Supporting Information

Multiplicity of Diverse Heterocycles from Polymer-Supported α-Acylamino Ketones

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Material and Methods

Solvents were used without further purification. The Rink amide resin (100-200 mesh, 1% DVB, 0.75 mmol/g), aminomethyl resin (100-200 mesh, 1% DVB, 0.9 mmol/g) and Wang resin (100-200 mesh, 1% DVB, 1.0 mmol/g) were used. Synthesis was carried out on Domino Blocks (www.torviq.com) in disposable polypropylene reaction vessels.

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.

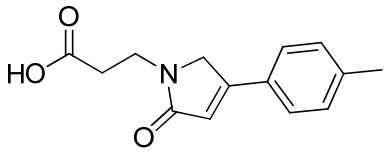
The LC/MS analyses were carried out using a 3 x 50 mm C18 reverse phase column. Mobile phases: 10 mM ammonium acetate in HPLC grade water (A) and HPLC grade acetonitrile (B), gradient of 5% to 80% of B in A, over 10 min at 0.7 mL/min. The MS electrospray source operated at capillary voltage 3.5 kV and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

Purification was carried out on C18 column 19 x 100 mm, 5 µm particles, gradient of acetonitrile in 10 mM aqueous ammonium acetate , 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).

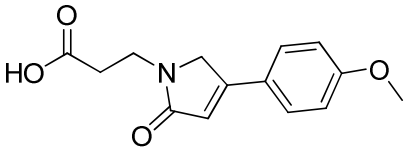
Analytical data of synthetic compounds

3-(2-Oxo-4-p-tolyl-2,3-dihydro-1*H*-pyrrol-1-yl)propanoic acid 5(1,1,1)



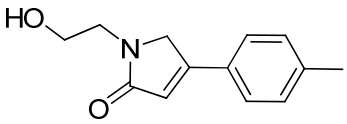
Yield (HPLC purified) 30.8 mg (44%). ESI-MS *m/z* = 246, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.52 (d, *J*=8.0 Hz, 2 H), 7.25 (d, *J*=8.3 Hz, 2 H), 6.48 (s, 1 H), 4.46 (s, 2 H), 3.55 (t, *J*=7.3 Hz, 2 H), 2.40 (t, *J*=7.0 Hz, 2 H), 2.33 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.4, 170.5, 154.6, 139.7, 129.4, 129.1, 125.9, 119.0, 52.1, 38.3, 34.5, 20.9. HRMS (FAB) *m/z* calcd for $C_{14}H_{16}O_3N$ $[M+H]^+$ 246.1130, found 246.1123

3-(4-(4-Methoxyphenyl)-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)propanoic acid 5(1,2,1)



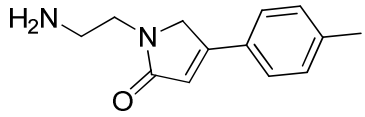
Yield (HPLC purified) 33.9 mg (75%). ESI-MS *m/z* = 262, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{14}H_{16}NO_4$ $[M+H]^+$ 262.1079, found 262.1080

1-(2-Hydroxyethyl)-4-p-tolyl-1*H*-pyrrol-2(5*H*)-one 5(2,1,1)



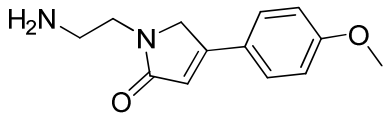
Yield (HPLC purified) 19.2 mg (77%). ESI-MS *m/z* = 218, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.54 (d, *J*=8.3 Hz, 2 H), 7.26 (d, *J*=8.0 Hz, 2 H), 6.51 (s, 1 H), 4.81 (t, *J*=5.4 Hz, 1 H), 4.51 (s, 2 H), 3.56 (q, *J*=5.6 Hz, 2 H), 3.43 (t, *J*=5.7 Hz, 2 H), 2.33 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 170.8, 154.8, 139.7, 129.5, 129.1, 125.9, 119.1, 59.4, 52.8, 44.2, 20.9. HRMS (FAB) *m/z* calcd for $C_{13}H_{16}NO_2$ $[M+H]^+$ 218.1181, found 218.1190

1-(2-Aminoethyl)-4-p-tolyl-1*H*-pyrrol-2(5*H*)-one 5(3,1,1)



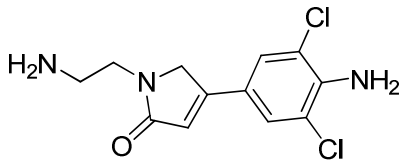
Yield (HPLC purified) 9.0 mg (37%). ESI-MS *m*/z = 217, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.54 (d, *J*=8.1 Hz, 2 H), 7.26 (d, *J*=7.9 Hz, 2 H), 6.51 (s, 1 H), 4.50 (d, *J*=0.9 Hz, 2 H), 3.46 (t, *J*=6.3 Hz, 2 H), 2.84 (t, *J*=6.5 Hz, 2 H), 2.33 (s, 3 H), 1.84 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.4, 172.0, 155.7, 140.5, 130.2, 129.8, 126.7, 119.6, 53.1, 43.5, 22.7. HRMS (FAB) *m/z* calcd for $C_{13}H_{17}N_2O$ $[M+H]^+$ 217.1341, found 217.1338

1-(2-Aminoethyl)-4-(4-methoxyphenyl)-1*H*-pyrrol-2(5*H*)-one 5(3,2,1)



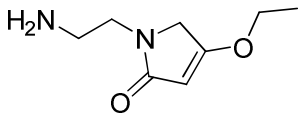
Yield (HPLC purified) 8.2 mg (23%). ESI-MS *m/z* = 233, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.60 (d, *J*=8.8 Hz, 2 H), 7.01 (d, *J*=8.8 Hz, 2 H), 6.45 (s, 1 H), 5.92 (br. s.), 4.48 (s, 2 H), 3.80 (s, 3 H), 3.49 (t, *J*=6.4 Hz, 2 H), 2.89 (t, *J*=6.4 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 171.5, 160.6, 154.8, 127.6, 124.5, 117.5, 114.3, 55.3, 52.3, 42.0. HRMS (FAB) *m/z* calcd for $C_{13}H_{17}N_2O_2$ $[M+H]^+$ 233.1290, found 233.1299

4-(4-Amino-3,5-dichlorophenyl)-1-(2-aminoethyl)-1*H*-pyrrol-2(5*H*)-one 5(3,3,1)



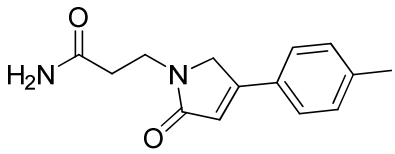
Yield (HPLC purified) 17.9 mg (41%). ESI-MS *m/z* = 286, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.57 (s, 2 H), 6.46 (s, 1 H), 6.02 (br. s.), 4.43 (s, 2 H), 3.42 (t, *J*=6.4 Hz, 2 H), 2.81 (t, *J*=6.5 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 171.2, 153.1, 142.5, 125.9, 120.8, 118.1, 117.6, 52.1, 42.9, 22.5. HRMS (FAB) *m/z* calcd for $C_{12}H_{14}N_3OCl_2$ $[M+H]^+$ 286.0514, found 286.0531

1-(2-Amino-ethyl)-4-ethoxy-1,5-dihydro-pyrrol-2-one 5(3,4,1)



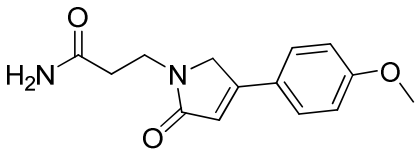
Yield (HPLC purified) 18.0 mg (44%), ESI-MS *m/z* = 171, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 5.14 (s, 1 H), 3.92 - 4.08 (m, 4 H), 3.48 (t, *J*=6.2 Hz, 2 H), 2.95 (t, *J*=6.2 Hz, 2 H), 1.30 (t, *J*=7.0 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.1, 172.1, 94.0, 66.9, 50.4, 39.1, 37.7, 14.0. HRMS (FAB) *m/z* calcd for $C_8H_{15}N_2O_2$ $[M+H]^+$ 171.1134, found 171.1121

3-(2-Oxo-4-p-tolyl-2,5-dihydro-1*H*-pyrrol-1-yl)propanamide 5(4,1,1)



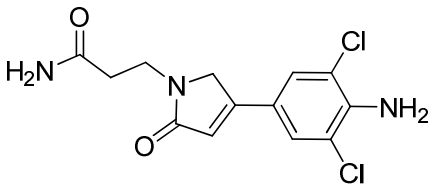
Yield (HPLC purified) 8.7 mg (28%). ESI-MS *m/z* = 245, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.52 (d, *J*=8.3 Hz, 2 H), 7.41 (br. s., 1 H), 7.26 (d, *J*=8.0 Hz, 2 H), 6.87 (br. s., 1 H), 6.50 (s, 1 H), 4.45 (d, *J*=1.4 Hz, 2 H), 3.57 (t, *J*=7.0 Hz, 2 H), 2.31 - 2.41 (m, 5 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.4, 170.6, 154.7, 139.8, 129.5, 129.1, 125.9, 119.0, 52.1, 38.2, 34.3, 21.0. HRMS (FAB) *m/z* calcd for $C_{14}H_{17}N_2O_2$ $[M+H]^+$ 245.1290, found 245.1282

3-(4-(4-Methoxyphenyl)-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)propanamide 5(4,2,1)



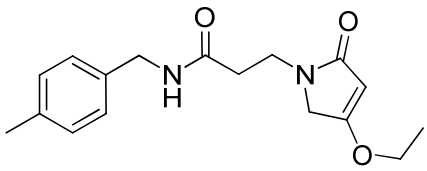
Yield (HPLC purified) 12.7 mg (38%). ESI-MS *m/z* = 261, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.57 (d, *J*=9.1 Hz, 2 H), 7.41 (br. s., 1 H), 7.00 (d, *J*=9.1 Hz, 2 H), 6.86 (br. s., 1 H), 6.42 (s, 1 H), 4.44 (s, 2 H), 3.80 (s, 3 H), 3.57 (t, *J*=7.0 Hz, 2 H), 2.36 (t, *J*=7.0 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.4, 170.8, 160.6, 154.4, 127.6, 124.4, 117.7, 114.3, 55.3, 52.1, 38.2, 34.4.

3-(4-(4-Amino-3,5-dichlorophenyl)-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)propanamide 5(4,3,1)



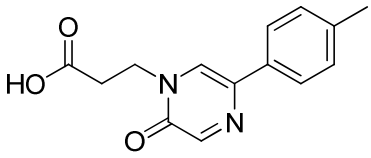
Yield (HPLC purified) 10.6 mg (27%). ESI-MS *m/z* = 314, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.55 (s, 2 H), 7.40 (br. s., 1 H), 6.86 (br. s., 1 H), 6.44 (s, 1 H), 6.01 (s, 2 H), 4.39 (s, 2 H), 3.54 (t, *J*=7.2 Hz, 2 H), 2.34 (t, *J*=7.0 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.4, 170.7, 152.9, 142.5, 125.8, 120.7, 118.1, 117.6, 51.9, 40.4, 34.4.

3-(4-Ethoxy-2-oxo-2,5-dihydro-pyrrol-1-yl)-*N*-(4-methyl-benzyl)-propionamide 5(5,4,1)



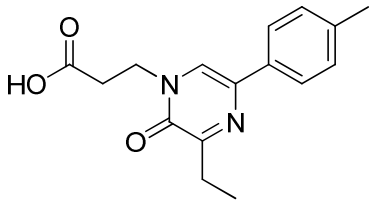
Yield (HPLC purified) 14.4 mg (53%). ESI-MS *m/z* = 303, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.39 (t, *J*=5.9 Hz, 1 H), 7.09 (s, 4 H), 5.07 (s, 1 H), 4.20 (d, *J*=5.9 Hz, 2 H), 3.98 (q, *J*=7.0 Hz, 2 H), 3.86 (s, 2 H), 3.48 (d, *J*=13.9 Hz, 2 H), 2.35 (t, *J*=6.9 Hz, 2 H), 2.26 (s, 3 H), 1.29 (t, *J*=7.1 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.6, 171.2, 170.3, 136.4, 135.8, 128.9, 127.2, 94.1, 66.8, 50.3, 41.8, 37.8, 34.8, 20.7, 14.1. HRMS (FAB) *m/z* calcd for $C_{17}H_{23}N_2O_3$ $[M+H]^+$ 303.1709, found 303.1696

3-(2-Oxo-5-p-tolylpyrazin-1(2*H*)-yl)propanoic acid 7(1,1,1)



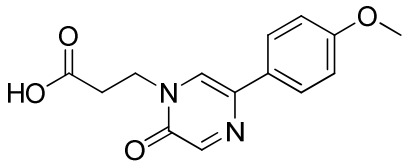
Yield (HPLC purified) 22.1 mg (30%). ESI-MS *m/z* = 259, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.26 (s, 1 H), 8.08 (s, 1 H), 7.71 (d, *J*=8.3 Hz, 2 H), 7.24 (d, *J*=8.0 Hz, 2 H), 4.11 (t, *J*=7.0 Hz, 2 H), 2.70 (t, *J*=7.0 Hz, 2 H), 2.32 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.3, 154.6, 146.9, 136.8, 132.9, 131.6, 129.3, 127.1, 124.3, 45.7, 32.8, 20.7. HRMS (FAB) *m/z* calcd for $C_{14}H_{15}N_2O_3$ $[M+H]^+$ 259.1083, found 259.1058

3-(3-Ethyl-2-oxo-5-p-tolylpyrazin-1(2*H*)-yl)propanoic acid 7(1,1,3)



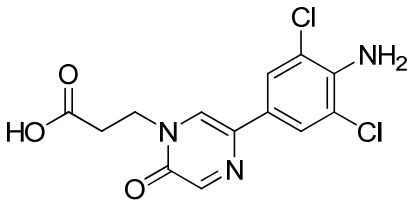
Yield (HPLC purified) 9.7 mg (24%). ESI-MS *m/z* = 287, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.13 (s, 1 H), 7.73 (d, *J*=8.4 Hz, 2 H), 7.22 (d, *J*=7.9 Hz, 2 H), 4.07 (t, *J*=7.1 Hz, 2 H), 2.76 (q, *J*=7.3 Hz, 2 H), 2.51 – 2.54 (m, 2 H), 2.31 (s, 3 H), 1.21 (t, *J*=7.4 Hz, 3 H)

3-(5-(4-Methoxyphenyl)-2-oxopyrazin-1(2*H*)-yl)propanoic acid 7(1,2,1)



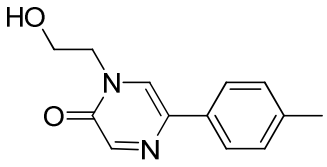
Yield (HPLC purified) 29.4 mg (38%). ESI-MS *m/z* = 275, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.20 (d, *J*=1.1 Hz, 1 H), 8.07 (d, *J*=1.1 Hz, 1 H), 7.74 (d, *J*=8.8 Hz, 2 H), 6.99 (d, *J*=8.8 Hz, 2 H), 4.11 (t, *J*=7.0 Hz, 2 H), 3.78 (s, 3 H), 2.69 (t, *J*=7.0 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.4, 158.9, 154.5, 146.9, 131.7, 128.2, 126.4, 125.8, 114.2, 55.2, 45.7, 32.9. HRMS (FAB) *m/z* calcd for $C_{14}H_{15}N_2O_4$ $[M+H]^+$ 275.0985, found 275.1028

3-(5-(4-Amino-3,5-dichlorophenyl)-2-oxopyrazin-1(2*H*)-yl)propanoic acid 7(1,3,1)



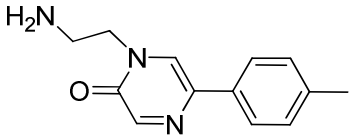
Yield (HPLC purified) 5.1 mg (12%). ESI-MS *m/z* = 328, $[M+H]^+$. HRMS (FAB) *m/z* calcd for $C_{13}H_{11}Cl_2N_3O_3$ $[M^{\bullet}]^+$ 327.0177, found 327.0178

1-(2-Hydroxyethyl)-5-p-tolylpyrazin-2(1*H*)-one 7(2,1,1)



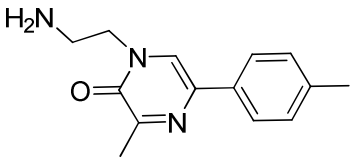
Yield (HPLC purified) 15.8 mg (61%). ESI-MS *m/z* = 231, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.16 (s, 1 H), 8.10 (s, 1 H), 7.72 (d, *J*=8.0 Hz, 2 H), 7.24 (d, *J*=8.0 Hz, 2 H), 4.99 (t, *J*=5.5 Hz, 1 H), 4.02 (t, *J*=5.4 Hz, 2 H), 3.70 (q, *J*=5.5 Hz, 2 H), 2.32 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 154.8, 146.8, 136.7, 132.9, 131.3, 129.3, 127.5, 124.3, 58.0, 51.4, 20.7. HRMS (FAB) *m/z* calcd for $C_{13}H_{15}N_2O_2$ $[M+H]^+$ 231.1134, found 231.1135

