Electronic Supplementary Material (ESI) for ChemComm.


# Supporting Information

Practical Synthesis of Fragment- and Lead-Like Molecules Enriched in $sp^3$ Character

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**General**

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods. Pd/C used is 10% Pd/C purchased from Sigma Aldrich.

**Experimental Details**

All reactions were carried out in oven-dried glassware, which was evacuated and purged with $N_2$ before use. Purging refers to a vacuum/nitrogen-refilling procedure. Room temperature was generally ca. 18 °C. Reactions were carried out at elevated temperatures using a temperature-regulated hotplate/stirrer and sand-bath.

**Purification of Products**

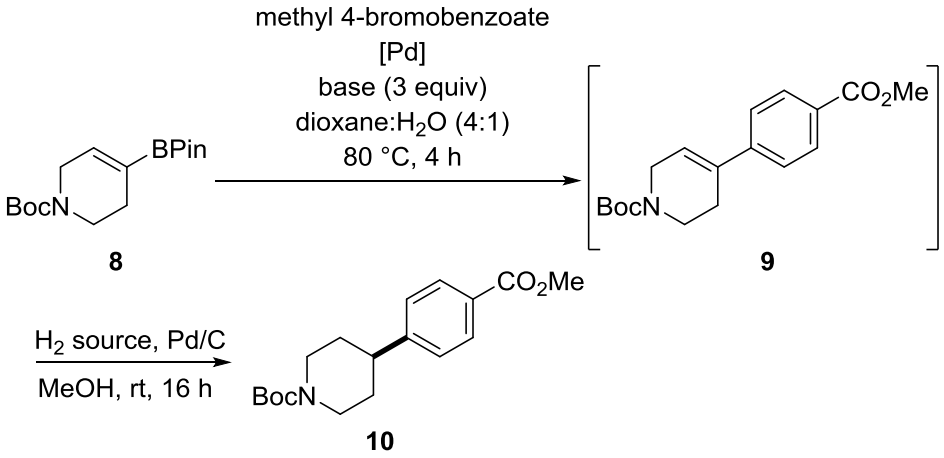
Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator UV254. These were analysed under 254 nm UV light or developed using potassium permanganate solution. Strong cation exchange chromatography was carried out using Silicycle SiliaPrepTM Propylsulfonic Acid (SCX-2) cartridges.

**Analysis of Products**

$^{1}$H NMR spectra were recorded at 400 or 500 MHz, and $^{13}$C NMR spectra were recorded at 101 or 126 MHz. Chemical shifts are reported in ppm and coupling constants are reported in Hz with $CDCl_3$ referenced at 7.26 ($^{1}$H) and 77.16 ppm ($^{13}$C), and Acetone-$d_6$ referenced at 2.05 ($^{1}$H) and 29.84 ppm ($^{13}$C). High-resolution mass spectra were obtained through analysis at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

## General Procedure A: Optimisation

To an oven dried 2-5 mL microwave vial was added *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), *catalysts*, *base* (3 eq.) and methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.). The vial was capped and purged, then 1,4-dioxane and water were added. The reaction mixture was stirred at 80 °C for 4 h, followed by the addition of MeOH (2 mL) and the appropriate hydrogen source. The reaction was stirred for 16 h at room temperature, before being diluted with ethyl acetate and filtered through Celite. The solvent was removed *in vacuo* and a $^{1}$H NMR was performed on the crude material.




| Entry | Catalyst (1 mol%, 2 mg) | Pd/C | Hydrogen Source | Base | 10:9 |
|---|---|---|---|---|---|
| 1 | Pd(dppf)$Cl_2$.DCM | 6 mol%, 16 mg | $H_2$ (balloon) | $K_2CO_3$, 104 mg | 100:0 |
| 2 | Pd(dppf)$Cl_2$.DCM | 6 mol%, 16 mg | $Et_3SiH$ (3 eq., 120 µL) | $K_2CO_3$, 104 mg | 74:26 |
| 3 | Pd(dppf)$Cl_2$.DCM | 10 mol%, 26 mg | $Et_3SiH$ (3 eq., 120 µL) | $K_2CO_3$, 104 mg | 39:61 |
| 4 | PdXPhosG2 | 10 mol%, 26 mg | $NH_4HCO_2$ (10 eq., 158 mg) | $K_2PO_4$, 159 mg | 28:72 |
| 5 | PdXPhosG2 | 10 mol%, 26 mg | $NH_4HCO_2$ (10 eq., 158 mg) | $K_2PO_4$, 159 mg | 80:20 |
| 6 | PdXPhosG2 | 12 mol%, 32 mg | $NH_4HCO_2$ (10 eq., 158 mg) | $K_2PO_4$, 159 mg | 100:0 |

## General Procedure B: General Substrate Scope

To an oven dried 2-5 mL microwave vial was added boronic ester/acid (0.25 mmol, 1 equiv.), PdXPhosG2 (2 mg, 0.0025 mmol, 0.01 equiv.), 10% Pd/C (32 mg, 0.04 mmol, 0.12 equiv.), $K_3PO_4$ (159 mg, 0.75 mmol, 3 equiv.) and aryl halide (0.25 mmol, 1 equiv.). The vial was capped and purged, then 1,4-dioxane (800 µL) and water (200 µL) were added. The reaction mixture was stirred at 80 °C for 4 h, followed by the addition of $NH_4HCO_2$ in MeOH (1.25 M) (158 mg $NH_4HCO_2$ in 2 mL MeOH, 10 eq. 2.5 mmol). After this, the reaction was stirred for 16 h at room temperature. The

vial was de-capped, and the reaction mixture was diluted with ethyl acetate, filtered through Celite and rinsed through with further ethyl acetate. The solvent was removed *in vacuo* and the crude material was taken forward to purification.

**General Procedure C: Wax capsule**

To a boiling tube was added *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), PdXPhosG2 (2 mg, 0.0025 mmol, 0.01 equiv.), 10% Pd/C (32 mg, 0.04 mmol, 0.12 equiv.), $K_3PO_4$ (159 mg, 0.75 mmol, 3 equiv.), aryl halide (0.25 mmol, 1 eq.) and a wax capsule containing ammonium formate (158 mg, 2.5 mmol, 10 equiv.). The tube was capped with a Suba Seal, purged then charged with 1,4-dioxane (800 µL), water (200 µL) and MeOH (2 mL). The reaction was stirred at 65 °C for 16 h, filtered through Celite then concentrated *in vacuo* before being taken forward to purification.

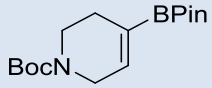
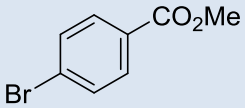
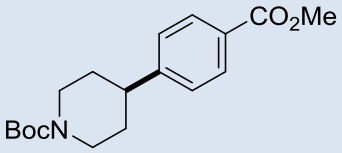
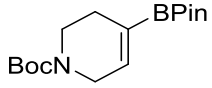
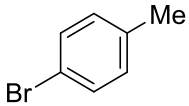
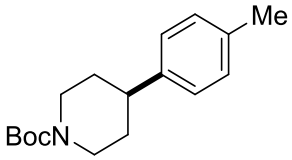
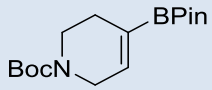
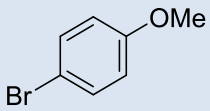
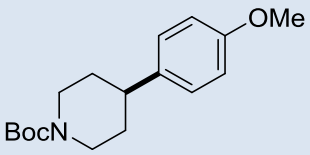
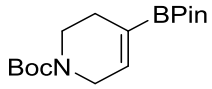
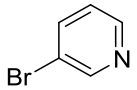
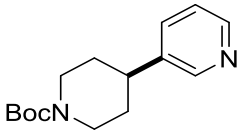
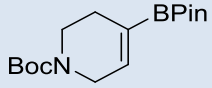
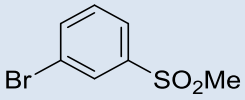
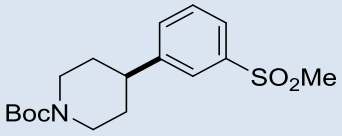
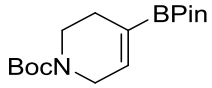
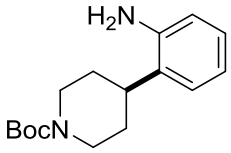
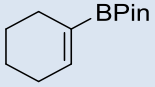
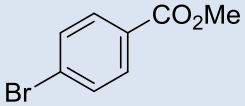
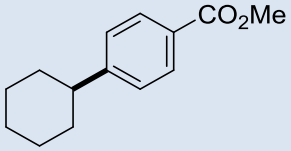
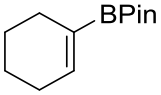
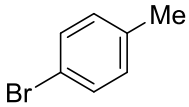
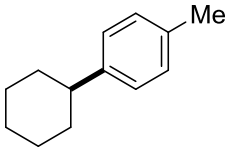
Synthesis of capsule: ≥65% paraffin wax was heated in a conical flask until fully melted and transferred to an unturned Suba Seal using a glass pipette. An NMR tube was placed in the molten wax to create a hollow centre and was held in position for ~1 minute until the wax had solidified. Following this, the Suba Seal was folded over to free the wax capsule, to which ammonium formate was added. Molten wax was dripped over the open capsule to fully encapsulate the ammonium formate, and then the full capsule was dipped in a conical flask of molten wax twice to ensure a full seal, then allowed to cool to room temperature.

**Chiral HPLC**

For Compound 22, Chiral HPLC was performed using a gradient of 5% IPA/hexanes to 10% IPA/hexanes over 20 minutes, using a ChiralpakIA column. For Compound 12s, Chiral HPLC was performed using an isocratic method of 30% IPA/hexanes over 20 minutes, using a ChiralpakIA column.

**Array Synthesis**

To an test tube was added Bpin (0.125 mmol, 1 eq.), PdXPhosG2 (1 mg, 0.00125 mmol, 0.01 eq.), Pd/C (16 mg, 0.015 mmol, 0.12 eq.), $K_3PO_4$ (79 mg, 0.375 mmol, 3 eq.) and aryl halide (0.125 mmol, 1 eq.). The test tube was sealed with a suba seal, purged with nitrogen, then 1,4-dioxane and water were added. The reaction mixture was stirred at 80 °C for 4 h, followed by the addition of $NH_4HCO_2$ in MeOH (1.25 M) (79 mg $NH_4HCO_2$ in 1 mL MeOH, 10 eq. 1.25 mmol). Following this, the reaction was stirred for 16 h at room temperature before 1,4-dinitrobenzene was added and the reaction was filtered through Celite. Concentration *in vacuo* afforded the crude material, on which a $^1$H NMR was performed. Conversion was determined by using 1,4-dinitrobenzene as an internal standard.

| Entry | BPin | Aryl Halide | Product | Conversion |
|---|---|---|---|---|
| **1** |  39 mg |  26 mg |  | 98% |
| **2** |  39 mg |  16 µL |  | Quant. |
| **3** |  39 mg |  16 µL |  | 94% |
| **4** |  39 mg |  12 µL |  | 79% |
| **5** |  39 mg |  30 mg |  | 99% |
| **6** |  39 mg |  26 mg |  | 95% |
| **7** |  26 mg |  26 mg |  | 95% |
| **8** |  26 mg |  16 µL |  | 80% |

| | | | | |
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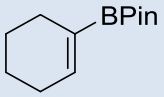
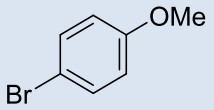
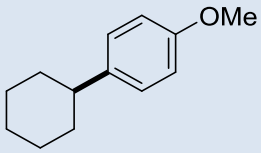
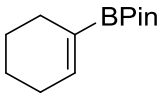
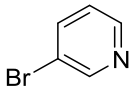
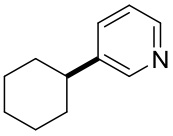
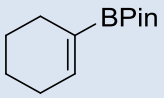
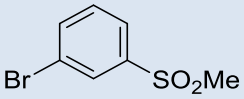
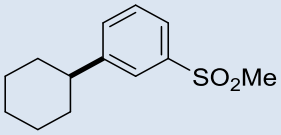
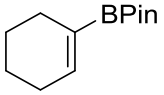
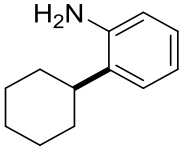
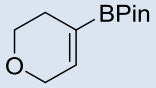
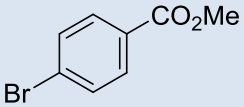
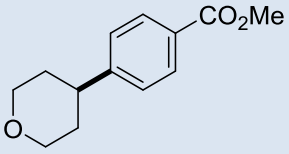
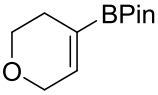
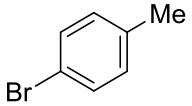
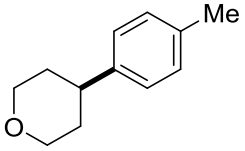
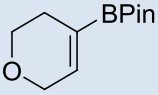
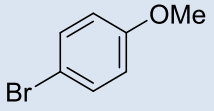
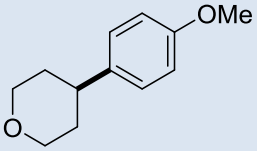
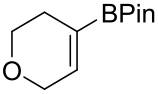
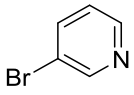
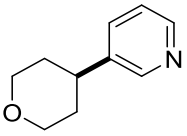
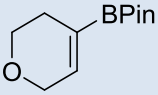
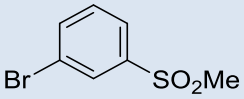
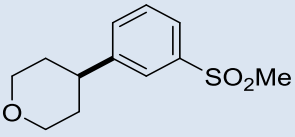
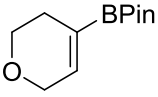
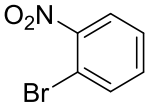
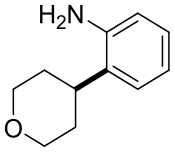
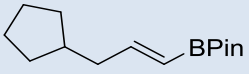
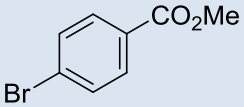
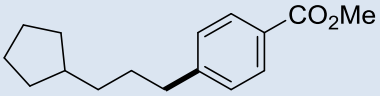
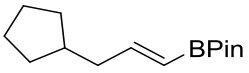
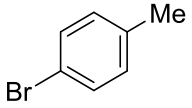
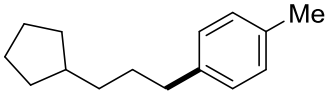
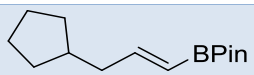
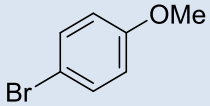
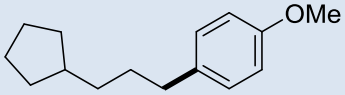
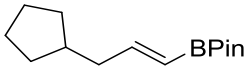
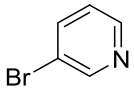
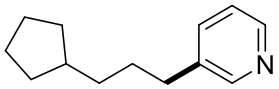
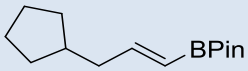
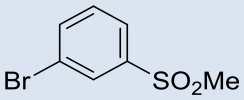
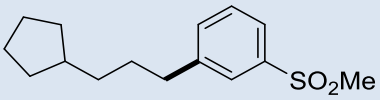
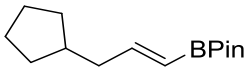
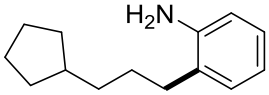
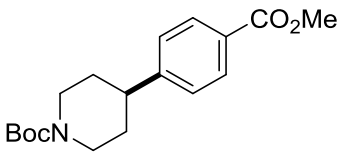
| **9** |  26 mg |  16 µL |  | 79% |
| **10** |  26 mg |  12 µL |  | 54% |
| **11** |  26 mg |  30 mg |  | 64% |
| **12** |  26 mg |  26 mg |  | 71% |
| **13** |  27 mg |  26 mg |  | 86% |
| **14** |  27 mg |  16 µL |  | 75% |
| **15** |  27 mg |  16 µL |  | 62% |
| **16** |  27 mg |  12 µL |  | 66% |
| **17** |  27 mg |  30 mg |  | 54% |
| **18** |  27 mg |  26 mg |  | 69% |
| **19** |  30 mg |  26 mg |  | 98% |
| **20** |  30 mg |  |  | 58% |

| | | | | |
|---|---|---|---|---|
| | | 16 µL | | |
| **21** |  30 mg |  16 µL |  | 70% |
| **22** |  30 mg |  12 µL |  | 38% |
| **23** |  30 mg |  30 mg |  | 50% |
| **24** |  30 mg |  26 mg |  | - |

**Compound 11a, *tert*-butyl 4-(4-(methoxycarbonyl)phenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.). The crude material was taken up in ethyl acetate and washed with water (2 x 10 mL) and brine (10 mL), dried with $Na_2SO_4$ and concentrated *in vacuo* to afford the title compound as a white amorphous solid (79.6 mg, 99%).

Synthesised according to General Procedure C using methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (20% EtOAc/PE) to afford the title compound as a white amorphous solid (36.7 mg, 46%).

$\upsilon_{max}$ (neat): 2973, 2930, 2848, 1719, 1688 $cm^{-1}$

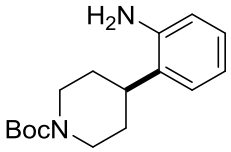
$^1$H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.26 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 4.25 (br. s, 2H, 2 x CH), 3.89 (s, 3H, $CH_3$), 2.80 (t, 2H, 2 x CH, *J* = 11.0 Hz), 2.70 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.82 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.62 (qd, 2H, 2 x CH, *J* = 12.7, 4.3 Hz), 1.47 (s, 9H, 3 x $CH_3$).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 167.1, 154.9, 151.2, 130.0, 128.5, 127.0, 79.7, 52.1, 44.3, 42.9, 33.0, 28.6.

HRMS ($C_{18}H_{26}O_4N$) $[M+H]^+$ requires: 320.1856, observed: 320.1856

Consistent with previously reported data.[1]

**Compound 11b, *tert*-butyl 4-(2-aminophenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 2-bromo nitrobenzene (51 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (40% EtOAc/PE) to afford the title compound as a dark yellow oil (66.2 mg, 96%).

$\upsilon_{max}$ (neat): 3456, 3357, 2971, 2921, 2850, 1677, 1625 $cm^{-1}$

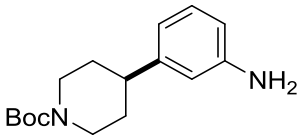
$^1$H NMR (500 MHz, $CDCl_3$): δ 7.10 – 7.02 (m, 2H, 2 x ArH), 6.79 (td, 1H, ArH, *J* = 7.5, 1.1 Hz), 6.70 (dd, 1H, ArH, *J* = 7.9, 1.1 Hz), 4.27 (br. s, 2H, 2 x CH), 3.64 (s, 2H, $NH_2$), 2.82 (t, 2H, 2 x CH, *J* =

11.3 Hz), 2.62 (tt, 1H, CH, *J* = 11.9, 3.2 Hz), 1.85 (d, 2H, 2 x CH, *J* = 13.3 Hz), 1.61 (qd, 2H, 2 x CH, *J* = 12.7, 4.3 Hz), 1.49 (s, 9H, 3 x $CH_3$).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 155.2, 154.4, 138.0, 127.9, 115.5, 79.8, 44.7, 41.9, 33.6, 28.7 (2C not observed).

HRMS ($C_{16}H_{25}O_2N_2$) $[M+H]^+$ requires: 277.1911, observed: 277.1911

**Compound 11c, *tert*-butyl 4-(3-aminophenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 3-bromoaniline (27 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (20% EtOAc/PE) to afford the title compound as an off-white solid (34.4 mg, 50%).

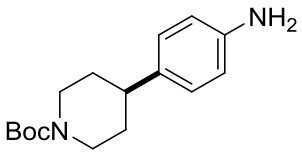
$\upsilon_{max}$ (neat): 3443, 3352, 2935, 2852, 1651, 1604 $cm^{-1}$

$^1$H NMR (500 MHz, $CDCl_3$): δ 7.09 (t, 1H, ArH, *J* = 7.9 Hz), 6.60 (d, 1H, ArH, *J* = 7.6 Hz), 6.56 – 6.51 (m, 2H, 2 x ArH), 4.22 (br. s, 2H, 2 x CH), 3.63 (s, 2H, $NH_2$), 2.77 (t, 2H, 2 x CH, *J* = 10.7 Hz), 2.54 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.79 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.65 – 1.53 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 155.0, 147.3, 146.7, 129.5, 117.3, 113.7, 113.3, 79.5, 44.6, 42.9, 33.2, 28.6.

HRMS ($C_{16}H_{25}O_2N_2$) $[M+H]^+$ requires: 277.1911, observed: 277.1912

**Compound 11d, *tert*-butyl 4-(4-aminophenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 4-bromo nitrobenzene (50 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a white solid (67.6 mg, 98%).

Synthesised according to General Procedure B using benzyl (4-bromophenyl)carbamate (77 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a white solid (53.0 mg, 77%).

Synthesised according to General Procedure C using 4-bromo nitrobenzene (50 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a white solid (47.6 mg, 69%).

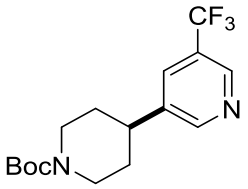
$\upsilon_{max}$ (neat): 3462, 3363, 2985, 2928, 2846, 1667 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 6.99 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 6.64 (d, 2 x ArH, *J* = 8.5 Hz), 4.21 (br. s, 2H, 2 x CH), 3.58 (br. s, 2H, $NH_2$), 2.77 (t, 2H, 2 x CH, *J* = 12.4 Hz), 2.53 (tt, 1H, CH, *J* = 12.1, 3.6 Hz), 1.77 (d, 2H, 2 x CH, *J* = 13.3 Hz), 1.62 – 1.50 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 144.8, 136.2, 127.7, 115.4, 79.5, 44.6, 42.0, 33.6, 28.6.

HRMS ($C_{16}H_{25}O_2N_2$) $[M+H]^+$ requires: 277.1911, observed: 277.1911

**Compound 11e, *tert*-butyl 4-(5-(trifluoromethyl)pyridin-3-yl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 3-bromo-5-(trifluoromethyl)pyridine (57 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (25% EtOAc/PE) to afford the title compound as a yellow oil (61.4 mg, 74%).

$\upsilon_{max}$ (neat): 2981, 2858, 1670, 1498 $cm^{-1}$

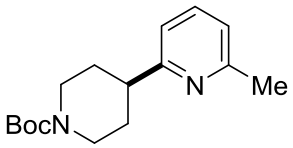
$^1H$ NMR (400 MHz, $CDCl_3$): δ 8.75 (s, 1H, ArH), 8.67 (s, 1H, ArH), 7.73 (s, 1H, ArH), 4.28 (br. s, 2H, 2 x CH), 2.89 – 2.73 (m, 3H, 3 x CH), 1.86 (d, 2H, 2 x CH, *J* = 13.3 Hz), 1.75 – 1.58 (m, 3H, 3 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, Acetone): δ 155.2, 153.8, 145.3 ($^3J_{CF}$, q, *J* = 4.2 Hz) 142.9, 132.2 ($^1J_{CF,}$ q, *J* = 3.3 Hz), 126.9 ($^2J_{CF,}$ app. d, *J* = 32.3 Hz), 125.1 ($^1J_{CF,}$ q, *J* = 272.3 Hz), 79.6, 45.0, 40.8, 33.5, 28.8.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ -62.42.

HRMS ($C_{16}H_{22}F_3O_2N_2$) $[M+H]^+$ requires: 331.1628, observed: 331.1630

**Compound 11f, *tert*-butyl 4-(6-methylpyridin-2-yl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 3-bromo-5-(trifluoromethyl)pyridine (28 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-

dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (40% EtOAc/PE) to afford the title compound as a yellow oil (40.9 mg, 59%).

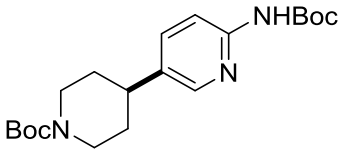
$\upsilon_{max}$ (neat): 2973, 2922, 2852, 1690, $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.50 (t, 1H, ArH, *J* = 7.7 Hz), 6.95 (dd, 2H, 2 x ArH, *J* = 18.4, 7.7 Hz), 4.23 (br. s, 2H, 2 x CH), 2.88 – 2.75 (m, 3H, 3 x CH), 2.52 (s, 3H, $CH_3$), 1.91 (d, 2H, 2 x CH, *J* = 13.4 Hz), 1.66 (qd, 2H, 2 x CH, *J* = 12.7, 4.8 Hz), 1.47 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 164.0, 157.9, 155.0, 136.9, 121.2, 117.5, 79.5, 44.9, 44.2, 32.0, 28.6, 24.7.

HRMS ($C_{16}H_{25}O_2N_2$) $[M+H]^+$ requires: 277.1911, observed: 277.1910

**Compound 11g, *tert*-butyl 4-(6-((tert-butoxycarbonyl)amino)pyridin-3-yl)piperidine-1 carboxylate**




Synthesised according to General Procedure B using *tert*-butyl (5-bromopyridin-2-yl)carbamate (68 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (20% EtOAc/PE) to afford the title compound as a white amorphous solid (70.7 mg, 75%).

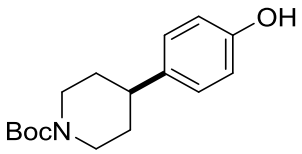
$\upsilon_{max}$ (neat): 3171, 2972, 2858, 1720, 1688 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H, NH), 8.14 (d, 1H, ArH, *J* = 2.2 Hz), 7.89 (d, 1H, ArH, *J* = 8.6 Hz), 7.49 (dd, 1H, ArH, *J* = 8.7, 2.4 Hz), 4.23 (br. s, 2H, 2 x CH), 2.78 (t, 2H, 2 x CH, *J* = 12.2 Hz), 2.60 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.78 (d, 2H, 2 x CH, *J* = 12.8 Hz), 1.67 – 1.53 (m, 2H, 2 x CH), 1.53 (s, 9H, 3 x $CH_3$), 1.47 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 154.9, 152.9, 151.0, 146.2, 136.6, 135.6, 112.5, 80.9, 79.7, 44.3, 39.8, 33.2, 28.6, 28.5.

HRMS ($C_{20}H_{32}N_3O_4$) $[M+H]^+$ requires: 378.2387, observed: 378.2385

**Compound 11h, *tert*-butyl 4-(4-hydroxyphenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 1-(benzyloxy)-4-bromobenzene (66 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-

1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a clear oil (53.0 mg, 77%).

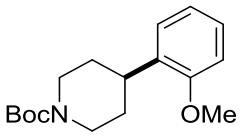
$\upsilon_{max}$ (neat): 3317, 3006, 2974, 2932, 2852, 1660 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.04 (d, 2H, 2 x ArH, *J* = 8.5 Hz), 6.79 (d, 2H, 2 x ArH, *J* = 8.6 Hz), 6.17 (s, 1H, OH), 4.21 (br. s, 2H, 2 x CH), 2.79 (t, 2H, 2 x CH, *J* = 12.0 Hz), 2.56 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.77 (d, 2H, 2 x CH, *J* = 14.0 Hz), 1.62 – 1.50 (m, 2H, 2 x CH), 1.49 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.2, 154.7, 137.7, 127.9, 115.5, 79.9, 44.8, 41.9, 33.6, 28.6.

HRMS ($C_{16}H_{24}NO_3$) $[M+H]^+$ requires: 278.1751, observed: 278.1752

**Compound 11i, *tert*-butyl 4-(2-methoxyphenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 2-bromoanisole (31 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound as a clear oil (71.3 mg, 98%).

$\upsilon_{max}$ (neat): 2999, 1667, 1520, 1403 $cm^{-1}$

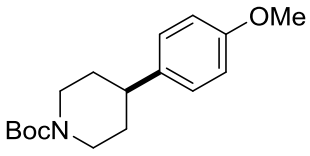
$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.21 – 7.17 (m, 1H, ArH), 7.15 (dd, 1H, ArH, *J* = 7.6, 1.4 Hz), 6.93 (t, 1H, ArH, *J* = 7.5 Hz), 6.86 (d, 1H, ArH, *J* = 8.2 Hz), 4.23 (br. s, 2H, 2 x CH), 3.83 (s, 3H, $OCH_3$), 3.09 (tt, 1H, CH, *J* = 12.1, 3.4 Hz), 2.83 (t, 2H, 2 x CH, *J* = 11.1 Hz), 1.79 (d, 2H, 2 x CH, *J* = 12.8 Hz,), 1.59 (qd, 2H, 2 x CH, *J* = 12.6, 4.0 Hz), 1.49 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 156.9, 155.1, 134.0, 127.2, 126.7, 120.8, 110.5, 79.4, 55.4, 44.9, 35.5, 32.0, 28.6.

HRMS ($C_{17}H_{26}O_3N$) $[M+H]^+$ requires: 292.1907, observed: 292.1909

Consistent with previously reported data.[2]

**Compound 11j, *tert*-butyl 4-(4-methoxyphenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 4-bromoanisole (31 µL, 0.25 mmol, 1 equiv.) and *tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound as a white solid (51.4 mg, 71%).

$\upsilon_{max}$ (neat): 2980, 1671, 1590, 1501 $cm^{-1}$

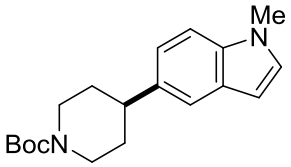
$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 7.12 (d, 2H, 2 x ArH, *J* = 8.6 Hz), 6.85 (d, 2H, 2 x ArH, *J* = 8.7 Hz), 4.23 (br. s, 2H, 2 x CH), 3.79 (s, 3H, $CH_3$), 2.79 (t, 2H, 2 x CH, *J* = 11.2 Hz), 2.59 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.79 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.65 – 1.52 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 158.2, 155.0, 138.2, 127.8, 114.0, 79.5, 55.4, 44.5, 42.0, 33.6, 28.6.

HRMS ($C_{17}H_{26}O_3N$) $[M+H]^+$ requires: 292.1907, observed: 292.1908

Consistent with previously reported data.[2]

**Compound 11k, *tert*-butyl 4-(1-methyl-1H-indol-5-yl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 5-bromo-1-methylindole (53 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound as a clear oil (45.3 mg, 58%).

$\upsilon_{max}$ (neat): 2973, 2928, 2848, 1688, 1422 $cm^{-1}$

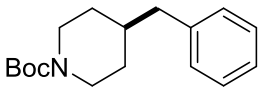
$^{1}H$ NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H, ArH), 7.27 (d, 1H, ArH, *J* = 8.4 Hz), 7.10 (dd, 1H, ArH, *J* = 8.5, 1.5 Hz), 7.04 (d, 1H, ArH, *J* = 3.1 Hz), 6.44 (d, 1H, ArH, *J* = 3.0 Hz), 4.27 (br. s, 2H, 2 x CH), 3.77 (s, 3H, $CH_3$), 2.84 (t, 2H, 2 x CH, *J* = 11.1 Hz), 2.75 (tt, 1H, CH, *J* = 12.1, 3.5 Hz), 1.88 (d, 2H, 2 x CH, *J* = 12.9 Hz), 1.71 (qd, 2H, 2 x CH, *J* = 12.7, 4.0 Hz), 1.51 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.1, 137.1, 135.7, 129.2, 128.8, 121.1, 118.5, 109.3, 100.8, 79.5, 44.7, 43.0, 34.1, 33.0, 28.7.

HRMS ($C_{19}H_{26}O_2N_2$) [M] requires: 314.1994, observed: 314.1986

Consistent with previously reported data.[3]

**Compound 11l, *tert*-butyl 4-benzylpiperidine-1-carboxylate**




Synthesised according to General Procedure B using benzyl bromide (30 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (8% EtOAc/PE) to afford the title compound as a yellow oil (33.0 mg, 48%).

$\upsilon_{max}$ (neat): 3021, 2999, 2939, 1688 $cm^{-1}$

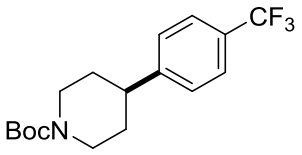
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.24 (m, 2H, 2 x ArH), 7.23 – 7.16 (m, 1H, ArH), 7.16 – 7.11 (m, 2H, 2 x ArH), 4.06 (br. s, 2H, 2 x CH), 2.63 (t, 2H, 2 x CH, *J* = 12.4 Hz), 2.53 (d, 2H, $CH_2$, *J* = 7.0 Hz), 1.69 – 1.57 (m, 3H, 3 x CH), 1.45 (s, 9H, 3 x $CH_3$), 1.21 – 1.08 (m, 2H, 2 x CH).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 155.0, 140.4, 129.3, 128.4, 126.1, 79.4, 44.1, 43.3, 38.3, 32.1, 28.6.

HRMS ($C_{13}H_{18}ON$) $[M\text{-}^{t}Bu+H]^+$ requires: 220.1338, observed: 220.1337

Consistent with previously reported data.[4]

**Compound 11m, *tert*-butyl 4-(4-(trifluoromethyl)phenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 4-bromobenzotrifluoride (36 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (10% EtOAc/PE) to afford the title compound as a yellow oil (70.0 mg, 85%).

Synthesised according to General Procedure C using 4-bromobenzotrifluoride (36 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (6% EtOAc/PE) to afford the title compound as a yellow oil (57.6 mg, 70%).

$\upsilon_{max}$ (neat): 3005, 2931, 2849, 1655 $cm^{-1}$

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 7.31 (d, 2H, 2 x ArH, *J* = 8.1 Hz), 4.26 (br. s, 2H, 2 x CH), 2.81 (t, 2H, 2 x CH, *J* = 11.4 Hz), 2.71 (tt, 1H, CH, *J* = 12.2, 3.5 Hz), 1.82 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.62 (qd, 2H, 2 x CH, *J* = 12.6, 4.1 Hz), 1.48 (s, 9H, 3 x $CH_3$).

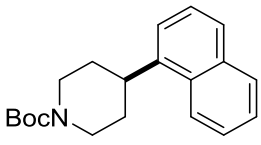
$^{13}$C NMR (126 MHz, $CDCl_3$): δ 155.0, 149.9, 128.9 ($^{2}J_{CF}$, q, *J* = 32.3 Hz), 127.3, 125.6 ($^{3}J_{CF}$, q, *J* = 3.6 Hz), 124.3 ($^{1}J_{CF}$, q, *J* = 218.2 Hz), 79.7, 44.4, 42.8, 33.1, 28.6.

$^{19}$F NMR (471 MHz, $CDCl_3$): δ -62.4.

HRMS ($C_{17}H_{23}F_3NO_2$) $[M+H]^+$ requires: 330.1675, observed: 330.1678

Consistent with previously reported data.[5]

**Compound 11n, *tert*-butyl 4-(naphthalen-1-yl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 1-bromonapthalene (52 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-

carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (10% EtOAc/PE) to afford the title compound as a yellow oil (45.9 mg, 59%).

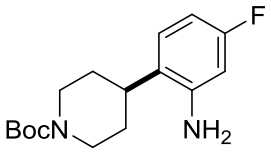
$\upsilon_{max}$ (neat): 2982, 2965, 2924, 2835, 1695 $cm^{-1}$

$^{1}H$ NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 3H, 3 x ArH), 7.64 (s, 1H, ArH), 7.49 – 7.41 (m, 2H, 2 x ArH), 7.36 (dd, 1H, ArH, *J* = 8.5, 1.7 Hz), 4.30 (br. s, 2H, 2 x CH), 2.93 – 2.76 (m, 3H, 3 x CH), 1.92 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.74 (qd, 2H, 2 x CH, *J* = 12.7, 4.1 Hz), 1.51 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 143.4, 133.7, 132.4, 128.2, 127.8, 127.7, 126.1, 125.9, 125.5, 124.9, 79.6, 44.6, 42.9, 33.3, 28.6.

HRMS ($C_{20}H_{26}NO_2$) $[M+H]^+$ requires: 312.1958, observed: 312.1958

**Compound 11o, *tert*-butyl 4-(2-amino-4-fluorophenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 2-bromo-5-fluoroaniline (48 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (35% EtOAc/PE) to afford the title compound as a yellow oil (58.1 mg, 79%).

$\upsilon_{max}$ (neat): 3460, 3363, 2930, 2850, 1673 $cm^{-1}$

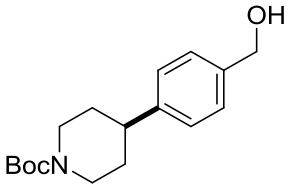
$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 6.98 (dd, 1H, ArH, *J* = 8.6, 6.4 Hz), 6.46 (td, 1H, ArH, *J* = 8.5, 2.6 Hz), 6.39 (dd, 1H, ArH, *J* = 10.5, 2.6 Hz), 4.25 (br. s, 2H, 2 x CH), 2.80 (t, 2H, 2 x CH, *J* = 12.4 Hz), 2.53 (tt, 1H, CH, *J* = 11.9, 3.2 Hz), 1.82 (d, 2H, 2 x CH, *J* = 13.3 Hz), 1.62 – 1.51 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$). 2H not observed (exchangeable).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 162.1 ($^{1}J_{CF}$, d, *J* = 242.5 Hz), 155.0, 145.0 ($^{3}J_{CF}$, d, *J* = 10.5 Hz), 127.4 ($^{3}J_{CF}$, d, *J* = 10.1 Hz), 125.4, 105.6 ($^{2}J_{CF}$, d, *J* = 21.1 Hz), 102.8 ($^{2}J_{CF}$, d, *J* = 24.4 Hz), 79.7, 44.7, 36.5, 31.8, 28.6, 25.0.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ -116.7.

HRMS ($C_{16}H_{24}FO_2N_2$) $[M+H]^+$ requires: 295.1816, observed: 295.1819

**Compound 11p, *tert*-butyl 4-(4-(hydroxymethyl)phenyl)piperidine-1-carboxylate**



Synthesised according to General Procedure B using 4-bromobenzyl alcohol (47 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a yellow oil (50.1 mg, 69%).

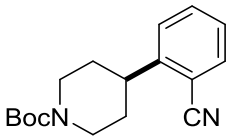
$\upsilon_{max}$ (neat): 3442, 3014, 2910, 2851, 1666 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.31 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 7.19 (d, 2H, 2 x ArH, *J* = 8.1 Hz), 4.66 (s, 2H, $CH_2$), 4.22 (br. s, 2H, 2 x CH), 2.79 (t, 2H, 2 x CH, *J* = 12.2 Hz), 2.64 (tt, 1H, CH, *J* = 12.1, 3.6 Hz), 1.89 (br. s, 1H, OH), 1.80 (d, 2H, 2 x CH, *J* = 13.5 Hz), 1.60 (qd, 2H, 2 x CH, *J* = 12.7, 4.4 Hz), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 145.4, 139.2, 127.4, 127.1, 79.6, 65.2, 44.5, 42.6, 33.3, 28.6.

HRMS ($C_{17}H_{26}O_3N$) $[M+H]^+$ requires: 292.1907, observed: 292.1909

**Compound 11q, *tert*-butyl 4-(2-cyanophenyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 2-bromobenzonitrile (46 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound as a yellow oil (54.0 mg, 76%).

$\upsilon_{max}$ (neat): 2999, 2923, 2222, 1681 $cm^{-1}$

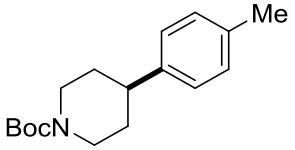
$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.63 (dd, 1H, ArH, J = 7.7, 1.0 Hz), 7.55 (td, 1H, ArH, J = 7.8, 1.2 Hz), 7.31 (ddd, 2H, 2 x ArH, J = 9.2, 8.5, 4.4 Hz), 4.27 (br. s, 2H, 2 x CH), 3.13 (tt, 1H, CH, J = 12.1, 3.5 Hz), 2.87 (br. s, 2H, 2 x CH), 1.86 (d, 2H, 2 x CH, *J* = 13.1 Hz), 1.71 – 1.57 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (126 MHz, $CDCl_3$): δ 154.8, 149.2, 133.1, 133.1, 126.9, 126.5, 117.9, 112.0, 79.6, 44.1, 40.9, 32.4, 28.5.

HRMS ($C_{17}H_{23}O_2N_2$) $[M+H]^+$ requires: 287.1754, observed: 287.1755

Consistent with previously reported data.[6]

**Compound 11r, *tert*-butyl 4-(p-tolyl)piperidine-1-carboxylate**




Synthesised according to General Procedure B using 4-bromotoluene (31µL, 0.25 mmol, 1 equiv.) and *tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.). The crude material was taken up in ethyl acetate and

washed with water (2 x 10 mL) and brine (10 mL), dried with $Na_2SO_4$ and concentrated *in vacuo* to afford the title compound as a clear oil (68.0 mg, 99%).

Synthesised according to General Procedure C using 4-bromobenzotrifluoride (36 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (5% EtOAc/PE) to afford the title compound as a yellow oil (67.6 mg, 99%).

$\upsilon_{max}$ (neat): 2971, 2926, 2848, 1688 $cm^{-1}$

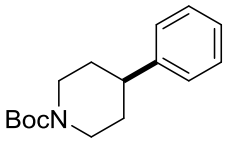
$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.13 – 7.09 (m, 4H, 4 x ArH), 4.24 (br. s, 2H), 2.79 (t, 2H, 2 x CH, *J* = 11.4 Hz), 2.60 (tt, 1H, *J* = 12.1, 3.5 Hz), 2.32 (s, 3H, $CH_3$), 1.80 (d, 2H, 2 x CH, *J* = 13.1 Hz), 1.69 – 1.55 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 143.0, 136.0, 129.3, 126.8, 79.5, 44.6, 42.4, 33.4, 28.6, 21.1.

HRMS ($C_{17}H_{26}O_2N$) $[M+H]^+$ requires: 276.1958, observed: 276.1958

Consistent with previously reported data.[5]

**Compound 11s, *tert*-butyl 4-phenylpiperidine-1-carboxylate**




Synthesised according to General Procedure B using bromobenzene (26 µL, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (10% EtOAc/PE) to afford the title compound as a yellow oil (61.3 mg, 94%).

$\upsilon_{max}$ (neat): 2945, 2843, 1667, $cm^{-1}$

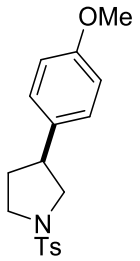
$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H, 2 x ArH), 7.24 – 7.18 (m, 3H, 3 x ArH), 4.24 (br. s, 2H, $CH_2$), 2.80 (t, 2H, *J* = 12.4 Hz, 2 x CH), 2.64 (tt, 1H, CH, *J* = 12.2, 3.6 Hz), 1.83 (d, 2H, 2 x CH, *J* = 13.3 Hz), 1.63 (qd, 2H, 2 x CH, *J* = 12.8, 4.3 Hz), 1.49 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 155.0, 145.9, 128.6, 126.9, 126.5, 79.5, 44.6, 42.9, 33.3, 28.6.

HRMS ($C_{16}H_{23}O_2NNa$) $[M+Na]^+$ requires: 284.1621, observed: 284.1621

Consistent with previously reported data.[7]

**Compound 12a, 3-(4-methoxyphenyl)-1-tosylpyrrolidine**




Synthesised according to General Procedure B using 3-bromo-1-tosyl-2,5-dihydro-1*H*-pyrrole (75 mg, 0.25 mmol, 1 equiv.) and 4-methoxyphenyl boronic acid (38 mg, 0.25 mmol, 1 eq.) and purified by flash column chromatography (7% EtOAc/PE) to afford the title compound an off-white amorphous solid (65.3mg, 79%).

$\upsilon_{max}$ (neat): 2930, 2815, 1523, 1493 $cm^{-1}$

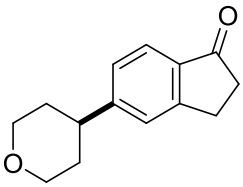
$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 7.74 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 7.34 (d, 2H, 2 x ArH, *J* = 8.0 Hz), 7.01 (d, 2H, 2 x ArH, *J* = 8.6 Hz), 6.80 (d, 2H, 2 x ArH, *J* = 8.7 Hz), 3.77 (s, 3H, $CH_3$), 3.69 (dd, 1H, CH, *J* = 8.8, 6.8 Hz), 3.51 (ddd, 1H, CH, *J* = 10.0, 8.5, 3.1 Hz), 3.34 (td, 1H, CH, *J* = 9.5, 7.0 Hz), 3.22 – 3.11 (m, 2H, 2 x CH), 2.45 (s, 3H, $CH_3$), 2.20 – 2.12 (m, 1H, CH), 1.87 – 1.76 (m, 1H, CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 158.7, 143.6, 134.2, 129.8, 128.0, 127.7, 114.2, 55.4, 54.4, 47.9, 43.3, 33.2, 21.7. (1C not observed).

HRMS ($C_{18}H_{22}NO_3S$) $[M+H]^+$ requires: 332.1315, observed: 332.1317

Consistent with previously reported data.[8]

**Compound 12b, 5-(tetrahydro-2*H*-pyran-4-yl)pyridin-2-amine**




Synthesised according to General Procedure B using 5-bromo-1-indanone (53 mg, 0.25 mmol, 1 equiv.) and 3,6-dihydro-2*H*-pyran-4-boronic acid pinacol ester (53 mg, 0.25 mmol, 1 eq.) and purified by flash column chromatography (25% EtOAc/PE) to afford the title compound an off-white amorphous solid (43.2mg, 80%).

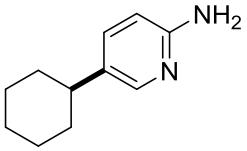
$\upsilon_{max}$ (neat): 2949, 2930, 2846, 1701, 1610 $cm^{-1}$

$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 7.70 (d, 1H, ArH, *J* = 8.2 Hz), 7.34 – 7.31 (m, 1H, ArH), 7.24 (ddd, 1H, ArH, *J* = 7.9, 1.4, 0.6 Hz), 4.12 – 4.07 (m, 2H, 2 x CH), 3.54 (td, 2H, 2 x CH, *J* = 11.7, 2.4 Hz), 3.14 – 3.10 (m, 2H, $CH_2$), 2.85 (tt, 1H, CH, *J* = 11.8, 4.1 Hz), 2.70 – 2.66 (m, 2H, 2 x CH), 1.89 – 1.75 (m, 4H, 2 x $CH_2$).

$^{13}C$ NMR (126 MHz, $CDCl_3$): δ 206.6, 156.0, 153.4, 135.8, 126.7, 124.8, 124.0, 68.3, 42.3, 36.6, 33.8, 25.9.

HRMS ($C_{14}H_{17}O_2$) $[M+H]^+$ requires: 217.1229, observed: 217.1233

**Compound 12c, 5-cyclohexylpyridin-2-amine**




Synthesised according to General Procedure B using 5-bromo-2-nitropyridine (51 mg, 0.25 mmol, 1 equiv.) and 1-cyclohexen-yl-boronic acid pinacol ester (52 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (80% PE/EtOAc) to afford the title compound an off-white amorphous solid (39.4 mg, 90%).

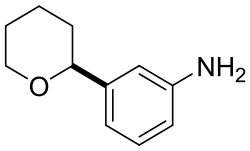
$\upsilon_{max}$ (neat): 3441, 3304, 3144, 2918, 2847, 1639, 1505 $cm^{-1}$

$^1$H NMR (600 MHz, acetone-$d_6$) δ 7.82 (d, 1H, ArH, *J* = 1.8 Hz), 7.27 (dd, 1H, ArH, *J* = 8.4, 2.3 Hz), 6.47 (d, 1H, ArH, *J* = 8.4 Hz), 5.11 (br. s, 2H, $NH_2$), 2.40 – 2.33 (m, 1H, CH), 1.84 – 1.74 (m, 4H, 4 x CH), 1.74 – 1.68 (m, 1H, CH), 1.41 – 1.35 (m, 4H, 4 x CH), 1.28 – 1.22 (m, 1H, CH).

$^{13}$C NMR (151 MHz, acetone-$d_6$): δ 159.1, 147.0, 136.4, 132.5, 108.7, 42.0, 35.3, 27.6, 26.7.

HRMS ($C_{11}H_{17}N_2$) $[M+H]^+$ requires: 177.1383, observed: 177.1386

**Compound 12d, 3-(tetrahydro-2*H*-pyran-2-yl)aniline**




Synthesised according to General Procedure B using 2-(3,4-dihydro-2*H*-pyran-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (53 mg, 0.25 mmol, 1 equiv.) and 3-nitrobromobenzene (50 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (30% EtOAc/PE) to afford the title compound as a clear oil (24.0 mg, 55%).

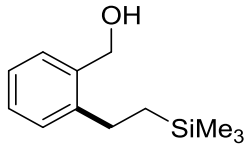
$\upsilon_{max}$ (neat): 3390, 3313, 3067, 2993, 2961, 2806, 1645, 1501 $cm^{-1}$

$^1$H NMR (500 MHz, $CDCl_3$): δ 7.11 (t, 1H, ArH, *J* = 7.9 Hz), 6.74 – 6.69 (m, 2H, 2 x ArH), 6.58 (dd, 1H, ArH, *J* = 7.9, 1.4 Hz), 4.24 (dd, 1H, CH, *J* = 10.7, 1.9 Hz), 4.17 – 4.09 (m, 1H, CH), 3.60 (td, 1H, CH, *J* = 11.7, 2.4 Hz), 1.96 – 1.90 (m, 1H, CH), 1.84 – 1.78 (m, 1H, CH), 1.71 – 1.55 (m, 4H, 4 x CH).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 146.5, 144.8, 129.3, 116.4, 114.3, 112.7, 80.3, 69.1, 34.1, 26.1, 24.2.

HRMS ($C_{11}H_{16}ON$) $[M+H]^+$ requires: 178.1226, observed: 178.1223

**Compound 12e, (2-(2-(trimethylsilyl)ethyl)phenyl)methanol**




Synthesised according to General Procedure B using (2-(hydroxymethyl)phenyl)boronic acid (38 mg, 0.25 mmol, 1 equiv.) and (E)-(2-bromovinyl)trimethylsilane (45 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (15% PE/EtOAc) to afford the title compound a clear oil (33.6 mg, 65%).

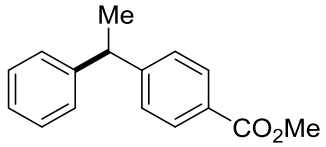
$\upsilon_{max}$ (neat): 3290 (br.), 2948, 2891, 1247 $cm^{-1}$

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.39 (d, 1H. ArH, *J* = 7.3 Hz), 7.29 – 7.19 (m, 3H, 3 x ArH), 4.74 (s, 2H, $CH_2$), 2.73 – 2.65 (m, 2H, $CH_2$), 0.89 – 0.82 (m, 2H, $CH_2$), 0.08 (s, 9H, 3 x $CH_3$) (1H not observed, exchangeable).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 143.6, 137.9, 128.8, 128.2, 126.1, 63.1, 26.5, 18.9, -1.7 (1C not observed).

HRMS ($C_{12}H_{21}OSi$) $[M-H]^-$ requires: 207.1205, observed: 207.1207

**Compound 12f, methyl 4-(1-phenylethyl)benzoate**




Synthesised according to General Procedure B using α-bromostyrene (36 µL, 0.25 mmol, 1 equiv.) and 4-methoxycarbonylphenylboronic acid (45 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound as a clear oil (49 mg, 82%).

$\upsilon_{max}$ (neat): 2920, 2852, 1719 $cm^{-1}$

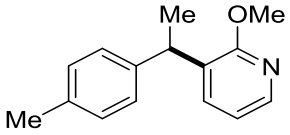
$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.98 – 7.93 (m, 2H, 2 x ArH), 7.32 – 7.27 (m, 4H, 4 x ArH), 7.23 – 7.17 (m, 3H, 3 x ArH), 4.20 (q, 1H, CH, *J* = 7.2 Hz), 3.89 (s, 3H, $CH_3$), 1.66 (d, 3H, $CH_3$, *J* = 7.2 Hz)

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 167.2, 151.9, 129.9, 128.7, 127.8, 127.8, 126.5, 52.1, 45.0, 21.7 (2C not observed).

HRMS ($C_{16}H_{17}O_2$) $[M+H]^+$ requires: 241.1223, observed: 241.1223

Consistent with previously reported data.[9]

**Compound 12g, 2-methoxy-3-(1-(*p*-tolyl)ethyl)pyridine**




Synthesised according to General Procedure B using 1-(1-bromovinyl)-4-methylbenzene (49 mg, 0.25 mmol, 1 equiv.) and (2-methoxypyridin-3-yl)boronic acid (38 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (6% EtOAc/PE) to afford the title compound as a clear oil (34.0 mg, 60%).

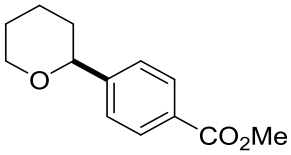
$\upsilon_{max}$ (neat): 3421, 2928, 1703, 1409, 1323 $cm^{-1}$

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, 1H, ArH, *J* = 5.0, 1.9 Hz), 7.37 (ddd, 1H, ArH, *J* = 7.3, 1.8, 0.5 Hz), 7.11 (app. q, 4H, 4 x ArH, *J* = 8.3 Hz), 6.81 (dd, 1H, ArH, *J* = 7.3, 5.0 Hz), 4.40 (q, 1H, CH, *J* = 7.2 Hz), 3.93 (s, 3H, $CH_3$), 2.31 (s, 3H, $CH_3$), 1.55 (d, 3H, $CH_3$, *J* = 7.2 Hz).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 161.6, 144.3, 142.2, 135.8, 135.7, 129.5, 129.1, 127.7, 116.9, 53.5, 37.4, 21.1, 20.6.

HRMS ($C_{15}H_{18}ON$) $[M+H]^+$ requires: 228.1383, observed: 228.1382

**Compound 12h, methyl 4-(tetrahydro-2H-pyran-2-yl)benzoate**




Synthesised according to General Procedure B using 2-(3,4-dihydro-2H-pyran-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (53 mg, 0.25 mmol, 1 equiv.) and methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (12% EtOAc/PE) to afford the title compound as a clear oil (32.5 mg, 59%).

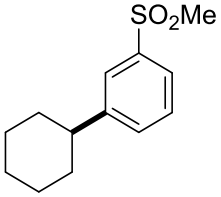
$\upsilon_{max}$ (neat): 2937, 2844, 1714, 1610, 1437 $cm^{-1}$

$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 8.00 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.41 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 4.38 (dd, 1H, CH, *J* = 11.1, 2.0 Hz), 4.18 – 4.13 (m, 1H, CH), 3.90 (s, 3H, $CH_3$), 3.62 (td, 1H, CH, *J* = 11.6, 2.5 Hz), 1.98 – 1.91 (m, 1H, CH), 1.85 (d, 1H, CH, *J* = 13.2 Hz), 1.73 – 1.65 (m, 2H, 2 x CH), 1.62 – 1.51 (m, 2H, 2 x CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 167.2, 148.7, 129.8, 129.1, 125.8, 79.7, 69.1, 52.2, 34.3, 25.9, 24.0.

HRMS ($C_{13}H_{17}O_3$) $[M+H]^+$ requires: 221.1178, observed: 221.1183

**Compound 12i, 1-cyclohexyl-3-(methylsulfonyl)benzene**



Synthesised according to General Procedure B using 4-bromophenyl methyl sulfone (59 mg, 0.25 mmol, 1 equiv.) and 1-cyclohexen-yl-boronic acid pinacol ester (52 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (30% PE/EtOAc) to afford the title compound an off-white solid (48.2 mg, 81%).

