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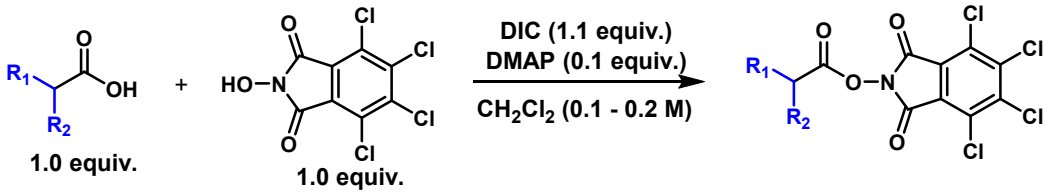
General Experimental

Tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF), and dichloromethane (CH_2Cl_2) were obtained by passing the previously degassed solvents through an activated alumina column. Extra dry 1,4-dioxane and DMF with molecular sieves were purchased from Acros (AcroSeal® bottles) and used directly. Et_3N was purchased from Sigma-Aldrich (sealed bottles). DIC (*N,N'*-diisopropylcarbodiimide) was purchased from Oakwood. $NiCl_2$•$6H_2O$ was purchased from Sigma-Aldrich. All the reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC), GC/MS GC/FID or LC/MS. TLC was performed using 0.25 mm E. Merck silica plates (60F-254), using short-wave UV light as the visualizing agent, and phosphomolybdic acid or $KMnO_4$ and heat as developing agents. NMR spectra were recorded on Bruker DRX-600, DRX-500, and AMX-400 instruments and are calibrated using residual undeuterated solvent ($CHCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Column chromatography was performed using E. Merck silica gel (60, particle size 0.043–0.063 mm), and preparative TLC was performed on Merck silica plates (60F-254). High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time of flight reflectron experiments. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus and are uncorrected. The UCSD small molecule X-ray facility collected and analyzed all X-ray diffraction data. Enantiomeric excesses (*ee*) were determined on an Agilent 1100 series HPLC system.

Handling of [Ni] Catalysts

All Ni catalysts were handled open to air on the bench top, and the bottles were neither flame dried nor stored under inert atmosphere.

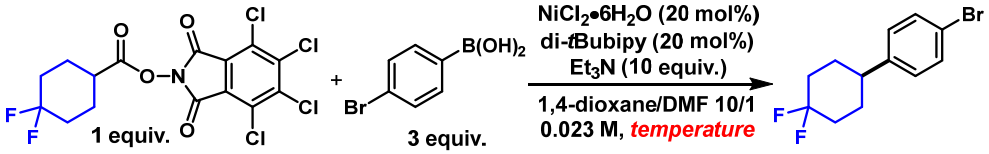
General Procedure for the Synthesis of TCNHPI Esters (General Procedure A)



Esters were prepared according to the previously reported procedure.[1,2] In short, a round-bottom flask or culture tube was charged with (if solid) carboxylic acid (1.0 equiv), *N*-hydroxy-tetrachlorophthalimide, 1.0 equiv.) and DMAP (0.1 equiv.). Dichloromethane was added (0.1 – 0.2 M), and the mixture was stirred vigorously. Carboxylic acid (1.0 equiv.) was added via syringe (if liquid). DIC (1.1 equiv.) was then added dropwise via syringe, and the mixture was allowed to stir until the acid was consumed (determined by TLC). Typical reaction times were between 0.5 h and 12 h. The mixture was filtered (over Celite, SiO_2, or through a fritted funnel) and rinsed with additional CH_2Cl_2/Et_2O. The solvent was removed under reduced pressure, and purification by column chromatography (and recrystallization, if necessary) afforded corresponding TCNHPI redox-active ester.

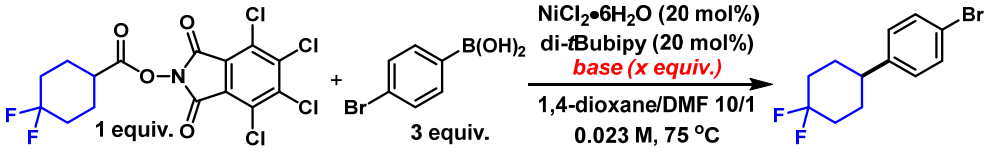
For graphical supporting information regarding the synthesis of TCNHPI esters, please address to our previous paper[1,2] for full details.

Optimization Details



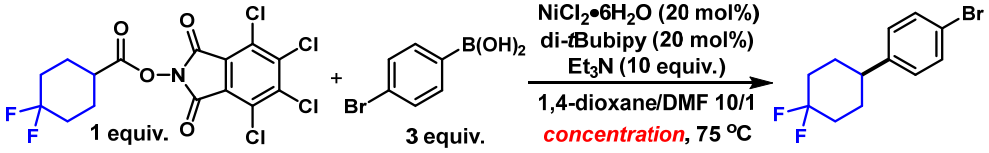
Temperature	Yield (%)[a]
55 °C	33
65 °C	36
75 °C	***82***
85 °C	54

[a]Yields determined by GC-FID with dodecane as internal standard



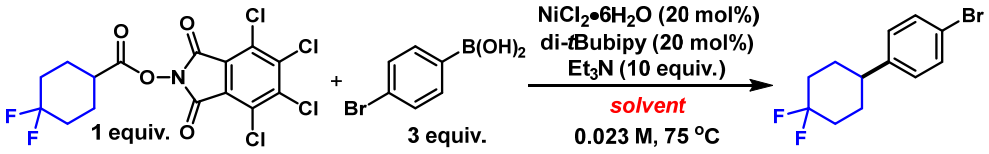
Base	Yield (%)[a]
No base	40
Et_3N (3.5 equiv.)	75
Et_3N (6.5 equiv.)	75
Et_3N (10 equiv.)	***82***
iPr$_2$NEt (10 equiv.)	68
nBu$_3$N (10 equiv.)	43
K_2CO_3 (3.5 equiv.)	35
Cs_2CO_3 (3.5 equiv.)	<5
K_3PO_4 (3.5 equiv.)	<5

[a]Yields determined by GC-FID with dodecane as internal standard



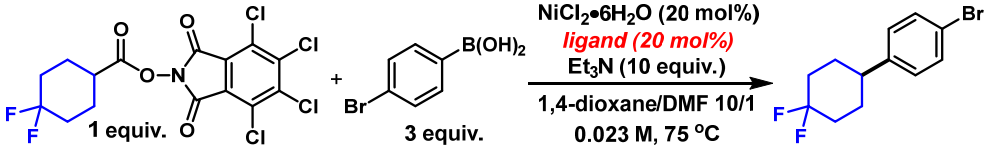
Concentration	Yield (%)[a]
0.091 M	6
0.045 M	35
0.023 M	***82***
0.011 M	73
0.009 M	63

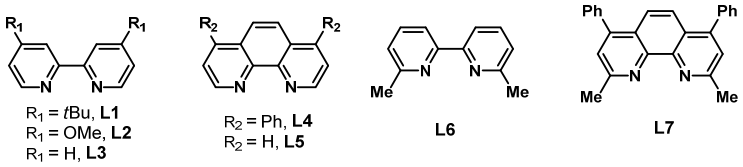
[a]Yields determined by GC-FID with dodecane as internal standard



Solvent	Yield (%)[a]
1,4-dioxane/DMF 10/1	***82***
THF/DMF 10/1	10
dioxane	20[b]
DMF	<5

[a]Yields determined by GC-FID with dodecane as internal standard, [b]isolated yield

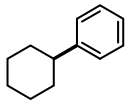




Ligand	Yield (%)[a]
L1	***82***
L2	64
L3	58
L4	***82***
L5	61
L6	<5
L7	<5
L1 (40 mol%)	44
No ligand	<5

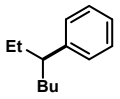
[a]Yields determined by GC-FID with dodecane as internal standard

Additional Optimization Details based on Various Substrates



$NiCl_2$-$6H_2O$, dtbbpy

1. DMF, 0%
2. EA, 18%
3. CDCl3, trace
4. MeCN, trace
5. acetone, 6%
6. benzene, 51%
7. DME, 0%
8. dioxane, 65%
9. DMA, trace
10. MTBE, 33%
11. THF, 86%



$NiCl_2$-$6H_2O$, dtbbpy

1. benzene, 4%
2. dioxane, 71%
3. MTBE, 52%
4. THF, 67%

$NiCl_2$-$6H_2O$, THF

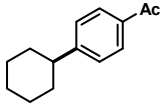
1. tBubpy, 67%
2. bipy, 25%
3. phen, 0
4. bathophen, 69%
5. TMEDA, 0
6. TMPDA, 0

$NiCl_2$-$6H_2O$, dioxane

1. tBubpy, 71%
2. bipy, 0%
3. phen, 2%
4. bathophen, 72%
5. TMEDA, 0
6. TMPDA, 0

$NiCl_2$-$6H_2O$, dtbbpy

1. CCl4, 0%
2. iPr2O, 7%
3. DMSO, 0%
4. NMP, 0%
5. CH3NO2, 0%
6. HMPA, 0%
7. anisole, 7%
8. toluene, 4%
9. DCE, 17%
10. EE, 11%
11. pyridine, 0%
12. Et3N, 4%



$NiCl_2$-$6H_2O$, dtbbpy

1. benzene, 6%
2. dioxane, 45%
3. MTBE, trace
4. THF, trace

$NiCl_2$-$6H_2O$, THF

1. tBubipy trace
2. bipy, 0
3. phen, 0
4. bathophen, 0
5. TMEDA, 0
6. TMPDA, 0

$NiCl_2$-$6H_2O$, dioxane

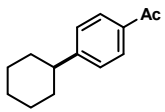
1. tBubpy, 45%
2. bipy, 0
3. phen, 0
4. bathophen, 42%
5. TMEDA, 0
6. TMPDA, 0

$NiCl_2$-glyme, dioxane

1. tBubipy 46%
2. bathophen, 30%

$NiCl_2$(dtbbpy)-solid

THF, 22%
dioxane, 42%

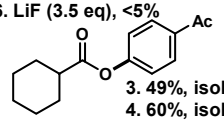


$NiCl_2$-$6H_2O$, dtbbpy, dioxane

MeOH (8 uL, 2 eq), 23%
iPrOH (15 uL, 2 eq), 38%
PhNMe2 (13 uL, 1.0 eq), trace
*t*BuOH (22 uL, 2 eq), 16%
Zn powder (3 mg, 0.5 eq), 43%
LiCl (4 mg, 1 eq), trace
LiF (2.6 mg, 1 eq), 46%
$B(C_6F_5)_3$ (26mg, 0.5 eq), 16%
$ZnCl_2$ (1.0 M, 50 uL, 0.5 eq), 26%
3A MS, 46%
4A MS, 39%
70 °C, 57%
75 °C, 68%
80 °C, 57%
90 °C, 35%
100 °C, 28%

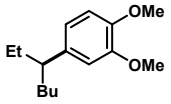
$NiCl_2$-$6H_2O$, dtbbpy, dioxane

1. K_2CO_3 (3.5 eq), 16%
2. CsOPiv (3.5 eq), 0%
3. Cs_2CO_3 (3.5 eq), ~ 10% prod
4. K_3PO_4 (3.5 eq), ~ 5% prod
5. KF (3.5 eq), < 5%
6. LiF (3.5 eq), <5%



3. 49%, isolated
4. 60%, isolated

1. Ni(acac)2, 0%
2. Ni(NO3)2-6H2O, 8%
3. Ni(OAc)2-4H2O, 0%
4. NiF2-4H2O, 0%
5. Ni(OMe)2, 0%
6. NiBr2-glyme, ~5%



$NiCl_2$•6H2O, dtbbpy

1. THF/DCE 1/1, 21%
2. THF/DCE 1/4, 10%
3. dioxane/DCE 1/1, 10%
4. dioxane/DCE 1/4, 7%

$NiCl_2$•6H2O, THF

1. tBubipy, 25%
2. bathophen, 20%

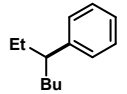
$NiCl_2$•6H2O, dioxane

1. tBubipy, 10%
2. bathophen, 24%

$NiCl_2$(dtbbpy)- solid

THF, 30%
dioxane, 27%

H_2O addition



$NiCl_2$-glyme, dtbbpy

1. 0 equiv H2O 56%
2. 1 equiv H2O 56%
3. 2 equiv H2O 61%
4. 3 equiv H2O 28%
5. 5 equiv H2O 11%
6. 10 equiv H2O 0%
7. 20 equiv H2O 0%

base screening

$NiCl_2$•6H2O, dtbbpy, THF

1. Et3N	45%
2. DIPEA	40%
3. pyridine	0%
4. DBU	0%
5. tBuTMG	0%
6. TMEDA	0%
7. Bu3N	35%
8. DMAP	0%
9. PhNMe2	0%
10. N-Me pyrrolidine	0%
11. N-Me pyperidine	0%
12. 1-Me imidazole	0%

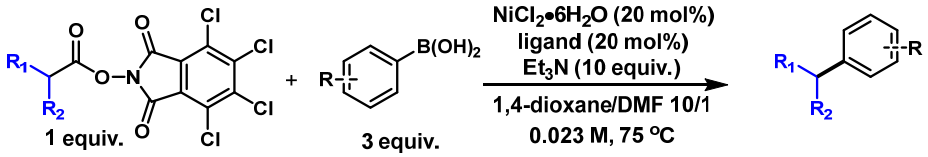
All screens are at 60 °C unless otherwise mentioned.

General Procedure for the Ni-Catalyzed Cross-Coupling of Alkyl Redox-Active Esters and Aryl Boronic Acids (General Procedure B)

Part I. Preparation of $NiCl_2$•$6H_2O$/ligand Stock Solution (0.05 M in DMF)

A culture tube was charged with $NiCl_2$•$6H_2O$ (71.3 mg, 0.3 mmol) and ligand (80.5 mg, 0.3 mmol for di-*t*Bubipy (**L1**) or 99.7 mg, 0.3 mmol for bathophenanthroline (**L4**)). The tube was then evacuated and backfilled with argon from a balloon 3 times. DMF (6.0 mL) was added and the resulting mixture was stirred at room temperature for 3 hours to give a homogeneous green solution, which could be used for several days without appreciable deterioration.

Part II. Ni-Catalyzed Cross-Coupling Reaction



A culture tube was charged with TCNHPI redox-active ester (0.1 mmol, 1.0 equiv.), aryl boronic acid (0.3 mmol, 3.0 equiv.) and a stir bar. The tube was then evacuated and backfilled with argon from a balloon. This process was repeated for three times in total. 1,4-Dioxane (4.0 mL) was added and the resulting mixture was stirred for 1 minutes before Et_3N (139 μL, 10.0 equiv.) was added. The mixture was stirred for 2-5 minutes until becoming homogeneous. Then, a solution of $NiCl_2$•$6H_2O$/ligand (0.05M in DMF, 0.4 mL, 20 mol%) was added and the tube was immediately placed in a preheated 75 °C oil bath for 12 hours under stirring. *NOTE: It is very important that the entirety of the reaction mixture is submerged in the heated oil bath to ensure the success and reproducibility of the reaction.* After 12 hours, the reaction mixture was allowed to cool to room temperature. The mixture was then diluted with ether or EtOAc, washed with 0.1 M aqueous HCl (not for acid-sensitive substrates), water and brine successively. The organic layer was dried over Na_2SO_4 and concentrated under vacuum by rotary evaporator in a water bath at 35 – 40 °C. The crude product was purified by silica gel flash column chromatography or preparative TLC (PTLC) to

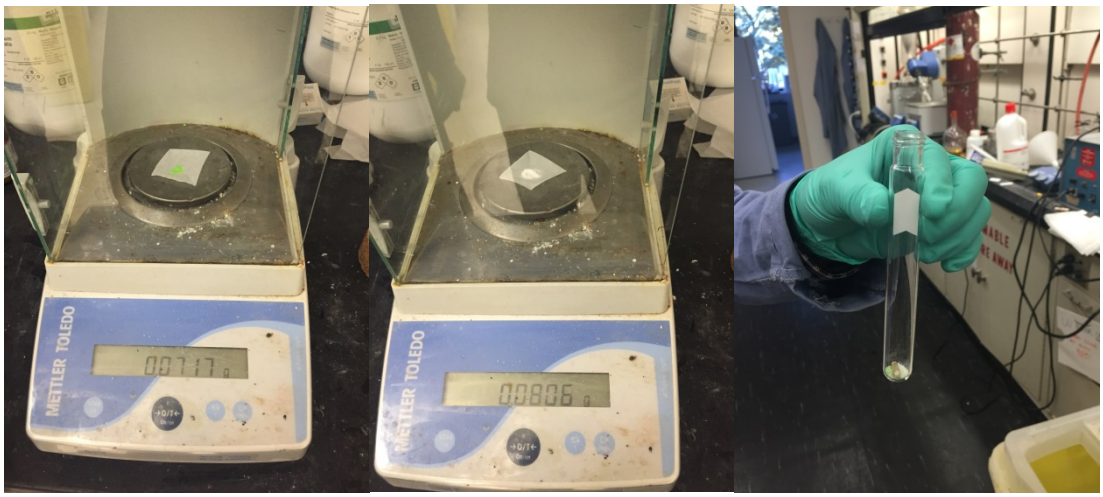
yield the pure compound.

Also see *Zero-Precaution Setup* section for a potentially more convenient setup for this reaction.

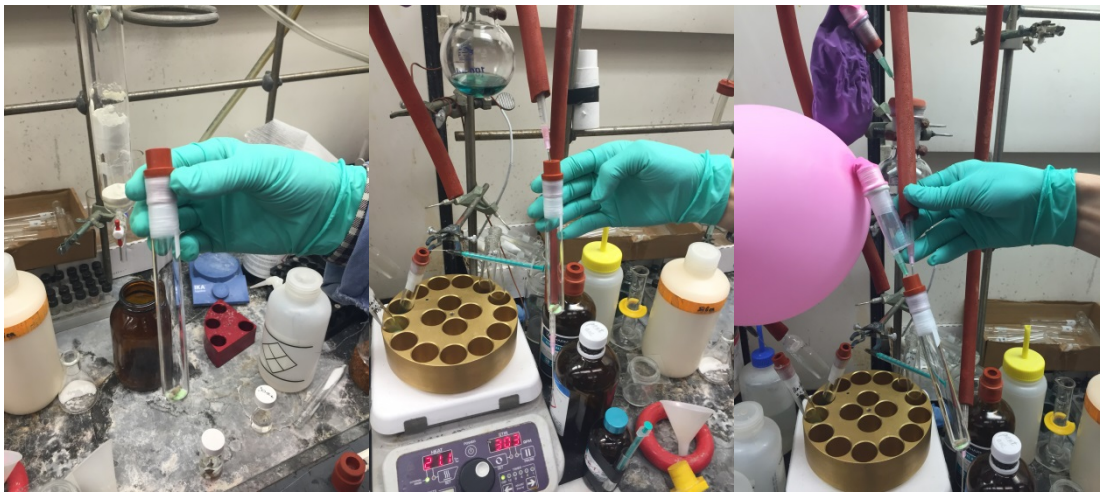
Graphical Supporting Information for the Ni-Catalyzed Cross-Coupling of Redox-Active Esters and Boronic Acids: *tert*-Butyl 4-(4-acetylphenyl) piperidine-1-carboxylate (22)

Part I. Preparation of $NiCl_2$•$6H_2O$/di-*t*Bubipy Stock Solution (0.05 M in DMF)

(Left) $NiCl_2$•$6H_2O$ (500 g, Sigma-Aldrich). **(Center)** di-*t*Bubipy (25 g, Sigma-Aldrich). **(Right)** DMF (1 L sealed bottle, Acros).



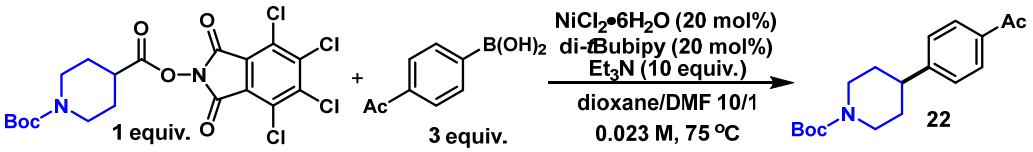
(Left) $NiCl_2$•$6H_2O$ (71 mg). **(Center)** di-*t*Bubipy (81 mg). **(Right)** $NiCl_2$•$6H_2O$ and di-*t*Bubipy were added to a medium-sized culture tube (without flame dry).

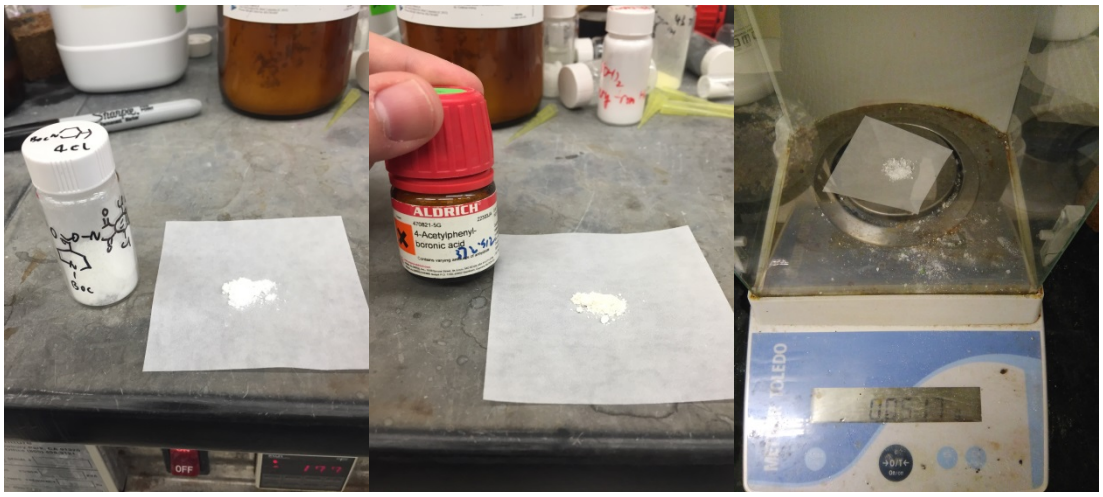


(Left) The tube is sealed with an inverted septum and parafilm. **(Center)** Evacuating the air from the tube. **(Right)** The tube is refilled with argon from a balloon. This was done 3 times in total.

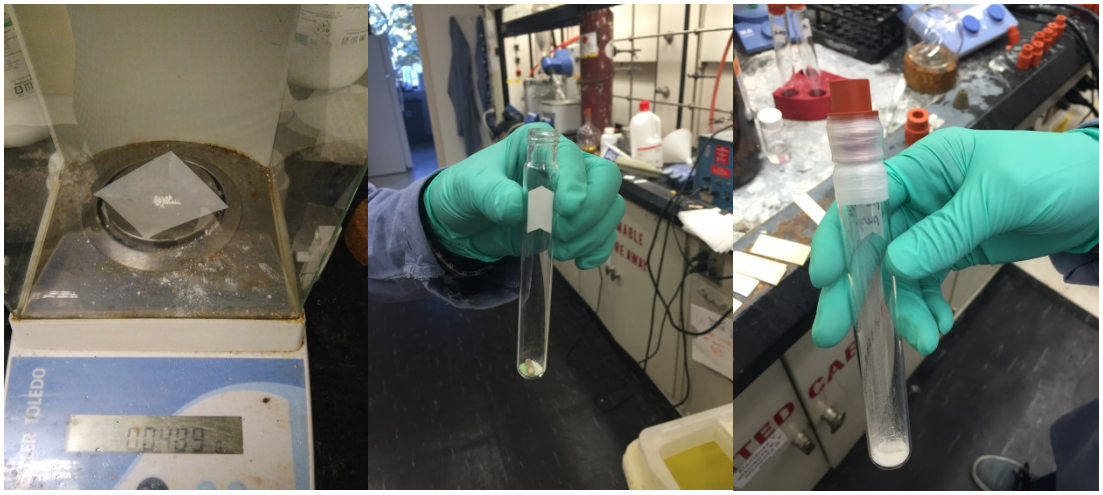
(Left) Addition of DMF (6.0 mL). **(Center)** After addition of DMF. **(Right)** After stirring for 3 hours. Note the clear and homogeneous green solution.

Part II. Ni-Catalyzed Cross-Coupling Reaction

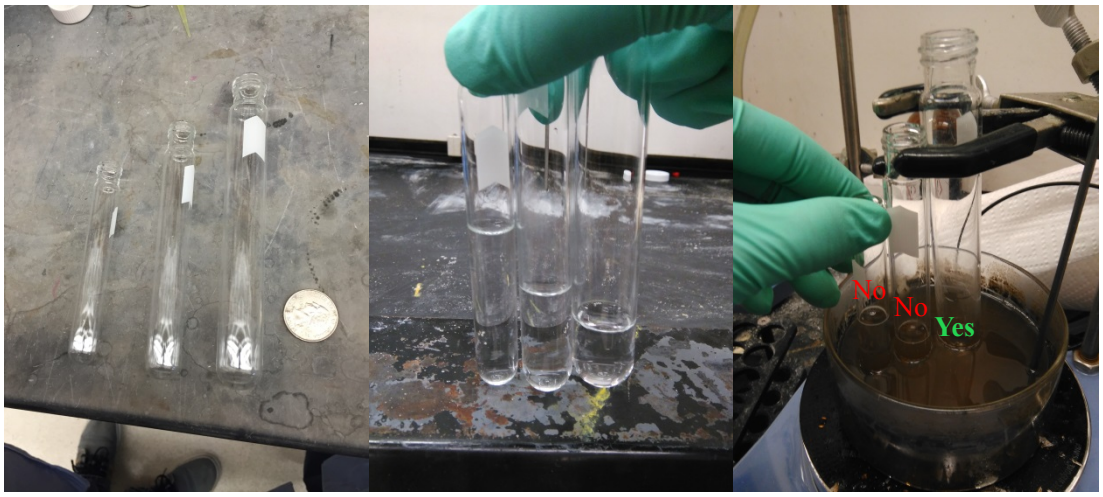




(Left) 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate. **(Center)** 4-acetylphenylboronic acid (Aldrich, off-white solid). **(Right)** 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate (51 mg, 0.1 mmol).

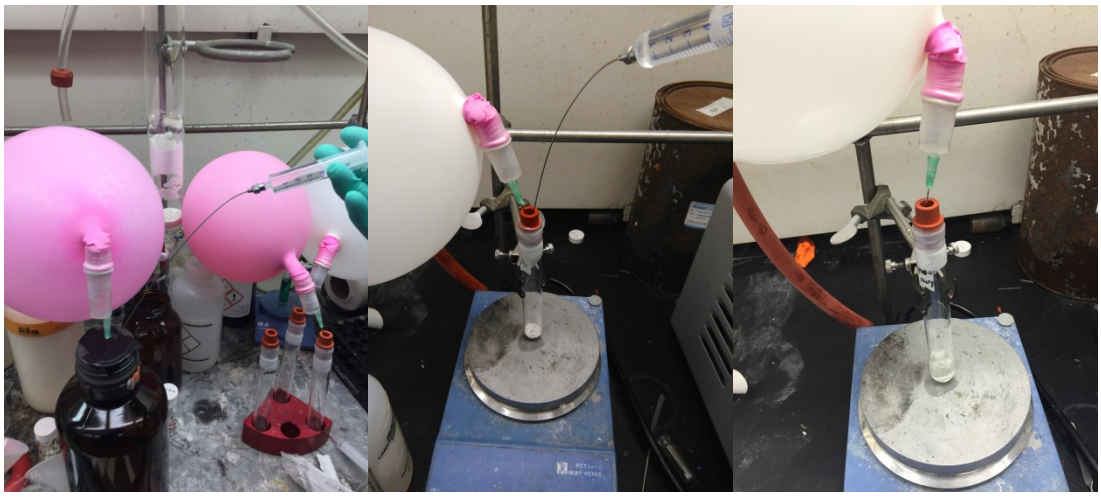


(Left) 4-acetylphenylboronic acid (49 mg, 0.3 mmol). **(Center)** Redox-active ester and boronic acid were added to a large-sized culture tube. **(Right)** The tube is sealed with an inverted septum and parafilm.

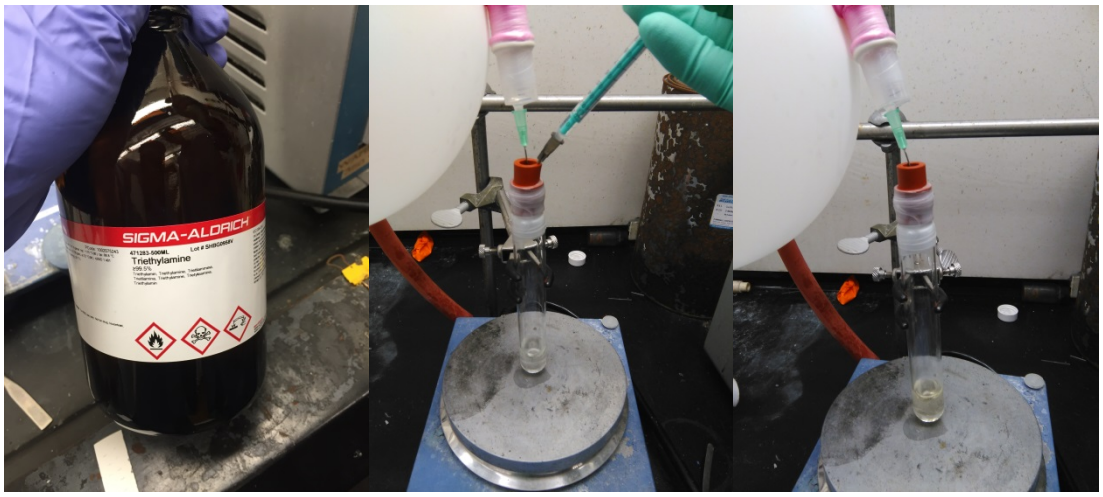


(Left) Three size of reaction tube: small, medium and large. **(Center)** The three different sized tubes containing 4.4 mL solvent each. **(Right)** Put them in the oil bath. *Note: we use the LARGE size for this reaction (the right one) to make sure the entirety of the reaction mixture is submerged in the heated oil bath. When we perform this reaction in the small or medium size tube, yield dropped 30% and 10% respectively because the mixture was not completely submerged.*

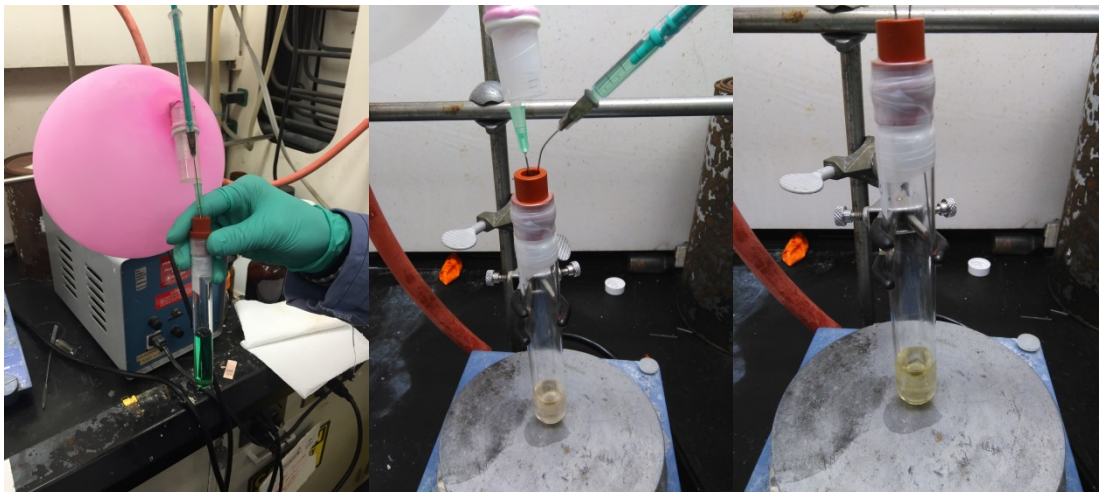
(Left) Evacuating the air from the tube. **(Center)** The tube is refilled with argon from a balloon. These steps are repeated for three times in total. **(Right)** 1,4-dioxane (1 L sealed bottle, Acros).



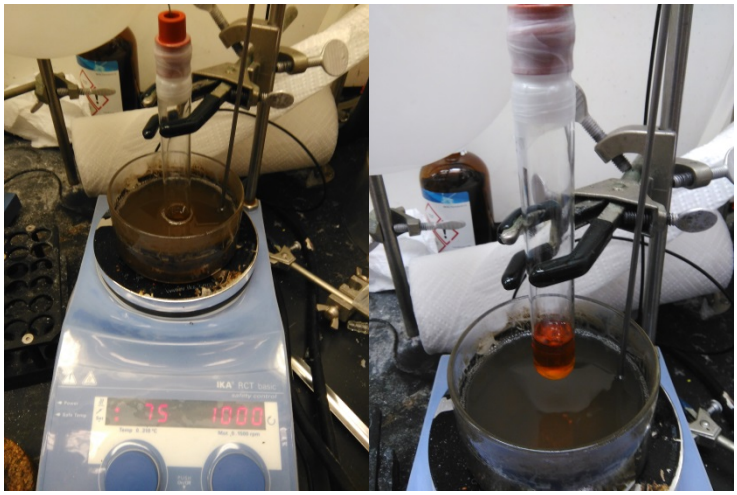
(Left) 1,4-dioxane is removed from the AcroSeal bottle. **(Center)** Addition of 1,4-dioxane. **(Right)** After addition, the mixture is stirred for 1 min.



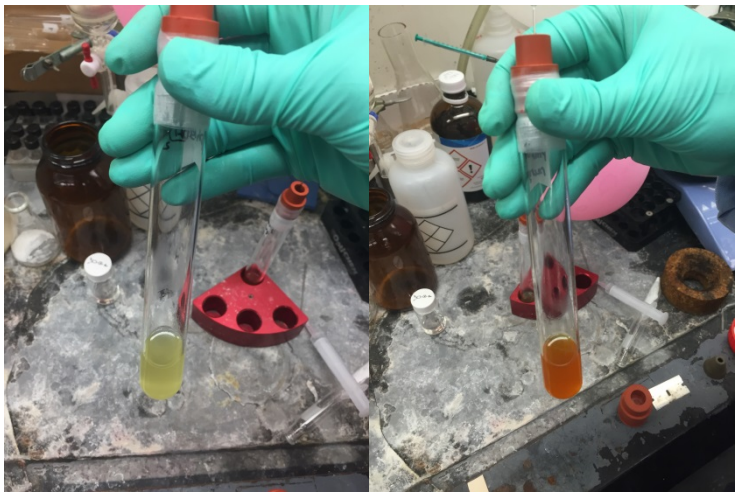
(Left) Triethylamine (500 mL sealed bottle, Sigma-Aldrich). **(Center)** Adding Et_3N (139 µL, 10.0 equiv.) to the reaction mixture. **(Right)** The reaction mixture was stirried for 2-5 min until it became homogenous. For this example, the mixture became homogeneous immediately. For some boronic acids, it could take a while, typically 2-5 min.



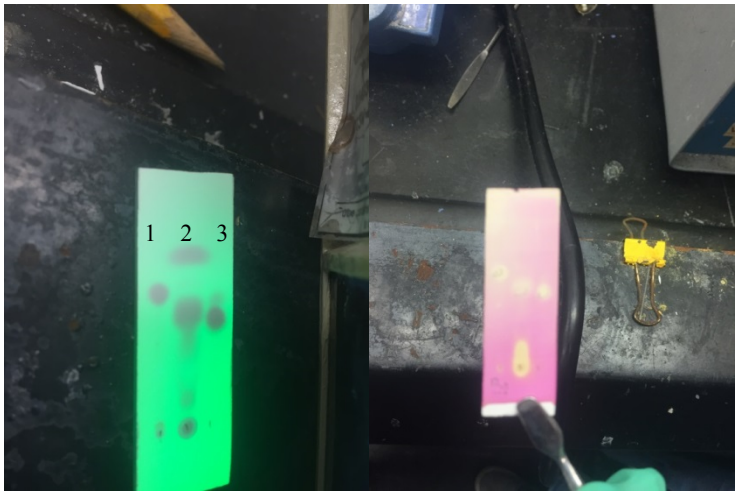
(Left) Prepared Ni/ligand complex stock solution in DMF. **(Center)** 0.4 mL Nickel complex DMF solution was adding into the tube while stirring. **(Right)** After addition.



(Left) After addition of Ni/ligand complex, directly placed in preheated 75 ºC oil bath. **(Right)** 5 min after heating, the reaction mixture turns red. Note: the red color changing is crucial for the success of the reaction.

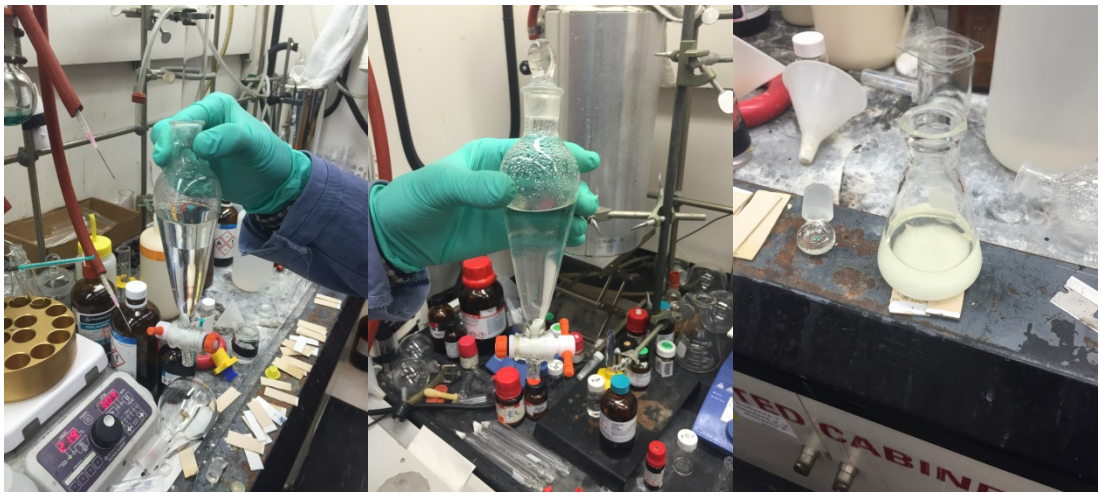


(Left) After 12 hours, the color turned light green, which is also observed for most substrates. **(Right)** For some other cases we have observed a reddish color.



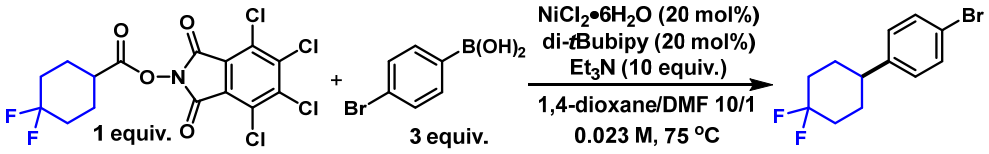
(Left) TLC under UV (hexanes/EtOAc 3:1), Lane 1: starting material, redox-active ester; Lane 2: reaction mixture (the front line spot is 4-acetylbenzene); Lane 3: pure product. **(Right)** After $KMnO_4$ stain.

(Left) Dilution with Et_2O. **(Center)** Transfer to a separatory funnel. **(Right)** 0.1 M HCl wash.



(Left) H_2O wash. (**Center**) Brine wash. **(Right)** Drying over Na_2SO_4.

Zero-Precaution Setup



Setup	Yield (%)[a]
General Procedure B	82
Procedure C	81
Procedure D	65[b]

[a]Yields determined by GC-FID with dodecane as internal standard, [b]Isolated yields.

Procedure C: following the *General Procedure B* except for both the precatalyst preparation and cross-coupling reaction were not setup and run under inert argon atmosphere. Setup and Run the reactions open-flask instead.

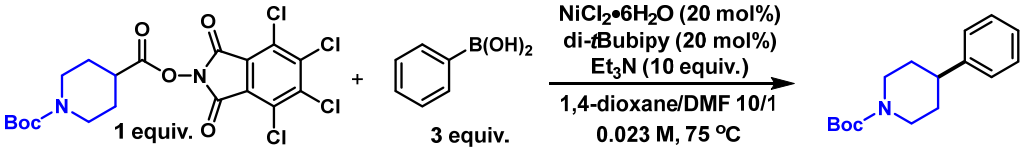
Procedure D: following *Procedure C* using wet dioxane, DMF, and Et_3N instead of anhydrous solvents.

Procedure C shows this reaction is not sensitive to air at all. However, we did not run every substrates open-flask due to unknown stabilities for various boronic acids. We believe this convenient zero-precaution setup could be potentially general for most substrates.

Procedure D shows that the reaction is somewhat sensitive to water but will still work in good yield with less than ideal quality of reagents.

Water Addition experiment

To better understand water tolerance of this reaction, we did water addition experiment and the results are listed below.



H_2O addition	Yield (%)[a]
0 equiv	90
1 equiv	89
2 equiv.	70
3 equiv	53
5 equiv	25

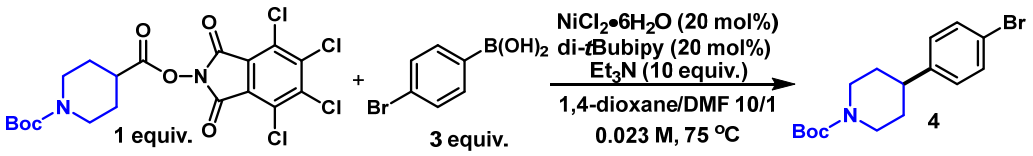
[a]Isolated yields.

General Procedure for the Gram-Scale Ni-Catalyzed Cross-Coupling Reaction: *tert*-Butyl 4-(4-bromophenyl)piperidine-1-carboxylate (4)

Part I. Preparation of $NiCl_2$•$6H_2O$/di-*t*Bubipy Stock Solution (0.05 M in DMF)

A 100 mL round bottom flask was charged with $NiCl_2$•$6H_2O$ (237.7 mg, 1.0 mmol) and di-*t*Bubipy (**L1**, 268.4 mg, 1.0 mmol). The flask was then evacuated and backfilled with argon from a balloon 3 times. DMF (20.0 mL) was added and the resulting mixture was stirred at room temperature for 3 hours to give a homogeneous green solution.

Part II. Ni-Catalyzed Cross-Coupling Reaction

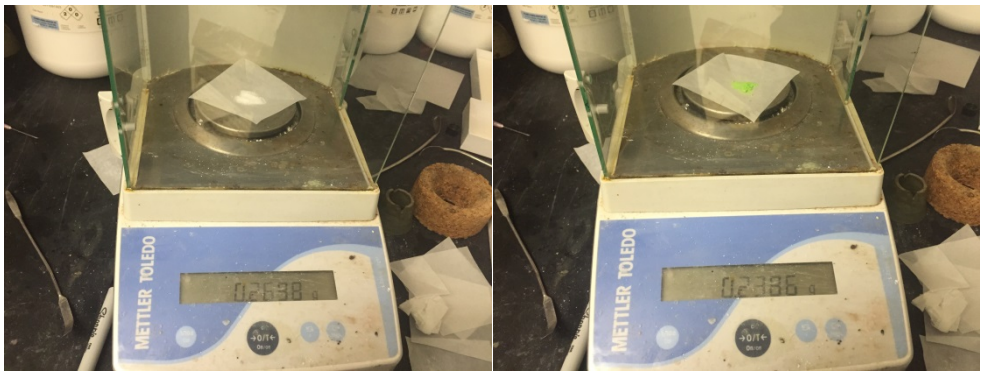


A 250 mL three-necked flask equipped with a thermometer was charged with 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate (1.28g, 2.5 mmol, 1.0 equiv.), 4-bromophenyl boronic acid (1.50 g, 3.0 equiv.) and a stir bar. The flask was then evacuated and backfilled with argon 3 times. Dioxane (100 mL) was added, and the resulting mixture was stirred for 2 minutes before being charged with Et_3N (3.5 mL, 10.0 equiv.). The mixture was placed into a preheated 75 °C oil bath. After the inner temperature of the solution reached 75 °C indicated by thermometer, a solution of $NiCl_2$•$6H_2O$/di-*t*Bubipy (0.05M in DMF, 10 mL, 20 mol%) was added in one portion. The reaction mixture immediately turned red and was stirred at 75 °C for 12 hours. The reaction mixture was cooled down to room temperature, and 1,4-dioxane was removed by rotary evaporator. The residue was diluted with Et_2O, washed with 0.1 M HCl, water, and brine successively. The organic layer was dried over Na_2SO_4 and concentrated under vacuum by rotary evaporator in a water bath at 35 °C. The crude product was purified by silica gel flash column chromatography (hexanes/EtOAc 9:1) and afforded the pure compound **4** in 61% yield (average of two runs, first run 516 mg, 61 %, second run 508 mg, 60%).

Graphical Supporting Information for the Gram-Scale Ni-Catalyzed Cross-Coupling Reaction: *tert*-Butyl 4-(4-bromophenyl)piperidine-1-carboxylate (4)

Part I. Preparation of $NiCl_2$•$6H_2O$/di-*t*Bubipy Stock Solution (0.05 M in DMF)

(Left) $NiCl_2$•$6H_2O$ (500 g, Sigma-Aldrich) used in this reaction. **(Center)** di-*t*Bubipy (25 g, Sigma-Aldrich). **(Right)** DMF (1 L bottle, Acros).

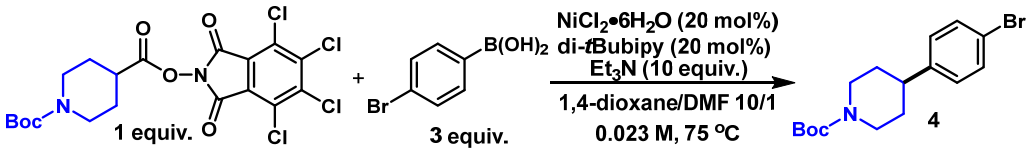


(Left) di-*t*Bubipy (270 mg). **(Right)** $NiCl_2$•$6H_2O$ (239 mg).

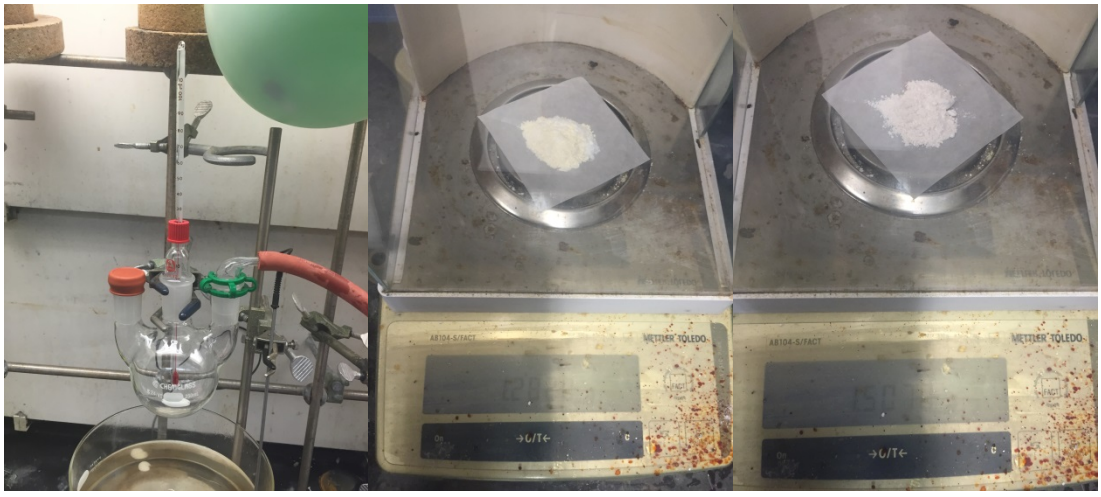
(**Left**) di-*t*Bubipy and $NiCl_2$•$6H_2O$ in a 100 mL round-bottom flask (not flame-dried) with a stir bar. (**Center**) The flask was sealed with a septum, wrapped with parafilm, and evacuated under vacuum. **(Right)** Refill the flask with argon. This was done 3 times in total.

(Left) Addition of 20 mL DMF into the flask. **(Center)** After addition of 20 mL of DMF. **(Right)** After stirring for 3 hours. Note the clear and homogeneous green solution.

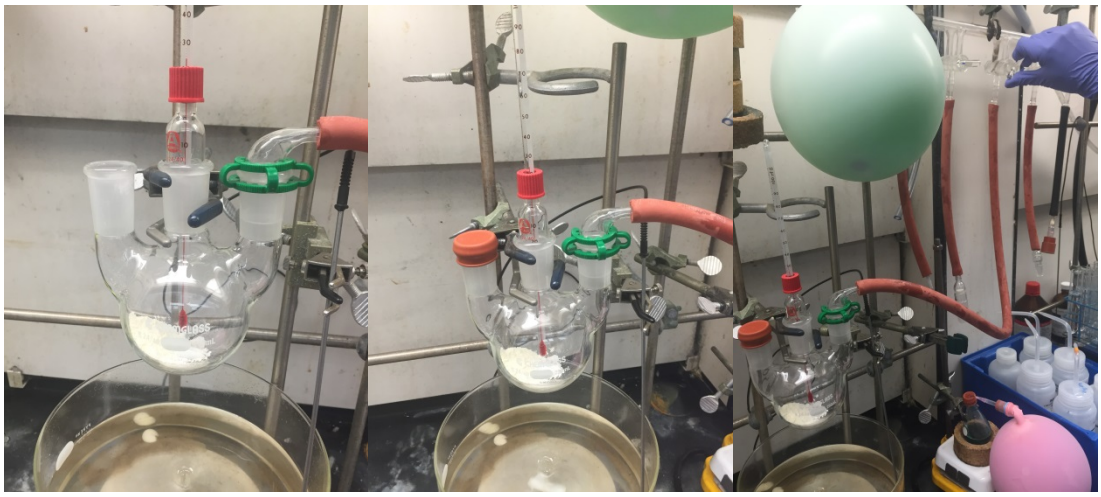
Part II. Ni-Catalyzed Cross-Coupling Reaction



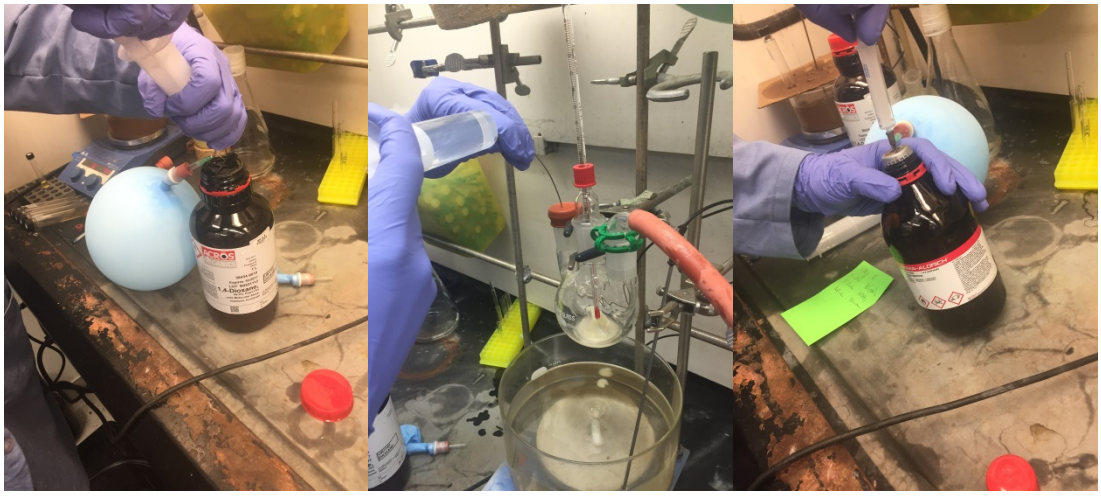
(Left) 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate (white powder) and 4-bromophenyl boronic acid (25 g, Combi-Blocks). **(Center)** 1,4-dioxane (1 L bottle, Acros). **(Right)** Et_3N (500 mL, Sigma-Aldrich).



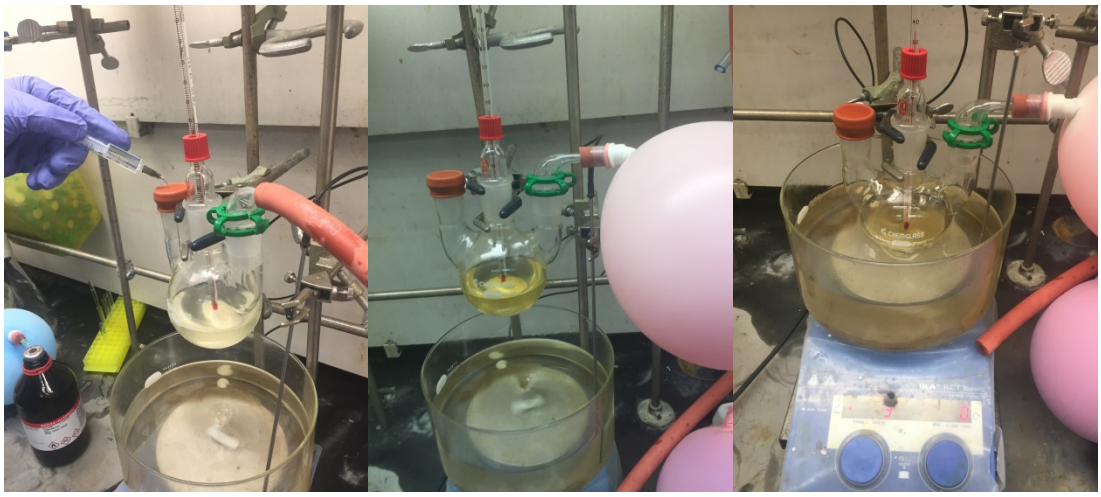
(Left) 250 mL three-necked flask equipped with thermometer. **(Center)** 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4- dicarboxylate (1.28 g, 2.5 mmol). **(Right)** 4-bromophenyl boronic acid (1.50 g, 3.0 equiv.).



(Left) Transfer 1-(*tert*-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate and 4-bromophenyl boronic acid to the three-necked flask. **(Center)** Evacuated the flask under vacuum. **(Right)** Refill the flask with argon. This process was repeated for three times in total.

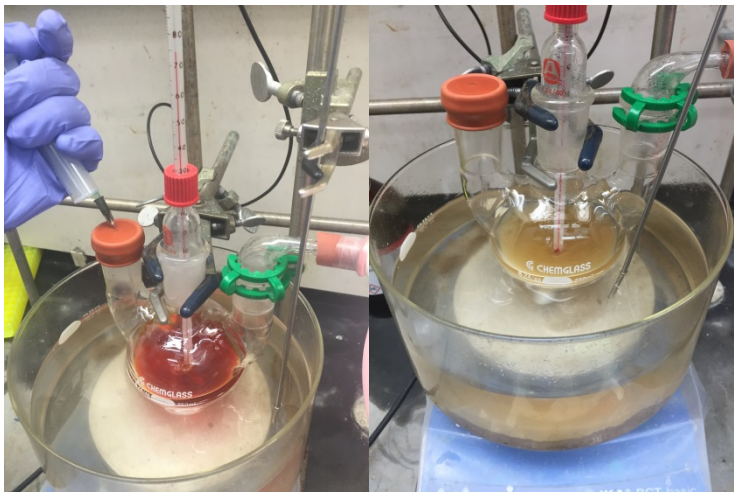


(Left) 1,4-dioxane (100 mL). **(Center)** Adding 1,4-dioxane to the 250 mL three-necked flask. **(Right)** Et_3N (3.47 mL).

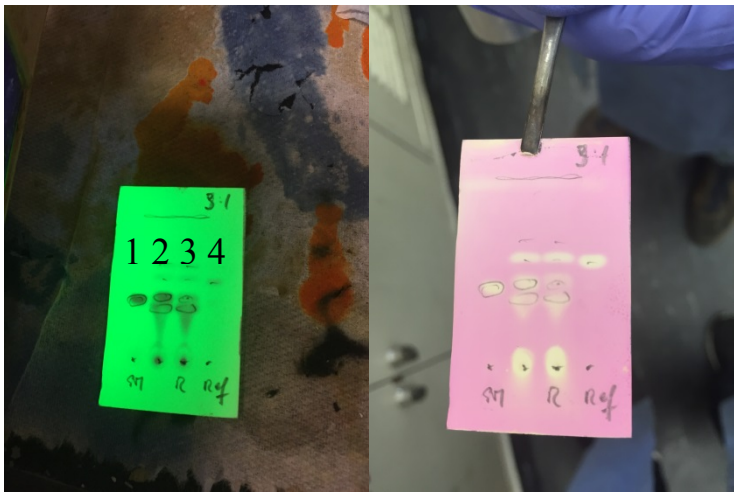


(Left) Addition of Et_3N (3.47 mL). **(Center)** After addition of Et_3N. (**Right**) The flask was placed in a preheated 75 °C oil bath.

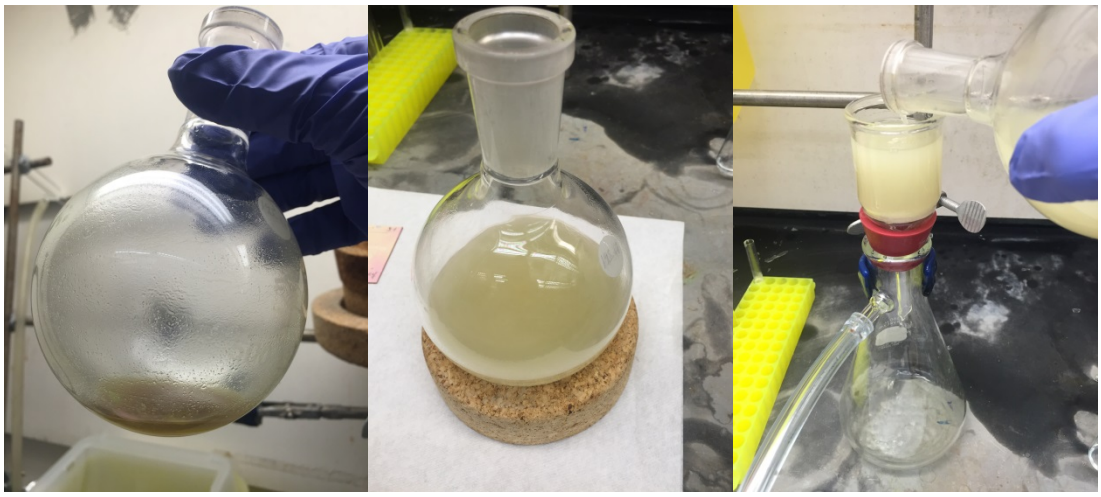
(Left) Internal temperature reached 75 °C indicated by thermometer. **(Center)** Adding Ni/ligand complex (0.05 M in DMF, 10.0 mL, 20 mol%). (**Right**) Reaction mixture immediately turned red after first drop of Ni/ligand complex.