1-(2-Aminoethyl)-5-p-tolylpyrazin-2(1*H*)-one 7(3,1,1)



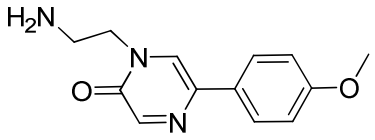
Yield (HPLC purified) 14.4 mg (40%). ESI-MS *m/z* = 230, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.21 (s, 1 H), 8.09 (s, 1 H), 7.73 (d, *J*=8.0 Hz, 2 H), 7.24 (d, *J*=8.0 Hz, 2 H), 4.53 (br. s.), 3.95 (t, *J*=6.1 Hz, 2 H), 2.90 (t, *J*=6.1 Hz, 2 H), 2.32 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 154.9, 146.9, 136.7, 133.0, 131.4, 129.3, 127.4, 124.3, 51.4, 39.6, 20.7. HRMS (FAB) *m/z* calcd for $C_{13}H_{16}N_3O$ $[M+H]^+$ 230.1293, found 230.1291

1-(2-Aminoethyl)-3-methyl-5-p-tolylpyrazin-2(1*H*)-one 7(3,1,2)



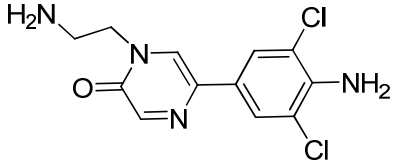
Yield (HPLC purified) 2.0 mg (12%). ESI-MS *m/z* = 244, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.06 (s, 1 H), 7.72 (d, *J*=8.4 Hz, 2 H), 7.23 (d, *J*=7.9 Hz, 2 H), 3.92 (t, *J*=6.2 Hz, 2 H), 2.89 (t, *J*=6.0 Hz, 2 H), 2.38 (s, 3 H), 2.32 (s, 3 H). HRMS (FAB) *m/z* calcd for $C_{14}H_{18}N_3O$ $[M+H]^+$ 244.1450, found 244.1467

1-(2-Aminoethyl)-5-(4-methoxyphenyl)pyrazin-2(1*H*)-one 7(3,2,1)



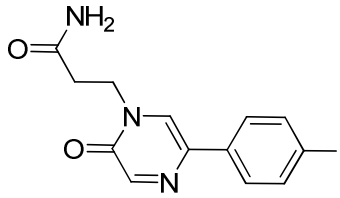
Yield (HPLC purified) 19.5 mg (52%). ESI-MS *m/z* = 246, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.15 (s, 1 H), 8.09 (d, *J*=1.1 Hz, 1 H), 7.73 - 7.79 (m, 2 H), 6.96 - 7.03 (m, 2 H), 6.12 (br. s.), 3.98 (t, *J*=6.1 Hz, 2 H), 3.78 (s, 3 H), 2.96 (t, *J*=6.1 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 158.9, 154.9, 146.9, 131.5, 128.3, 126.6, 125.8, 114.1, 55.2, 50.6.

5-(4-Amino-3,5-dichlorophenyl)-1-(2-aminoethyl)pyrazin-2(1*H*)-one 7(3,3,1)



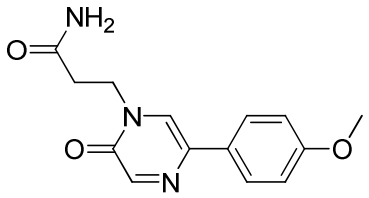
Yield (HPLC purified) 28.2 mg (62%). ESI-MS *m/z* = 299, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.22 (s, 1 H), 8.04 (s, 1 H), 7.71 (s, 2 H), 6.24 (br. s.), 5.65 (s, 2 H), 3.95 (t, *J*=6.1 Hz, 2 H), 2.93 (t, *J*=6.1 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 154.8, 146.9, 140.4, 129.7, 126.8, 125.0, 123.9, 118.6, 50.8, 39.2. HRMS (FAB) *m/z* calcd for $C_{12}H_{13}N_4OCl_2$ $[M+H]^+$ 299.0466, found 299.0483

3-(2-Oxo-5-p-tolylpyrazin-1(2*H*)-yl)propanamide 7(4,1,1)



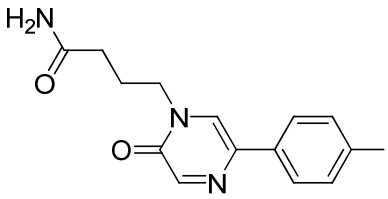
Yield (HPLC purified) 6.8 mg (21%). ESI-MS *m/z* = 258, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.18 (s, 1 H), 8.09 (d, *J*=1.1 Hz, 1 H), 7.70 (d, *J*=8.3 Hz, 2 H), 7.43 (br. s., 1 H), 7.25 (d, *J*=8.0 Hz, 2 H), 6.95 (br. s., 1 H), 4.12 (t, *J*=6.9 Hz, 2 H), 2.59 (t, *J*=6.9 Hz, 2 H), 2.32 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 171.4, 154.6, 146.9, 136.8, 131.6, 129.3, 127.2, 124.3, 45.9, 33.2, 20.7. HRMS (FAB) *m/z* calcd for $C_{14}H_{16}N_3O_2$ $[M+H]^+$ 258.1243, found 258.1246

3-(5-(4-Methoxyphenyl)-2-oxopyrazin-1(2*H*)-yl)propanamide 7(4,2,1)



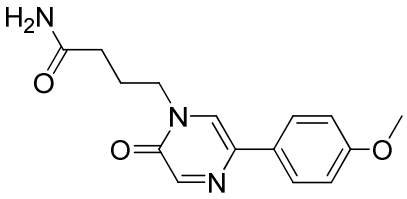
Yield (HPLC purified) 12.4 mg (36%). ESI-MS *m/z* = 274, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.13 (s, 1 H), 8.08 (s, 1 H), 7.74 (d, *J*=8.8 Hz, 2 H), 7.43 (br. s., 1 H), 7.00 (d, *J*=8.8 Hz, 2 H), 6.95 (br. s., 1 H), 4.11 (t, *J*=6.9 Hz, 2 H), 3.78 (s, 3 H), 2.59 (t, *J*=6.9 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 171.4, 158.9, 154.5, 146.9, 131.6, 128.1, 126.5, 125.8, 114.2, 55.2, 45.8, 33.2. HRMS (FAB) *m/z* calcd for $C_{14}H_{16}N_3O_3$ $[M+H]^+$ 274.1192, found 274.1207

4-(2-Oxo-5-p-tolylpyrazin-1(2*H*)-yl)butanamide 7(6,1,1)



Yield (HPLC purified) 10.9 mg (39%). ESI-MS *m/z* = 272, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.24 (d, *J*=1.1 Hz, 1 H), 8.10 (d, *J*=1.1 Hz, 1 H), 7.74 (d, *J*=8.3 Hz, 2 H), 7.32 (br. s., 1 H), 7.24 (d, *J*=8.0 Hz, 2 H), 6.78 (br. s., 1 H), 3.95 (t, *J*=7.0 Hz, 2 H), 2.32 (s, 3 H), 2.11 (t, *J*=7.7 Hz, 2 H), 1.87 - 1.99 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.2, 154.7, 147.1, 136.8, 132.8, 131.9, 129.3, 126.5, 124.4, 48.4, 31.9, 24.2, 20.7. HRMS (FAB) *m/z* calcd for $C_{15}H_{17}N_3O_2$ $[M^{\bullet}]^+$ 271.1321, found 271.1340

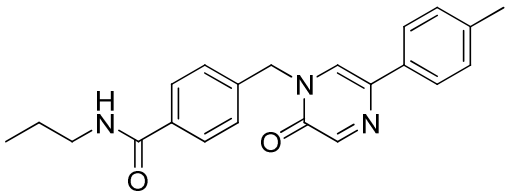
4-(5-(4-Methoxyphenyl)-2-oxopyrazin-1(2*H*)-yl)butanamide 7(6,2,1)



Yield (HPLC purified) 12.4 mg (42%). ESI-MS *m/z* = 288, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.18 (d, *J*=0.8 Hz, 1 H), 8.09 (d, *J*=0.8 Hz, 1 H), 7.78 (d, *J*=8.8 Hz, 2 H), 7.32 (br. s., 1 H), 7.00 (d, *J*=8.8 Hz, 2 H), 6.79 (br. s., 1 H), 3.94 (t, *J*=7.0 Hz, 2 H), 3.78 (s, 3 H), 2.10 (t,

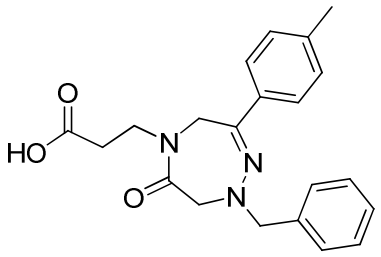
J=7.5 Hz, 2 H), 1.87 - 1.99 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.3, 158.9, 154.6, 147.1, 131.9, 128.2, 125.8, 114.1, 55.2, 48.4, 31.9, 24.2. HRMS (FAB) *m/z* calcd for $C_{15}H_{18}N_3O_3$ $[M+H]^+$ 288.1348, found 288.1325

4-((2-Oxo-5-p-tolylpyrazin-1(2*H*)-yl)methyl)-*N*-propylbenzamide 7(7,1,1)



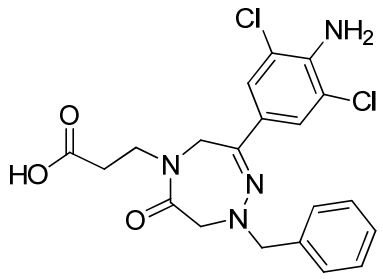
Yield (HPLC purified) 6.4 mg (11%). ESI-MS *m/z* = 362, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.39 - 8.47 (m, 2 H), 8.16 (d, *J*=0.7 Hz, 1 H), 7.81 (d, *J*=8.1 Hz, 2 H), 7.74 (d, *J*=8.1 Hz, 2 H), 7.46 (d, *J*=8.1 Hz, 2 H), 7.25 (d, *J*=8.4 Hz, 2 H), 5.19 (s, 2 H), 3.15 - 3.24 (m, 2 H), 2.32 (s, 3 H), 1.51 (tq, *J*=7.4, 7.2 Hz, 2 H), 0.86 (t, *J*=7.4 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 165.8, 154.6, 147.7, 138.9, 137.0, 134.3, 132.6, 132.1, 129.3, 127.8, 127.5, 126.4, 124.4, 51.6, 40.9, 22.4, 20.7, 11.4. HRMS (FAB) *m/z* calcd for $C_{22}H_{23}N_3O_2$ $[M^{\bullet}]^+$ 361.1790, found 361.1786

3-(1-Benzyl-6-oxo-3-p-tolyl-1*H*-1,2,5-triazepin-5(4*H*,6*H*,7*H*)-yl)propanoic acid 9(1,1,1)



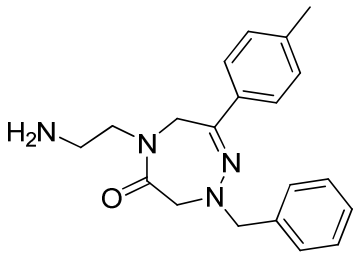
Yield (HPLC purified) 9.7 mg (19%). ESI-MS *m/z* = 366, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.62 (d, *J*=8.4 Hz, 2 H), 7.23 - 7.38 (m, 5 H), 7.20 (d, *J*=8.6 Hz, 2 H), 4.59 (s, 2 H), 4.23 (s, 2 H), 3.69 (s, 2 H), 3.60 (t, *J*=7.4 Hz, 2 H), 2.37 (t, *J*=7.4 Hz, 2 H), 2.30 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 173.0, 167.5, 153.5, 138.9, 138.0, 133.3, 129.1, 128.8, 128.2, 127.1, 125.9, 63.0, 58.5, 45.2, 44.6, 33.3, 20.8. HRMS (FAB) *m/z* calcd for $C_{21}H_{24}N_3O_3$ $[M+H]^+$ 366.1818, found 366.1840

3-(3-(4-Amino-3,5-dichlorophenyl)-1-benzyl-6-oxo-1*H*-1,2,5-triazepin-5(4*H*,6*H*,7*H*)-yl)propanoic acid 9(1,4,1)



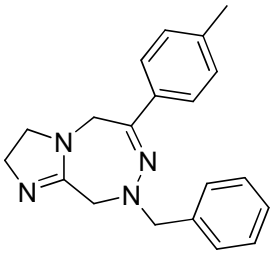
Yield (HPLC purified) 17.7 mg (25%). ESI-MS *m/z* = 435, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.62 (s, 2 H), 7.21 - 7.37 (m, 5 H), 5.86 (s, 2 H), 4.55 (s, 2 H), 4.22 (s, 2 H), 3.67 (s, 2 H), 3.60 (t, *J*=7.2 Hz, 2 H), 2.42 (t, *J*=7.2 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.8, 167.7, 150.8, 142.0, 138.0, 128.7, 128.2, 127.1, 125.6, 124.8, 118.0, 63.0, 58.4, 44.8, 44.2, 32.6.

5-(2-Aminoethyl)-1-benzyl-3-p-tolyl-4,5-dihydro-1*H*-1,2,5-triazepin-6(7*H*)-one 9(3,1,1)



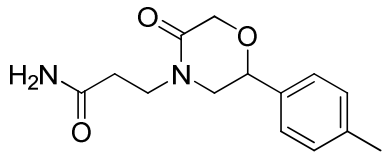
Yield (HPLC purified) 7.2 mg (18%). ESI-MS *m/z* = 337, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.63 (d, *J*=8.3 Hz, 2 H), 7.23 - 7.39 (m, 5 H), 7.20 (d, *J*=8.3 Hz, 2 H), 4.60 (s, 2 H), 4.25 (s, 2 H), 3.72 (s, 2 H), 3.45 (t, *J*=6.6 Hz, 2 H), 2.66 (t, *J*=6.6 Hz, 2 H), 2.31 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.3, 167.7, 153.0, 138.9, 138.0, 133.4, 129.1, 128.8, 128.2, 127.1, 125.9, 63.0, 58.4, 50.1, 45.4, 20.8.

