Calcium Catalysed Strecker-Type Reactions Towards α-Aminonitriles

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General Information

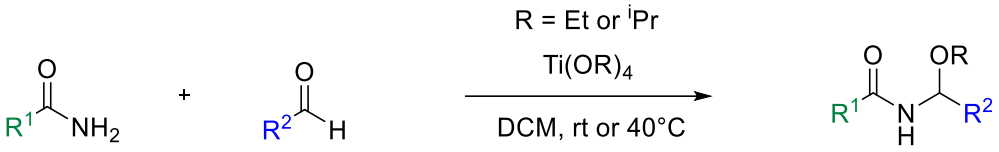
Solvents & reagents Reagents were purchased in the highest purity available from Acros Organics, Alfa Aesar, Fluorochem, TCI, Fisher Scientific or Merck. All solvents were purchased from commercial sources and used without purification (reagent grade). Metal salts and ligands were stored in a desiccator when not in use. Anhydrous solvent was prepared by storing solvent over activated 4Å MS for 72 hours. Standard vacuum line techniques were used and glassware was oven dried prior to use. Organic solvents were dried during workup using anhydrous Na_2SO_4. All reactions were performed using DrySyn heating mantles and pressure regulated vials or round bottom flasks.

Thin Layer Chromatography (TLC) was carried out using aluminium plates coated with 60 F_{254} silica gel. Plates were visualised using UV light (254 or 365 nm) and developed with iodine, basic permanganate solution or ninhydrin. Flash chromatography was performed on VWR Silica gel 60, 40–63 microns RE as the stationary phase and the solvents employed were of reagent grade.

^{1}H NMR spectroscopic data were obtained at 400 MHz (Bruker Ultrashield 400 Plus) or 600 MHz (Bruker Ultrashield 600 Plus) and ^{13}C NMR data were obtained at 100 MHz (Bruker Ultrashield 400 Plus) or 151 MHz (Bruker Ultrashield 600 Plus) at 298 K. Infrared spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer. High resolution mass spectrometry data were recorded using electron spray ionization (ESI) or atmospheric pressure chemical ionization (APCI) on a Shimadzu LCMS-IT-TOF mass spectrometer.

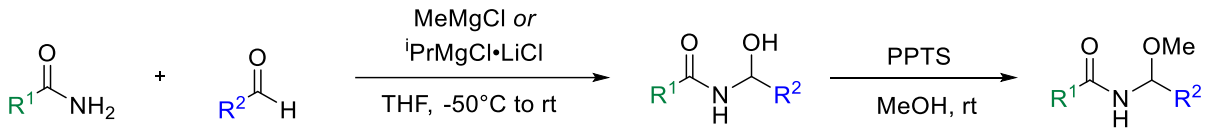
General Procedures

General Procedure A



Amide (1.0 equiv.) and aldehyde (1.2 equiv.) were dissolved in anhydrous DCM (0.25M) under an argon atmosphere. $Ti(OEt)_4$ or $Ti(O^iPr)_4$ (1.5 equiv.) was added dropwise and the reaction was stirred at room temperature or 40°C overnight (condenser fitted for 40°C reaction). The reaction was then diluted with ethanol and quenched through dropwise addition of a 0.5M K_2CO_3 solution. The resulting precipitate was then removed via slow filtration through Celite and washed 3 times with ethanol. The solution was then concentrated, and the resulting solid was purified by flash column chromatography (EtOAc:Hex) to afford the pure product.

General Procedure B



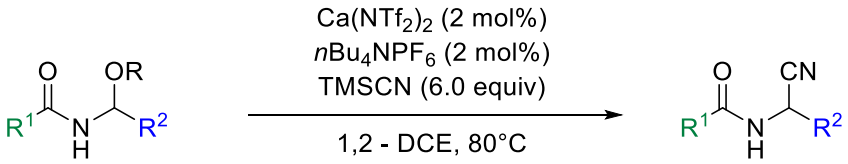
Amide (1.0 equiv) was dissolved in anhydrous THF (0.66 M) and cooled to -50°C. MeMgCl soln. or ^{i}PrMgCl•LiCl (1.05 equiv) was added dropwise with strong stirring. Mixture was allowed to come to room temperature and stirred for 30 mins. Mixture was cooled again to -50°C and aldehyde (1.05 equiv) was added in one portion and the reaction was warmed to room temperature and stirred for 3 hours.

Reaction was quenched by adding aq. sat. $NaHCO_3$ and organic layer was separated. Aqueous phase was extracted with DCM (x3). Organic layers were combined and washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to obtain the crude hemiaminal.

Immediately, the crude hemiaminal was dissolved in MeOH (3 mL/mmol) or 1:1 DCM/MeOH if insoluble. PPTS was added (0.05 equiv) and the reaction was stirred at room temperature overnight. Reaction was quenched with aq. sat. $NaHCO_3$ and the reaction was diluted with DCM. Organic layer was separated, and aqueous layer was extracted with DCM (x3). Combined

organic layers were dried over aq. sat. $NaHCO_3$, filtered and concentrated *in vacuo.* The crude solid was purified by flash column chromatography (EtOAc:Hex) to afford the pure product.

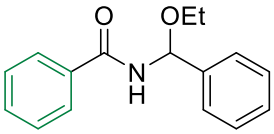
General Procedure C



To a screw top vial capped with a capped with Teflon cap was added *N*-acyl-*N,O*-acetal (1 equiv.), trimethylsilyl cyanide (TMSCN, 6 equiv.), $Ca(NTf_2)_2$ (2 mol%) and nBu$_4$NPF$_6$ (2 mol%) in 1,2-DCE (0.2 M). The reaction was stirred at 80 °C until TLC analysis indicated full conversion to the product (typically 12 h). The reaction was then quenched with sat. aq. $NaHCO_3$, and extracted into DCM (x3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The product was then purified by FCC (EtOAc:Hex or Hept) to afford the pure compound.

Synthesis of Starting Materials – N-acyl-N,O-acetals

_N_-[ethoxy(phenyl)methyl]benzamide (1a)



The title compound was prepared according to general procedure **A** from benzamide (6 g, 50 mmol), benzaldehyde (6.3 g, 60 mmol) and $Ti(OEt)_4$ (17 g, 74 mmol) in DCM (165 mL). Purification by flash column chromatography (1:20 EtOAc:Hex) afforded the pure product as a white solid (4.9 g, 39%).

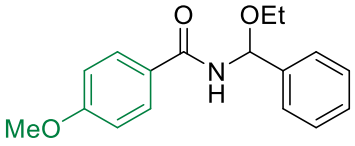
RF (1:3 EtOAc:Hept): 0.30

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.18 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 7.0 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.52 – 7.44 (m, 4H), 7.42 – 7.36 (m, 2H), 7.36 – 7.29 (m, 1H), 6.37 (d, *J* = 8.9 Hz, 1H), 3.71 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.57 (dq, *J* = 9.5, 7.0 Hz, 1H), 1.20 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.7, 140.1, 133.8, 131.6, 128.3, 128.1, 127.9, 127.7, 126.4, 80.1, 62.9, 15.1.

*Data in accordance with literature[1]

_N_-(ethoxy(phenyl)methyl)-4-methoxybenzamide (1b)



The title compound was prepared according to general procedure **A** from 4-methoxybenzamide (500 mg, 3.31 mmol), benzaldehyde (422 mg, 3.97 mmol) and $Ti(OEt)_4$ (1.132 g, 4.97 mmol) in anhydrous DCM (13.2 mL) at room temperature. Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (651 mg, 69%).

RF (1:3 EtOAc:Hex): 0.43

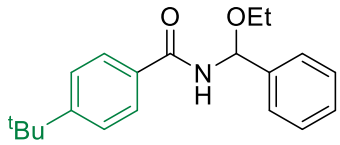
IR ν_{max} (cm^{-1}): 3266, 3017, 2969, 1632, 1492, 1027

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{19}NO_3Na$ 308.1263; Found 308.1256

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.40 – 7.31 (m, 3H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.56 (d, *J* = 9.1 Hz, 1H), 6.47 (d, *J* = 9.3 Hz, 1H), 3.84 (s, 3H), 3.84 (dq, *J* = 14.4 7.1 Hz, 1H), 3.70 (dq, *J* = 14.4 7.1 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 162.6, 139.9, 129.0, 128.6, 128.4, 126.0, 125.9, 113.8, 80.2, 64.1, 55.5, 15.2.

4-(*tert*-butyl)-*N*-(ethoxy(phenyl)methyl)benzamide (1c)



The title compound was prepared according to general procedure **A** from 4-tertbutylbenzamide (500 mg, 2.82 mmol), benzaldehyde (359 mg, 3.39 mmol) and $Ti(OEt)_4$ (965 mg, 4.23 mmol) in anhydrous DCM (11.3 mL) at room temperature. Purification by FCC (1:9 EtOAc:Hex) afforded the pure product as a white solid (529 mg, 60%).

RF (1:9 EtOAc:Hex): 0.29

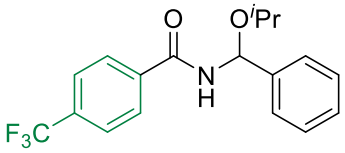
IR ν_{max} (cm^{-1}): 3280, 2905, 2870, 1649, 1612, 1532, 1500, 1273, 1090, 588, 749

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{25}NO_2Na$ 334.1783; Found 334.1772

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.41 – 7.30 (m, 3H), 6.62 (d, *J* = 9.2 Hz, 1H), 6.48 (d, *J* = 9.4 Hz, 1H), 3.84 (dq, *J* = 14.4, 7.1 Hz, 1H), 3.72 (dq, *J* = 14.4, 7.1 Hz, 1H), 1.33 (s, 9H), 1.29 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.1, 155.6, 139.8, 130.9, 128.6, 128.4, 12.0, 126.0, 125.6, 80.1, 64.12, 35.0, 31.1, 15.2.

***N*-(phenyl[(propan-2-yl)oxy]methyl)-4-(trifluoromethyl)benzamide (1d)**



The title compound was prepared according to general procedure **A** from 4-(trifluoromethyl)benzamide (400 mg, 2.10 mmol), benzaldehyde (270 mg, 2.50 mmol) and Ti(O^{i}Pr)$_4$ (900 mg, 3.20 mmol) in DCM (9 mL). Purification by flash column chromatography (0 to 5% EtOAc:Hex) afforded the pure product as a white solid (206 mg, 30%).

RF (1:5 EtOAc:Hex): 0.51

IR ν_{max} (cm^{-1}): 3282, 2977, 1652, 1534, 1326, 1126, 859

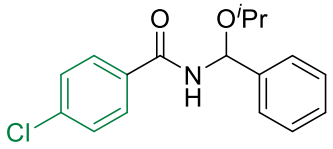
HRMS (ESI) m/z: $[M - C_3H_8O]^+$ Calcd for $C_{15}H_{11}F_3NO$ 278.0793; Found 278.0792

^{1}H NMR (400 MHz, DMSO-d$_6$): δ ^{1}H NMR (400 MHz,) δ 9.48 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.35 – 7.29 (m, 1H), 6.46 (d, *J* = 8.8 Hz, 1H), 3.92 (hept, *J* = 6.0 Hz, 1H), 1.21 (dd, *J* = 9.9, 6.1 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ ^{13}C NMR (101 MHz,) δ 165.5, 140.3, 137.6, 131.4 (q, *J* = 31.8 Hz), 128.6, 128.2, 127.9, 126.4, 125.3 (d, *J* = 3.7 Hz), 124.0 (q, *J* = 272.9 Hz), 78.2, 68.6, 23.1, 21.6.

^{19}F NMR (376 MHz, DMSO-d$_6$): 61.27

4-chloro-*N*-(phenyl[(propan-2-yl)oxy]methyl)benzamide (1e)



The title compound was prepared according to general procedure **A** from 4-chlorobenzamide (500 mg, 3.20 mmol), benzaldehyde (410 mg, 3.90 mmol) and Ti(O^{i}Pr)$_4$ (1.40 g, 4.80 mmol) in DCM (13 mL). Purification by flash column chromatography (0 to 10% EtOAc:Hex) afforded the pure product as a white solid (222 mg, 23%).

RF (1:5 EtOAc:Hex): 0.54

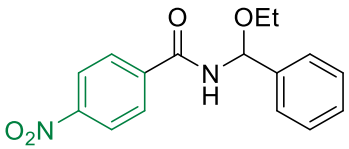
IR ν_{max} (cm^{-1}): 3263, 3064, 2974, 1635, 1532, 1486, 1031,850

HRMS (ESI) m/z: [M + C_3H_8O]$^+$ Calcd for $C_{17}H_{19}ClNO$ 244.0529; Found 244.0534

^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.30 (d, *J* = 8.9 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.35 – 7.28 (m, 1H), 6.44 (d, *J* = 8.9 Hz, 1H), 3.89 (hept, *J* = 6.1 Hz, 1H), 1.20 (dd, *J* = 10.1, 6.1 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d$_6$): δ 165.6, 140.4, 136.5, 132.6, 129.7, 128.4, 128.1, 127.9, 126.4, 78.1, 68.56, 23.1, 21.6.

***N*-(ethoxy(phenyl)methyl)-4-nitrobenzamide (1f)**



The title compound was prepared according to general procedure **A** from 4-nitrobenzamide (500 mg, 3.01 mmol), benzaldehyde (383 mg, 3.61 mmol) and Ti(OEt)$_4$ (1.029 g, 4.51 mmol) in anhydrous DCM (12.0 mL) at 40 °C. Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (698 mg, 77%).

RF (1:3 EtOAc:Hex): 0.47

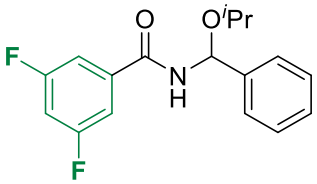
IR ν_{max} (cm^{-1}): 3287, 3063, 2974, 2898, 1656, 1519, 1338, 1272, 1075

HRMS (ESI) m/z: [M - NO_2]$^+$ Calcd for $C_{16}H_{16}NO_2$ 254.1176

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.51 (d, *J* = 7.1 Hz, 2H), 7.43 – 7.31 (m, 3H), 6.77 (d, *J* = 9.0 Hz, 1H), 6.44 (d, *J* = 9.1 Hz, 1H), 3.83 (dq, *J* = 9.3, 7.1 Hz, 1H), 3.70 (dq, *J* = 9.4, 7.0 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.2, 149.8, 139.3, 139.1, 128.8, 128.4, 126.0, 123.9, 80.7, 64.5, 15.2.

3,5-difluoro-*N*-(phenyl[(propan-2-yl)oxy]methyl)benzamide (1g)



The title compound was prepared according to general procedure **A** from 3,5-difluorobenzamide (400 mg, 2.60 mmol), benzaldehyde (324 mg, 3.06 mmol) and Ti(O^{i}Pr)$_4$ (1.10 g, 3.80 mmol) in DCM (10 mL). Purification by flash column chromatography (0 to 5% EtOAc:Hex) afforded the pure product as a white solid (275 mg, 35%).

RF (1:5 EtOAc:Hex): 0.65

IR ν_{max} (cm^{-1}): 3264, 3063, 2970, 1654, 1534, 1330, 1119

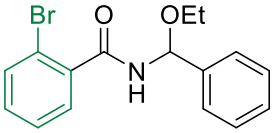
HRMS (ESI) m/z: $[M - C_3H_8O]^+$ Calcd for $C_{14}H_{10}F_2NO$ 246.0730; Found 246.0729

^{1}H NMR (400 MHz, DMSO-d_6): δ ^{1}H NMR (400 MHz,) δ 9.39 (d, *J* = 8.7 Hz, 1H), 7.68 (dd, *J* = 8.5, 2.3 Hz, 2H), 7.54 – 7.44 (m, 3H), 7.41 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 6.44 (d, *J* = 8.7 Hz, 1H), 3.89 (hept, *J* = 6.1 Hz, 1H), 1.20 (dd, *J* = 8.5, 6.1 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 163.9, 163.5 (d, *J* = 12.7 Hz), 161.0 (d, *J* = 12.6 Hz), 140.2, 137.2 (t, *J* = 8.4 Hz), 128.2, 128.0, 126.4, 111.2 (d, *J* = 7.2 Hz), 111.0 (d, *J* = 7.2 Hz), 107.2 (t, *J* = 25.9 Hz), 78.2, 68.6, 23.1, 21.6.

^{19}F NMR (376 MHz, DMSO-d_6): 108.86

2-bromo-*N*-(ethoxy(phenyl)methyl)benzamide (1h)



The title compound was prepared according to general procedure **A** from 2-bromobenzamide (500 mg, 2.51 mmol), benzaldehyde (320 mg, 3.02 mmol) and $Ti(OEt)_4$ (860 mg, 3.77 mmol) in anhydrous DCM (10.0 mL) at 40°C. Purification by FCC (1:9 EtOAc:Hex) afforded the pure product as a white solid (578 mg, 69%).

RF (1:3 EtOAc:Hex): 0.55

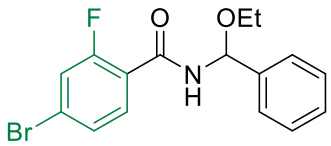
IR ν_{max} (cm^{-1}): 3264, 3083, 2987, 1652, 1513, 1098, 1029

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{16}NO_2BrNa$ 356.0262; Found 356.0263

^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.52 (d, *J* = 7.3 Hz, 3H), 7.40 – 7.30 (m, 4H), 7.27 (dd, *J* = 11.1, 4.2 Hz, 1H), 6.51 (d, *J* = 9.3 Hz, 1H), 6.44 (d, *J* = 9.4 Hz, 1H), 3.97 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.77 (dq, *J* = 14.1, 7.0 Hz, 1H), 1.32 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.6, 139.3, 137.4, 133.5, 131.5, 129.5, 128.6, 128.5, 127.6, 126.0, 119.2, 80.2, 64.4, 15.2.

4-bromo-*N*-(ethoxy(phenyl)methyl)-2-fluorobenzamide (1i)



The title compound was prepared according to general procedure **A** from 4-bromo-2-fluorobenzamide (500 mg, 2.29 mmol), benzaldehyde (292 mg, 2.75 mmol) and $Ti(OEt)_4$ (785 mg, 3.44 mmol) in anhydrous DCM (9.2 mL) at 40°C. Purification by FCC (1:11 EtOAc:Hex) afforded the pure product as a white solid (446 mg, 55%).

RF (1:9 EtOAc:Hex): 0.42

IR ν_{max} (cm^{-1}): 3263, 3058, 2970, 2918, 1647, 1602, 1541, 1479, 1092, 872

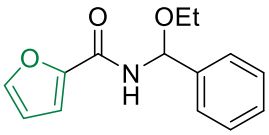
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{15}NO_2FBrNa$ 374.0168; Found 374.0163

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (t, *J* = 8.4 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.33 (dd, *J* = 18.9, 9.3 Hz, 2H), 7.11 (t, *J* = 10.2 Hz, 1H), 3.84 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.70 (dq, *J* = 14.2, 7.1 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 162.40 (d, *J* = 3.2 Hz), 160.19 (d, *J* = 252.2 Hz), 139.36 (s), 133.41 (d, *J* = 2.6 Hz), 128.70 (s), 128.61 (s), 128.51 (d, *J* = 3.3 Hz), 126.97 (d, *J* = 10.5 Hz), 125.96 (s), 119.75 (d, *J* = 28.1 Hz), 119.74 (d, *J* = 11.4 Hz), 80.54 (s), 64.26 (s), 15.15 (s).

^{19}F NMR (376 MHz, $CDCl_3$): δ -110.64

***N*-(ethoxy(phenyl)methyl)furan-2-carboxamide (1j)**



The title compound was prepared according to general procedure **A** from 2-furancarboxamide (200 mg, 1.80 mmol), benzaldehyde (229 mg, 2.16 mmol) and $Ti(OEt)_4$ (616 mg, 2.70 mmol) in anhydrous DCM (9.0 mL) at 40°C. Purification by FCC (1:9 to 1:5 EtOAc:Hex) afforded the pure product as a white solid (219 mg, 50%).

RF (1:3 EtOAc:Hex): 0.36

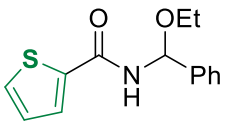
IR ν_{max} (cm^{-1}): 3343, 3118, 2976, 2909, 1653, 1568, 1504, 1470, 1269, 1008, 770

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{15}NO_3Na$ 268.0950; Found 268.0966

^1H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.48 (m, 2H), 7.43 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.42 – 7.30 (m, 3H), 7.19 (dd, *J* = 3.5, 0.7 Hz, 1H), 6.83 (d, *J* = 9.3 Hz, 1H), 6.51 (dd, *J* = 3.5, 1.7 Hz, 1H), 6.41 (d, *J* = 9.6 Hz, 1H), 3.83 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.69 (dq, *J* = 9.4, 7.0 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.14, 147.33, 144.30, 139.52, 128.64, 128.51, 125.99, 115.31, 112.38, 79.49, 64.10, 15.14.

***N*-[ethoxy(phenyl)methyl]thiophene-2-carboxamide (1k)**



The title compound was prepared according to general procedure **A** from thiophene-2-carboxamide (400 mg, 3.15 mmol), benzaldehyde (400 mg, 3.80 mmol) and $Ti(O^iPr)_4$ (1.30 g, 4.70 mmol) in DCM (13 mL). Purification by flash column chromatography (0 to 5% EtOAc:Hex) afforded the pure product as a white solid (206 mg, 24%).

RF (1:5 EtOAc:Hex): 0.40

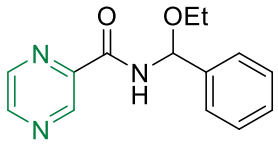
IR ν_{max} (cm^{-1}): 3330, 3090, 2969, 1625, 1533, 1030, 745

HRMS (ESI) m/z: $[M - C_3H_8O]^+$ Calcd for $C_{15}H_{18}NO_2S$ 216.0483; Found 216.0478

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.25 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 3.8 Hz, 1H), 7.81 (d, *J* = 5.0 Hz, 1H), 7.47 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.18 – 7.14 (m, 1H), 6.41 (d, *J* = 9.0 Hz, 1H), 3.90 (hept, *J* = 6.1 Hz, 1H), 1.20 (dd, *J* = 8.0, 6.2 Hz, 6H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 161.4, 140.4, 139.4, 131.8, 129.1, 128.2, 128.1, 127.9, 126.3, 77. 8, 68.4, 23.1, 21.6.

_N_-(ethoxy(phenyl)methyl)pyrazine-2-carboxamide (1l)



The title compound was prepared according to general procedure **A** from pyrazinamide (500 mg, 4.06 mmol), benzaldehyde (517 mg, 4.87 mmol) and $Ti(OEt)_4$ (1.389 g, 6.09 mmol) in anhydrous DCM (16.2 mL) at 40°C. Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (269 mg, 26%).

RF (1:3 EtOAc:Hex): 0.40

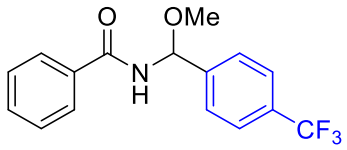
IR ν_{max} (cm^{-1}): 3360, 3088, 2980, 2907, 2871, 1666, 1584, 1494, 1477, 1095, 1023

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{15}N_3O_2Na$ 280.1062; Found 280.1056

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.76 (d, *J* = 2.2 Hz, 1H), 8.51 (s, 1H), 8.31 (d, *J* = 9.3 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.43 – 7.32 (m, 3H), 6.45 (d, *J* = 9.8 Hz, 1H), 3.83 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.71 (dq, *J* = 14.3, 7.0 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.07, 147.62, 144.78, 143.98, 142.64, 139.29, 128.68, 128.62, 126.01, 80.02, 64.19, 15.14.

***N*-(methoxy[4-(trifluoromethyl)phenyl]methyl)benzamide (1m)**



The title compound was prepared according to general procedure **B** from benzamide (300 mg, 2.50 mmol), *i*PrMgCl.LiCl (2 mL, 2.60 mmol, 1.3M in THF) and 4-(Trifluoromethyl)benzaldehyde (475 mg, 2.72 mmol) in THF (6 mL) to afford the hemiaminal. Transacetalisation in MeOH (4 mL) and PPTS (21 mg, 0.085 mmol) followed by column chromatography (1:4 EtOAc:Hex, 1% NEt_3) afforded the pure product as a white solid (365 mg, 53%)

RF (1:3 EtOAc:Hex): 0.42

IR ν_{max} (cm^{-1}): 3275, 3017, 2970, 1642, 1519, 1325,

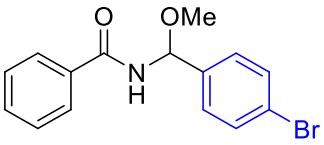
HRMS (ESI) m/z: $[M - CH_4O]^+$ Calcd for $C_{15}H_{10}F_3NO$ 278.0793; Found 278.0796

^1H NMR (400 MHz, DMSO-d_6): δ 9.30 (d, *J* = 8.9 Hz, 1H), 7.98 (d, *J* = 7.4 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 6.38 (d, *J* = 8.9 Hz, 1H), 3.44 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): 167.1, 144.4, 133.6, 131.8, 128.4, 128.6 (q, *J* = 31.6 Hz), 127.8, 127.3, 125.2 (d, *J* = 3.6 Hz), 124.3 (q, *J* = 272.1 Hz), 81.1, 55.4.

^{19}F NMR (376 MHz, DMSO-d_6): 60.88

***N*-[(4-bromophenyl)(methoxy)methyl]benzamide (1n)**



The title compound was prepared according to general procedure **B** from benzamide (400 mg, 3.30 mmol), *i*PrMgCl.LiCl (3.70 mL, 3.50 mmol, 0.94M in THF) and 4-bromo benzaldehyde (670 mg, 3.60 mmol) in THF (7 mL) to afford the hemiaminal. Transacetalisation in MeOH (5 mL) and PPTS (25 mg, 0.1 mmol) followed by column chromatography (1:4 EtOAc:Hex, 1% NEt_3) afforded the pure product as a white solid (440 mg, 47%)

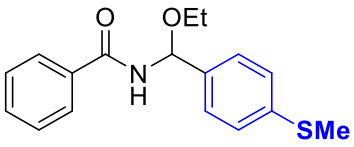
RF (1:3 EtOAc:Hex): 0.43

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.22 (d, *J* = 8.9 Hz, 1H), 7.99 – 7.92 (m, 2H), 7.63 – 7.52 (m, 3H), 7.52 – 7.40 (m, 4H), 6.25 (d, *J* = 8.9 Hz, 1H), 3.39 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.9, 139.3, 133.6, 131.8, 131.1, 128.7, 128.4, 127.7, 121.2, 81.2, 55.3.

*Data in accordance with literature.[2]

***N*-[ethoxy-(4-methylsulfanylphenyl)methyl]benzamide (1o)**



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), 4-(methylthio)benzaldehyde (450 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 EtOAc:Hex) afforded the pure product as a white solid (458 mg, 61%).

RF (1:3 EtOAc:Hept): 0.33

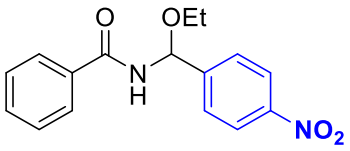
IR ν_{max} (cm^{-1}): 3282, 2973, 2876, 1644, 1519, 1273, 1090

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}NO_2S$ 302.1215; Found 302.1225

^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.1 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.39 (m, 4H), 7.25 (d, *J* = 8.3 Hz, 2H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.43 (d, *J* = 9.3 Hz, 1H), 3.83 (dq, *J* = 9.5, 7.0 Hz, 1H), 3.70 (dq, *J* = 9.5, 7.0 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.3, 139.0, 136.7, 133.9, 132.1, 128.8, 127.2, 126.7, 126.6, 80.1, 64.3, 15.9, 15.3.

_N_-[ethoxy-(4-nitrophenyl)methyl]benzamide (1p)



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), 4-nitrobenzladehyde (450 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 EtOAc:Hex) afforded the pure product as a pale yellow solid (338 mg, 45%).

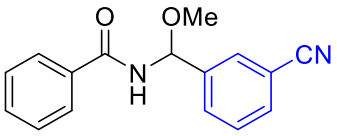
RF (1:3 EtOAc:Hept): 0.31

^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.6 Hz, 2H), 7.85 – 7.79 (m, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 6.67 (s, 1H), 6.57 (d, *J* = 9.5 Hz, 1H), 3.95 – 3.80 (m, 1H), 3.80 – 3.68 (m, 1H), 1.32 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.4, 148.0, 146.9, 133.3, 132.5, 128.9, 127.3, 123.9, 79.5, 64.7, 15.2.

*Data in accordance with literature[1]

_N_-[(3-cyanophenyl)(methoxy)methyl]benzamide (1q)



The title compound was prepared according to general procedure **B** from benzamide (300 mg, 2.50 mmol), *i*PrMgCl.LiCl (2.4 mL, 2.60 mmol, 1.097M in THF) and 3-Formylbenzonitrile (360 mg, 2.70 mmol) in THF (5 mL) to afford the hemiaminal. Transacetalisation in MeOH (5 mL) and PPTS (20 mg, 0.08 mmol) followed by column chromatography (3:10 EtOAc:Hex, 1% NEt_3) afforded the pure product as a white solid (350 mg, 64%)

RF (3:10 EtOAc:Hex): 0.48

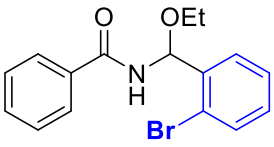
IR ν_{max} (cm^{-1}): 3246, 2950, 2232, 1637, 1515, 1108, 1046

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}N_2O_2Na$ 289.0953; Found 289.0950

^1H NMR (400 MHz, DMSO-d_6): δ ^1H NMR (400 MHz,) δ 9.19 (d, *J* = 9.0 Hz, 1H), 7.98 – 7.93 (m, 2H), 7.59 – 7.53 (m, 1H), 7.50 – 7.44 (m, 4H), 7.41 – 7.36 (m, 2H), 7.35 – 7.29 (m, 1H), 6.27 (d, *J* = 9.0 Hz, 1H), 3.39 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 167.0, 141.3, 133.5, 131.9, 131.8, 131.5, 130.1, 129.6, 128.4, 127.8, 118.8, 111.2, 80.9, 55.4.

_N_-[(2-bromophenyl)-ethoxy-methyl]benzamide (1r)



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), 2-bromobenzladehyde (550 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (718 mg, 87%).

RF (1:3 EtOAc:Hept): 0.39

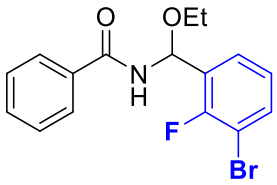
IR ν_{max} (cm^{-1}): 3286, 2973, 2928, 1642, 1517, 1263, 1088

HRMS (APCI) m/z: $[M - C_2H_6O]^+$ Calcd for $C_{16}H_{17}BrNO_2$ 334.0443; Found 334.0453

^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.1 Hz, 2H), 7.72 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.59 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.22 (td, *J* = 7.7, 1.7 Hz, 1H), 6.64 – 6.52 (m, 2H), 3.87 (dq, *J* = 9.4, 7.0 Hz, 1H), 3.73 (dq, *J* = 9.4, 7.0 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.1, 138.7, 133.9, 133.5, 132.1, 130.2, 128.8, 127.9, 127.8, 127.3, 122.8, 80.4, 64.5, 15.3.

***N*-[(3-bromo-2-fluoro-phenyl)-ethoxy-methyl]benzamide (1s)**



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), 3-bromo-2-fluorobenzaldehyde (603 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (163 mg, 19%).

RF (1:3 EtOAc:Hept): 0.18

IR ν_{max} (cm^{-1}): 3267, 2971, 2919, 1643, 1517, 1353, 1051, 841

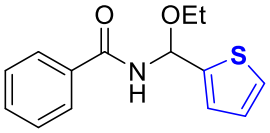
HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}BrFNO_2$ 352.0348; Found 352.0358

^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.1 Hz, 2H), 7.60 – 7.51 (m, 3H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.09 (td, *J* = 7.9, 0.9 Hz, 1H), 6.84 (d, *J* = 9.2 Hz, 1H), 6.62 (d, *J* = 9.4 Hz, 1H), 3.86 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.72 (dq, *J* = 9.5, 7.0 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.0, 156.8 (d, *J* = 249.5 Hz), 133.9, 133.7, 132.2, 128.8, 127.3, 127.2, 128.5 (d, *J* = 13.8 Hz), 125.4 (d, *J* = 4.4 Hz), 109.9 (d, *J* = 20.9 Hz), 64.5, 15.2.

^{19}F NMR (376 MHz, $CDCl_3$): -110.9

***N*-[ethoxy(2-thienyl)methyl]benzamide (1t)**



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), 2-thiophenecarboxaldehyde (333 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (340 mg, 53%).

RF (1:3 EtOAc:Hept): 0.21

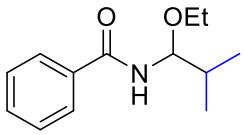
IR ν_{max} (cm^{-1}): 3278, 2976, 1646, 1523, 1273, 1072

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}NO_2S$ 262.0902; Found 262.0900

^1H NMR (400 MHz, DMSO-d_6): δ 9.40 (d, *J* = 8.9 Hz, 1H), 7.97 (d, *J* = 7.1 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.53 – 7.42 (m, 3H), 7.08 (dt, *J* = 3.5, 1.2 Hz, 1H), 7.02 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.58 (dd, *J* = 8.9, 0.8 Hz, 1H), 3.70 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.61 (dq, *J* = 9.7, 7.0 Hz, 1H), 1.20 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.6, 143.7, 133.5, 131.7, 128.3, 127.8, 126.7, 125.8, 124.7, 77.3, 63.0, 15.0.

N-(1-ethoxy-2-methyl-propyl)benzamide (1u)



The title compound was prepared according to general procedure **A** from benzamide (300 mg, 2.5 mmol), isobutraldehyde (214 mg, 3.0 mmol) and $Ti(OEt)_4$ (850 mg, 3.7 mmol) in DCM (6 mL). Purification by flash column chromatography (1:20 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (385 mg, 70%).

RF (1:3 EtOAc:Hept): 0.41

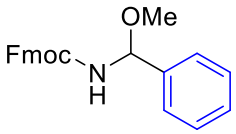
IR ν_{max} (cm^{-1}): 3283, 3058, 2976, 2872, 1633, 1530, 1489, 1092

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{20}NO_2$ 222.1494; Found 222.1504

^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.0 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 6.29 (d, *J* = 9.1 Hz, 1H), 5.18 (dd, *J* = 9.7, 6.3 Hz, 1H), 3.69 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.56 (dq, *J* = 9.7, 7.0 Hz, 1H), 1.99 – 1.83 (m, 1H), 1.19 (t, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.6, 134.4, 131.9, 128.8, 127.1, 84.4, 64.2, 33.6, 18.1, 17.6, 15.3.

(9*H*-fluoren-9-yl)methyl (methoxy(phenyl)methyl)carbamate (3a)



The title compound was prepared according to general procedure **B** from Fmoc-NH_2 (2.393 g, 10 mmol), MeMgCl (1.92M in Et_2O) (5.47 mL, 10.5 mmol) and benzaldehyde (1.114 g, 10.5 mmol) in anhydrous THF (15.0 mL) then *p*-toluenesulfonic acid (126 mg, 0.5 mmol) in MeOH (30.0 mL). . Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (380 mg, 11%).

RF (1:3 EtOAc:Hex): 0.63

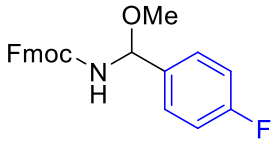
IR ν_{max} (cm^{-1}): 3298, 3039, 2950, 2894, 2838, 1697, 1526, 1250, 1034, 980, 741

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{21}NO_3Na$ 382.1419; Found 382.1413

^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.3 Hz, 2H), 7.57 (d, *J* = 7.0 Hz, 2H), 7.45 – 7.25 (m, 9H), 5.87 (d, *J* = 9.6 Hz, 1H), 5.36 (d, *J* = 8.8 Hz, 1H), 4.49 (dt, *J* = 15.9, 9.5 Hz, 1H), 4.21 (s, 1H), 3.41 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.07, 143.76, 141.41, 139.10, 128.66, 127.80, 127.14, 125.91, 125.05, 125.02, 120.08, 83.94, 66.82, 55.75, 47.27.

(9*H*-fluoren-9-yl)methyl ((4-fluorophenyl)(methoxy)methyl)carbamate (3b)



The title compound was prepared according to general procedure **B** from Fmoc-NH_2 (500 mg, 2.09 mmol), MeMgCl (1.92M in Et_2O) (1.41 mL, 2.19 mmol) and 4-fluorobenzaldehyde (272 mg, 2.19 mmol) in anhydrous THF (3.0 mL) then *p*-toluenesulfonic acid (26 mg, 0.105 mmol) in 1:1 DCM/MeOH (6.0 mL). . Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (142 mg, 18%).

RF (1:3 EtOAc:Hex): 0.61

IR ν_{max} (cm^{-1}): 3293, 2991, 2916, 2834, 1695, 1534, 1507, 1254, 1220, 1041, 982, 734

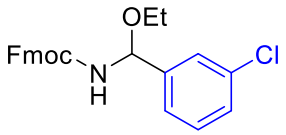
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{20}NO_3FNa$ 400.1325; Found 400.1314

^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.44 – 7.29 (m, 6H), 7.04 (t, *J* = 8.5 Hz, 2H), 5.86 (d, *J* = 9.8 Hz, 1H), 5.22 (d, *J* = 9.4 Hz, 1H), 4.53 (ddd, *J* = 17.1, 10.6, 7.3 Hz, 1H), 4.23 (t, *J* = 6.4 Hz, 1H), 3.42 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.73 (d, *J* = 247.1 Hz), 155.96 (s), 143.68 (d, *J* = 2.2 Hz), 141.41 (s), 134.99 (s, *J* = 27.0 Hz), 127.79 (s), 127.69 (d, *J* = 8.3 Hz), 127.11 (s), 124.94 (s), 119.97 (d, *J* = 19.2 Hz), 115.47 (d, *J* = 21.6 Hz), 83.31 (s, *J* = 7.4 Hz), 66.76 (s, *J* = 9.0 Hz), 55.76 (s, *J* = 10.9 Hz), 47.27 (s, *J* = 17.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ -113.44.

(9*H*-fluoren-9-yl)methyl ((3-chlorophenyl)(ethoxy)methyl)carbamate (3c)



The title compound was prepared according to general procedure **A** from Fmoc-NH_2 (500 mg, 2.09 mmol), 3-chlorobenzaldehyde (353 mg, 2.51 mmol) and $Ti(OEt)_4$ (716 mg, 3.14 mmol) in anhydrous DCM (8.0 mL) at 40°C. Purification by FCC (1:9 EtOAc:Hex) afforded the pure product as a white solid (230 mg, 27%).

RF (1:3 EtOAc:Hex): 0.61

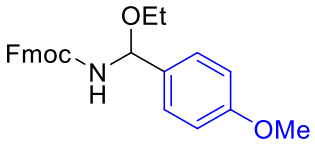
IR ν_{max} (cm^{-1}): 3289, 2970, 2894, 1690, 1526, 1248, 1101, 1026, 738

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{22}NO_3ClNa$ 430.1186; Found 430.1189

^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.4 Hz, 2H), 7.47 – 7.36 (m, 3H), 7.35 – 7.22 (m, 5H), 5.95 (d, *J* = 9.9 Hz, 1H), 5.30 (d, *J* = 9.8 Hz, 1H), 4.51 (dt, *J* = 17.1, 10.6 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 1H), 3.74 – 3.51 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 155.94, 143.67, 141.55, 141.41, 134.50, 129.85, 128.61, 127.81, 127.11, 126.24, 124.98, 124.25, 120.07, 81.59, 66.77, 63.83, 47.27, 15.09.

(9*H*-fluoren-9-yl)methyl (ethoxy(4-methoxyphenyl)methyl)carbamate (3d)



The title compound was prepared according to general procedure **A** from Fmoc-NH_2 (500 mg, 2.09 mmol), 4-methoxybenzaldehyde (342 mg, 2.51 mmol) and $Ti(OEt)_4$ (716 mg, 3.14 mmol) in anhydrous DCM (8.0 mL) at 40°C. Purification by FCC (1:9 to 1:3 EtOAc:Hex) afforded the pure product as a white solid (77 mg, 9%).

RF (1:5 EtOAc:Hex): 0.39

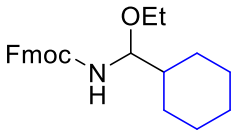
IR ν_{max} (cm^{-1}): 3291, 3037, 2972, 2898, 2834, 1694, 1511, 1237, 1032, 736

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{25}NO_4Na$ 426.1681; Found 426.1679

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.27 (m, 4H), 6.88 (d, *J* = 8.2 Hz, 2H), 5.93 (d, *J* = 9.6 Hz, 1H), 5.31 (d, *J* = 9.4 Hz, 1H), 4.48 (dt, *J* = 16.9, 10.3 Hz, 2H), 4.22 (t, *J* = 6.2 Hz, 1H), 3.79 (s, 3H), 3.75 – 3.51 (m, 2H), 1.25 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.66, 155.92, 143.77, 141.38, 131.74, 127.75, 127.10, 125.02, 120.04, 113.90, 82.12, 66.73, 63.59, 55.34, 47.27, 15.15.

(9*H*-fluoren-9-yl)methyl (cyclohexyl(ethoxy)methyl)carbamate (3e)



The title compound was prepared according to general procedure **A** from Fmoc-NH_2 (500 mg, 2.09 mmol), cyclohexanecarboxaldehyde (282 mg, 2.51 mmol) and $Ti(OEt)_4$ (716 mg, 3.14 mmol) in anhydrous DCM (8.0 mL) at 40°C. Purification by FCC (1:9 EtOAc:Hex) afforded the pure product as a white solid (96 mg, 12%).

RF (1:3 EtOAc:Hex): 0.68

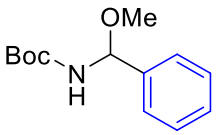
IR ν_{max} (cm^{-1}): 3289, 3064, 2970, 2920, 2849, 1694, 1530, 1254, 1079, 1012, 738

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{29}NO_3Na$ 402.2045; Found 402.2046

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 4.97 (d, *J* = 9.9 Hz, 1H), 4.68 (dd, *J* = 9.8, 7.0 Hz, 1H), 4.53 – 4.38 (m, 2H), 4.22 (t, *J* = 6.3 Hz, 1H), 3.64 – 3.53 (m, 1H), 3.47 – 3.36 (m, 1H), 1.90 – 0.91 (m, 11H), 1.15 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.30, 143.89, 143.82, 141.39, 127.71, 127.06, 125.00, 120.01, 85.65, 66.35, 63.54, 47.38, 42.81, 28.54, 27.90, 26.33, 25.71, 15.10.

tert-butyl (methoxy(phenyl)methyl)carbamate (3f)



The title compound was prepared according to general procedure **B** from *tert*-butyl carbamate (1.172 g, 10 mmol), MeMgCl (1.92M in Et_2O) (5.47 mL, 10.5 mmol) and benzaldehyde (1.114 g, 10.5 mmol) in anhydrous THF (15.0 mL) then *p*-toluenesulfonic acid (88 mg, 0.35 mmol) in MeOH (20.9 mL). Purification by FCC (1:7 EtOAc:Hex) afforded the pure product as an off - white solid (444 mg, 19%).

RF (1:5 EtOAc:Hex): 0.31

IR ν_{max} (cm^{-1}): 3317, 3002, 2974, 2931, 2830, 1707, 1551, 1244, 1169, 1049, 959

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{19}NO_3Na$ 260.1263; Found 260.1262

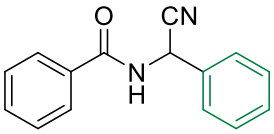
^1H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.29 (m, 5H), 5.82 (d, *J* = 9.8 Hz, 1H), 5.20 (d, *J* = 8.9 Hz, 1H), 3.44 (s, 3H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 155.32, 139.45, 128.56, 128.42, 125.92, 83.50, 80.09, 55.55, 28.33.

Data in accordance with literature.[2]

Synthesis of α-amido nitriles

_N_-[cyano(phenyl)methyl]benzamide (2a)



The title compound was prepared according to general procedure **C** from **1a** (50 mg, 0.196 mmol), TMSCN (117 mg, 147 µL, 1.18 mmol), $Ca(NTf_2)_2$ (2.4 mg, 0.0039 mmol), $n$$Bu_4NPF_6$ (1.5 mg, 0.0039 mmol) in 1,2-DCE (1 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (40 mg, 86 %).

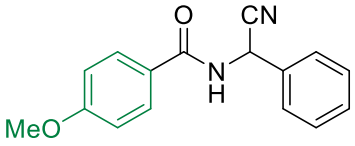
RF (1:3 EtOAc:Hept): 0.26

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (dt, J = 8.5, 1.7 Hz, 2H), 7.60 – 7.53 (m, 3H), 7.51 – 7.41 (m, 5H), 6.64 (d, J = 7.0 Hz, 1H), 6.36 (d, J = 8.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 133.4, 132.7, 132.5, 129.8, 129.6, 128.9, 127.4, 127.2, 117.6, 44.7.

*Data in accordance with literature[3]

_N_-(cyano(phenyl)methyl)-4-methoxybenzamide (2b)



The title compound was prepared according to general procedure **C** from **1b** (100 mg, 0.35 mmol), TMSCN (208 mg, 263 µL, 2.10 mmol), $Ca(NTf_2)_2$ (4.2 mg, 0.007 mmol) and $n$$Bu_4NPF_6$ (2.7 mg, 0.007 mmol) in 1,2-DCE (1.75 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:2 EtOAc:Hex) afforded the pure compound as an off-white solid (70 mg, 75 %).

RF (1:3 EtOAc:Hex): 0.22

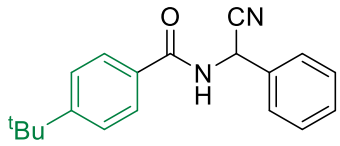
IR ν_{max} (cm^{-1}): 3293, 2920, 2842, 1634, 1602, 1592, 1581, 1500, 1321, 1243, 1179

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_2O_2$ 267.1134; Found 267.1140

^1H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.73 (m, 2H), 7.55 – 7.51 (m, 2H), 7.46 – 7.40 (m, 3H), 6.95 – 6.88 (m, 2H), 6.83 (d, *J* = 8.3 Hz, 1H), 6.32 (d, *J* = 8.3 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.02, 162.99, 133.41, 129.57, 129.42, 129.31, 127.12, 124.57, 117.65, 114.01, 55.50, 44.53.

4-(*tert*-butyl)-N-(cyano(phenyl)methyl)benzamide (2c)



The title compound was prepared according to general procedure **C** from **1c** (100 mg, 0.32 mmol), TMSCN (191 mg, 241 µL, 1.93 mmol), $Ca(NTf_2)_2$ (3.9 mg, 0.006 mmol) and nBu_4NPF_6 (2.5 mg, 0.006 mmol) in 1,2-DCE (1.60 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:5 EtOAc:Hex) afforded the pure compound as an white solid (71 mg, 76 %).

RF (1:5 EtOAc:Hex): 0.36

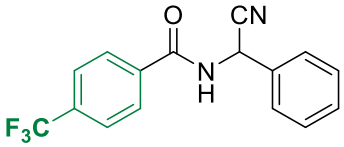
IR ν_{max} (cm^{-1}): 3243, 2953, 2922, 2863, 1638, 1604, 1522, 1492, 1455, 1319, 874

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}N_2O$ 293.1654; Found 293.1655

^1H NMR (400 MHz, $CDCl_3$): δ 7.77 – 7.71 (m, 2H), 7.56 – 7.51 (m, 2H), 7.48 – 7.40 (m, 5H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.35 (d, *J* = 8.4 Hz, 1H), 1.32 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.36, 156.30, 133.36, 129.60, 129.49, 129.44, 127.19, 127.08, 125.79, 117.55, 44.49, 35.07, 31.11.

***N*-[cyano(phenyl)methyl]-4-(trifluoromethyl)benzamide (2d)**



The title compound was prepared according to general procedure **C** from **1d** (56 mg, 0.174 mmol), TMSCN (104 mg, 131 µL, 1.1 mmol), $Ca(NTf_2)_2$ (5.2 mg, 0.0087 mmol), nBu_4NPF_6 (3.4 mg, 0.0087 mmol) in 1,2-DCE (0.9 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a white solid (32 mg, 60 %).

RF (1:3 EtOAc:Hept): 0.44

IR ν_{max} (cm^{-1}): 3241, 2021, 1644, 1528, 1325, 1109, 1062

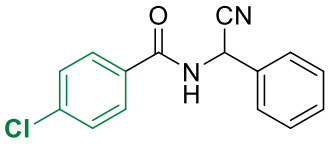
HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}F_3N_2O$ 305.0902; Found 305.0898

^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.59 – 7.54 (m, 2H), 7.51 – 7.44 (m, 3H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.33 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.4, 135.8, 134.4 (q, *J* = 32.7 Hz), 132.9, 130.0, 129.7, 128.0, 127.3, 126.0 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.7 Hz), 117.4, 44.9.

^{19}F NMR (376 MHz, $CDCl_3$): -63.1

4-chloro-*N*-[cyano(phenyl)methyl]benzamide (2e)



The title compound was prepared according to general procedure **C** from **1e** (53 mg, 0.174 mmol), TMSCN (104 mg, 131 µL, 1.1 mmol), $Ca(NTf_2)_2$ (5.2 mg, 0.0087 mmol), nBu_4NPF_6 (3.4 mg, 0.0087 mmol) in 1,2-DCE (0.9 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (26 mg, 55 %).

RF (1:3 EtOAc:Hept): 0.30

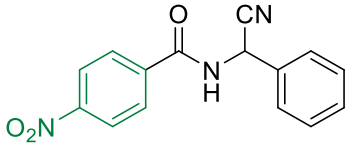
IR ν_{max} (cm^{-1}): 3319, 2917, 1644, 1517, 1482, 1092

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}ClN_2O$ 271.0638; Found 271.0640

^1H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.7 Hz, 2H), 7.60 – 7.52 (m, 2H), 7.51 – 7.38 (m, 5H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.32 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.5, 139.2, 133.1, 130.9, 130.0, 129.7, 129.3, 128.9, 127.3, 117.4, 44.9.

***N*-(cyano(phenyl)methyl)-4-nitrobenzamide (2f)**



The title compound was prepared according to general procedure **C** from **1f** (100 mg, 0.33 mmol), TMSCN (198 mg, 250 µL, 2.00 mmol), $Ca(NTf_2)_2$ (4.0 mg, 0.007 mmol) and $n$$Bu_4NPF_6$ (2.6 mg, 0.007 mmol) in 1,2-DCE (1.67 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:3 EtOAc:Hex) afforded the pure compound as an orange solid (70 mg, 75 %).

RF (1:3 EtOAc:Hex): 0.34

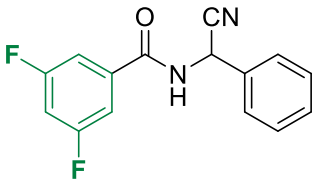
IR ν_{max} (cm^{-1}): 3267, 2920, 2853, 1640, 1593, 1518, 1345

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{11}N_3O_3Na$ 304.0698

^{1}H NMR (400 MHz, DMSO): δ 10.12 (d, *J* = 7.7 Hz, 1H), 8.38 – 8.34 (m, 2H), 8.17 – 8.13 (m, 2H), 7.59 – 7.56 (m, 2H), 7.52 – 7.41 (m, 3H), 6.45 (d, *J* = 7.6 Hz, 1H).

^{13}C NMR (101 MHz, DMSO): δ 165.00, 149.96, 138.74, 134.57, 129.73, 129.46, 129.43, 127.65, 124.15, 118.71, 44.62.

_N_-[cyano(phenyl)methyl]-3,5-difluoro-benzamide (2g)



The title compound was prepared according to general procedure **C** from **1g** (90 mg, 0.295 mmol), TMSCN (175 mg, 221 µL, 1.8 mmol), $Ca(NTf_2)_2$ (5.7 mg, 0.015 mmol), $n Bu_4NPF_6$ (5.7 mg, 0.015 mmol) in 1,2-DCE (1.5 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (31 mg, 38 %).

RF (1:3 EtOAc:Hept): 0.35

IR ν_{max} (cm^{-1}): 3297, 3088, 2924, 1655, 1595, 1526, 1336, 1124, 988

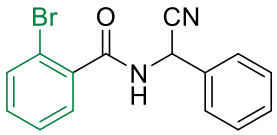
HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}F_2N_2OS$ 273.0839; Found 273.0827

^1H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.52 (m, 2H), 7.50 – 7.43 (m, 3H), 7.36 – 7.28 (m, 2H), 7.00 (tt, *J* = 8.5, 2.3 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 6.28 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR (101 MHz, CDCl3): δ 164.5 (d, *J* = 12.1 Hz), 164.2, 161.9 (d, *J* = 12.1 Hz), 135.8 (t, *J* = 8.4 Hz), 132.8, 130.1, 129.8, 127.3, 117.2, 110.9 (d, *J* = 7.9 Hz), 110.7 (d, *J* = 7.9 Hz), 108.2 (t, *J* = 25.2 Hz), 45.0.

^{19}F NMR (376 MHz, $CDCl_3$): -107.0

2-bromo-*N*-(cyano(phenyl)methyl)benzamide (2h)



The title compound was prepared according to general procedure **C** from **1h** (100 mg, 0.30 mmol), TMSCN (179 mg, 225 µL, 1.80 mmol), $Ca(NTf_2)_2$ (3.6 mg, 0.006 mmol) and nBu_4NPF_6 (2.3 mg, 0.006 mmol) in 1,2-DCE (1.50 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:3 EtOAc:Hex) afforded the pure compound as a pale yellow solid (76 mg, 80 %).

RF (1:3 EtOAc:Hex): 0.32

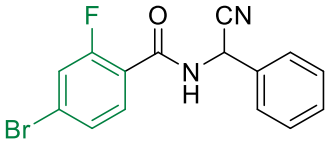
IR ν_{max} (cm^{-1}): 3207, 3032, 2901, 2883, 1653, 1591, 1522, 1314, 746

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{11}N_2OBrNa$ 336.9952; Found 336.9949

^1H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.52 (m, 4H), 7.48 – 7.42 (m, 3H), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 (td, *J* = 7.7, 1.8 Hz, 1H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.28 (d, *J* = 8.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.65, 135.59, 133.59, 132.65, 132.17, 129.93, 129.74, 129.46, 127.76, 127.19, 119.35, 116.94, 44.60.

4-bromo-*N*-(cyano(phenyl)methyl)-2-fluorobenzamide (2i)



The title compound was prepared according to general procedure **C** from **1i** (100 mg, 0.285 mmol), TMSCN (169 mg, 214 µL, 1.71 mmol), $Ca(NTf_2)_2$ (3.4 mg, 0.006 mmol) and nBu_4NPF_6 (2.2 mg, 0.006 mmol) in 1,2-DCE (1.40 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:3 EtOAc:Hex) afforded the pure compound as a yellow solid (65 mg, 72 %).

RF (1:3 EtOAc:Hex): 0.59

IR ν_{max} (cm^{-1}): 3367, 2922, 1649, 1602, 1504, 1472, 1401, 1132, 885

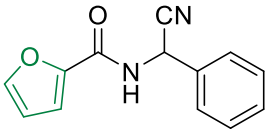
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{10}N_2OFBrNa$ 354.9858; Found 354.9847

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (t, *J* = 8.4 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.50 – 7.42 (m, 4H), 7.34 (dd, *J* = 11.4, 1.7 Hz, 1H), 7.17 (dd, *J* = 12.4, 8.2 Hz, 1H), 6.31 (dd, *J* = 7.9, 1.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.78 (d, *J* = 3.2 Hz), 160.19 (d, *J* = 252.4 Hz), 133.47 (d, *J* = 2.5 Hz), 132.73 (s), 129.83 (s), 129.57 (s), 128.80 (d, *J* = 3.3 Hz), 127.88 (d, *J* = 10.6 Hz), 127.08 (s), 119.86 (d, *J* = 27.9 Hz), 118.35 (d, *J* = 11.3 Hz), 117.08 (s), 44.70 (s).

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.29

_N_-(cyano(phenyl)methyl)furan-2-carboxamide (2j)



The title compound was prepared according to general procedure **C** from **1j** (100 mg, 0.408 mmol), TMSCN (243 mg, 306 µL, 2.45 mmol), $Ca(NTf_2)_2$ (4.9 mg, 0.008 mmol) and $n$$Bu_4NPF_6$ (3.2 mg, 0.008 mmol) in 1,2-DCE (2.04 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:2 EtOAc:Hex) afforded the pure compound as a pale red solid (71 mg, 77 %).

RF (1:2 EtOAc:Hex): 0.37

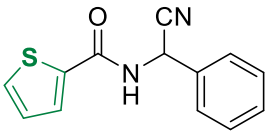
IR ν_{max} (cm^{-1}): 3267, 3125, 3035, 2922, 2249, 1654, 1522, 1474, 1321, 1202, 771

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{10}N_2O_2Na$ 249.0640; Found 249.0638

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 – 7.51 (m, 2H), 7.49 – 7.41 (m, 4H), 7.24 (d, *J* = 3.5 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.54 (dd, *J* = 3.5, 1.7 Hz, 1H), 6.31 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 157.13, 146.32, 144.88, 133.05, 129.70, 129.47, 127.11, 117.20, 116.33, 112.61, 43.72.

***N*-[cyano(phenyl)methyl]thiophene-2-carboxamide (2k)**



The title compound was prepared according to general procedure **C** from **1k** (60 mg, 0.230 mmol), TMSCN (137 mg, 172 µL, 1.4 mmol), $Ca(NTf_2)_2$ (6.9 mg, 0.012 mmol), $n$$Bu_4NPF_6$ (4.5 mg, 0.012 mmol) in 1,2-DCE (1.2 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (38 mg, 68 %).