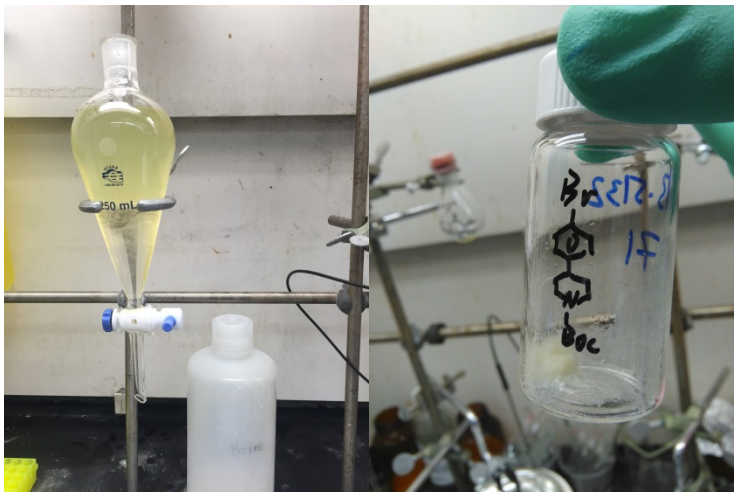
(Left) Completed addition of Ni/Ligand solution. (**Right**) Reaction mixture after stirring for 3 hours.



(Left) TLC under UV (hexanes/EtOAc 3:1), Lane 1: starting material, redox-active ester; Lane 2: co-spot of starting material and reaction mixture; Lane 3: reaction mixture. Lane 4: pure product. **(Right)** The same TLC after $KMnO_4$ stain.



(Left) Residue after 1,4-dioxane was removed by rotavapor. **(Center)** Dilution with ether. **(Right)** Vacuum filtration.



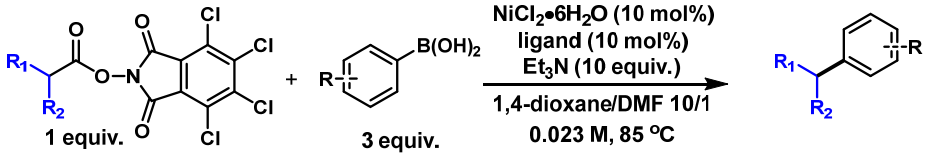
(Left) Wash with brine. **(Right)** Pure product after flash column chromatography.

General Procedure for Cross-Coupling of Alkyl Redox-Active Esters and Aryl Boronic Acids with 10 mol% Nickel/ligand (General Procedure C)

Part I. Preparation of $NiCl_2$•$6H_2O$/di-*t*Bubipy (L1) Stock Solution (0.025 M in DMF)

A culture tube was charged with $NiCl_2$•$6H_2O$ (35.7 mg, 0.15 mmol) and di-*t*Bubipy (40.3 mg, 0.15 mmol). The tube was then evacuated and backfilled with argon from a balloon 3 times. DMF (6.0 mL) was added and the resulting mixture was stirred at room temperature for 3 hours to give a homogeneous green solution, which could be used for several days without appreciable deterioration.

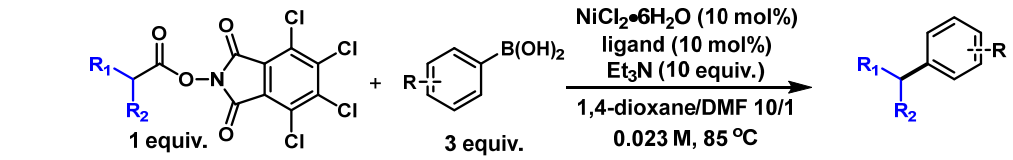
Part II. Ni-Catalyzed Cross-Coupling Reaction

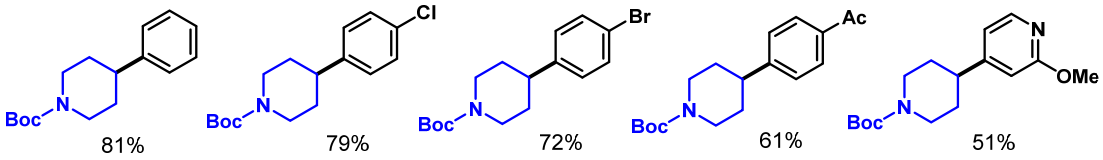


A culture tube was charged with TCNHPI redox-active ester (0.1 mmol, 1.0 equiv.), aryl boronic acid (0.3 mmol, 3.0 equiv.) and a stir bar. The tube was then evacuated and backfilled with argon from a balloon 3 times. 1,4-Dioxane (4.0 mL) was added and the resulting mixture was stirred for 1 minute before Et_3N (139 μL, 10.0 equiv.) was added. The mixture was stirred for 2-5 minutes until becoming homogeneous. Then, a solution of $NiCl_2$•$6H_2O$/ di-*t*Bubipy (0.025M in DMF, 0.4 mL, 10 mol%) was added and the tube was immediately placed in a preheated 85 °C oil bath for 12 hours under stirring. *NOTE: It is very important that the entirety of the reaction mixture is submerged in the heated oil bath to ensure the success and reproducibility of the reaction.* After 12 hours, the reaction mixture was allowed to cool to room temperature, diluted with ether or EtOAc, washed with 0.1 M aqueous HCl (not for acid-sensitive substrates), water and brine successively. The organic layer was dried over Na_2SO_4 and concentrated under vacuum by rotary evaporator in a water bath at 35 – 40 °C. The crude product was purified by silica gel flash column chromatography or preparative TLC (PTLC) to yield the pure compound.

Examples of Cross-Coupling with 10 mol% Nickel

We demonstrated this 10 mol% nickel catalyzed cross-coupling with 5 examples based on *General Procedure C*.



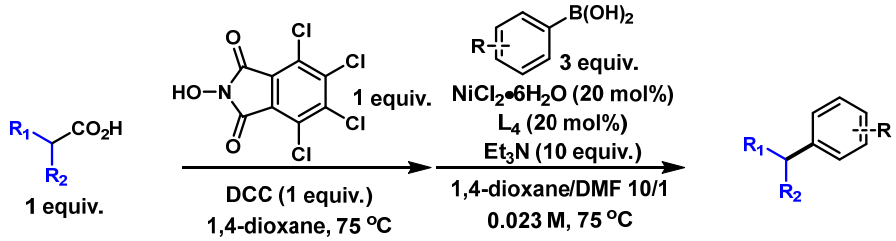


General Procedure for *in situ* Ni-Catalyzed Cross-Coupling of Alkyl Carboxylic Acids and Aryl Boronic Acids (General Procedure D)

Part I. Preparation of $NiCl_2$•$6H_2O$/bathophenanthroline (L4) Stock Solution (0.05 M in DMF)

A culture tube was charged with $NiCl_2$•$6H_2O$ (71.3 mg, 0.3 mmol) and bathophenanthroline (99.7 mg, 0.3 mmol). The tube was then evacuated and backfilled with argon from a balloon 3 times. DMF (6.0 mL) was added and the resulting mixture was stirred at room temperature for 3 hours to give a homogeneous green solution, which could be used for several days without appreciable deterioration.

Part II. Ni-Catalyzed Cross-Coupling Reaction



A culture tube was charged with alkyl carboxylic acid (1.0 equiv.), *N*-hydroxy-tetrachlorophthalimide (1.0 equiv.), *N,N′*-dicyclohexylcarbodiimide (1.0 equiv.) and a stir bar. The tube was then evacuated and backfilled with argon from a balloon. This process was repeated for three times in total. 1,4-Dioxane (3.0 mL) was added and the resulting mixture was placed in a preheated 75 °C oil bath and stirred until completion as indicated by TLC (typically 30-45 minutes). Aryl boronic acid (3 equiv.) was added quickly and more 1,4-dioxane (1 mL) was added for rinse. Et_3N (139 μL, 10.0 equiv.) and a solution of $NiCl_2$•$6H_2O$/**L4** (0.05M in DMF, 0.4 mL, 20 mol%) was added successively and the tube was immediately placed in a preheated 75 °C oil bath for 12 hours under stirring. *NOTE: It is very important that the entirety of the reaction mixture is submerged in the heated oil bath to ensure the success and reproducibility of the reaction.* After 12 hours, the reaction mixture was allowed to cool to room temperature. The mixture was then diluted with ether or EtOAc, washed

with 0.1 M aqueous HCl (not for acid-sensitive substrates), water and brine successively. The organic layer was dried over Na_2SO_4 and concentrated under vacuum by rotary evaporator in a water bath at 35 – 40 °C. The crude product was purified by silica gel flash column chromatography or preparative TLC (PTLC) to yield the pure compound.

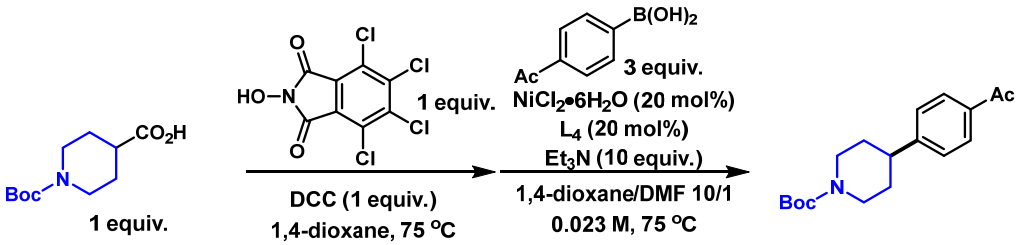
Graphical Supporting Information for *in situ* Ni-Catalyzed Cross-Coupling of Alkyl Carboxylic Acids and Aryl Boronic Acids: *tert*-Butyl 4-(4-acetylphenyl) piperidine-1-carboxylate (22)

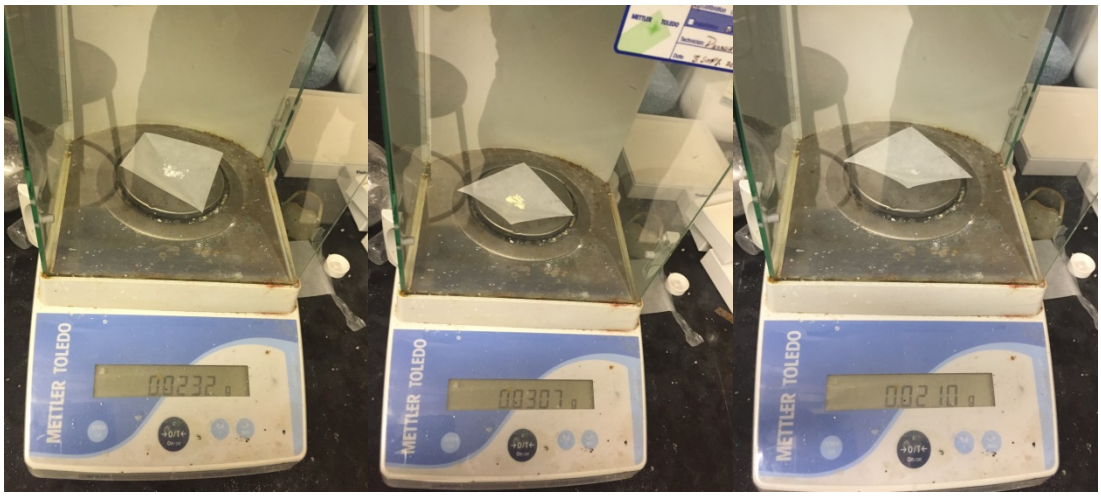
Part I. Preparation of $NiCl_2•6H_2O$/bathophenanthroline Stock Solution (0.05 M in DMF)

(Left) $NiCl_2•6H_2O$ (72 mg). **(Center)** bathophenanthroline (100 mg). **(Right)** $NiCl_2•6H_2O$ and bathophenanthroline in vial.

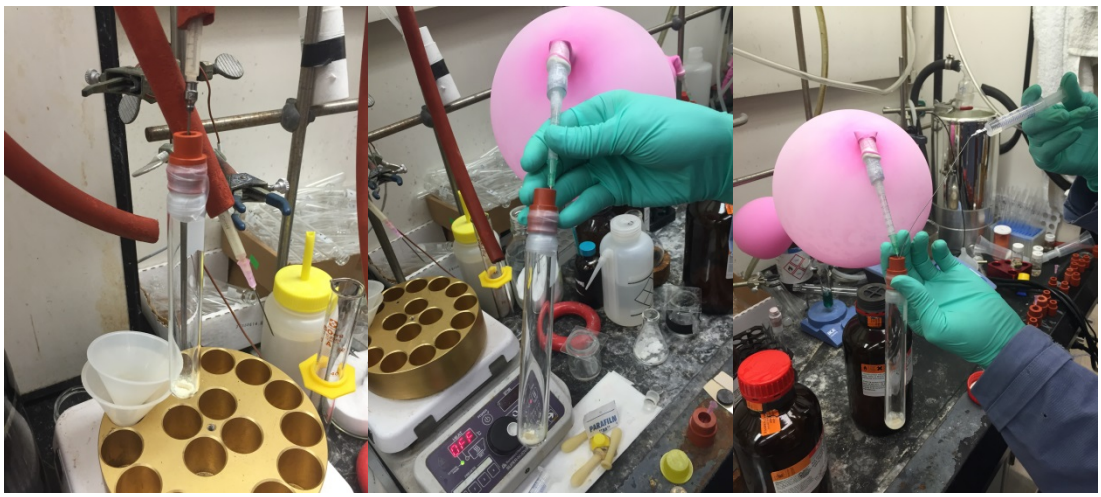
(Left) The flask with a stir bar was sealed with a septum, wrapped with parafilm, evacuated under vacuum and refilled with argon. This was done 3 times in total. **(Center)** Add DMF (6 mL) into the vial. **(Right)** After stirring for 3 hours at room temperature.

Part II. Ni-Catalyzed Cross-Coupling Reaction



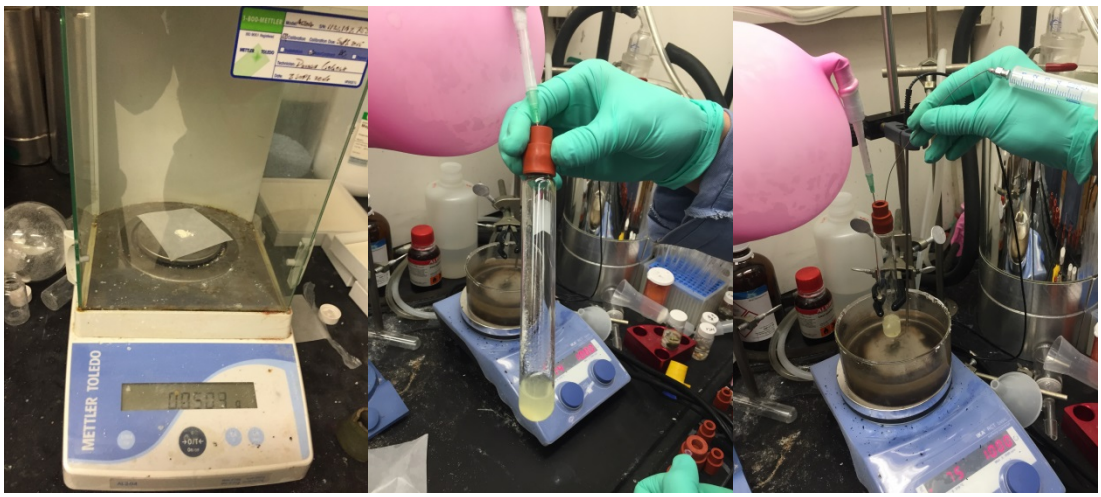


(Left) 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid (23 mg, 0.1 mmol). **(Center)** *N*-hydroxy-tetrachlorophthalimide (30 mg, 0.1 mmol). **(Right)** *N,N′*-dicyclohexylcarbodiimide (21 mg, 0.1 mmol).

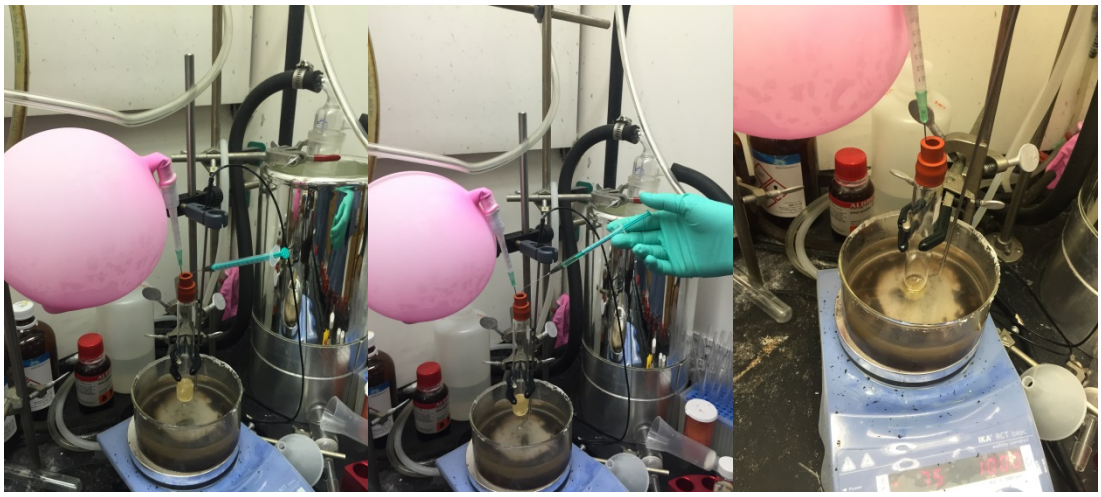


(Left) Put them into a vial with a stir bar. The vial was sealed with a septum, wrapped with parafilm and evacuated under vacuum. **(Center)** Refill the vial with argon. This was done 3 times in total. **(Right)** Add 1,4-dioxane (3 mL) into the vial.

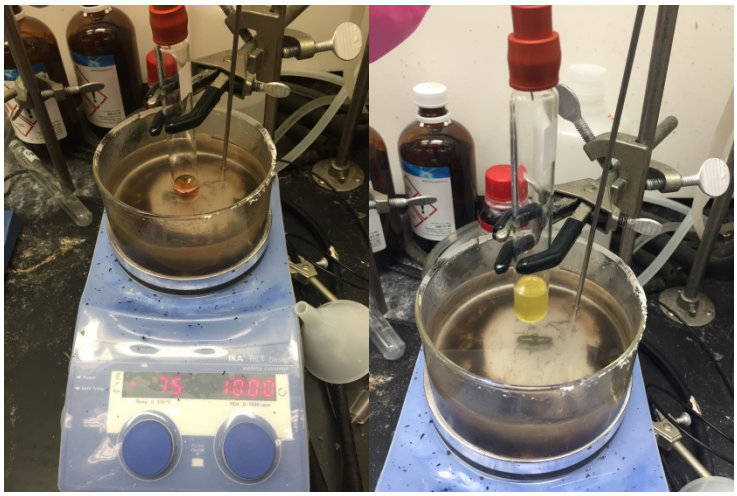
(Left) The vial was put in a preheated 75 ^{o}C oil bath. **(Center)** After heating for 30 min. **(Right)** TLC (hexanes/EtOAc 2:1) under UV indicates completion of the redox-active ester formation. Lane 1: starting material of *N*-hydroxy-tetrachlorophthalimide; Lane 2: co-spot of starting material and reaction mixture; Lane 3: reaction mixture.



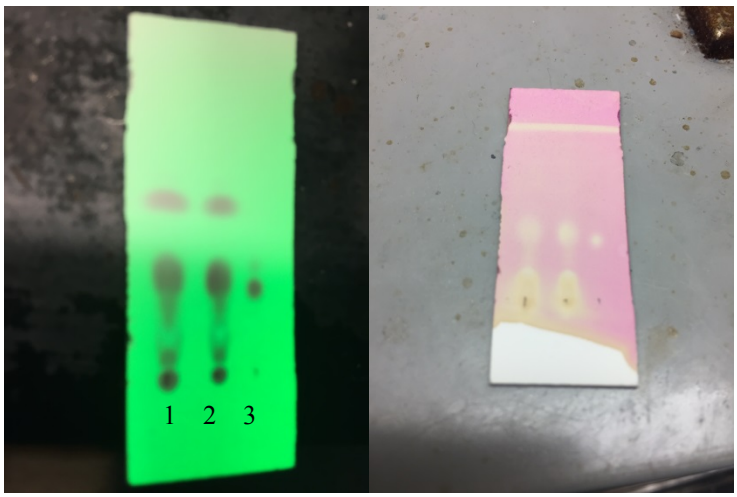
(Left) 4-Acyl phenyl boronic acid. **(Center)** Add 4-Acyl phenyl boronic acid to reaction mixture quickly. **(Right)** Add 1,4-dioxane (1 mL) for rinse.



(Left) Add Et_3N (0.14 mL). **(Center)** Add $NiCl_2$•$6H_2O$/bathophenanthroline stock solution (0.4 mL). **(Right)** Place the vial in a preheated 75 ^oC oil bath immediately.



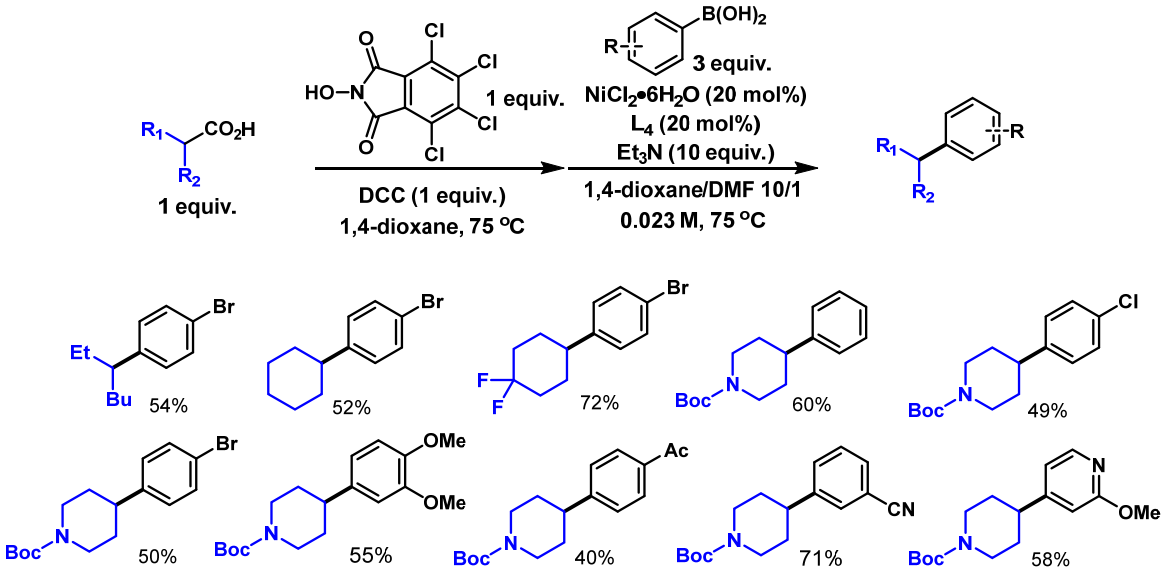
(Left) After heating for 5 min, the reaction mixture turned red. **(Right)** Reaction mixture after stirring for 12 hours.



(Left) TLC under UV (hexanes/EtOAc 5:1), Lane 1: reaction mixture; Lane 2: co-spot; Lane 3: desired product. **(Right)** The same TLC after $KMnO_4$ stain.

Examples of *In Situ* Cross-Coupling of Alkyl Carboxylic Acids and Aryl Boronic Acids

We demonstrated this *in situ* cross-coupling of alkyl acids and aryl boronic acids with 10 examples based on *General Procedure D*.



Troubleshooting: Frequently Asked Questions

Part I. Redox-Active Ester Synthesis

Question 1:

I am trying to get high-resolution mass spec data for my redox-active ester, but I am having trouble. What do I do?

Answer:

For these types of compounds, obtaining HRMS data by ESI is difficult. We normally rely heavily on ^{1}H and ^{13}C NMR data to determine if we have the correct compound. If necessary, a crystal structure can typically be obtained for most redox-active esters.

Question 2:

Can you use DCC or EDC-HCl or other common coupling reagents like HATU/PyBOP etc. to synthesis the TCNHPI redox-active esters?

Answer:

We occasionally used DCC or EDC-HCl and they gave similar yields while we never tried HATU/PyBOP.

For other questions regarding synthesis, purification, characterization, stability and storage of the redox-active ester, please address to our previous paper[2] for fully-detailed answers.

Part II. Nickel-Catalyzed Cross-Coupling

Question 1:

Have you tried any other nickel sources for this reaction?

Answer:

During our initial screening, we tried several nickel sources, such as $NiCl_2$•glyme, $NiBr_2$, NiI_2, $Ni(OTf)_2$, $Ni(acac)_2$ etc. As soon as we realized $NiCl_2$•$6H_2O$ worked well for this reaction, we focused the optimization to $NiCl_2$•$6H_2O$. When we finally came up with the best solvent (1,4-dioxane/DMF 10/1), we did not re-screen the nickel

sources due to the inexpensive nature of $NiCl_2$•$6H_2O$ ($9.5/mol).

Question 2:

How do you monitor the reactions?

Answer:

We monitor the reactions by a combination of TLC (and appropriate staining or UV visualization), GC/MS, and LC/MS. For smaller molecules, GC/MS typically shows the formation of the product. For compounds containing basic nitrogen atoms, LC/MS works well. *N*-Boc-4-piperidyl derivatives on LC/MS typically shows [M+1], [M-99] (de-Boc), or very rarely [M-55] (de-*t*Bu of Boc).

Question 3:

Do I need a glovebox to run this reaction?

Answer:

We do not set up or run the reaction in a glovebox. A glovebox is not necessary to run this reaction. We usually did degas-refill three times for the culture tube before adding 1,4-dioxane. We don't degas for the solvents or Et_3N. You also don't need to be very cautious of water. As mentioned in the *Zero-Precaution Setup* section, we can even setup and run the reaction open-flask and see basically no erosion in yield.

Question 4:

Is it necessary to purify the boronic acids used in this reaction?

Answer:

It is not necessary to purify the boronic acids before running the reaction. We directly use the commercial boronic acids without any purification. However, we recommend to analyze the boronic acids by ^1H NMR to make sure it is the boronic acid itself rather than the corresponding hydrate or something else. Low levels of hydrate in the boronic acids don't affect the reaction much, but elevated amount of water could lead to a diminished yield due to competing hydrolysis of the redox-active ester (See *Water Addition Experiment* for more details).

Question 5:

Can the reaction be run only in 1,4-dioxane, or is the DMF cosolvent necessary?

Answer:

It is detrimental to the yield if the reaction is only run in 1,4-dioxane.

Question 6:

Is it necessary to run the reaction for a 12 hours period, or can I quench it sooner?

Answer:

The reaction can be stopped sooner if there is complete consumption of the redox-active ester starting material. The best way to determine if the starting material has been completely consumed is by TLC analysis with a co-spot of the reaction mixture and starting material.

Question 7:

The catalyst solution precipitates, can I still use it?

Answer:

We sometimes observe precipitation of the catalyst solution after placing for some time, especially for $NiCl_2$•$6H_2O$/bathophenanthroline. We don't use it any more after it precipitates.

Question 8:

Are there any indicative color changes during the reaction?

Answer:

We often observe that the reaction mixture becomes red upon heating. After a long period of 12 hours, the mixture typically turns to a green or yellow color.

Question 9:

How do I work up the reaction?

Answer:

We work up the reaction by diluting the reaction with Et_2O or EtOAc. We then wash

the organic layer with 0.1 M HCl, water, and brine. For acid-sensitive substrates, the 0.1 M HCl wash is omitted and only water and brine wash are used. The organic layer is then dried and concentrated on a rotary evaporator. The crude product often contains solids that are tetrachlorophthalimide byproducts, which can be easily removed by flash column chromatography.

Question 10:

How do I purify my product?

Answer:

We use both silica gel flash column chromatography and PTLC. Reverse-phase HPLC can be used for very polar compounds.

Question 11:

How do I determine which redox-active ester to use?

Answer:

It is necessary to use the *N*-hydroxy-tetrachlorophthalimide ester for this reaction.

Question 12:

What other possible byproducts could be observed in this reaction?

Answer:

We occasionally observed the decarboxylated product, ester formation, and arylation on 1,4-dioxane.

Question 13:

Can I use other coupling reagent instead of DCC in the *in situ* cross coupling?

Answer:

The cross coupling is not working at all while using HATU, PyBOP or T3P as coupling reagent. We recommend to use diimide-type coupling reagent, among which DCC can get a better yield than DIC.

Question 14:

Is the *in situ* cross coupling procedure general to every substrate?

Answer:

So far the *in situ* procedure is working for every substrate we tried and we believe it's general. However, the yields droped up to 30% for some substrates. We recommend to try the cross coupling reaction with isolated redox-active ester when the *in situ* procedure gives you a low yield.

Question 15:

I obtained the product, but the yield is not satisfactory for my purposes. What do you recommend I try to optimize the reaction?

Answer:

For optimization, we recommend the following:

1. Try heating the reaction at temperatures higher than 75 °C. We found empirically that primary alkyl substrates perform better at 85 °C.

2. Make sure that the internal temperature of the reaction is the desired temperature. This is particularly important on larger scale.

3. Check the quality of boronic acid. We find that most boronic acids are contaminated with their hydrate. As mentioned in *Question 4* and *Water Addition Experiment*, low levels of hydrate in the boronic acids do not affect this reaction much, but elevated amount of water could lead to a diminished yield due to competing hydrolysis of the redox-active ester.

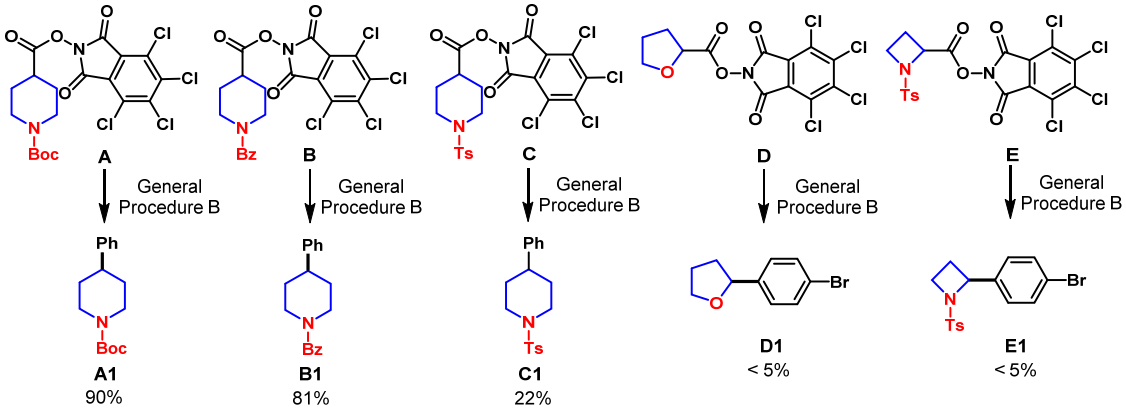
4. Add more equivalents of boronic acid.

5. Try different bipyridine- or phenanthroline-type ligands. We found that bathophenanthroline works quite well for some of our substrates (**8**, **11**, **27**) as well as the *in situ* cross-coupling from alkyl acids.

6. Try a higher loading of Ni precatalyst.

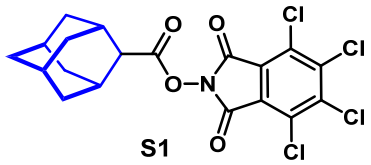
Question 16: Do you have some examples of "hydroytically labile" activated esters in the discussion of limitations?

Answer: As seen below, the cross coupling yields with redox-active esters **A, B, C** are 90%, 81% and 22% respectively. The major byproducts we obtained were the corresponding alkyl carboxylic acids. We assume the relative stability of redox-active esters is A>B>C. We believe the electron-withdrawing nature of Ts and Bz contributes to hydrolytic lability but we can't rule out that a downstream process after interaction with the Ni-catalyst is also responsible for this trend. In addition, compounds D and E also give very low yield of coupling product with the corresponding acid as the major byproduct.



Experimental Procedures and Characterization Data for Redox-Active Esters

Compound S1



S1

4,5,6,7-Tetrachloro-1,3-dioxoisoindolin-2-yl adamantane-2-carboxylate (S1)

Following the General Procedure A on 1.0 mmol scale. Purification by flash column chromatography (silica gel, CH_2Cl_2) and recrystallized from CH_2Cl_2/MeOH afforded 223 mg (48%) of the title compound **S1**.

Physical State: colorless needles. **m.p.** 193-196 °C.

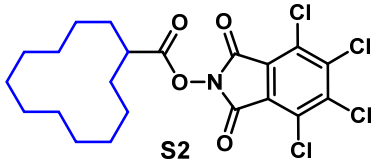
R_f = 0.4 (15:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.08 (p, *J* = 2.0 Hz, 1H), 2.48 (q, *J* = 2.9 Hz, 2H), 2.11 – 2.05 (m, 2H), 1.99 – 1.89 (m, 4H), 1.87 – 1.81 (m, 2H), 1.80 – 1.76 (m, 2H), 1.75 – 1.69 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 170.15, 158.03, 141.07, 130.53, 124.97, 47.61, 37.95, 37.22, 33.26, 29.86, 27.34, 27.22.

HRMS (ESI-TOF): High resolution mass spectroscopic data could not be obtained for this compound.

Compound S2



S2

4,5,6,7-Tetrachloro-1,3-dioxoisoindolin-2-yl cyclododecanecarboxylate (S2)

Following the General Procedure A on 1.0 mmol scale. Purification by flash column chromatography (silica gel, CH_2Cl_2) and recrystallized from CH_2Cl_2/MeOH afforded 306 mg (62%) of the title compound **S2**.

Physical State: off-white solid. **m.p.** 159-161 °C.

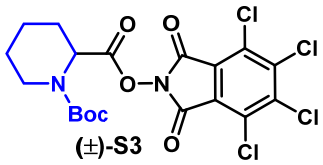
R_f = 0.6 (15:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 2.93 – 2.85 (m, 1H), 1.85 – 1.74 (m, 4H), 1.57 – 1.49 (m, 2H), 1.52 – 1.32 (m, 16H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 172.41, 157.89, 141.11, 130.57, 124.93, 38.26, 26.81, 23.82, 23.76, 23.60, 23.48, 22.20.

HRMS (ESI-TOF): High resolution mass spectroscopic data could not be obtained for this compound.

Compound (±)-S3



1-(tert-Butyl) 2-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,2-dicarboxylate ((±)-S3)

Following the General Procedure A on 5.0 mmol scale. Purification by flash column chromatography (silica gel, 3:1:1 hexanes:CH_2Cl_2:EtOAc) and recrystallized from CH_2Cl_2/MeOH afforded 1.96 g (78%) of the title compound **(±)-S3.**

Physical State: yellow solid. **m.p.** 180-183 °C.

R_f = 0.4 (6:1 hexanes:EtOAc).

Mixture of rotamers, ratio: 65%/35%.

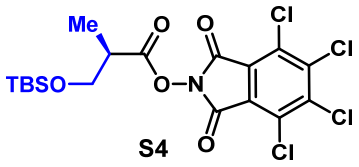
^{1}H NMR (600 MHz, $CDCl_3$):δ 5.37 (br s, 0.35H), 5.13 (br d, J = 4.5 Hz, 0.65 H), 4.07 (d, J = 12.6 Hz, 0.65H), 3.97 (br d, J = 12.7 Hz, 0.35H), 3.07 (t, J = 12.6 Hz, 0.35H), 2.99 (t, J = 11.2 Hz, 0.65H), 2.35 – 2.32 (m, 1H), 1.87 – 1.66 (m, 3H), 1.59 – 1.38 (m, 2H), 1.49 (s, 5.85H), 1.47 (s, 3.15H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 168.53, 168.30 (minor), 157.48, 155.43 (minor), 155.07, 141.21, 130.61, 124.83, 81.29, 80.82 (minor), 53.70, 52.63 (minor), 42.27 (minor), 41.26, 28.42 (minor), 28.28, 27.31, 24.82 (minor), 24.45, 20.68 (minor), 20.36.

HRMS (ESI-TOF): High resolution mass spectroscopic data could not be obtained

for this compound.

Compound S4



4,5,6,7-Tetrachloro-1,3-dioxoisoindolin-2-yl (R)-3-((tert-butyldimethylsilyl)oxy)-2-methylpropanoate (S4)

Following the General Procedure A on 1.0 mmol scale. Purification by flash column chromatography (silica gel, 5:1 hexanes:EtOAc) afforded 400 mg (63%) of the title compound **S4**.

Physical State: white solid. **m.p.** 78-80 °C.

R_f= 0.50 (5:1 hexanes:EtOAc).

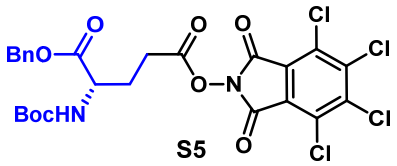
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.93 (dd, *J* = 12.5, 9.0 Hz, 1H), 3.78 (dd, *J* = 12.5, 8.0 Hz, 1H), 3.06 – 2.99 (m, 1H), 1.35 (d, *J* = 8.5 Hz, 3H), 0.91 (s, 9H), 0.09 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 170.78, 141.07, 130.56, 124.94, 64.50, 40.60, 25.95, 18.35, 13.67, -5.38. -5.48.

HRMS (ESI-TOF): calc'd for $C_{18}H_{22}Cl_4O_5Si$ $[M+H]^+$ 500.0016; found 500.0016.

$[\alpha]_D^{20}$ = -22.5 (c 1.02, $CHCl_3$).

Compound S5



1-Benzyl 5-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) (tert-butoxycarbonyl)-L-glutamate (S5)

Following the General Procedure A on 1.6 mmol scale. Purification by flash column chromatography (silica gel, 5:1 hexanes:EtOAc) afforded 462 mg (47%) of the title compound **S5**.

Physical State: white solid. **m.p.** 153-155 °C.

R_f = 0.43 (4:1 hexanes:EtOAc).

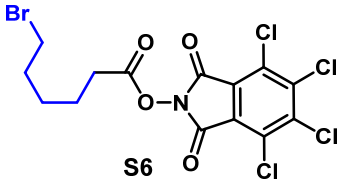
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 – 7.21 (m, 5H), 5.13 – 5.10 (m, 1H), 5.10 (s, 2H), 4.38 – 4.32 (m, 1H), 2.68 (ddd, *J* = 17.0, 9.3, 6.3 Hz, 1H), 2.59 (ddd, *J* = 17.0, 9.3, 6.0 Hz, 1H), 2.30 – 2.21 (m, 1H), 2.01 (dddd, *J* = 14.3, 9.2, 8.3, 6.0 Hz, 1H), 1.34 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.56, 168.56, 157.48, 155.49, 141.18, 135.18, 130.62, 128.82, 128.74, 128.52, 124.78, 80.47, 67.67, 52.77, 28.40, 27.76, 27.41.

HRMS (ESI-TOF): calc'd for $C_{25}H_{23}Cl_4N_2O_8$ $[M+H]^+$ 619.0203; found 619.0203.

$[\alpha]_D^{20}$ = +3.8 (c 1.0, CH_2Cl_2).

Compound S6



S6

4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl 6-bromohexanoate

Following the General Procedure A on 5 mmol scale. Purification by flash column chromatography (silica gel, CH_2Cl_2) and recrystallized from CH_2Cl_2/MeOH afforded 1.50 g (63%) of the title compound **S6**.

Physical State: yellowish solid. **m.p.** 77-78 ºC.

R_f = 0.53 (7:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.43 (t, *J* = 6.7 Hz, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 1.95-1.90 (m, 2H), 1.85-1.80 (m, 2H), 1.66 – 1.57 (m, 2H).

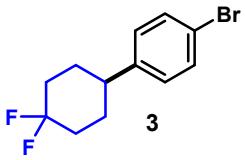
^{13}C NMR (151 MHz, $CDCl_3$): δ 169.02, 157.68, 141.19, 130.63, 124.83, 33.25, 32.32, 30.88, 27.44, 24.03.

HRMS (ESI-TOF): High resolution mass spectroscopic data could not be obtained for this compound.

Characterization of other TCNHPI esters employed in this paper are fully described in literature[1,2].

Experimental Procedures and Characterization Data for Cross-Coupling Products

Compound 3



3

1-Bromo-4-(4,4-difluorocyclohexyl)benzene (3)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 hexanes:EtOAc) afforded 21.5 mg (78%) of the title compound **3**.

Physical State: white solid. **m.p.** 71-72 ºC.

R_f = 0.5 (15:1 hexanes:EtOAc).

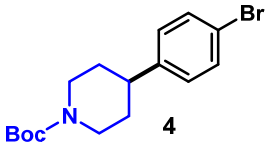
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.40 (m, 2H), 7.13 – 7.07 (m, 2H), 2.56 (dt, *J* = 12.2, 3.3 Hz, 1H), 2.23 – 2.18 (m, 2H), 1.94 – 1.83 (m, 3H), 1.86 – 1.72 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 144.29, 131.74, 128.65, 123.11 (dd, *J* = 242.4, 239.9 Hz, 1C), 121.51, 42.17, 34.12 (dd, *J* = 26.0, 23.3 Hz, 2C), 30.32 (d, *J* = 10.0 Hz, 2C).

^{19}F NMR (376 MHz, $CDCl_3$): δ -92.07 (d, *J* = 236.9 Hz), -102.67 (d, *J* = 236.9 Hz).

MS (GCMS, EI): m/z = 274 (25%), 195 (20%), 116 (100%), 91 (27%), 77 (25%).

Compound 4



4

tert-Butyl 4-(4-bromophenyl)piperidine-1-carboxylate (4)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 23.8 mg (70%) of the title compound **4**.

Physical State: white solid. **m.p.** 41-42 °C.

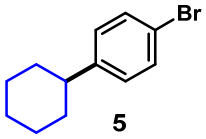
R_f = 0.50 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.39 (m, 2H), 7.10 – 7.04 (m, 2H), 4.24 (br s, 2H), 2.80 – 2.77 (m, 2H), 2.60 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.79 (d, *J* = 13.1 Hz, 2H), 1.65 – 1.54 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.94, 144.88, 131.69, 128.67, 120.12, 79.66, 44.35 (br), 42.36, 33.21, 28.62.

Spectroscopic data matches that reported in the literature.[3]

Compound 5



5

1-Bromo-4-cyclohexylbenzene (5)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, pentane) afforded 16.7 mg (70%) of the title compound **5**.

Physical State: colorless oil.

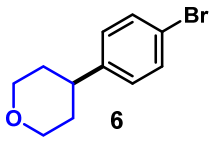
R_f = 0.70 (pentane).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.37 (m, 2H), 7.11 – 7.05 (m, 2H), 2.48 – 2.43 (m, 1H), 1.89 – 1.79 (m, 4H), 1.79 – 1.71 (m, 1H), 1.45 – 1.32 (m, 4H), 1.30 – 1.19 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 147.16, 131.42, 128.75, 119.46, 44.20, 34.50, 26.93, 26.20.

Spectroscopic data matches that reported in the literature.[4]

Compound 6



6

4-(4-Bromophenyl)tetrahydro-2H-pyran (6)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand

at 75 °C. Purification by PTLC (silica gel, 6:1 hexanes:EtOAc) afforded 20.8 mg (86%) of the title compound **6**.

Physical State: white solid. **m.p**. 61-62 ºC.

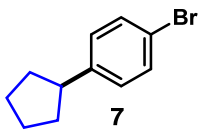
R_f = 0.50 (4:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46 – 7.40 (m, 2H), 7.12 – 7.07 (m, 2H), 4.19 – 4.06 (m, 2H), 3.51 (td, *J* = 11.5, 2.8 Hz, 2H), 2.72 (tt, *J* = 11.3, 4.6 Hz, 1H), 1.83 – 1.70 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 144.93, 131.67, 128.63, 120.09, 68.38, 41.20, 33.93.

HRMS (ESI-TOF): calc'd for $C_{11}H_{14}BrO$ $[M+H]^+$ 241.0222; found 241.0223.

Compound 7



7

1-Bromo-4-(cyclopentyl)benzene (7)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, pentane) afforded 11.0 mg (49%) of the title compound **7**.

Physical State: colorless oil.

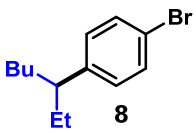
R_f = 0.6 (pentane).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.36 (m, 2H), 7.14 – 7.08 (m, 2H), 2.94 (tt, *J* = 9.8, 7.5 Hz, 1H), 2.10 – 2.01 (m, 2H), 1.84 – 1.75 (m, 2H), 1.73 – 1.64 (m, 2H), 1.59 – 1.49 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.65, 131.36, 129.02, 119.36, 45.53, 34.70, 25.60.

MS (GCMS, EI): m/z = 224 (40%), 182 (35%), 145 (100%), 116 (90%), 91 (75%).

Compound 8



8

1-Bromo-4-(heptan-3-yl)benzene (8)

Following the General Procedure B on 0.1 mmol scale with bathophenanthroline (**L4**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 hexanes:EtOAc) afforded 17.8 mg (70%) of the title compound **8**.

Physical State: colorless oil.

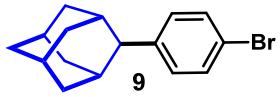
R_f = 0.9 (50:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.5, 2H), 7.01 (d, *J* = 8.0, 2H), 2.39 – 2.33 (m, 1H), 1.70 – 1.59 (m, 2H), 1.54 – 1.45 (m, 2H), 1.31 – 1.19 (m, 2H), 1.18 – 1.02 (m, 2H), 0.83 (t, *J* = 7.5 Hz, 3H), 0.75 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.23, 131.37, 129.65, 119.46, 47.54, 36.29, 29.91, 29.77, 22.88. 14.14, 12.24.

MS (GCMS, EI): m/z = 254 (20%), 225 (25%), 197 (42%), 169 (100%), 118 (28%).

Compound 9



9

2-(4-Bromophenyl)adamantane (9)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, pentane) afforded 14.3 mg (49%) of the title compound **9**.

Physical State: white solid. **m.p**. 41-42 ºC.

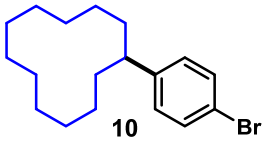
R_f = 0.7 (pentane).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.41 (m, 2H), 7.24 – 7.21 (m, 2H), 2.94 (br s, 1H), 2.42 (br s, 2H), 2.04 – 1.95 (m, 3H), 1.96 – 1.89 (m, 2H), 1.80 – 1.76 (m, 5H), 1.57 – 1.54 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.57, 131.29, 128.89, 119.03, 46.54, 39.17, 37.92, 32.00, 31.11, 28.11, 27.78.

Spectroscopic data matches that reported in the literature.[5]

Compound 10



(4-Bromophenyl)cyclododecane (10)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, hexanes) afforded 23.5 mg (73%) of the title compound **10**.

Physical State: white solid. **m.p.** 58-59 ºC.

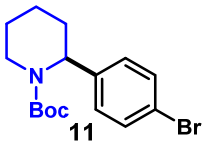
R_f = 0.9 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.36 (m, 2H), 7.09 – 7.04 (m, 2H), 2.72 (p, *J* = 6.4 Hz, 1H), 1.81 – 1.74 (m, 2H), 1.51 – 1.22 (m, 20H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 146.77, 131.33, 129.56, 119.37, 39.41, 31.62, 24.07, 23.96, 23.56, 23.34, 22.75.

MS (GCMS, EI): m/z = 324 (50%), 243 (50%), 182 (100%), 171 (95%), 131 (70%), 117 (70%), 55 (55%).

Compound 11



tert-Butyl-2-(4-bromophenyl)piperidine-1-carboxylate (11)

Following the General Procedure B on 0.1 mmol scale with bathophenanthroline (**L4**) as ligand at 85 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 13.6 mg (40%) of the title compound **11**.

Physical State: colorless oil.

R_f= 0.40 (10:1 hexanes:EtOAc).

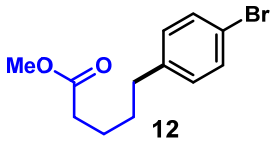
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.5, 2H), 7.09 (d, *J* = 9.0, 2H), 5.34(br s, 1H), 4.04 (d, *J* = 14.0 Hz, 1H), 2.72(dt, *J* = 13.0, 3.5 Hz, 1H), 2.23 (d, *J* = 16.5 Hz, 1H), 1.92 – 1.84 (m, 1H), 1.62 – 1.56 (m, 2H), 1.53 – 1.48 (m, 1H), 1.46 (s, 9H), 1.42

– 1.36 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.70, 139.80, 131.75, 128.51, 120.38, 79.92, 53.05, 40.26, 28.56, 28.23, 25.49, 19.42.

HRMS (ESI-TOF): calc'd for $C_{16}H_{23}BrNO_2$ $[M+H]^+$ 340.0907; found 340.0910.

Compound 12



Methyl 5-(4-bromophenyl)pentanoate (12)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 85 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 17.4 mg (54%) of the title compound **12**.

Physical State: colorless oil.

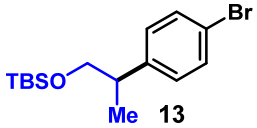
R_f = 0.65 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.3 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 3.66 (s, 3H), 2.58 (t, *J* = 7.1 Hz, 2H), 2.33 (t, *J* = 6.9 Hz, 2H), 1.69 – 1.60 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 174.09, 141.16, 131.50, 130.28, 119.64, 51.67, 35.10, 33.99, 30.83, 24.58.

Spectroscopic data matches that reported in the literature.[6]

Compound 13



(2-(4-Bromophenyl)propoxy)(tert-butyl)dimethylsilane (13)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 hexanes:EtOAc) afforded 25.7 mg (78%) of the title compound **13**.

Physical State: colorless oil.

R_f = 0.50 (50:1 hexanes:EtOAc).

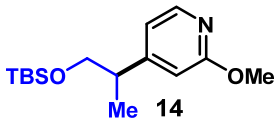
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, *J* = 10.0 Hz, 2H), 7.09 (d, *J* = 10.0 Hz, 2H), 3.65 – 3.55 (m, 2H), 2.90 – 2.81 (m, 1H), 1.24 (d, *J* = 8.5 Hz, 3H), 0.85 (s, 9H), -0.04 (s, 3H), -0.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 143.77, 131.31, 129.52, 120.01, 69.01, 42.07, 26.00, 18.37, 17.47, -5.38.

HRMS (ESI-TOF): calc'd for $C_{15}H_{26}BrOSi$ $[M+H]^+$ 329.0931; found 329.0930.

$[\alpha]_D^{20}$ = 0 (c 1.0, $CHCl_3$).

Compound 14



14

4-(1-(tert-Butyldimethylsilyloxy)propan-2-yl)-2-methoxypyridine (14)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 15:1 hexanes:EtOAc) afforded 22.9 mg (81%) of the title compound **14**.

Physical State: colorless oil.

R_f = 0.50 (15:1 hexanes:EtOAc).

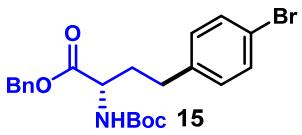
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 5.0 Hz, 2H), 6.74 (dd, *J* = 5.0, 1.5 Hz, 2H), 6.59 (s, 1H), 3.92 (s, 3H), 3.68 – 3.58 (m, 2H), 2.87 – 2.80 (m, 1H), 1.24 (d, *J* = 7.0 Hz, 1H), 0.84 (s, 9H), -0.03 (s, 3H), -0.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 164.57, 156.65, 146.51, 116.86, 109.73, 68.32, 53.43, 42.00, 25.97, 18.40, 16.87, -5.38.

HRMS (ESI-TOF): calc'd for $C_{15}H_{28}BrNO_2Si$ $[M+H]^+$ 282.1884; found 282.1885.

$[\alpha]_D^{20}$ = 0 (c 1.0, $CHCl_3$).

Compound 15



15

Benzyl (S)-4-(4-bromophenyl)-2-((tert-butoxycarbonyl)amino)butanoate (15)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 6:1 hexanes:EtOAc) afforded 22.9 mg (51%) of the title compound **15**.

Physical State: colorless oil.

R_f = 0.24 (10:1 hexanes:EtOAc).

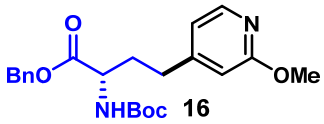
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.33 (m, 7H), 6.99 – 6.95 (m, 2H), 5.19 (d, *J* = 12.3 Hz, 1H), 5.12 (d, *J* = 12.3 Hz, 1H), 5.08 (d, *J* = 8.4 Hz, 1H), 4.41 – 4.34 (m, 1H), 2.60 (ddd, *J* = 13.9, 10.2, 6.3 Hz, 1H), 2.53 (ddd, *J* = 14.3, 10.1, 5.6 Hz, 1H), 2.18 – 2.07 (m, 1H), 1.96 – 1.85 (m, 1H), 1.45 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 172.45, 155.41, 139.85, 135.43, 131.63, 130.29, 128.78, 128.66, 128.53, 120.03, 80.16, 67.27, 53.31, 34.38, 31.08, 28.45.

HRMS (ESI-TOF): calc'd for $C_{22}H_{27}BrNO_4$ $[M+H]^+$ 448.1118; found 448.1118.

$[\alpha]_D^{20}$ = +6.8 (c 1.0, CH_2Cl_2).

Compound 16



16

Benzyl (S)-2-((tert-butoxycarbonyl)amino)-4-(2-methoxypyridin-4-yl)butanoate (16)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 4:1 hexanes:EtOAc) afforded 18.2 mg (45%) of the title compound **16** as a pure enantiomer indicated by chiral HPLC.

Physical State: colorless oil.

R_f = 0.21 (4:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (d, *J* = 5.2 Hz, 1H), 7.39 – 7.32 (m, 5H), 6.62

(dd, J = 5.3, 1.5 Hz, 1H), 6.49 (dd, J = 1.5, 0.8 Hz, 1H), 5.20 (d, J = 12.2 Hz, 1H), 5.13 (d, J = 12.5 Hz, 1H), 5.10 (s, 1H), 4.39 (d, J = 6.9 Hz, 1H), 3.90 (s, 3H), 2.58 (ddd, J = 14.0, 10.4, 6.1 Hz, 1H), 2.51 (ddd, J = 14.4, 10.3, 5.5 Hz, 1H), 2.18 – 2.08 (m, 1H), 1.96 – 1.87 (m, 1H), 1.44 (s, 9H).

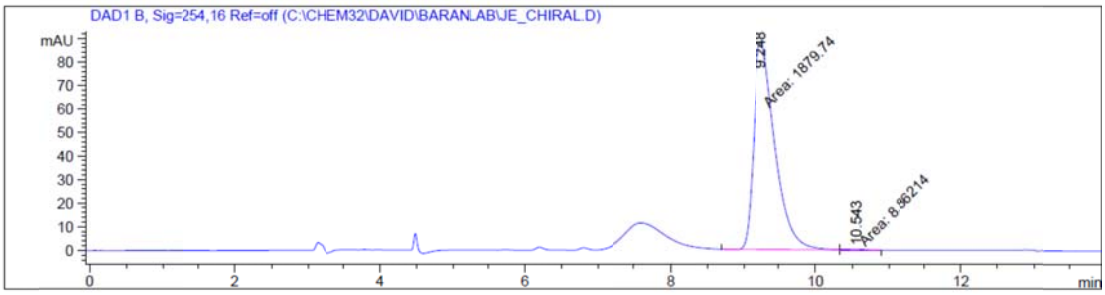
^{13}C NMR (151 MHz, $CDCl_3$): δ 172.30, 164.67, 155.40, 152.65, 146.88, 135.36, 128.80, 128.71, 128.54, 117.40, 110.40, 80.23, 67.35, 53.45, 53.31, 33.30, 30.87, 28.43.

HRMS (ESI-TOF): calc'd for $C_{22}H_{29}N_2O_5$ $[M+H]^+$ 401.2071; found 401.2071.

$[\alpha]_D^{20}$ = +6.4 ° (c 1.0, CH_2Cl_2).

>99% *ee*. HPLC conditions: OZ3 Column, isocratic 90:10 (Hexane:*i*PrOH), 25 °C, 1.0 mL/min, UV detection, 254 nm.

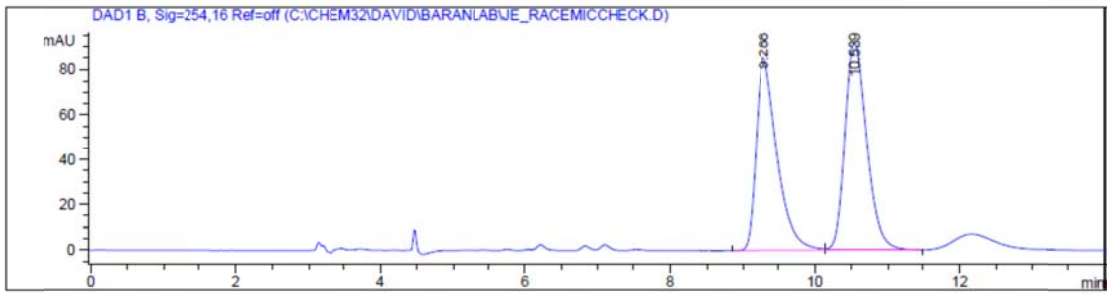
For cross-coupling product 16:



Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.248	MF	0.3563	1879.73682	87.92305	99.5308
2	10.543	MF	0.3807	8.86214	3.87956e-1	0.4692
Totals :				1888.59895	88.31101	

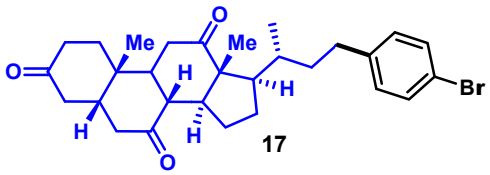
For racemic sample of (±)-16:



Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.288	BV	0.3238	1826.38696	85.29803	49.0379
2	10.539	VV	0.3193	1898.05225	91.75673	50.9621
Totals :				3724.43921	177.05476	

Compound 17



17

(5S,8R,10S,13R,14S,17R)-17-((R)-4-(4-Bromophenyl)butan-2-yl)-10,13-dimethyldodecahydro-3H-cyclopenta[a]phenanthrene-3,7,12(2H,4H)-trione (17)

Following the General Procedure B on 0.05 mmol scale with di-*t*Bubipy (**L1**) as ligand at 85 °C. Purification by PTLC (silica gel, 50:1 CH_2Cl_2:MeOH) afforded 15.5 mg (60%) of the title compound **17**.

