Supporting Information

Efficient Traceless Solid-Phase Synthesis of 3,4-Dihydropyrazino[1,2-b]indazoles and their 6-Oxides

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Material and Methods

Solvents were used without further purification. The Wang resin (100-200 mesh, 1% DVB, 1.0 mmol/g) was used. Synthesis was carried out on Domino Blocks (www.torviq.com) in disposable polypropylene reaction vessels.

All reactions were carried out at ambient temperature (~21 ^{o}C) unless stated otherwise. The volume of wash solvent was 10 mL per 1 g of resin. For washing, resin slurry was shaken with the fresh solvent for at least 1 min before changing the solvent. After adding a reagent solution, the resin slurry was manually vigorously shaken to break any potential resin clumps. Resin-bound intermediates were dried by a stream of nitrogen for prolonged storage and/or quantitative analysis.

For the LC/MS analysis a sample of resin (~5 mg) was treated by 50% TFA in DCM, the cleavage cocktail was evaporated by a stream of nitrogen, and cleaved compounds extracted into 1 mL of MeOH.

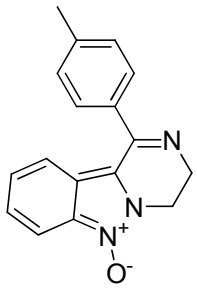
The LC/MS analyses were carried out using a 3 x 50 mm C18 reverse phase column. Mobile phases: 10 mM ammonium acetate in HPLC grade water (A) and HPLC grade acetonitrile (B). A gradient was formed from 5% to 80% of B in 10 minutes at 0.7 mL/min. The MS electrospray source operated at capillary voltage 3.5 kV and a desolvation temperature 300 ^{o}C.

Purification was carried out on C18 column 19 x 100 mm, 5 um particles, gradient was formed from 10 mM aqueous ammonium acetate and acetonitrile, flow rate 15 mL/min.

NMR spectroscopy. All ^{1}H and ^{13}C-NMR experiments were performed at magnetic field strengths of 7.05 T corresponding to ^{1}H resonance frequencies of 299.89 MHz, and at ambient temperature (~21 ^{o}C). ^{1}H spectra and ^{13}C spectra were referenced relative to the signal of DMSO (^{1}H δ = 2.49 ppm, ^{13}C δ = 39.50 ppm).

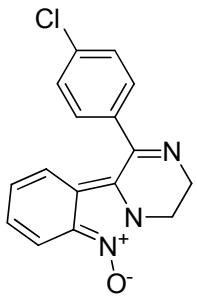
Analytical data of synthetic compounds

1-p-Tolyl-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,1,1)



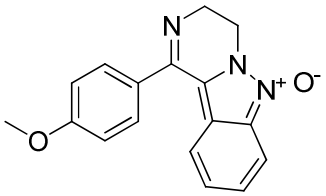
Yield 41.3 mg (72%). ESI-MS *m/z* = 278, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.42 (s, 3 H) 4.11 (t, *J*=6.91 Hz, 2 H) 4.42 (t, *J*=6.77 Hz, 2 H) 7.00 (d, *J*=8.56 Hz, 1 H) 7.16 - 7.24 (m, 1 H) 7.29 - 7.38 (m, 3 H) 7.59 (d, *J*=8.01 Hz, 2 H) 7.73 (d, *J*=8.84 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.77, 38.08, 47.57, 110.80, 113.69, 115.51, 120.77, 126.61, 126.84, 129.11, 129.56, 129.72, 135.05, 140.85, 156.34. HRMS (FAB) *m/z* calcd for $C_{17}H_{16}N_3O$ [M + H]+ 278.1293, found 278.1316

1-(4-Chlorophenyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,1,2)



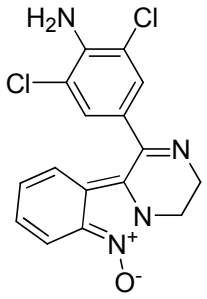
Yield 26.0 mg (43%). ESI-MS *m/z* = 298, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.18 (t, *J*=6.77 Hz, 2 H) 4.63 (t, *J*=6.63 Hz, 2 H) 7.04 (d, *J*=8.29 Hz, 1 H) 7.41 - 7.54 (m, 2 H) 7.71 - 7.76 (m, 2 H) 7.76 - 7.81 (m, 2 H) 7.91 (d, *J*=8.29 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 39.48, 44.16, 109.99, 114.70, 120.40, 127.78, 129.36, 129.92, 130.94, 131.41, 131.85, 137.87, 155.04. HRMS (FAB) *m/z* calcd for $C_{16}H_{13}ClN_3O$ [M + H]+ 298.0747, found 298.0734

1-(4-Methoxyphenyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,1,3)



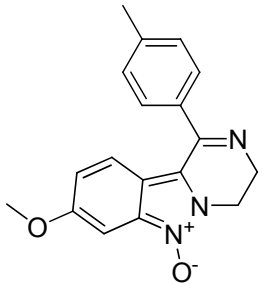
Yield 30.1 mg (50%). ESI-MS *m/z* = 294, [M+H]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.89 (s, 3 H) 4.13 (t, *J*=6.49 Hz, 2 H) 4.65 (t, *J*=6.49 Hz, 2 H) 7.16 (d, *J*=7.73 Hz, 1 H) 7.21 (d, *J*=8.84 Hz, 2 H) 7.49 (dd, *J*=9.25, 7.60 Hz, 2 H) 7.76 (d, *J*=8.84 Hz, 2 H) 7.92 (d, *J*=7.73 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 39.80, 42.67, 56.46, 109.74, 114.91, 115.37, 120.44, 121.17, 123.76, 127.94, 130.48, 131.82, 132.46, 155.70, 163.91. HRMS (FAB) *m/z* calcd for $C_{17}H_{16}N_3O_2$ [M + H]+ 294.1243, found 294.1228

1-(4-Amino-3,5-dichlorophenyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,1,4)



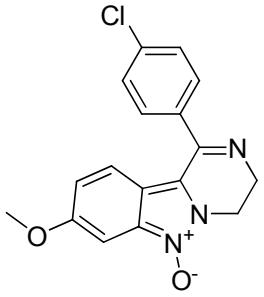
Yield 69.0 mg (96%). ESI-MS *m/z* = 347, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.12 (t, *J*=6.35 Hz, 2 H) 4.67 (t, *J*=6.49 Hz, 2 H) 6.86 (s, 2 H) 7.38 - 7.44 (m, 1 H) 7.54 - 7.64 (m, 2 H) 7.76 (s, 2 H) 8.01 (dd, *J*=6.49, 2.62 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 37.17, 41.24, 109.27, 115.26, 116.88, 118.46, 120.28, 122.56, 128.32, 130.96, 131.46, 132.39, 147.03, 153.50. HRMS (FAB) *m/z* calcd for $C_{16}H_{13}Cl_2N_4O$ [M + H]+ 347.0466, found 347.0482

8-Methoxy-1-p-tolyl-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,2,1)



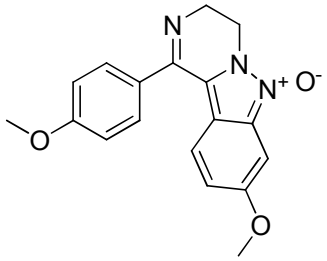
Yield (HPLC purified) 10.1 mg (16%). ESI-MS *m/z* = 308, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}N_3O_2$ [M + H]+ 308.1399, found 308.1424

1-(4-Chlorophenyl)-8-methoxy-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,2,2)



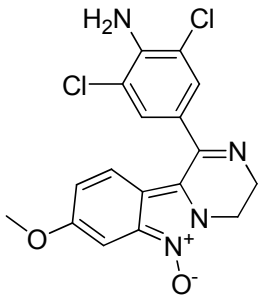
Yield (HPLC purified) 11.0 mg (16%). ESI-MS *m/z* = 328, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}N_3O_2Cl$ [M + H]+ 328.0853, found 328.0868

8-Methoxy-1-(4-methoxyphenyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,2,3)



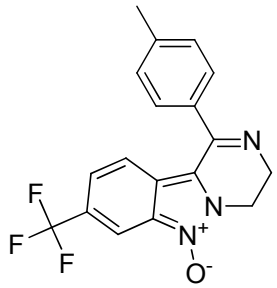
Yield (HPLC purified) 12.7 mg (20%). ESI-MS *m/z* = 324, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.85 (s, 6 H) 4.07 (t, *J*=6.77 Hz, 2 H) 4.36 (t, *J*=6.91 Hz, 2 H) 6.89 (d, *J*=2.21 Hz, 1 H) 6.92 - 6.97 (m, 1 H) 6.98 (d, *J*=2.21 Hz, 1 H) 7.05 - 7.11 (m, 2 H) 7.60 - 7.67 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 37.93, 47.64, 56.05, 56.42, 91.38, 111.27, 111.32, 114.48, 121.24, 122.02, 130.15, 130.19, 130.67, 155.77, 158.84, 161.70. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}N_3O_3$ [M + H]+ 324.1348, found 324.1332

1-(4-Amino-3,5-dichlorophenyl)-8-methoxy-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,2,4)



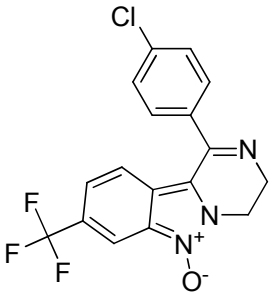
Yield (HPLC purified) 15.0 mg (20%). ESI-MS *m/z* = 377, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}Cl_2N_4O_2$ [M + H]+ 377.0572, found 377.0564

1-p-Tolyl-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,3,1)



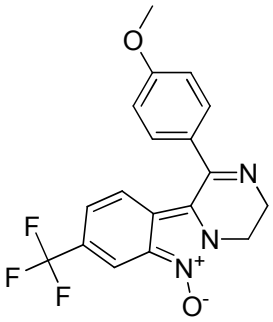
Yield 56.5 mg (78%). ESI-MS *m/z* = 346, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.47 (s, 3 H) 4.21 (t, *J*=6.77 Hz, 2 H) 4.70 (t, *J*=6.63 Hz, 2 H) 7.27 (d, *J*=8.84 Hz, 1 H) 7.50 (d, *J*=8.01 Hz, 2 H) 7.66 - 7.74 (m, 3 H) 8.33 (s, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.97, 42.97, 110.10, 113.41 (q, *J*=5.2 Hz), 121.84, 122.43, 125.61 (d, *J*=2.1 Hz), 126.05, 127.84 (q, *J*=32.4 Hz), 128.84, 130.31, 130.53, 130.70, 144.56, 156.78. HRMS (FAB) *m/z* calcd for $C_{18}H_{15}F_3N_3O$ [M + H]+ 346.1167, found 346.1140

1-(4-Chlorophenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,3,2)



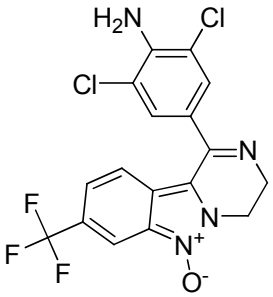
Yield 47.7 mg (62%). ESI-MS *m/z* = 366, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{12}ClF_3N_3O$ [M + H]+ 366.0621, found 366.0584

1-(4-Methoxyphenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,3,3)



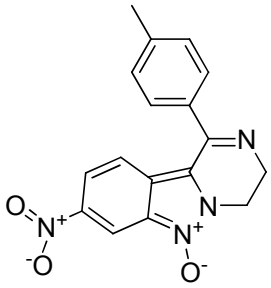
Yield 32.0 mg (81%). ESI-MS *m/z* = 362, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{18}H_{15}F_3N_3O_2$ [M + H]+ 362.1116, found 362.1155

1-(4-Amino-3,5-dichlorophenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,3,4)



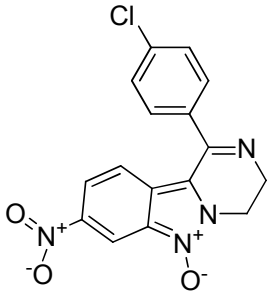
Yield 50.8 mg (58%). ESI-MS *m/z* = 415, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{12}Cl_2F_3N_4O$ [M + H]+ 415.0340, found 415.0361

8-Nitro-1-p-tolyl-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,4,1)



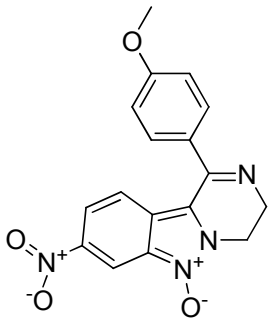
Yield 42.9 mg (60%). ESI-MS *m/z* = 323, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}O_3N_4$ [M + H]+ 323.1144, found 323.1129

1-(4-Chlorophenyl)-8-nitro-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,4,2)



Yield 44.4 mg (59%). ESI-MS *m/z* = 343, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{16}H_{12}O_3N_4Cl$ [M + H]+ 343.0598, found 343.0608

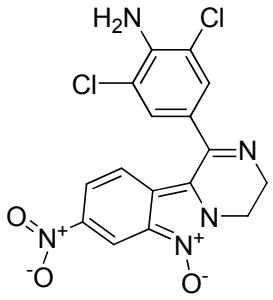
1-(4-Methoxyphenyl)-8-nitro-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,4,3)



Yield 56.3 mg (75%). ESI-MS *m/z* = 339, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.93 (s, 3 H) 4.23 (t, *J*=6.63 Hz, 2 H) 4.74 (t, *J*=6.49 Hz, 2 H) 7.28 (d, *J*=8.84 Hz, 2 H) 7.36 (d, *J*=9.39 Hz, 1 H) 7.81 (d, *J*=8.84 Hz, 2 H) 8.17 (dd, *J*=9.25, 2.07 Hz, 1 H) 8.78 (d, *J*=1.93 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 37.17, 56.31, 56.59, 110.01, 112.57, 115.01, 115.69,

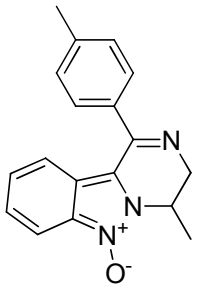
122.20, 124.18, 130.88, 131.63, 132.93, 146.39, 156.84, 164.63. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}N_4O_4$ [M + H]+ 339.1093, found 339.1137

1-(4-Amino-3,5-dichlorophenyl)-8-nitro-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(1,4,4)



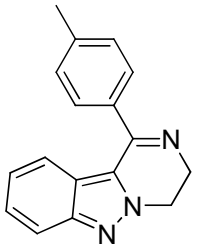
Yield 57.9 mg (67%). ESI-MS *m/z* = 392, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{16}H_{12}Cl_2N_5O_3$ [M + H]+ 392.0317, found 392.0283

4-Methyl-1-p-tolyl-3,4-dihydropyrazino[1,2-b]indazole 6-oxide 7(2,1,1)