RF (1:3 EtOAc:Hept): 0.14

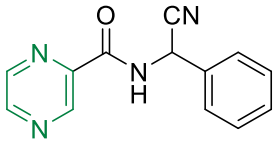
IR ν_{max} (cm^{-1}): 3241, 3029, 1627, 1532, 1299, 853

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{11}N_2OS$ 243.0592; Found 243.0597

^1H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.52 (m, 4H), 7.50 – 7.40 (m, 3H), 7.10 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.68 (d, *J* = 7.4 Hz, 1H), 6.33 (d, *J* = 8.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.4, 161.0, 136.7, 133.3, 131.8, 129.8, 129.6, 128.1, 127.3, 117.4, 44.6.

***N*-(cyano(phenyl)methyl)pyrazine-2-carboxamide (2l)**



The title compound was prepared according to general procedure C from **1j** (100 mg, 0.389 mmol), TMSCN (231 mg, 292 µL, 2.23 mmol), $Ca(NTf_2)_2$ (11.7 mg, 0.020 mmol) and $n$$Bu_4NPF_6$ (7.6 mg, 0.020 mmol) in 1,2-DCE (1.95 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:2 EtOAc:Hex) afforded the pure compound as a yellow solid (50 mg, 54 %).

RF (1:2 EtOAc:Hex): 0.22

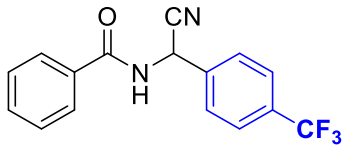
IR ν_{max} (cm^{-1}): 3289, 2922, 2851, 1664, 1578, 1498, 1150, 1019

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{11}N_4O$ 239.0933; Found 239.0930

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (d, *J* = 1.2 Hz, 1H), 8.82 (d, *J* = 2.4 Hz, 1H), 8.54 (dd, *J* = 2.2, 1.6 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H), 7.57 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.51 – 7.44 (m, 3H), 6.33 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.34, 148.21, 144.81, 143.05, 142.78, 132.83, 129.81, 129.55, 127.11, 116.99, 44.14.

N-[cyano-[4-(trifluoromethyl)phenyl]methyl]benzamide (2m)



The title compound was prepared according to general procedure **C** from **1m** (80 mg, 0.259 mmol), TMSCN (154 mg, 194 µL, 1.55 mmol), $Ca(NTf_2)_2$ (7.8 mg, 0.0129 mmol), *n*Bu_4NPF_6 (5 mg, 0.0129 mmol) in 1,2-DCE (1.3 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:9 to 1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (56 mg, 71 %).

RF (1:3 EtOAc:Hept): 0.30

IR ν_{max} (cm^{-1}): 3263, 2937, 1646, 1521, 1323, 1113

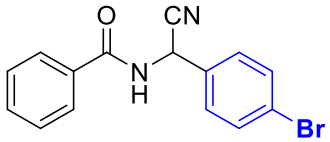
HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}F_3N_2O$ 305.0902; Found 305.0912

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.78 (m, 2H), 7.75 – 7.67 (m, 3H), 7.64 (d, *J* = 1.5 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.52 – 7.45 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 8.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.6, 133.0, 132.2, 129.1, 129.0, 127.7, 127.4, 127.2, 126.6 (q, *J* = 3.7 Hz), 126.6, 116.9, 44.2.

^{19}F NMR (376 MHz, $CDCl_3$): -62.9

***N*-[(4-bromophenyl)-cyano-methyl]benzamide (2n)**



The title compound was prepared according to general procedure **C** from **1n** (25 mg, 0.0781 mmol), TMSCN (47 mg, 60 µL, 0.468 mmol), $Ca(NTf_2)_2$ (2.3 mg, 0.0039 mmol), $n$$Bu_4NPF_6$ (1.55 mg, 0.0039 mmol) in 1,2-DCE (0.4 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:9 to 1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (19 mg, 77 %).

RF (1:3 EtOAc:Hept): 0.29

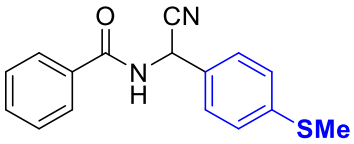
IR ν_{max} (cm^{-1}): 3248, 2917, 1642, 1517, 1325, 1012

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}BrN_2O$ 315.0133; Found 315.0143

^1H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.76 (m, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.46 – 7.39 (m, 3H), 6.68 (d, *J* = 8.2 Hz, 1H), 6.34 (d, *J* = 8.5 Hz, 1H).z

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.5, 132.9, 132.8, 132.5, 132.3, 129.1, 128.9, 127.4, 124.2, 117.1, 44.2.

***N*-[cyano-(4-methylsulfanylphenyl)methyl]benzamide (2o)**



The title compound was prepared according to general procedure **C** from **1o** (100 mg, 0.333 mmol), TMSCN (198 mg, 250 µL, 2.0 mmol), $Ca(NTf_2)_2$ (4 mg, 0.0066 mmol), $n$$Bu_4NPF_6$ (2.6 mg, 0.0066 mmol) in 1,2-DCE (1.7 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:9 to 1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (72 mg, 77 %).

RF (1:3 EtOAc:Hept): 0.16

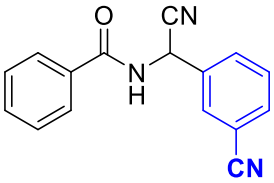
IR ν_{max} (cm^{-1}): 3267, 2917, 1644, 1513, 1489, 1320, 960

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2OS$ 283.0905; Found 283.0895

^1H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.76 (m, 2H), 7.55 (tt, *J* = 2.0, 1.3 Hz, 1H), 7.48 – 7.42 (m, 4H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.29 (d, *J* = 8.3 Hz, 1H), 2.49 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): 166.6, 141.3, 132.7, 132.5, 129.7, 129.0, 127.7, 127.4, 126.9, 117.5, 44.4, 15.5.

***N*-[cyano-(3-cyanophenyl)methyl]benzamide (2q)**



The title compound was prepared according to general procedure **C** from **1q** (74 mg, 0.278 mmol), TMSCN (165 mg, 209 µL, 1.7 mmol), $Ca(NTf_2)_2$ (8.3 mg, 0.014 mmol), $n$$Bu_4NPF_6$ (5.4 mg, 0.014 mmol) in 1,2-DCE (1.4 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (67 mg, 92 %).

RF (1:3 EtOAc:Hept): 0.10

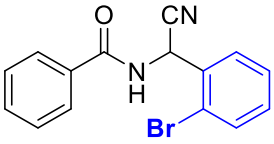
IR ν_{max} (cm^{-1}): 3260, 3036, 2234, 1646, 1517, 1321

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}N_3OS$ 262.0980; Found 262.0973

^1H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.77 (m, 4H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 1H), 6.46 (d, *J* = 8.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.7, 135.4, 133.3, 133.1, 132.0, 131.7, 130.7, 130.5, 129.1, 127.5, 117.9, 116.7, 113.8, 43.9.

***N*-[(2-bromophenyl)-cyano-methyl]benzamide (2r)**



The title compound was prepared according to general procedure **C** from **1r** (100 mg, 0.299 mmol), TMSCN (178 mg, 225 µL, 1.8 mmol), $Ca(NTf_2)_2$ (3.6 mg, 0.006 mmol), $n$$Bu_4NPF_6$ (2.3 mg, 0.006 mmol) in 1,2-DCE (1.5 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:9 to 1:3 EtOAc:Heptane) afforded the pure compound as a white solid (78 mg, 83 %).

RF (1:3 EtOAc:Hept): 0.29

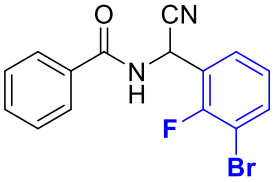
IR ν_{max} (cm^{-1}): 3265, 2920, 1640, 1523, 1325, 1077

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}BrN_2OS$ 315.0133; Found 315.0143

^1H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.73 (m, 3H), 7.67 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.55 (tt, *J* = 2.0, 1.3 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.33 (td, *J* = 7.7, 1.7 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.43 (d, *J* = 7.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.4, 134.2, 132.7, 132.5, 132.4, 131.6, 130.3, 129.0, 128.5, 127.4, 123.4, 116.9, 45.6.

***N*-[(3-bromo-2-fluoro-phenyl)-cyano-methyl]benzamide (2s)**



The title compound was prepared according to general procedure **C** from **1s** (100 mg, 0.284 mmol), TMSCN (169 mg, 213 µL, 1.7 mmol), $Ca(NTf_2)_2$ (3.4 mg, 0.0057 mmol), $n$$Bu_4NPF_6$ (2.2 mg, 0.0057 mmol) in 1,2-DCE (1.4 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a yellow solid (58 mg, 61 %).

RF (1:3 EtOAc:Hept): 0.19

IR ν_{max} (cm^{-1}): 3258, 2920, 1638, 1517, 1456, 1329, 788

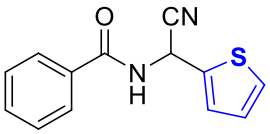
HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}BrFN_2OS$ 333.0039; Found 333.0039

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.1 Hz, 2H), 7.66 (ddd, *J* = 8.1, 6.7, 1.6 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.14 (td, *J* = 8.0, 0.9 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.43 (d, *J* = 8.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3, 135.6, 132.9, 132.3, 129.0, 128.8 (d, *J* = 2.2 Hz), 127.4, 126.1 (d, *J* = 4.7 Hz), 122.6 (d, *J* = 14.4 Hz), 116.3, 110.5 (d, *J* = 20.2 Hz), 40.4.

^{19}F NMR (376 MHz, $CDCl_3$): -109.6

***N*-[cyano(2-thienyl)methyl]benzamide (2t)**



The title compound was prepared according to general procedure **C** from **1t** (74 mg, 0.284 mmol), TMSCN (169 mg, 213 µL, 1.7 mmol), $Ca(NTf_2)_2$ (3.4 mg, 0.0057 mmol), $n$$Bu_4NPF_6$ (2.2 mg, 0.0057 mmol) in 1,2-DCE (1.4 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as an orange solid (60 mg, 87 %).

RF (1:3 EtOAc:Hept): 0.21

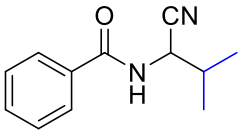
IR ν_{max} (cm^{-1}): 3271, 3107, 2909, 1642, 1508, 1485, 1238, 848

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{11}N_2OS$ 243.0592; Found 243.0600

^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.1 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.36 (dt, *J* = 3.6, 1.1 Hz, 1H), 7.04 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.52 (dd, *J* = 8.4, 0.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.4, 135.7, 132.8, 132.4, 129.0, 128.0, 127.8, 127.5, 127.5, 117.0, 40.5.

_N_-(1-cyano-2-methyl-propyl)benzamide (2u)



The title compound was prepared according to general procedure **C** from **1u** (60 mg, 0.271 mmol), TMSCN (161 mg, 204 µL, 1.6 mmol), $Ca(NTf_2)_2$ (8.1 mg, 0.014 mmol), $n$$Bu_4NPF_6$ (5.3 mg, 0.014 mmol) in 1,2-DCE (1.4 mL). Following completion of the reaction (12 h) and work-up, purification by FCC (1:3 EtOAc:Heptane) afforded the pure compound as a white solid (48 mg, 88 %).

RF (1:3 EtOAc:Hept): 0.21

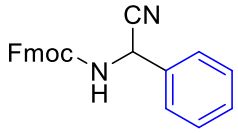
IR ν_{max} (cm^{-1}): 3267, 2969, 2876, 1636, 1522, 1306, 855

HRMS (APCI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}N_2O$ 203.1184; Found 203.1189

^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 6.62 (d, *J* = 7.5 Hz, 1H), 5.03 (dd, *J* = 8.9, 6.4 Hz, 1H), 2.24 – 2.10 (m, 1H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.9, 133.0, 132.5, 129.0, 127.3, 118.0, 47.1, 32.0, 18.8, 18.2.

(9*H*-fluoren-9-yl)methyl (cyano(phenyl)methyl)carbamate (4a)



The title compound was prepared according to general procedure **C** from **3a** (50 mg, 0.139 mmol), TMSCN (83 mg, 104 µL, 0.835 mmol), $Ca(NTf_2)_2$ (1.7 mg, 0.003 mmol) and nBu$_4$NPF$_6$ (1.1 mg, 0.003 mmol) in 1,2-DCE (0.70 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:7 EtOAc:Hex) afforded the pure compound as a white solid (27 mg, 51 %).

RF (1:3 EtOAc:Hex): 0.59

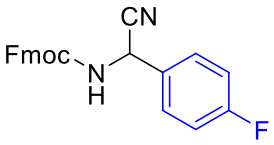
IR ν_{max} (cm^{-1}): 3280, 2918, 2849, 1687, 1523, 1449, 1245, 728

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{18}N_2O_2Na$ 377.1266; Found 377.1264

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 7.1 Hz, 2H), 7.47 – 7.37 (m, 7H), 7.30 (t, *J* = 7.0 Hz, 2H), 5.83 (d, *J* = 8.1 Hz, 1H), 5.36 (d, *J* = 6.8 Hz, 1H), 4.52 (d, *J* = 5.5 Hz, 2H), 4.21 (s, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 155.06, 143.47, 143.38, 141.39, 133.01, 129.72, 129.44, 127.90, 127.19, 126.94, 124.90, 120.12, 117.36, 67.61, 47.08.

(9*H*-fluoren-9-yl)methyl (cyano(4-fluorophenyl)methyl)carbamate (4b)



The title compound was prepared according to general procedure **C** from **3b** (50 mg, 0.132 mmol), TMSCN (79 mg, 99 µL, 0.795 mmol), $Ca(NTf_2)_2$ (1.6 mg, 0.003 mmol) and nBu$_4$NPF$_6$ (1.0 mg, 0.003 mmol) in 1,2-DCE (0.66 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:5 to 1:3 EtOAc:Hex) afforded the pure compound as a white solid (40 mg, 81 %).

RF (1:3 EtOAc:Hex): 0.69

IR ν_{max} (cm^{-1}): 3274, 3039, 2980, 2914, 2849, 1692, 1526, 1269, 1222

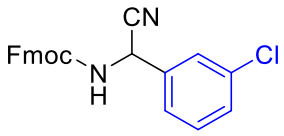
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{17}N_2O_2FNa$ 395.1172; Found 395.1183

^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.58 – 7.52 (m, 2H), 7.41 (t, *J* = 7.4 Hz, 4H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.10 (t, *J* = 8.2 Hz, 2H), 5.81 (d, *J* = 8.5 Hz, 1H), 5.36 (d, *J* = 8.2 Hz, 1H), 4.54 (d, *J* = 6.1 Hz, 1H), 4.20 (t, *J* = 6.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.28 (d, *J* = 249.9 Hz), 155.00 (s), 143.40 (s), 143.30 (s), 141.38 (d, *J* = 2.8 Hz), 128.94 (d, *J* = 8.5 Hz), 127.93 (s), 127.20 (s), 124.87 (d, *J* = 4.0 Hz), 120.13 (d, *J* = 2.0 Hz), 117.10 (d, *J* = 14.0 Hz), 116.59 (s), 116.37 (s), 67.59 (s), 47.06 (s).

^{19}F NMR (376 MHz, $CDCl_3$): δ -111.00.

(9*H*-fluoren-9-yl)methyl ((3-chlorophenyl)(cyano)methyl)carbamate (4c)



The title compound was prepared according to general procedure **C** from **3c** (50 mg, 0.123 mmol), TMSCN (73 mg, 92 µL, 0.735 mmol), $Ca(NTf_2)_2$ (1.5 mg, 0.002 mmol) and $n$$Bu_4NPF_6$ (1.0 mg, 0.002 mmol) in 1,2-DCE (0.62 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:5 EtOAc:Hex) afforded the pure compound as a white solid (30 mg, 63 %).

RF (1:5 EtOAc:Hex): 0.29

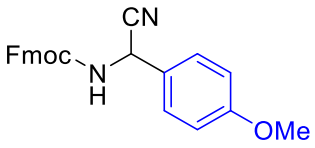
IR ν_{max} (cm^{-1}): 3295, 2918, 2851, 1690, 1528, 1310, 1258, 726

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{17}ClN_2O_2$ 411.0876; Found 411.0879

^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 7.0 Hz, 2H), 7.50 – 7.28 (m, 8H), 5.82 (d, *J* = 8.5 Hz, 1H), 5.40 (d, *J* = 7.7 Hz, 1H), 4.54 (d, *J* = 5.6 Hz, 2H), 4.21 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.99, 143.37, 143.27, 141.36, 135.40, 134.92, 130.70, 129.97, 127.94, 127.21, 127.11, 125.07, 124.85, 120.14, 116.81, 67.73, 47.04.

(9*H*-fluoren-9-yl)methyl (cyano(4-methoxyphenyl)methyl)carbamate (4d)



The title compound was prepared according to general procedure **C** from **3d** (35 mg, 0.087 mmol), TMSCN (52 mg, 65 µL, 0.522 mmol), $Ca(NTf_2)_2$ (1.1 mg, 0.002 mmol) and $n$$Bu_4NPF_6$ (0.7 mg, 0.002 mmol) in 1,2-DCE (0.44 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:5 to 1:3 EtOAc:Hex) afforded the pure compound as a white solid (20 mg, 60 %).

RF (1:3 EtOAc:Hex): 0.38

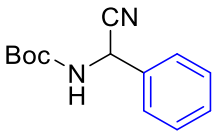
IR ν_{max} (cm^{-1}): 3280, 2953, 2918, 2849, 1686, 1530, 1511, 1302, 1250, 1014, 730

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{20}N_2O_3Na$ 407.1372; Found 407.1387

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.45 – 7.28 (m, 6H), 6.92 (d, *J* = 8.4 Hz, 2H), 5.75 (d, *J* = 8.3 Hz, 1H), 5.30 (d, *J* = 6.0 Hz, 1H), 4.51 (d, *J* = 6.3 Hz, 1H), 4.26 – 4.17 (m, 1H), 3.81 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.54, 154.98, 143.47, 143.40, 141.37, 128.42, 127.89, 127.18, 124.92, 120.11, 117.60, 114.71, 67.55, 55.46, 47.05.

***tert*-butyl (cyano(phenyl)methyl)carbamate (4f)**



The title compound was prepared according to general procedure **C*** from **3f** (50 mg, 0.21 mmol), TMSCN (125 mg, 158 µL, 1.26 mmol), $Ca(NTf_2)_2$ (2.5 mg, 0.004 mmol) and $n$$Bu_4NPF_6$ (1.6 mg, 0.004 mmol) in 1,2-DCE (1.0 mL). Following completion of the reaction (18 h) and work-up, purification by FCC (1:5 EtOAc:Hex) afforded the pure compound as a white solid (28 mg, 57 %).

*Reaction at 60°C.

RF (1:3 EtOAc:Hex): 0.36

IR ν_{max} (cm^{-1}): 3326, 3013, 2980, 2935, 2907, 1692, 1507, 1161

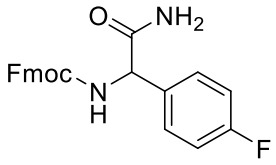
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.46 (m, 2H), 7.46 – 7.39 (m, 3H), 5.80 (d, *J* = 6.5 Hz, 1H), 5.14 (s, 1H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.19, 133.49, 129.52, 129.34, 126.91, 117.76, 81.60, 46.08, 28.24.

Data in accordance with literature.[4]

Derivatisation of Products

(9H-fluoren-9-yl)methyl (2-amino-1-(4-fluorophenyl)-2-oxoethyl)carbamate (5)



To a screw top vial capped with a capped with Teflon cap was added **4b** (21 mg, 0.056 mmol) and Ghaffar-Parkins catalyst (0.5 mg, 0.001 mmol). EtOH (0.5 mL) and H_2O (0.1 mL) were added and the reactions was stirred at 80°C for 4 hours. The reaction was cooled to room temperature, diluted with DCM and organic layer was separated. Aqueous layer was washed with DCM (x3) and combined organic fractions were dried over Na_2SO_4 filtered and concentrated *in vacuo*. The product was purified by FCC (1:1 EtOAc:Hex) to afford the pure product as a white solid. (22 mg, quant.)

RF (1:1 EtOAc:Hex): 0.40

IR ν_{max} (cm^{-1}): 3383, 3300, 3200, 3063, 2954, 2920, 2850, 1692, 1662, 1539, 1507, 1254, 1231, 1072, 731

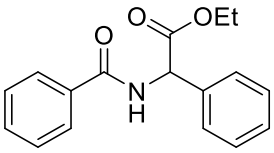
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}FN_2O_3$ 391.1458; Found 391.1468

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 7.4 Hz, 2H), 7.72 (s, 1H), 7.60 – 7.52 (m, 2H), 7.52 – 7.44 (m, 2H), 7.38 (dd, *J* = 17.0, 7.8 Hz, 2H), 7.26 (t, *J* = 8.5 Hz, 3H), 5.26 (d, *J* = 8.3 Hz, 1H), 4.35 – 4.25 (m, 3H).

^{13}C NMR (101 MHz, d_6-DMSO): δ 172.07 (s), 162.07 (d, *J* = 243.4 Hz), 156.06 (s), 144.26 (d, *J* = 13.8 Hz), 141.14 (s), 135.60 (s), 129.72 (d, *J* = 8.2 Hz), 128.12 (s), 127.53 (s), 125.90 (d, *J* = 4.0 Hz), 120.55 (s), 115.48 (d, *J* = 21.4 Hz), 66.38 (s), 57.77 (s), 47.06 (s).

^{19}F NMR (376 MHz, DMSO-d_6): δ -115.01.

ethyl 2-benzamido-2-phenyl-acetate (6)



2a (20 mg, 0.085 mmol) was dissolved in a 1:1 solution of conc. HCl (0.7 mL) and EtOH (0.7 mL) and the reaction was heated to reflux overnight. Upon completion of the reaction, indicated by TLC, the reaction was allowed to cool and the pH was adjusted to pH = 9 by slow addition of 1M NaOH. The solution was then transferred to a separating funnel whereby the aqueous layer was extracted into DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated. The product was purified by FCC (1:3 EtOAc:Heptane) to afford the pure compound as a white solid (16 mg, 67%).

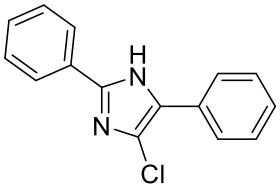
RF (1:3 EtOAc:Hept): 0.21

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.0 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.40 (m, 4H), 7.41 – 7.31 (m, 3H), 7.16 (d, *J* = 6.8 Hz, 1H), 5.77 (d, *J* = 7.0 Hz, 1H), 4.28 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.19 (dq, *J* = 10.8, 7.1 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 171.2, 166.7, 136.9, 133.8, 132.0, 129.1, 128.8, 128.7, 127.4, 127.3, 62.2, 57.0, 14.2.

*Data in accordance with literature[5]

5-Chloro-2,4-diphenyl-1*H*-imidazole (7)



In a round bottom flask, **2a** (80 mg, 0.339 mmol) was dissolved in MeCN (3.4mL) and triphenylphosphine (222mg, 0.848 mmol) and carbon tetrachloride (130 mg, 0.848 mmol) were added successively. Condenser was fitted and the reaction was heated at 45°C overnight. Upon completion, the reaction mixture is concentrated and resuspended in DCM (4 mL). 0.5 M NaOH (4mL) was added and the two-phase solution was stirred for 10 mins at room temperature. Organic layer was separated, washed with H_2O (x2) and brine and then

concentrated *in vacuo*. The product was purified by FCC (1:3 EtOAc:Hex) to afford pure compound as an orange solid (53 mg, 61%).

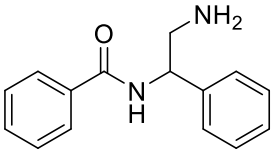
RF (1:3 EtOAc:Hex): 0.47

^{1}H NMR (400 MHz,): δ 12.93 (s, 1H), 8.03 (d, *J* = 7.9 Hz, 2H), 7.81 (d, *J* = 7.9 Hz, 2H), 7.56 – 7.47 (m, 4H), 7.45 – 7.36 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 144.97, 129.88, 129.31, 129.26, 129.19, 128.91, 128.11, 126.95, 126.27, 126.20, 125.71.

*Data in accordance with literature[6]

***N*-(2-amino-1-phenyl-ethyl)benzamide (8)**



In an oven dried round bottom flask, **2a** (100 mg, 0.423 mmol) was added and the flask was flushed with argon

. Anhydrous THF (2 mL) was added and the reaction was cooled to 0°C. $LiAlH_4$ (2.0 M in THF, 2.12 mL) was added dropwise and the reaction was warmed to room temperature for 1.5 hr. Upon completion, a stirred sat. solution of Rochelle's salt was cooled to in an ice bath and the reaction mixture was quenched by dropwise addition to the aqueous solution. A few drops of 1M NaOH was added to pH = 9 and quenched solution was extracted with DCM (x3). Organic fractions were combined, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The product was purified by FCC (1:9 MeOH:DCM) to afford the pure compound as a white solid (58 mg, 57%).

RF (1:9 MeOH:DCM): 0.24

IR ν_{max} (cm^{-1}): 3323, 2926, 1634. 1489, 1284, 853, 751

HRMS (ESI) m/z: [M+H]+ Calcd for C15H17N2O 241.1341; Found 241.1351

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.72 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 6.9 Hz, 2H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.37 (d, *J* = 7.0 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.1 Hz, 1H), 4.96 (dd, *J* = 13.6, 8.2 Hz, 1H), 3.22 (s, 2H), 2.89 (ddd, *J* = 18.4, 13.1, 7.1 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6): δ 166.4, 142.4, 134.7, 131.1, 128.2, 127.4, 126.7, 126.6, 56.7, 47.1.

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3. M. J. Thompson, H. Adams and B. Chen, *J. Org. Chem.*, 2009, **74**, 3856-3865.
4. J. Xia, J. Xu, Y. Fan, T. Song, L. Wang and J. Zheng, *Inorg. Chem.*, 2014, **53**, 10024-10026.
5. Q.-H. Deng, H.-W. Xu, A. W.-H. Yuen, Z.-J. Xu and C.-M. Che, *Org. Lett.*, 2008, **10**, 1529-1532.
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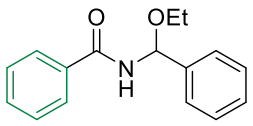
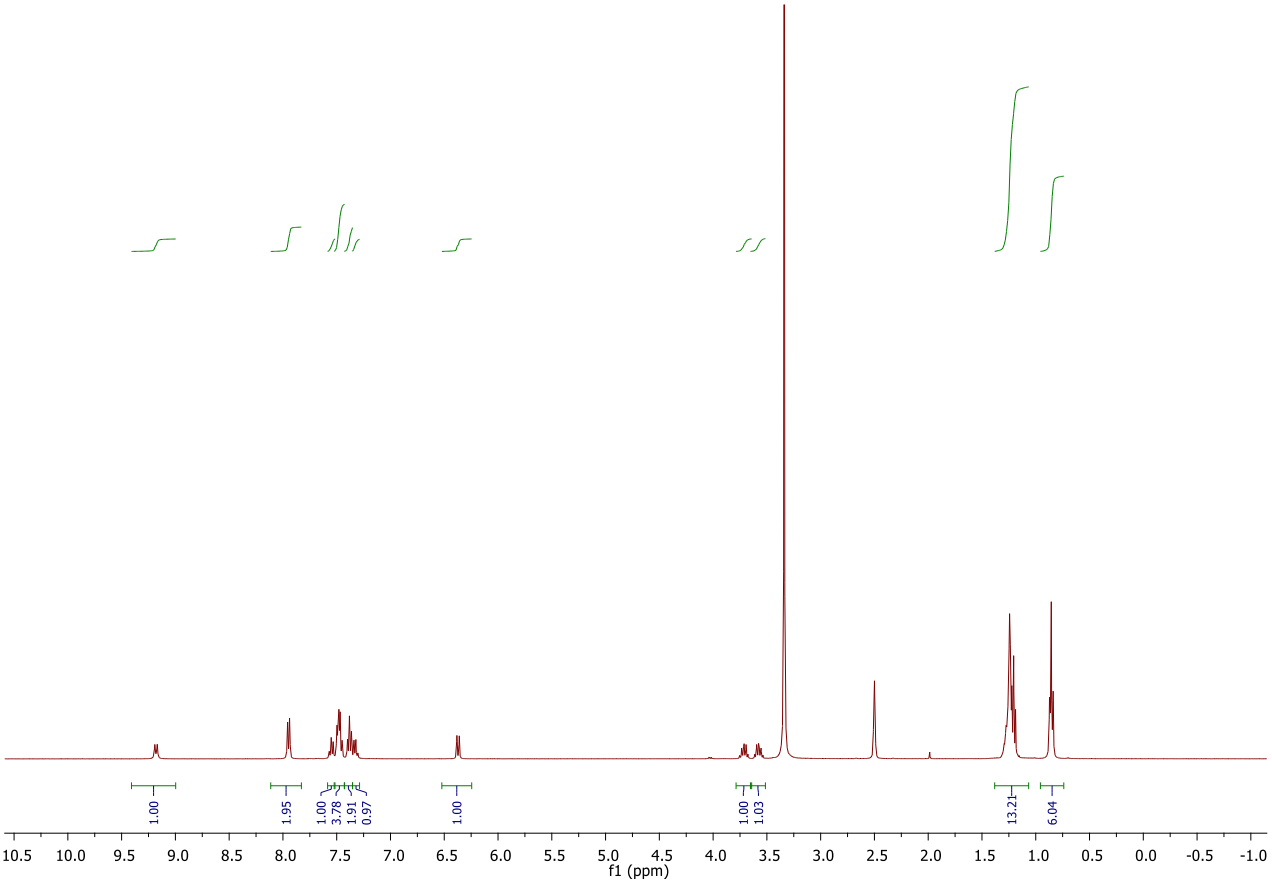
Copies of NMR Spectra

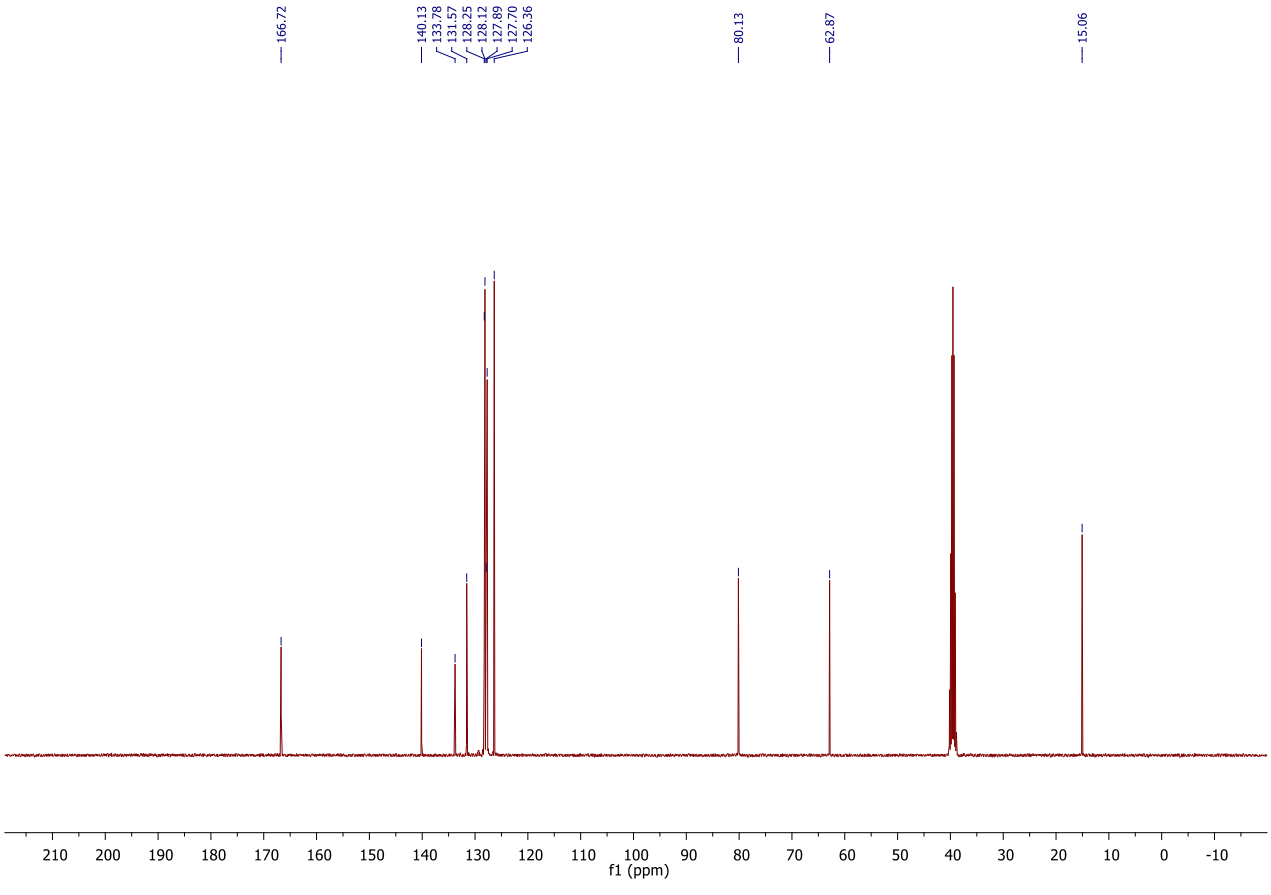
_N_-[ethoxy(phenyl)methyl]benzamide (1a)



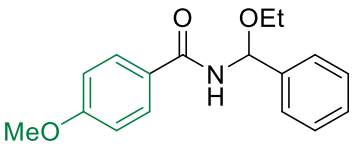
^{1}H NMR (400 MHz, DMSO-d_6)



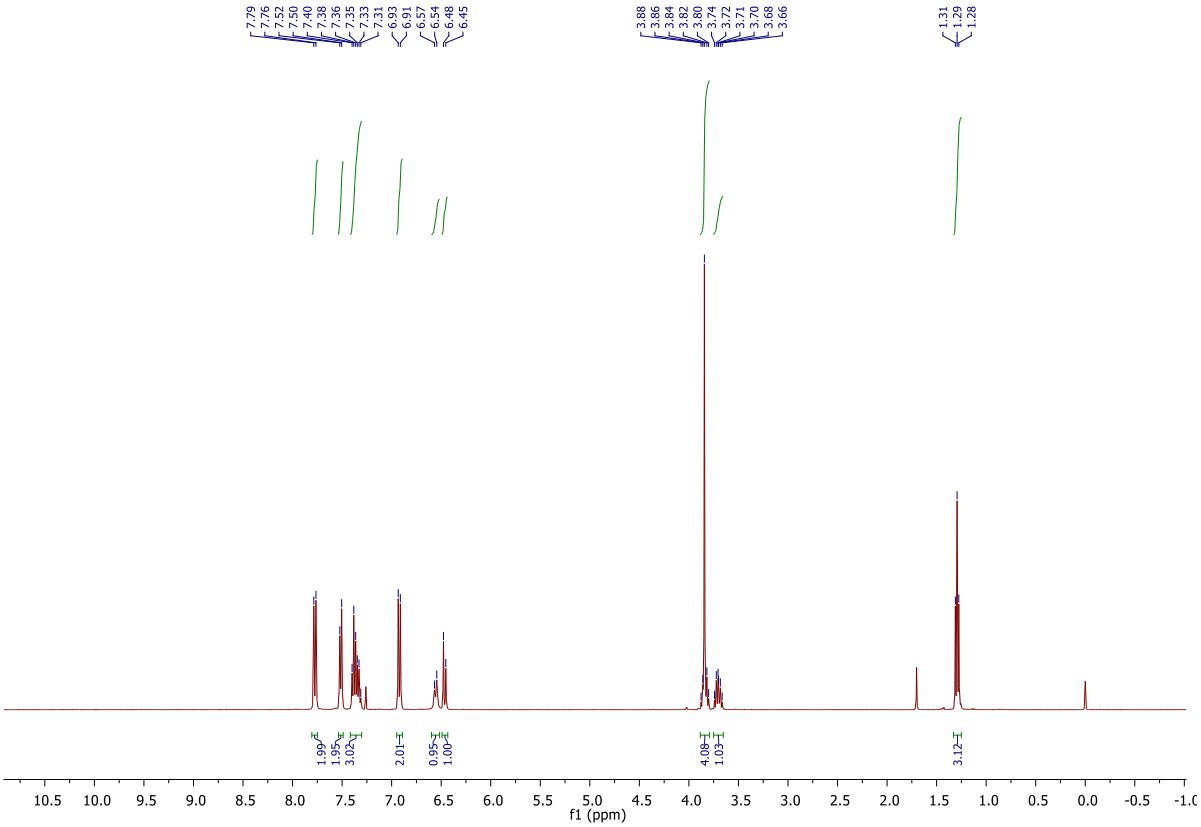
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)



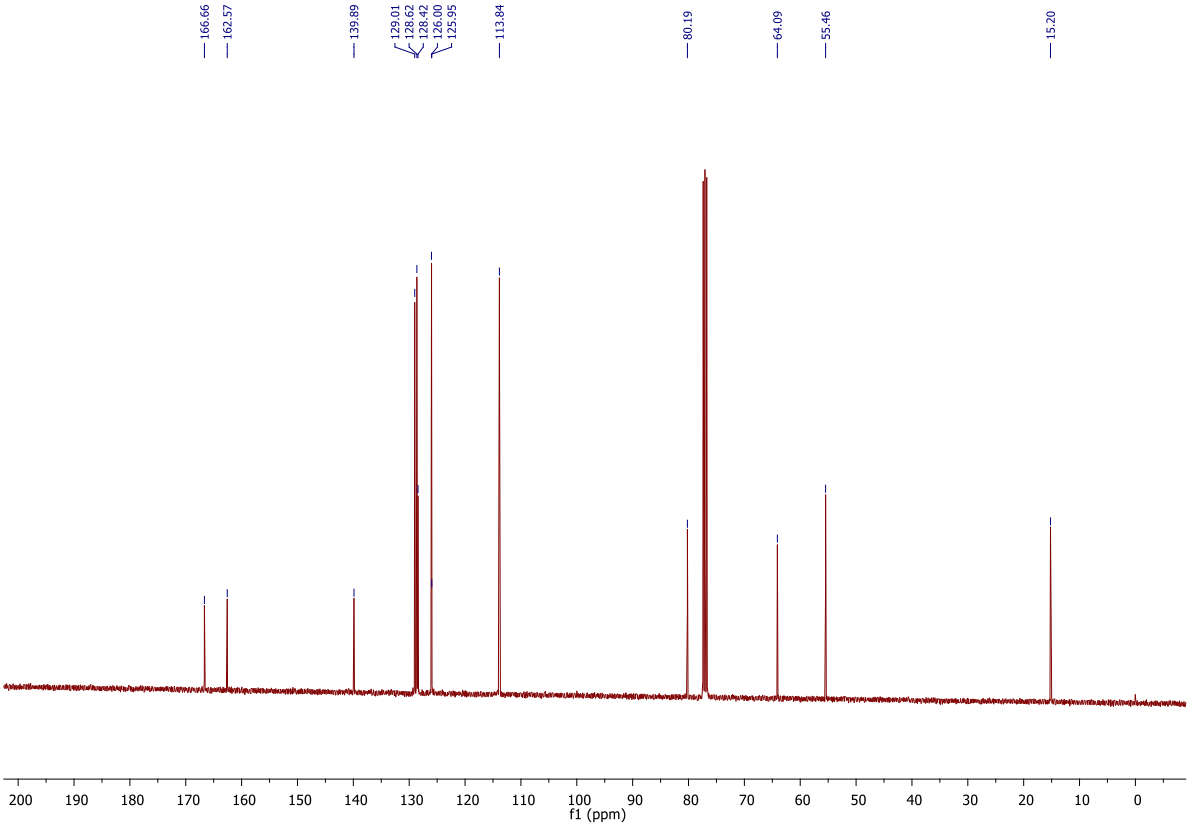
N-(ethoxy(phenyl)methyl)-4-methoxybenzamide (1b)



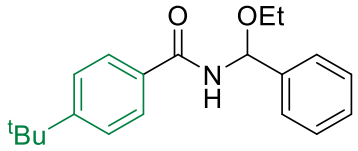
^{1}H NMR (400 MHz, $CDCl_3$)



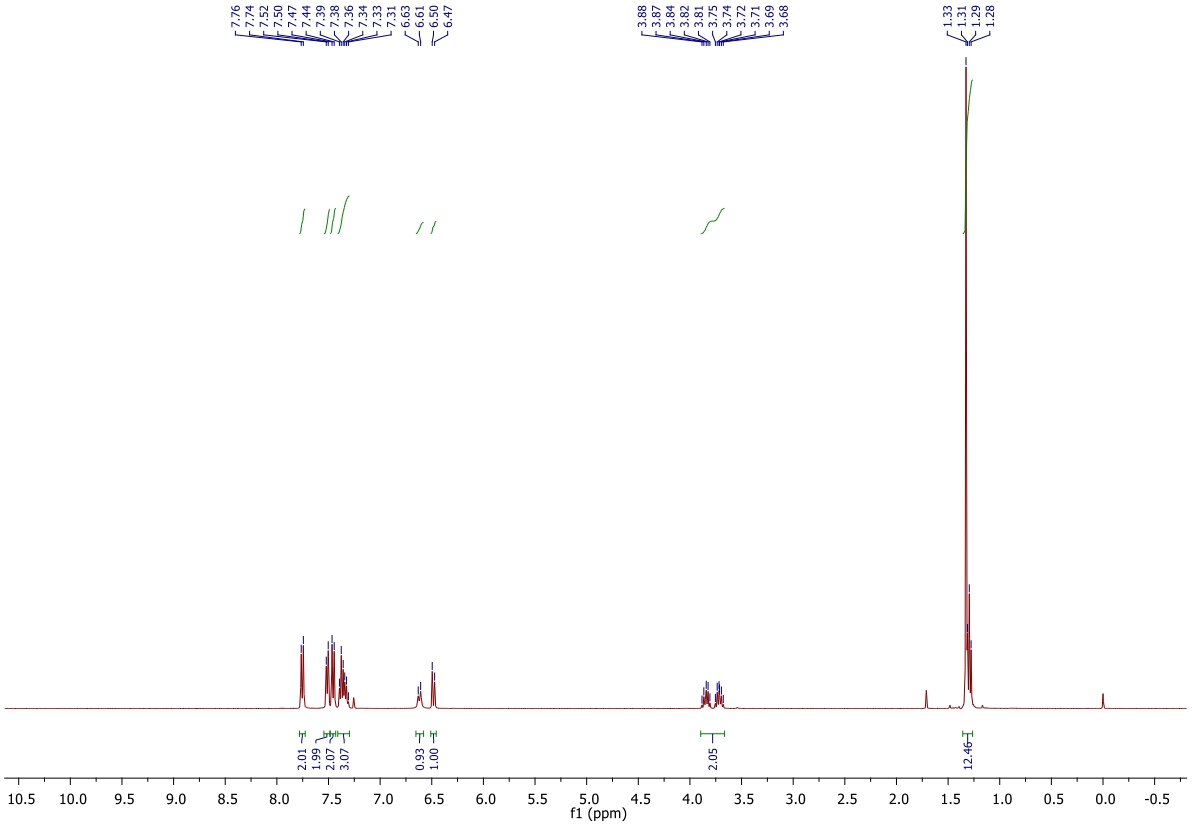
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



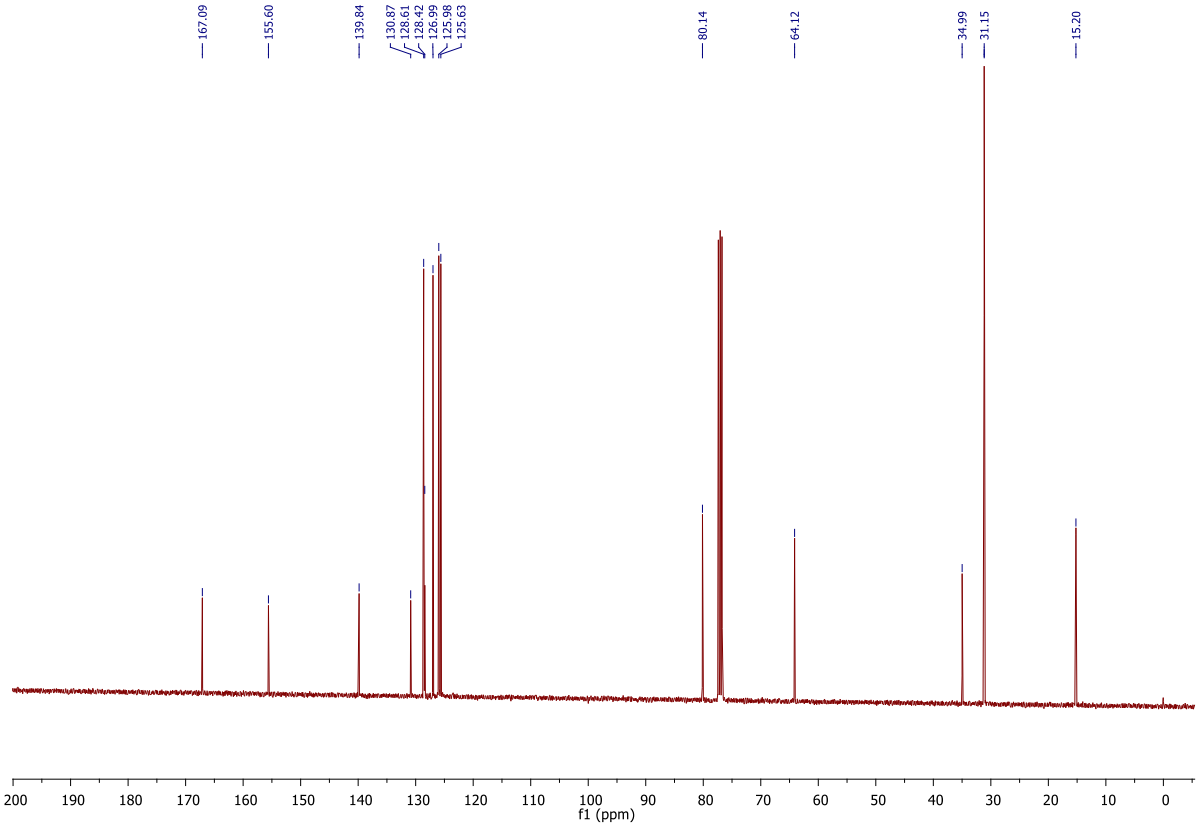
4-(*tert*-butyl)-*N*-(ethoxy(phenyl)methyl)benzamide (1c)



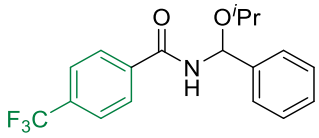
^{1}H NMR (400 MHz, $CDCl_3$)



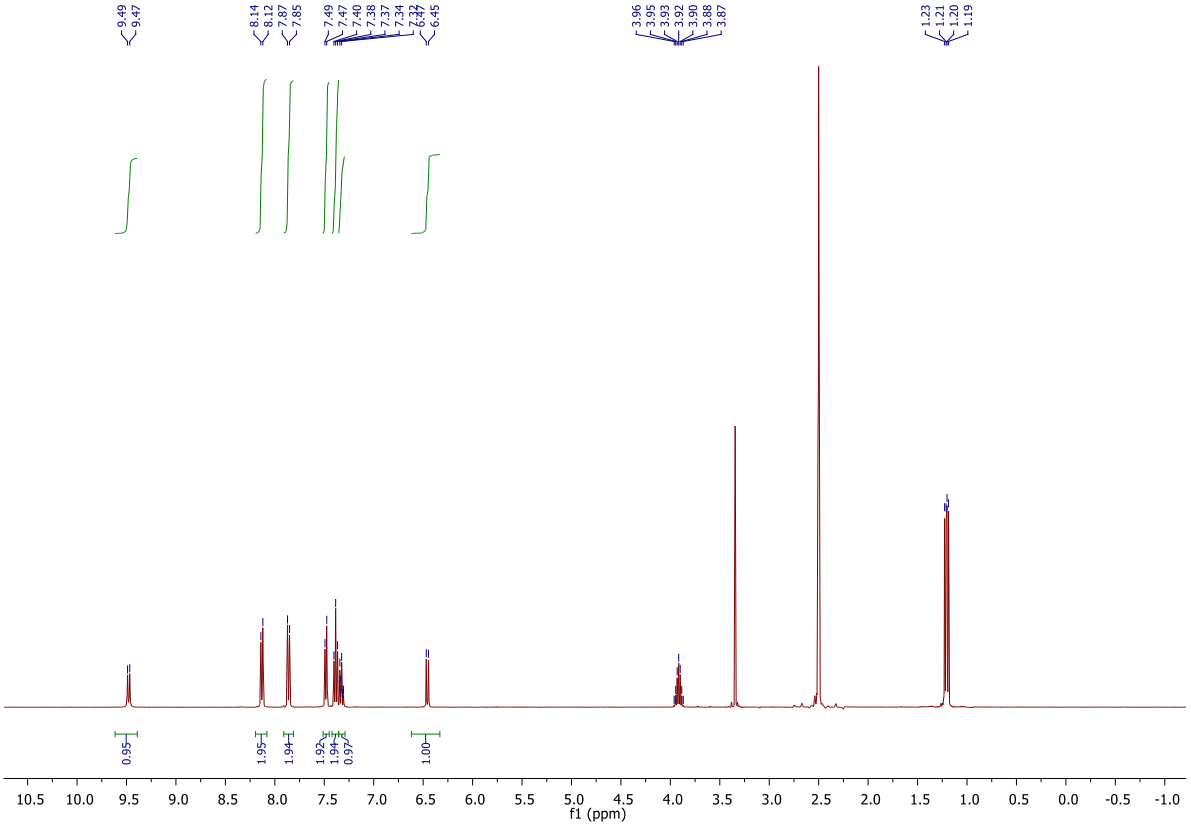
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



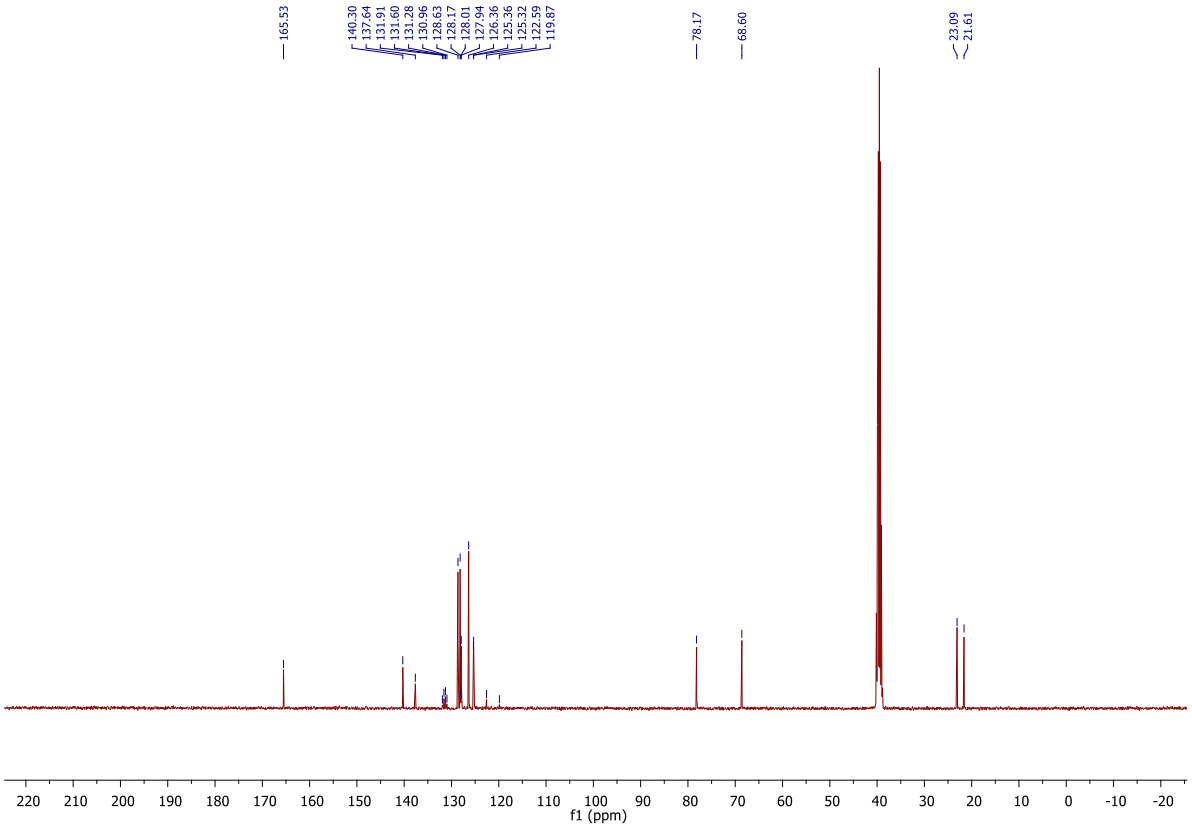
N-{phenyl[(propan-2-yl)oxy]methyl}-4-(trifluoromethyl)benzamide (1d)



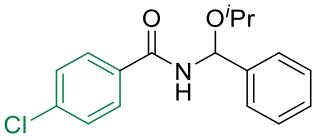
^{1}H NMR (400 MHz, DMSO-d$_6$)



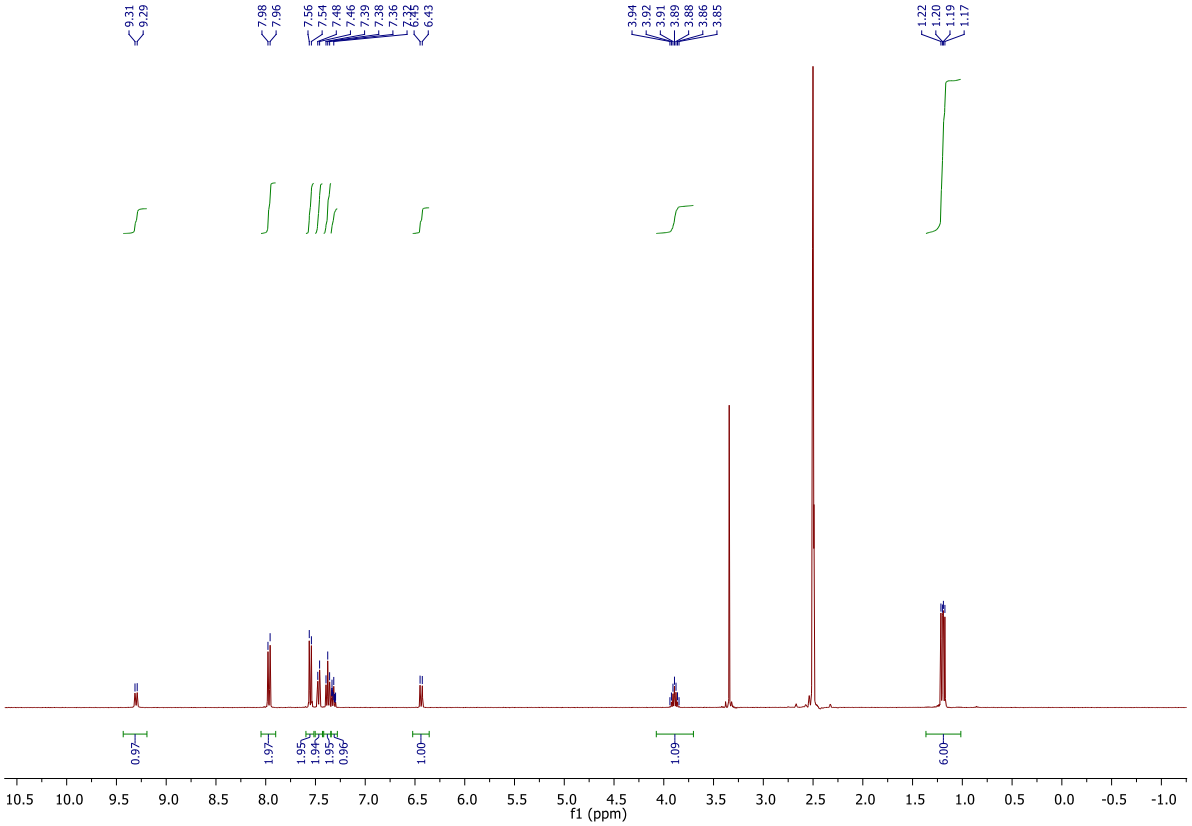
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$)



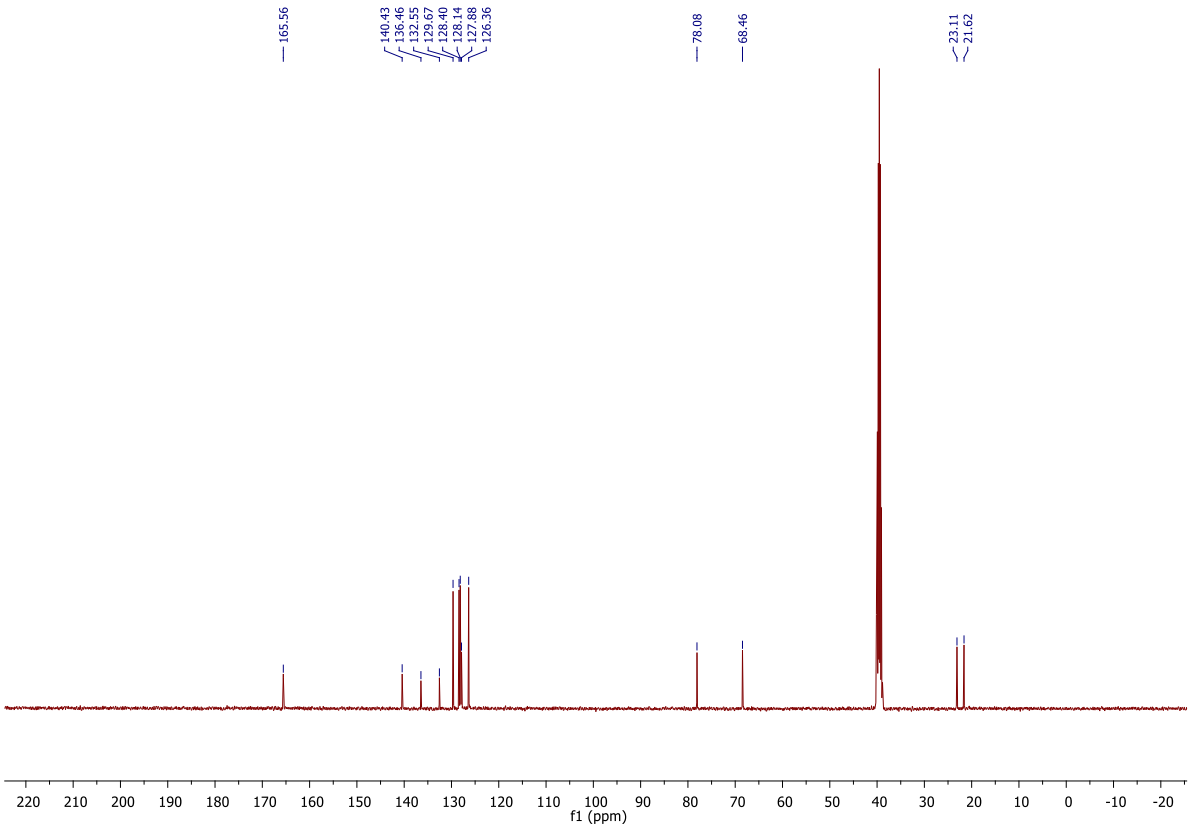
4-chloro-*N*-{phenyl[(propan-2-yl)oxy]methyl}benzamide (1e)