Physical State: white solid. **m.p.** 200-202 ºC.

R_f = 0.6 (20:1 CH_2Cl_2:MeOH).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.35 (m, 2H), 7.07 – 7.01 (m, 2H), 2.93 – 2.83 (m, 3H), 2.68 (ddd, *J* = 13.7, 10.7, 4.9 Hz, 1H), 2.44 (ddd, *J* = 13.7, 10.4, 6.5 Hz, 1H), 2.36 – 2.20 (m, 6H), 2.16 – 1.94 (m, 6H), 1.85 (td, *J* = 11.1, 7.1 Hz, 1H), 1.71 (dddd, *J* = 13.5, 10.6, 6.5, 2.8 Hz, 1H), 1.61 (td, *J* = 14.4, 4.7 Hz, 2H), 1.40 (s, 3H), 1.32 – 1.22 (m, 3H), 1.05 (s, 3H), 0.92 (d, *J* = 6.7 Hz, 3H).

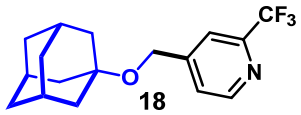
^{13}C NMR (151 MHz, $CDCl_3$): δ 212.16, 209.18, 208.87, 142.14, 131.46, 130.26,

119.39, 57.05, 51.93, 49.15, 46.99, 45.81, 45.73, 45.12, 42.93, 38.79, 37.45, 36.63, 36.15, 35.81, 35.42, 32.46, 27.92, 25.29, 22.06, 19.04, 11.99.

HRMS (ESI-TOF): calc'd for $C_{29}H_{38}BrO_3$ $[M+H]^+$ 513.1999; found 513.1998.

$[\alpha]_D^{20}$ = +13.0 (c 1.04, $CHCl_3$).

Compound 18



4-(((-Adamantan-1-yl)oxy)methyl)-2-(trifluoromethyl)pyridine (18)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 85 °C. Purification by PTLC (silica gel, 4:1 hexanes:EtOAc) afforded 18.0 mg (58%) of the title compound **18**.

Physical State: colorless oil.

R_f = 0.41 (4:1 hexanes:EtOAc).

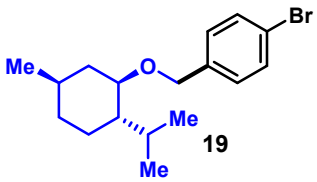
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.9 Hz, 1H), 7.68 (s, 1H), 7.48 (d, *J* = 4.5 Hz, 1H), 4.60 (s, 2H), 2.26 – 2.17 (m, 3H), 1.83 (d, *J* = 3.0 Hz, 6H), 1.68 (d, *J* = 12.1 Hz, 3H), 1.62 (d, *J* = 12.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 151.89, 149.89, 148.30 (q, *J* = 34.2 Hz), 124.42, 120.80 (q, *J* = 123.2 Hz), 118. 65 (q, *J* = 2.6 Hz), 73.72, 60.64, 41.72, 36.49, 30.68.

^{19}F NMR (376 MHz, $CDCl_3$): δ -68.27.

HRMS (ESI-TOF): calc'd for $C_{17}H_{21}F_3NO$ $[M+H]^+$ 312.1570; found 312.1671.

Compound 19



1-Bromo-4-((((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)methyl)benzene (19)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 85 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 17.4 mg (54%)

of the title compound **19**.

Physical State: colorless oil.

R_f = 0.70 (10:1 hexanes:EtOAc).

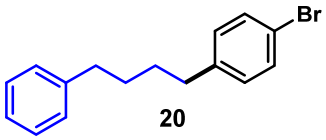
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47 – 7.43 (m, 2H), 7.24 – 7.20 (m, 2H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.34 (d, *J* = 11.7 Hz, 1H), 3.16 (td, *J* = 10.6, 4.2 Hz, 1H), 2.26 (pd, *J* = 7.0, 2.8 Hz, 1H), 2.16 (dtd, *J* = 12.1, 3.8, 1.9 Hz, 1H), 1.68 – 1.60 (m, 2H), 1.41 – 1.32 (m, 1H), 1.31 – 1.24 (m, 1H), 1.01 – 0.82 (m, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 7.1 Hz, 3H), 0.72 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 138.35, 131.52, 129.55, 121.33, 79.13, 69.77, 48.46, 40.43, 34.69, 31.71, 25.73, 23.41, 22.52, 21.15, 16.25.

$[\alpha]_D^{20}$ = -68.7 (c 1.0, CH_2Cl_2).

Spectroscopic data matches that reported in the literature.[7]

Compound 20



20

1-Bromo-4-(4-phenylbutyl)benzene (20)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 85 °C. Purification by PTLC (silica gel, hexanes) afforded 18.5 mg (64%) of the title compound **20**.

Physical State: colorless oil.

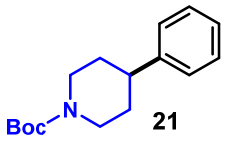
R_f = 0.8 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$):δ 7.42 – 7.37 (m, 2H), 7.29 (dd, *J* = 8.3, 6.8 Hz, 2H), 7.23 – 7.15 (m, 3H), 7.07 – 7.02 (m, 2H), 2.66 – 2.63 (m, 2H), 2.61 – 2.59 (m, 2H), 1.67 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 142.51, 141.59, 131.42, 131.40, 130.30, 128.42, 125.85, 119.49, 35.89, 35.32, 31.07, 31.00.

MS (GCMS, EI): m/z = 288 (16%), 171 (19%), 131 (30%), 117 (21%), 91 (100%).

Compound 21



21

tert-Butyl 4-phenylpiperidine-1-carboxylate (21)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 23.6 mg (90%) of the title compound **21**.

Physical State: colorless oil.

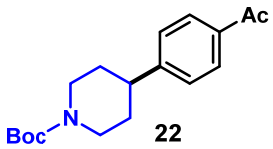
R_f = 0.50 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (dd, *J* = 8.5, 7.0 Hz, 2H), 7.24 – 7.18 (m, 3H), 4.25 (br s, 2H), 2.80 (t, *J* = 10.2 Hz, 2H), 2.64 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.85 – 1.79 (m, 2H), 1.68 – 1.57 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.01, 145.94, 128.64, 126.91, 126.47, 79.57, 44.50 (br), 42.87, 33.33, 28.64.

Spectroscopic data matches that reported in the literature.[8]

Compound 22



22

tert-Butyl 4-(4-acetylphenyl)piperidine-1-carboxylate (22)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 CH_2Cl_2:MeOH) afforded 20.5 mg (68%) of the title compound **22**.

Physical State: colorless oil.

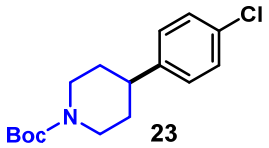
R_f = 0.60 (3:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93 – 7.88 (m, 2H), 7.32 – 7.27 (m, 2H), 4.26 (br s, 2H), 2.82 – 2.79 (m, 2H), 2.71 (tt, *J* = 12.3, 3.6 Hz, 1H), 2.58 (s, 3H), 1.85 – 1.79 (m, 2H), 1.66 – 1.58 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 197.89, 154.94, 151.44, 135.66, 128.85, 127.16, 79.73, 44.36 (br), 42.94, 32.99, 28.62, 26.71.

Spectroscopic data matches that reported in the literature.[9]

Compound 23



23

tert-Butyl 4-(4-chlorophenyl)piperidine-1-carboxylate (23)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 23.7 mg (80%) of the title compound **23**.

Physical State: colorless oil.

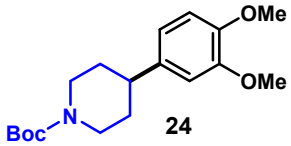
R_f = 0.50 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 2H), 7.15 – 7.10 (m, 2H), 4.24 (br s, 2H), 2.79 (br t, *J* = 13.0 Hz, 2H), 2.62 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.79 (d, *J* = 13.7 Hz, 2H), 1.57 (qd, *J* = 12.7, 4.4 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.96, 144.35, 132.10, 128.74, 128.26, 79.66, 44.39 (br), 42.29, 33.28, 28.62.

Spectroscopic data matches that reported in the literature.[3]

Compound 24



24

tert-Butyl 4-(3,4-dimethoxyphenyl)piperidine-1-carboxylate (24)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 CH_2Cl_2:MeOH) afforded 19.4 mg (60%) of the title compound **24**.

Physical State: colorless oil.

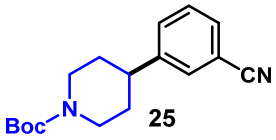
R_f = 0.40 (4:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.81 (d, *J* = 8.1 Hz, 1H), 6.77 – 6.71 (m, 2H), 4.24 (br s, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 2.79 (br t, *J* = 11.9 Hz, 2H), 2.59 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.81 (d, *J* = 13.0 Hz, 2H), 1.64 – 1.56 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.01, 149.03, 147.61, 138.75, 118.58, 111.40, 110.32, 79.58, 56.06, 55.98, 44.52 (br), 42.49, 33.58, 28.63.

HRMS (ESI-TOF): calc'd for $C_{18}H_{28}NO_4$ $[M+H]^+$ 322.2013; found 322.2013.

Compound 25



tert-Butyl 4-(3-cyanophenyl)piperidine-1-carboxylate (25)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 50:1 CH_2Cl_2:MeOH) afforded 20.3 mg (71%) of the title compound **25**.

Physical State: colorless oil.

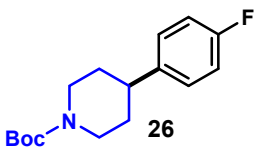
R_f = 0.35 (4:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54 – 7.47 (m, 2H), 7.47 – 7.36 (m, 2H), 4.26 (br s, 2H), 2.82 – 2.78 (m, 2H), 2.68 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.81 (d, *J* = 13.1 Hz, 2H), 1.59 (qd, *J* = 12.6, 4.4 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.86, 147.20, 131.52, 130.65, 130.28, 129.47, 119.05, 112.70, 79.80, 44.19 (br), 42.48, 33.00, 28.59.

HRMS (ESI-TOF): calc'd for $C_{17}H_{23}N_2O_2$ $[M+H]^+$ 287.1754; found 287.1755.

Compound 26



tert-Butyl 4-(4-fluorophenyl)piperidine-1-carboxylate (26)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 21.0 mg (75%) of the title compound **26**.

Physical State: colorless oil.

R_f = 0.5 (10:1 hexanes:EtOAc).

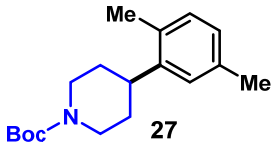
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18 – 7.11 (m, 2H), 7.03 – 6.95 (m, 2H), 4.24 (d, *J* = 13.2 Hz, 2H), 2.79 (td, *J* = 13.0, 2.5 Hz, 2H), 2.62 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.83 – 1.76 (m, 2H), 1.61 – 1.54 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 161.53 (d, *J* = 244.4 Hz), 154.97, 141.59 (d, *J* = 3.0 Hz), 128.22 (d, *J* = 7.5 Hz), 115.35 (d, *J* = 21.1 Hz), 79.63, 44.48 (br), 42.14, 33.50, 28.62.

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.51.

Spectroscopic data matches that reported in the literature.[9]

Compound 27



27

***tert*-Butyl 4-(2,5-dimethylphenyl)piperidine-1-carboxylate (27)**

Following the General Procedure B on 0.1 mmol scale with bathophenanthroloine (**L4**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 15.0 mg (52%) of the title compound **27**.

Physical State: colorless oil.

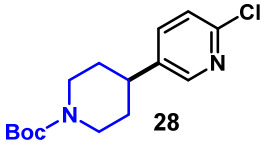
R_f = 0.5 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.04 (d, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 1.9 Hz, 1H), 6.93 (dd, *J* = 7.6, 1.8 Hz, 1H), 4.26 (br s, 2H), 2.84 – 2.79 (m, 3H), 2.30 (s, 6H), 1.75 – 1.72 (m, 2H), 1.65 – 1.58 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.01, 143.57, 135.77, 132.04, 130.44, 126.82, 126.36, 79.54, 44.78 (br), 38.46, 32.59, 28.65, 21.31, 19.03.

HRMS (ESI-TOF): calc'd for $C_{18}H_{28}NO_2$ $[M+H]^+$ 290.2114; found 290.2114.

Compound 28



28

tert-Butyl 4-(6-chloropyridin-3-yl)piperidine-1-carboxylate (28)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 4:1 hexanes:EtOAc) afforded 15.6 mg (53%) of the title compound **28**.

Physical State: colorless oil.

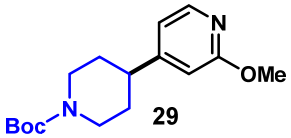
R_f = 0.32 (4:1 hexanes:EtOAc);

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (d, *J* = 2.5 Hz, 1H), 7.47 (dd, *J* = 8.2, 2.6 Hz, 1H), 7.27 (d, *J* = 7.4 Hz, 1H), 4.37 – 4.16 (m, 2H), 2.86 – 2.73 (m, 2H), 2.67 (tt, *J* = 12.3, 3.6 Hz, 1H), 1.81 (d, *J* = 13.0 Hz, 2H), 1.59 (qd, *J* = 12.3, 4.0 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.85, 149.62, 148.65, 139.90, 137.14, 124.27, 79.86, 44.28 (br), 39.72, 32.95, 28.60.

HRMS (ESI-TOF): calc'd for $C_{15}H_{21}ClN_2O_2$ $[M+H]^+$ 297.1364; found 297.1366.

Compound 29



29

tert-Butyl 4-(2-methoxypyridin-4-yl)piperidine-1-carboxylate (29)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 4:1 hexanes:EtOAc) afforded 16.3 mg (56%) of the title compound **29**.

Physical State: colorless oil.

R_f = 0.41 (4:1 hexanes:EtOAc);

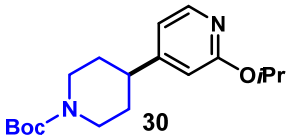
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 5.4, 0.7 Hz, 1H), 6.71 (dd, *J* = 5.5, 1.5 Hz, 1H), 6.58 – 6.54 (m, 1H), 4.35 – 4.13 (m, 2H), 3.91 (s, 3H), 2.85 – 2.72 (m, 2H),

2.59 (tt, J = 12.2, 3.6 Hz, 1H), 1.80 (d, J = 13.2 Hz, 2H), 1.62 – 1.53 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 164.75, 157.36, 154.89, 146.97, 115.96, 108.85, 79.73, 53.49, 44.06 (br), 42.05, 32.32, 28.59.

HRMS (ESI-TOF): calc'd for $C_{16}H_{24}N_2O_3$ $[M+H]^+$ 293.1860; found 293.1860.

Compound 30



30

tert-Butyl 4-(2-isopropoxypyridin-4-yl)piperidine-1-carboxylate (30)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 8:1 hexanes:EtOAc) afforded 15.2 mg (47%) of the title compound **30**.

Physical State: colorless oil.

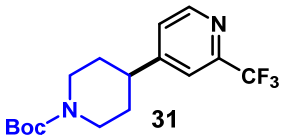
R_f = 0.50 (4:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 5.3 Hz, 1H), 6.66 (dd, J = 5.4, 1.6 Hz, 1H), 6.53 – 6.47 (m, 1H), 5.28 (hept, J = 6.2 Hz, 1H), 4.41 – 4.08 (m, 2H), 2.85 – 2.67 (m, 2H), 2.57 (ddd, J = 12.2, 8.6, 3.6 Hz, 1H), 1.80 (d, J = 13.1 Hz, 2H), 1.62 – 1.52 (m, 2H), 1.47 (s, 9H), 1.33 (d, J = 6.2 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 164.07, 157.31, 146.98, 115.54, 109.51, 79.71, 67.96, 44.55 (br), 42.06, 32.32, 28.61, 28.59, 22.25.

HRMS (ESI-TOF): calc'd for $C_{16}H_{24}N_2O_3$ $[M+H]^+$ 293.1860; found 293.1860.

Compound 31



31

tert-Butyl 4-(2-(trifluoromethyl)pyridin-4-yl)piperidine-1-carboxylate (31)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand

at 75 °C. Purification by PTLC (silica gel, 6:1 hexanes:EtOAc) afforded 18.7 mg (57%) of the title compound **31**.

Physical State: colorless oil.

R_f = 0.27 (4:1 hexanes:EtOAc).

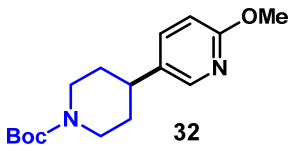
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63 (d, *J* = 5.0 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.32 (dd, *J* = 5.0, 1.6 Hz, 1H), 4.28 (s, 2H), 2.81 (s, 2H), 2.75 (tt, *J* = 12.0, 3.6 Hz, 1H), 1.85 (d, *J* = 13.0 Hz, 2H), 1.63 (qd, *J* = 12.6, 4.4 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 156.51, 154.78, 150.33, 148.67 (q, *J* = 34.2 Hz), 124.92, 121.71 (q, *J* = 247.6 Hz), 119.17 (q, *J* = 2.4 Hz), 79.96, 43.95 (br), 42.26, 32.32, 28.58.

^{19}F NMR (376 MHz, $CDCl_3$): δ -68.26.

HRMS (ESI-TOF): calc'd for $C_{16}H_{22}F_3N_2O_2$ $[M+H]^+$ 331.1628; found 331.1630.

Compound 32



32

tert-butyl 4-(6-methoxypyridin-3-yl)piperidine-1-carboxylate (32)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 4:1 hexanes:EtOAc) afforded 12.3 mg (42%) of the title compound **32**.

Physical State: colorless oil.

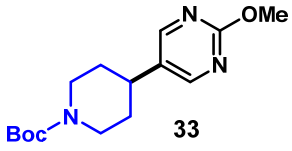
R_f = 0.46 (silica gel, 4:1 hexanes:EtOAc);

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (d, *J* = 2.4 Hz, 1H), 7.41 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 4.24 (br s, 2H), 3.92 (s, 3H), 2.79 (br s, 2H), 2.61 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.78 (d, *J* = 13.1 Hz, 2H), 1.57 (qd, *J* = 12.4, 4.3 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 163.12, 154.96, 145.00, 137.27, 133.78, 110.82, 79.69, 53.50, 44.35, 39.53, 33.24, 28.62.

HRMS (ESI-TOF): calc'd for $C_{16}H_{25}N_2O_3$ $[M+H]^+$ 293.1860; found 293.1856.

Compound 33



33

tert-butyl 4-(2-methoxypyrimidin-5-yl)piperidine-1-carboxylate (33)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 5:1 CH_2Cl_2:EtOAc) afforded 10.0 mg (34%) of the title compound **33**.

Physical State: colorless oil.

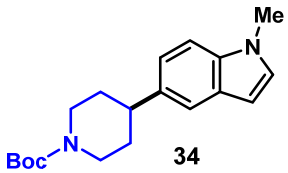
R_f = 0.38 (silica gel, 5:1 CH_2Cl_2:EtOAc);

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (s, 2H), 4.26 (br s, 2H), 4.00 (s, 3H), 2.80 (br s, 2H), 2.63 (tt, *J* = 12.3, 3.6 Hz, 1H), 1.82 (d, *J* = 13.1 Hz, 2H), 1.60 (qd, *J* = 12.6, 4.3 Hz, 2H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 164.84, 157.87, 154.86, 131.60, 79.90, 55.02, 44.29, 37.48, 32.92, 28.60.

HRMS (ESI-TOF): calc'd for $C_{15}H_{24}N_3O_3$ $[M+H]^+$ 294.1812; found 294.1813.

Compound 34



34

tert-butyl 4-(1-methyl-1H-indol-5-yl)piperidine-1-carboxylate (34)

Following the General Procedure B with 1-(tert-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate (0.1 mmol) and 1-methylindole-5-boronic acid (0.5 mmol), di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 13.6 mg (43%) of the title compound **34**.

Physical State: white solid. **m.p.** 95-96 ºC.

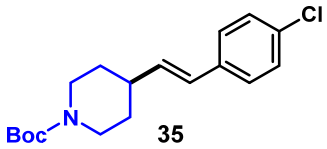
R_f = 0.55 (silica gel, 7:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.28 (s, 1H), 7.09 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.03 (d, *J* = 3.0 Hz, 1H), 6.43 (dd, *J* = 3.1, 0.9 Hz, 1H), 4.26 (d, *J* = 13.1 Hz, 2H), 3.77 (s, 3H), 2.83 (t, *J* = 12.9 Hz, 2H), 2.74 (tt, *J* = 12.2, 3.6 Hz, 1H), 1.87 (d, *J* = 12.7 Hz, 2H), 1.70 (qd, *J* = 12.7, 4.3 Hz, 2H), 1.50 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.08, 137.06, 135.72, 129.24, 128.74, 121.06, 118.45, 109.27, 100.79, 79.46, 44.78, 42.99, 34.07, 32.99, 28.67.

HRMS (ESI-TOF): calc'd for $C_{19}H_{27}N_2O_2$ $[M+H]^+$ 315.2067; found 315.2066.

Compound 35



35

tert-Butyl (E)-4-(4-chlorostyryl)piperidine-1-carboxylate (35)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 20.7 mg (64%) of the title compound **35**.

Physical State: colorless oil.

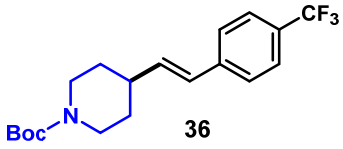
R_f = 0.24 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 – 7.25 (m, 4H), 6.33 (dd, *J* = 16.0, 1.3 Hz, 1H), 6.12 (dd, *J* = 16.0, 6.9 Hz, 1H), 4.28 – 3.99 (br s, 2H), 2.87 – 2.63 (m, 2H), 2.27 (qdd, *J* = 7.9, 3.4, 1.3 Hz, 1H), 1.74 (d, *J* = 12.4 Hz, 2H), 1.47 (s, 9H), 1.42 – 1.35 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.96, 136.13, 135.20, 132.78, 128.77, 127.45, 127.37, 79.53, 44.05 (br), 39.50, 31.87, 28.61.

HRMS (ESI-TOF): calc'd for $C_{18}H_{24}NO_2Cl$ $[M+H]^+$ 322.1568; found 322.1568.

Compound 36



36

tert-Butyl (E)-4-(4-(trifluoromethyl)styryl)piperidine-1-carboxylate (36)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 19.9 mg (56%) of the title compound **36**.

Physical State: white solid.

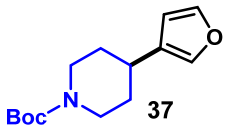
R_f = 0.22 (10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 6.41 (d, *J* = 16.0 Hz, 1H), 6.25 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.26 – 4.05 (m, 2H), 2.88 – 2.72 (m, 2H), 2.31 (dtd, *J* = 10.9, 7.0, 3.1 Hz, 1H), 1.76 (d, *J* = 12.6 Hz, 2H), 1.47 (s, 9H), 1.39 (qd, *J* = 12.3, 4.0 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 154.96, 141.13, 137.24, 128.06 (q, *J* = 32.3 Hz), 127.47, 126.31, 125.59 (q, *J* = 3.7 Hz), 124.37 (q, *J* = 271.9 Hz), 79.58, 43.83 (br), 39.57, 31.75, 28.61.

Spectroscopic data matches that reported in the literature.[10]

Compound 37



37

tert-Butyl 4-(furan-3-yl)piperidine-1-carboxylate (37)

Following the General Procedure B with 1-(tert-butyl) 4-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl) piperidine-1,4-dicarboxylate (0.1 mmol) and 3-furyl boronic acid (0.5 mmol), di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 10.2 mg (41%) of the title compound **37**.

Physical State: colorless oil.

R_f = 0.46 (10:1 hexanes:EtOAc).

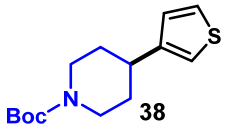
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (t, *J* = 1.7 Hz, 1H), 7.25 – 7.23 (m, 1H), 6.31 (dd, *J* = 1.8, 0.9 Hz, 1H), 4.27 – 4.11 (m, 2H), 2.90 – 2.77 (m, 2H), 2.61 (tt, *J* = 11.7, 3.7 Hz, 1H), 1.89 (d, *J* = 12.4 Hz, 2H), 1.55 – 1.48 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.00, 143.01, 137.91, 129.64, 109.51, 79.56,

44.16, 33.04, 32.66, 28.62.

Spectroscopic data matches that reported in the literature.[11]

Compound 38



38

tert-Butyl 4-(thiophen-3-yl)piperidine-1-carboxylate (38)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 10:1 hexanes:EtOAc) afforded 11.2 mg (42%) of the title compound **38**.

Physical State: colorless oil.

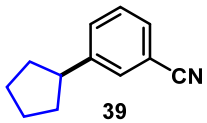
R_f = 0.46 (10:1 hexanes:EtOAc);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 1H), 6.98 (d, *J* = 4.9 Hz, 1H), 6.96 – 6.94 (m, 1H), 4.20 (s, 2H), 2.85 – 2.79 (m, 2H), 2.76 (tt, *J* = 11.9, 3.7 Hz, 1H), 1.91 (d, *J* = 13.1 Hz, 2H), 1.57 (qd, *J* = 12.7, 4.5 Hz, 2H), 1.47 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.00, 146.89, 126.78, 125.63, 119.07, 79.56, 44.40 (br), 37.87, 33.15, 28.63.

HRMS (ESI-TOF): calc'd for $C_{14}H_{22}NO_2S$ $[M+H]^+$ 268.1366; found 268.1366.

Compound 39



39

3-cyclopentylbenzonitrile (39)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, 15:1 hexanes:EtOAc) afforded 9.5 mg (56%) of the title compound **39**.

Physical State: colorless oil.

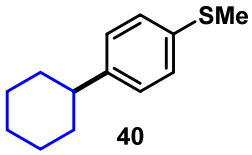
R_f = 0.60 (silica gel, 10:1 hexanes:EtOAc).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52 (t, *J* = 1.8 Hz, 1H), 7.46 (dt, *J* = 8.1, 1.5 Hz, 2H), 7.37 (t, *J* = 7.7 Hz, 1H), 3.01 (tt, *J* = 9.8, 7.6 Hz, 1H), 2.14 – 2.05 (m, 2H), 1.86 – 1.78 (m, 2H), 1.77 – 1.66 (m, 2H), 1.62 – 1.52 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 148.09, 131.93, 130.90, 129.59, 129.11, 119.38, 112.34, 45.60, 34.57, 25.58.

Spectroscopic data matches that reported in the literature.[12]

Compound 40



40

(4-cyclohexylphenyl)(methyl)sulfane (40)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, pentane) afforded 18.8 mg (91%) of the title compound **40**.

Physical State: colorless solid. **m.p.** 34-35 ºC.

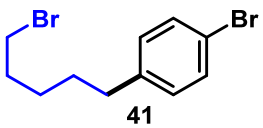
R_f = 0.65 (silica gel, pentane).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.23 – 7.20 (m, 2H), 7.16 – 7.12 (m, 2H), 2.49-2.45 (m, 1H), 2.47 (s, 3H), 1.89 – 1.80 (m, 4H), 1.75 (dtt, *J* = 12.7, 2.9, 1.5 Hz, 1H), 1.43-1.35 (m, 4H), 1.29 – 1.21 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 145.49, 135.17, 127.51, 127.32, 44.20, 34.58, 27.01, 26.26, 16.54.

Spectroscopic data matches that reported in the literature.[13]

Compound 41



41

1-bromo-4-(5-bromopentyl)benzene (41)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand

at 85 °C. Purification by PTLC (silica gel, hexanes) afforded 15.4 mg (50%) of the title compound **41**.

Physical State: colorless oil.

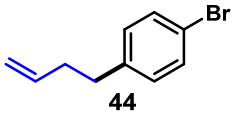
R_f = 0.55 (silica gel, hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.37 (m, 2H), 7.07 – 7.02 (m, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.58 (t, *J* = 7.7 Hz, 2H), 1.92 – 1.81 (m, 2H), 1.66 – 1.58 (m, 2H), 1.51 – 1.45 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 141.33, 131.50, 130.28, 119.61, 35.26, 33.82, 32.75, 30.57, 27.84.

Spectroscopic data matches that reported in the literature.[14]

Compound 44



44

1-Bromo-4-(but-3-en-1-yl)benzene (44)

Following the General Procedure B on 0.1 mmol scale with di-*t*Bubipy (**L1**) as ligand at 75 °C. Purification by PTLC (silica gel, hexanes) afforded 7.5 mg (36%) of the title compound **44**.

Physical State: colorless oil.

R_f = 0.65 (hexanes).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 – 7.37 (m, 2H), 7.09 – 7.04 (m, 2H), 5.82 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 5.06 – 4.95 (m, 2H), 2.66 (dd, *J* = 8.7, 6.8 Hz, 2H), 2.35 (dtt, *J* = 7.8, 6.6, 1.4 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 140.90, 137.73, 131.46, 130.36, 119.68, 115.43, 35.42, 34.89.

Spectroscopic data matches that reported in the literature.[15]

X-Ray Crystallographic Data for Compound 17

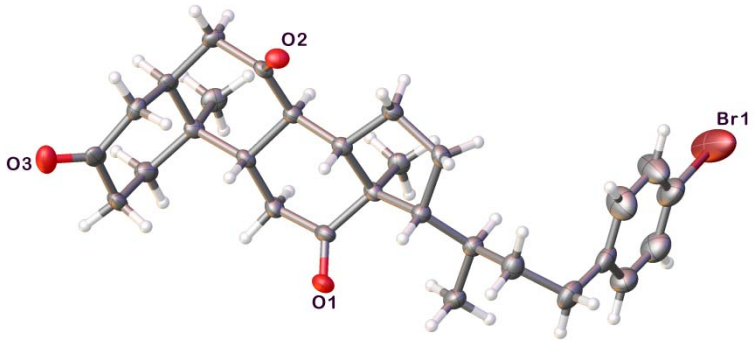


Table S1. Crystal data and structure refinement for **17**.

Identification code	CCDC 1477360	
Empirical formula	C29 H37 Br O3	
Formula weight	513.49	
Temperature	100.0 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 38.768(6) Å	a= 90°.
	b = 6.6812(10) Å	b= 100.947(4)°.
	c = 11.1118(15) Å	g = 90°.
Volume	2825.8(7) $Å^3$	
Z	4	
Density (calculated)	1.207 Mg/m^3	
Absorption coefficient	1.480 mm^{-1}	
F(000)	1080	
Crystal size	0.29 x 0.16 x 0.1 mm^3	
Theta range for data collection	1.867 to 26.450°.	
Index ranges	-37<=h<=48, -8<=k<=8, -13<=l<=13	
Reflections collected	17682	
Independent reflections	5803 [R(int) = 0.0852]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.333 and 0.277	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5803 / 1 / 301	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0648, wR2 = 0.1456	
R indices (all data)	R1 = 0.1073, wR2 = 0.1650	
Absolute structure parameter	0.055(17)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.386 and -0.879 e.$Å^{-3}$	
SQUEEZE	found 125e/uc;calcd for 4 CH_2Cl_2, 168e/uc	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for baran577_a_sq. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	5185(1)	7930(2)	12387(1)	109(1)
O(1)	3502(1)	1667(6)	5521(3)	32(1)
O(2)	2606(1)	8494(5)	5413(3)	27(1)
O(3)	2212(1)	4951(7)	499(4)	39(1)
C(23)	2797(1)	8187(8)	2506(5)	24(1)
C(15)	3558(1)	4875(8)	6538(5)	22(1)
C(17)	3534(2)	3470(8)	5457(5)	24(1)
C(24)	3138(2)	6970(8)	2707(5)	24(1)
C(28)	2467(2)	5291(8)	1311(5)	29(1)
C(16)	3881(2)	6256(9)	6654(5)	28(1)
C(20)	3160(2)	7262(8)	5055(4)	22(1)
C(19)	3179(2)	5835(8)	3947(4)	22(1)
C(14)	3201(1)	6056(8)	6242(4)	22(1)
C(29)	2465(2)	6867(9)	2256(5)	26(1)
C(18)	3509(2)	4504(9)	4225(5)	27(1)
C(13)	3192(2)	7149(8)	7435(5)	28(1)
C(21)	2828(2)	8458(8)	4766(5)	22(1)
C(22)	2779(2)	9614(8)	3578(5)	26(1)
C(9)	3861(1)	3101(10)	8598(4)	26(1)
C(25)	3451(2)	8383(9)	2691(5)	32(2)
C(10)	4056(2)	1564(9)	7936(5)	34(1)
C(11)	3528(2)	3936(9)	7779(5)	24(1)
C(12)	3365(2)	5666(9)	8432(5)	28(1)
C(7)	4068(2)	1415(11)	10718(6)	43(2)
C(26)	3120(2)	5542(9)	1621(5)	32(1)
C(8)	3756(2)	2140(10)	9749(5)	36(2)
C(6)	4341(2)	2976(11)	11148(5)	36(1)
C(27)	2804(2)	4131(9)	1420(5)	34(2)
C(5)	4690(2)	2696(12)	11106(6)	46(2)
C(4)	4937(2)	4132(13)	11476(7)	54(2)
C(3)	4844(2)	5907(12)	11905(7)	55(2)
C(1)	4253(2)	4803(13)	11590(7)	58(2)
C(2)	4499(2)	6280(14)	11964(8)	68(2)

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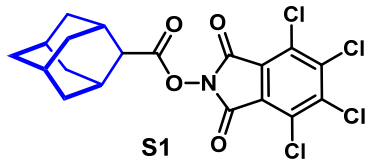
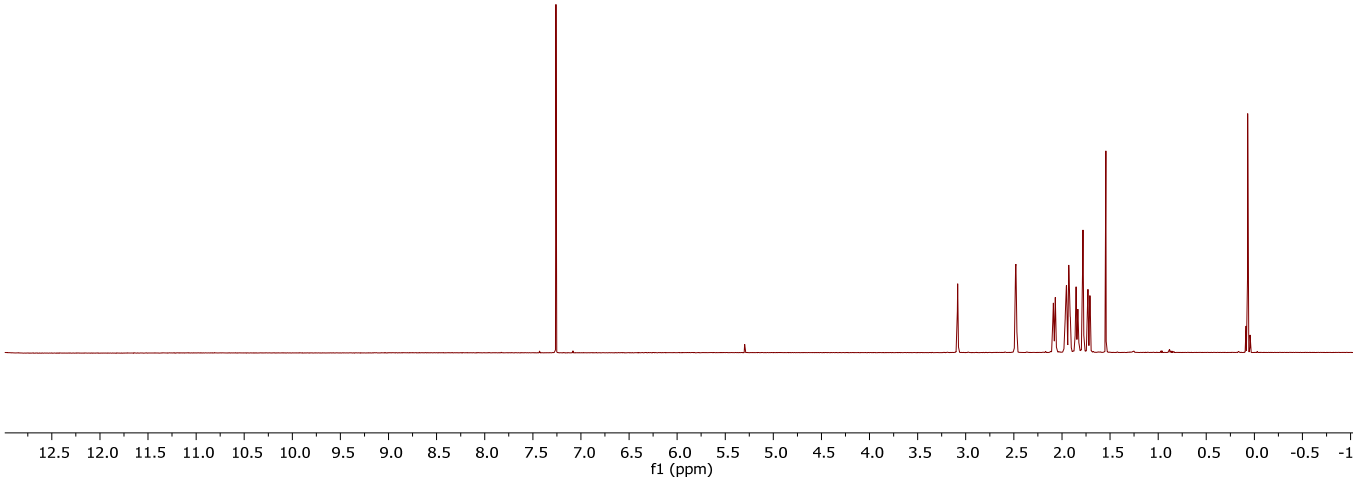
Spectra for Compounds

