Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information

Iron-catalysed carbene-transfer reactions of diazo acetonitrile

Claire Empel, Katharina J. Hock and Rene M. Koenigs*

Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074 Aachen, Germany

rene.koenigs@rwth-aachen.de

Table of Contents

Supporting information **1**
General Information **3**
Important safety note **3**
Experimental Procedures **4**
Analytical data **5**

General Information

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Chemicals used in this manuscript were purchased from Sigma Aldrich, Alfa Aesar, Fluorochem and Carl Roth. Amino acetonitrile hydrochloride used in this manuscript was purchased from Alfa Aesar and Fluorochem, though it can be readily synthesized on 50 mmol scale in a single step starting from formaldehyde, ammonium hydroxide and sodium cyanide, followed by precipitation of the hydrochloride salt with 69% yield.[i]

Solvents used in reactions were p.A. grade. All reactions were performed under argon using degassed solvents. Solvents for chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on Macherey-Nagel silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.063 – 0.2 mm). Solvent mixtures are understood as volume/volume.
^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR were recorded on a Varian AV600/AV400 or an Agilent DD2 400 NMR spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated br (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); coupling constants (J) are in Hertz (Hz).
HRMS data were recorded on a ThermoFisher Scientific LTQ Orbitrap XL using ESI ionization or on a Finnigan MAT 95 using EI ionization at 70 eV.
IR spectra were recorded on a Perkin Elmer-100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}).

The following equipment was utilized for the continuous-flow generation of diazo acetonitrile: Syringe pump: Chemyx Inc. Model Fusion 710. Micromixer: Little Things Factory, MR Lab MX. PTFE tubing: CS Chromatographie PTFE tubing, Art Nr. 590515, 1/16” AD, 0.8 mm ID, max. pressure 37 bar. Back pressure regulator: IDEX back pressure assembly, 20 psi.

Important safety note

Safety hazards of diazo acetonitrile, described within this manuscript, have not been investigated. However, it should be noted this particular diazo compound was reported to be highly explosive.
Handling of diazo compounds should only be done in a well-ventilated fume cupboard using an additional blast shield. No incidents occurred handling of diazoalkanes during the preparation of this manuscript, yet the reader should be aware of carcinogenicity and explosiveness of the herein described diazo compounds. General safety precautions when working with diazomethane and its derivatives should be followed. Any reactions described in this manuscript should not be performed without strict risk assessment and proper safety precautions.

Experimental Procedures

Standard procedure for the X—H Insertion reactions

For the X—H insertion reactions, aqueous degassed solutions of aminoacetonitrile hydrochloride (c = 2.0 mol / L, 2.0 mL, 4.0 eq., 148 mg) and sodium nitrite (c = 2.4 mol / L, 2.0 mL, 4.8 eq., 132 mg) were both added at a flow rate of 100 µL / min into the LTF MR Lab MX microreactor at 55 °C and then passed through an ice bath. The microreactor was connected to an IDEX backpressure vent and the outlet was connected to a standard reaction vessel. This solution of diazoacetonitrile was added drop wise over 20 min to a degassed solution of the amine (1.0 eq.) and catalyst (1 mol-%) in toluene (100 µL) and stirred for 1 h or 3 h at room temperature. The reaction mixture was then extracted three times with 5-10 mL of DCM. The combined organic phases were dried over $MgSO_4$ and the solvent removed. The crude product thus obtained was purified by column chromatography on silica gel.

Procedure for the gram-scale N—H insertion reaction

For the gram-scale N—H insertion reactions, aqueous degassed solutions of aminoacetonitrile hydrochloride (c = 2.0 mol / L, 4.0 eq.) and sodium nitrite (c = 2.4 mol / L, 4.8 eq.) were both added at a flow rate of 100 µL / min into the LTF MR Lab MX microreactor at 55 °C and then passed through an ice bath. The microreactor was connected to an IDEX backpressure vent and the outlet was connected to a standard reaction vessel. This solution of diazoacetonitrile was added drop wise at this flowrate to a degassed solution of the *N*-benzylanlinine (1.24g, 6.8 mmol, 1.0 eq.) and FeTPPCl (1 mol-%) in 2.4 mL toluene and stirred after addition for another 1 h at room temperature. The reaction mixture was then extracted three times with 50 mL of DCM. The combined organic phases were dried over $MgSO_4$ and the solvent removed. The crude product thus obtained was purified by column chromatography on silica gel.

Analysis of the formation of diazo acetonitrile

Degassed solutions of aminoacetonitrile hydrochloride (c = 2.0 mol / L, 2.0 mL, 4.0 eq., 148 mg) and sodium nitrite (c = 2.4 mol / L, 2.0 mL, 4.8 eq., 132 mg) in deuterium oxide were both added at a flow rate of 100 µL / min into the LTF MR Lab MX microreactor at 55 °C and then passed through an ice bath. The microreactor was connected to an IDEX backpressure vent and the outlet was connected to a standard reaction vessel. After 10 minutes, an aliquot was taken and investigated by ^{1}H-NMR, revealing quantitative consumption of the starting amine.

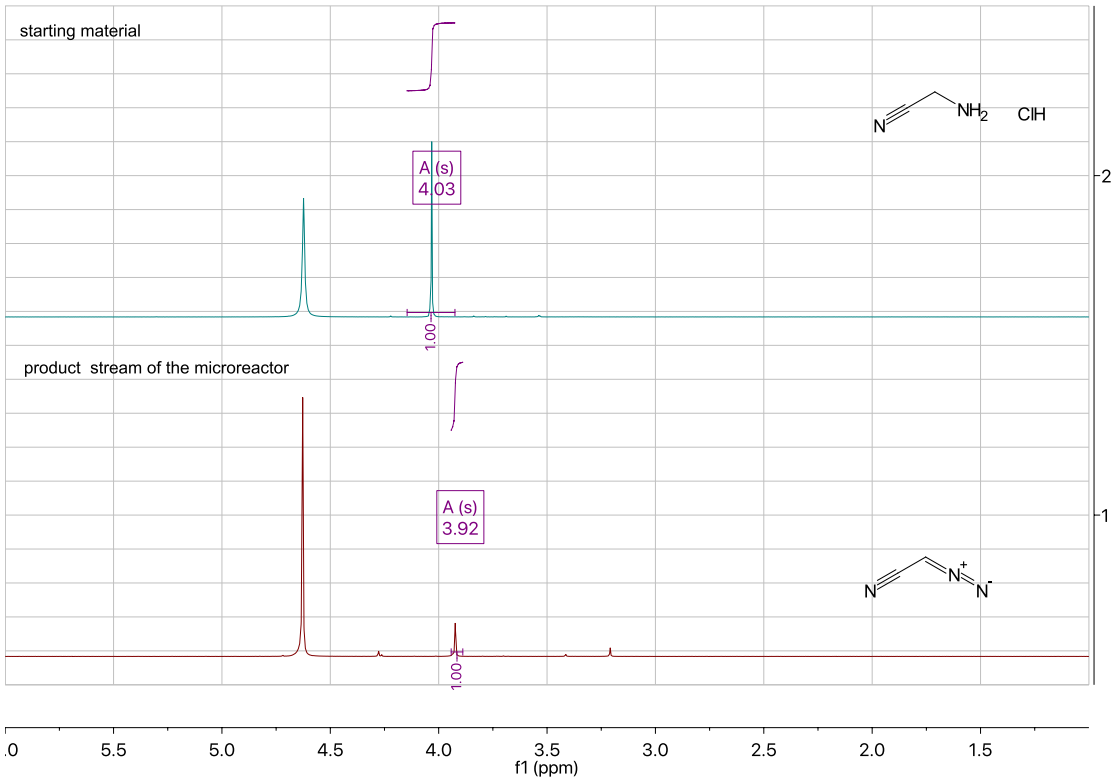
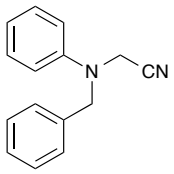


Figure 1: ^{1}H-NMR data of amino acetonitrile hydrochloride and of the product stream of the microreactor.

Analytical data

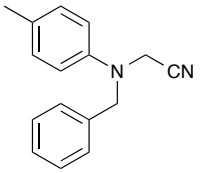
Amines

2-(benzyl(phenyl)amino)acetonitrile (7a)



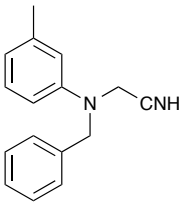
Compound **7a** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 98% yield (50 mg): ^{1}H NMR (300 MHz, Chloroform-*d*): = δ 7.49 – 7.27 (m, 7H), 7.04 – 6.91 (m, 3H), 4.53 (s, 2H), 4.08 (s, 2H) ppm; ^{13}C NMR (75 MHz, Chloroform-*d*): δ = 147.9, 136.8, 129.5, 128.9, 127.8, 127.6, 120.7, 115.7, 115.6, 55.7, 39.5 ppm; MS(EI): *m/z*(%) = 222.4 ($[M]^{+}$, 70.1%), 196.4 ($[M - CN]^{+}$, 100%), 91.2 ($[M – C_8H_7N_2]^{+}$, 31.4%); IR(KBr): 3854, 3394, 3034, 2851, 2665, 2328, 2110, 1943, 1676, 1596, 1498, 1453, 1355, 1214, 1160, 1076, 1029, 937, 873, 818, 744, 694 cm^{-1}.
The data is in accordance to the literature.[ii]

2-(benzyl(*p*-tolyl)amino)acetonitrile (7b)



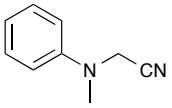
Compound **7b** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 99% yield (78 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.41 – 7.34 (m, 4H), 7.32 (td, *J* = 6.4, 2.7 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.93 – 6.87 (m, 2H), 4.46 (s, 2H), 4.02 (s, 2H), 2.30 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 145.8, 136.9, 130.5, 130.0, 128.8, 127.8, 120.4, 116.4, 115.7, 55.9, 40.0, 20.4 ppm; HRMS(ESI): mass found: 237.13858, calculated mass for $C_{16}H_{17}N_2^+$: 237.13862; IR(KBr): 3653, 3030, 2922, 2860, 2734, 2328, 2236, 2162, 2020, 1961, 1874, 1813, 1679, 1614, 1515, 1450, 1356, 1206, 1161, 1076, 1032, 938, 868, 805, 738, 700 cm^{-1}.

3-(benzyl(*m*-tolyl)amino)acetonitrile (7c)



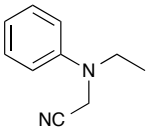
Compound **7c** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 99% yield (78 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.41 – 7.29 (m, 5H), 7.23 – 7.17 (m, 1H), 6.80 – 6.77 (m, 3H), 4.50 (s, 2H), 4.06 (s, 2H), 2.35 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 148.0, 139.4, 136.9, 129.3, 128.8, 127.8, 127.6, 121.6, 116.3, 115.8, 112.8, 55.6, 39.4, 21.7 ppm; HRMS(ESI): mass found: 237.13858, calculated mass for $C_{16}H_{17}N_2^+$: 237.13863; IR(KBr): 3655, 3384, 3035, 2921, 2858, 2327, 2095, 1924, 1814, 1681, 1597, 1495, 1451, 1356, 1247, 1174, 1075, 1033, 947, 862, 766, 696 cm^{-1}.

2-(methyl(phenyl)amino)acetonitrile (7d)



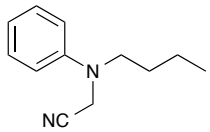
Compound **7d** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 70% yield (41 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.35 – 7.30 (m, 2H), 6.93 (tt, *J* = 7.3, 1.0 Hz, 1H), 6.90 – 6.85 (m, 2H), 4.18 (s, 2H), 3.02 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 147.7, 129.4, 120.2, 115.4, 114.8, 42.3, 39.2 ppm; MS(EI): *m/z*(%) = 146.0 ([M]$^+$, 100%), 145.0 ([M – H]$^+$, 38.7%), 120.0 ([M – CN]$^+$, 44.2%), 106.0 ([M – CH_2CN]$^+$ 16.1%), 77.1 ([M – CH_2CN – CH_3 – N]$^+$, 16.3%); IR(KBr): 3036, 2958, 2891, 2818, 2660, 2326, 2239, 2176, 2084, 1997, 1949, 1854, 1774, 1674, 1598, 1500, 1454, 1423, 1346, 1244, 1199, 1117, 1033, 007, 924, 869, 753, 691 cm^{-1}.
The data is in accordance to the literature.[iii]

2-(ethyl(phenyl)amino)acetonitrile (7e)



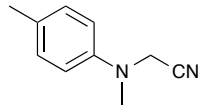
Compound **7e** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 68% yield (44 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.31 (dd, *J* = 8.7, 7.2 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 1H), 6.89 – 6.85 (m, 2H), 4.15 (s, 2H), 3.45 (q, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 146.8, 129.5, 119.8, 116.3, 114.9, 46.2, 39.5, 12.2 ppm; MS(EI): *m/z*(%)= 160.0 ([M]$^{+}$, 59.7%), 145 ([M – CH_3]$^{+}$, 100%), 105.0 ([M – C_2H_5 – CN]$^{+}$, 63.1%), 77.1 ([M – CH_2CN – C_2H_5 – N]$^{+}$, 41.9%); IR(KBr): 3196, 3063, 2975, 2933, 2876, 26858, 2326, 2239, 2089, 1998, 1924, 1836, 1675, 1598, 1500, 1455, 1430, 1380, 1350, 1243, 1185, 1128, 1075, 1037, 1011, 978, 873, 797, 750, 692 cm^{-1}.
The data is in accordance to the literature.[ii]

2-(butyl(phenyl)amino)acetonitrile (7f)



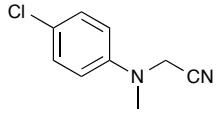
Compound **7f** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 93% yield (70 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.30 (dd, *J* = 8.8, 7.3 Hz, 2H), 6.89 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.85 (dt, *J* = 7.7, 1.0 Hz, 2H), 4.15 (s, 2H), 3.63 – 3.26 (m, 2H), 1.70 – 1.60 (m, 2H), 1.40 (heptet, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 147.1, 129.4, 119.6, 116.2, 114.7, 51.8, 40.0, 29.2, 20.2, 13.8 ppm; HRMS(ESI): mass found: 189.13858, calculated mass for $C_{12}H_{17}N_2^{+}$: 189.13862; IR(KBr): 3197, 3064, 2957, 2932, 2869, 2325, 2080, 1993, 1924, 1675, 1598, 1501, 1463, 1430, 1367, 1251, 1218, 1178, 1132, 1040, 925, 868, 749, 692 cm^{-1}.
The data is in accordance to the literature.[ii]

2-(methyl(*p*-tolyl)amino)acetonitrile (7g)



Compound **7g** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 71% yield (46 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.12 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.14 (s, 2H), 2.97 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 145.7, 129.97, 129.91, 115.4, 42.9, 39.5, 20.4 ppm; MS(EI): *m/z*(%) = 160.3 ([M]$^{+}$, 100%), 134.3 ([M – CN]$^{+}$, 31.7%), 120.3 ([M – CH_2CN]$^{+}$, 69.3%), 91.2 ([M – $C_3H_5N_2$]$^{+}$, 45.6%; IR(KBr): 3853, 3628, 3343, 3029, 2918, 2729, 2326, 2234, 2116, 2029, 1880, 1724, 1673, 1610, 1514, 1345, 1248, 1195, 1116, 999, 925, 867, 802, 701 cm^{-1}.
The data is in accordance to the literature.[iv]

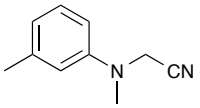
2-((4-chlorophenyl)(methyl)amino)acetonitrile (7h)



Compound **7h** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 72% yield (52 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.38 – 7.18 (m, 2H), 6.83 – 6.74 (m, 2H), 4.15 (s, 2H), 2.99 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 146.3, 129.3, 125.3, 116.0, 115.1, 42.3, 39.4 ppm; MS(EI): *m/z*(%): 180.3; 182.3 ([M]$^{+}$, 59.0%; 18.3%), 154.3; 156.4 ([M – CN]$^{+}$, 23.9%; 7.7%), 140.2; 142.2 ([M – CH_2CN]$^{+}$, 86.6%; 24.2%), 111.1; 113.1 ([M

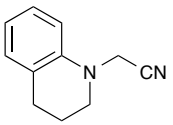
– $C_3H_5N_2]^+$, 66.5%; 24.4 %); IR(KBr): 3388, 3068, 2914, 2827, 2688, 2322, 2239, 2179, 1873, 1751, 1678, 1593, 1494, 1360, 1327, 1248, 1200, 1111, 998, 927, 877, 807, 698 cm^{-1}.
The data is in accordance to the literature.[iii]

2-(methyl(*m*-tolyl)amino)acetonitrile (7i)



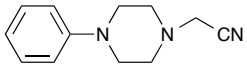
Compound **7i** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 50% yield (32 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.24 – 7.17 (m, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.71 – 6.67 (m, 2H), 4.17 (s, 2H), 3.00 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 147.8, 139.2, 129.2, 121.1, 115.7, 115.5, 112.1, 42.3, 39.2, 21.8 ppm; MS(EI): *m/z*(%) = 160.3 ($[M]^+$, 100%), 134.3 ($[M – CN]^+$, 48.2%), 120.2 ($[M – CH_2CN]^+$, 18.4%), 91.2 ($[M – C_3H_5N_2]^+$, 19.6%; IR(KBr): 3646, 3040, 2918, 2237, 2025, 1918, 1685, 1598, 1493, 1345, 1253, 1179, 1116, 1016, 938, 859, 771, 691 cm^{-1}.
The data is in accordance to the literature.[v]

2-(3,4-dihydroquinolin-1(2*H*)-yl)acetonitrile (7j)



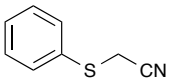
Compound **7j** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 9:1 → 4:1 → 1:1) as a yellow oil in 68% yield (47 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.17 – 7.11 (m, 1H), 7.04 – 7.01 (m, 1H), 6.78 (td, *J* = 7.3, 1.0 Hz, 1H), 6.67 (dd, *J* = 8.2, 1.0 Hz, 1H), 4.17 (s, 2H), 3.34 – 3.25 (m, 2H), 2.80 (t, *J* = 6.5 Hz, 2H), 2.10 – 1.97 (m, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 143.1, 129.5, 127.2, 124.6, 119.1, 115.7, 111.8, 50.0, 40.1, 27.3, 22.1 ppm; MS(EI): *m/z*(%) = 172.3 ($[M]^+$, 18.1%), 130.2 ($[M – C_3H_6]^+$, 24.8%; IR(KBr): 3034, 2939, 2843, 2767, 2637, 2315, 2236, 2157, 1898, 1736, 1670, 1598, 1498, 1446, 1331, 1239, 1187, 1115, 1063, 963, 927, 866, 800, 747 cm^{-1}.
The data is in accordance to the literature.[iii]

2-(4-phenylpiperazin-1-yl)acetonitrile (7k)



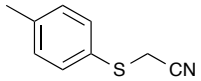
Compound **7k** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 4:1 → 1:1) as a red oil in 30% yield (24 mg): ^{1}H NMR (400 MHz, Chloroform-*d*): δ = 7.30 – 7.22 (m, 2H), 6.95 – 6.90 (m, 2H), 6.87 (tt, *J* = 7.3, 1.1 Hz, 1H), 3.56 (s, 2H), 3.30 – 3.19 (m, 4H), 2.78 – 2.69 (m, 4H); ^{13}C NMR (101 MHz, Chloroform-*d*): δ = 150.9, 129.1, 120.1, 116.3, 114.5, 51.8, 48.9, 45.9 ppm; MS(EI): *m/z*(%) = 201.1 ($[M]^+$, 100%), 161.1 ($[M – C_2HCN]^+$, 58.8%); IR(KBr): 3348, 3064, 3038, 2940, 2879, 2829, 2771, 2698, 2454, 2329, 2232, 2162, 2068, 2015, 1932, 1849, 1779, 1676, 1597, 1496, 1452, 1427, 1378, 1326, 1303, 1229, 1193, 1140, 1055, 1053, 1003, 917, 861, 820, 757, 692 cm^{-1}.
The data is in accordance to the literature.[vi]

2-(phenylthio)acetonitrile (9a)



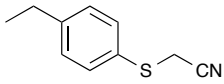
Compound **9a** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 40:1 → 20:1 → 9:1) as a yellow oil in 48% yield (14 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.66 – 7.52 (m, 2H), 7.45 – 7.33 (m, 3H), 3.57 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 132.5, 132.0, 129.6, 129.0, 116.5, 21.4 ppm; MS(EI): *m/z*(%) = 149.0 ([M]$^{+}$, 53.1%), 109.0 ([M – CH_2CN]$^{+}$, 100%), 109.0 ([M – CH_2CN – CH – S]$^{+}$, 21.2%); IR(KBr): 3166, 3061, 2970, 2930, 2325, 2245, 2155, 2085, 1954, 1883, 1806, 1723, 1670, 1580, 1478, 1439, 1399, 1304, 1231, 1179, 1071, 1023, 923, 860, 741, 689 cm^{-1}.
The data is in accordance to the literature.[vii]

2-(*p*-tolylthio)acetonitrile (9b)



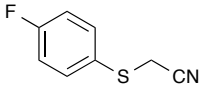
Compound **9b** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 53% yield (35 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.32 – 7.23 (m, 2H), 6.83 – 6.76 (m, 2H), 4.15 (s, 2H), 3.00 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 146.3, 129.3, 125.3, 116.0, 115.1, 42.3, 39.4; MS(EI): *m/z*(%) = 163.0 ([M]$^{+}$, 100%), 123.0 ([M – CH_2CN]$^{+}$, 94.6%), 79.1 ([M – CH_2CNSC]$^{+}$, 10.6%); IR(KBr): 3169, 3026, 2969, 2925, 2868, 2664, 2325, 2244, 2179, 2109, 1995, 1902, 1802, 1637, 1644, 1596, 1492, 1448, 1400, 1303, 1213, 1180, 1094, 1018, 926, 864, 805, 753, 701 cm^{-1}.
The data is in accordance to the literature.[vii]

2-((4-ethylphenyl)thio)acetonitrile (9c)



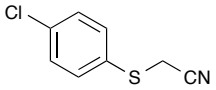
Compound **9c** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 52% yield (18 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.50 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 3.52 (s, 2H), 2.66 (q, *J* = 7.6 Hz, 2H), 1.24 (td, *J* = 7.6, 0.8 Hz, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 145.7, 133.2, 129.1, 128.5, 116.6, 28.5, 21.9, 15.3 ppm; MS(EI): *m/z*(%) = 177.5 ([M]$^{+}$, 100%), 162.3 ([M – CH_3]$^{+}$, 23.8%), 137.4 ([M – CH_2CN]$^{+}$, 97.4%); IR(KBr): 3850, 3650, 3028, 2966, 2875, 2676, 2501, 2317, 2243, 2114, 2026, 1909, 1713, 1594, 1489, 1403, 1328, 1182, 1093, 1015, 964, 825 cm^{-1}.
The data is in accordance to the literature.[vii]

2-((4-fluorophenyl)thio)acetonitrile (9d)



Compound **9d** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 45% yield (30 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.66 – 7.52 (m, 2H), 7.21 – 6.95 (m, 2H), 3.51 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 163.5 (d, *J* = 250.7 Hz), 135.9 (d, *J* = 8.6 Hz), 126.8 (d, *J* = 3.4 Hz), 116.8 (d, *J* = 22.0 Hz), 116.3, 22.3 ppm; ^{19}F NMR (564 MHz, Chloroform-*d*): δ = -110.78 (tt, *J* = 8.8, 5.2 Hz) ppm; MS(EI): *m/z*(%) = 167.0 ([M]$^{+}$, 81.0%), 127 ([M – CH_2CN]$^{+}$, 100%), 83.1 ([M – C_3H_3NS]$^{+}$, 28.5%); HRMS(ESI): mass found: 167.01995 , calculated mass for $C_8H_6NFS^{+}$: 167.02050; IR(KBr): 3169, 3098, 2965, 2928, 2854, 2655, 2453, 2328, 2244, 2176, 2042, 1884, 1762, 1639, 1589, 1489, 1402, 1304, 1224, 1160, 1089, 1011, 923, 870, 818, 727 cm^{-1}.

