 1H), 3.93–3.86* (m, 1H), 3.82 (s, 3H), 3.14* (dd, *J* = 13.5, 6.5 Hz, 1H), 3.05–2.96* (m, 1H), 2.83 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.78* (s, 3H), 2.60* (dd, *J* = 13.5, 8.0 Hz, 1H), 2.51–2.42 (m, 1H), 2.28 (dd, *J* =13.5, 6.0 Hz, 1H), 2.19 (s, 3H), 0.98* (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.72* (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.6, 176.8*, 162.9,

162.8*, 146.9, 146.7, 142.4, 141.7*, 139.9*, 139.6, 128.7, 128.5*, 128.3, 128.2*, 128.1*, 127.6, 126.9*, 126.4, 110.3, 110.2*, 76.3, 75.3*, 57.9, 53.4, 38.9, 37.7*, 36.3, 35.9*, 32.4, 27.4*, 17.4, 15.6*, 14.3; IR (neat) 3422, 1618 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{26}N_2O_3Na$ $[M+Na]^+$ 365.1841, found 365.1827.

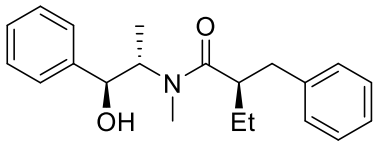


(*R*)-3-(6-Fluoropyridin-3-yl)-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,2-dimethylpropanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (66 mg, 0.20 mmol) was obtained as a light yellow oil in 80% yield.

$[\alpha]^{20}_D$ +32.2 (c 0.75, $CHCl_3$); ^1H NMR (2:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 8.10* (s, 1H), 7.86 (s, 1H), 7.39–7.02 (m, 6H), 6.47–6.42* (m, 1H), 6.40–6.33 (m, 1H), 4.66 (br, 1H), 4.52 (s, 1H), 4.48 (s, 1H), 4.29* (d, *J* = 7.5 Hz, 1H), 4.16* (s, 1H), 3.90–3.80* (m, 1H), 3.12–2.98 (m, 1H), 2.74* (s, 3H), 2.52–2.44* (m, 1H), 2.44–2.33 (m, 1H), 2.01 (s, 3H), 2.22–2.14 (m, 1H), 0.92* (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H), 0.72* (d, *J* = 6.5 Hz, 3H), ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.0, 176.2*, 162.5 (d, *J* = 236.3 Hz), 162.3* (d, *J* = 236.3 Hz), 147.7* (d, *J* = 13.8 Hz), 147.5* (d, *J* = 15.0 Hz), 142.3, 142.0 (d, *J* = 30.0 Hz), 142.0* (d, *J* = 60.0 Hz), 133.6* (d, *J* = 3.8 Hz), 133.3 (d, *J* = 3.8 Hz), 128.7*, 128.4, 128.3*, 127.7, 126.8*, 126.4, 109.0 (d, *J* = 37.5 Hz), 108.8* (d, *J* = 37.5 Hz), 76.2, 75.1*, 57.9, 38.8, 37.6*, 36.1, 35.8*,

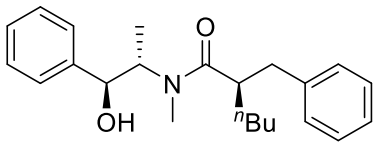
27.4, 17.7*, 17.6, 15.6*, 14.3; IR (neat) cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{23}N_2O_2FNa$ $[M+Na]^+$ 353.1641, found 353.1642.



(*R*)-2-Benzyl-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*-methylbutanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (57 mg, 0.18 mmol) was obtained as a white solid in 70% yield.

$[\alpha]^{20}_D$ +7.4 (c 1.37, $CHCl_3$); mp: 85–88 °C; ^1H NMR (4:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.40–6.84 (m, 10H), 4.62 (br, 1H), 4.57–4.38 (m, 2H), 4.26* (d, *J* = 8.0 Hz, 1H), 4.12–4.01* (m, 1H), 3.42–3.31* (m, 2H), 3.12–3.02* (m, 1H), 2.95 (dd, *J* = 11.5, 8.5 Hz, 1H), 2.88–2.78* (m, 1H), 2.81* (s, 3H), 2.66–2.49 (m, 2H), 2.16 (s, 3H), 1.90–1.77 (m, 1H), 1.51–1.42* (m, 1H), 1.42–1.31 (m, 1H), 0.81 (t, *J* = 7.5 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H), 0.71* (d, 3H, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 177.7, 176.5*, 142.4, 141.4*, 140.7*, 140.1, 129.3*, 129.0, 128.7*, 128.5*, 128.4, 128.3, 128.3*, 127.7, 127.0*, 126.6, 126.4*, 126.3, 76.4, 75.2*, 58.3, 46.5, 45.5*, 39.4, 39.1*, 32.3, 27.2*, 26.2, 26.0*, 15.6*, 14.4, 12.1*, 12.0; IR (neat) 3370, 2965, 1615 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{27}NO_2Na$ $[M+Na]^+$ 348.1939, found 348.1927.

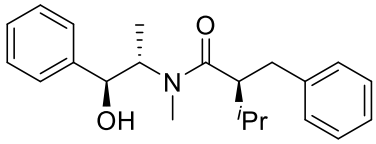


(*R*)-2-Benzyl-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*-methylhexanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (42 mg, 0.12 mmol) was obtained as a white solid in 47% yield.

^{1}H NMR (4:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.40–6.99 (m, 10H), 4.58 (br, 1H), 4.50 (d, *J* = 7.5 Hz, 1H), 4.20* (d, *J* = 8.5 Hz, 1H), 4.11–4.03* (m, 1H), 3.40* (dd, *J* = 13.5, 6.5 Hz, 1H), 3.18–3.07* (m, 1H), 2.98 (dd, *J* = 12.5, 9.0 Hz, 1H), 2.85* (dd, *J* = 13.0, 7.5 Hz, 1H), 2.79* (s, 3H), 2.72–2.63 (m, 1H), 2.58 (dd, *J* = 13.0, 5.0 Hz, 1H), 2.17 (s, 3H), 1.92–1.82 (m, 1H), 1.51–1.06 (m, 6H), 2.92* (t, *J* = 7.5 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.76 (d, *J* = 7.5 Hz, 3H), 0.72* (d, *J* = 6.5 Hz, 3H).

Data is consistent with that reported in the literature.[16b]



(*S*)-2-Benzyl-*N*-{(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl}-*N*,3-dimethylbutanamide.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (25 mg, 0.08 mmol) was obtained as a white solid in 30% yield.

^{1}H NMR (10:1 rotamer ratio, asterisk denotes minor rotamer peaks, 500 MHz, C_6D_6) δ 7.42–6.96 (m, 10H), 4.63 (br, 1H), 4.37 (d, *J* = 7.5 Hz, 1H), 4.02–3.81 (m, 1H), 3.34* (dd, *J* = 12.5, 10.0 Hz, 1H), 2.99 (dd, *J* = 11.5, 11.5 Hz, 1H), 2.85* (dd, *J* = 13.0, 4.5 Hz, 1H), 2.72 (dd, *J* = 12.5, 3.5 Hz, 1H), 2.63* (s, 3H), 2.51–2.41 (m, 1H), 2.09 (s, 3H), 2.07–2.01 (m, 1H), 0.95 (dd, *J* = 13.5, 6.5 Hz, 6H), 0.64* (d, *J* = 6.5 Hz, 3H), 0.60 (d, *J* = 7.0 Hz, 3H).

Data is consistent with that reported in the literature.[16b]

2.6 References

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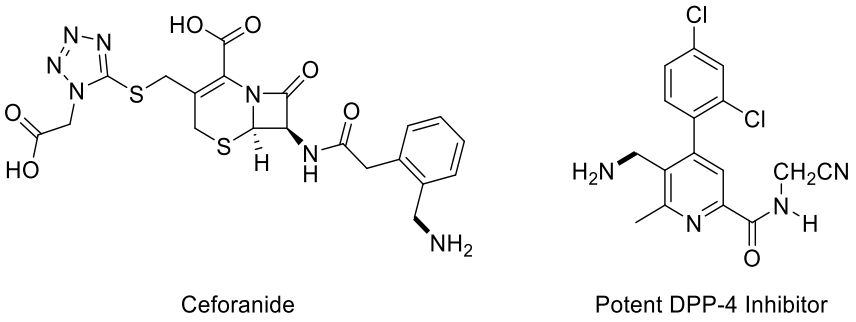
Chapter 3. Potassium Boc-Protected Aminomethyltrifluoroborates

3.1 Introduction

Aminomethylated arenes can be considered privileged substructures because they appear in many bioactive natural products and drugs, such as ceforanide and a potent DPP-4 inhibitor (Figure 3.1).[1] Moreover, aminomethyl arenes are also readily found as important intermediates in synthetic organic chemistry.[2]



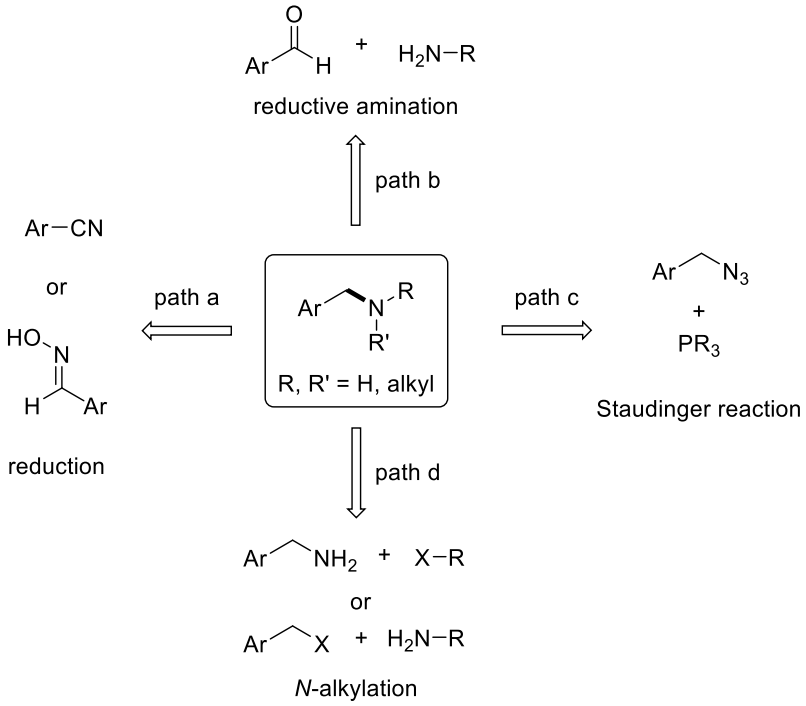
Ceforanide Potent DPP-4 Inhibitor

Figure 3.1 Bioactive Molecules Containing the Aminomethyl Moiety

3.1.1 Traditional Preparation of Aminomethylated Compounds

Because of the importance of aminomethyl moieties in organic and pharmaceutical chemistry, many different ways to install aminomethyl substructures have been studied. Reduction of cyanides[3] or oximes,[4] reductive amination,[5] Staudinger reaction,[6] and *N*-alkylation[7] are representative ways to prepare aminomethyl moieties (Scheme 3.1). However, these approaches do not provide a general synthesis of target subunits, and many limitations exist.

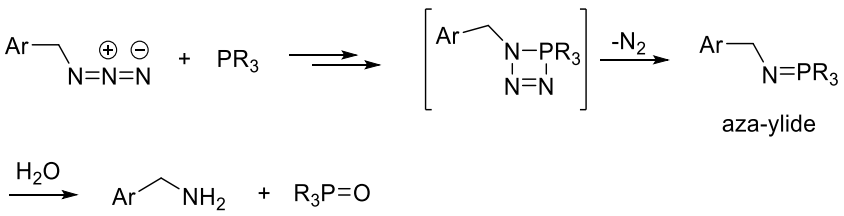
Scheme 3.1 Traditional Ways to Prepare Aminomethyl Moieties



Reductions of aryl cyanides or oximes are often applied to the synthesis of aminomethylated arenes (Scheme 3.1, path a).[3,4] However, many reducible functional groups, such as esters or aldehydes, are not compatible with this method. Another way to prepare aminomethyl substructures is reductive amination using the corresponding aldehyde and an amine (Scheme 3.1, path b).[5] This method is one of the most popular ways to build such a moiety. However, similar to the reduction pathway of cyanides and oximes, many functional groups cannot be embedded in desirable substrates because of the harsh reduction conditions required. Therefore, the scope of functional groups are limited by these two methods.

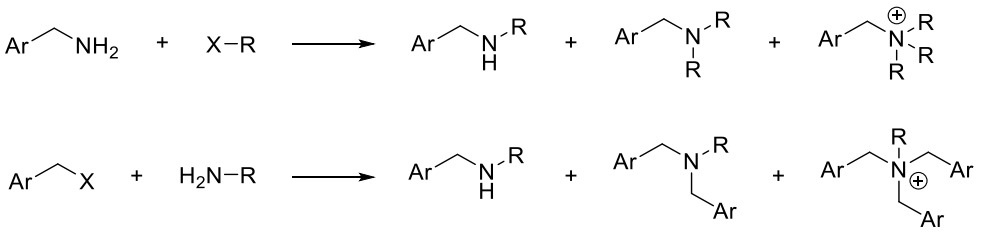
An alternative route to install the aminomethyl moieties is the Staudinger reaction using organic azides with phosphorus compounds (Scheme 3.1, path c).[6] The Staudinger reaction has been widely utilized in many organic syntheses over several decades. Reaction of an azide and a trivalent phosphorus compound produces the iminophosphorane intermediate, an aza-ylide, which is followed by hydrolysis to give the corresponding aminomethyl moiety and phosphine oxide (Scheme 3.2). Unfortunately, some azides exhibit significant thermal or shock sensitivity.[8] Therefore, these chemicals are avoided in many laboratories. Moreover, the benzylic or pseudobenzylic halide precursors required to prepare the azides are often not readily available.

Scheme 3.2 Staudinger Reaction



Lastly, another conventional approach is the *N*-alkylation of primary amines (Scheme 3.1, path d).[7] One of the drawbacks of this pathway is polyalkylation, which is frequently hard to control.[7a] *N*-Alkylation methods often give a mixture of secondary amines, tertiary amines, and even ammonium salts (Scheme 3.3).

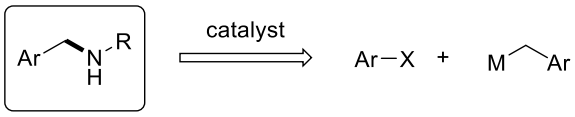
Scheme 3.3 *N*-Alkylation



3.1.2 Amidomethylation and Aminomethylation in Suzuki–Miyaura Reactions

A more straightforward route to the synthesis of aminomethyl substructures is transition metal catalyzed cross-coupling reactions of aminomethylmetallic reagents (Scheme 3.4).

Scheme 3.4 Synthesis of Aminomethyl Moieties by Transition Metal Catalyzed Cross-Coupling Reactions

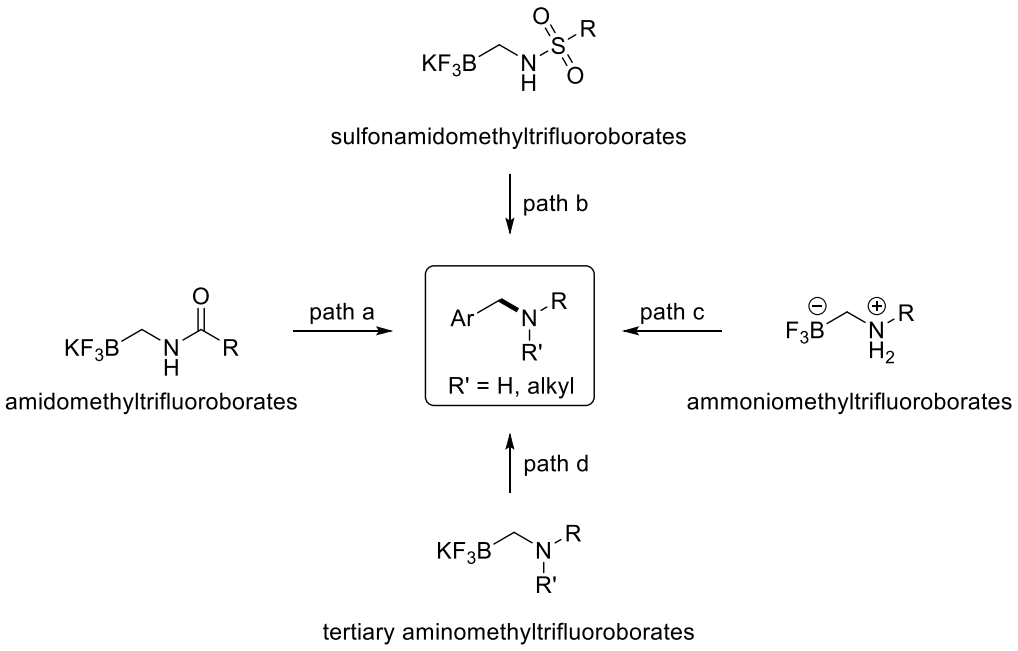


Particularly, Suzuki–Miyaura cross-coupling reactions compared to other cross-coupling reactions are more functional group tolerant.[9] A wide range of functional groups can be utilized in Suzuki–Miyaura coupling reactions which provides an advantage over the reduction or reductive amination methods to build aminomethyl substructures. Therefore, the reactions are not limited by sensitive functional groups. Additionally, there is a much greater diversity of commercially available aryl and hetaryl halides for cross-coupling reactions compared to corresponding substrate partners for reductive amination,

Staudinger reaction, or *N*-alkylation. Furthermore, the preparation of sensitive reagents, such as azides, is not required in cross-coupling reactions. In general, fewer synthetic steps are required in cross-coupling approaches and reaction conditions are much milder and more efficient compared to other synthetic pathways of aminomethyl subunits.

Syntheses and transition metal catalyzed cross-coupling reactions of aminomethyl organometallics or their equivalents are rare. Recently, Molander and co-workers have demonstrated the synthesis and Suzuki–Miyaura cross-coupling reactions of amidomethyltrifluoroborates [10] and sulfonamidomethyltrifluoroborates. [11] They also reported the synthesis and cross-coupling reactions of secondary ammoniomethyltrifluoroborates [12] and tertiary aminomethyltrifluoroborates (Scheme 3.5).[13] Development of these methods have proven to be efficient to prepare primary, secondary, and tertiary aminomethyl moieties by transition metal catalyzed coupling reactions.

Scheme 3.5 Amidomethylation and Aminomethylation in Suzuki–Miyaura Cross-Coupling Reactions



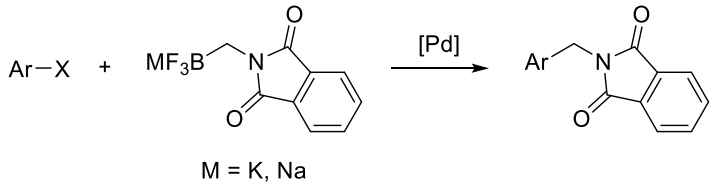
Amidomethyl arenes can be easily installed in organic compounds using amidomethyltrifluoroborates (Scheme 3.5, path a).[10] Amidomethyltrifluoroborates have been prepared by a 'one-pot' process using chloromethyl pinacol boronate and also explored as the nucleophiles in Suzuki–Miyaura reactions. A wide range of amidomethyltrifluoroborates have proven to be efficient nucleophilic partners in cross-coupling reactions with aryl and hetaryl chlorides.

Primary aminomethyl substructures can be prepared from sulfonamidomethyltrifluoroborate derivatives (Scheme 3.5, path b).[11] Among these various aryl sulfonamidomethyltrifluoroborates, the *p*-toluenesulfonyl (tosyl) group as an amine protecting group is utilized in synthesis and also tested in Suzuki–Miyaura cross-coupling

reactions. Although cross-coupling has successfully been performed with the tosyl group, the removal of this protecting group requires the use of harsh conditions.[14] Therefore, use of tosyl group is not ideal for preparation of primary aminomethyl moieties.

On the other hand, several reports exist that refer to the use of the *N*-phthalimido group as an amine protecting group (Scheme 3.6).[15] Although the preparation of phthalimidomethyltrifluoroborates and their application in Suzuki–Miyaura coupling reactions have been studied several times, the reactions are not efficient due to longer reaction times and low yields. Furthermore, hydrazine is often used to remove the phthalimido group,[14a] and its toxicity and instability to storage and handling prevent its routine use in this capacity.

Scheme 3.6 Phthalimidomethyltrifluoroborates in Suzuki–Miyaura Cross-Coupling Reactions



Secondary aminomethylated moieties have been prepared using secondary ammoniomethyltrifluoroborates (Scheme 3.5, path c).[12] This method proved to be a good synthetic pathway to access the secondary aminomethyl moieties, but the scope of the coupling reactions is limited to bromides as the electrophiles, which are more expensive

and appear in a less diverse range of substructures compared to chlorides. Furthermore, this previously developed method proved effective for only a few select hetaryl bromides.

To the best of our knowledge, only one Suzuki–Miyaura reaction has been reported to prepare the tertiary aminomethyl arenes from *N*,*N*-dialkyl aminomethyltrifluoroborates (Scheme 3.5, path d).[13] A variety of *N*,*N*-dialkyl aminomethyltrifluoroborates have been synthesized in this report and have been shown to be good nucleophiles in cross-coupling reactions with aryl bromides as the electrophiles.

3.2 Results and Discussion

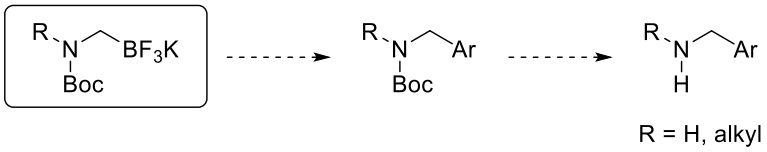
Several synthetic procedures have been studied to prepare aminomethyl substructures. However, many limitations exist in terms of the stability of reagents, inefficient protecting groups, and reaction conditions.

Particularly, we were interested in development of primary and secondary aminomethylating reagents or their equivalents. The sulfonamidomethylating[10] and phthalimidomethylating[15] procedures by the Molander and Tanaka laboratories led us to investigate the synthesis of alternative protected primary and secondary aminomethyltrifluoroborates. Although tosyl and phthalimido groups as amine protecting groups have already been developed, the removal of these groups requires the use of harsh reaction conditions as discussed above.

The Boc group is a good candidate for an amine protecting group. The Boc protecting group is commonly found in many organic synthetic steps, and also can be easily removed under either acidic or basic conditions.[14a,16] After deprotection of a Boc group,

the corresponding primary or secondary aminomethyl arenes are readily accessed. Therefore, the development of Boc-protected aminomethyltrifluoroborates as aminomethylating reagents and their applications in Suzuki–Miyaura coupling reactions could be envisioned (Scheme 3.7).

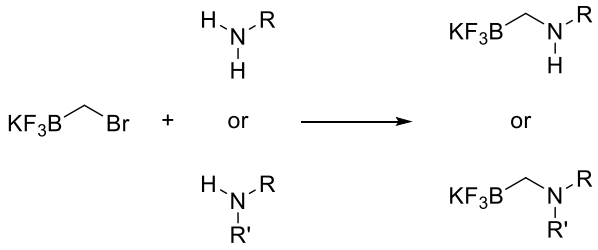
Scheme 3.7 Boc-Protected Aminomethyltrifluoroborates and Suzuki–Miyaura Reactions



3.2.1 Synthesis of Potassium Boc-Protected Primary Aminomethyltrifluoroborate

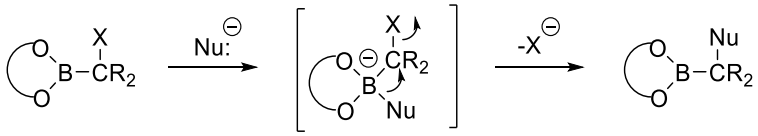
Previously, the Molander group reported the synthesis of *N*,*N*-dialkyl aminomethyltrifluoroborates by a direct nucleophilic displacement of bromomethyltrifluoroborate with primary or secondary amines (Scheme 3.8).[13] Unfortunately, Boc-protected aminomethyltrifluoroborate could not be prepared by this method using halomethyltrifluoroborates.

Scheme 3.8 Synthesis of *N*,*N*-Dialkyl Aminomethyltrifluoroborates



Instead of halomethyltrifluoroborates, we were inspired by one-carbon homologation of halomethylboronate esters developed by Matteson.[17] In this chemical process, boronate esters are not prepared by simple S_N2 displacement of halogen with a nucleophile. A nucleophile attacks the boron center instead of the carbon attached to the halogen, and, an 'ate' complex is generated as the reaction intermediate. Next, the nucleophile on the boron atom is α-transferred to the neighboring carbon to provide the corresponding boronate ester (Scheme 3.9).

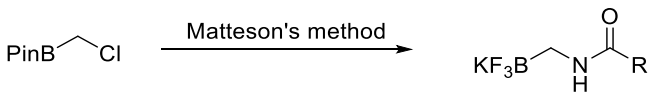
Scheme 3.9 Matteson's One-Carbon Homologation of Boronate Esters



nucleophile (Nu:) = organolithium, Grignard, alkoxides, enolates, alkylamines

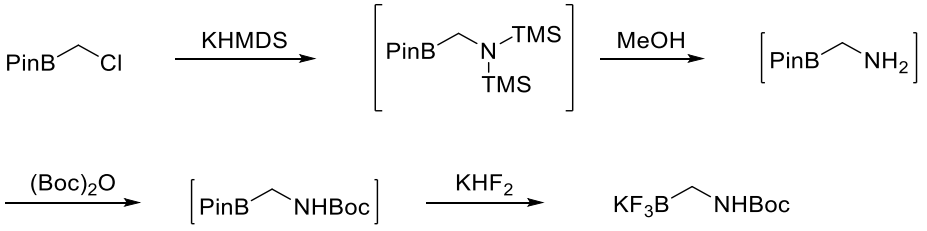
Recently, Molander and Hiebel applied Matteson's method effectively for the synthesis of amidomethyltrifluoroborates from chloromethyl pinacol boronate ester (Scheme 3.10).[10] Several amidomethyltrifluoroborates were prepared by a 'one-pot' synthetic process, and these moieties were successfully employed as nucleophiles in Suzuki–Miyaura coupling reactions.

Scheme 3.10 Preparation of Amidomethyltrifluoroborates



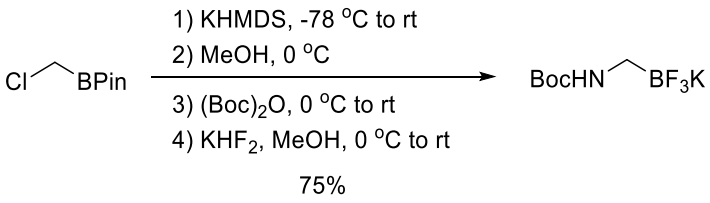
As an adaptation of Matteson's homologation and amidomethyltrifluoroborates synthesis, we designed our synthesis of potassium Boc-protected primary aminomethyltrifluoroborate. First, reaction of 2-(chloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and potassium hexamethyldisilazide (KHMDS) gave the disilylated aminoboronate ester as the intermediate, which was followed by deprotection of silyl groups using methanol. After 1 h stirring at 0 °C, the corresponding primary amine was protected with a Boc group by addition of di-*tert*-butyl dicarbonate. Then, all solvents were removed after overnight stirring at rt. The crude reaction mixture was dissolved in methanol, and saturated KHF_2 solution was added to afford the desired Boc-protected aminomethyltrifluoroborate (Scheme 3.11).

Scheme 3.11. Preparation of Boc-Protected Primary Aminomethyltrifluoroborate



The desired potassium Boc-protected primary aminomethyltrifluoroborate, which is a primary aminomethyl equivalent, was obtained in 75% overall yield over four steps in a 'one-pot' process (Equation 3.1). The aminomethyltrifluoroborate was revealed to be air stable and could be stored on the bench without decomposition. Moreover, this Boc-protected primary aminomethyltrifluoroborate is now commercially available.

Equation 3.1 'One-Pot' Synthesis of Potassium Boc-Protected Primary Aminomethyltrifluoroborate

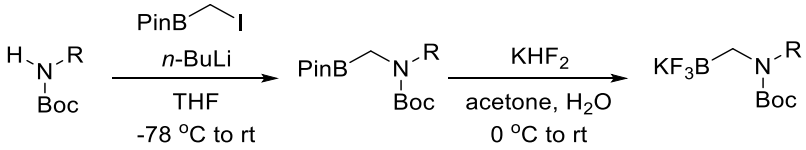


3.2.2 Synthesis of Potassium Boc-Protected Secondary Aminomethyltrifluoroborates

To extend the study of aminomethyltrifluoroborates, the development of Boc-protected secondary aminomethyltrifluoroborates would be envisioned to allow the synthesis of secondary aminomethyl moieties. Based on the synthesis of Boc-protected primary aminomethyltrifluoroborate, the 'one-pot' process was tested first for the preparation of secondary aminomethyltrifluoroborates. Unfortunately, all attempts were unsuccessful. Only traces of the desired products were detected.

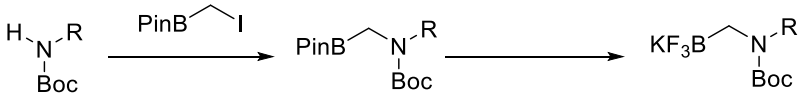
As an alternative, we designed the two step synthesis of the secondary aminomethyltrifluoroborates from Boc-protected primary amines. First, *N*-alkylation was conducted with Boc-protected primary amines and iodomethylpinacol boronate in the presence of *n*-butyllithium at –78 °C. After stirring overnight at room temperature, the aminomethylpinacol boronates were purified by column chromatography. Then, addition of KHF_2 gave the expected secondary aminomethyltrifluoroborates as white solids (Equation 3.2).

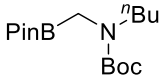
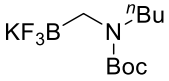
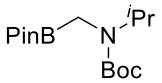
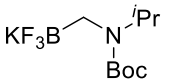
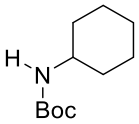
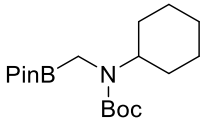
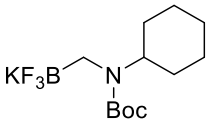
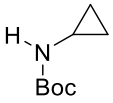
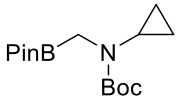
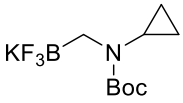
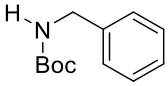
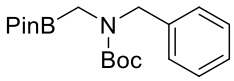
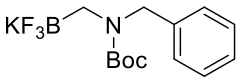
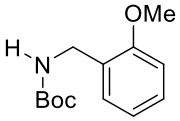
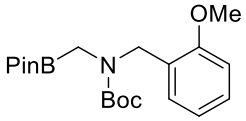
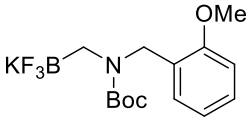
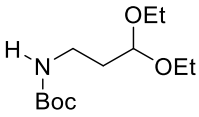
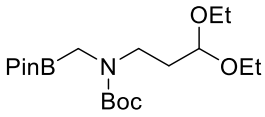
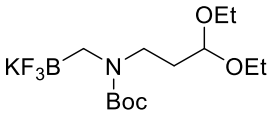
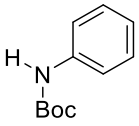
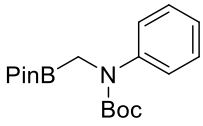
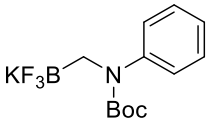
Equation 3.2 Two-Step Synthesis of Potassium Boc-Protected Secondary Aminomethyltrifluoroborates



Pleasingly, seven different Boc-protected secondary aminomethyltrifluoroborates were prepared over two steps in moderate to good yields (Table 3.1). However, initial attempts to prepare a trifluoroborate bearing an acetal protecting group failed. Although the corresponding aminomethyl pinacol boronate was successfully prepared in 75% isolated yield, conversion to the trifluoroborate by addition of KHF_2 led to low yields due to the acidic reaction media. By modifying the reaction conditions to include the addition of 1 equiv of K_2CO_3 before addition of KHF_2, the expected acetal derivative trifluoroborate was obtained as a white solid in 53% isolated yield (Table 3.1, entry 7). An aniline derivative was also tried, however, attempted conversions from the pinacol boronate to the corresponding trifluoroborate with KHF_2 provided a mixture of the desired Boc-protected trifluoroborate as well as Boc-deprotected trifluoroborate, even buffering with K_2CO_3. These two trifluoroborates were inseparable with many attempts of purifications (Table 3.1, entry 8). All of the prepared secondary aminomethyltrifluoroborates were white solids. They were air stable and could be stored at room temperature without decomposition over several months.

Table 3.1 Preparation of Potassium Boc-Protected Secondary Aminomethyltrifluoroborates



entry	amine	pinacol boronate	yield (%)	trifluoroborate	yield (%)
1			65		67
2			69		71
3			68		87
4			53		90
5			41		74
6			60		88
7			75		53[a]
8			41		74[a,b]

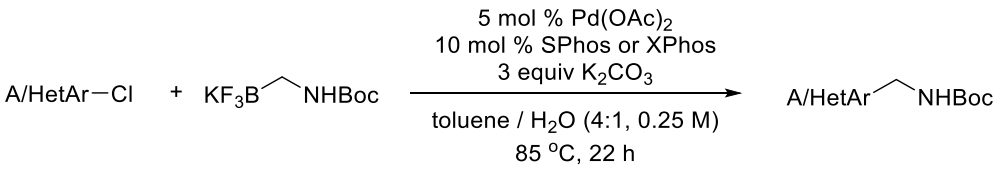
[a] 1 equiv of K_2CO_3 was added before addition of KHF_2. [b] A mixture of Boc-protected and Boc-deprotected trifluoroborates.

3.2.3 Suzuki–Miyaura Reactions with Aryl and Hetaryl Chlorides

3.2.3.1 Cross-Coupling with Primary Aminomethyltrifluoroborate

With the successfully prepared Boc-protected primary aminomethyltrifluoroborate, its application in Suzuki–Miyaura cross-coupling reactions was investigated. Optimization was conducted with 4-chlorobenzonitrile and 4-chloroanisole as the electrophilic coupling partners. After extensive screening with several catalysts, ligands, bases, and reaction times, the combination of 5 mol % of $Pd(OAc)_2$, 10 mol % of SPhos or XPhos, and 3 equiv of K_2CO_3 in toluene / H_2O (4:1, 0.25 M) for 22 h emerged as the best reaction conditions. Two different ligands, SPhos and XPhos, were required depending on the substrates. Moreover, the trifluoroborate was required only in a stoichiometric amount, 1.05 equiv, in the cross-coupling reactions (Equation 3.3).

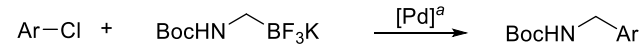
Equation 3.3 Optimization of Cross-Coupling Reactions with Boc-Protected Primary Aminomethyltrifluoroborate

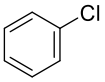
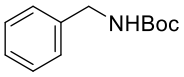
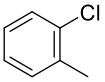
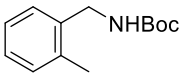
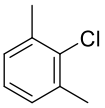
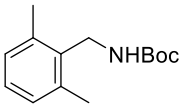
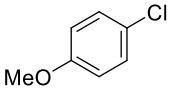
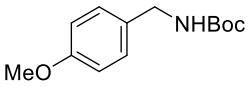
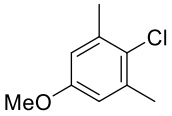
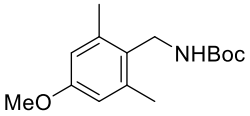
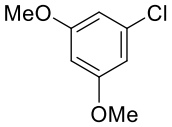
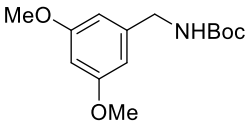
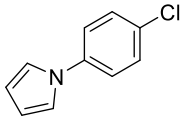
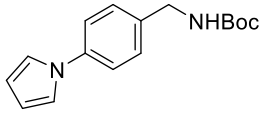
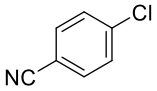
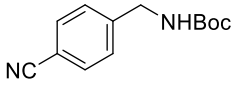
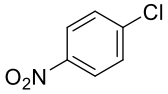
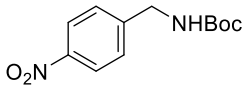
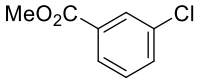
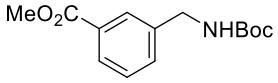
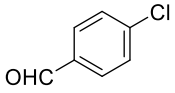
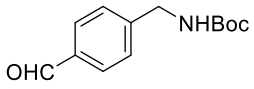
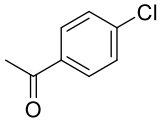
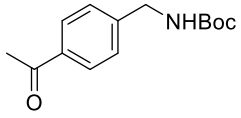


First, we applied these conditions to explore cross-couplings with a variety of aryl chlorides as electrophiles (Table 3.2). Electron neutral, electron donating, and electron withdrawing groups were all successfully coupled to provide the corresponding products

using the optimized conditions. More sterically hindered di-*ortho* substituted electrophiles provided the desired products in high yields as the less hindered electrophiles (Table 3.2, entries 2 and 3). In the case of 4-chloroanisole as an electrophile, the expected product was obtained in 88% isolated yield using XPhos as the ligand on a 0.25 mmol scale. When the scale was increased to 4.0 mmol, a lower catalyst loading (2 mol %, instead of 5 mol %) was required to provide the desired product in 78% isolated yield (Table 3.2, entry 4). Various functional groups were compatible to coupling reactions (Table 3.2, entries 8–12). Importantly, aminomethylated arenens with various functional groups, such as nitrile, aldehyde, ketone, ester, and nitro group, could be prepared by this developed coupling pathway, which can not be accessed by traditional preparations, such as reduction and reductive amination. Therefore, this protocol could be a complementary synthetic pathway to build such substrates with functional groups.

Table 3.2 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Aryl Chlorides

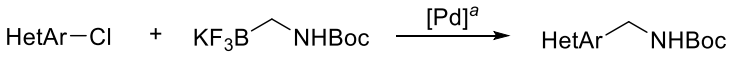


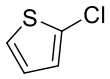
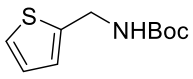
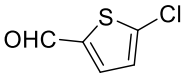
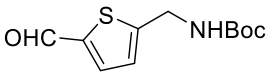
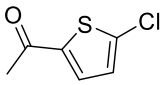
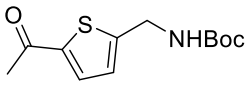
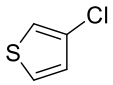
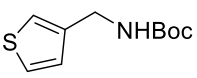
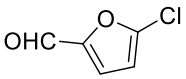
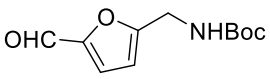
entry	Ar−Cl	product	isolated yield (%) A[b]	isolated yield (%) B[c]
1			91	74
2			76	90
3			90	76
4			69	88(78)[d]
5			78	71
6			75	79
7			86	87
8			90	88
9			90	88
10			90	86
11			70	77
12			69	71

[a] Reaction conditions: 1.0 equiv of aryl halide, 1.05 equiv of trifluoroborate, 5 mol % $Pd(OAc)_2$, 10 mol % SPhos or XPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] SPhos. [c] XPhos. [d] 4.0 mmol of 4-chloroanisole, 2 mol % of $Pd(OAc)_2$, 4 mol % of XPhos

Then, various hetaryl chlorides were employed as electrophilic coupling partners. Sulfur and oxygen containing hetaryl chlorides, such as thiophenes and furans, were successfully coupled to provide the desired products (Table 3.3). Several sensitive functional groups, such as aldehydes and ketones, were tolerated under these conditions, providing the desired products in moderate to good yields (Table 3.3, entries 2, 3 and 5). When 3-chlorothiophene was applied to coupling reactions, XPhos provided the product in mcuh higher yield compared to SPhos (Table 3.3, entry 4), even though other substrates showed a resonable range of yield differences.

Table 3.3 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluroborate with Various Hetaryl Chlorides



entry	HetAr—Cl	product	isolated yield(%) A[b]	isolated yield(%) B[c]
1			78	60
2			70	75
3			85	80
4			45	73
5			66	73

[a] Reaction coditions: 1.0 equiv of aryl halide, 1.05 equiv of trifluoroborate, 5 mol % $Pd(OAc)_2$, 10 mol % SPhos or XPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] SPhos. [c] XPhos.

Moreover, pyridine, quinoline and indole derivatives proved to the efficient coupling partners as electrophiles to provide the coupled products in moderate to good yields (Table 3.4). 2-Chloropyridine provided much lower yield compared to other hetaryl chlorides (Table 3.4, entry 3). Presumably, oxidative addition of Pd(0) to 2-halopyridines forms a dimeric metalated pyridine species (Figure 3.2).[18] This complex have been utilized as an precatalyst in Suzuki-Miyaura cross-coupling reactions with boronic acid derivatives. However, we assumed that this complex in some way inhibits effective cross-coupling in our transformations. In the case of indoles as the electrophiles, protection of free amines was not required, and also the coupling reactions proceeded effectively to provide the desired products in good yields (Table 3.4, entries 9 and 10).

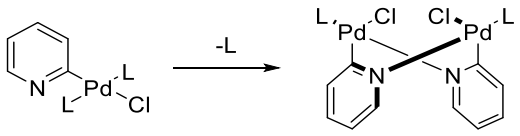
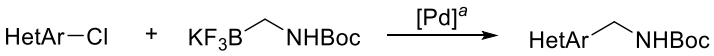
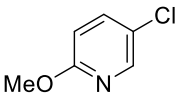
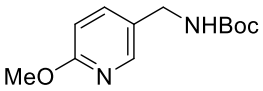
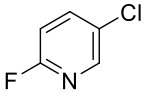
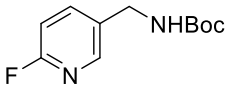
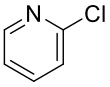
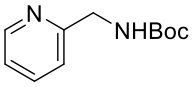
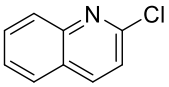
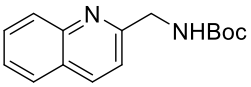
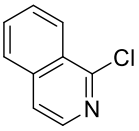
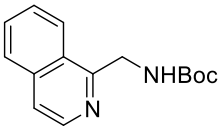
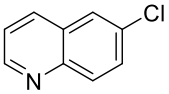
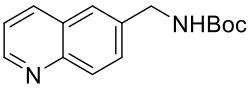
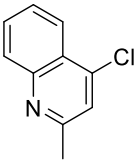
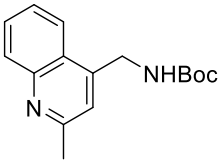
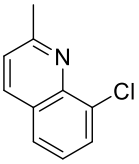
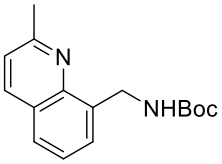
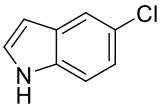
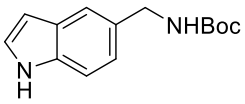
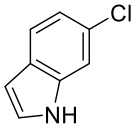
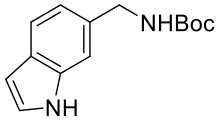


Figure 3.2 Dimeric Metalated Pyridine

Table 3.4 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Hetaryl Chlorides

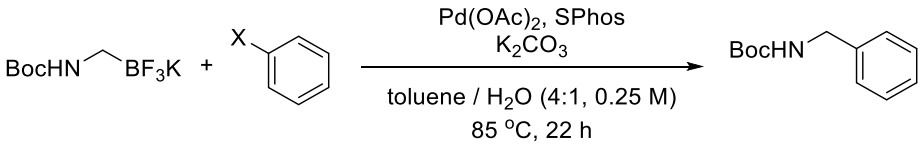


entry	HetAr—Cl	product	isolated yield(%) A[b]	B[c]
1			86	62
2			67	74
3			35	33
4			51	36
5			37	62
6			57	70
7			59	37
8			76	87
9			65	67
10			67	70

[a] Reaction coditions: 1.0 equiv of aryl halide, 1.05 equiv of trifluoroborate, 5 mol % $Pd(OAc)_2$, 10 mol % SPhos or XPhos, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.25 M), 85 °C, 22 h. [b] SPhos. [c] XPhos.

We then examined electrophile compatibility using the developed conditions, but only with SPhos as a ligand (Table 3.5). Phenyl bromide and phenyl triflate gave moderate yields, 72% and 70%, respectively (Table 3.5, entries 2 and 4). In the case of iodobenzene, the desired product was prepared in only 41% isolated yield (Table 3.5, entry 3). Unfortunately, phenyl mesylate and tosylate proved to be inefficient coupling partners under the same set of reaction conditions (Table 3.5, entries 5 and 6). Presumably, a different set of conditions would have to be developed to successfully couple with these substrates.

Table 3.5 Electrophile Compatibility

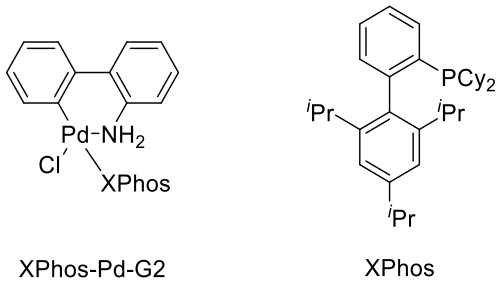


entry	X	isolated yield (%)
1	Cl	91
2	Br	72
3	I	41
4	OTf	70
5	OMs	trace
6	OTs	trace

3.2.3.2 Cross-Coupling with Secondary Aminomethyltrifluoroborates

Based on the development of the Suzuki–Miyaura reaction with Boc-protected primary aminomethyltrifluoroborate, the optimizations of Boc-protected secondary aminomethyltrifluoroborate cross-coupling reactions were investigated. *n*-Butyl Boc-

protected aminomethyltrifluoroborate as a nucleophile and 4-chloroanisole as an eletrophile were selected for the optimization study. Reaction conditions were screened with various palladium catalysts, ligands, bases, solvents, concentrations, temperatures, and times. Buchwald's second generation preformed catalyst with XPhos, XPhos-Pd-G2, proved to be most efficient (Figure 3.3).[19]

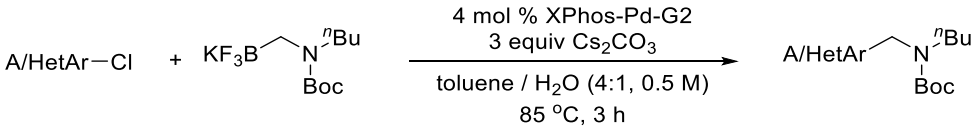


XPhos-Pd-G2 XPhos

Figure 3.3 Buchwald's Preformed Catalyst

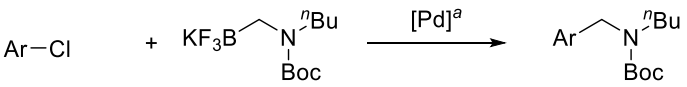
The best combination for the cross-coupling reations was 4 mol % of XPhos-Pd-G2 and 3 equiv of Cs_2CO_3 in toluene / H_2O (4:1, 0.5 M) at 85 °C. Use of Buchwald's preformed catalyst allowed the completion in only 3 h (Equation 3.4).

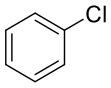
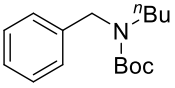
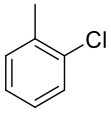
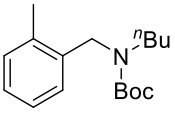
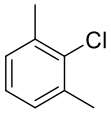
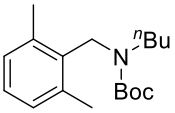
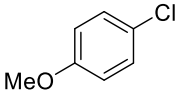
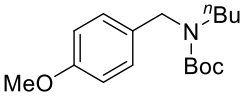
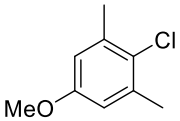
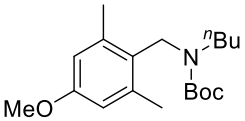
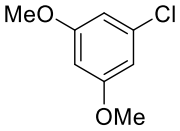
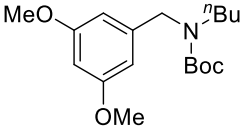
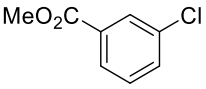
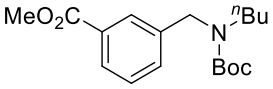
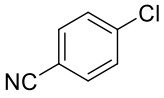
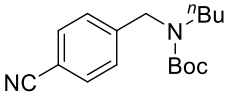
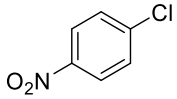
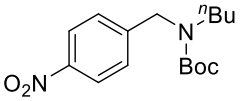
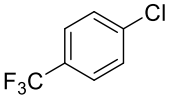
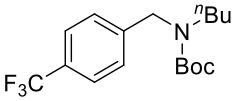
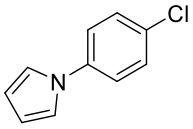
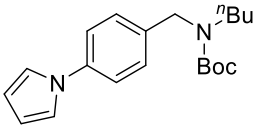
Equation 3.4 Optimization of Cross-Coupling Reactions with Boc-Protected Secondary Aminomethyltrifluoroborate



First, we employed these optimized conditions with various aryl chlorides as the electrophile (Table 3.6). A variety of aryl chlorides was successfully cross-coupled to provide the expected products in good to excellent yields. In general, electrophiles with electron-neutral (Table 3.6, entries 1–3) and electron-donating groups (Table 3.6, entries 4–6) gave slightly better results than electrophiles containing electron-withdrawing functional groups (Table 3.6, entries 7–11). Particularly, more sterically demanding substrates at the *ortho* position gave higher yields than less hindered electrophiles (Table 3.6, entries 3 and 5). Once again, sensitive functional groups, such as esters, nitriles, and nitro groups, were compatible with the reaction conditions to provide the corresponding products in excellent yields (Table 3.6, entries 7–10). These functional groups are not able to survive under harsh reduction conditions. Therefore, cross-coupling reactions could be an ideal and more direct way to install the aminomethyl moieties. A larger scale reaction (4 mmol) with 4-chloroanisole was tested under same set of reaction conditions. Luckily, the catalyst loading was lowering to 2 mol % to provide the desired product in 93% isolated yield (Table 3.6, entry 4).

Table 3.6 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Various Aryl Chlorides



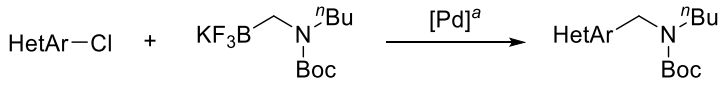
entry	Ar−Cl	product	isolated yield (%)
1			91
2			89
3			95
4			97(93)[b]
5			100
6			96
7			97
8			93
9			86
10			80
11			94

[a] Reaction coditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroborate, 5 mol % XPhos-Pd-G2, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.5 M), 85 °C, 3 h. [b] 4 mmole scale of 4-chloroanisole, 2 mol % of XPhos-Pd-G2

Next, hetaryl chlorides were tested as the electrophilic coupling partners (Table 3.7 and Table 3.8). Even though most of the reactions went to completion under the same set of reaction conditions, some of substrates were not complete in 3 h. In these cases, a longer reaction time, 18 h, was required.

Sulfur and oxygen containing hetaryl chlorides proved to be good coupling partners with *n*-butyl Boc-protected secondary aminomethyltrifluoroborate (Table 3.7). As shown, sensitive functional groups, such as aldehydes and esters, remained intact throughout the coupling reactions (Table 3.7, entries 3, 4, and 5).

Table 3.7 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Various Hetaryl Chlorides



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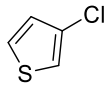
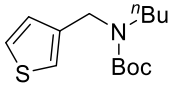
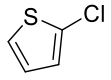
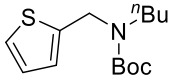
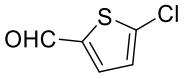
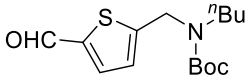
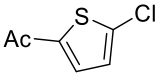
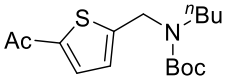
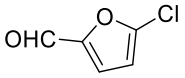
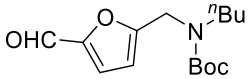
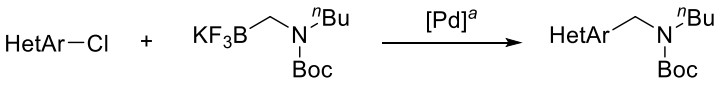
1			94
2			80
3			91
4			91[b]
5			91

[a] Reaction coditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroborate, 5 mol % XPhos-Pd-G2, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.5 M), 85 °C, 3 h. [b] 18 h

Nitrogen containing hetaryl chlorides were also investigated as the electrophilic coupling partners (Table 3.8). 3-Chloropyridine and 5-chloro-2-methoxypyridine provided the desired products in 85% and 92% isolated yields, respectively (Table 3.8, entries 1 and 2). Moreover, the expected product was obtained in 49% isolated yield with 2-chloro-6-methoxypyridine (Table 3.8, entry 3). However, the product was not detected when the 2-chloropyridine was applied. For some reason, 2-chloropyridine derivatives might require a substituent on the pyridine ring to afford the products. Quinolines and isoquinolines were also good coupling partners (Table 3.8, entries 3–6), although quinoline with a methyl substituent on the ring gave a slightly lower yield even after 18 h (Table 3.8, entry 6). In case of indole derivatives, a protecting group was required to obtain the desired products. When the reactions were performed with chloroindoles without the protecting groups, the products were not formed. After Boc-protection of indoles, the corresponding products were successfully formed in good to excellent yields (Table 3.8, entries 7 and 8). As an additional note, cross-coupling reactions of Boc-protected primary aminomethyltrifluoroborate with indole derivatives did not require any protecting groups.

Table 3.8 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Various Aryl Chlorides



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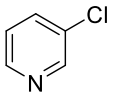
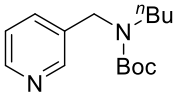
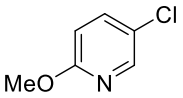
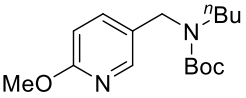
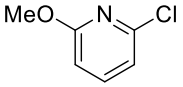
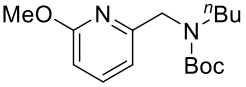
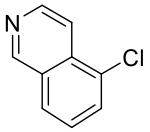
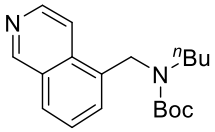
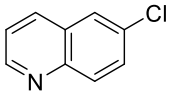
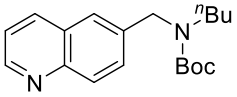
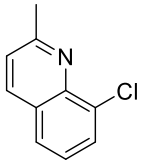
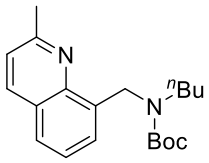
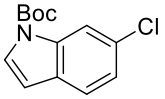
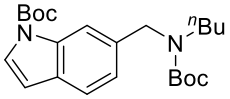
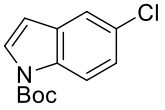
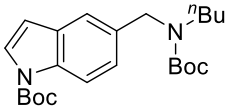
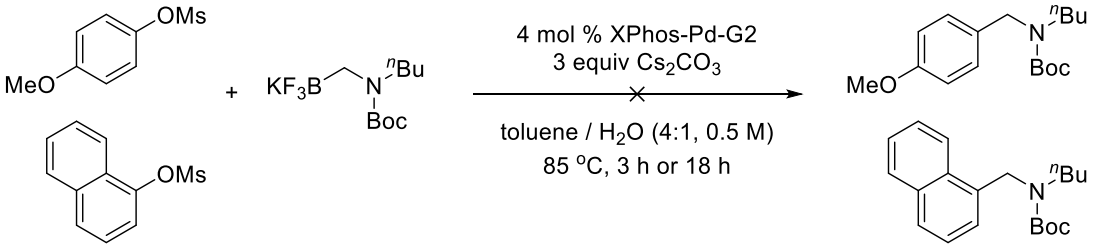
1			85[b]
2			92
3			49[b]
4			98[b]
5			99
6			77[b]
7			82
8			93

[a] Reaction coditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroborate, 5 mol % XPhos-Pd-G2, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.5 M), 85 °C, 3 h. [b] 18 h

Moreover, mesylates were tested as the electrophiles under the same set of conditions (Equation 3.5). Even though two different mesylates were applied, the desired

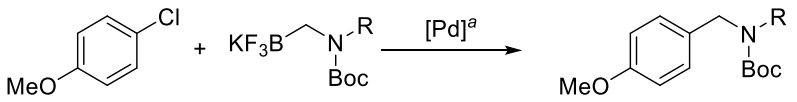
products were not obtained after 3 h and 18 h stirring at 85 °C. Only starting mesylates were observed. Therefore, a different set of conditions would have to be developed to couple these electrophiles effectively.

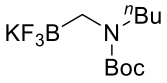
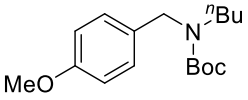
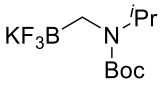
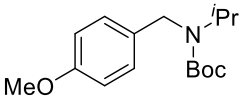
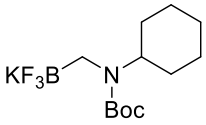
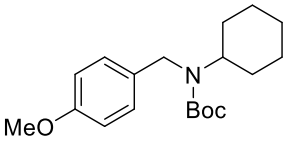
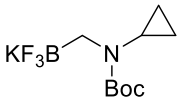
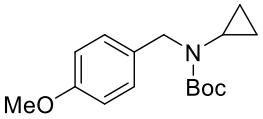
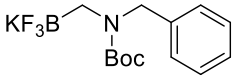
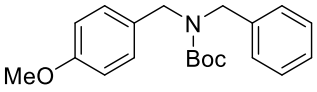
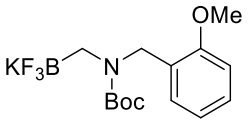
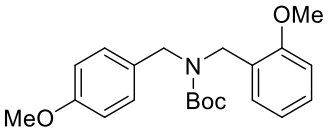
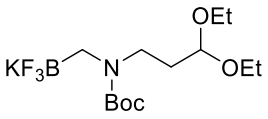
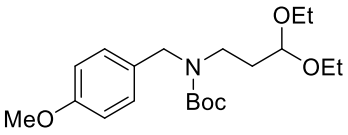
Equation 3.5 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Aryl Mesylates



Next, coupling reactions with seven different Boc-protected secondary aminomethyltrifluoroborates were examined as the nucleophiles under the same reaction conditions (Table 3.9). All of them gave the expected products in good to excellent isolated yields. Aliphatic alkyl (Table 3.9, entries 1 and 2) and cyclic alkyl groups, cyclohexyl (Table 3.9, entry 3) and cyclopropyl groups (Table 3.9, entry 4), on the nitrogen proved to be good nucleophiles. A benzyl group on the nitrogen gave the desired product in 90% isolated yield (Table 3.9, entry 5). However, a benzyl group with an electron-donating substituent on the aryl ring provided the corresponding product in a lower yield, 73% (Table 3.9, entry 6). The acetal-containing trifluoroborate also proved to be a good coupling partner to afford the desired product in 85% isolated yield, and the acetal group was tolerated under the coupling reactions (Table 3.9, entry 7).

Table 3.9 Cross-Coupling of Various Boc-Protected Secondary Aminomethyltrifluoroborates with 4-Chloroanisole



entry	trilfuoroborate	product	isolated yield (%)
1			97
2			83
3			69
4			81
5			90
6			73
7			85

[a] Reaction coditions: 1.0 equiv of aryl chloride, 1.05 equiv of trifluoroborate, 5 mol % XPhos-Pd-G2, 3 equiv K_2CO_3, toluene / H_2O (4:1, 0.5 M), 85 ^oC, 3 h.

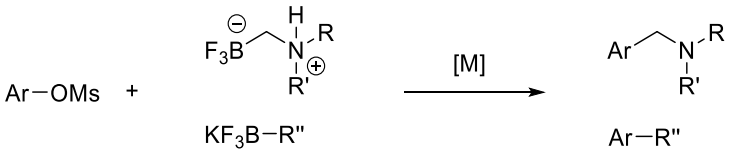
3.2.4 Suzuki–Miyaura Reactions with Aryl and Hetaryl Mesylates

3.2.4.1 Introduction

Aryl and hetaryl halides, such as chlorides, bromides, and iodides, have been widely studied as the electrophilic partners in cross-coupling reactions. A wide range of halides are commercially available, and their substrate scope is broad. More recently, pseudo-halides, such as sulfonated groups, have been utilized successfully in Suzuki–Miyaura coupling reactions as alternative coupling partners.[20] Among several sulfonated phenolic derivatives, tosylates or mesylates are more attractive because they are easily prepared from the corresponding phenol with tosyl or mesyl chloride, respectively. These sulfonated counterparts are easy to handle and show high stability. Particularly, mesylates are of great interest in terms of atom economy and low cost.[21] Even though mesylates show the lowest reactivity among sulfonated derivatives, they have proven to be good coupling partners in cross-coupling reactions.

Recently, the Molander[22] and Kwong groups[23] have reported the Suzuki–Miyaura reaction of potassium organotrifluoroborates with mesylates as the electrophilic coupling partners. Organotrifluoroborate salts have proven to be efficient coupling partners with mesylates in the presence of transition metals (Scheme 3.12).

Scheme 3.12 Cross-Coupling Reactions of Organotrifluoroborate Salts and Mesylates

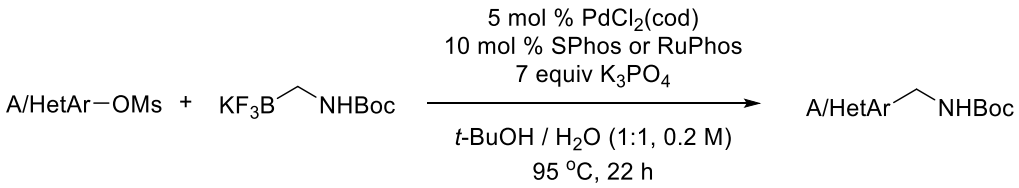


3.2.4.2 Cross-Coupling with Primary Aminomethyltrifluoroborate

Boc-Protected primary aminomethyltrifluoroborate proved to be a good nucleophile with aryl and hetaryl chlorides in Suzuki–Miyaura cross-coupling reactions. To expand the scope of reactivity of aminomethyltrifluoroborate, we explored the Suzuki–Miyaura reaction with mesylates as an electrophile.

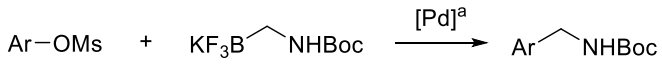
Initially, we applied the previously developed coupling conditions of primary aminomethyltrifluoroborate with aryl and hetaryl chlorides to reactions with mesylates. Unfortunately, only trace amounts of product were detected. This results showed that a new set of conditions would have to be developed for effective couplings with mesylates. Based on the coupling reaction conditions with mesylates reported previously, K_3PO_4 was chosen as the base, and a mixture of *t*-BuOH / H_2O was selected as the solvent system. Next, we screened extensively with palladium catalysts, ligands, reaction concentrations, ratio of two solvents, and temperature. After optimization, the combination of 5 mol % of $PdCl_2$(cod), 10 mol % of SPhos or RuPhos, and 7 equiv of K_3PO_4 in *t*-BuOH / H_2O (1:1, 0.2 M) at 95 °C for 22 h emerged as the best conditions (Equation 3.6). Two different ligands, SPhos and RuPhos, were used because reactions with various substrates were not general.

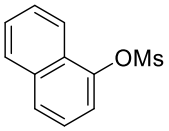
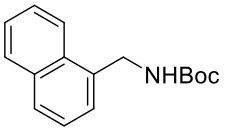
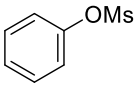
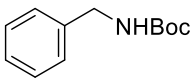
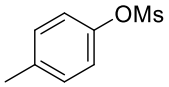
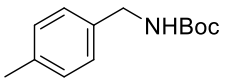
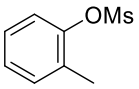
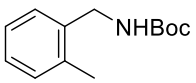
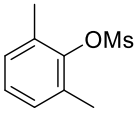
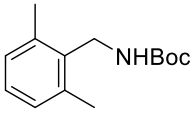
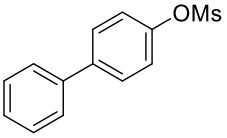
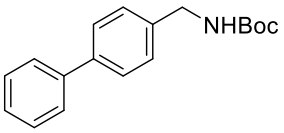
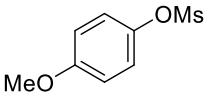
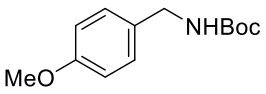
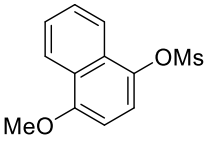
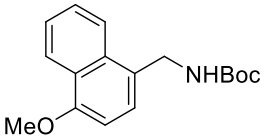
Equation 3.6 Optimization of Cross-Coupling Reactions with Boc-Protected Primary Aminomethyltrifluoroborate with Mesylates



We employed these optimized conditions for various aryl mesylates containing electron-neutral and electron-donating substituents on the aryl ring (Table 3.10). Both electron-neutral (Table 3.10, entries 1–6) and electron-rich mesylates (Table 3.10, entries 7 and 8) proved to be good electrophilic partners in this process. RuPhos was the most efficient ligand for all these cases. The yields dropped dramatically with substrates possessed more steric hindrance *ortho* to the mesylates compared to less hindered substrates (Table 3.10, entries 4, and 5). The di-*ortho* substituted aryl mesylate gave the desired product in only 22% isolated yield. When the scale was increased to 4 mmol of mesylated 1-naphthol, a lower catalyst loading, 3 mol %, could be employed to give the expected product in 87% isolated yield (Table 3.10, entry 1).

Table 3.10 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Aryl Mesylates



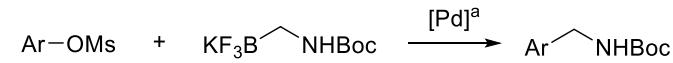
entry	Ar−OMs	product	ligand	isolated yield (%)
1			RuPhos	79(87)[b]
2			RuPhos	66
3			RuPhos	72
4			RuPhos	72
5			RuPhos	22
6			RuPhos	86
7			RuPhos	59
8			RuPhos	84

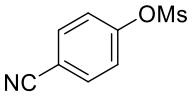
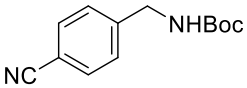
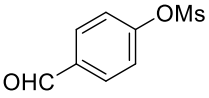
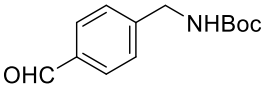
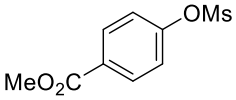
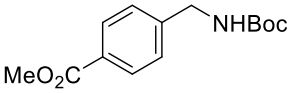
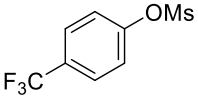
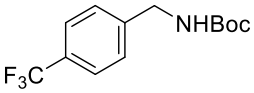
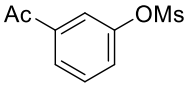
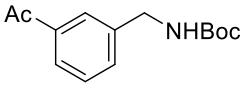
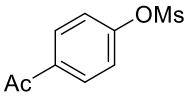
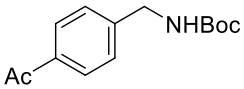
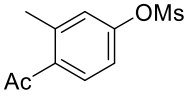
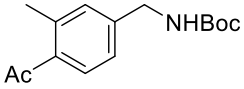
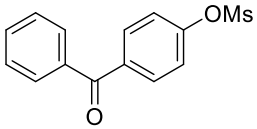
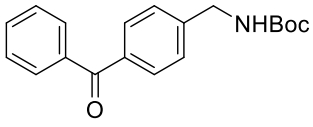
[a] Reaction conditions: 1.0 equiv of aryl mesylate, 1.1 equiv of trifluoroborate, 5 mol % $PdCl_2$(cod), 10 mol % SPhos or RuPhos, 7 equiv K_3PO_4, *t*-BuOH / H_2O (1:1, 0.2 M), 95 °C, 22 h. [b] 4.0 mmol of mesylated 1-naphthol, 3.0 mol % of $PdCl_2$(cod), 6 mol % RuPhos

To expand the scope of the aryl mesylates, electron-deficient aryl mesylates were tested (Table 3.11). Two different ligands, SPhos and RuPhos, were used to obtain the optimal depending on substrates. All electron-poor electrophilic coupling partners

provided the corresponding products in moderate to good yields. Several functional groups, such as nitriles, aldehydes, esters, and ketones, were tolerated under coupling reaction conditions. However, the aldehyde and methyl ester substituted aryl mesylates gave lower yields compared to other substrates (Table 3.11, entries 2 and 3).

Table 3.11 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Aryl Mesylates

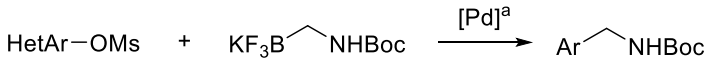


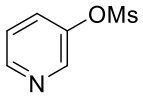
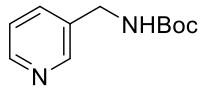
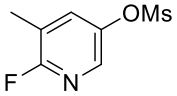
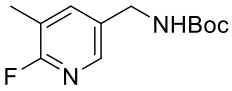
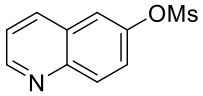
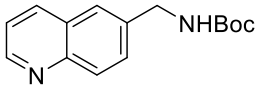
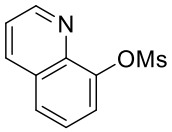
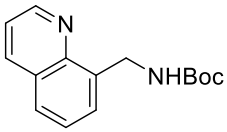
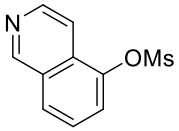
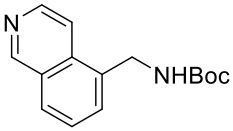
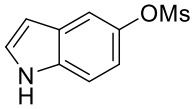
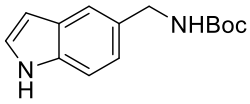
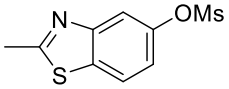
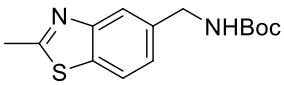
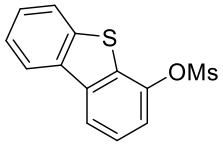
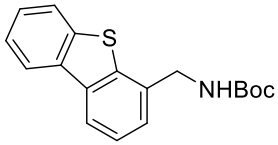
entry	Ar−OMs	product	ligand	isolated yield (%)
1			SPhos	72
2			RuPhos	46
3			SPhos	42
4			RuPhos	83
5			RuPhos	82
6			SPhos	80
7			RuPhos	81
8			RuPhos	86

[a] Reaction conditions: 1.0 equiv of aryl mesylate, 1.1 equiv of trifluoroborate, 5 mol % $PdCl_2$(cod), 10 mol % SPhos or RuPhos, 7 equiv K_3PO_4, *t*-BuOH / H_2O (1:1, 0.2 M), 95 °C, 22 h.

Various hetaryl mesylates were also investigated as the electrophilic coupling partners with the same set of reaction conditions (Table 3.12). Once again, for better results two ligands, SPhos and RuPhos, were used depending on the substrates. Pyridine, quinoline, isoquinoline, indole and thiazole were successfully coupled with Boc-protected primary aminomethyltrifluoroborate to provide the desired products in moderate to good yields (Table 3.12, entries 1–7). In the case of the mesylated indole, protection of the free amine was not required, and the expected product was obtained in 75% isolated yield (Table 3.12, entry 6). As an additional note, coupling reactions of primary aminomethyltrifluoroborate with chloroindoles did not require protection, while those of secondary aminomethyltrifluoroborates couplings did require protection prior to cross-coupling reactions. Moreover, sulfur containing hetaryl mesylates proved to be efficient coupling partners to give the desired products in good yields (Table 3.12, entries, 7 and 8).

Table 3.12 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Hetaryl Mesylates



entry	HetAr−OMs	product	ligand	isolated yield (%)
1			SPhos	52
2			RuPhos	78
3			SPhos	84
4			RuPhos	87
5			SPhos	57
6			SPhos	75
7			RuPhos	86
8			RuPhos	88

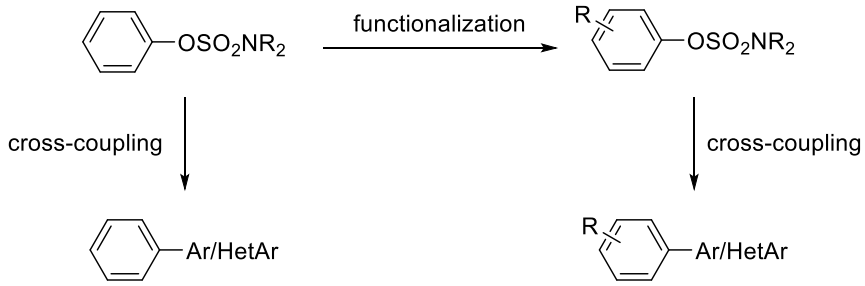
[a] Reaction conditions: 1.0 equiv of aryl mesylate, 1.1 equiv of trifluoroborate, 5 mol % $PdCl_2$(cod), 10 mol % SPhos or RuPhos, 7 equiv K_3PO_4, *t*-BuOH / H_2O (1:1, 0.2 M), 95 °C, 22 h.

3.2.5 Suzuki–Miyaura Reactions with Aryl and Hetaryl Sulfamates

3.2.5.1 Introduction

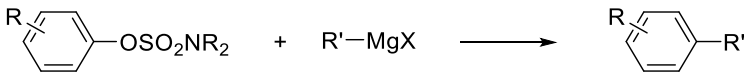
Transition metal catalyzed Suzuki–Miyaura couplings with phenolic derivatives have often been demonstrated because these substrates are inexpensive and easy to prepare from the corresponding phenols. Phenol derivatives are readily found in many natural compound syntheses, and can be utilized as the coupling partners after protection. More recently, sulfamates are of interest in terms of easy preparation and further functionalization.[24] The direct installation of functional groups *ortho* or *para* to the sulfamate have also been reported, because these substrates are known to be stable to various reaction conditions (Scheme 3.13). Moreover, the cross-coupling reactions, such as Kumada[25] and Suzuki–Miyaura coupling reactions,[24, 26] have been demonstrated. Therefore, more complex molecules can be synthesized by further functionalizations and couplings.

Scheme 3.13 Utilities of Sulfamates



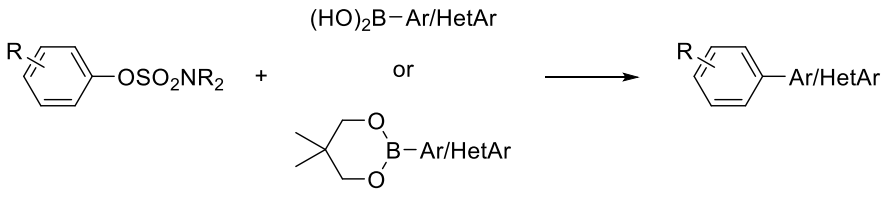
Previously, sulfamates have been utilized as the coupling partners in Kumada couplings (Scheme 3.14).[25] In general, many functional groups, such as esters and ketones, are not compatible with Grignard reagents for Kumada couplings. Therefore, Kumada couplings cannot be widely applied to build new carbon-carbon bonds.

Scheme 3.14 Kumada Couplings with Sulfamates



Recently, Suzuki–Miyaura reactions with sulfamates have been reported by Garg, Snieckus and Percec (Scheme 3.15).[24,26] Several boron reagents, such as boronic acids and neopentylglycolboronates, are successfully utilized in nickel-catalyzed Suzuki–Miyaura reactions with sulfamates. Even though carbon(sp^2)-carbon(sp^2) bonds can be effectively formed under these processes, the reaction conditions are harsh and inefficient due to high temperatures required and longer reaction times. Moreover, since palladium catalysts are known to be inefficient for coupling reactions with sulfamates, only nickel catalyzed reactions have been studied.[24a]

Scheme 3.15 Suzuki–Miyaura Couplings with sulfamates



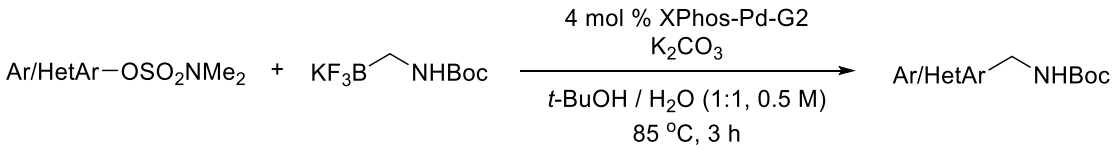
To the best of our knowledge, palladium catalyzed Suzuki–Miyaura coupling reactions with potassium organotrifluoroborates and sulfamates have not been reported.

3.2.5.2 Cross-Coupling with Primary Aminomethyltrifluoroborate

To extend our study of phenolic derivatives in the Suzuki–Miyaura reaction with aminomethyltrifluoroborates, sulfamates were chosen as the electrophilic coupling partners with potassium Boc-protected primary and secondary aminomethyltrifluoroborates. The carbon(sp^3)-carbon(sp^2) bonds could be prepared by this development, which were previously demostrated only with carbon(sp^2)-carbon(sp^2) bond formation.[24,26] To the best of our knowledge, potassium organotrifluoroborates have not been reported as the nucleophilic coupling partner in Suzuki–Miyaura coupling reactions of sulfamates.

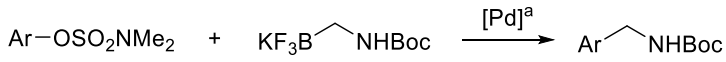
The coupling reactions were screened with the 1-naphthol sulfamate and Boc-protected primary aminomethyltrifluoroborate. After the screening of various palladium catalysts, ligands, bases, solvents, and reaction times, the combination of 4 mol % of XPhos-Pd-G2 and K_2CO_3 in *t*-BuOH / H_2O (1:1, 0.5 M) at 85 °C for 3 h emerged as the optimal conditions (Equation 3.7). Again, use of Buchwald's second generation preformed catalysts allowed the reaction times shortened to 3 h. Moreover, the reactions could be concentrated to 0.5 M.

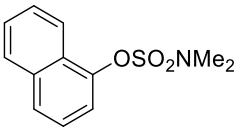
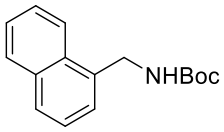
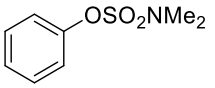
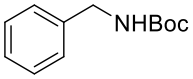
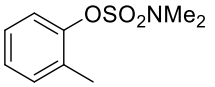
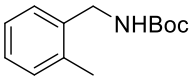
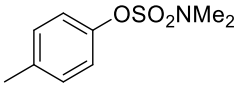
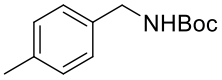
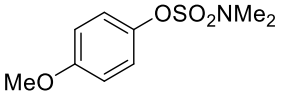
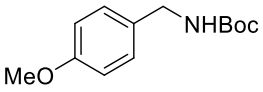
Equation 3.7 Optimization of Cross-Coupling Reactions with Boc-Protected Primary Aminomethyltrifluoroborate with Sulfamates



Then, we applied these optimized conditions to aryl sulfamates as electrophiles. First, electron-neutral and electron-rich aryl sulfamates were applied (Table 3.13). Electron-neutral sulfamates, such as 1-naphthol and phenol derivatives, were effectively coupled to provide the desired products in 93% and 85% isolated yields (Table 3.13, entries 1 and 2). In the case of phenolic substrates required a slightly higher amount of base, 5 equiv instead of 3 equiv. Methyl substituted derivatives on the aryl ring, such as the *ortho* or *para* to sulfamates, were observed in low conversions and yields by ^{1}H NMR (Table 3.13, entries 3 and 4). Unfortunately, electron-donating aryl sulfamates were not efficient coupling partners because only low conversions and yields were detected (Table 3.13, entry 5).

Table 3.13 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Aryl Sulfamates



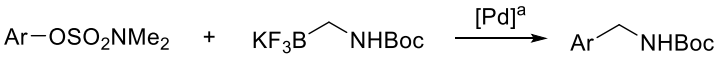
entry	$Ar-OSO_2NMe_2$	product	equiv of K_2CO_3	conversion (%)[b]	isolated yield (%)
1			3	100	93
2			5	90	85
3			3	27	13[b]
4			3	38	38[b]
5			3	25	23[b]

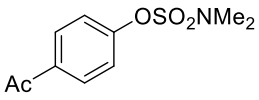
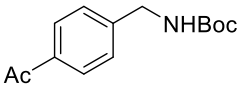
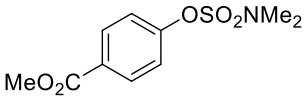
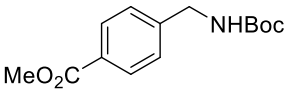
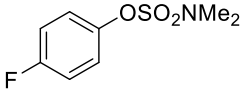
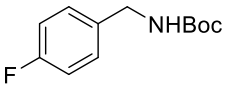
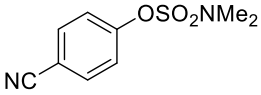
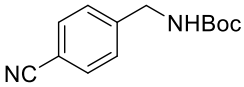
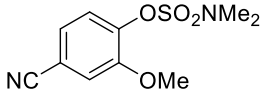
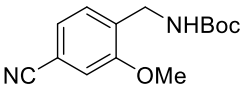
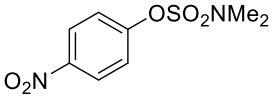
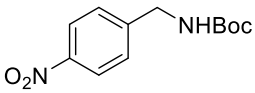
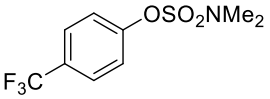
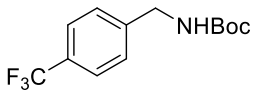
[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 3 h. [b] calculated by ^1H NMR with 30 μL of CH_2Cl_2.

We then studied electron-deficient aryl sulfamates as the electrophilic coupling partners (Table 3.14). All sulfamates with electron-withdrawing groups provided the desired products in good to excellent yields. In general, electron-poor aryl sulfamates showed better results than the electron-neutral and electron-rich substrates. A mixture of *t*-BuOH / H_2O gave low conversion and yields when the fluoro substituted aryl sulfamate was applied. After optimization the solvent system again, a mixture of *n*-PrOH / H_2O was better for this substrate to provide the corresponding product in a higher yield with a better

conversion (Table 3.14, entry 3). Several functional groups, such as ketones, esters, nitriles, and nitro groups, were compatible throughout the coupling reactions. In the case of aryl sulfamate with both electron-donating and electron-withdrawing groups on the aryl ring, the desired product was obtained in 90% isolated yield with full conversion (Table 3.14, entry 5). As shown above, low yields and low conversion were observed with electron-rich substituted aryl sulfamates (Table 3.13, entry 5). Unfortunately, a slightly lower yield and conversion were obtained with a nitro group on the aryl ring compared to other electron-poor substrates (Table 3.14, entry 6).

Table 3.14 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Aryl Sulfamates



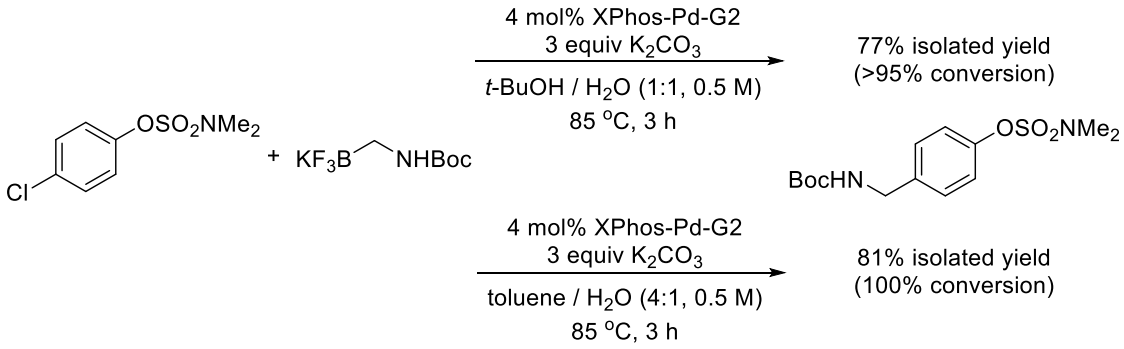
entry	$Ar-OSO_2NMe_2$	product	equiv of K_2CO_3	conversion (%)[b]	isolated yield (%)
1			3	100	87
2			3	100	93
3[c]			7	98	89
4			3	100	88
5			3	100	90
6			5	80	60
7			5	100	76

[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 3 h. [b] calculated by ^1H NMR with 30 μL of CH_2Cl_2. [c] *n*-PrOH / H_2O.

Then, we tested 4-chlorophenyl *N*,*N*-dimethylsulfamate as the electrophilic coupling partner using the same set of conditions (Equation 3.8). Initially, we expected the product from the coupling of the sulfamate site. However, the aminomethyltrifluoroborate was coupled only with the chloride instead of the sulfamate. The other site coupled product was not detected at all. We also applied the modified conditions of couplings with aryl

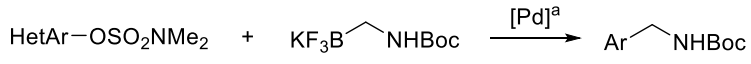
chlorides and primary aminomethyltrifluoroborate, but the same result was observed. Therefore, we assumed oxidative addition to chlorides is faster than sulfamates if the two substrates exist on the same aryl ring.

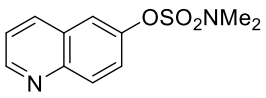
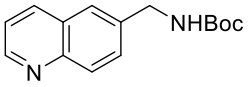
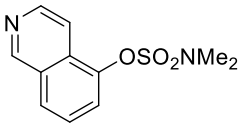
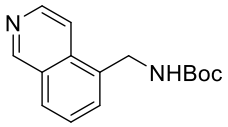
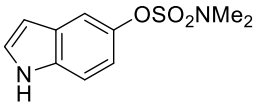
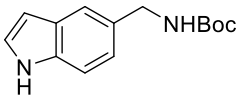
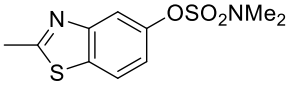
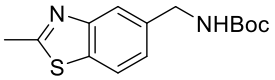
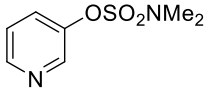
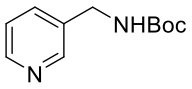
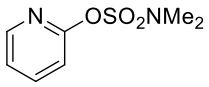
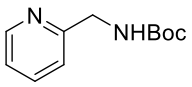
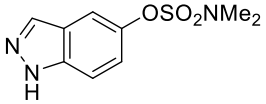
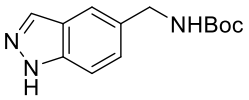
Equation 3.8 Cross-Coupling Reactions with Boc-Protected Primary Aminomethyltrifluoroborate with 4-Chlorophenyl Dimethylsulfamate



Next, hetaryl sulfamates were investigated as the electrophilic coupling partners (Table 3.15). Various hetaryl sulfamates proved to be good electrophiles. The proctection was not required to effectively couple with indole derivatives, the desired product was obtained in 68% isolated yield (Table 3.15, entry 3). Even though 2-pyridyl sulfamate gave the product, the isolated yield was a lot lower compared to other substrates (Table 3.15, entry 5). Unfortunately, indazole derivatives were not efficient coupling partners using the same set of conditions (Table 3.15, entry 7).

Table 3.15 Cross-Coupling of Boc-Protected Primary Aminomethyltrifluoroborate with Various Hetaryl Sulfamates



entry	HetAr−OSO_2NMe_2	product	equiv of K_2CO_3	conversion (%)[b]	isolated yield (%)
1			3	100	88
2			7	100	91
3			7	79	68
4			3	89	85
5			5	83	83
6			5	100	58
7			3	0	0

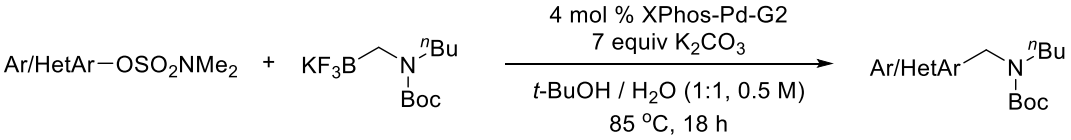
[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 3 h. [b] Calculated by ^1H NMR with 30 μL of CH_2Cl_2.

3.2.5.3 Cross-Coupling with Secondary Aminomethyltrifluoroborates

We screened the coupling reactions of Boc-protected secondary aminomethyltrifluoroborates with various bases, solvents and times. The combination of 4 mol % of XPhos-Pd-G2 and 7 equiv of K_2CO_3 in *t*-BuOH / H_2O (1:1, 0.5 M) at 85 °C for 18 h was optimal for the secondary aminomethyltrifluoroborates couplings (Equation 3.9).

Only 7 equiv of base was more efficient in the case of secondary aminomethyltrifluoroborates. Moreover, the longer reaction time, 18 h, was required for the better results.

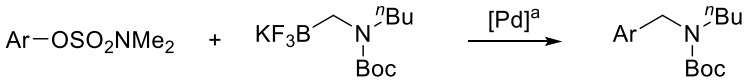
Equation 3.9 Optimization of Cross-Coupling Reactions with Boc-Protected Secondary Aminomethyltrifluoroborate with Sulfamates

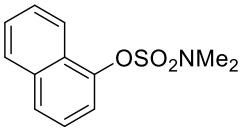
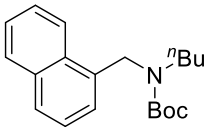
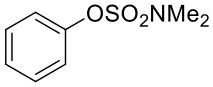
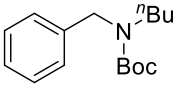
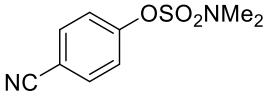
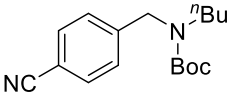
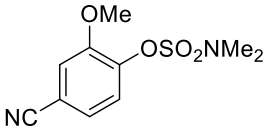
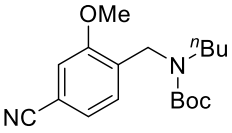
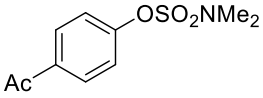
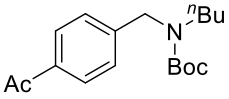
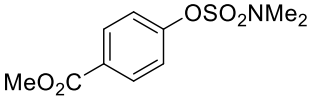
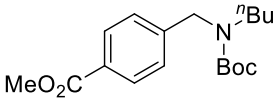
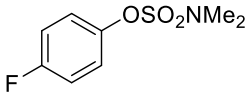
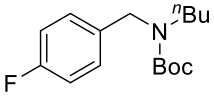
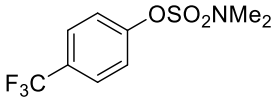
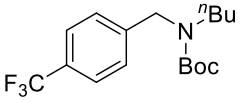
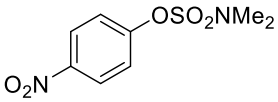
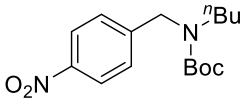
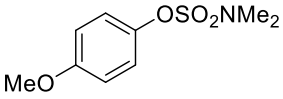
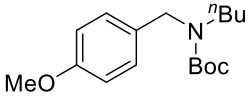


We first studied aryl sulfamates as the electrophilic coupling partners using the optimized conditions (Table 3.16). The coupling reactions were not effective as the coupling reactions of primary aminomethyltrifluoroborate. Several functional groups, such as nitrile, ketones, and esters, were intact throughout the coupling reactions. In the case of an acyl substituted sulfamate, the corresponding product was obtained in only 42% isolated yield even though full conversion was detected (Table 3.16, entry 5). A sulfmate with nitrile group on the ring required a lower amount of base, 5 equiv of K_2CO_3 (Table 3.16, entry 3). Although a sulfamate with only an electron-donating substituent proved to be an inefficient electrophilic coupling partner (Table 3.16, entry 10), an aryl sulfamate with both electron-rich and electron-poor substituents on the same ring gave the better result, 63% isolated yield (Table 3.16, entry 4). Sulfamates with fluoro and trifluoromethyl groups on the aryl rings, the desired products were obtained in lower yields, 47% and 42%,

respetively (Table 3.16, entries 7 and 8). Unfortunately, a nitro group-containing aryl sulfamate proved to be an inefficient coupling partner (Table 3.16, entry 9).

Table 3.16 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Various Aryl Sulfamates

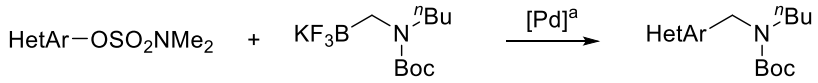


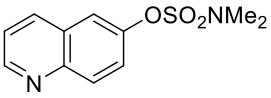
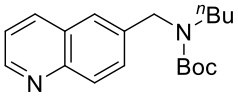
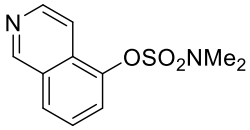
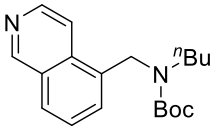
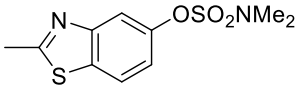
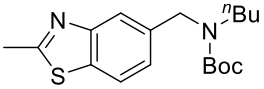
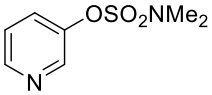
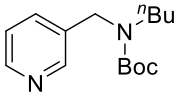
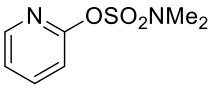
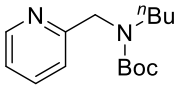
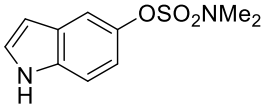
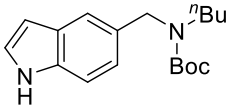
entry	HetAr−OSO_2NMe_2	product	conversion (%)[b]	isolated yield (%)
1			100	92
2			76	33
3[c]			80	53
4			100	63
5			100	42
6			100	76
7			68	47
8			60	42
9			0	0
10			16	15[b]

[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, 7 equiv K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 18 h. [b] Calculated by ^1H NMR with 30 μL of CH_2Cl_2. [c] 5 equiv of K_2CO_3.

Then, various sulfur and nitrogen containing hetaryl sulfamates were tested as the electrophiles (Table 3.17). Unfortunately, only a few hetaryl sulfamates were successfully coupled to provide the desired products. The expected products were obtained in good yields when quinoline, isoquinoline, and thiazole derivatives were applied (Table 3.17, entries 1–3). Unfortunately, pyridines and indoles were not efficient, and did not afford the corresponding products under the developed conditions, even though more studies were conducted (Table 3.17, entries 4–6).

Table 3.17 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborate with Various Hetaryl Sulfamates

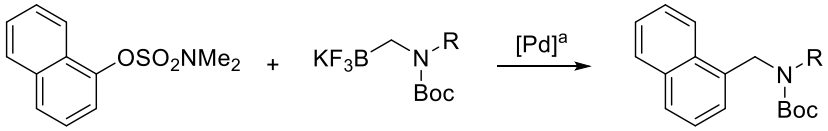


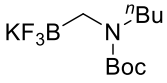
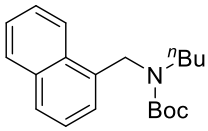
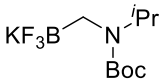
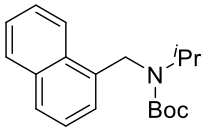
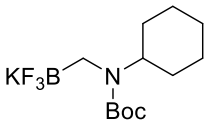
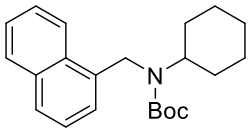
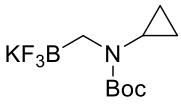
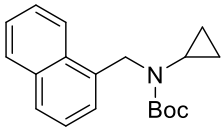
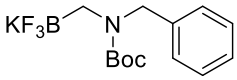
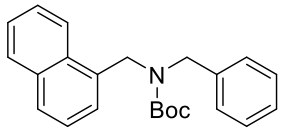
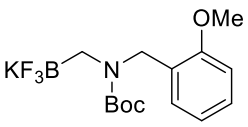
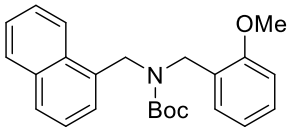
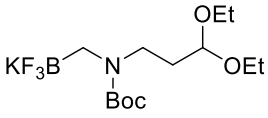
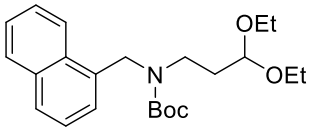
entry	HetAr−OSO_2NMe_2	product	conversion (%)[b]	isolated yield (%)
1			100	84
2			100	83
3			92	85
4			100	29[b]
5			0	0
6			0	0

[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, 7 equiv K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 18 h. [b] Calculated by ^1H NMR with 30 μL of CH_2Cl_2

The scope of the reactions were expanded seven Boc-protected secondary aminomethyltrifluoroborates (Table 3.18). The same set of coupling conditions were applied. The desired products were prepared in good yields with full conversions, when the aliphatic alkyl substrates on the nitrogen were tested (Table 3.18, entries 1 and 2). Even though cyclohexyl substrate provided the expected product in 68% isolated yield (Table 3.18, entry 3), the desired product was not detected by ^{1}H NMR with a cyclopropyl group on the nitrogen (Table 3.18, entry 4). Benzyl groups, even with electron-rich substituent on an aryl ring, afforded the corresponding products in 74% and 82% isolated yields, respectively (Table 3.18, entries 5 and 6). The acetal derivative trifluoroborate was also effectively coupled to provide the desired product in 86% isolated yield (Table 3.18, entry 7).

Table 3.18 Cross-Coupling of Boc-Protected Secondary Aminomethyltrifluoroborates with *N,N*-Dimethylsulfamated 1-Naphthol



entry	trifluoroborate	product	conversion (%)[b]	isolated yield (%)
1			100	92
2			100	71
3			100	68
4			0	0
5			89	74
6			97	82
7			100	86

[a] Reaction conditions: 1.0 equiv of aryl sulfamate, 1.05 equiv of trifluoroborate, 4 mol% XPhos-Pd-G2, 7 equiv K_2CO_3, *t*-BuOH / H_2O (1:1, 0.5 M), 85 °C, 18 h. [b] Calculated by ^1H NMR with 30 μL of CH_2Cl_2

3.3 Conclusions

We successfully synthesized Boc-protected primary aminomethyltrifluoroborate, the primary aminomethyl equivalent, in 75% isolated yield over four steps through a 'one-pot' process. Moreover, seven Boc-protected secondary aminomethyltrifluoroborates were prepared in a two-step synthesis. All of the prepared trifluoroborates are air stable and could be stored at room temperature without decomposition. Then, the Suzuki–Miyaura cross-coupling reaction of these aminomethyltrifluoroborates were investigated with various electrophilic coupling partners. Aryl and hetaryl chlorides, mesylates, and sulfamates all proved to be effective electrophiles in Suzuki–Miyaura cross-couplings under developed reaction conditions. The development of the aminomethyltrifluoroborates and applications in coupling reactions allowed access to the aminomethyl moieties more efficiently. Moreover, this proved to be a complementary way to build such substructure compared to traditional pathways.

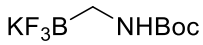
3.4 Experimental

General.

$Pd(OAc)_2$, $PdCl_2(cod)$, SPhos, XPhos, RuPhos and K_2CO_3 were used as received. All halides were used as received. XPhos-Pd-G2 was synthesized prior to use.[19] Toluene was distilled from sodium/benzophenone prior to use or used from Grubbs distillation.[27] *tert*-Butanol and H_2O was degassed prior to use. Melting points (°C) are uncorrected. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at 500, 125.8, and 470.8 MHz, respectively. ^{19}F NMR chemical shifts were referenced to external $CFCl_3$ (0.0 ppm). ^{11}B NMR spectra at

128.4 MHz were obtained on a spectrometer equipped with the appropriate decoupling accessories. All ^{11}B NMR chemical shifts were referenced to external $BF_3 \bullet OEt_2$ (0.0 ppm) with a negative sign indicating an upfield shift. Analytical thin layer chromatography (TLC) was performed on TLC silica gel plates (250 μm) precoated with a fluorescent indicator. Standard flash chromatography procedures[28] were followed using 32–63 μm silica gel. Visualization was effected with ultraviolet light and ninhydrin and *p*-anisaldehyde solution.

Procedure for the Preparation of Potassium Boc-Protected Primary Aminomethyltrifluoroborate.



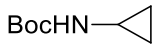
Potassium *tert*-Butoxycarbonyl Aminomethyltrifluoroborate.

KHMDS (4.0 g, 19.8 mmol, 1.0 equiv) in THF (40 mL) was added slowly to 2-(chloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.5 g, 19.84 mmol, 1.0 equiv) in THF (40 mL) at –78 °C. The reaction mixture was stirred for 15 min at –78 °C and then stirred for an additional 2 h at rt. The reaction mixture was cooled to 0 °C. MeOH (1.3 g, 39.7 mmol, 2.0 equiv) was added to the flask at 0 °C. After stirring for 1 h at 0 °C, $(Boc)_2O$ (8.7 g, 39.7 mmol, 2.0 equiv) was added in one portion. The reaction flask was warmed to rt and stirred overnight at rt. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in MeOH (40 mL), and then KHF_2 in H_2O (4.5 M, 18 mL, 4.0 equiv) was added slowly at 0 °C. After vigorous stirring for 30 min at rt, the solution was concentrated in vacuo and then dried in vacuo overnight. The crude mixture was extracted with acetone (3 × 30 mL), and the extracts were combined and concentrated. Et_2O (60 mL)

was added to precipitate the product. The resulting precipitate (3.5 g, 14.9 mmol) was filtered and dried in vacuo to provide the product as a white solid in 75% yield.

mp (transition): 178–181 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.57 (s, 1H), 1.81, (s, 2H), 1.33 (s, 9H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 156.4, 76.4, 28.3, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –145.5; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.13; IR (neat) 3426, 1680 cm^{-1}; HRMS (ES–) calcd. For $C_6H_{12}BF_3NO_2$ $[M–K]^-$ 198.0913, found 198.0906.

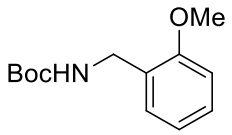
General Procedure for Boc Protection of Amines.



***tert*-Butyl Cyclopropylcarbamate.**

A round bottomed flask was charged with $(Boc)_2O$ (1.6 g, 7.22 mmol, 1.0 equiv). Cyclopropanamine (412 mg, 0.5 mL, 7.22 mmol, 1.0 equiv) was slowly added to the flask at rt. The reaction mixture was stirred at rt for 2 h. The crude reaction mixture was purified by column chromatography (hexanes/EtOAc = 10:1 to 3:1) to afford the product (1.09 g, 6.95 mmol) as a white solid in 96% yield.

mp: 60–62 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.78 (br, 1H), 2.53 (s, 1H), 1.45 (s, 9H), 0.68 (d, J = 6.0 Hz, 2H), 0.49 (s, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.8, 79.5, 28.5, 22.9, 6.8; IR (neat) 3360, 1687, 1508, 1160 cm^{-1}; HRMS (CI^+) calcd. for $C_8H_{16}NO_2$ $[M+H]^+$ 158.1181, found 158.1180.

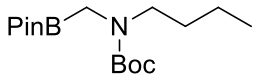


***tert*-Butyl 2-Methoxybenzylcarbamate.**

The reaction was carried out with 2-methoxybenzylamine (1.05 g, 1.0 mL, 7.66 mmol, 1.0 equiv) according to the general procedure for Boc protection of amines to obtain product (1.82 g, 7.66 mmol) as a colorless oil in quantitative yield after column chromatography (hexanes/EtOAc = 6:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.21 (m, 2H), 6.91 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 5.06 (br, 1H), 4.30 (d, *J* = 6.0 Hz, 2H), 3.82 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.5, 156.0, 129.4, 128.7, 127.1, 120.6, 110.2, 79.2, 55.3, 40.5, 28.5; IR (neat) 3357, 2976, 1699, 1493, 1242, 1168 cm^{-1}; HRMS (ES^+) calcd. for $C_{13}H_{19}NO_3Na$ $[M+Na]^+$ 260.1263, found 260.1253.

General Procedure for the Preparation of Boc-Protected Secondary Aminomethyl Pinacolborates.

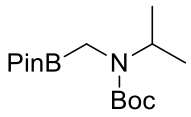


***tert*-Butyl *n*-Butyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.**

A round bottomed flask was charged with *tert*-butyl *n*-butylcarbamate (5.9 g, 34.2 mmol, 1.2 equiv) in THF (171 mL). The solution was cooled to –78 ºC, and *n*-BuLi in hexanes (2.5 M, 14 mL, 34.2 mmol, 1.2 equiv) was added slowly to the solution at –78 ºC. The resulting mixture was stirred at rt for 10 min. Iodomethylpinacolboronate (7.4 g, 27.6 mmol,

1.0 equiv) was added to reaction mixture at rt, and stirred at rt overnight. Then the reaction was quenched by the addition of saturated aq. NH4Cl solution (30 mL). The mixture was extracted with EtOAc (2 ×40 mL). The organic layer was dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography (hexanes/EtOAc = 9:1 to 1:1) to afford the product (5.6 g, 18.0 mmol) as a colorless oil in 65% yield.

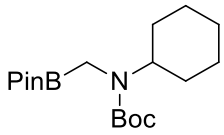
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.18 (t, *J* = 7.0 Hz, 2H), 2.35 (s, 2H), 1.59–1.40 (m, 11H), 1.31–1.19 (m, 14H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 161.1, 85.3, 80.5, 46.3, 29.2, 28.5, 25.2, 19.8, 13.7, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 15.2; IR (neat) 2972, 1682, 1613, 1369, 1161, 1143 cm^{-1}; HRMS (ES^+) calcd. for $C_{16}H_{32}NO_4BNa$ $[M+Na]^+$ 336.2322, found 336.2328.



***tert*-Butyl Isopropyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.** The reaction was carried out with *tert*-butyl isopropylcarbamate (705 mg, 4.43 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolborates to obtain product (761 mg, 2.54 mmol) as a white solid in 69% yield after column chromatography (hexanes/EtOAc = 7:1 to 3:1).

mp: 54–58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12–3.88 (m, 1H), 2.23 (s, 2H), 1.52 (s, 9H), 1.19 (s, 12H), 1.09 (d, *J* = 6.5 Hz, 6 H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.8, 86.2, 80.0, 45.4, 28.6, 25.2, 19.9, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$)

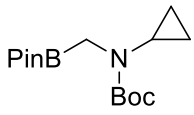
δ 13.1; IR (neat) 2975, 1688, 1602, 1523, 1371, 1162 cm^{-1}; HRMS (ES^+) calcd. for $C_{15}H_{30}BNO_4Na$ $[M+Na]^+$ 322.2166, found 322.2173.



***tert*-Butyl Cyclohexyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.**

The reaction was carried out with *tert*-butyl cyclohexylcarbamate (1.5 g, 7.53 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolboronates to obtain product (1.45 g, 4.27 mmol) as a colorless oil in 68% yield after column chromatography (hexanes/EtOAc = 8:1 to 2:1).

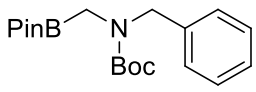
^1H NMR (500 MHz, $CDCl_3$) δ 3.52–3.44 (m, 1H), 2.56 (s, 2H), 1.82–1.74 (m, 2H), 1.66–1.57 (m, 3H), 1.52 (s, 9H), 1.46–1.35 (m, 2H), 1.33–1.20 (s, 2H), 1.19 (s, 12H), 1.13–1.02 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 161.0, 86.2, 79.9, 53.9, 30.2, 28.6, 25.5, 25.4, 25.2, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 13.9; IR (neat) 2932, 1600, 1519, 1158, 1124 cm^{-1}; HRMS (ES^+) calcd. for $C_{18}H_{35}BNO_4$ $[M+H]^+$ 340.2659, found 340.2659.



***tert*-Butyl Cyclopropyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.**

The reaction was carried out with *tert*-butyl cyclopropylcarbamate (641 mg, 4.08 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolborates to obtain product (556 mg, 1.87 mmol) as a colorless oil in 55% yield after column chromatography (hexanes/EtOAc = 6:1 to 3:1).

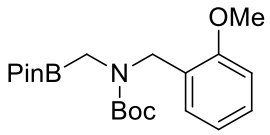
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55 (s, 1H), 2.35 (s, 2H), 1.51 (s, 9H), 1.20 (s, 12H), 0.69–0.61 (m, 4H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ□161.8, 84.9, 80.6, 37.8, 28.4, 28.2*, 25.0, 24.8*, 6.3, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 16.8; IR (neat) 2975, 1686, 1366, 1144 cm^{-1}; HRMS (ES^+) calcd. for $C_{15}H_{29}BNO_4$ $[M+H]^+$ 298.2190, found 298.2197.



***tert*-Butyl Benzyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.**

The reaction was carried out with *tert*-butyl benzylcarbamate (800 mg, 3.86 mmol, 1.1 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolborates to obtain product (556 mg, 1.87 mmol) as a colorless oil in 41% yield after column chromatography (hexanes/EtOAc = 10:1 to 5:1).

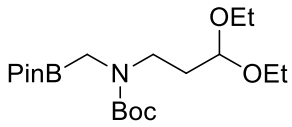
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.23 (m, 3H), 7.20–7.16 (m, 2H), 4.35 (s, 2H), 2.36 (s, 2H), 1.52 (s, 9H), 1.21 (s, 12H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.3, 136.3, 128.6, 128.0, 127.7, 84.9, 81.0, 51.3, 28.5, 25.1, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 18.2; IR (neat) 2977, 2358, 1695, 1455, 1368, 1152 cm^{-1}; HRMS (ES^+) calcd. for $C_{19}H_{30}BNO_4Na$ $[M+Na]^+$ 370.2166, found 370.2170.



***tert*-Butyl 2-Methoxybenzyl{(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl} carbamate.**

The reaction was carried out with *tert*-butyl 2-methoxybenzylcarbamate (1.1 g, 4.64 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolborates to obtain product (877 mg, 2.32 mmol) as a white solid in 60% yield after column chromatography (hexanes/EtOAc = 8:1 to 2:1).

mp: 78–81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26–7.20 (m, 1H), 7.13–7.08 (m, 1H), 6.92–6.87 (m, 1H), 6.86–6.81 (m, 1H), 4.38 (s, 2H), 3.80 (s, 3H), 2.34 (s, 2H), 1.52 (s, 9H), 1.20 (s, 12H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.8, 157.5, 129.4, 128.9, 124.2, 120.4, 110.3, 84.9, 80.6, 55.2, 45.8, 28.5, 25.2, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 17.0; IR (neat) 2970, 1610, 1532, 1158, 1158, 1140, 1110 cm^{-1}; HRMS (ES^+) calcd. for $C_{20}H_{33}BNO_5$ $[M+H]^+$ 378.2452, found 378.2462.

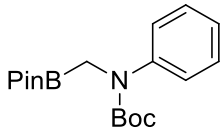


***tert*-Butyl (3,3-Diethoxypropyl){(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl}carbamate.**

The reaction was carried out with *tert*-butyl (3,3-diethoxypropyl)carbamate (1.5 g, 6.18 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected

secondary aminomethyl pinacolborates to obtain product (1.5 g, 3.88 mmol) as a colorless oil in 49% yield after column chromatography (hexanes/EtOAc = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.48 (dd, *J* = 5.5, 5.5 Hz, 1H), 3.68–3.59 (m, 2H), 3.52–3.44 (m, 2H), 3.26 (dd, *J* = 7.5, 7.5 Hz, 2H), 2.39 (s, 2H), 1.85–1.78 (m, 2H), 1.23 (s, 9H), 1.23–1.18 (m, 18H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.6, 100.5, 85.1, 80.5, 61.2, 42.9, 31.4, 28.4, 25.0, 15.3, one carbon was not detected; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 16.3; IR (neat) 2975, 1693, 1611, 1371, 1141, 1062 cm^{-1}; HRMS (ES^+) calcd. for $C_{19}H_{38}BNO_6Na$ $[M+Na]^+$ 410.2690, found 410.2687.

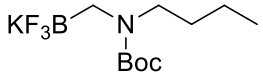


***tert*-Butyl Phenyl((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)carbamate.**

The reaction was carried out with *tert*-butyl phenylcarbamate (1.0 g, 5.17 mmol, 1.2 equiv) according to the general procedure for the preparation of Boc-protected secondary aminomethyl pinacolborates to obtain product (916 mg, 2.75 mmol) as a light yellow oil in 64% yield after column chromatography (hexanes/EtOAc = 7:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.28 (m, 2H), 7.27–7.21 (m, 2H), 7.18–7.13 (m, 1H), 2.93 (s, 2H), 1.50 (s, 9H), 1.25 (s, 12H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 159.1, 140.9, 128.6, 125.7, 124.1, 85.6, 81.3, 40.8, 28.4, 25.1; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 18.3; IR (neat) 2976, 1686, 1369, 1143 cm^{-1}; HRMS (ES^+) calcd. for $C_{18}H_{28}BNO_4Na$ $[M+Na]^+$ 356.2009, found 356.2005.

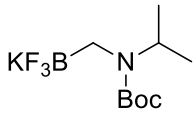
General Procedure for the Preparation of Potassium Boc-Protected Secondary Aminomethyltrifluoroborates.



Potassium *tert*-Butyl Butyl{(trifluoroborato)methyl}carbamate.

The corresponding boronate ester (7.0 g, 22.2 mmol, 1.0 equiv) was dissolved in acetone (44 mL) and cooled to 0 ºC. KHF_2 (5.2 g, 66.7 mmol, 3.0 equiv) was added to solution, and then H_2O (15 mL) was added at 0 ºC. The reaction mixture was stirred for 30 min at rt. The solution was concentrated in vacuo and then dried in vacuo overnight. The crude mixture was extracted with acetone (3 × 30 mL), and the extracts were combined and concentrated. Et_2O (100 mL) was added to precipitate the product. The solution was sonicated for 15 min and stored in the refrigerator overnight. The solid was filtered and dried in vacuo to provide the product (4.4 g, 14.9 mmol) as a white solid in 67% yield.

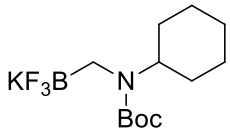
mp (transition): 135–138 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 3.21 (dd, J = 7.5, 7.5 Hz, 2H), 2.35–2.29 (m, 2H), 1.55–1.47 (m, 2H), 1.41 (s, 9H), 1.31–1.23 (m, 2H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 156.6, 77.9, 48.6, 30.7, 28.9, 20.7, 14.3, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –142.5; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.03; IR (neat) 2956, 2928, 1664 cm^{-1}; HRMS (ES$^-$) calcd. for $C_{10}H_{20}BF_3NO_2$ $[M–K]^-$ 254.1539, found 254.1538.



Potassium *tert*-Butyl Isopropyl{(trifluoroborato)methyl}carbamate.

The reaction was carried out with the corresponding boronate ester (688 mg, 2.30 mmol, 1.0 equiv) according to the general procedure for the preparation of potassium Boc-protected secondary aminomethyltrifluoroborates to obtain product (456 mg, 1.63 mmol) as a white solid in 71% yield.

mp: 203–206 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 4.02–3.91 (m, 1H), 2.21 (s, 2H), 1.41 (s, 9H), 1.12 (d, J = 6.5 Hz, 6H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 156.4, 77.8, 49.1, 29.1, 20.8, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –141.6; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.24; IR (neat) 2973, 1677, 1099 cm^{-1}; HRMS (ES^{-}) calcd. for $C_{10}H_{21}BF_2NO_3$ [M–(FK)+(OMe)]$^{-}$ 252.1583, found 252.1596.

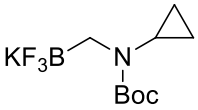


Potassium *tert*-Butyl Cyclohexyl{(trifluoroborato)methyl}carbamate.

The reaction was carried out with the corresponding boronate ester (1.35 g, 3.98 mmol, 1.0 equiv) according to the general procedure for the preparation of potassium Boc-protected secondary aminomethyltrifluoroborates to obtain product (1.11 g, 3.48 mmol) as a white solid in 87% yield.

mp (transition): 207–210 °C; ^{1}H NMR (500 MHz, MeOD) δ 3.66–3.59 (m, 1H), 2.34–2.21 (m, 2H), 1.85–1.02 (m, 19H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 162.8, 90.9, 79.3, 55.6,

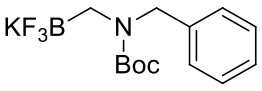
31.6*, 30.9, 29.1, 28.5*, 27.5, 26.9*, 26.7, 26.2*; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –144.4, –146.7*; ^{11}B NMR (128.4 MHz, MeOD) δ 3.71; IR (neat) 2931, 1679, 1109 cm^{-1}; HRMS (ES$^-$) calcd. for $C_{14}H_{28}BFNO_4$ [M–(F_2K)+(OMe)]$^-$ 304.2095, found 304.2093.



Potassium *tert*-Butyl Cyclopropyl{(trifluoroborato)methyl}carbamate.

The reaction was carried out with the corresponding boronate ester (384 mg, 1.29 mmol, 1.0 equiv) according to the general procedure for the preparation of potassium Boc-protected secondary aminomethyltrifluoroborates to obtain product (322 mg, 1.16 mmol) as a white solid in 90% yield.

mp (transition): 113–115 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 2.57–2.50 (m, 1H), 2.33–2.25 (m, 2H), 1.41 (s, 9H), 0.61–0.51 (m, 4H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 158.1, 78.0, 31.4, 29.0, 8.8, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –141.9; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.01; IR (neat) 2976, 1669, 1408, 1128 cm^{-1}; HRMS (ES$^-$) calcd. for $C_9H_{16}BF_3NO_2$ [M–K]$^-$ 238.1226, found 238.1226.

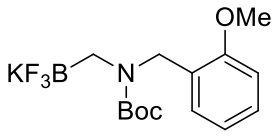


Potassium *tert*-Butyl Benzyl{(trifluoroborato)methyl}carbamate.

The reaction was carried out with the corresponding boronate ester (439 mg, 1.26 mmol, 1.0 equiv) according to the general procedure for the preparation of potassium Boc-

protected secondary aminomethyltrifluoroborates to obtain product (305 mg, 0.93 mmol) as a white solid in 74% yield.

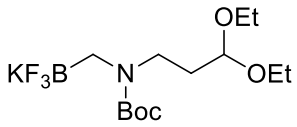
mp: 210–213 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 7.29–7.14 (m, 5H), 4.48 (s, 2H), 2.37–2.31 (m, 2H), 1.37 (s, 9H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 156.8, 141.2, 128.8, 128.1, 127.1, 78.4, 51.9, 28.8, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –142.1; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.16; IR (neat) 2987, 1665, 997 cm^{-1}; HRMS (ES$^-$) calcd. for $C_{13}H_{18}BF_3NO_2$ [M–K]$^-$ 288.1383, found 288.1386.



Potassium *tert*-Butyl 2-Methoxybenzyl{(trifluoroborato)methyl}carbamate.

The reaction was carried out with the corresponding boronate ester (613 mg, 1.62 mmol, 1.0 equiv) according to the general procedure for the preparation of potassium Boc-protected secondary aminomethyltrifluoroborates to obtain product (511 mg, 1.43 mmol) as a white solid in 88% yield.

mp (transition): 158–161 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 7.17 (dd, J = 7.5, 7.5 Hz, 1H), 7.08 (d, J = 7.0 Hz, 1H), 6.94–6.87 (m, 2H), 4.49 (s, 2H), 3.80 (s, 3H), 2.40–2.34 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 158.0, 157.2, 128.6, 127.9, 127.4, 120.8, 110.8, 78.2, 55.5, 47.4, 28.8, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –142.4; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.40; IR (neat) 2969, 1680, 1240, 1000 cm^{-1}; HRMS (ES$^-$) calcd. for $C_{14}H_{20}BF_3NO_3$ [M–K]$^-$ 318.1488, found 318.1493.



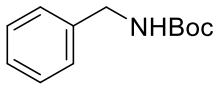
Potassium *tert*-Butyl (3,3-Diethoxypropyl){(trifluoroborato)methyl}carbamate.

The corresponding boronate ester (787 mg, 2.03 mmol, 1.0 equiv) was dissolved in theacetone (4 mL) and cooled to 0 ºC. K_2CO_3 (280 mg, 2.03 mmol, 1.0 equiv) was added to the solution, then H_2O (2 mL) was added at 0 ºC. After stirring for 10 min at 0 ºC, KHF_2 (793 mg, 10.15 mmol, 5 equiv) was added. The reaction mixture was stirred for 1.5 h at rt. The solution was concentrated in vacuo and then dried in vacuo overnight. The crude mixture was extracted with acetone (3 × 15 mL), and the extracts were combined and concentrated. Hexanes (40 mL) were added to precipitate the product. The solution was sonicated for 15 min and the solid was filtered and dried in vacuo to provide the product (395 mg, 1.08 mmol) as a white solid in 53% yield.

mp (transition): 138–140 °C; ^{1}H NMR (500 MHz, acetone-d_6) δ 4.47 (dd, J = 5.5, 5.5 Hz, 1H), 3.64–3.57 (m, 2H), 3.50–3.41 (m, 2H), 3.35–3.20 (m, 2H), 2.30 (s, 2H), 1.88–1.79 (m, 2H), 1.42 (s, 9H), 1.14 (dd, J = 7.0, 7.0 Hz, 6H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 156.5, 102.0, 78.0, 60.9, 45.3, 32.7, 28.9, 15.7, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –142.3; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.11; IR (neat) 2975, 1660, 1061 cm^{-1}; HRMS (ES$^-$) calcd. for $C_{13}H_{26}BF_3NO_4$ $[M–K]^-$ 328.1907, found 328.1898.

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction of Boc-Protected Primary Aminomethyltrifluoroborate with Aryl and Hetaryl Chlorides.

A sealed tube was charged with potassium *tert*-butoxycarbonyl aminomethyltrifluoroborate (62 mg, 0.263 mmol, 1.05 equiv), an aryl or hetaryl chloride (0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (3 mg, 0.013 mmol, 0.05 equiv), SPhos or XPhos ligand (0.03 mmol, 0.1 equiv) and K_2CO_3 (104 mg, 0.75 mmol, 3.0 equiv). The mixture was then was purged 3 times with argon. (Liquid electrophiles were added last, after purging with argon). Toluene / H_2O (4:1, 0.8 mL/0.2 mL) was then added to the reaction tube. The reaction mixture was stirred for 22 h at 85 °C and then cooled to rt. A solution of pH 7 buffer (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$) and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.



***tert*-Butyl Benzylcarbamate.**

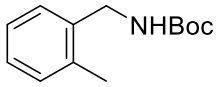
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 91% yield (47 mg, 0.23 mmol).

XPhos: 74% yield (38 mg, 0.18 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.22 (m, 5H), 4.89 (br, 1H), 4.31 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 139.0, 128.7, 127.6, 127.4, 79.5, 44.8, 28.5.

Data is consistent with that reported in the literature.[29]



***tert*-Butyl 2-Methylbenzylcarbamate.**

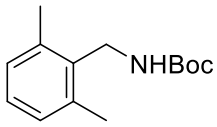
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 76% yield (42 mg, 0.19 mmol).

XPhos: 90% yield (50 mg, 0.23 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.12 (m, 4H), 4.71 (br, 1H), 4.31 (d, *J* = 5.5 Hz, 2H), 2.31 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 136.6, 136.4, 130.5, 128.1, 127.6, 126.2, 79.5, 42.9, 28.5, 19.0.

Data is consistent with that reported in the literature.[30]



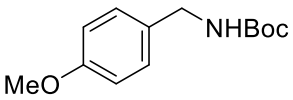
***tert*-Butyl 2,6-Dimethylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 10:1).

SPhos: 90% yield (53 mg, 0.23 mmol).

XPhos: 76% yield (45 mg, 0.19 mmol).

mp: 73–74 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12–7.00 (m, 3H), 4.39 (br, 1H), 4.35 (d, *J* = 4.0 Hz, 2H), 2.37 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 137.5, 134.5, 128.5, 127.9, 79.5, 39.2, 28.5, 19.8; IR (neat) 3385, 1682, 1504 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{21}NO_2Na$ $[M+Na]^+$ 258.1470, found 258.1475.



***tert*-Butyl 4-Methoxybenzylcarbamate.**

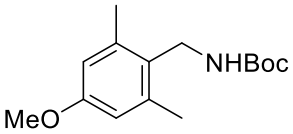
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 5:1).

SPhos: 69% yield (41 mg, 0.17 mmol).

XPhos: 88% yield (52 mg, 0.22 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.84 (br, 1H), 4.24 (d, *J* = 5.5 Hz, 2H), 3.79 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 159.0, 156.0, 131.2, 128.9, 114.1, 79.5, 55.4, 44.3, 28.5.

Data is consistent with that reported in the literature.[31]



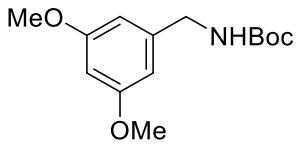
***tert*-Butyl 4-Methoxy-2,6-dimethylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 15:1).

SPhos: 78% yield (52 mg, 0.20 mmol).

XPhos: 71% yield (47 mg, 0.18 mmol).

mp: 108–110 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.36 (br, 1H), 4.29 (m, 2H), 3.76 (s, 3H), 2.34 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.8, 155.8, 139.0, 126.9, 113.7, 79.3, 55.2, 38.7, 28.5, 20.1; IR (neat) 3374, 3318, 1680, 1522 cm^{-1}; HRMS (CI+) calcd. for $C_{15}H_{24}NO_3$ $[M+H]^+$ 266.1756, found 266.1768.



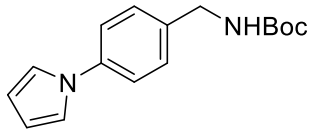
***tert*-Butyl 3,5-Dimethoxybenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 6:1).

SPhos: 75% yield (50 mg, 0.19 mmol).

XPhos: 79% yield (52 mg, 0.20 mmol).

mp: 64–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44–6.41 (m, 2H), 6.35 (t, J = 2.0 Hz, 1H), 4.89 (br, 1H), 4.25 (d, J = 6.0 Hz, 2H), 3.77 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 161.1, 156.0, 141.5, 105.4, 99.4, 79.6, 55.4, 44.9, 28.5; IR (neat) 3318, 1677, 1597, 1535 cm^{-1}; HRMS (CI+) calcd. for $C_{14}H_{22}NO_4$ $[M+H]^+$ 268.1549, found 268.1528.



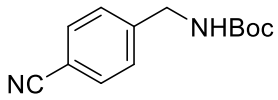
***tert*-Butyl 4-(1H-Pyrrol-1-yl)benzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 5:1).

SPhos: 86% yield (58 mg, 0.21 mmol).

XPhos: 87% yield (59 mg, 0.22 mmol).

mp: 118–119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.27 (m, 4H), 7.08–7.03 (m, 2H), 6.34 (t, *J* = 2.5 Hz, 2H), 4.94 (br, 1H), 4.31 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 140.0, 136.5, 128.7, 120.7, 119.4, 110.5, 79.7, 44.2, 28.5; IR (neat) 3385, 1685, 1520 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{20}N_2O_2Na$ $[M+Na]^+$ 295.1422, found 295.1419.



***tert*-Butyl 4-Cyanobenzylcarbamate.**

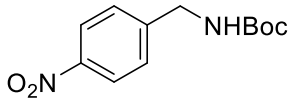
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 90% yield (52 mg, 0.22 mmol).

XPhos: 88% yield (51 mg, 0.22 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 5.11 (br, 1H), 4.37 (d, *J* = 6.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 144.8, 132.5, 127.9, 118.9, 111.1, 80.1, 44.2, 28.4.

Data is consistent with that reported in the literature.[32]



***tert*-Butyl 4-Nitrobenzylcarbamate.**

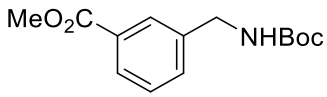
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 90% yield (57 mg, 0.23 mmol).

XPhos: 88% yield (55 mg, 0.22 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 5.13 (br, 1H), 4.12 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 147.3, 146.9, 127.9, 123.9, 80.2, 44.1, 28.4.

Data is consistent with that reported in the literature.[33]



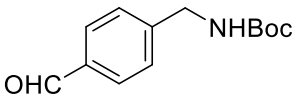
Methyl 3-[{(*tert*-Butoxycarbonyl)amino}methyl]benzoate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 90% yield (60 mg, 0.23 mmol).

XPhos: 86% yield (57 mg, 0.22 mmol).

mp: 86–90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.90 (m, 2H), 7.51–7.46 (m, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 5.05 (br, 1H), 4.36 (d, *J* = 5.5 Hz, 2H), 3.91 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.9, 156.0, 139.5, 132.1, 130.5, 128.8, 128.6, 128.5, 79.8, 44.3, 28.5; IR (neat) 3380, 1713, 1698 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{19}NO_4Na$ $[M+Na]^+$ 288.1212, found 288.1218.



***tert*-Butyl 4-Formylbenzylcarbamate.**

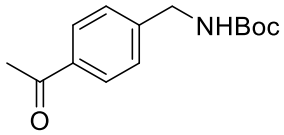
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 70% yield (41 mg, 0.17 mmol).

XPhos: 77% yield (45 mg, 0.19 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 7.5 Hz, 2H), 5.09 (br, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 192.0, 156.0, 146.3, 135.6, 130.2, 127.8, 80.0, 44.4, 28.5.

Data is consistent with that reported in the literature.[34]



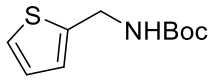
***tert*-Butyl 4-Acetylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 69% yield (43 mg, 0.17 mmol).

XPhos: 71% yield (44 mg, 0.18 mmol).

mp: 67–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.09 (br, 1H), 4.37 (d, *J* = 6.0 Hz, 2H), 2.59 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 197.8, 156.0, 144.7, 136.3, 128.8, 127.4, 79.9, 44.4, 28.5, 26.7; IR (neat) 3318, 1677, 1530 cm^{-1}; HRMS (CI+) calcd. for $C_{14}H_{20}NO_3$ $[M+H]^+$ 250.1443, found 250.1438.



***tert*-Butyl (Thiophen-2-ylmethyl)carbamate.**

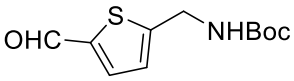
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow oil after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 78% yield (42 mg, 0.20 mmol).

XPhos: 60% yield (32 mg, 0.15 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22–7.18 (m, 1H), 6.96–6.91 (m, 2H), 4.95 (br, 1H), 4.47 (d, *J* = 5.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.6, 142.0, 126.9, 125.6, 125.0, 79.8, 39.6, 28.5.

Data is consistent with that reported in the literature.[35]



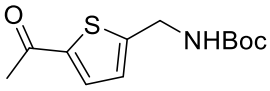
***tert*-Butyl {(5-Formylthiophen-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a yellow oil after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 70% yield (42 mg, 0.17 mmol).

XPhos: 75% yield (45 mg, 0.19 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.63 (d, *J* = 4.0 Hz, 1H), 7.05 (d, *J* = 3.5 Hz, 1H), 5.34 (br, 1H), 4.51 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 183.0, 155.7, 154.1, 142.7, 136.9, 126.1, 80.2, 40.1, 28.4; IR (neat) 3333, 1697, 1665 cm^{-1}; HRMS (ES+) calcd. for $C_{11}H_{15}NO_3SNa$ $[M+Na]^+$ 264.0670, found 264.0671.



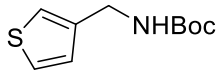
***tert*-Butyl {(5-Acetylthiophen-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a yellow oil after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 85% yield (54 mg, 0.21 mmol).

XPhos: 80% yield (51 mg, 0.20 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 4.0 Hz, 1H), 6.97 (d, *J* = 3.5 Hz, 1H), 5.01 (br, 1H), 4.48 (d, *J* = 5.5 Hz, 2H), 2.52 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 190.7, 155.7, 152.1, 143.5, 132.8, 126.0, 80.2, 40.1, 28.5, 26.7; IR (neat) 3339, 1698, 1655 cm^{-1}; HRMS (ES+) calcd. for $C_{12}H_{17}NO_3SNa$ $[M+Na]^+$ 278.0827, found 278.0837.



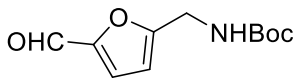
***tert*-Butyl (Thiophen-3-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 10:1).

SPhos: 45% yield (24 mg, 0.11 mmol).

XPhos: 73% yield (39 mg, 0.18 mmol).

mp: 54–56 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.25 (m, 1H), 7.12 (s, 1H), 7.04–7.00 (m, 1H), 4.85 (br, 1H), 4.31–4.29 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.9, 140.0, 127.3, 126.4, 121.9, 79.6, 40.0, 28.5; IR (neat) 3300, 1679, 1534 cm^{-1}; HRMS (ES+) calcd. for $C_{10}H_{15}NO_2SNa$ $[M+Na]^+$ 236.0721, found 236.0714.



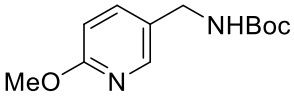
***tert*-Butyl {(5-Formylfuran-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a dark brown oil after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 66% yield (37 mg, 0.16 mmol).

XPhos: 73% yield (41 mg, 0.18 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.20 (d, *J* = 3.0 Hz, 1H), 6.45 (s, 1H), 5.12 (br, 1H), 4.40–4.35 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 177.5, 159.2, 155.6, 152.4, 123.1, 109.9, 80.3, 38.0, 28.4; IR (neat) 3328, 1699, 1673 cm^{-1}; HRMS (CI+) calcd. for $C_{11}H_{16}NO_4$ $[M+H]^+$ 226.1079, found 226.1079.



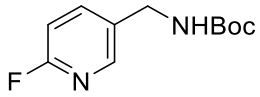
***tert*-Butyl {(6-Methoxypyridin-3-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 5:1).

SPhos: 86% yield (51 mg, 0.21 mmol).

XPhos: 62% yield (37 mg, 0.16 mmol).

mp: 55–58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.5 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 4.93 (br, 1H), 4.23 (d, *J* = 5.0 Hz, 2H), 3.92 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.7, 155.9, 145.9, 138.6, 127.4, 111.0, 79.7, 53.5, 41.7, 28.5; IR (neat) 3358, 1685, 1522, 1495 cm^{-1}; HRMS (ES+) calcd. for $C_{12}H_{19}N_2O_3$ $[M+H]^+$ 239.1396, found 239.1404.



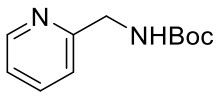
***tert*-Butyl {(6-Fluoropyridin-3-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 67% yield (38 mg, 0.17 mmol).

XPhos: 74% yield (42 mg, 0.19 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.76 (dd, *J* = 7.0, 7.0 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.12 (br, 1H), 4.31 (d, *J* = 5.0 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.1 (d, *J* = 238.5 Hz), 156.0, 146.6 (d, *J* = 14.7 Hz), 140.8, 132.6 (d, *J* = 4.5 Hz), 109.6 ((d, *J* = 37.5 Hz), 80.1, 41.4, 28.4; IR (neat) 3323, 1697 cm^{-1}; HRMS (ES+) calcd. for $C_{11}H_{16}N_2O_2F$ $[M+H]^+$ 227.1196, found 227.1196.



***tert*-Butyl (Pyridin-2-ylmethyl)carbamate.**

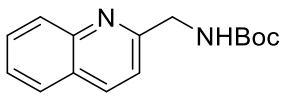
According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow oil after flash chromatography (hexanes/EtOAc = 1:1).

SPhos: 35% yield (18 mg, 0.09 mmol).

XPhos: 33% yield (17 mg, 0.08 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 5.0 Hz, 1H), 7.65 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 7.27 (dd, *J* = 4.0, 4.0 Hz, 1H), 7.18 (dd, *J* = 7.0, 5.0 Hz, 1H), 5.59 (br, 1H), 4.45 (d, *J* = 5.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.6, 156.1, 149.2, 136.8,

122.3, 121.8, 79.6, 45.9, 28.5; IR (neat) 3344, 1781, 1709 cm^{-1}; HRMS (ES+) calcd. for $C_{11}H_{16}N_2O_2Na$ $[M+Na]^+$ 231.1109, found 231.1113.



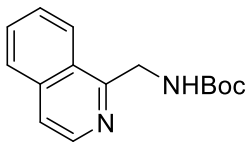
***tert*-Butyl (Quinolin-2-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow solid after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 51% yield (33 mg, 0.13 mmol).

XPhos: 36% yield (23 mg, 0.09 mmol).

mp: 54–58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.71 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.52 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 5.96 (br, 1H), 4.63 (d, *J* = 4.5 Hz, 2H), 1.50 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.4, 156.2, 147.5, 136.8, 129.8, 129.0, 127.7, 127.4, 126.4, 119.9, 79.6, 46.3, 28.6; IR (neat) 3235, 1709 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1447, found 259.1436.



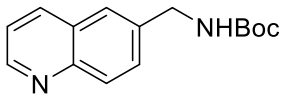
***tert*-Butyl (Isoquinolin-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a yellow oil after flash chromatography (hexanes/EtOAc = 5:1).

SPhos: 37% yield (24 mg, 0.09 mmol).

XPhos: 62% yield (40 mg, 0.16 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 5.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.71 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.65 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.58 (d, *J* = 5.5 Hz, 1H), 6.36 (br, 1H), 4.98 (d, *J* = 4.0 Hz, 2H), 1.51 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.2, 155.2, 141.2, 136.1, 130.4, 127.8, 127.5, 126.0, 124.0, 120.5, 79.5, 43.3, 28.6; IR (neat) 3344, 1776, 1706 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1447, found 259.1447.



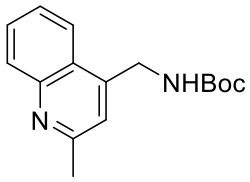
***tert*-Butyl (Quinolin-6-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 1:1).

SPhos: 57% yield (37 mg, 0.14 mmol).

XPhos: 70% yield (45 mg, 0.17 mmol).

mp: 75–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92–8.86 (m, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 9.0 Hz, 1H), 7.69 (s, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.39 (dd, *J* = 8.5, 4.5 Hz, 1H), 5.14 (br, 1H), 4.50 (d, *J* = 5.5 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 150.4, 147.8, 137.5, 136.0, 130.0, 129.4, 128.3, 125.7, 121.5, 79.9, 44.6, 28.5; IR (neat) 3256, 1708 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1447, found 259.1457.



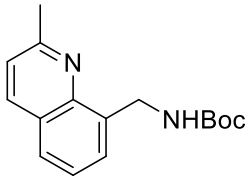
***tert*-Butyl {(2-Methylquinolin-4-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 1:1).

SPhos: 59% yield (40 mg, 0.15 mmol).

XPhos: 37% yield (25 mg, 0.09 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.66 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.49 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.19 (s, 1H), 5.17 (br, 1H), 4.73 (d, *J* = 5.0 Hz, 2H), 2.69 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.9, 155.9, 148.1, 144.0, 129.5, 129.4, 126.0, 124.7, 122.8, 120.2, 80.0, 41.5, 28.5, 25.5; IR (neat) 3333, 1699 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{21}N_2O_2$ $[M+H]^+$ 273.1603, found 273.1595.



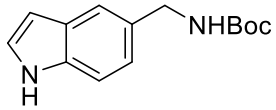
***tert*-Butyl {(2-Methylquinolin-8-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow oil after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 76% yield (52 mg, 0.19 mmol).

XPhos: 87% yield (59 mg, 0.22 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.5 Hz, 1H), 7.68–7.61 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 5.92 (br, 1H), 4.84 (d, *J* = 6.0 Hz, 2H), 2.73 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.4, 156.2, 146.5, 136.4, 136.3, 128.9, 127.2, 126.6, 125.5, 121.9, 79.1, 42.4, 28.6, 25.8; IR (neat) 3344, 1704 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{21}N_2O_2$ $[M+H]^+$ 273.1603, found 273.1596.



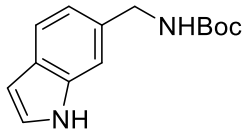
***tert*-Butyl {(1H-Indol-5-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 65% yield (40 mg, 0.16 mmol).

XPhos: 67% yield (41 mg, 0.17 mmol).

mp: 86–89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (br, 1H), 7.53 (s, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.18 (dd, *J* = 2.5, 2.5 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.52–6.47 (m, 1H), 4.85 (br, 1H), 4.39 (d, *J* = 5.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 135.3, 130.2, 128.1, 124.9, 122.2, 119.9, 111.4, 102.5, 79.4, 45.4, 28.6; IR (neat) 3356, 3318, 1697, 1655 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{18}N_2O_2Na$ $[M+Na]^+$ 269.1266, found 269.1265.



***tert*-Butyl {(1H-Indol-6-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 65% yield (41 mg, 0.17 mmol).

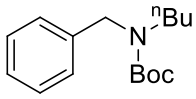
XPhos: 70% yield (43 mg, 0.18 mmol).

mp: 106–108 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (br, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.29 (s, 1H), 7.17 (dd, *J* = 2.5, 2.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.54–6.49 (m, 1H), 4.89 (br, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 136.1, 132.8, 127.3, 124.7, 120.9, 119.9, 110.4, 102.5, 79.5, 45.4, 28.6; IR (neat) 3390, 3351, 1670 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{18}N_2O_2Na$ $[M+Na]^+$ 269.1266, found 269.1265.

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction of Boc-Protected Secondary Aminomethyltrifluoroborates with Aryl and Hetaryl Chlorides.

A sealed tube was charged with potassium *tert*-butyl butyl{(trifluoroborato)methyl}carbamate (77 mg, 0.263 mmol, 1.05 equiv), an aryl or hetaryl chloride (0.250 mmol, 1.0 equiv), XPhos-Pd-G2 (8 mg, 0.010 mmol, 0.04 equiv), and Cs_2CO_3 (244 mg, 0.750 mmol, 3.0 equiv). The mixture was then was purged three times with argon. Toluene / H_2O (0.5 M, 4:1, 0.4 mL/0.1 mL) was then added to the reaction tube. The reaction mixture was stirred for 3 or 18 h as denoted at 85 °C and then

cooled to rt. H_2O (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$) and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.

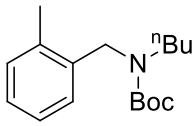


***tert*-Butyl Benzyl(butyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (60 mg, 0.228 mmol) was obtained as a colorless oil in 91% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.37–7.18 (m, 5H), 4.44 (s, 2H), 4.41* (s, 2H), 3.26–3.09 (m, 2H), 1.56–1.37 (m, 11H), 1.33–1.21 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.8*, 139.0, 138.8*, 128.5, 127.8, 127.1, 79.6, 50.5, 49.8*, 46.6, 46.2*, 30.3, 30.1*, 28.6, 20.1, 14.0.

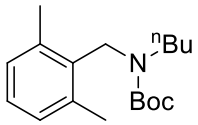
Data is consistent with that reported in the literature.[36]



***tert*-Butyl Butyl(2-methylbenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (62 mg, 0.224 mmol) was obtained as a colorless oil in 89% yield after column chromatography (hexanes/EtOAc = 20:1).

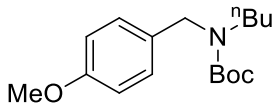
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.18–7.09 (m, 4H), 4.46 (s, 2H), 4.40* (s, 2H), 3.22–3.04 (m, 2H), 2.28 (s, 3H), 1.53–1.37 (m, 11H), 1.31–1.22 (m, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.9, 136.5, 136.0, 130.4, 127.7, 127.1, 126.0, 79.5, 48.3, 47.8*, 46.3, 45.9*, 30.3, 28.5, 28.2*, 20.2, 19.1, 14.0; IR (neat) 2961, 1693, 1414, 1249, 1170, 1143 cm^{-1}; HRMS (ES+) calcd. for $C_{17}H_{27}NO_2Na$ $[M+Na]^+$ 300.1939, found 300.1949.



***tert*-Butyl Butyl(2,6-dimethylbenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (69 mg, 0.237 mmol) was obtained as a colorless oil in 95% yield after column chromatography (hexanes/EtOAc = 20:1).

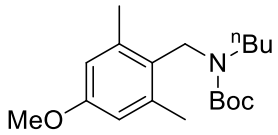
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10–7.06 (m, 1H), 7.00 (d, *J* = 7.5 Hz, 2H), 4.58 (s, 2H), 2.85 (s, 2H), 2.32 (s, 6H), 1.49 (s, 9H), 1.41–1.33 (m, 2H), 1.21–1.12 (m, 2H), 0.82 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (.8 MHz, $CDCl_3$) δ 155.6, 138.1, 133.9, 128.6, 127.5, 79.4, 44.3, 43.3, 30.5, 28.6, 20.2, 20.1, 13.9; IR (neat) 2961, 1692, 1413, 1172, 1141 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{29}NO_2Na$ $[M+Na]^+$ 314.2096, found 314.2084.



***tert*-Butyl Butyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (71 mg, 0.242 mmol) was obtained as a colorless oil in 97% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.16 (s, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.36 (s, 2H), 3.79 (s, 3H), 3.17* (s, 2H), 3.09 (s, 2H), 1.52–1.40 (m, 11H), 1.31–1.21 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 158.9, 130.9, 129.2, 128.5, 113.9, 79.5, 55.4, 49.8, 49.2*, 46.2, 46.0*, 30.3, 28.6, 20.1, 14.0; IR (neat) 2960, 1690, 1512, 1412, 1247, 1170, 1141 cm^{-1}; HRMS (ES+) calcd. for $C_{17}H_{27}NO_3Na$ $[M+Na]^+$ 316.1889, found 316.1896.

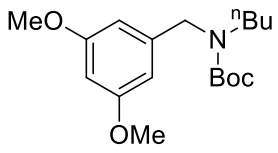


***tert*-Butyl Butyl(4-methoxy-2,6-dimethylbenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (80 mg, 0.249 mmol) was obtained as a colorless oil in 100% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.52 (s, 2H), 3.77 (s, 3H), 2.84 (s, 2H), 2.30 (s, 6H), 1.49 (s, 9H), 1.41–1.33 (m, 2H), 1.22–1.13 (m, 2H), 0.82 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 1158.4, 155.6, 139.5, 126.2, 113.8, 79.3, 55.1, 44.0, 42.8,

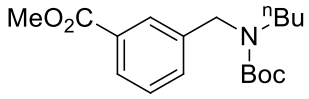
30.4, 28.6, 20.4, 20.2, 13.9; IR (neat) 2970, 1689, 1172, 1140 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{31}NO_3Na$ $[M+Na]^+$ 344.2202, found 344.2191.



***tert*-Butyl Butyl(3,5-dimethoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (78 mg, 0.241 mmol) was obtained as a colorless oil in 96% yield after column chromatography (hexanes/EtOAc = 20:1).

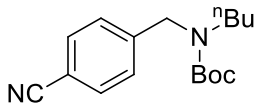
^1H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 6.42–6.33 (m, 3H), 4.38 (s, 2H), 4.34* (s, 2H), 3.77 (s, 6H), 3.23–3.09 (m, 2H), 1.54–1.41 (m, 11H), 1.33–1.23 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 161.0, 156.2, 155.7*, 141.5, 141.2*, 105.6, 105.1*, 99.0, 79.6, 55.4, 50.6, 49.9*, 46.5, 46.3*, 30.4, 30.1*, 28.6, 20.1, 14.0; IR (neat) 2960, 1691, 1597, 1414, 1205, 1156 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{29}NO_4Na$ $[M+Na]^+$ 346.1994, found 346.1989.



Methyl 3-[{(*tert*-Butoxycarbonyl)(butyl)amino}methyl]benzoate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (78 mg, 0.243 mmol) was obtained as a colorless oil in 97% yield after column chromatography (hexanes/EtOAc = 15:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.96–7.87 (m, 2H), 7.49–7.36 (m, 2H), 4.49 (s, 2H), 4.44* (s, 2H), 3.91 (s, 3H), 3.32–3.08 (m, 2H), 1.57–1.37 (m, 11H), 1.34–1.23 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 167.1, 156.2, 155.6*, 139.5, 139.2*, 132.2, 131.6, 130.4, 128.6, 79.8, 52.2, 50.3, 49.6*, 46.8, 46.5*, 30.3, 30.2*, 28.5, 20.0, 13.9; IR (neat) 2965, 2360, 2342, 1725, 1692, 1285, 1170 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{27}NO_4Na$ $[M+Na]^+$ 344.1838, found 344.1843.

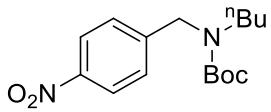


***tert*-Butyl Butyl(4-cyanobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (67 mg, 0.232 mmol) was obtained as a colorless oil in 93% yield after column chromatography (hexanes/EtOAc = 10:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.33 (s, 2H), 4.54–4.41 (m, 2H), 3.25–3.15 (m, 2H), 1.62–1.23 (m, 13H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.1, 144.8*, 144.5, 132.4, 128.1, 127.5*, 118.9, 111.0, 80.5, 50.6*, 49.9, 47.0, 30.4, 28.4, 20.0,

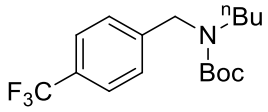
13.9; IR (neat) 2961, 2359, 2228, 1691, 1409, 1169, 1146 cm^{-1}; HRMS (ES+) calcd. for $C_{17}H_{24}N_2O_2Na$ $[M+Na]^+$ 311.1735, found 311.1726.



***tert*-Butyl Butyl(4-nitrobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (66 mg, 0.214 mmol) was obtained as a yellow oil in 86% yield after column chromatography (hexanes/EtOAc = 10:1).

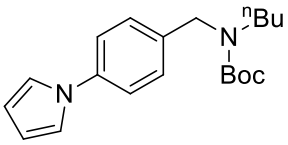
^1H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.5 Hz, 2H), 7.39 (s, 2H), 4.54–4.92 (m, 2H), 3.31–3.10 (m, 2H), 1.63–1.19 (m, 13H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.1, 147.2, 146.6*, 128.1, 127.5, 123.8, 80.2, 50.4*, 49.8, 47.4*, 47.1, 30.5, 28.5, 20.1, 13.9; IR (neat) 2963, 2360, 1692, 1521, 1344 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{24}N_2O_4Na$ $[M+Na]^+$ 331.1634, found 331.1629.



***tert*-Butyl Butyl{4-(trifluoromethyl)benzyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (66 mg, 0.199 mmol) was obtained as a colorless oil in 80% yield after column chromatography (hexanes/EtOAc = 20:1).

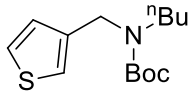
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2H), 7.39–7.30 (m, 2H), 4.51–4.45 (m, 2H), 3.29–3.12 (m, 2H), 1.58–1.37 (m, 11H), 1.33–1.25 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.6*, 143.3*, 143.0, 129.5 (q, *J* = 32.2 Hz), 127.8, 127.2*, 125.5 (q, *J* = 3.4 Hz), 124.3 (q, *J* = 271.7 Hz), 80.0, 50.4*, 49.7*, 46.7, 30.4, 28.5, 28.1*, 20.1, 13.9; IR (neat) 2966, 2360, 1693, 1325, 1163, 1126 cm^{-1}; HRMS (ES+) calcd. for $C_{17}H_{24}F_3NO_2Na$ $[M+Na]^+$ 354.1657, found 354.1648.



***tert*-Butyl 4-(1H-Pyrrol-1-yl)benzyl(butyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (77 mg, 0.234 mmol) was obtained as a colorless oil in 94% yield after column chromatography (hexanes/EtOAc = 20:1).

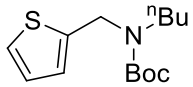
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.5 Hz, 2H), 7.32–7.25 (m, 2H), 7.09–7.05 (m, 2H), 6.36–6.31 (m, 2H), 4.47–4.39 (m, 2H), 3.26–3.09 (m, 2H), 1.56–1.38 (m, 11H), 1.33–1.24 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.7*, 139.9, 136.3, 128.9, 128.4*, 120.6, 119.4, 110.5, 79.8, 50.1*, 49.4, 46.7*, 46.5, 30.4, 30.3*, 28.6, 20.1, 14.0; IR (neat) 2961, 2360, 1689, 1522, 1413, 1329, 1169, 1143 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{28}N_2O_2Na$ $[M+Na]^+$ 351.2048, found 351.2037.



***tert*-Butyl Butyl(thiophen-3-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (63 mg, 0.234 mmol) was obtained as a colorless oil in 94% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 1H), 7.11–6.96 (m, 2H), 4.41 (s, 2H), 4.37* (s, 2H), 3.24–3.11 (m, 2H), 1.53–1.40 (m, 11H), 1.31–1.22 (m, 2H), 0.81 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.0, 155.5*, 139.9, 127.7, 127.3*, 126.0, 122.1, 121.6*, 79.5, 46.3, 46.0, 45.3*, 30.4, 30.2*, 28.6, 20.1, 14.0; IR (neat) 2961, 2931, 1689, 1169 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{23}NO_2SNa$ $[M+Na]^+$ 292. 1347, found 292.1342.

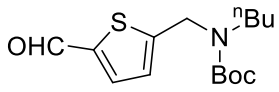


***tert*-Butyl Butyl(thiophen-2-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (54 mg, 0.200 mmol) was obtained as a light yellow oil in 80% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.24–7.18 (m, 1H), 6.95–6.88 (m, 2H), 4.56* (s, 2H), 4.51 (s, 2H), 3.33–3.15 (m, 2H), 1.55–1.43 (m, 11H), 1.33–1.23 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.8*, 155.2, 141.8, 126.5, 126.0*, 125.8, 125.1, 80.0, 79.7*,

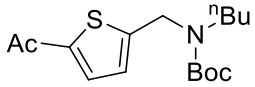
46.2, 45.6, 45.0*, 30.5*, 30.2, 28.6, 20.2, 14.0; IR (neat) 2960, 2932, 1693, 1154 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{23}NO_2SNa$ $[M+Na]^+$ 292.1347, found 292.1341.



***tert*-Butyl Butyl{(5-formylthiophen-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (68 mg, 0.229 mmol) was obtained as a yellow oil in 91% yield after column chromatography (hexanes/EtOAc = 6:1).

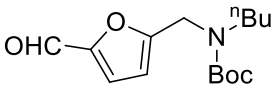
^1H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.64 (d, *J* = 3.5 Hz, 1H), 7.03 (s, 1H), 4.59 (s, 2H), 4.56* (s, 2H), 3.23 (s, 2H), 1.52–1.46 (m, 11H), 1.34–1.27 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 182.9, 155.7, 154.8*, 153.5, 143.0, 136.6, 126.6, 80.5*, 80.3, 47.0, 46.4*, 45.9, 30.6, 30.3*, 28.5, 20.0, 13.9; IR (neat) 2962, 2932, 1673, 1152 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{23}NO_3SNa$ $[M+Na]^+$ 320.1296, found 320.1287.



***tert*-Butyl {(5-Acetylthiophen-2-yl)methyl}(butyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, 18 h instead of 3 h, the product (71 mg, 0.228 mmol) was obtained as a light yellow oil in 93% yield after column chromatography (hexanes/EtOAc = 10:1).

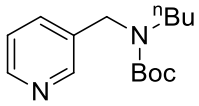
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.55 (s, 1H), 6.95 (s, 1H), 4.56 (s, 2H), 4.54* (s, 2H), 3.22 (s, 2H), 2.52 (s, 3H), 1.52–1.44 (m, 11H), 1.32–1.25 (m, 2H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 190.6, 155.7*, 154.9, 151.6, 143.5, 132.5, 132.4*, 126.5, 126.3*, 80.4*, 80.1, 46.8, 46.2*, 45.7, 30.5, 30.2*, 28.5, 26.6, 19.9, 13.9; IR (neat) 2960, 2931, 1691, 1662, 1275, 1153 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{25}NO_3SNa$ $[M+Na]^+$ 334.1453, found 334.1458.



***tert*-Butyl Butyl{(5-formylfuran-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (64 mg, 0.227 mmol) was obtained as a yellow oil in 91% yield after column chromatography (hexanes/EtOAc = 9:1).

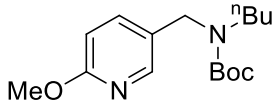
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 9.58 (s, 1H), 7.20 (d, *J* = 3.0 Hz, 1H), 6.46–6.44 (m, 1H), 4.42 (s, 2H), 4.43* (s, 2H), 3.32–3.25 (m, 2H), 1.54–1.38 (m, 11H), 1.35–1.25 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 177.4, 159.5, 155.7, 155.1*, 152.3, 127.8, 110.4, 109.6*, 80.3, 47.5, 44.6*, 43.9, 30.5, 29.8*, 28.5, 20.0, 13.9; IR (neat) 2962, 2932, 1682, 1165 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{23}NO_4Na$ $[M+Na]^+$ 304.1525, found 304.1524.



***tert*-Butyl Butyl(pyridin-3-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (56 mg, 0.212 mmol) was obtained as a colorless oil in 85% yield after column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.55–8.50 (m, 2H), 7.64–7.55 (m, 1H), 7.27 (dd, *J* = 7.5, 4.5 Hz, 1H), 4.51–4.48 (m, 2H), 3.24–3.10 (m, 2H), 1.57–1.37 (m, 11H), 1.33–1.22 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.2, 149.1, 148.7, 135.7, 134.9*, 134.4, 123.6, 80.0, 48.4*, 47.7, 47.0*, 46.6, 30.4, 28.5, 20.1, 13.9; IR (neat) 2961, 2932, 1690, 1412, 1168, 1144 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{25}N_2O_2$ $[M+H]^+$ 265.1916, found 265.1909.

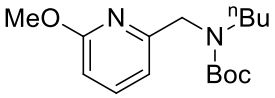


***tert*-Butyl Butyl{(6-methoxypyridin-3-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (68 mg, 0.231 mmol) was obtained as a light yellow oil in 92% yield after column chromatography (hexanes/EtOAc = 10:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.0 Hz, 1H), 7.52 (s, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 4.35 (s, 2H), 3.93 (s, 3H), 3.23–3.09 (m, 2H),

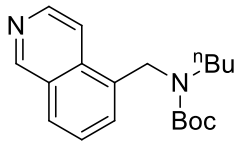
1.51–1.45 (m, 11H), 1.32–1.26 (m, 2H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 163.7, 156.1, 155.4*, 145.9, 138.8, 138.2*, 127.0, 110.9, 79.7, 53.4, 47.5, 46.9*, 46.1, 30.4, 28.5, 20.1, 13.9; IR (neat) 2960, 1691, 1493, 1289, 1169 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{27}N_2O_3$ $[M+H]^+$ 295.2022, found 295. 2020.



***tert*-Butyl Butyl{(6-methoxypyridin-2-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (36 mg, 0.122 mmol) was obtained as a colorless oil in 49% yield after column chromatography (hexanes/EtOAc = 20:1).

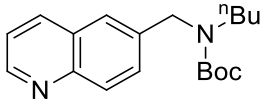
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.51 (dd, J = 7.5, 7.5 Hz, 1H), 6.76 (dd, J = 25.0, 6.0 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 4.45* (s, 2H), 4.38 (s, 2H), 3.90 (s, 3H), 3.37–3.19 (m, 2H), 1.60–1.22 (m, 13H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 163.8, 156.8, 156.4*, 156.2*, 155.8, 139.1*, 138.9, 113.8*, 113.3, 108.6, 79.5, 53.3, 52.4, 51.8*, 47.6, 47.4*, 30.6*, 30.4, 28.6*, 28.5, 20.3, 20.1*, 14.0; IR (neat) 2958, 2931, 1696, 1467, 1171 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{27}N_2O_3$ $[M+H]^+$ 295.2022, found 295. 2018.



***tert*-Butyl Butyl(isoquinolin-5-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (77 mg, 0.245 mmol) was obtained as a light yellow oil in 98% yield after column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.57 (d, *J* = 6.0 Hz, 1H), 8.01–7.78 (m, 2H), 7.62–7.54 (m, 2H), 4.90 (s, 2H), 3.29–3.02 (m, 2H), 1.59–1.32 (m, 11H), 1.31–1.18 (m, 2H), 0.92–0.81 (m, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.9, 153.2, 143.3, 134.7, 133.5, 130.3, 129.0, 128.6*, 127.7, 126.9, 117.2, 116.2*, 80.0, 47.6*, 47.2, 46.5*, 45.8, 30.1, 28.5, 20.1, 13.9; IR (neat) 2970, 1687, 1170, 1144 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{27}N_2O_2$ $[M+H]^+$ 315.2073, found 315. 2072.

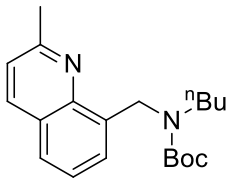


***tert*-Butyl Butyl(quinolin-6-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (78 mg, 0.248 mmol) was obtained as a light yellow oil in 99% yield after column chromatography (hexanes/EtOAc = 3:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.68–7.51 (m, 2H), 7.42–7.31 (m, 1H), 4.66–

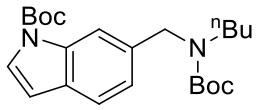
4.47 (m, 2H), 3.32–3.10 (m, 2H), 1.59–1.34 (m, 11H), 1.34–1.18 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.7*, 150.2, 147.8, 137.2, 135.9, 129.8, 129.6, 129.0*, 128.3, 125.9, 125.2*, 121.4, 79.8, 50.5*, 49.8, 46.8*, 46.5, 30.3, 28.5, 20.1, 13.9; IR (neat) 2961, 2931, 1690, 1170, 1145 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{27}N_2O_2$ $[M+H]^+$ 315.2073, found 315.2064.



***tert*-Butyl Butyl{(2-methylquinolin-8-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (63 mg, 0.192 mmol) was obtained as a yellow oil in 77% yield after column chromatography (hexanes/EtOAc = 20:1).

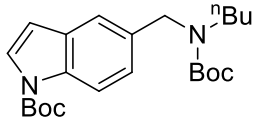
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.06–8.98 (m, 1H), 7.69–7.47 (m, 2H), 7.43 (dd, J = 7.5, 7.5 Hz, 1H), 7.29–7.21 (m, 1H), 5.16* (s, 2H), 5.12 (s, 2H), 3.43–3.26 (m, 2H), 2.73 (s, 3H), 2.71* (s, 3H), 1.64–1.53 (m, 2H), 1.51* (s, 9H), 1.40 (s, 9H), 1.38–1.25 (m, 2H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 158.0, 156.4, 146.3*, 146.1, 136.2, 127.6, 126.6, 126.4, 126.3, 125.6*, 125.3, 121.9, 121.7*, 79.3, 79.2*, 47.2, 46.6, 45.7*, 30.7*, 30.4, 28.6*, 28.5, 25.6, 20.3, 20.1*, 14.0; IR (neat) 2960, 2931, 1690, 1172, 1143 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{29}N_2O_2$ $[M+H]^+$ 329. 2229, found 329.2223.



***tert*-Butyl 6-[{(tert-Butoxycarbonyl)(butyl)amino}methyl]-1H-indole-1-carboxylate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (83 mg, 0.206 mmol) was obtained as a colorless oil in 82% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.56 (s, 1H), 7.49 (d, *J* =7.5 Hz, 1H), 7.18–7.04 (m, 1H), 6.53 (s, 1H), 4.58* (s, 2H), 4.54 (s, 2H), 3.26–3.10 (m, 2H), 1.67 (s, 9H), 1.56–1.38 (m, 11H), 1.31–1.22 (m, 2H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.2, 155.7*, 149.8, 135.4, 135.1, 129.7, 122.0*, 121.0, 114.6, 114.1*, 107.2, 83.7, 79.4, 50.8*, 50.1, 46.3*, 45.9, 30.3, 30.0*, 28.6, 28.3, 20.1, 14.0; IR (neat) 2973, 1735, 1693, 1168, 1145 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{34}N_2O_4$ Na $[M+Na]^+$ 425.2416, found 425.2413.

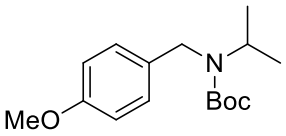


***tert*-Butyl 5-[{(tert-Butoxycarbonyl)(butyl)amino}methyl]-1H-indole-1-carboxylate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (96 mg, 0.138 mmol) was obtained as a yellow oil in 95% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.12–8.05 (m, 1H), 7.59–7.54 (m, 1H), 7.44–7.36 (m, 1H), 7.26–7.13 (m, 1H), 6.52 (d, *J* = 3.5 Hz, 1H), 4.56–

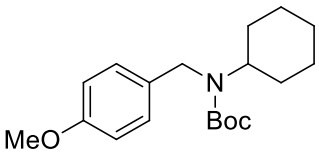
4.47 (m, 2H), 3.26–3.18 (m, 2H), 1.66 (s, 9H), 1.52–1.44 (m, 11H), 1.29–1.23 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.2, 155.8*, 149.8, 134.5, 133.1, 131.0, 126.3, 124.4, 123.7*, 120.2, 119.4*, 115.2, 107.3, 83.7, 79.5, 50.4*, 49.8, 46.3, 45.9*, 30.2, 28.6, 28.3, 20.1, 14.0; IR (neat) 2974, 1734, 1691, 1368, 1354, 1163 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{35}N_2O_4$ $[M+H]^+$ 403.2597, found 403.2592.



***tert*-Butyl Isopropyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (58 mg, 0.208 mmol) was obtained as a colorless oil in 83% yield after column chromatography (hexanes/EtOAc = 20:1).

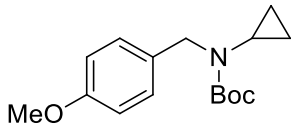
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 7.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 4.37–4.25 (m, 3H), 3.79 (s, 3H), 1.42 (s, 9H), 1.09 (d, J = 7.0 Hz, 6H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 158.4, 155.7, 132.6, 128.0, 113.7, 79.5, 55.3, 48.5*, 47.2, 45.6, 28.6, 21.0; IR (neat) 2974, 1687, 1245, 1161 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{25}NO_3Na$ $[M+Na]^+$ 302.1732, found 302.1733.



***tert*-Butyl Cyclohexyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (55 mg, 0.172 mmol) was obtained as a colorless oil in 69% yield after column chromatography (hexanes/EtOAc = 25:1).

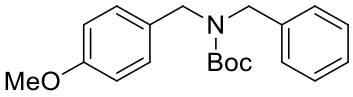
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.0 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.30 (s, 2H), 3.99 (s, 1H), 3.79 (s, 3H), 1.78–0.94 (m, 19H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.4, 155.8, 132.7, 127.8, 113.6, 79.5, 57.2, 55.3, 46.1, 31.4, 28.6, 26.2, 25.7; IR (neat) 2932, 1685, 1244, 1166 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{30}NO_3$ $[M+H]^+$ 320.2226, found 320.2233.



***tert*-Butyl Cyclopropyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (56 mg, 0.202 mmol) was obtained as a colorless oil in 81% yield after column chromatography (hexanes/EtOAc = 25:1).

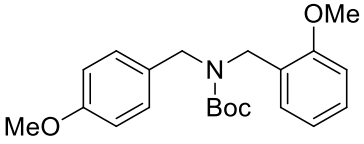
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 4.36 (s, 2H), 3.79 (s, 3H), 2.40 (s, 1H), 1.46 (s, 9H), 0.71–0.63 (m, 4H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.8, 156.9, 131.1, 128.9, 113.9, 79.7, 55.3, 50.9, 29.1, 28.6, 8.2.; IR (neat) 2976, 1694, 1247, 1171 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{23}NO_3Na$ $[M+Na]^+$ 300.1576, found 300.1585.



***tert*-Butyl Benzyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (74 mg, 0.226 mmol) was obtained as a colorless oil in 90% yield after column chromatography (hexanes/EtOAc = 25:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.06 (m, 7H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.42–4.21 (m, 4H), 3.79 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 159.0, 156.1, 138.3, 130.1, 129.5, 128.9*, 128.6, 128.1*, 127.5, 127.3, 114.0, 80.1, 55.3, 49.1, 48.7, 48.5*, 28.6; IR (neat) 2974, 1690, 1245, 1163 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{25}NO_3Na$ $[M+Na]^+$ 350.1732, found 350.1724.

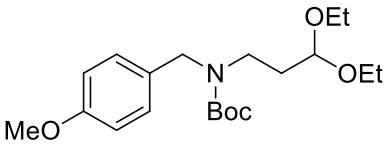


***tert*-Butyl 2-Methoxybenzyl(4-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (65 mg, 0.182 mmol) was obtained as a colorless oil in 73% yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.26–7.10 (m, 4H), 6.93 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.88–6.82 (m, 3H), 4.48–4.30 (m, 4H), 3.79 (s, 3H), 3.77 (s, 3H), 1.48* (s, 9H), 1.46 (s, 9H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 158.8, 157.6*, 157.3, 156.4, 156.0*, 130.8*, 130.7, 129.3, 128.9*, 128.8,

128.2, 126.4, 120.6*, 120.5, 113.8, 110.2, 79.8, 55.3, 55.2, 49.5*, 49.0, 44.4, 44.1*, 29.8*, 28.6; IR (neat) 2931, 1690, 1239, 1161 cm^{-1}; HRMS (ES+) calcd. for $C_{21}H_{27}NO_4Na$ $[M+Na]^+$ 300.1838, found 380.1826.



***tert*-Butyl (3,3-Diethoxypropyl)(4-methoxybenzyl)carbamate.**

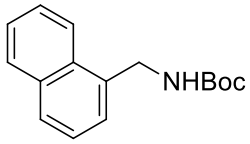
According to the general procedure for Suzuki–Miyaura cross-coupling, the product (78 mg, 0.212 mmol) was obtained as a colorless oil in 85% yield after column chromatography (hexanes/EtOAc = 10:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.17 (s, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.51–4.41 (m, 1H), 4.41–4.32 (m, 2H), 3.79 (s, 3H), 3.65–3.58 (m, 2H), 3.50–3.41 (m, 2H), 3.25* (s, 2H), 3.17 (s, 2H), 1.85–1.79 (m, 2H), 1.48 (s, 9H), 1.18 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 158.9, 156.0, 155.6*, 130.7, 129.2, 128.7*, 113.9, 101.0, 79.6, 61.0, 55.3, 50.3*, 49.7, 42.5, 32.4, 32.1*, 28.5, 15.4; IR (neat) 2975, 1691, 1247, 1169 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{33}NO_5Na$ $[M+Na]^+$ 390.2256, found 390.2261.

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction of Boc-Protected Primary Aminomethyltrifluoroborate with Aryl and Hetaryl Mesylates.

A sealed tube was charged with potassium *tert*-butoxycarbonyl aminomethyltrifluoroborate (65 mg, 0.275 mmol, 1.1 equiv), an aryl or hetaryl mesylates

(0.250 mmol, 1.0 equiv), $PdCl_2$(cod) (4 mg, 0.013 mmol, 0.05 equiv), RuPhos or SPhos ligand (0.025 mmol, 0.1 equiv) and K_3PO_4 (371 mg, 1.750 mmol, 7.0 equiv). The mixture was then was purged three times with argon. *t*-BuOH / H_2O (1:1, 0.6 mL/0.6 mL) was then added to the reaction tube. The reaction mixture was stirred for 22 h at 95 °C and then cooled to rt. H_2O (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$) and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.

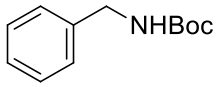


***tert*-Butyl (Naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 6:1).

RuPhos: 79% yield (51 mg, 0.198 mmol).

mp: 97–98 °C (lit.: 99–100 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.57–7.46 (m, 2H), 7.45–7.38 (m, 2H), 4.83 (br, 1H), 4.77 (d, *J* = 4.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.9, 134.4, 134.1, 131.6, 129.0, 128.6, 126.7, 126.4, 126.1, 125.6, 123.7, 79.7, 43.0, 28.7. Data is consistent with that reported in the literature.[37]



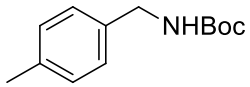
***tert*-Butyl Benzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

RuPhos: 66% yield (34 mg, 0.164 mmol).

mp: 54–56 °C (lit.: 57 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5H), 4.89 (br, 1H), 4.31 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 139.0, 128.7, 127.6, 127.4, 79.5, 44.8, 28.5.

Data is consistent with that reported in the literature.[29]



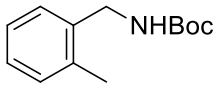
***tert*-Butyl 4-Methylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

RuPhos: 72% yield (40 mg, 0.181 mmol).

mp: 72–74 °C (lit.: 72.5–73 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.81 (br, 1H), 4.27 (d, *J* = 5.0 Hz, 2H), 2.33 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 137.1, 136.0, 129.4, 127.6, 79.5, 44.6, 28.5, 21.2.

Data is consistent with that reported in the literature.[33]



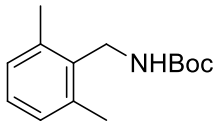
***tert*-Butyl 2-Methylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

RuPhos: 72% yield (40 mg, 0.181 mmol).

mp: 51–53 °C (lit.: 50–51 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.6–7.13 (m, 4H), 4.72 (br, 1H), 4.31 (d, *J* = 5.0 Hz, 2H), 2.32 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 136.6, 136.3, 130.5, 128.1, 127.6, 126.2, 79.5, 42.8, 28.5, 19.0.

Data is consistent with that reported in the literature.[30]



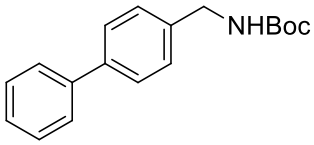
***tert*-Butyl 2,6-Dimethylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 10:1).

RuPhos: 22% yield (13 mg, 0.055 mmol).

mp: 73–75 °C (lit.: 73–74 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (dd, *J* = 8.0, 6.5 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 2H), 4.42–4.33 (m, 3H), 2.37 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 137.5, 134.5, 128.5, 127.9, 79.5, 39.2, 28.6, 19.8.

Data is consistent with that reported in the literature.[38]



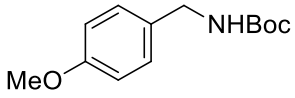
***tert*-Butyl {(1,1'-Biphenyl)-4-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

RuPhos: 86% yield (61 mg, 0.215 mmol).

mp: 102–105 °C (lit.: 101–103 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.53 (m, 4H), 7.45–7.40 (m, 2H), 7.36–7.30 (m, 3H), 4.92 (br, 1H), 4.35 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 140.9, 140.4, 138.1, 128.9, 128.0, 127.5, 127.4, 127.2, 79.6, 44.5, 28.5.

Data is consistent with that reported in the literature.[37]



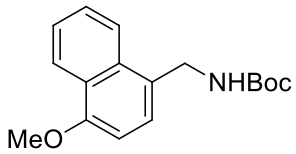
***tert*-Butyl 4-Methoxybenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 5:1).

RuPhos: 59% yield (35 mg, 0.147 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.81 (br, 1H), 4.24 (d, *J* = 5.5 Hz, 2H), 3.79 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 159.0, 156.0, 131.2, 129.0, 114.1, 79.5, 55.4, 44.3, 28.5.

Data is consistent with that reported in the literature.[31]

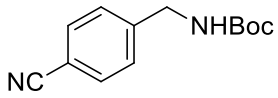


***tert*-Butyl {(4-Methoxynaphthalen-1-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light brown solid after flash chromatography (hexanes/EtOAc = 7:1).

RuPhos: 84% yield (60 mg, 0.209 mmol).

mp: 85–88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.55 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.49 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 4.78 (br, 1H), 4.67 (d, *J* = 5.0 Hz, 2H), 3.97 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 155.6, 132.4, 127.1, 126.8, 126.2, 126.1, 125.3, 123.5, 122.8, 103.1, 79.5, 55.6, 42.8, 28.5; IR (neat) 3370, 1678, 1493, 1479, 1243, 1166 cm^{-1}; HRMS (ES+) calcd. for $C_{17}H_{21}NO_3Na$ $[M+Na]^+$ 310.1419, found 310.1422.



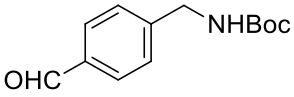
***tert*-Butyl 4-Cyanobenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 72% yield (42 mg, 0.181 mmol).

mp: 108–110 °C (lit.: 111–113 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 5.05 (br, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 144.8, 132.5, 127.9, 118.9, 111.2, 80.1, 44.3, 28.5.

Data is consistent with that reported in the literature.[32]



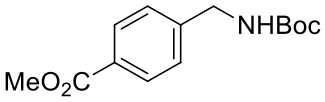
***tert*-Butyl 4-Formylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

RuPhos: 46% yield (27 mg, 0.115 mmol).

mp: 80–82 °C (lit.: 82–88 °C);^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 5.04 (br, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 192.0, 156.0, 146.3, 135.7, 130.2, 127.8, 80.0, 44.5, 28.5.

Data is consistent with that reported in the literature.[34]



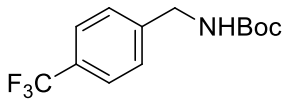
Methyl 4-[{(*tert*-Butoxycarbonyl)amino}methyl]benzoate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

SPhos: 42% yield (28 mg, 0.106 mmol).

mp: 88–90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 4.97 (br, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 3.91 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.0, 156.0, 144.4, 130.0, 129.3, 127.3, 79.9, 52.2, 44.5, 28.5; IR (neat)

3314, 2925, 1723, 1682, 1535, 1275, 1258, 1164 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{19}NO_4Na$ $[M+Na]^+$ 288.1212, found 288.1220.



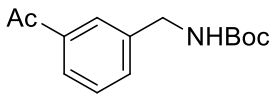
***tert*-Butyl 4-(Trifluoromethyl)benzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 6:1).

RuPhos: 83% yield (57 mg, 0.207 mmol).

mp: 72–74 °C (lit.: 70–71 °C);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 5.00 (br, 1H), 4.36 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 143.3, 129.7 (q, *J* = 32.4 Hz), 127.6, 125.7 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 270.0 Hz), 80.0, 44.3, 28.5.

Data is consistent with that reported in the literature.[39]

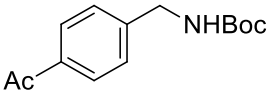


***tert*-Butyl 3-Acetylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 3:1).

RuPhos: 82% yield (51 mg, 0.205 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 7.5, 7.5 Hz, 1H), 5.04 (br, 1H), 4.37 (d, *J* = 6.0 Hz, 2H), 2.60 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.2, 156.1, 139.8, 137.5, 132.2, 129.0, 127.4, 127.1, 79.8, 44.4, 28.5, 26.8; IR (neat) 3347, 1682, 1367, 1270, 1251, 1164 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{19}NO_3Na$ $[M+Na]^+$ 272.1263, found 272.1255.



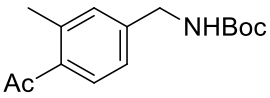
***tert*-Butyl 4-Acetylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 80% yield (50 mg, 0.201 mmol).

mp: 68–72 °C (lit.: 67–69 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.10 (br, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 2.59 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 197.9, 156.0, 144.7, 136.2, 128.8, 127.4, 79.9, 44.4, 28.5, 26.7.

Data is consistent with that reported in the literature.[38]

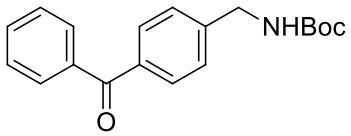


***tert*-Butyl 4-Acetyl-3-methylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 4:1).

RuPhos: 81% yield (53 mg, 0.201 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.14 (s, 1H), 5.04 (br, 1H), 4.31 (d, *J* = 6.0 Hz, 2H), 2.56 (s, 3H), 2.52 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 201.3, 156.0, 142.8, 139.2, 136.5, 131.0, 130.1, 124.5, 79.8, 44.3, 29.6, 28.5, 21.8; IR (neat) 3351, 1680, 1251, 1166 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{21}NO_3Na$ $[M+Na]^+$ 286.1419, found 286.1418.



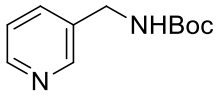
***tert*-Butyl 4-Benzoylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 5:1).

RuPhos: 86% yield (67 mg, 0.215 mmol).

mp: 124–127 °C (lit.: 127–130 °C); °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.74 (m, 4H), 7.60–7.55 (m, 1H), 7.50–7.44 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 5.07 (br, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 196.4, 156.1, 144.0, 137.8, 136.7, 132.5, 130.6, 130.1, 128.4, 127.2, 79.9, 44.4, 28.5.

Data is consistent with that reported in the literature.[40]



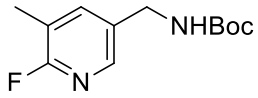
***tert*-Butyl (Pyridin-3-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 1:1).

SPhos: 52% yield (27 mg, 0.130 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56–8.47 (m, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.30–7.24 (m, 1H), 5.04 (br, 1H), 4.34 (d, *J* = 5.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 149.1, 148.9, 135.4, 134.7, 123.6, 80.0, 42.3, 28.5.

Data is consistent with that reported in the literature.[41]

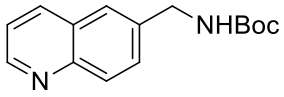


***tert*-Butyl ((6-Fluoro-5-methylpyridin-3-yl)methyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

RuPhos: 78% yield (47 mg, 0.196 mmol).

mp: 37–39 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.55 (d, *J* = 9.5 Hz, 1H), 5.00 (br, 1H), 4.27 (d, *J* = 5.0 Hz, 2H), 2.27 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 161.8 (d, *J* = 238.0 Hz), 156.0, 143.6 (d, *J* = 14.6 Hz), 141.3, 132.6 (d, *J* = 4.5 Hz), 119.7 (d, *J* = 32.7 Hz), 80.0, 41.4, 28.4, 14.5; IR (neat) 3359, 1676, 1512, 1249, 1164, 1144 cm^{-1}; HRMS (ES+) calcd. for $C_{12}H_{18}N_2O_2F$ $[M+H]^+$ 241.1352, found 241.1355.



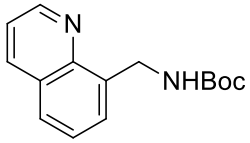
***tert*-Butyl (Quinolin-6-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 1:1).

SPhos 84% yield (54 mg, 0.209 mmol).

mp: 75–78 °C (lit.: 75–77 °C);^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J* = 3.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.68 (s, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, *J* = 8.5, 4.5 Hz, 1H), 5.25 (br, 1H), 4.49 (d, *J* = 5.5 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 150.3, 147.8, 137.5, 136.0, 129.9, 129.3, 128.2, 125.7, 121.4, 79.8, 44.6, 28.5.

Data is consistent with that reported in the literature.[38]



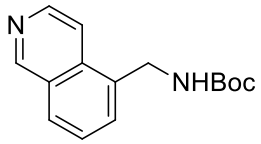
***tert*-Butyl (Quinolin-8-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a colorless oil after flash chromatography (hexanes/EtOAc = 3:1).

RuPhos: 87% yield (56 mg, 0.217 mmol).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (dd, *J* = 4.5, 2.0 Hz, 1H), 8.13 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.73–7.65 (m, 2H), 7.47 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.39 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.85 (br, 1H), 4.87 (d, *J* = 6.0 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1,

149.7, 146.9, 137.0, 136.5, 129.0, 128.5, 127.5, 126.5, 121.2, 79.1, 42.3, 28.6; IR (neat) 3343, 1706, 1498, 1164 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{18}N_2O_2Na$ $[M+Na]^+$ 281.1266, found 281.1262.

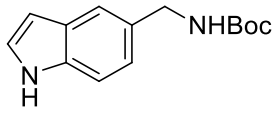


***tert*-Butyl (Isoquinolin-5-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 1:1).

SPhos: 57% yield (37 mg, 0.143 mmol).

mp: 156–160 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.59 (d, *J* = 6.0 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 5.5 Hz, 1H), 7.68 (d, *J* = 7.0 Hz, 1H), 7.58 (dd, *J* = 7.5, 7.5 Hz, 1H), 4.89 (br, 1H), 4.76 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 153.1, 143.5, 134.2, 133.9, 130.0, 129.0, 127.8, 127.0, 116.6, 79.9, 42.0, 28.5; IR (neat) 3351, 1680, 1529, 1383, 1251, 1164 cm^{-1}; HRMS (ES+) calcd. for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1447, found 259.1454.



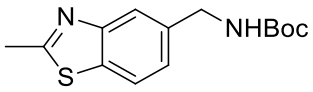
***tert*-Butyl{(1H-Indol-5-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a light yellow solid after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 75% yield (46 mg, 0.187 mmol).

mp: 86–89 °C (lit.: 86–89 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (br, 1H), 7.53 (s, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.18 (dd, *J* = 3.0, 3.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.56–6.43 (m, 1H), 4.85 (br, 1H), 4.39 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 135.3, 130.2, 128.1, 124.9, 122.2, 119.9, 111.4, 102.5, 79.4, 45.4, 28.6.

Data is consistent with that reported in the literature.[38]

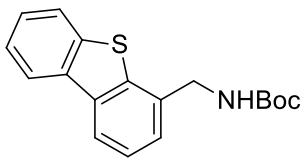


***tert*-Butyl {(2-Methylbenzo[d]thiazol-5-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

SPhos: 91% yield (63 mg, 0.226 mmol).

mp: 93–95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.28 (d, *J* = 9.5 Hz, 1H), 5.03 (br, 1H), 4.44 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.7, 156.0, 153.8, 137.5, 134.6, 124.5, 121.6, 121.0, 79.7, 44.6, 28.5, 20.3; IR (neat) 3367, 1680, 1521, 1253, 1177 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{18}N_2O_2SNa$ $[M+Na]^+$ 301.0987, found 301.0981.



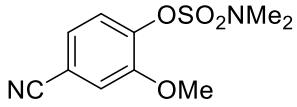
***tert*-Butyl (Dibenzo[b,d]thiophen-4-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product was obtained as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

SPhos: 91% yield (71 mg, 0.227 mmol).

mp: 150–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15–8.09 (m, 1H), 8.04 (d, *J* = 7.5 Hz, 1H), 7.87–7.82 (m, 1H), 7.47–7.35 (m, 4H), 5.03 (br, 1H), 4.58 (d, *J* = 5.0 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 139.3, 138.2, 136.2, 135.8, 133.0, 126.9, 125.6, 124.9, 124.6, 122.9, 121.8, 120.8, 79.8, 44.0, 28.6; IR (neat) 3355, 1678, 1521, 1282, 1168 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{19}NO_2SNa$ $[M+Na]^+$ 336.1034, found 336.1020.

General Procedure A for the Synthesis of Sulfamates.



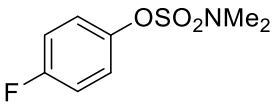
4-Cyano-2-methoxyphenyl Dimethylsulfamate.

A round bottomed flask was charged with 4-hydroxy-3-methoxybenzonitrile (300 mg, 1.0 equiv) and DMAP (12 mg, 0.10 mmol, 0.05 equiv) in CH_2Cl_2 (7 mL). Et_3N (244 mg, 2.41 mmol, 1.2 equiv) was slowly added to reaction flask at rt and the reaction mixture was stirred for 10 min. Dimethylsulfamoyl chloride (342 mg, 2.41 mmol, 1.2 equiv) was slowly added to reaction flask at rt, then the reaction was stirred at rt for 16 h. The reaction mixture was extracted with CH_2Cl_2 (10 mL) and H_2O (8 mL). The organic layer was washed with 1 M KOH (5 mL), then washed with H_2O (10 mL). The combined aqueous layers were extracted with CH_2Cl_2 (10 mL). All organic layers were combined, washed with brine (5 mL), and dried ($MgSO_4$). The crude mixture was concentrated under vacuo and purified

by column chromatography (hexanes/EtOAc = 3:1) to afford the product (494 mg, 2.01 mmol) as a white solid in quantitative yield.

mp: 64–66 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 3.93 (s, 3H), 3.01 (s, 6H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 152.1, 142.9, 125.5, 124.4, 118.1, 116.1, 111.1, 56.5, 38.8; IR (neat) 2231, 1380, 1169, 838, 759 cm^{-1}; HRMS (ES+) calcd. for $C_{10}H_{13}N_2O_4S$ $[M+H]^+$ 257.0596, found 257.0593.

General Procedure B for the Synthesis of Sulfamates.

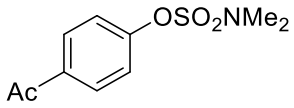


4-Fluorophenyl Dimethylsulfamate.

A round bottomed flask was charged with NaH (60% in mineral oil, 107 mg, 1.2 equiv) and the flask was cooled to 0 °C. 4-fluorophenol (250 mg, 2.23 mmol, 1 equiv) in DME (7 mL) was slowly added to reaction flask at 0 °C. The reaction mixture was warmed to rt for 10 min, then cooled to 0 °C again. Dimethylsulfamoyl chloride (320 mg, 2.23 mmol, 1 equiv) was slowly added to reaction flask at 0 °C and stirred at rt for 16 h. The reaction was quenched by addition of H_2O (5 mL). The crude mixture was extracted with Et_2O (15 mL). The organic layer was washed with 1 M KOH (5 mL), then washed with H_2O (10 mL). The combined aqueous layers were extracted with Et_2O (10 mL). All organic layers were combined, washed with brine (5 mL), and dried ($MgSO_4$). The crude mixture was

concentrated under vacuo and purified by column chromatography (hexanes/EtOAc = 4:1) to afford the product (485 mg, 2.21 mmol) as a white solid in 99% yield.

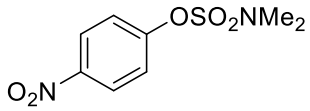
mp: 52–55 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 8.5, 4.0 Hz, 2H), 7.07 (dd, *J* = 8.5, 8.5 Hz, 2H), 2.98 (s, 6H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 160.9 (d, *J* = 246.1 Hz), 146.1 (d, *J* =2.6 Hz), 125.1 (d, *J* = 8.4 Hz), 116.6 (d, *J* = 23.6 Hz), 38.9; IR (neat) 2923, 1498, 1360, 1185, 844, 797 cm^{-1}; HRMS (CI+) calcd. for $C_8H_{11}NO_3SF$ $[M+H]^+$ 220.0444, found 220.0439.



4-Acetylphenyl Dimethylsulfamate.

According to the general procedure B for the synthesis of sulfamates, the product was obtained as a white solid in 70% isolated yield after column chromatography (hexanes/EtOAc = 3:1).

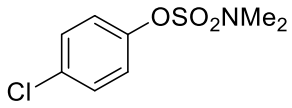
mp: 65–67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 9.0 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 3.01 (s, 6H), 2.61 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 196.8, 154.0, 135.4, 130.4, 121.7, 38.9, 26.8; IR (neat) 1690, 1361, 1171, 848, 763 cm^{-1}; HRMS (ES+) calcd. for $C_{10}H_{14}NO_4S$ $[M+H]^+$ 244.0644, found 244.0644.



4-Nitrophenyl Dimethylsulfamate.

According to the general procedure A for the synthesis of sulfamates, the product was obtained as a white solid in 90% isolated yield after column chromatography (hexanes/EtOAc = 4:1).

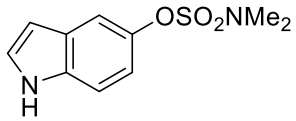
mp: 120–123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 9.5 Hz, 2H), 7.45 (d, *J* = 9.5 Hz, 2H), 3.05 (s, 6H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.0, 145.8, 125.7, 122.2, 38.9; IR (neat) 2980, 1521, 1361, 1172, 1146, 862, 748 cm^{-1}; HRMS (CI+) calcd. for $C_8H_{11}N_2O_5S$ $[M+H]^+$ 247.0389, found 247.0388.