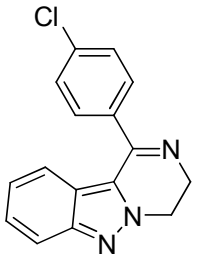
Yield (HPLC purified) 33.2 mg (78%). ESI-MS *m/z* = 292, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.34 (d, *J*=6.63 Hz, 3 H) 2.42 (s, 3 H) 3.96 (dd, *J*=16.57, 6.35 Hz, 1 H) 4.36 (d, *J*=16.57 Hz, 1 H) 5.09 - 5.20 (m, 1 H) 7.01 (d, *J*=8.84 Hz, 1 H) 7.17 - 7.24 (m, 1 H) 7.30 - 7.38 (m, 3 H) 7.57 - 7.63 (m, 2 H) 7.74 (d, *J*=8.56 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 16.28, 21.02, 44.26, 52.92, 108.8, 112.99, 114.90, 120.16, 125.99, 126.17, 128.36, 128.82, 128.97, 134.34, 140.06, 155.05. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}N_3O$ [M + H]+ 292.1450, found 292.1456

1-p-Tolyl-3,4-dihydropyrazino[1,2-b]indazole 8(1,1,1)



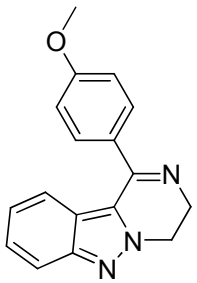
Yield 29.0 mg (54%). ESI-MS *m/z* = 262, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.47 (s, 3 H) 4.24 (t, *J*=6.91 Hz, 2 H) 4.81 (t, *J*=6.77 Hz, 2 H) 7.06 (d, *J*=8.56 Hz, 1 H) 7.22 - 7.29 (m, 1 H) 7.38 - 7.51 (m, 3 H) 7.69 (d, *J*=8.01 Hz, 2 H) 7.91 (d, *J*=8.56 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.93, 45.75, 46.68, 119.44, 120.30, 121.05, 124.33, 126.30, 127.20, 129.90, 130.12, 131.05, 143.35, 148.36, 160.66. HRMS (FAB) *m/z* calcd for $C_{17}H_{16}N_3$ [M + H]+ 262.1344, found 262.1342

1-(4-Chlorophenyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,1,2)



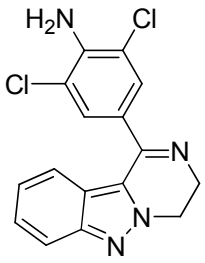
Yield 34.5 mg (60%). ESI-MS *m/z* = 282, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.18 (t, *J*=6.91 Hz, 2 H) 4.62 - 4.70 (m, 2 H) 7.03 (d, *J*=8.56 Hz, 1 H) 7.14 - 7.22 (m, 1 H) 7.32 - 7.40 (m, 1 H) 7.63 - 7.69 (m, 2 H) 7.72 - 7.78 (m, 2 H) 7.83 (d, *J*=8.84 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 46.21, 47.90, 118.91, 119.13, 120.45, 124.34, 125.09, 126.71, 129.43, 131.07, 135.52, 136.41, 147.99, 158.29. HRMS (FAB) *m/z* calcd for $C_{16}H_{13}N_3Cl$ [M + H]+ 282.0798, found 282.0776

1-(4-Methoxyphenyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,1,3)



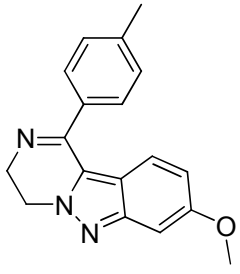
Yield 19.5 mg (34%). ESI-MS *m/z* = 278, [M+H]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.88 (s, 3 H) 4.17 (t, *J*=6.91 Hz, 2 H) 4.77 (t, *J*=6.77 Hz, 2 H) 7.13 (d, *J*=8.56 Hz, 1 H) 7.18 (d, *J*=8.84 Hz, 2 H) 7.22 - 7.28 (m, 1 H) 7.38 - 7.44 (m, 1 H) 7.74 (d, *J*=8.84 Hz, 2 H) 7.89 (d, *J*=8.56 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 45.64, 46.74, 56.34, 114.98, 119.37, 120.41, 120.94, 124.31, 126.17, 127.13, 131.02, 131.91, 148.29, 159.99, 163.30. HRMS (FAB) *m/z* calcd for $C_{17}H_{16}N_3O$ [M + H]+ 278.1293, found 278.1288

2,6-Dichloro-4-(3,4-dihydropyrazino[1,2-b]indazol-1-yl)aniline 8(1,1,4)



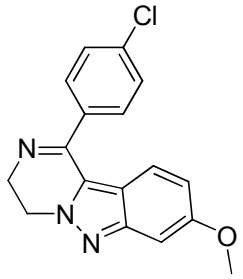
Yield 67.6 mg (99%). ESI-MS *m/z* = 331, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.12 (t, *J*=6.63 Hz, 2 H) 4.70 (t, *J*=6.63 Hz, 2 H) 6.42 (br. s., 2 H) 7.26 (d, *J*=3.59 Hz, 2 H) 7.39 (ddd, *J*=8.42, 4.14, 4.01 Hz, 1 H) 7.65 (s, 2 H) 7.87 (d, *J*=8.56 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 46.10, 46.68, 118.29, 119.30, 120.24, 122.38, 124.02, 125.88, 126.96, 129.73, 145.24, 148.18, 157.57. HRMS (FAB) *m/z* calcd for $C_{16}H_{13}N_4Cl_2$ [M + H]+ 331.0517, found 331.0517

8-Methoxy-1-p-tolyl-3,4-dihydropyrazino[1,2-b]indazole 8(1,2,1)



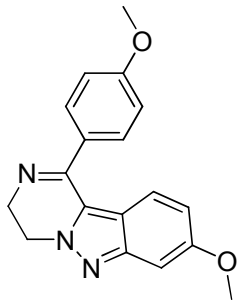
Yield (HPLC purified) 12.2 mg (21%). ESI-MS *m/z* = 292, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.41 (s, 3 H) 3.80 (s, 3 H) 4.10 (t, *J*=6.91 Hz, 2 H) 4.51 (t, *J*=6.91 Hz, 2 H) 6.75 - 6.81 (m, 1 H) 6.87 - 6.93 (m, 1 H) 7.11 (d, *J*=1.93 Hz, 1 H) 7.34 (d, *J*=8.01 Hz, 2 H) 7.58 (d, *J*=8.01 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.74, 45.75, 48.58, 55.95, 96.39, 113.93, 118.41, 121.52, 124.68, 128.89, 129.66, 135.12, 140.78, 148.94, 158.40, 158.64. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}N_30$ [M + H]+ 292.1450, found 292.1465

1-(4-Chlorophenyl)-8-methoxy-3,4-dihydropyrazino[1,2-b]indazole 8(1,2,2)



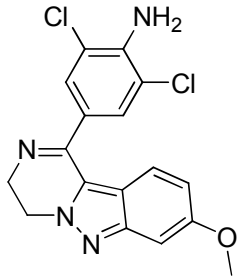
Yield (HPLC purified) 53.9 mg (86%). ESI-MS *m/z* = 312, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}ClN_3O$ [M + H]+ 312.0904, found 312.0911

8-Methoxy-1-(4-methoxyphenyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,2,3)



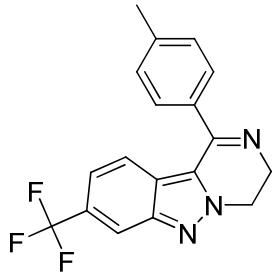
Yield (HPLC purified) 22.6 mg (36%). ESI-MS *m/z* = 308, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}N_3O_2$ [M + H]+ 308.1399, found 308.1392

2,6-Dichloro-4-(8-methoxy-3,4-dihydropyrazino[1,2-b]indazol-1-yl)aniline 8(1,2,4)



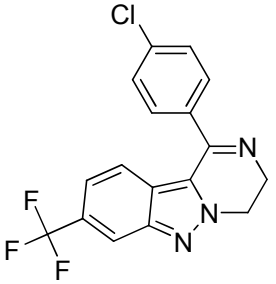
Yield (HPLC purified) 13.6 mg (19%). ESI-MS *m/z* = 361, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}Cl_2N_4O$ [M + H]+ 361.0623, found 361.0618

1-p-Tolyl-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,3,1)



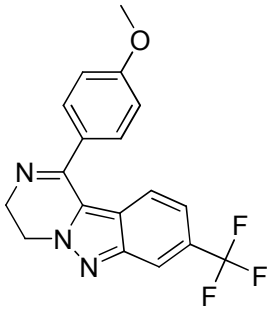
Yield 8.3 mg (12%). ESI-MS *m/z* = 330, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{18}H_{15}F_3N_3$ [M + H]+ 330.1218, found 330.1219

1-(4-Chlorophenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,3,2)



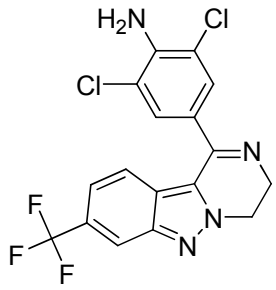
Yield 44.5 mg (61%). ESI-MS *m/z* = 350, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{12}F_3N_3Cl$ [M + H]+ 350.0672, found 350.0685

1-(4-Methoxyphenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazole 8(1,3,3)



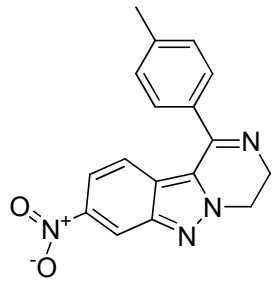
Yield 46.1 mg (64%). ESI-MS *m/z* = 346, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.88 (s, 3 H) 4.18 (t, *J*=6.77 Hz, 2 H) 4.75 (t, *J*=6.91 Hz, 2 H) 7.12 - 7.18 (m, 2 H) 7.30 - 7.35 (m, 1 H) 7.41 - 7.47 (m, 1 H) 7.69 - 7.76 (m, 2 H) 8.31 (s, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 46.72, 47.03, 56.20, 114.80, 117.36 (q, *J*=4.2 Hz), 120.40 (d, *J*=3.2 Hz), 120.88, 122.69, 125.07 (q, *J*=272.7 Hz), 125.27, 127.30 (q, *J*=31.3 Hz), 127.96, 131.24, 146.45, 158.68, 162.61. HRMS (FAB) *m/z* calcd for $C_{18}H_{15}N_3OF_3$ $[M + H]+$ 346.1167, found 346.1178

2,6-Dichloro-4-(8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-b]indazol-1-yl)aniline 8(1,3,4)



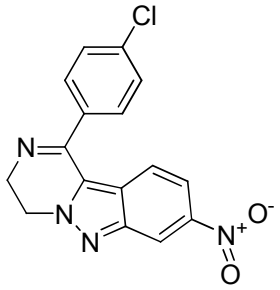
Yield 81.7 mg (98%). ESI-MS *m/z* = 399, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{12}F_3N_4Cl_2$ $[M + H]+$ 399.0391, found 399.0398

8-Nitro-1-p-tolyl-3,4-dihydropyrazino[1,2-b]indazole 8(1,4,1)



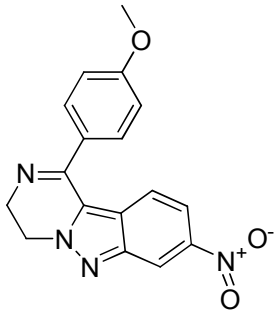
Yield 37.8 mg (56%). ESI-MS *m/z* = 307, $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ: 2.45 (s, 3 H) 4.22 (t, *J*=6.91 Hz, 2 H) 4.78 (t, *J*=6.91 Hz, 2 H) 7.25 (d, *J*=9.12 Hz, 1 H) 7.42 (d, *J*=7.73 Hz, 2 H) 7.65 (d, *J*=8.29 Hz, 2 H) 7.95 (dd, *J*=9.25, 2.07 Hz, 1 H) 8.84 (d, *J*=1.93 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 21.85, 34.30, 46.86, 47.49, 116.41, 116.88, 118.47, 121.71, 122.46,125.69, 129.25, 130.01, 142.04, 146.09, 146.60. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}N_4O_2$ [M + H]+ 307.1195, found 307.1202

1-(4-Chlorophenyl)-8-nitro-3,4-dihydropyrazino[1,2-b]indazole 8(1,4,2)



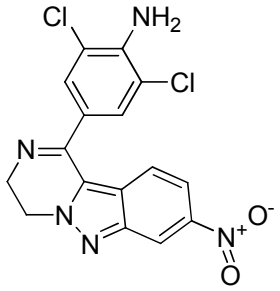
Yield 4.0 mg (7%). ESI-MS *m/z* = 327, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{16}H_{12}N_4O_2Cl$ [M + H]+ 327.0649, found 327.0640

1-(4-Methoxyphenyl)-8-nitro-3,4-dihydropyrazino[1,2-b]indazole 8(1,4,3)



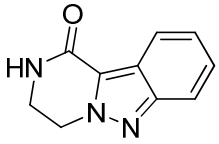
Yield 40.0 mg (56%). ESI-MS *m/z* = 323, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{17}H_{15}N_4O_3$ [M + H]+ 323.1144, found 323.1136

2,6-Dichloro-4-(8-nitro-3,4-dihydropyrazino[1,2-b]indazol-1-yl)aniline 8(1,4,4)



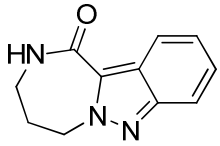
Yield 10.5 mg (12%). ESI-MS *m/z* = 376, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{16}H_{12}Cl_2N_5O_2$ [M + H]+ 376.0368, found 376.0358

3,4-Dihydropyrazino[1,2-b]indazol-1(2H)-one 10(1,1,5)