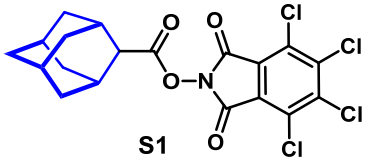
Compound S1 ^{1}H NMR



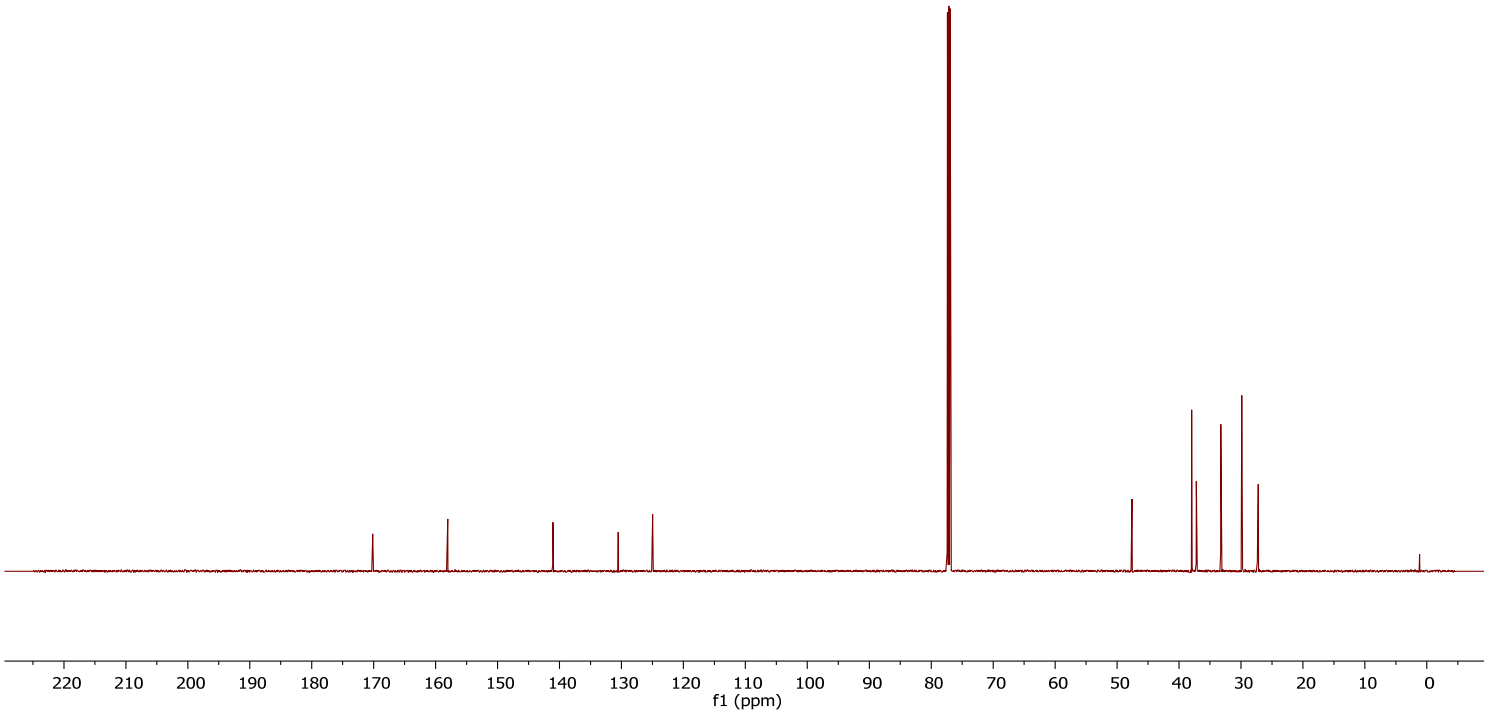
S1



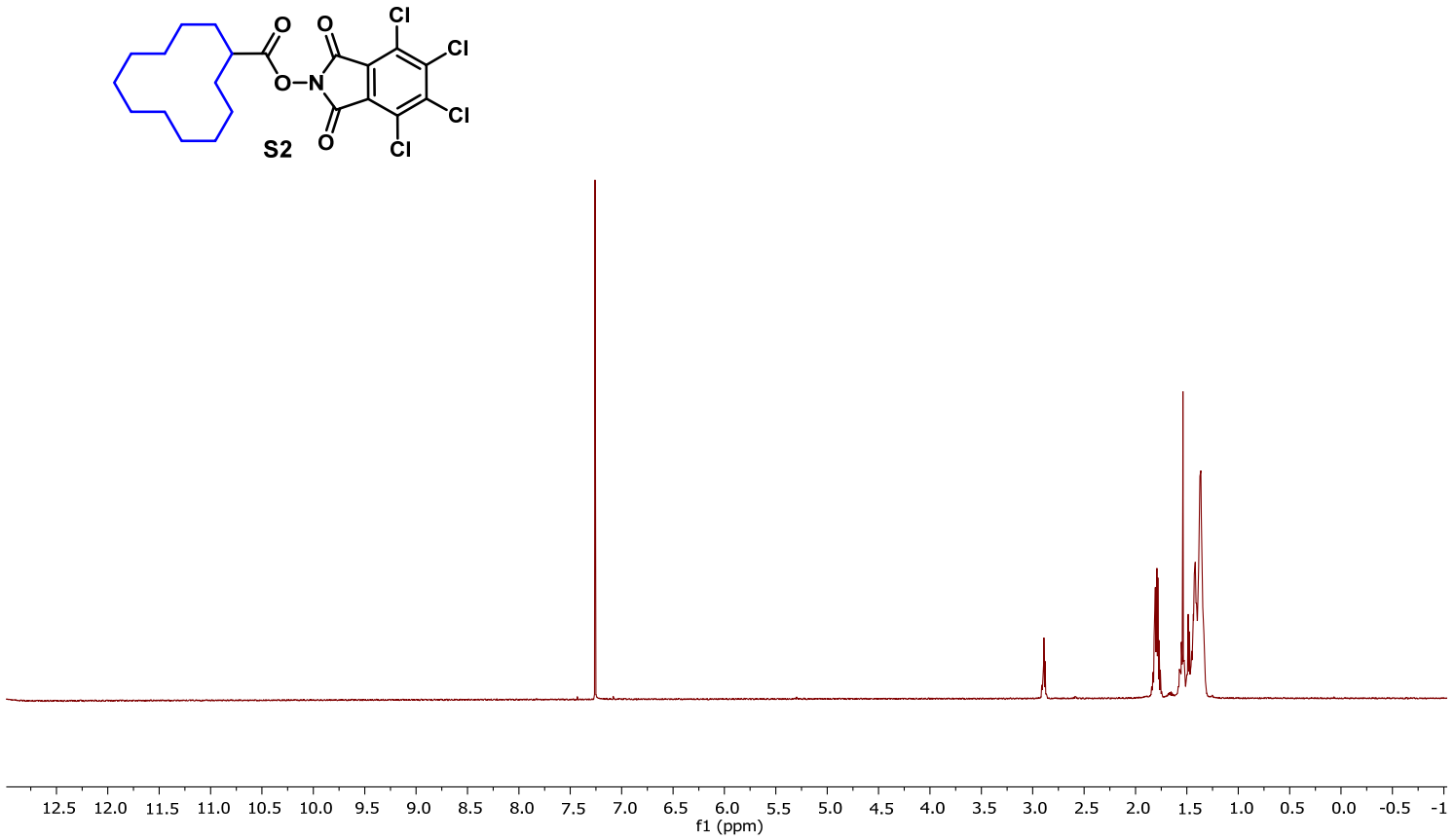
Compound S1 ^{13}C NMR



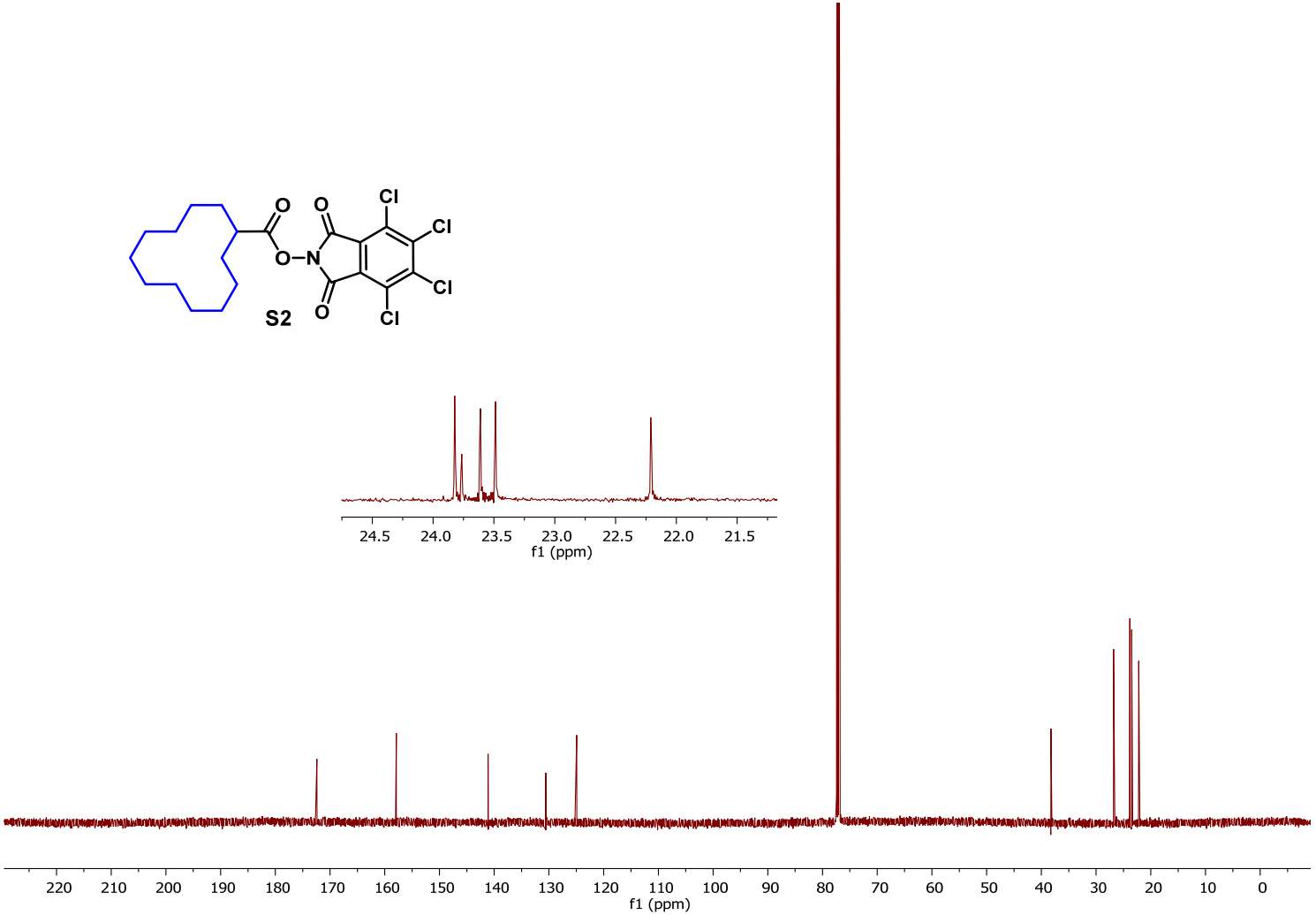
S1



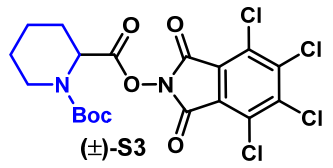
Compound S2 ^{1}H NMR



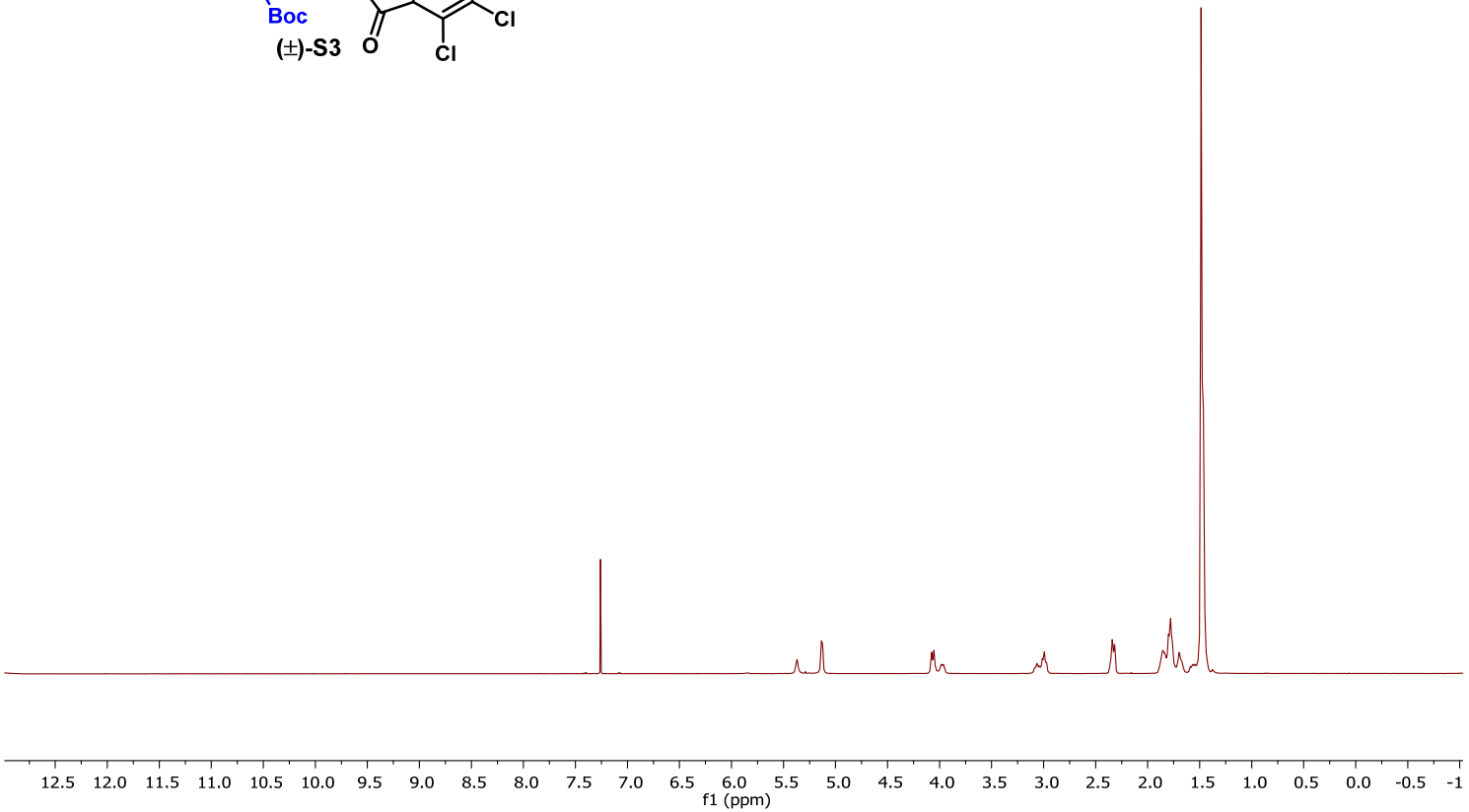
Compound S2 ^{13}C NMR



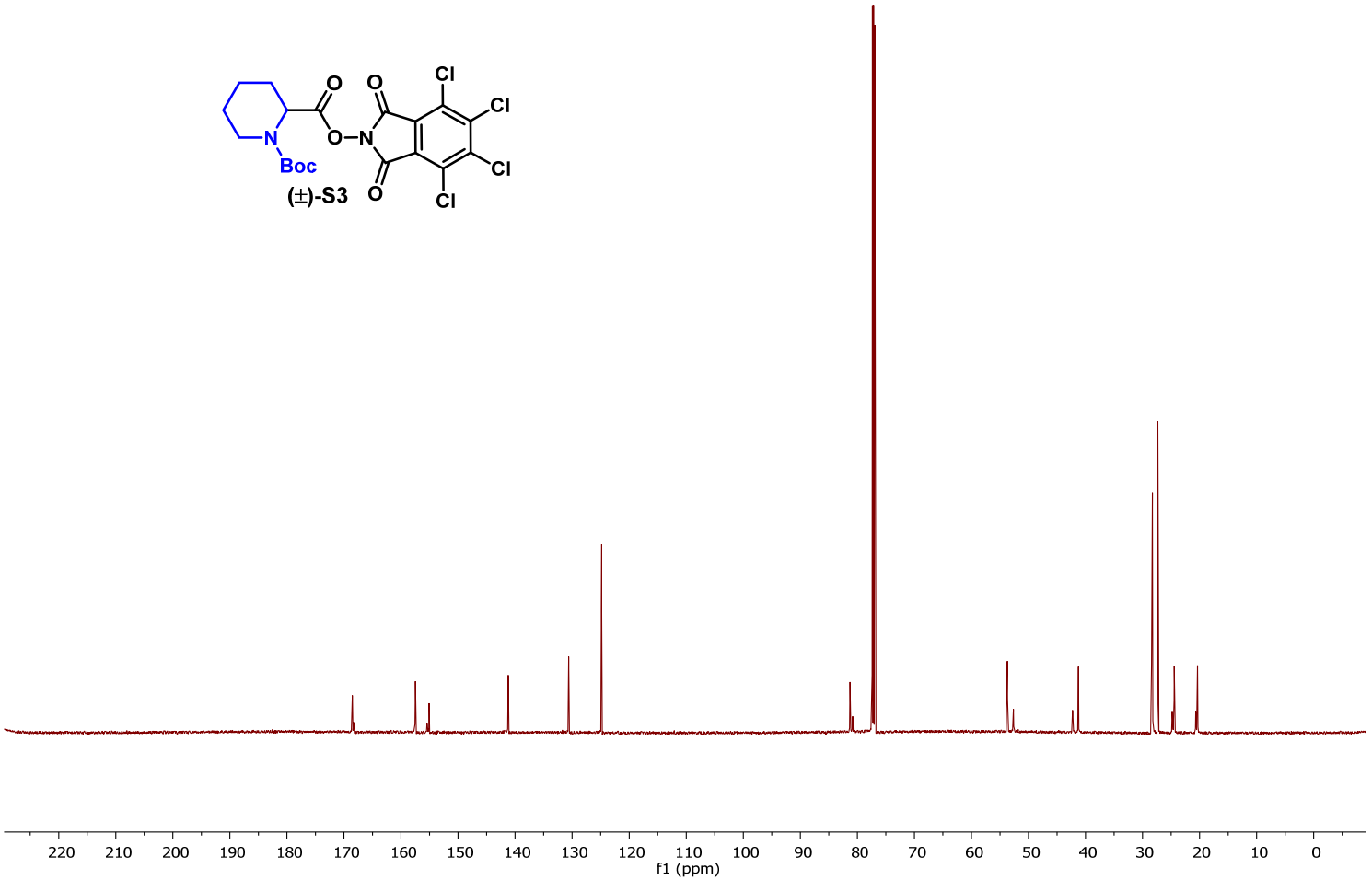
Compound (±)-S3 ^{1}H NMR



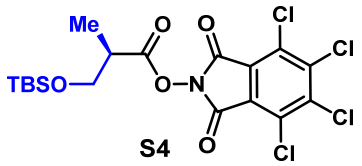
(±)-S3



Compound (±)-S3 ^{13}C NMR

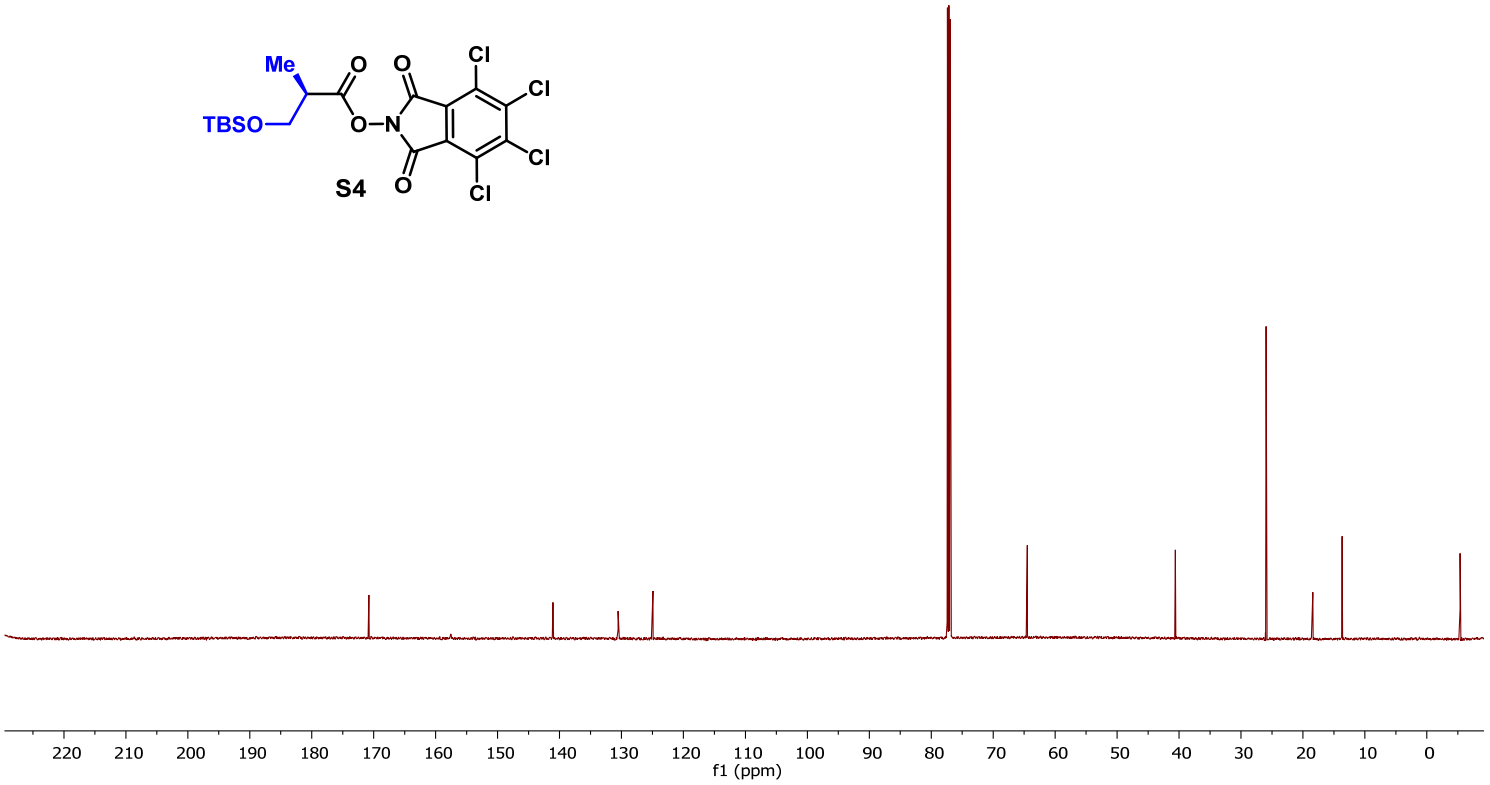


Compound S4 ^{1}H NMR

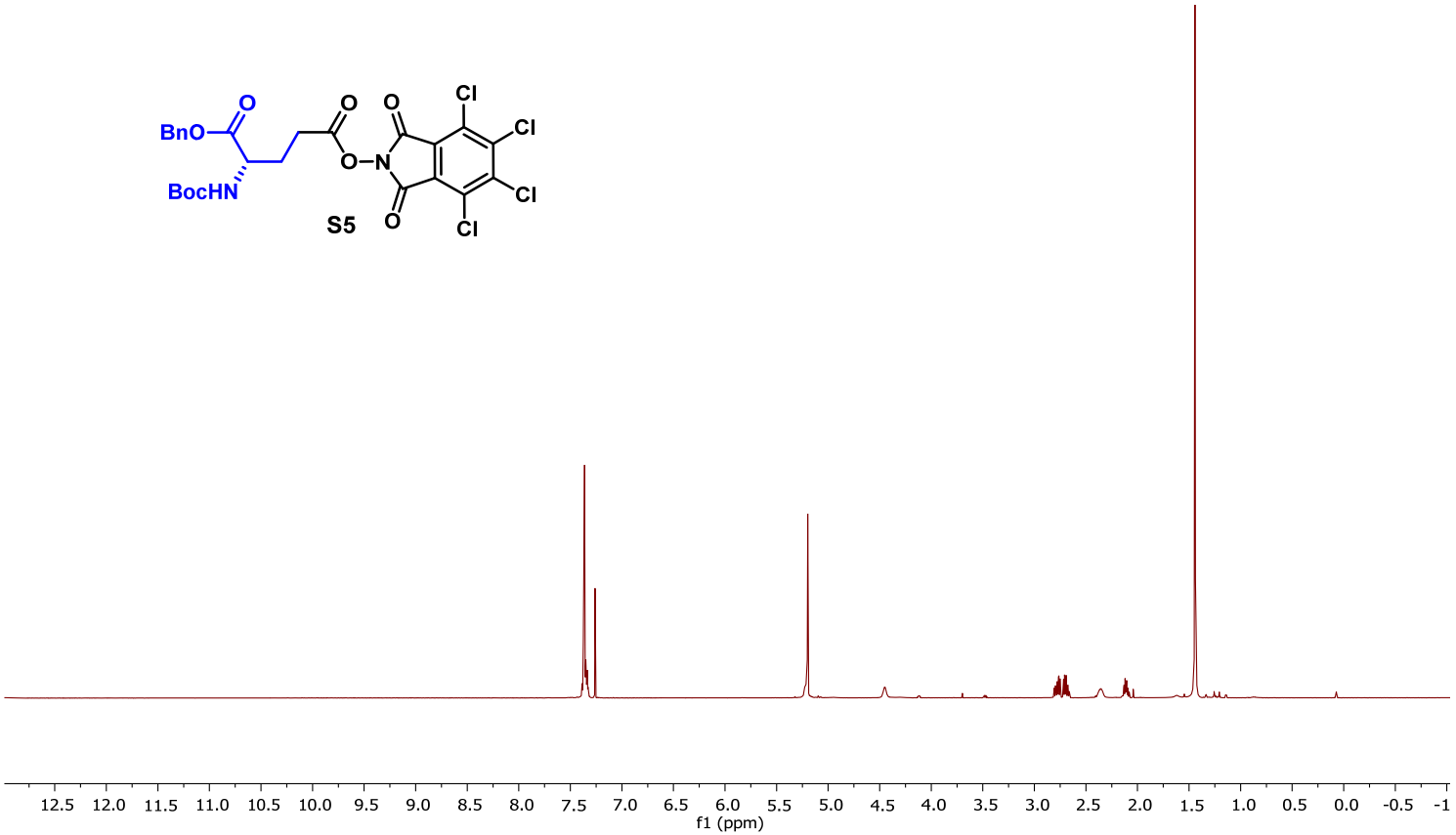


S4

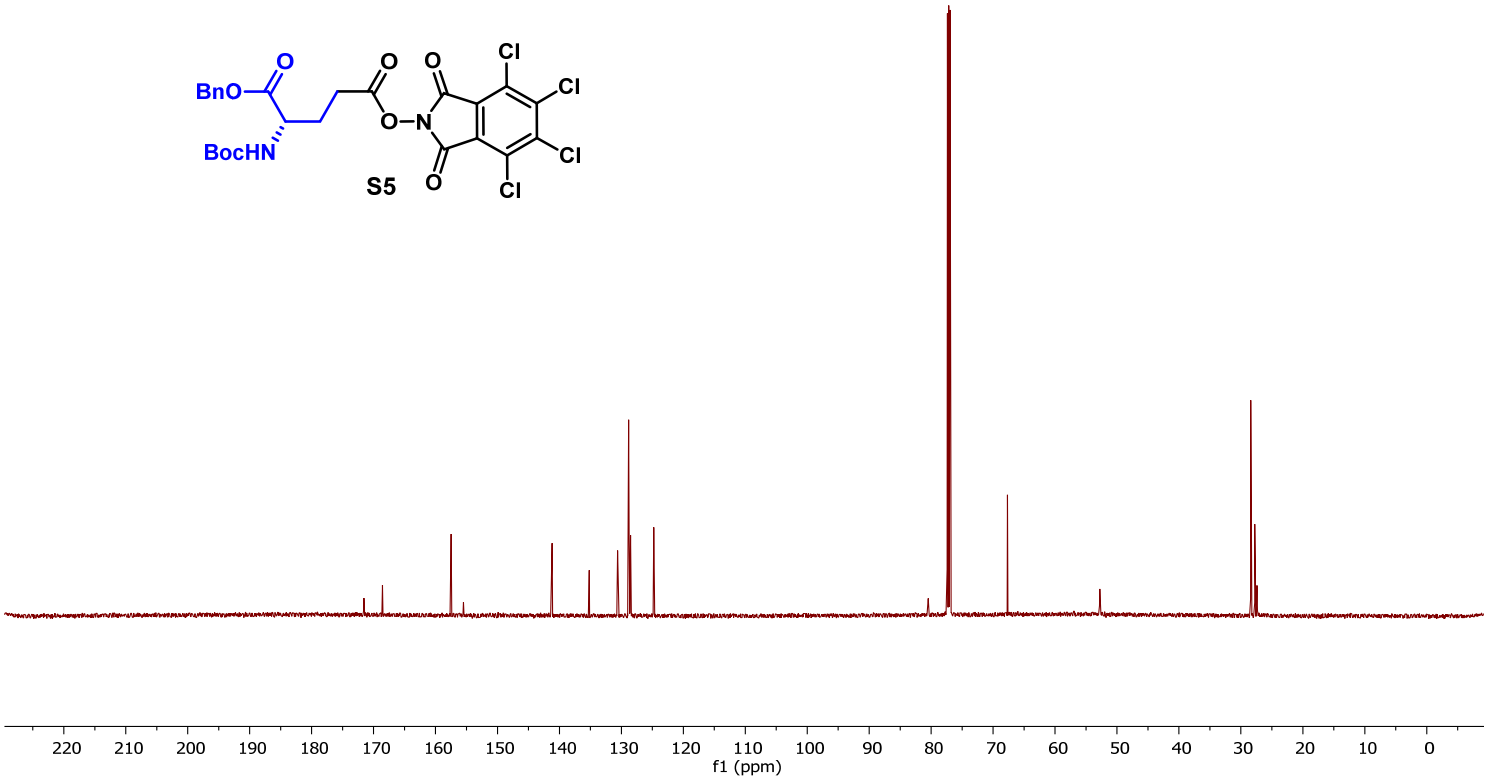
Compound S4 ^{13}C NMR



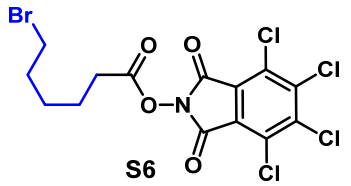
Compound S5 ^{1}H NMR

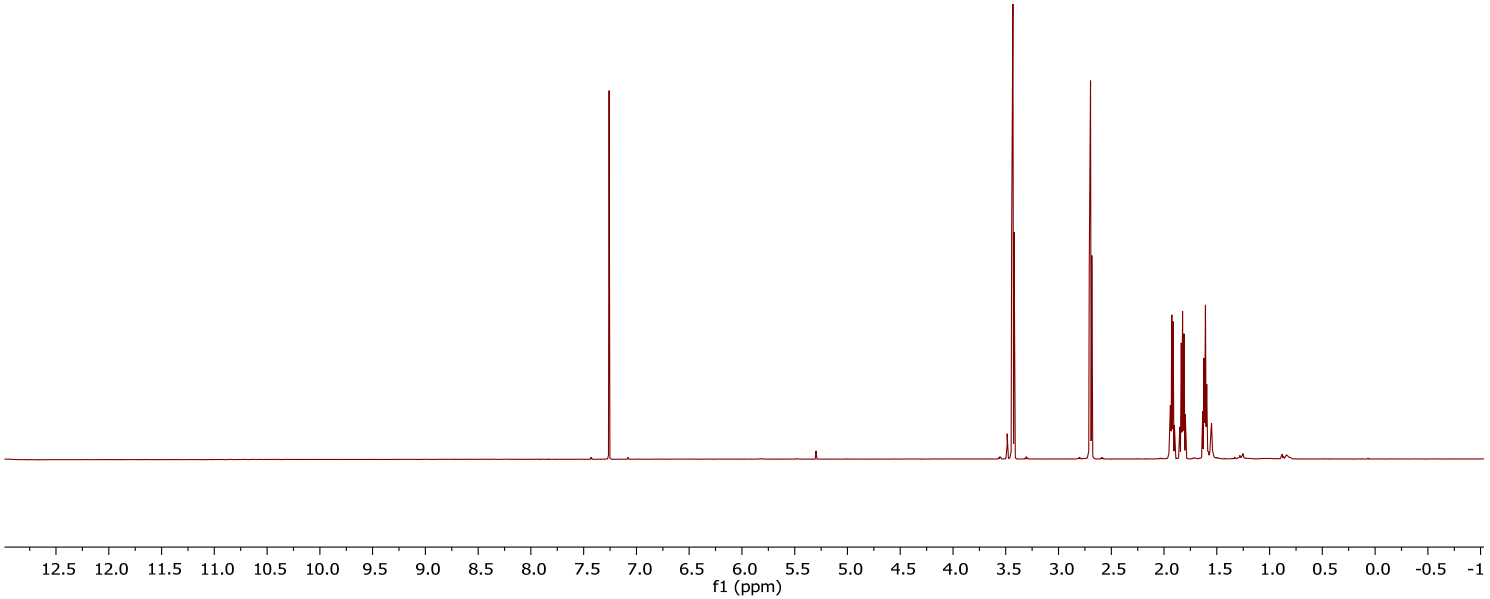


Compound S5 ^{13}C NMR

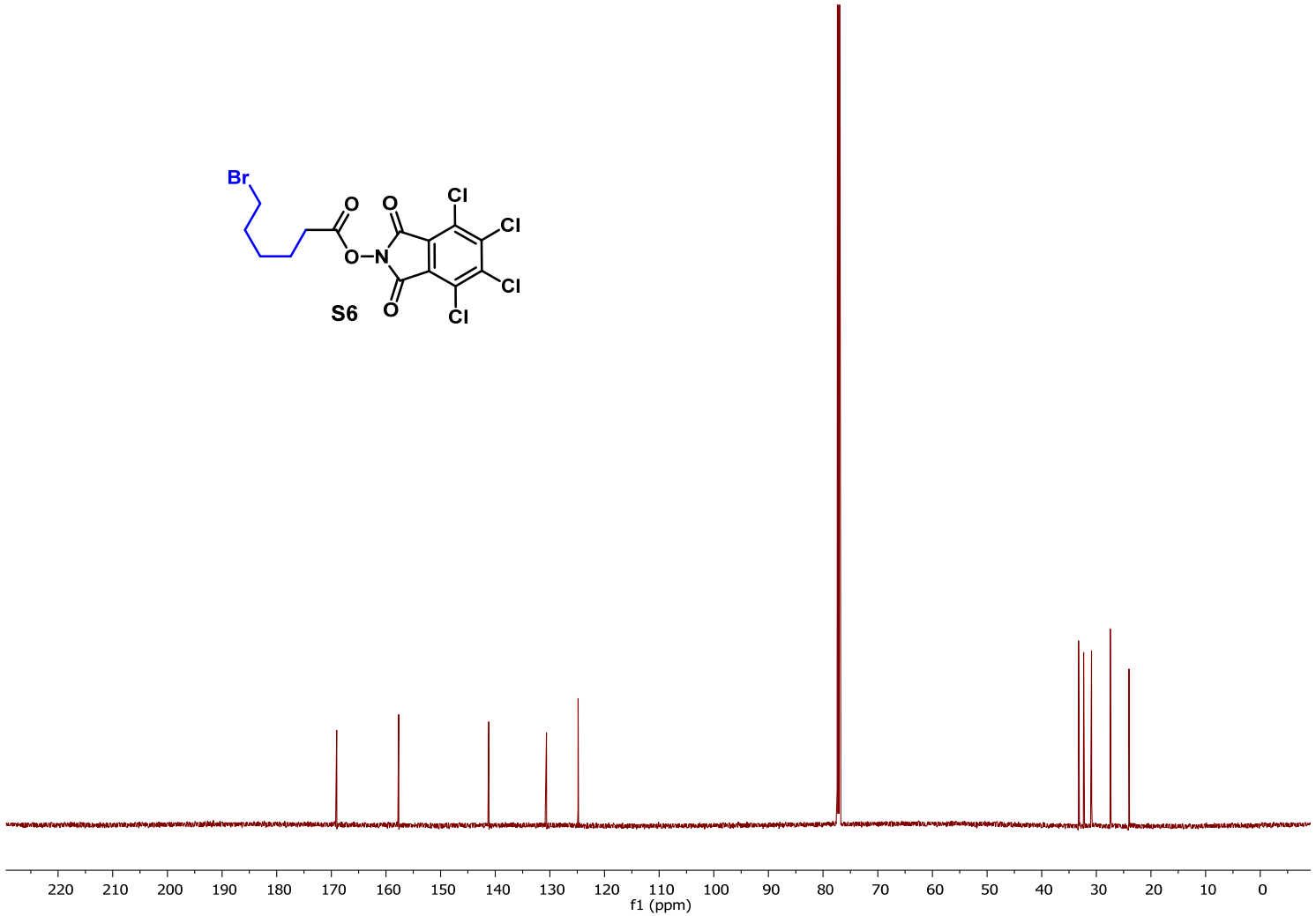


Compound S6 ^{1}H NMR

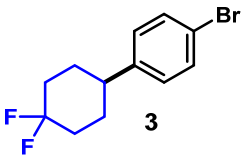




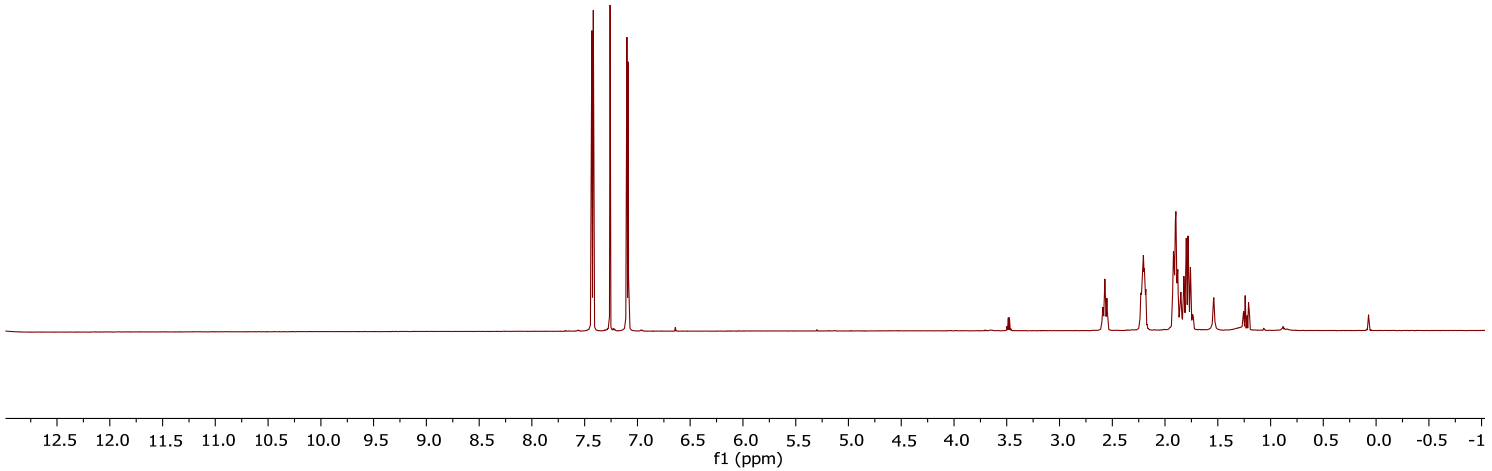
Compound S6 ^{13}C NMR



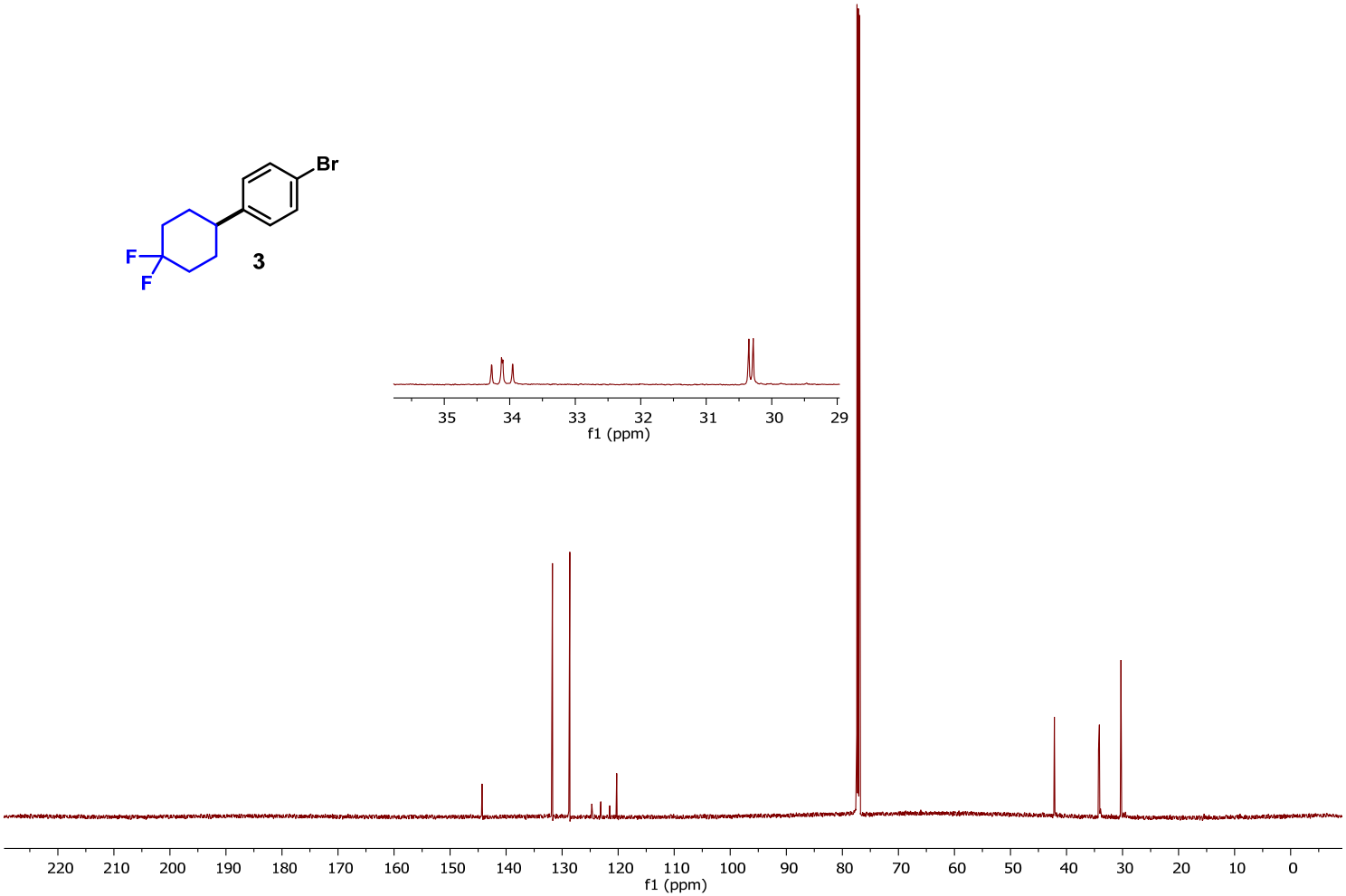
Compound 3 ^{1}H NMR



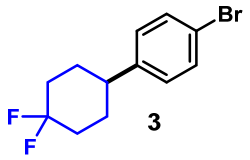
3



Compound 3 ^{13}C NMR



Compound 3 ^{19}F NMR



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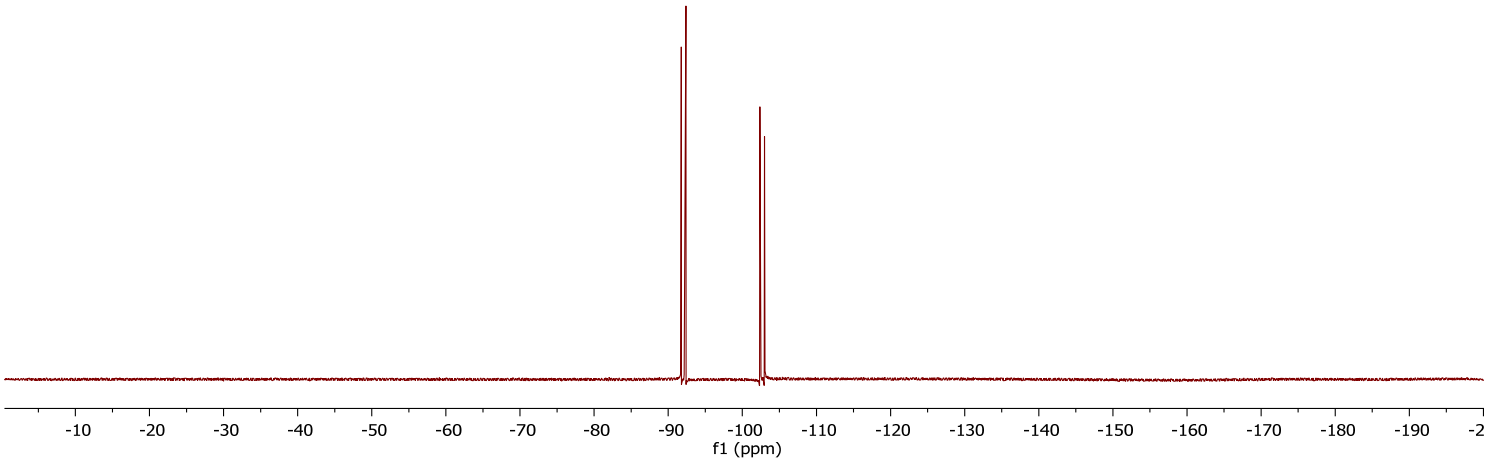
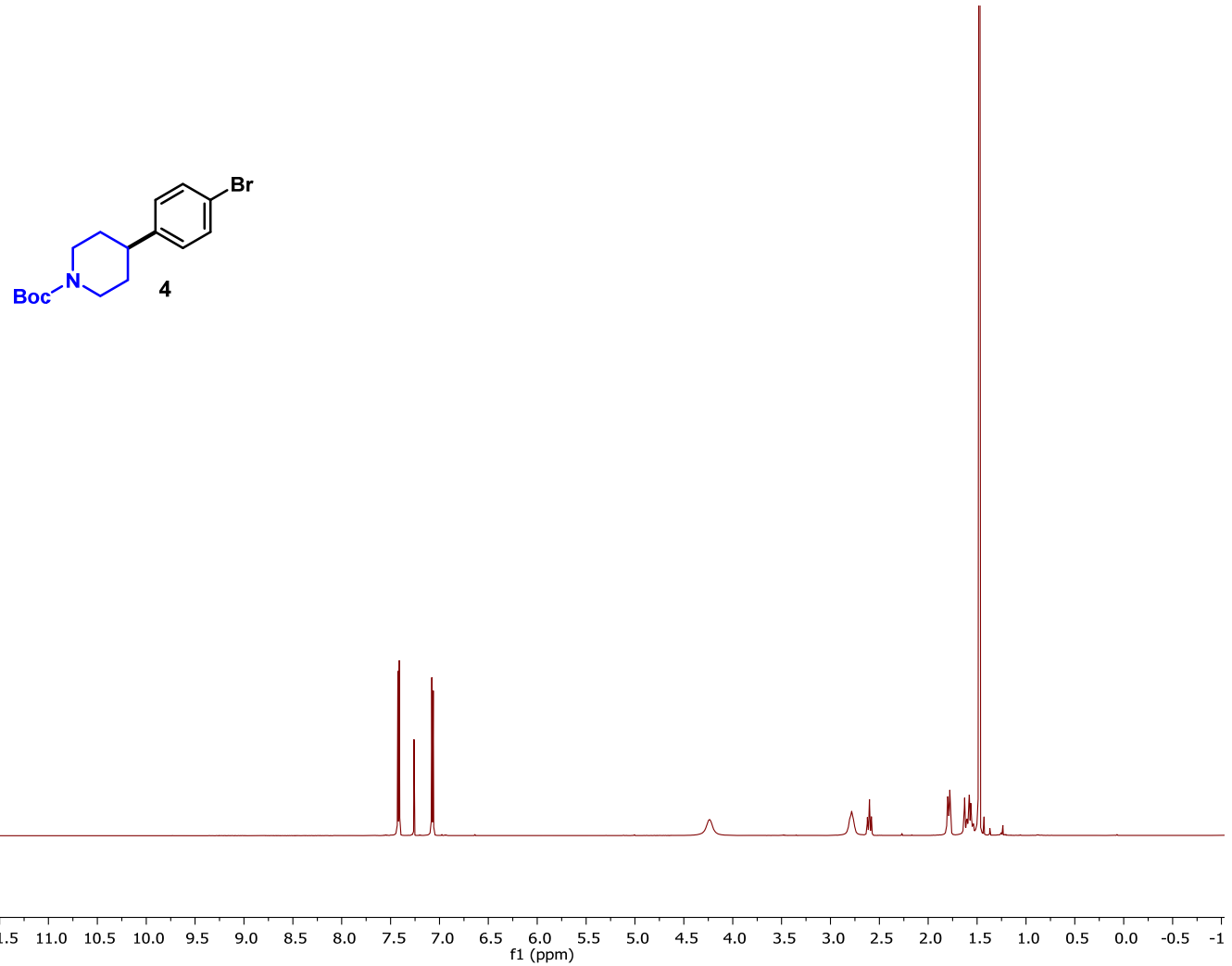
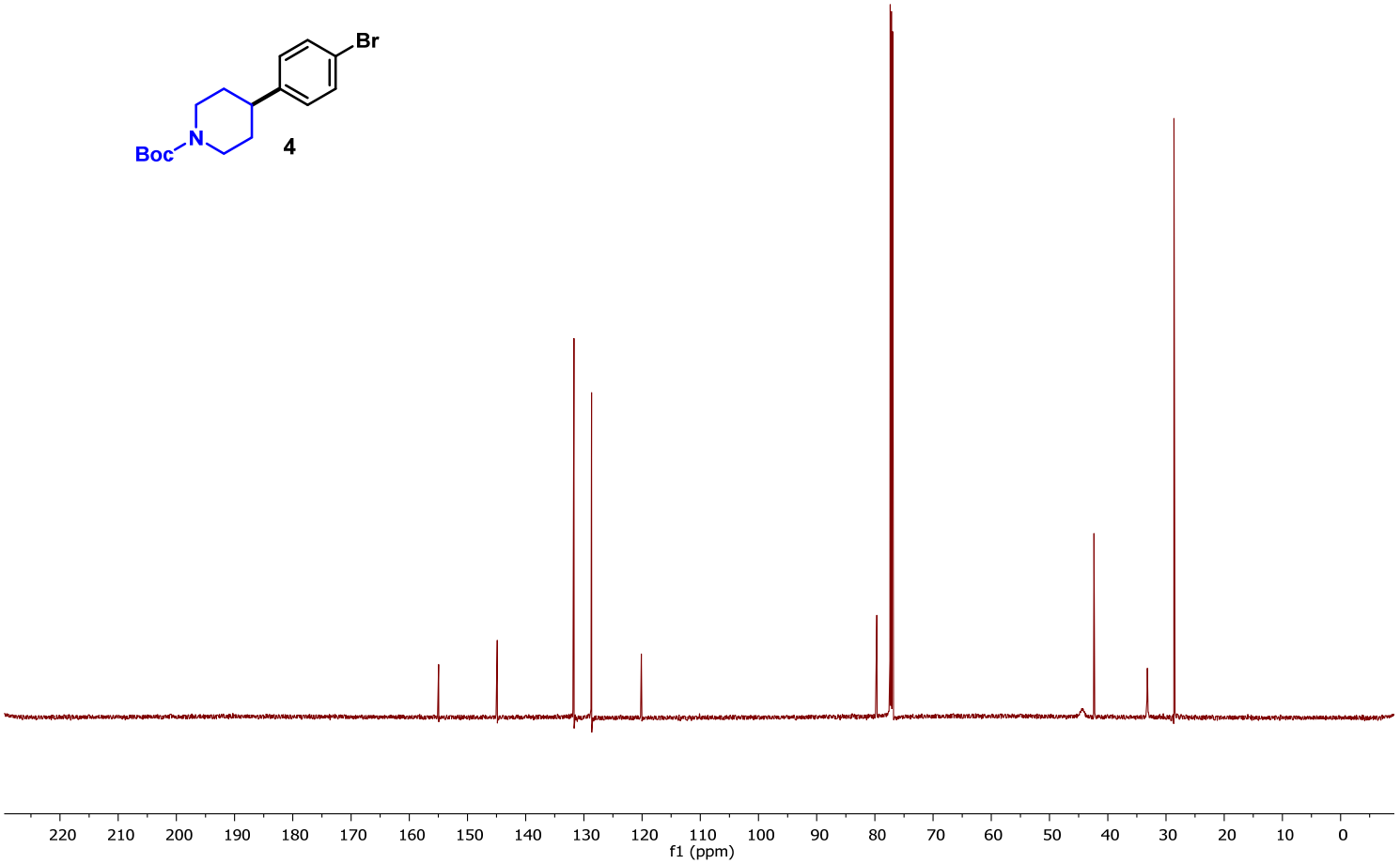


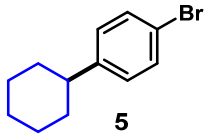
Compound 4 ^{1}H NMR



Compound 4 ^{13}C NMR



Compound 5 ^{1}H NMR



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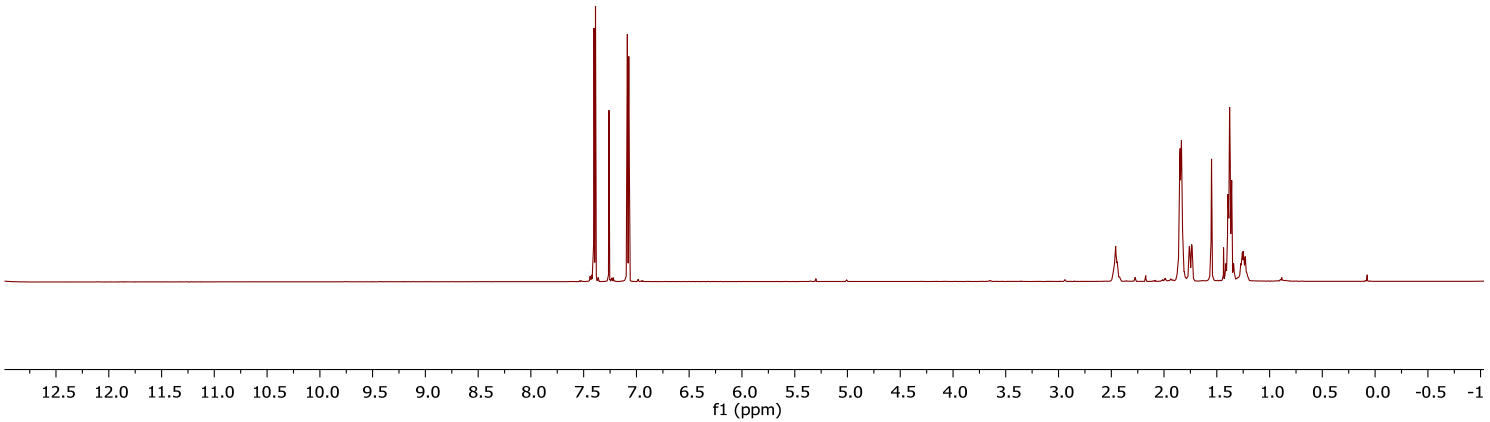
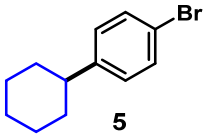


Compound 5 ^{13}C NMR



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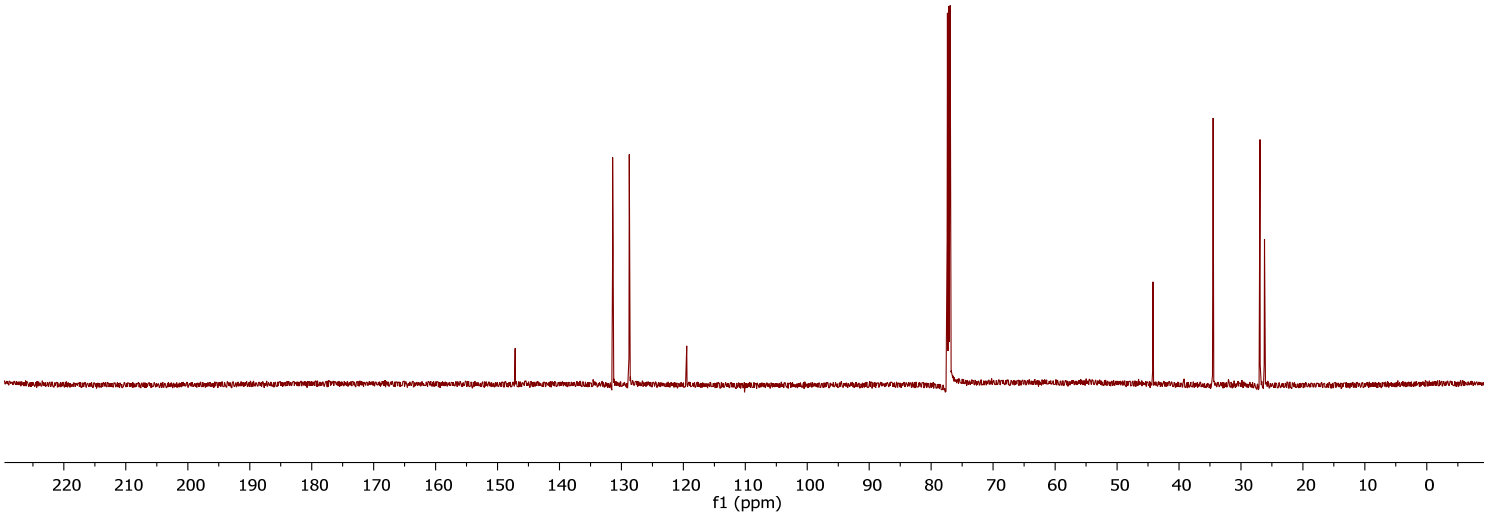
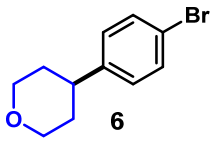
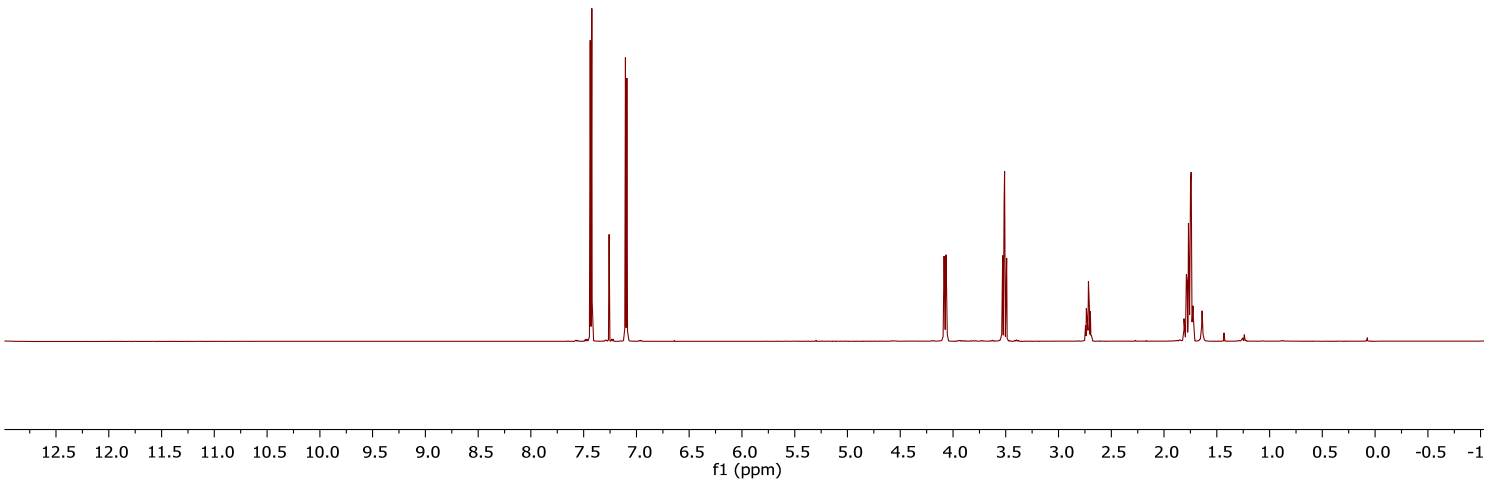
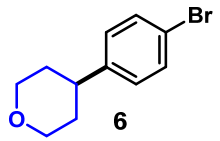


Compound 6 ^{1}H NMR





Compound 6 ^{13}C NMR



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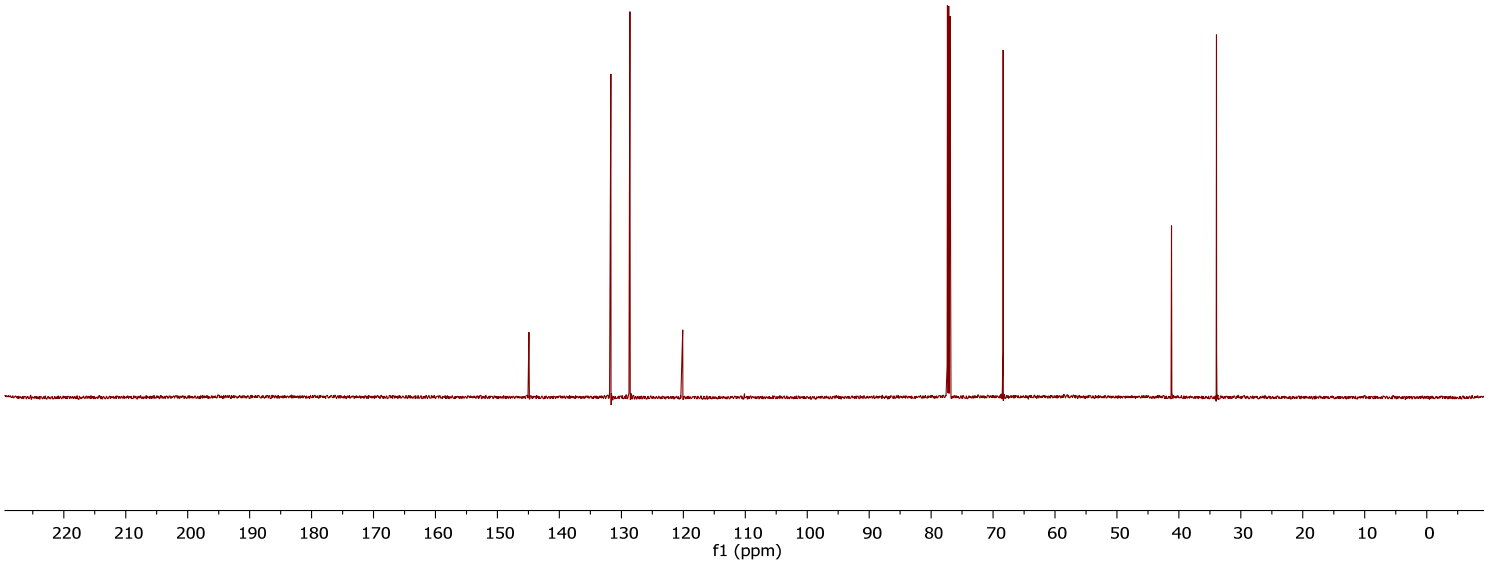
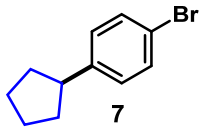


Compound 7 ^{1}H NMR



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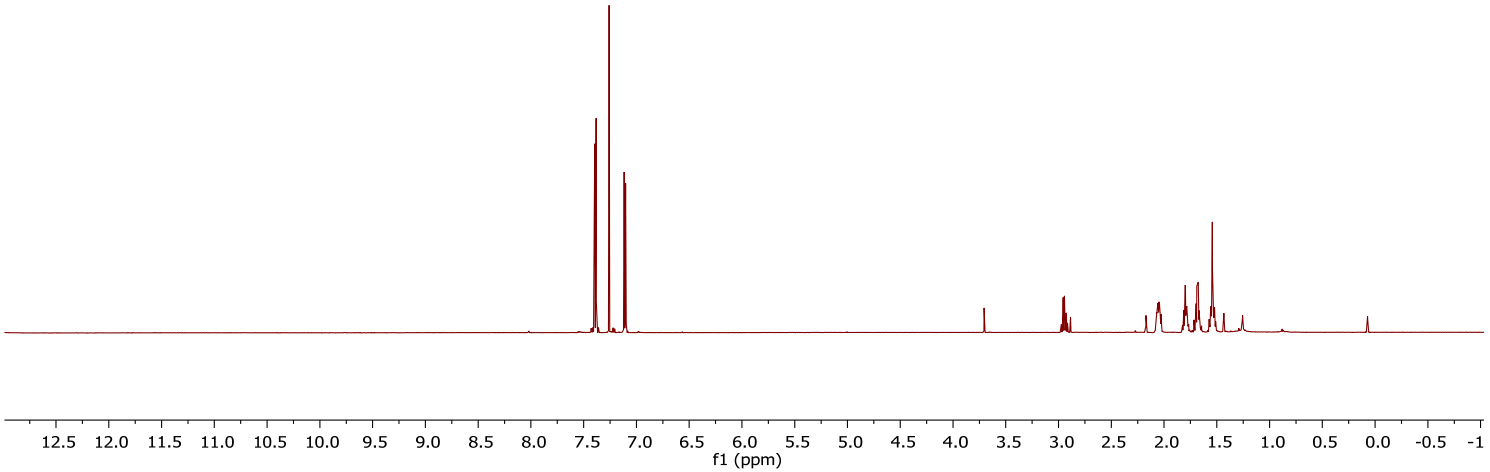
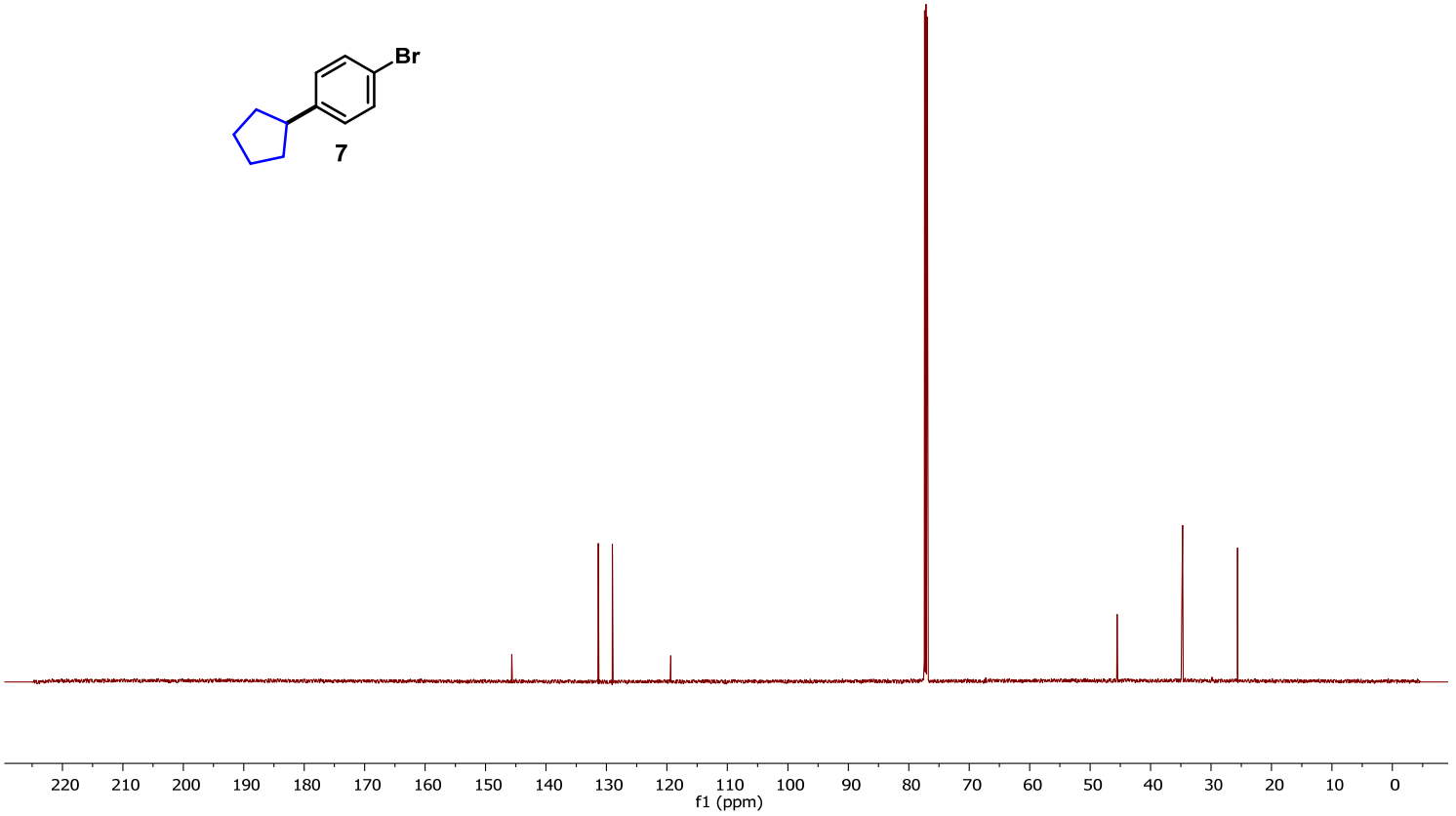
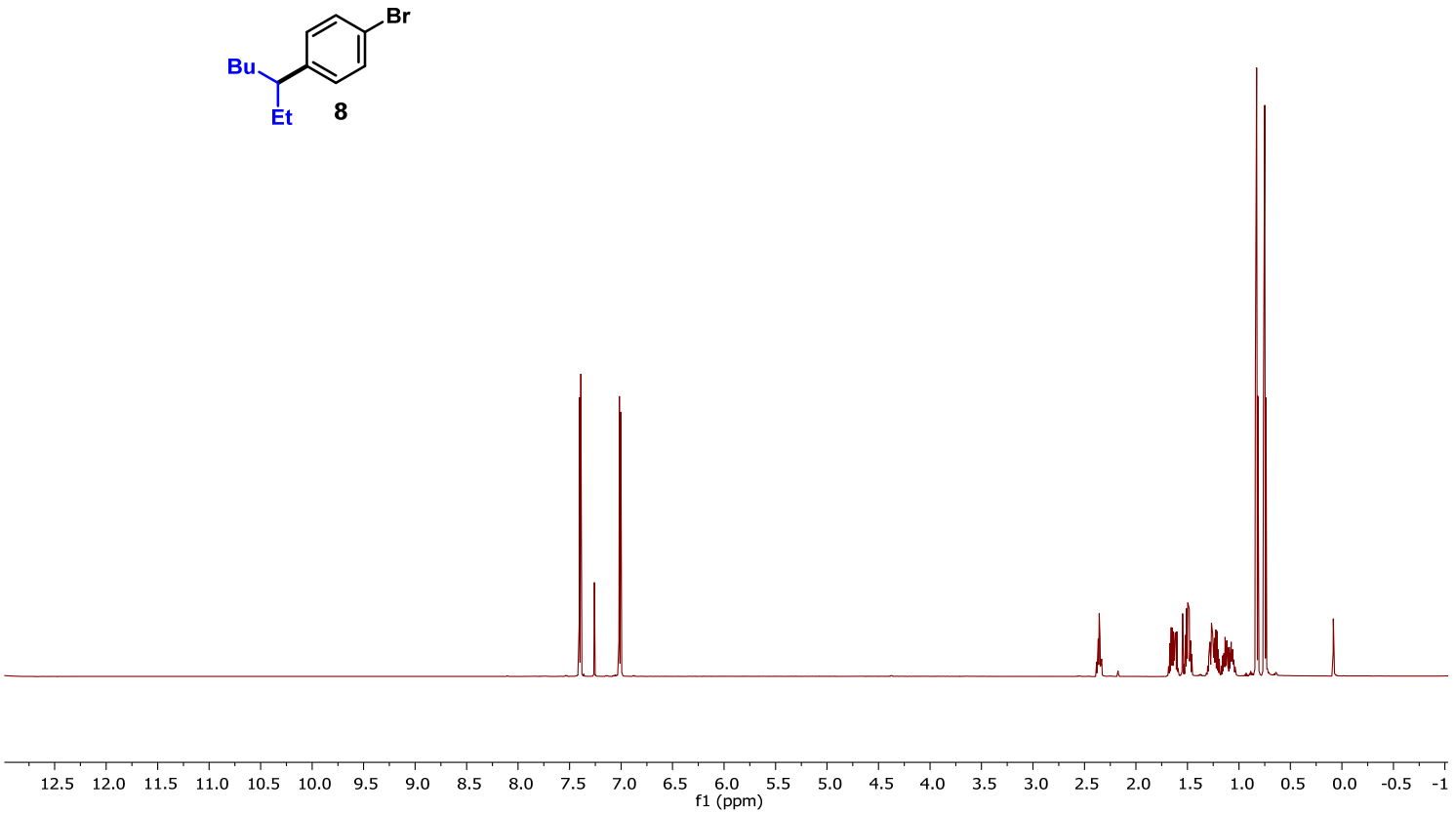


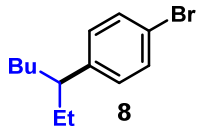
Compound 7 ^{13}C NMR



Compound 8 ^{1}H NMR



Compound 8 ^{13}C NMR



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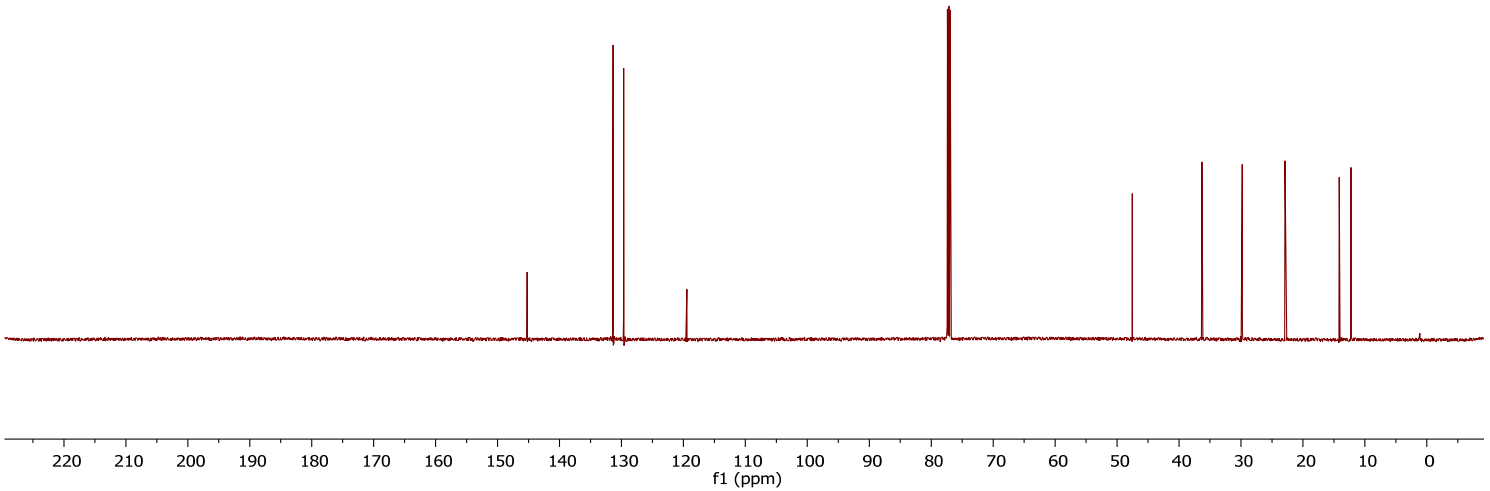
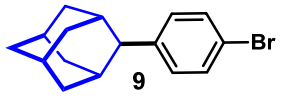
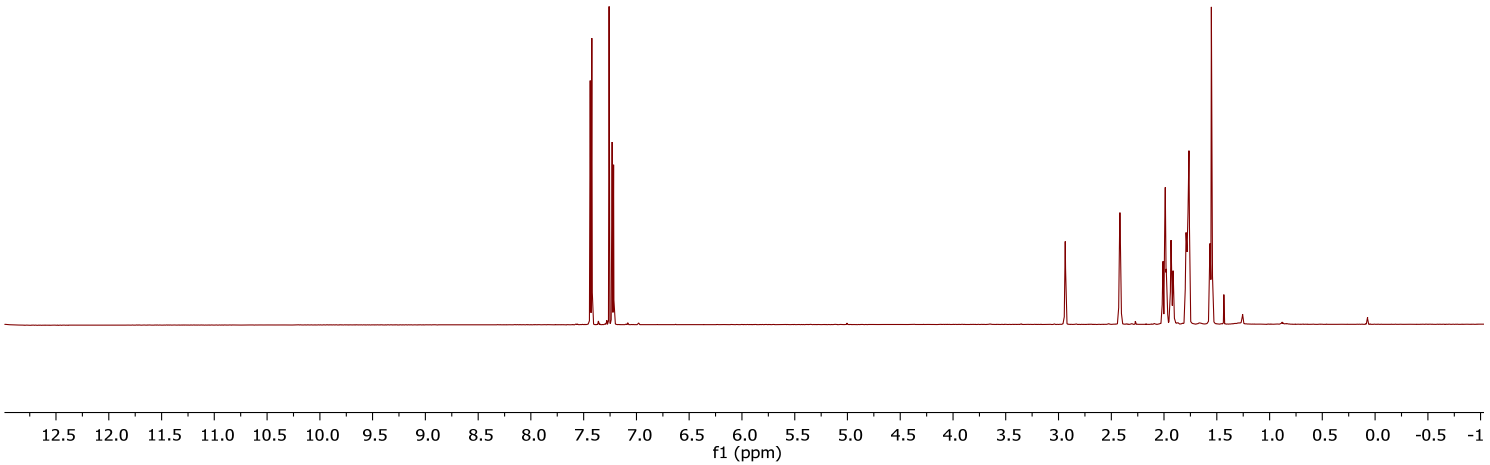
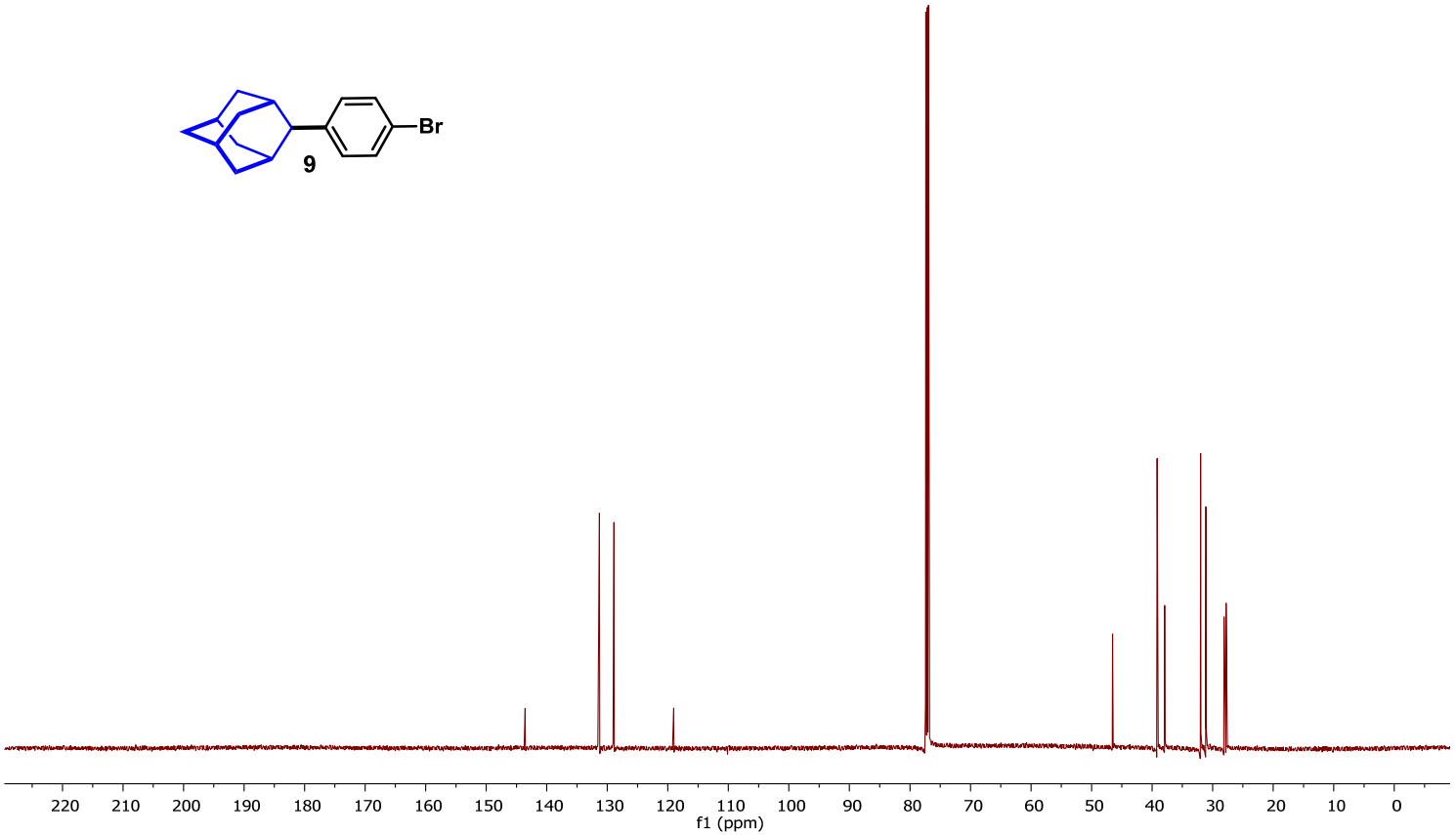