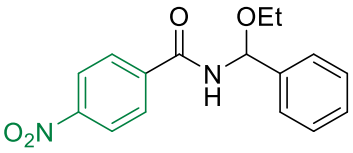
^{1}H NMR (400 MHz, DMSO-d$_6$)



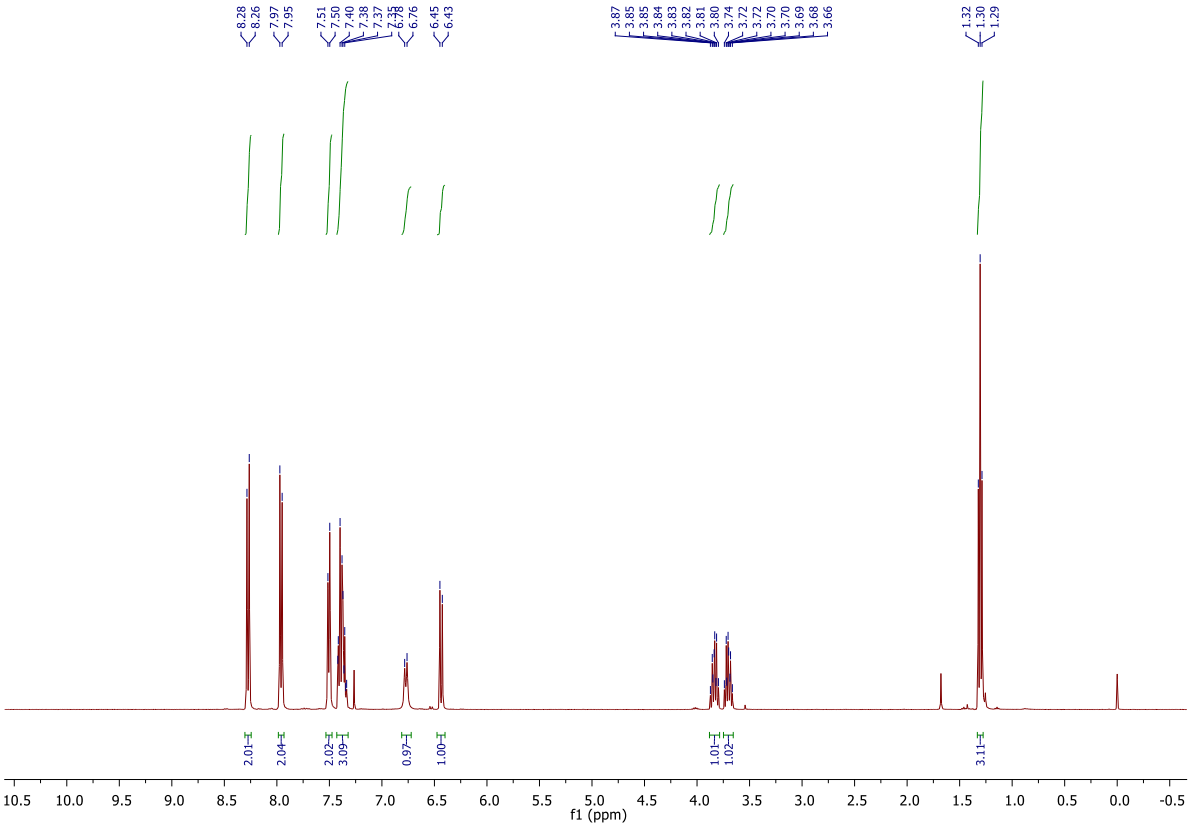
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$)



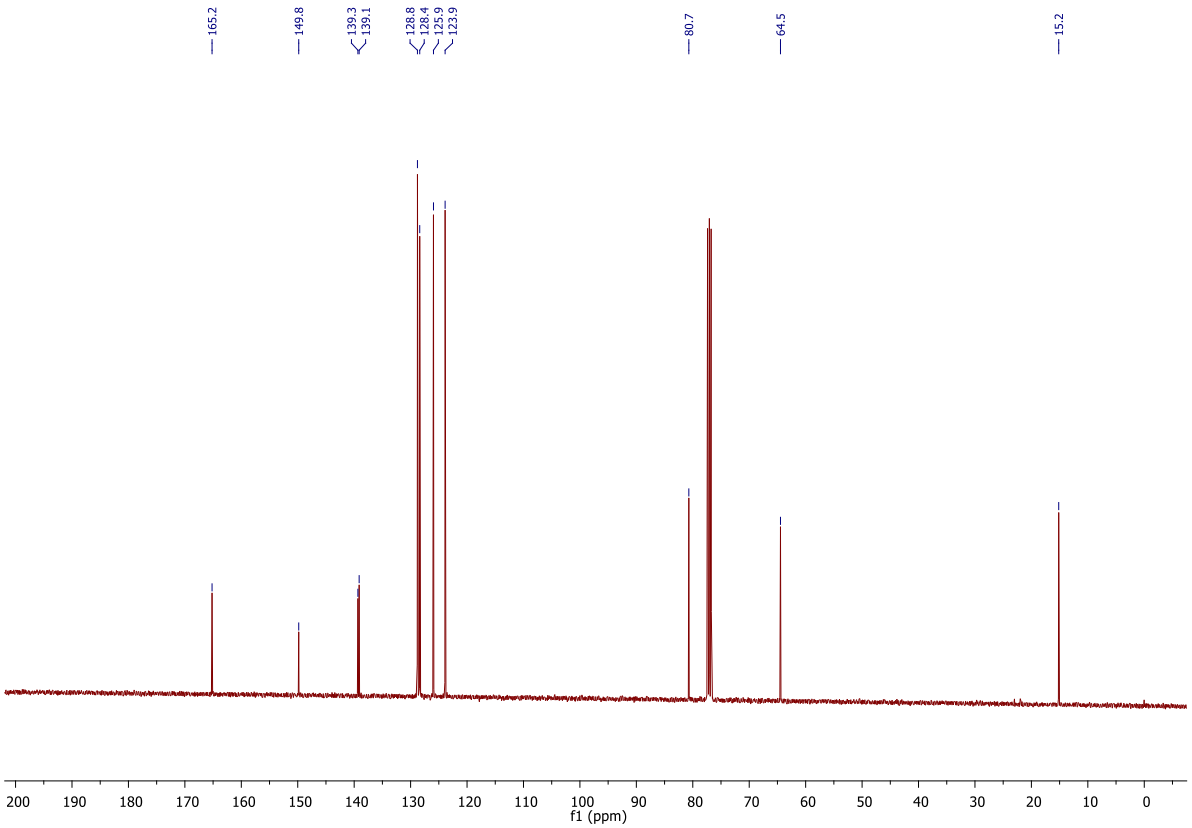
N-(ethoxy(phenyl)methyl)-4-nitrobenzamide (1f)



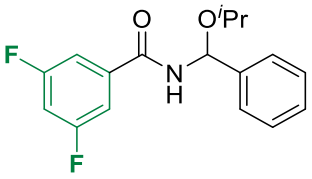
^{1}H NMR (400 MHz, $CDCl_3$)



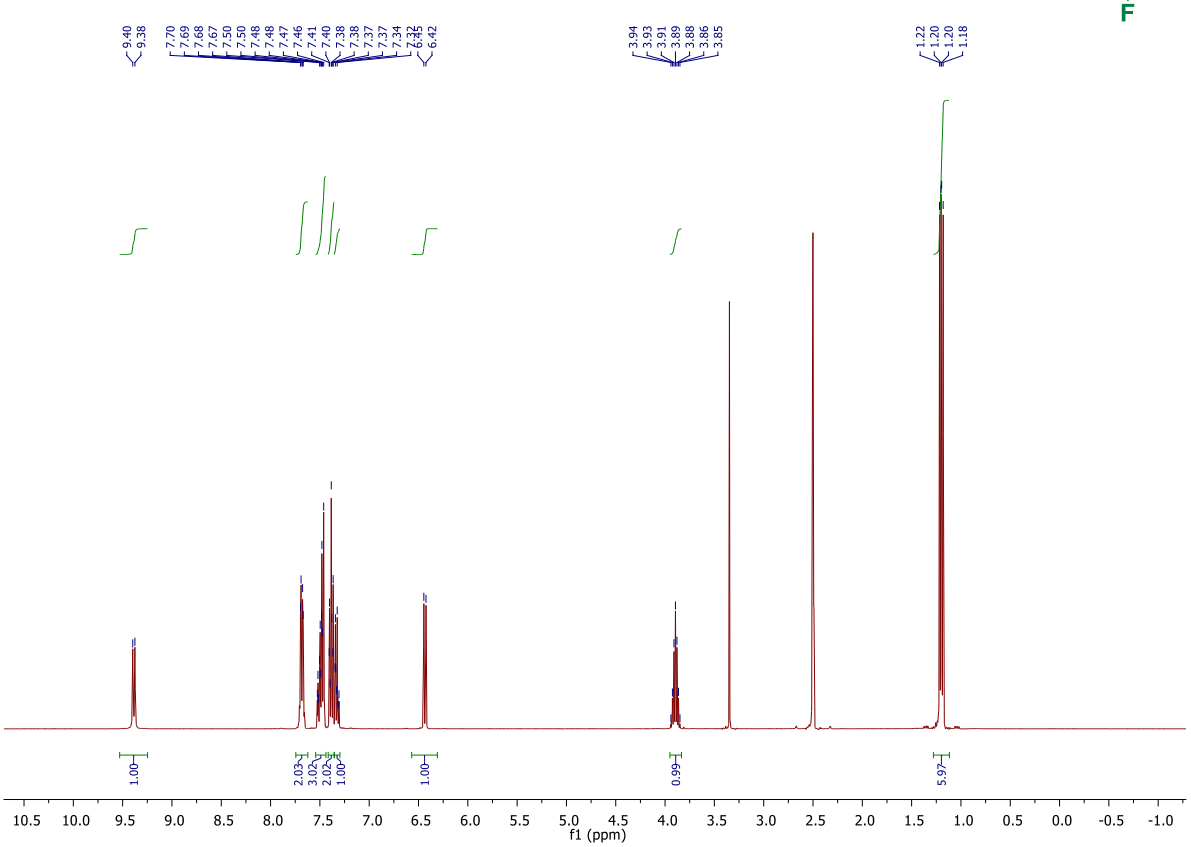
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



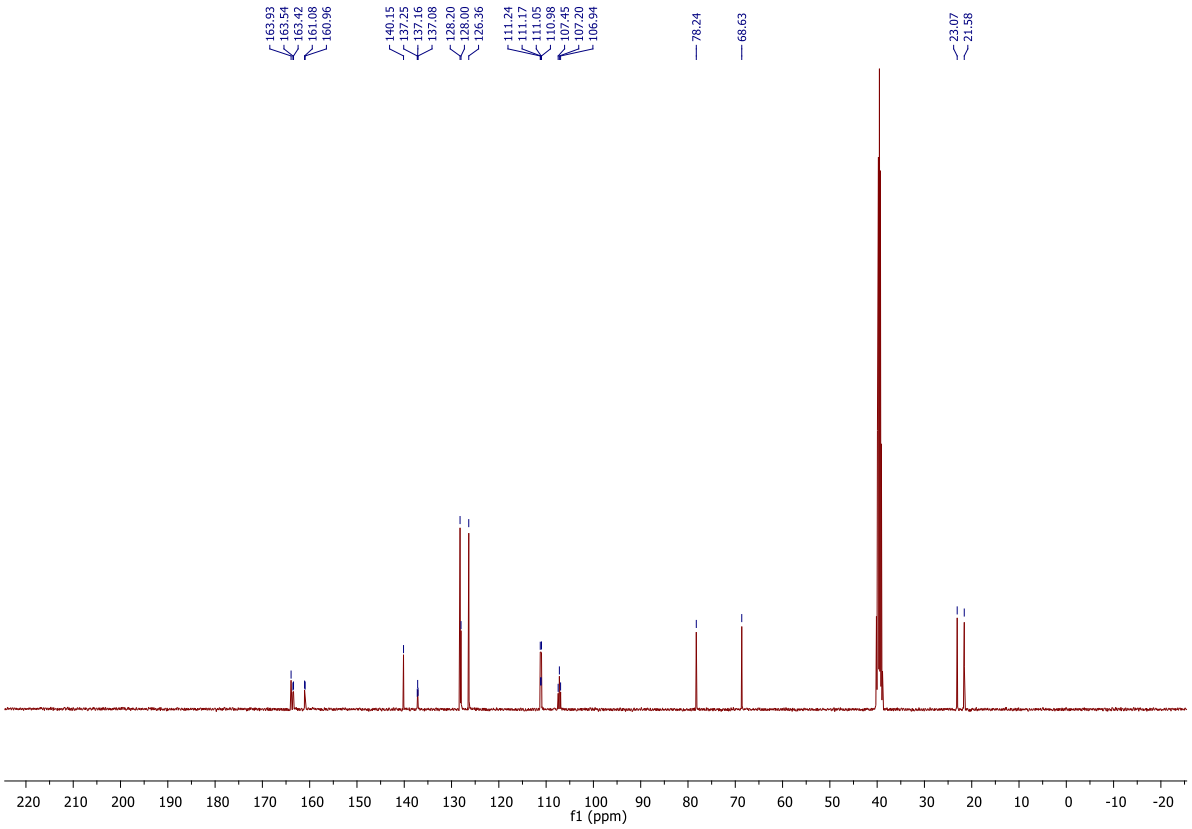
3,5-difluoro-*N*-{phenyl[(propan-2-yl)oxy]methyl}benzamide (1g)



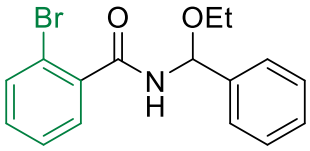
^{1}H NMR (400 MHz, DMSO-d$_6$)



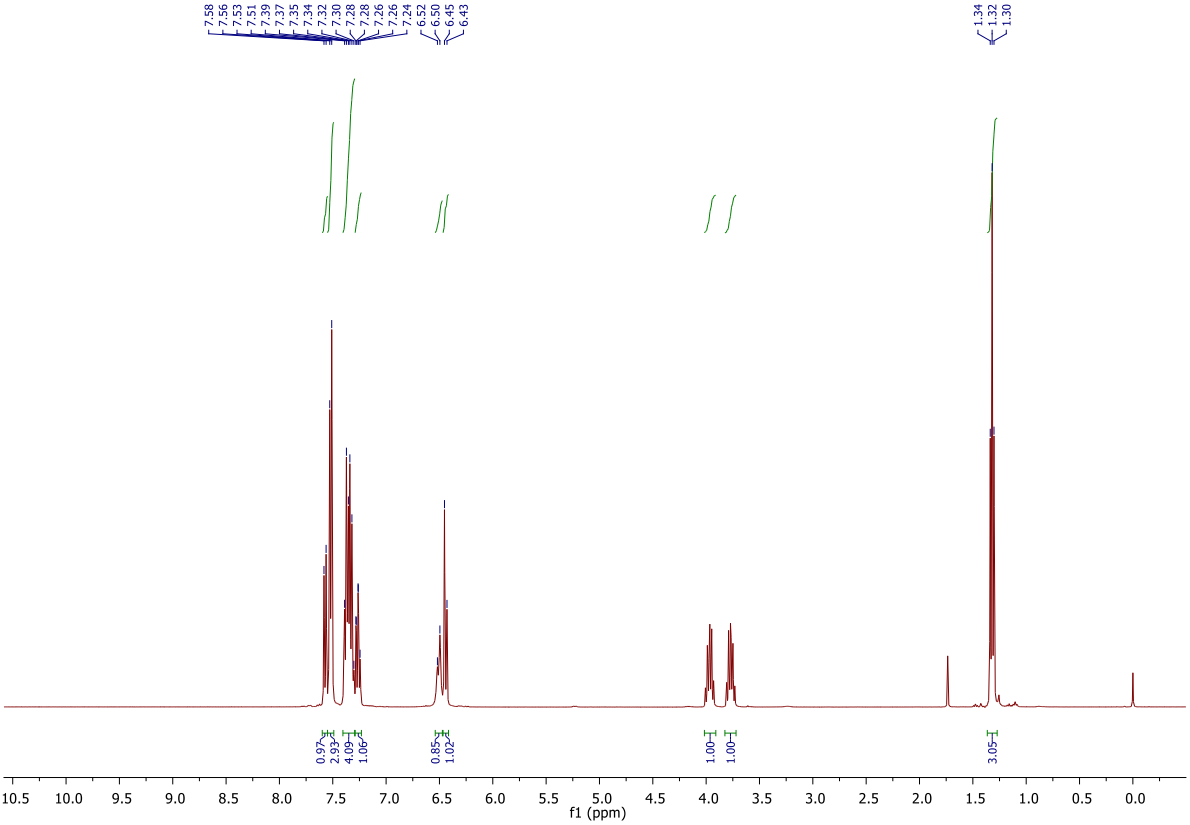
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$)



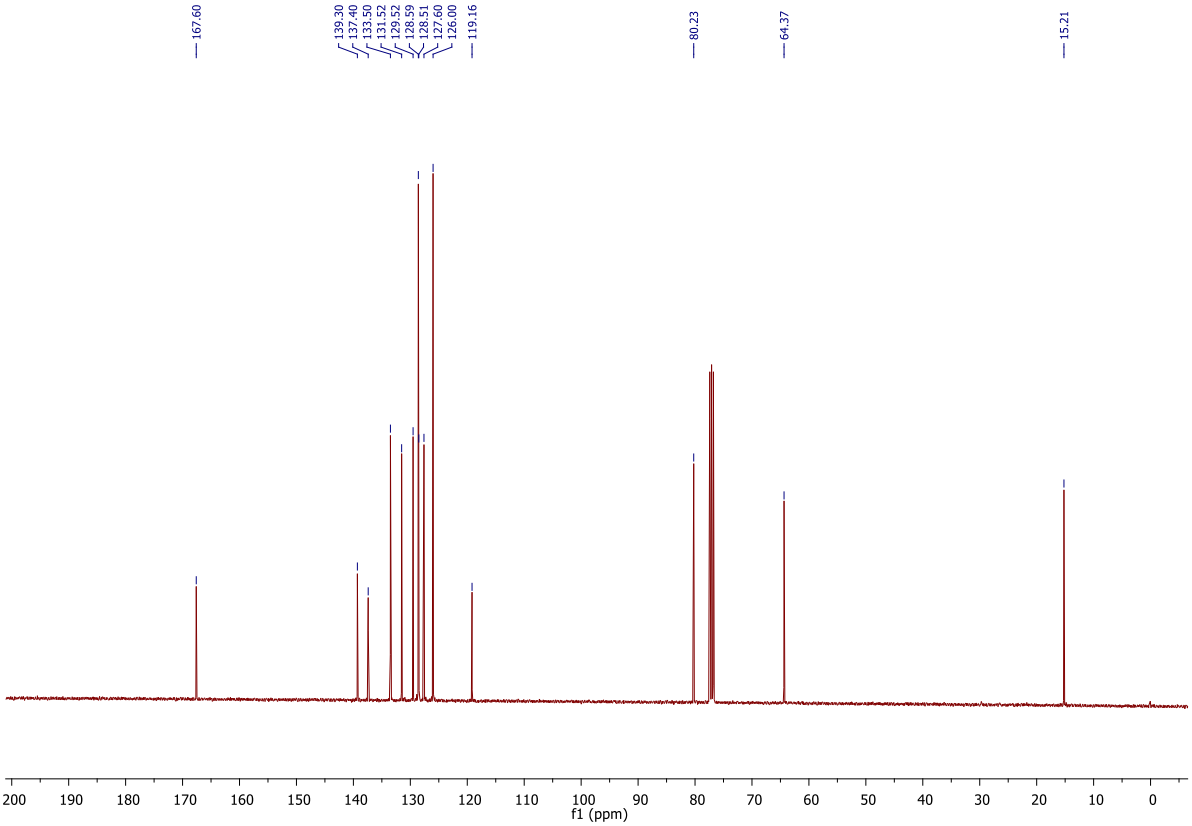
2-bromo-*N*-(ethoxy(phenyl)methyl)benzamide (1h)



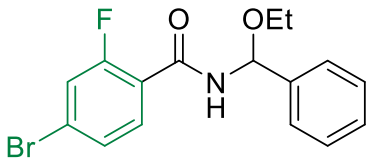
^{1}H NMR (400 MHz, $CDCl_3$)



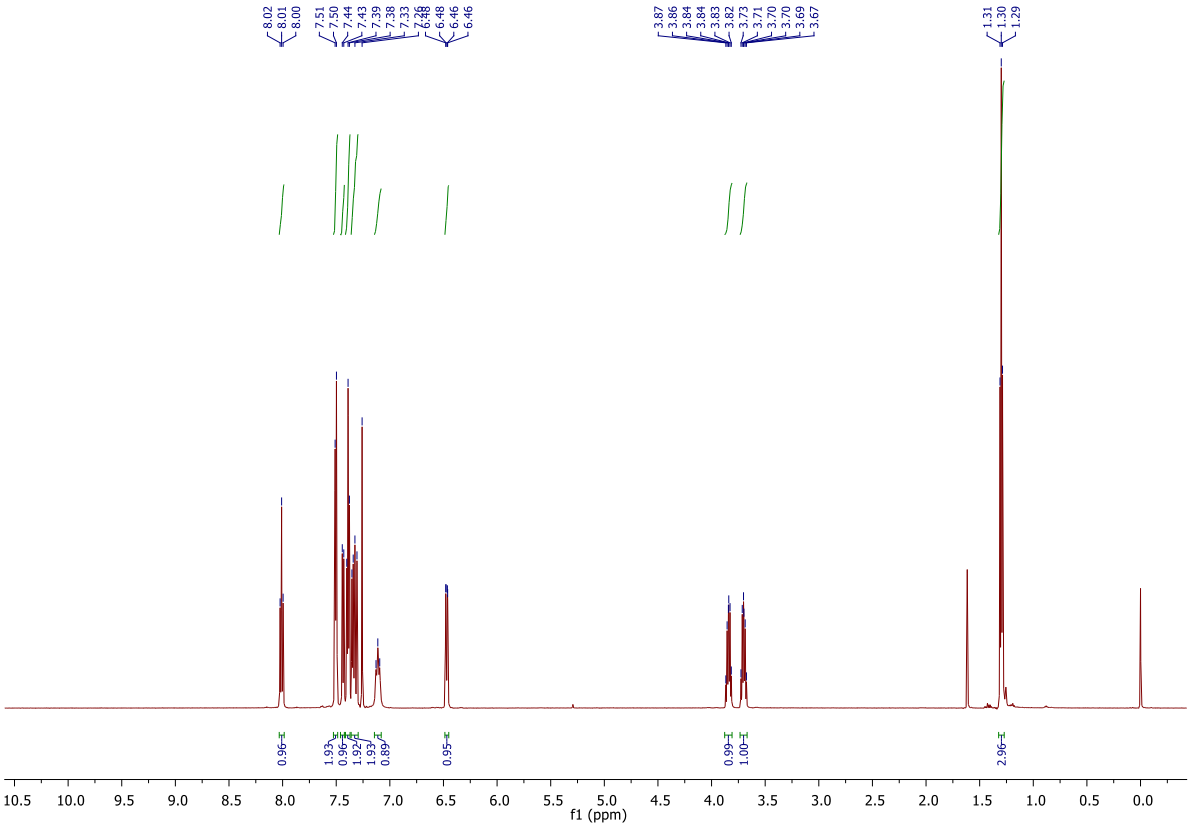
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



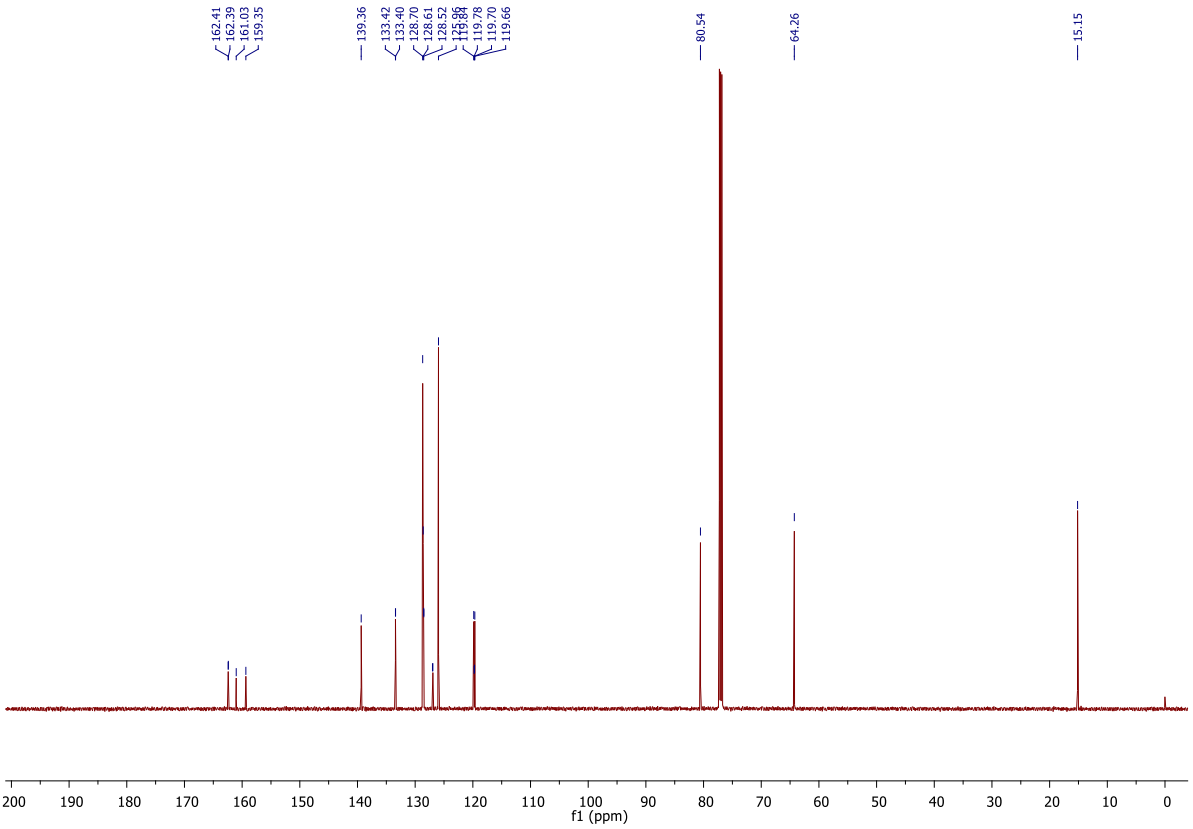
4-bromo-*N*-(ethoxy(phenyl)methyl)-2-fluorobenzamide (1i)



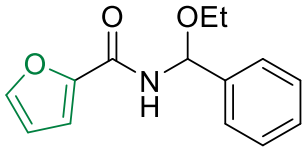
^{1}H NMR (600 MHz, $CDCl_3$)



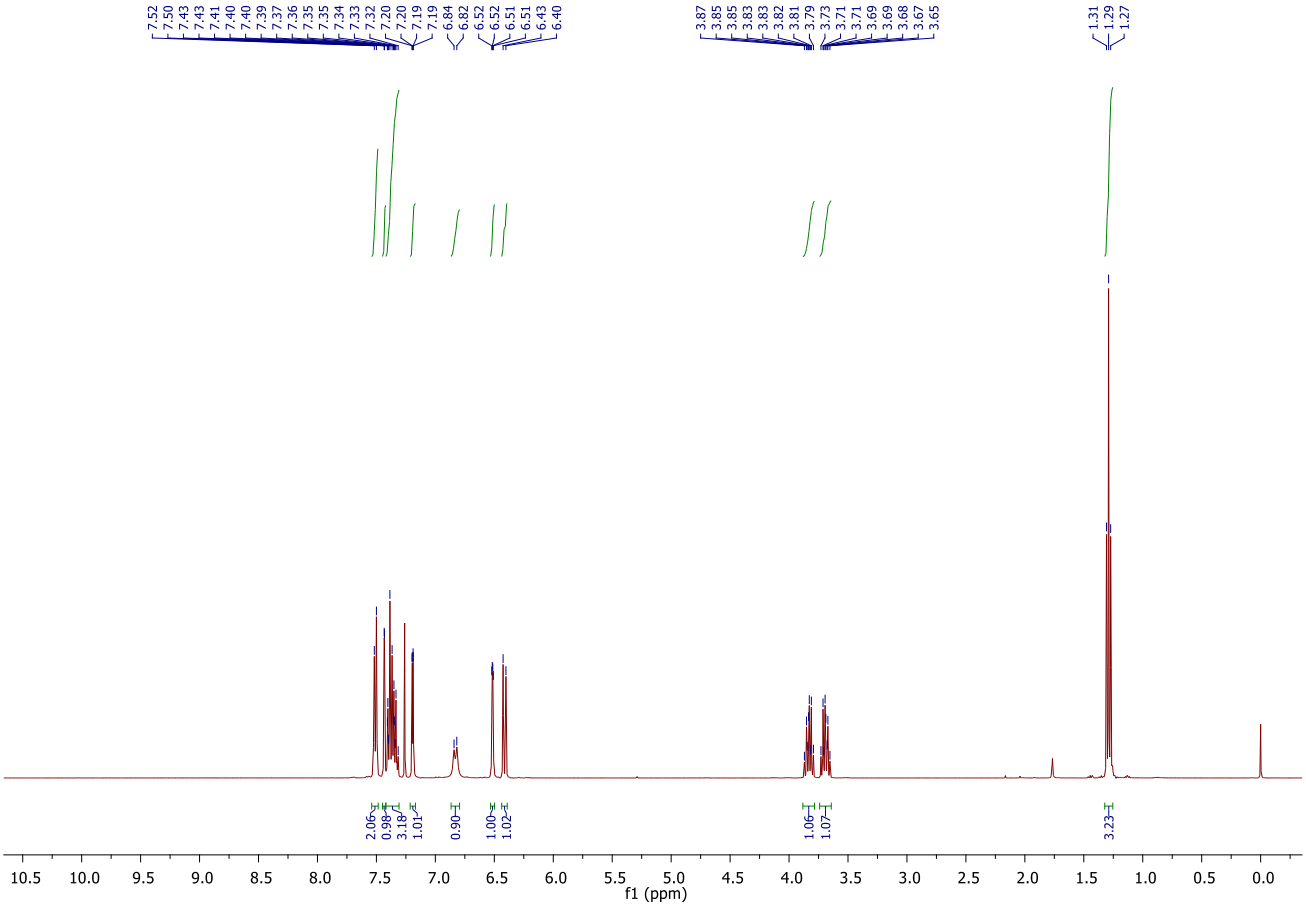
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)



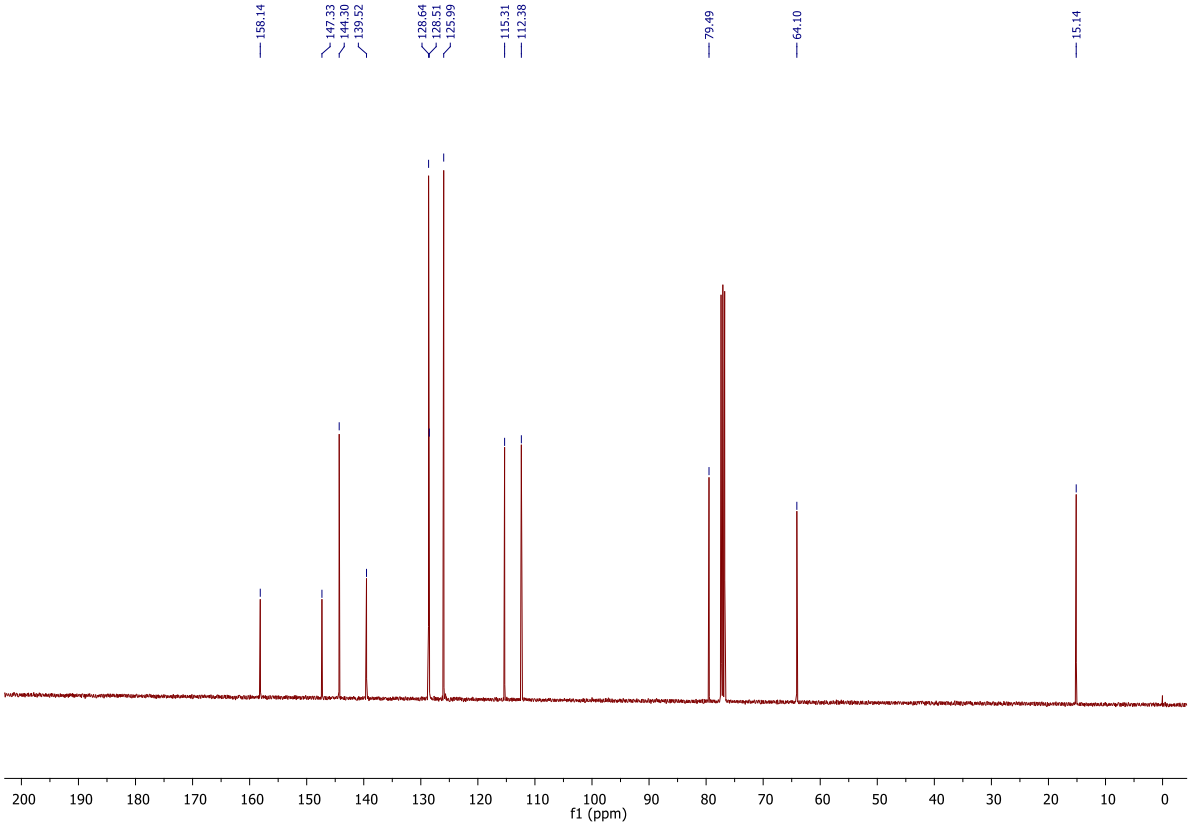
N-(ethoxy(phenyl)methyl)furan-2-carboxamide (1j)



^{1}H NMR (400 MHz, $CDCl_3$)

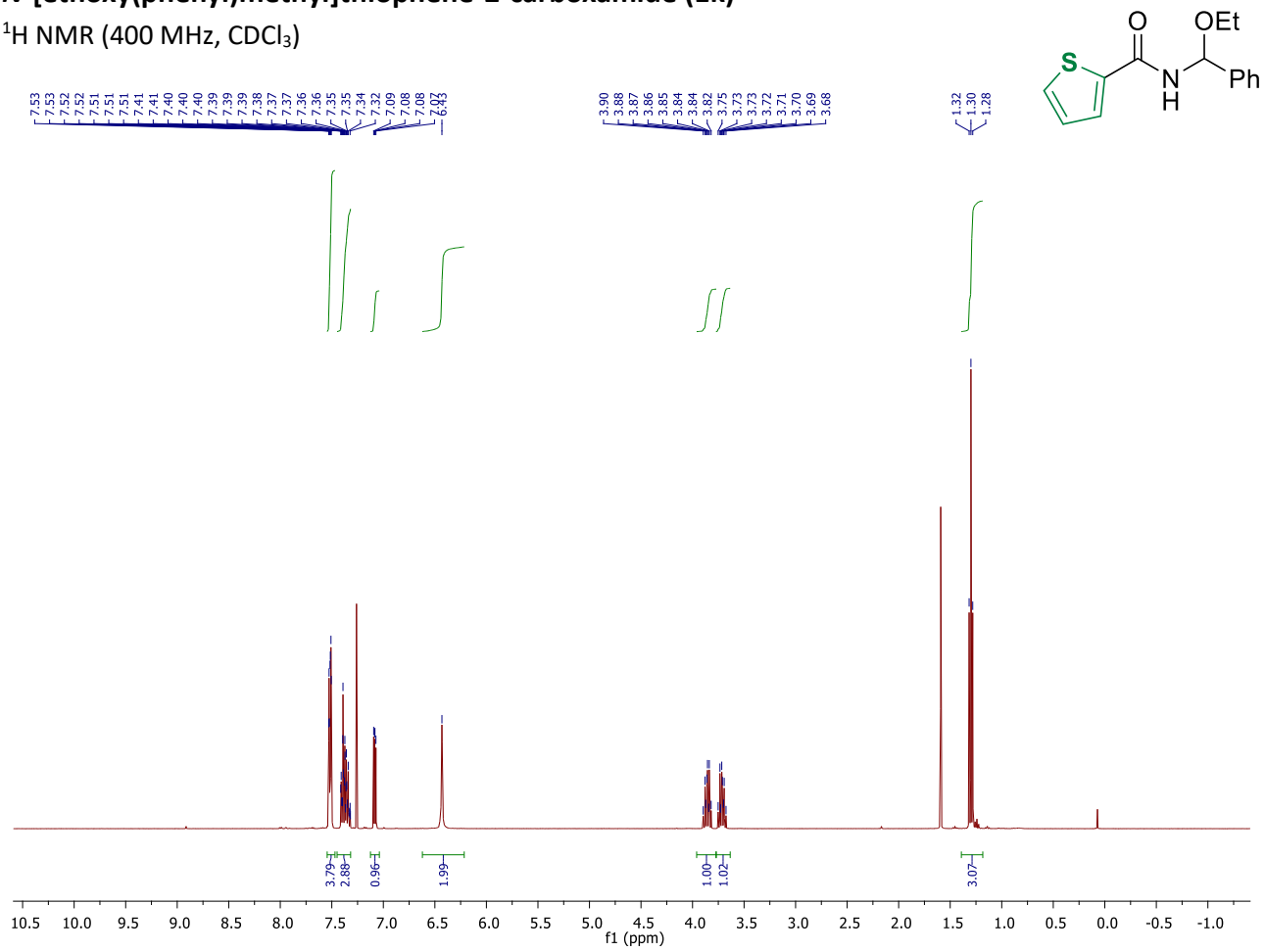


^{13}C{1H} NMR (101 MHz, $CDCl_3$)

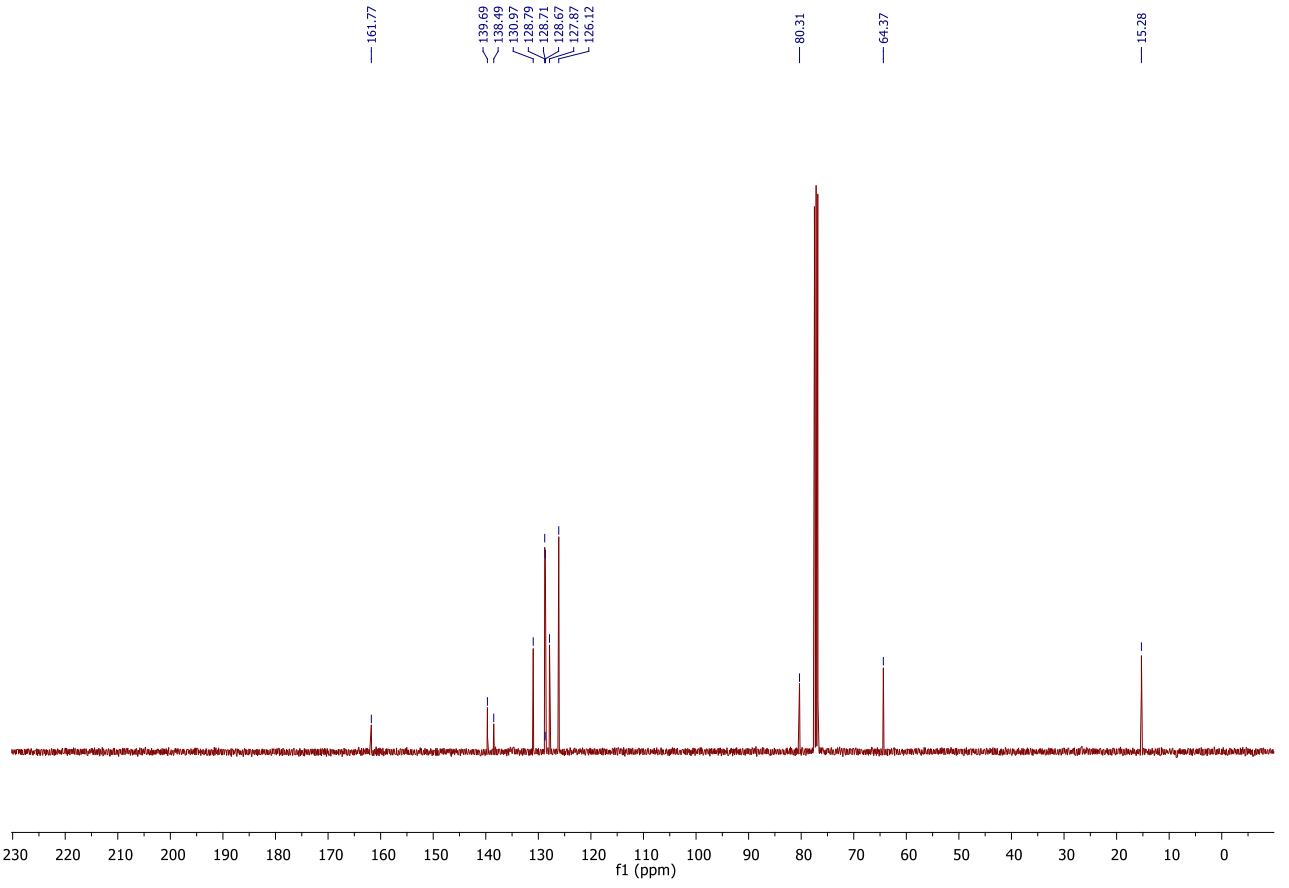


N-[ethoxy(phenyl)methyl]thiophene-2-carboxamide (1k)

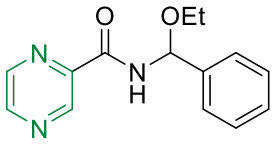
^{1}H NMR (400 MHz, $CDCl_3$)



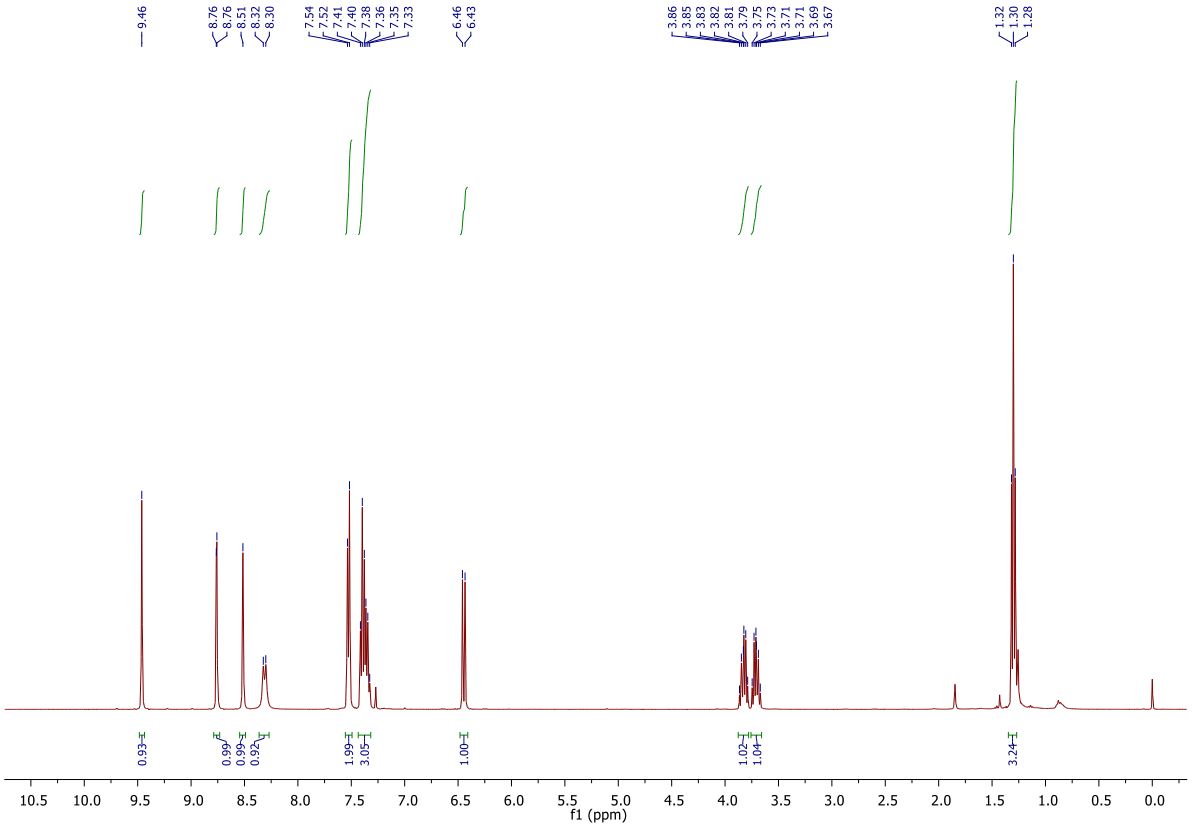
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



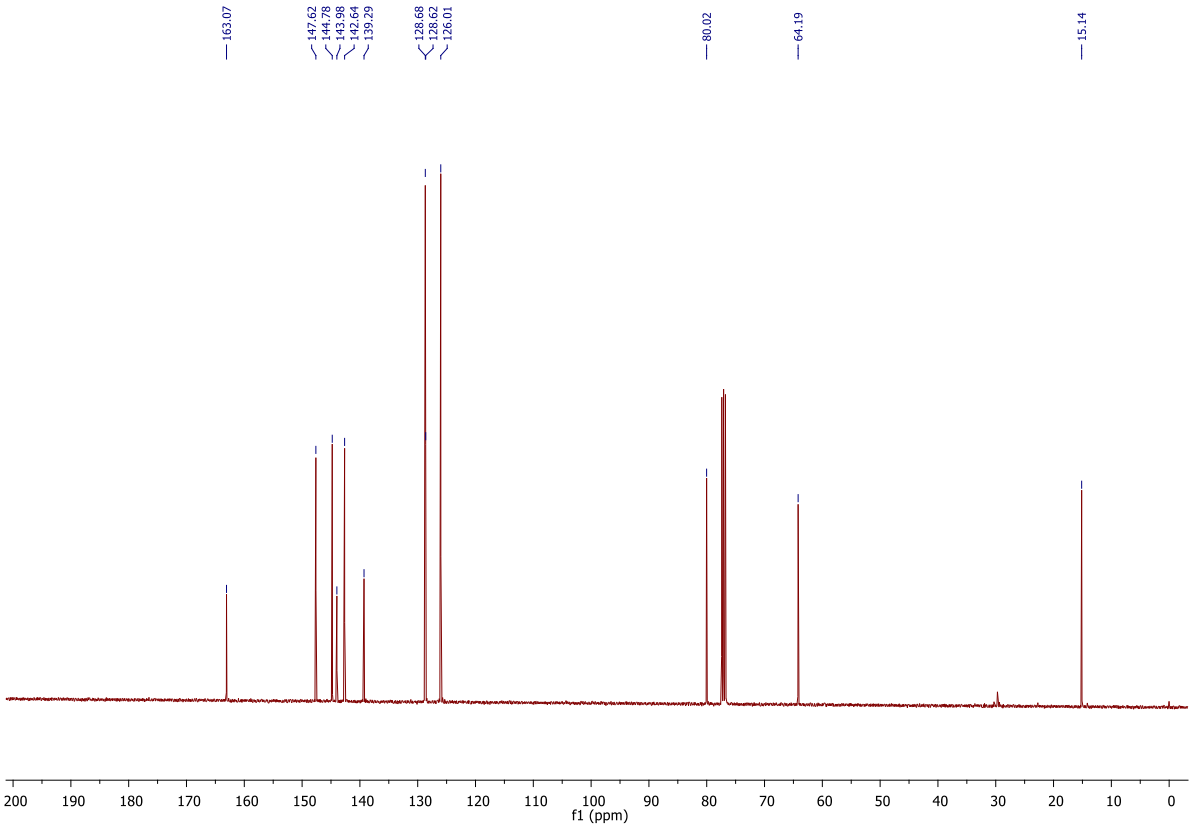
N-(ethoxy(phenyl)methyl)pyrazine-2-carboxamide (1l)



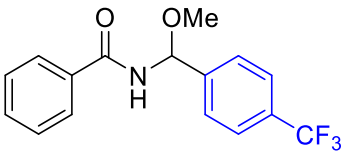
^{1}H NMR (400 MHz, $CDCl_3$)



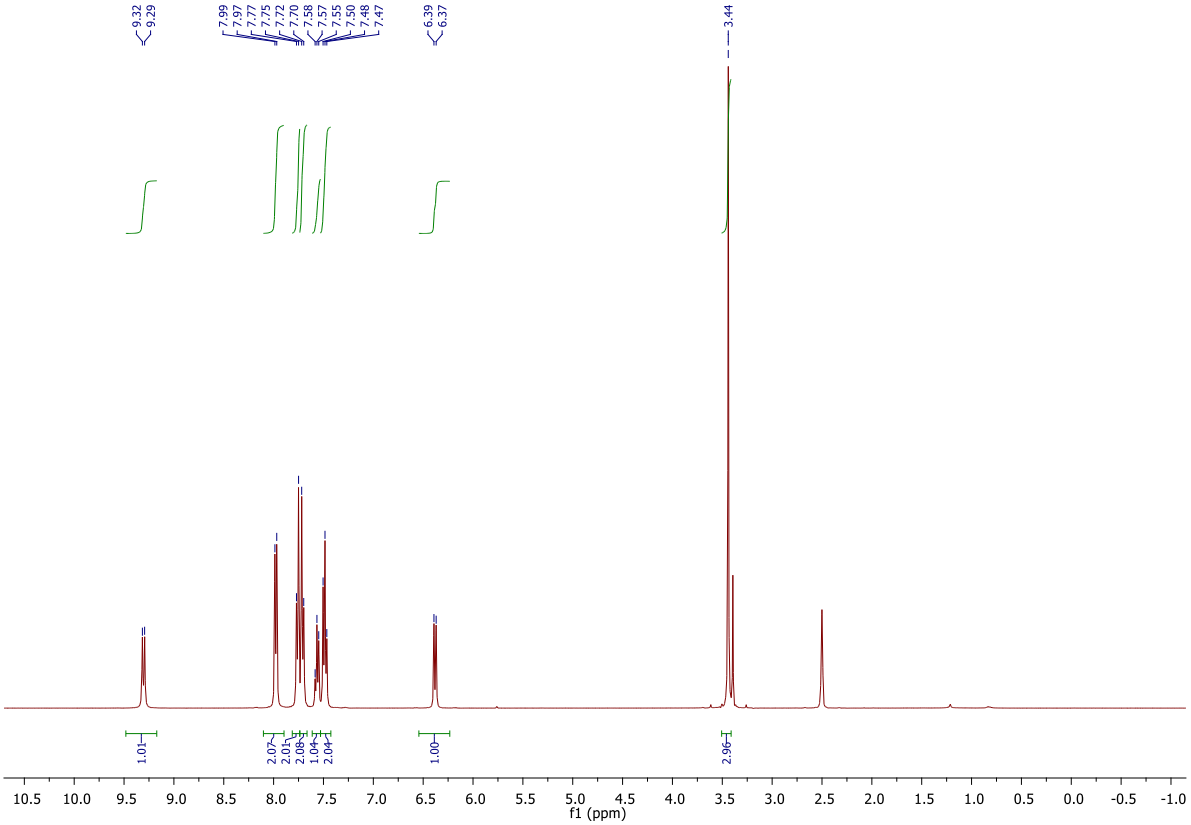
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



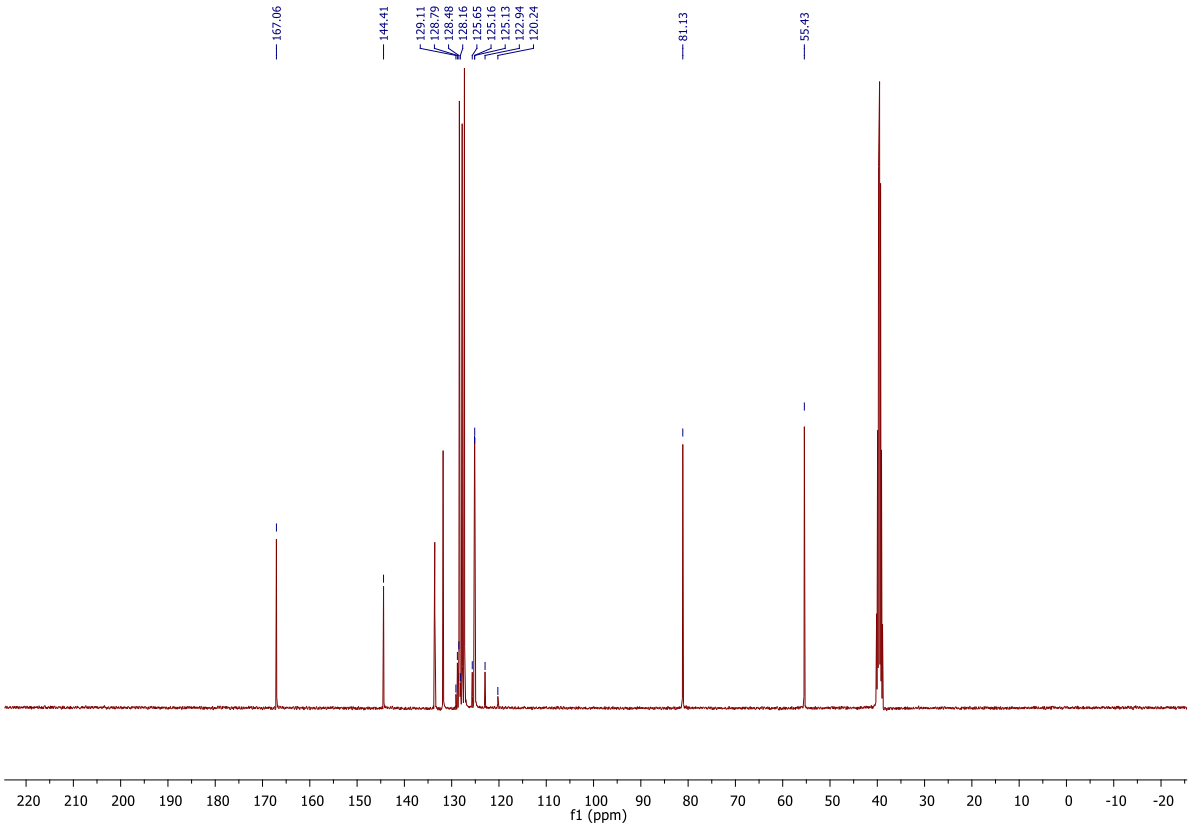
N-{methoxy[4-(trifluoromethyl)phenyl]methyl}benzamide (1m)



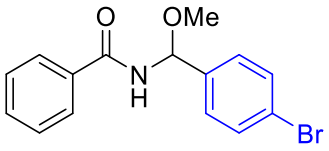
^{1}H NMR (400 MHz, DMSO-d$_6$)



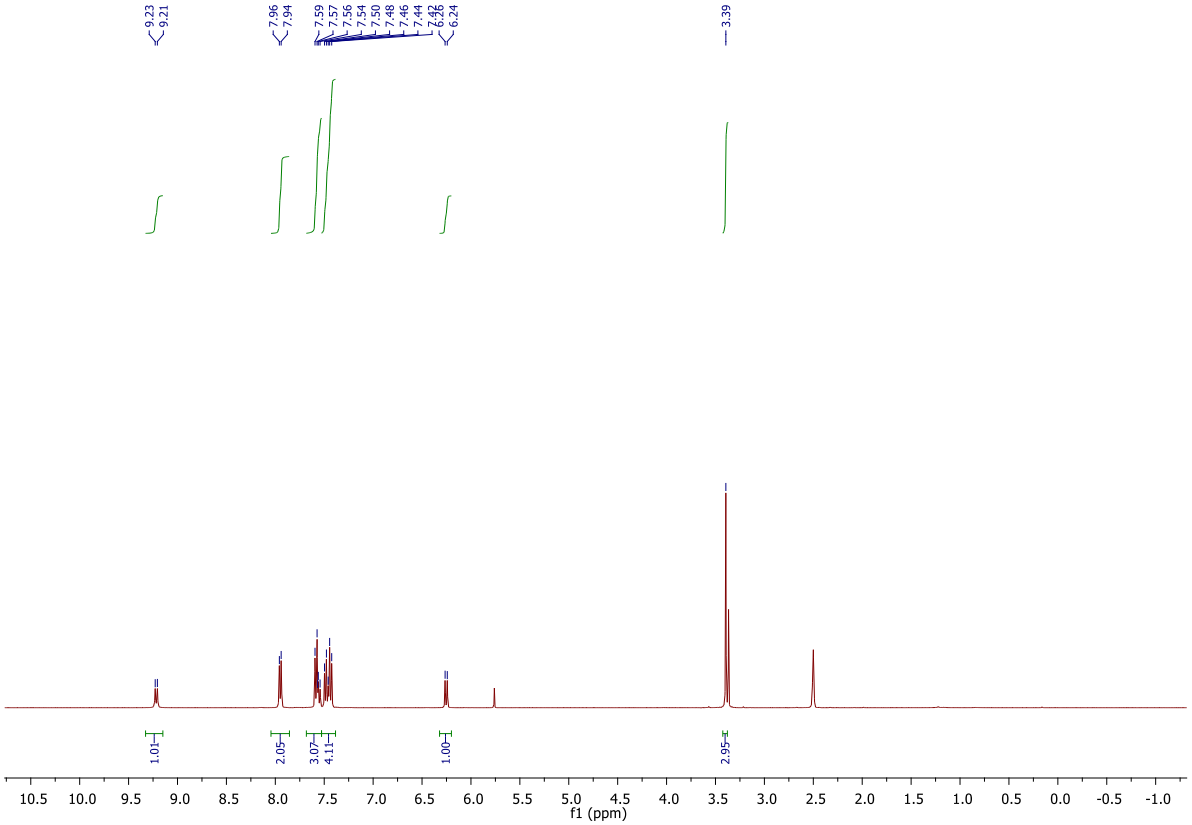
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$)