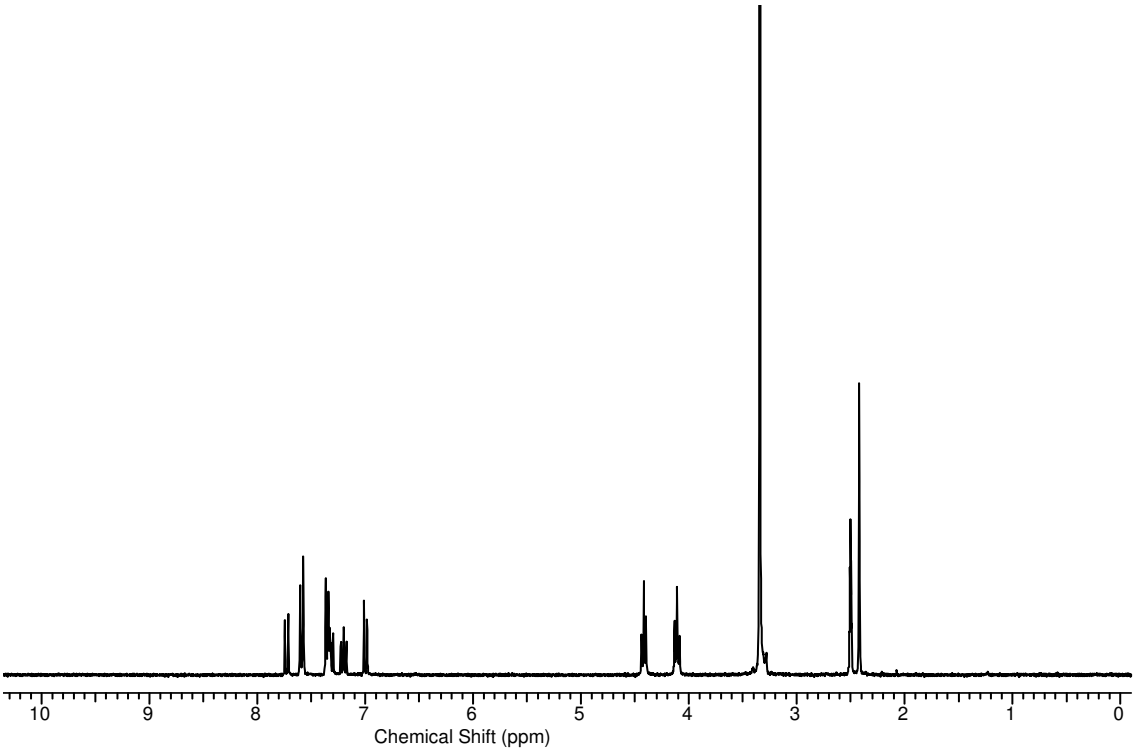
Yield (HPLC purified) 5.8 mg (33%). ESI-MS *m/z* = 188, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.69 - 3.78 (m, 2 H) 4.61 - 4.67 (m, 2 H) 7.22 - 7.30 (m, 1 H) 7.36 (ddd, *J*=8.42, 6.91, 1.24 Hz, 1 H) 7.75 (d, *J*=8.84 Hz, 1 H) 7.98 (d, *J*=8.29 Hz, 1 H) 8.29 (br. s., 1 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 39.61, 48.30, 118.44, 121.20, 121.53, 124.69, 126.02, 126.82, 147.97, 159.84. HRMS (FAB) *m/z* calcd for $C_{10}H_{10}N_3O$ [M + H]+ 188.0824, found 188.0809

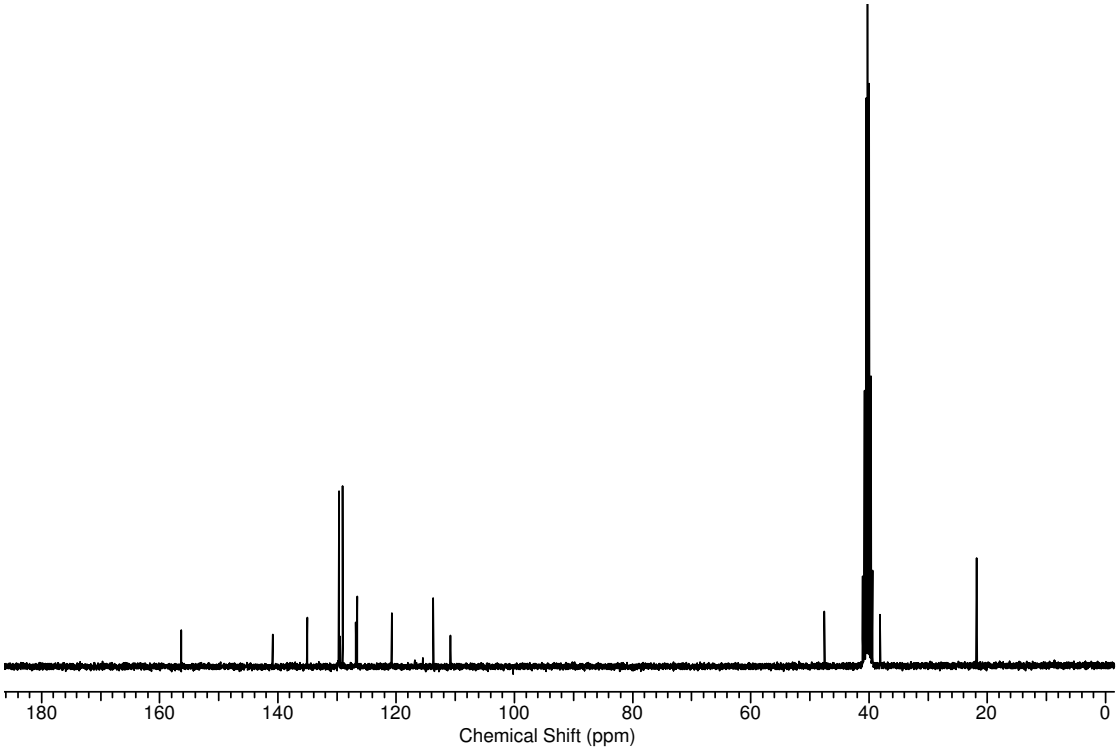
2,3,4,5-Tetrahydro-1H-[1,4]diazepino[1,2-b]indazol-1-one 11



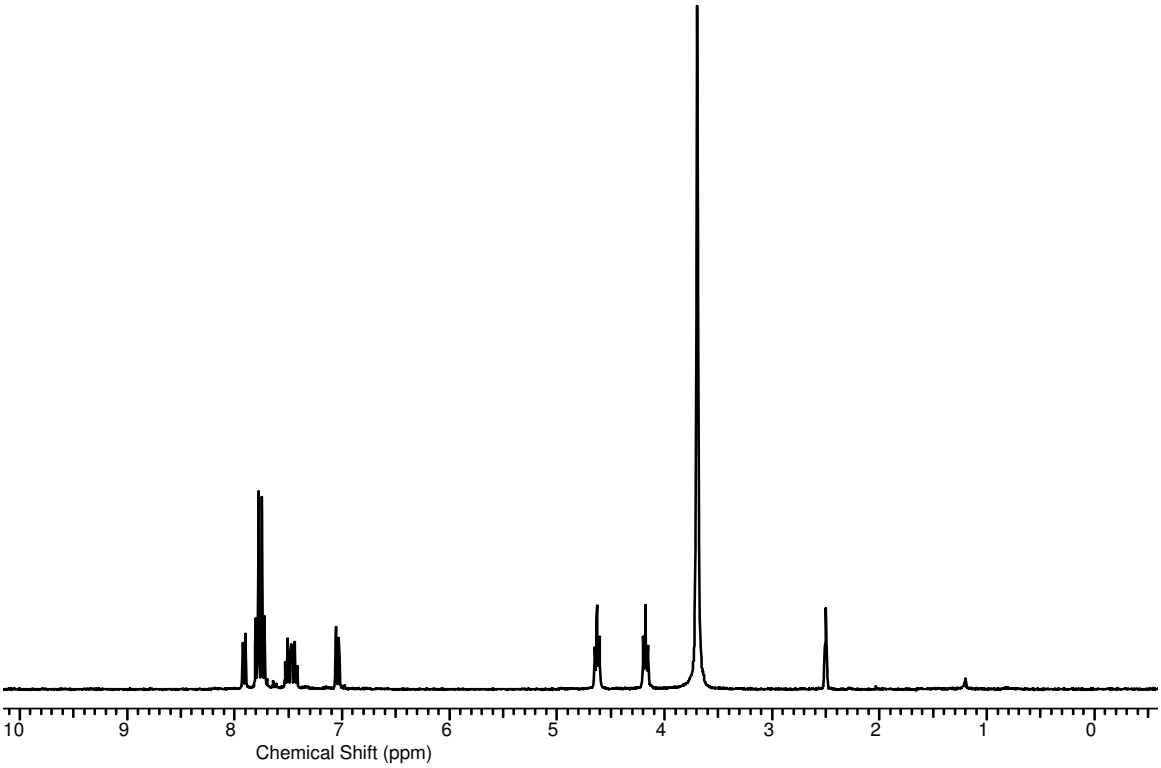
Yield (HPLC purified) 2.4 mg (10%). ESI-MS *m/z* = 202, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{11}H_{12}N_3O$ [M + H]+ 202.0980, found 202.0976

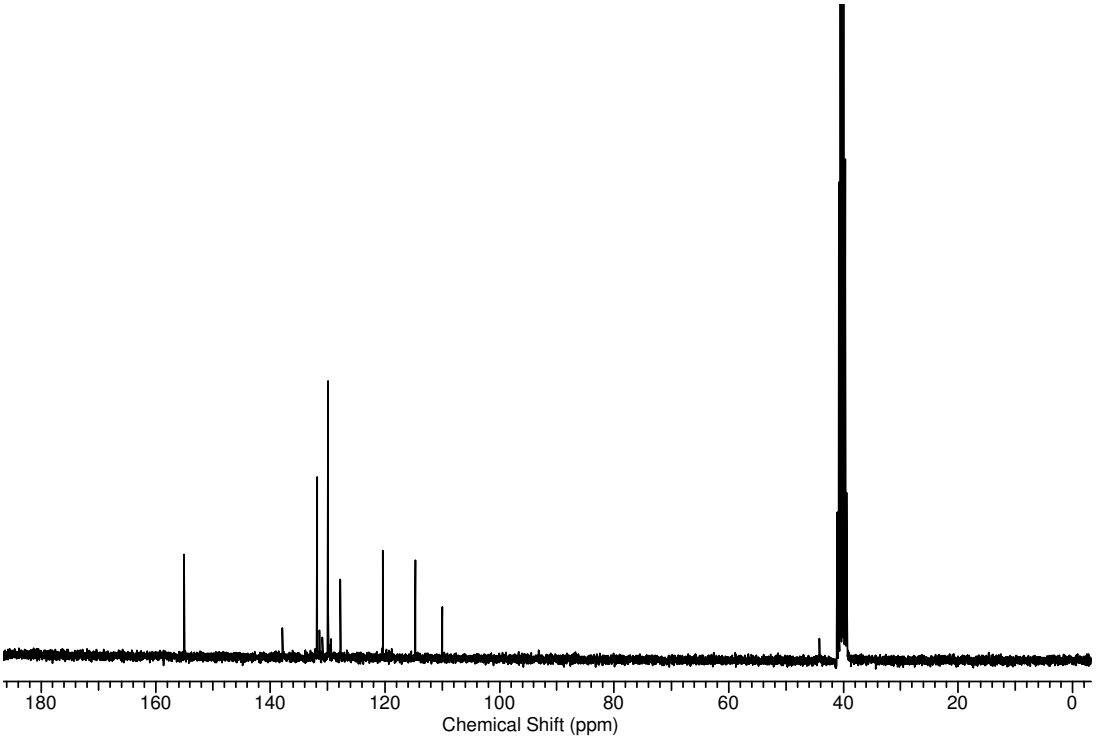
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1,1)



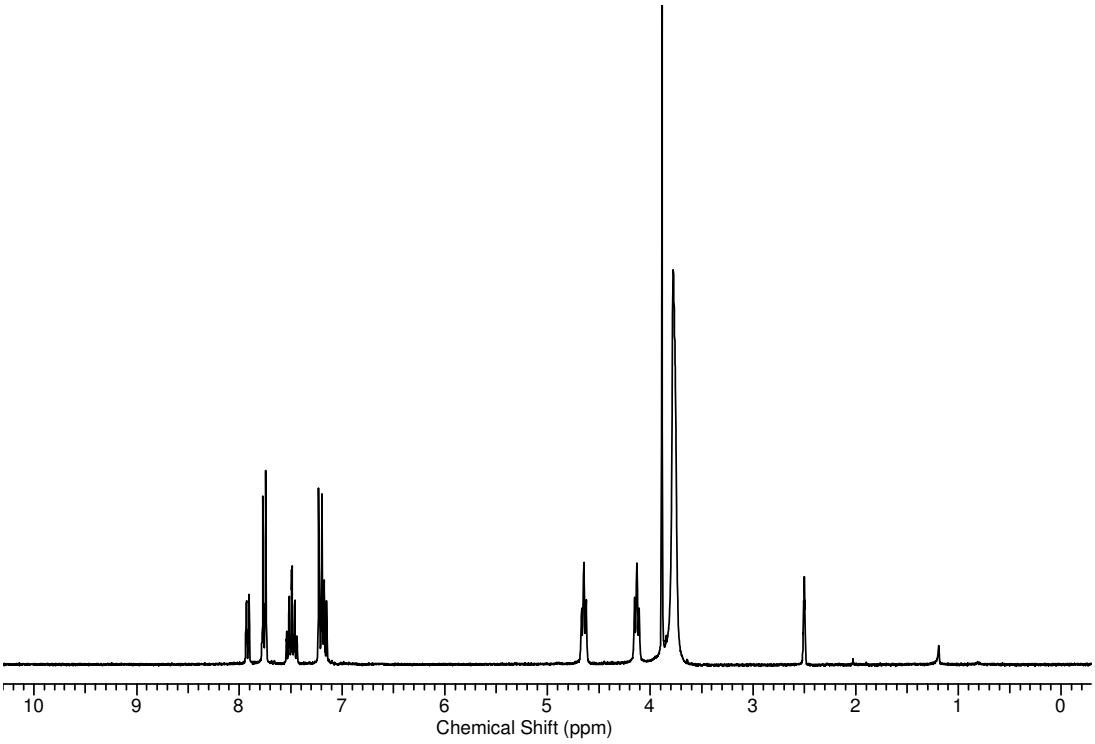


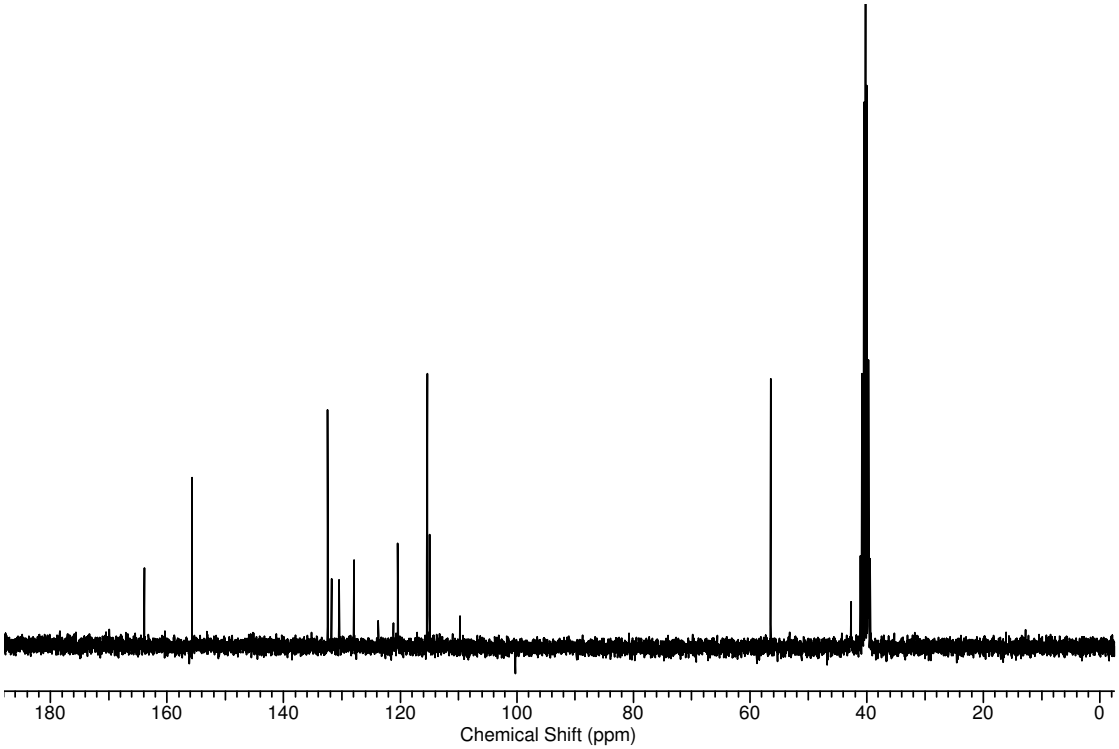
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1,2)



