Supporting Information

Synthesis and Suzuki–Miyaura Cross-Coupling Reactions of Potassium Boc-Protected Aminomethyltrifluoroborate with Aryl- and Hetaryl Halides

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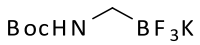
Contents:

General.

$Pd(OAc)_2$, SPhos, XPhos, and K_2CO_3 were used as received. All halides were used as received. Toluene was distilled from sodium/benzophenone prior to use. H_2O was degassed prior to use. Melting points (°C) are uncorrected. ^1H, ^{13}C and ^{19}F NMR spectra were recorded at 500, 125.8, and 470.8 MHz, respectively. ^{19}F NMR chemical shifts were referenced to external $CFCl_3$ (0.0 ppm). ^{11}B NMR spectra at 128.4 MHz were obtained on a spectrometer equipped with the appropriate decoupling accessories. All ^{11}B NMR chemical shifts were referenced to external $BF_3 \bullet OEt_2$ (0.0 ppm) with a negative sign indicating an upfield shift. Analytical thin layer chromatography (TLC) was performed on TLC silica gel plates (0.25 nm) precoated with a fluorescent indicator. Standard flash chromatography procedures were followed using 32–63 μm silica gel. Visualization was effected with ultraviolet light and ninhydrin solution.

Procedure for the Preparation of Potassium Boc-Protected Aminomethyltrifluoroborate.

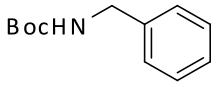


Potassium (*tert*-Butoxycarbonyl)amino)methyl)trifluoroborate 2.

KHMDS (4.0 g, 19.8 mmol, 1.0 equiv) in THF (40 mL) was added slowly to 2-(chloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1** (3.5 g, 19.84 mmol, 1.0 equiv) in THF (40 mL) at –78 °C. The reaction mixture was stirred for 15 min at –78 °C and then stirred for an additional 2 h at rt. The reaction mixture was cooled to 0 °C. MeOH (1.3 g, 39.7 mmol, 2.0 equiv) was added to the flask at 0 °C. After stirring for 1 h at 0 °C, $(Boc)_2O$ (8.7 g, 39.7 mmol, 2.0 equiv) was added in one portion. The reaction flask was warmed to rt and stirred overnight at rt. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in MeOH (40 mL), and then KHF_2 in H_2O (4.5 M, 18 mL, 4.0 equiv) was added slowly at 0 °C. After vigorous stirring for 30 min at rt, the solution was concentrated in vacuo and then dried in vacuo overnight. The crude mixture was extracted with acetone (3 × 30 mL), and the extracts were combined and concentrated. Et_2O (60 mL) was added to precipitate the product. The resulting precipitate (3.5 g, 14.9 mmol) was filtered and dried in vacuo to provide the product **2** as a white solid in 75% yield. mp (transition): 178–181 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 4.57 (s, 1H), 1.81, (s, 2H), 1.33 (s, 9H); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 156.4, 76.4, 28.3, one carbon was not detected; ^{19}F NMR (470.8 MHz, acetone-d_6) δ –145.5; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 4.13; IR (neat) 3426, 1680 cm^{-1}; HRMS (ES$^-$) calcd. for $C_6H_{12}BF_3NO_2$ $[M–K]^-$ 198.0913, found 198.0906.

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

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



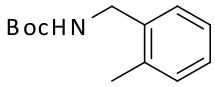
***tert*-Butyl Benzylcarbamate (3a).**

Obtained **3a** as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.22 (m, 5H), 4.89 (br, 1H), 4.31 (d, J = 5.5 Hz, 2H), 1.46 (s, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 139.0, 128.7, 127.6, 127.4, 79.5, 44.8, 28.5. Data is consistent with that reported in the literature.[a]



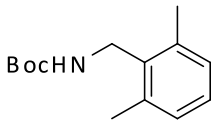
***tert*-Butyl 2-Methylbenzylcarbamate (3b).**

Obtained **3b** as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.12 (m, 4H), 4.71 (br, 1H), 4.31 (d, J = 5.5 Hz, 2H), 2.31 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.8, 136.6, 136.4, 130.5, 128.1, 127.6, 126.2, 79.5, 42.9, 28.5, 19.0. Data is consistent with that reported in the literature.[b]



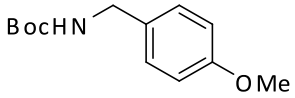
***tert*-Butyl 2,6-Dimethylbenzylcarbamate (3c).**

Obtained **3c** as a white solid after flash chromatography (hexanes/EtOAc = 10:1).

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

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

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



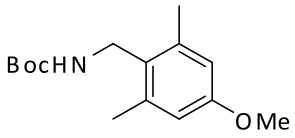
***tert*-Butyl 4-Methoxybenzylcarbamate (3d).**

Obtained **3d** as a colorless oil after flash chromatography (hexanes/EtOAc = 5:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 4.84 (br, 1H), 4.24 (d, J = 5.5 Hz, 2H), 3.79 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 159.0, 156.0, 131.2, 128.9, 114.1, 79.5, 55.4, 44.3, 28.5. Data is consistent with that reported in the literature.[c]



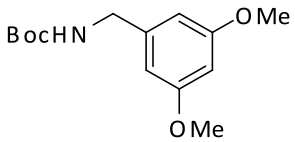
***tert*-Butyl 4-Methoxy-2,6-dimethylbenzylcarbamate (3e).**

Obtained **3e** as a white solid after flash chromatography (hexanes/EtOAc = 15:1).

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

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

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



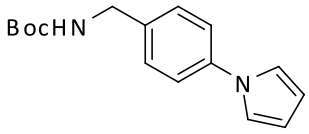
***tert*-Butyl 3,5-Dimethoxybenzylcarbamate (3f).**

Obtained **3f** as a white solid after flash chromatography (hexanes/EtOAc = 6:1).

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

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

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



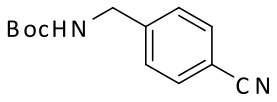
***tert*-Butyl 4-(1H-Pyrrol-1-yl)benzylcarbamate (3g).**

Obtained **3g** as a white solid after flash chromatography (hexanes/EtOAc = 5:1).

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

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

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



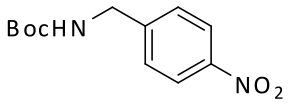
***tert*-Butyl 4-Cyanobenzylcarbamate (3h).**

Obtained **3h** as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

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

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

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



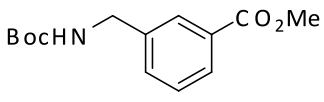
***tert*-Butyl 4-Nitrobenzylcarbamate (3i).**

Obtained **3i** as a yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 5.13 (br, 1H), 4.12 (d, *J* = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 156.0, 147.3, 146.9, 127.9, 123.9, 80.2, 44.1, 28.4. Data is consistent with that reported in the literature.[e]



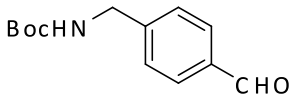
Methyl 3-(((*tert*-Butoxycarbonyl)amino)methyl)benzoate (3j).

Obtained **3j** as a white solid after flash chromatography (hexanes/EtOAc = 7:1).

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

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

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



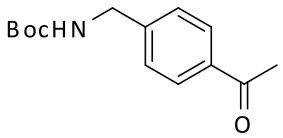
***tert*-Butyl 4-Formylbenzylcarbamate (3k).**

Obtained **3k** as a white solid after flash chromatography (hexanes/EtOAc = 4:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 7.5 Hz, 2H), 5.09 (br, 1H), 4.40 (d, J = 5.5 Hz, 2H), 1.47 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 192.0, 156.0, 146.3, 135.6, 130.2, 127.8, 80.0, 44.4, 28.5. Data is consistent with that reported in the literature.[f]



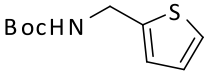
***tert*-Butyl 4-Acetylbenzylcarbamate (3l).**

Obtained **3l** as a white solid after flash chromatography (hexanes/EtOAc = 3:1).

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

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

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



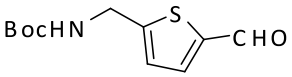
***tert*-Butyl (Thiophen-2-ylmethyl)carbamate (4a).**

Obtained **4a** as a light yellow oil after flash chromatography (hexanes/EtOAc = 7:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22–7.18 (m, 1H), 6.96–6.91 (m, 2H), 4.95 (br, 1H), 4.47 (d, J = 5.0 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 155.6, 142.0, 126.9, 125.6, 125.0, 79.8, 39.6, 28.5. Data is consistent with that reported in the literature.[g]



***tert*-Butyl ((5-Formylthiophen-2-yl)methyl)carbamate (4b).**

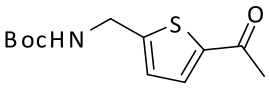
Obtained **4b** as a yellow oil after flash chromatography (hexanes/EtOAc = 4:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.63 (d, J = 4.0 Hz, 1H), 7.05 (d, J = 3.5 Hz, 1H), 5.34 (br, 1H), 4.51 (d, J = 5.5 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$)

δ 183.0, 155.7, 154.1, 142.7, 136.9, 126.1, 80.2, 40.1, 28.4; IR (neat) 3333, 1697, 1665 cm^{-1}; HRMS (ES+) calcd. for $C_{11}H_{15}NO_3SNa$ $[M+Na]^+$ 264.0670, found 264.0671.



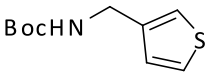
***tert*-Butyl ((5-Acetylthiophen-2-yl)methyl)carbamate (4c).**

Obtained **4c** as a yellow oil after flash chromatography (hexanes/EtOAc = 3:1).

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

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

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



***tert*-Butyl (Thiophen-3-ylmethyl)carbamate (4d).**

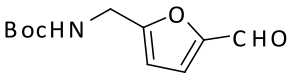
Obtained **4d** as a white solid after flash chromatography (hexanes/EtOAc = 10:1).

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

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

mp: 54–56 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.25 (m, 1H), 7.12 (s, 1H), 7.04–7.00 (m, 1H), 4.85 (br, 1H), 4.31–4.29 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$)

δ 155.9, 140.0, 127.3, 126.4, 121.9, 79.6, 40.0, 28.5; IR (neat) 3300, 1679, 1534 cm^{-1}; HRMS (ES+) calcd. for $C_{10}H_{15}NO_2SNa$ $[M+Na]^+$ 236.0721, found 236.0714.



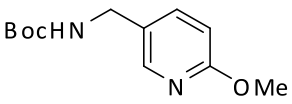
***tert*-Butyl ((5-Formylfuran-2-yl)methyl)carbamate (4e).**

Obtained **4e** as a dark brown oil after flash chromatography (hexanes/EtOAc = 3:1).

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

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

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



***tert*-Butyl ((6-Methoxypyridin-3-yl)methyl)carbamate (4f).**

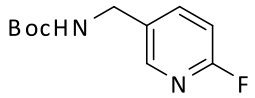
Obtained **4f** as a white solid after flash chromatography (hexanes/EtOAc = 5:1).

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

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

mp: 55–58 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 1.5 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 4.93 (br, 1H), 4.23 (d, J = 5.0 Hz, 2H), 3.92 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.7, 155.9, 145.9, 138.6, 127.4, 111.0,

79.7, 53.5, 41.7, 28.5; IR (neat) 3358, 1685, 1522, 1495 cm^{-1}; HRMS (ES+) calcd. for $C_{12}H_{19}N_2O_3$ $[M+H]^+$ 239.1396, found 239.1404.



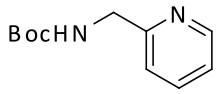
***tert*-Butyl ((6-Fluoropyridin-3-yl)methyl)carbamate (4g).**

Obtained **4g** as a colorless oil after flash chromatography (hexanes/EtOAc = 3:1).

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

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

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



***tert*-Butyl (Pyridin-2-ylmethyl)carbamate (4h).**

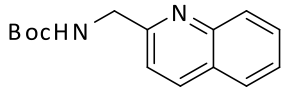
Obtained **4h** as a light yellow oil after flash chromatography (hexanes/EtOAc = 1:1).