8-Benzyl-6-p-tolyl-3,5,8,9-tetrahydro-2*H*-imidazo[2,1-*d*][1,2,5]triazepine 13(10,1,1)



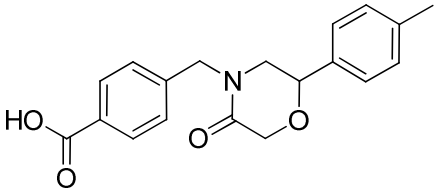
Yield (HPLC purified) 2.4 mg (yield not calculated due to HPLC malfunction). ESI-MS *m/z* = 319, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.66 (d, *J*=8.0 Hz, 2 H), 7.31 - 7.43 (m, 5 H), 7.25 (d, *J*=7.7 Hz, 2 H), 4.69 (s, 2 H), 4.28 (s, 2 H), 4.00 - 4.13 (m, 4 H), 3.82 (t, *J*=10.4 Hz, 2 H), 2.33 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 165.7, 157.9, 140.3, 137.3, 132.2, 129.1, 129.0, 128.4, 127.4, 126.8, 63.0, 51.8, 50.0, 43.9, 43.5, 20.9. HRMS (FAB) *m/z* calcd for $C_{20}H_{23}N_4$ $[M+H]^+$ 319.1923, found 319.1917

3-(3-Oxo-6-p-tolyl-2,3-dihydro-[1,4]oxazin-4-yl)-propionamide 15(4,1,1)



Yield (HPLC purified) 6.4 mg (23%). ESI-MS *m/z* = 263, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.40 (br. s., 1 H), 7.25 - 7.31 (m, 2 H), 7.16 - 7.22 (m, 2 H), 6.87 (br. s., 1 H), 4.80 (dd, *J*=9.7, 3.9 Hz, 1 H), 4.21 (s, 2 H), 3.54 - 3.66 (m, 1 H), 3.41 - 3.48 (m, 3 H), 2.35 (t, *J*=7.2 Hz, 2 H), 2.30 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 172.5, 165.6, 137.3, 135.4, 128.9, 126.0, 74.5, 67.4, 52.3, 42.8, 33.1, 20.7. HRMS (FAB) *m/z* calcd for $C_{14}H_{19}N_2O_3$ $[M+H]^+$ 263.1396, found 263.1409

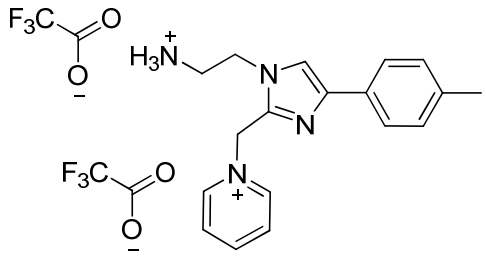
4-((5-Oxo-2-p-tolylmorpholino)methyl)benzoic acid 15(8,1,1)



Yield (HPLC purified) 4.9 mg (22%). ESI-MS *m/z* = 326, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.89 (d, *J*=8.3 Hz, 2 H), 7.34 (d, *J*=8.3 Hz, 2 H), 7.24 (d, *J*=8.0 Hz, 2 H), 7.15 (d, *J*=7.7

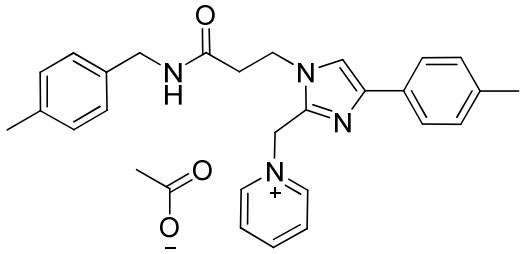
Hz, 2 H), 4.90 (dd, *J*=9.7, 3.6 Hz, 1 H), 4.67 (d, *J*=15.2 Hz, 1 H), 4.56 (d, *J*=15.2 Hz, 1 H), 4.34 (s, 2 H), 3.33 - 3.41 (m, 2 H), 2.27 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 167.8, 166.3, 140.7, 137.6, 135.3, 129.8, 129.1, 127.8, 126.2, 74.4, 67.6, 51.9, 48.7, 20.9. HRMS (FAB) *m/z* calcd for $C_{19}H_{20}NO_4$ $[M+H]^+$ 326.1392, found 326.1390

1-((1-(2-Ammonioethyl)-4-p-tolyl-1*H*-imidazol-2-yl)methyl)pyridinium 2,2,2-trifluoroacetate 19(3,1,4)



Yield (HPLC purified) 4.2 mg (16%). ESI-MS *m/z* = 293, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 9.14 (d, *J*=5.5 Hz, 2 H), 8.71 (t, *J*=7.9 Hz, 1 H), 8.19 - 8.35 (m, 2 H), 8.11 (br. s., 3 H), 7.80 (s, 1 H), 7.53 (d, *J*=8.1 Hz, 2 H), 7.15 (d, *J*=7.9 Hz, 2 H), 6.04 (s, 2 H), 4.34 (t, *J*=6.3 Hz, 2 H), 3.24 - 3.38 (m, 2 H), 2.27 (s, 3 H). HRMS (FAB) *m/z* calcd for $C_{18}H_{21}N_4$ $[M+H]^+$ 293.1766.1042, found 293.1762

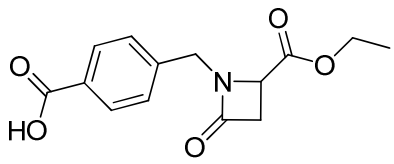
1-((1-(3-(4-Methylbenzylamino)-3-oxopropyl)-4-p-tolyl-1*H*-imidazol-2-yl)methyl)pyridinium acetate 19(5,1,4)



Yield (HPLC purified) 11.6 mg (29%). ESI-MS *m/z* = 425, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 9.11 (d, *J*=6.7 Hz, 2 H), 8.73 (t, *J*=5.6 Hz, 1 H), 8.61 (t, *J*=7.8 Hz, 1 H), 8.09 (t, *J*=7.5 Hz, 2 H), 7.73 (s, 1 H), 7.54 (d, *J*=8.1 Hz, 2 H), 7.15 (d, *J*=7.9 Hz, 2 H), 6.88 (d, *J*=8.1 Hz, 2 H), 6.83 (d, *J*=8.1 Hz, 2 H), 6.07 (s, 2 H), 4.36 (t, *J*=6.2 Hz, 2 H), 4.16 (d, *J*=6.0 Hz, 2 H), 2.78 (t, *J*=6.1 Hz, 2 H), 2.28 (s, 3 H), 2.15 (s, 3 H), 1.77 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-

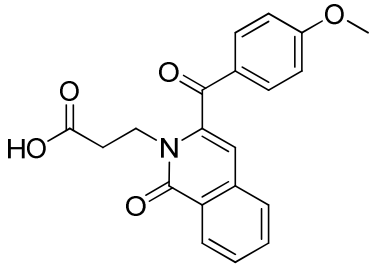
d_6) δ: 173.0, 169.6, 146.1, 145.5, 140.5, 140.3, 136.0, 135.8, 135.6, 129.1, 128.9, 128.8, 127.8, 126.7, 124.2, 117.1, 55.3, 42.1, 41.7, 36.1, 22.7, 20.8, 20.6. HRMS (FAB) *m/z* calcd for $C_{27}H_{29}N_4O$ $[M+H]^+$ 425.2341, found 425.2358

1-(4-Carboxy-benzyl)-4-oxo-azetidine-2-carboxylic acid ethyl ester 21(8,4,1)



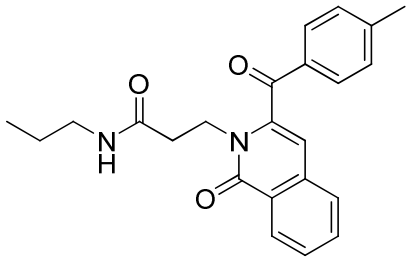
Yield (HPLC purified) 4.4 mg (23%). ESI-MS *m/z* = 278, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.91 (d, *J*=8.0 Hz, 2 H), 7.39 (d, *J*=8.0 Hz, 2 H), 4.60 (d, *J*=16.0 Hz, 1 H), 4.30 (d, *J*=16.0 Hz, 1 H), 4.14 (dd, *J*=5.8, 2.5 Hz, 1 H), 4.06 (q, *J*=7.0 Hz, 2 H), 3.28 (d, *J*=5.5 Hz, 1 H), 2.97 (dd, *J*=14.4, 2.2 Hz, 1 H), 1.13 (t, *J*=7.2 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 170.4, 167.1, 165.9, 140.9, 129.9, 129.5, 128.1, 61.0, 50.5, 44.9, 41.7, 13.8. HRMS (FAB) *m/z* calcd for $C_{14}H_{16}NO_5$ $[M+H]^+$ 278.1028, found 278.1040

3-(3-(4-Methoxybenzoyl)-1-oxoisoquinolin-2(1*H*)-yl)propanoic acid 23(1,2,5)



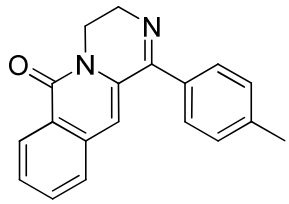
Yield (HPLC purified) 3.0 mg (5%). ESI-MS *m/z* = 352, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.29 (d, *J*=7.5 Hz, 1 H), 7.99 (d, *J*=9.1 Hz, 2 H), 7.75 - 7.79 (m, 2 H), 7.65 (ddd, *J*=8.4, 4.7, 3.5 Hz, 1 H), 7.14 (d, *J*=8.8 Hz, 2 H), 6.87 (s, 1 H), 4.17 (t, *J*=7.3 Hz, 2 H), 3.89 (s, 3 H), 2.69 (t, *J*=7.5 Hz, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 188.9, 172.3, 164.3, 161.5, 139.8, 134.6, 133.1, 132.9, 128.7, 128.4, 127.6, 127.1, 125.8, 114.3, 110.5, 55.8, 41.5, 33.0

3-(3-(4-Methylbenzoyl)-1-oxoisoquinolin-2(1*H*)-yl)-*N*-propylpropanamide 23(9,1,5)



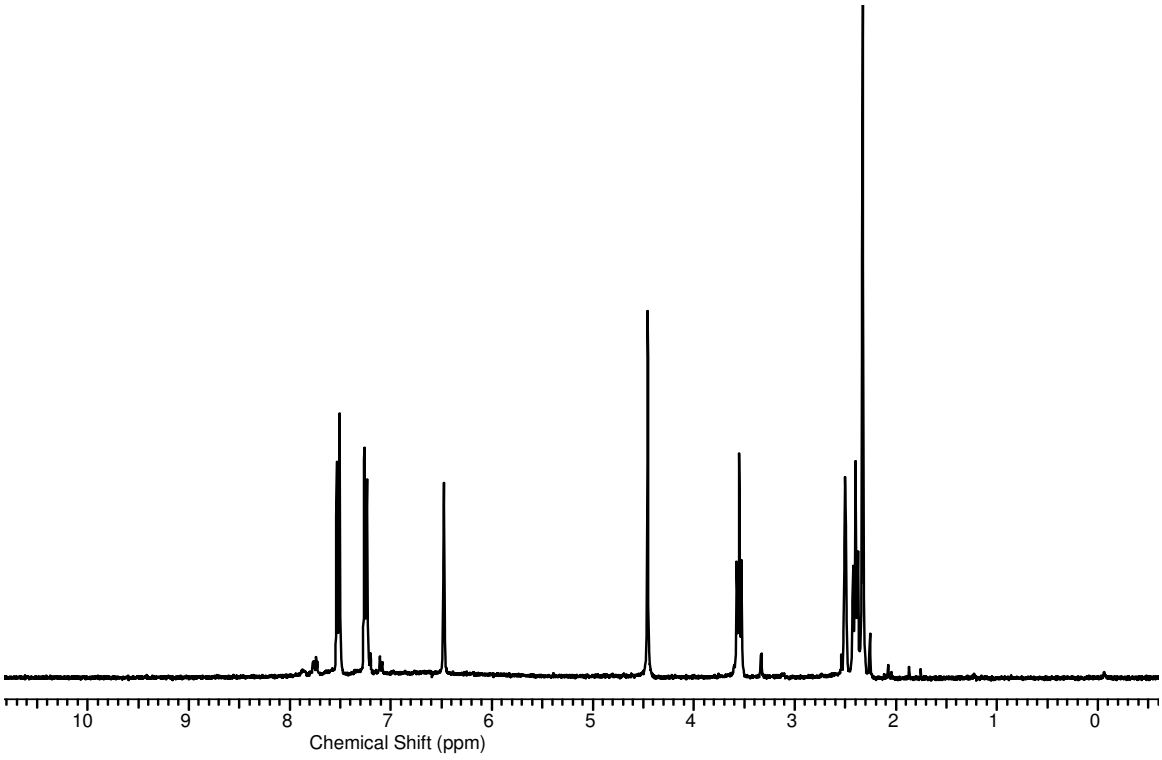
Yield (HPLC purified) 7.5 mg (15%). ESI-MS *m/z* = 377, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.28 (d, *J*=8.0 Hz, 1 H), 7.87 (d, *J*=8.0 Hz, 2 H), 7.74 - 7.79 (m, 2 H), 7.61 - 7.68 (m, 1 H), 7.42 (d, *J*=8.3 Hz, 2 H), 6.84 (s, 1 H), 4.23 (t, *J*=7.0 Hz, 2 H), 2.83 - 2.93 (m, 2 H), 2.51 - 2.58 (m, 2 H), 2.44 (s, 3 H), 1.22 - 1.36 (m, 2 H), 0.74 (t, *J*=7.5 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 189.8, 169.3, 161.4, 145.0, 139.9, 134.5, 133.3, 132.9, 130.7, 129.3, 128.8, 127.6, 127.1, 125.8, 111.0, 41.8, 40.2, 34.1, 22.2, 21.3, 11.3. HRMS (FAB) *m/z* calcd for $C_{23}H_{25}N_2O_3$ $[M+H]^+$ 377.1865, found 377.1871

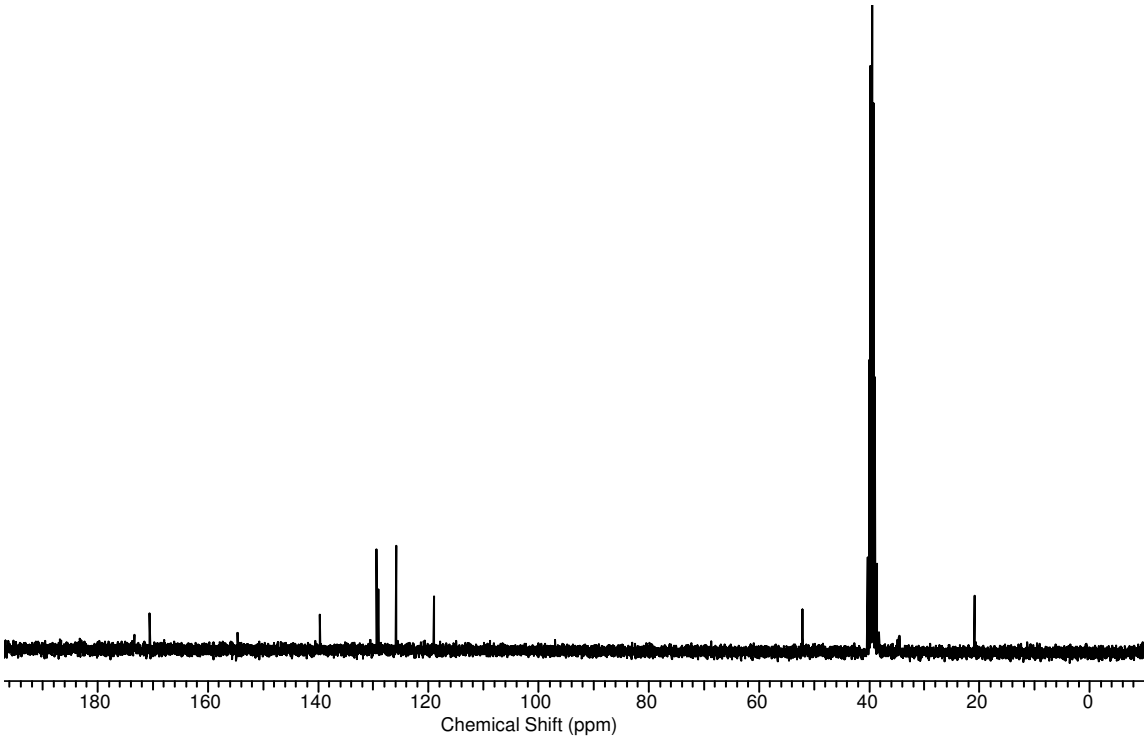
1-p-Tolyl-3,4-dihydro-pyrazino[1,2-*b*]isoquinolin-6-one 24(10,1,5)



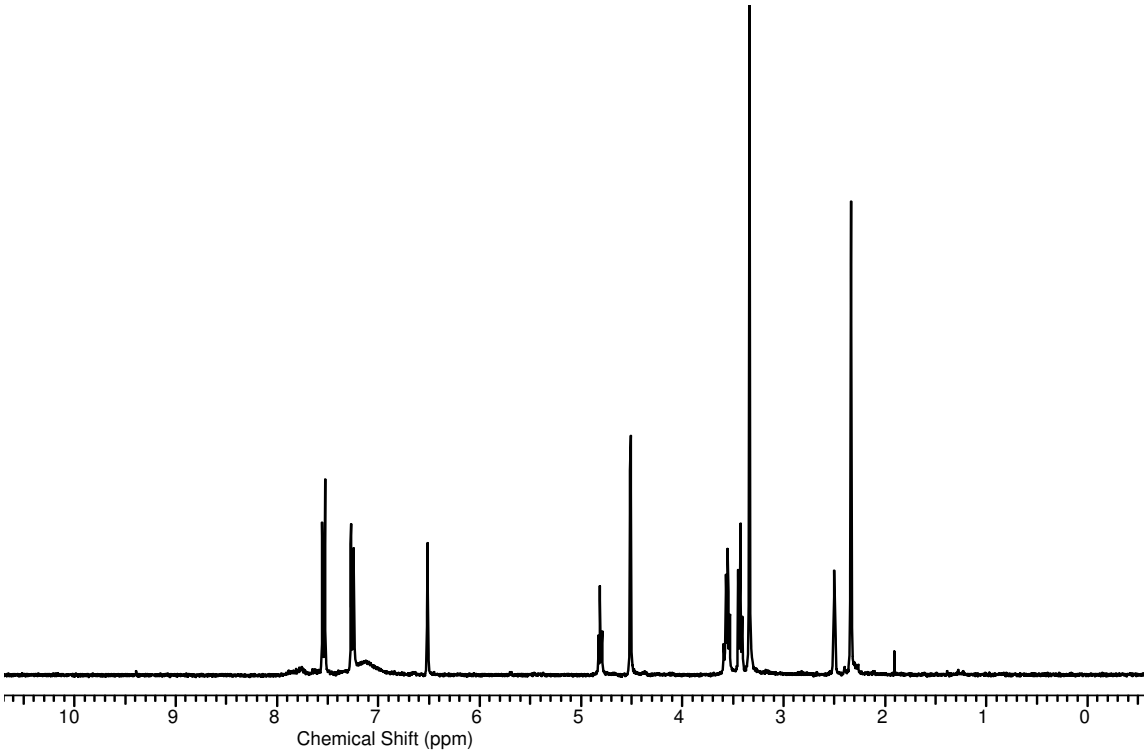
Yield (HPLC purified) 4.1 mg (13%). ESI-MS *m/z* = 289, $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.33 (dt, *J*=7.7, 0.69 Hz, 1 H), 7.90 (d, *J*=6.9 Hz, 1 H), 7.80 (td, *J*=7.4, 1.5 Hz, 1 H), 7.74 (td, *J*=7.6, 1.0 Hz, 1 H), 7.66 (d, *J*=8.0 Hz, 2 H), 7.43 (d, *J*=8.3 Hz, 2 H), 7.02 (s, 1 H), 4.21 (t, *J*=5.5 Hz, 2 H), 4.04 (t, *J*=5.5 Hz, 2 H), 2.44 (s, 3 H). HRMS (FAB) *m/z* calcd for $C_{19}H_{17}N_2O$ $[M+H]^+$ 289.1341, found 289.1333