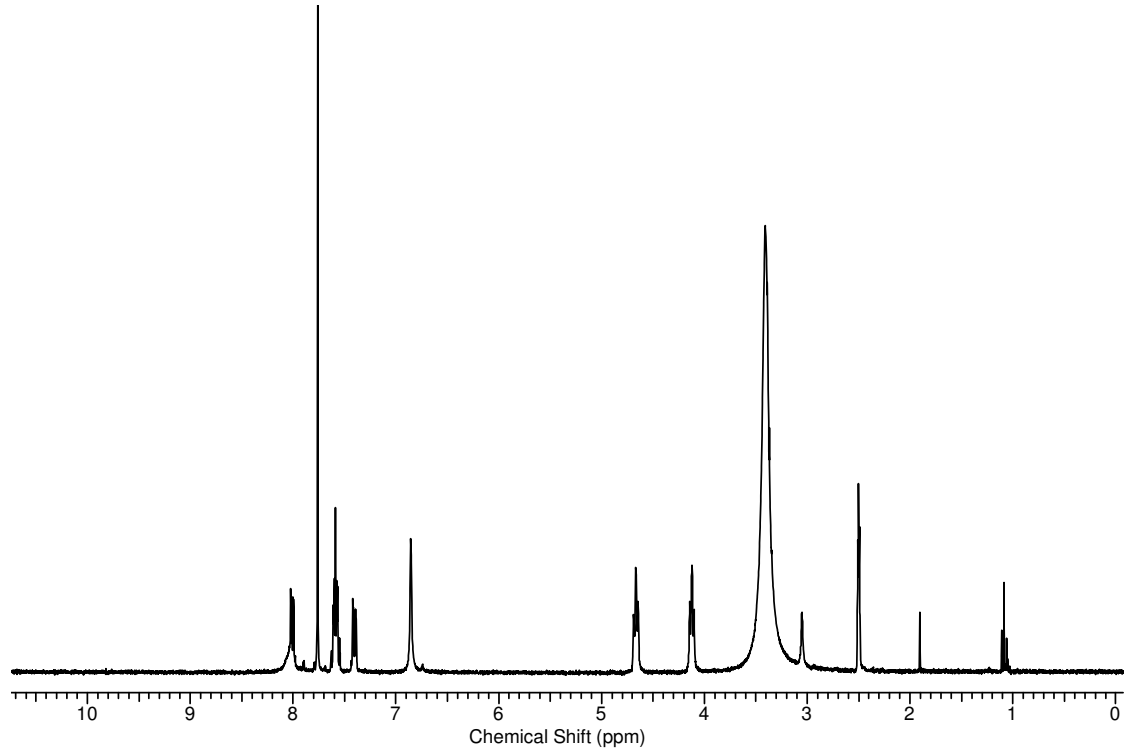


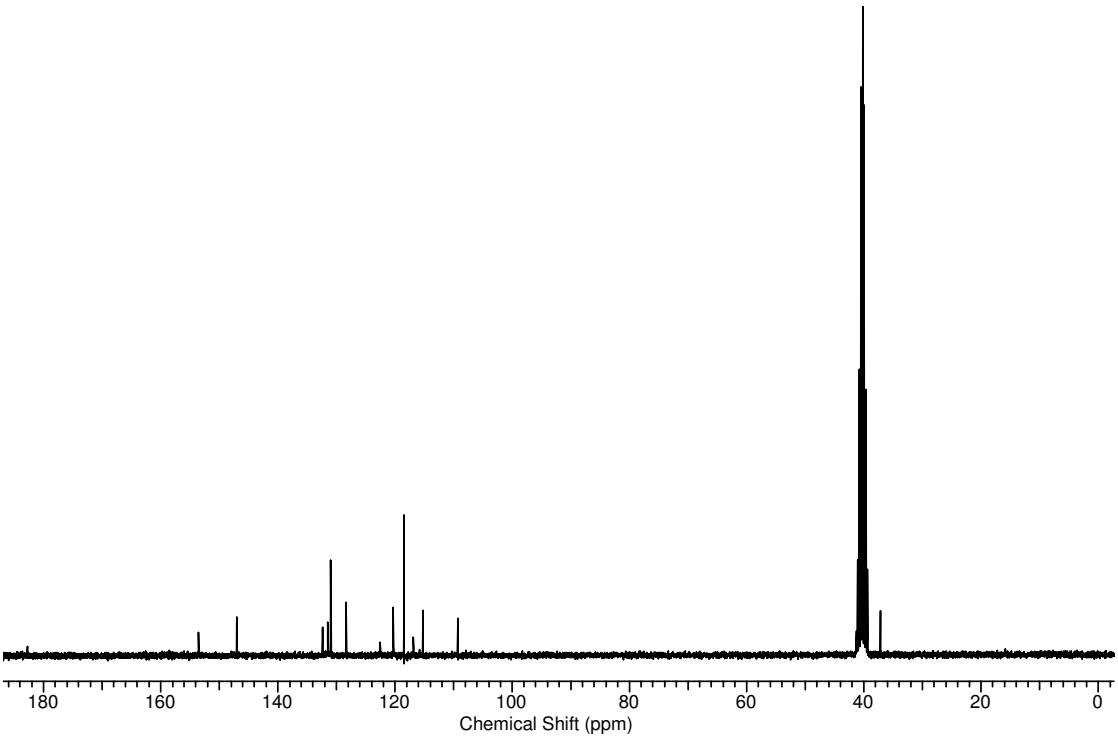
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1,3)



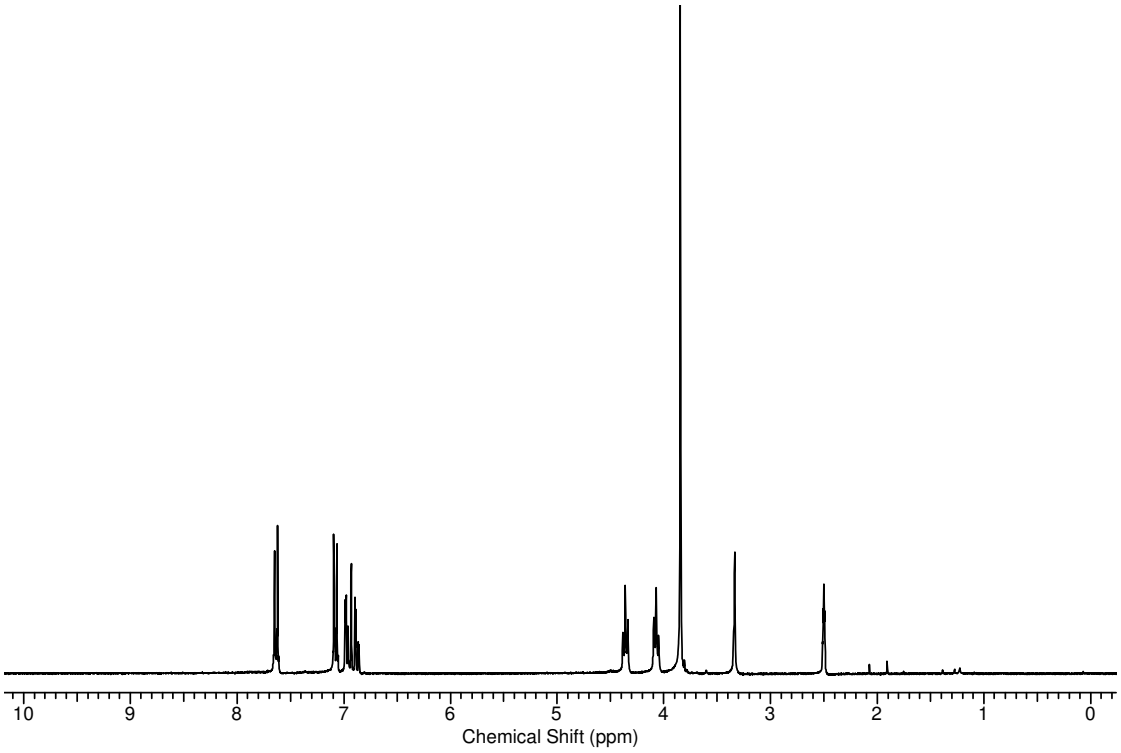


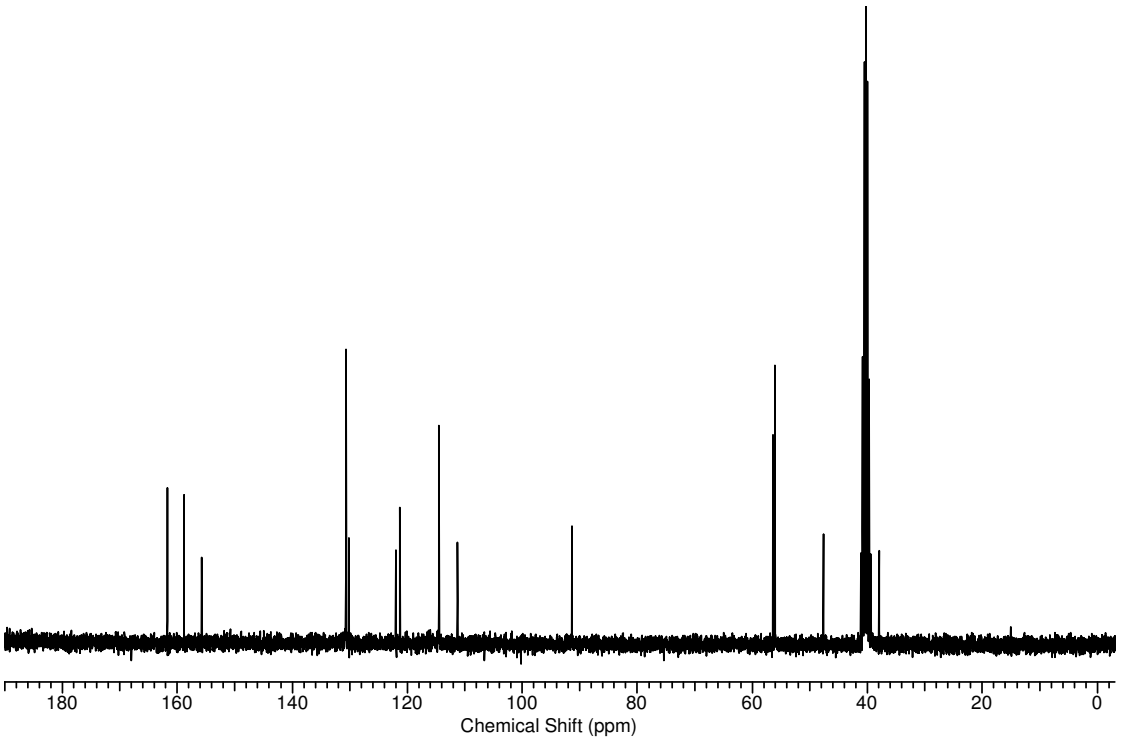
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1,4)