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

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

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

136.8, 122.3, 121.8, 79.6, 45.9, 28.5; IR (neat) 3344, 1781, 1709 cm^{-1}; HRMS (ES+) calcd. for $C_{11}H_{16}N_2O_2Na$ $[M+Na]^+$ 231.1109, found 231.1113.



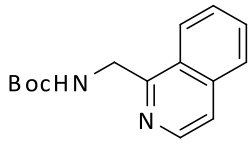
***tert*-Butyl (Quinolin-2-ylmethyl)carbamate (4i).**

Obtained **4i** as a light yellow solid after flash chromatography (hexanes/EtOAc = 3:1).

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

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

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



***tert*-Butyl (Isoquinolin-1-ylmethyl)carbamate (4j).**

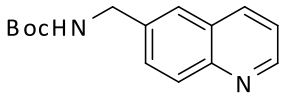
Obtained **4j** as a yellow oil after flash chromatography (hexanes/EtOAc = 5:1).

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

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

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, J = 5.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.71 (dd, J = 7.0, 7.0 Hz, 1H), 7.65 (dd, J = 7.0, 7.0 Hz, 1H), 7.58 (d, J =

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



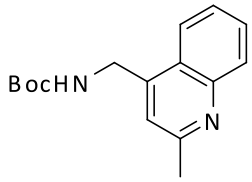
***tert*-Butyl (Quinolin-6-ylmethyl)carbamate (4k).**

Obtained **4k** as a white solid after flash chromatography (hexanes/EtOAc = 1:1).

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

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

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



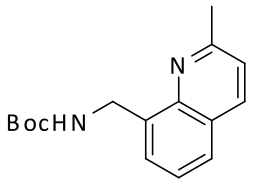
***tert*-Butyl ((2-Methylquinolin-4-yl)methyl)carbamate (4l).**

Obtained **4l** as a colorless oil after flash chromatography (hexanes/EtOAc = 1:1).

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

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

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



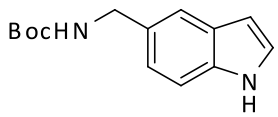
***tert*-Butyl ((2-Methylquinolin-8-yl)methyl)carbamate (4m).**

Obtained **4m** as a light yellow oil after flash chromatography (hexanes/EtOAc = 7:1).

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

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

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



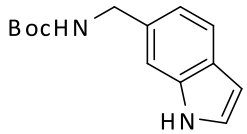
***tert*-Butyl ((1H-Indol-5-yl)methyl)carbamate (4n).**

Obtained **4n** as a light yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

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

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

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



***tert*-Butyl ((1H-Indol-6-yl)methyl)carbamate (4o).**

Obtained **4o** as a light yellow solid after flash chromatography (hexanes/EtOAc = 4:1).

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

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

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

References:

(a) Varala, R.; Nuvula, S.; Adapa, S. R. *J. Org. Chem.* **2006**, *71*, 8283.

(b) Clark, R. D.; Jahangir *J. Heterocyclic Chem.* **1995**, *32*, 81.

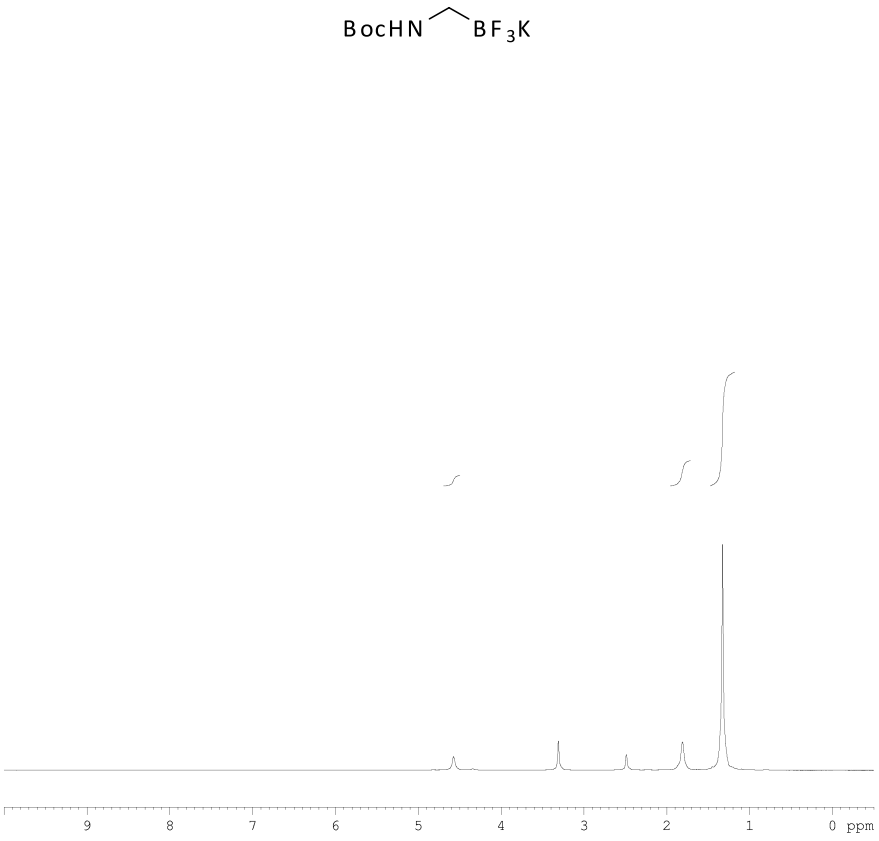
(c) Kapeller, D. C.; Hammerschmidt, F. *Chem. Eur. J.* **2009**, *15*, 5729.

(d) Ilas, J.; Kikelj, D. *Hev. Chimica Acta* **2008**, *91*, 654.

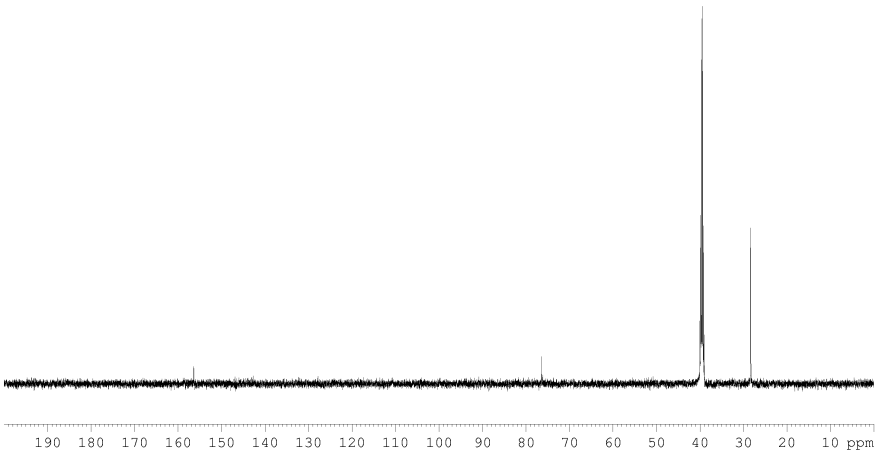
(e) Tanaka, K.-I.; Yoshifuji, S.; Nitta, Y. *Chem. Pharm. Bull.* **1988**, *36*, 3125.

(f) Far, A. R.; Cho, Y. L.; Rang, A.; Rudkevich, D. M.; Rebek, J. Jr. *Tetrahedron* **2002**, *58*, 741.

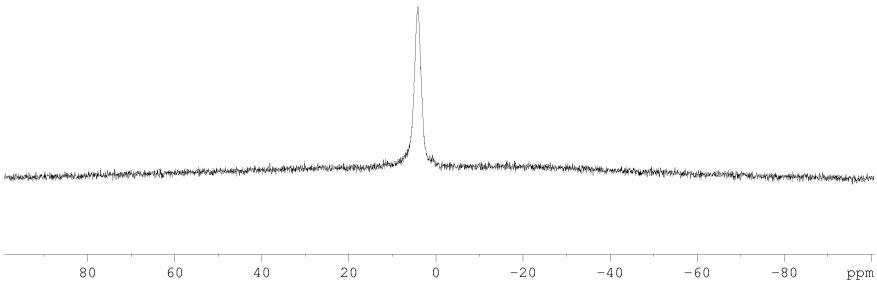
(g) Klare, J. E.; Murrary, I. P.; Goldberger, J.; Stupp, S. I. *Chem. Commun*. **2009**, 3705.



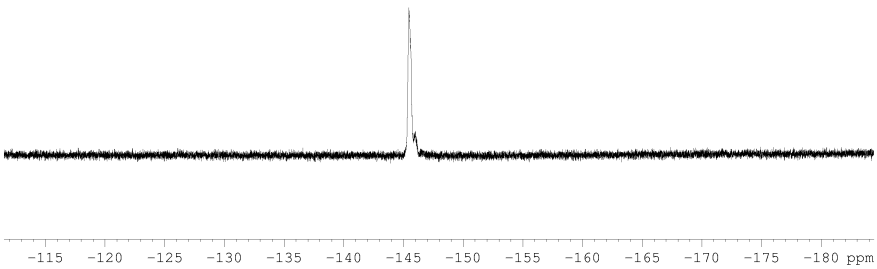
^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **2**



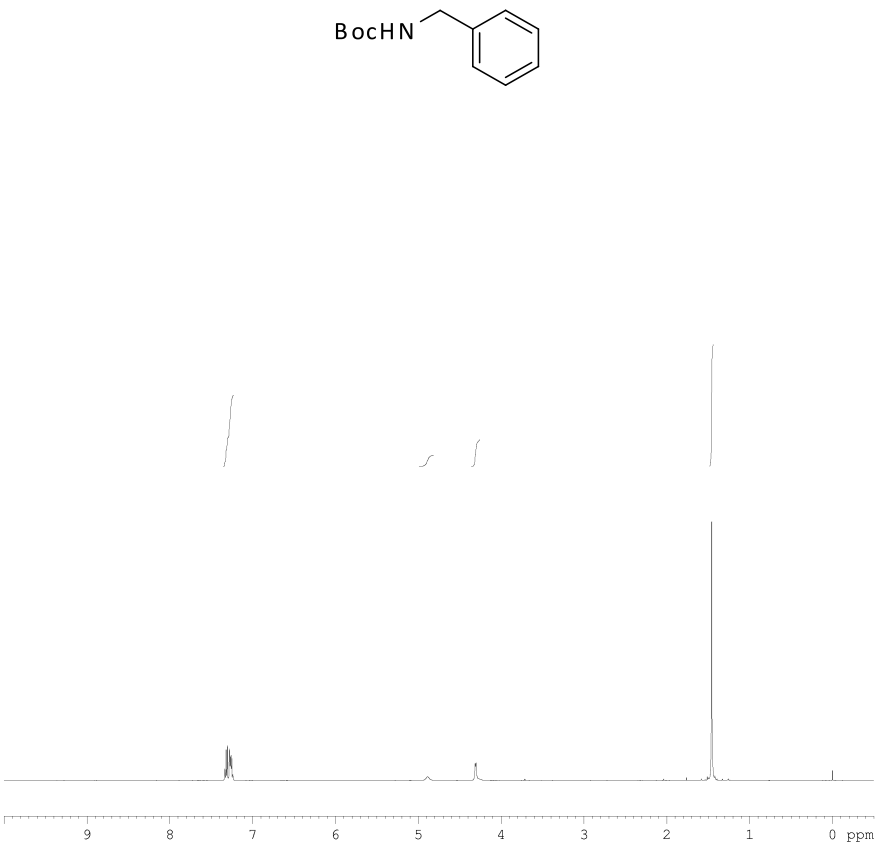
^{13}C NMR (125.8 MHz, DMSO-d_6) Spectrum of **2**