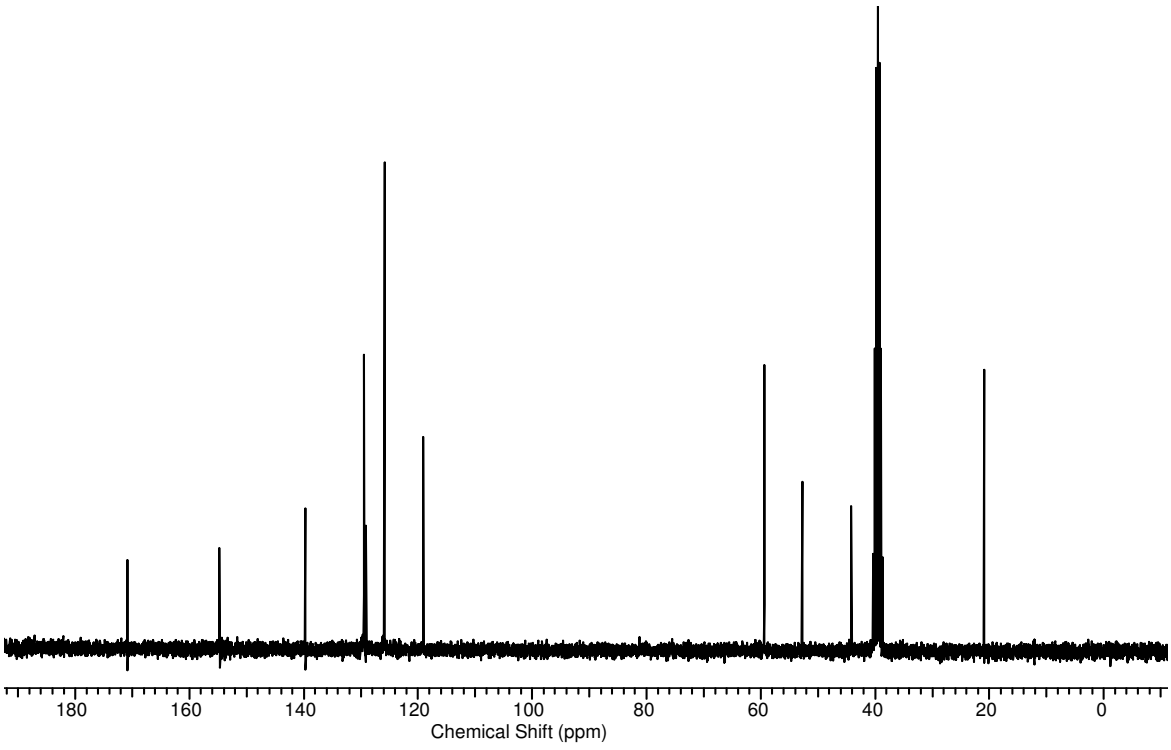
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(1,1,1)



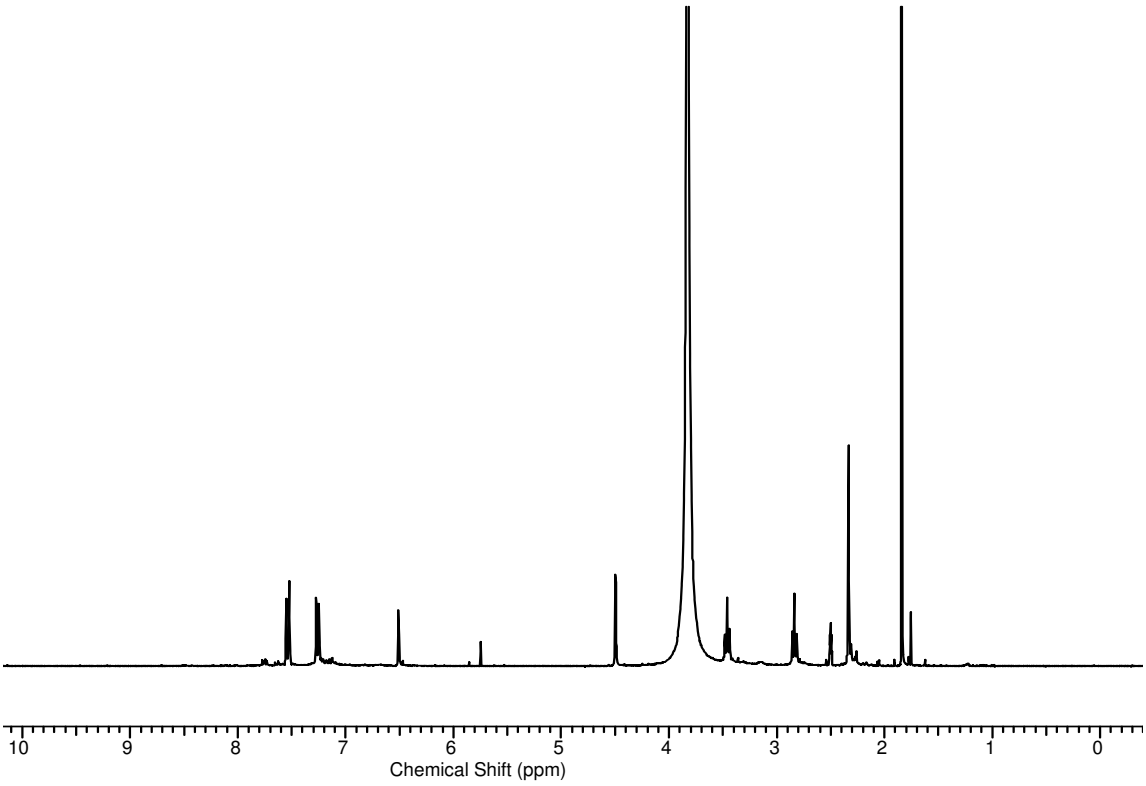


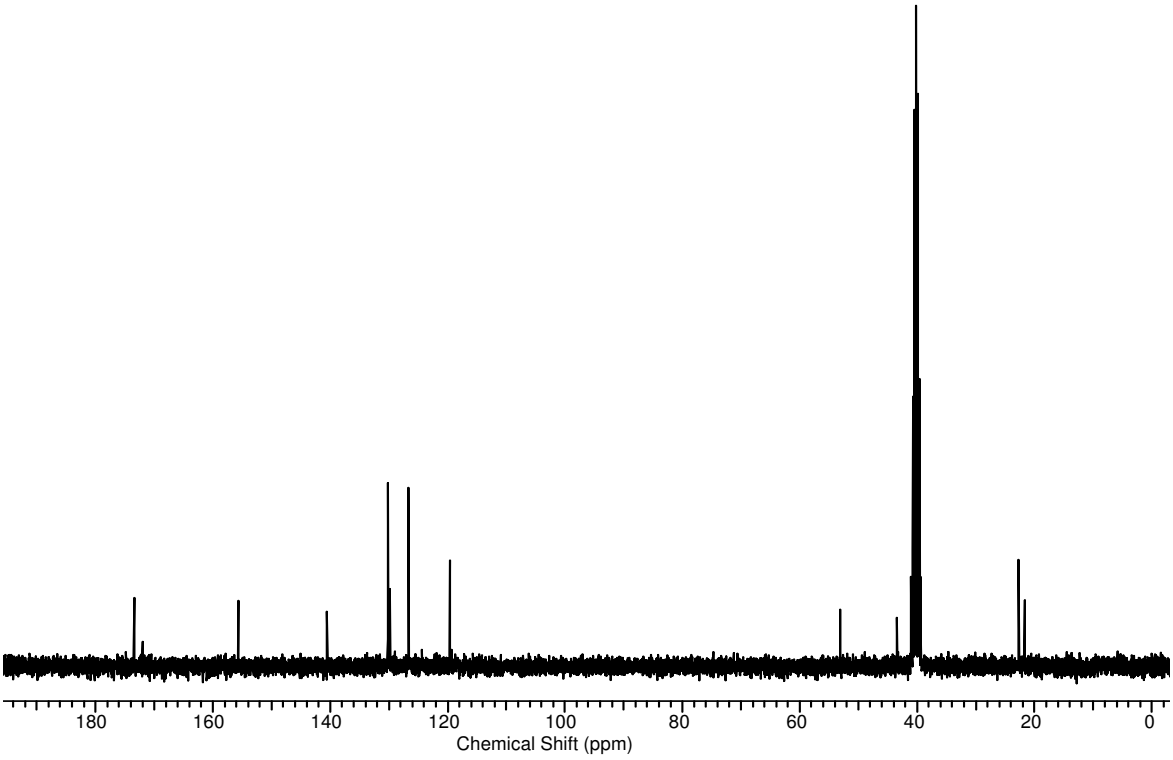
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(2,1,1)



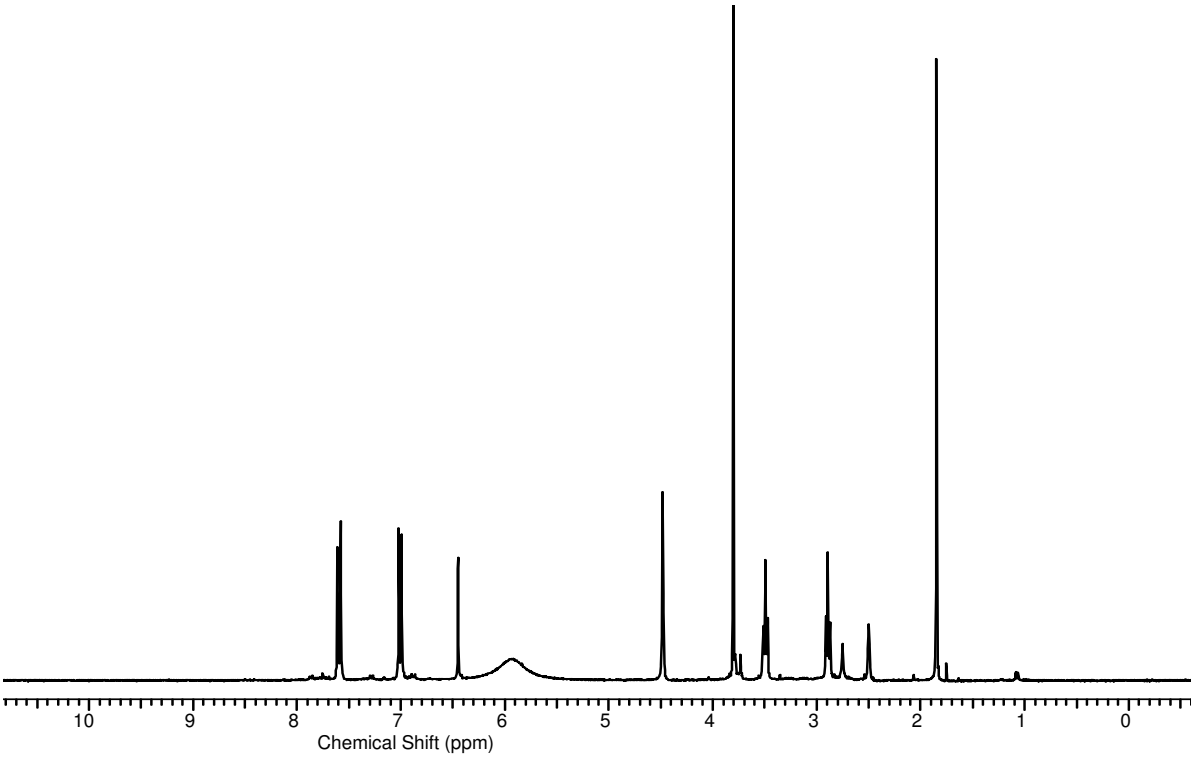


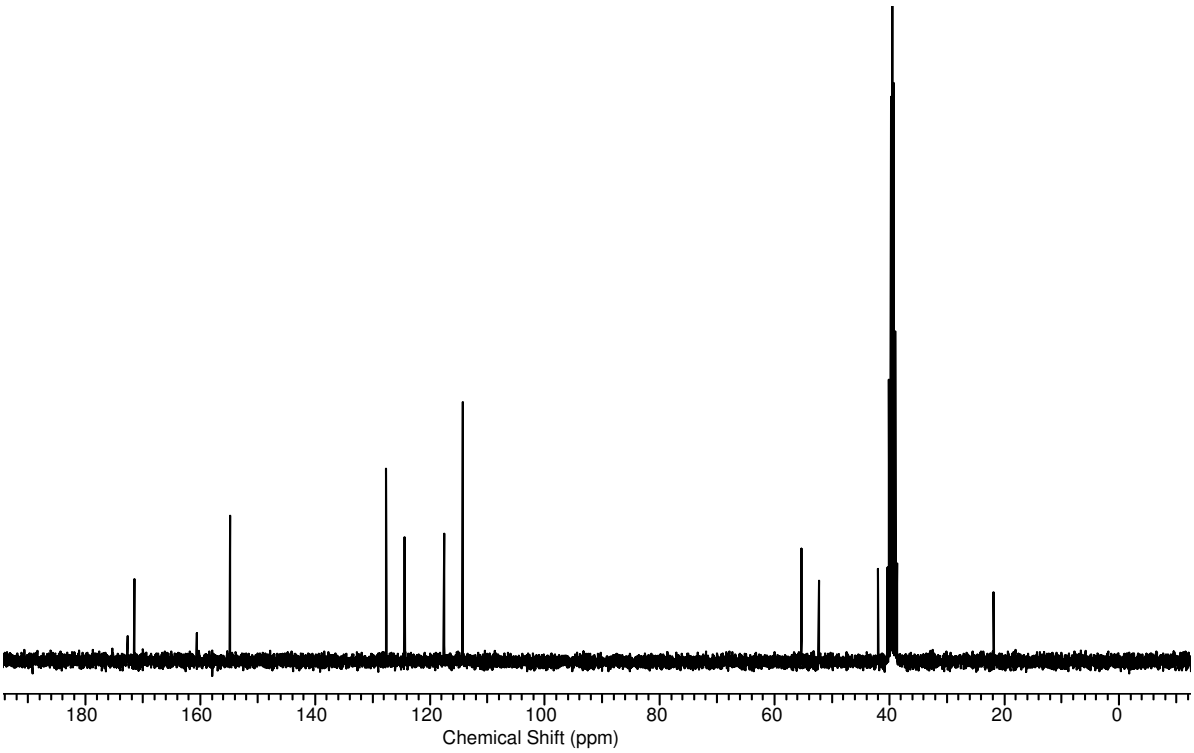
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(3,1,1)