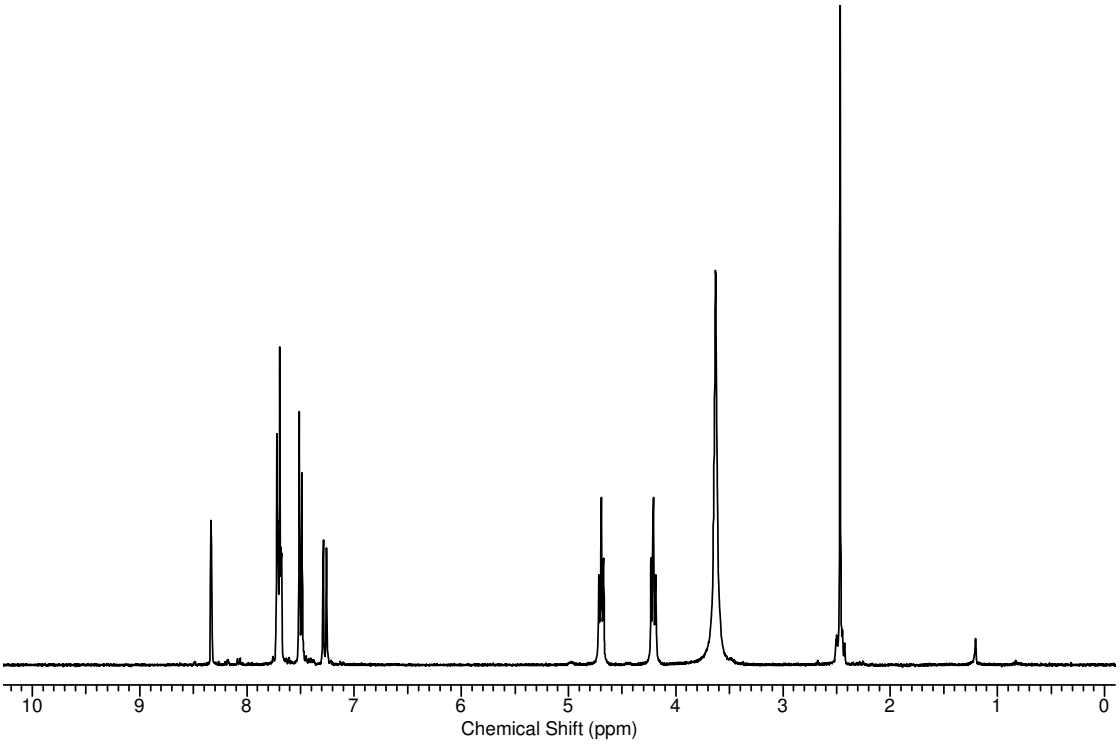


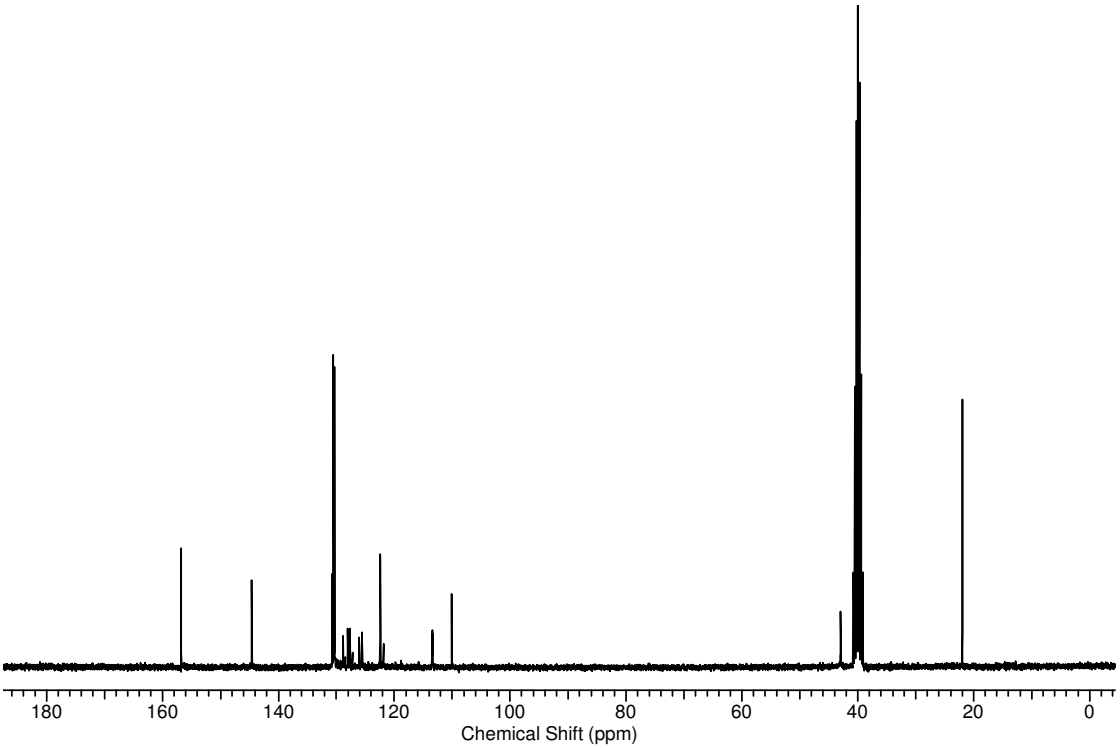
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,2,3)



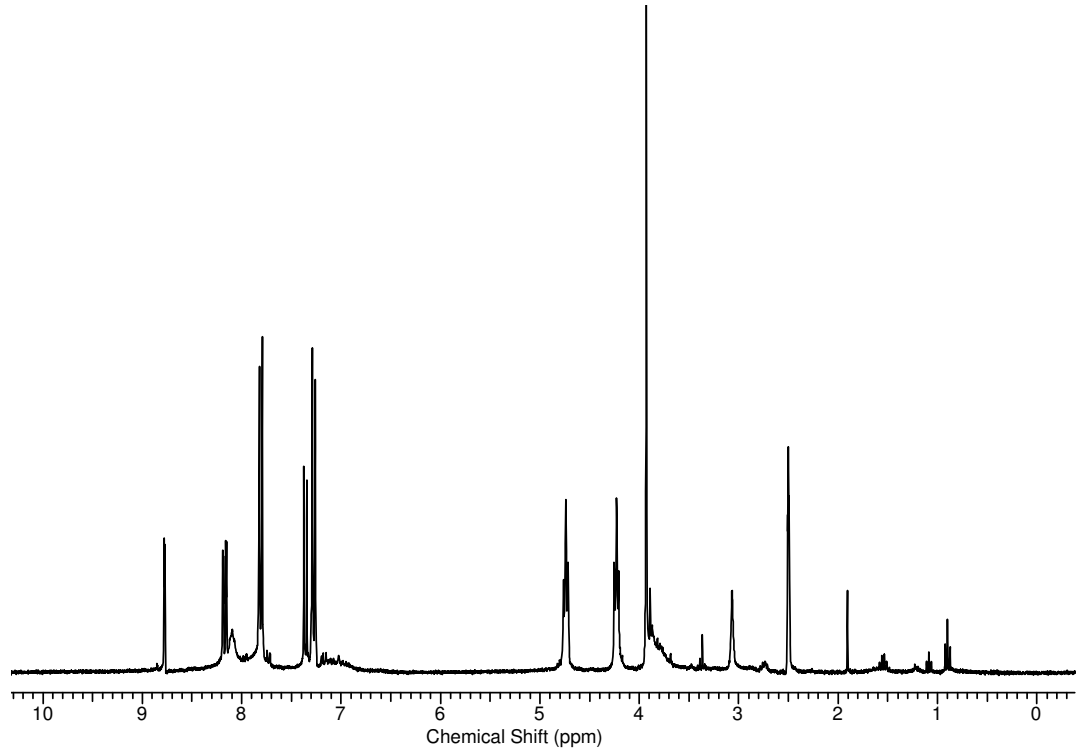


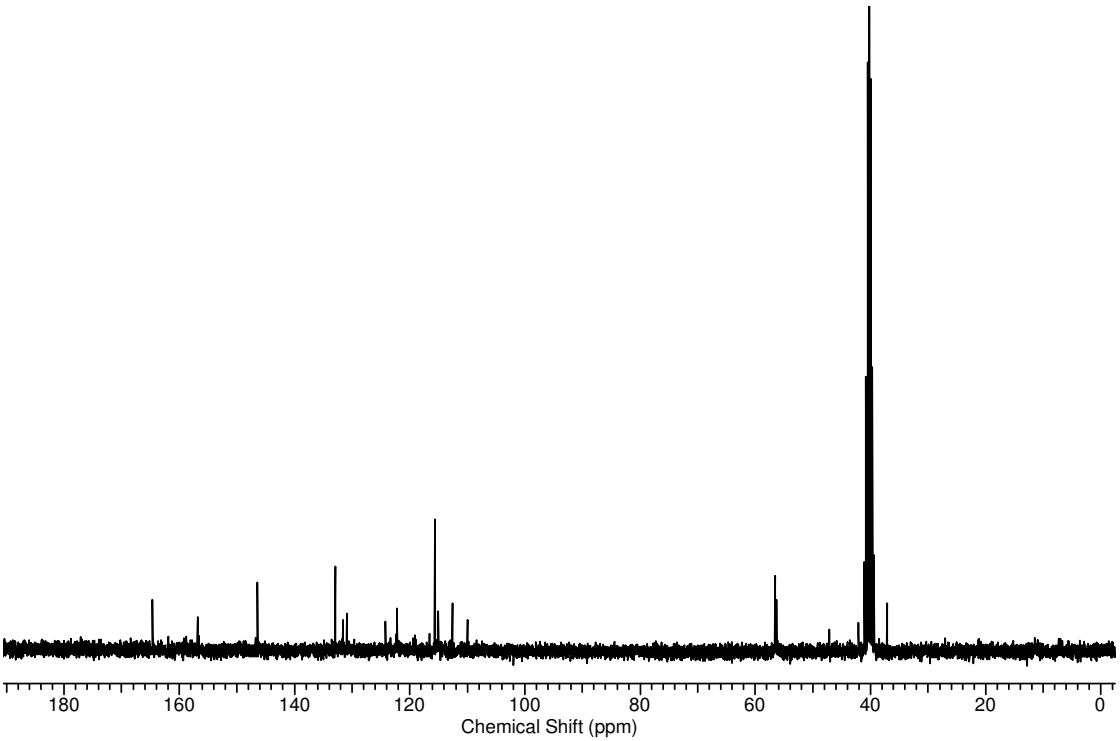
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,3,1)



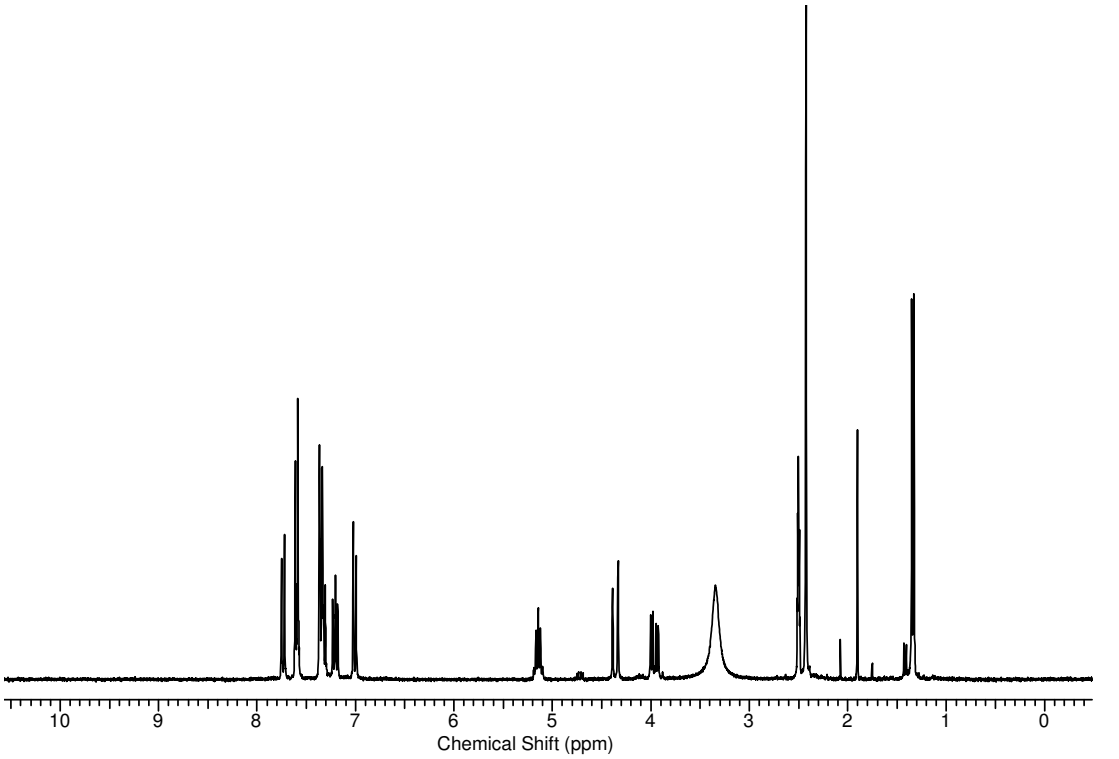


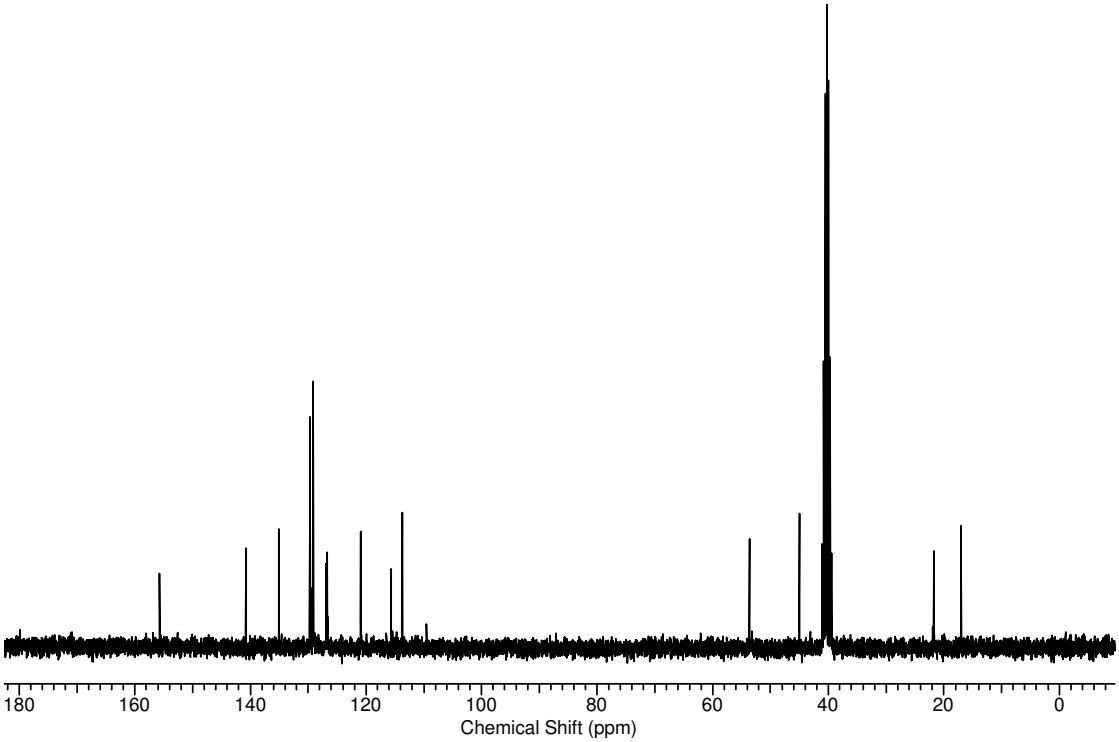
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,4,3)