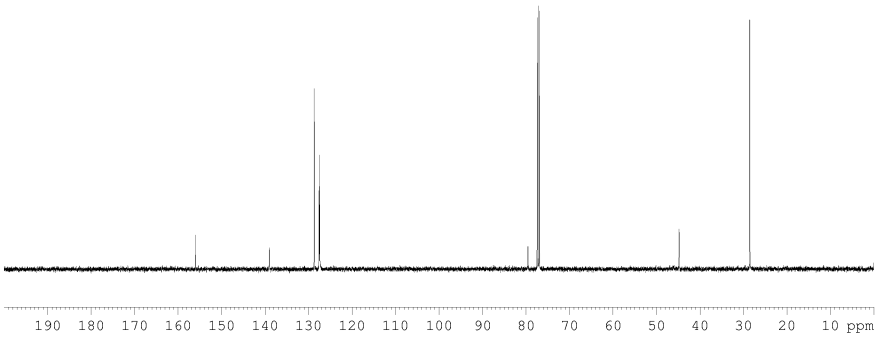
^{11}B NMR (128.4 MHz, acetone- d_6) Spectrum of **2**



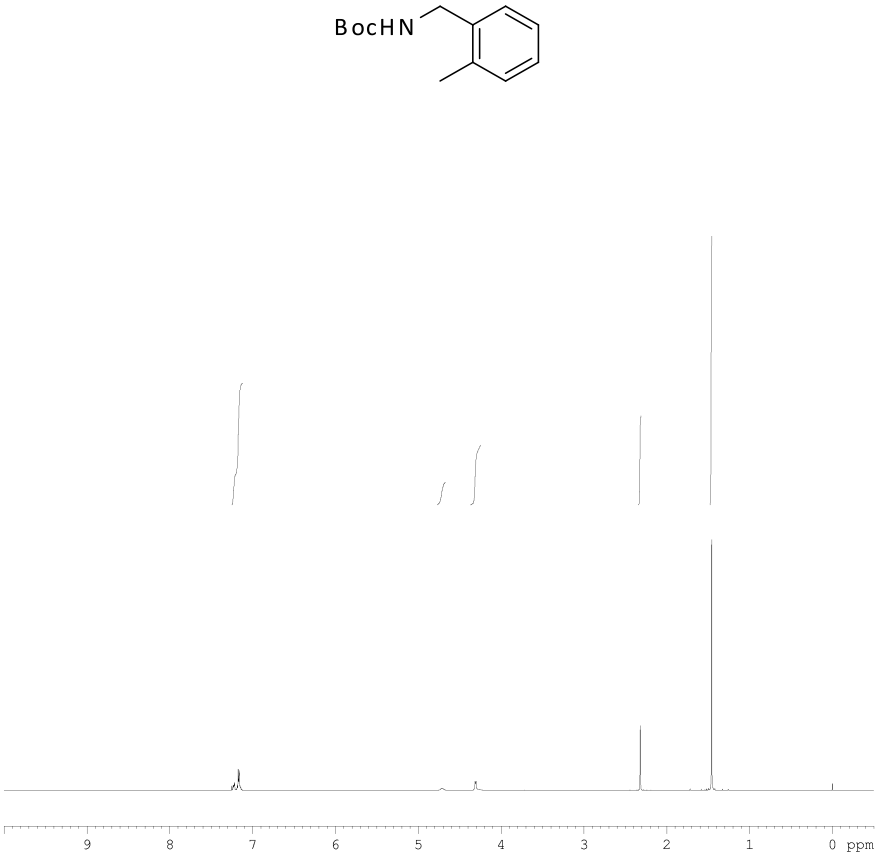
^{19}F NMR (470.8 MHz, acetone- d_6) Spectrum of **2**



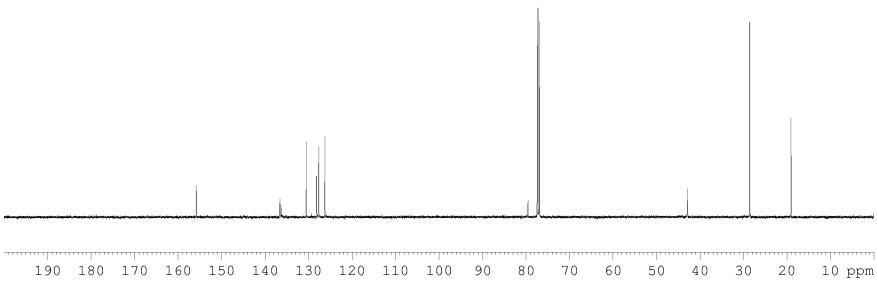
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3a**



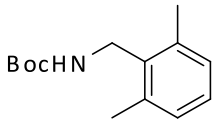
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3a**