Compound 9 ^{1}H NMR

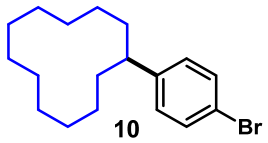


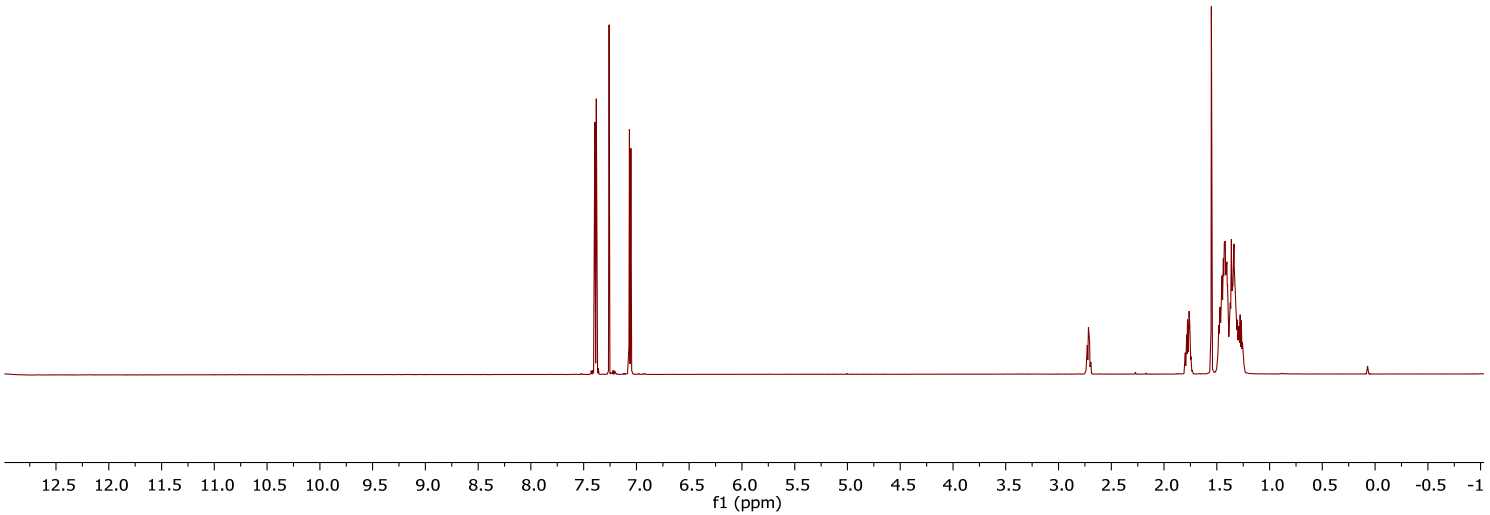


Compound 9 ^{13}C NMR

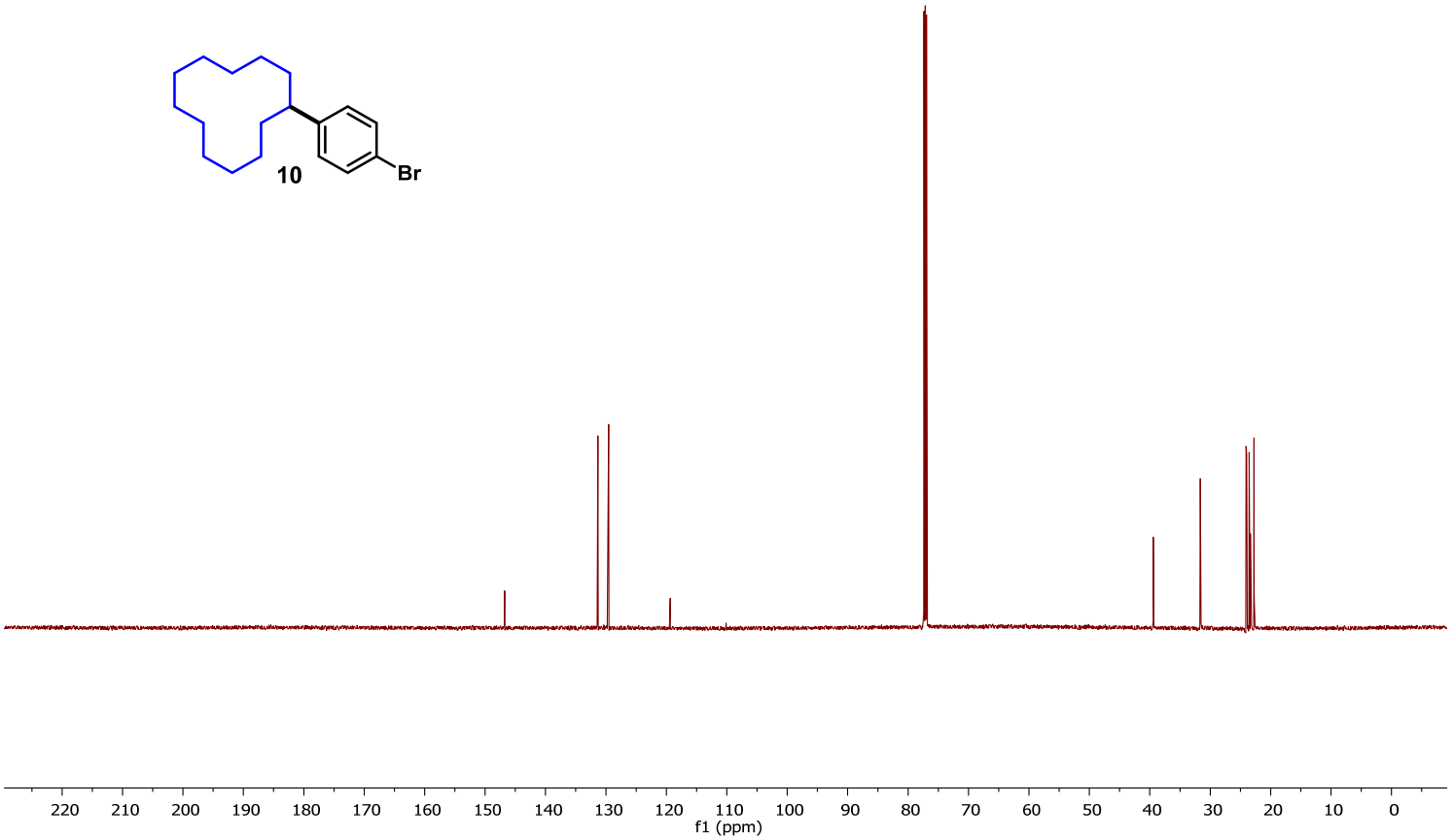


Compound 10 ^{1}H NMR

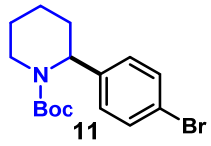


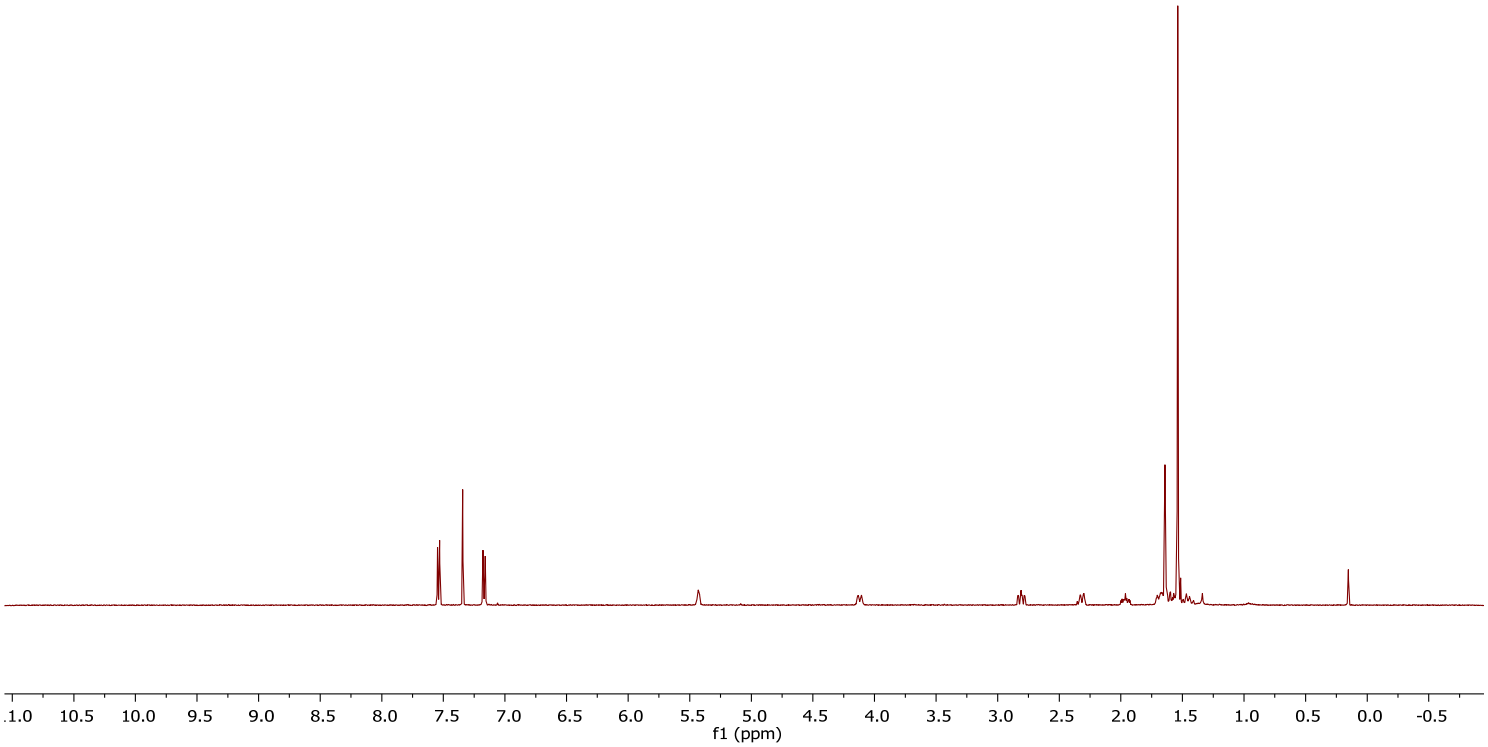


Compound 10 ^{13}C NMR

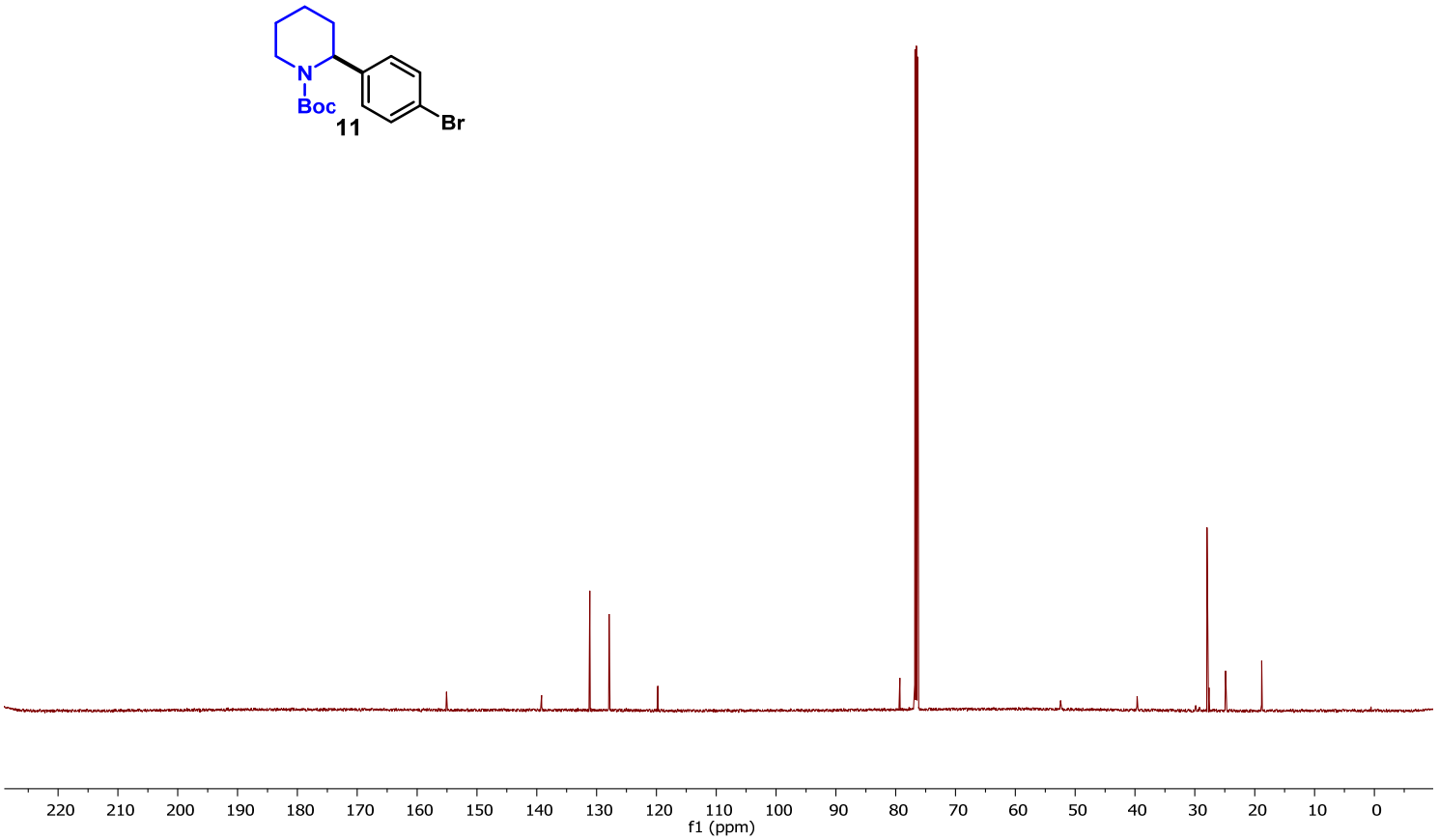


Compound 11 ^{1}H NMR

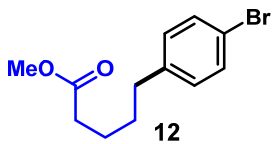




Compound 11 ^{13}C NMR



Compound 12 ^{1}H NMR



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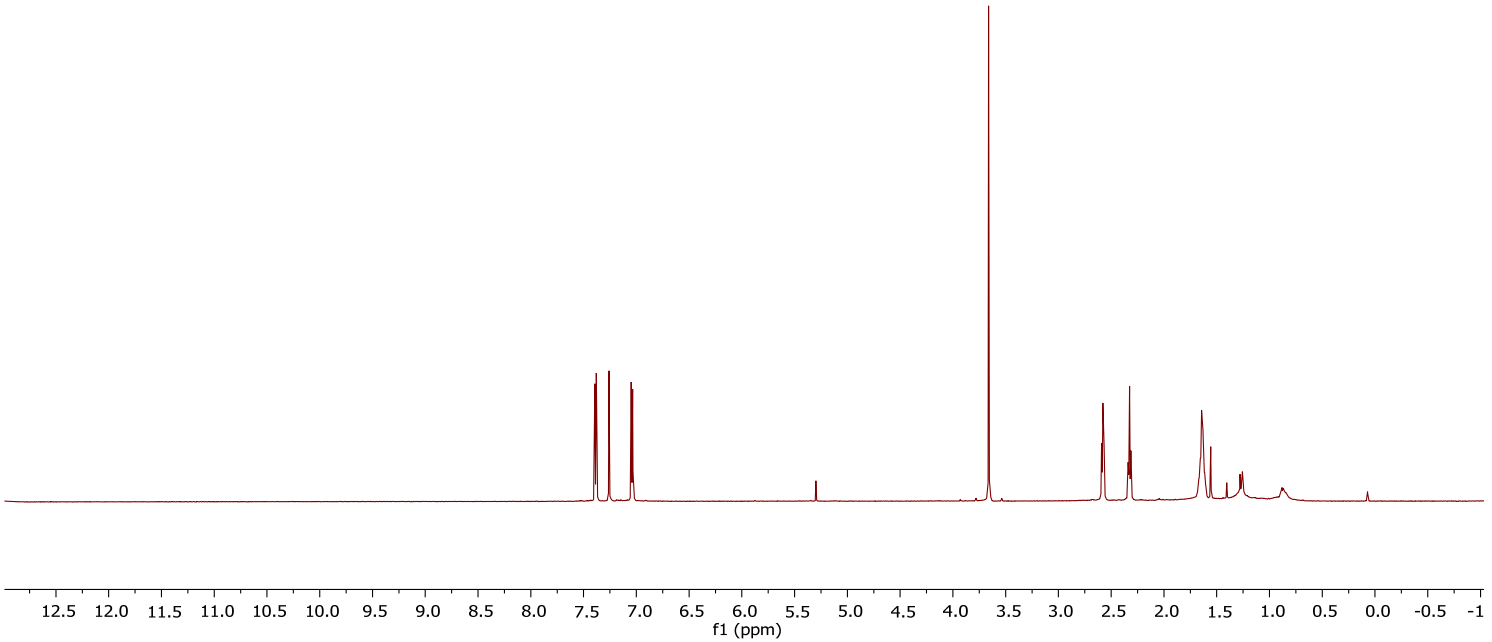
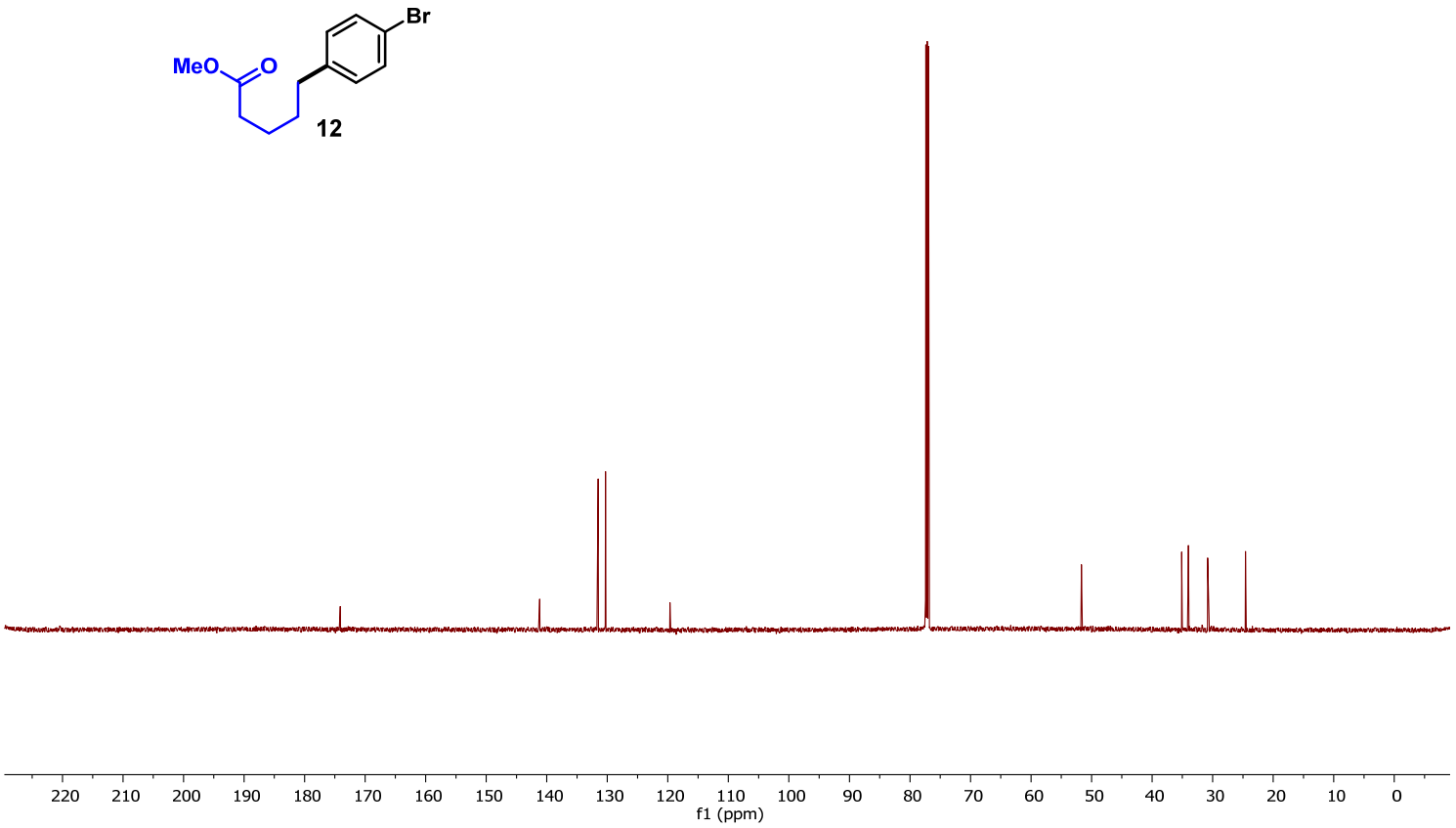


Compound 12 ^{13}C NMR



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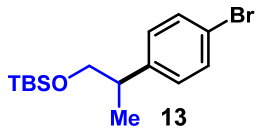

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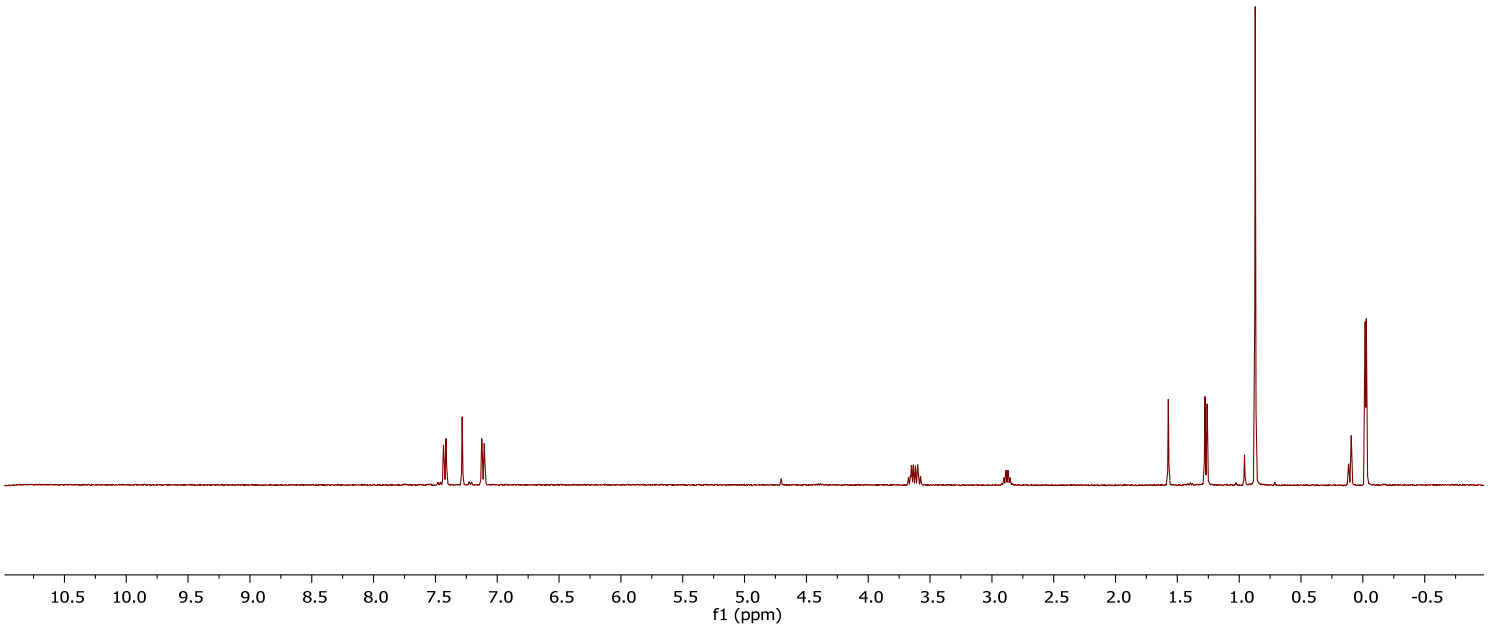
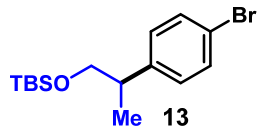


Compound 13 ^{13}C NMR



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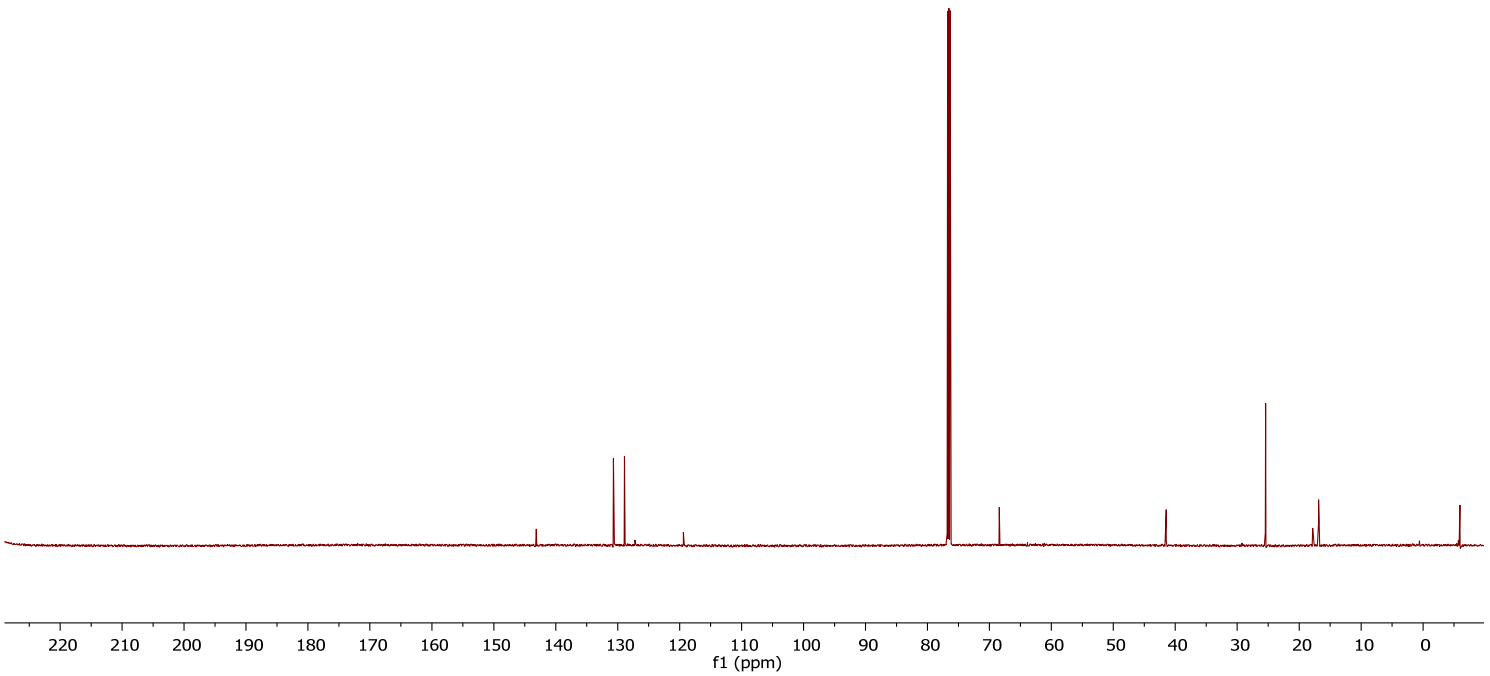
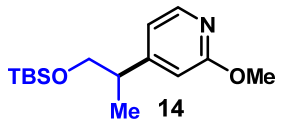


Compound 14 ^{1}H NMR



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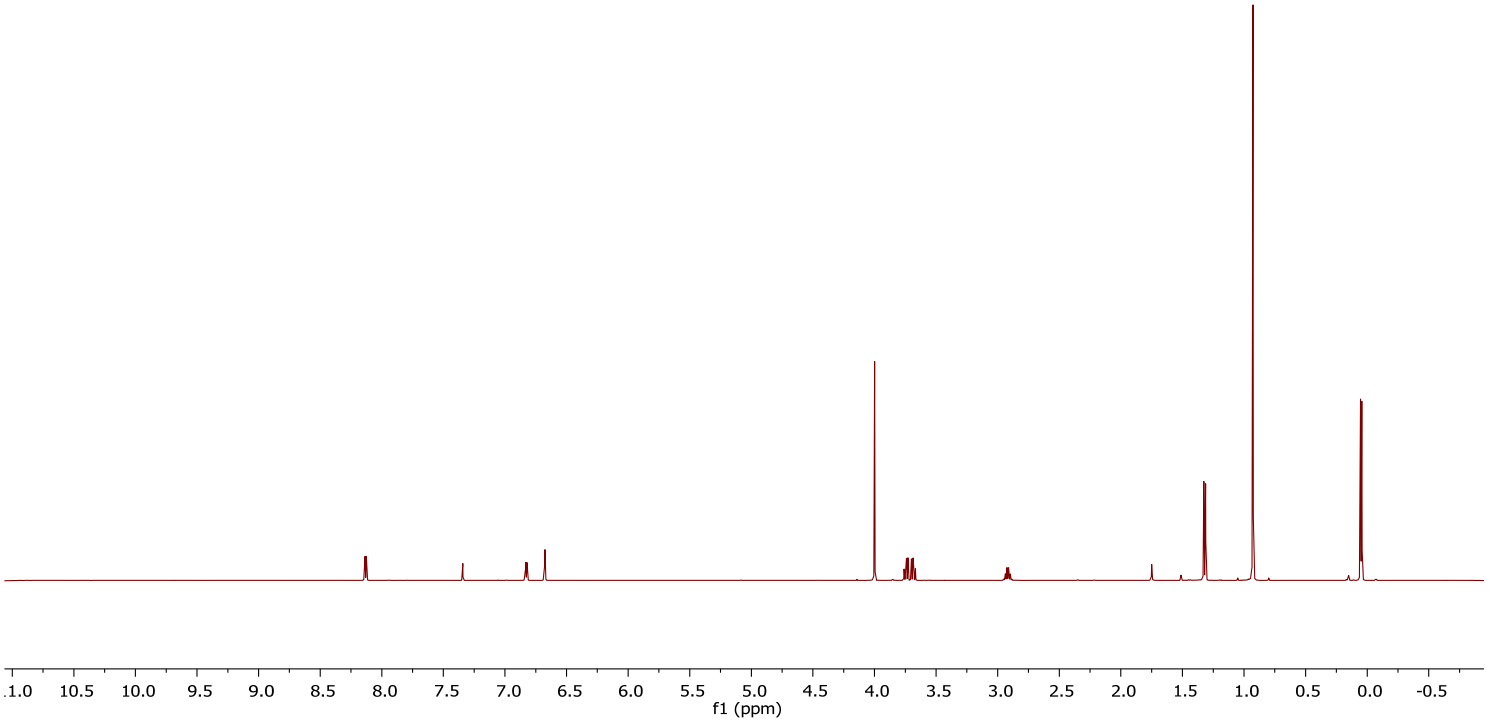
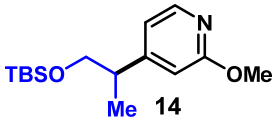
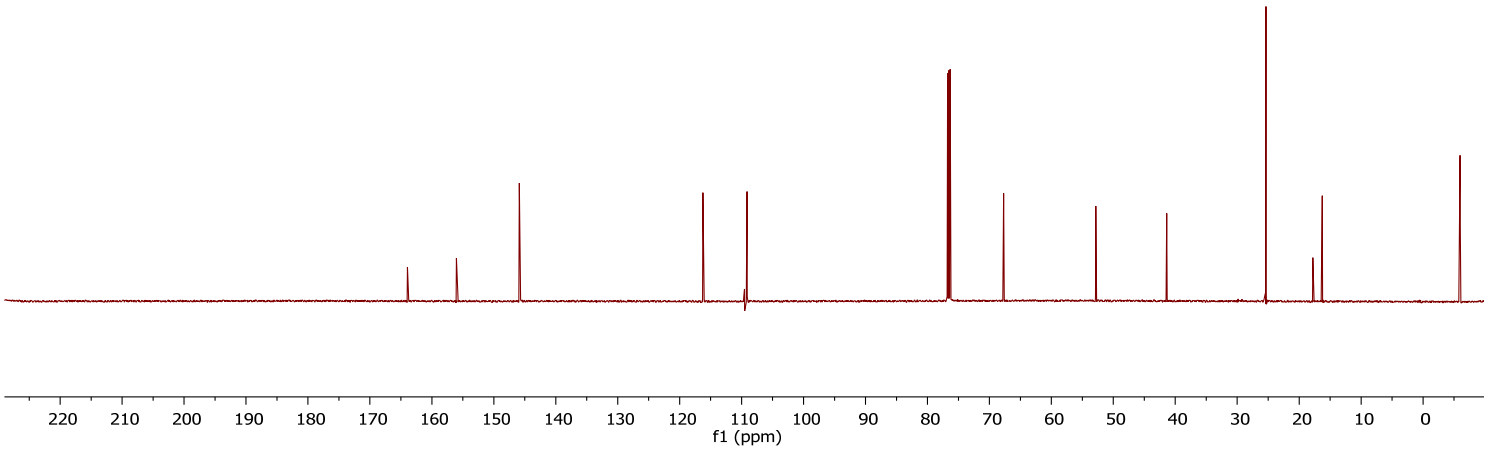
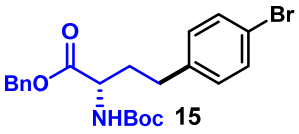


Compound 14 ^{13}C NMR





Compound 15 ^{1}H NMR



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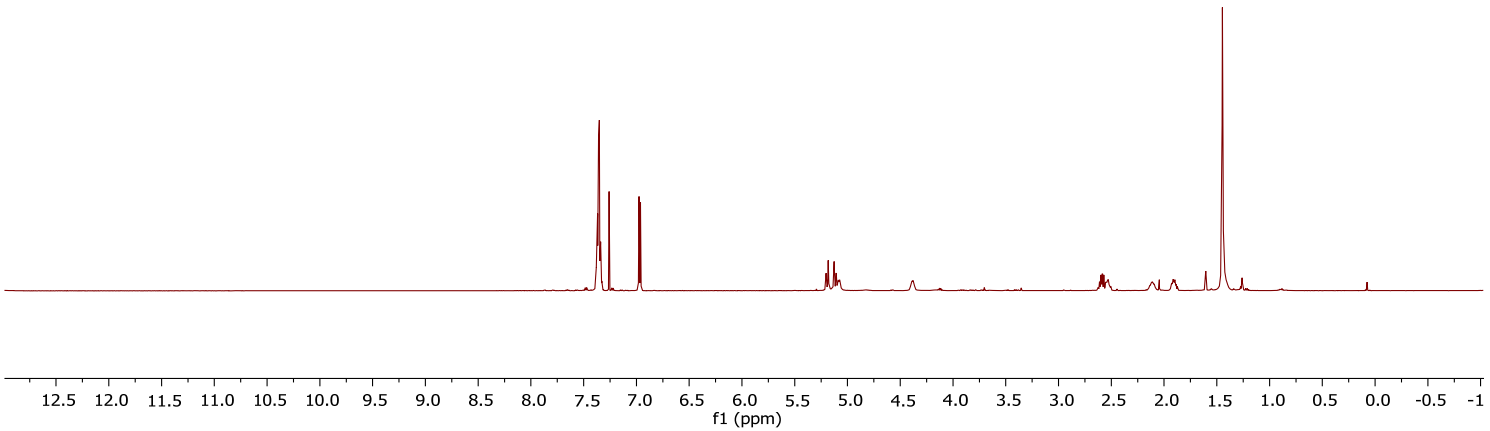
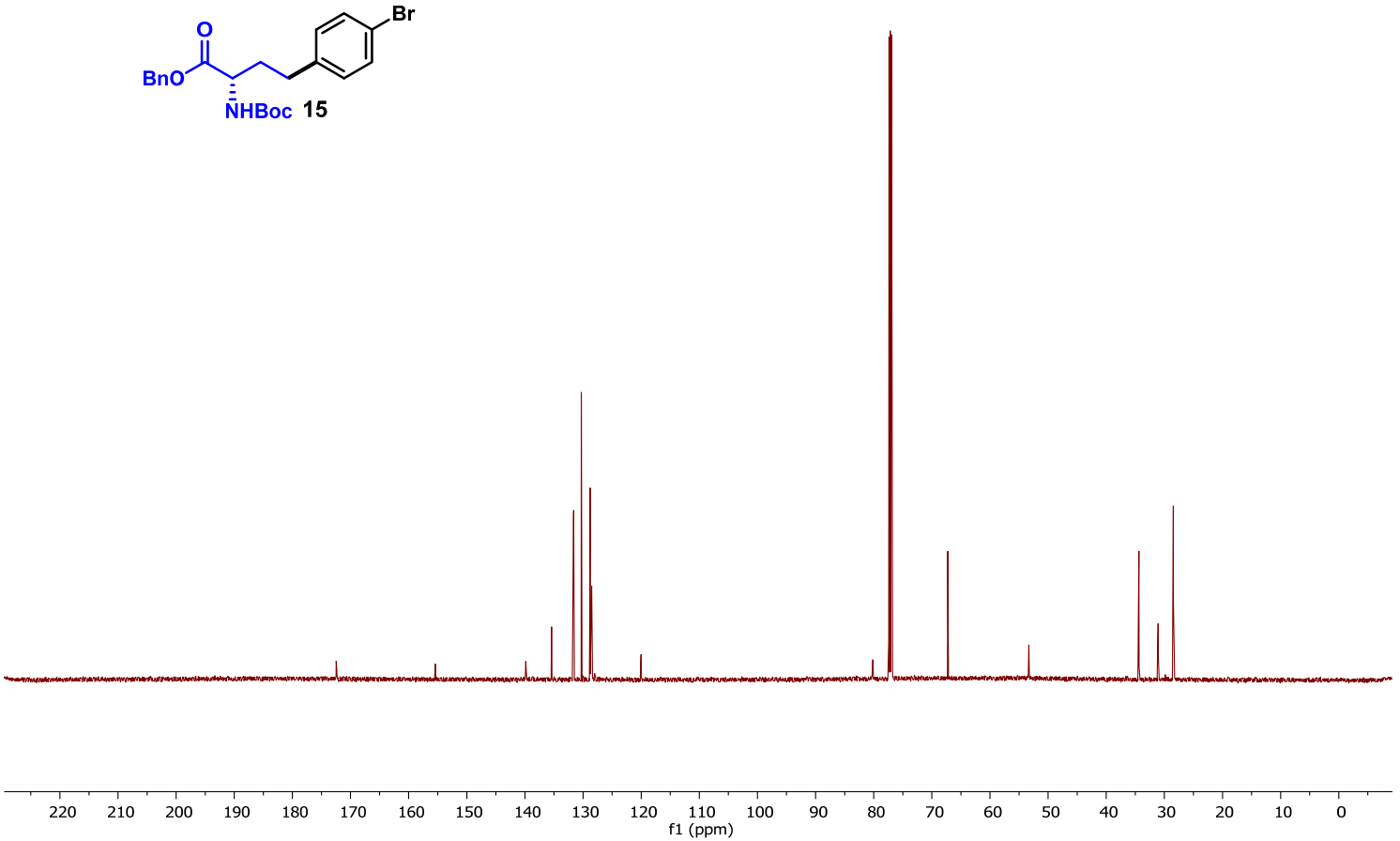
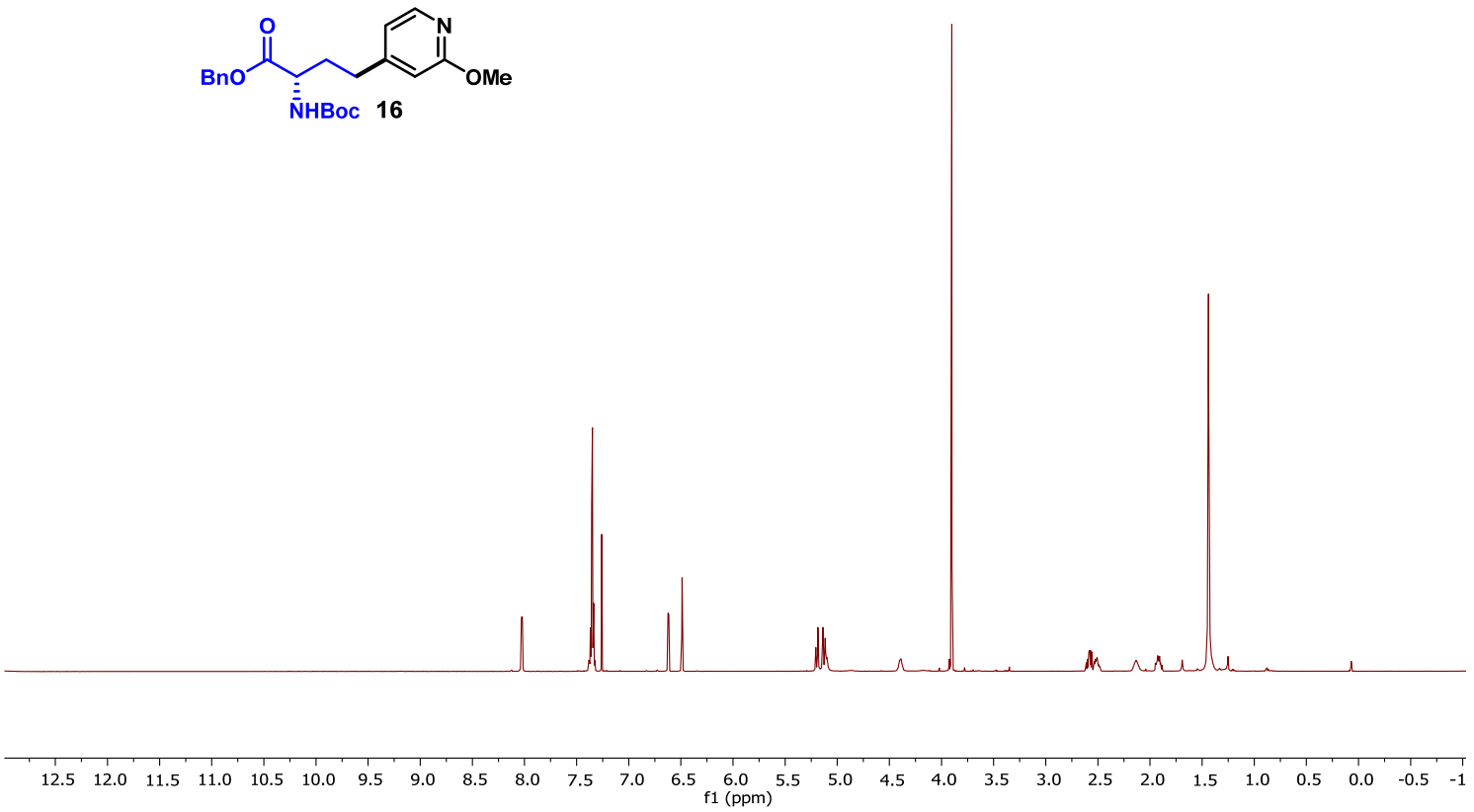