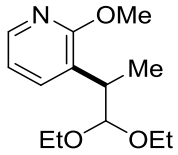
$\upsilon_{max}$ (neat): 2921, 2848, 1597, 1297, 1143 $cm^{-1}$

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.77 (s, 1H, ArH), 7.74 (dt, 1H, ArH, *J* = 6.4, 2.1 Hz), 7.50 – 7.44 (m, 2H, 2 x ArH), 3.04 (s, 3H, $CH_3$), 2.60 (ddd, 1H, CH, *J* = 11.8, 7.4, 3.2 Hz), 1.92 – 1.82 (m, 4H, 4 x CH), 1.80 – 1.72 (m, 1H, CH), 1.49 – 1.36 (m, 4H, 4 x CH), 1.31 – 1.23 (m, 1H, CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 149.9, 140.6, 132.5, 129.4, 125.7, 124.9, 44.7, 44.6, 34.3, 26.8, 26.0.

HRMS ($C_{13}H_{19}O_2S$) $[M+H]^+$ requires: 239.1106, observed: 239.1107

**Compound 12j, 3-(1,1-diethoxypropan-2-yl)-2-methoxypyridine**




Synthesised according to General Procedure B using 2-bromopropenal diethyl acetal (42 µL, 0.25 mmol, 1 equiv.) and 2-methoxy-3-pyridinylboronic acid (38 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (10% EtOAc/PE) to afford the title compound a colourless oil (32.4 mg, 54%).

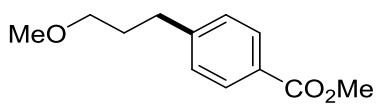
$\upsilon_{max}$ (neat): 2973, 2876, 1584, 1461, 1413 $cm^{-1}$

$^1H$ NMR (500 MHz, $CDCl_3$): δ 8.02 (dd, 1H, ArH, *J* = 5.0, 1.8 Hz), 7.51 (dd, 1H, ArH, *J* = 7.3, 1.8 Hz), 6.83 (dd, 1H, ArH, *J* = 7.3, 5.0 Hz), 4.60 (d, 1H, CH, *J* = 5.8 Hz), 3.95 (s, 3H, $CH_3$), 3.69 (dq, 1H, CH, *J* = 9.3, 7.0 Hz), 3.58 (dq, 1H, CH, *J* = 9.4, 7.0 Hz), 3.48 – 3.38 (m, 2H, 2 x CH), 3.38 – 3.31 (m, 1H, CH), 1.25 (d, 3H, $CH_3$, *J* = 7.1 Hz), 1.14 (t, 3H, $CH_3$, *J* = 7.0 Hz), 1.08 (t, 3H, $CH_3$, *J* = 7.0 Hz).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 161.8, 144.4, 137.3, 125.9, 116.9, 105.2, 63.3, 62.4, 53.4, 37.1, 15.3, 14.6.

HRMS ($C_{13}H_{22}O_3N$) $[M+H]^+$ requires: 240.1594, observed: 240.1592

**Compound 12k, methyl 4-(3-methoxypropyl)benzoate**




Synthesised according to General Procedure B using using methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.) and *trans*-3-methoxy-1-propenylboronic acid pinacol ester (50 mg, 0.25 mmol, 1

equiv.), and purified by flash column chromatography (15% EtOAc/PE) to afford the title compound an yellow oil (30.6 mg, 59%).

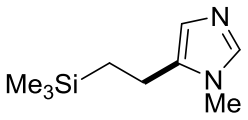
$\upsilon_{max}$ (neat): 2973, 2922, 1690, 1167 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.95 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.25 (d, 2H, 2 x ArH, *J* = 8.4 Hz), 3.90 (s, 3H, $CH_3$), 3.37 (t, 2H, 2 x CH, *J* = 6.3 Hz), 3.34 (s, 3H, $CH_3$, *J* = 2.6 Hz), 2.78 – 2.70 (m, 2H, 2 x CH), 1.94 – 1.86 (m, 2H, 2 x CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 167.3, 147.7, 129.9, 128.6, 128.0, 71.8, 58.7, 52.1, 32.5, 31.0.

HRMS ($C_{12}H_{17}O_3$) $[M+H]^+$ requires: 209.1178, observed: 209.1181

**Compound 12l, 1-methyl-5-(2-(trimethylsilyl)ethyl)-1*H*-imidazole**




Synthesised according to General Procedure B using (2-bromovinyl)trimethylsilane (45 mg, 0.25 mmol, 1 equiv.) 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-imidazole (52 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (7% PE/EtOAc) to afford the title compound an off-white solid (32.1mg, 71%).

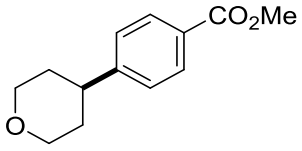
$\upsilon_{max}$ (neat): 2921, 2850, 1736 $cm^{-1}$

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.36 (d, 1H, ArH, *J* = 1.8 Hz), 6.02 (d, 1H, ArH, *J* = 1.7 Hz), 3.77 (s, 3H, $CH_3$), 2.60 – 2.54 (m, 2H, $CH_2$), 0.90 – 0.84 (m, 2H, $CH_2$), 0.04 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 145.4, 138.1, 103.8, 36.1, 20.2, 15.6, -1.7.

HRMS ($C_9H_{19}N_2Si$) $[M+H]^+$ requires: 183.1318, observed: 183.1321

**Compound 12m, methyl 4-(tetrahydro-2*H*-pyran-4-yl)benzoate**




Synthesised according to General Procedure B using methyl 4-bromobenzoate (54 mg, 0.25 mmol, 1 equiv.) and MeOH (1 mL) and purified by flash column chromatography (25% EtOAc/PE) to afford the title compound as an off white amorphous solid (47.3 mg, 86%).

$\upsilon_{max}$ (neat): 3099, 2983, 2799, 1744 $cm^{-1}$

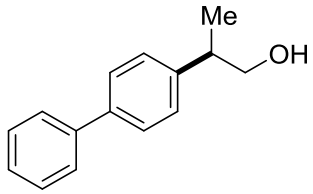
$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.98 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.29 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 4.09 (dd, 2H, 2 x CH, *J* = 11.2, 3.9 Hz), 3.90 (s, 3H, $CH_3$), 3.53 (td, 2H, 2 x CH, *J* = 11.6, 2.3 Hz), 2.82 (tt, 1H, CH, *J* = 11.7, 4.1 Hz), 1.87 – 1.85 (m, 4H, 2 x $CH_2$).

$^{13}$C NMR (151 MHz, $CDCl_3$): δ 167.1, 151.2, 130.0, 128.4, 126.9, 68.3, 52.1, 41.8, 33.7.

HRMS ($C_{13}H_{16}O_3Na$) $[M+Na]^+$ requires: 243.0993, observed: 243.0992

Consistent with previously reported data.[1]

**Compound 12n, 2-([1,1'-biphenyl]-4-yl)propan-1-ol**




Synthesised according to General Procedure B using 2-bromoallyl alcohol (22 µL, 0.25 mmol, 1 equiv.) and 4-biphenylboronic acid (50 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (70% EtOAc/PE) to afford the title compound a clear oil (39 mg, 73%).

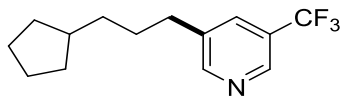
$\upsilon_{max}$ (neat): 3301, 3060, 2902, 1491 $cm^{-1}$

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.61 – 7.54 (m, 4H, 4 x ArH), 7.48 – 7.40 (m, 2H, 2 x ArH), 7.37 – 7.29 (m, 3H, 3 x ArH), 3.76 (d, 2H, $CH_2$, $J$ = 6.8 Hz), 3.06 – 2.96 (m, 1H, CH), 1.40 (s, 1H, OH), 1.33 (d, 3H, $CH_3$ $J$ = 7.0 Hz).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 142.9, 141.1, 139.8, 128.9, 128.1, 127.5, 127.3, 127.2, 68.8, 42.3, 17.7.

HRMS ($C_{15}H_{20}ON$) $[M+NH_4]^+$ requires: 230.1540, observed: 230.1539

**Compound 12o, 3-(3-cyclopentylpropyl)-5-(trifluoromethyl)pyridine**




Synthesised according to General Procedure B using using 3-bromo-5-(trifluoromethyl)pyridine (57 mg, 0.25 mmol, 1 equiv.) and (*E*)-2-(3-cyclopentylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (59 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (8% EtOAc/PE) to afford the title compound an yellow oil (33.6 mg, 52%).

$\upsilon_{max}$ (neat): 2941, 2861, 1338, 1132 $cm^{-1}$

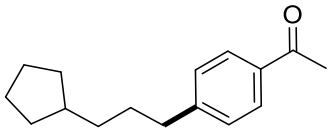
$^1$H NMR (400 MHz, $CDCl_3$): δ 8.71 (s, 1H, ArH), 8.63 (s, 1H, ArH), 7.71 (s, 1H, ArH), 2.71 – 2.65 (m, 2H, 2 x CH), 1.78 – 1.74 (m, 2H, 2 x CH), 1.72 – 1.62 (m, 3H, 3 x CH), 1.62 – 1.54 (m, 2H, 2 x CH), 1.54 – 1.45 (m, 2H, 2 x CH), 1.40 – 1.31 (m, 2H, 2 x CH), 1.13 – 0.99 (m, 2H, 2 x CH).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 153.3, 144.1 ($^3J_{CF}$, q, $J$ = 4.0 Hz), 138.4, 132.7 ($^3J_{CF}$, q, $J$ = 3.7 Hz), 123.8 ($^1J_{CF}$, q, $J$ = 247.3 Hz), 40.0, 35.8, 33.2, 32.8, 30.2, 25.3 (1C not observed).

$^{19}$F NMR (471 MHz, $CDCl_3$): δ -62.43.

HRMS ($C_{14}H_{19}F_3N$) $[M+H]^+$ requires: 258.1470, observed: 258.1466

**Compound 12p, 1-(4-(3-cyclopentylpropyl)phenyl)ethan-1-one**



Synthesised according to General Procedure B using (E)-2-(3-cyclopentylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (59 mg, 0.25 mmol, 1 equiv.) and 4 bromoacetophenone (50 mg, 0.25 mmol, 1 equiv.) and purified by flash column chromatography (8% EtOAc/PE) to afford the title compound as a clear oil (28.5 mg, 60%).

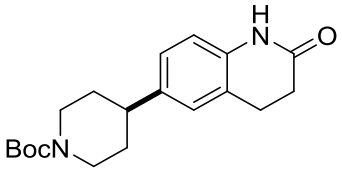
$\upsilon_{max}$ (neat): 2934, 2855, 1680, 1606, 1266 $cm^{-1}$

$^1H$ NMR (500 MHz, $CDCl_3$) δ 7.85 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.24 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 2.67 – 2.60 (m, 2H, 2 x CH), 2.55 (s, 3H, $CH_3$), 1.73 – 1.68 (m, 2H, 2 x CH), 1.65 – 1.59 (m, 2H, 2 x CH), 1.58 – 1.52 (m, 2H, 2 x CH), 1.50 – 1.42 (m, 2H, 2 x CH), 1.34 – 1.28 (m, 2H, 2 x CH), 1.24 – 1.20 (m, 1H, CH), 1.07 – 1.00 (m, 2H, 2 x CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 198.0, 149.0, 135.1, 128.7, 128.6, 127.4, 40.1, 36.4, 35.9, 32.8, 30.4, 26.7, 25.3.

HRMS ($C_{16}H_{22}O$) [M] requires: 230.1671, observed: 230.1670

**Compound 12q, *tert*-butyl 4-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)piperidine-1-carboxylate**



Synthesised according to General Procedure B using ethyl 3-(5-bromo-2-nitrophenyl)acrylate (75 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (60% EtOAc/PE) to afford the title compound as a white solid (65.9 mg, 80%).

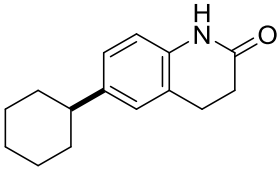
$\upsilon_{max}$ (neat): 3066, 2944, 1683, 1670 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H, NH), 7.03 – 6.96 (m, 2H, 2 x ArH), 6.73 (d, 1H, ArH, *J* = 8.7 Hz), 4.22 (br. s, 2H, 2 x CH), 2.97 – 2.91 (m, 2H, 2 x CH), 2.78 (t, 2H, 2 x CH, *J* = 12.3 Hz), 2.66 – 2.53 (m, 3H, 3 x CH), 1.79 (d, 2H, 2 x CH, *J* = 13.0 Hz), 1.58 (ddd, 2H, 2 x CH, *J* = 25.4, 12.8, 4.3 Hz), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 171.8, 155.0, 141.0, 135.7, 126.5, 125.9, 123.9, 115.6, 79.6, 44.5, 42.3, 33.5, 30.9, 28.6, 25.6.

HRMS ($C_{19}H_{27}O_3N_2$) $[M+H]^+$ requires: 331.2016, observed: 331.2018

**Compound 12r, 6-cyclohexyl-3,4-dihydroquinolin-2(1H)-one**




Synthesised according to General Procedure B using 1-cyclohexen-yl-boronic acid pinacol ester (52 mg, 0.25 mmol, 1 equiv.) and ethyl (E)-3-(5-bromo-2-nitrophenyl)acrylate (75 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (50% EtOAc/PE) to afford the title compound an off-white amorphous solid (40.5 mg, 71%).

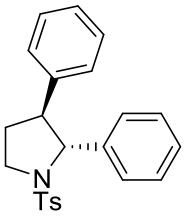
$\upsilon_{max}$ (neat): 3052, 2921, 2834, 1694 $cm^{-1}$

$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 8.60 (s, 1H, NH), 7.01 (d, 2H, 2 x ArH, *J* = 6.9 Hz), 6.73 (d, 1H, ArH, *J* = 8.6 Hz), 2.94 (t, 2H, 2 x CH, *J* = 7.6 Hz), 2.65 – 2.60 (t, 2H, 2 x CH, *J* = 7.6 Hz), 2.48 – 2.40 (m, 1H, CH), 1.89 – 1.79 (m, 4H, 4 x CH), 1.74 (d, 1H, CH, *J* = 13.1 Hz), 1.44 – 1.32 (m, 4H, 4 x CH), 1.30 – 1.18 (m, 1H, CH).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 172.0, 143.3, 135.2, 126.5, 125.9, 123.6, 115.4, 44.1, 34.7, 31.0, 27.0, 26.3, 25.7.

HRMS ($C_{15}H_{20}NO$) $[M+H]^+$ requires: 230.1539, observed: 230.1538

**Compound 12s, (2*R*,3*S*)-2,3-diphenyl-1-tosylpyrrolidine (12:1, *trans:cis*)**




Synthesised according to General Procedure B using phenyl boronic acid (31 mg, 0.25 mmol, 1 equiv.) and (*S*)-3-bromo-2-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole (95 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (14% EtOAc/PE) to afford the title compound an off-white amorphous solid (66.0 mg, 70%).

$\upsilon_{max}$ (neat): 3002, 2990, 2713, 1515, $cm^{-1}$

$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 7.70 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 7.29 (d, 2H, 2 x ArH, *J* = 8.2 Hz), 7.10 – 6.99 (m, 6H, 6 x ArH), 6.74 (d, 2H, 2 x ArH, *J* = 7.2 Hz), 6.65 (d, 2H, 2 x ArH, *J* = 6.6 Hz), 5.03 (d, 1H, CH, *J* = 8.1 Hz), 3.87 (t, 1H, CH, *J* = 8.7 Hz), 3.52 (ddd, 1H, CH, *J* = 10.9, 9.6, 6.6 Hz), 3.29 (ddd, 1H, CH, *J* = 13.6, 8.0, 5.7 Hz), 2.44 (s, 3H, $CH_3$), 2.41 – 2.34 (m, 1H, CH), 2.06 (dt, 1H, CH, *J* = 12.3, 6.1 Hz).

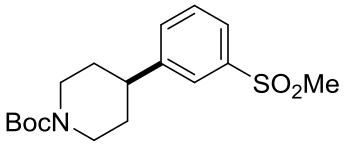
$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 143.5, 138.8, 137.0, 135.5, 129.7, 128.6, 128.0, 127.6, 127.6, 127.5, 127.0, 67.2, 50.6, 48.0, 27.8, 21.7.

*cis* isomer observed in $^{1}H$ and $^{13}C$ NMR but not reported. Diastereomeric ratio determined by $^{1}H$ NMR, ratio between doublet at 5.03 and 4.65.

HRMS ($C_{23}H_{24}O_2NS$) $[M+H]^+$ requires: 378.1522, observed: 378.1522

ee = >97% (by chiral HPLC)

**Compound 13, 4-(3-(methylsulfonyl)phenyl)piperidine**




Synthesised according to General Procedure B using 3-bromophenylmethylsulfone (59 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (40% EtOAc/PE) to afford the title compound as a yellow oil (75.4 mg, 89%).

Synthesised according to General Procedure C using 3-bromophenylmethylsulfone (59 mg, 0.25 mmol, 1 equiv.) and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-6-dihydropyridine-1(2*H*)-carboxylate (77 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography (40% EtOAc/PE) to afford the title compound as a yellow oil (68.6 mg, 81%).

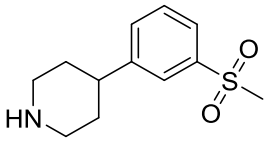
$\upsilon_{max}$ (neat): 2974, 2926, 1683, 1423 $cm^{-1}$

$^{1}H$ NMR (600 MHz, $CDCl_3$) δ 7.80 – 7.76 (m, 2H, 2 x ArH), 7.53 – 7.47 (m, 2H, 2 x ArH), 4.26 (br. s, 2H, $CH_2$), 3.04 (s, 3H, $CH_3$), 2.86 – 2.72 (m, 3H, 3 x CH), 1.84 (d, 2H, 2 x CH, *J* = 12.8 Hz), 1.69 – 1.60 (m, 2H, 2 x CH), 1.48 (s, 9H, 3 x $CH_3$).

$^{13}C$ NMR (151 MHz, $CDCl_3$): δ 154.9, 147.7, 141.0, 132.3, 129.8, 125.7, 125.5, 79.8, 44.6, 42.7, 33.1, 28.6. (1C not observed).

HRMS ($C_{17}H_{26}O_4N_2S$) $[M+H]^+$ requires: 357.1843, observed: 357.1843

**Compound 14, 4-(3-(methylsulfonyl)phenyl)piperidine**




To a vial containing Compound 13 (60 mg, 0.18 mmol, 1 equiv.) was added DCM (1 mL), then TFA (138 μL, 1.8 mmol, 10 equiv.) dropwise. The reaction mixture was stirred at room temperature for 4 hours before being concentrated under compressed air. The crude material was dissolved in minimal MeOH and applied to a 2g SCX cartridge which had been equilibrated with MeOH. The cartridge was washed with 2 column volumes of MeOH, followed by 2 column volumes of $NH_3$/MeOH (3M). The $NH_3$/MeOH fractions were combined and concentrated *in vacuo* to afford the title compound as a white amorphous solid (39 mg, 91%).

$\upsilon_{max}$ (neat): 3210, 2901, 1688, 1499, 1300 $cm^{-1}$

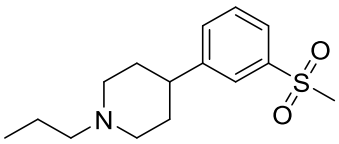
$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.81 – 7.74 (m, 2H, 2 x ArH), 7.53 – 7.47 (m, 2H, 2 x ArH), 3.21 (d, 2H, $CH_2$, *J* = 12.0 Hz), 3.04 (s, 3H, $CH_3$), 2.74 (m, 2H, $CH_2$,), 2.11 (br. s, 1H, NH), 1.86 (d, 2H, $CH_2$, *J* = 12.8 Hz), 1.67 (q, 2H, $CH_2$, *J* = 12.4 Hz).

$^{13}$C NMR (101 MHz, $CDCl_3$) δ 148.6, 140.8, 132.3, 129.7, 125.8, 125.3, 47.0, 44.6, 43.0, 34.3.

HRMS ($C_{12}H_{18}O_2NS$) $[M+H]^+$ requires: 240.1052, observed: 240.1053

Consistent with reported data.[10]

**Compound 3, 4-(3-(methylsulfonyl)phenyl)-1-propylpiperidine**




To an oven dried round bottom flask was added $K_2CO_3$ (45 mg, 0.39 mmol, 2.5 equiv.) and was purged with nitrogen. Compound 14 (30 mg, 0.13 mmol, 1 equiv.) was added in MeCN (2 mL) and the reaction mixture was stirred at room temperature for 15 minutes. 1-Iodopropane (15 μL, 0.16 mmol, 1.2 equiv.) was added dropwise at 0 ˚C and the reaction mixture was heated to 70 ˚C and stirred for 24 h. The reaction was then allowed to cool to room temperature and applied directly to an SCX cartridge which had been equilibrated with MeOH. The cartridge was washed with 2 column volumes of MeOH, followed by 2 column volumes of $NH_3$/MeOH (3M). The $NH_3$/MeOH fractions were combined and concentrated *in vacuo* to afford a clear gum which was purified by flash column chromatography (10% MeOH/DCM) to afford the title compound as a colourless gum (25 mg, 69%).

$\upsilon_{max}$ (neat): 2991, 2920, 1646, 1333 $cm^{-1}$

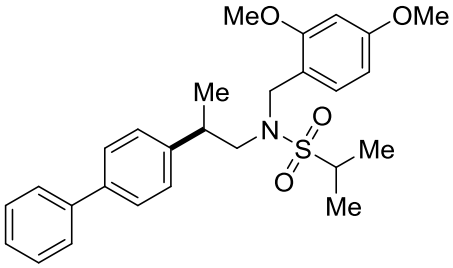
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 2H, 2 x ArH), 7.57 – 7.47 (m, 2H, 2 x ArH), 3.19 (d, 2H, 2 x CH, *J* = 11.6 Hz), 3.04 (s, 3H, $CH_3$), 2.67 (tt, 1H, CH, *J* = 11.9, 4.0 Hz), 2.49 – 2.42 (m, 2H, 2 x CH), 2.20 (t, 2H, 2 x CH, *J* = 11.8 Hz), 2.02 – 1.85 (m, 4H, 4 x CH), 1.68 – 1.58 (m, 2H, 2 x CH), 0.94 (t, 3H, $CH_3$, *J* = 7.4 Hz).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 147.7, 140.9, 132.2, 129.8, 126.0, 125.4, 60.7, 54.0, 44.6, 42.3, 32.7, 19.8, 12.0.

HRMS ($C_{15}H_{24}O_2NS$) $[M+H]^+$ requires: 282.1528, observed: 282.1532

Consistent with reported data.[11]

**Compound 17, *N*-(2-([1,1'-biphenyl]-4-yl)propyl)-*N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide**




Synthesised according to General Procedure C using *N*-(2-bromoallyl)-*N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide (98 mg, 0.25 mmol, 1 equiv.) and 4-biphenylboronic acid (50 mg, 0.25 mmol, 1 equiv.), and purified by flash column chromatography to afford the title compound as a white solid (116.7 mg, 71%).

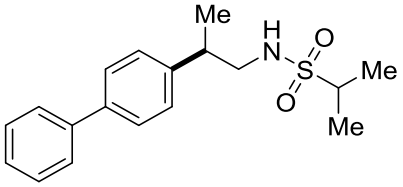
$\upsilon_{max}$ (neat): 2931, 2834, 1612, 1508 $cm^{-1}$

$^{1}H$ NMR (400 MHz, Acetone): δ 7.66 – 7.56 (m, 4H, 4 x ArH), 7.47 – 7.41 (m, 2H, 2 x ArH), 7.38 – 7.28 (m, 4H, 4 x ArH), 6.59 (d, 1H, ArH, *J* = 2.4 Hz), 6.55 (dd, 1H, ArH, *J* = 8.3, 2.4 Hz), 4.45 (d, 1H, CH, *J* = 15.0 Hz), 4.29 (d, 1H, CH, *J* = 15.0 Hz), 3.89 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 3.38 (qd, 2H, 2 x CH, *J* = 14.2, 7.6 Hz), 3.17 – 3.05 (m, 1H, CH), 2.91 (dt, 1H, CH, *J* = 13.6, 6.8 Hz), 1.22 (d, 3H, $CH_3$, *J* = 7.0 Hz), 1.14 (dd, 6H, 2 x $CH_3$, *J* = 6.8, 1.7 Hz).

$^{13}C$ NMR (101 MHz, Acetone): δ 161.9, 159.7, 144.9, 141.7, 140.2, 132.6, 129.7, 128.8, 128.0, 127.8, 127.6, 117.7, 105.6, 99.0, 55.8, 55.7, 54.1, 46.3, 39.1, 19.4, 17.0, 16.9.

HRMS ($C_{27}H_{34}NO_4S$) $[M+H]^+$ requires: 468.2203, observed: 468.2201

**Compound 18, *N*-(2-([1,1'-biphenyl]-4-yl)propyl)propane-2-sulfonamide**




To a solution of *N*-(2-([1,1'-biphenyl]-4-yl)propyl)-*N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide (100 mg, 0.21 mmol, 1 eq.) in DCM (2 mL) was added TFA (161 µL, 2.1 mmol, 10 eq.). The reaction was stirred for 1 h at room temperature before being concentrated *in vacuo*. The crude material was dissolved in minimal MeOH and applied to a 2g SCX cartridge which had been equilibrated with MeOH. The cartridge was washed with 2 column volumes of MeOH, followed by 2 column volumes of $NH_3$/MeOH (3M). The $NH_3$/MeOH fractions were combined and concentrated *in vacuo* to afford the title compound as an off-white amorphous solid (64.5 mg, 97%).

$\upsilon_{max}$ (neat): 3284, 2925, 1612, 1315 $cm^{-1}$

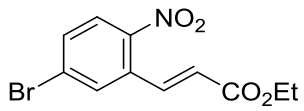
$^{1}H$ NMR (400 MHz, Acetone): δ 7.70 – 7.57 (m, 4H, 4 x ArH), 7.48 – 7.42 (m, 2H, 2 x ArH), 7.39 – 7.32 (m, 3H, 3 x ArH), 5.88 (app. t, 1H, NH, *J* = 5.8 Hz), 3.39 – 3.25 (m, 2H, 2 x CH), 3.14 – 3.00 (m, 2H, 2 x CH), 1.34 (d, 3H, $CH_3$, *J* = 7.0 Hz), 1.25 (d, 1H, *J* = 6.8 Hz), 1.21 (d, 1H, *J* = 6.8 Hz).

$^{13}$C NMR (101 MHz, Acetone): δ 144.6, 141.7, 140.1, 129.7, 128.8, 128.0, 127.8, 127.6, 53.0, 50.9, 41.4, 19.5, 16.9, 16.8.

HRMS ($C_{18}H_{24}NO_2S$) $[M+H]^+$ requires: 318.1522, observed: 318.1527

## Synthesis of starting materials and intermediates

**Compound 19, Ethyl 3-(5-bromo-2-nitrophenyl)acrylate (*20:1, E:Z*)**




To a round bottom flask containing 5-bromo-2-nitrobenzaldehyde (300 mg, 1.3 mmol, 1 eq.) and triphenylcarbethoxymethylenephosphorane (1.044 g, 3 mmol, 2.3 eq.) was added DCM (6 mL). The reaction was stirred at room temperature for 16 h before being washed with water (10 mL) and brine (10 mL). The organic layer was dried with $Na_2SO_4$ before being concentrated *in vacuo*. Purification by flash column chromatography (30% EtOAc/PE) afforded the title compound a yellow amorphous solid (385 mg, 99%).

$\upsilon_{max}$ (neat): 3096, 2977, 1727, 1709 cm$^{-1}$

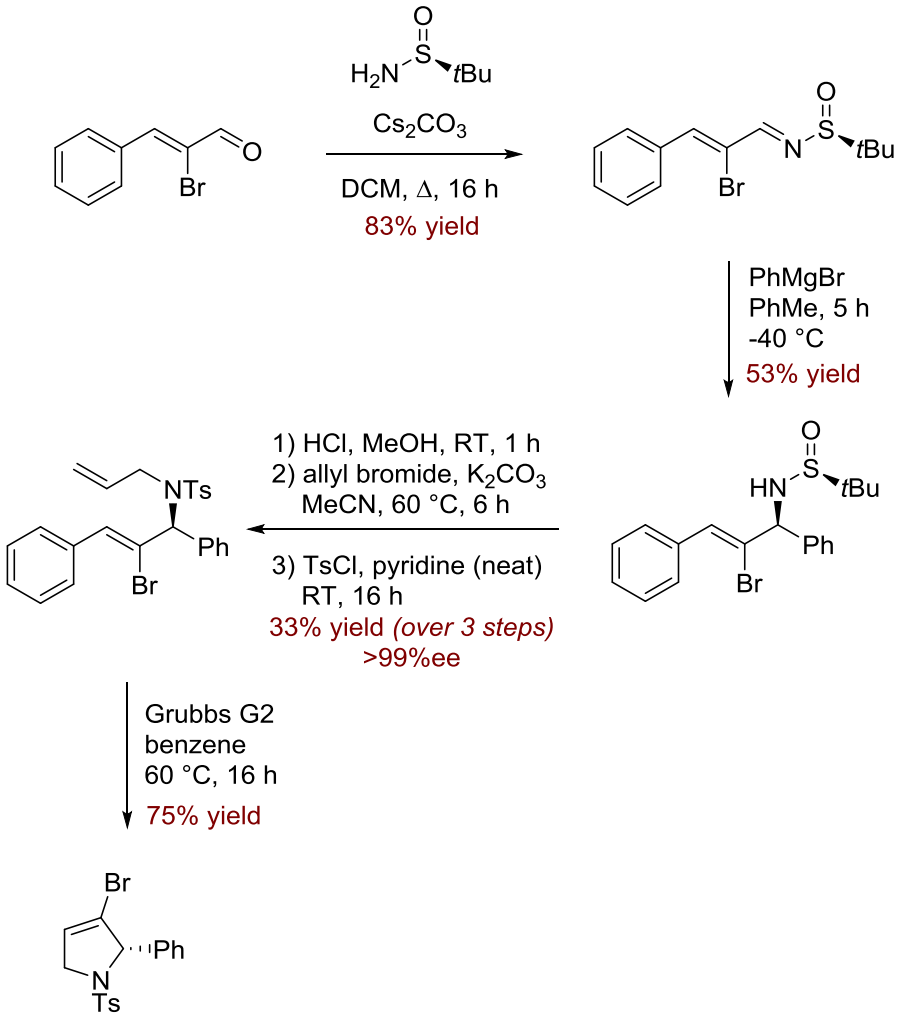
$^1$H NMR (500 MHz, $CDCl_3$): δ 8.07 (d, 1H, alkene CH, *J* = 15.8 Hz), 7.95 (d, 1H, ArH, *J* = 8.7 Hz), 7.78 (d, 1H, ArH, *J* = 2.1 Hz), 7.67 (dd, 1H, ArH, *J* = 8.7, 2.1 Hz), 6.37 (d, 1H, alkene CH, *J* = 15.8 Hz), 4.30 (q, 2H, $CH_2$, *J* = 7.1 Hz), 1.35 (t, 3H, $CH_3$, *J* = 7.1 Hz).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 165.5, 147.0, 138.8, 133.3, 132.7, 132.2, 128.5, 126.5, 124.6, 61.2, 14.3.

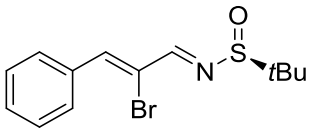
(Inconsequential *Z* (~5%) isomer observed in $^1$H and $^{13}$C NMR but not reported).

HRMS ($C_{11}H_{11}NO_4Br$) $[M+H^+]$ requires: 299.9872, observed: 299.9868

**Synthetic route to 12r starting material:**




**Compound 20, (*S*)-*N*-((1E,2Z)-2-bromo-3-phenylallylidene)-2-methylpropane-2-sulfinamide**



To a solution of (*Z*)-2-bromo-3-phenylacrylaldehyde (422 mg, 2 mmol, 1 eq.) in DCM (8 mL) was added (*R*)-2-methyl-2-propanesulfinamide (242 mg, 2 mmol, 1 eq.) and $Cs_2CO_3$ (704 mg, 2 mmol, 1 eq.) and the reaction was stirred at 40 °C with a reflux condenser for 16 h. Following this, the reaction was filtered through Celite, rinsed with DCM and concentrated *in vacuo*. Purification by flash chromatography (14% EtOAc) gave the title compound as a yellow oil (521.2 mg 83%).

$\upsilon_{max}$ (neat): 3100, 2977, 1726, 1709, 1519 $cm^{-1}$

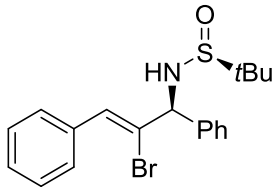
$^1$H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H, imine CH), 7.95 – 7.88 (m, 2H, 2 x ArH), 7.64 (s, 1H, alkene CH), 7.48 – 7.40 (m, 3H, 3 x ArH), 1.27 (s, 9H, 3 x $CH_3$).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 161.7, 144.7, 134.0, 130.7, 130.6, 128.7, 120.9, 58.4, 22.7.

HRMS ($C_{13}H_{17}NOS$) $[M+H]^+$ requires: 316.0187, observed: 316.0187

$[\alpha]_D^{20}$: +18.6 (c=0.1, $CH_2Cl_2$)

**Compound 21, (S)-N-((S,Z)-2-bromo-1,3-diphenylallyl)-2-methylpropane-2-sulfinamide**




$\upsilon_{max}$ (neat): 3107, 2988, 1729, 1709, 1517 $cm^{-1}$

To a solution of (*S*)-*N*-((1E,2Z)-2-bromo-3-phenylallylidene)-2-methylpropane-2-sulfinamide (500 mg, 1.59 mmol, 1 eq.) in dry toluene (10 mL) was added PhMgBr (3M in $Et_2O$) (793 µL, 2.38 mmol, 1.5 eq.) dropwise at -40°C. The reaction was stirred for 5 h at -40 °C before being quenched with $NH_4Cl$ and washed between water and ethyl acetate. The organic layer was dried with $Na_2SO_4$, concentrated *in vacuo* and purified by flash chromatography (55% EtOAc/PE) to afford the title compound as a clear oil (330.3 mg, 53%).

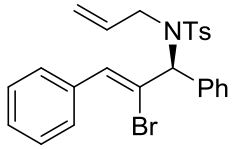
$^1$H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, 2H, 2 x ArH, *J* = 7.3 Hz), 7.50 (d, 2H, 2 x ArH, *J* = 7.3 Hz), 7.42 – 7.29 (m, 7H, 6 x ArH, 1 x alkene CH), 5.38 (d, 1H, CH, *J* = 3.4 Hz), 3.76 (d, 1H, CH, *J* = 3.2 Hz), 1.32 (s, 9H, 3 x$CH_3$).

$^{13}$C NMR (126 MHz, $CDCl_3$): δ 139.4, 135.1, 130.9, 129.4, 128.9, 128.6, 128.5, 128.3, 127.6, 127.1, 66.4, 56.3, 22.9.

HRMS ($C_{19}H_{23}NOS$) $[M+H]^+$ requires: 394.0657, observed: 394.0655

$[\alpha]_D^{20}$: +8.9 (c=0.1, $CH_2Cl_2$)

**Compound 22, (*S*,Z)-N-allyl-N-(2-bromo-1,3-diphenylallyl)-4-methylbenzenesulfonamide**




To a solution of (S)-*N*-((S,Z)-2-bromo-1,3-diphenylallyl)-2-methylpropane-2-sulfinamide (300 mg, 0.77 mmol, 1 eq.) in MeOH (2 mL) was added AcCl (540 µL, 7.7 mmol, 10 eq.) at 0 °C. The reaction mixture was stirred at room temperature for 1 h before being concentrated *in vacuo*. The resulting HCl salt was taken up in MeCN (4 mL) and $K_2CO_3$ (638, 4.62 mmol, 6 eq.) was added. After stirring for 15 minutes at room temperature, allyl bromide (80 µL, 0.92, 1.2 eq.) was added dropwise. The reaction was stirred 60 °C for 6 h before being quenched with $NH_4Cl$. The mixture was washed between water and EtOAc and the organic layer was dried with $Na_2SO_4$, filtered and concentrated *in vacuo*. To this was added pyridine (3 mL) and tosyl chloride (195 µL, 1.54 mmol, 2 eq.)and the reaction was stirred at room temperature for 16 h. HCl (1M) was added and the mixture was washed with DCM. The organic layer was dried with $Na_2SO_4$, filtered, concentrated *in vacuo* and purified by flash chromatography (10% EtOAc/PE) to afford the title compound as a yellow oil (122.2 mg, 33%, >99% ee).

$\upsilon_{max}$ (neat): 3057, 2920, 1597, 1493, 1342 $cm^{-1}$

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.45 – 7.39 (m, 2H, 2 x ArH), 7.37 – 7.24 (m, 10H, 10 x ArH), 6.80 (s, 1H, alkene CH), 6.09 (s, 1H, CH), 5.53 – 5.41 (m, 1H, CH), 4.90 – 4.79 (m, 2H, 2 x CH), 4.03 – 3.81 (m, 2H, $CH_2$), 2.40 (s, 3H, $CH_3$)

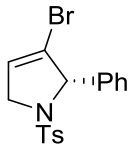
$^{13}$C NMR (101 MHz, $CDCl_3$) δ 143.57, 137.66, 136.50, 135.09, 134.78, 131.58, 129.66, 129.44, 129.40, 129.17, 128.71, 128.46, 128.41, 128.20, 127.78, 123.71, 117.39, 77.48, 77.16, 76.84, 69.59, 49.07, 21.61.

HRMS ($C_{25}H_{28}N_2O_2S$) $[M+NH_4]^+$ requires: 501.1029, observed: 501.1022

$[\alpha]_D^{20}$: -2.4 (c=0.05, $CH_2Cl_2$)

%ee: >99% (by chiral HPLC)

**Compound 23, (*S*)-3-bromo-2-phenyl-1-tosyl-2,5-dihydro-1*H*-pyrrole**



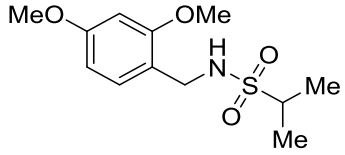

To an oven dried 2-5 mL microwave vial was added Grubbs G2 catalyst (17 mg, 0.02 mmol, 0.1 eq.). The vial was capped, dry benzene (2 mL) was added and the reaction was stirred for 5 minutes at 60 °C. Following this, (*S*,Z)-*N*-allyl-*N*-(2-bromo-1,3-diphenylallyl)-4-methylbenzenesulfonamide (100 mg, 0.2 mmol, 1 eq.) in dry benzene (2 mL) was added dropwise at 60 °C. The reaction was stirred at 60 °C for 16 h then was purified directly by flash chromatography (7% EtOAc/PE) to afford the title compound as an orange oil (56.6 mg, 75%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, 2H, 2 x ArH, *J* = 8.3 Hz), 7.32 – 7.27 (m, 3H, 3 x ArH), 7.25 – 7.20 (m, 2H, 2 x ArH), 7.17 (d, 2H, 2 x ArH, *J* = 8.0 Hz), 5.99 (dd, 1H, CH, *J* = 4.0, 2.0 Hz), 5.40 – 5.36 (m, 1H, CH), 4.33 (dt, 1H, CH, *J* = 14.2, 2.5 Hz), 4.21 (ddd, 1H, CH, *J* = 14.2, 5.8, 2.0 Hz), 2.38 (s, 3H, $CH_3$).

$^{13}$C NMR (101 MHz, $CDCl_3$): δ 143.6, 138.2, 135.4, 129.7, 128.6, 128.2, 127.4, 125.5, 119.8,73.0, 55.1, 21.6.

HRMS ($C_{11}H_{11}NO_4Br$) $[M+H]^+$ requires: 299.9872, observed: 299.9868

***N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide**




To an oven dried round bottom flask containing 2,4-dimethoxybenzylamine (417 mg, 2.5 mmol, 1 eq.) in DCM (10 mL) was added $Et_3N$ (1043 µL, 7.5 mmol, 3 eq.) at room temperature. The reaction mixture was cooled to 0 °C and 2-propanesulfonyl chloride (280 µL, 2.5 mmol, 1 eq.) was added dropwise. The reaction was stirred at room temperature for 3 hours before being quenched with water

then washed between 1 M HCl and DCM, and then water and DCM. The organic layers were dried with $Na_2SO_4$ and concentrated *in vacuo* before being purified by flash chromatography (40% EtOAc) to afford the title compound as a yellow solid (552.8 mg, 81%).

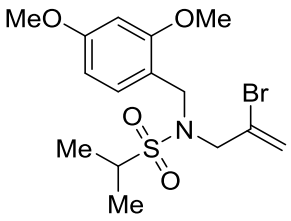
$\upsilon_{max}$ (neat): 3275, 2936, 2836, 1612 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.15 (d, 1H, ArH, *J* = 8.1 Hz), 6.48 – 6.41 (m, 2H, 2 x ArH), 4.69 (t, 1H, CH, *J* = 5.9 Hz), 4.22 (d, 2H, $CH_2$, *J* = 6.2 Hz), 3.83 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 2.95 (hept, 1H, CH, *J* = 6.8 Hz), 1.27 (d, 6H, 2 x $CH_3$, *J* = 6.8 Hz).

$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 161.1, 158.7, 130.6, 118.2, 104.2, 98.8, 55.6, 55.5, 53.6, 43.8, 16.6.

HRMS ($C_{12}H_{19}NO_4SNa$) $[M+Na]^+$ requires: 296.0927, observed: 296.0928

**Compound 16, *N*-(2-bromoallyl)-*N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide**




To a round bottom flask containing *N*-(2,4-dimethoxybenzyl)propane-2-sulfonamide (532 mg, 1.95 mmol, 1 eq.) in MeCN (10 mL) was added $Cs_2CO_3$ (950 mg, 2.93, 1.5 eq.) at 0 °C. After stirring for 5 minutes, 2,3-dibromopropene (80%) (286 µL, 2.34 mmol, 1.2 eq.) was added at 0 °C. The reaction mixture was then stirred at 80 °C for 2 hours before being quenched with water and washed between water and EtOAc. The organic layers were then dried with $Na_2SO_4$ and concentrated *in vacuo* before being purified by flash chromatography (30% EtOAc) to afford the title compound as a yellow oil (588.4 mg, 77%).

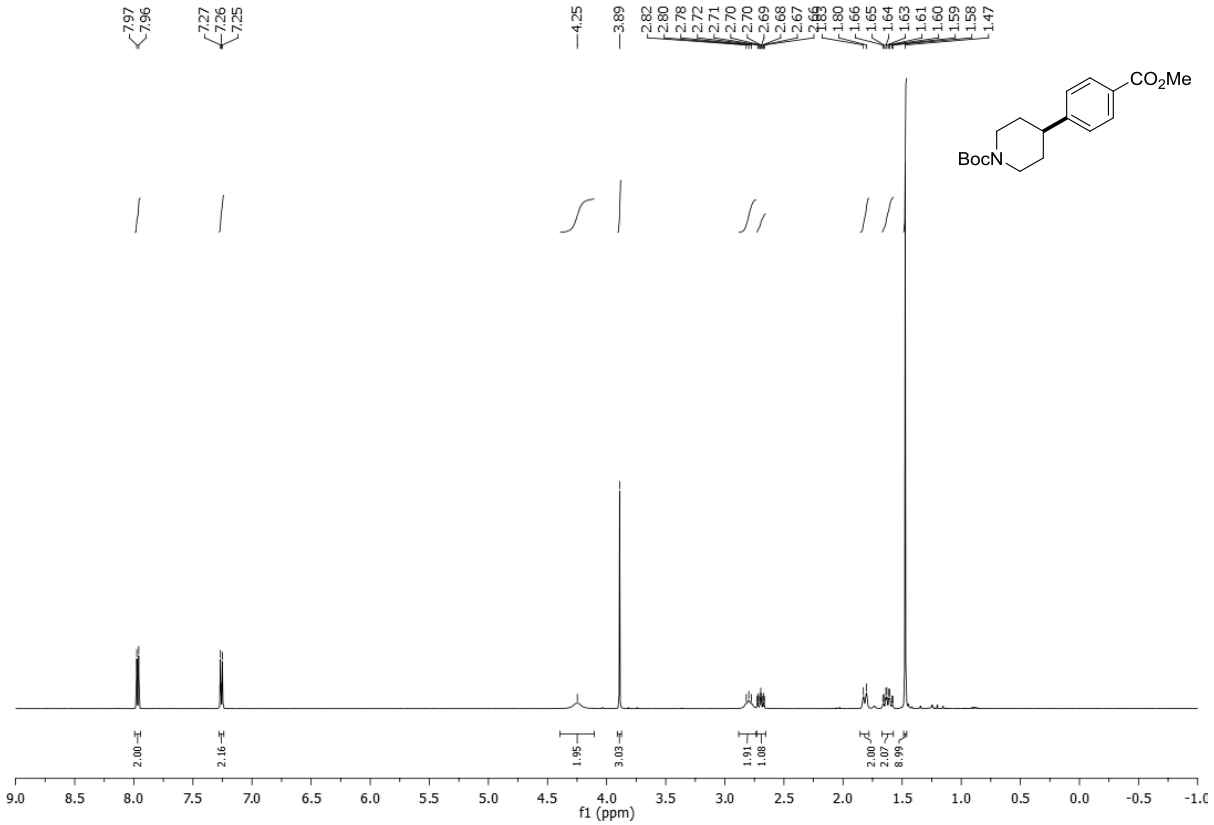
$\upsilon_{max}$ (neat): 2973, 2936, 1612, 1588 $cm^{-1}$

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.21 (d, 1H, ArH, *J* = 8.2 Hz), 6.46 – 6.41 (m, 2H, 2 x ArH), 5.84 (d, 1H, CH, *J* = 1.3 Hz), 5.60 (br. s, 1H, CH), 4.39 (s, 2H, 2 x CH), 4.02 (s, 2H, 2 x CH), 3.78 (s, 6H, 2 x $CH_3$), 3.05 (hept, 1H, CH, *J* = 6.8 Hz), 1.26 (d, 6H, 2 x $CH_3$, *J* = 6.9 Hz).

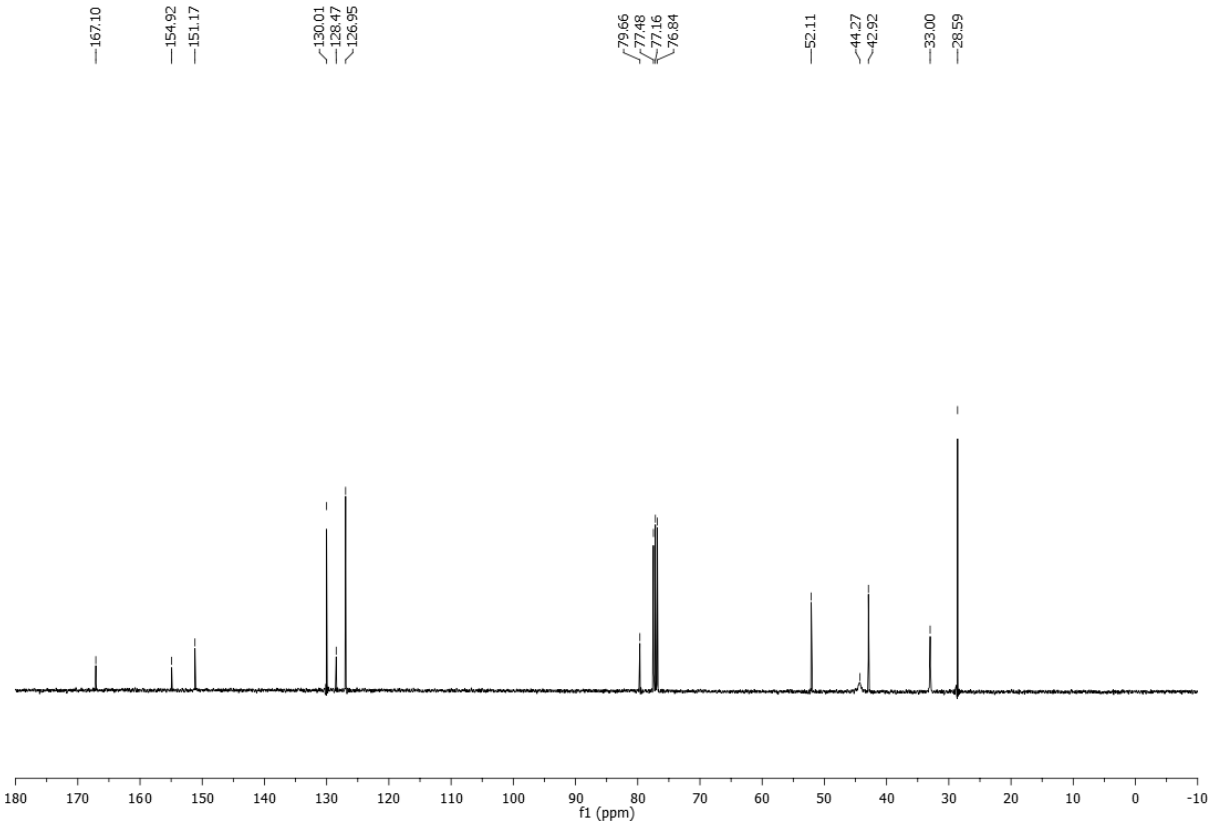
$^{13}C$ NMR (101 MHz, $CDCl_3$): δ 161.0, 158.7, 131.9, 128.8, 118.6, 116.1, 104.3, 98.4, 55.4, 55.2, 54.6, 46.0, 16.5.