4-Chlorophenyl Dimethylsulfamate.

According to the general procedure B for the synthesis of sulfamates, the product was obtained as a light yellow oil in quantitative yield after column chromatography (hexanes/EtOAc = 7:1).

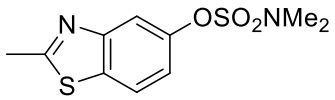
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 9.0 Hz, 2H), 2.98 (s, 6H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 148.8, 132.4, 130.0, 123.3, 38.9; IR (neat) 1484, 1371, 1171, 856, 754 cm^{-1}; HRMS (ES+) calcd. for $C_8H_{11}NO_3SCl$ $[M+H]^+$ 236.0148, found 236.0149.



1H-Indol-5-yl Dimethylsulfamate.

According to the general procedure B for the synthesis of sulfamates, the product was obtained as a white solid in 80% isolated yield after column chromatography (hexanes/EtOAc = 3:1).

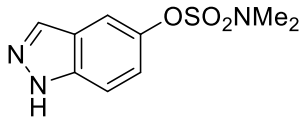
mp: 77–80 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (br, 1H), 7.54 (s, 1H), 7.33 (d, *J* =8.5 Hz, 1H), 7.26–7.23 (m, 1H), 7.13–7.06 (m, 1H), 6.54 (s, 1H), 2.96 (s, 6H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.1, 134.3, 128.3, 126.1, 116.4, 113.5, 111.8, 103.3, 38.9; IR (neat) 3384, 1350, 1169, 843 cm^{-1}; HRMS (ES-) calcd. for $C_{10}H_{11}N_2O_3S$ $[M-H]^-$ 239.0490, found 239. 0503.



2-Methylbenzo[d]thiazol-5-yl Dimethylsulfamate.

According to the general procedure B for the synthesis of sulfamates, stirred for 18 h at 70 °C instead of rt, the product was obtained as a white solid in 89% isolated yield after column chromatography (hexanes/EtOAc = 3:1 to 2:1).

mp: 95–97 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.5 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.34 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.00 (s, 6H), 2.85 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 169.6, 154.2, 148.9, 134.1, 122.2, 119.3, 115.7, 38.9, 20.4; IR (neat) 1365, 1176, 815, 750 cm^{-1}; HRMS (CI+) calcd. for $C_{10}H_{13}N_2O_3S_2$ $[M+H]^+$ 273.0368, found 273.0361.



1H-Indazol-5-yl Dimethylsulfamate.

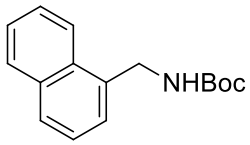
According to the general procedure B for the synthesis of sulfamates, stirred for 18 h at 70 °C instead of rt, the product was obtained as a white solid in 32% isolated yield after column chromatography (hexanes/EtOAc = 1:1).

mp: 143–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.11 (br, 1H), 8.10 (s, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 9.0 Hz, 1H), 7.35 (dd, *J* = 9.0 2.5 Hz, 1H), 3.01 (s, 6H); ^{13}C NMR (125.8 MHz, CD_2Cl_2) δ 144.7, 138.8, 135.2, 123.5, 122.1, 113.6, 111.2, 39.0; IR (neat) 3152, 1502, 1360, 1170, 838 cm^{-1}; HRMS (ES+) calcd. for $C_9H_{12}N_3O_3S$ $[M+H]^+$ 242.0599, found 242.0591.

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction of Boc-Protected Primary Aminomethyltrifluoroborate with Aryl and Hetaryl Sulfamates.

A microwave vial was charged with potassium *tert*-butoxycarbonyl aminomethyltrifluoroborate (62 mg, 0.263 mmol, 1.05 equiv), aryl or hetaryl sulfamates (0.250 mmol, 1.0 equiv), XPhos-Pd-G2 (8 mg, 0.010 mmol, 0.04 equiv), and K_2CO_3 (3.0, 5.0, or 7.0 equiv). The vial was capped, and then the mixture was degassed under vacuum and purged with argon. This procedure was repeated three times. *t*-BuOH / H_2O (0.5 M, 1:1, 0.25 mL/0.25 mL) was then added to the reaction vial. The reaction mixture was stirred for 3 h at 85 °C and then cooled to rt. H_2O (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$)

and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.

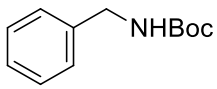


***tert*-Butyl (Naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (60 mg, 0.233 mmol) was obtained as a white solid in 93% isolated yield after column chromatography (hexanes/EtOAc = 7:1).

mp: 95–98 °C (lit.: 99–100 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.80–7.75 (m, 1H), 7.56–7.46 (m, 2H), 7.44–7.37 (m, 2H), 4.85 (br, 1H), 4.76 (d, *J* = 5.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 134.3, 134.0, 131.5, 128.9, 128.9, 126.6, 126.2, 126.0, 125.5, 123.6, 79.6, 42.9, 28.5.

Data is consistent with that reported in the literature.[37]

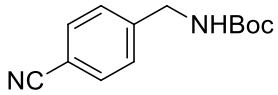


***tert*-Butyl Benzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (44 mg, 0.212 mmol) was obtained as a white solid in 85% isolated yield after column chromatography (CH_2Cl_2/hexanes = 9:1).

mp: 54–56 °C (lit.: 57 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.23 (m, 5H), 4.86 (br, 1H), 4.31 (d, *J* = 4.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 139.1, 128.7, 127.6, 127.4, 79.6, 44.8, 28.5.

Data is consistent with that reported in the literature.[29]

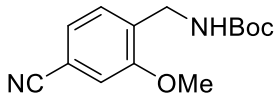


***tert*-Butyl 4-Cyanobenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (51 mg, 0.220 mmol) was obtained as a white solid in 88% isolated yield after column chromatography (hexanes/EtOAc = 4:1).

mp: 106–109 °C (lit.: 111–113 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 5.04 (br, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 144.8, 132.5, 127.9, 118.9, 111.2, 80.1, 44.3, 28.5.

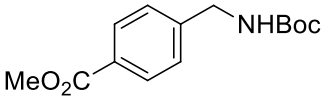
Data is consistent with that reported in the literature.[32]



***tert*-Butyl (4-Cyano-2-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (59 mg, 0.225 mmol) was obtained as a white solid in 90% isolated yield after column chromatography (hexanes/EtOAc = 4:1).

mp: 100–102 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.0 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.07 (s, 1H), 5.08 (br, 1H), 4.32 (d, *J* = 5.5 Hz, 2H), 3.88 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.4, 155.9, 133.2, 129.3, 125.0, 118.9, 113.1, 111.9, 79.8, 55.8, 40.0, 28.5; IR (neat) 3363, 3323, 2982, 2227, 1696, 1504, 1282, 1152 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{19}N_2O_3$ $[M+H]^+$ 263.1396, found 263.1392.

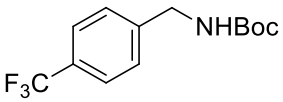


Methyl 4-[{(*tert*-Butoxycarbonyl)amino}methyl]benzoate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (62 mg, 0.234 mmol) was obtained as a white solid in 93% isolated yield after column chromatography (hexanes/EtOAc = 4:1).

mp: 86–89 °C(lit.: 88–90 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.97 (br, 1H), 4.37 (d, *J* = 5.0 Hz, 2H), 3.91 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.0, 156.0, 144.4, 130.0, 129.3, 127.3, 79.9, 52.2, 44.5, 28.5.

Data is consistent with that reported in the literature.[42]

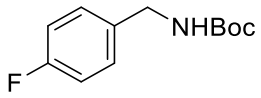


***tert*-Butyl 4-(Trifluoromethyl)benzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (52 mg, 0.189 mmol) was obtained as a white solid in 76% isolated yield after column chromatography (hexanes/EtOAc = 6:1).

mp: 70–72 °C (lit.: 70–71 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 5.03 (br, 1H), 4.36 (d, *J* = 6.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 143.3, 129.7 (q, *J* = 32.5 Hz), 127.6, 125.6 (q, *J* = 3.5 Hz), 124.3 (q, *J* = 271.9 Hz), 80.0, 44.3, 28.5.

Data is consistent with that reported in the literature.[39]

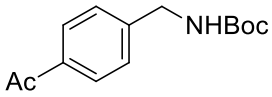


***tert*-Butyl (4-Fluorobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, *n*-PrOH instead of *t*-BuOH, the product (50 mg, 0.222 mmol) was obtained as a white solid in 89% isolated yield after column chromatography (hexanes/EtOAc = 10:1).

mp: 64–66 °C (lit.: 68–70 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.21 (m, 2H), 7.03–6.97 (m, 2H), 4.84 (br, 1H), 4.27 (d, *J* = 5.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 162.3 (d, *J* = 245.0 Hz), 156.0, 134.9, 129.2 (d, *J* = 7.5 Hz), 115.5 (d, *J* = 21.4 Hz), 79.8, 44.2, 28.5.

Data is consistent with that reported in the literature.[37]

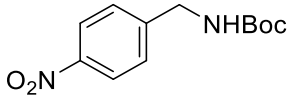


***tert*-Butyl 4-Acetylbenzylcarbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (54 mg, 0.217 mmol) was obtained as a white solid in 87% isolated yield after column chromatography (hexanes/EtOAc = 3:1).

mp: 69–71 °C (lit.: 67–69 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.04 (br, 1H), 4.37 (d, *J* = 5.0 Hz, 2H), 2.59 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 197.9, 156.0, 144.7, 136.3, 128.8, 127.4, 79.9, 44.4, 28.5, 26.7.

Data is consistent with that reported in the literature.[38]

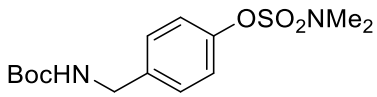


***tert*-Butyl (4-Nitrobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (38 mg, 0.151 mmol) was obtained as a yellow solid in 60% isolated yield after column chromatography (hexanes/EtOAc = 10:1).

mp: 107–109 °C (lit.: 109–110 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 5.08 (br, 1H), 4.42 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 147.3, 146.8, 127.9, 123.9, 80.3, 44.1, 28.5.

Data is consistent with that reported in the literature.[33]

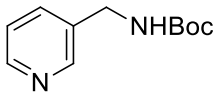


4-[{(*tert*-Butoxycarbonyl)amino}methyl]phenyl Dimethylsulfamate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (64 mg, 0.194 mmol) was obtained as a white solid in 77% isolated yield after column chromatography (hexanes/EtOAc = 3:1).

When the solvents were toluene / H_2O (0.5 M, 4:1, 0.4 mL/0.1 mL), obtained product (67 mg, 0.203 mmol) as a white solid in 81% isolated yield after column chromatography (hexanes/EtOAc = 3:1).

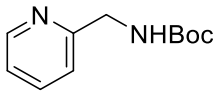
mp: 94–96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 4.93 (br, 1H), 4.30 (d, *J* = 5.0 Hz, 2H), 2.96 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 149.5, 137.9, 128.9, 122.0, 79.8, 44.1, 38.8, 28.5; IR (neat) 3328, 2976, 1676, 1356, 1170, 1149 cm^{-1}; HRMS (ES+) calcd. for $C_{14}H_{22}N_2O_5SNa$ $[M+Na]^+$ 353.1147, found 353.1131.



***tert*-Butyl (Pyridin-3-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (43 mg, 0.206 mmol) was obtained as a colorless oil in 83% isolated yield after column chromatography (CH_2Cl_2/EtOAc = 2:1).

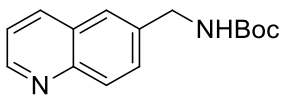
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.50 (d, *J* = 4.5 Hz, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 3.84 (dd, *J* = 7.5, 5.0 Hz, 1H), 5.17 (br, 1H), 4.32 (d, *J* = 4.0 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 149.1, 148.8, 135.3, 134.7, 123.6, 79.9, 42.3, 28.5. Data is consistent with that reported in the literature.[41]



***tert*-Butyl (Pyridin-2-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (30 mg, 0.144 mmol) was obtained as a colorless oil in 58% isolated yield after column chromatography (hexanes/EtOAc = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.5 Hz, 1H), 7.68–7.62 (m, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.20–7.17 (m, 1H), 5.65 (br, 1H), 4.45 (d, *J* = 5.0 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.6, 156.1, 149.2, 136.8, 122.3, 121.8, 79.6, 45.9, 28.5. Data is consistent with that reported in the literature.[38]

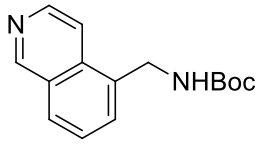


***tert*-Butyl (Quinolin-6-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (57 mg, 0.221 mmol) was obtained as a white solid in 88% isolated yield after column chromatography (hexanes/EtOAc = 1:1).

mp: 78–81 °C (lit.: 75–77 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90–8.85 (m, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.67 (s, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.26 (br, 1H), 4.49 (d, *J* = 5.5 Hz, 2H), 1.48 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.1, 150.3, 147.8, 137.5, 135.9, 129.9, 129.3, 128.2, 125.7, 121.4, 79.8, 44.6, 28.5.

Data is consistent with that reported in the literature.[38]

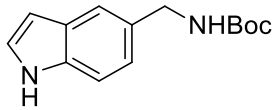


***tert*-Butyl (Isoquinolin-5-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (59 mg, 0.228 mmol) was obtained as a white solid in 91% isolated yield after column chromatography (hexanes/EtOAc = 1:1).

mp: 155–158 °C (lit.: 156–160 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.54 (d, *J* = 5.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 5.5 Hz, 1H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.54 (dd, *J* = 7.5, 7.5 Hz, 1H), 5.17 (br, 1H), 4.75 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 153.1, 143.5, 134.2, 133.9, 129.9, 128.9, 127.7, 126.9, 116.5, 79.8, 42.0, 28.5.

Data is consistent with that reported in the literature.[42]

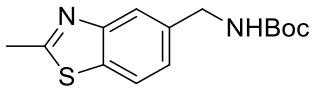


***tert*-Butyl {(1H-Indol-5-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (42 mg, 0.171 mmol) was obtained as a brown solid in 68% isolated yield as a light yellow solid after column chromatography (CH_2Cl_2/hexanes = 40:1).

mp: 86–89 °C (lit.: 86–89 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (br, 1H), 7.54 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 2.5, 2.5 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.53–6.49 (m, 1H), 4.84 (br, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0 135.3, 130.2, 128.1, 124.9, 122.3, 119.9, 111.4, 102.6, 79.4, 45.4, 28.6.

Data is consistent with that reported in the literature.[38]



***tert*-Butyl {(2-Methylbenzo[d]thiazol-5-yl)methyl}carbamate.**

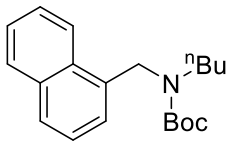
According to the general procedure for Suzuki–Miyaura cross-coupling, the product (59 mg, 0.212 mmol) was obtained as a white solid in 85% isolated yield after column chromatography (CH_2Cl_2/EtOAc = 6:1 to 4:1).

mp: 93–95 °C (lit.: 93–95 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 5.10 (br, 1H), 4.43 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 167.6, 156.0, 153.7, 137.5, 134.5, 124.4, 121.5, 121.0, 79.6, 44.5, 28.5, 20.2.

Data is consistent with that reported in the literature.[42]

General Procedure for the Suzuki–Miyaura Cross-coupling Reaction of Boc-Protected Secondary Aminomethyltrifluoroborates with Aryl and Hetaryl Sulfamates.

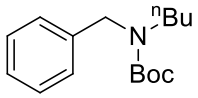
A microwave vial was charged with potassium *tert*-butyl butyl{(trifluoroborato)methyl}carbamate secondary (77 mg, 0.263 mmol, 1.05 equiv), aryl or hetaryl sulfamates (0.250 mmol, 1.0 equiv), XPhos-Pd-G2 (8 mg, 0.010 mmol, 0.04 equiv), and K_2CO_3 (7.0 equiv). The vial was capped, and then the mixture was degassed under vacuum and purged with argon. This procedure was repeated three times. *t*-BuOH / H_2O (0.5 M, 1:1, 0.25 mL/0.25 mL) was then added to the reaction vial. The reaction mixture was stirred for 18 h at 85 °C and then cooled to rt. H_2O (2 mL) was added, and the resulting mixture was extracted with EtOAc (2 × 3 mL). The organic layer was combined, dried ($MgSO_4$) and filtered. The solvent was removed in vacuo and the product was purified by column chromatography.



***tert*-Butyl Butyl(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (72 mg, 0.230 mmol) was obtained as a colorless oil in 92% isolated yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.18–7.98 (m, 1H), 7.89–7.81 (m, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.54–7.46 (m, 2H), 7.46–7.39 (m, 1H), 7.34–7.28 (m, 1H), 5.00–4.89 (m, 2H), 3.22* (s, 2H), 3.07 (s, 2H), 1.57–1.36 (m, 11H), 1.29–1.18 (m, 2H), 0.88–0.82 (m, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.9, 155.7*, 133.9, 133.7, 131.9, 131.4*, 128.7, 128.2, 127.8*, 126.3*, 126.2, 125.8, 125.3, 124.5*, 124.0, 123.1, 79.6, 48.2*, 47.7, 46.3*, 45.4, 30.1, 28.6, 20.1, 13.9; IR (neat) 2962, 1689, 1415, 1171, 1142 cm^{-1}; HRMS (ES+) calcd. for $C_{20}H_{28}NO_2$ $[M+H]^+$ 314.2120, found 314.2122.

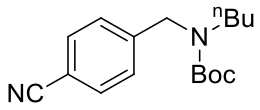


***tert*-Butyl Benzyl(butyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (22 mg, 0.084 mmol) was obtained as a colorless oil in 33% isolated yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.38–7.19 (m, 5H), 4.45 (s, 2H), 4.41* (s, 2H), 3.23–3.10 (m, 2H), 1.59–1.397 (m, 11H), 1.35–1.22 (m, 2H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.8*, 139.0*, 138.7, 128.5, 127.8, 127.1, 79.6, 50.5*, 49.8, 46.6*, 46.2, 30.4*, 30.1, 28.6, 20.1, 14.0.

Data is consistent with that reported in the literature.[36]

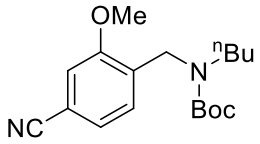


***tert*-Butyl Butyl(4-cyanobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, 5 equiv of K_2CO_3 instead of 7 equiv, the product (38 mg, 0.132 mmol) was obtained as a colorless oil in 53% isolated yield after column chromatography (hexanes/EtOAc = 15:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.35–7.27 (m, 2H), 4.50–4.39 (m, 2H), 3.28–3.08 (m, 2H), 1.56–1.34 (m, 11H), 1.34–1.22 (m, 2H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.2, 155.4*, 144.9*, 144.5, 132.4, 128.1, 127.5*, 118.9, 111.0, 80.1, 50.6*, 49.9, 47.3*, 47.0, 30.4, 28.5, 20.0, 13.9.

Data is consistent with that reported in the literature.[43]

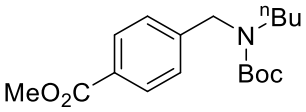


***tert*-Butyl Butyl(4-cyano-2-methoxybenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (50 mg, 0.157 mmol) was obtained as a white solid in 63% isolated yield after column chromatography (hexanes/EtOAc = 10:1).

mp: 63–66 °C; ^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.27–7.17 (m, 2H), 7.09–7.04 (m, 1H), 4.46 (s, 2H), 4.41* (s, 2H), 3.86 (s, 3H), 3.28–3.14 (m, 2H), 1.52–1.36 (m, 11), 1.36–1.24 (m, 2H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk

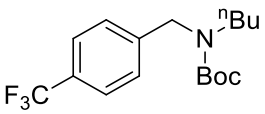
denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 157.3, 157.0*, 156.1, 155.7*, 133.3*, 133.0, 128.3, 127.8*, 124.9, 124.8*, 119.1, 123.0, 111.4, 79.8, 55.7, 47.4, 45.6*, 45.0, 30.6, 30.3*, 28.5, 28.4*, 20.2*, 20.0, 13.9; IR (neat) 2969, 2229, 1677, 1406, 1142 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{26}N_2O_3Na$ $[M+Na]^+$ 341.1841, found 341.1847.



Methyl 4-[{(*tert*-Butoxycarbonyl)(butyl)amino}methyl]benzoate.

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (61 mg, 0.190 mmol) was obtained as a colorless oil in 76% isolated yield after column chromatography (hexanes/EtOAc = 20:1).

^1H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 2H), 7.32–7.26 (m, 2H), 4.49 (s, 2H), 4.44* (s, 2H), 3.91 (s, 3H), 3.29–3.10 (m, 2H), 1.55–1.34 (m, 11), 1.34–1.23 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 167.0, 156.2, 155.6*, 144.5, 144.2*, 129.9, 129.1, 127.5, 126.9*, 79.9, 52.2, 50.6*, 49.9, 47.1*, 46.7, 30.4, 28.5, 20.1, 13.9; IR (neat) 2961, 1724, 1693, 1277, 1174 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{27}NO_4Na$ $[M+Na]^+$ 344.1838, found 344.1839.

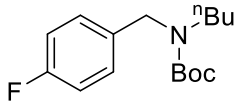


***tert*-Butyl Butyl{4-(trifluoromethyl)benzyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (35 mg, 0.106 mmol) was obtained as a colorless oil in 42% isolated yield after column chromatography (hexanes/EtOAc = 20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.34 (s, 2H), 4.49 (s, 2H), 4.46* (s, 2H), 3.24* (s, 2H), 3.14 (s, 2H), 1.55–1.38 (m, 11H), 1.35–1.26 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.2, 155.6*, 143.3*, 143.0, 129.5 (q, *J* = 32.3 Hz), 127.8, 127.2*, 125.5 (q, *J* = 3.5 Hz), 124.3 (q, *J* = 271.6 Hz), 80.0, 50.3*, 49.7, 47.0*, 46.8, 30.4, 30.3*, 28.5, 20.1, 13.9.

Data is consistent with that reported in the literature.[43]

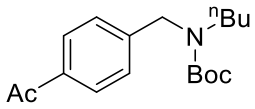


***tert*-Butyl Butyl(4-fluorobenzyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (33 mg, 0.117 mmol) was obtained as a colorless oil in 47% isolated yield after column chromatography (hexanes/EtOAc = 30:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.26–7.15 (m, 2H), 7.00 (dd, *J* = 8.5, 8.5 Hz, 2H), 4.48–4.32 (m, 2H), 3.22–3.07 (m, 2H), 1.55–1.42 (m, 11H), 1.33–1.25 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 162.1 (d, *J* = 244.7), 156.2, 155.6*, 134.5, 129.4, 128.8*, 115.5, 115.3*, 79.7, 49.9*, 49.3, 46.6*, 46.3, 30.4, 28.6, 20.1, 14.0; IR (neat) 2961, 2929,

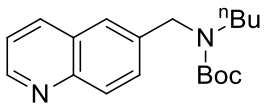
1692, 1509, 1410, 1222, 1171, 1143 cm^{-1}; HRMS (ES+) calcd. for $C_{16}H_{24}NO_2FNa$ $[M+Na]^+$ 304.1689, found 304.1689.



***tert*-Butyl (4-Acetylbenzyl)(butyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (32 mg, 0.105 mmol) was obtained as a colorless oil in 42% isolated yield after column chromatography (hexanes/EtOAc = 10:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 2H), 7.31 (s, 2H), 4.49 (s, 2H), 4.45* (s, 2H), 3.28–3.11 (m, 2H), 2.60 (s, 3H), 1.55–1.37 (m, 11H), 1.33–1.25 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 197.9, 156.2, 144.7*, 144.4, 136.2, 128.7, 127.7, 127.1*, 79.9, 50.6*, 49.9, 47.1*, 46.8, 30.3, 28.5, 26.7, 20.1, 13.9; IR (neat) 2960, 2929, 1685, 1408, 1266, 1170, 1144cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{27}NO_3Na$ $[M+Na]^+$ 328.1889, found 328.1886.

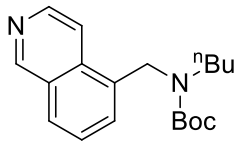


***tert*-Butyl Butyl(quinolin-6-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (66 mg, 0.210 mmol) was obtained as a colorless oil in 84% isolated yield after column chromatography (CH_2Cl_2/EtOAc = 7:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 9.0 Hz, 1H), 7.67–7.58 (m, 2H), 7.43–7.37 (m, 1H), 4.63 (s, 2H), 4.60* (s, 2H), 3.29* (s, 2H), 3.18 (s, 2H), 1.59–1.37 (m, 11H), 1.36–1.25 (m, 2H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.3, 155.7*, 150.2, 147.8, 137.3, 135.9, 129.8, 129.6, 129.0*, 128.2, 125.9, 125.1*, 121.4, 79.8, 50.5*, 49.8, 46.8*, 46.4, 30.3, 28.5, 20.1, 13.9.

Data is consistent with that reported in the literature.[43]

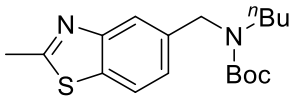


***tert*-Butyl Butyl(isoquinolin-5-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (65 mg, 0.207 mmol) was obtained as a colorless oil in 83% isolated yield after column chromatography (hexanes/EtOAc = 5:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.57 (d, *J* = 6.0 Hz, 1H), 8.00–7.78 (m, 2H), 7.61–7.53 (m, 2H), 4.90 (s, 2H), 3.26–3.04 (m, 2H), 1.59–1.38 (m, 11H), 1.36–1.21 (m, 2H), 0.91–0.85 (m, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.8, 153.2, 143.5, 134.6, 133.4, 130.1, 129.0, 128.6, 127.3*, 126.7, 116.9, 116.1*, 79.9, 47.6*, 47.1, 46.5*, 45.7, 30.1, 28.5, 20.1, 13.9.

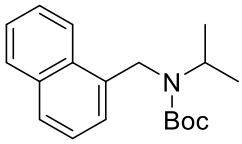
Data is consistent with that reported in the literature.[43]



***tert*-Butyl Butyl{(2-methylbenzo[d]thiazol-5-yl)methyl}carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (71 mg, 0.212 mmol) was obtained as a colorless oil in 85% isolated yield after column chromatography (hexanes/EtOAc = 7:1).

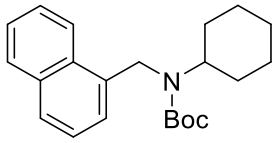
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.30–7.21 (m, 1H), 4.58 (s, 2H), 4.53* (s, 2H), 3.30–3.13 (m, 2H), 2.83 (s, 3H), 1.58–1.42 (m, 11H), 1.33–1.23 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 167.4, 156.2, 155.5*, 153.7, 137.2*, 137.0, 134.3, 124.7, 124.1*, 121.4, 121.1, 121.0*, 79.6, 50.4*, 49.7, 46.5*, 46.2, 30.3, 30.1*, 28.5, 20.2, 20.1*, 20.0, 13.9; IR (neat) 2966, 2929, 1691, 1412, 1171 cm^{-1}; HRMS (ES+) calcd. for $C_{18}H_{27}N_2O_2S$ $[M+H]^+$ 335.1793, found 335.1782.



***tert*-Butyl Isopropyl(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (53 mg, 0.177 mmol) was obtained as a colorless oil in 71% isolated yield after column chromatography (hexanes/EtOAc = 25:1).

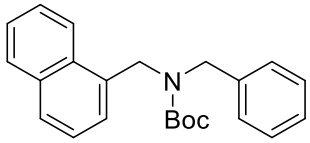
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.54–7.46 (m, 2H), 7.43 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.37–7.33 (m, 1H), 4.82 (s, 2H), 4.53 (s, 1H), 3.98* (s, 1H), 1.62–1.23 (m, 9H), 1.17–1.08 (m, 6H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.9, 135.0, 133.7, 131.0, 128.9, 127.2, 126.0, 125.6, 125.4, 123.4, 122.6, 79.7, 48.5*, 47.3, 45.7*, 43.5, 28.5, 20.7; IR (neat) 2973, 1690, 1365, 1164 cm^{-1}; HRMS (ES+) calcd. for $C_{19}H_{25}NO_2Na$ $[M+Na]^+$ 322.1783, found 322.1786.



***tert*-Butyl Cyclohexyl(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (58 mg, 0.171 mmol) was obtained as a colorless oil in 68% isolated yield after column chromatography (hexanes/EtOAc = 25:1).

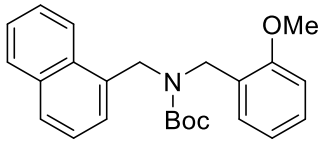
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.54–7.46 (m, 2H), 7.42 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 4.84 (s, 2H), 4.16 (s, 1H), 3.67* (s, 1H), 1.88–0.93 (m, 19H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 156.0, 135.1, 133.6, 130.6, 128.9, 127.0, 125.9, 125.5, 125.3, 123.2, 122.4, 79.6, 57.2*, 55.4, 45.4*, 44.0, 31.0, 28.4, 26.0, 25.6; IR (neat) 2929, 1687, 1364, 1246, 1167 cm^{-1}; HRMS (ES+) calcd. for $C_{22}H_{29}NO_2Na$ $[M+Na]^+$ 362.2096, found 362.2094.



***tert*-Butyl Benzyl(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (64 mg, 0.184 mmol) was obtained as a colorless oil in 74% isolated yield after column chromatography (hexanes/EtOAc = 30:1).

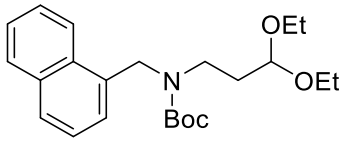
^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.17–7.94 (m, 1H), 7.88–7.83 (m, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.53–7.37 (m, 3H), 7.35–7.15 (m, 6H), 4.93 (s, 2H), 4.84* (s, 2H), 4.44* (s, 2H), 4.28 (s, 2H), 1.52 (s, 9H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.9, 138.2, 134.0, 133.1, 132.0, 131.6*, 128.9*, 128.7, 128.6, 128.4*, 128.0, 127.5*, 127.3, 126.8*, 126.4, 126.2*, 125.9, 125.3, 124.9, 124.1, 123.2, 80.3, 48.8, 47.1, 28.6; IR (neat) 2970, 1691, 1245, 1163 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{25}NO_2Na$ $[M+Na]^+$ 370.1783, found 370.1784.



***tert*-Butyl (2-Methoxybenzyl)(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (77 mg, 0.204 mmol) was obtained as a light yellow oil in 82% isolated yield after column chromatography (hexanes/EtOAc =20:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.19–7.82 (m, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.53–7.17 (m, 6H), 6.95–6.77 (m, 2H), 4.99 (s, 2H), 4.91* (s, 2H), 4.53* (s, 2H), 4.35 (s, 2H), 3.68 (s, 3H), 3.62* (s, 3H), 1.48 (s, 9H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 157.6*, 157.4, 156.4, 134.0, 133.6, 132.0, 131.5*, 128.9*, 128.8, 128.4*, 128.2, 128.1, 127.7*, 126.3, 126.1, 125.9, 125.8*, 125.6*, 125.4, 124.3*, 124.0, 123.4*, 123.2, 120.7, 120.5, 110.8*, 110.3, 80.1, 55.2, 48.1*, 47.7, 44.5*, 44.4, 28.6; IR (neat) 1689, 1242, 1159 cm^{-1}; HRMS (ES+) calcd. for $C_{24}H_{27}NO_3Na$ $[M+Na]^+$ 400.1889, found 400.1895.



***tert*-Butyl (3,3-Diethoxypropyl)(naphthalen-1-ylmethyl)carbamate.**

According to the general procedure for Suzuki–Miyaura cross-coupling, the product (83 mg, 0.214 mmol) was obtained as a colorless oil in 86% isolated yield after column chromatography (hexanes/EtOAc = 20:1 to 10:1).

^{1}H NMR (asterisk denotes minor rotamer peaks, 500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.04* (s, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.53–7.45 (m, 2H), 7.418 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.37–7.28 (m, 1H), 4.93 (s, 2H), 4.46* (s, 1H), 4.37 (s, 1H), 3.59–3.11 (m, 6H), 1.88–1.74 (m, 2H), 1.56–1.44 (m, 9H), 1.14 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (asterisk denotes minor rotamer peaks, 125.8 MHz, $CDCl_3$) δ 155.7, 133.9, 133.5, 131.9, 131.5*, 128.7, 128.3, 128.0*, 126.5*, 126.3, 125.8, 125.3, 124.9*, 124.0, 123.1, 101.0, 79.9, 61.0,

48.7*, 48.2, 42.6*, 41.9, 32.1, 28.5, 15.3; IR (neat) 2975, 1690, 1167, 1136, 1062 cm^{-1}; HRMS (ES+) calcd. for $C_{23}H_{33}NO_4Na$ $[M+Na]^+$ 410.2307, found 410.2307.

3.5 References

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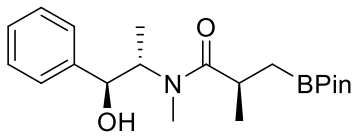
Appendix A1

Spectra Relevant to Chapter 2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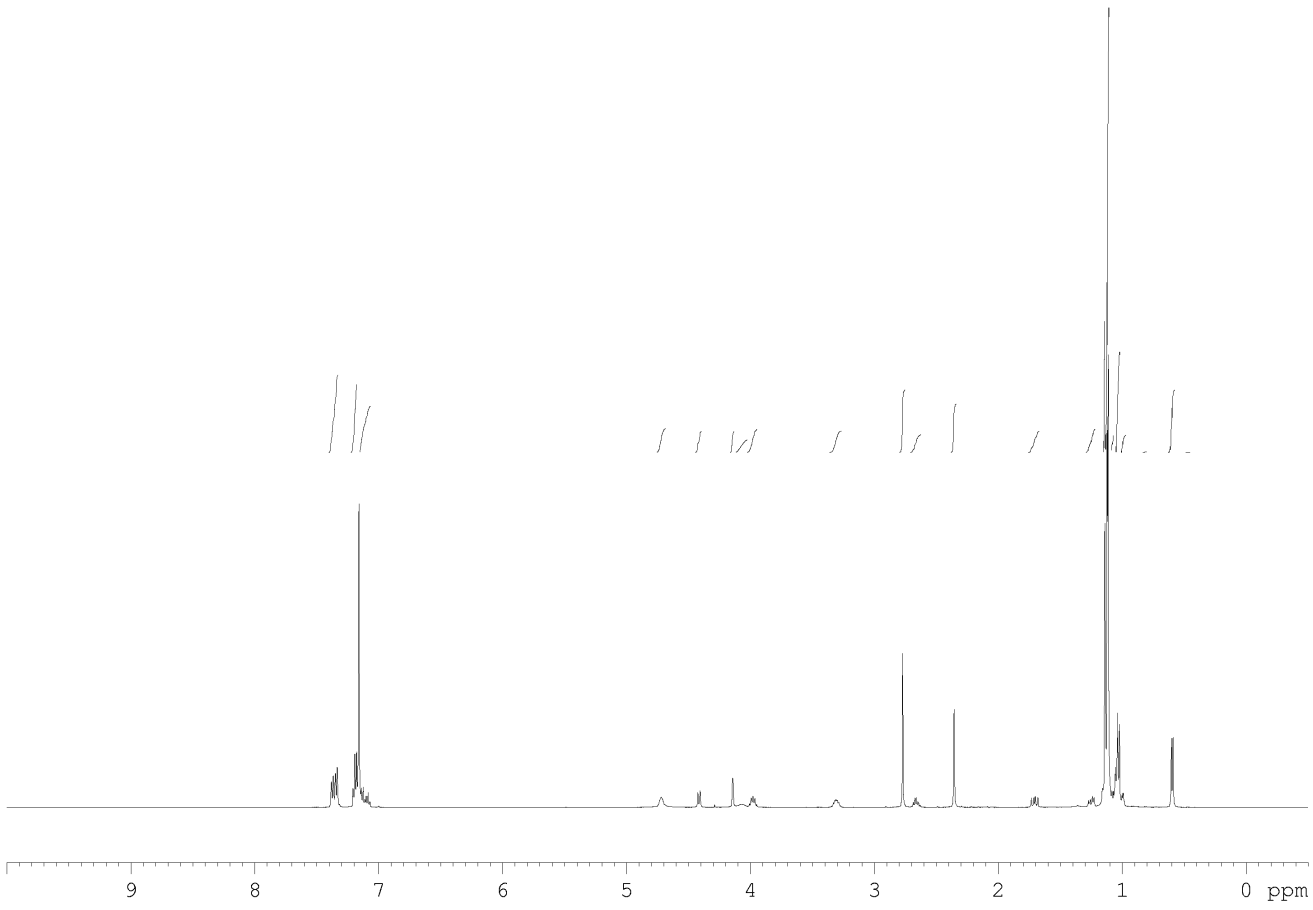
N
BPin
OH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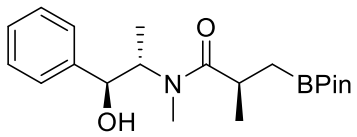
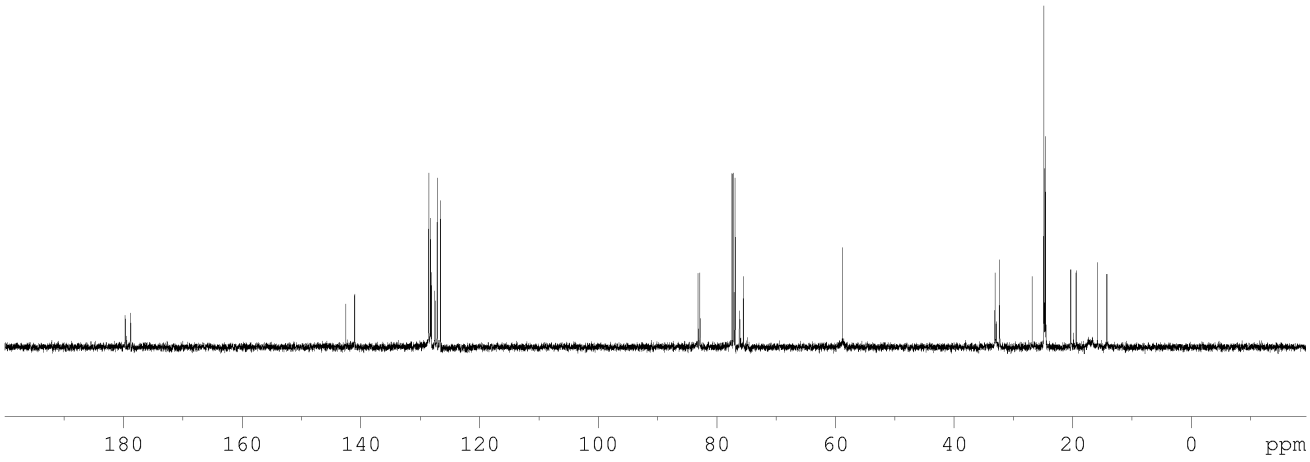
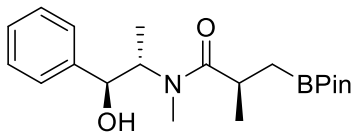
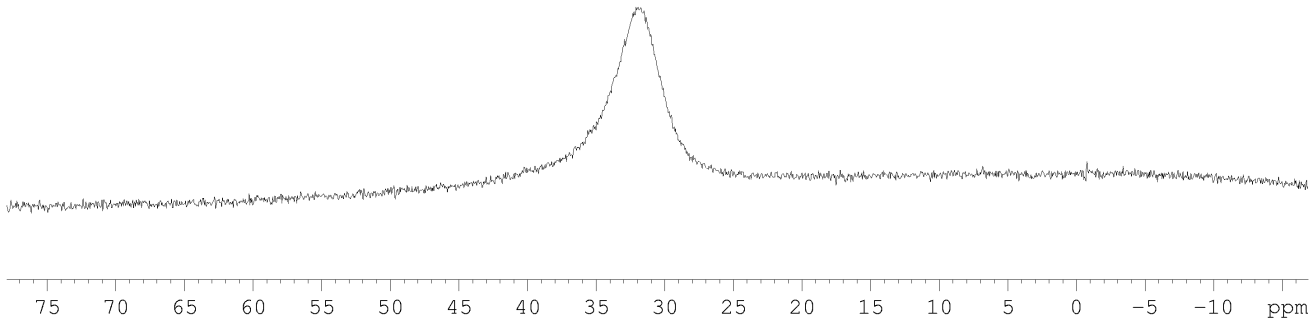
8
7
6
5
4
3
2
1
0 ppm


O
N
BPin
OH


180
160
140
120
100
80
60
40
20
0
ppm


O
N
BPin
OH


75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 −5 −10 ppm

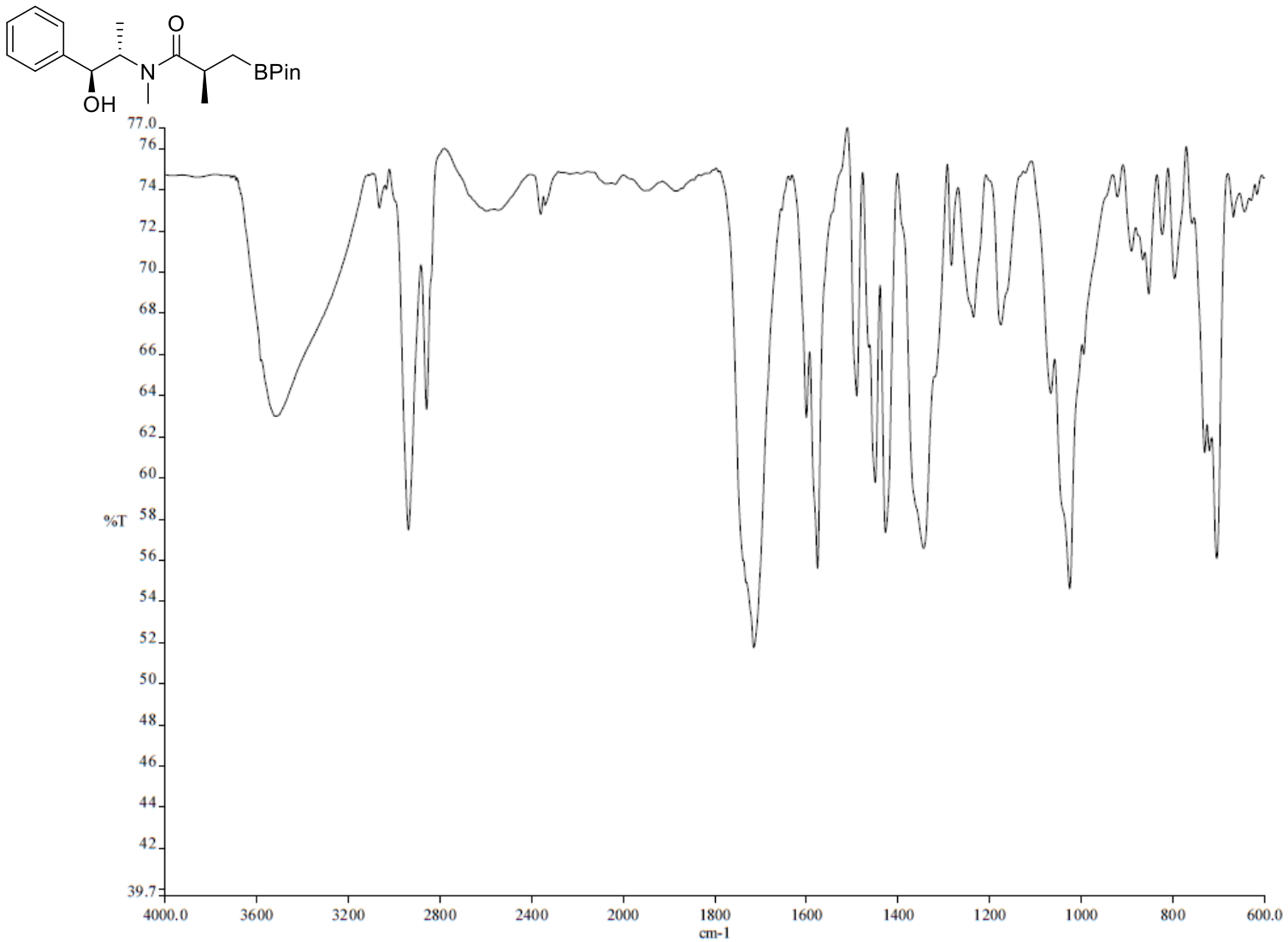


Figure A1.4 Infrared Spectrum

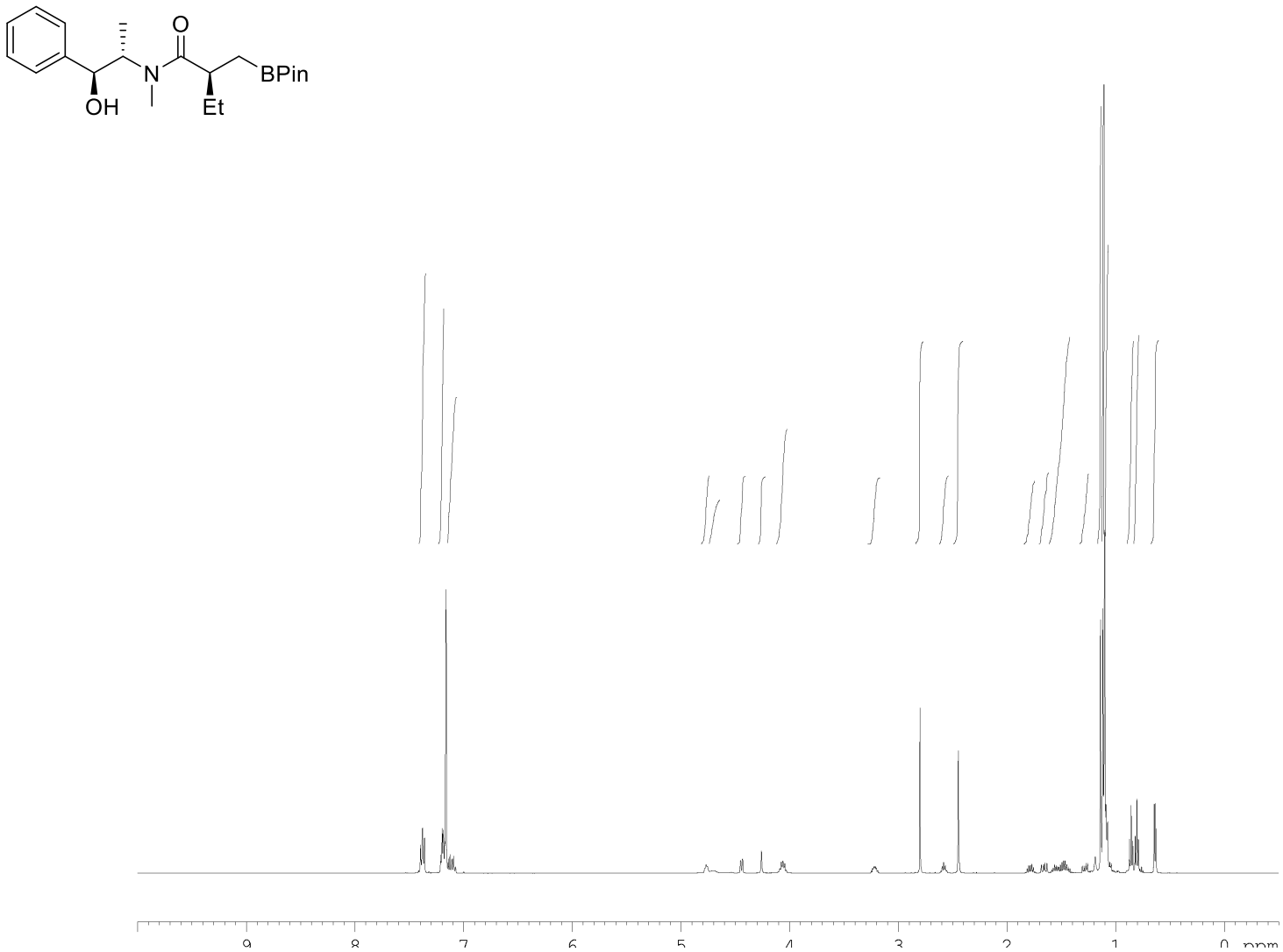
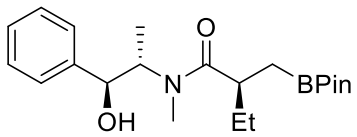
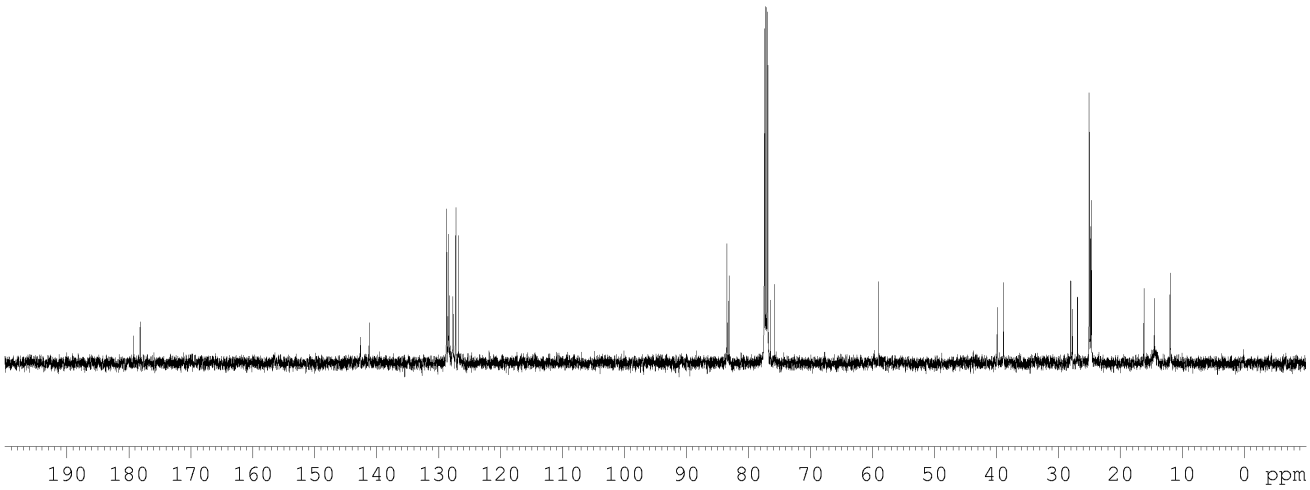


Figure A1.5 ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum


O
N
BPin
OH
Et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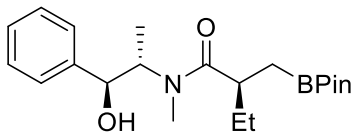
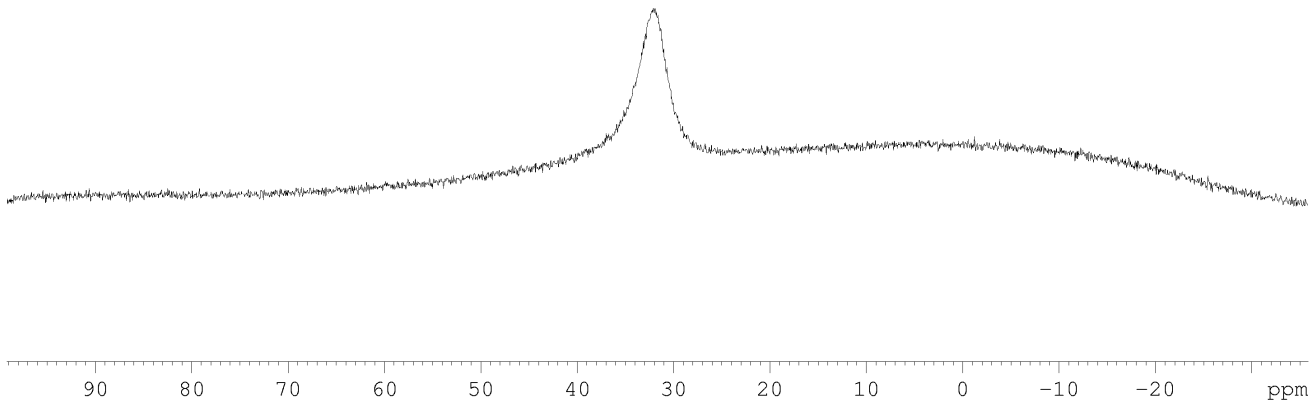

O
N
BPin
OH
Et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80
70
60
50
40
30
20
10
0
−10
−20
ppm

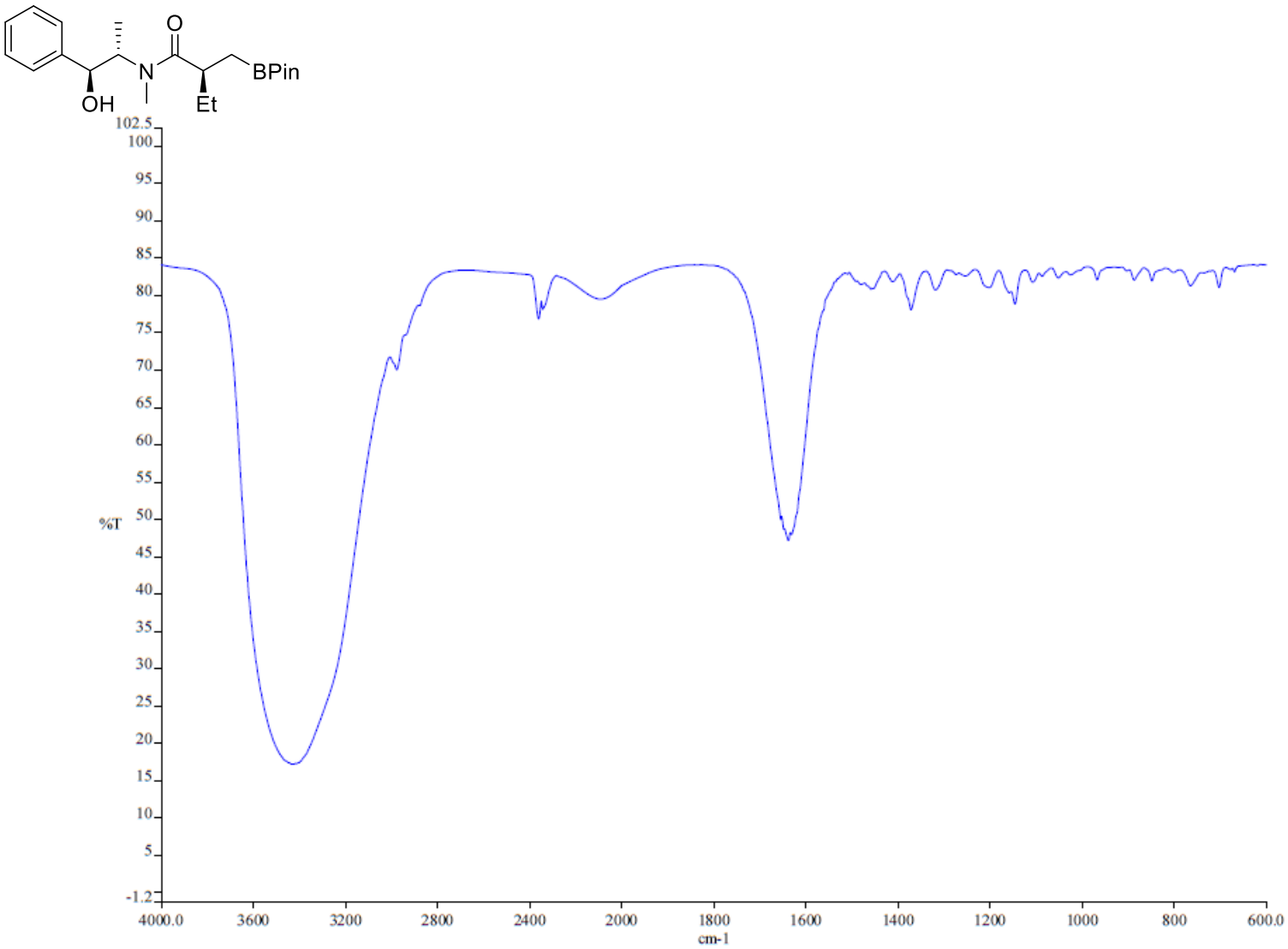
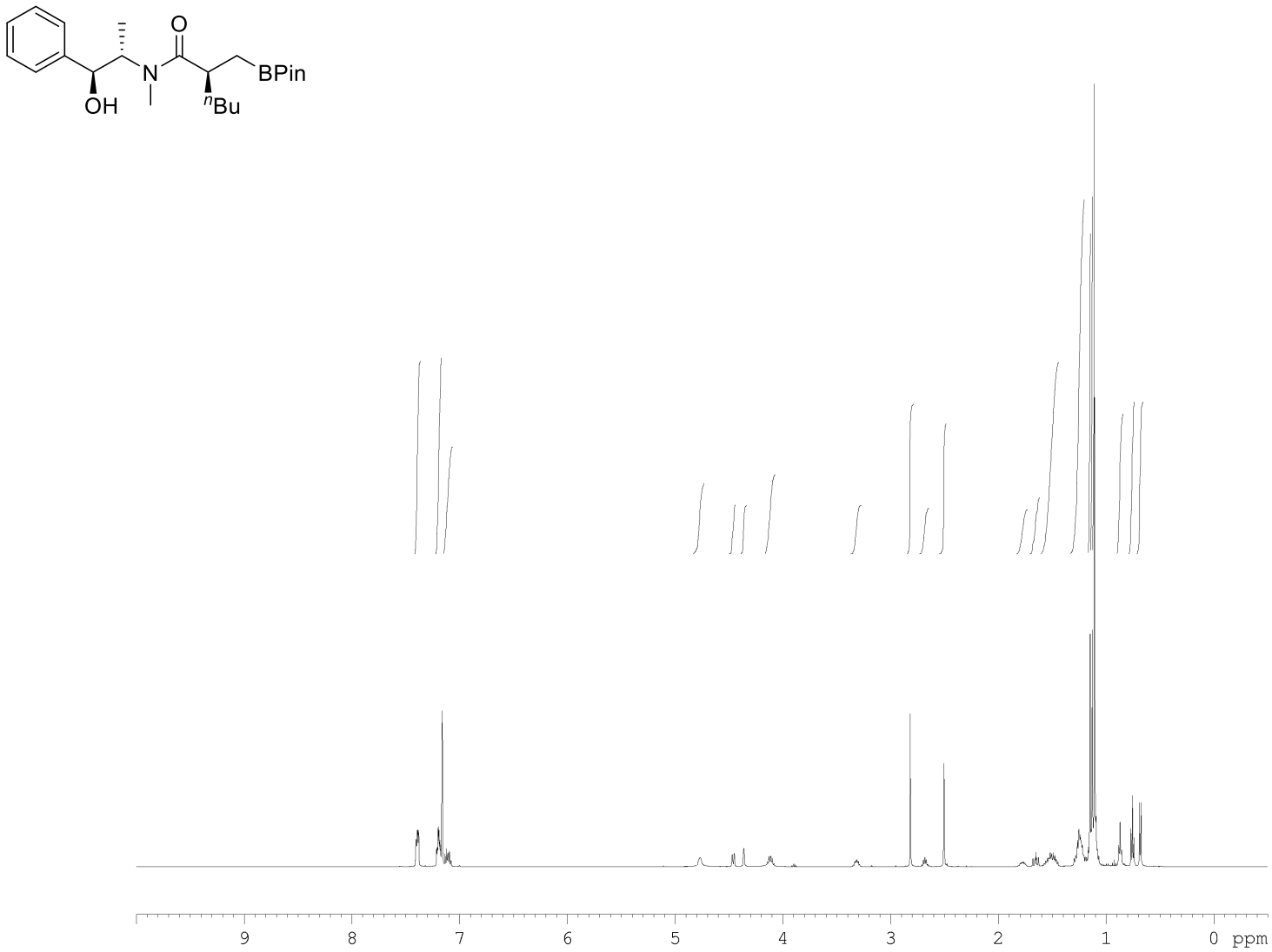
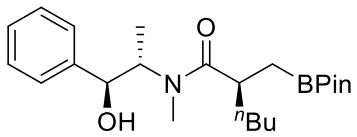
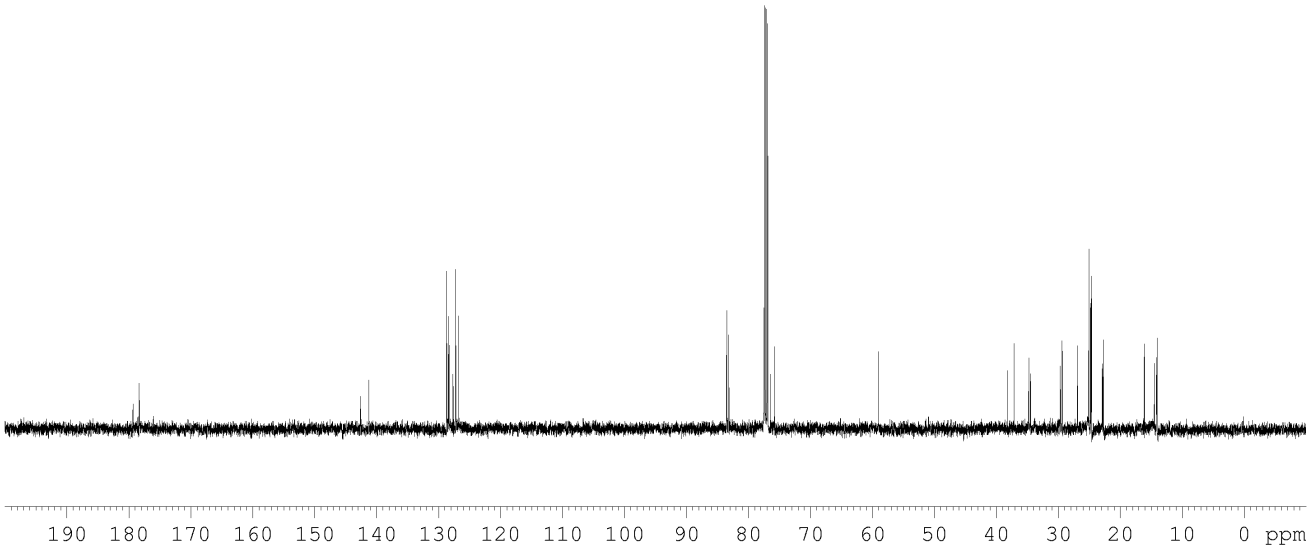


Figure A1.8 Infrared Spectrum


O
N
BPin
OH
nBu
9
8
7
6
5
4
3
2
1
0 ppm


O
N
BPin
OH
nBu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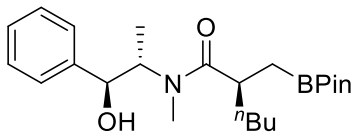
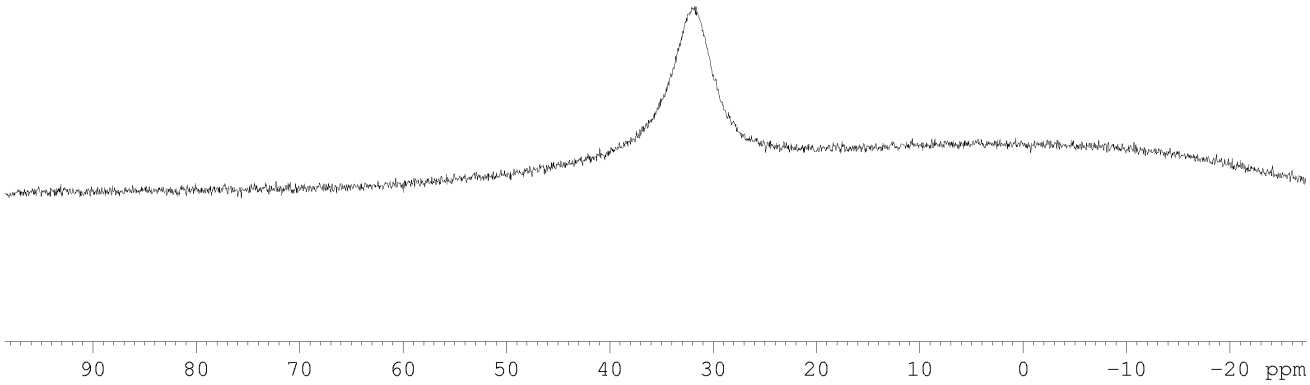

O
N
BPin
OH
nBu


90
80
70
60
50
40
30
20
10
0
−10
−20 ppm

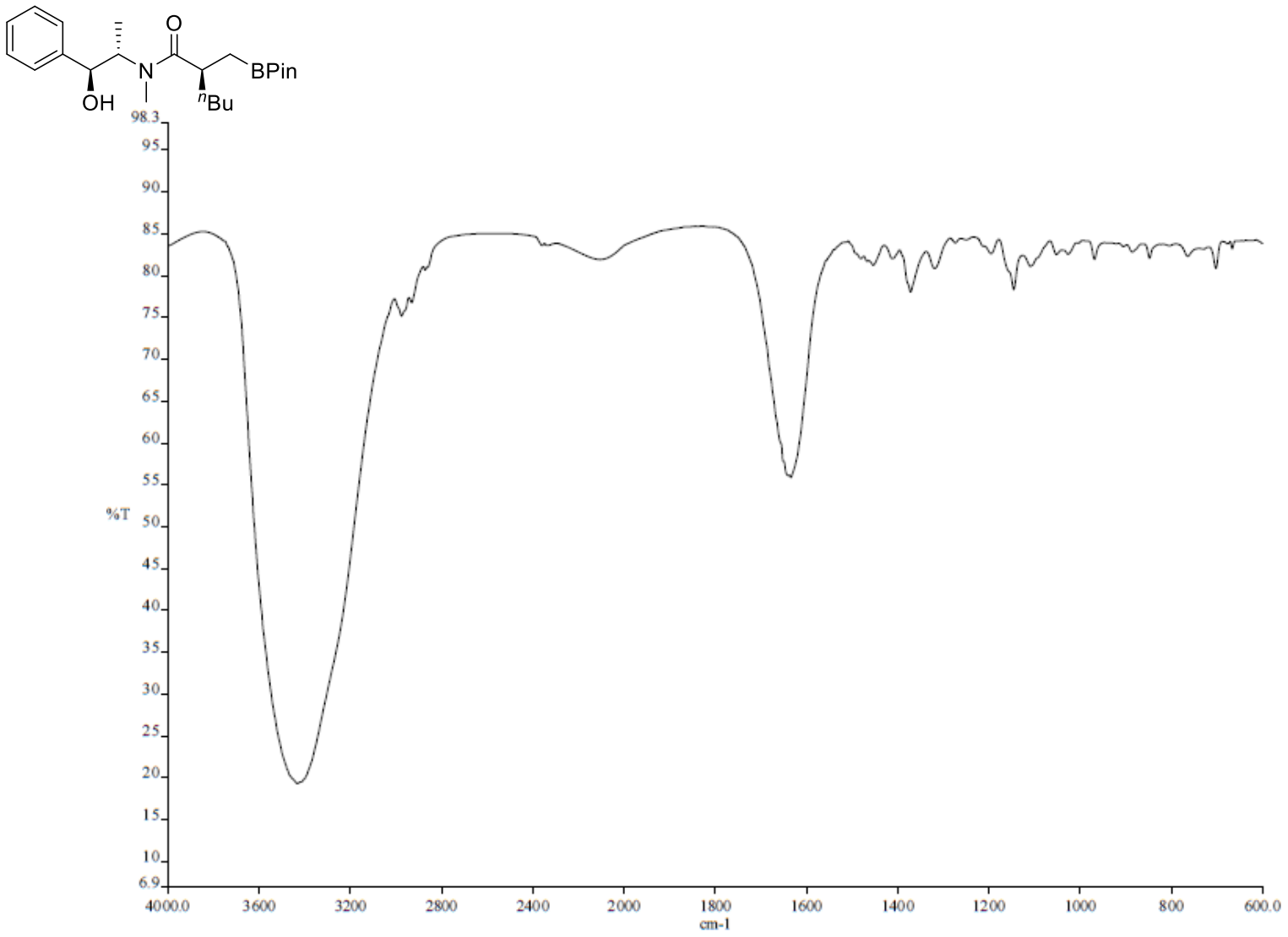
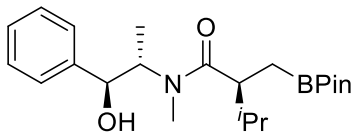


Figure A1.12 Infrared Spectrum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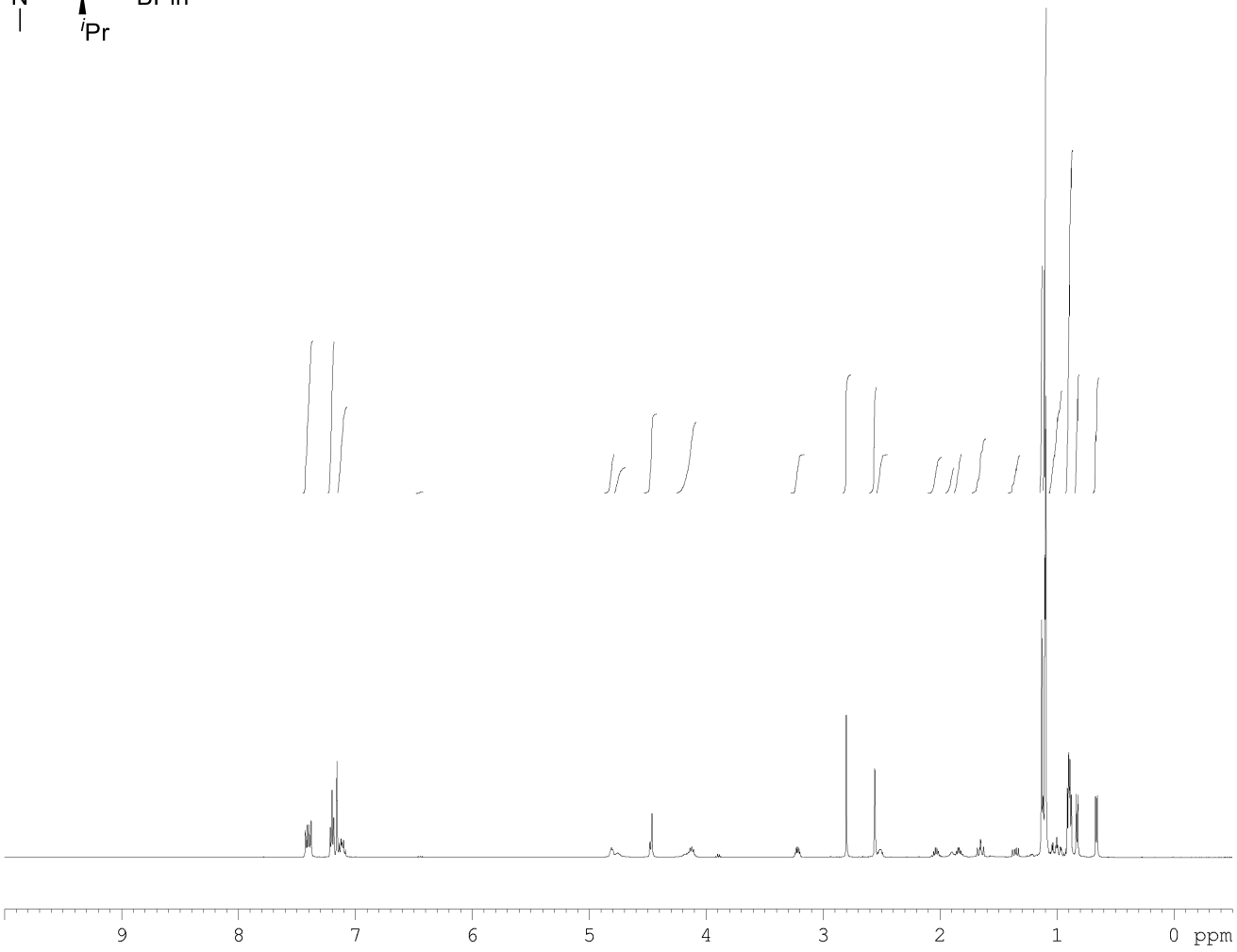
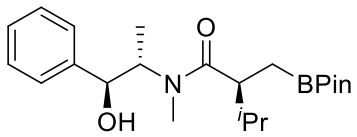
N
BPin
OH
iPr


9
8
7
6
5
4
3
2
1
0 ppm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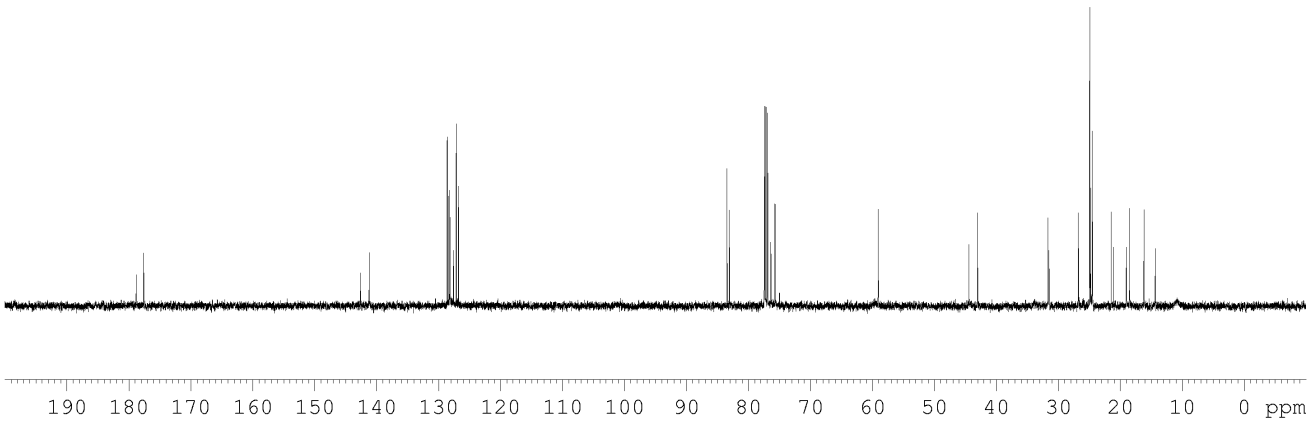
N
BPin
OH
iPr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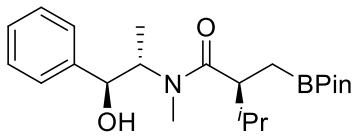
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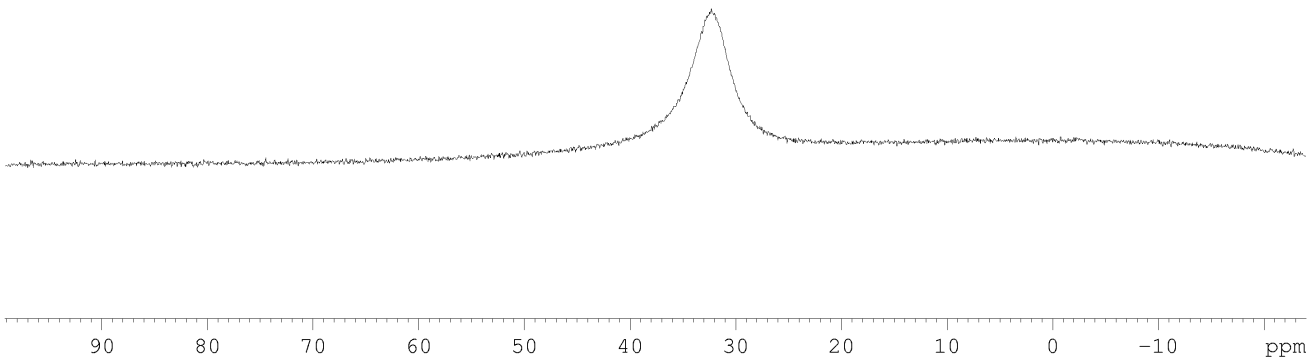
BPin
OH
iPr


90
80
70
60
50
40
30
20
10
0
−10
ppm

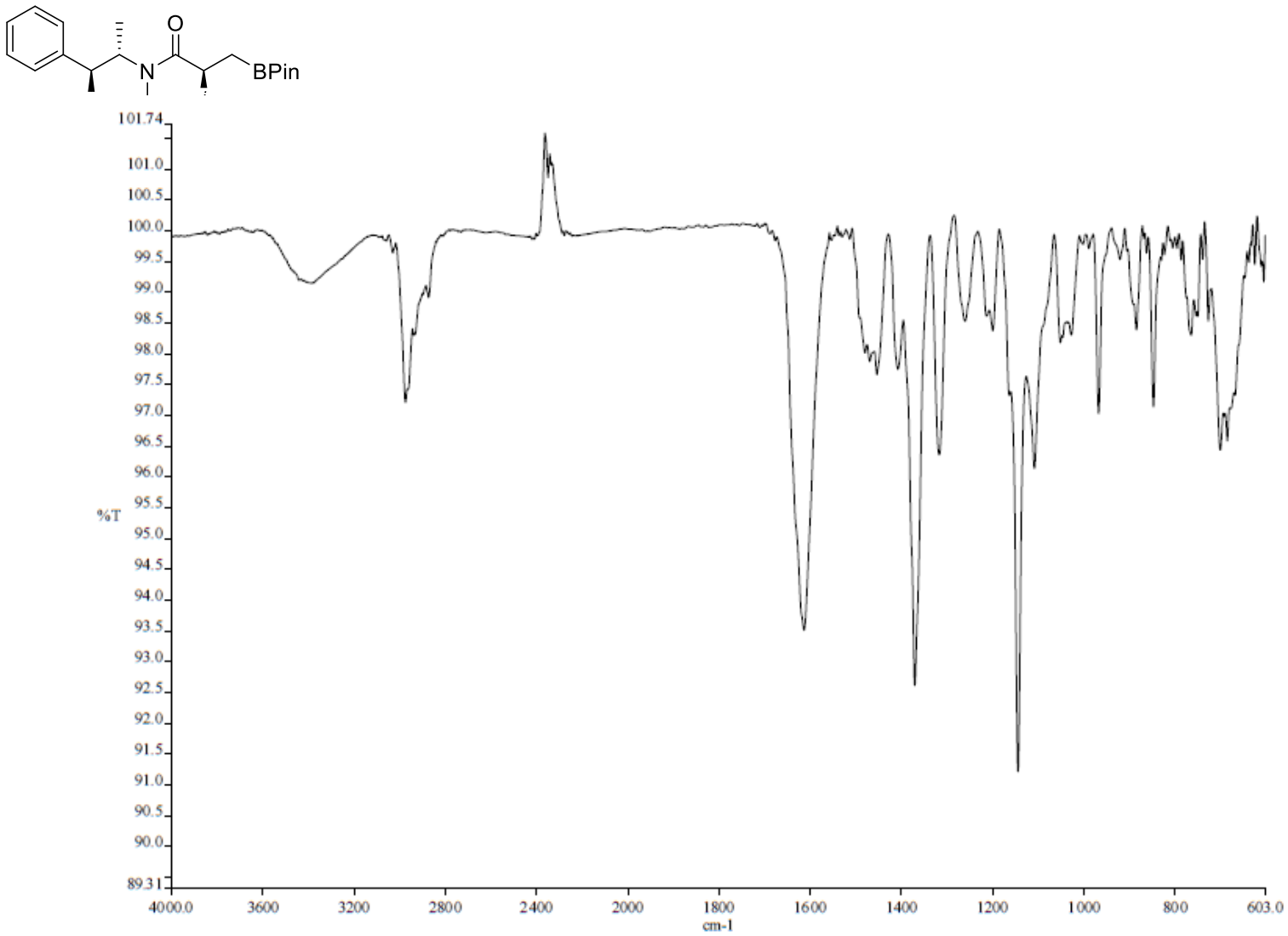
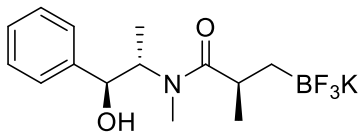


Figure A1.16 Infrared Spectrum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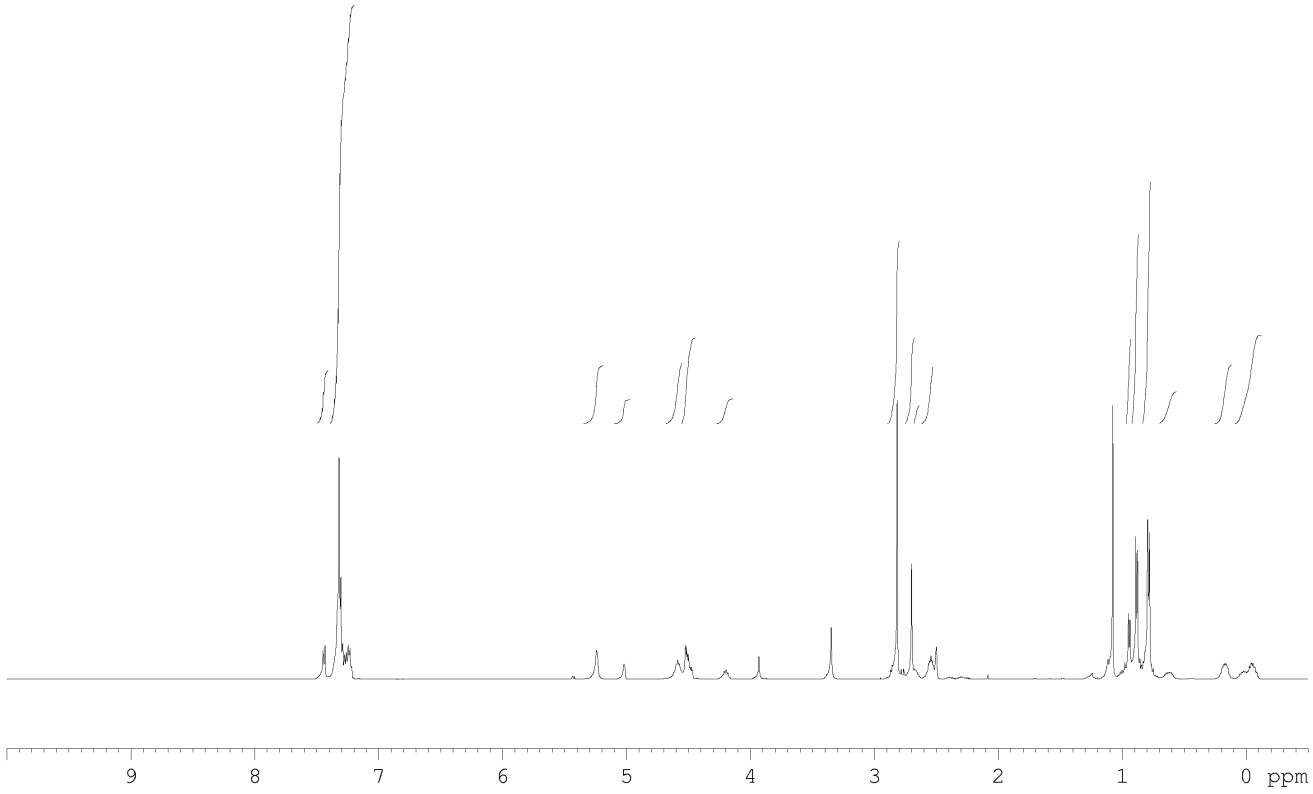
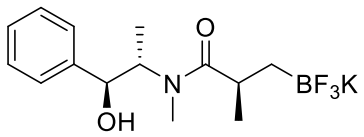
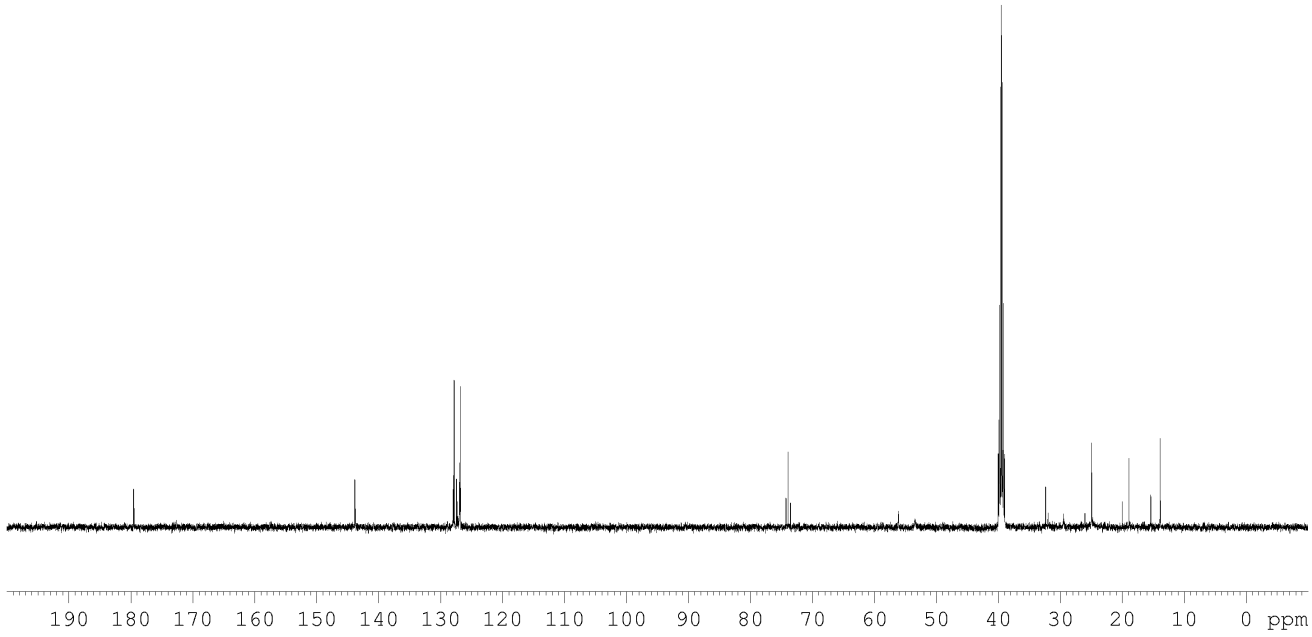
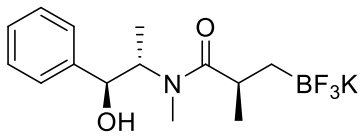
BF3K
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
N
BF3K
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



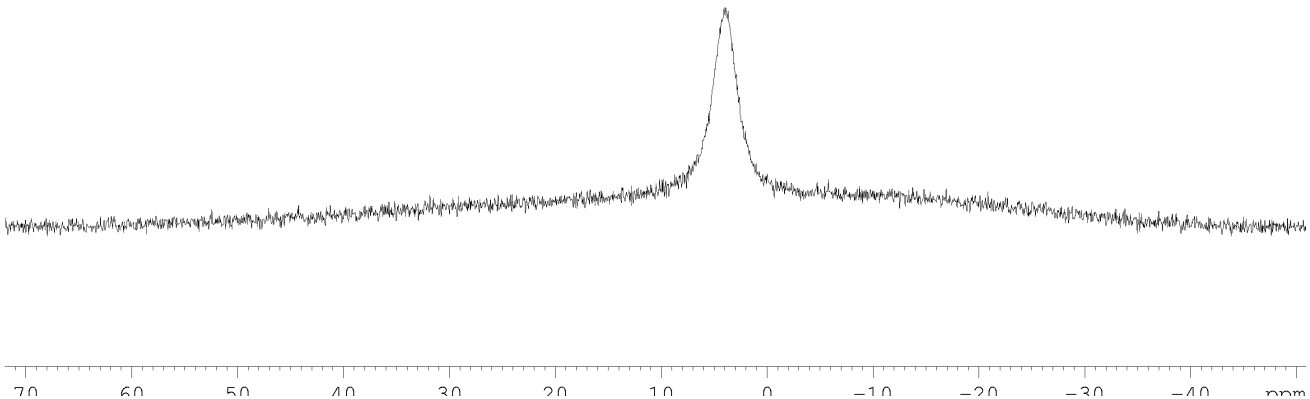
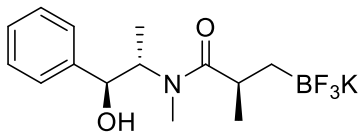
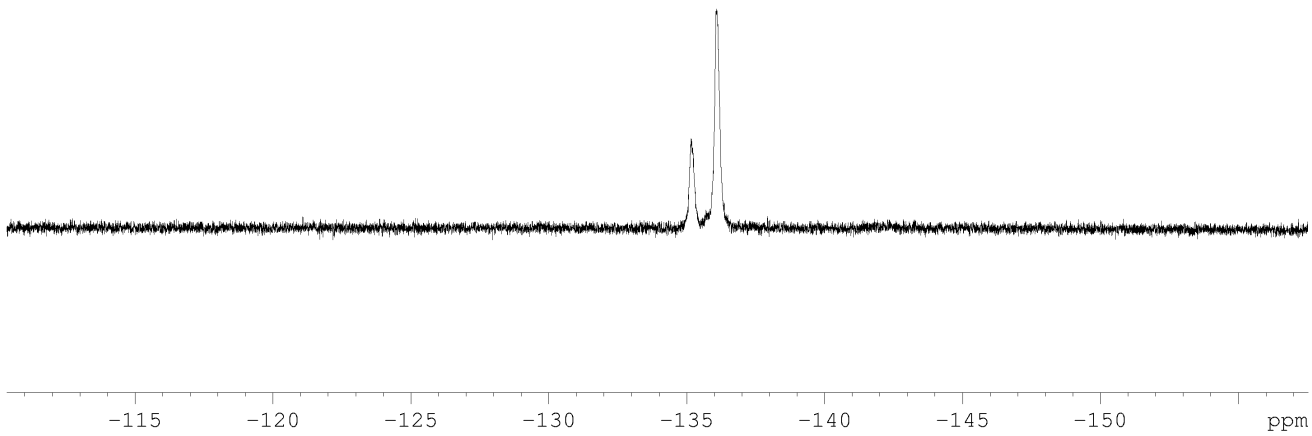


Figure A1.19 ^{11}B NMR (128.4 MHz, DMSO-d_6) Spectrum


O
N
BF3K
OH


−115
−120
−125
−130
−135
−140
−145
−150
ppm

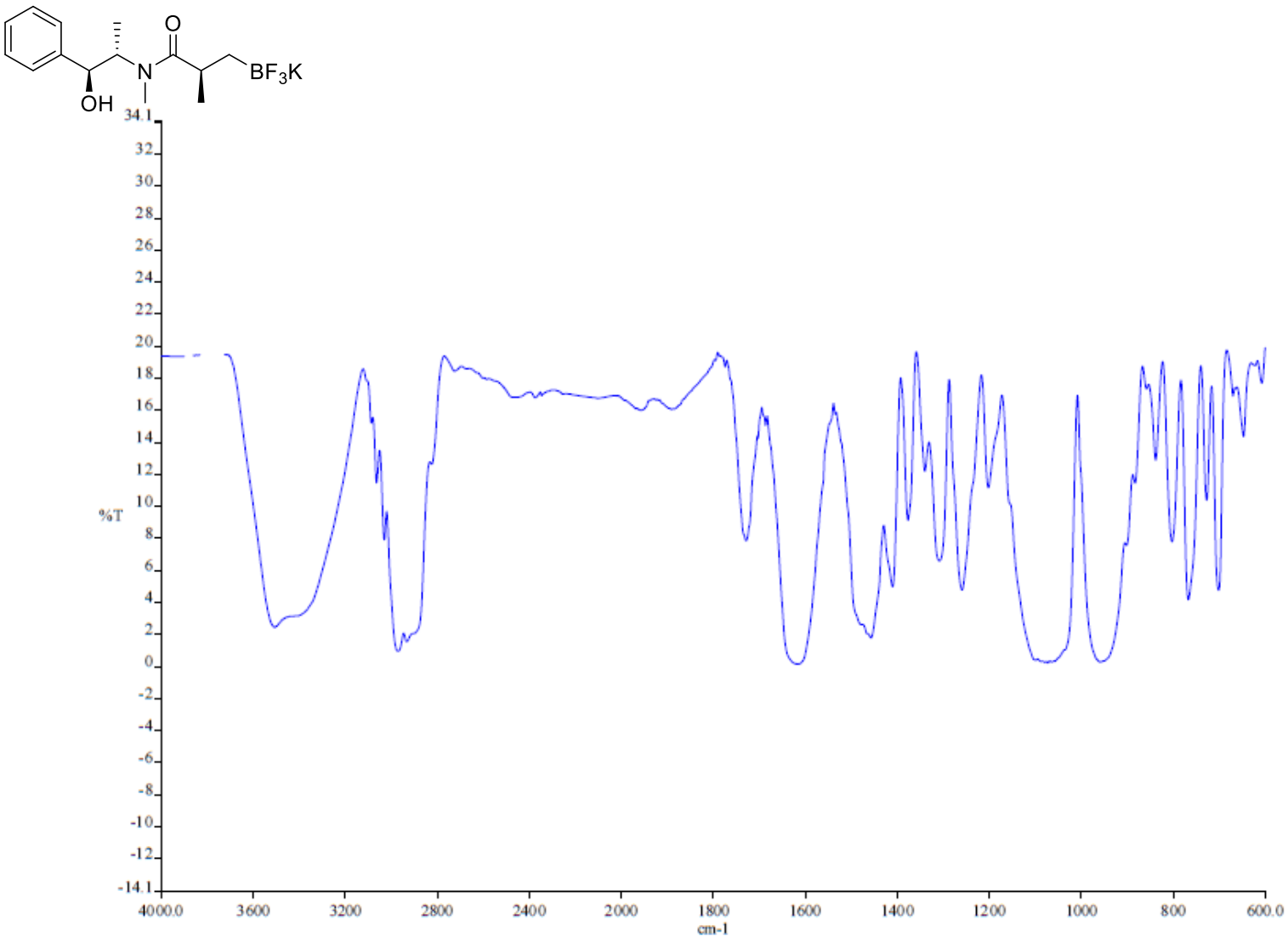
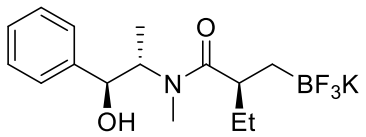
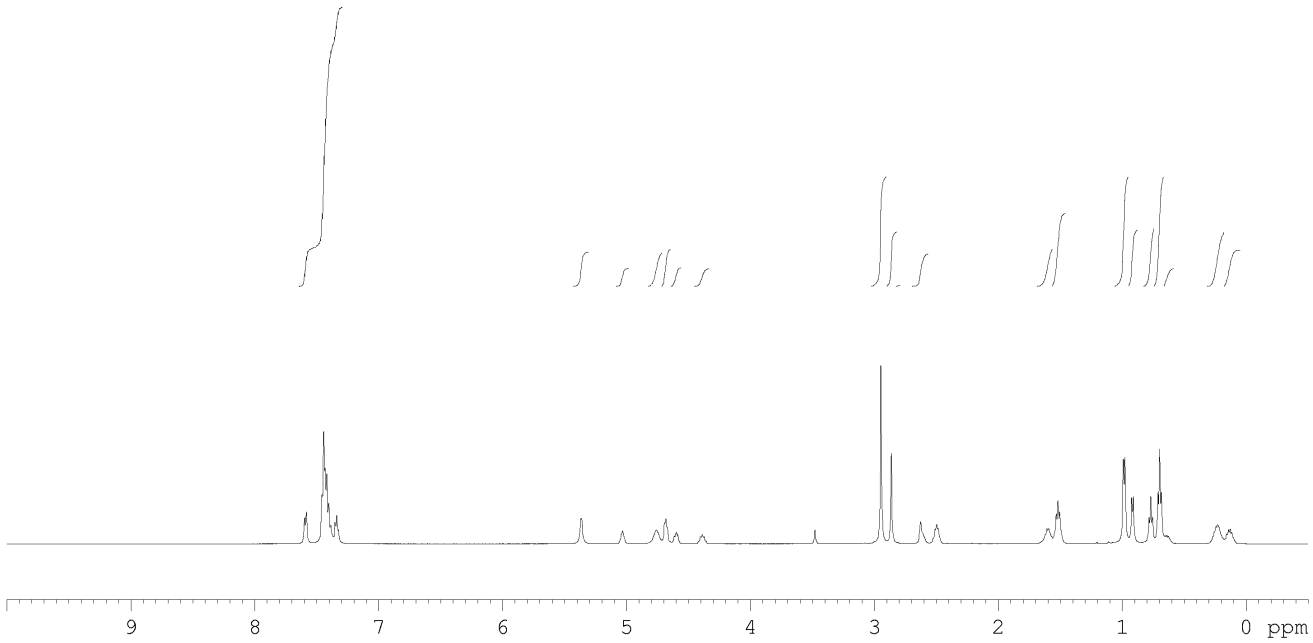
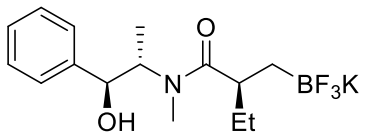
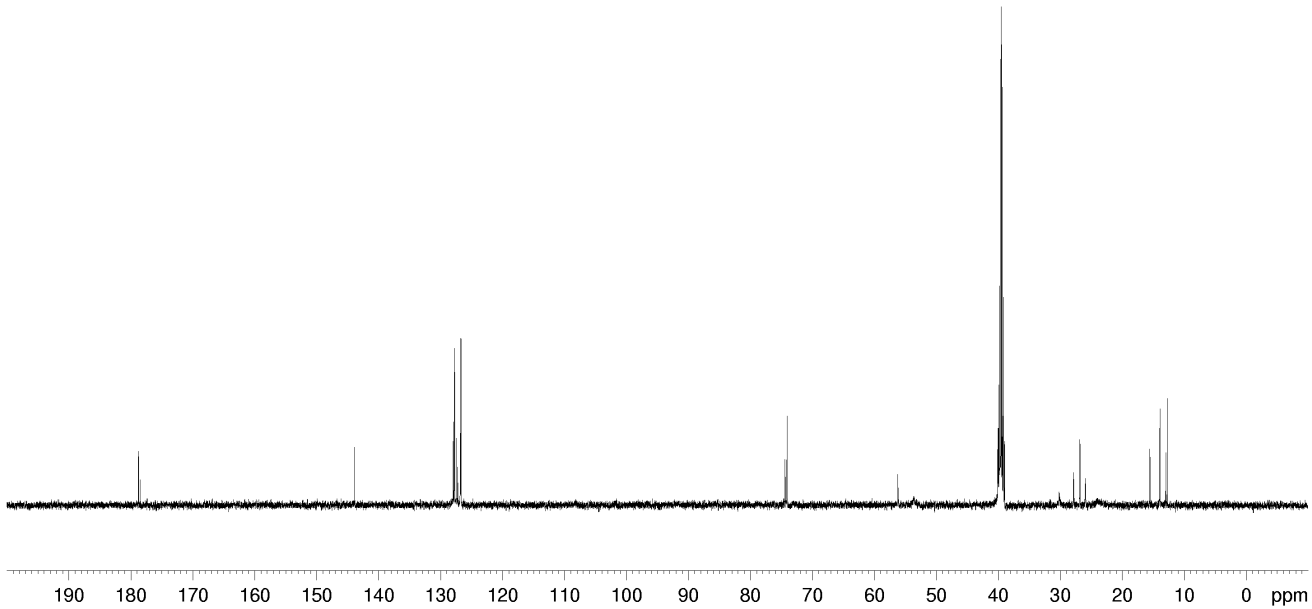


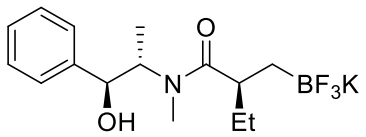
Figure A1.21 Infrared Spectrum

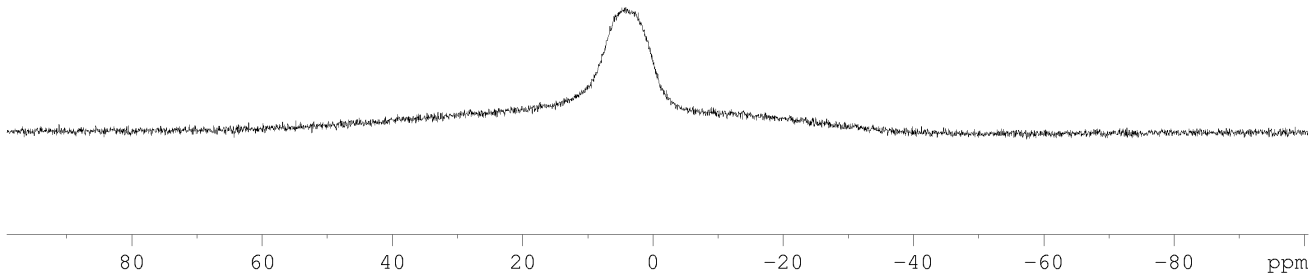

O
N
BF3K
OH
Et

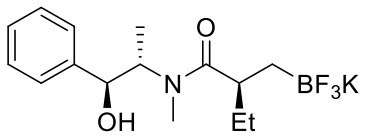

9
8
7
6
5
4
3
2
1
0 ppm

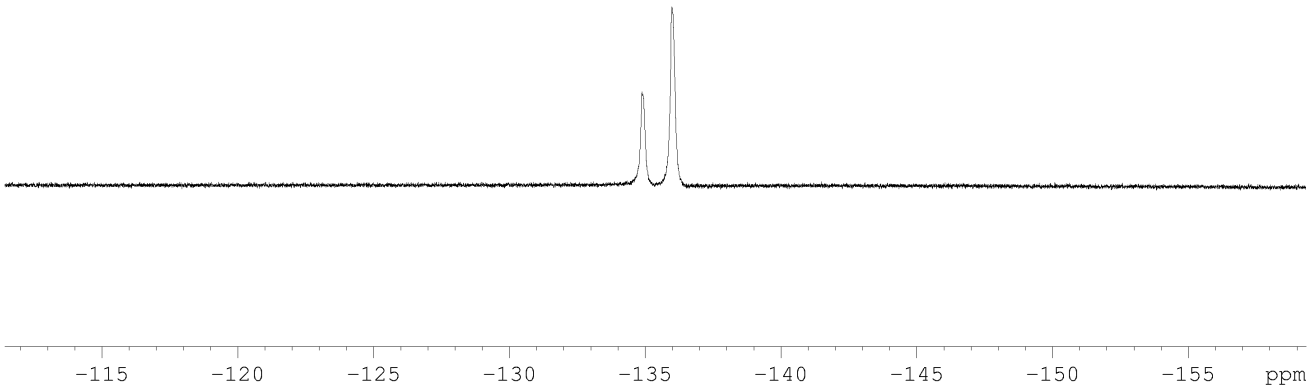

O
N
BF3K
OH
Et


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


O
N
BF3K
OH
Et


80
60
40
20
0
−20
−40
−60
−80
ppm


O
N
BF3K
OH
Et


−115
−120
−125
−130
−135
−140
−145
−150
−155
ppm

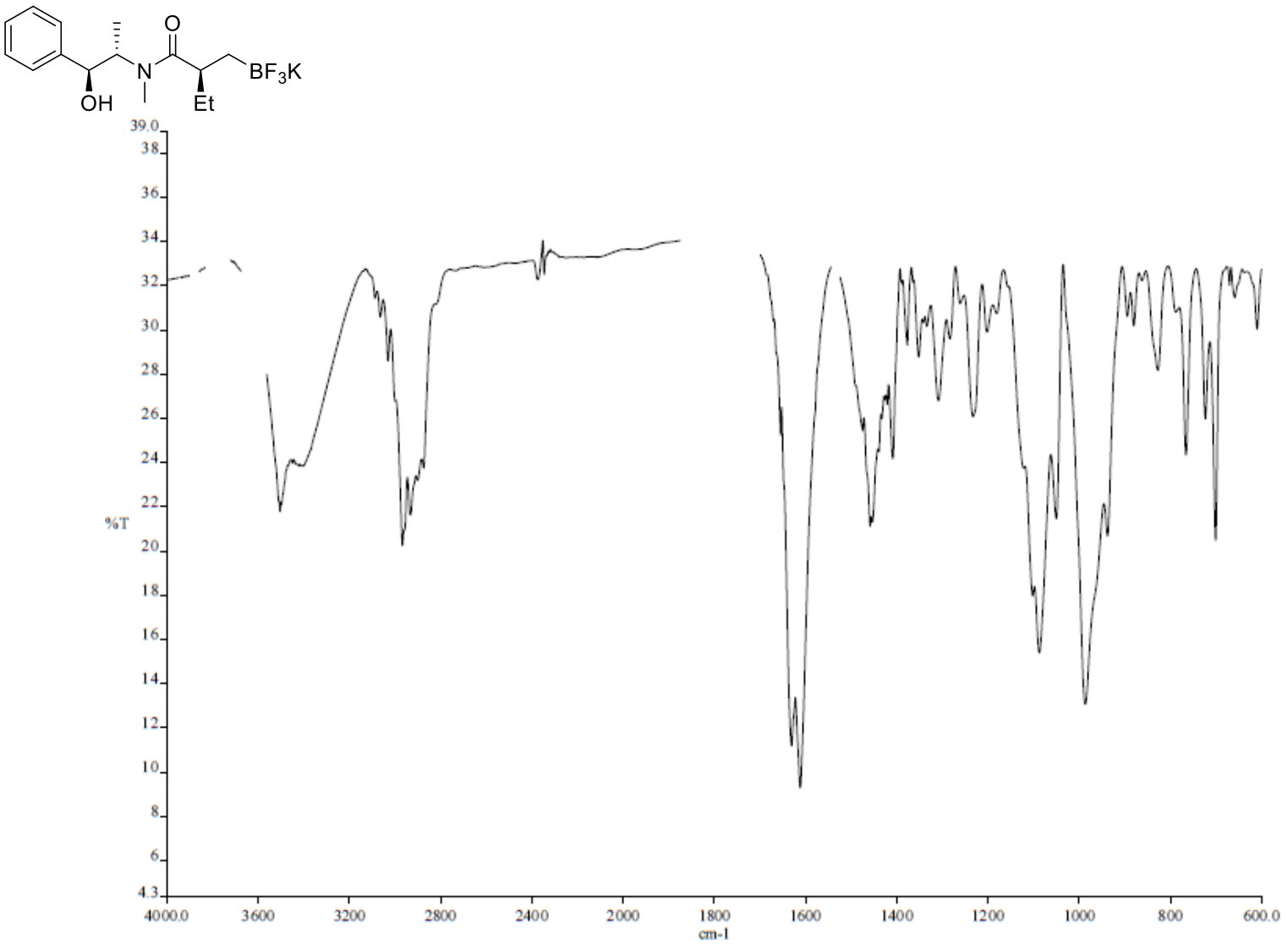
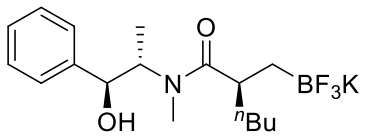
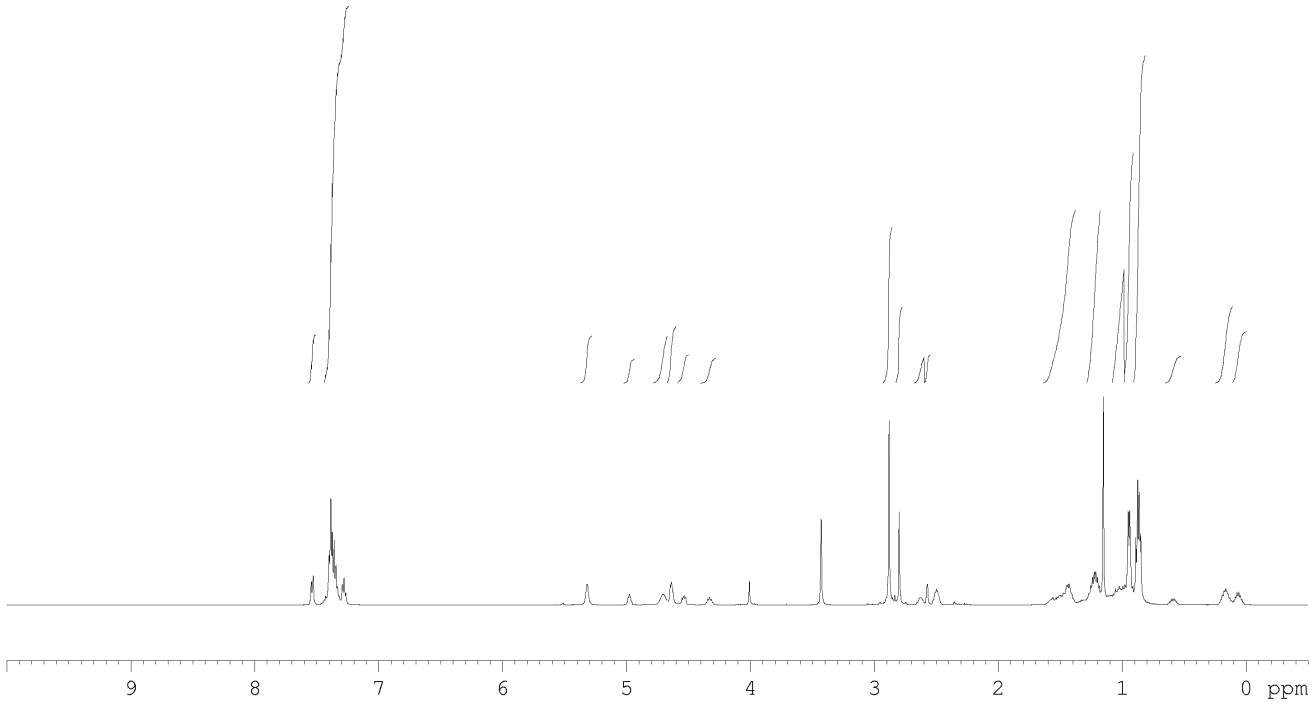
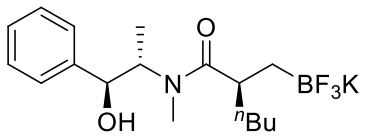
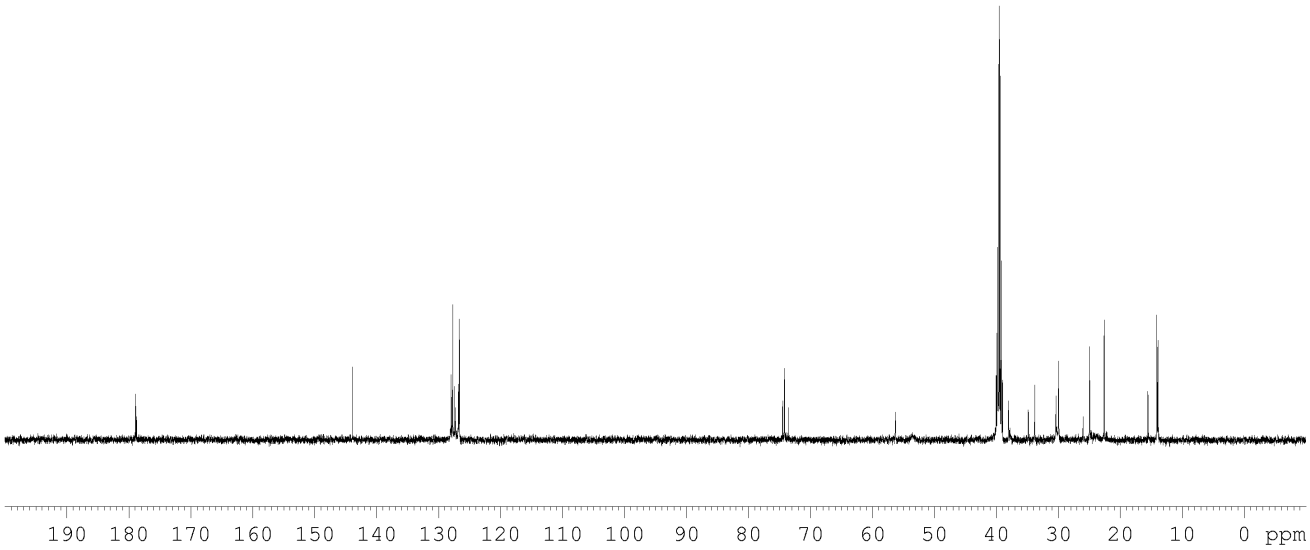


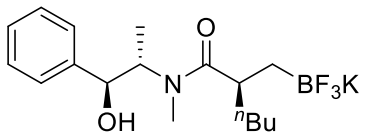
Figure A1.20 Infrared Spectrum

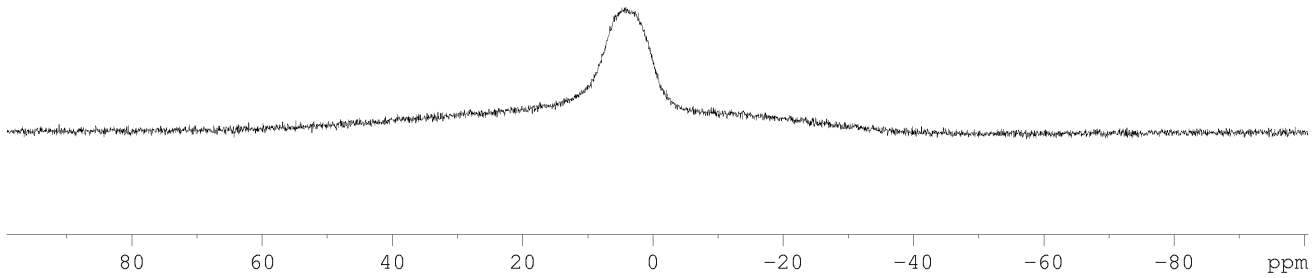

O
N
BF3K
OH
nBu

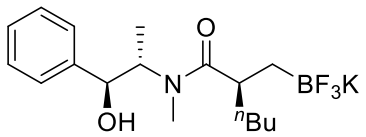

9
8
7
6
5
4
3
2
1
0 ppm

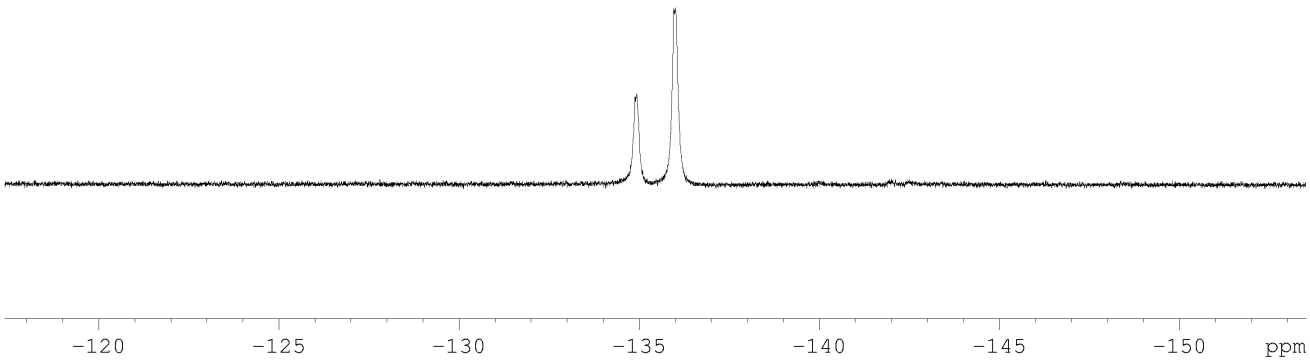

O
N
BF3K
OH
nBu


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
N
BF3K
OH
nBu


80
60
40
20
0
−20
−40
−60
−80
ppm


O
N
BF3K
OH
nBu


−120
−125
−130
−135
−140
−145
−150
ppm

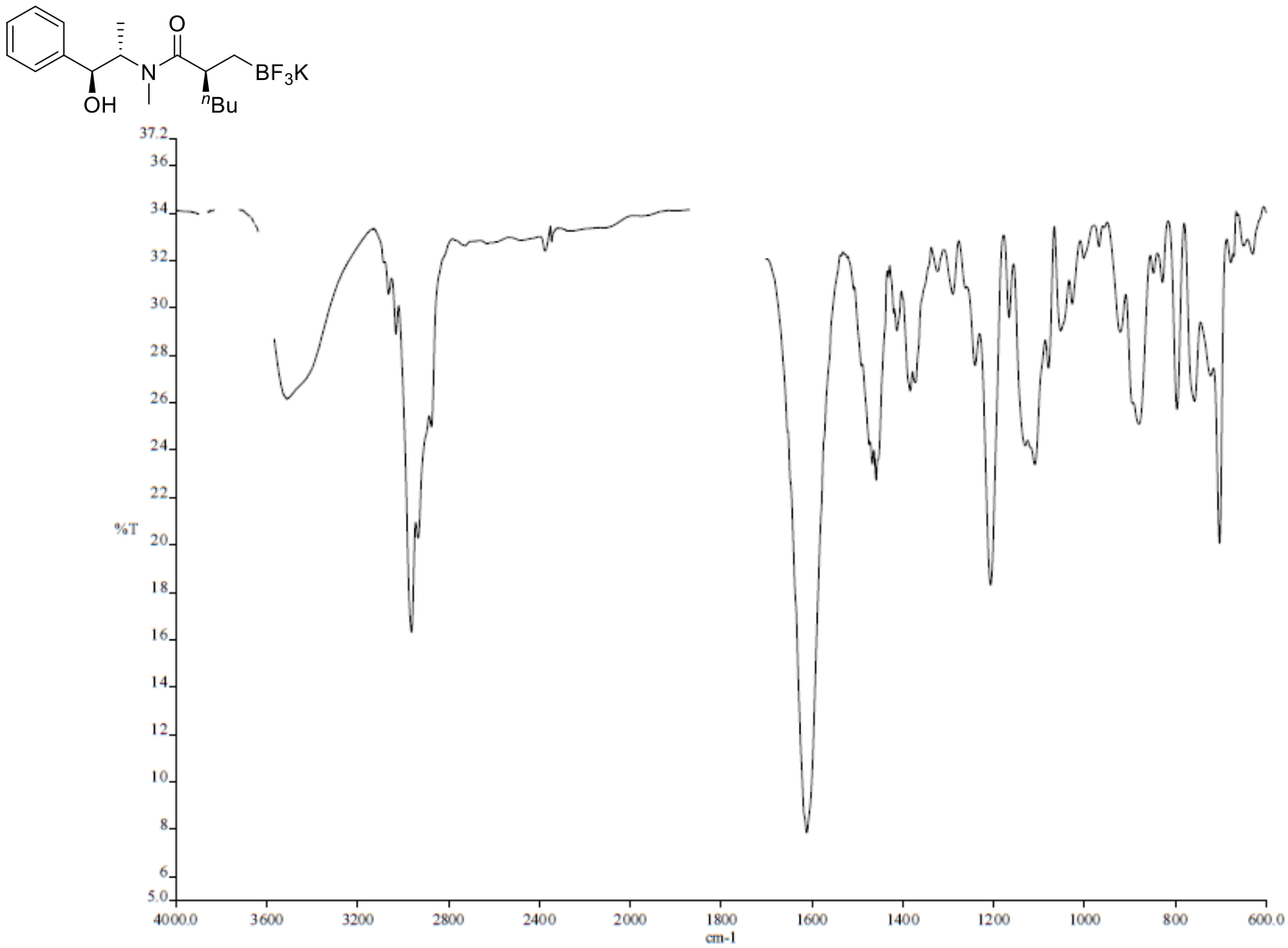
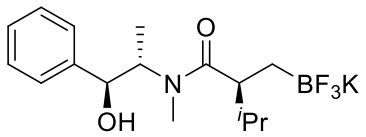
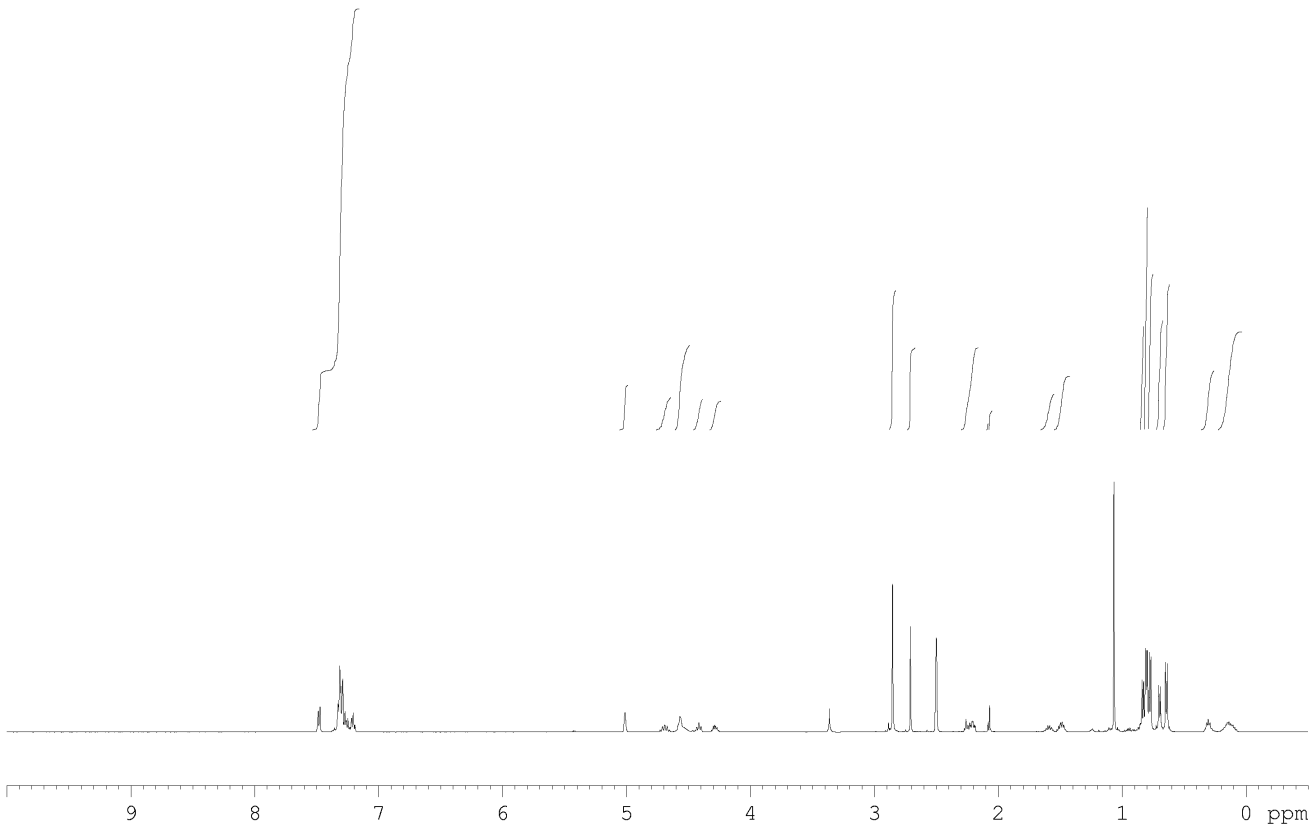


Figure A1.31 Infrared Spectrum


O
N
BF3K
OH
iPr


9
8
7
6
5
4
3
2
1
0 ppm

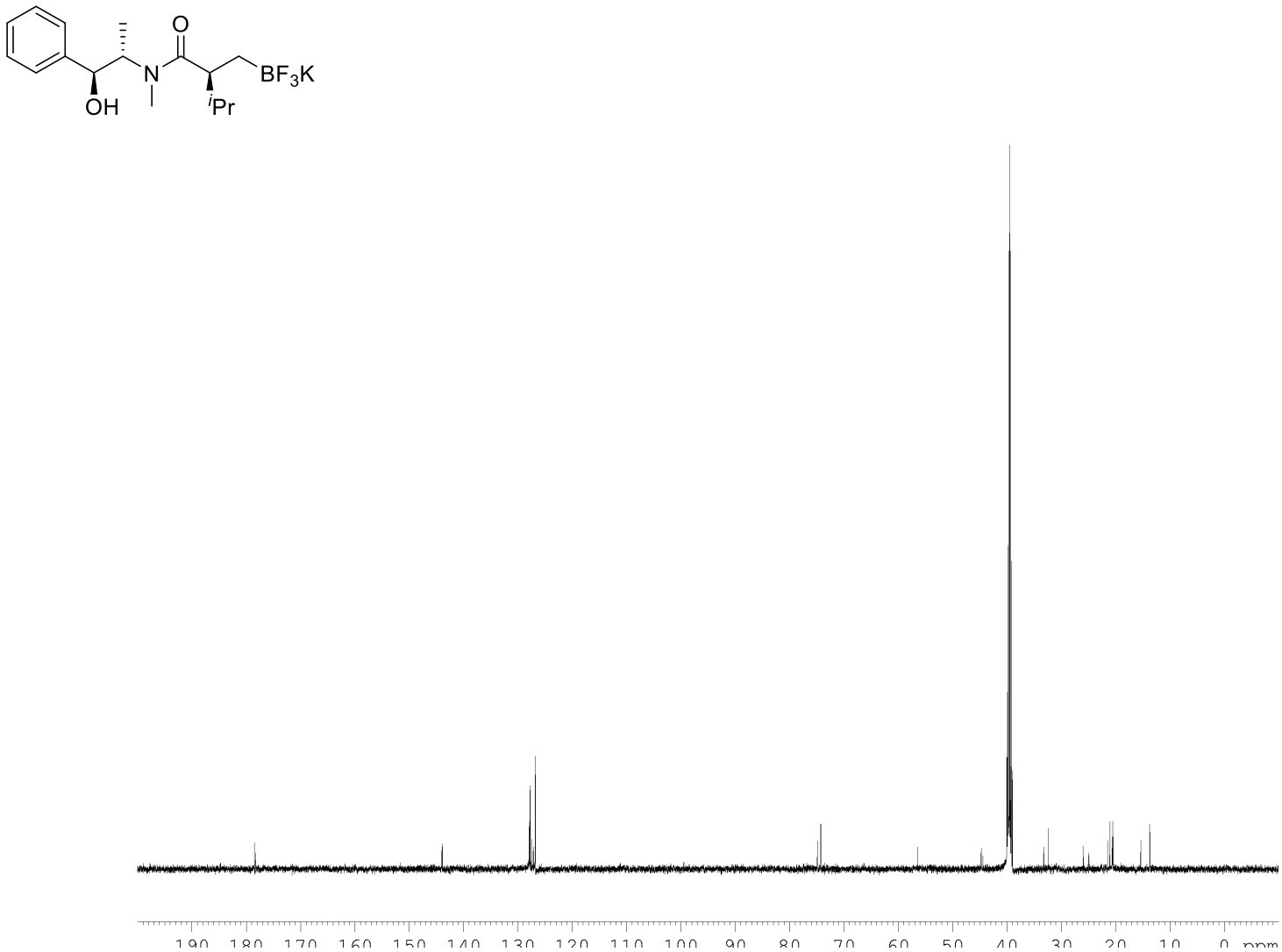
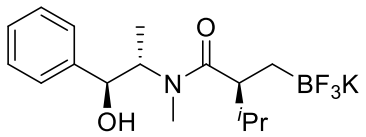
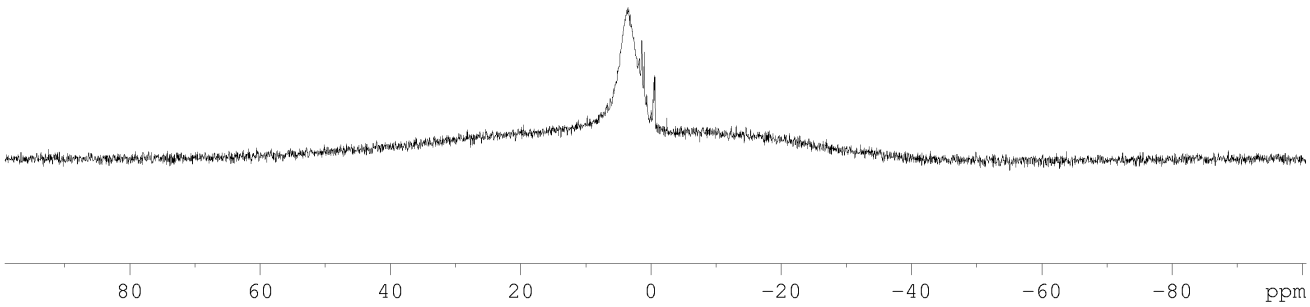
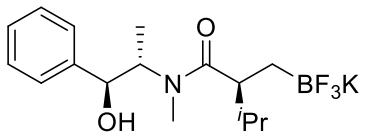
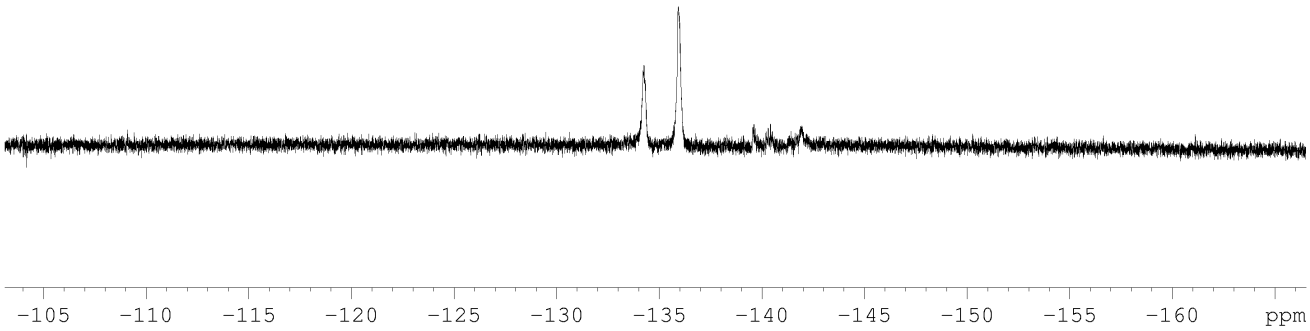


Figure A1.33 ^{13}C NMR (125.8 MHz, DMSO-d_6) Spectrum


O
N
BF3K
OH
iPr


80
60
40
20
0
−20
−40
−60
−80
ppm


O
N
BF3K
OH
iPr


−105
−110
−115
−120
−125
−130
−135
−140
−145
−150
−155
−160
ppm

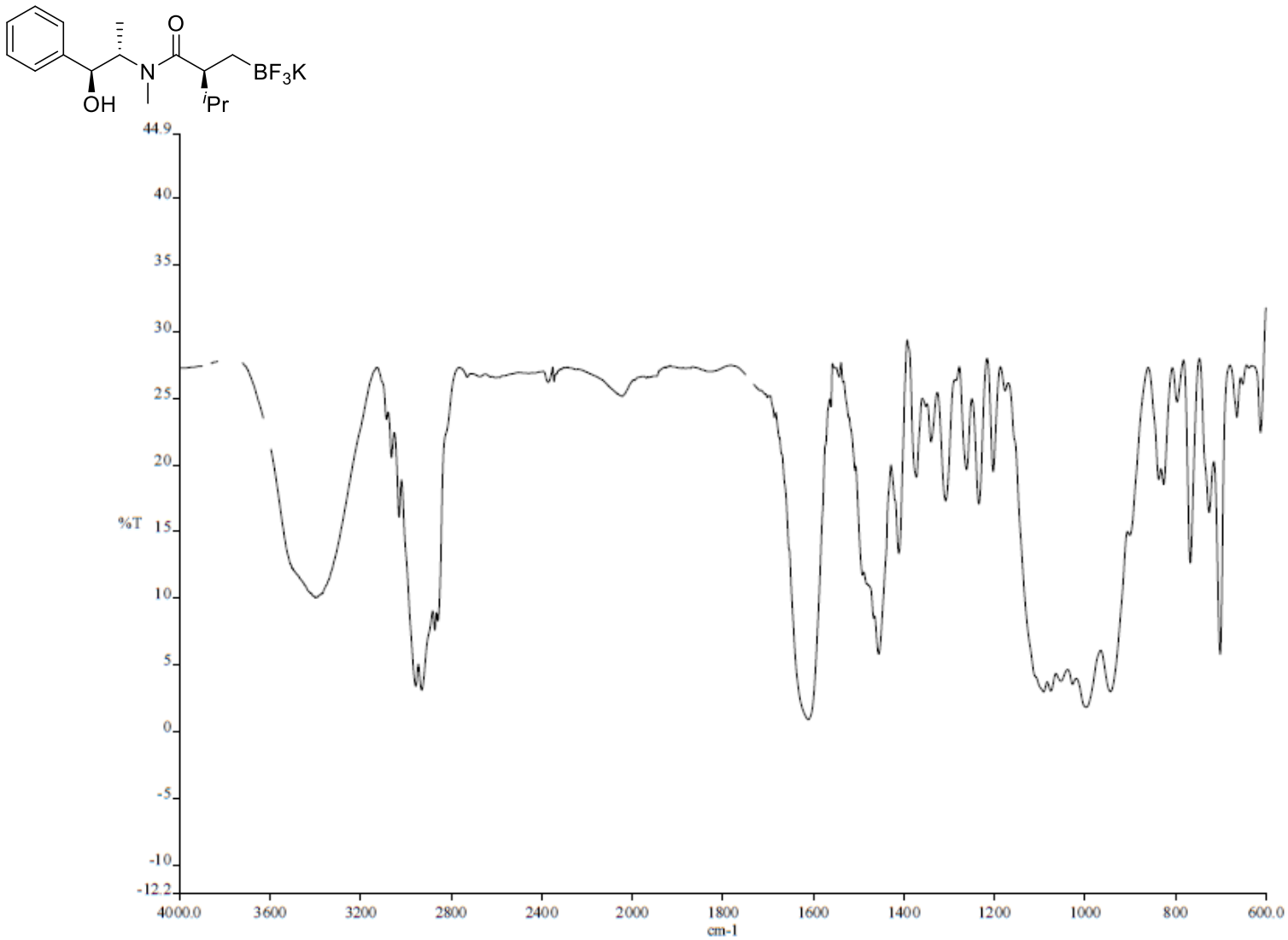
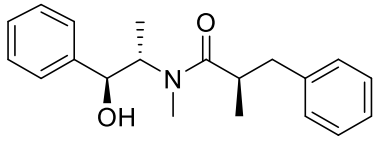
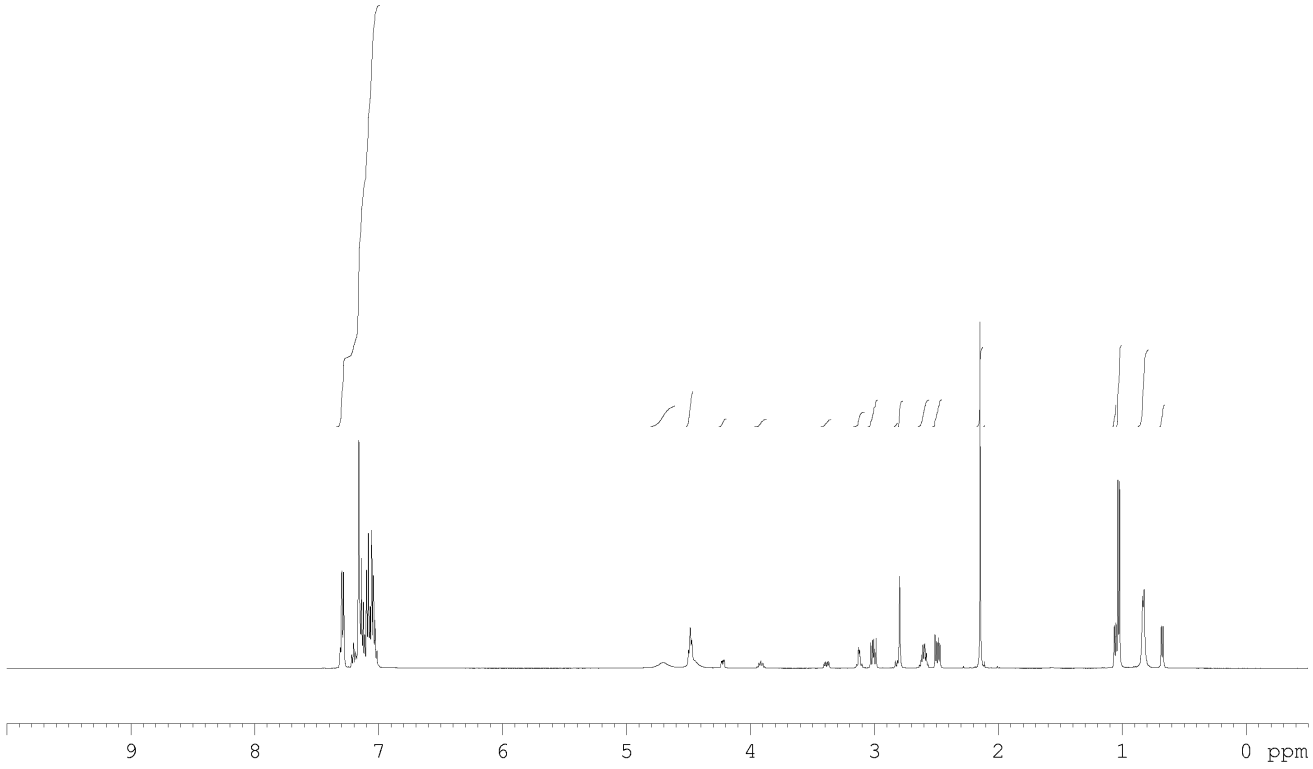
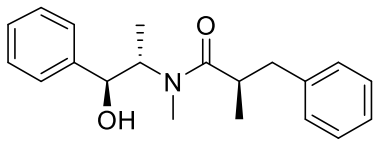
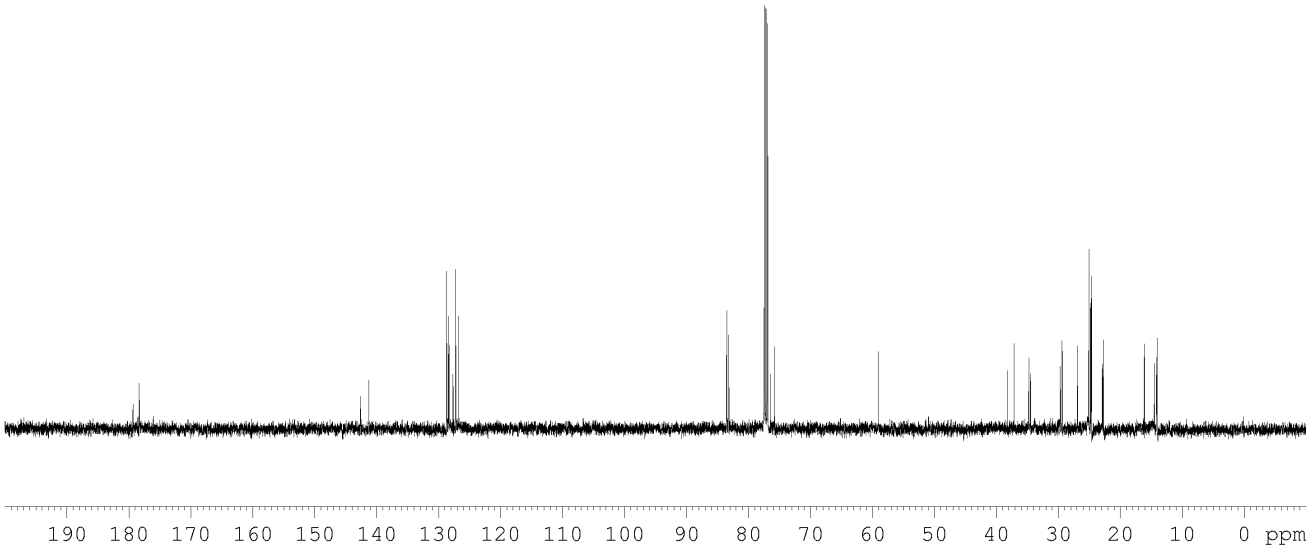


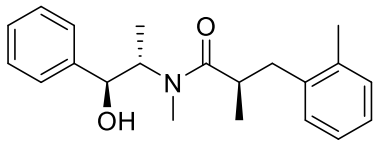
Figure A1.36 Infrared Spectrum

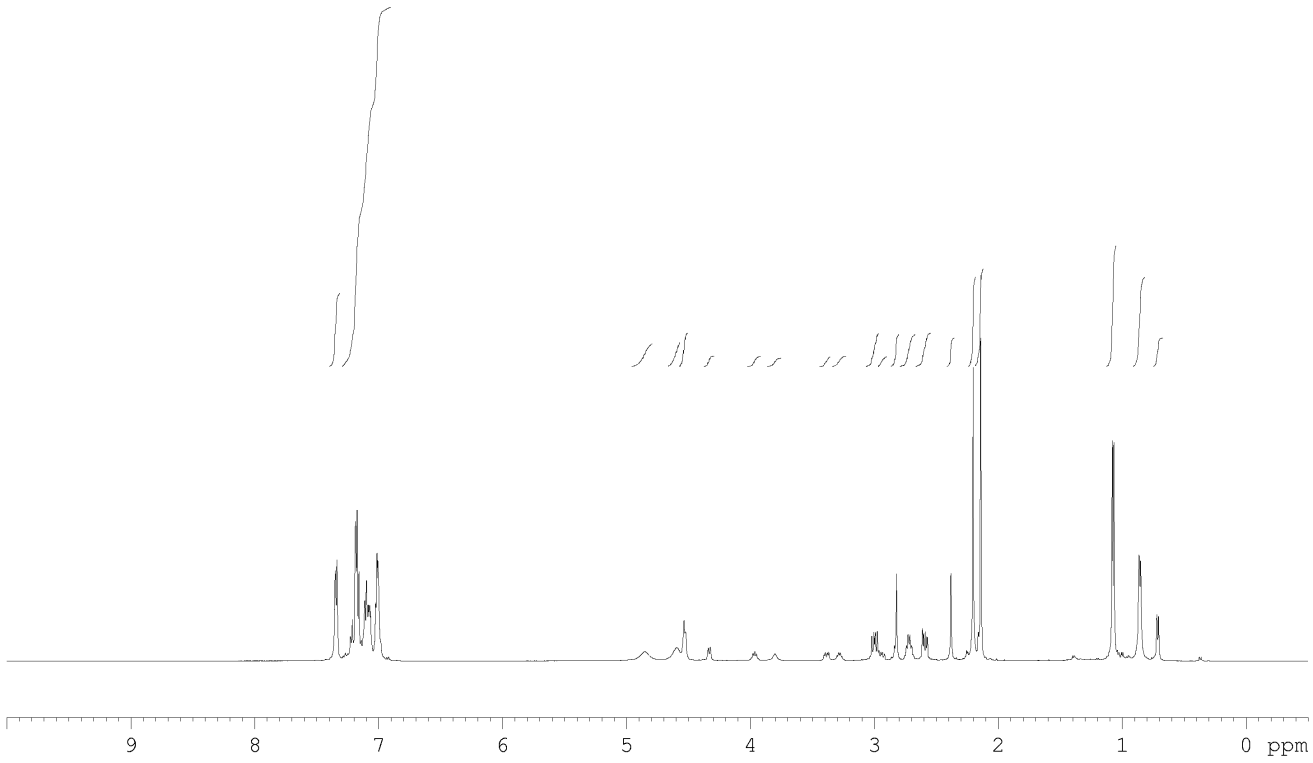

O
N
OH

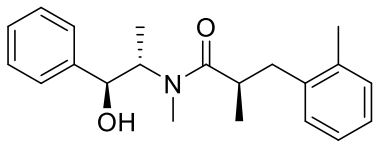

9
8
7
6
5
4
3
2
1
0 ppm

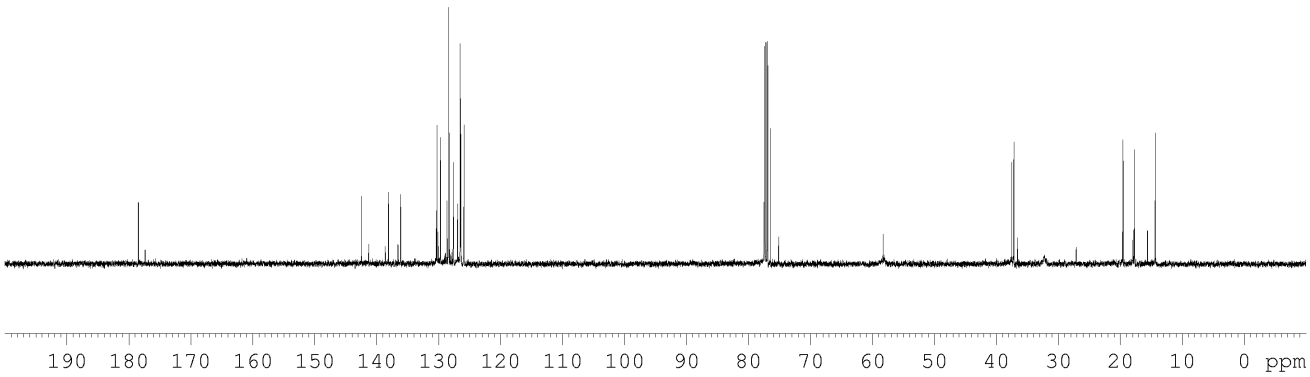

O
N
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
N
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

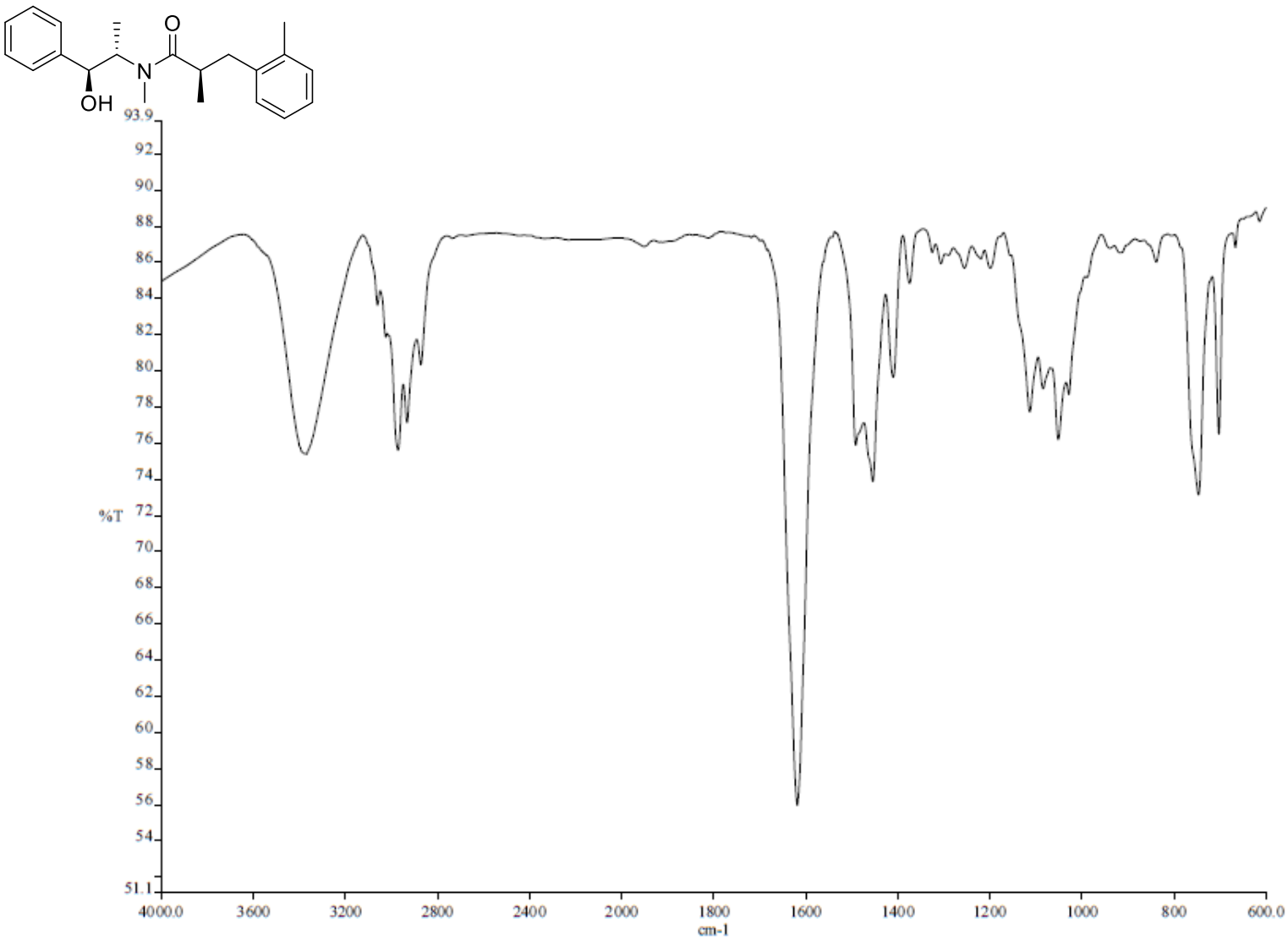
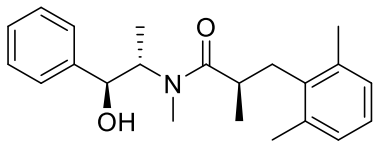
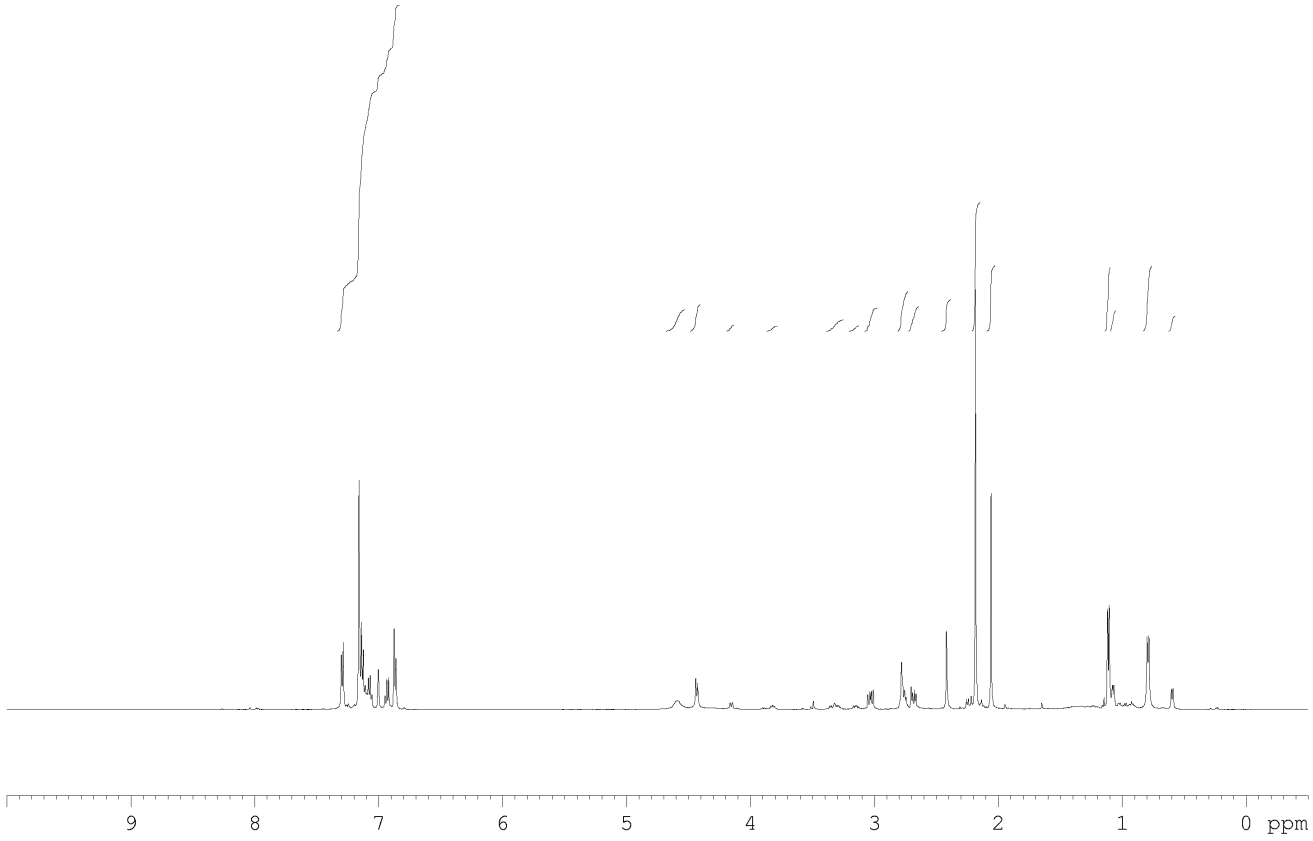
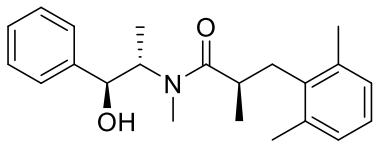
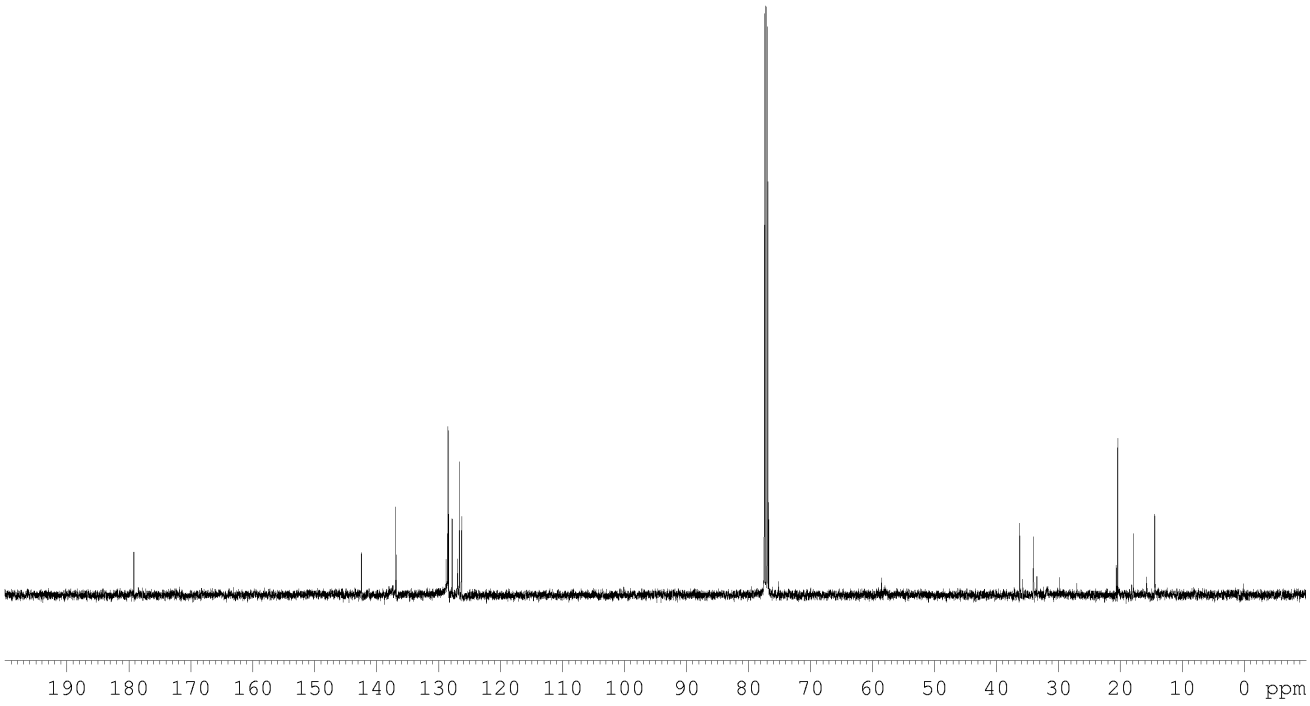


Figure A1.41 Infrared Spectrum


O
N
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

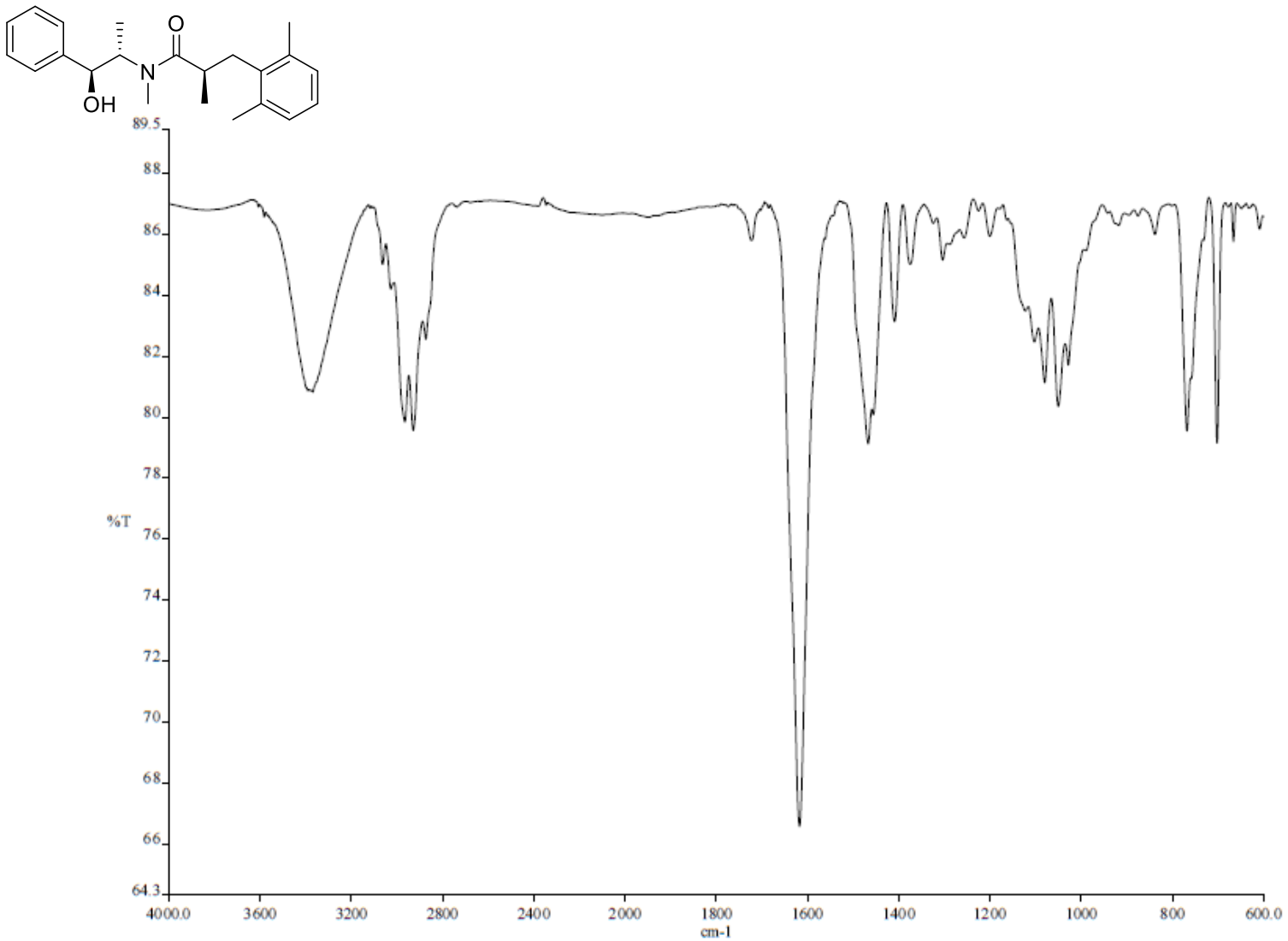
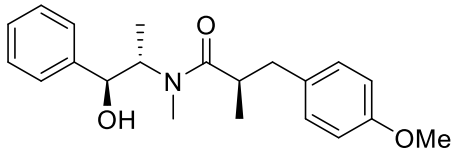
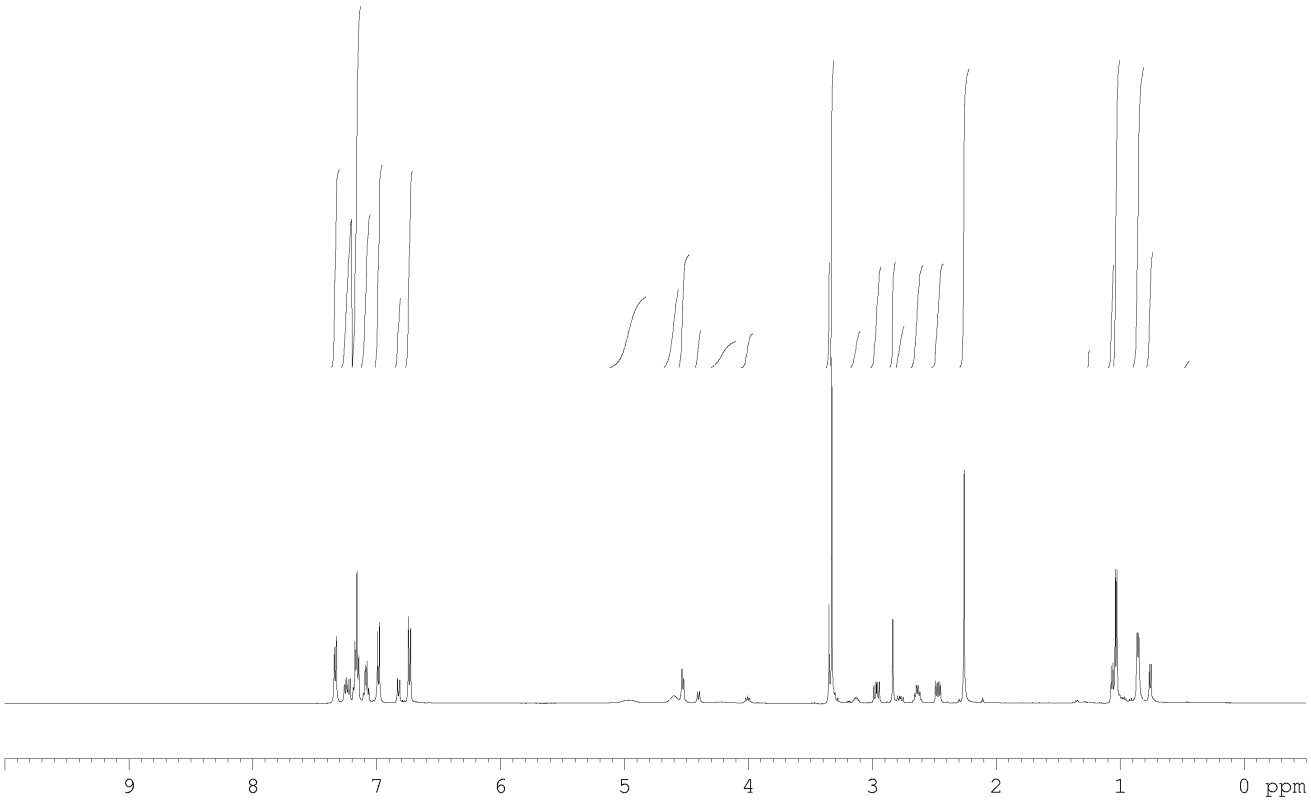
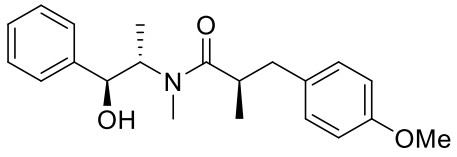
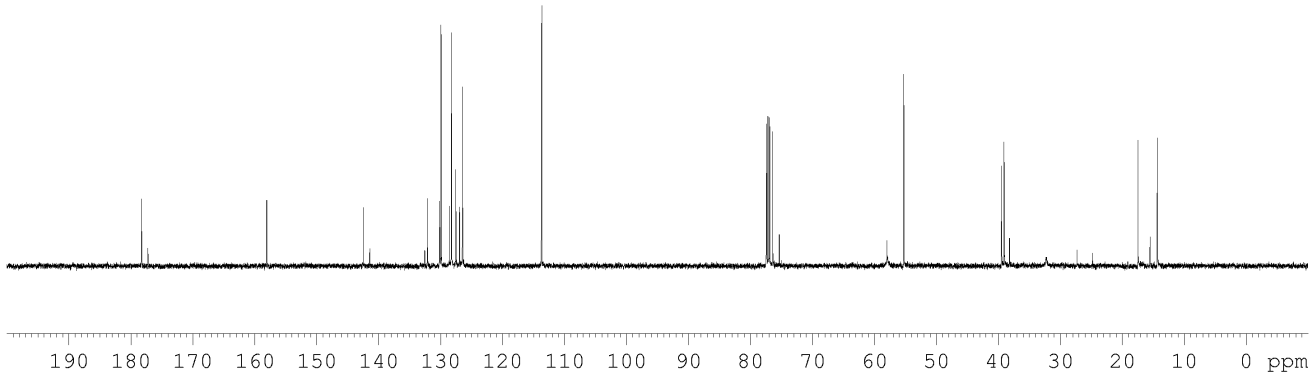


Figure A1.44 Infrared Spectrum


O
N
OH
OMe


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
OMe


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

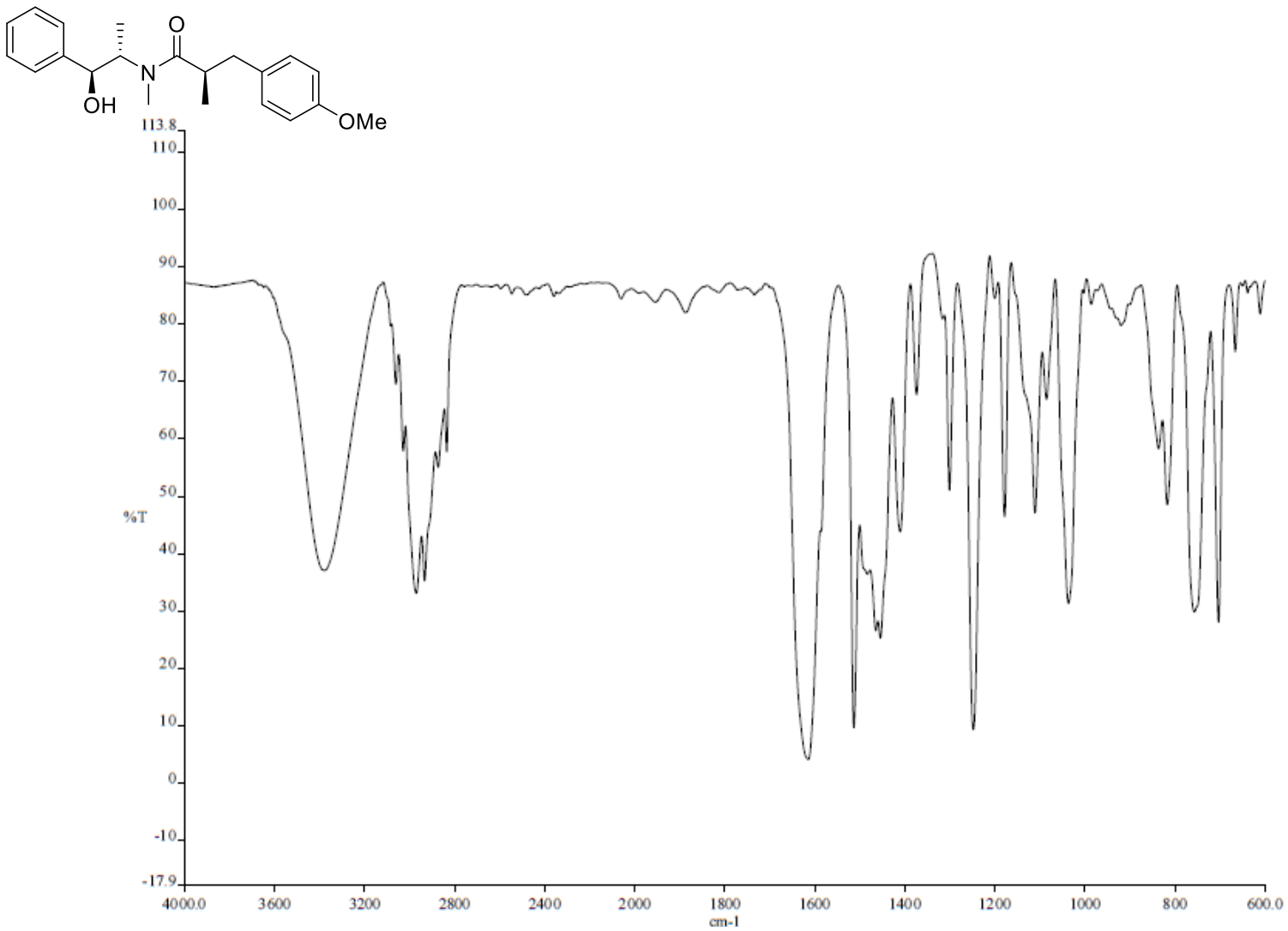
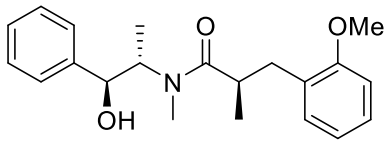
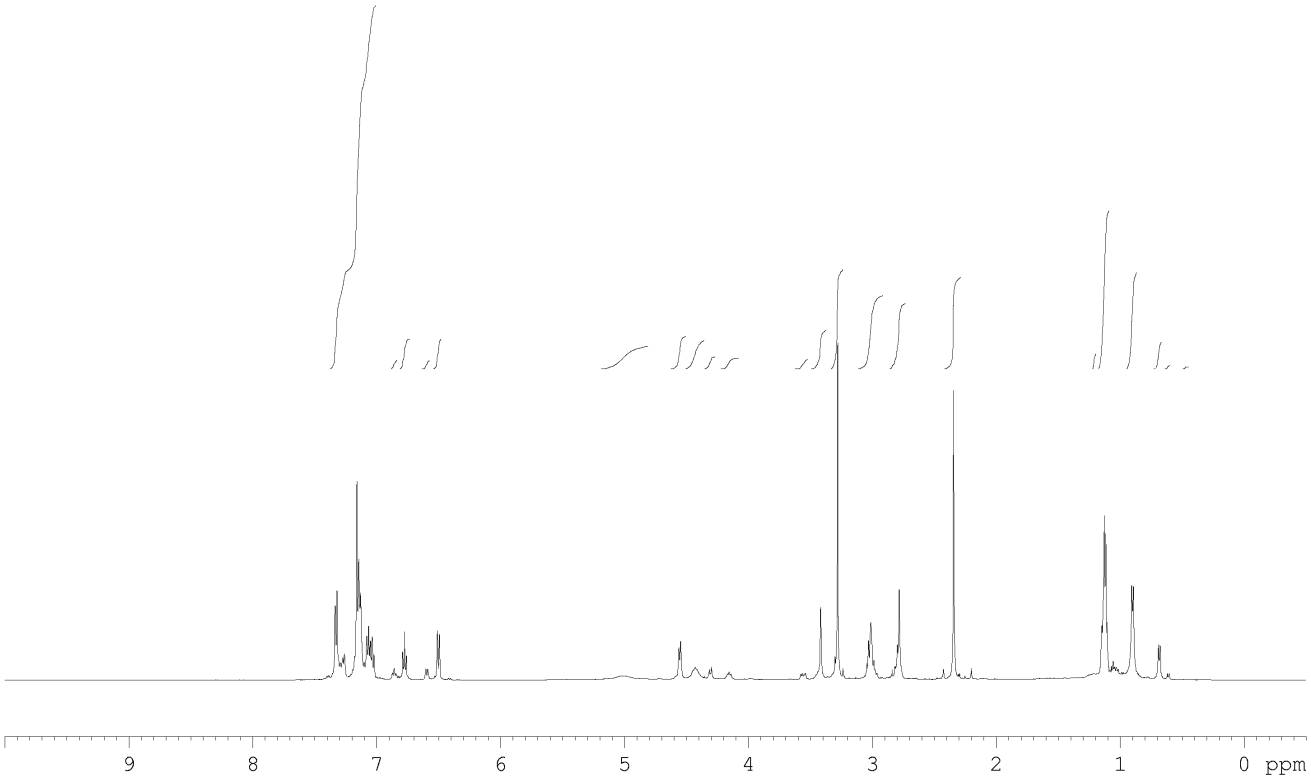
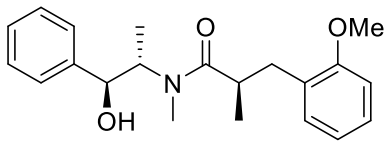
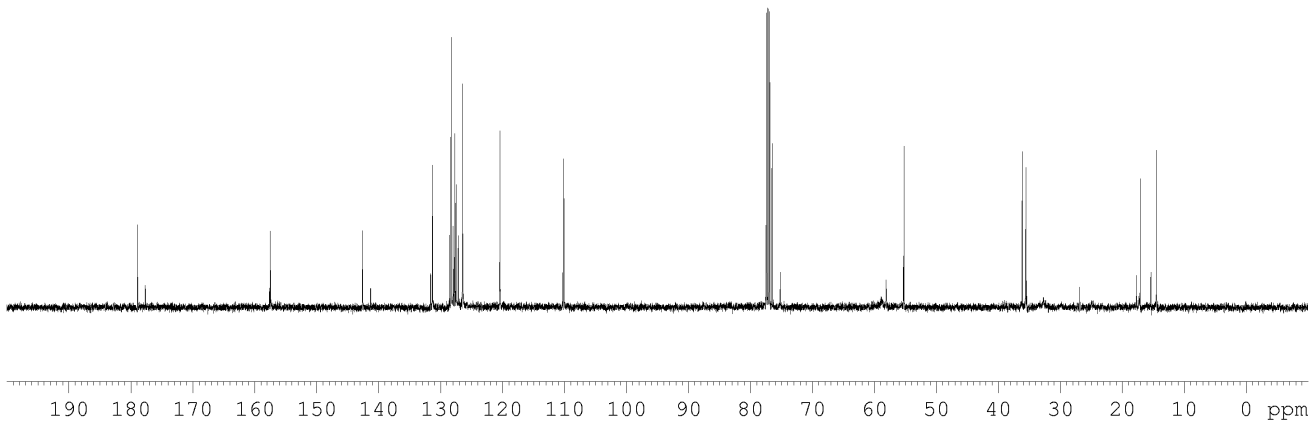


Figure A1.47 Infrared Spectrum


O
OMe
N
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
OMe
N
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

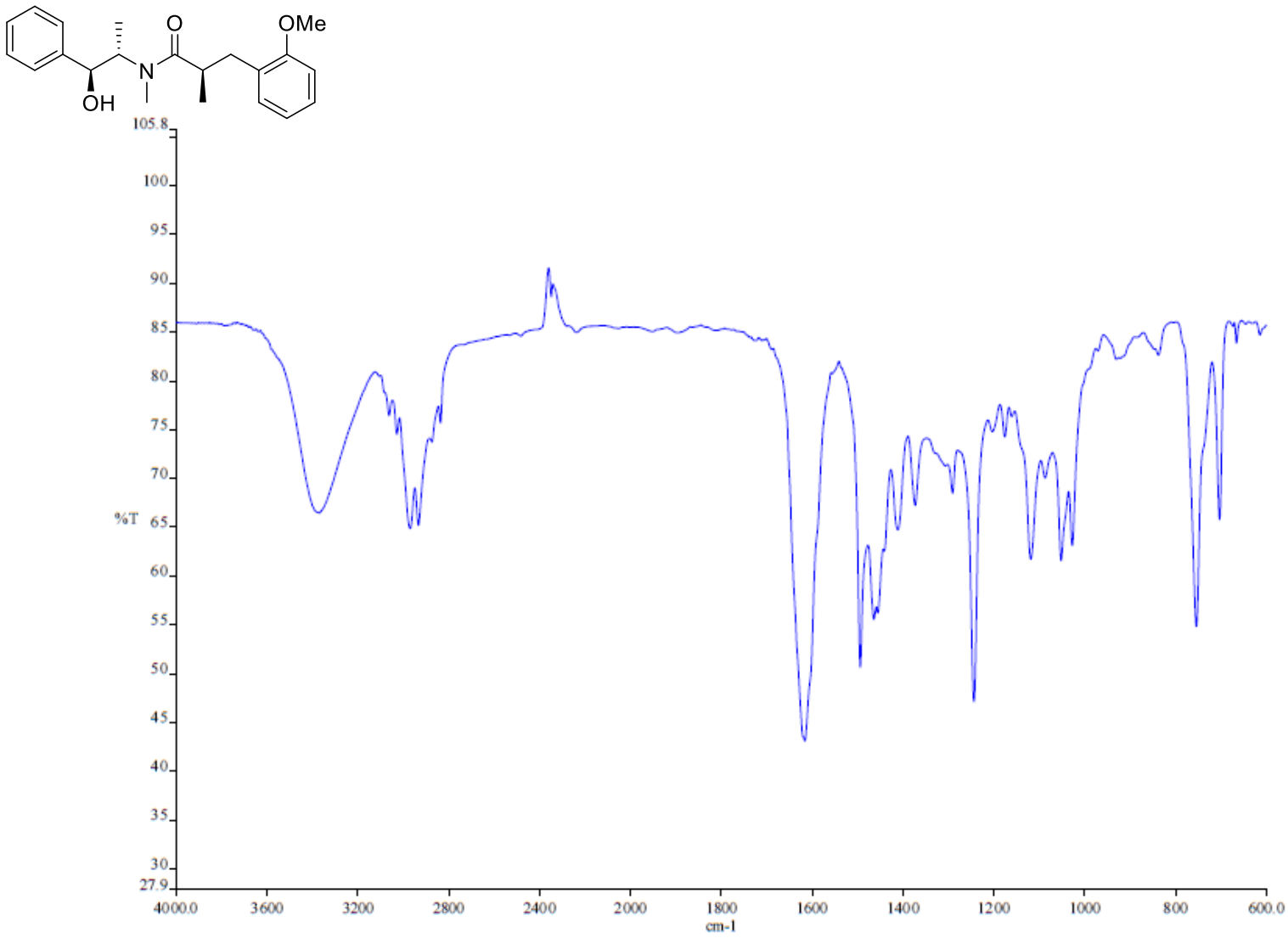
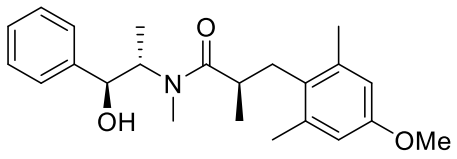
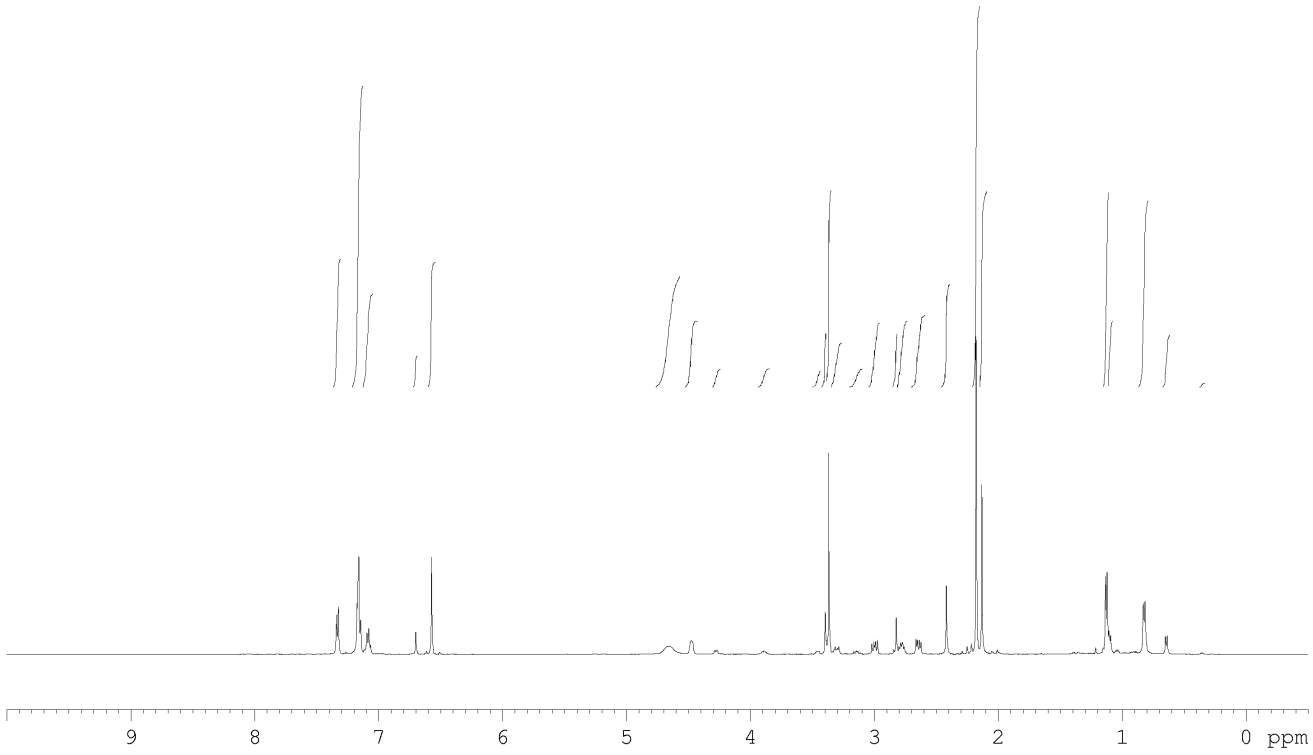
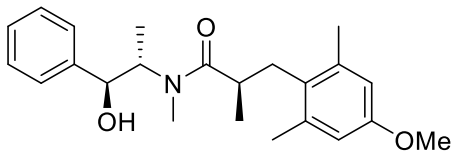
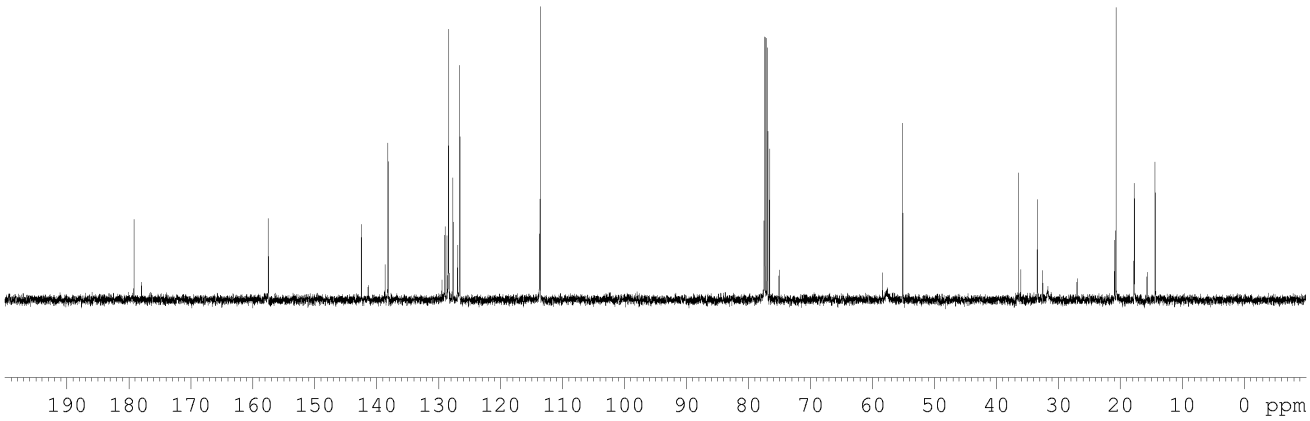


Figure A1.50 Infrared Spectrum


O
N
OH
OMe


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
OMe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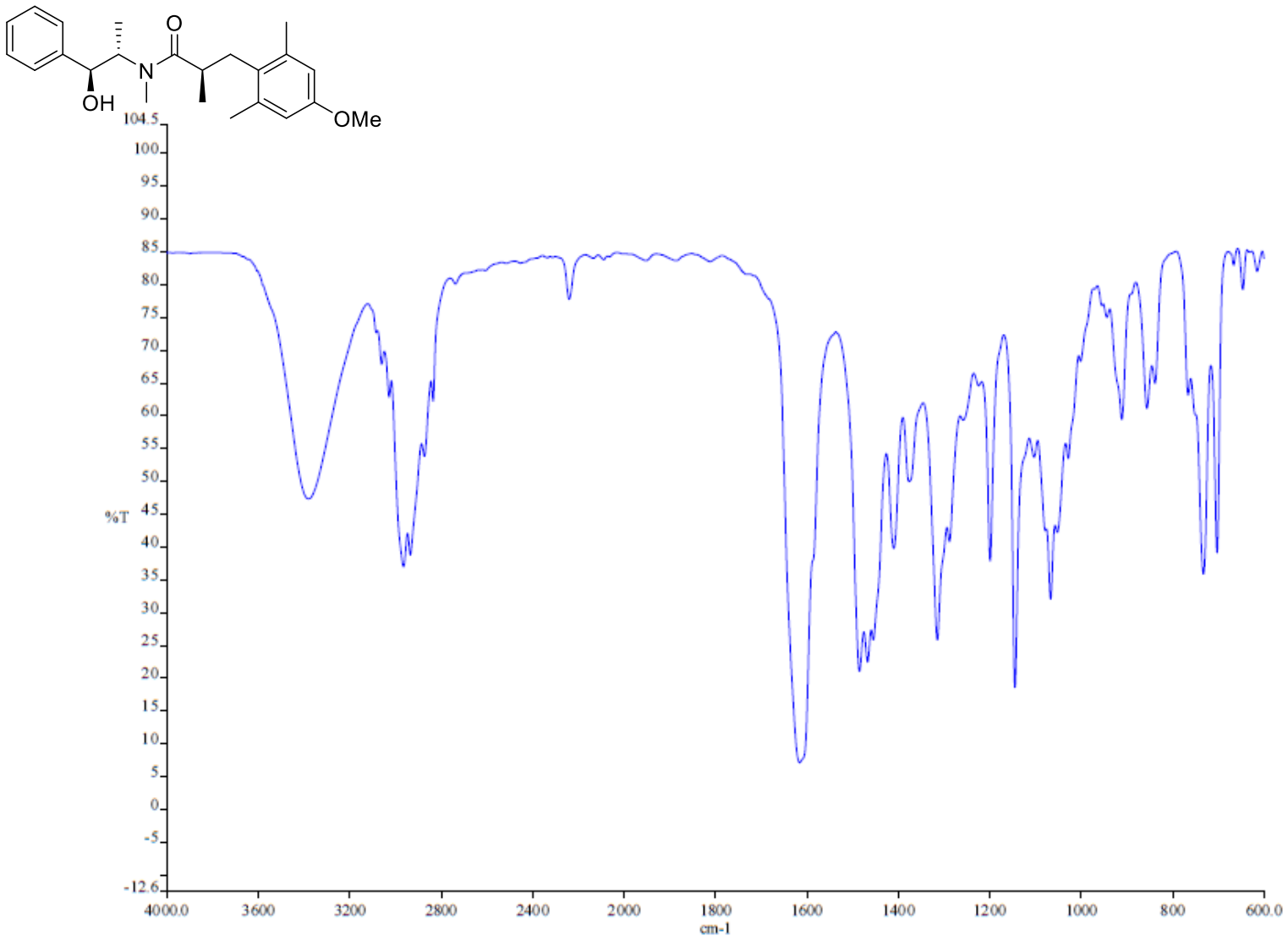
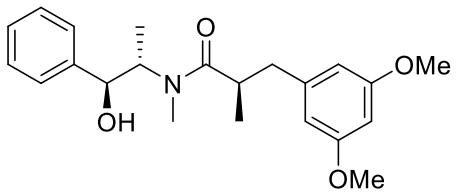
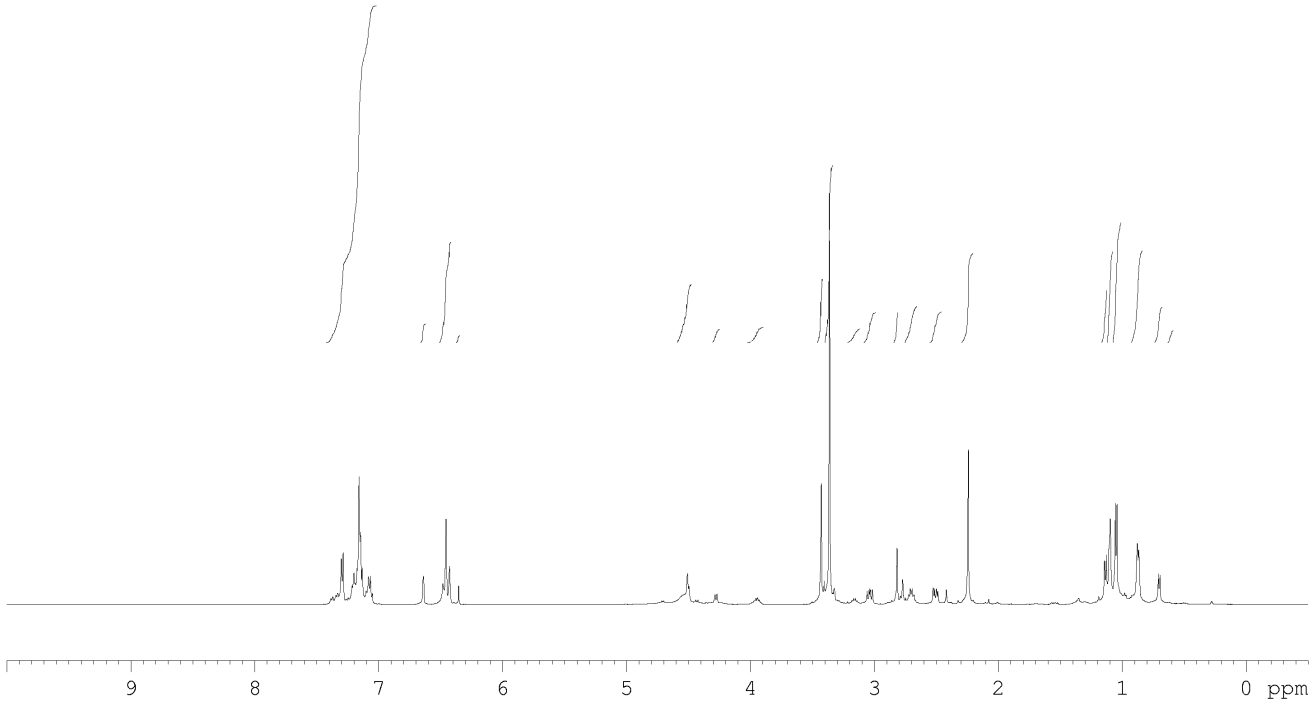
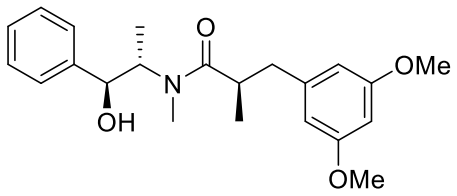
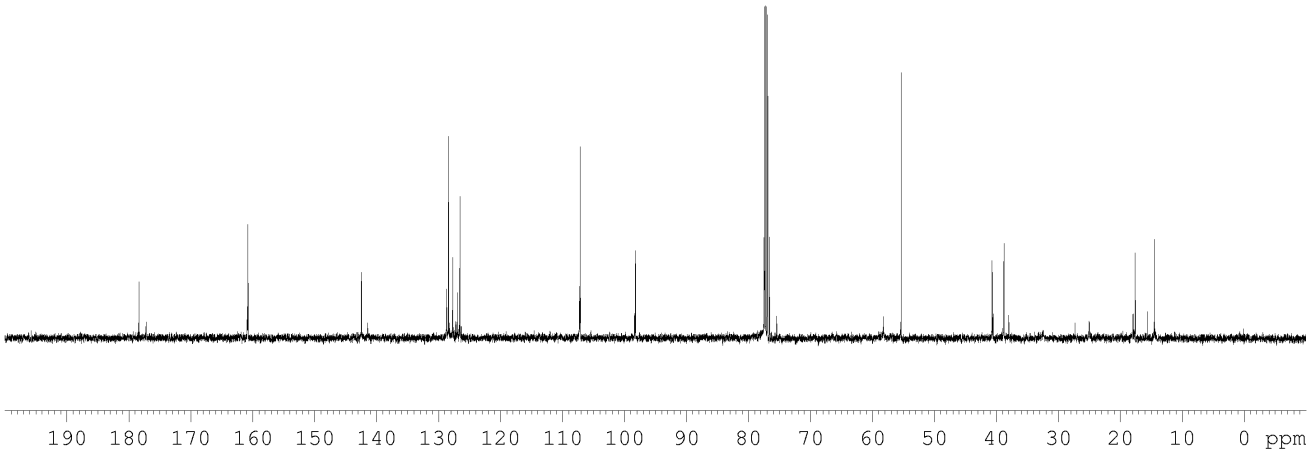