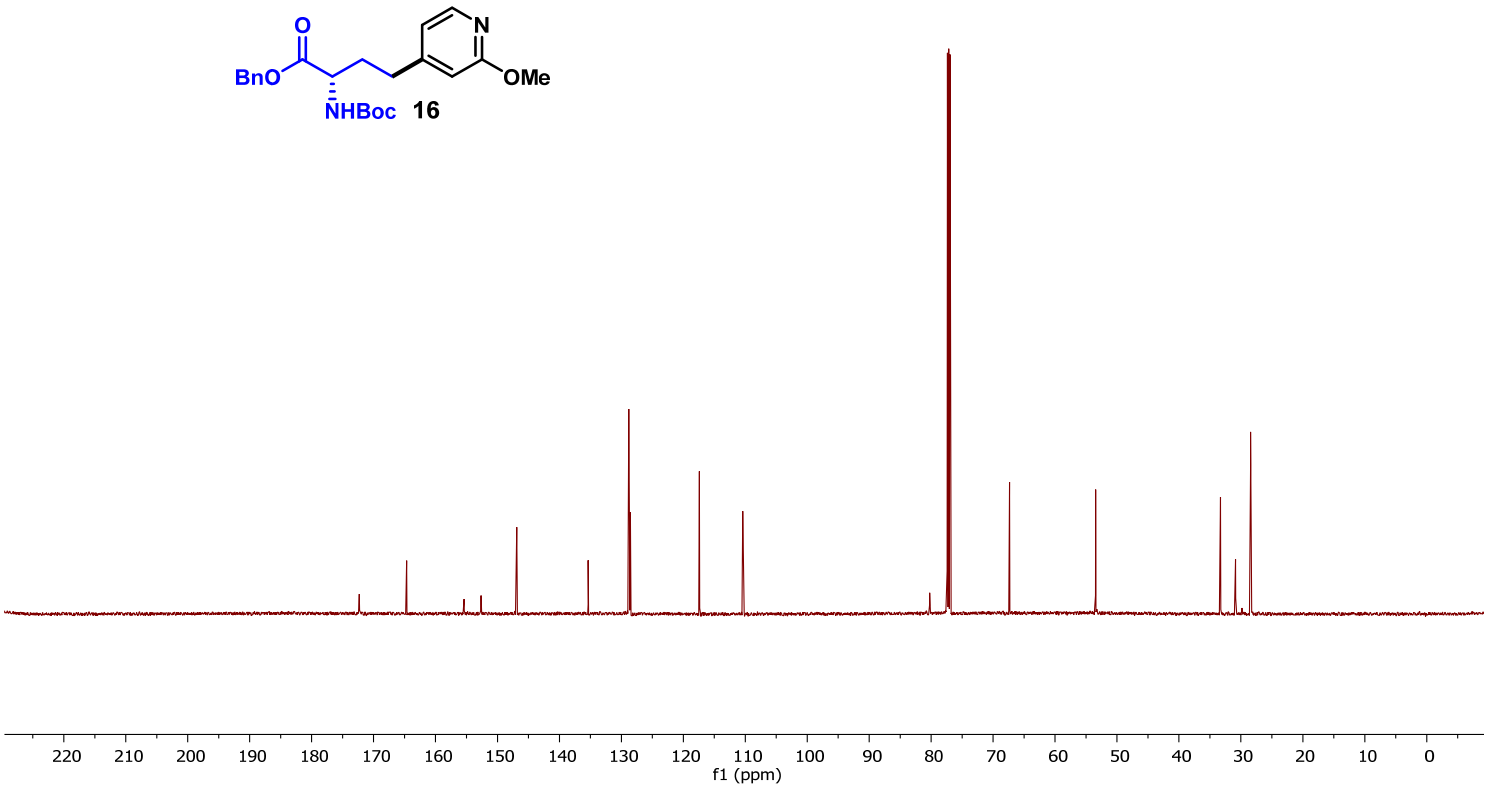
Compound 15 ^{13}C NMR



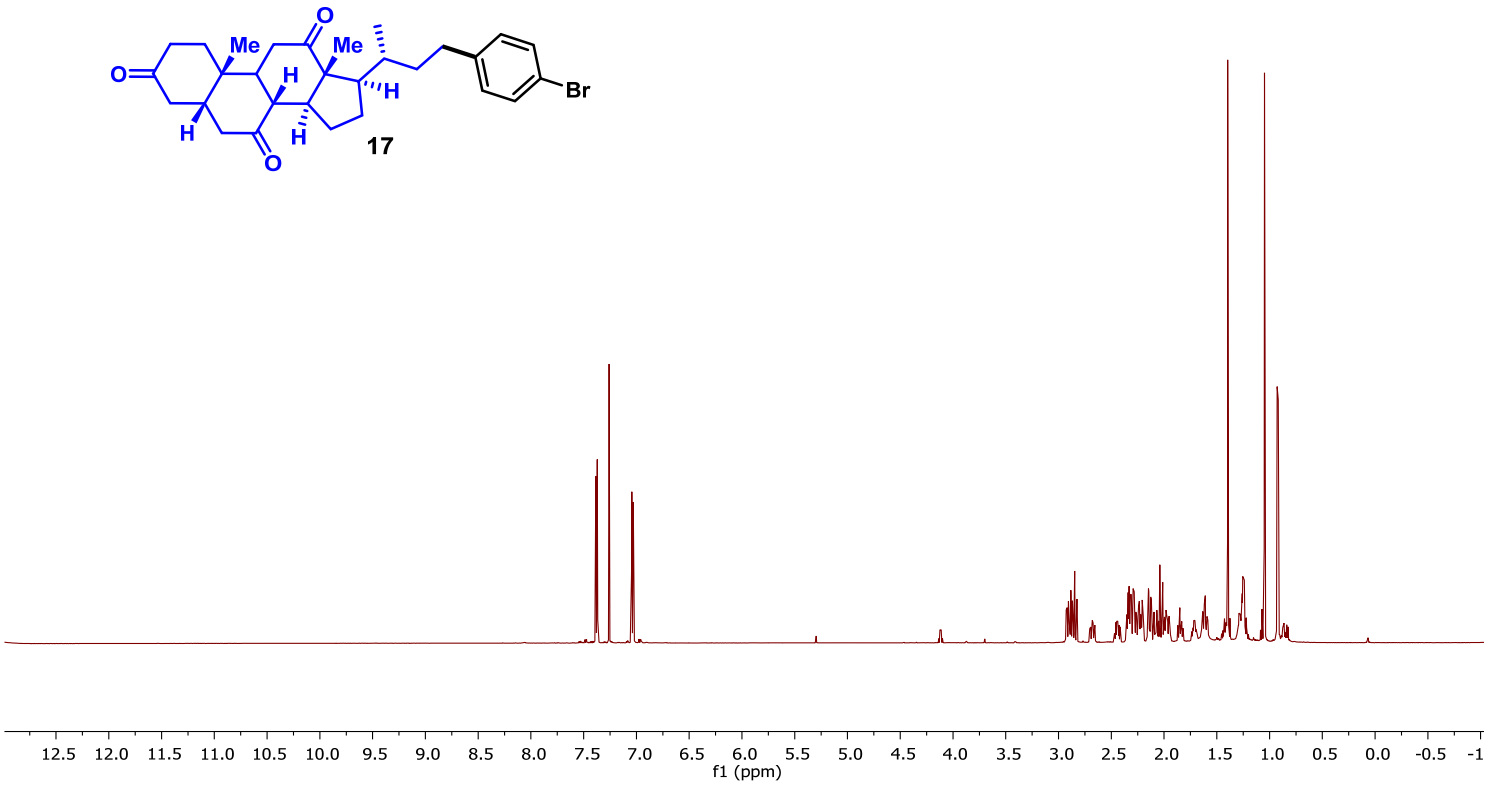
Compound 16 ^{1}H NMR



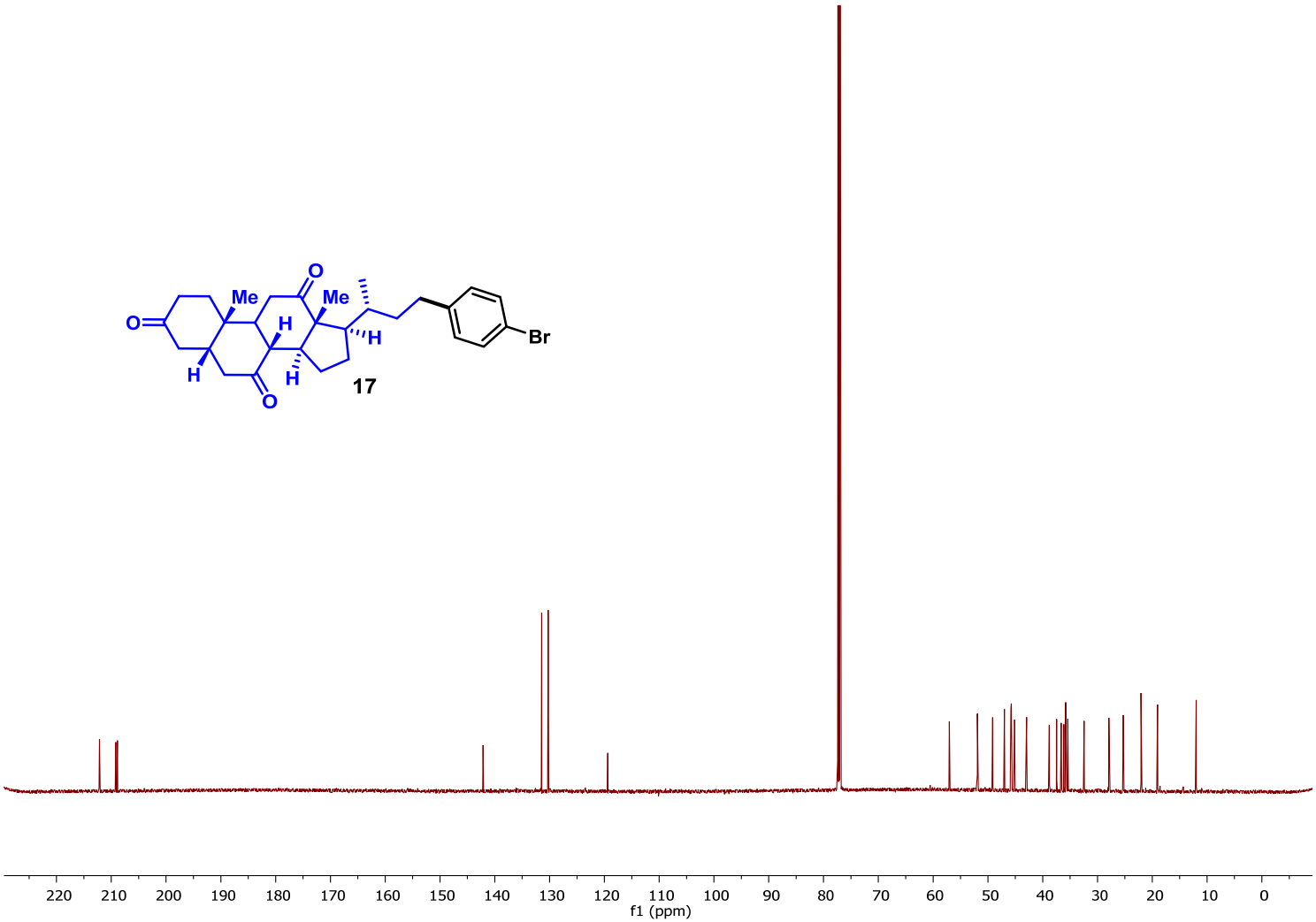
Compound 16 ^{13}C NMR



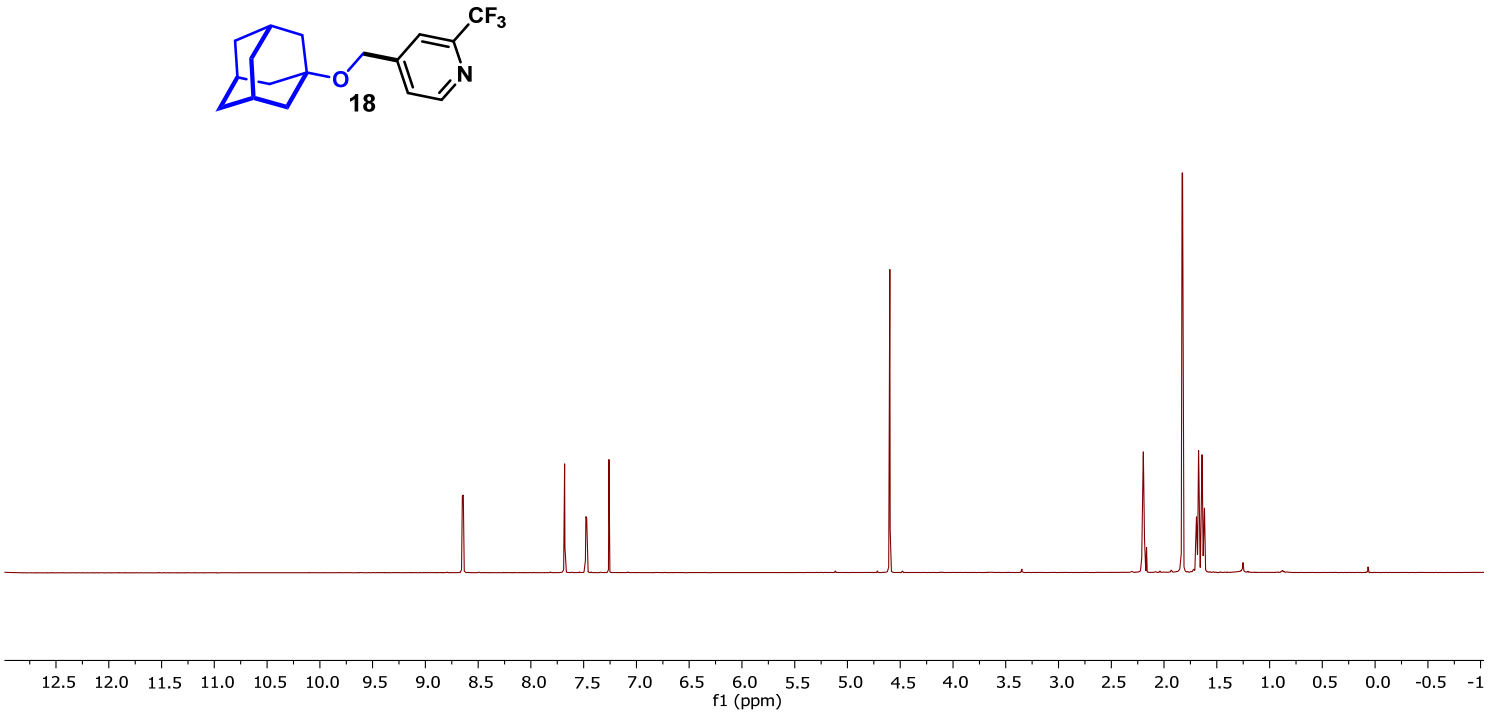
Compound 17 ^{1}H NMR



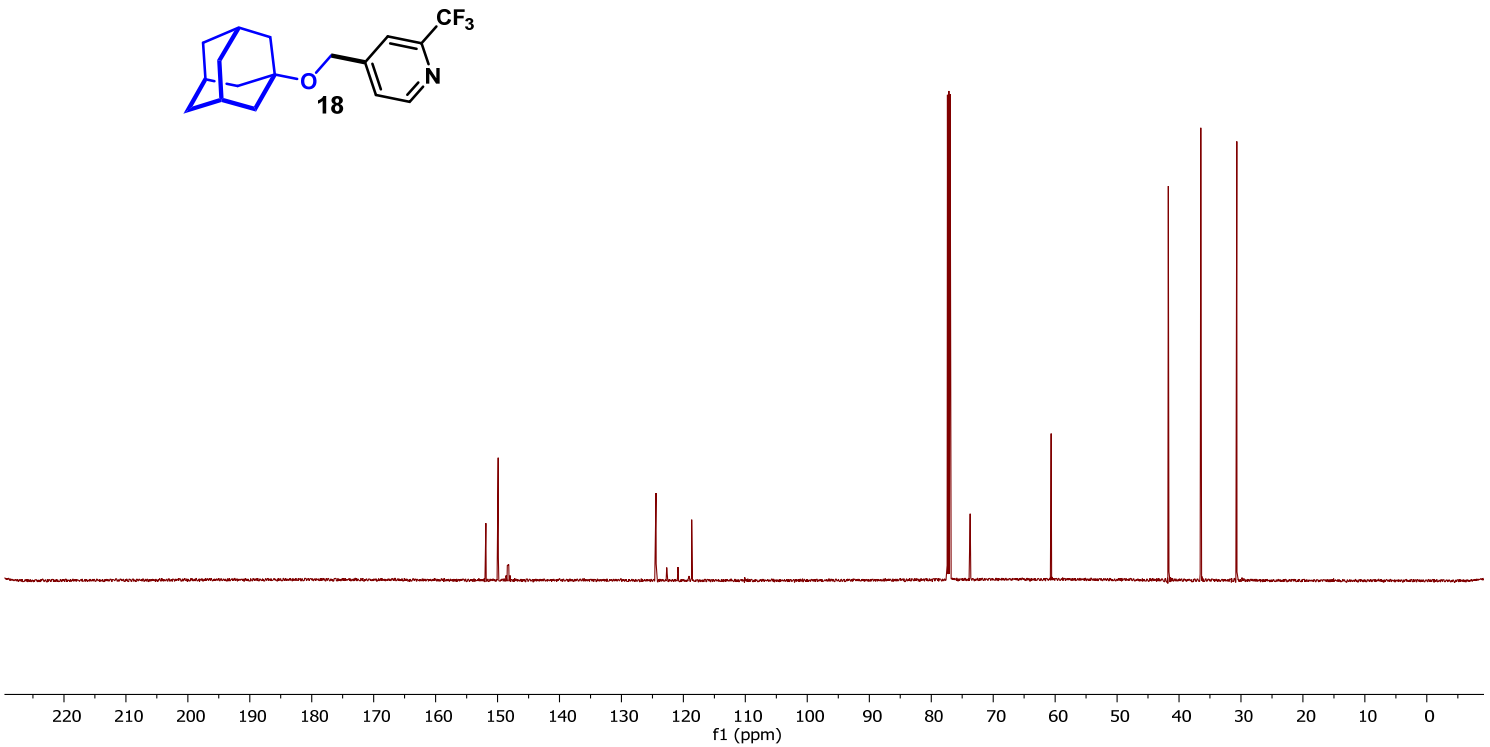
Compound 17 ^{13}C NMR



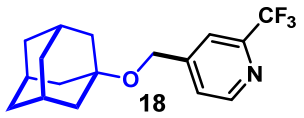
Compound 18 ^{1}H NMR

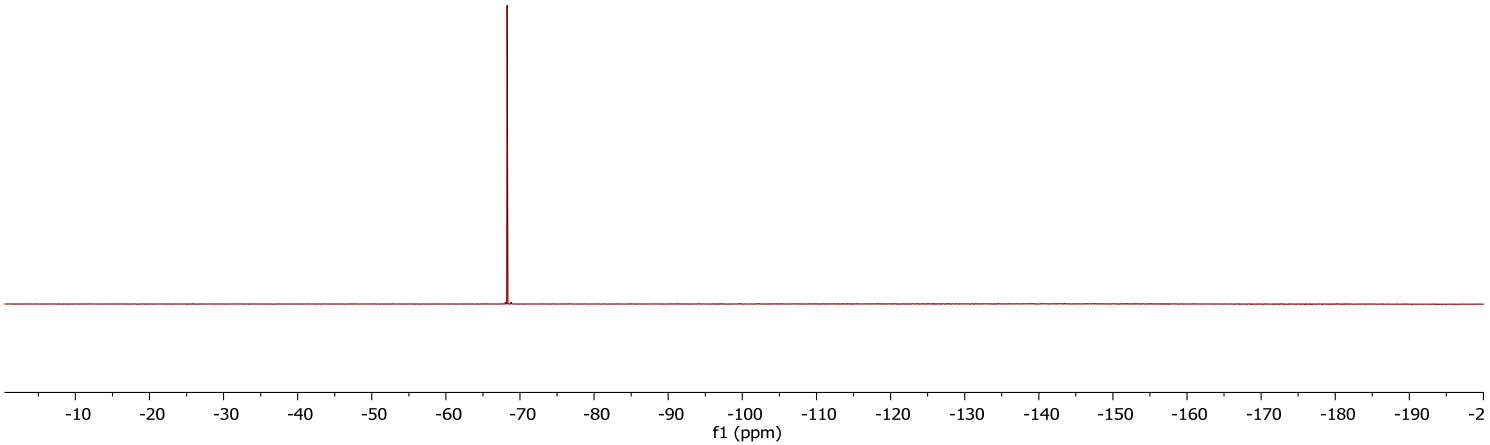


Compound 18 ^{13}C NMR

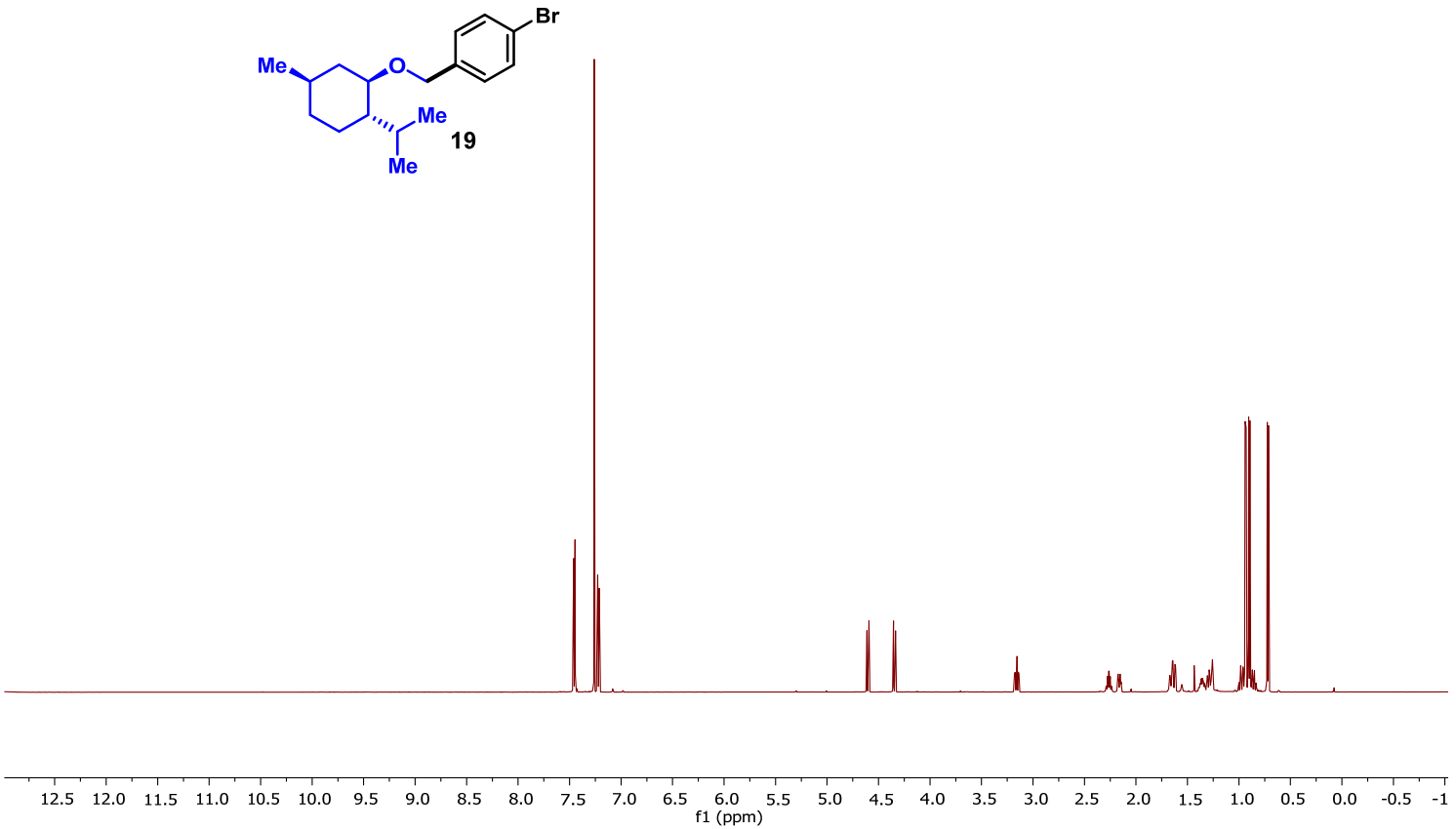


Compound 18 ^{19}F NMR

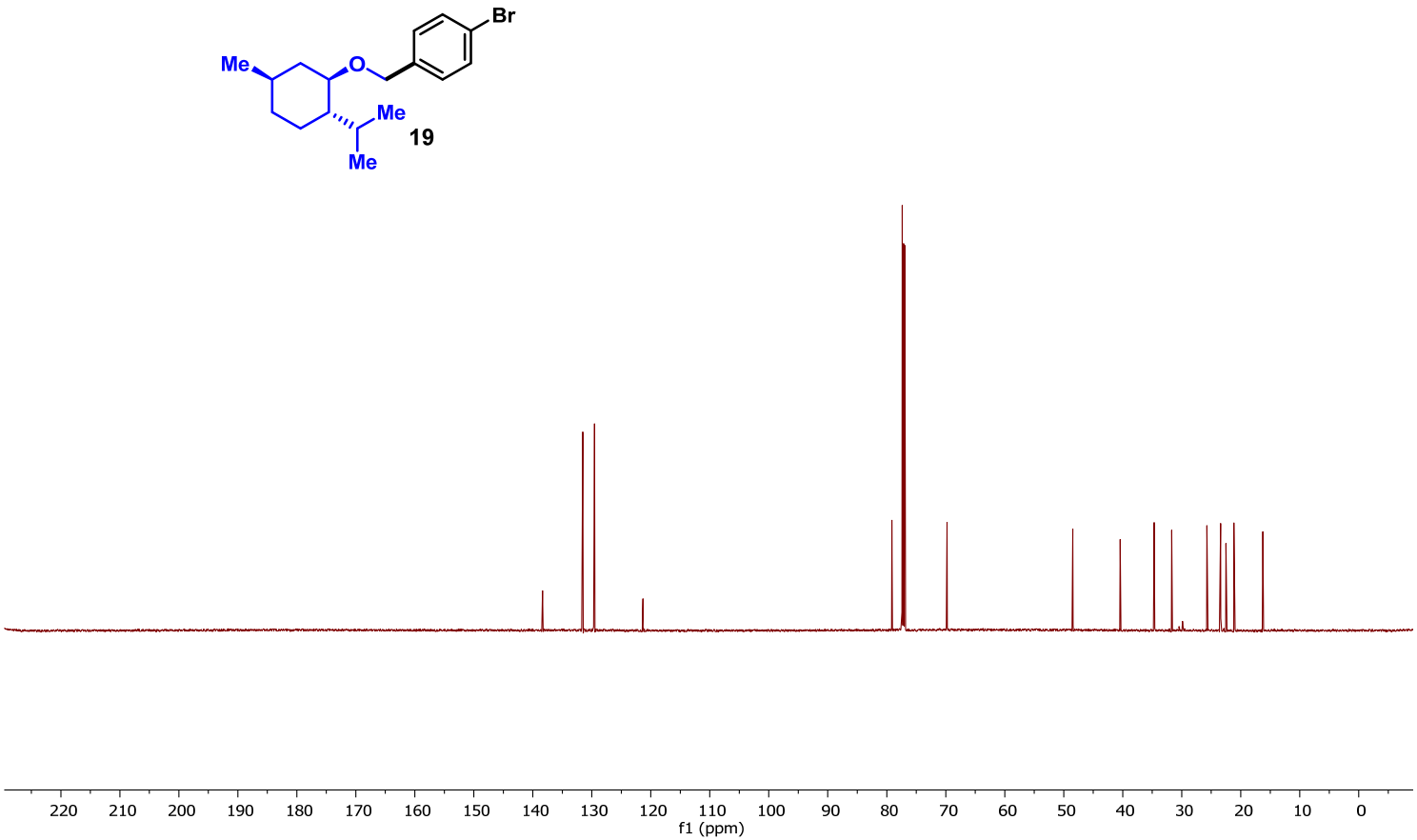




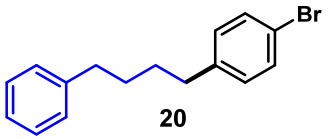
Compound 19 ^{1}H NMR



Compound 19 ^{13}C NMR



Compound 20 ^{1}H NMR



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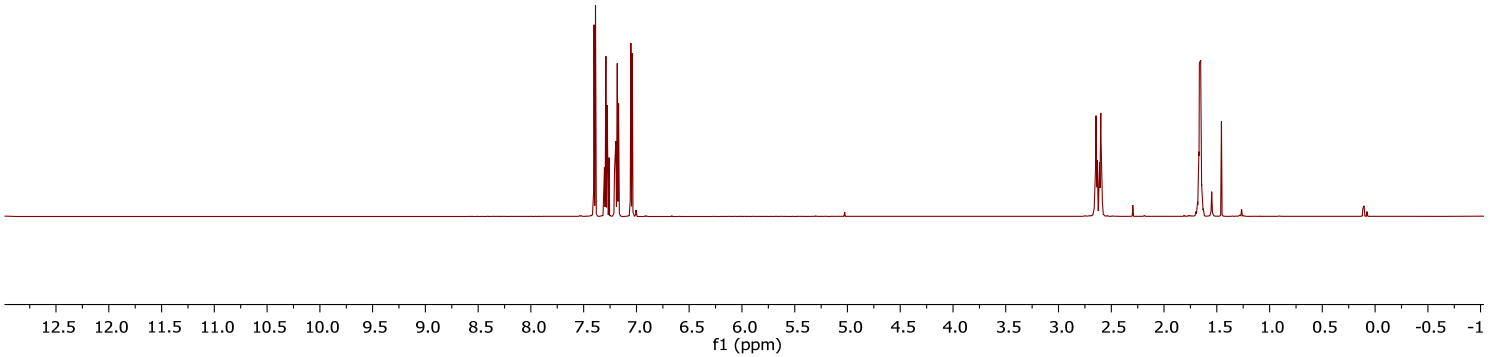
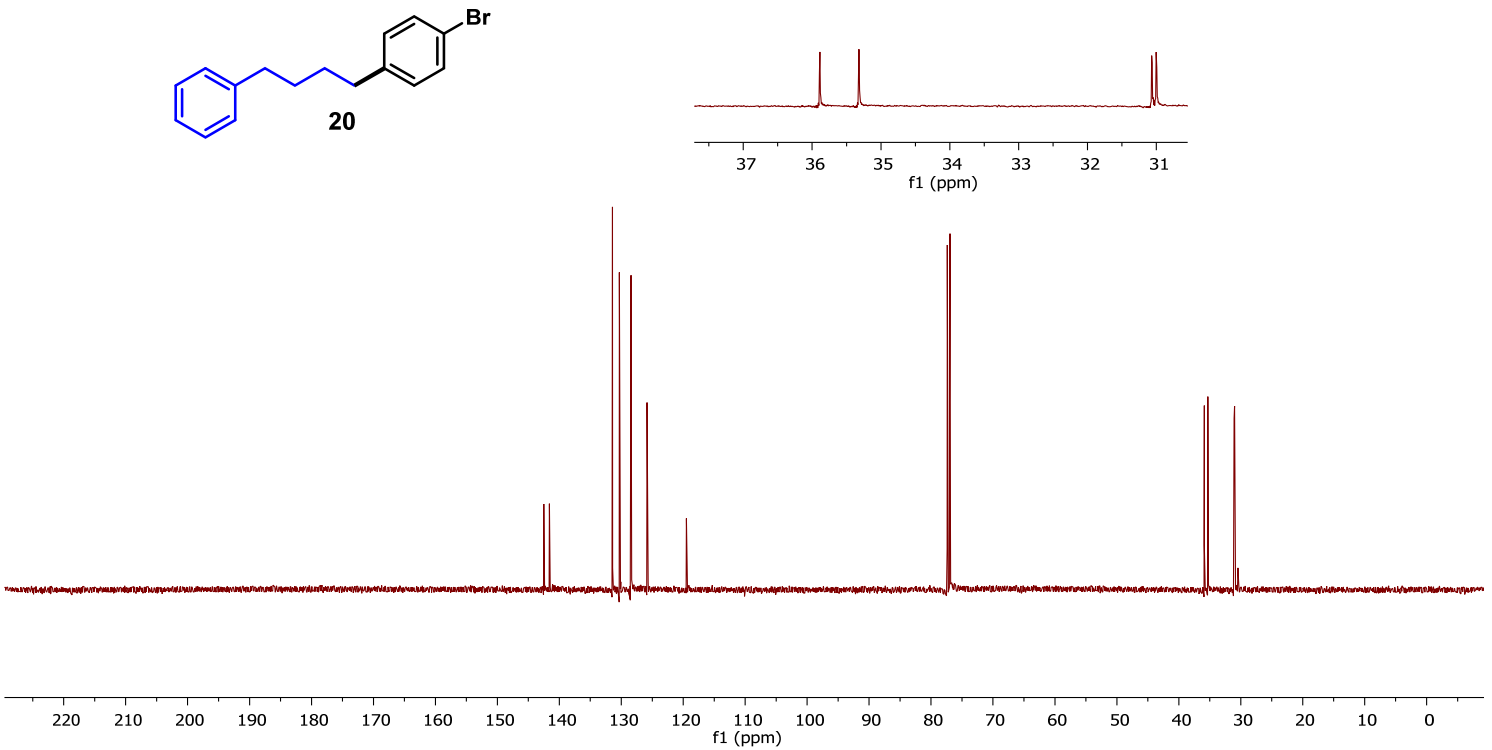
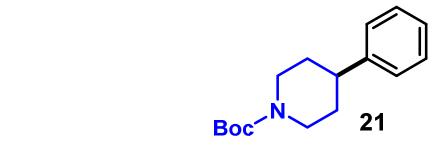


Compound 20 ^{13}C NMR

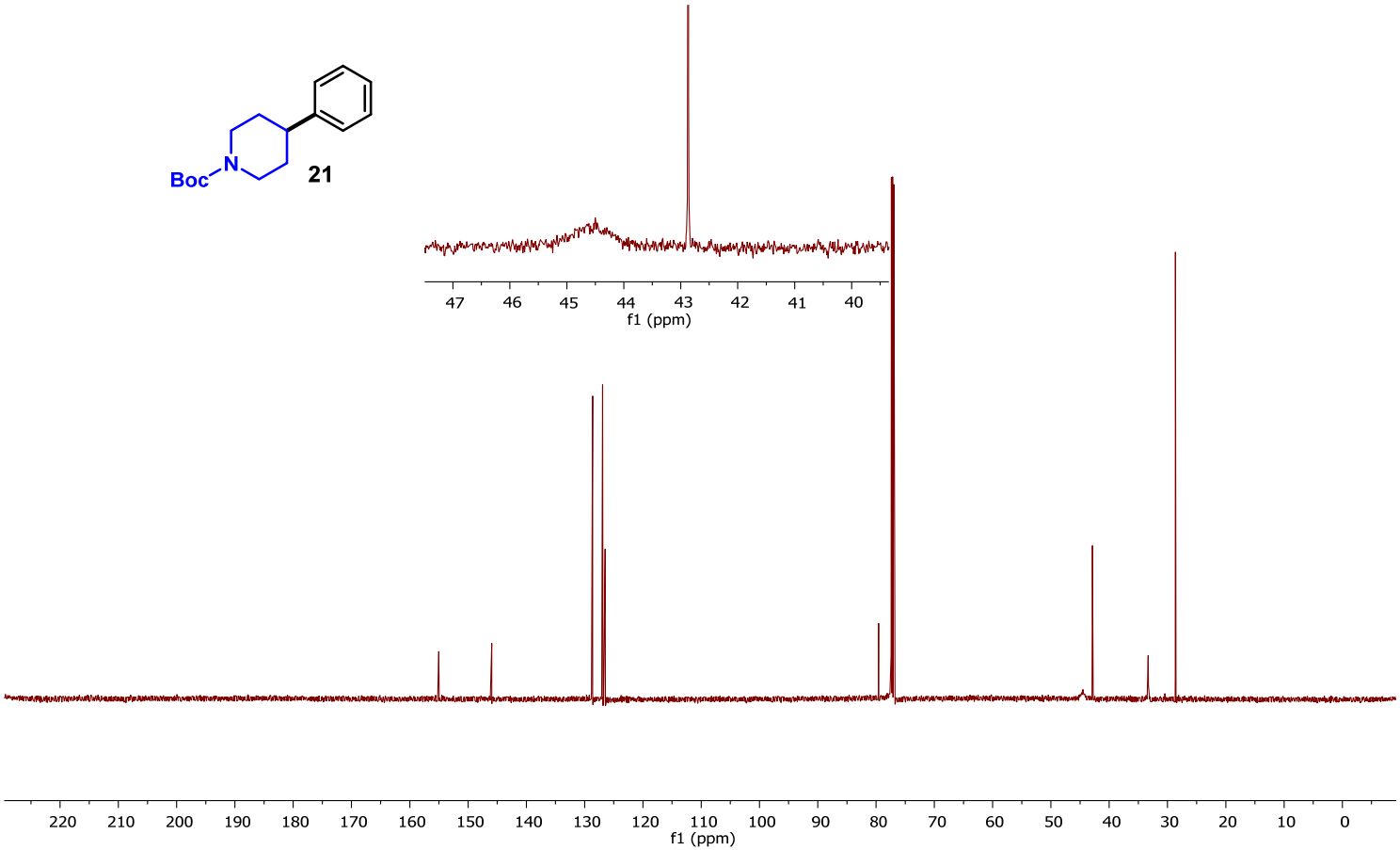


Compound 21 ^{1}H NMR

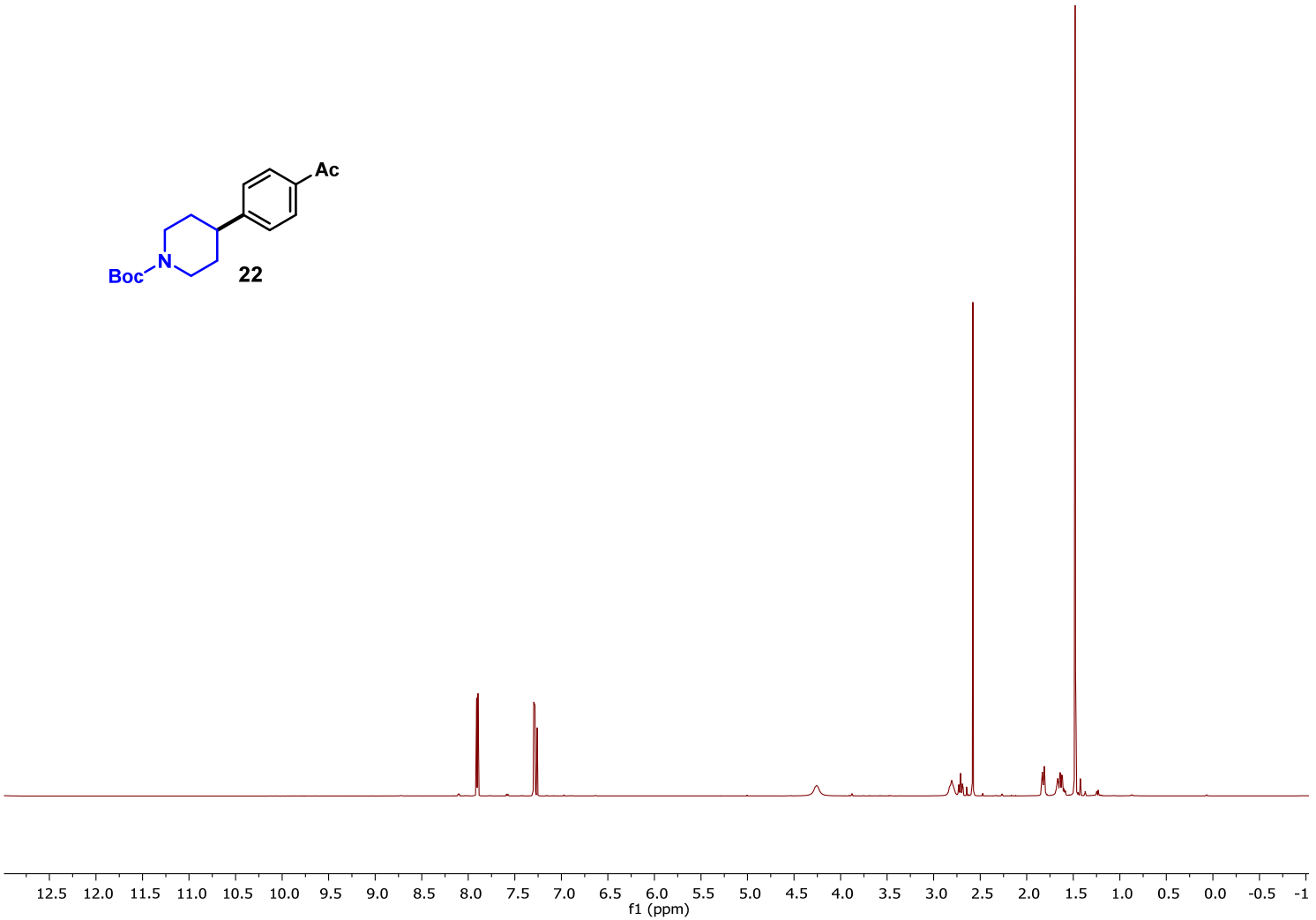


21

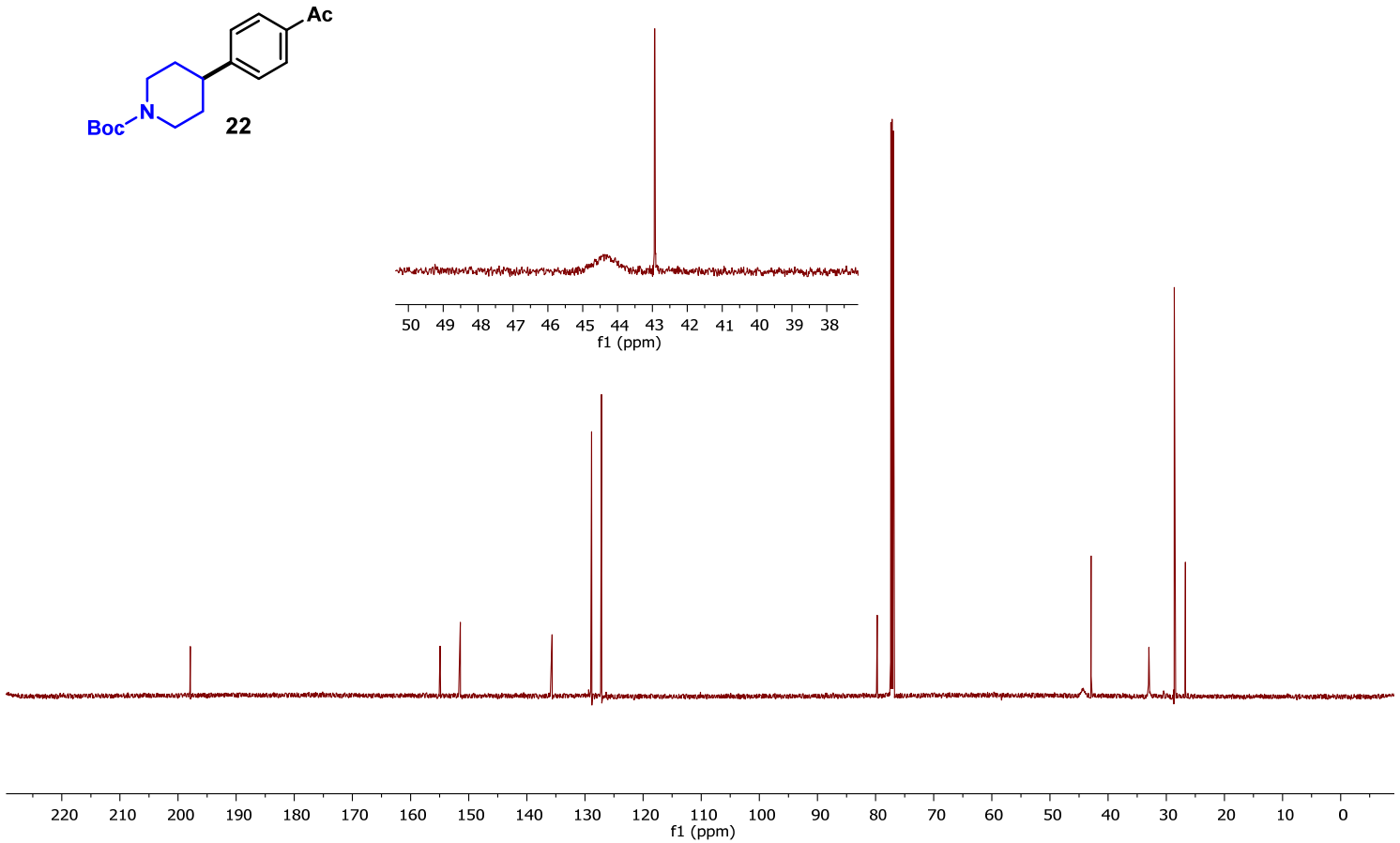
Compound 21 ^{13}C NMR



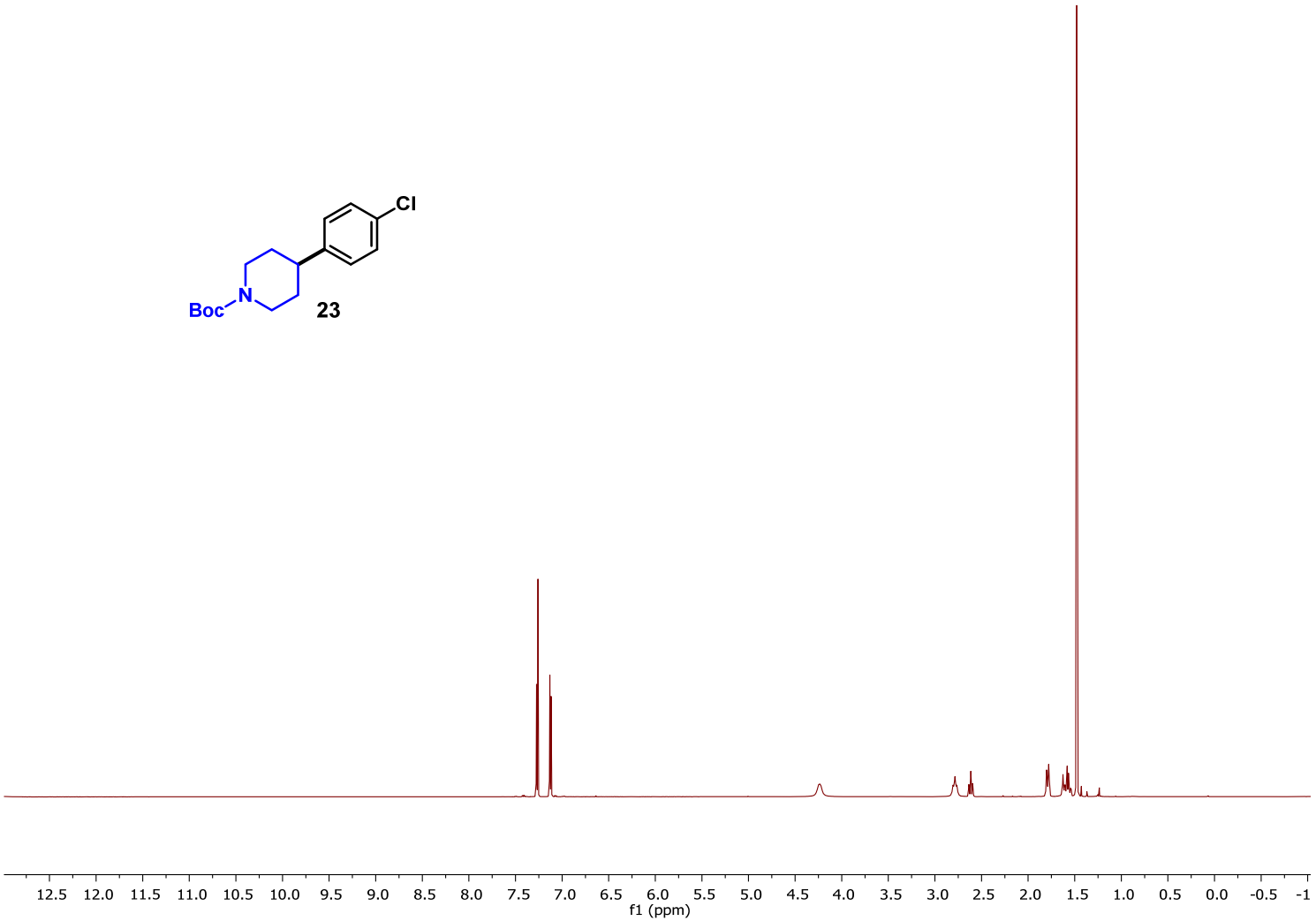
Compound 22 ^{1}H NMR



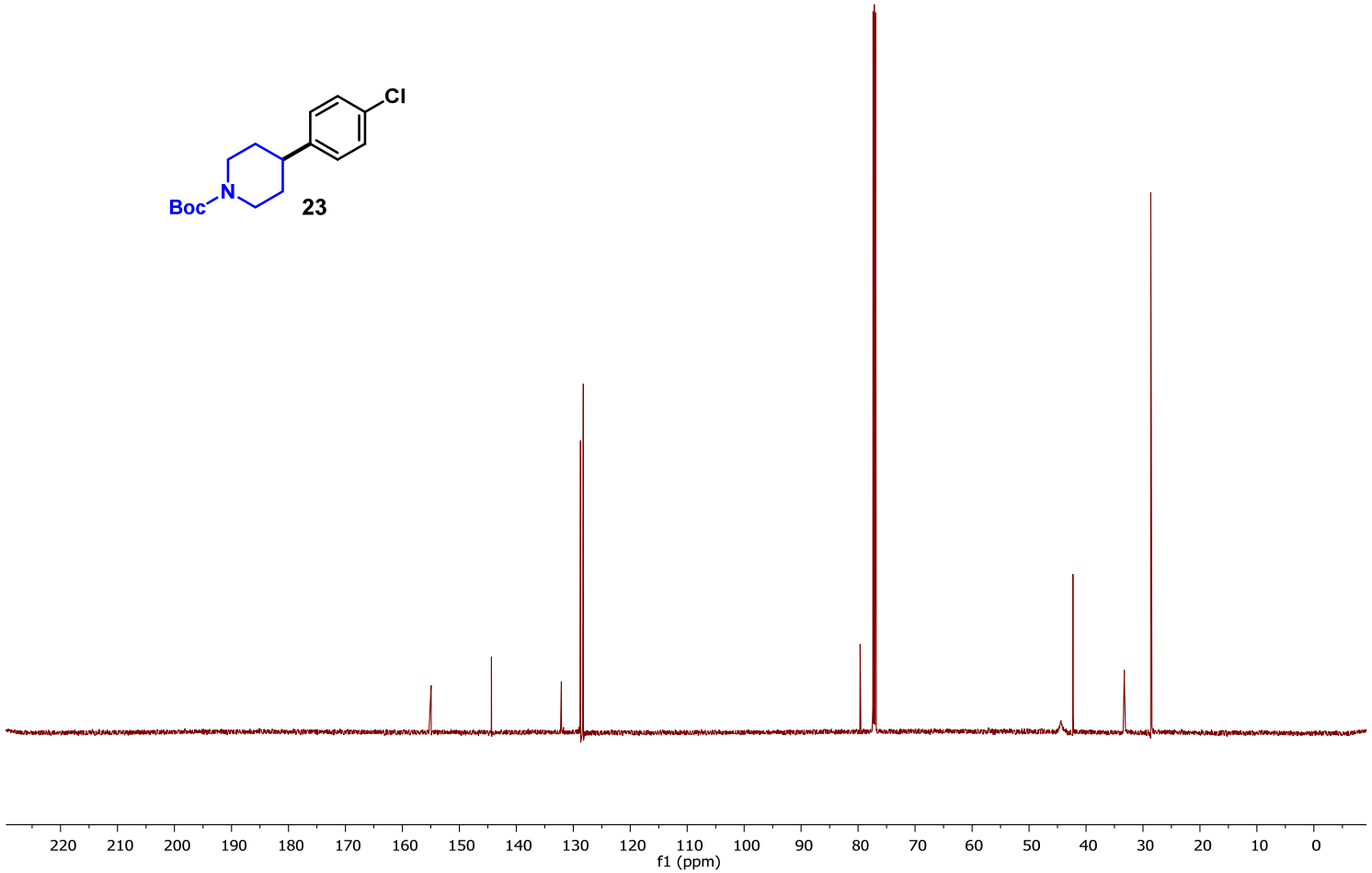
Compound 22 ^{13}C NMR



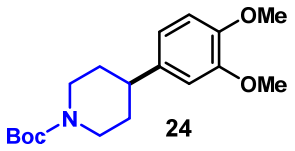
Compound 23 ^{1}H NMR



Compound 23 ^{13}C NMR

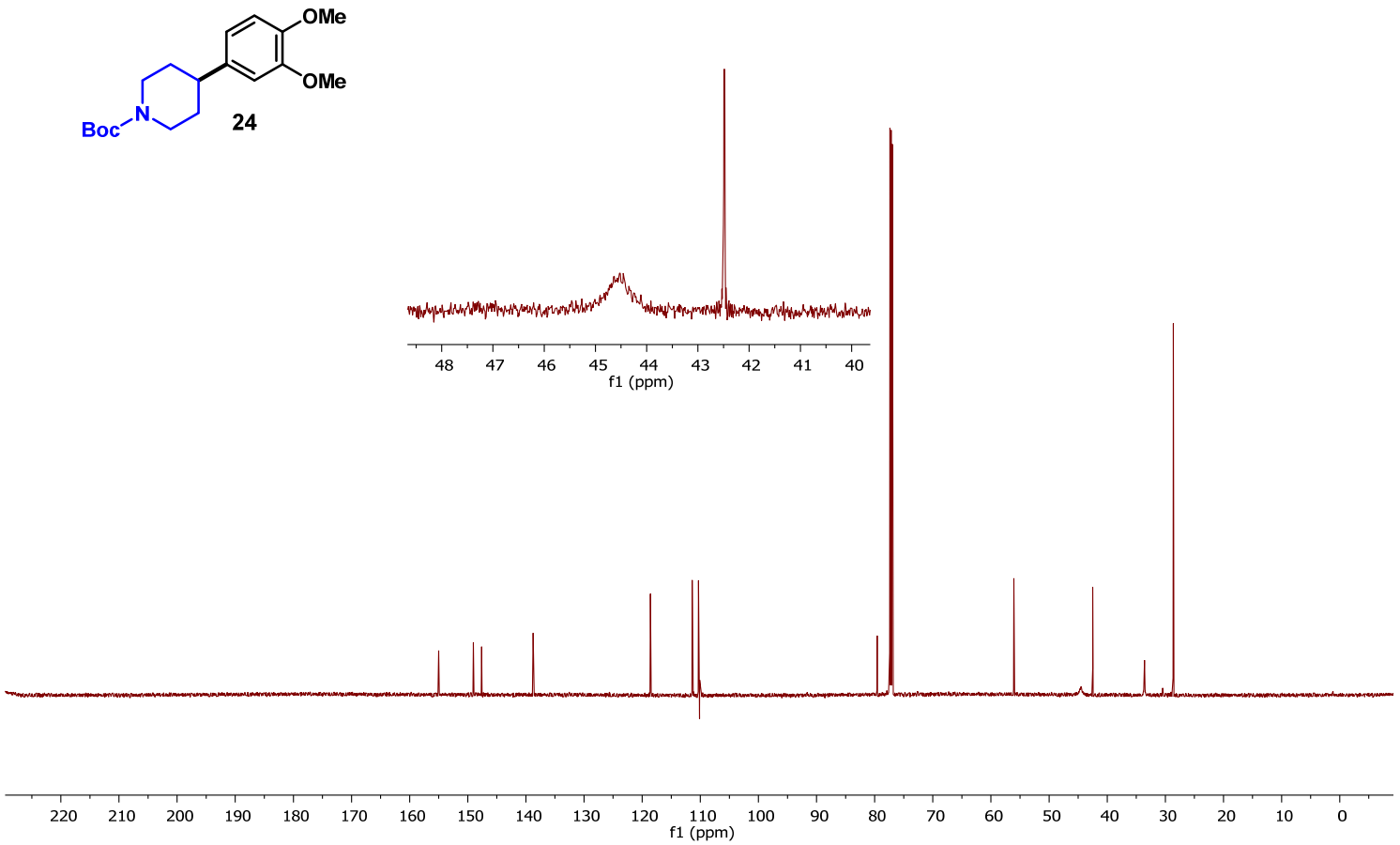


Compound 24 ^{1}H NMR

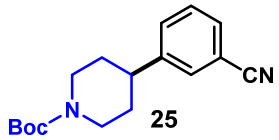


24

Compound 24 ^{13}C NMR

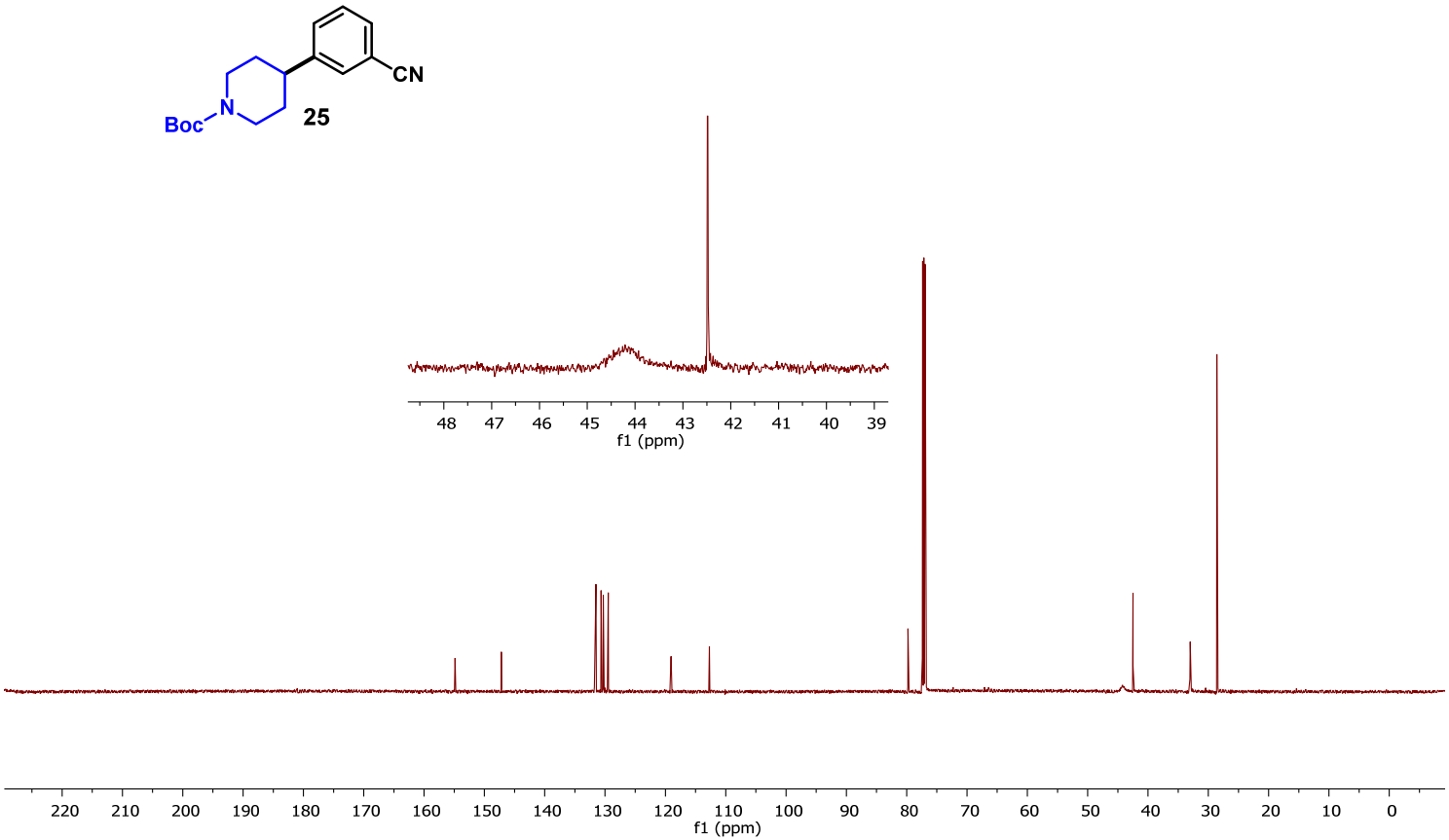


Compound 25 ^{1}H NMR

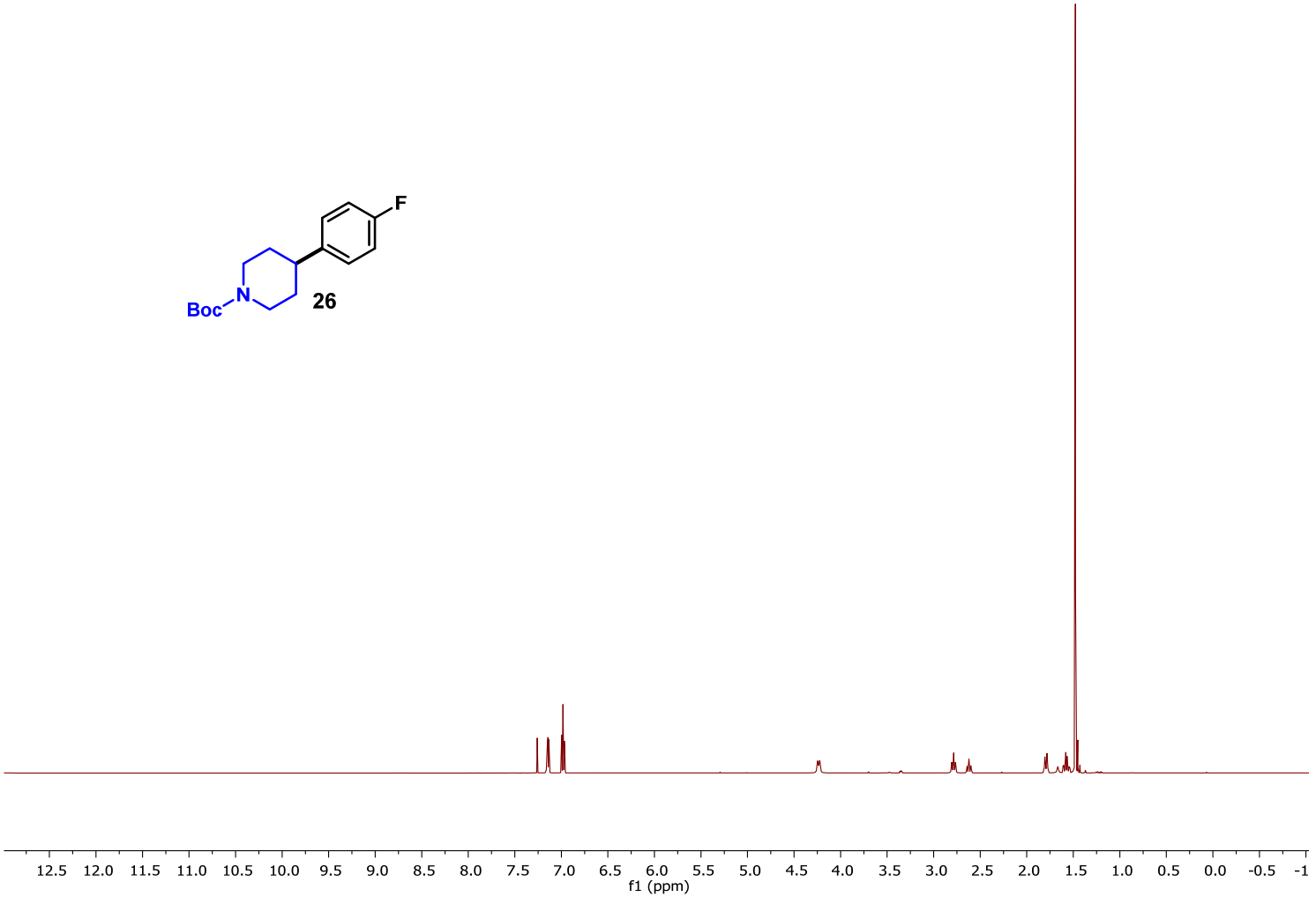


25

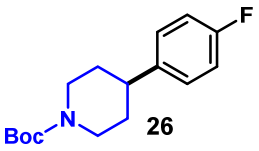
Compound 25 ^{13}C NMR



Compound 26 ^{1}H NMR



Compound 26 ^{13}C NMR



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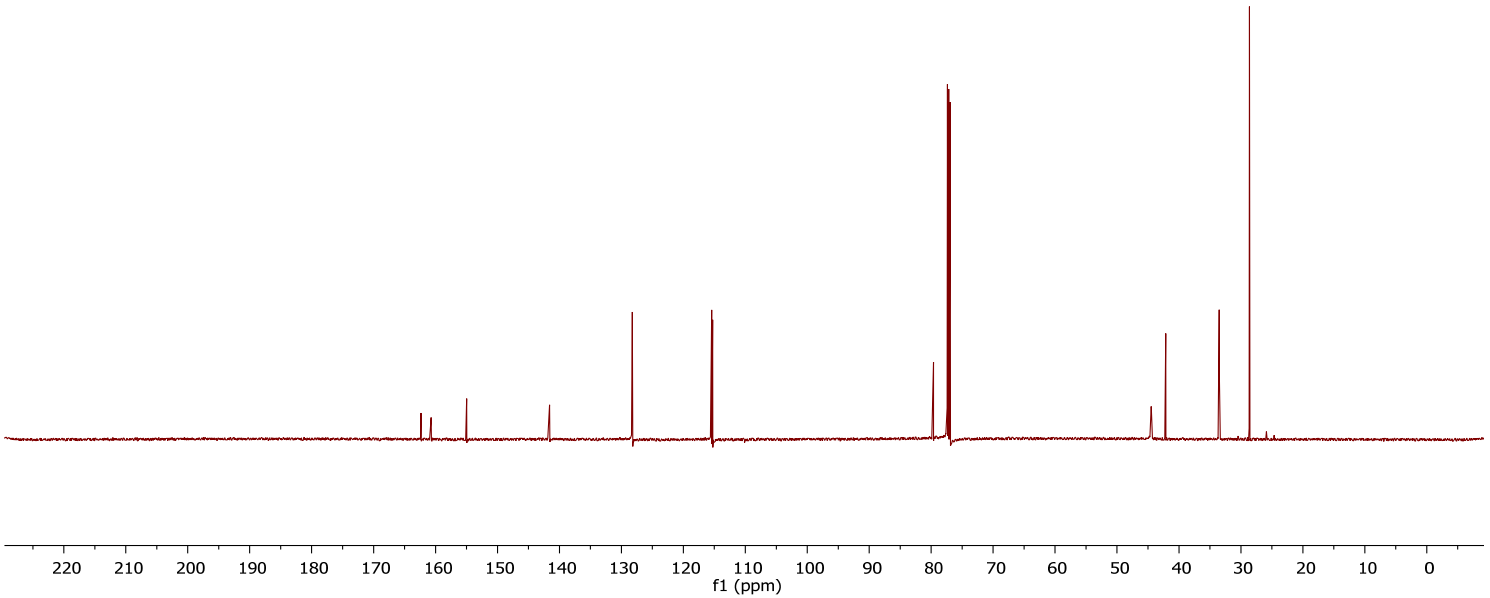
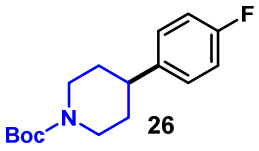


Compound 26 ^{19}F NMR



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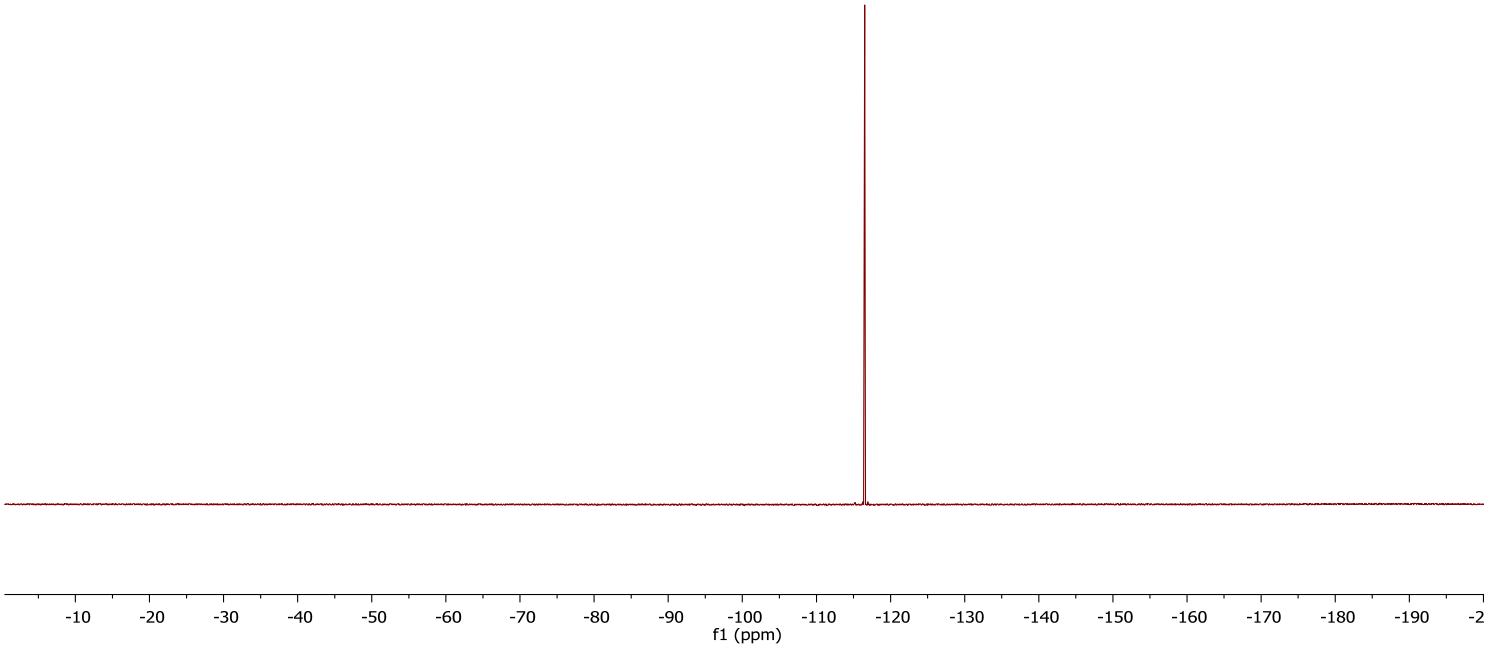
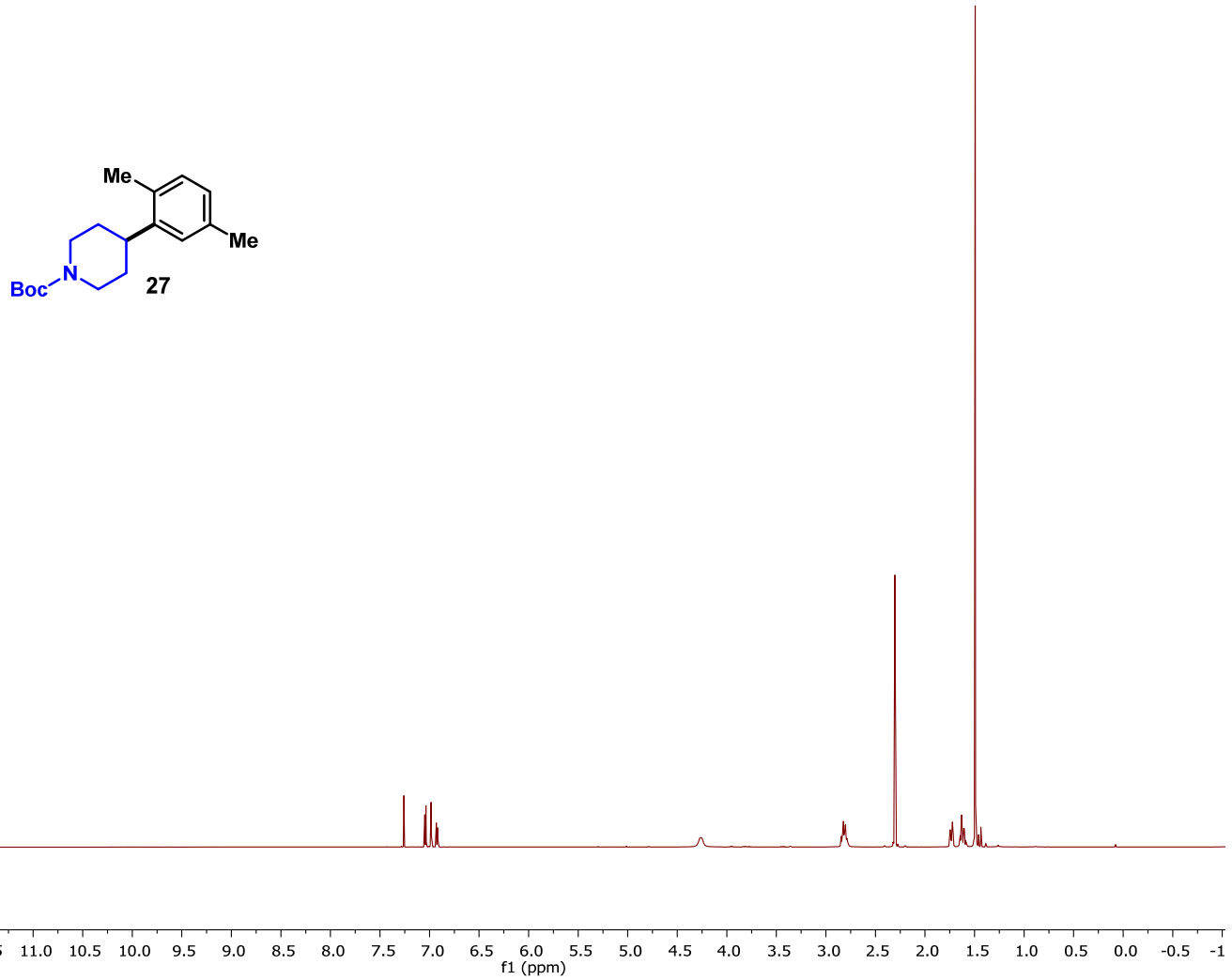
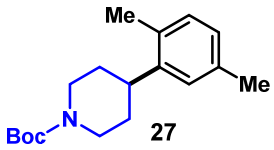