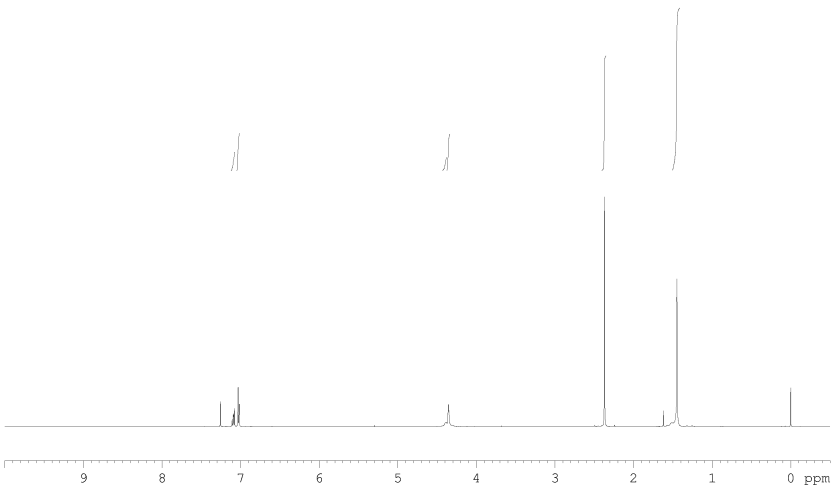


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3b**

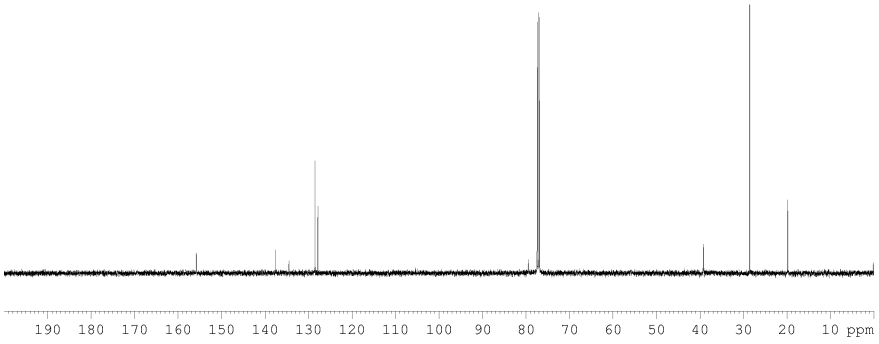


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3b**

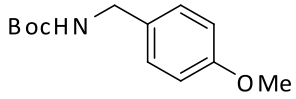


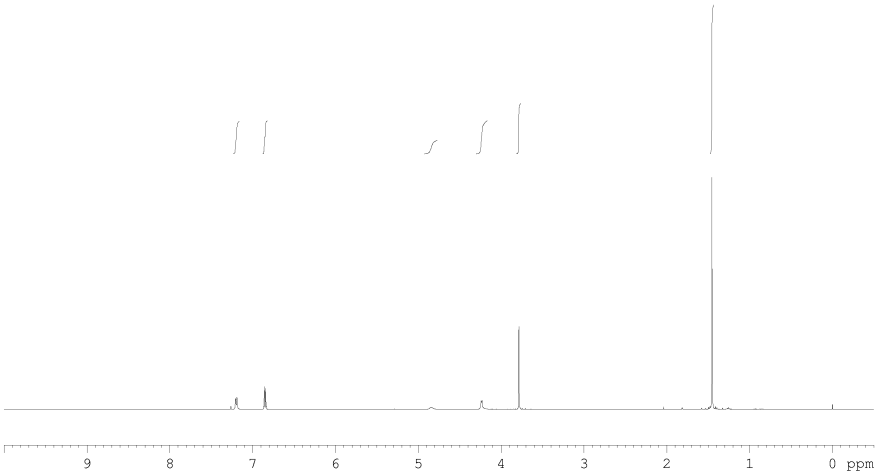


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3c**

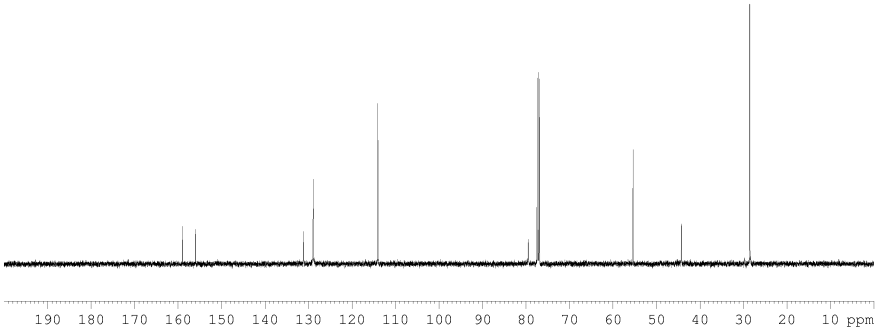


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3c**

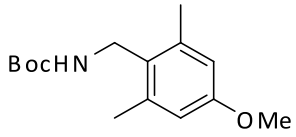


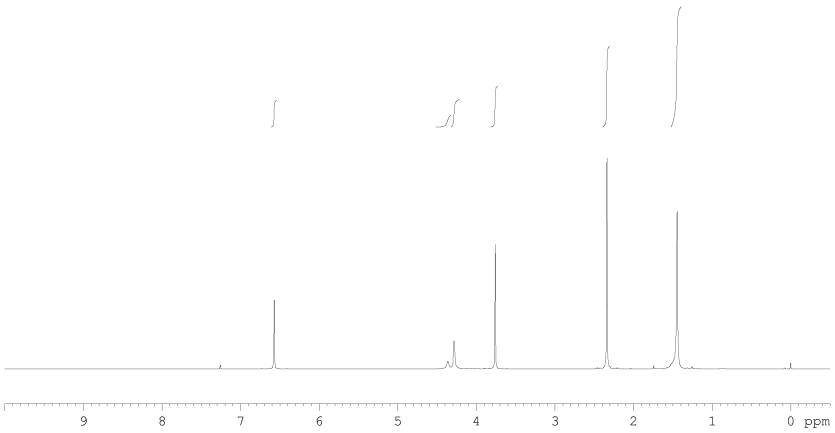


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3d**

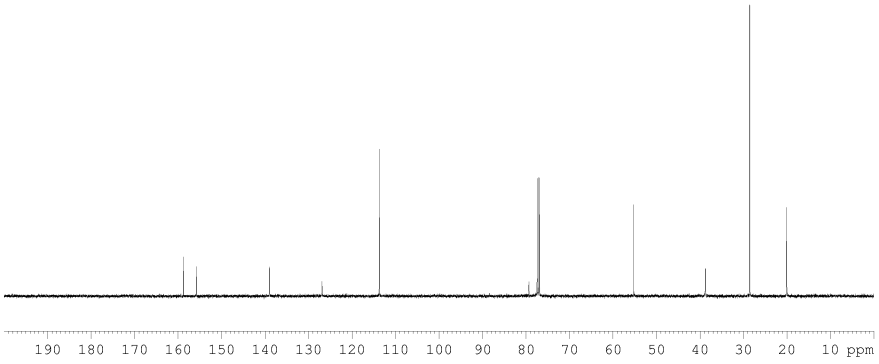


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3d**

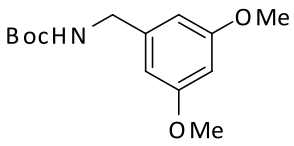


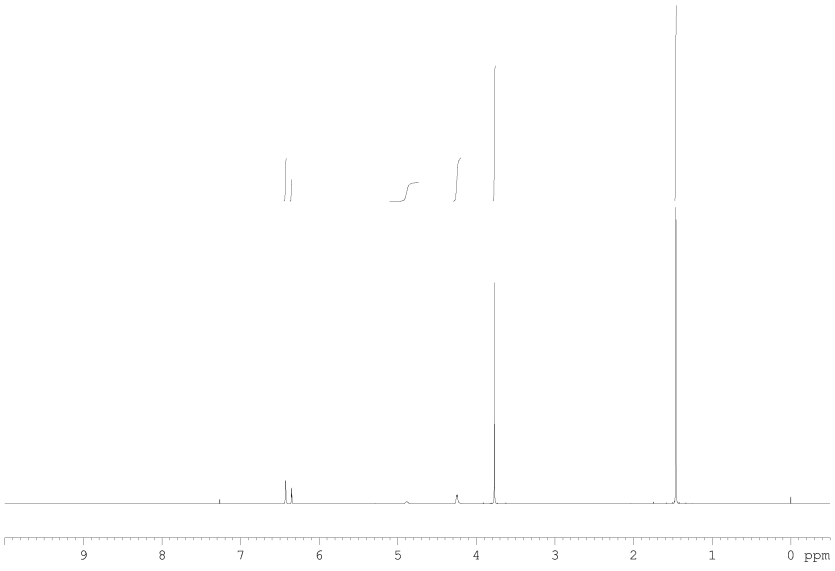


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3e**

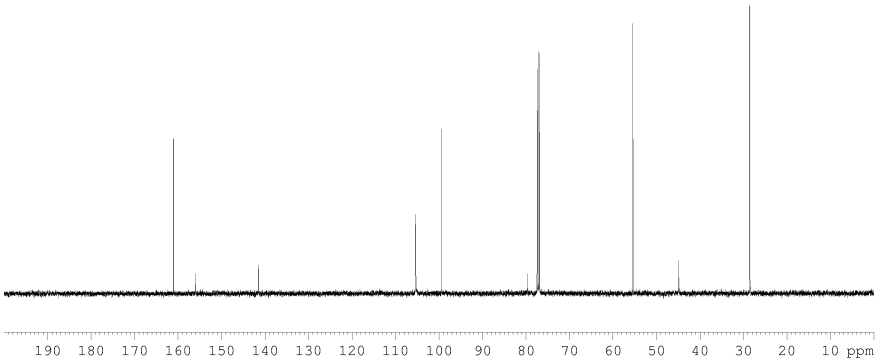


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3e**

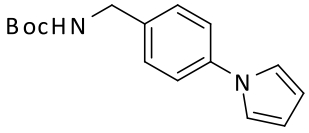


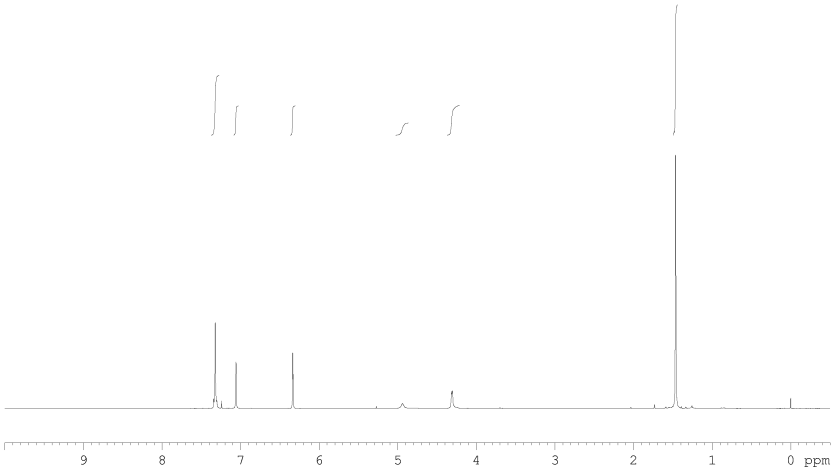


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3f**

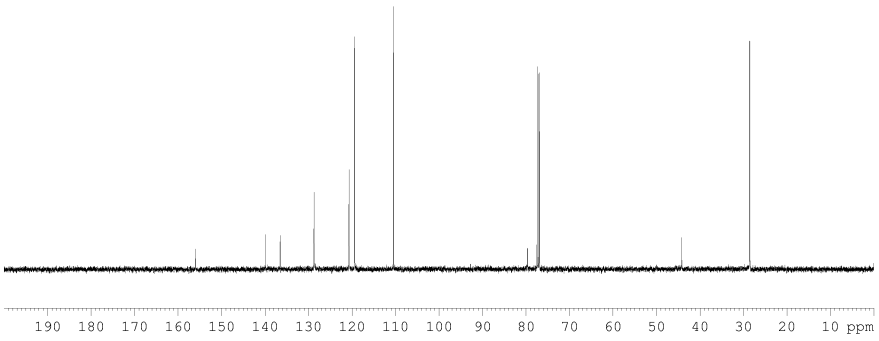


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3f**

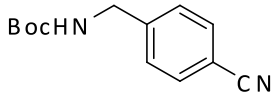


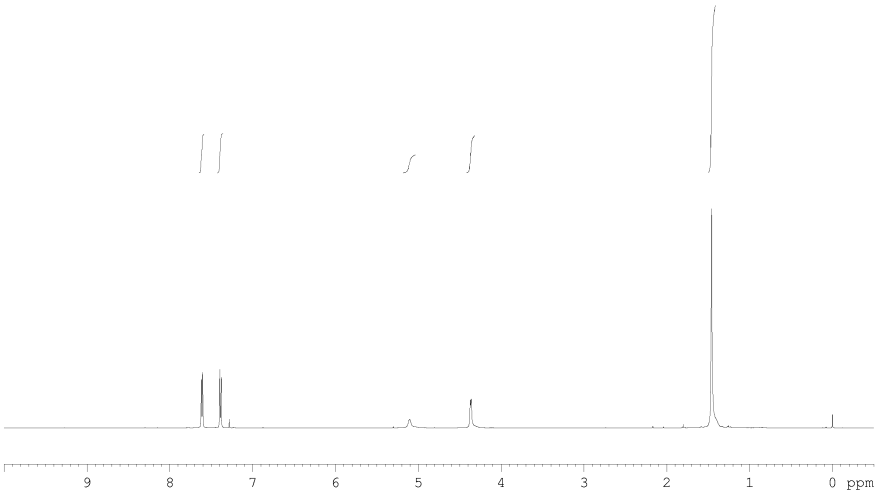


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3g**