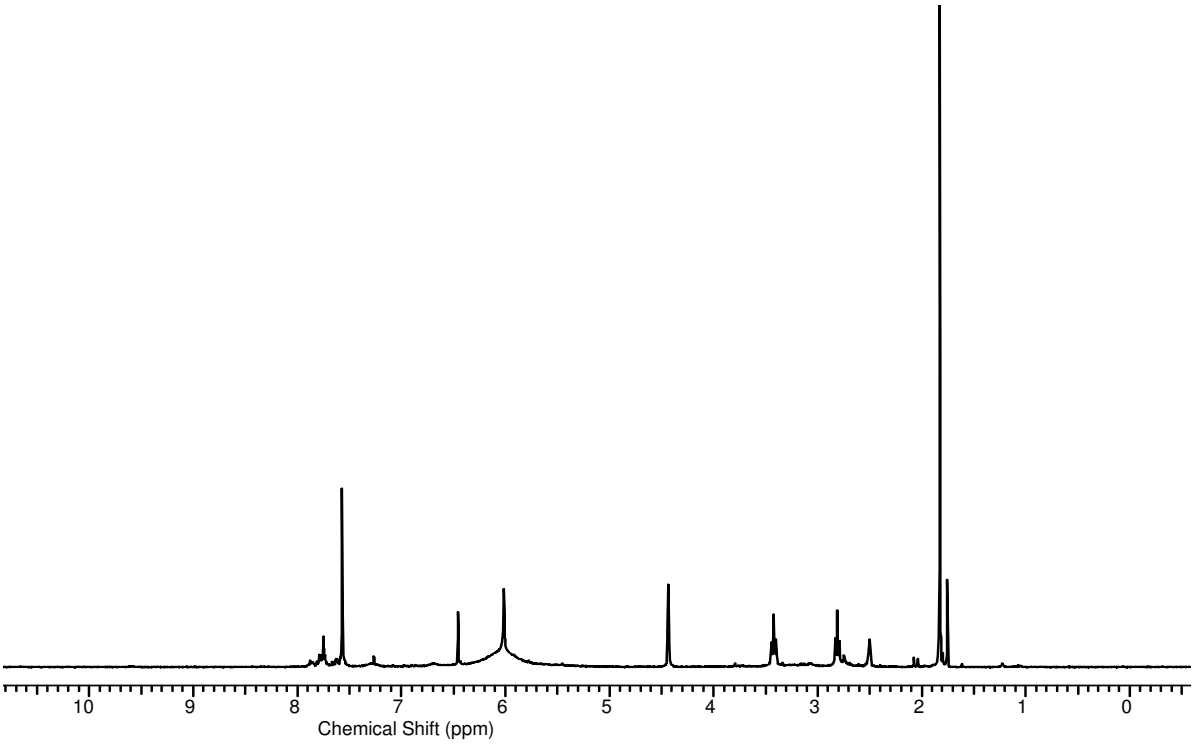


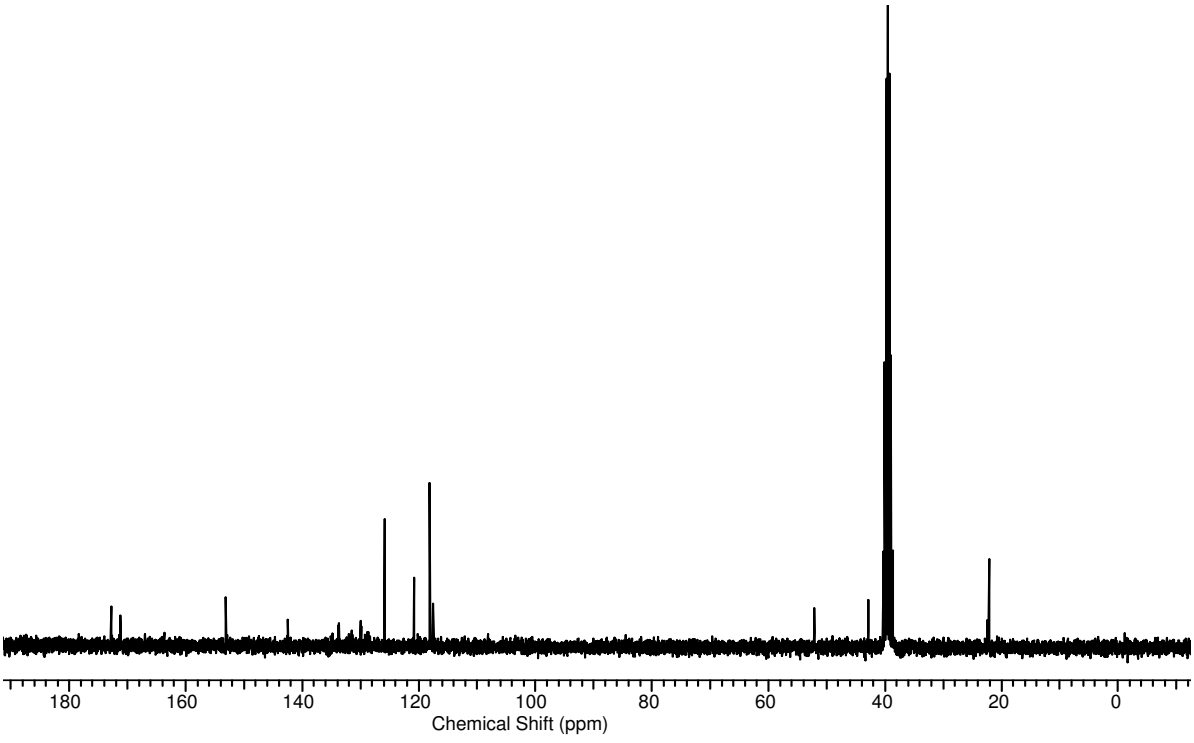
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(3,2,1)



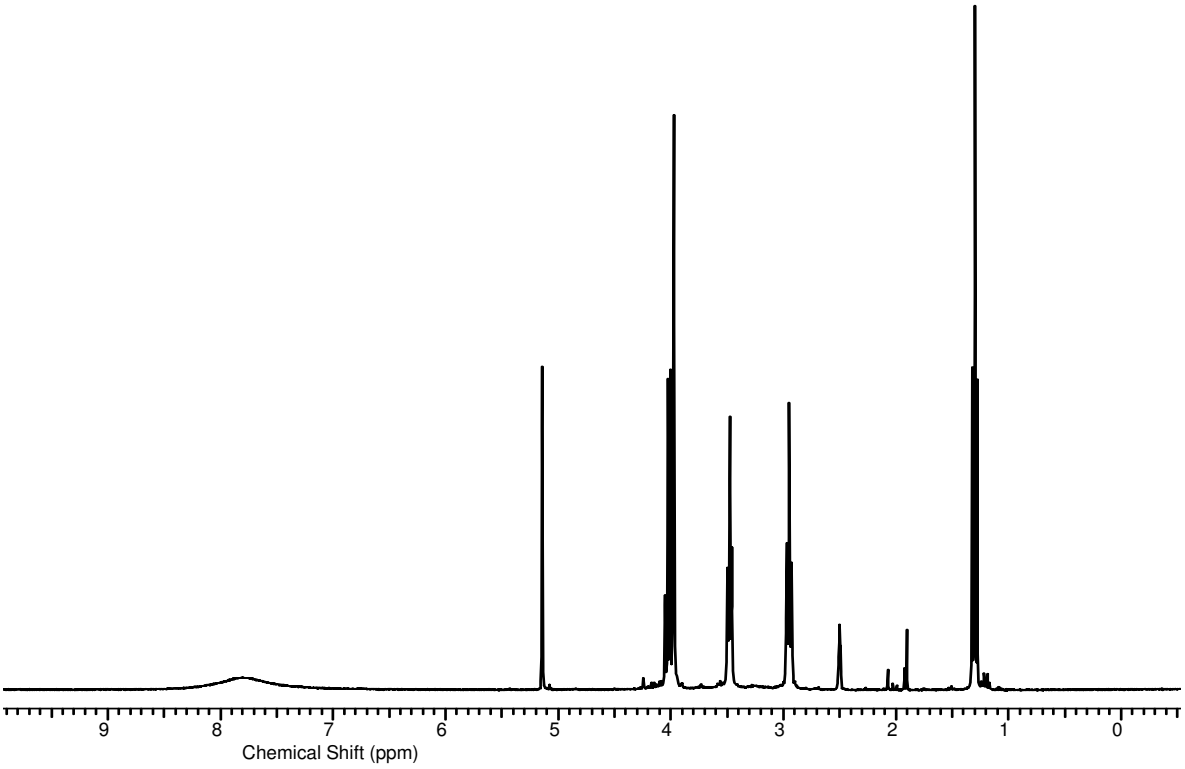


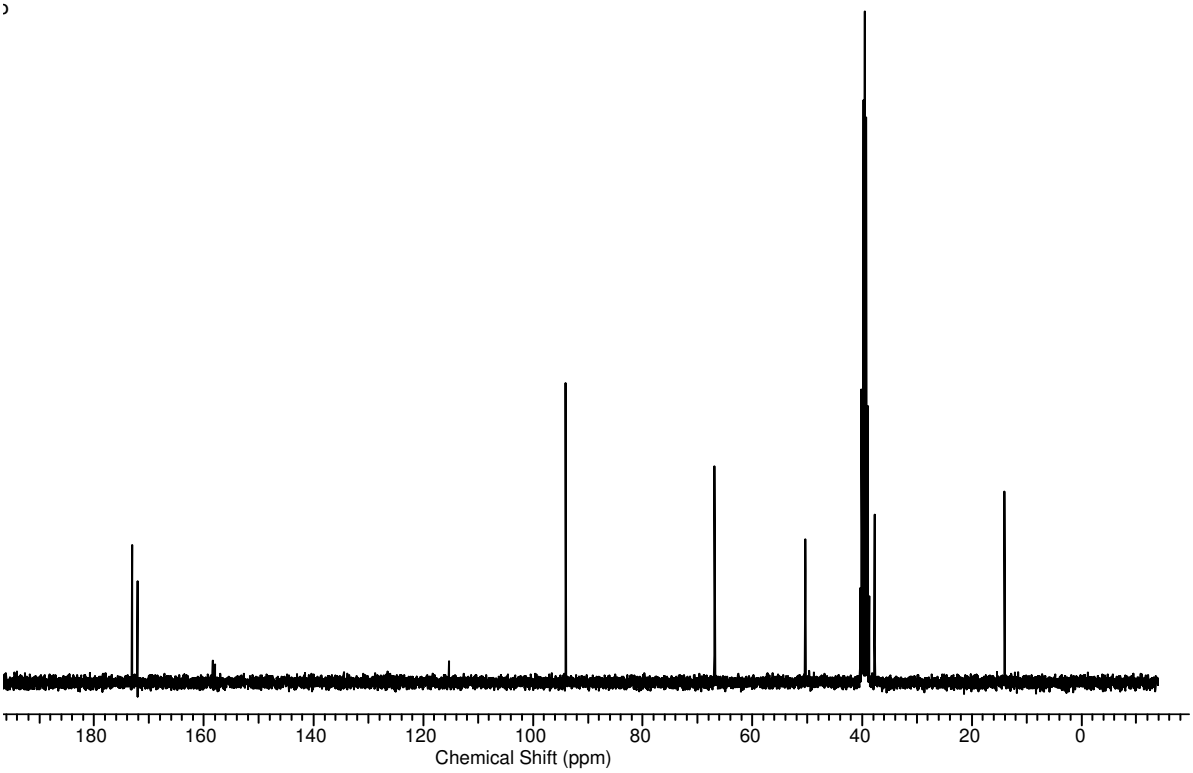
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(3,3,1)



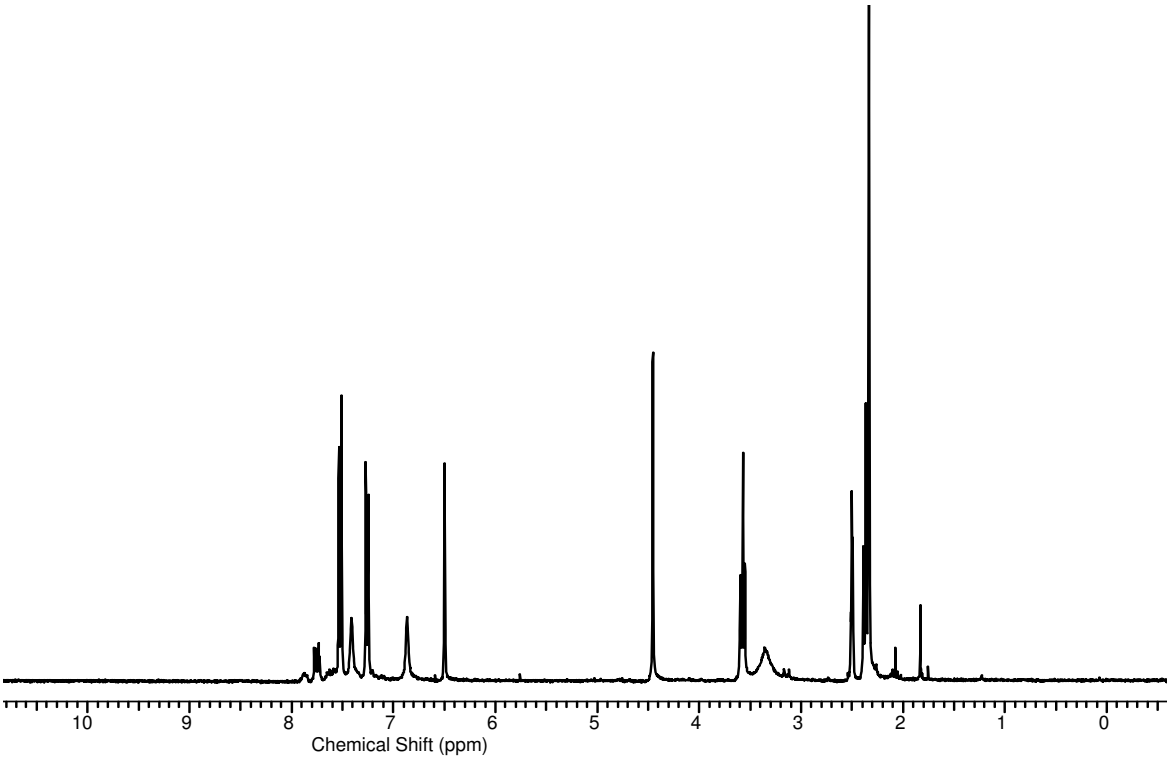


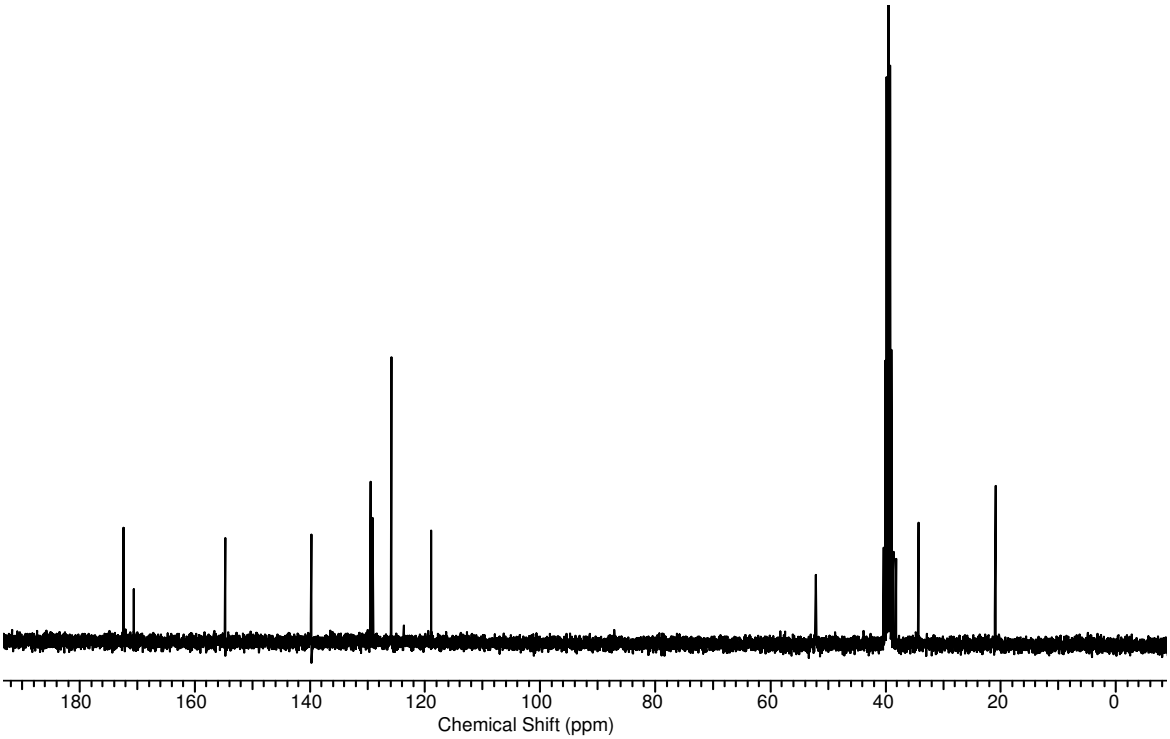
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(3,4,1)