HRMS ($C_{15}H_{22}BrNO_4SNa$) $[M+Na]^+$ requires: 414.0345, observed: 414.0344

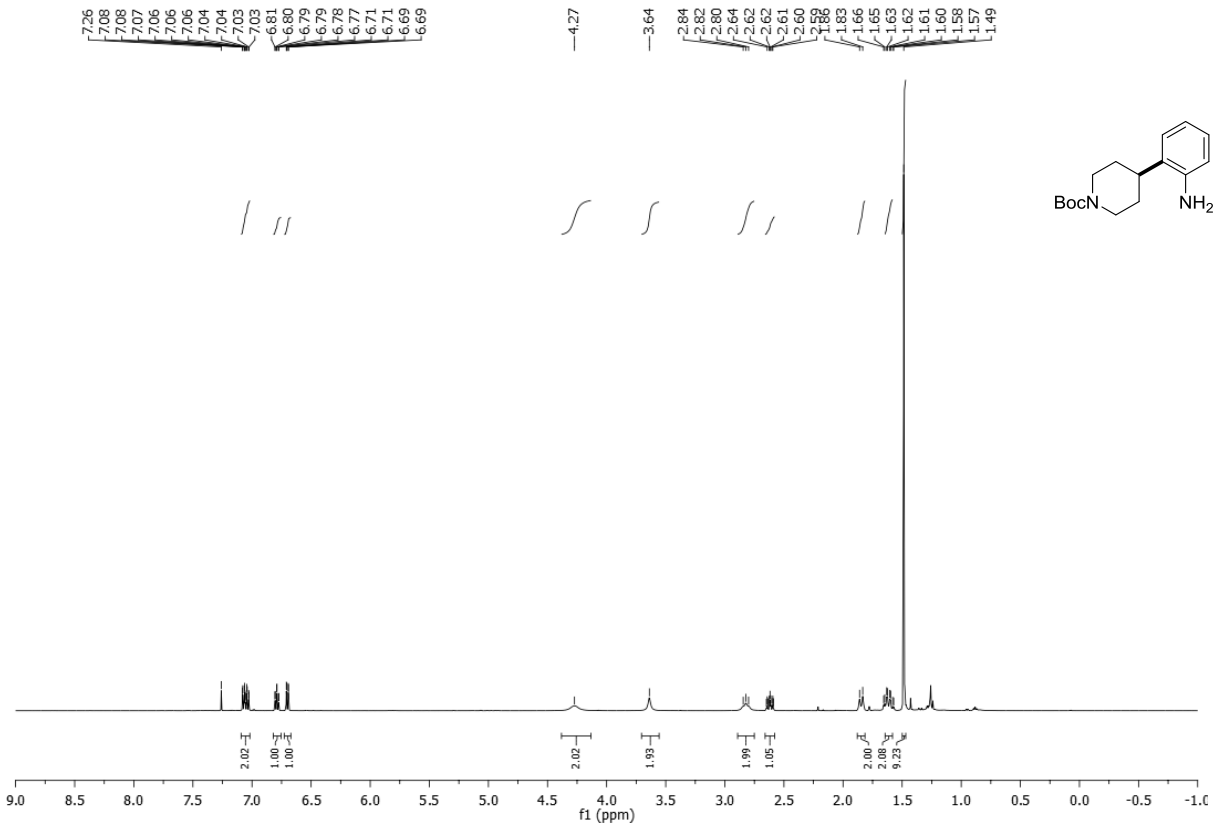
$^{1}$H NMR of Compound 11a



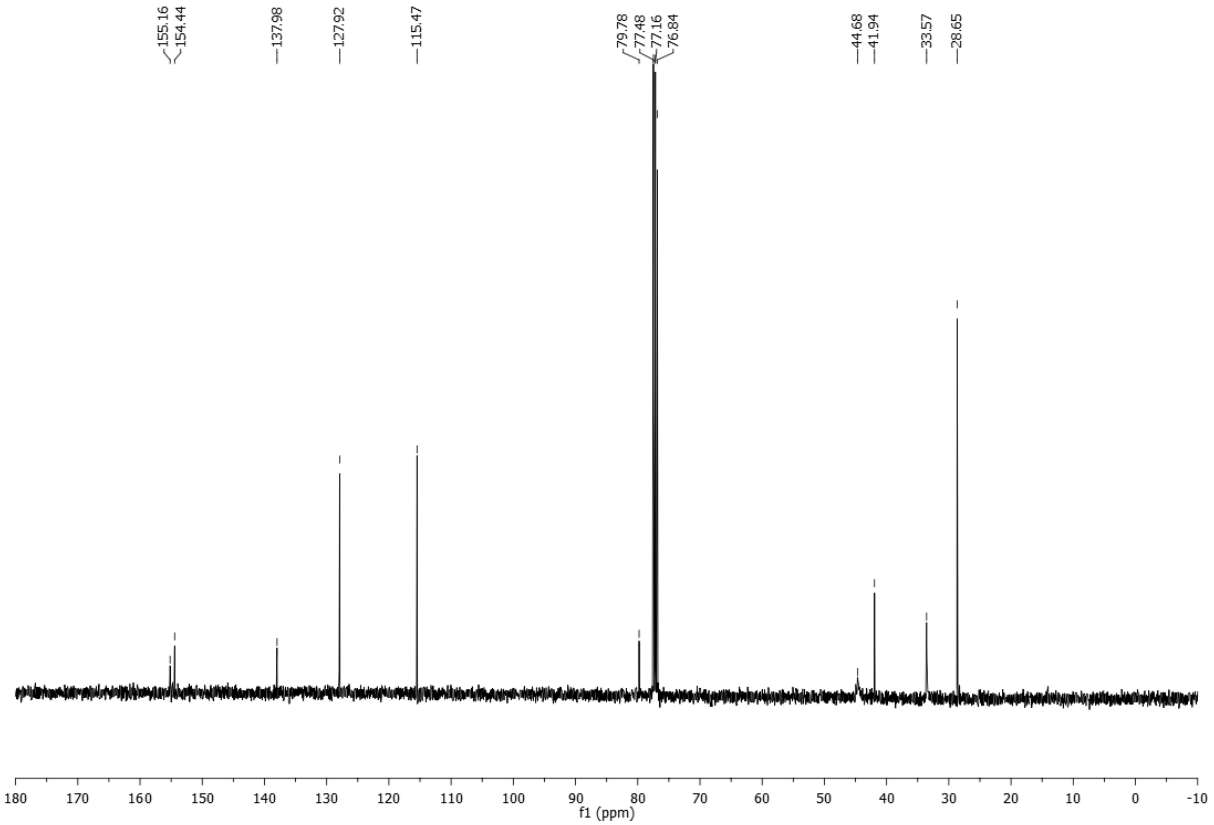

$^{13}$C NMR of Compound 11a



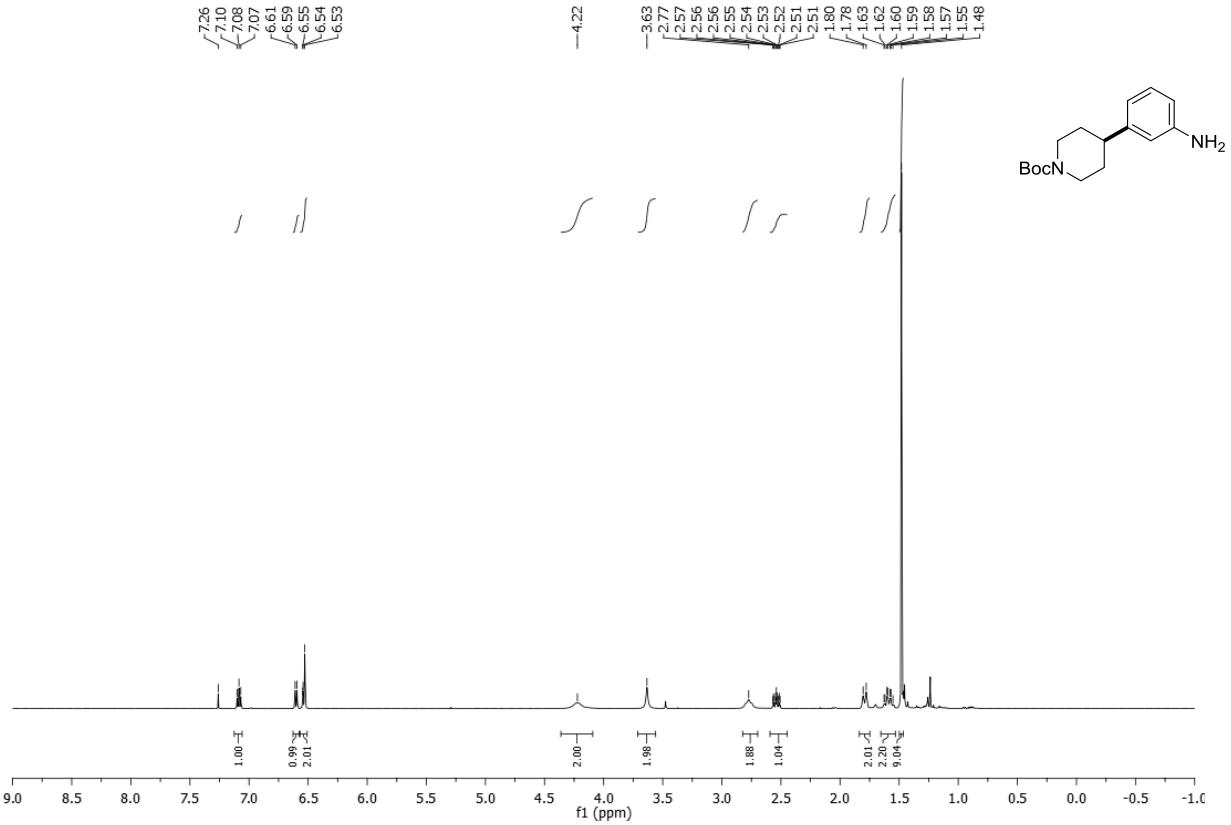
$^{1}$H NMR of Compound 11b



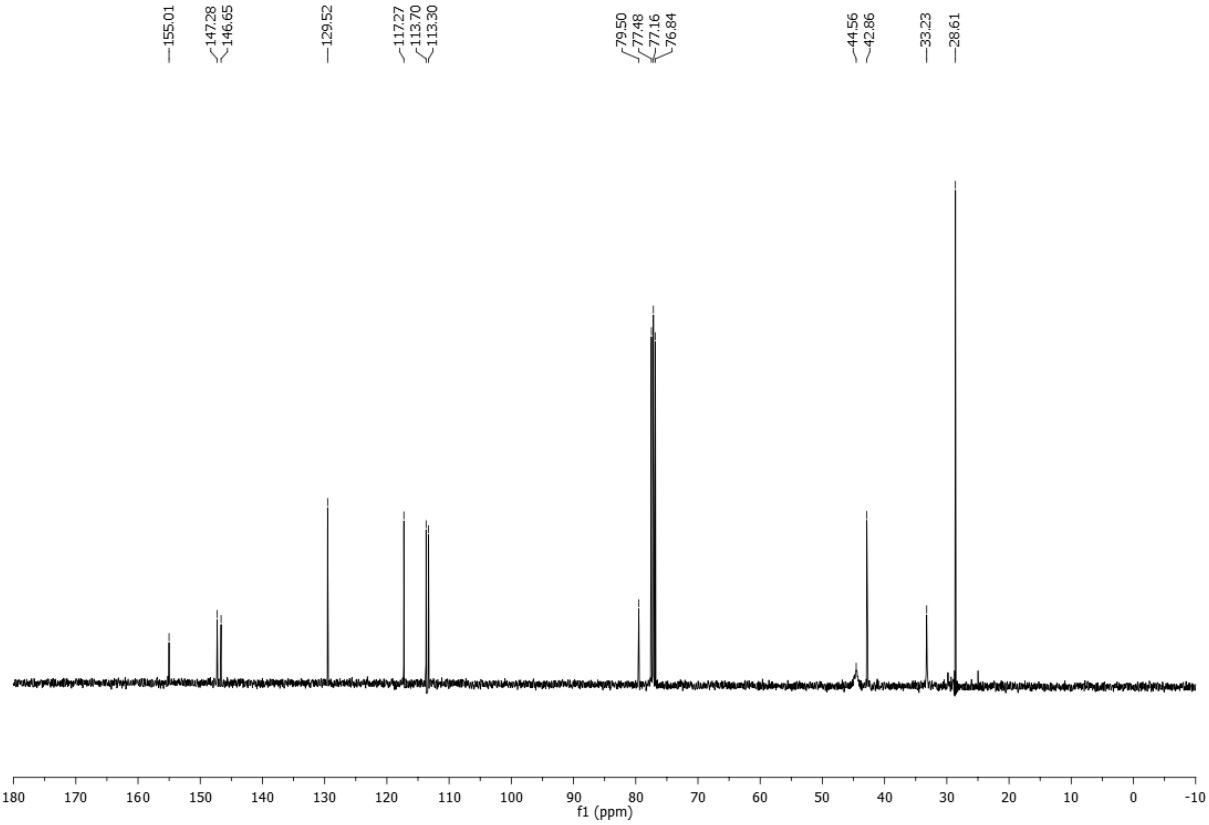

$^{13}$C NMR of Compound 11b



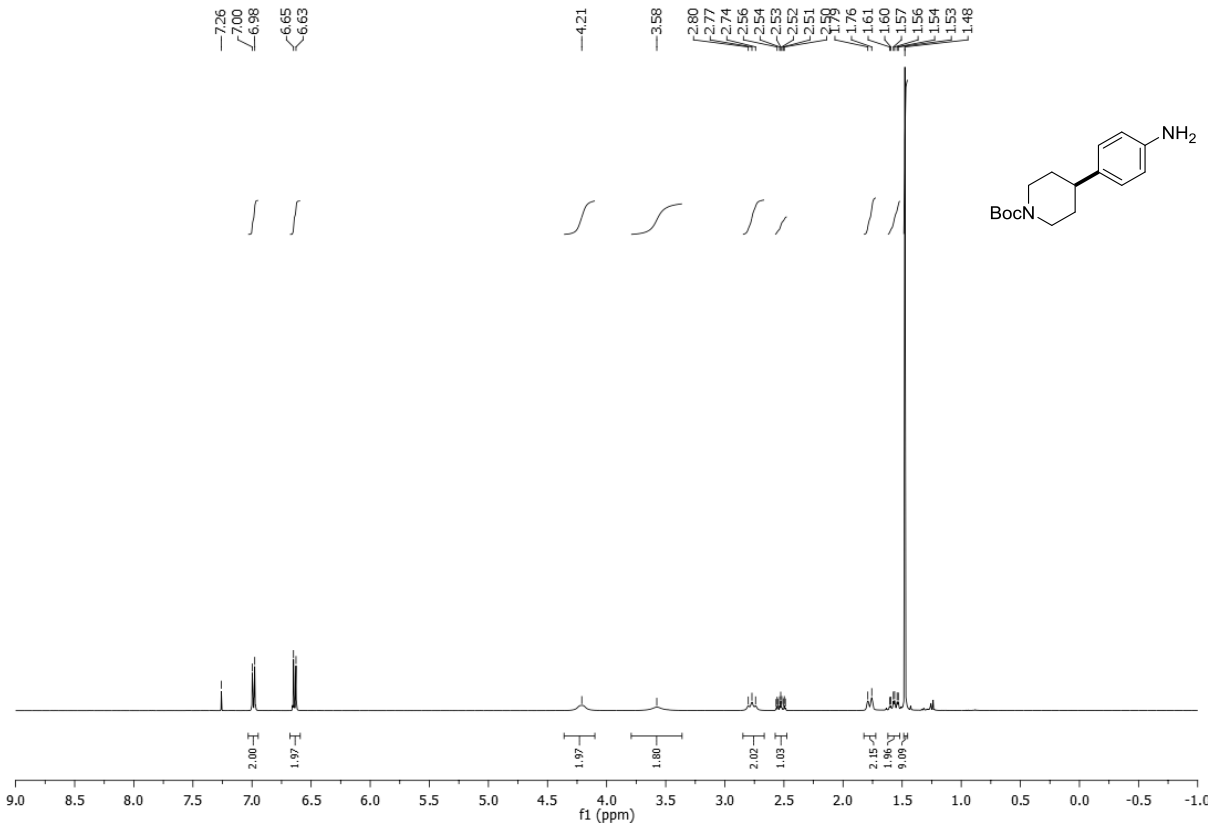
$^{1}$H NMR of Compound 11c



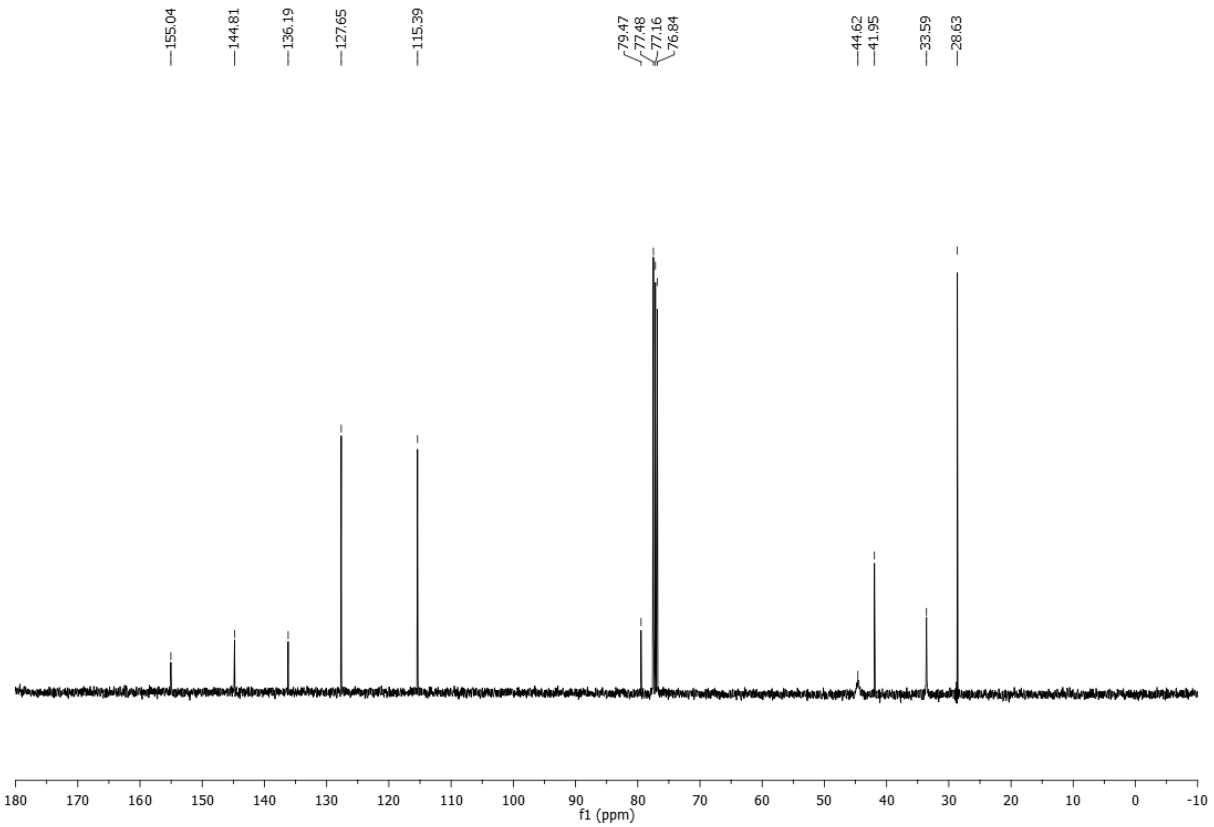

$^{13}$C NMR of Compound 11c



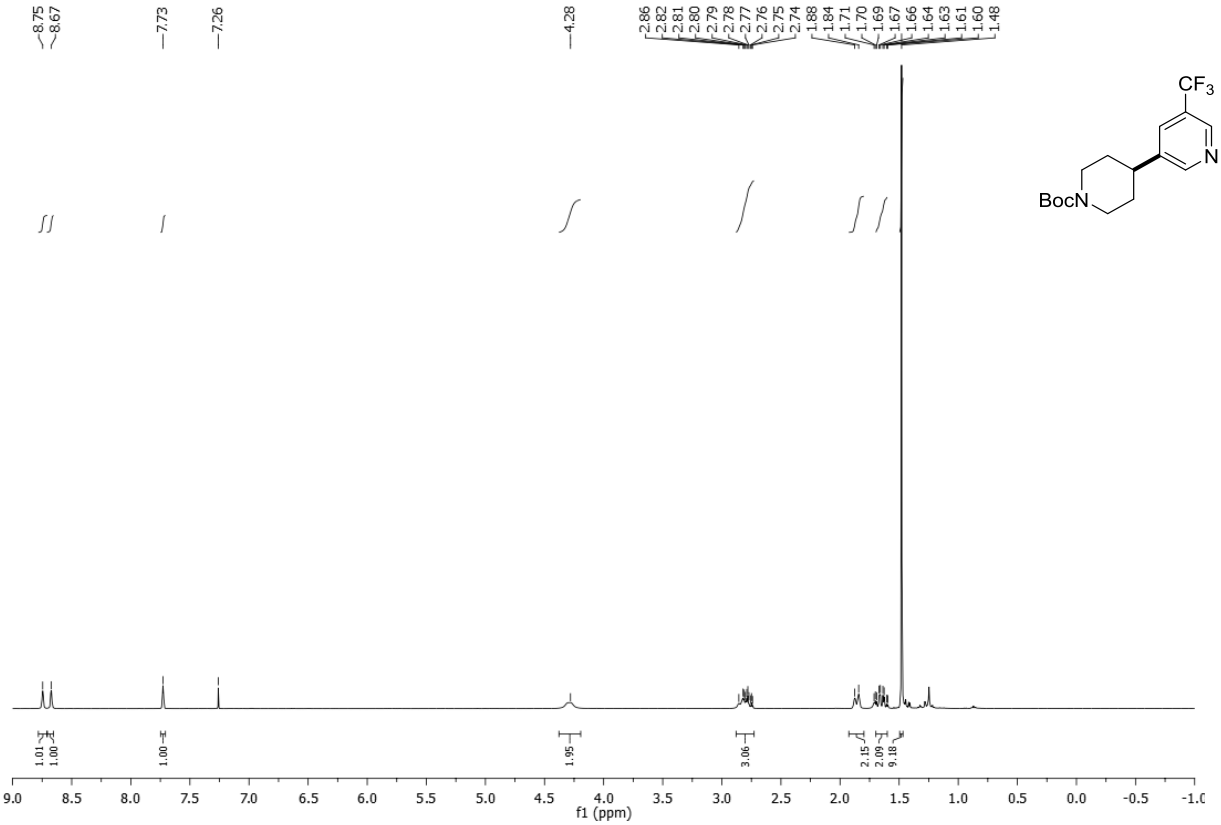
[1]H NMR of Compound 11d



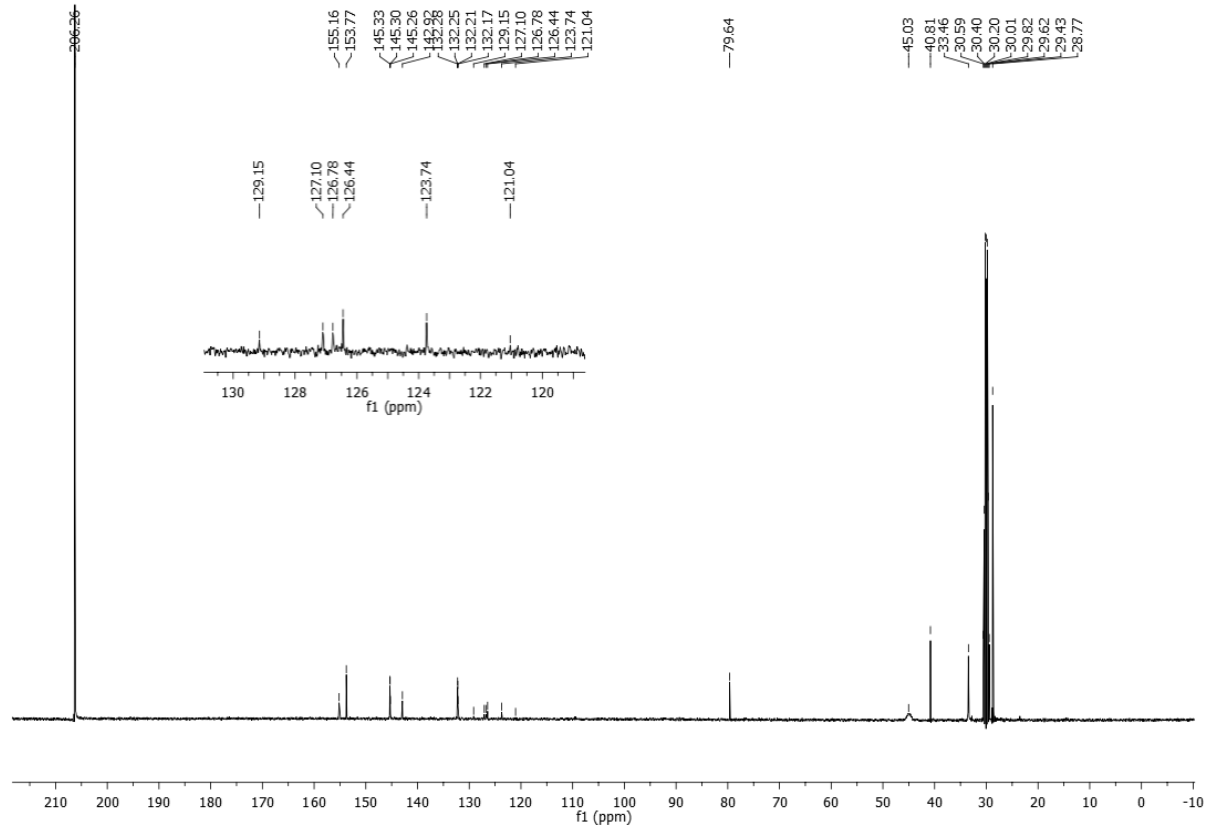

[13]C NMR of Compound 11d



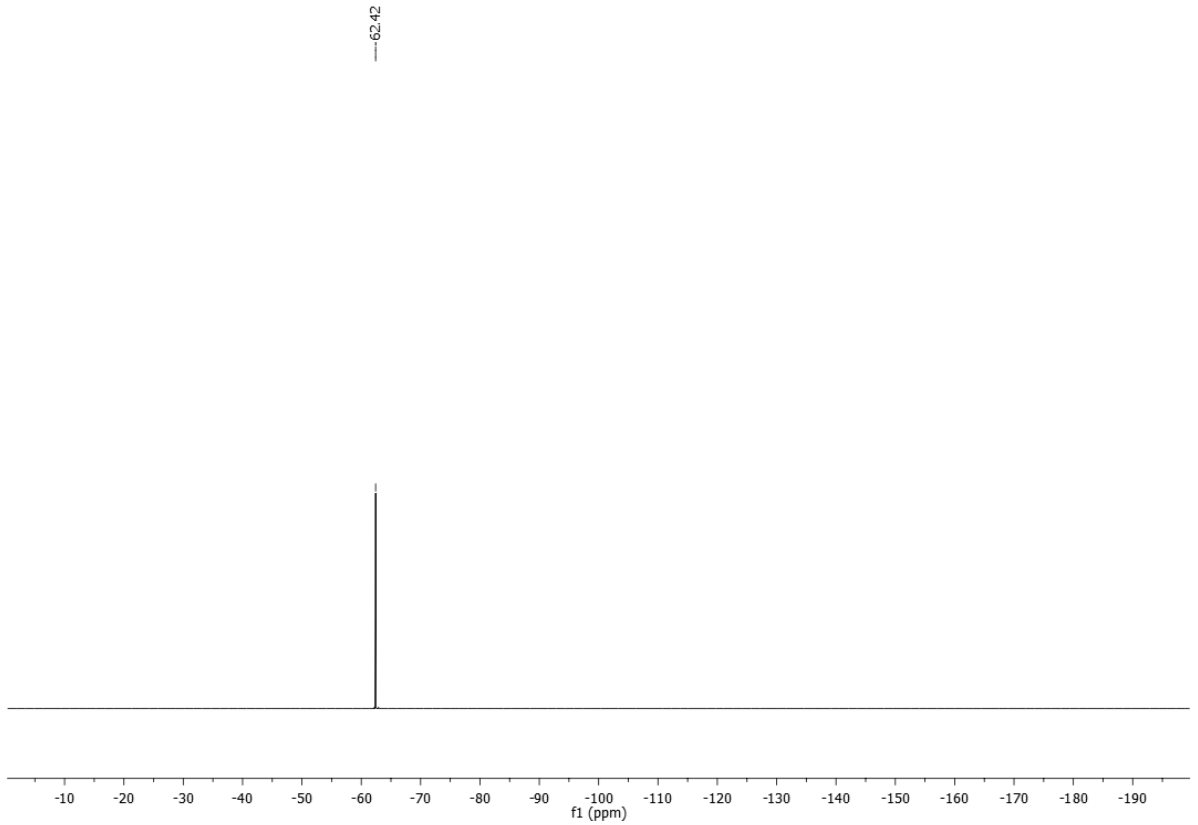
$^{1}$H NMR of Compound 11e



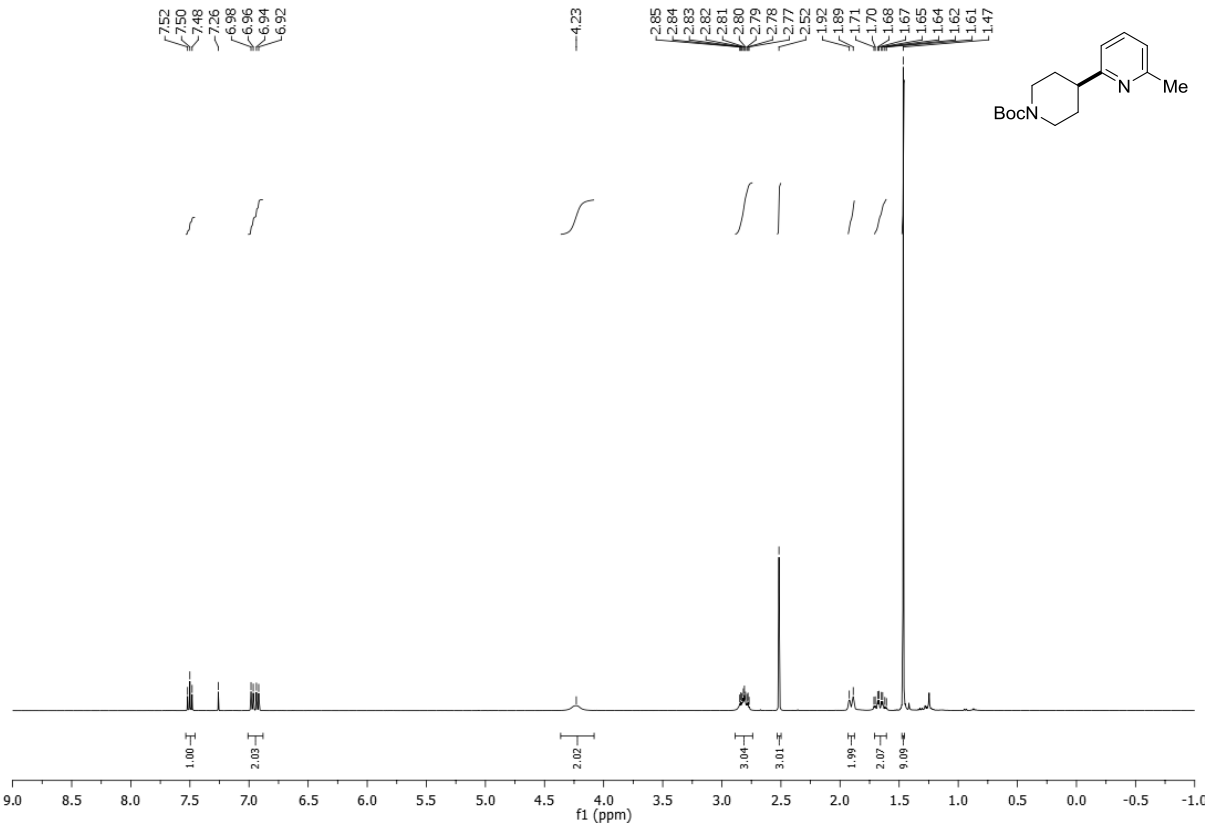

$^{13}$C NMR of Compound 11e



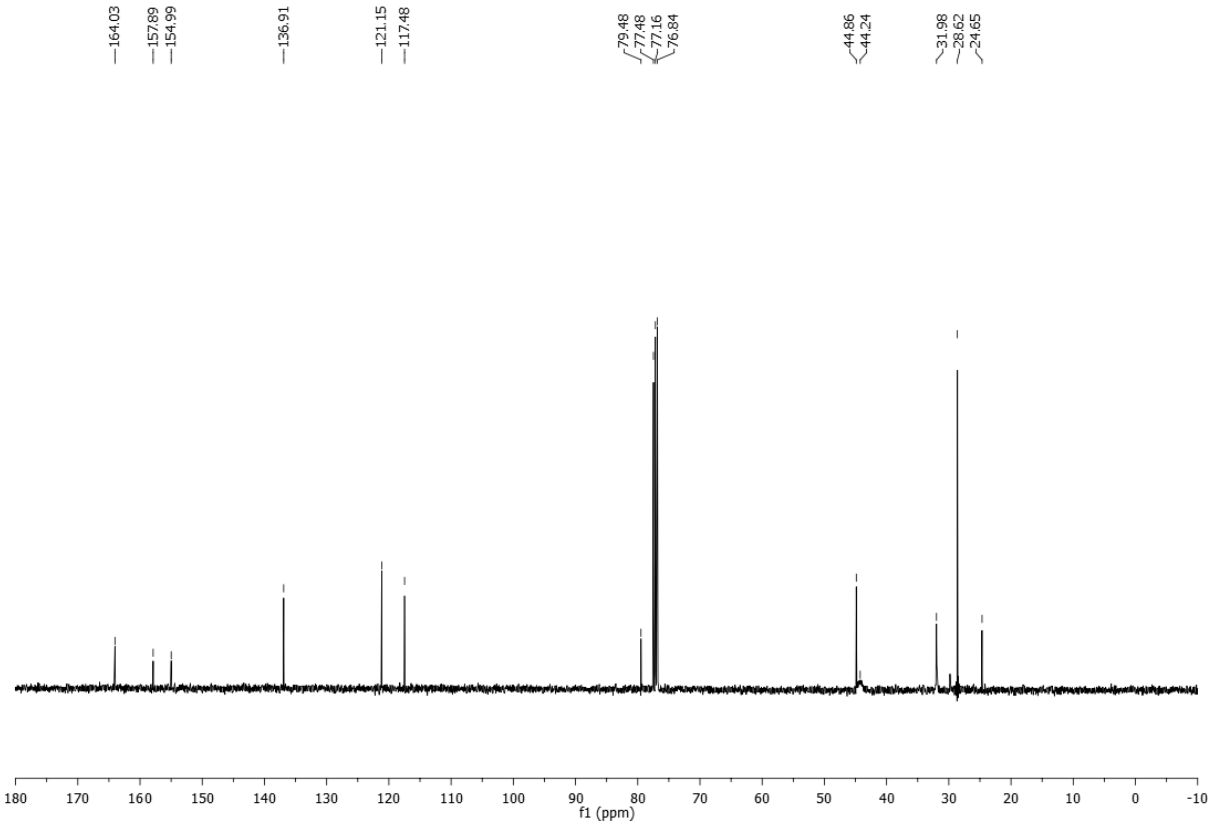
$^{19}$F of Compound 11e



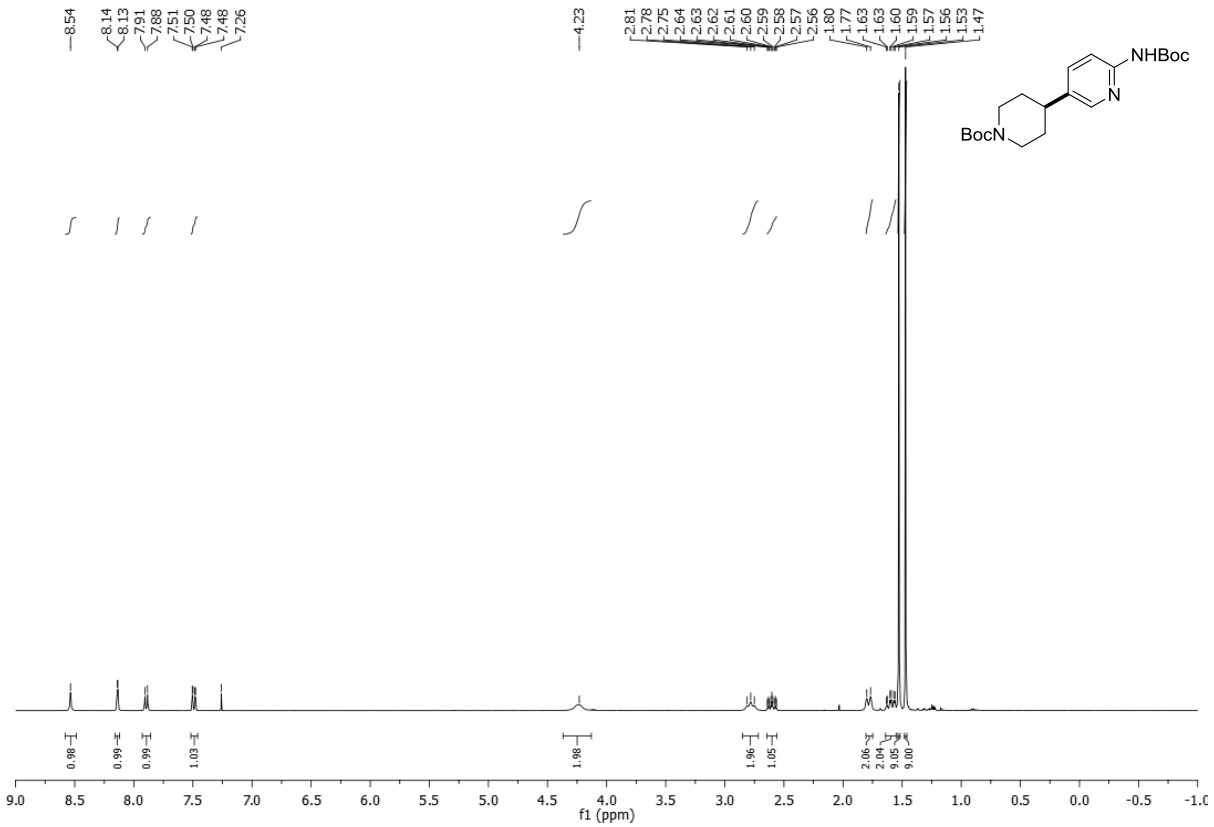

$^{1}$H NMR of Compound 11f



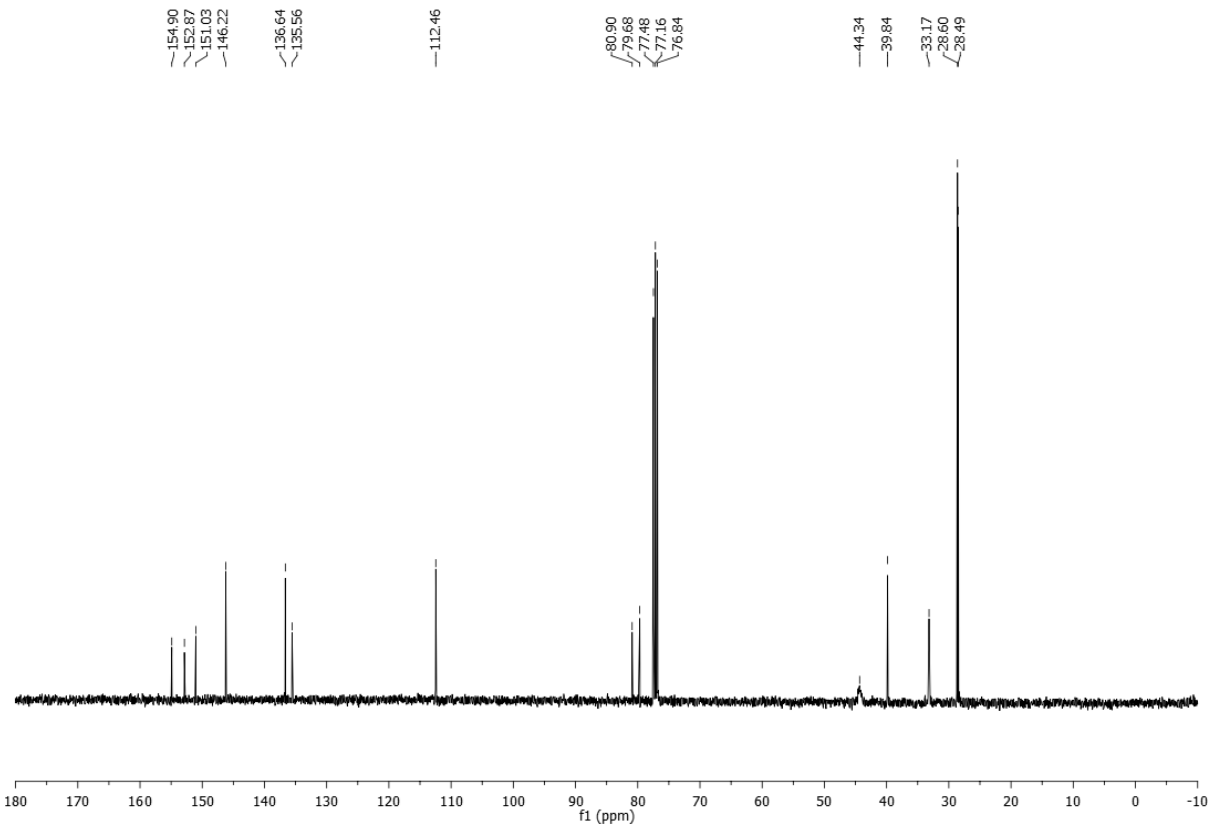
$^{13}$C NMR of Compound 11f



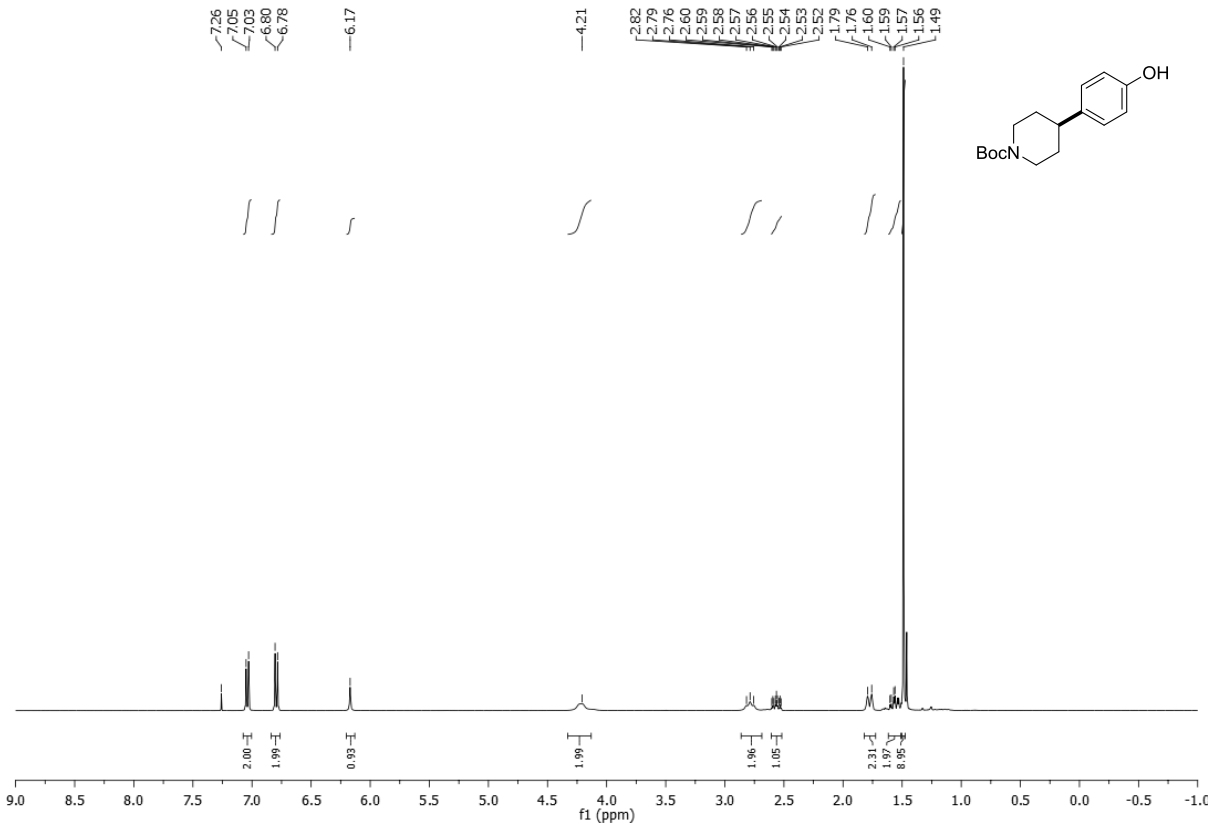

$^{1}$H NMR of Compound 11g



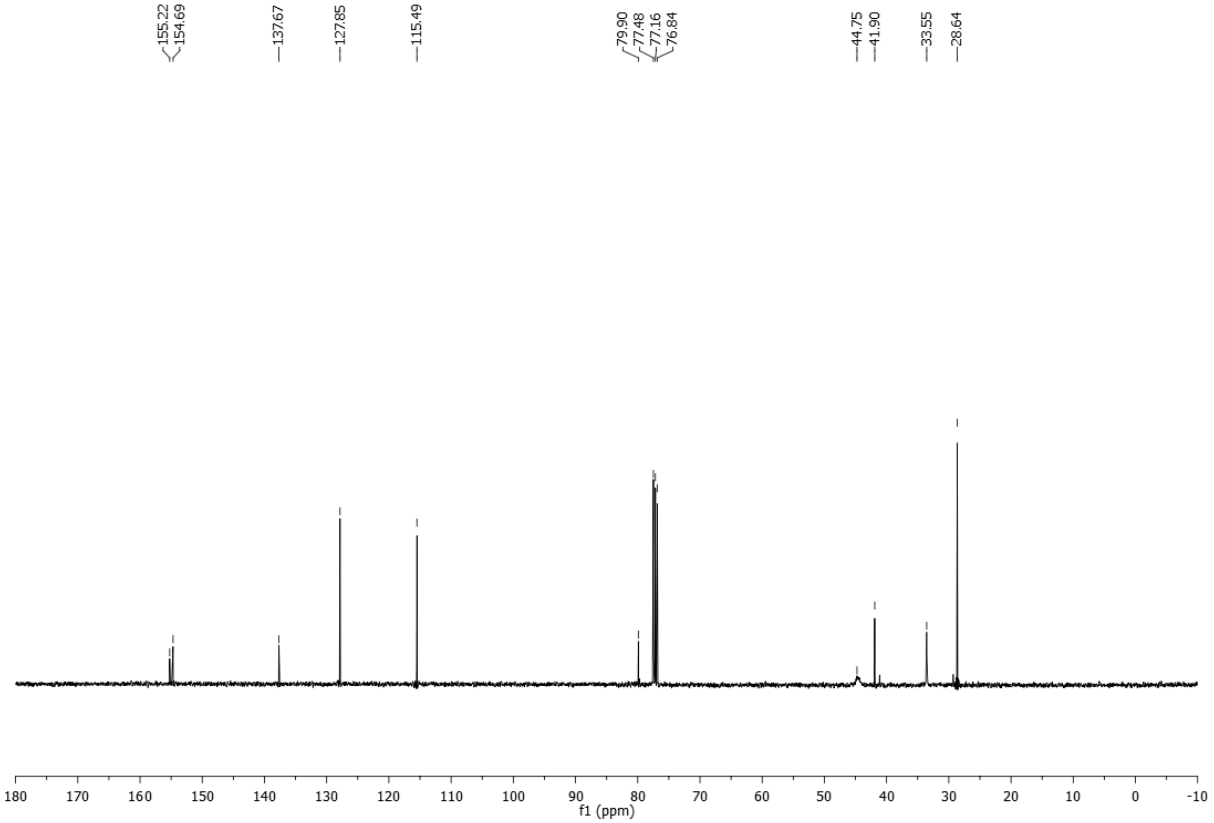
$^{13}$C NMR of Compound 11g



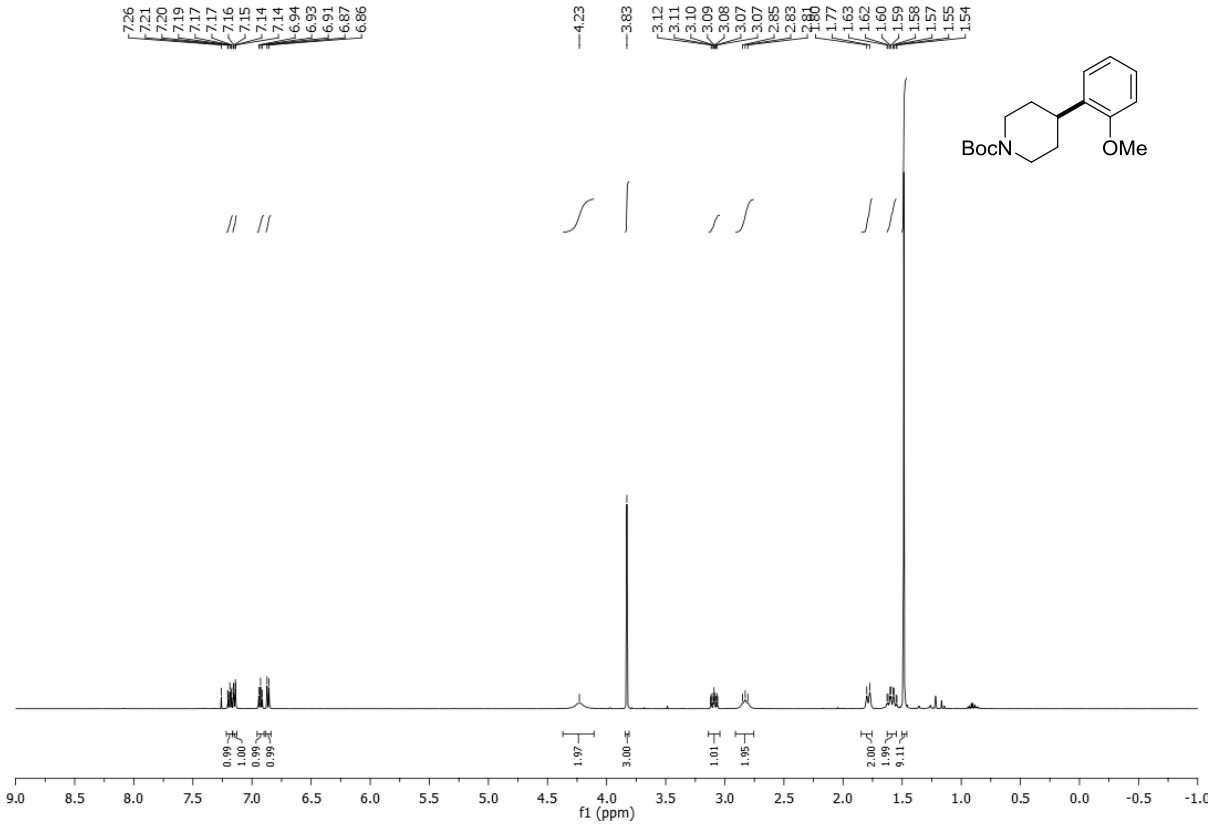

$^{1}$H NMR of Compound 11h



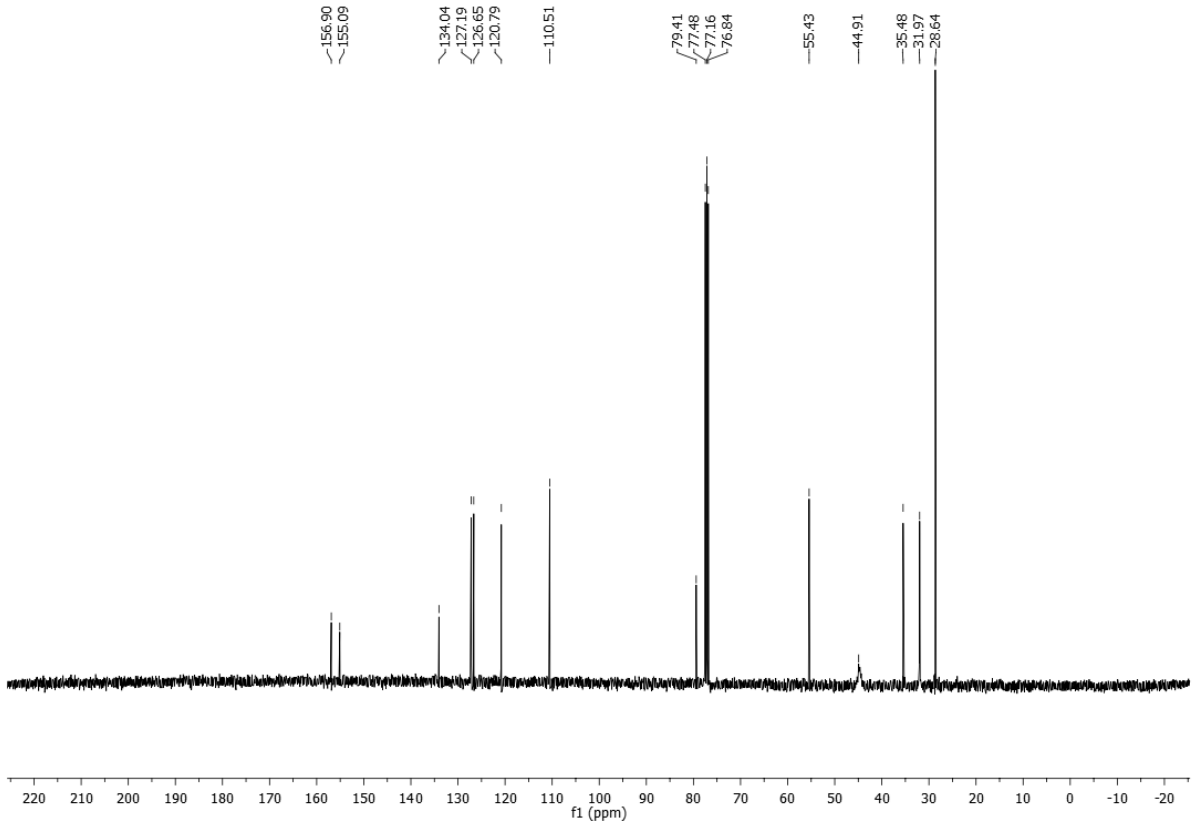
$^{13}$C NMR of Compound 11h



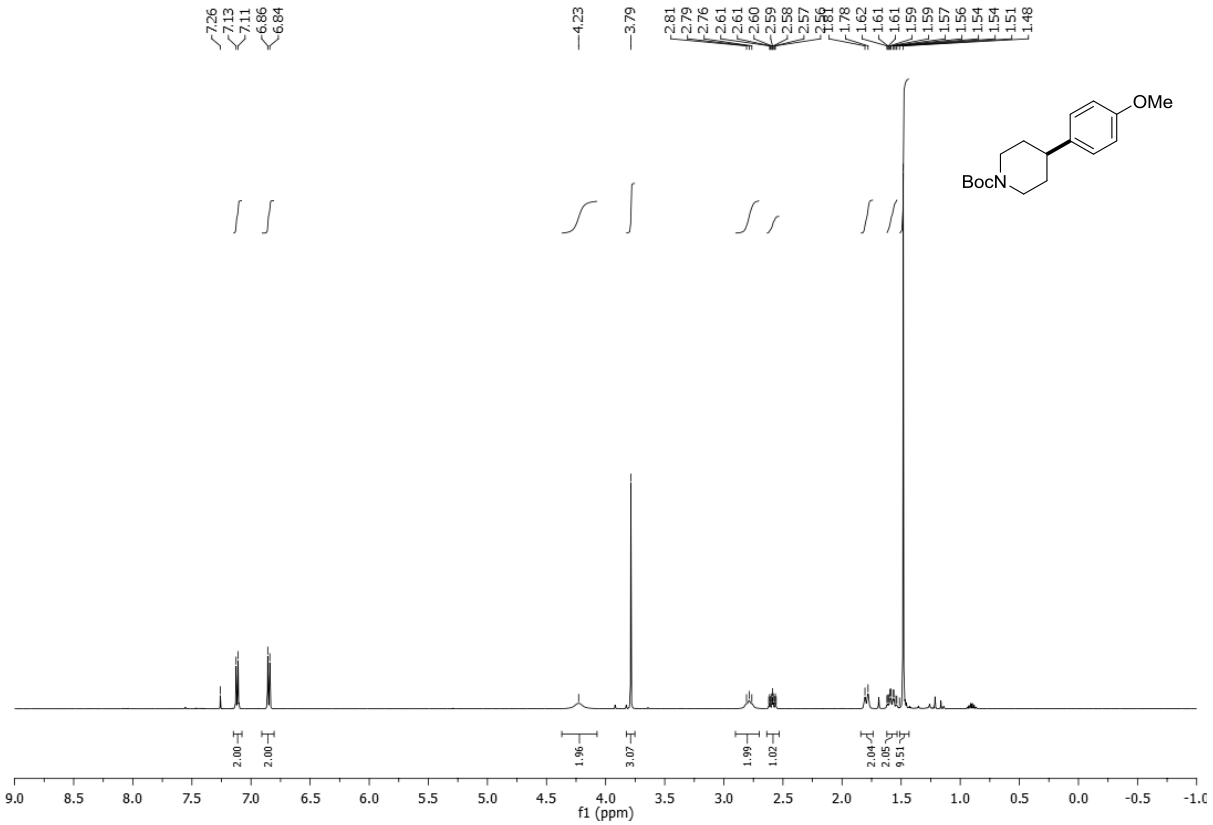

$^{1}$H NMR of Compound 11i



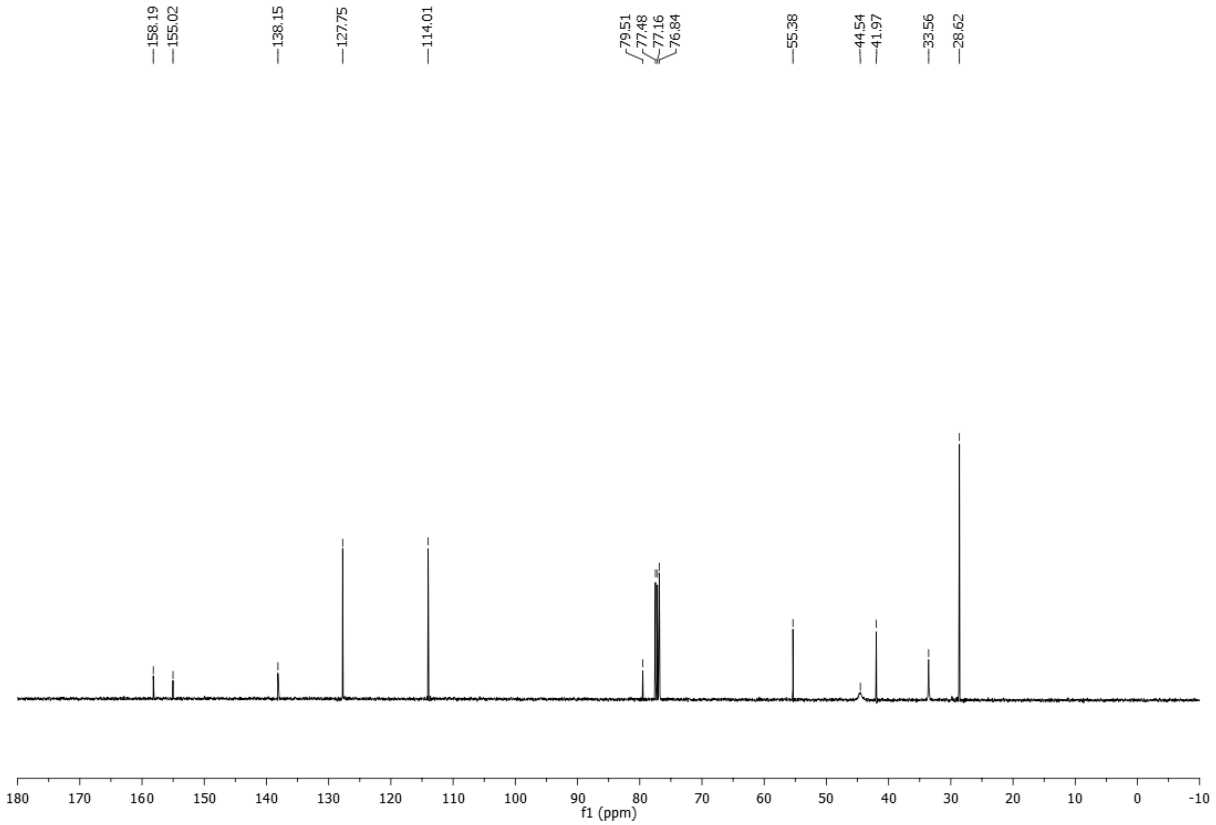
$^{13}$C NMR of Compound 11i



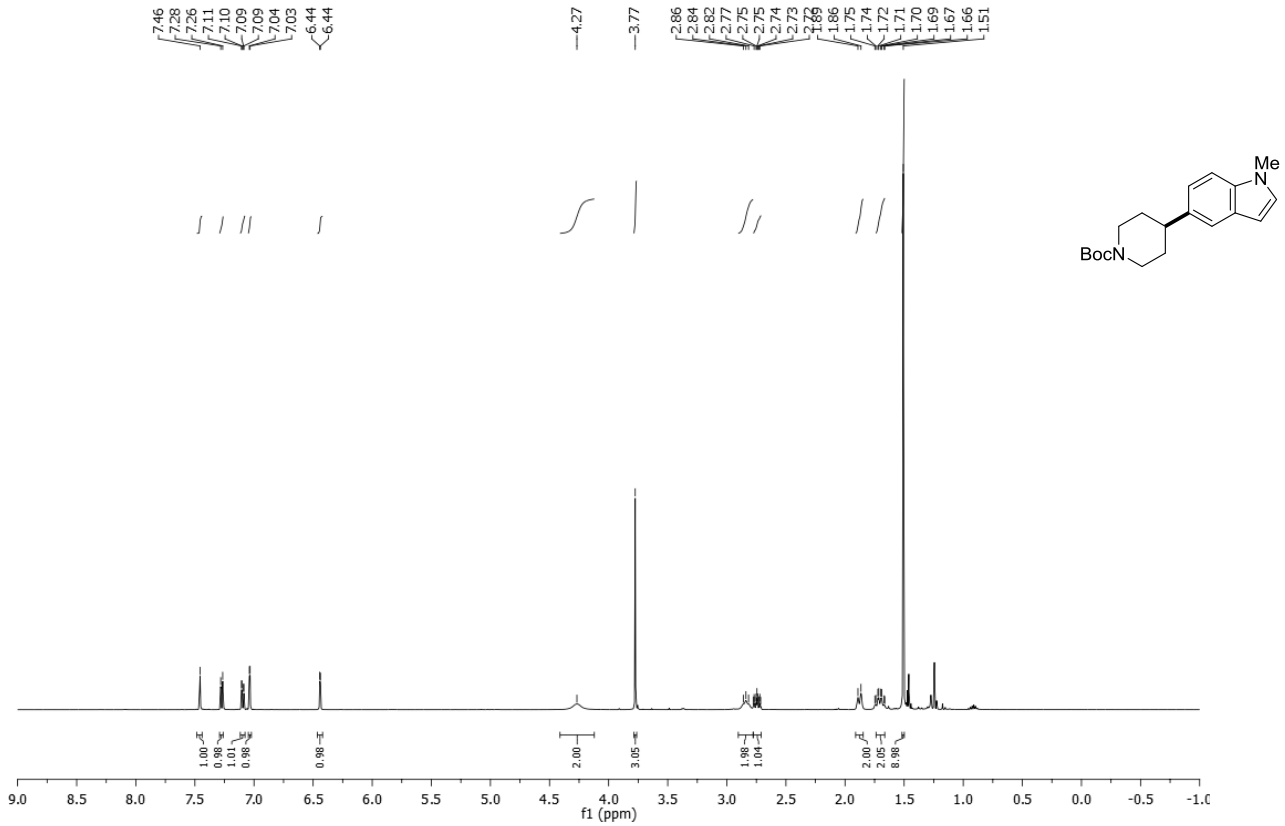

$^{1}$H NMR of Compound 11j



$^{13}$C NMR of Compound 11j




$^{1}$H NMR of Compound 11k



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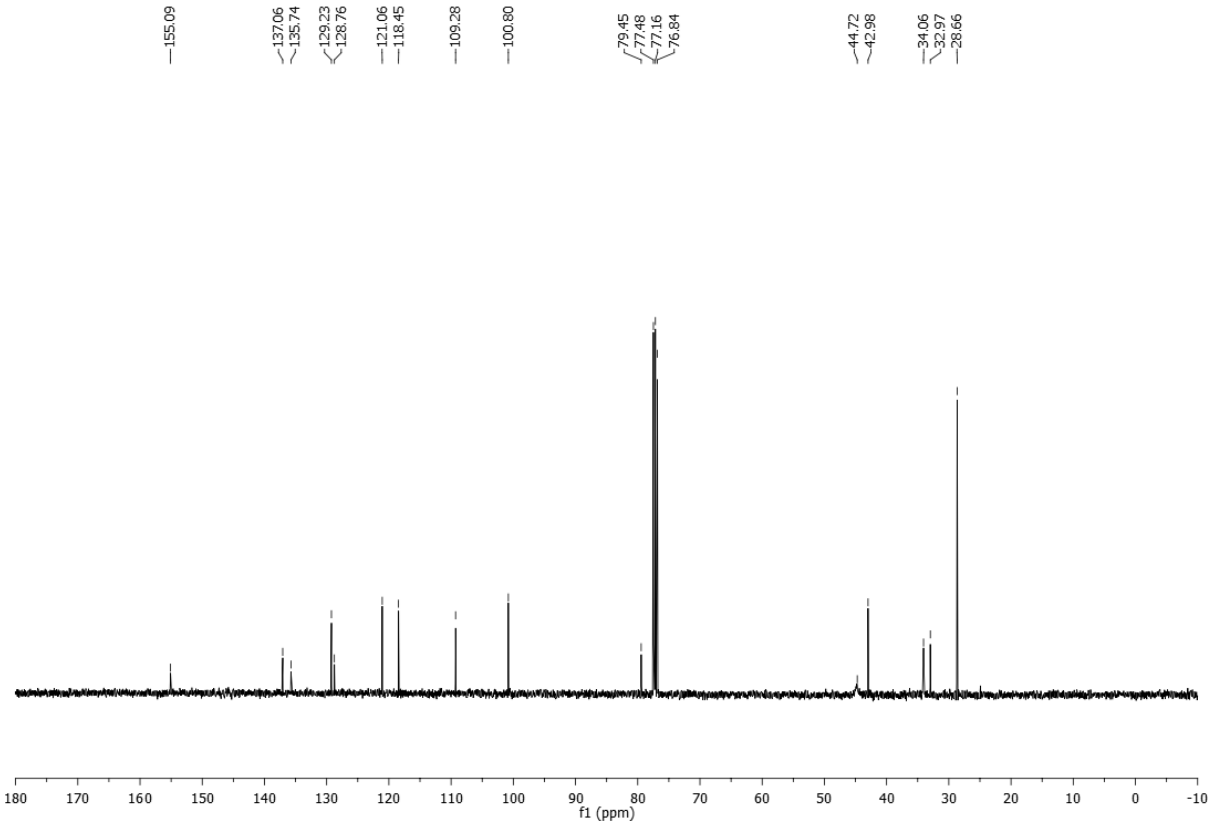