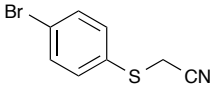
2-((4-chlorophenyl)thio)acetonitrile (9e)



Compound **9e** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 52% yield (39 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.51 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 3.55 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 135.6, 134.1, 130.3, 129.8, 116.1, 21.6 ppm; MS(EI): *m/z*(%) = 183.0; 185.0 ([M]$^{+}$, 86.4%; 33.6%), 143.0; 144.9 ([M – CH_2CN]$^{+}$, 100%; 42.0%), 108.0 ([M – $ClCH_2CN$]$^{+}$, 42.2%); IR(KBr): 3343, 3165, 3071, 3022, 2962, 2926, 2855, 2661, 2454, 2311, 2243, 2182, 2108, 1989, 1897, 1841, 1781, 1735, 1638, 1571, 1475, 1403, 1303, 1259, 1232, 1178, 1092, 1006, 949, 922, 871, 809, 748, 723 cm^{-1}.

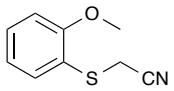
The data is in accordance to the literature.[vii]

2-((4-bromophenyl)thio)acetonitrile (9f)



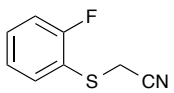
Compound **9f** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a pale brown oil in 35% yield (32 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.53 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 3.55 (s, 2H) ppm;^{13}C NMR (151 MHz, Chloroform-*d*): δ = 134.1, 132.8, 131.0, 123.7, 116.2, 21.4 ppm; MS(EI): *m/z*(%) = 227.3; 229.3 ([M]$^{+}$ 10.8%; 9.7%) , 187.2; 189.2 ([M – CH_2CN]$^{+}$ 25.9%; 27.1%), 108.2 ([M – $BrCH_2CN$]$^{+}$ 100%); HRMS(ESI): mass found: 226.94053, calculated mass for $C_8H_6BrNS^{+}$: 226.94043; IR(KBr): 3661, 3165, 3066, 3012, 2963, 2928, 2839, 2772, 2651, 2552, 2458, 2328, 2243, 2203, 2176, 2086, 1989, 1951, 1895, 1742, 1663, 1580, 1473, 1403, 1274, 1246, 1178, 1130, 1087, 1002, 921, 871, 806, 752, 717, 677 cm^{-1}.

2-((2-methoxyphenyl)thio)acetonitrile (9g)



Compound **9g** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1 → 4:1) as a pale brown oil in 60% yield (43 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.38 (ddd, *J* = 8.3, 7.4, 1.7 Hz, 1H), 6.98 (td, *J* = 7.6, 1.2 Hz, 1H), 6.94 (dd, *J* = 8.3, 1.2 Hz, 1H), 3.93 (s, 3H), 3.62 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 158.9, 134.5, 130.9, 121.3, 119.2, 116.7, 111.1, 55.8, 19.1 ppm; MS(EI): *m/z*(%) = 179.0 ([M]$^{+}$, 100%), 139.0 ([M – CH_2CN]$^{+}$, 23.0%); HRMS(ESI): mass found: 218.00363, calculated mass for $C_9H_9NOKS^{+}$: 218.00364; IR(KBr): 3171, 3065, 2971, 2933, 2836, 2540, 2245, 2148, 2028, 1949, 1914, 1877, 1789, 1700, 1578, 1470, 1430, 1403, 1268, 1243, 1181, 1158, 1126, 1067, 1015, 940, 860, 794, 752, 714, 679 cm^{-1}.

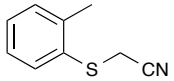
2-((2-fluorophenyl)thio)acetonitrile (9h)



Compound **9h** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 99% yield (67 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.60 (td, *J* = 7.5, 1.7 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.22 – 7.12 (m, 2H), 3.61 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 162.4 (d, *J* =

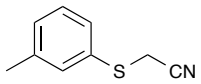
248.6 Hz), 135.3, 131.7 (d, *J* = 8.3 Hz), 125.09 (d, *J* = 3.9 Hz), 118.4 (d, *J* = 17.7 Hz), 116.3 (d, *J* = 22.1 Hz), 116.0, 20.0 (d, *J* = 3.8 Hz) ppm; ^{19}F NMR (564 MHz, Chloroform-*d*): δ= -107.65 (ddd, *J* = 9.5, 7.4, 5.2 Hz) ppm; MS(EI): *m/z*(%) = 167.3 ([M]$^+$, 61.2%), 127.2 ([M – CH_2CN]$^+$, 100%), 83.2 ([M – C_3H_3NS]$^+$, 45.3%); IR(KBr): 3892, 3663, 3446, 3178, 3071, 2976, 2935, 2657, 2523, 2465, 2328, 2245, 2211, 2169, 2087, 1991, 1949, 1803, 1572, 1472, 1446, 1402, 1314, 1261, 1222, 1156, 1123, 1070, 1029, 927, 867, 819, 758, 698, 674, 667 cm^{-1}.
The data is in accordance to the literature.[viii]

2-(*o*-tolylthio)acetonitrile (9i)



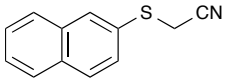
Compound **9i** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a pale yellow oil in 97% yield (32 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.52 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.22 (m, 3H), 3.54 (s, 2H), 2.49 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 140.4, 132.7, 131.2, 130.8, 129.0, 127.1, 116.3, 20.5, 20.4 ppm; MS(EI): *m/z*(%) = 163.3 (26.3%), 123.2 (48.6%), 45.3 (100%); IR(KBr): 3856, 3409, 3167, 3061, 2966, 2927, 2669, 2329, 2247, 2091, 1994, 1906, 1667, 1586, 1464, 1391, 1331, 1277, 1163, 1045, 925, 859, 750 cm^{-1}.
The data is in accordance to the literature.[vii]

2-((3-methylphenyl)thio)acetonitrile (9j)



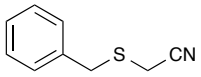
Compound **9j** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 44% yield (29 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.38 – 7.33 (m, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.56 (s, 2H), 2.37 (s, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 139.5, 132.9, 131.7, 129.8, 129.4, 129.3, 116.5, 21.3, 21.2 ppm; MS(EI): *m/z*(%) = 163.2 ([M]$^+$, 90.7%), 123.2 ([M – CH_2CN]$^+$, 100%), 79.2 ([M – C_3H_3NS]$^+$, 16.3%); IR(KBr): 3544, 3176, 2966, 2926, 2335, 2245, 2170, 2077, 1998, 1946, 1881, 1784, 1674, 1591, 1473, 1402, 1302, 1225, 1171, 1081, 1042, 998, 924, 854, 777, 687 cm^{-1}.
The data is in accordance to the literature.[viii]

2-(naphthalen-2-ylthio)acetonitrile (9k)



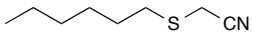
Compound **9k** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 51% yield (20 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 8.06 (d, *J* = 1.8 Hz, 1H), 7.89 – 7.81 (m, 3H), 7.58 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.56 – 7.51 (m, 2H), 3.66 (s, 2H); ^{13}C NMR (151 MHz, CDCl3): δ = 133.6, 133.0, 131.9, 129.4, 129.2, 128.8, 127.78, 127.75, 127.0, 126.9, 116.5, 21.3 ppm; MS(EI): *m/z*(%) = 199.1 ([M]$^+$, 80.3%), 159.1 ([M – CH_2CN]$^+$, 100%), 115.1 ([M – C_3H_2SN]$^+$, 85.5%); HRMS(ESI): mass found: 222.03471, calculated mass for $C_{12}H_9NNaS^+$: 222.03479; IR(KBr): 3896, 3859, 3748, 3627, 3166, 3053, 2963, 2927, 2857, 2456, 2348, 2244, 2153, 2063, 2003, 1953. 1912. 1841, 1767, 1711, 1620, 1583, 1498, 1458, 1429, 1402, 1337, 1260, 1196, 1125, 1074, 1019, 940, 889, 857, 809, 732, 698 cm^{-1}.
The data is in accordance to the literature.[vii]

2-(benzylthio)acetonitrile (9l)



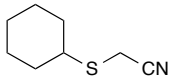
Compound **9l** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 20:1 → 9:1) as a yellow oil in 66% yield (21 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 7.39 – 7.33 (m, 4H), 7.34 – 7.27 (m, 1H), 3.92 (s, 2H), 3.08 (s, 2H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 135.6, 129.0, 128.8, 127.8, 116.2, 36.0, 15.8 ppm; MS(EI): *m/z*(%) = 163.2 ($[M]^+$,14.8%), 91.2 ($[M - C_2H_2NS]^+$, 100%), 65.2 ($[M - C_4H_5NS]^+$, 17.5%); IR(KBr): 3641, 3029, 2964, 2923, 2666, 2325, 2243, 2177, 2061, 1893, 1814, 1613, 1493, 1450, 1399, 1241. 1185, 1070, 1026, 919, 824, 768, 700 cm^{-1}. The data is in accordance to the literature.[ix]

2-(hexylthio)acetonitrile (9m)



Compound **9m** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 40:1 → 20:1 → 9:1) as a yellow oil in 87% yield (55 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 3.29 (s, 2H), 2.83 – 2.68 (m, 2H), 1.64 (p, *J* = 7.5 Hz, 2H), 1.45 – 1.27 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 116.6, 32.6, 31.3, 28.5, 28.3, 22.5, 16.9, 14.0 ppm; MS(EI): *m/z*(%) = 158.3 ($[M + H^+]$, 48.3%), 157.3 ($[M]^+$, 29.2%), 131.2 ($[M - CN]^+$, 29.2%), 117.2 ($[M - CH_2CN]^+$; 100%); HRMS(ESI): mass found: 180.08089, calculated mass for $C_8H_{15}NNaS^+$: 180.08174; IR(KBr): 3668, 3165, 2926, 2857, 2662, 2327, 2243, 2201, 2171, 2088, 1991, 1946, 1805, 1622, 1553, 1459, 1401, 1295, 1234, 1179, 1110, 1048, 990, 922, 866, 726 cm^{-1}.

2-(cyclohexylthio)acetonitrile (9n)



Compound **9n** was prepared according to general procedure and was obtained after column chromatography (*n*-hexane : ethyl acetate 40:1 → 20:1 → 9:1) as a pale yellow oil in 56% yield (34 mg): ^{1}H NMR (600 MHz, Chloroform-*d*): δ = 3.30 (s, 2H), 2.93 (tt, *J* = 10.4, 3.9 Hz, 1H), 2.06 – 1.99 (m, 2H), 1.83 – 1.74 (m, 2H), 1.69 – 1.60 (m, 1H), 1.43 – 1.31 (m, 4H), 1.30 – 1.22 (m, 1H) ppm; ^{13}C NMR (151 MHz, Chloroform-*d*): δ = 117.1, 44.3, 32.7, 25.5, 15.2 ppm; HRMS(ESI): mass found: 156.14929, calculated mass for $C_8H_{14}NS^+$:156.08415; IR(KBr): 3853, 3747, 3629, 2928, 2855, 2662, 2334, 2243, 2084, 1881, 1619, 1447, 1401, 1341, 1267, 1206, 1000, 921, 886, 818, 735 cm^{-1}.

References

[i] B. Binkowski, L. P. Encell, M. Hall, M. B. Robers, M. R. Slater, K. V. Wood and M. G. Wood, WO2012061530, 2012, (Promega Corporation).

[ii] A. Wagner, W. Han, P. Mayer and A. R. Ofial, *Adv. Synth. Catal.*, 2013, **355**, 3058.

[iii] Z. Yuan, N. Li, C. Zhu and C. Xia, *Chem. Commun.*, 2018, **54**, 2854.

[iv] M.-X. Sun, Y.-F. Wang, B.-H. Xu, X.-Q. Ma and S.-J. Zhang, *Org. Biomol. Chem.*, 2018, **16**, 1971.

[v] P.-Y. Liu, C. Zhang, S.-C. Zhao, F. Yu, F. Li and Y.-P. He, *J. Org. Chem.*, 2017, **82**, 12786

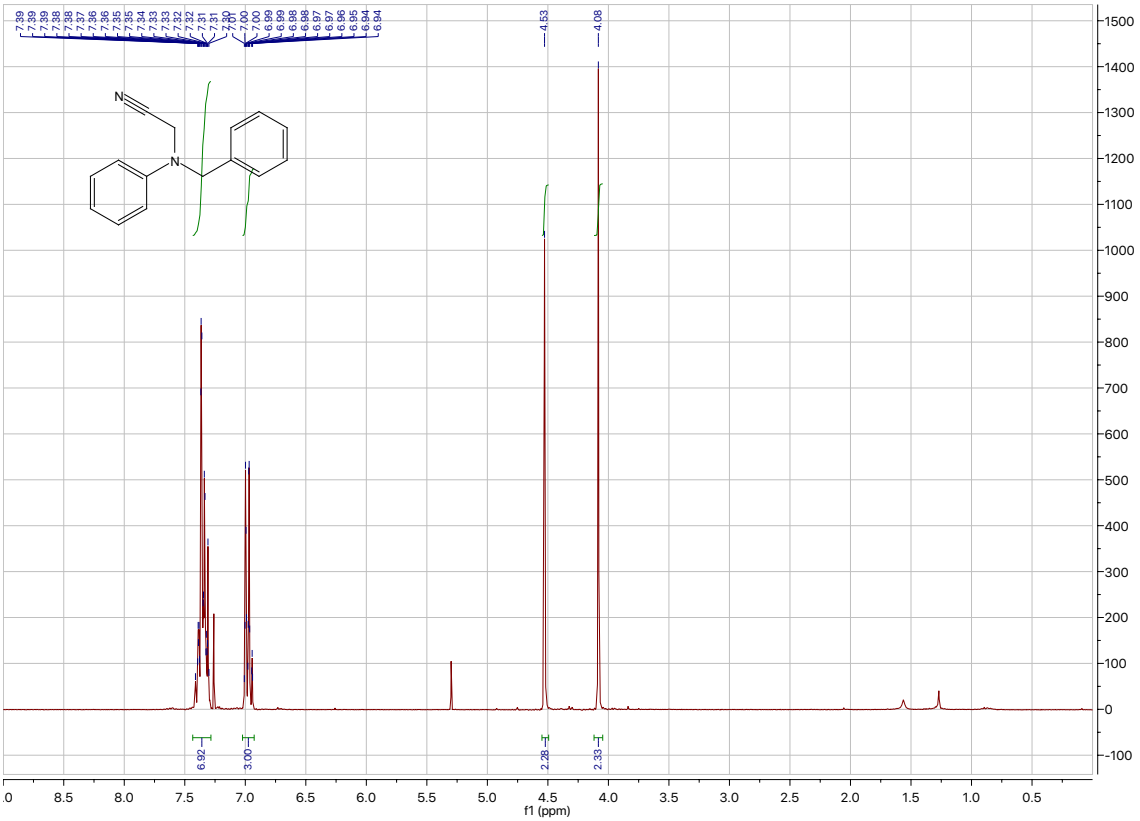
[vi] H. Wang, Y. Shao, H. Zheng, H. Wang, J. Cheng and X. Wan, *Chem. Eur. J.*, 2015, **21**, 18333.

[vii] Q. Chen, Y. Huang, X. Wang, C. Wen, X. Yan, J. Zeng, *Tetrahedron Lett.* **2017**, *58*, 3928-3931.
[viii] Q. Chen, Y. Huang, X. Wang, C. Wen, X. Yan and J. Zeng, *Tetrahedron Lett.*, 2017, **58**, 3928.
[ix] C.-H. Tan, X. Ye and L. Zong, WO2017164813, 2017, (Nanyang Technological University).

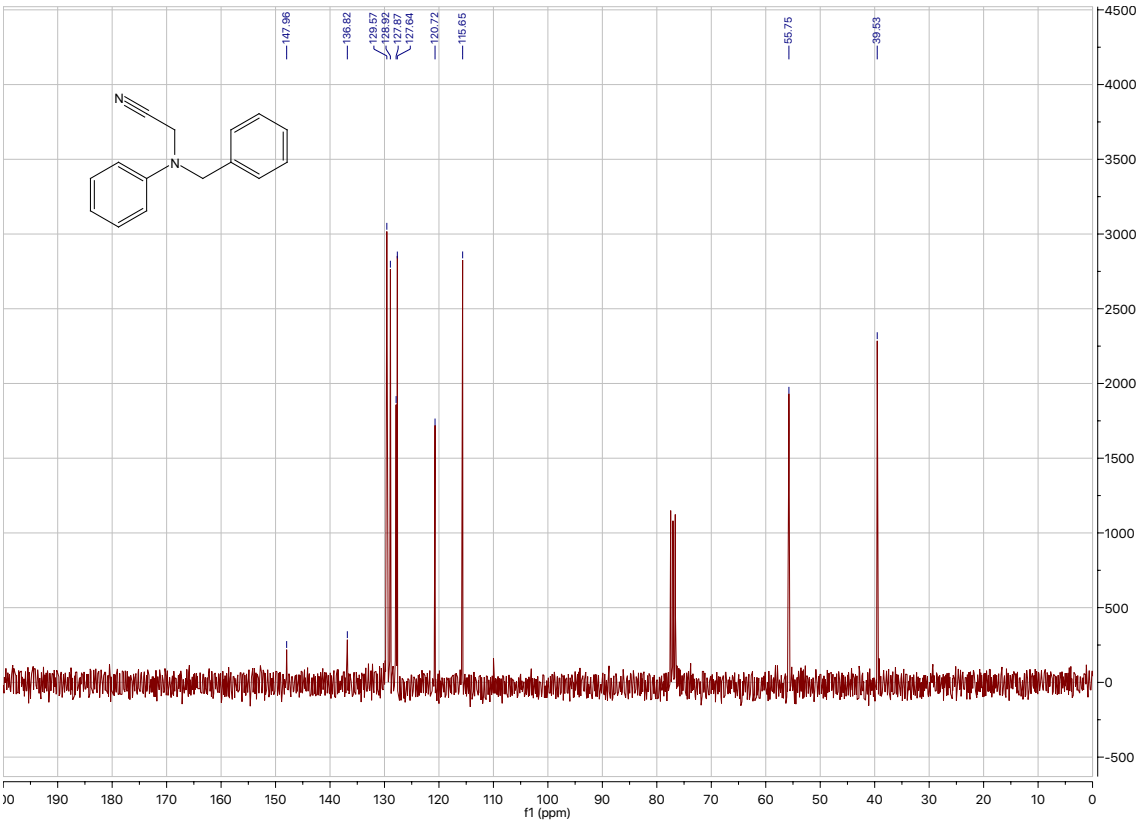
α-aminonitriles

2-(benzyl(phenyl)amino)acetonitrile (7a)

^{1}H NMR (300 MHz, $CDCl_3$)

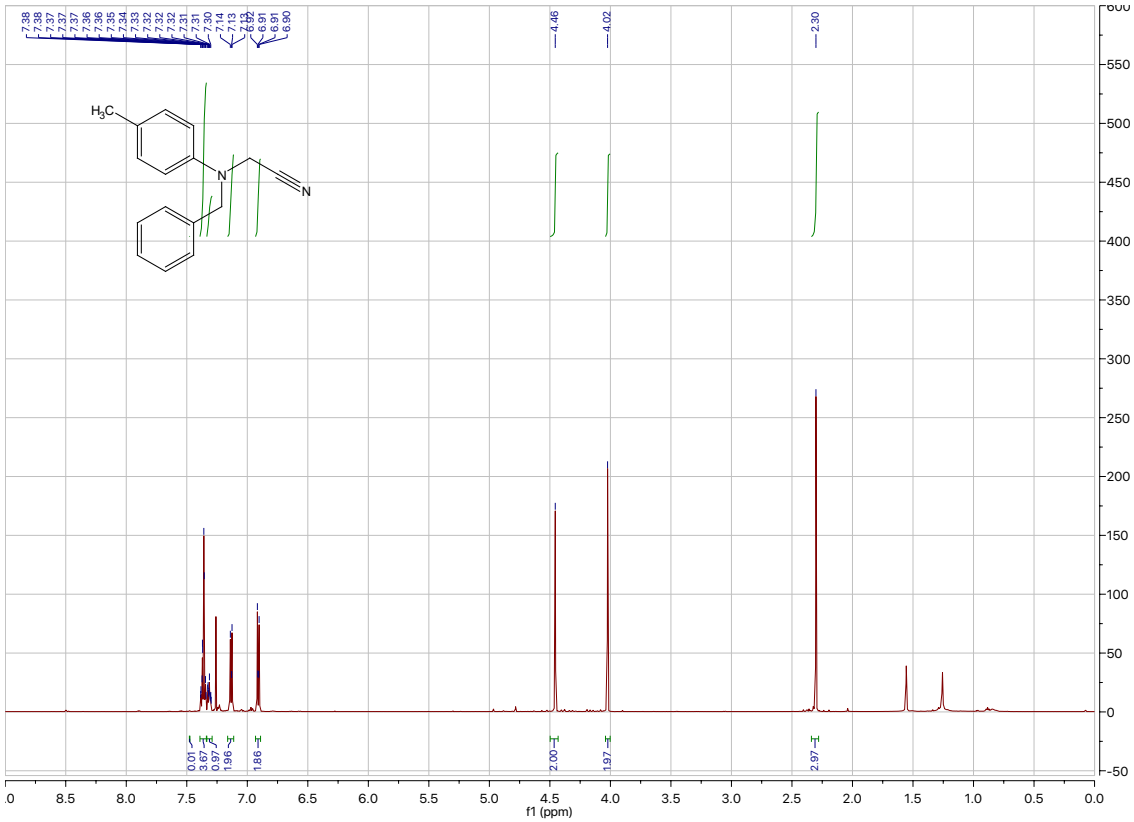


^{13}C NMR (75 MHz, $CDCl_3$)

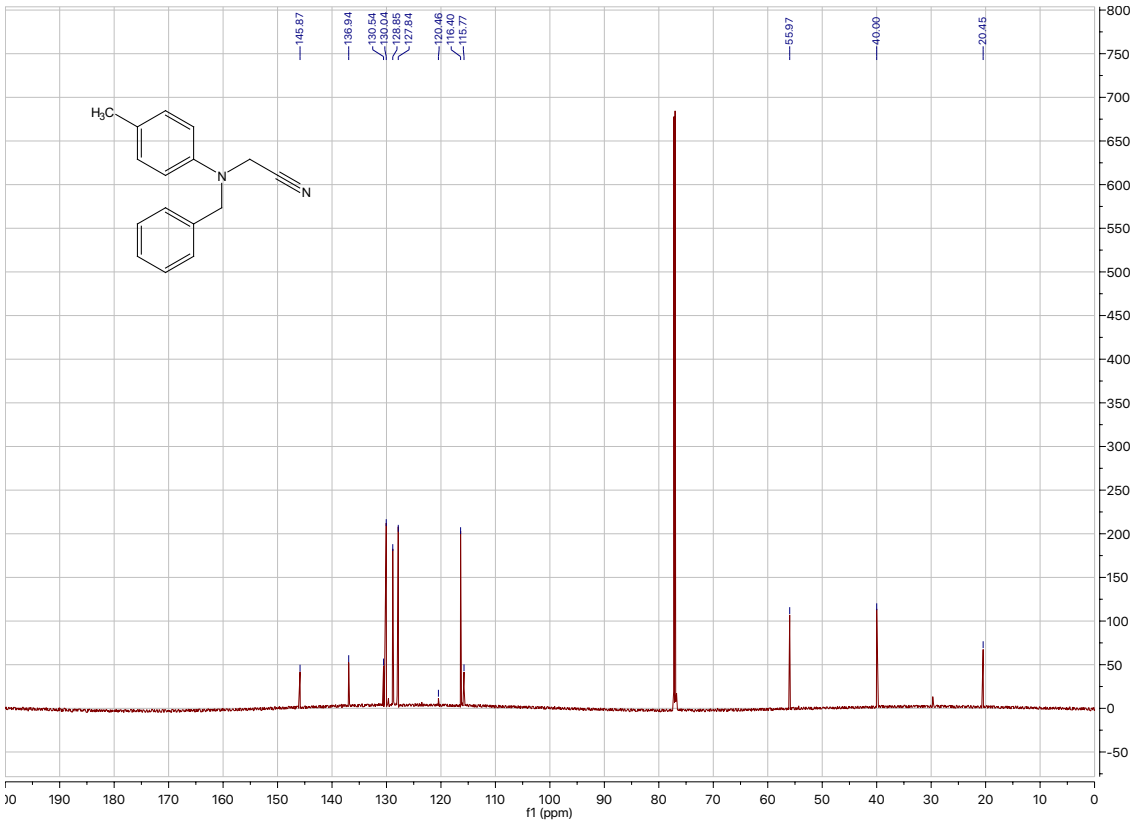


2-(benzyl(*p*-tolyl)amino)acetonitrile (7b)