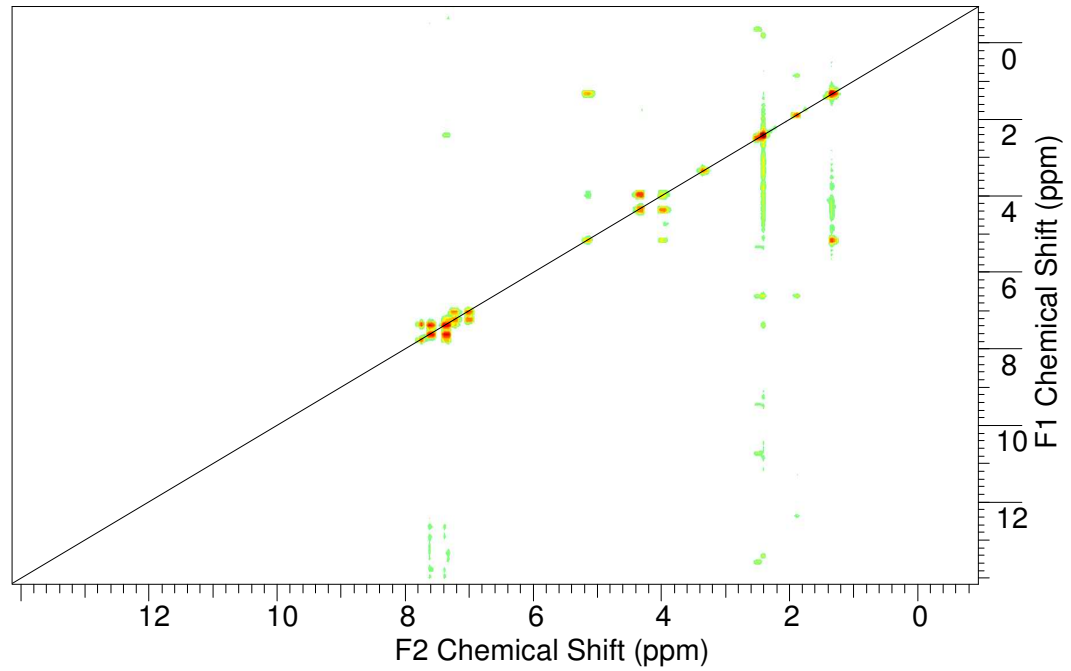


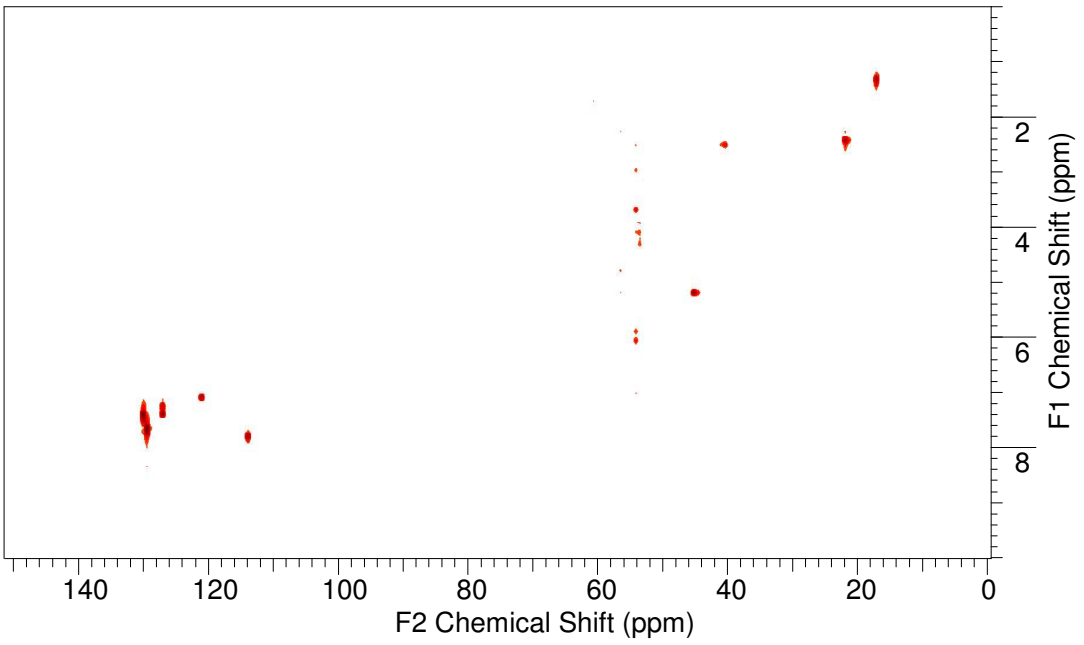
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(2,1,1)



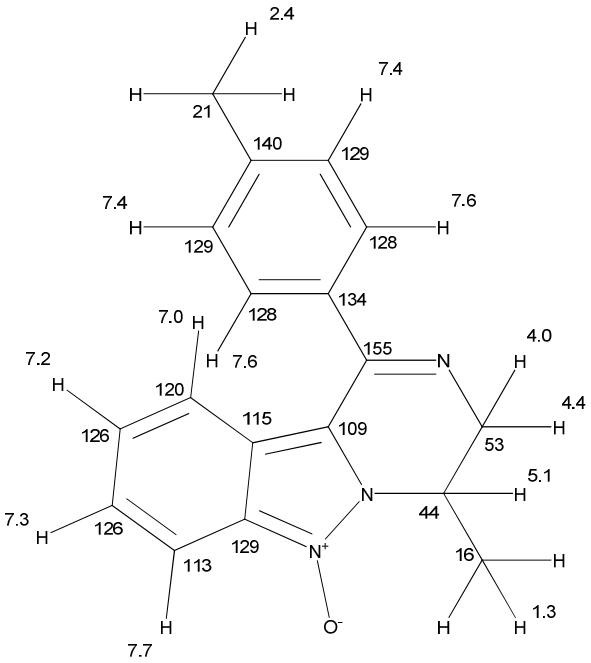


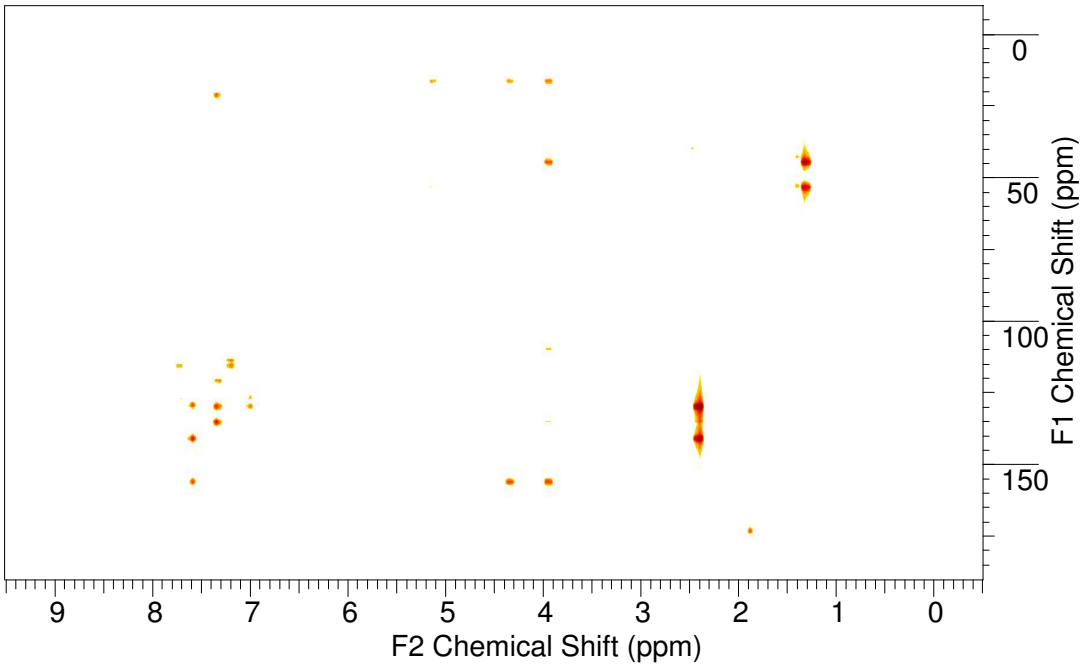
COSY and HETCOR NMR spectra (d_6-DMSO) for compound 7(2,1,1)



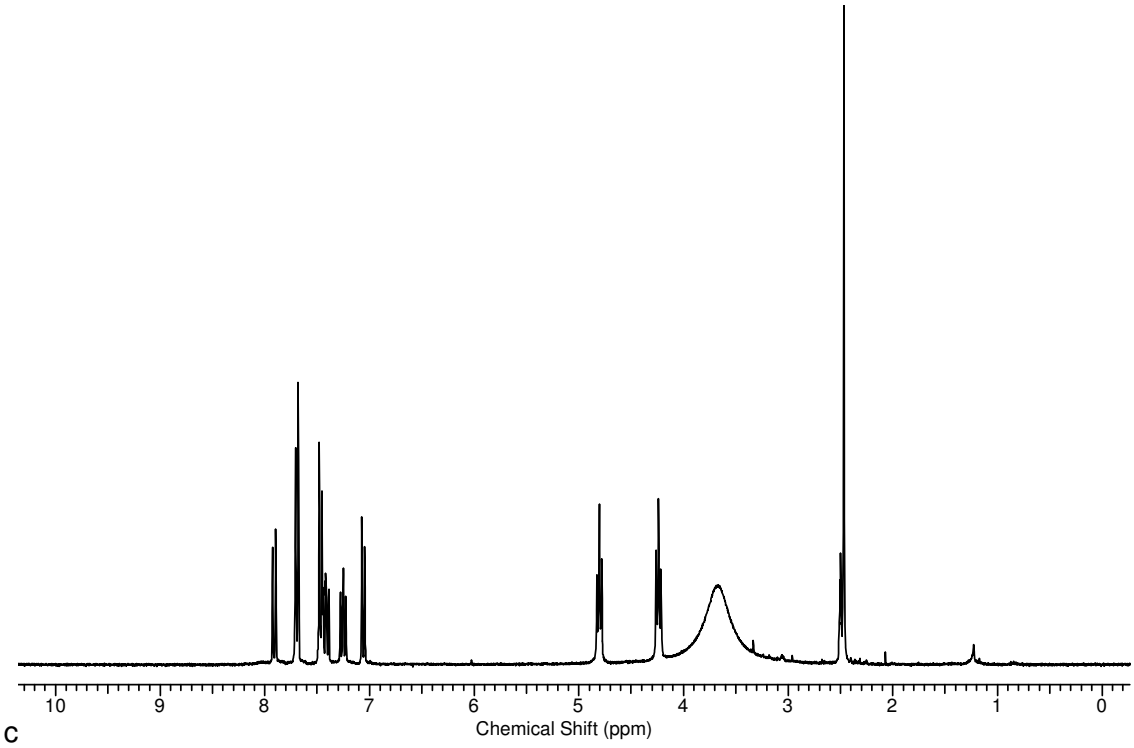


Chemical shifts and gHMBC NMR spectrum (d_6-DMSO) for compound 7(2,1,1)

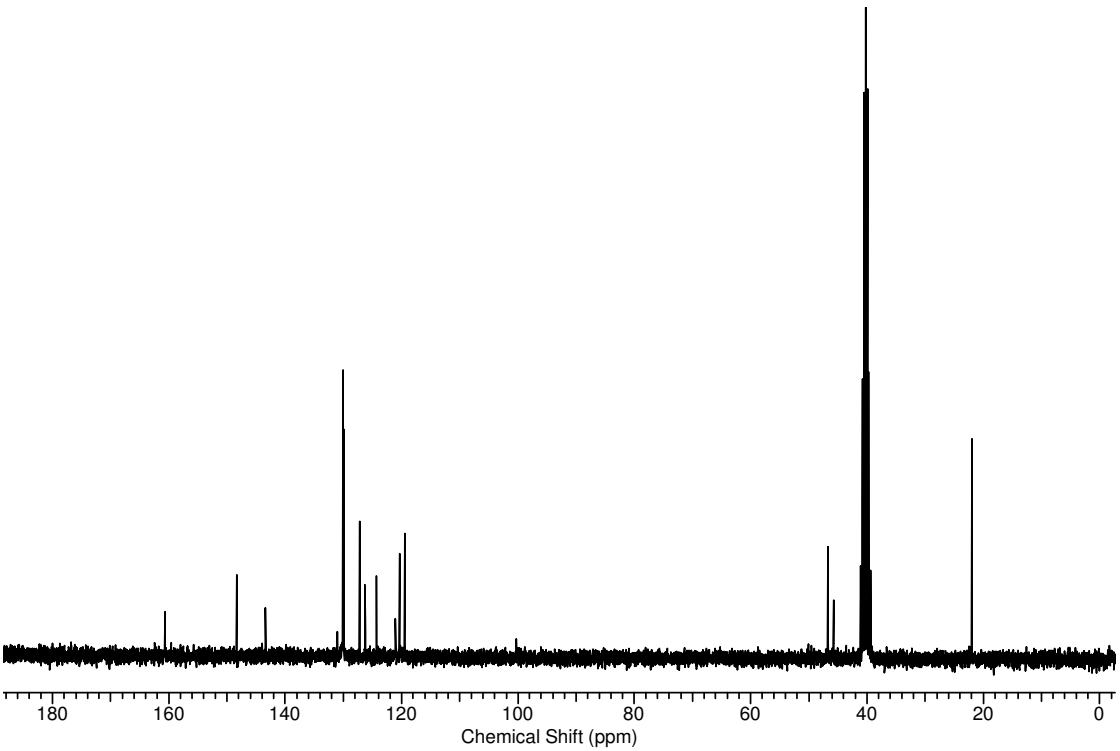




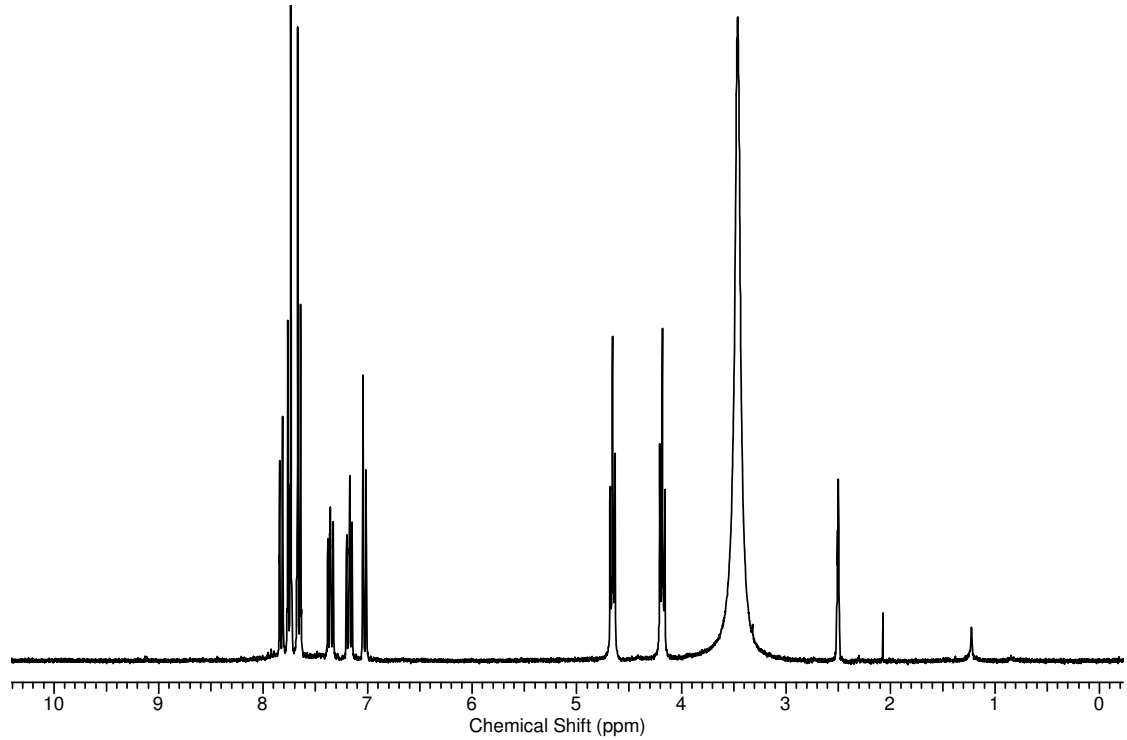
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,1,1)