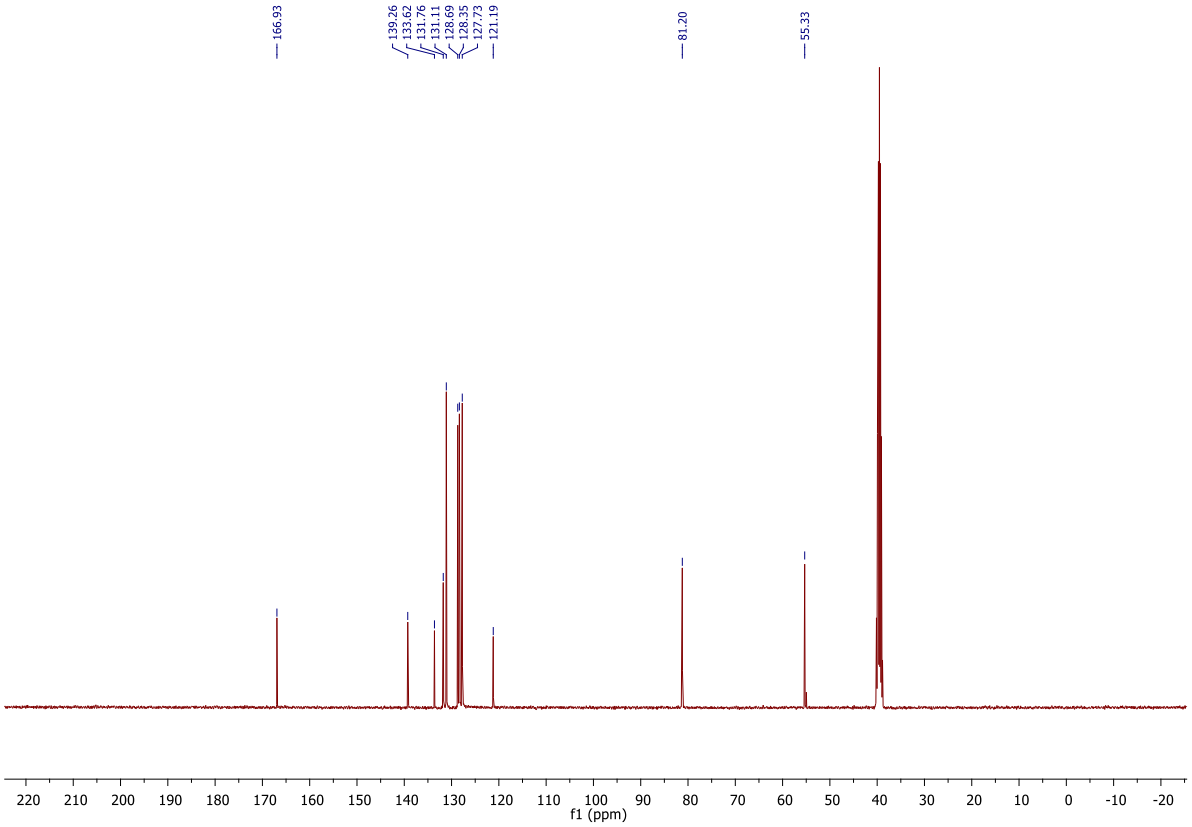
N-[(4-bromophenyl)(methoxy)methyl]benzamide (1n)



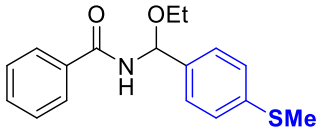
^{1}H NMR (400 MHz, DMSO-d$_6$)



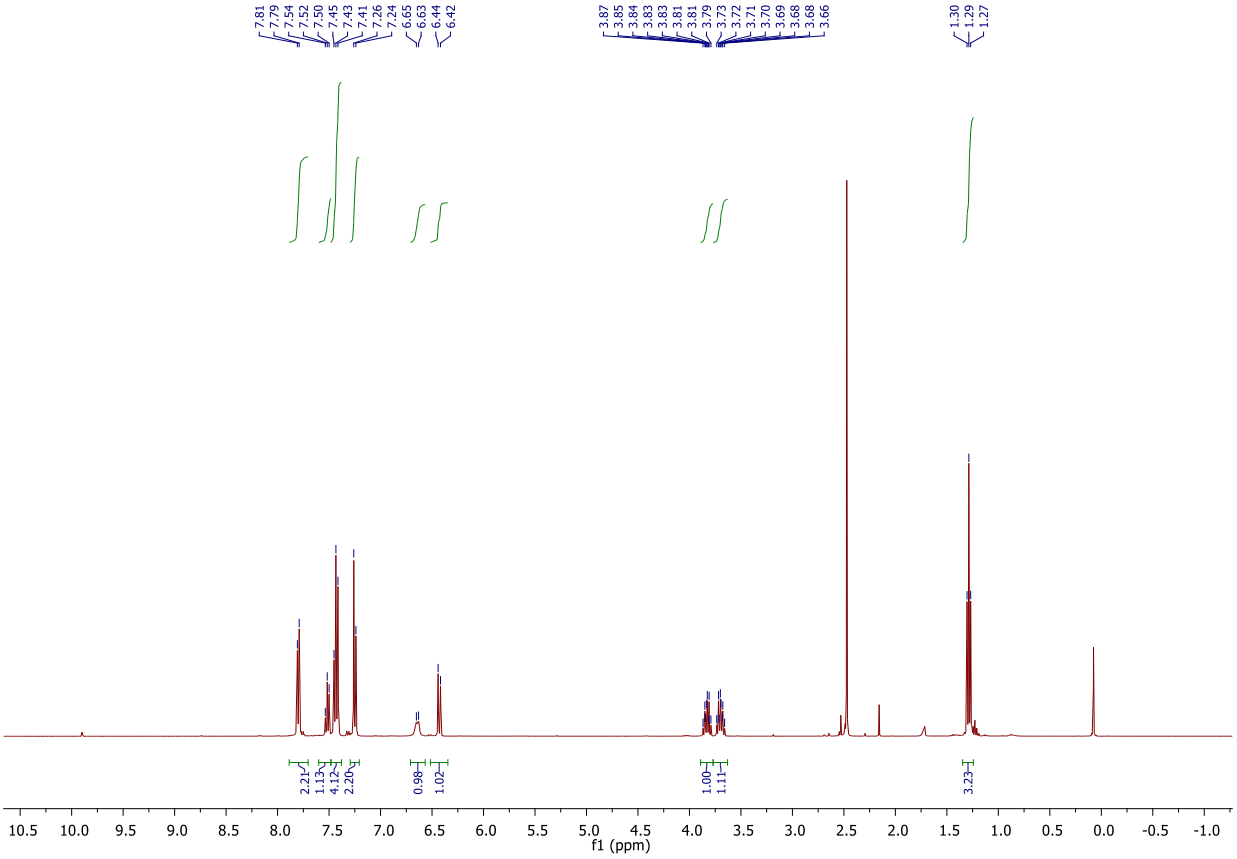
^{13}C{^{1}H} NMR (101 MHz, DMSO-d$_6$)



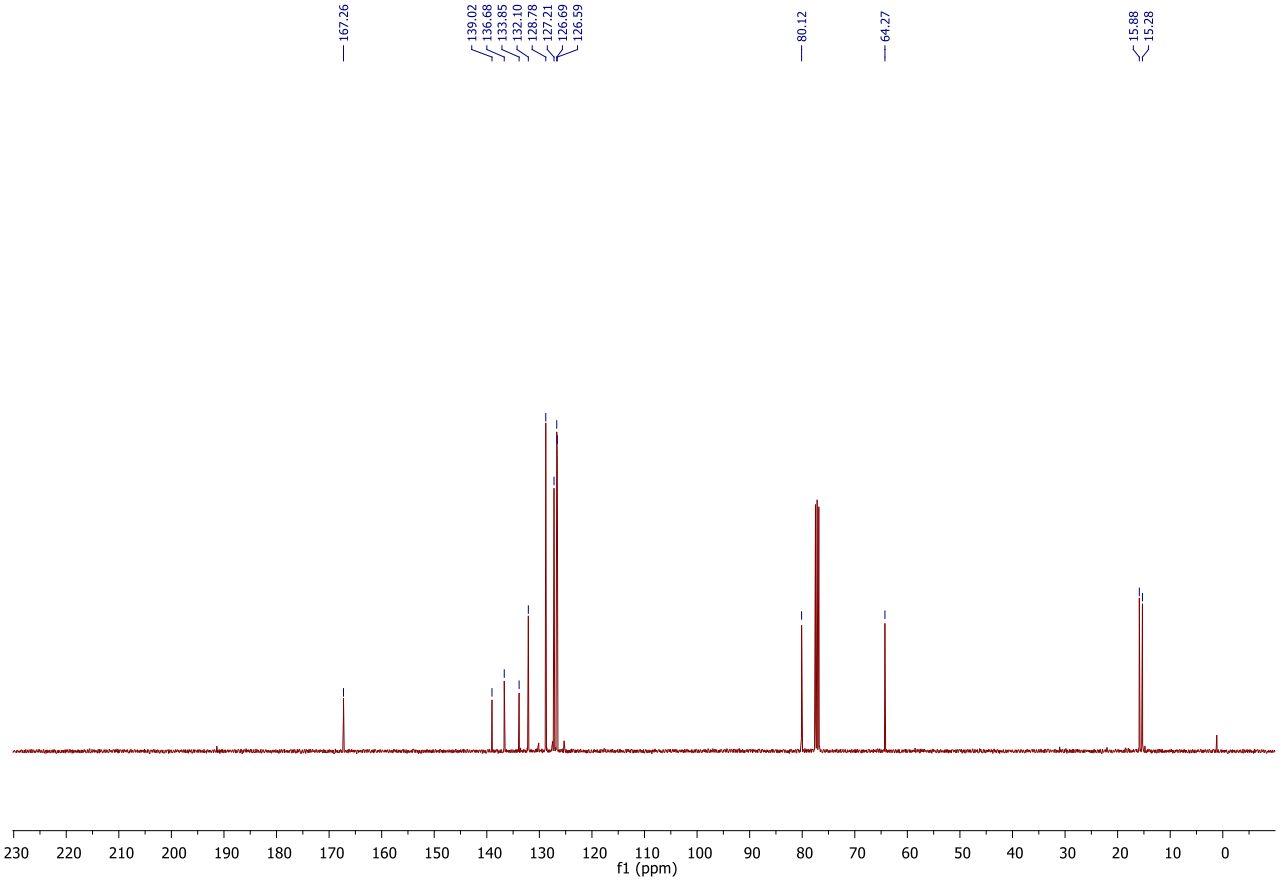
N-[ethoxy-(4-methylsulfanylphenyl)methyl]benzamide (1o)



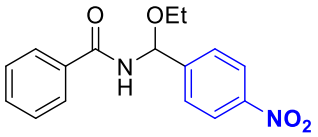
^{1}H NMR (400 MHz, $CDCl_3$)



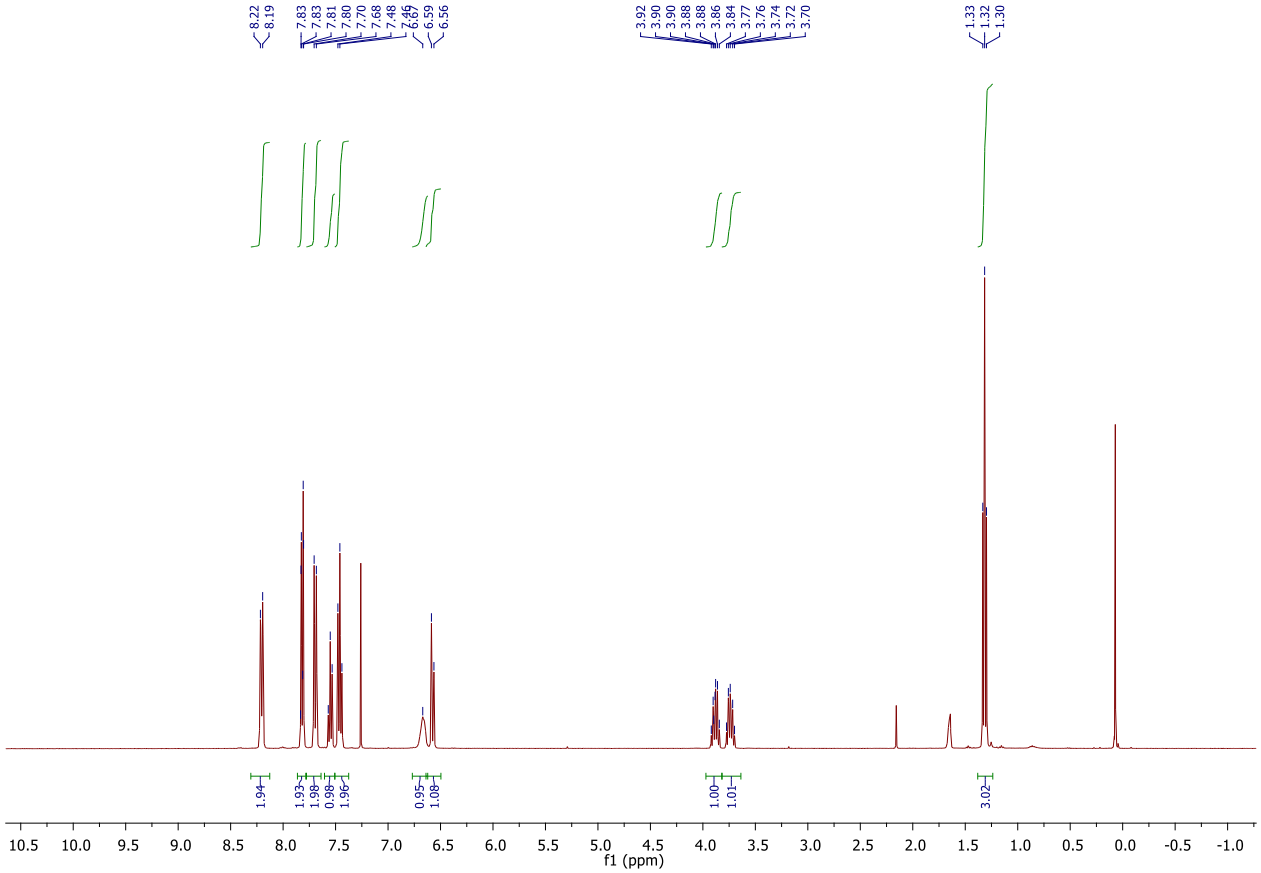
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



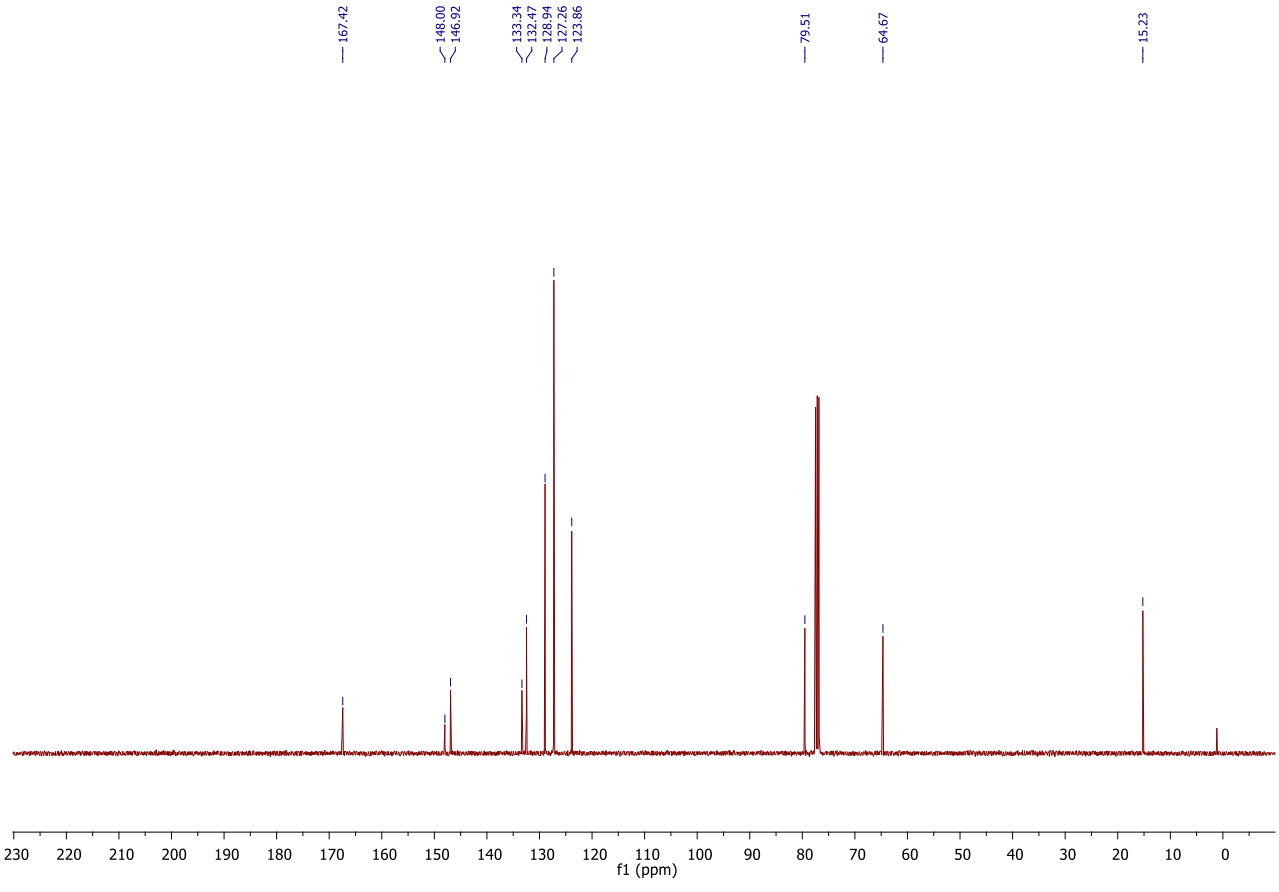
_N_-[ethoxy-(4-nitrophenyl)methyl]benzamide (1p)



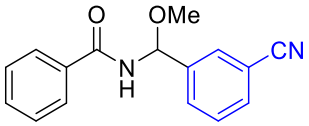
^{1}H NMR (400 MHz, $CDCl_3$)



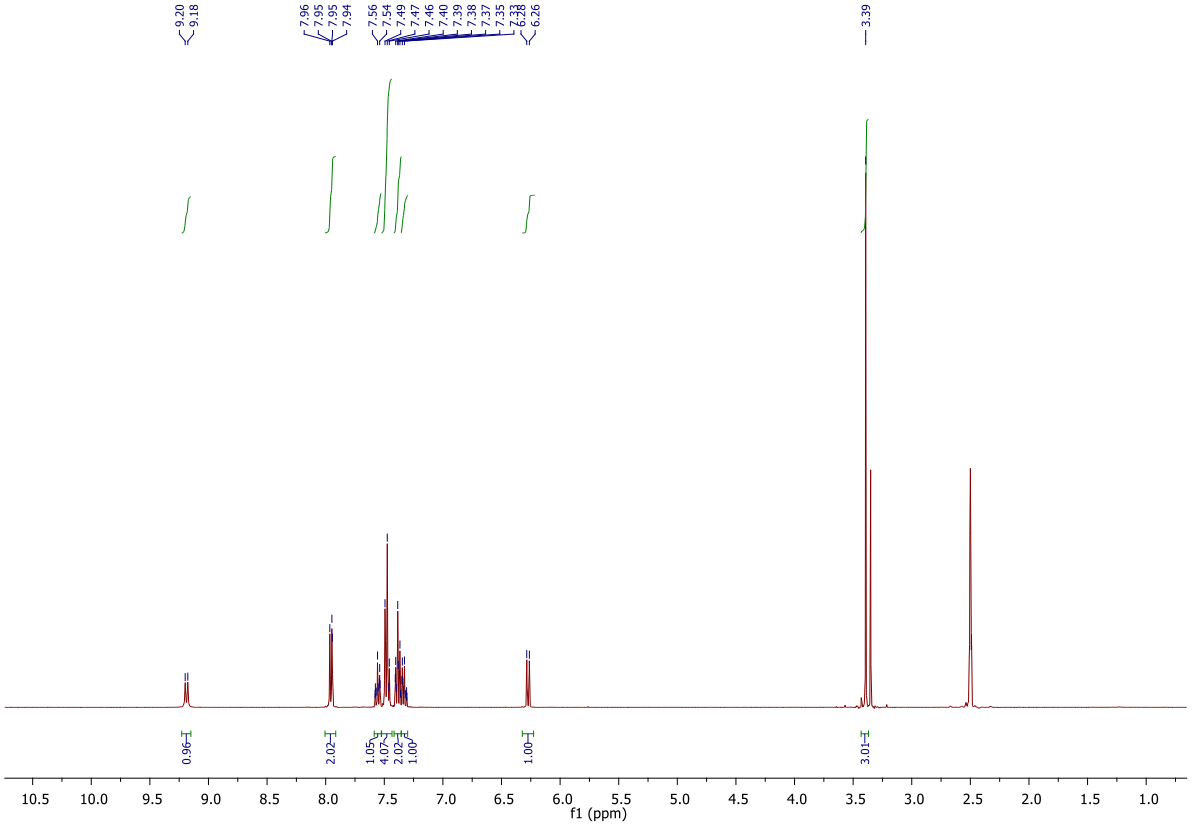
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



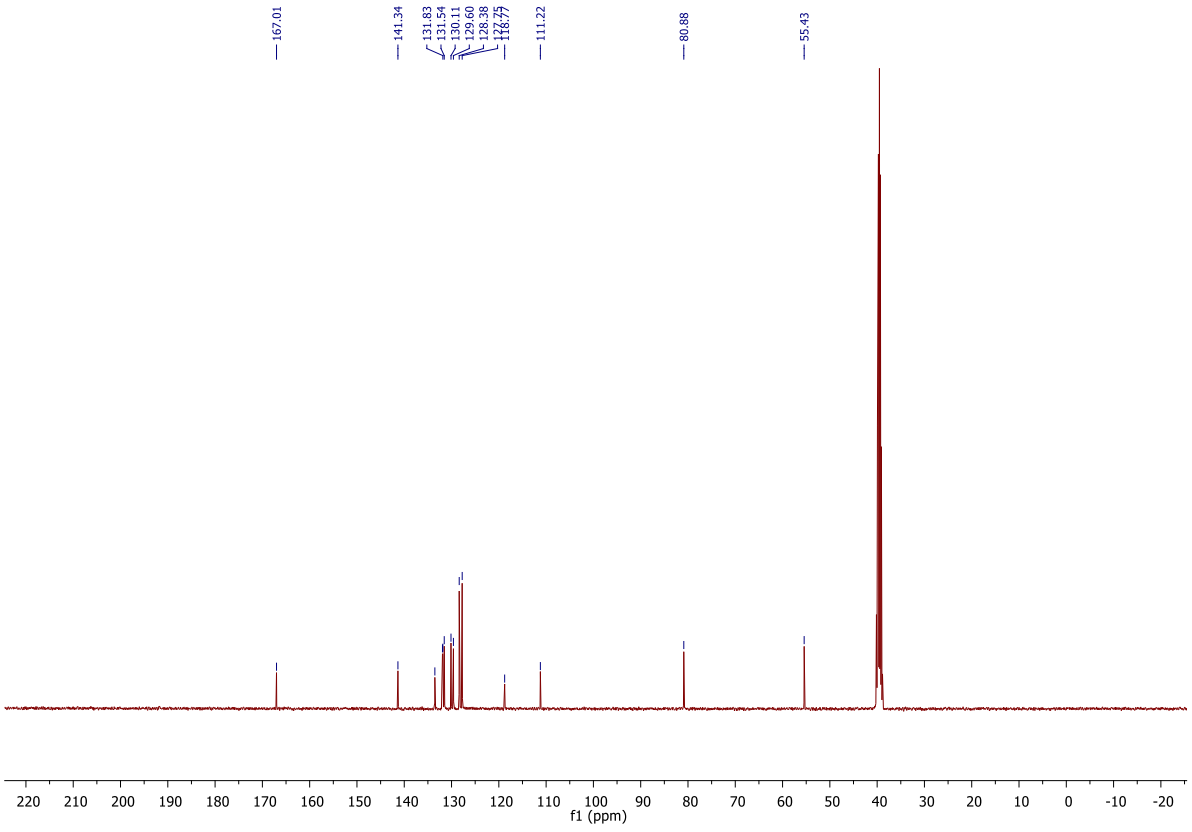
N-[(3-cyanophenyl)(methoxy)methyl]benzamide (1q)



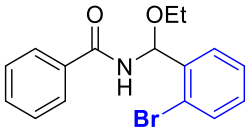
^{1}H NMR (400 MHz, DMSO-d_6)



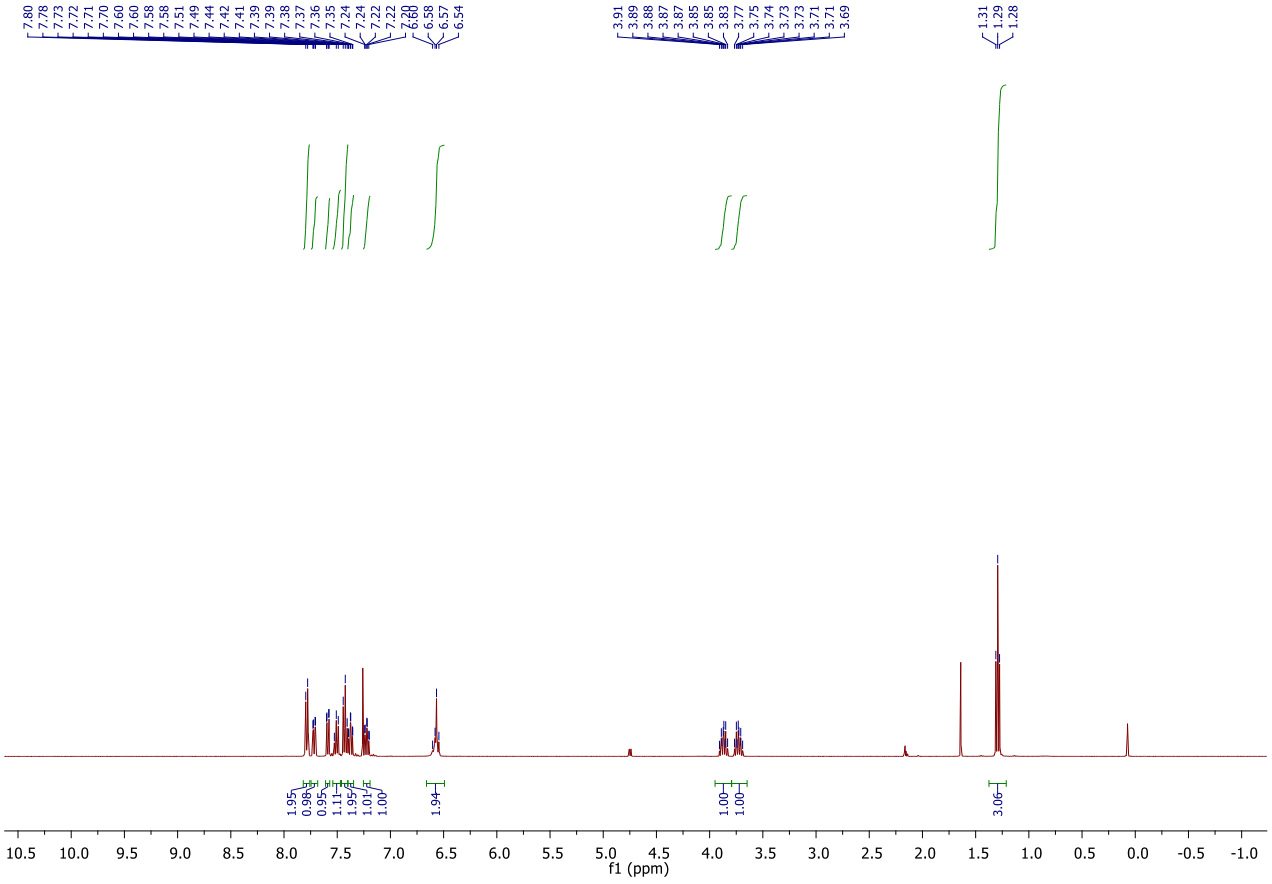
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)



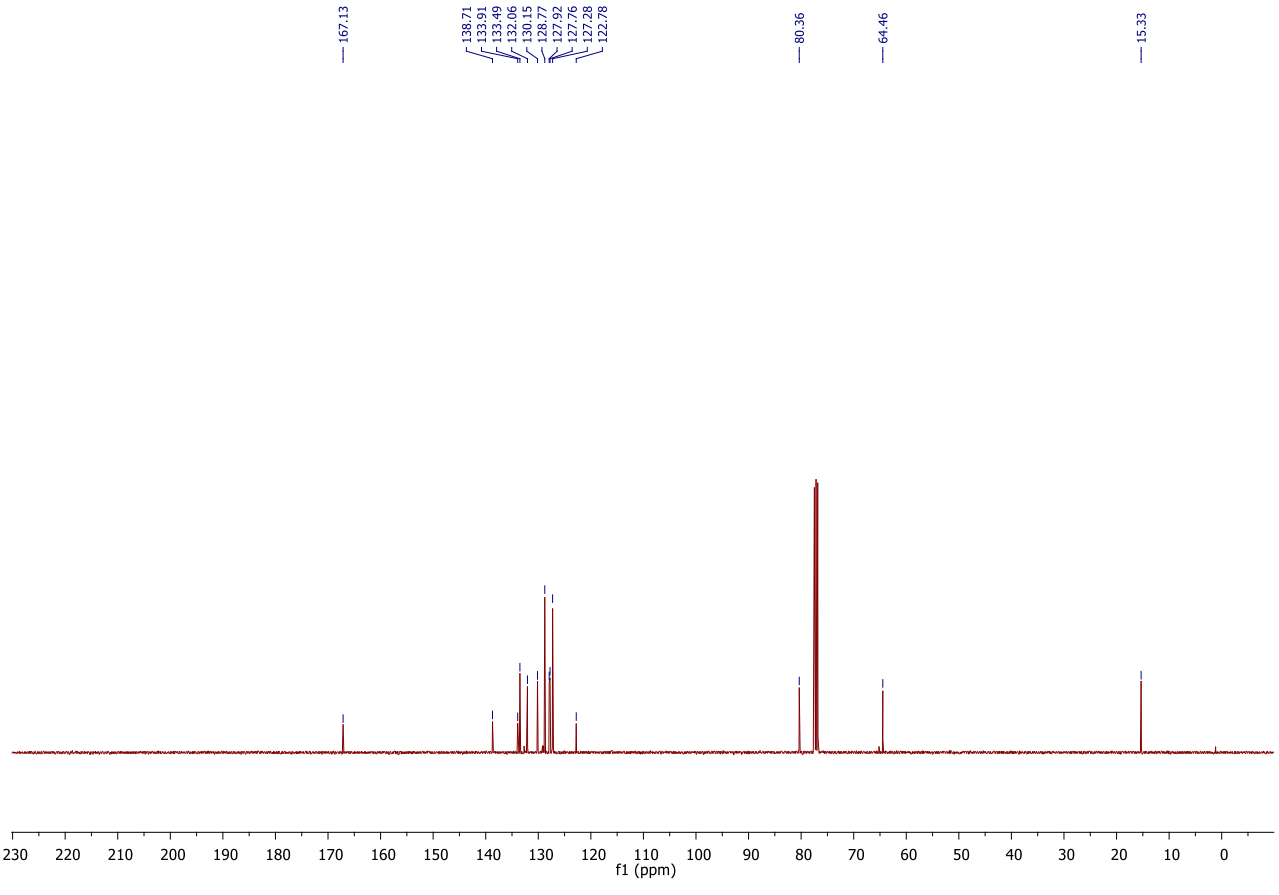
_N_-[(2-bromophenyl)-ethoxy-methyl]benzamide (1r)



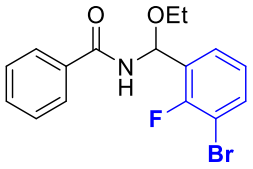
^{1}H NMR (400 MHz, $CDCl_3$)



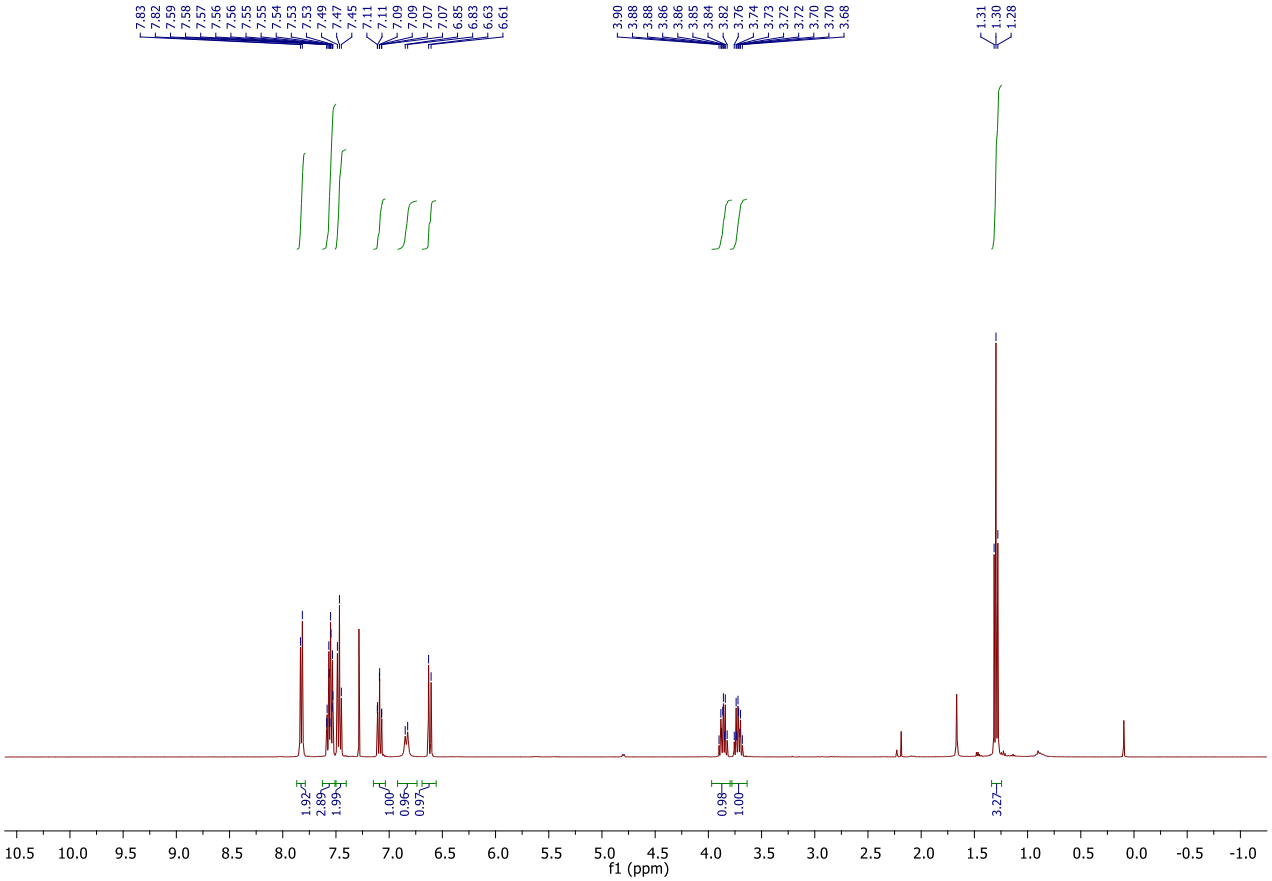
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



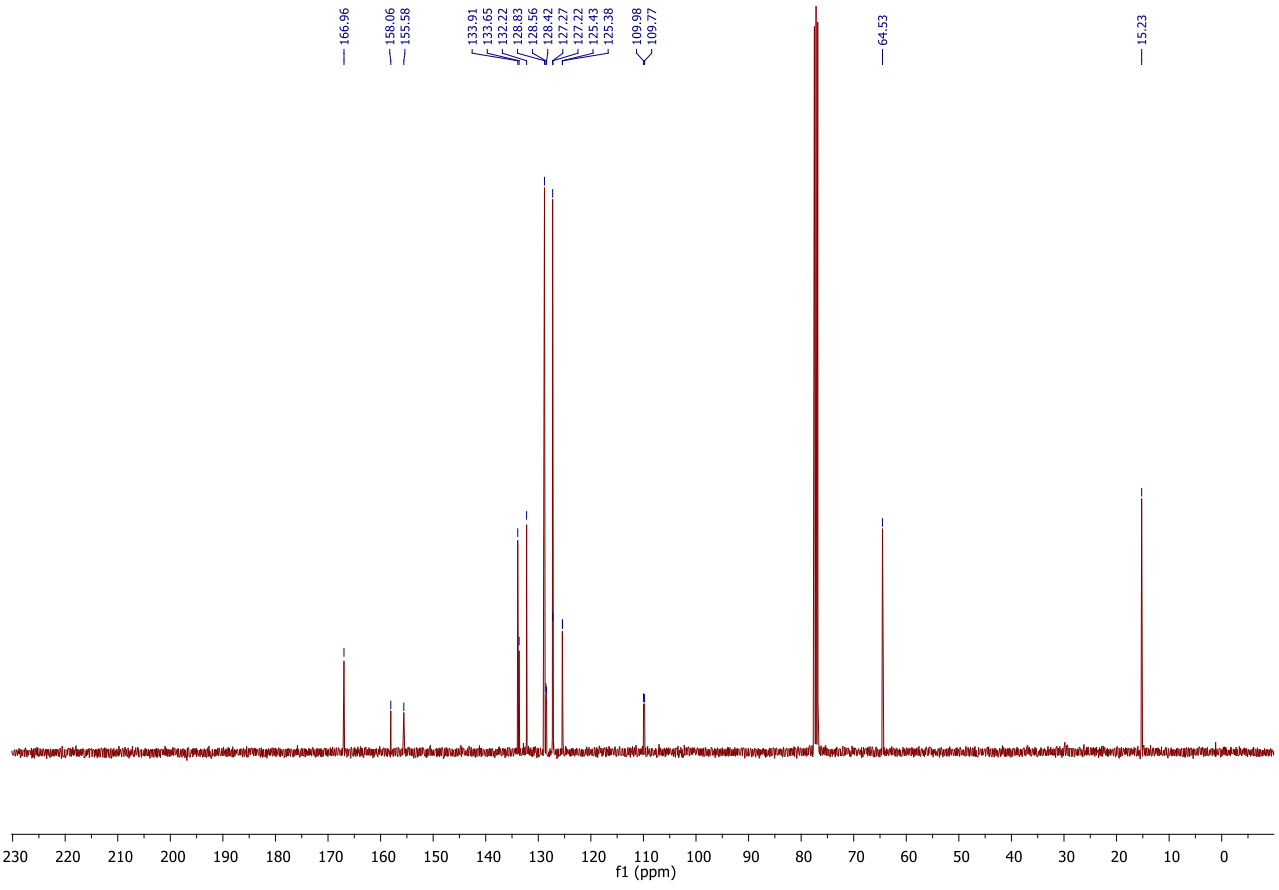
_N_-[(3-bromo-2-fluoro-phenyl)-ethoxy-methyl]benzamide (1s)



^{1}H NMR (400 MHz, $CDCl_3$)

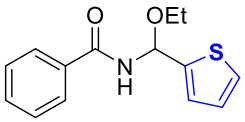


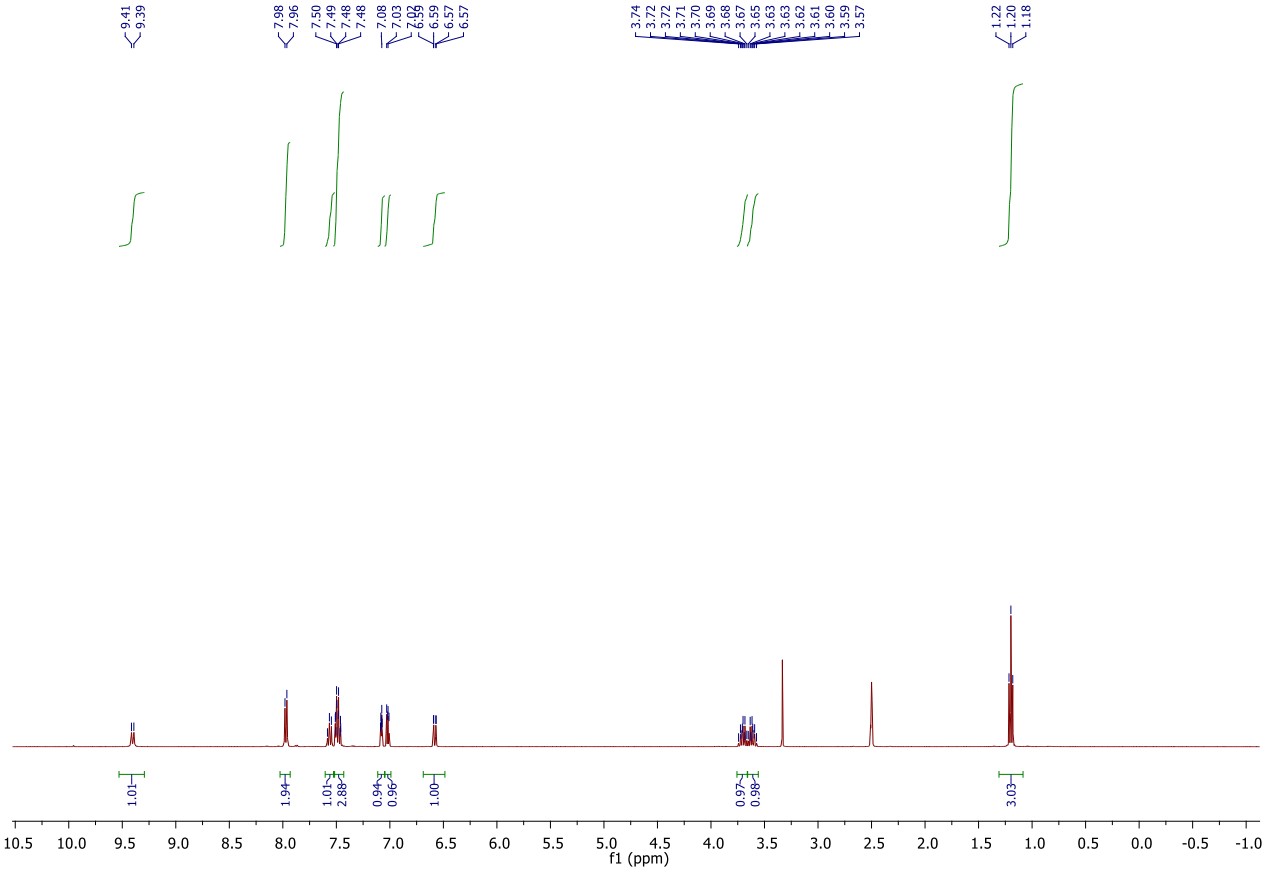
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



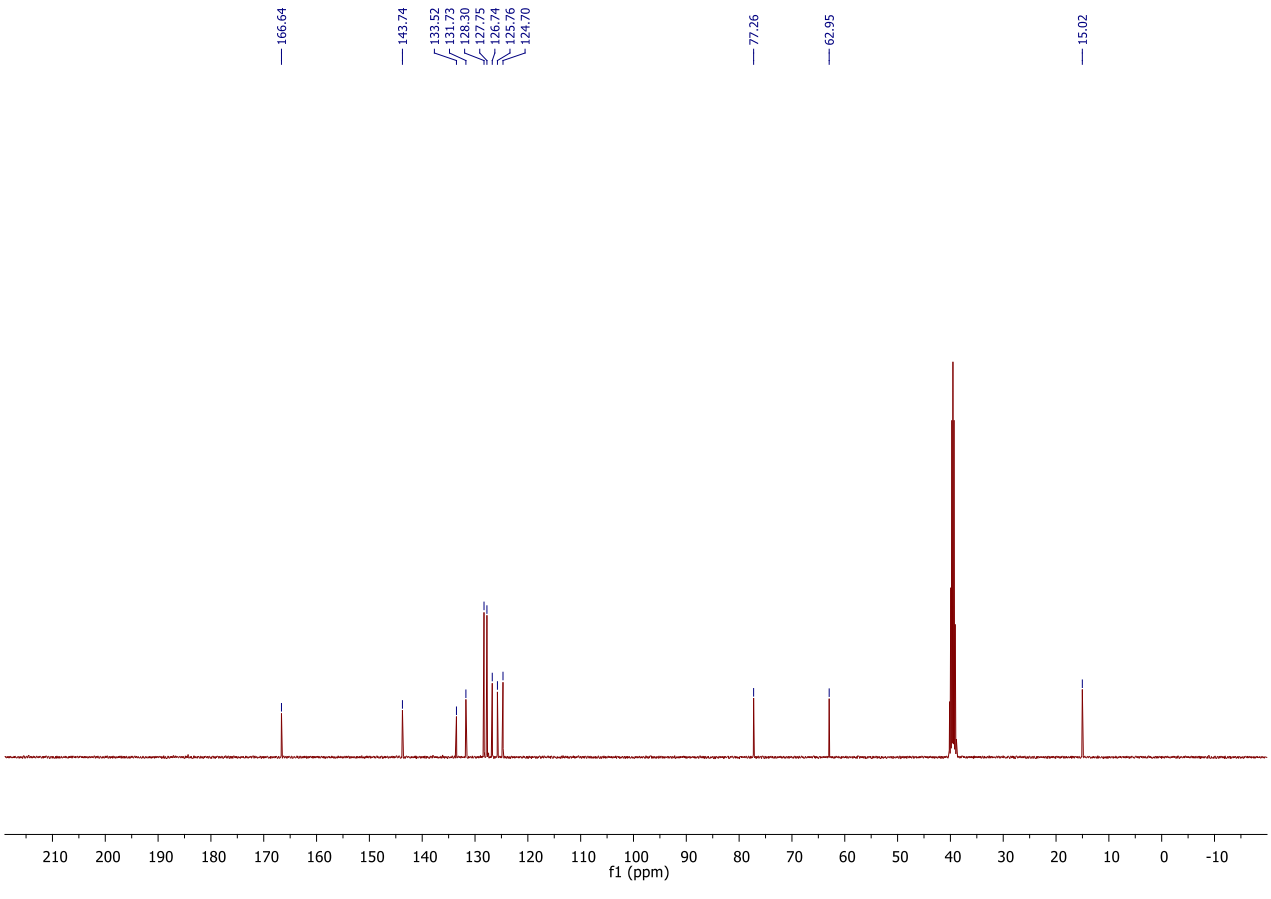
N-[ethoxy(2-thienyl)methyl]benzamide (1t)

^{1}H NMR (400 MHz, DMSO-d_6)

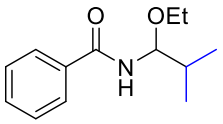




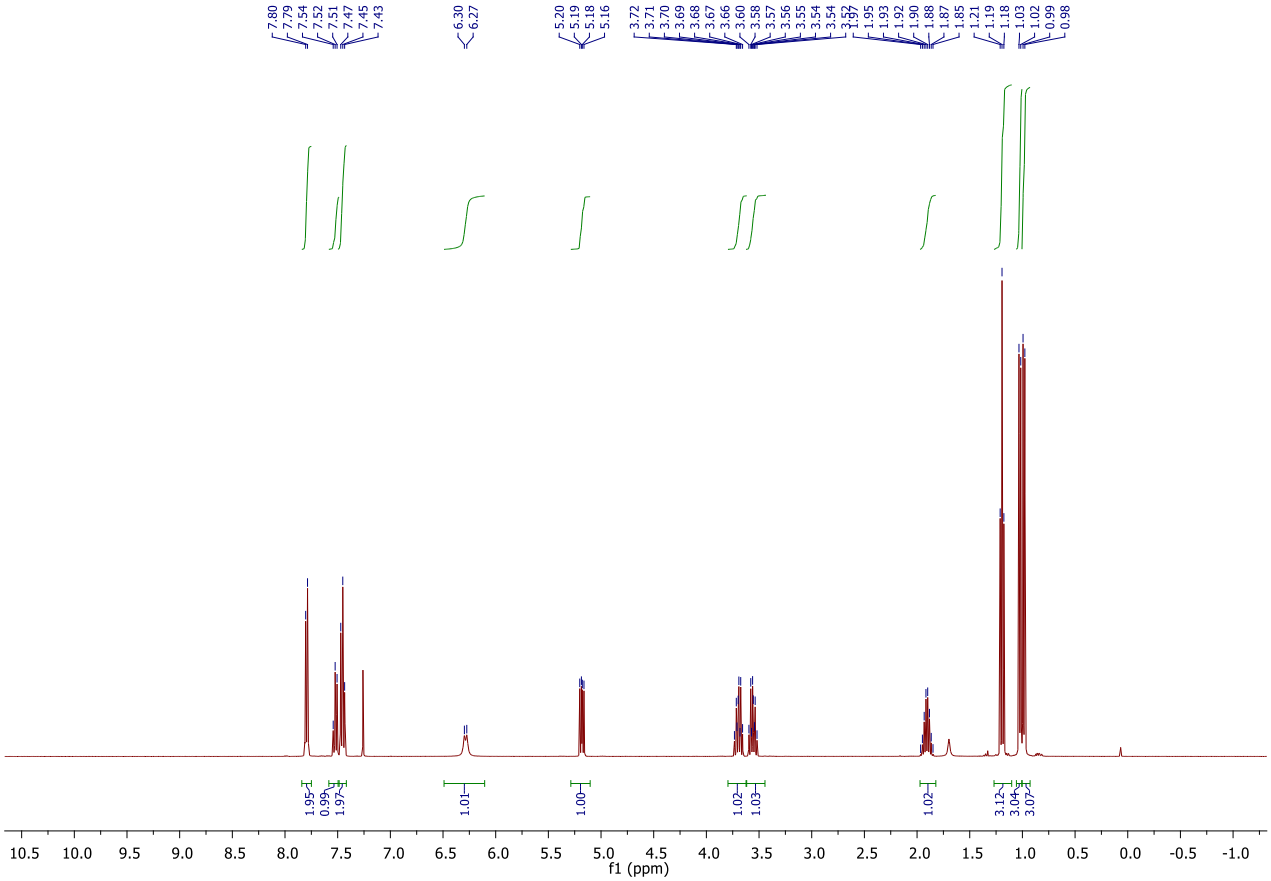
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)



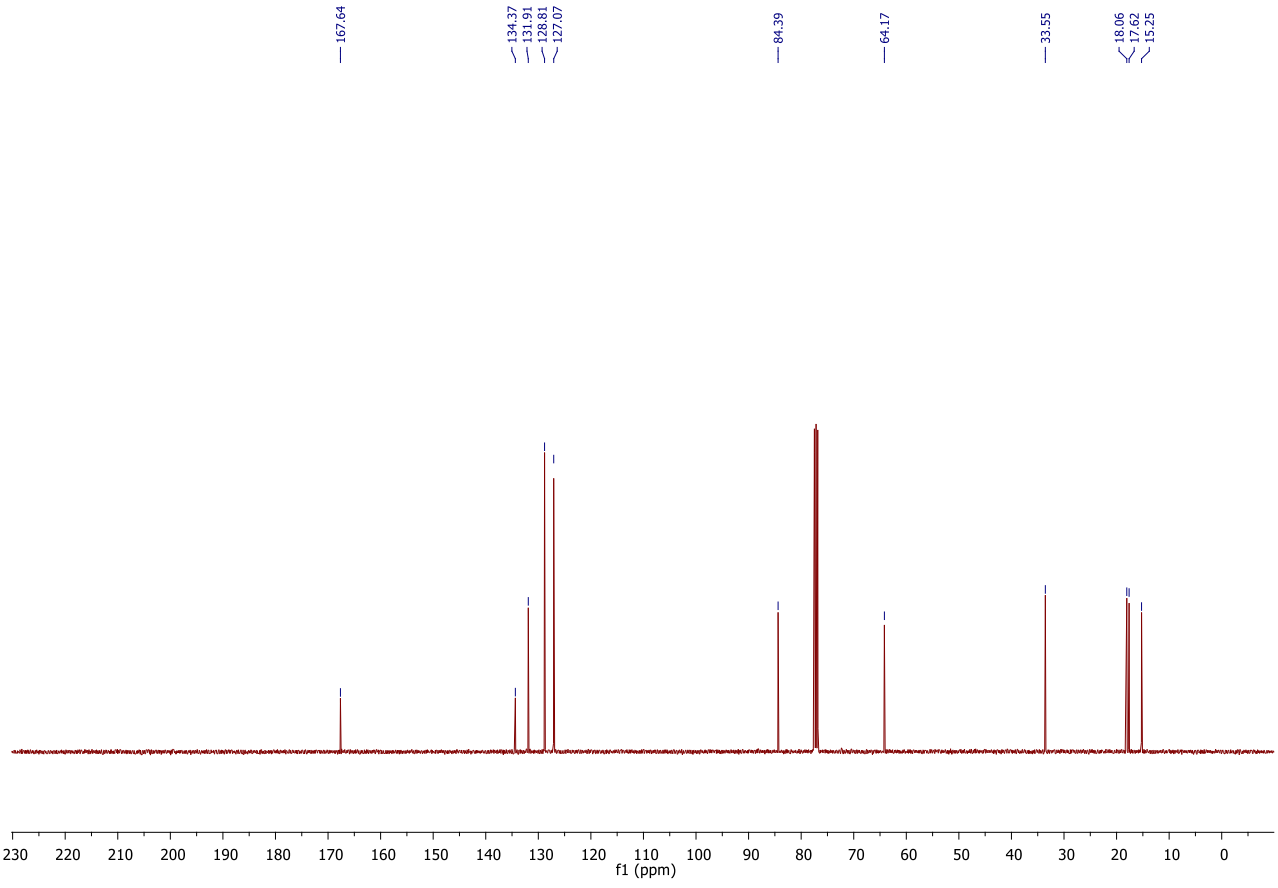
N-(1-ethoxy-2-methyl-propyl)benzamide (1u)

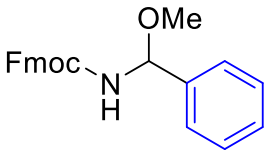


^{1}H NMR (400 MHz, $CDCl_3$)



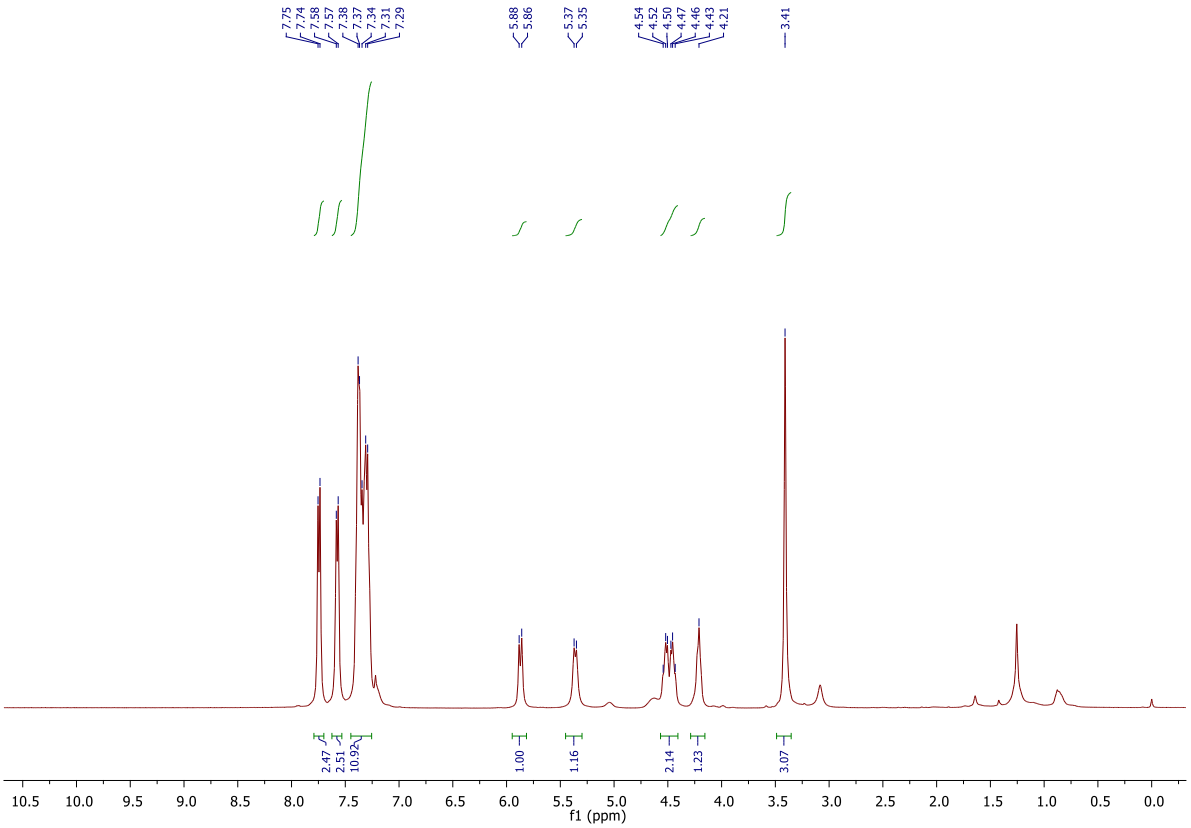
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