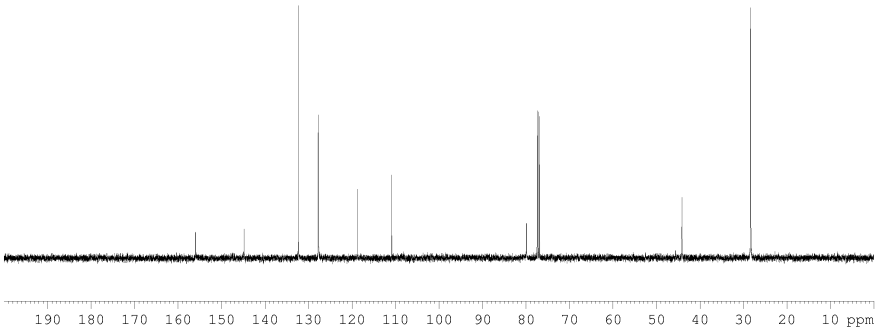


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3g**

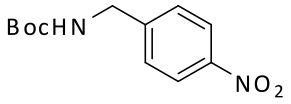


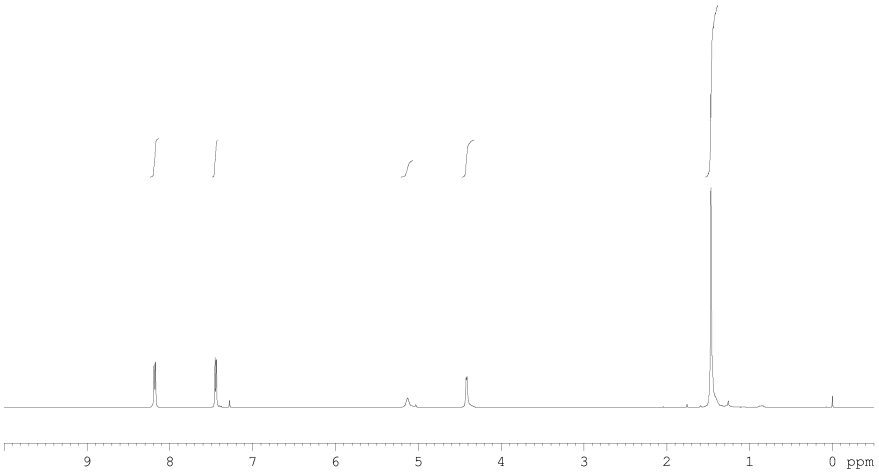


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3h**

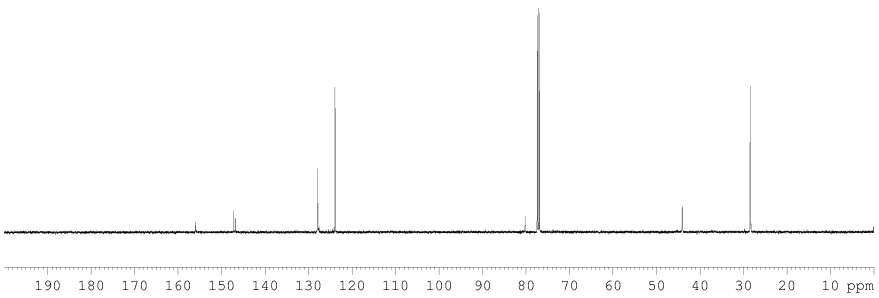


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3h**

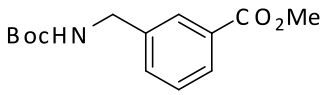


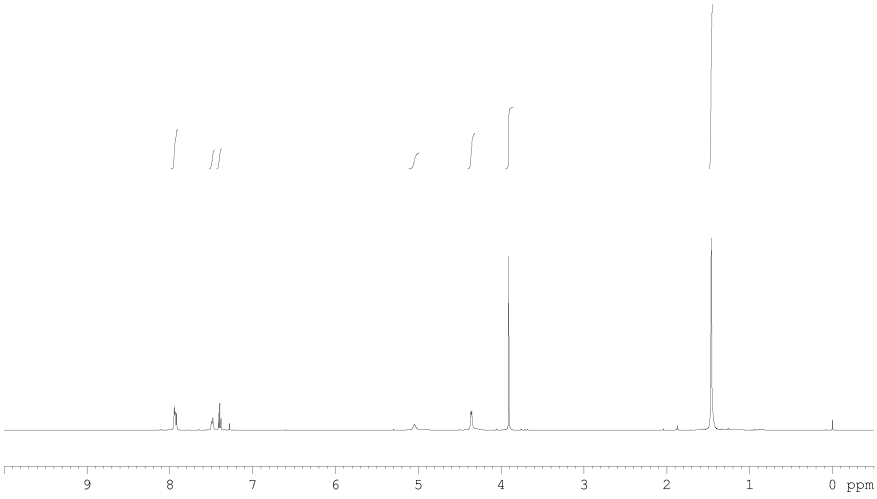


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3i**

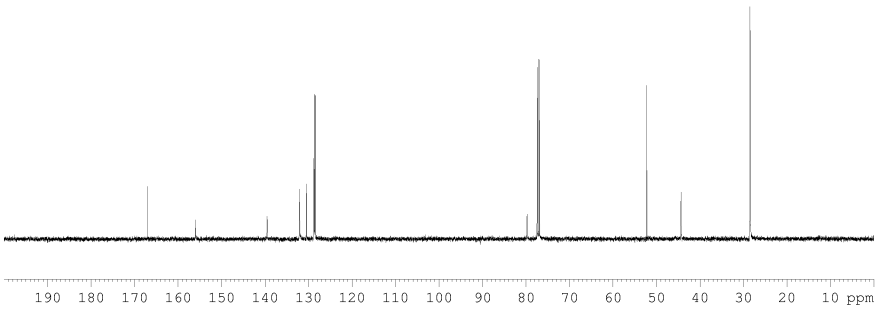


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3i**

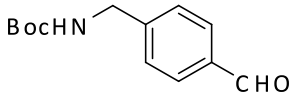


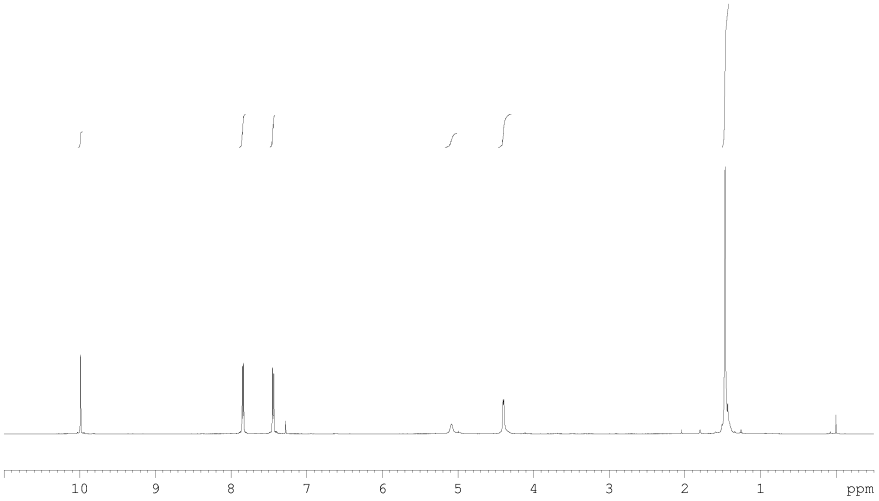


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3j**

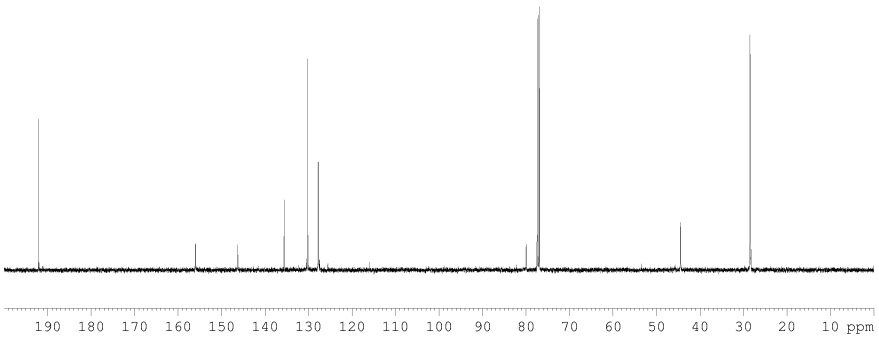


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3j**

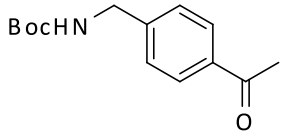


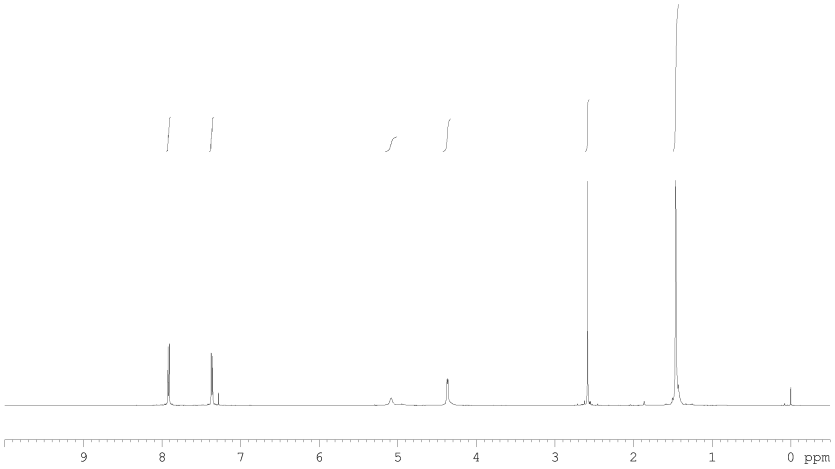


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3k**

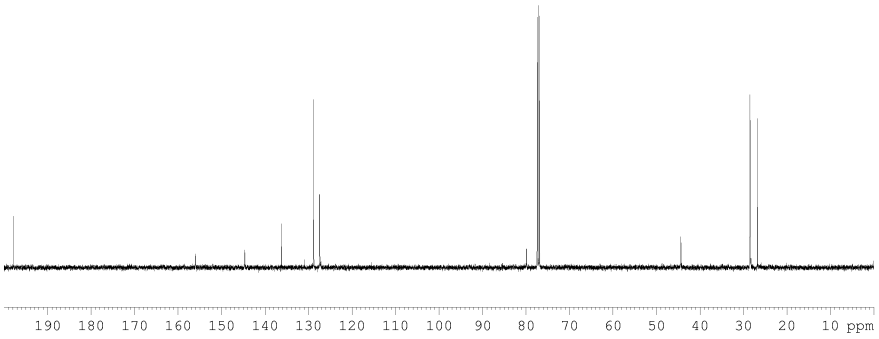


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3k**

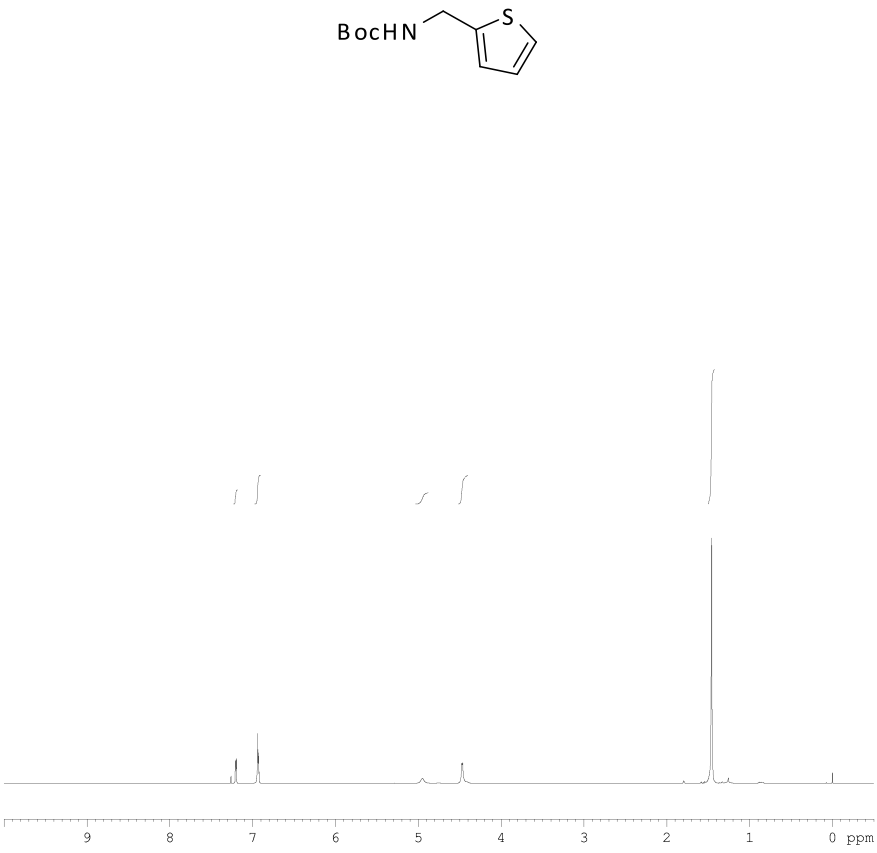




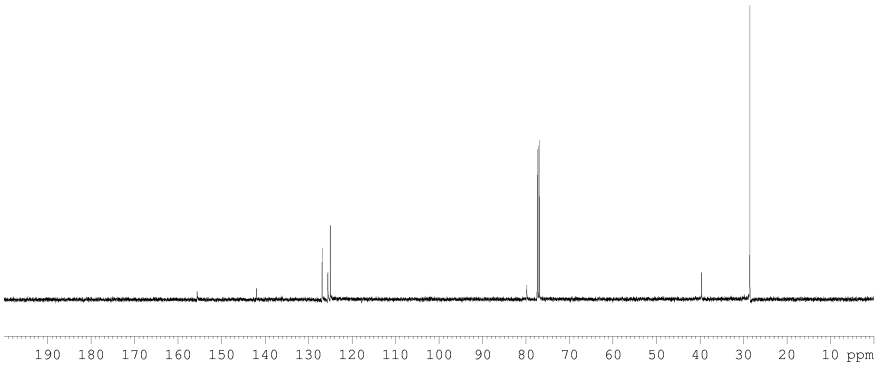
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **3l**



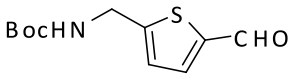
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **3l**