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

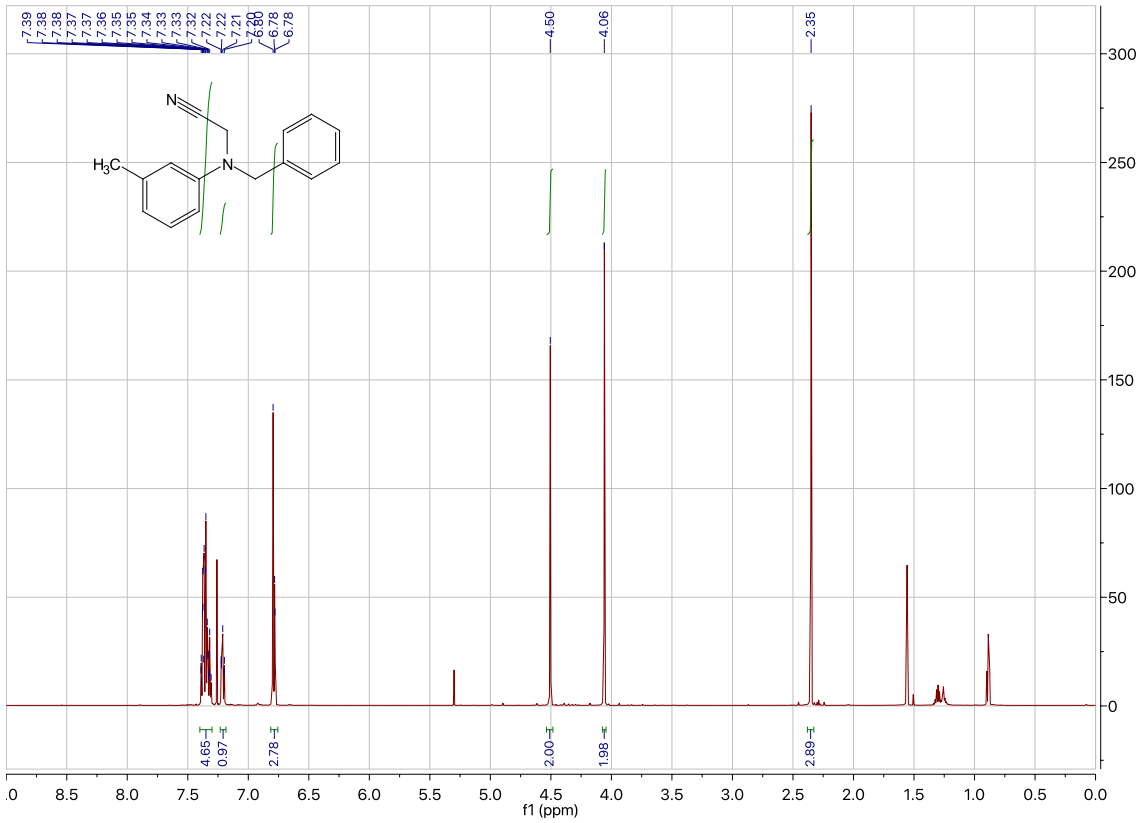


^{13}C NMR (151 MHz, $CDCl_3$)

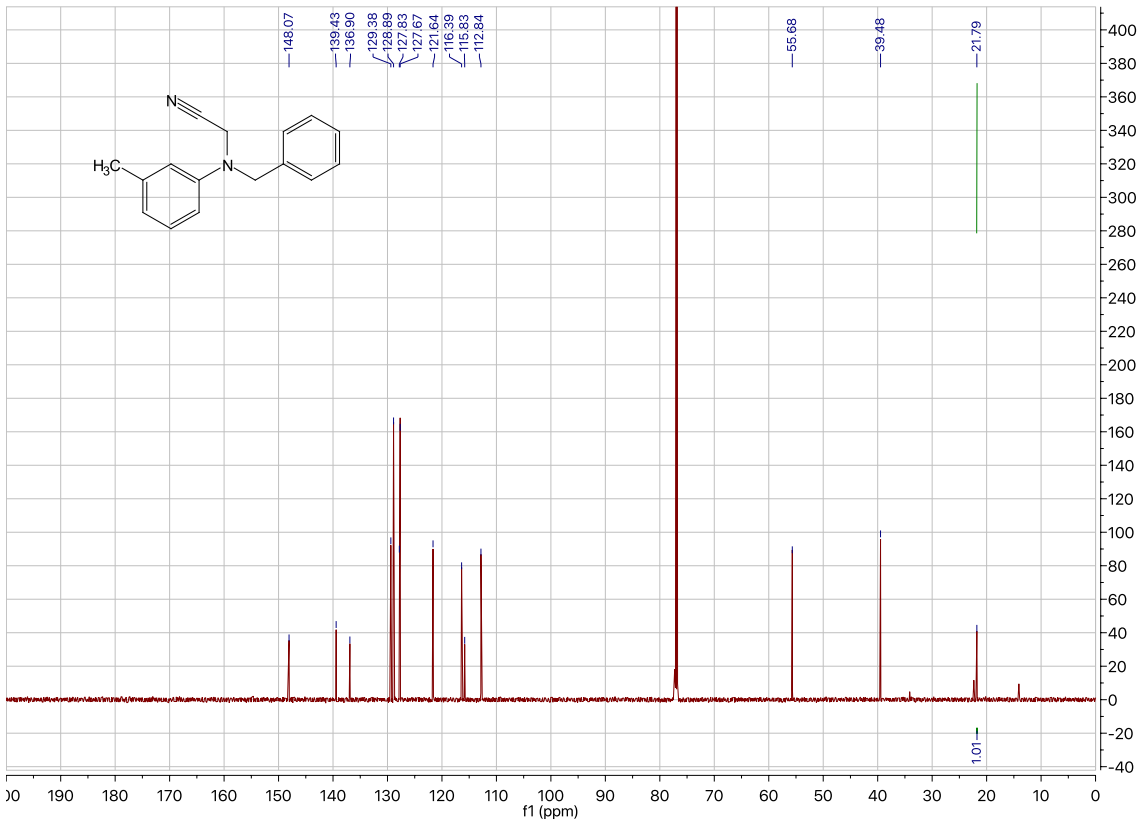


2-(benzyl(*m*-tolyl)amino)acetonitrile (7c)

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

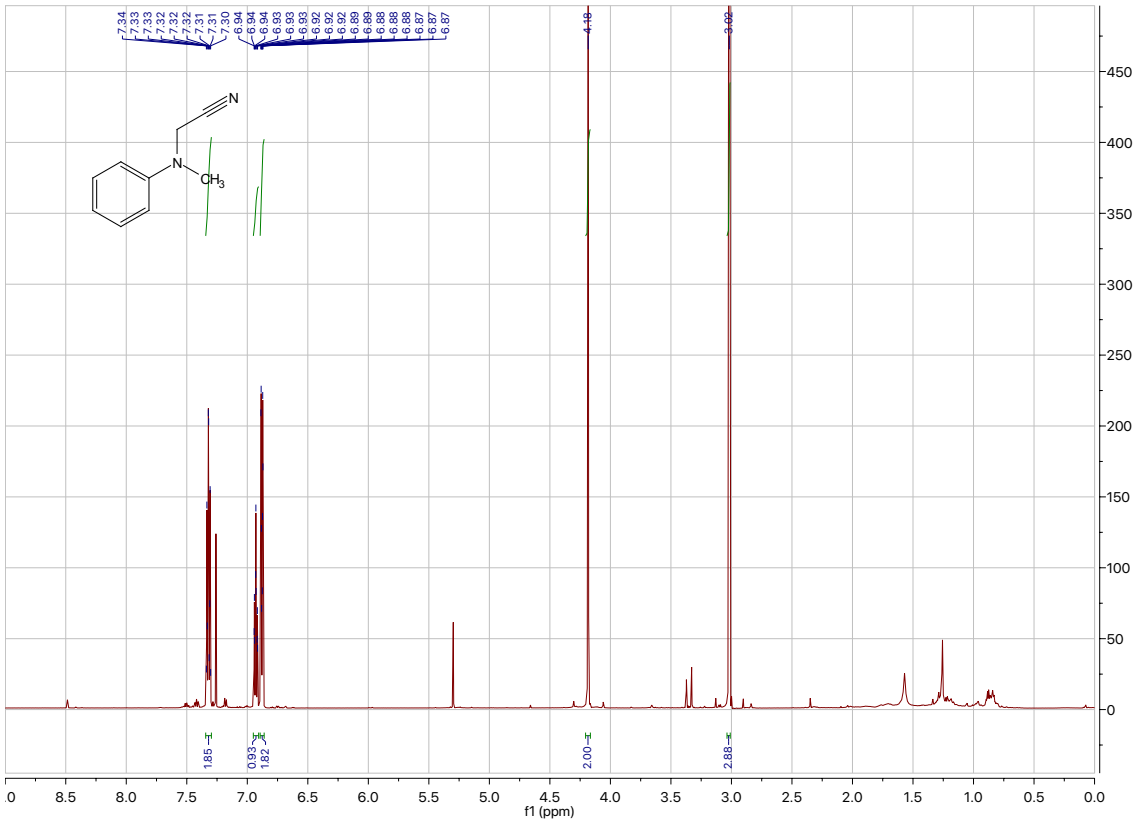


^{13}C NMR (151 MHz, $CDCl_3$)

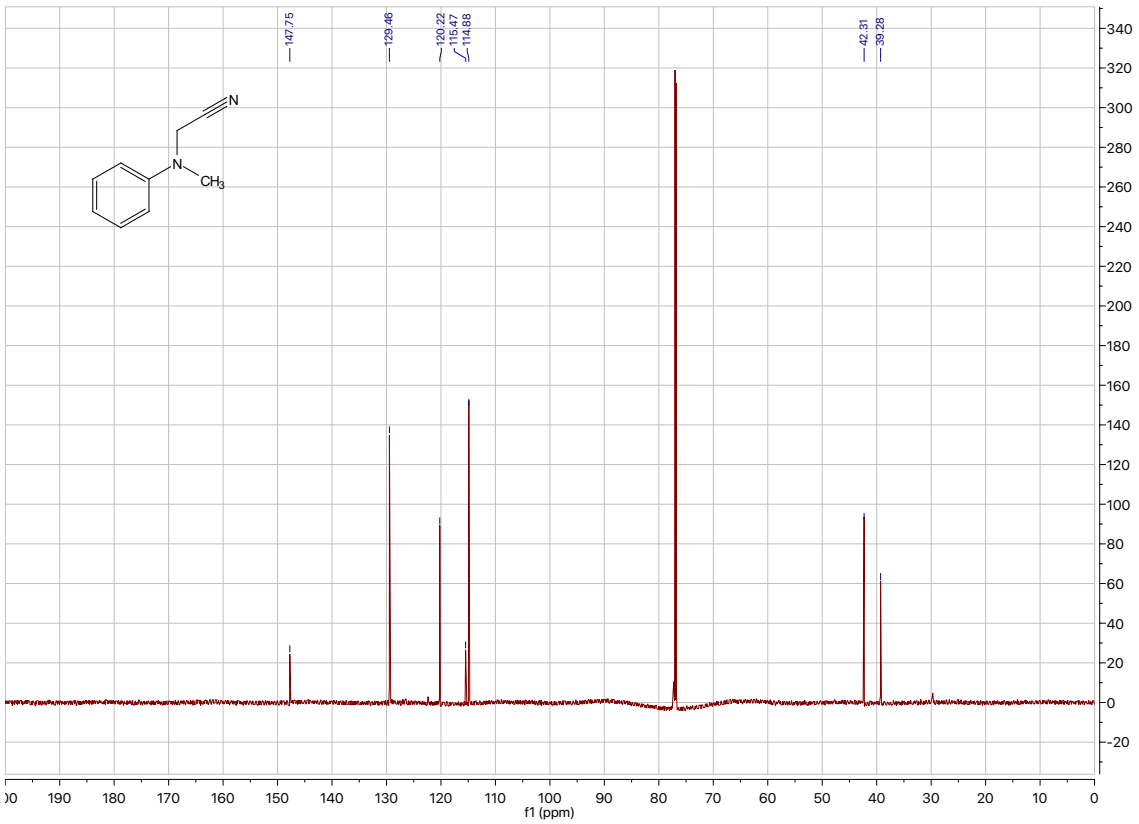


2-(methyl(phenyl)amino)acetonitrile (7d)

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

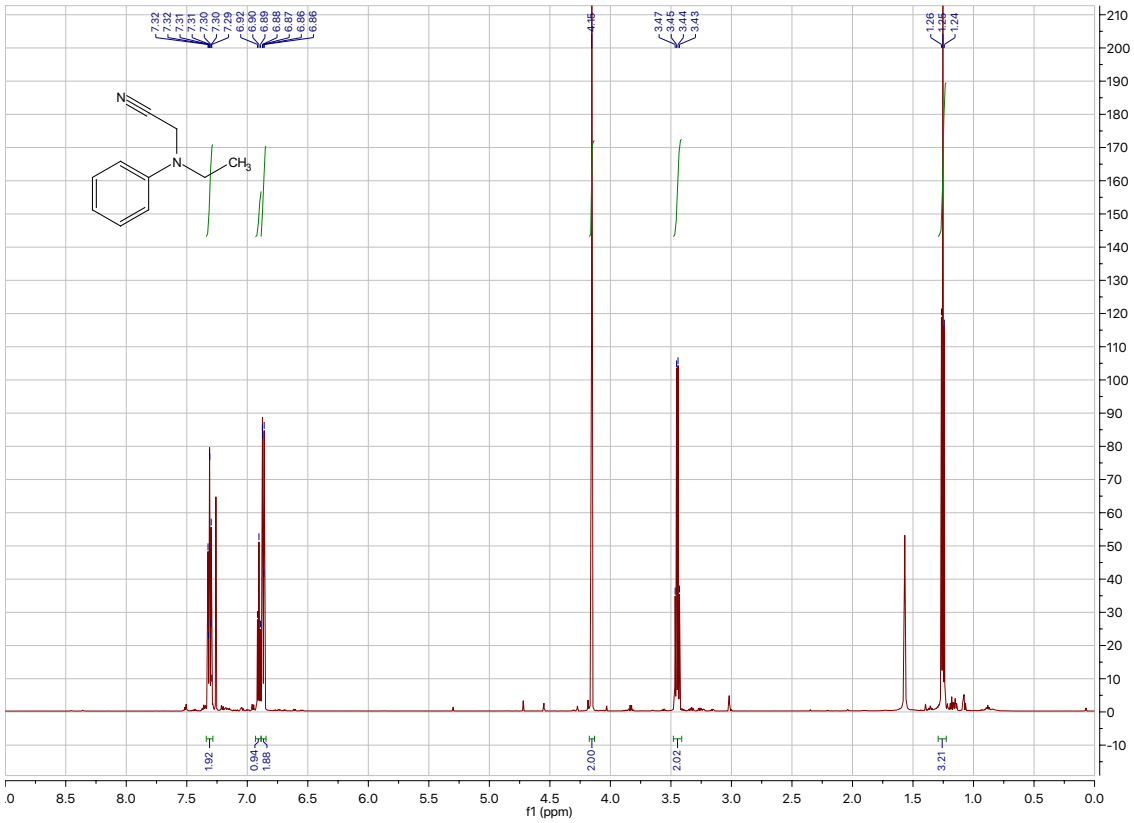


^{13}C NMR (151 MHz, $CDCl_3$)

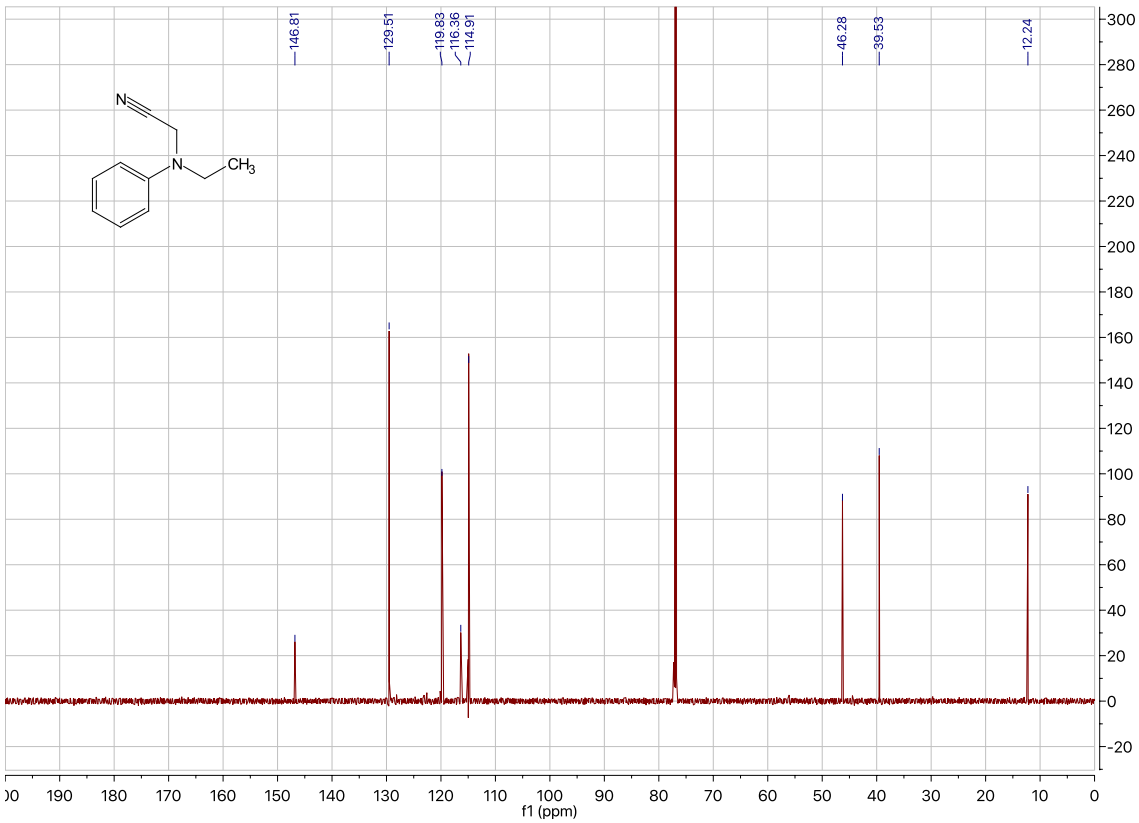


2-(ethyl(phenyl)amino)acetonitrile (7e)

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

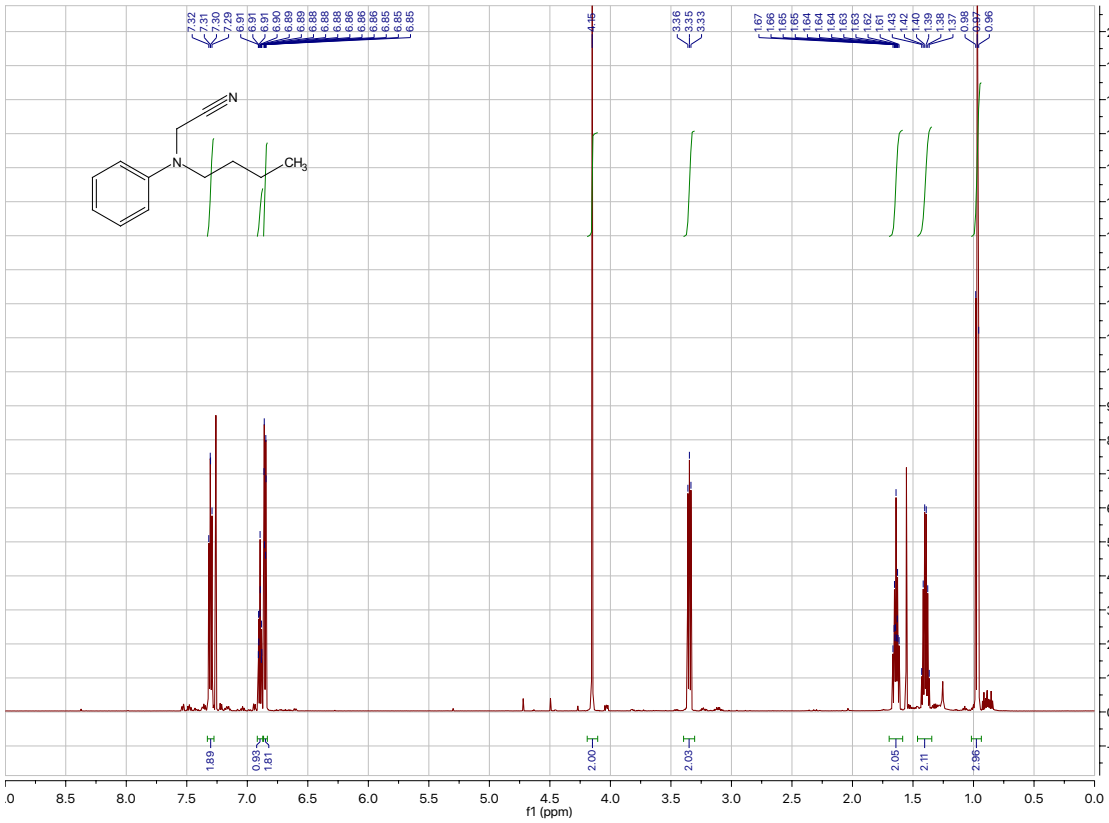


^{13}C NMR (151 MHz, $CDCl_3$)

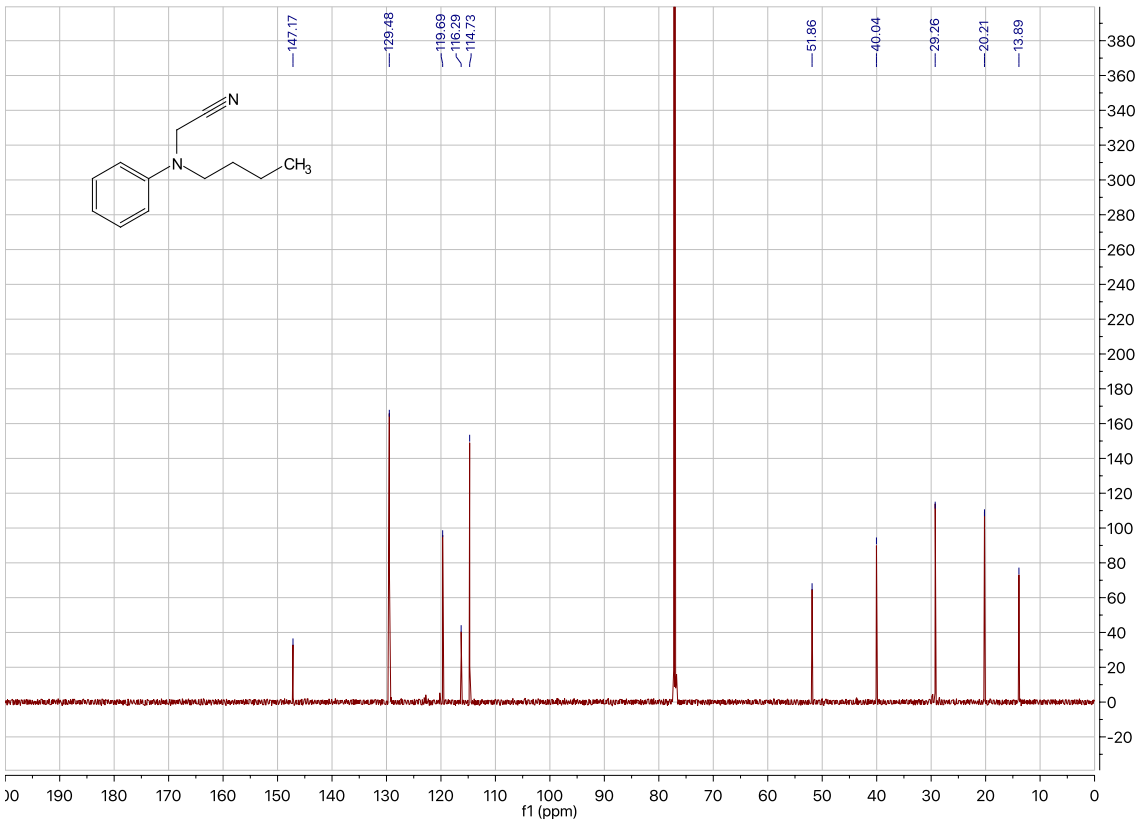


2-(butyl(phenyl)amino)acetonitrile (7f)