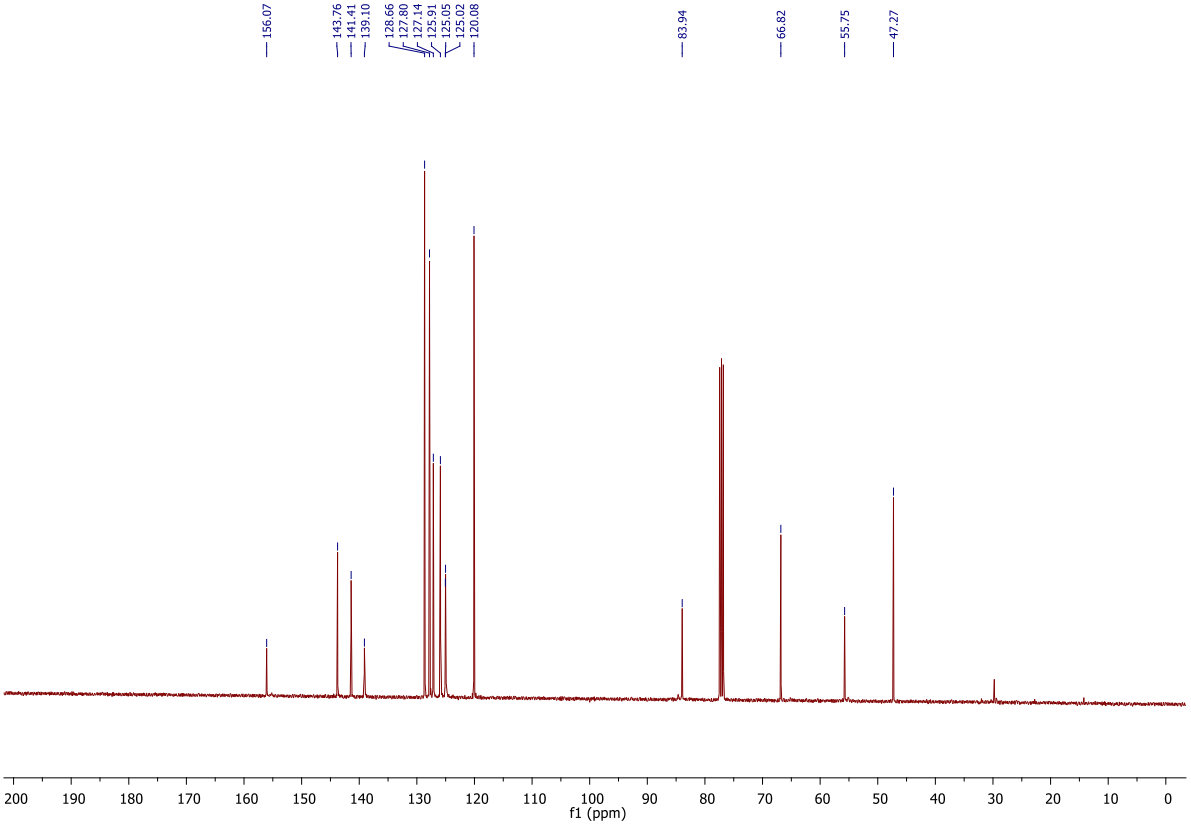


(9*H*-fluoren-9-yl)methyl (methoxy(phenyl)methyl)carbamate (3a)

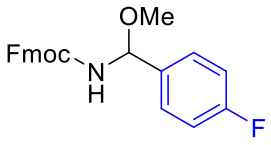
^{1}H NMR (400 MHz, $CDCl_3$)



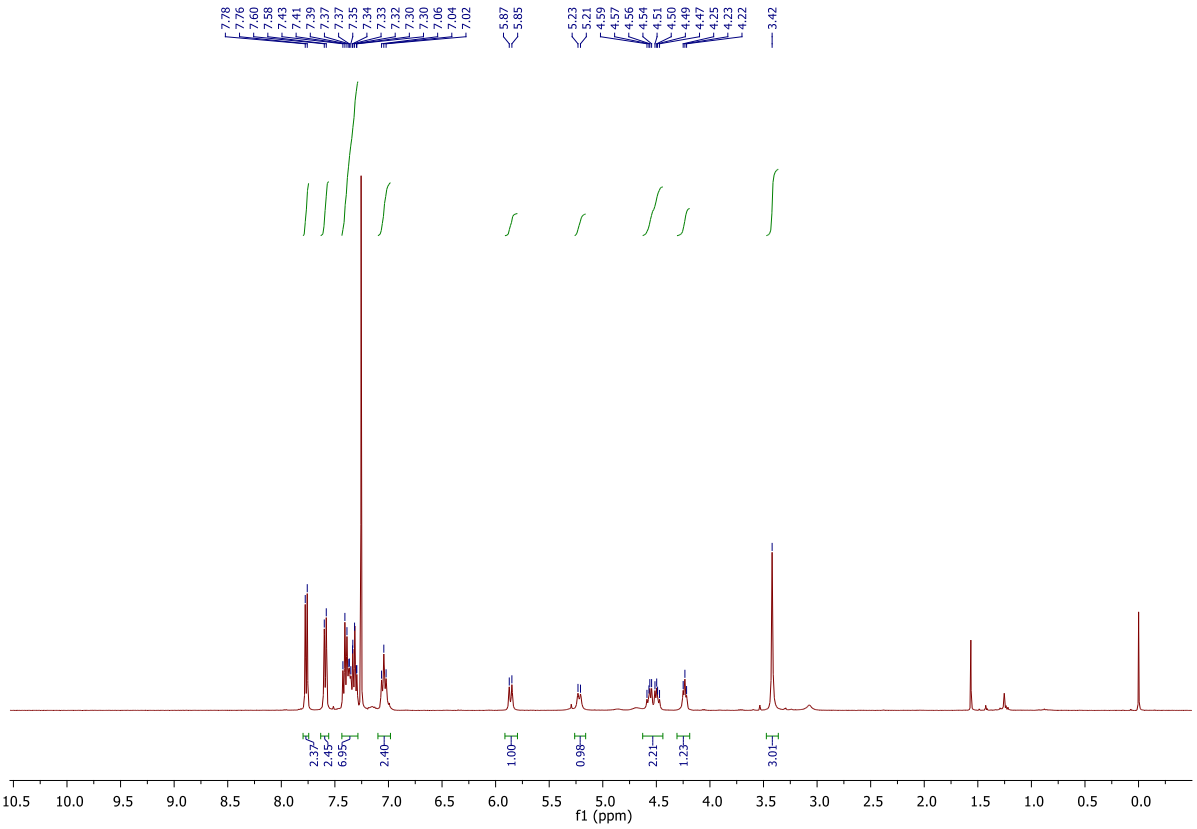
^{13}C NMR (101 MHz, $CDCl_3$)



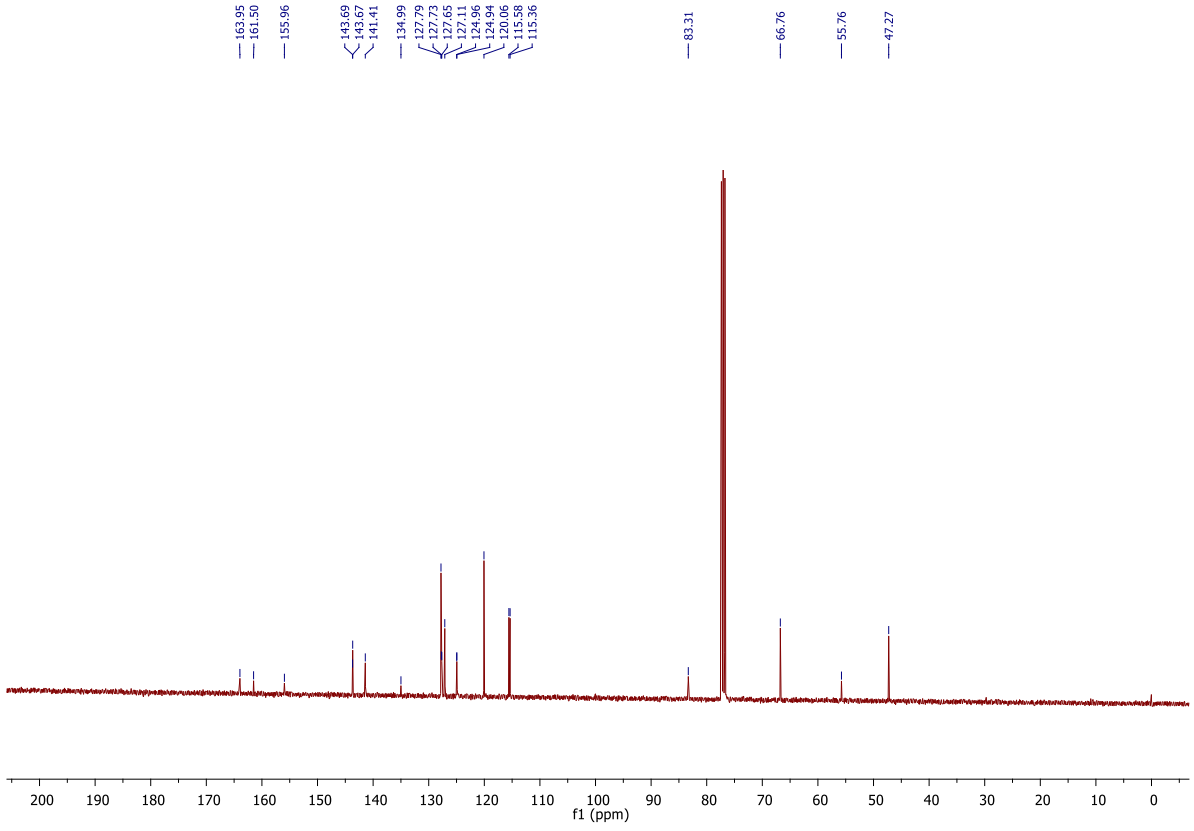
(9*H*-fluoren-9-yl)methyl ((4-fluorophenyl)(methoxy)methyl)carbamate (3b)



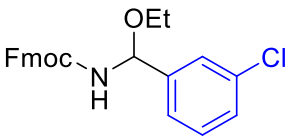
^{1}H NMR (400 MHz, $CDCl_3$)



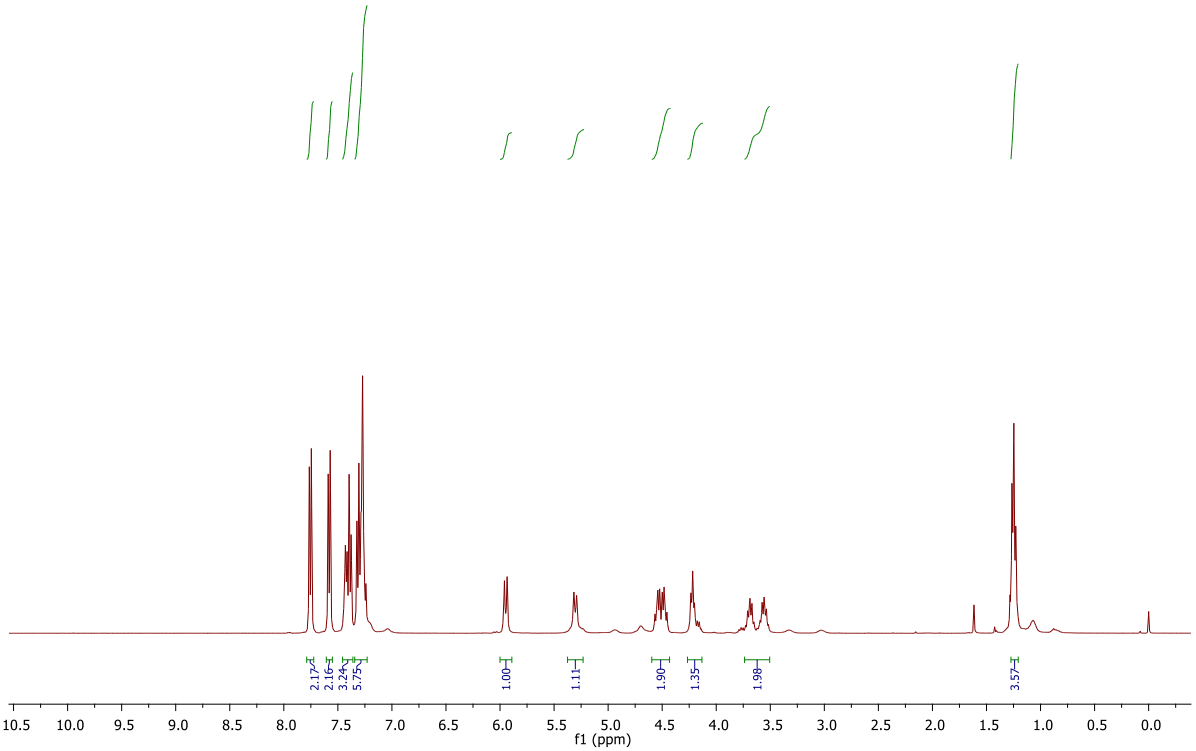
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



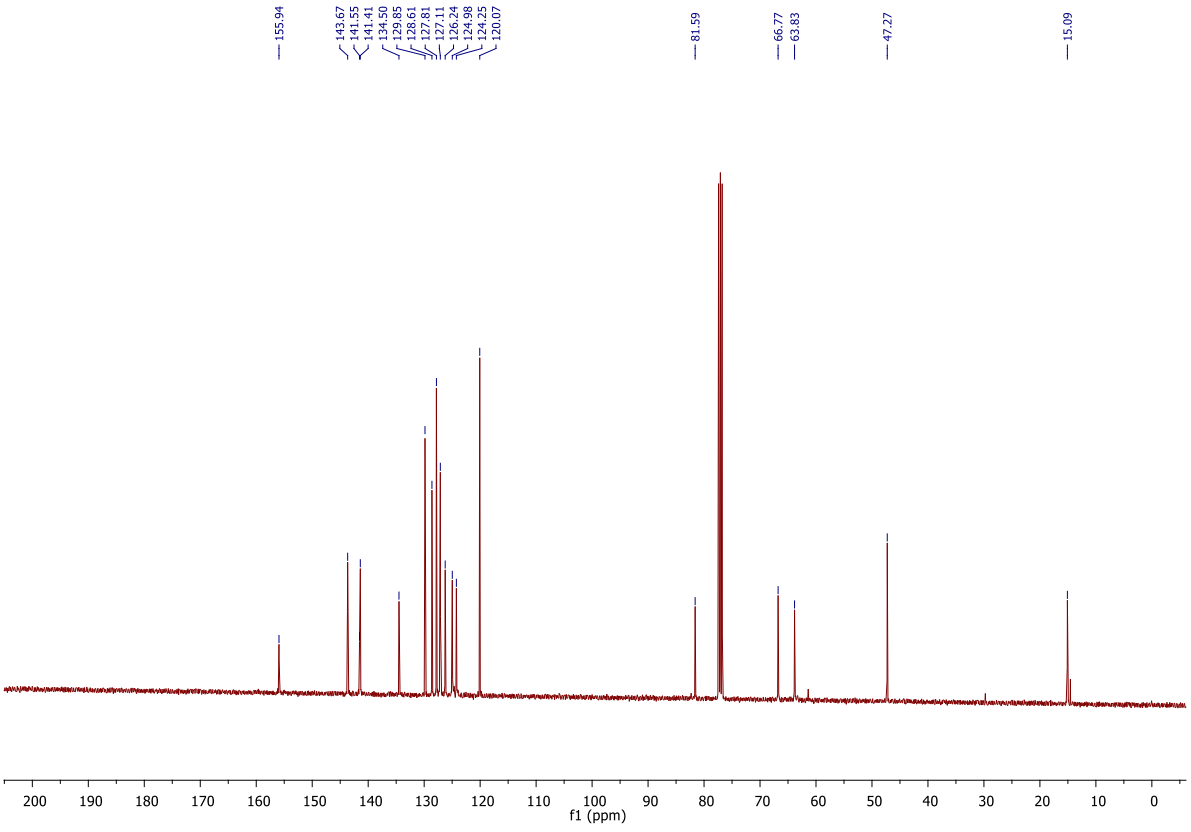
(9*H*-fluoren-9-yl)methyl ((3-chlorophenyl)(ethoxy)methyl)carbamate (3c)



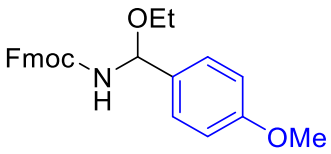
^{1}H NMR (400 MHz, $CDCl_3$)



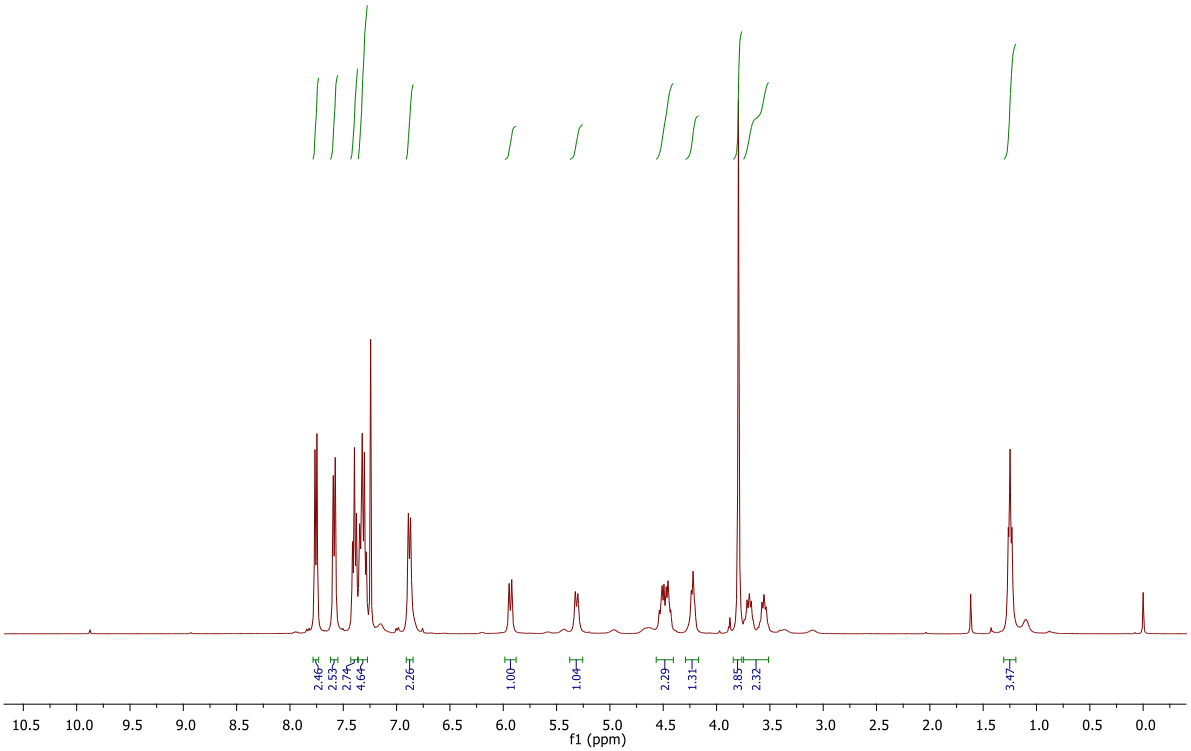
^{13}C NMR (101 MHz, $CDCl_3$)



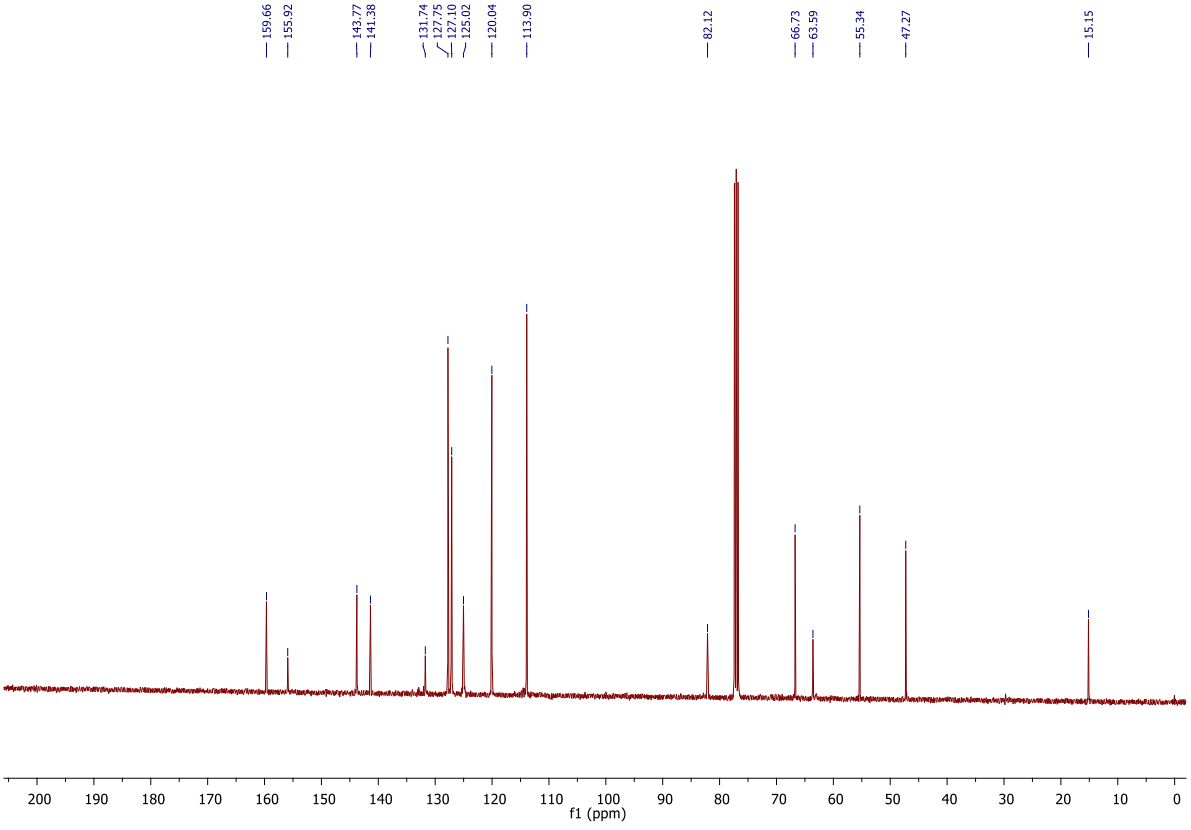
(9*H*-fluoren-9-yl)methyl (ethoxy(4-methoxyphenyl)methyl)carbamate (3d)



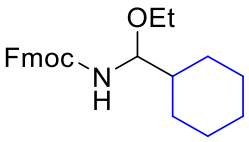
^{1}H NMR (400 MHz, $CDCl_3$)



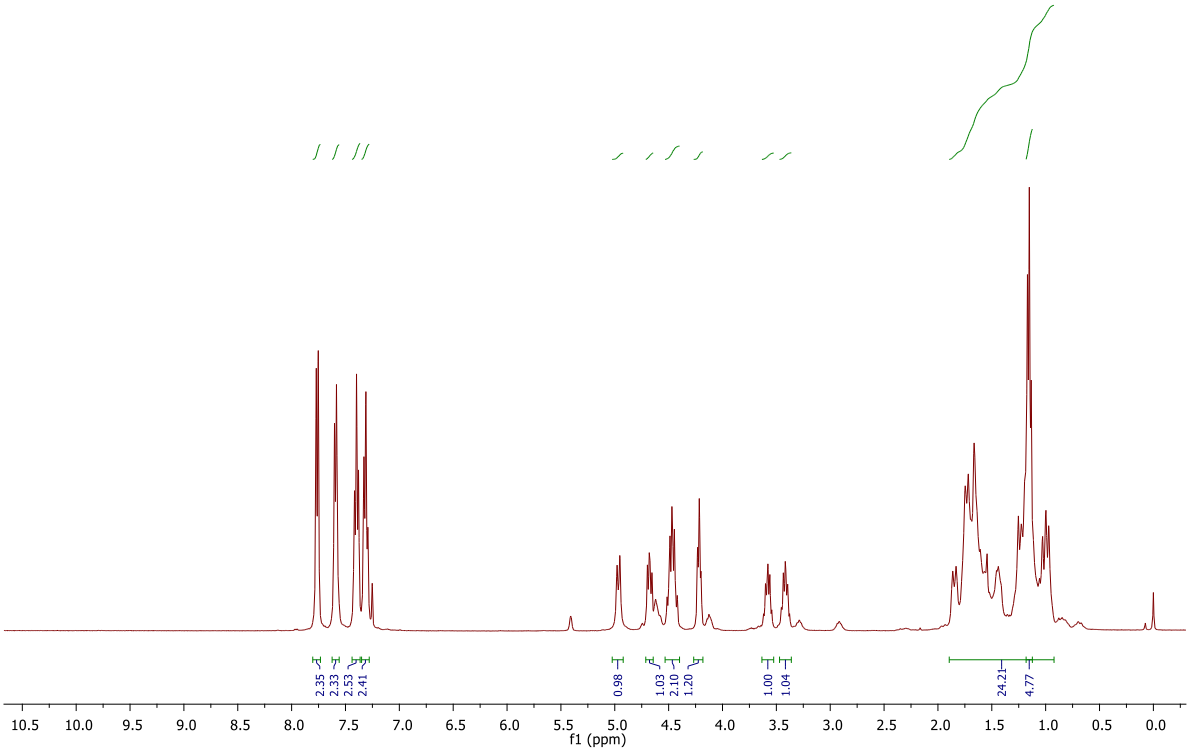
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



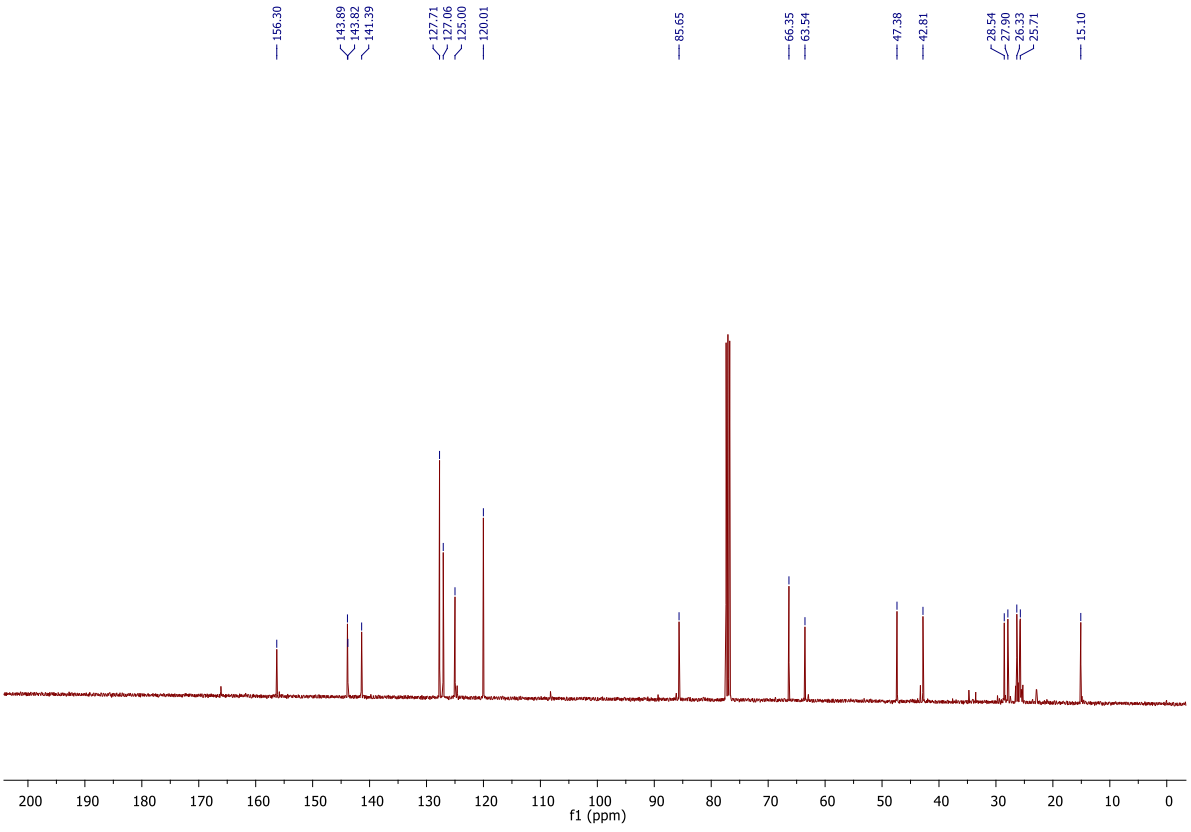
(9*H*-fluoren-9-yl)methyl (cyclohexyl(ethoxy)methyl)carbamate (3e)



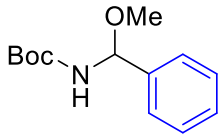
^{1}H NMR (400 MHz, $CDCl_3$)



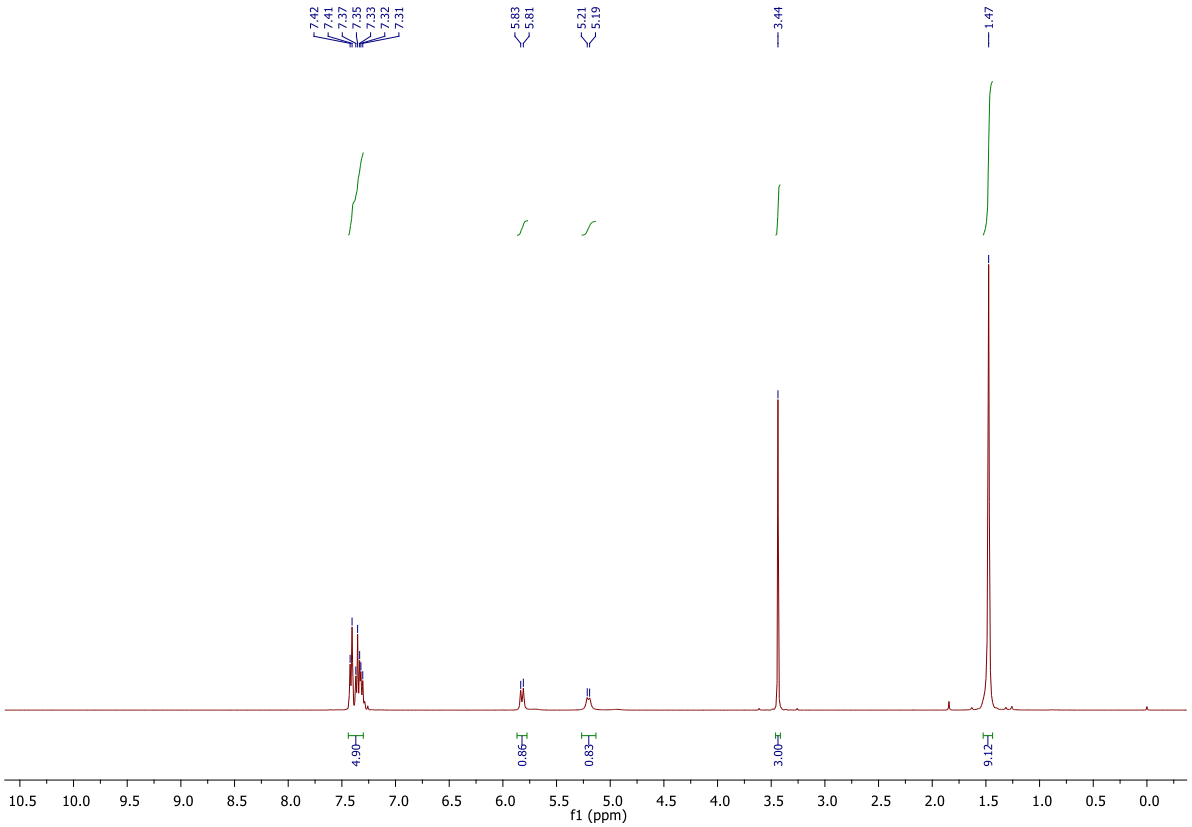
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



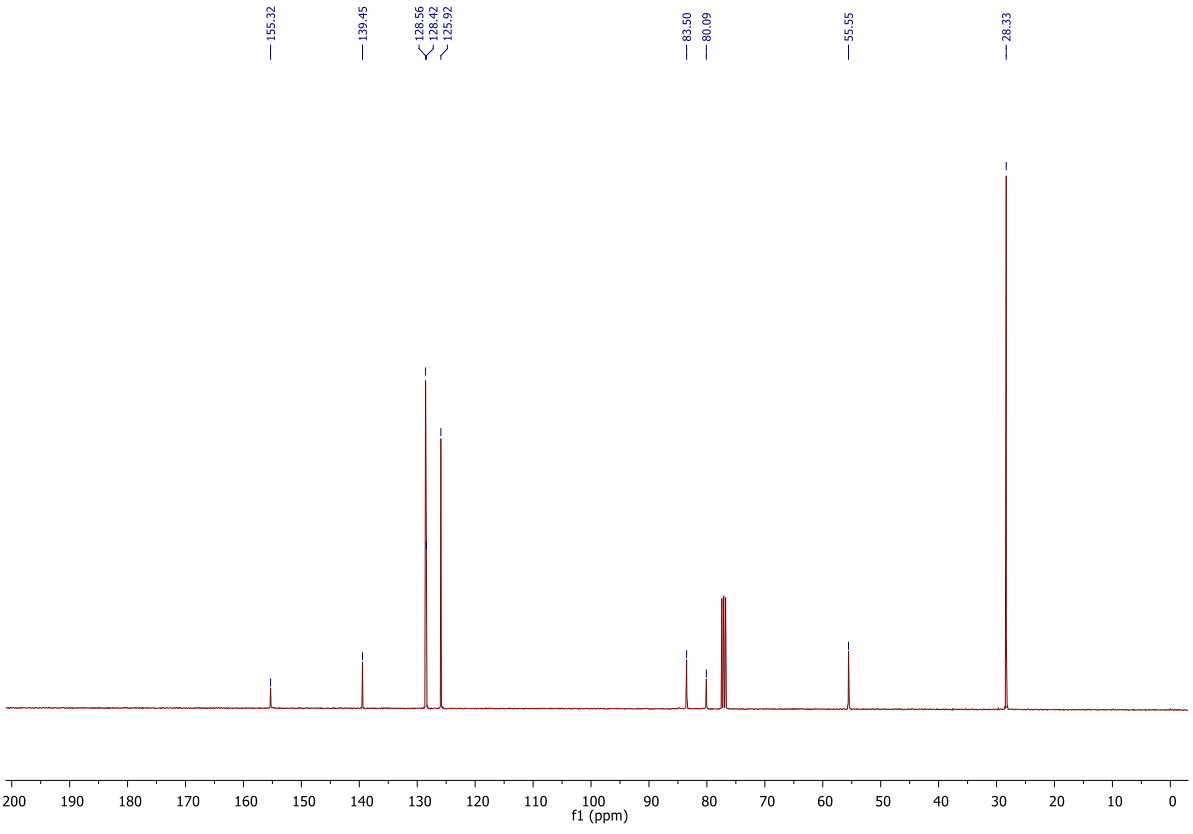
tert-butyl (methoxy(phenyl)methyl)carbamate (3f)



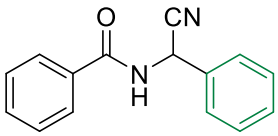
^{1}H NMR (400 MHz, $CDCl_3$)



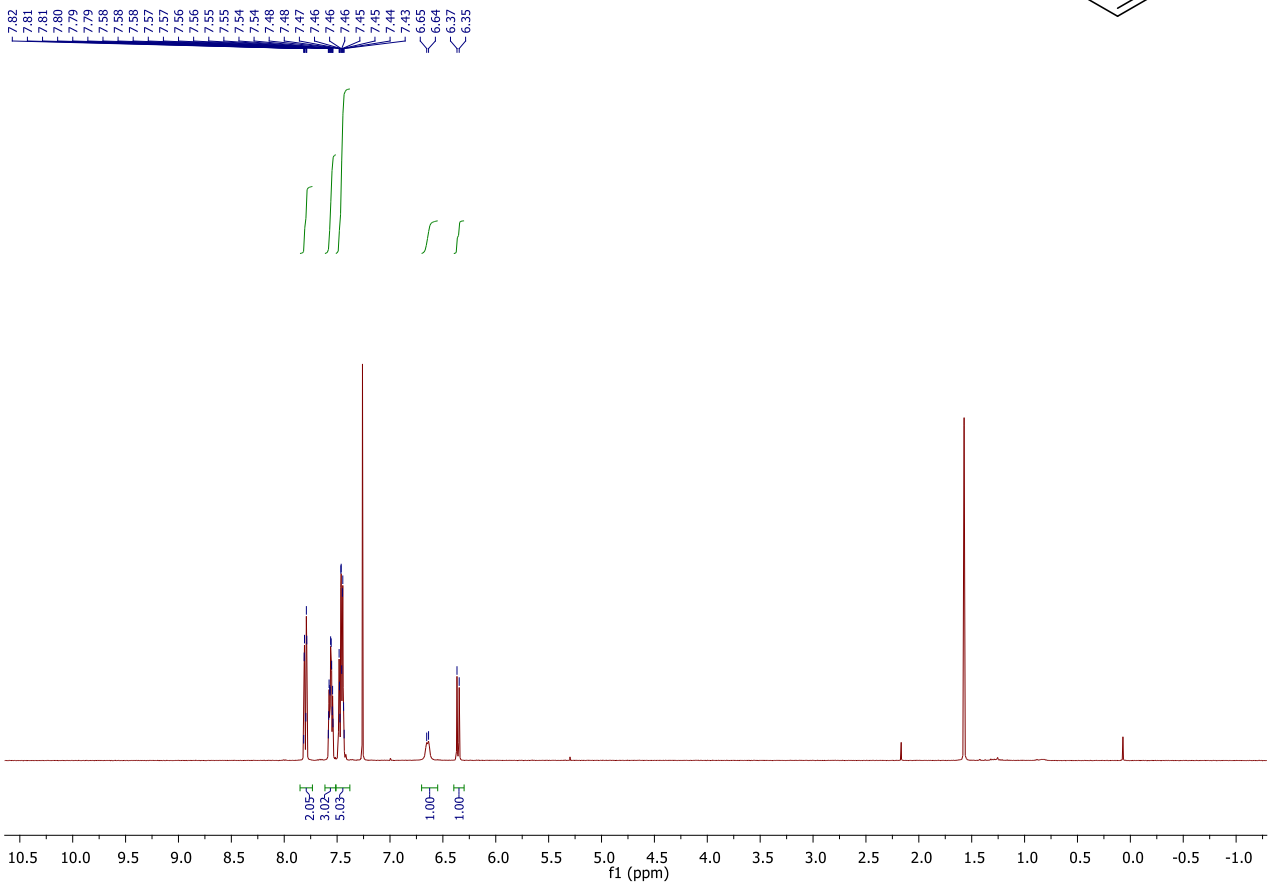
^{13}C NMR (101 MHz, $CDCl_3$)



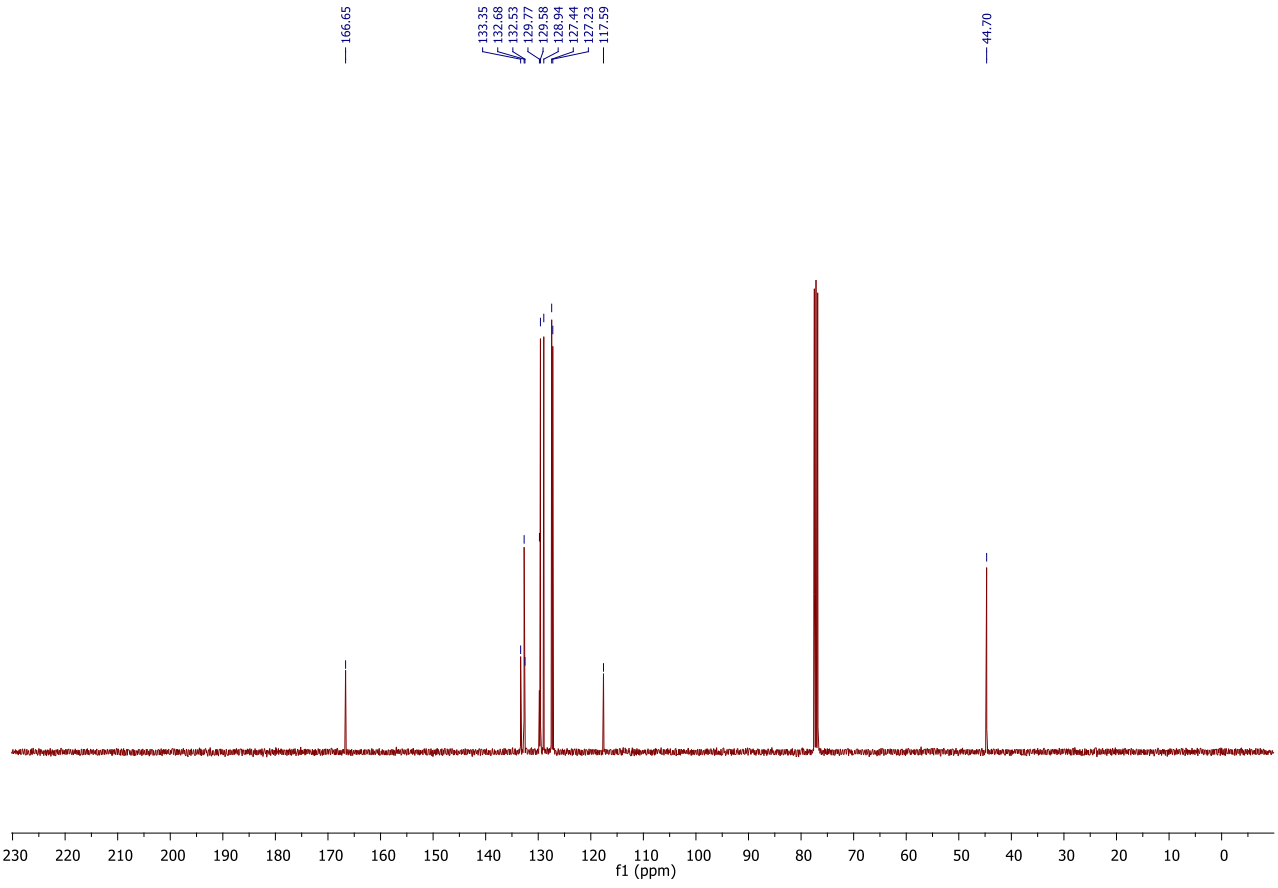
N-[cyano(phenyl)methyl]benzamide (2a)



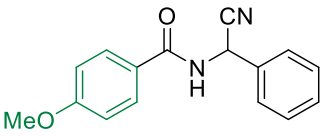
^{1}H NMR (400 MHz, $CDCl_3$)



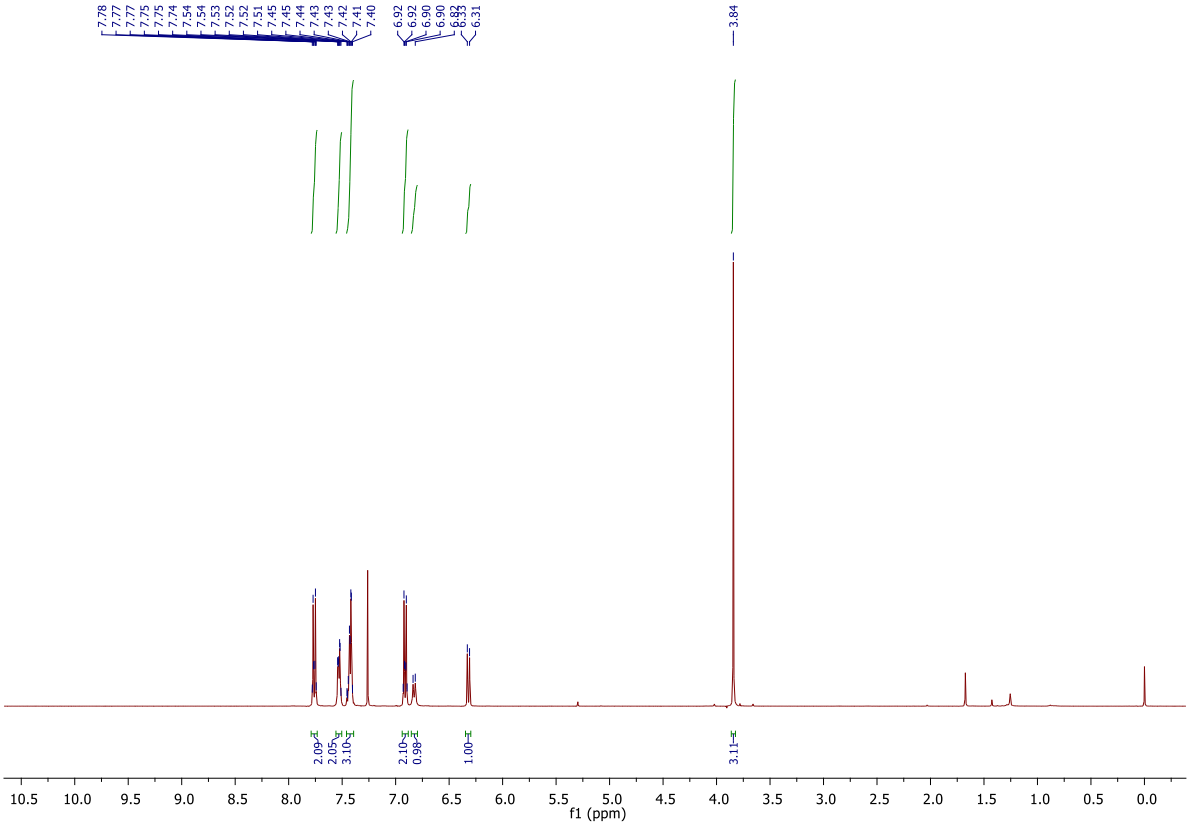
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



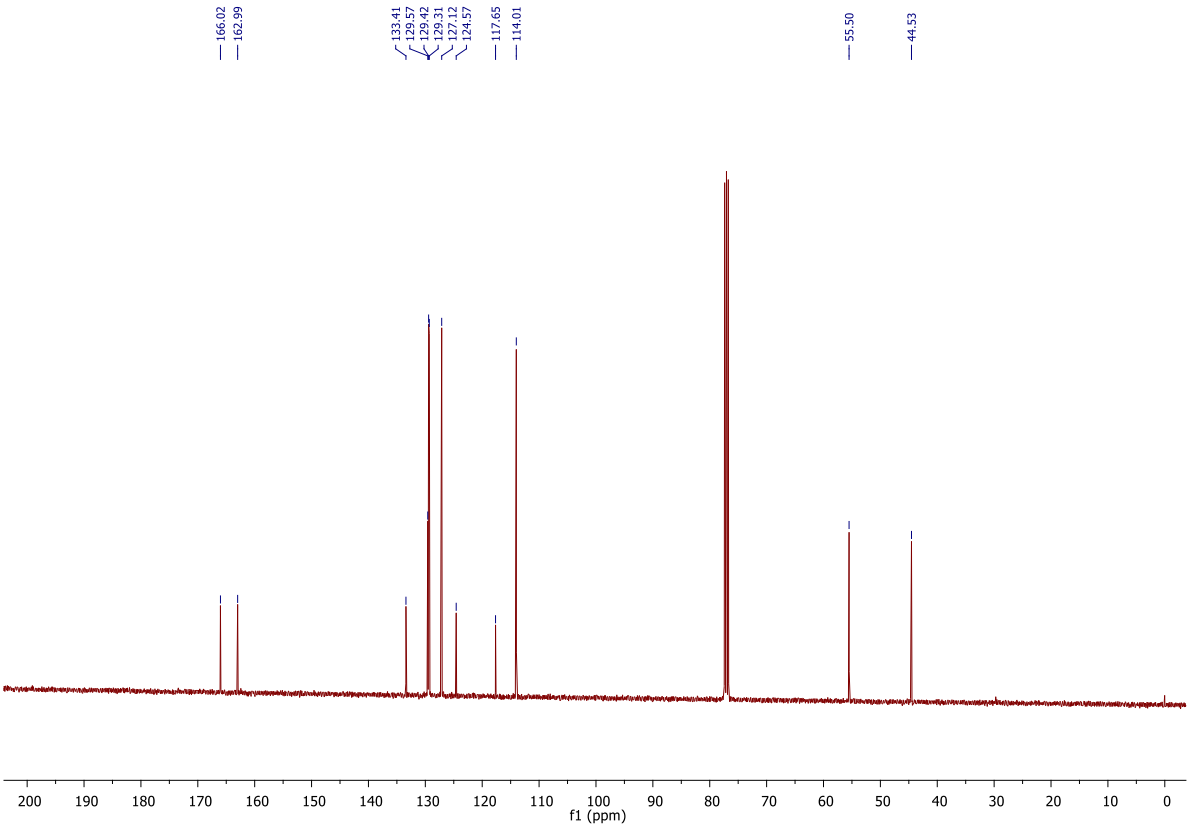
N-(cyano(phenyl)methyl)-4-methoxybenzamide (2b)



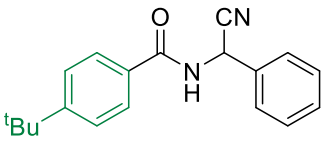
^{1}H NMR (400 MHz, $CDCl_3$)



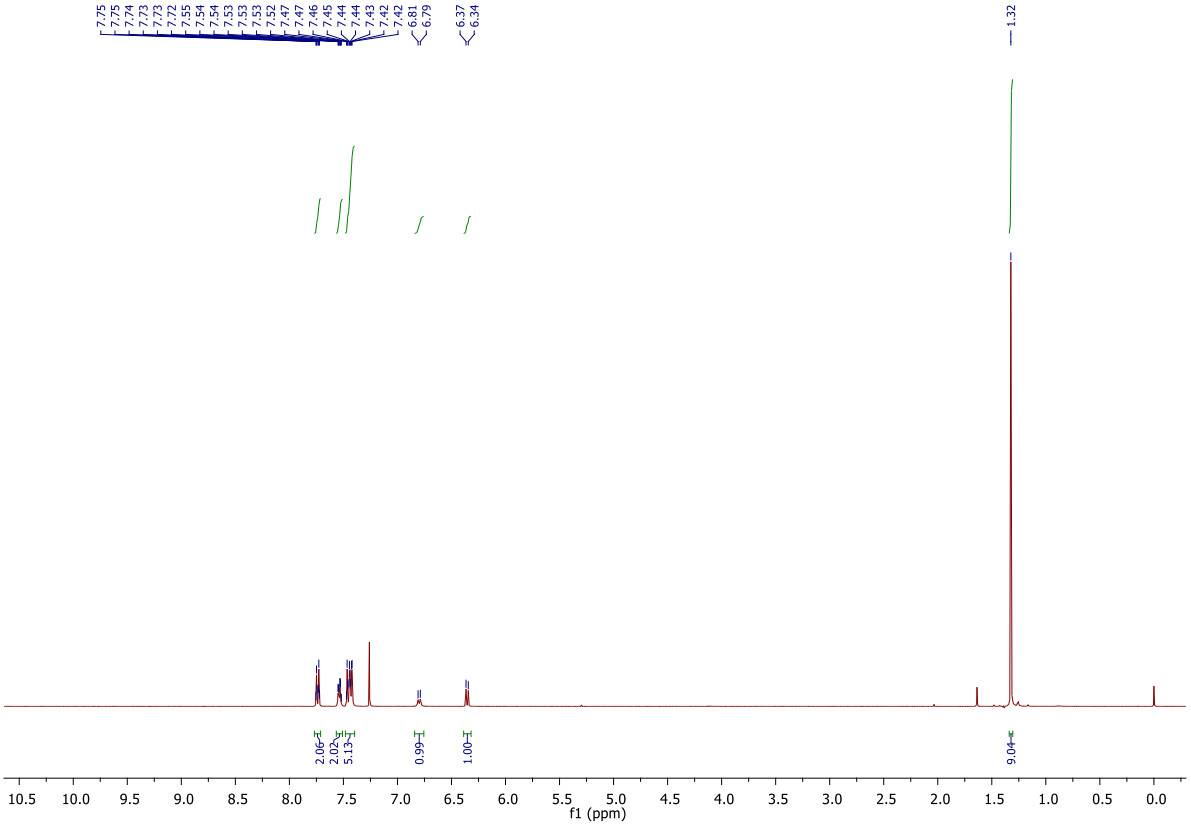
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



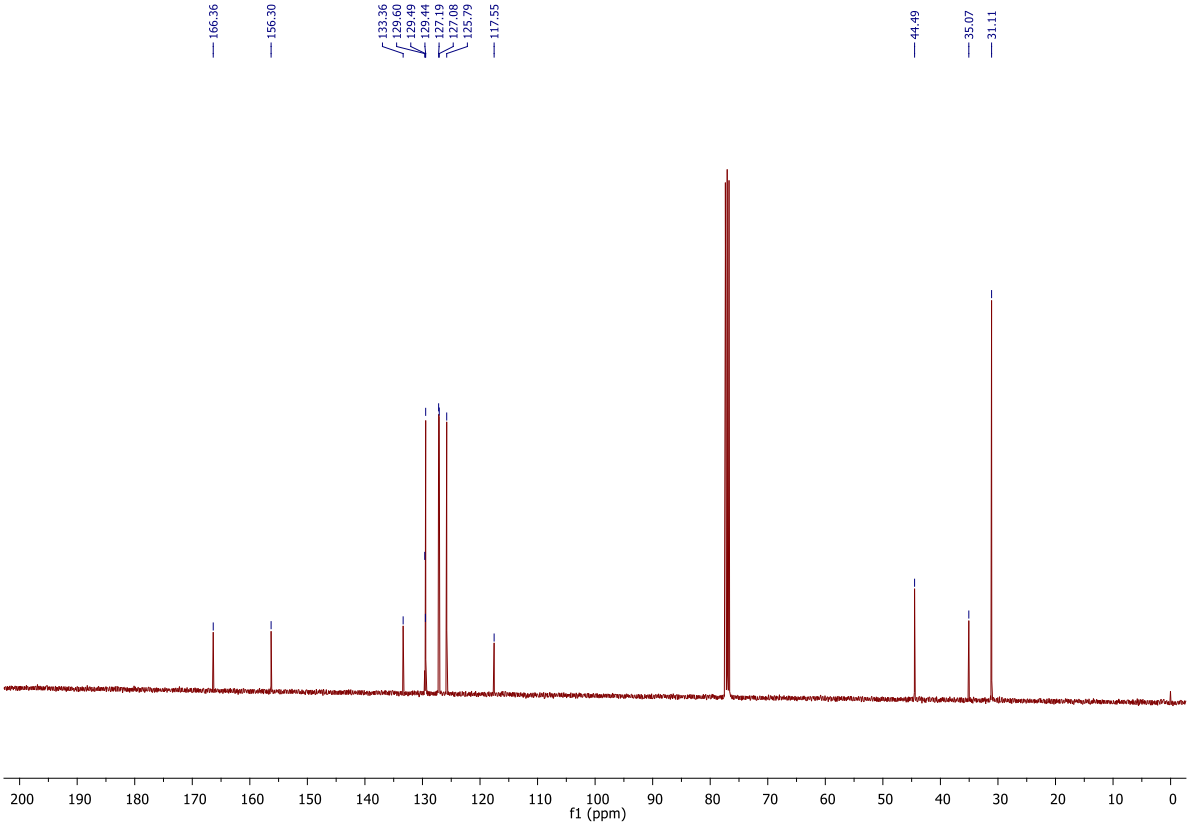
4-(*tert*-butyl)-N-(cyano(phenyl)methyl)benzamide (2c)



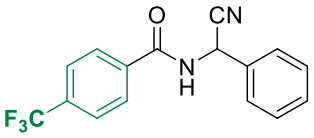
^{1}H NMR (400 MHz, $CDCl_3$)