Figure A1.33 Infrared Spectrum


O
N
OH
OMe
OMe


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
OMe
OMe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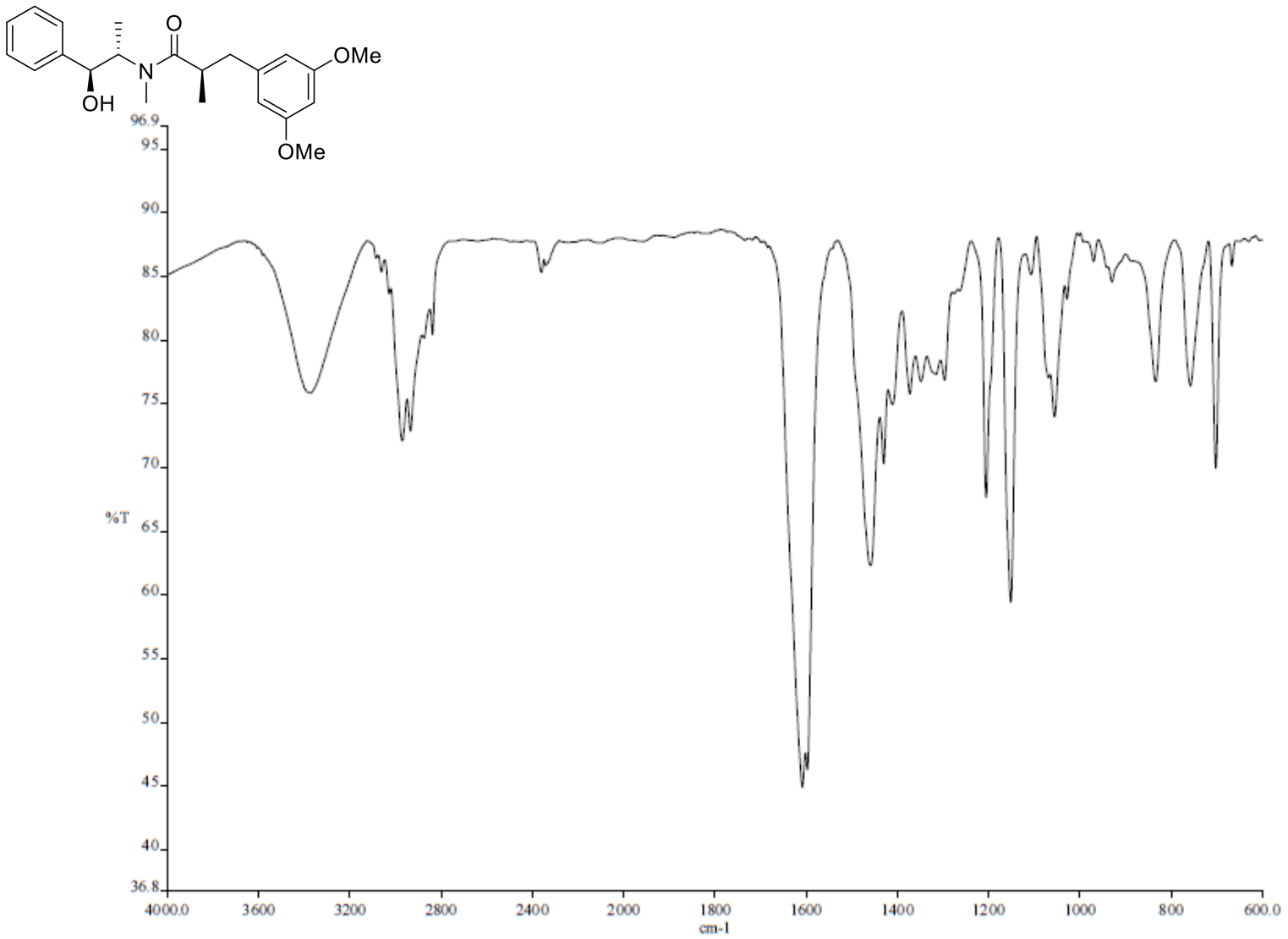
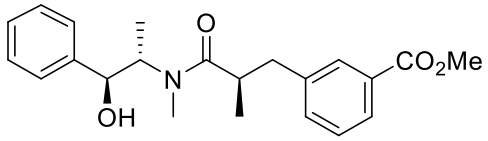
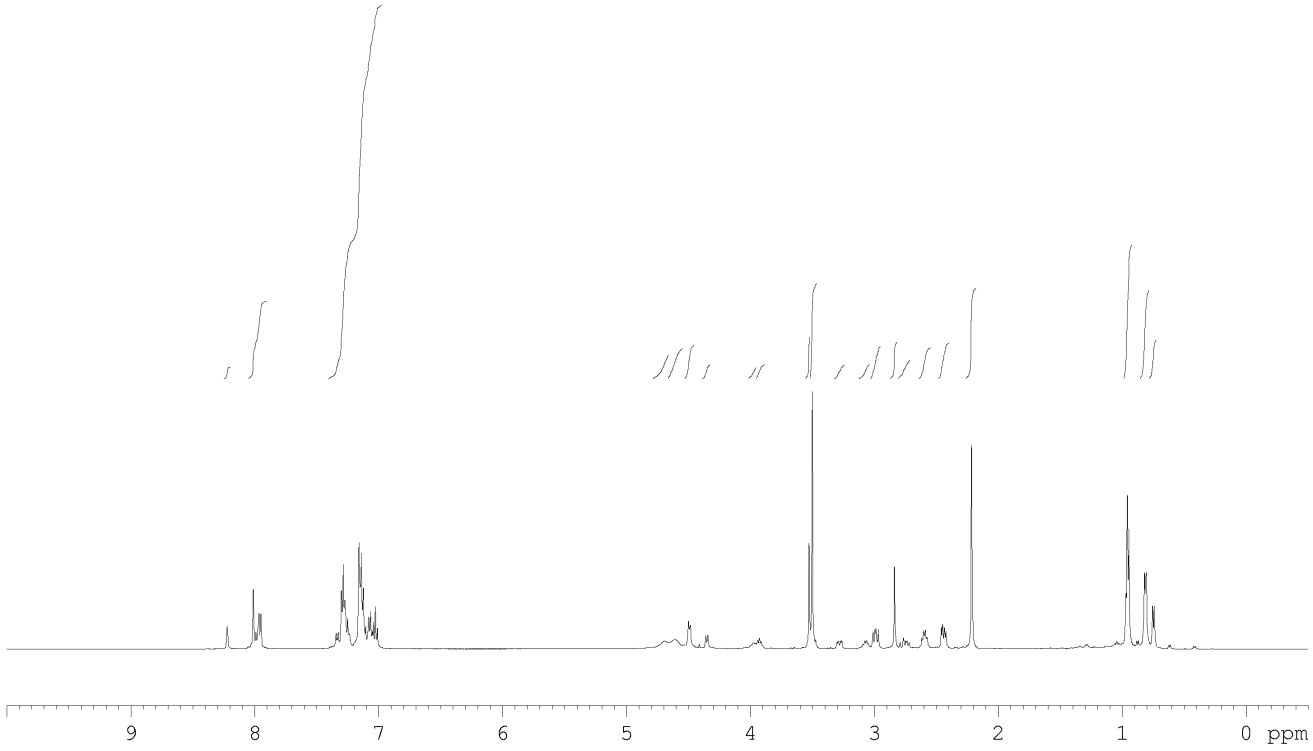
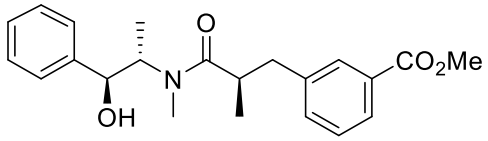
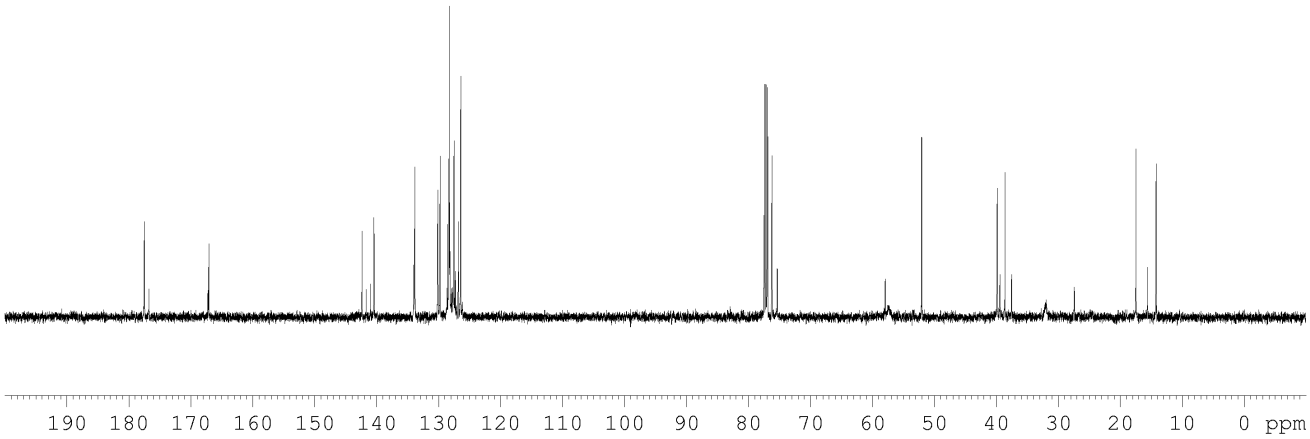


Figure A1.56 Infrared Spectrum


O
N
OH
CO2Me


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
CO2Me


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

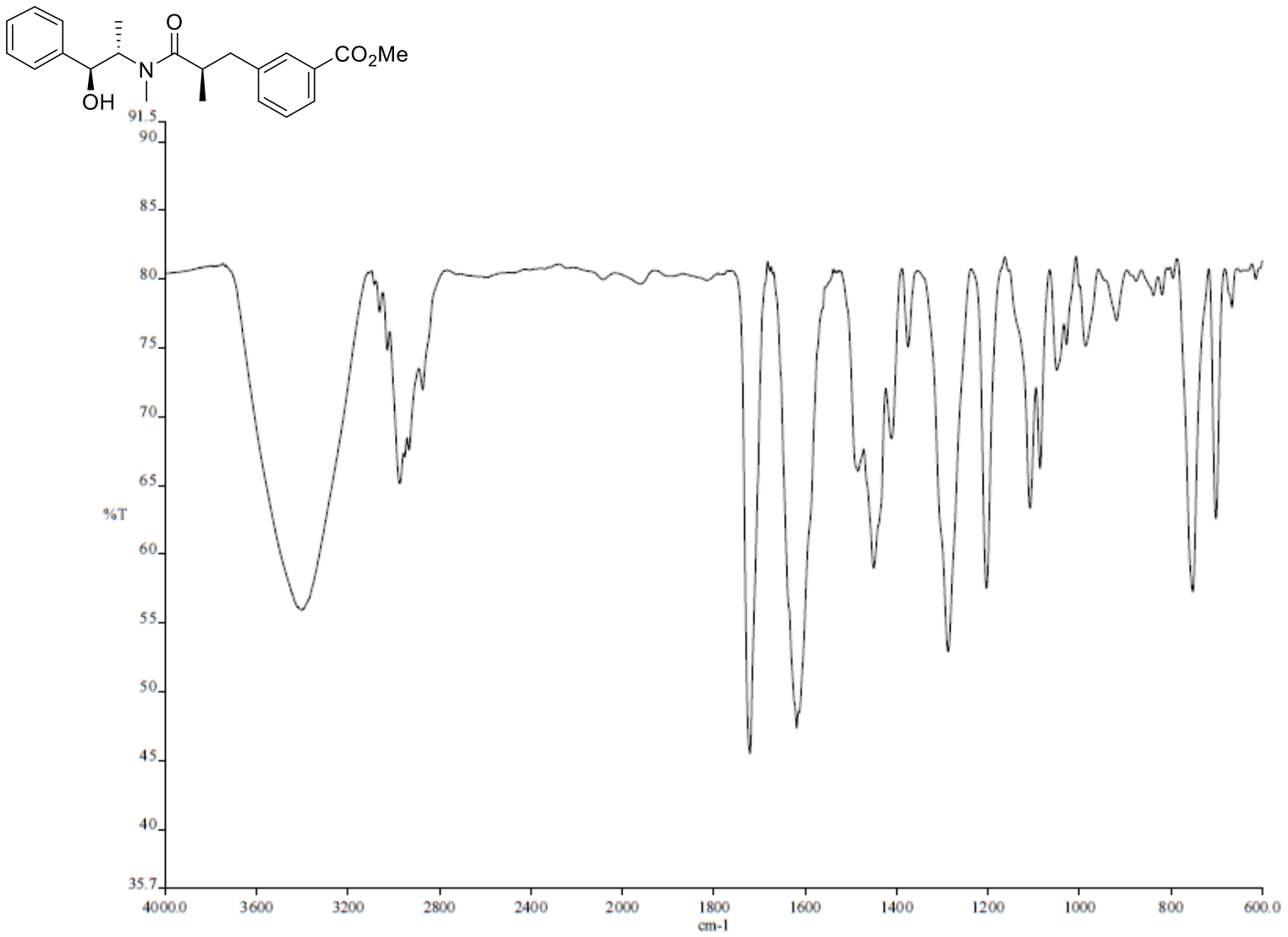
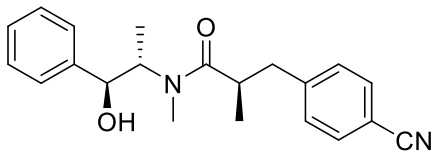
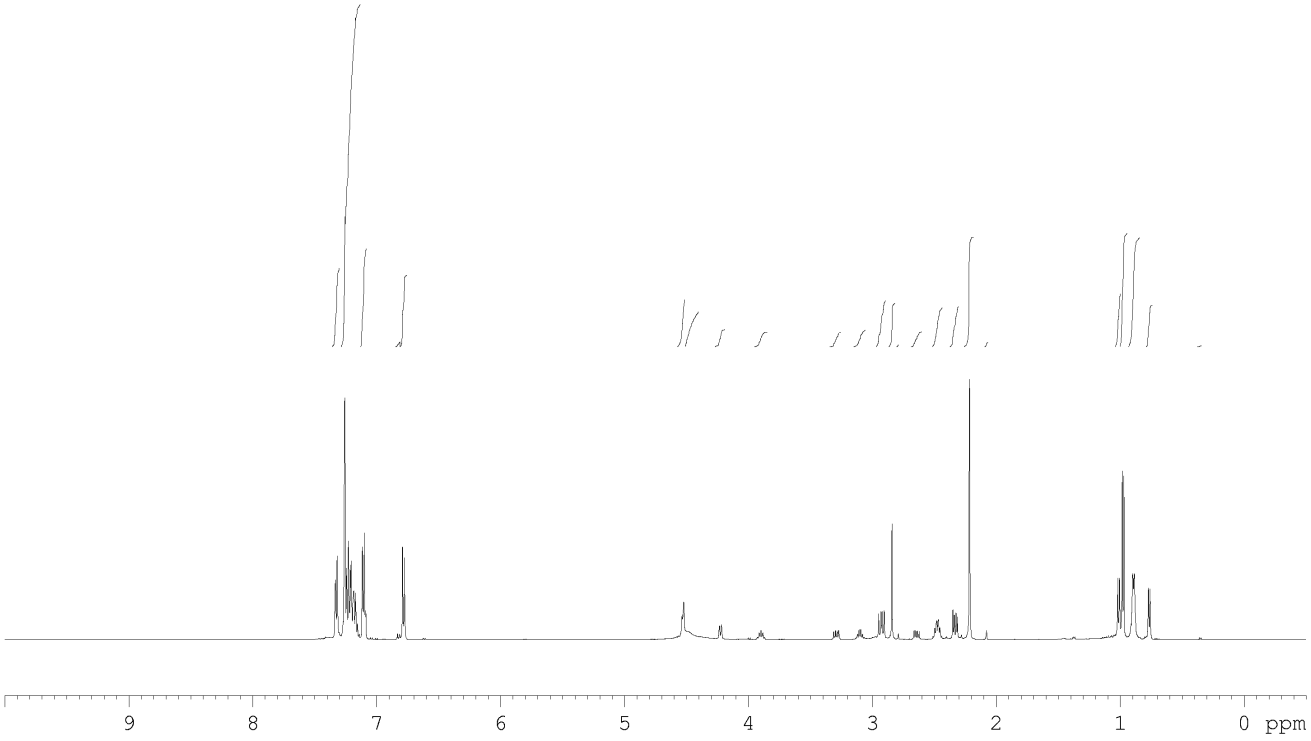
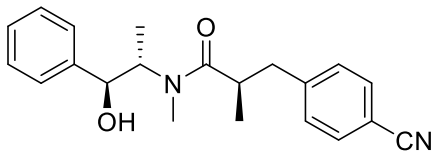


Figure A1.59 Infrared Spectrum


O
N
OH
CN


9
8
7
6
5
4
3
2
1
0 ppm



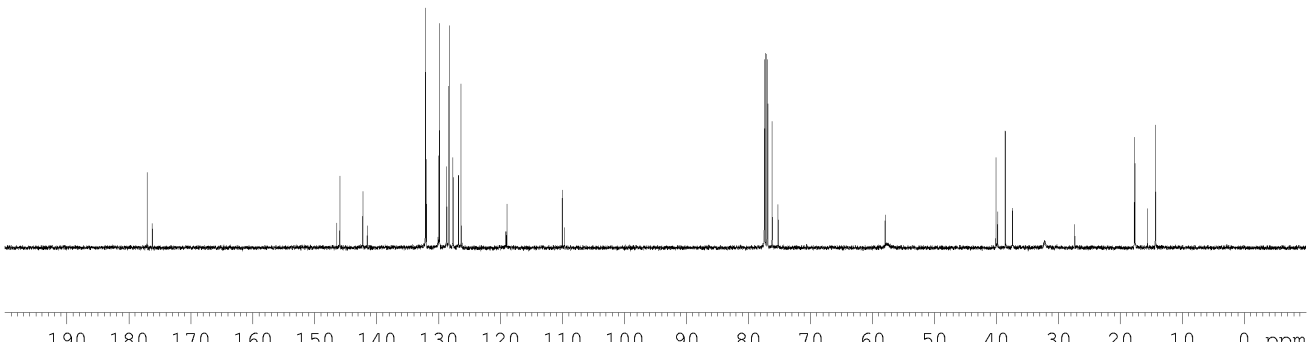


Figure A1.61 ^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum

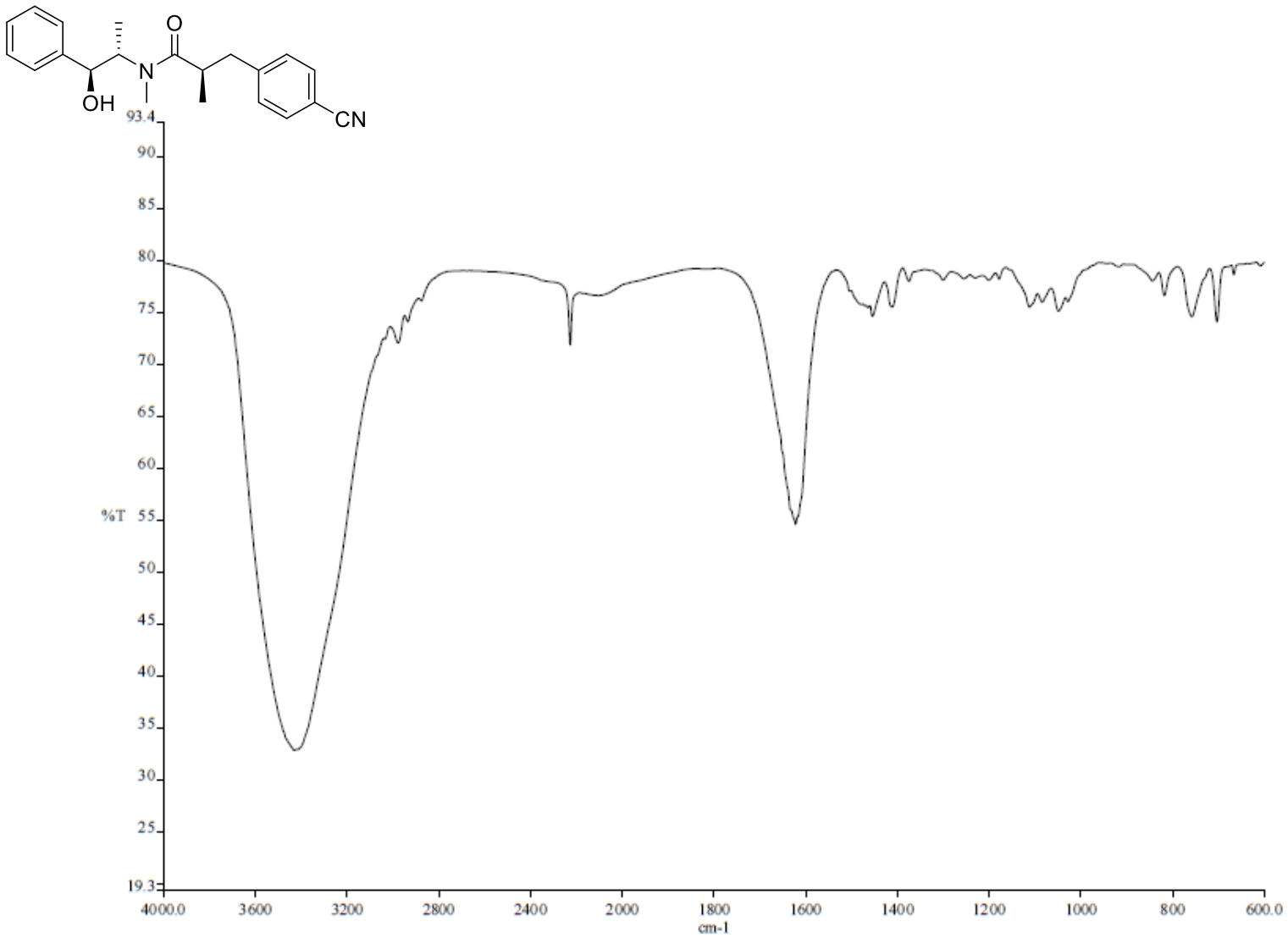
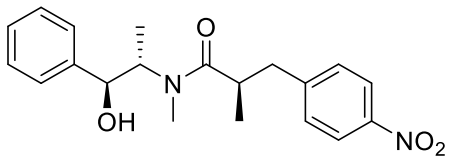
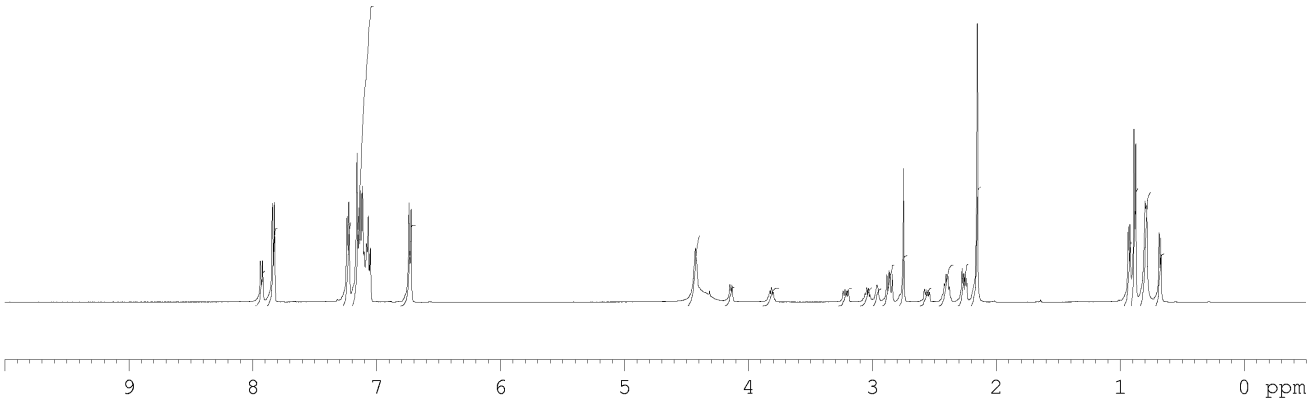
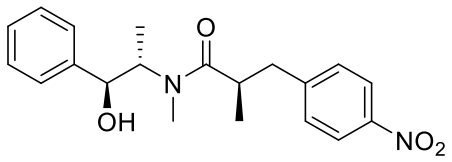
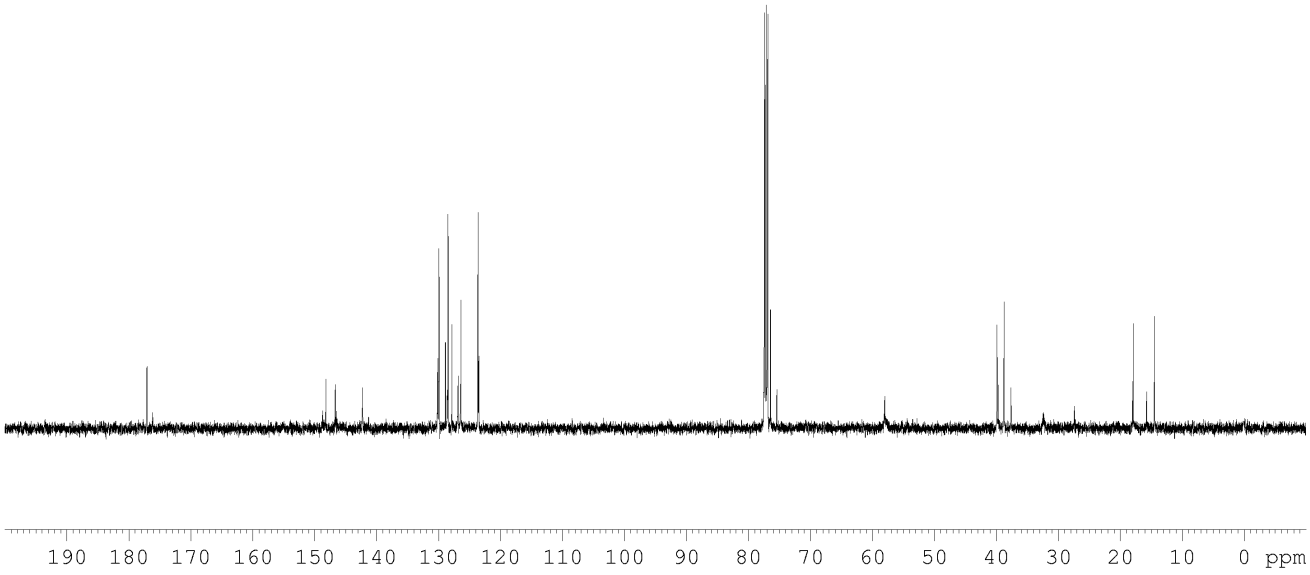


Figure A1.62 Infrared Spectrum


O
N
OH
NO2


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
NO2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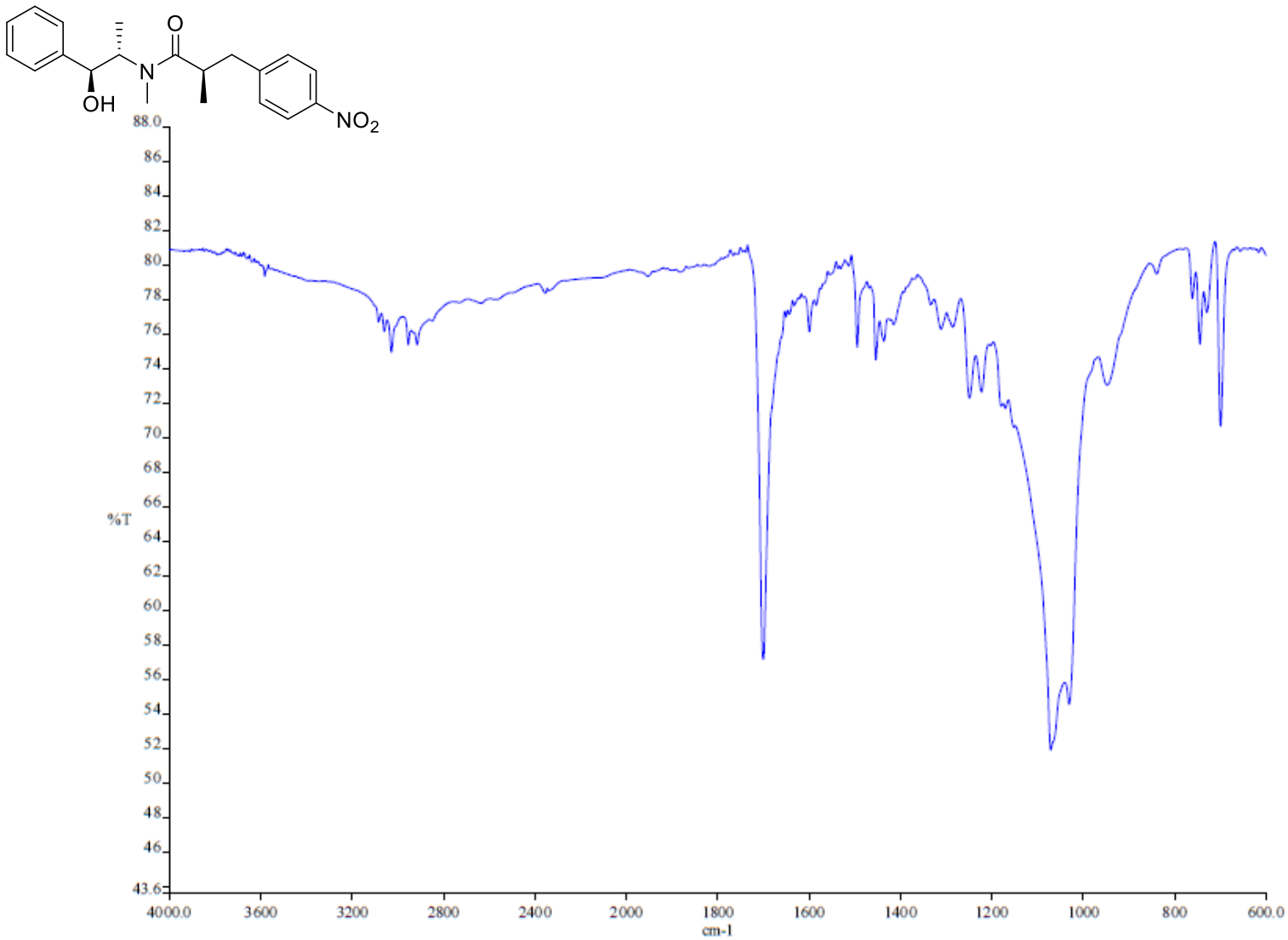
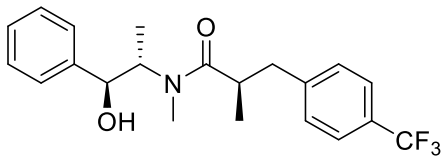
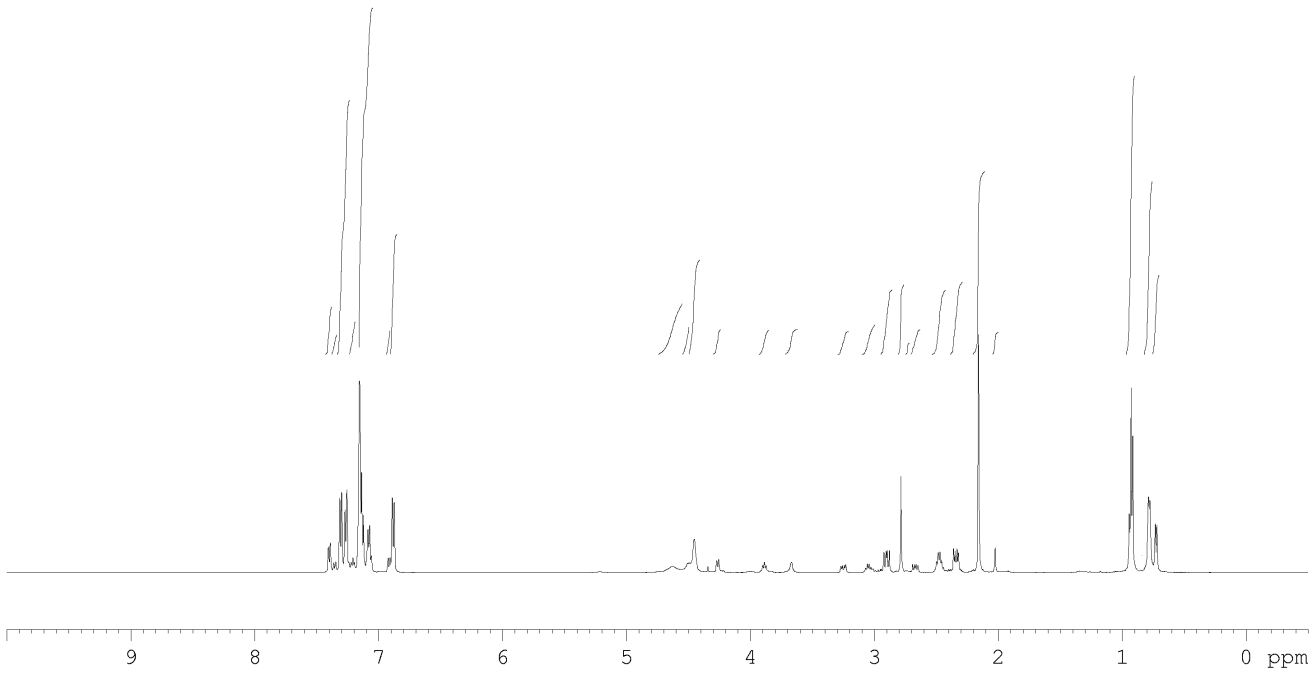
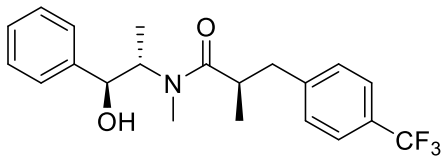
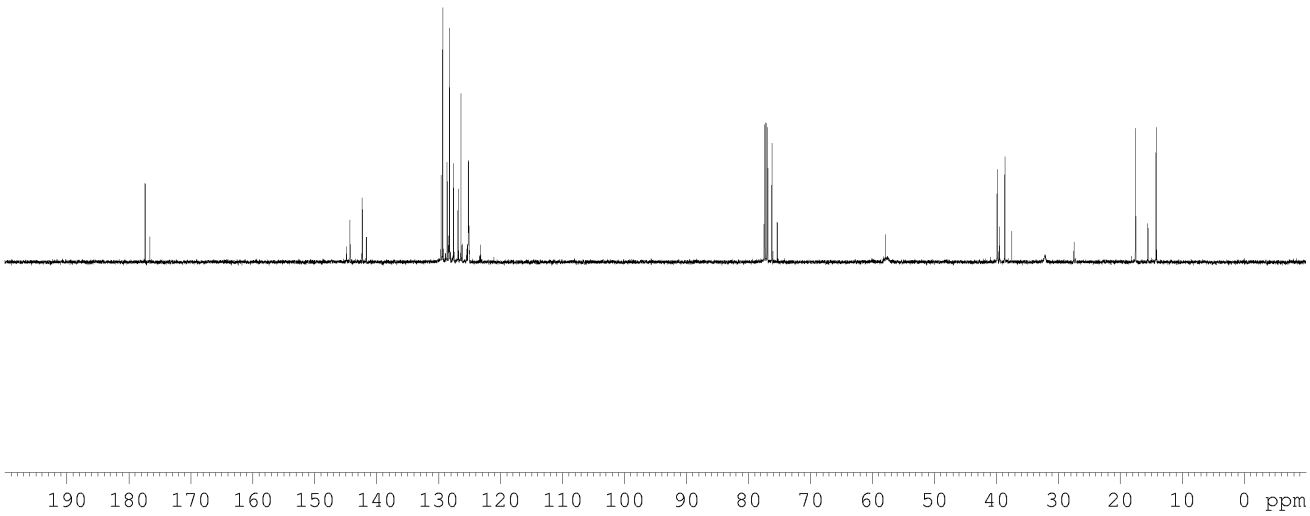


Figure A1.65 Infrared Spectrum


O
N
OH
CF3


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
CF3


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

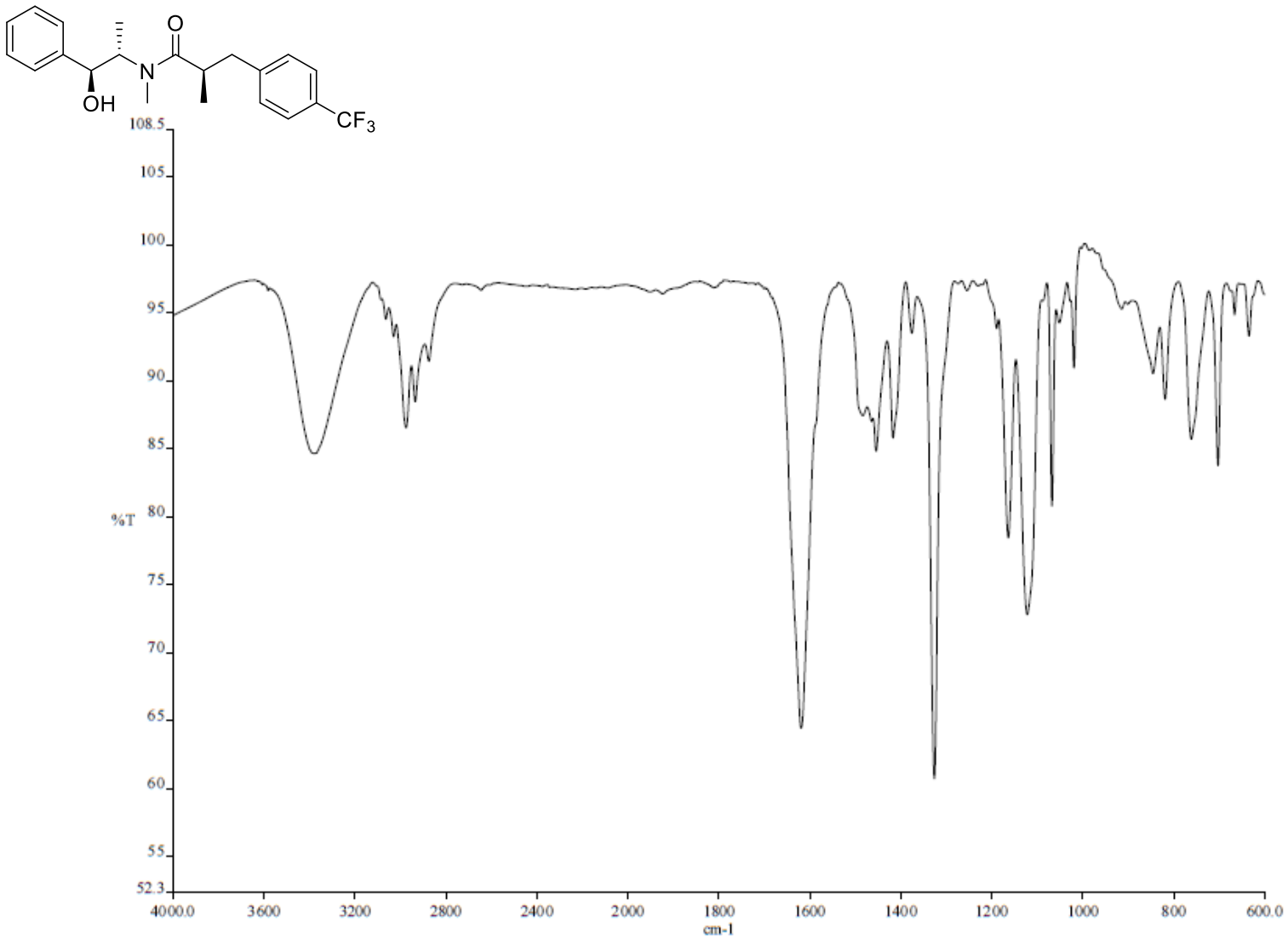
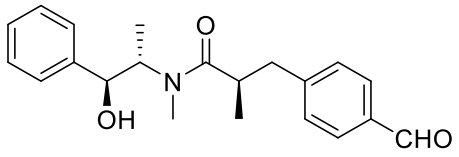
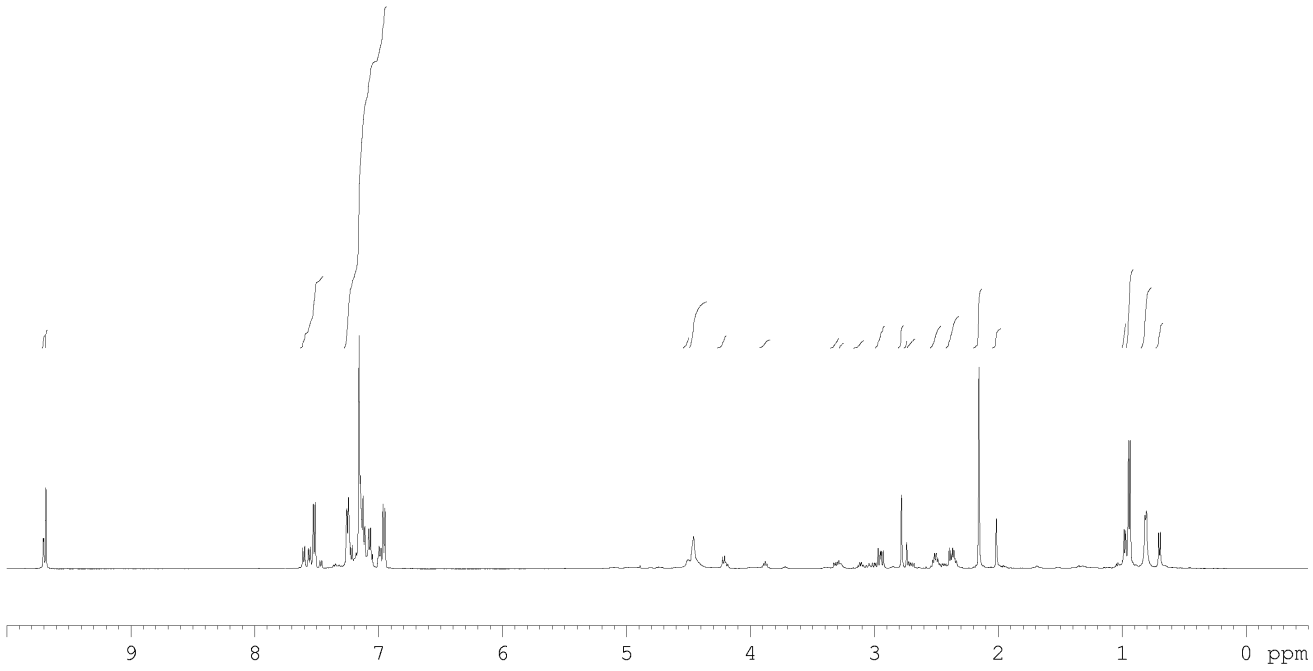
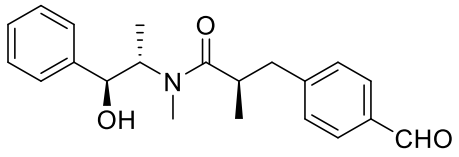
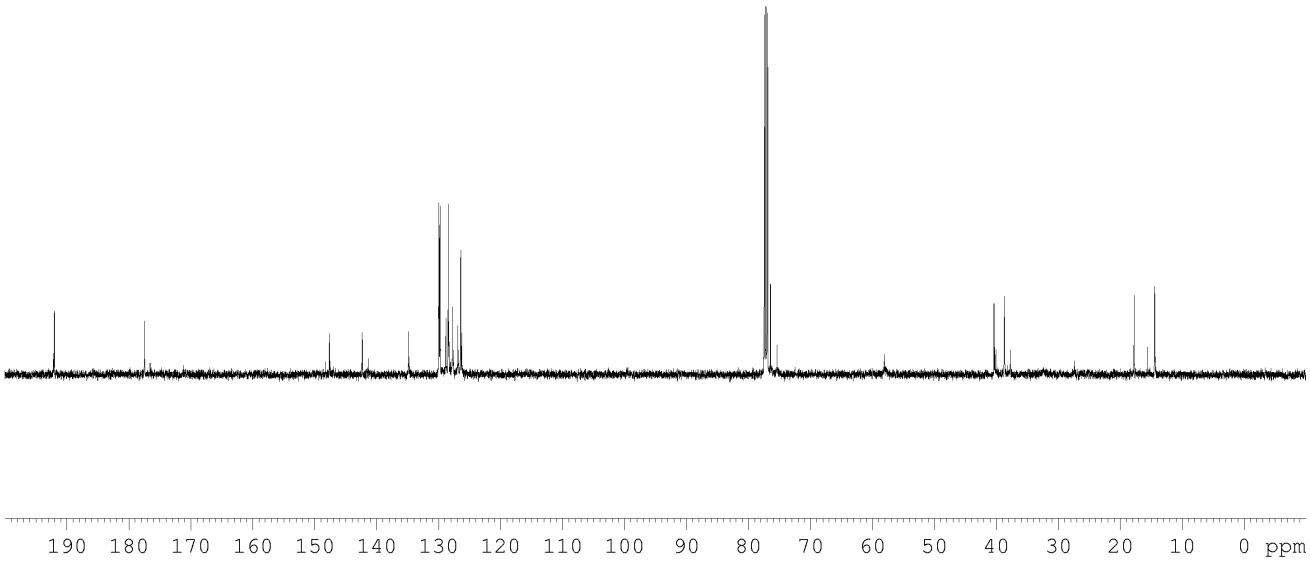


Figure A1.68 Infrared Spectrum


O
N
OH
CHO


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
CHO


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

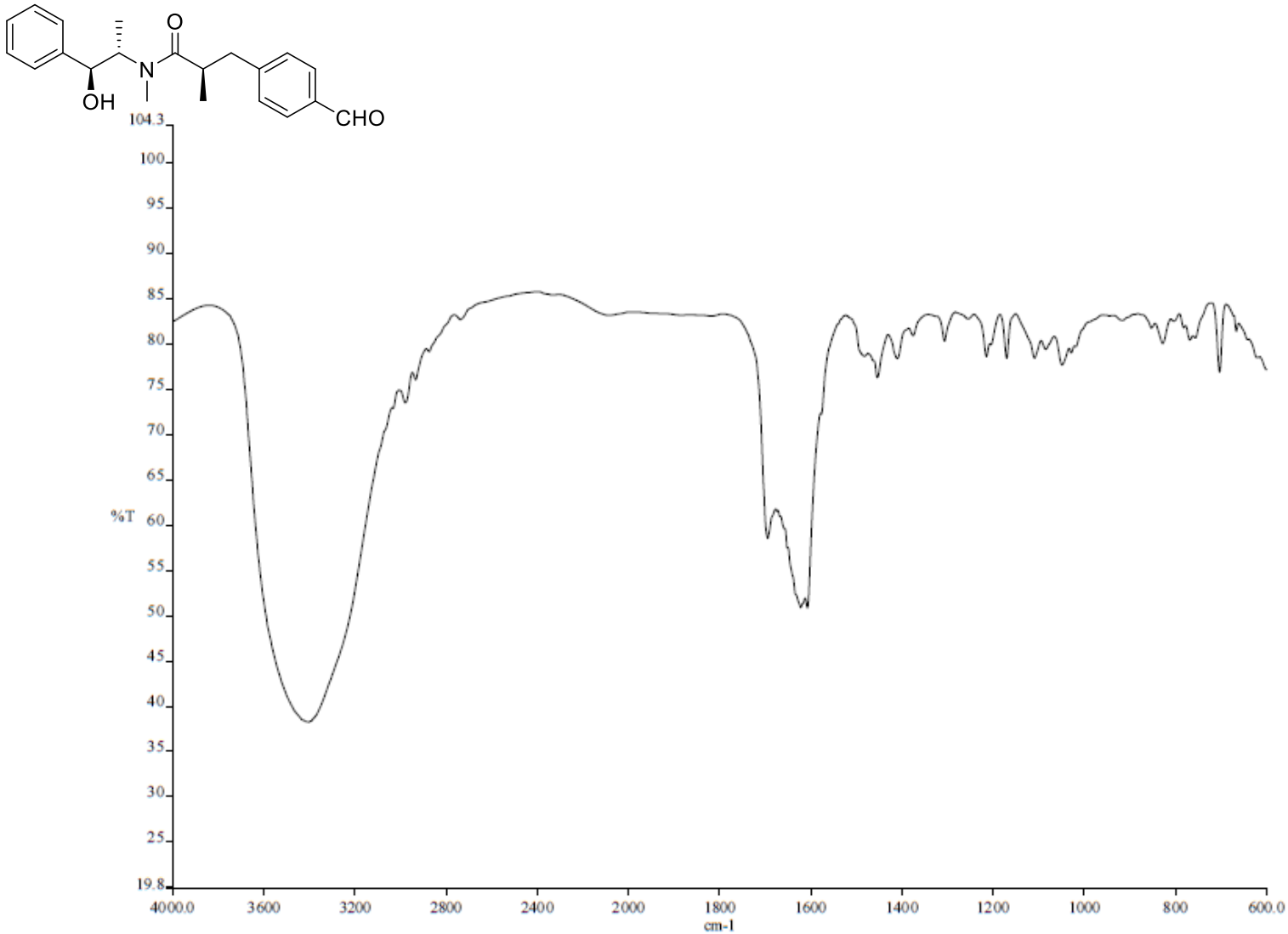
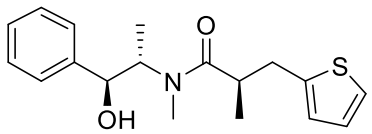
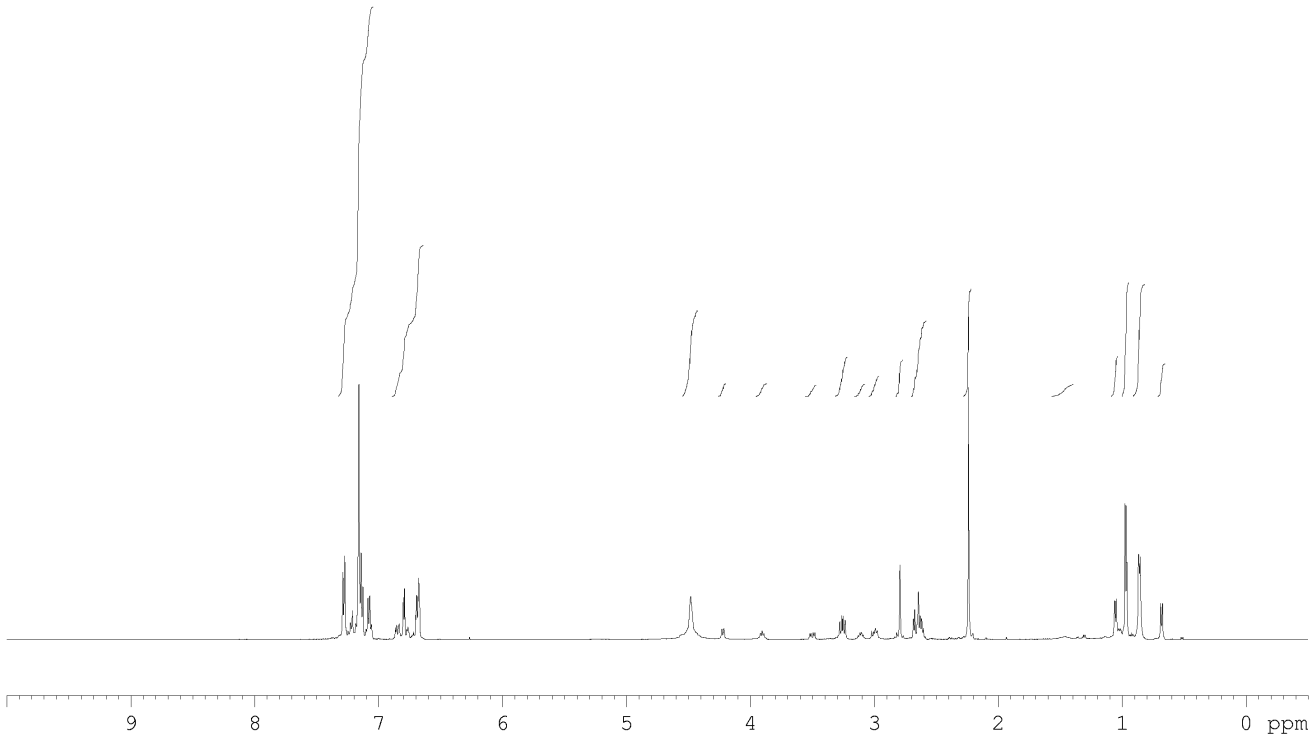
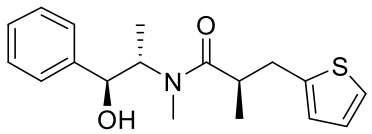
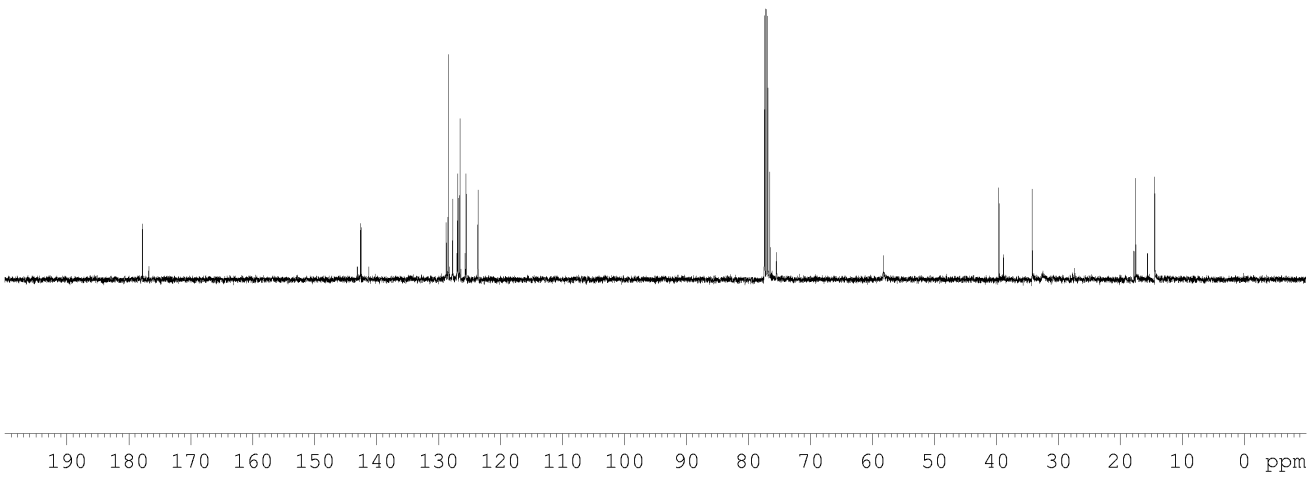


Figure A1.71 Infrared Spectrum


O
S
N
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
S
N
OH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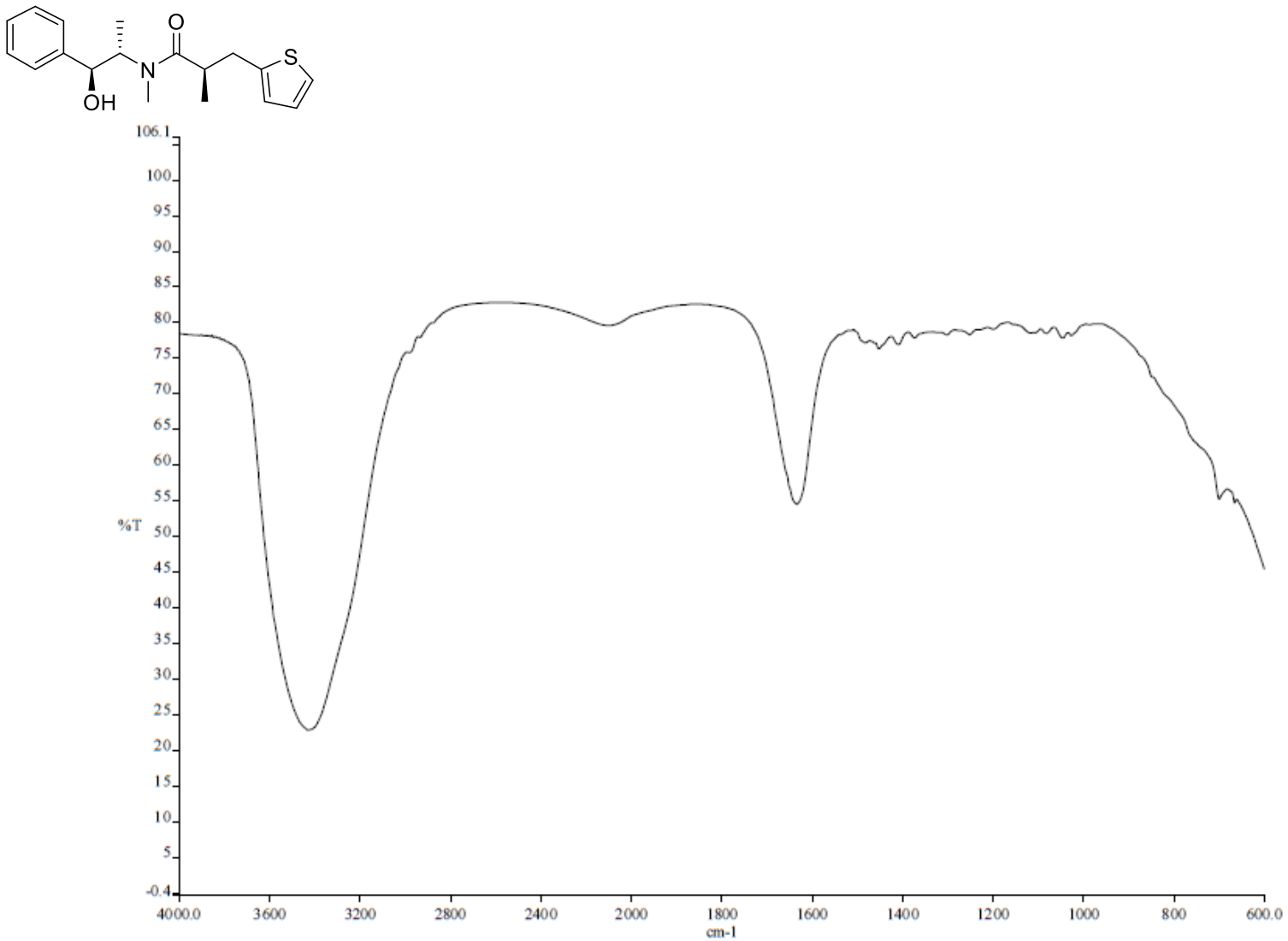
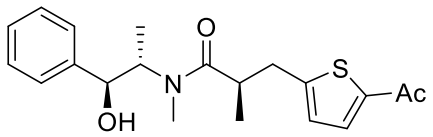
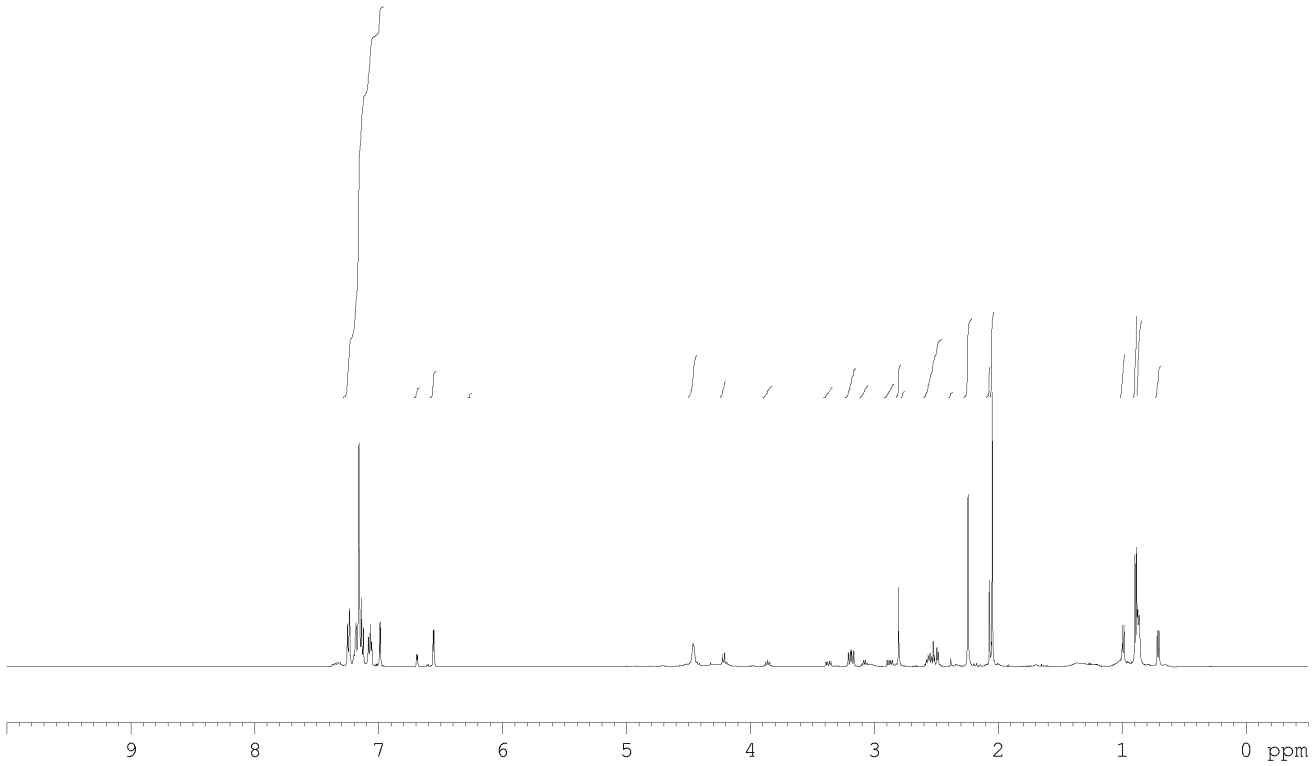
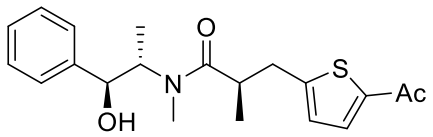
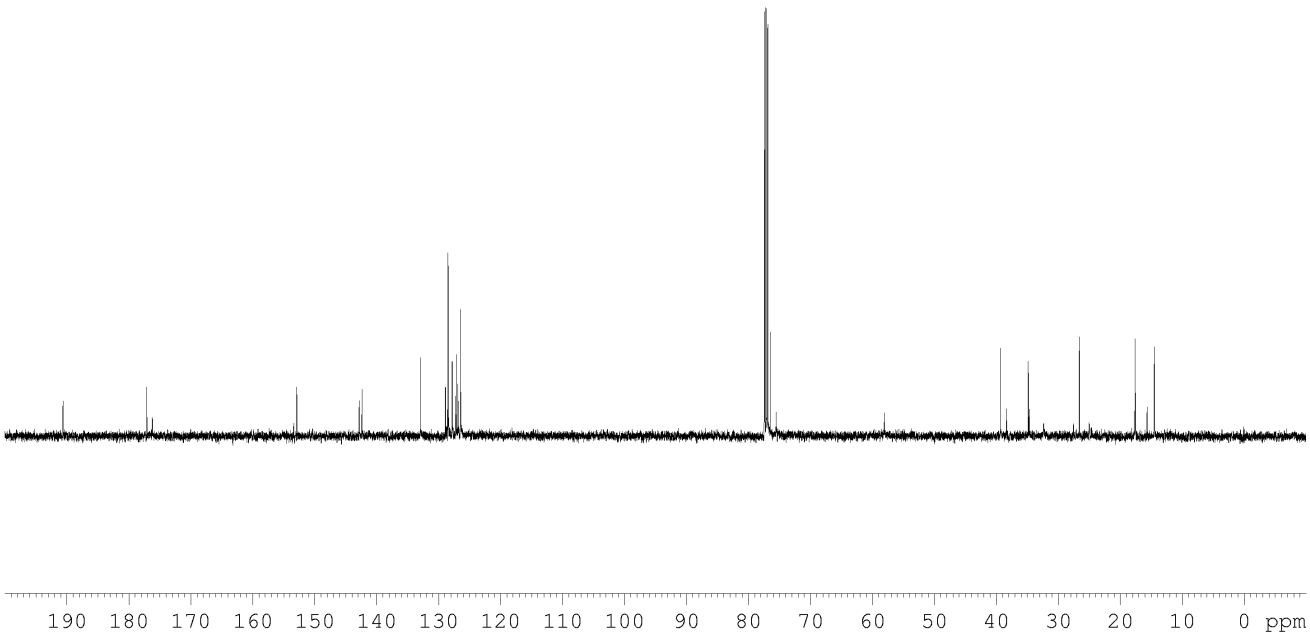


Figure A1.74 Infrared Spectrum


O
S
N
Ac
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
S
N
Ac
OH


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

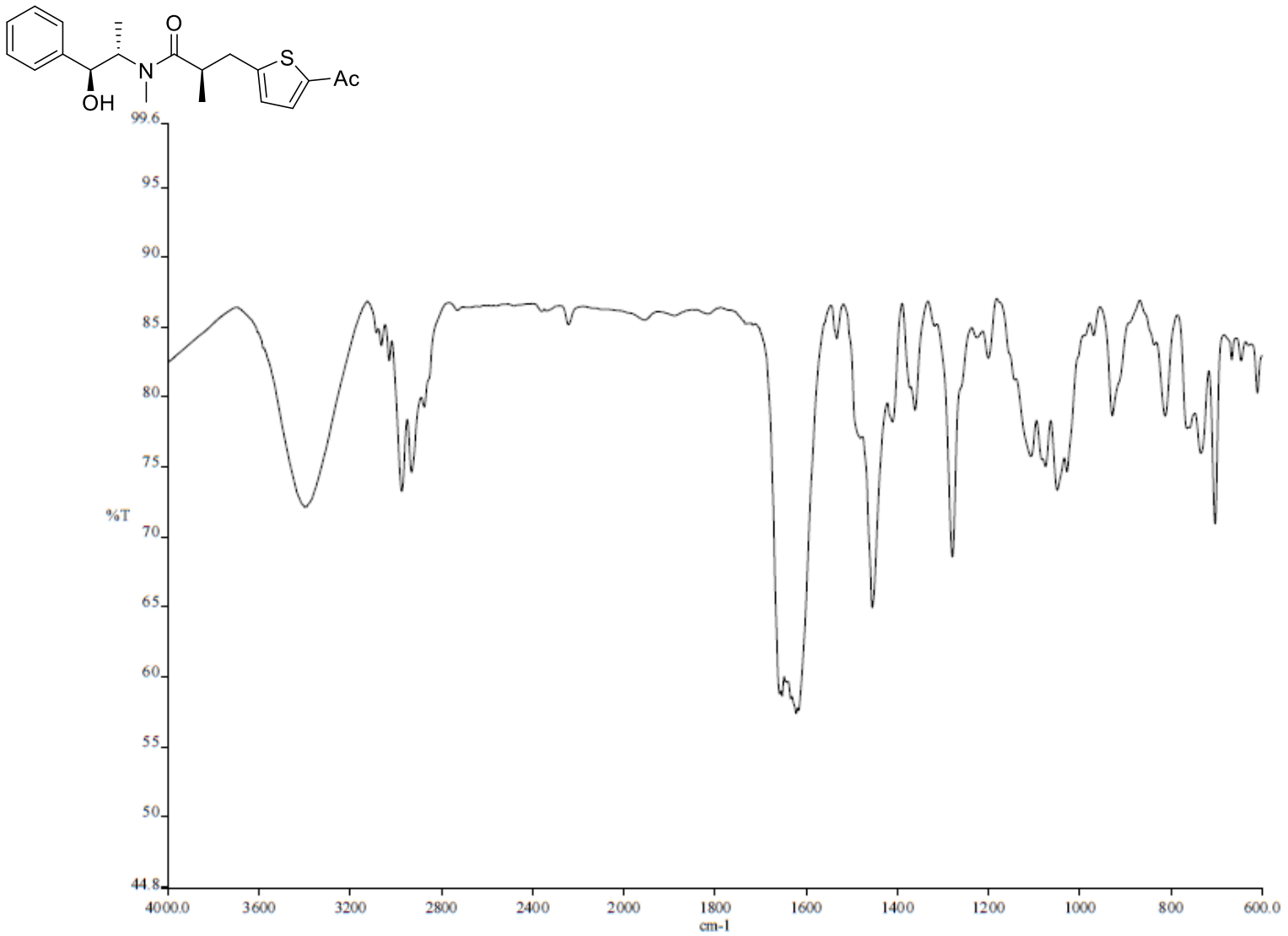
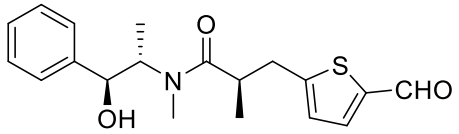
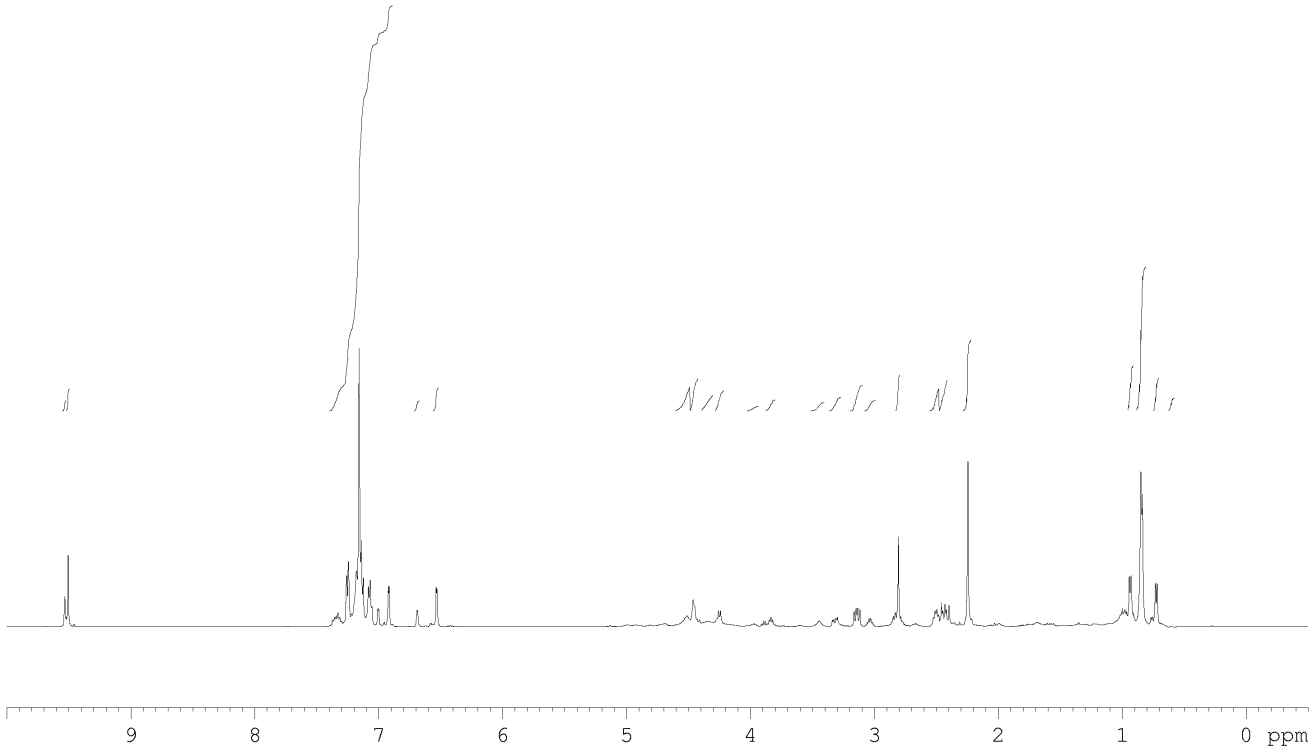
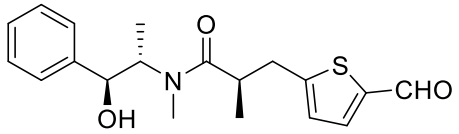
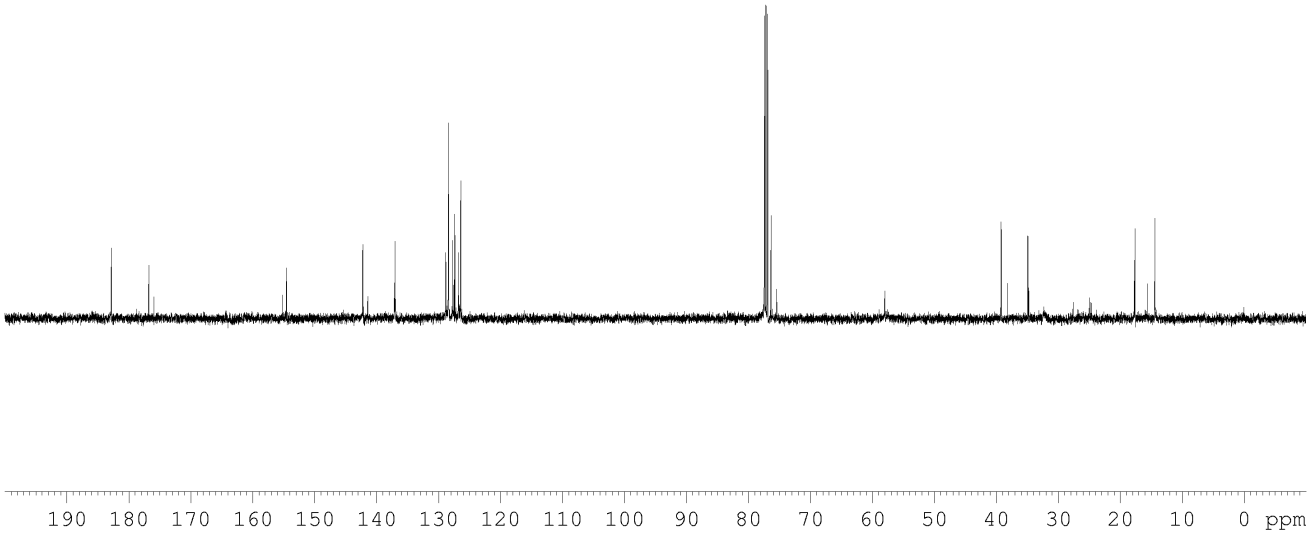


Figure A1.77 Infrared Spectrum


O
S
N
CHO
OH


9
8
7
6
5
4
3
2
1
0 ppm


O
S
N
CHO
OH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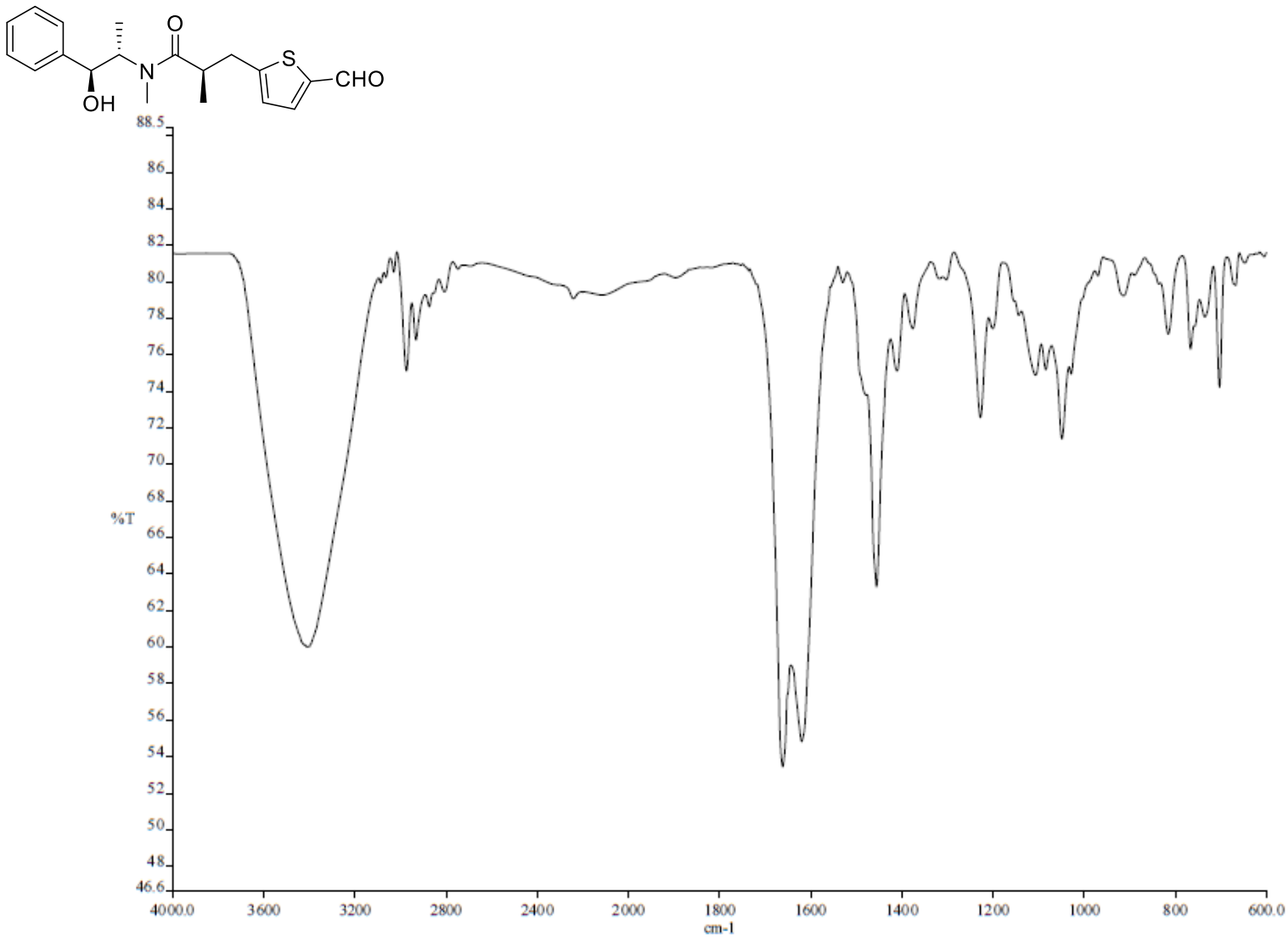
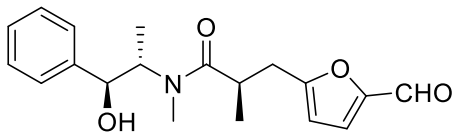
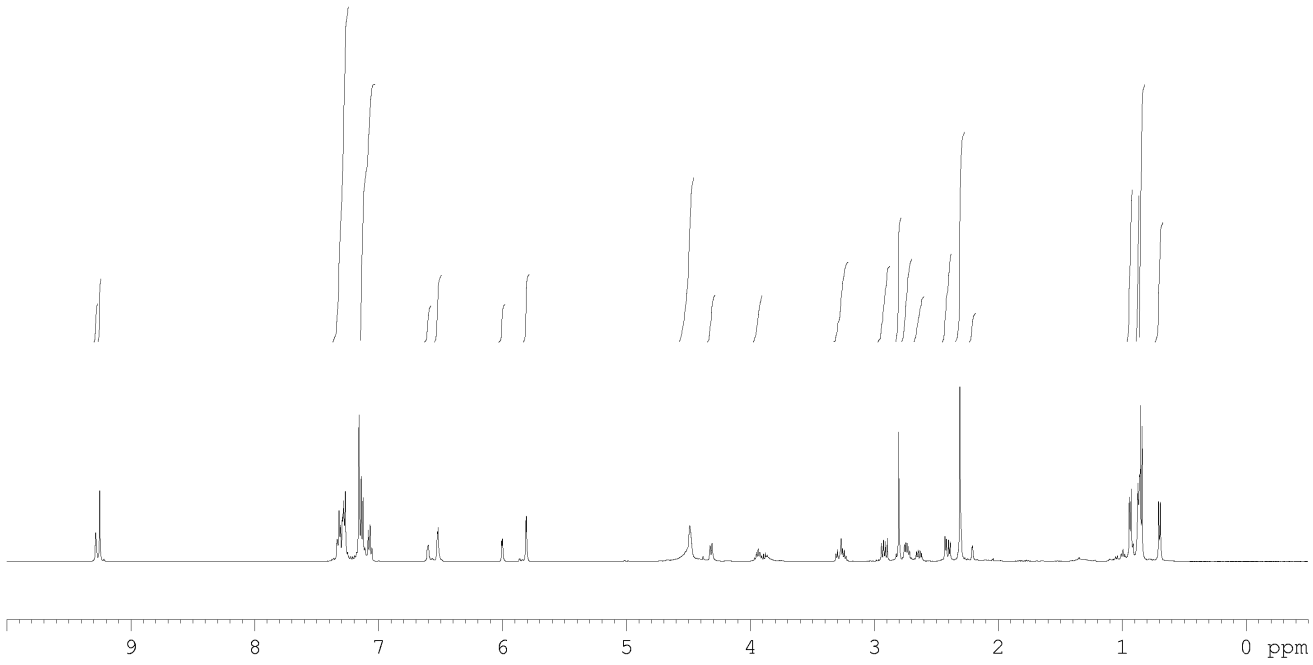
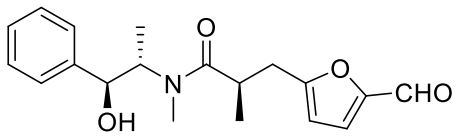
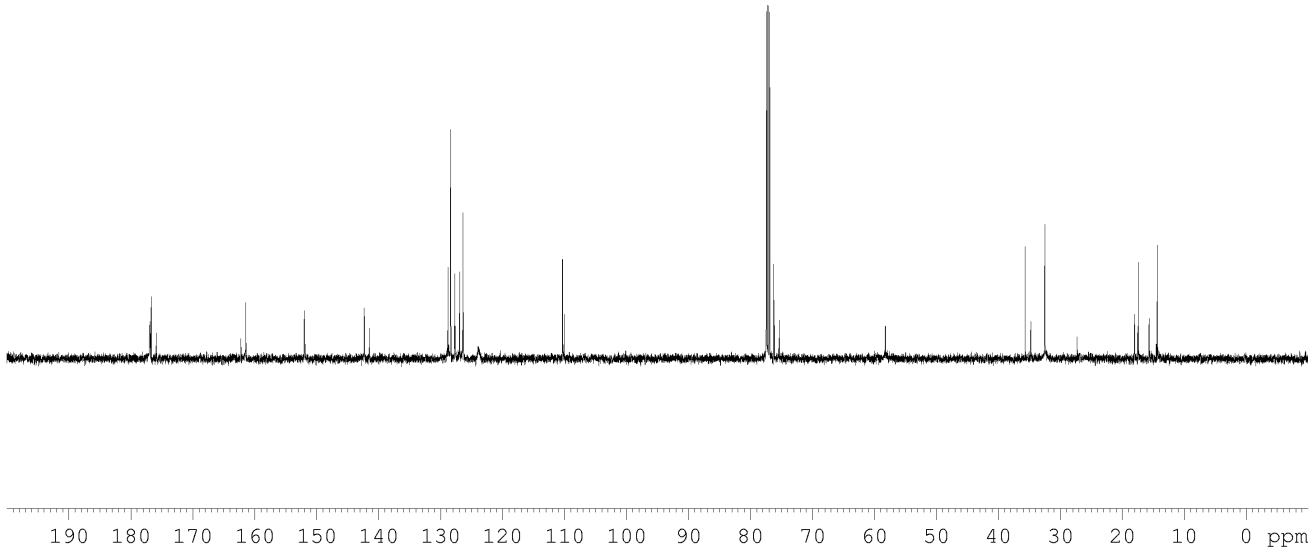


Figure A1.80 Infrared Spectrum


O
N
OH
O
CHO


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
O
CHO


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

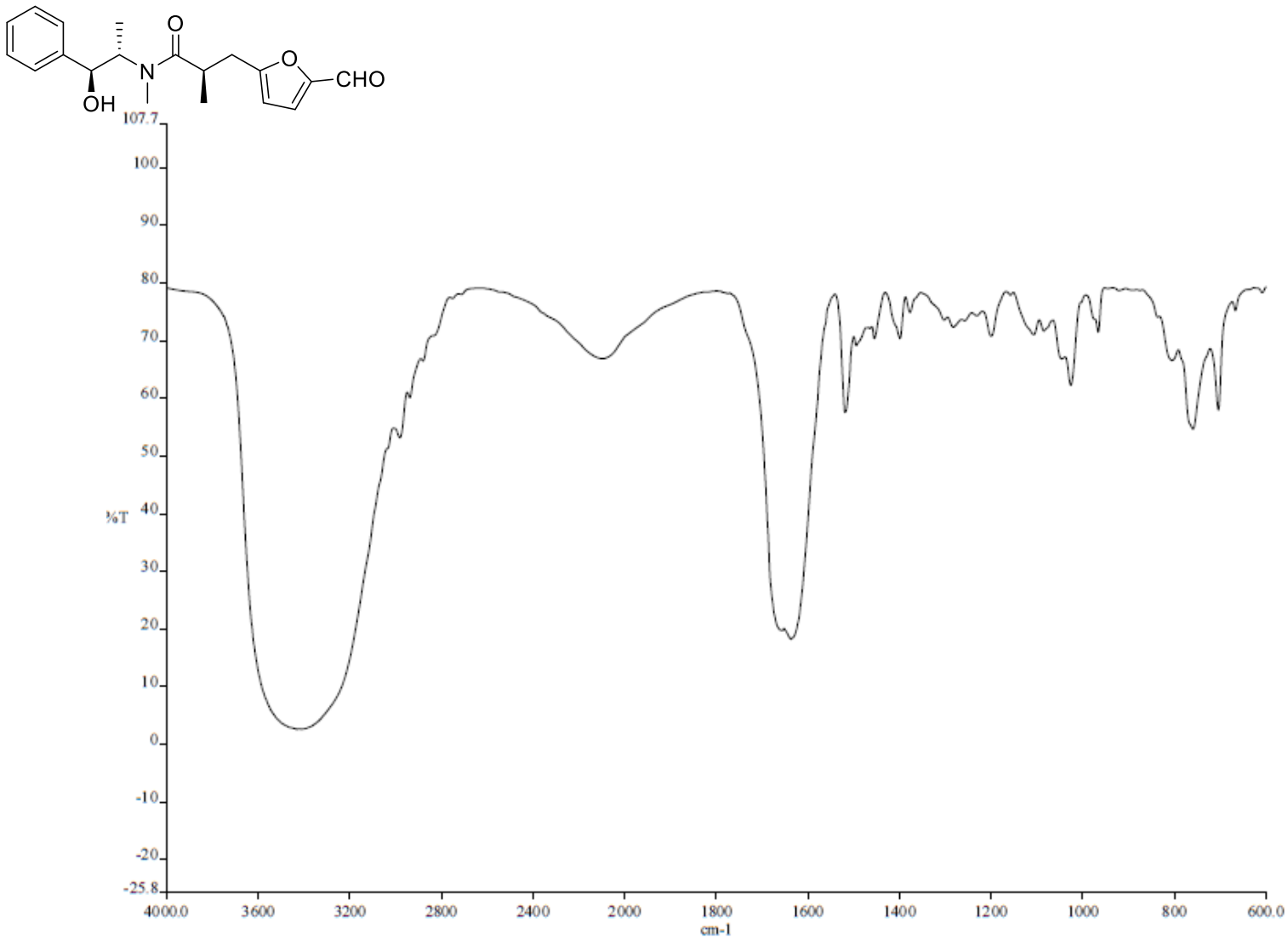
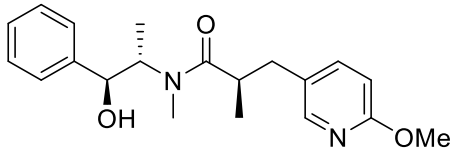
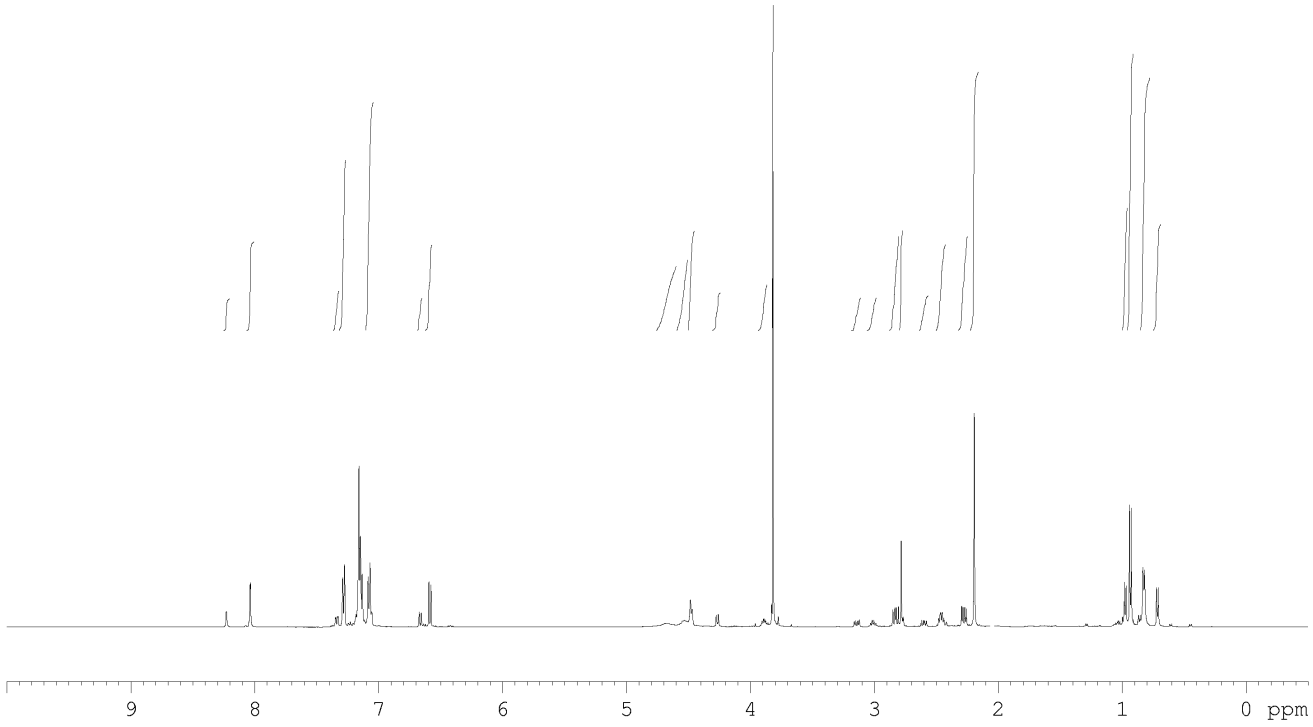
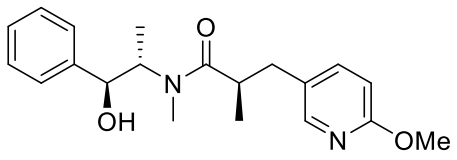
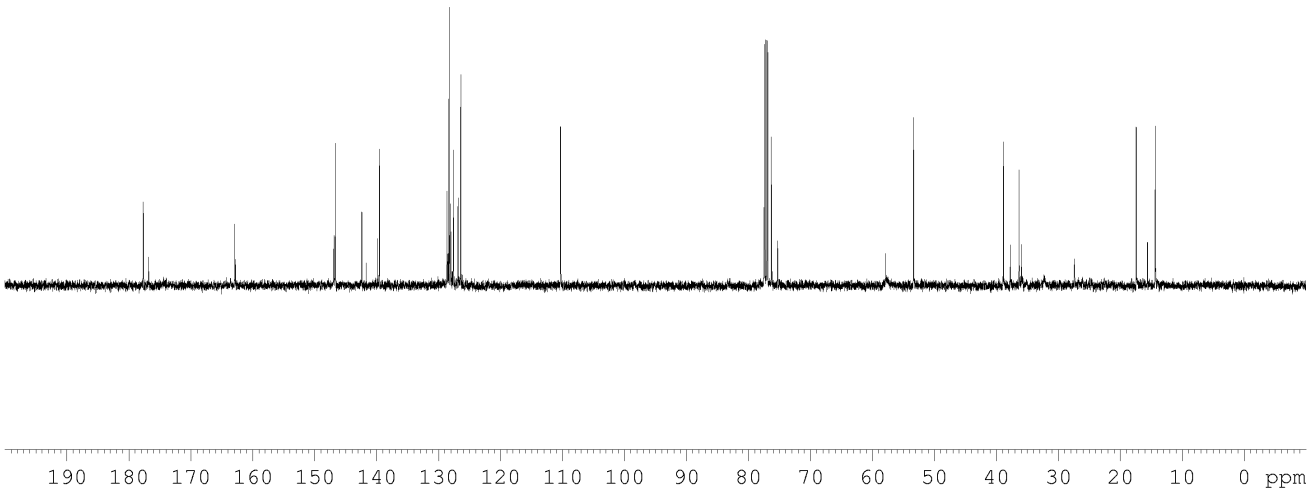


Figure A1.83 Infrared Spectrum


O
N
OH
N
OMe


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
N
OMe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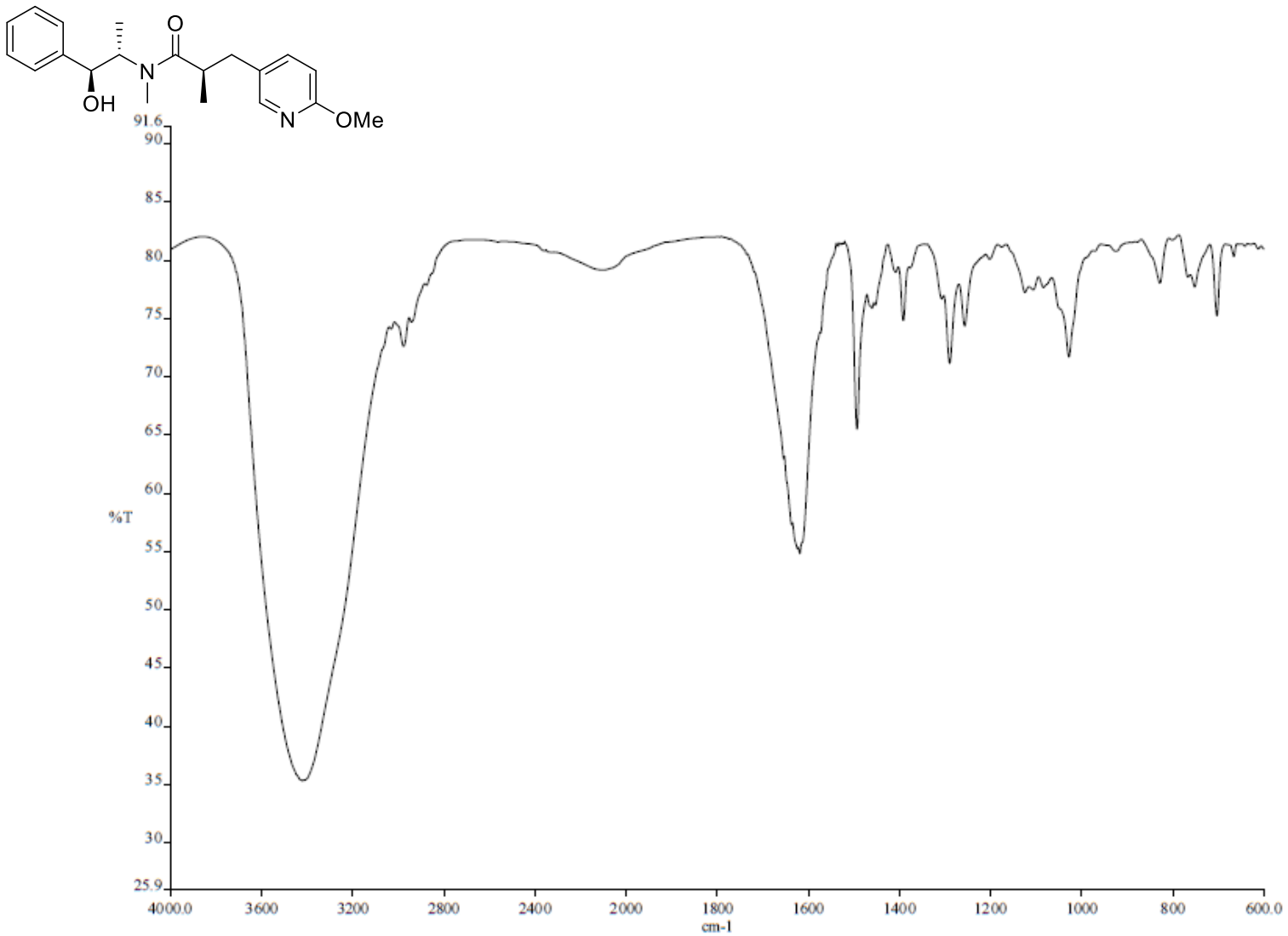
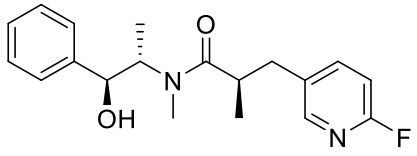
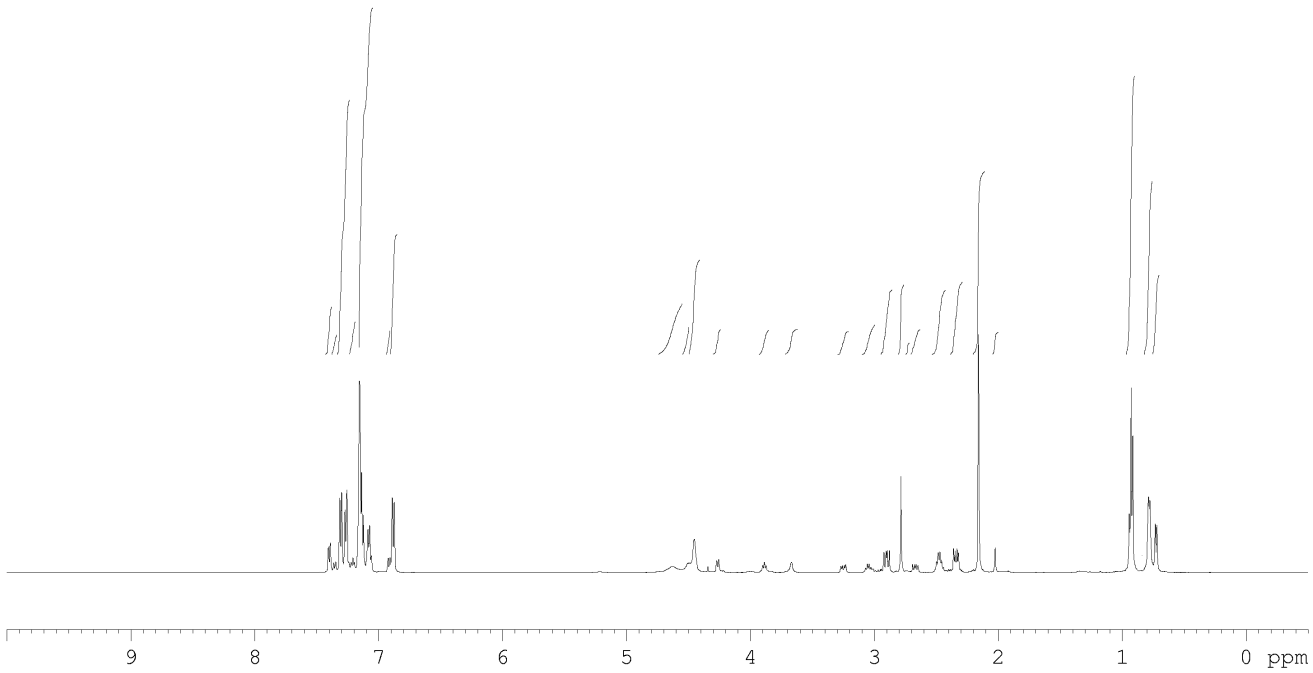
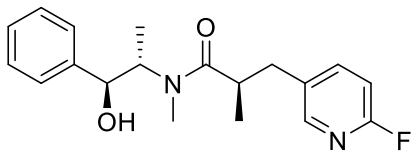
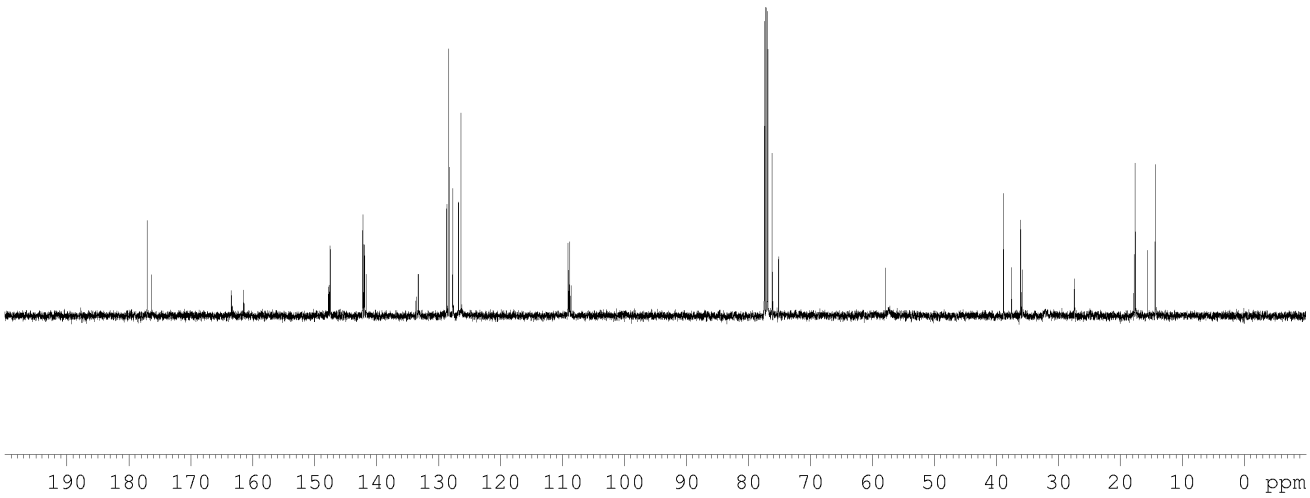


Figure A1.86 Infrared Spectrum


O
N
OH
N
F


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
N
F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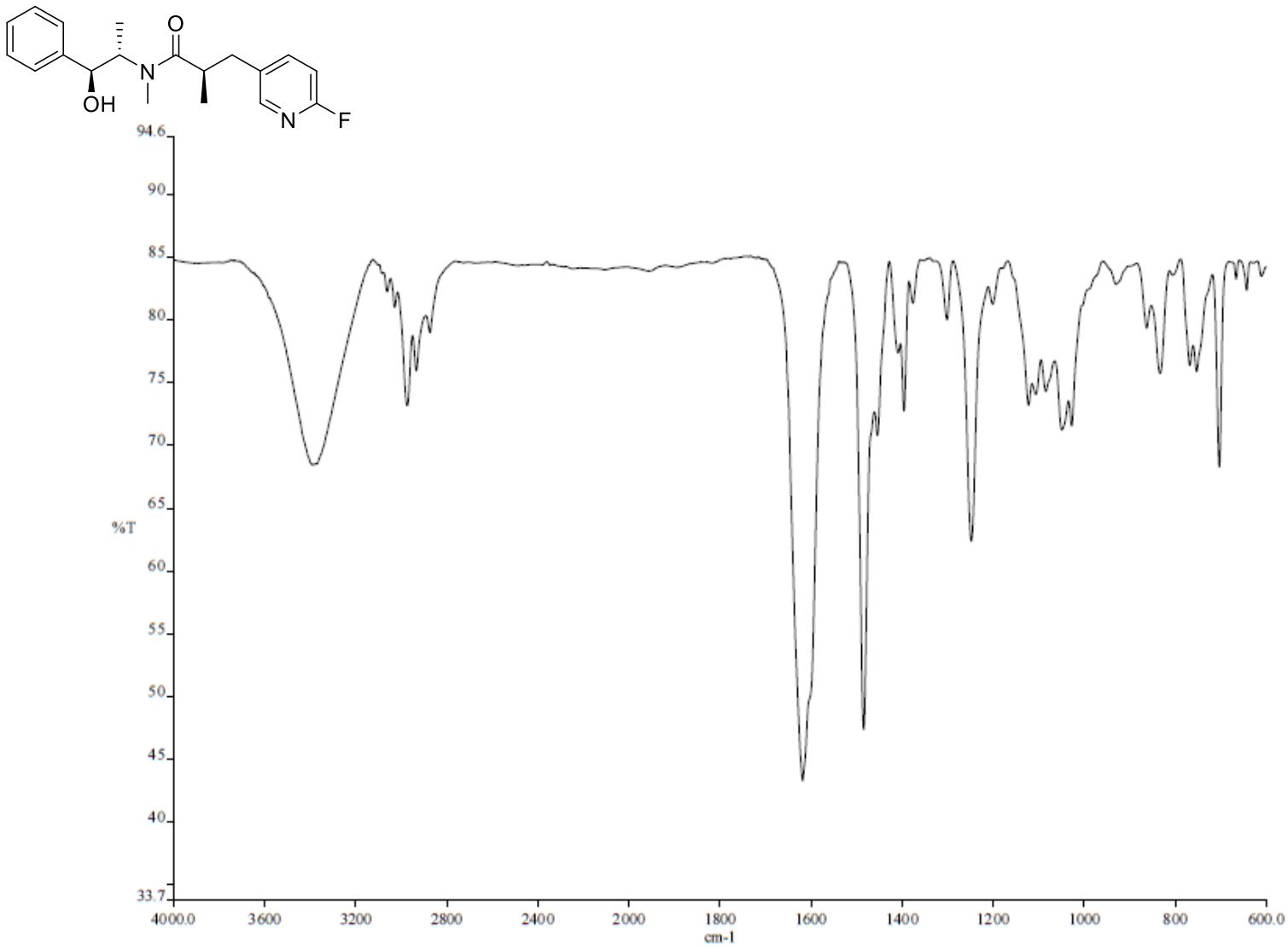
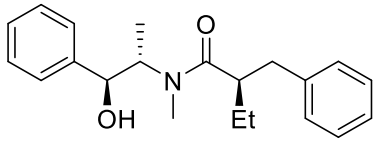
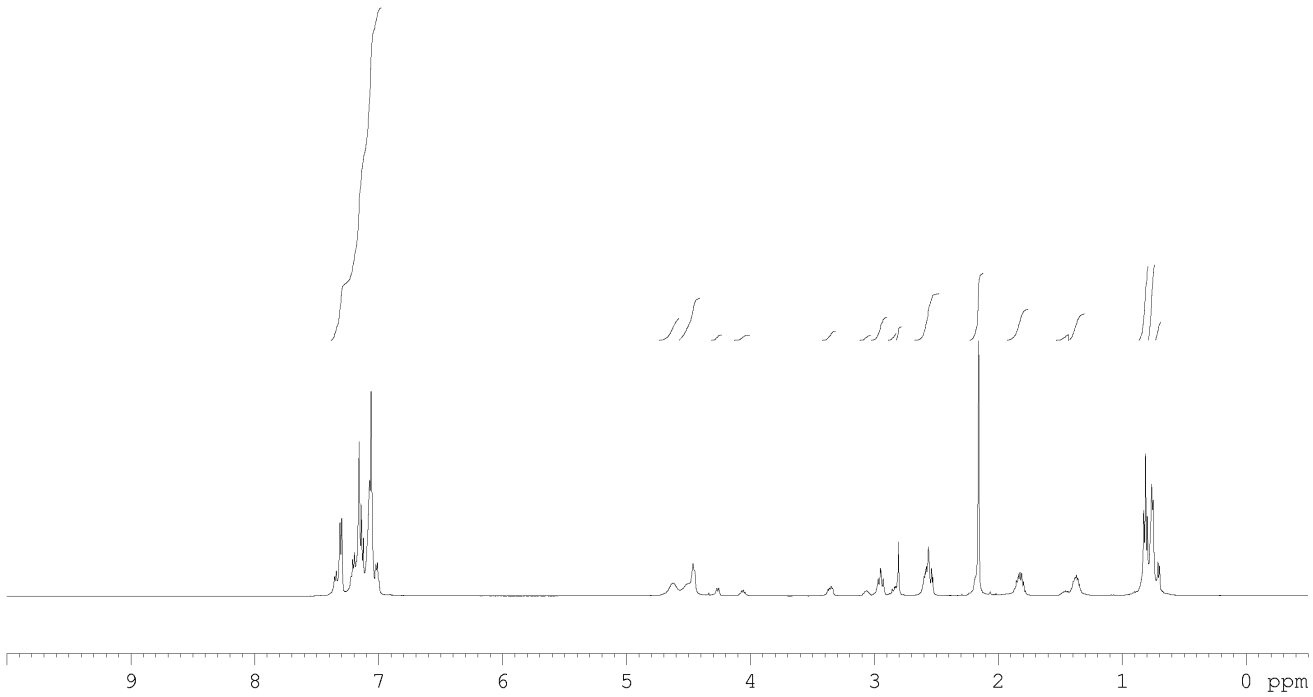
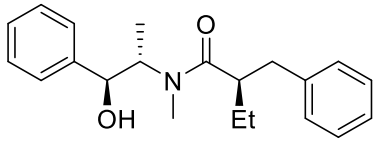
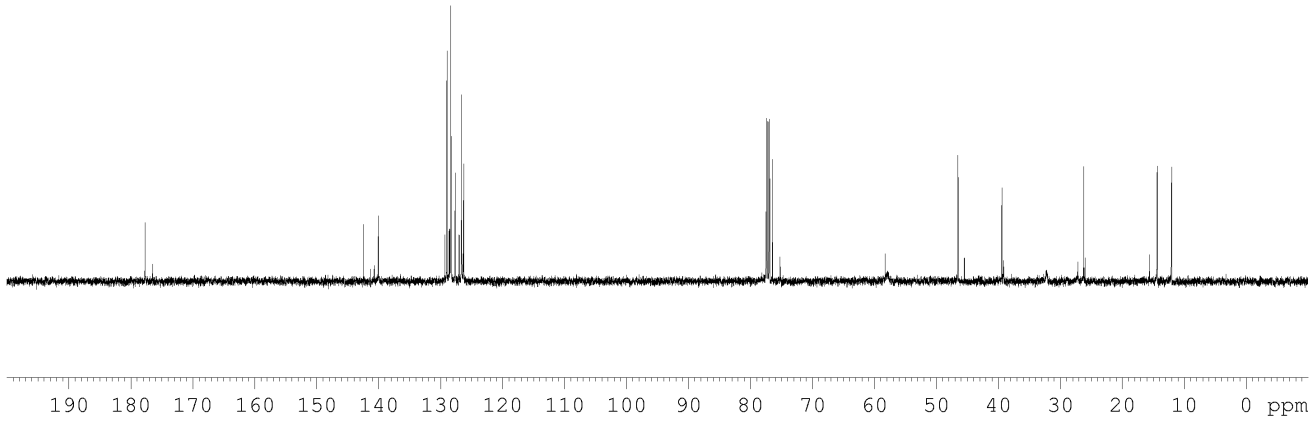


Figure A1.69 Infrared Spectrum


O
N
OH
Et


9
8
7
6
5
4
3
2
1
0 ppm


O
N
OH
Et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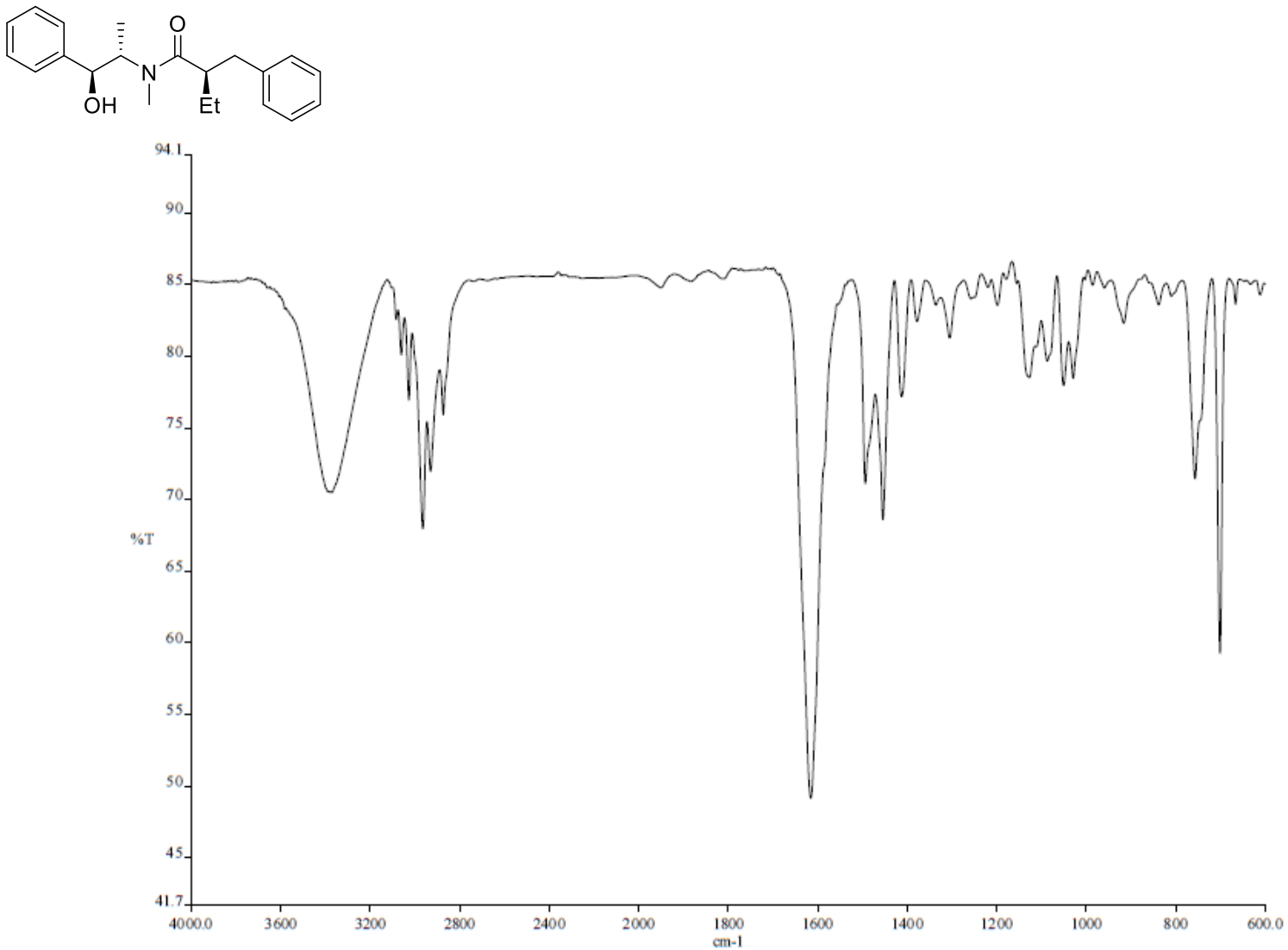
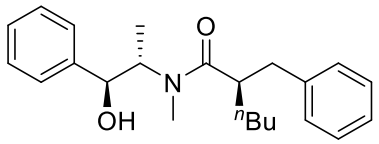
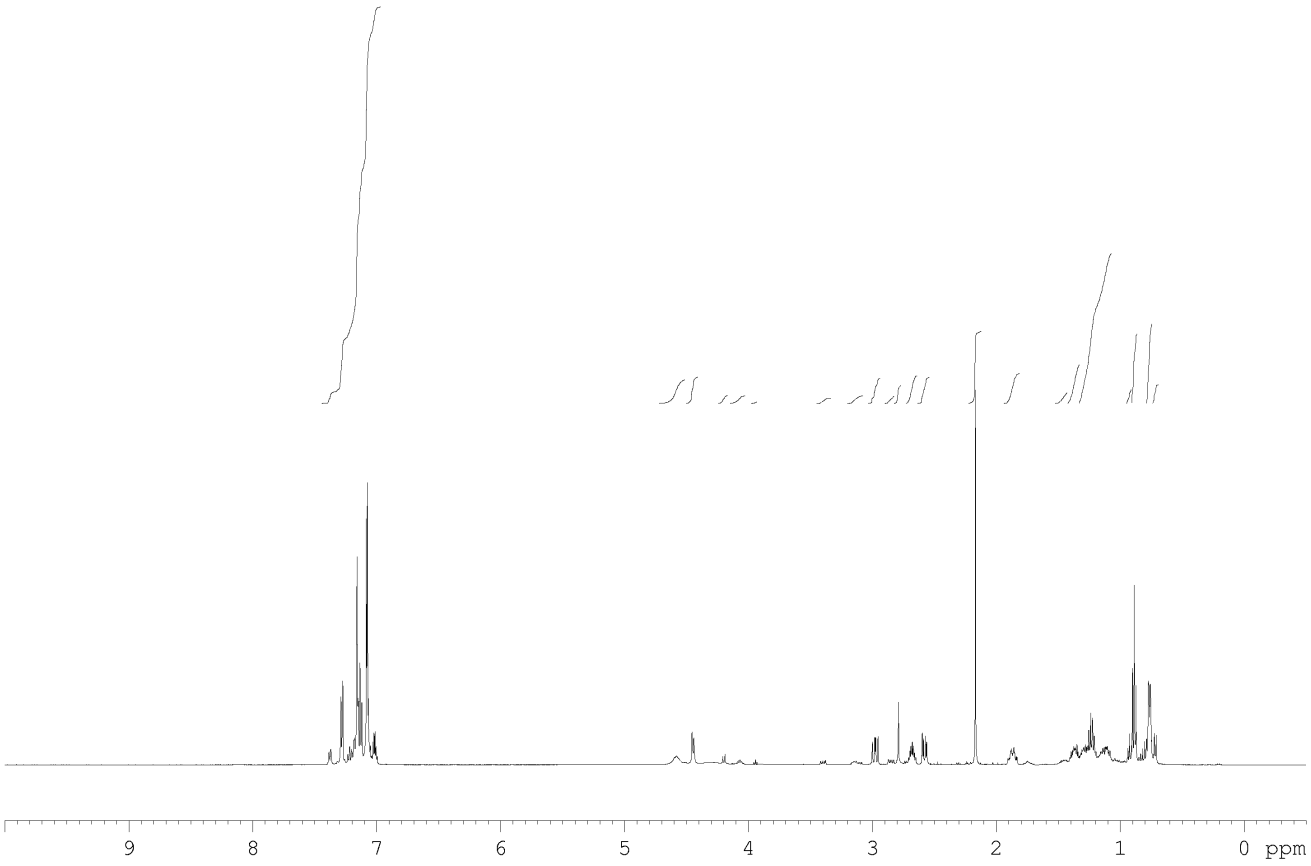
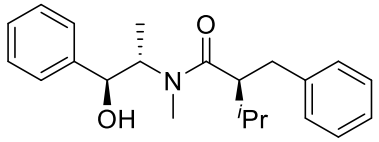
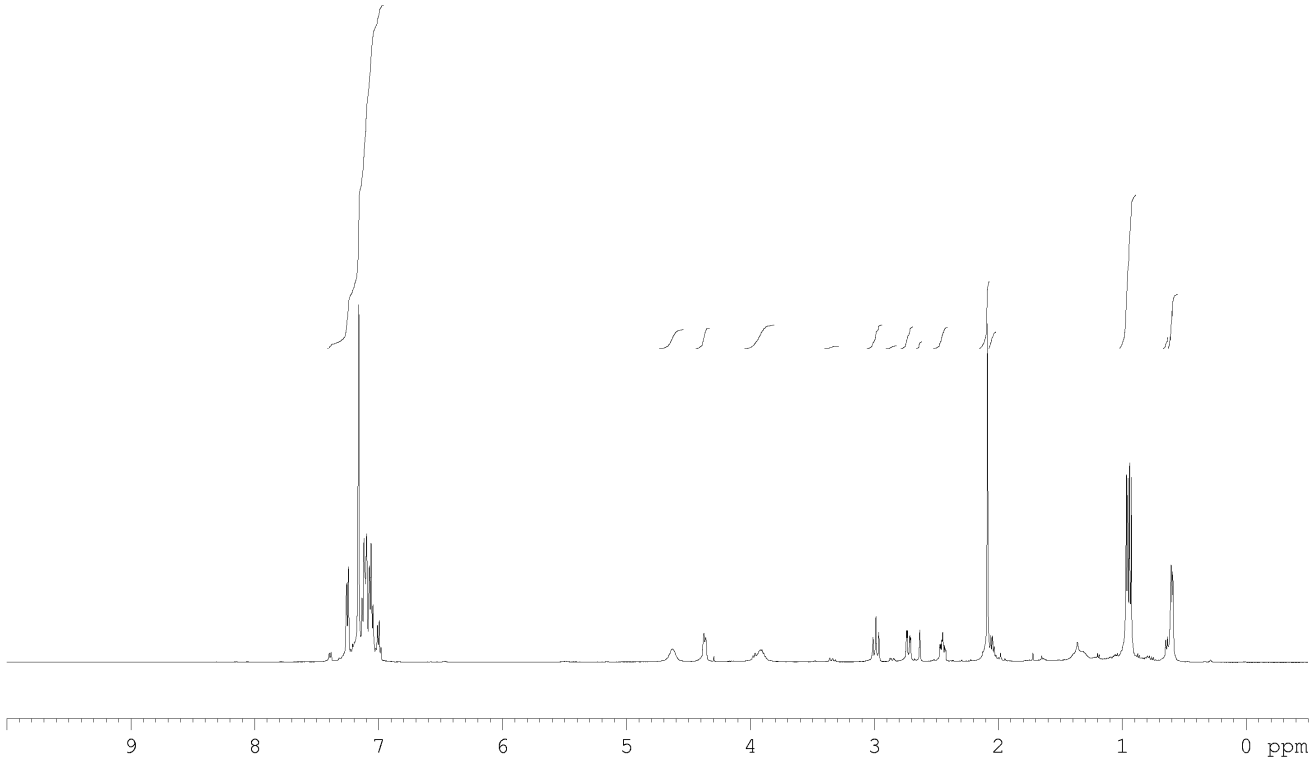


Figure A1.92 Infrared Spectrum


O
N
OH
nBu

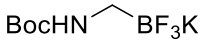

9
8
7
6
5
4
3
2
1
0 ppm

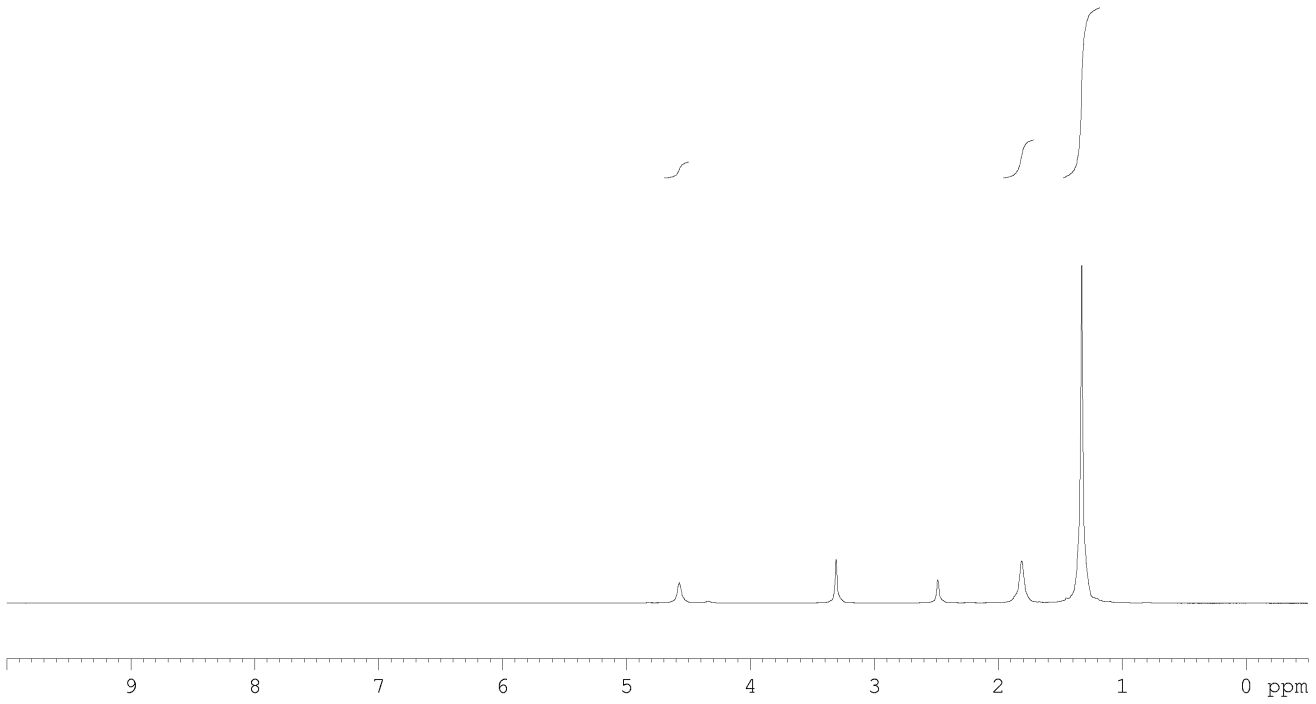

O
N
OH
iPr

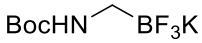

9
8
7
6
5
4
3
2
1
0 ppm

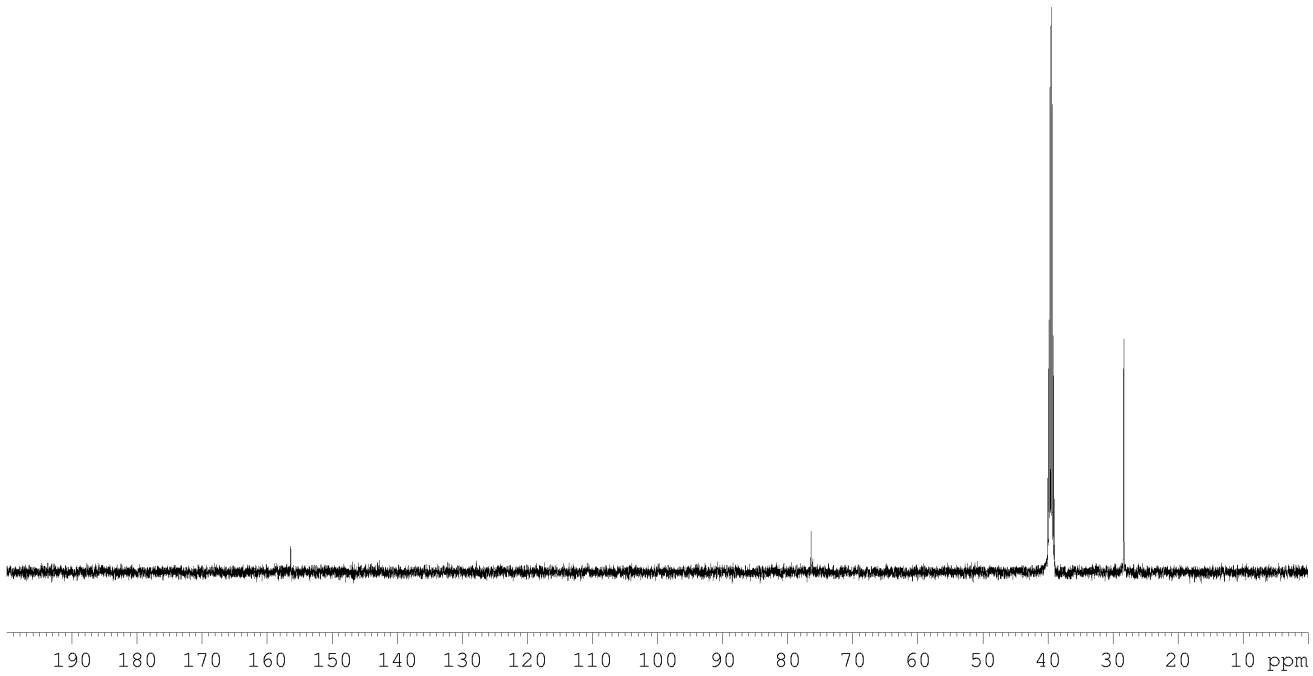
Appendix A2

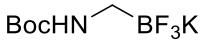
Spectra Relevant to Chapter 3

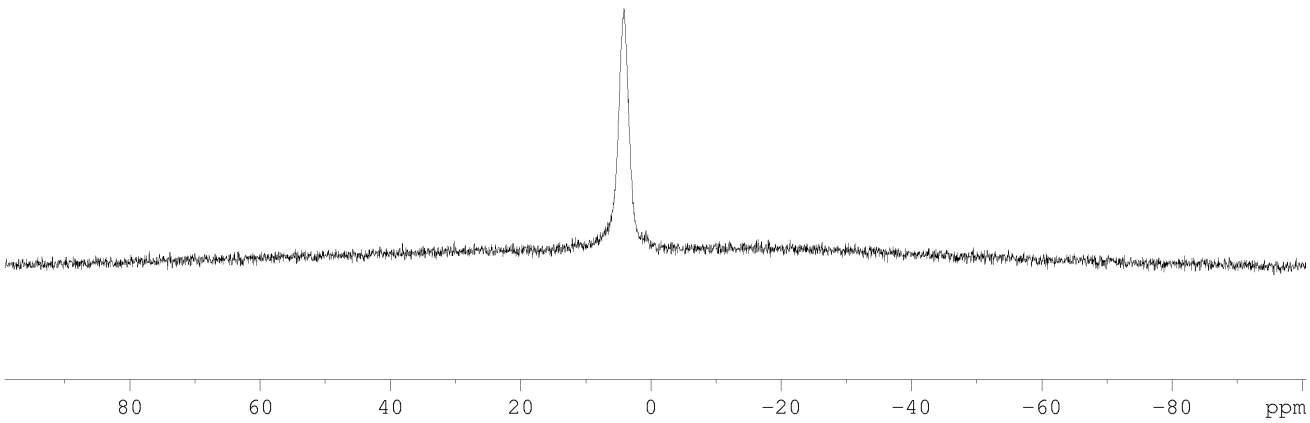

BocHN
BF3K

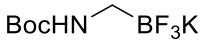

9
8
7
6
5
4
3
2
1
0 ppm

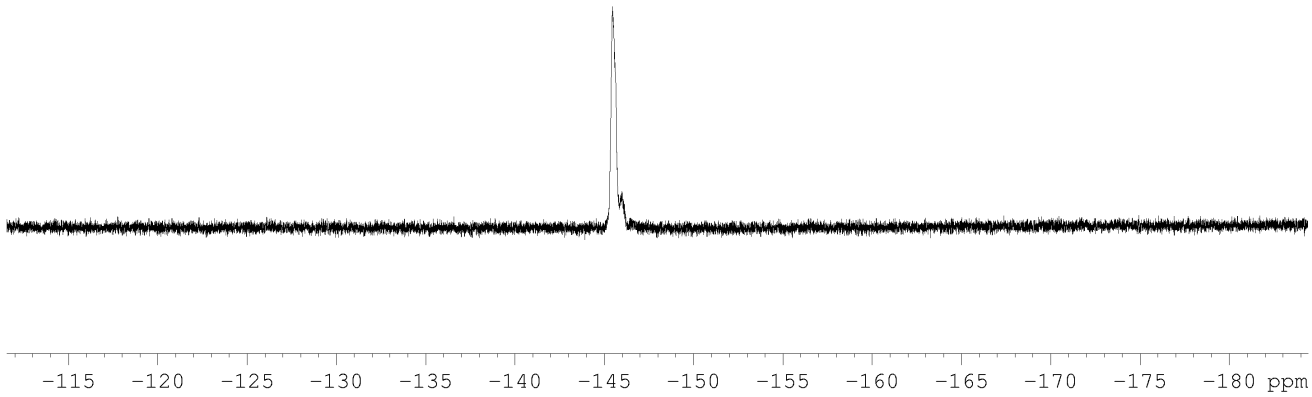

BocHN
BF3K


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


BocHN
BF3K


80
60
40
20
0
−20
−40
−60
−80
ppm


BocHN
BF3K


−115
−120
−125
−130
−135
−140
−145
−150
−155
−160
−165
−170
−175
−180 ppm

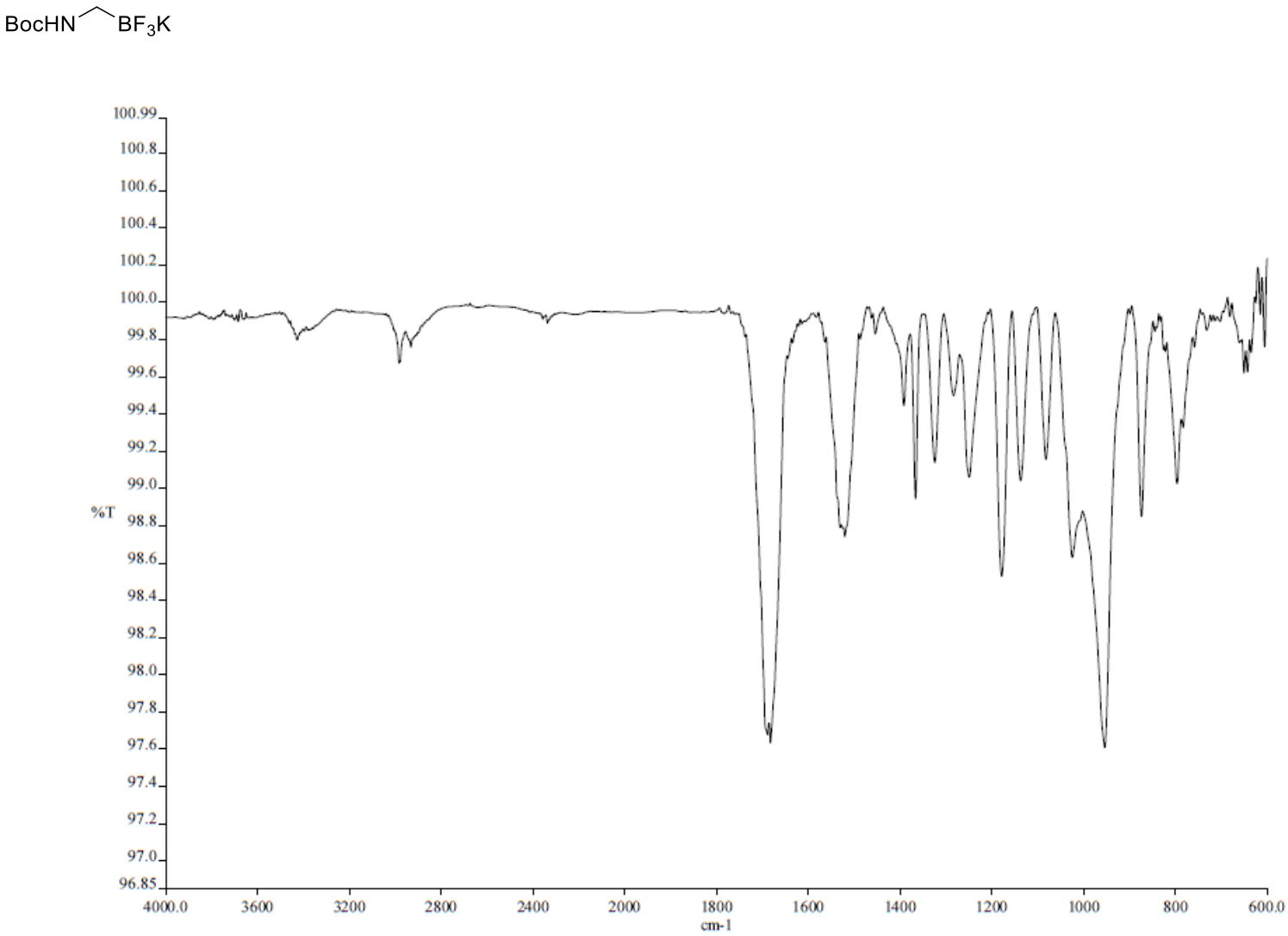
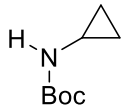
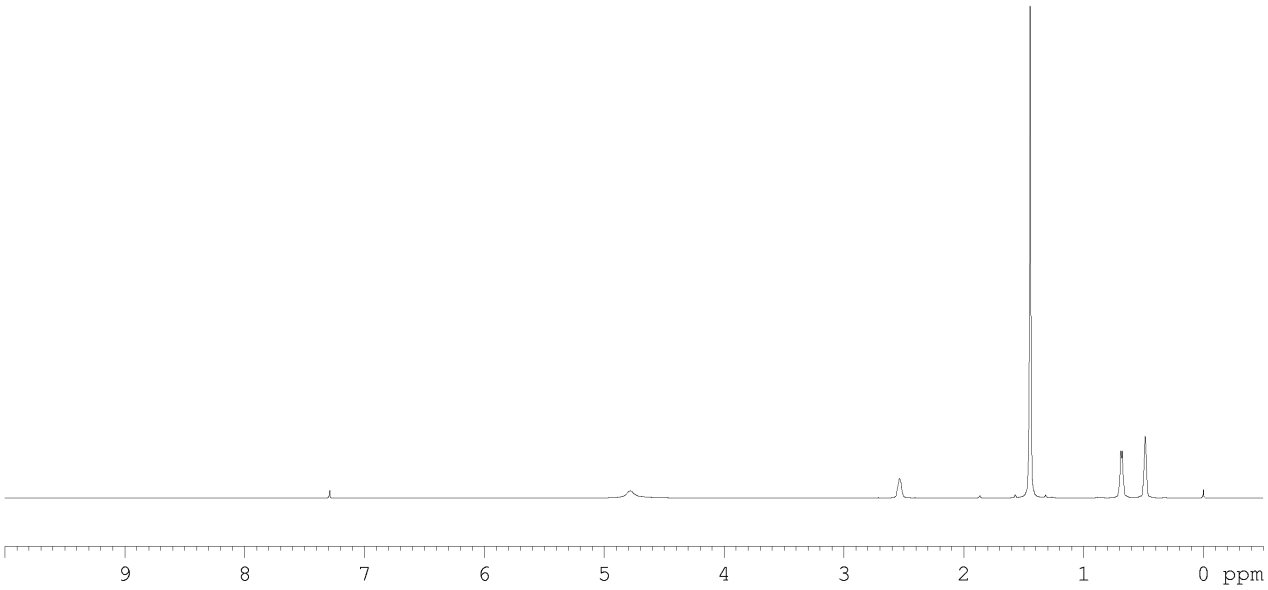
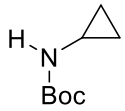


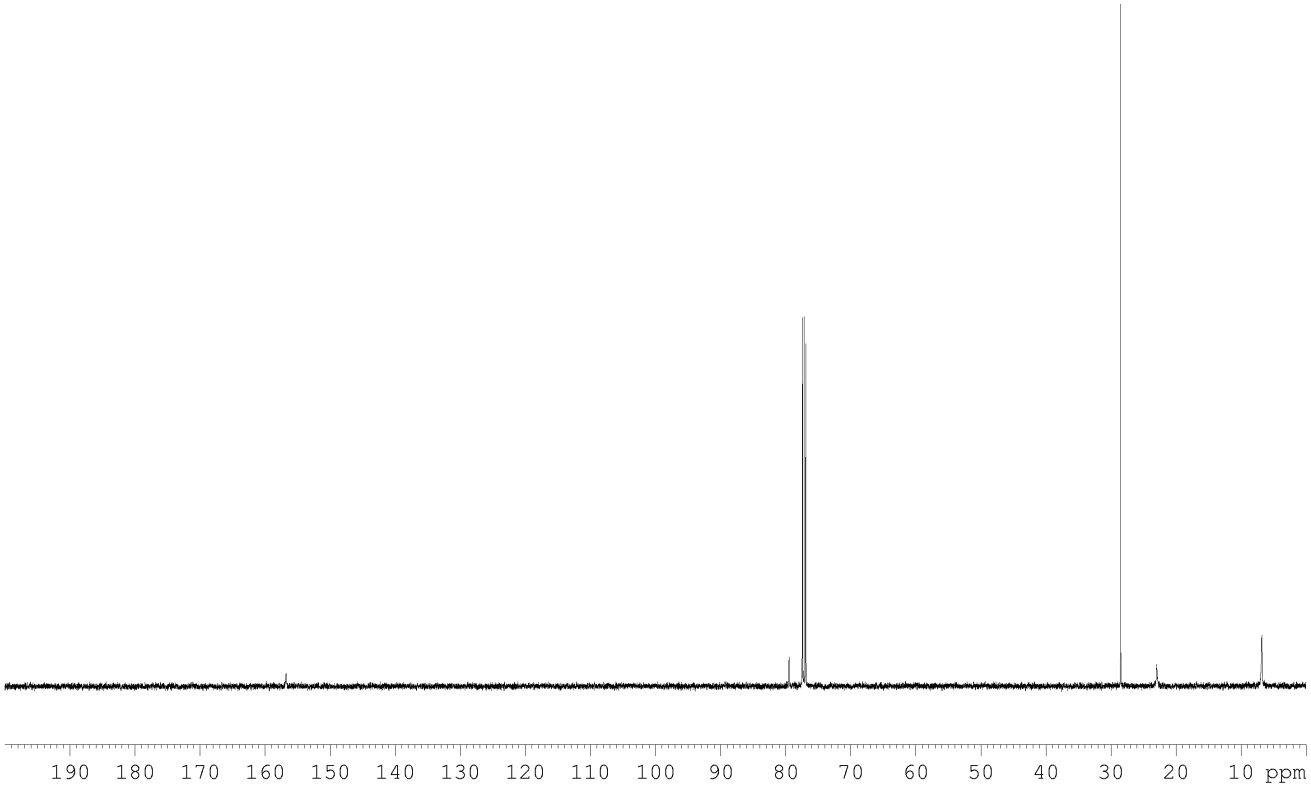
Figure A2.5 Infrared Spectrum



309




H
N
Boc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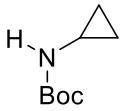


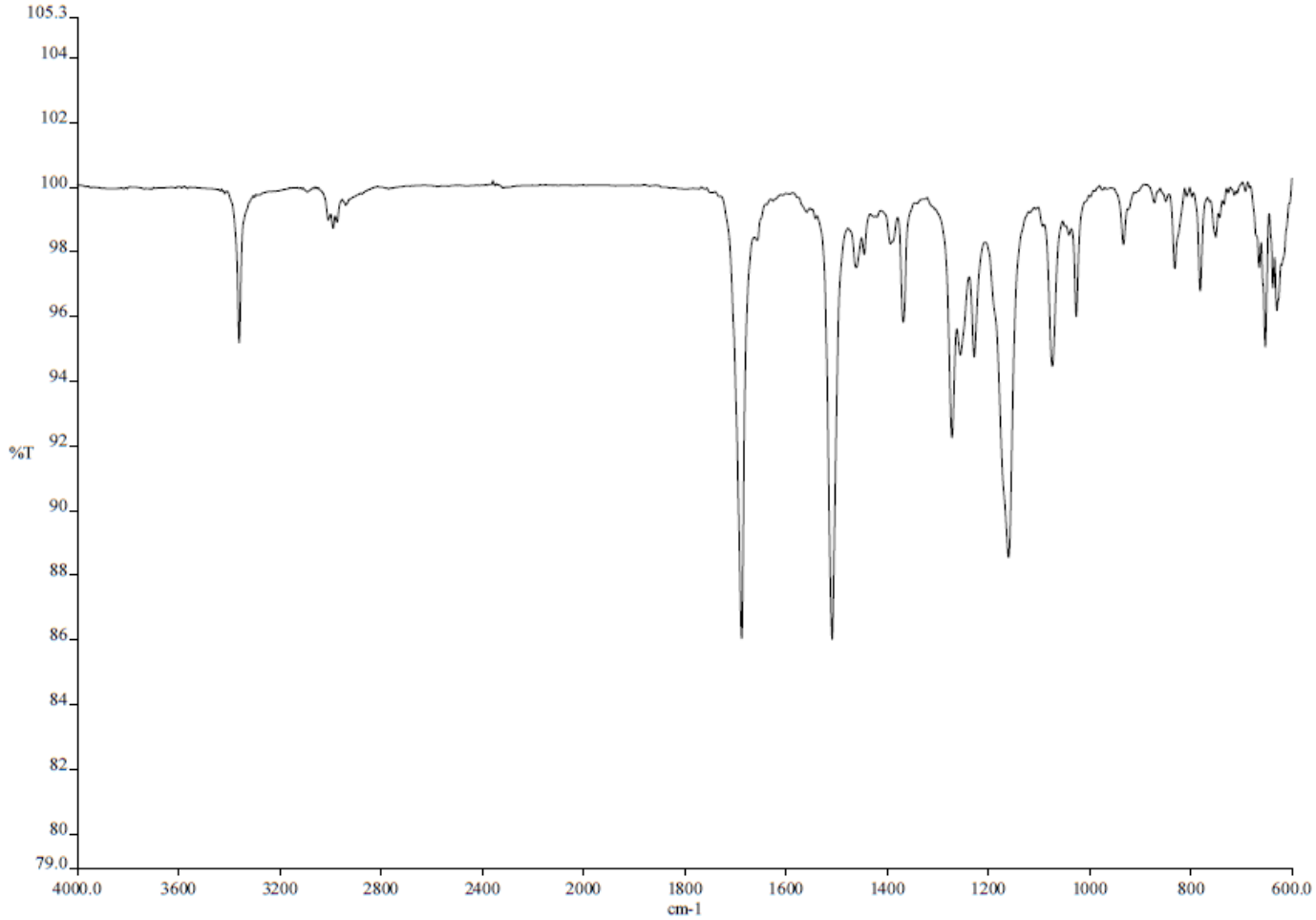
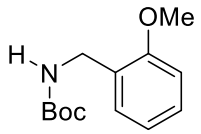
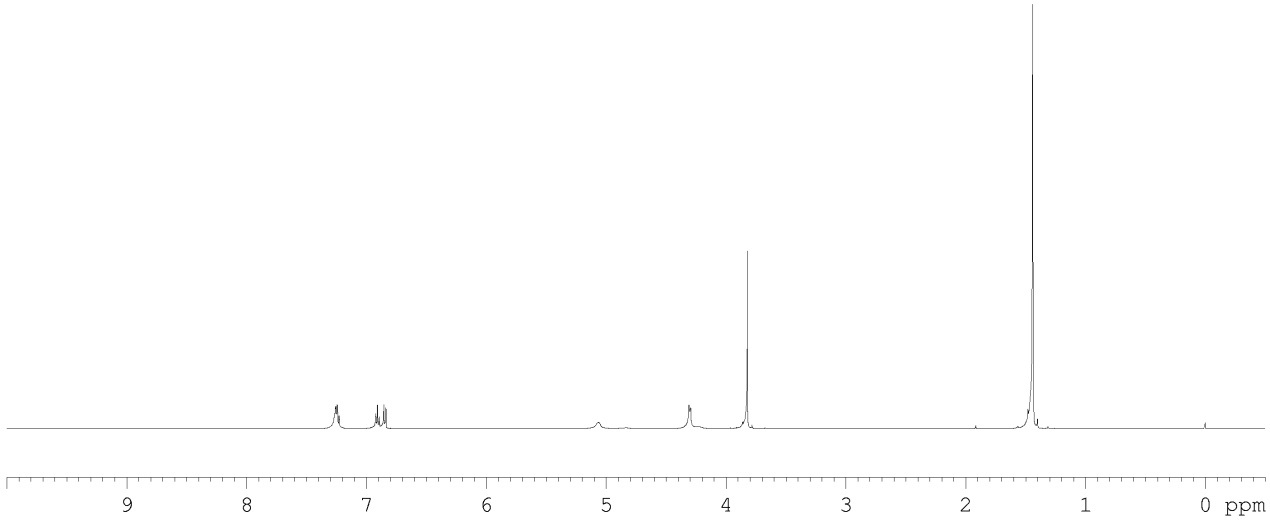
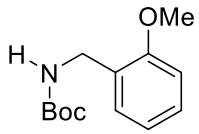
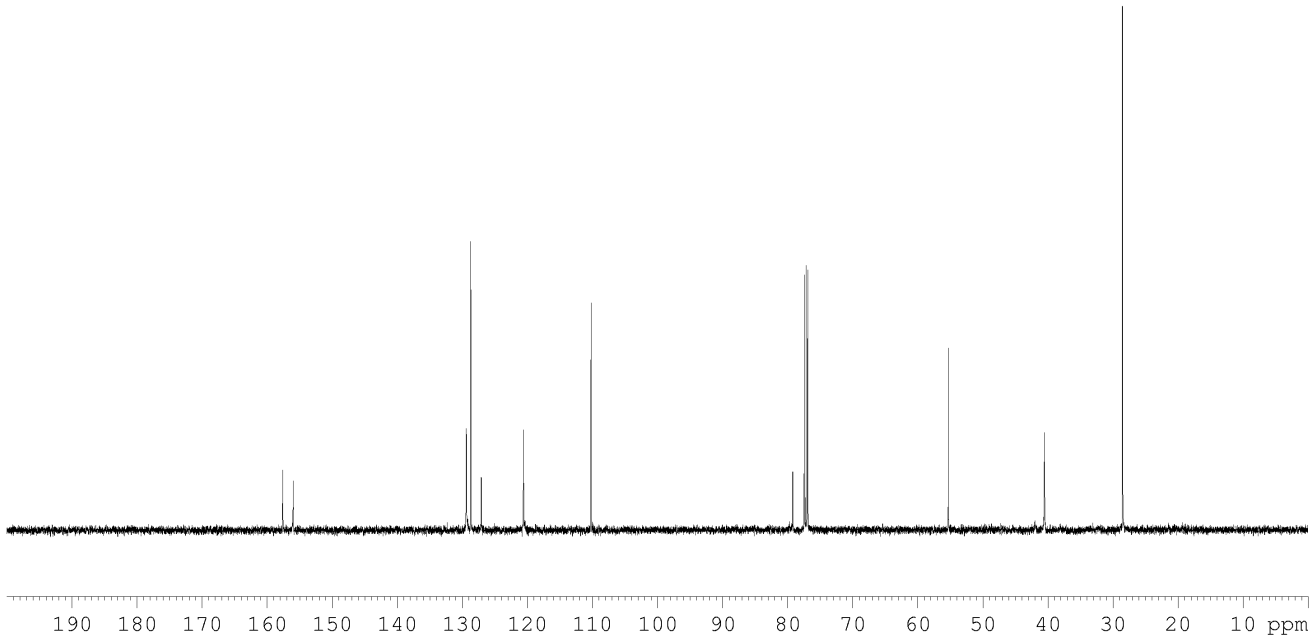


Figure A2.8 Infrared Spectrum


OMe
H
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


OMe
H
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

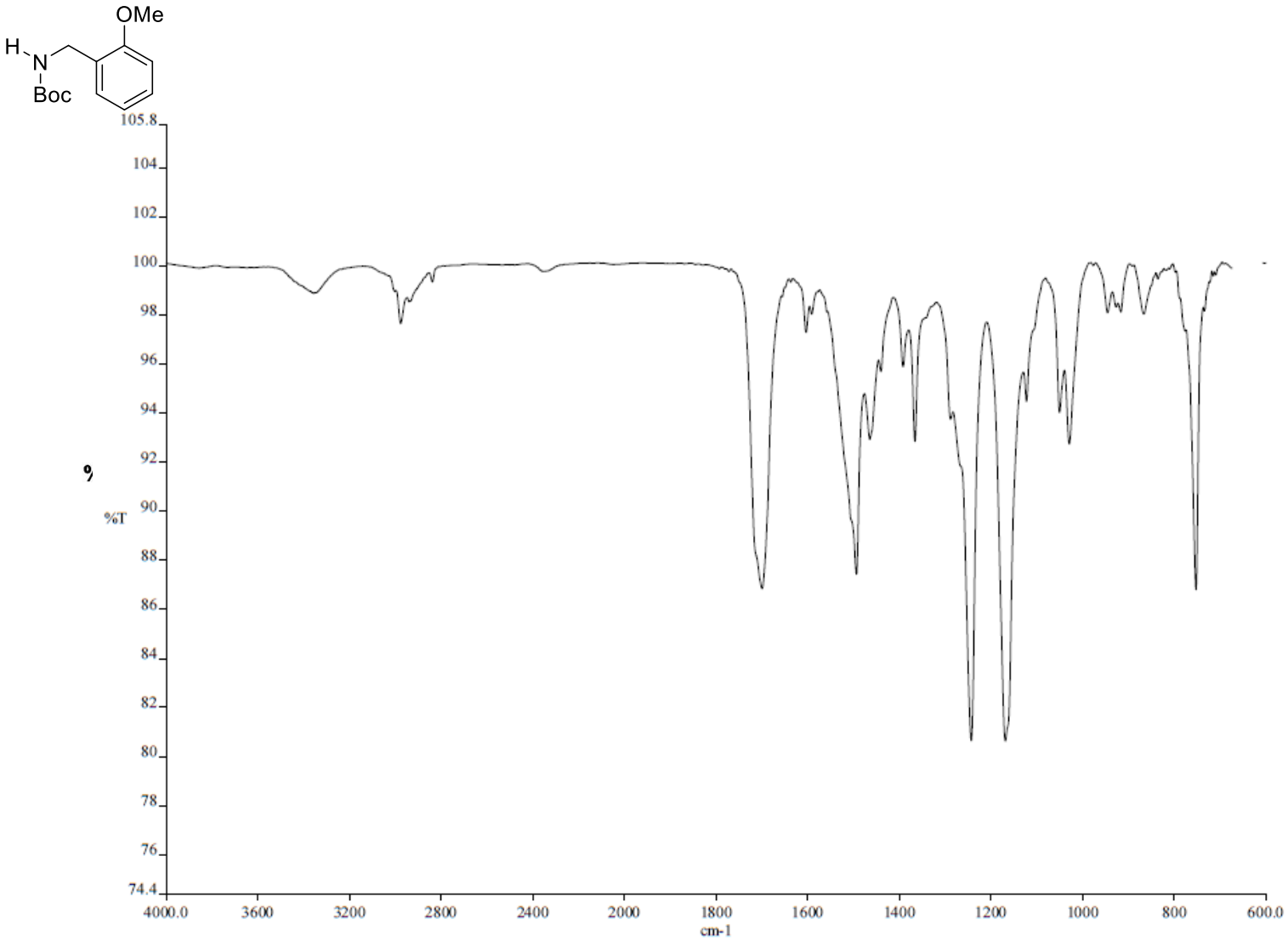
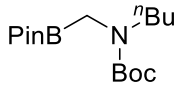
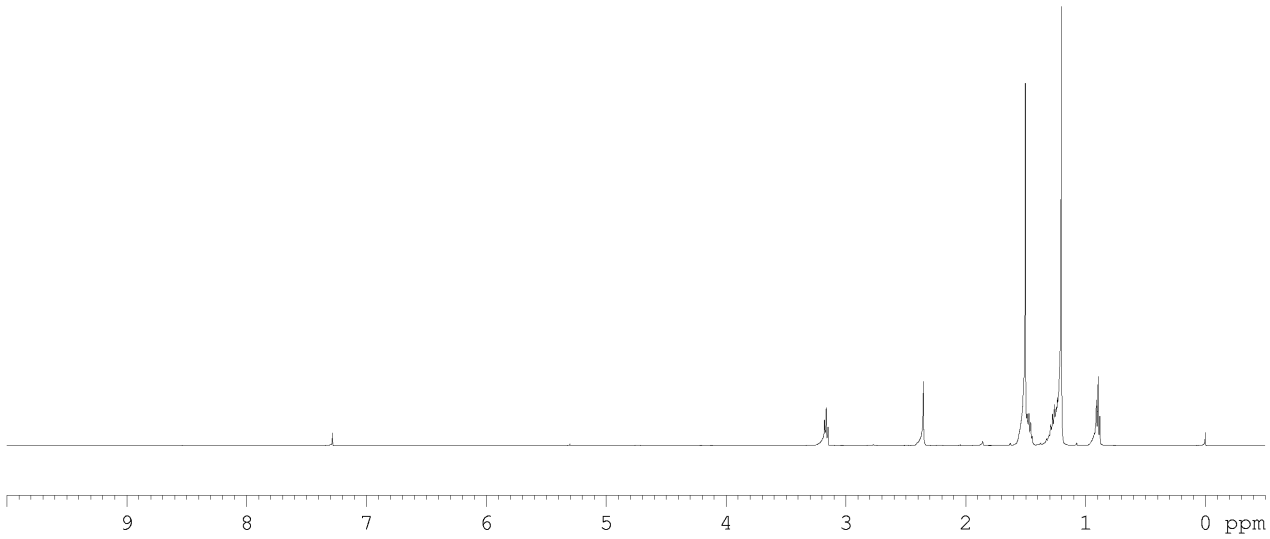
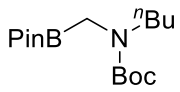
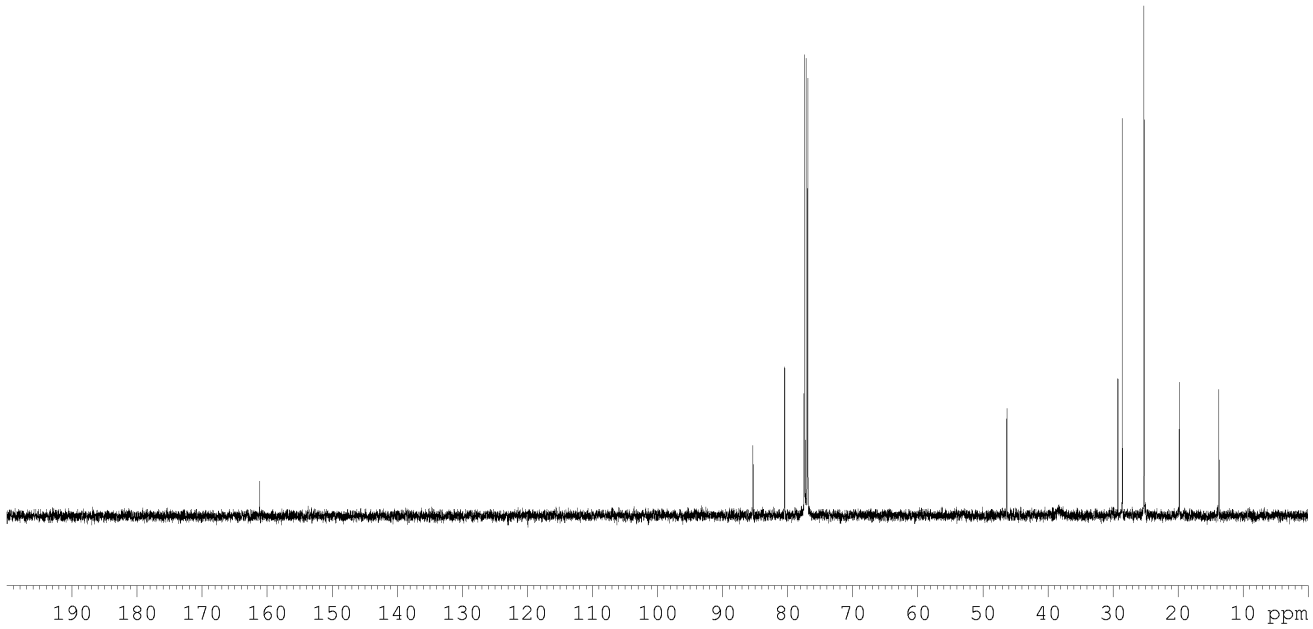


Figure A2.11 Infrared Spectrum


PinB
N
nBu
Boc


9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
nBu
Boc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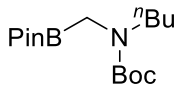
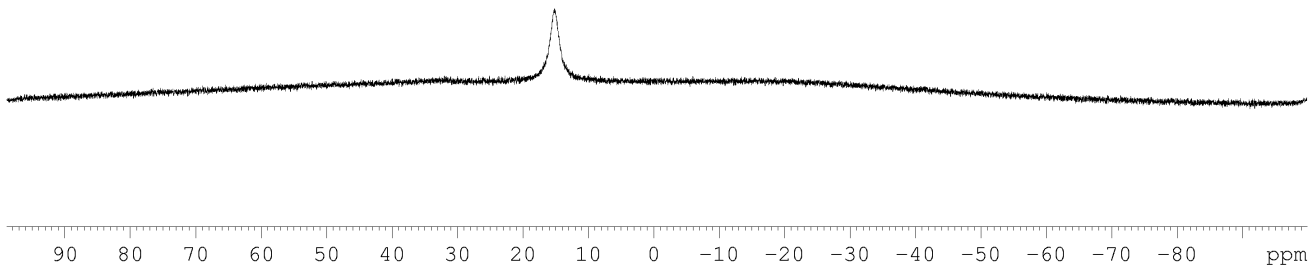

PinB
N
nBu
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 ppm

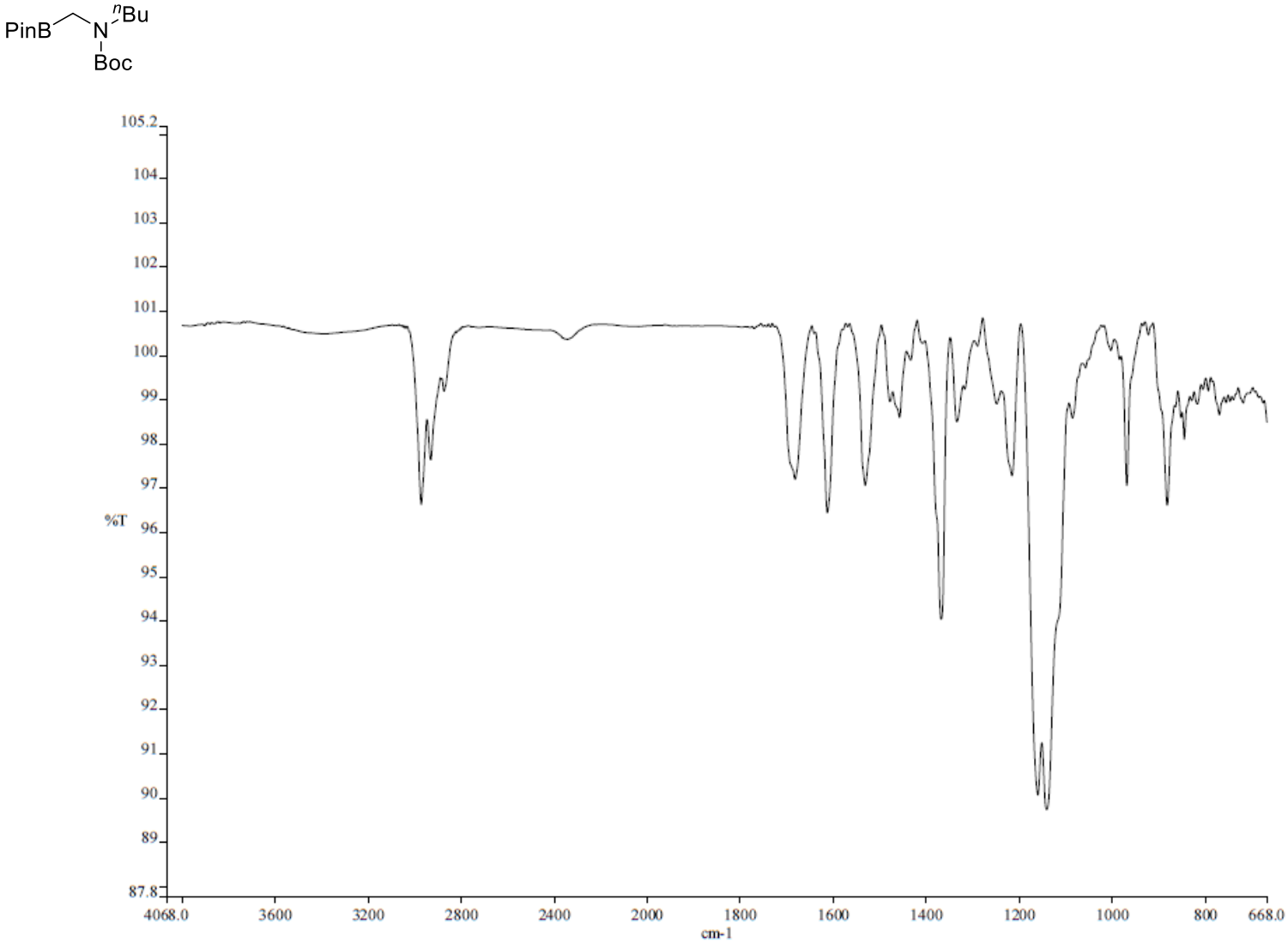
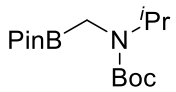
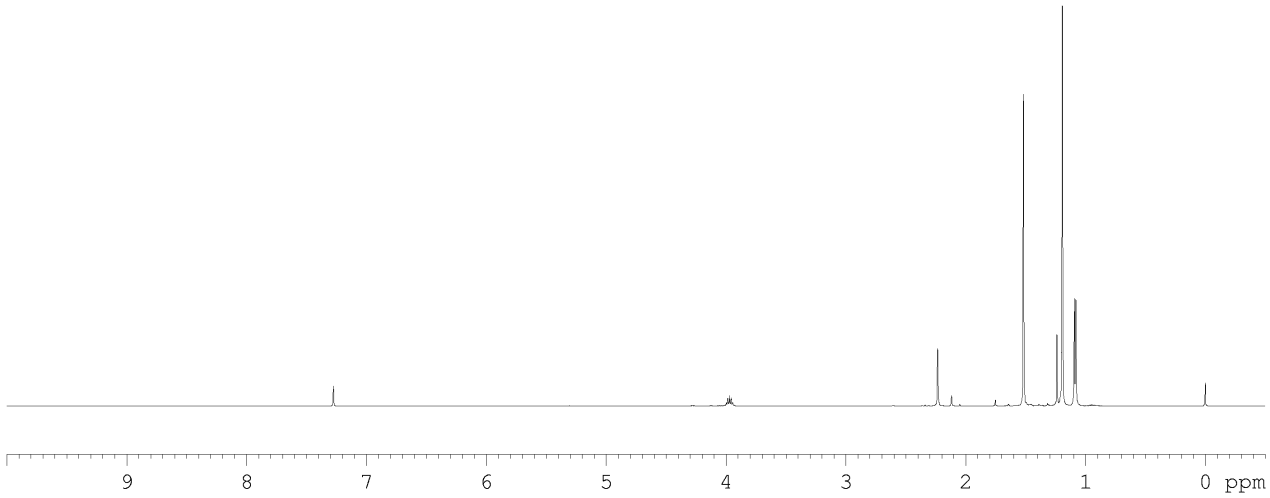
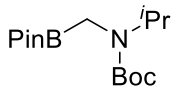
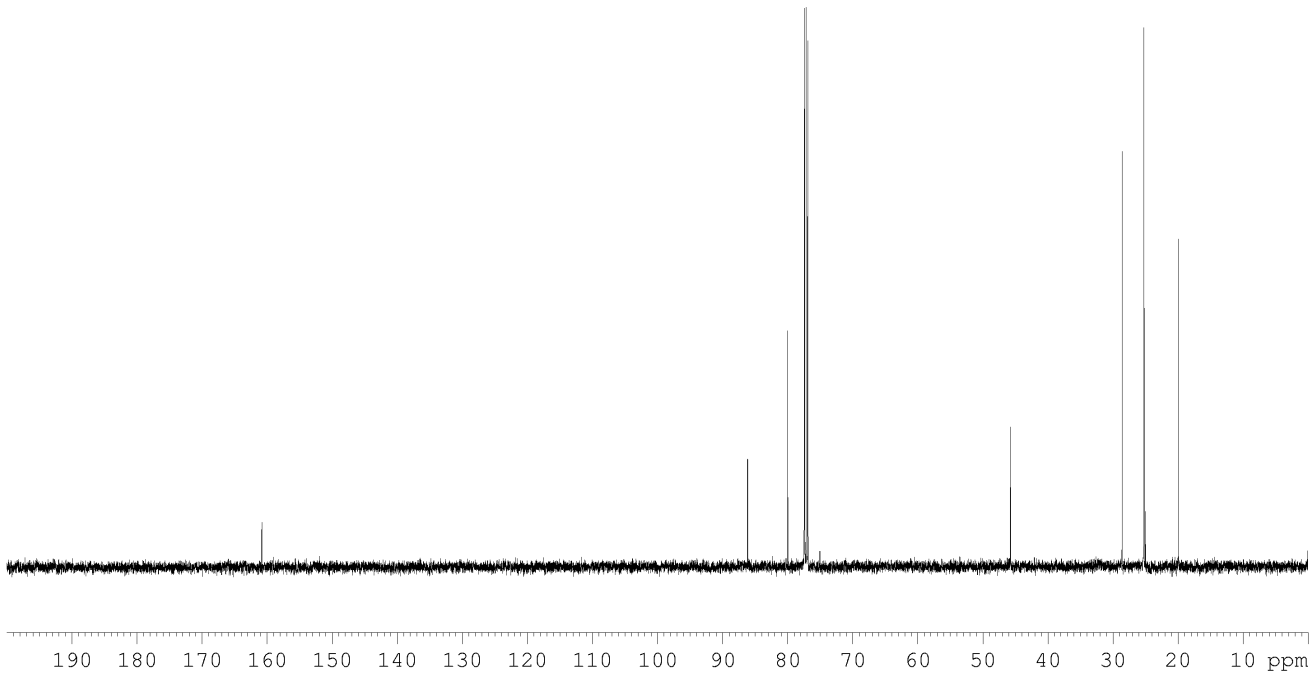


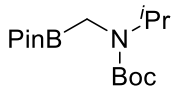
Figure A2.15 Infrared Spectrum

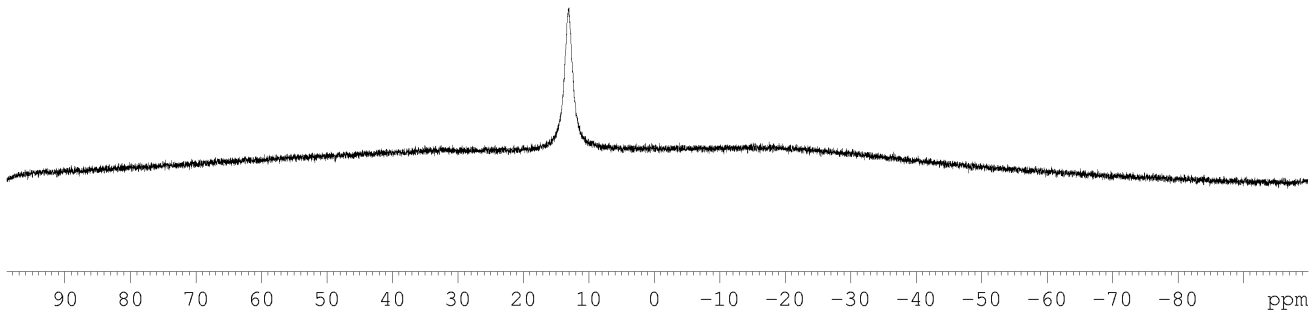

PinB
N
iPr
Boc


9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
iPr
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


PinB
N
iPr
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80
ppm

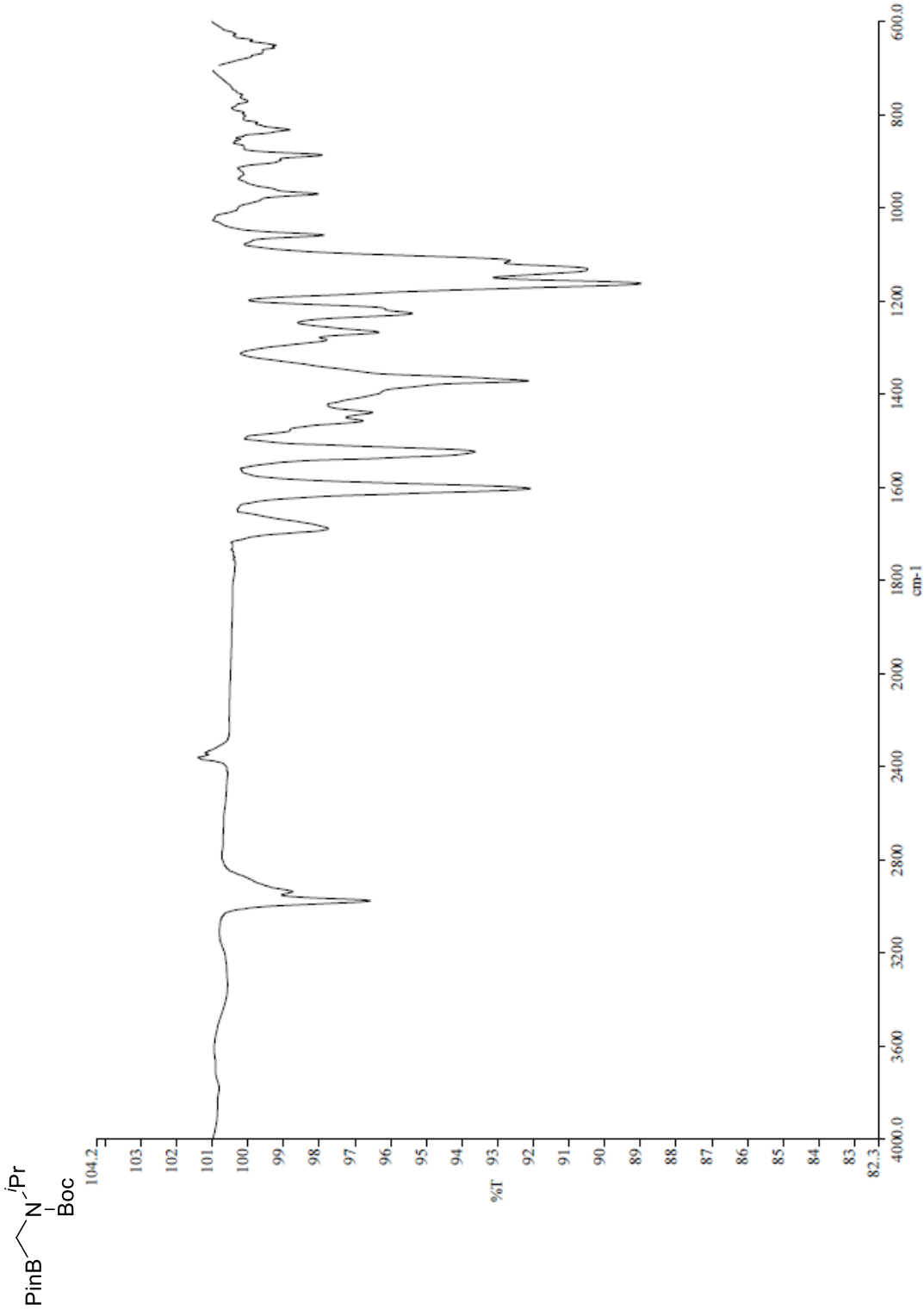
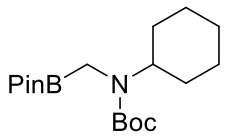
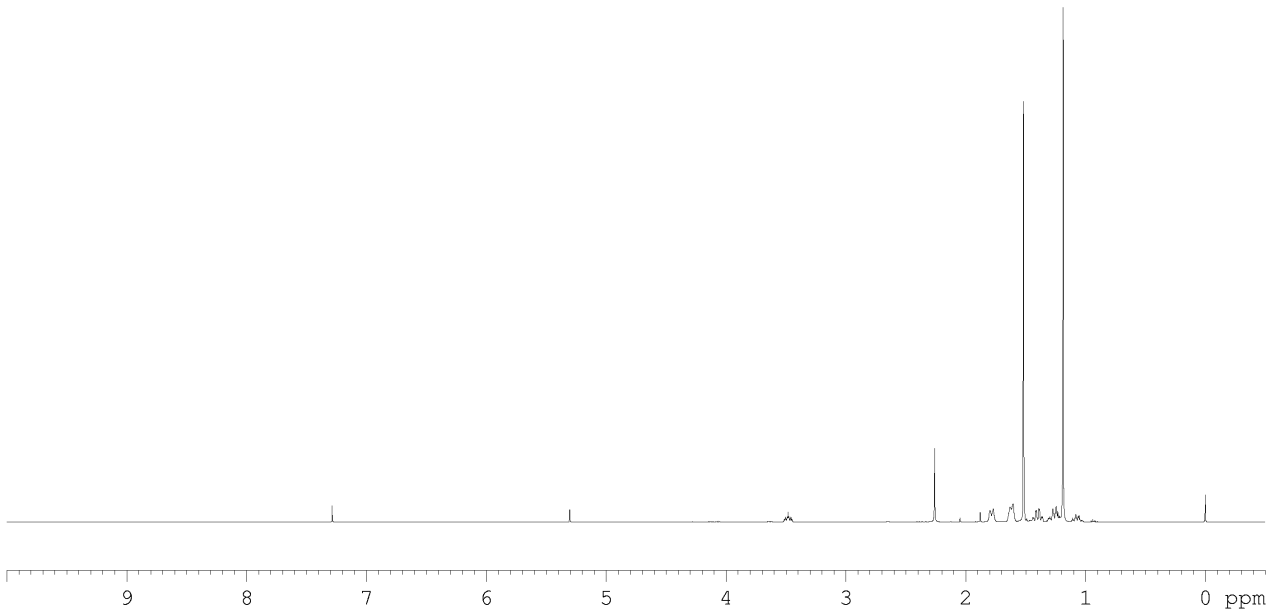
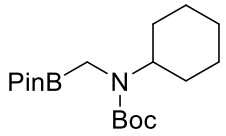
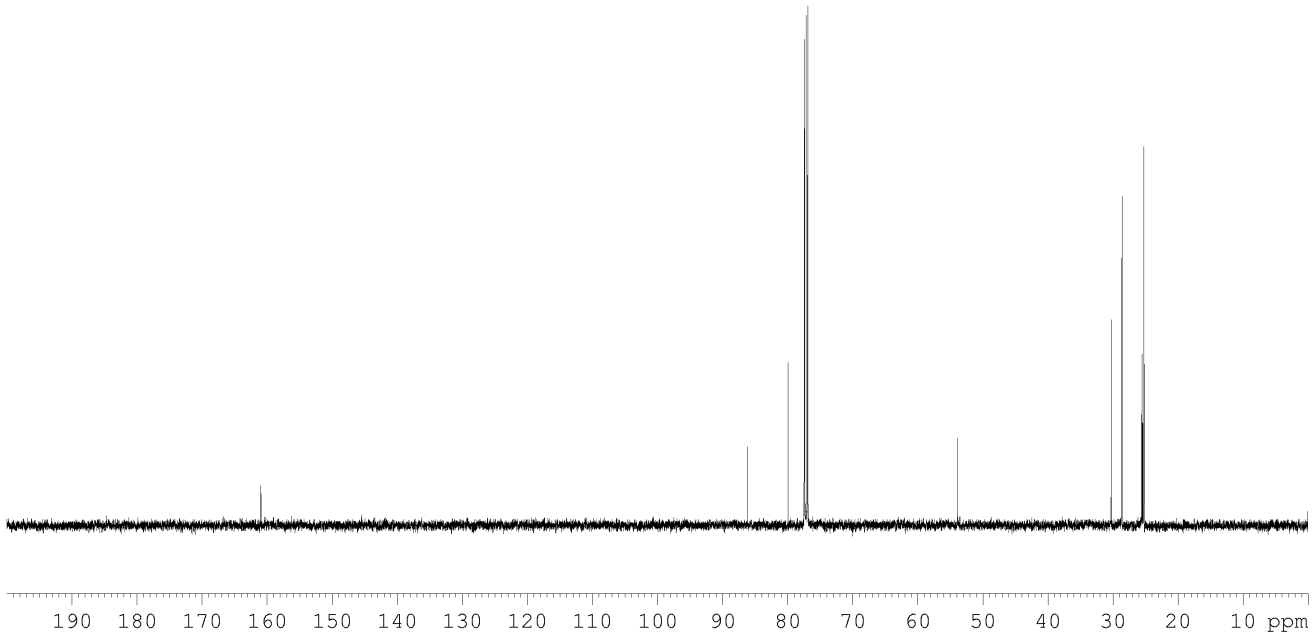


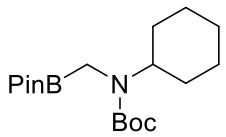
Figure A2.19 Infrared Spectrum

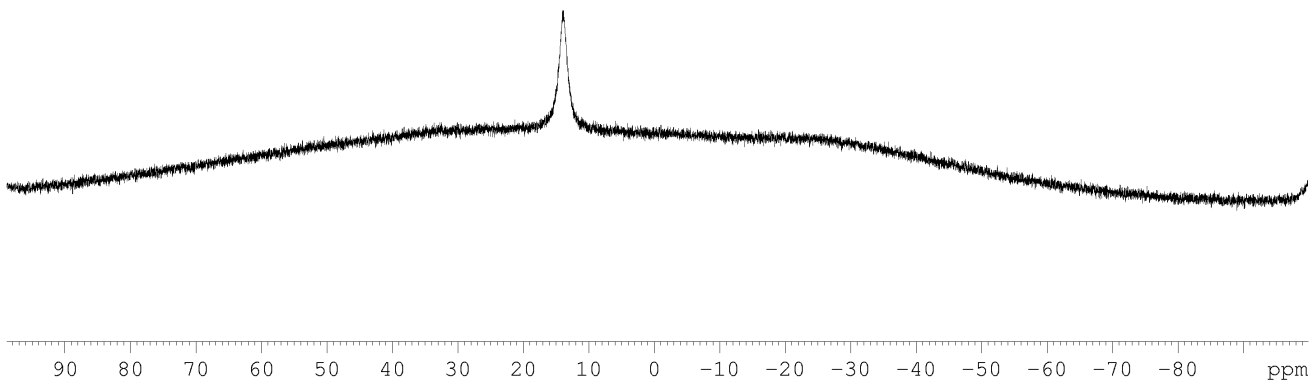

PinB
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


PinB
N
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 ppm

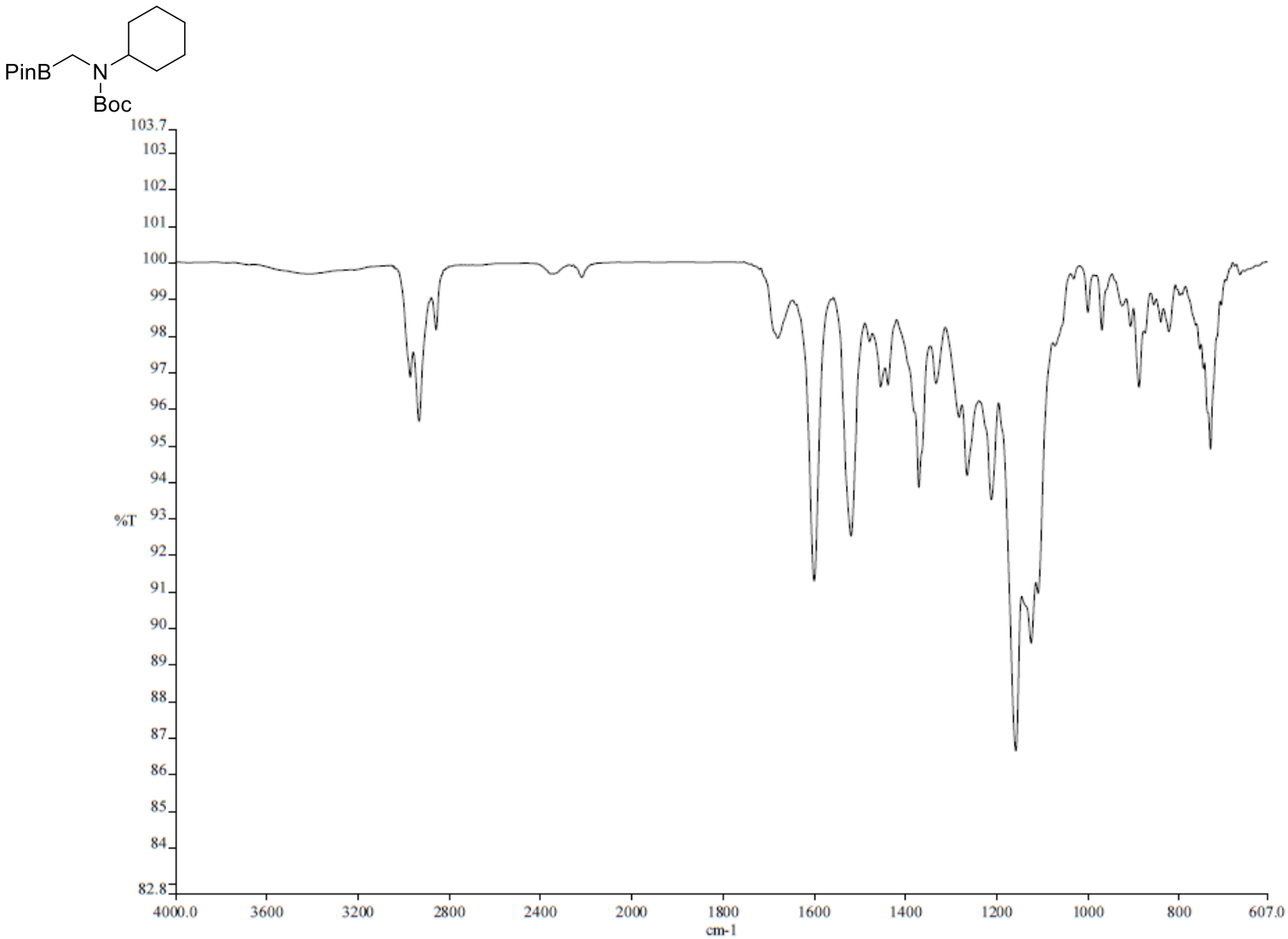
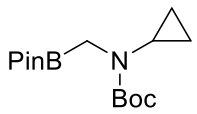
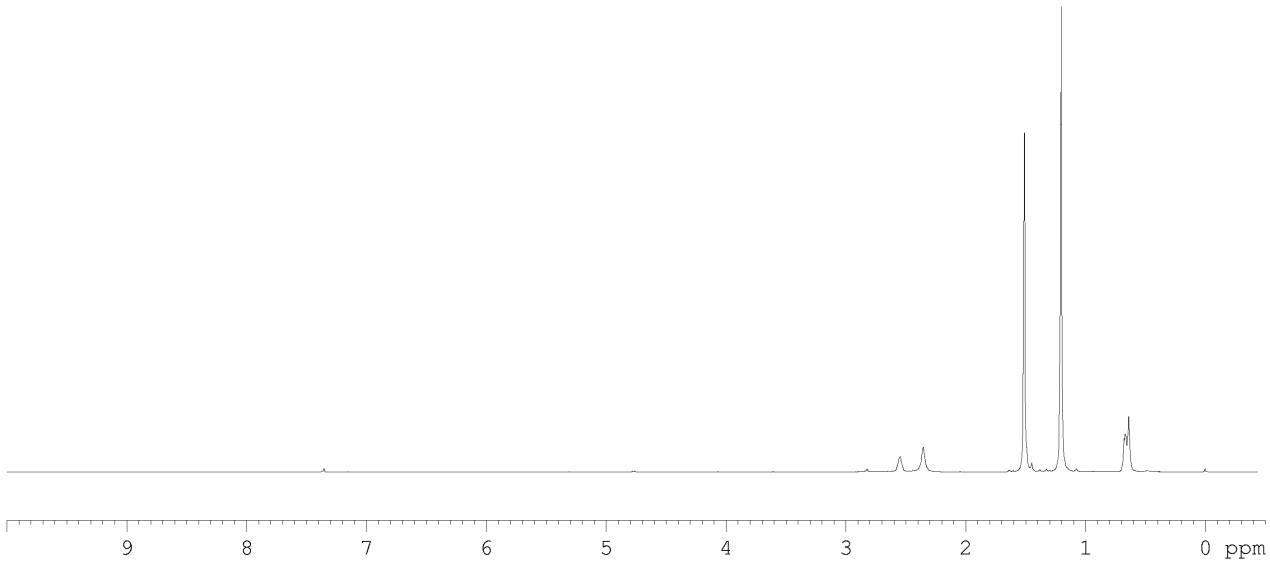
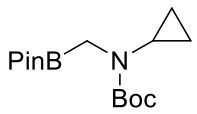
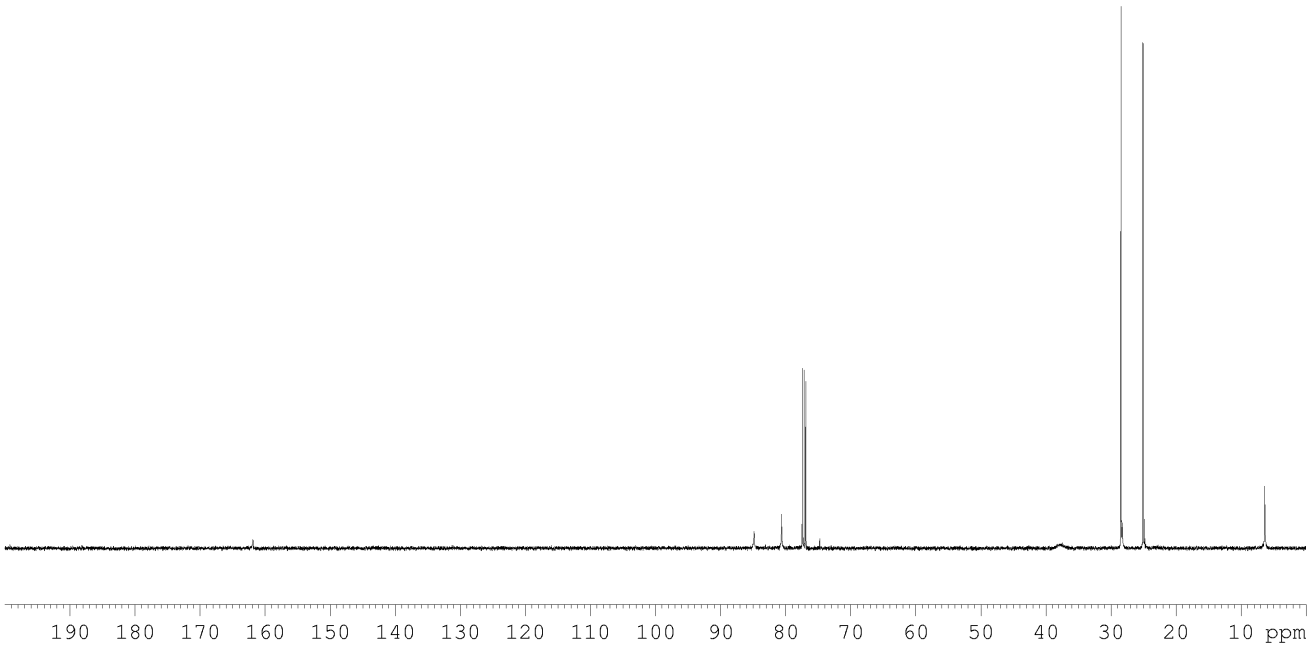