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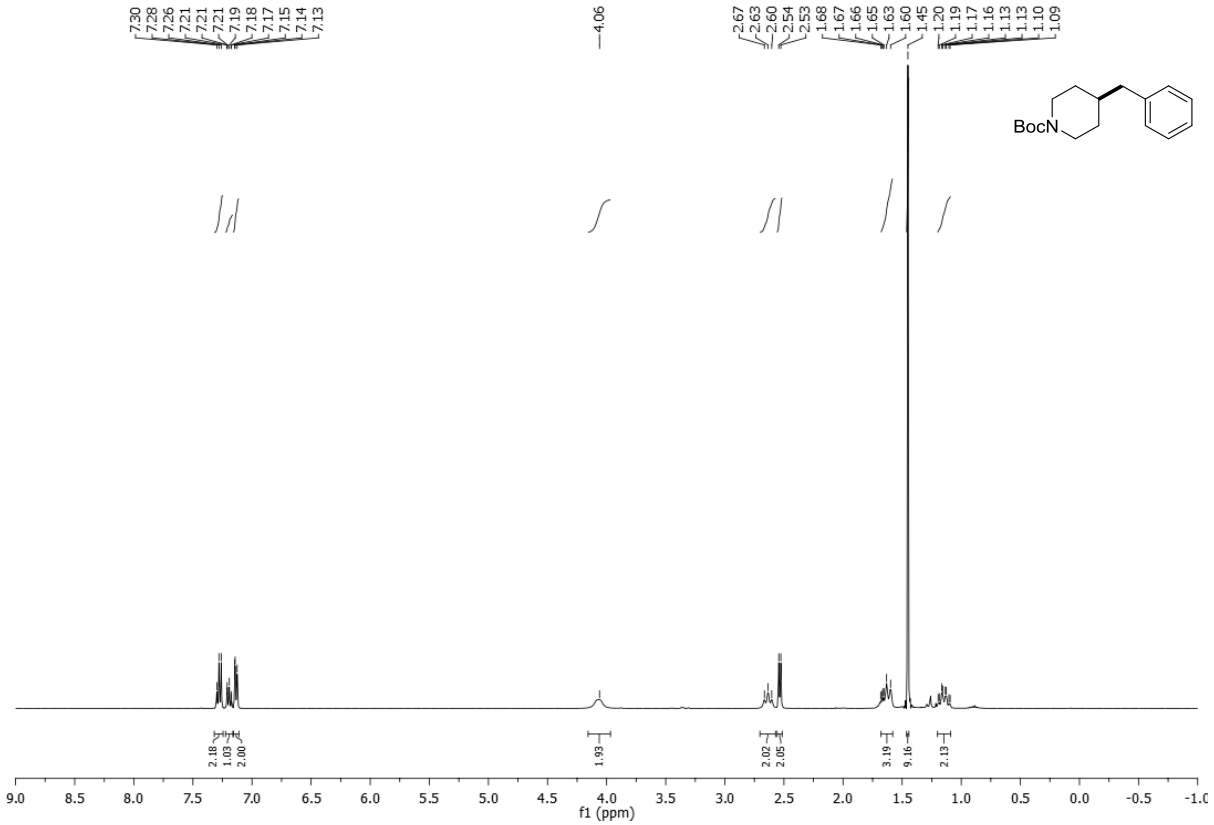
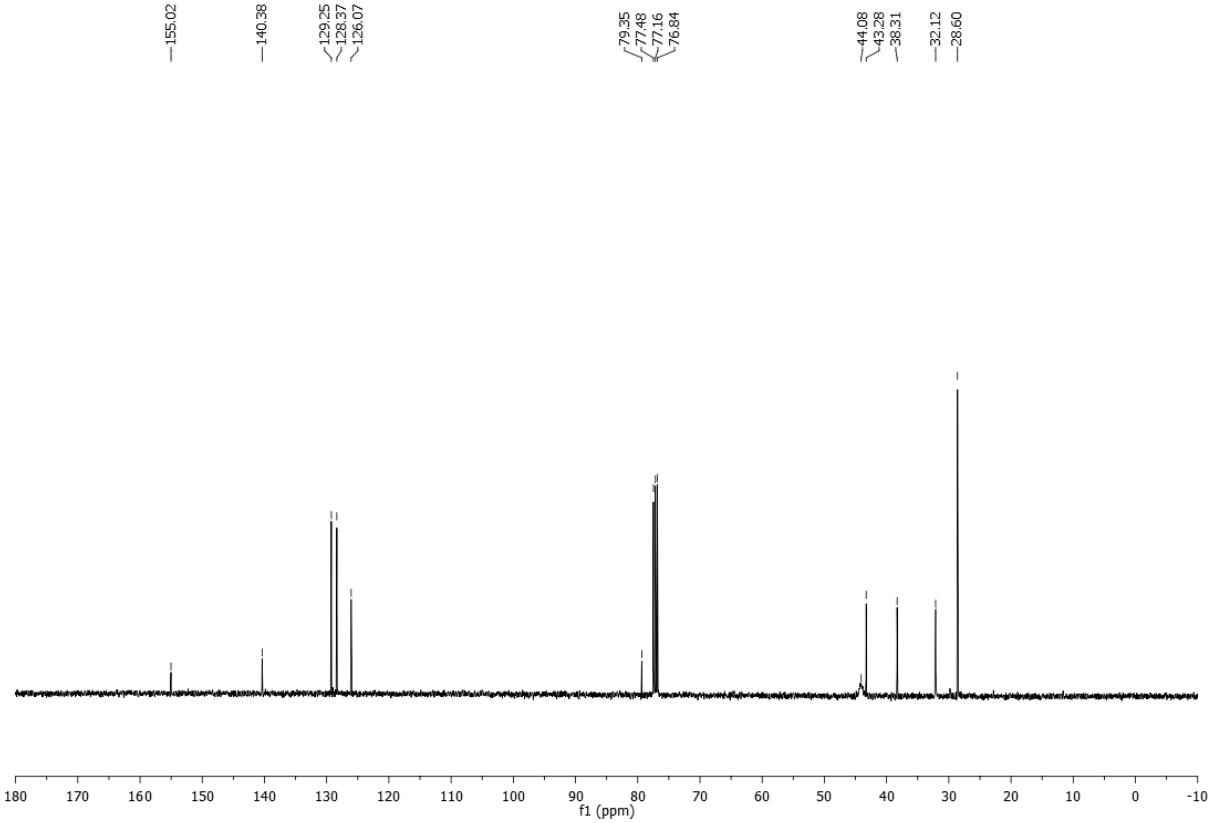
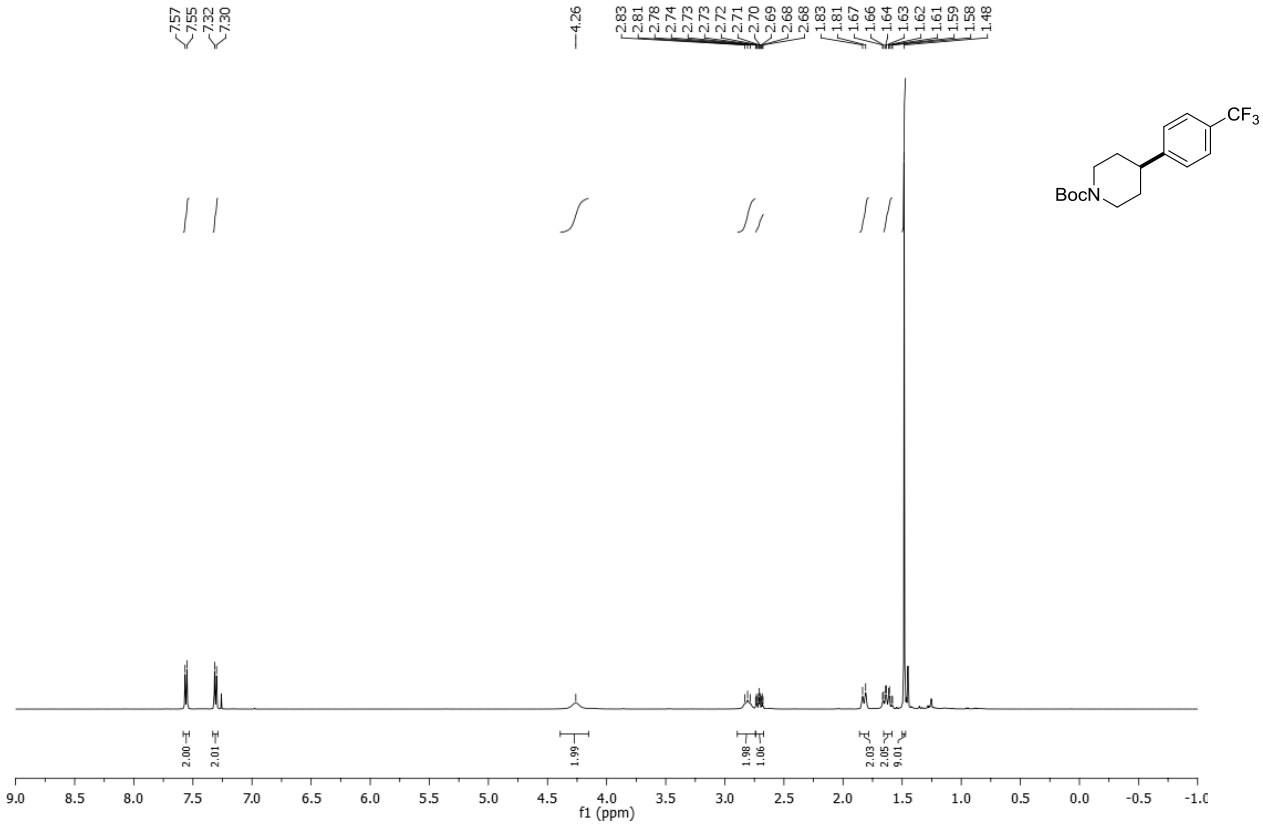


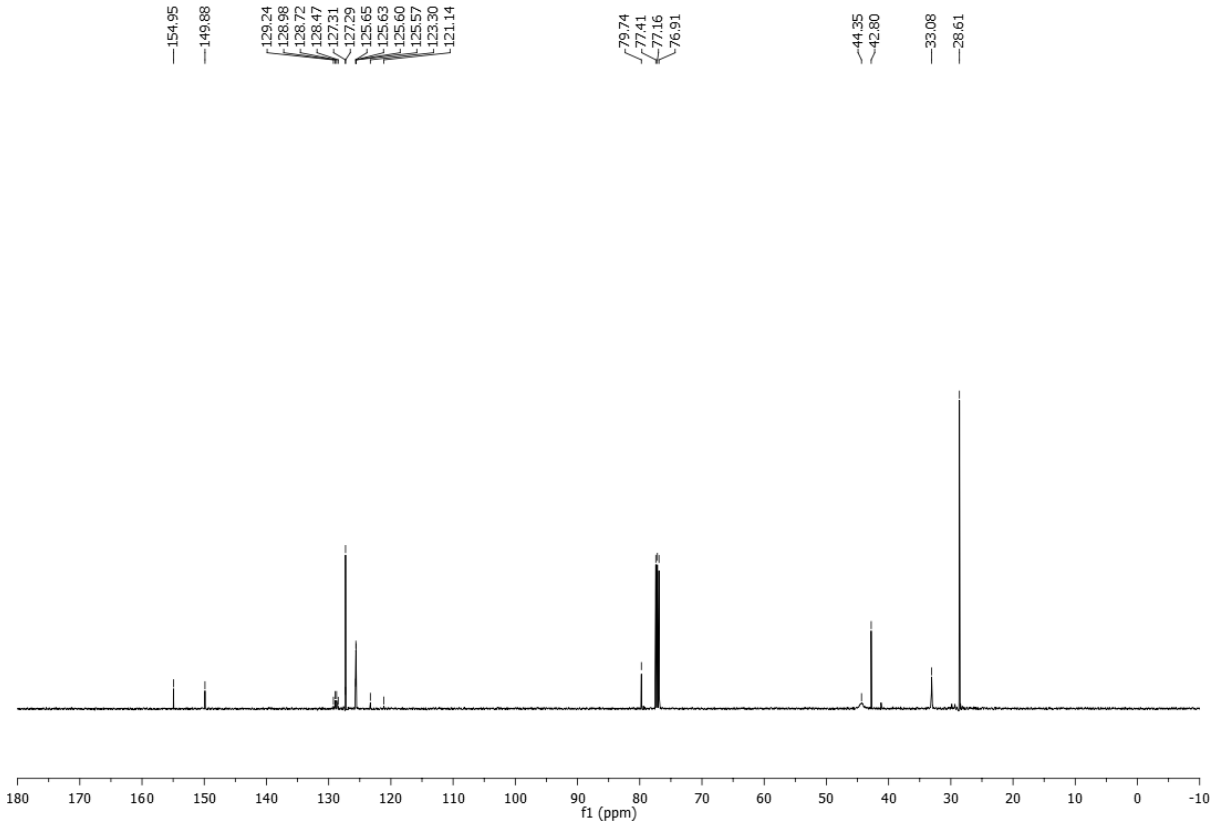
$^{13}$C NMR of Compound 11l



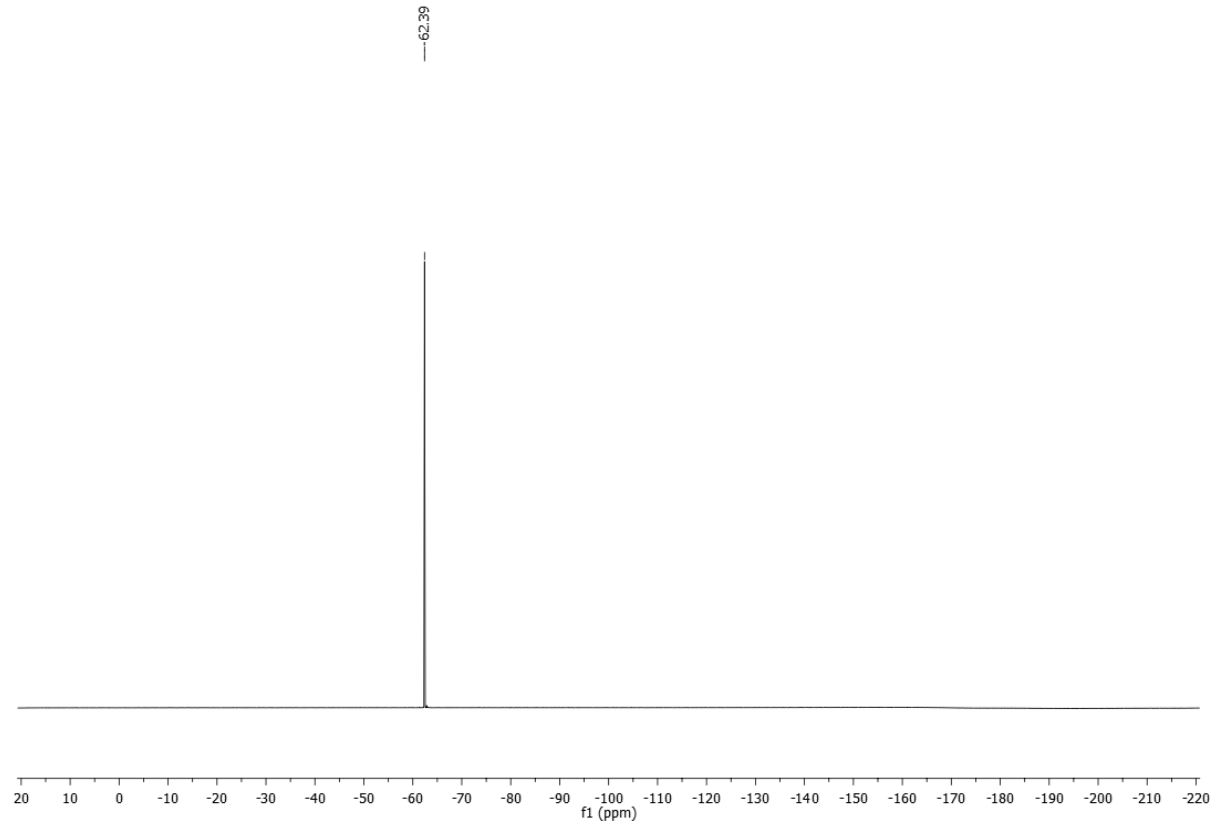

$^{1}$H NMR of Compound 11m



$^{13}$C NMR of Compound 11m




$^{19}$F NMR of Compound 11m



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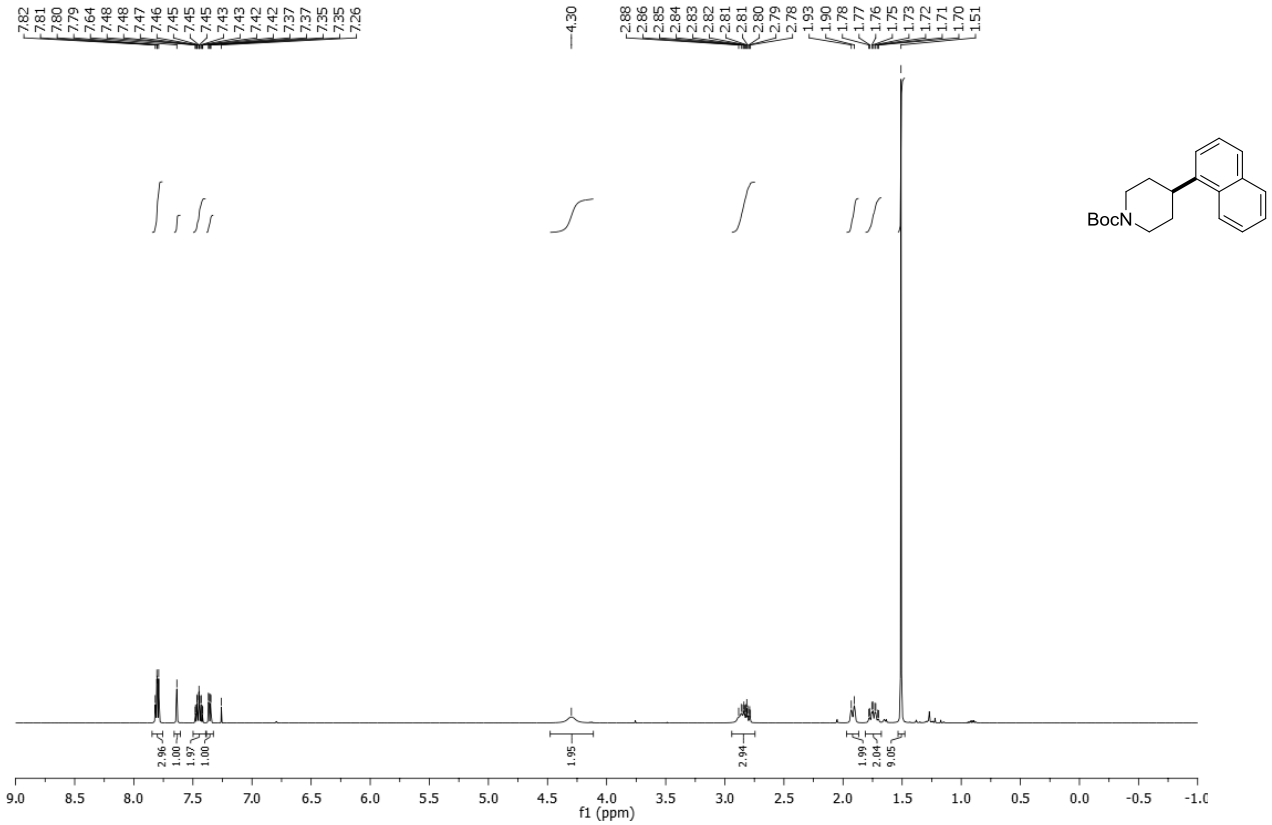


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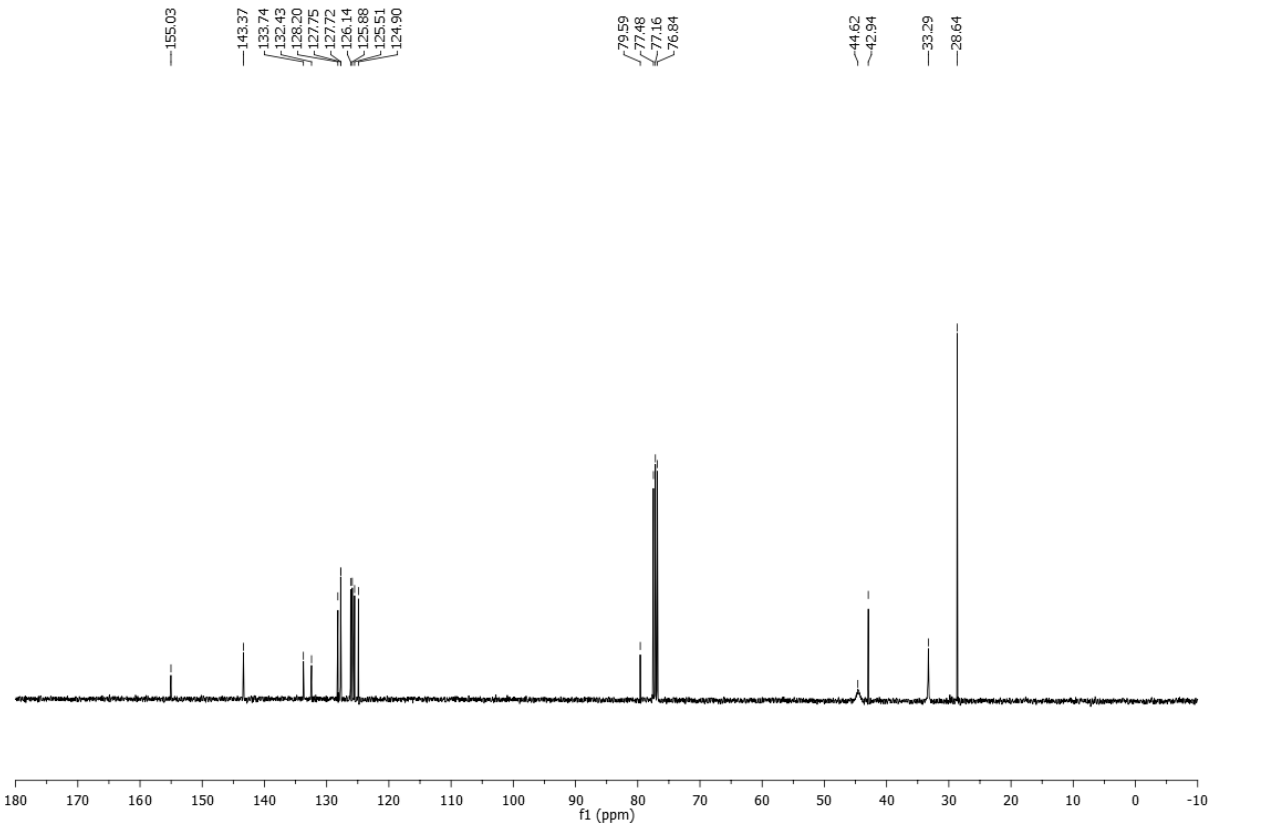
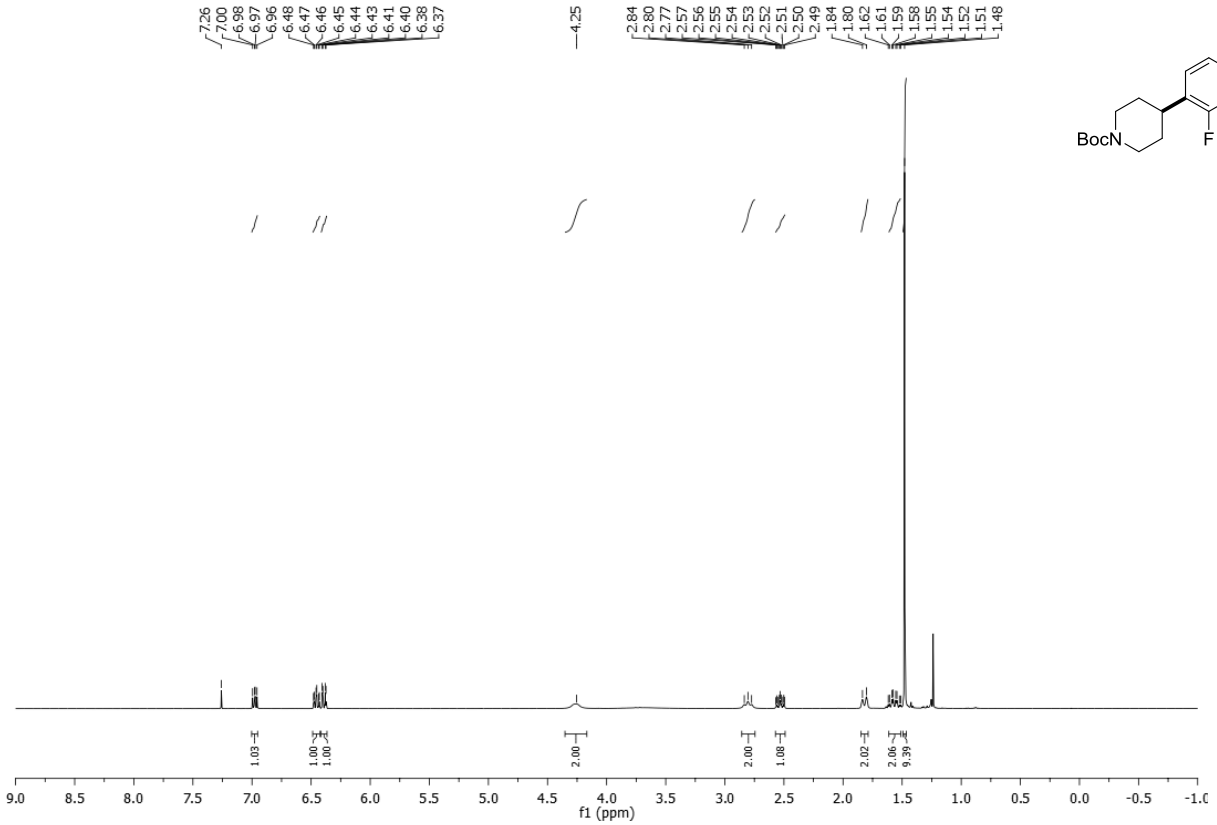


$^{1}$H NMR of Compound 11o

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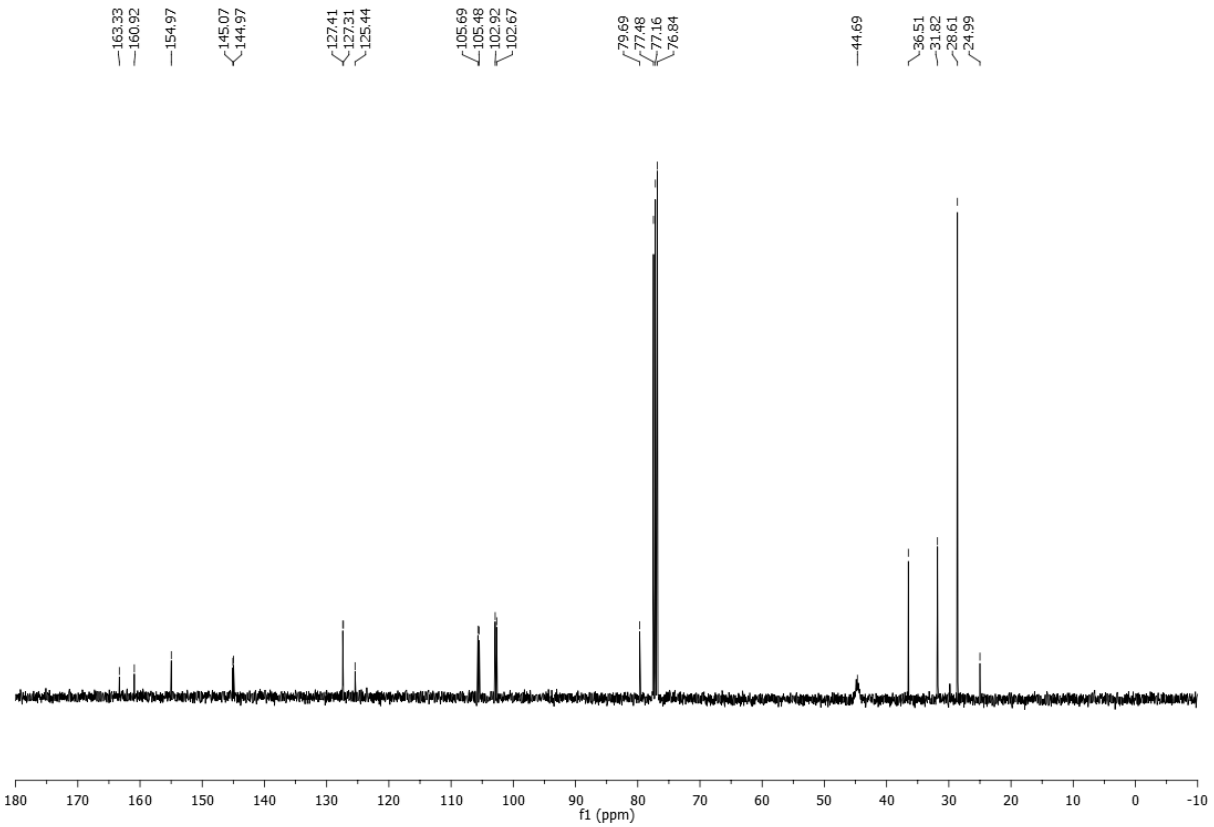

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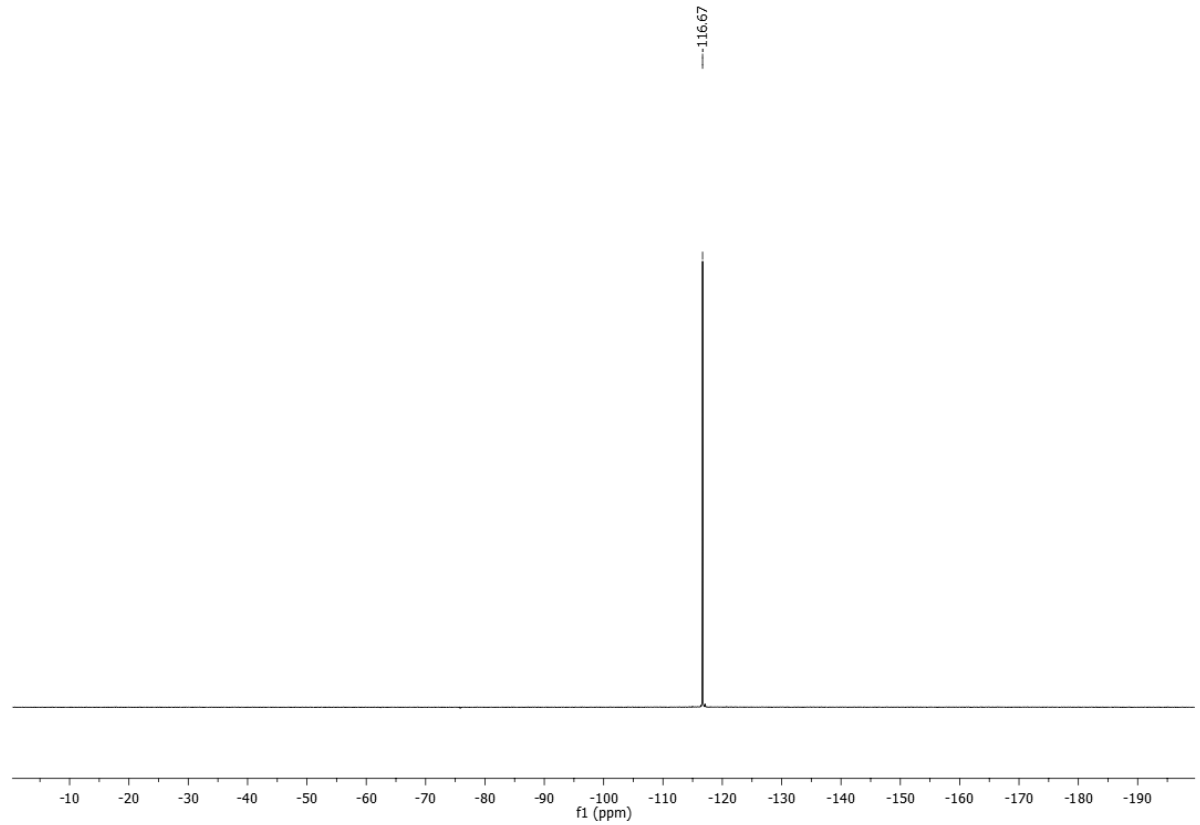
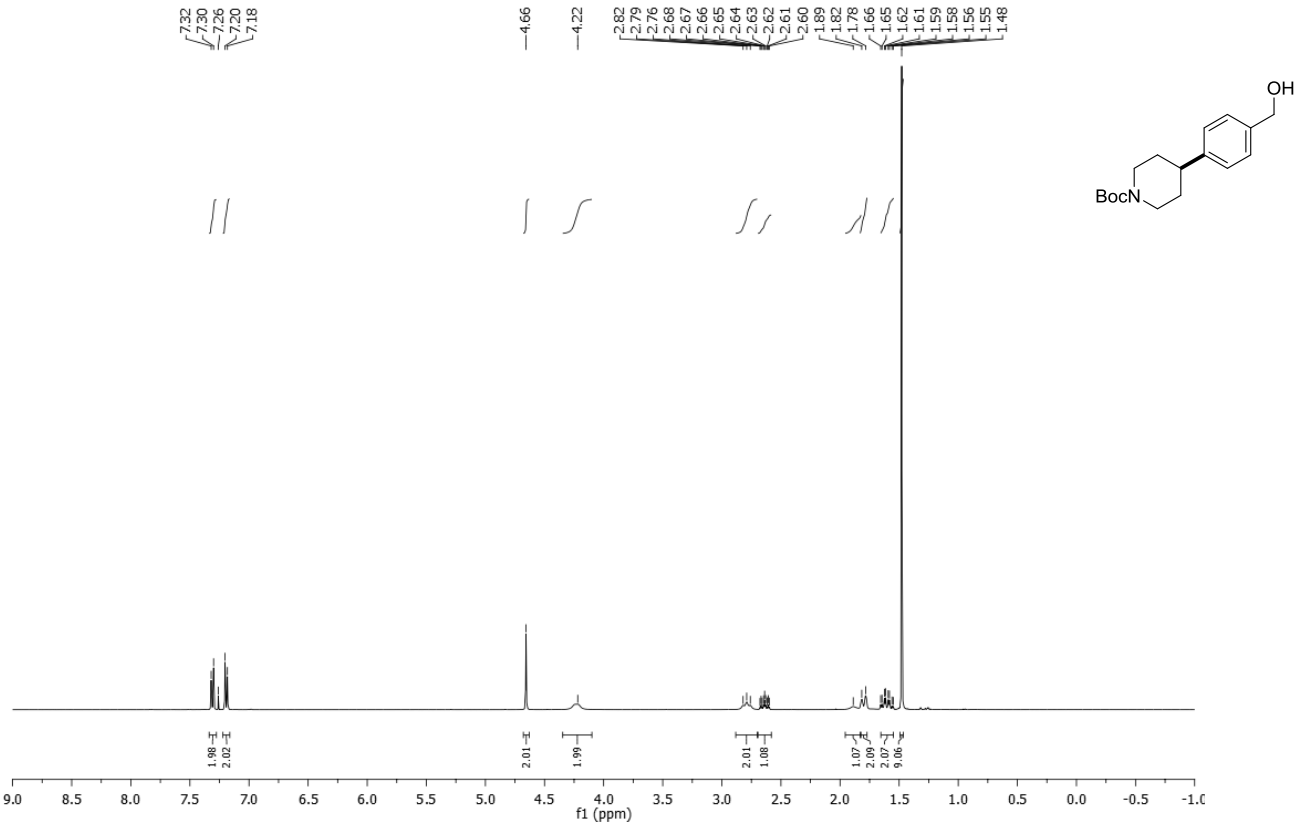
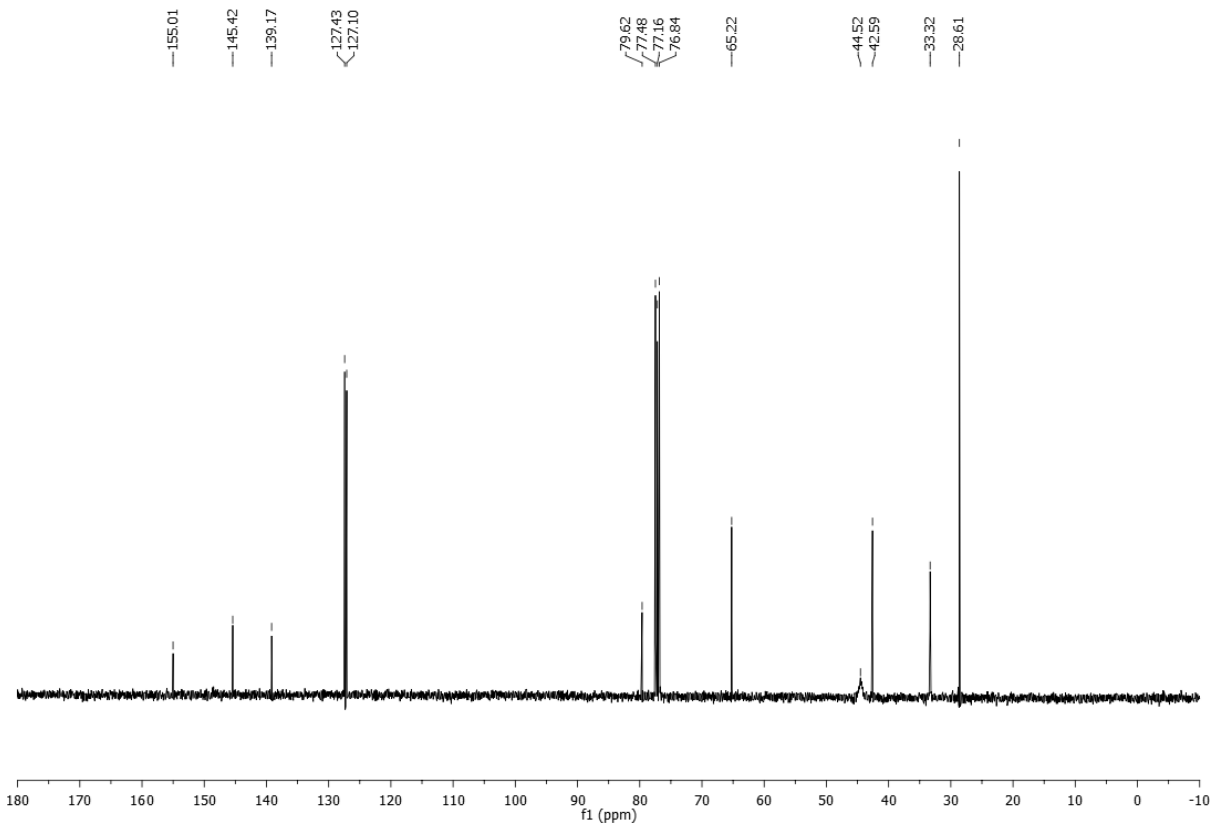


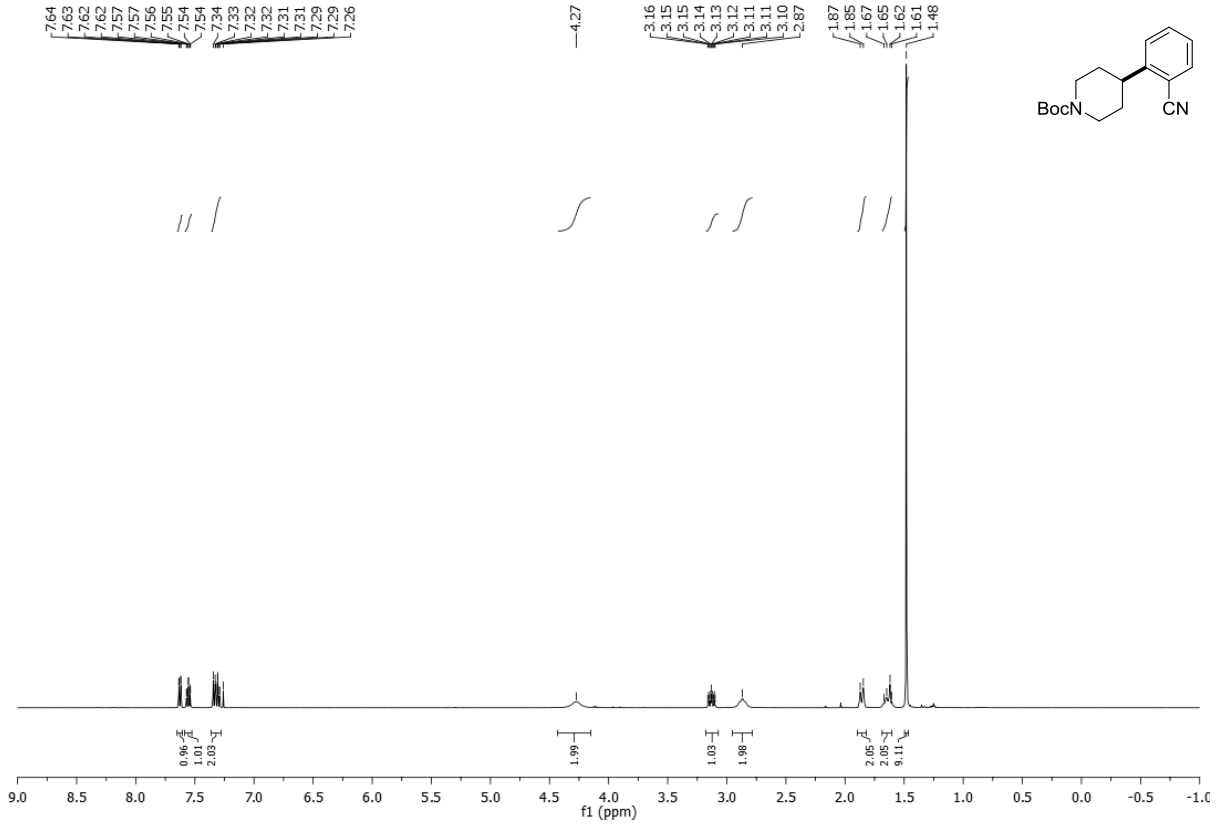

$^{1}$H NMR of Compound 11p



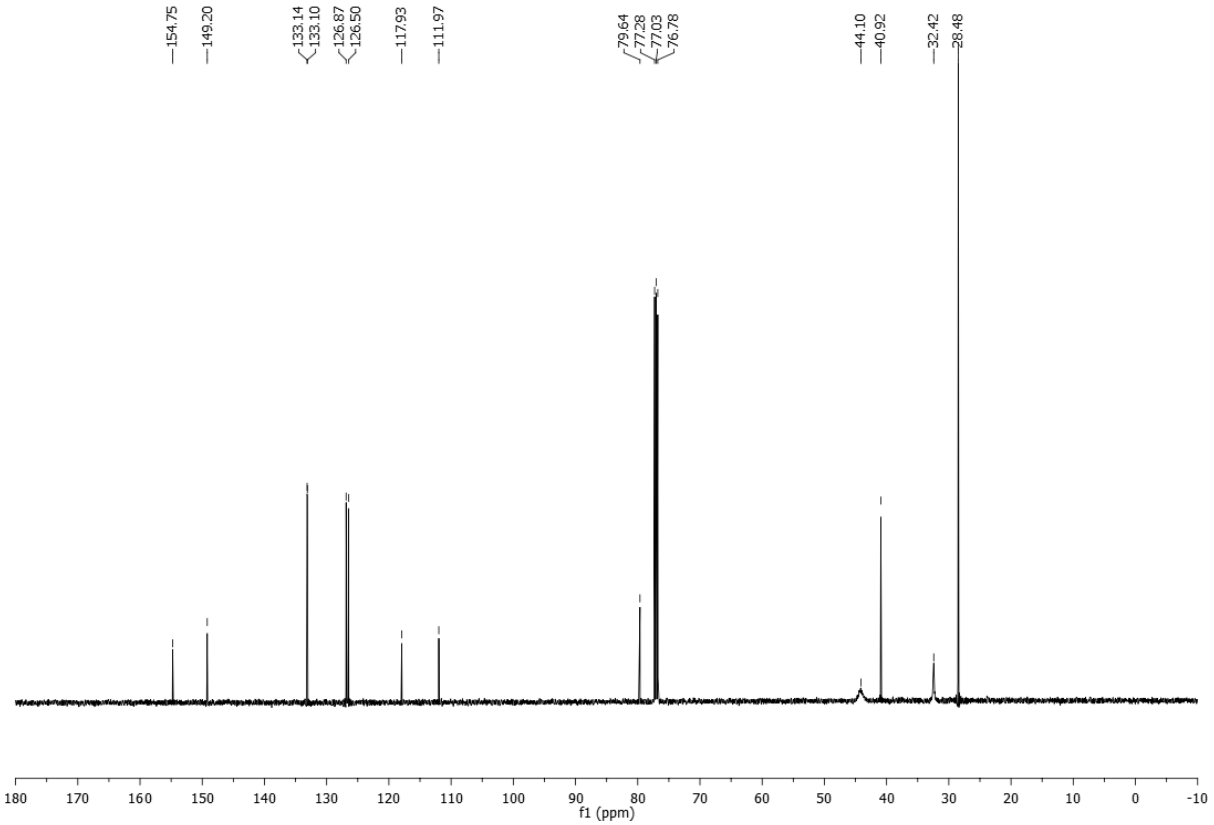

$^{13}$C NMR of Compound 11p



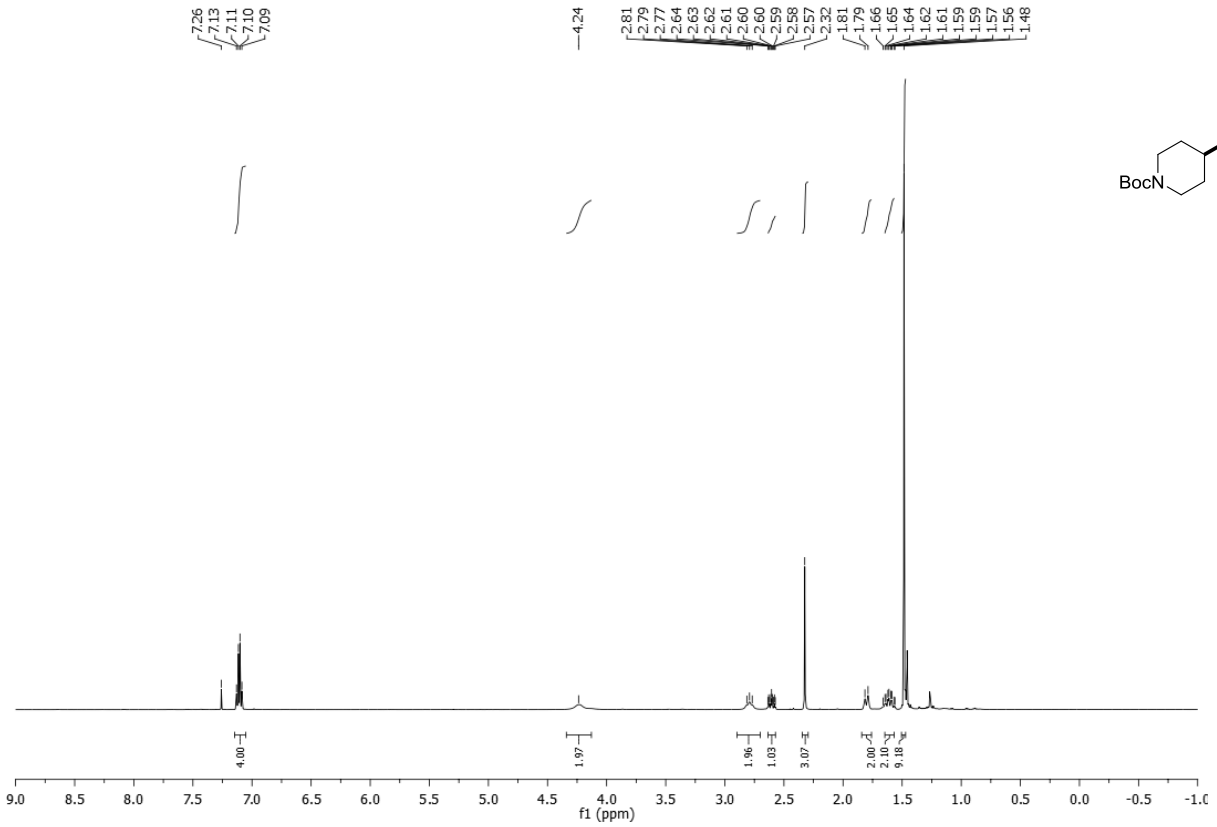

$^{1}$H NMR of Compound 11q

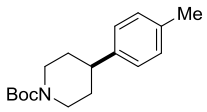


$^{13}$C NMR of Compound 11q




$^{1}$H NMR of Compound 11r



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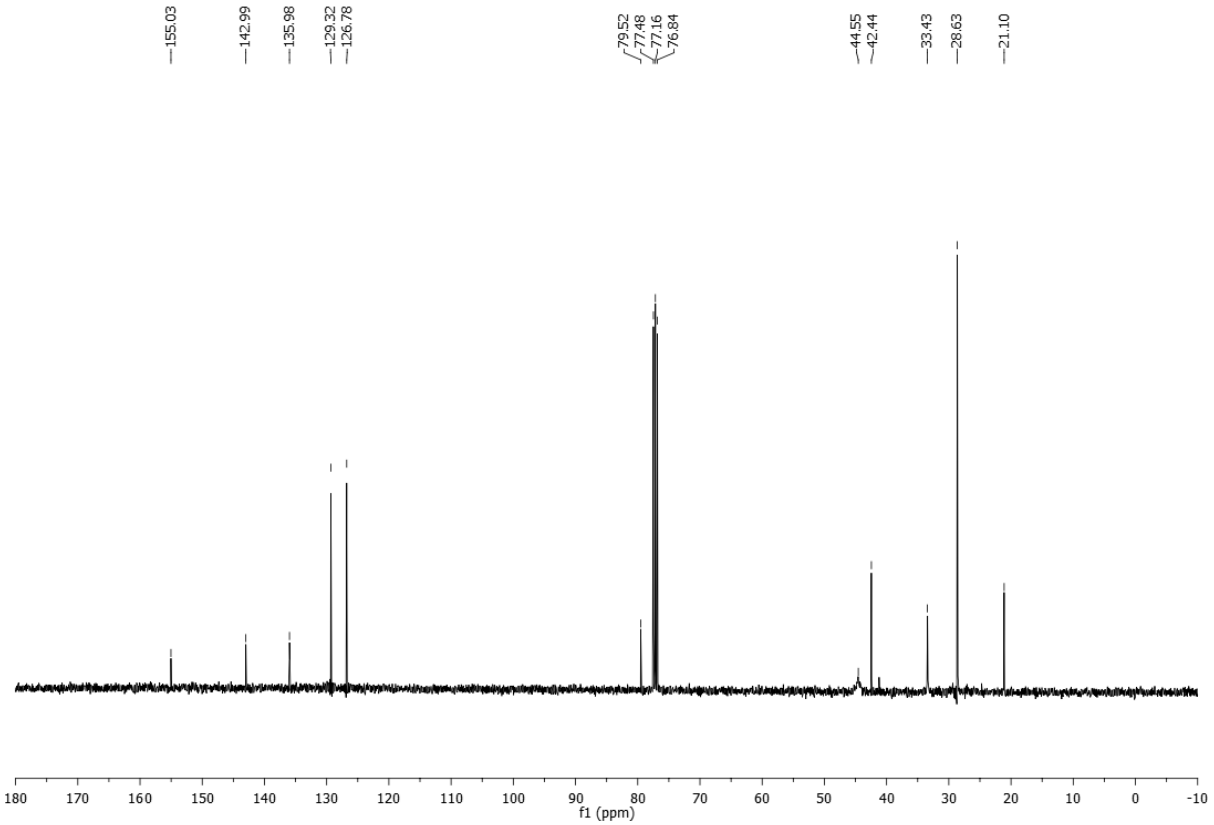
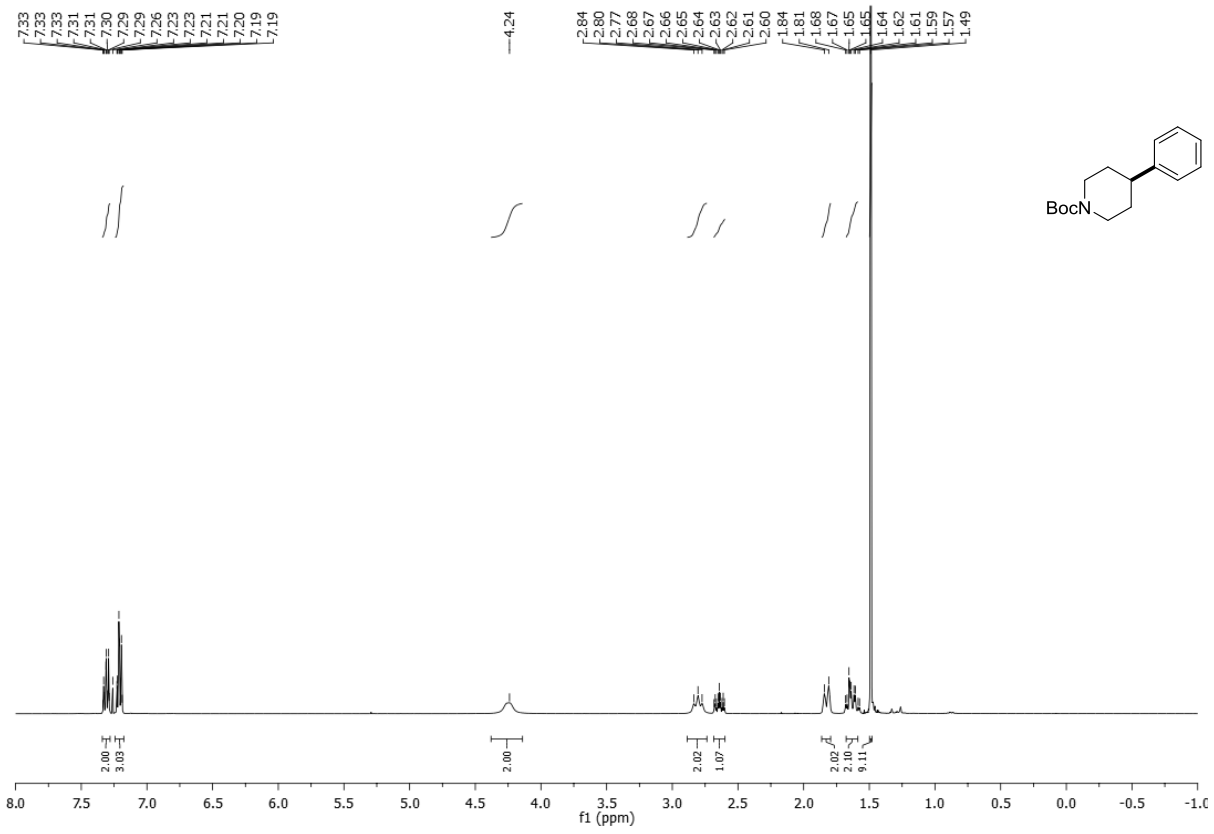