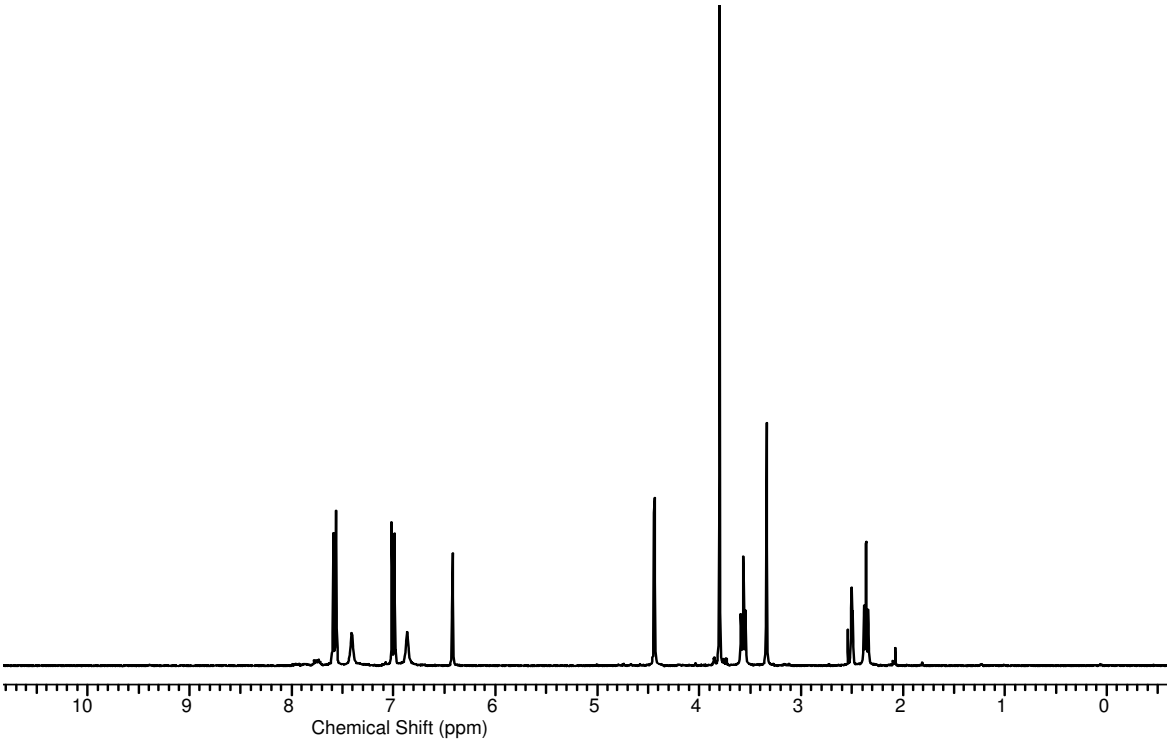


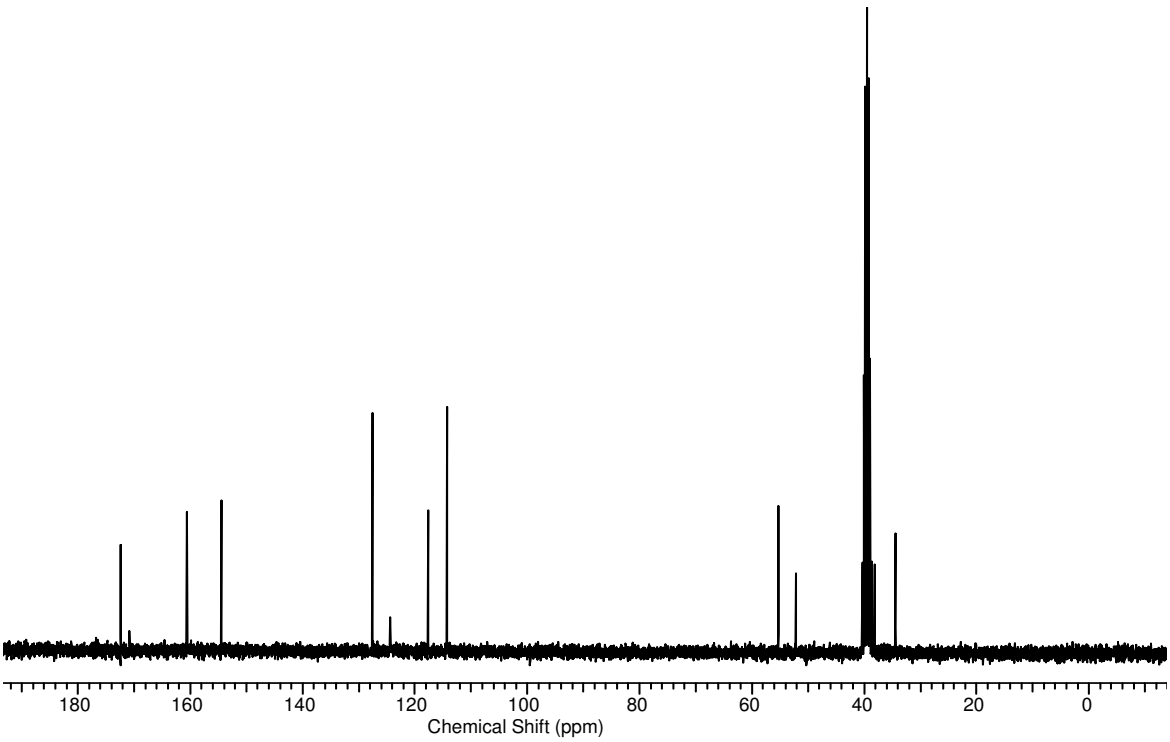
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(4,1,1)



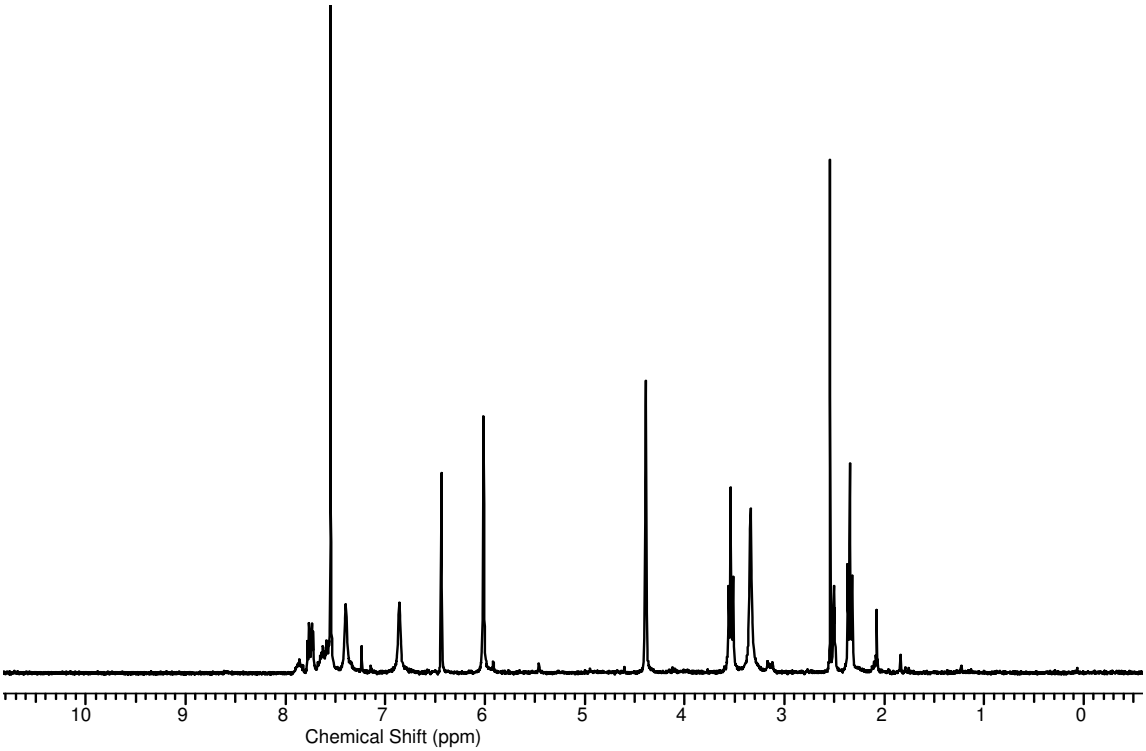


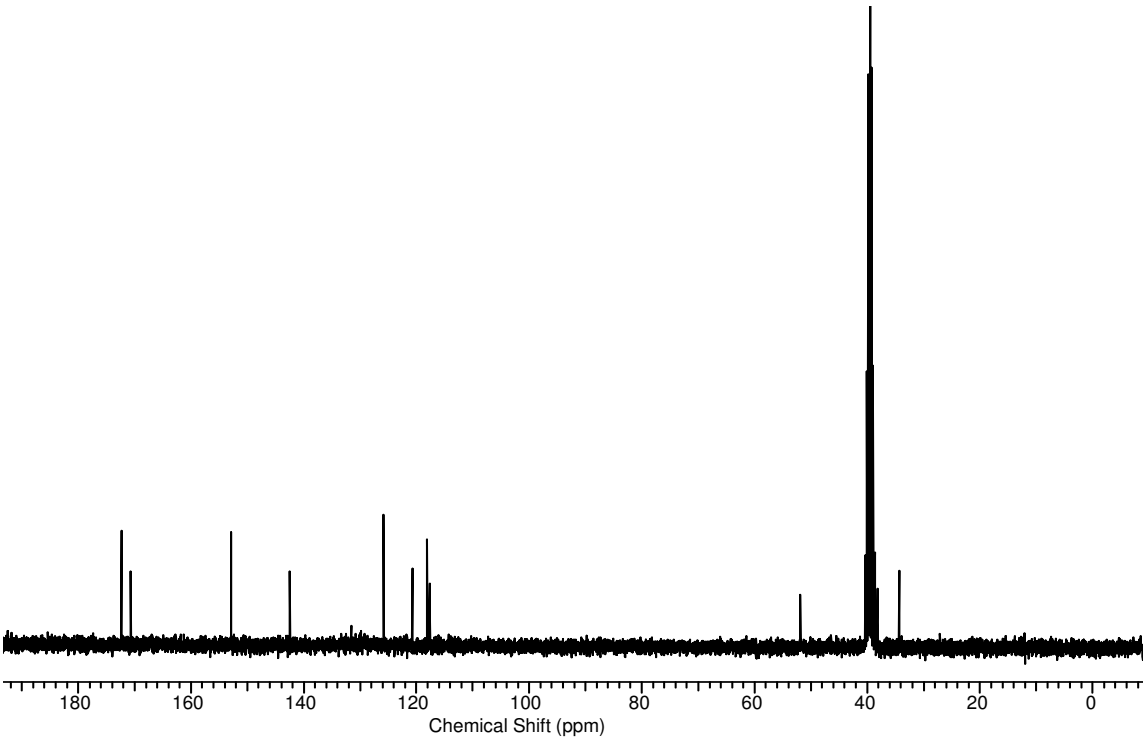
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(4,2,1)



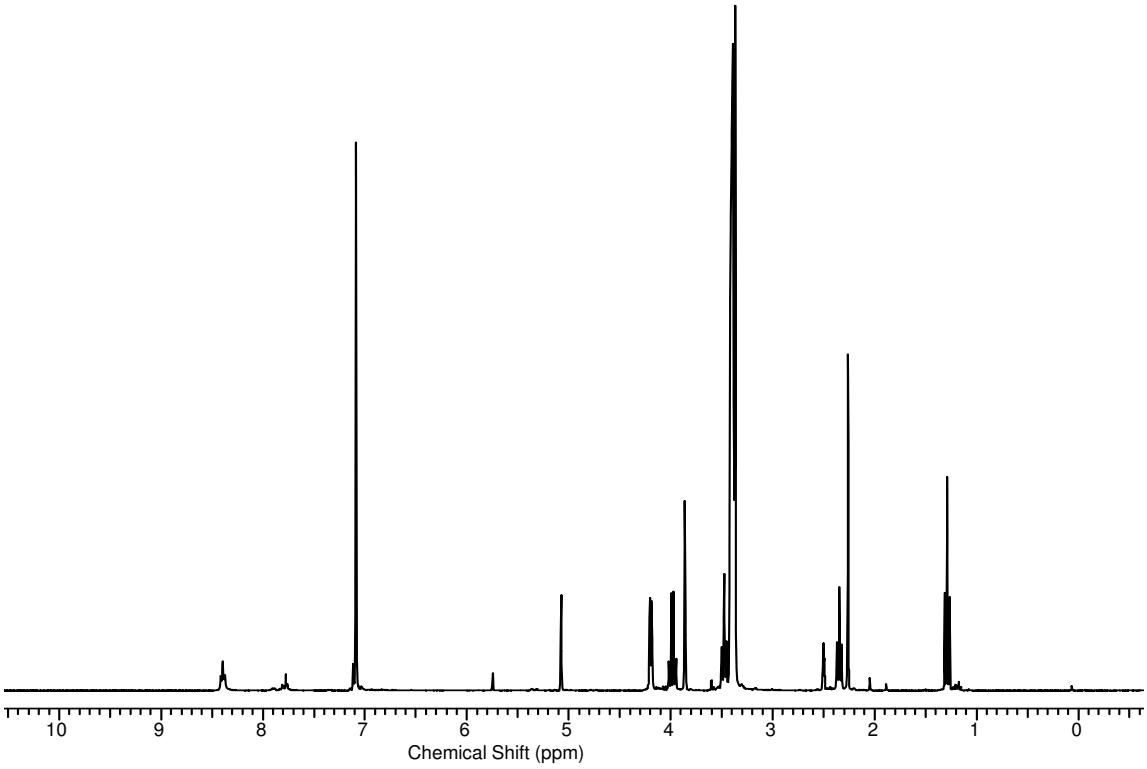


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(4,3,1)