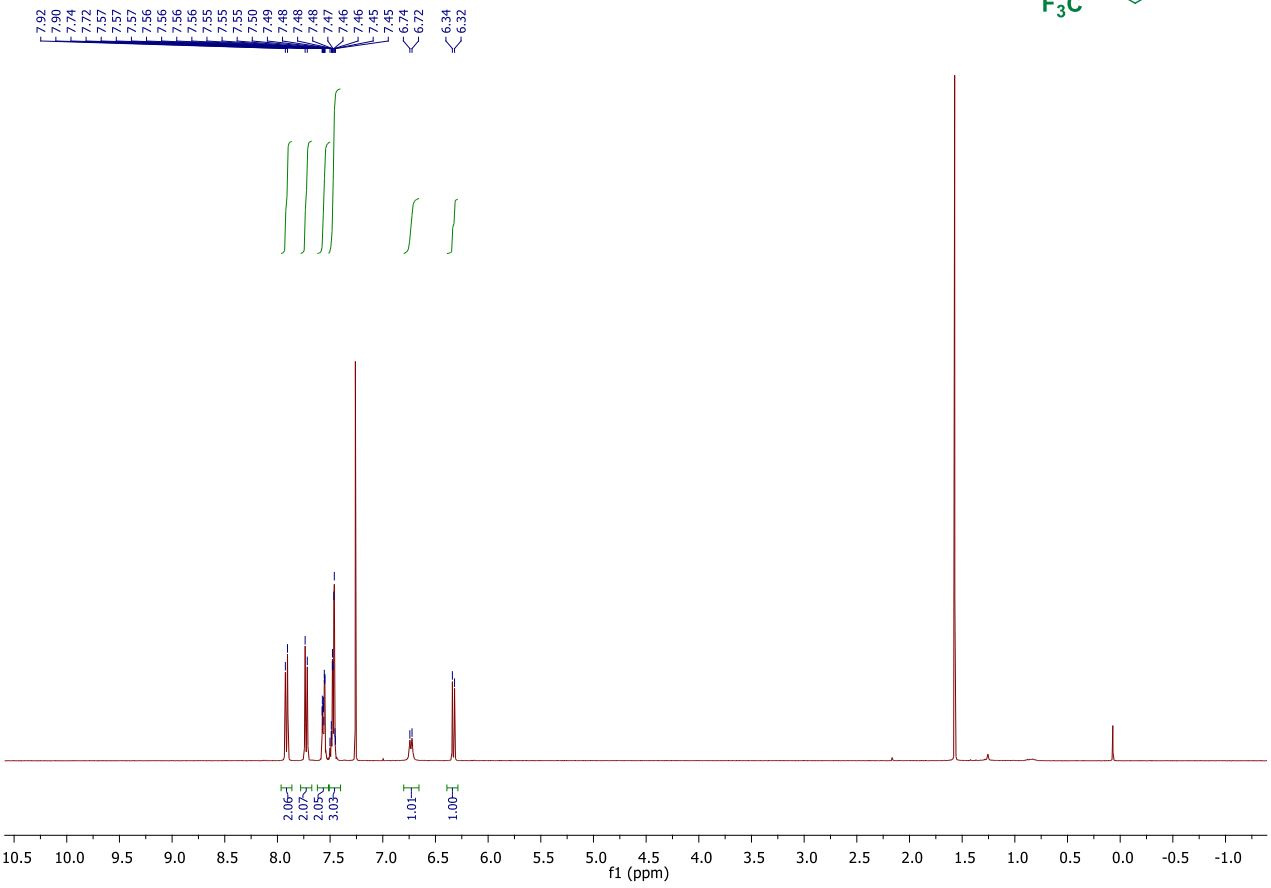
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



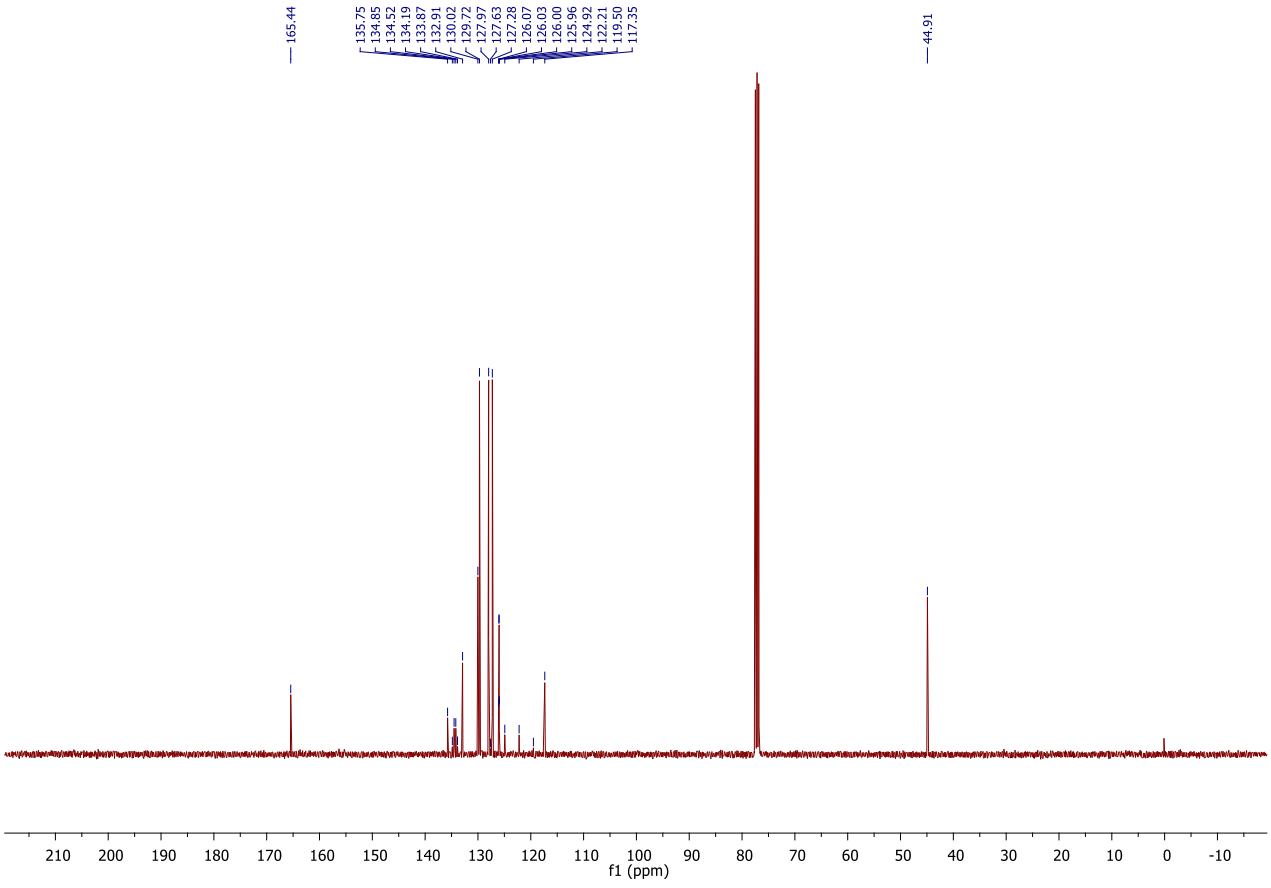
_N_-[cyano(phenyl)methyl]-4-(trifluoromethyl)benzamide (2d)



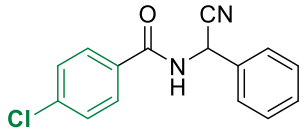
^{1}H NMR (400 MHz, $CDCl_3$)



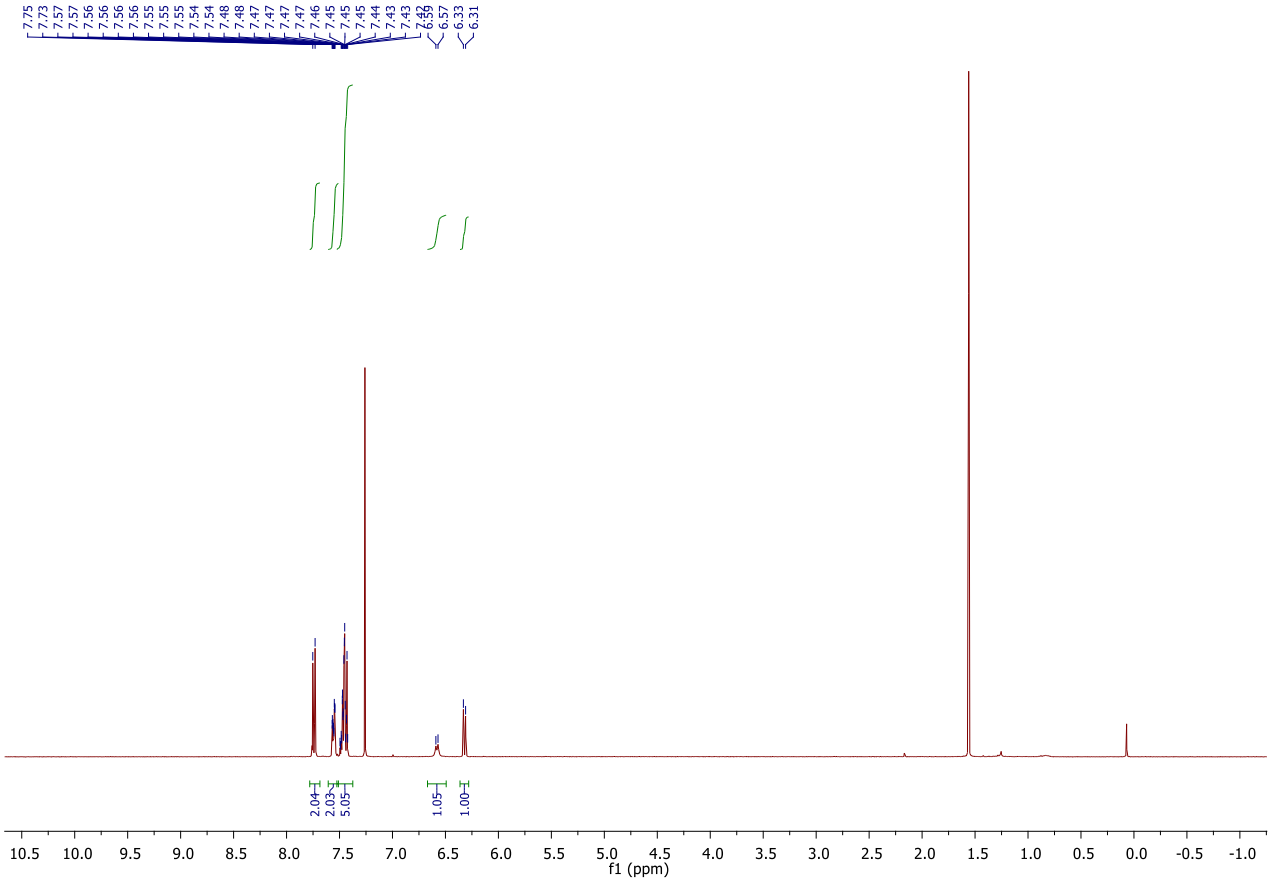
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



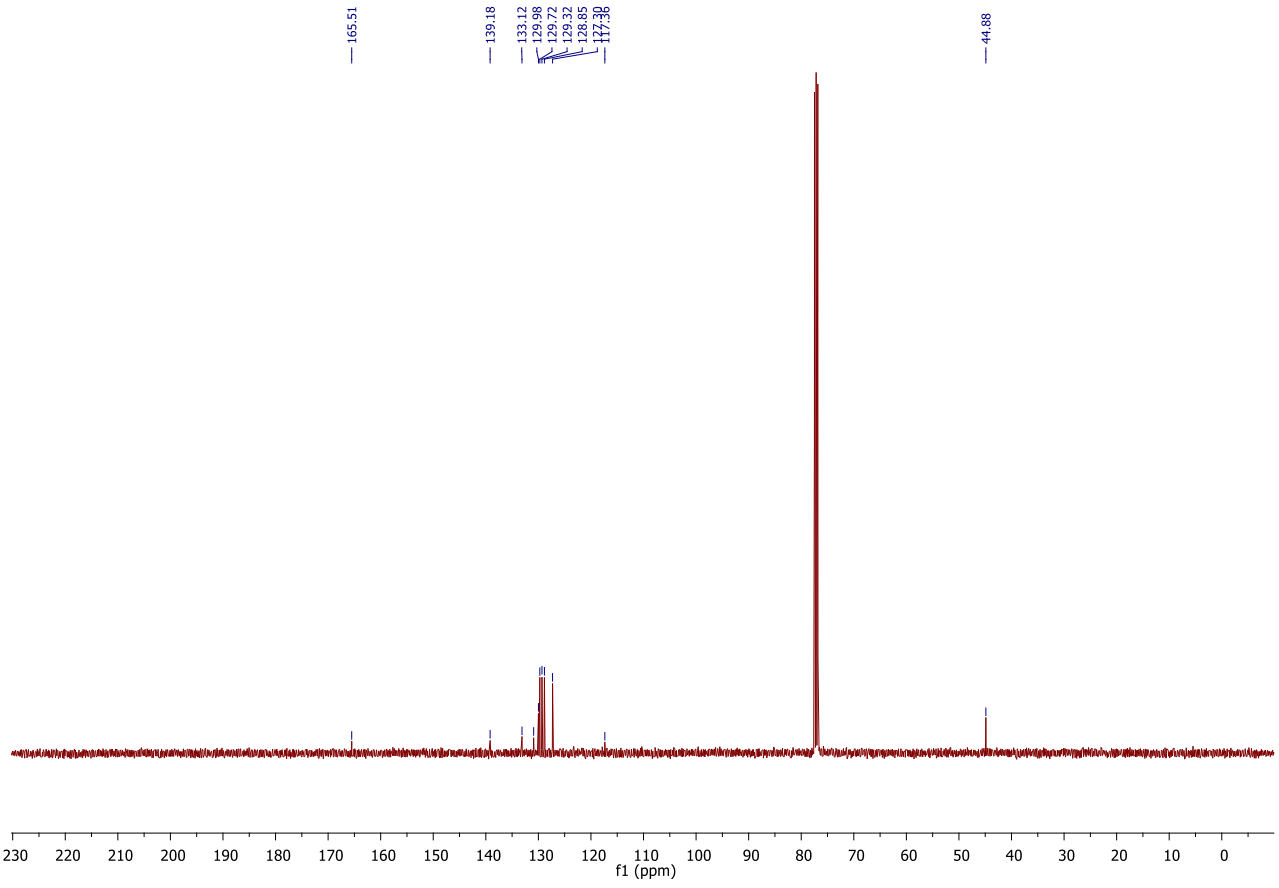
4-chloro-*N*-[cyano(phenyl)methyl]benzamide (2e)



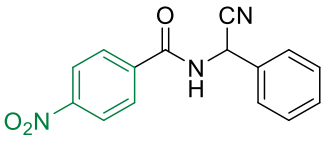
^{1}H NMR (400 MHz, $CDCl_3$)



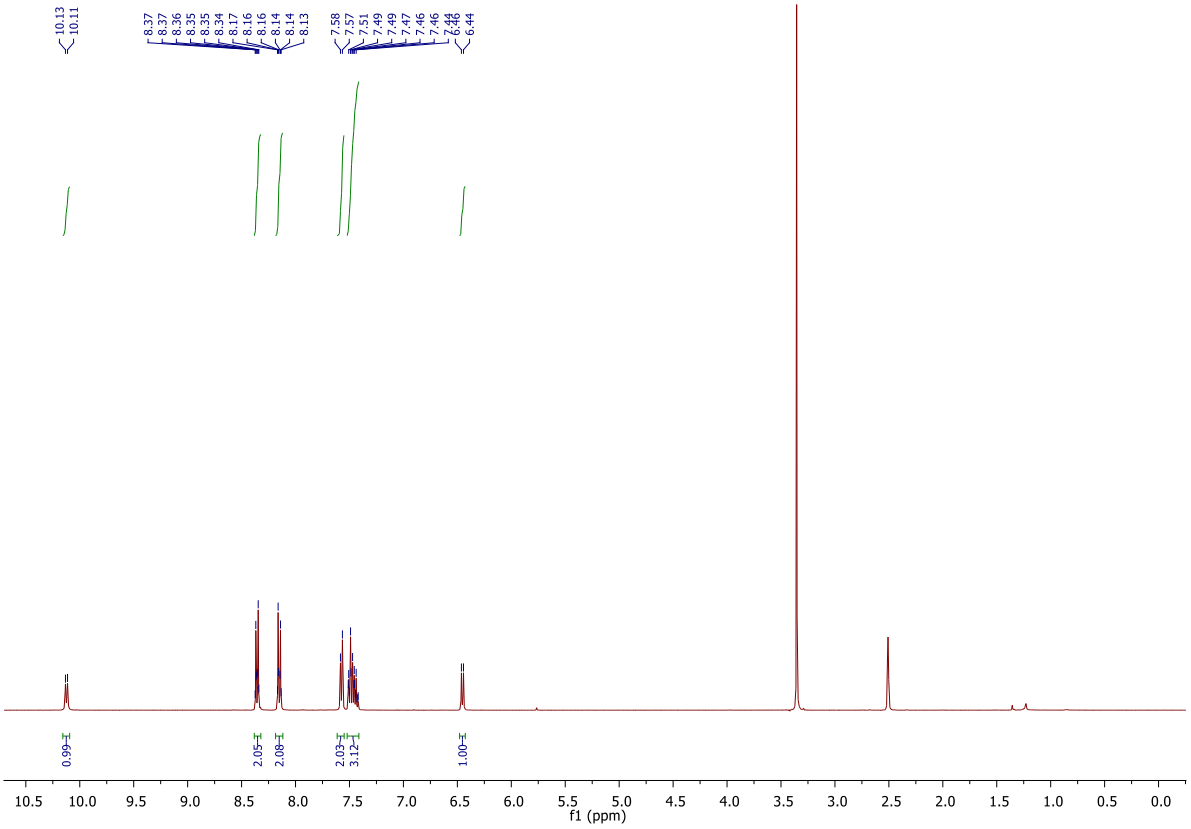
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



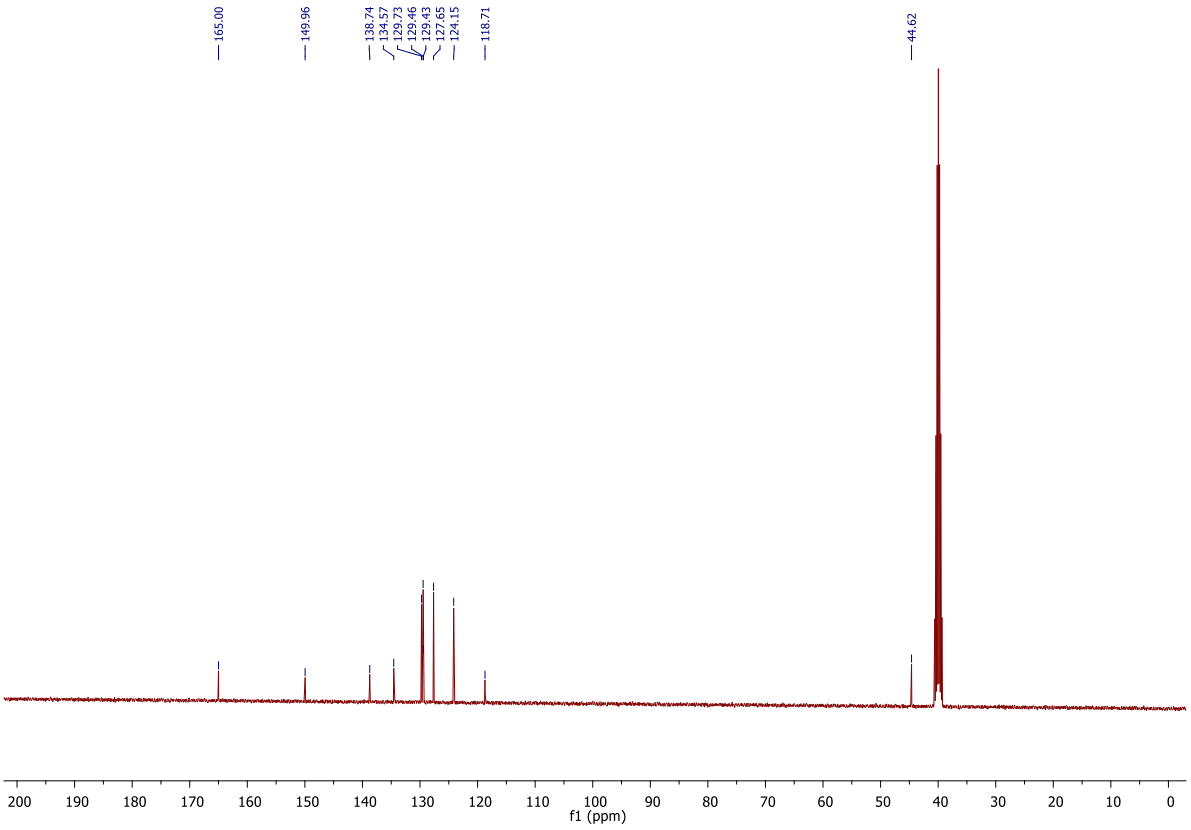
N-(cyano(phenyl)methyl)-4-nitrobenzamide (2f)



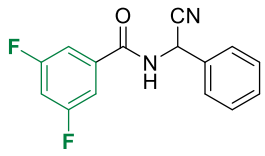
^{1}H NMR (400 MHz, DMSO-d_6)



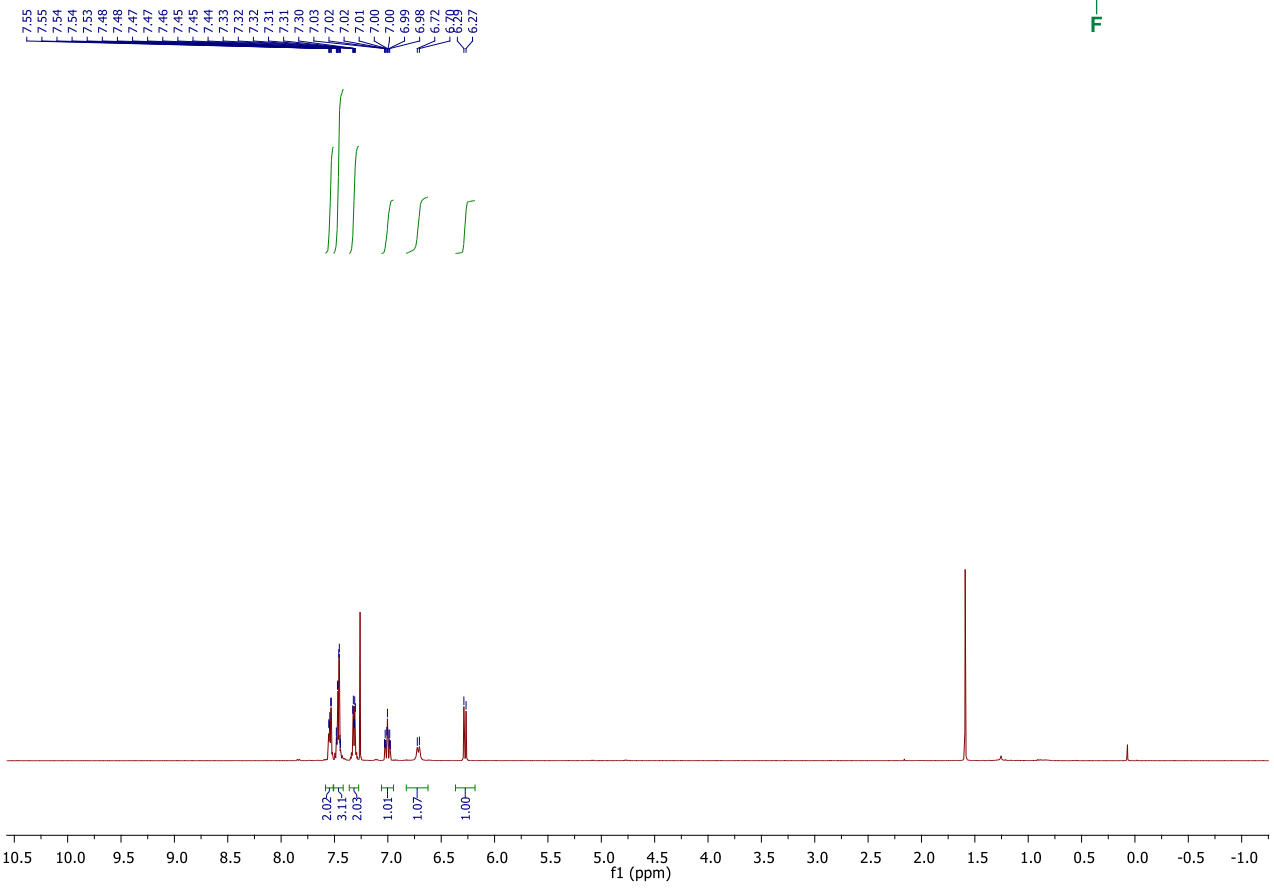
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)



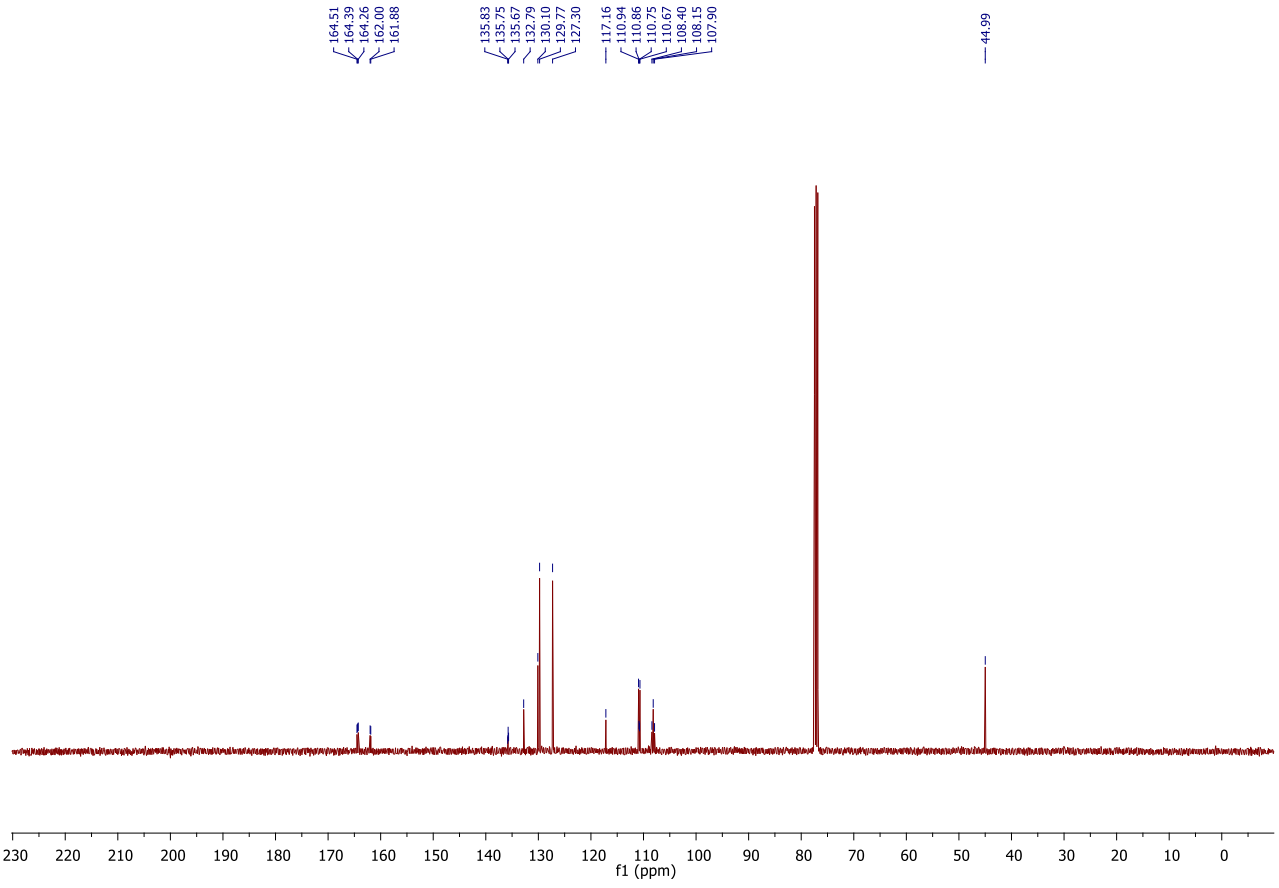
N-[cyano(phenyl)methyl]-3,5-difluoro-benzamide (2g)



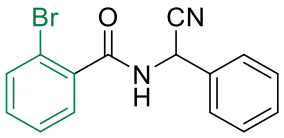
^{1}H NMR (400 MHz, $CDCl_3$)



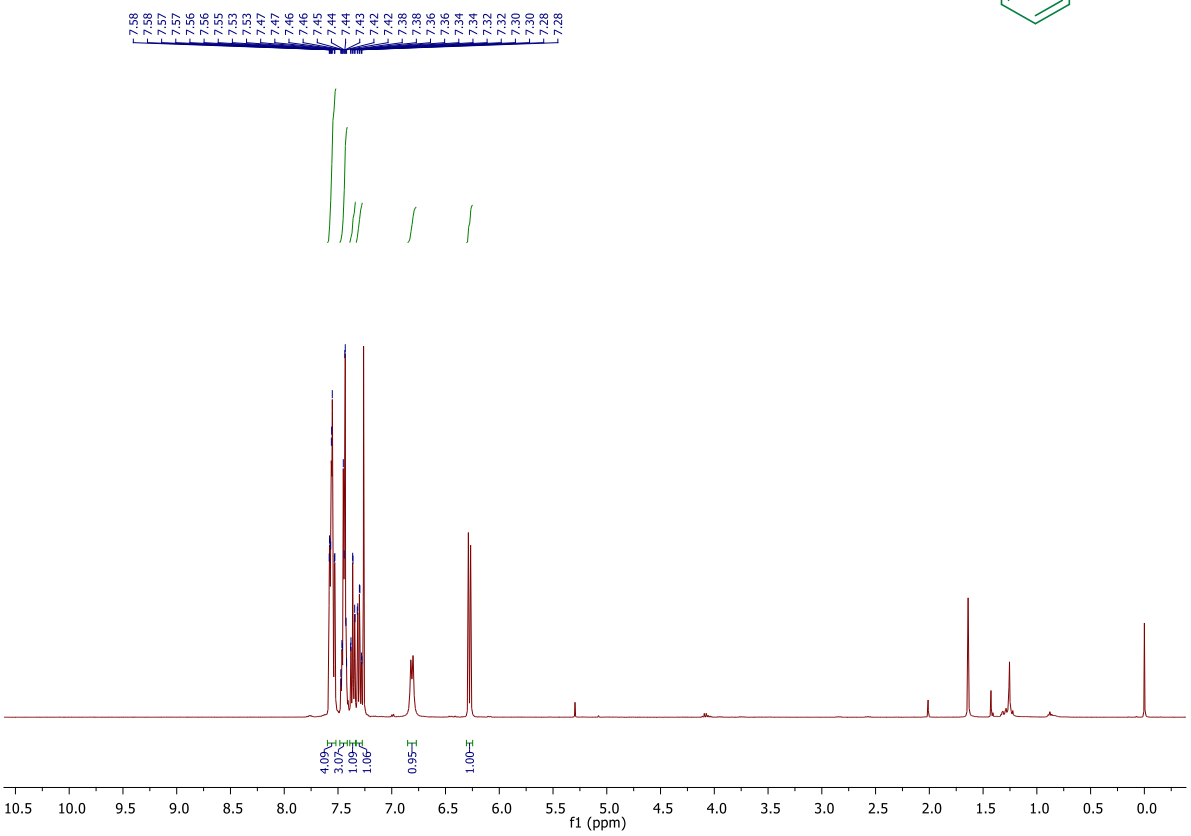
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



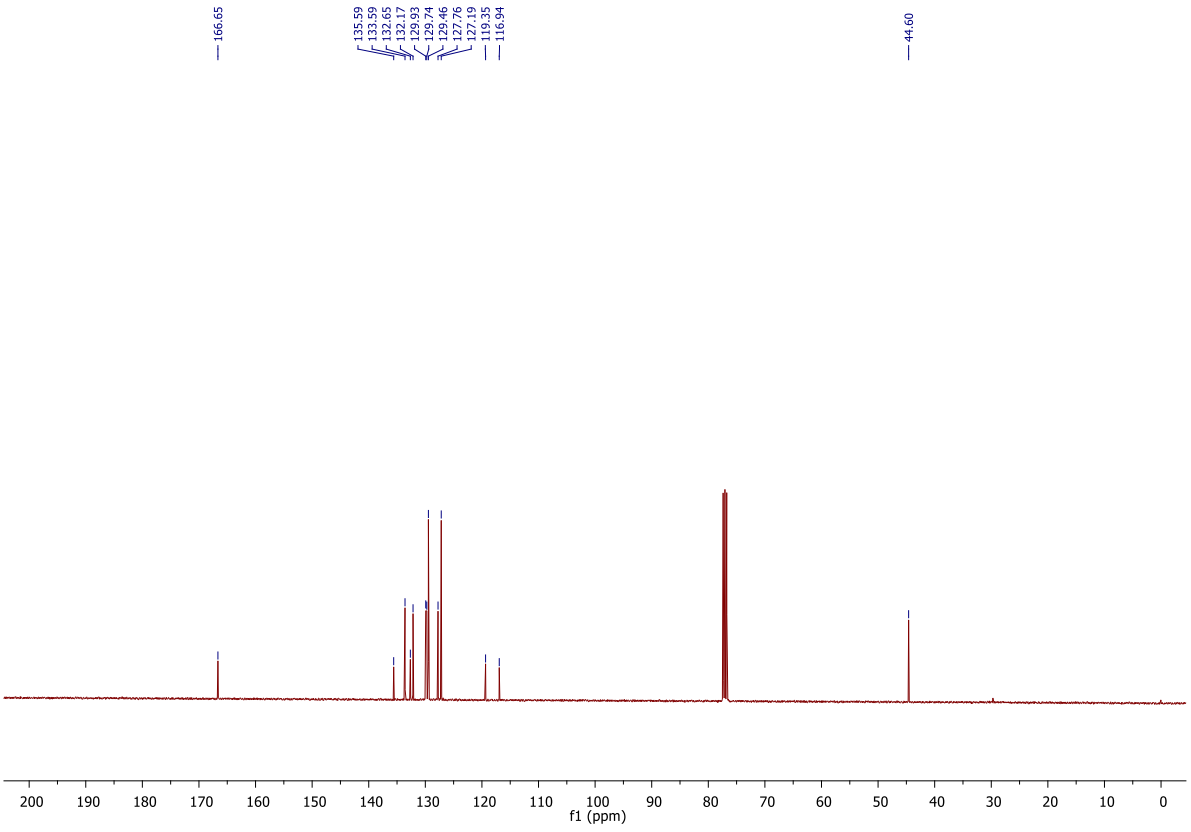
2-bromo-*N*-(cyano(phenyl)methyl)benzamide (2h)



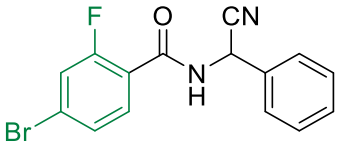
^{1}H NMR (400 MHz, $CDCl_3$)



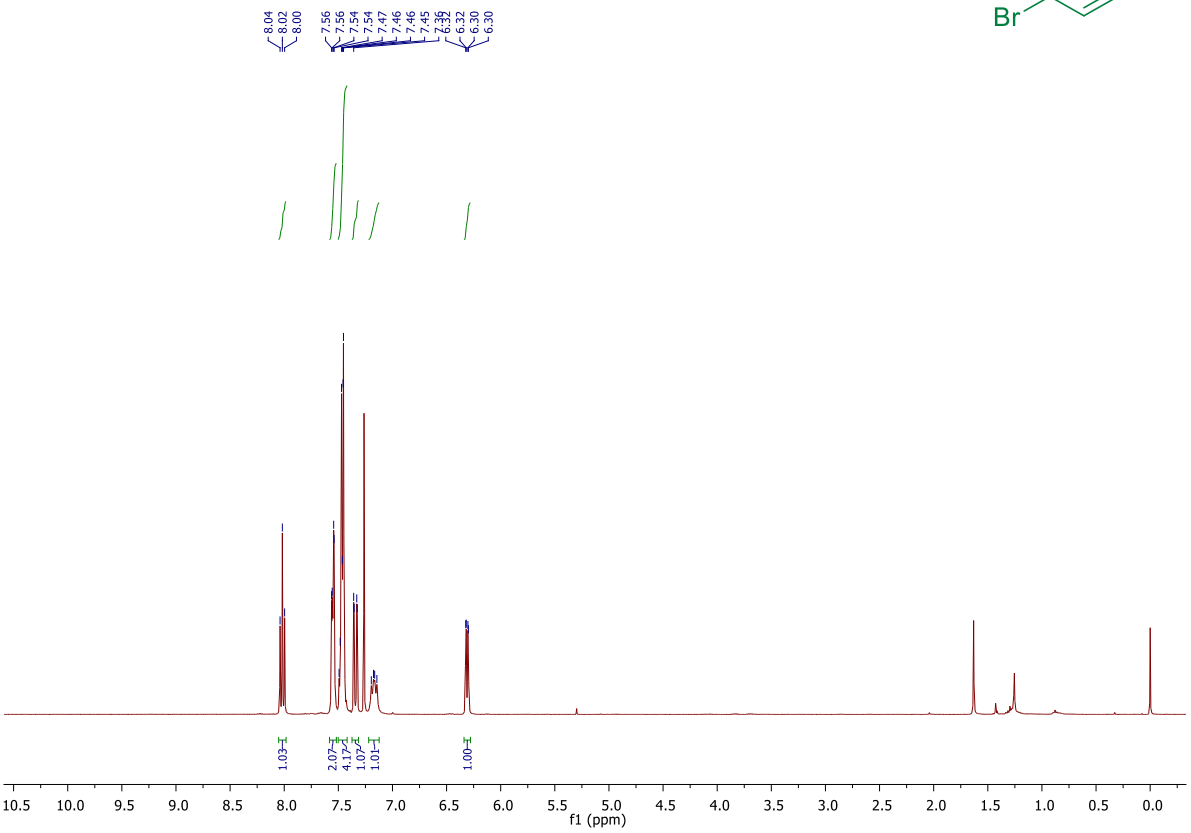
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



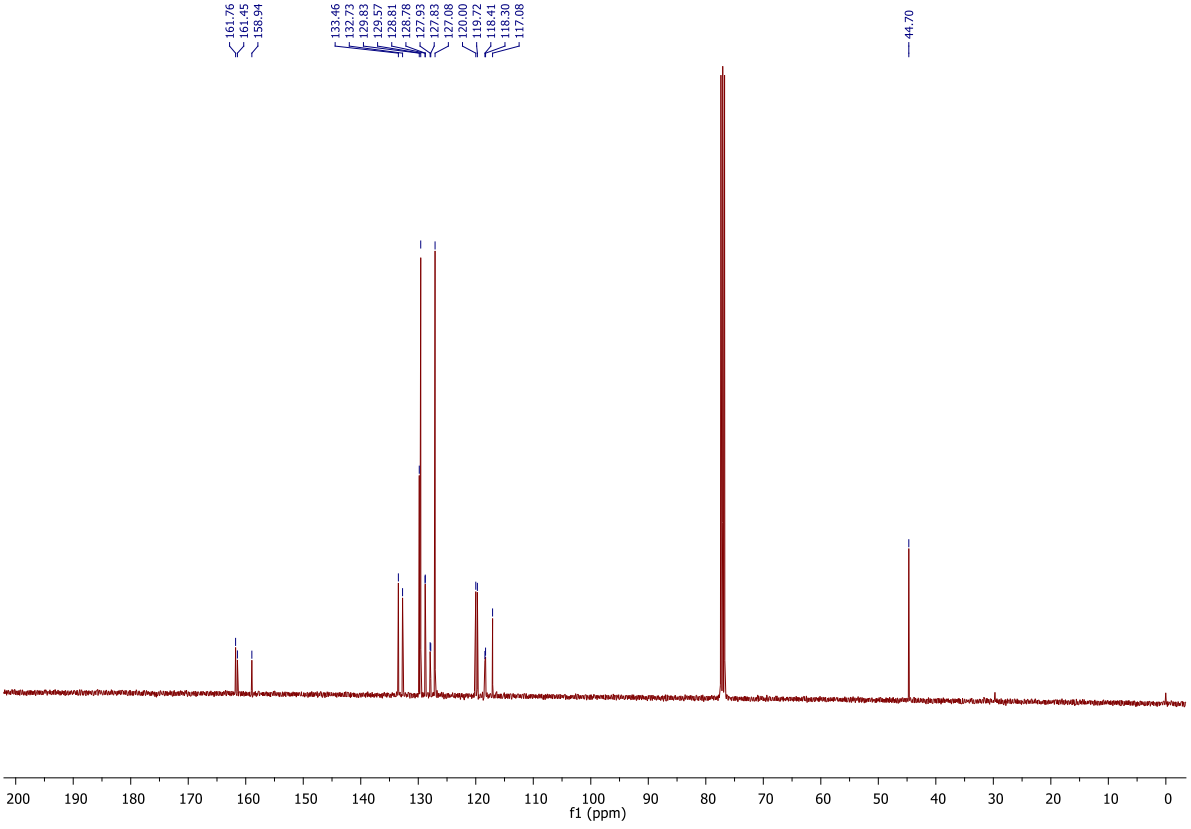
4-bromo-*N*-(cyano(phenyl)methyl)-2-fluorobenzamide (2i)



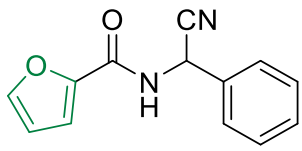
^{1}H NMR (400 MHz, $CDCl_3$)



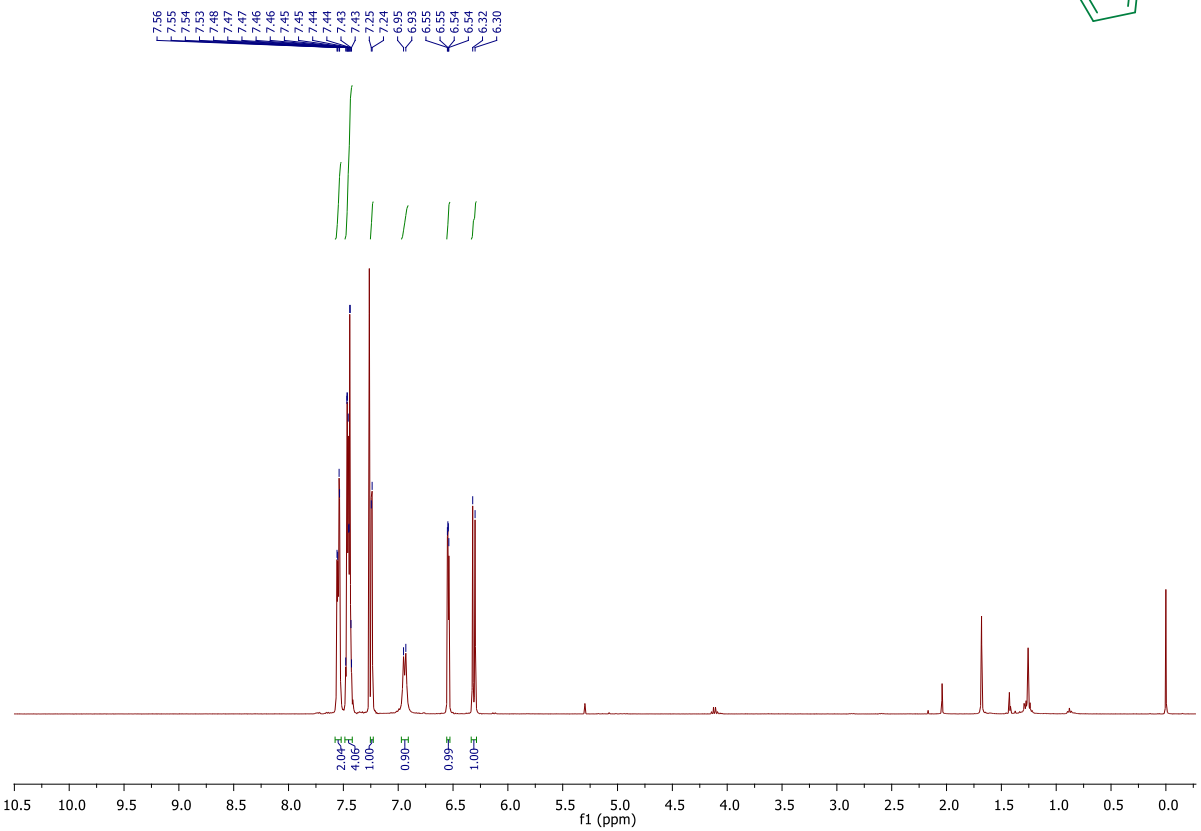
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



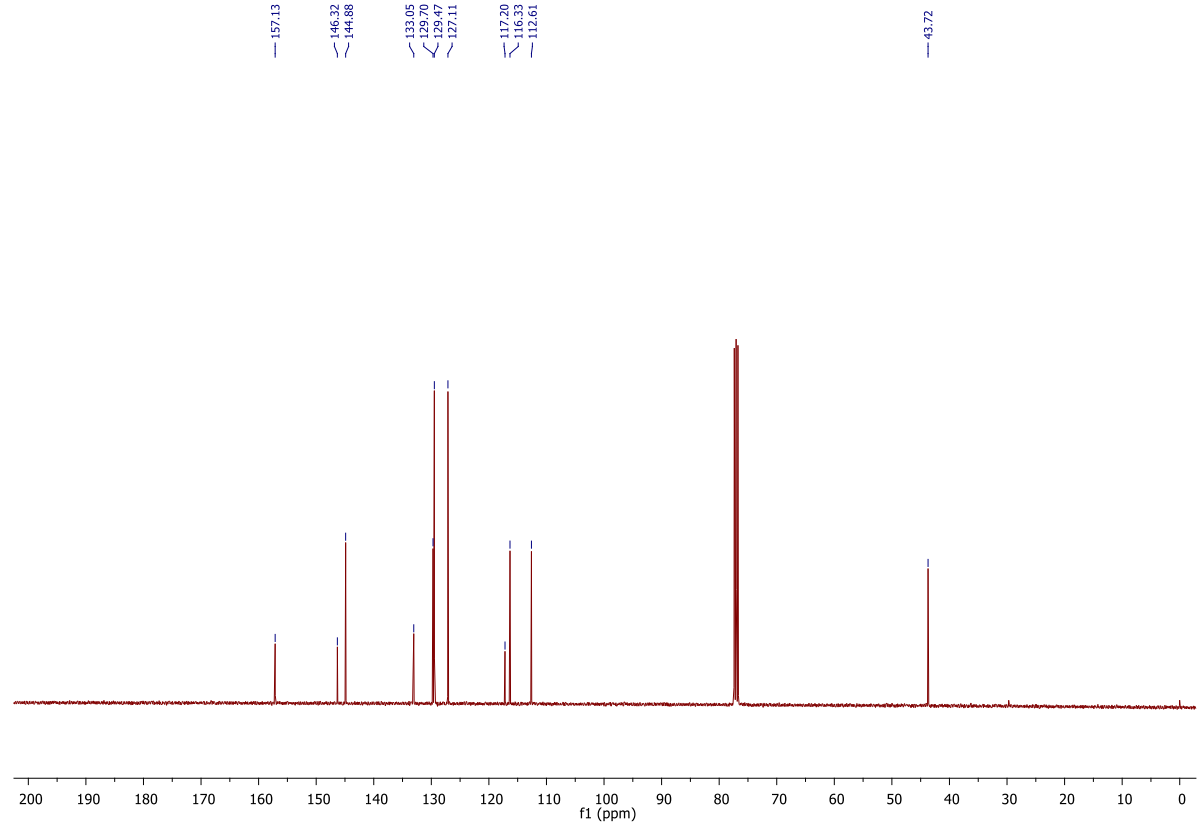
N-(cyano(phenyl)methyl)furan-2-carboxamide (2j)



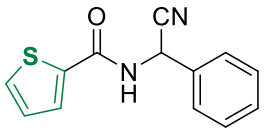
^{1}H NMR (400 MHz, $CDCl_3$)



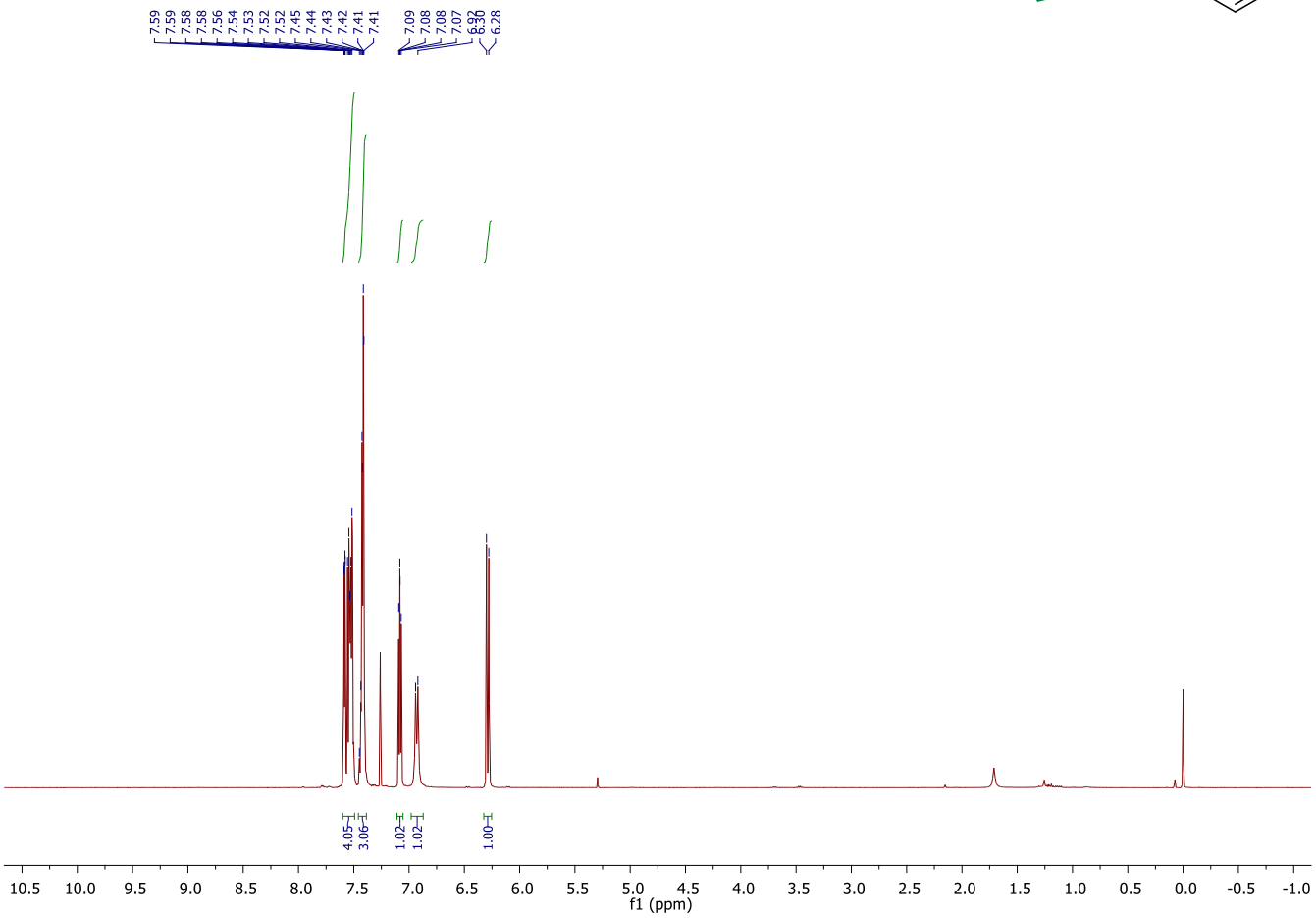
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



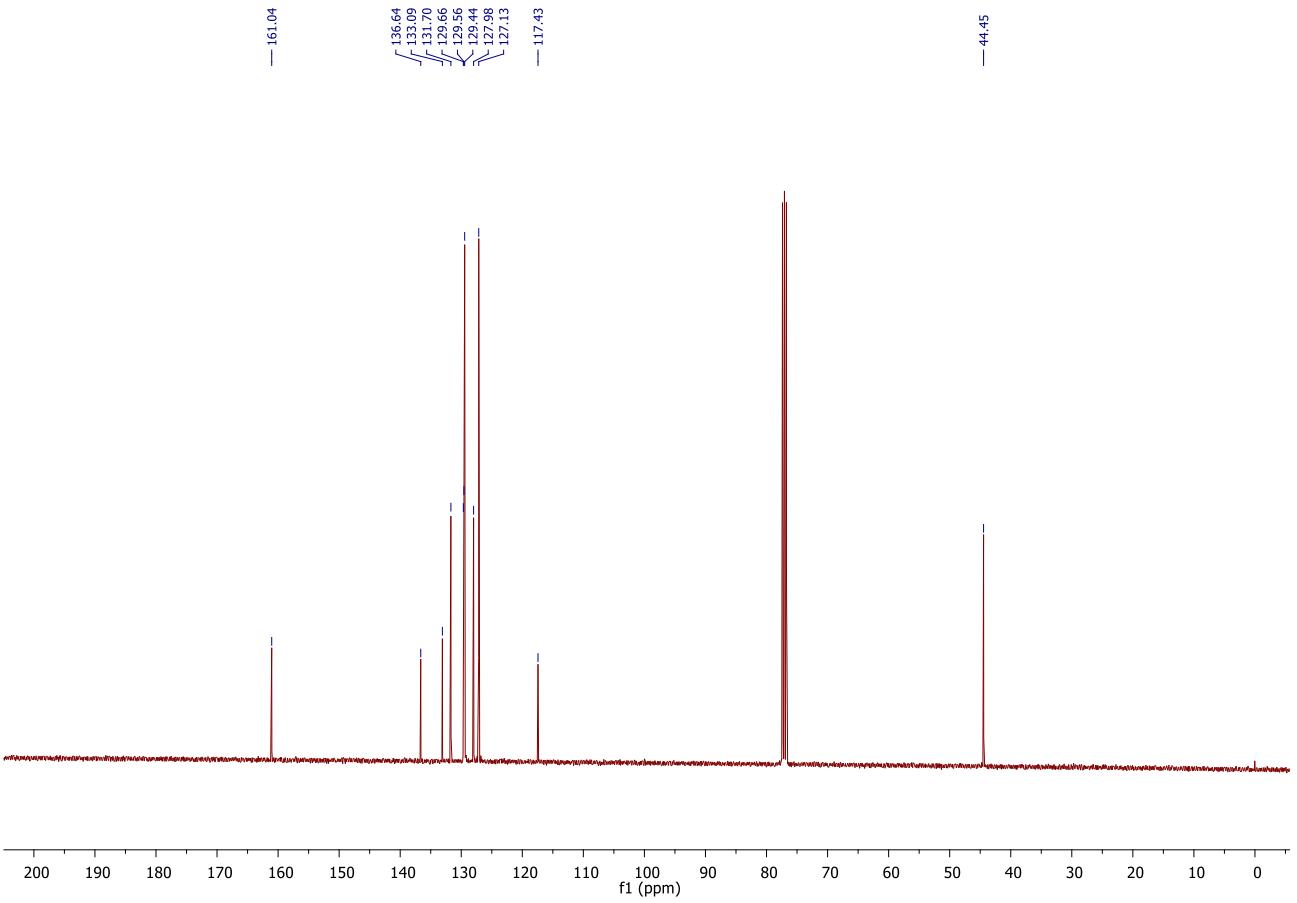
N-[cyano(phenyl)methyl]thiophene-2-carboxamide (2k)



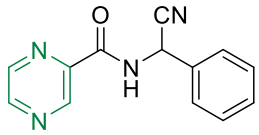
^{1}H NMR (400 MHz, $CDCl_3$)



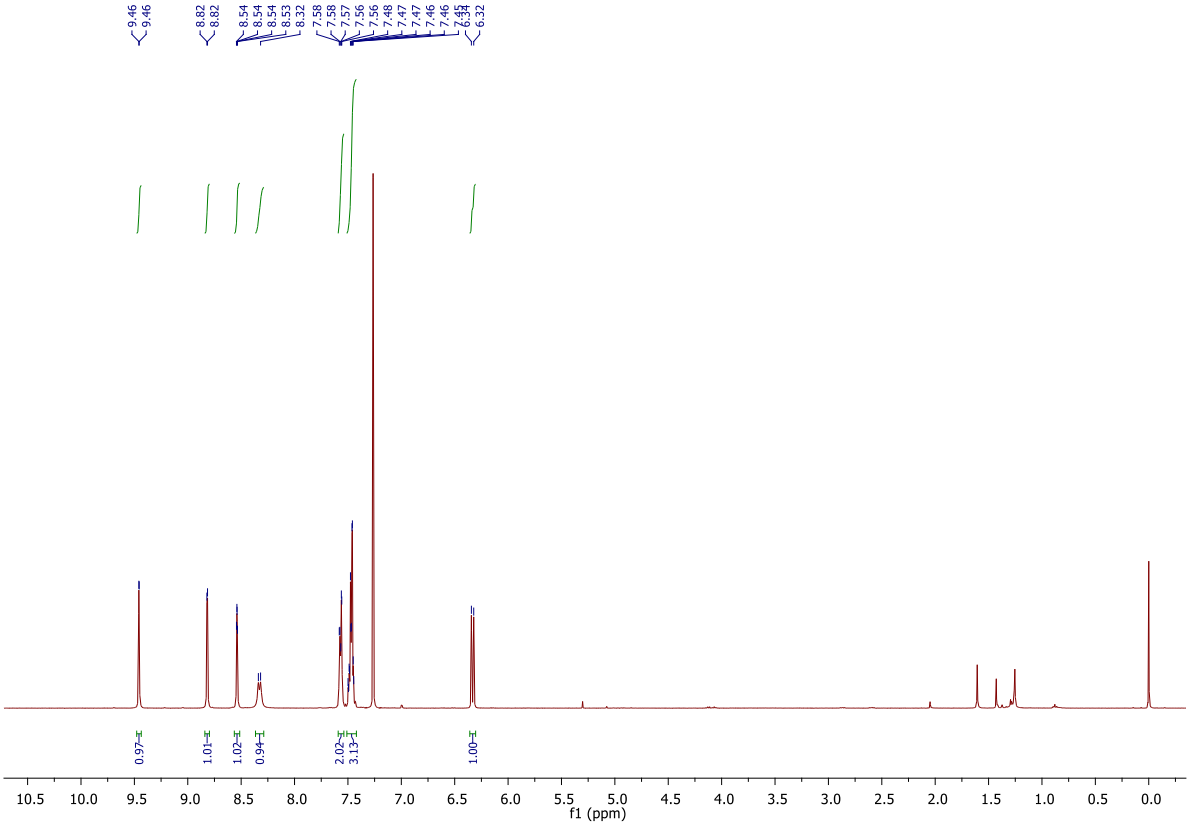
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