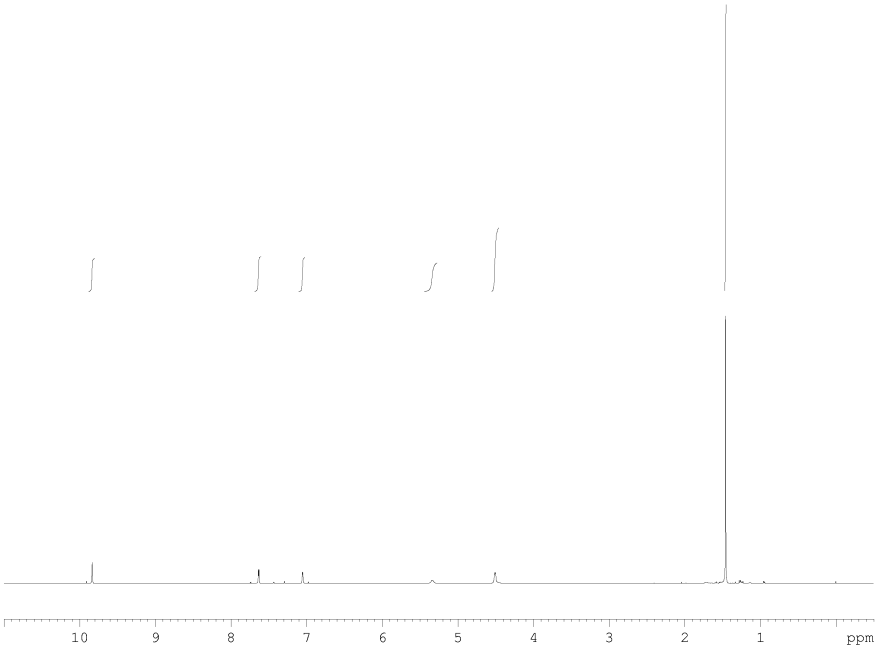


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4a**

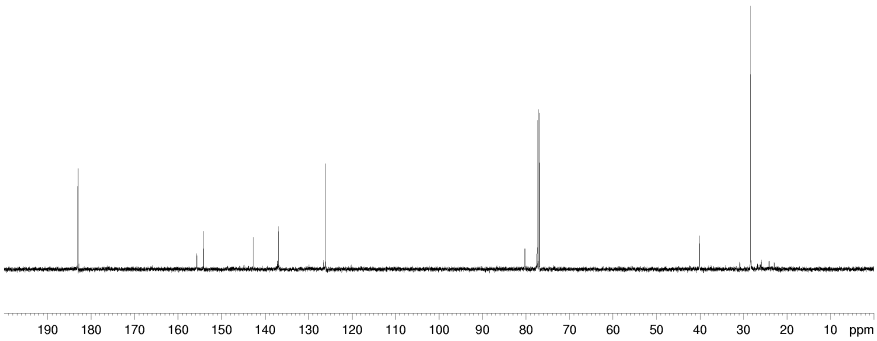


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4a**

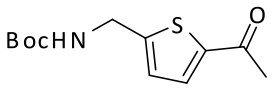


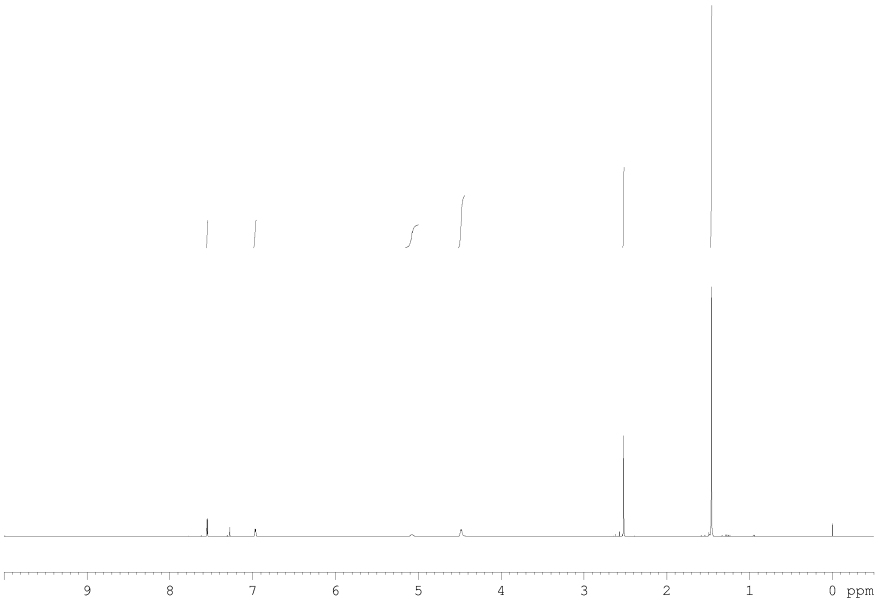


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4b**

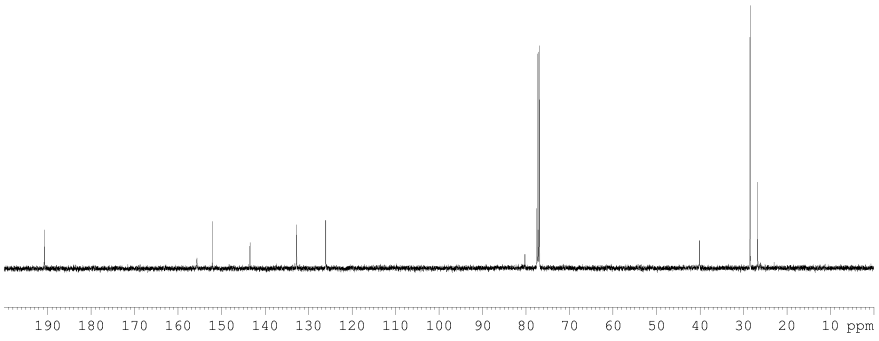


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4b**

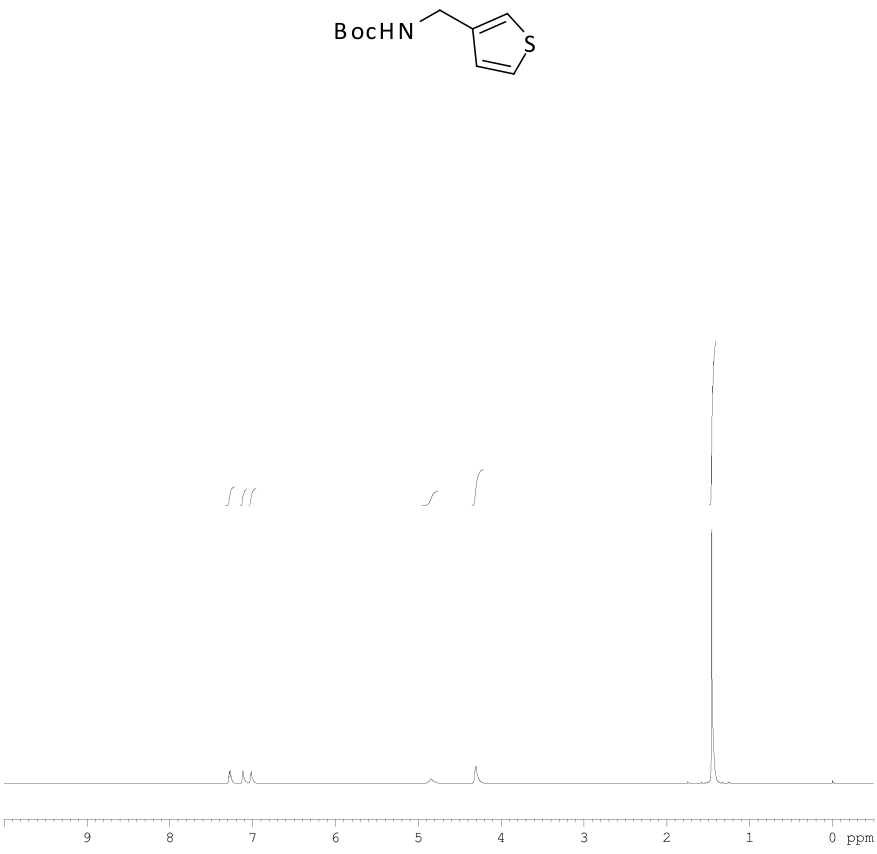




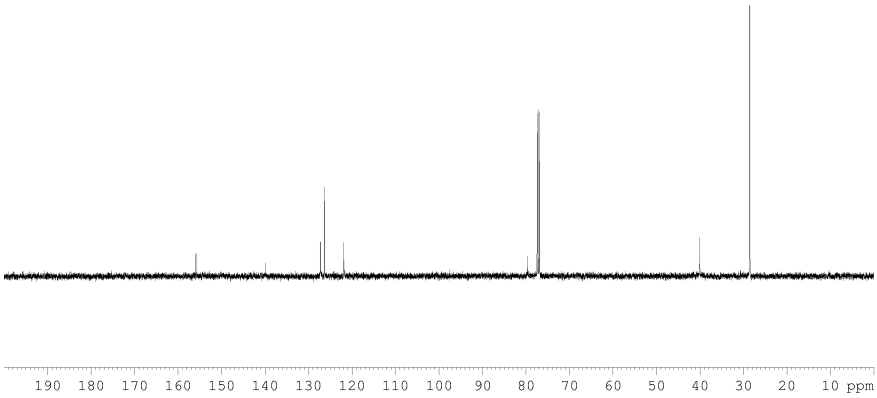
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4c**



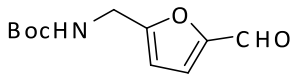
^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4c**