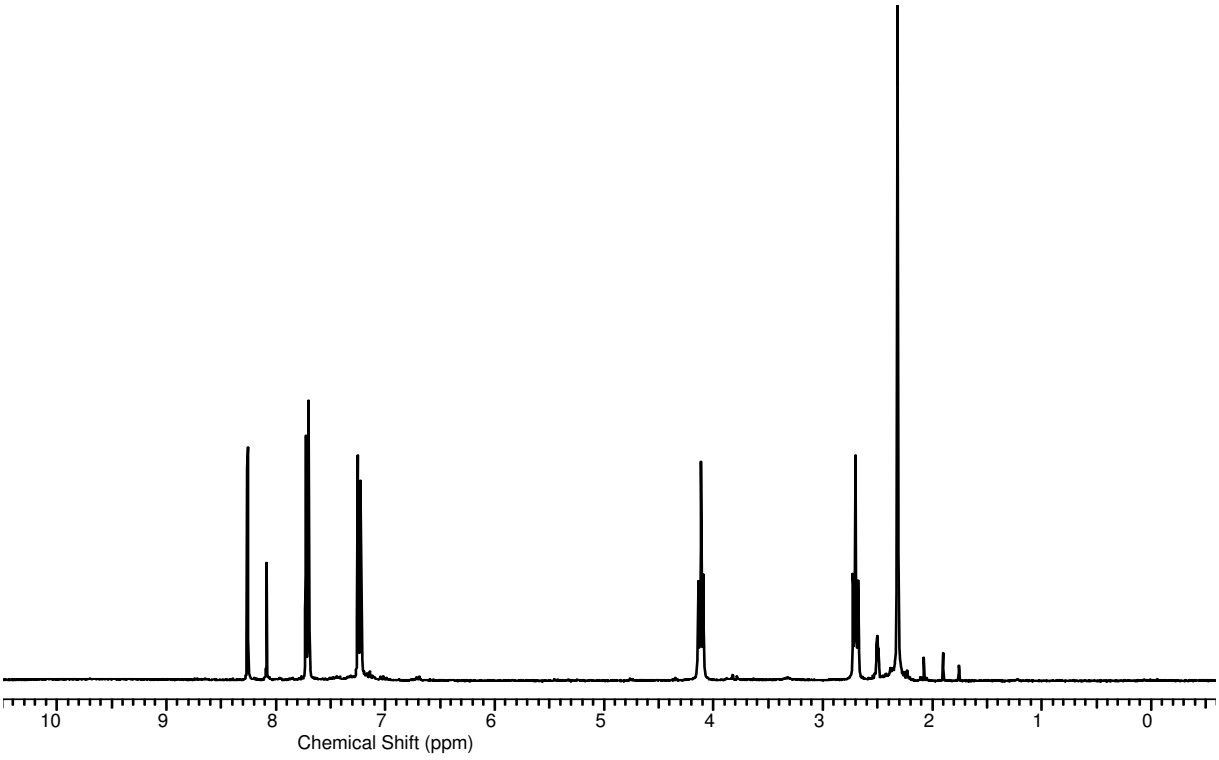


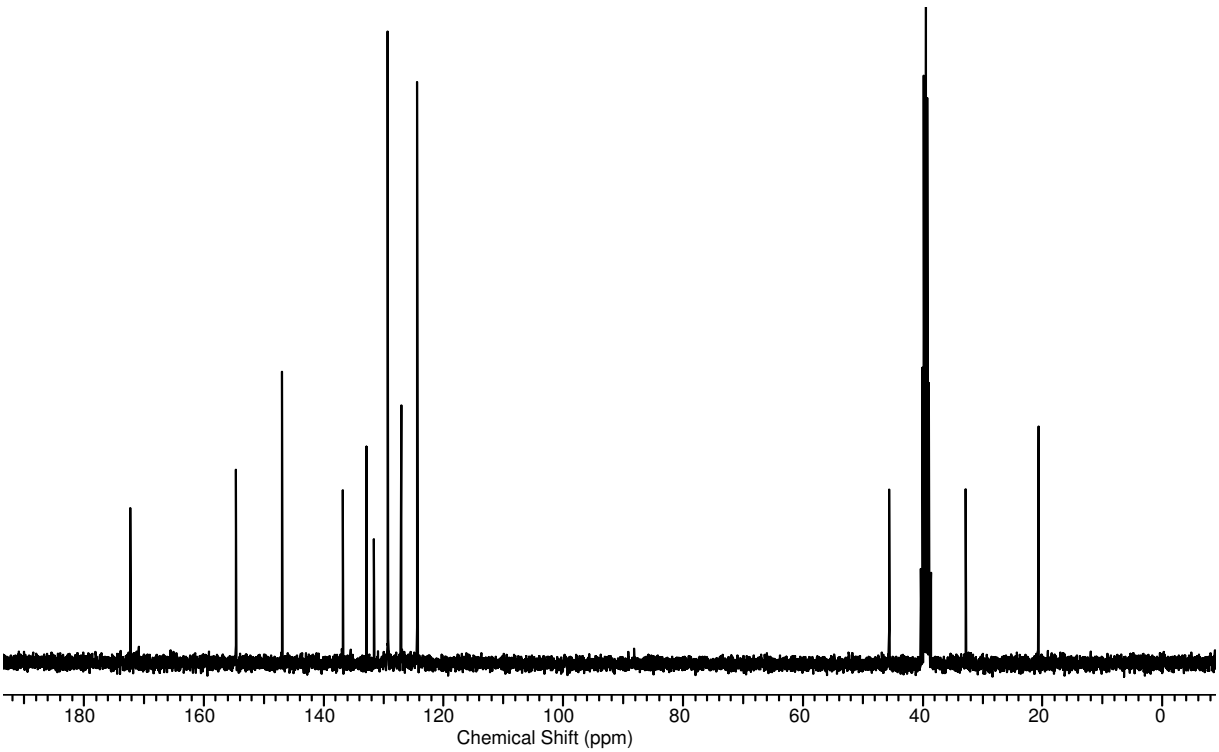


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 5(5,4,1)

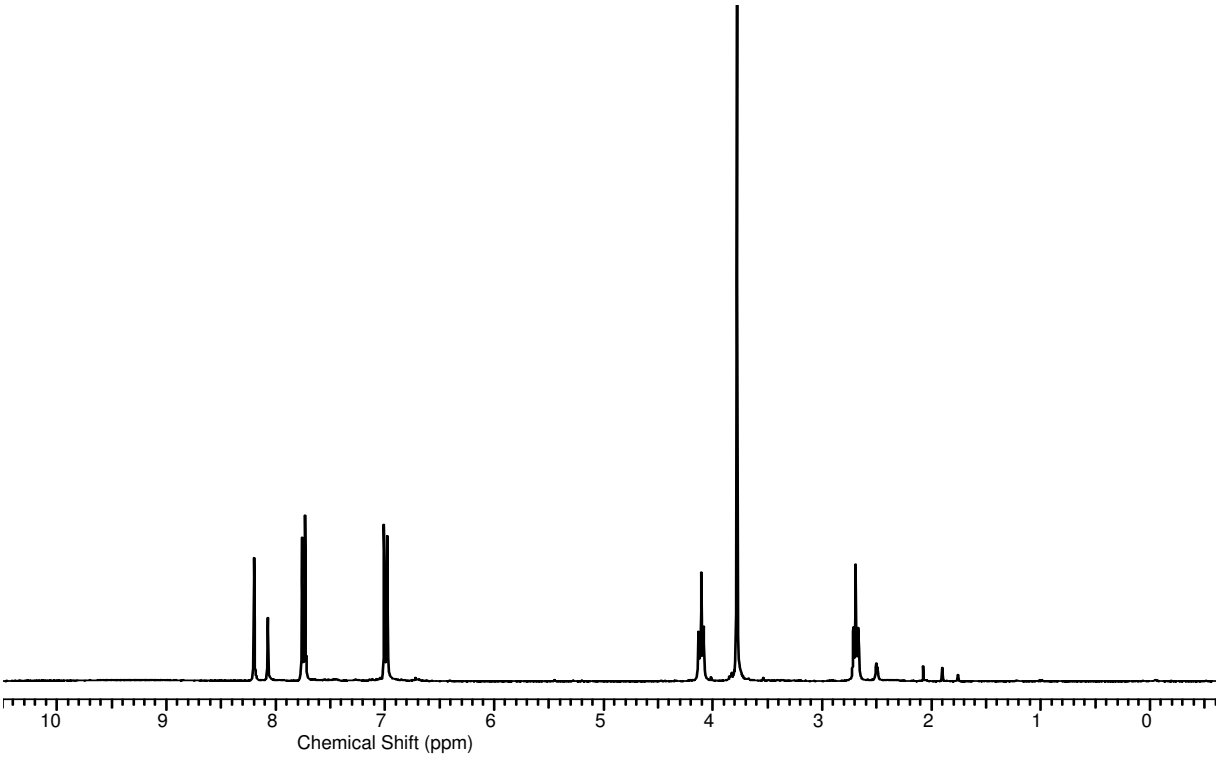


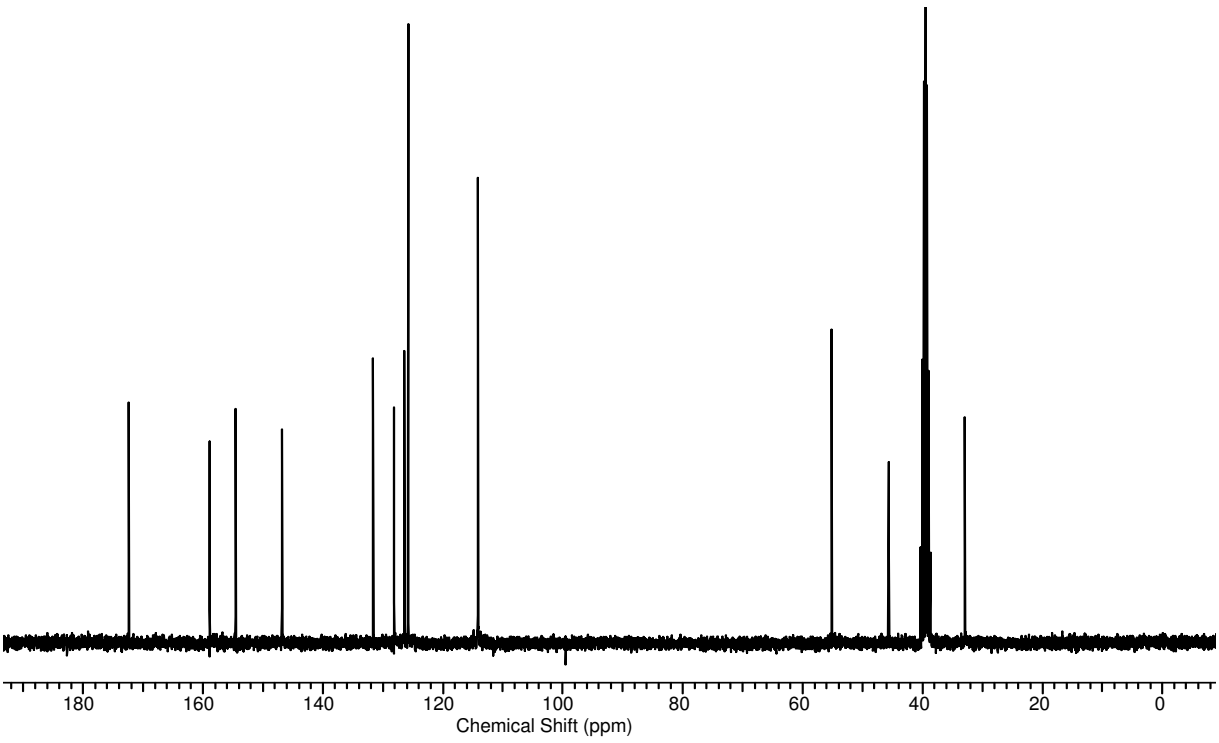
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1,1)



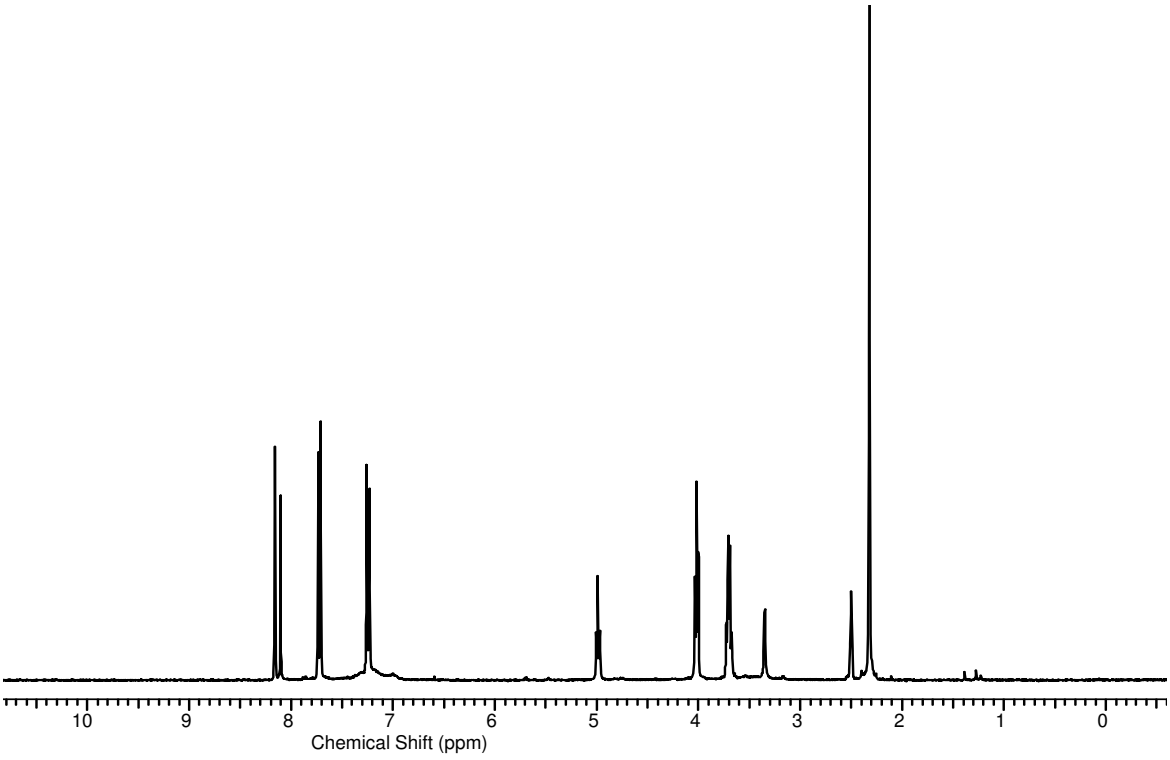


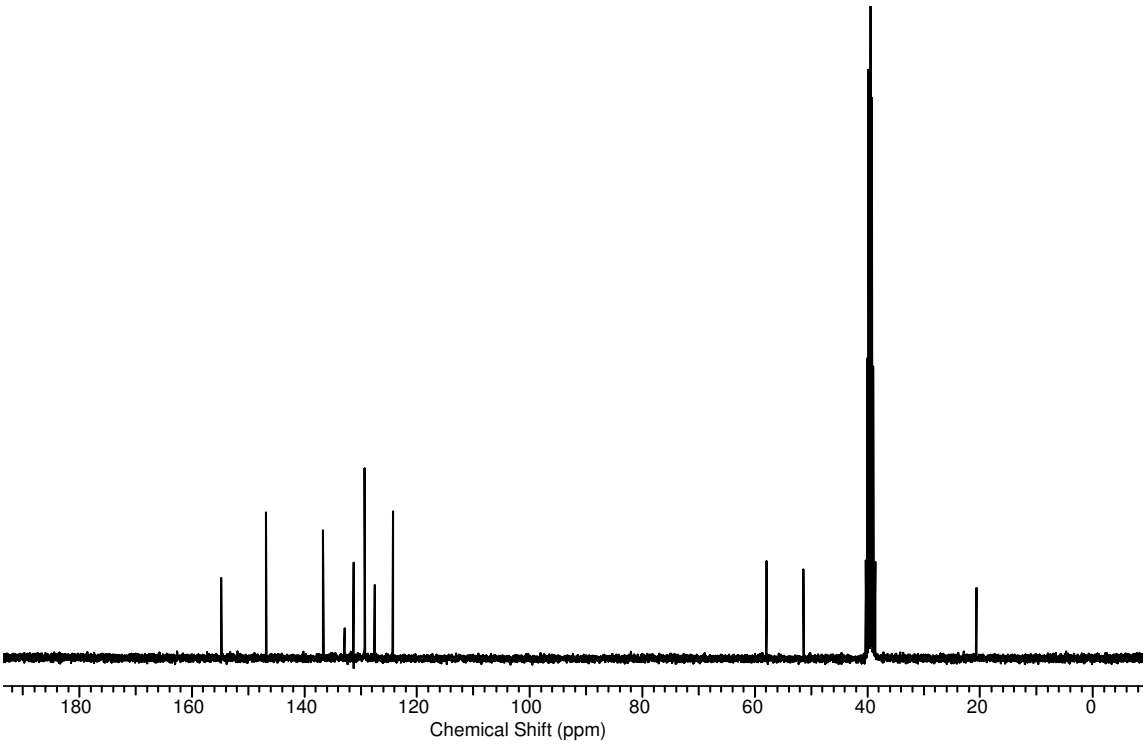
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,2,1)