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

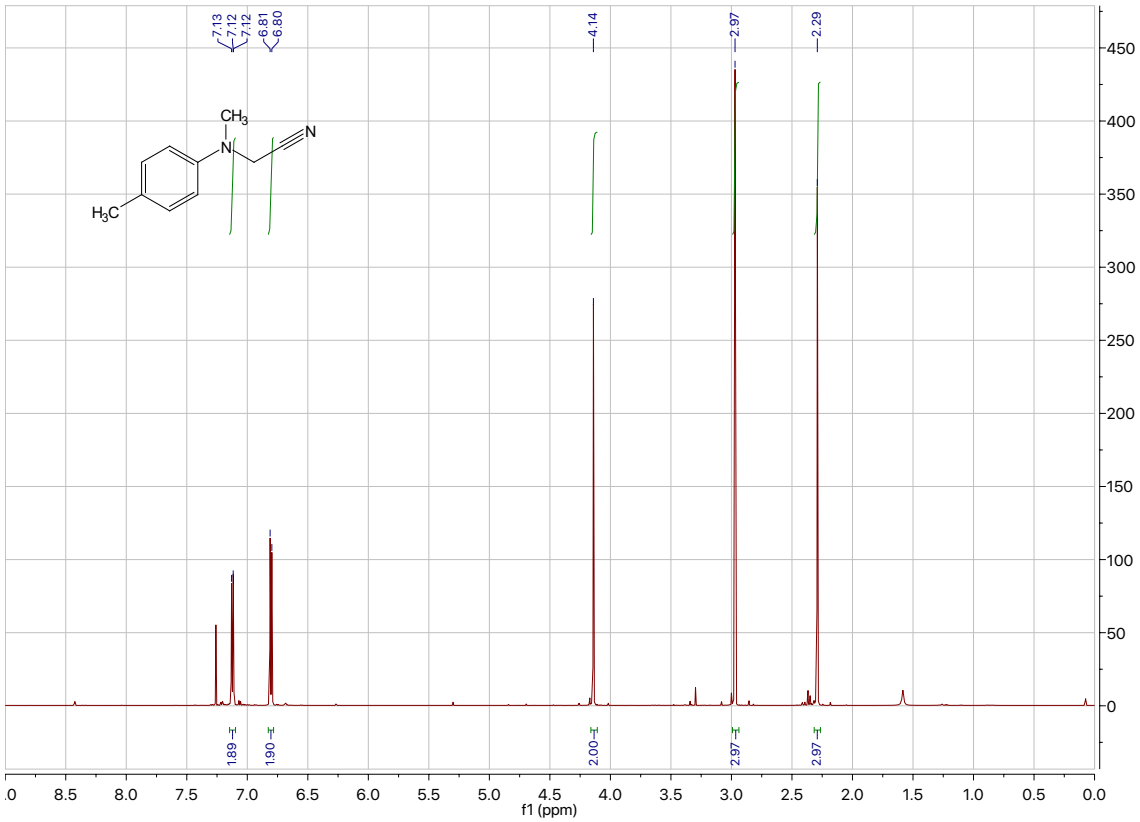


^{13}C NMR (151 MHz, $CDCl_3$)

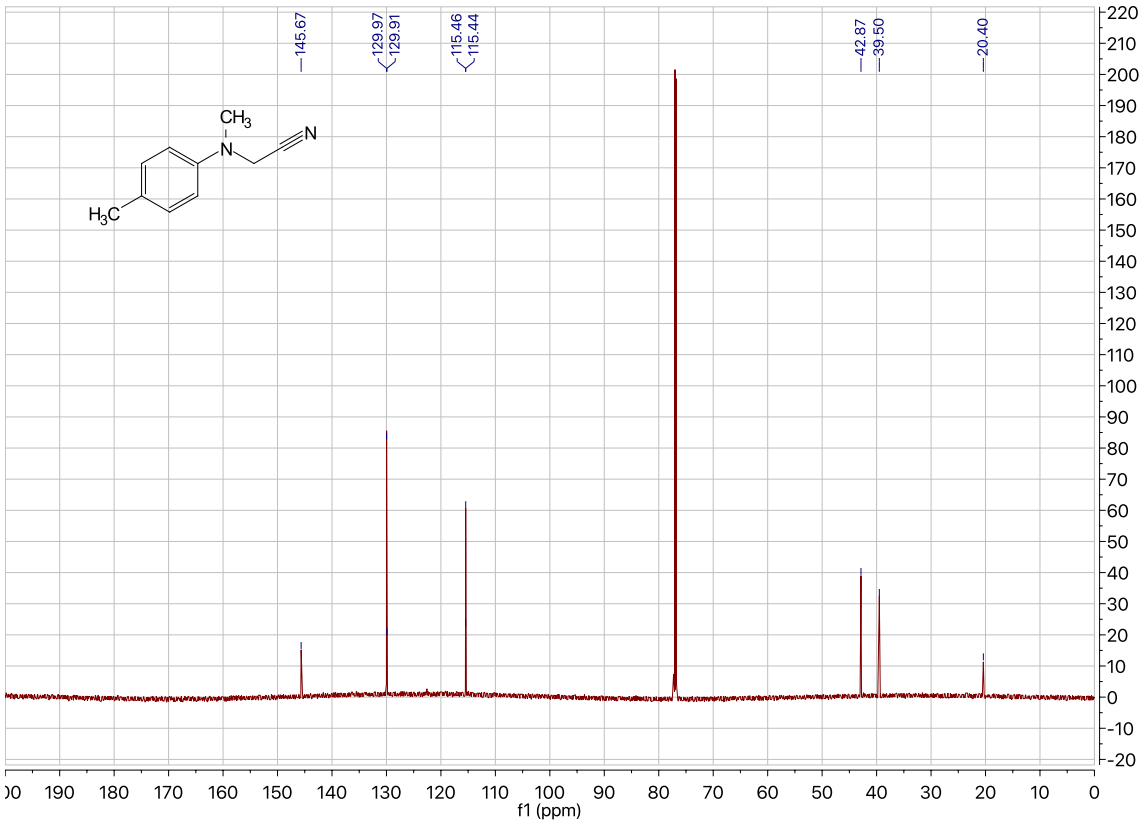


2-(methyl(*p*-tolyl)amino)acetonitrile (7g)

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

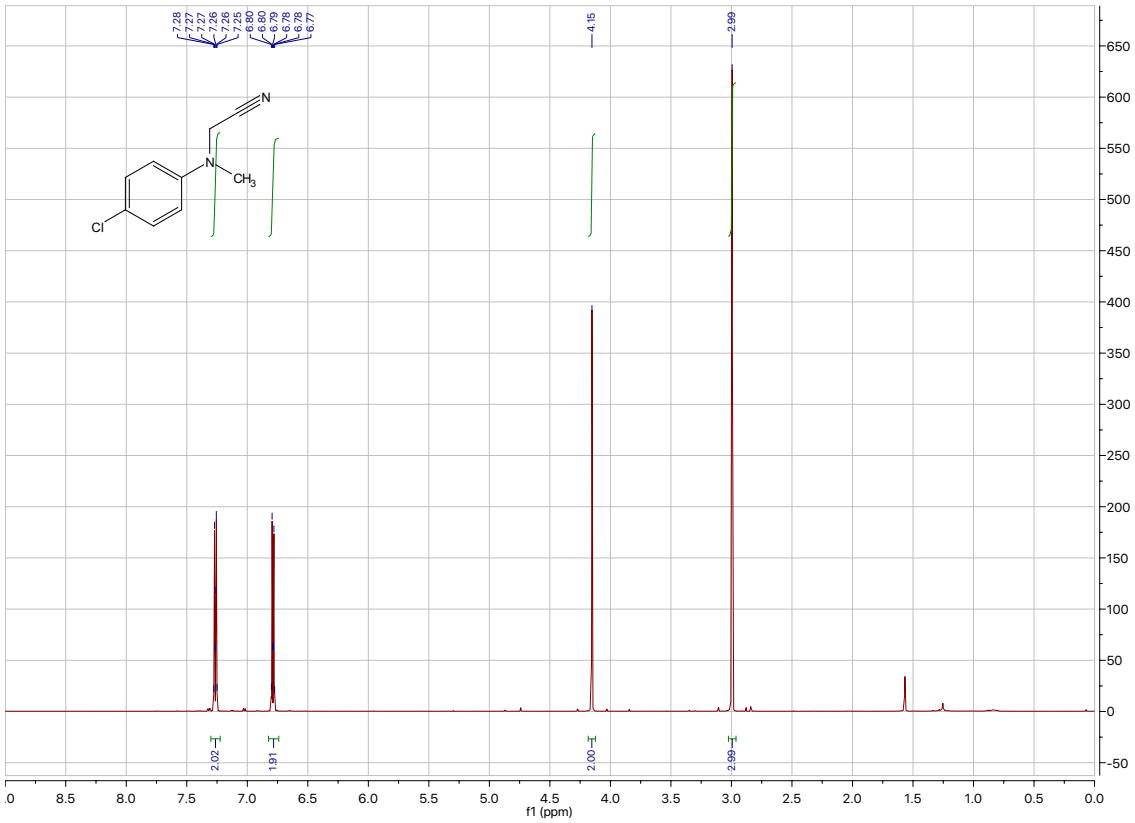


^{13}C NMR (151 MHz, $CDCl_3$)

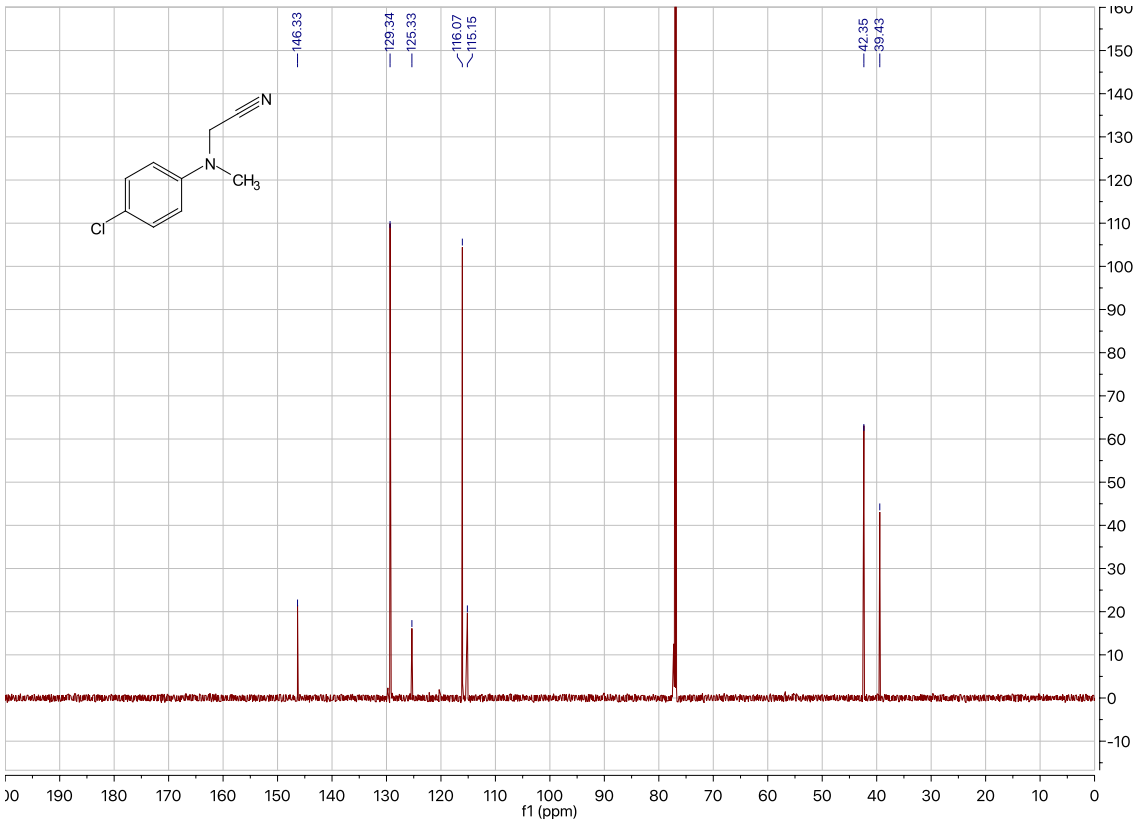


2-((4-chlorophenyl)(methyl)amino)acetonitrile (7h)

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

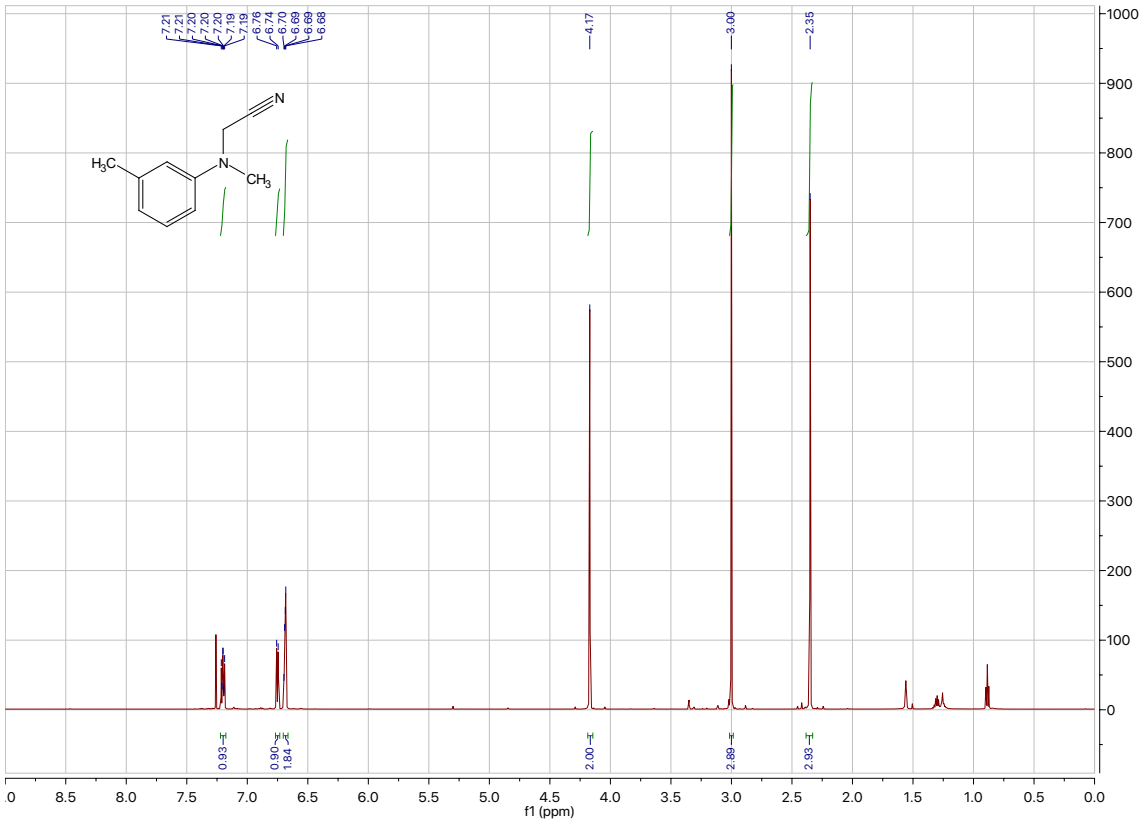


^{13}C NMR (151 MHz, $CDCl_3$)

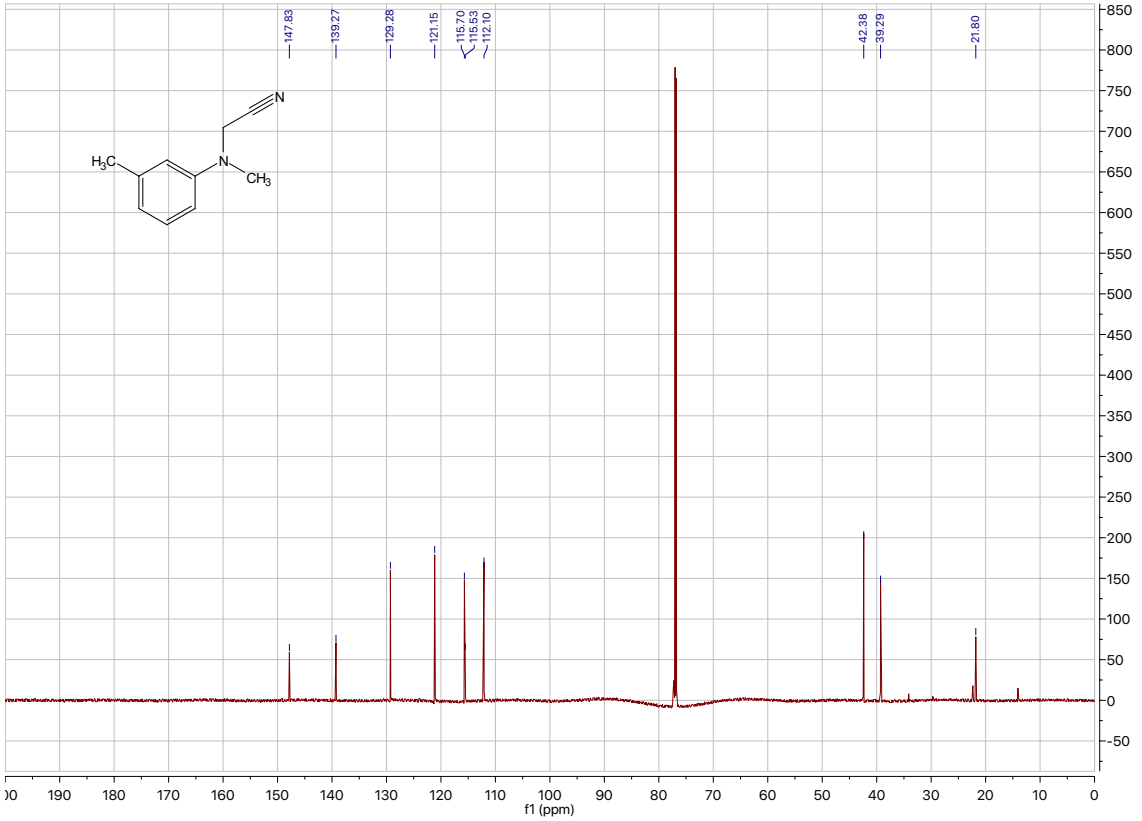


2-(methyl(*m*-tolyl)amino)acetonitrile (7i)

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

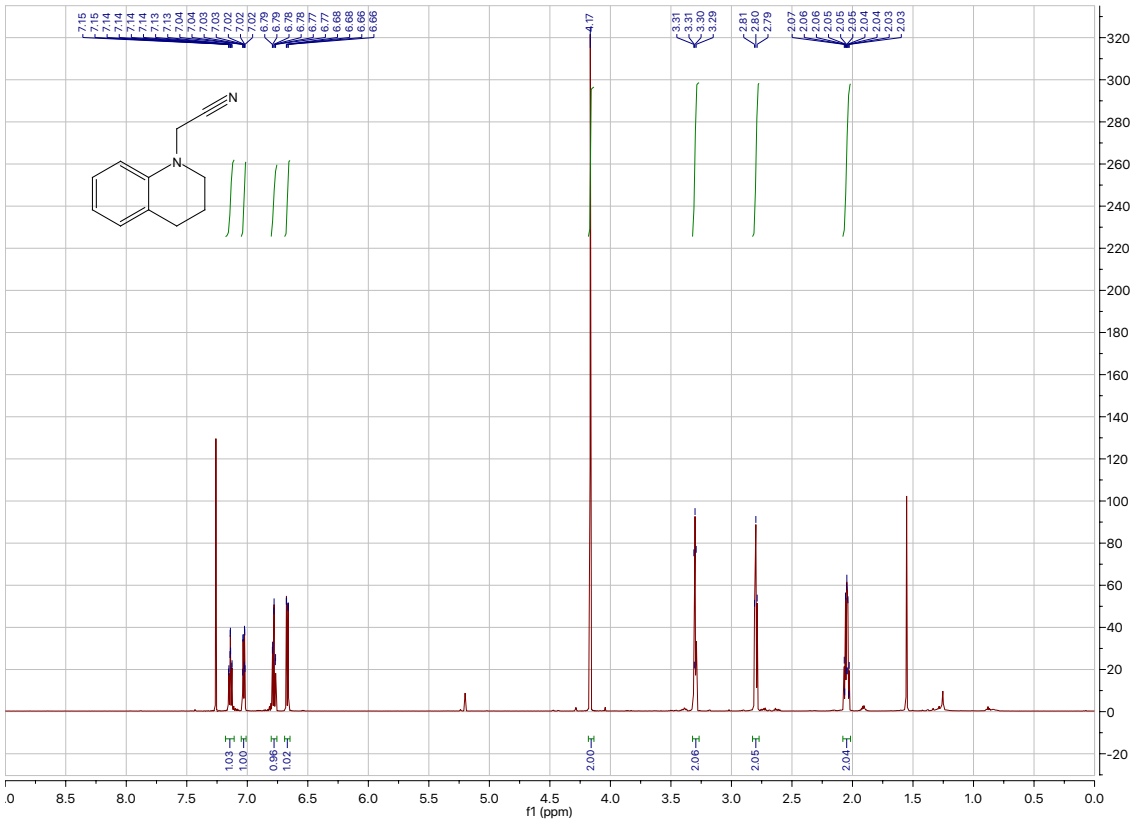


^{13}C NMR (151 MHz, $CDCl_3$)

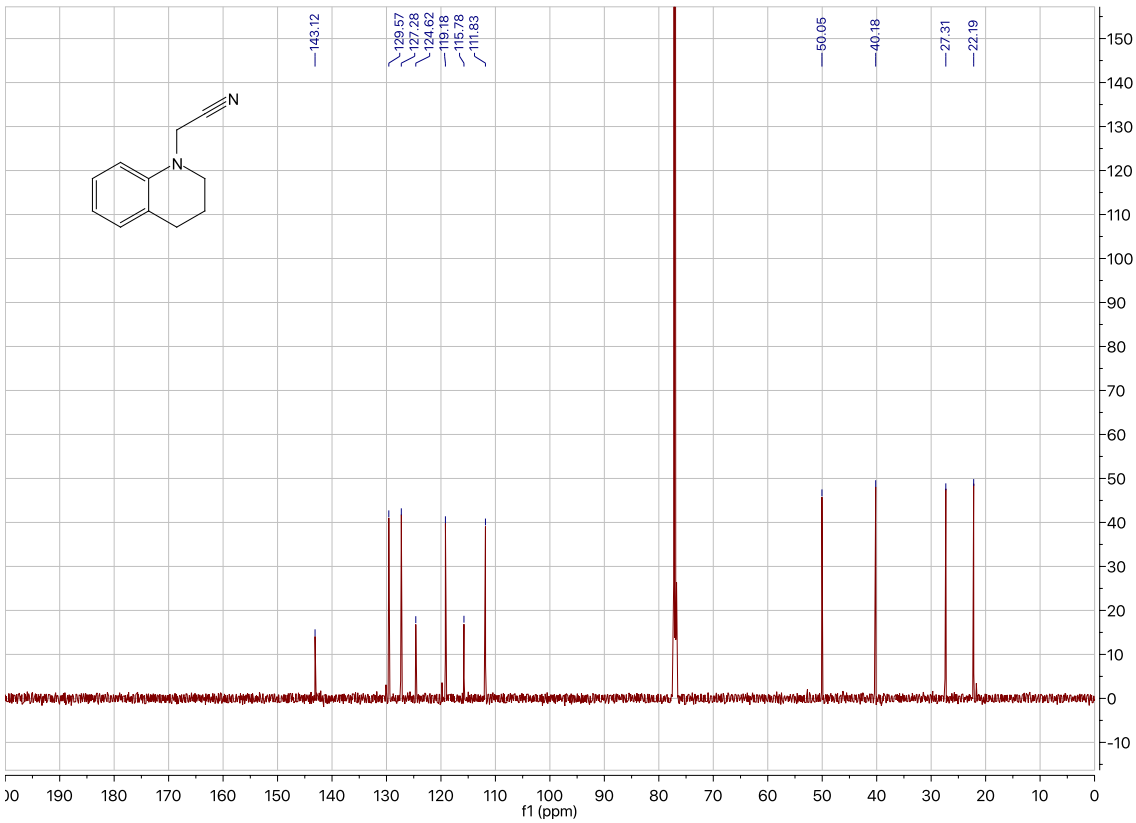


2-(3,4-dihydroquinolin-1(2*H*)-yl)acetonitrile (7j)