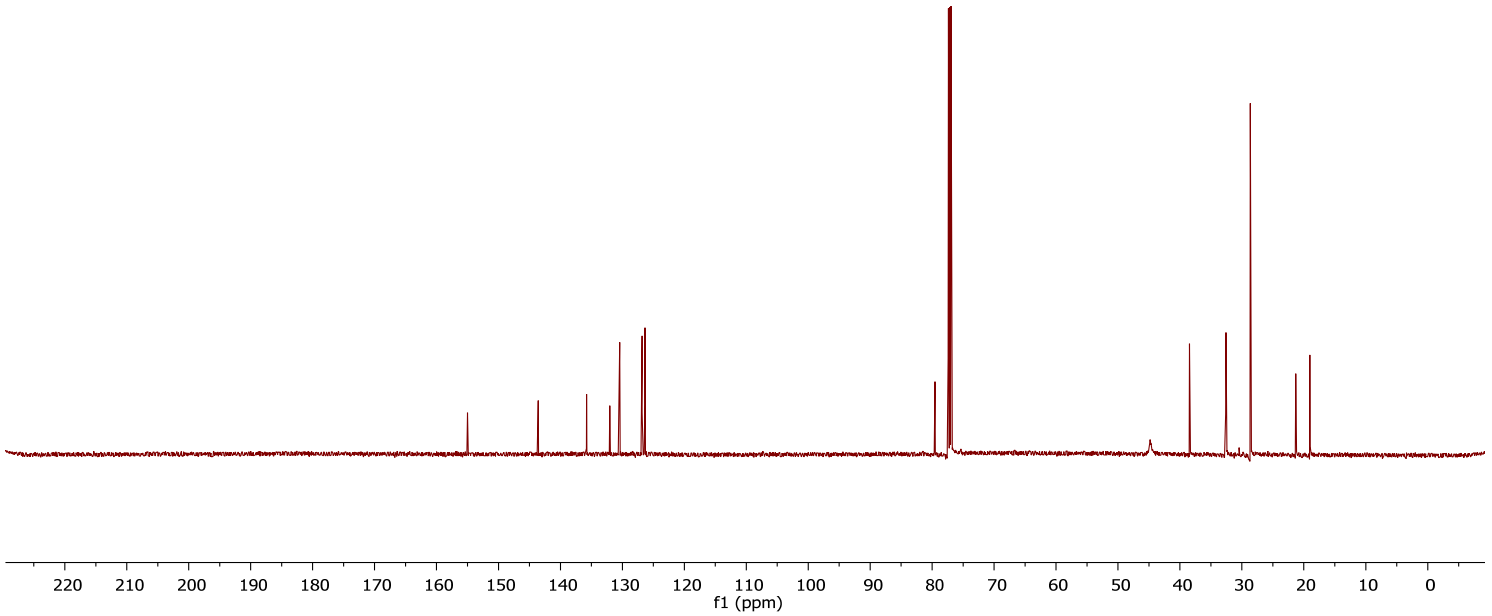
Compound 27 ^{1}H NMR



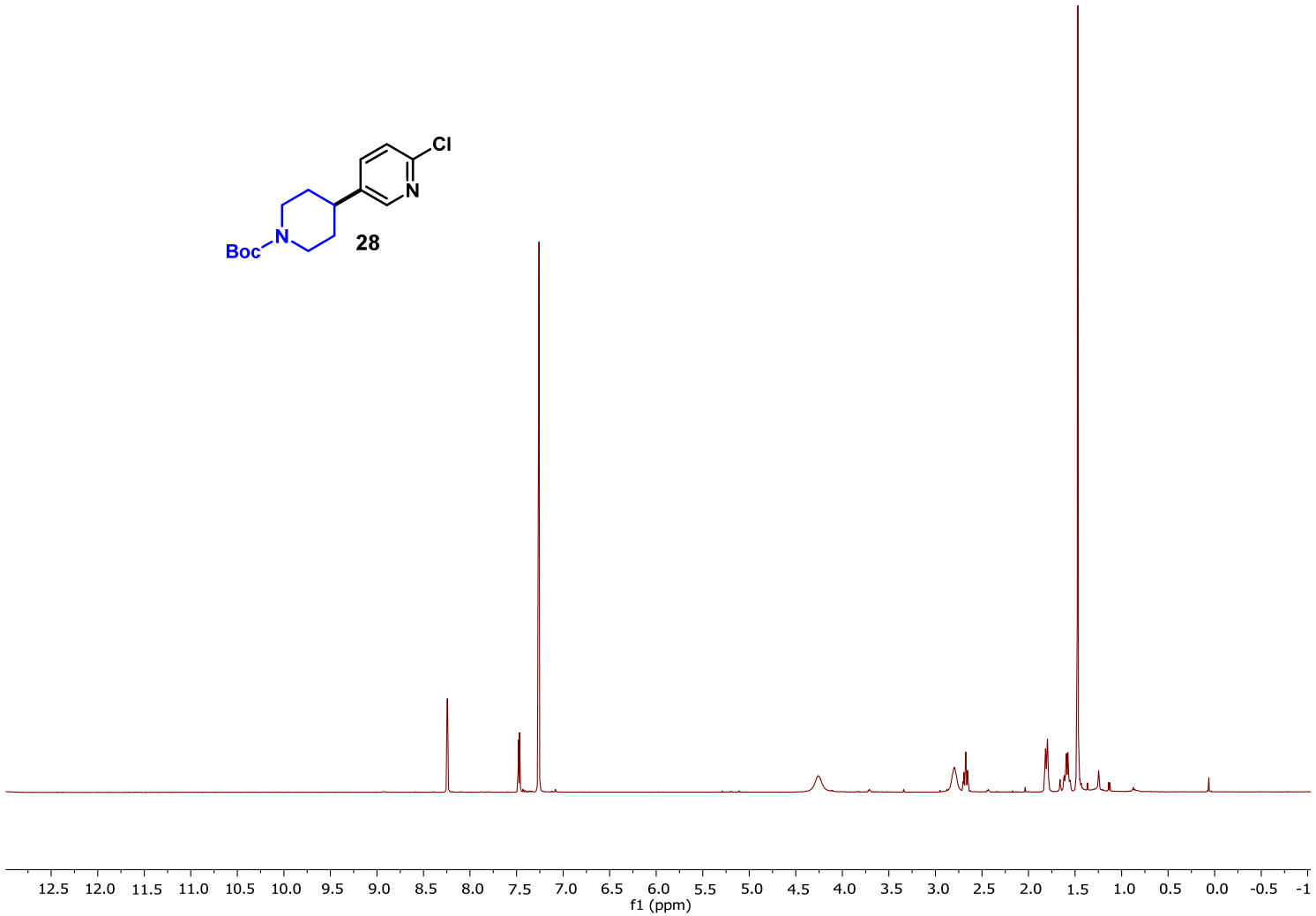
Compound 27 ^{13}C NMR



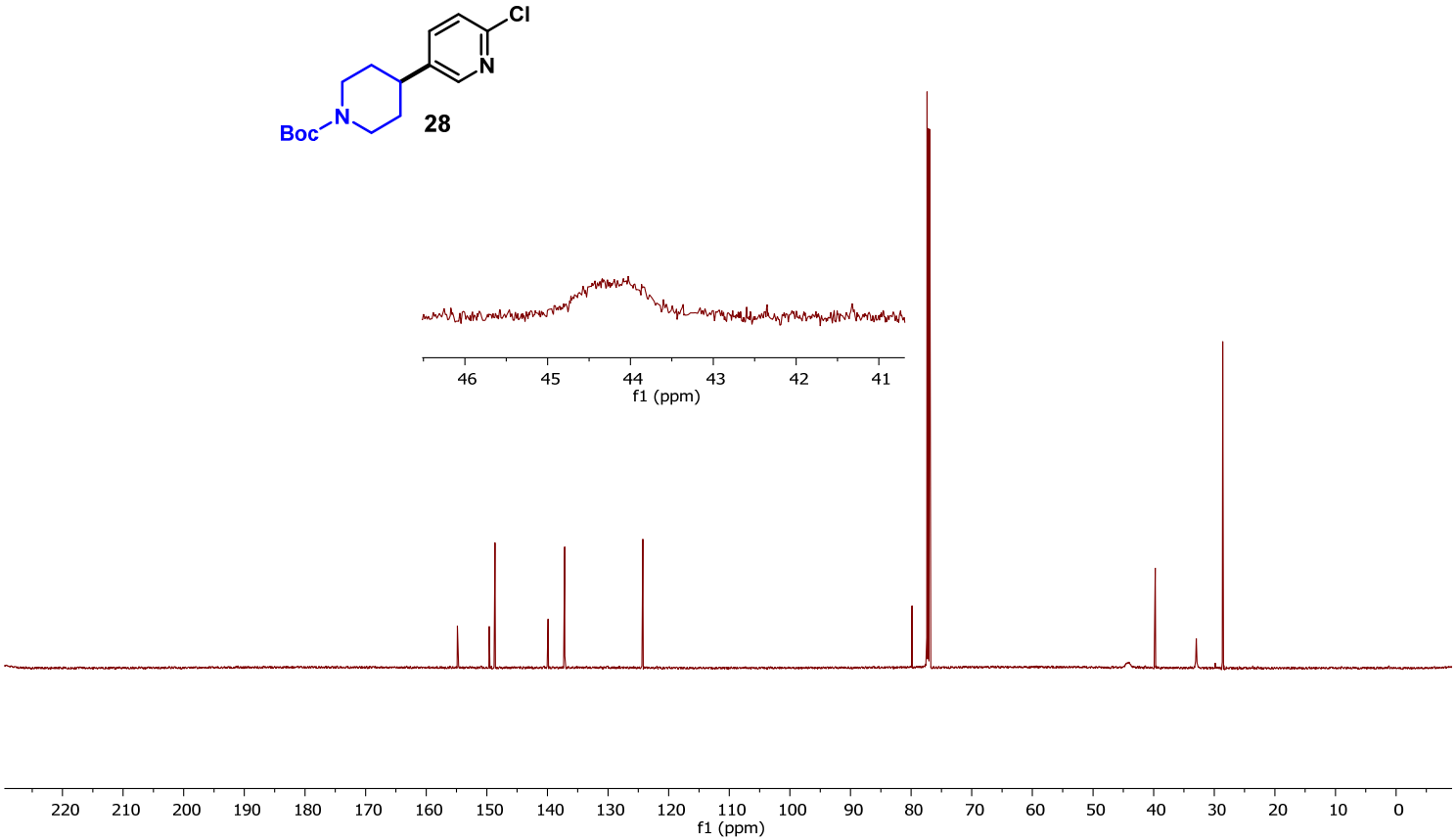
27



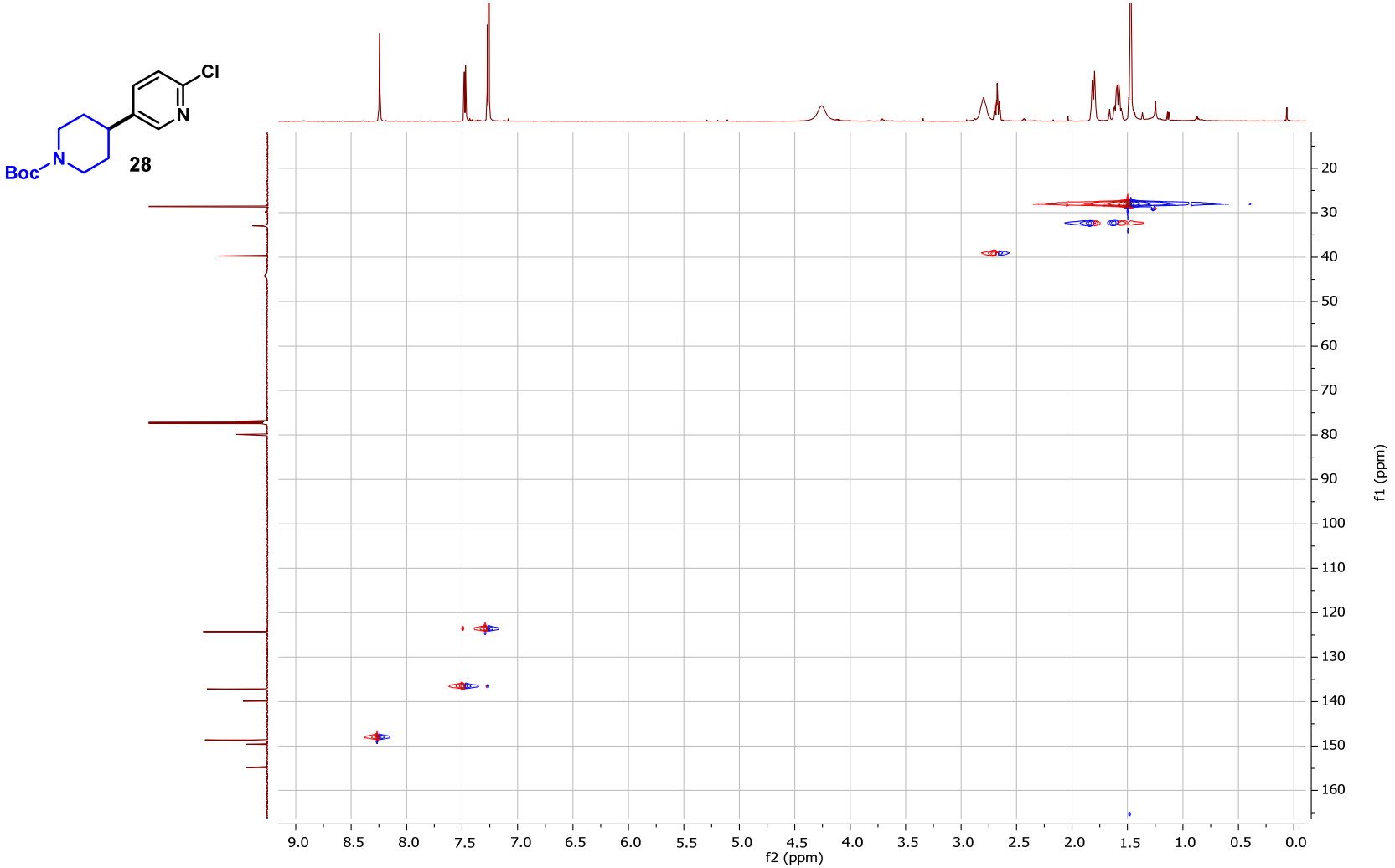
Compound 28 ^{1}H NMR



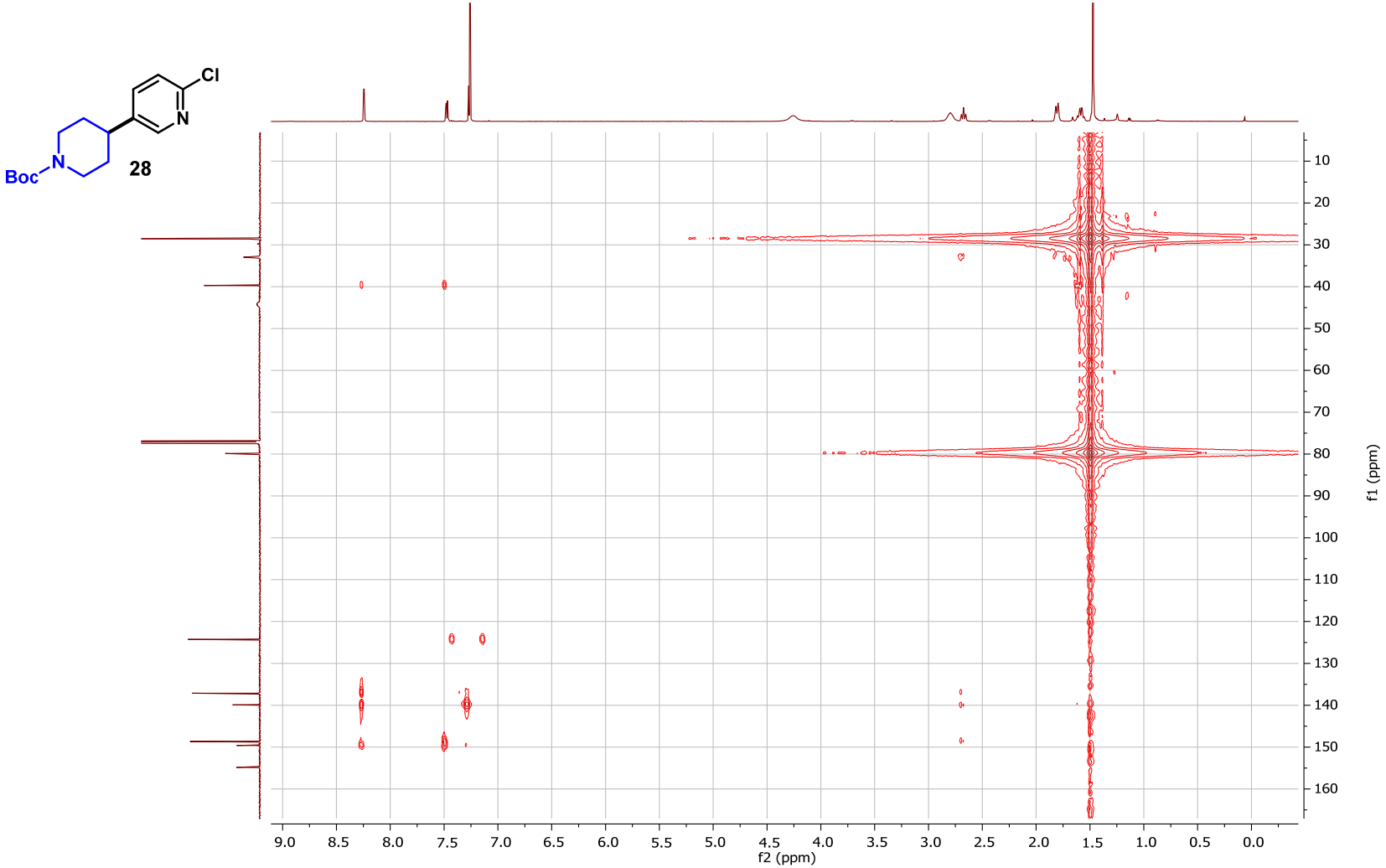
Compound 28 ^{13}C NMR



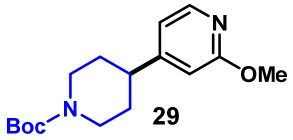
Compound 28 HSQC



Compound 28 HMBC

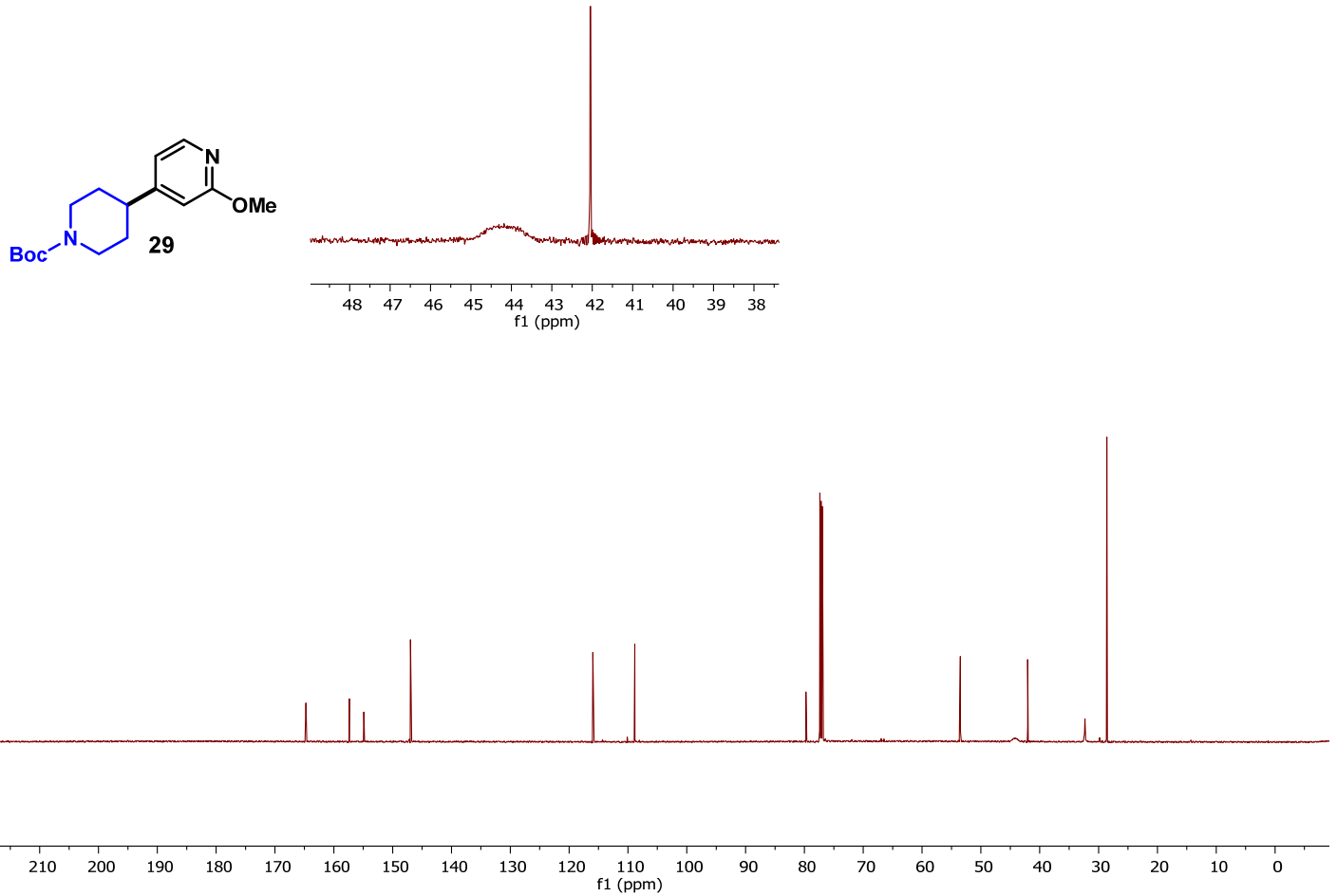


Compound 29 ^{1}H NMR

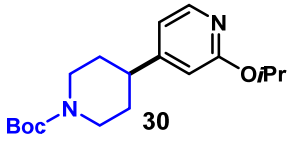


29

Compound 29 ^{13}C NMR

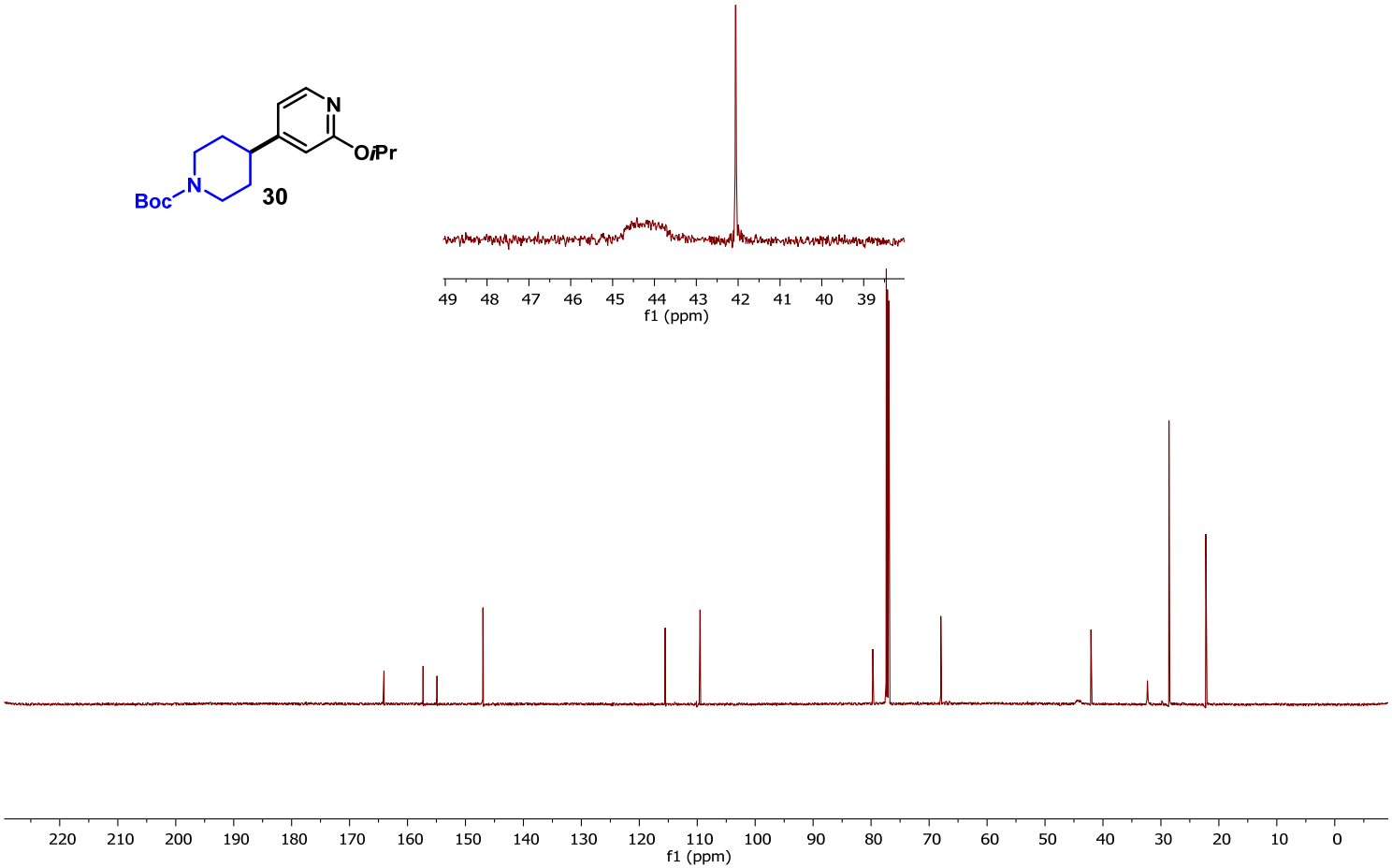


Compound 30 ^{1}H NMR

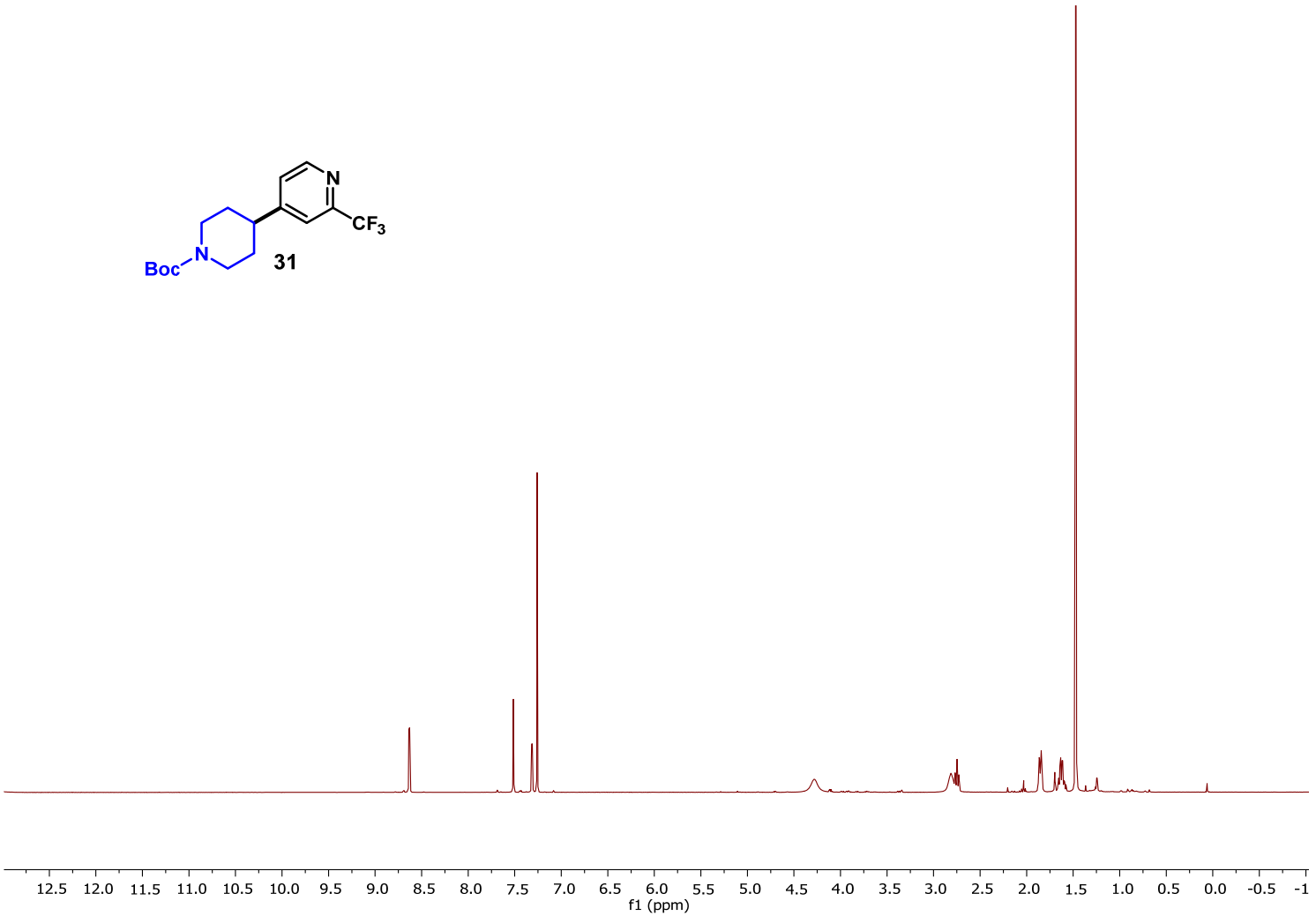


30

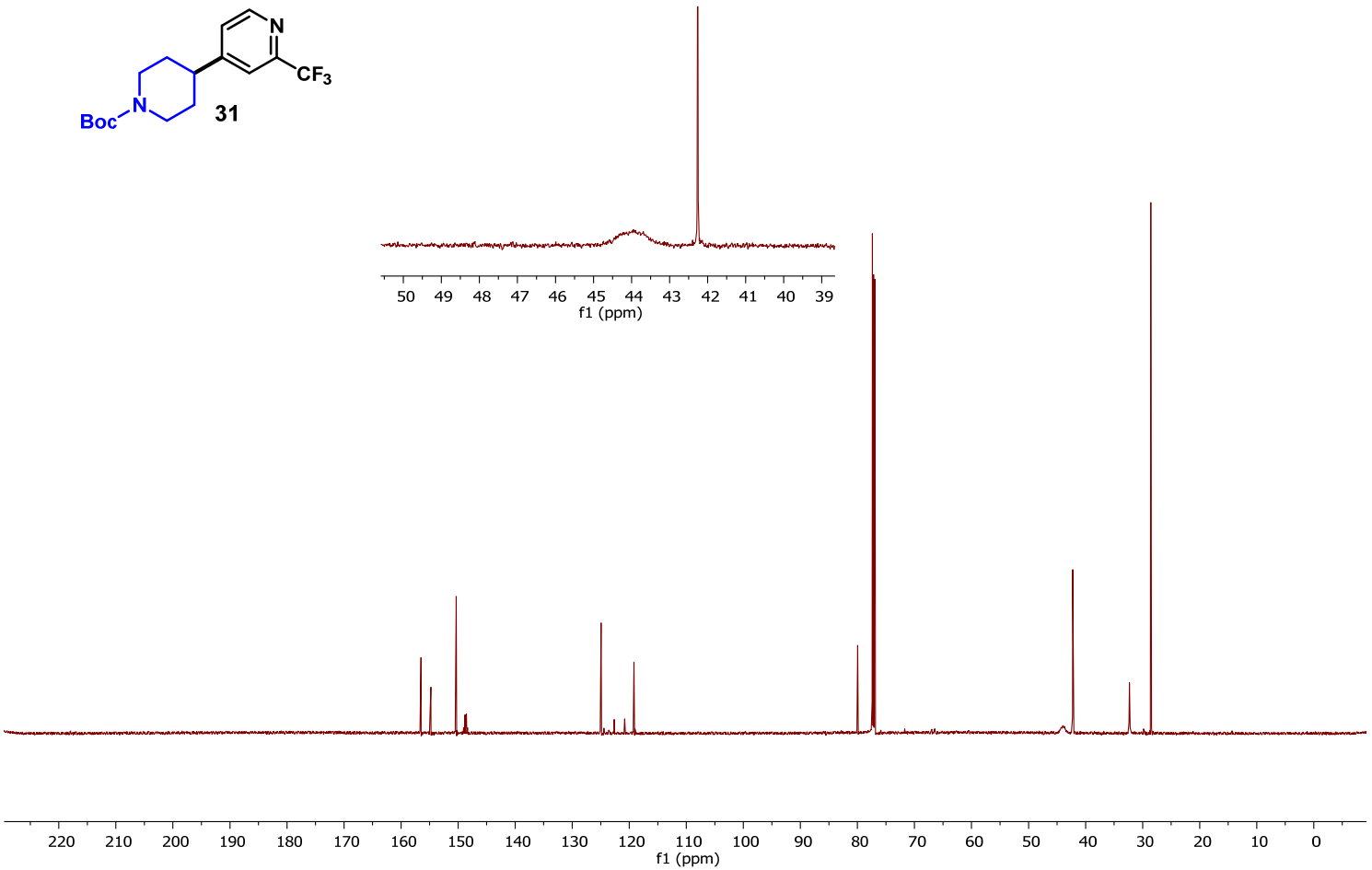
Compound 30 ^{13}C NMR



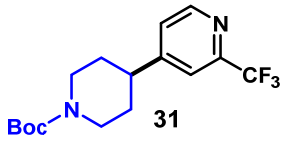
Compound 31 ^{1}H NMR



Compound 31 ^{13}C NMR



Compound 31 ^{19}F NMR



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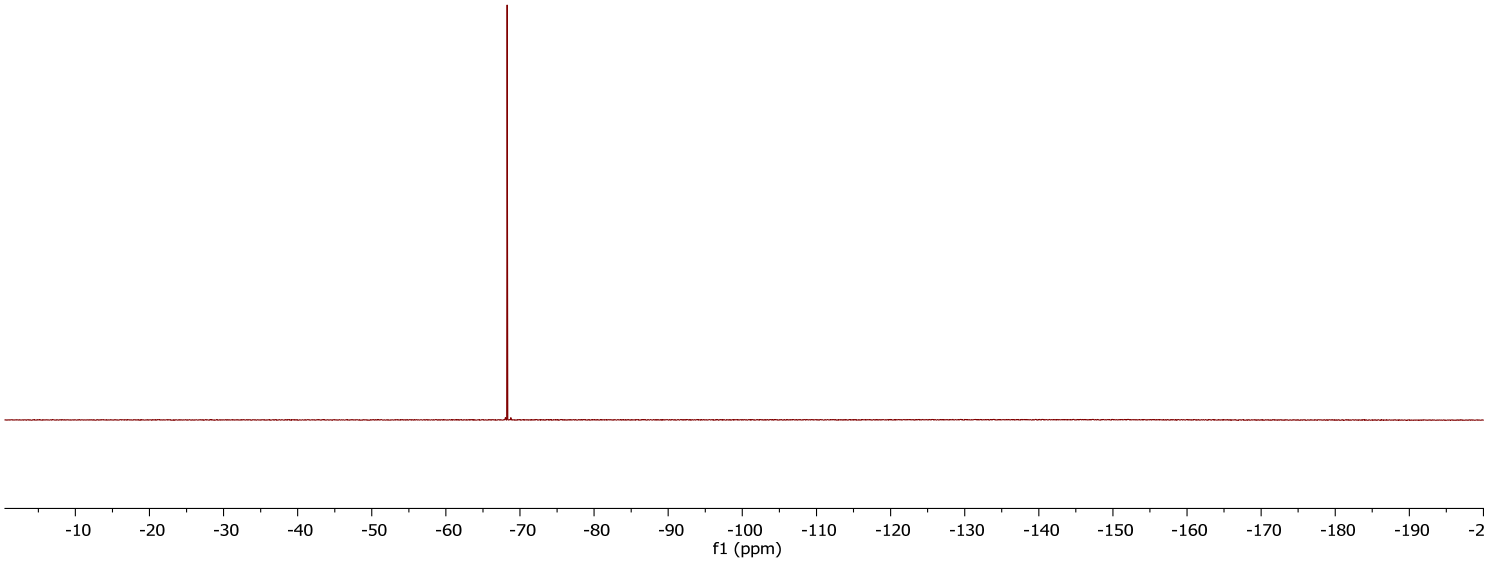
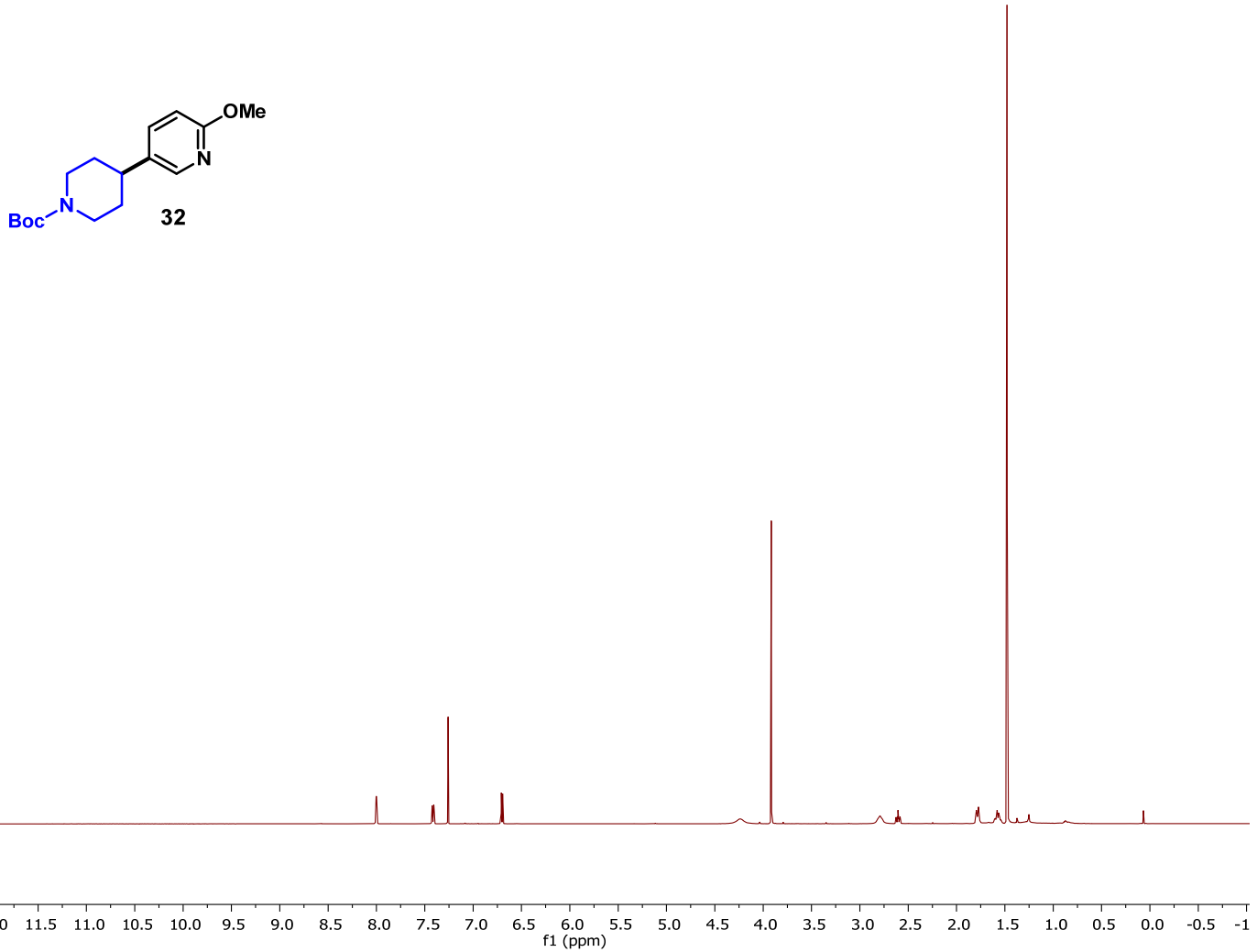
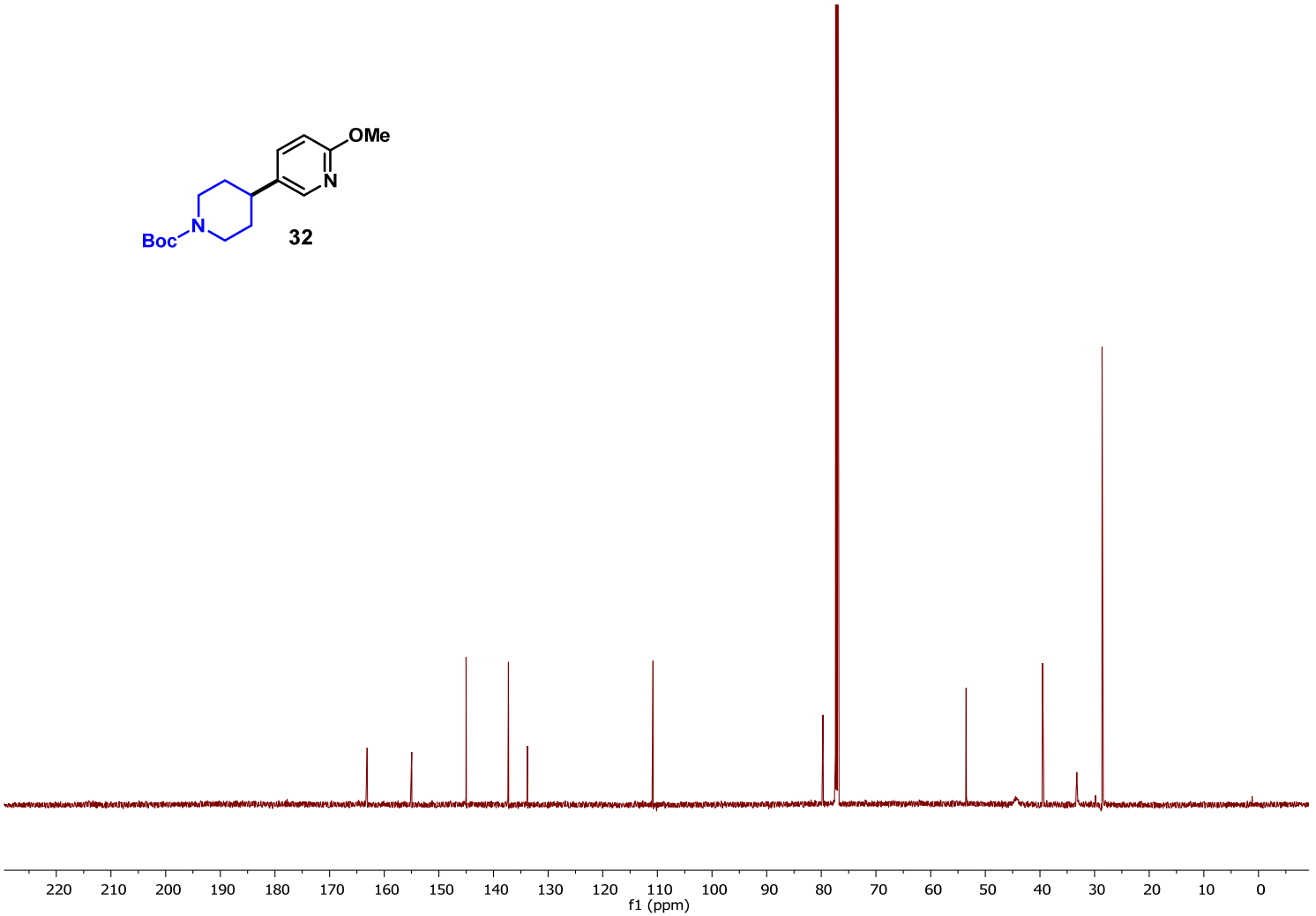