$^{1}$H NMR of Compound 11s



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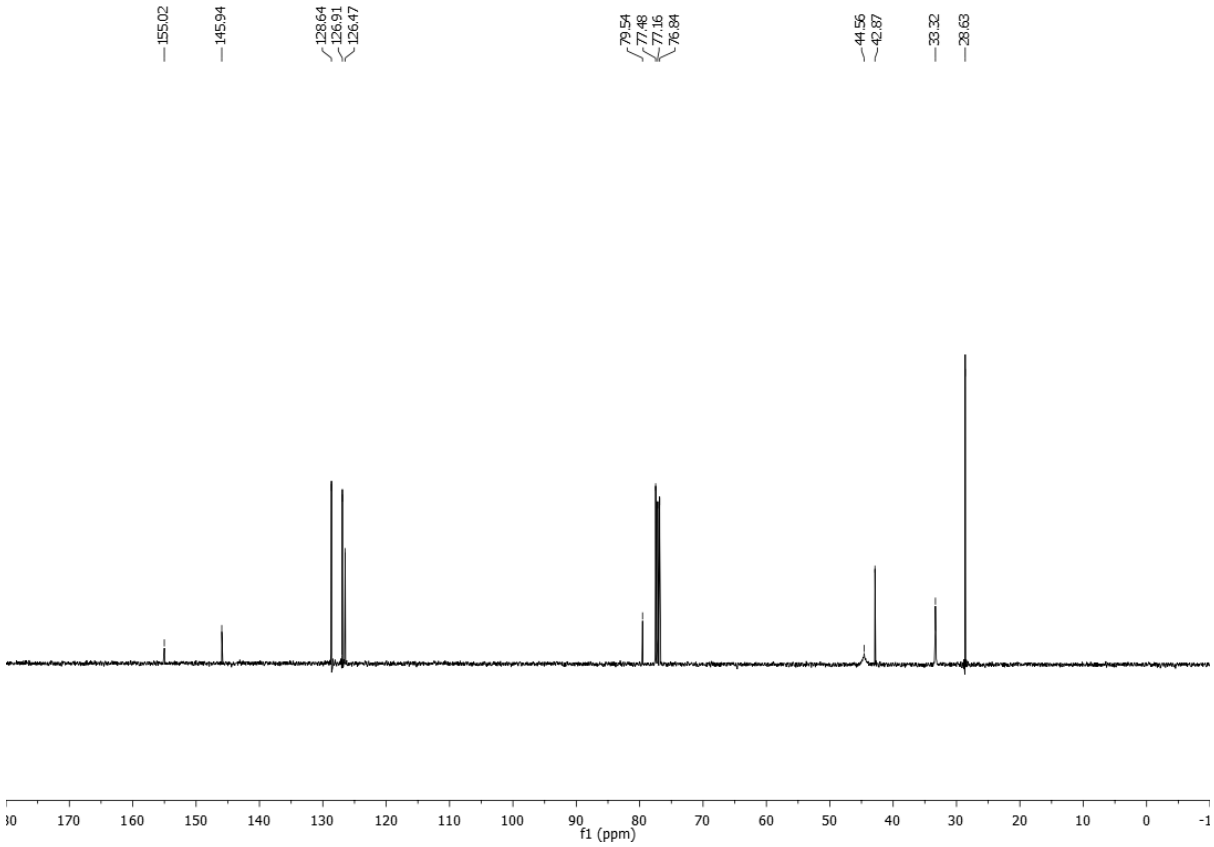
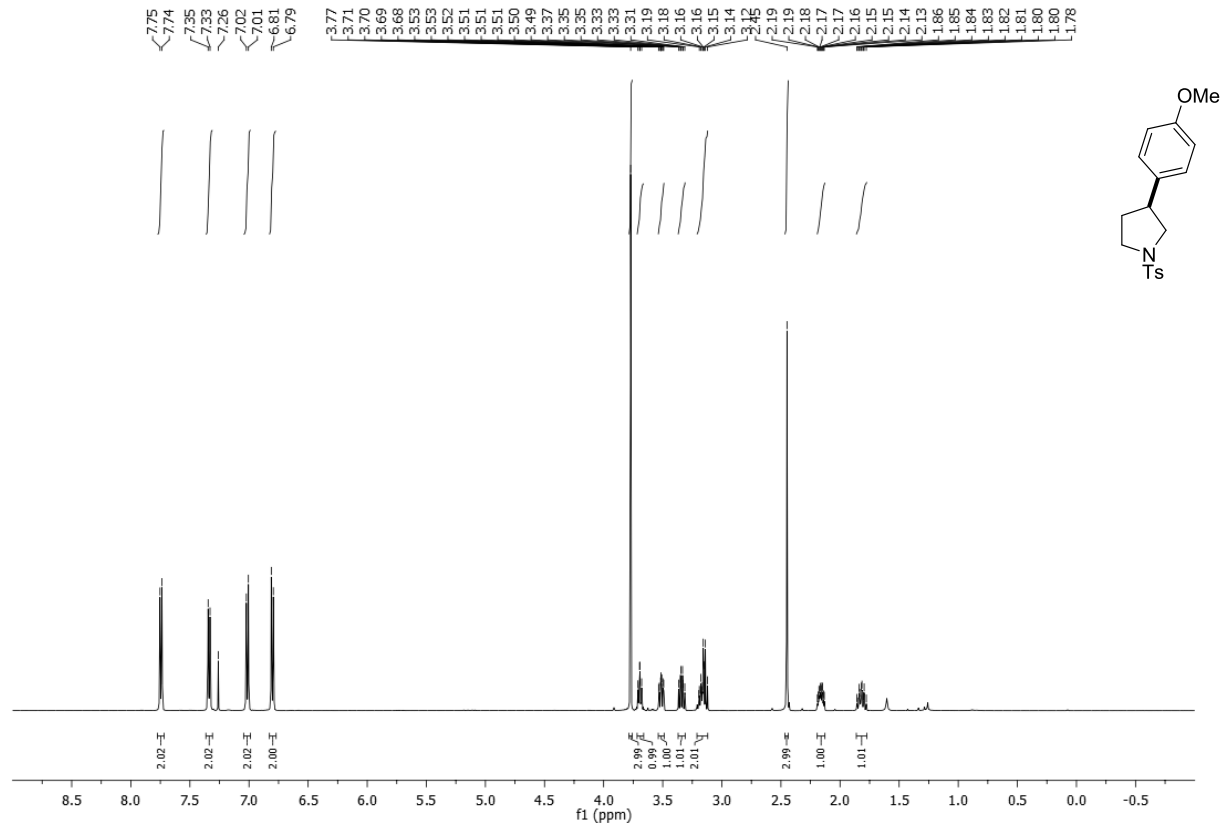



$^{1}$H NMR of Compound 12a

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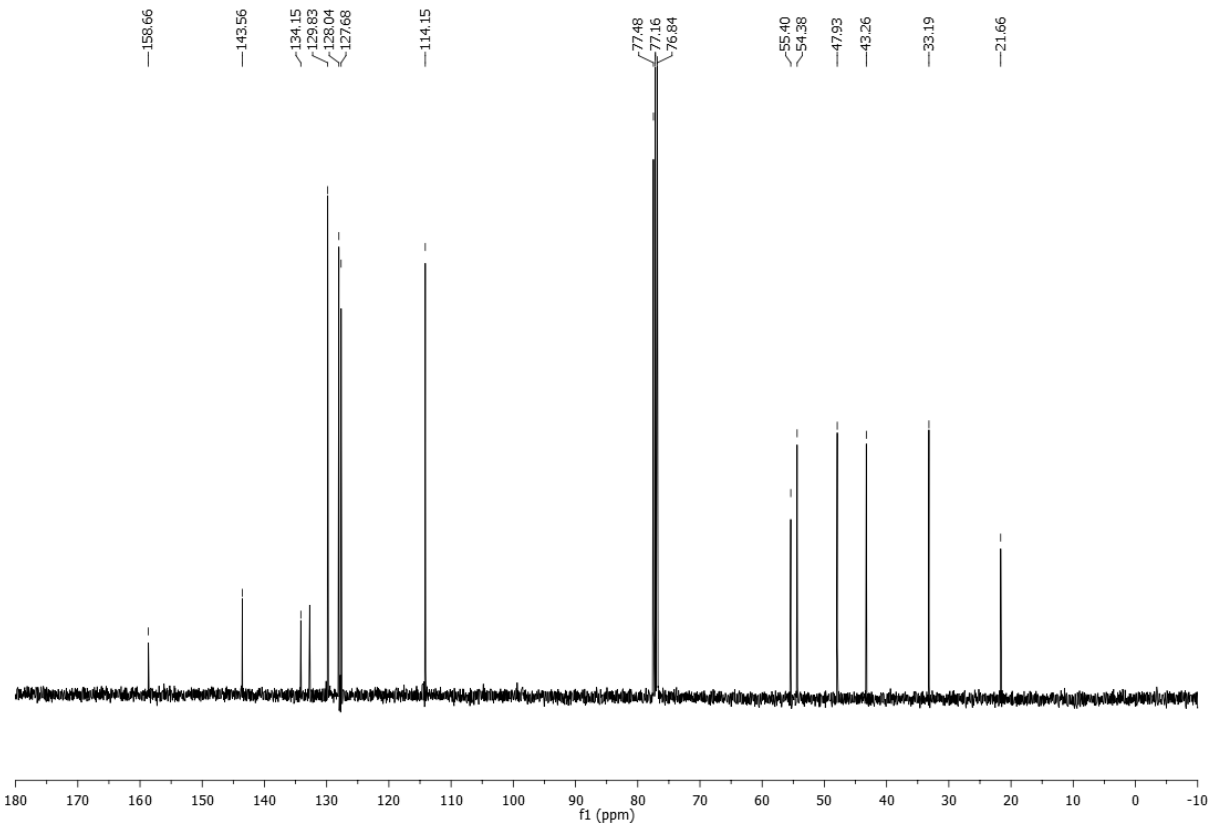
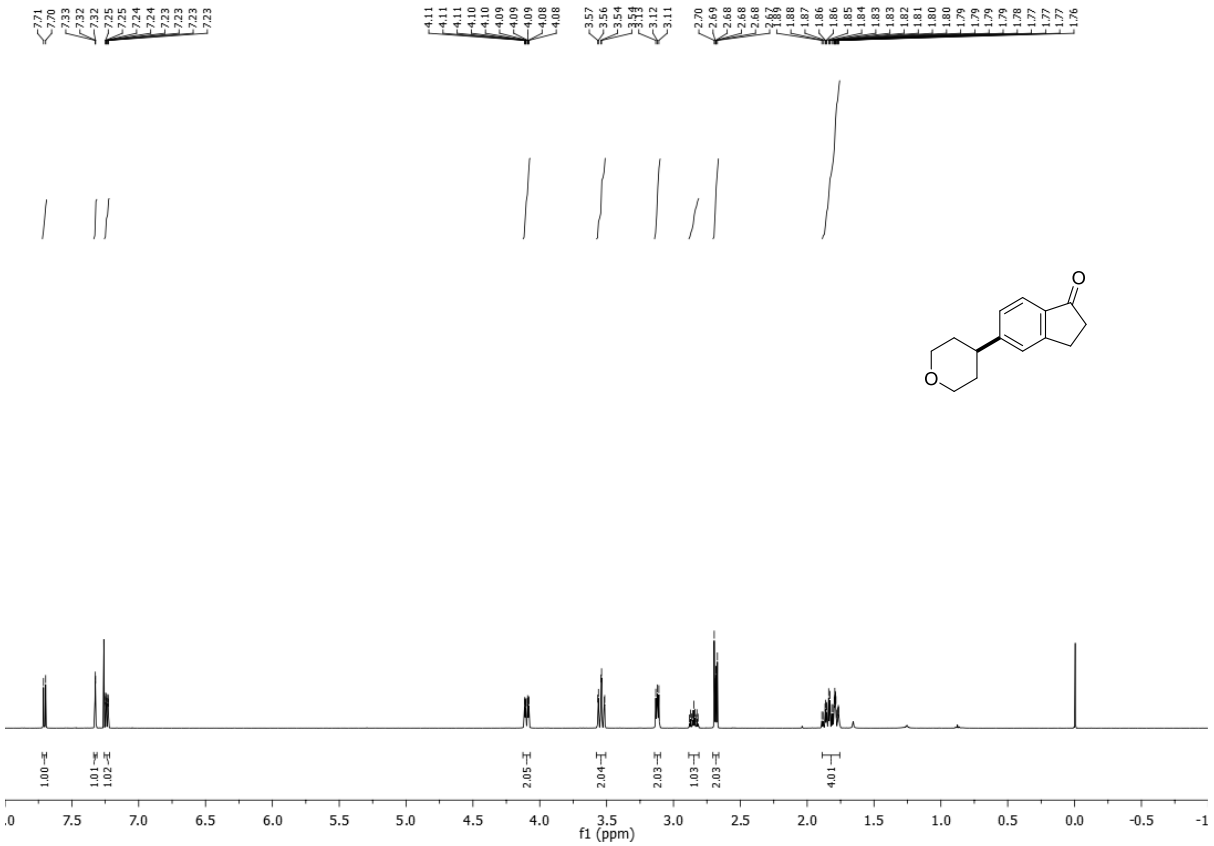
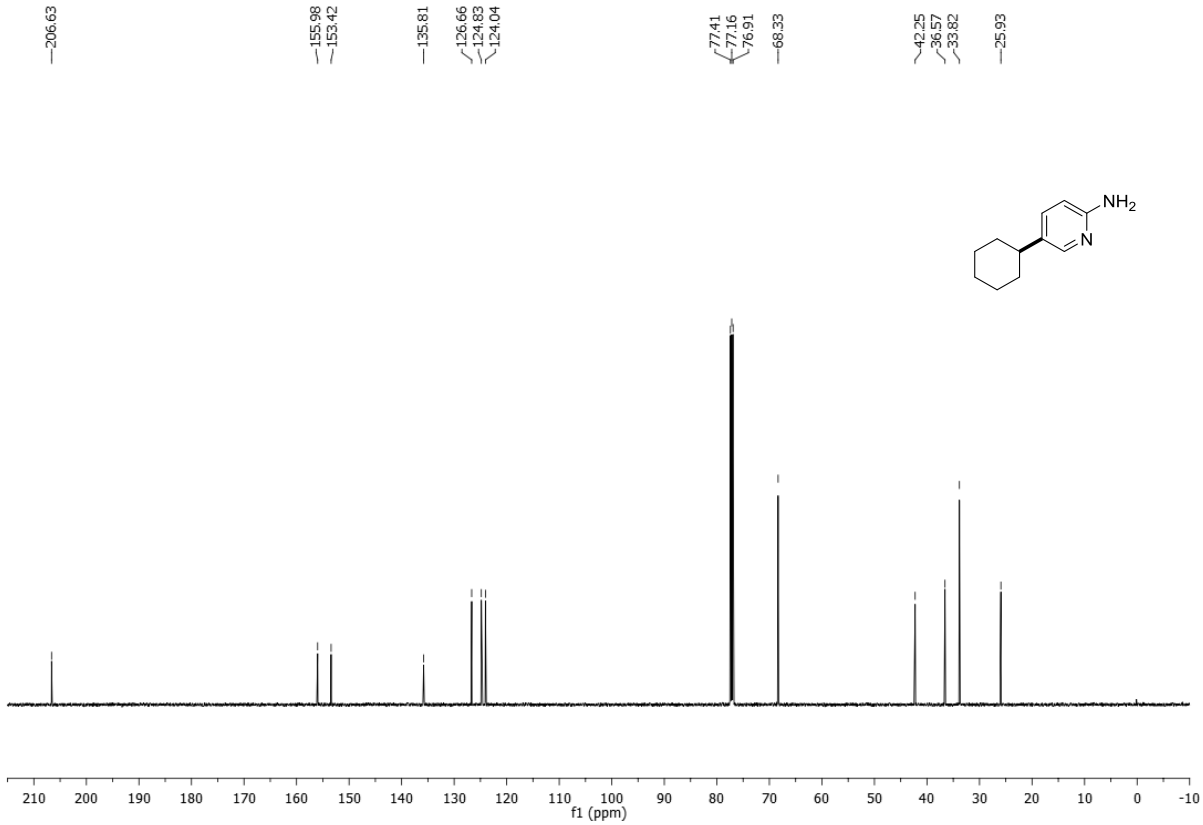


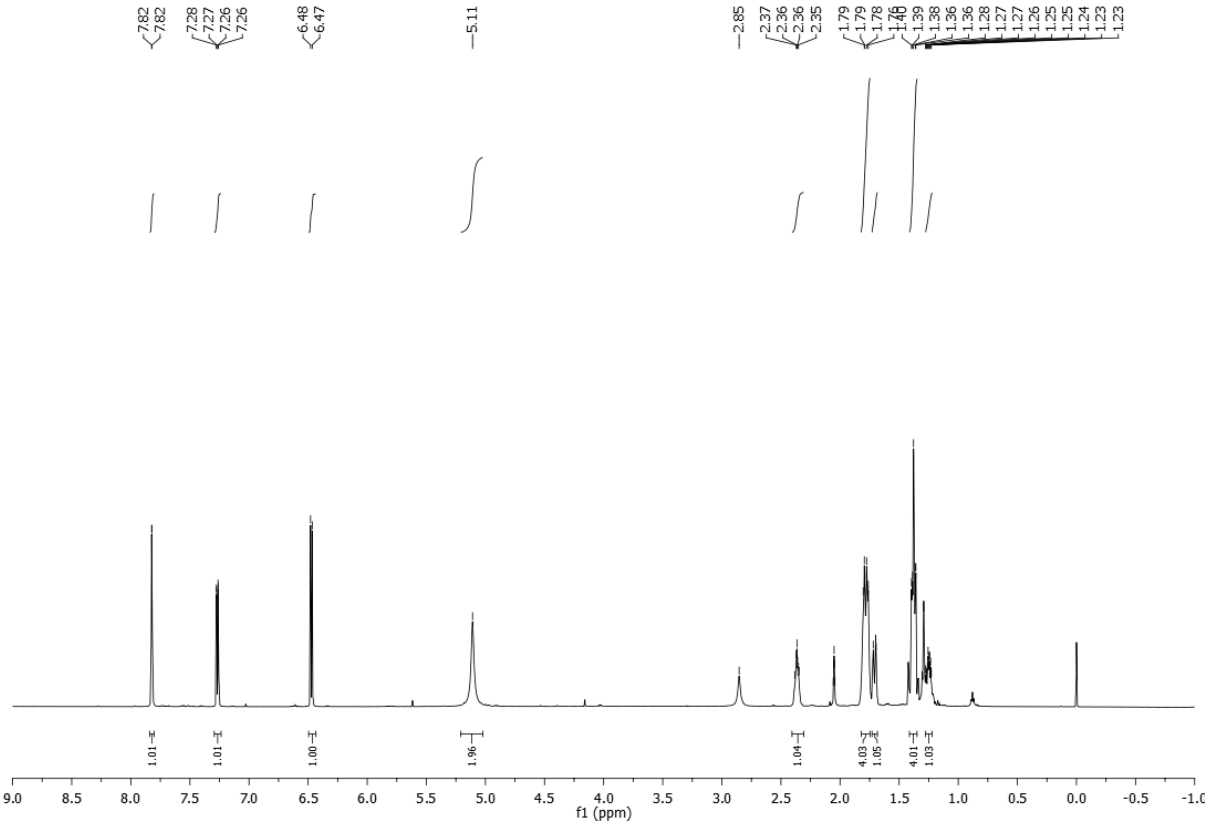

$^{1}$H NMR of Compound 12b



$^{13}$C NMR of Compound 12b




$^{1}$H NMR of Compound 12c



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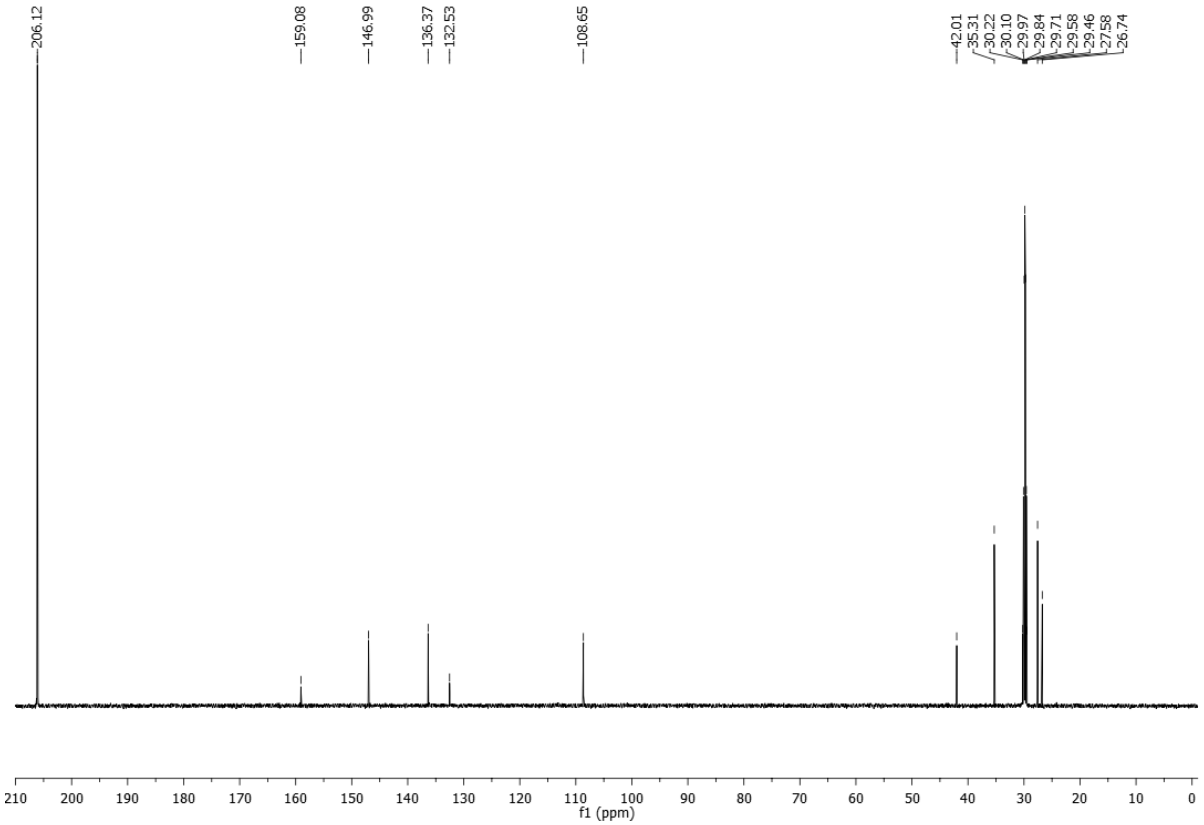
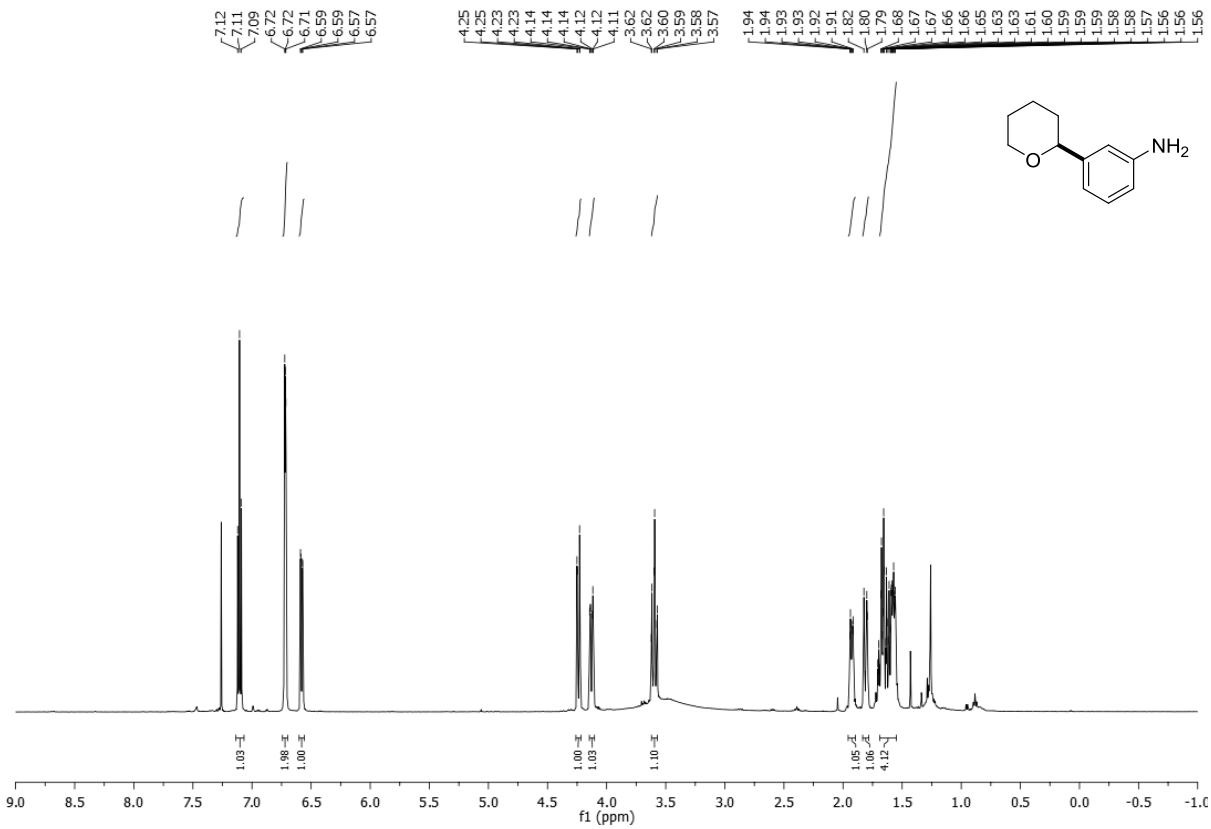



$^{1}$H NMR of Compound 12d



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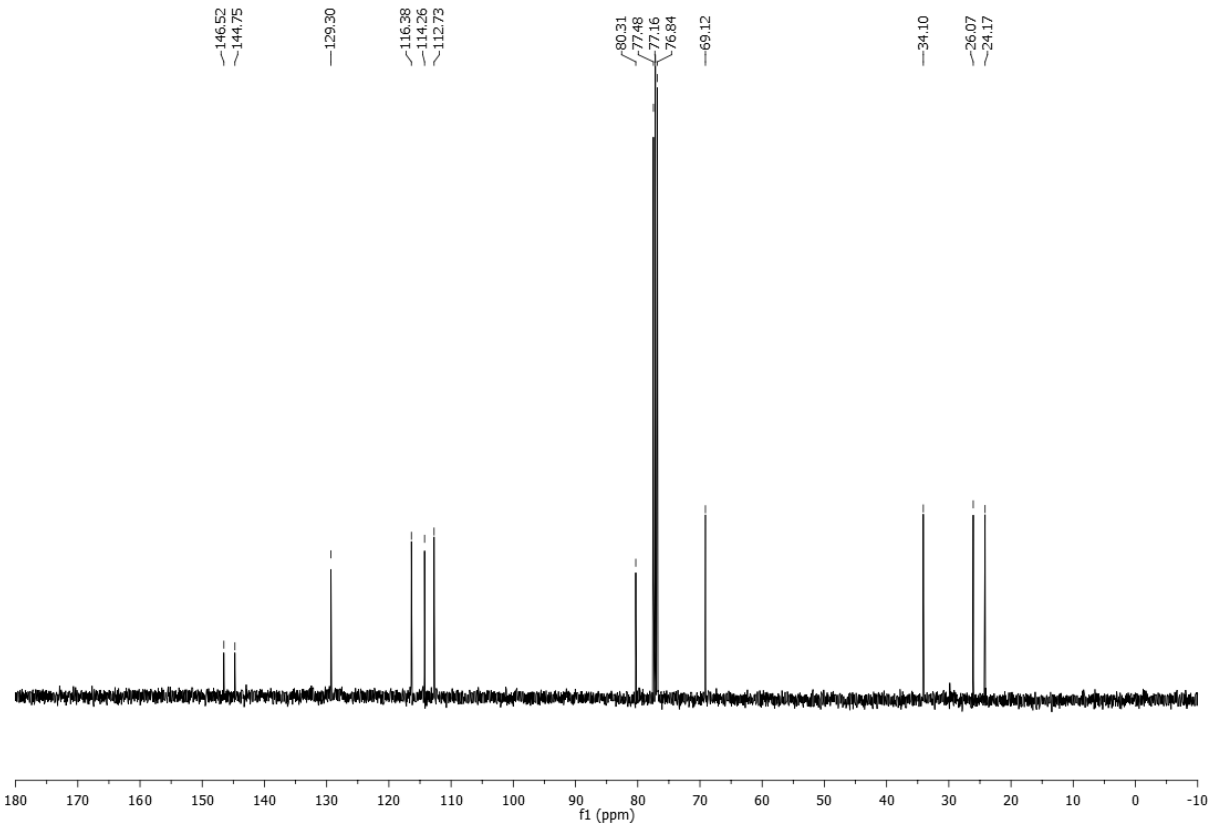


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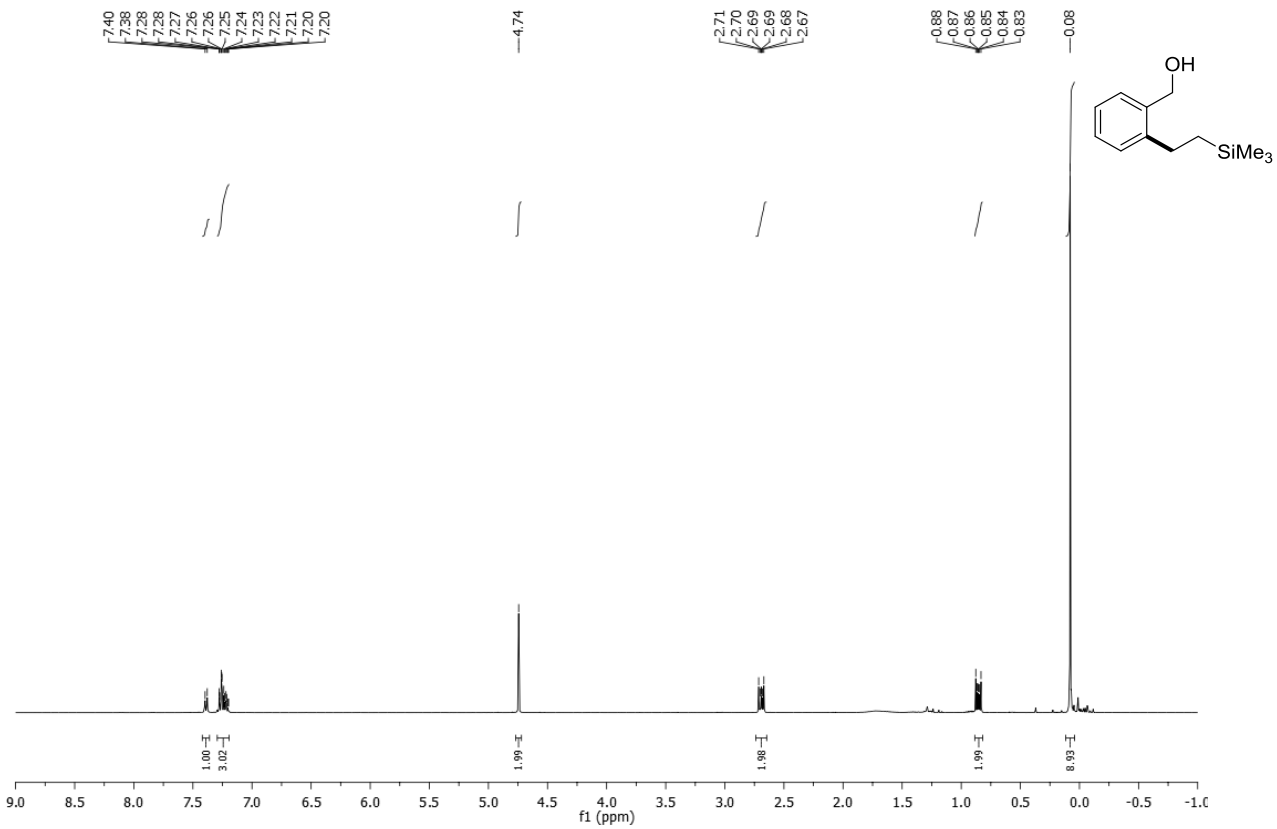

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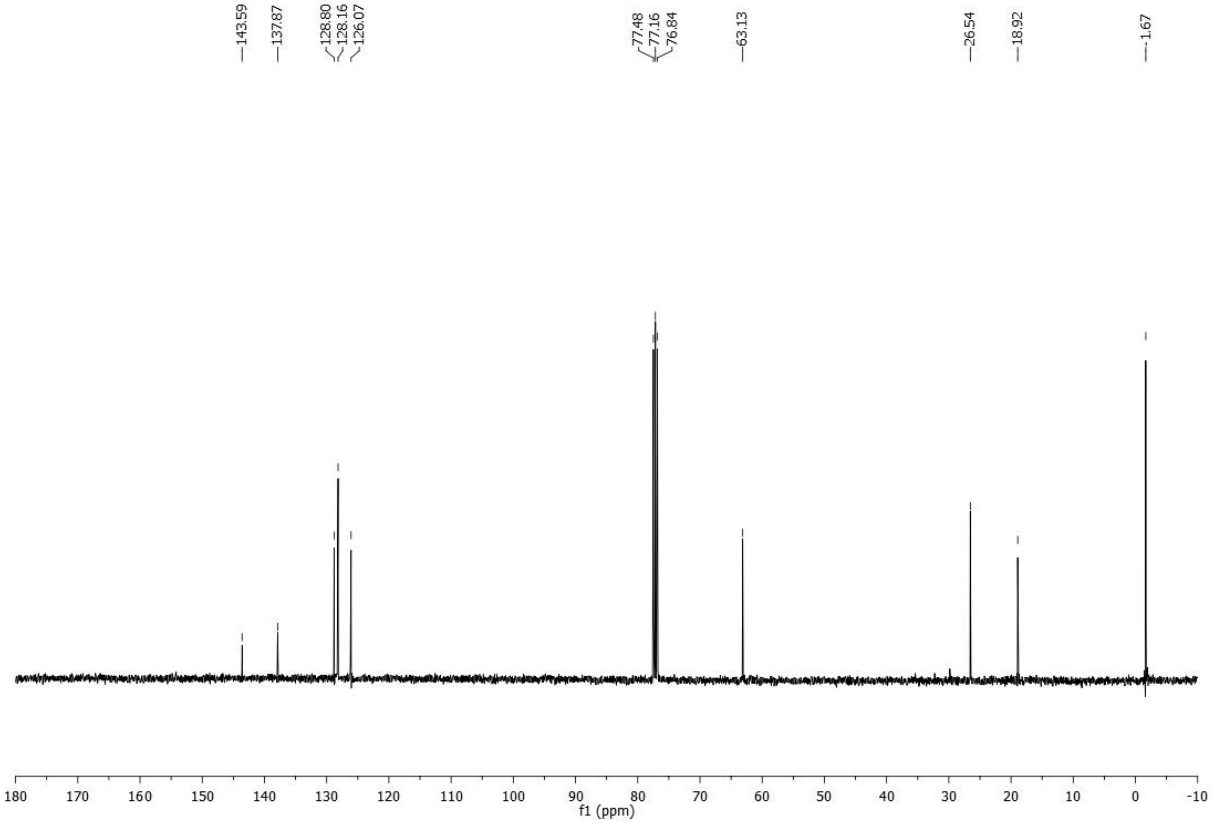
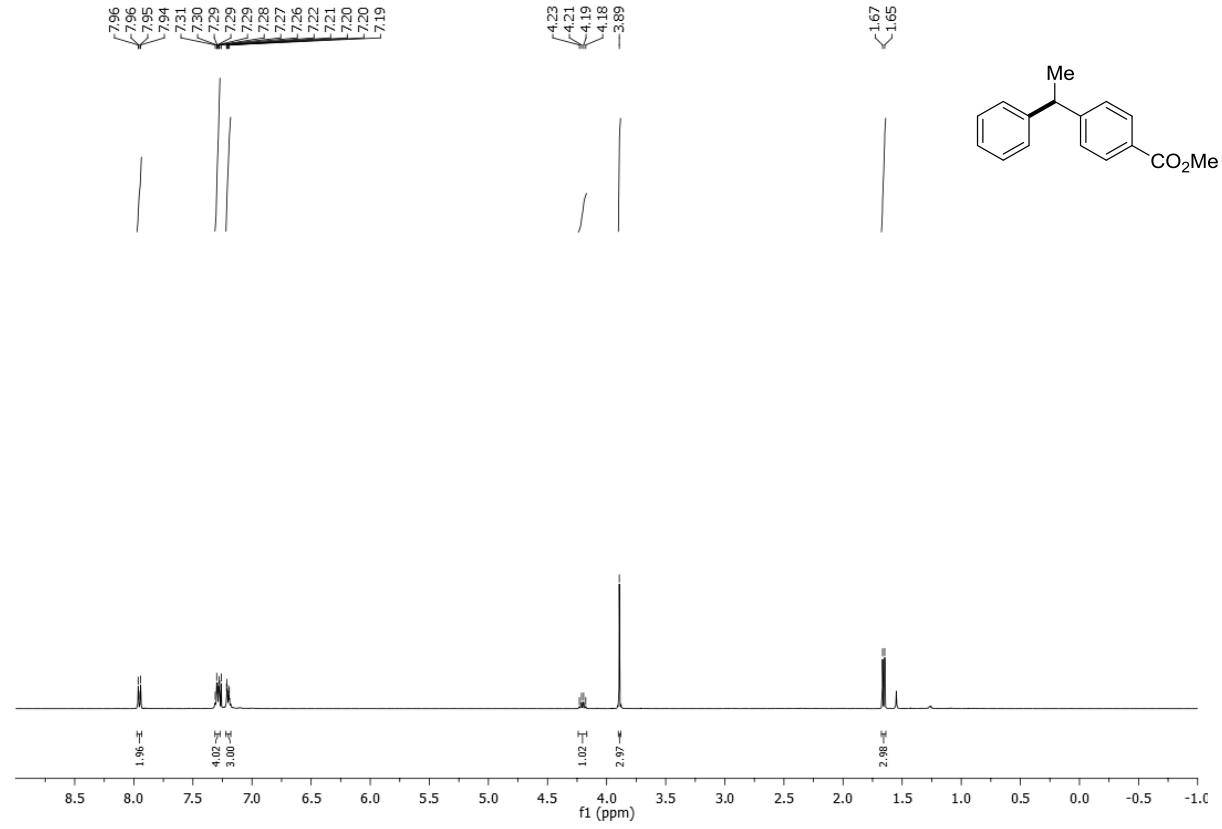



$^{1}$H NMR of Compound 12f



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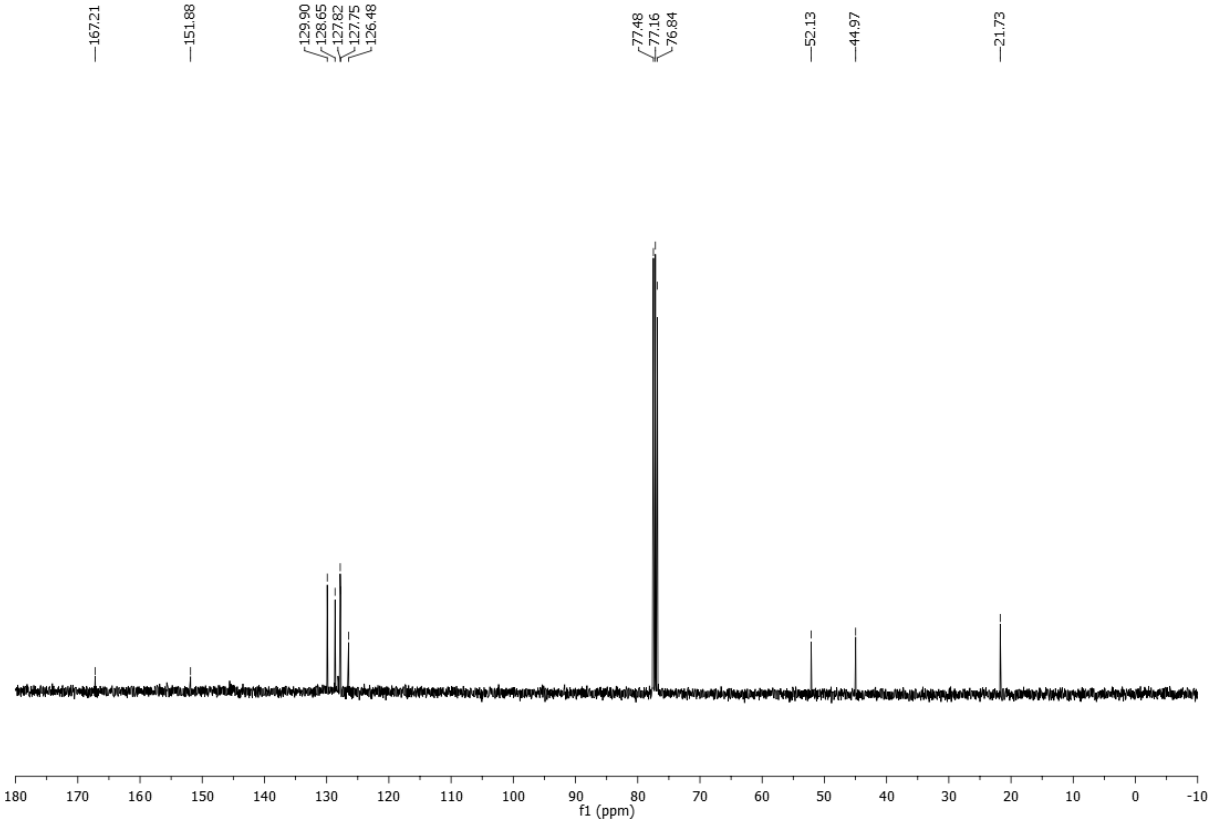
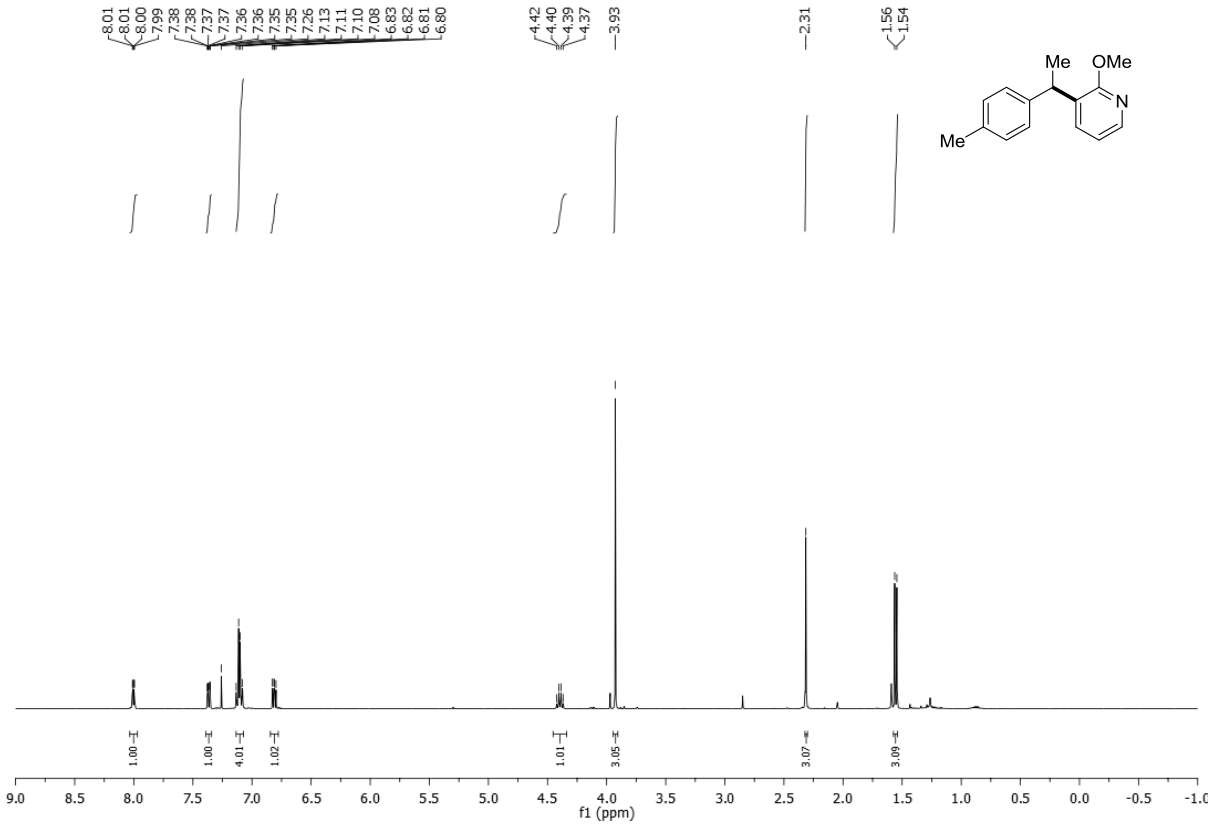
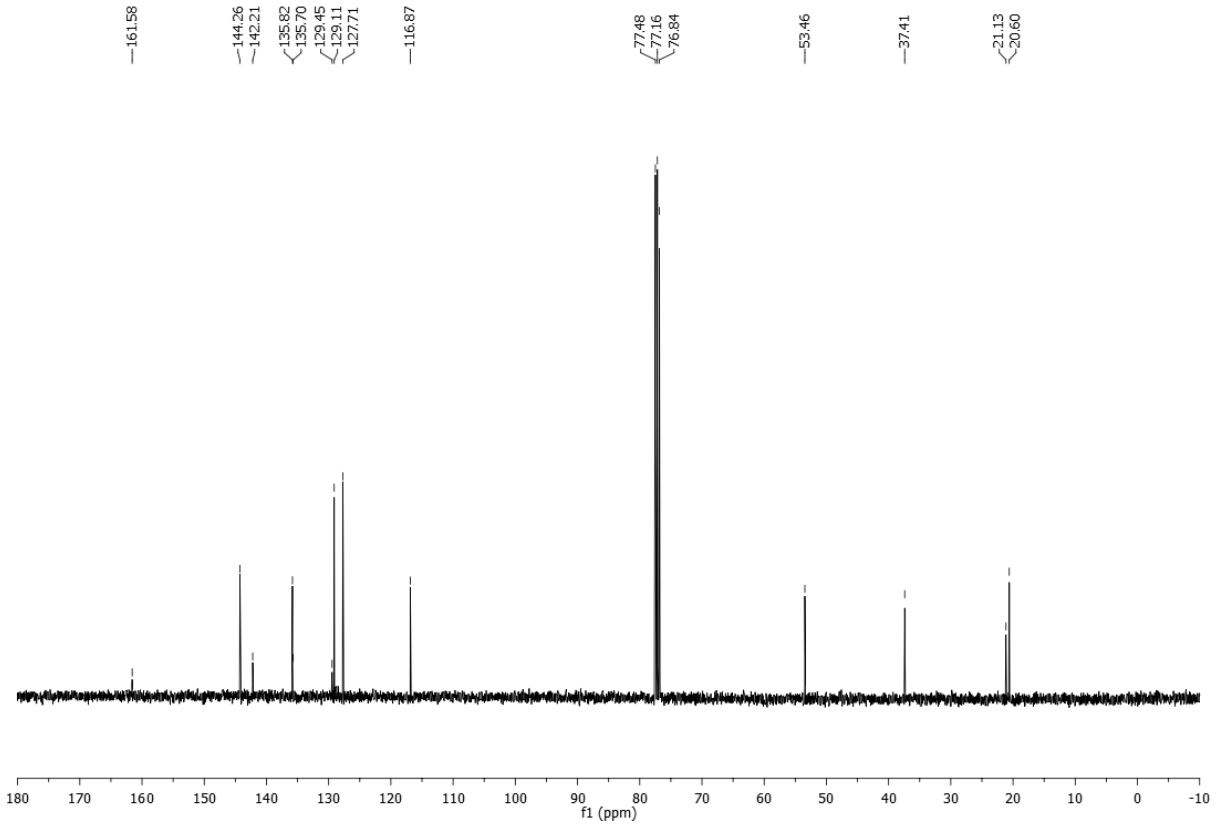