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

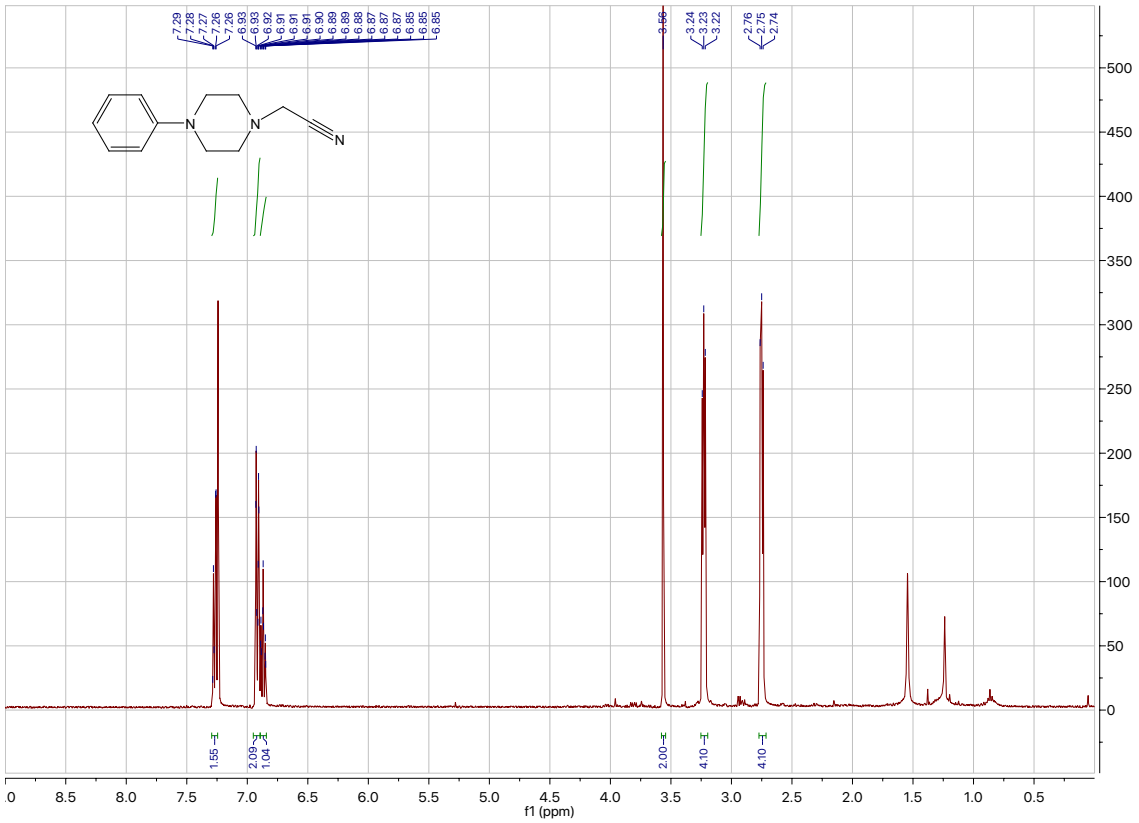


^{13}C NMR (151 MHz, $CDCl_3$)

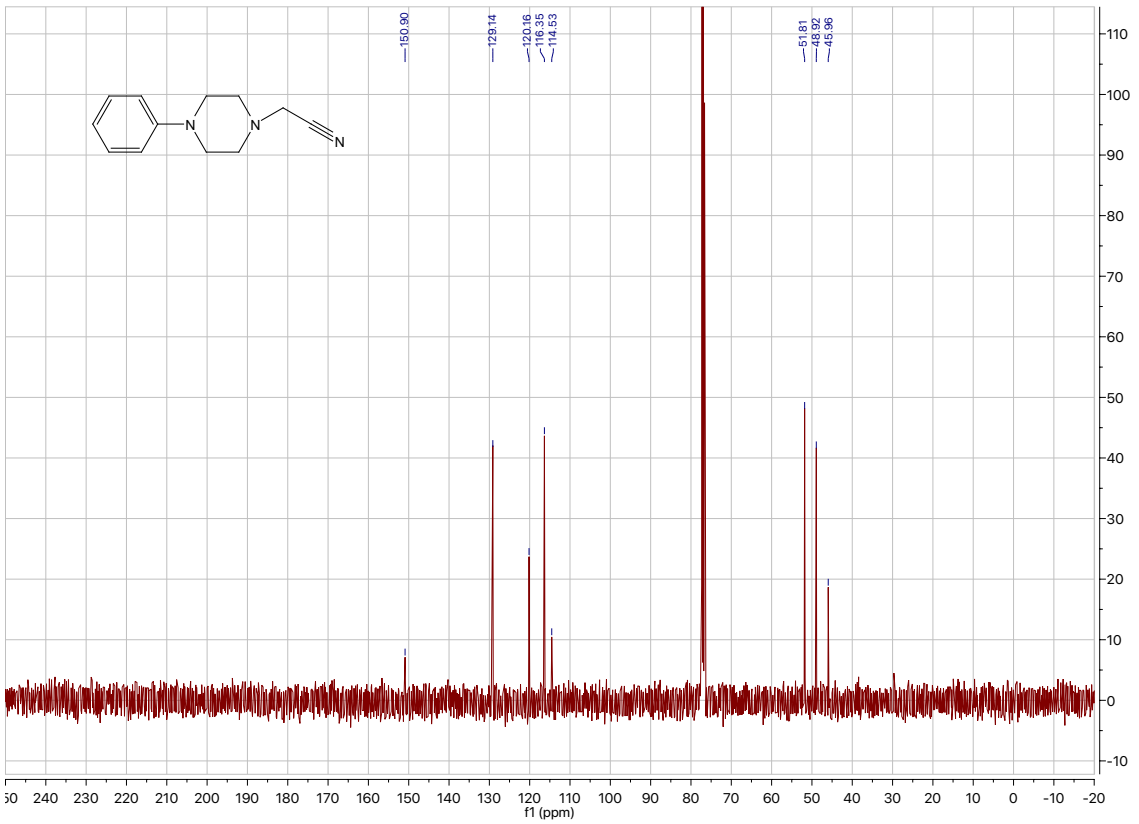


2-(4-phenylpiperazin-1-yl)acetonitrile (7k)

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



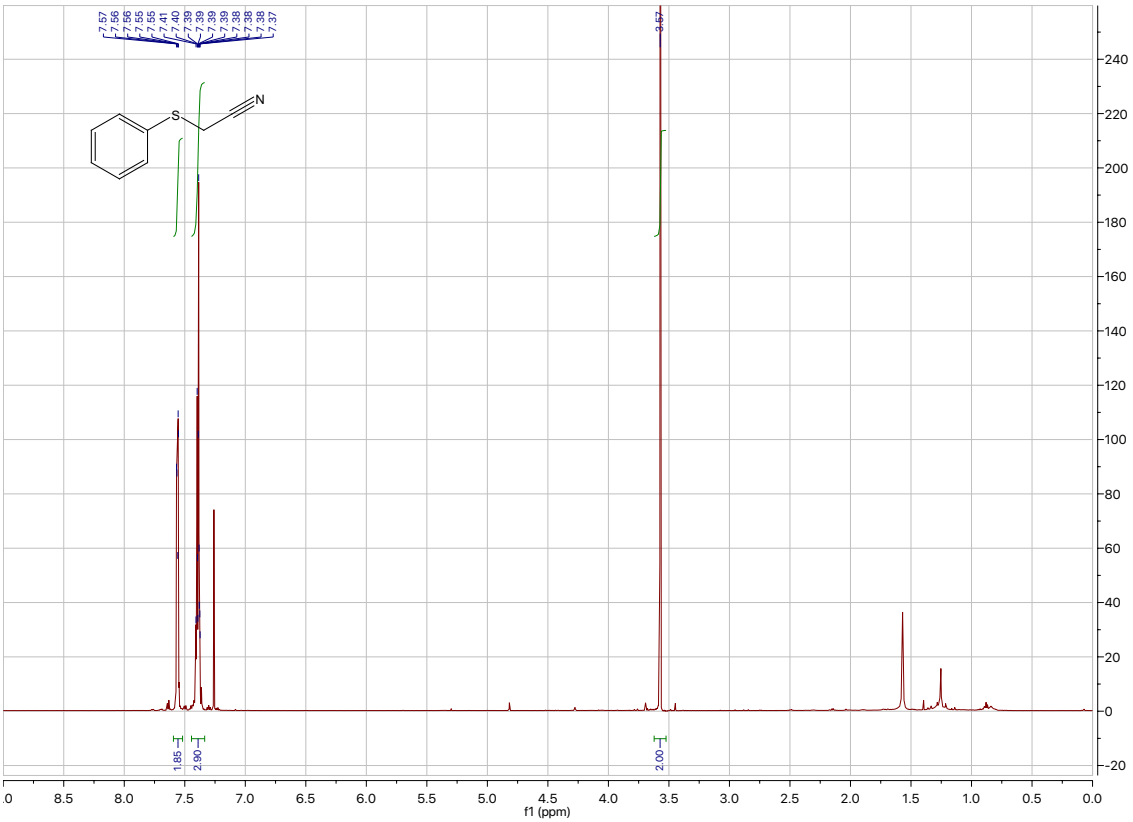
^{13}C NMR (101 MHz, $CDCl_3$)



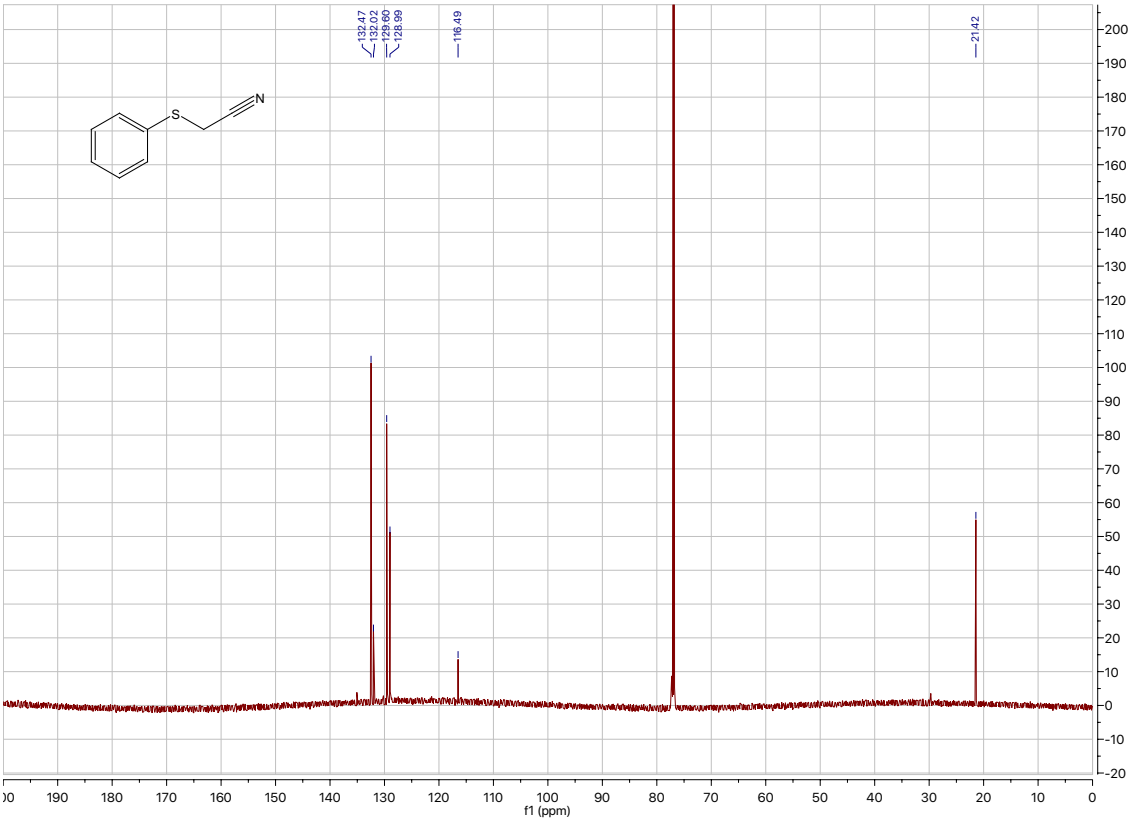
α-mercaptonitriles

2-(phenylthio)acetonitrile (9a)

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

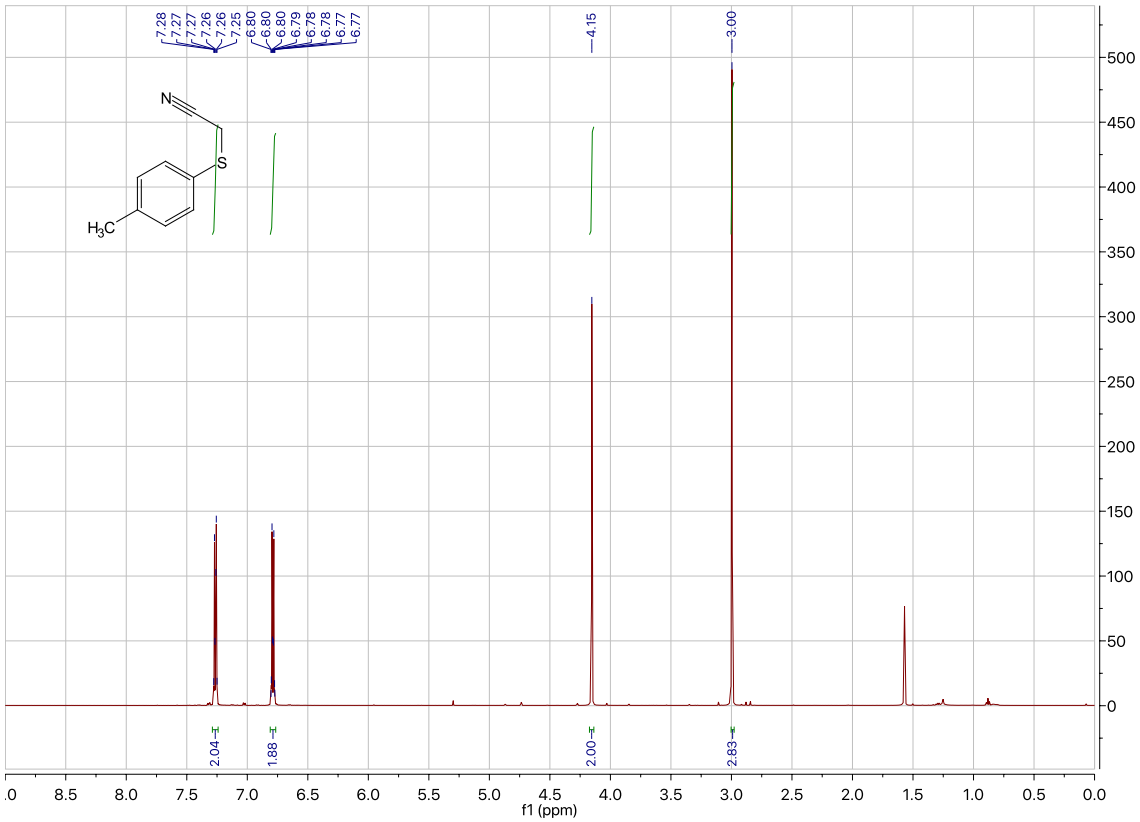


^{13}C NMR (151 MHz, $CDCl_3$)

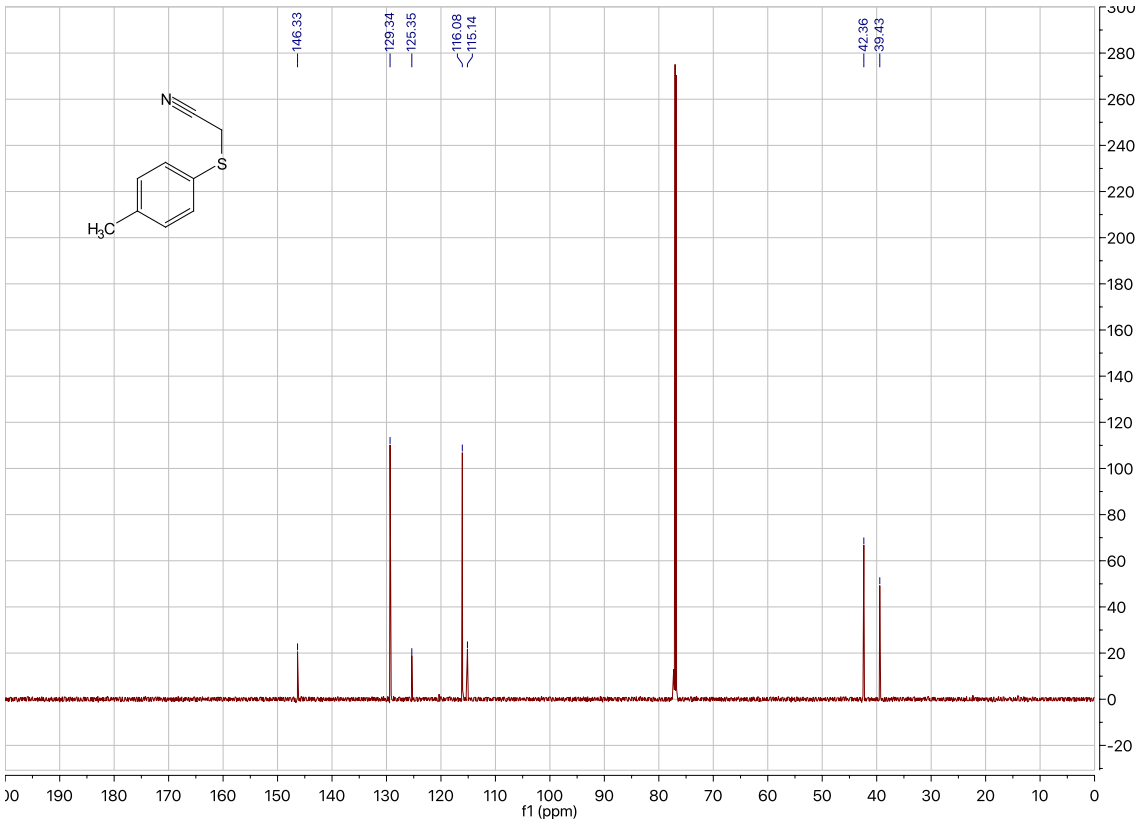


2-(*p*-tolylthio)acetonitrile (9b)

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

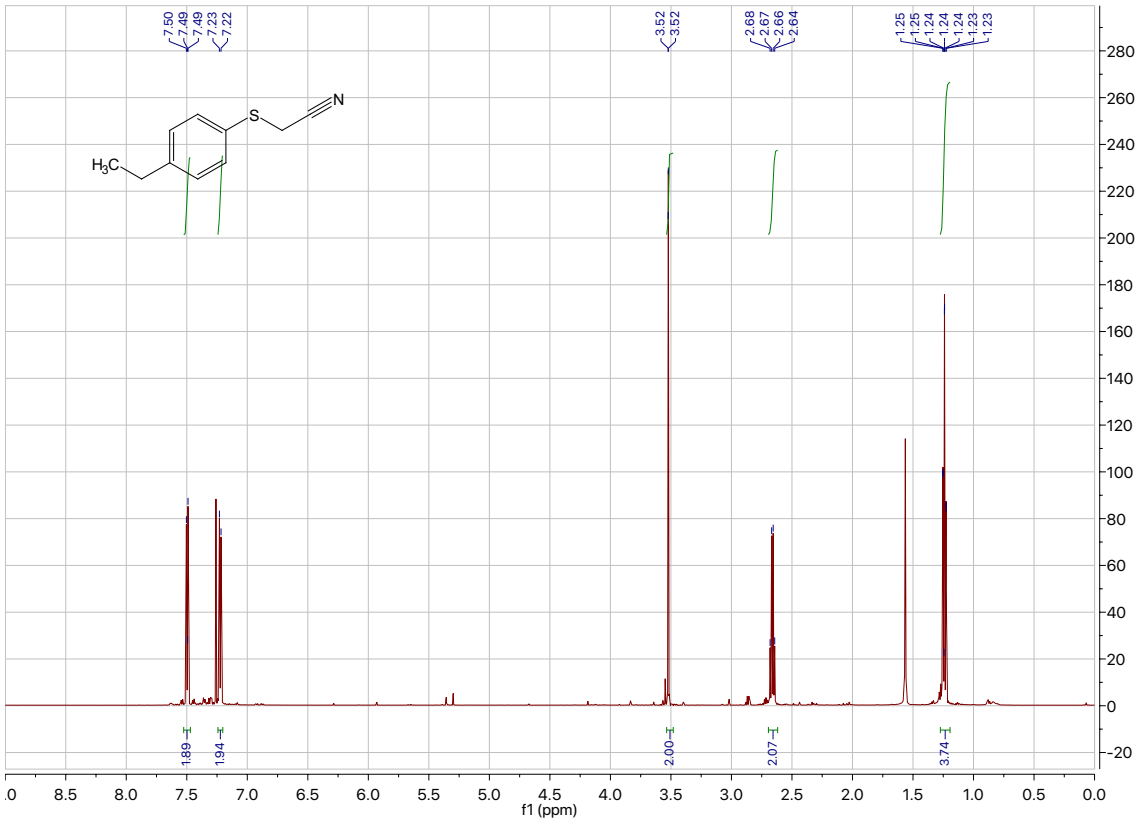


^{13}C NMR (151 MHz, $CDCl_3$)