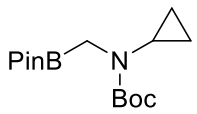
Figure A2.23 Infrared Spectrum

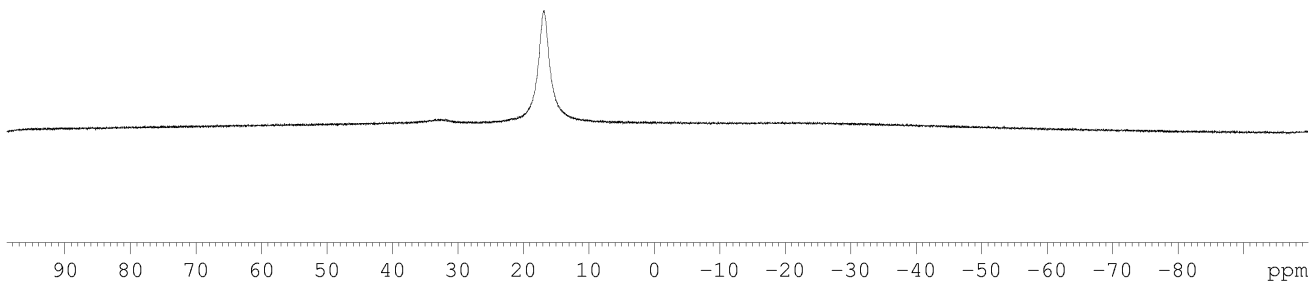

PinB
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


PinB
N
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 ppm

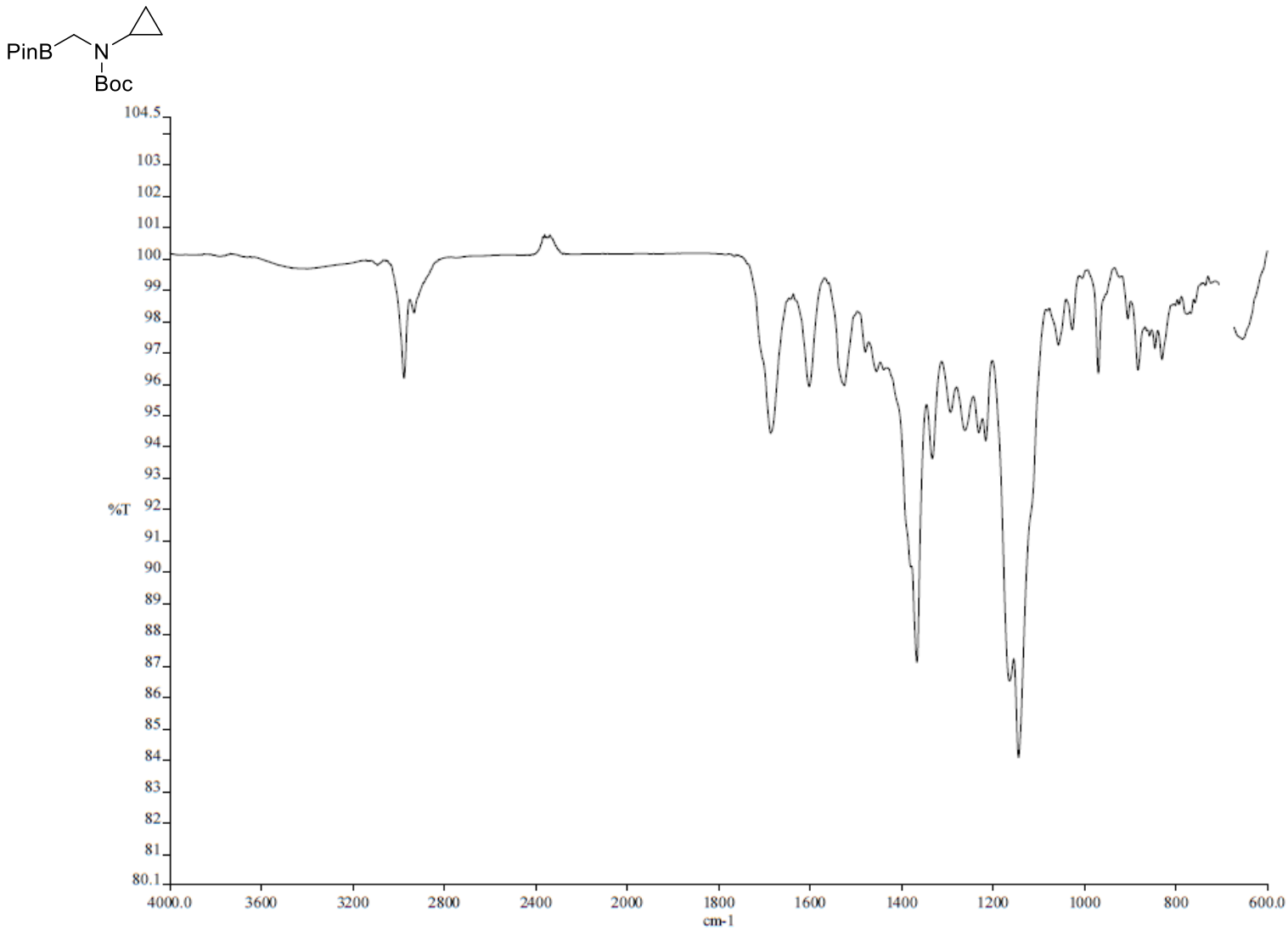
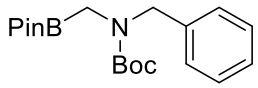
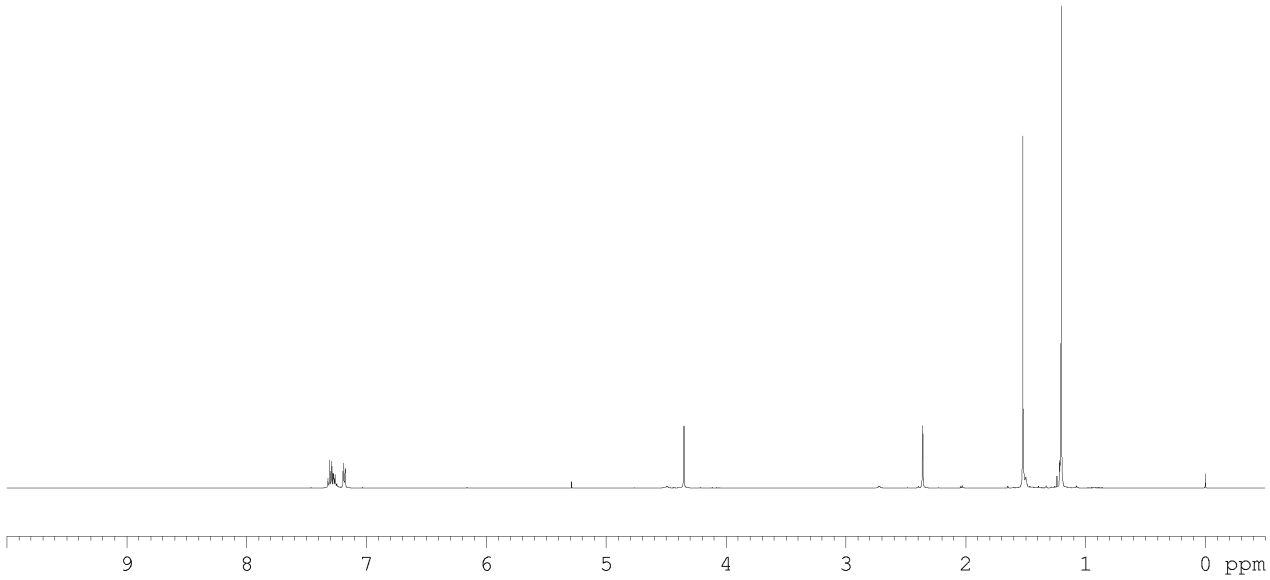
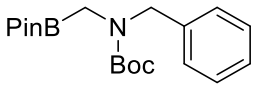
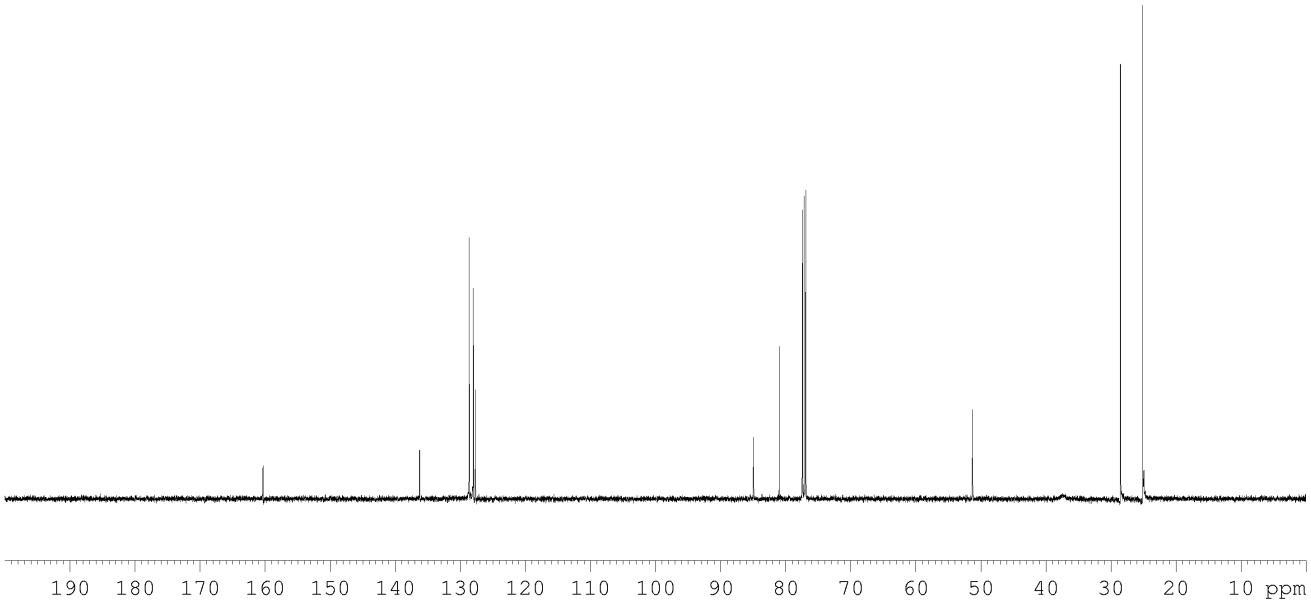


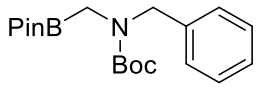
Figure A2.27 Infrared Spectrum

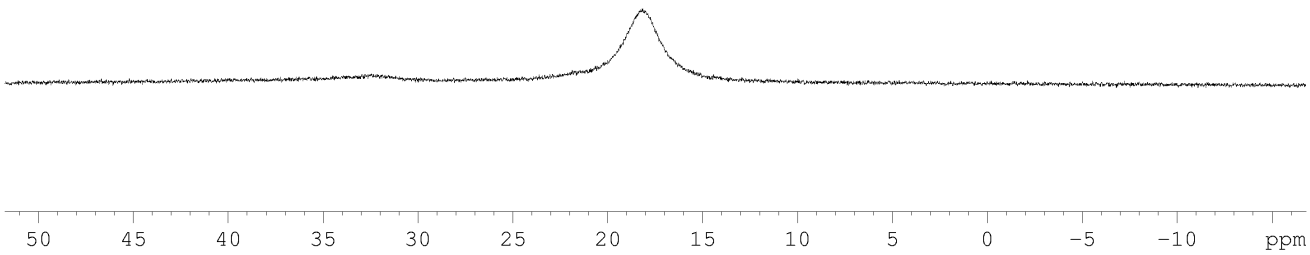

PinB
N
Boc

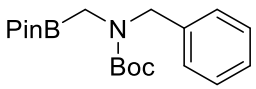

9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


PinB
N
Boc


50
45
40
35
30
25
20
15
10
5
0
−5
−10
ppm



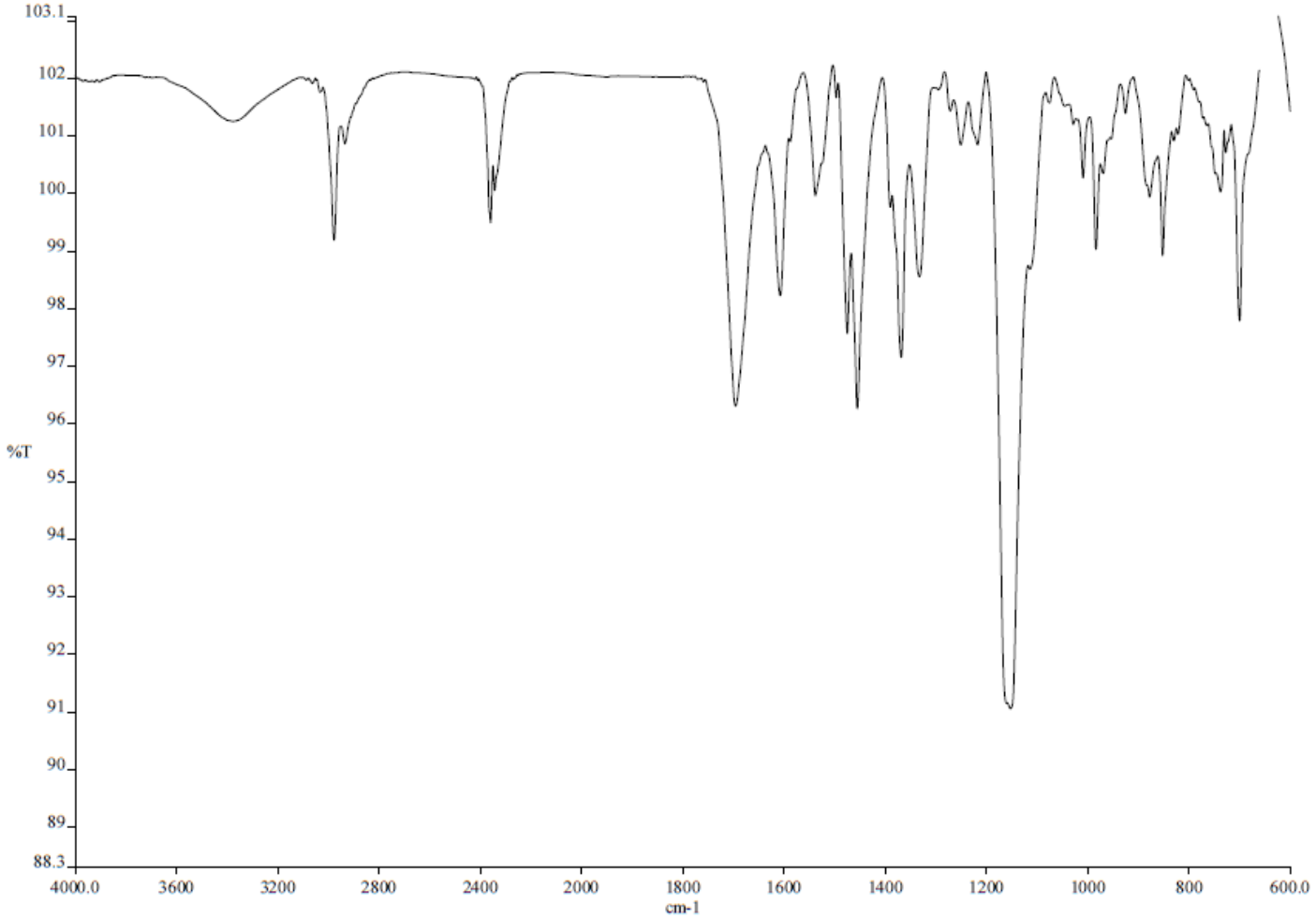
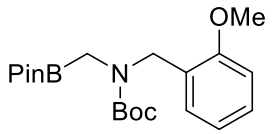
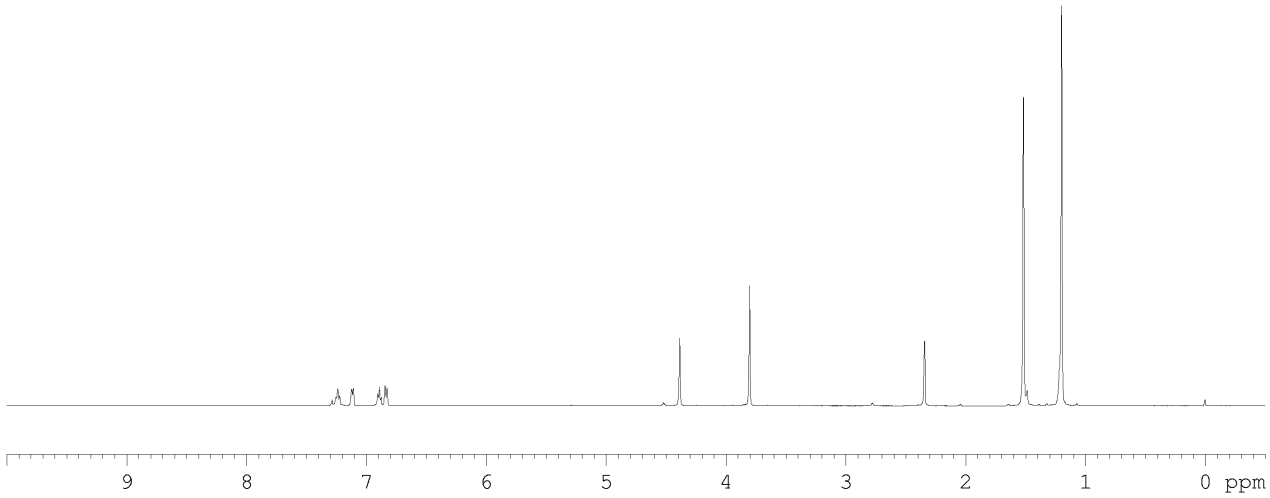
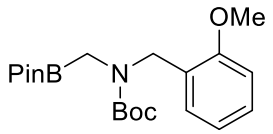


Figure A2.31 Infrared Spectrum


OMe
PinB
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm



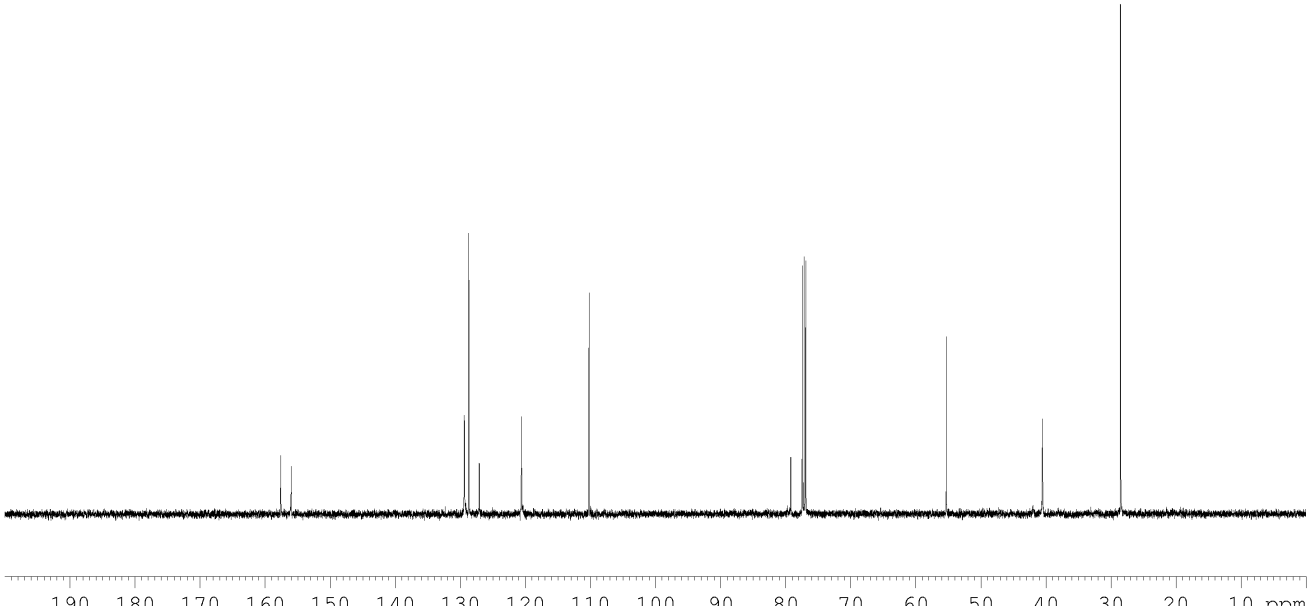
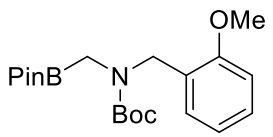
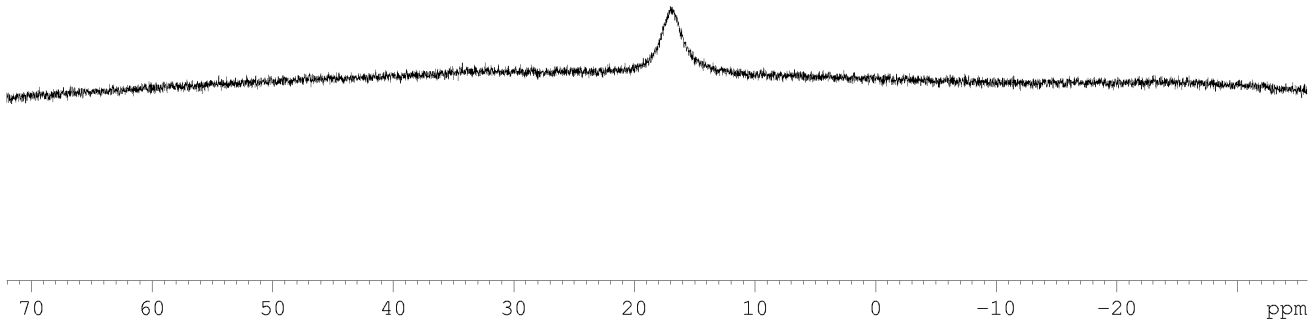


Figure A2.33 ^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum


OMe
PinB
N
Boc


70
60
50
40
30
20
10
0
−10
−20
ppm

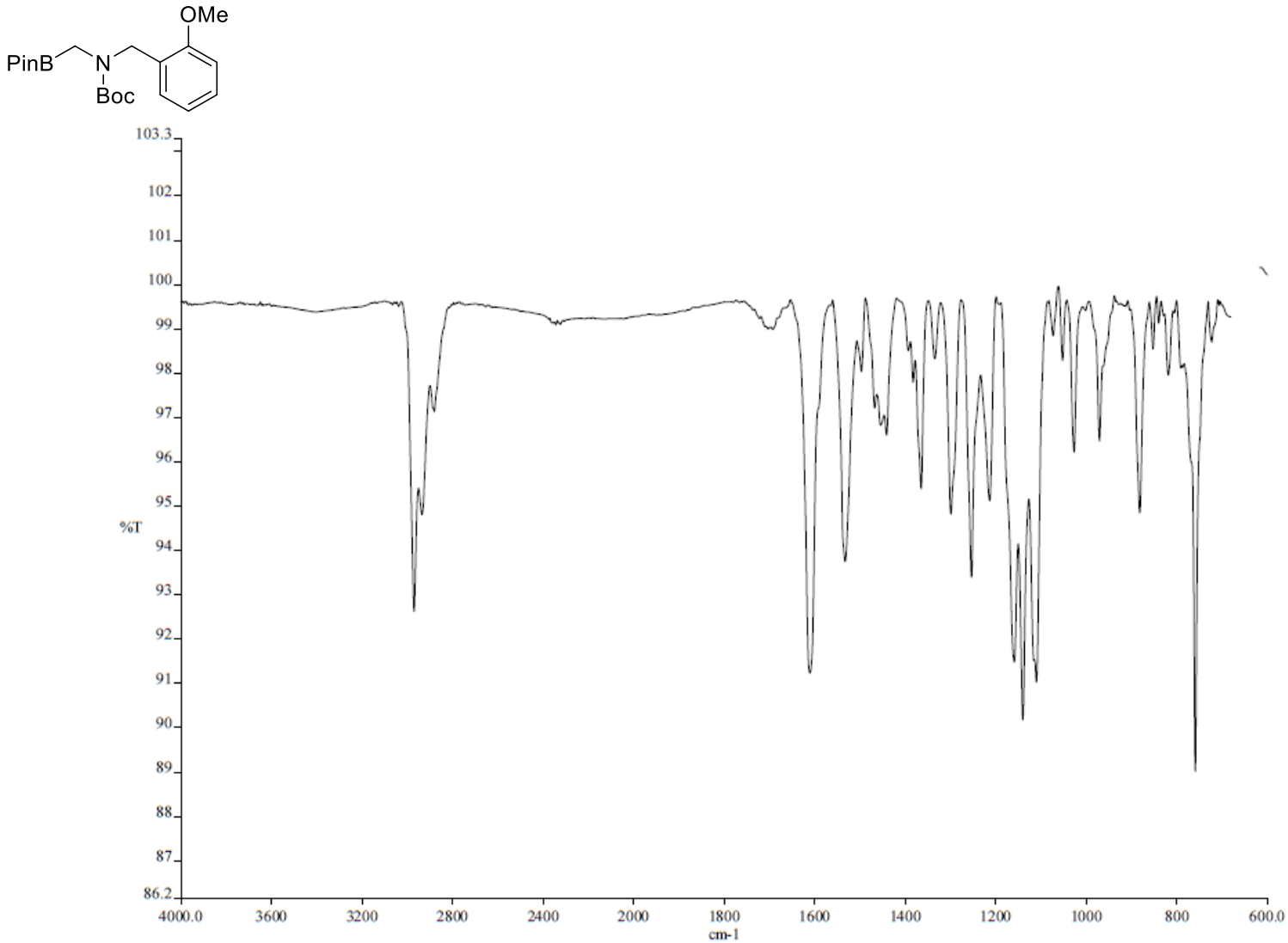
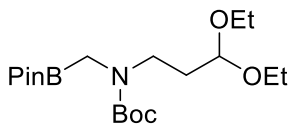
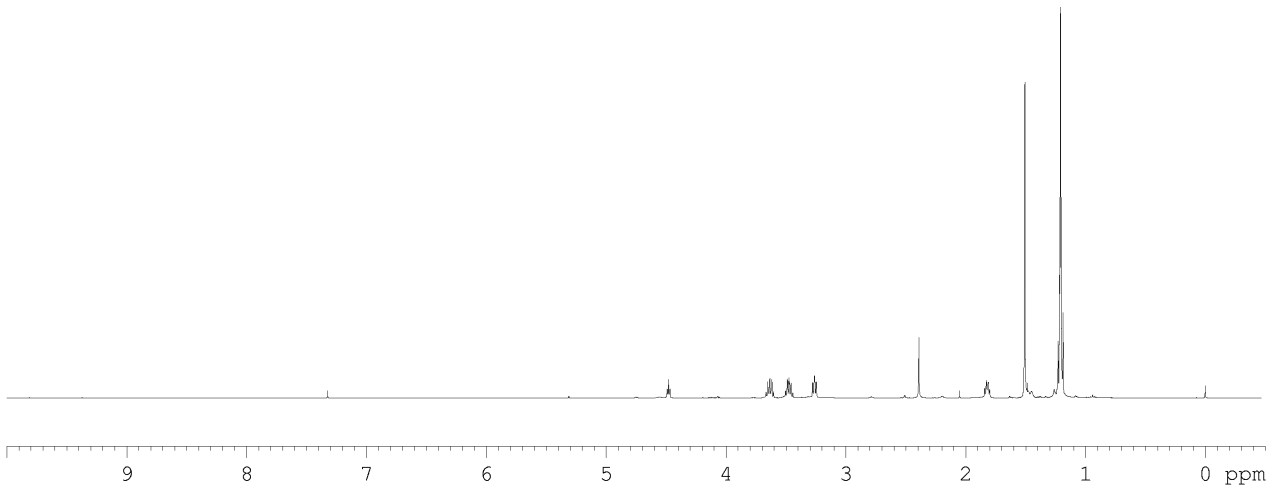
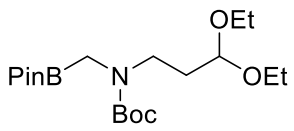
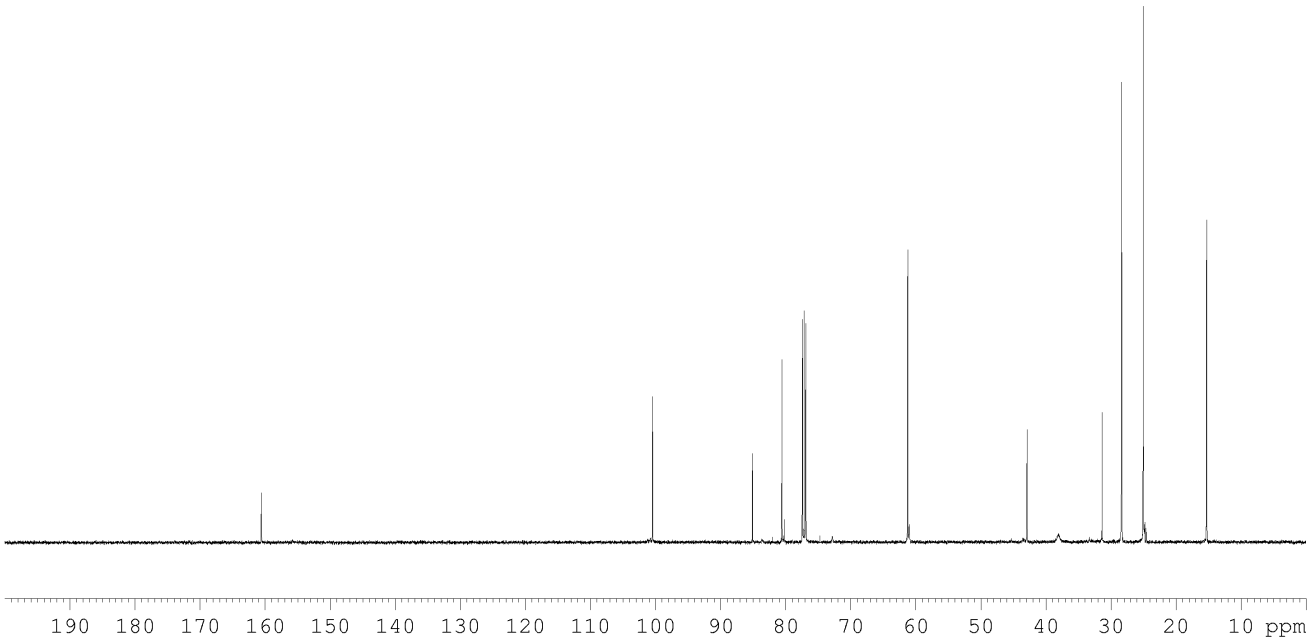


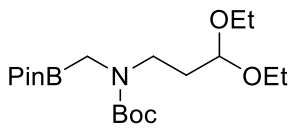
Figure A2.35 Infrared Spectrum

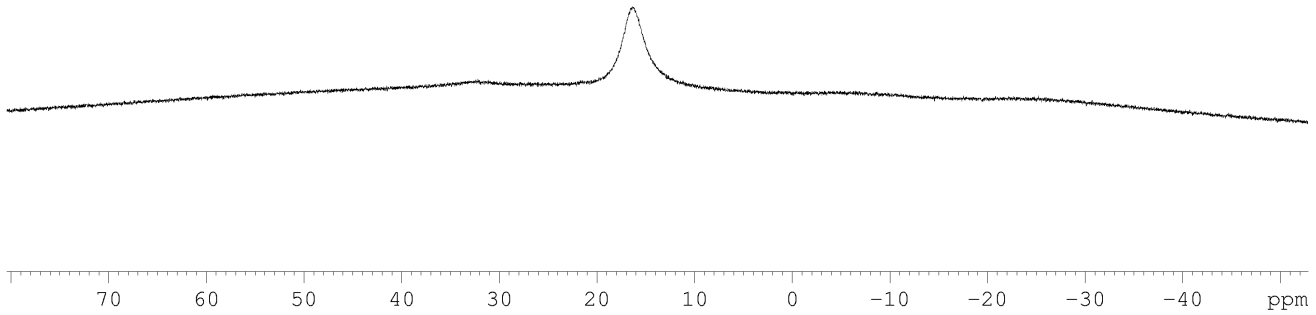

OEt
PinB
N
OEt
Boc

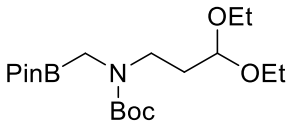

9
8
7
6
5
4
3
2
1
0 ppm


OEt
PinB
N
OEt
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OEt
PinB
N
OEt
Boc


70
60
50
40
30
20
10
0
−10
−20
−30
−40
ppm



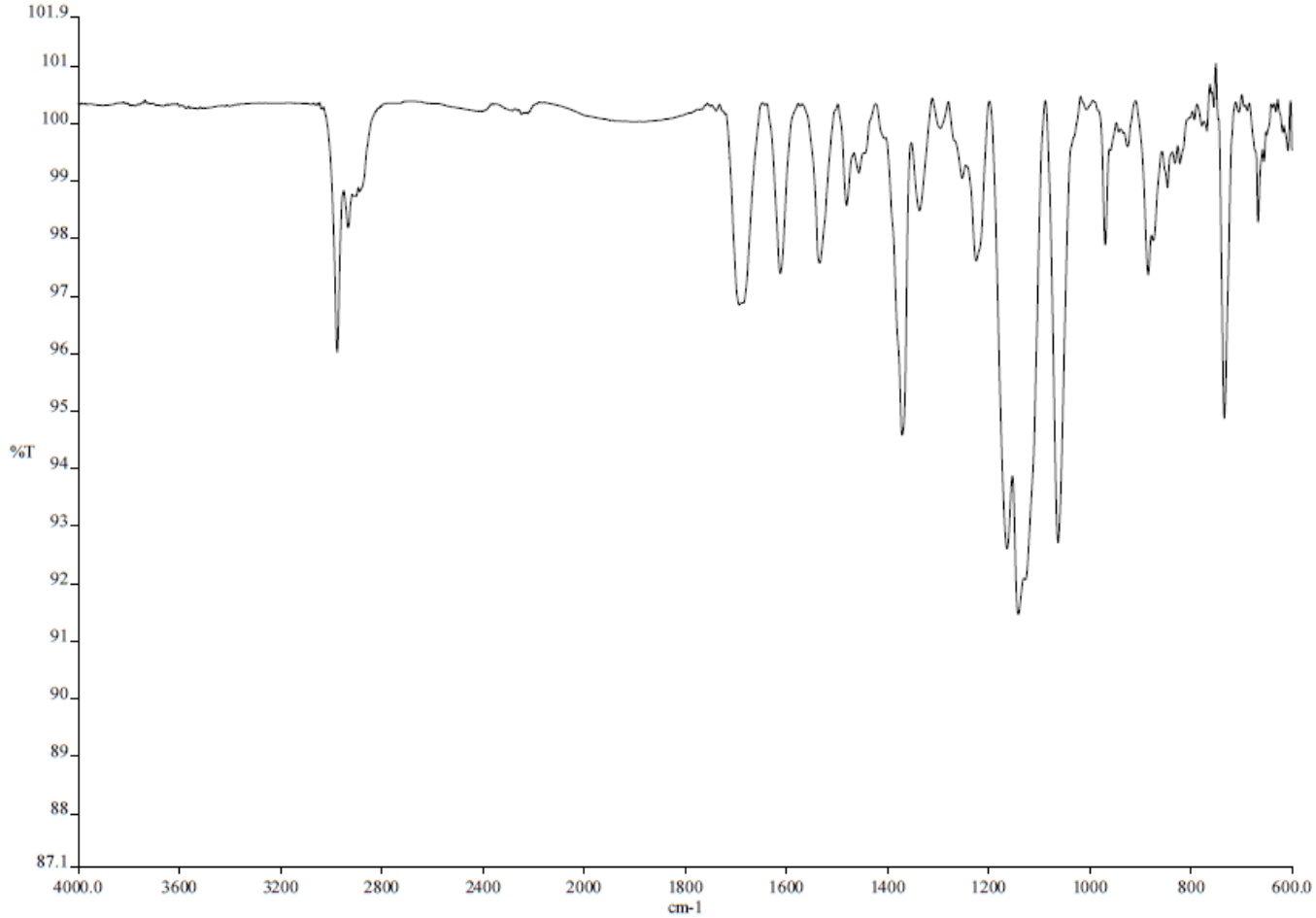
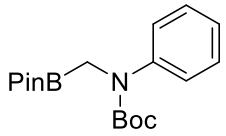
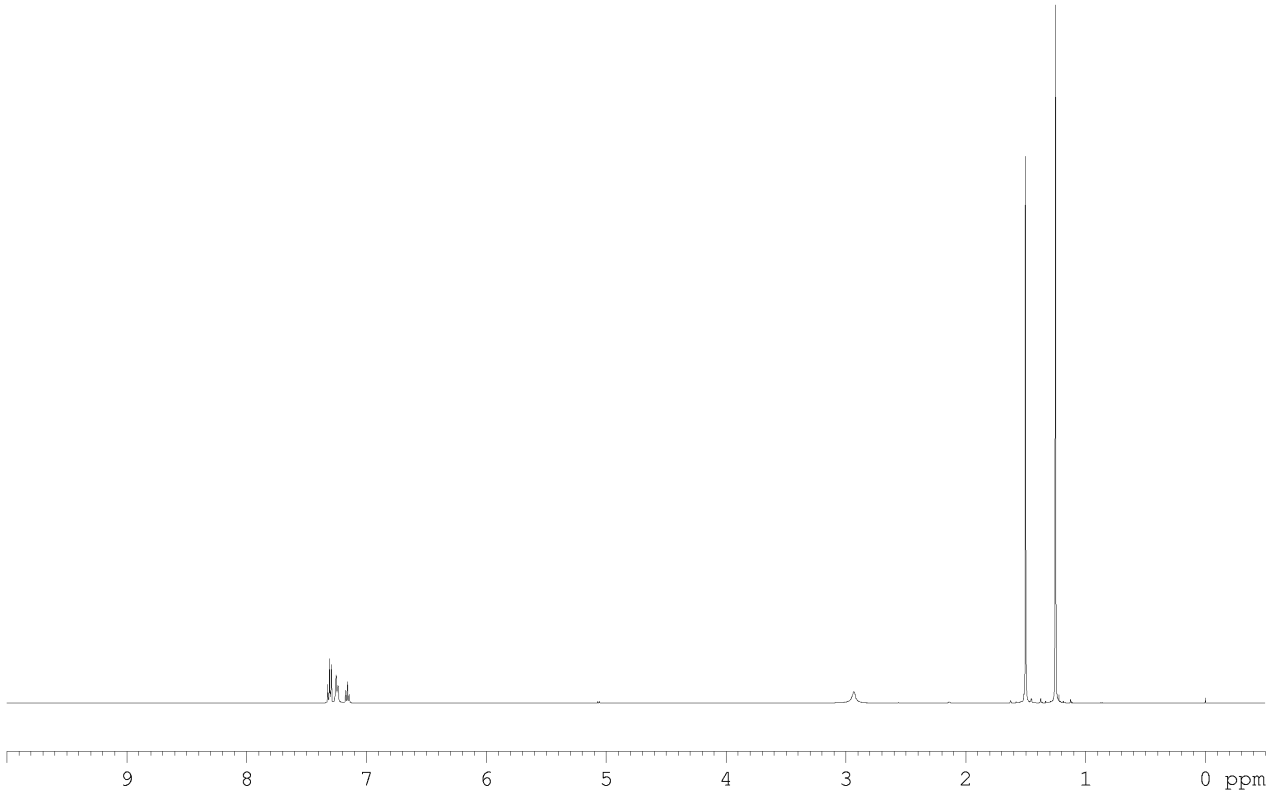
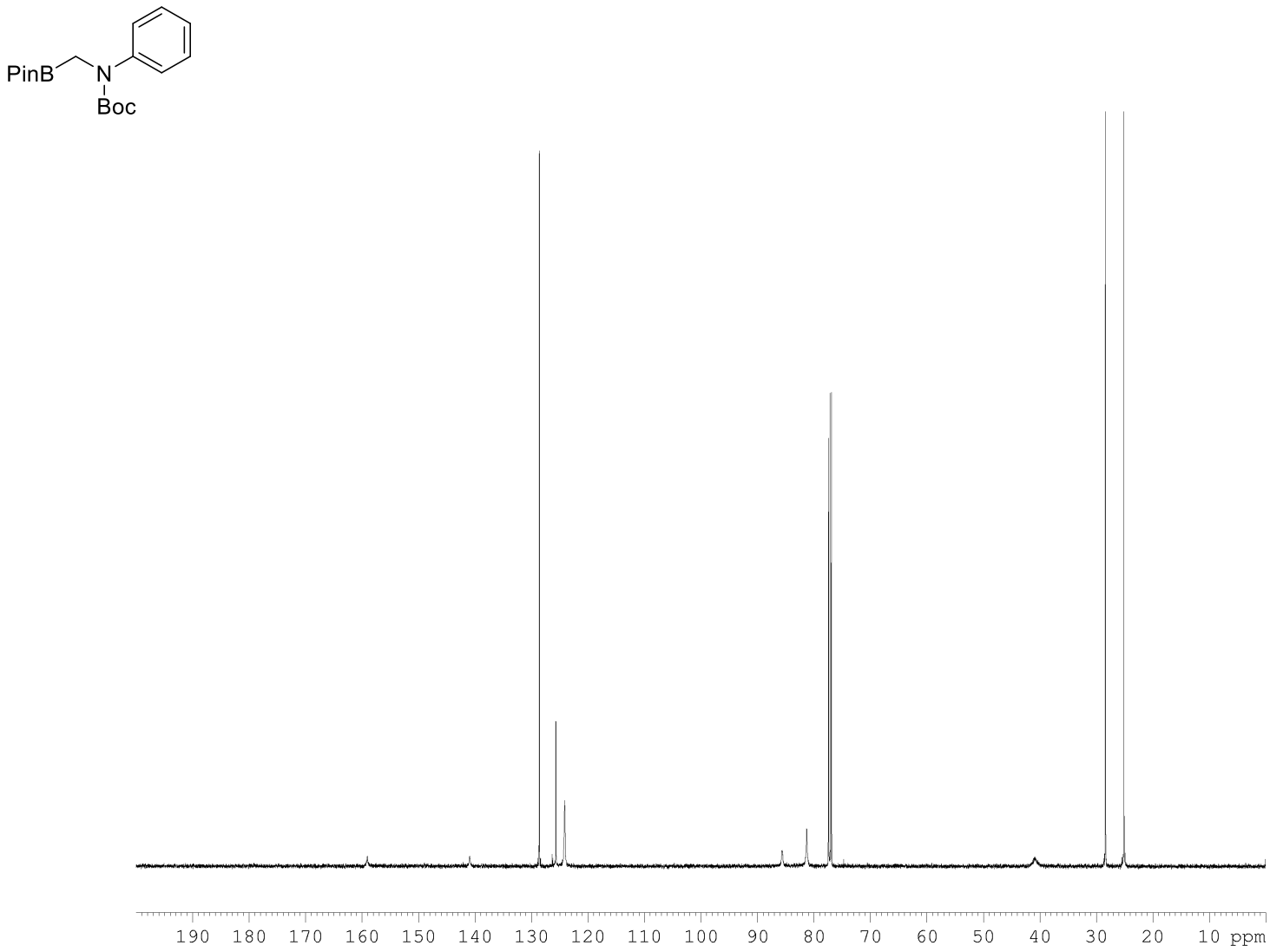
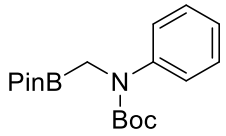


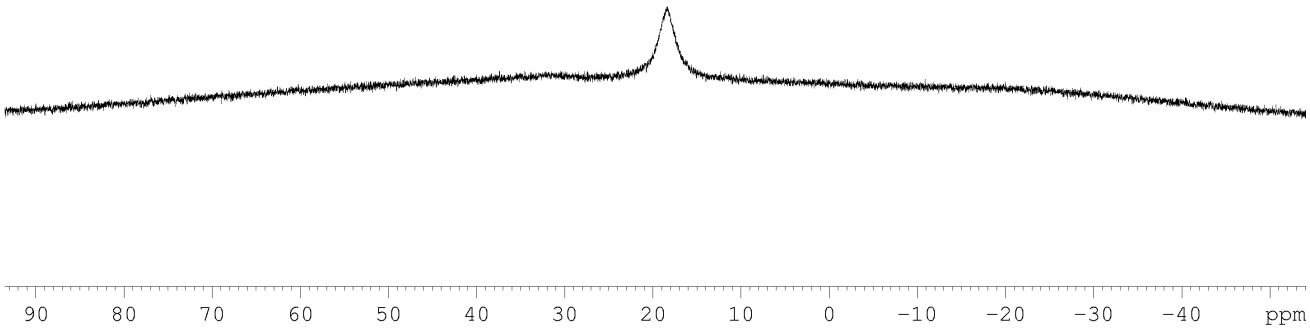
Figure A2.39 Infrared Spectrum


PinB
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


PinB
N
Boc
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


PinB
N
Boc


90
80
70
60
50
40
30
20
10
0
−10
−20
−30
−40
ppm

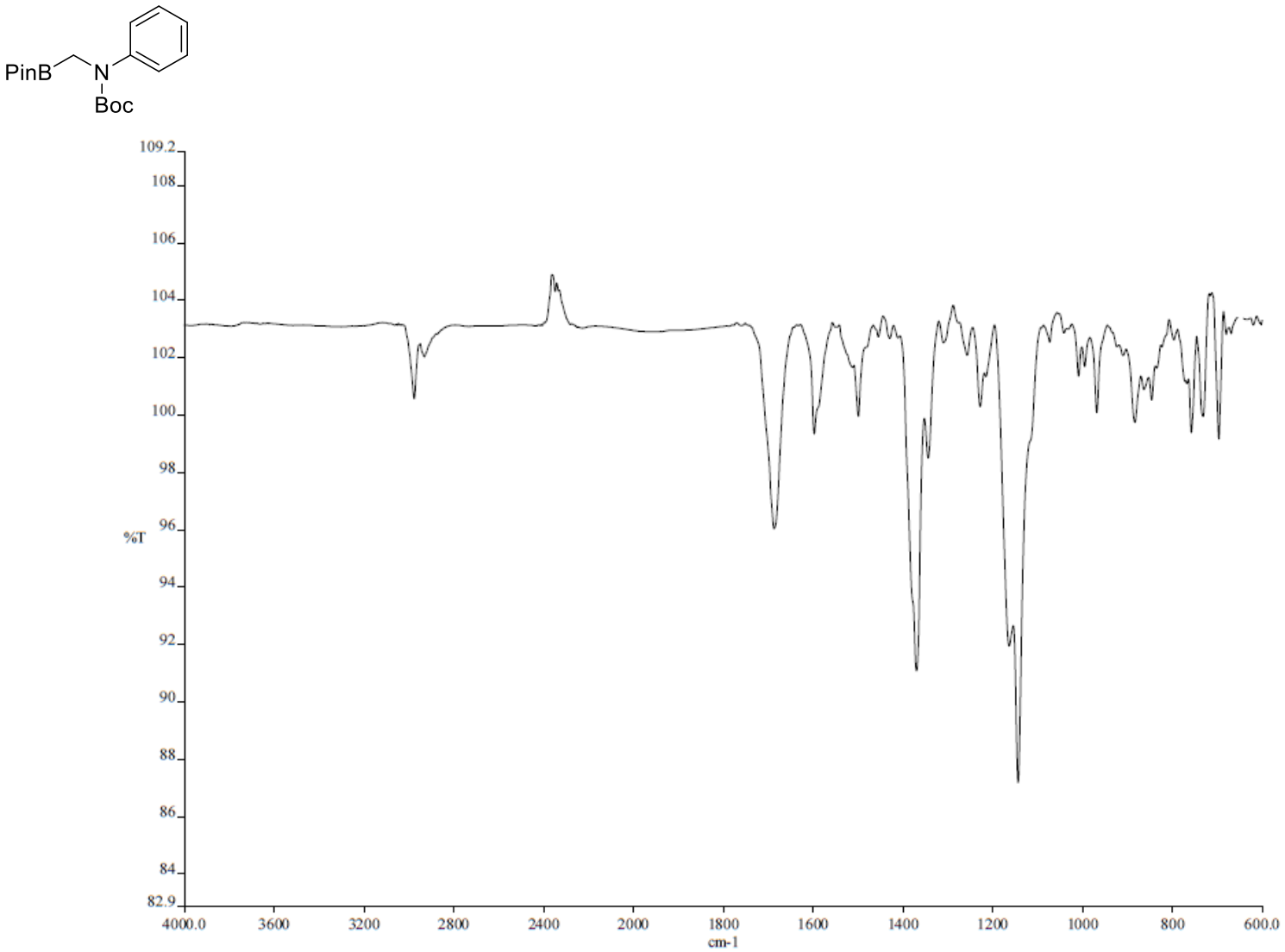
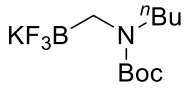
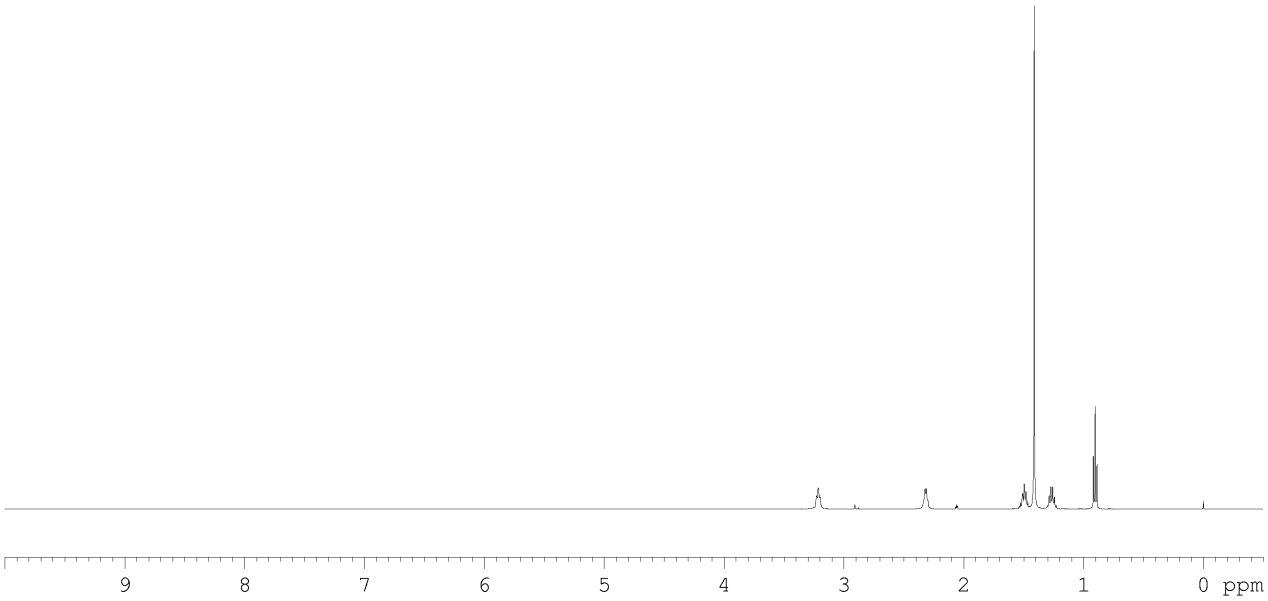
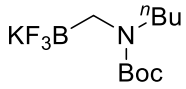
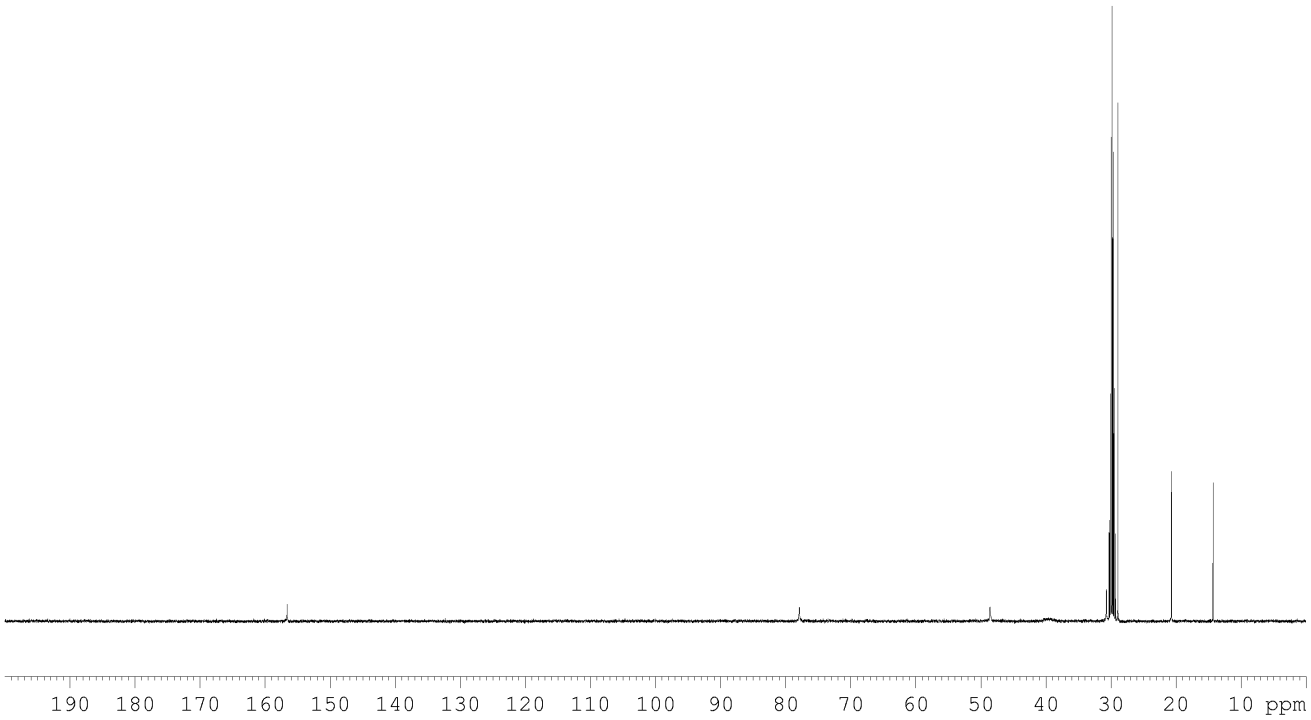


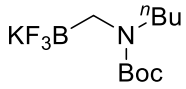
Figure A2.43 Infrared Spectrum

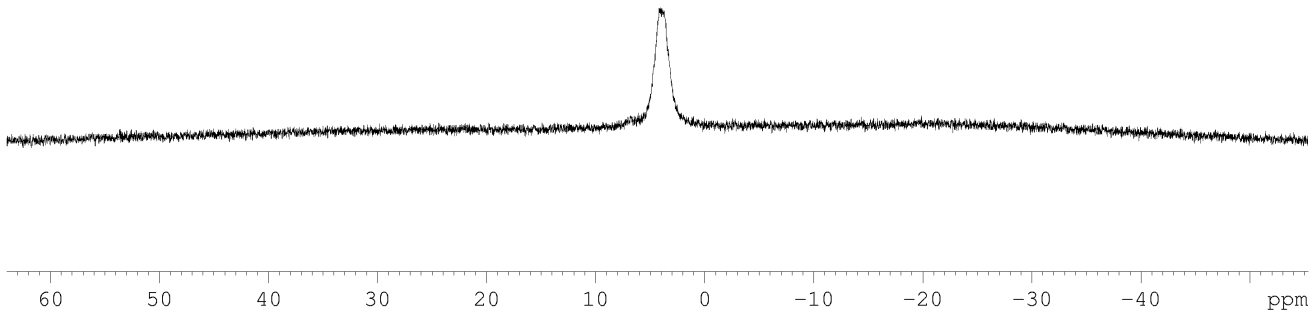

KF3B
N
nBu
Boc

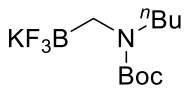

9
8
7
6
5
4
3
2
1
0 ppm


KF3B
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


KF3B
N
nBu
Boc


60
50
40
30
20
10
0
−10
−20
−30
−40
ppm



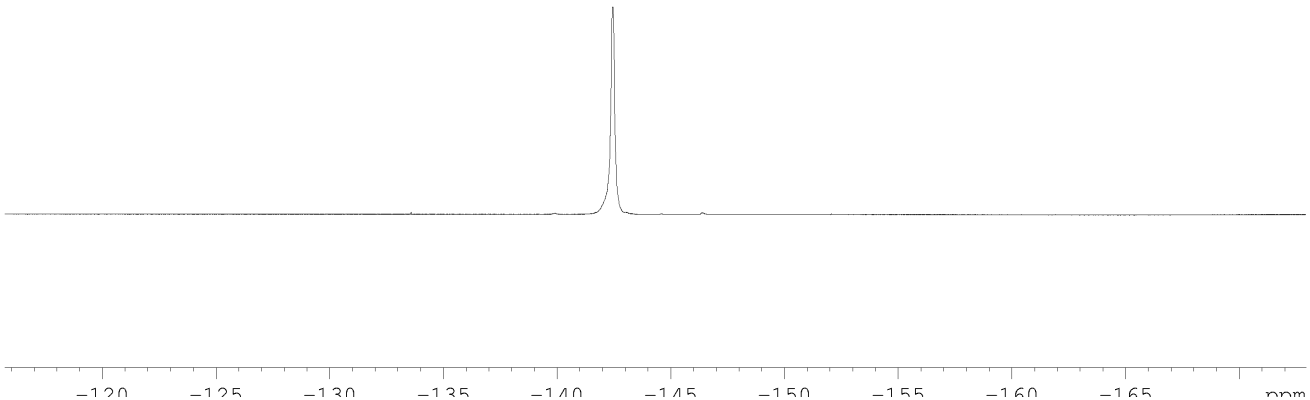
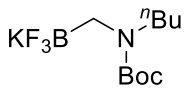


Figure A2.47 ^{19}F NMR (470.8 MHz, acetone-d_6) Spectrum



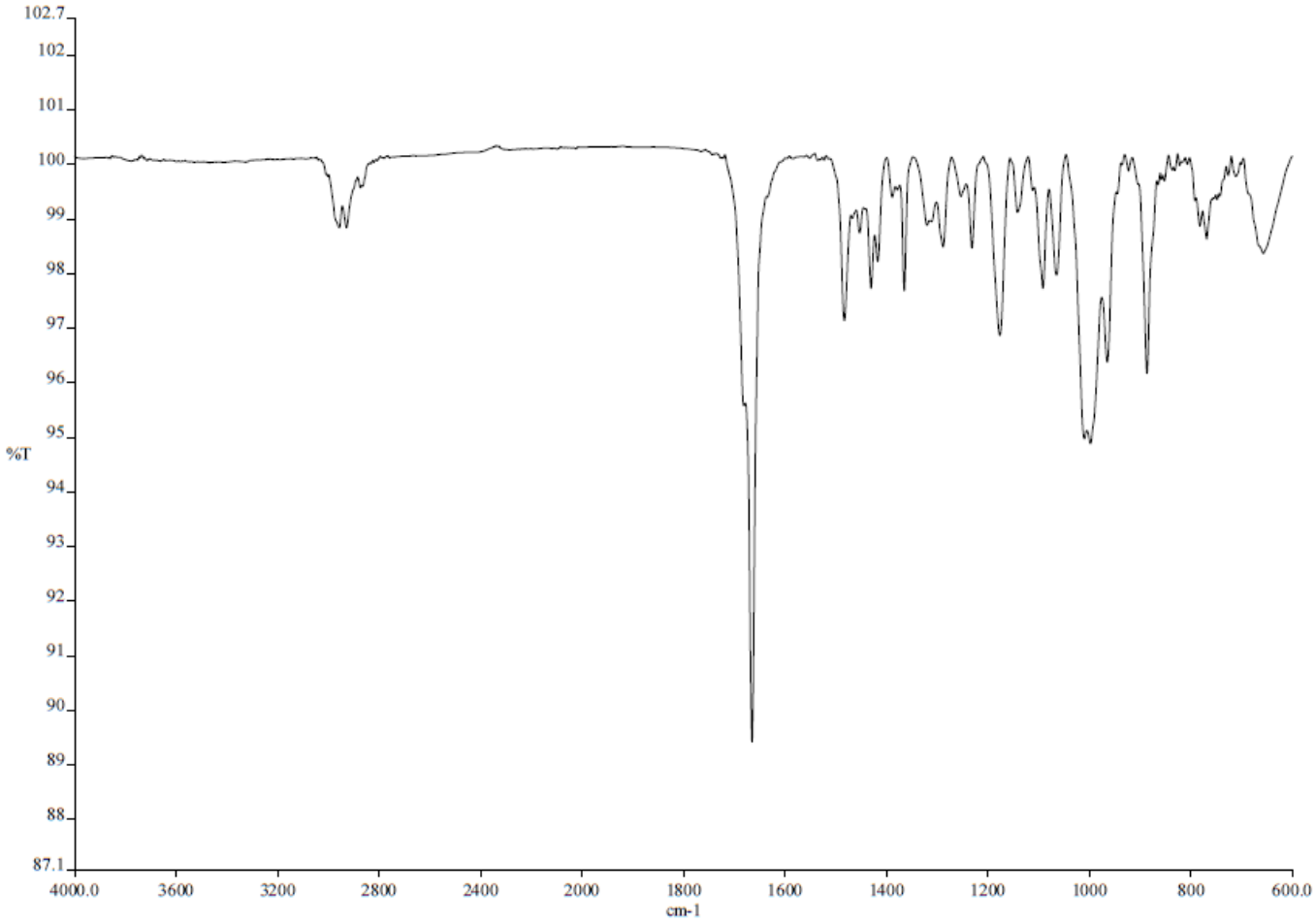
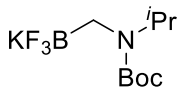
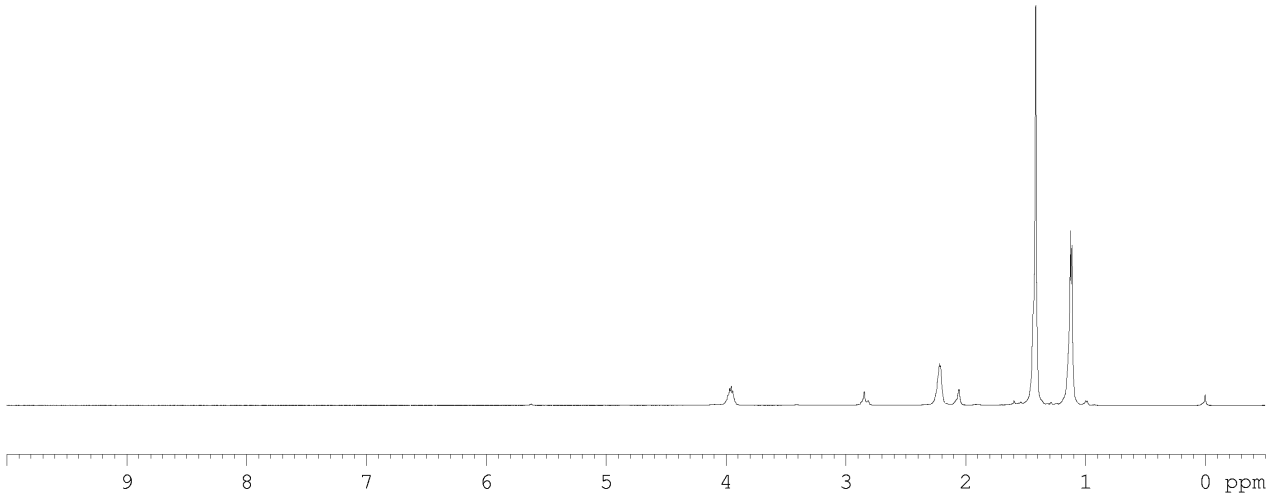
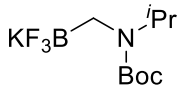
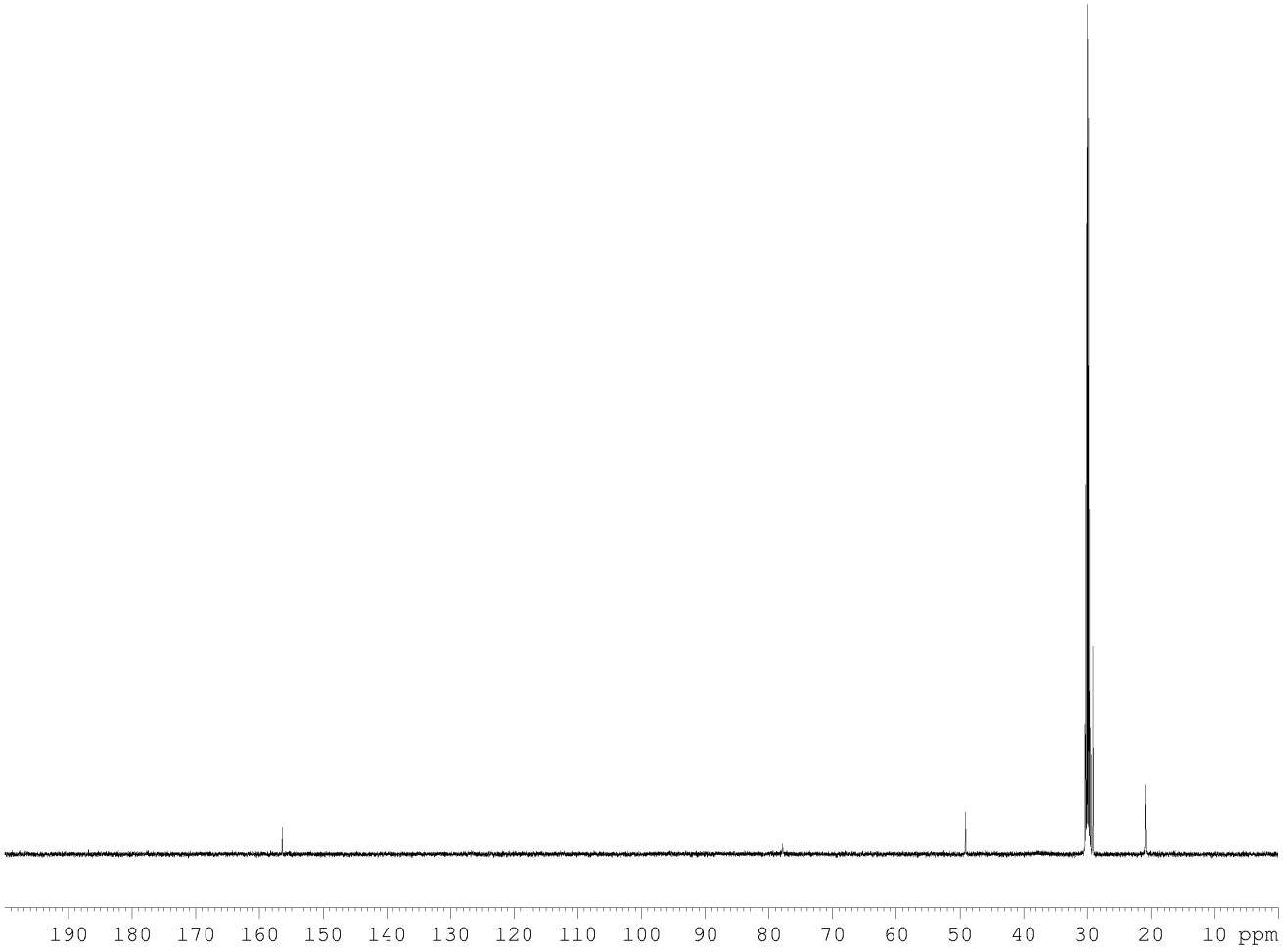


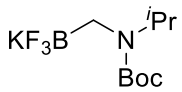
Figure A2.48 Infrared Spectrum

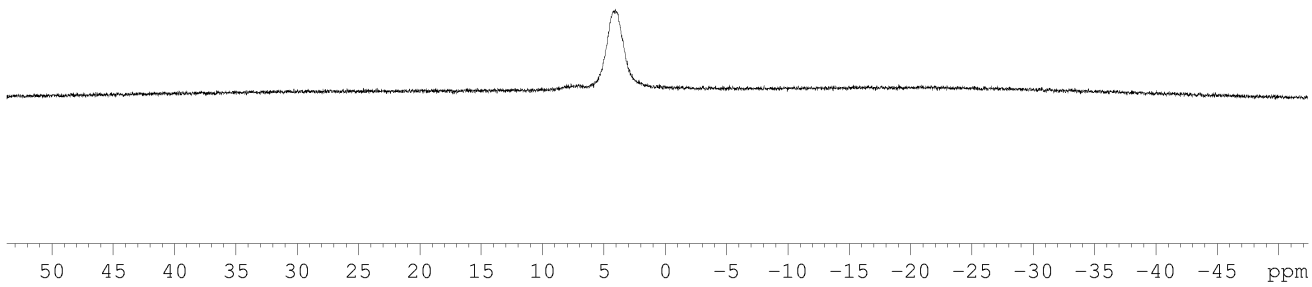

KF3B
N
iPr
Boc

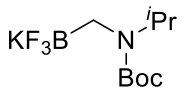

9
8
7
6
5
4
3
2
1
0 ppm

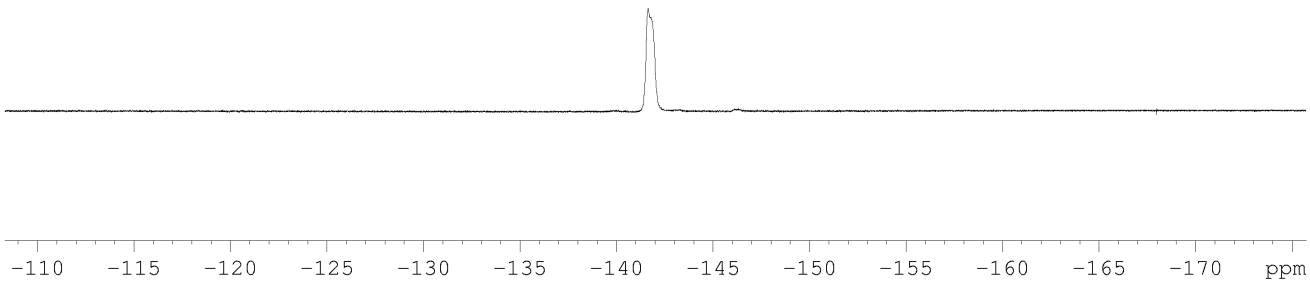

KF3B
N
iPr
Boc

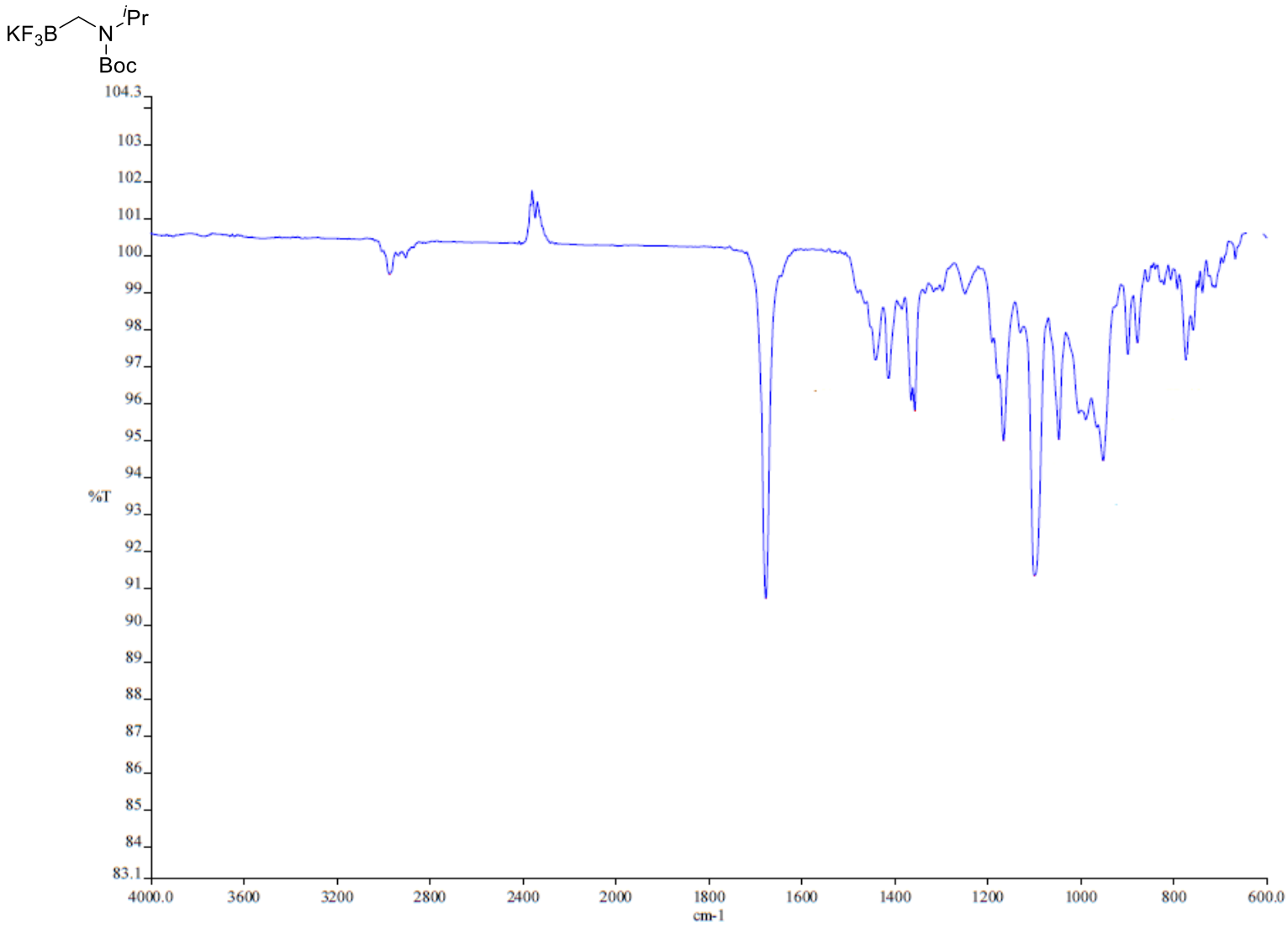

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

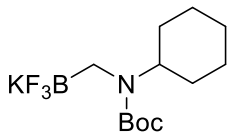

KF3B
N
iPr
Boc

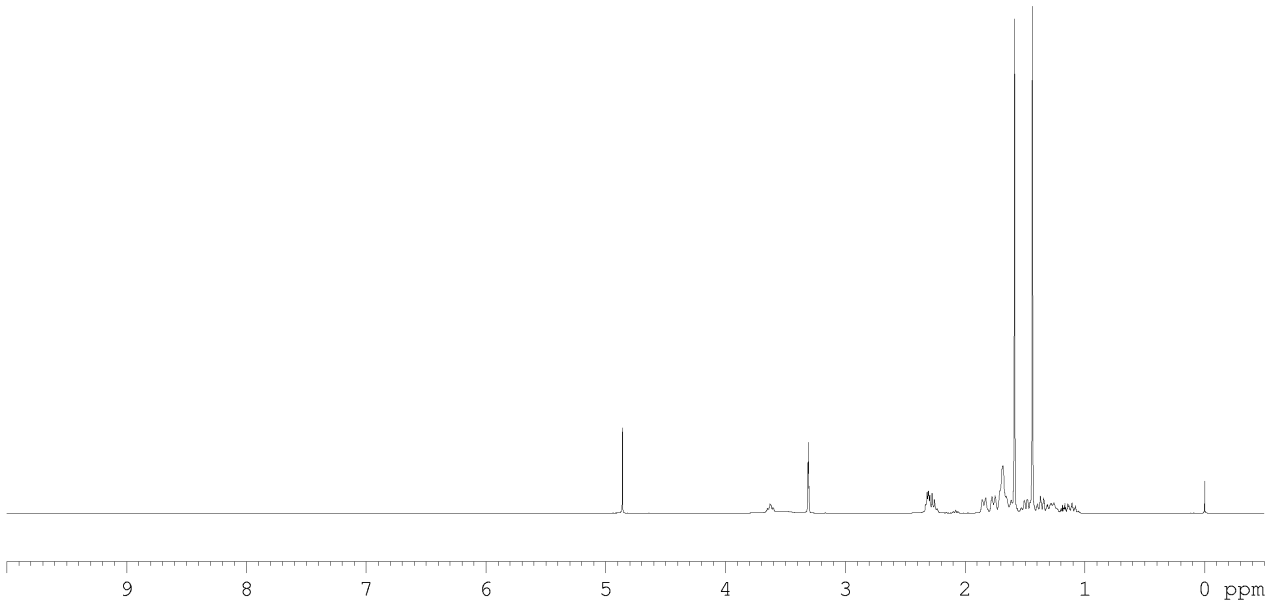

50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 ppm

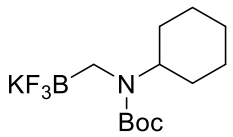

KF3B
N
iPr
Boc

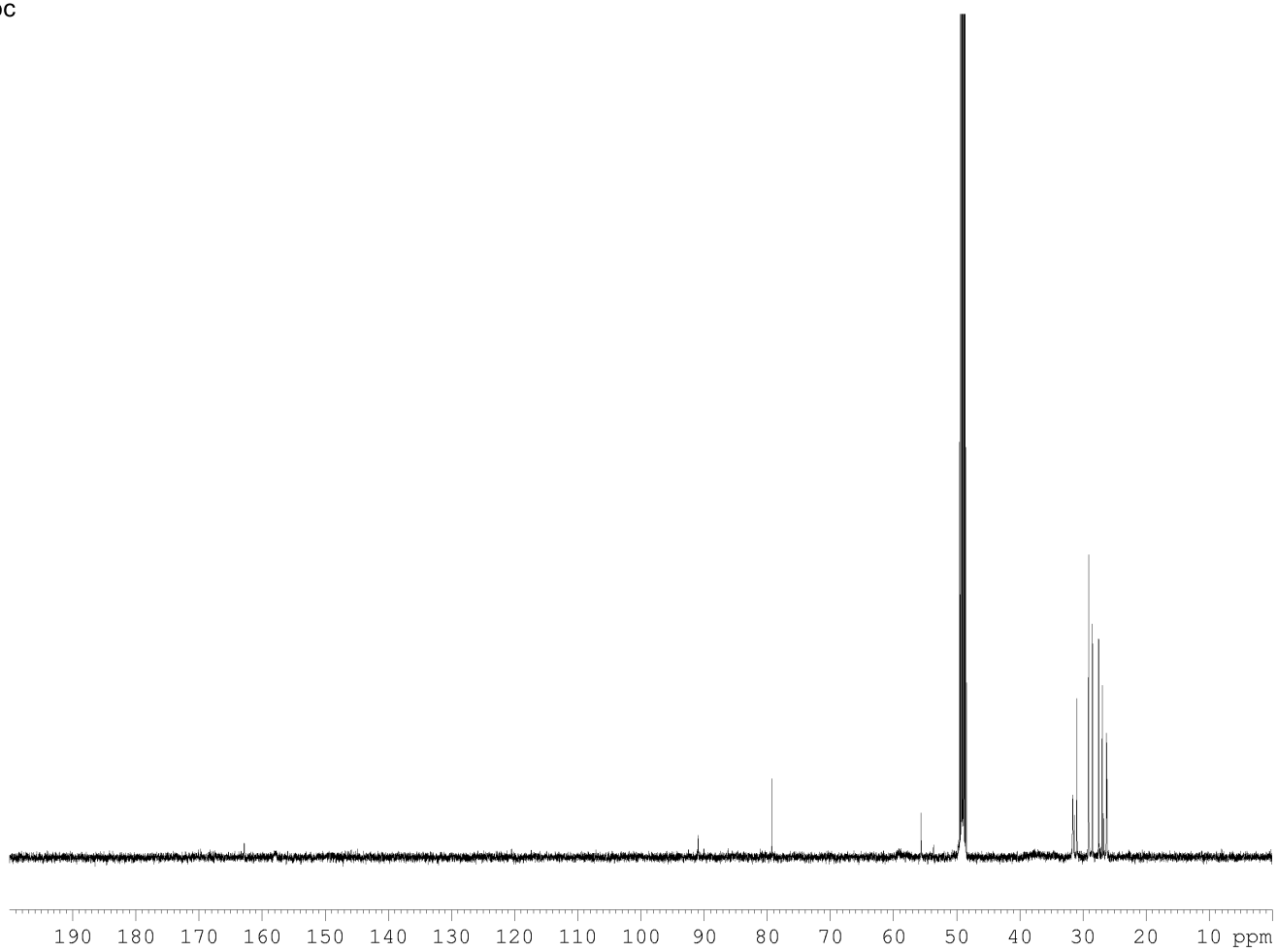

−110
−115
−120
−125
−130
−135
−140
−145
−150
−155
−160
−165
−170
ppm

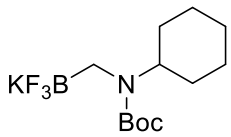

KF3B
N
iPr
Boc
104.3
103
102
101
100
99
98
97
96
95
94
%T
93
92
91
90
89
88
87
86
85
84
83.1
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

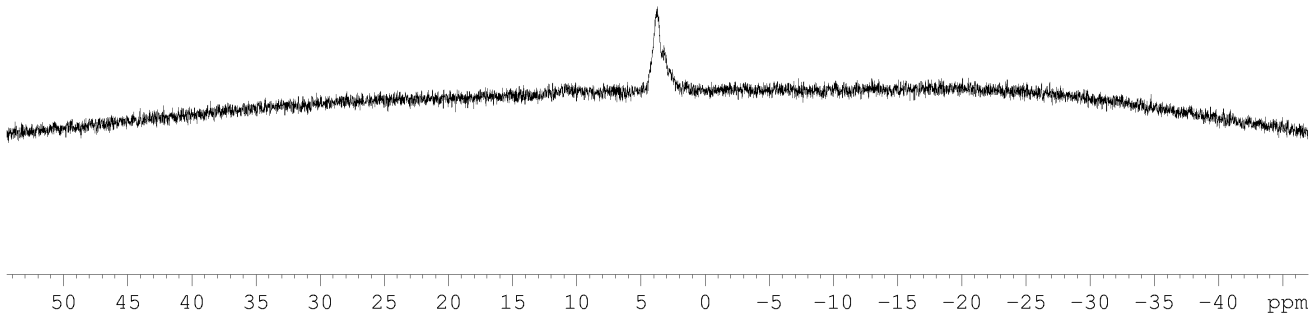

KF3B
N
Boc

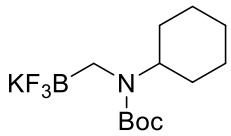

9
8
7
6
5
4
3
2
1
0 ppm

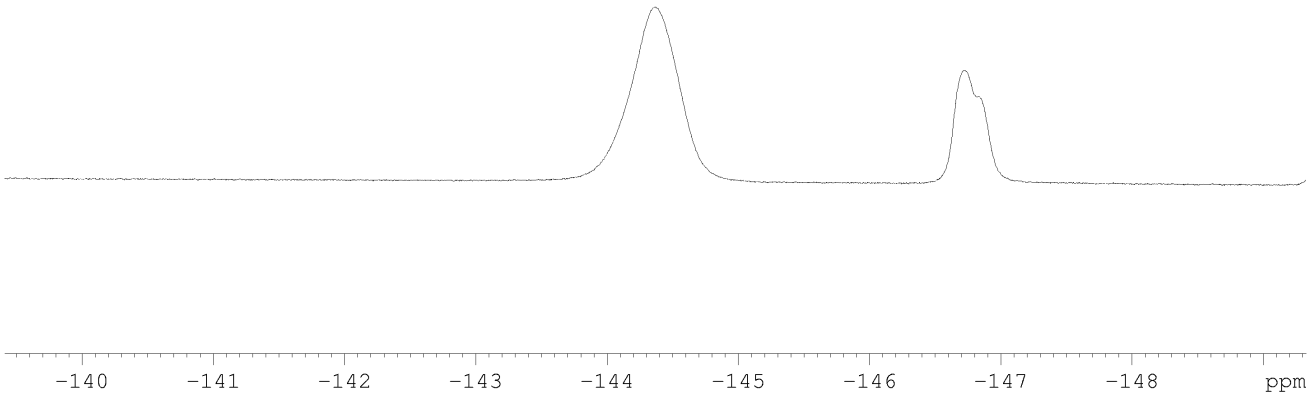

KF3B
N
Boc

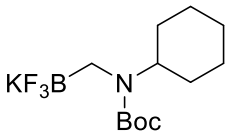

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


KF3B
N
Boc


50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 ppm


KF3B
N
Boc


−140
−141
−142
−143
−144
−145
−146
−147
−148
ppm



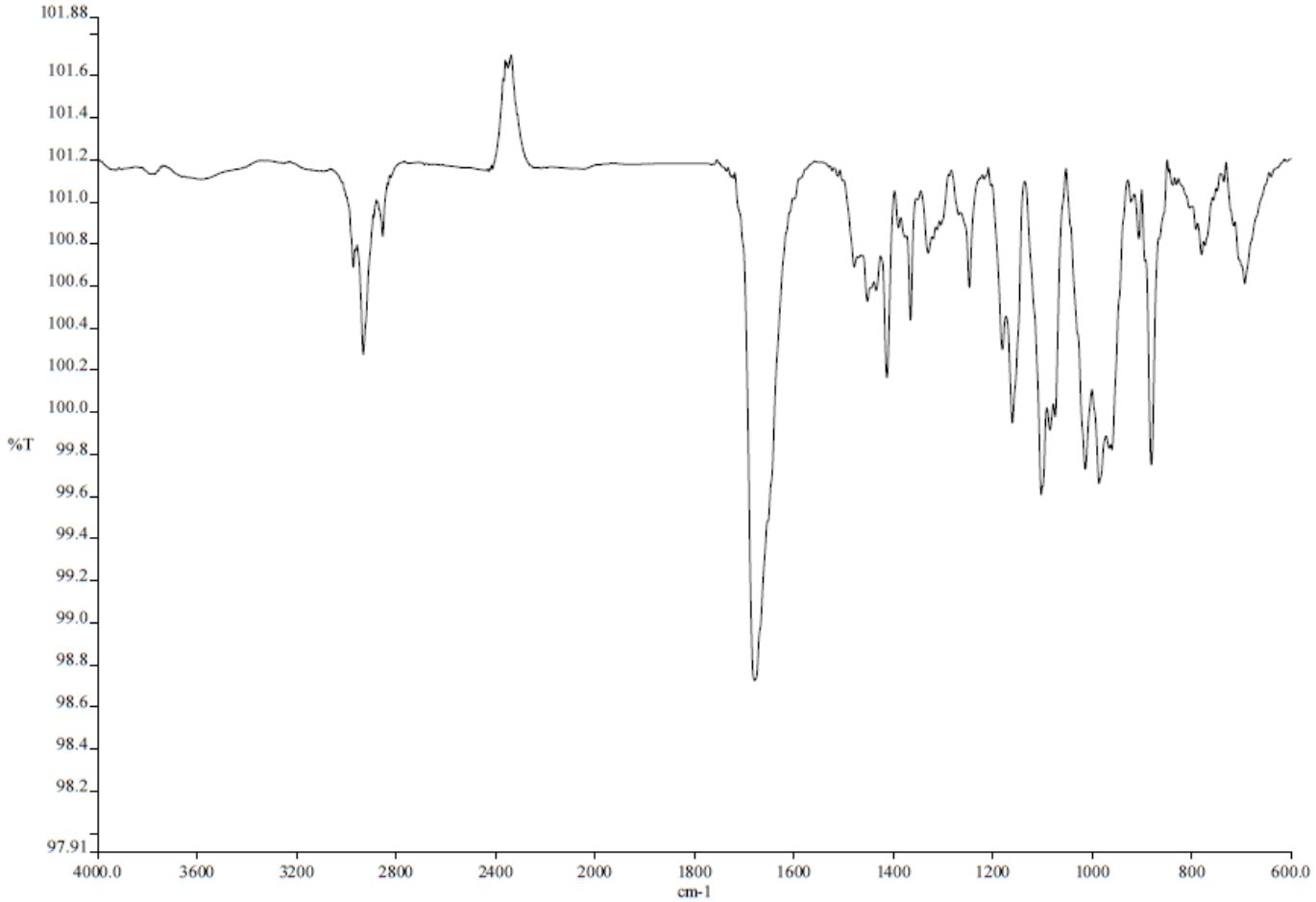
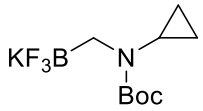
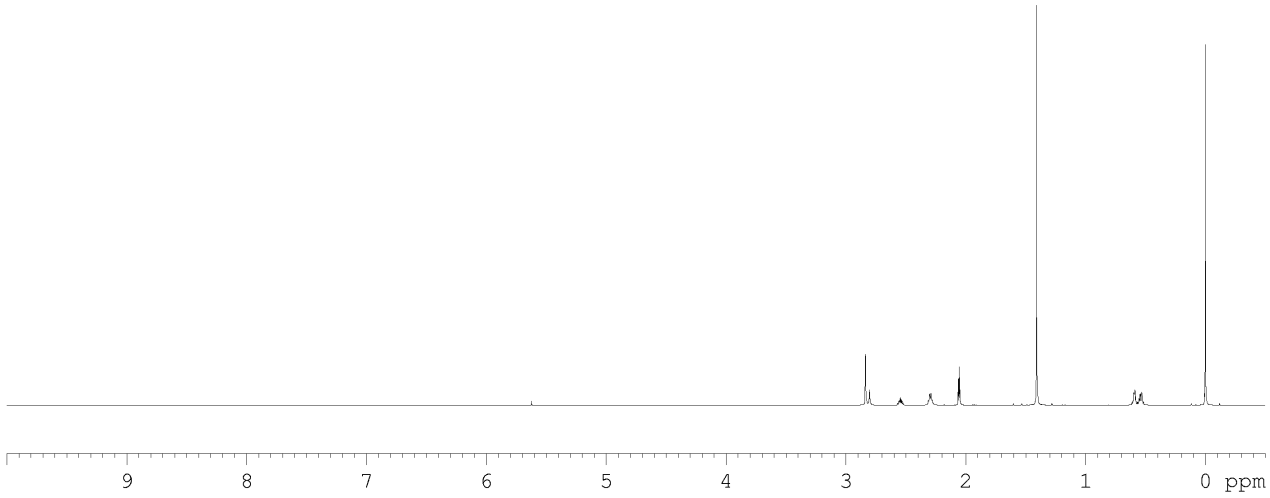
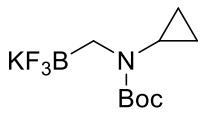
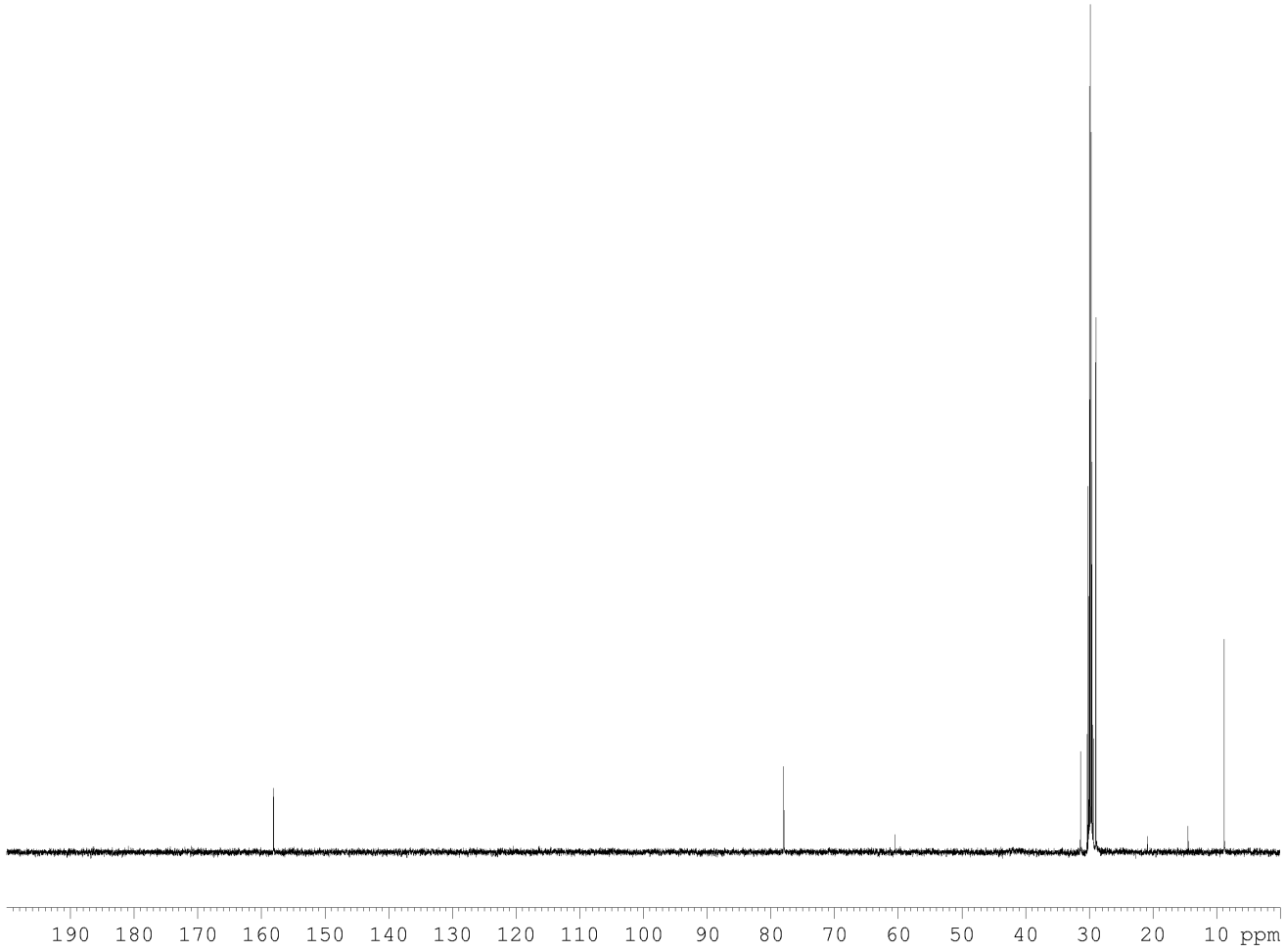


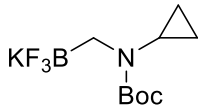
Figure A2.58 Infrared Spectrum


KF3B
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


KF3B
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



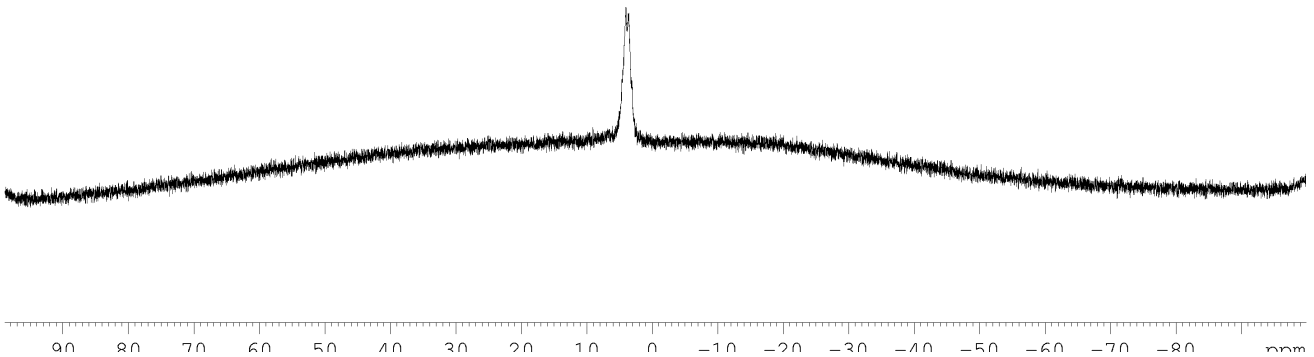
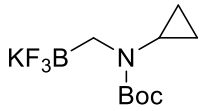
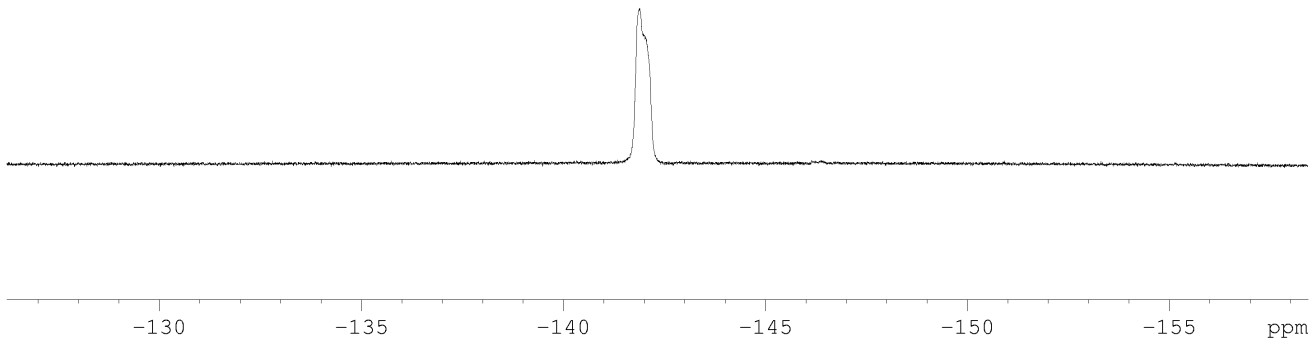


Figure A2.61 ^{11}B NMR (128.4 MHz, acetone-d_6) Spectrum


KF3B
N
Boc


−130
−135
−140
−145
−150
−155
ppm

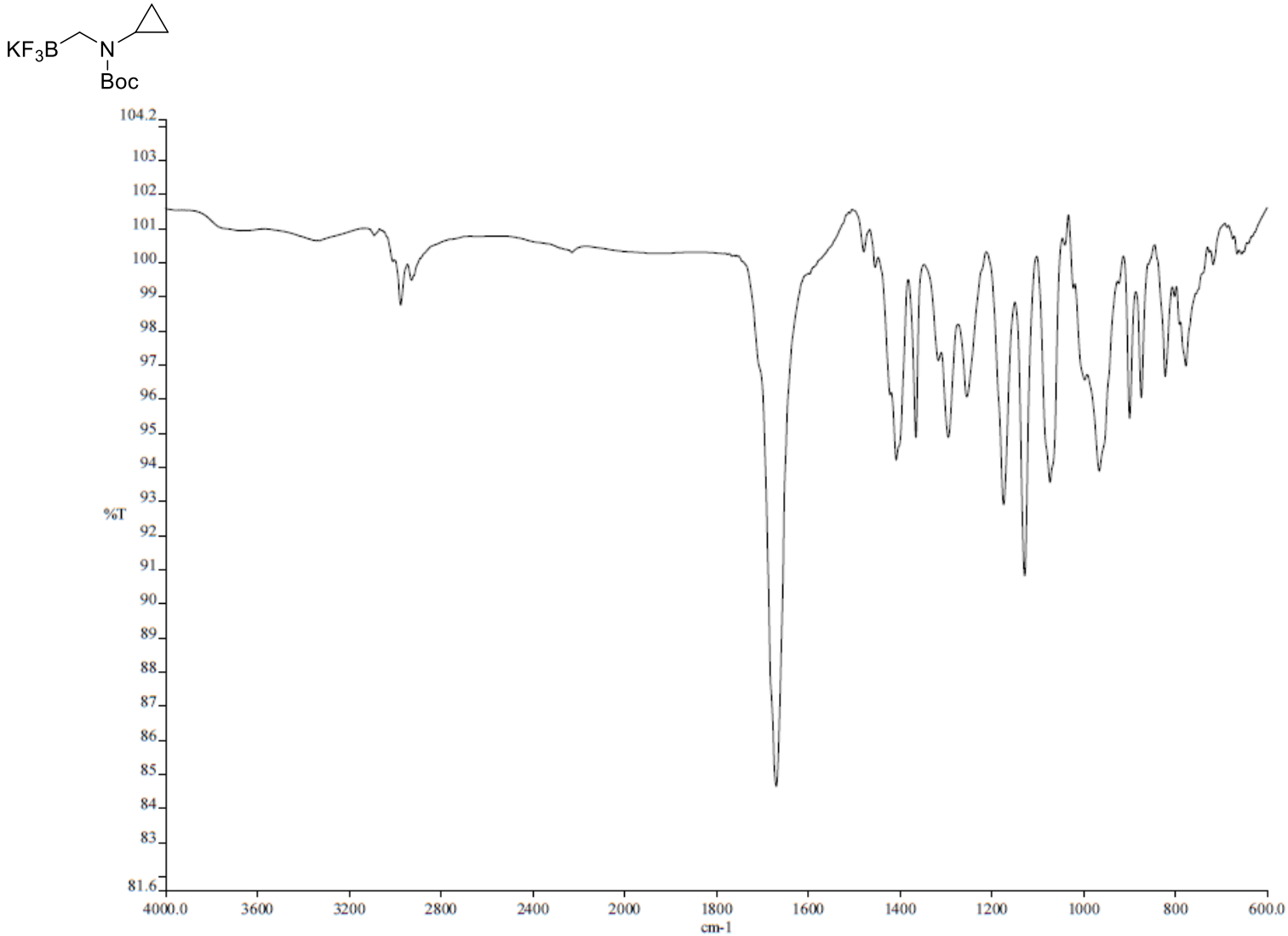
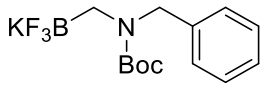
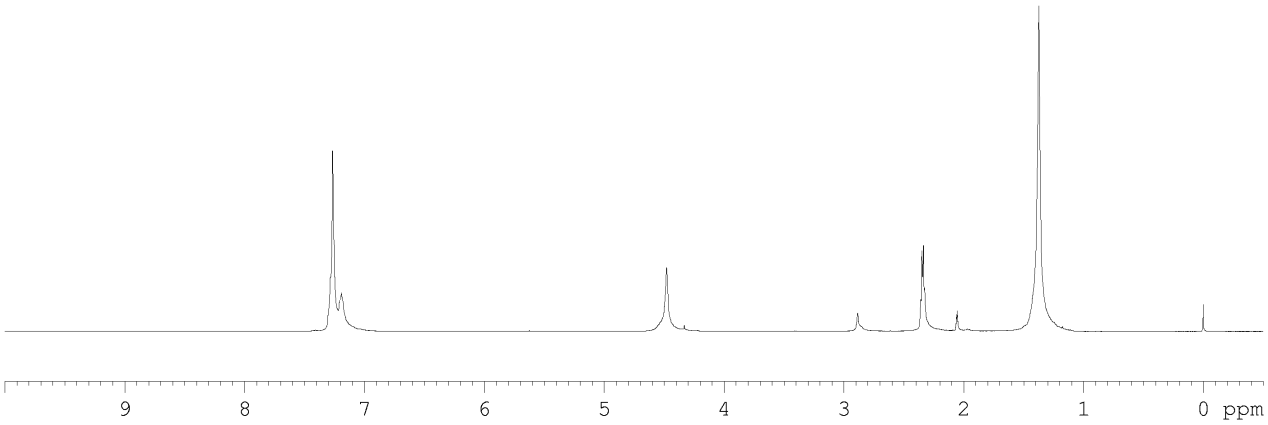
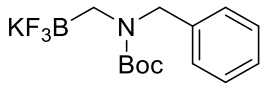
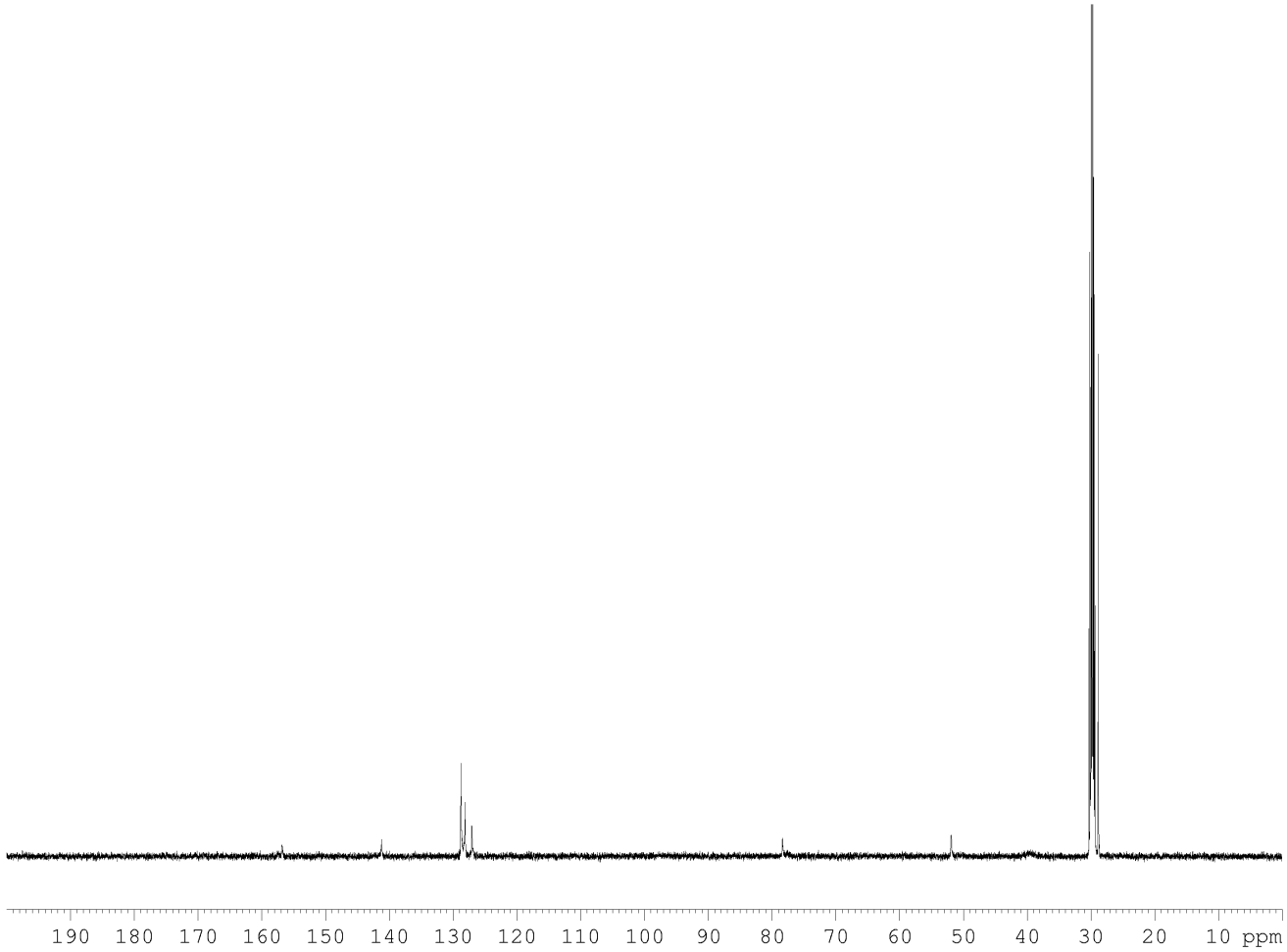


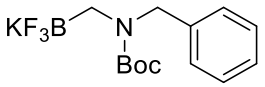
Figure A2.63 Infrared Spectrum

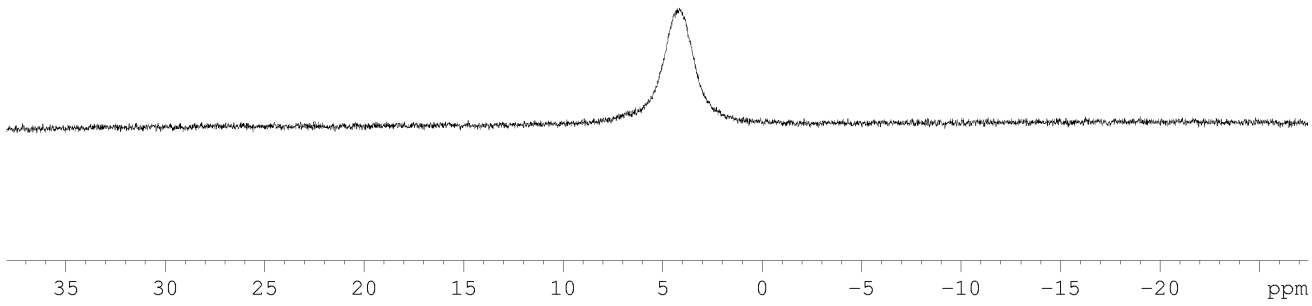

KF3B
N
Boc

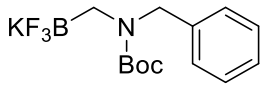

9
8
7
6
5
4
3
2
1
0 ppm

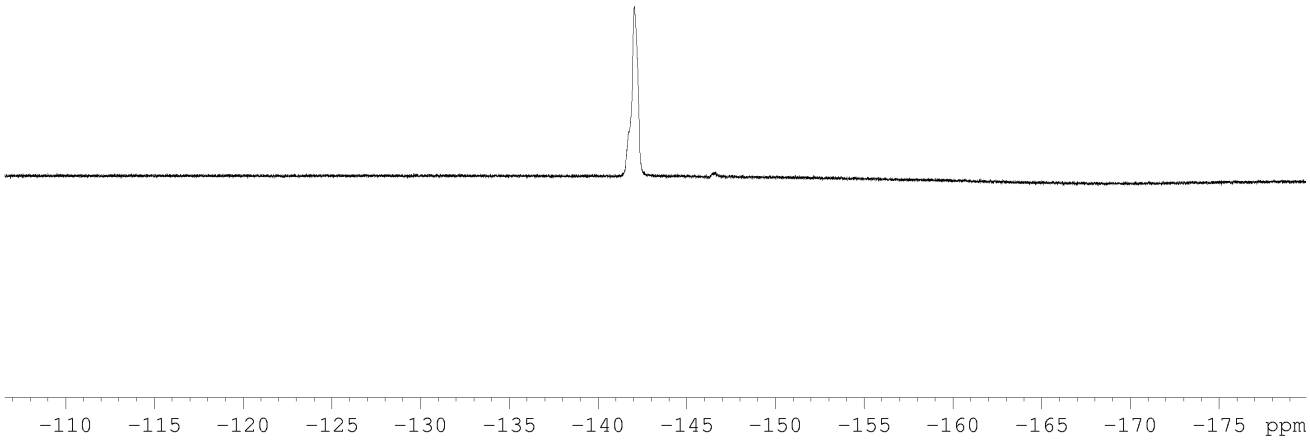

KF3B
N
Boc

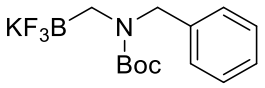

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


KF3B
N
Boc


35
30
25
20
15
10
5
0
-5
-10
-15
-20
ppm


KF3B
N
Boc


-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175
ppm



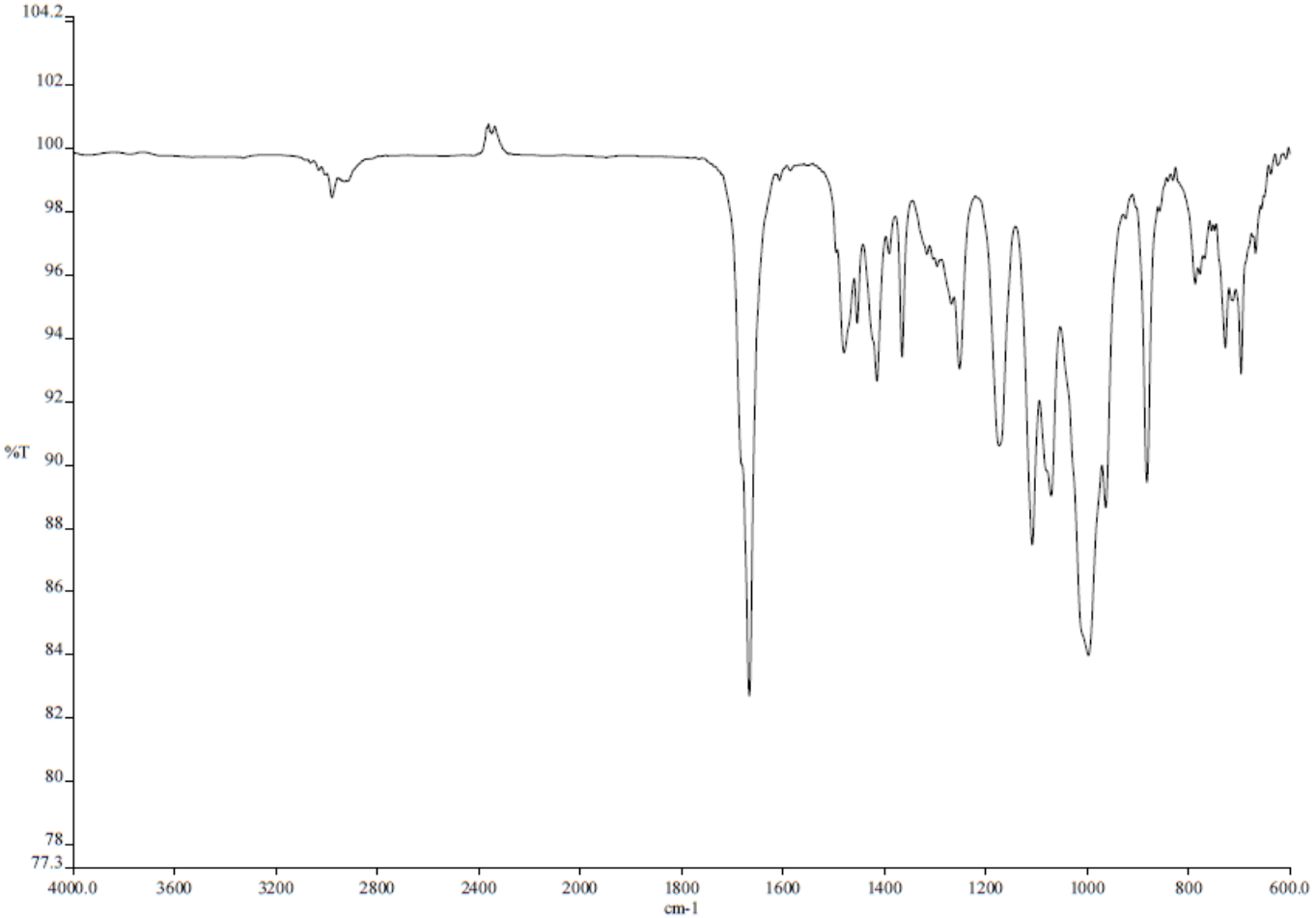
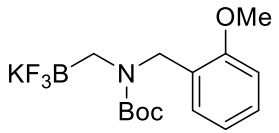
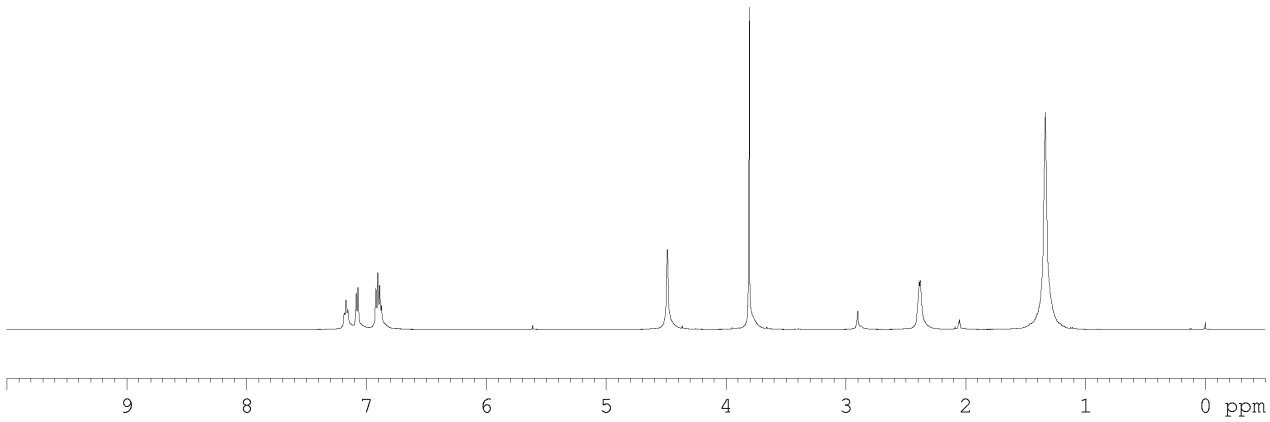
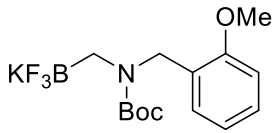
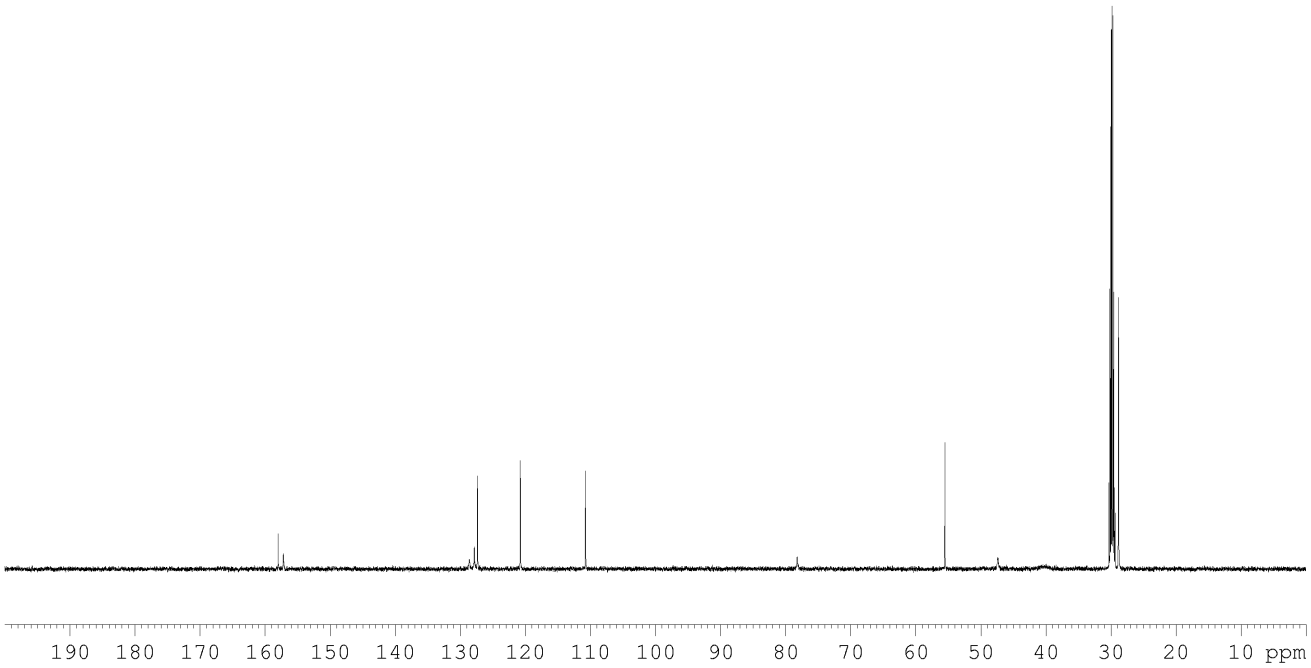


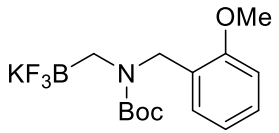
Figure A2.68 Infrared Spectrum

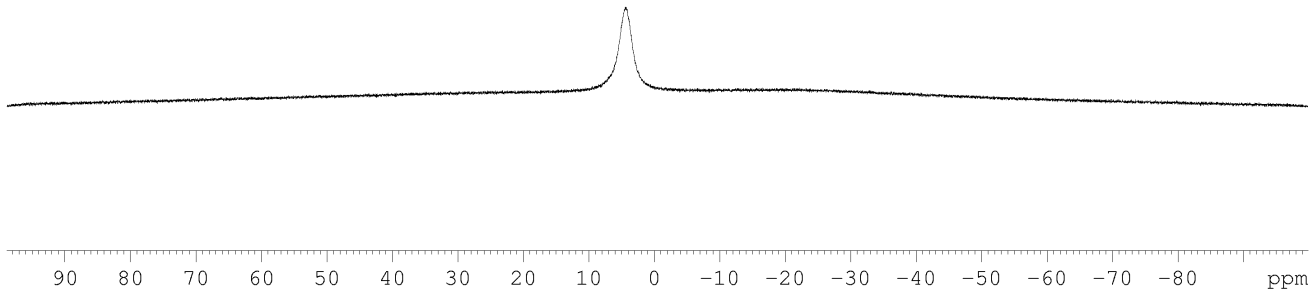

OMe
KF3B
N
Boc

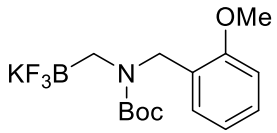

9
8
7
6
5
4
3
2
1
0 ppm

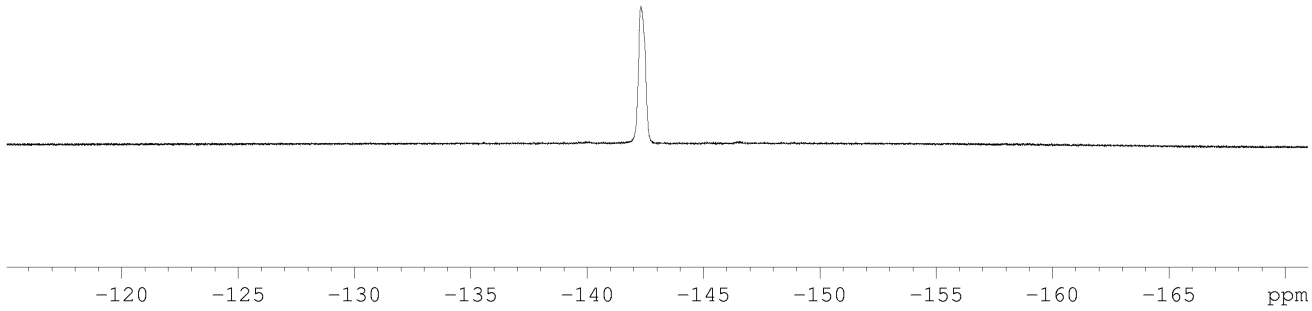

OMe
KF3B
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OMe
KF3B
N
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 ppm


OMe
KF3B
N
Boc


−120
−125
−130
−135
−140
−145
−150
−155
−160
−165
ppm

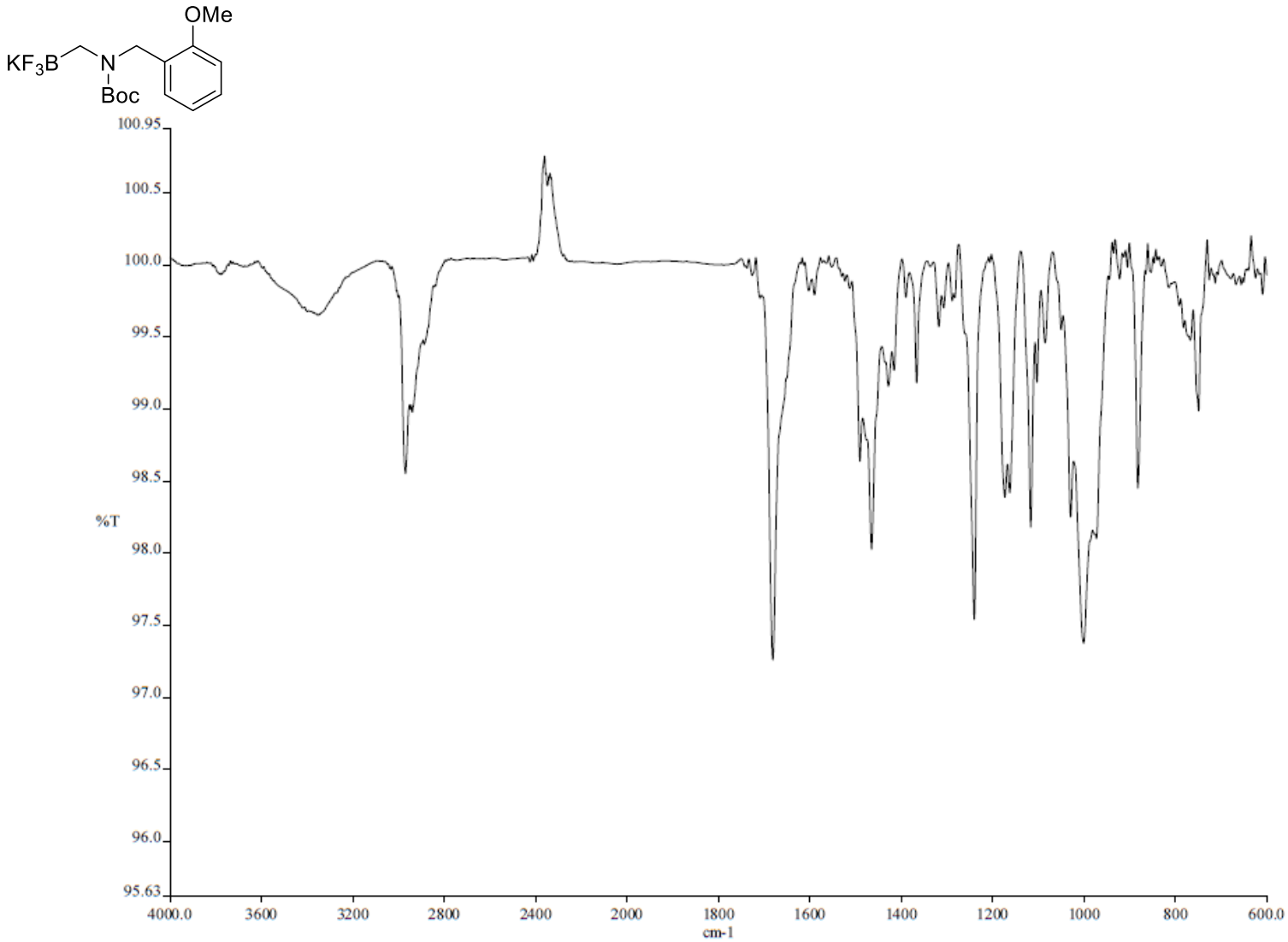
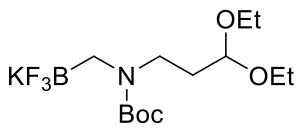
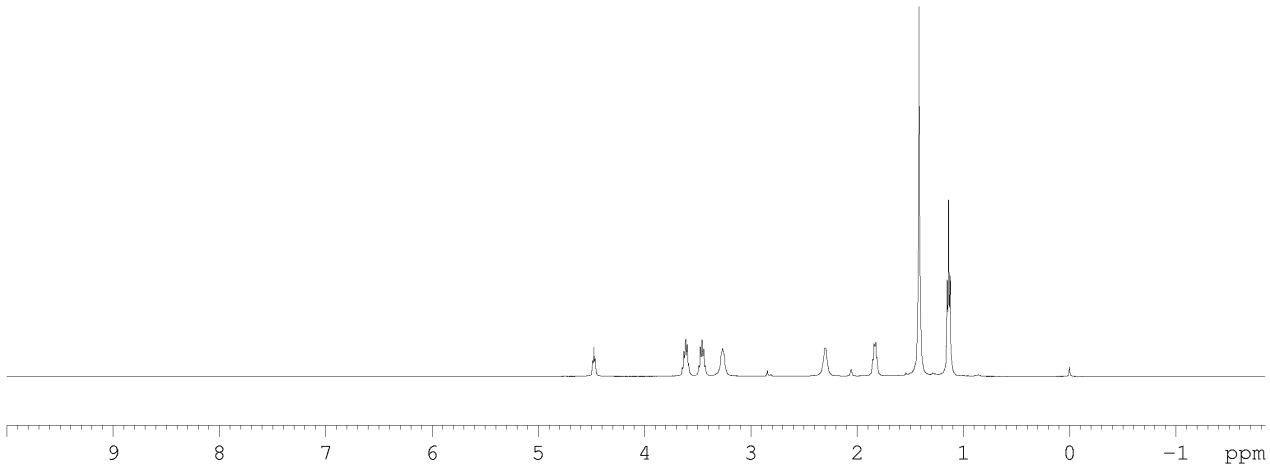
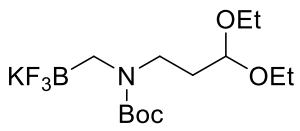
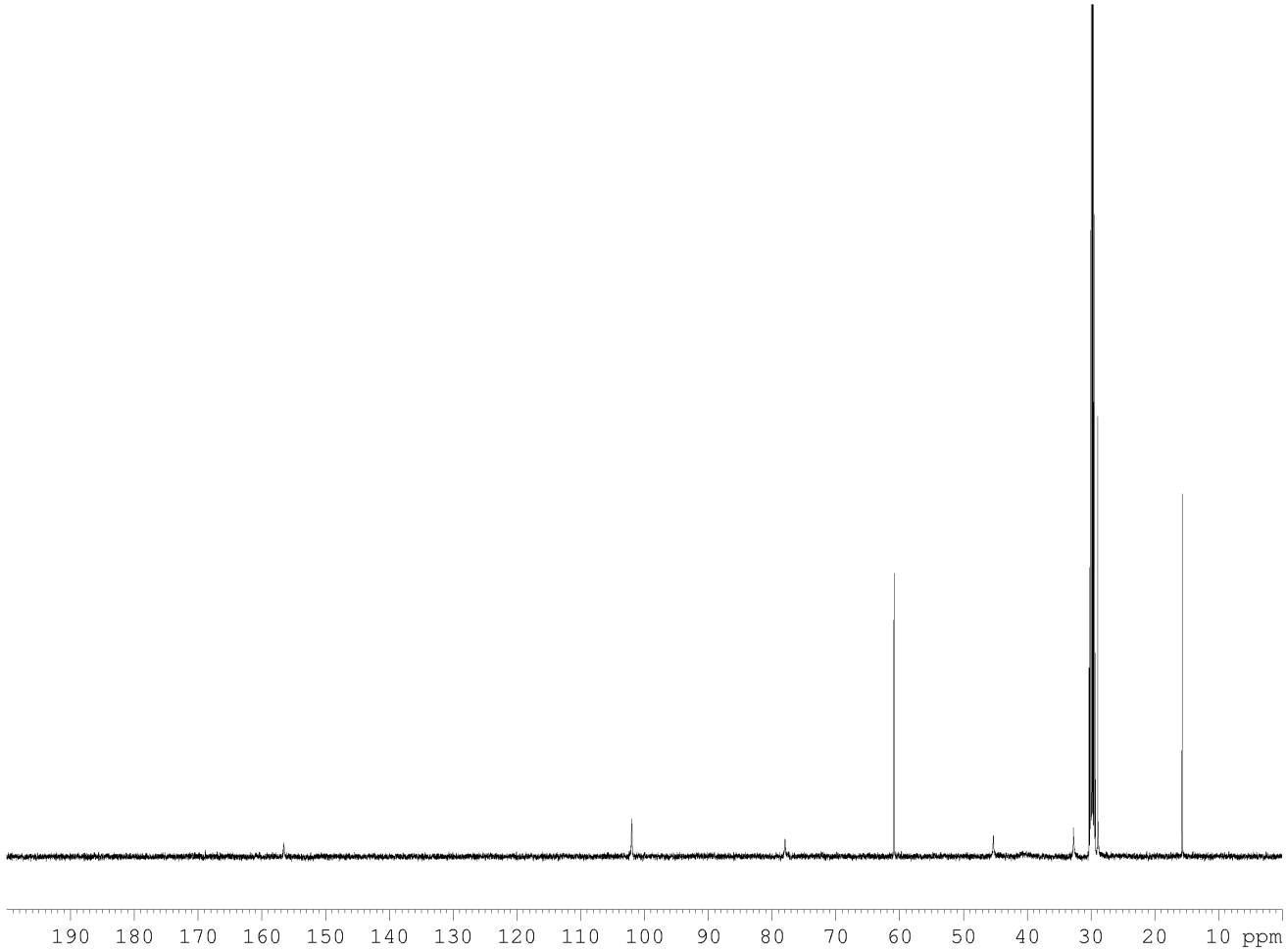


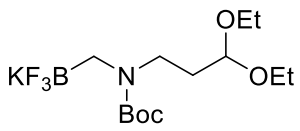
Figure A2.73 Infrared Spectrum

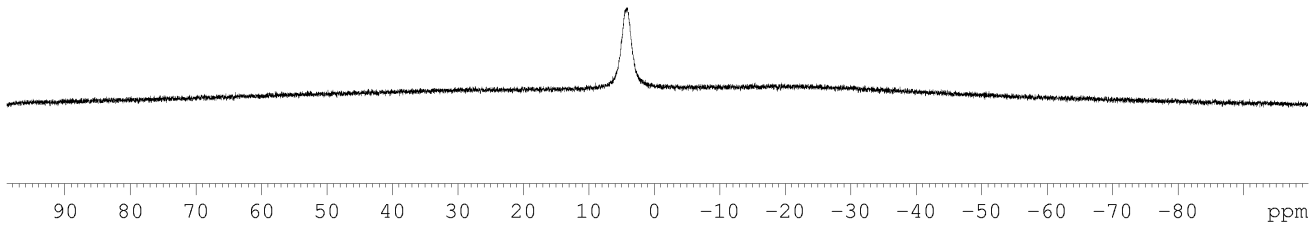

OEt
KF3B
N
OEt
Boc

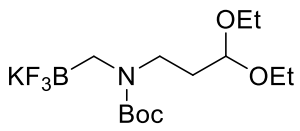

9
8
7
6
5
4
3
2
1
0
−1
ppm

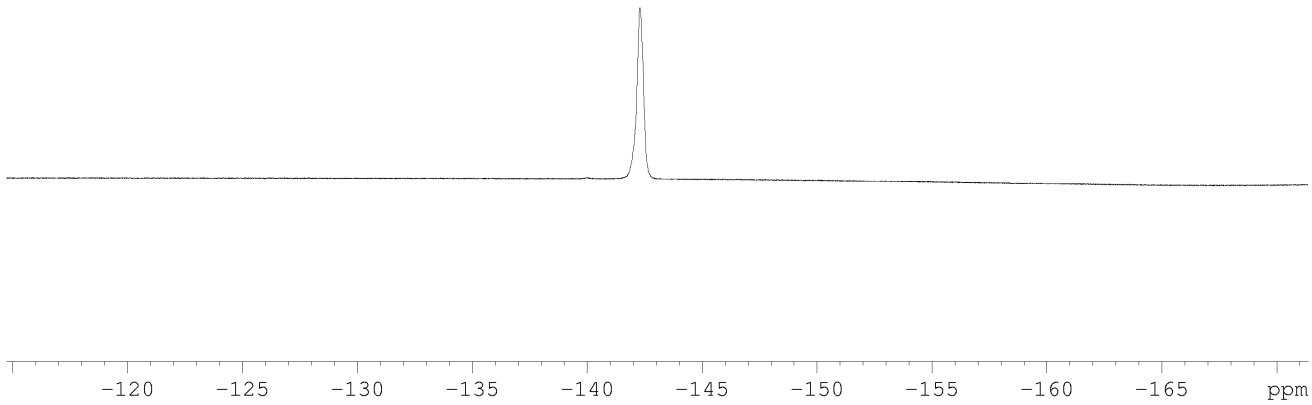

OEt
KF3B
N
OEt
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OEt
KF3B
N
OEt
Boc


90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80
ppm


OEt
KF3B
N
OEt
Boc


−120
−125
−130
−135
−140
−145
−150
−155
−160
−165
ppm

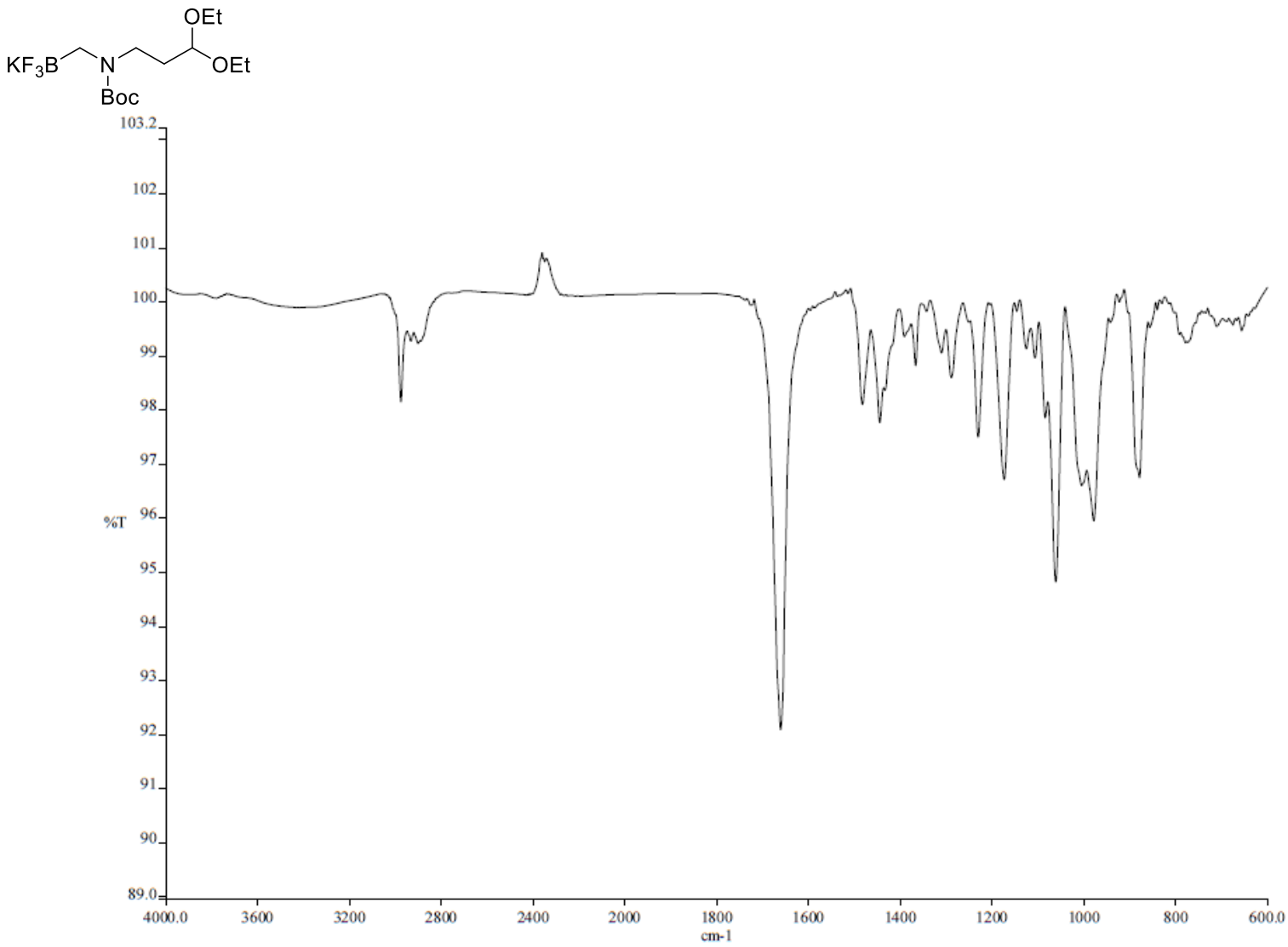
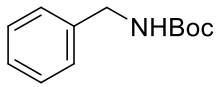
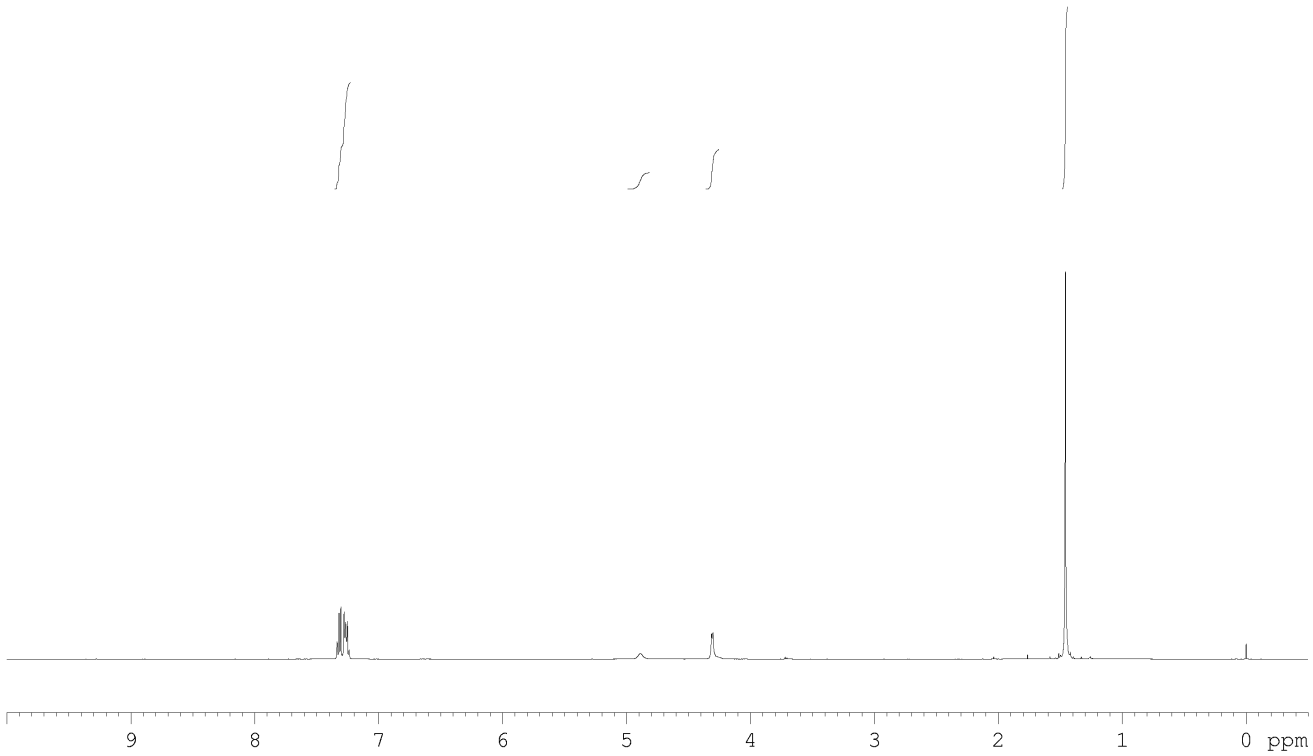
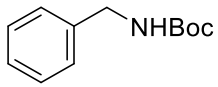
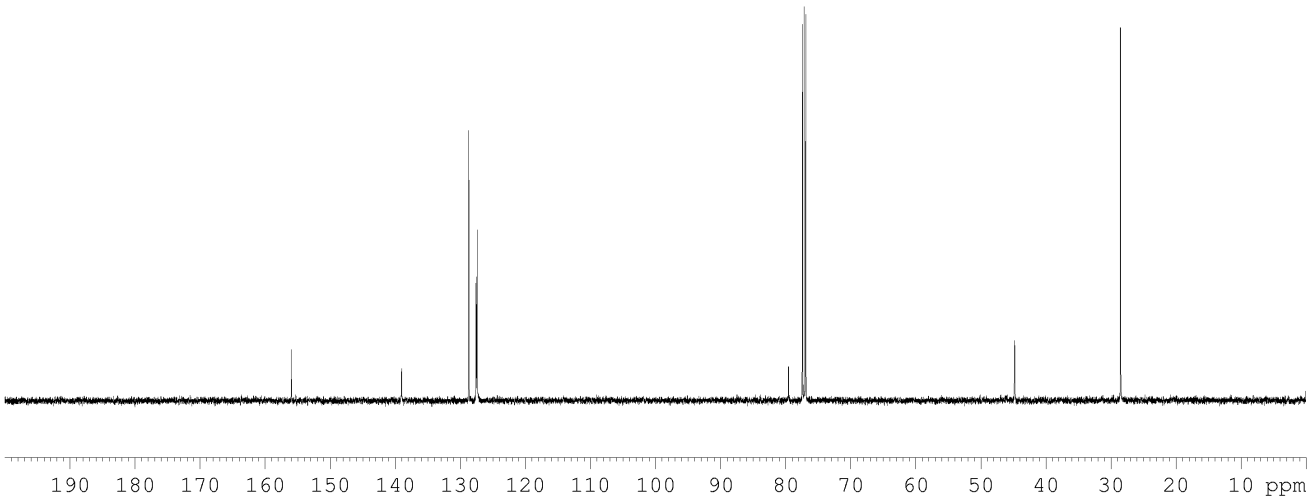


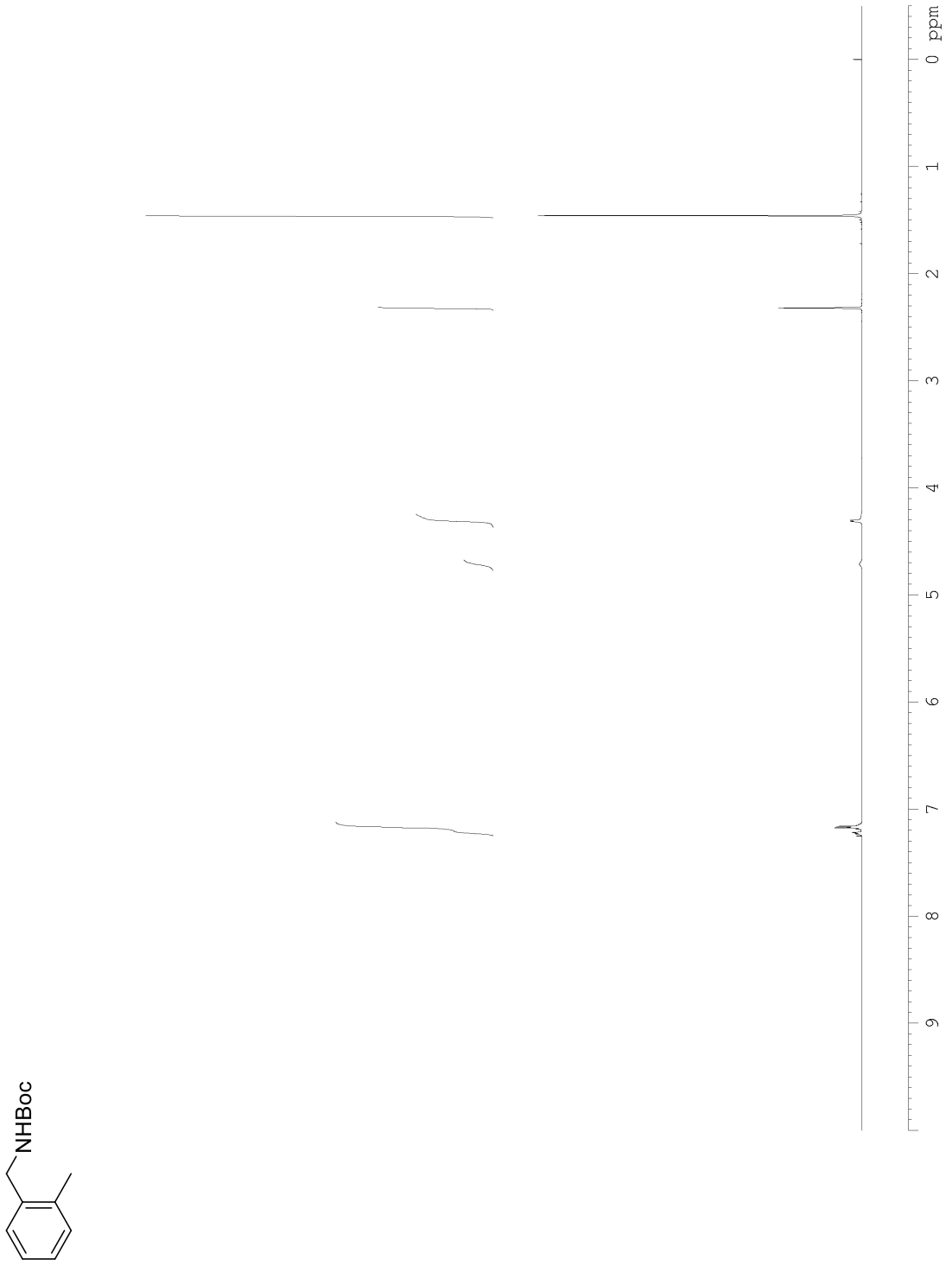
Figure A2.78 Infrared Spectrum

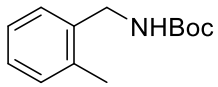

NHBoc

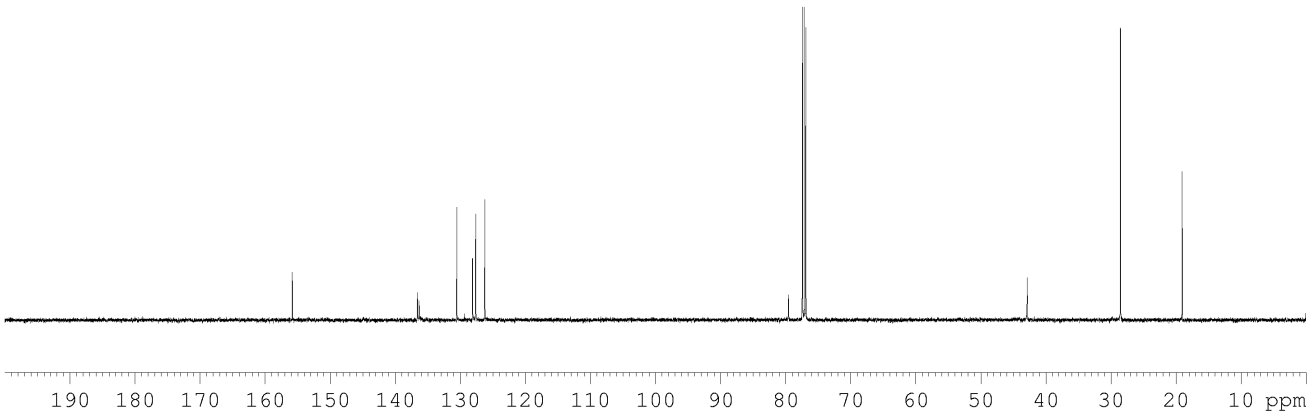

9
8
7
6
5
4
3
2
1
0 ppm

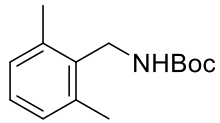

NHBoc

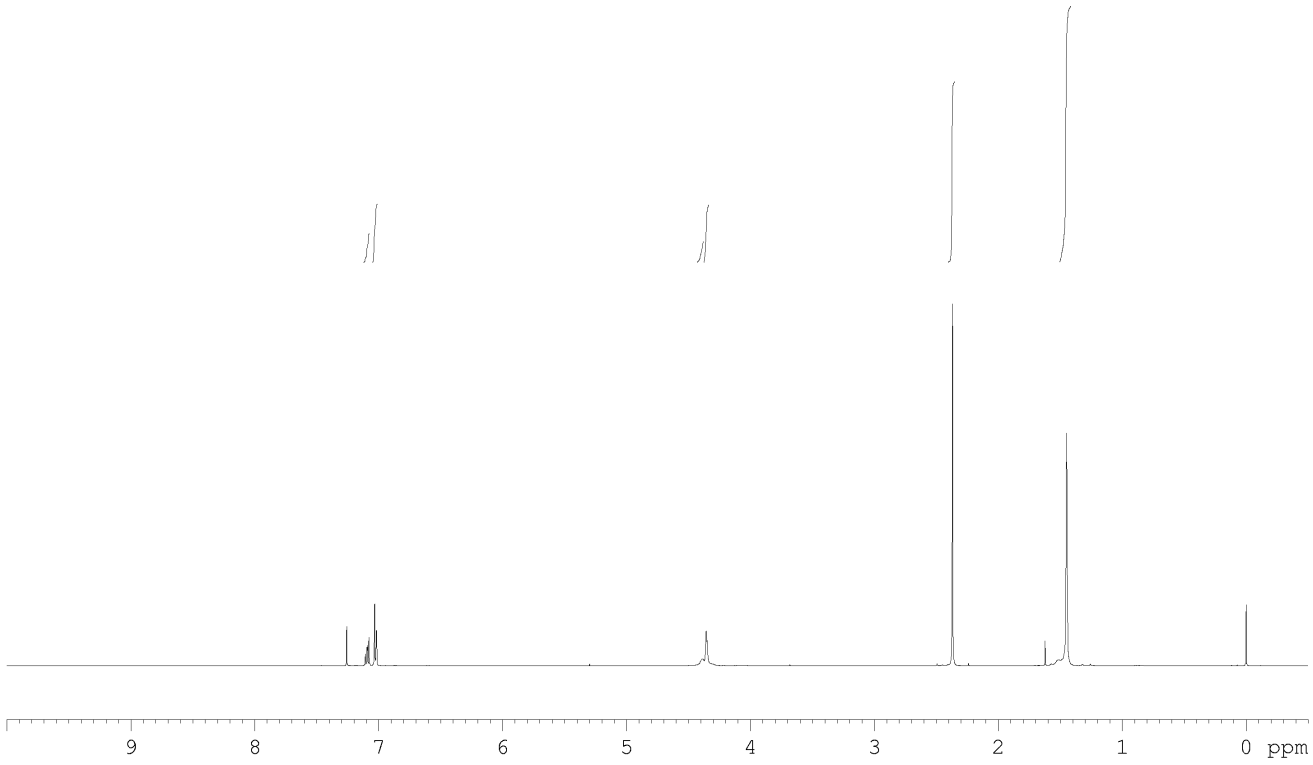

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

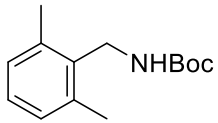

NHBoc
9
8
7
6
5
4
3
2
1
0 ppm

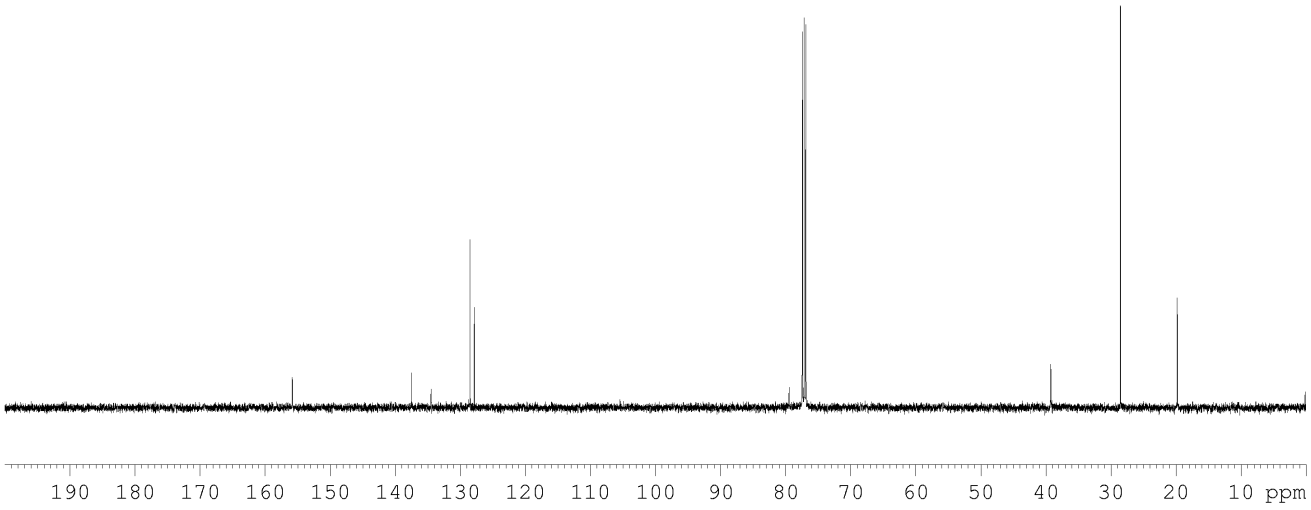

NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc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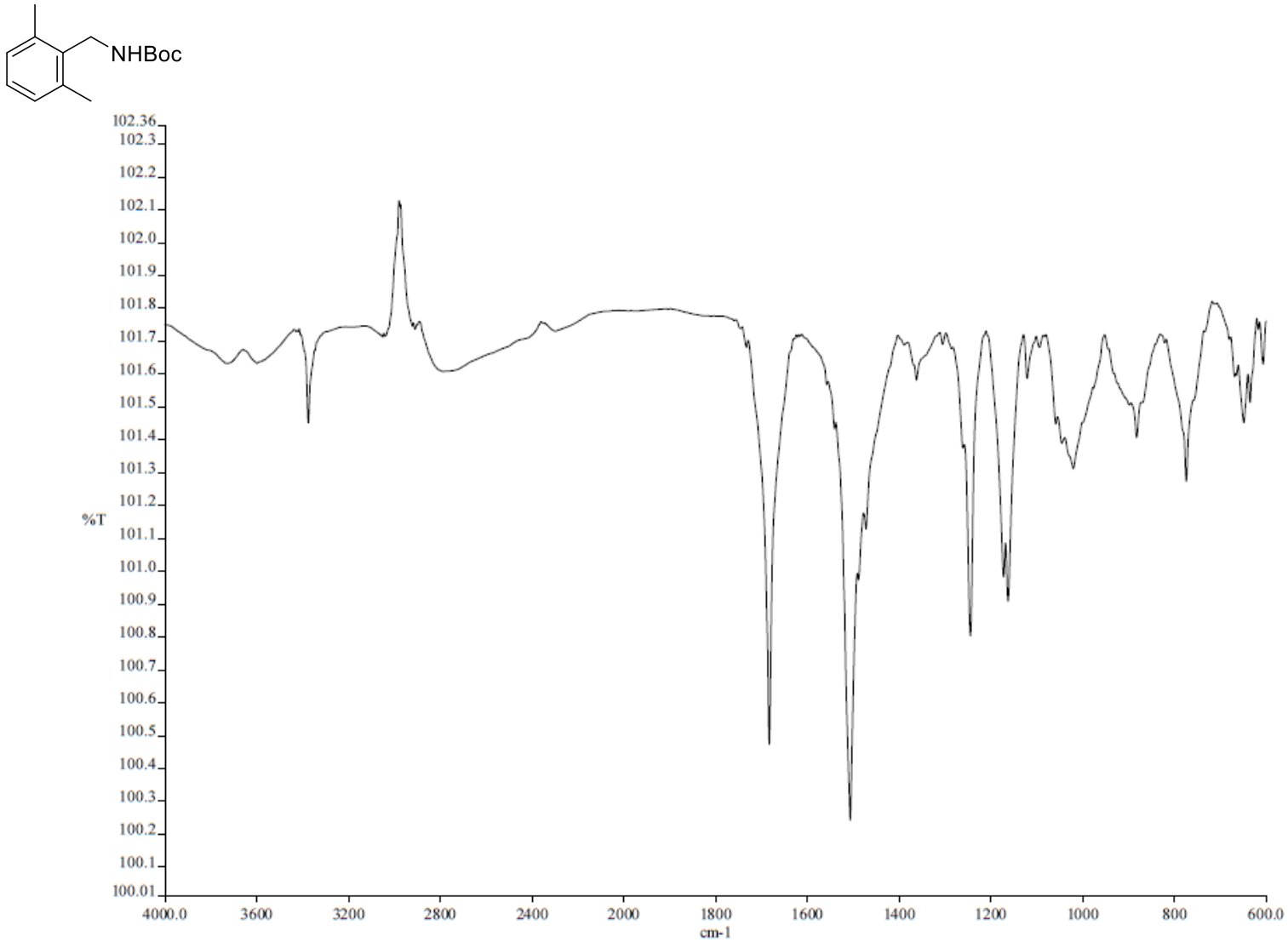
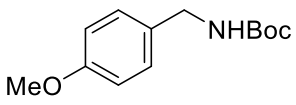
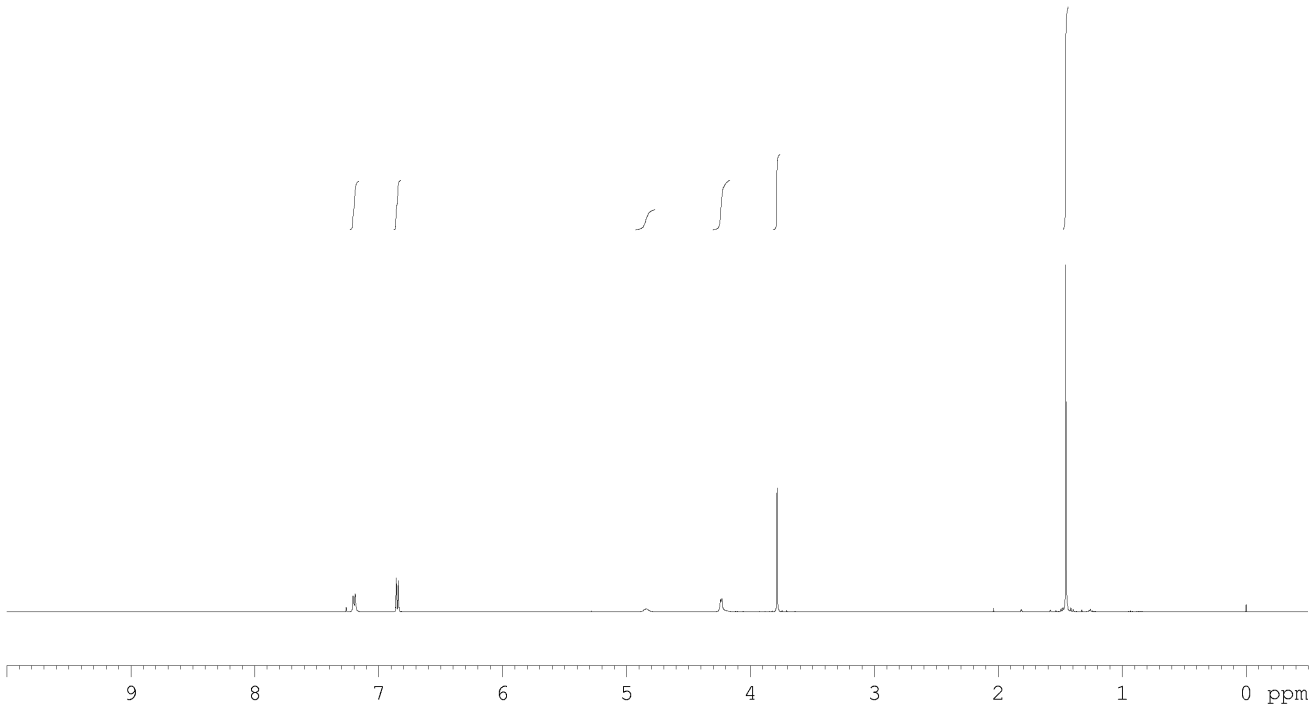
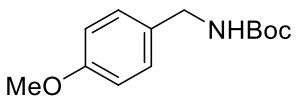
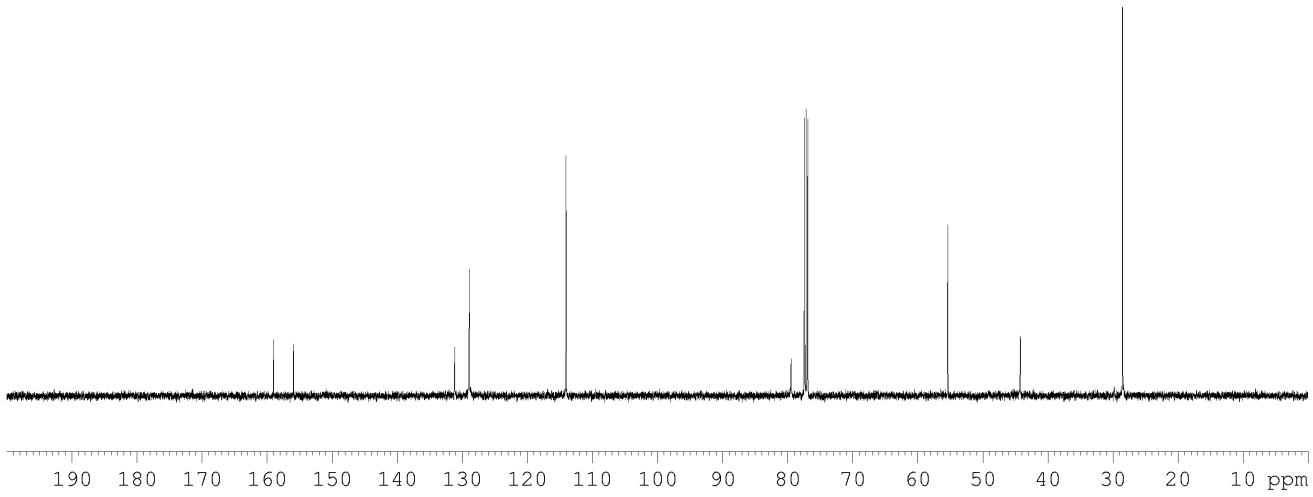


Figure A2.85 Infrared Spectrum


NHBoc
MeO


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
MeO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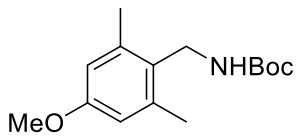
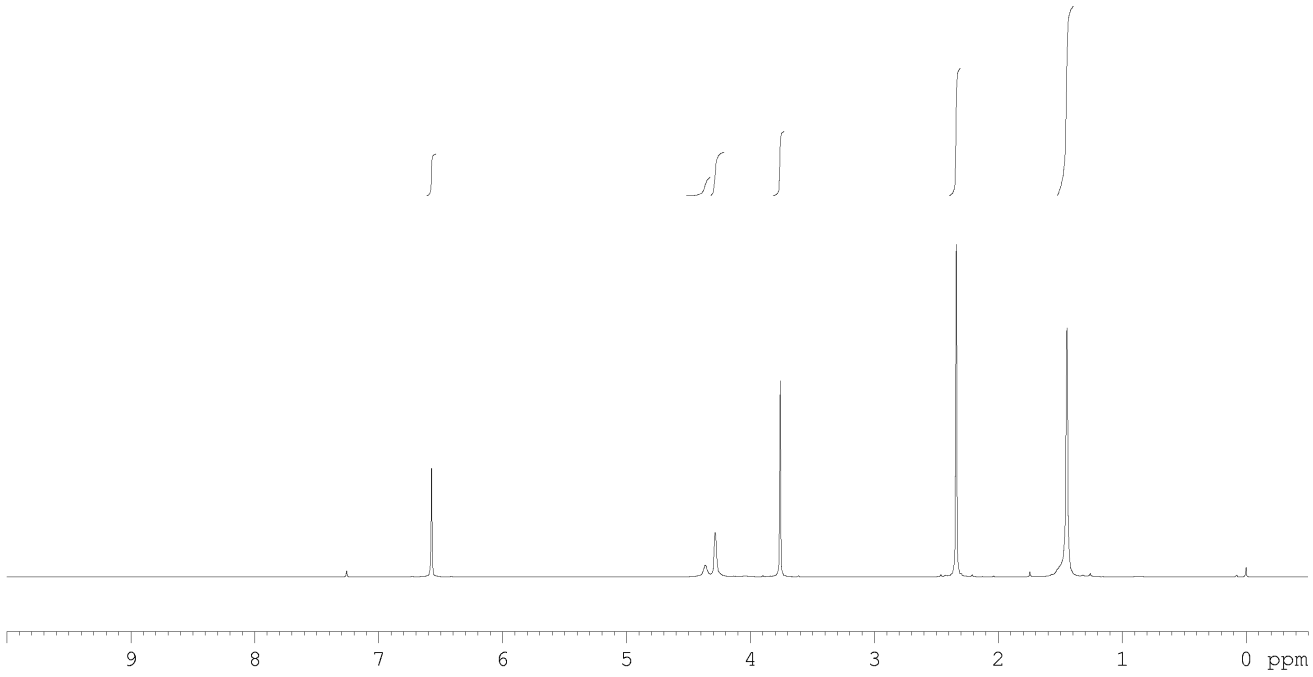
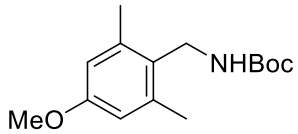
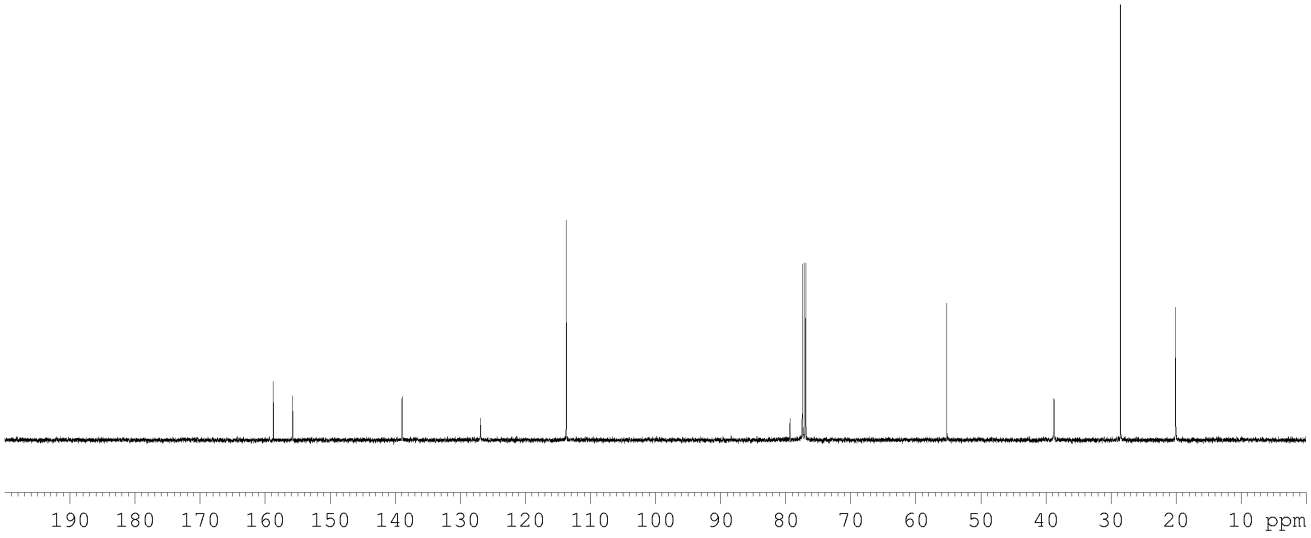

NHBoc
MeO


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
MeO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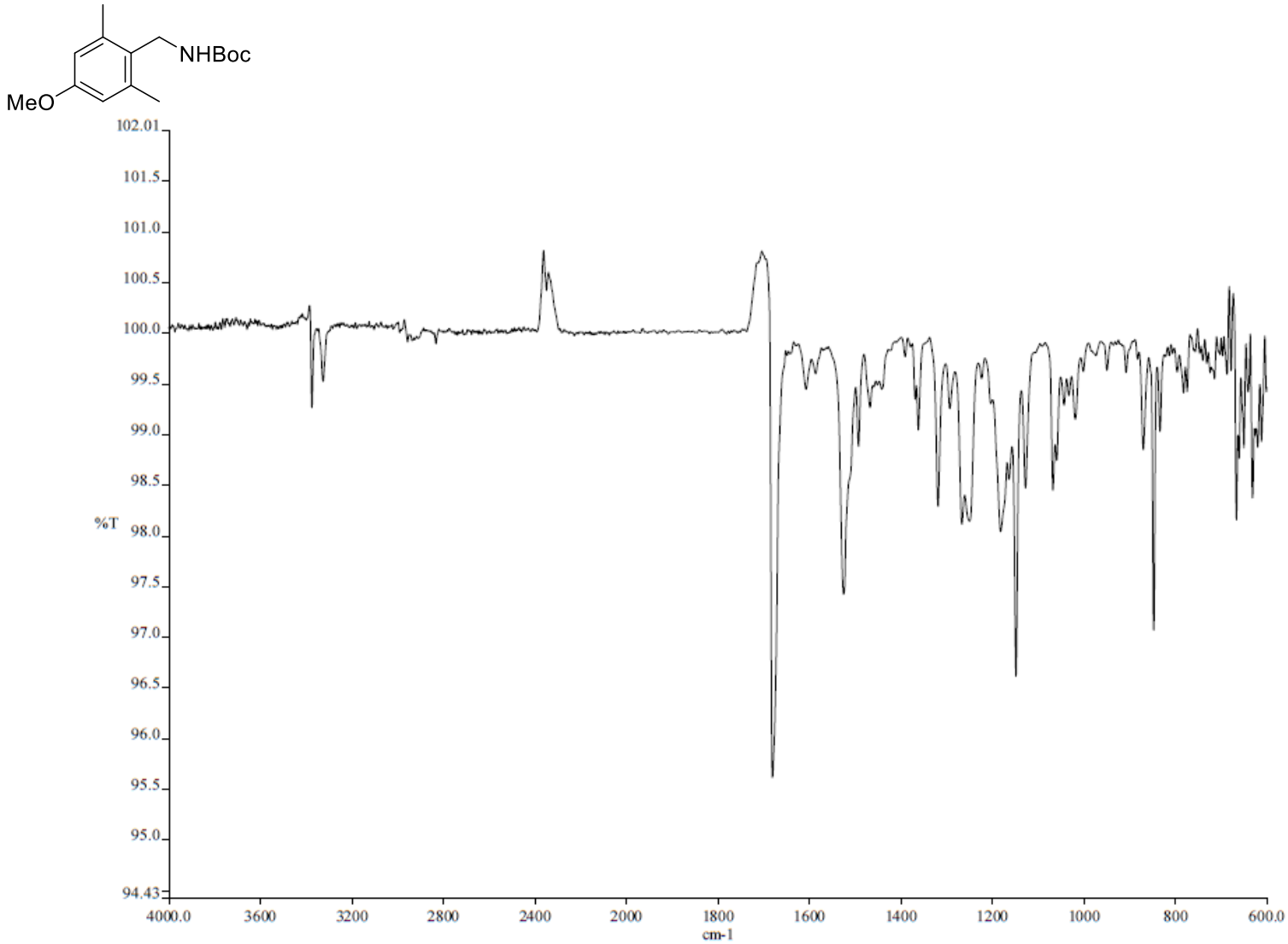
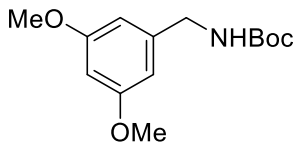
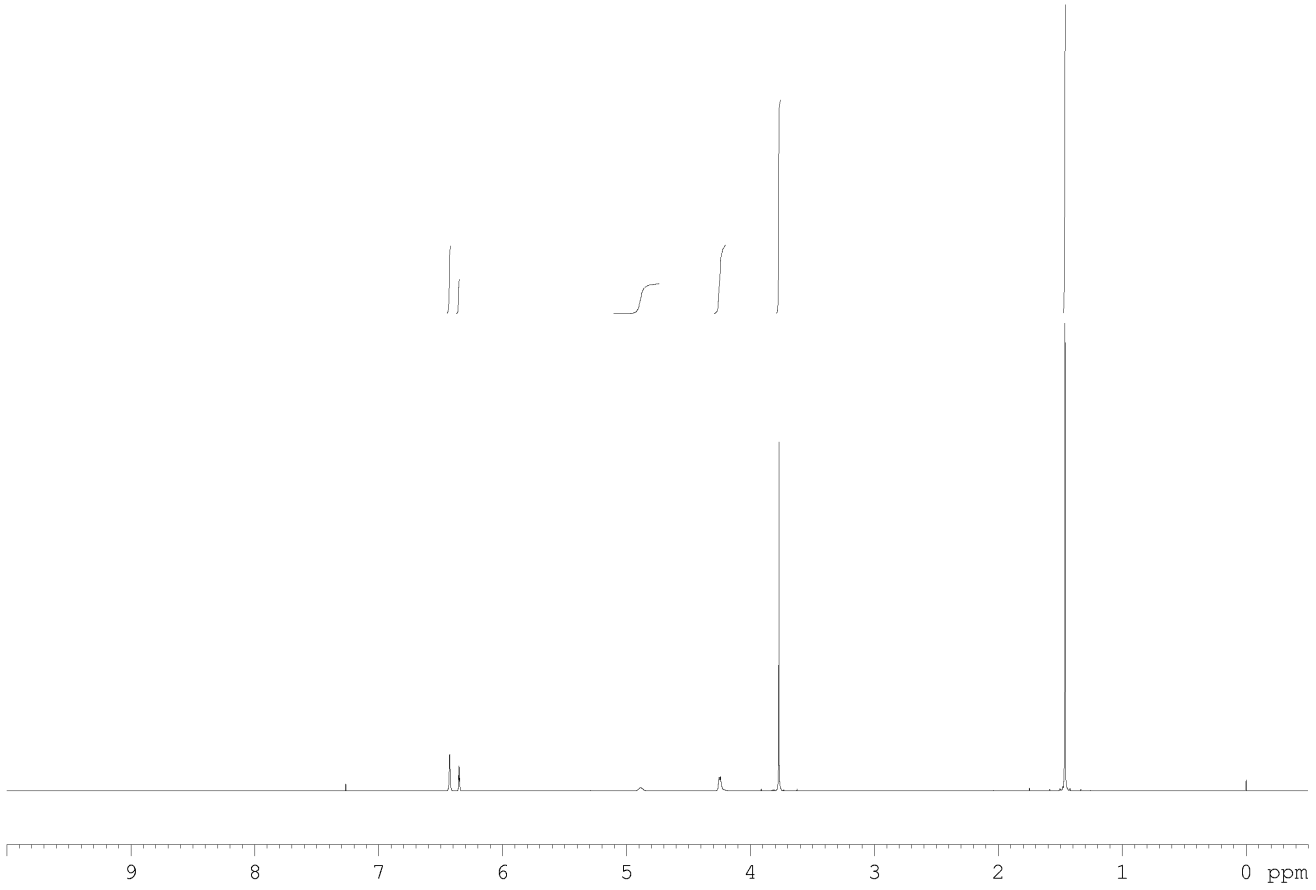
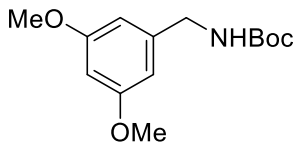
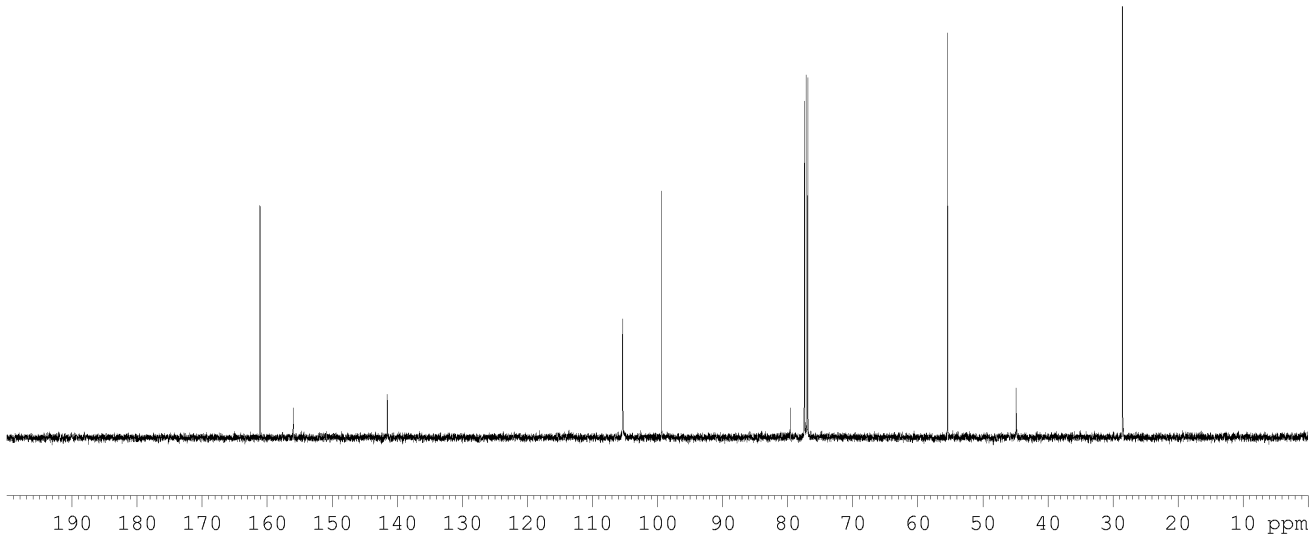


Figure A2.90 Infrared Spectrum


MeO
NHBoc
OMe


9
8
7
6
5
4
3
2
1
0 ppm


MeO
NHBoc
OMe


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

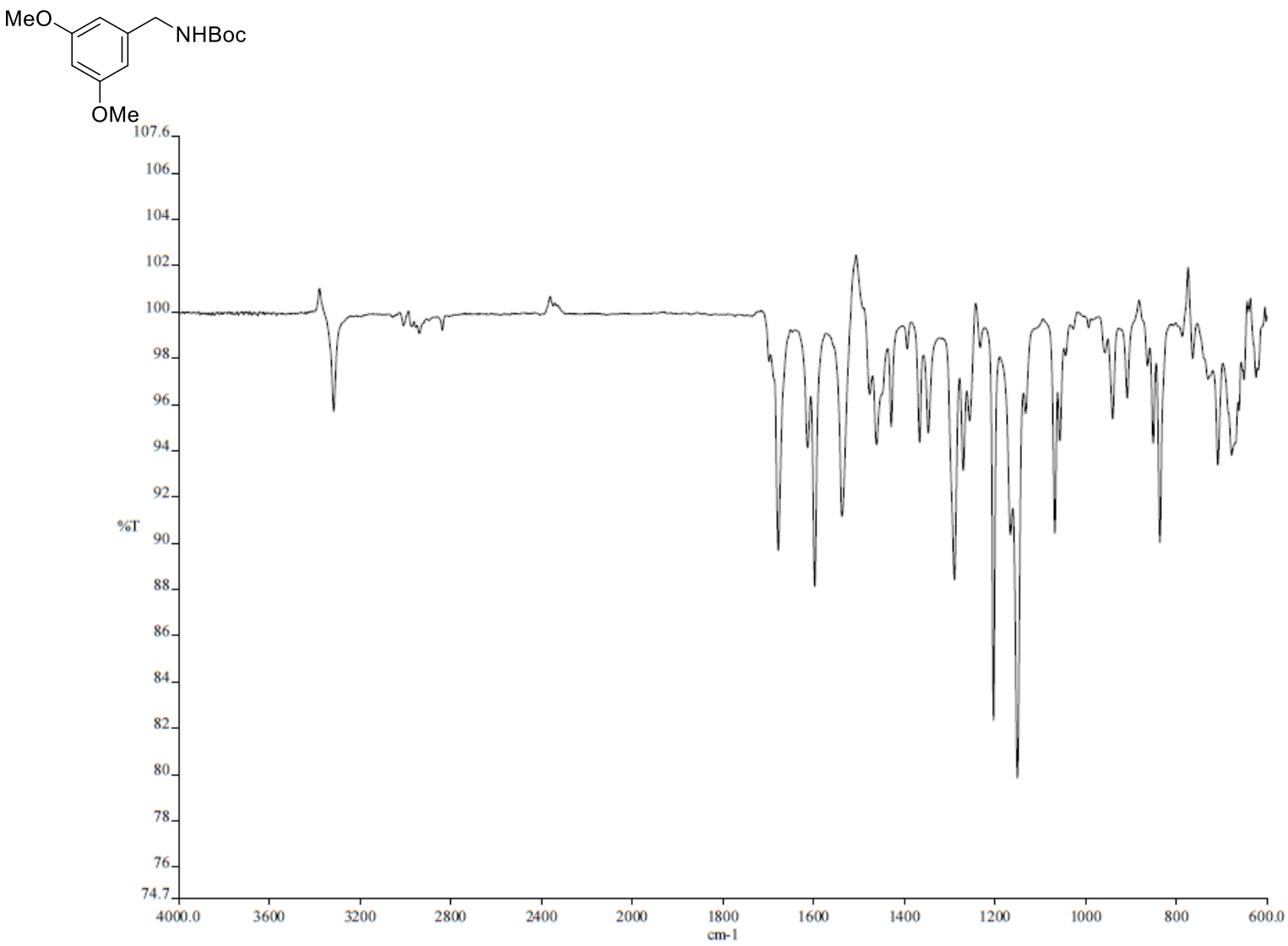


Figure A2.93 Infrared Spectrum

NHBoc
N

9
8
7
6
5
4
3
2
1
0 ppm

NHBoc
N

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

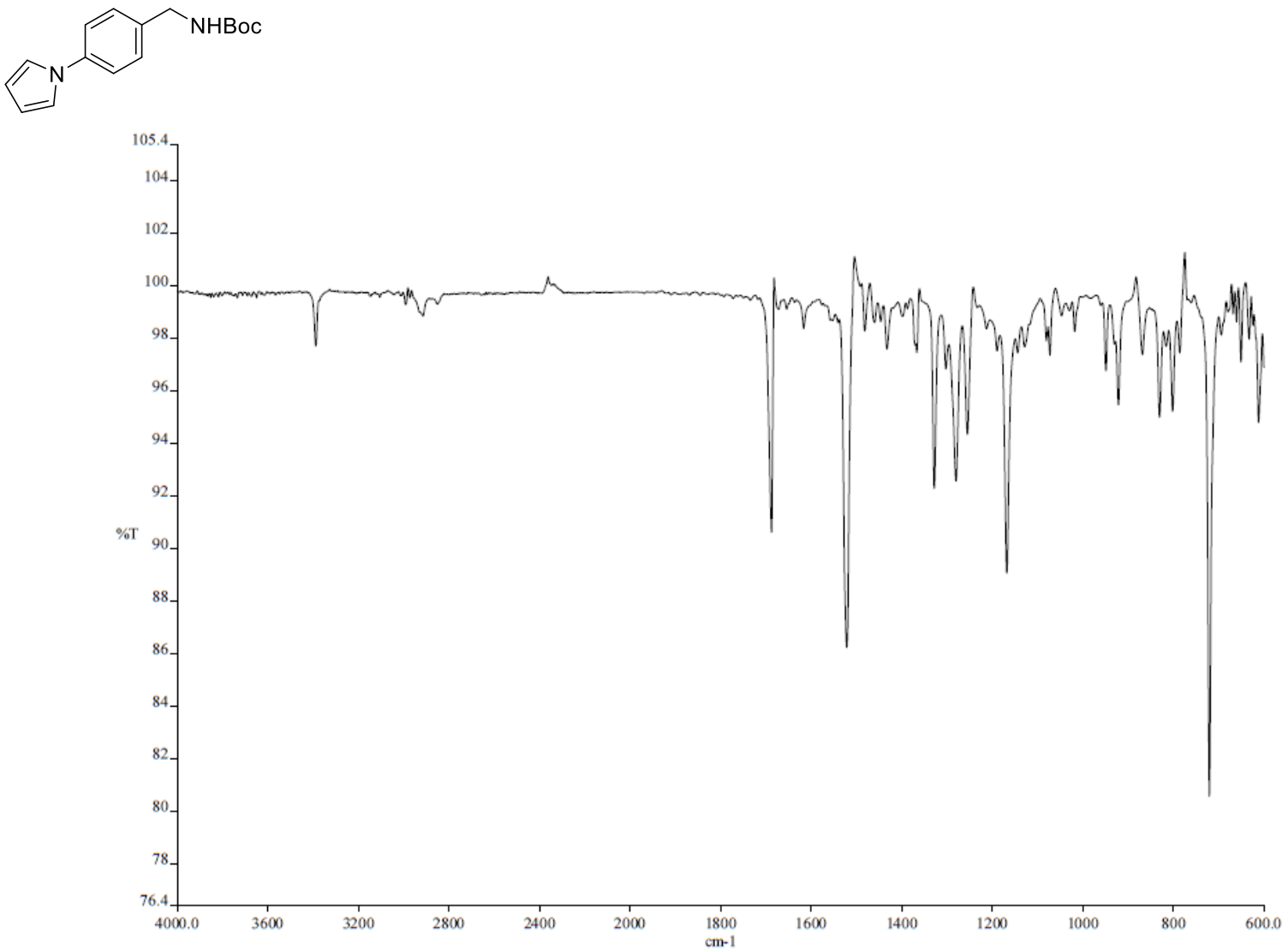
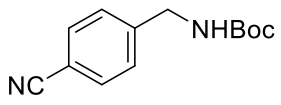
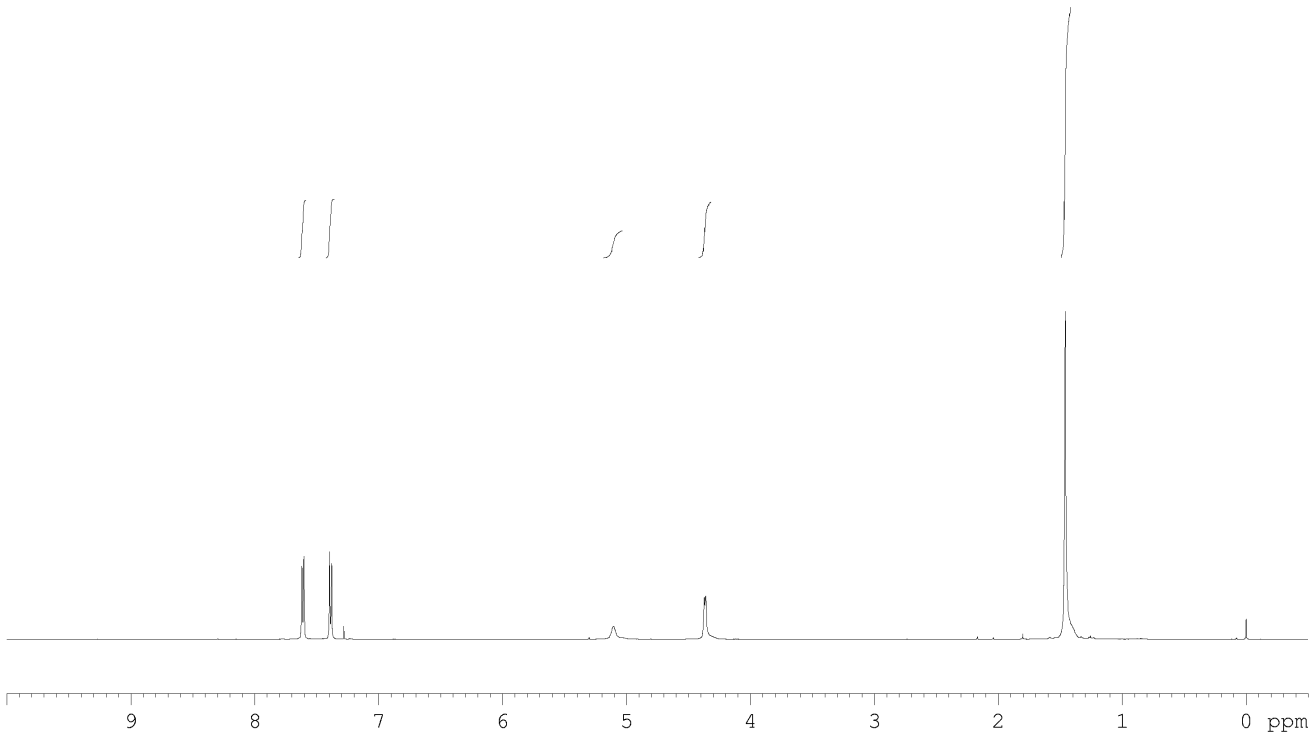
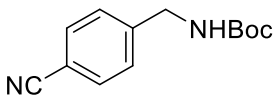