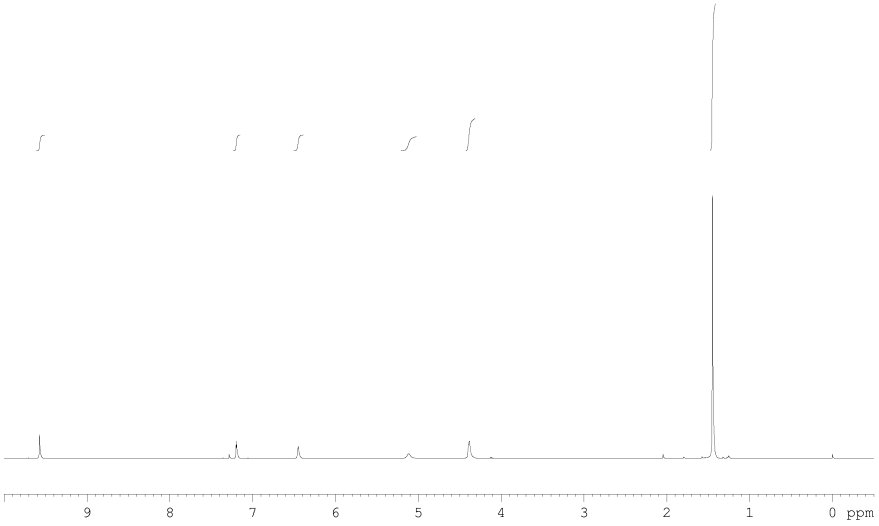


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4d**

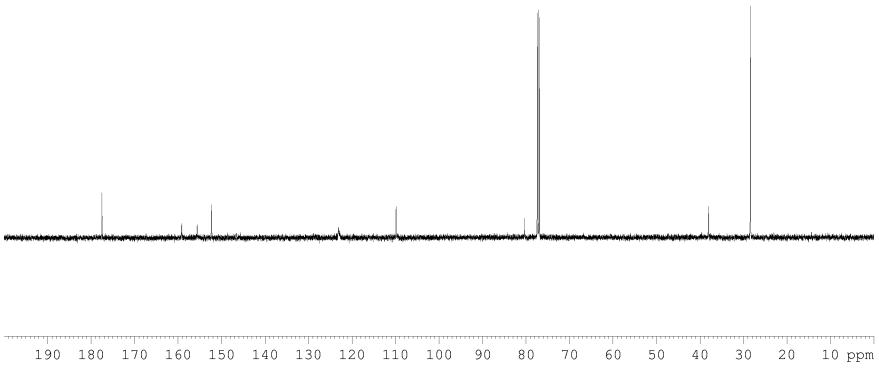


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4d**

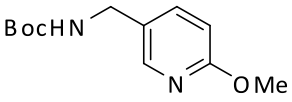


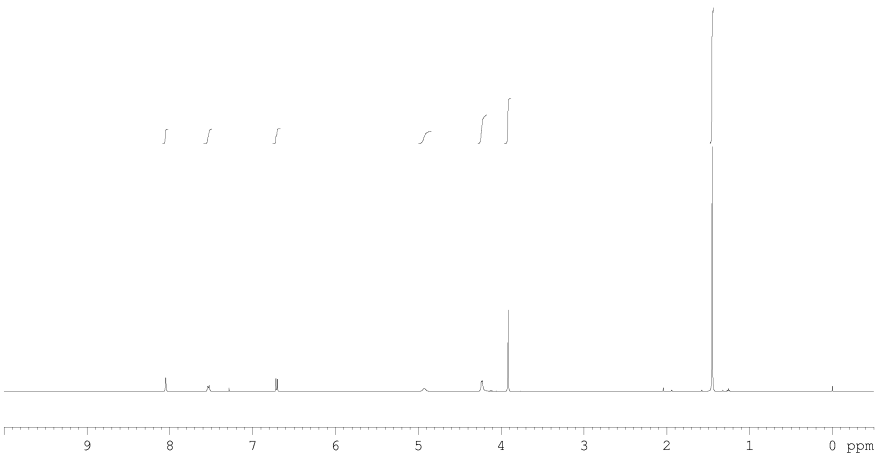


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4e**

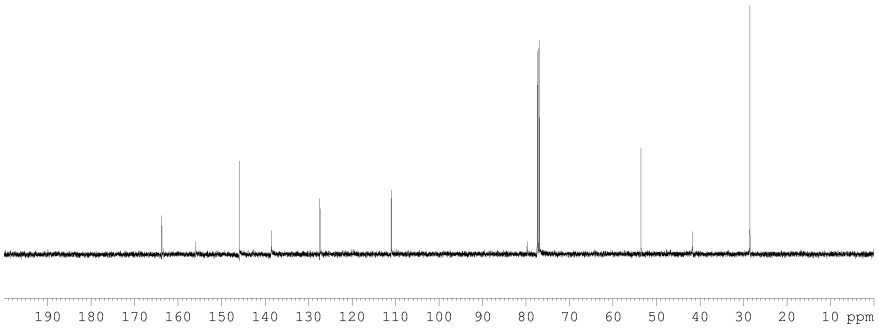


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4e**

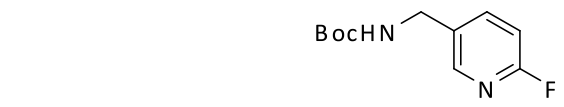


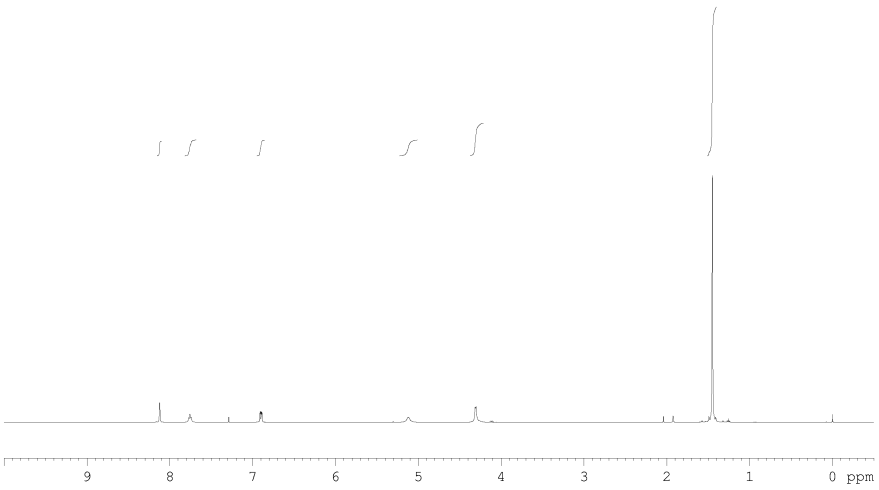


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4f**

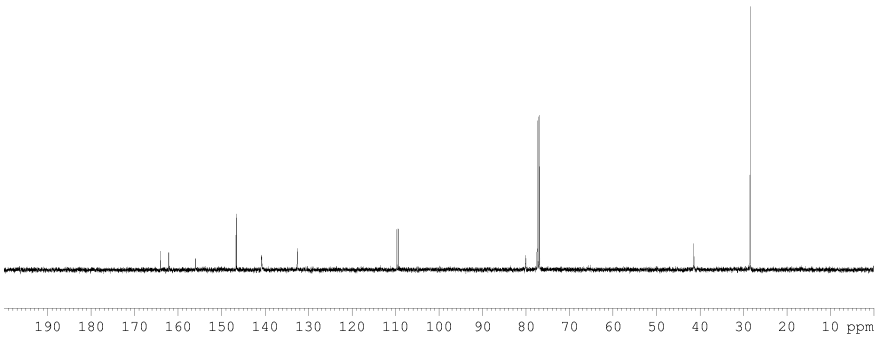


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4f**

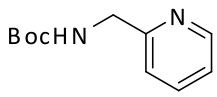


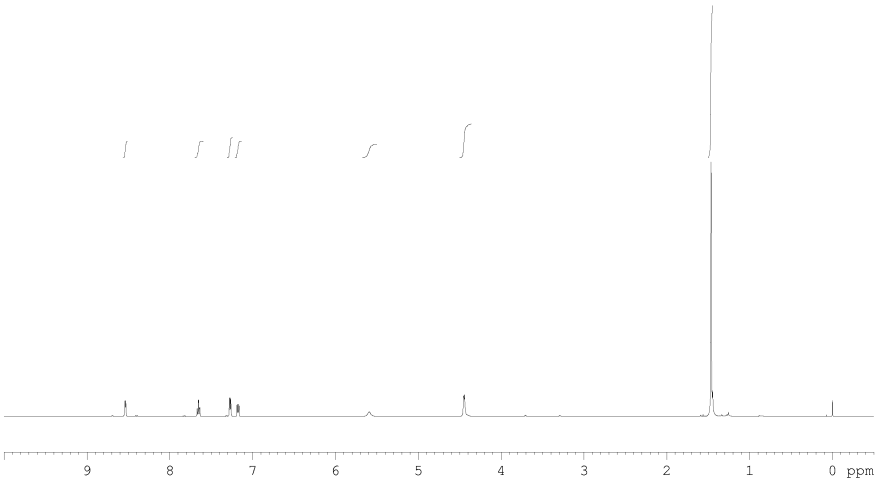


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4g**

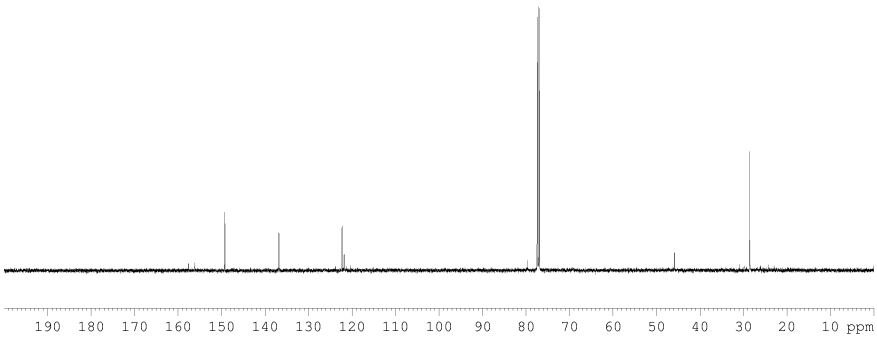


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4g**

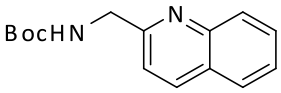


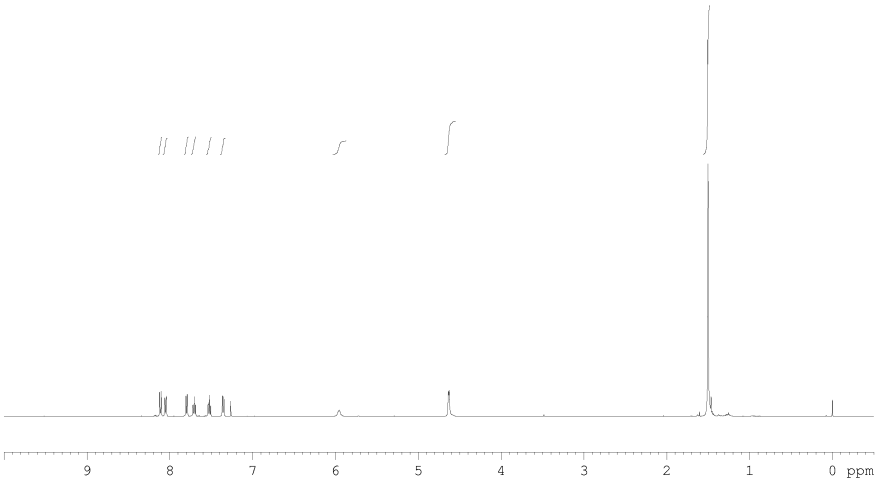


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4h**

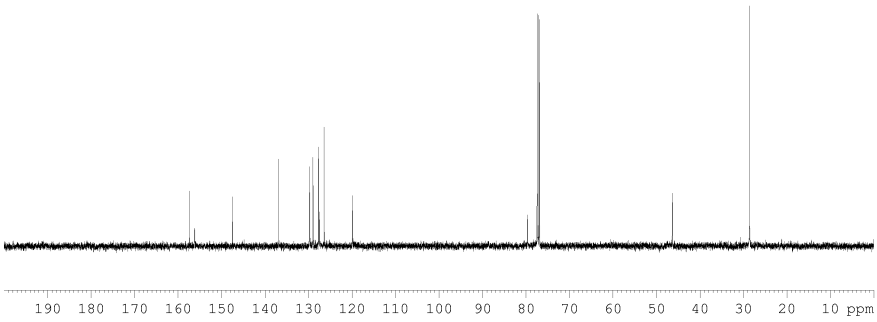


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4h**

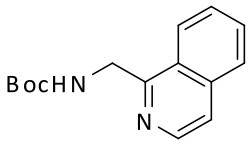


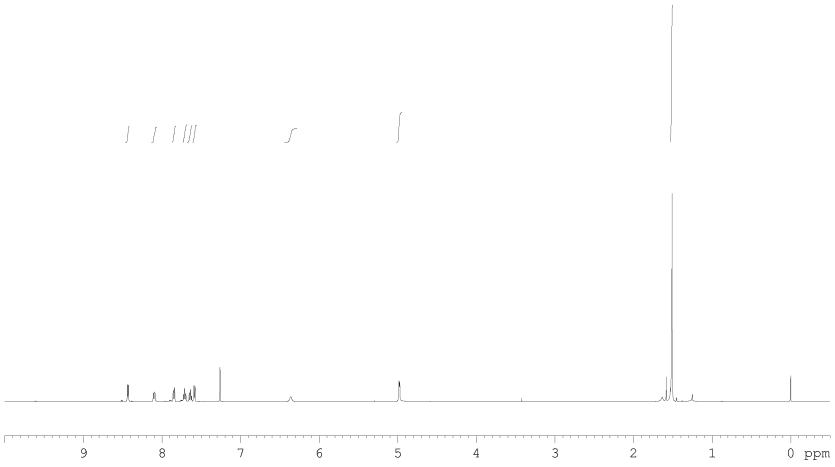


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4i**

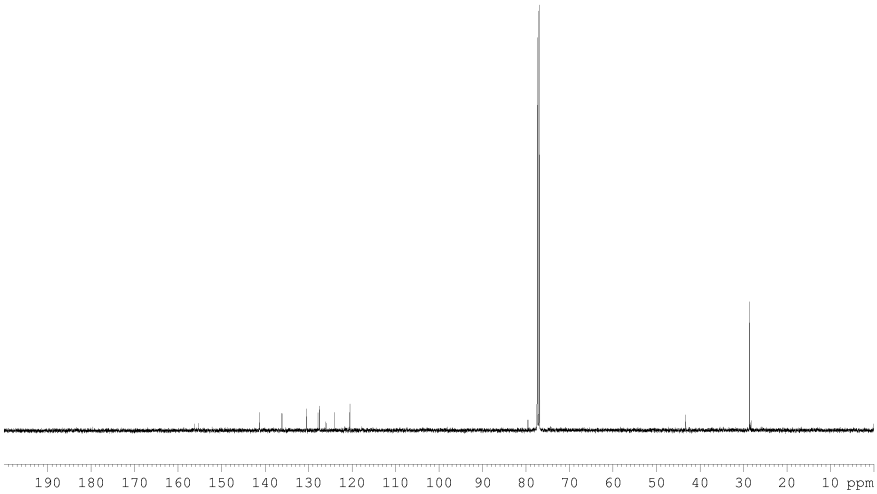