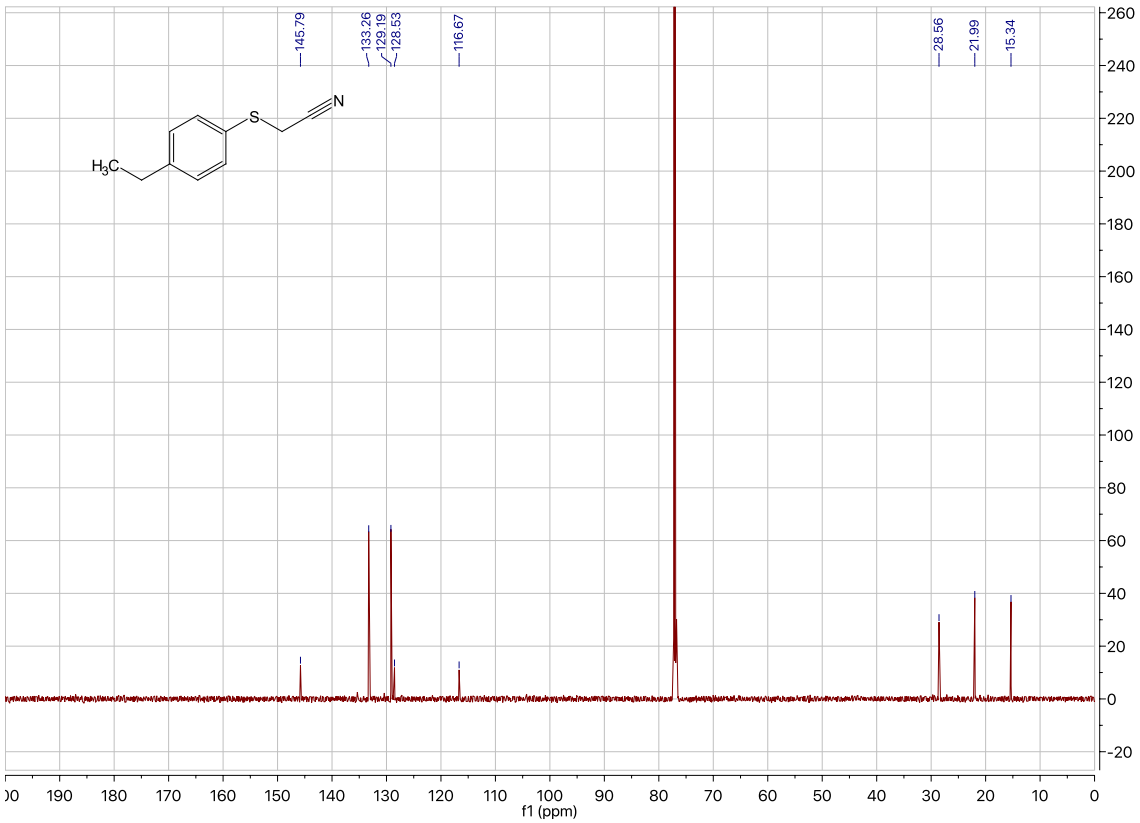


2-((4-ethylphenyl)thio)acetonitrile (9c)

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

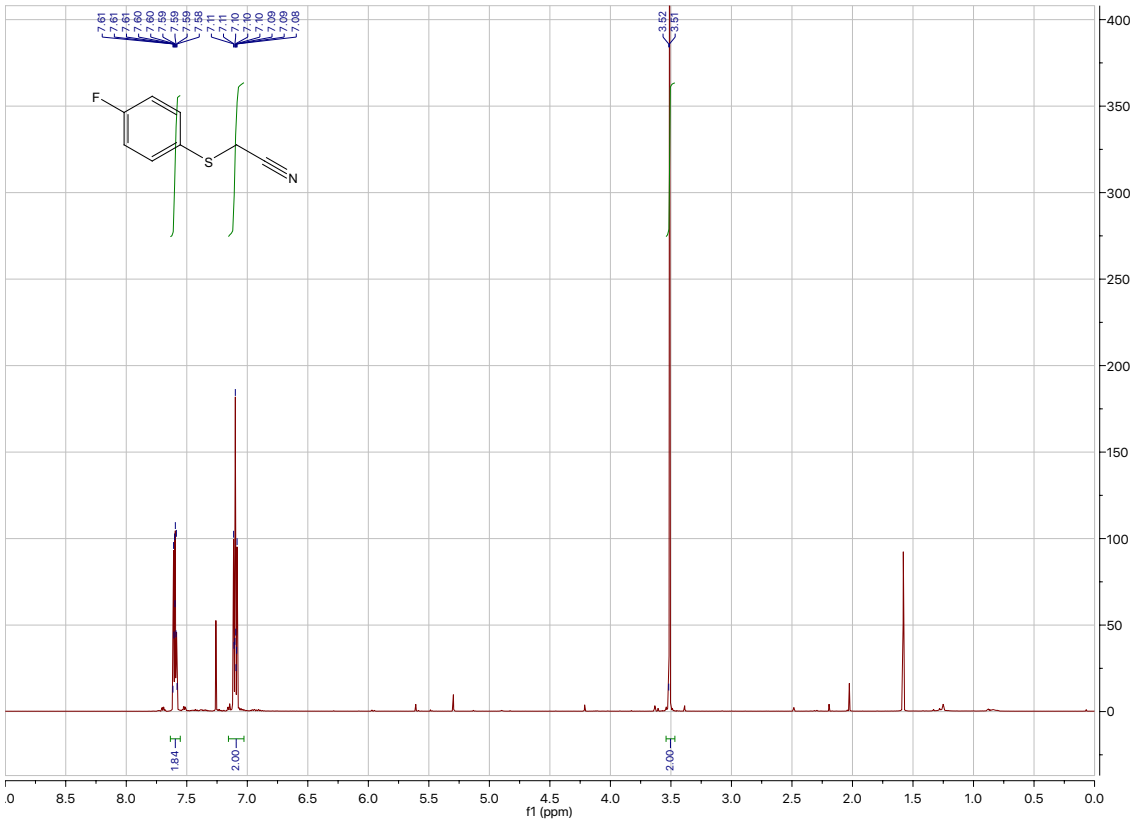


^{13}C NMR (151 MHz, $CDCl_3$)

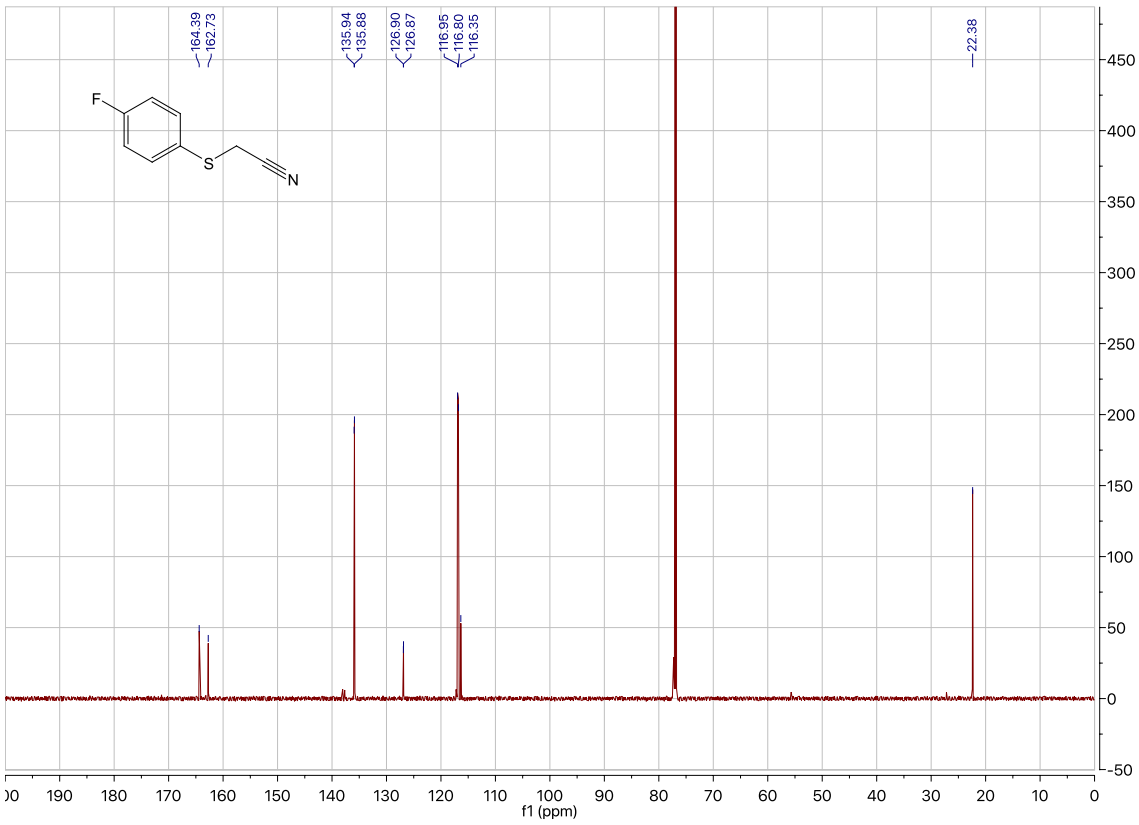


2-((4-fluorophenyl)thio)acetonitrile (9d)

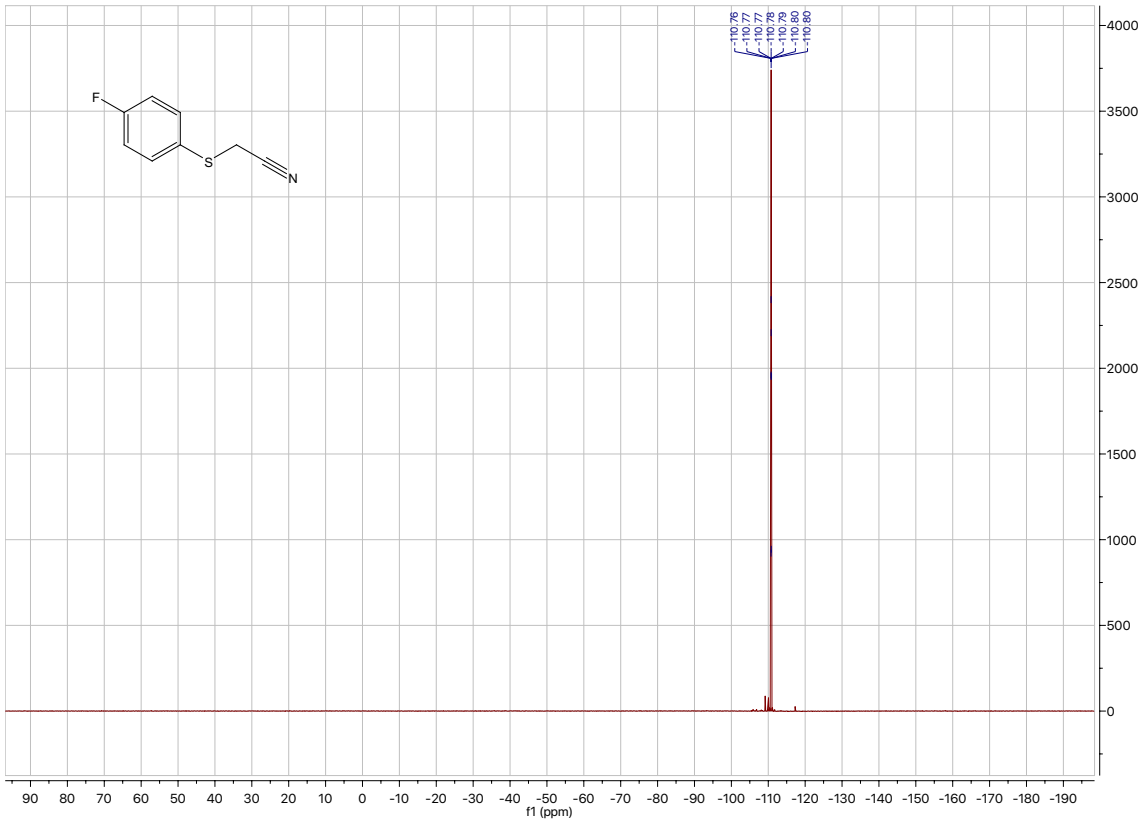
^{1}H NMR (600 MHz, $CDCl_3$)



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

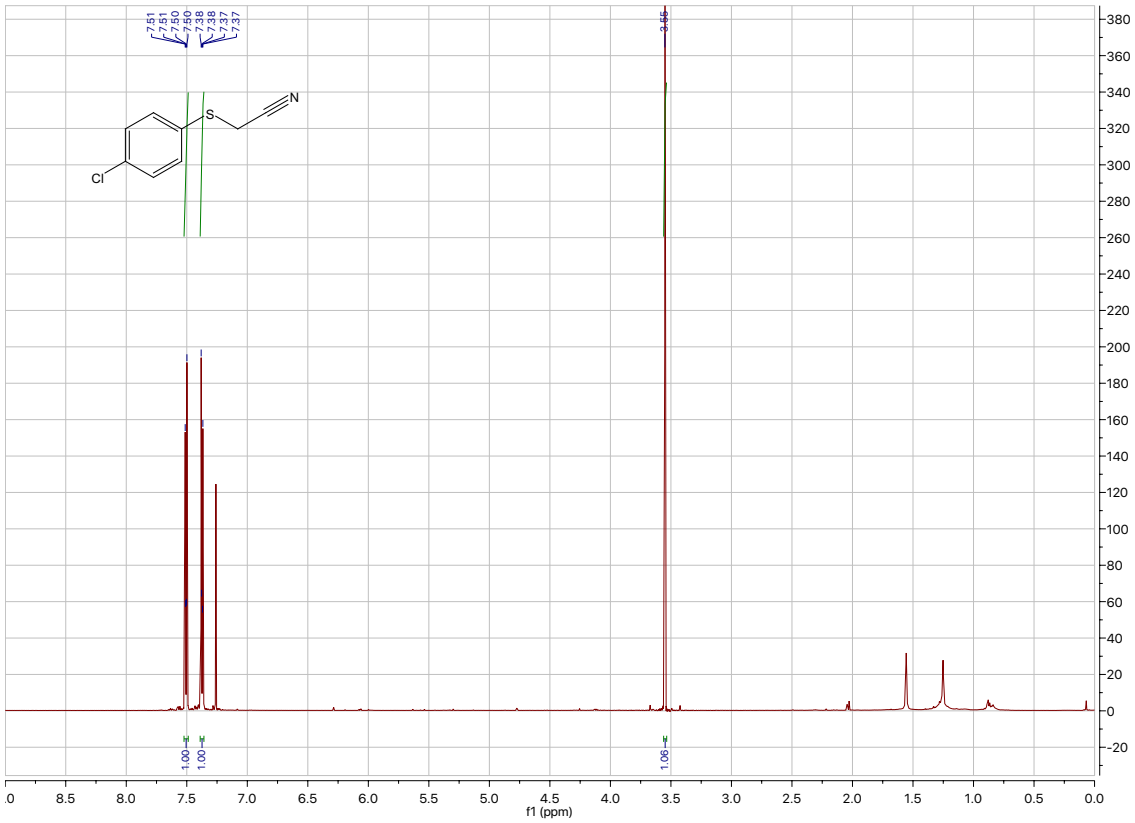


^{19}F NMR (564 MHz, $CDCl_3$)

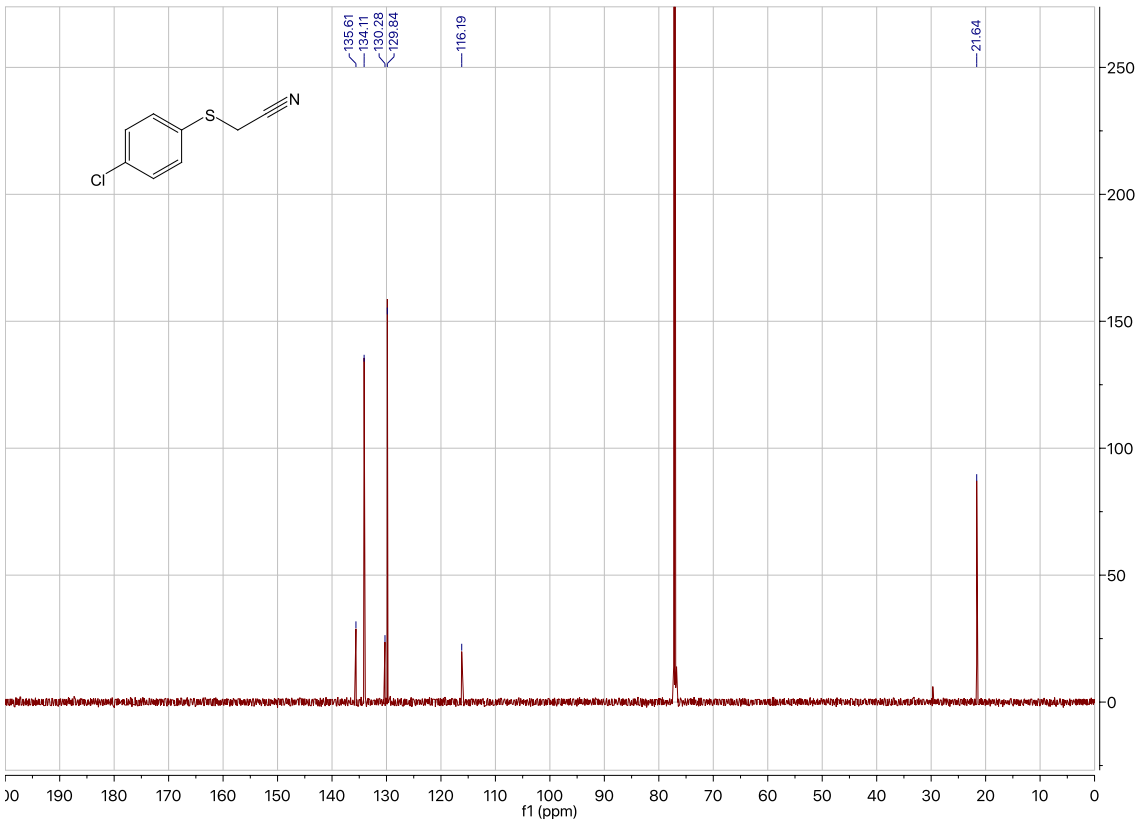


2-((4-chlorophenyl)thio)acetonitrile (9e)

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

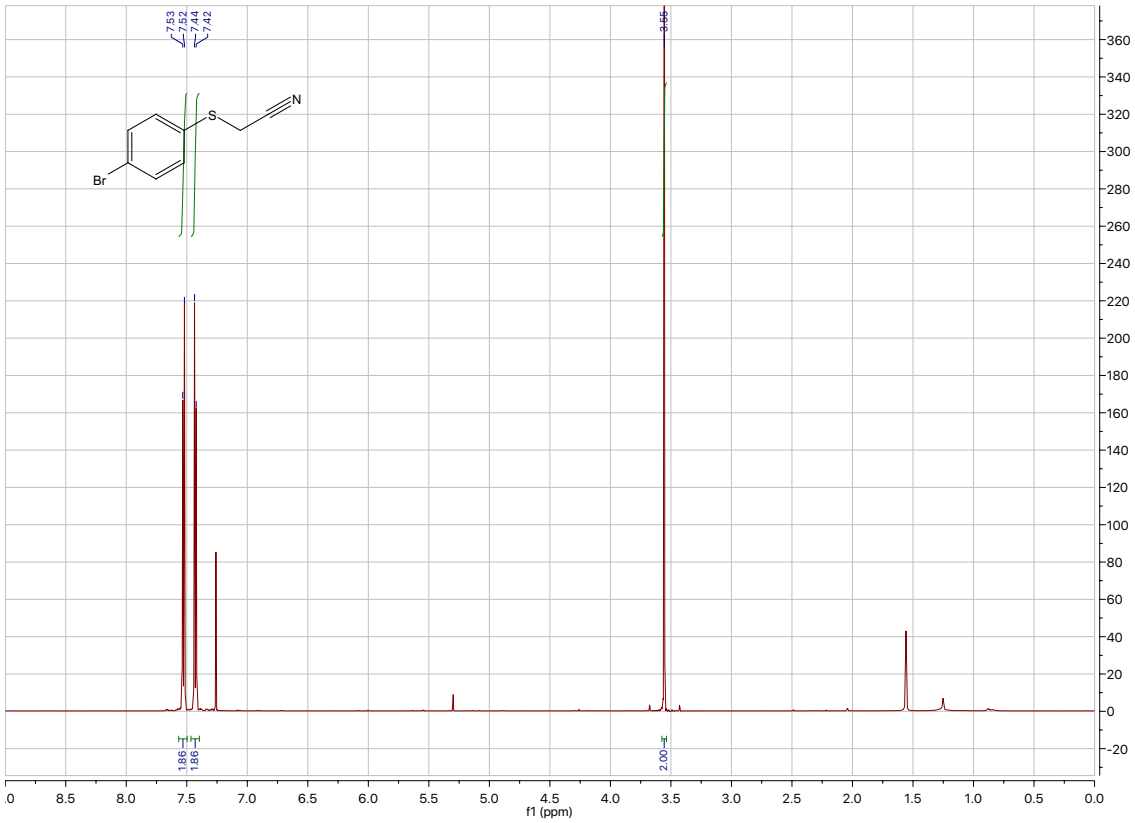


NMR (151 MHz, $CDCl_3$)

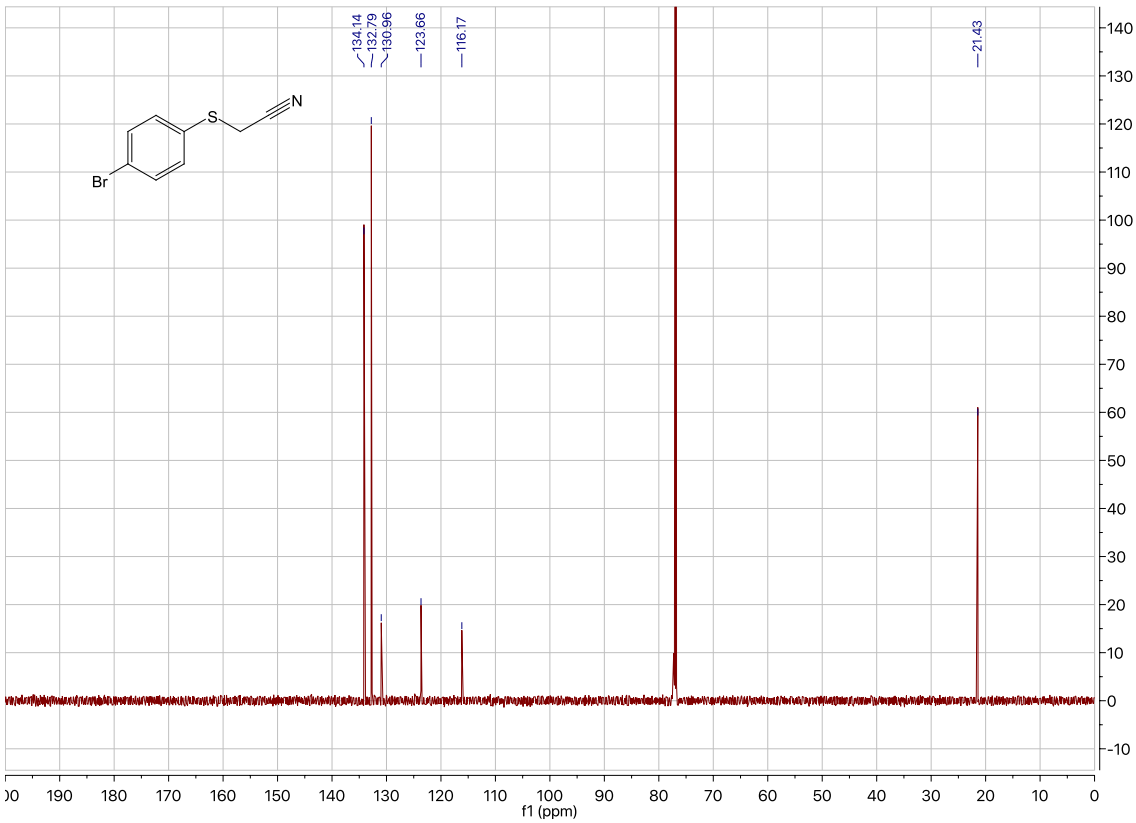


2-((4-bromophenyl)thio)acetonitrile (9f)