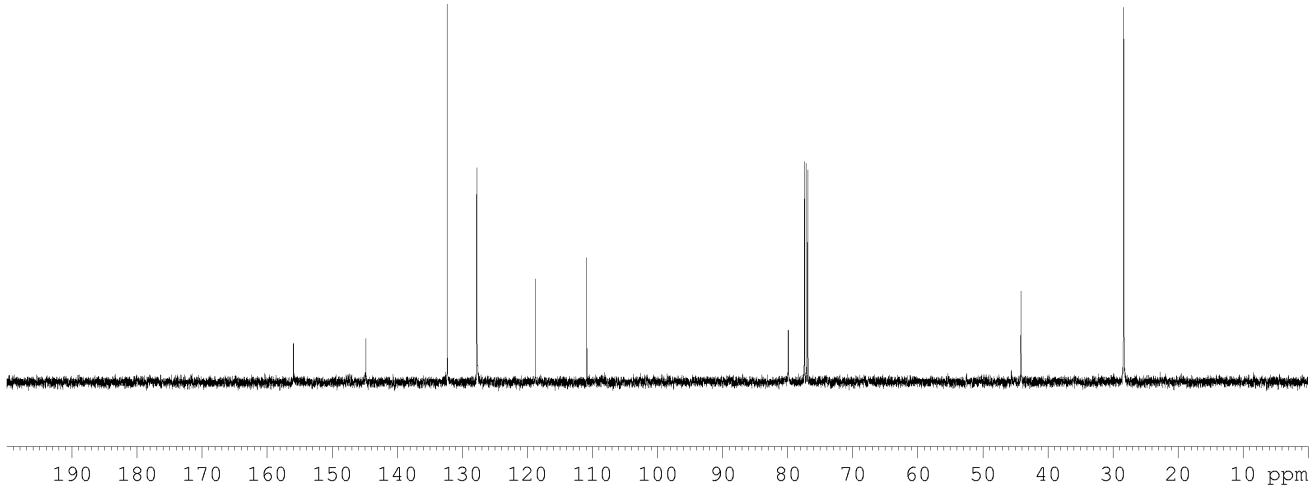
Figure A2.96 Infrared Spectrum

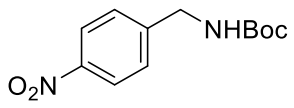


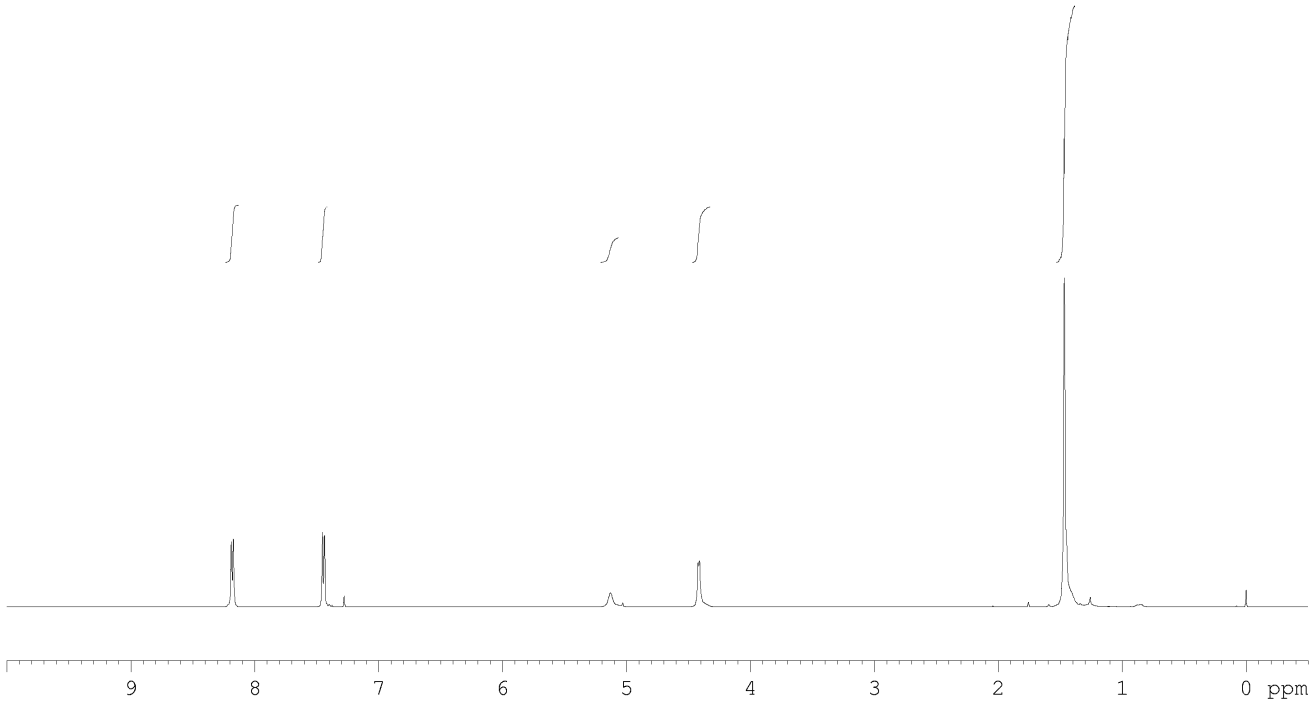
400

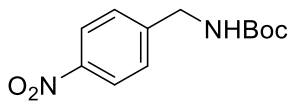


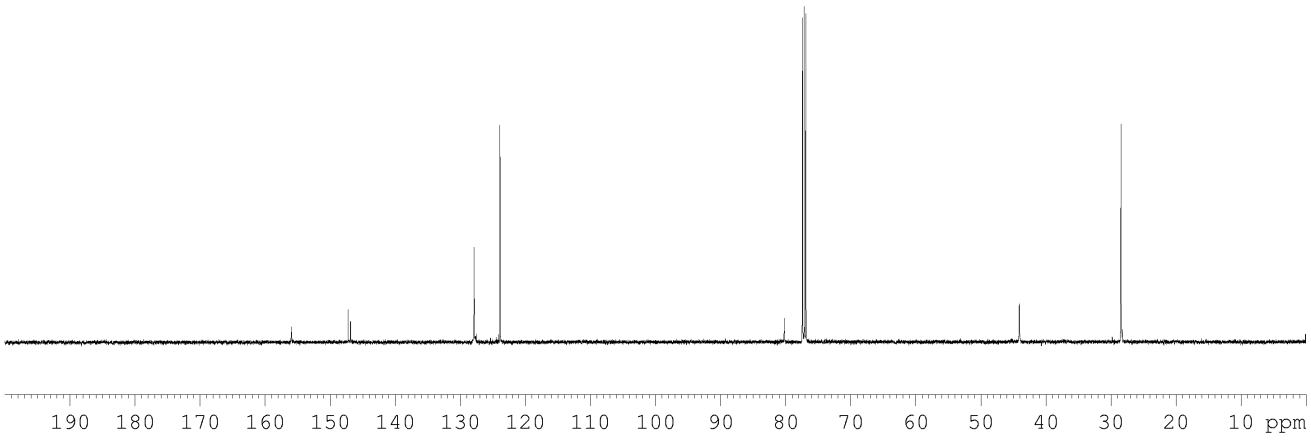

NHBoc
NC

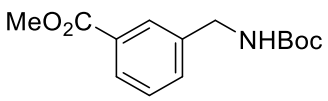

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

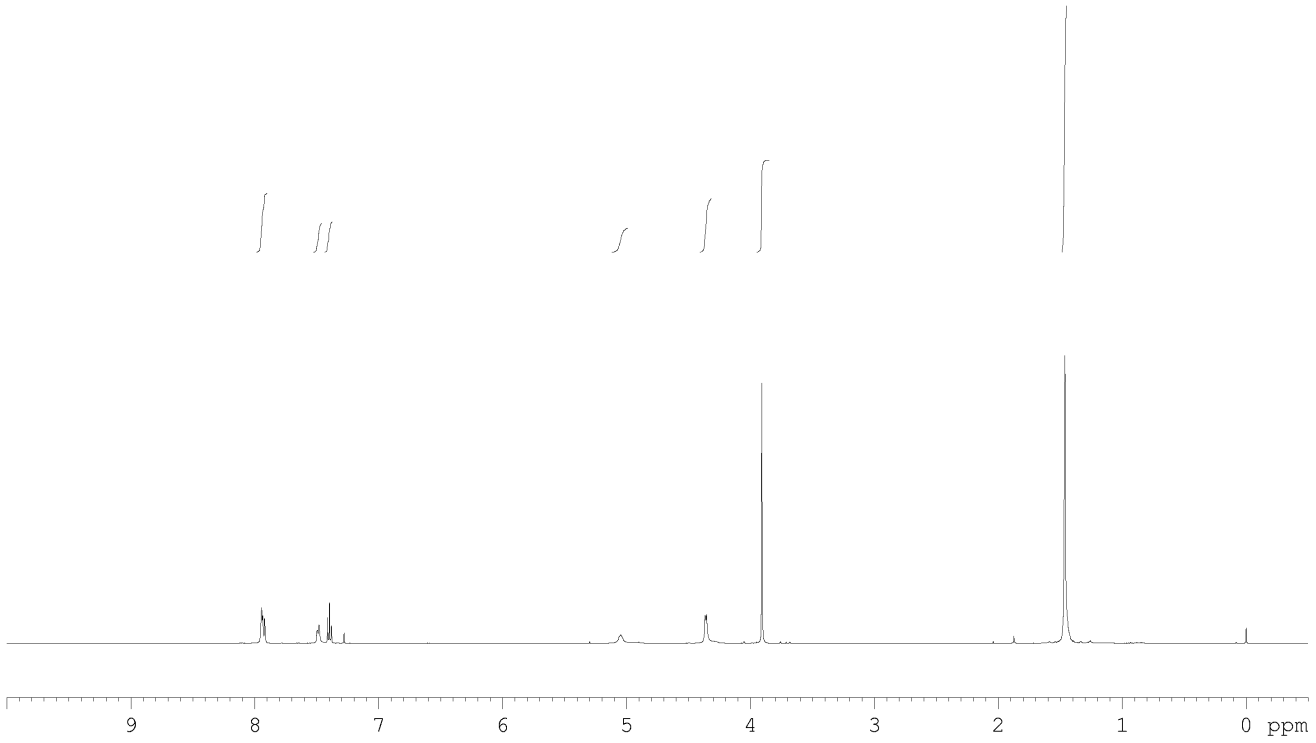

NHBoc
O2N

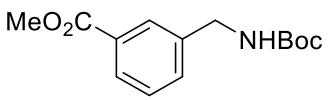

9
8
7
6
5
4
3
2
1
0 ppm

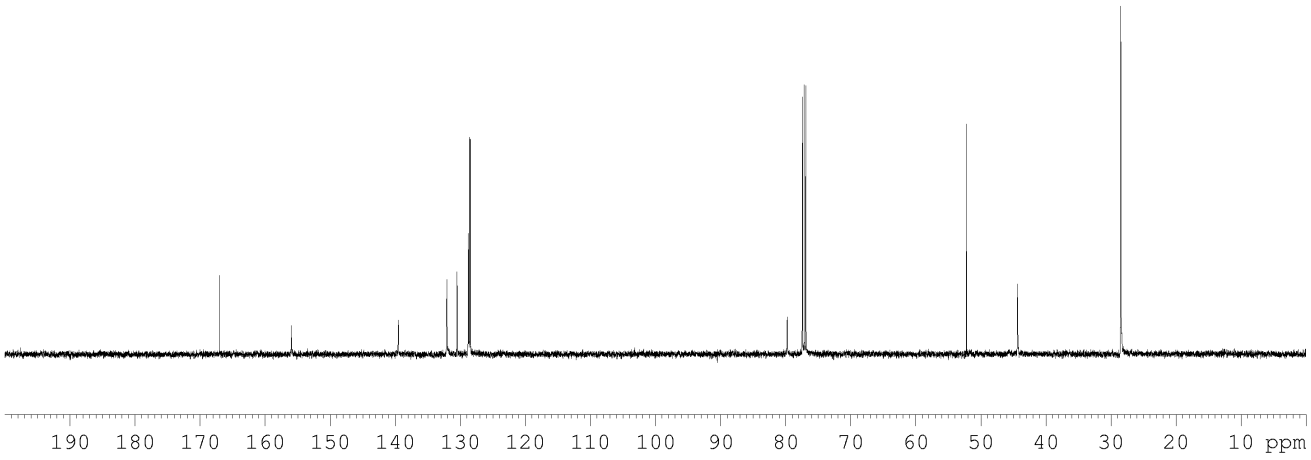

NHBoc
O2N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


MeO2C
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


MeO2C
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

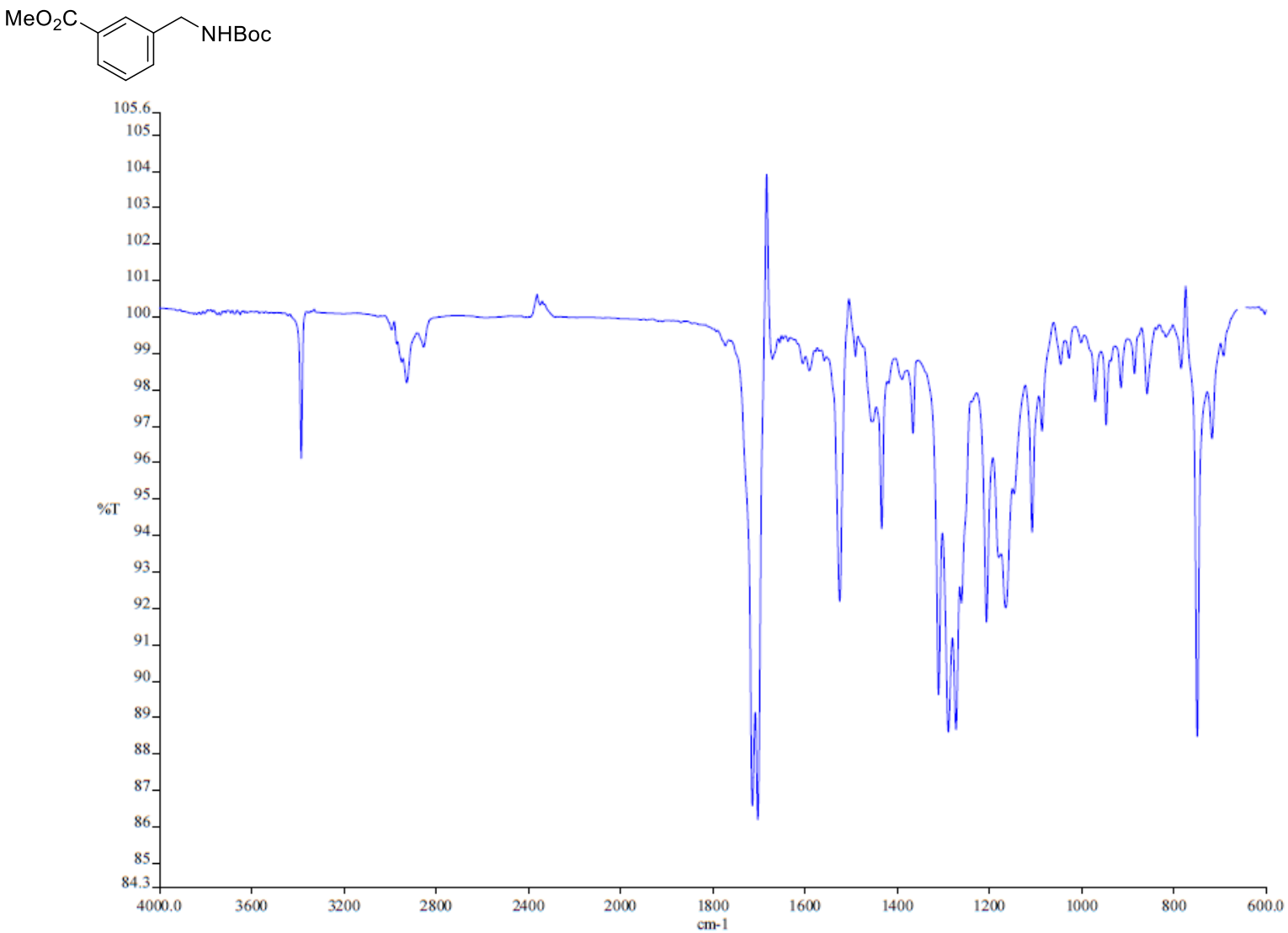
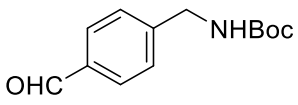
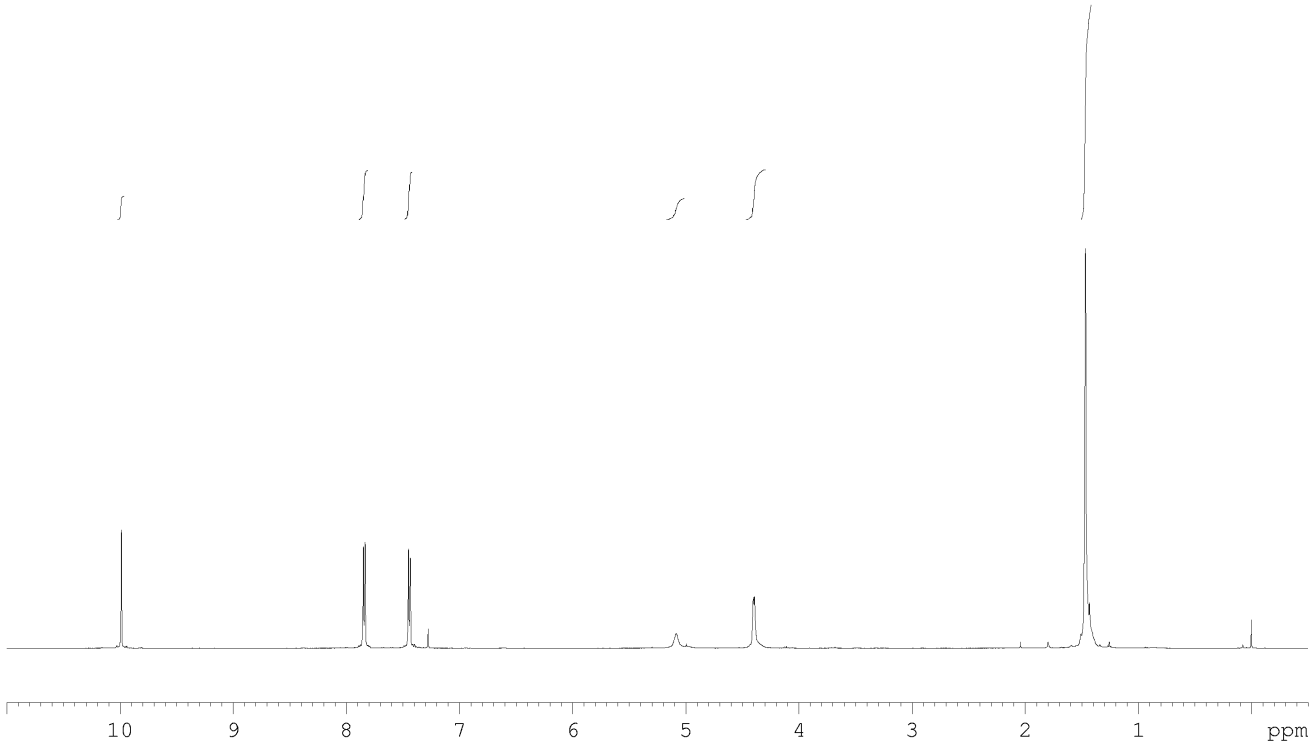
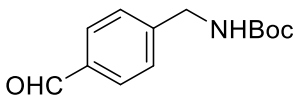
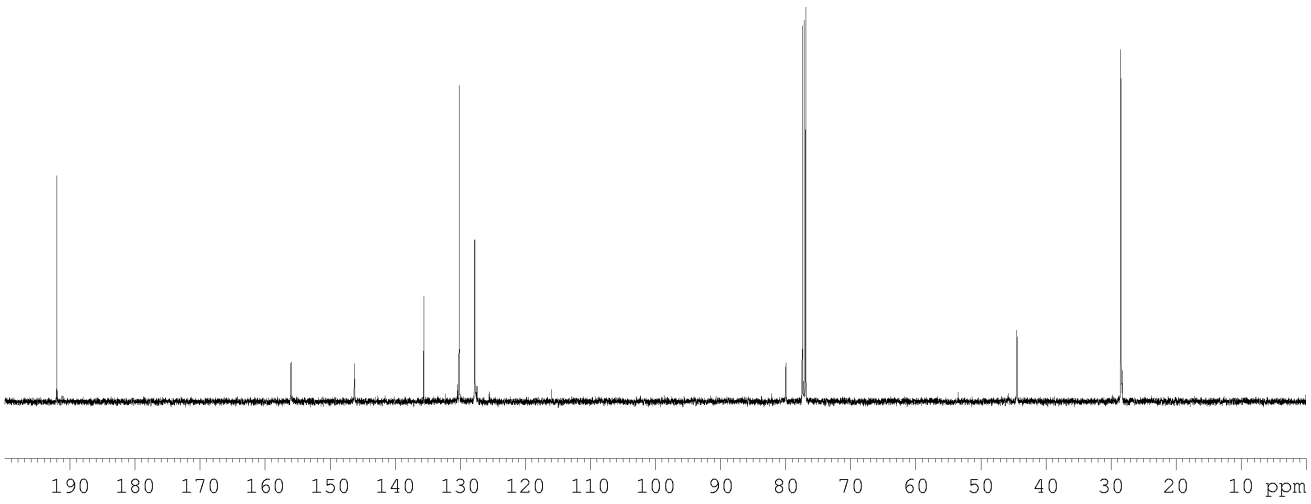


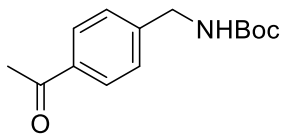
Figure A2.103 Infrared Spectrum

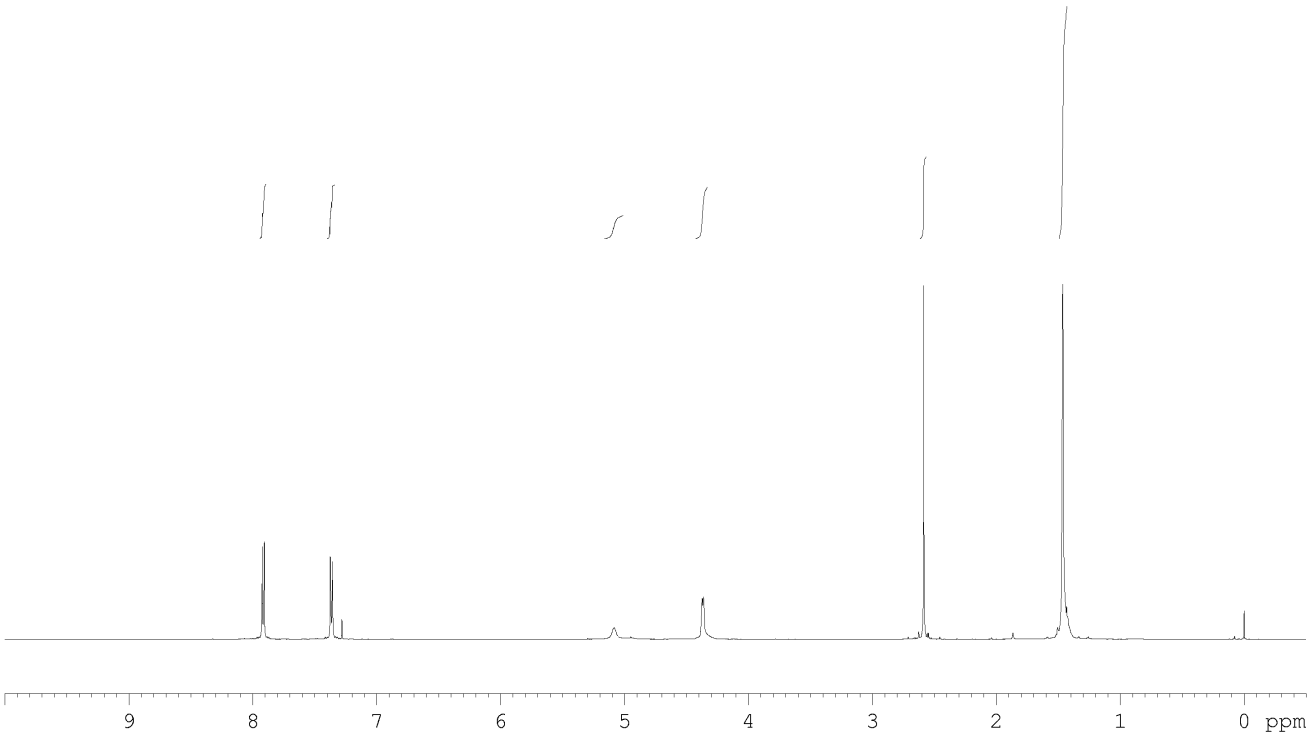

NHBoc
OHC

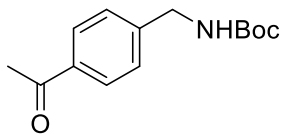

10
9
8
7
6
5
4
3
2
1
ppm

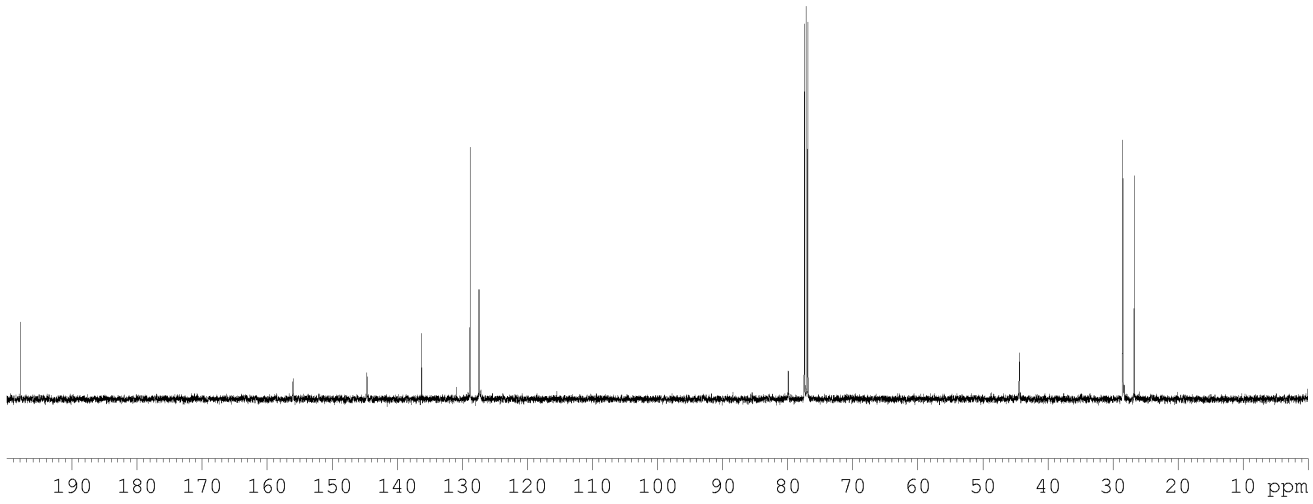

NHBoc
OHC


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBoc
O


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
O


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

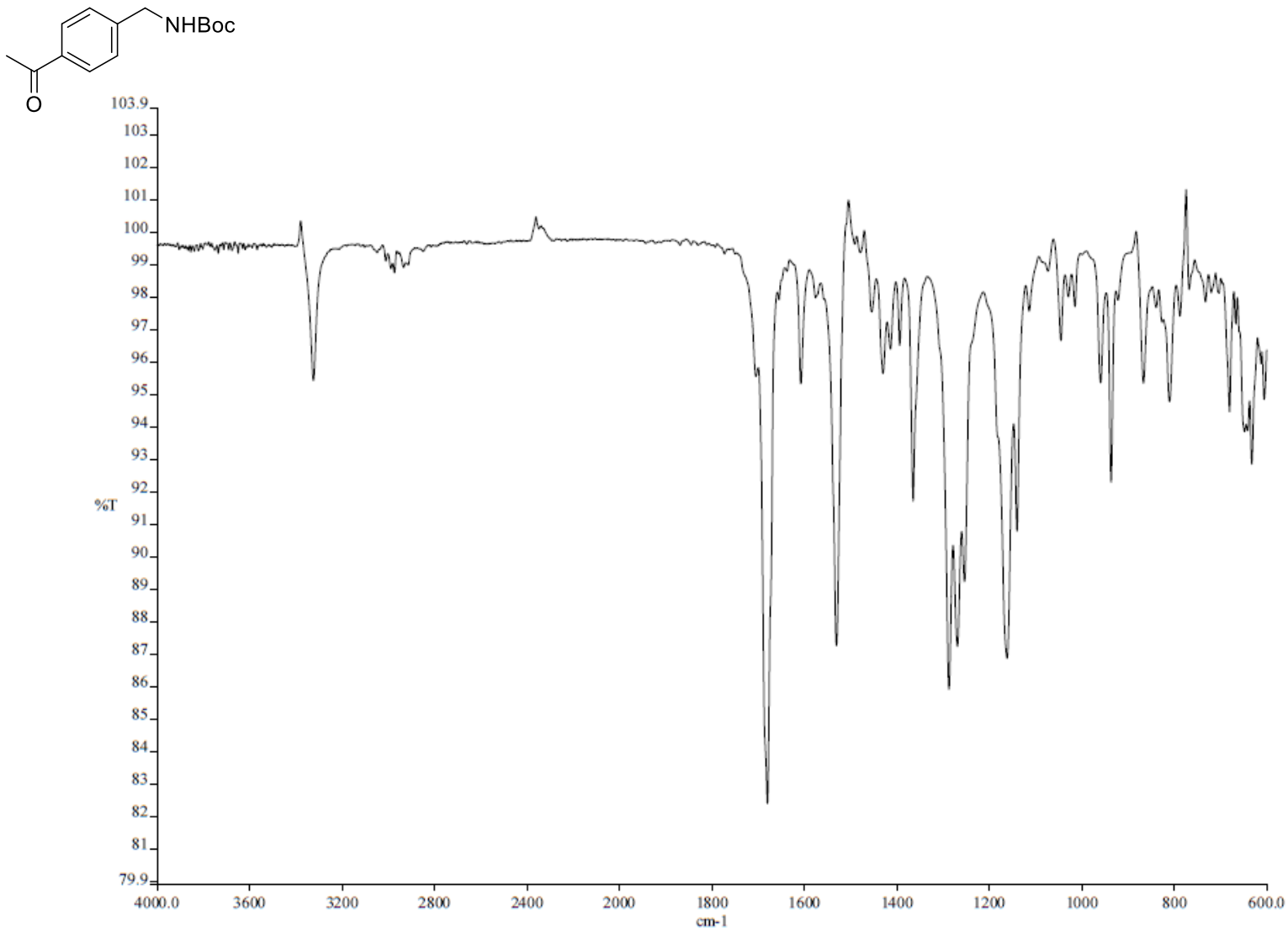
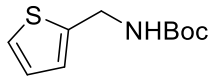
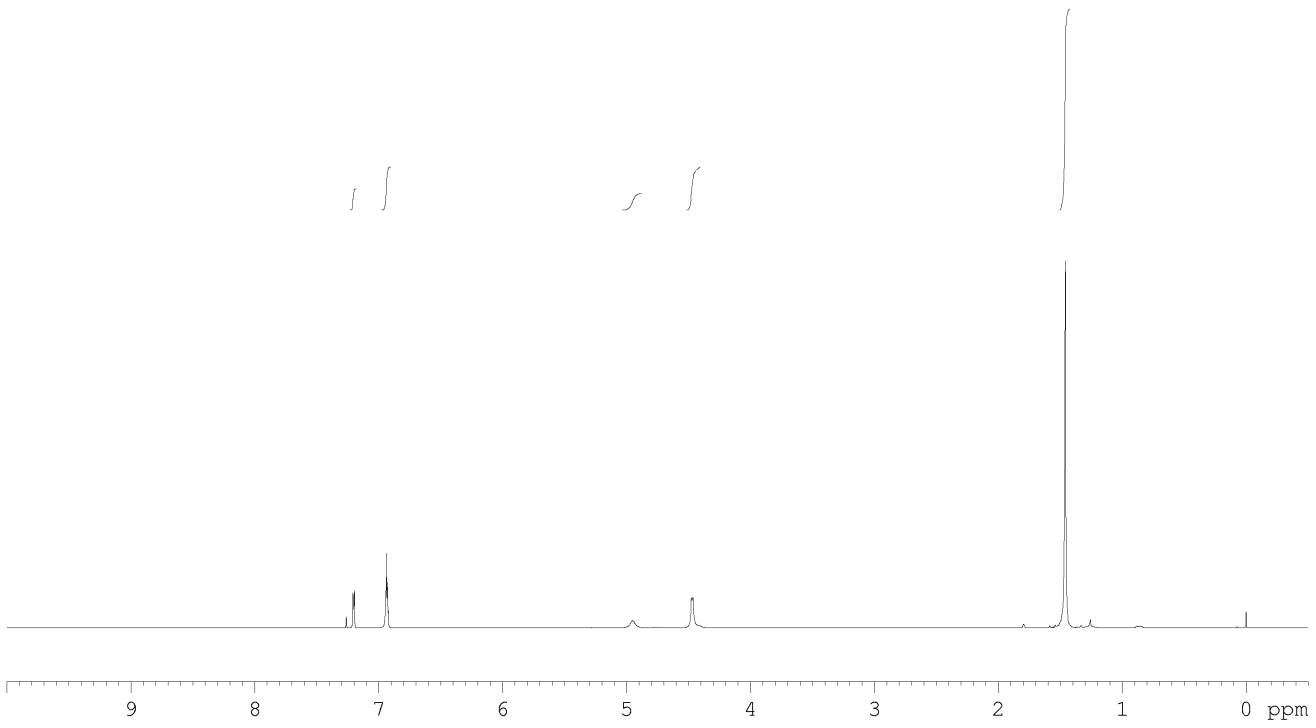
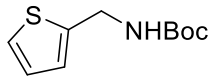
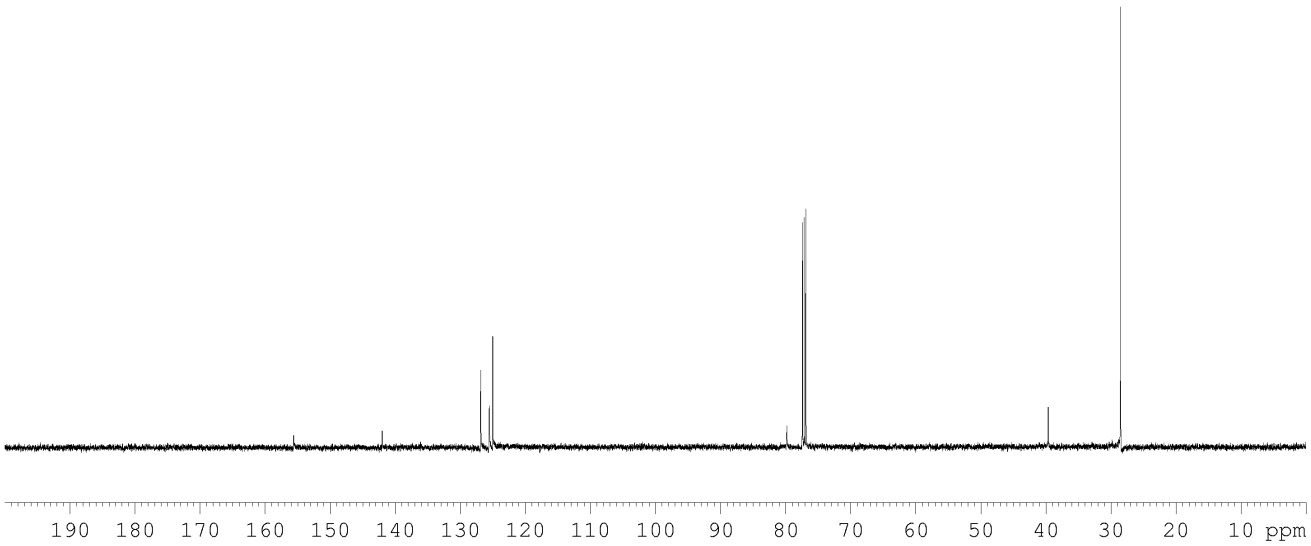


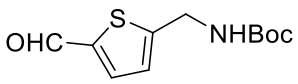
Figure A2.108 Infrared Spectrum

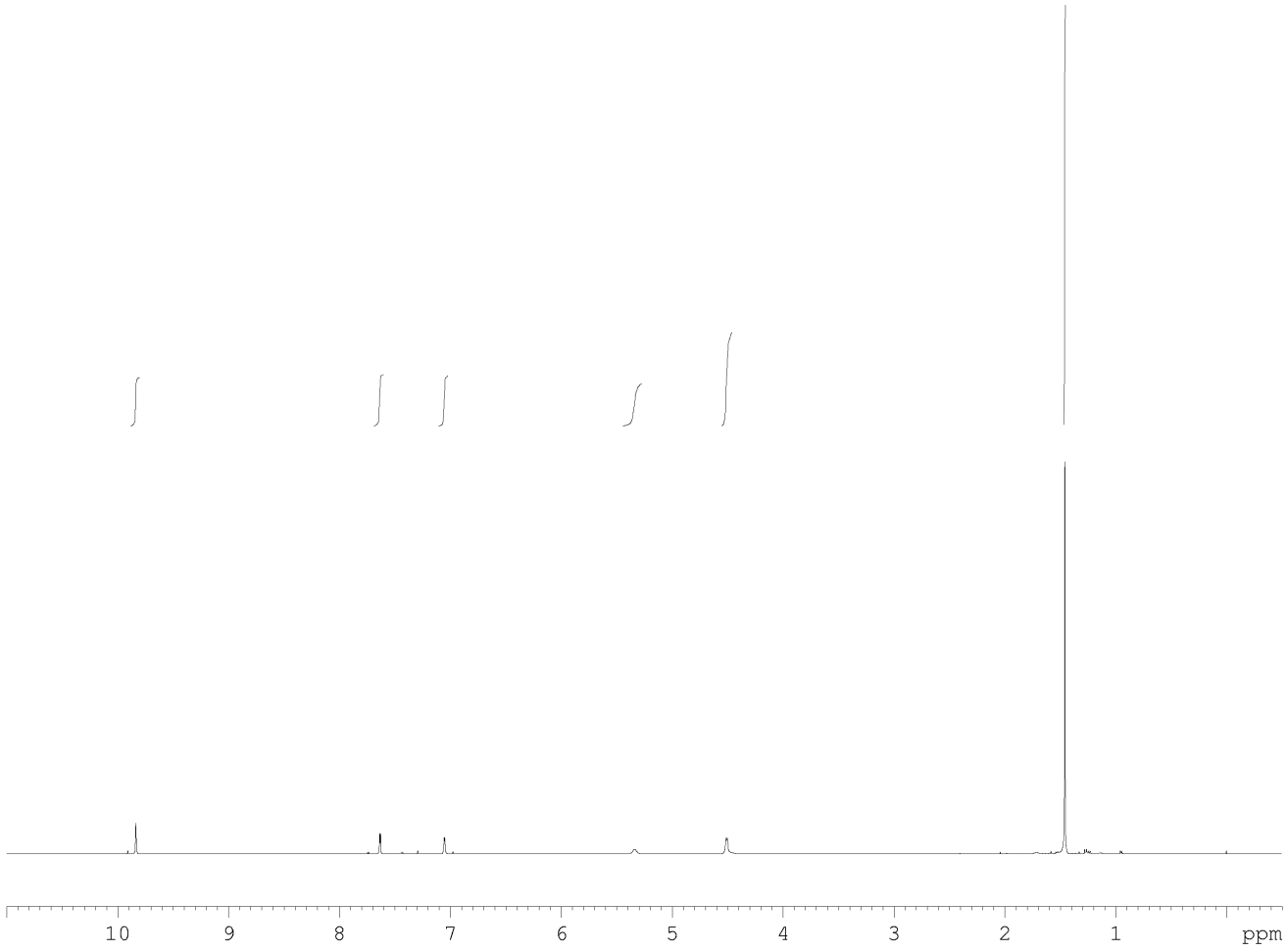

S
NHBoc

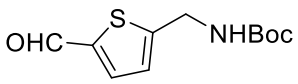

9
8
7
6
5
4
3
2
1
0 ppm

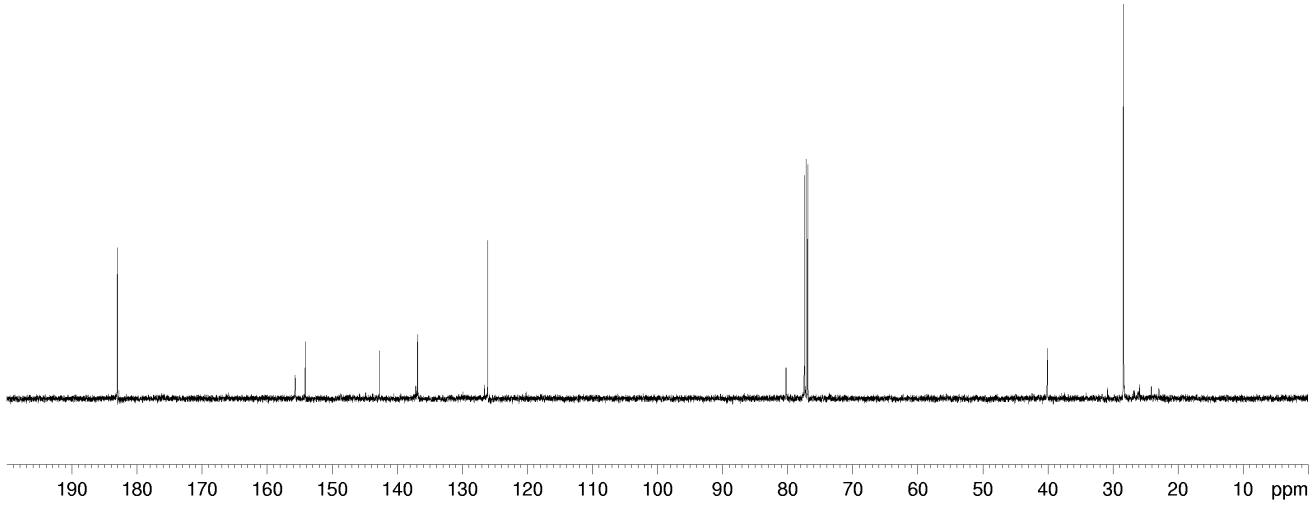

S
NHBoc

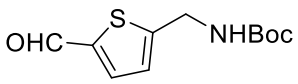

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OHC
S
NHBoc


10
9
8
7
6
5
4
3
2
1
ppm


OHC
S
NHBoc


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



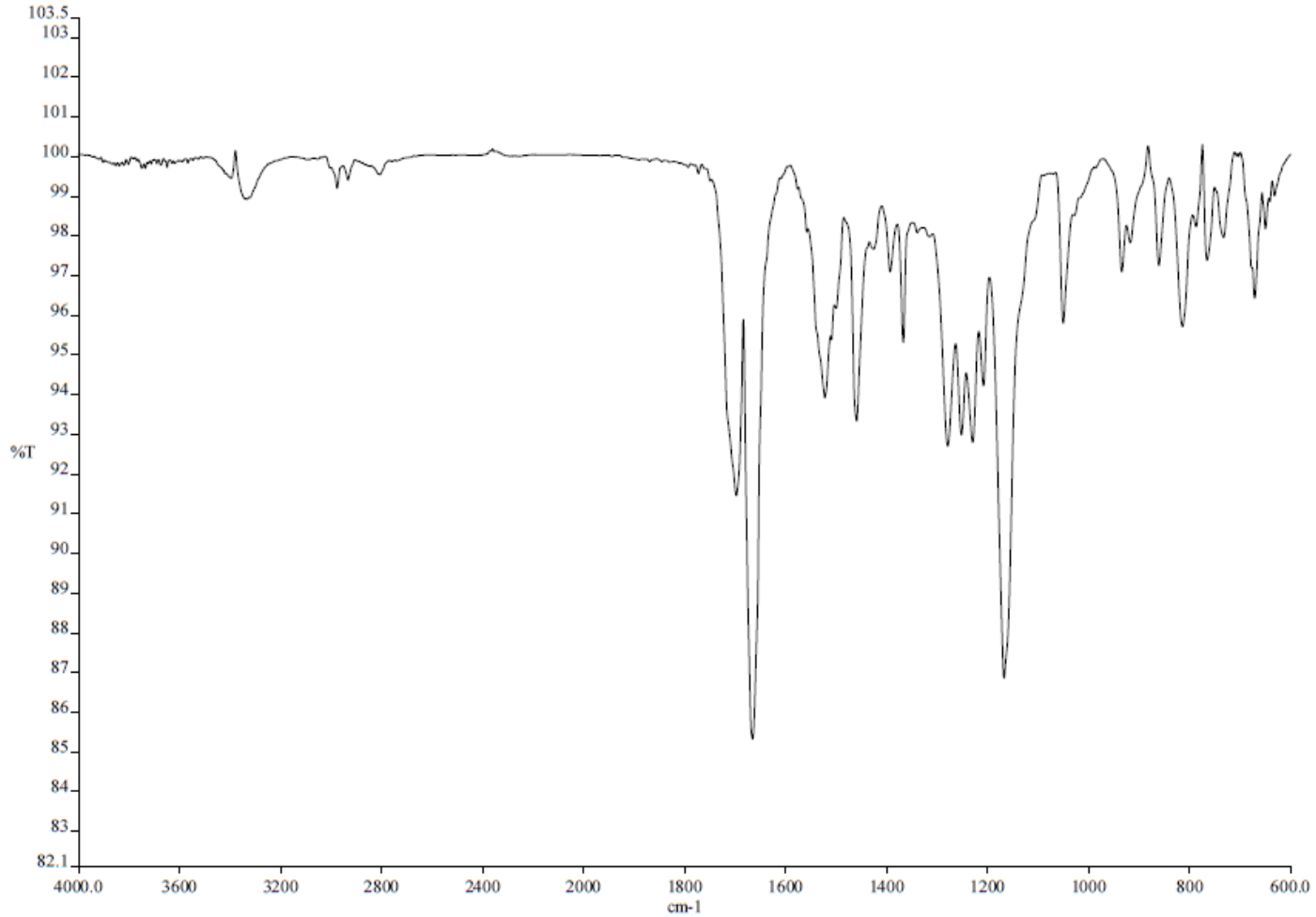
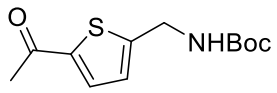
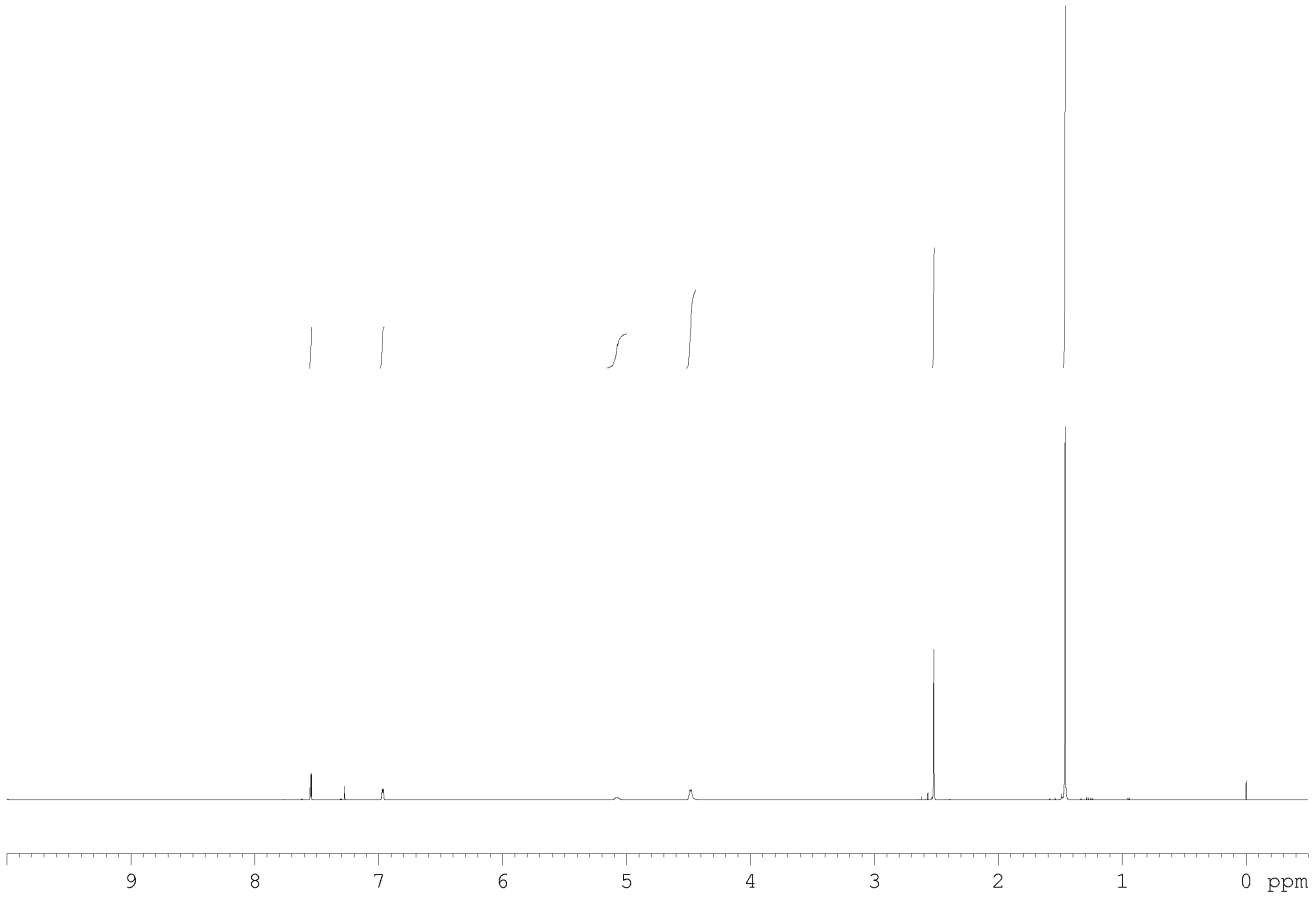
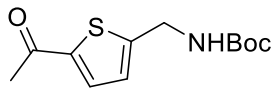
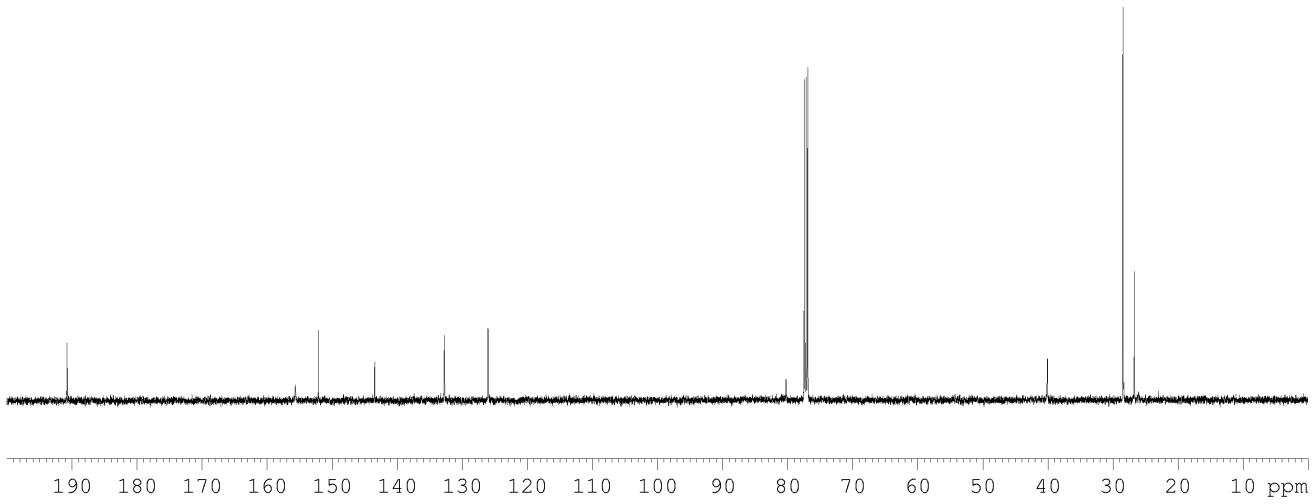


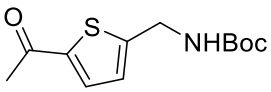
Figure A2.113 Infrared Spectrum


O
S
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


O
S
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



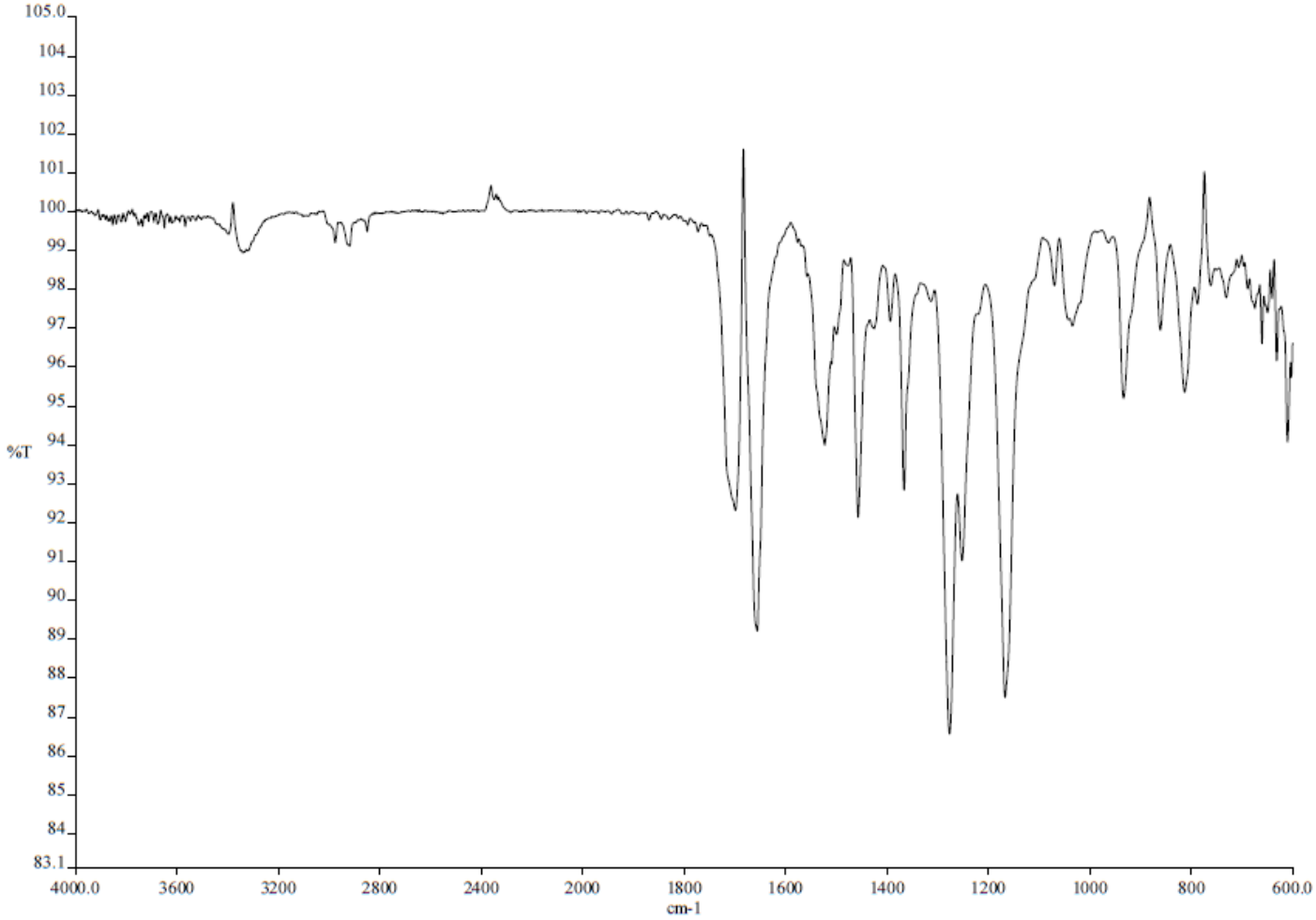
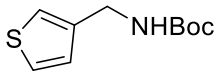
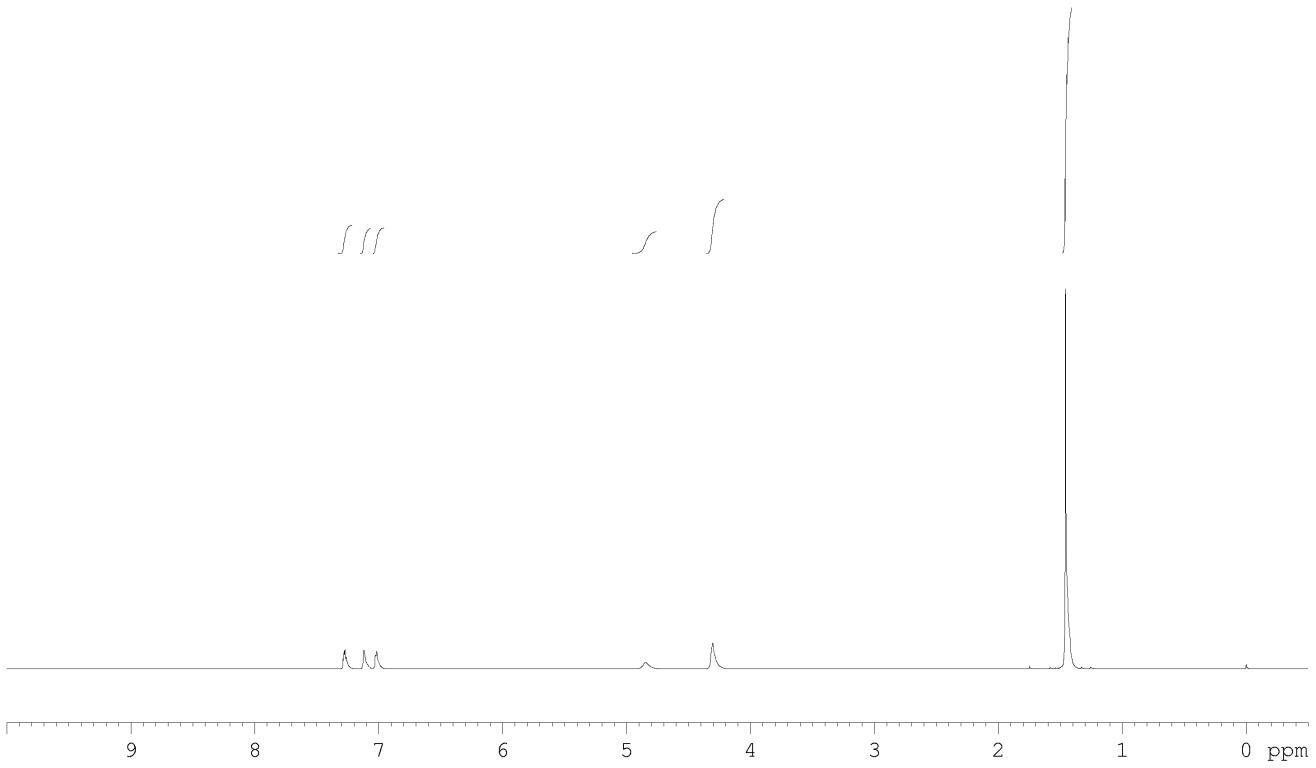
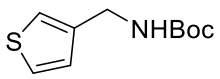
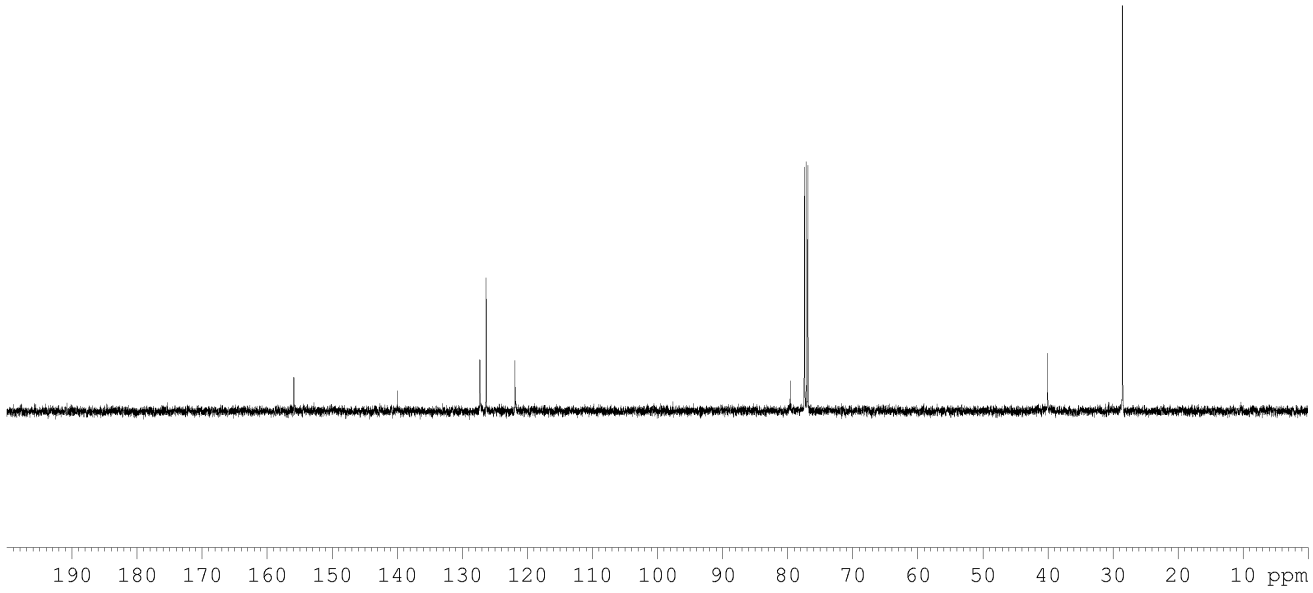


Figure A2.116 Infrared Spectrum


S
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


S
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

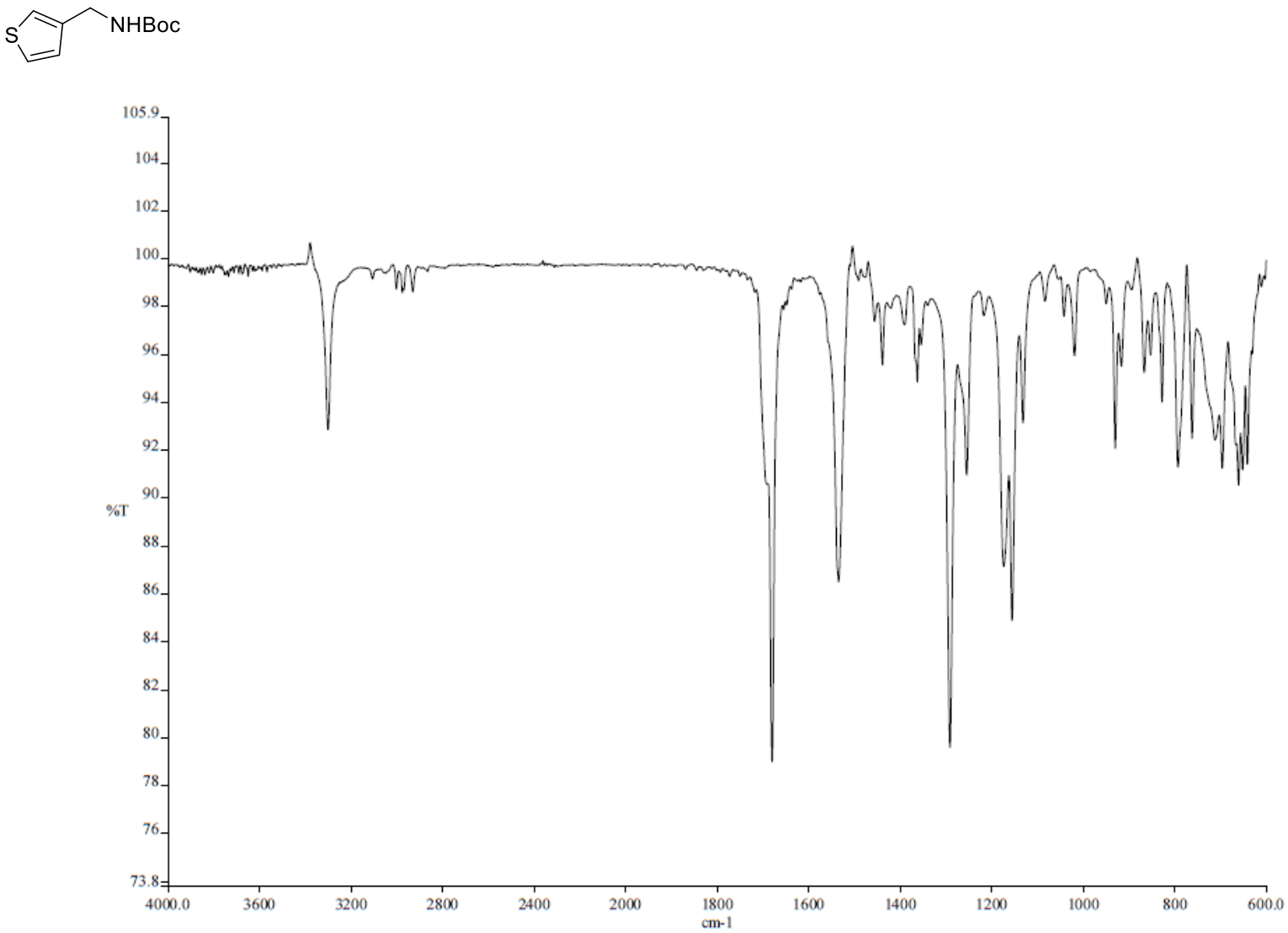
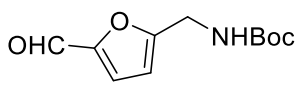
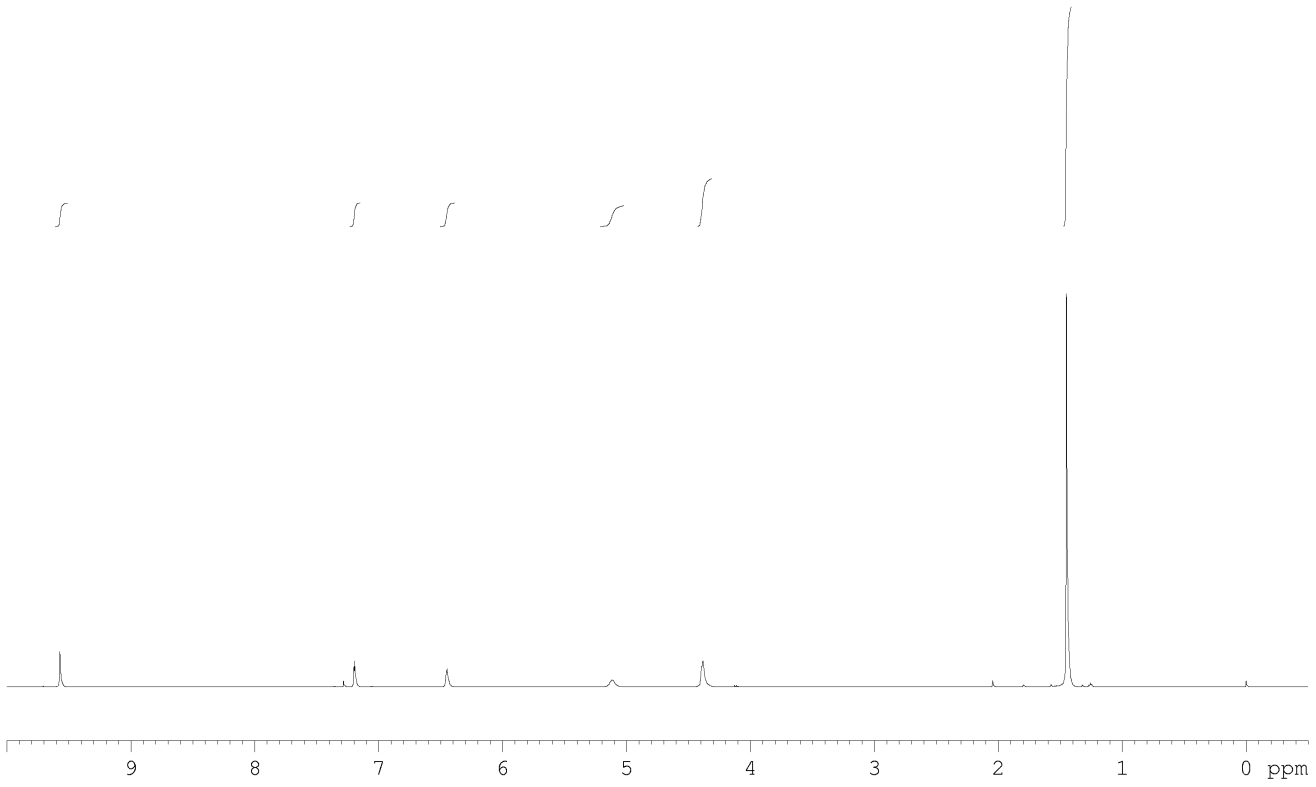
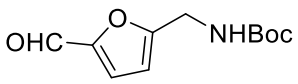
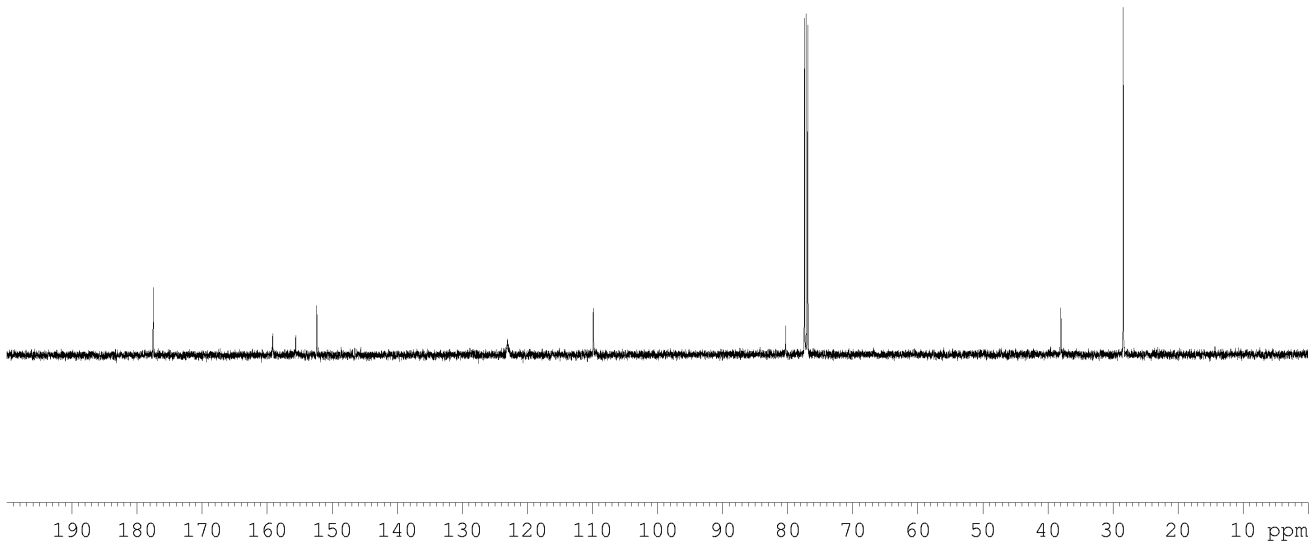


Figure A2.119 Infrared Spectrum


OHC
O
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


OHC
O
NHBoc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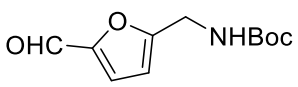


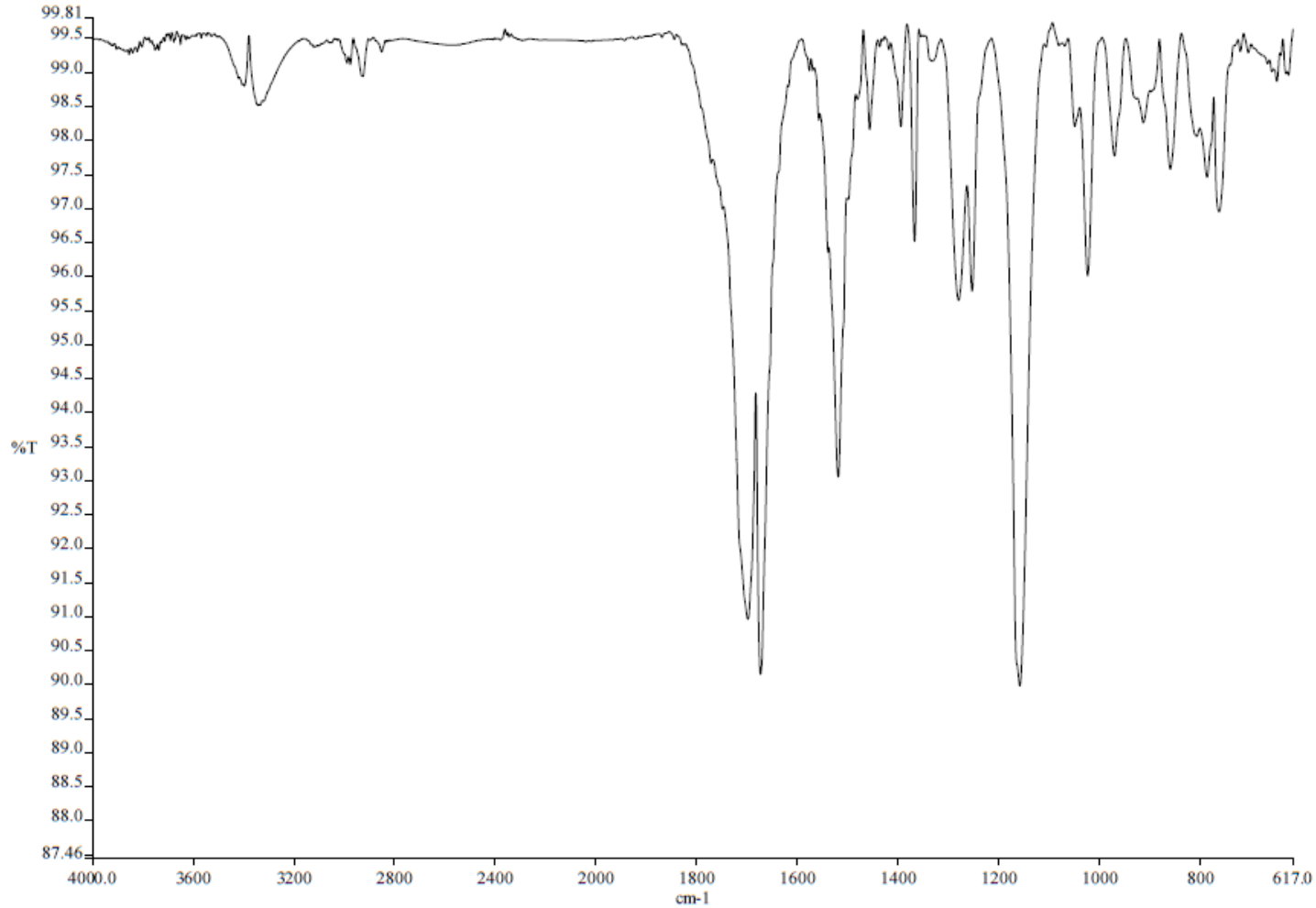
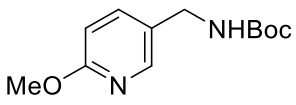
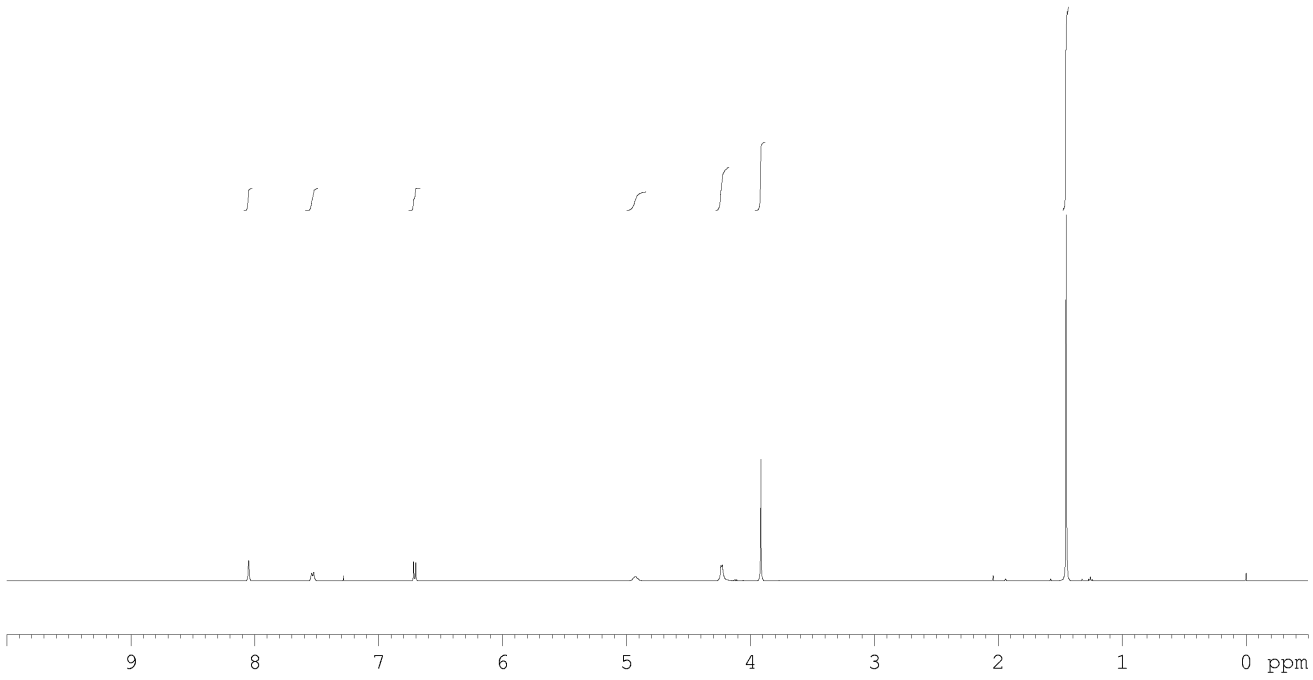
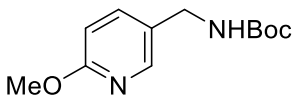
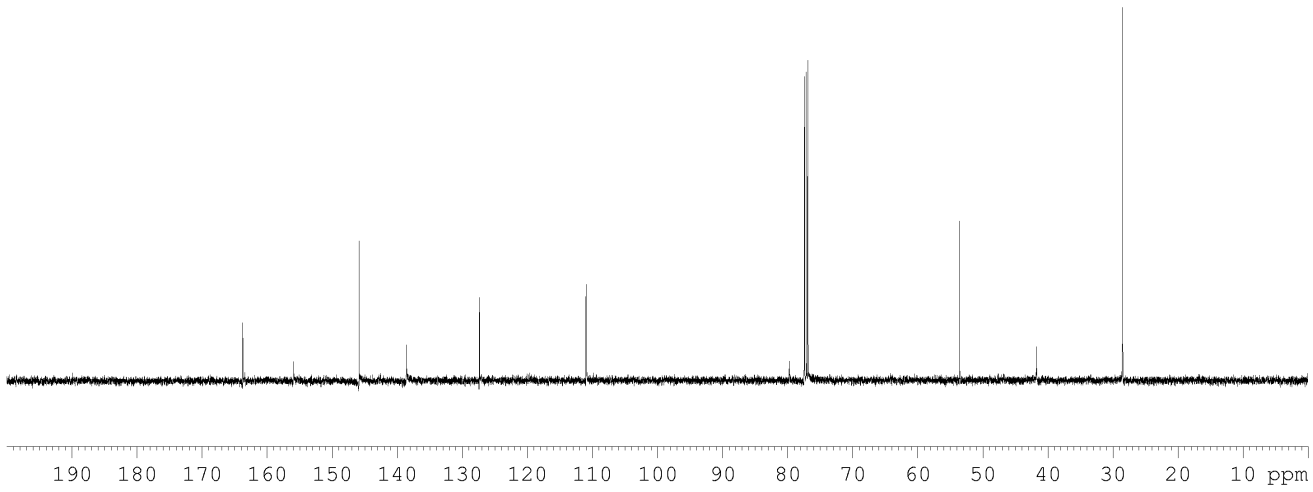


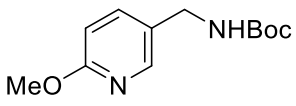
Figure A2.122 Infrared Spectrum


NHBoc
MeO
N


9
8
7
6
5
4
3
2
1
0
ppm


NHBoc
MeO
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



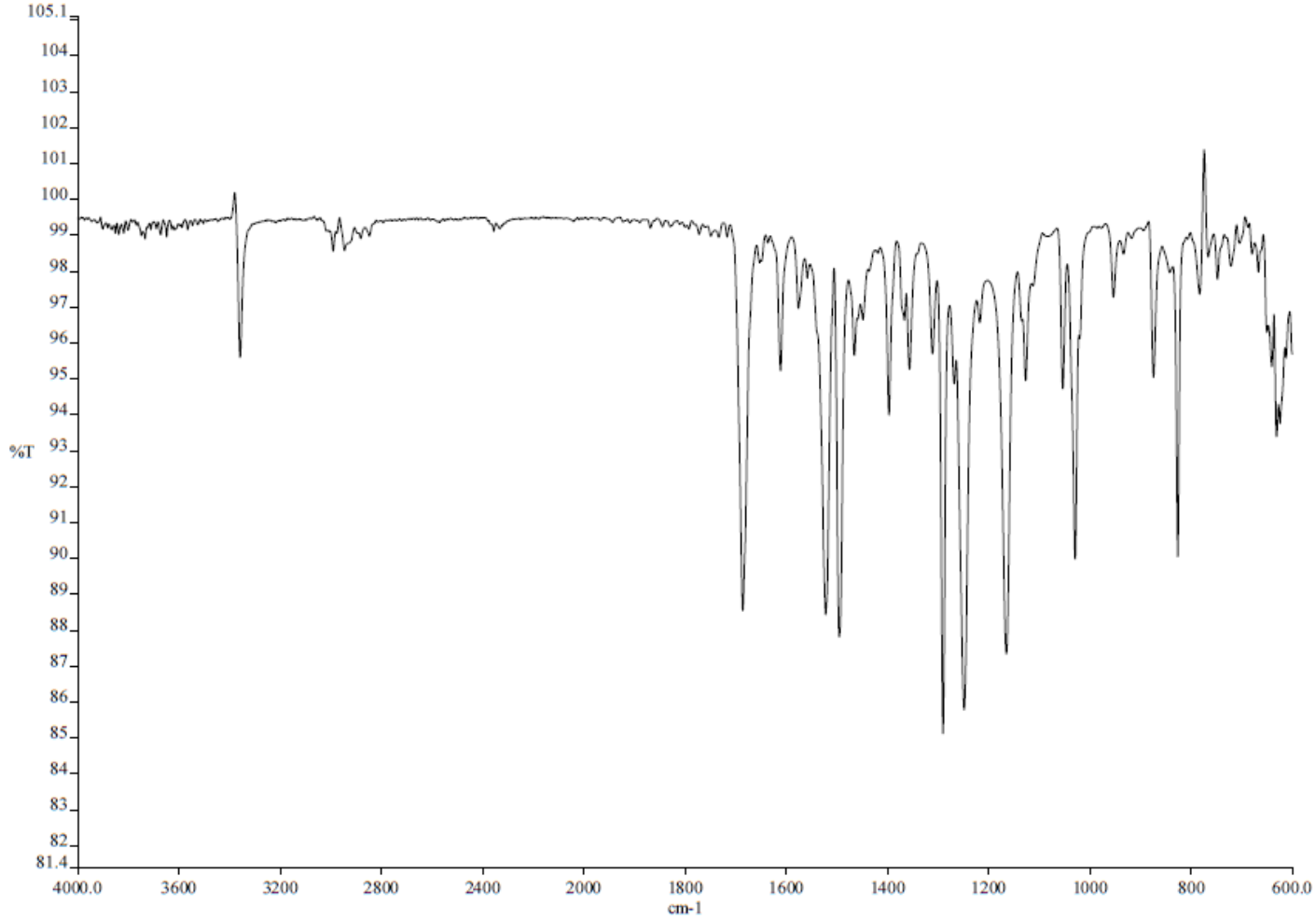
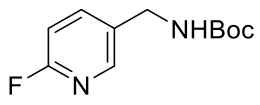
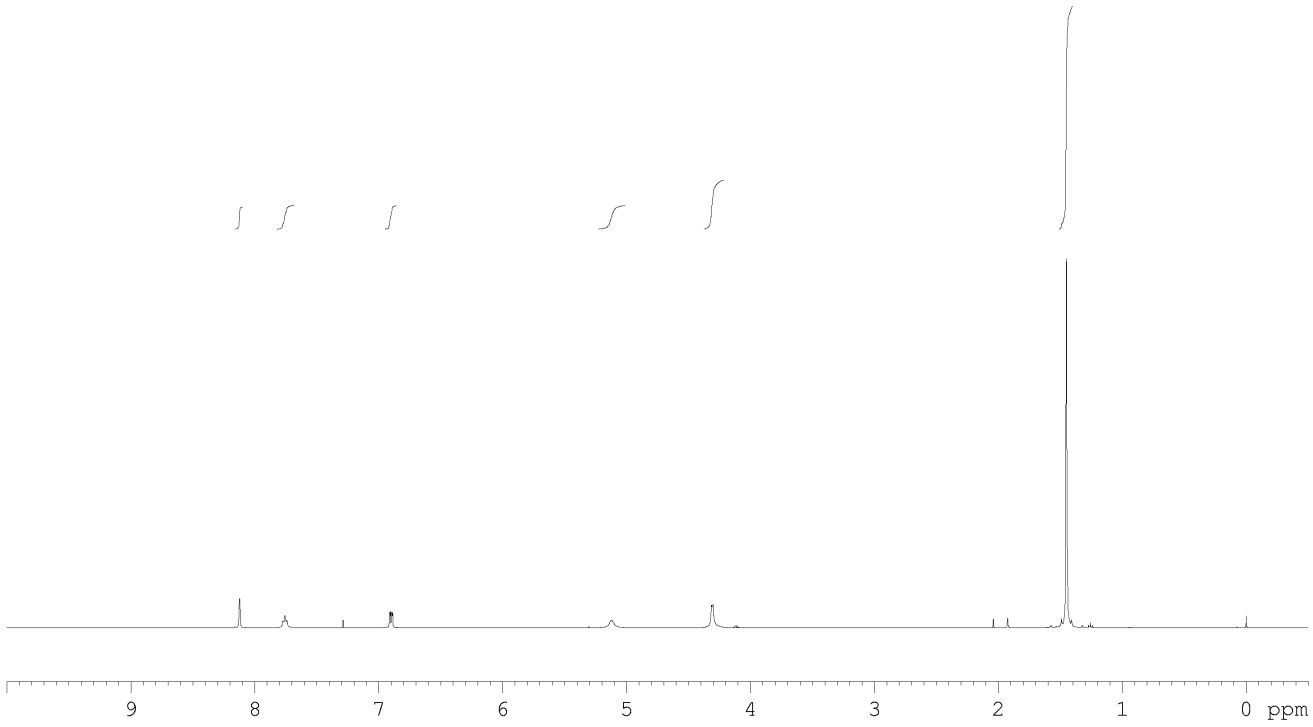
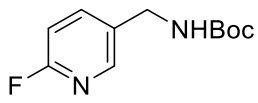
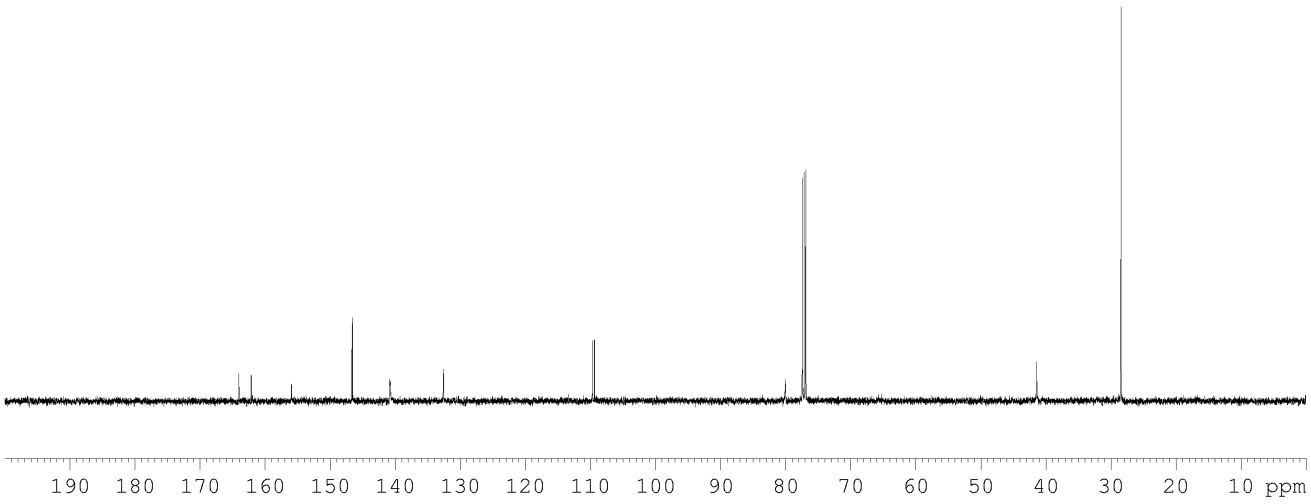


Figure A2.125 Infrared Spectrum


NHBoc
F
N


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
F
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

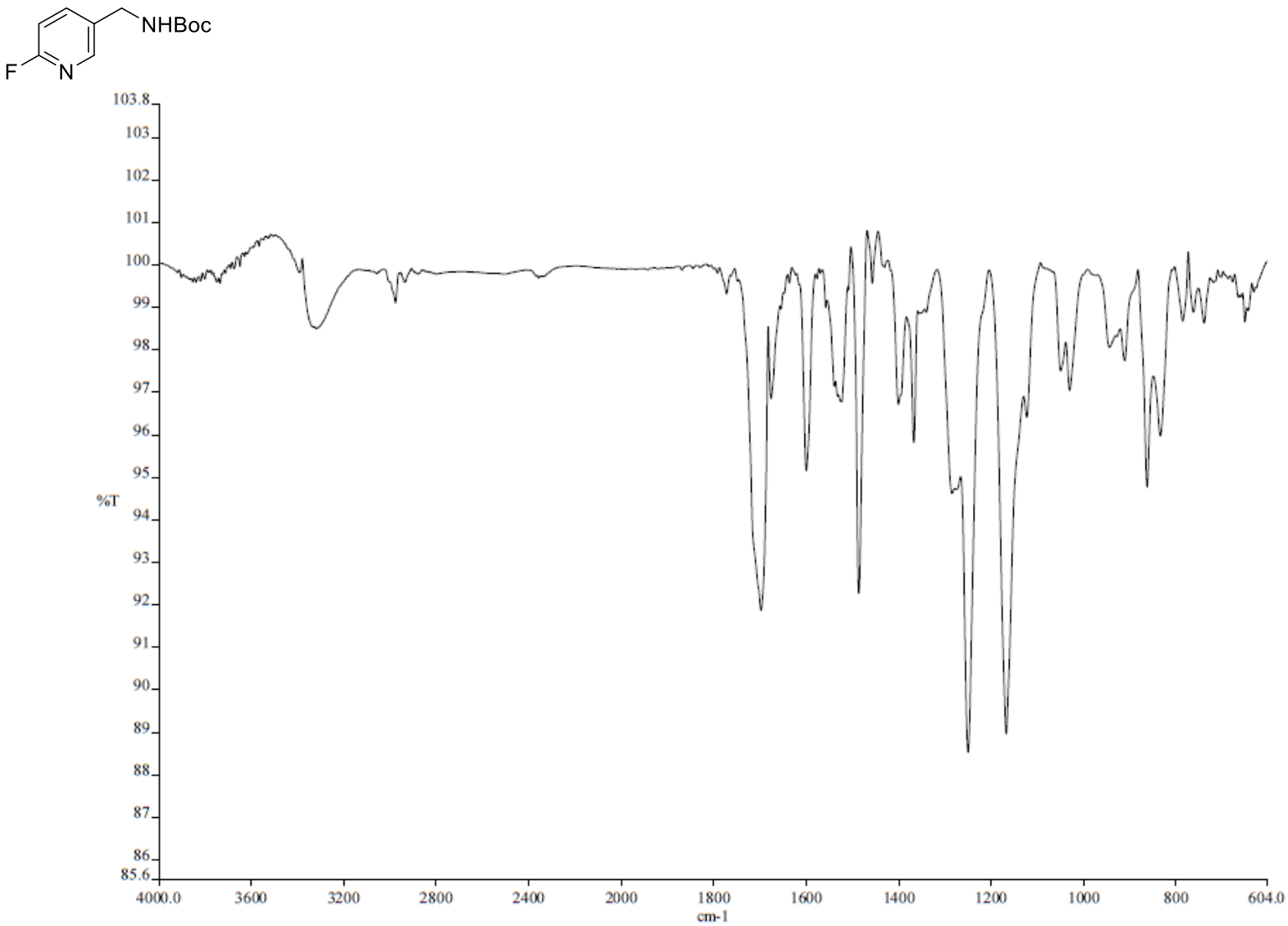
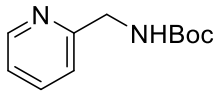
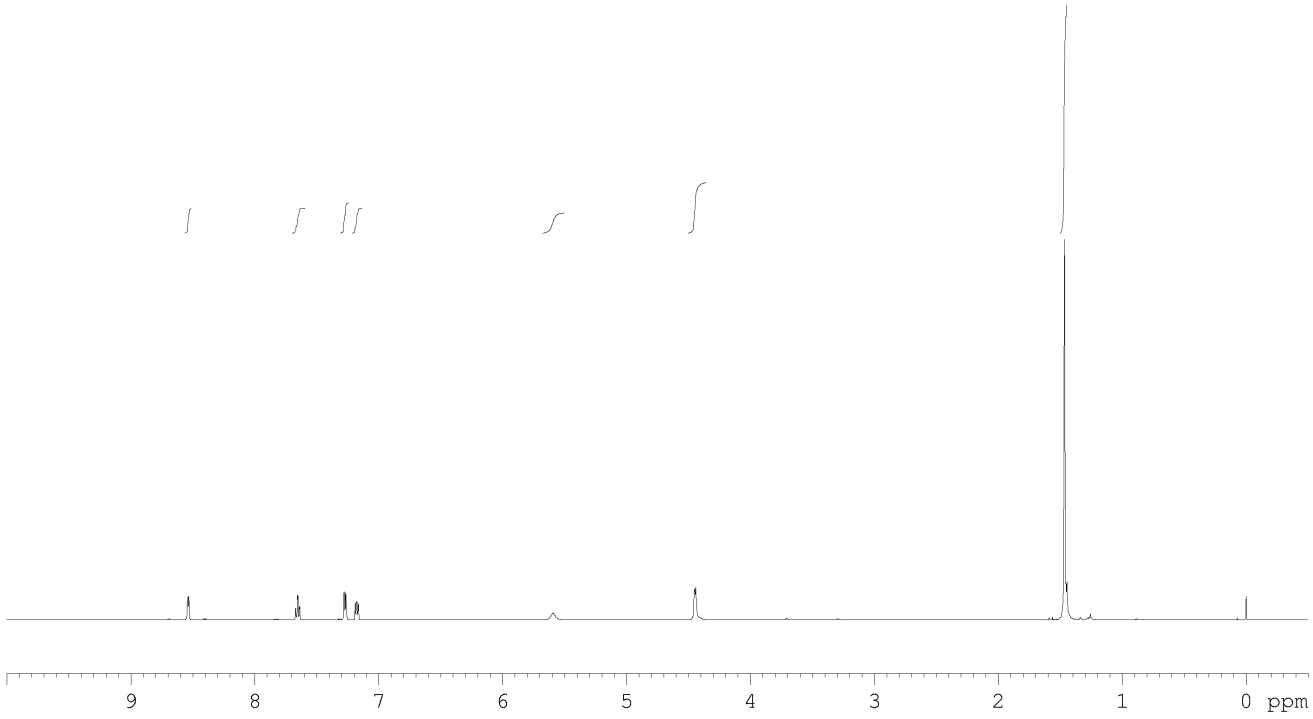
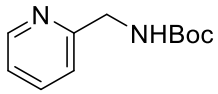
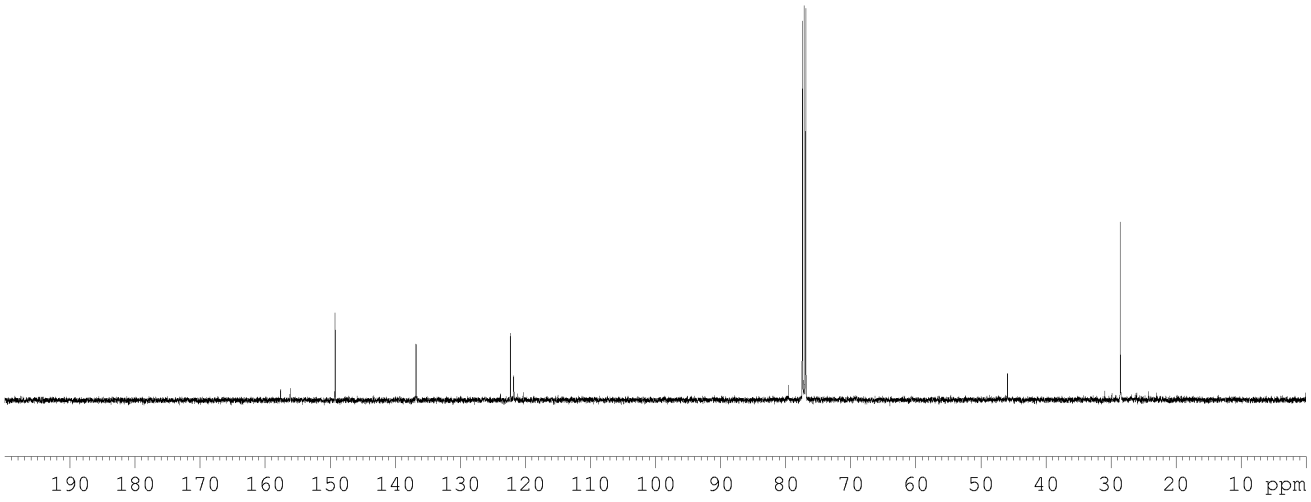


Figure A2.128 Infrared Spectrum


N
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


N
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

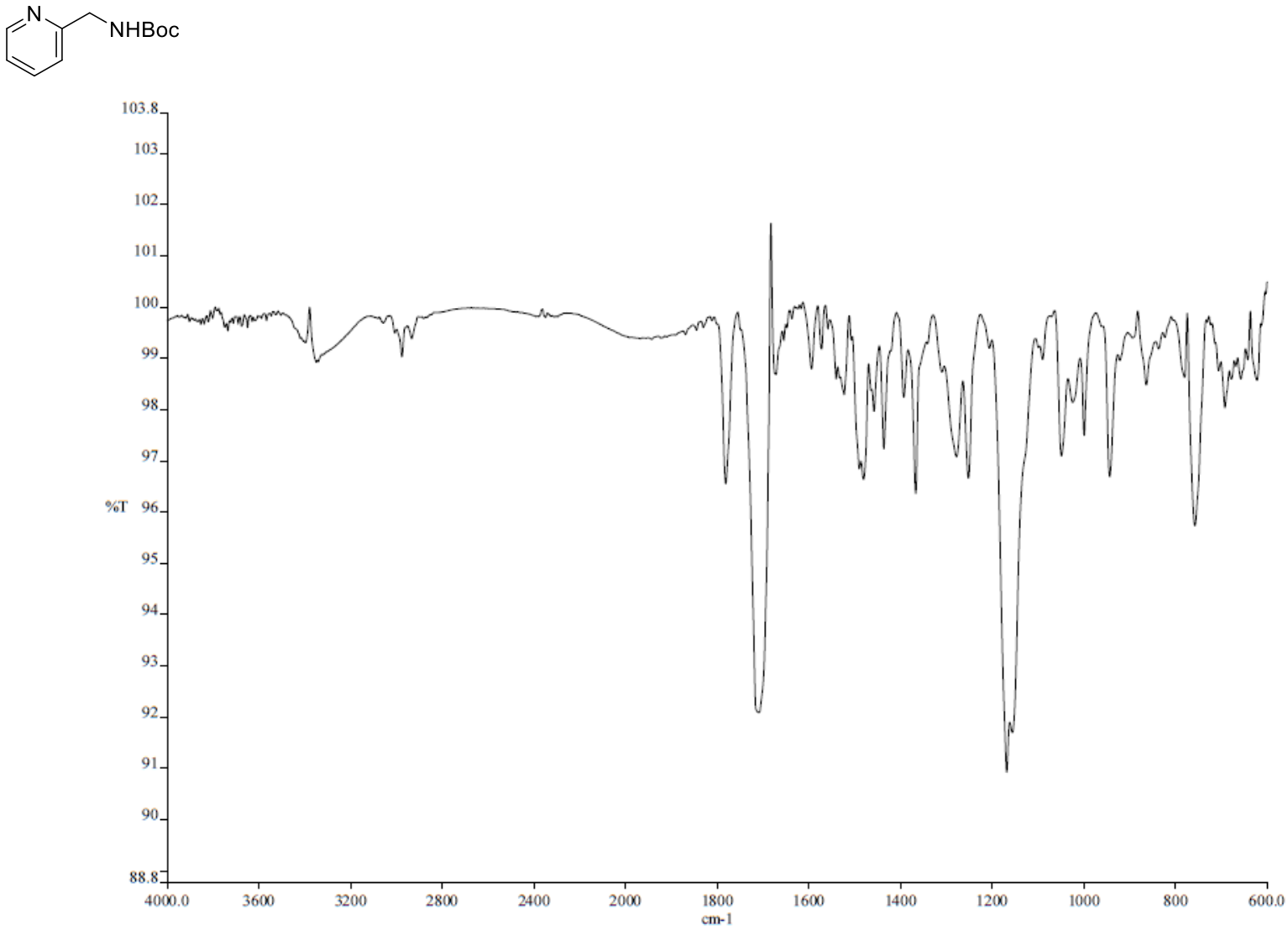
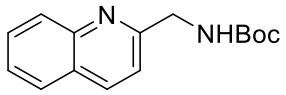
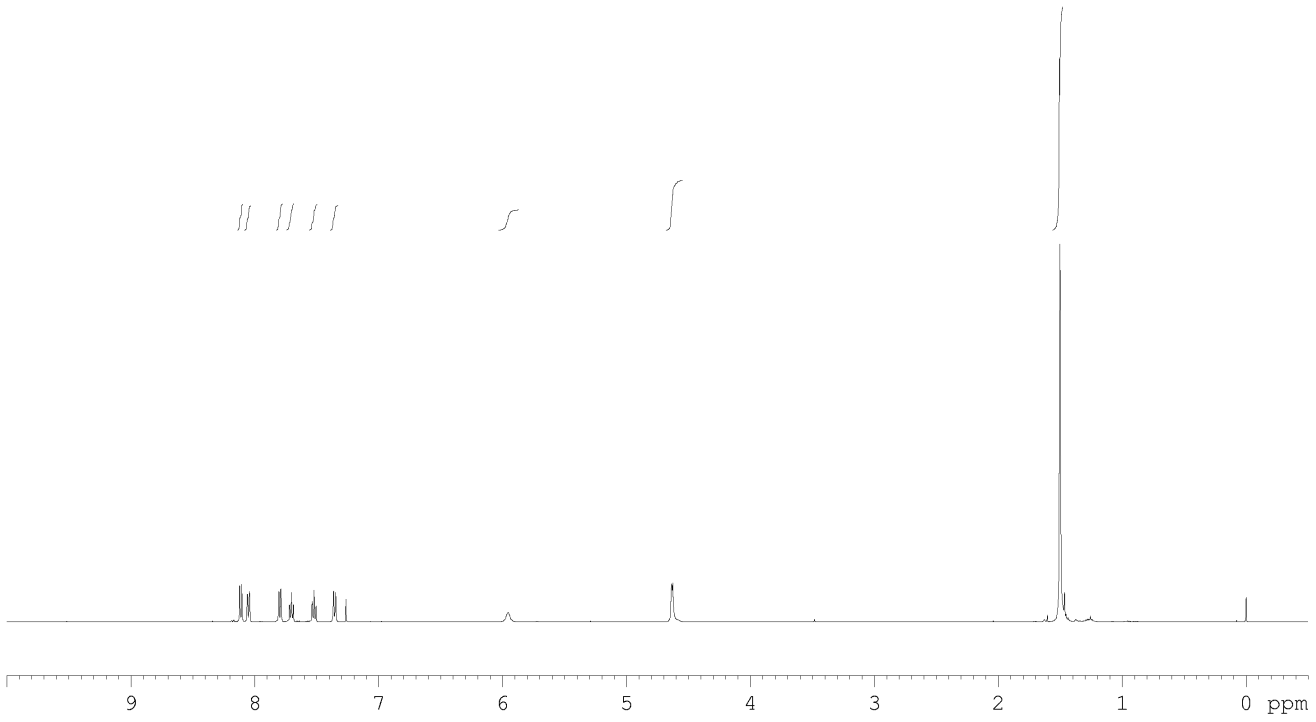
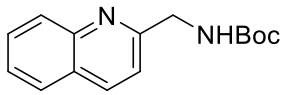
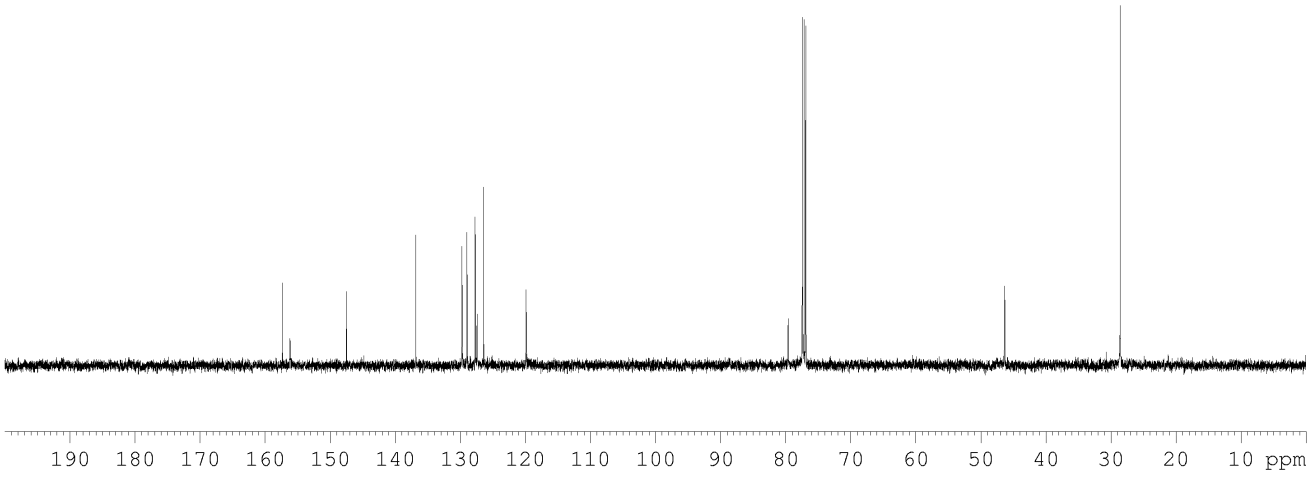


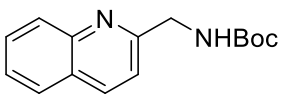
Figure A2.131 Infrared Spectrum


N
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


N
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



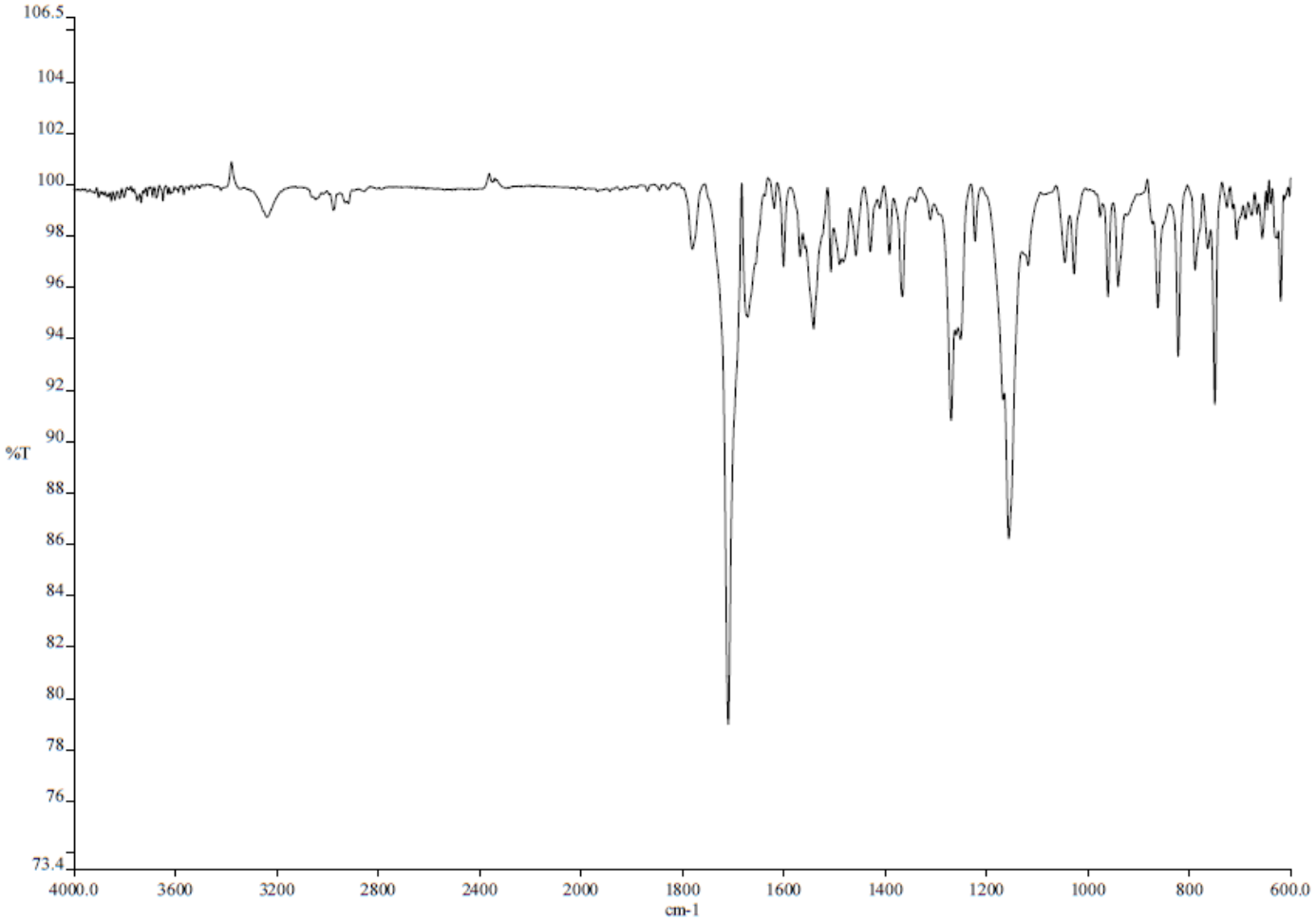
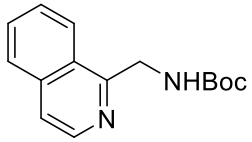
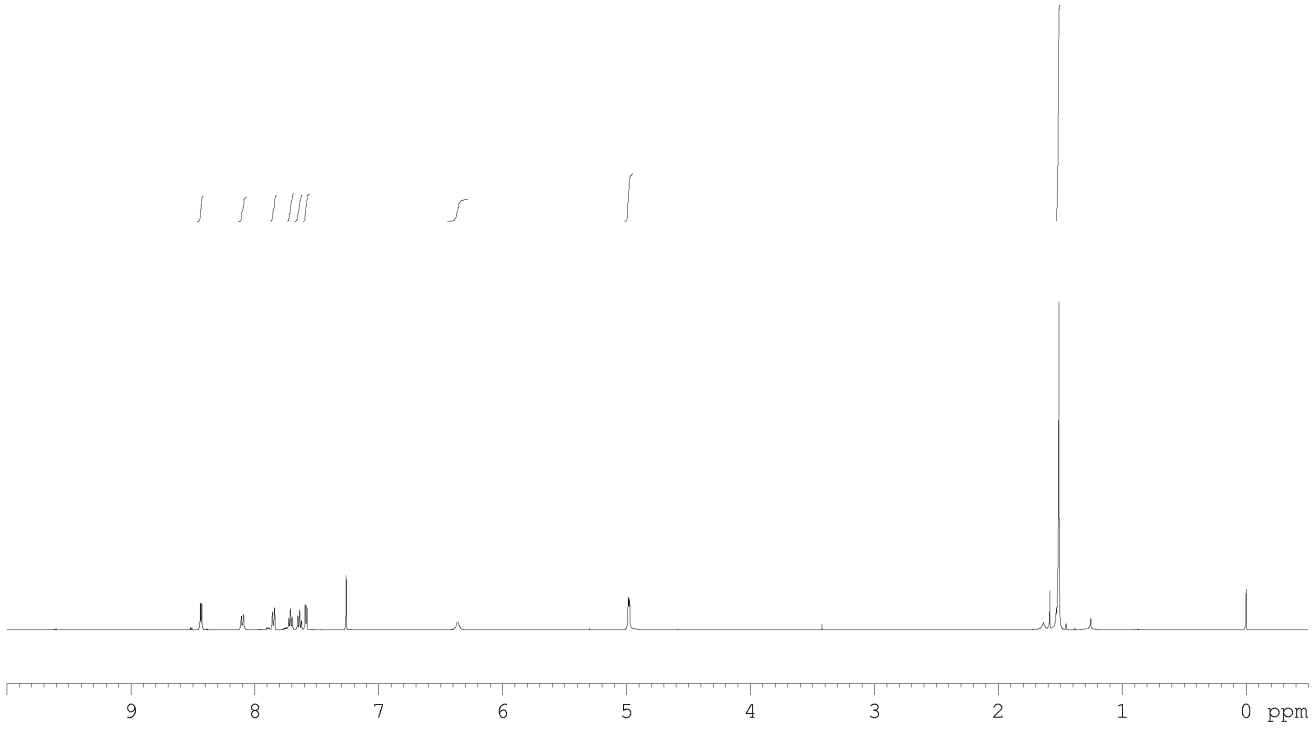
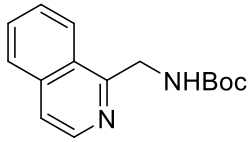
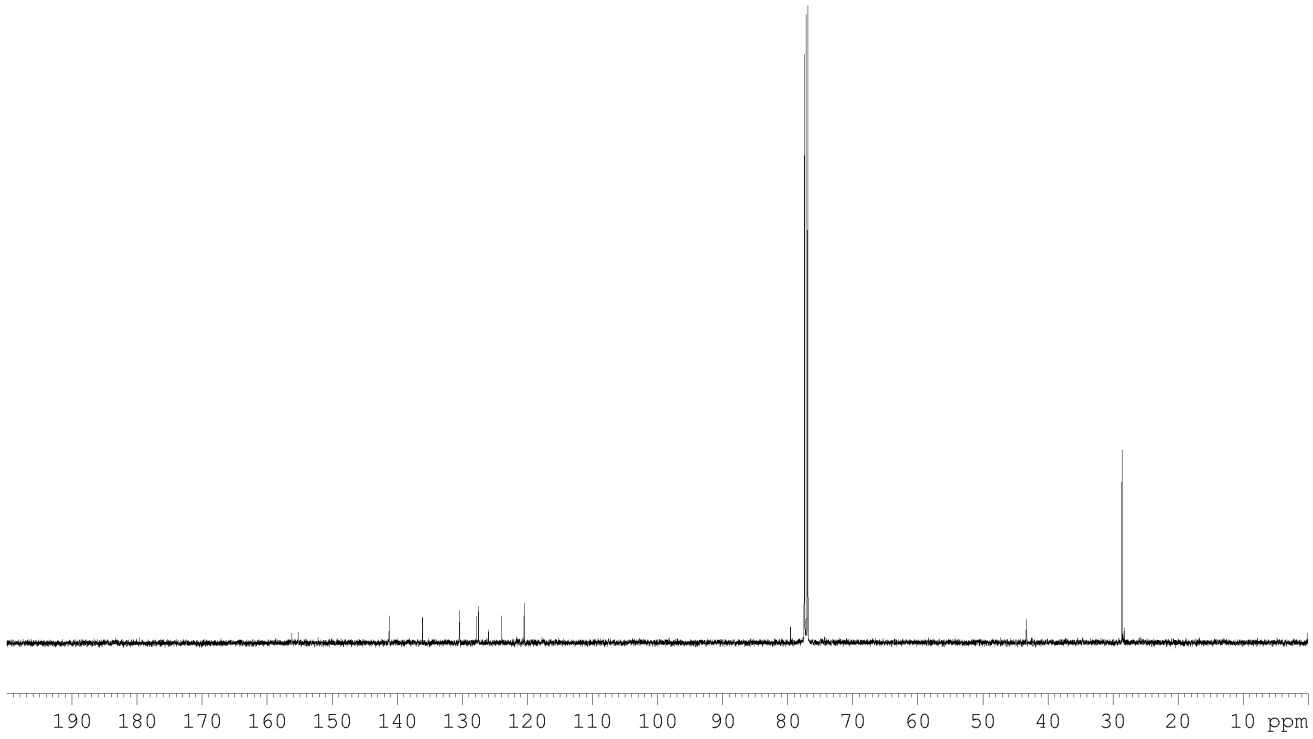


Figure A2.134 Infrared Spectrum


NHBoc
N


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

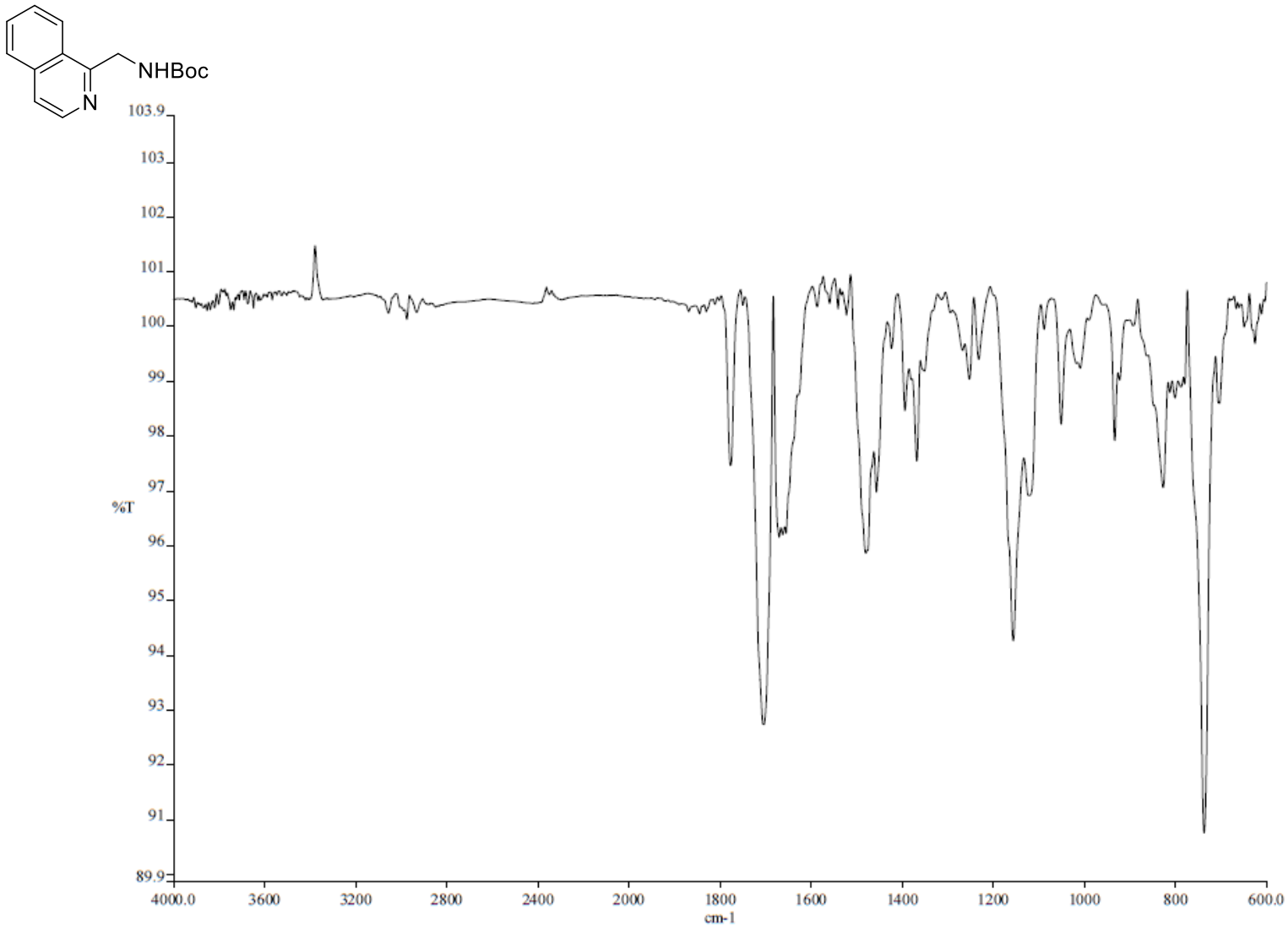
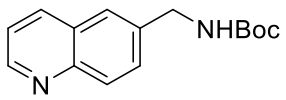
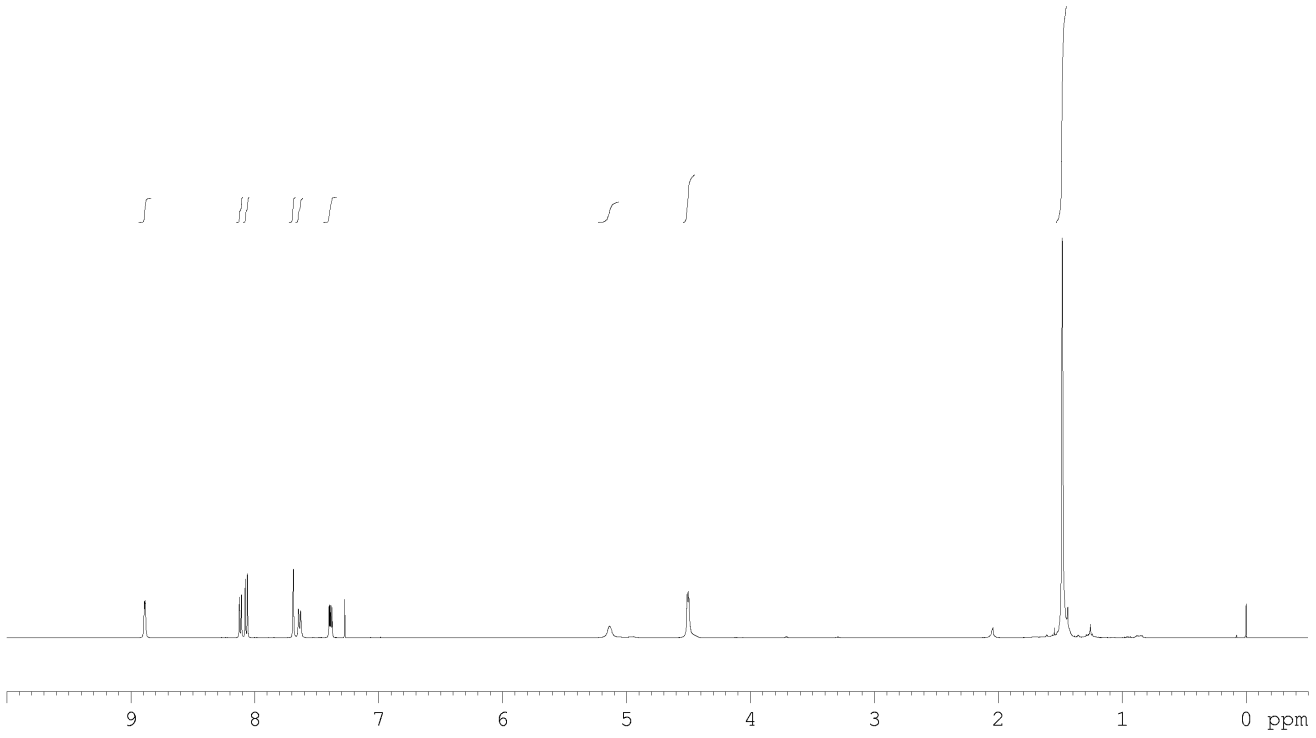


Figure A2.137 Infrared Spectrum


NHBoc
N


9
8
7
6
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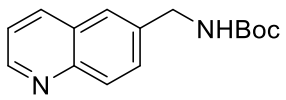
3
2
1
0 ppm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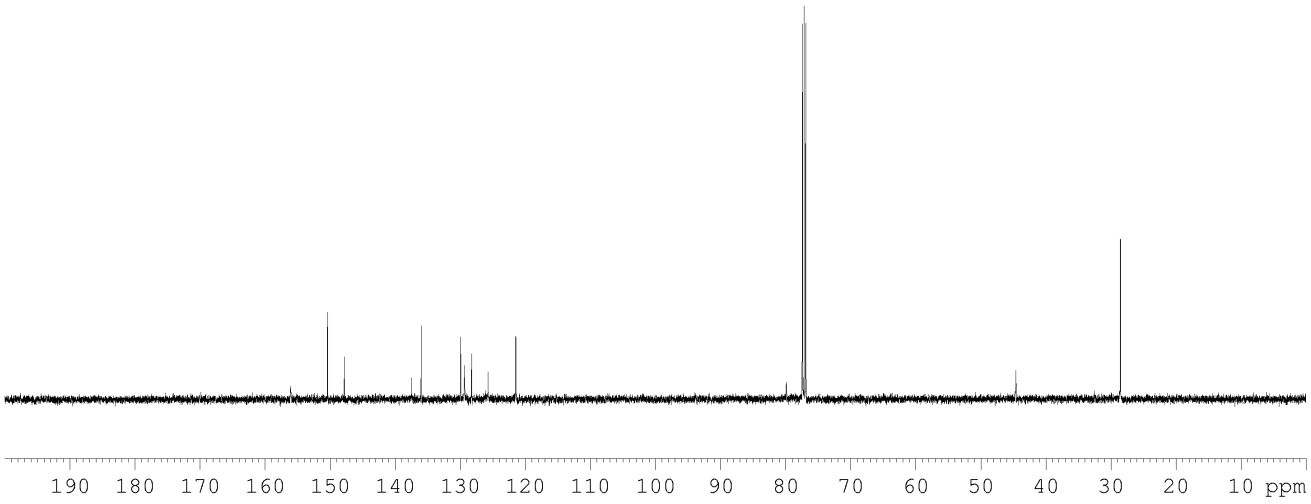
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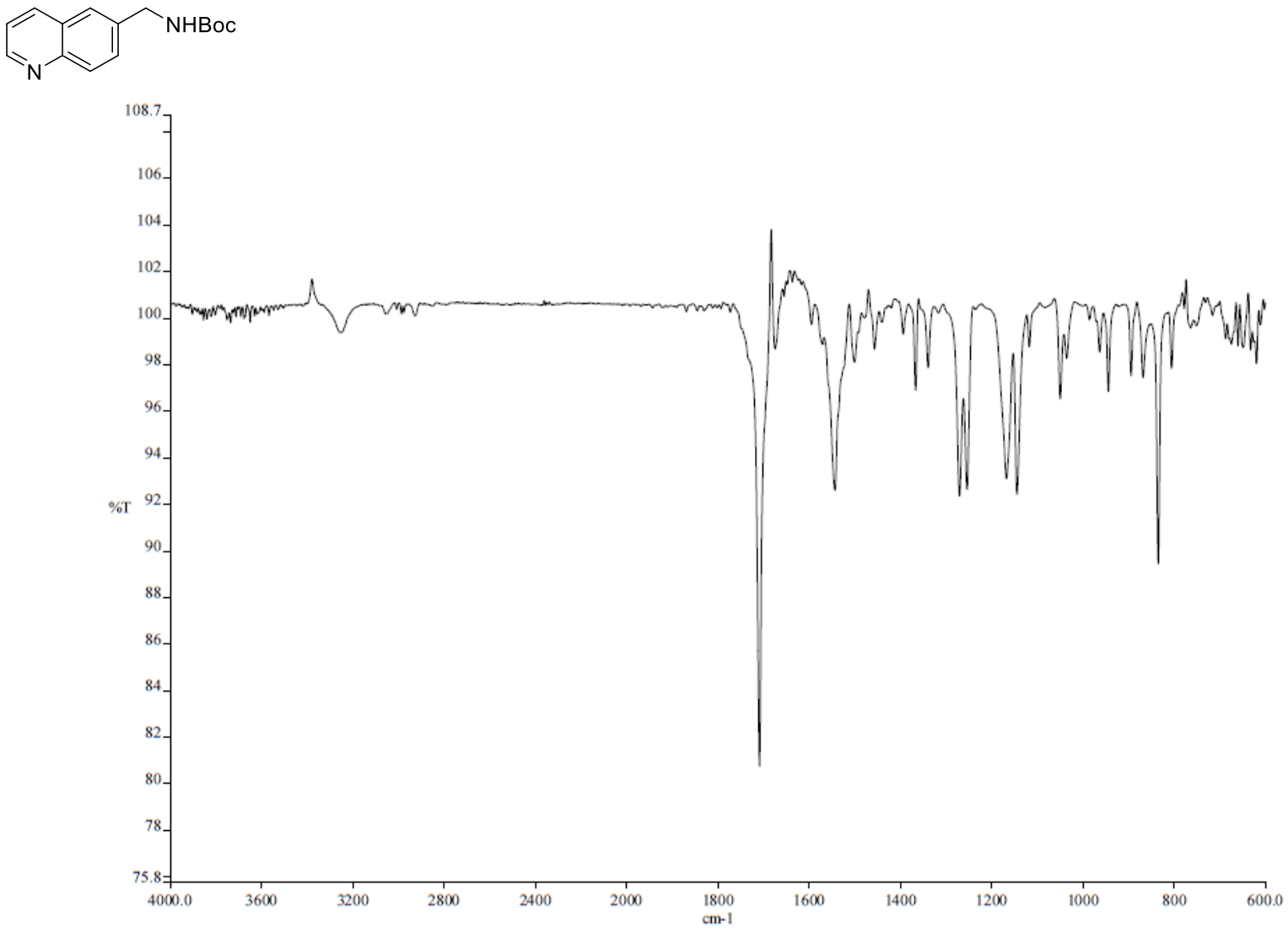
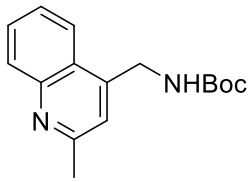


Figure A2.140 Infrared Spectrum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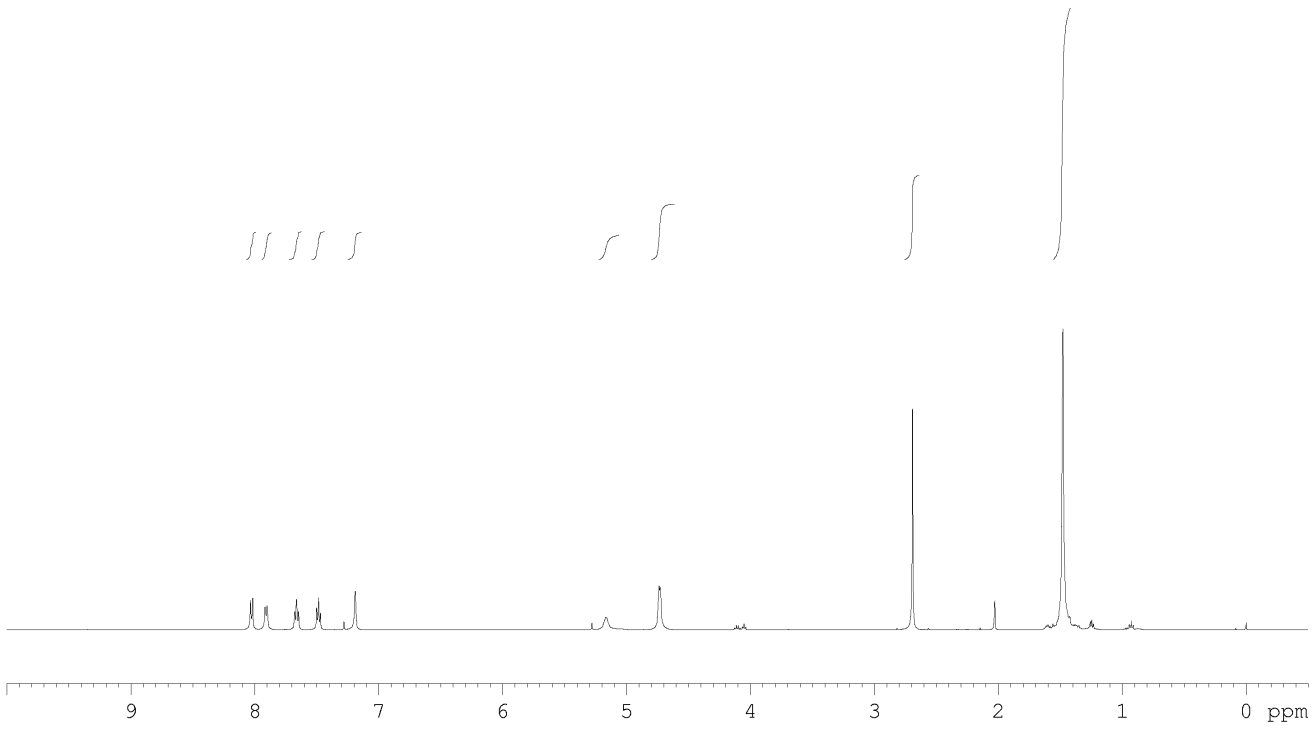
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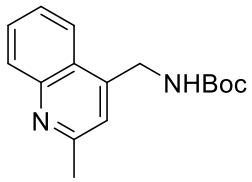
0 ppm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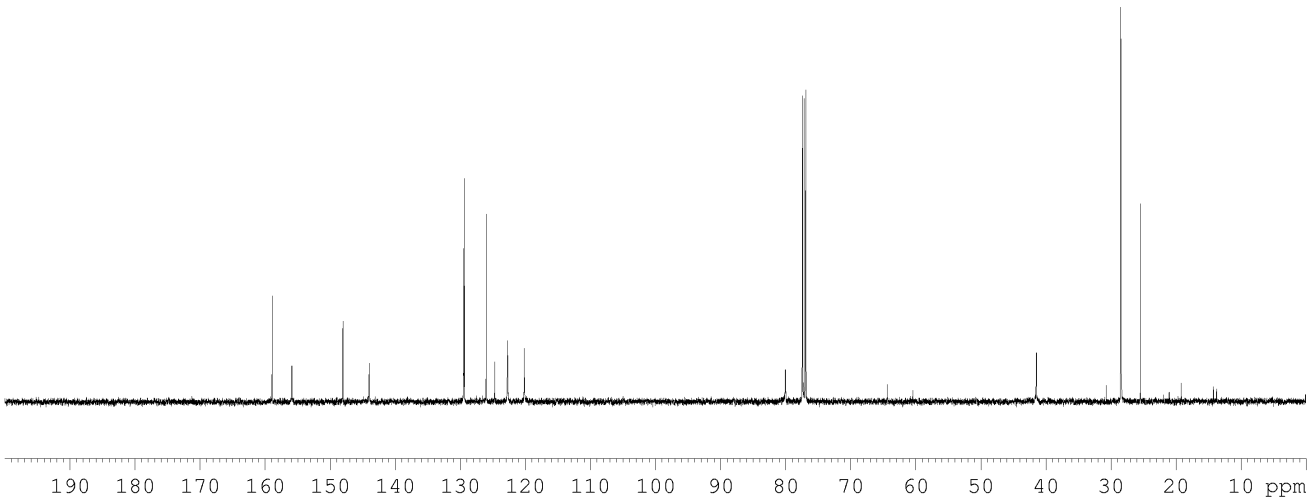
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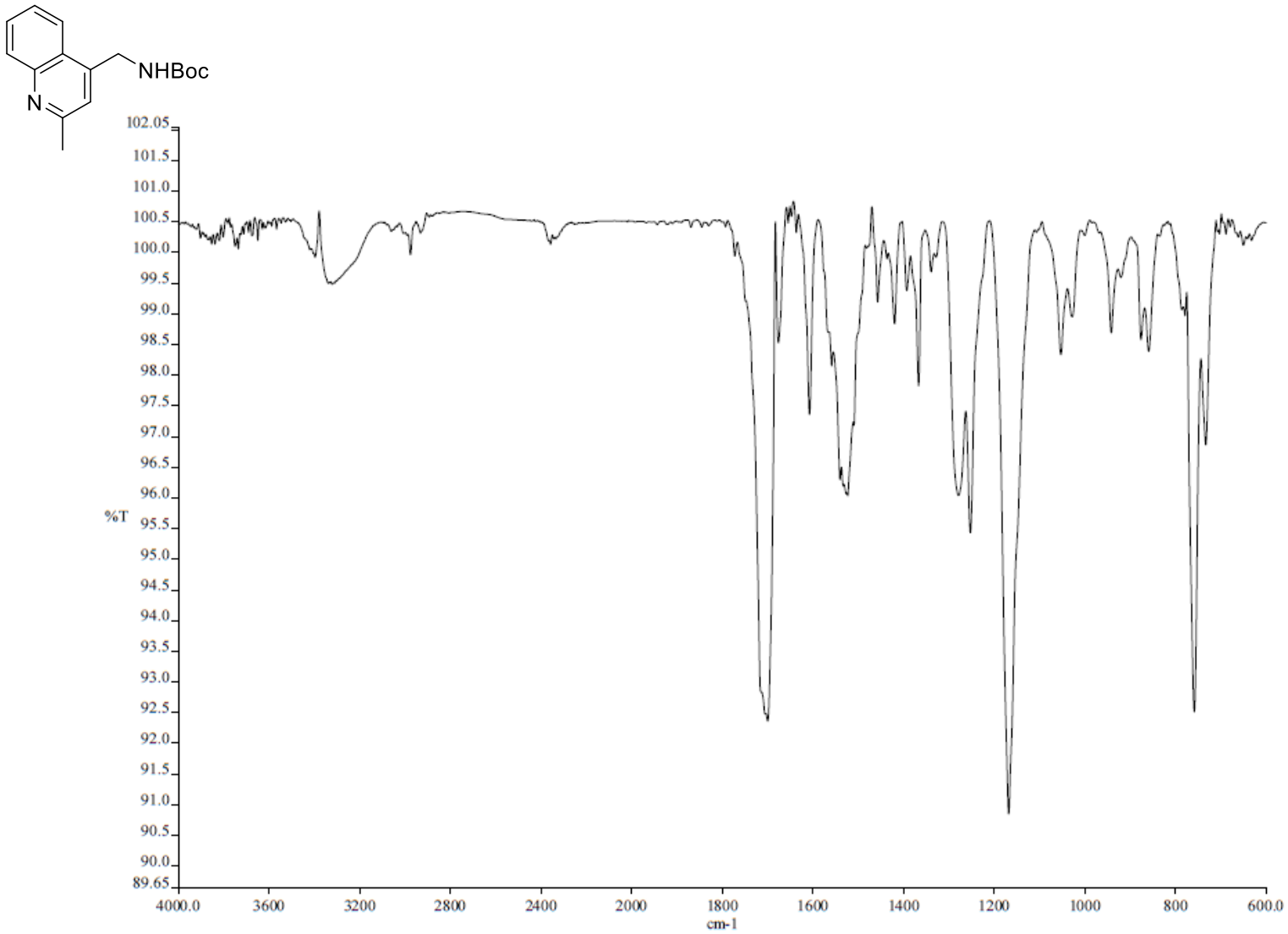
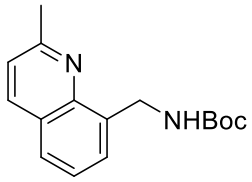


Figure A2.143 Infrared Spectrum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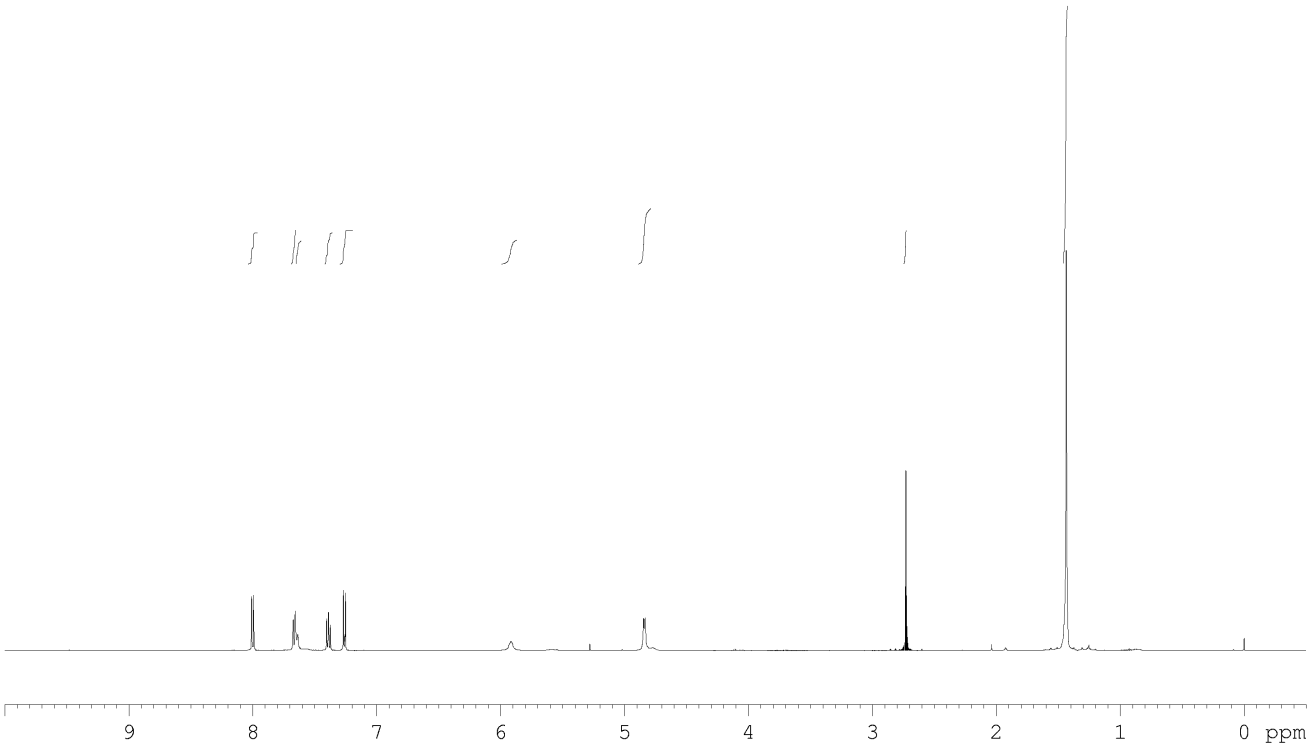
NHBoc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2
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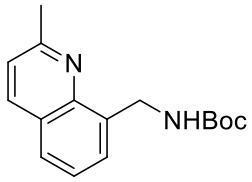
0 ppm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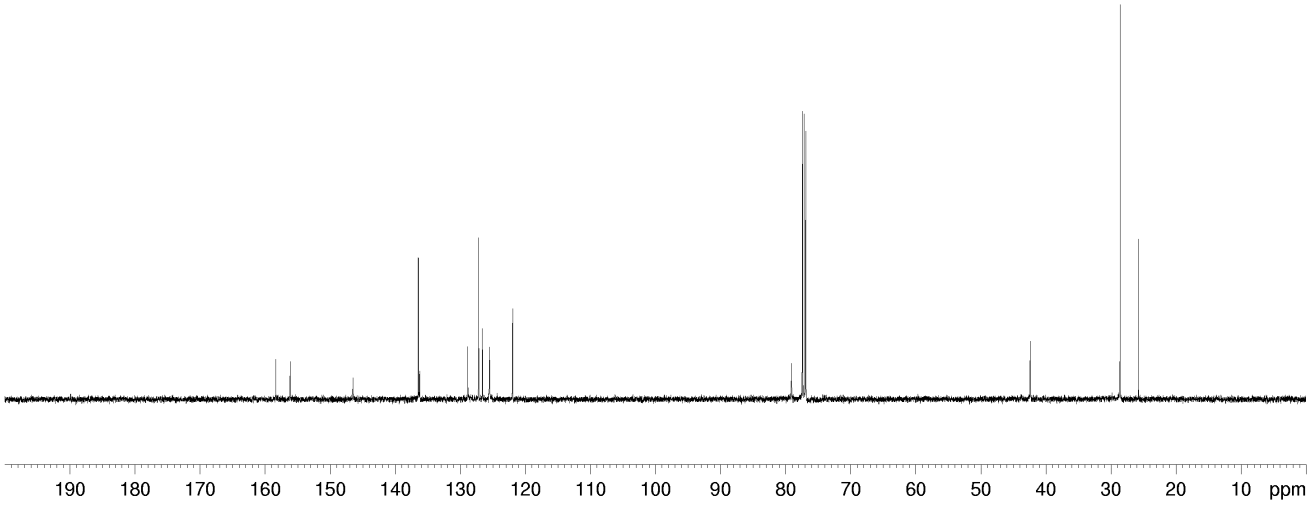
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ppm

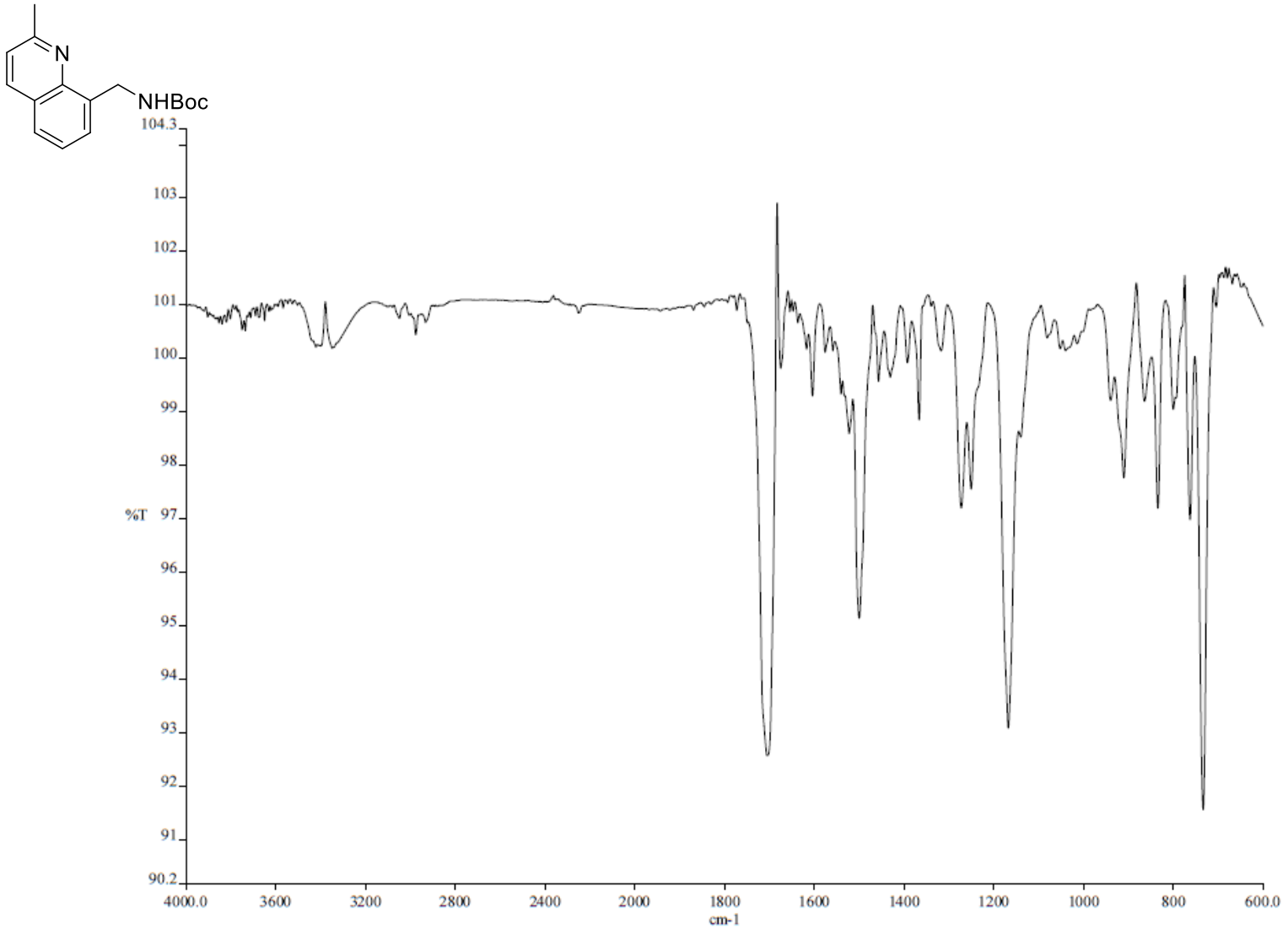
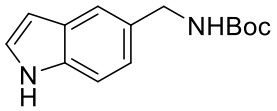
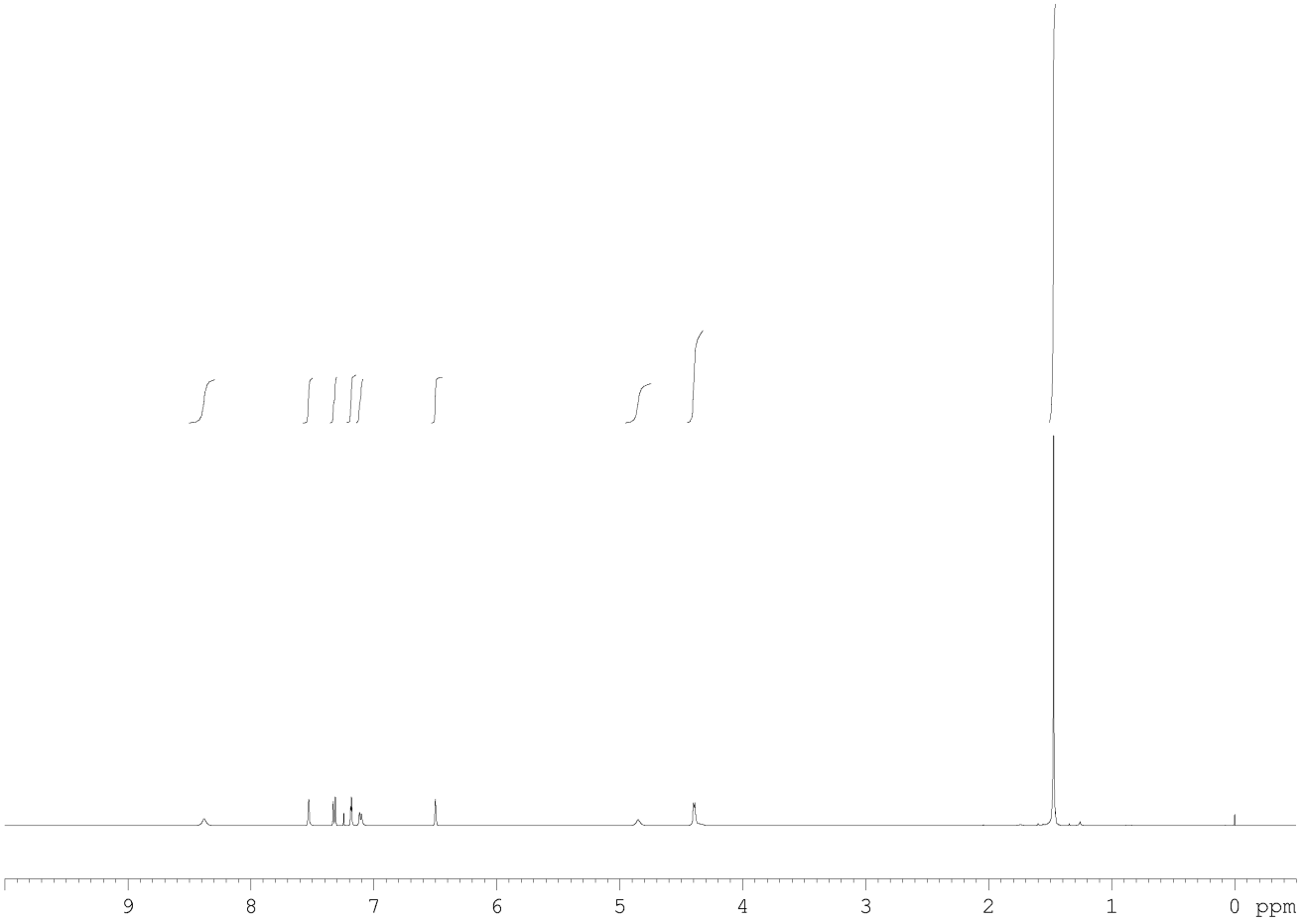


Figure A2.146 Infrared Spectrum


NHBoc
N
H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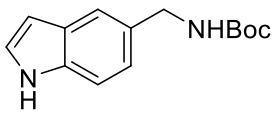
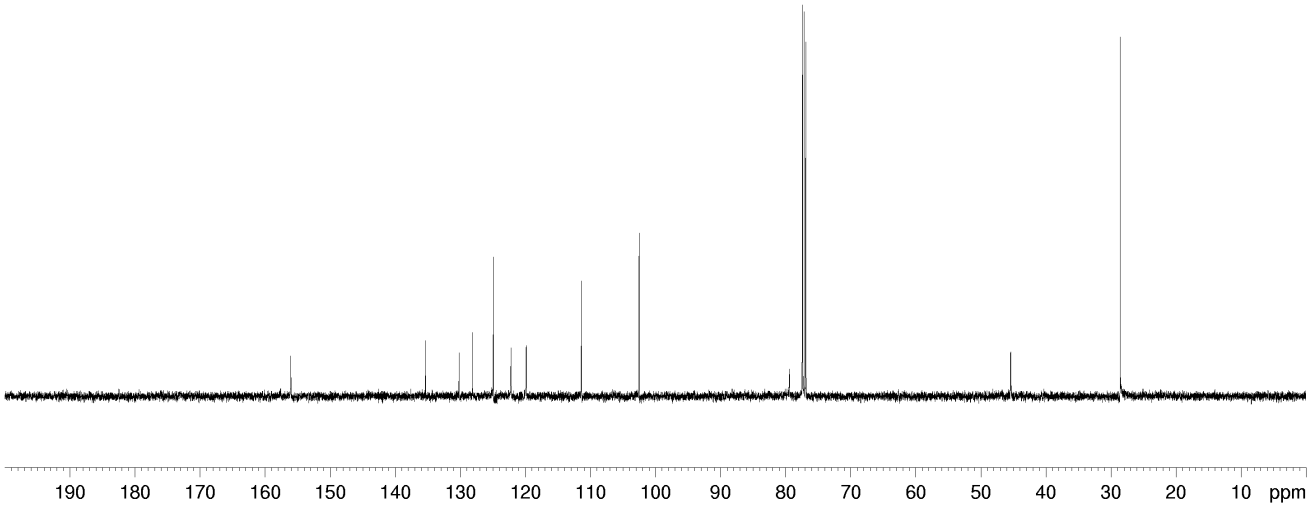
0 ppm


NHBoc
N
H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ppm

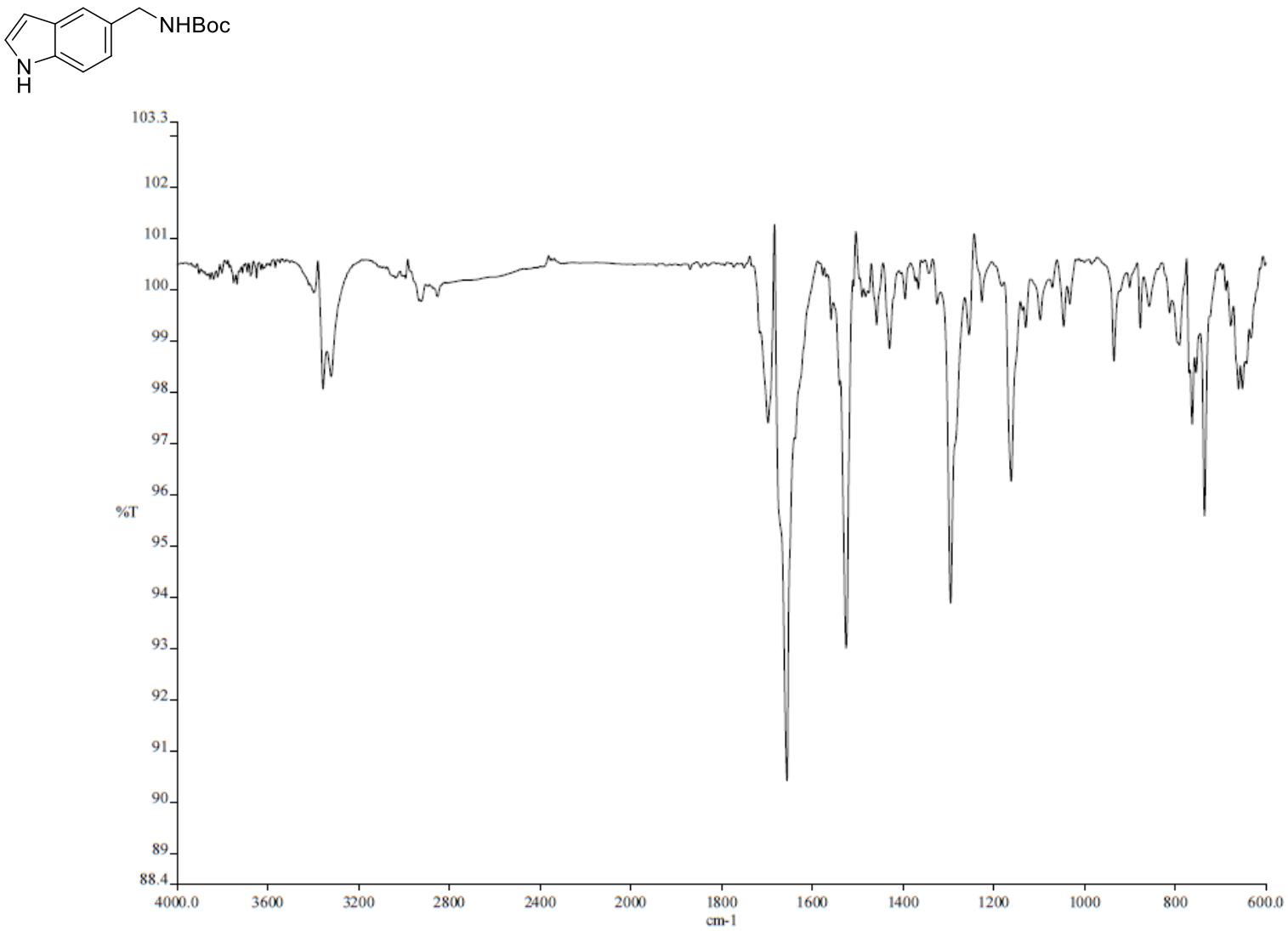
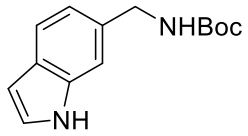


Figure A2.149 Infrared Spectrum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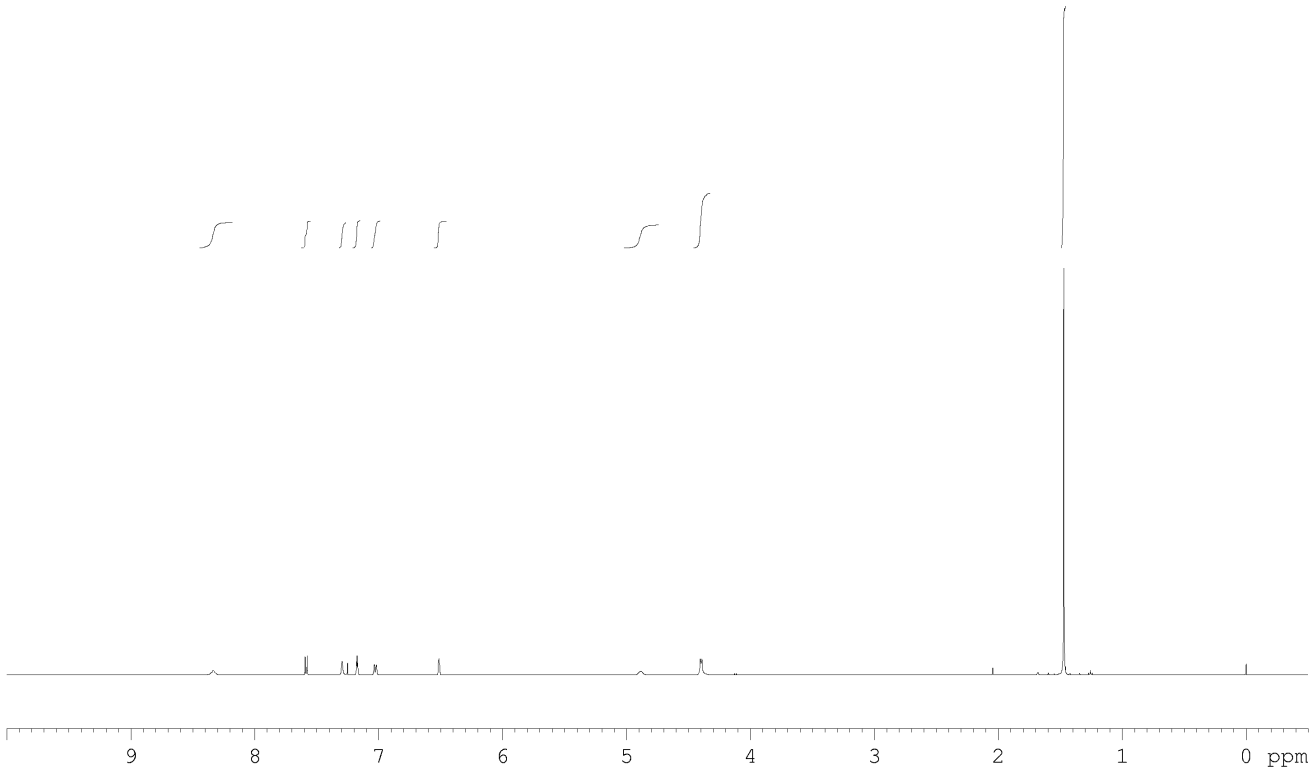
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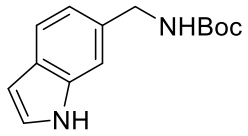
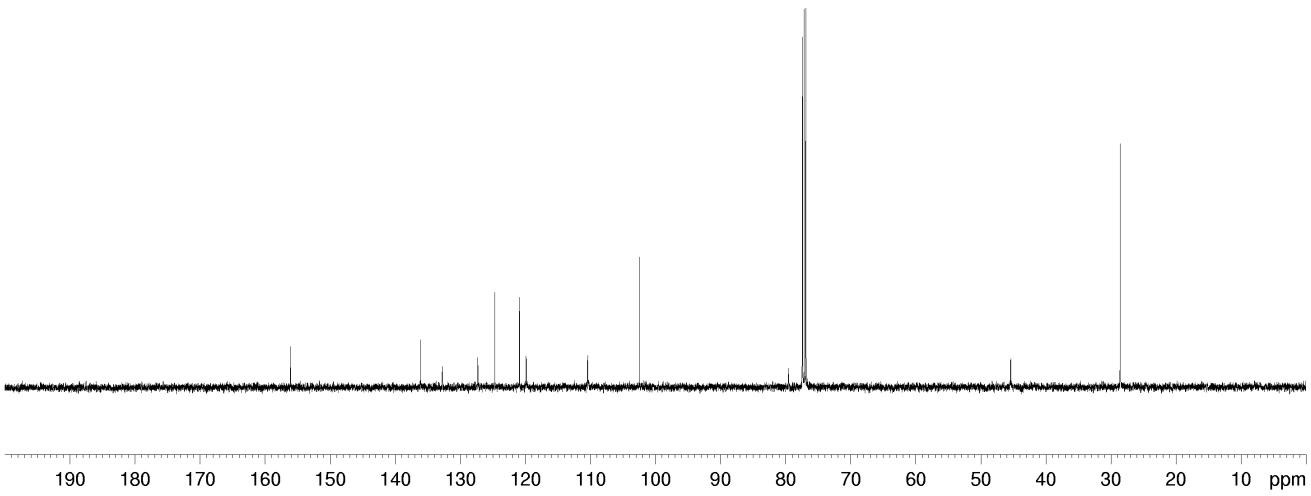
0 ppm


NHBoc
NH


190
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ppm

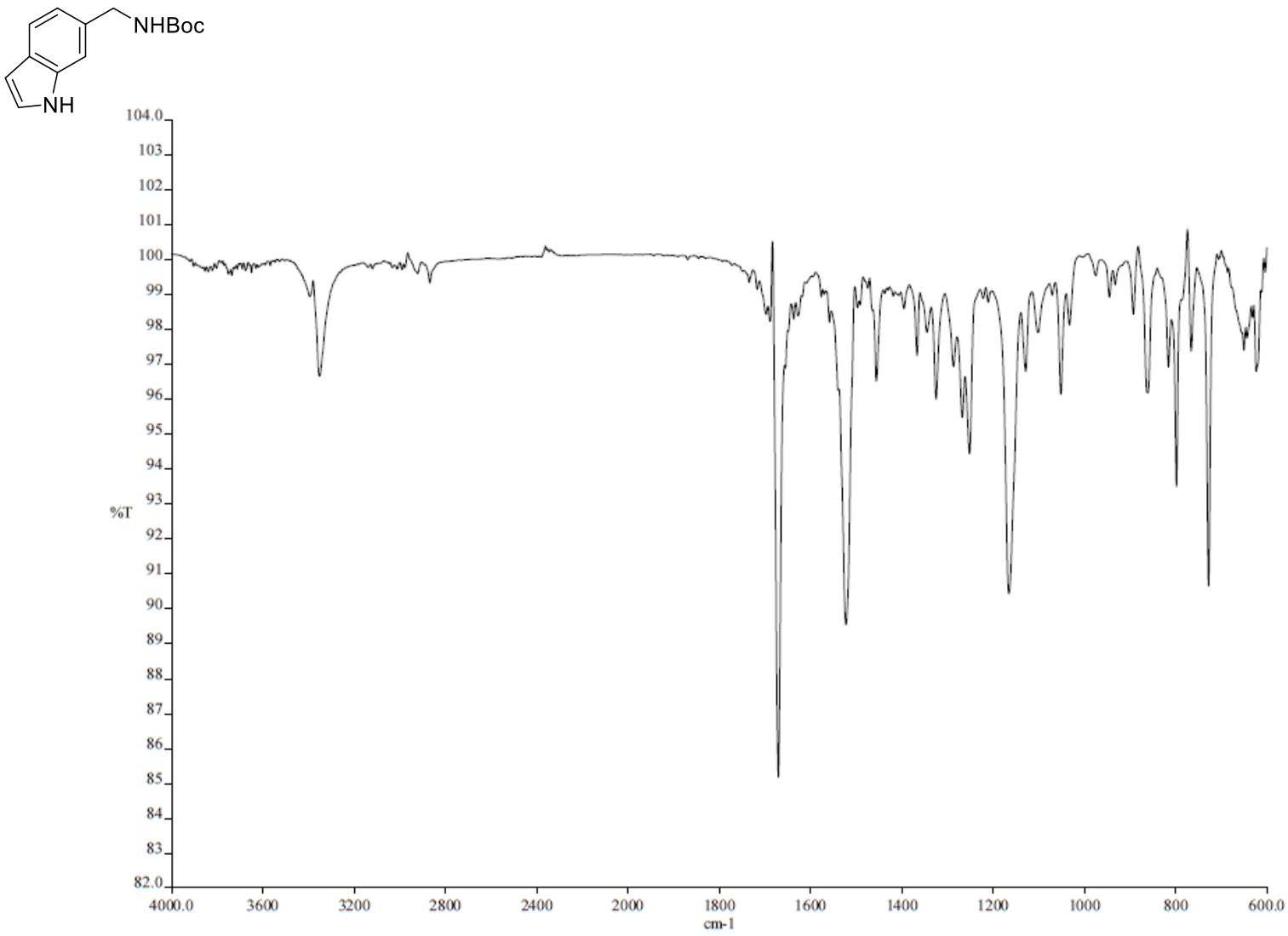
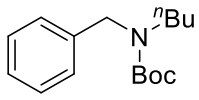
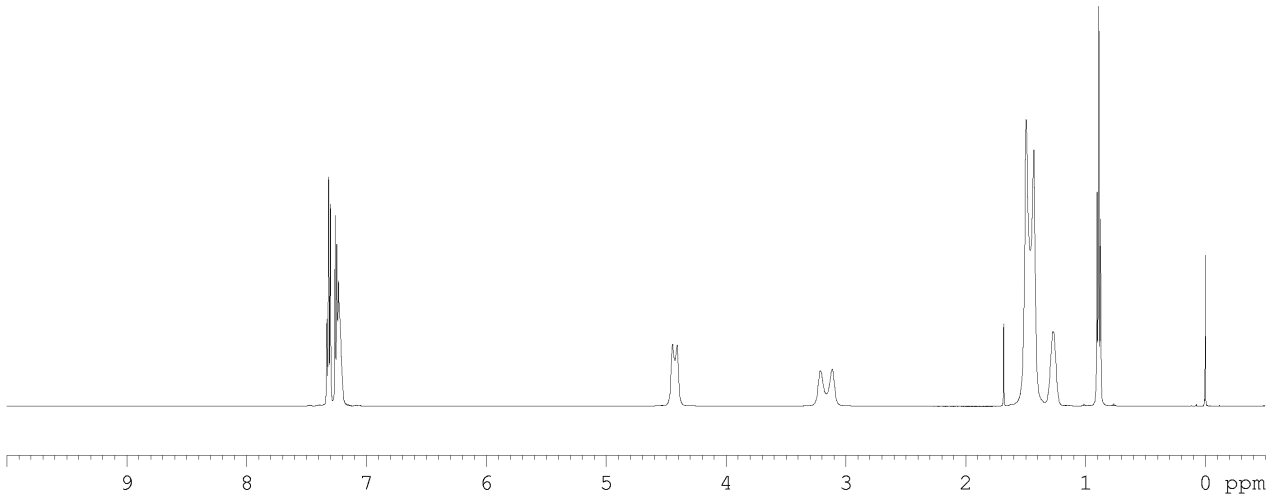


Figure A2.152 Infrared Spectrum


nBu
N
Boc


9
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3
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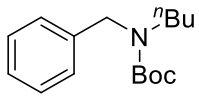
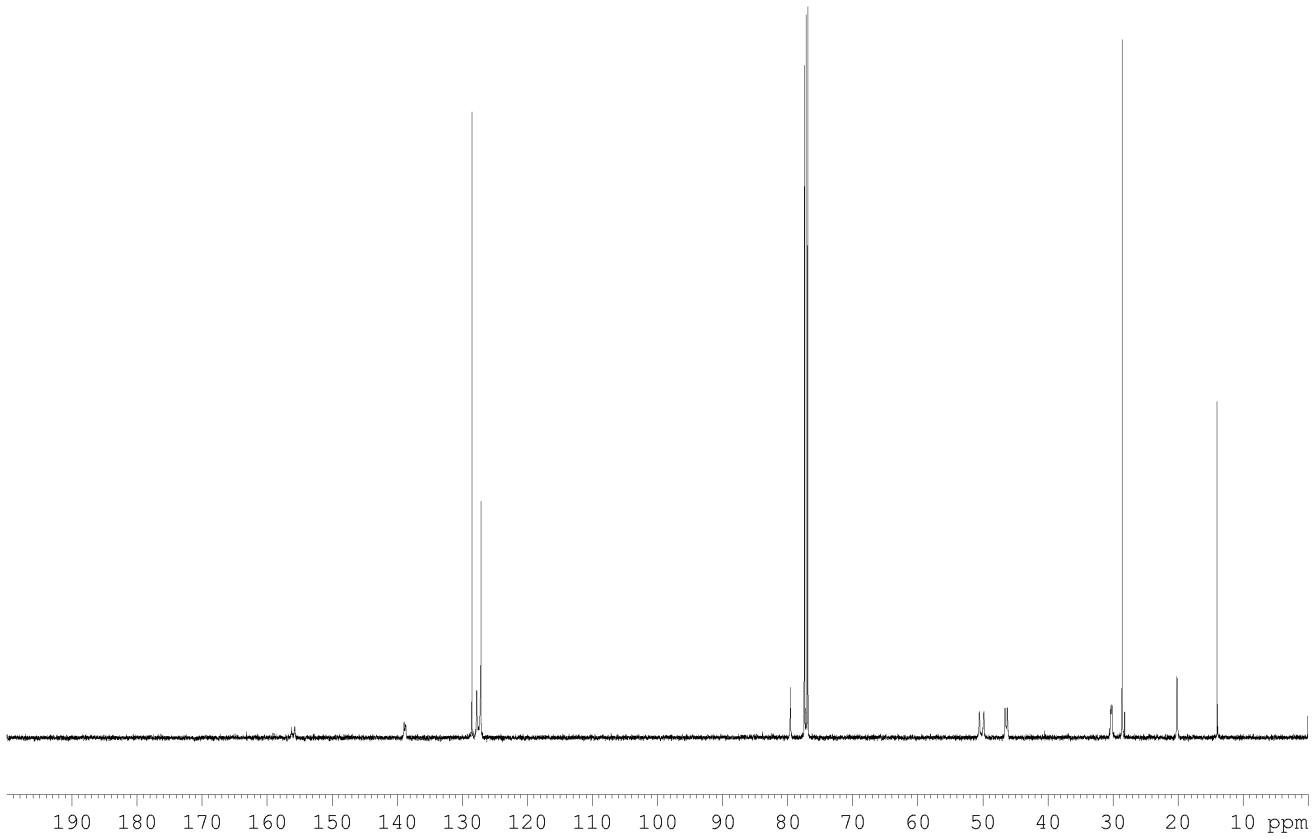
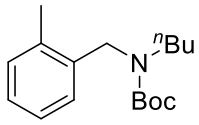
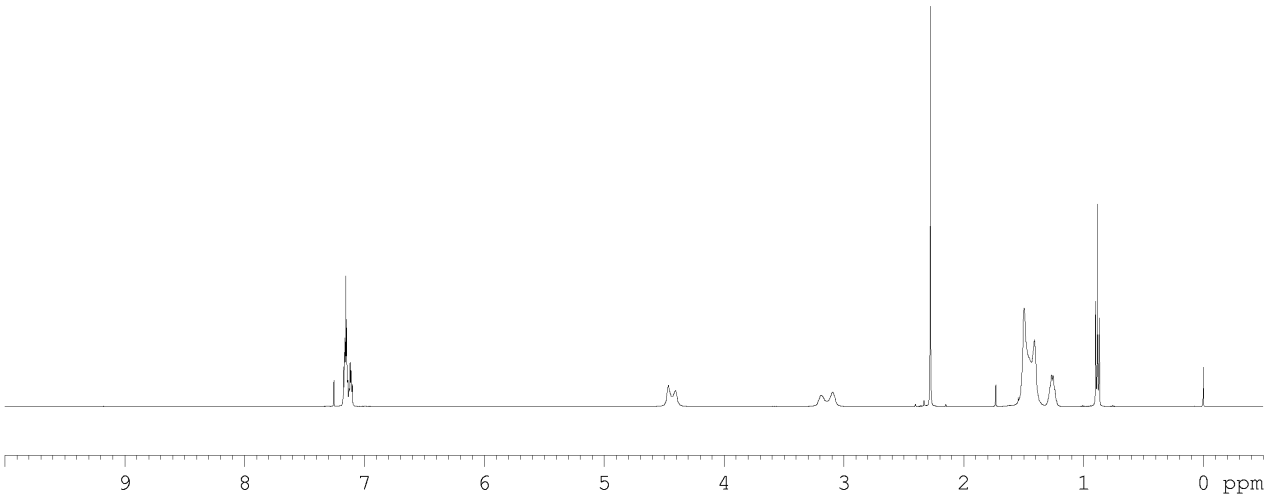
1
0 ppm


nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


nBu
N
Boc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6
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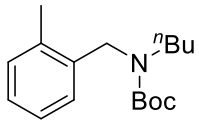
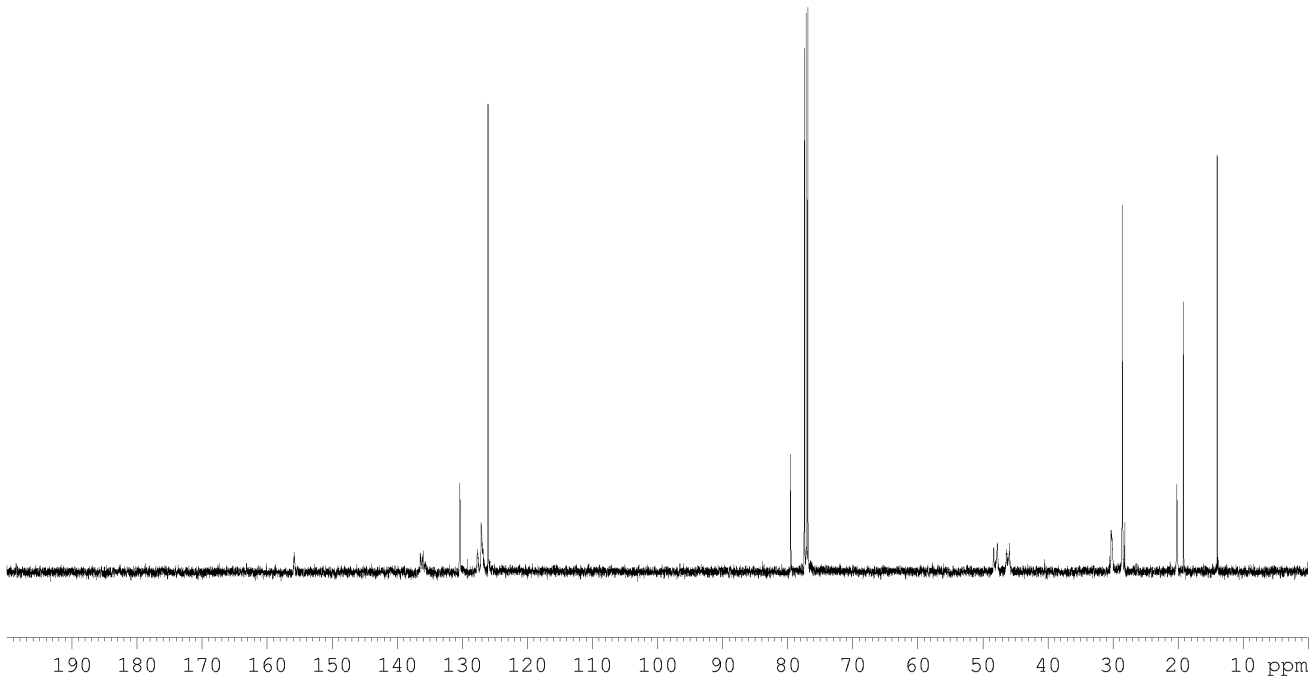
4
3
2
1
0 ppm


nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

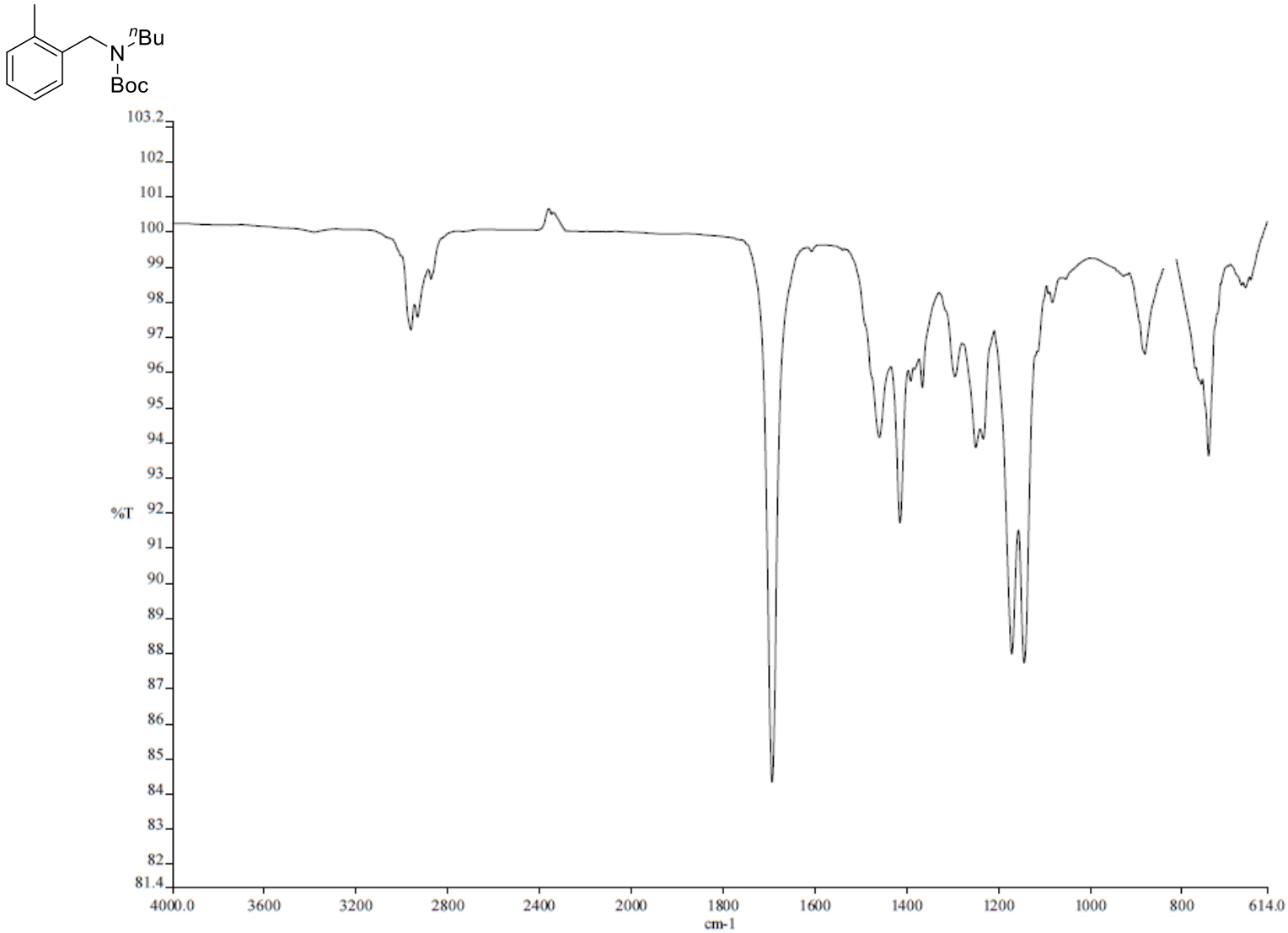
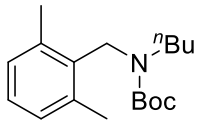
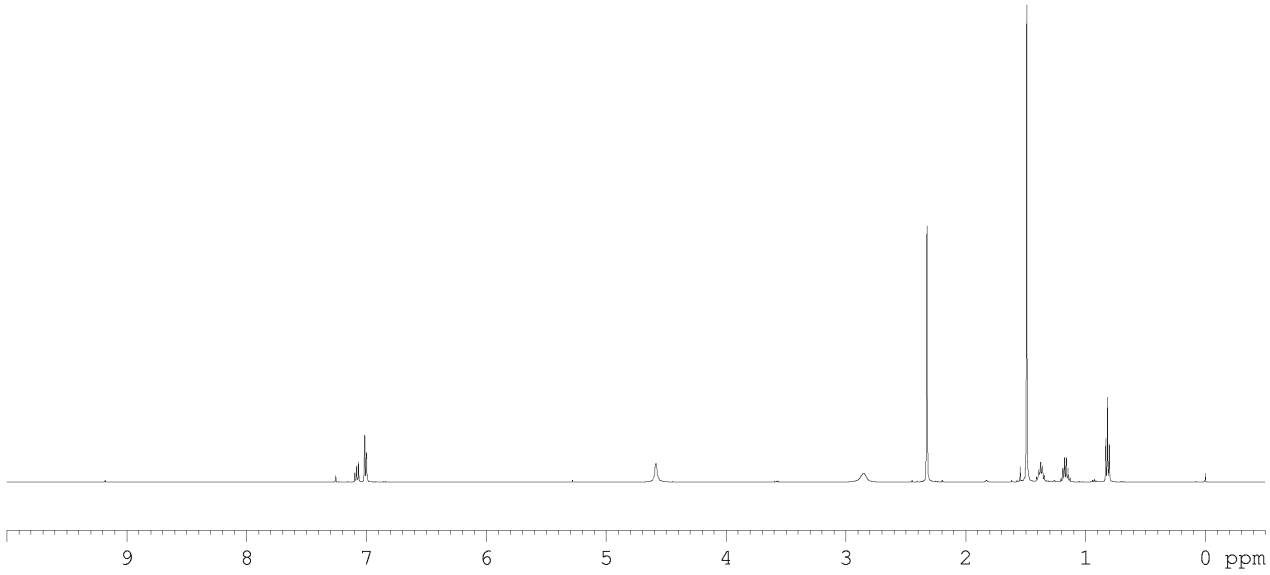