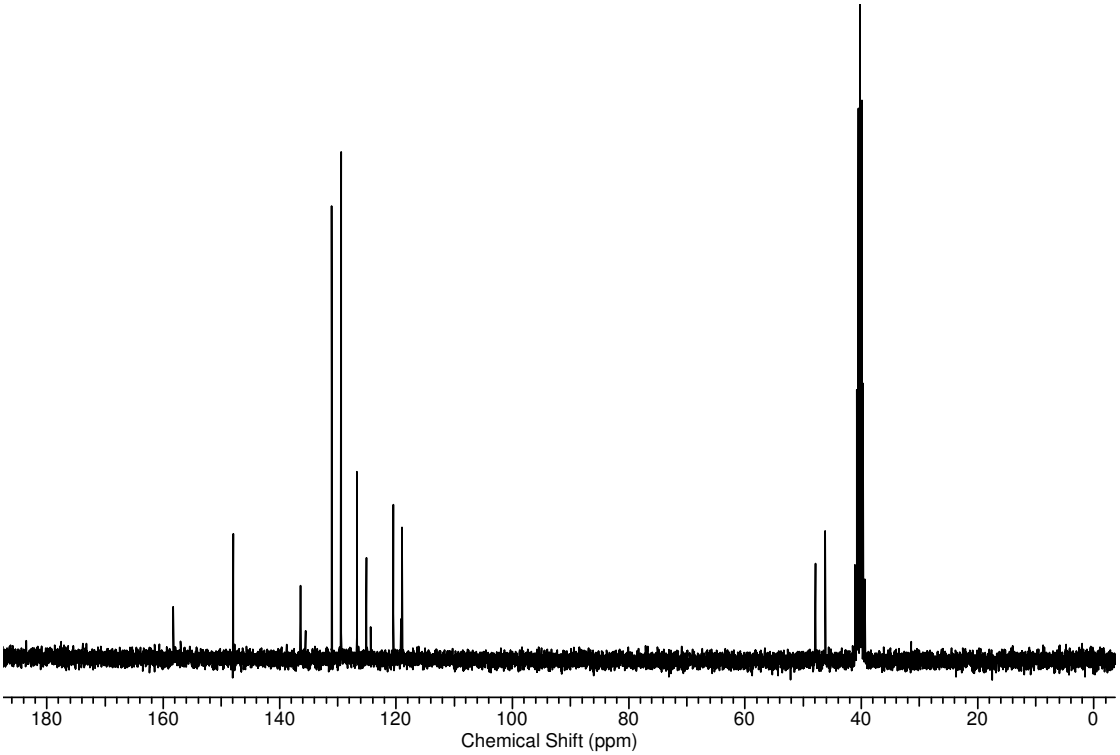


C

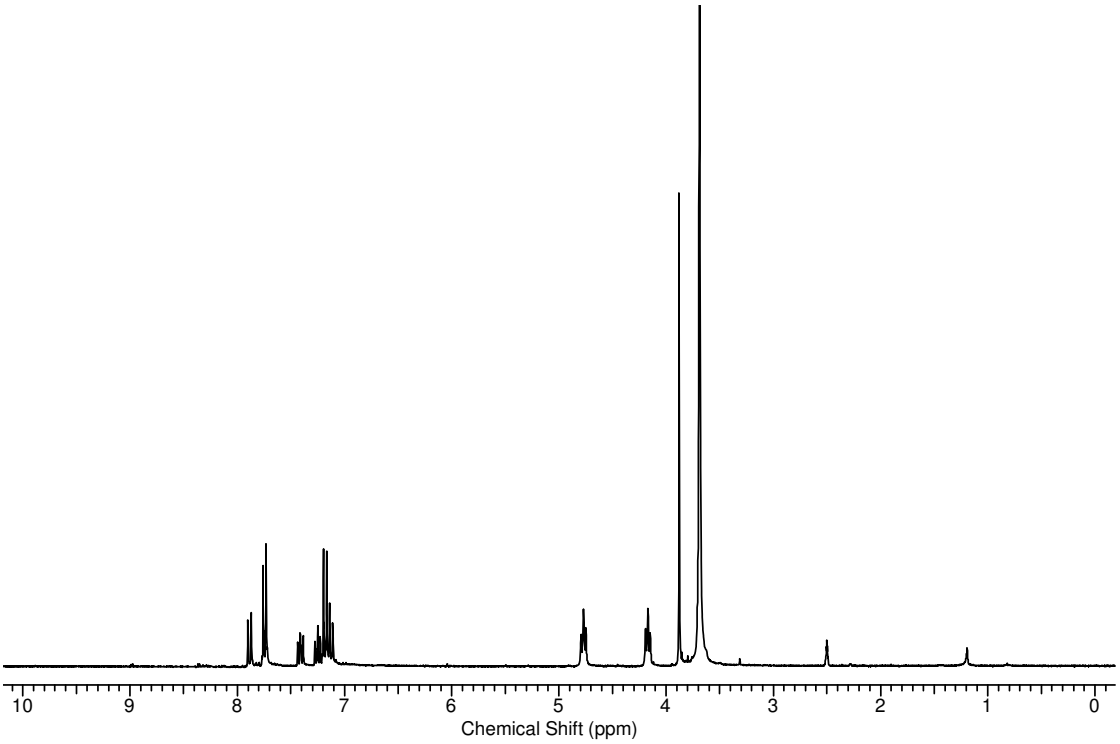


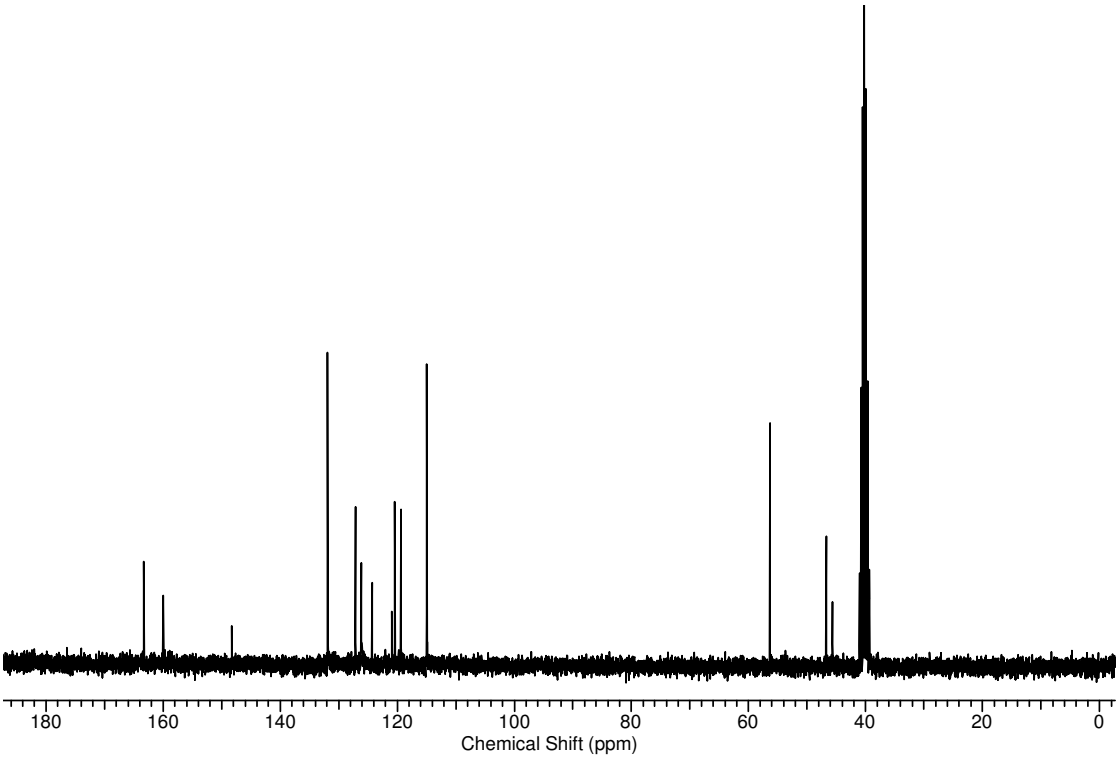
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,1,2)



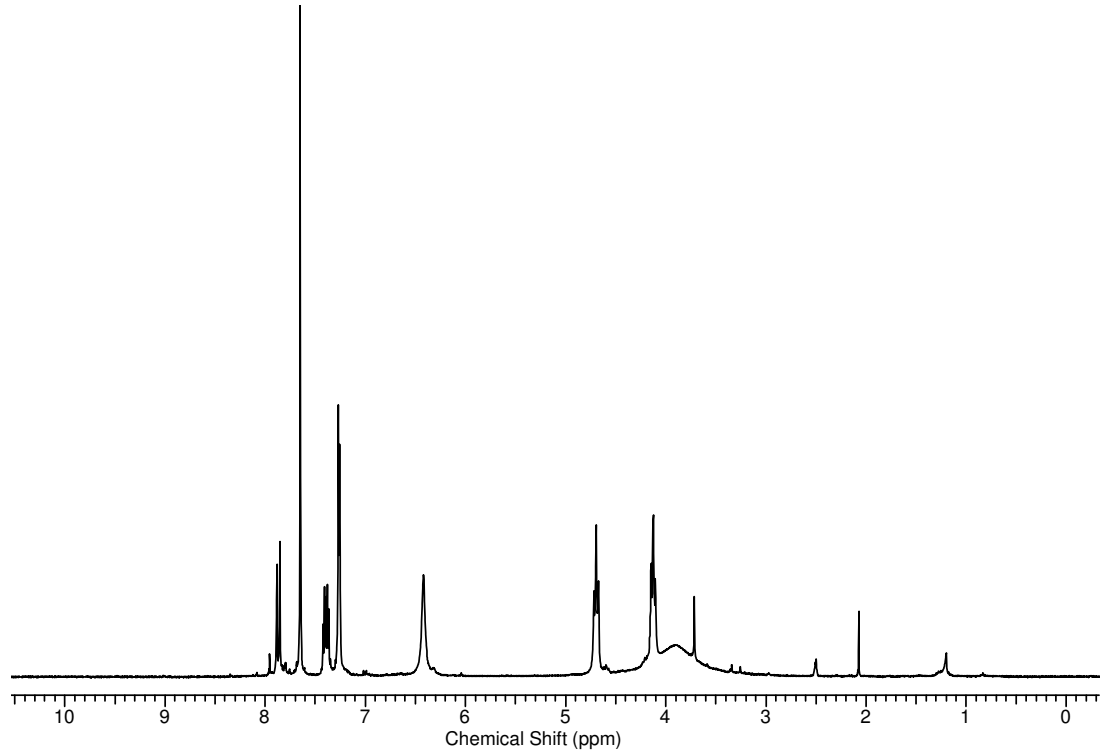


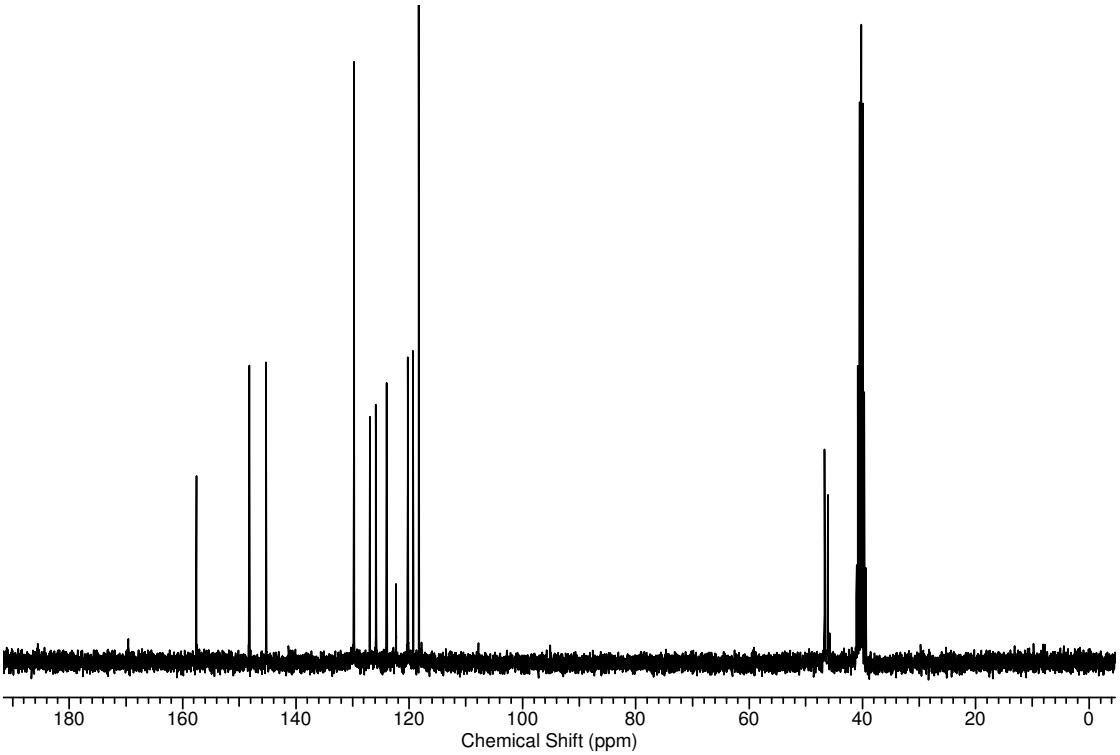
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,1,3)