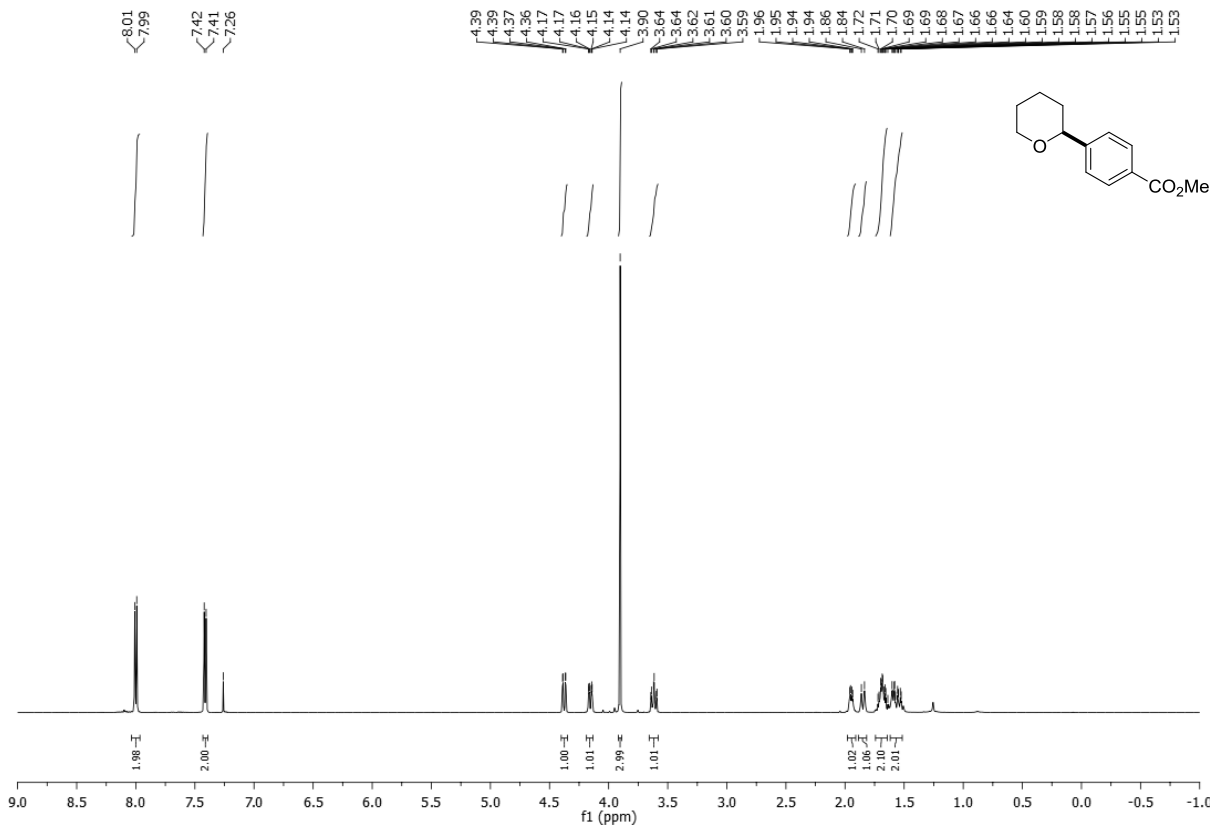

$^{1}$H NMR of Compound 12g



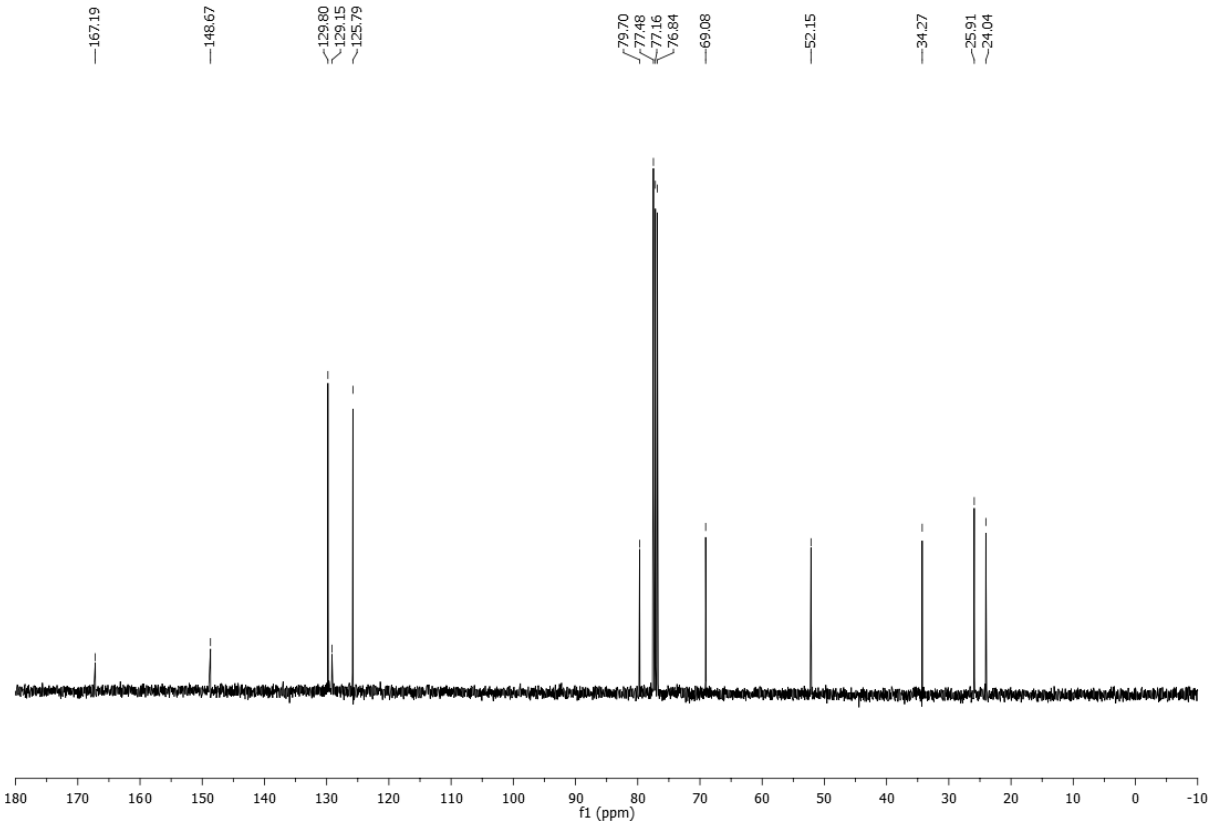
$^{13}$C NMR of Compound 12g



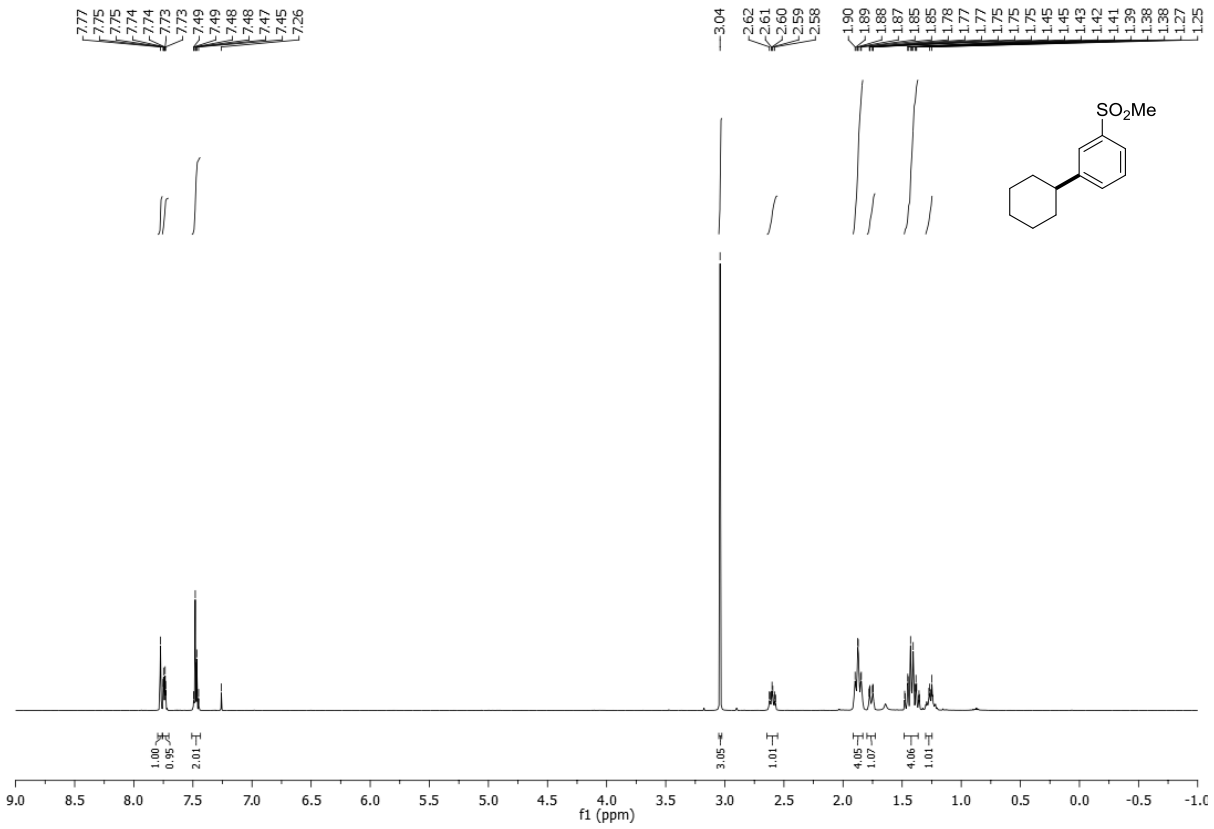

$^{1}$H NMR of Compound 12h



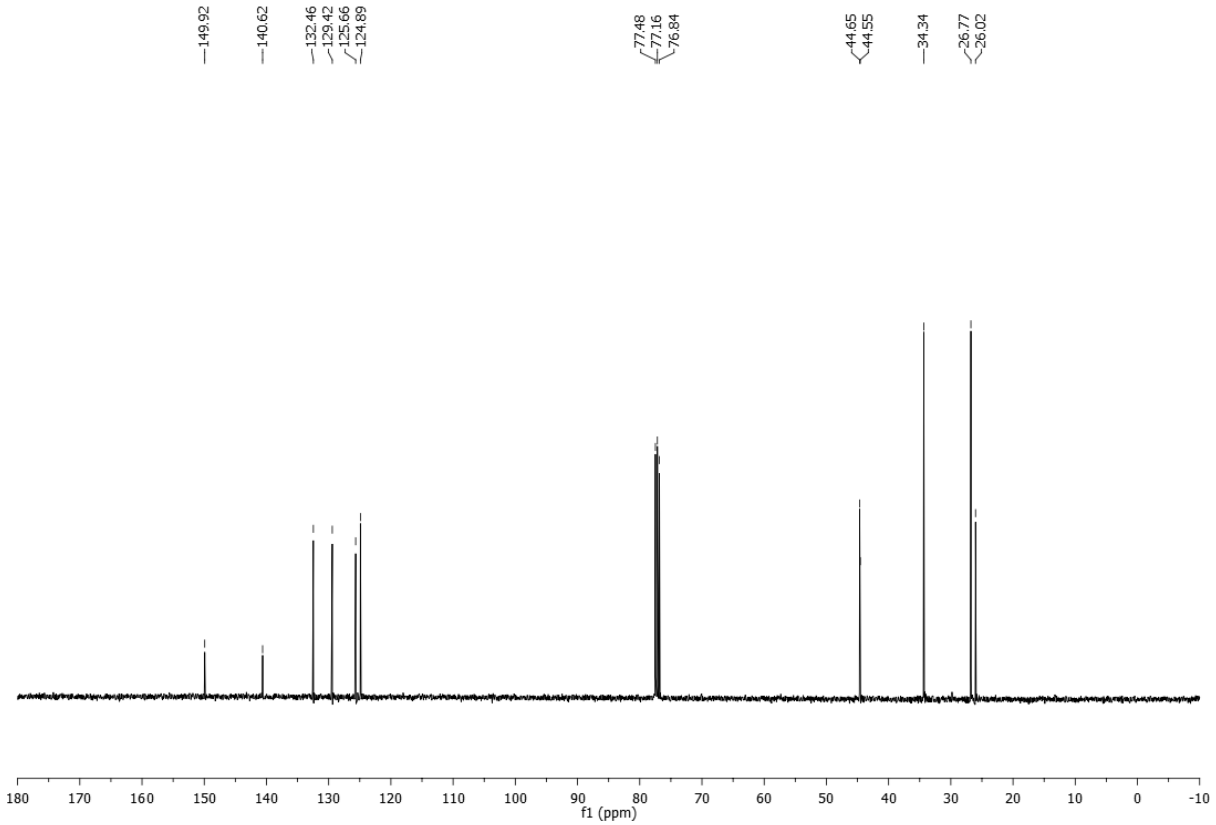
$^{13}$C NMR of Compound 12h




$^{1}$H NMR of Compound 12i



$^{13}$C NMR of Compound 12i

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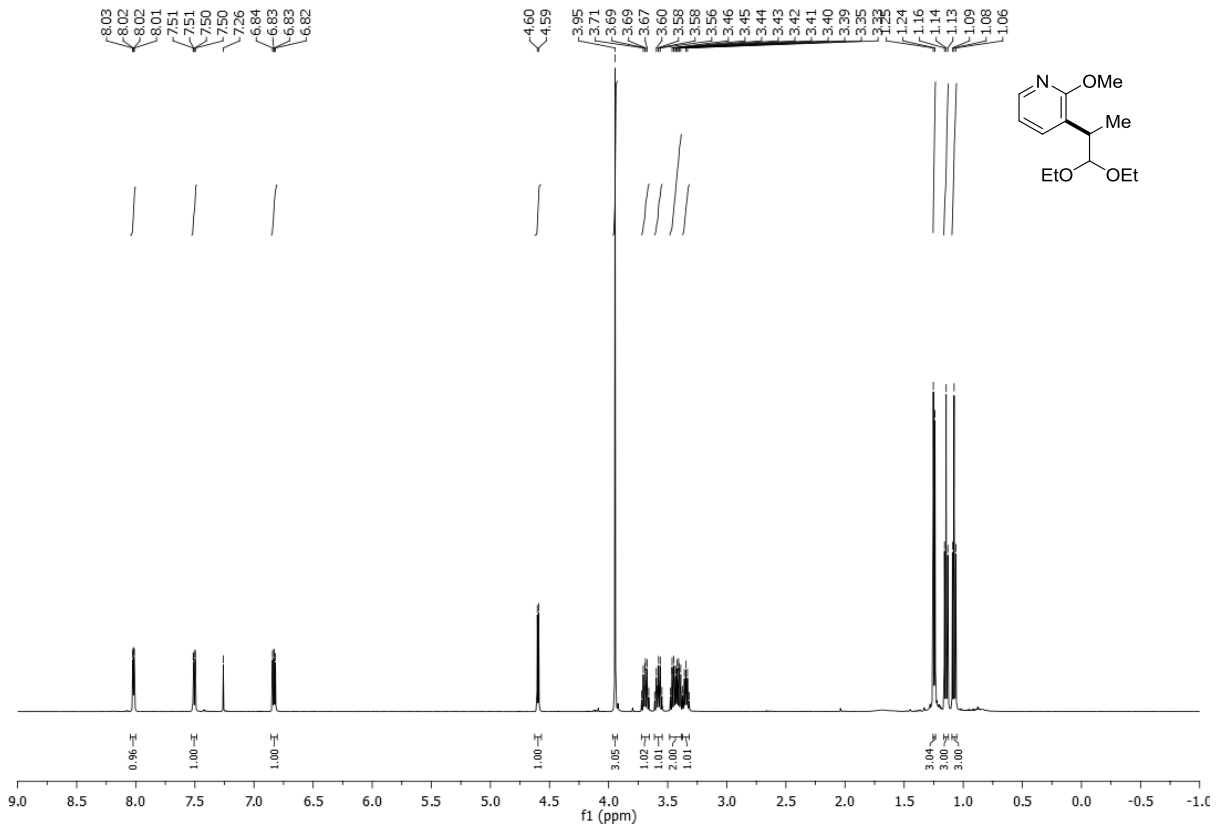

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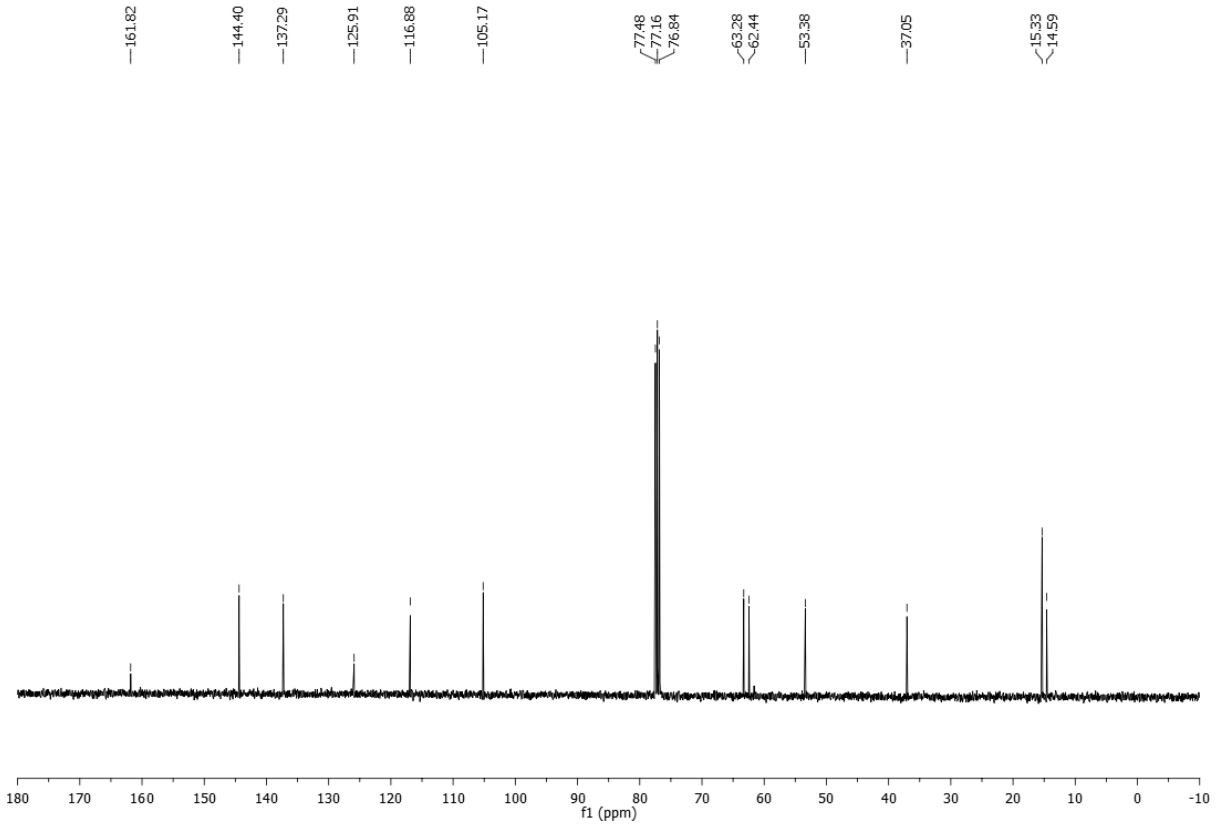
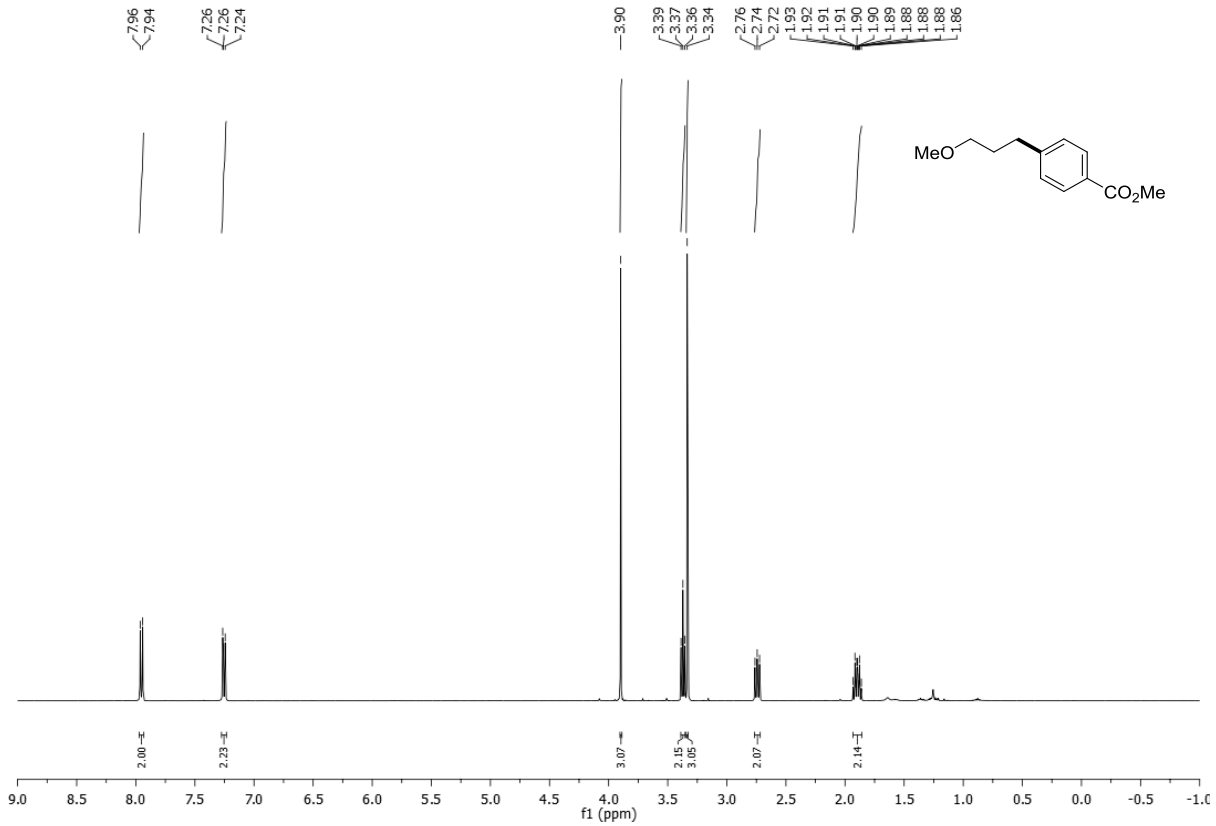



$^{1}$H NMR of Compound 12k



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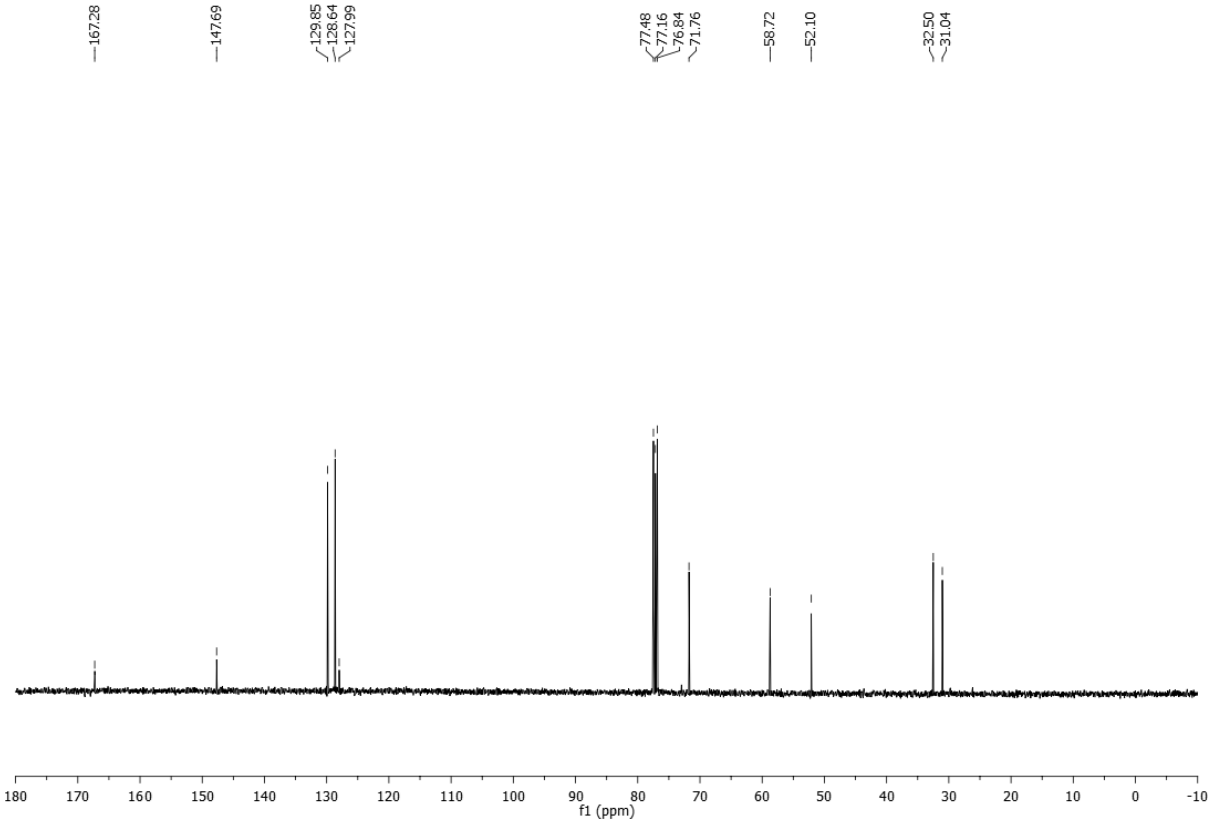


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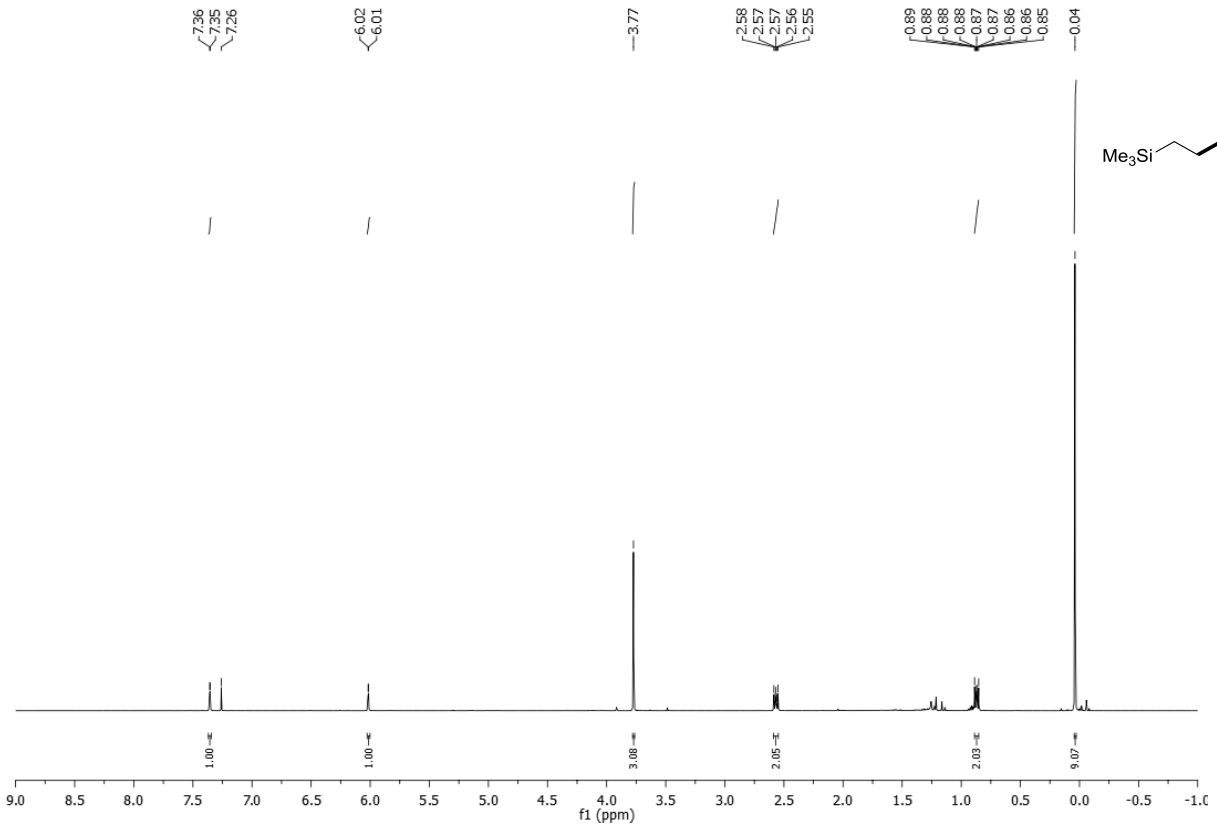

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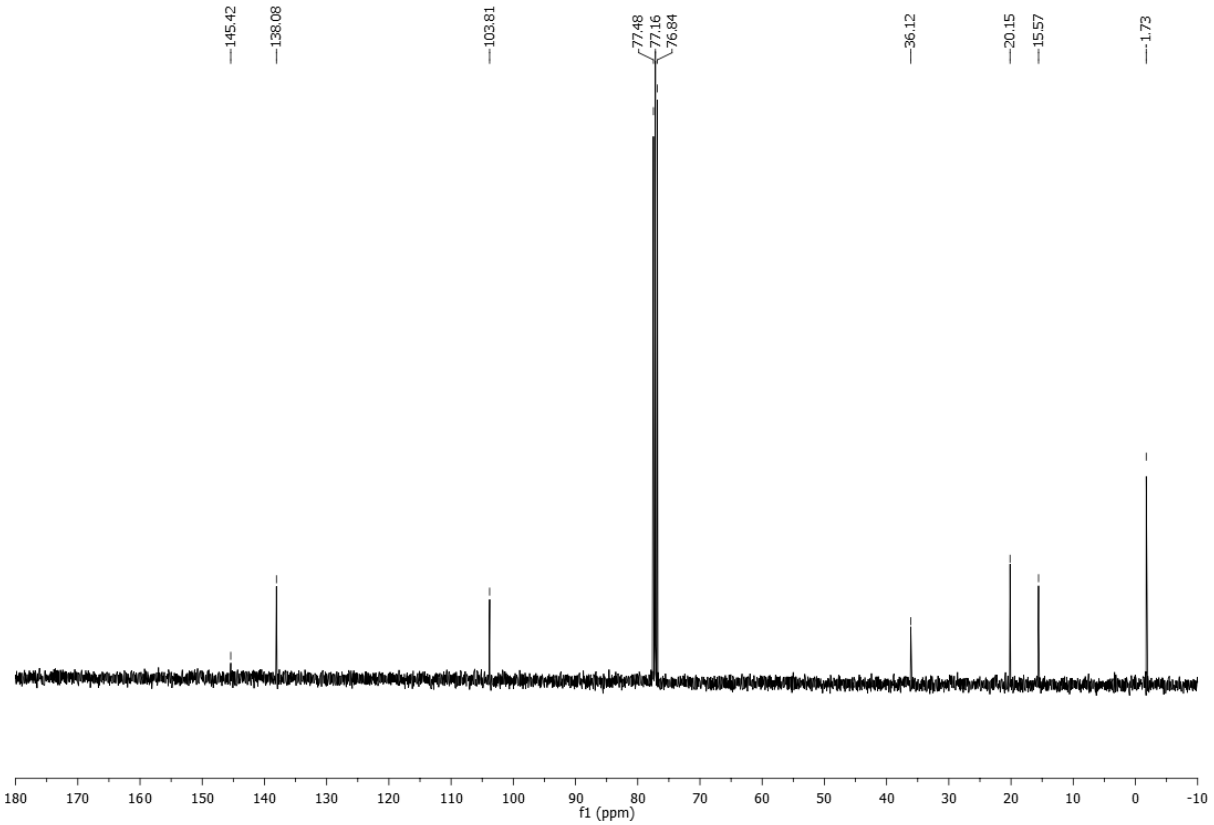
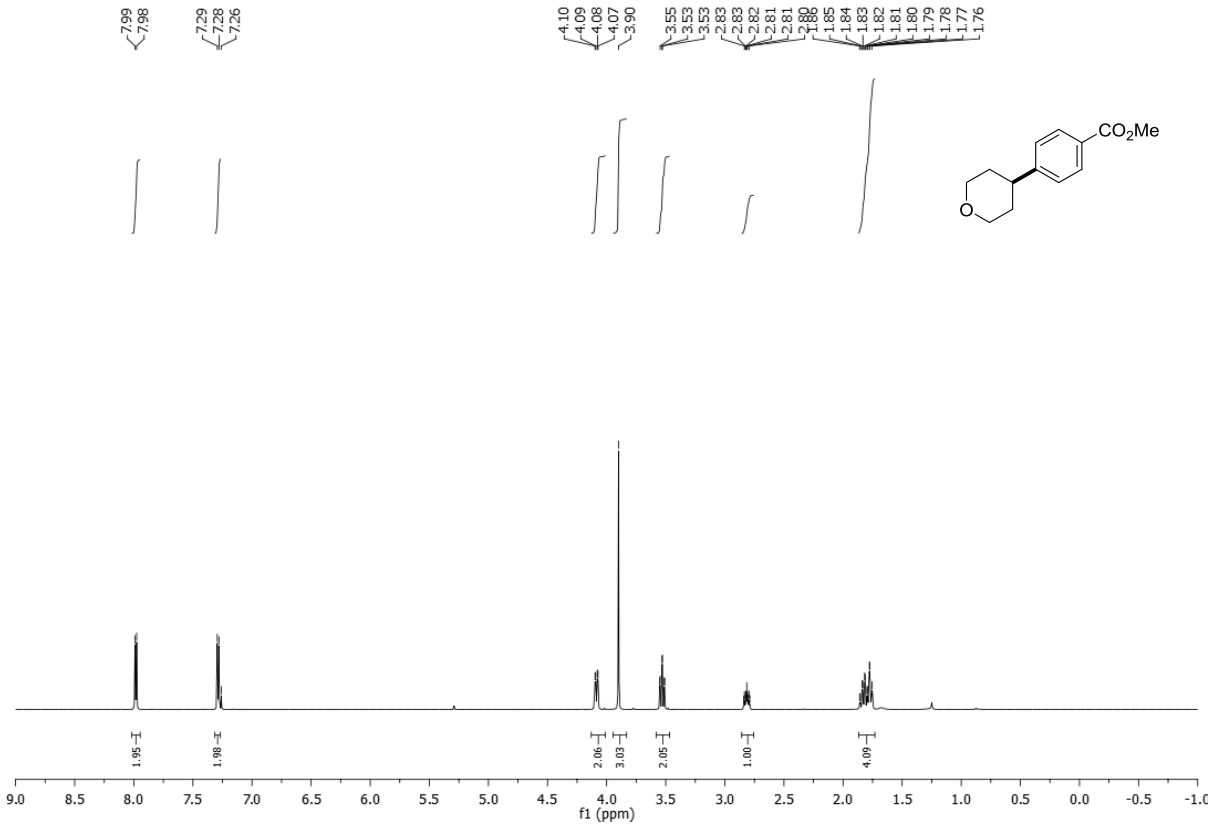



$^{1}$H NMR of Compound 12m



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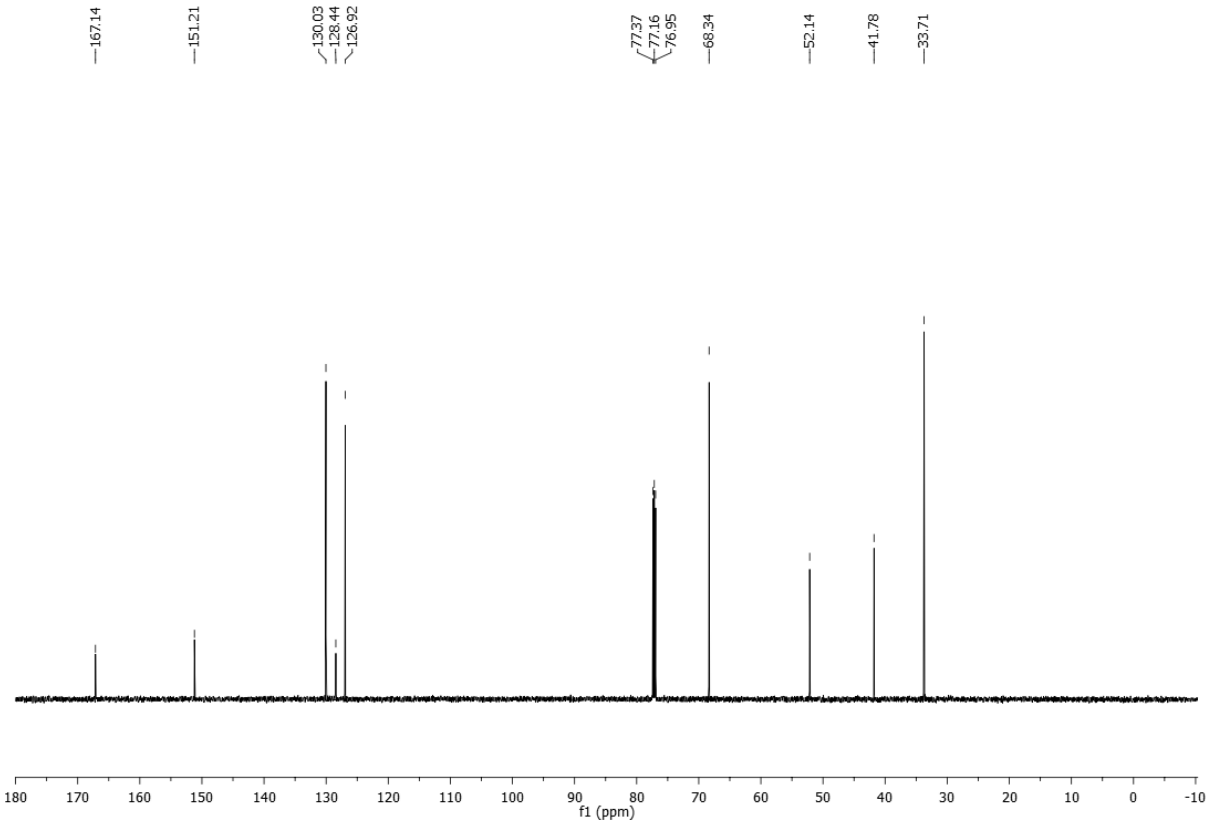


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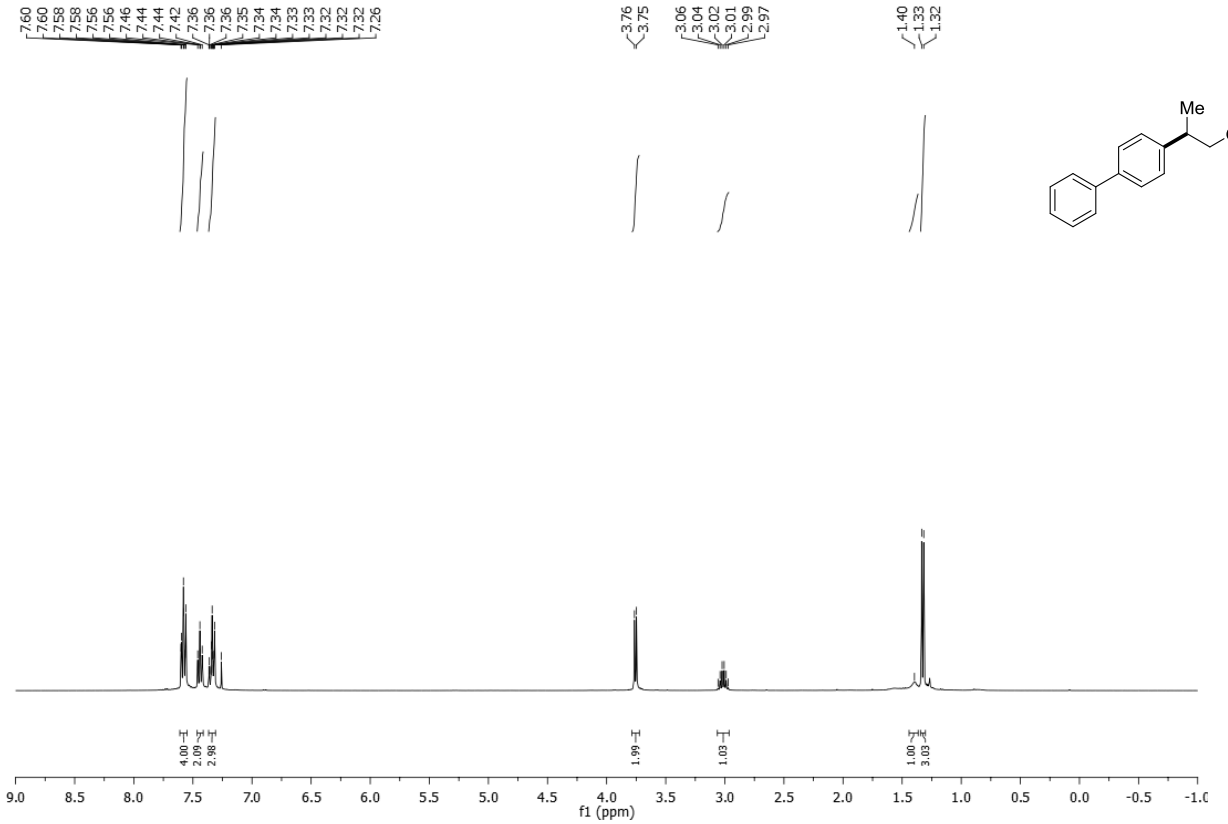

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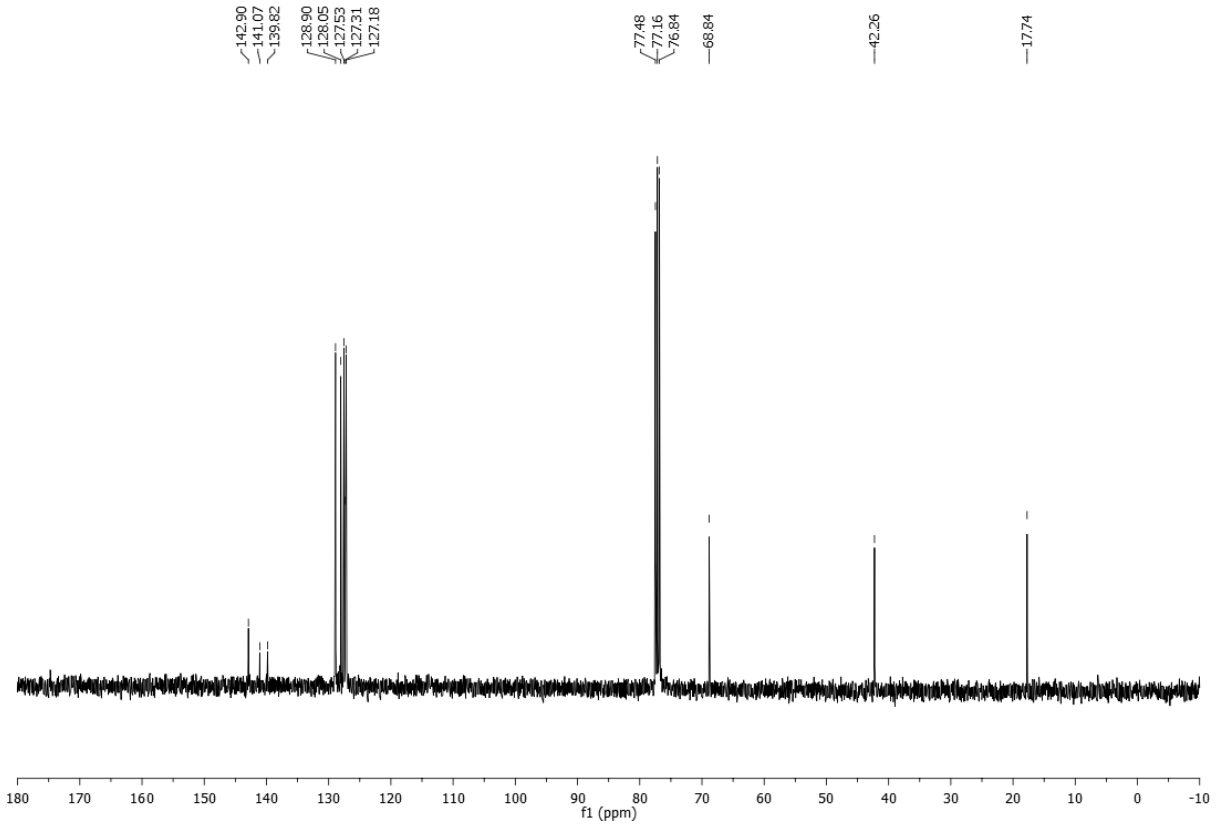


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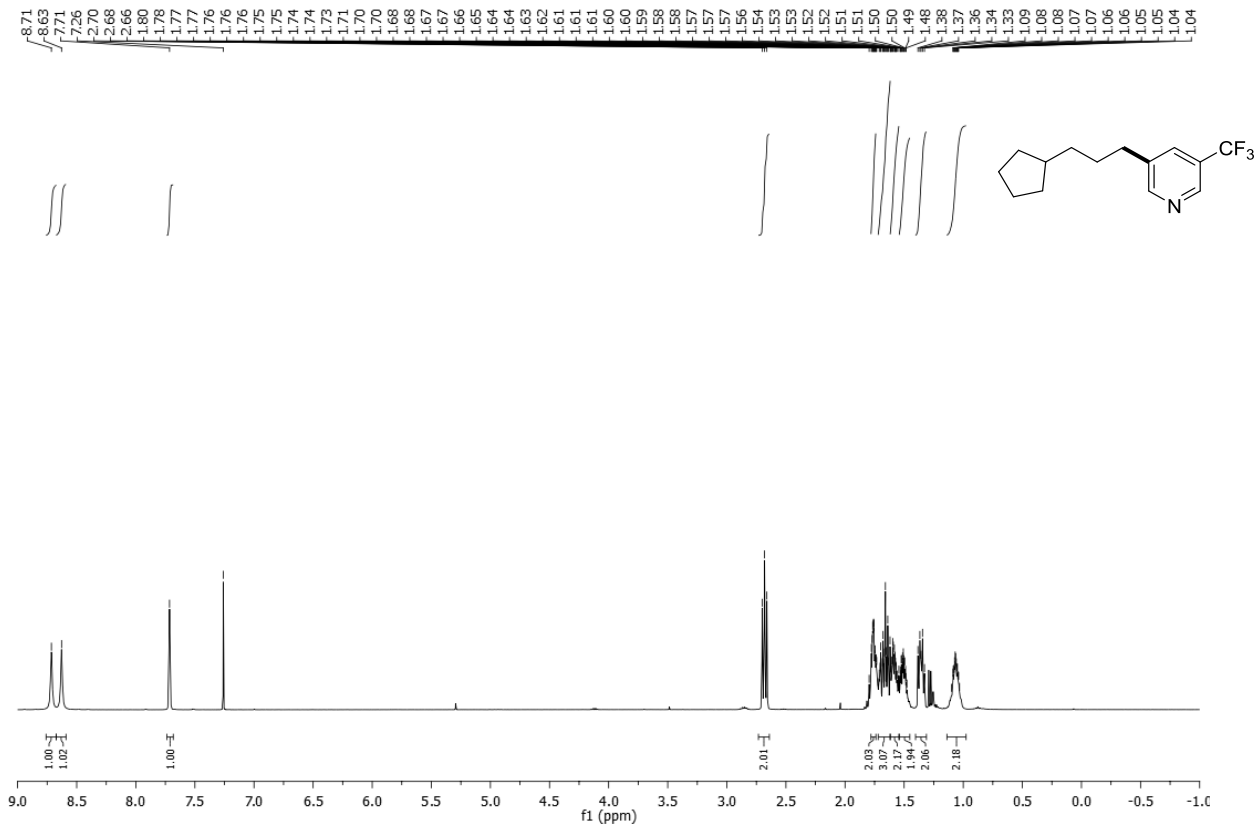

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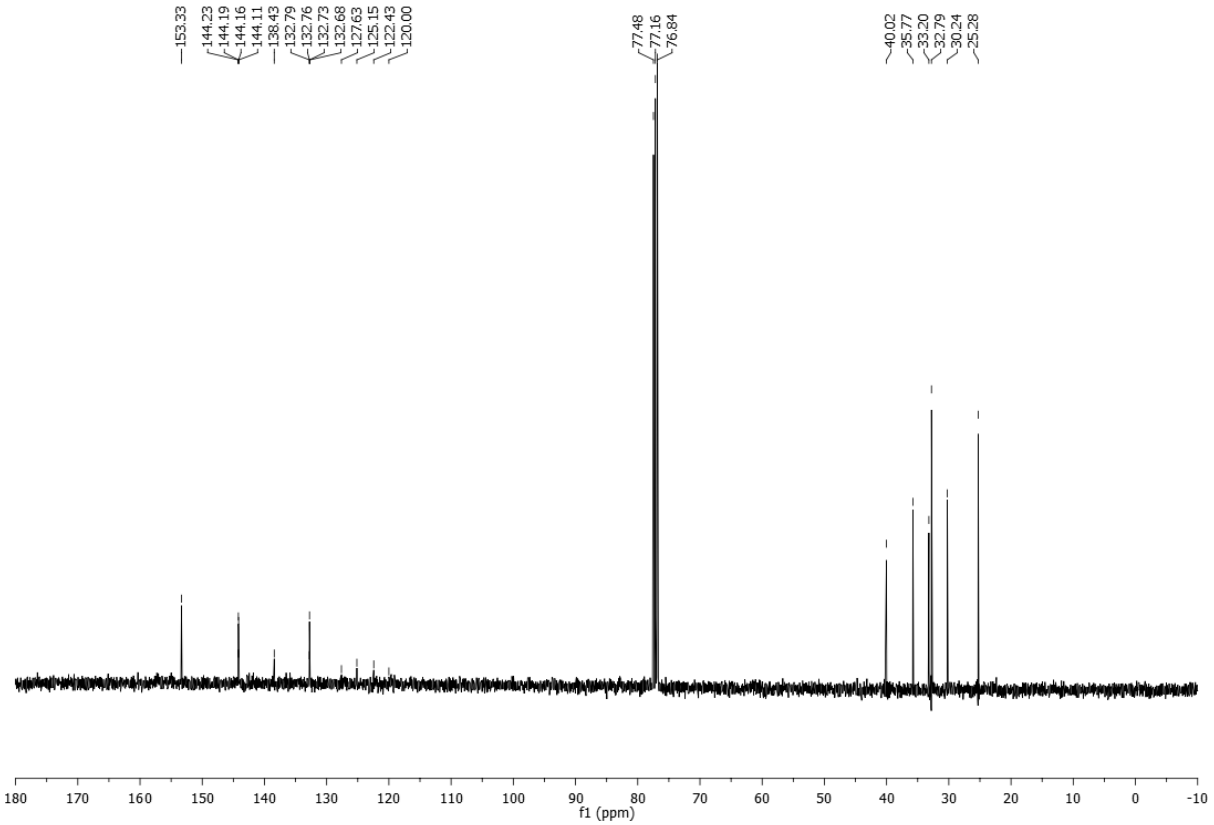
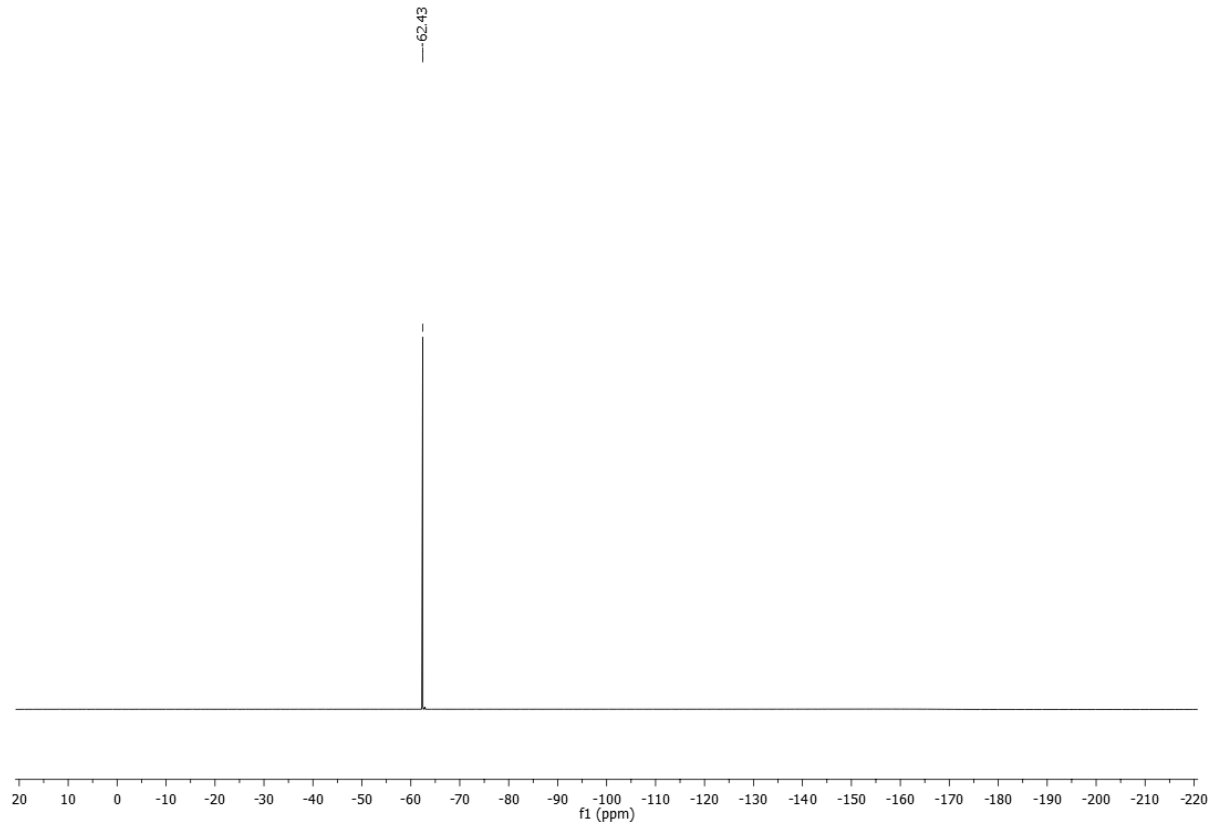
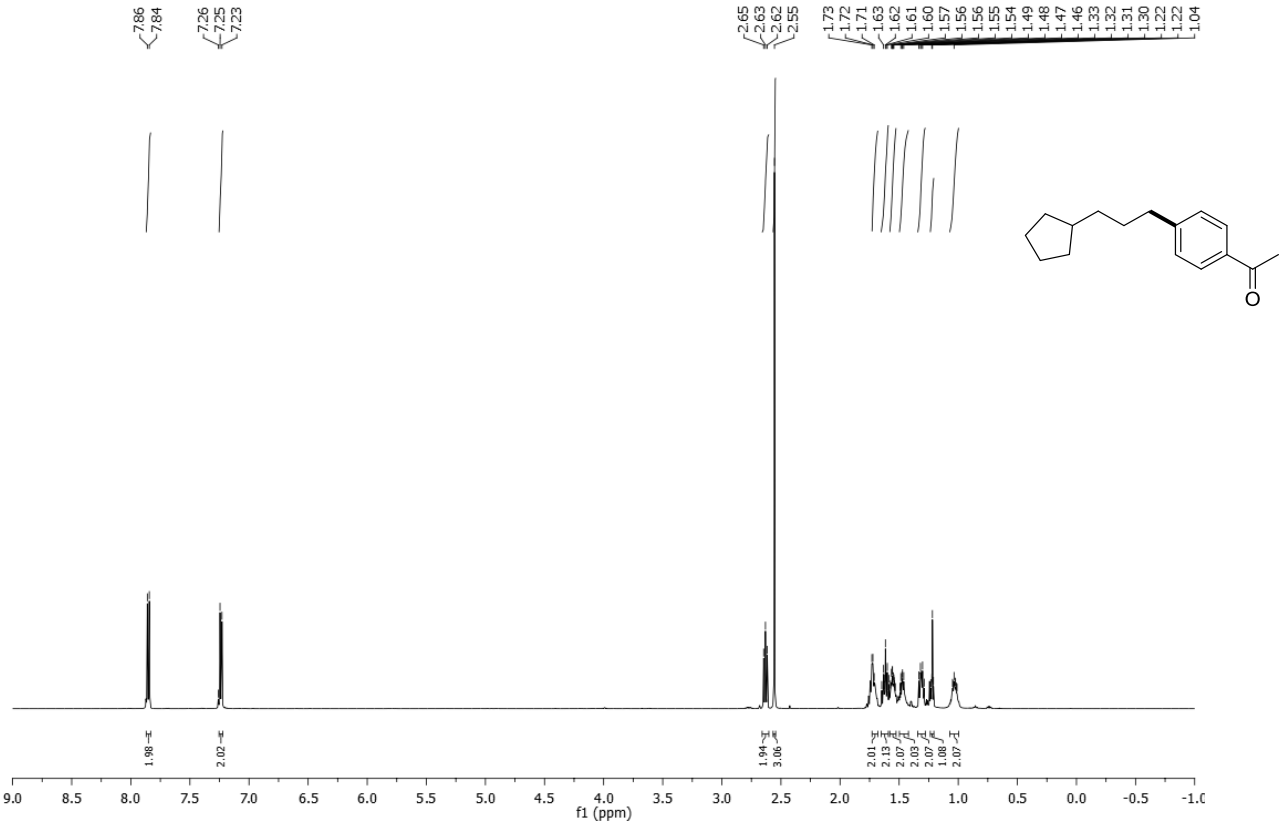