Figure A2.157 Infrared Spectrum


nBu
N
Boc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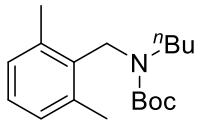
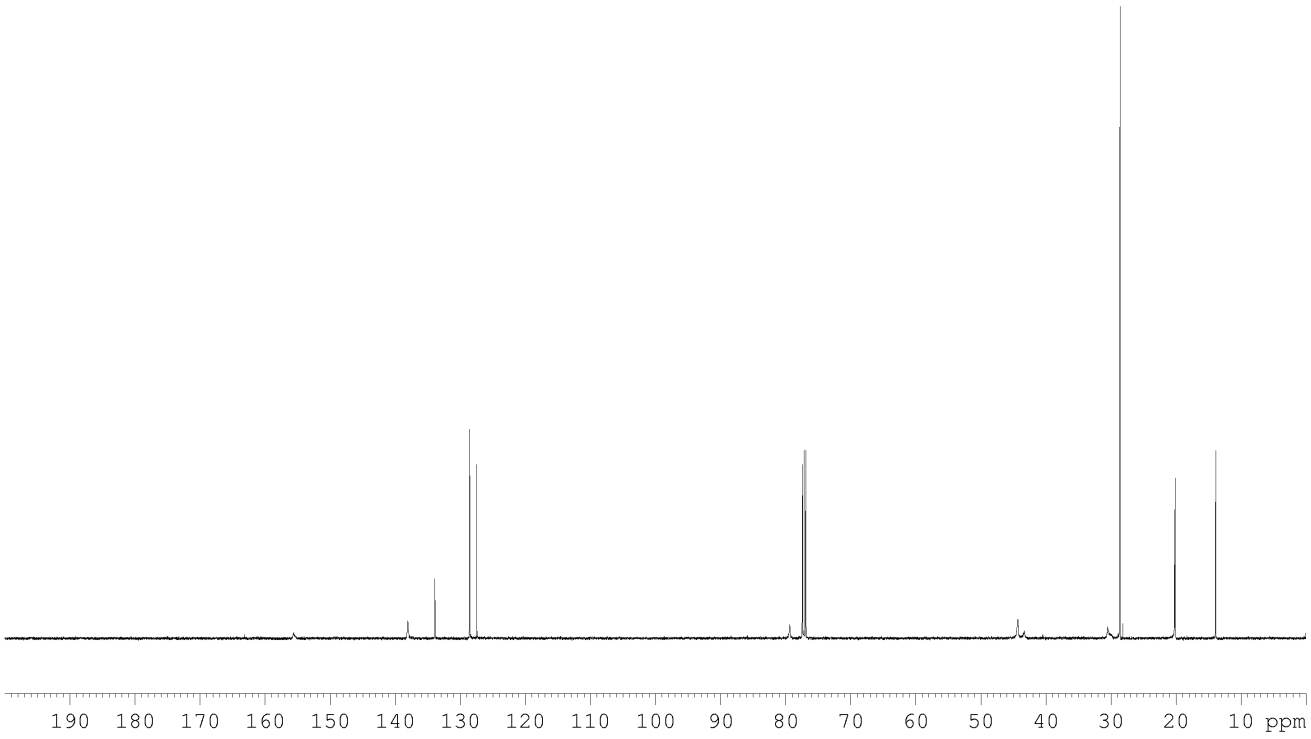
6
5
4
3
2
1
0 ppm


nBu
N
Boc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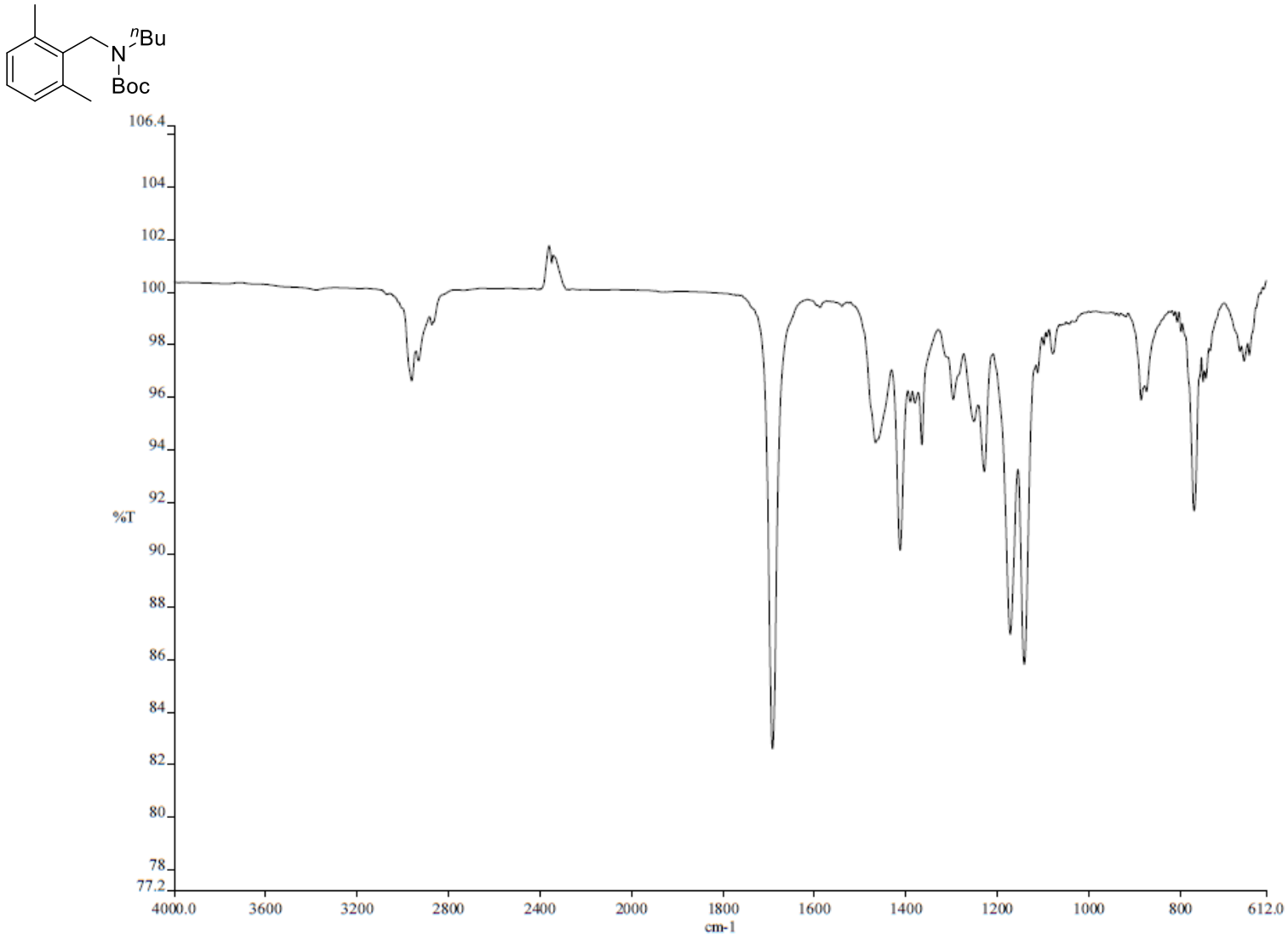
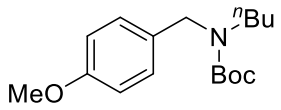
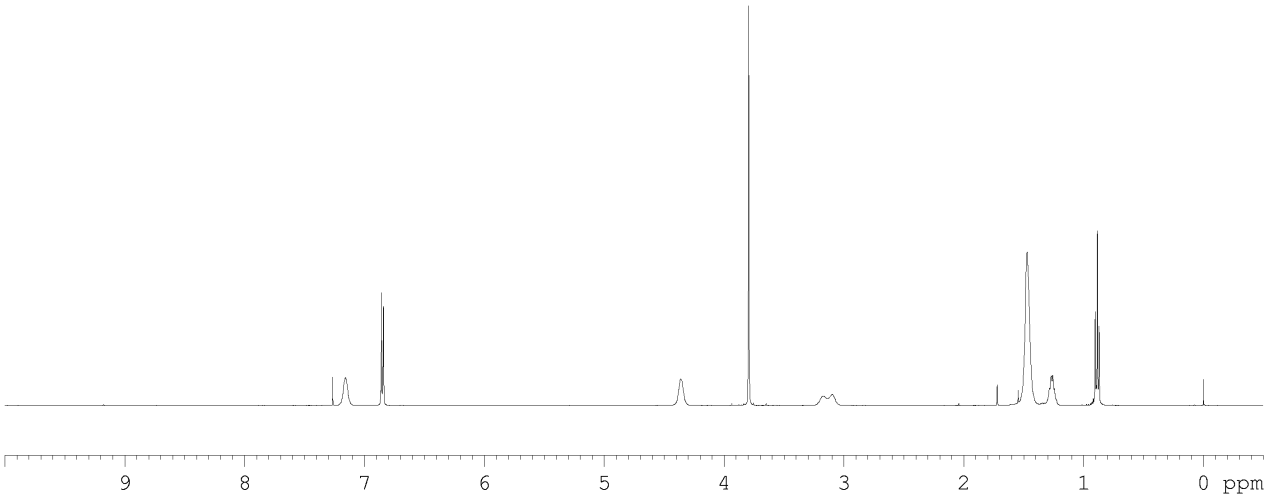


Figure A2.160 Infrared Spectrum


nBu
N
Boc
MeO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6
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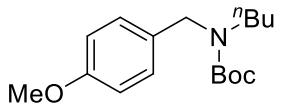
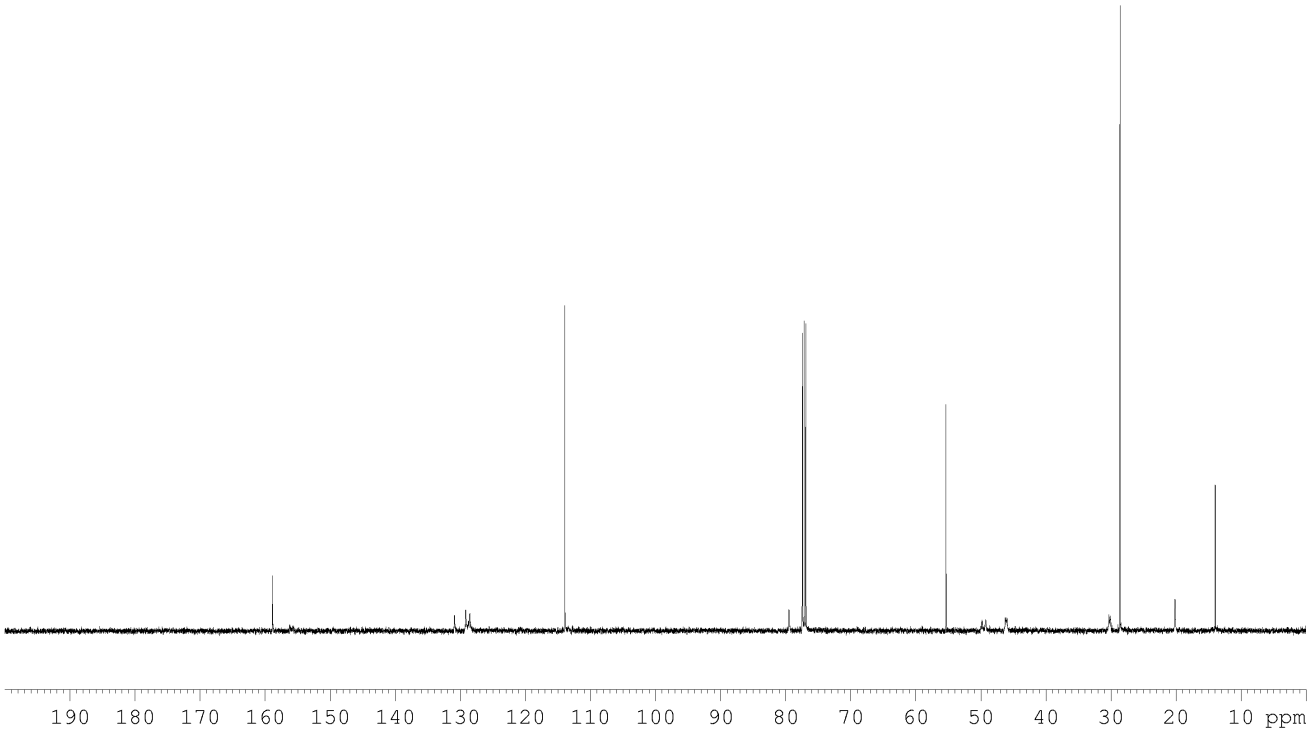
4
3
2
1
0 ppm


MeO
N
nBu
Boc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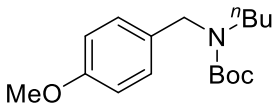


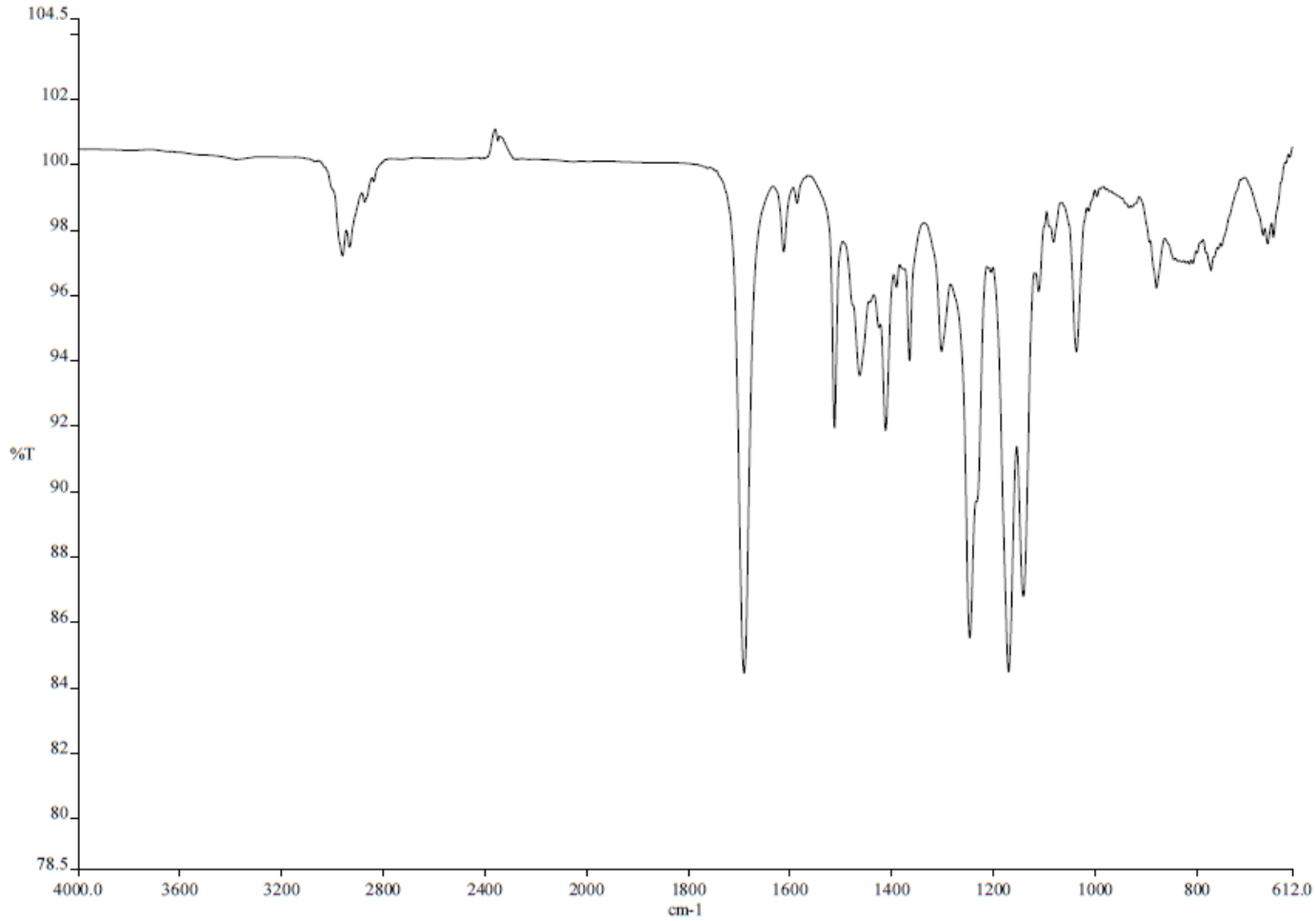
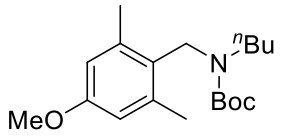
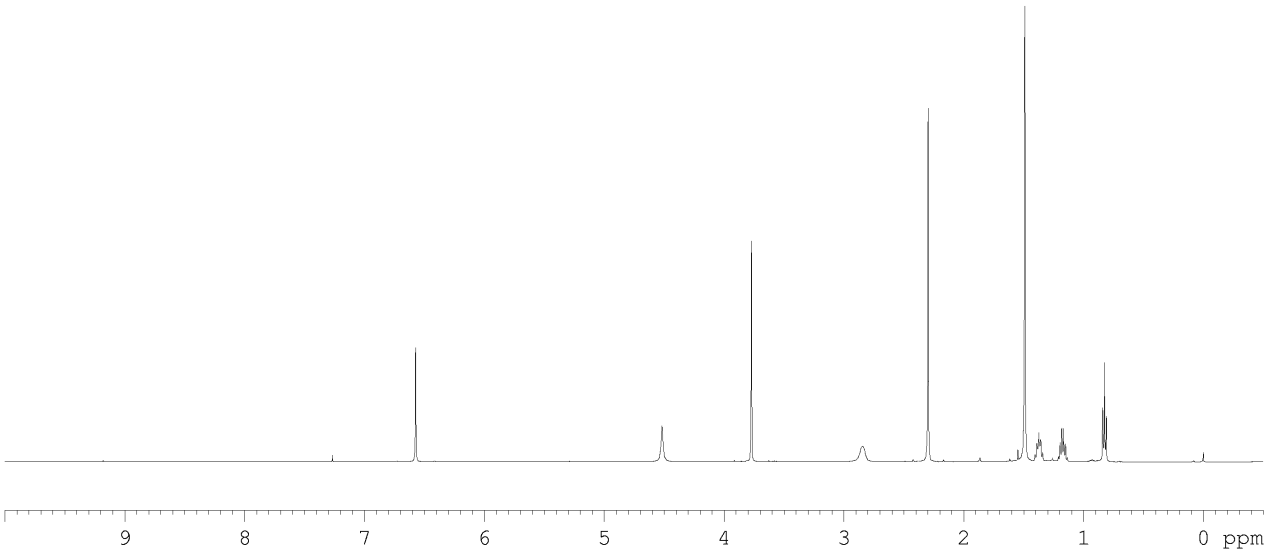


Figure A2.163 Infrared Spectrum


MeO
N
nBu
Boc


9
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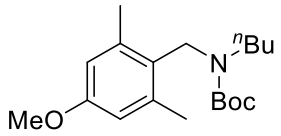
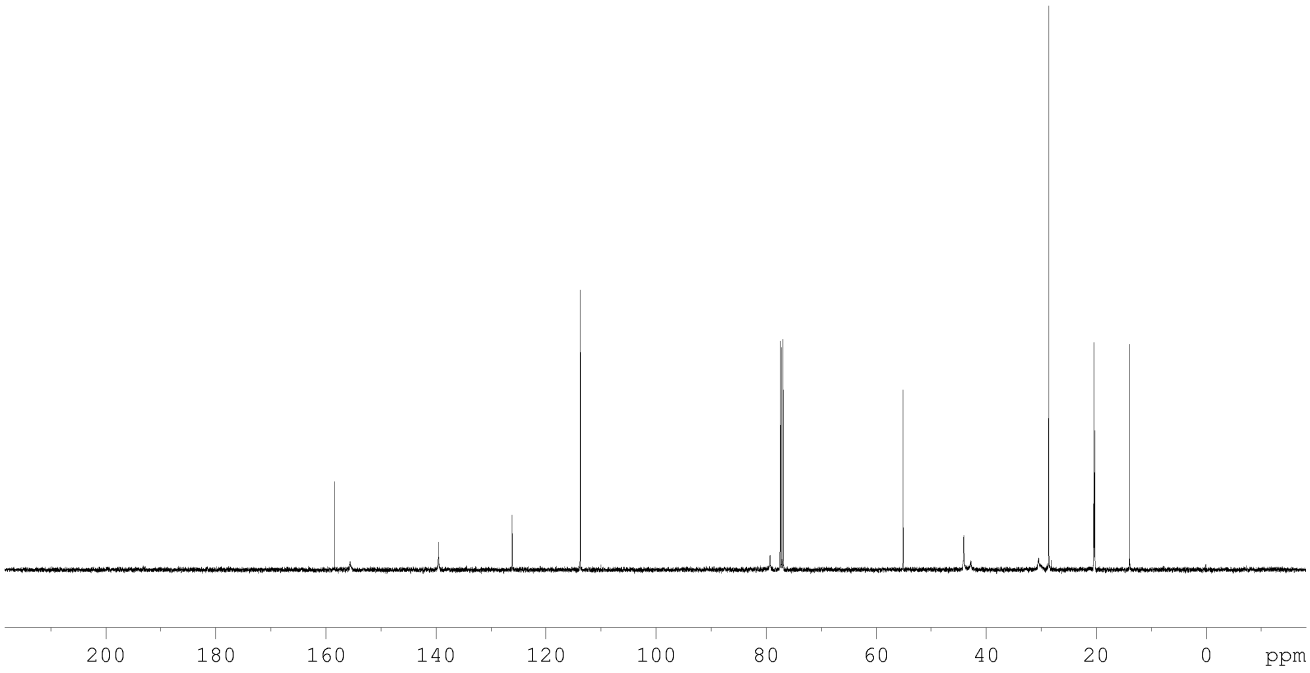
1
0 ppm


MeO
N
nBu
Boc


200
180
160
140
120
100
80
60
40
20
0
ppm

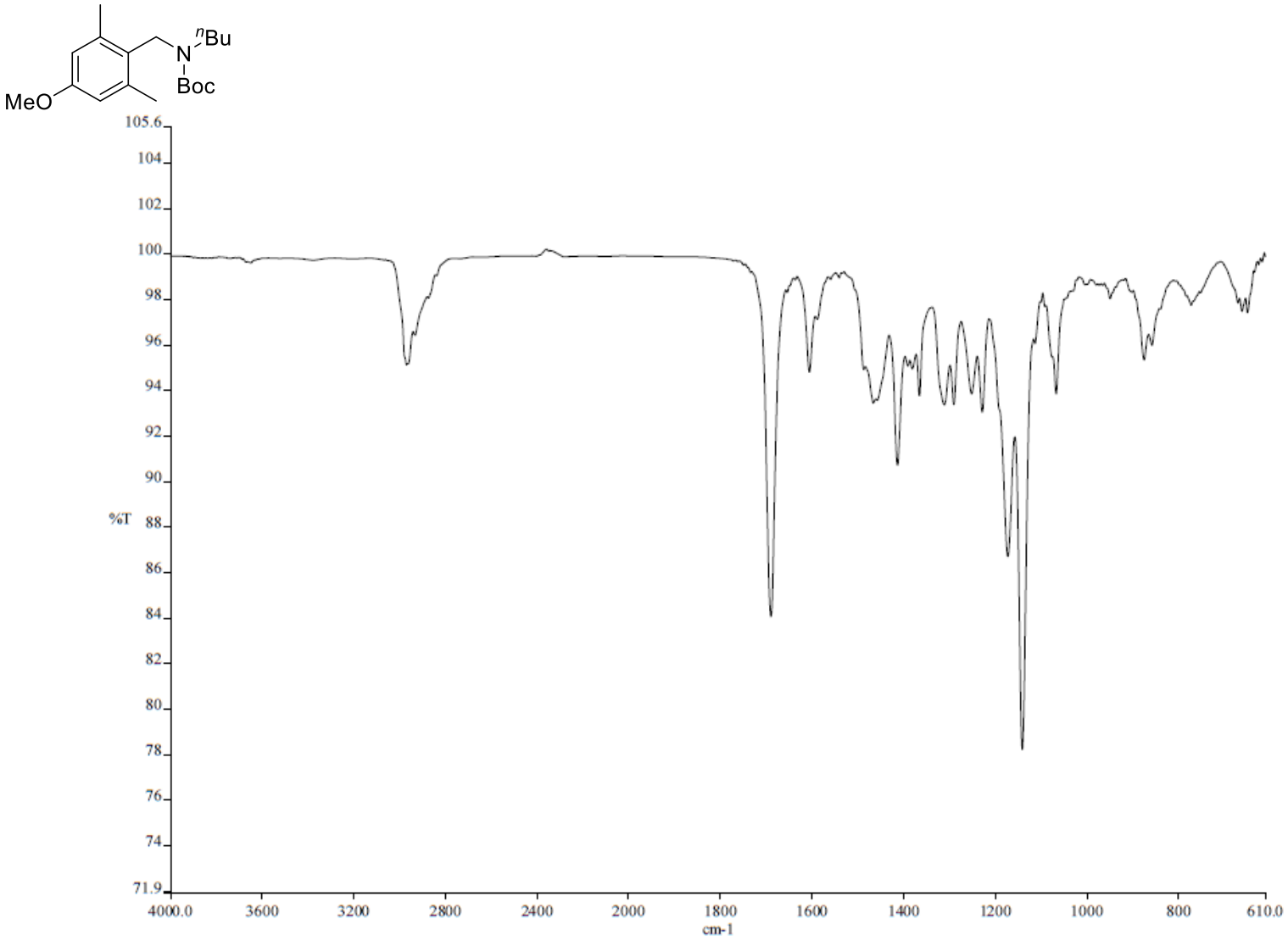
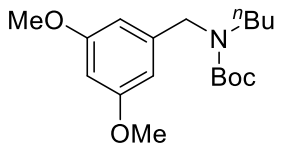
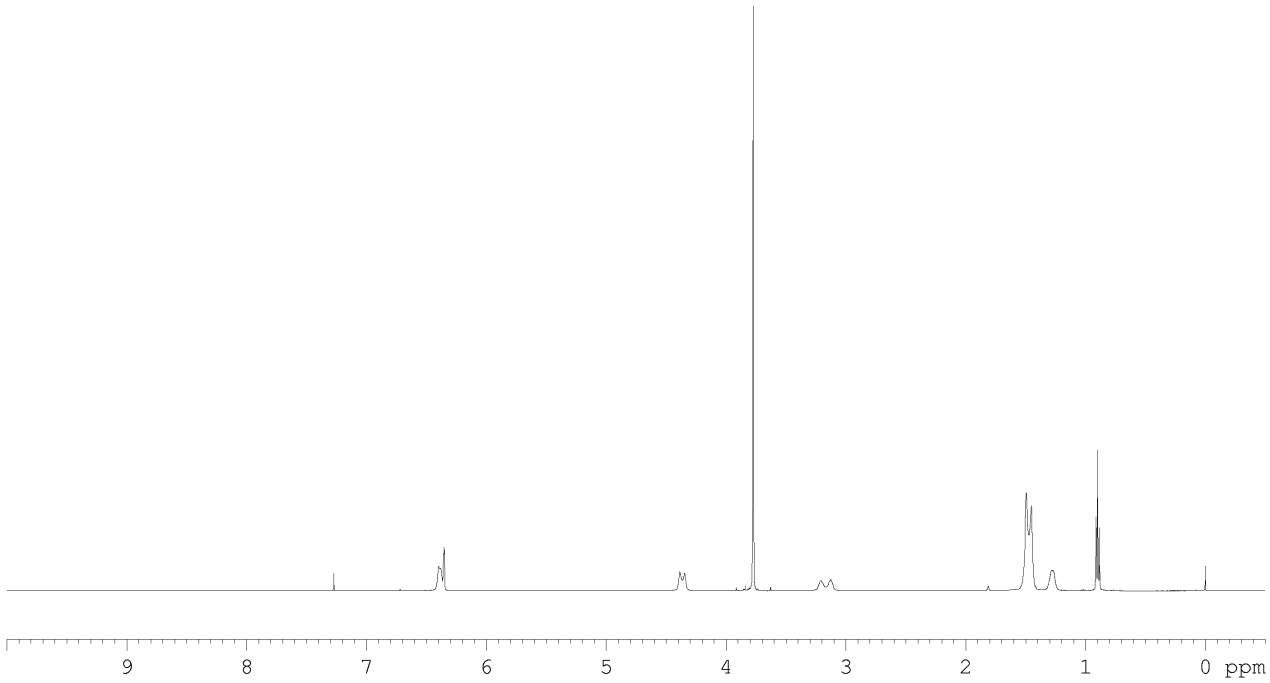
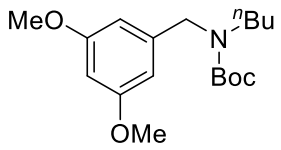
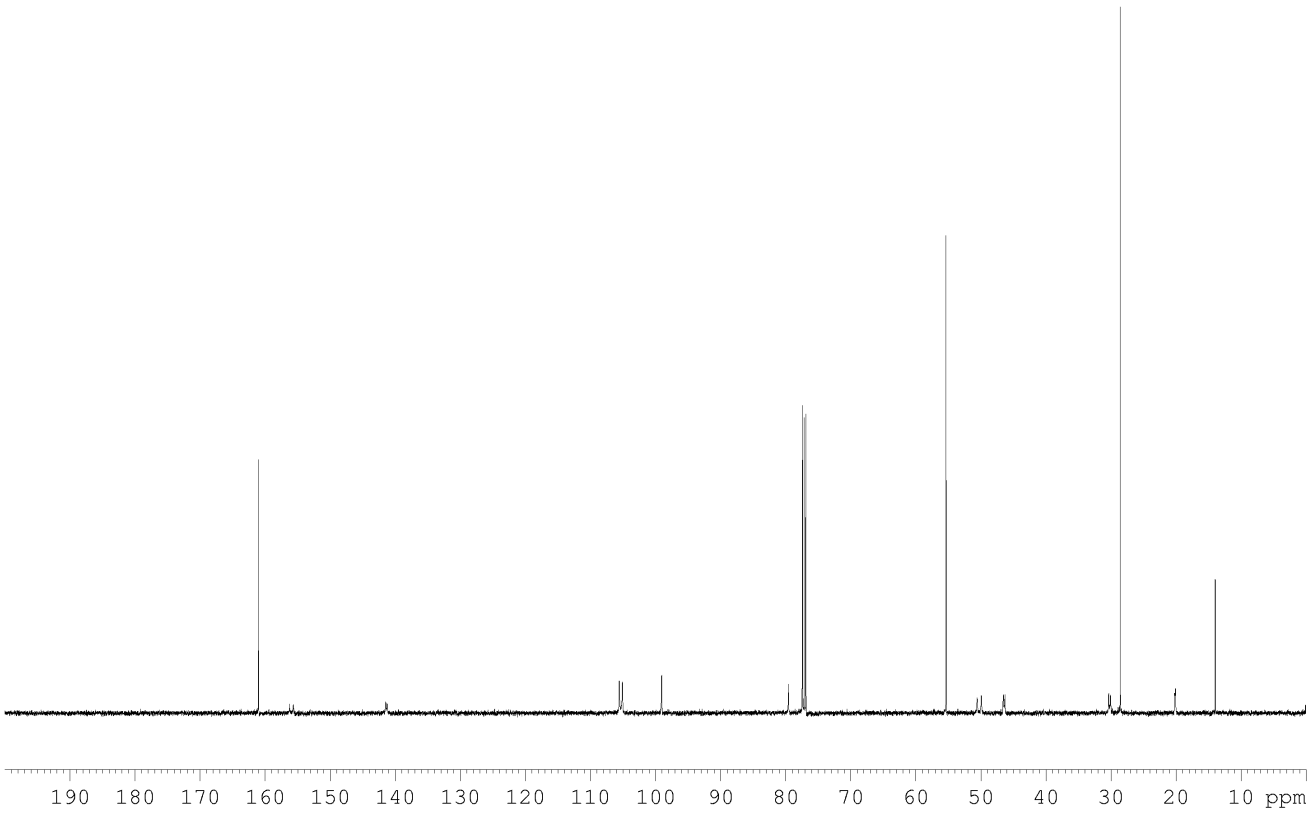


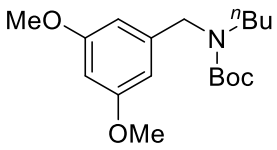
Figure A2.100 Infrared Spectrum


MeO
N
nBu
Boc
OMe


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
nBu
Boc
OMe


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



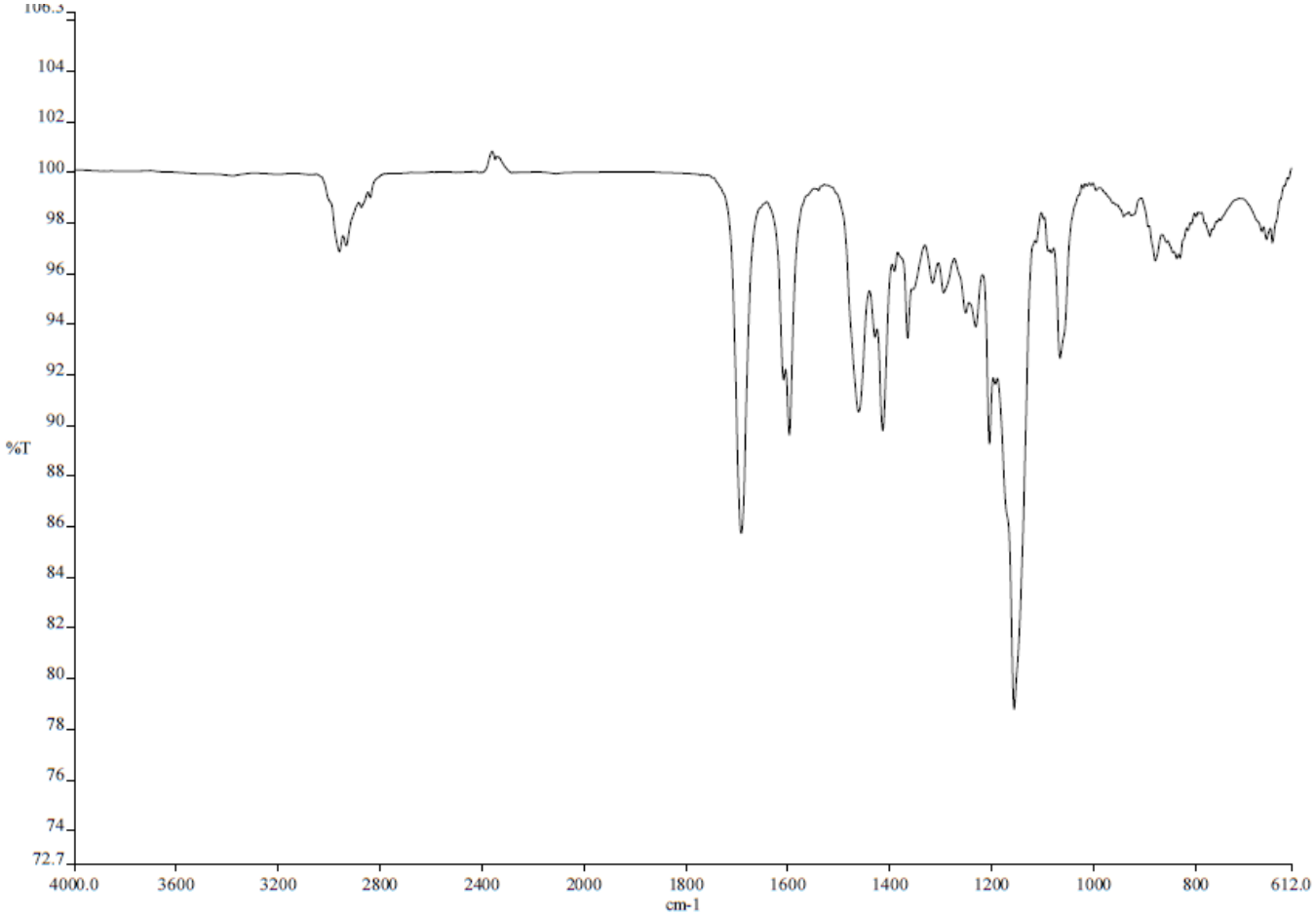
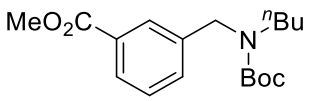
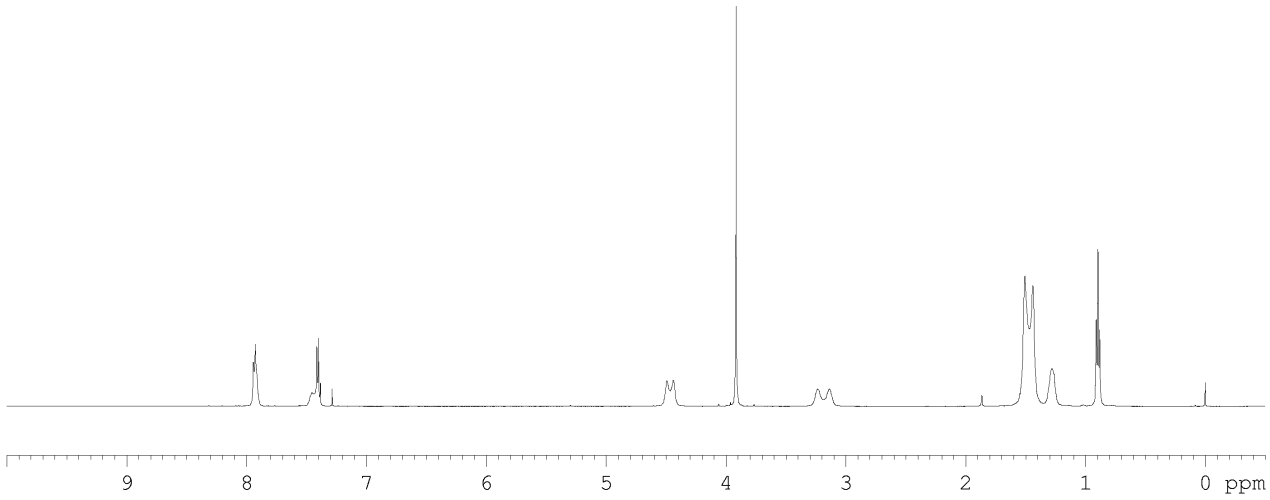
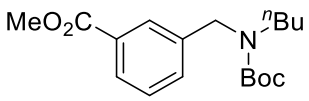
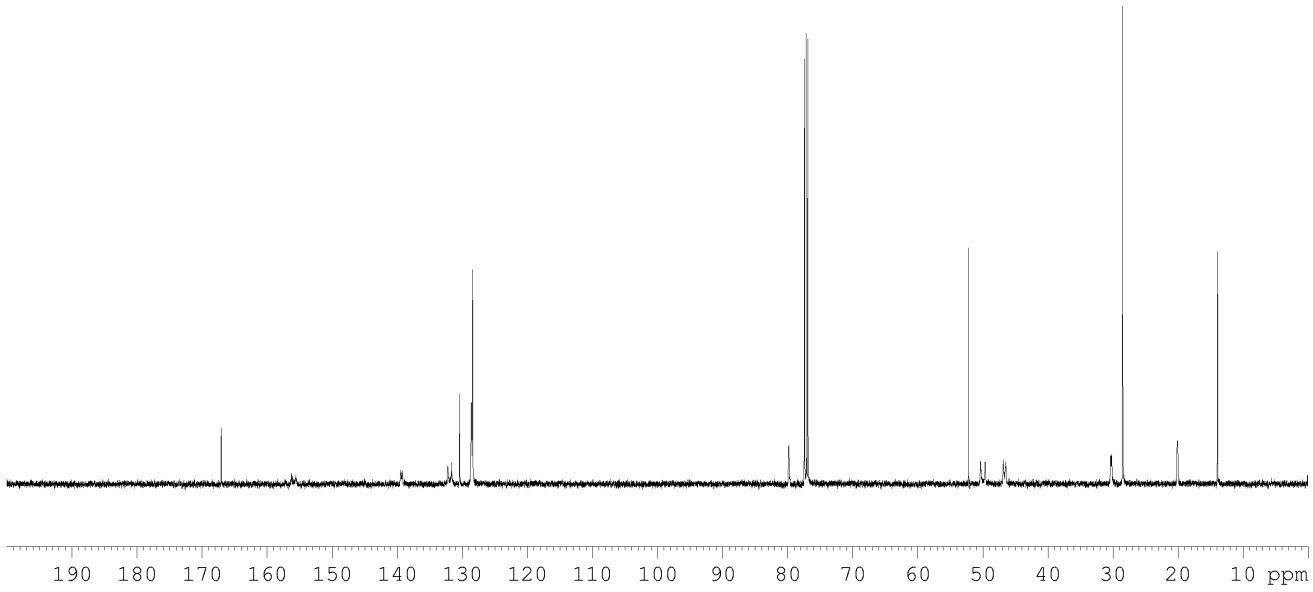


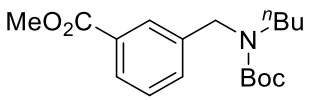
Figure A2.169 Infrared Spectrum


MeO2C
nBu
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO2C
nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



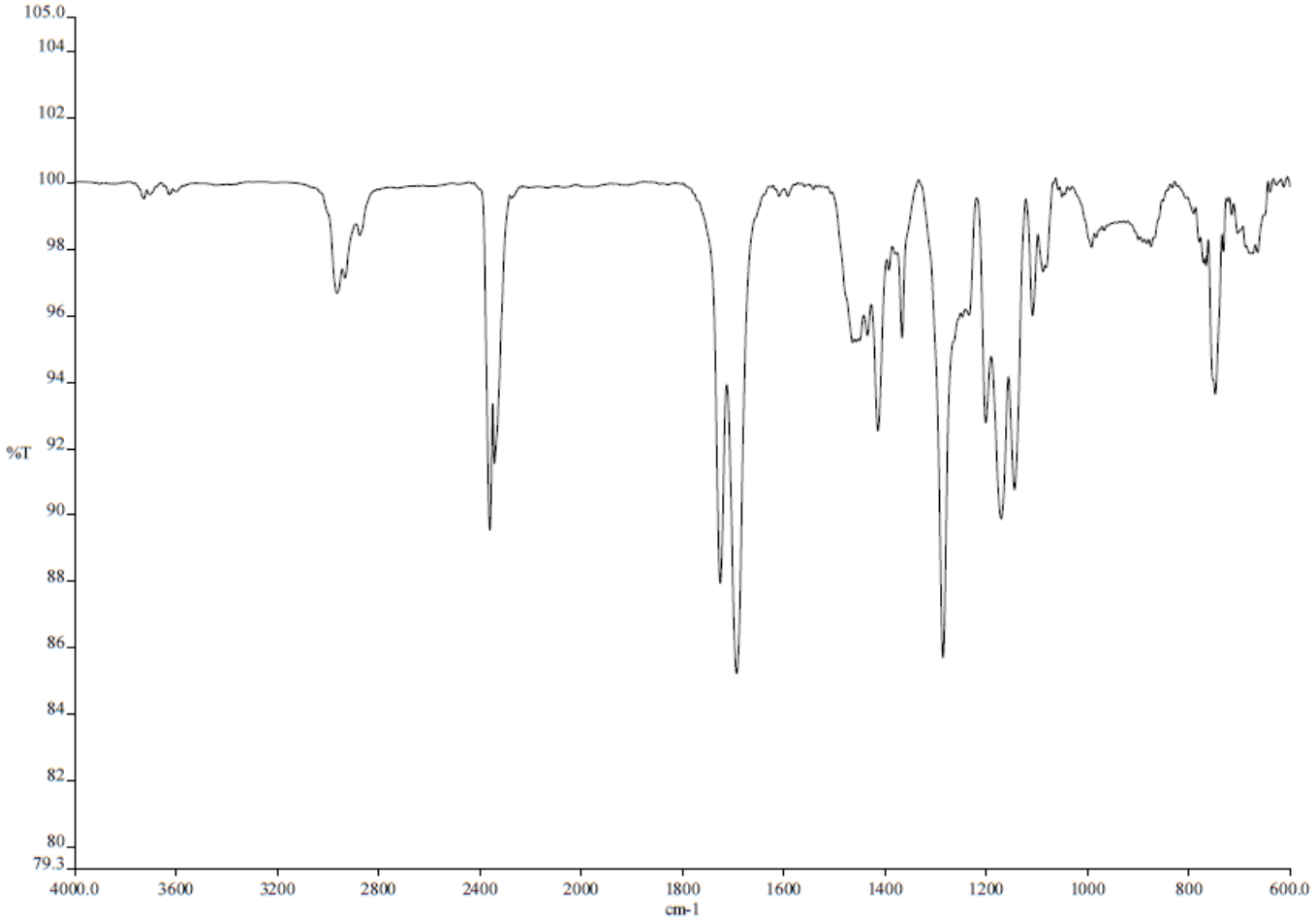
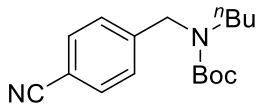
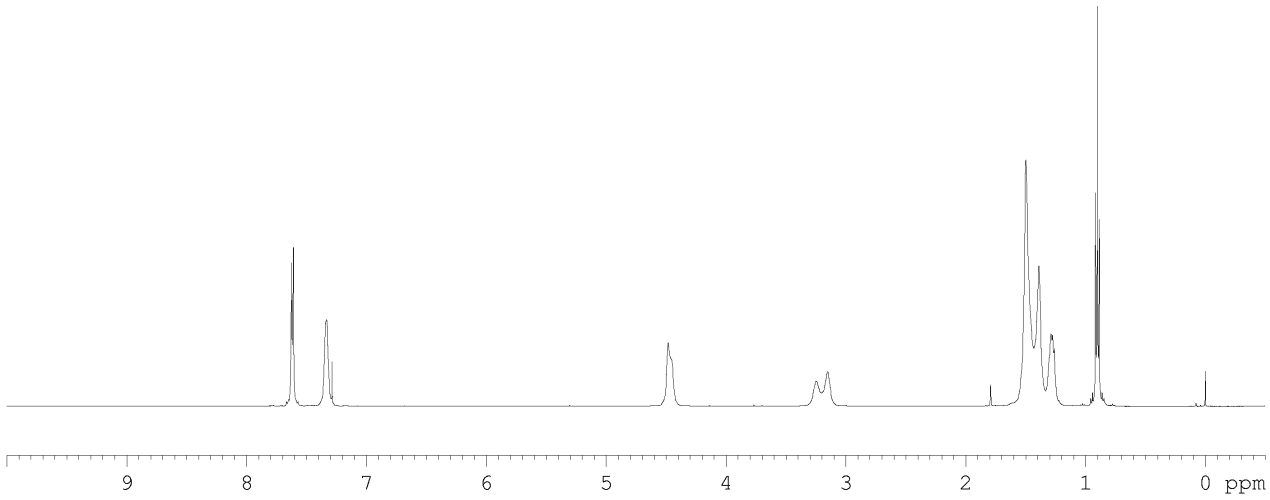
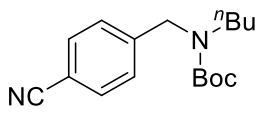
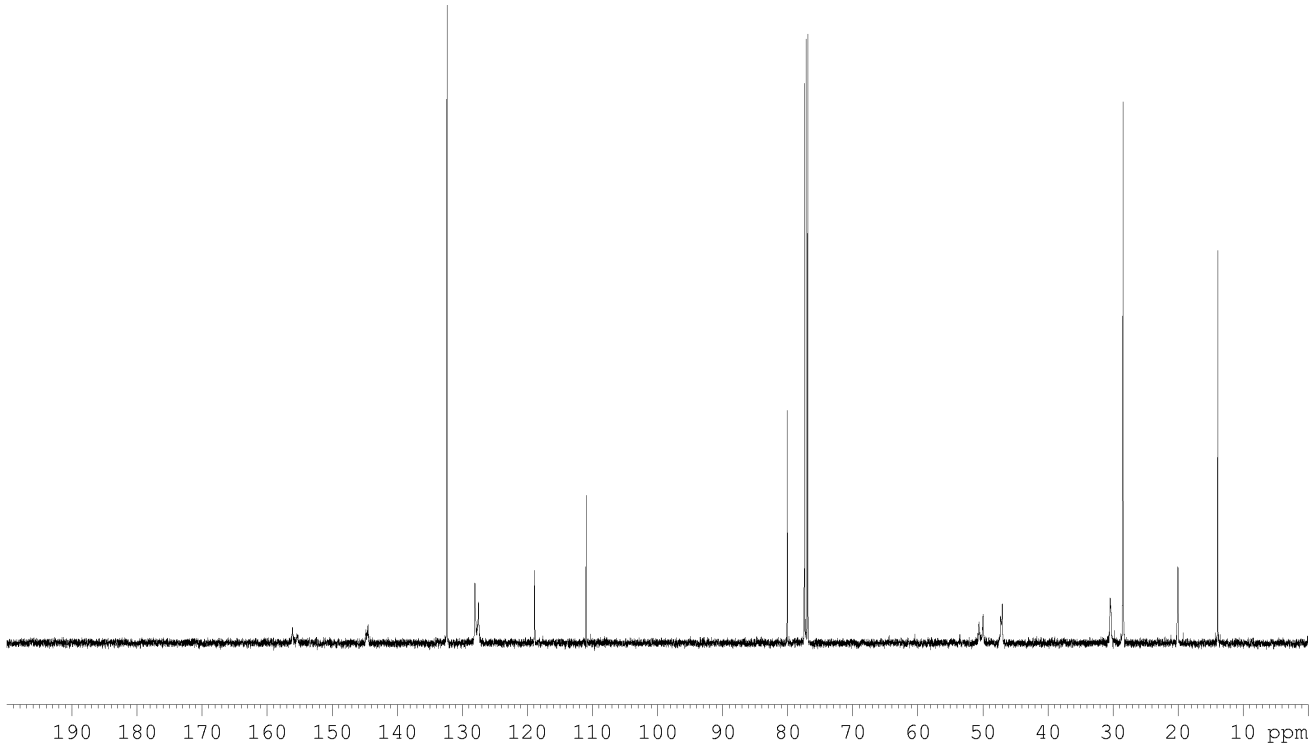


Figure A2.172 Infrared Spectrum


nBu
N
Boc
NC


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
NC


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

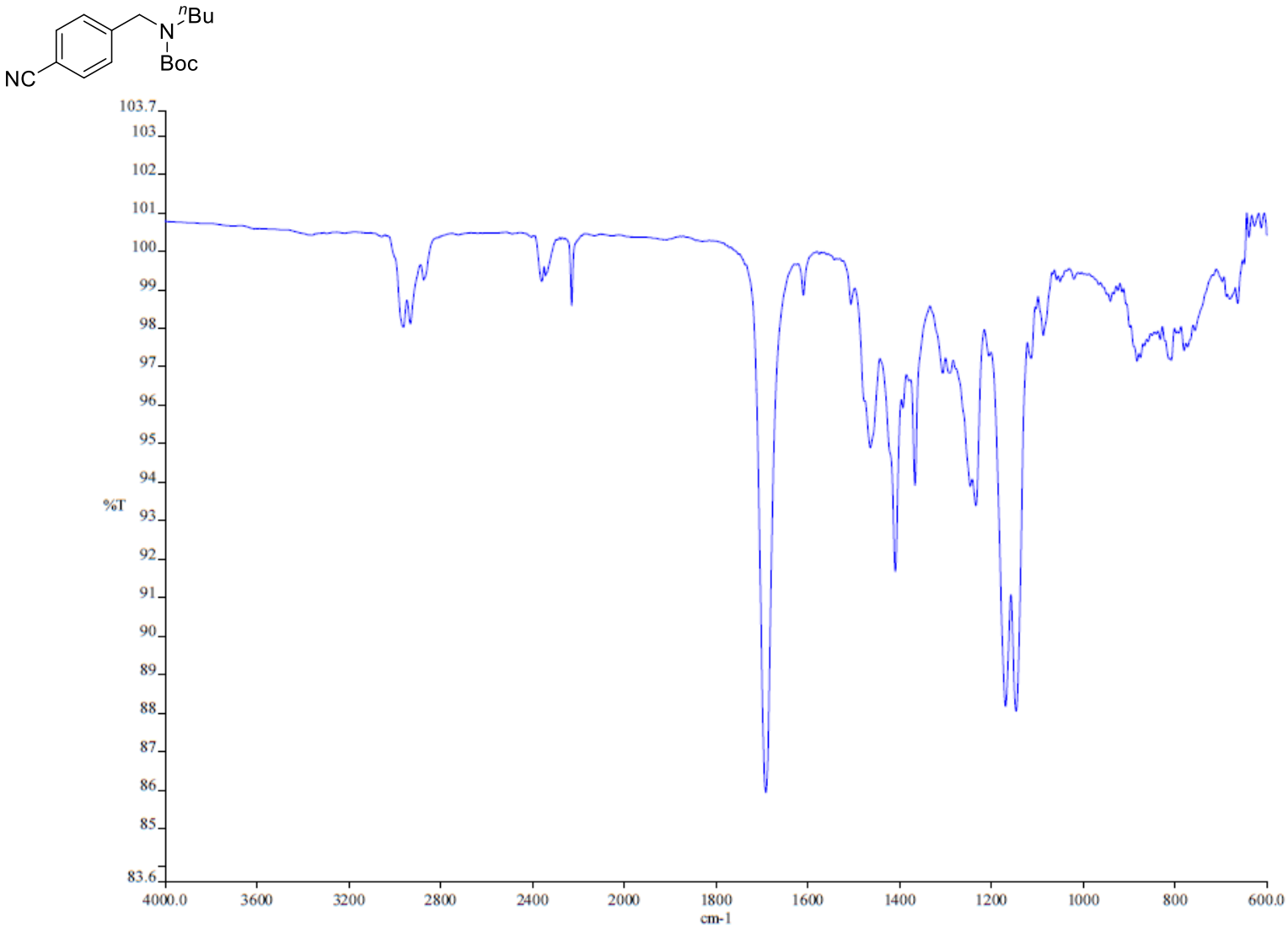
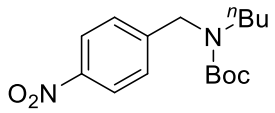
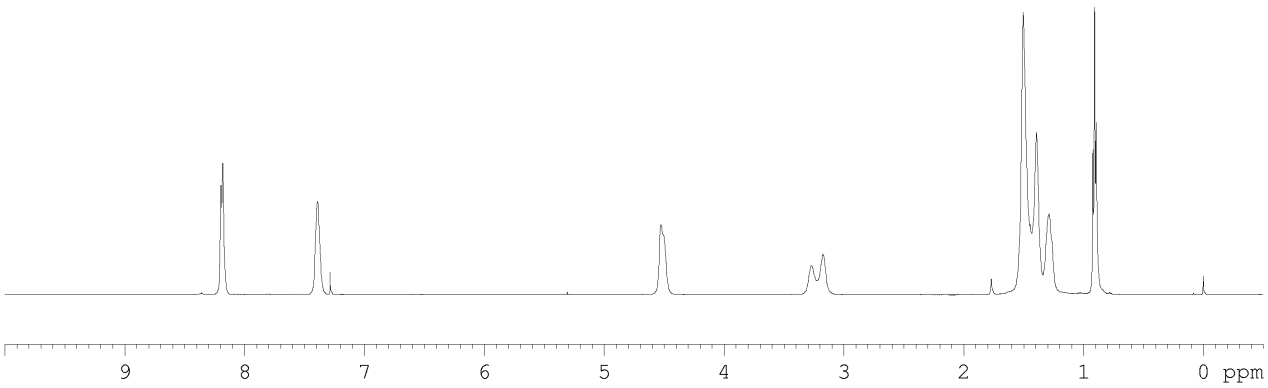
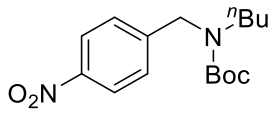
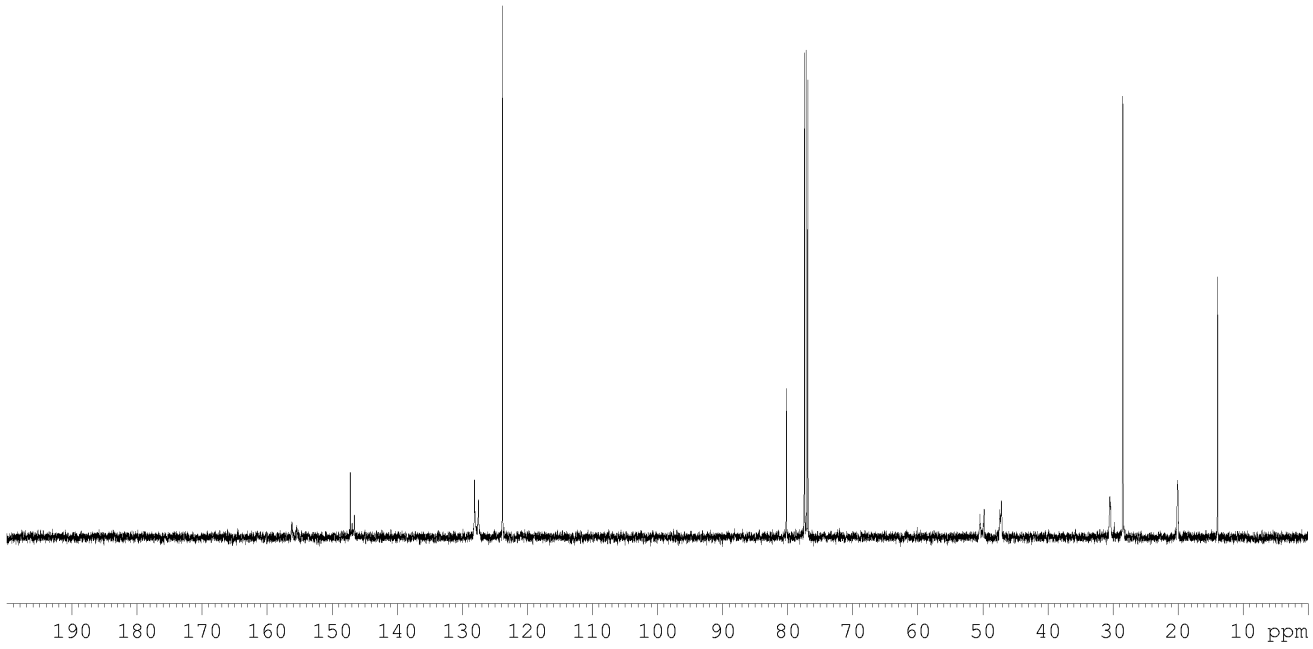


Figure A2.175 Infrared Spectrum


^{n}Bu
N
Boc
O_2N


9
8
7
6
5
4
3
2
1
0 ppm


^{n}Bu
N
Boc
O_2N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

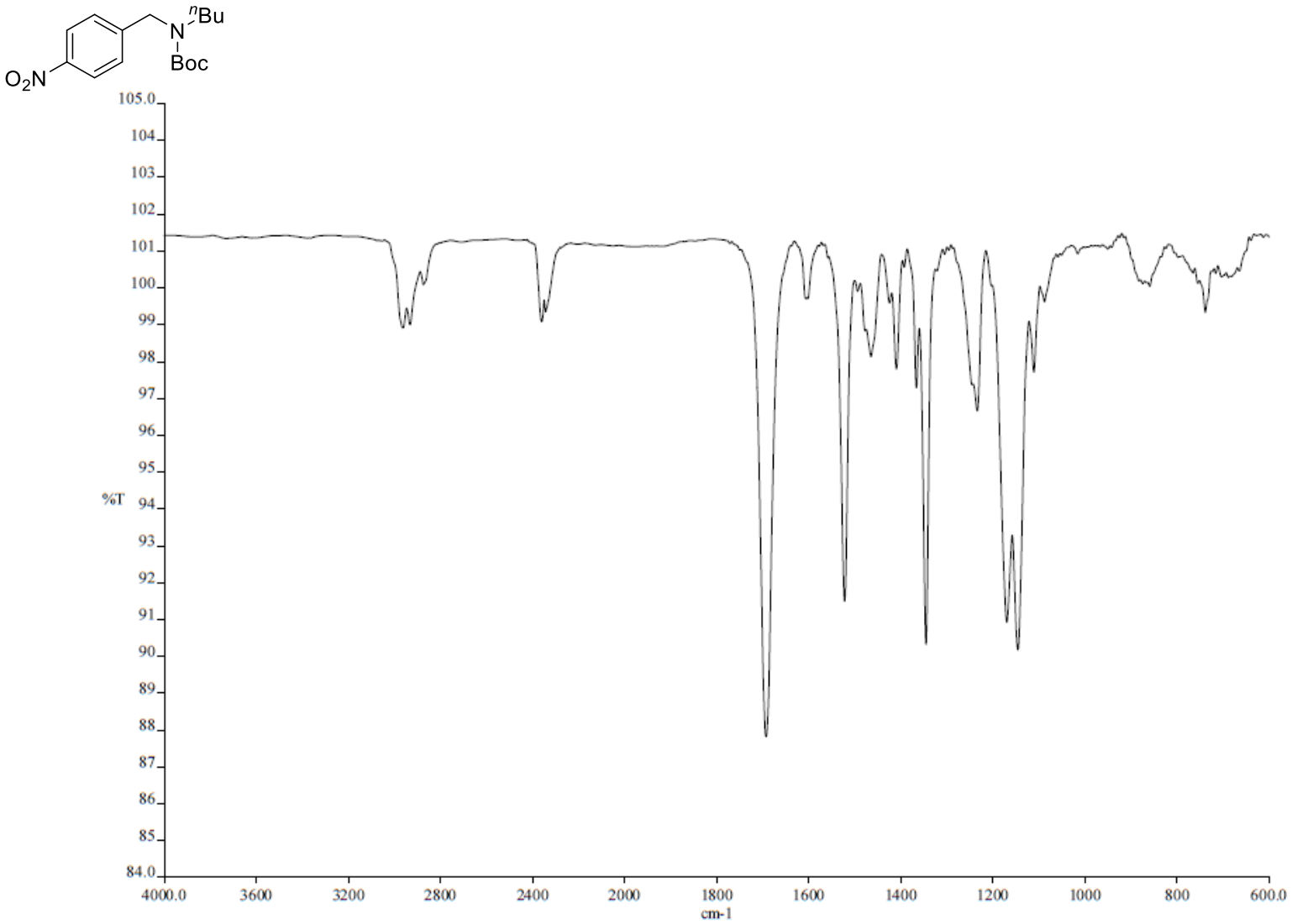
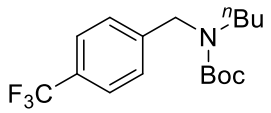
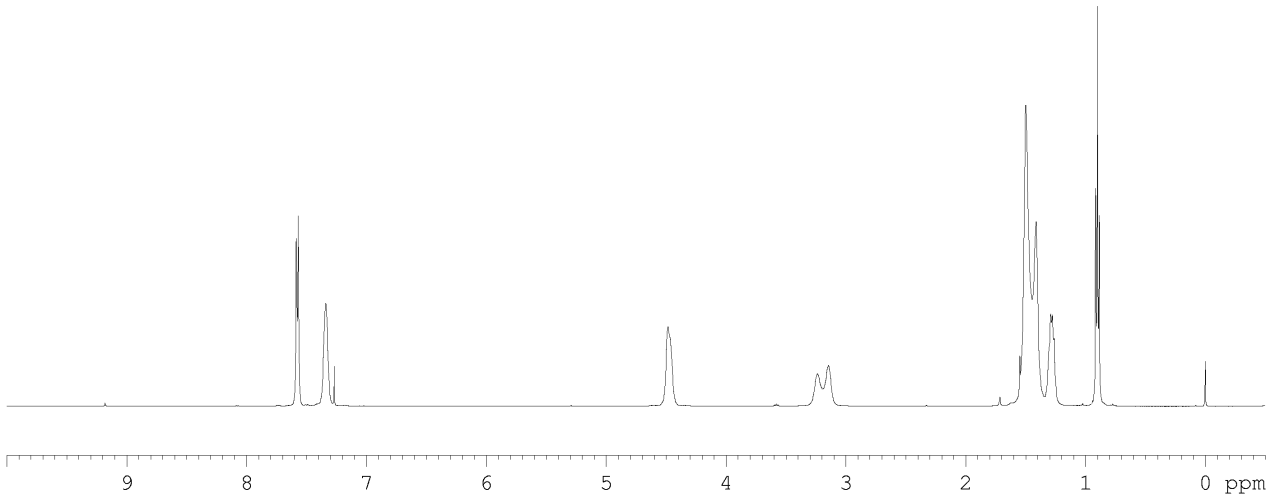
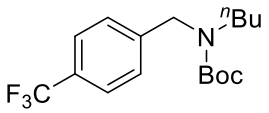
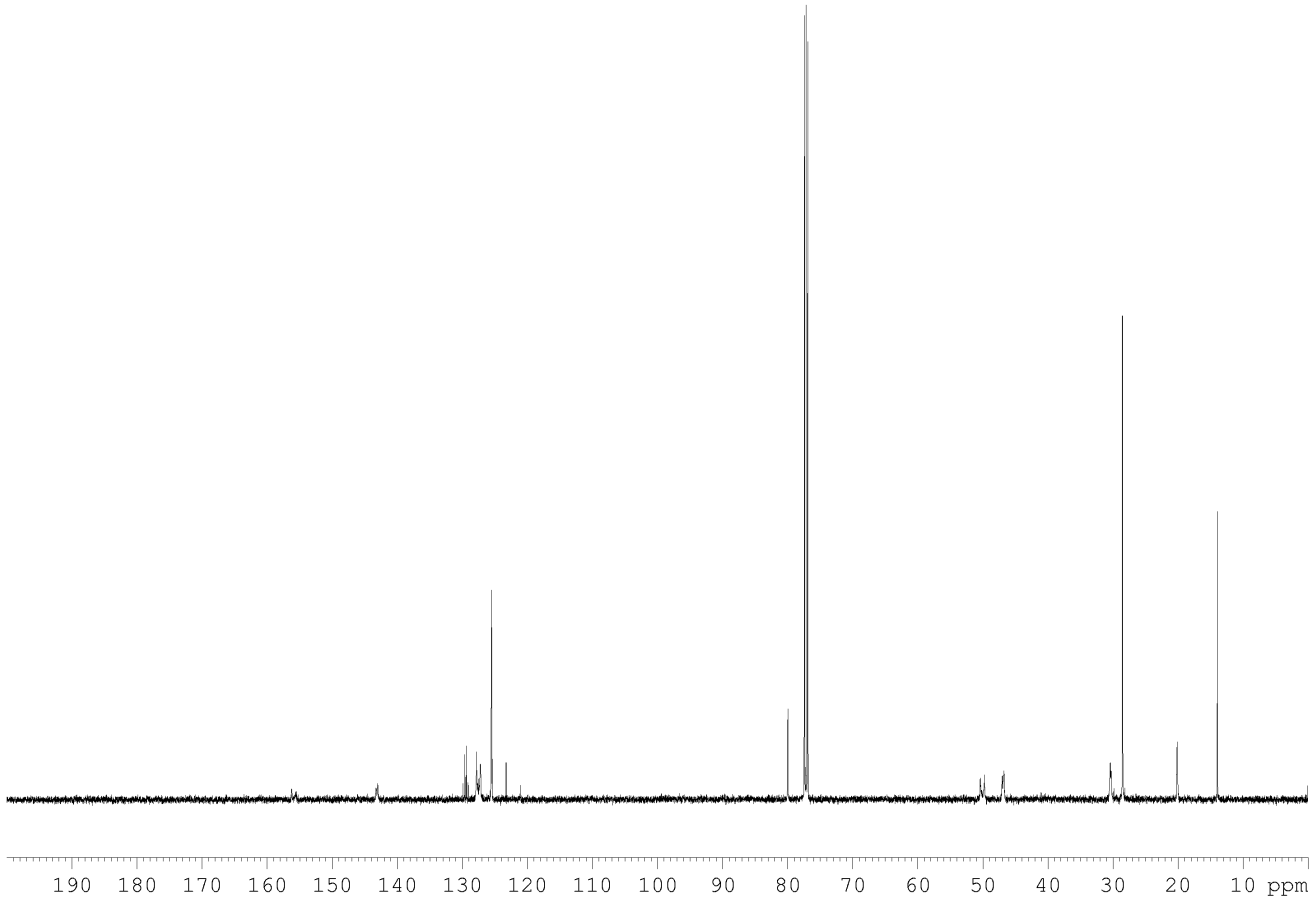


Figure A2.178 Infrared Spectrum


nBu
N
Boc
F3C


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
F3C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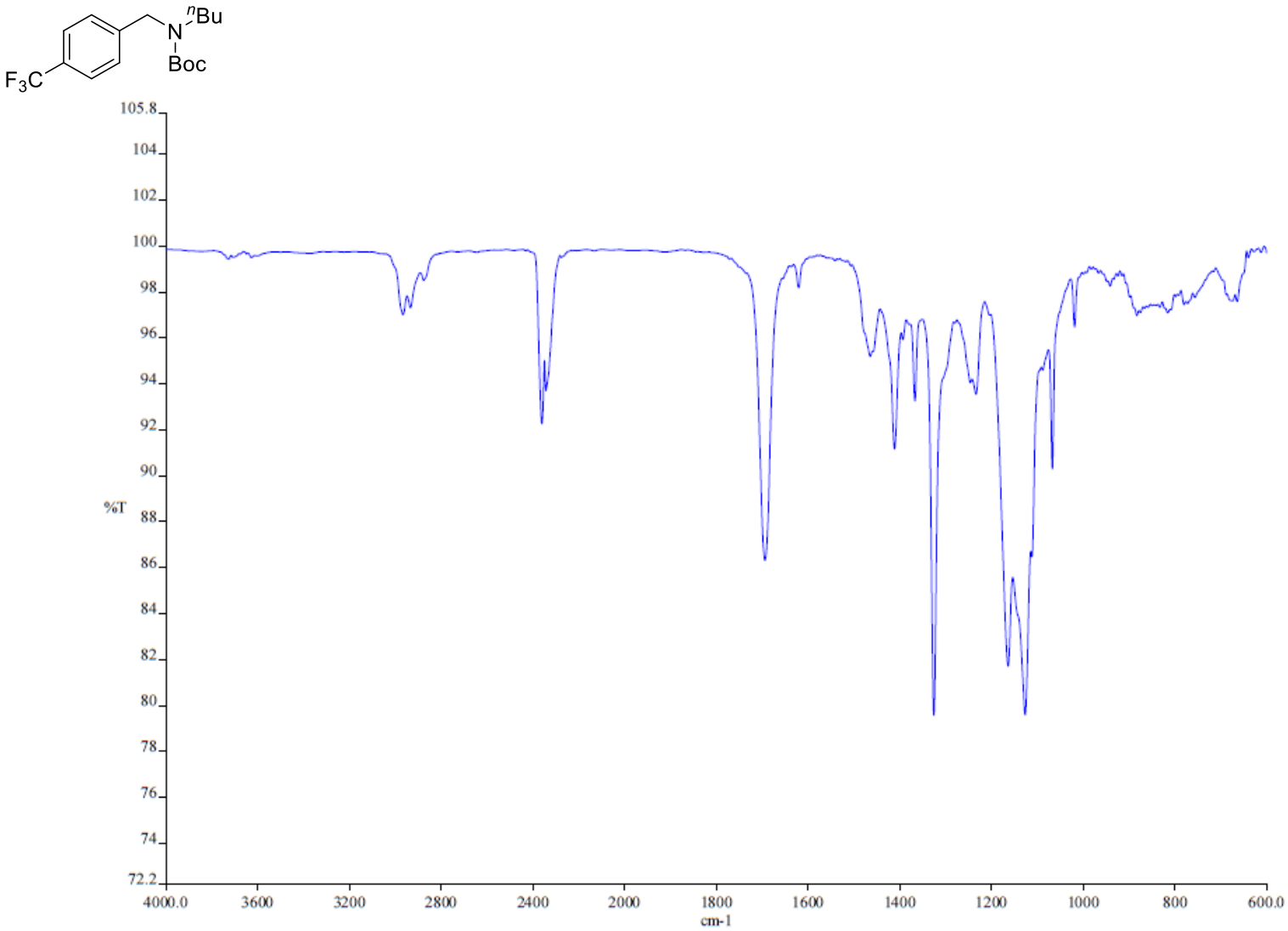
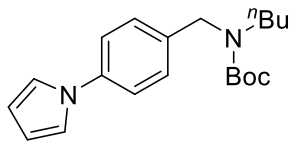
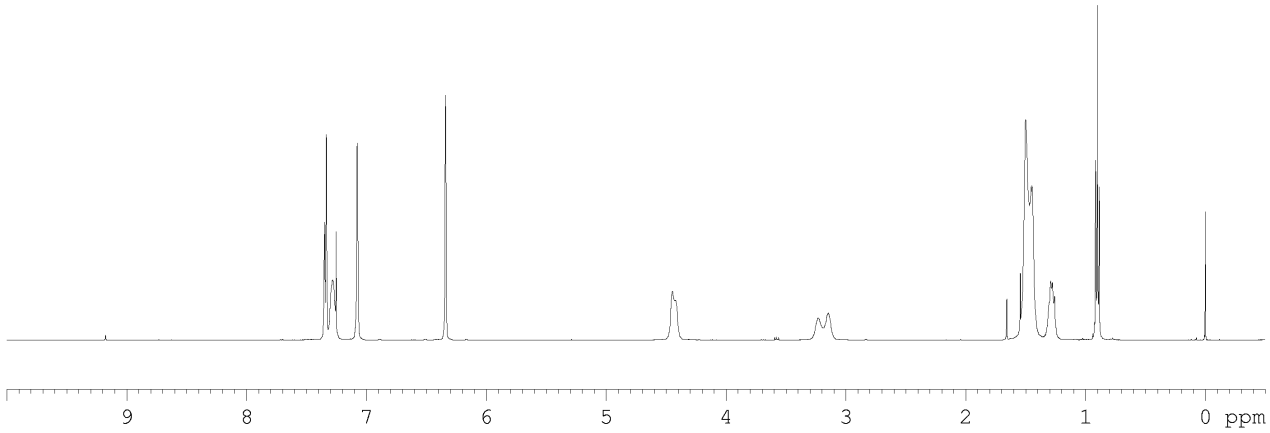
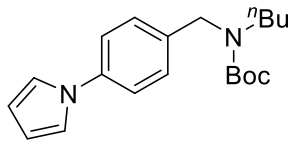
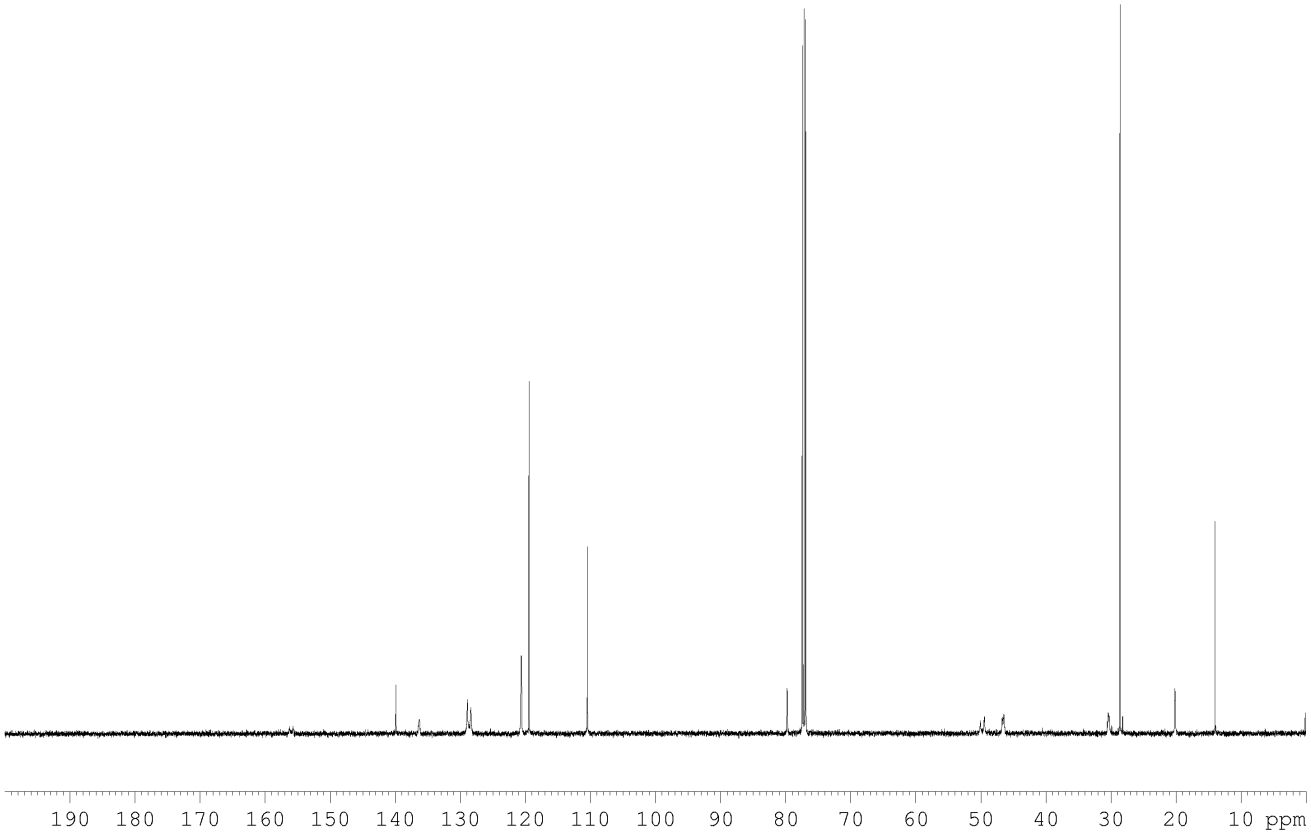


Figure A2.181 Infrared Spectrum


N
nBu
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

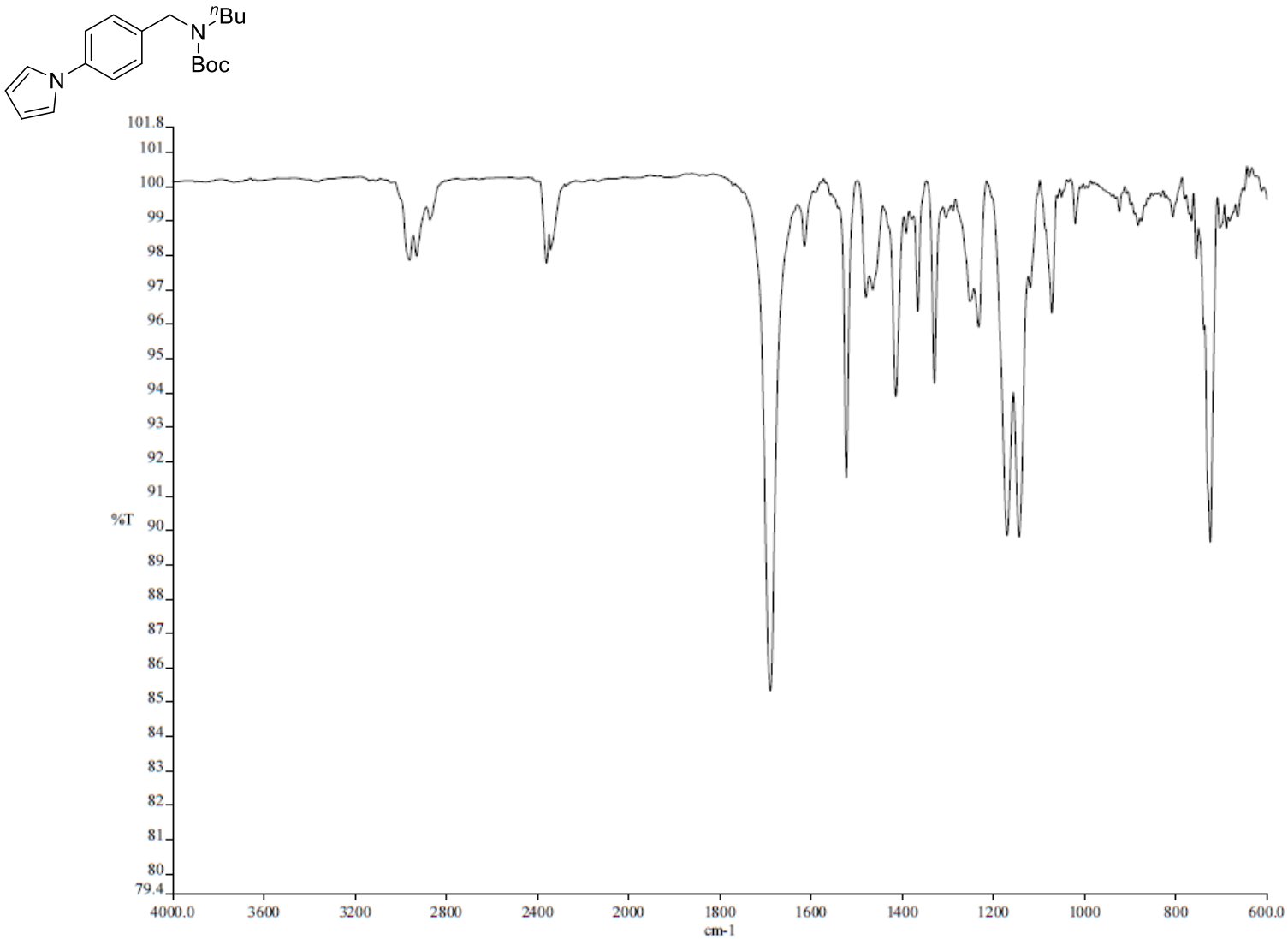
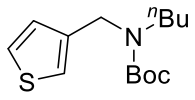
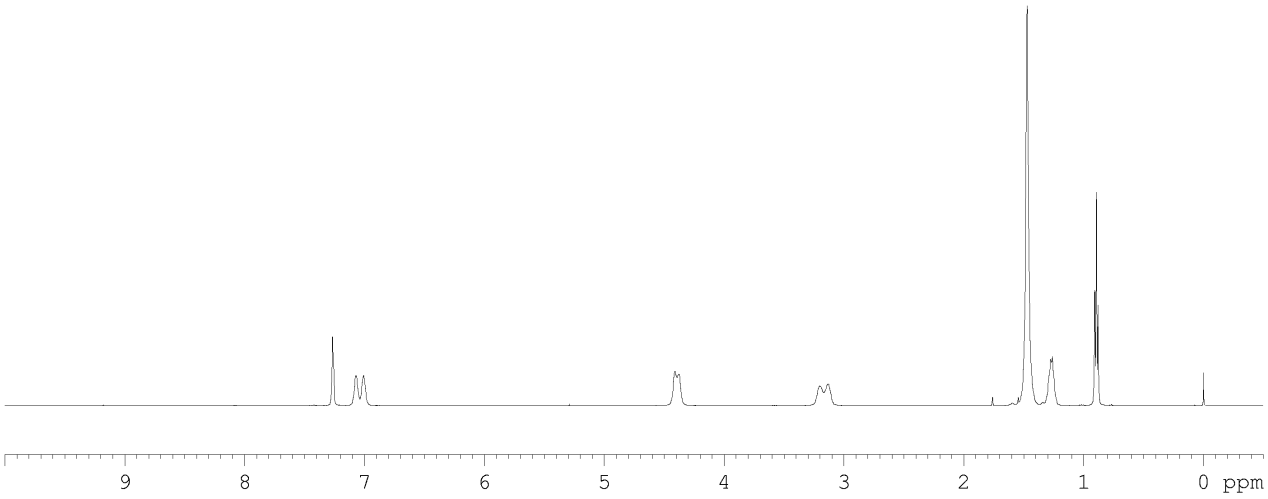
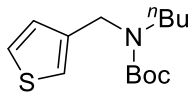
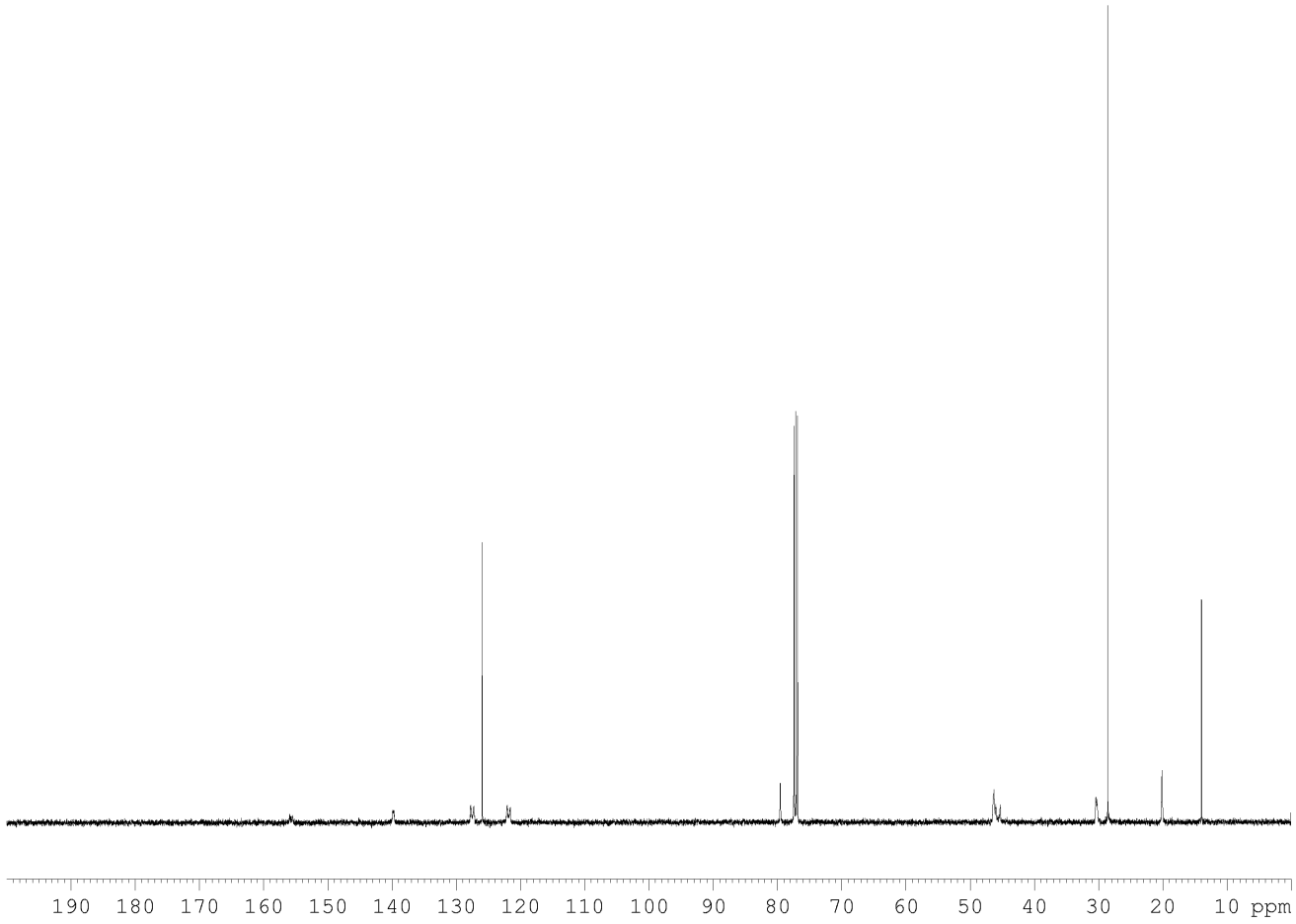


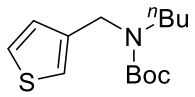
Figure A2.184 Infrared Spectrum


nBu
N
Boc
S


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
S


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



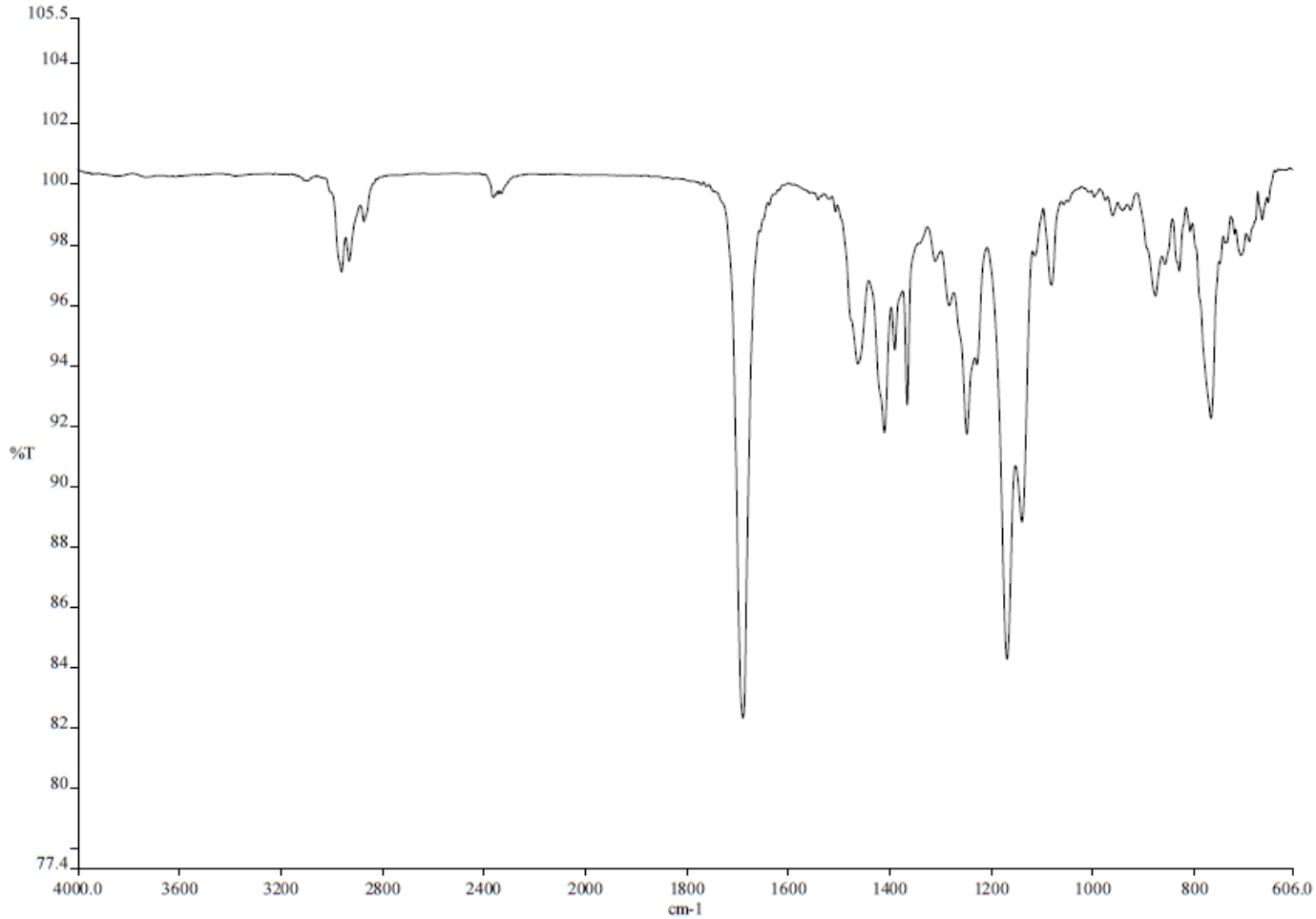
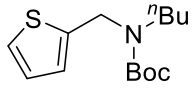
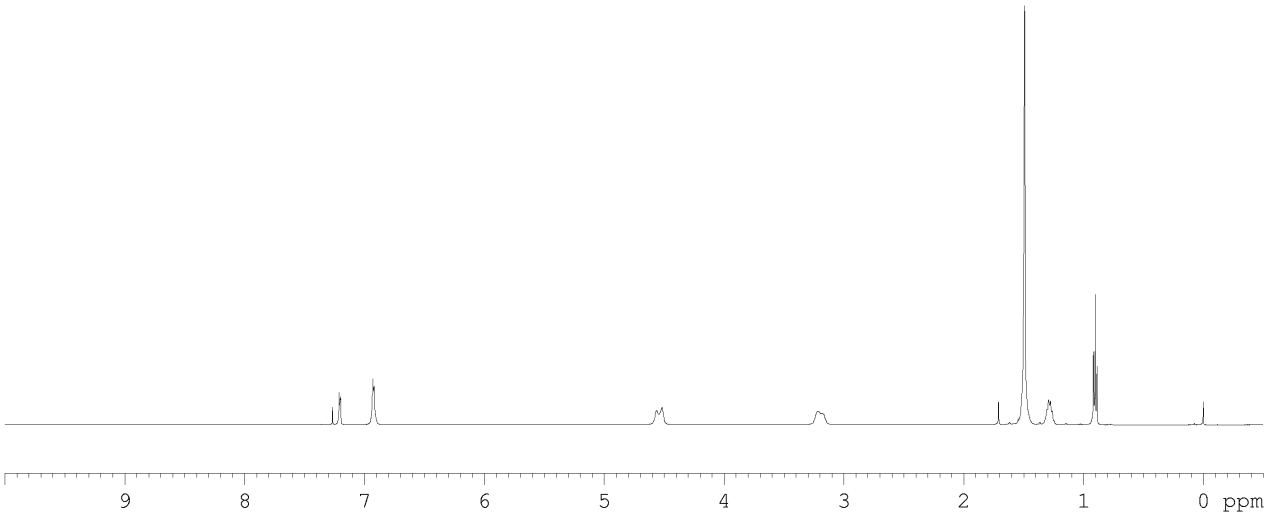
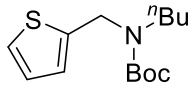
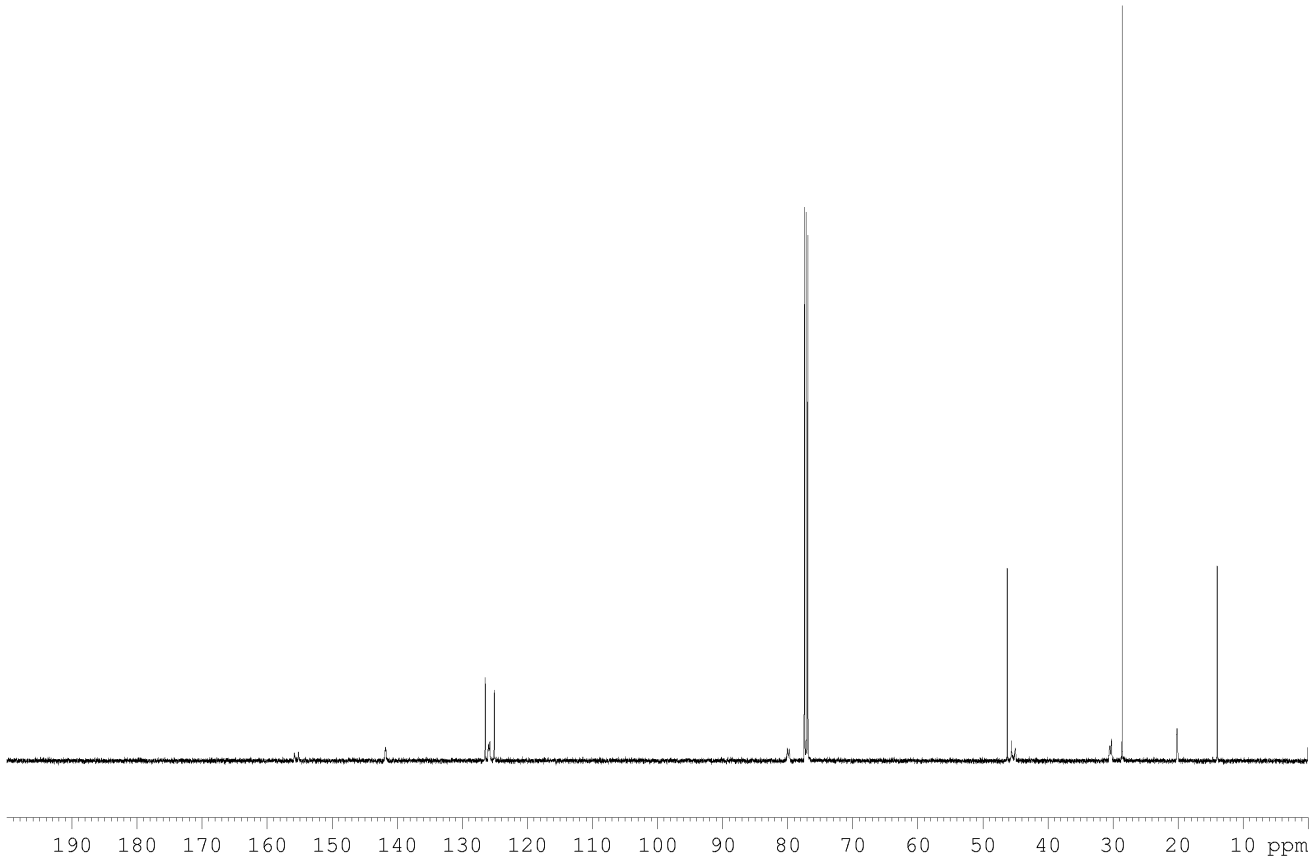


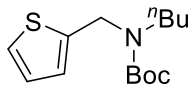
Figure A2.187 Infrared Spectrum


S
N
nBu
Boc


9
8
7
6
5
4
3
2
1
0 ppm


S
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



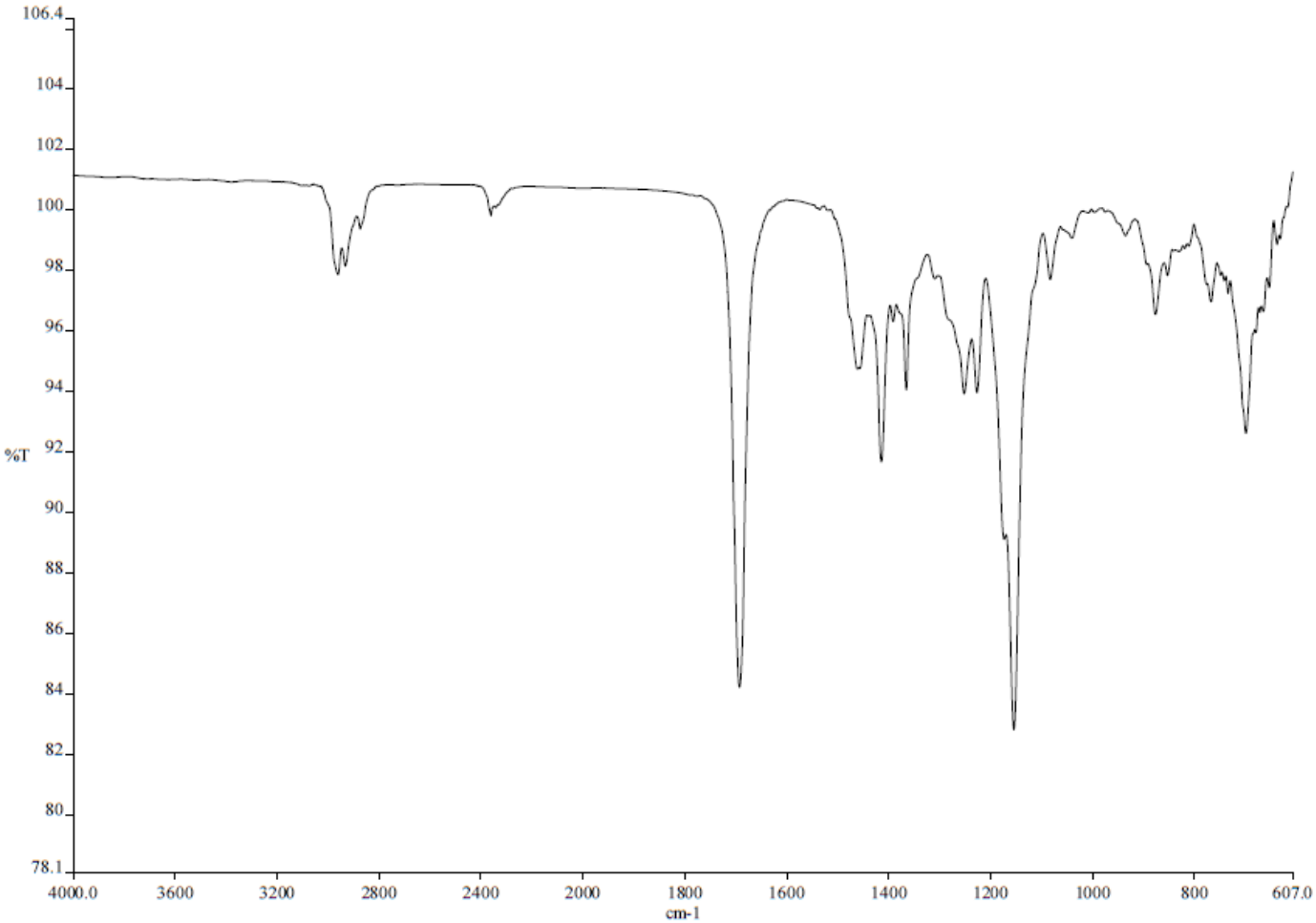
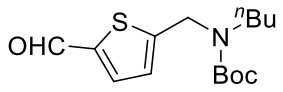
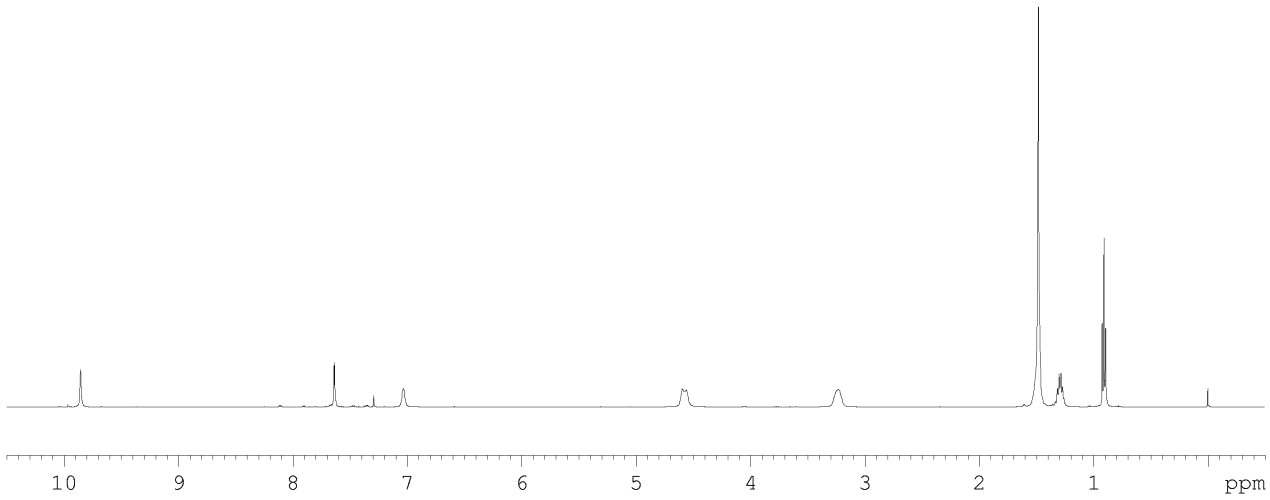
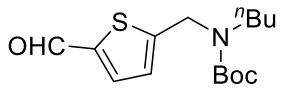
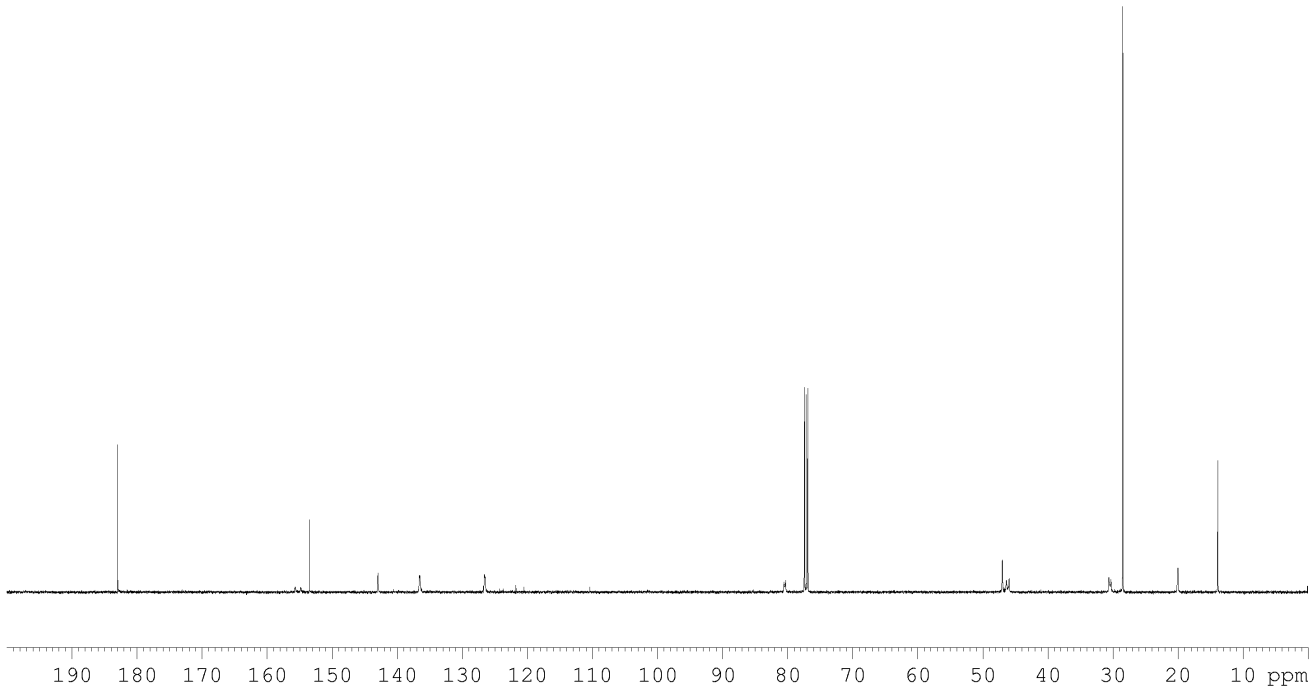


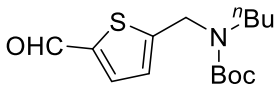
Figure A2.190 Infrared Spectrum


OHC
S
N
nBu
Boc


10
9
8
7
6
5
4
3
2
1
ppm


OHC
S
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



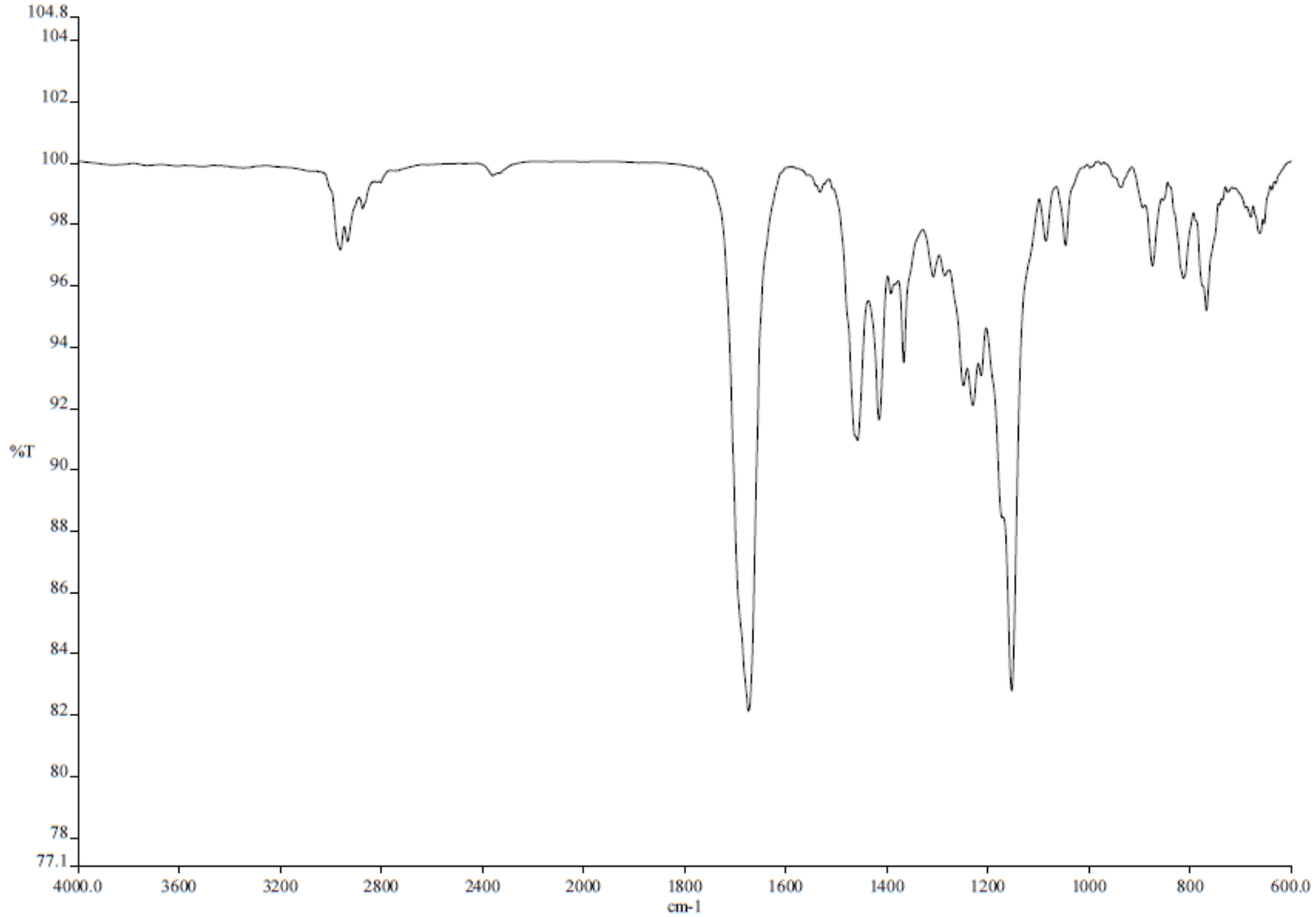
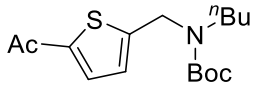
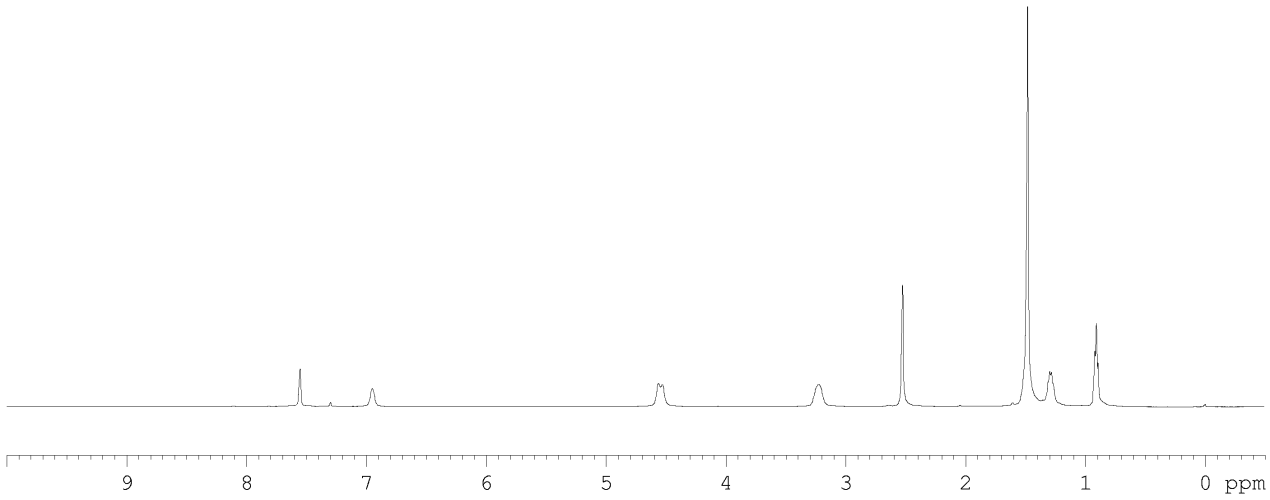
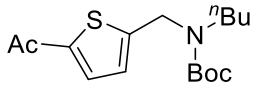
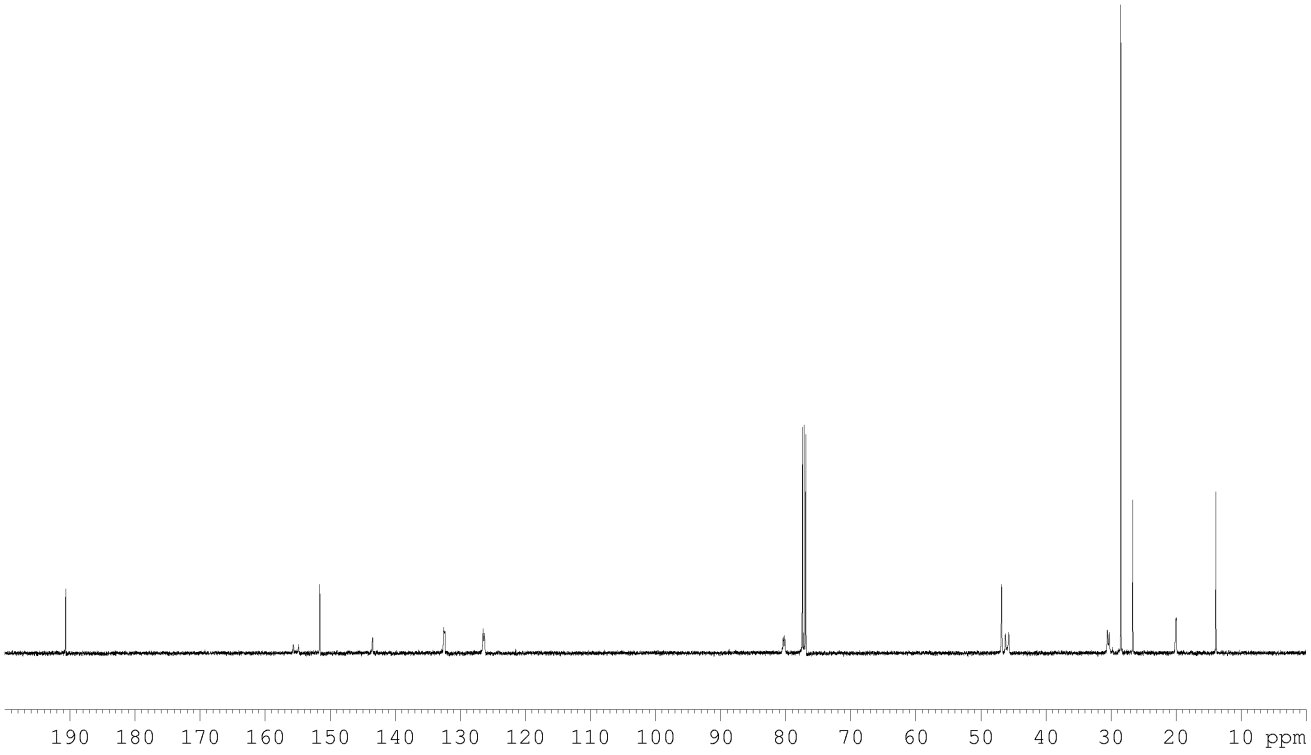


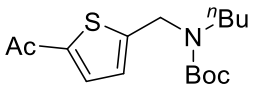
Figure A2.193 Infrared Spectrum


Ac
S
N
nBu
Boc


9
8
7
6
5
4
3
2
1
0 ppm


S
Ac
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



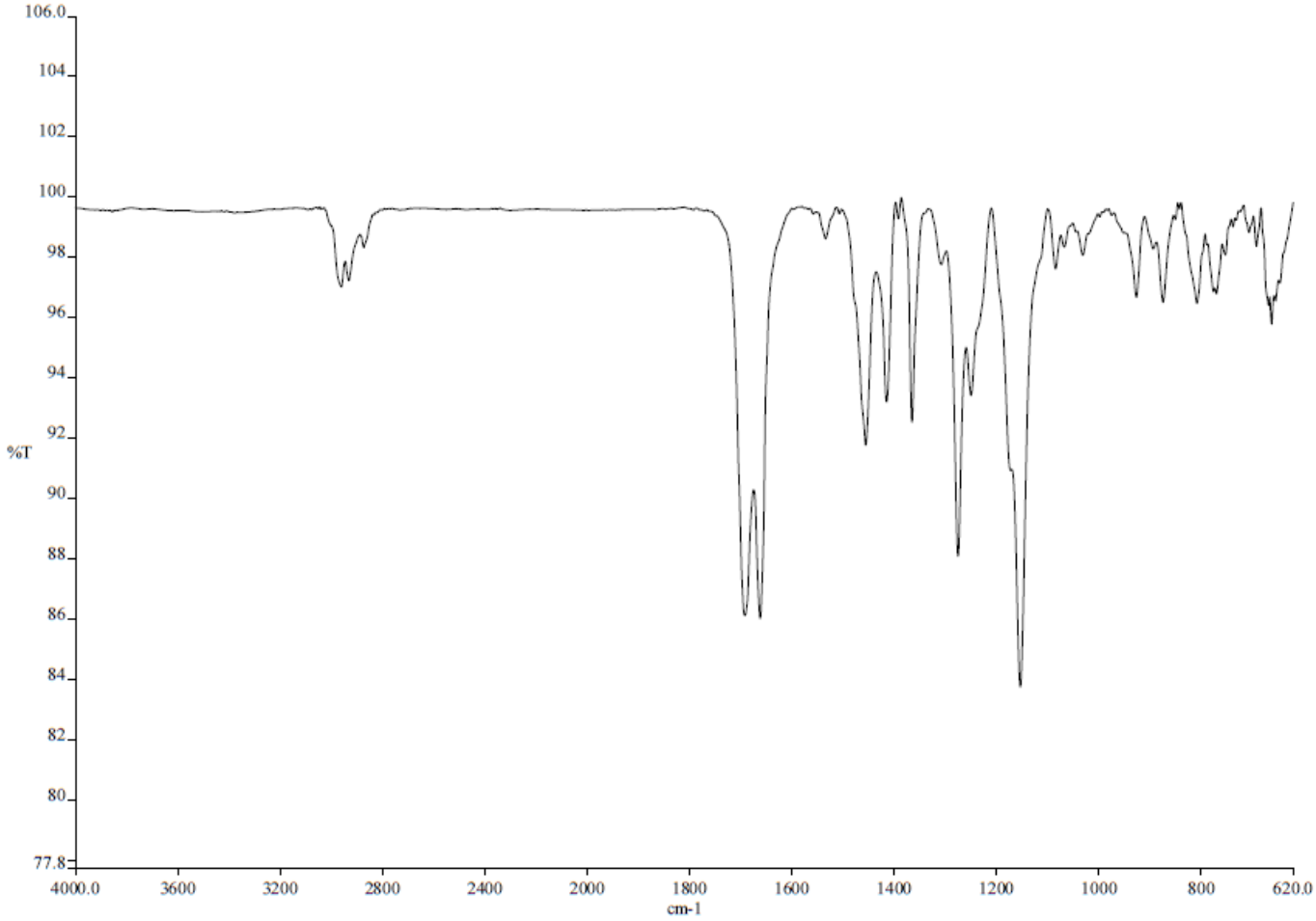
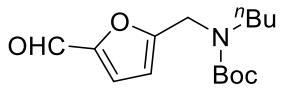
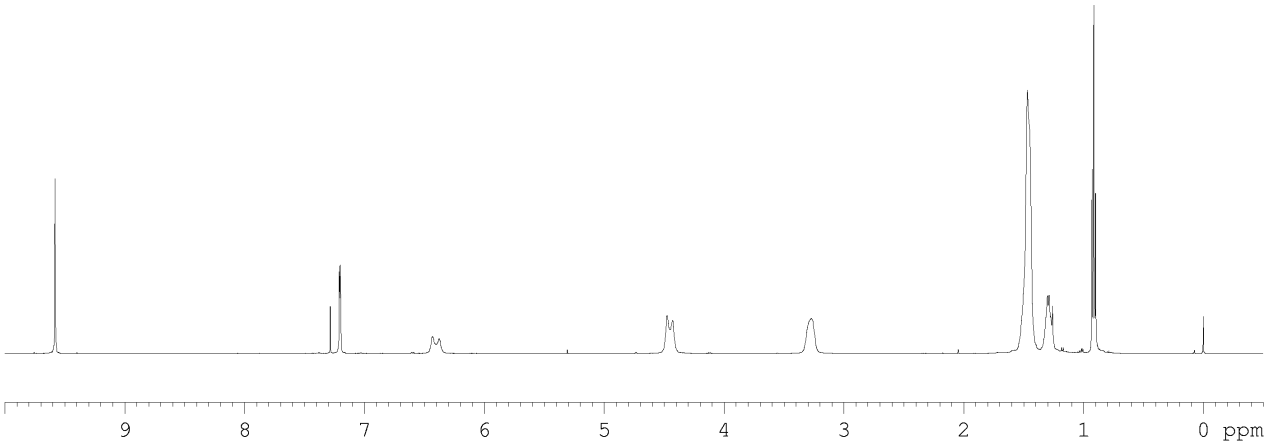
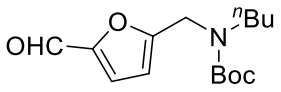


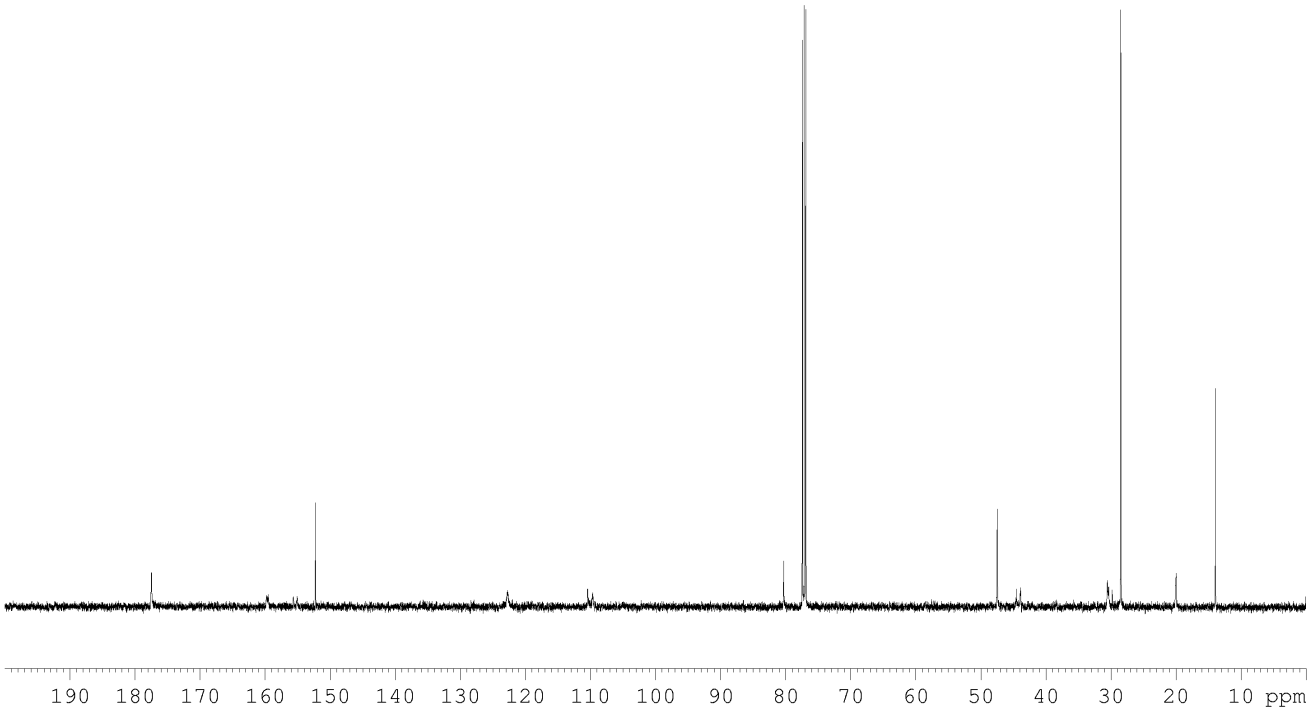
Figure A2.196 Infrared Spectrum

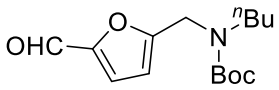


500




OHC
O
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



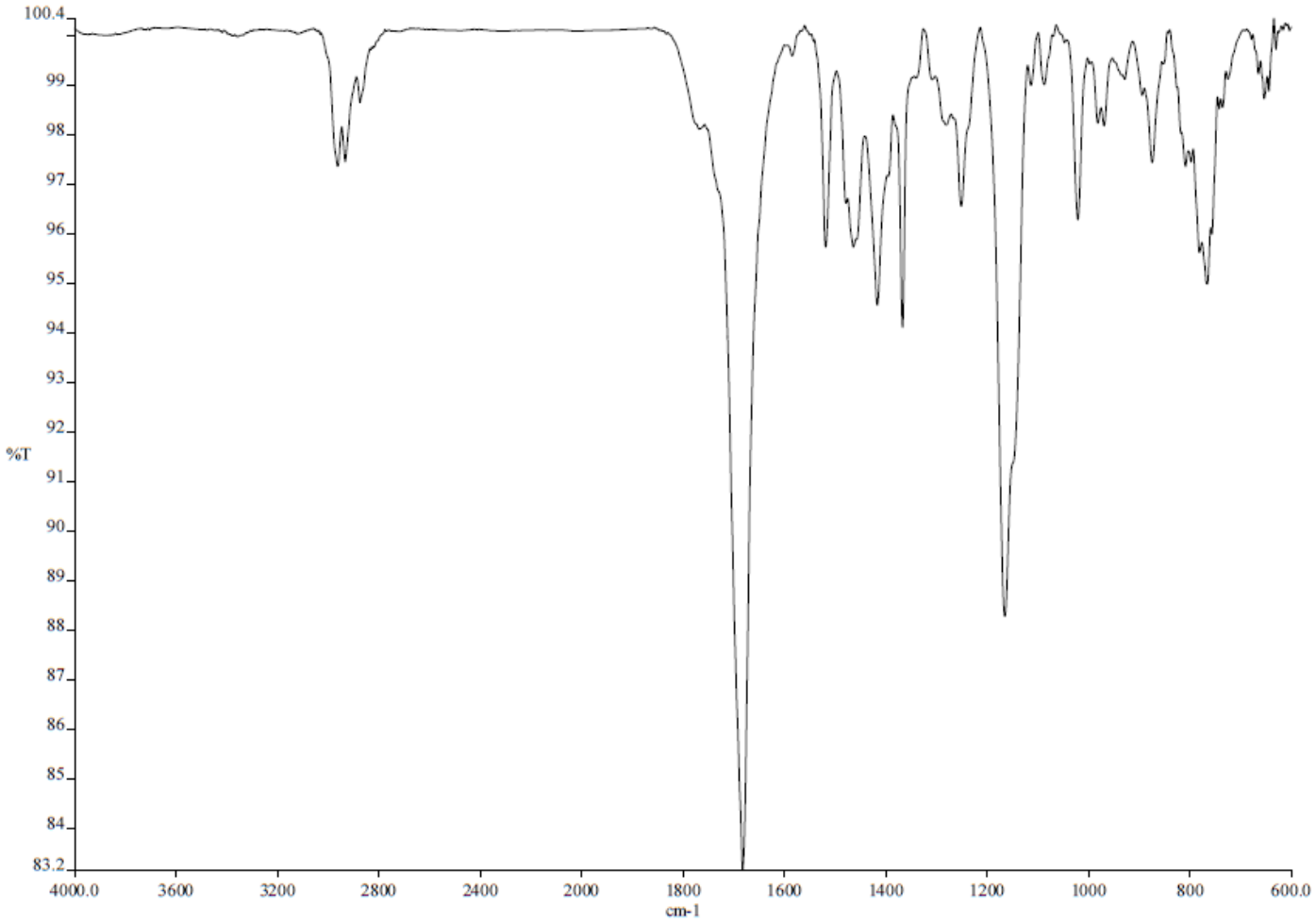
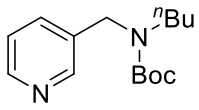
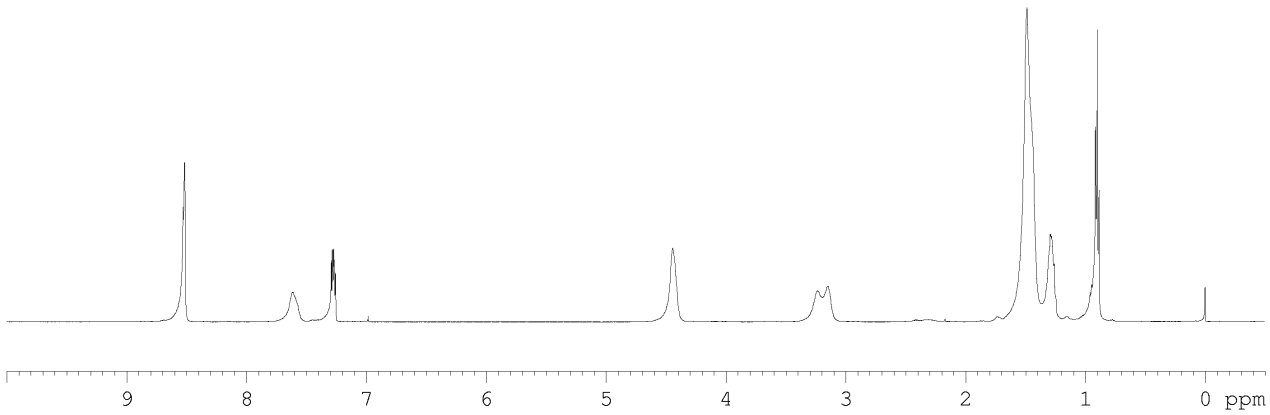
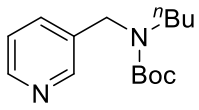
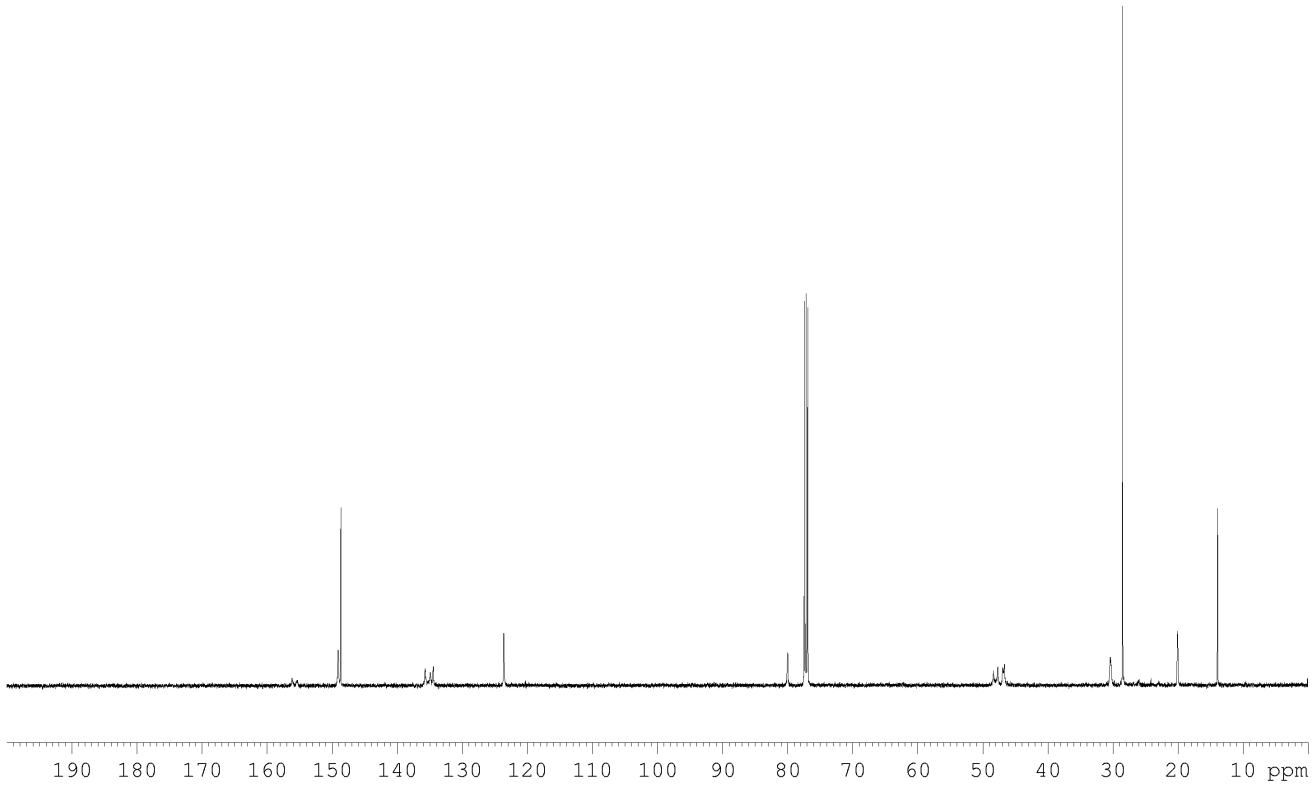


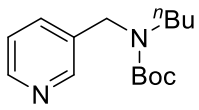
Figure A2.199 Infrared Spectrum


nBu
N
Boc
N


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



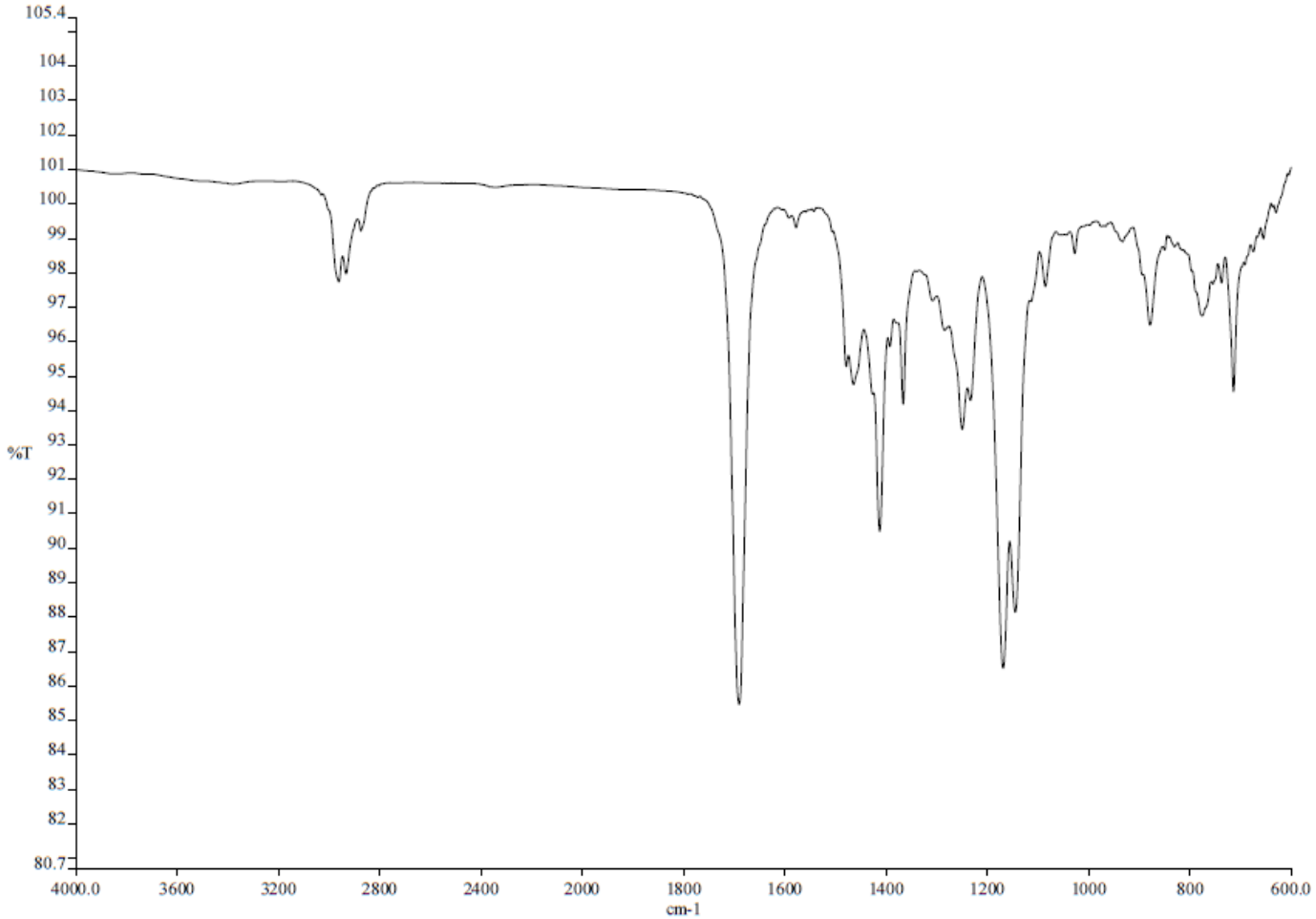
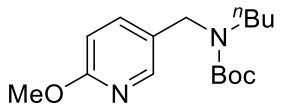
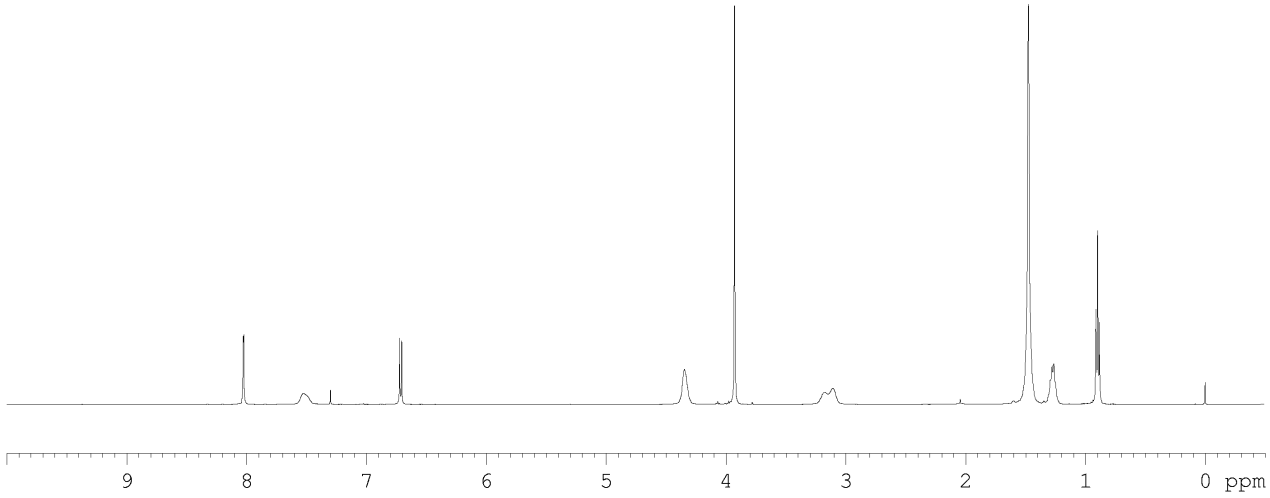
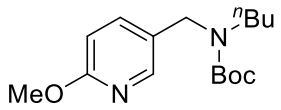
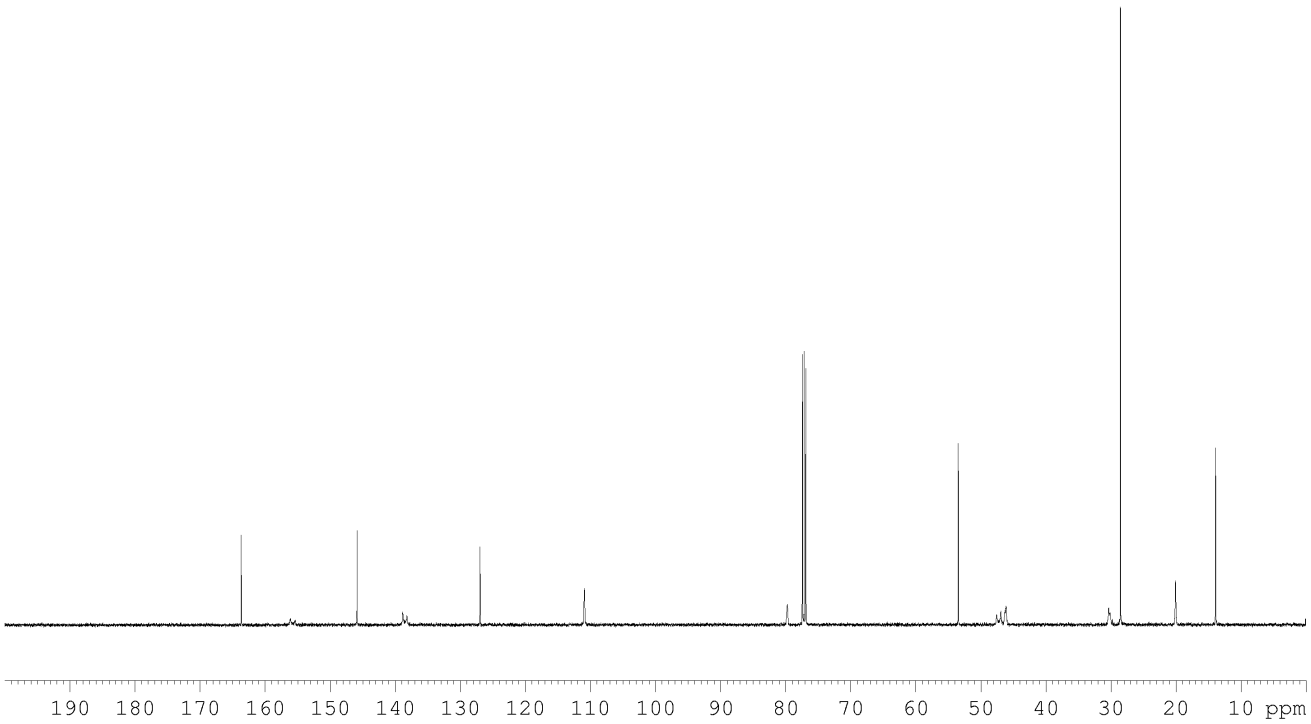


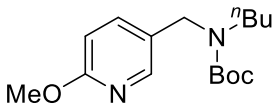
Figure A2.202 Infrared Spectrum


nBu
N
Boc
MeO
N


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



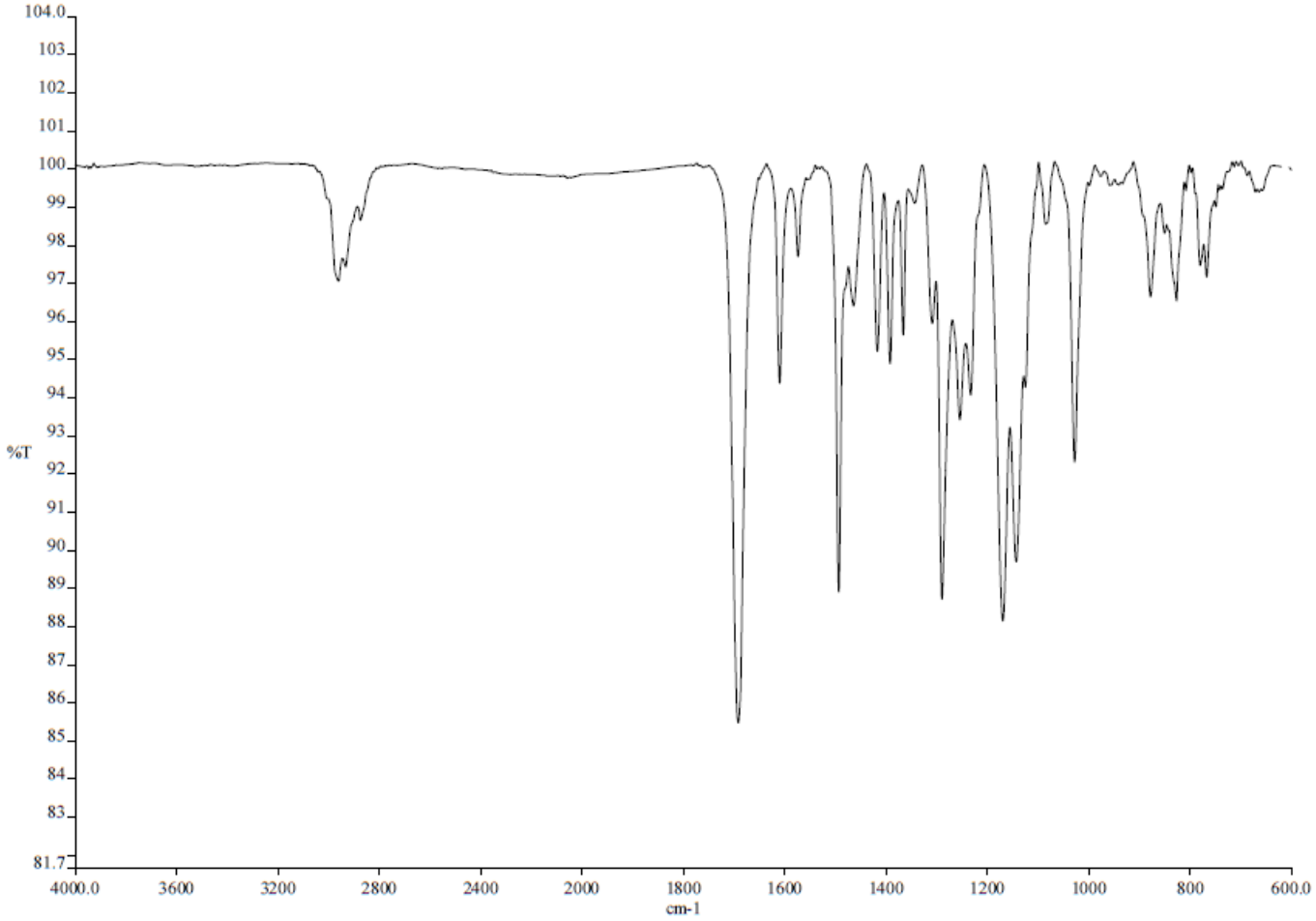
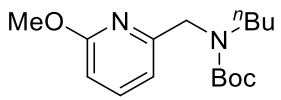
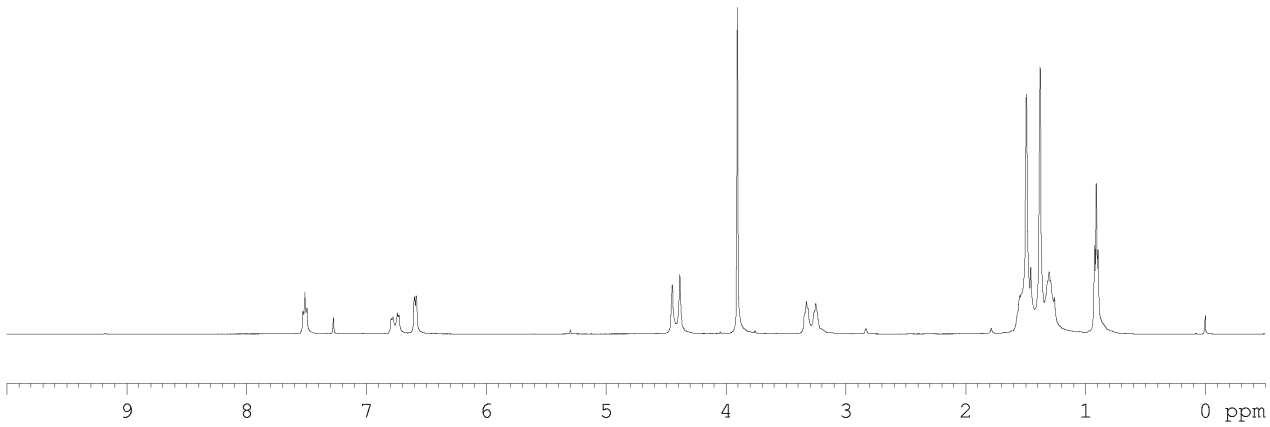
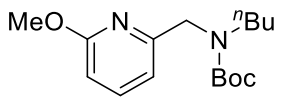
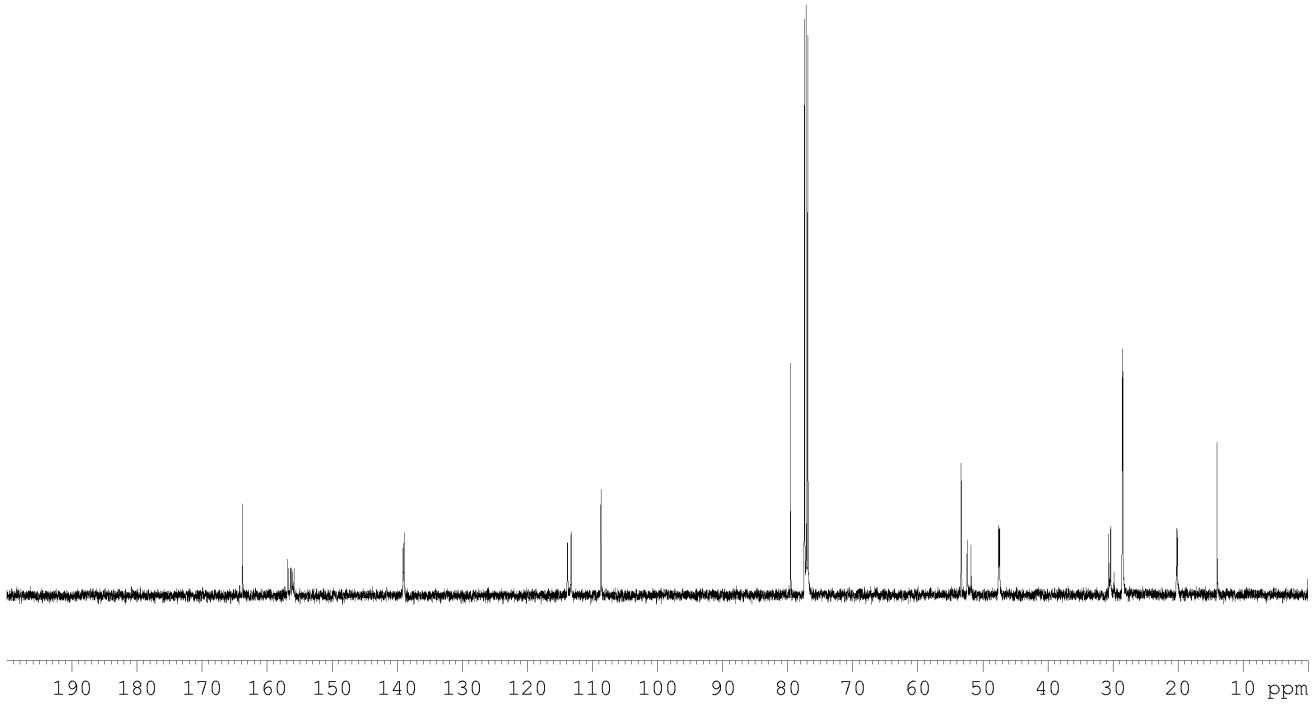


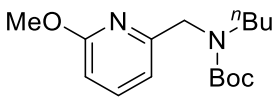
Figure A2.205 Infrared Spectrum


MeO
N
N
nBu
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



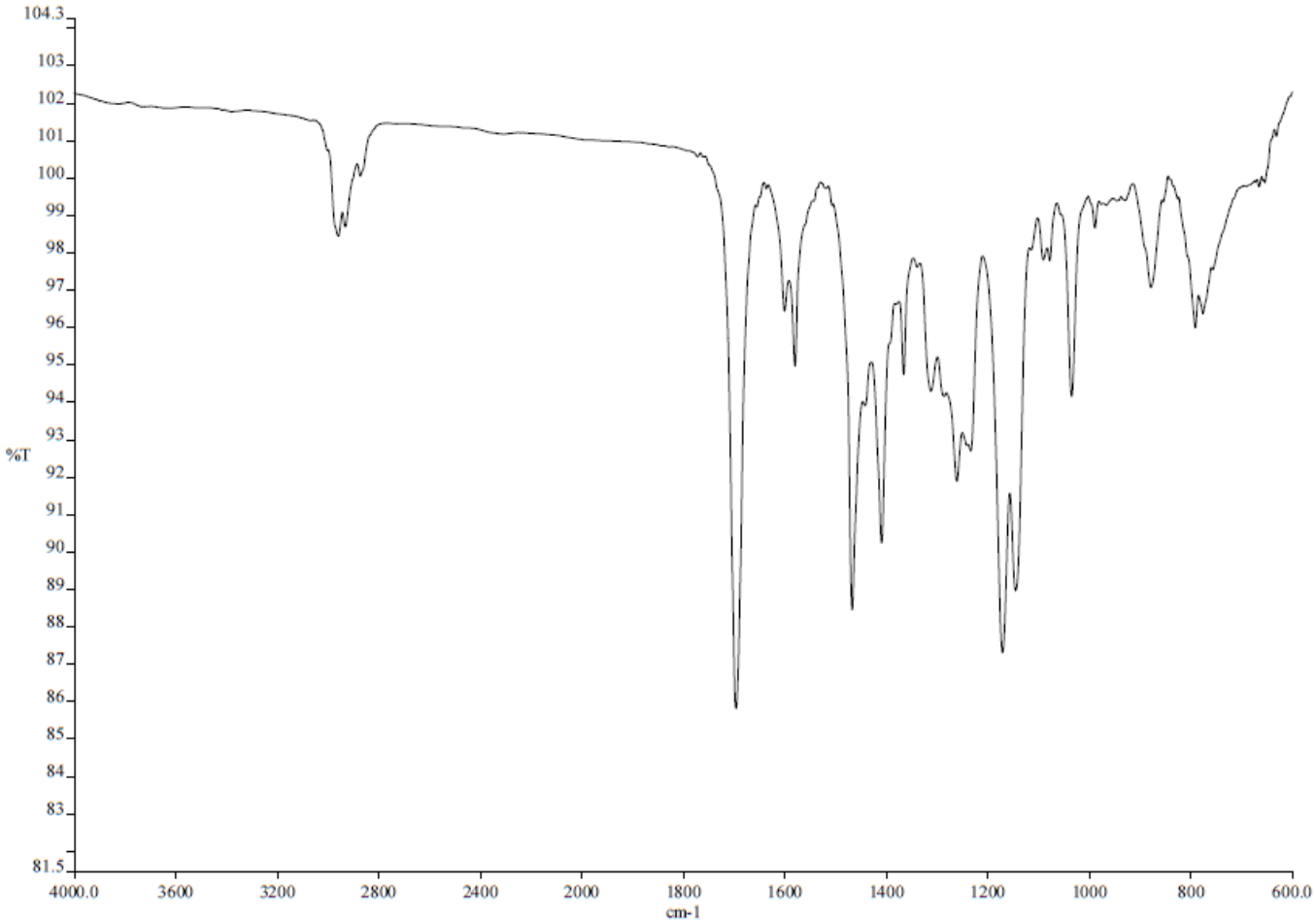
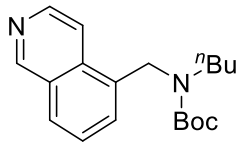
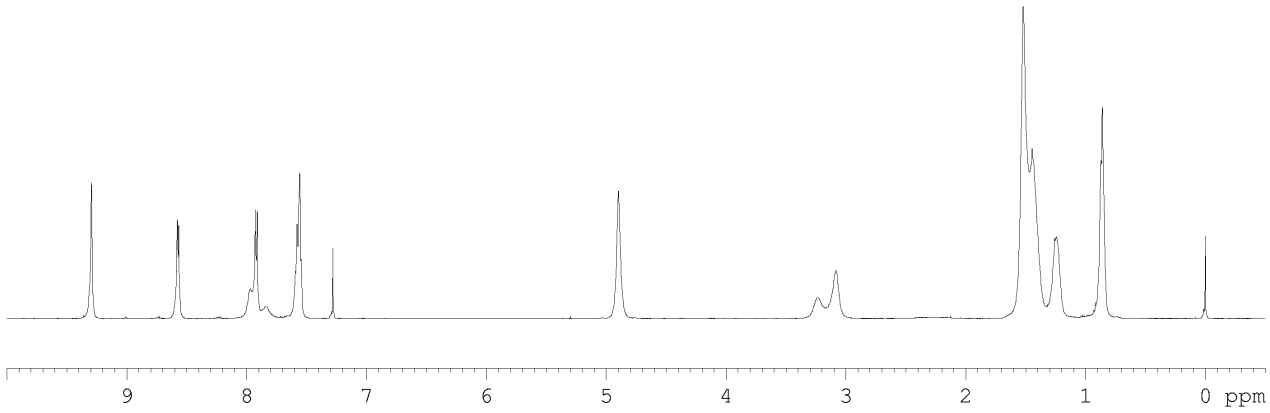
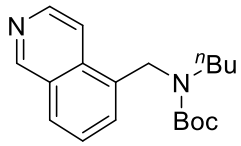
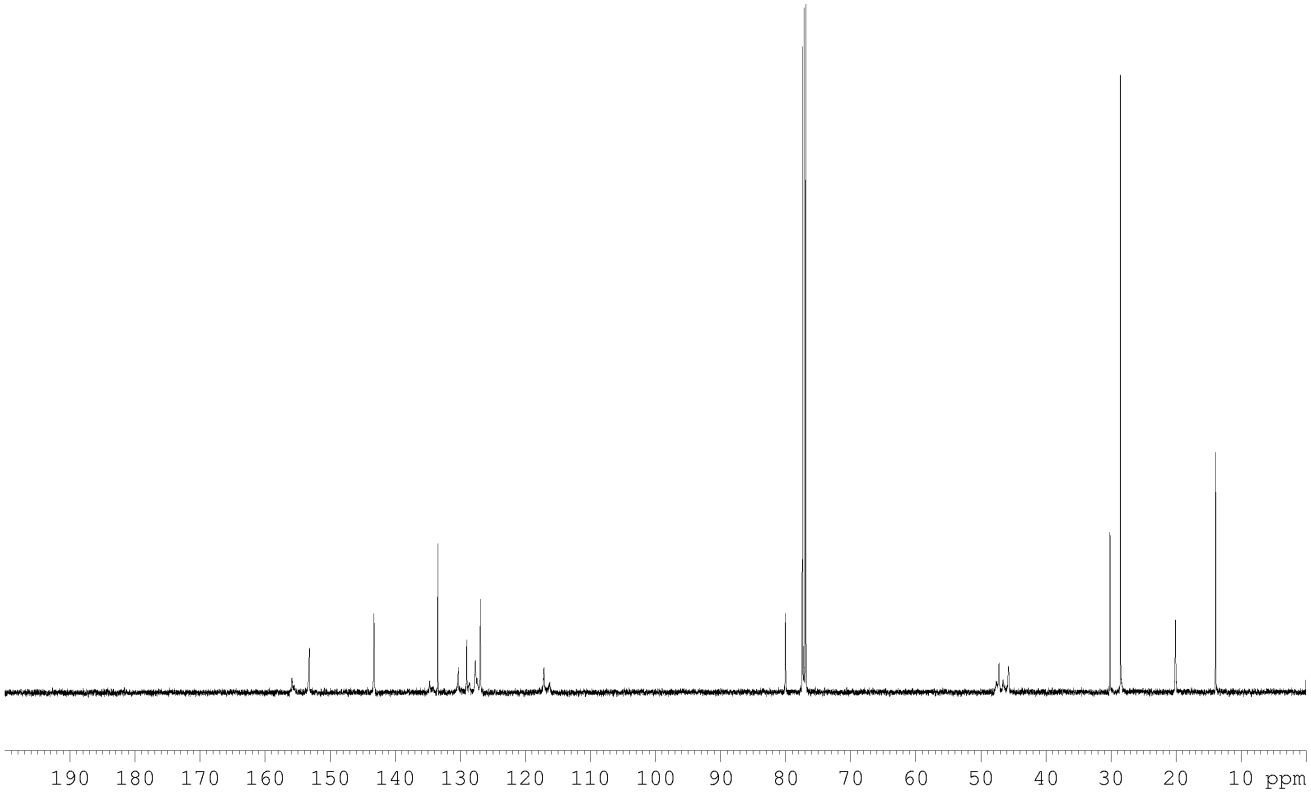


Figure A2.208 Infrared Spectrum


N
nBu
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


N
nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

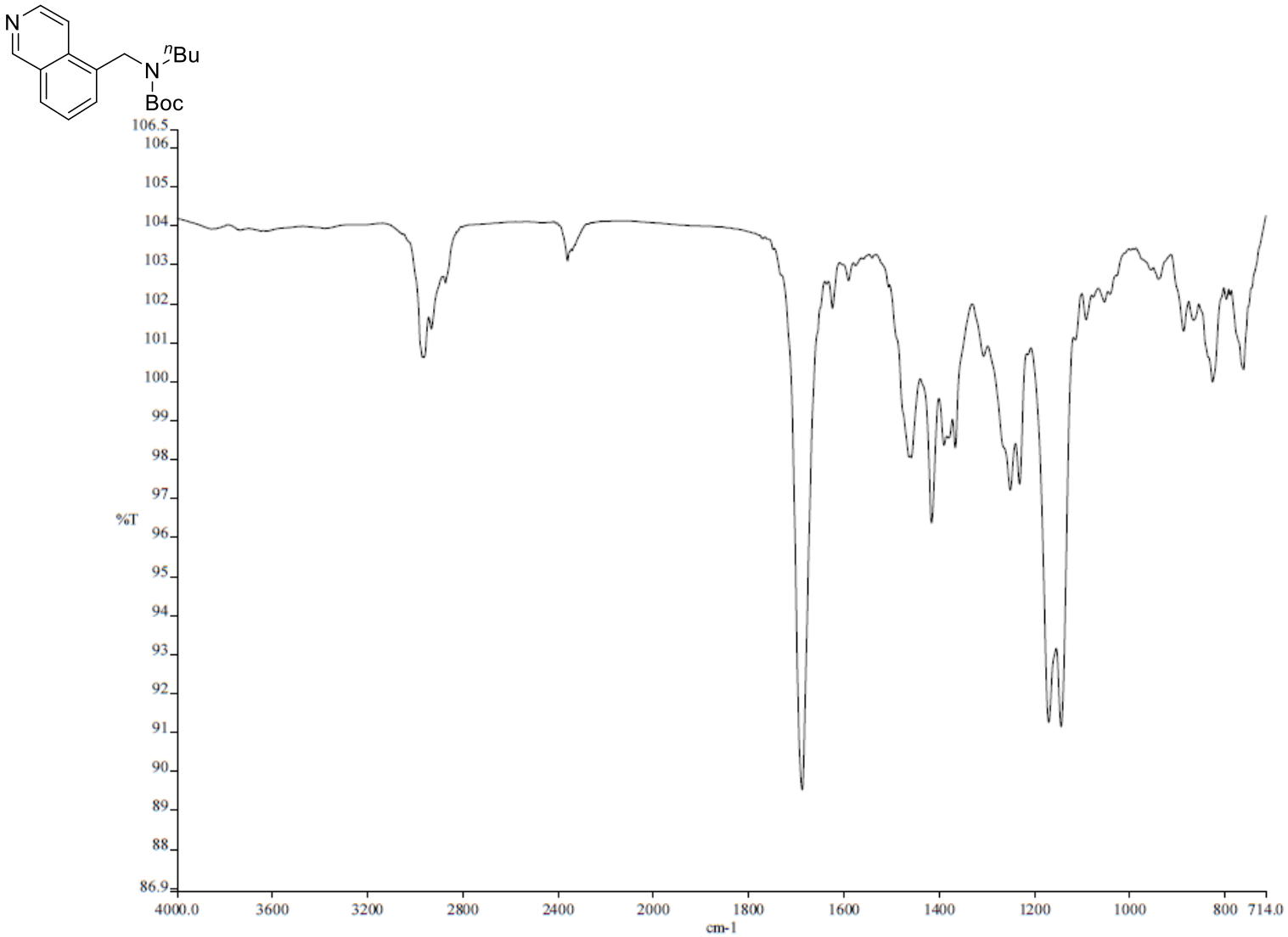
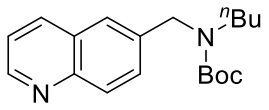
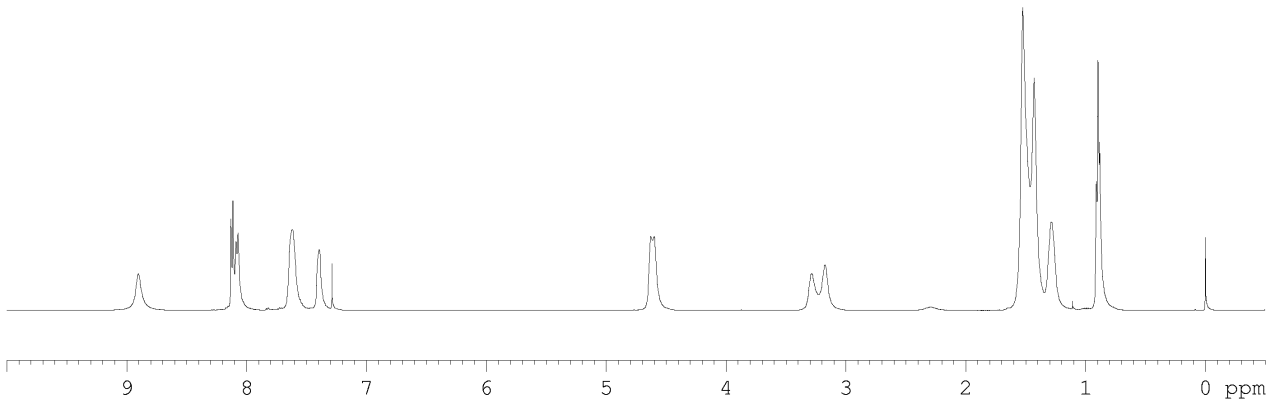
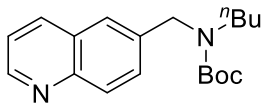
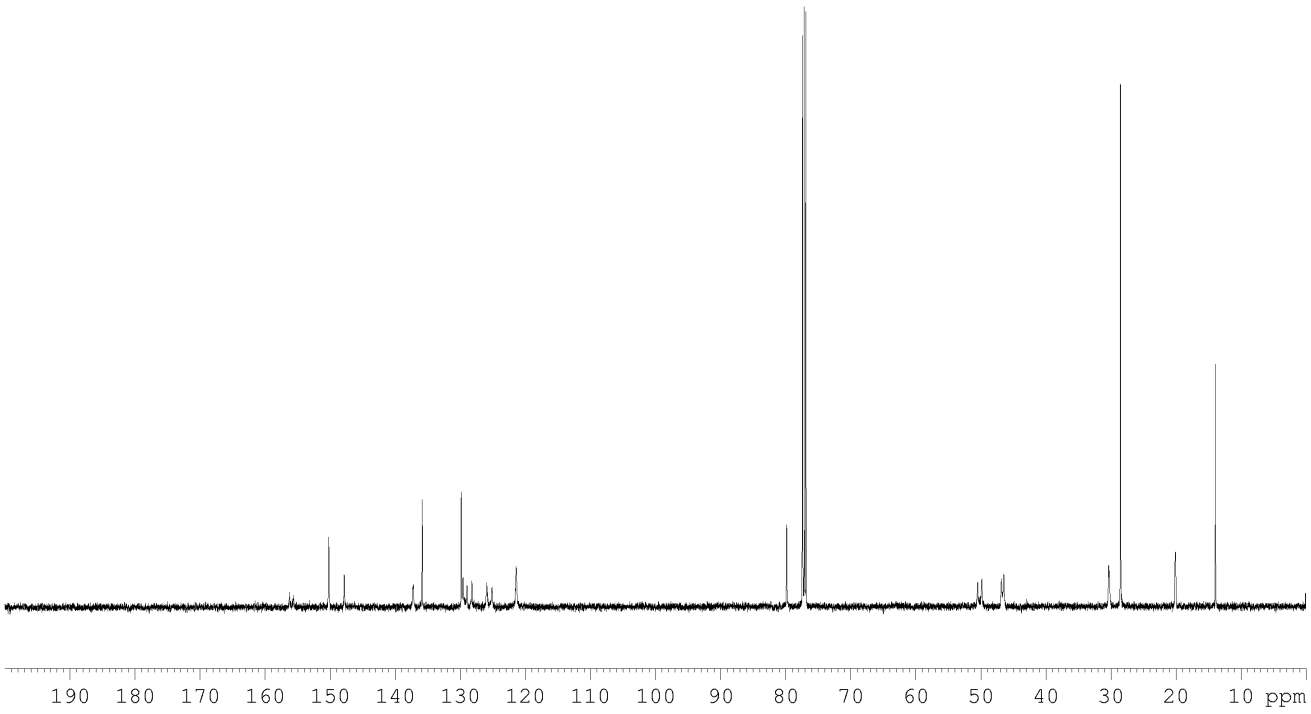


Figure A2.211 Infrared Spectrum


nBu
N
Boc
N


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

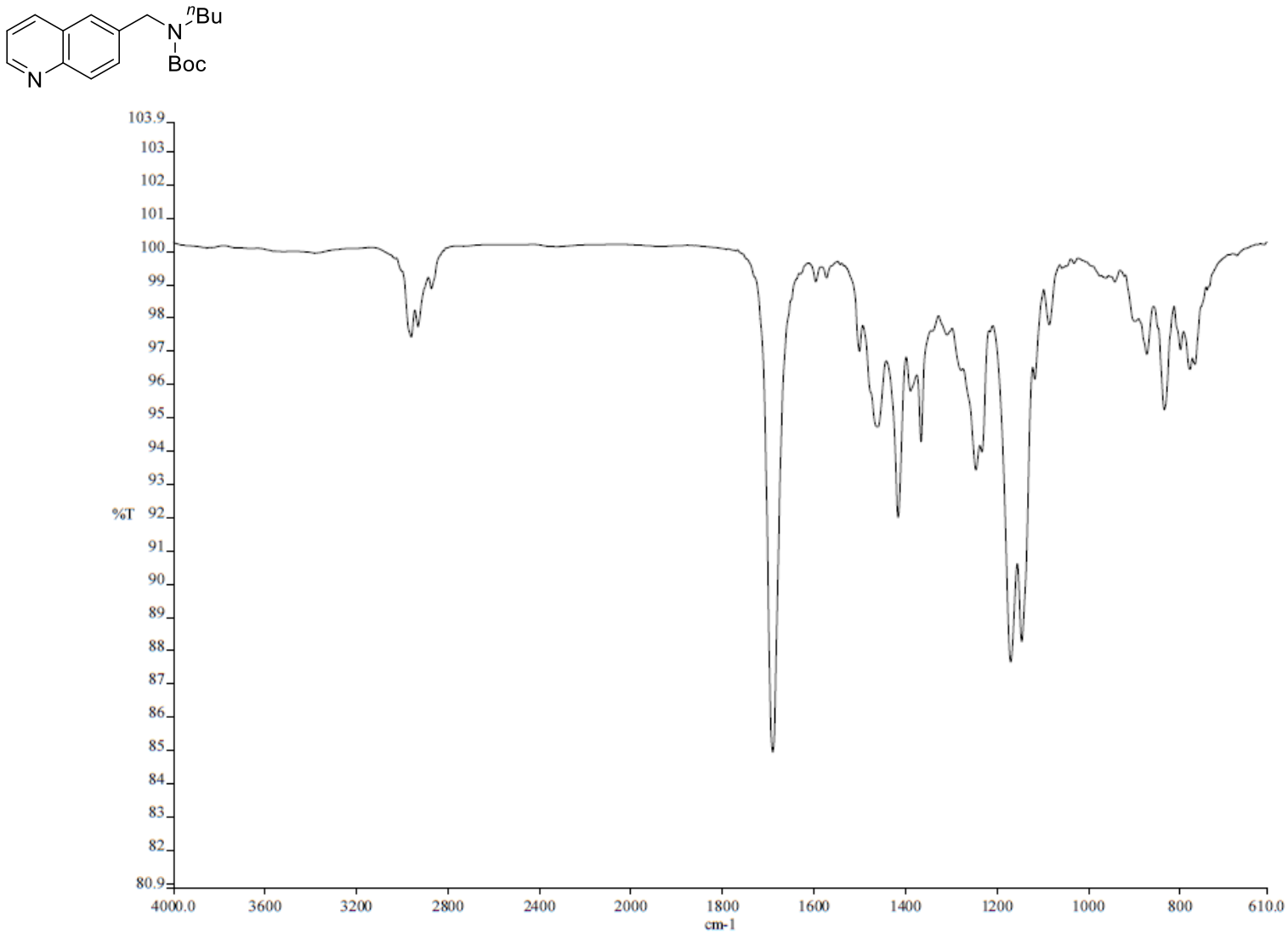
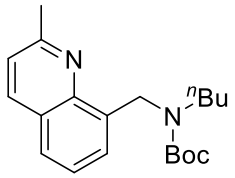
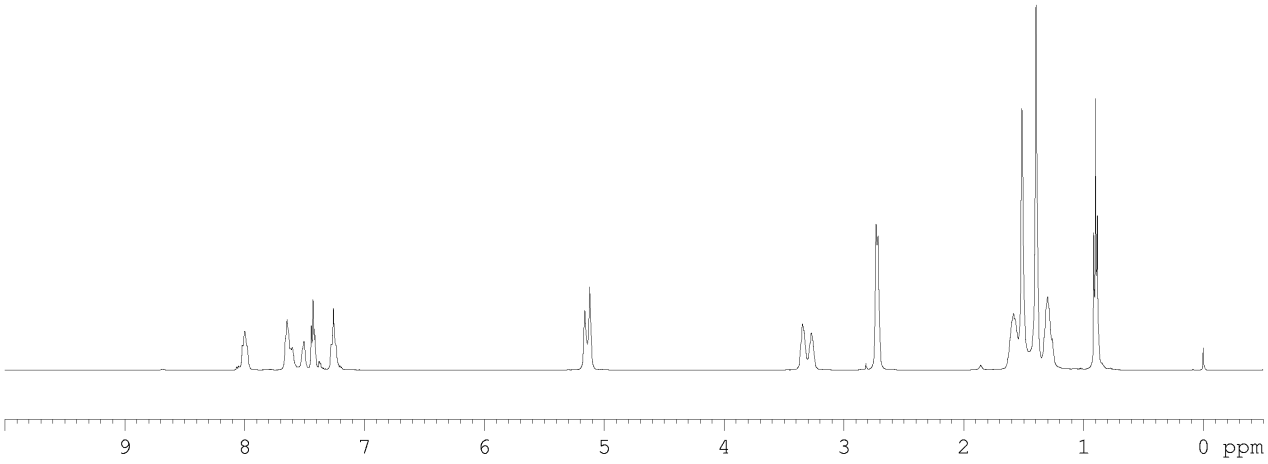
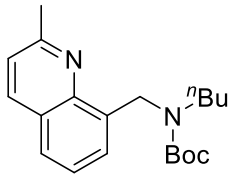
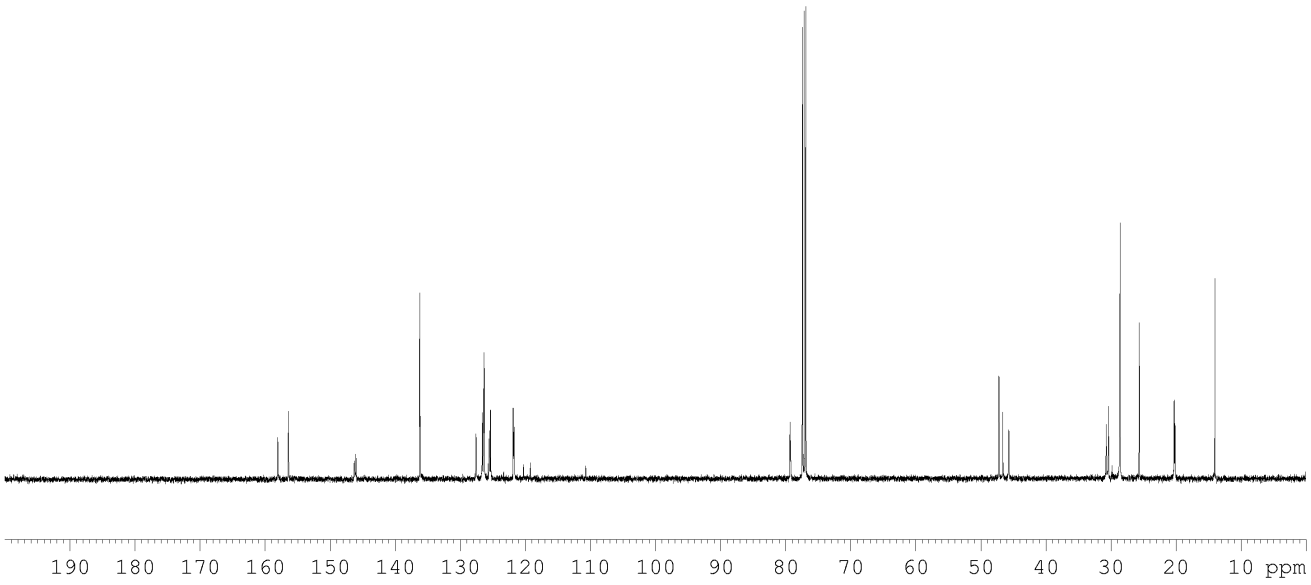


Figure A2.214 Infrared Spectrum


N
nBu
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


N
nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

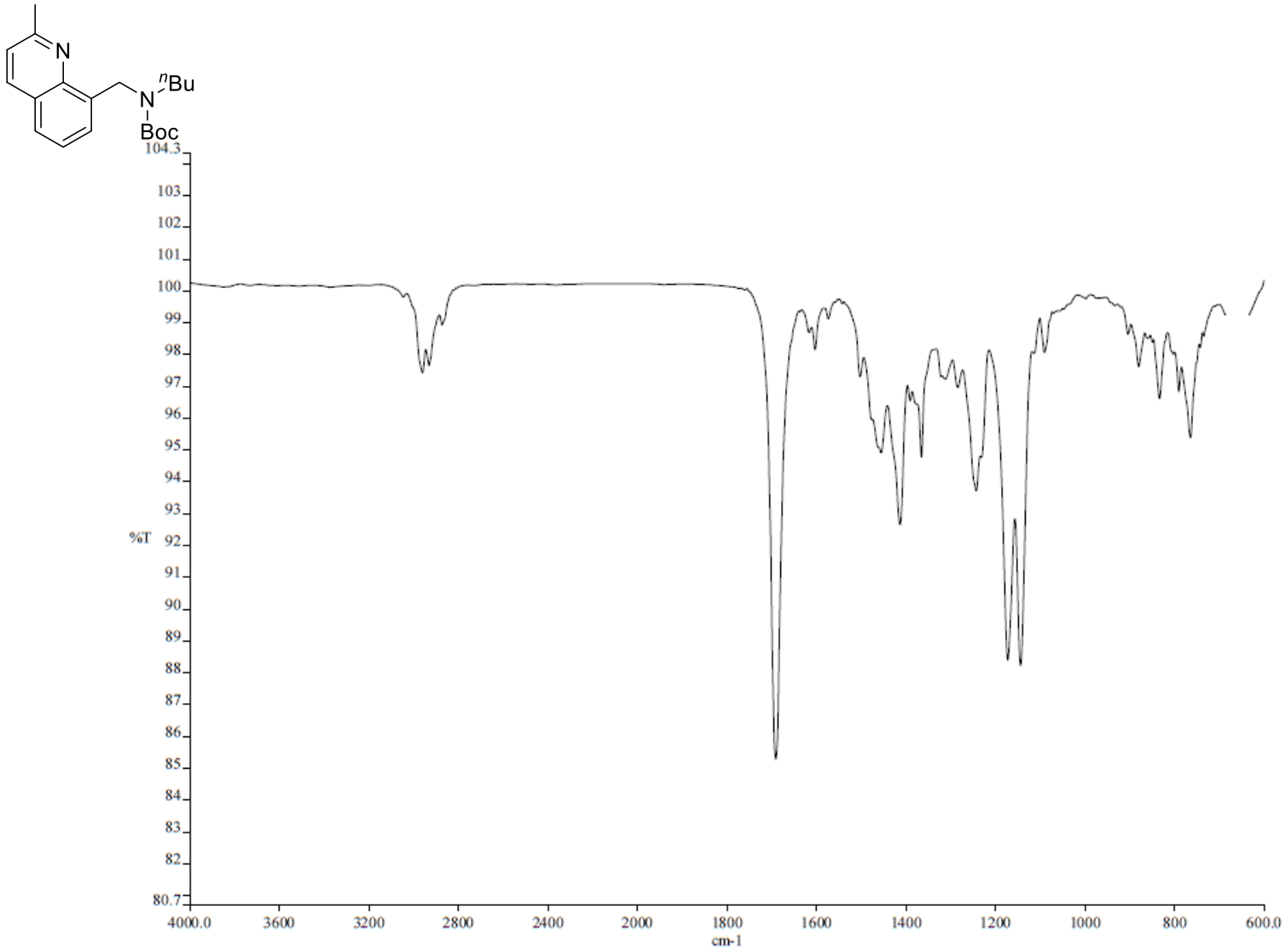
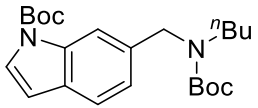
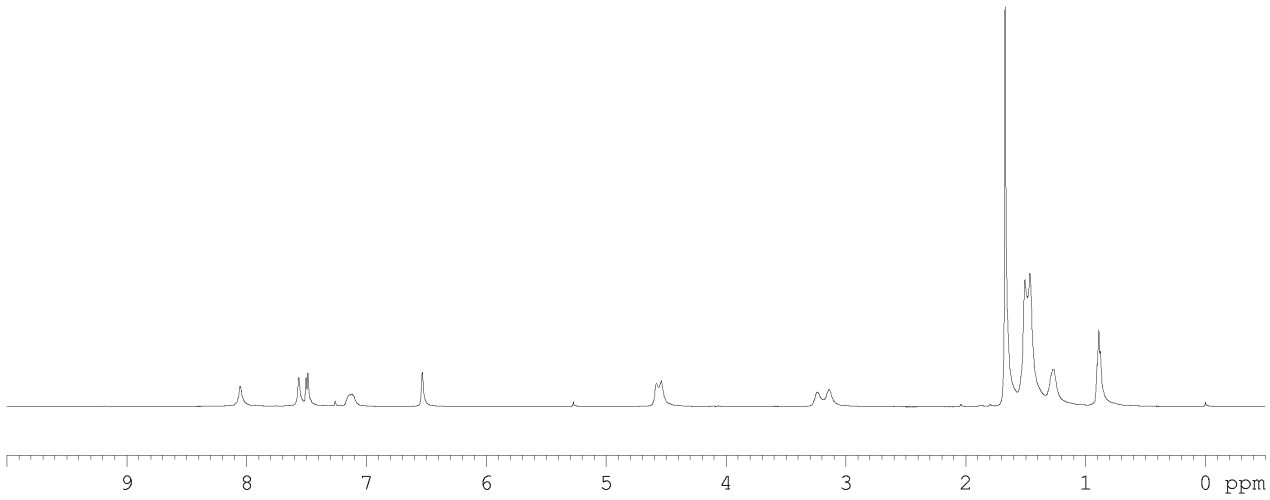
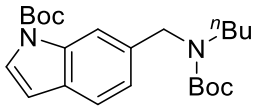
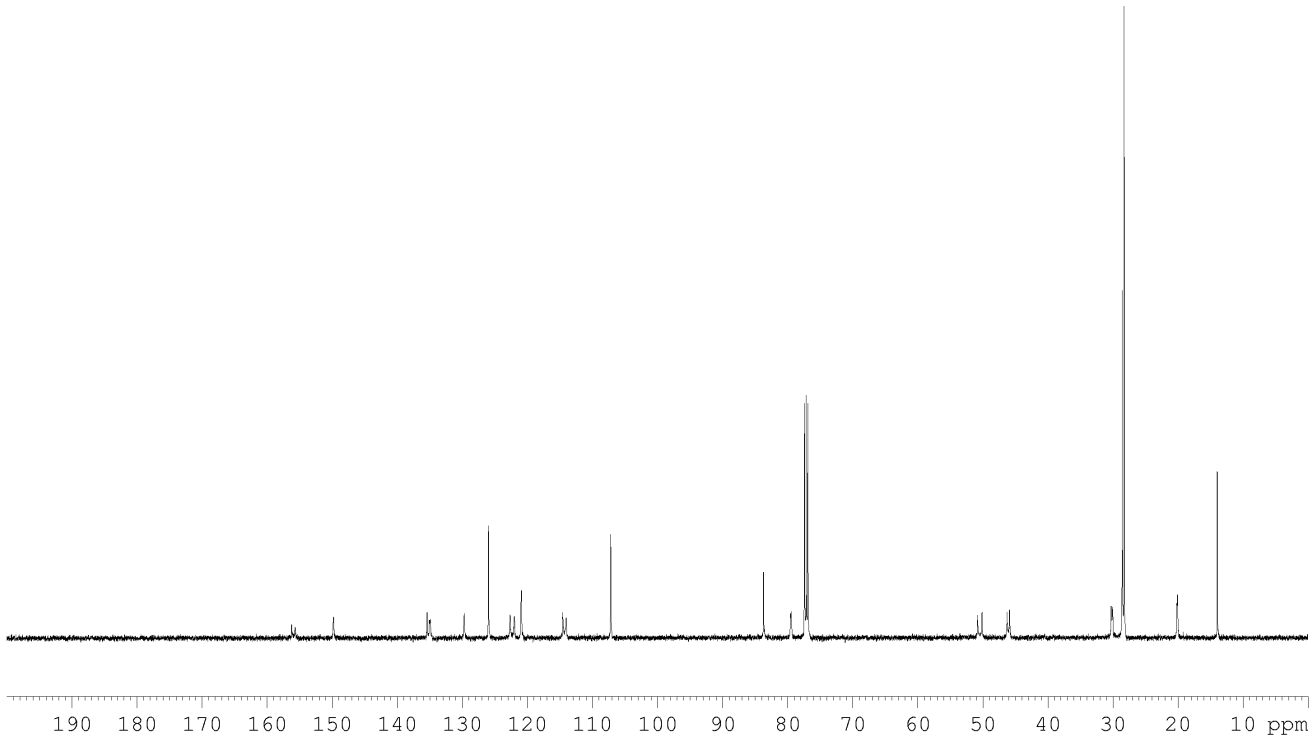


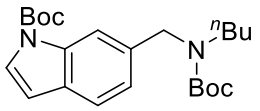
Figure A2.217 Infrared Spectrum


Boc
N
N
nBu
Boc


9
8
7
6
5
4
3
2
1
0 ppm


Boc
N
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



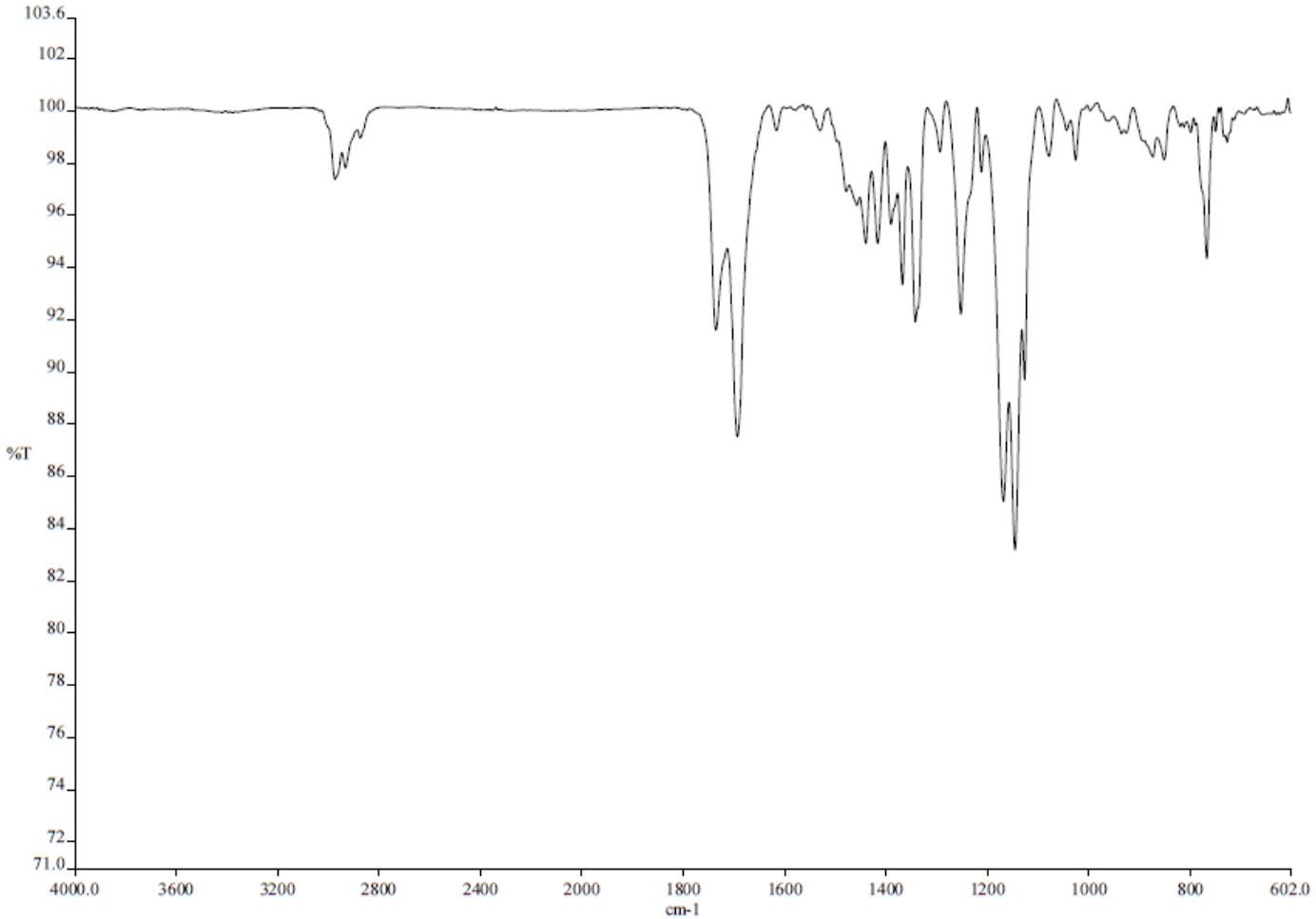
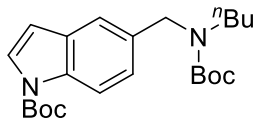
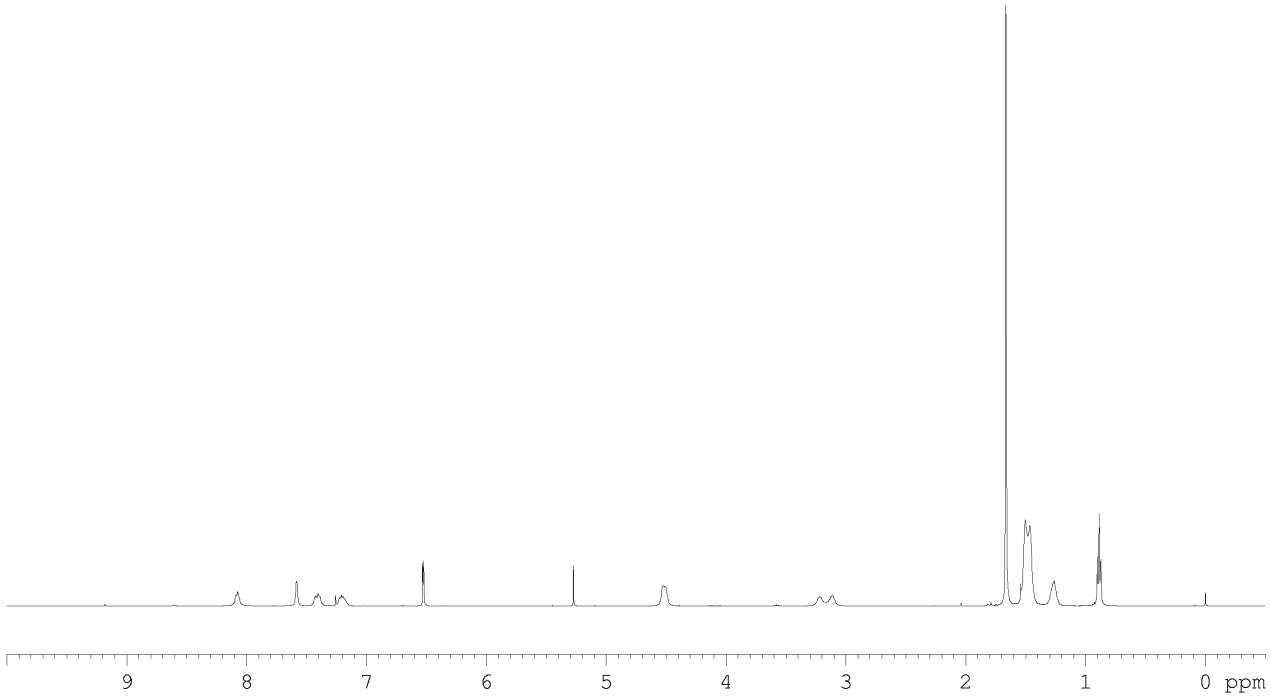
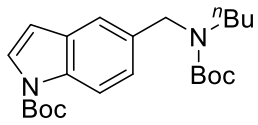
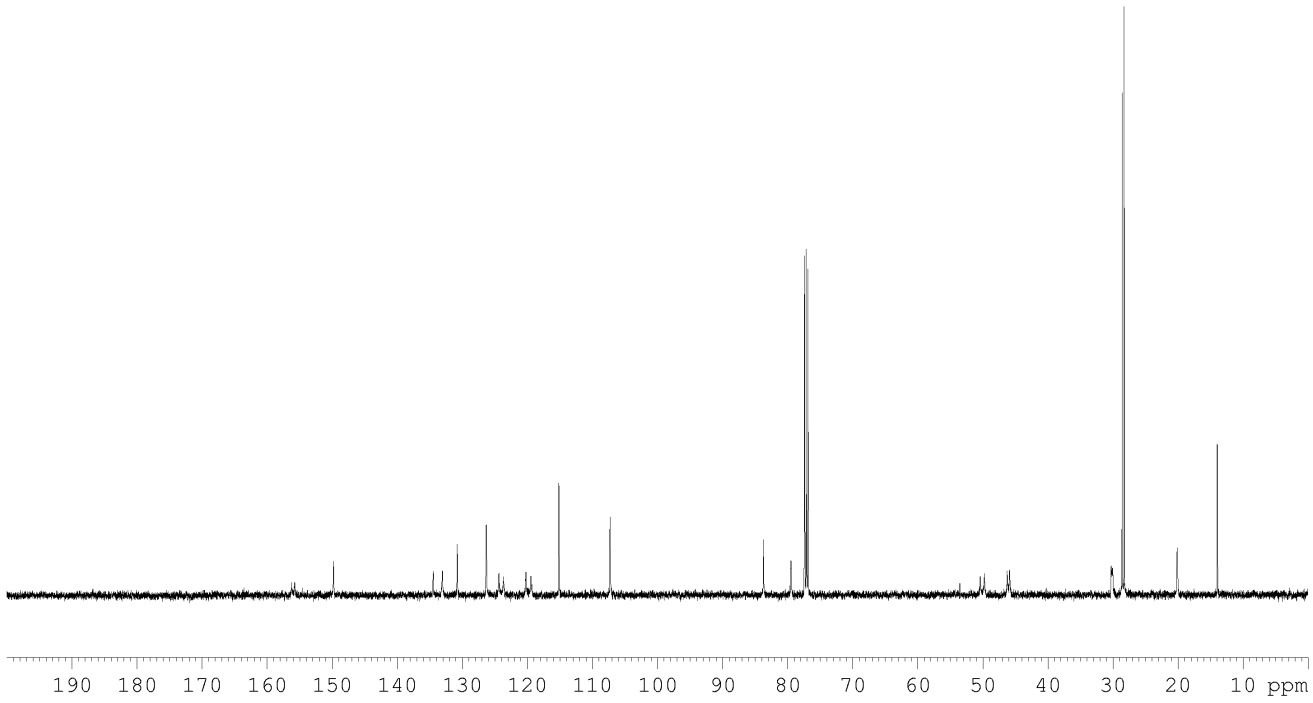