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

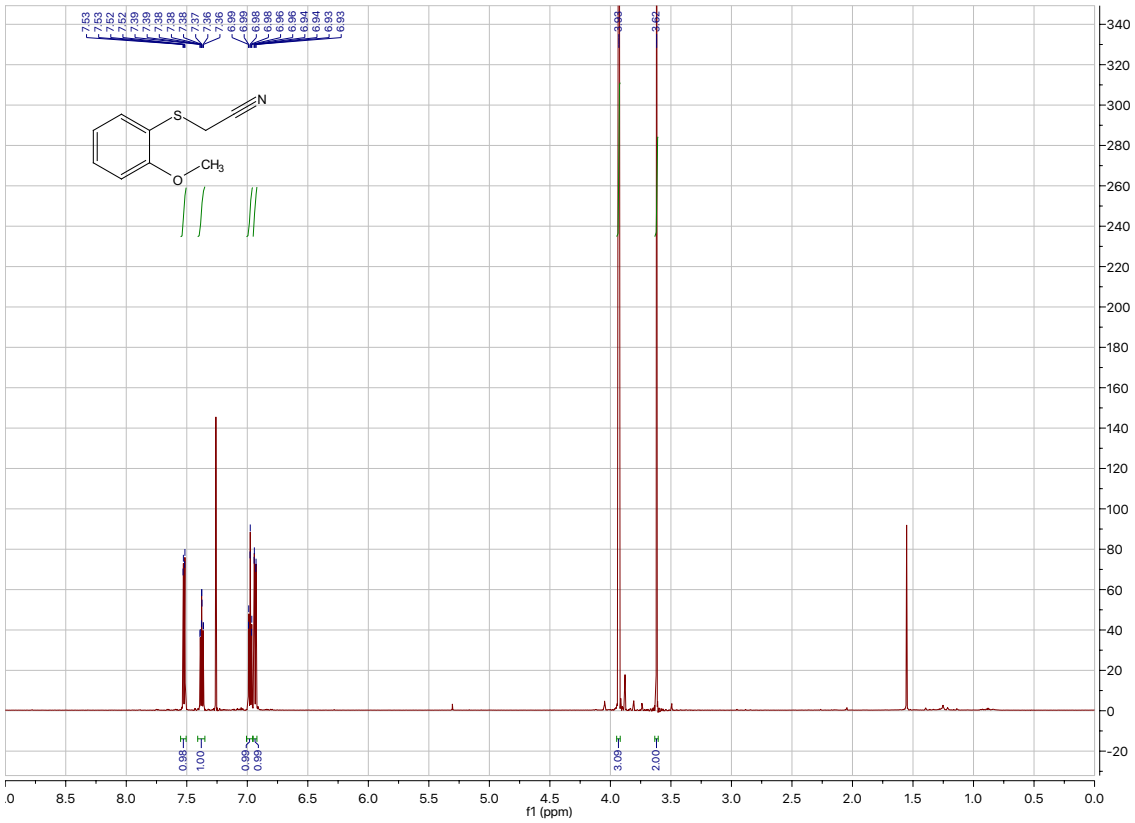


^{13}C NMR (151 MHz, $CDCl_3$)

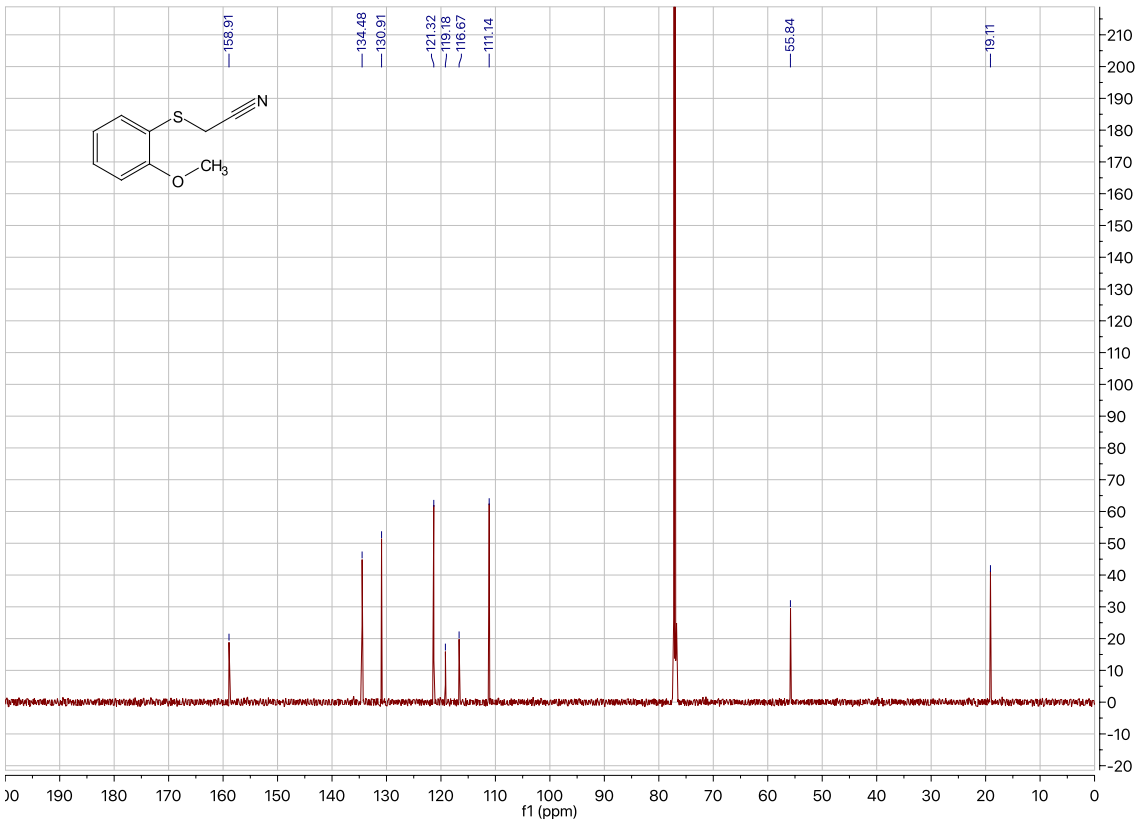


2-((2-methoxyphenyl)thio)acetonitrile (9g)

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

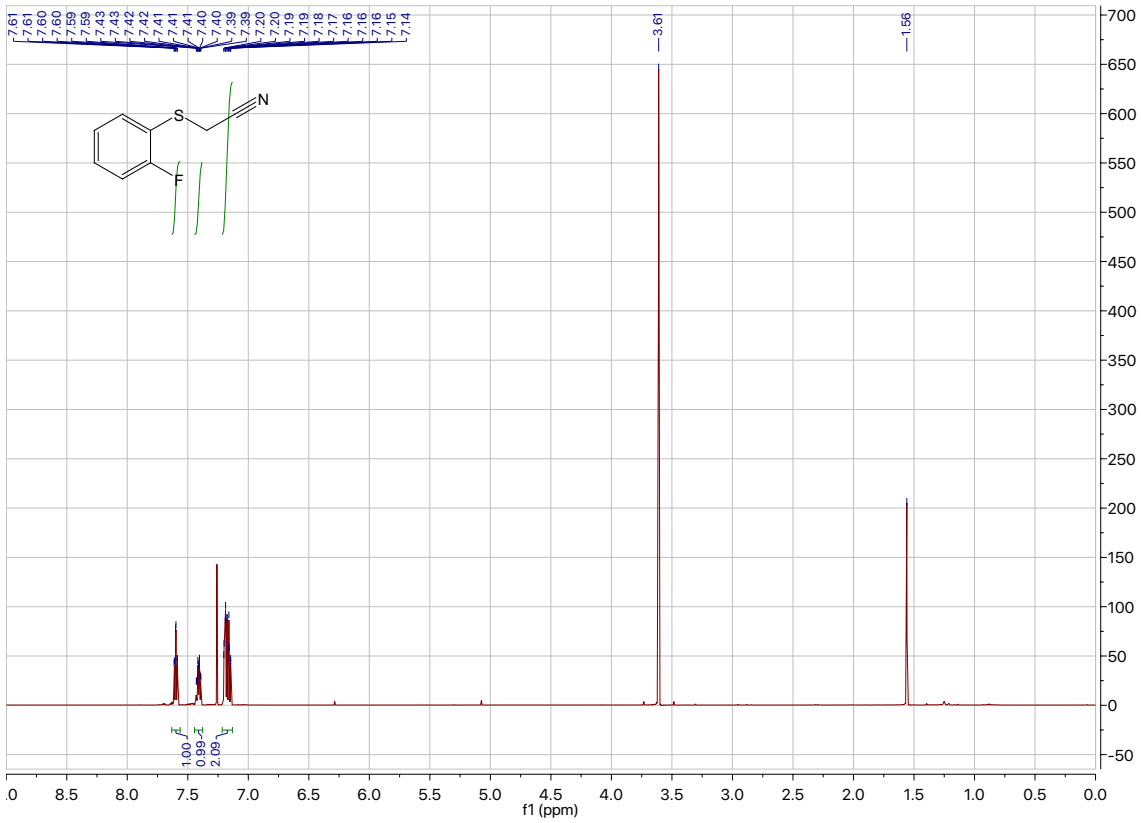


^{13}C NMR (151 MHz, $CDCl_3$)

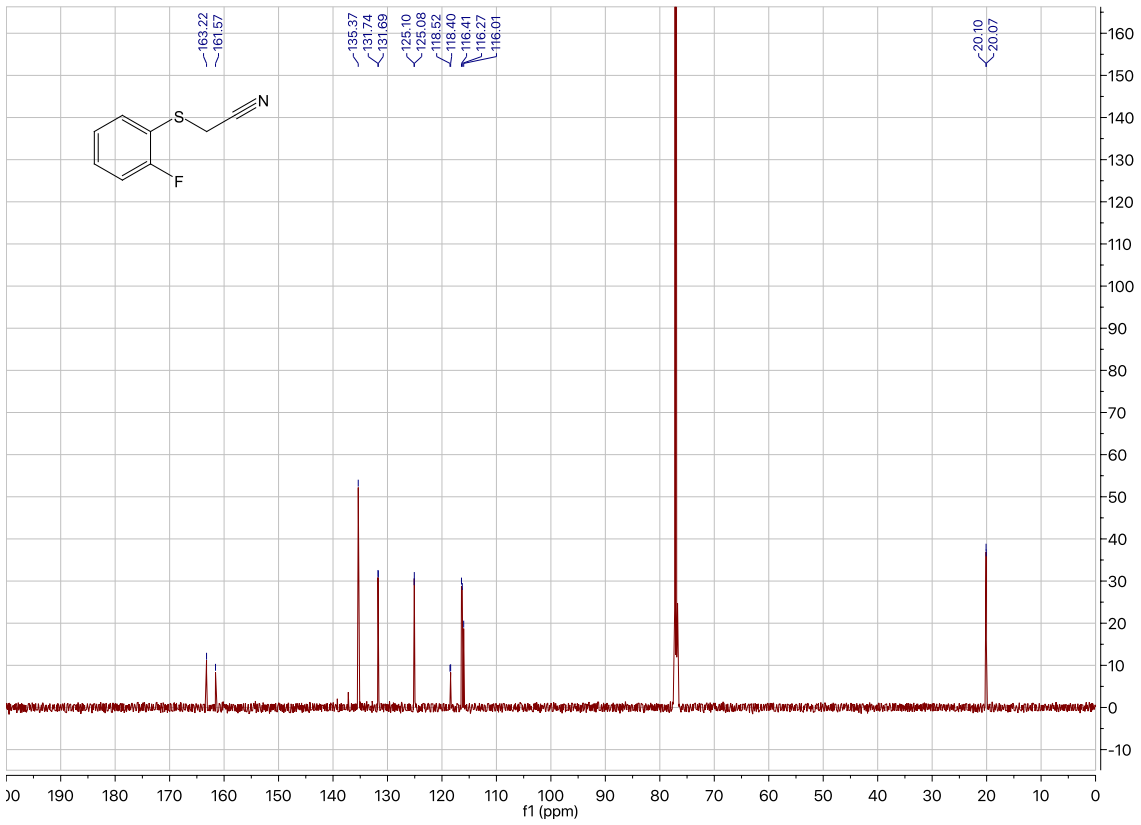


2-((2-fluorophenyl)thio)acetonitrile (9h)

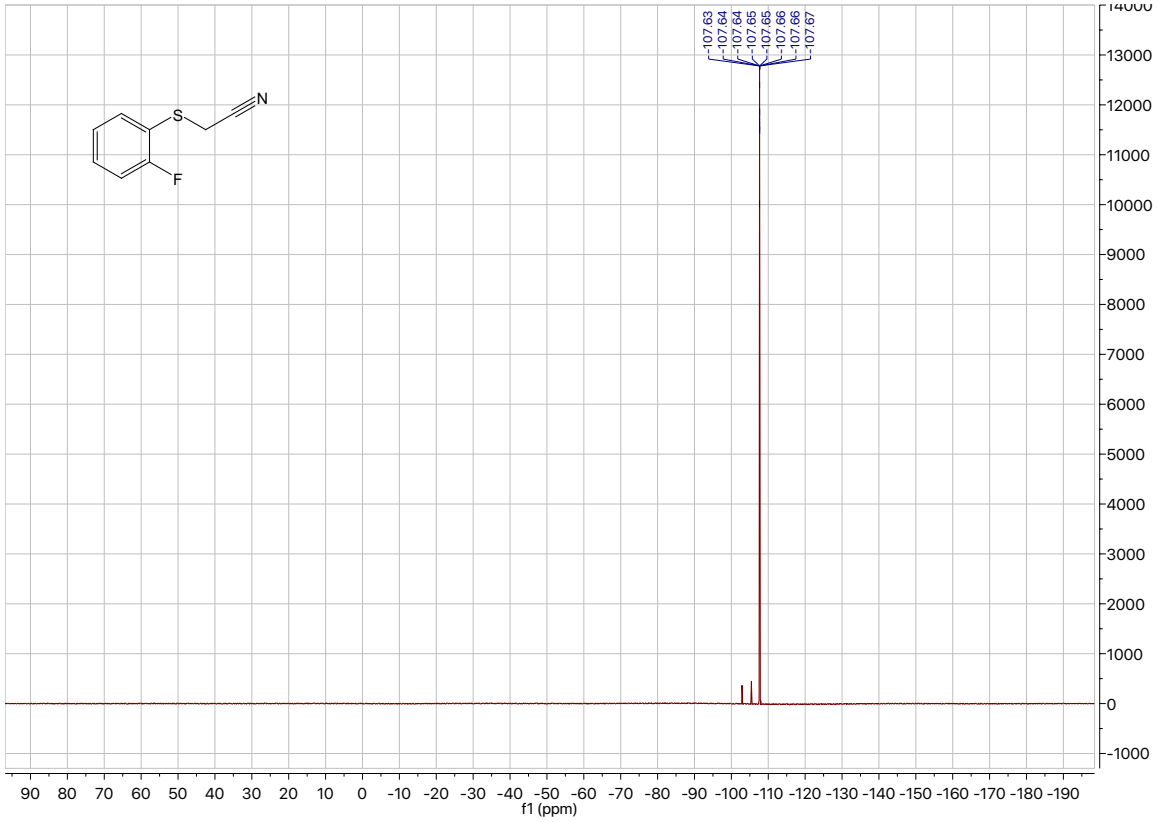
^{1}H NMR (600 MHz, $CDCl_3$)



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

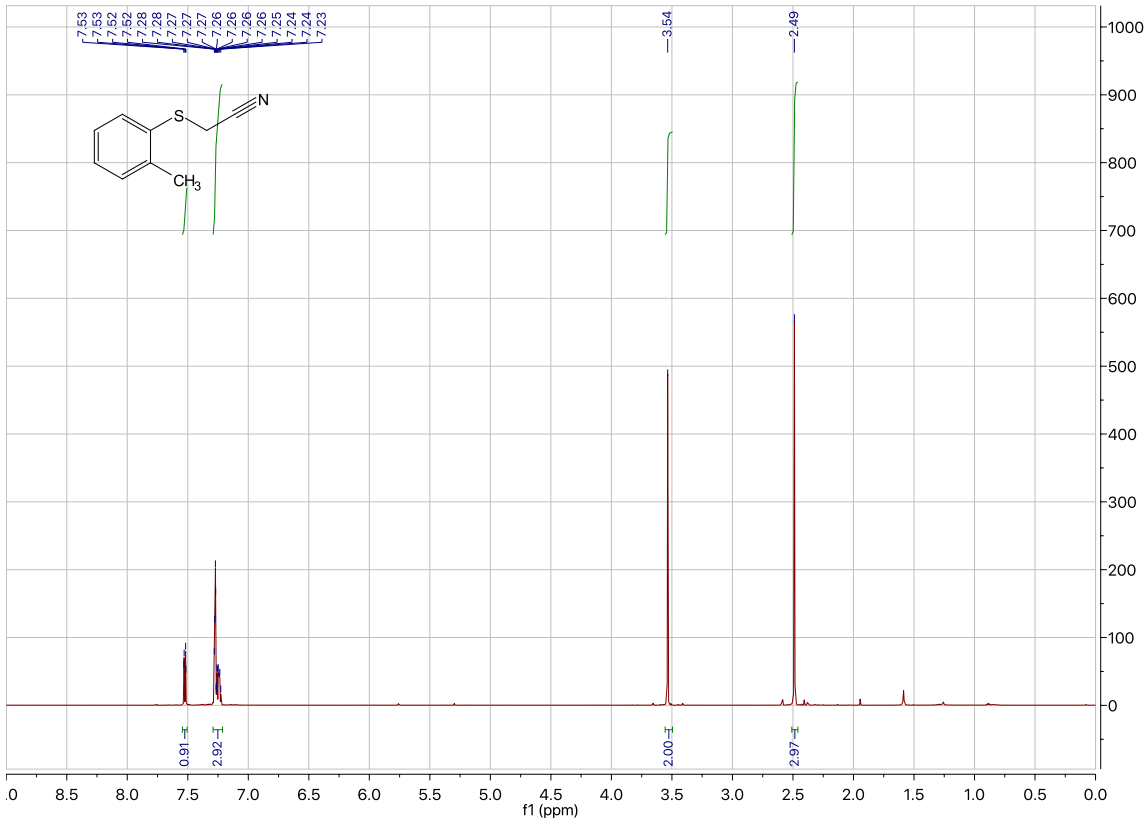


^{19}F NMR (564 MHz, $CDCl_3$)

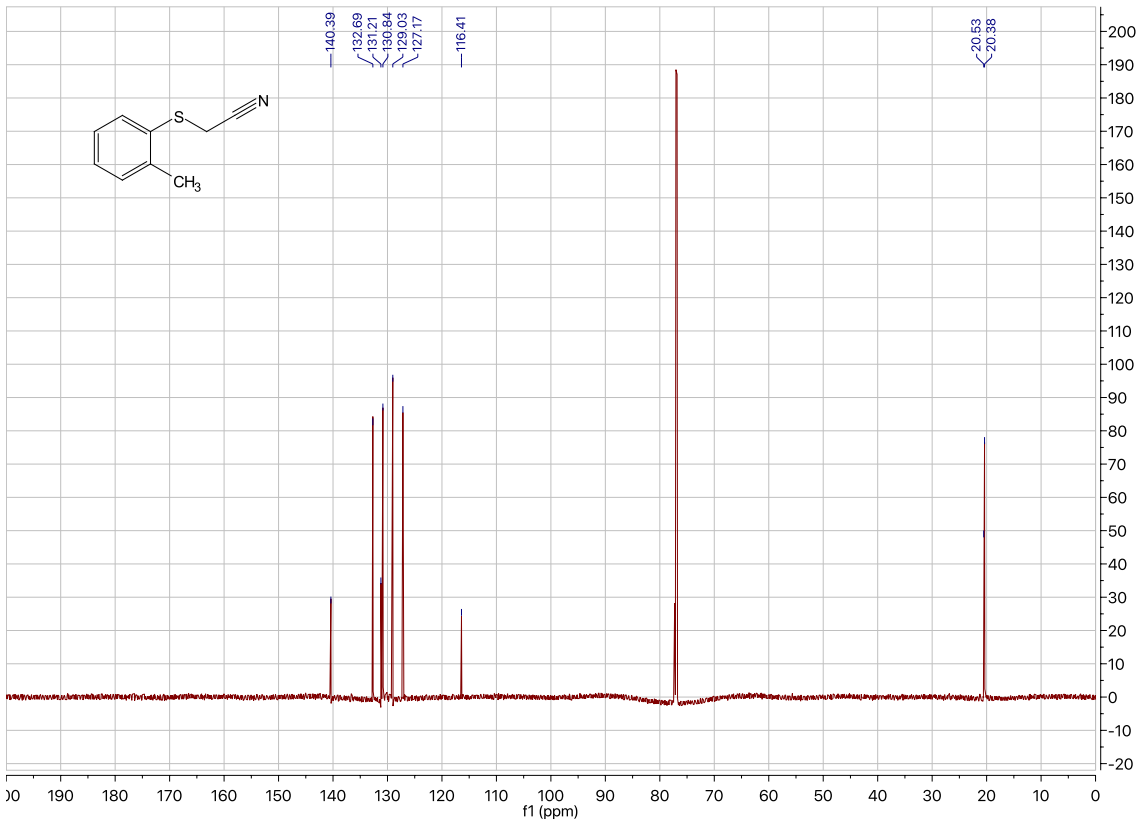


2-(*o*-tolylthio)acetonitrile (9i)

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

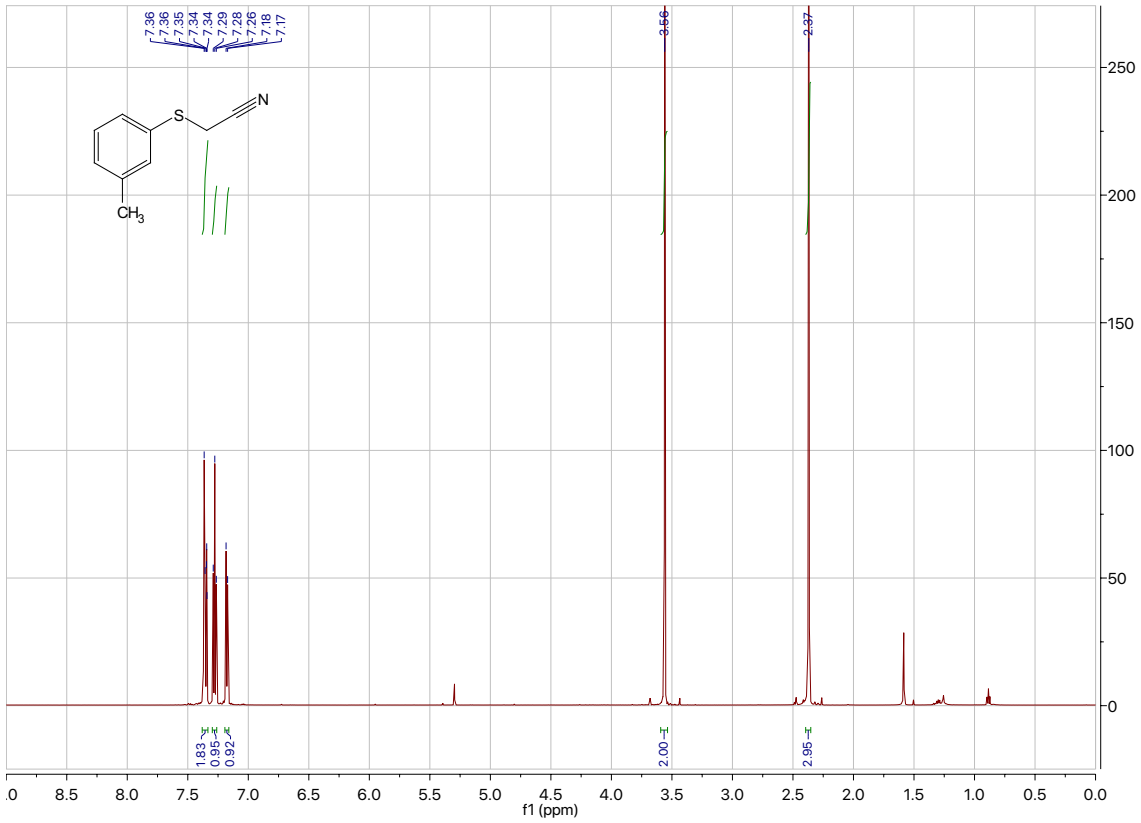


^{13}C NMR (151 MHz, $CDCl_3$)