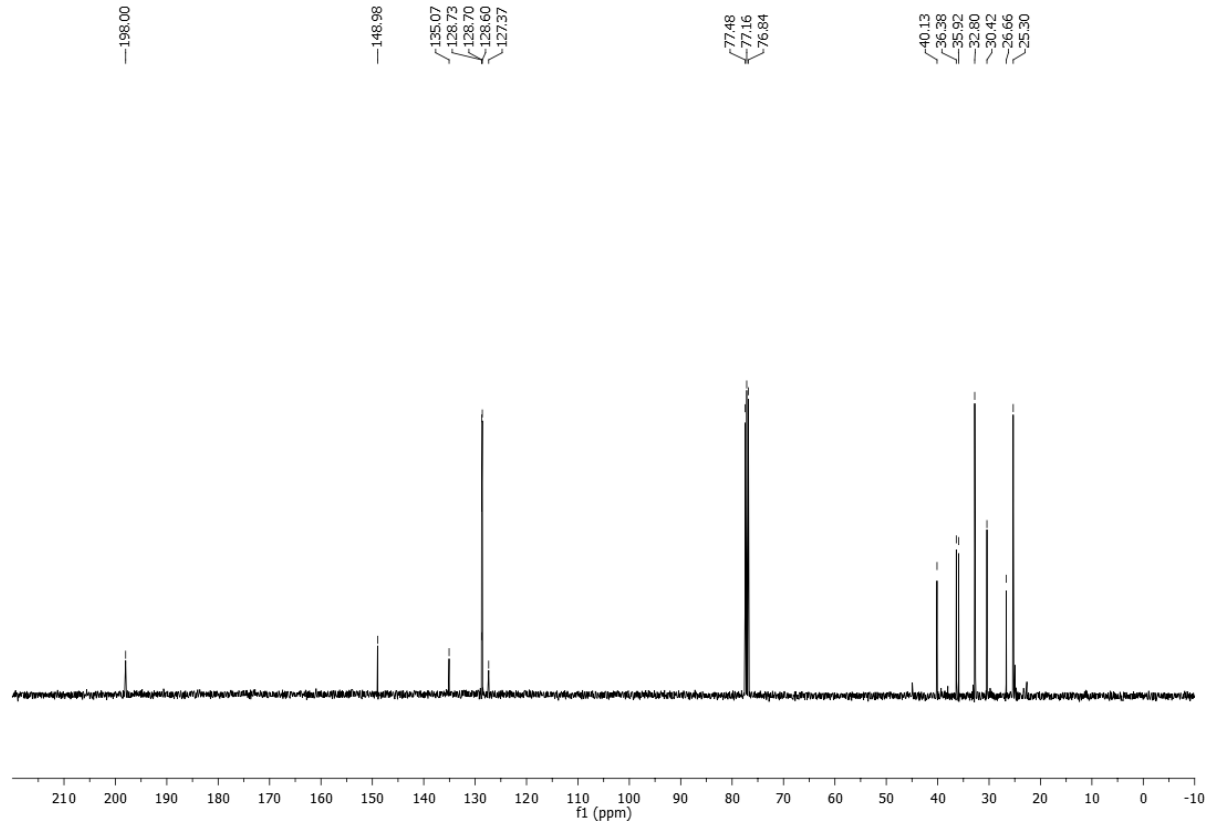

$^{19}$F NMR of Compound 12o



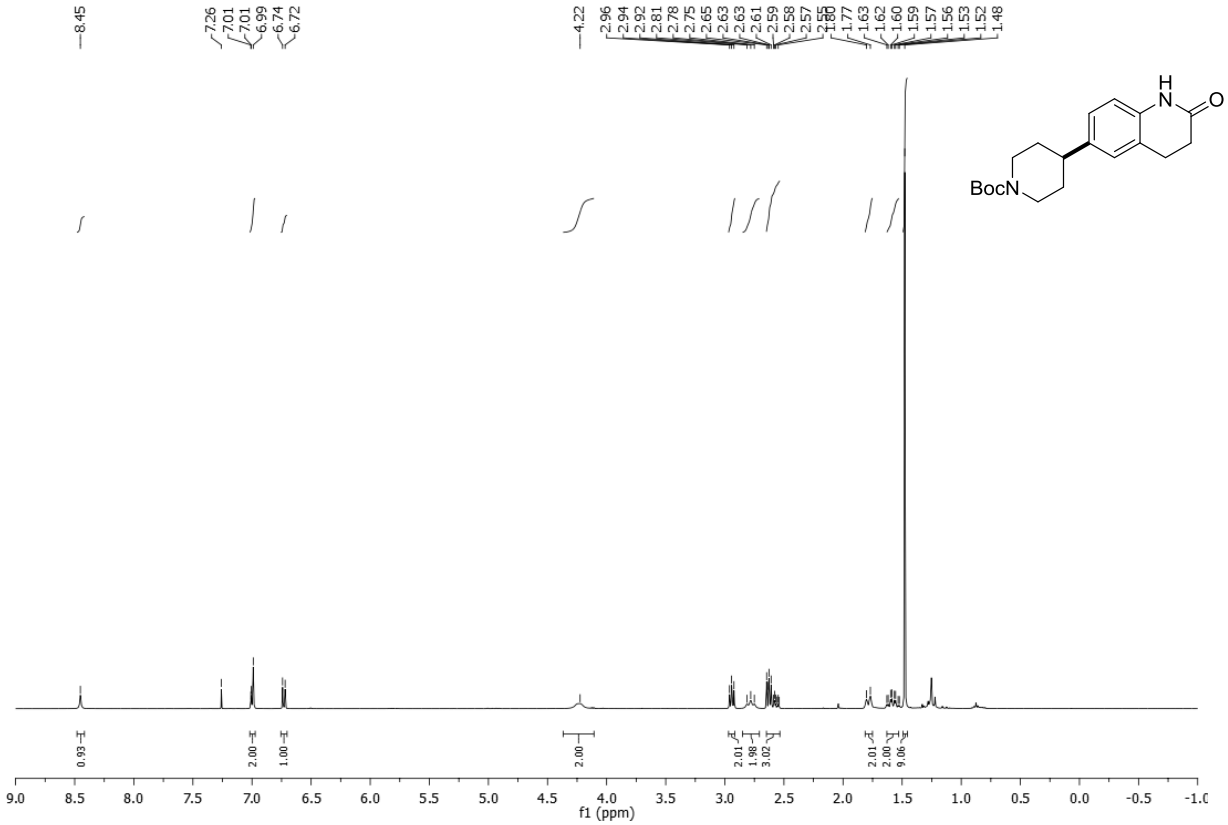
$^{1}$H NMR of Compound 12p



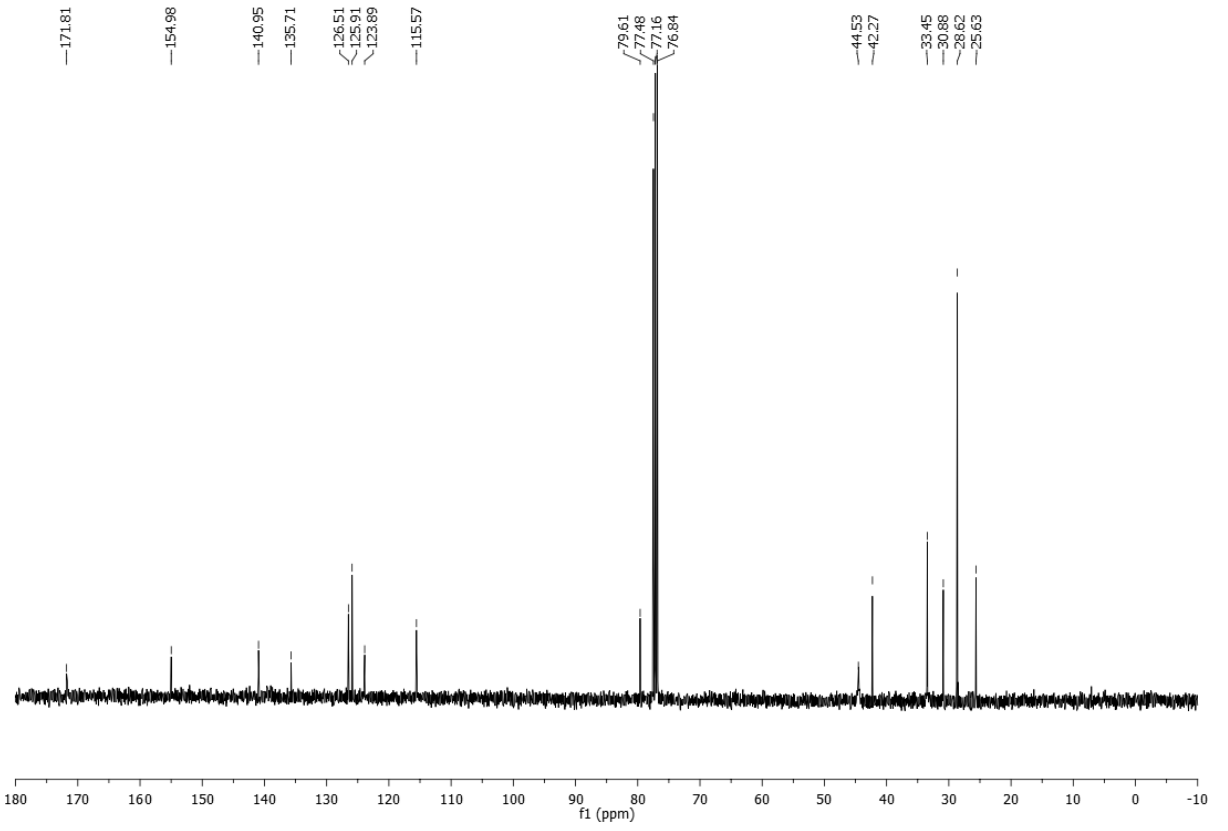

$^{13}$C NMR of Compound 12p



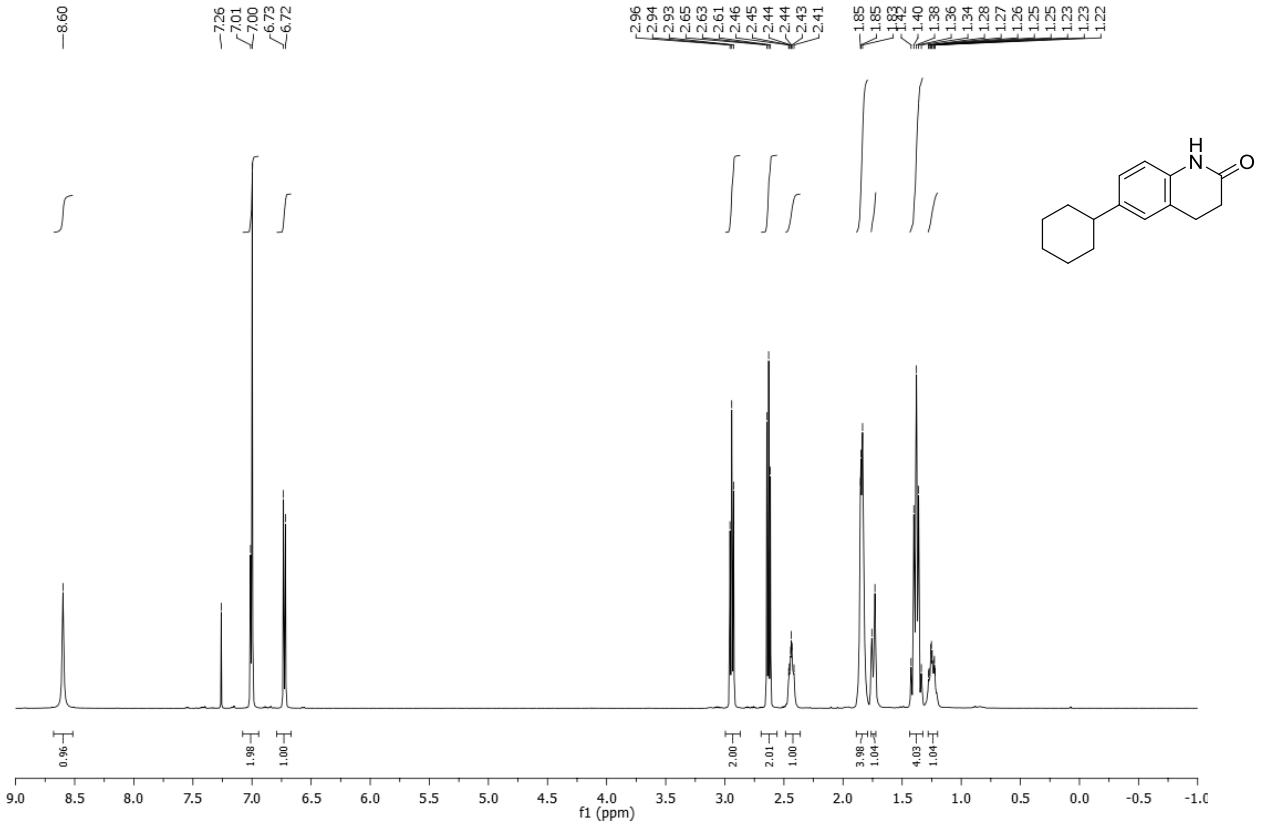
$^{1}$H NMR of Compound 12q



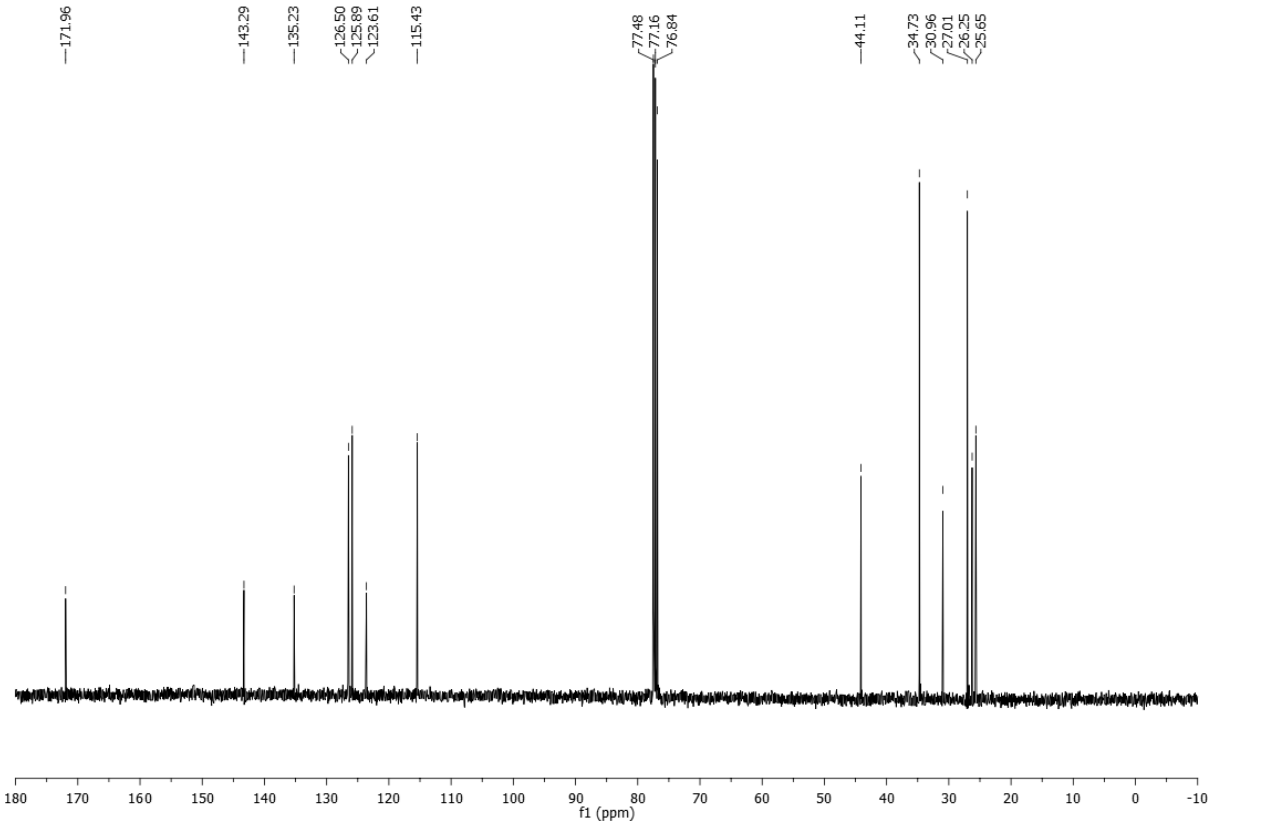

$^{13}$C NMR of Compound 12q



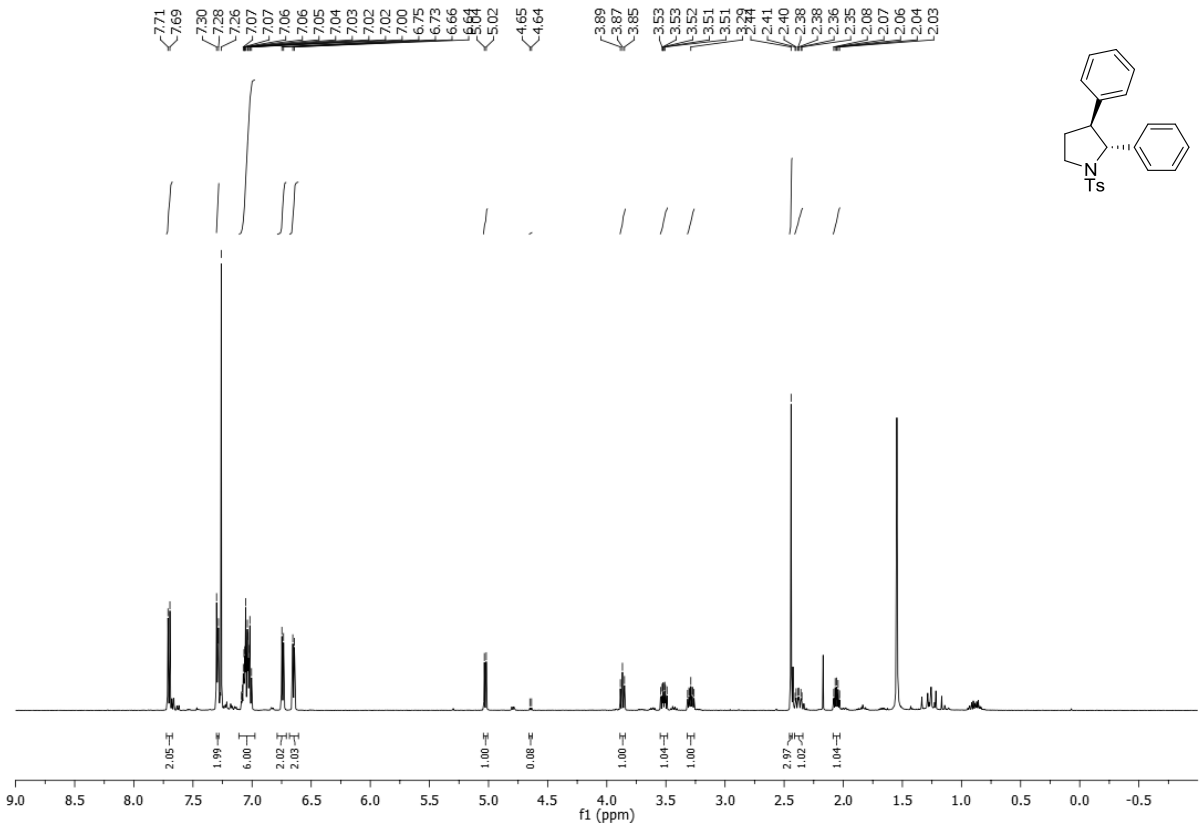
$^{1}$H NMR of Compound 12r



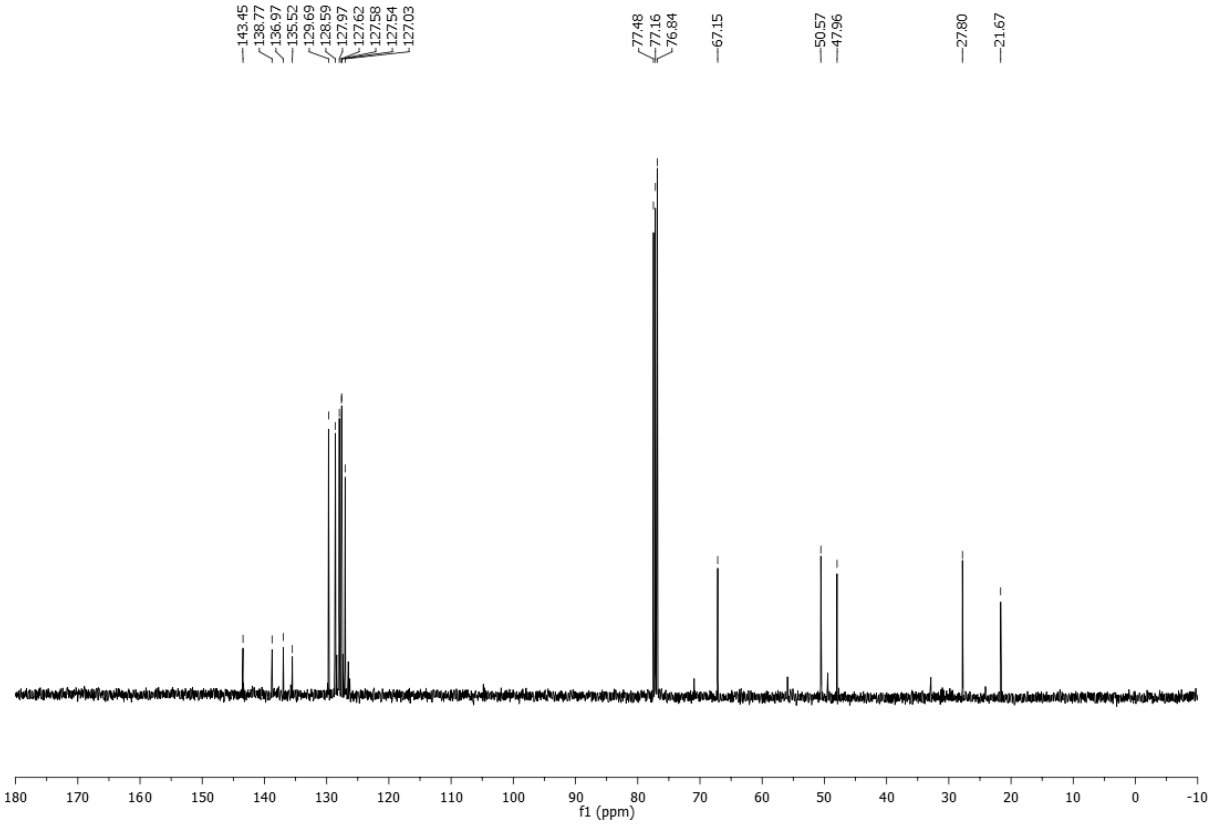

$^{13}$C NMR of Compound 12r



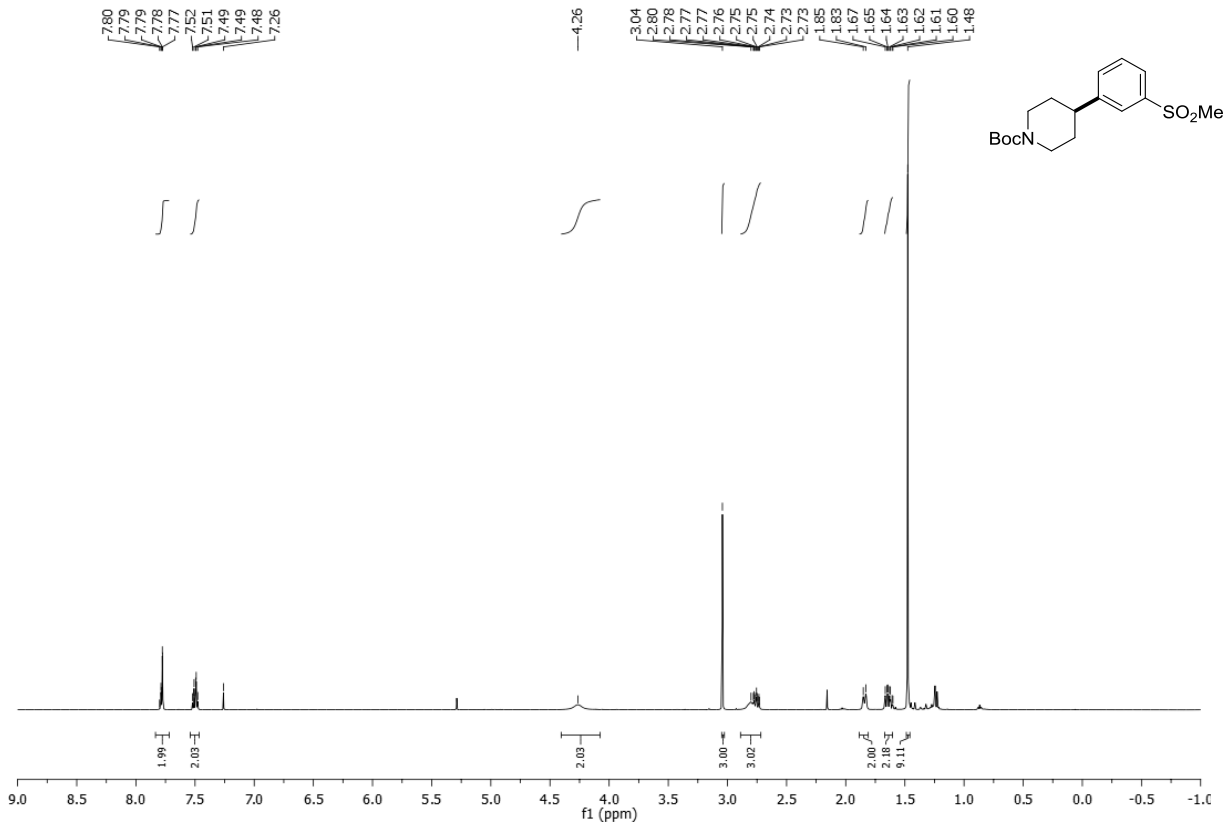
$^{1}$H NMR of Compound 12s



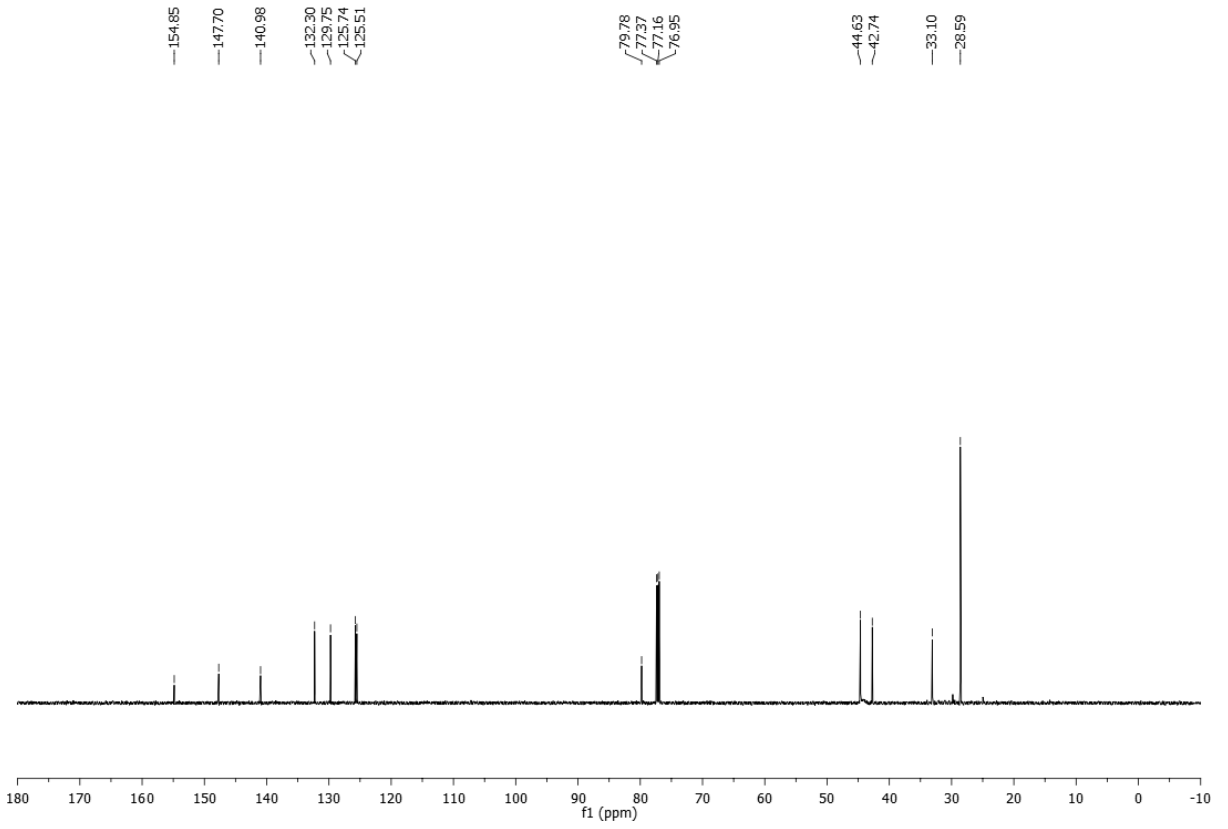

$^{13}$C NMR of Compound 12s



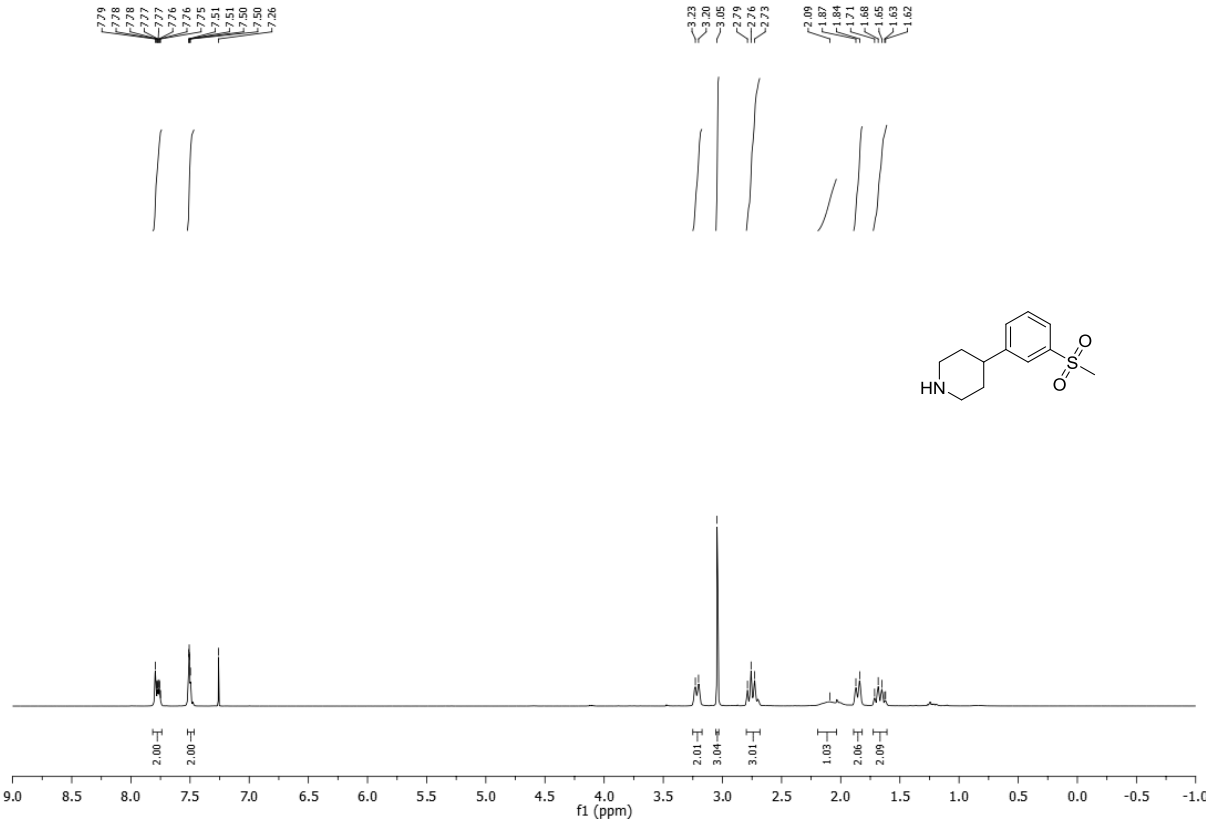
[1]H NMR of Compound 13



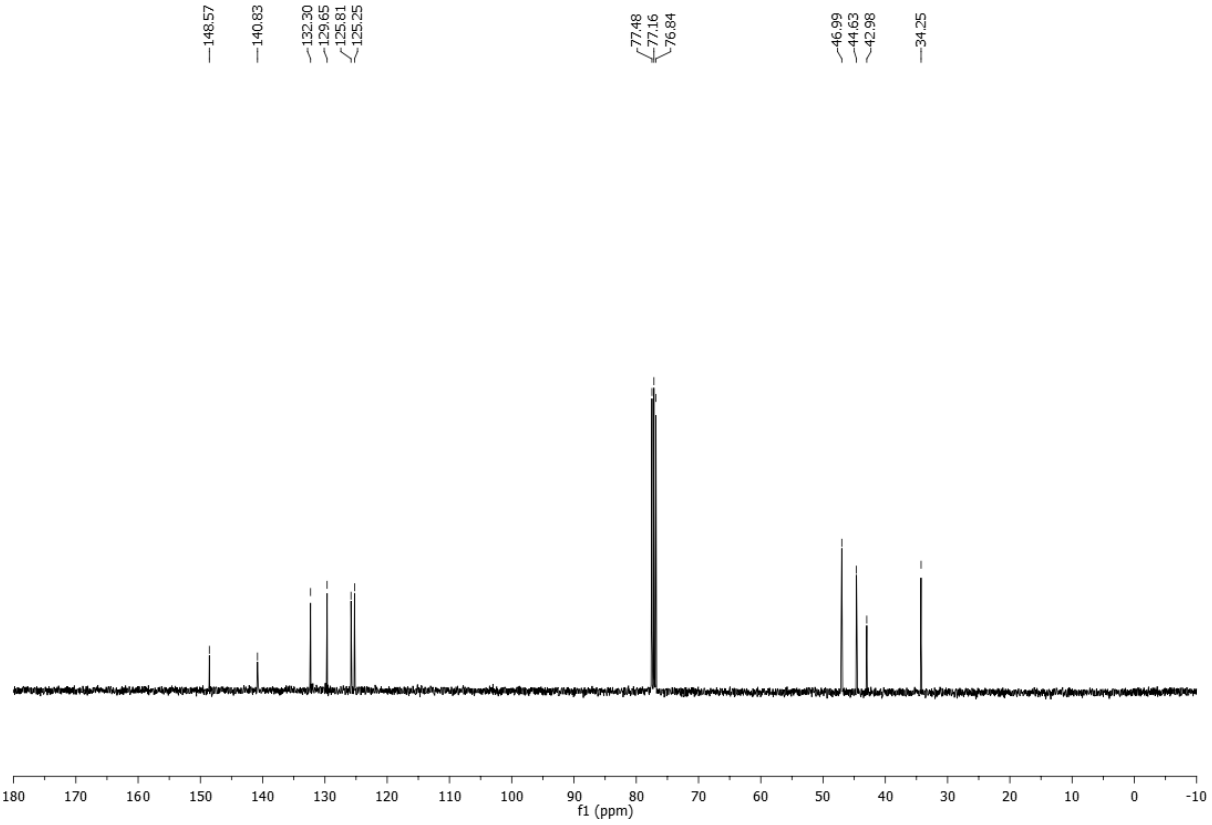

[13]C NMR of Compound 13



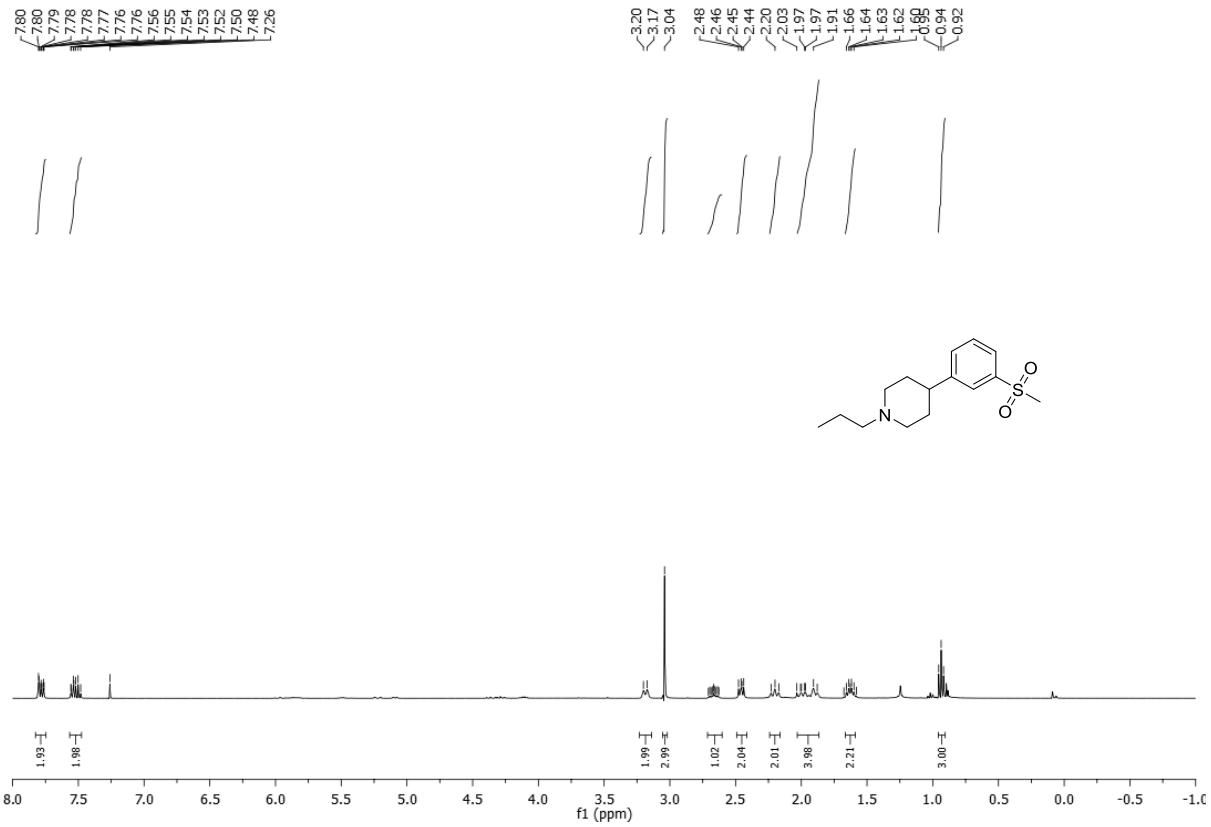
[1]H NMR of Compound 14



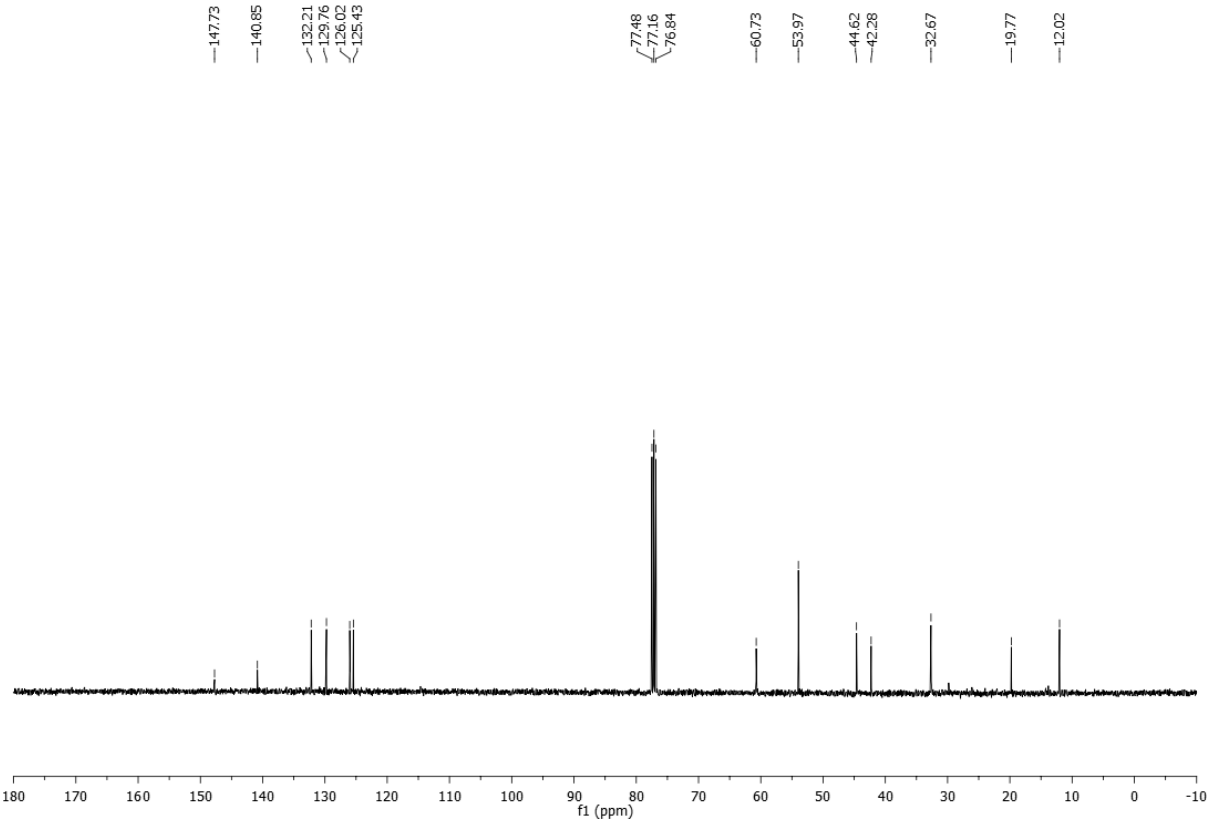

[13]C NMR of Compound 14



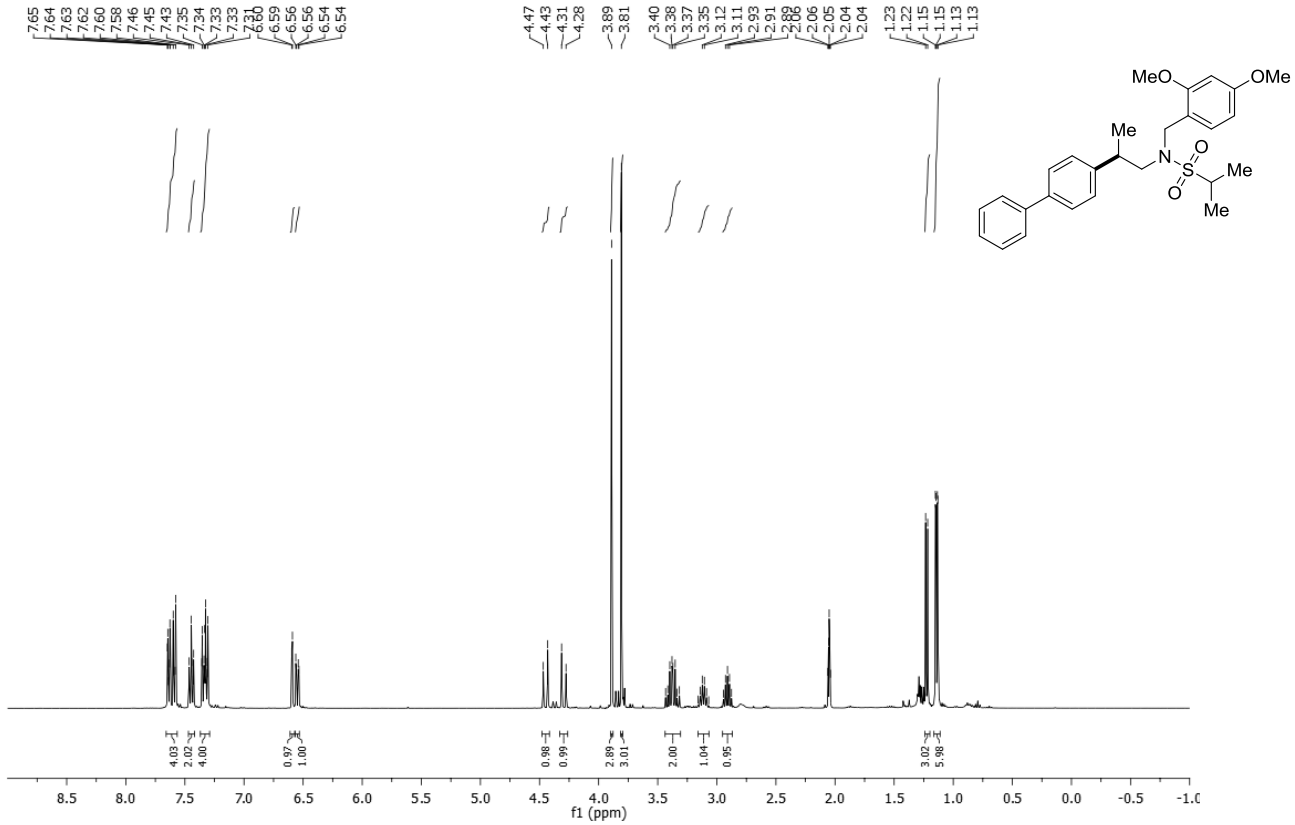
$^{1}$H NMR of Compound 3



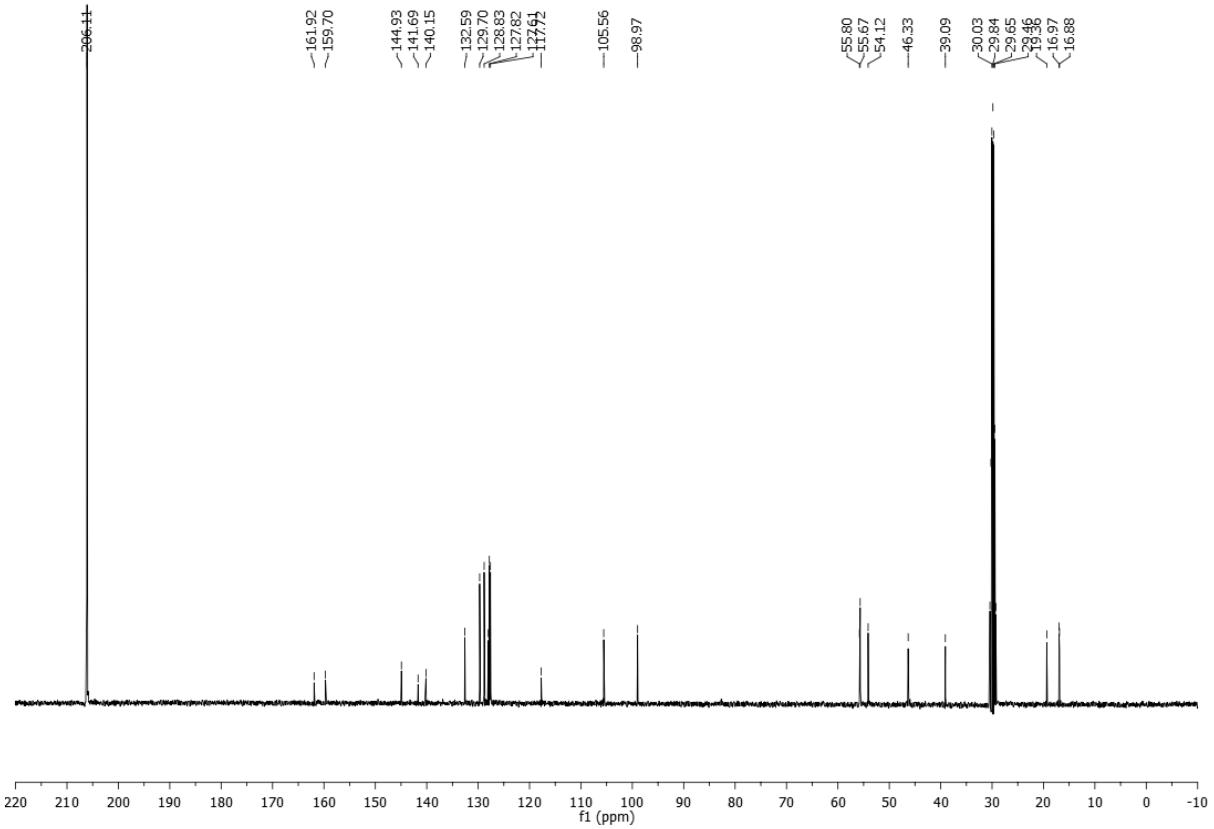

$^{13}$C NMR of Compound 3



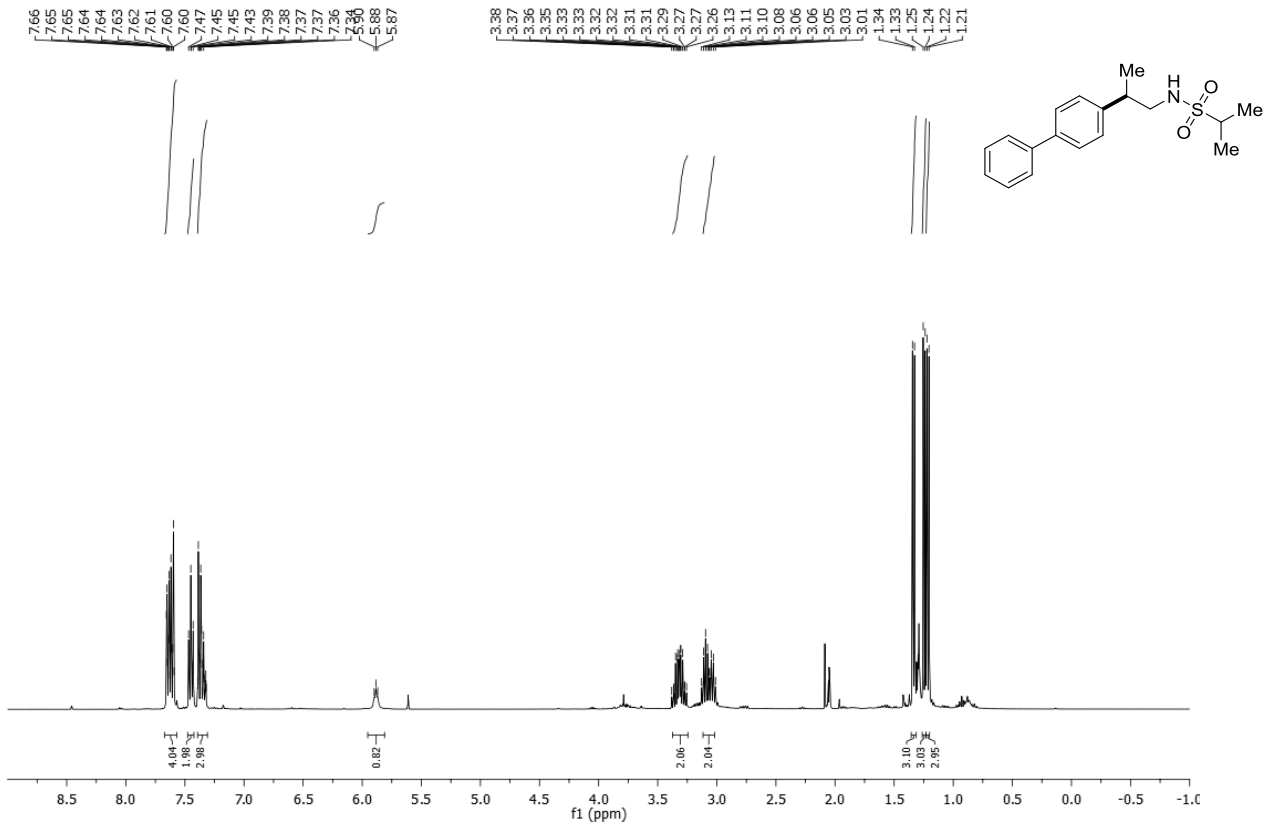
$^{1}$H NMR of Compound 17



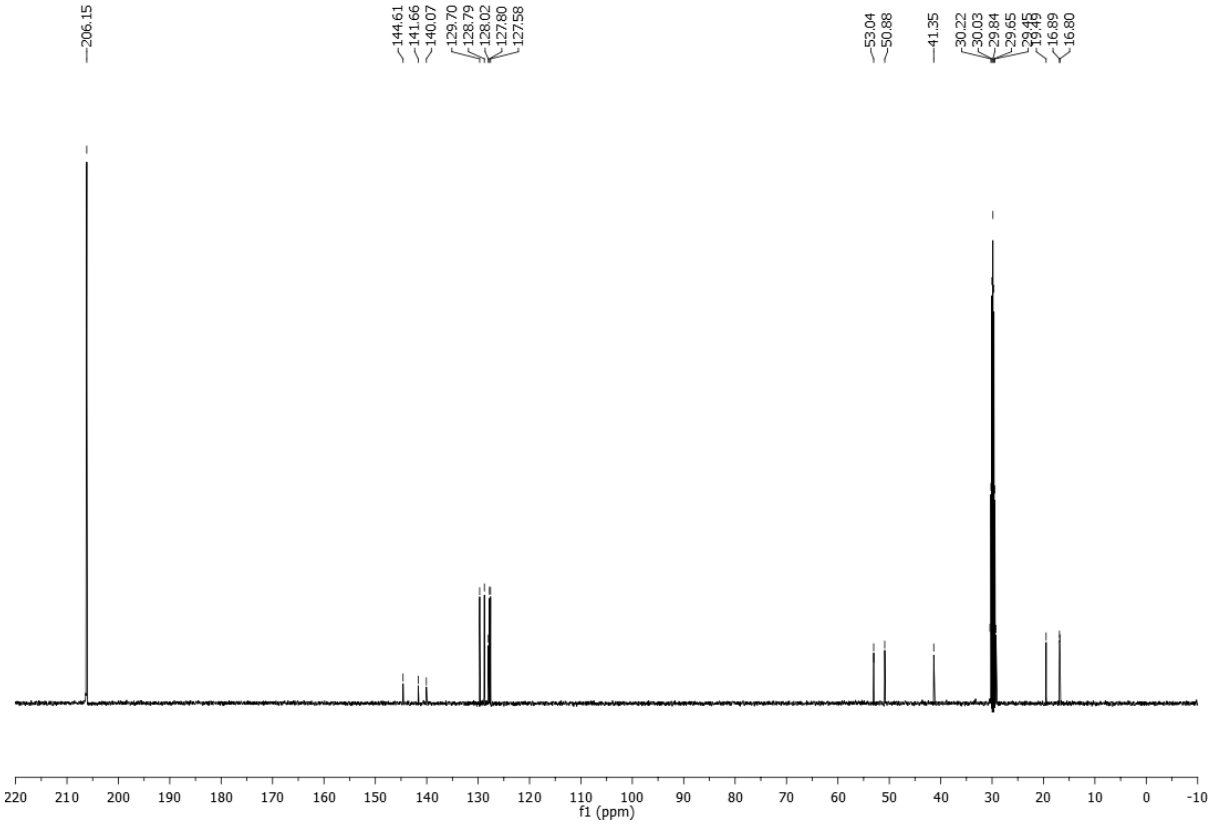

$^{13}$C NMR of Compound 17



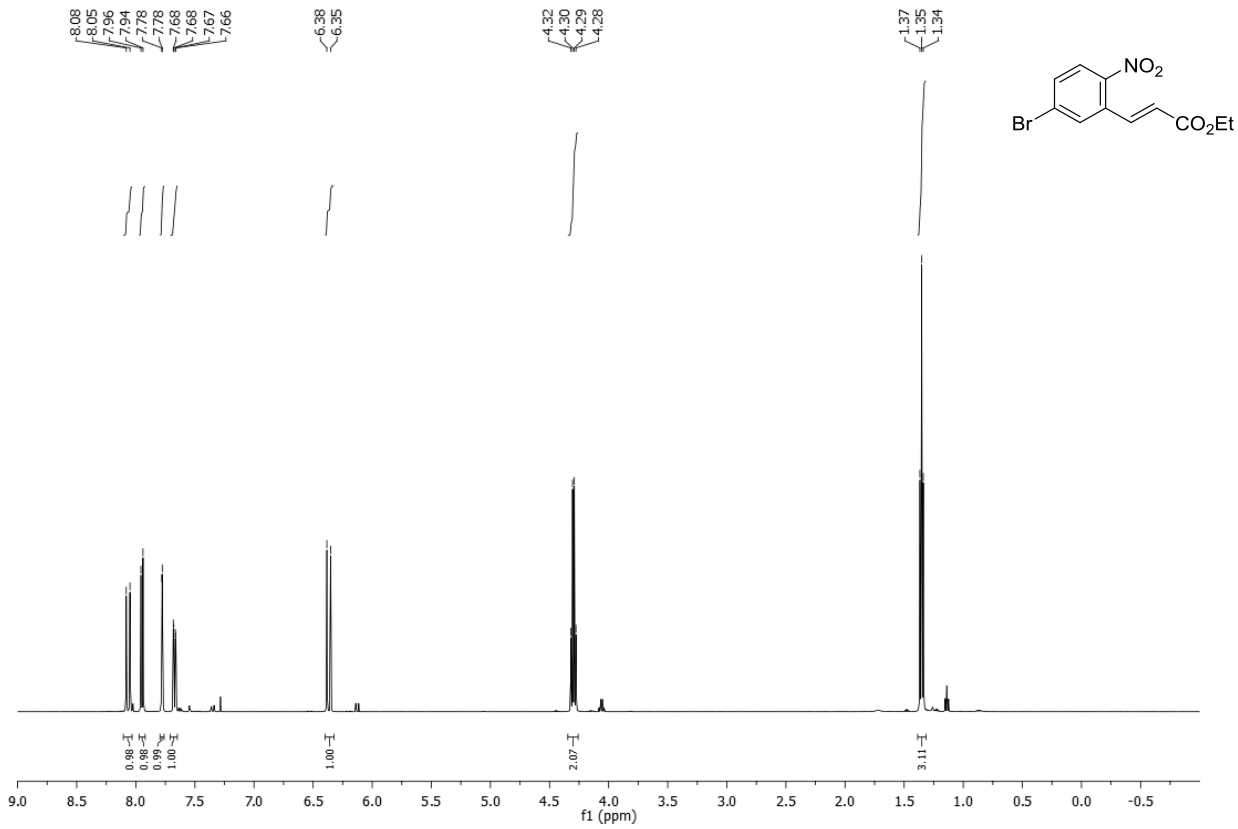
$^{1}$H NMR of Compound 18



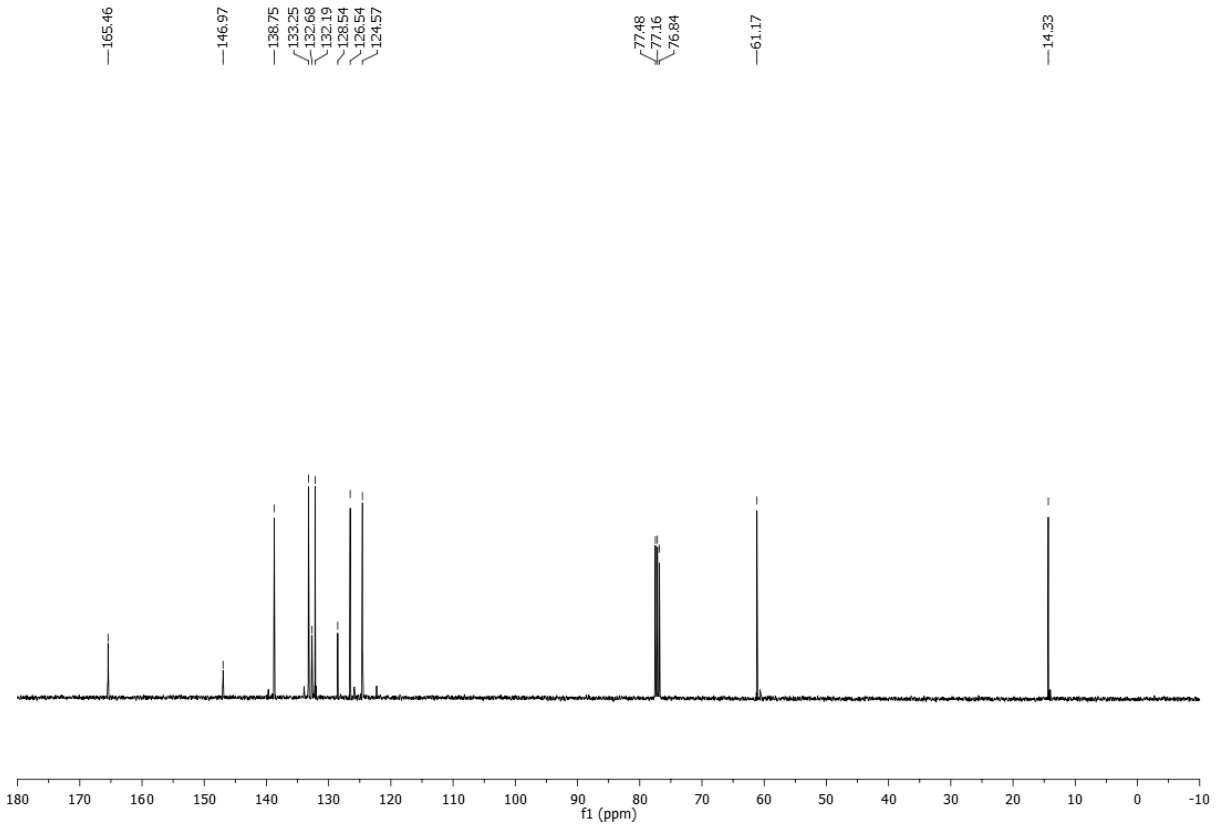

$^{1}$H NMR of Compound 18



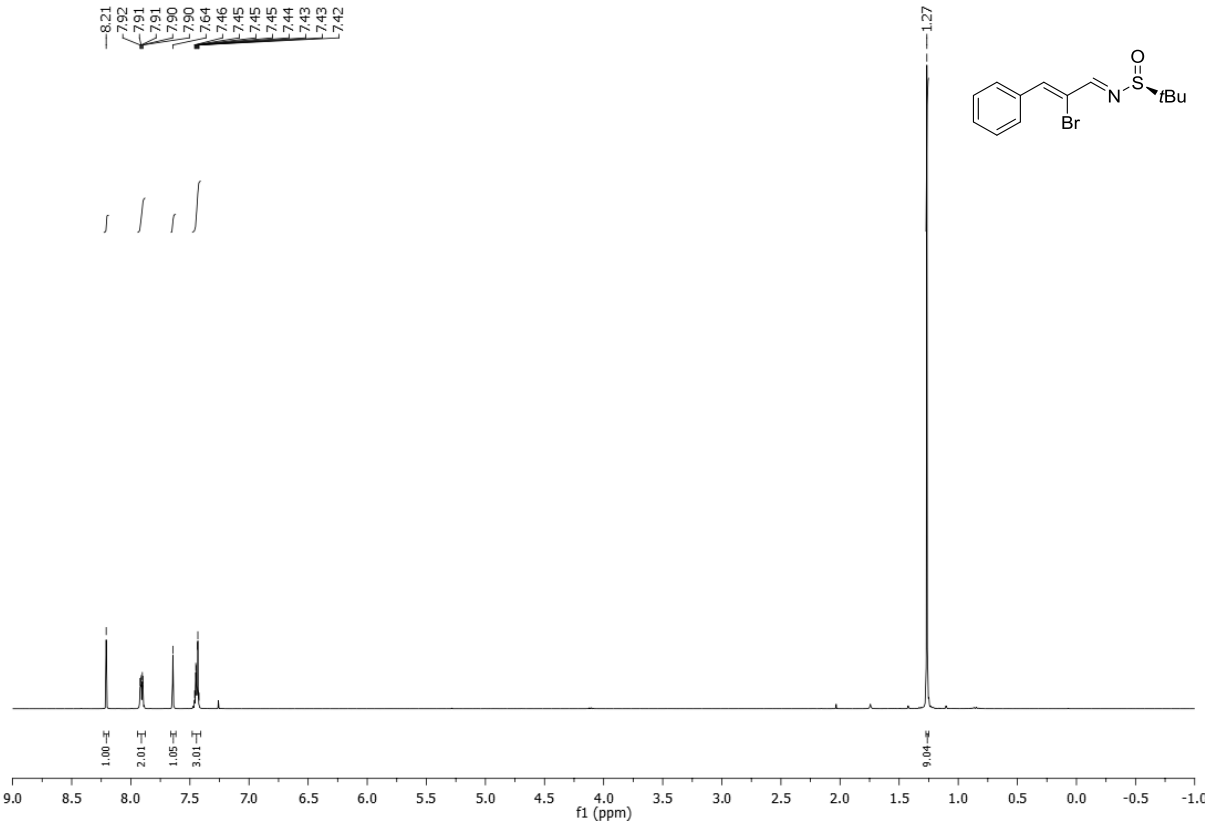
$^{1}$H NMR of Compound 19



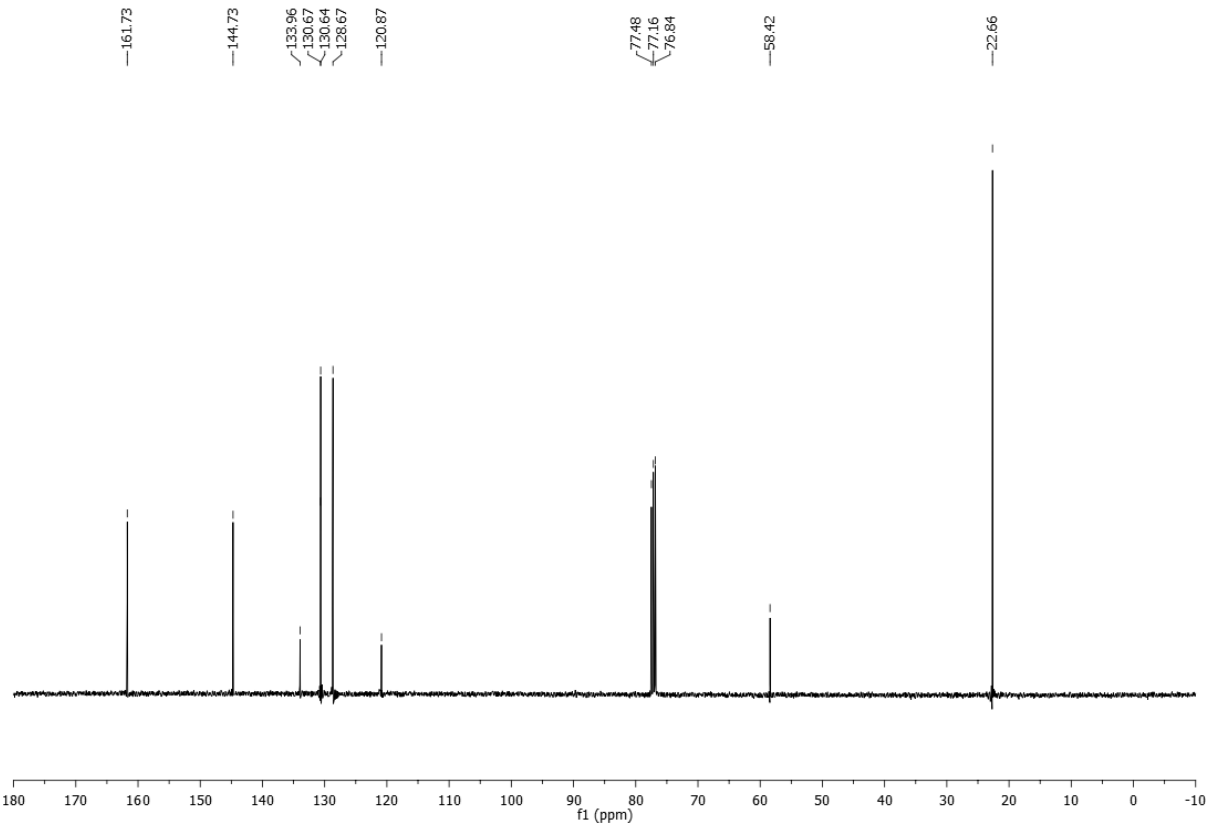

$^{13}$C NMR of Compound 19



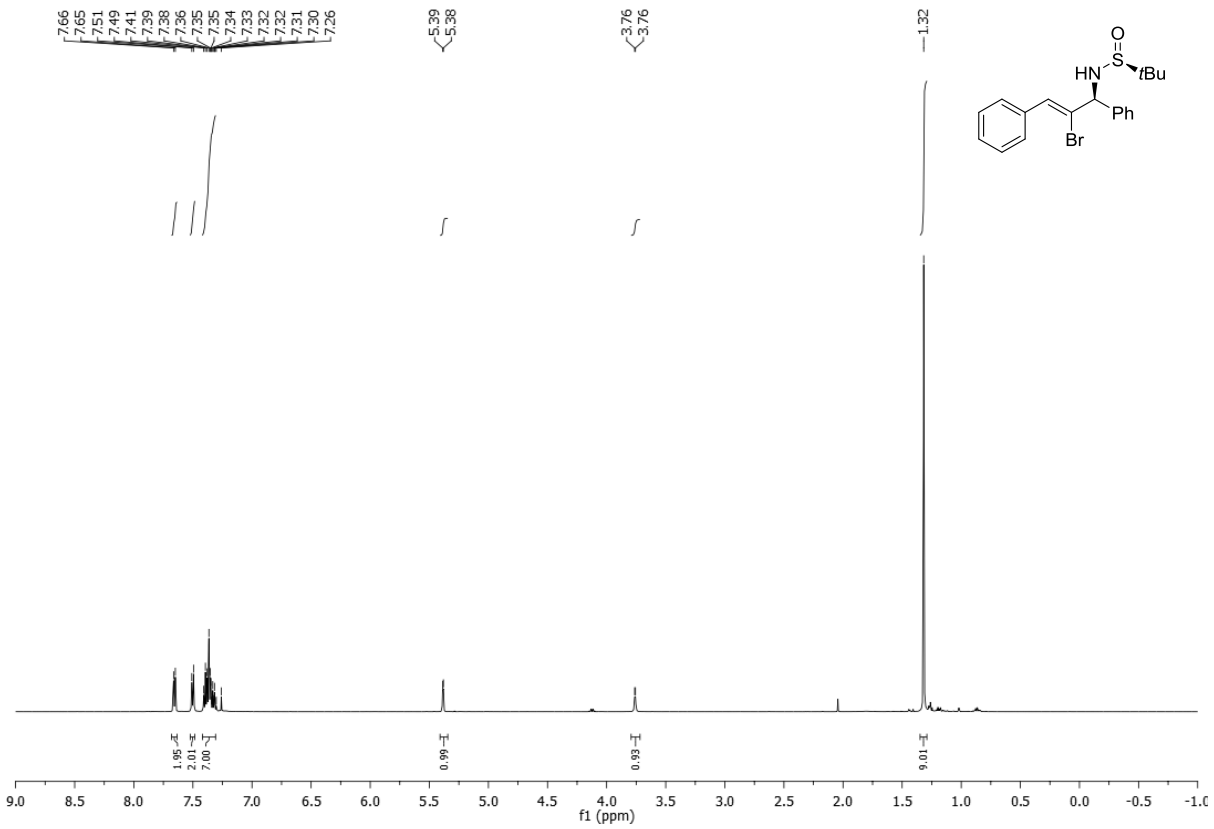
$^{1}$H NMR of Compound 20



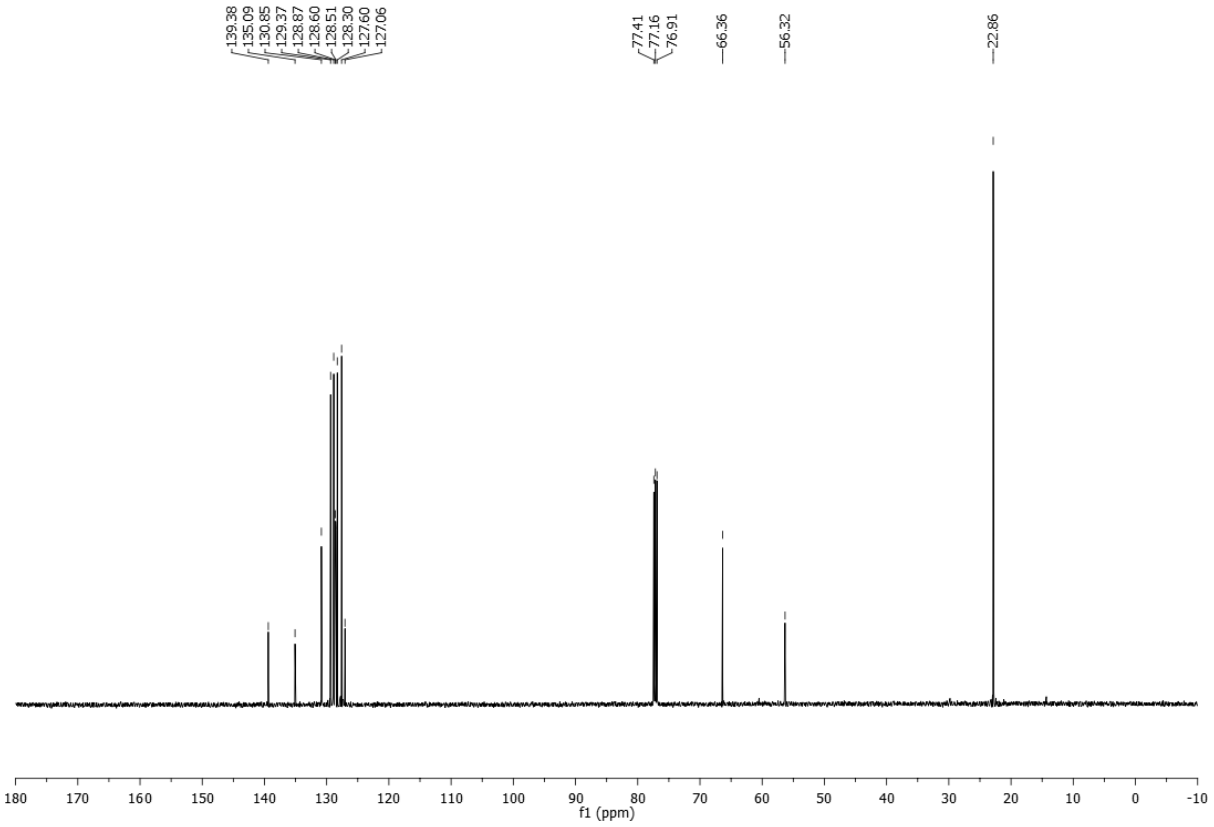

$^{13}$C NMR of Compound 20



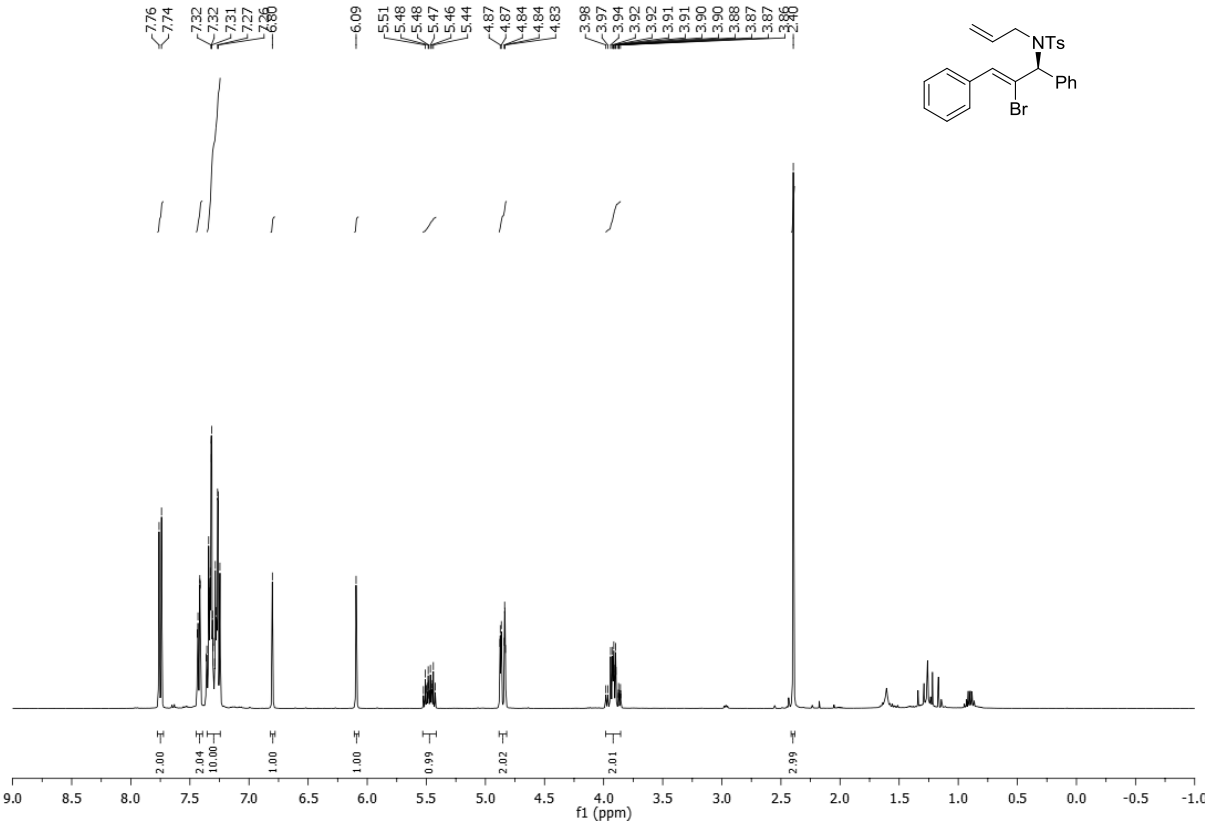
$^{1}$H NMR of Compound 21




$^{13}$C NMR of Compound 21



$^{1}$H NMR of Compound 22

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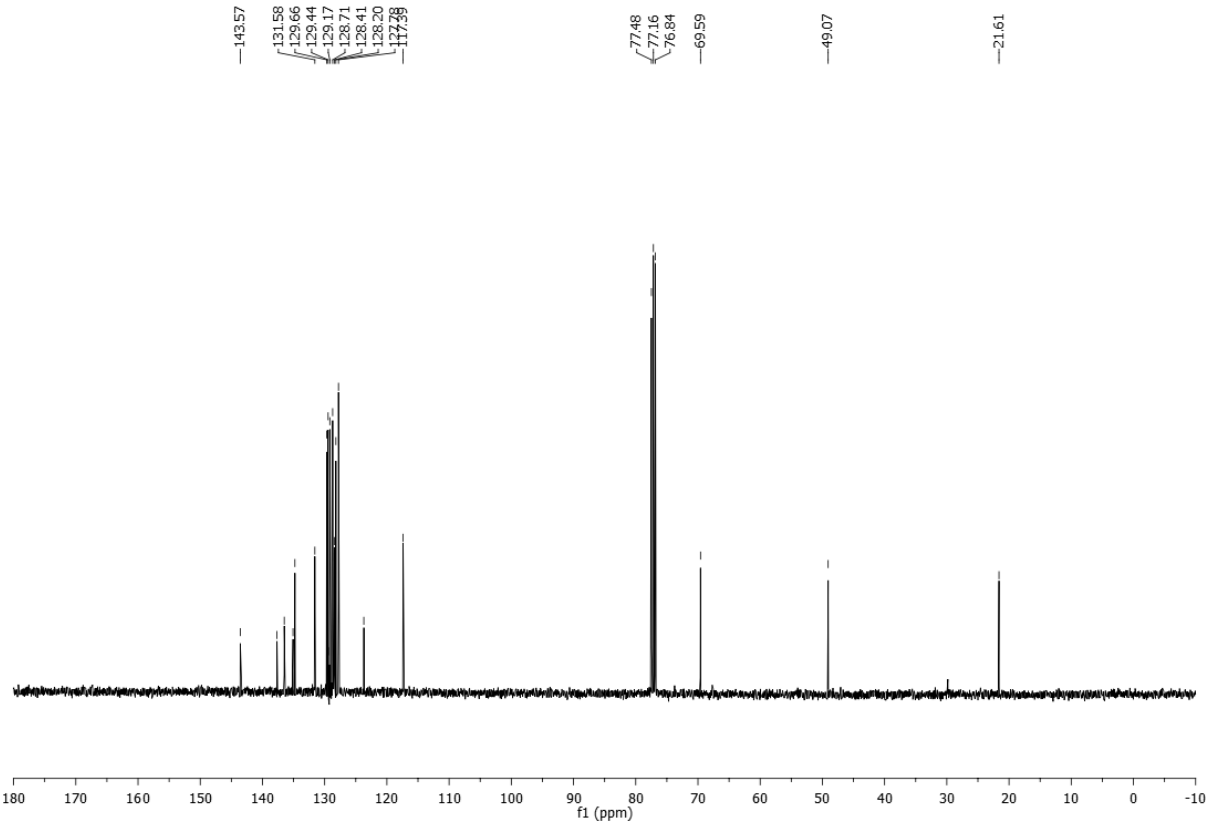

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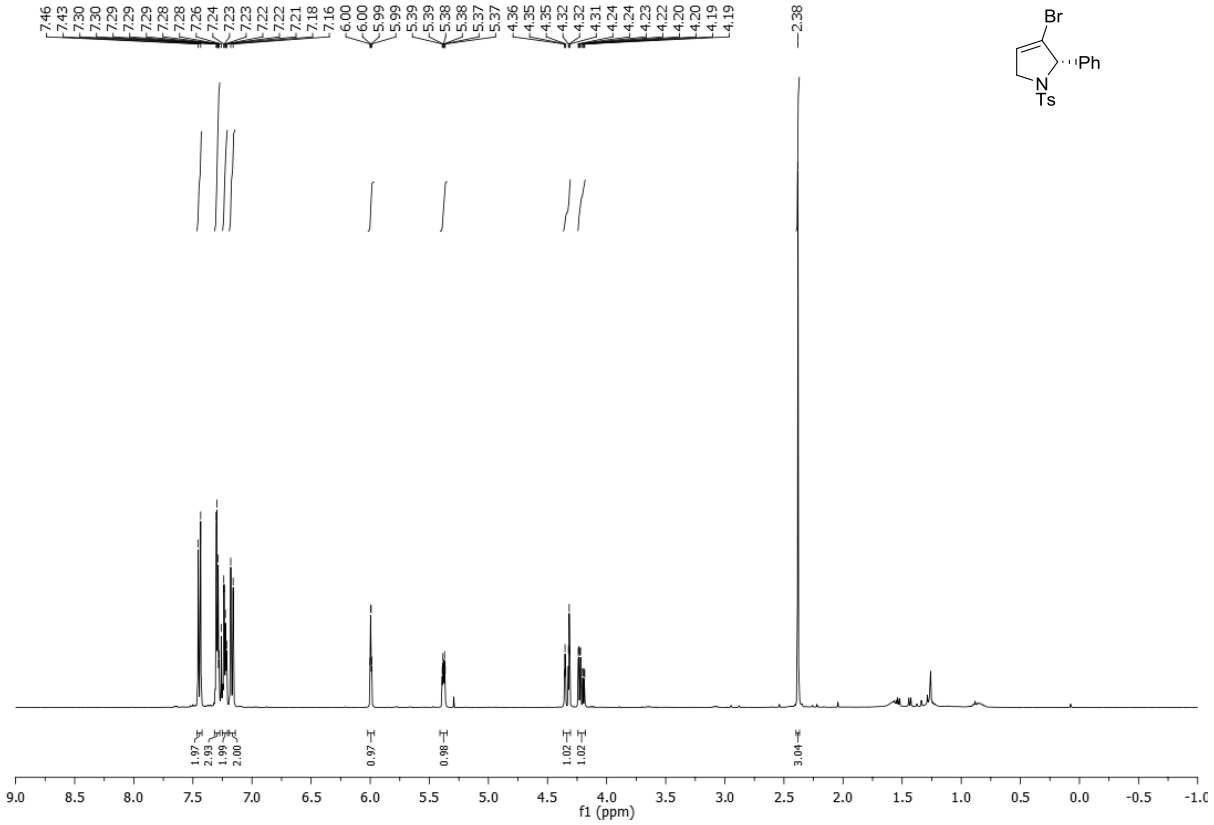
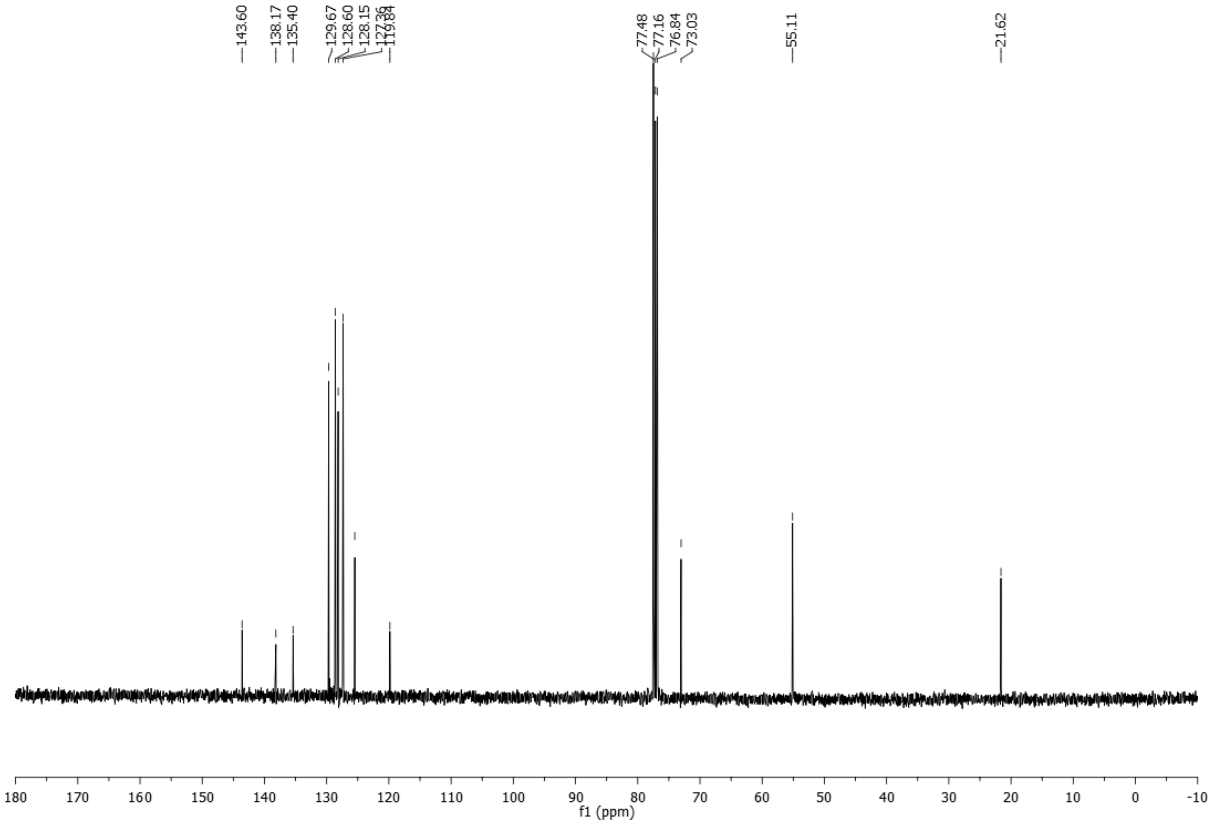
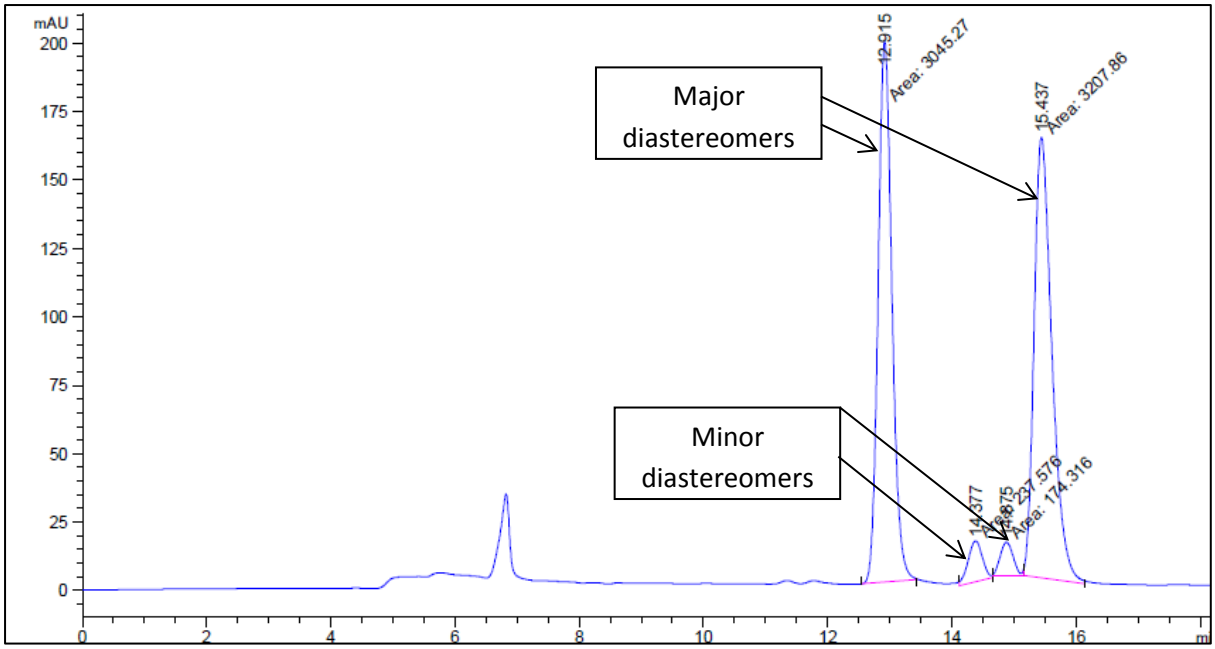