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4i**

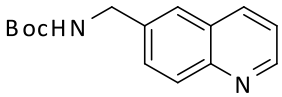


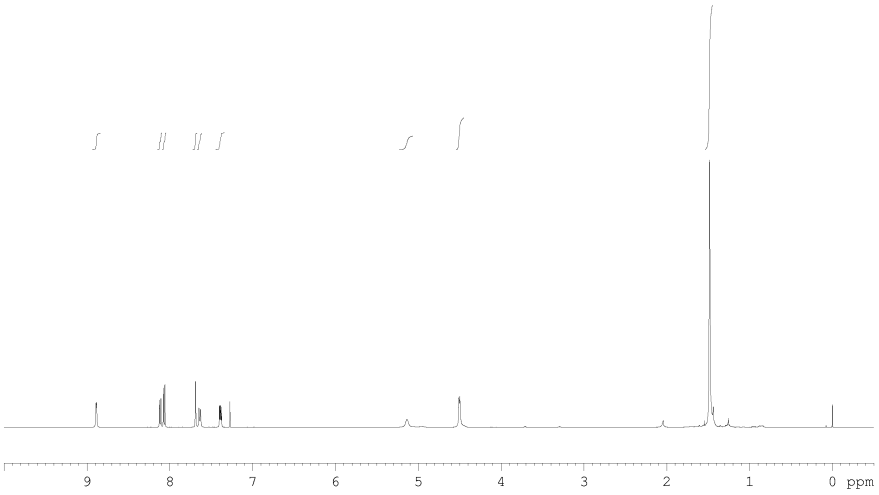


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4j**

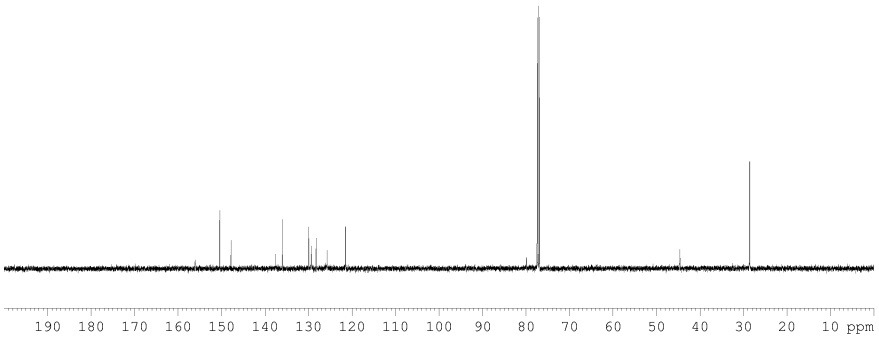


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4j**

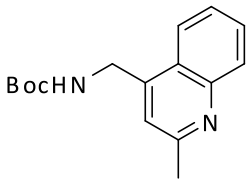


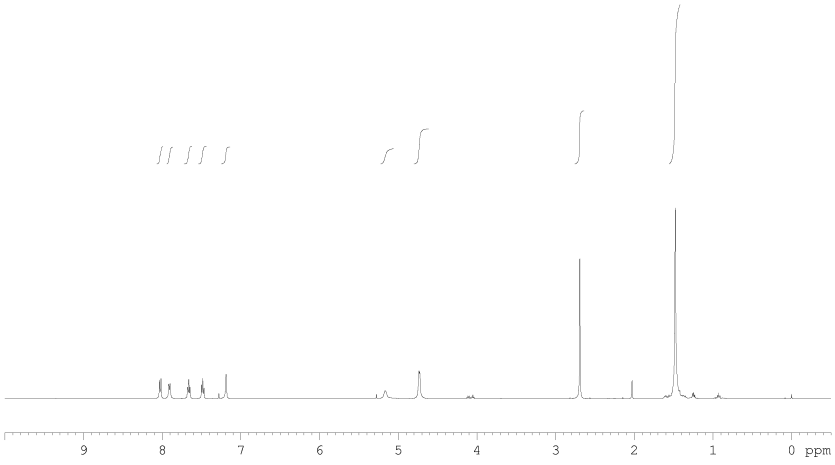


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4k**

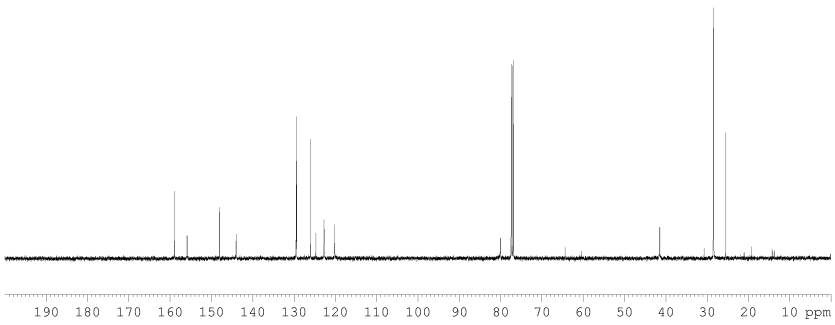


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4k**

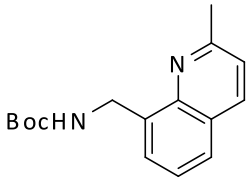


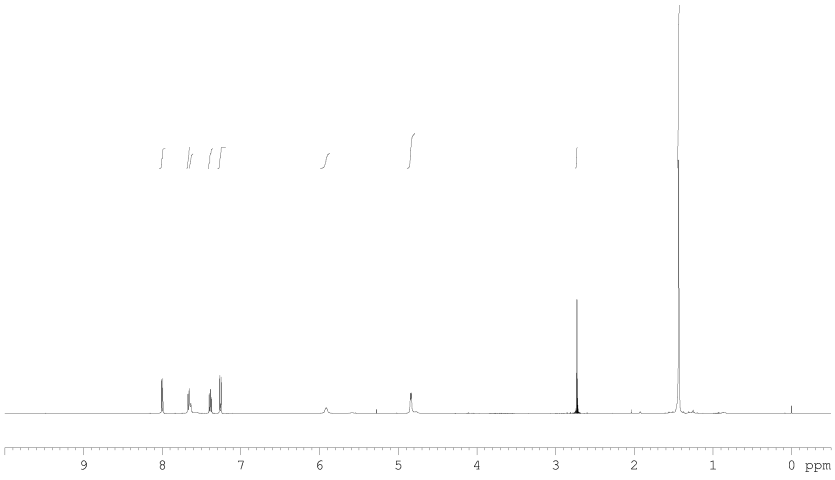


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4l**

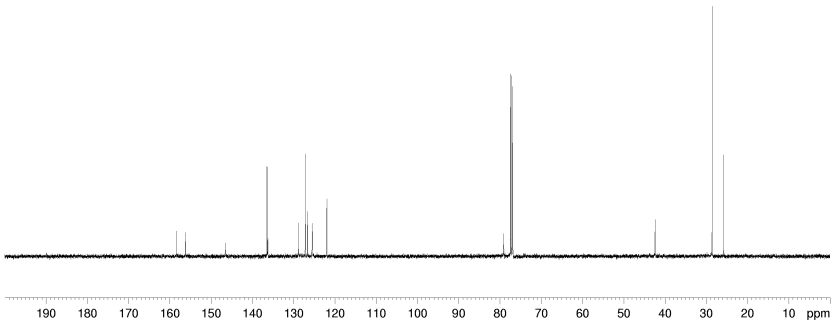


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4l**

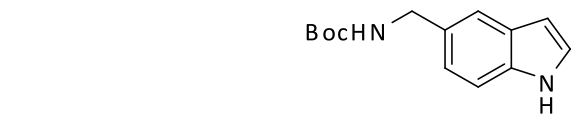


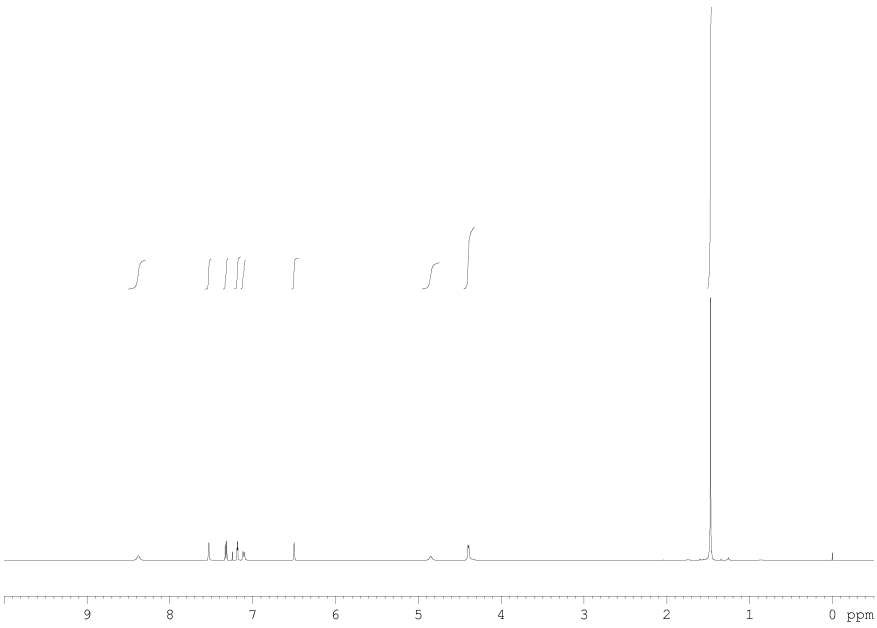


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4m**

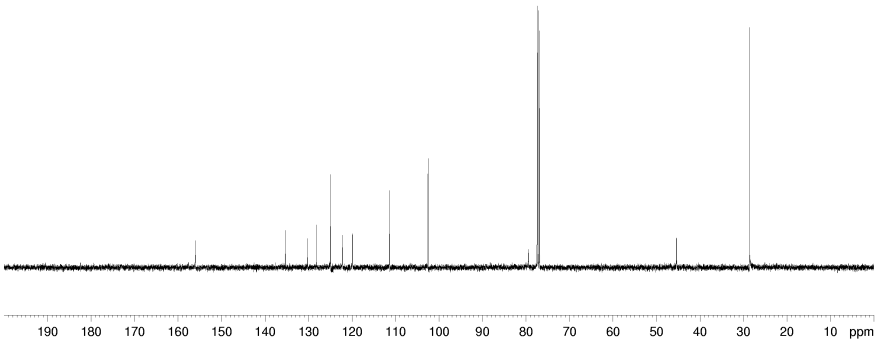


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4m**

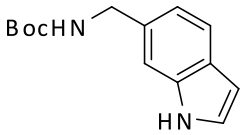


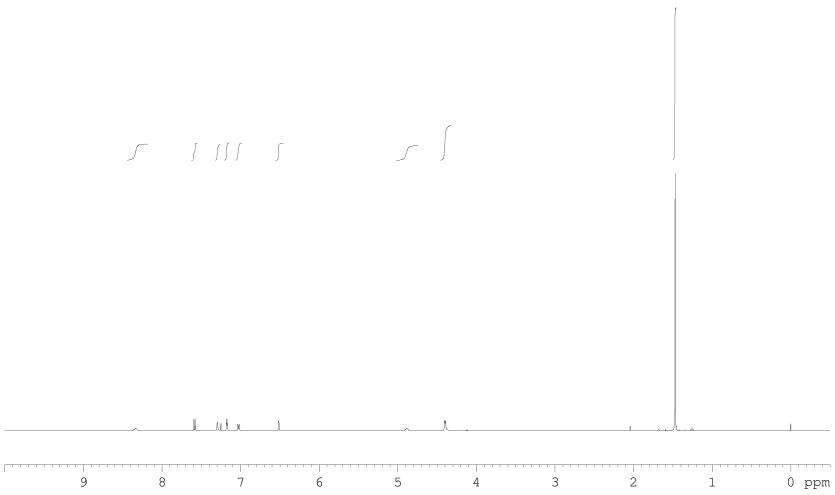


^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4n**

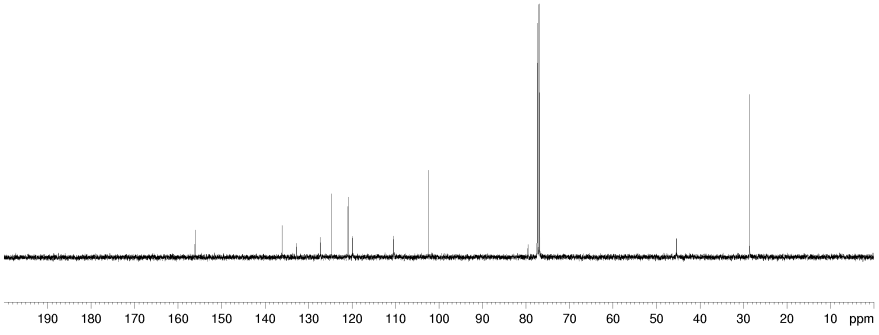


^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4n**





^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4o**



^{13}C NMR (125.8 MHz, $CDCl_3$) Spectrum of **4o**