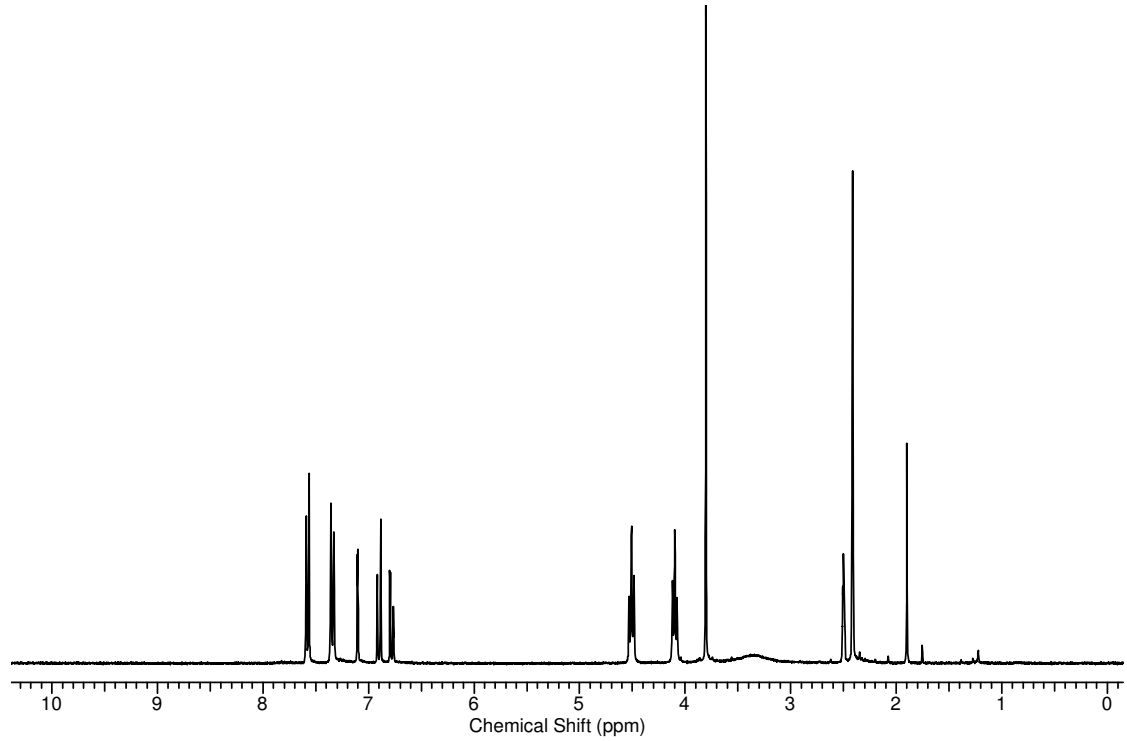


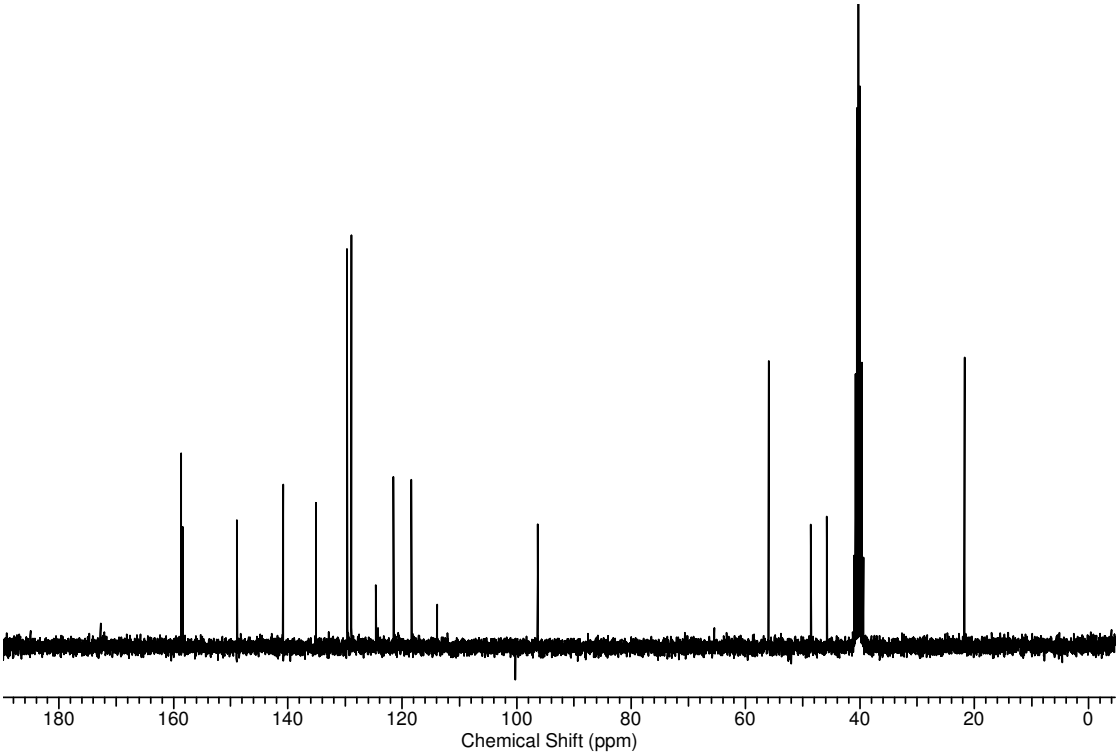
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,1,4)



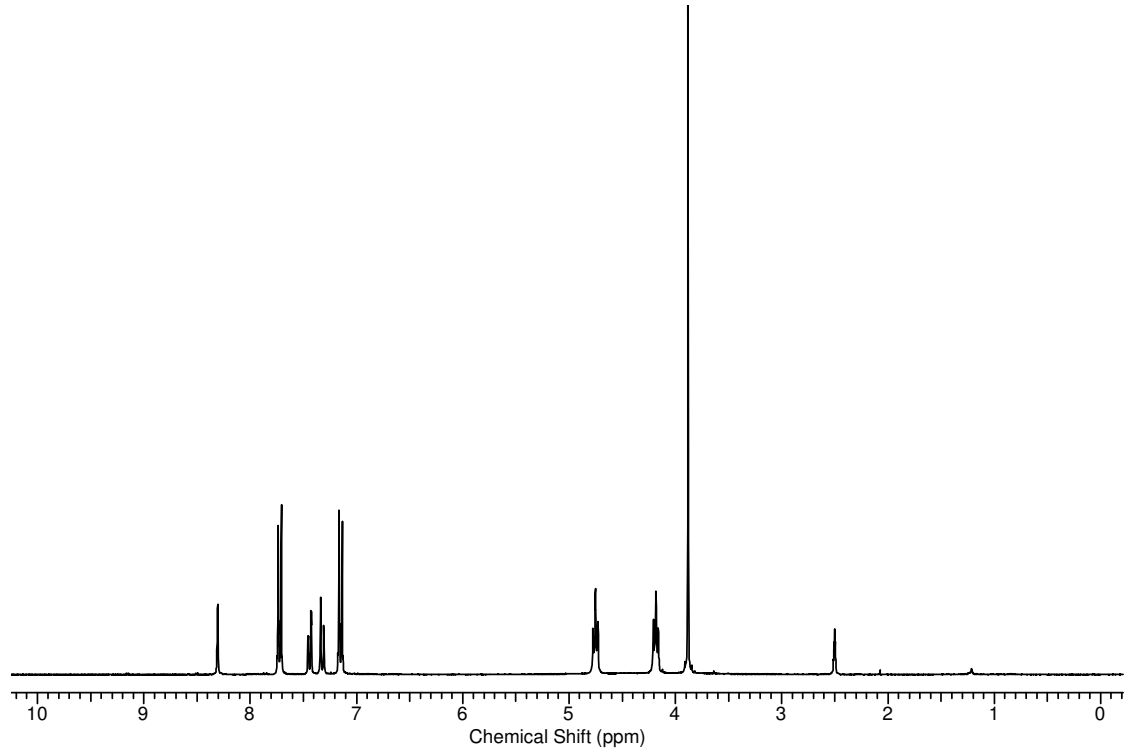


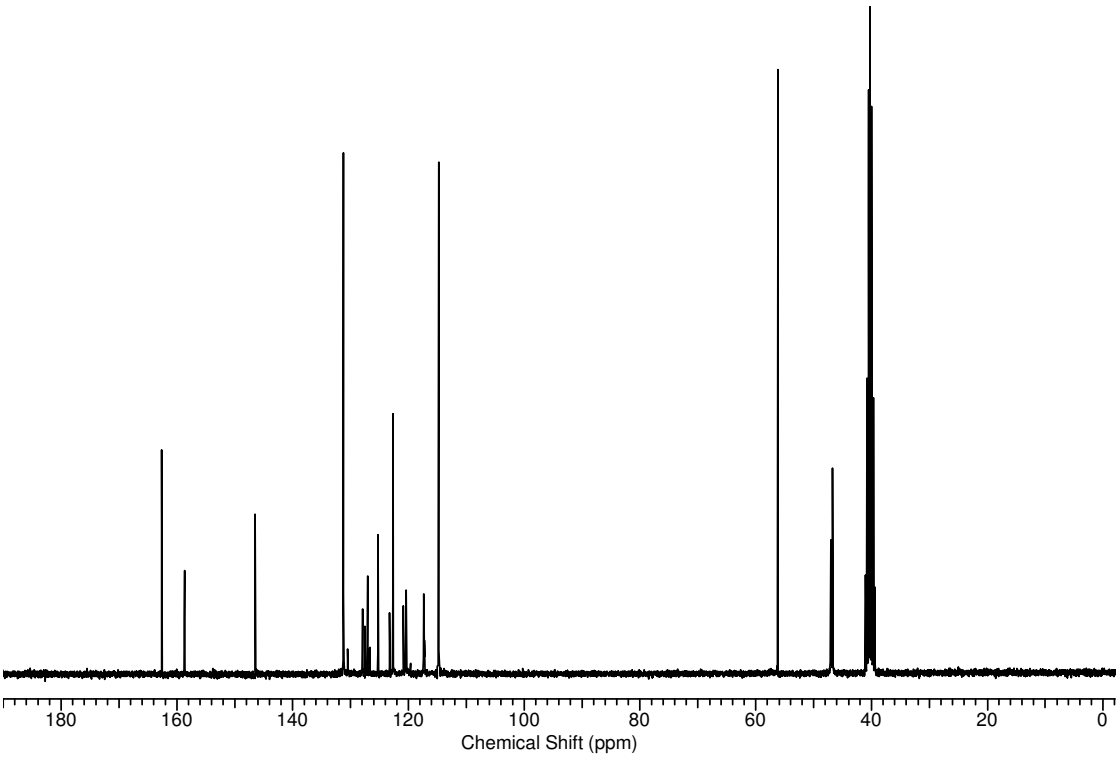
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,2,1)



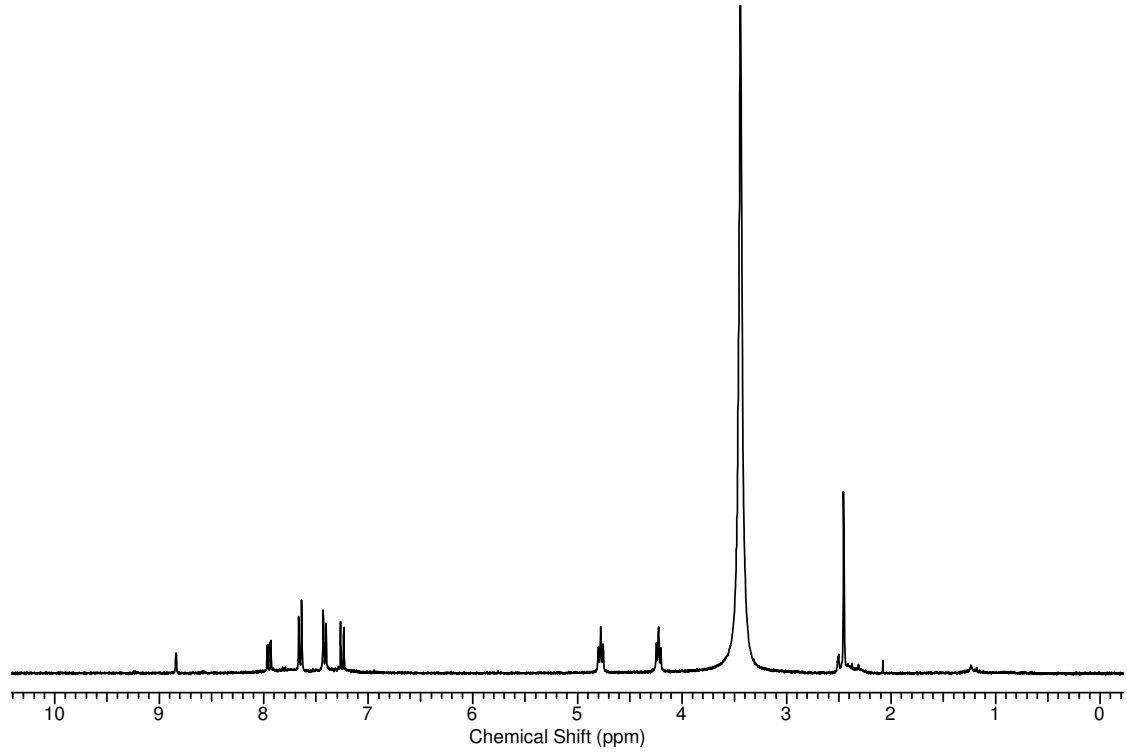


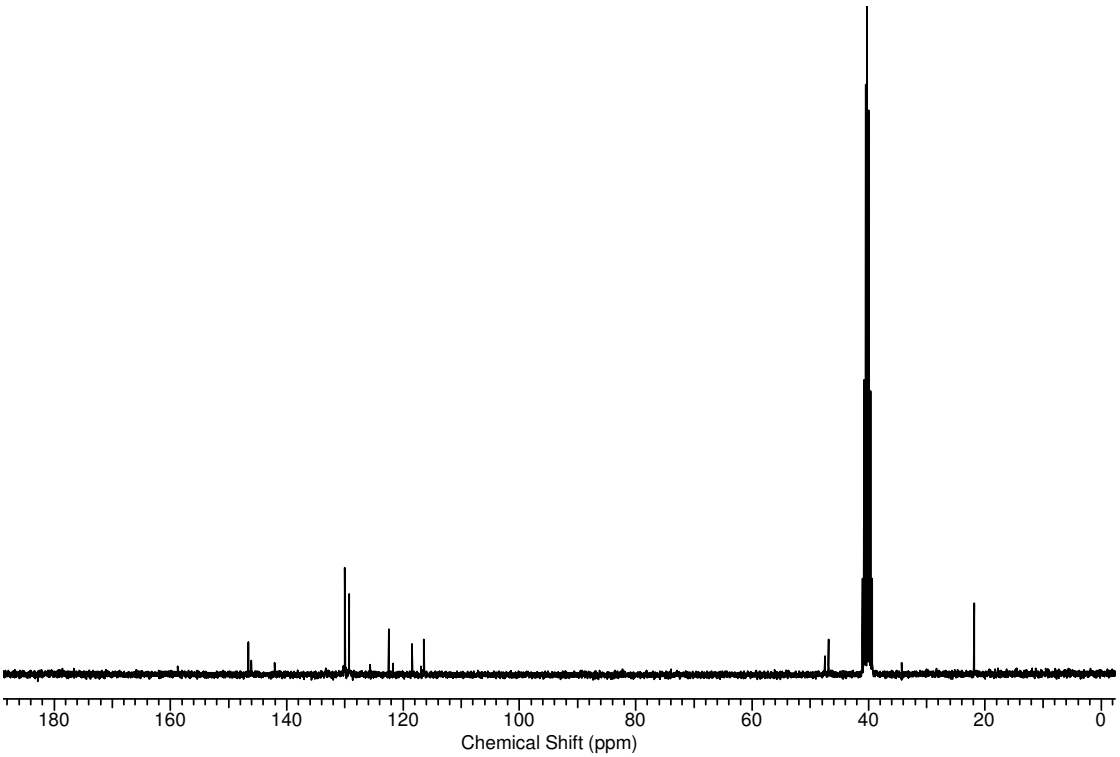
^{1}H and ^{13}C NMR spectra (d6-DMSO) for compound 8(1,3,3)





^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,4,1)





^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(1,1,5)