$^{13}$C NMR of Compound 23



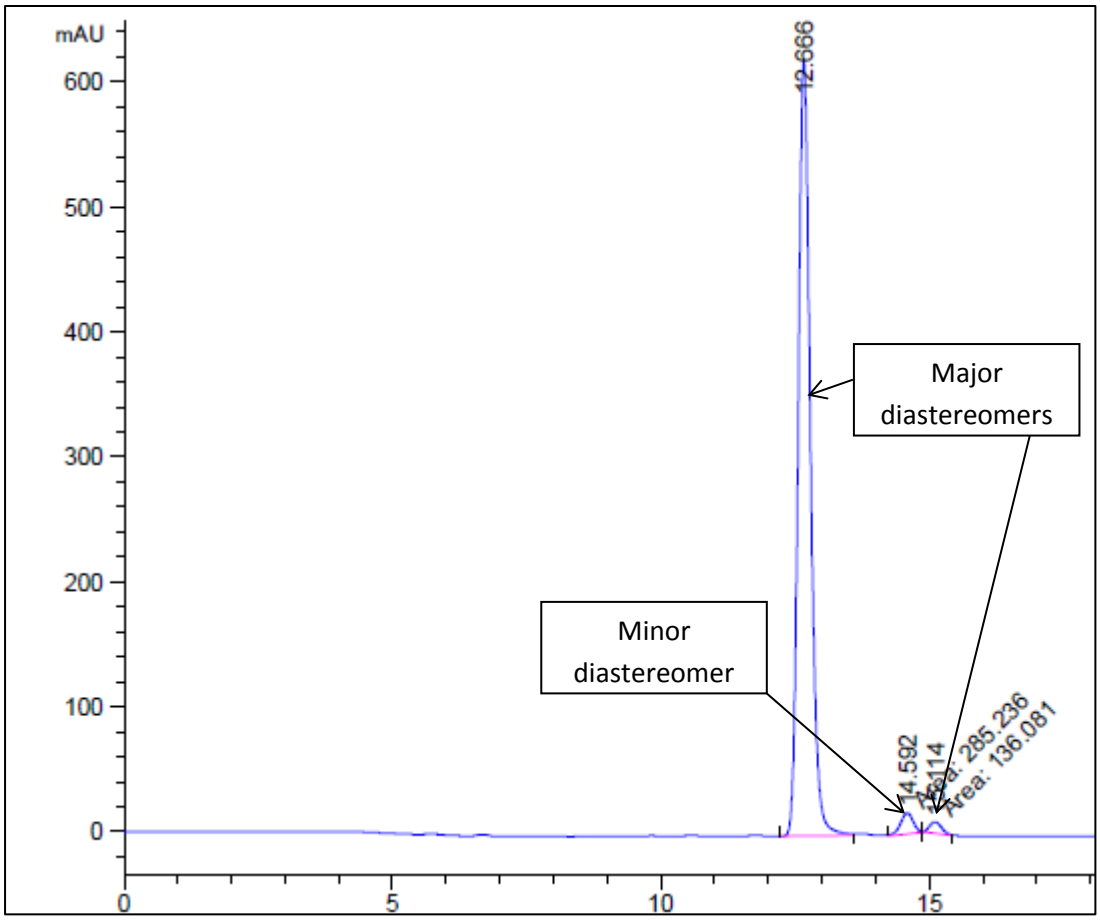
**HPLC Data**

*Racemic Compound 12s*

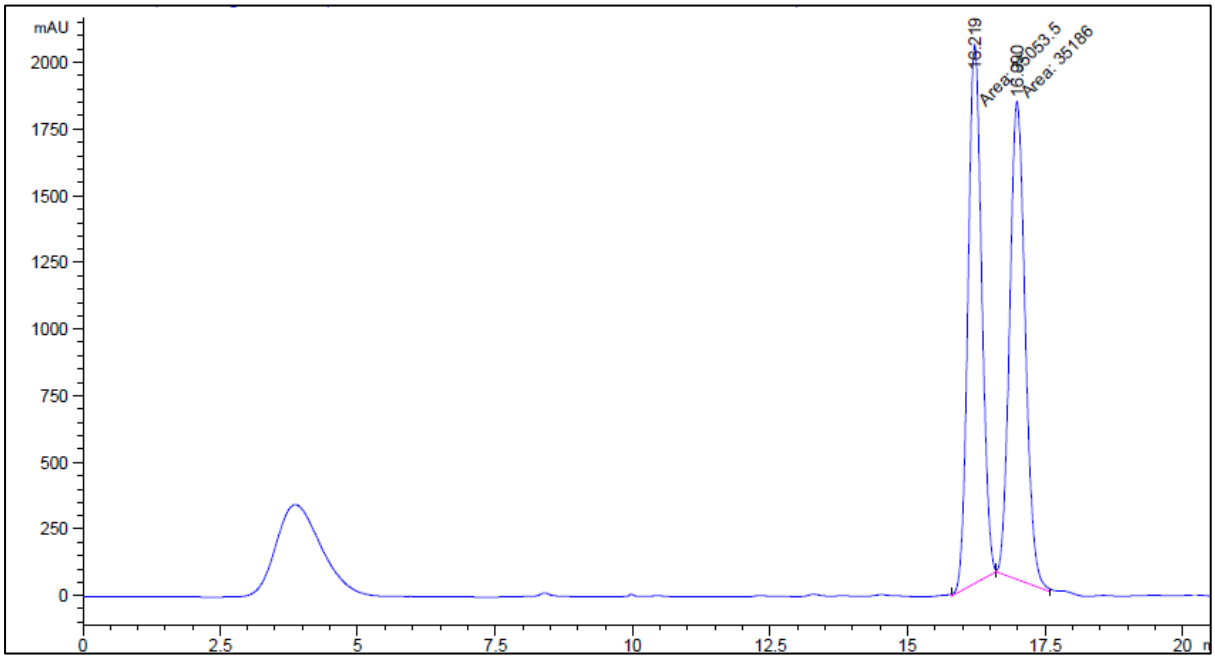



*Compound 12s*

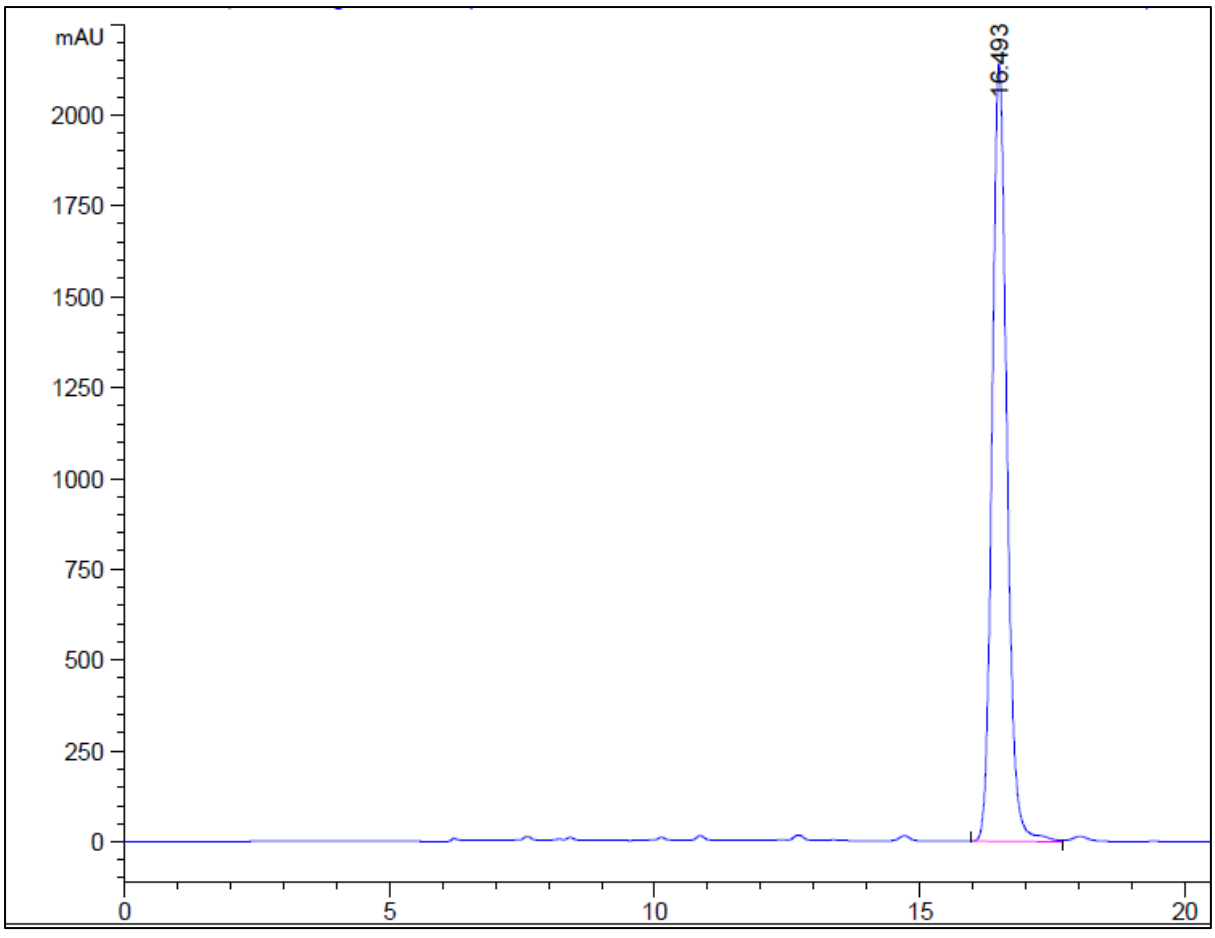
Due to a lower solubility of minor diastereomer in 2-propanol, *dr* appears greater by HPLC.



*Racemic Compound 22*

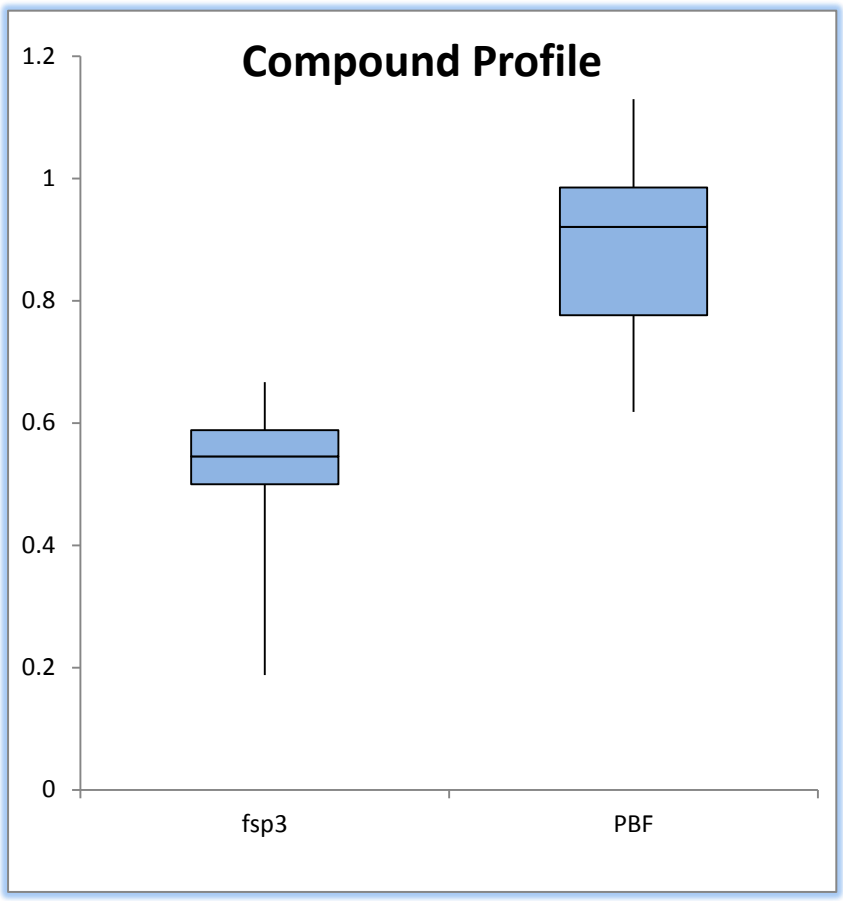


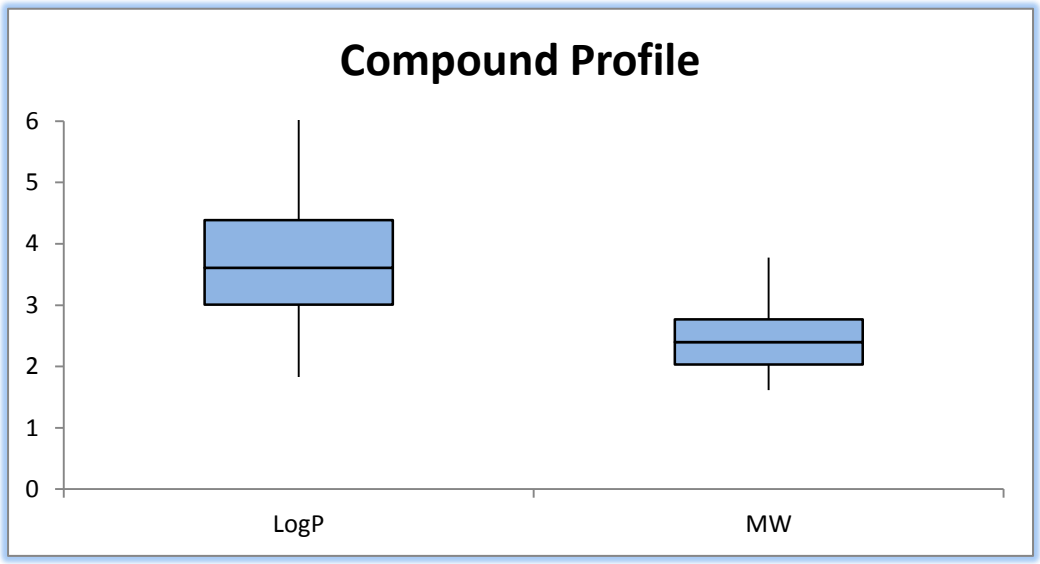

*Compound 22*



**Physicochemical Analysis of Products**

$fsp^3$ data, PBF values, log P and molecular weight were generated using the LLAMA platform at the University of Leeds, UK.[12] Data obtained was analysed using Microsoft Excel to generate the following box-plots.



**References**


1. D. N. Primer, I. Karakaya, J. C. Tellis, G. A. Molander, *J. Am. Chem. Soc.*, **2015**, *137*, 2195-2198

2. G. A. Molander, K. M. Traister, B. T. O'Neill, *J. Org. Chem.*, **2014**, *79*, 5771-5780

3. J. Wang, T. Qin, T-G. Chen, L. Wimmer, J. T. Edwards, J. Cornella, B. Vokits, S. A. Shaw, P. S. Baran, *Angew. Chem. Int. Ed.*, **2016**, *55*, 9676 –9679

4. D. F. Thomas, *Synthesis*, **2013**, *45*, 2949-2958

5. E. G. Corley, K. Conrad, J. A. Murry, C. Savarin, J. Holko, G. Boice, *J. Org. Chem.*, **2004**, *69*, 5120

6. C. Han, S. L. Buchwald, *J. Am. Chem. Soc.*, **2009**, *131*, 7532-7533

*7.* F. Toriyama, J. Cornella, L. Wimmer, T-G. Chen, D. D. Dixon, G. Creech, and P. S. Baran, *J. Am. Chem. Soc.*, **2016**, *138*, 11132–11135

8. P. Evans, T. McCabe, B. S. Morgan, S. Reau, *Org. Lett.*, **2005**, *7*, 43-46

9. Y. Iwai, K. M. Gligorich, and M. S. Sigman, *Angew. Chem. Int. Ed.*, **2008**, *47*, 3219 –3222

10. Iwai, Y.; Gligorich, K. M.; Sigman, M. S.; *Angew. Chem. Int. Ed*., **2008**, *47*, 3219 –3222.

11. Pettersson, F.; Pontén, H.; Waters, N.; Waters, S.; Sonesson, C.; *J. Med. Chem*. **2010**, *53*, 2510–2520.

12. (a) https://llama.leeds.ac.uk/ (b) Colomer, I.; Empson, C. J.; Craven, P.; Owen, Z.; Doveston, R. G.; Churcher, I.; Marsden, S. P.; Nelson, A. *Chem. Commun.* **2016**, *52*, 7209 – 7212.