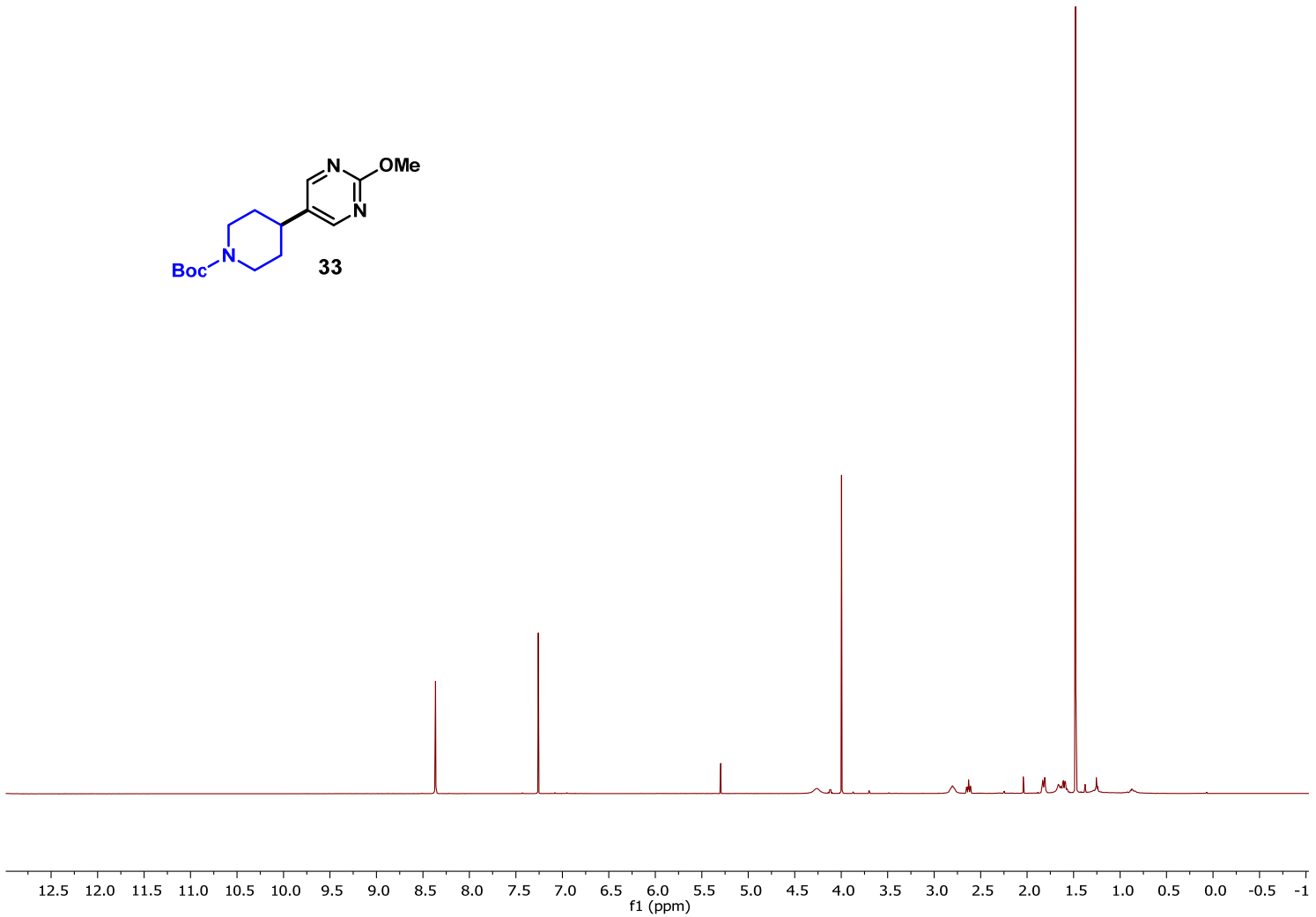
Compound 32 ^{1}H NMR



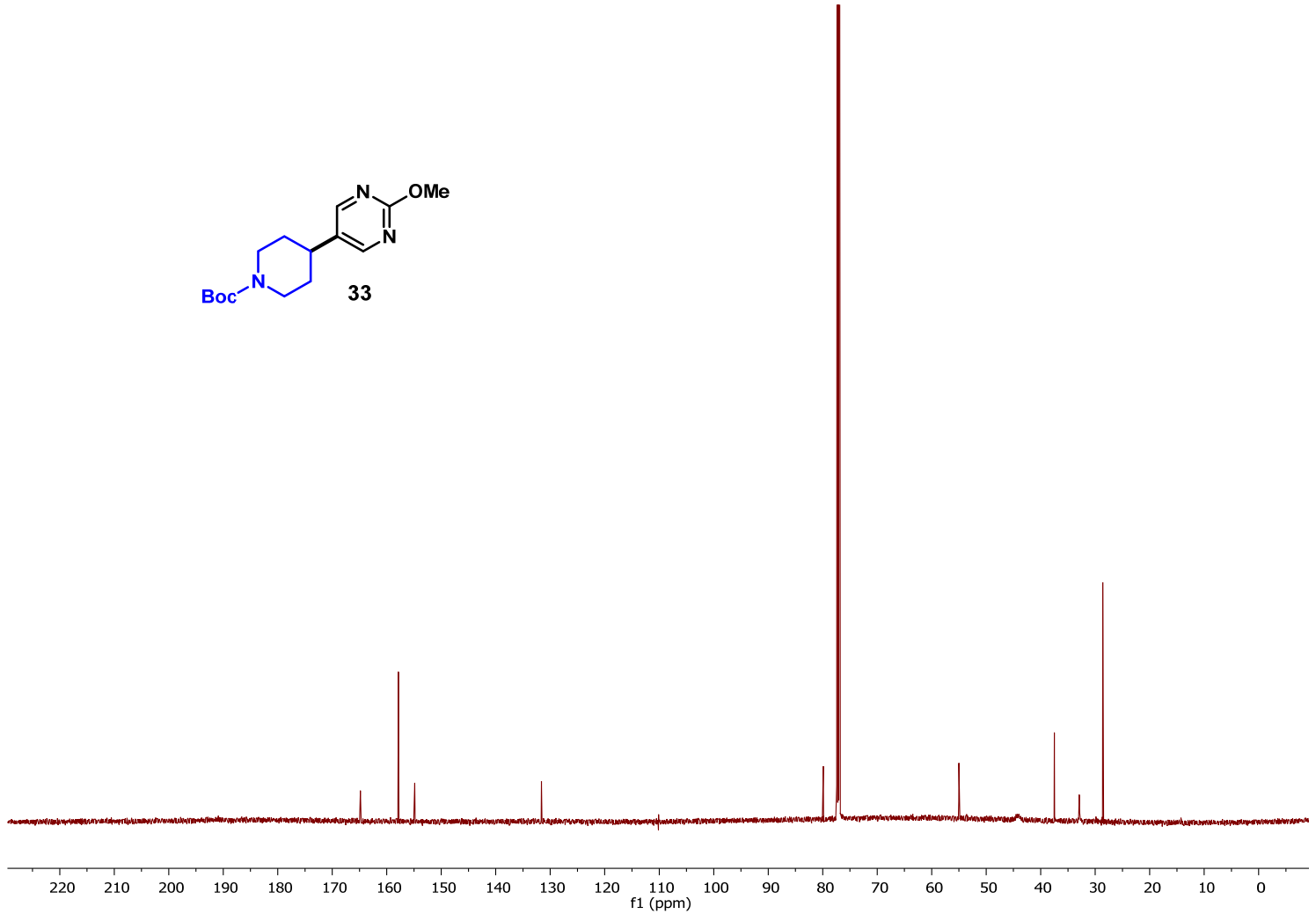
Compound 32 ^{13}C NMR



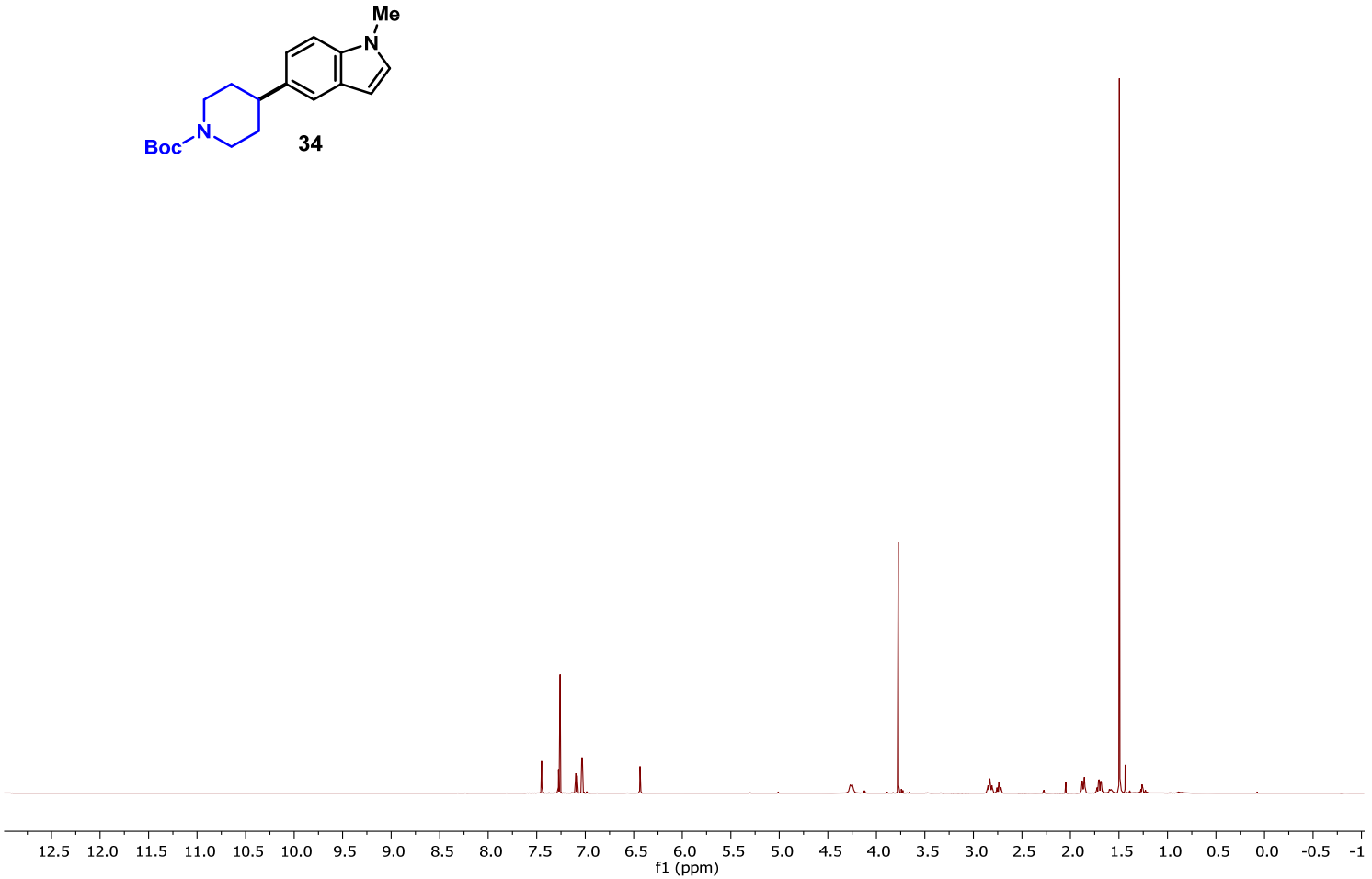
Compound 33 ^{1}H NMR



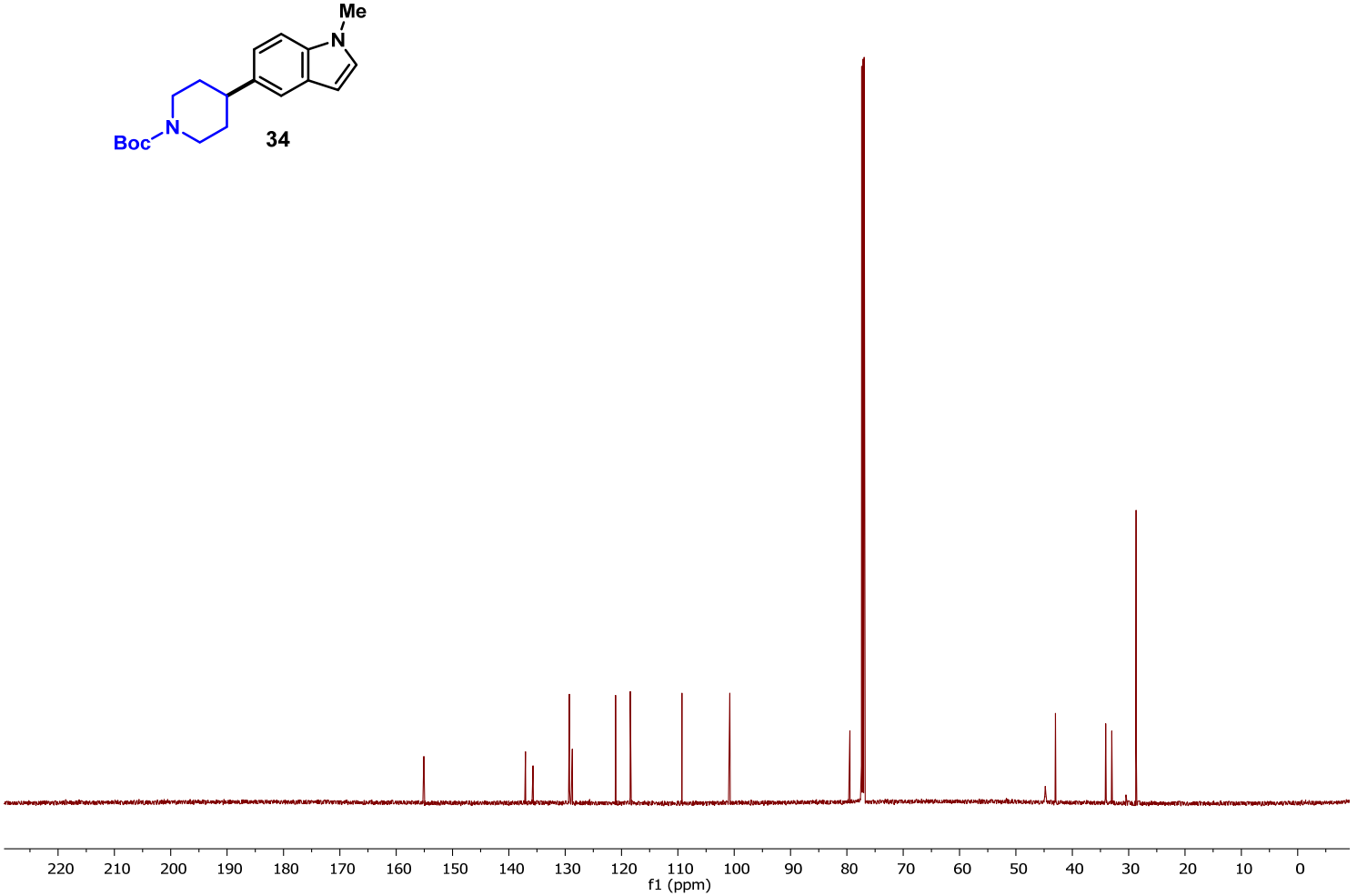
Compound 33 ^{13}C NMR



Compound 34 ^{1}H NMR



Compound 34 ^{13}C NMR



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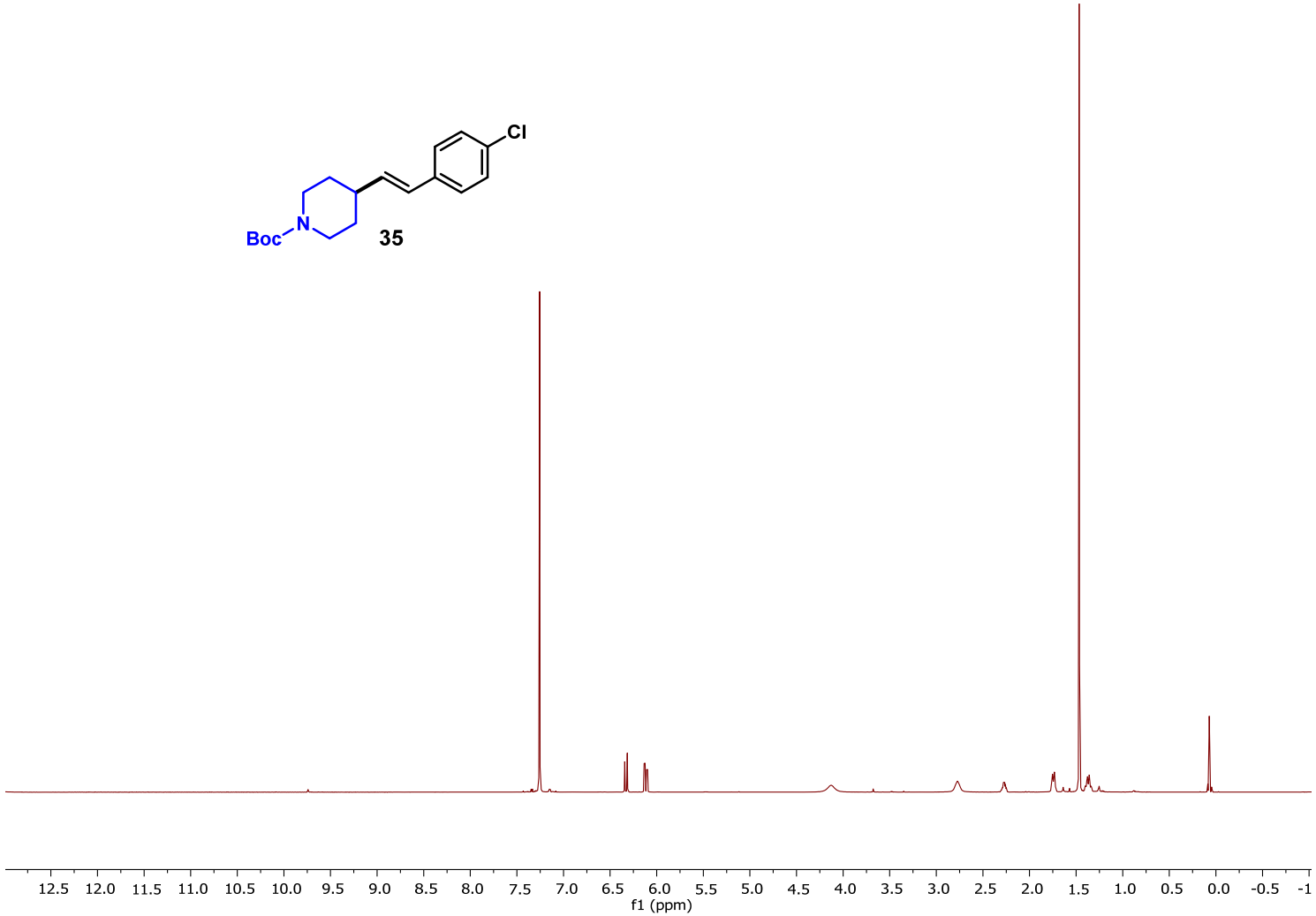
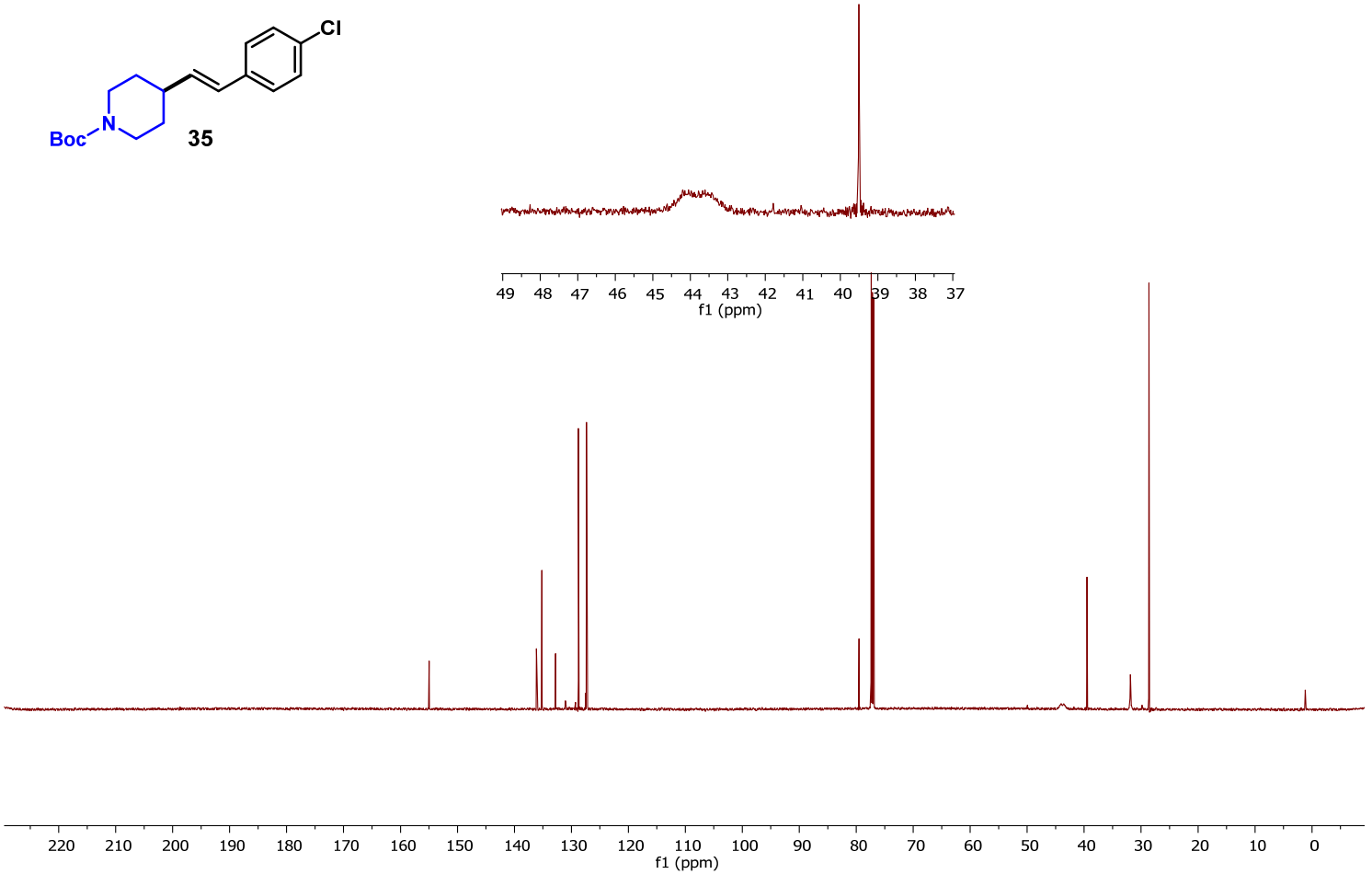
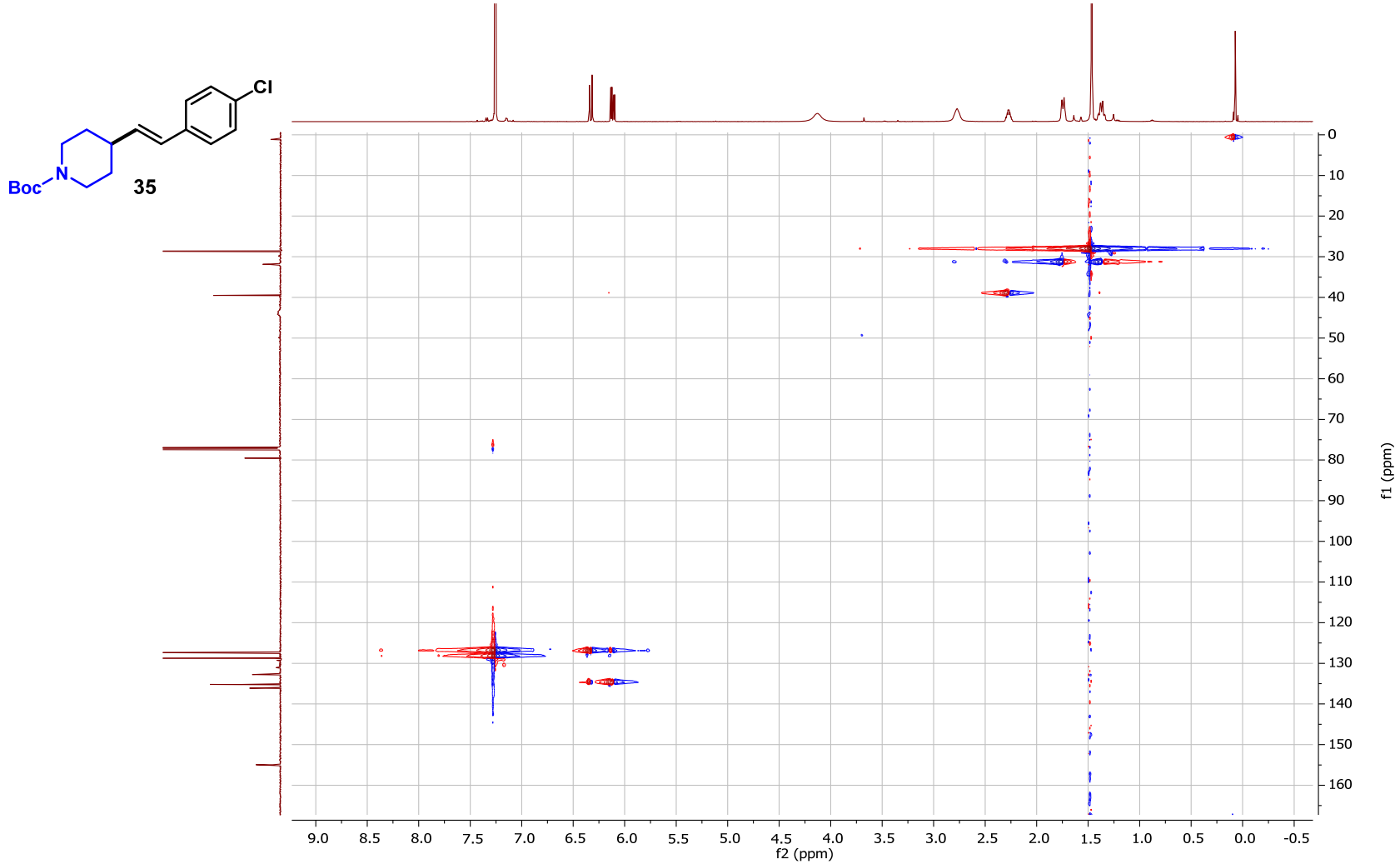


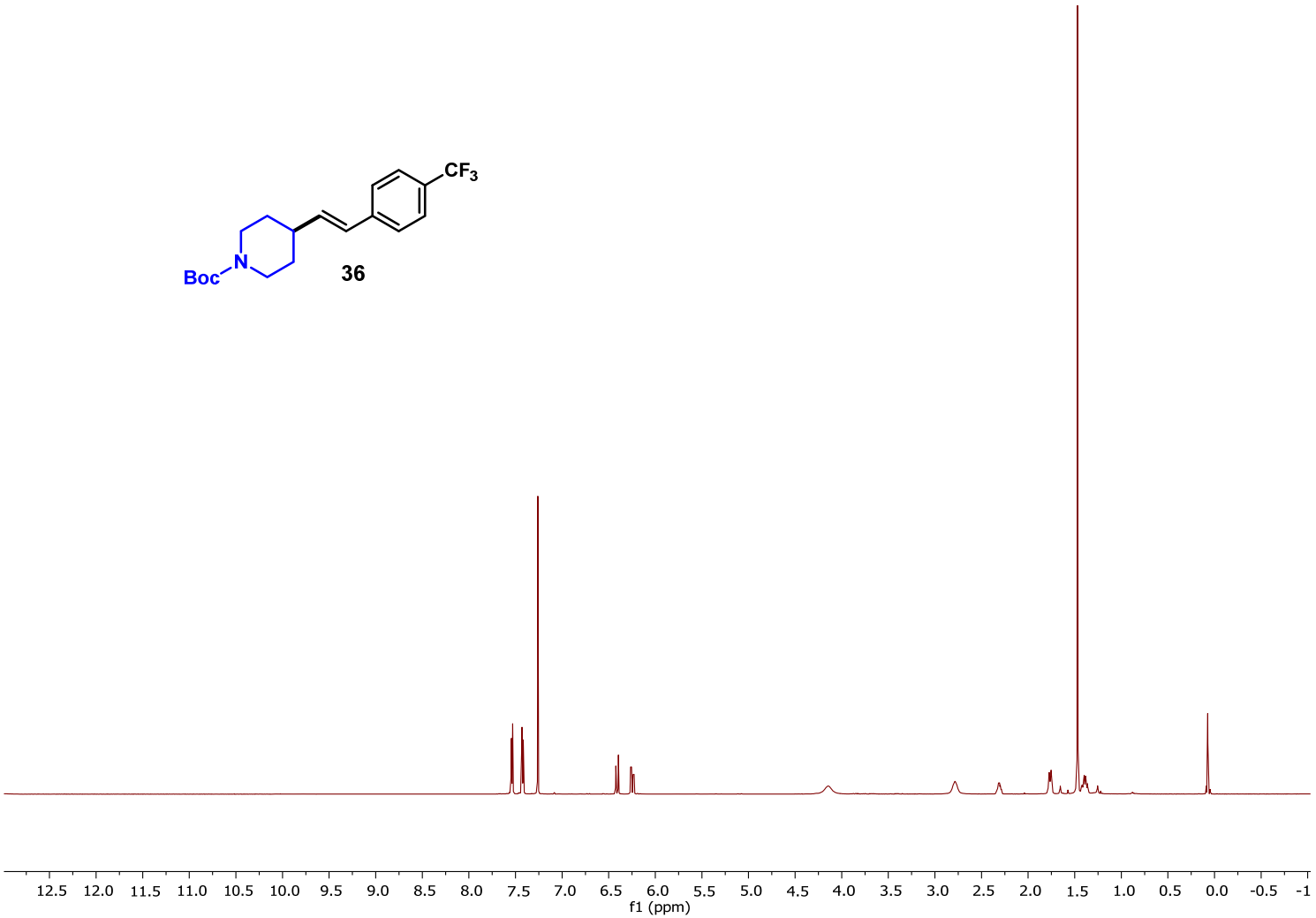
Compound 35 ^{13}C NMR



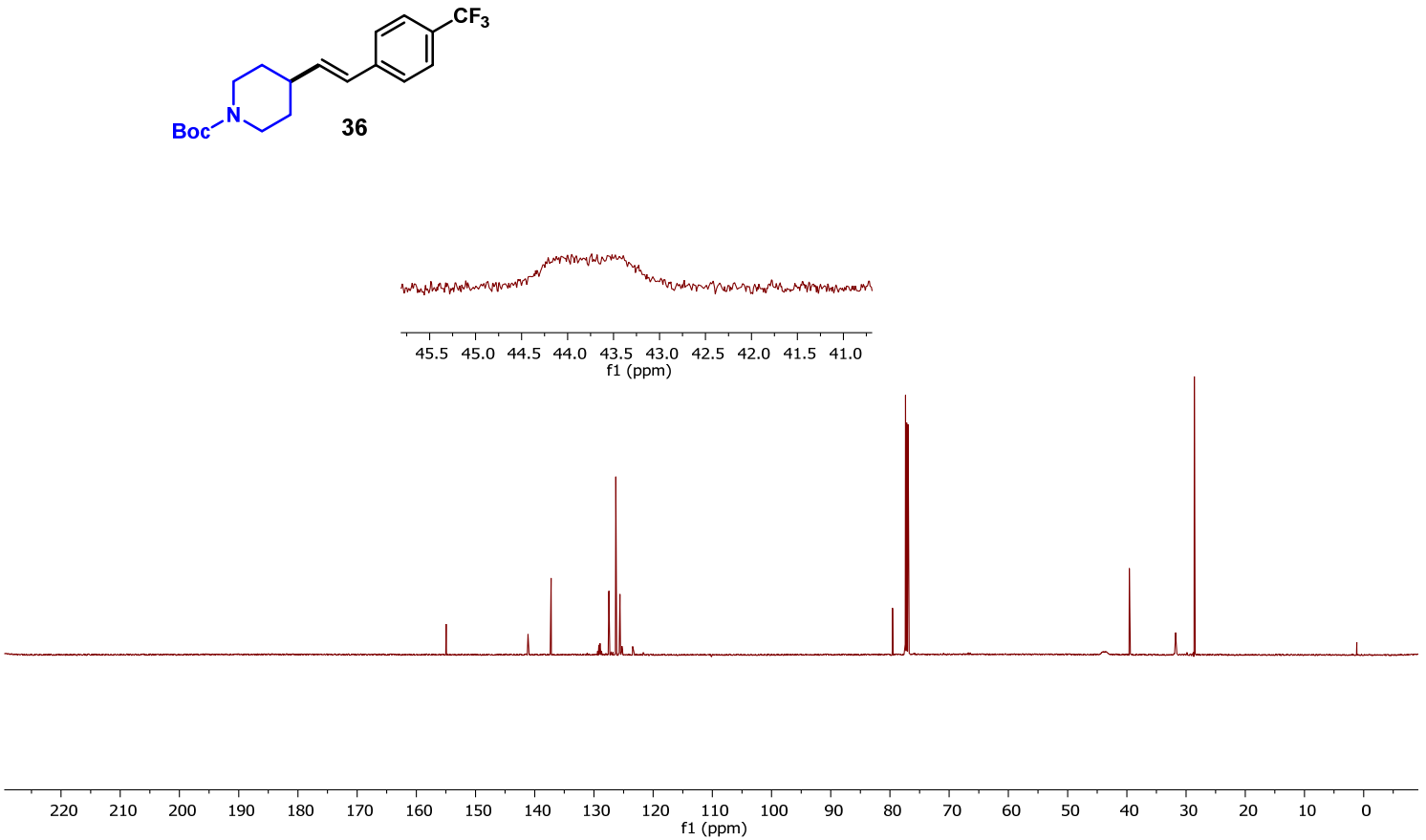
Compound 35 HSQC



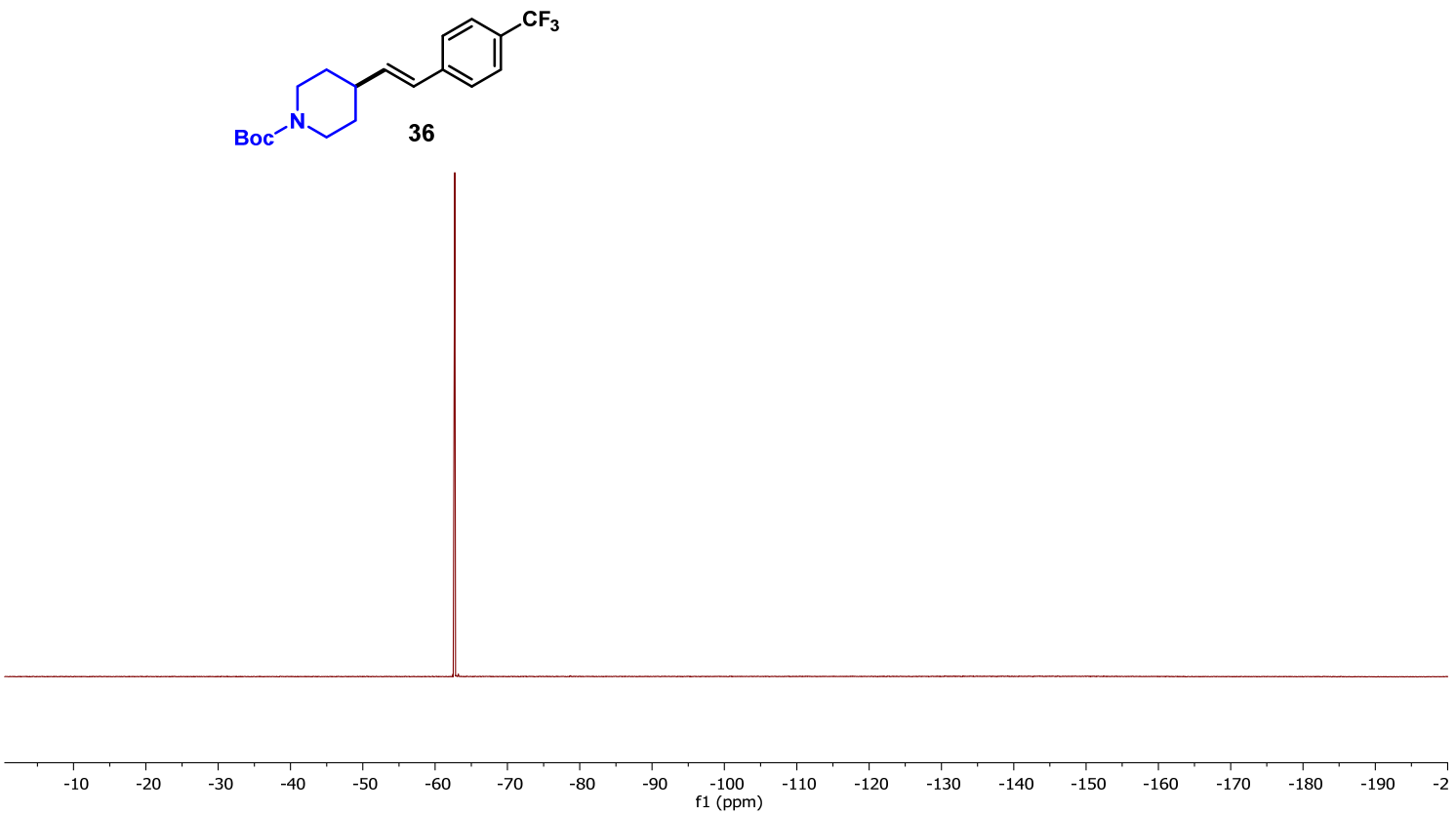
Compound 36 ^{1}H NMR



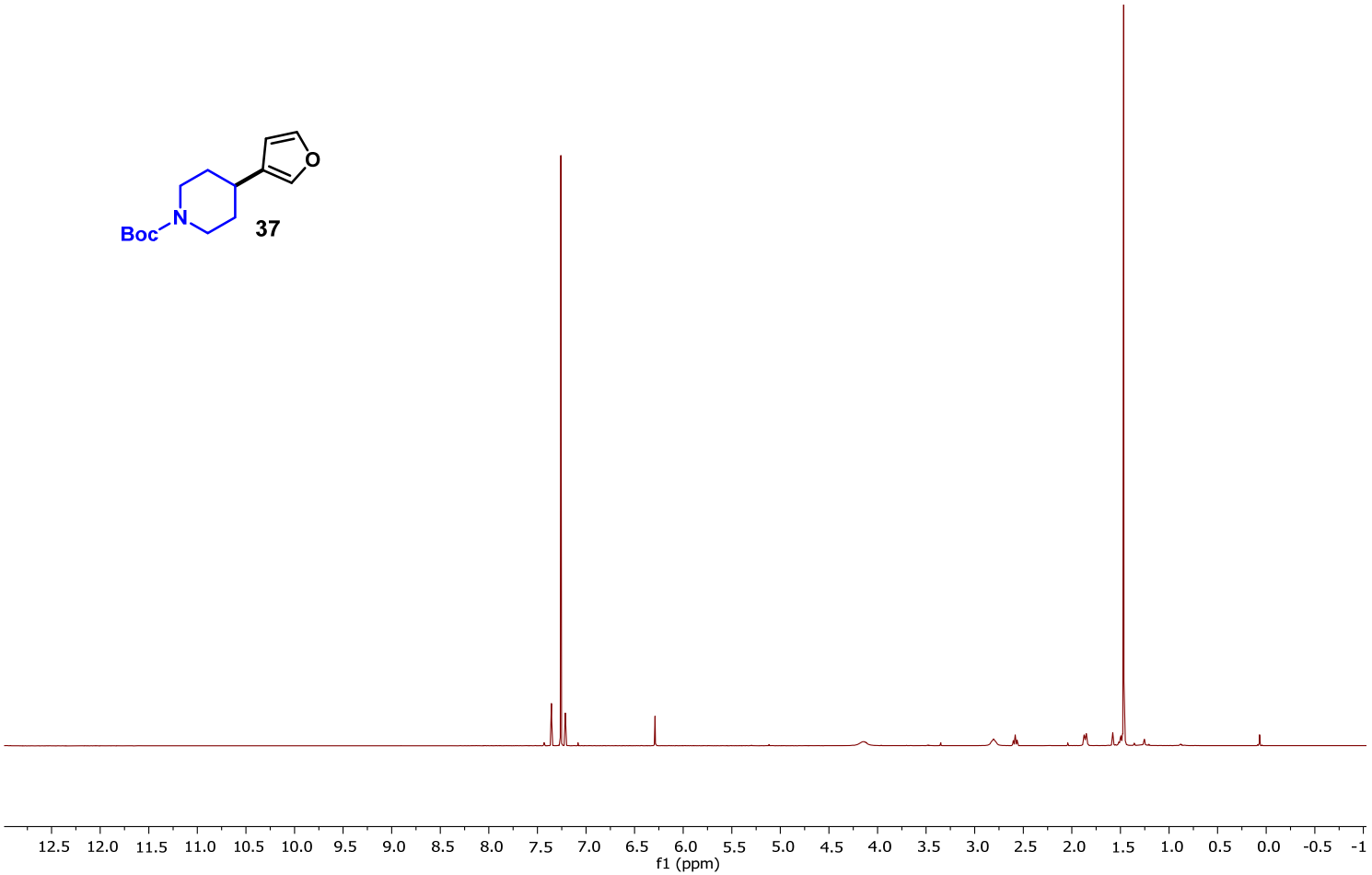
Compound 36 ^{13}C NMR



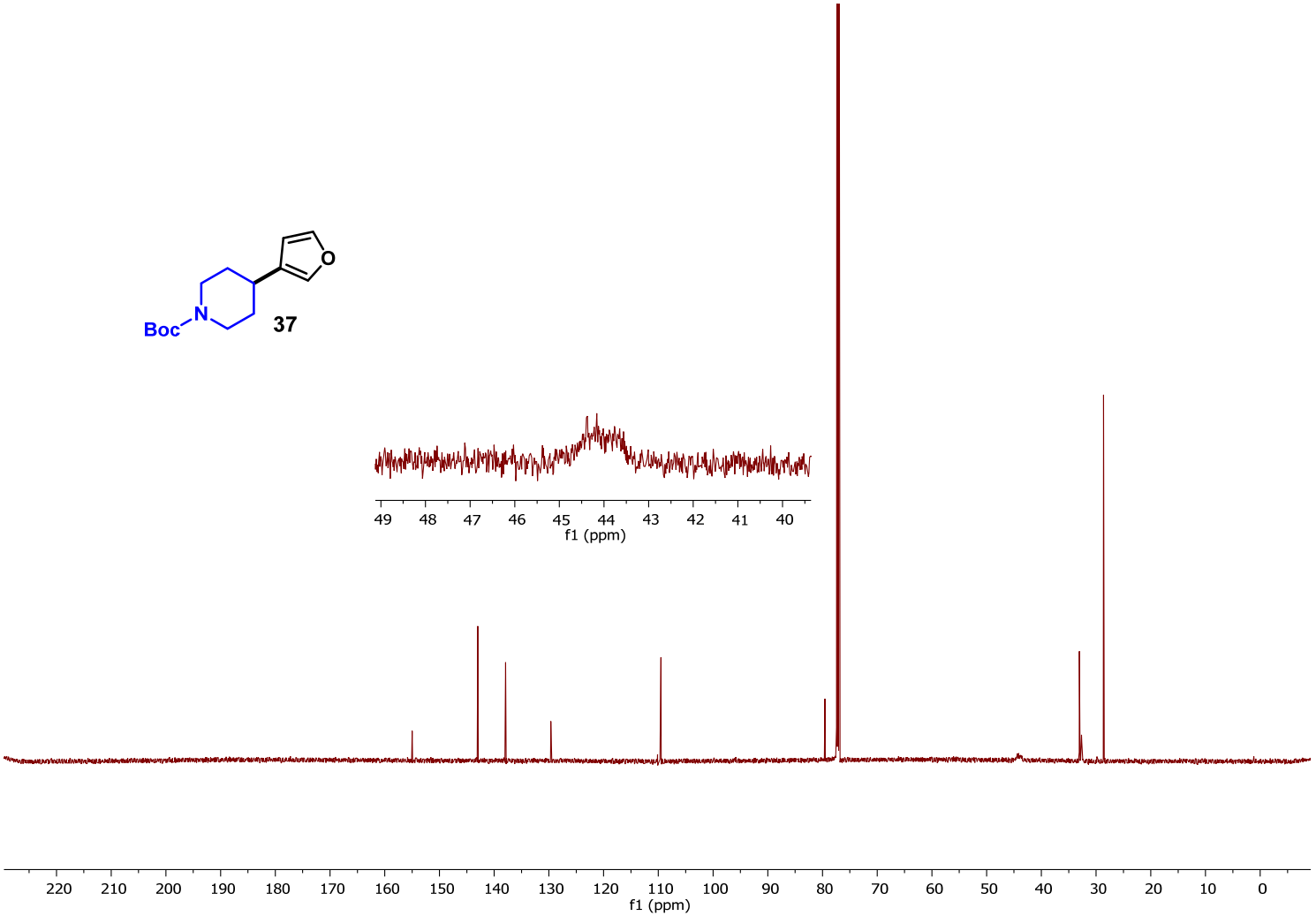
Compound 36 ^{19}F NMR



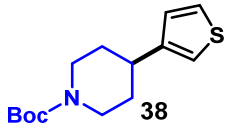
Compound 37 ^{1}H NMR



Compound 37 ^{13}C NMR

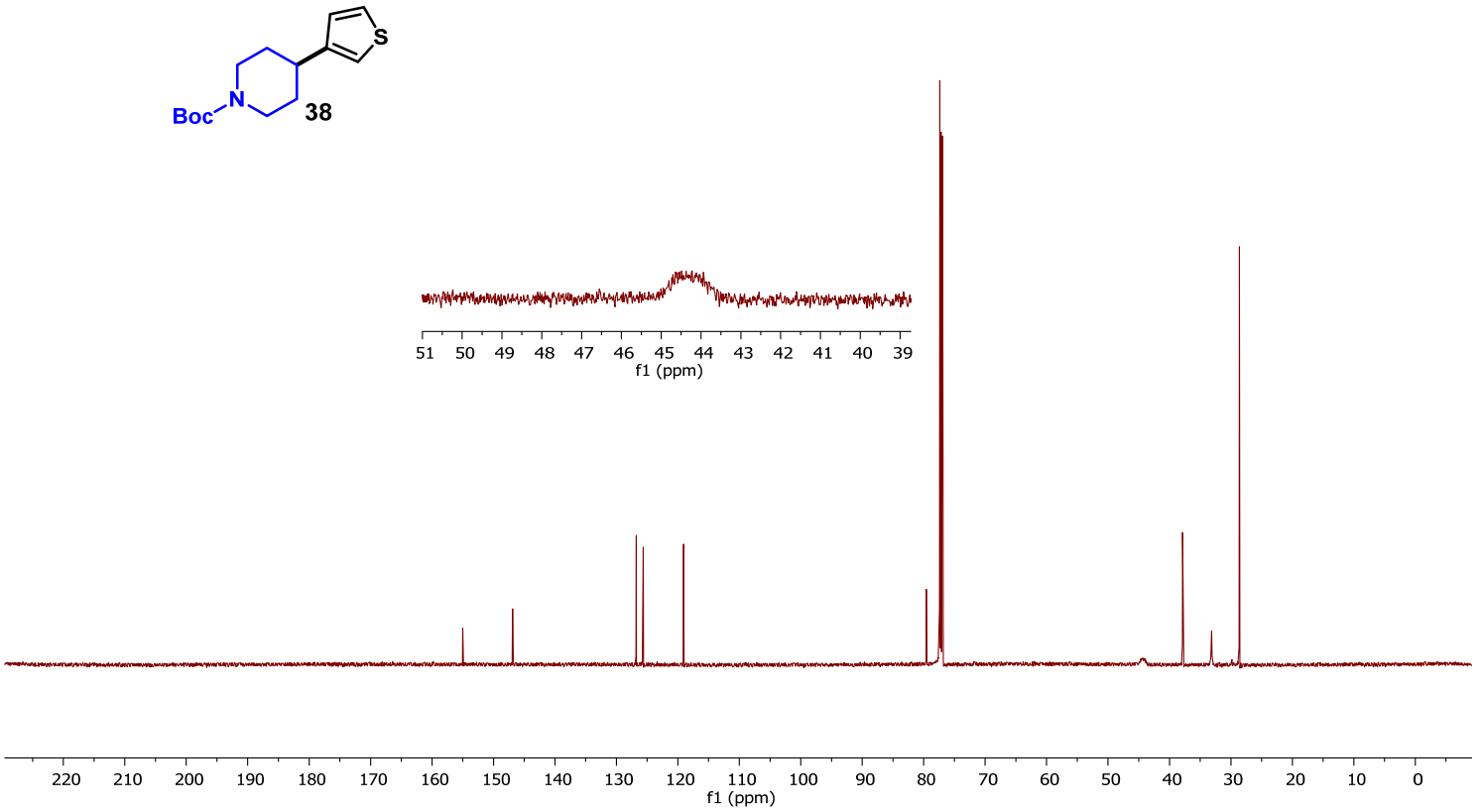


Compound 38 ^{1}H NMR

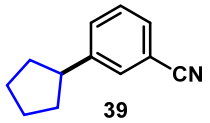


38

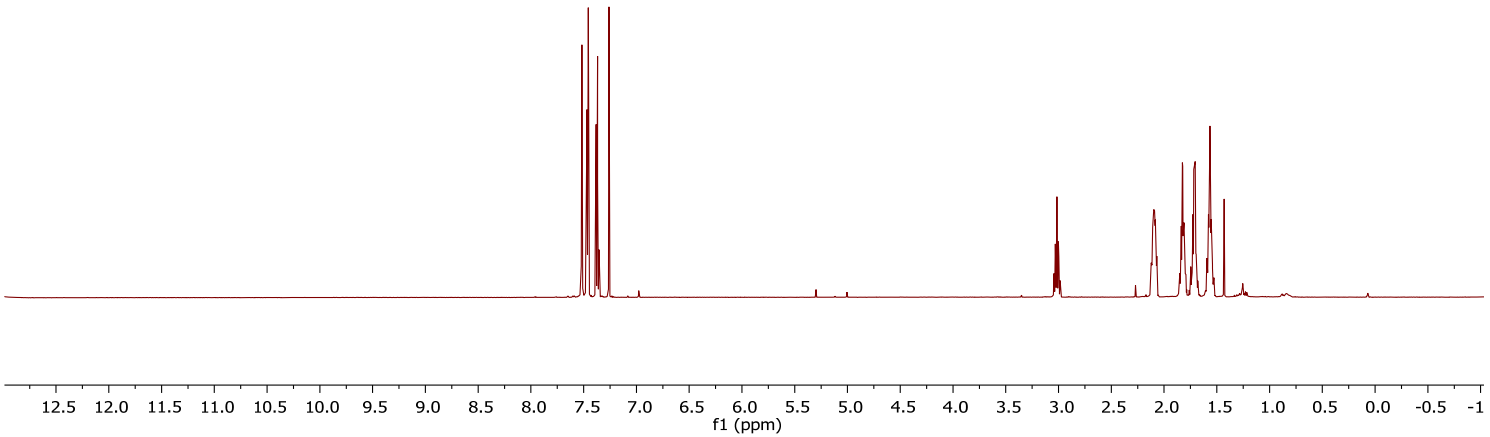
Compound 38 ^{13}C NMR



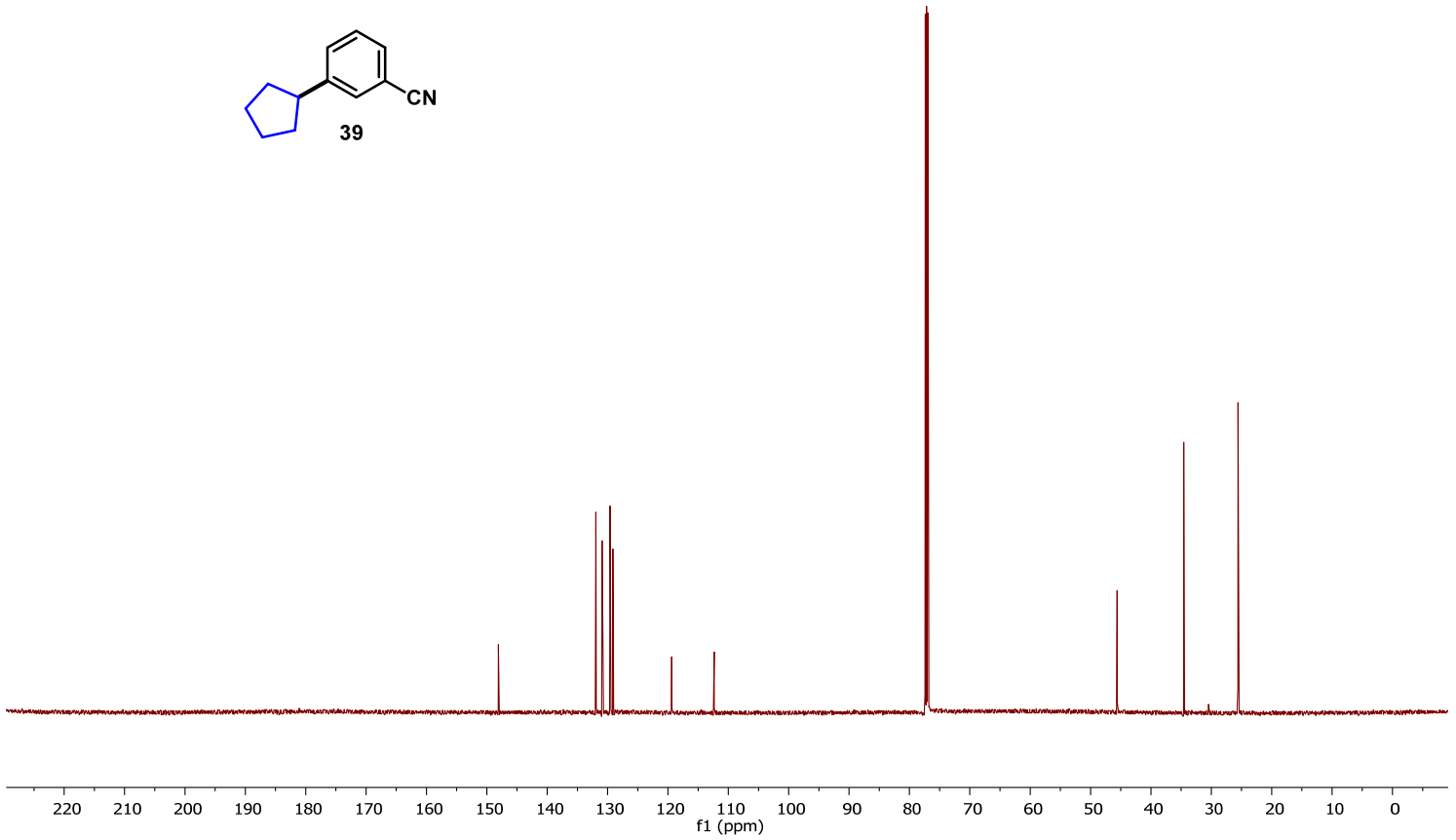
Compound 39 ^{1}H NMR



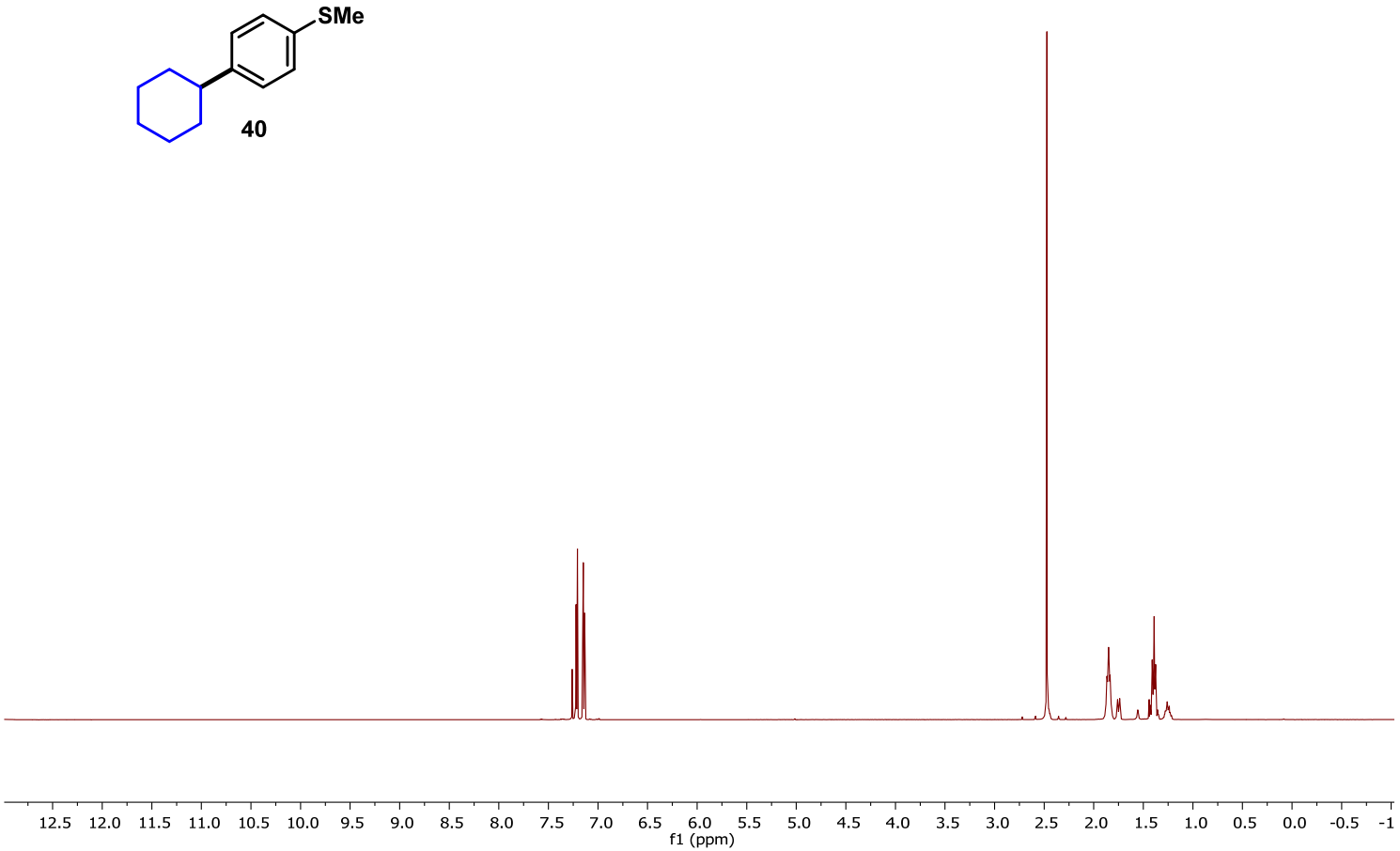
39



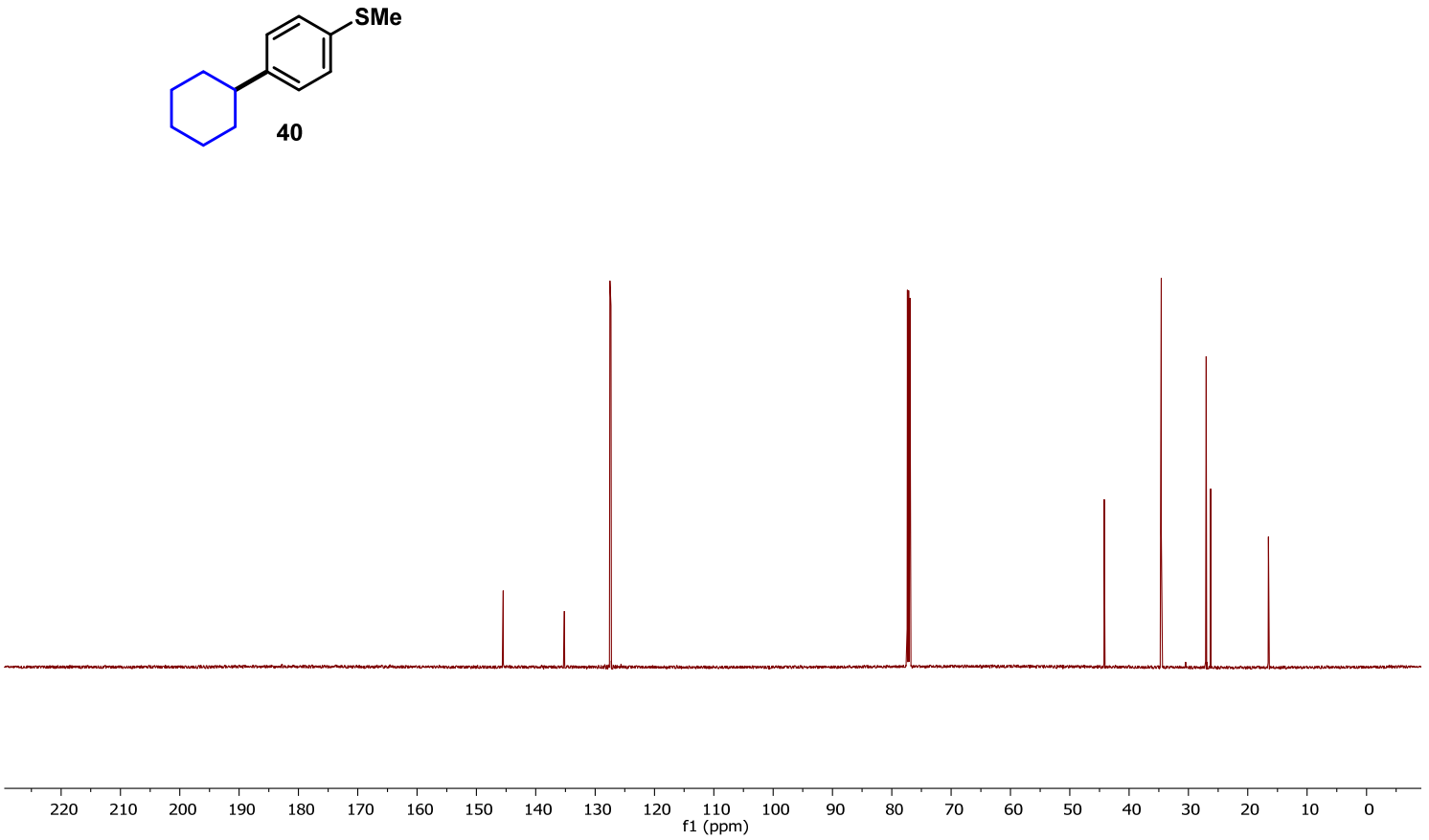
Compound 39 ^{13}C NMR



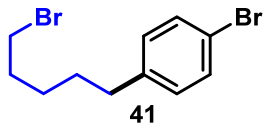
Compound 40 ^{1}H NMR



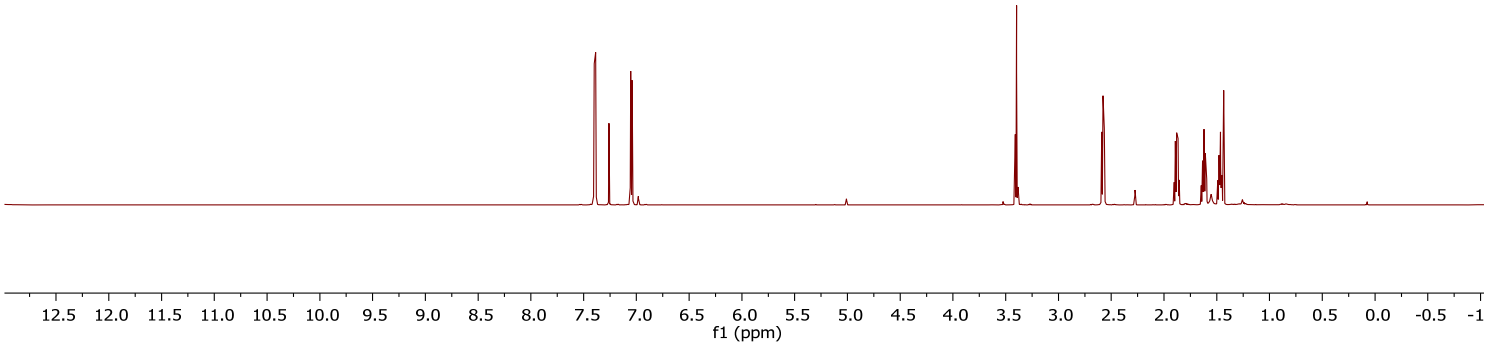
Compound 40 ^{13}C NMR



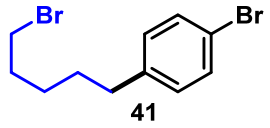
Compound 41 ^{1}H NMR



41



Compound 41 ^{13}C NMR



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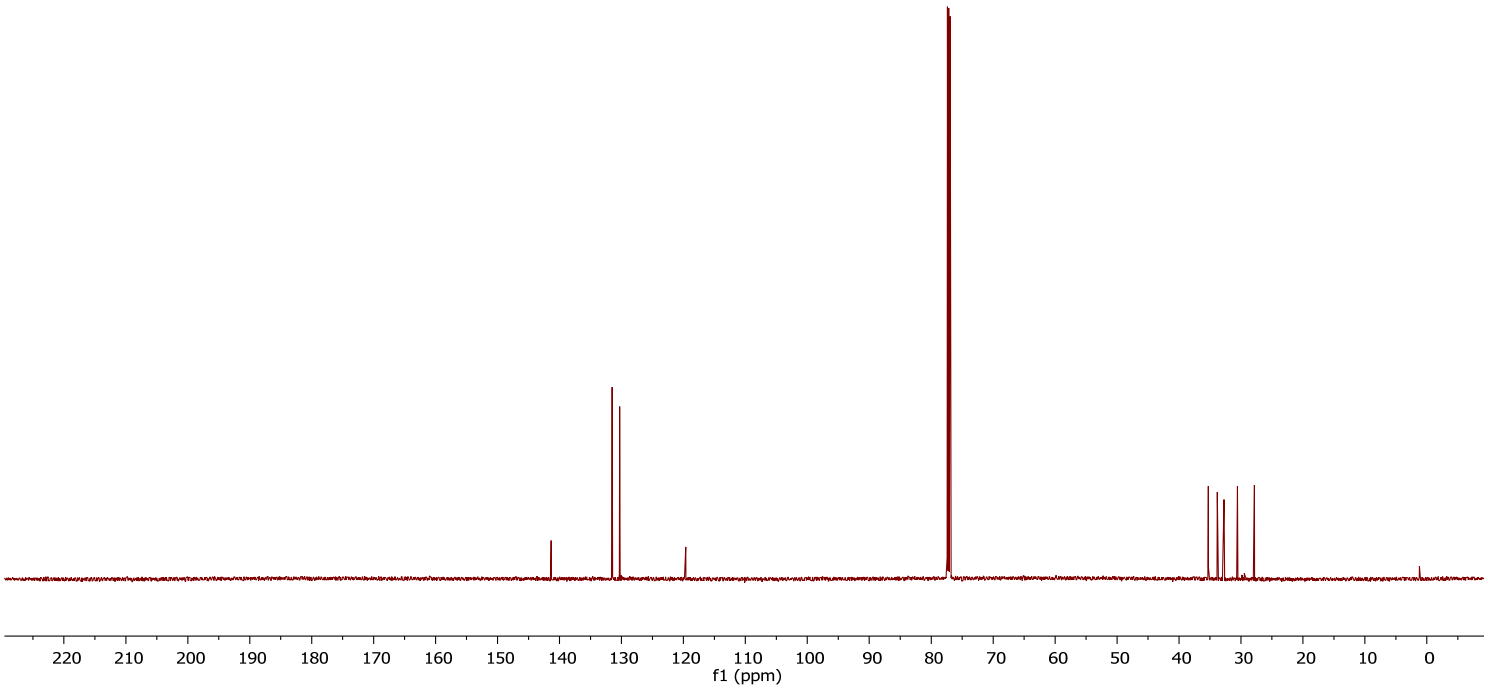
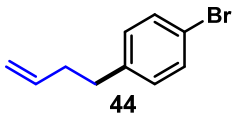
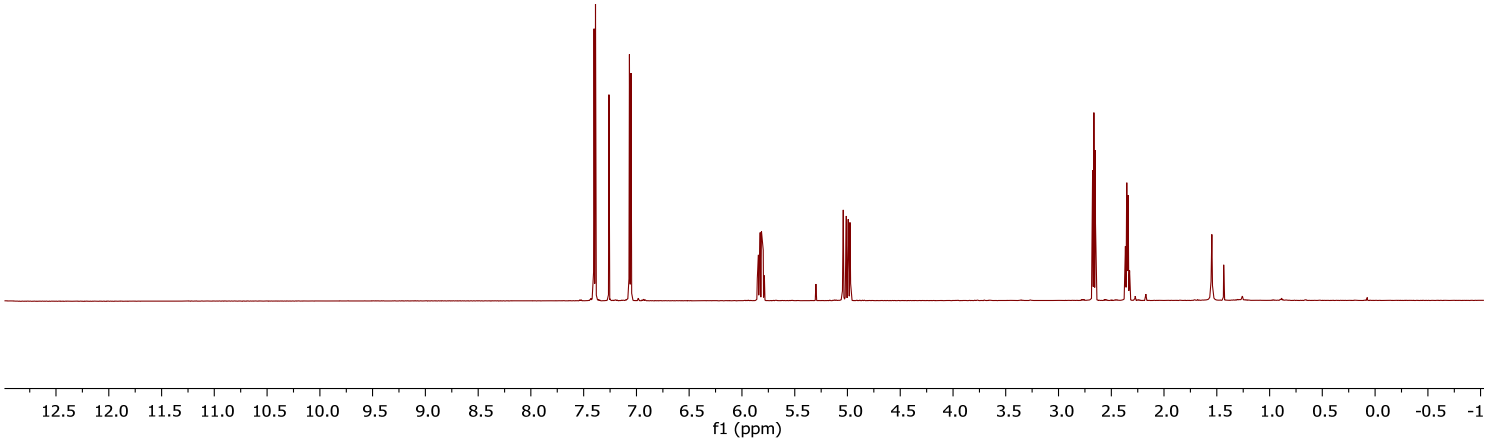


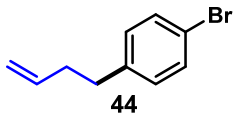
Compound 44 ^{1}H NMR



44



Compound 44 ^{13}C NMR



44