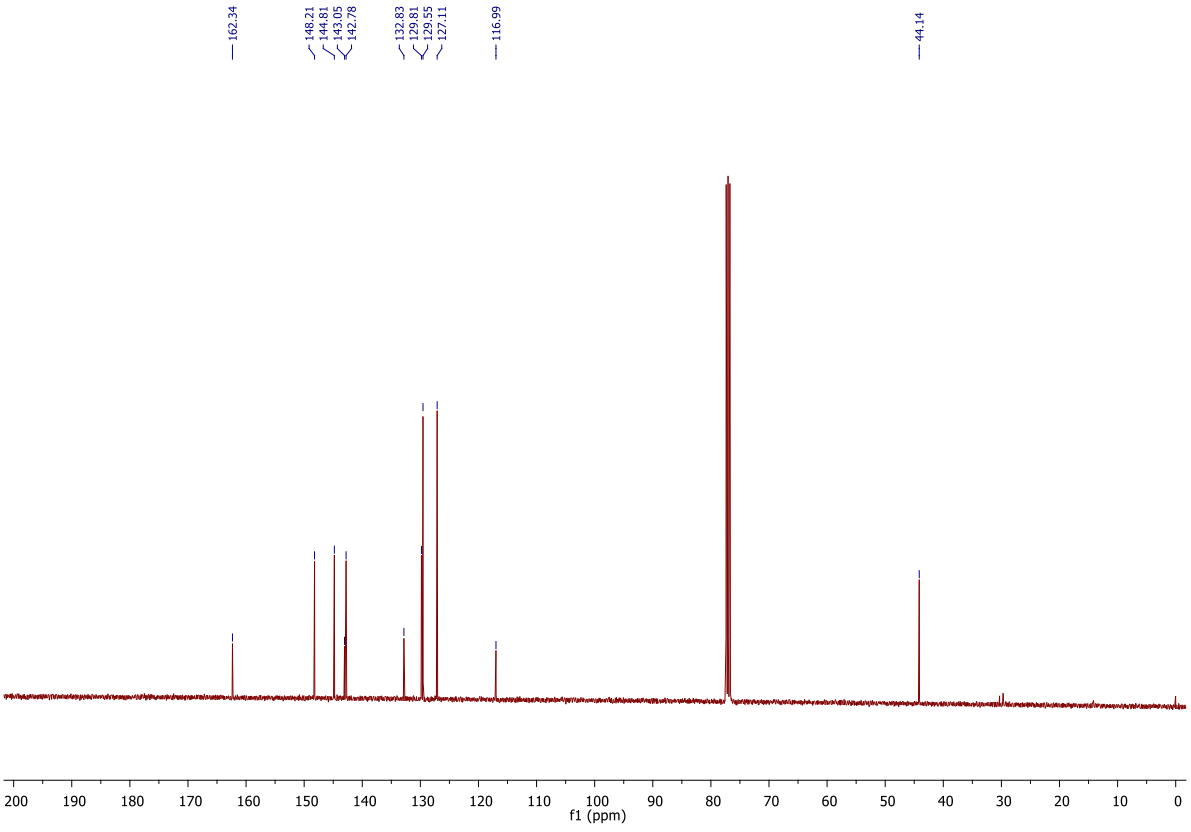
N-(cyano(phenyl)methyl)pyrazine-2-carboxamide (2l)



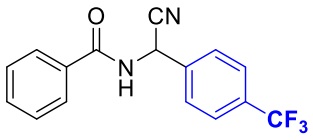
^{1}H NMR (400 MHz, $CDCl_3$)



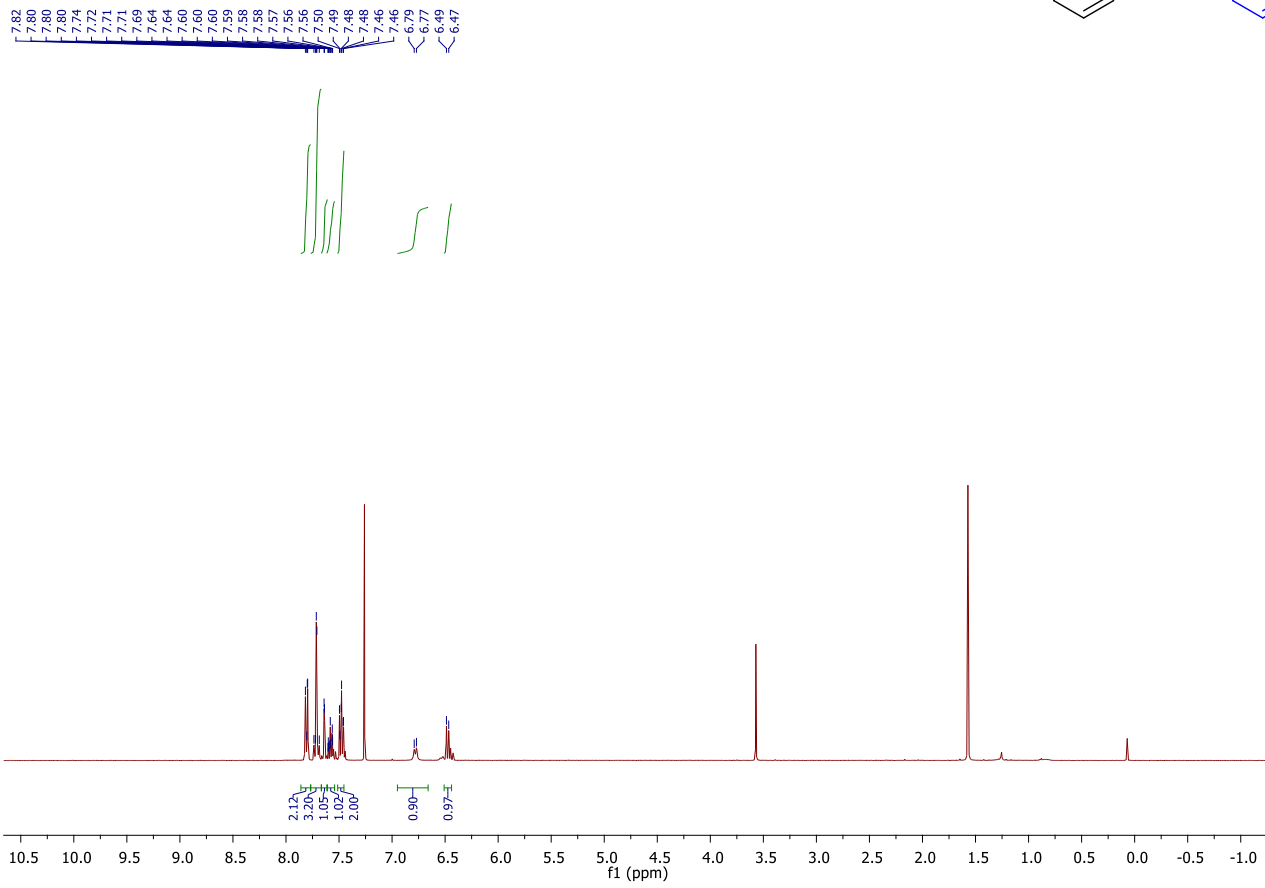
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)



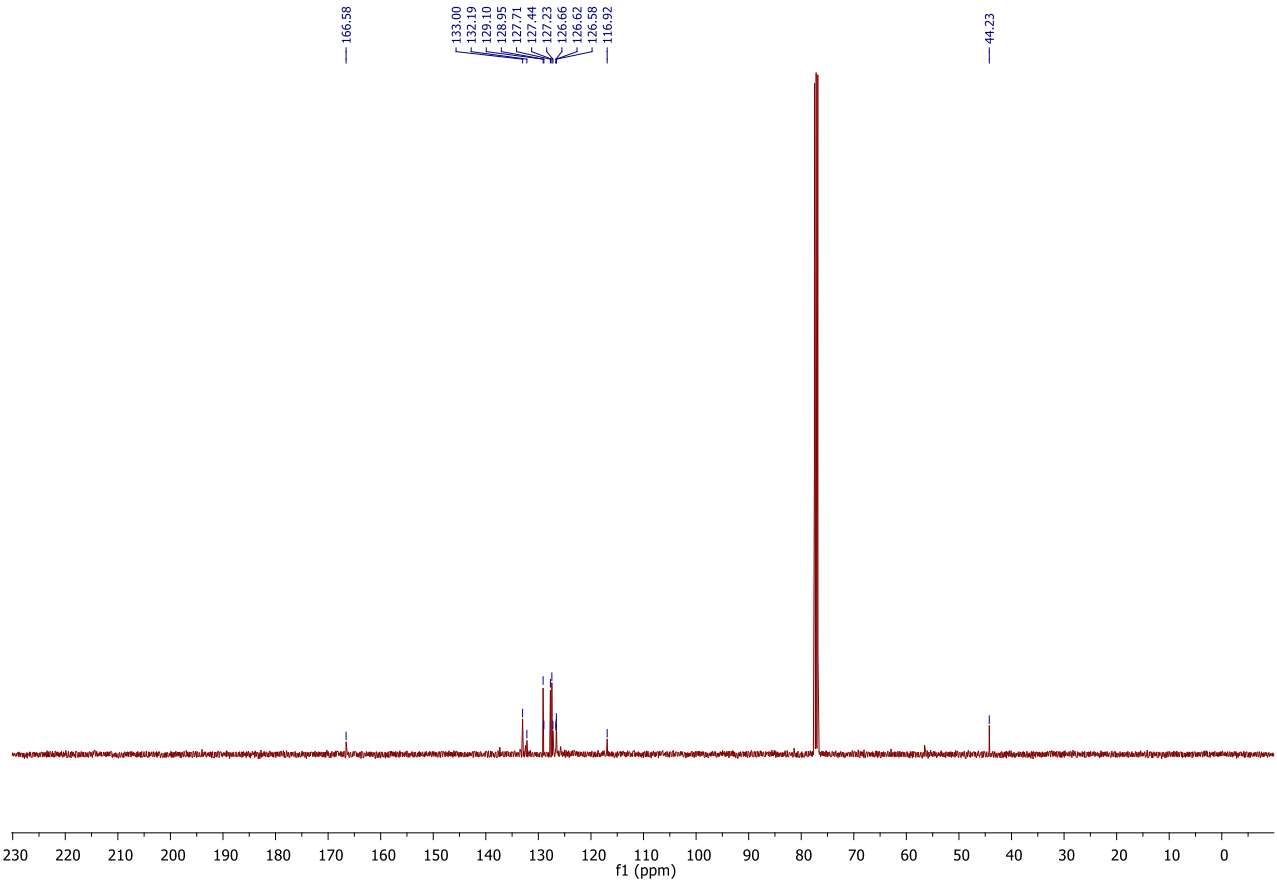
N-[cyano-[4-(trifluoromethyl)phenyl]methyl]benzamide (2m)



^{1}H NMR (400 MHz, $CDCl_3$)

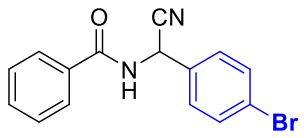


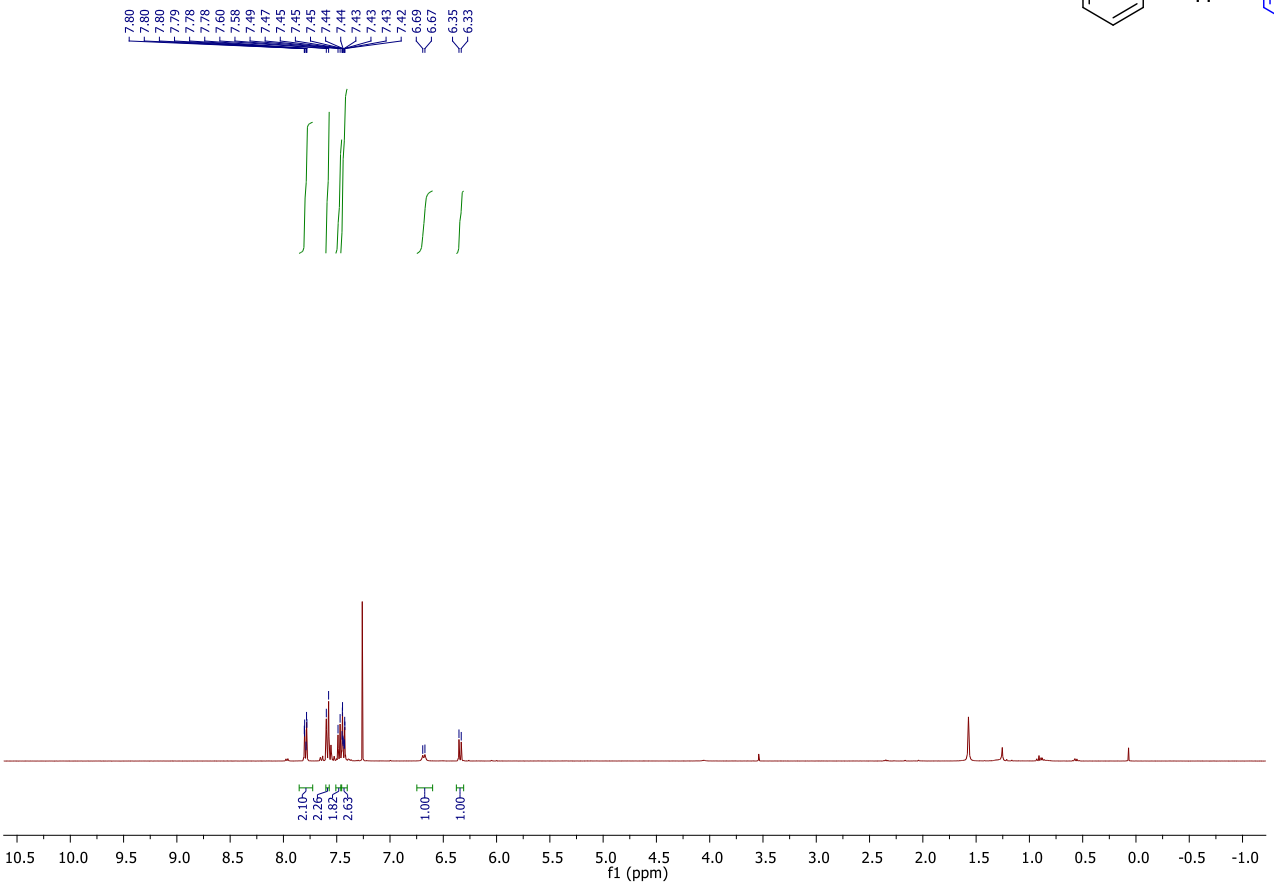
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



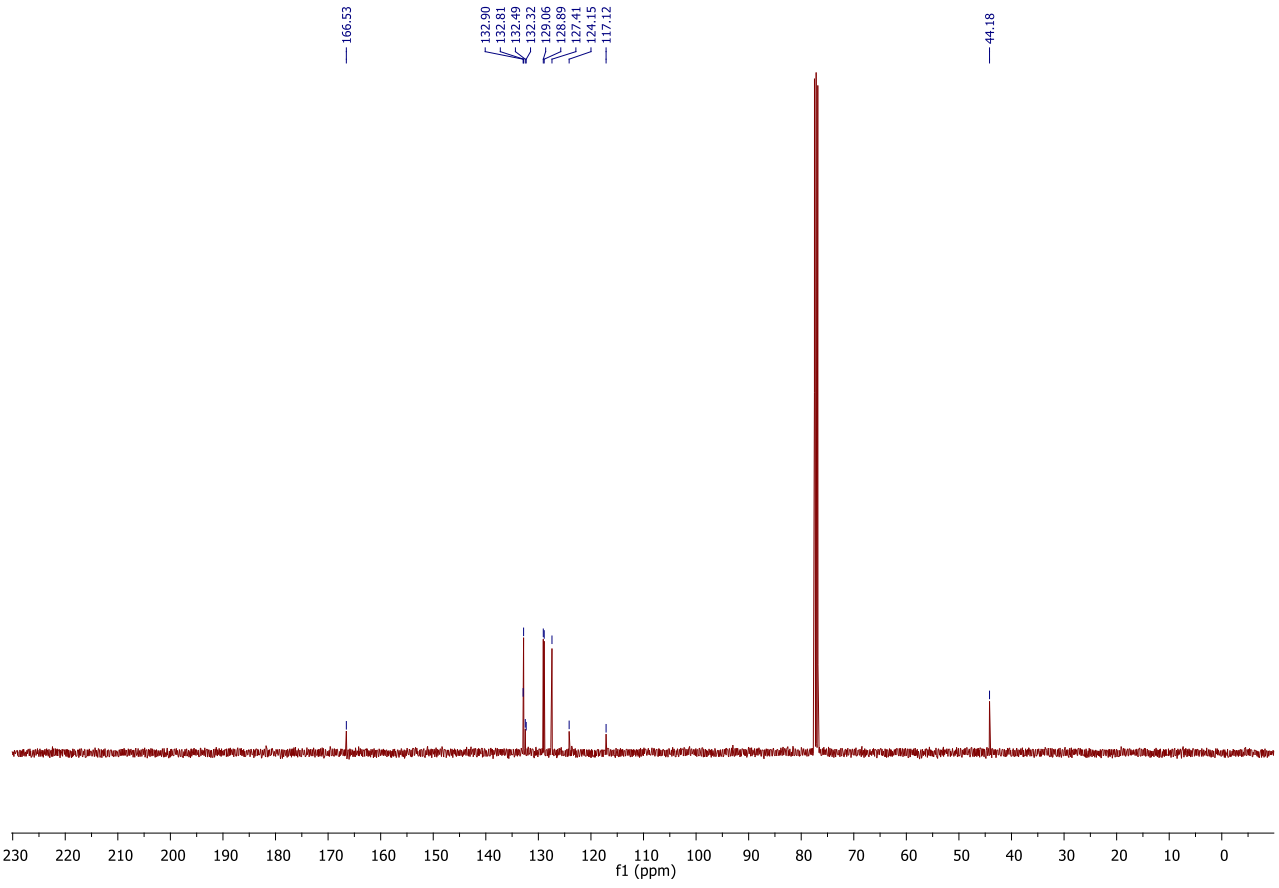
N-[(4-bromophenyl)-cyano-methyl]benzamide (2n)

^{1}H NMR (400 MHz, $CDCl_3$)

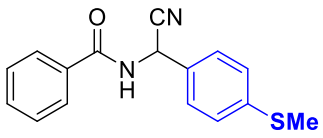




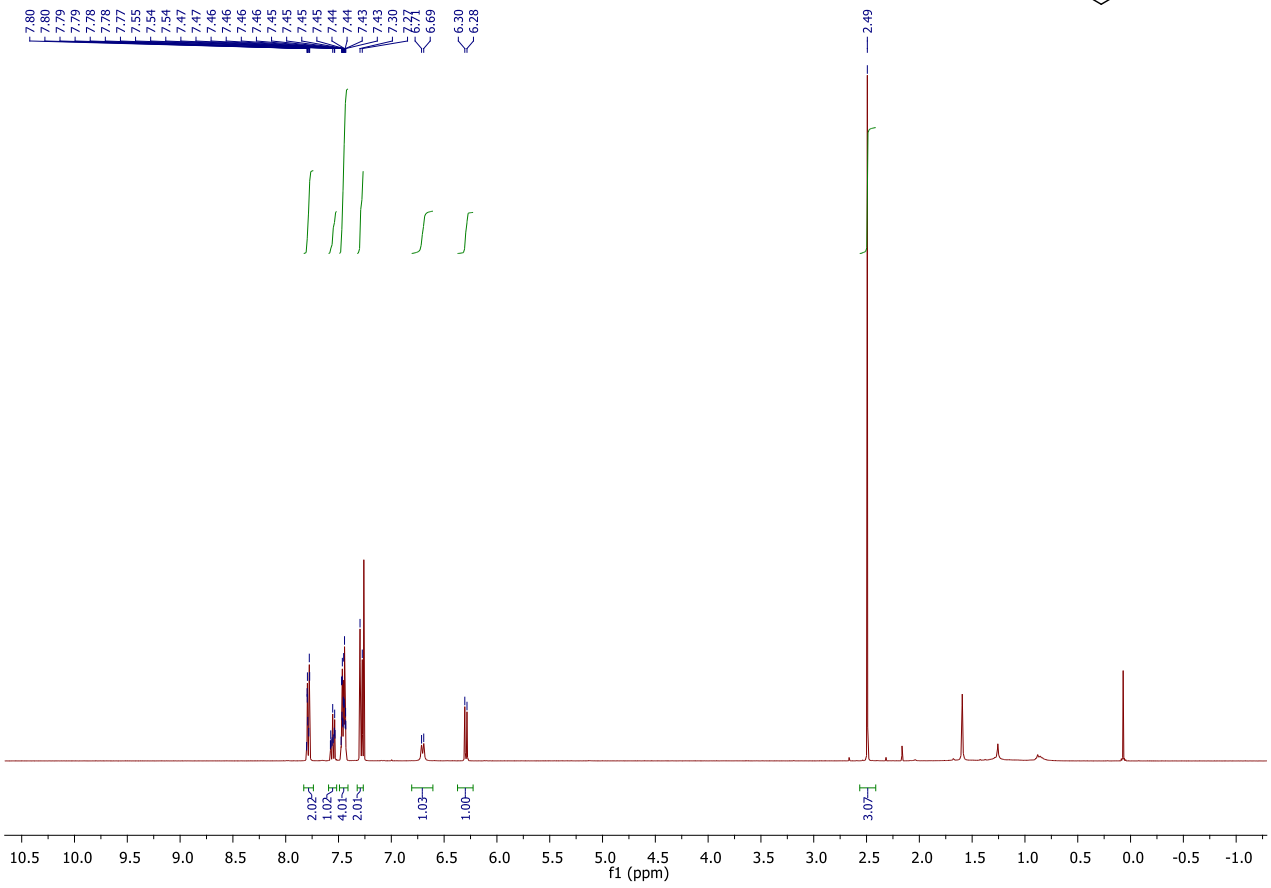
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



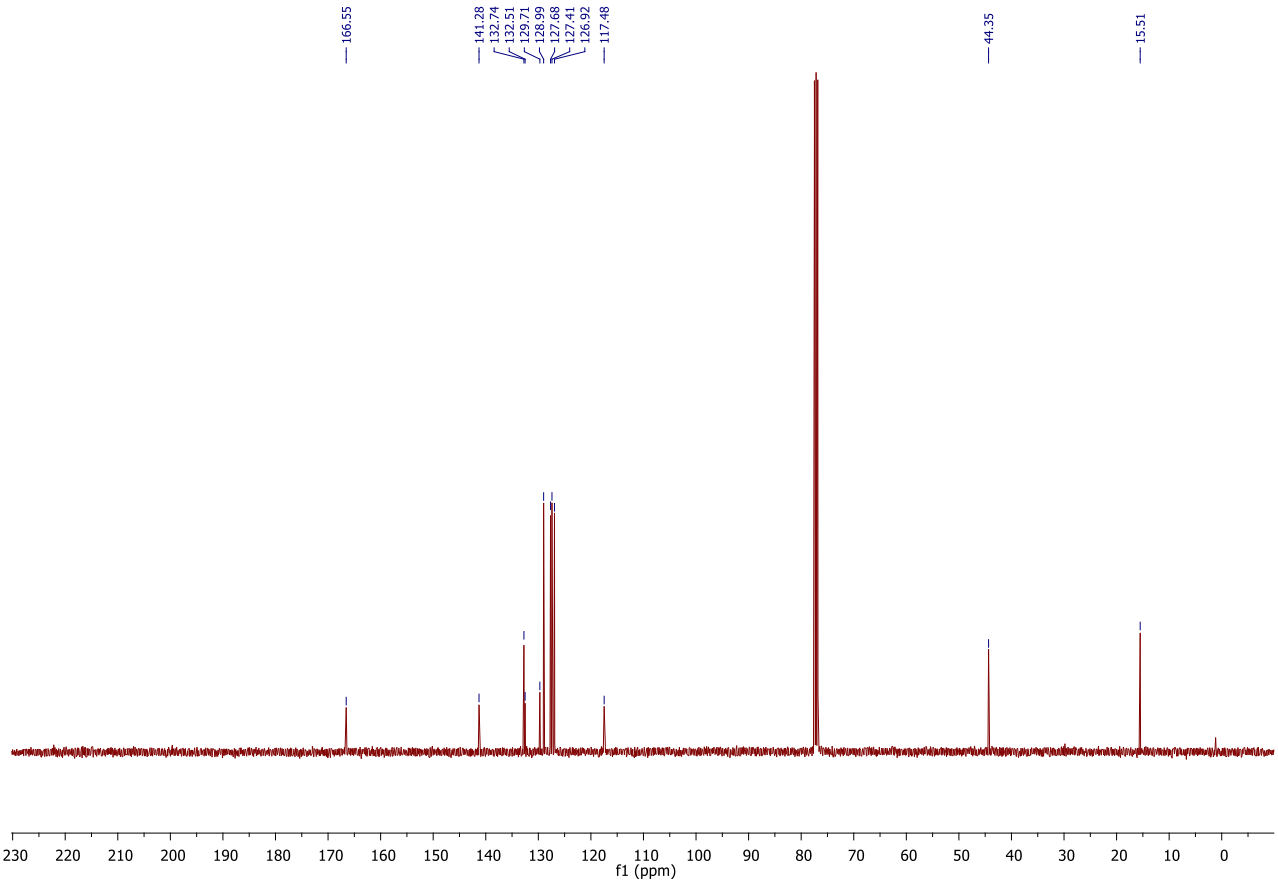
N-[cyano-(4-methylsulfanylphenyl)methyl]benzamide (2o)



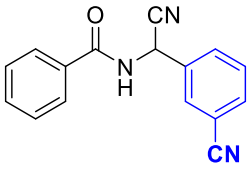
^{1}H NMR (400 MHz, $CDCl_3$)



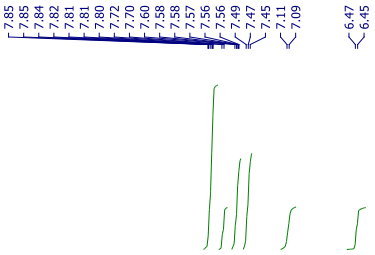
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

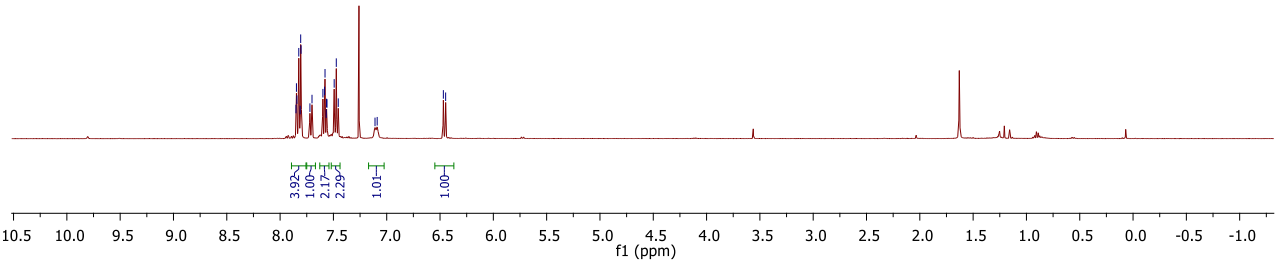


N-[cyano-(3-cyanophenyl)methyl]benzamide (2q)

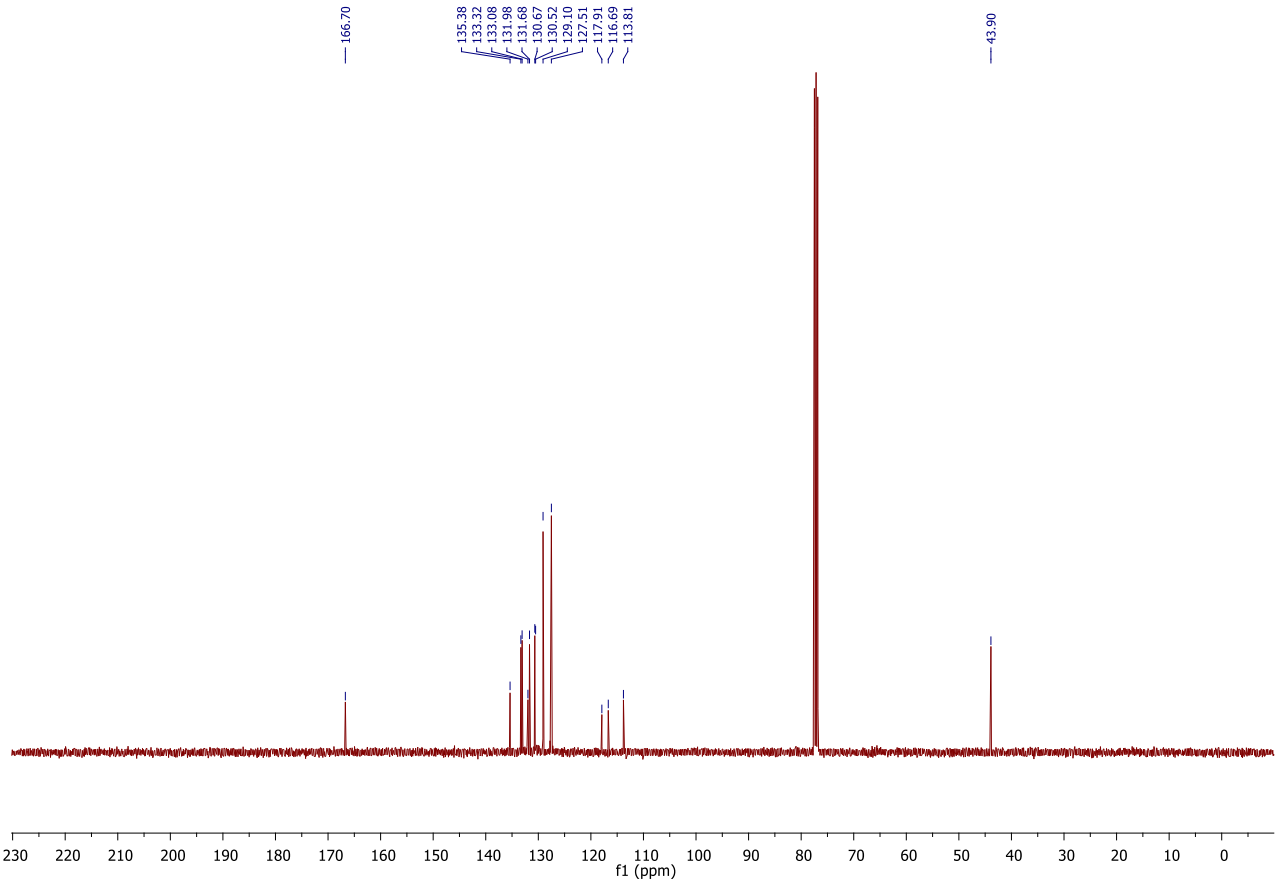


^{1}H NMR (400 MHz, $CDCl_3$)

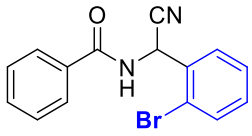




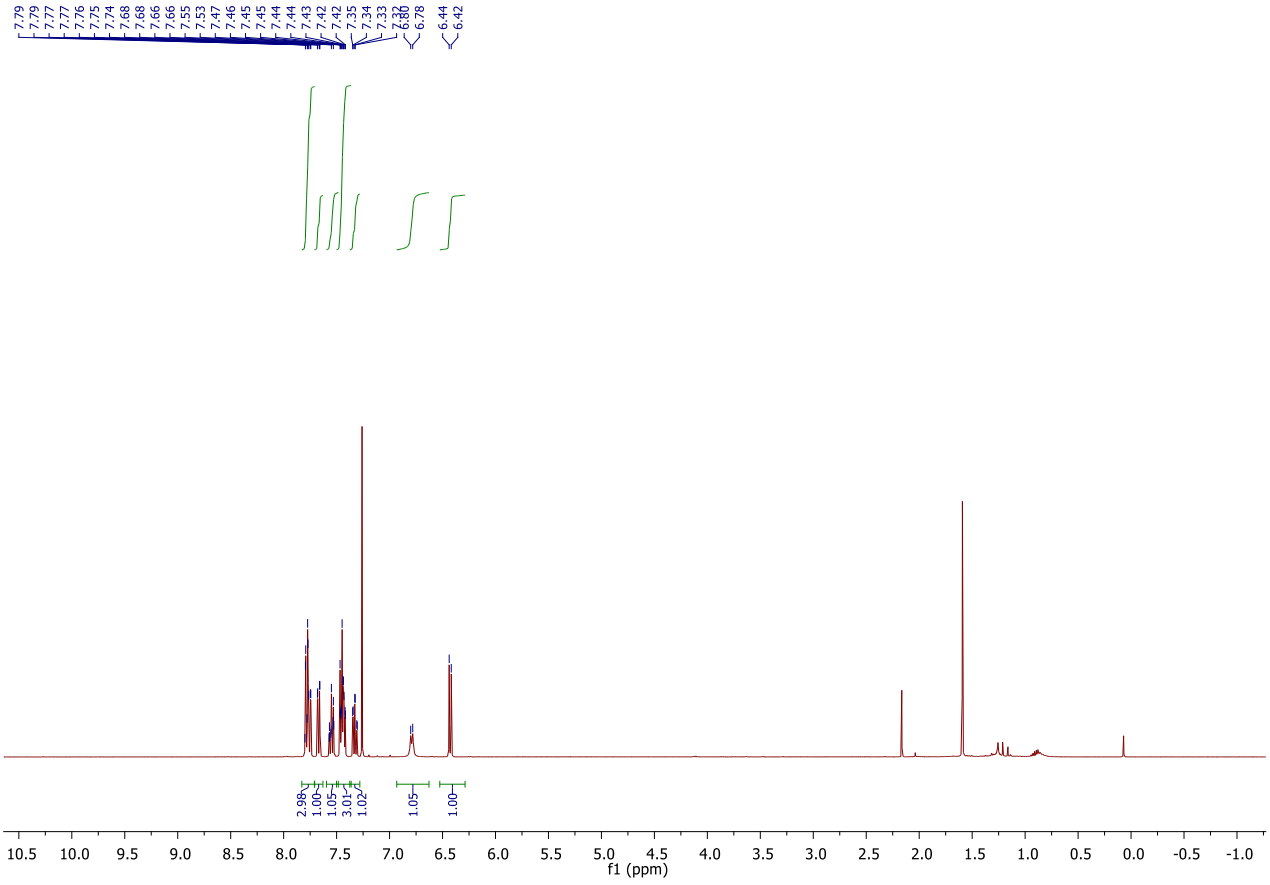
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



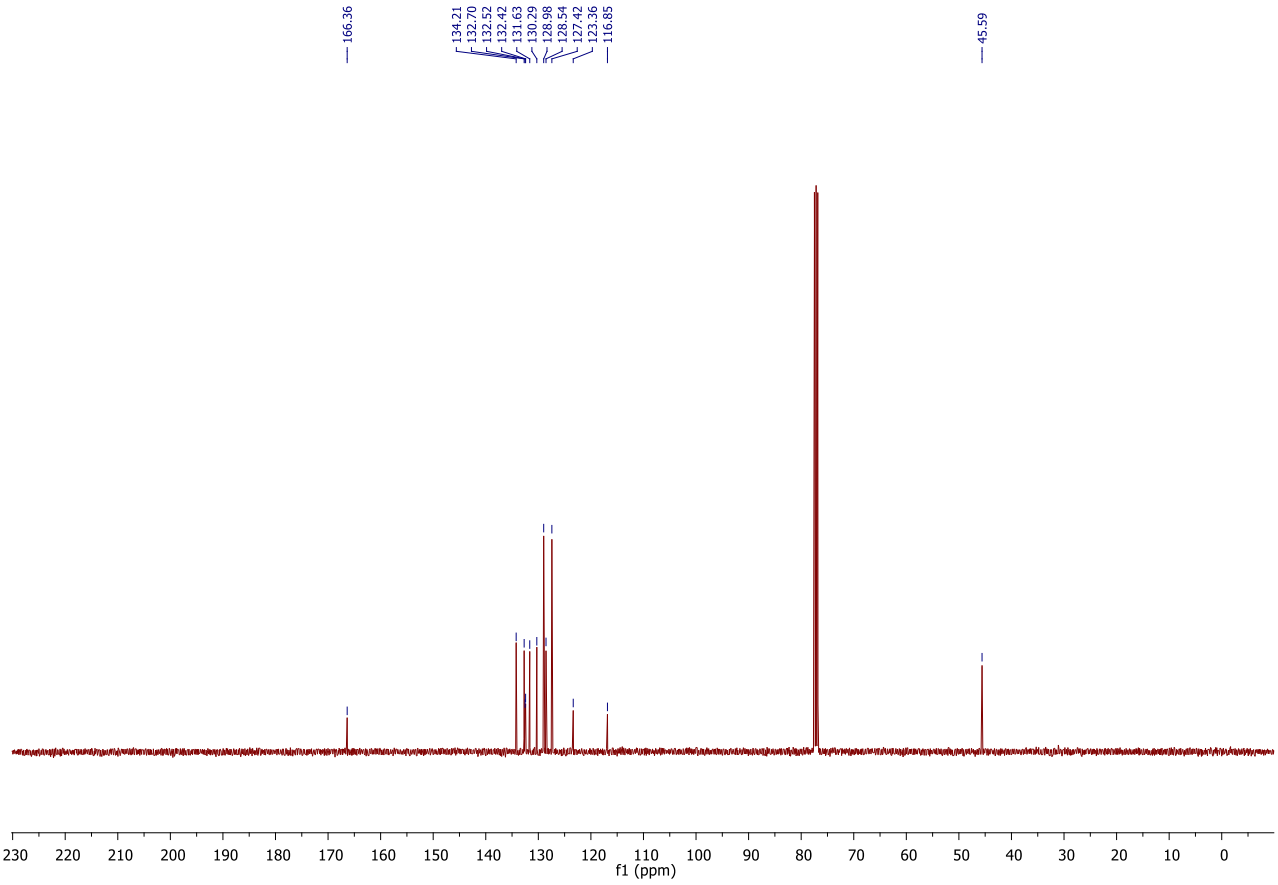
N-[(2-bromophenyl)-cyano-methyl]benzamide (2r)



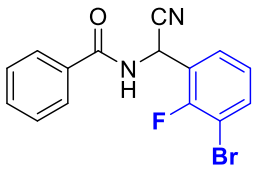
^{1}H NMR (400 MHz, $CDCl_3$)



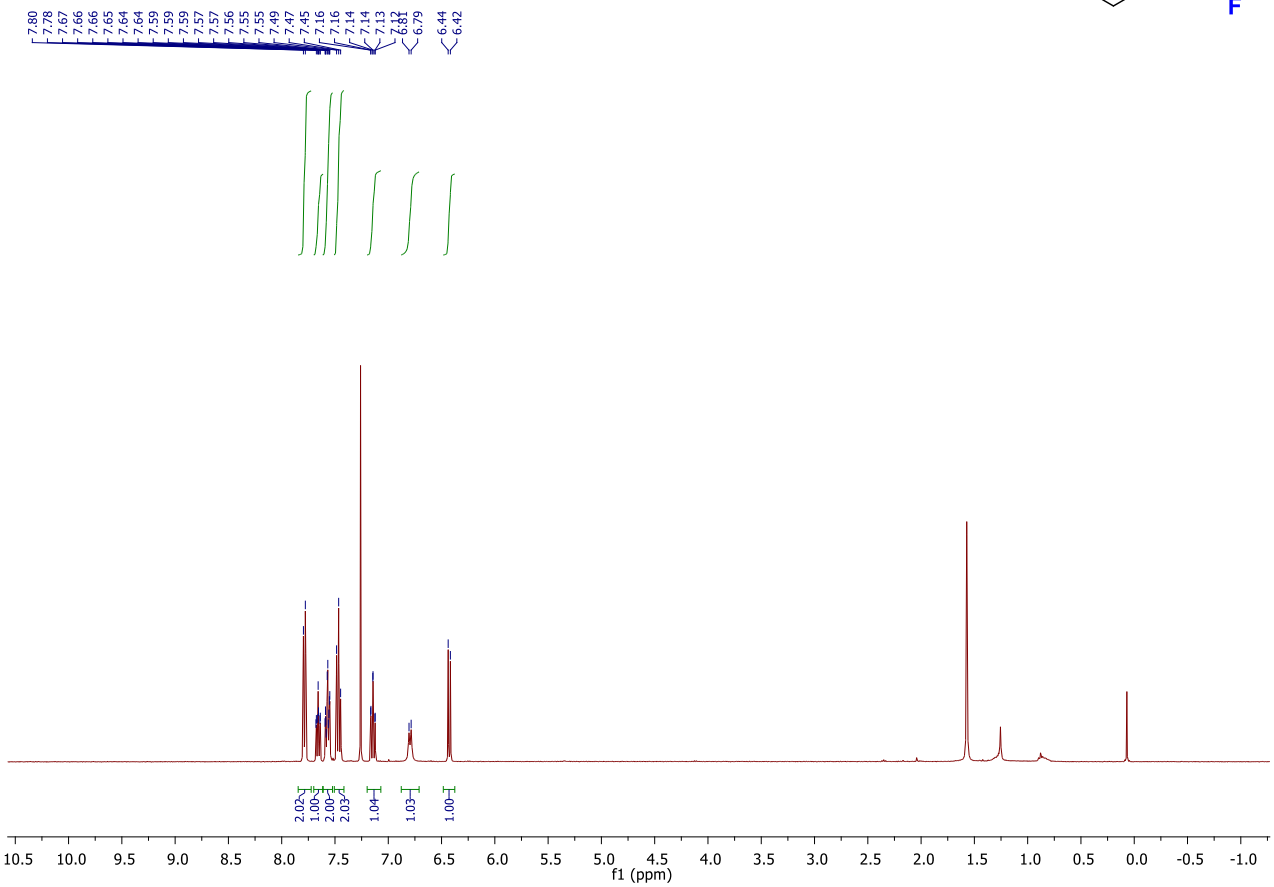
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



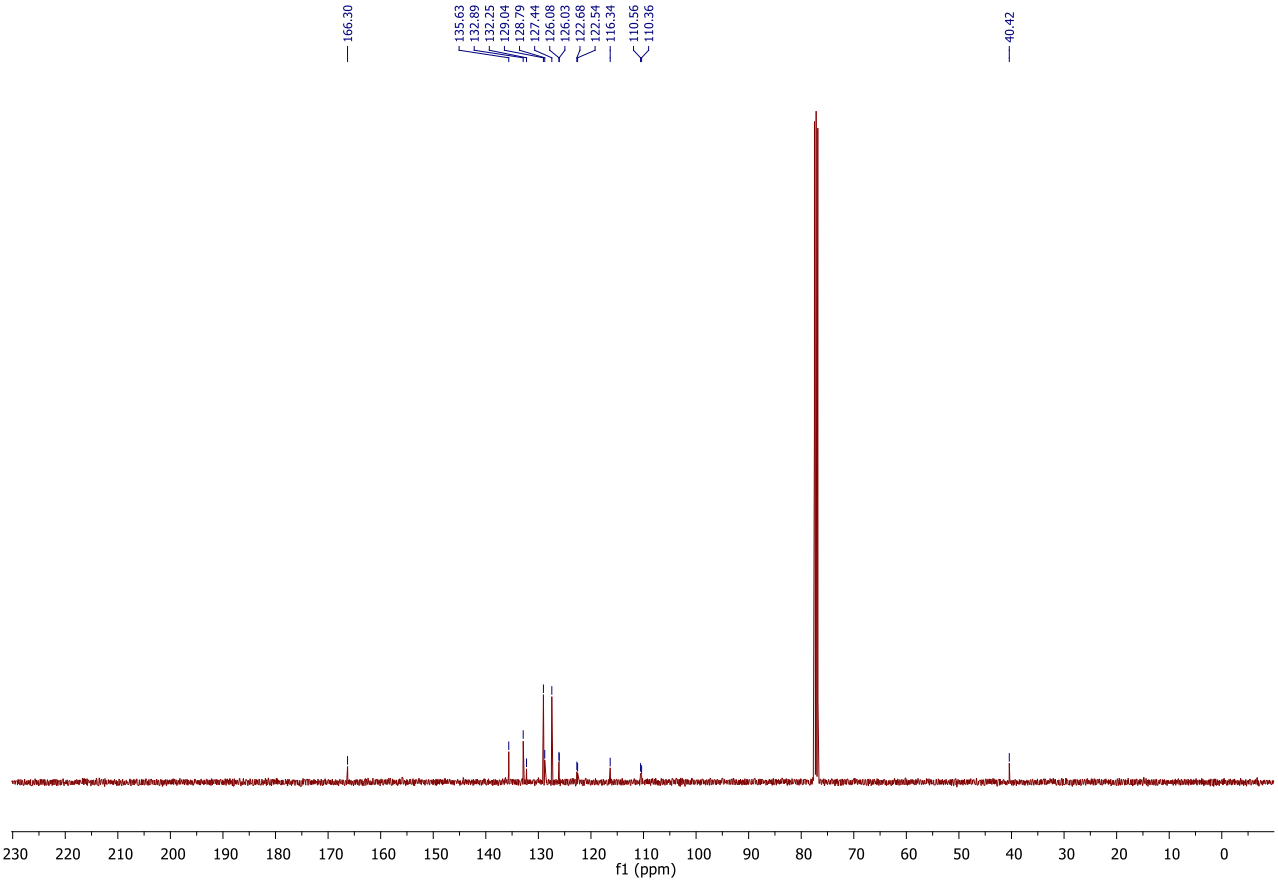
N-[(3-bromo-2-fluoro-phenyl)-cyano-methyl]benzamide (2s)



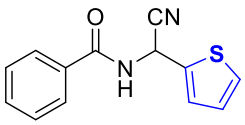
^{1}H NMR (400 MHz, $CDCl_3$)



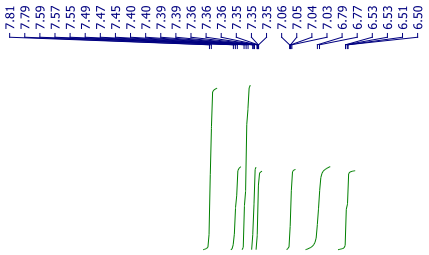
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

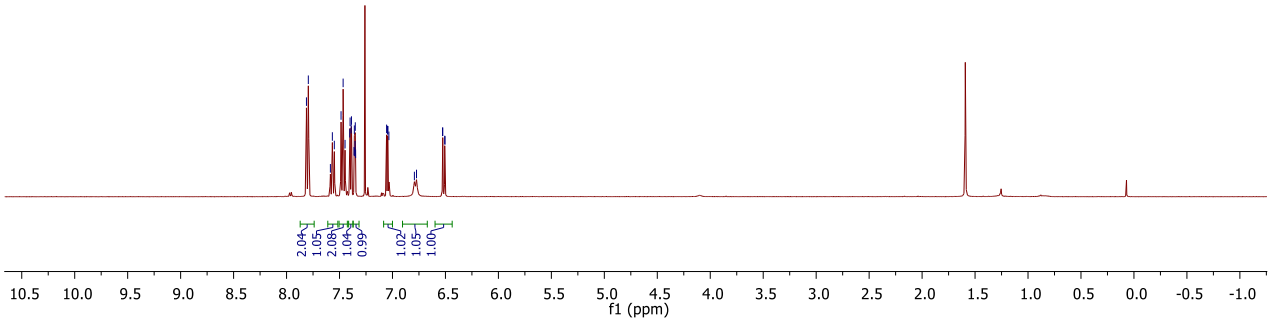


N-[cyano(2-thienyl)methyl]benzamide (2t)

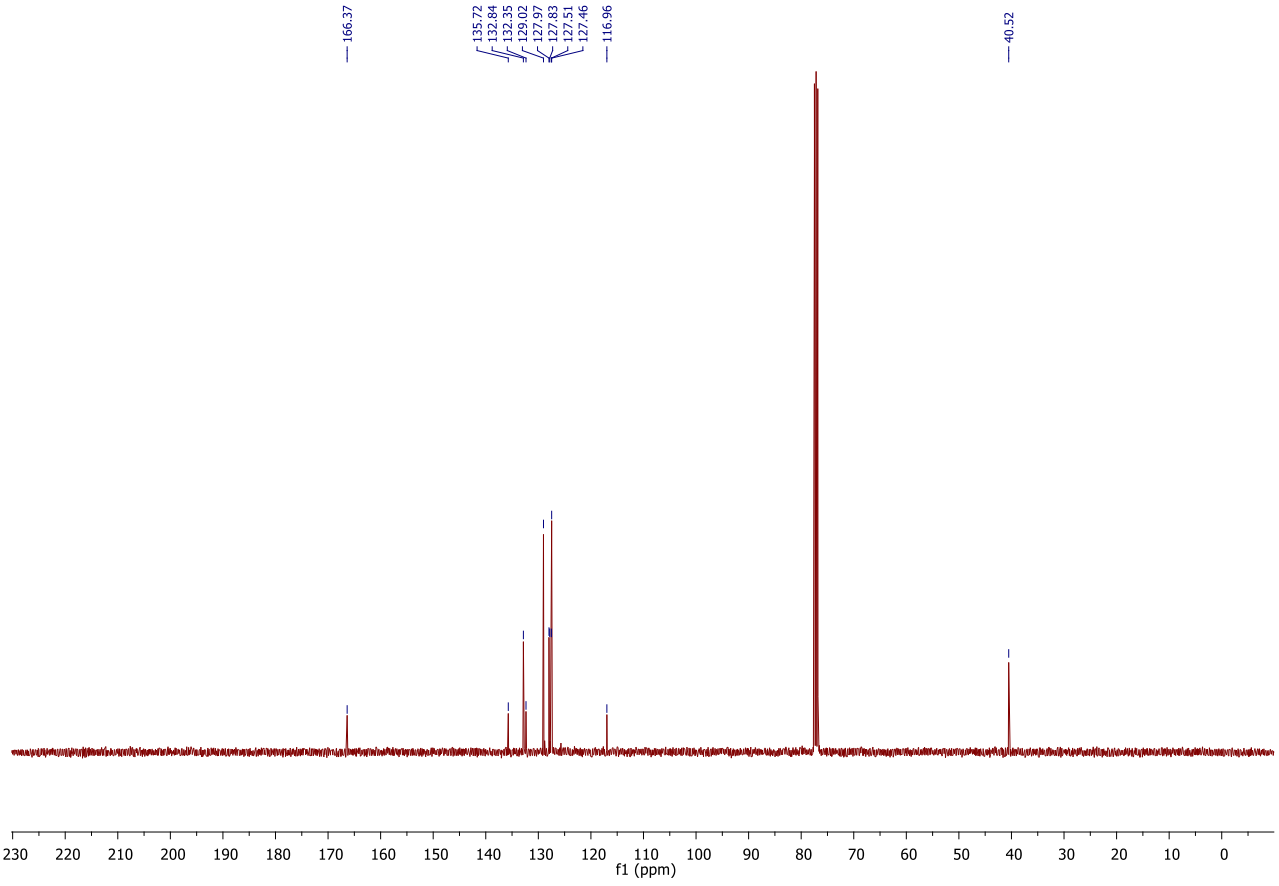


^{1}H NMR (400 MHz, $CDCl_3$)

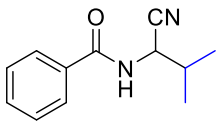




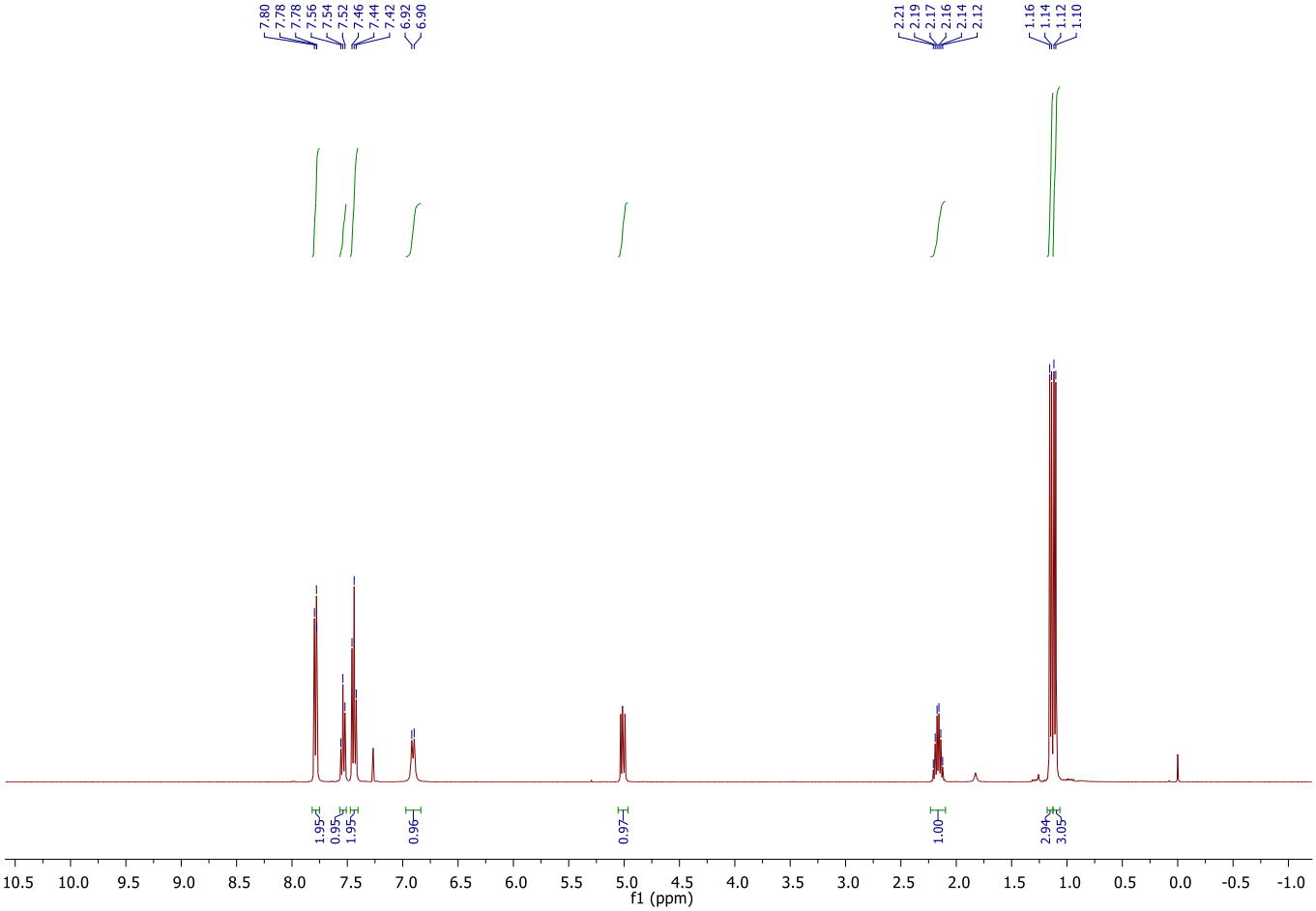
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



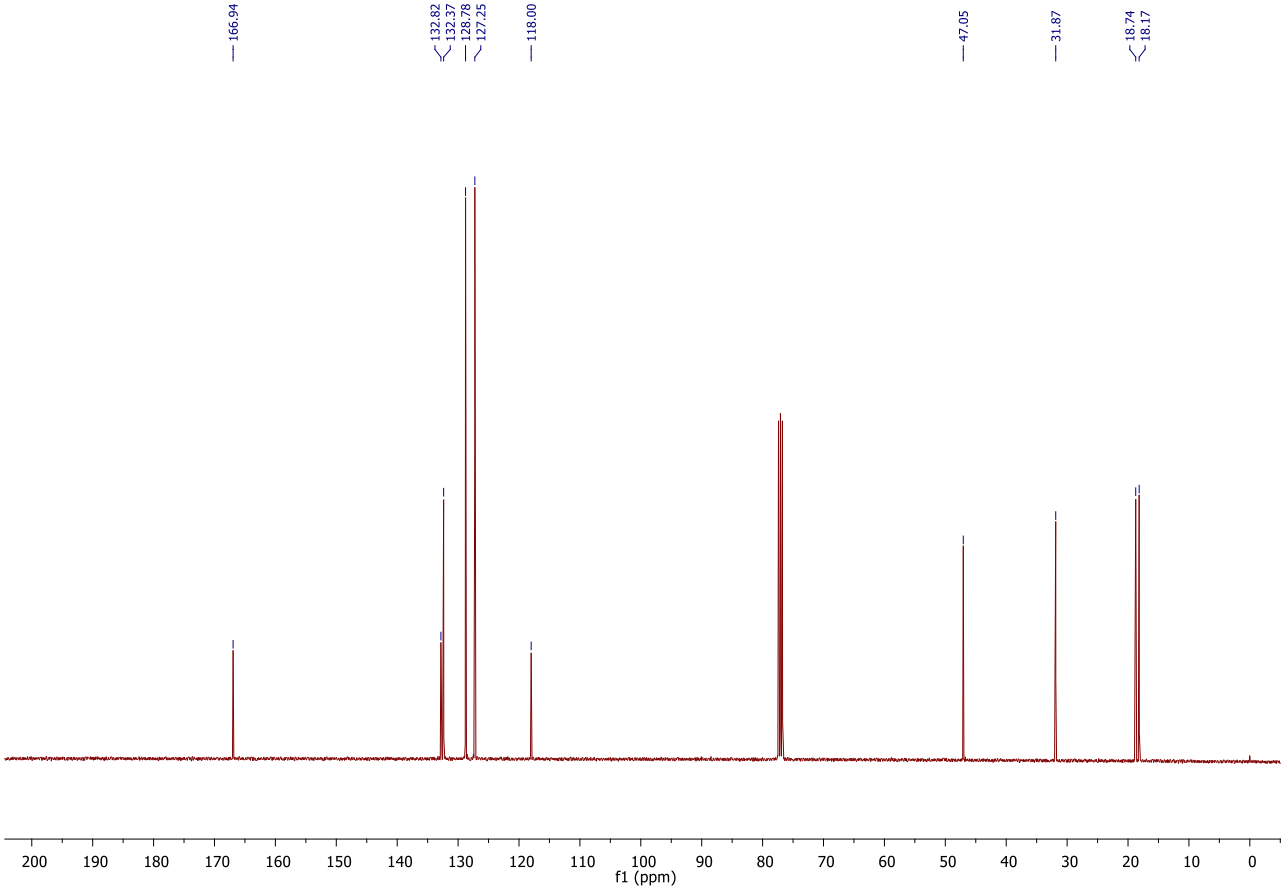
_N_-(1-cyano-2-methyl-propyl)benzamide (2u)