Figure A2.220 Infrared Spectrum


nBu
N
Boc
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

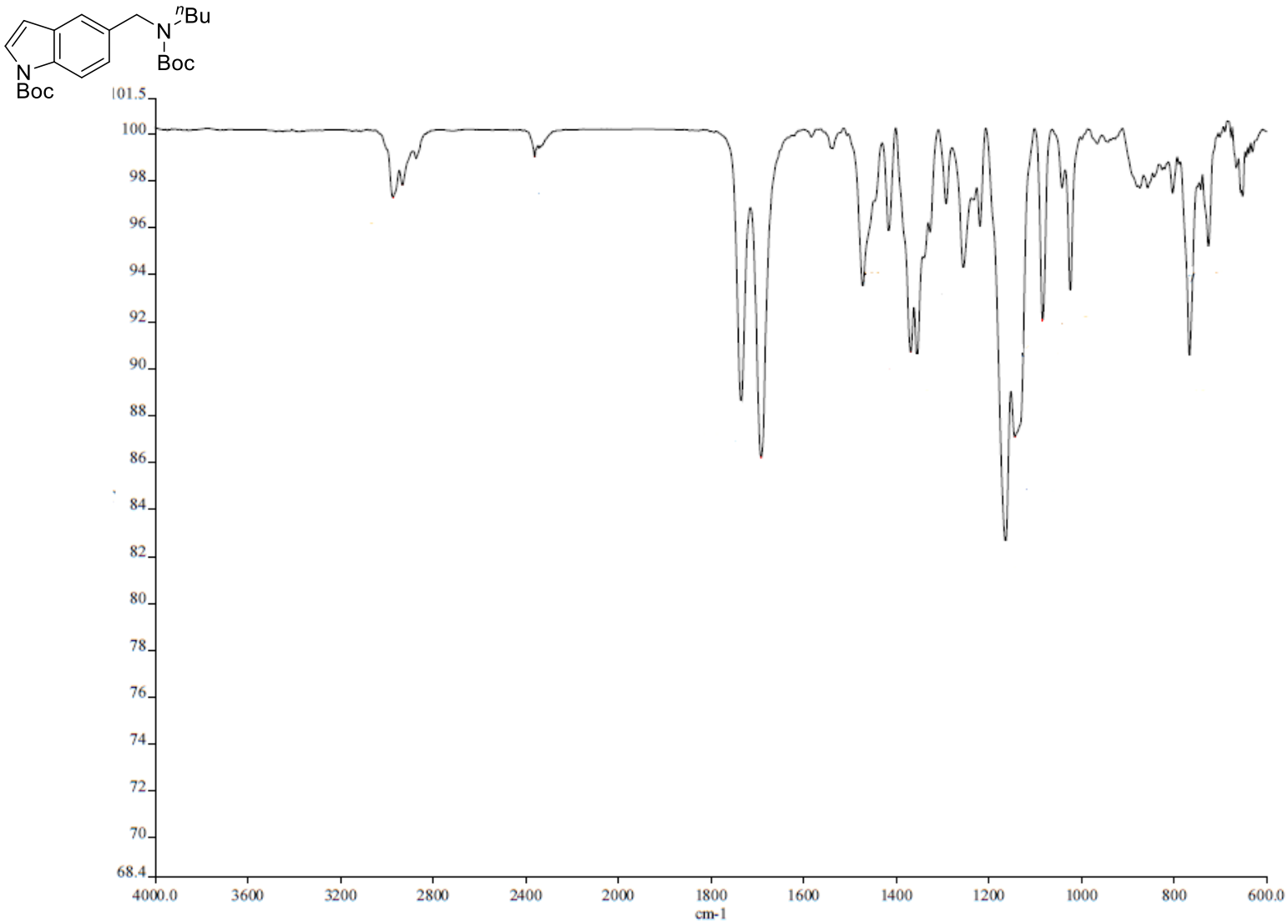
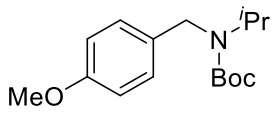
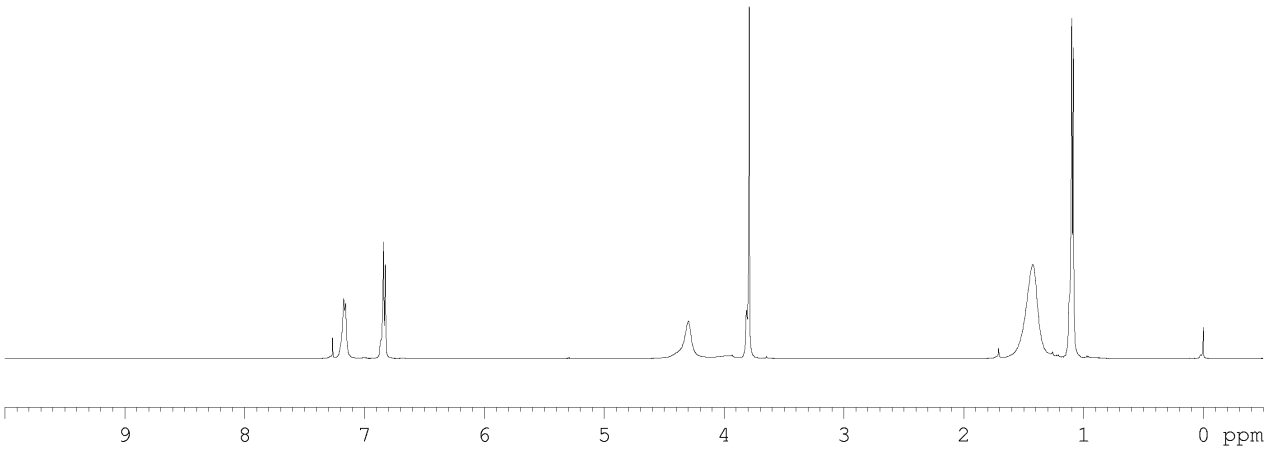
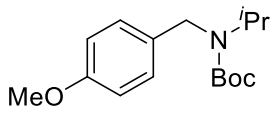
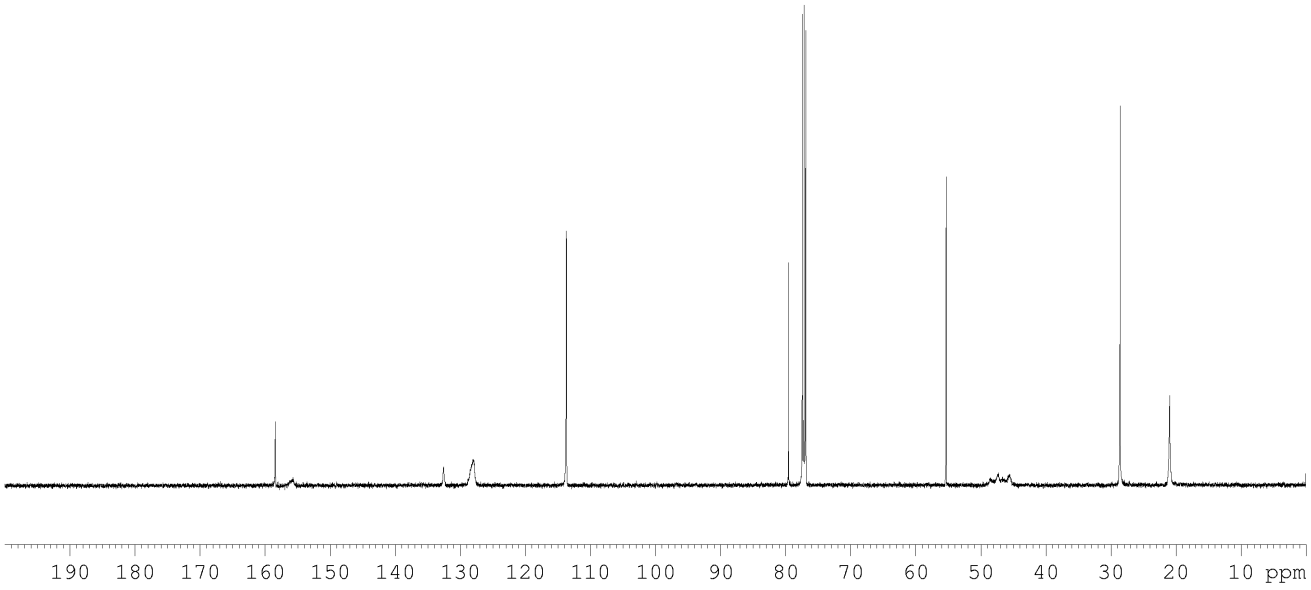


Figure A2.223 Infrared Spectrum


MeO
N
iPr
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
iPr
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

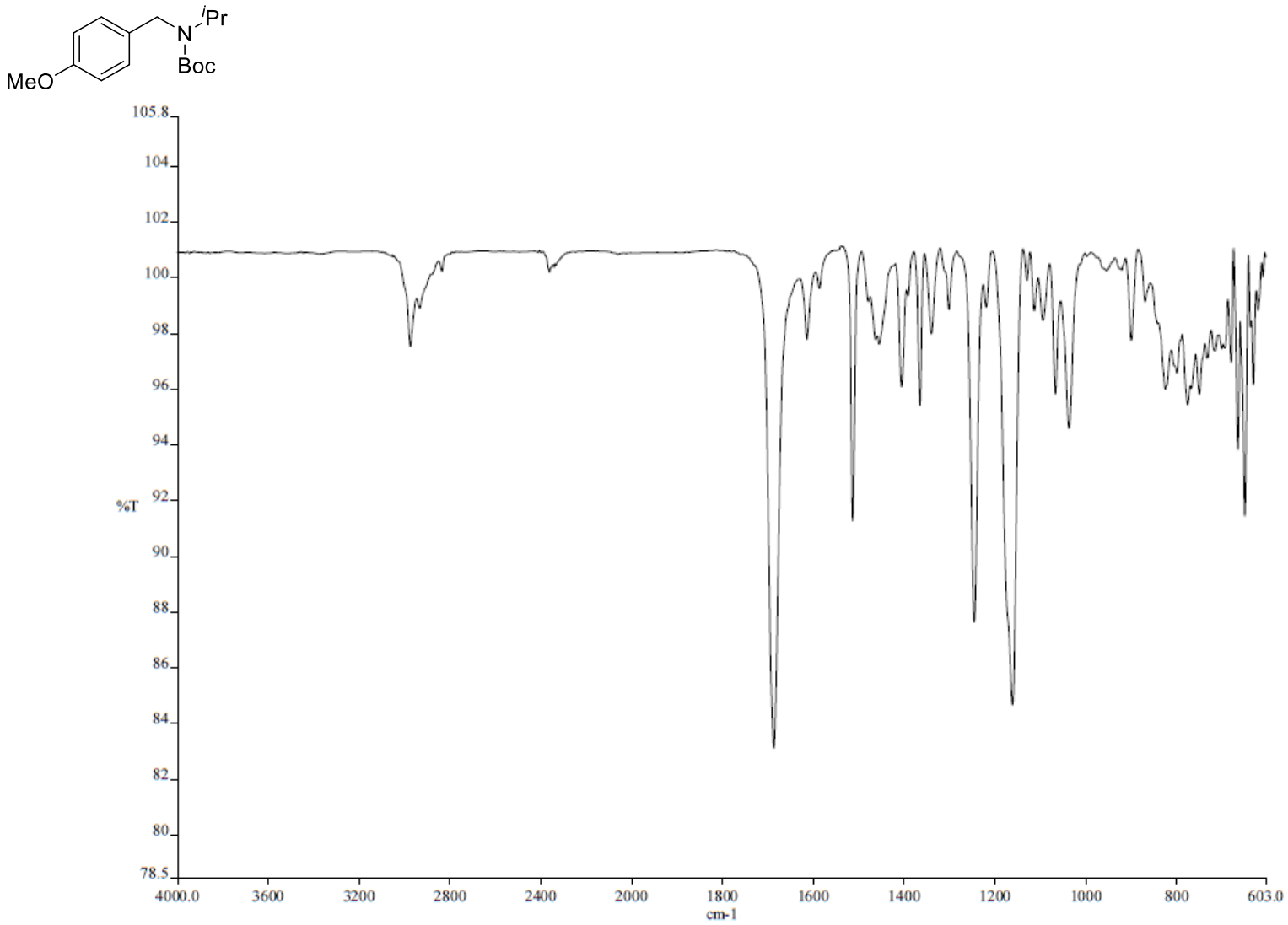
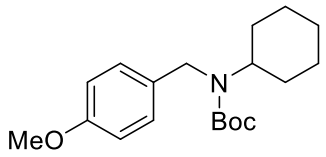
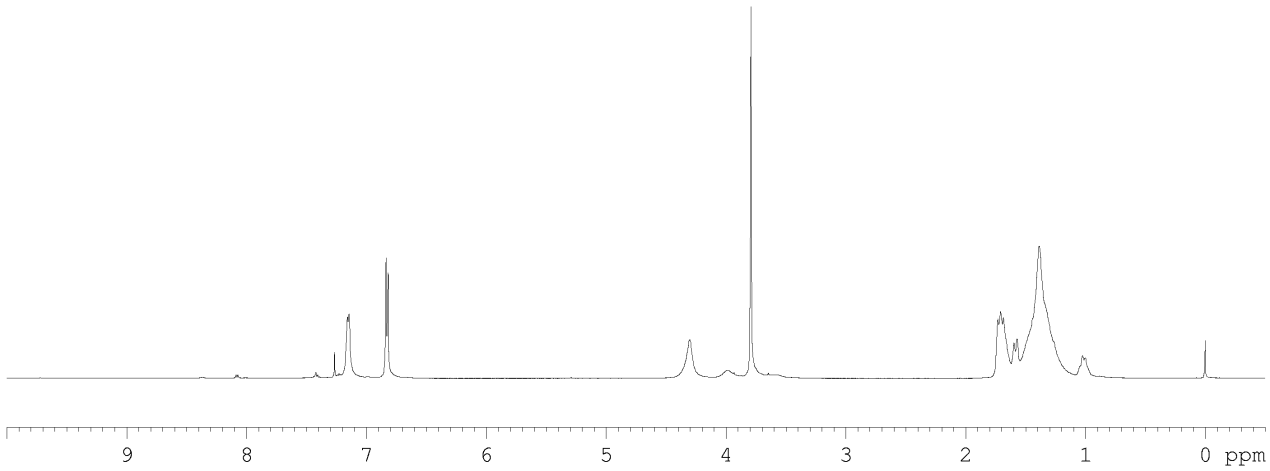
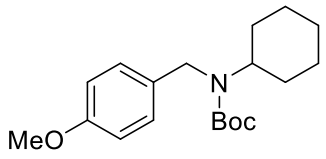
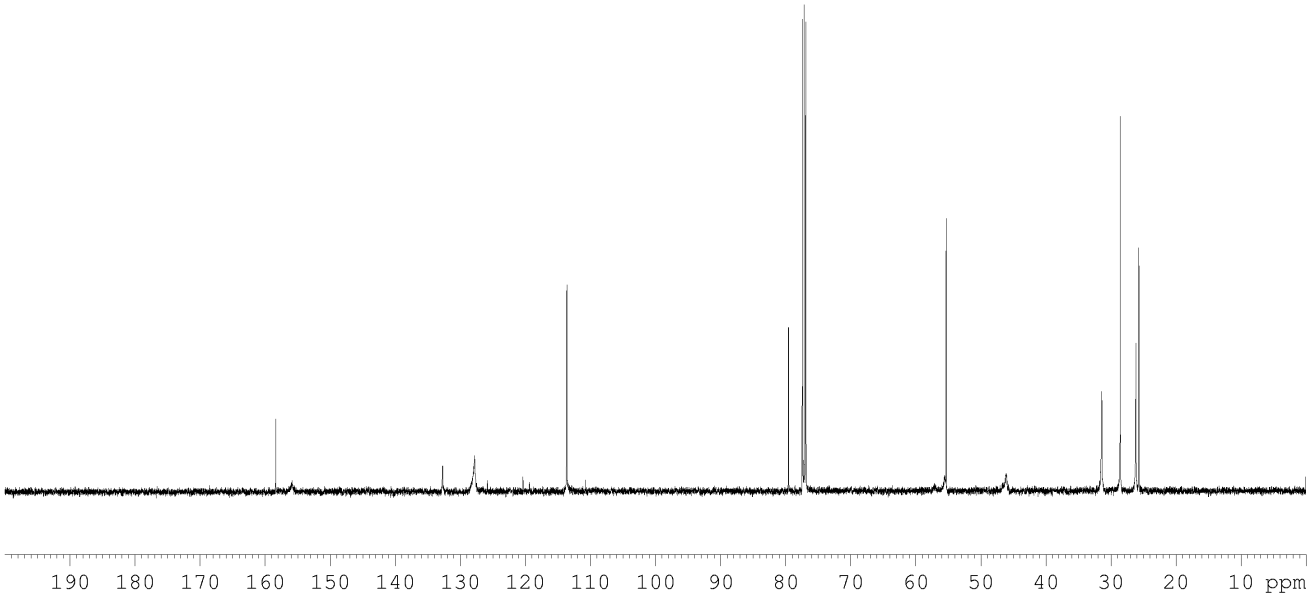


Figure A2.226 Infrared Spectrum


MeO
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

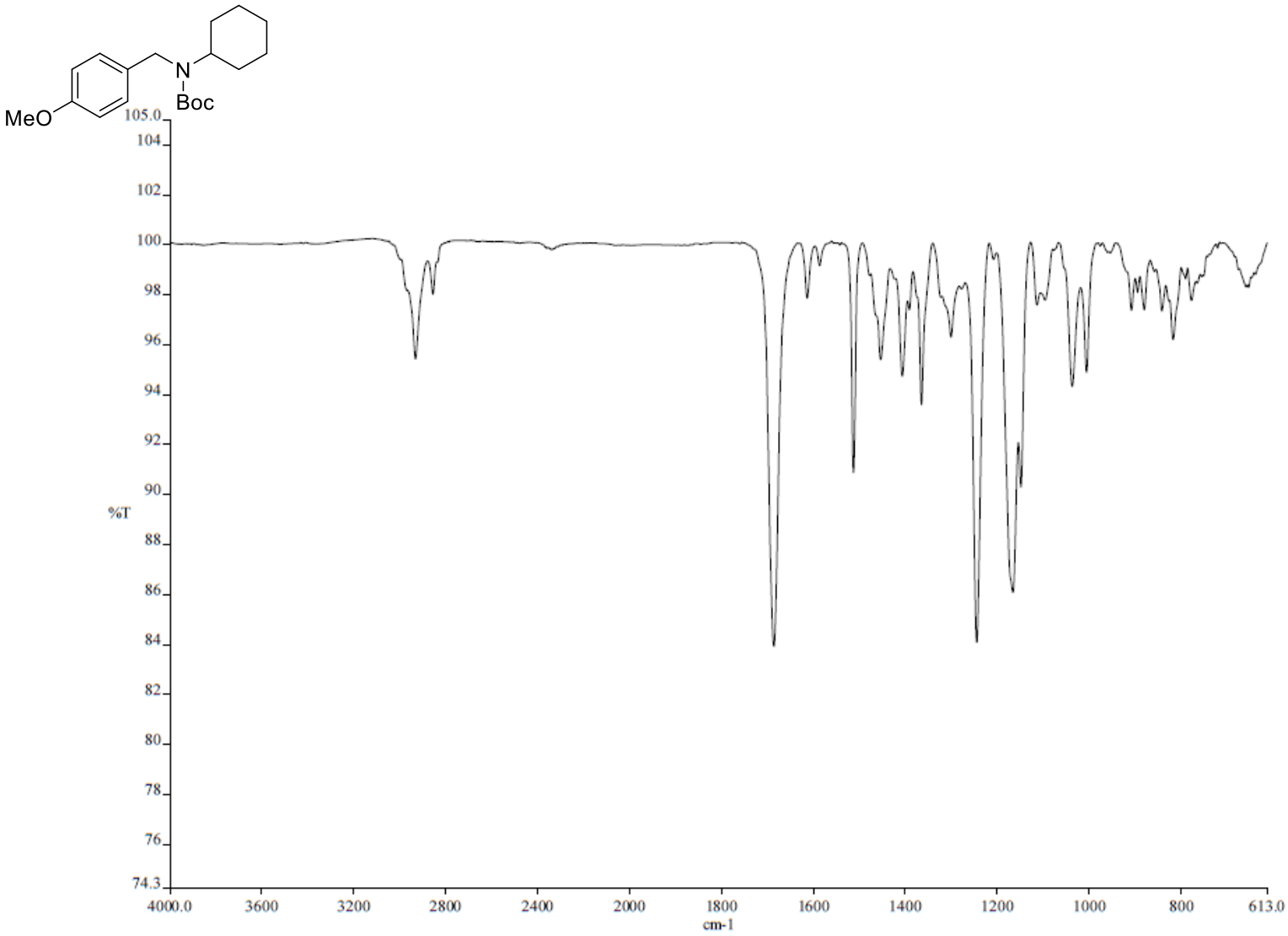
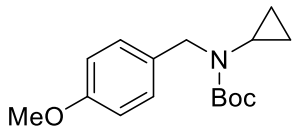
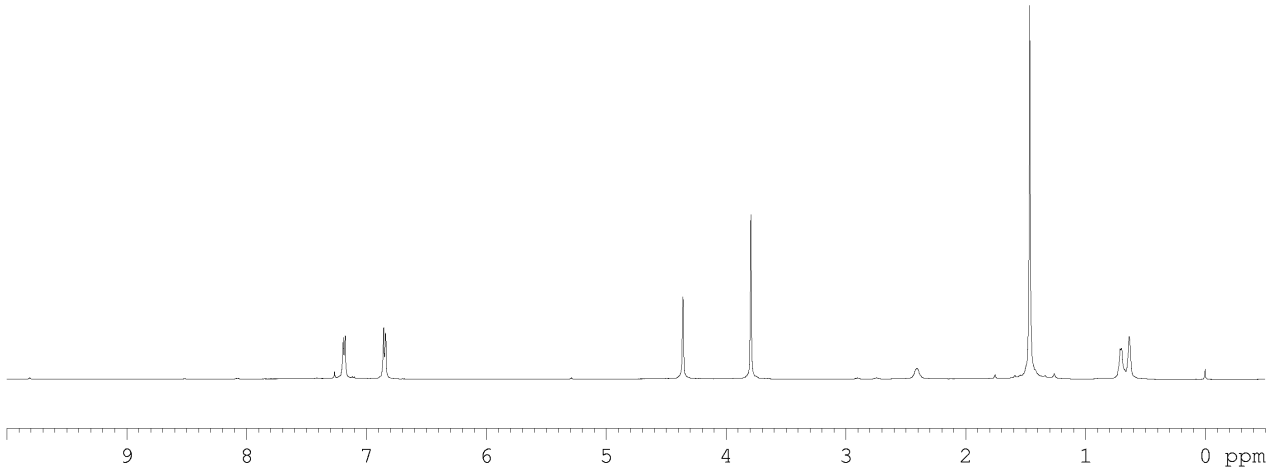
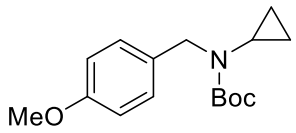
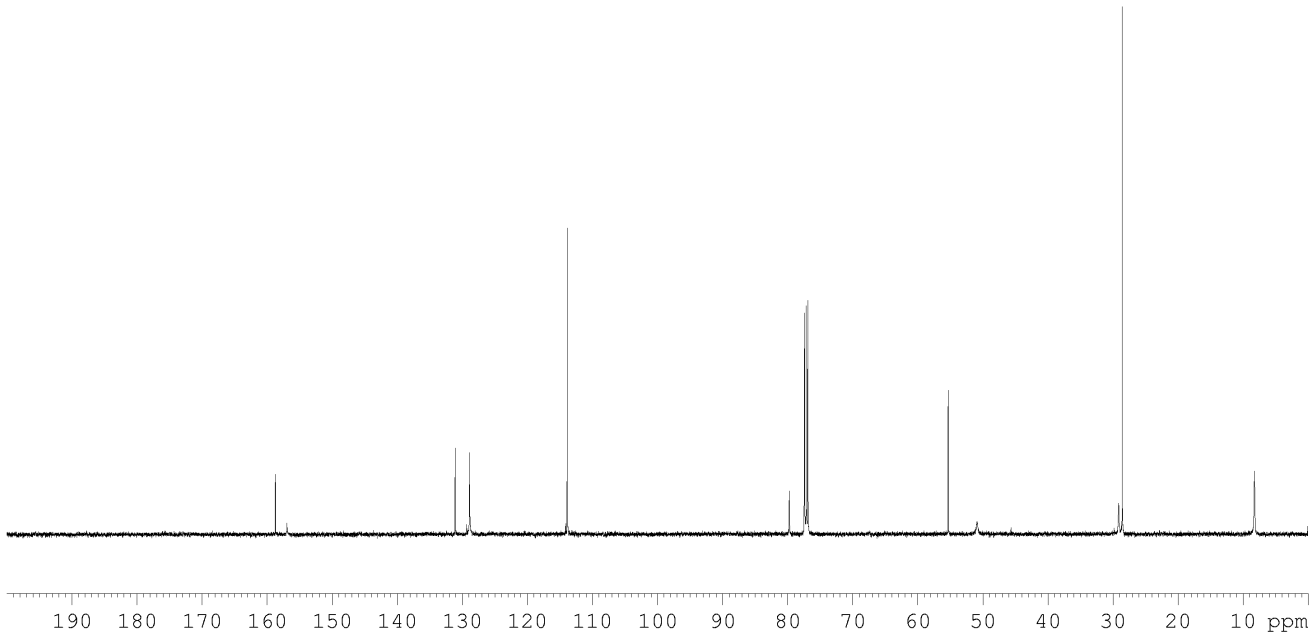


Figure A2.229 Infrared Spectrum


MeO
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

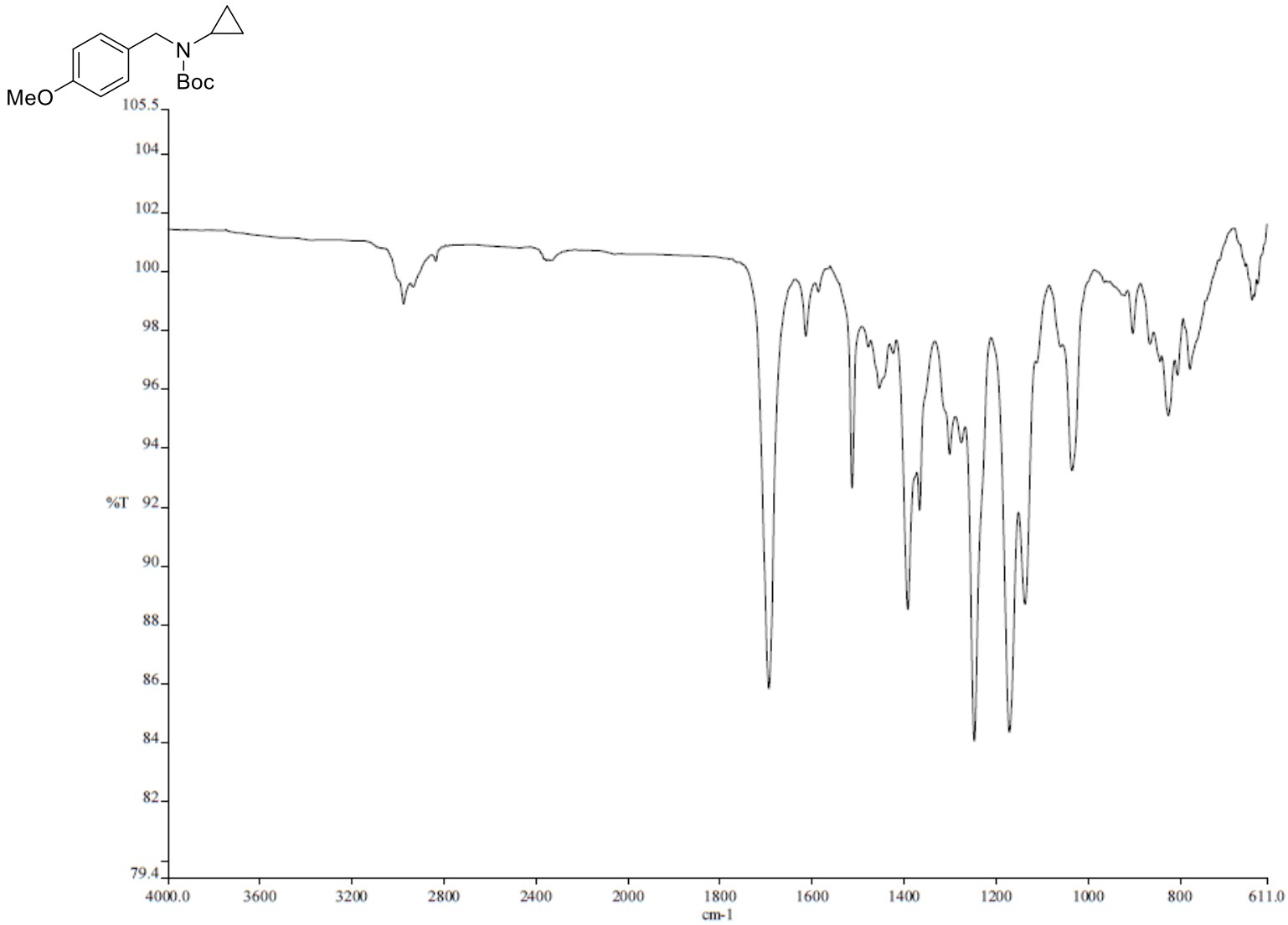
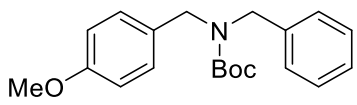
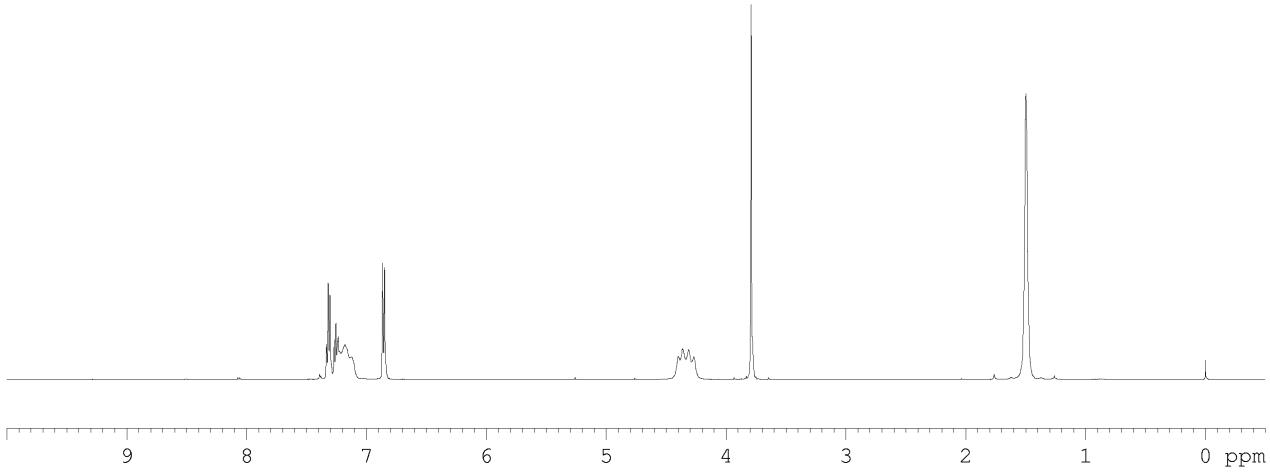
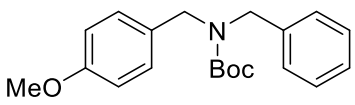
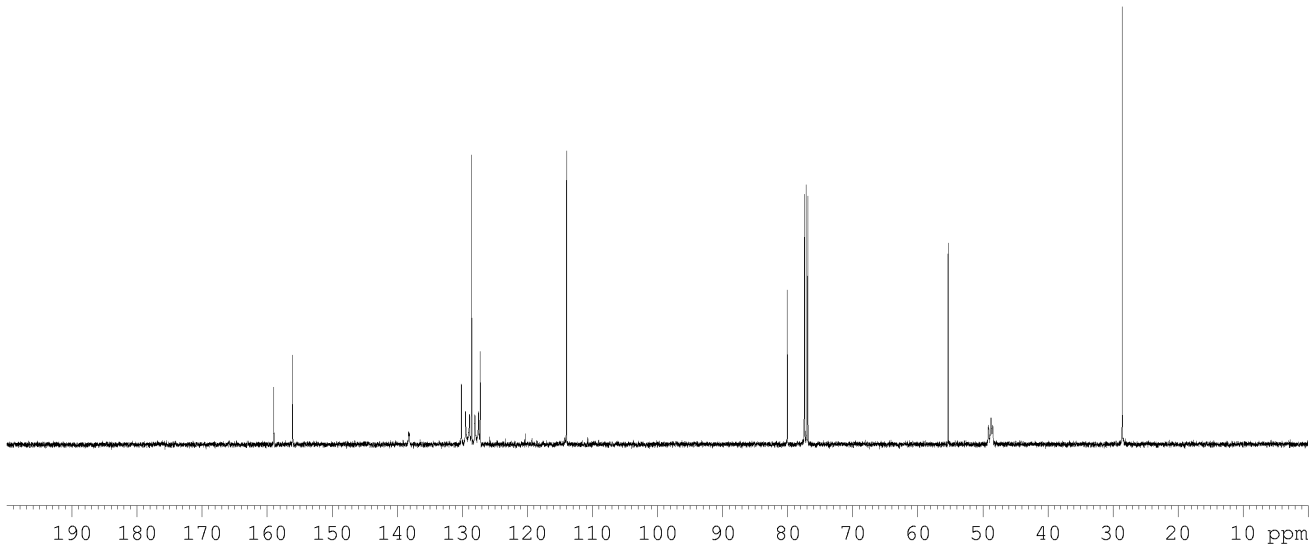


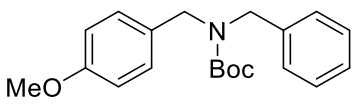
Figure A2.232 Infrared Spectrum


MeO
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


MeO
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



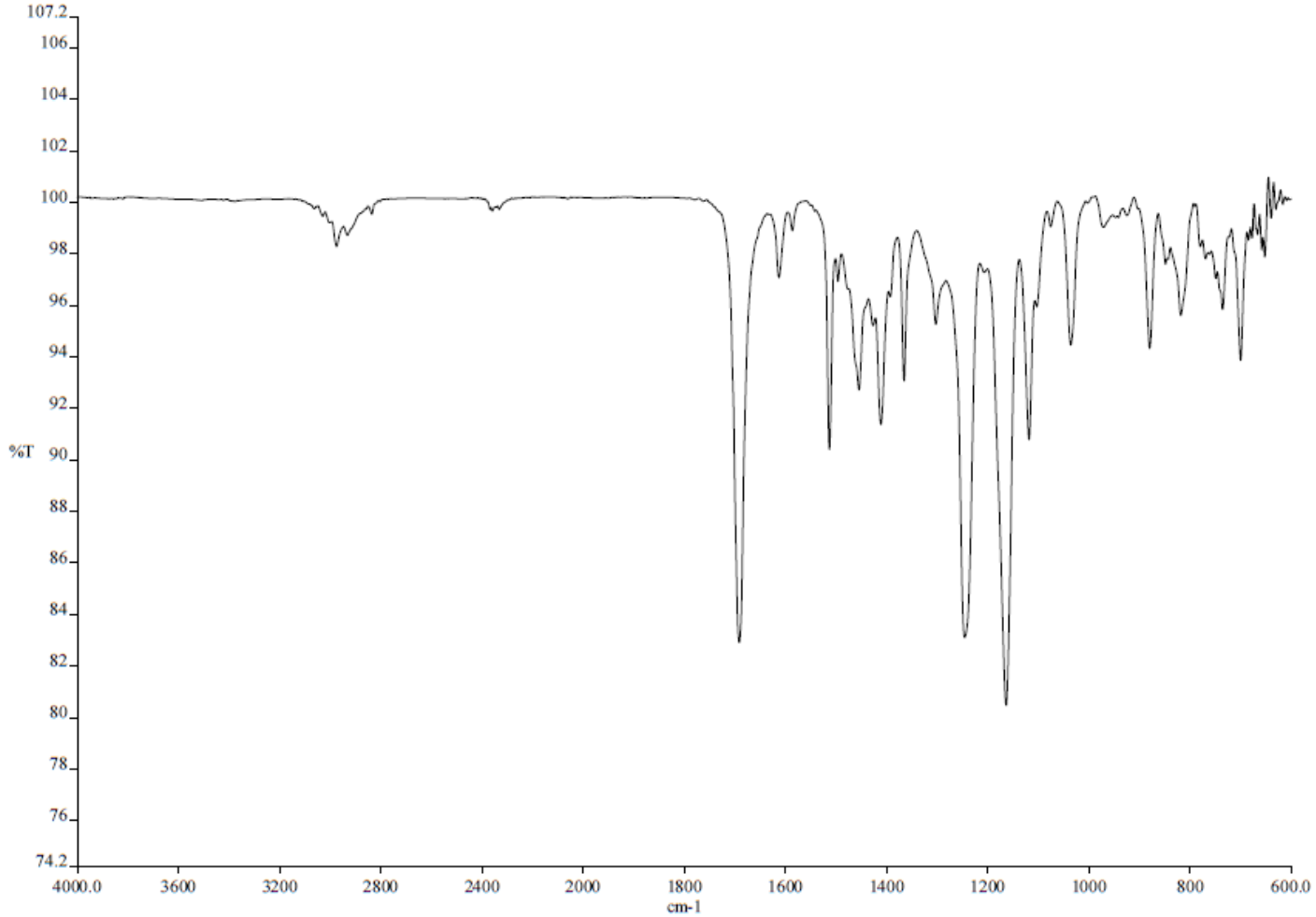
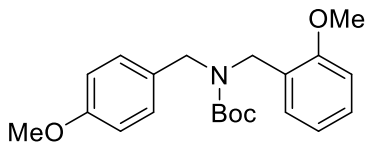
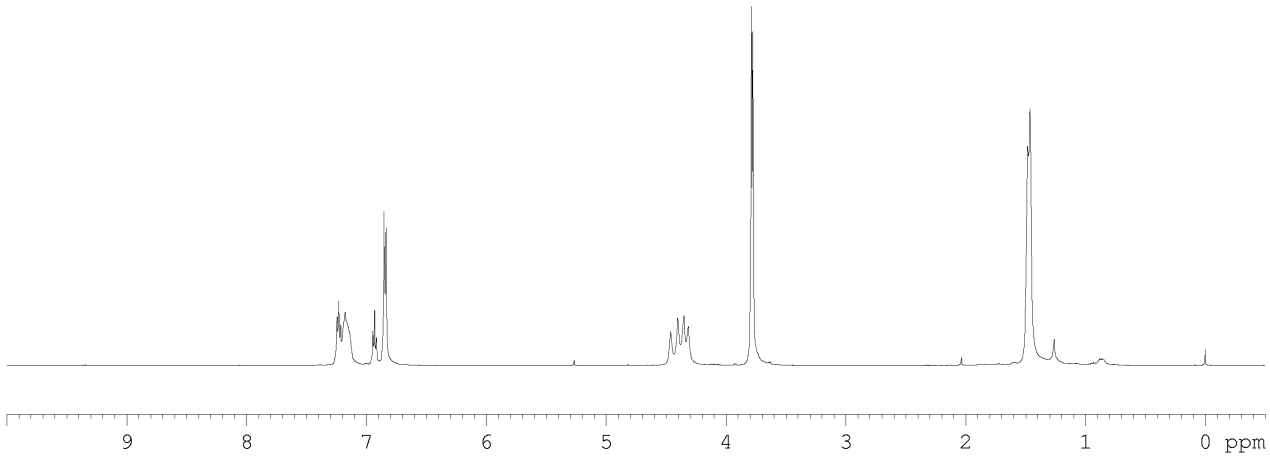
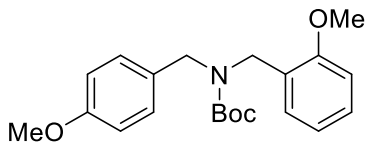
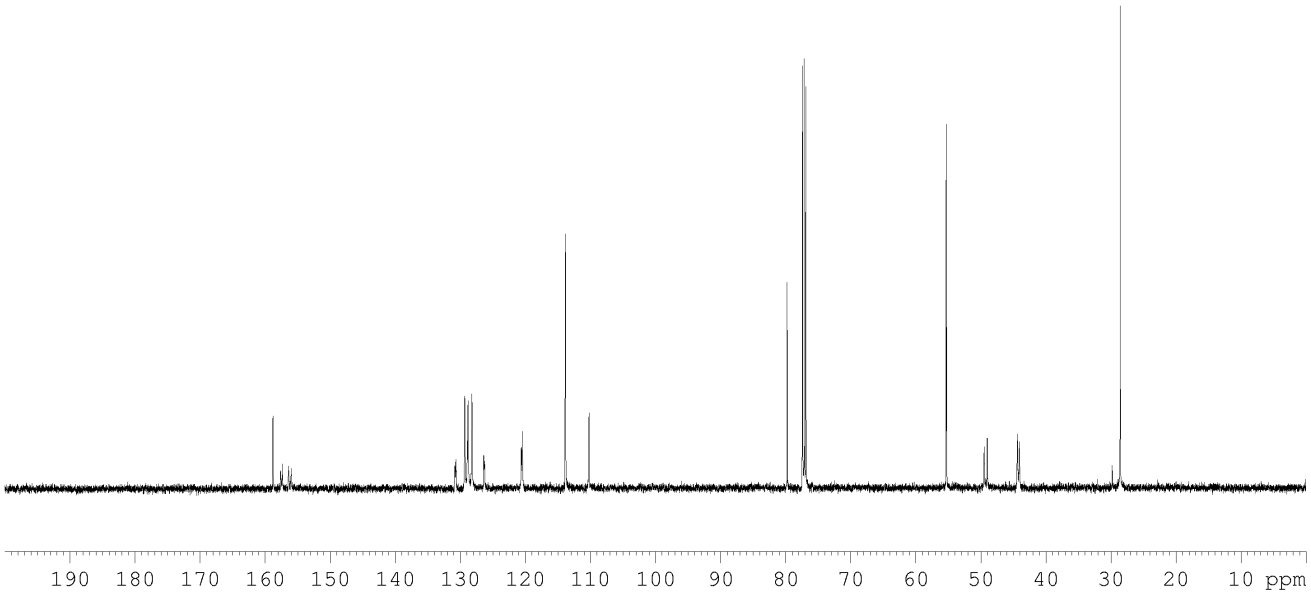


Figure A2.235 Infrared Spectrum


OMe
N
Boc
MeO


9
8
7
6
5
4
3
2
1
0 ppm


OMe
N
Boc
MeO


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

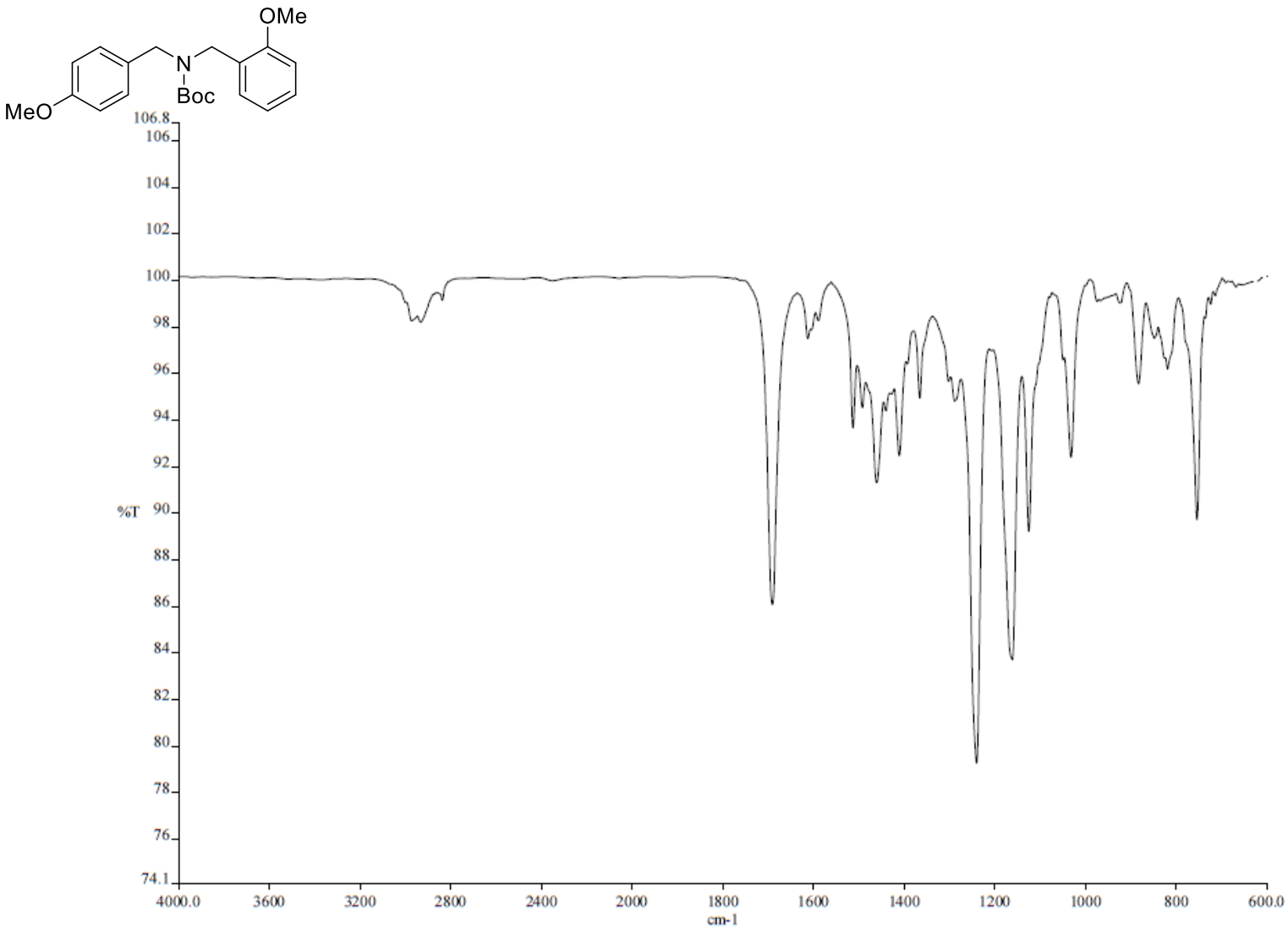
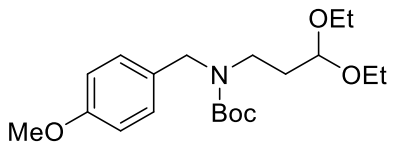
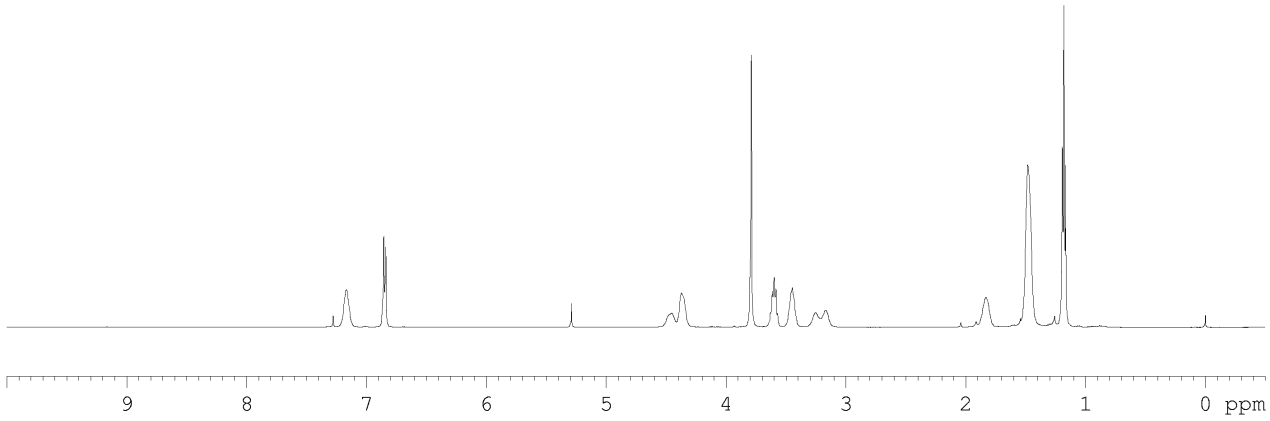
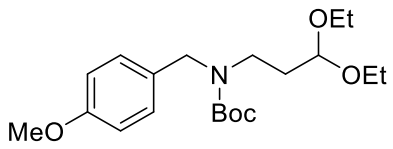
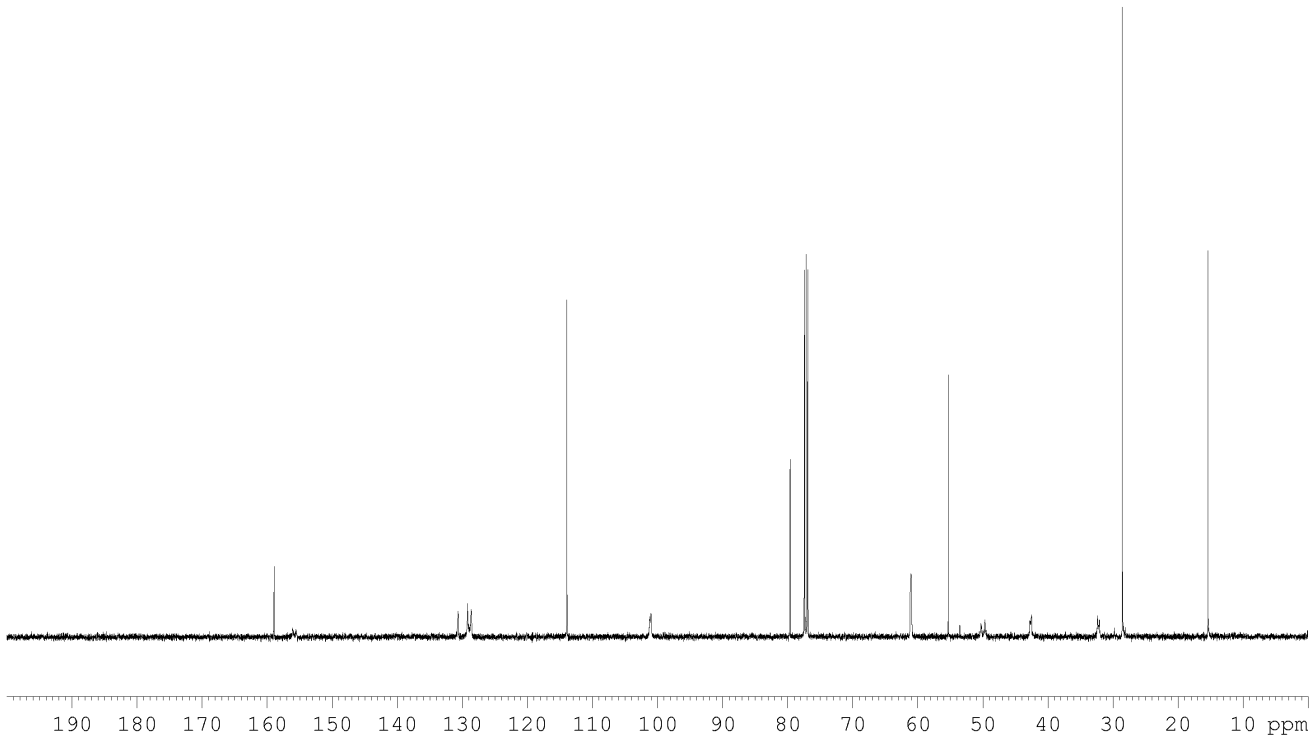


Figure A2.238 Infrared Spectrum


OEt
OEt
N
Boc
MeO


9
8
7
6
5
4
3
2
1
0 ppm


OEt
N
OEt
Boc
MeO


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

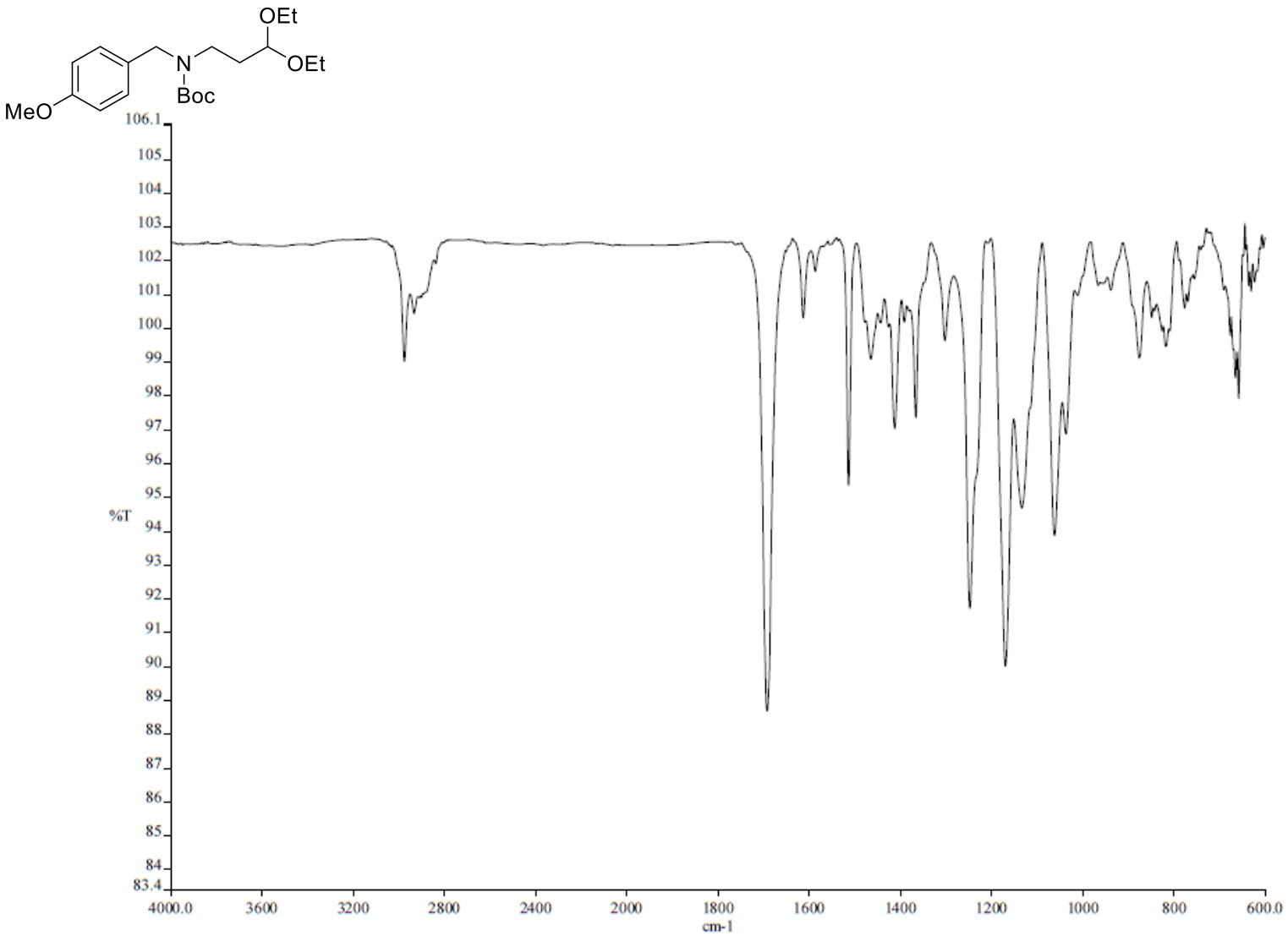
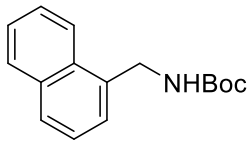
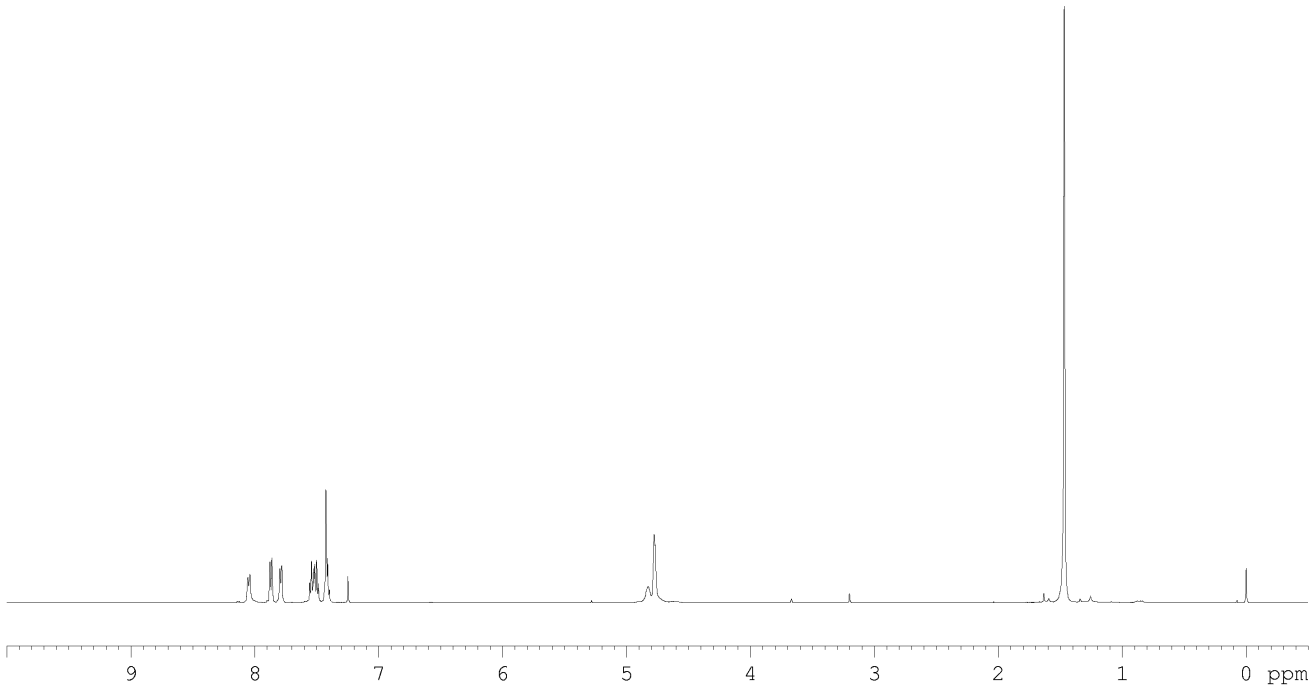
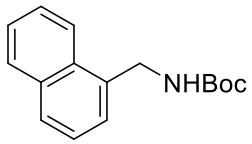
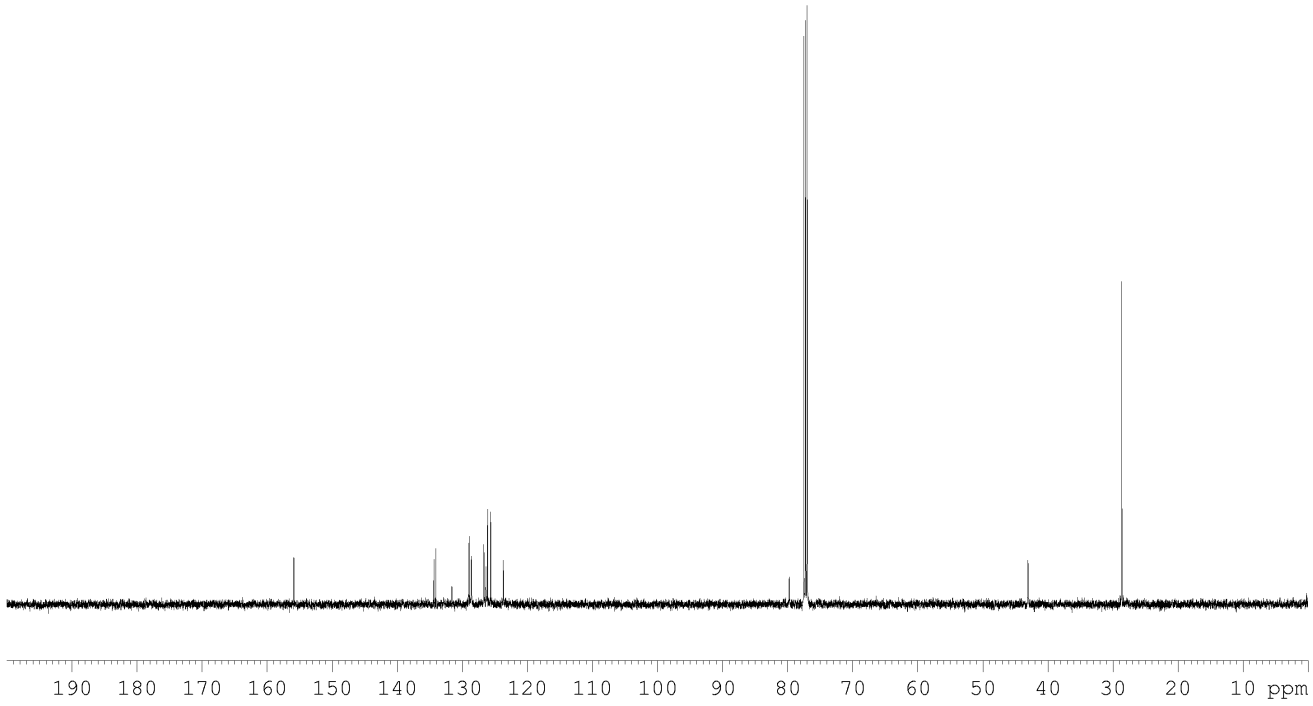


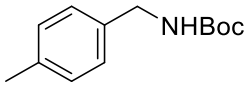
Figure A2.241 Infrared Spectrum

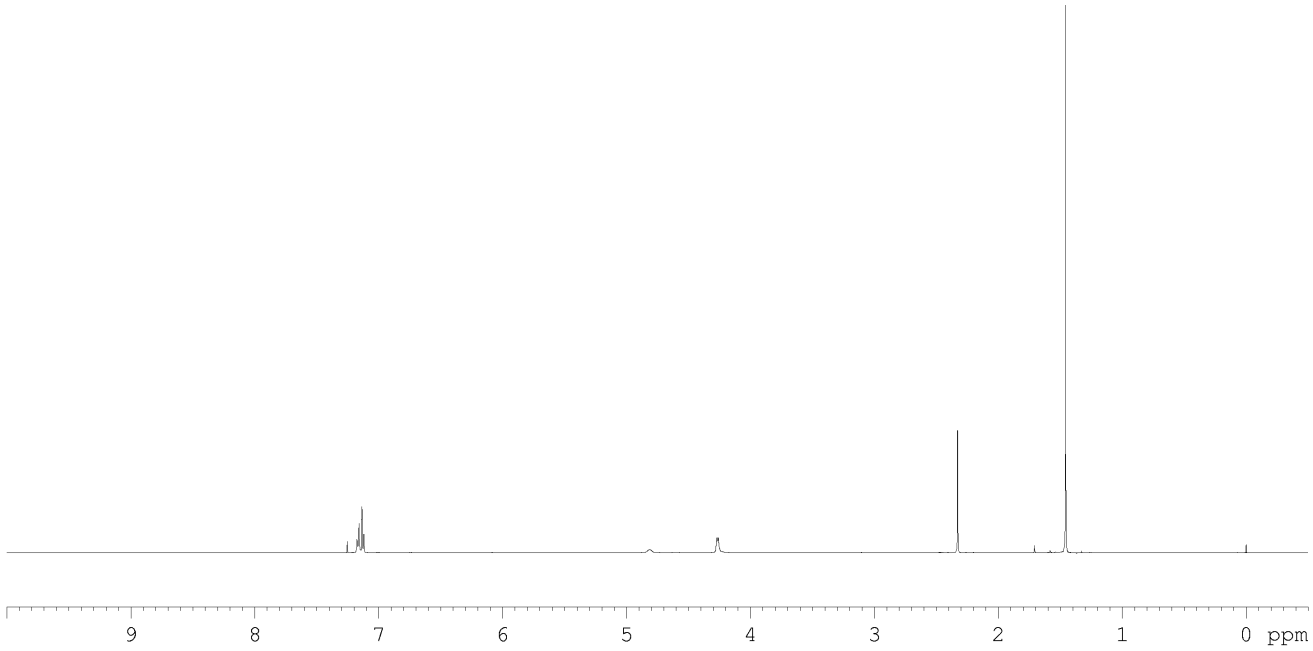

NHBoc

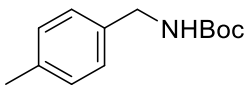

9
8
7
6
5
4
3
2
1
0 ppm


NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


NHBoc


9
8
7
6
5
4
3
2
1
0 ppm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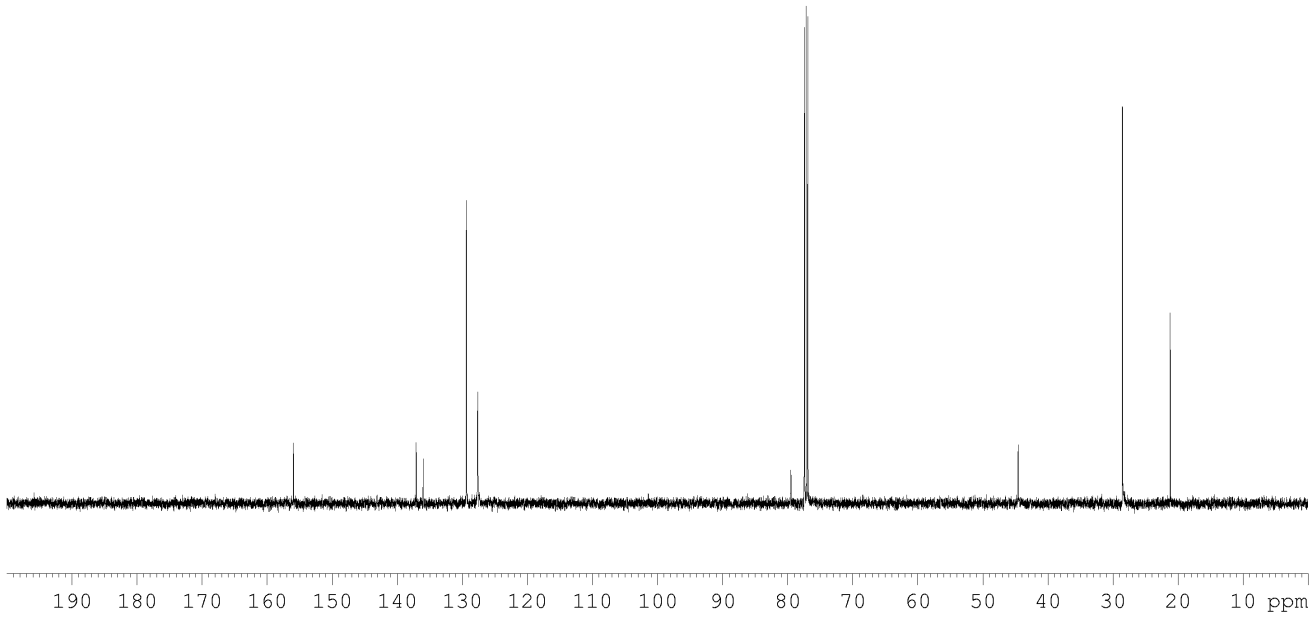
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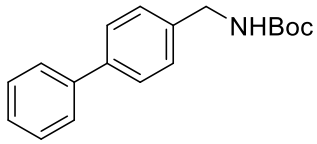
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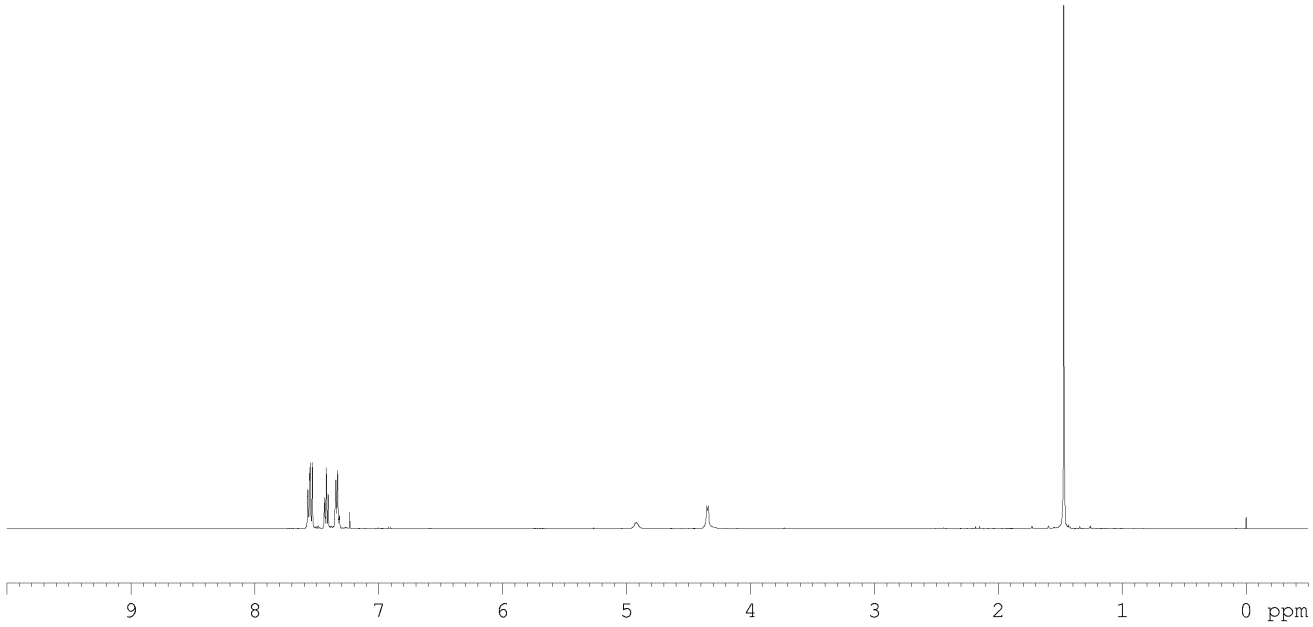
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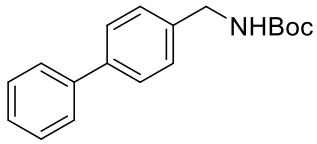
6
5
4
3
2
1
0 ppm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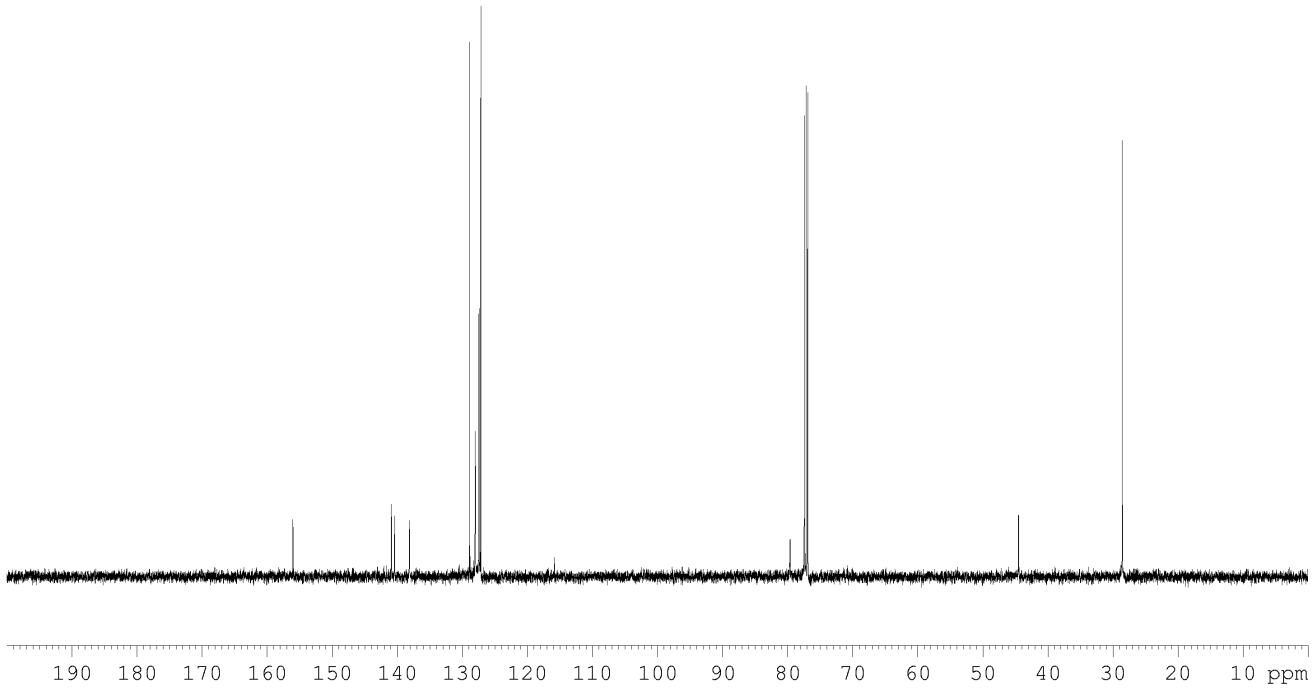
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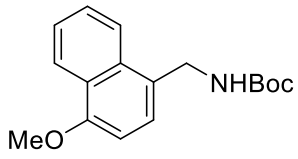
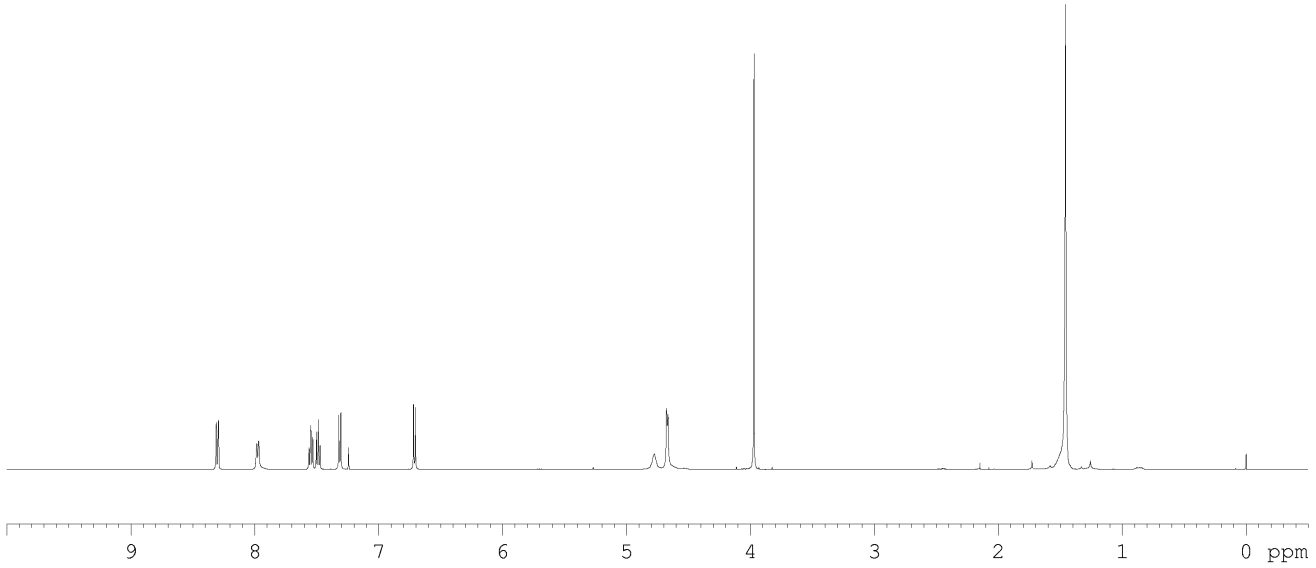
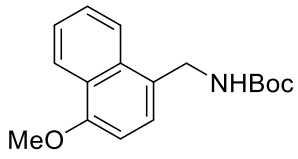
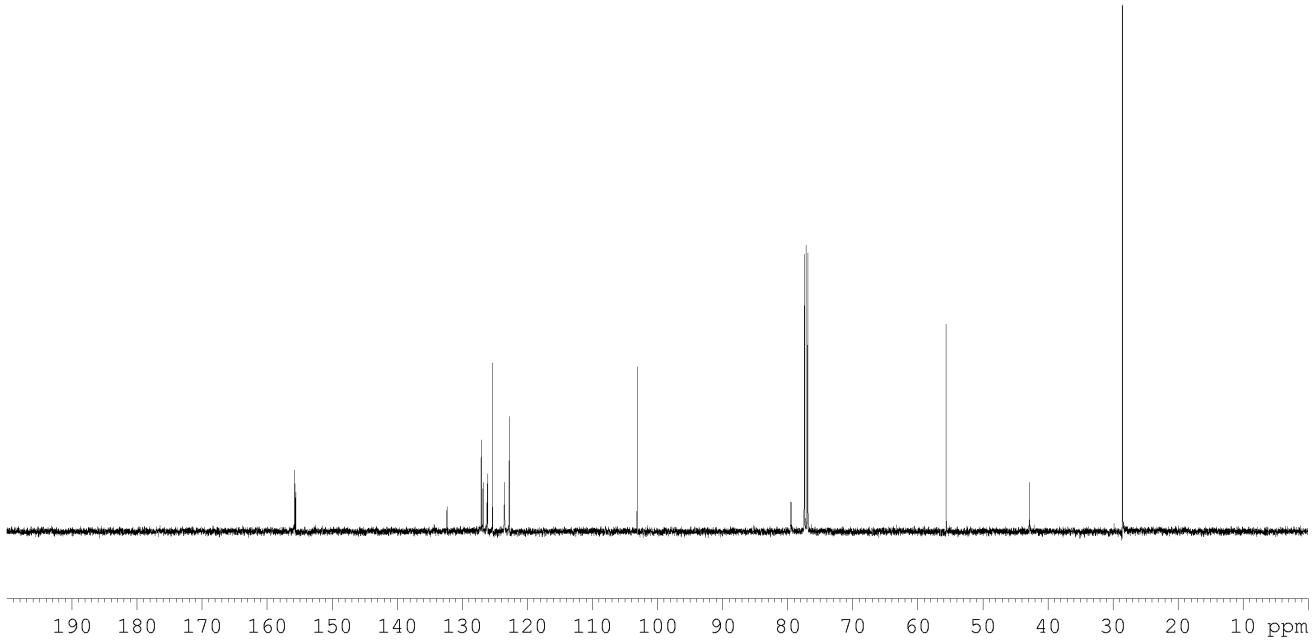


551




NHBoc
MeO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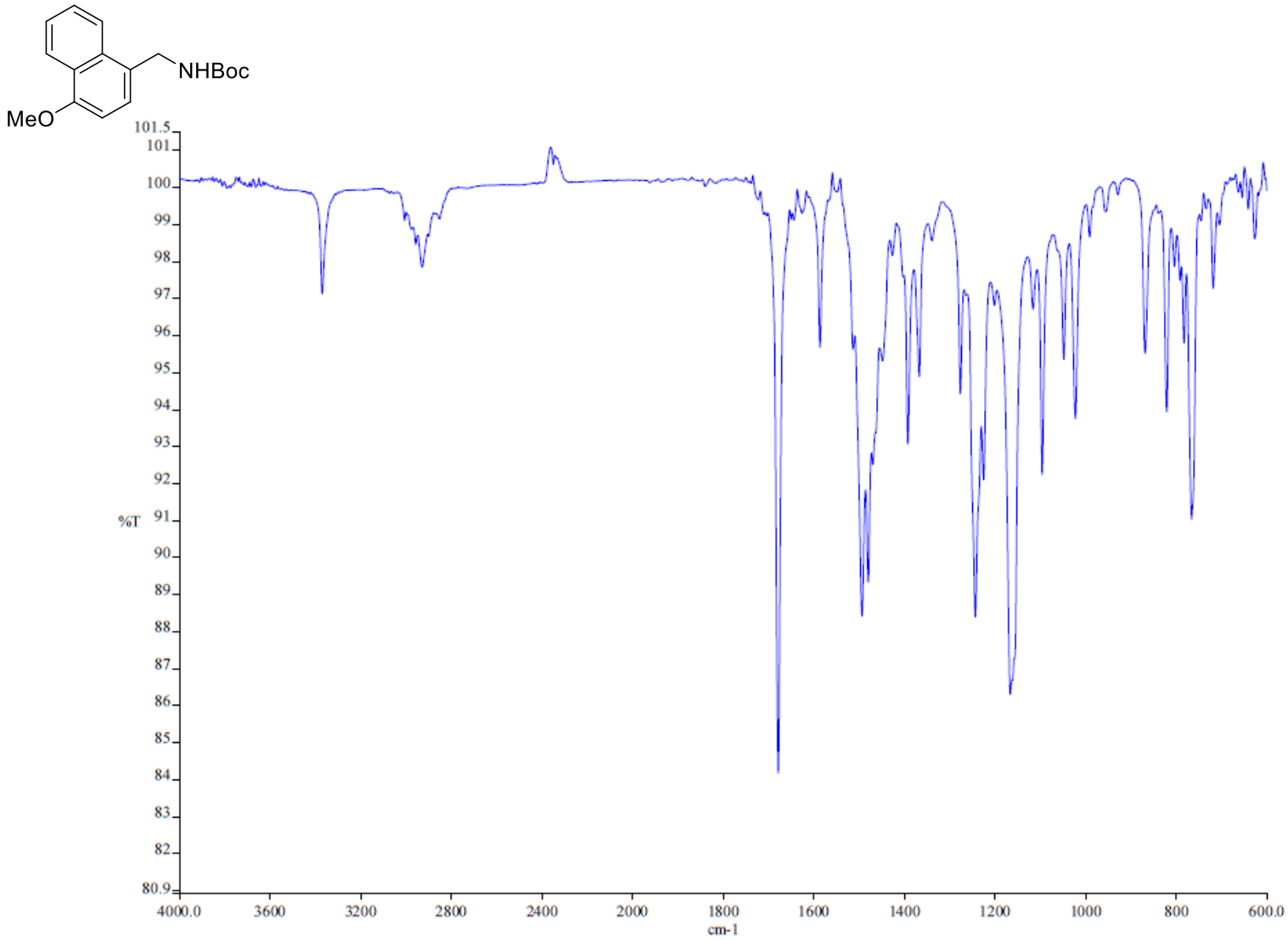
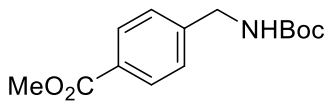


Figure A2.250 Infrared Spectrum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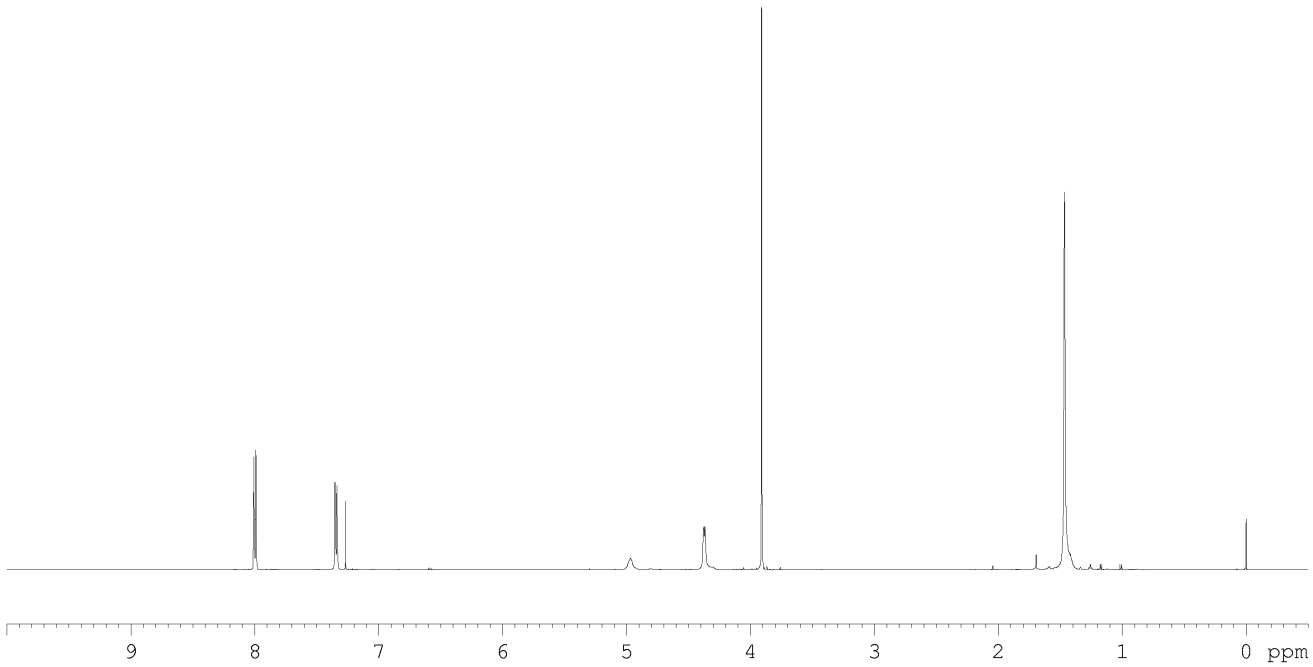
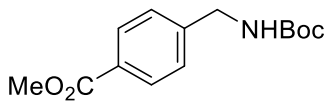
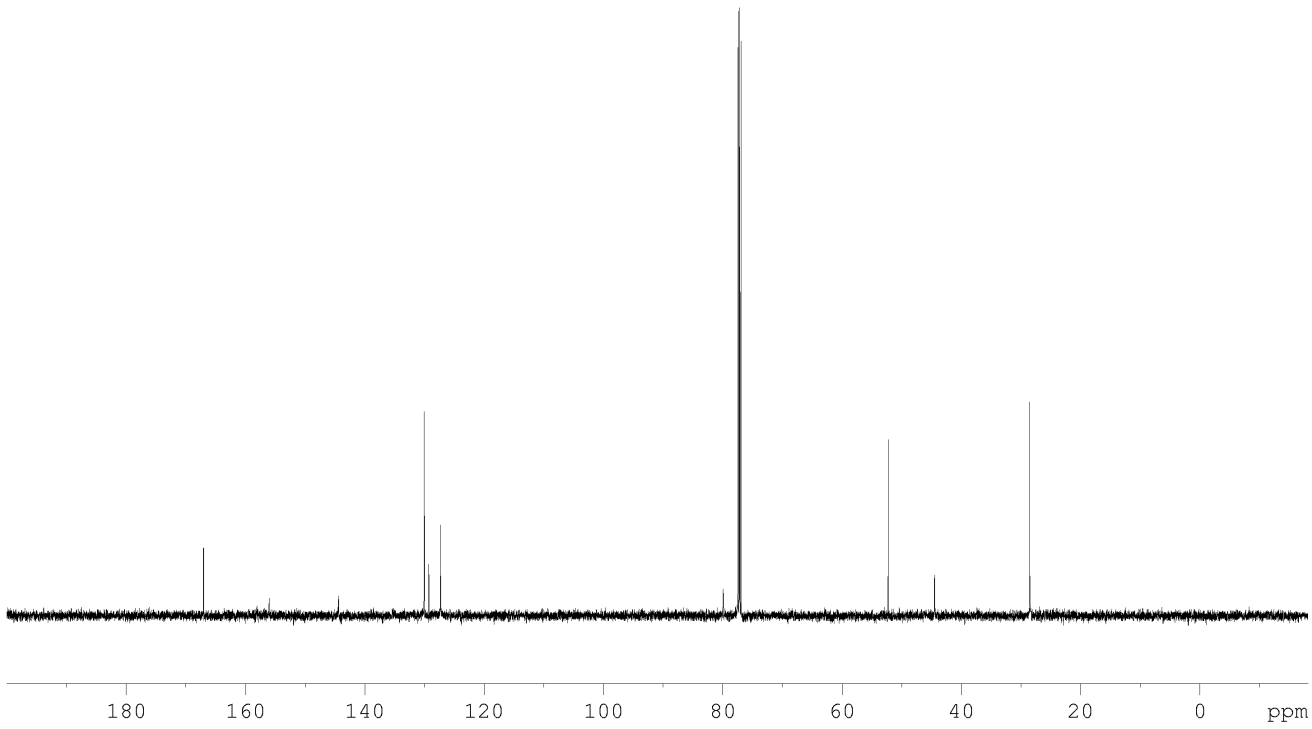
MeO2C


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
MeO2C


180
160
140
120
100
80
60
40
20
0
ppm

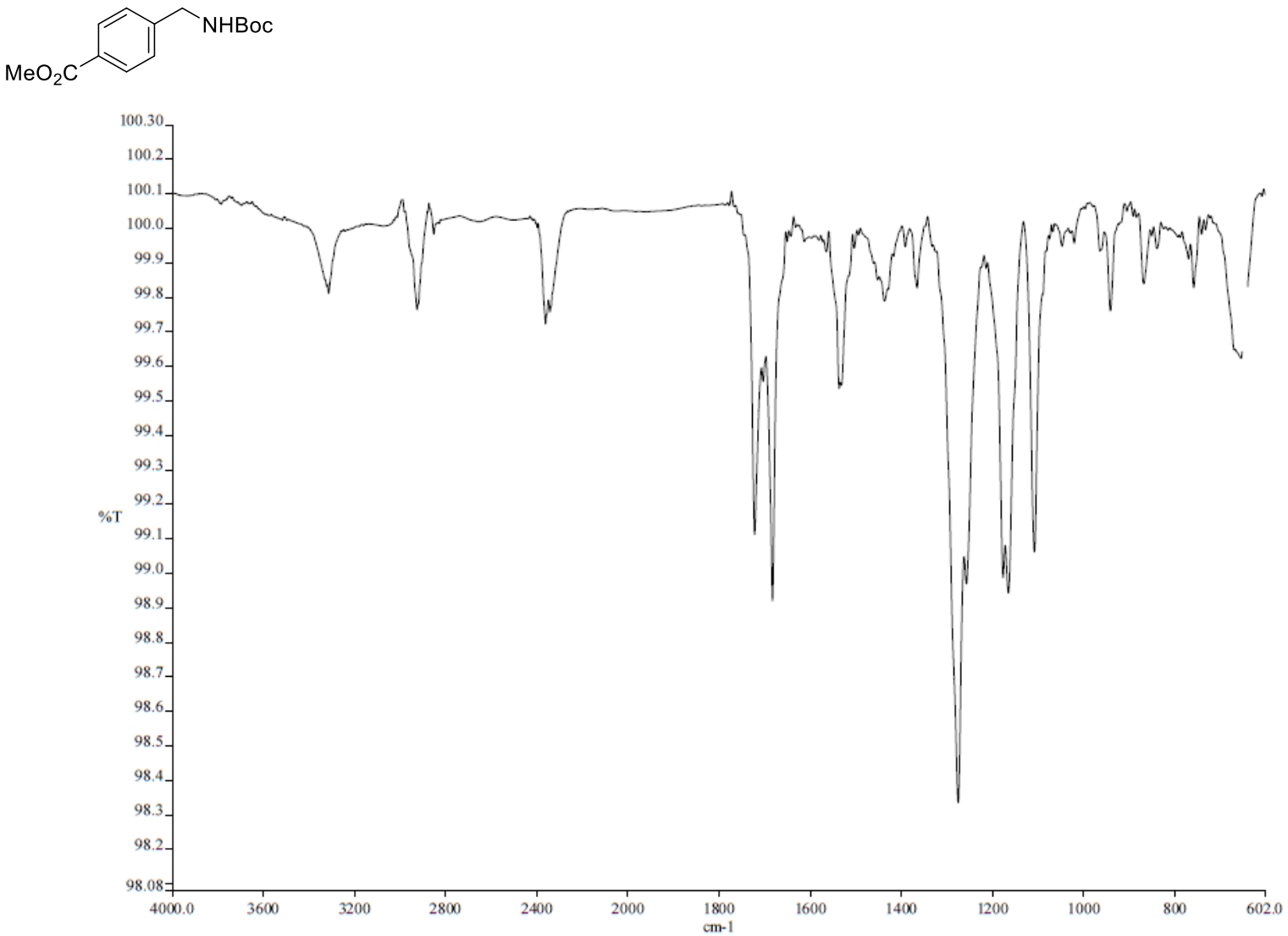
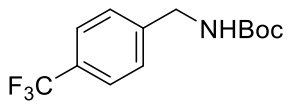
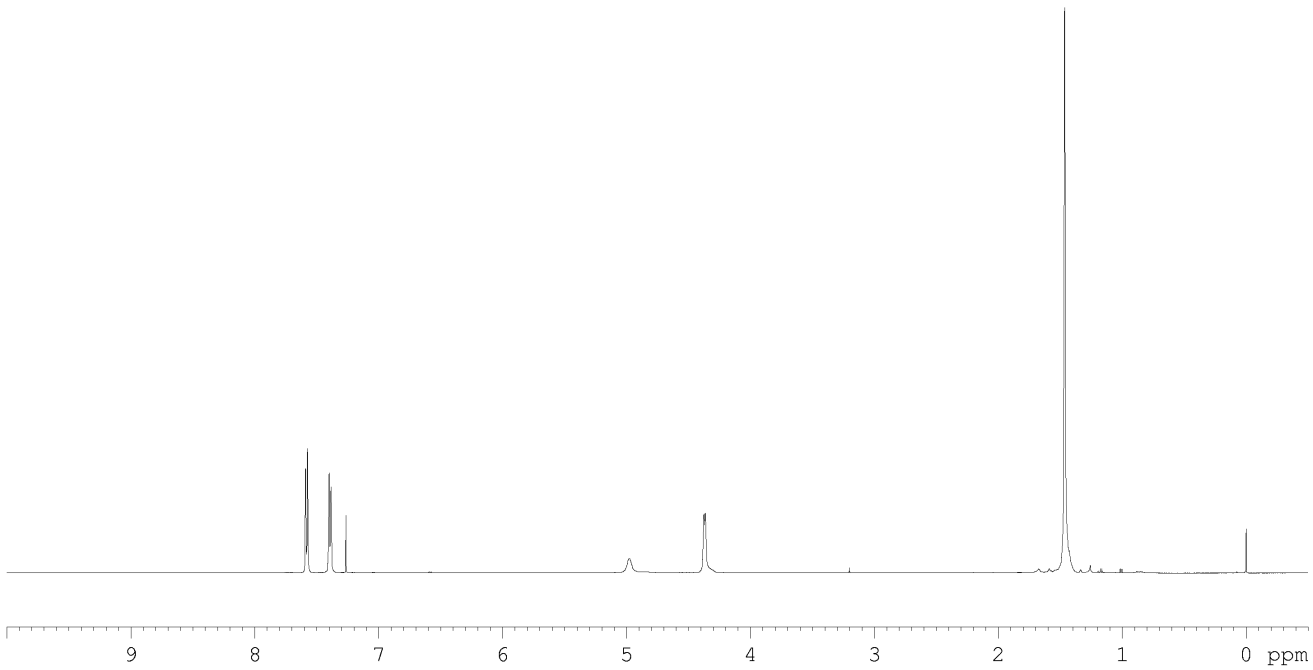
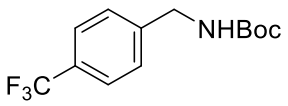
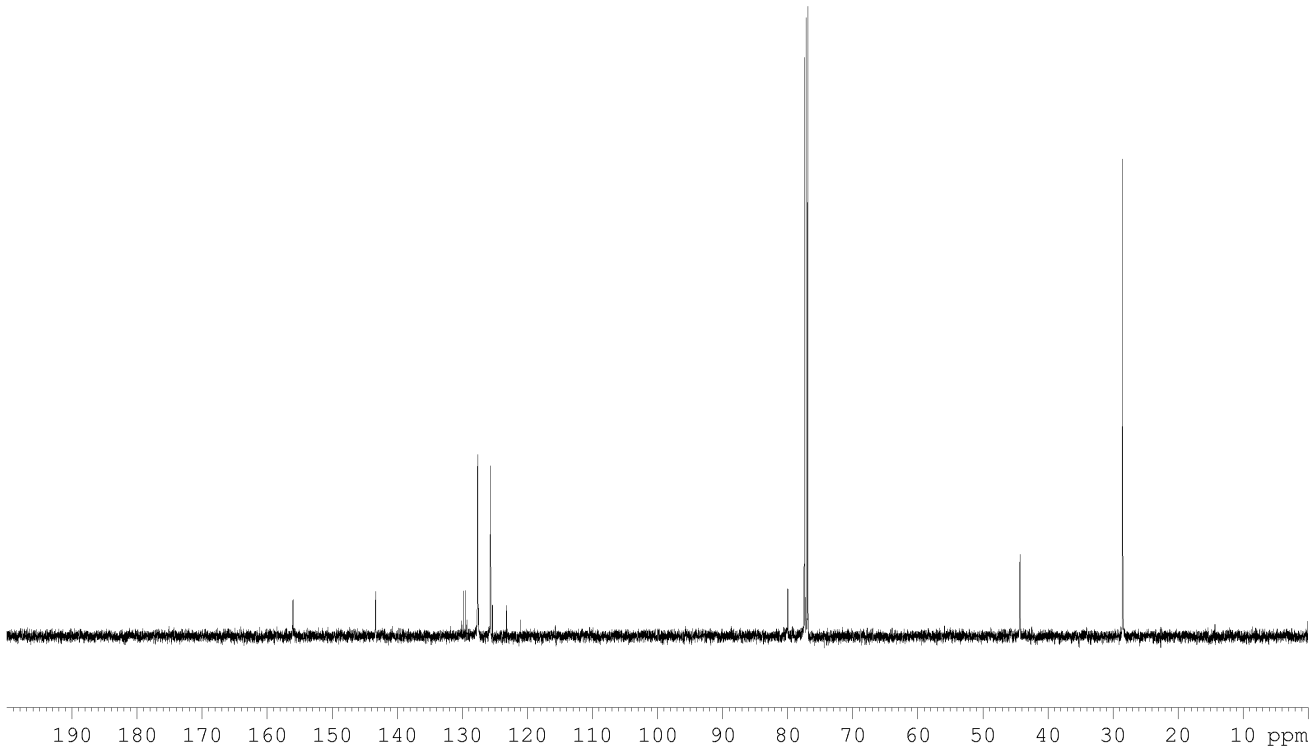


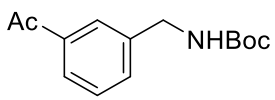
Figure A2.253 Infrared Spectrum


NHBoc
F3C

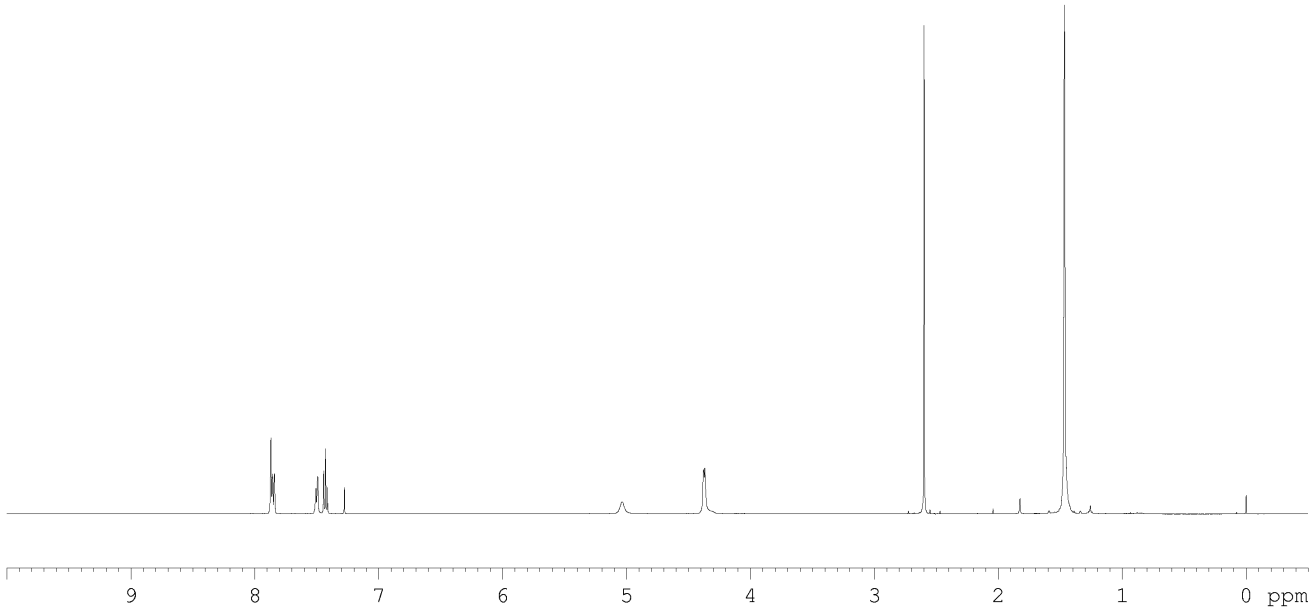

9
8
7
6
5
4
3
2
1
0 ppm

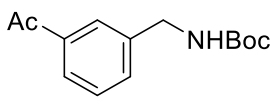

NHBoc
F3C


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

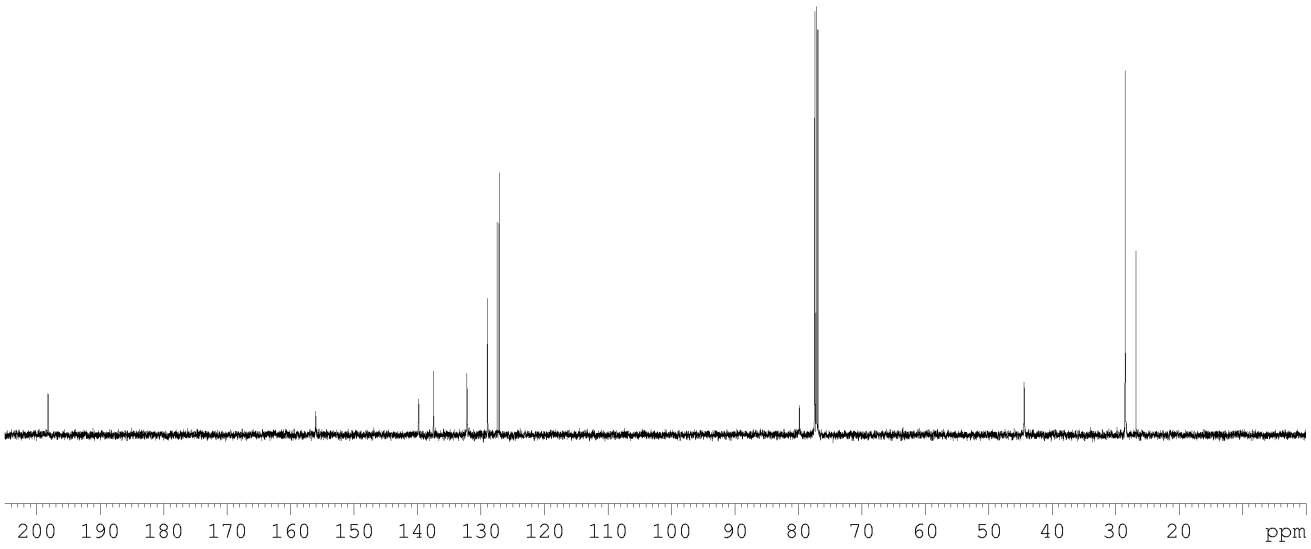


559




Ac
NHBoc

560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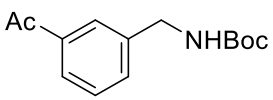


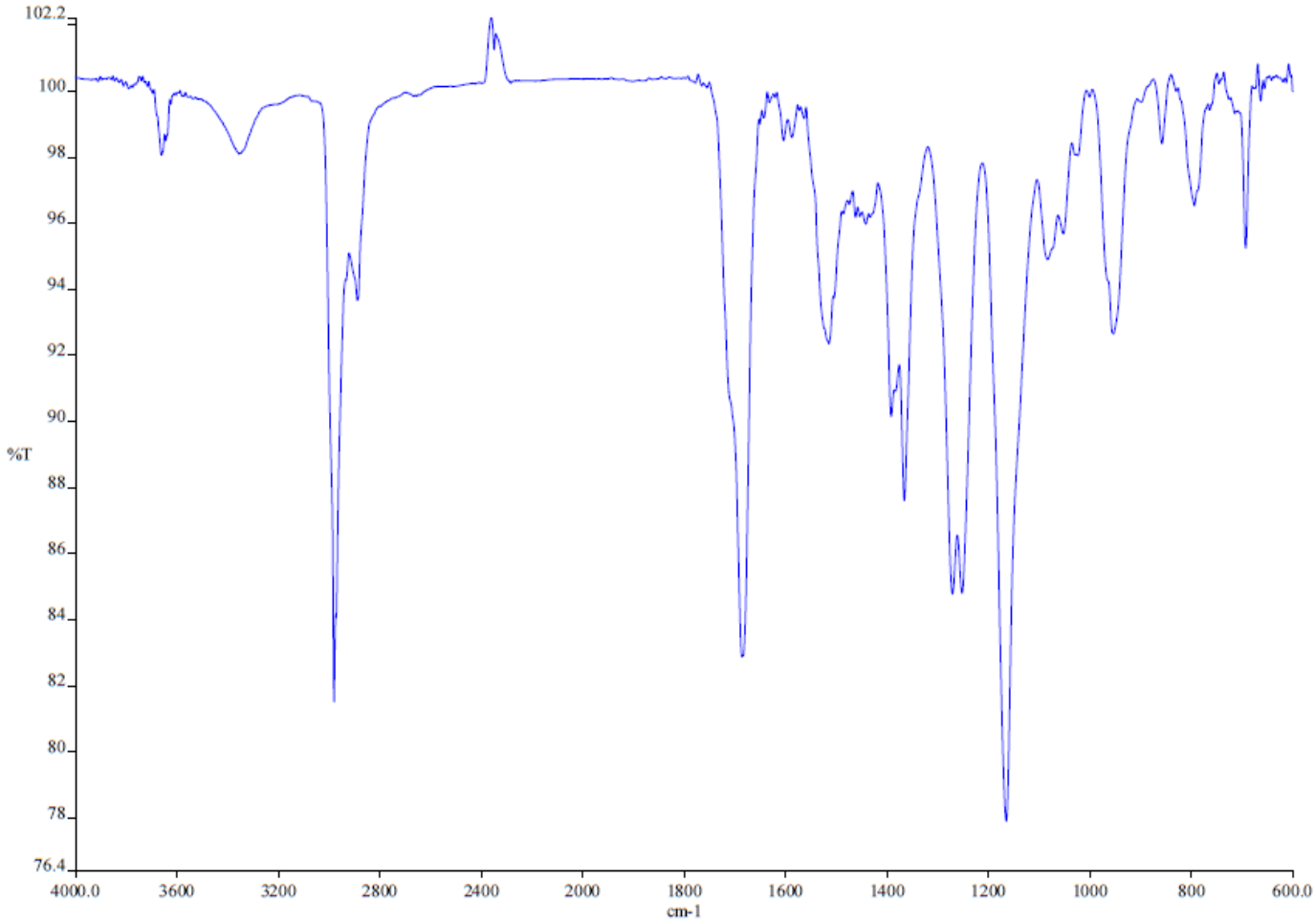
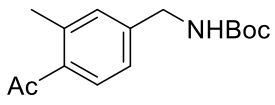
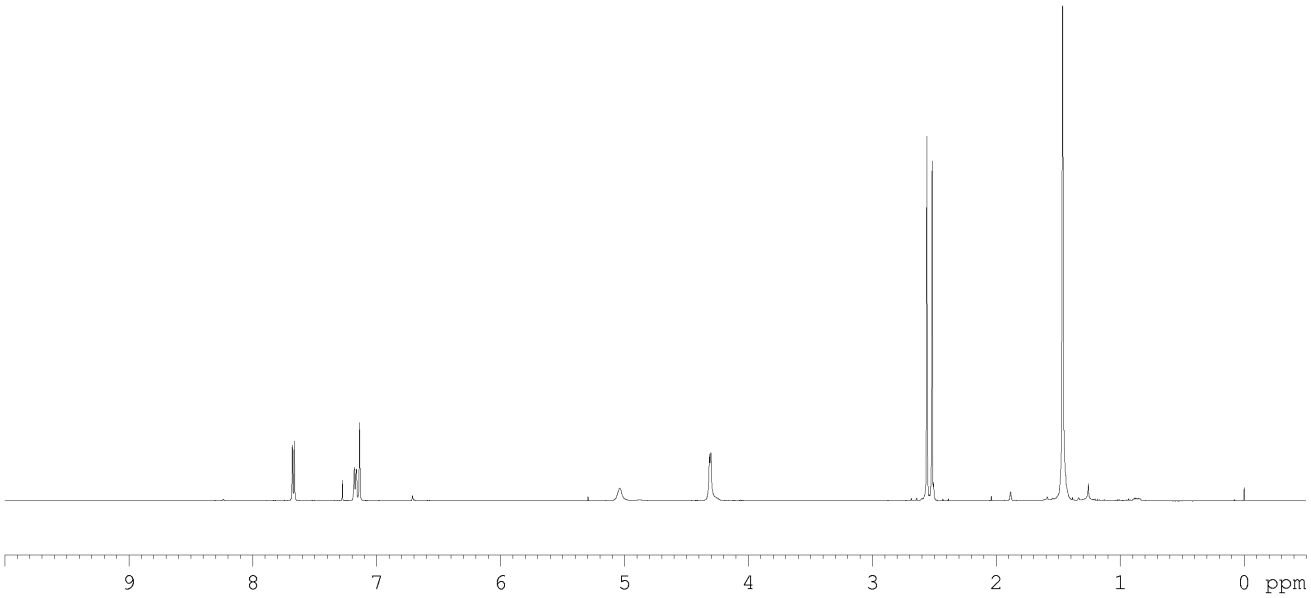
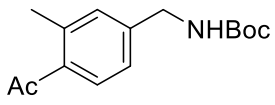
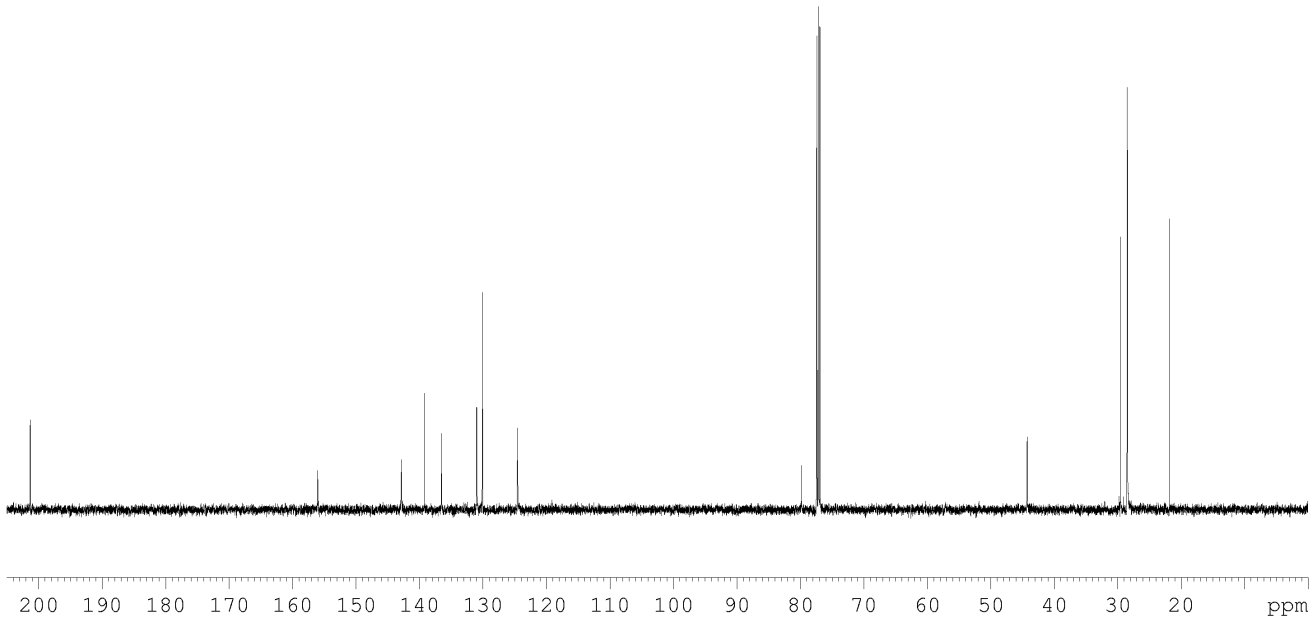


Figure A2.258 Infrared Spectrum


NHBoc
Ac


9
8
7
6
5
4
3
2
1
0 ppm


NHBoc
Ac


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

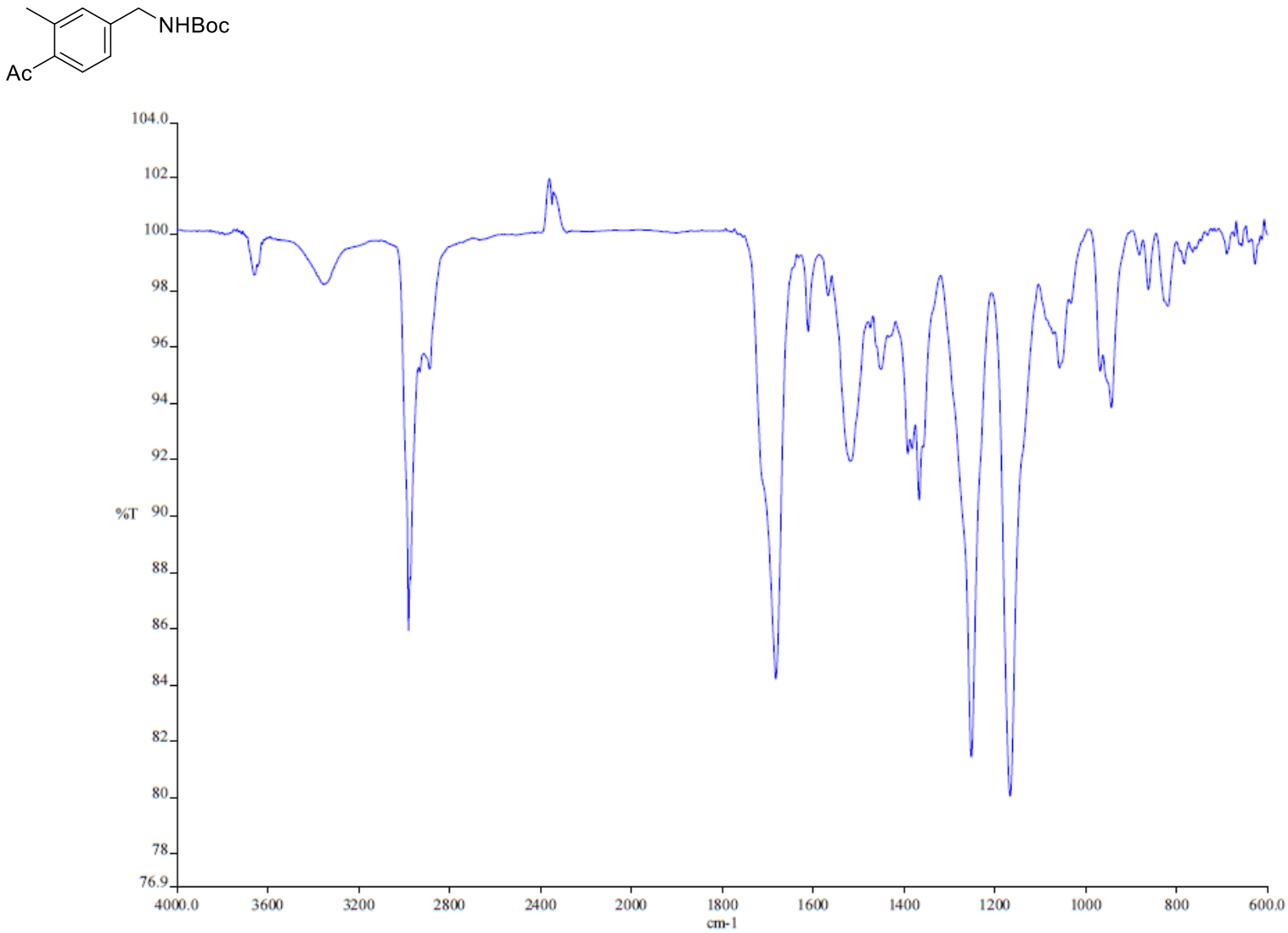
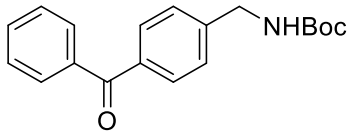
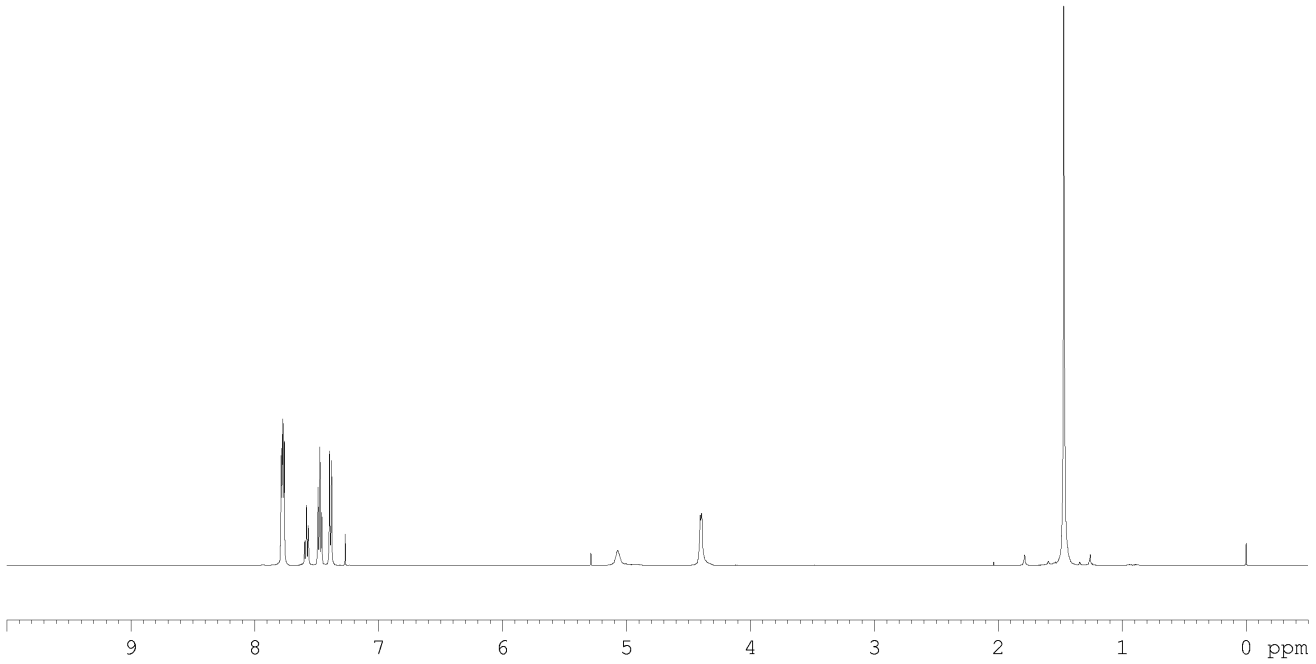


Figure A2.261 Infrared Spectrum


NHBoc
O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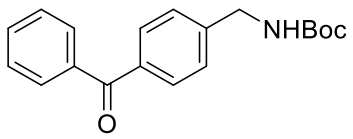
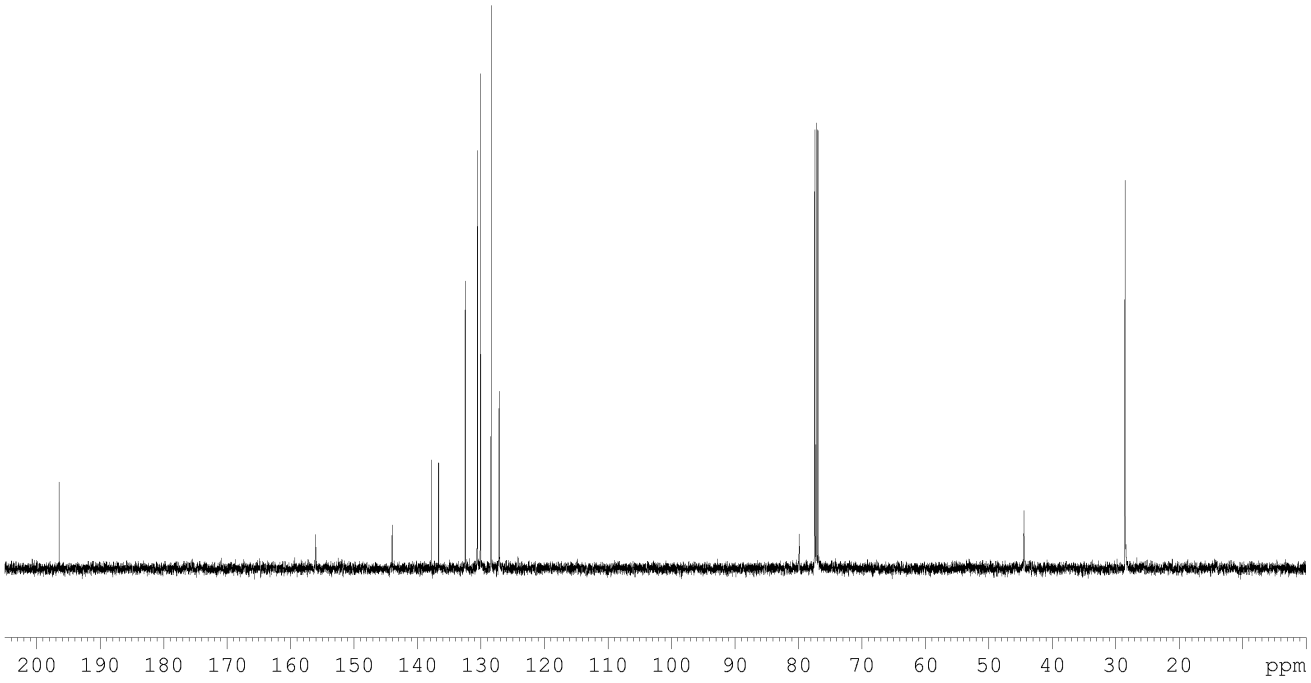
6
5
4
3
2
1
0 ppm


NHBoc
O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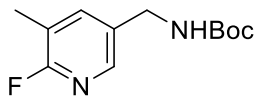
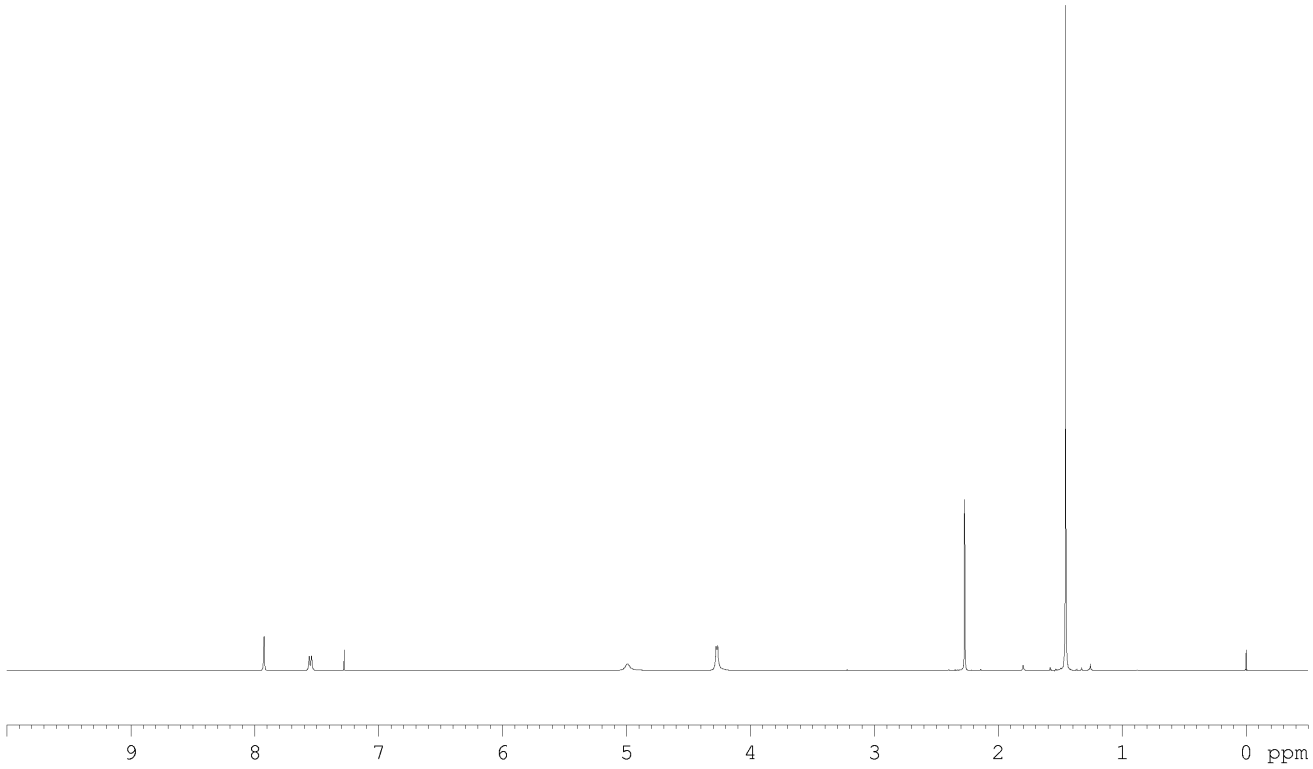

NHBoc
F
N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5
4
3
2
1
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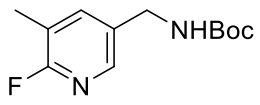
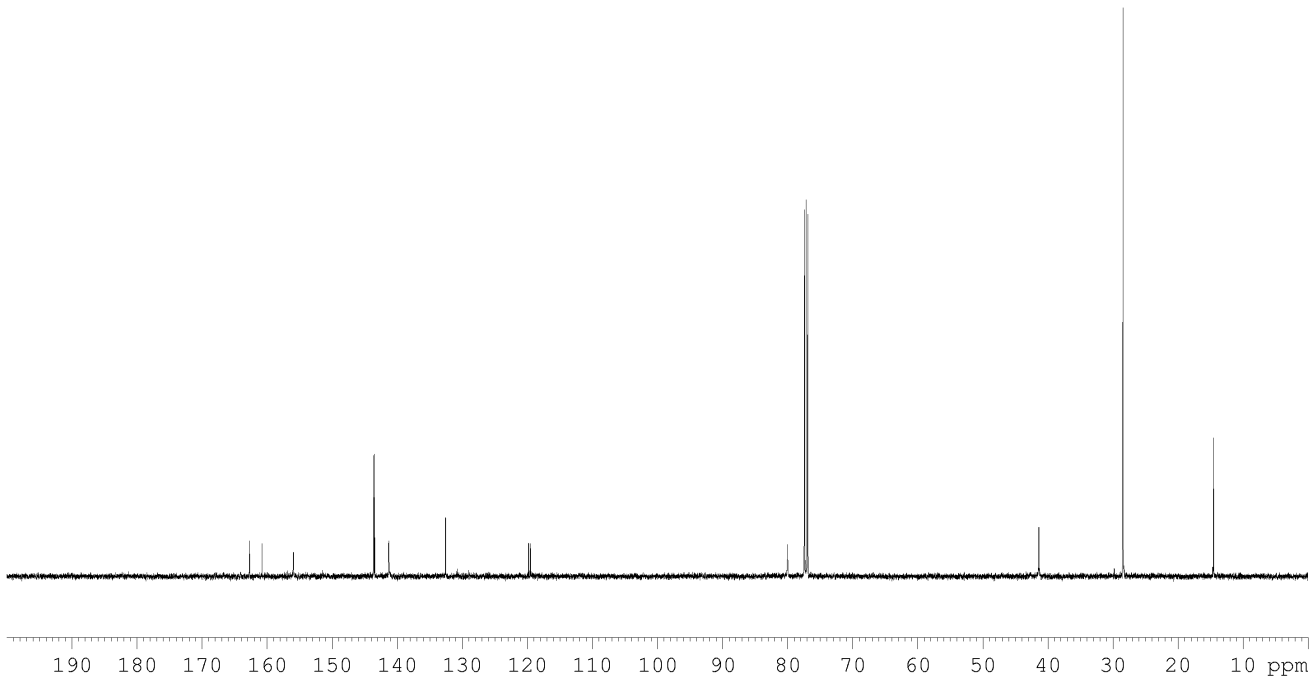

NHBoc
F
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

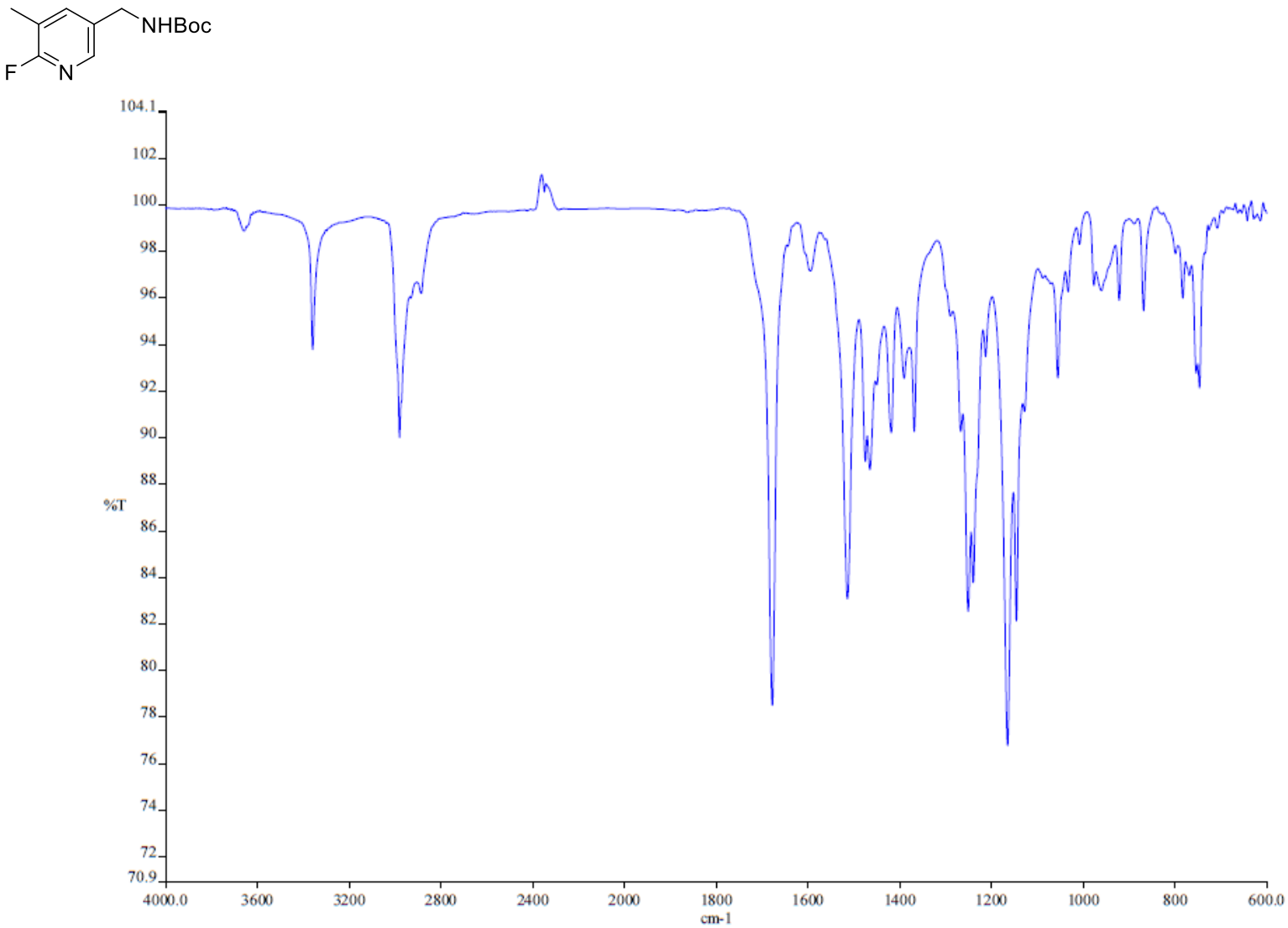
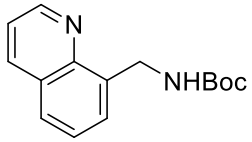


Figure A2.266 Infrared Spectrum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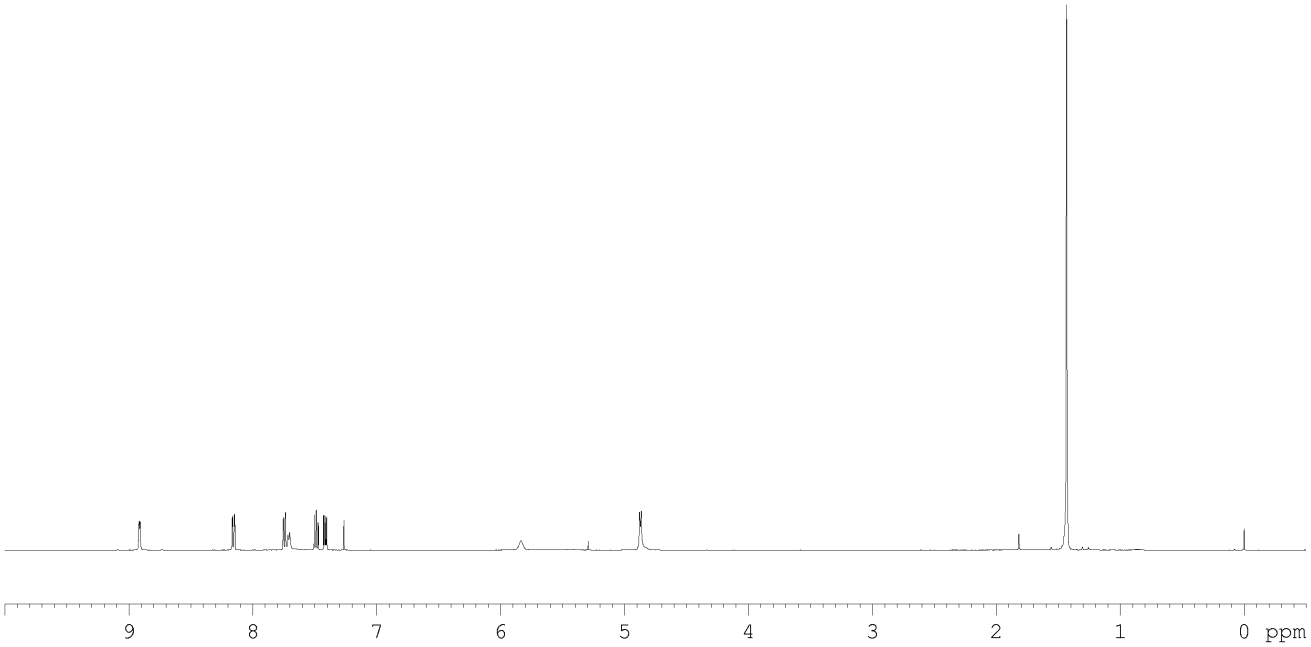
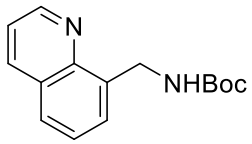
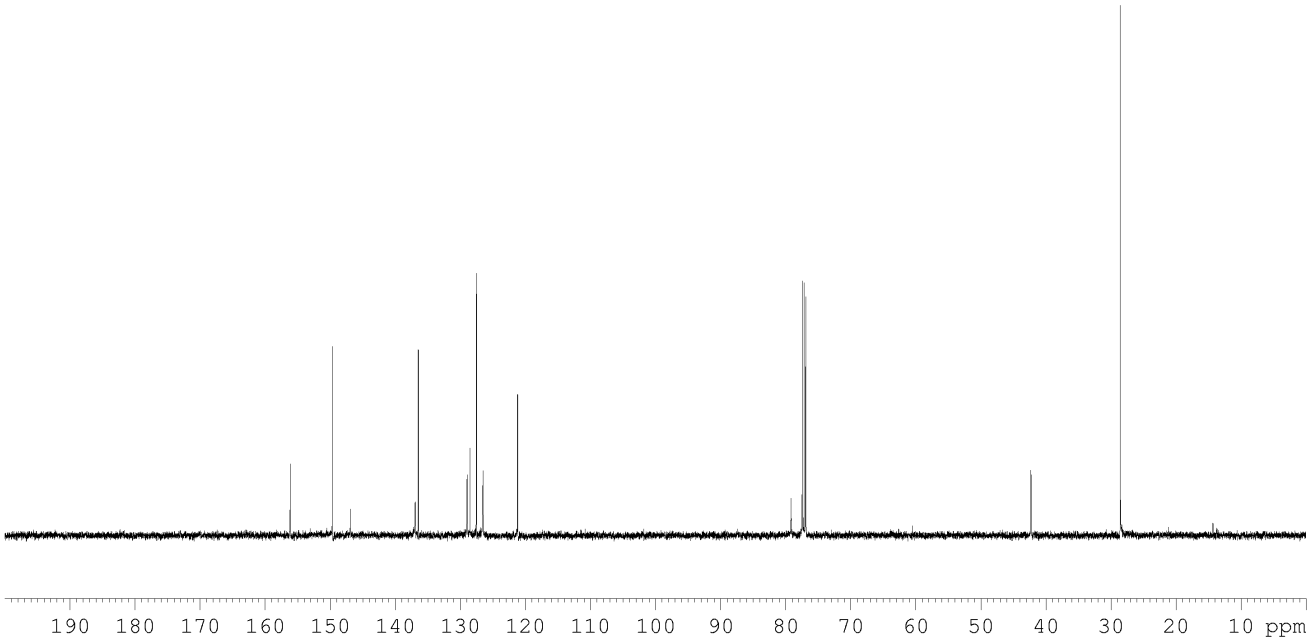
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm


N
NHBoc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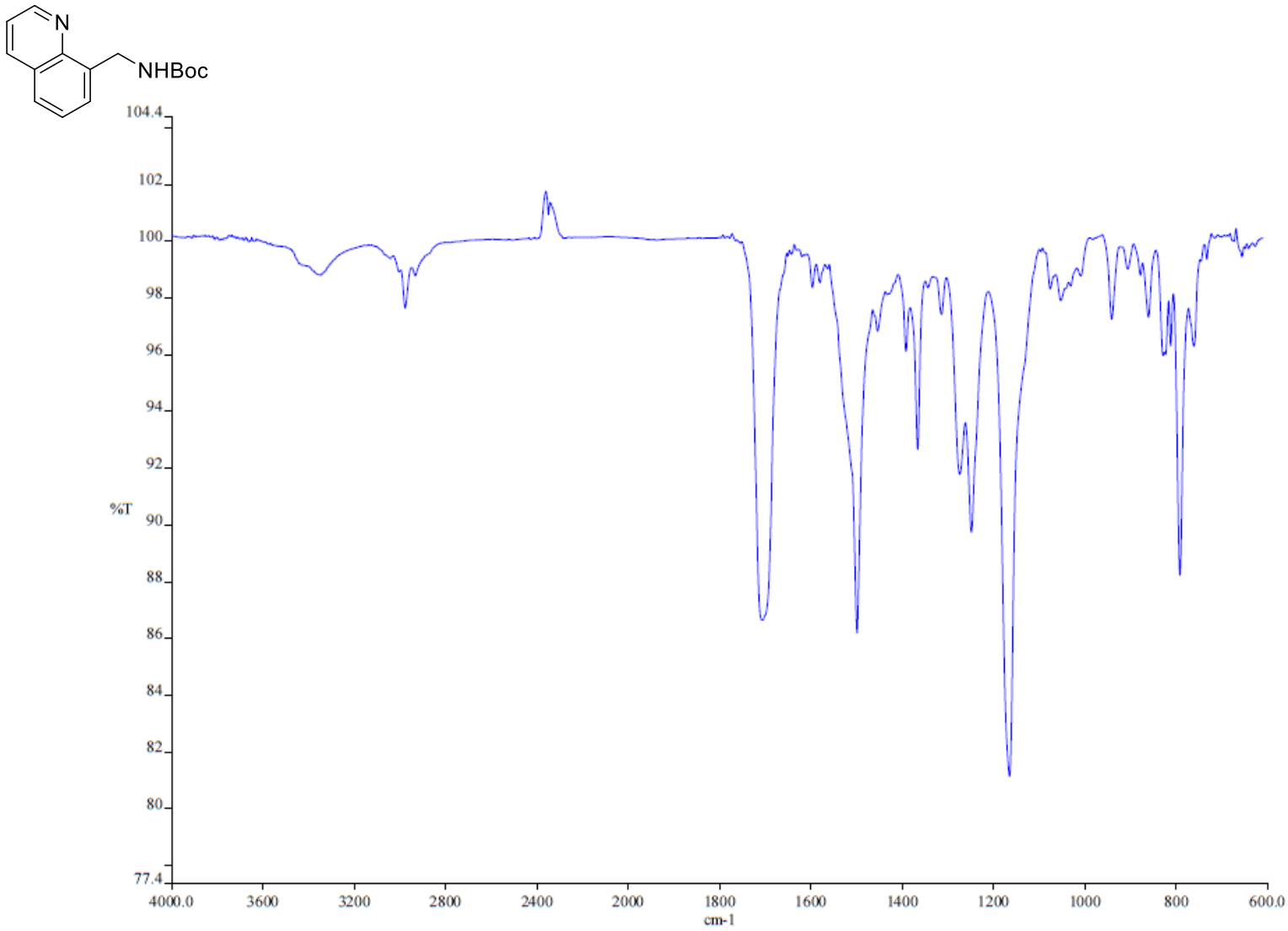
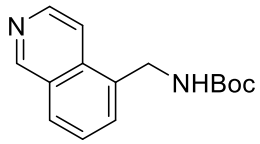
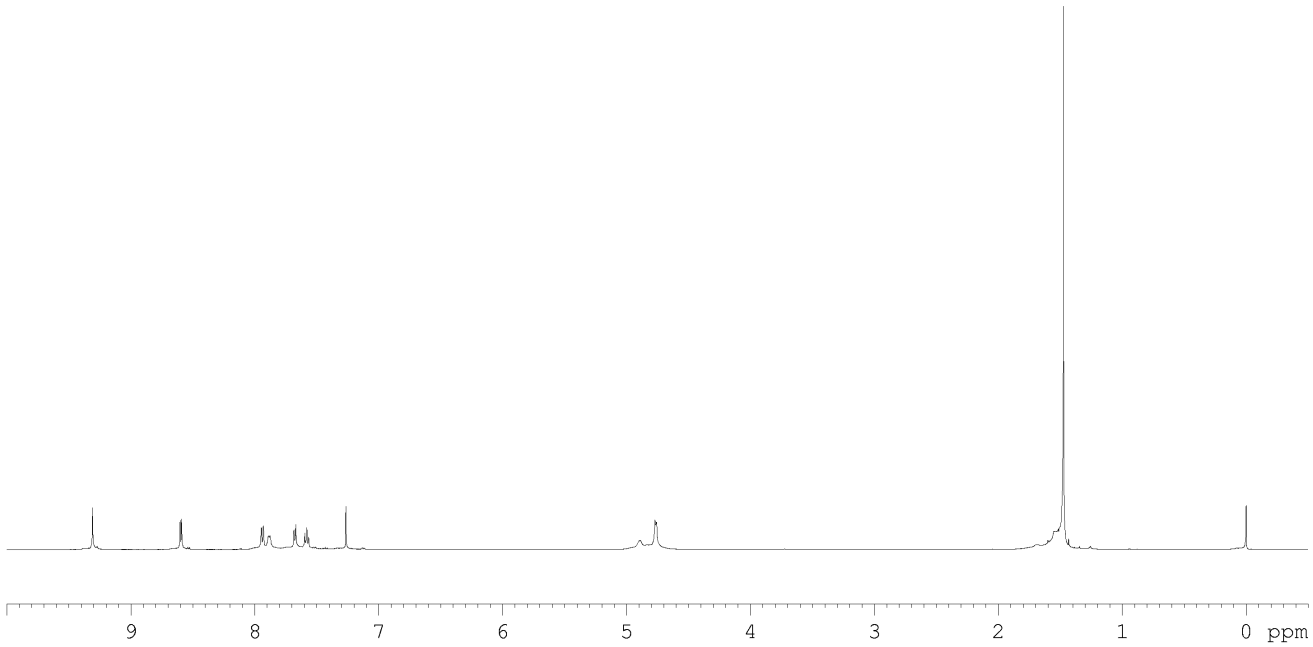
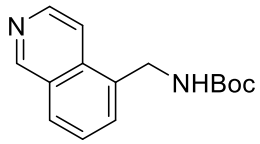


Figure A2.269 Infrared Spectrum


N
NHBoc


9
8
7
6
5
4
3
2
1
0 ppm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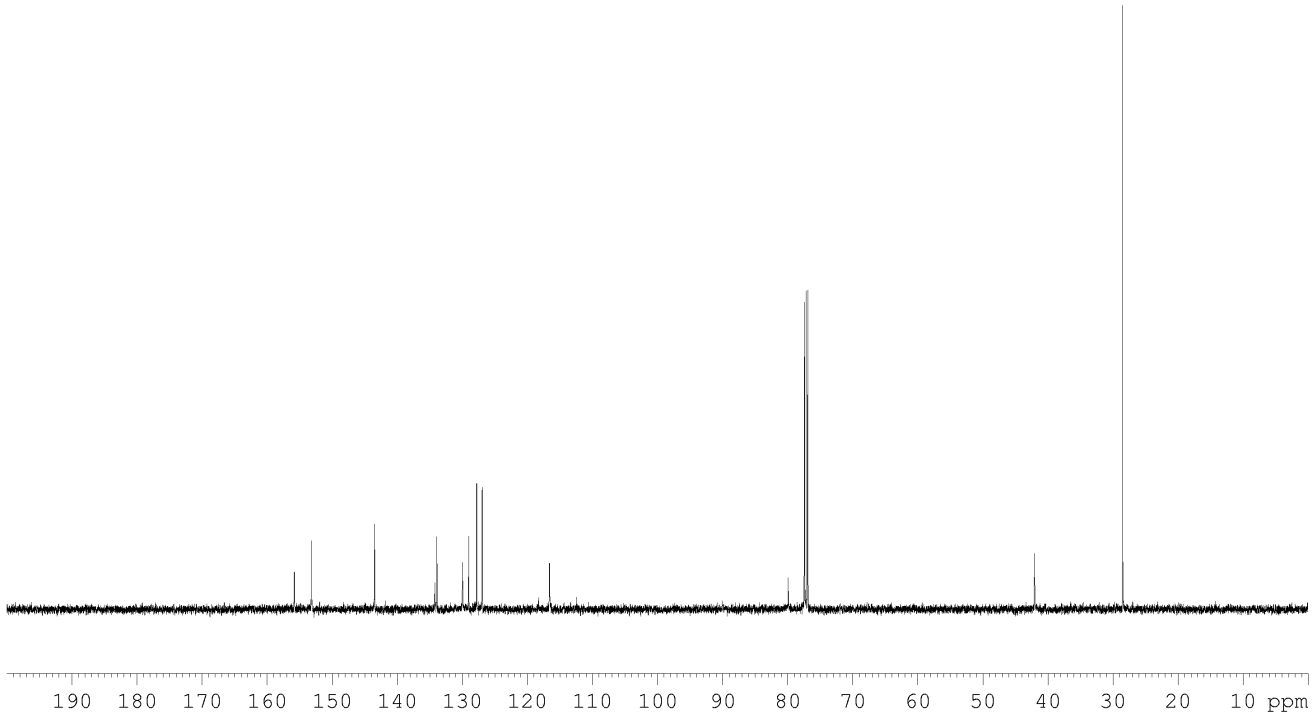
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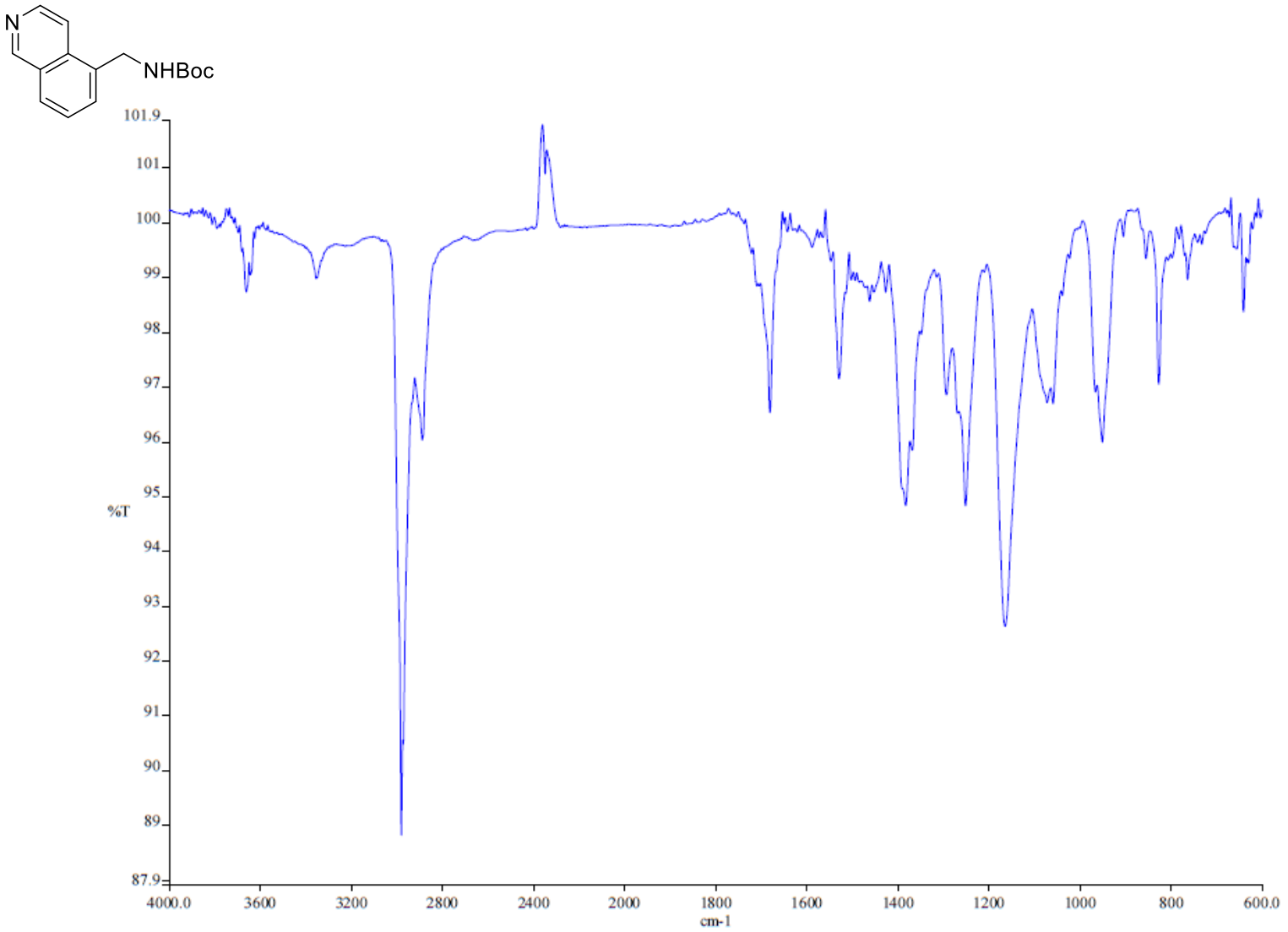
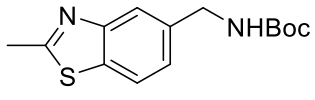


Figure A2.272 Infrared Spectrum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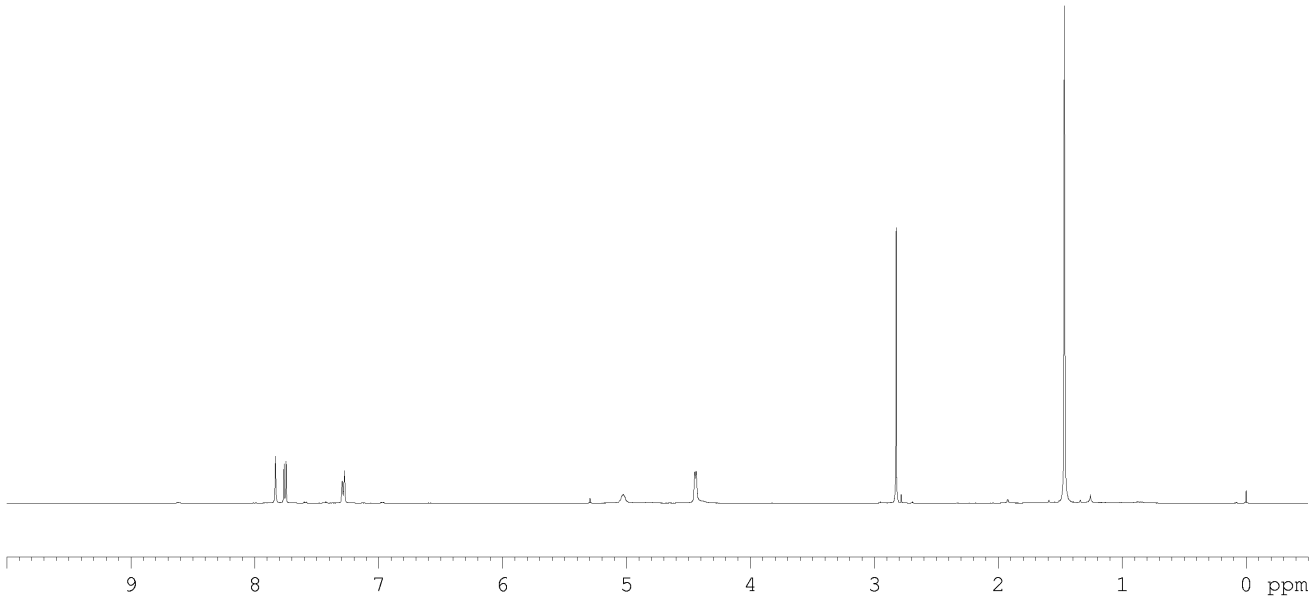
S
NHBoc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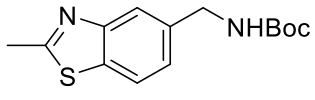
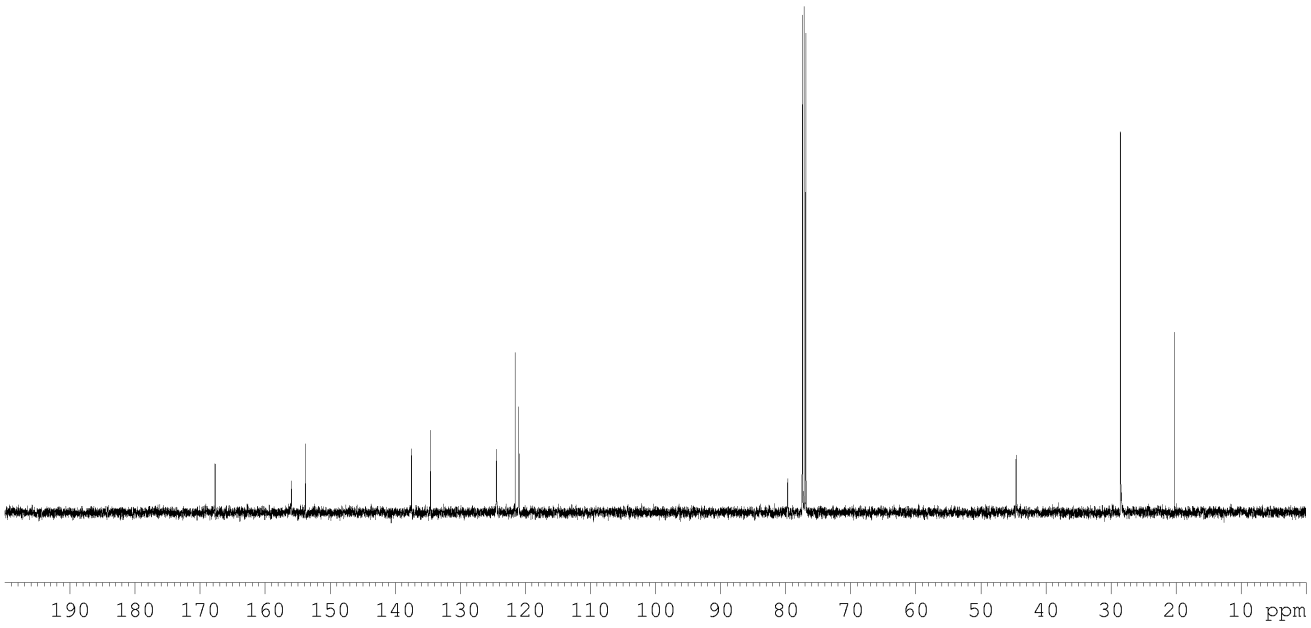
8
7
6
5
4
3
2
1
0 ppm


N
S
NHBoc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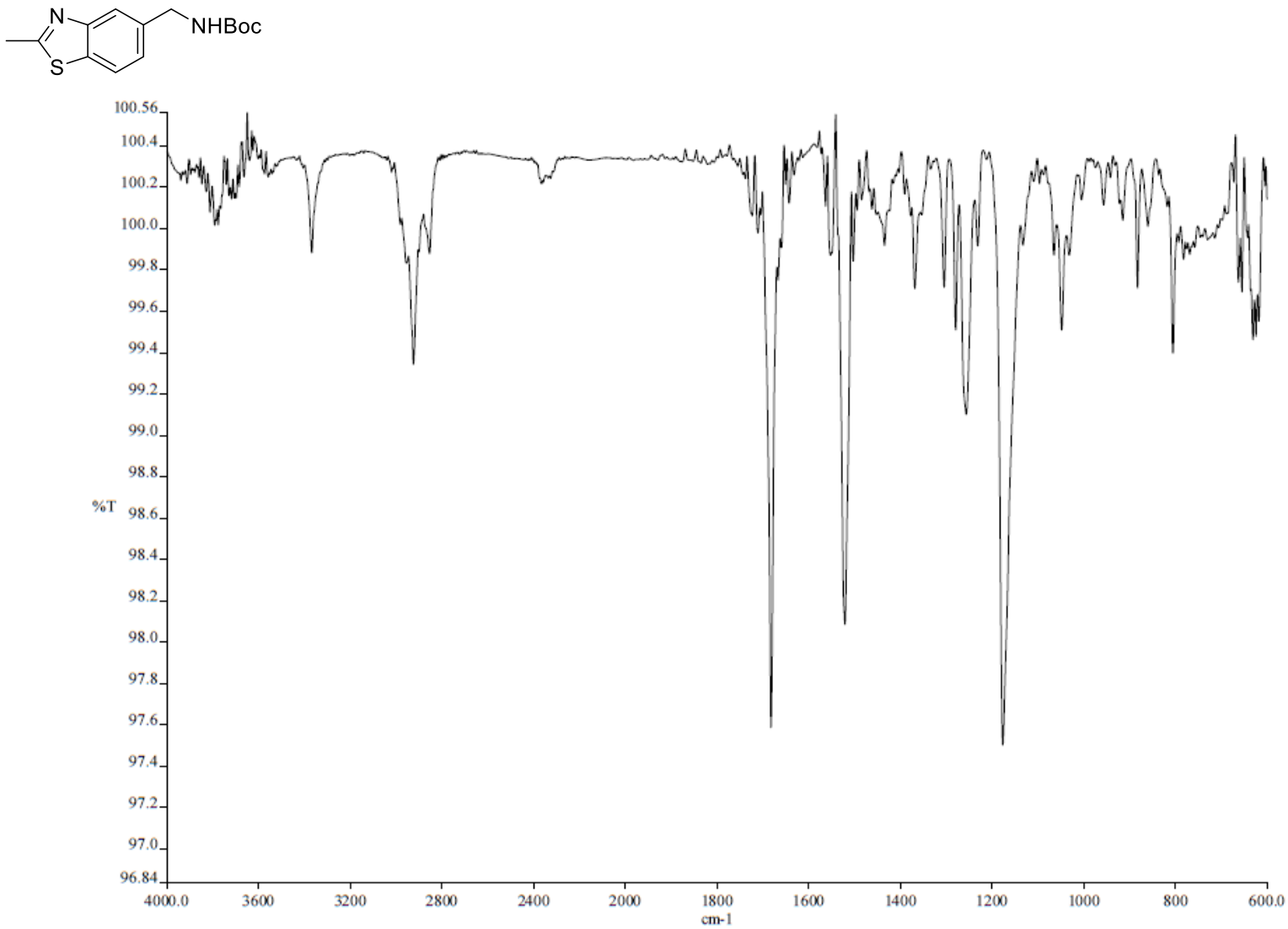
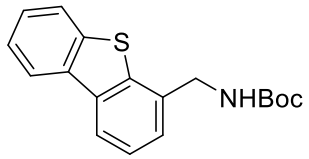


Figure A2.275 Infrared Spectrum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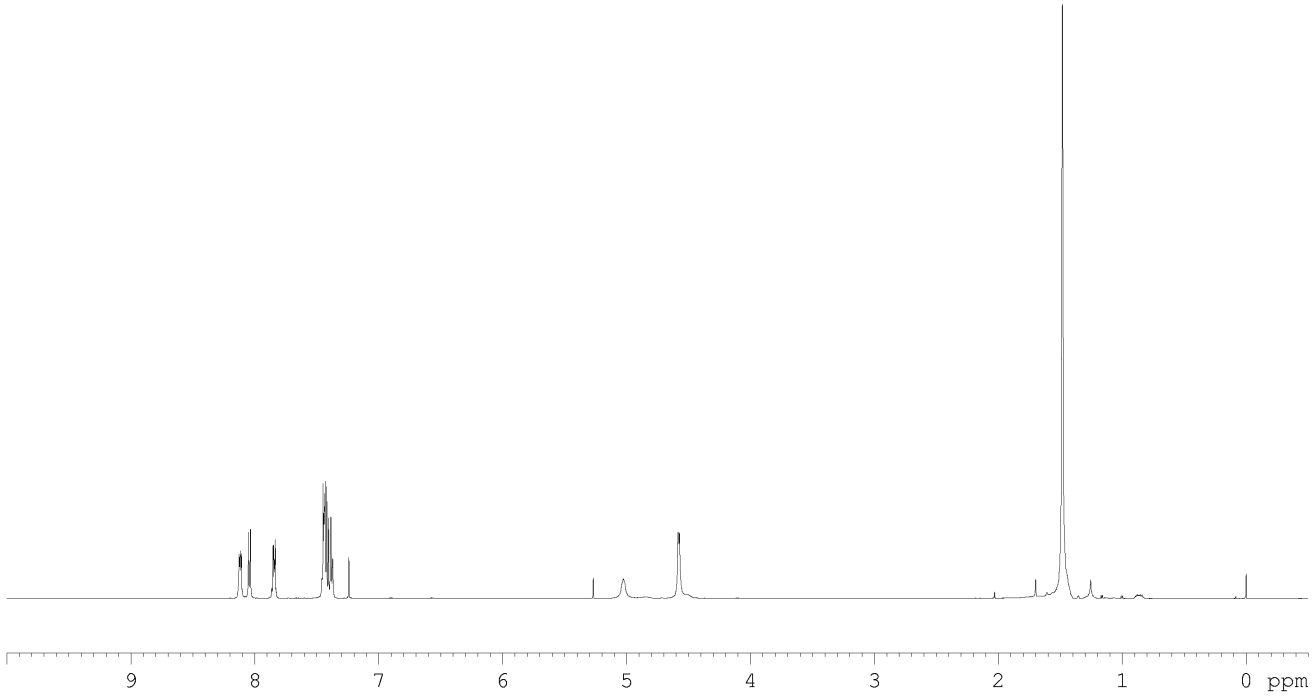
NHBoc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8
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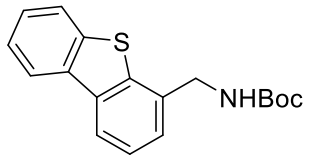
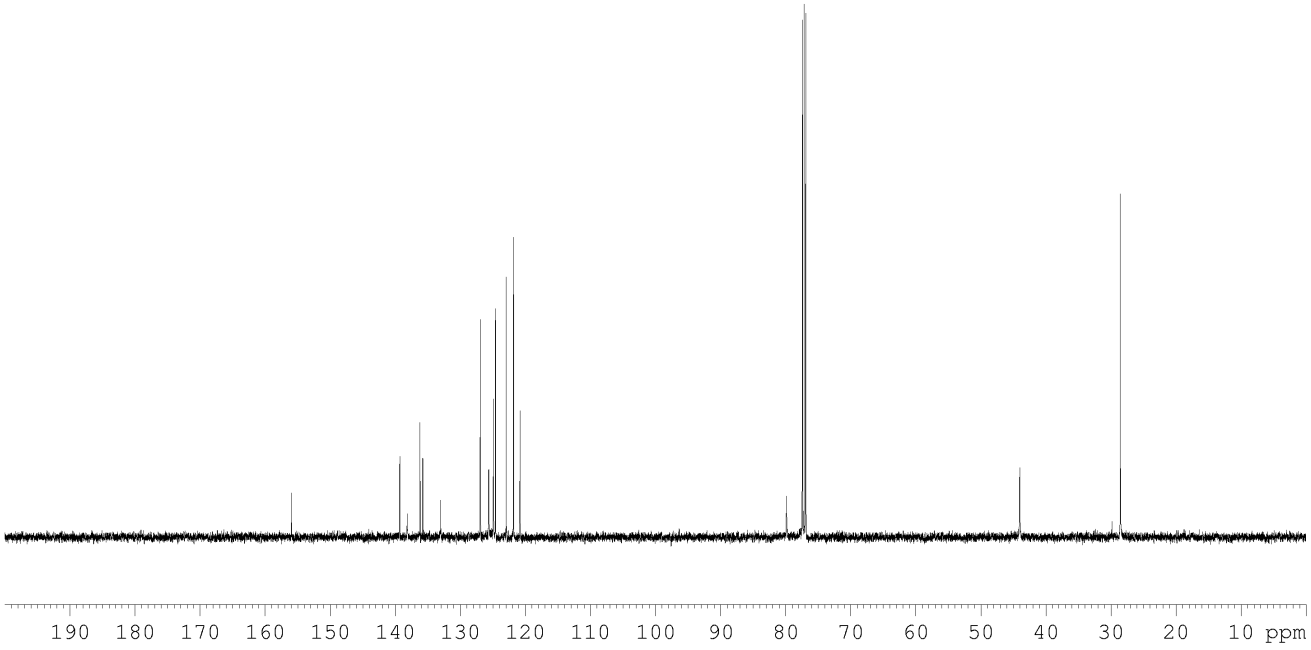
6
5
4
3
2
1
0 ppm


S
NHBoc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

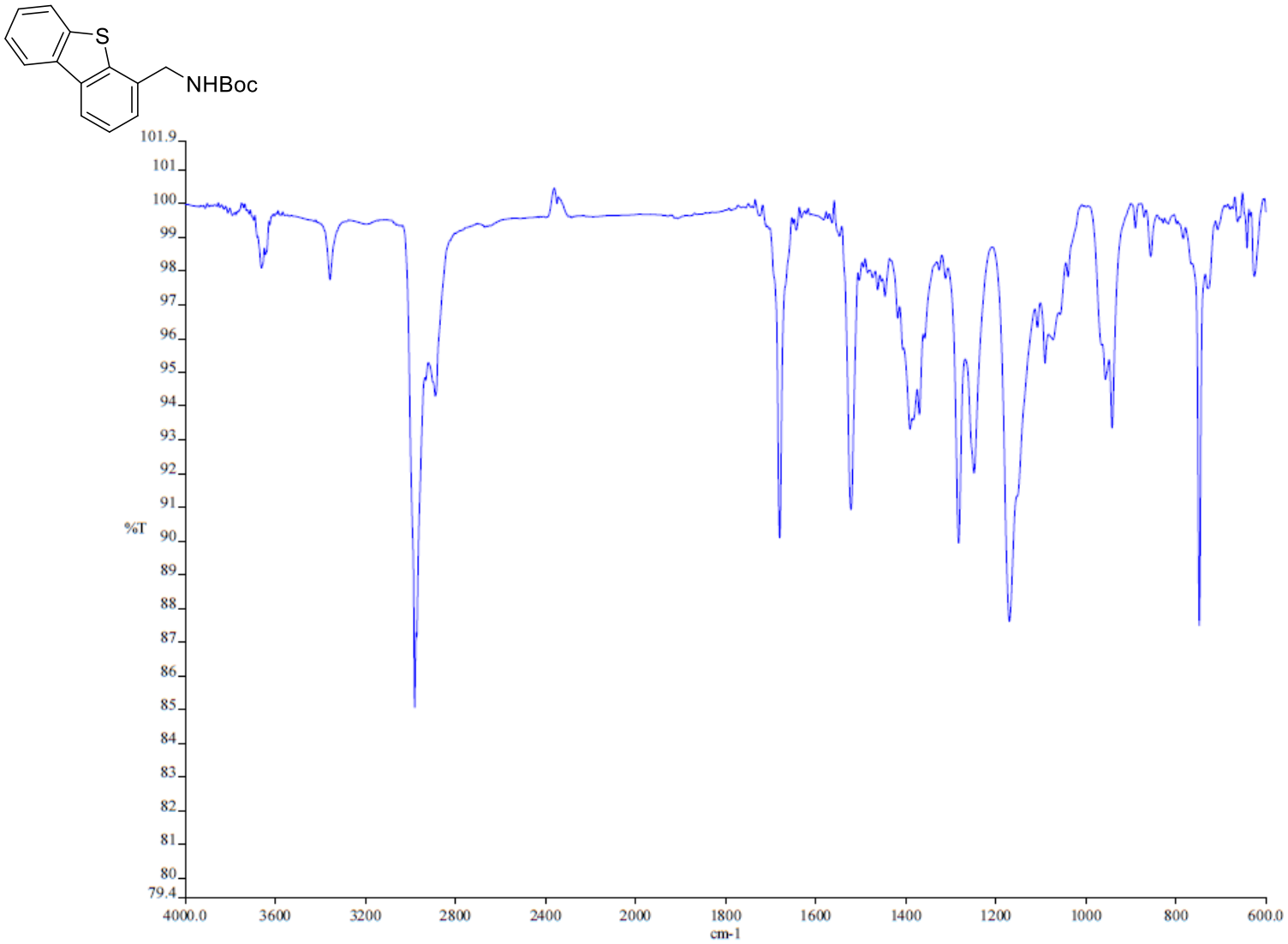
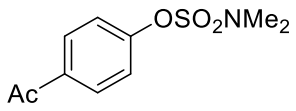
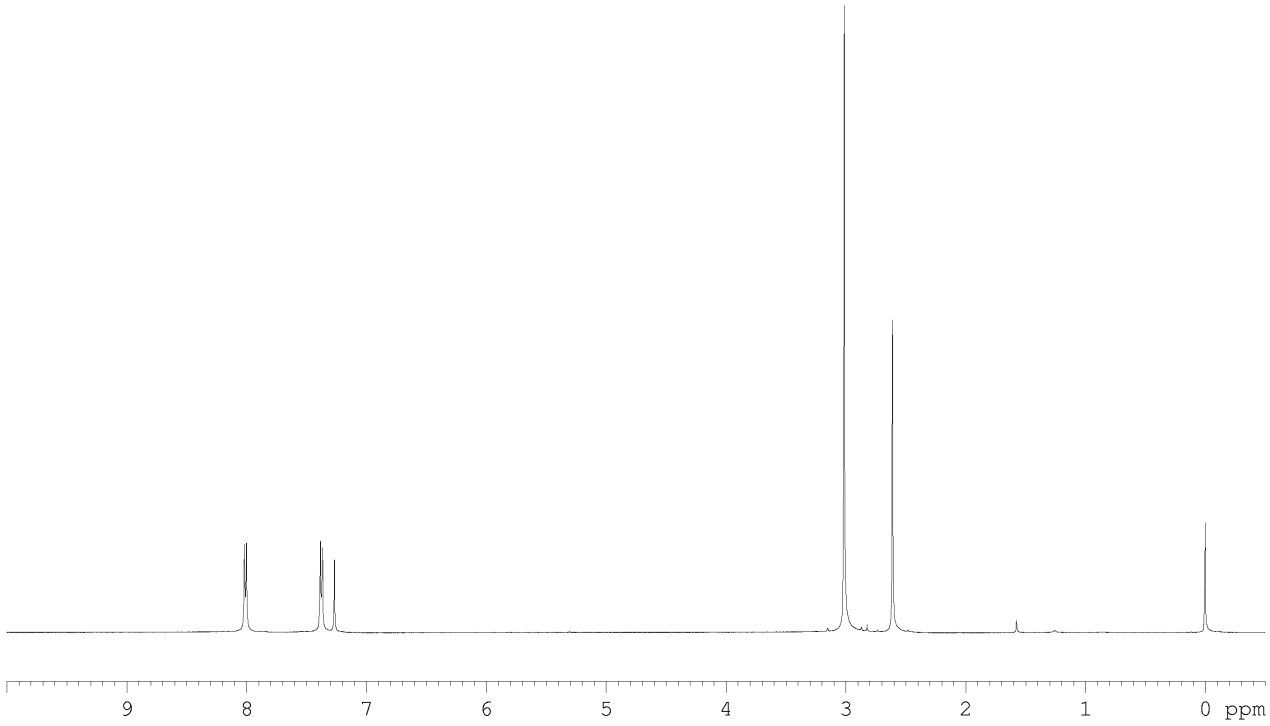


Figure A2.278 Infrared Spectrum


OSO2NMe2
Ac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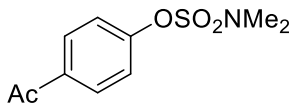
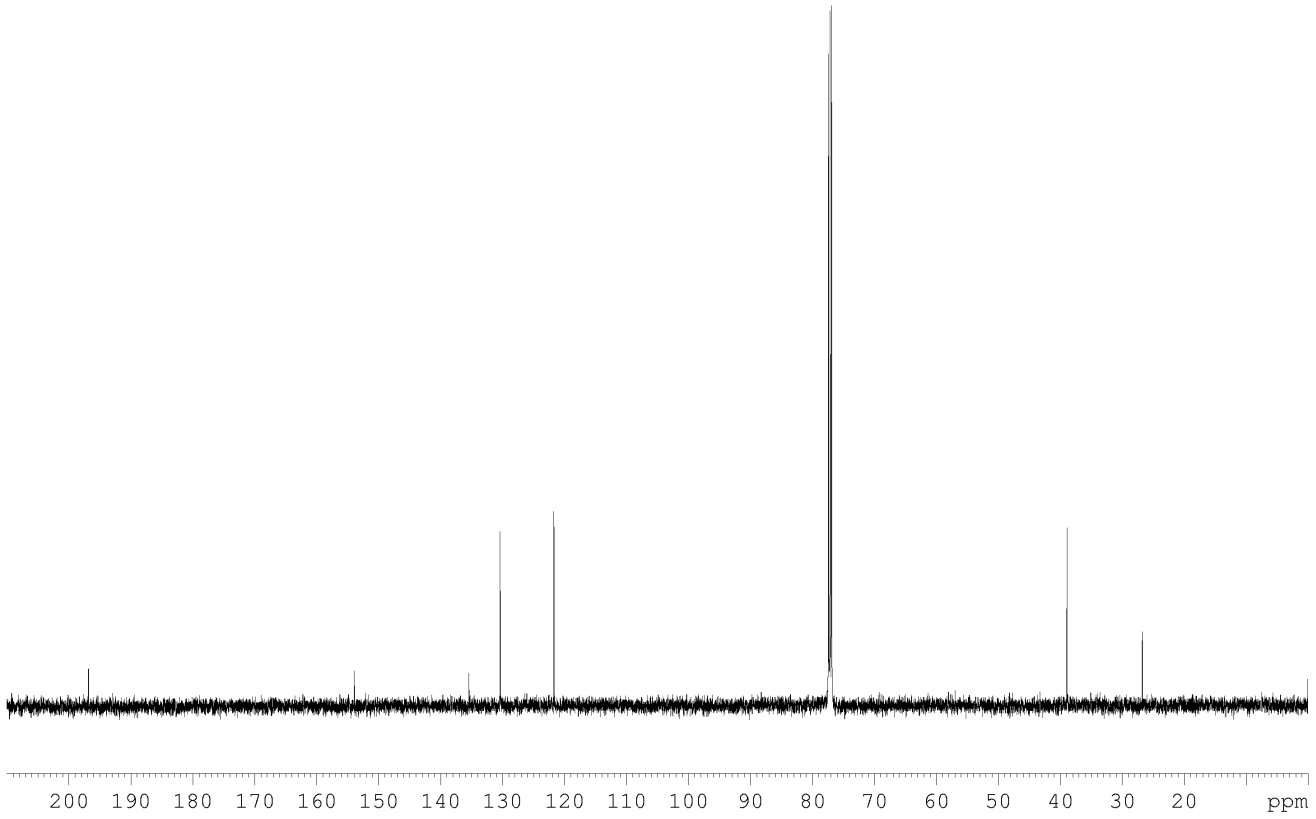
8
7
6
5
4
3
2
1
0 ppm


OSO2NMe2
Ac


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

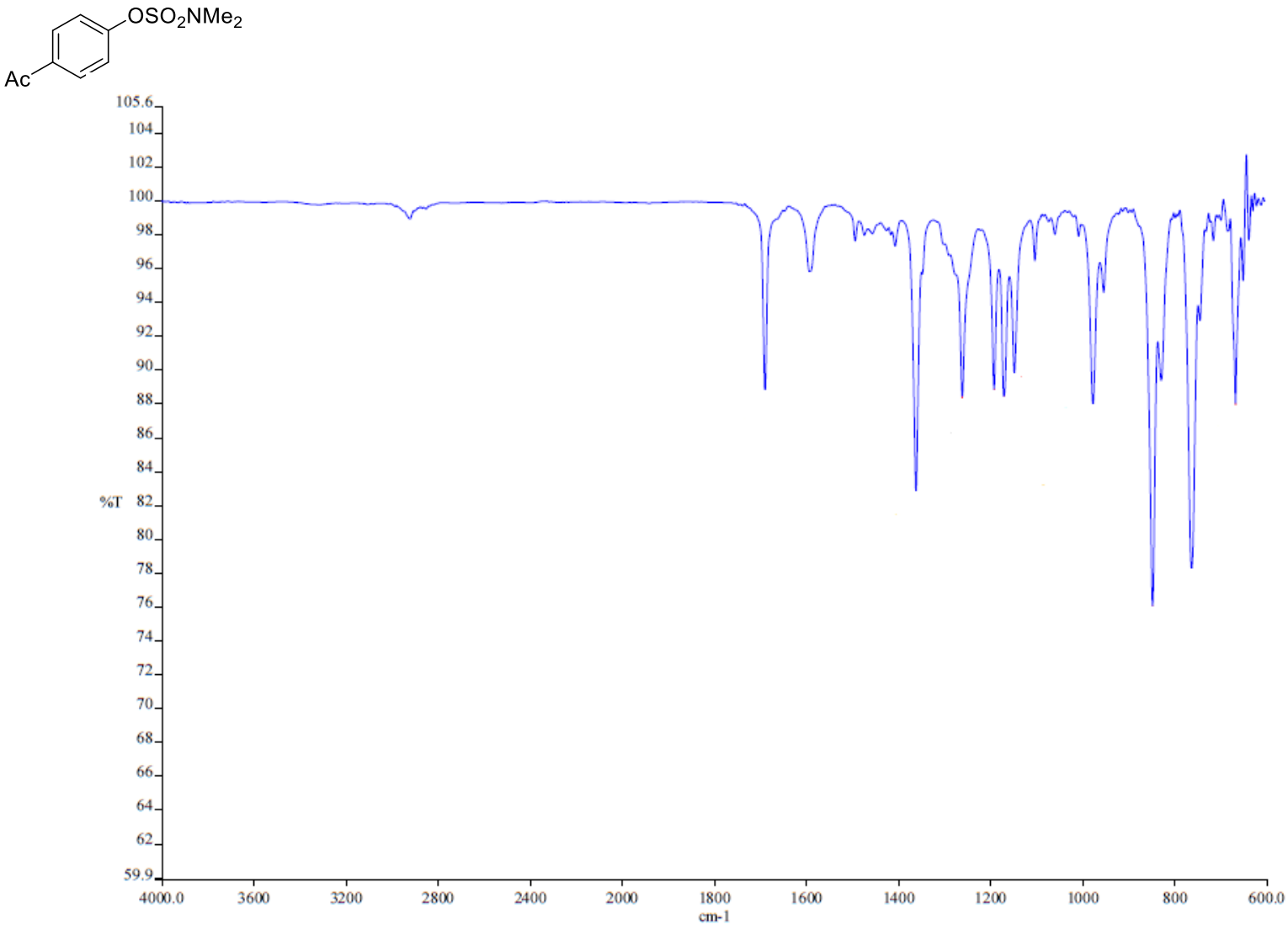
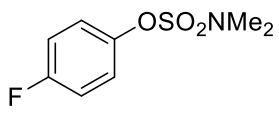
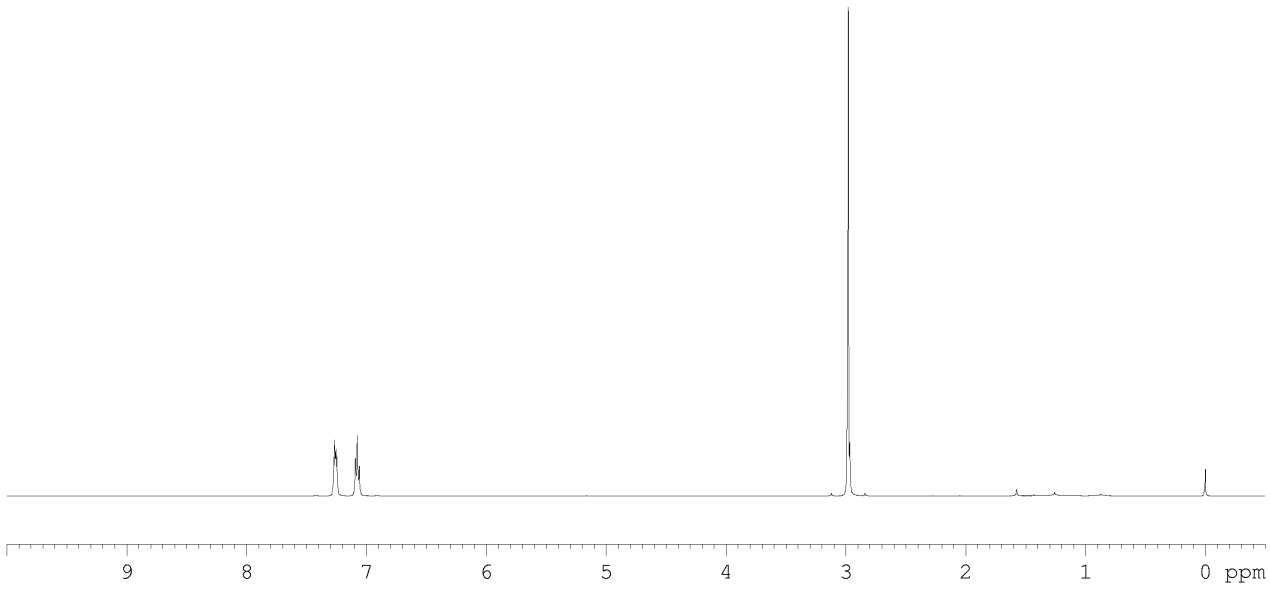
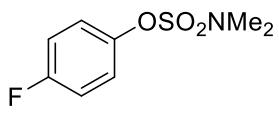
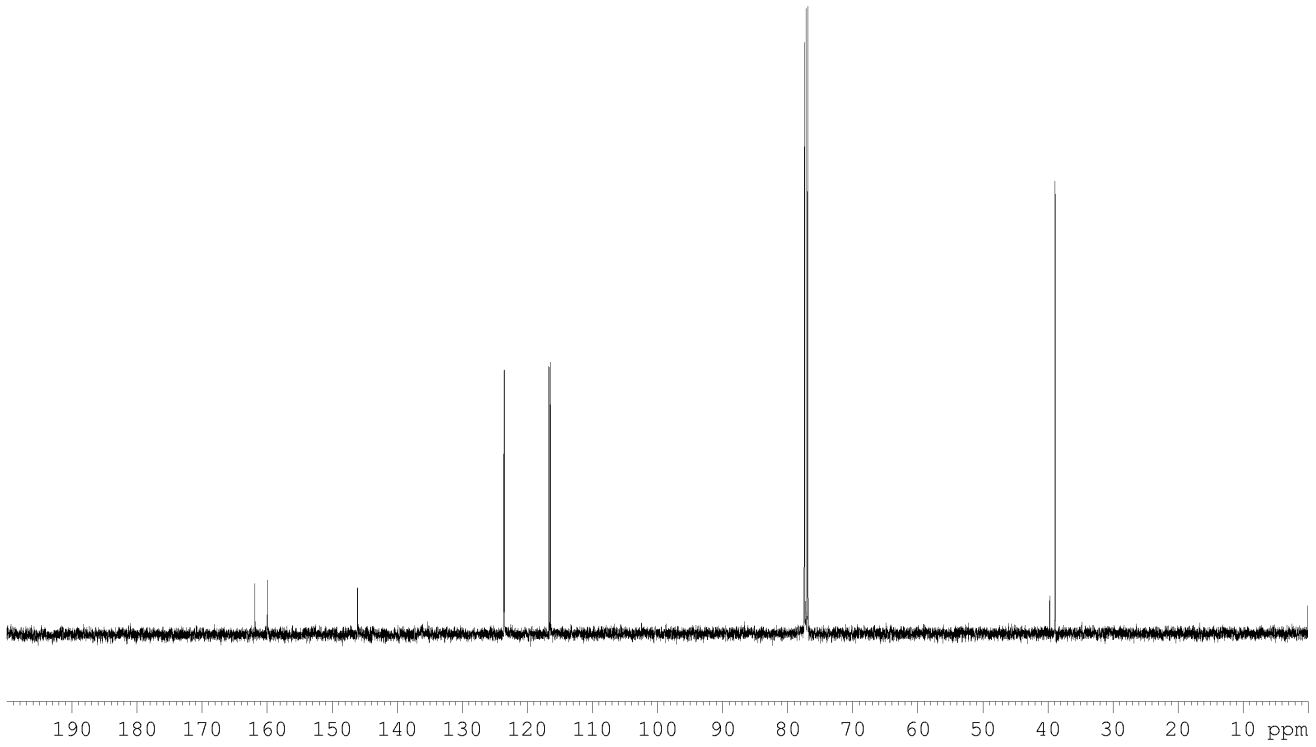