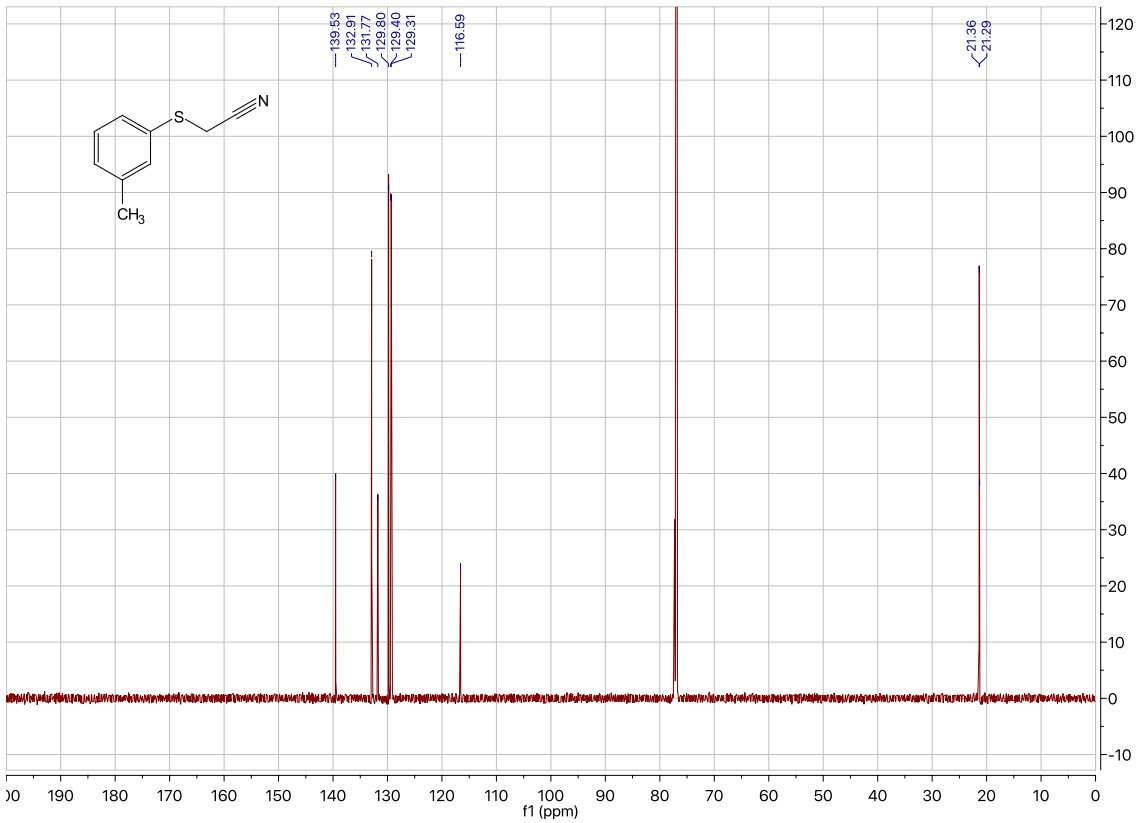


2-((3-methylphenyl)thio)acetonitrile (9j)

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

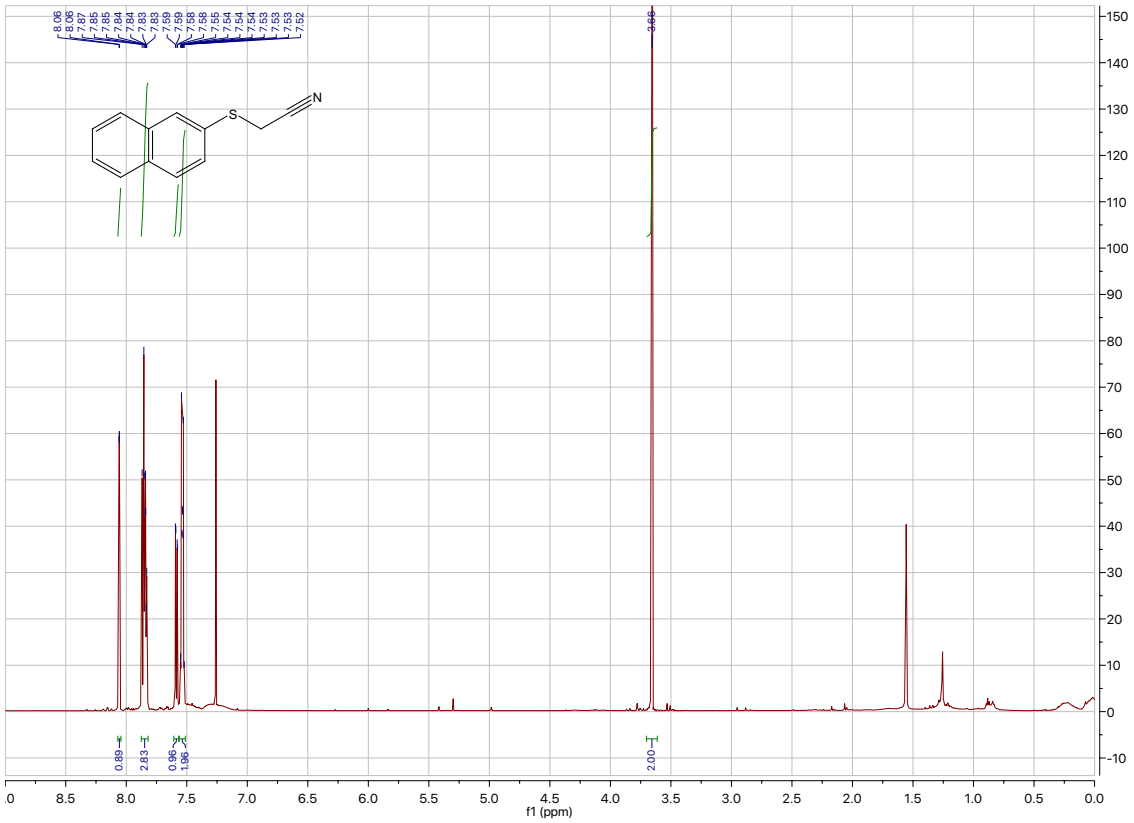


^{13}C NMR (151 MHz, $CDCl_3$)

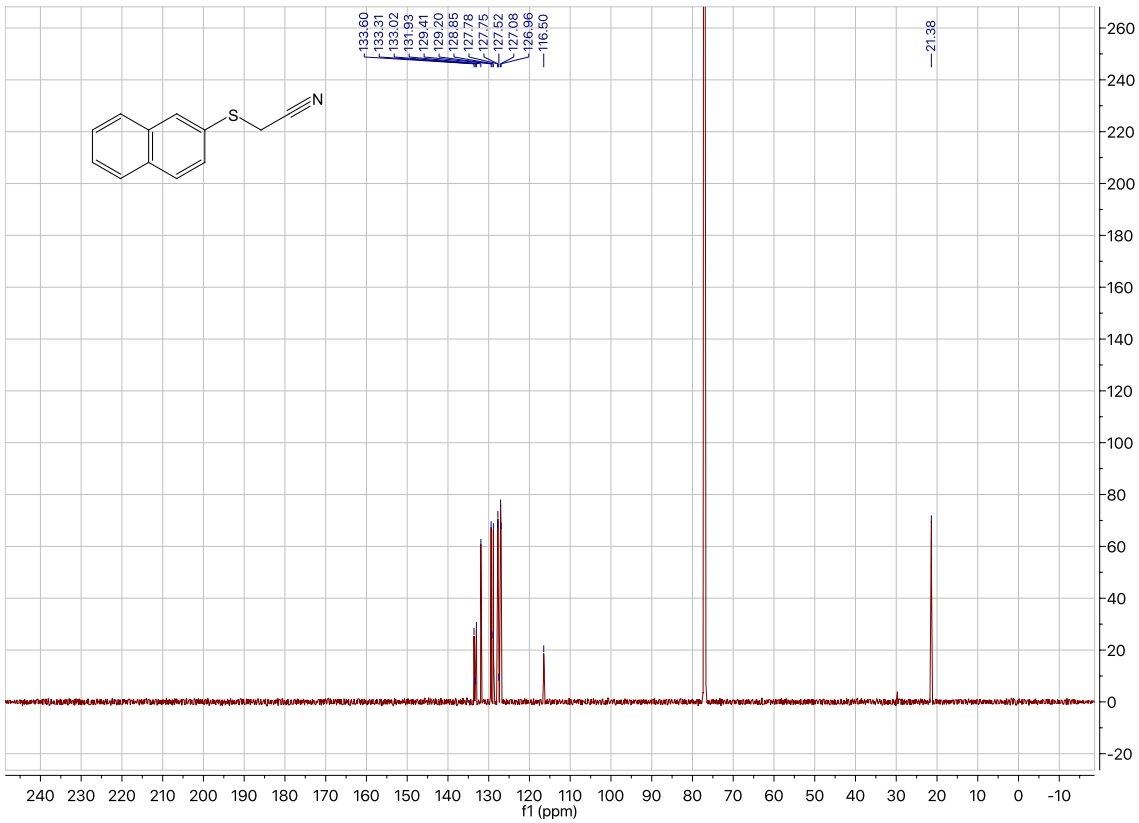


2-(naphthalen-2-ylthio)acetonitrile (9k)

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

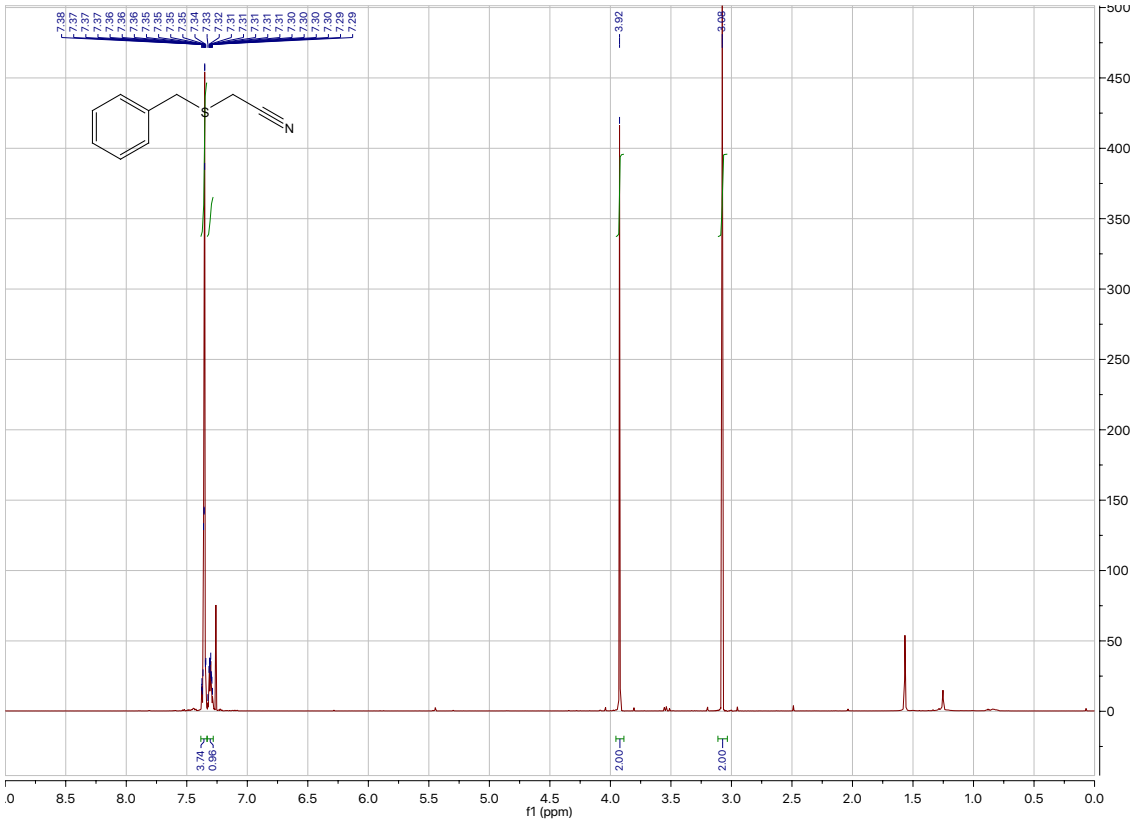


^{13}C NMR (151 MHz, $CDCl_3$)

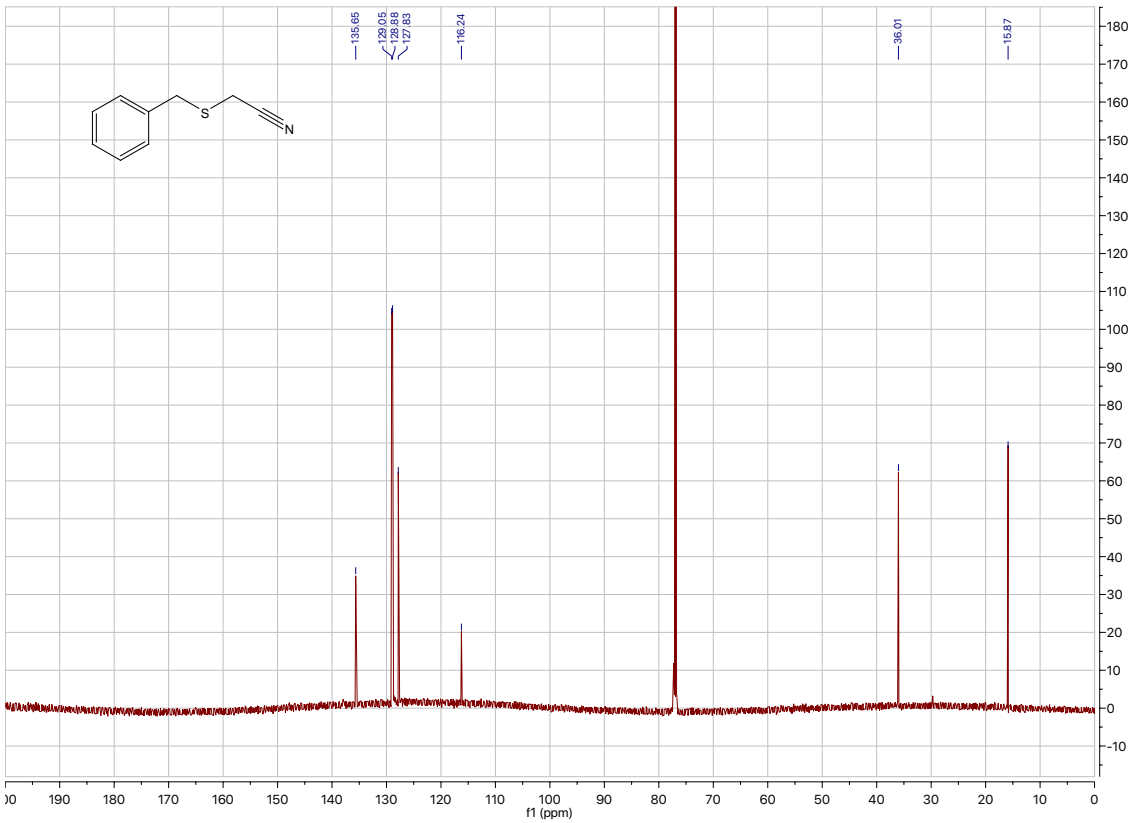


2-(benzylthio)acetonitrile (9l)

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

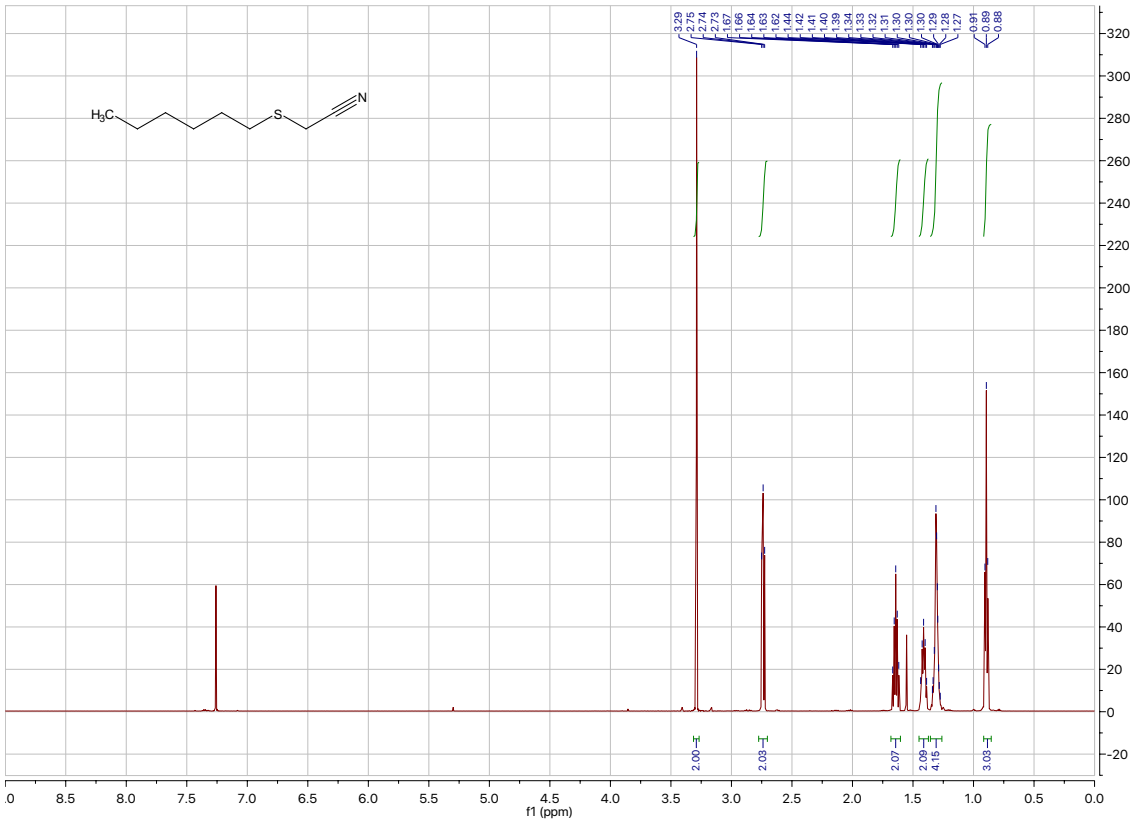


^{13}C NMR (151 MHz, $CDCl_3$)

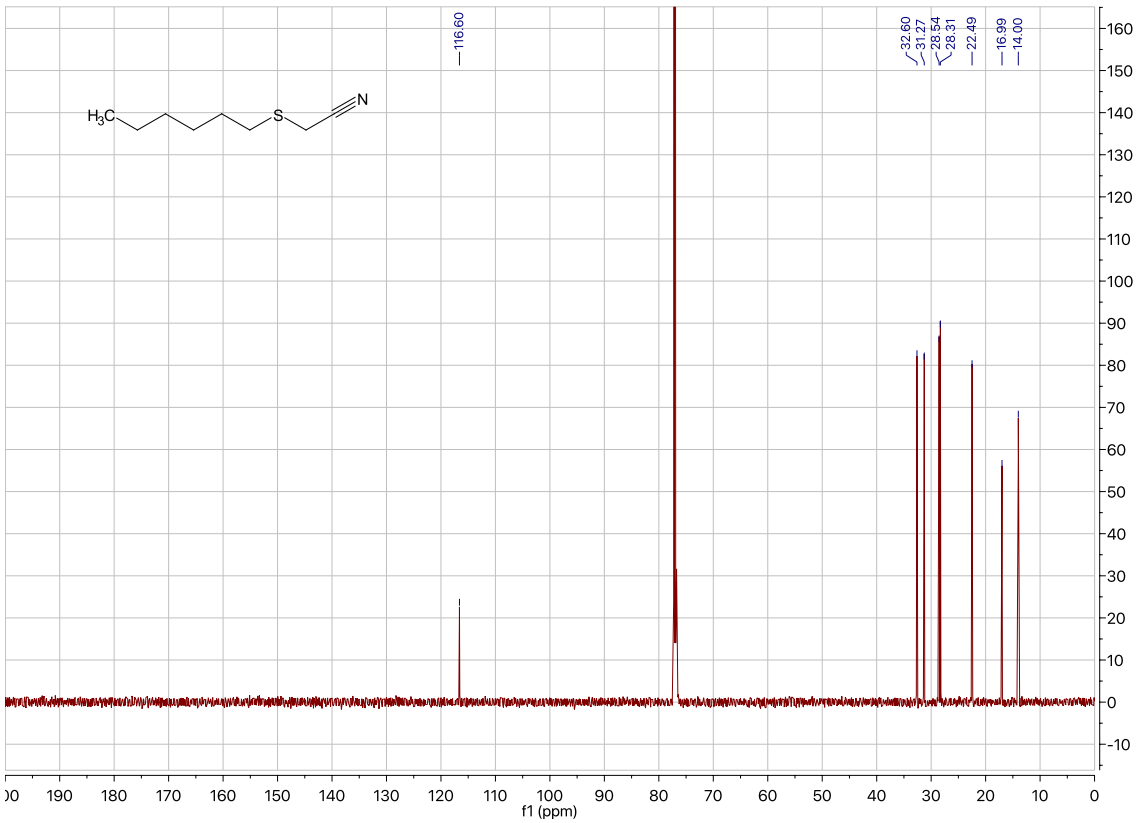


2-(hexylthio)acetonitrile (9m)

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

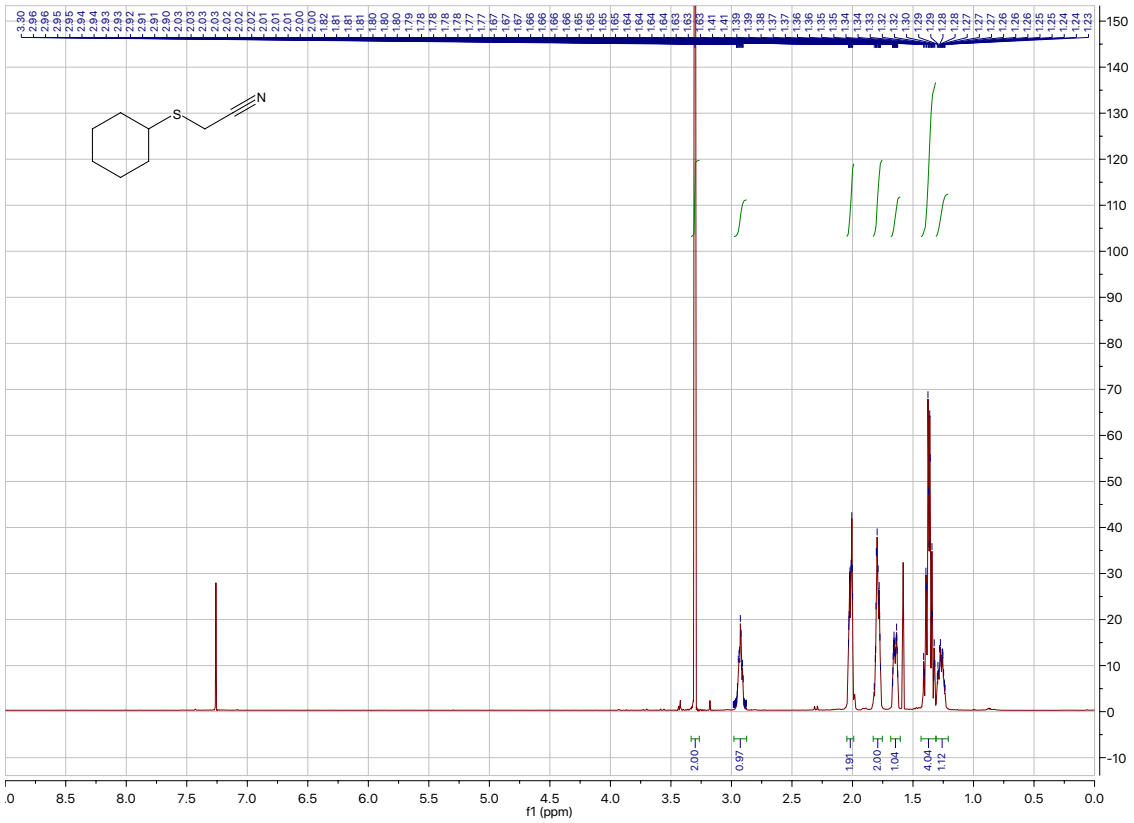


^{13}C NMR (151 MHz, $CDCl_3$)



2-(cyclohexylthio)acetonitrile (9n)

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



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