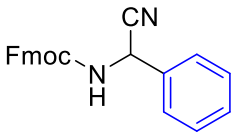
^{1}H NMR (400 MHz, $CDCl_3$)



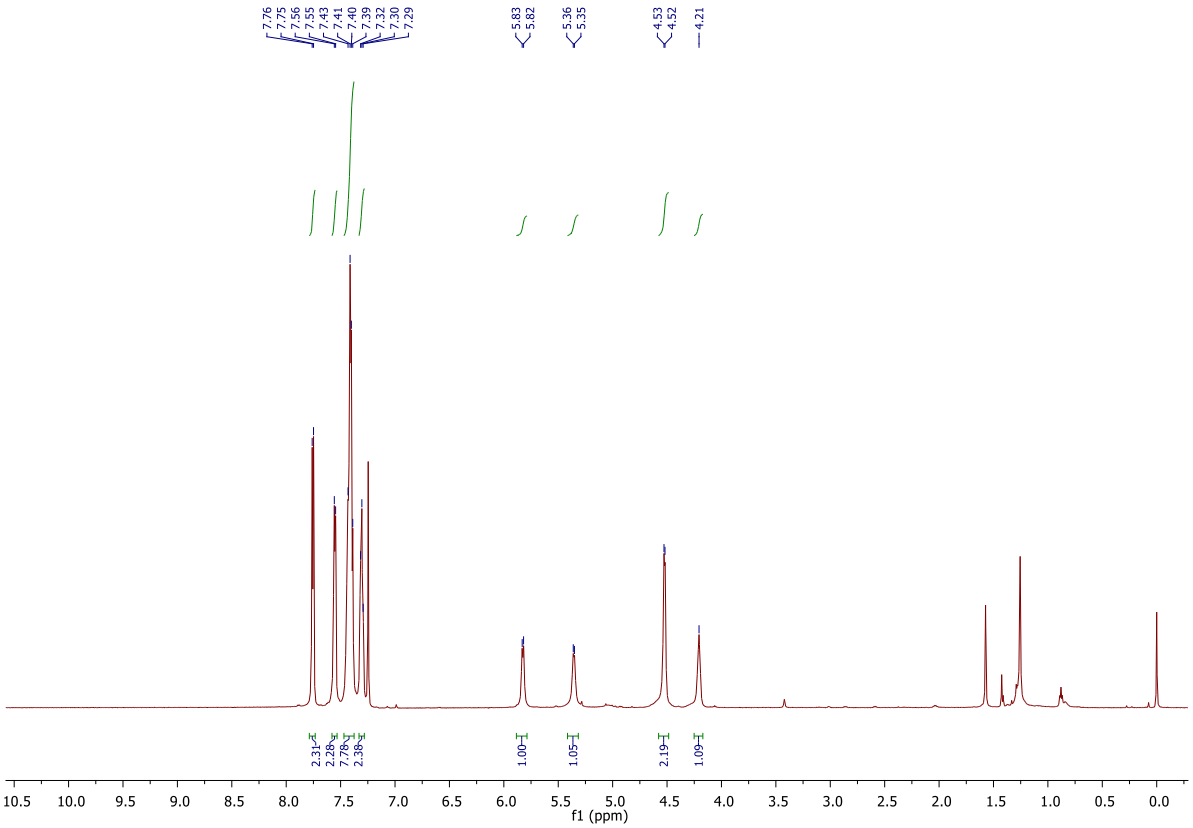
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



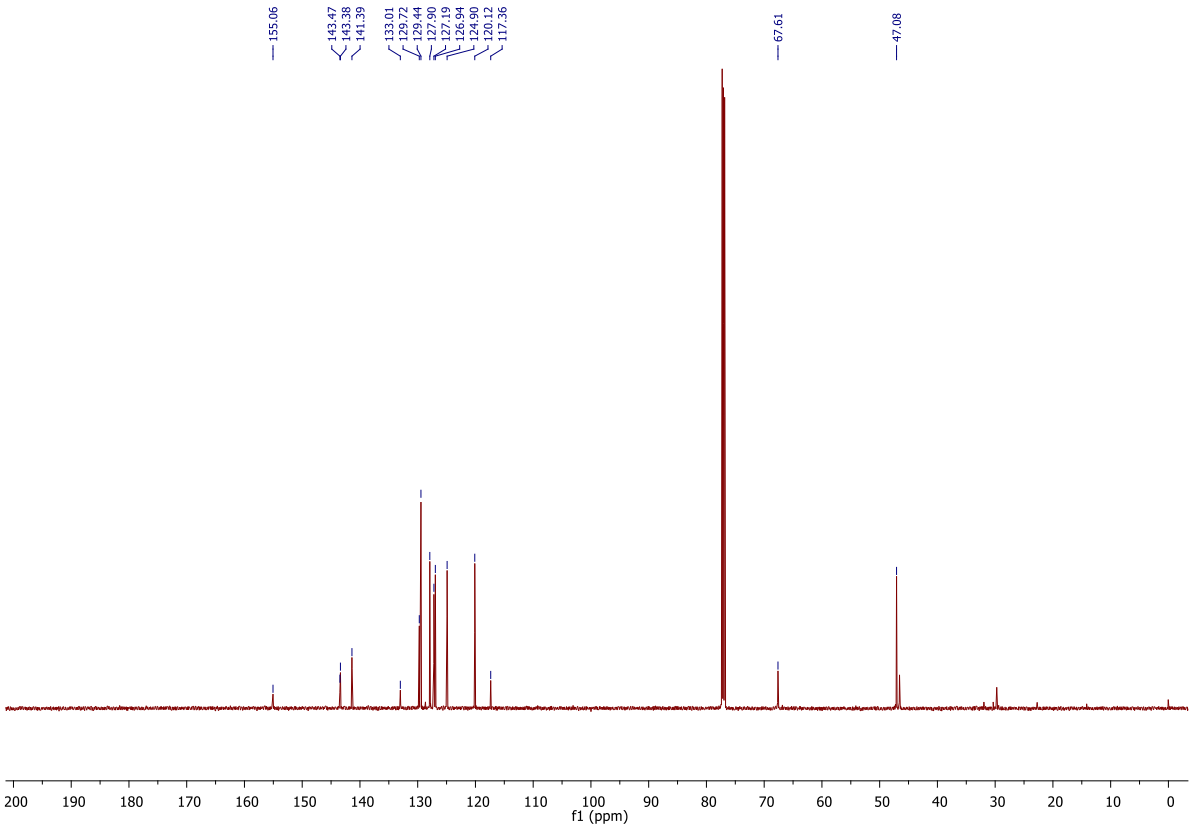
(9*H*-fluoren-9-yl)methyl (cyano(phenyl)methyl)carbamate (4a)



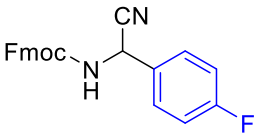
^{1}H NMR (600 MHz, $CDCl_3$)



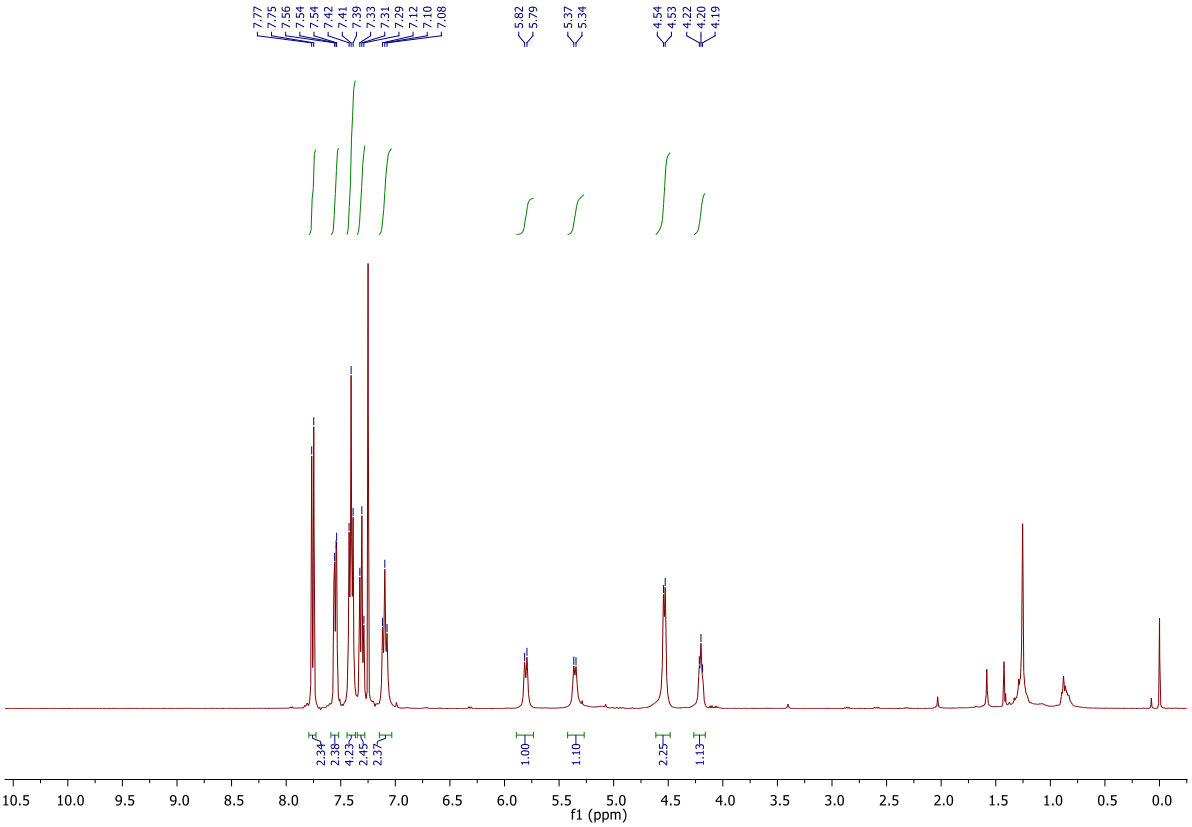
^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)



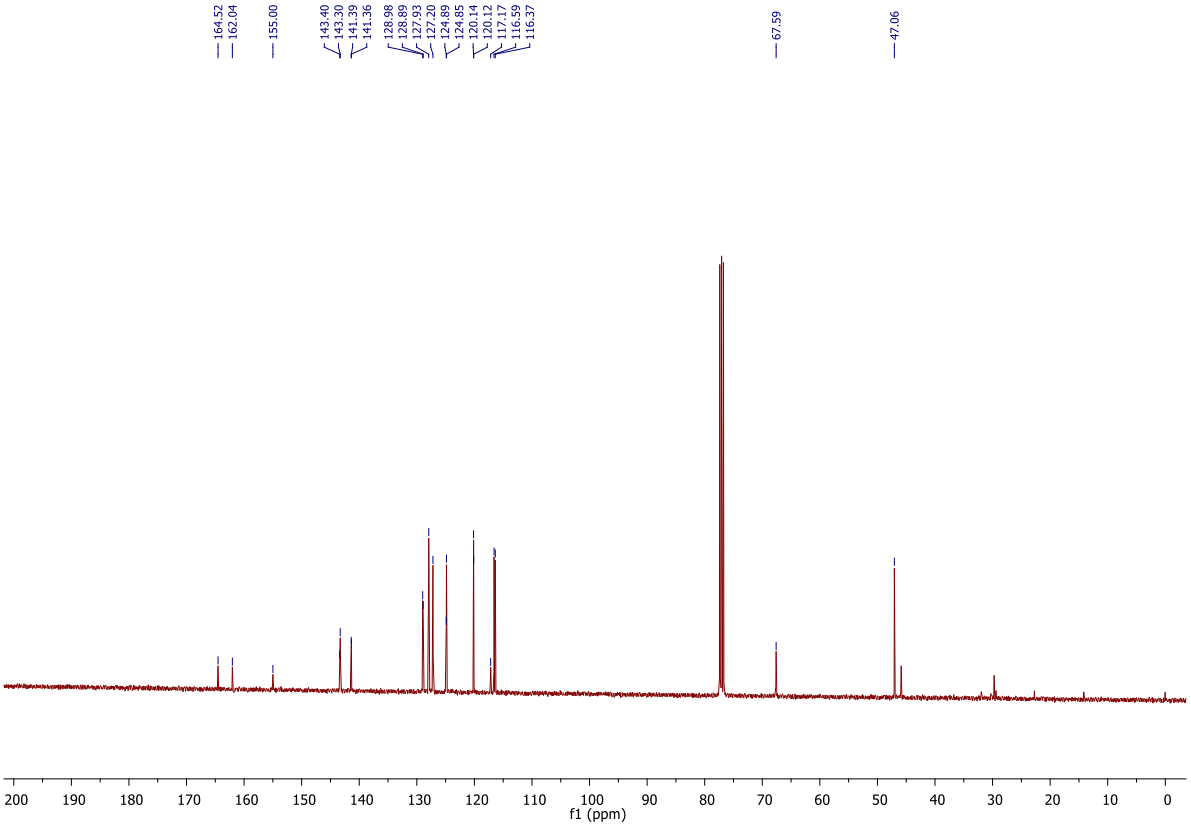
(9*H*-fluoren-9-yl)methyl (cyano(4-fluorophenyl)methyl)carbamate (4b)



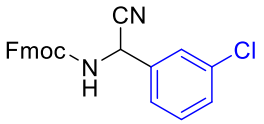
^{1}H NMR (400 MHz, $CDCl_3$)



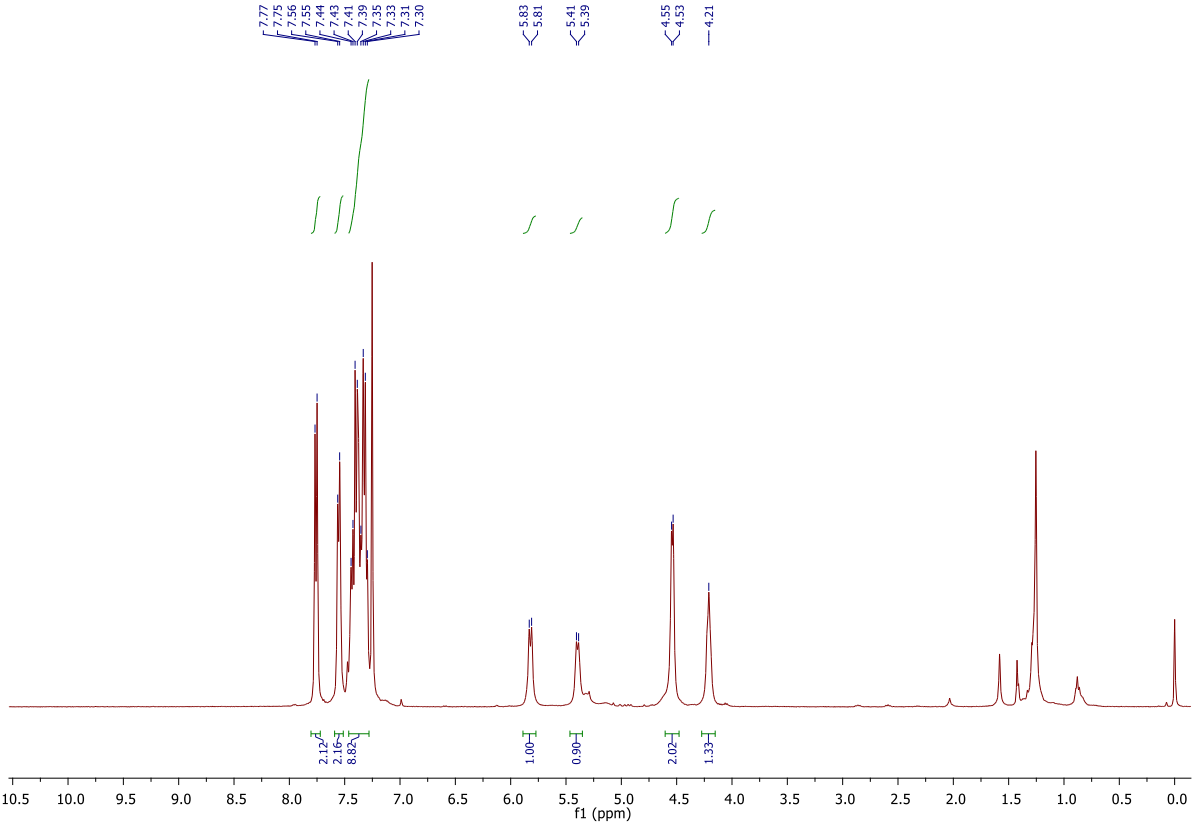
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



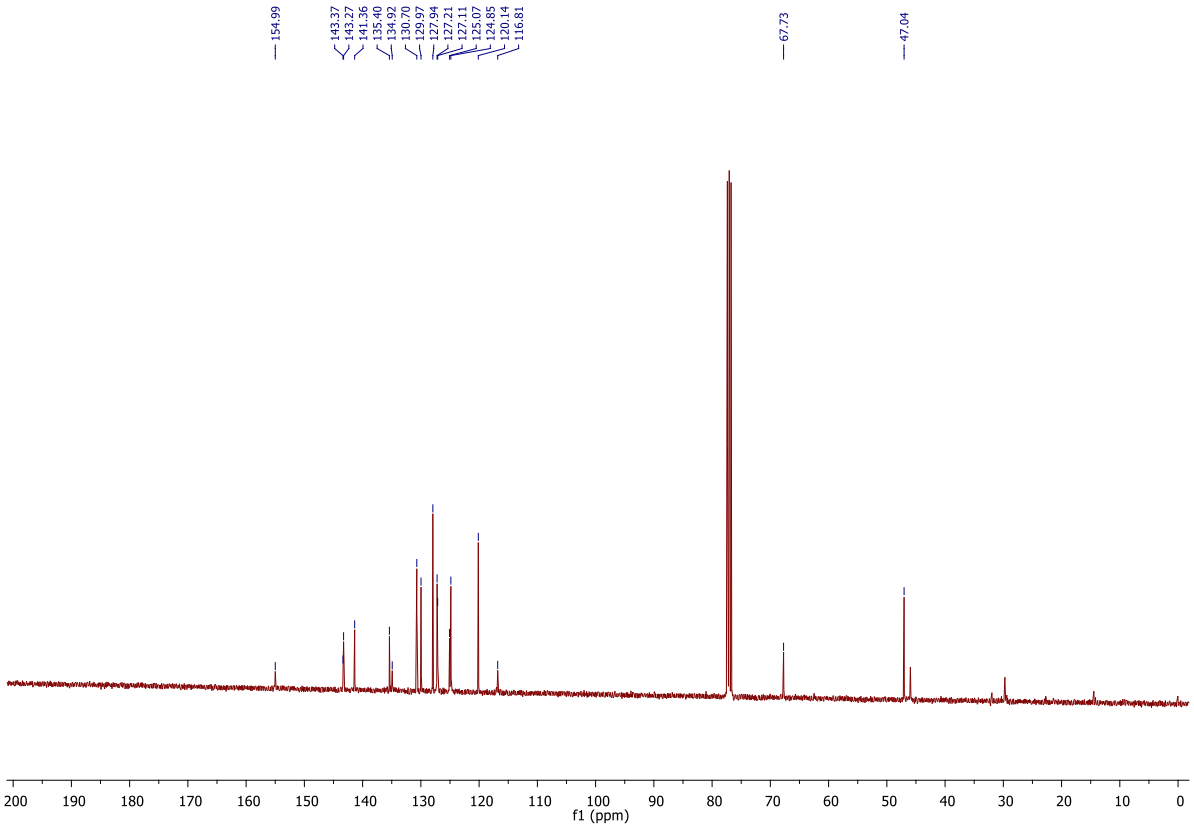
(9*H*-fluoren-9-yl)methyl ((3-chlorophenyl)(cyano)methyl)carbamate (4c)



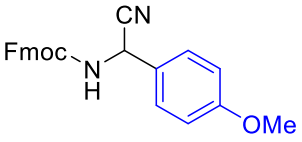
^{1}H NMR (400 MHz, $CDCl_3$)



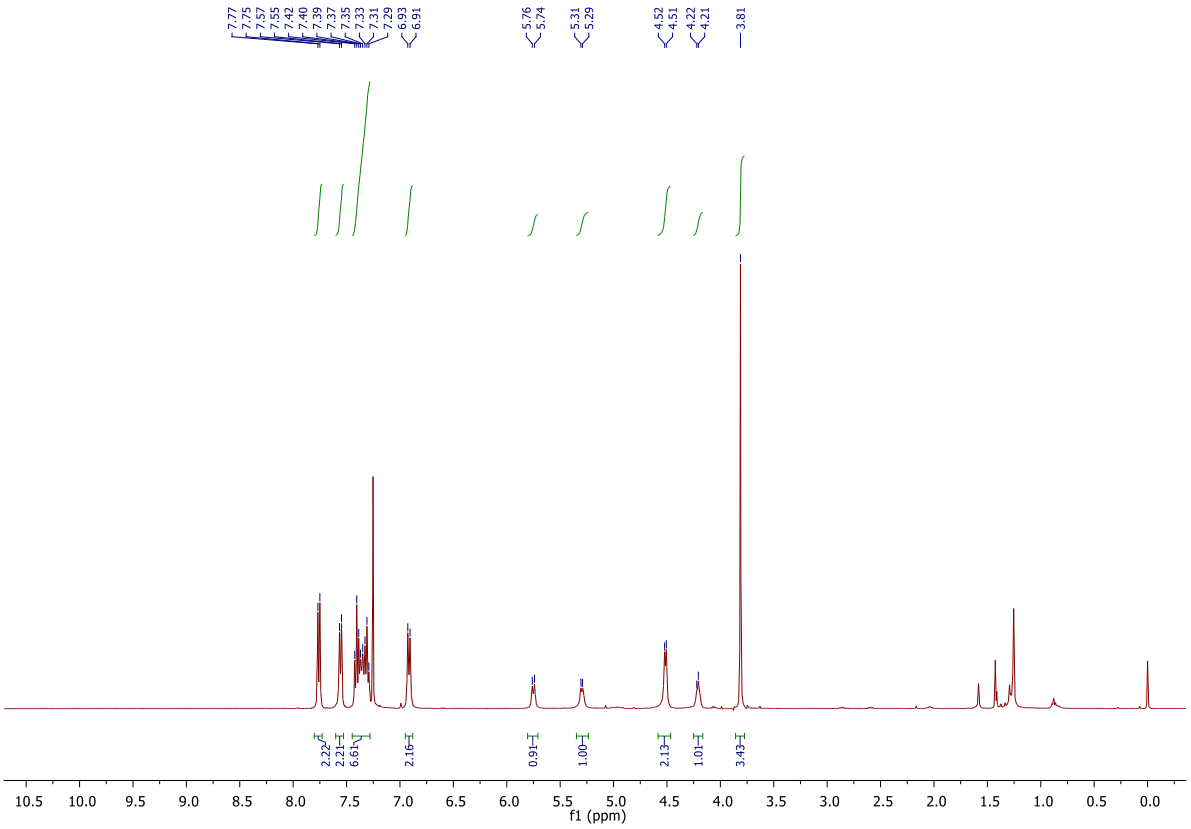
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



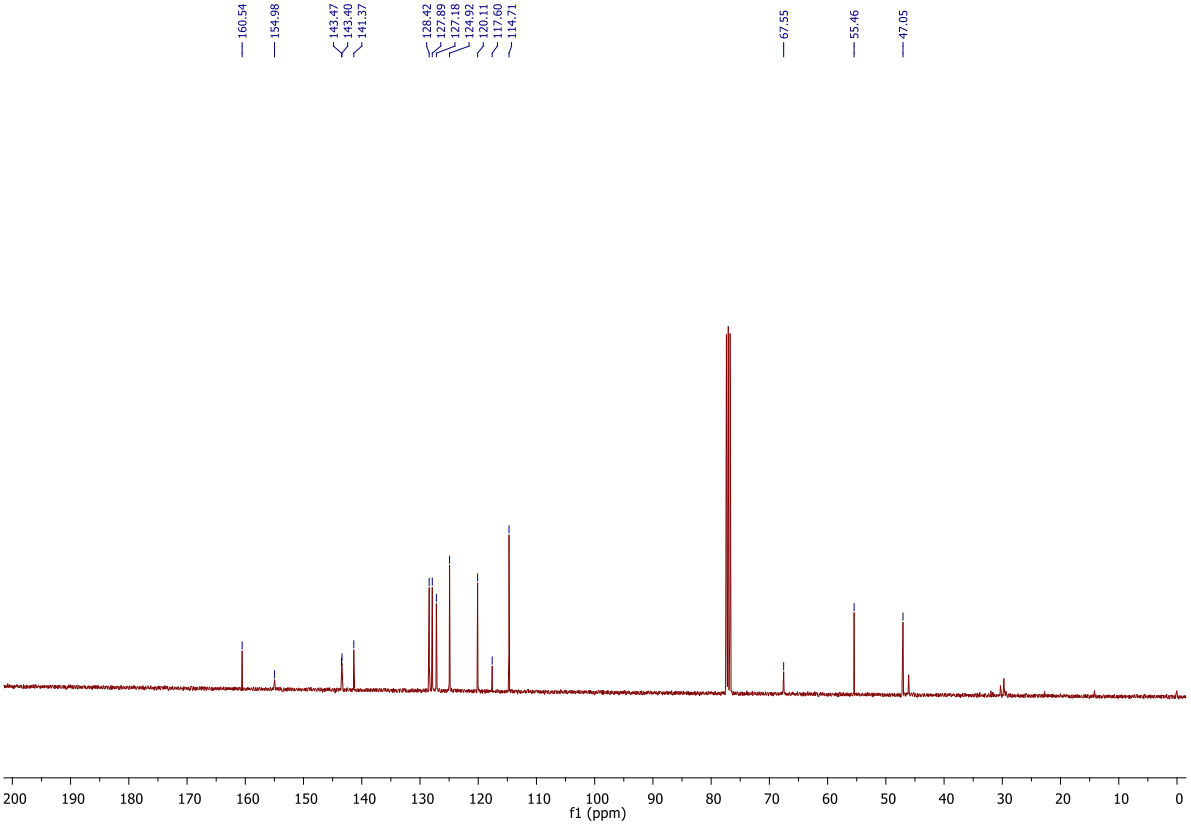
(9*H*-fluoren-9-yl)methyl (cyano(4-methoxyphenyl)methyl)carbamate (4d)



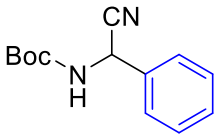
^{1}H NMR (400 MHz, $CDCl_3$)



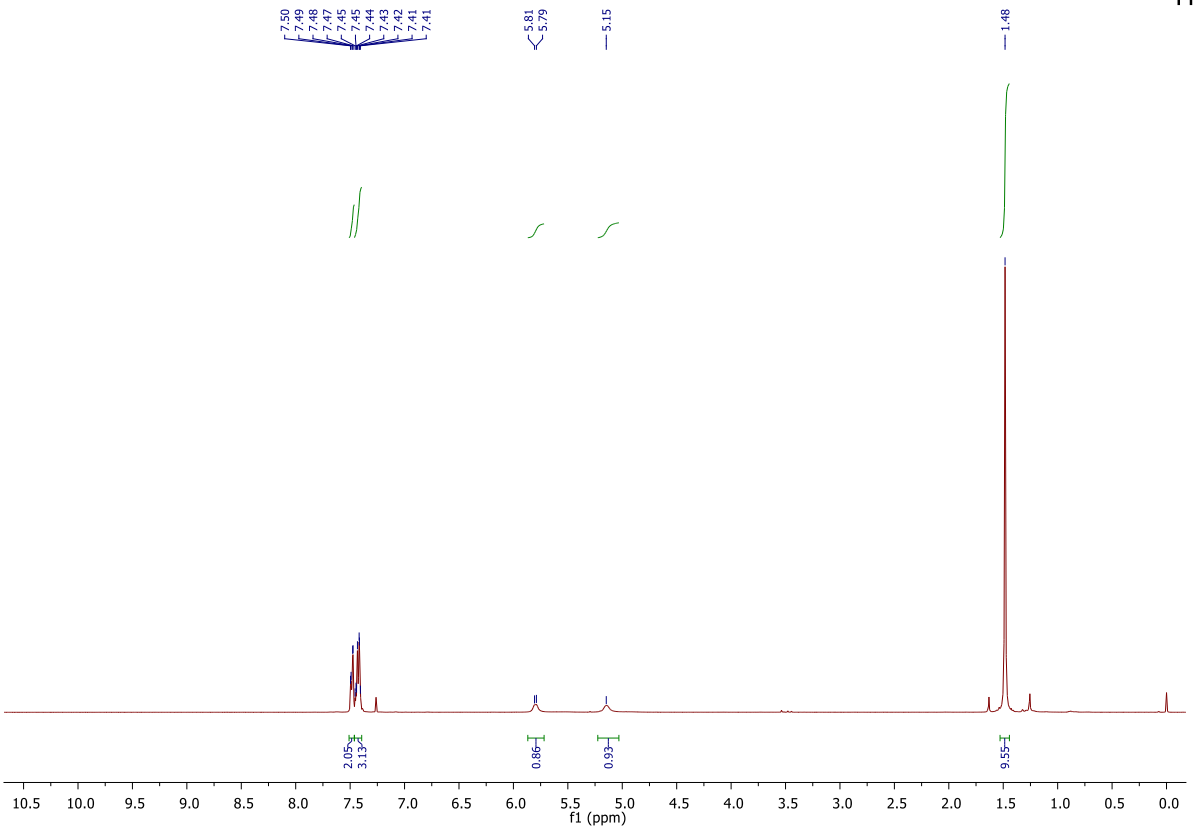
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



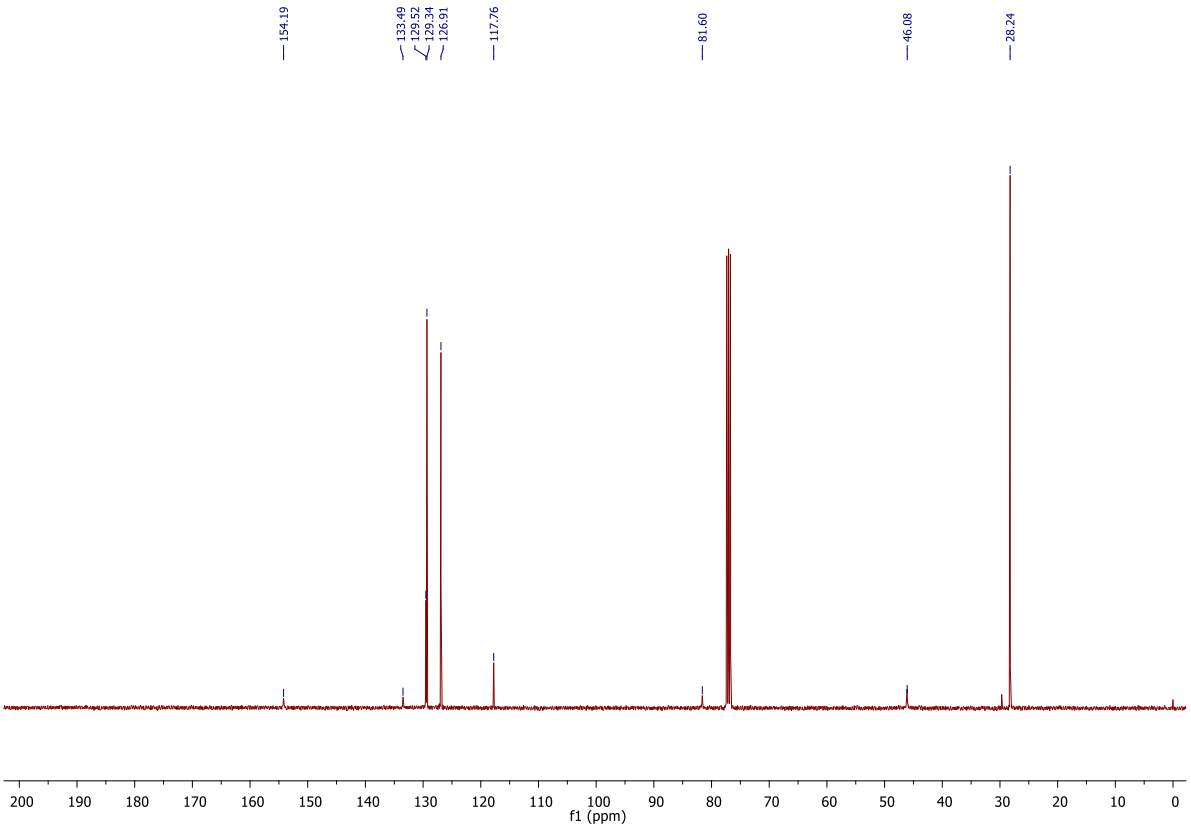
tert-butyl (cyano(phenyl)methyl)carbamate (4f)



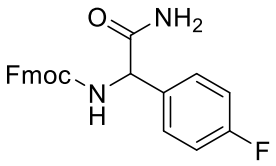
^{1}H NMR (400 MHz, $CDCl_3$)



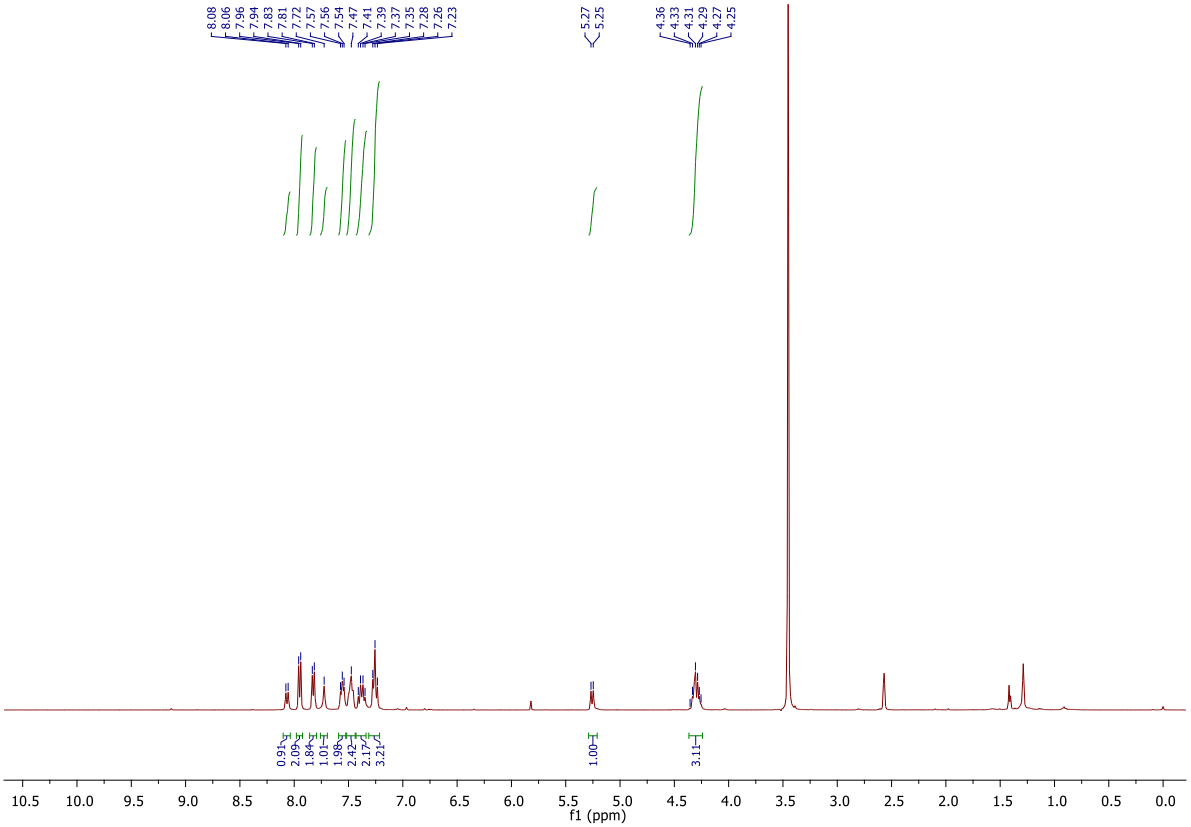
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



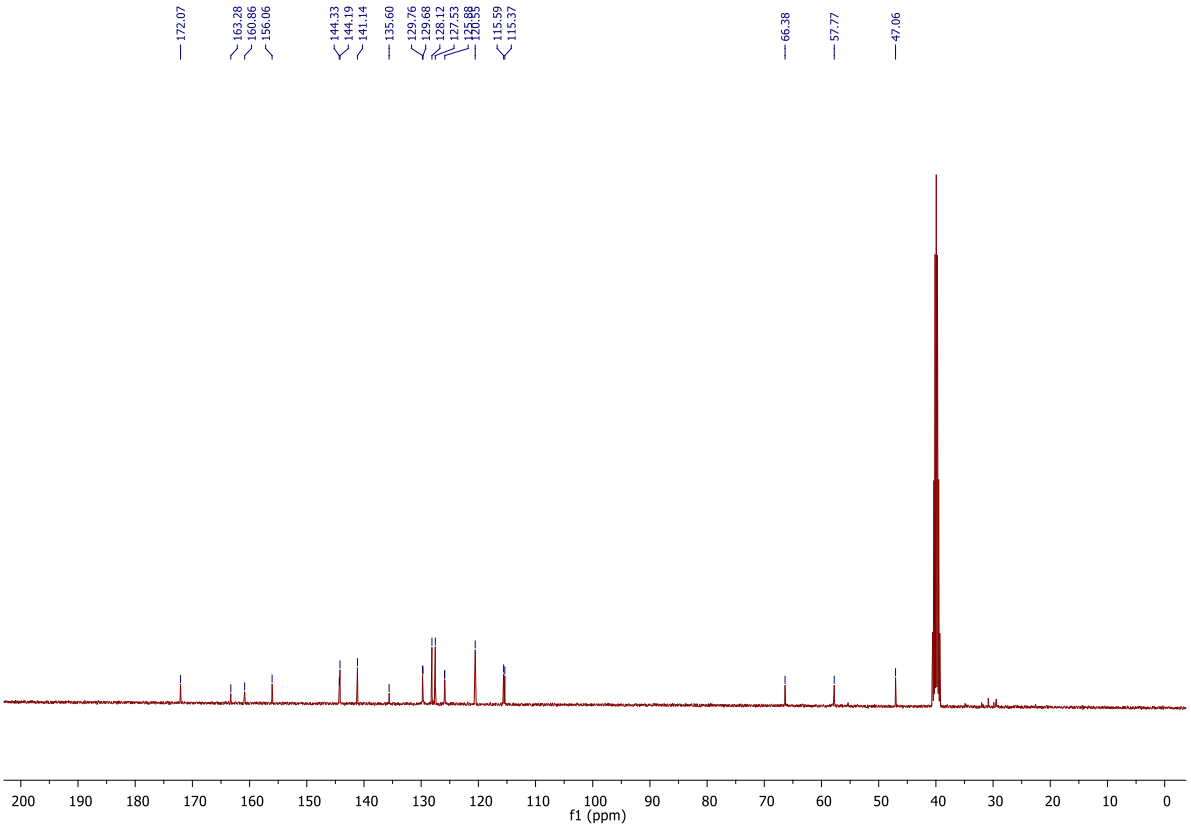
(9H-fluoren-9-yl)methyl (2-amino-1-(4-fluorophenyl)-2-oxoethyl)carbamate (5)



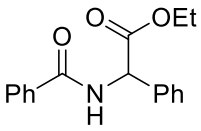
^{1}H NMR (400 MHz, DMSO-d_6)



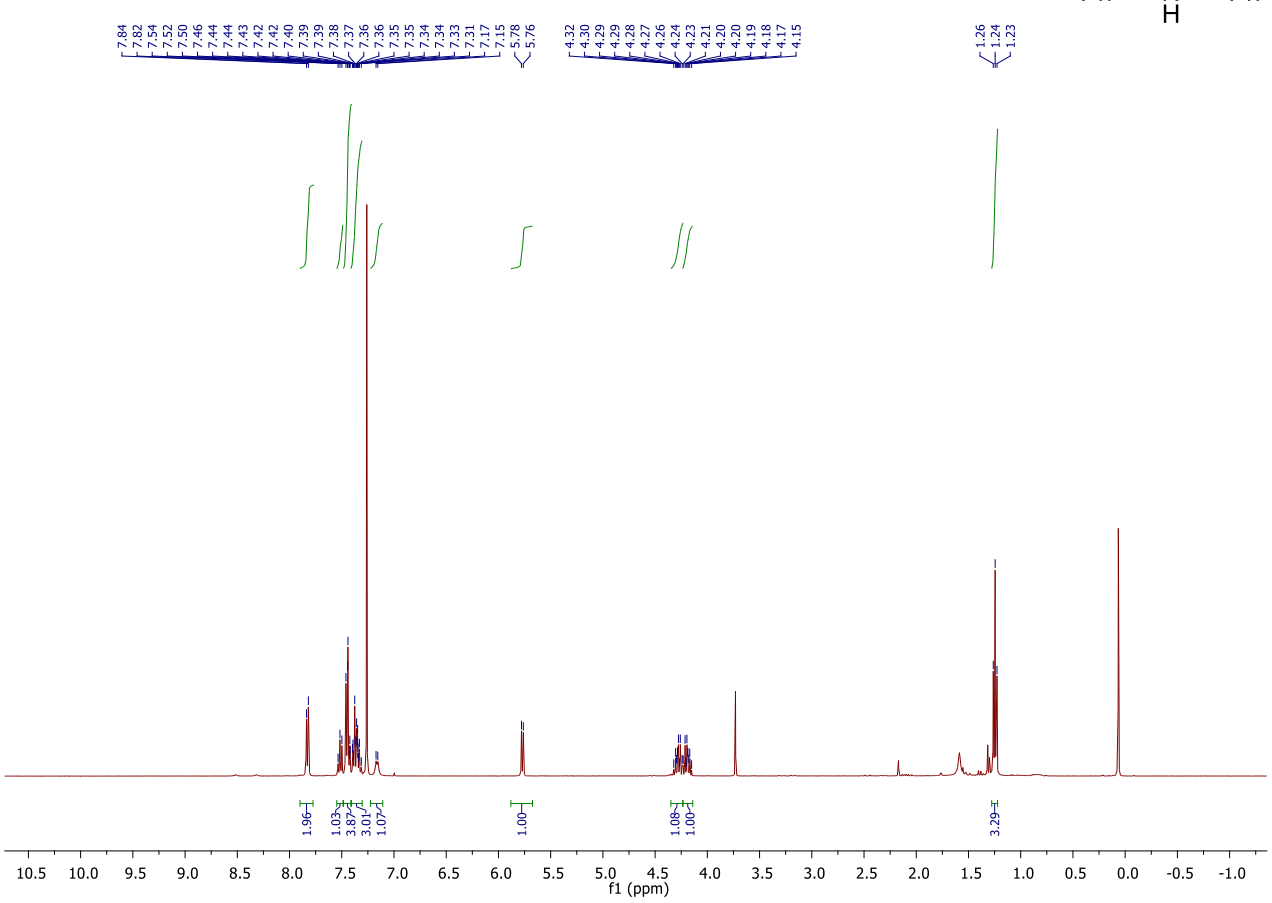
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)



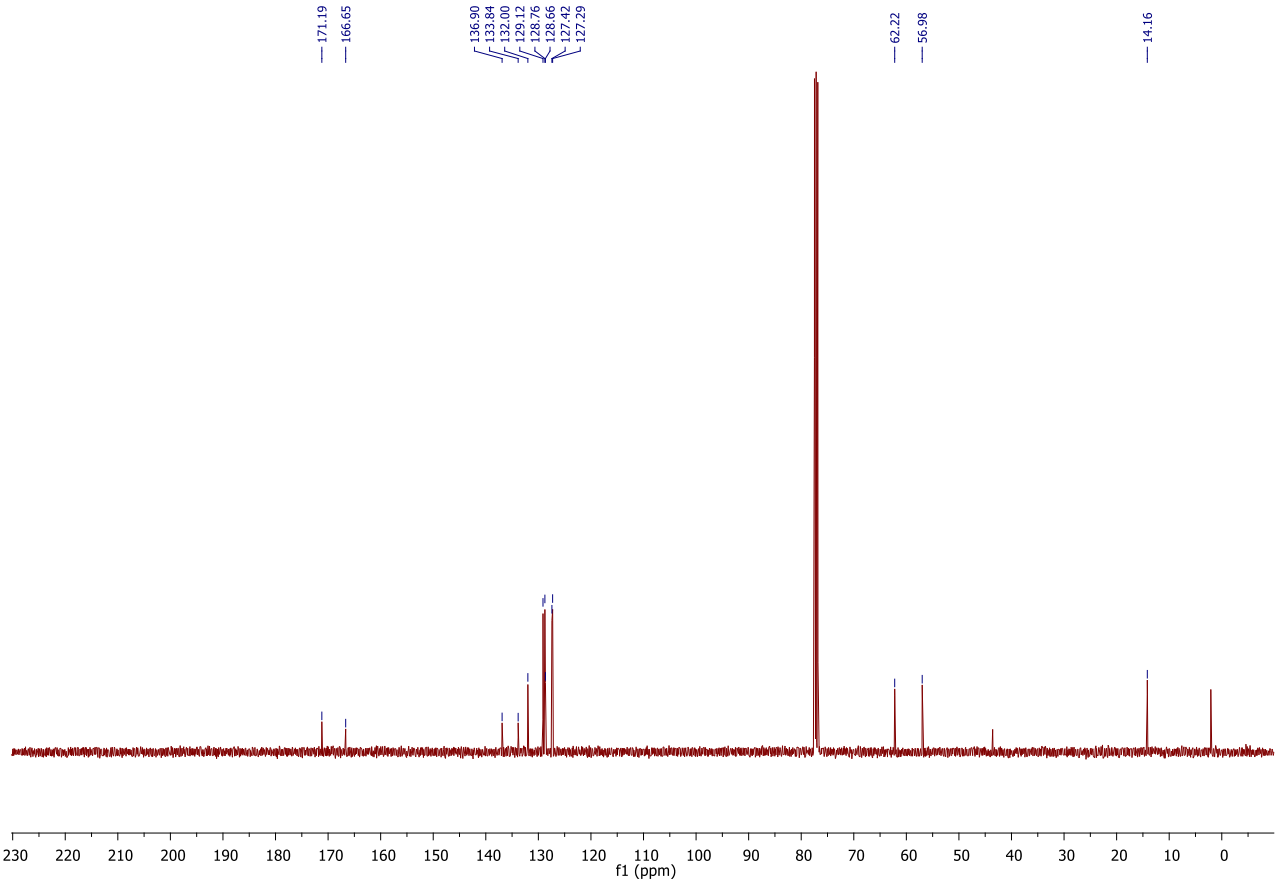
ethyl 2-benzamido-2-phenyl-acetate (6)



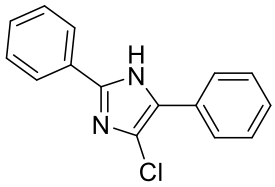
^{1}H NMR (400 MHz, $CDCl_3$)



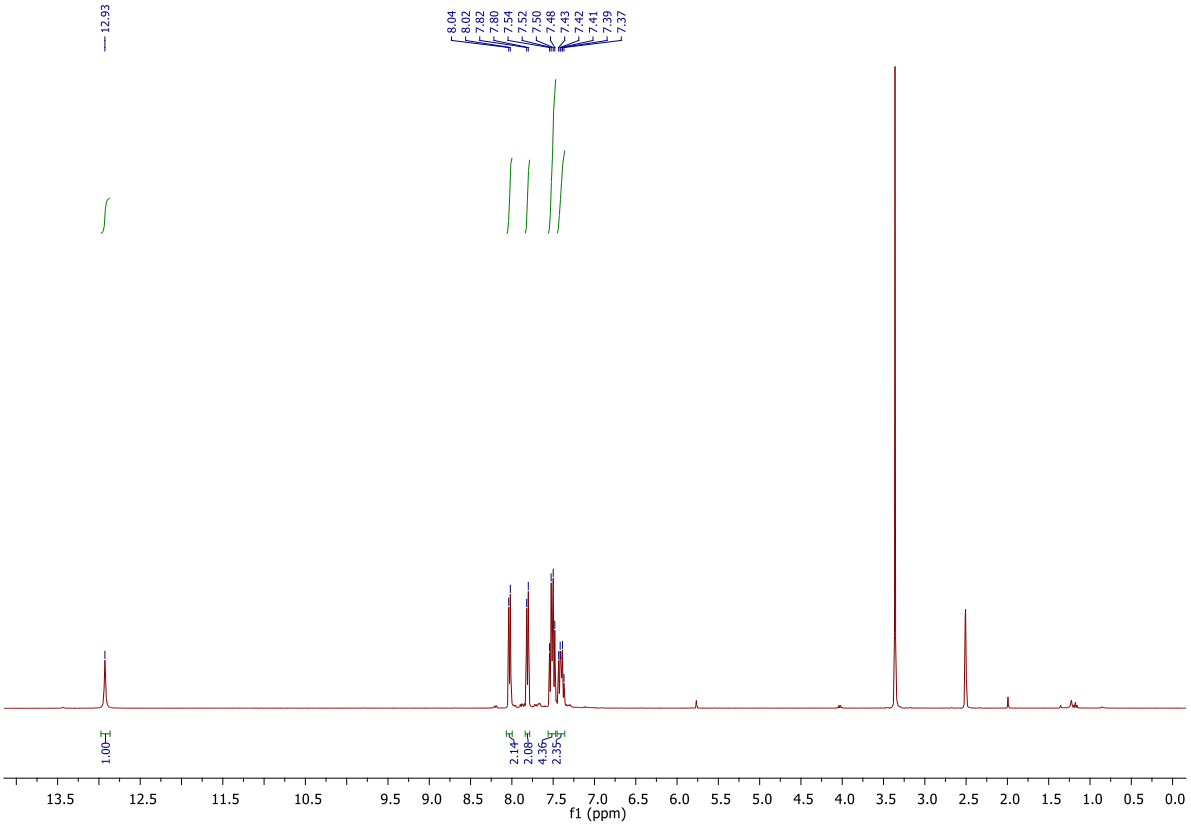
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)



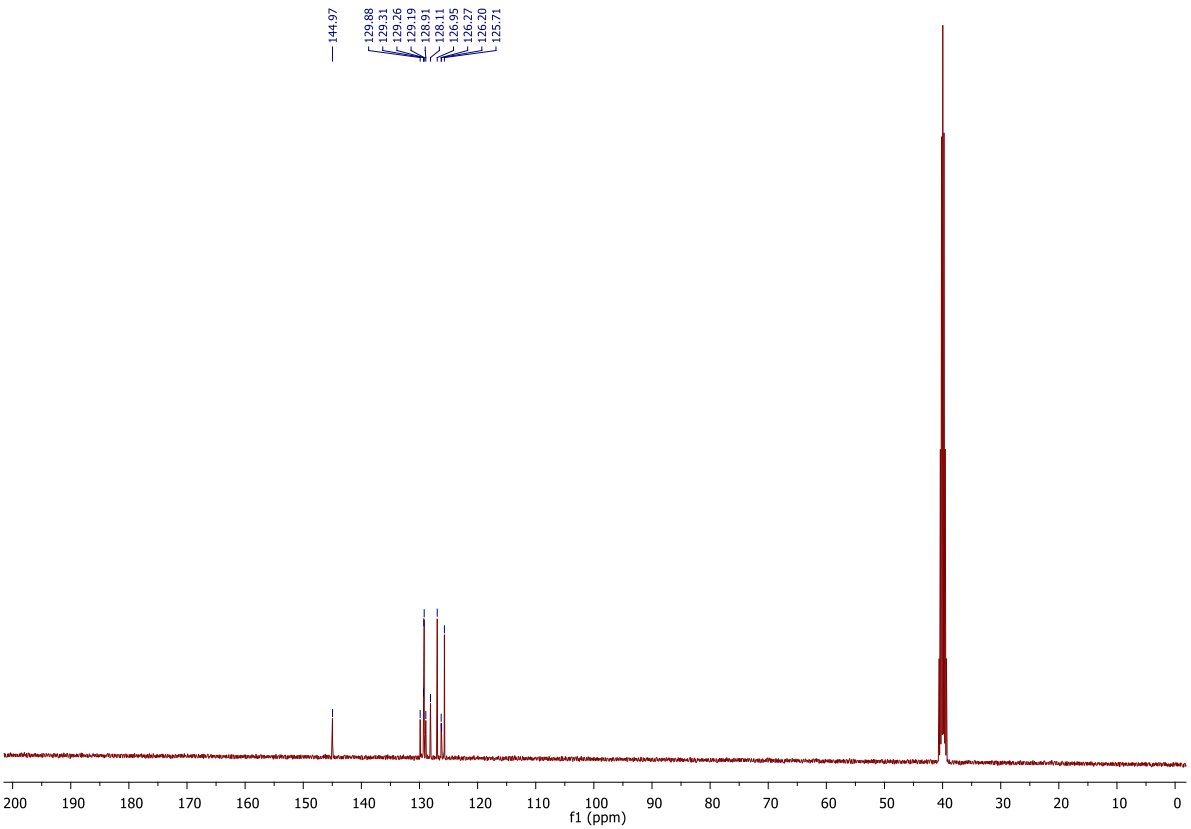
5-Chloro-2,4-diphenyl-1*H*-imidazole (7)



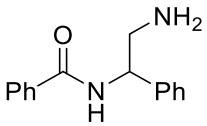
^{1}H NMR (400 MHz, DMSO-d_6)



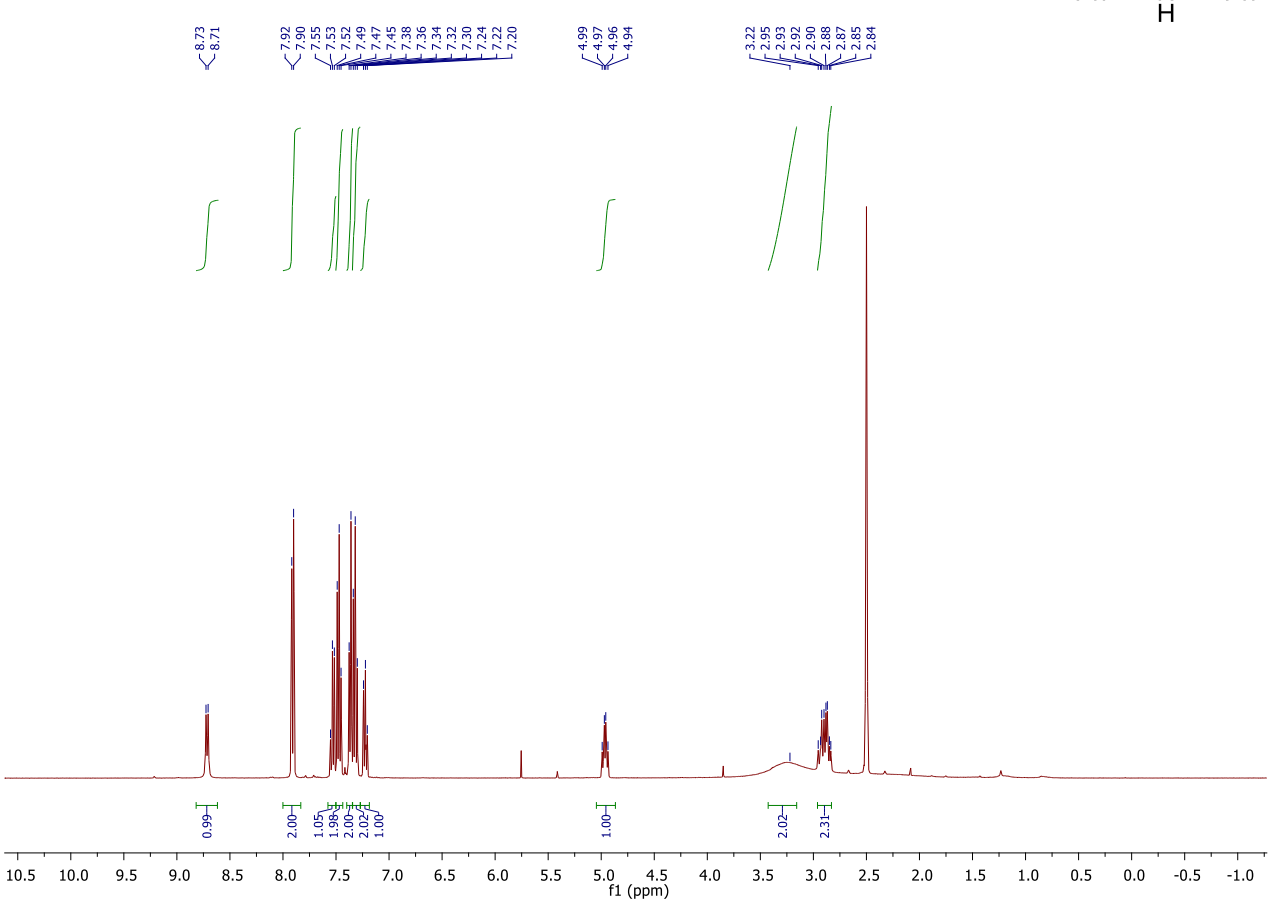
^{13}C NMR (101 MHz, DMSO-d_6)



N-(2-amino-1-phenyl-ethyl)benzamide (8)



^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6)