Figure A2.201 Infrared Spectrum


OSO2NMe2
F


9
8
7
6
5
4
3
2
1
0 ppm


OSO2NMe2
F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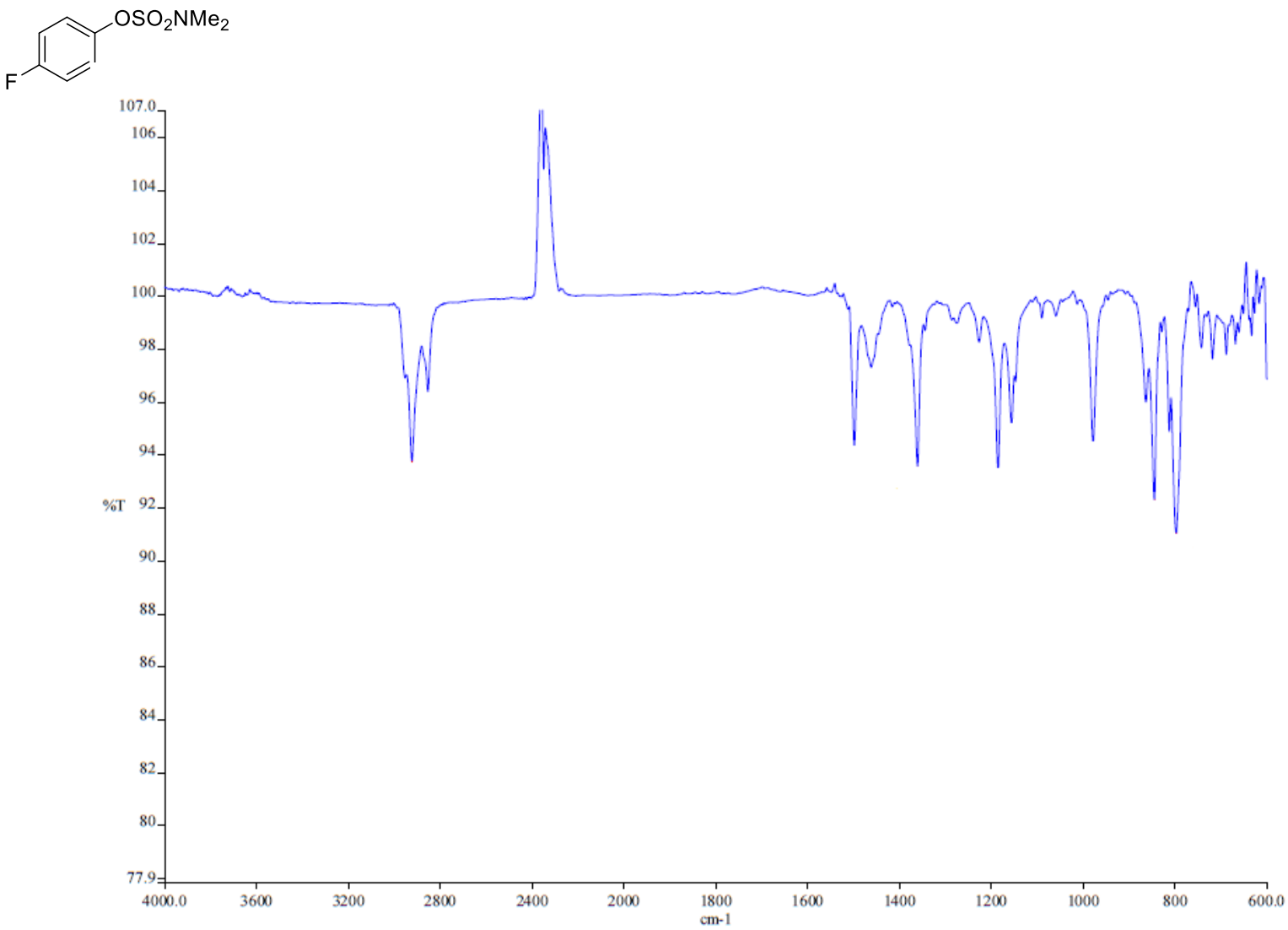
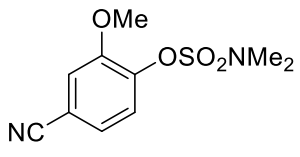
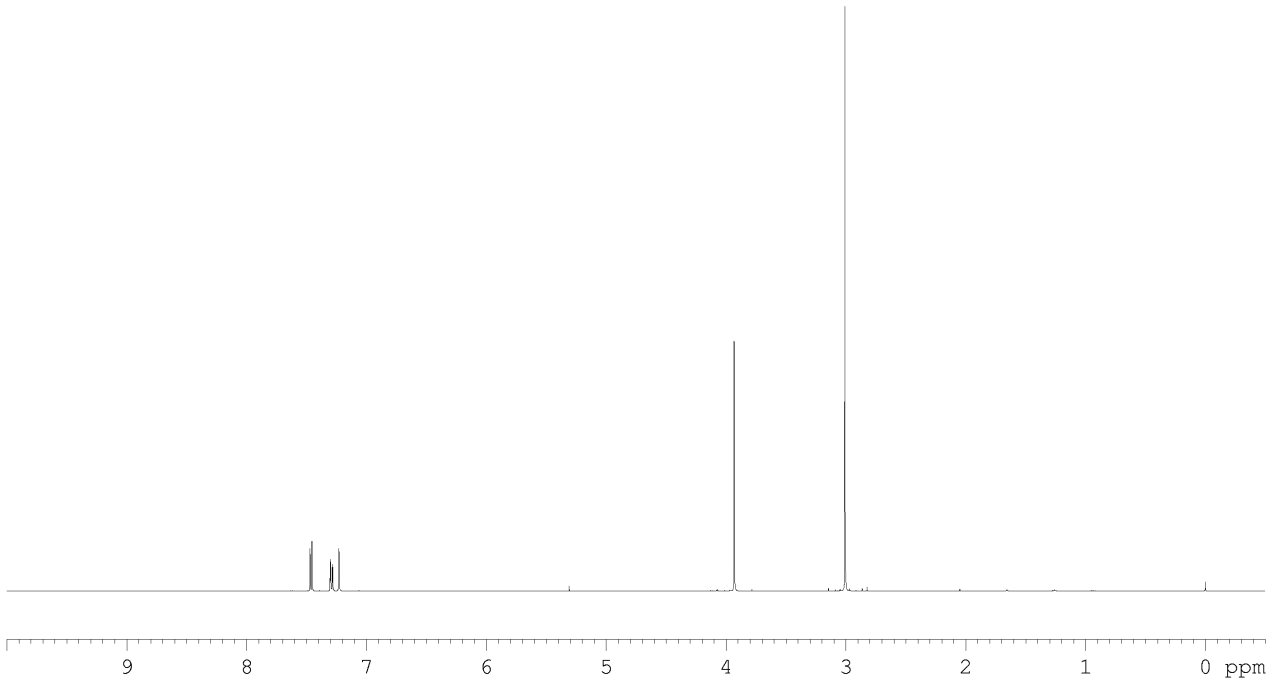


Figure A2.284 Infrared Spectrum


OMe
OSO2NMe2
NC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8
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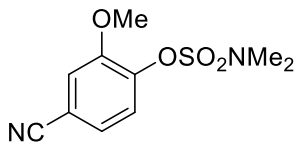
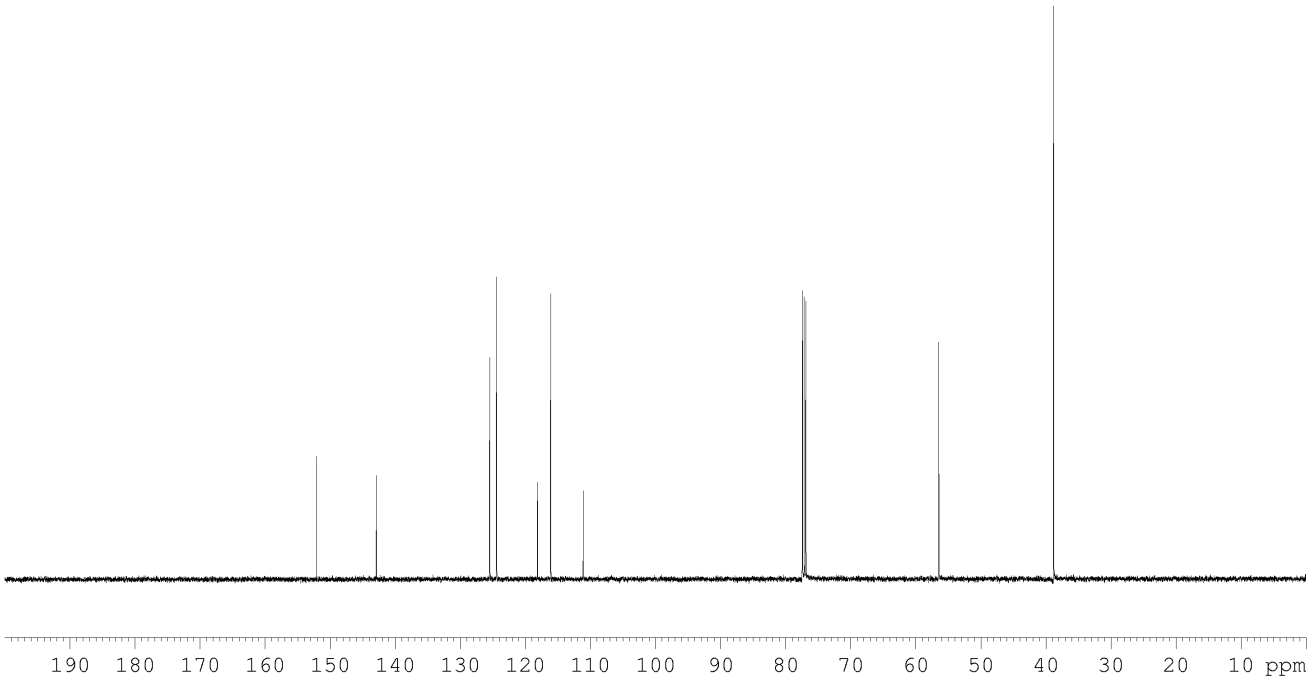
1
0 ppm


OMe
OSO2NMe2
NC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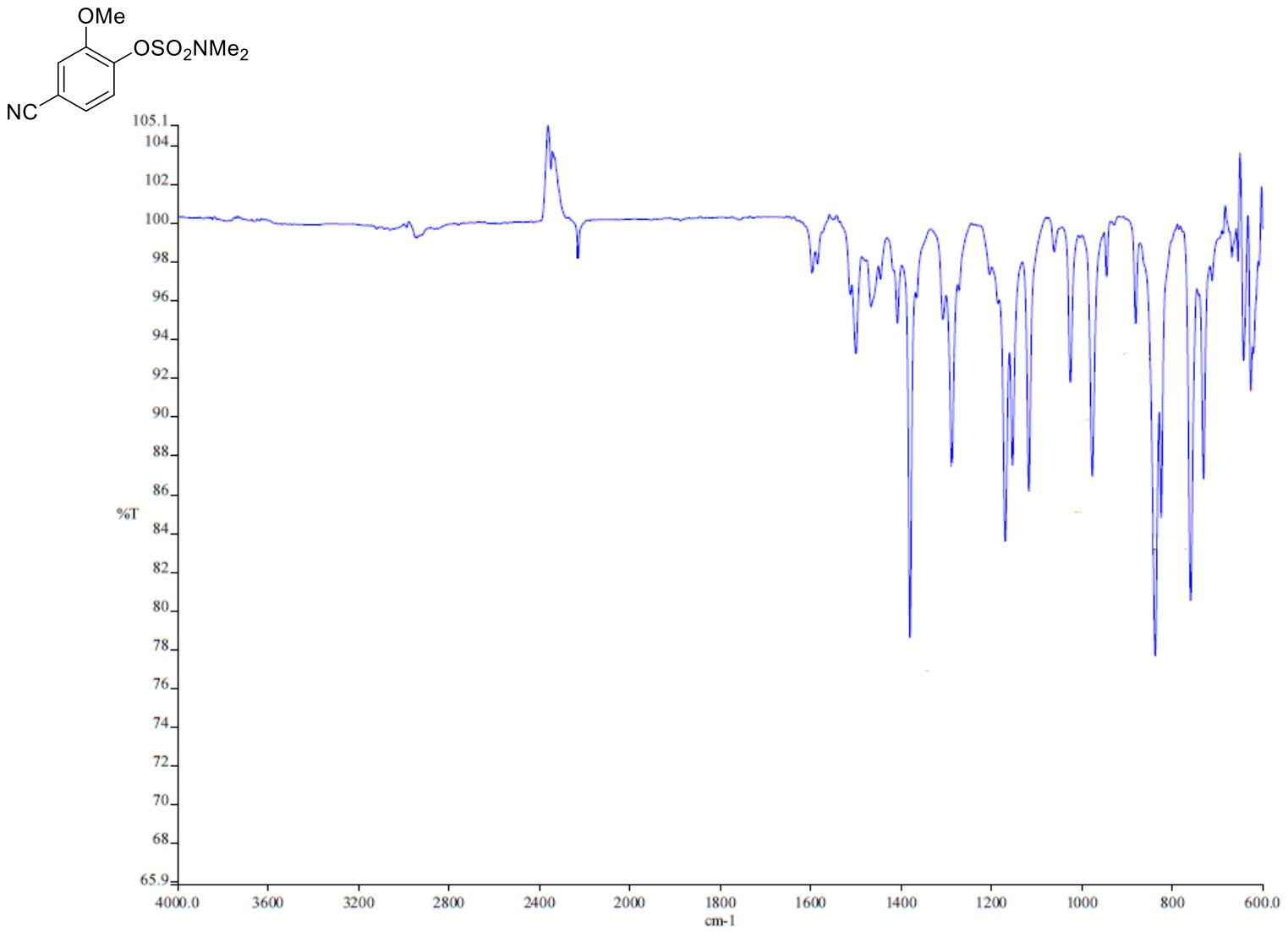
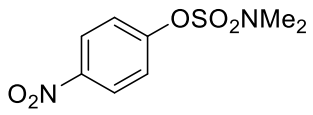


Figure A2.287 Infrared Spectrum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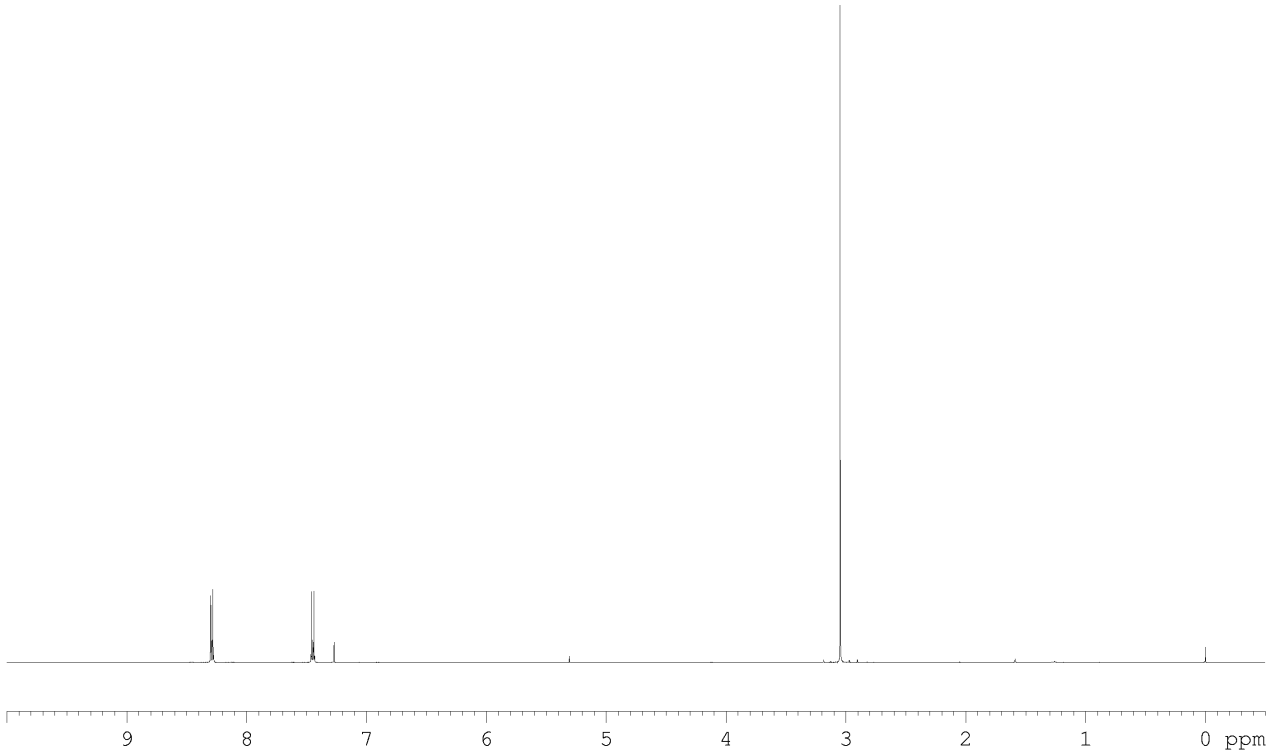
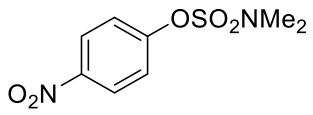
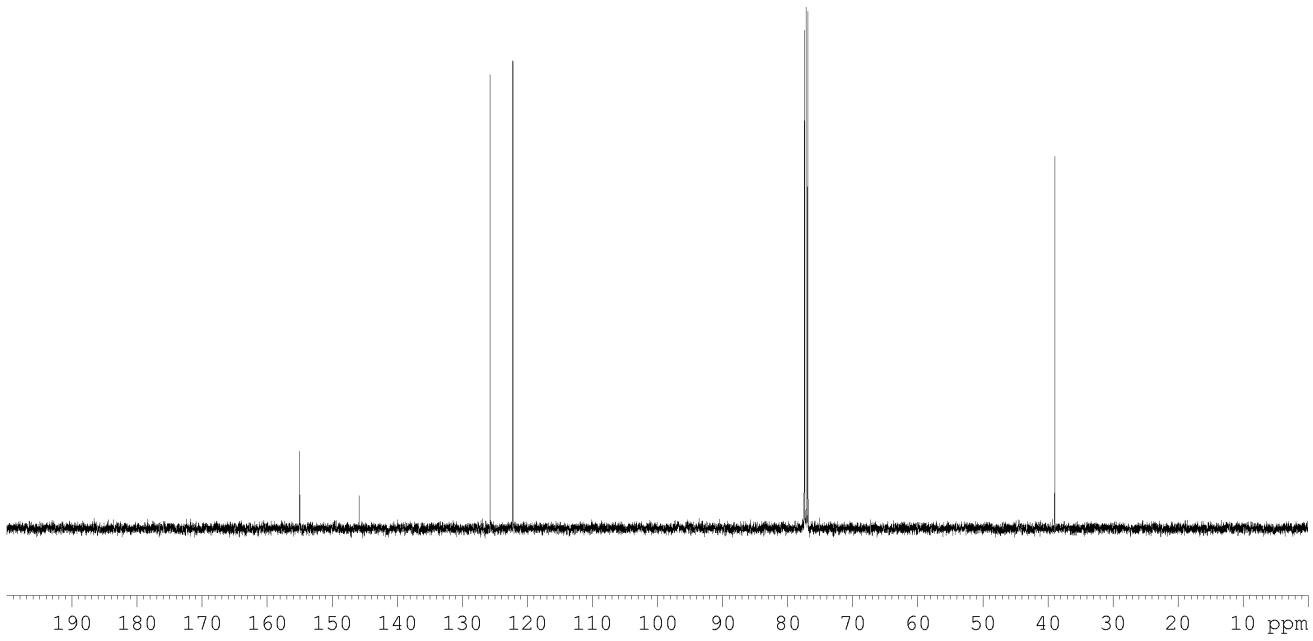
O2N


9
8
7
6
5
4
3
2
1
0 ppm


OSO2NMe2
O2N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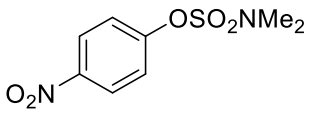
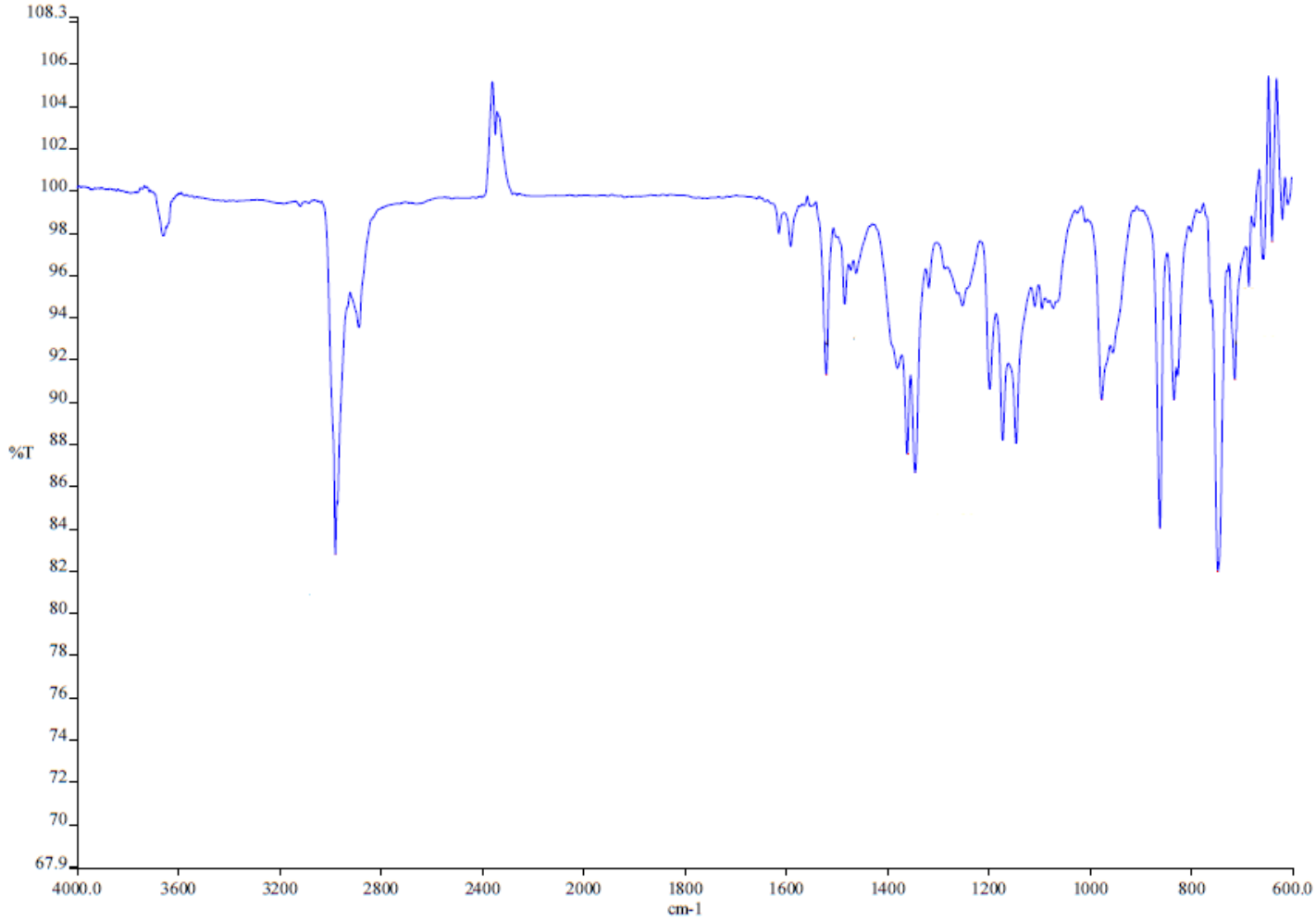

OSO2NMe2
O2N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90
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86
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80
78
76
74
72
70
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%T
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2800
2400
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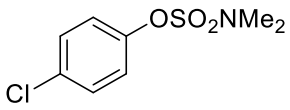
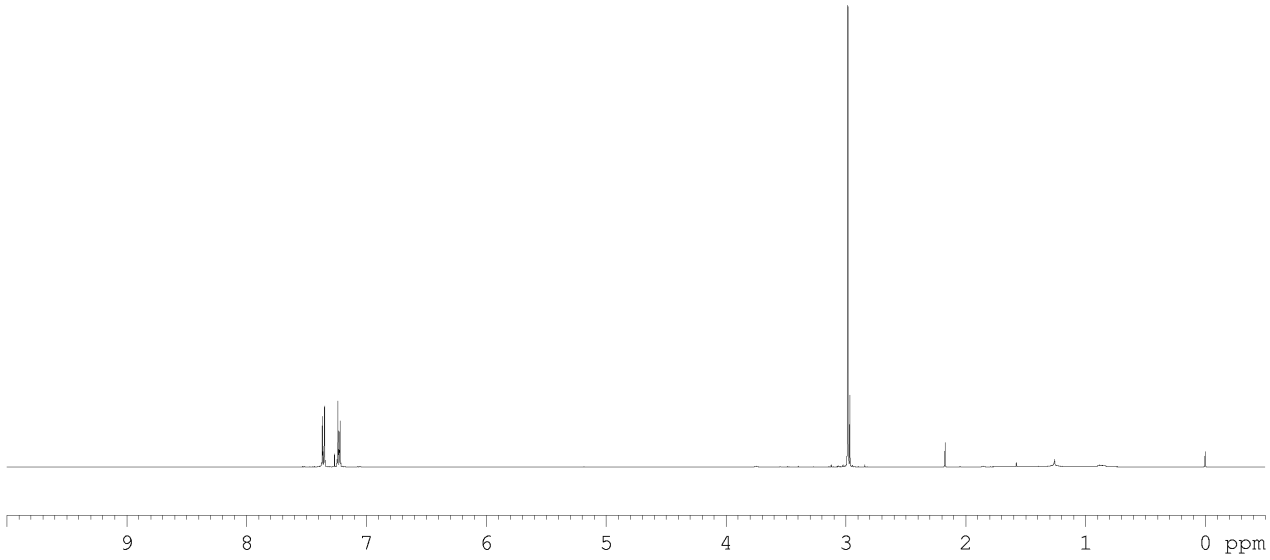
1600
1400
1200
1000
800
600.0
cm-1


OSO2NMe2
Cl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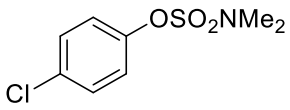
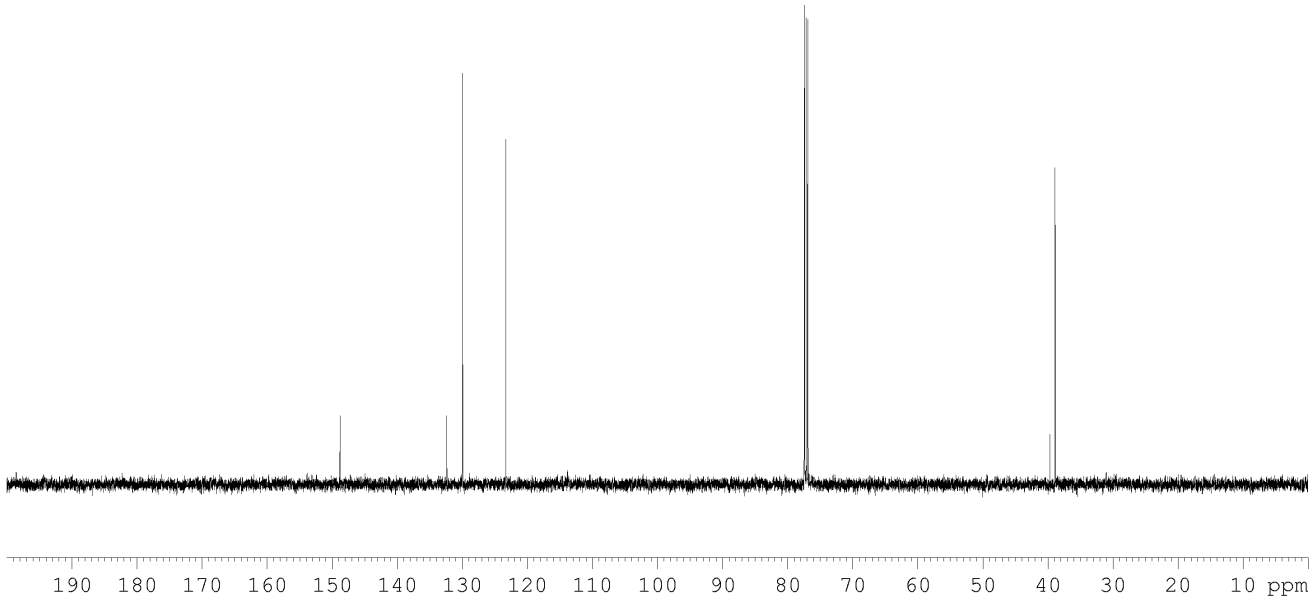
6
5
4
3
2
1
0 ppm


OSO2NMe2
Cl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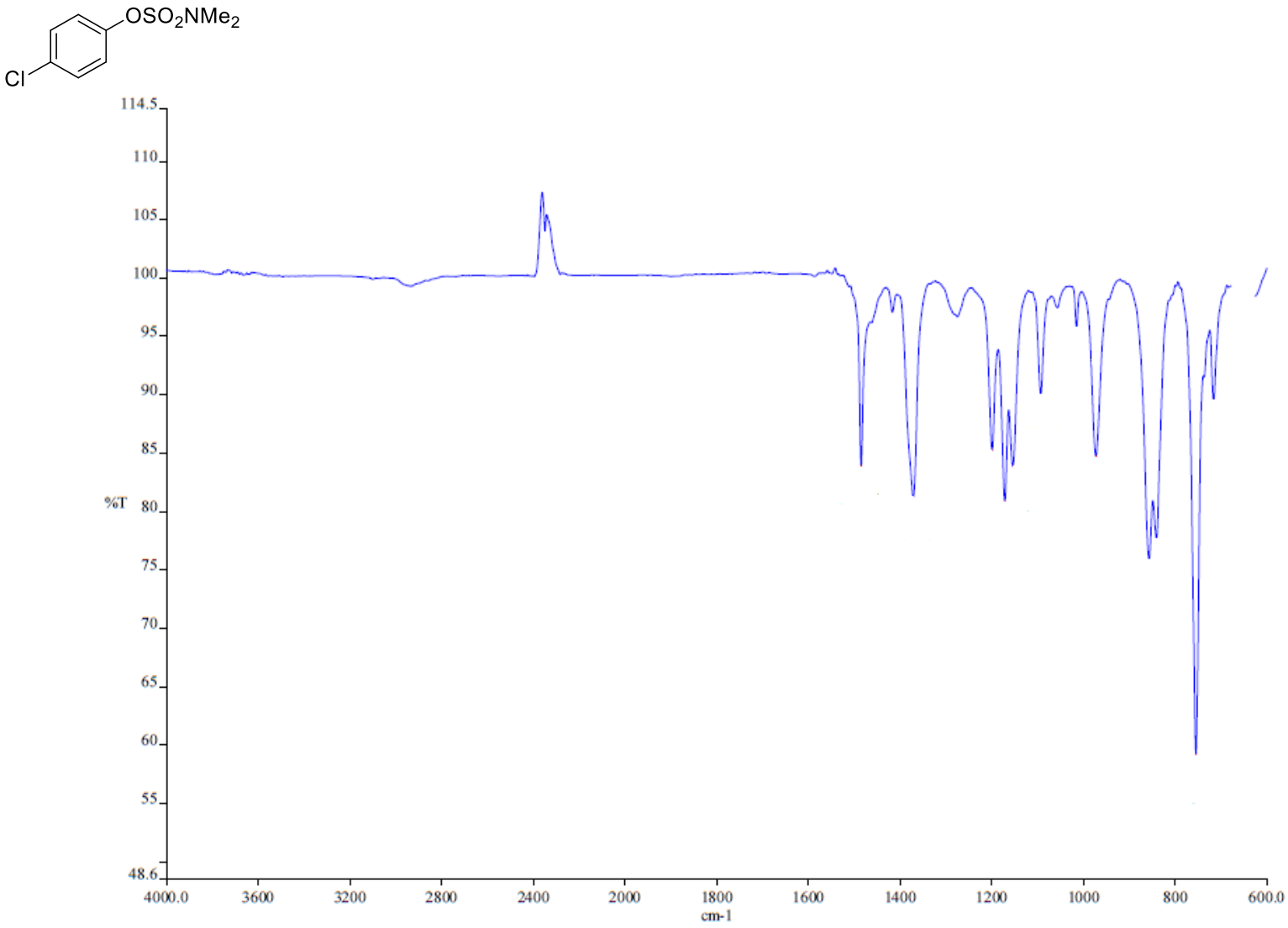
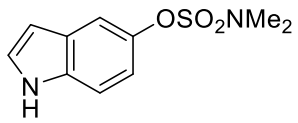
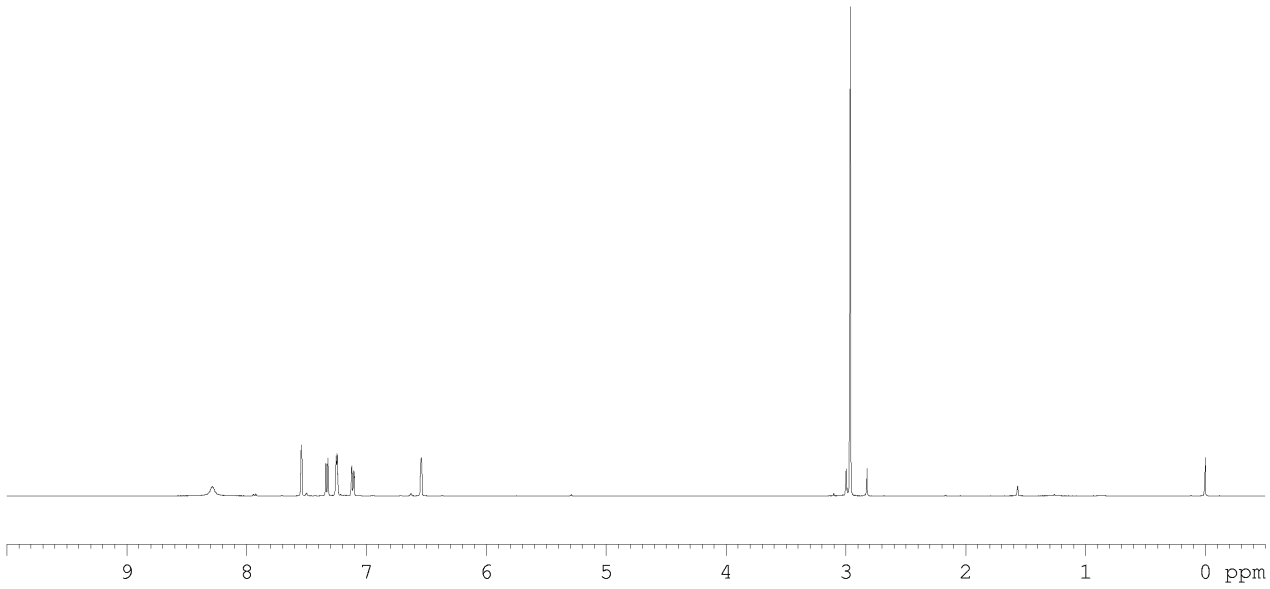


Figure A2.253 Infrared Spectrum


OSO2NMe2
N
H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4
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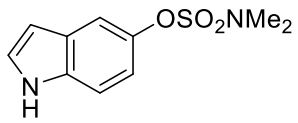
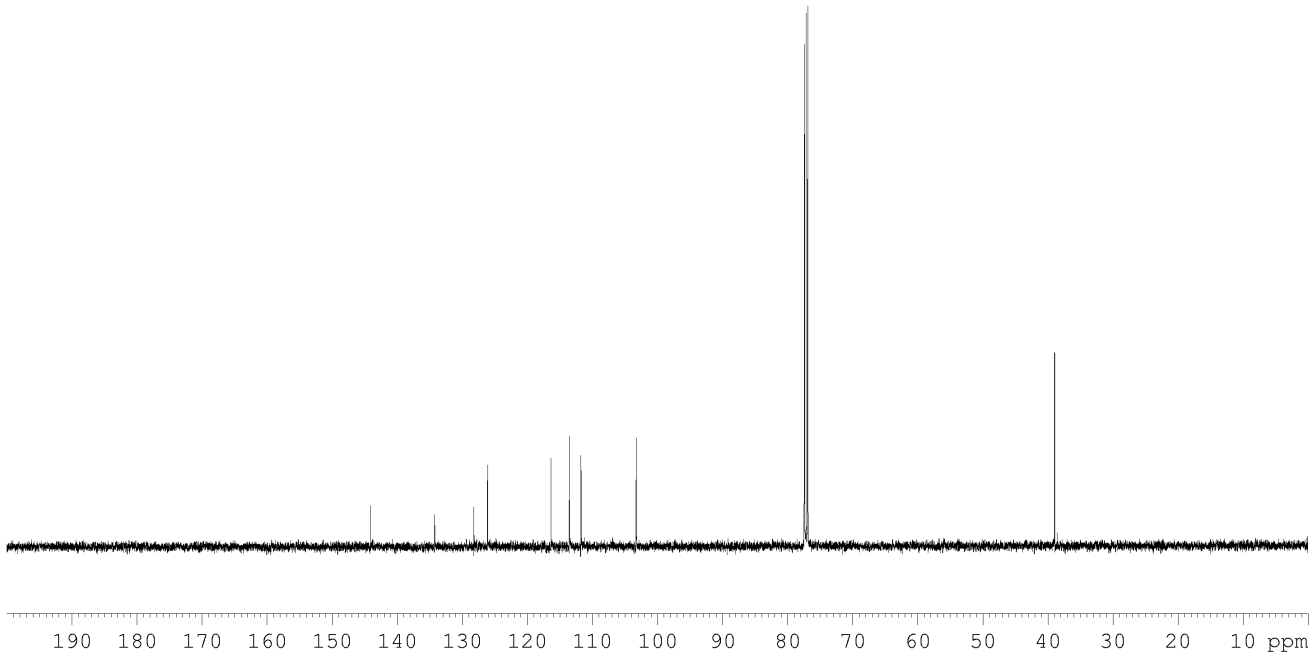
2
1
0 ppm


OSO2NMe2
N
H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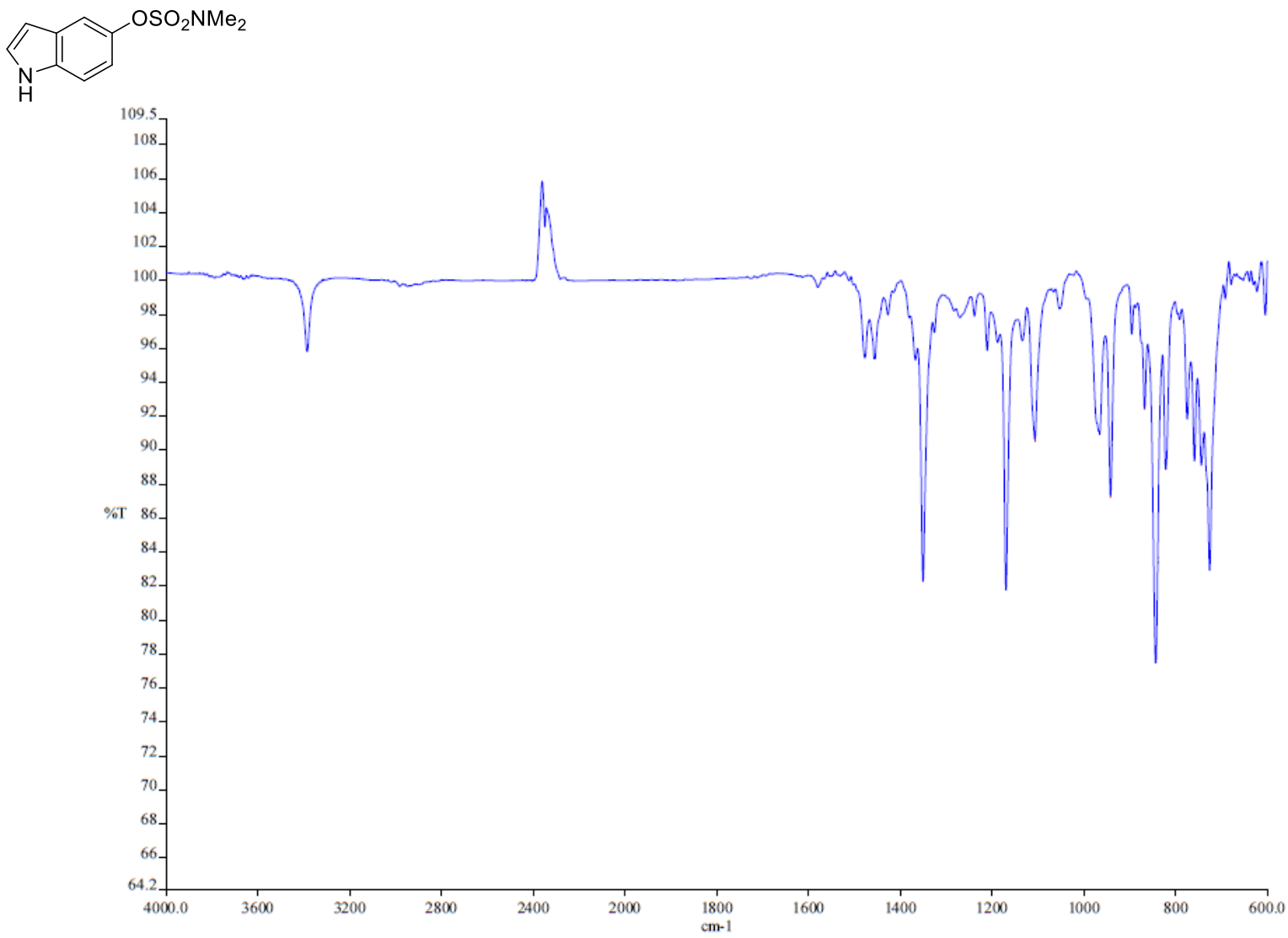
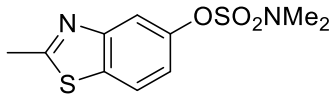
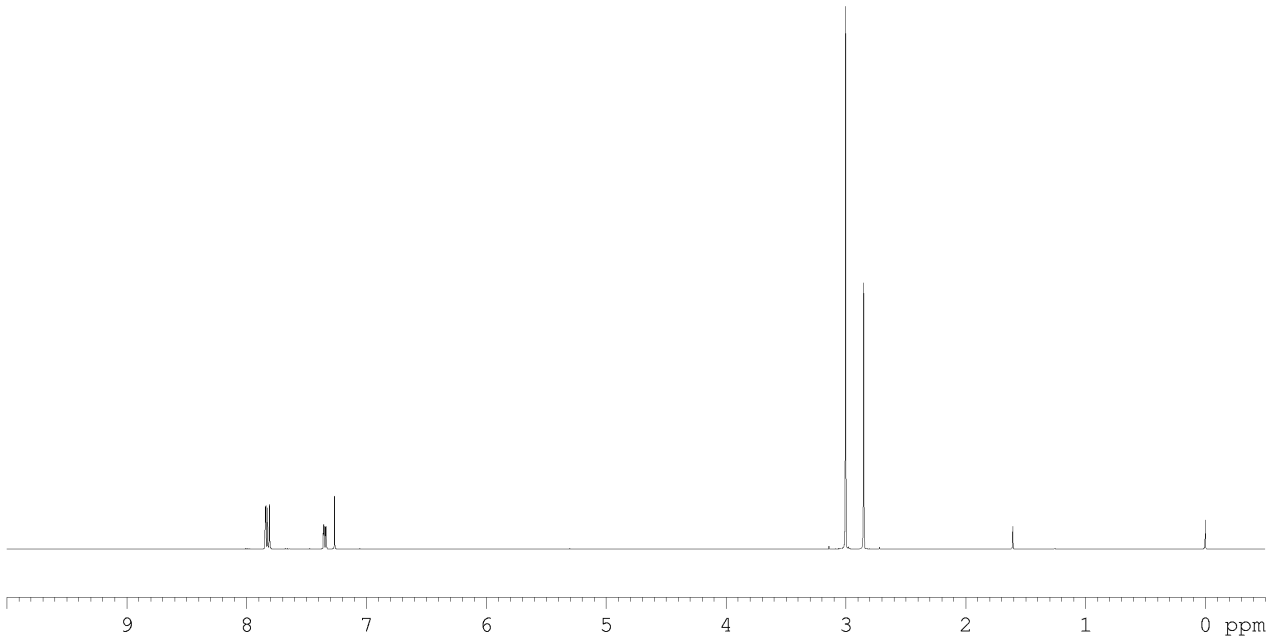
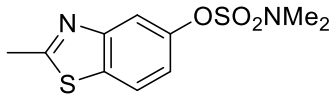


Figure A2.290 Infrared Spectrum

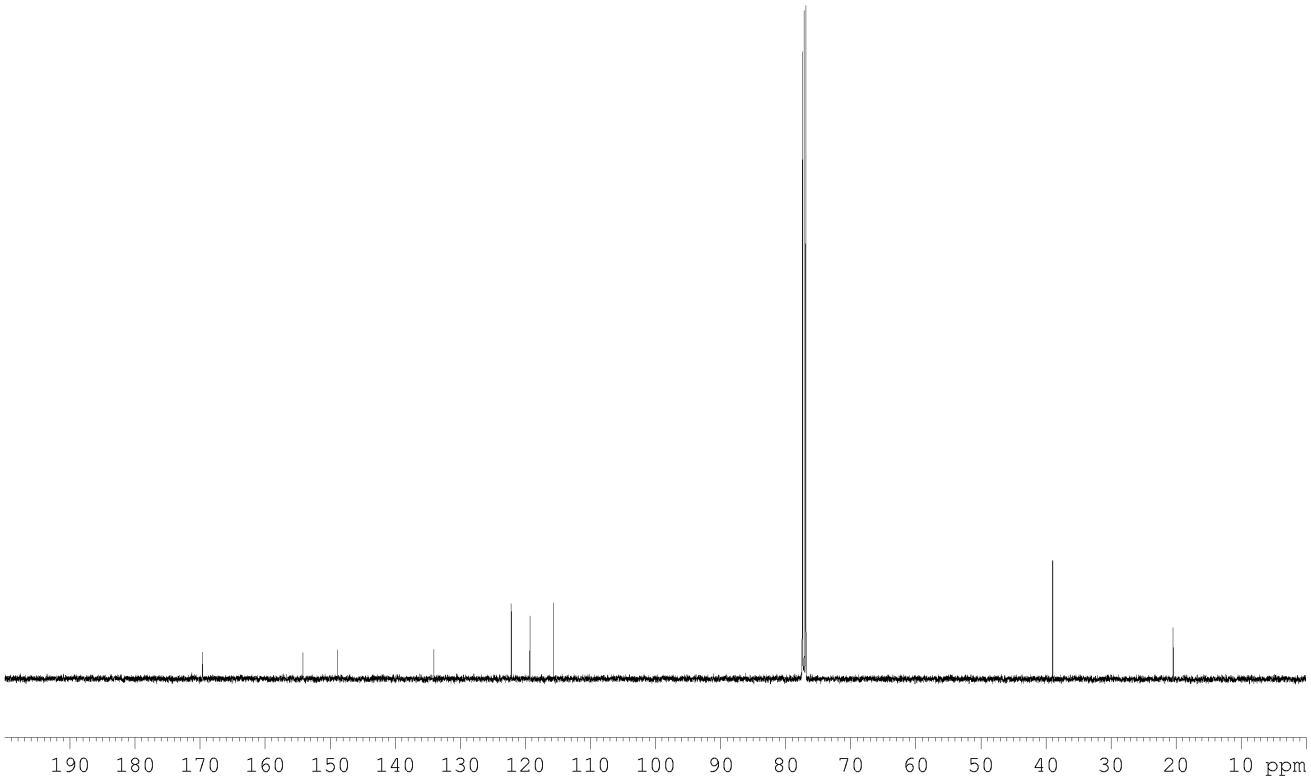


600




N
S
OSO2NMe2

601


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

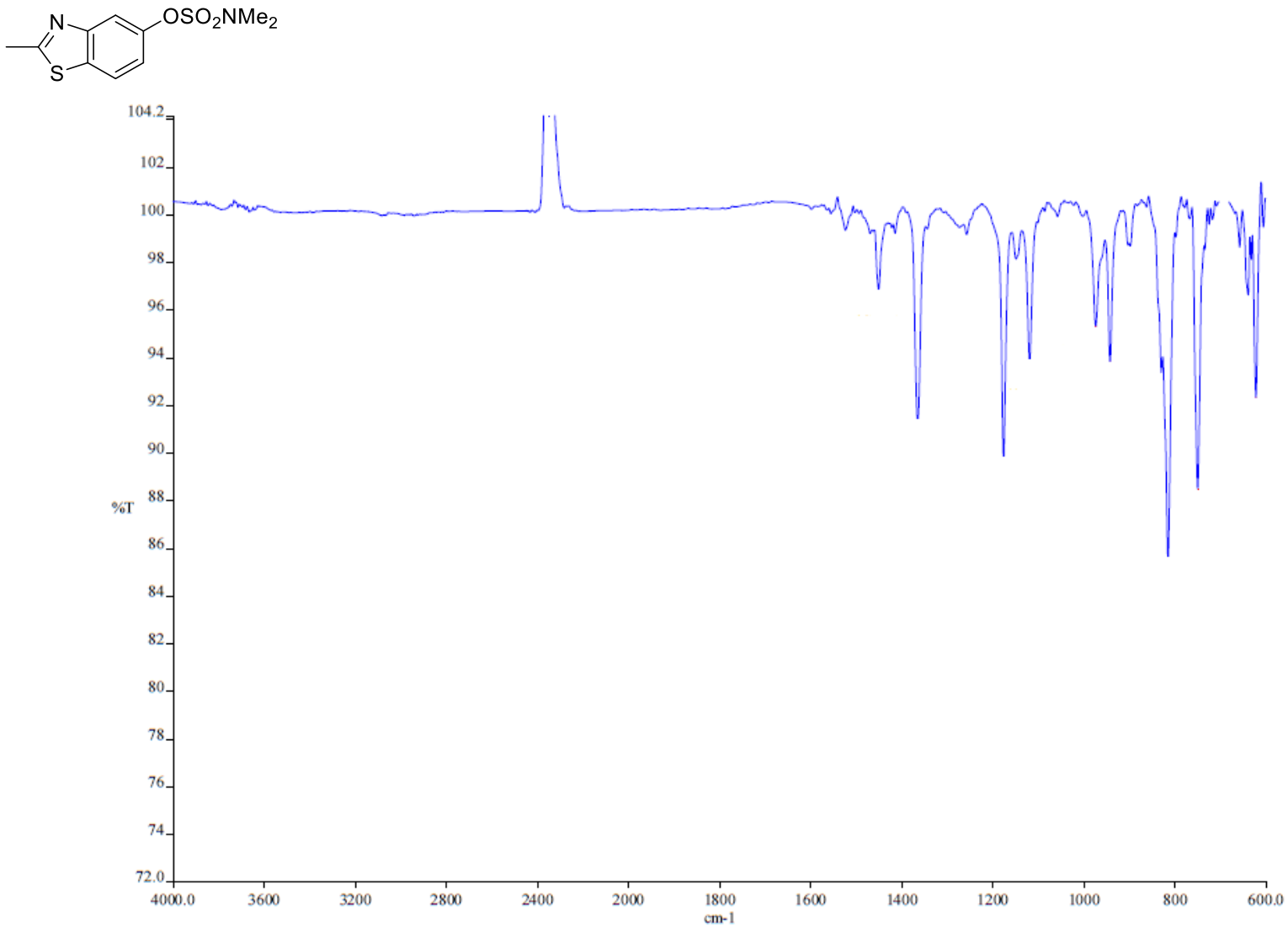
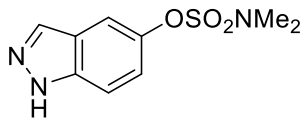
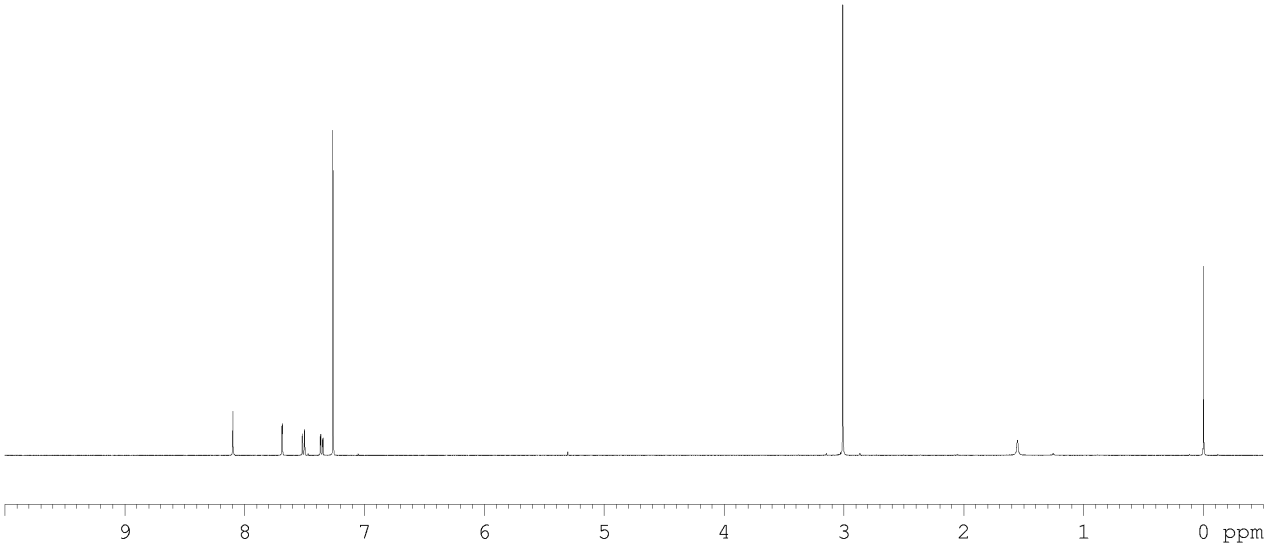
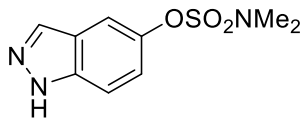


Figure A2.299 Infrared Spectrum

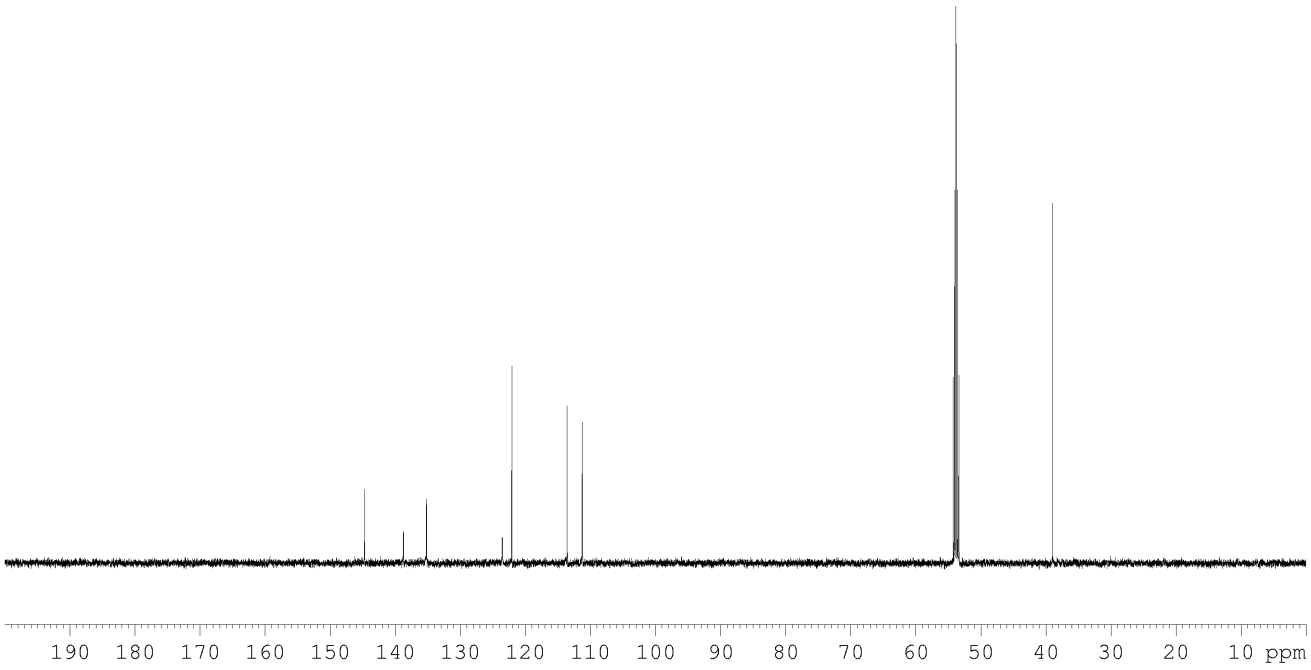


603




OSO2NMe2
N
N
H

604


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

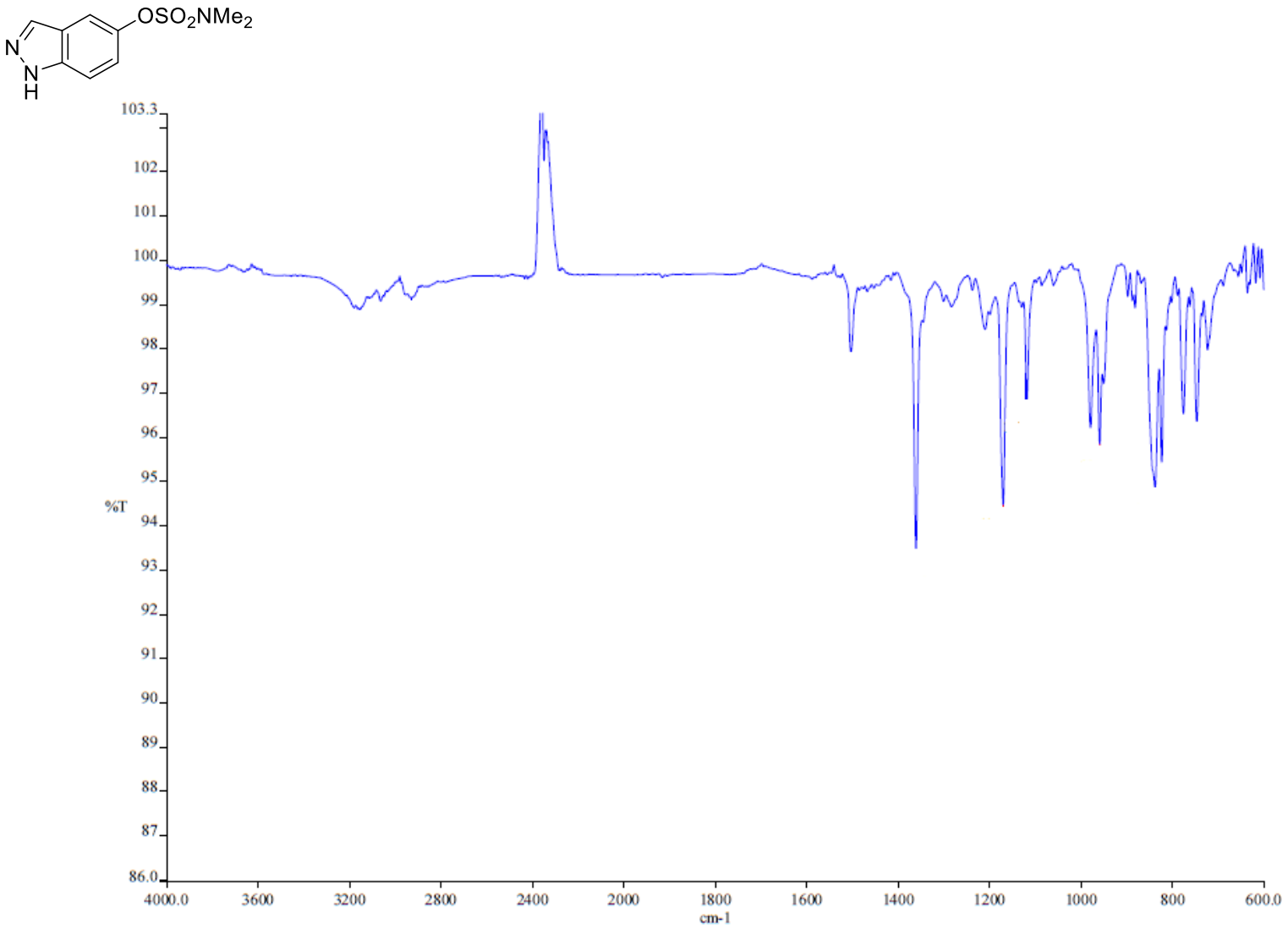
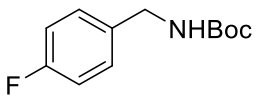
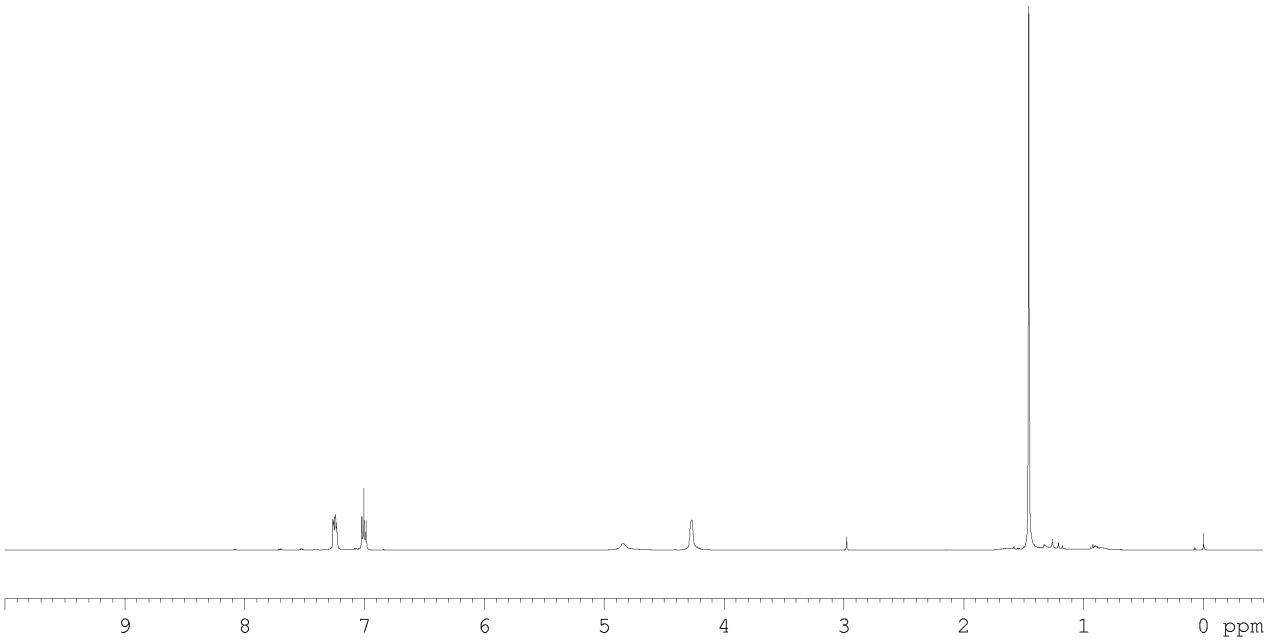
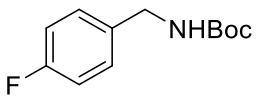


Figure A2.302 Infrared Spectrum

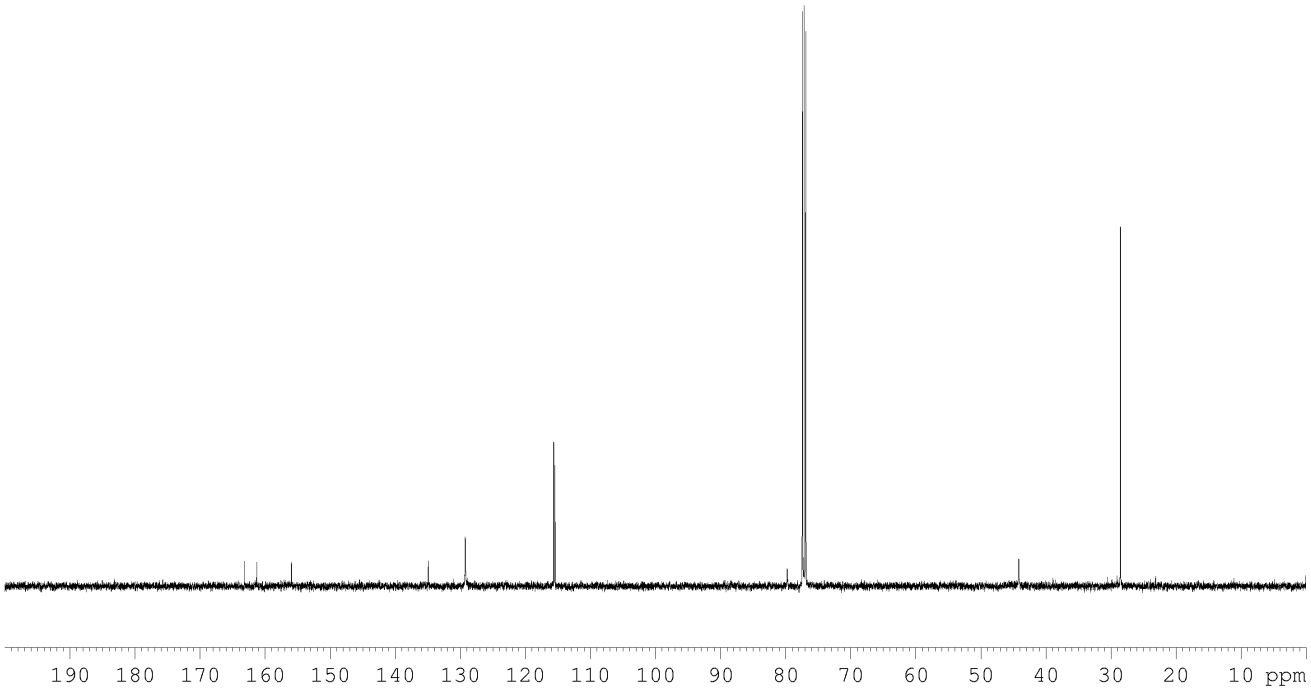


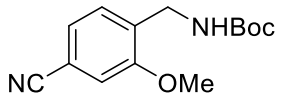
909



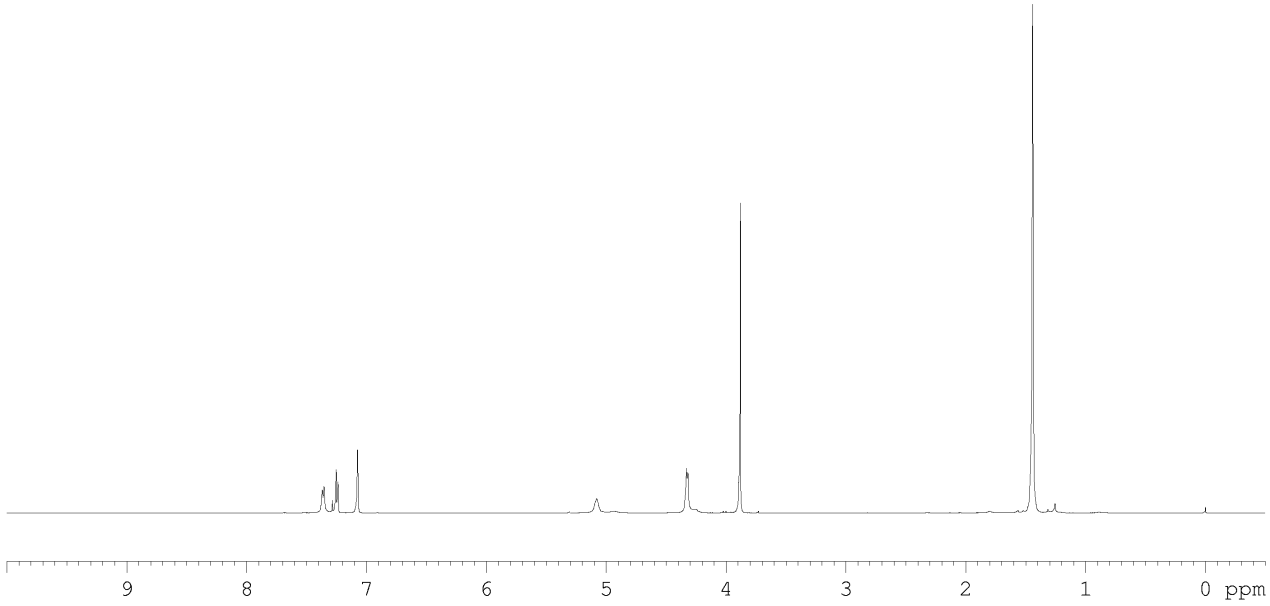

NHBoc
F

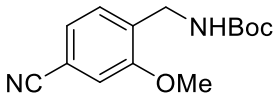
607


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

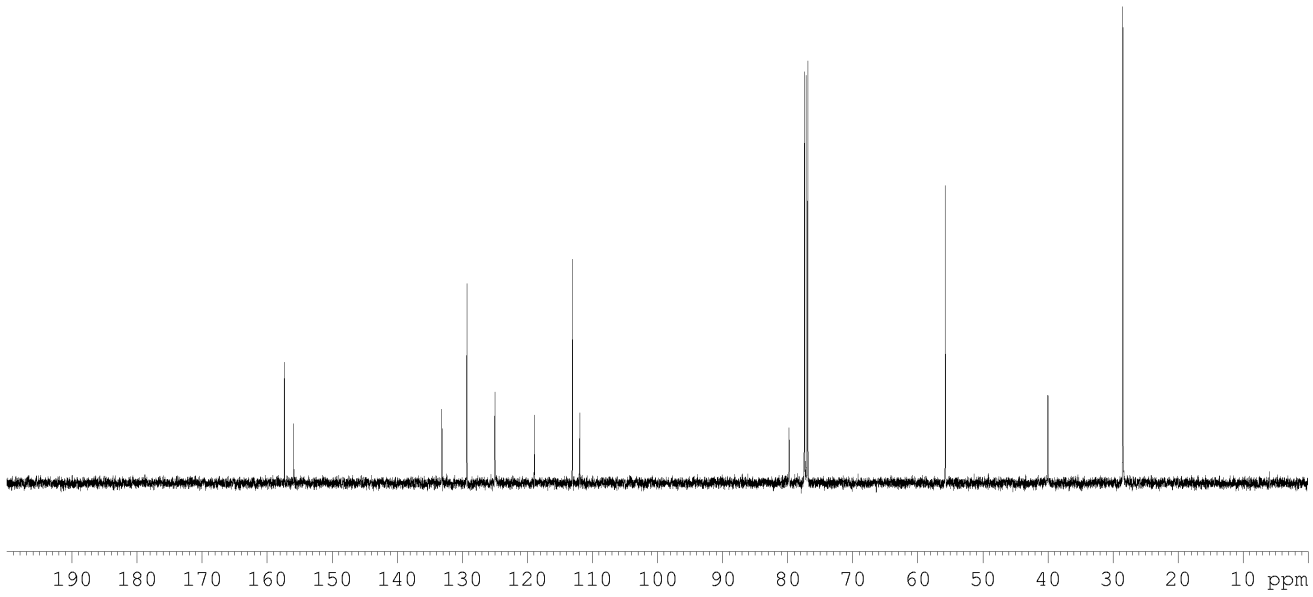


809




NHBoc
NC
OMe

609


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

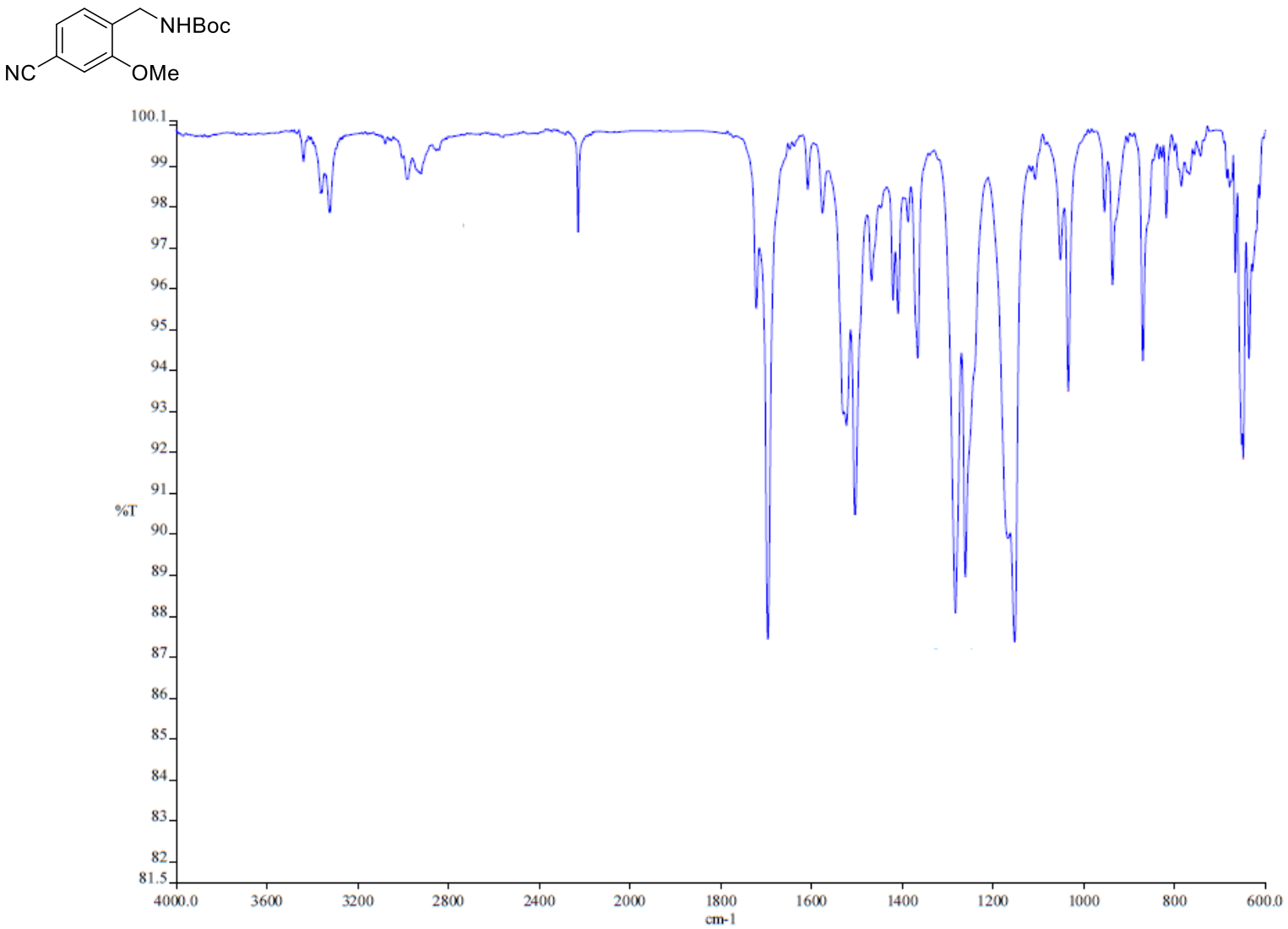
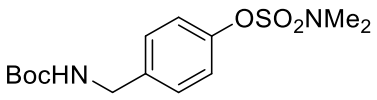
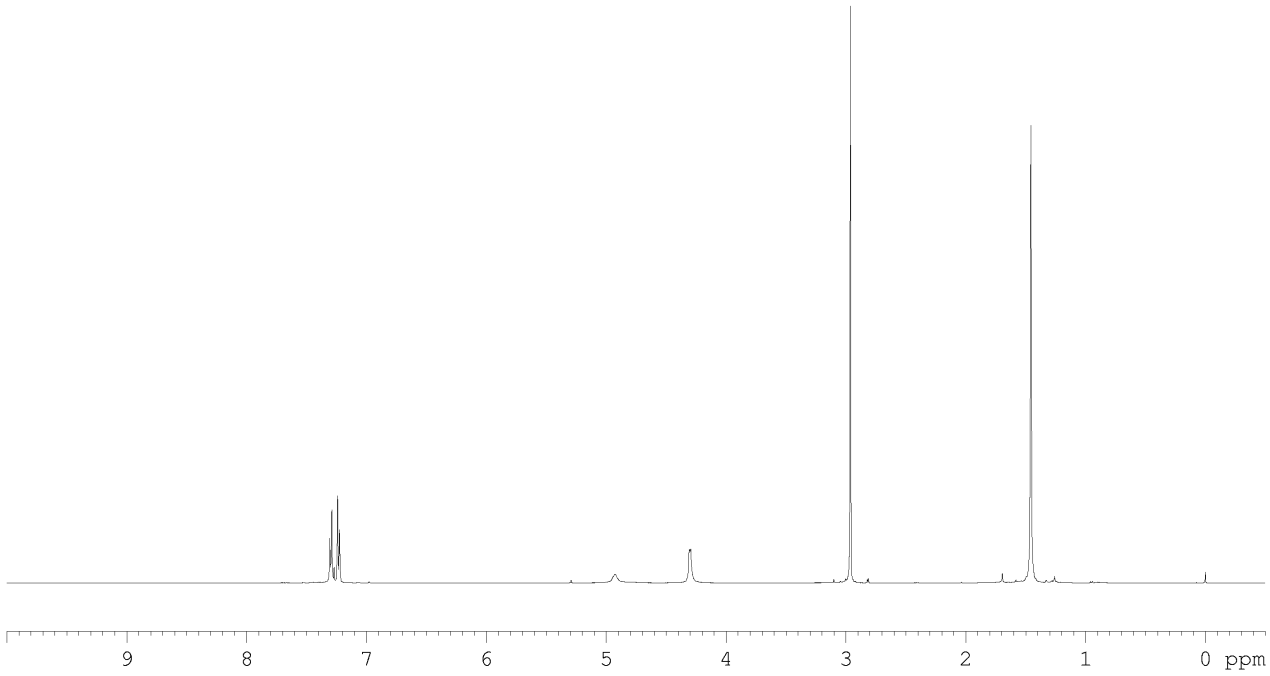
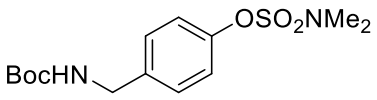


Figure A2.307 Infrared Spectrum

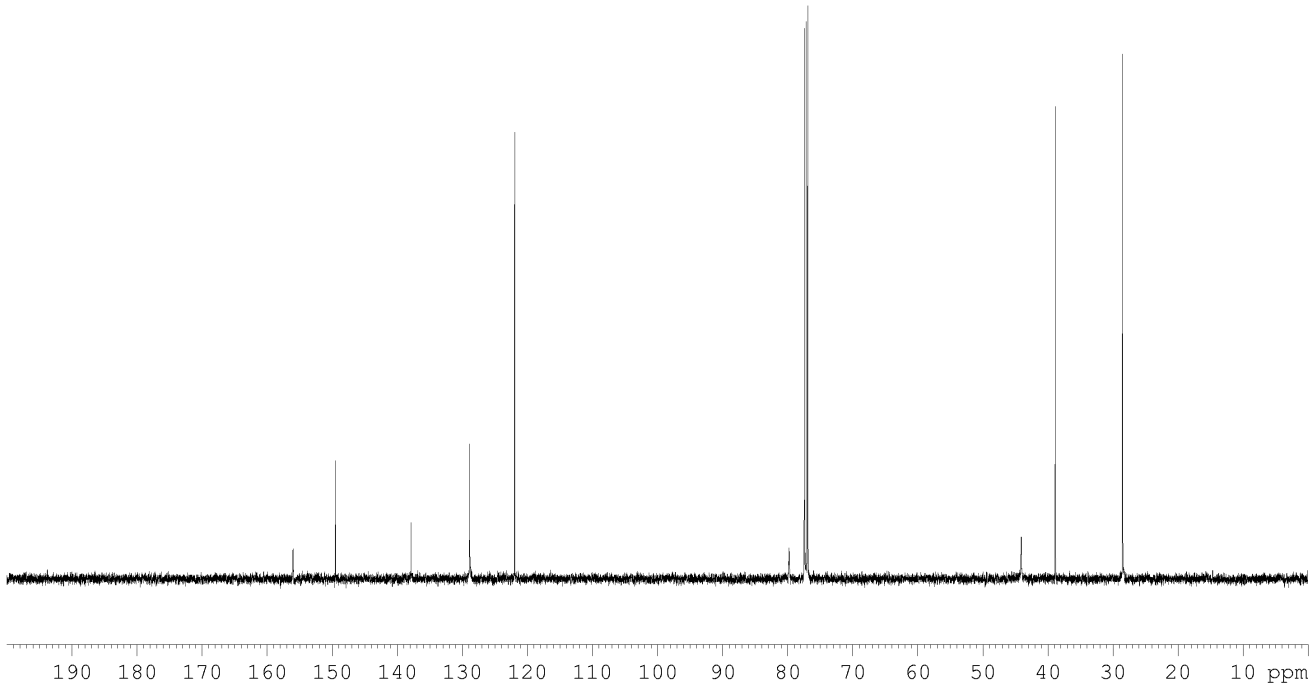




611


OSO2NMe2
BocHN

612


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

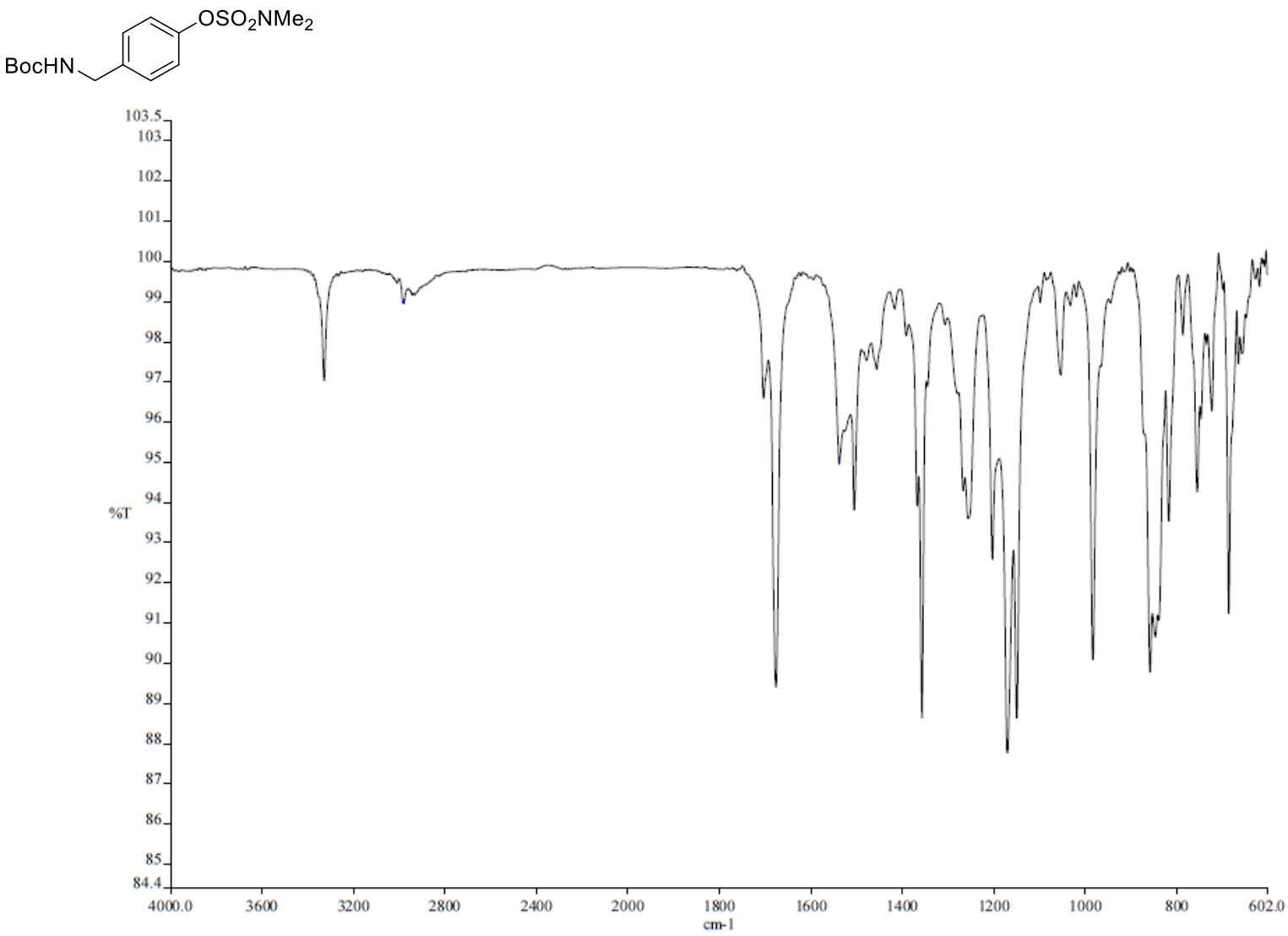
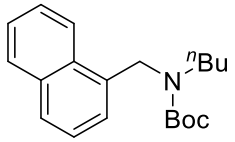
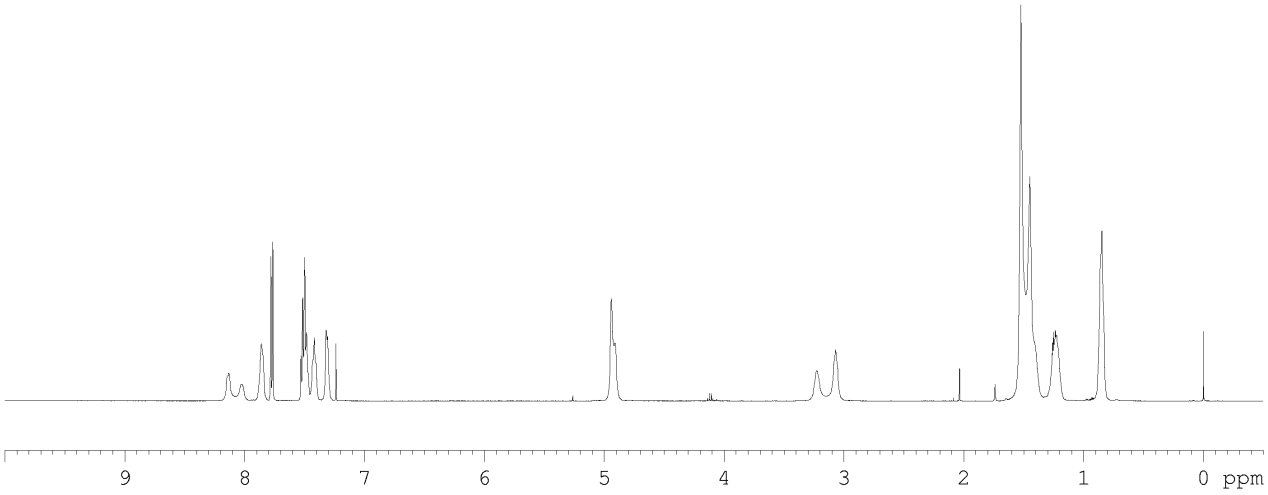
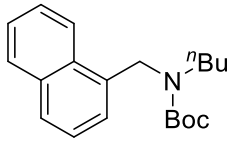
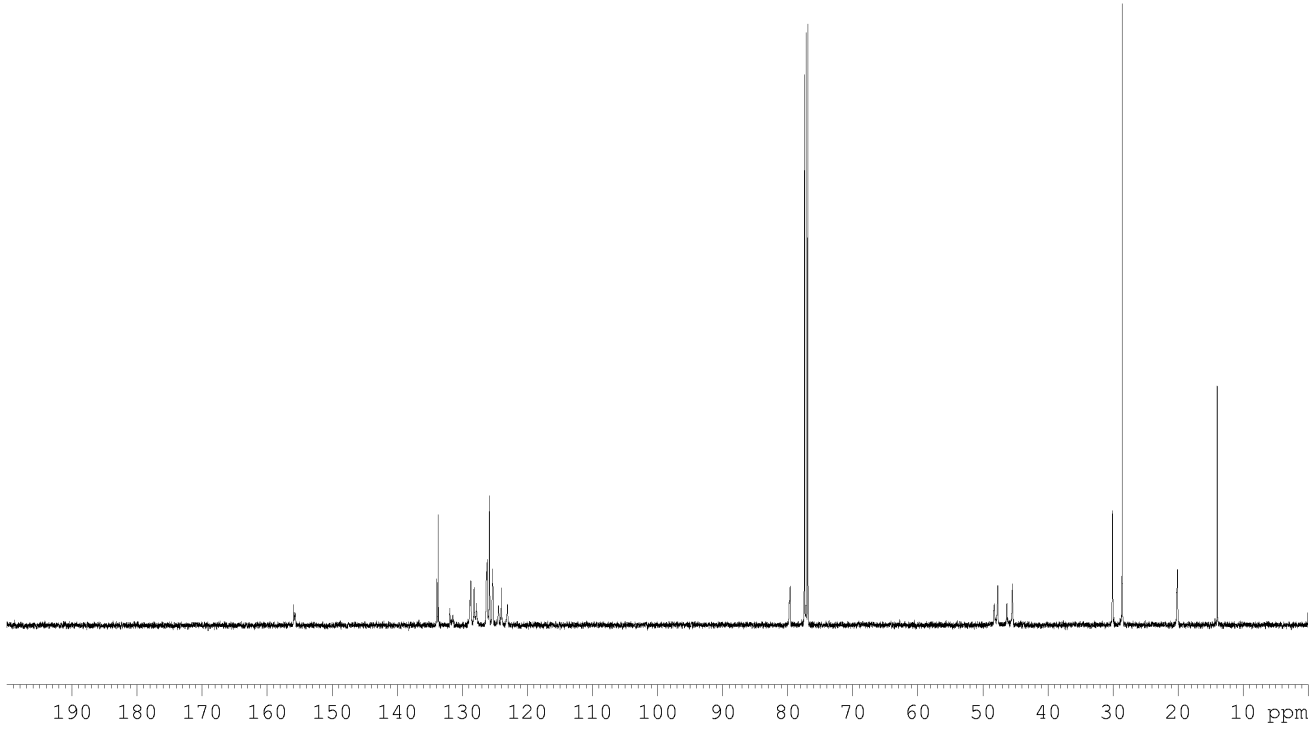


Figure A2.310 Infrared Spectrum


nBu
N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


nBu
N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

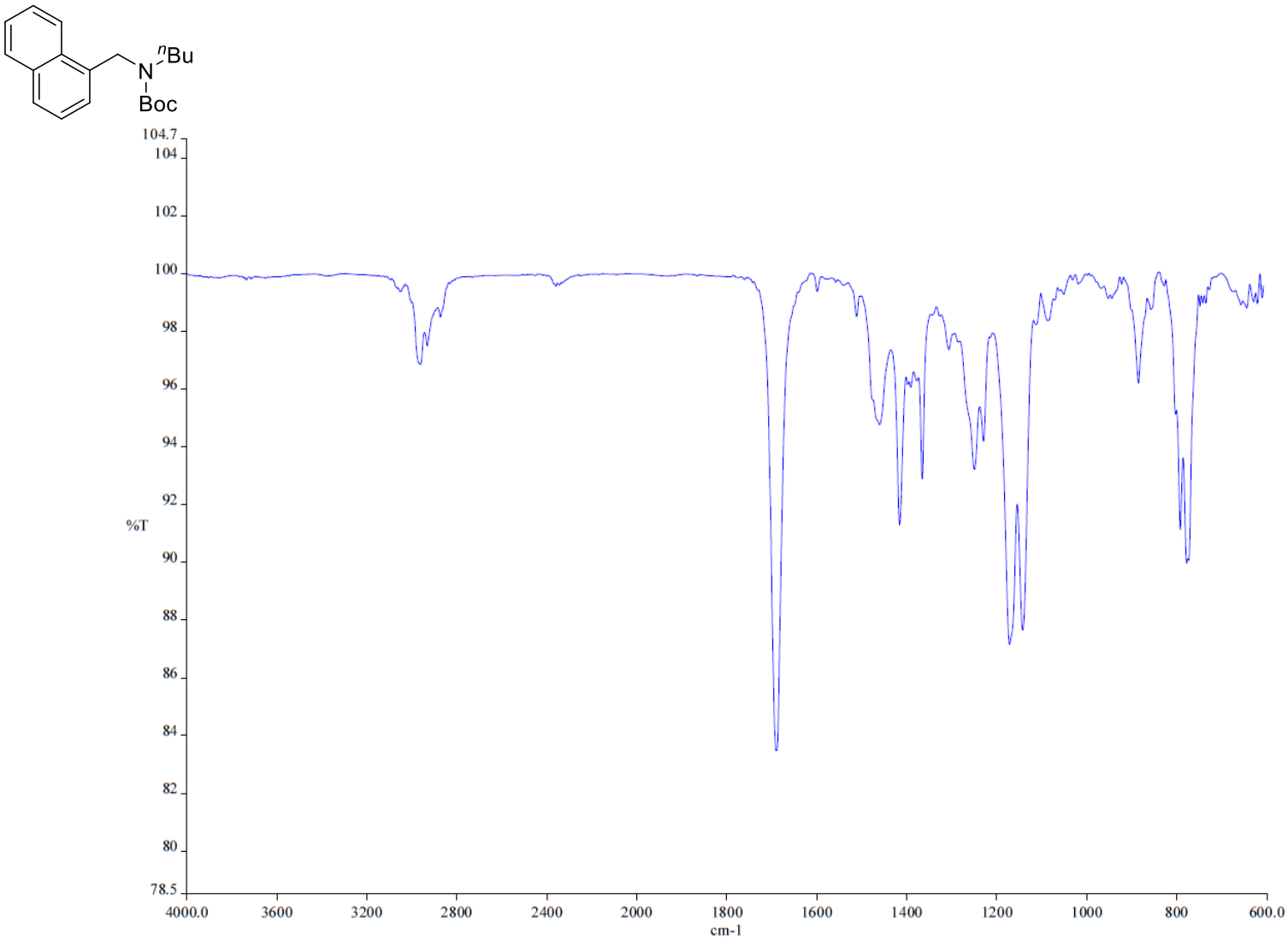
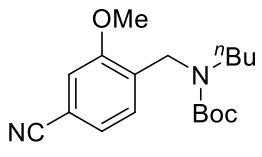
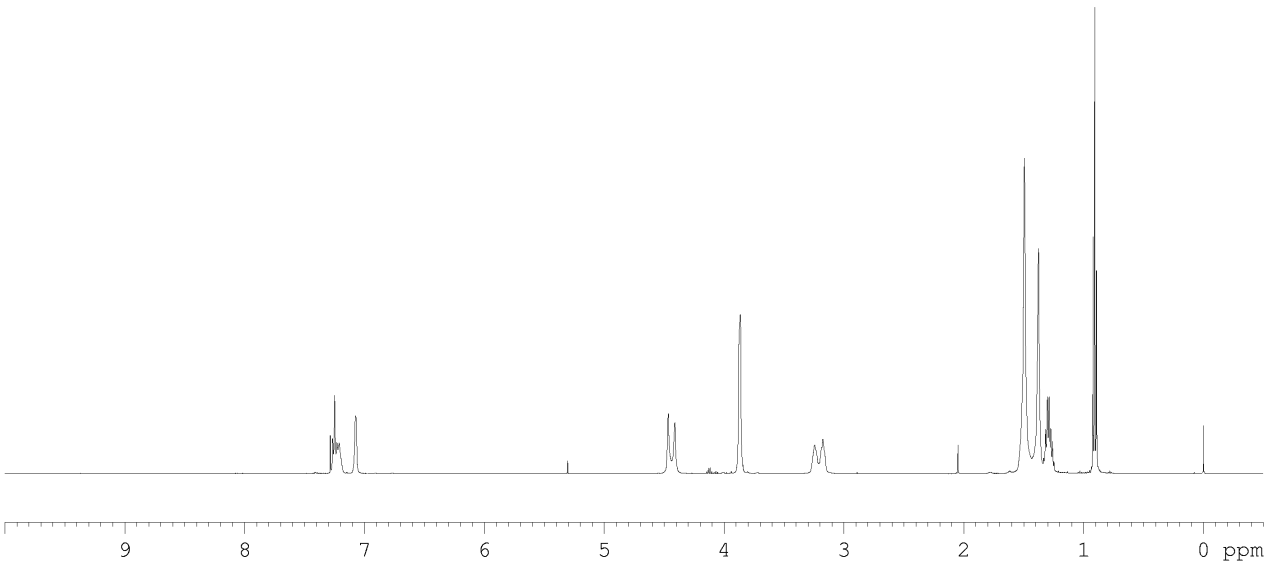
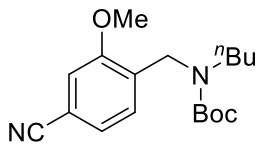
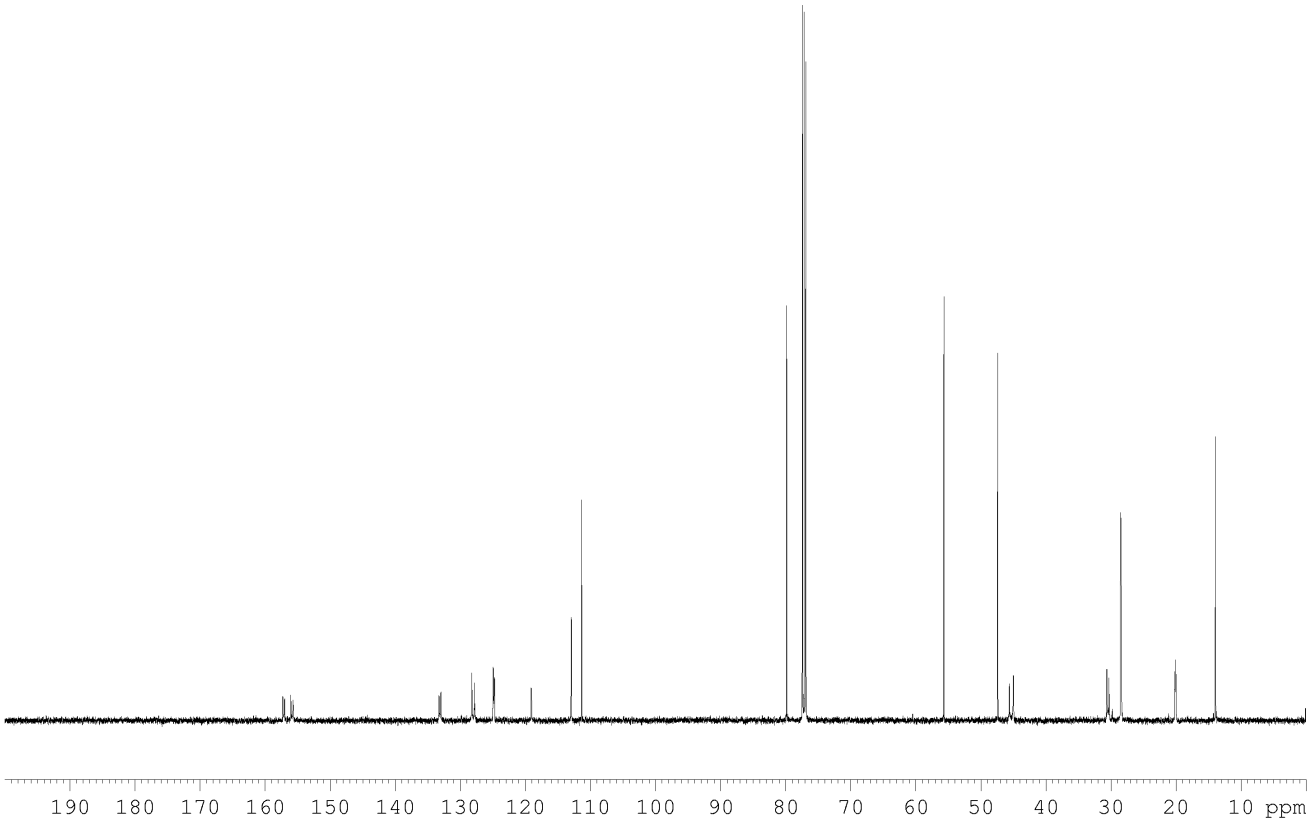


Figure A2.313 Infrared Spectrum


OMe
nBu
N
Boc
NC


9
8
7
6
5
4
3
2
1
0 ppm


OMe
nBu
N
Boc
NC


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

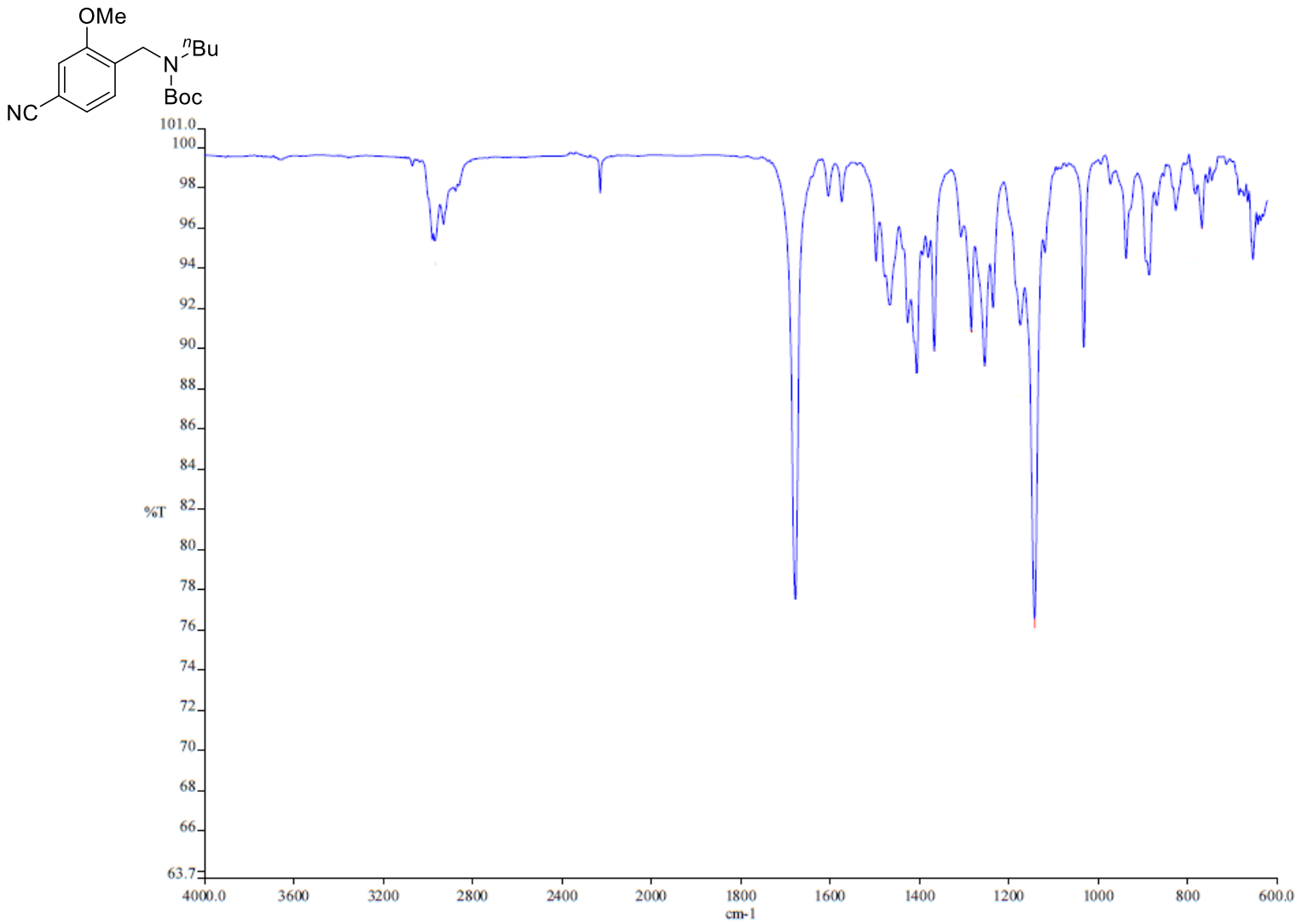
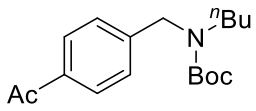
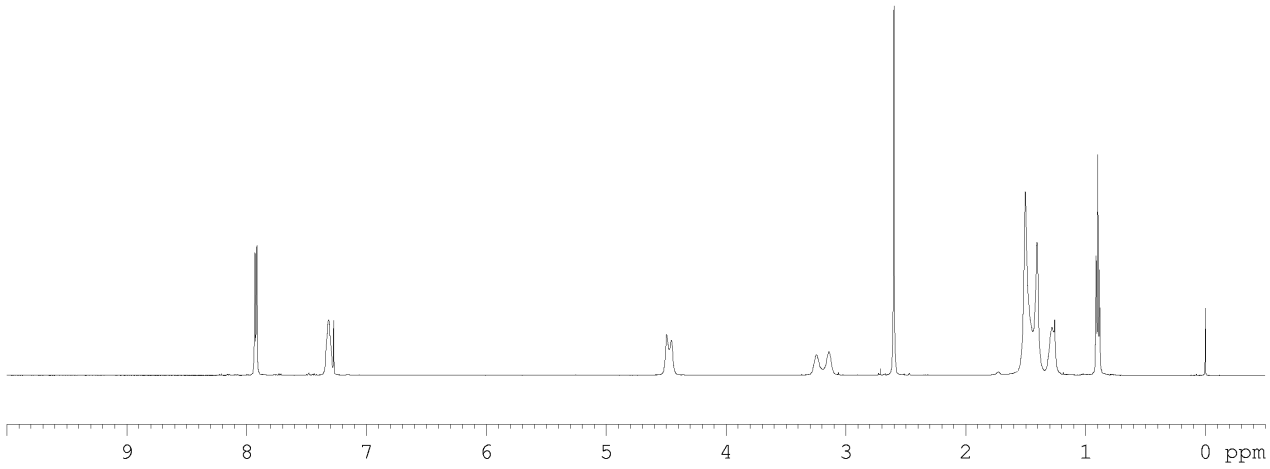
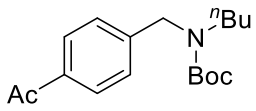


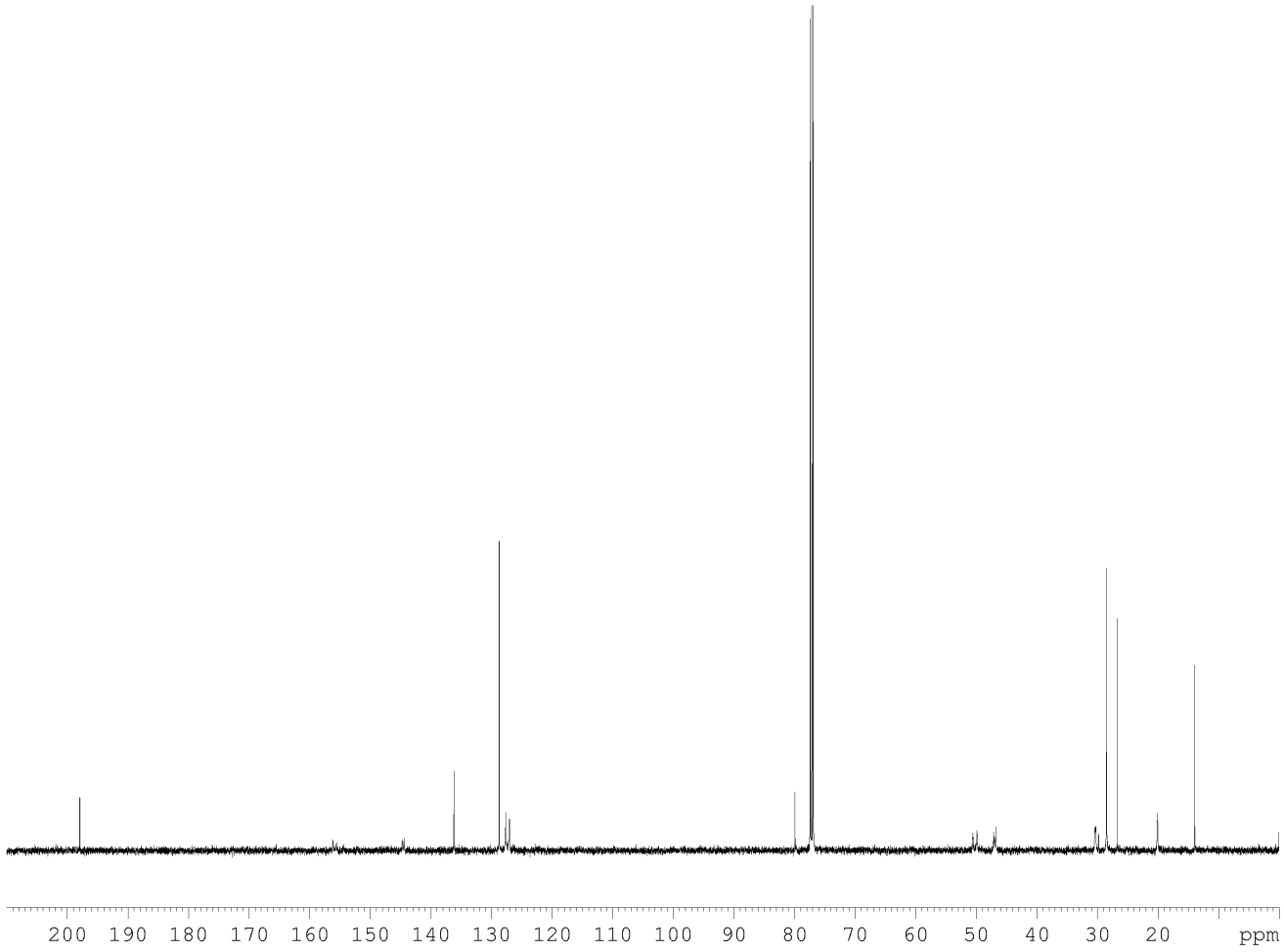
Figure A2.316 Infrared Spectrum



620




nBu
N
Boc
Ac


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

621

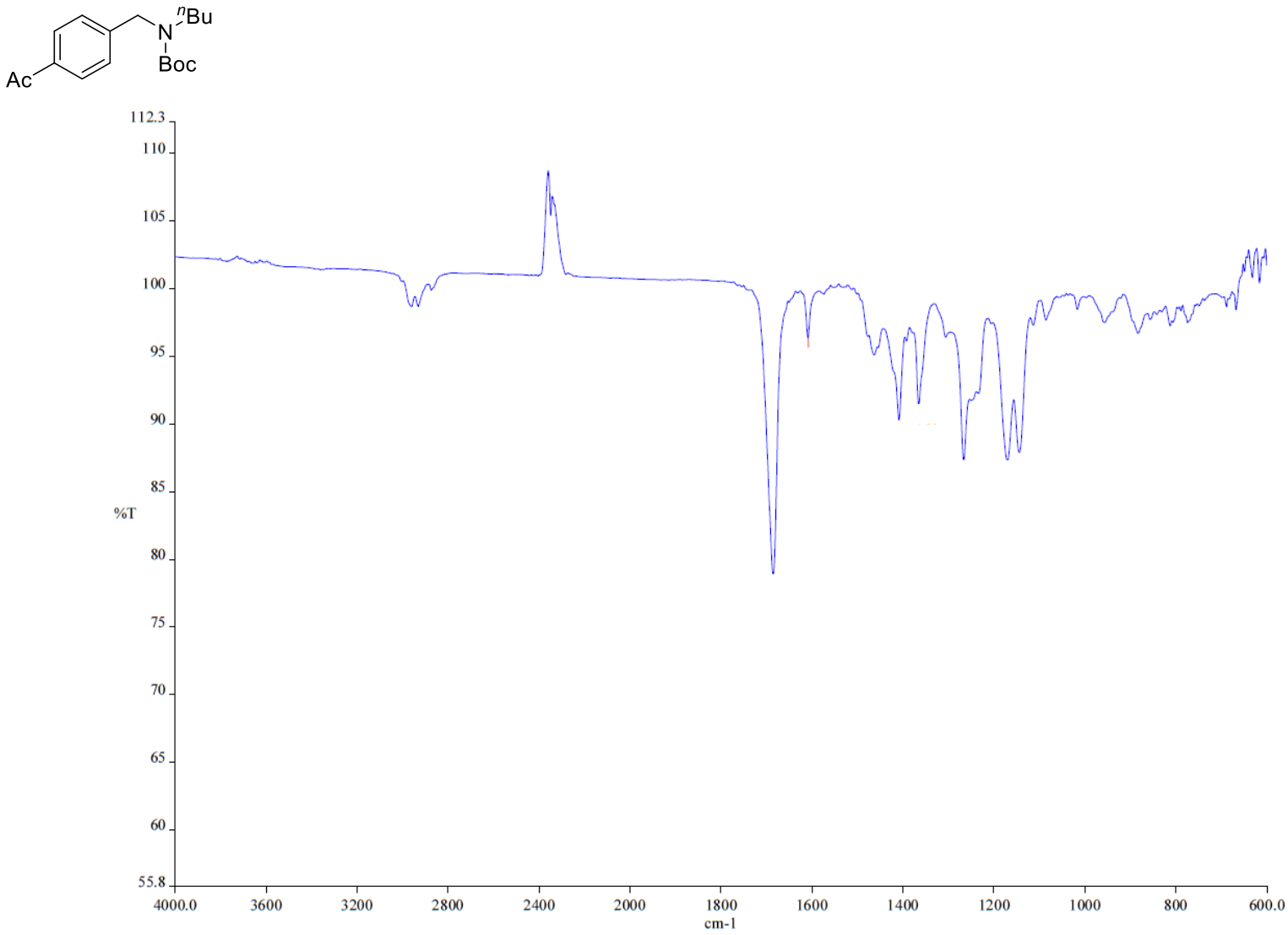
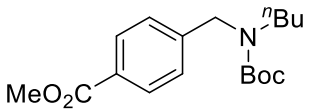
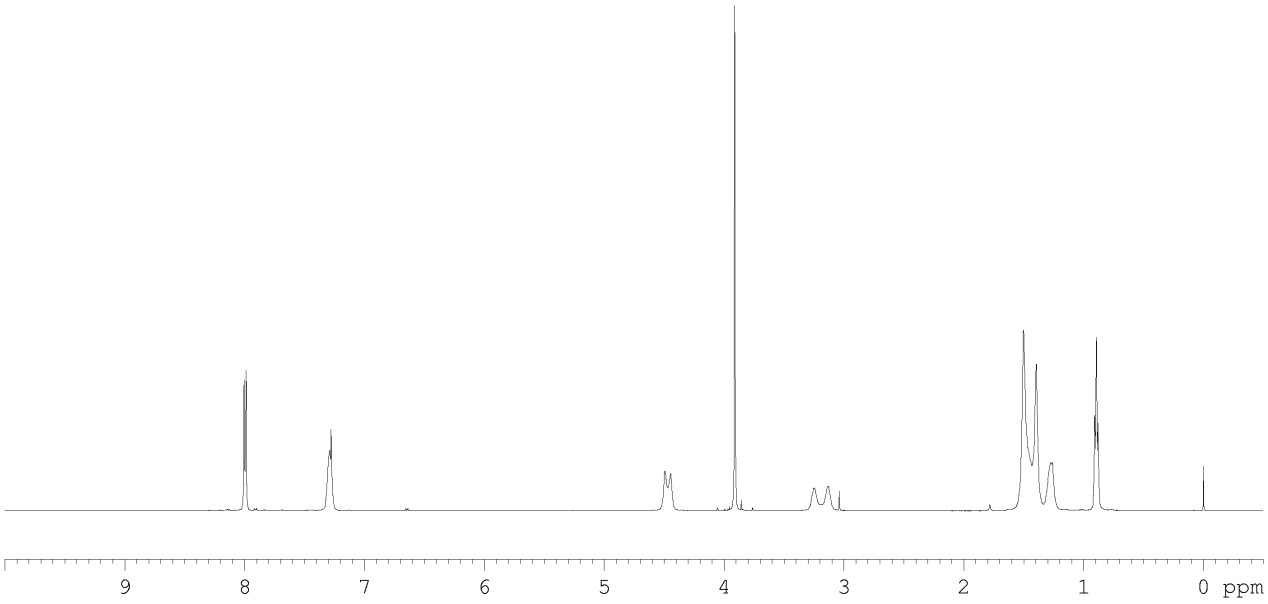
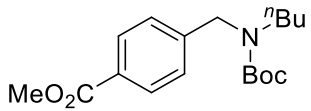


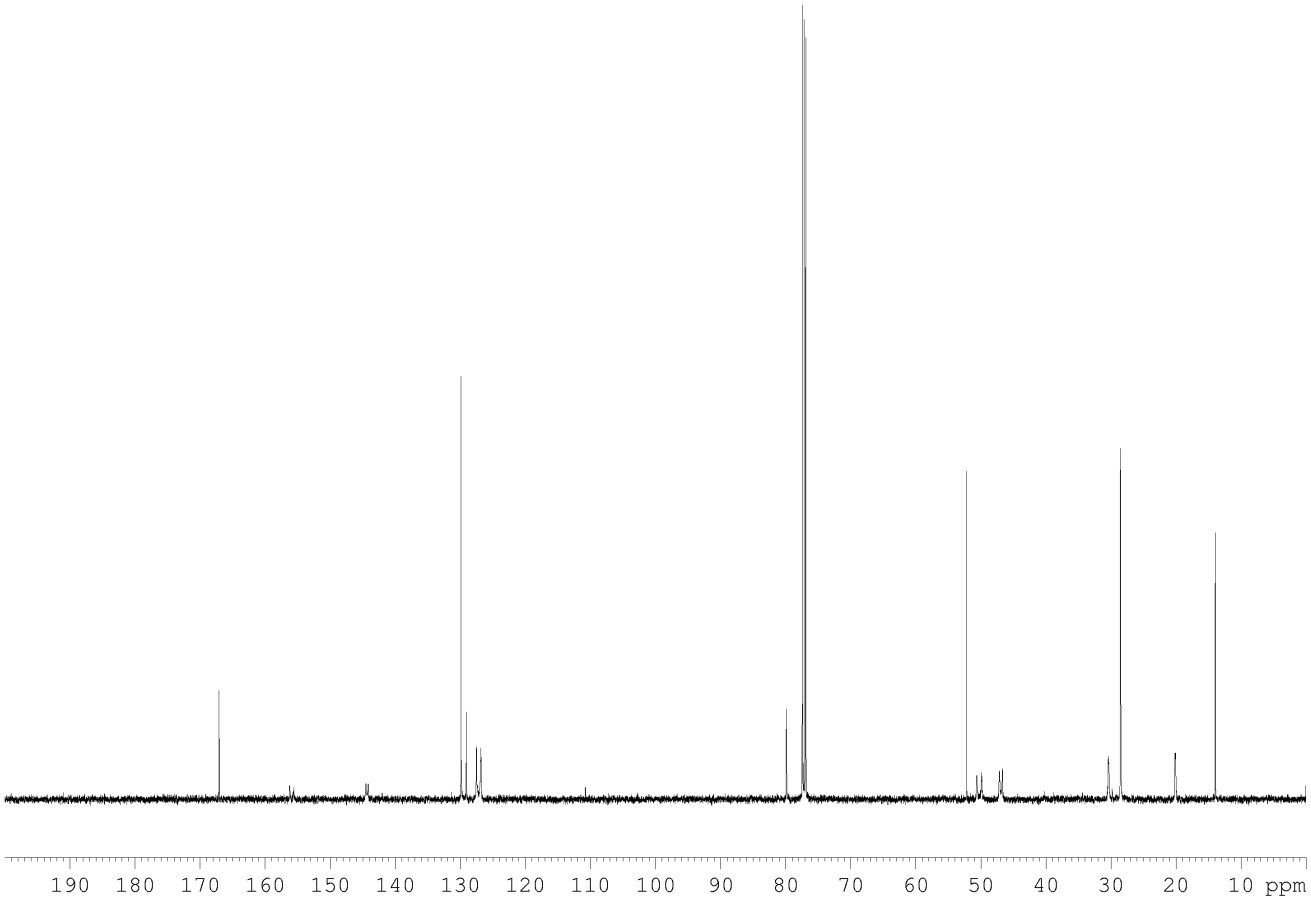
Figure A2.51b Infrared Spectrum

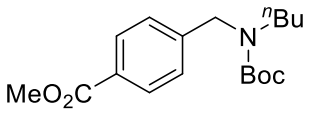


623




nBu
N
Boc
MeO2C


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



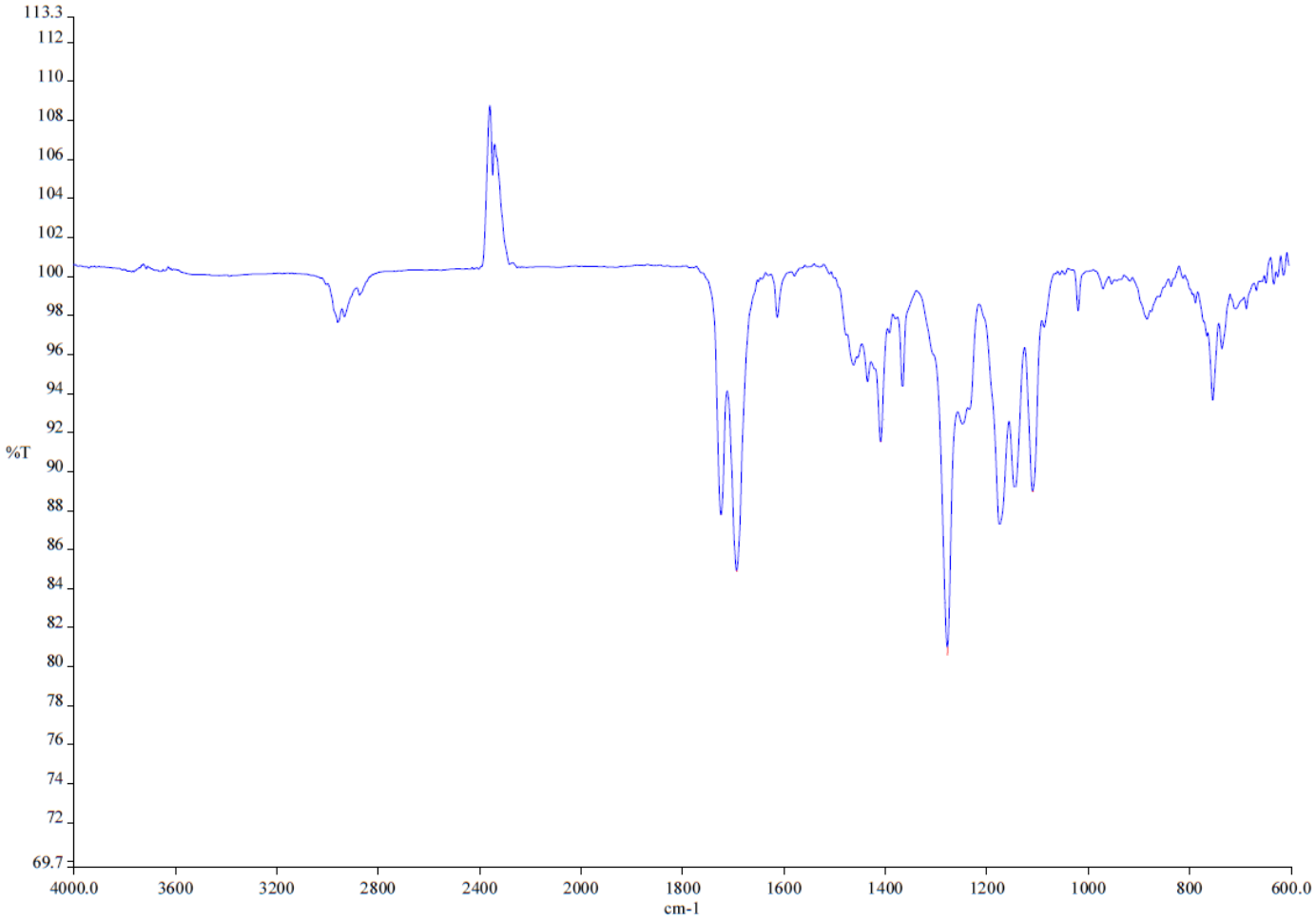
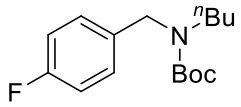
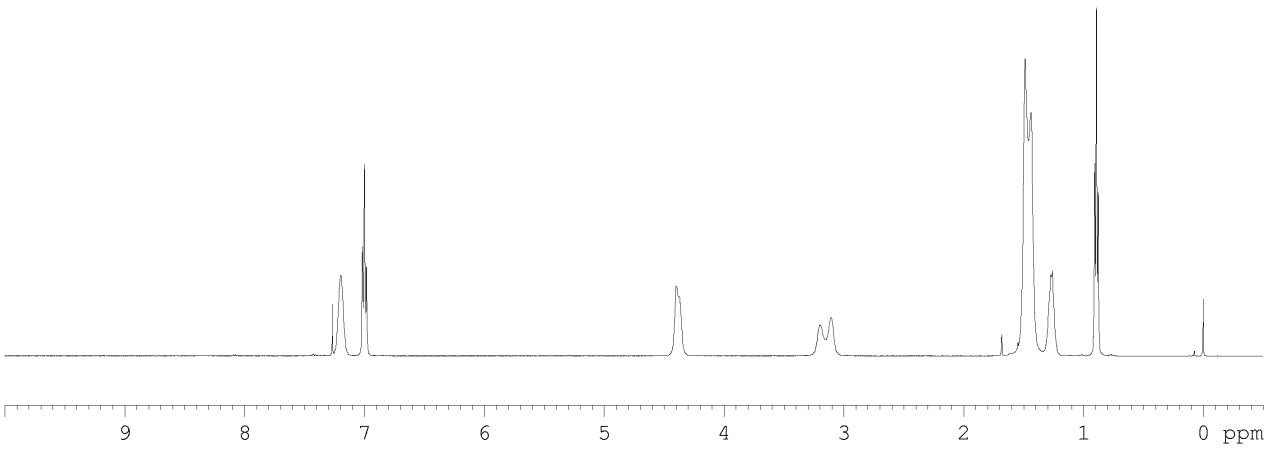
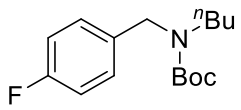


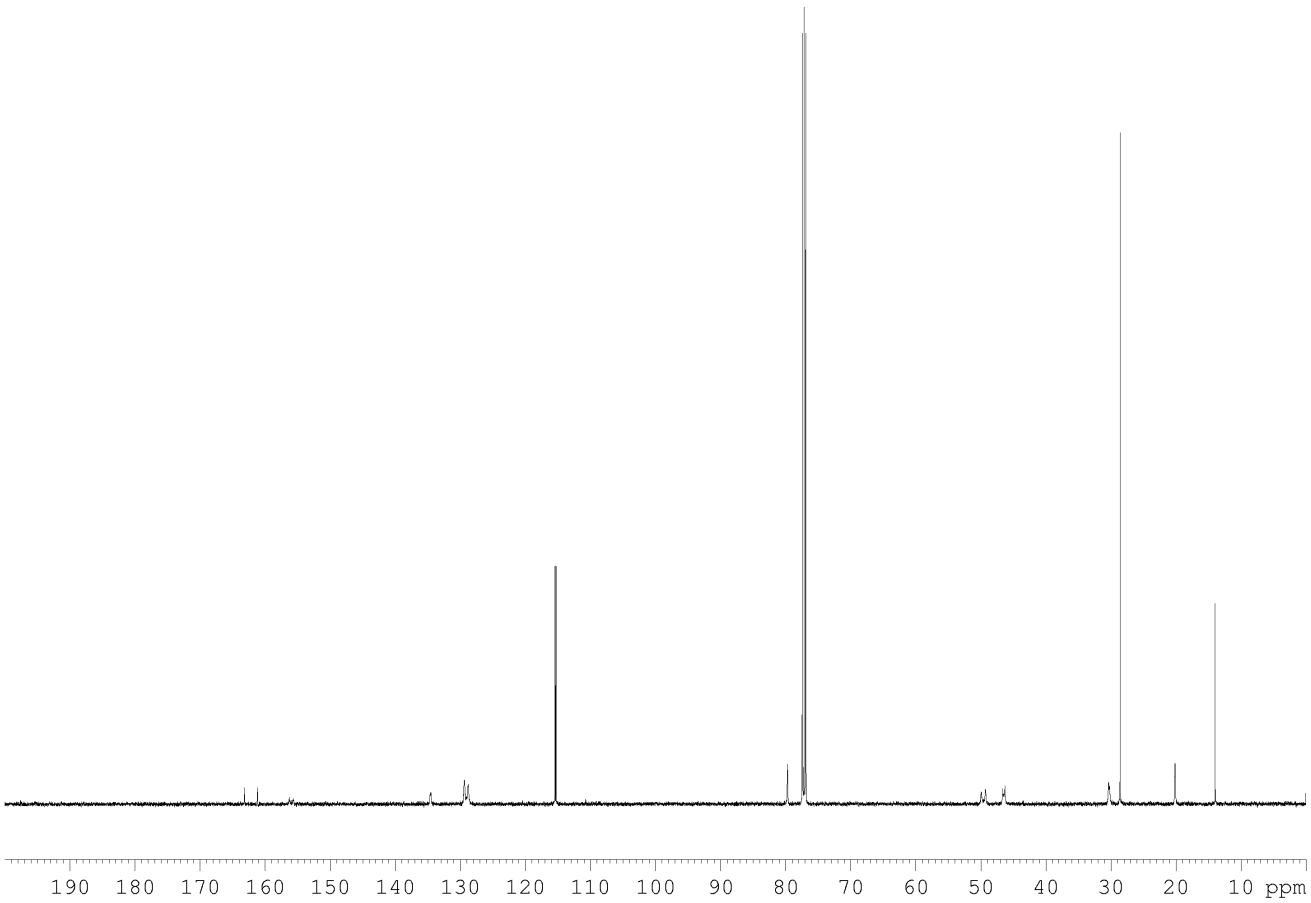
Figure A2.322 Infrared Spectrum



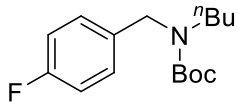
626




F
N
nBu
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

627



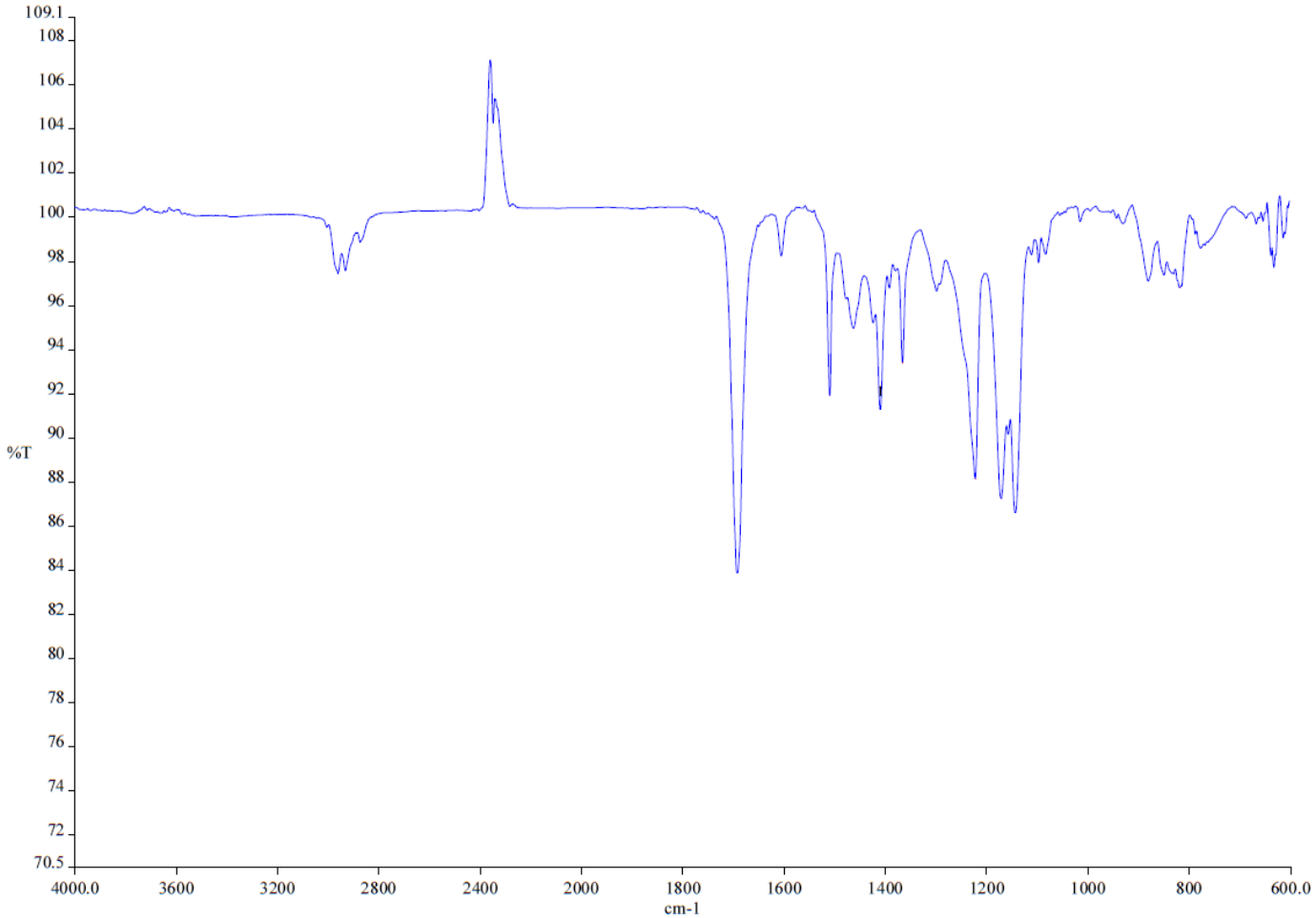
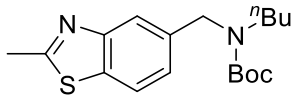
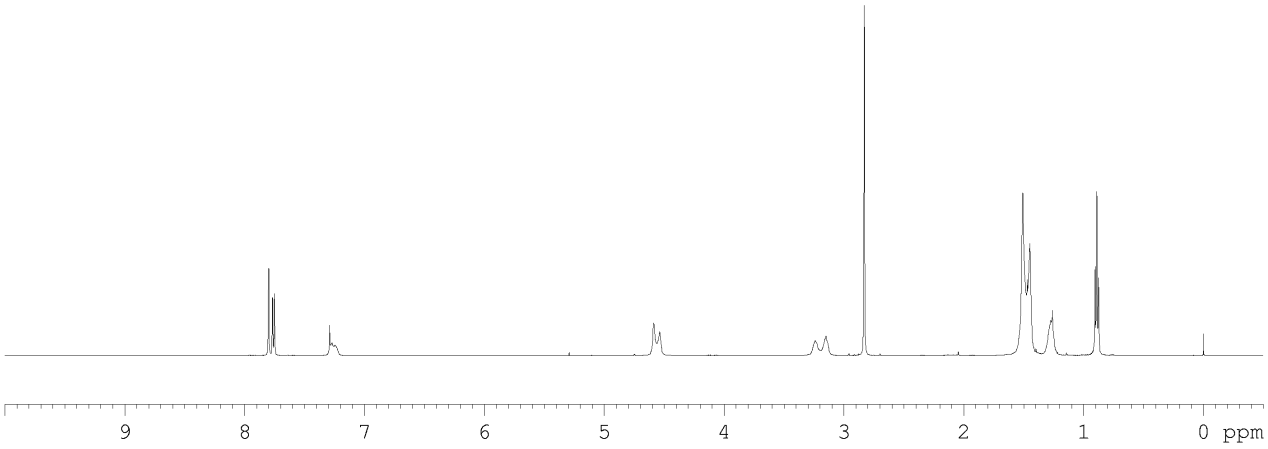
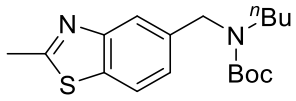


Figure A2.325 Infrared Spectrum

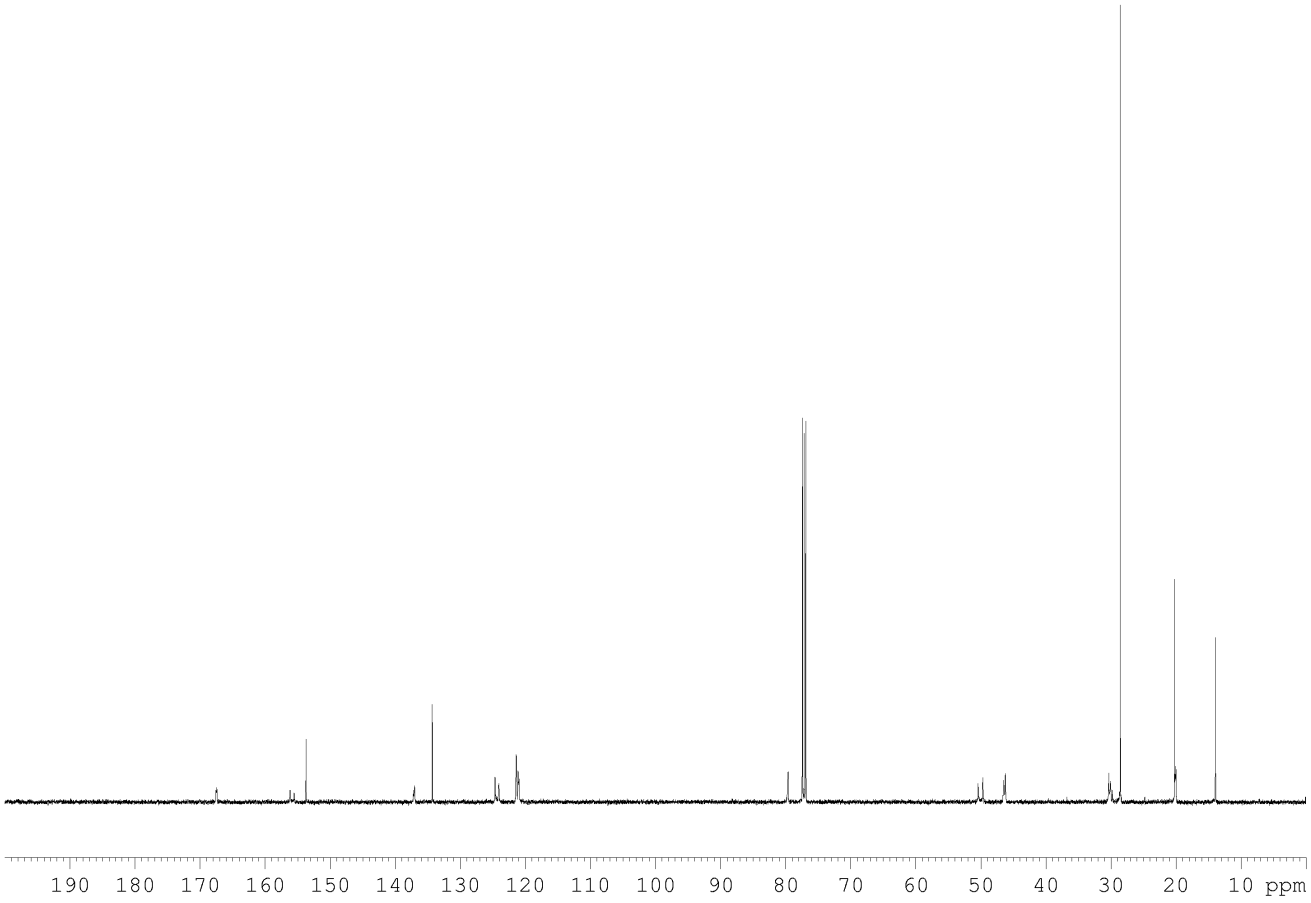


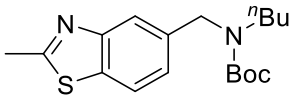
629




N
S
nBu
N
Boc

630


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



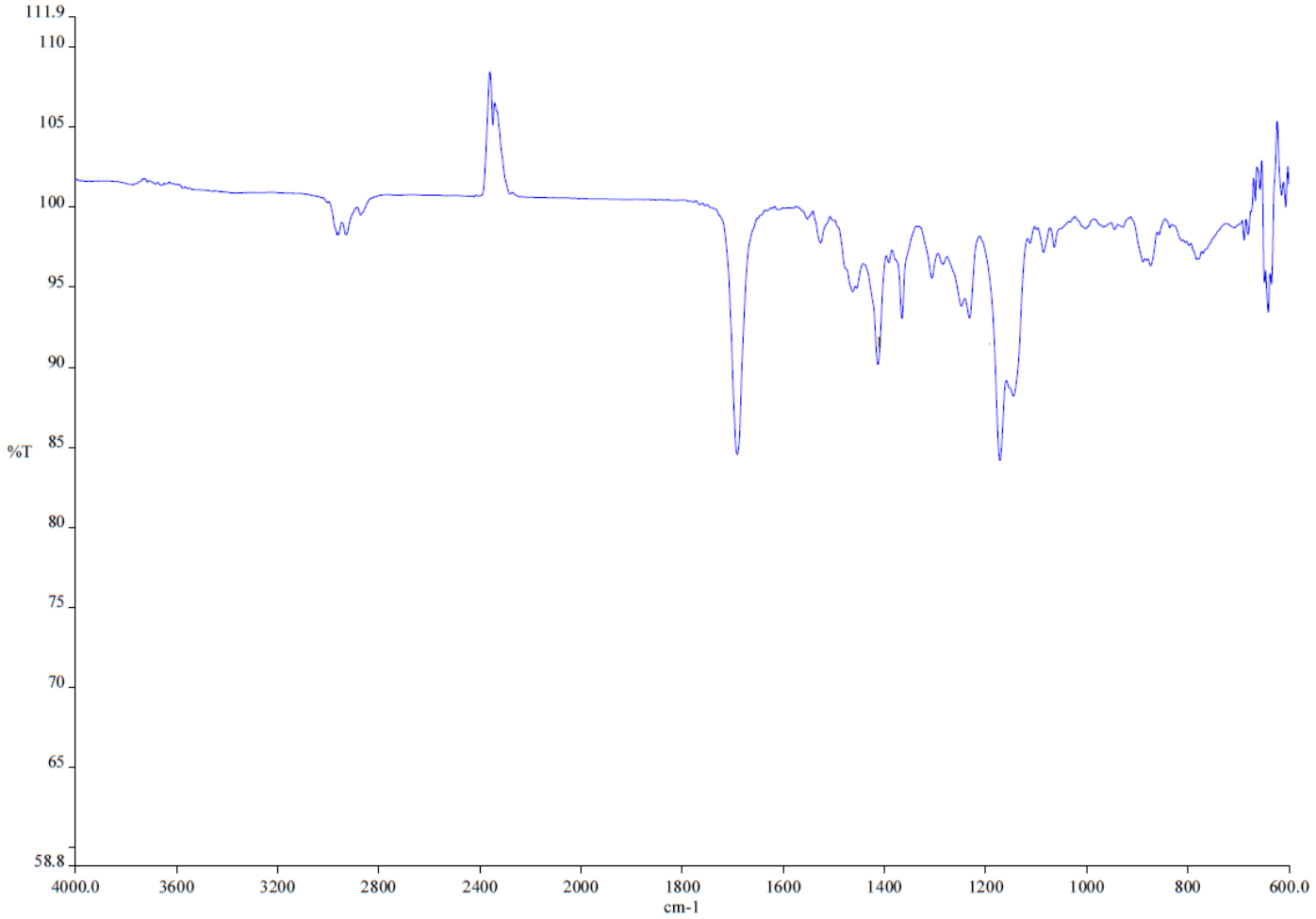
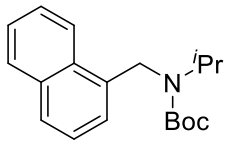
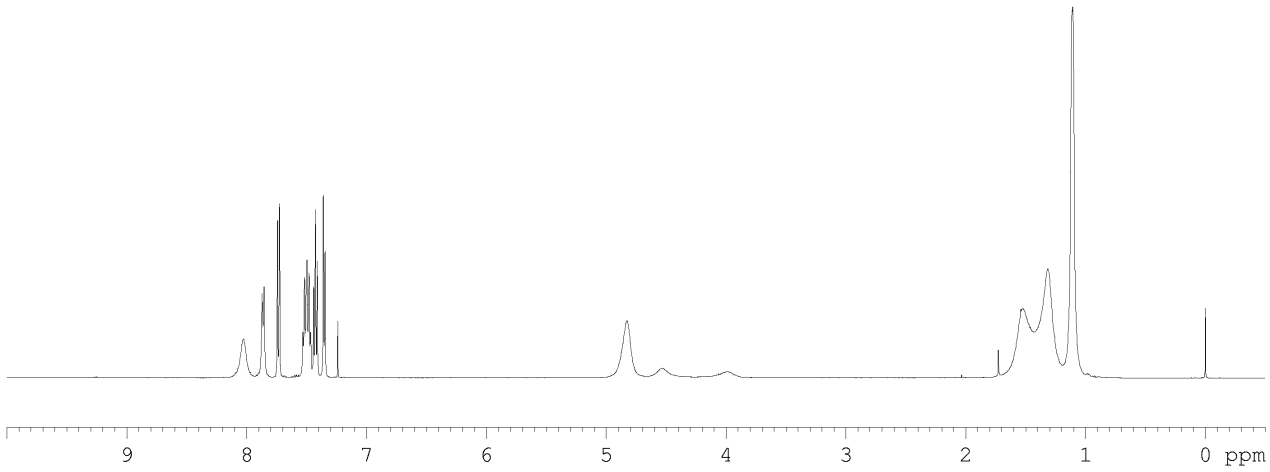
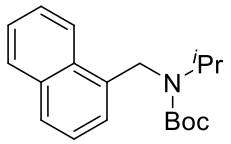


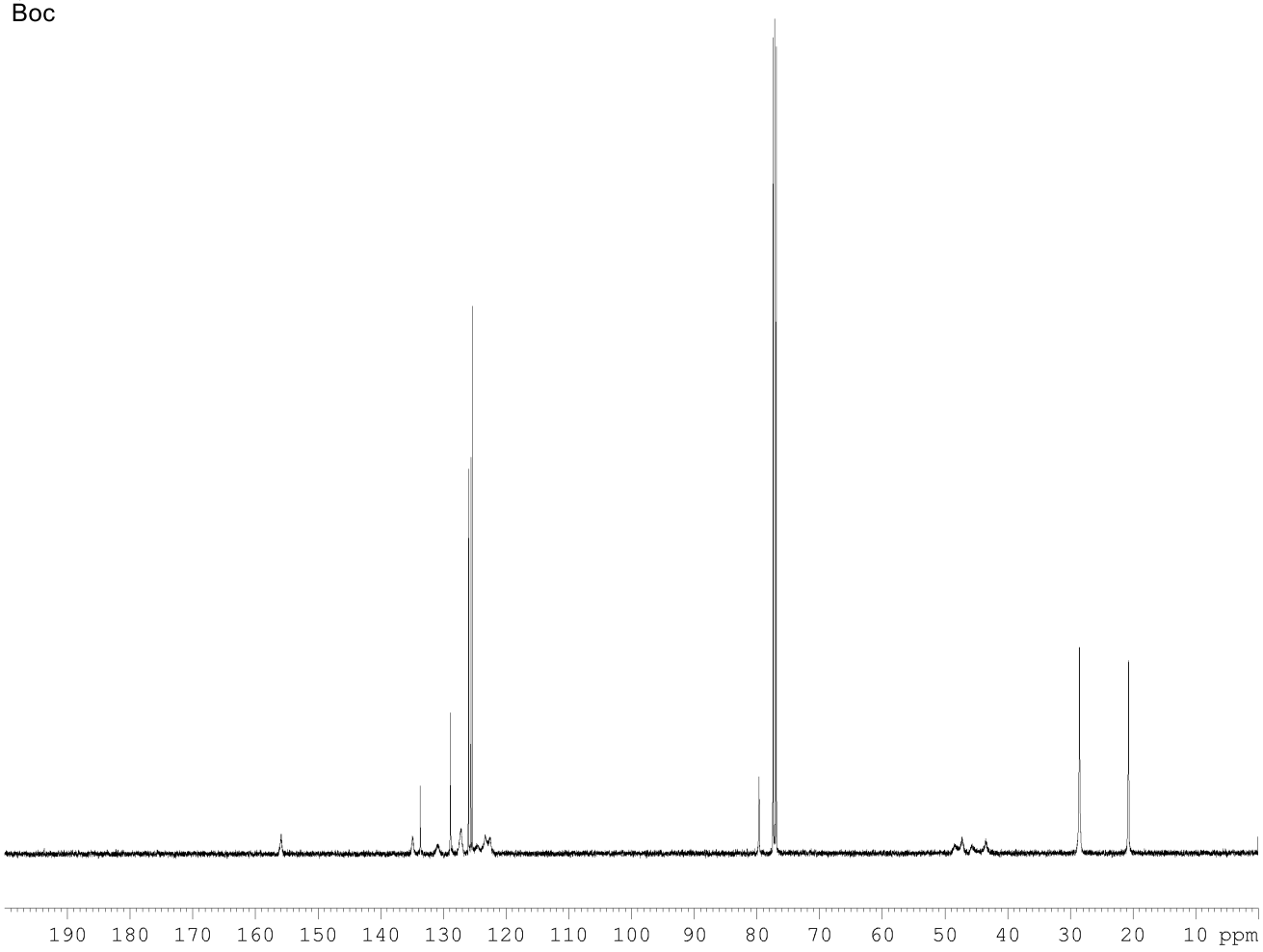
Figure A2.328 Infrared Spectrum



632




N
iPr
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

633

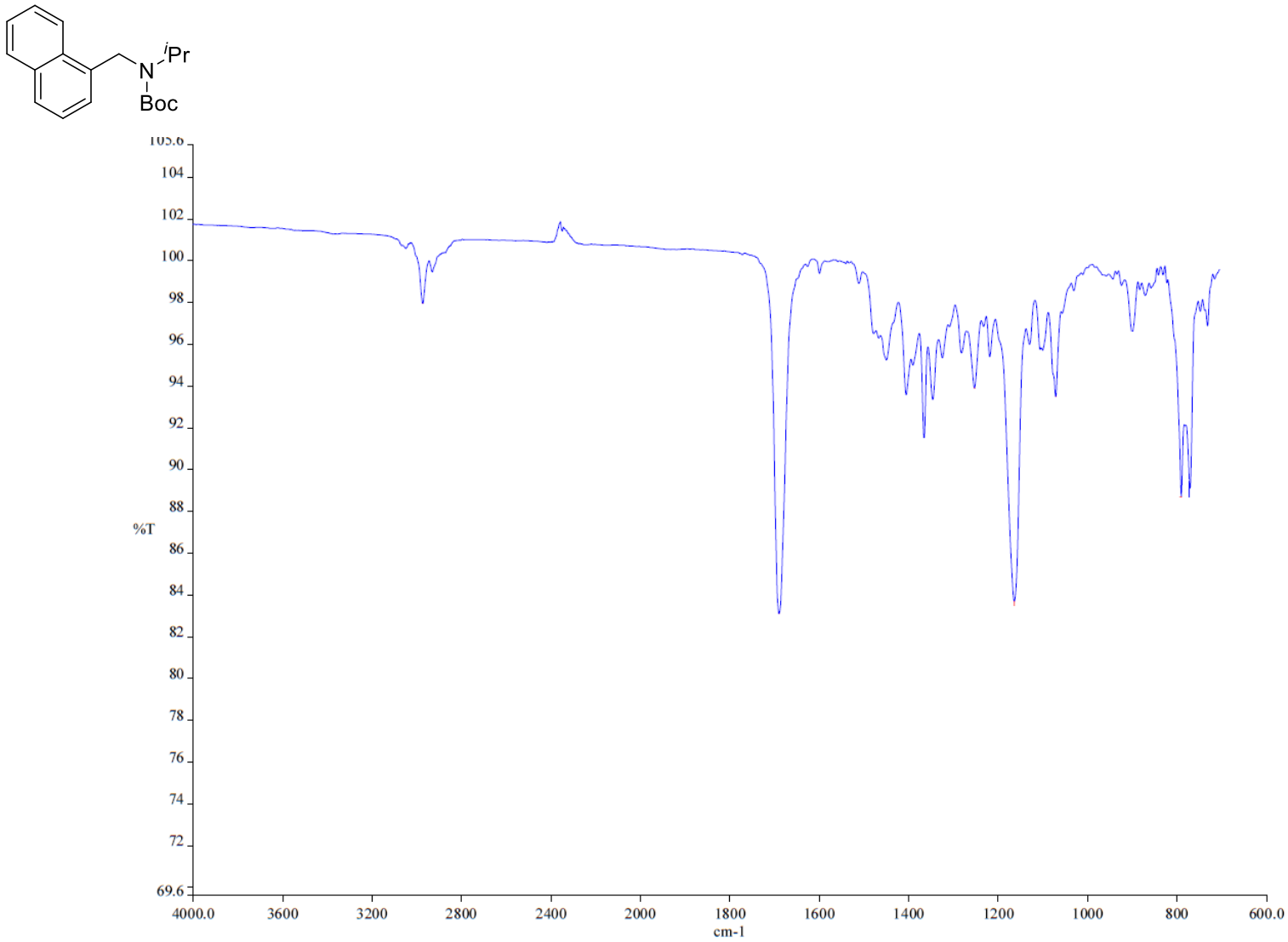
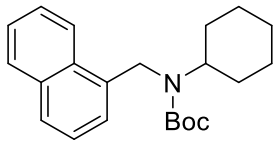
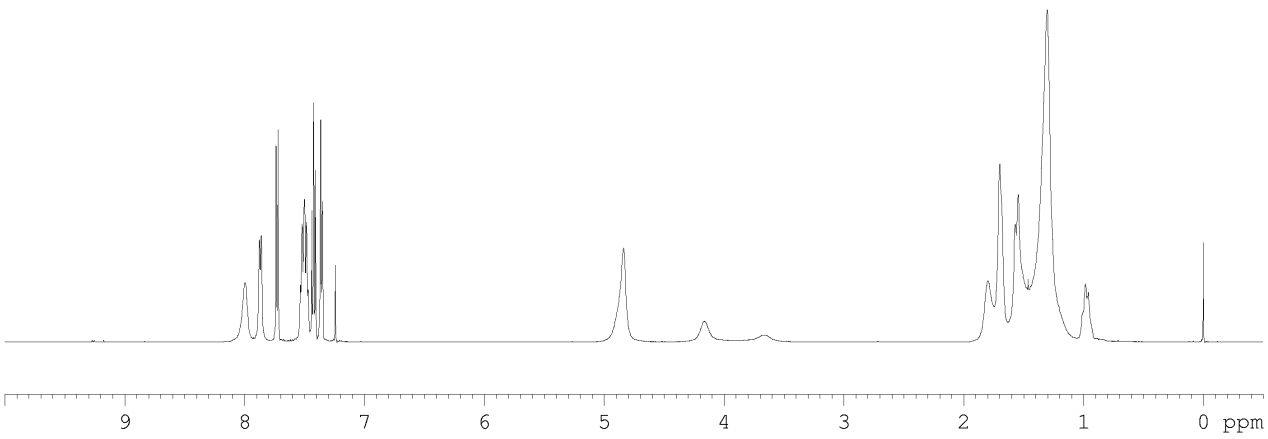


Figure A2.331 Infrared Spectrum



635



N
Boc

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

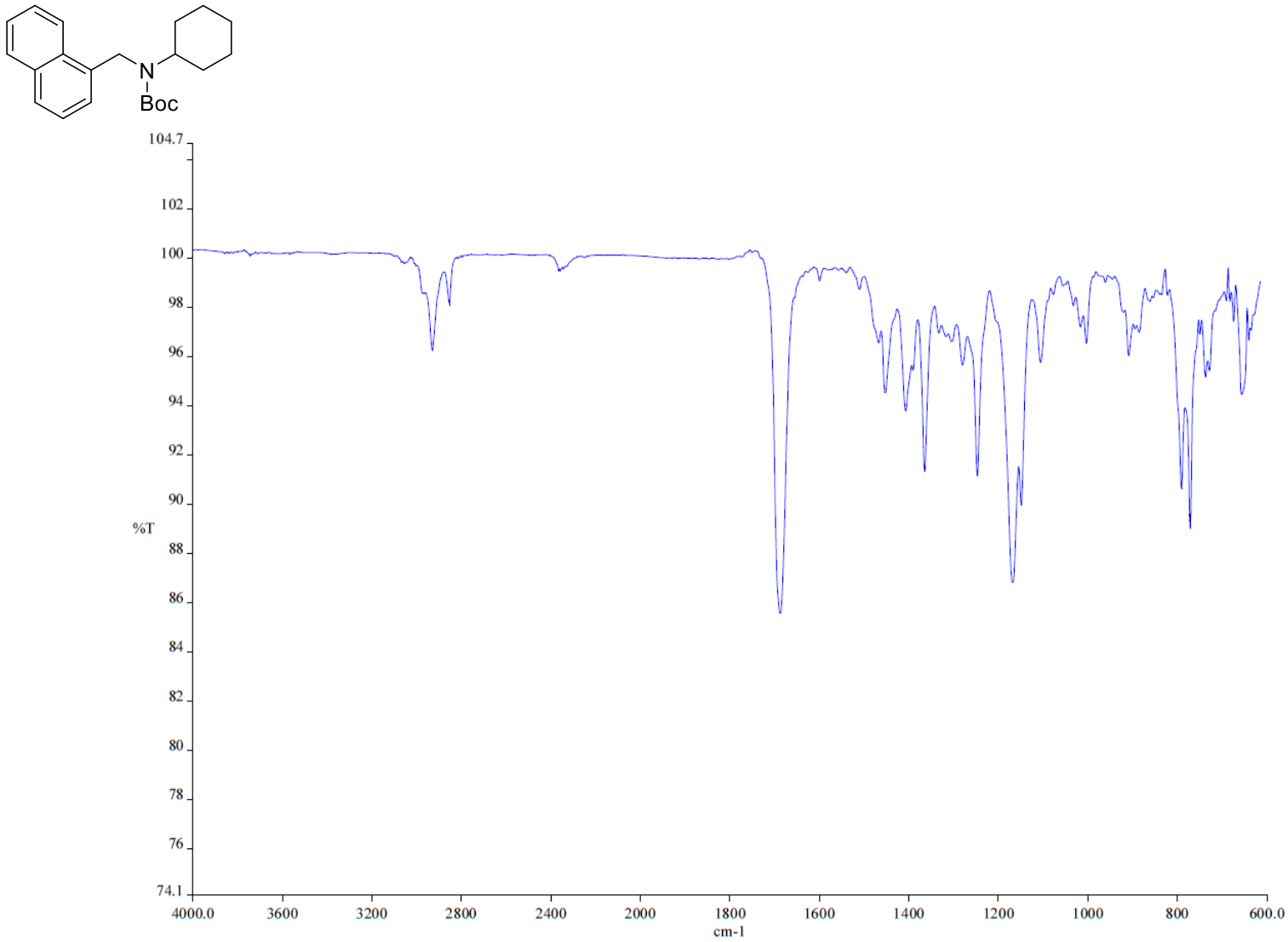
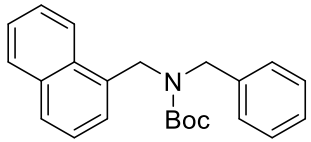
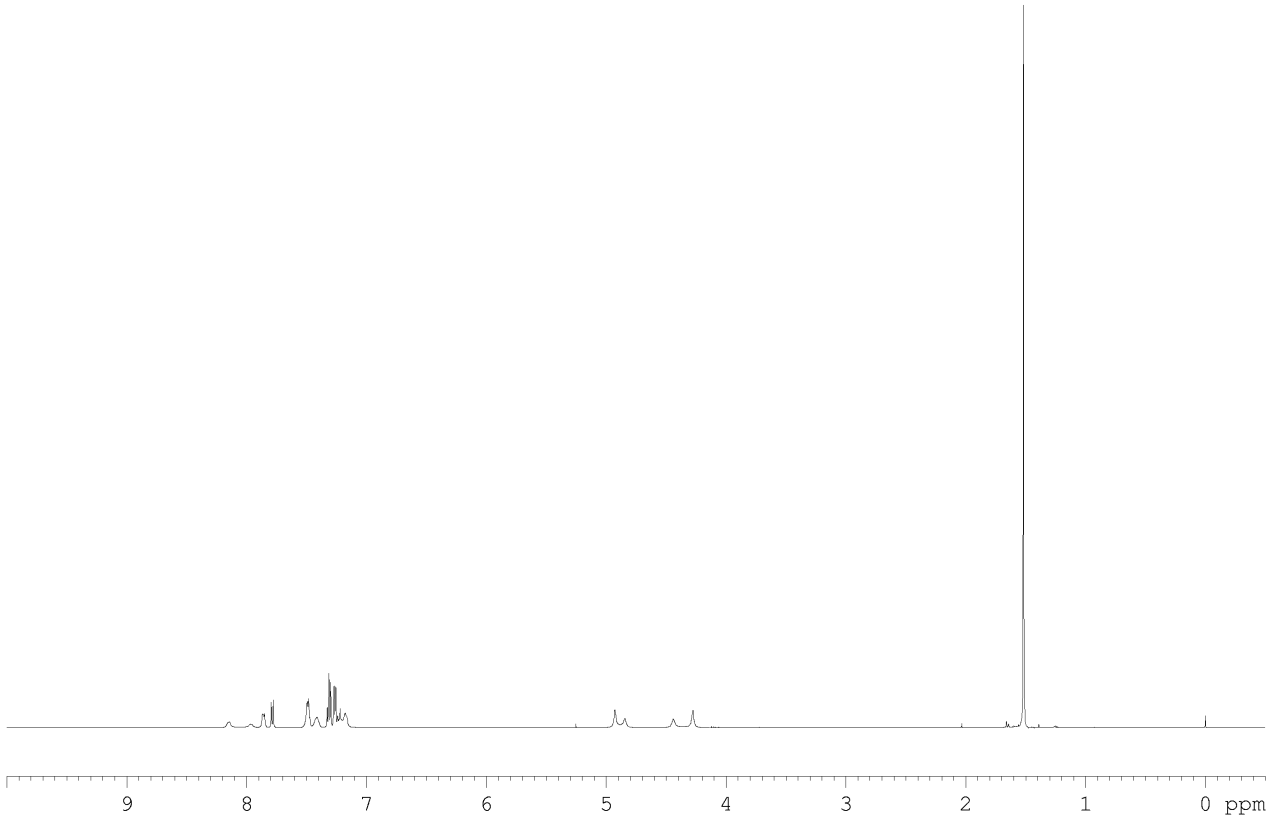
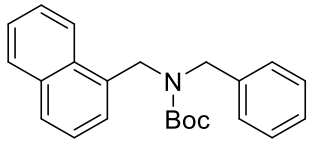
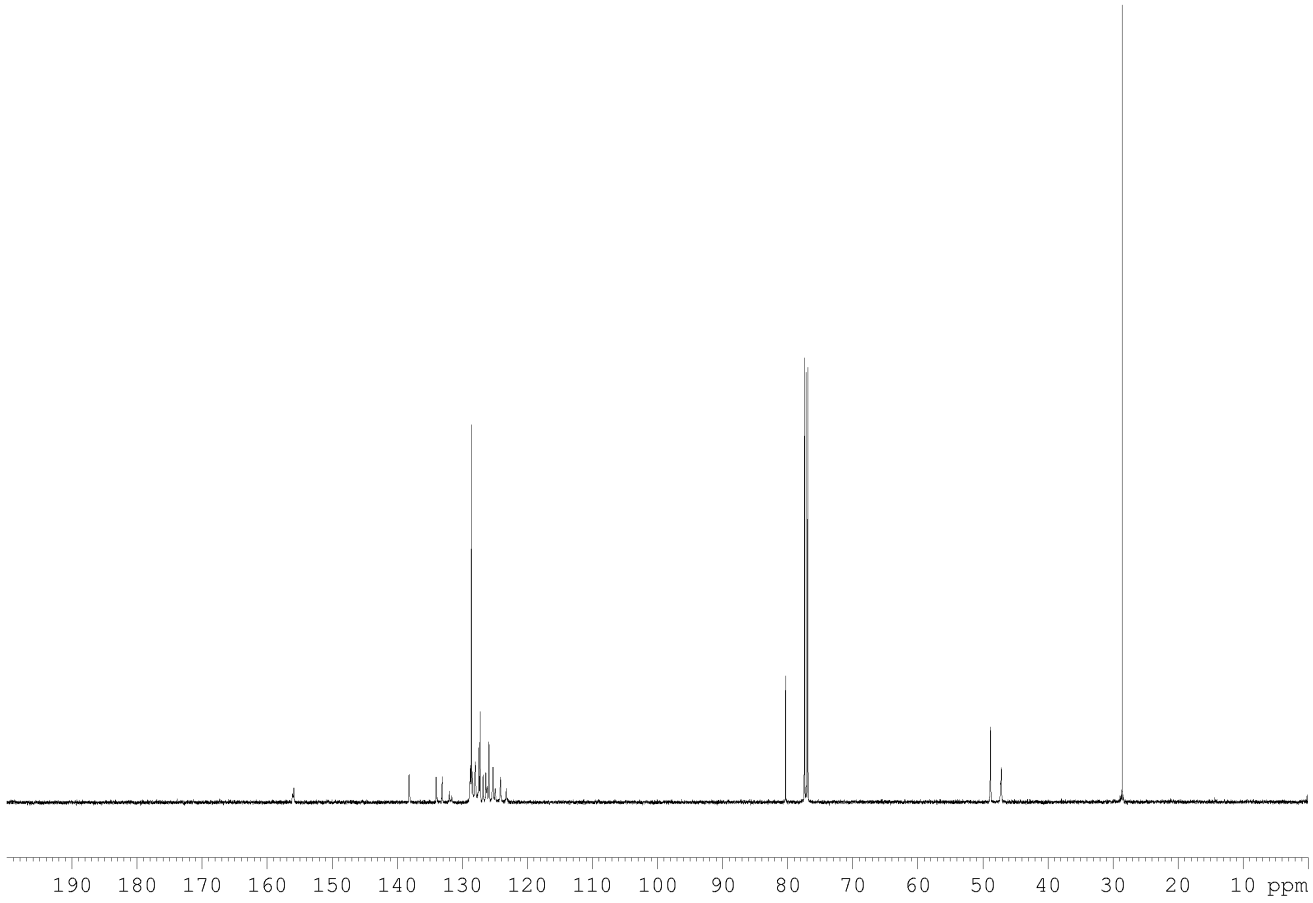


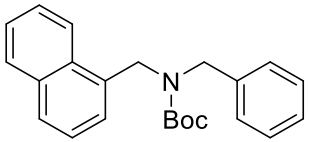
Figure A2.334 Infrared Spectrum


N
Boc


9
8
7
6
5
4
3
2
1
0 ppm


N
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



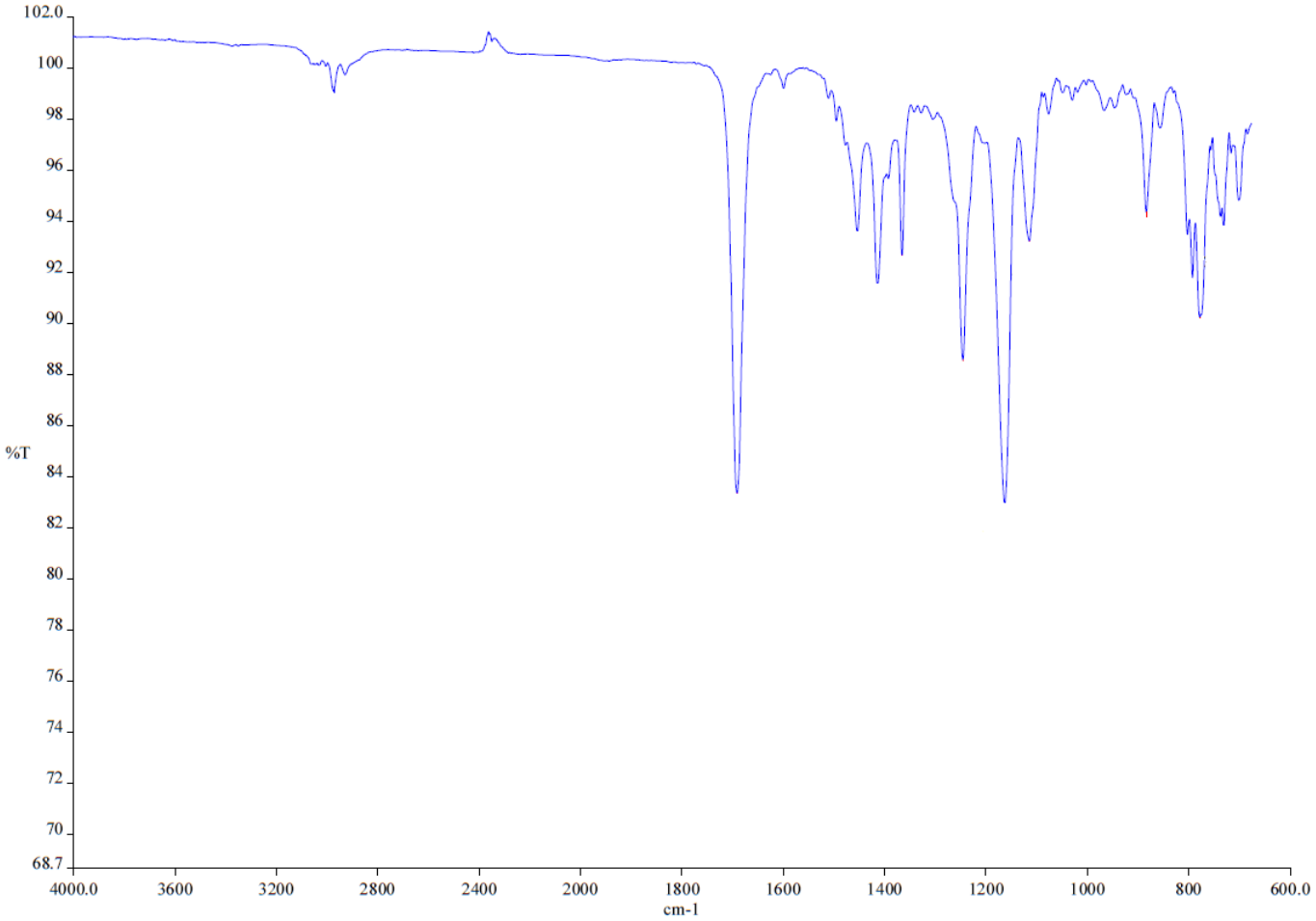
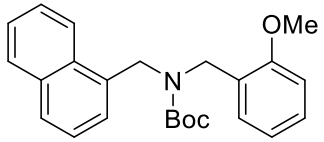
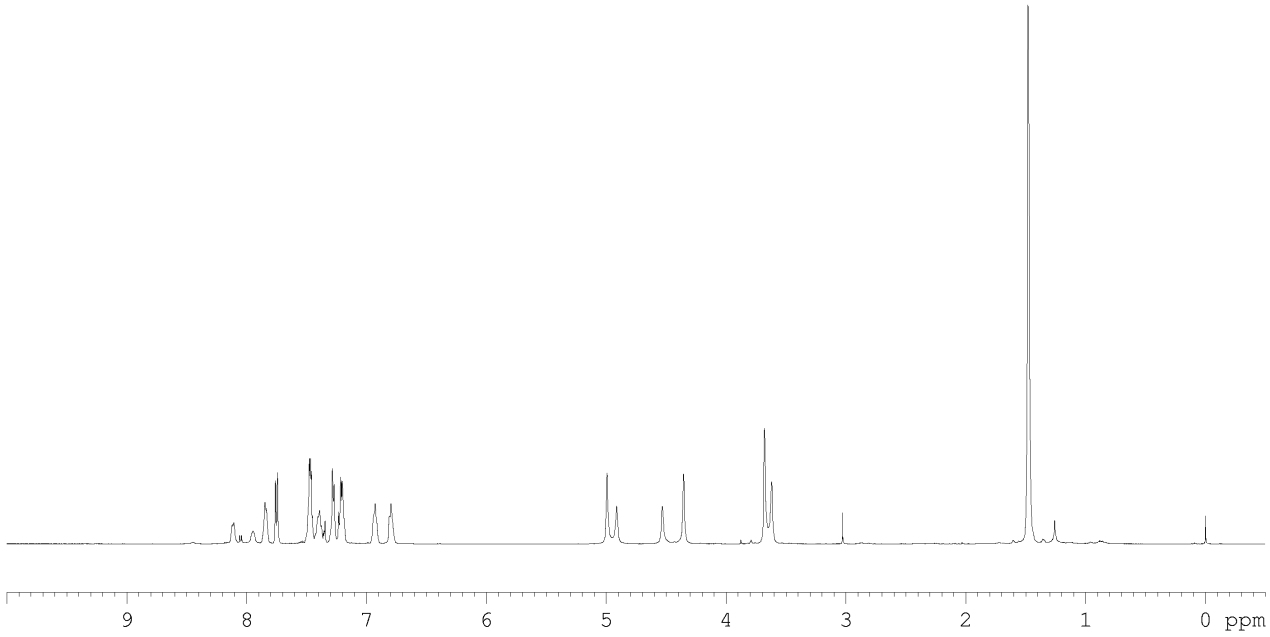
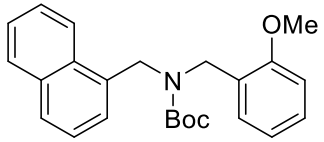


Figure A2.357 Infrared Spectrum

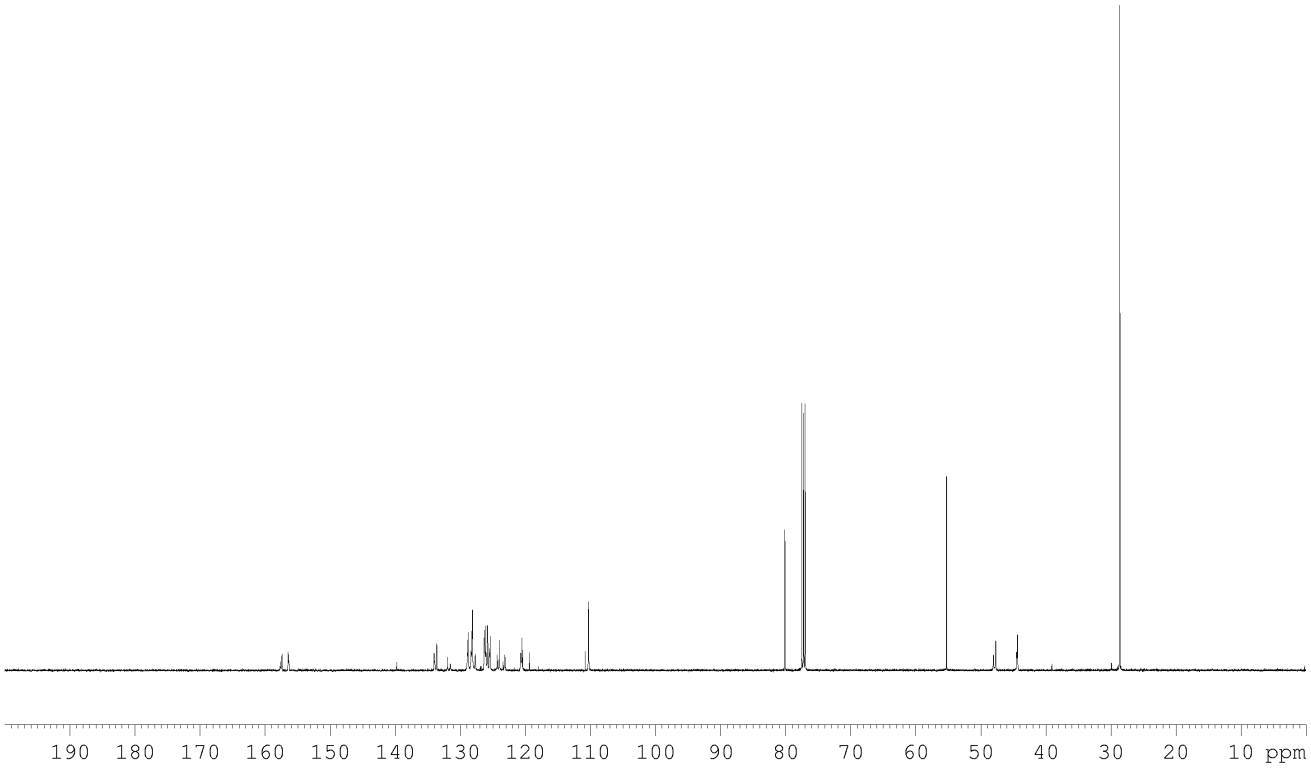




641


OMe
N
Boc

642


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

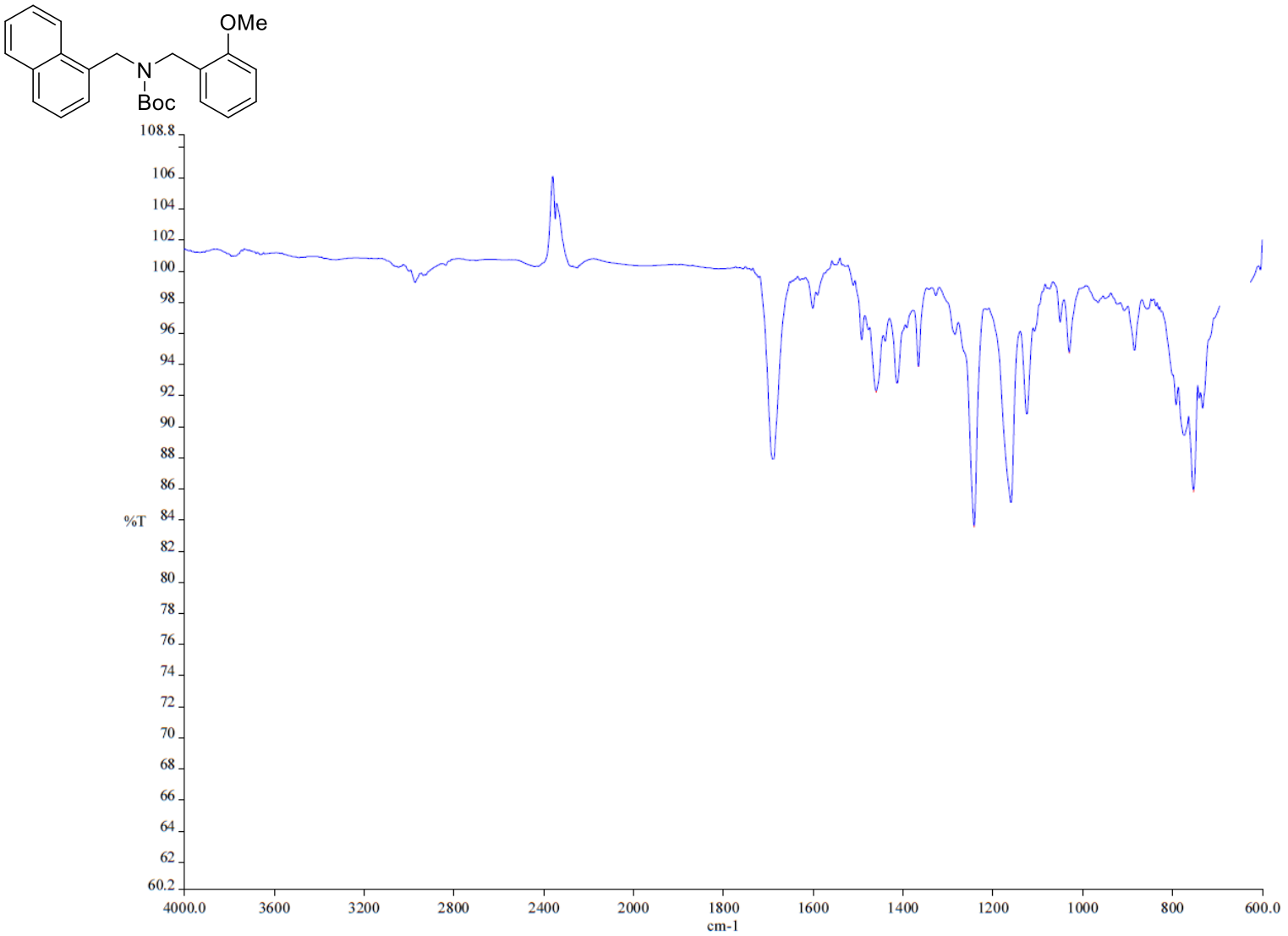
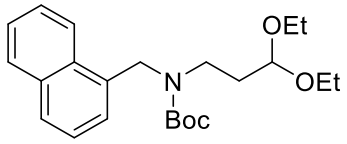
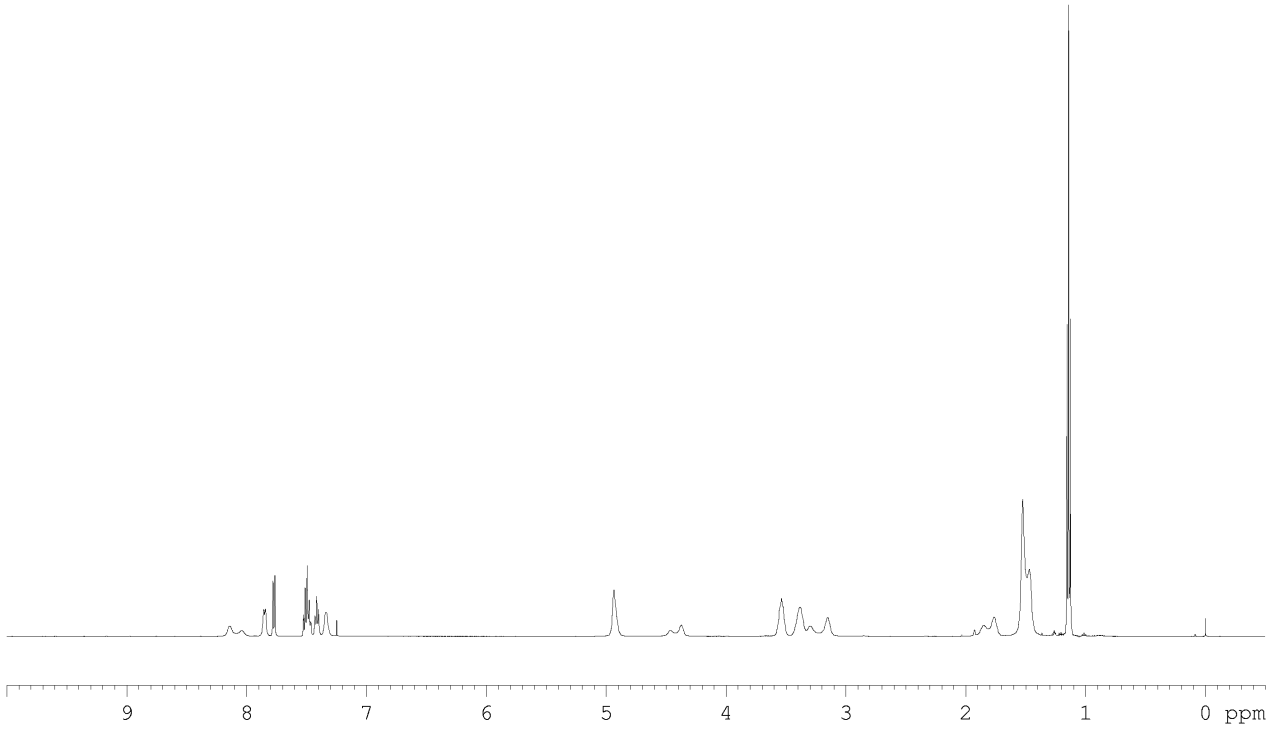
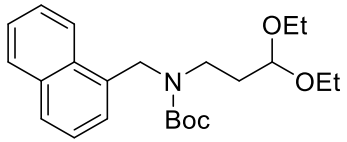
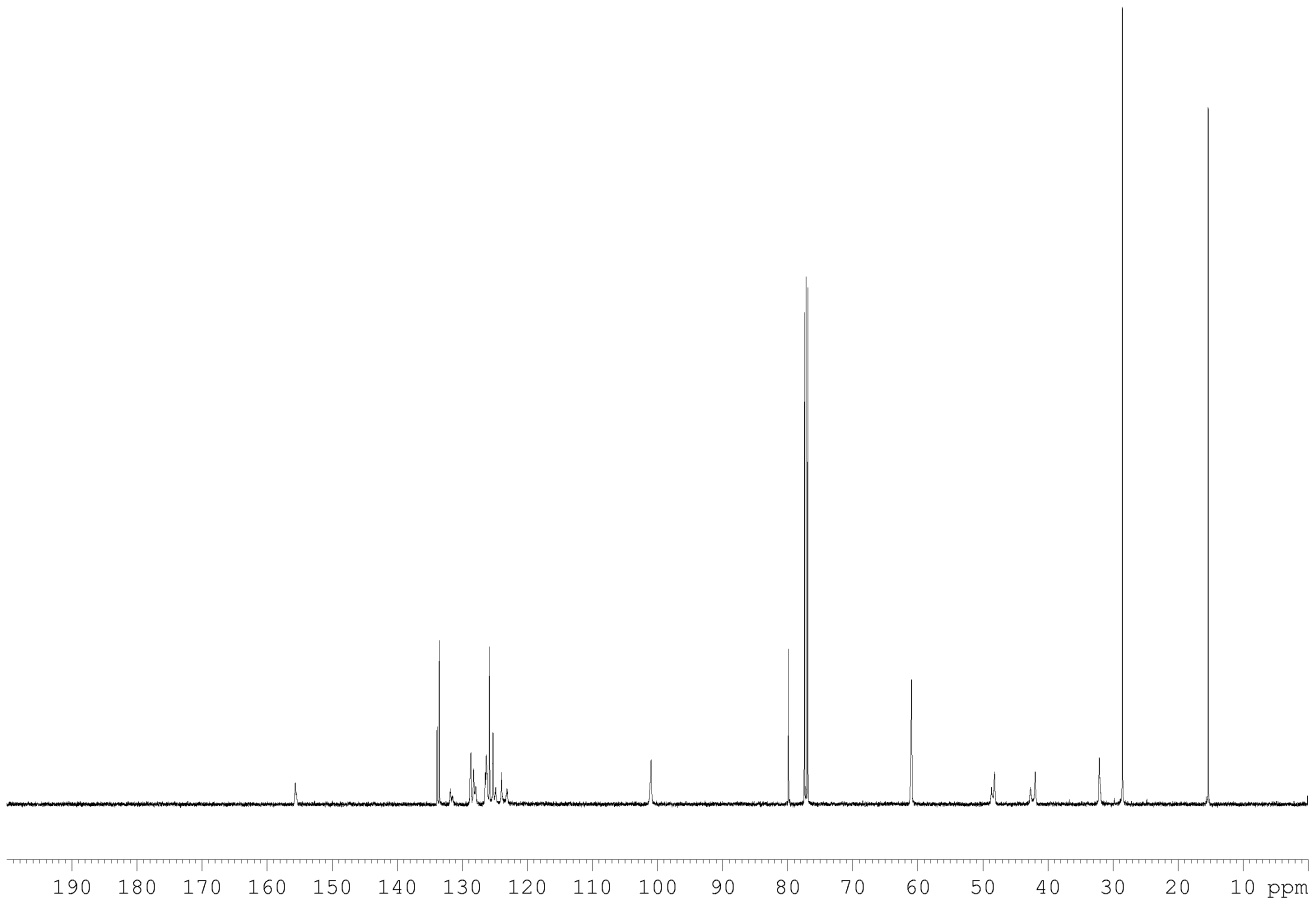


Figure A2.340 Infrared Spectrum


OEt
N
OEt
Boc


9
8
7
6
5
4
3
2
1
0 ppm


OEt
N
OEt
Boc


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

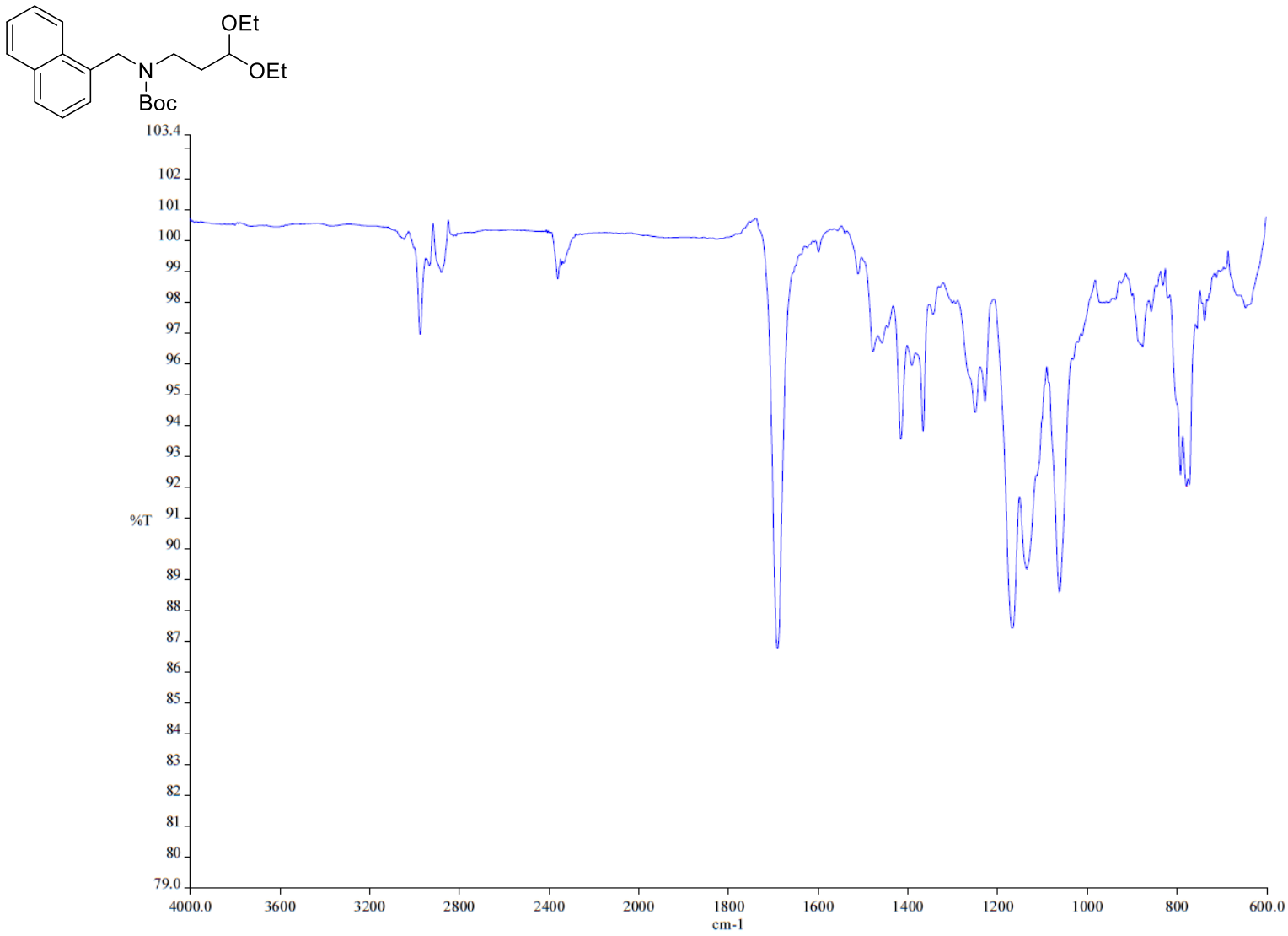


Figure A2.345 Infrared Spectrum

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About the Author

Inji Shin was born on April 28, 1982 in Seoul, South Korea. She is the first child of two children in her family. She grew up in Busan, Korea.

She was interested in chemistry since middle school, and she majored in chemistry when she attended Hanyang University in 2001. She graduated from Hanyang University as the top student in her class in February 2005. She then started her graduate research in organic chemistry under the supervision of Professor Cheon-Gyu Cho at Hanyang University. In February 2007, she obtained her master's degree in Chemistry with her thesis "The First Total Synthesis of (±)-*trans*-Dihydronarciclasine Utilizing the Highly *endo*-Selective Diels-Alder Cycloaddition of 3,5-Dibromo-2-pyrone", and she published three papers.

She decided to pursue her Ph.D. because she wanted to study further in organic chemistry. In the fall of 2008, she started the Ph.D. program at the University of Pennsylvania, and started the research under the supervision Professor Gary A. Molander in 2009. Since joining the Molander group, she focused on design, synthesis, and Suzuki–Miyaura cross-coupling reactions. After her graduate study at the University of Pennsylvania, she will post-doc for Professor Michael J. Krische at University of Texas in Austin.

In May 2007, she married Wonsuk Kim, who is an assistant professor at Ewha Womans University in Korea. They have a lovely son, Steve H. Kim, who was born on March 28, 2008.