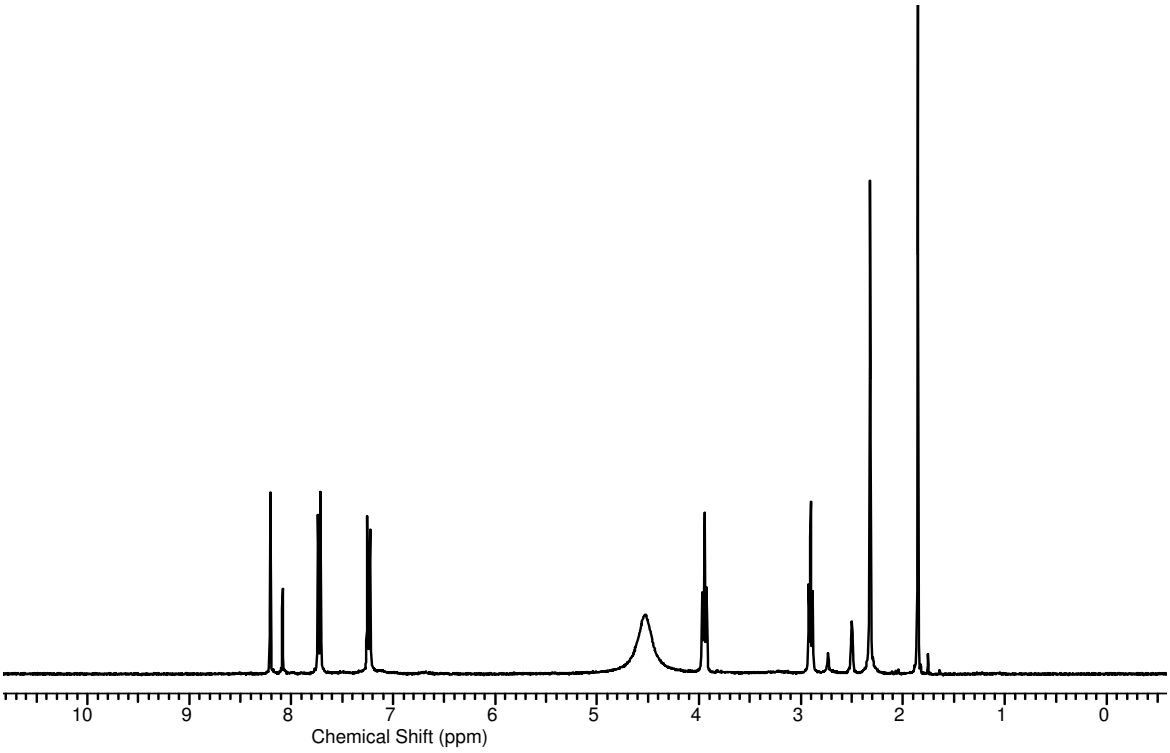


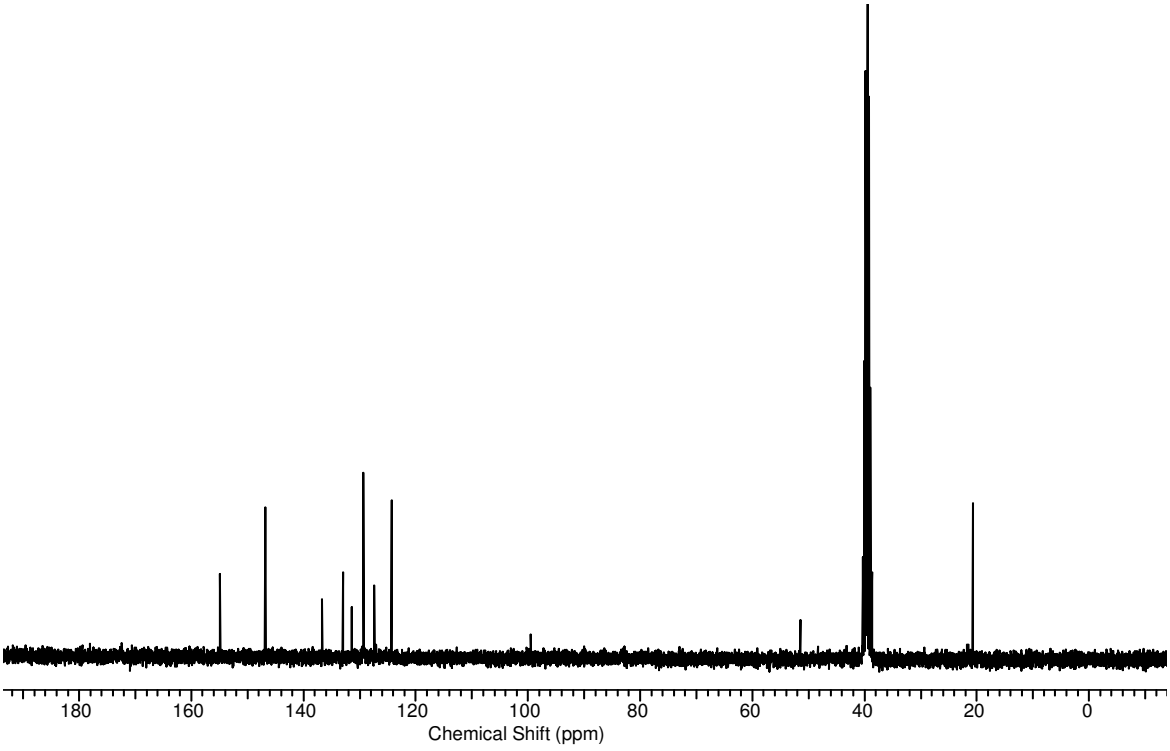
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(2,1,1)



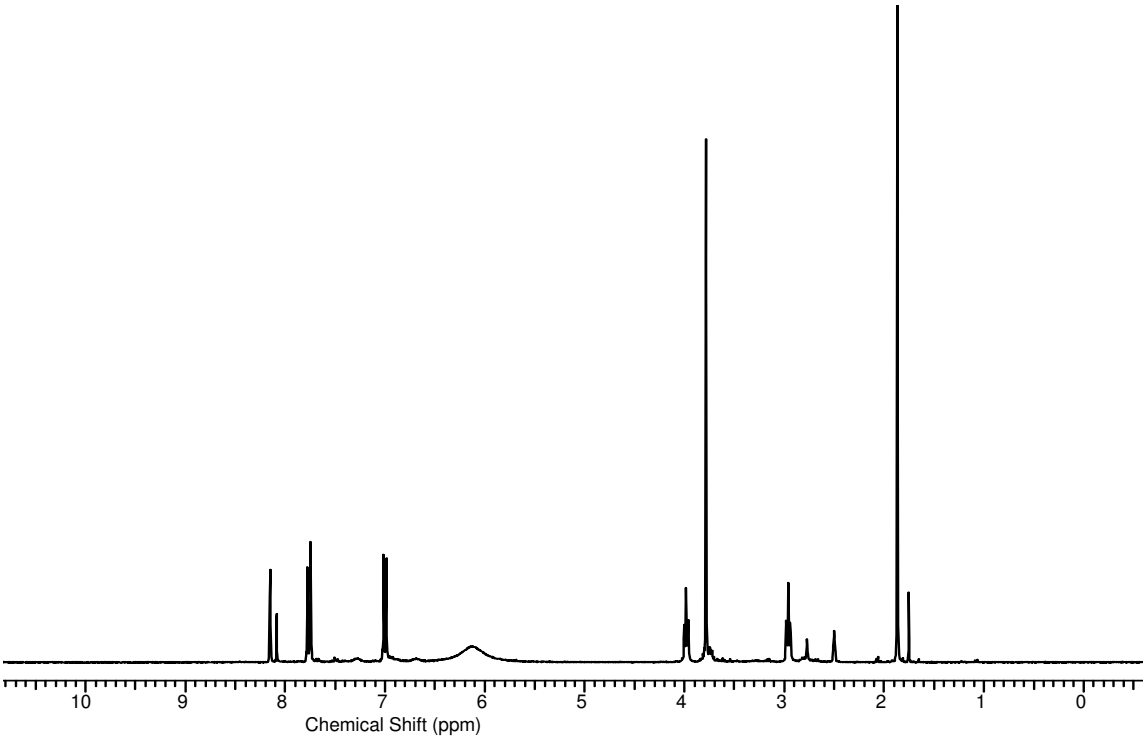


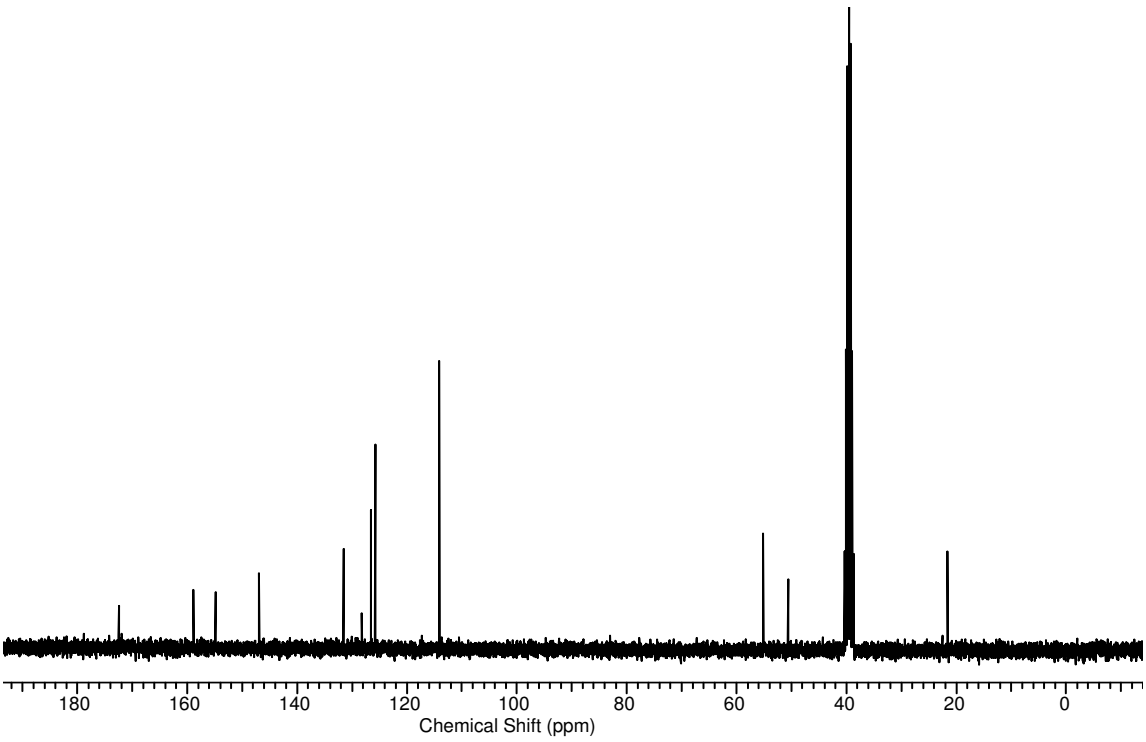
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(3,1,1)



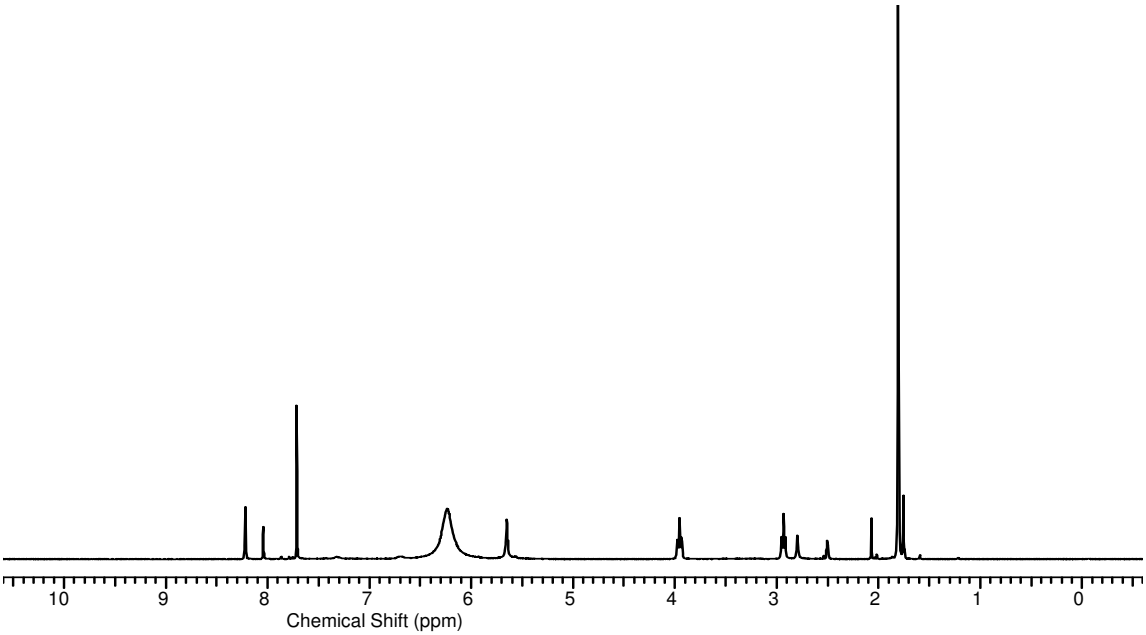


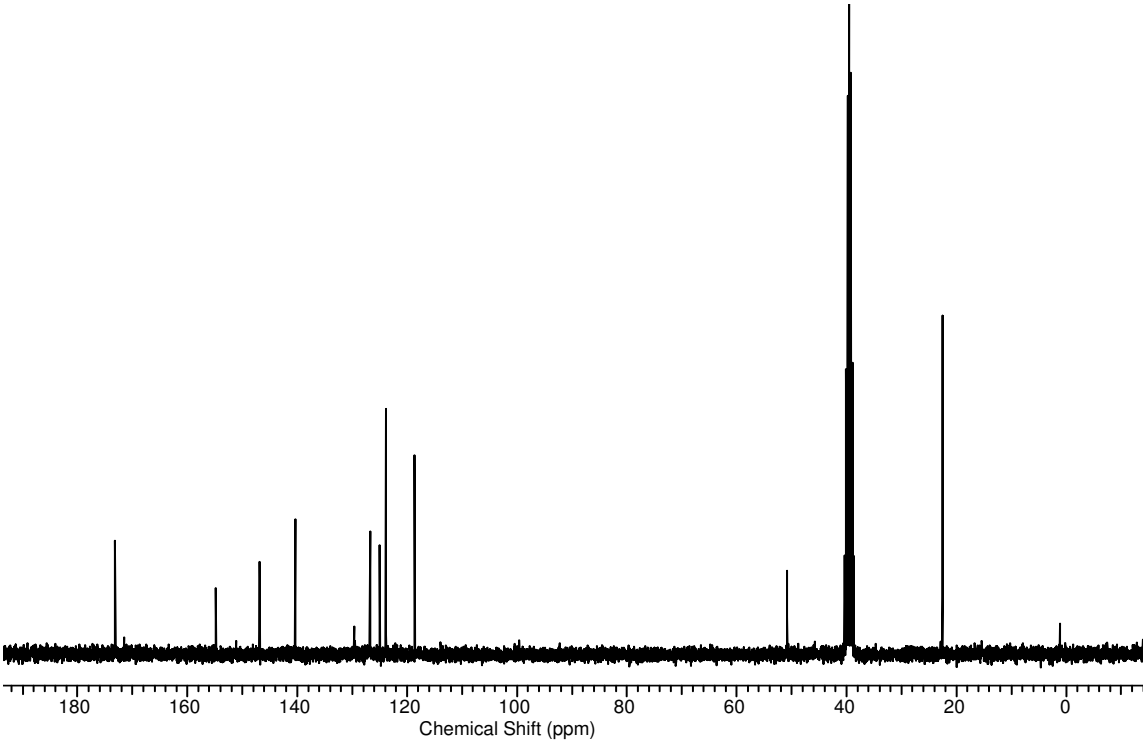
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(3,2,1)



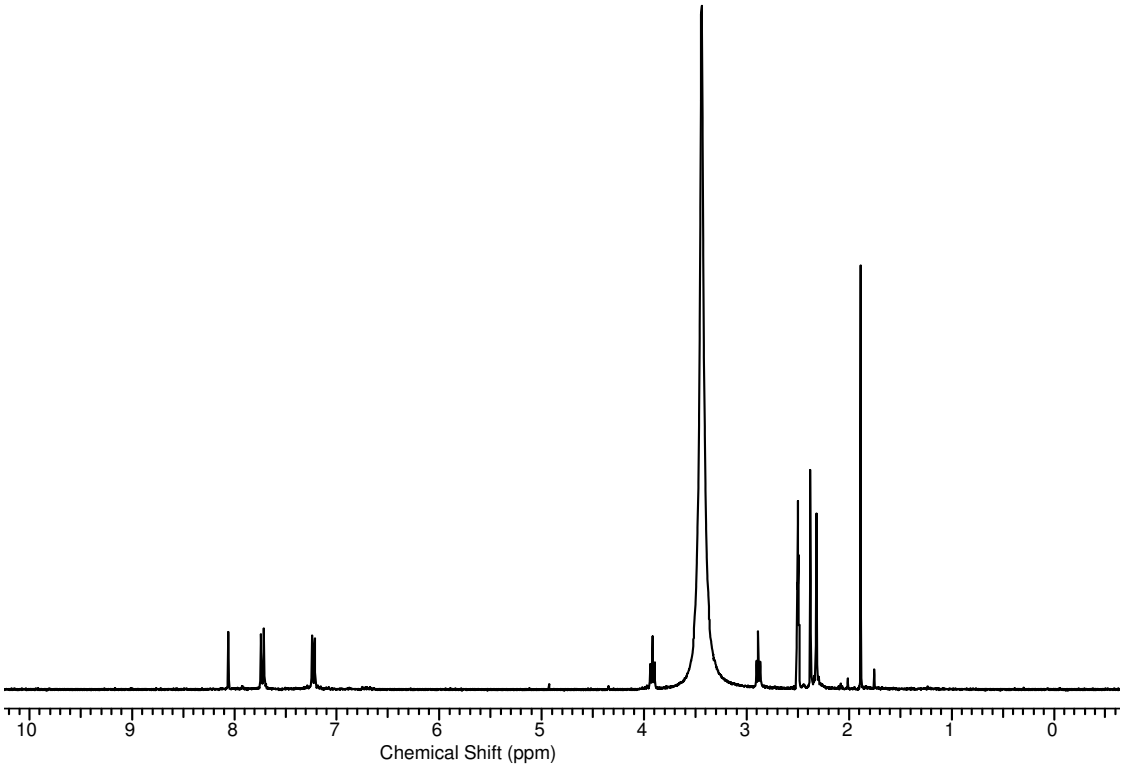


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(3,3,1)

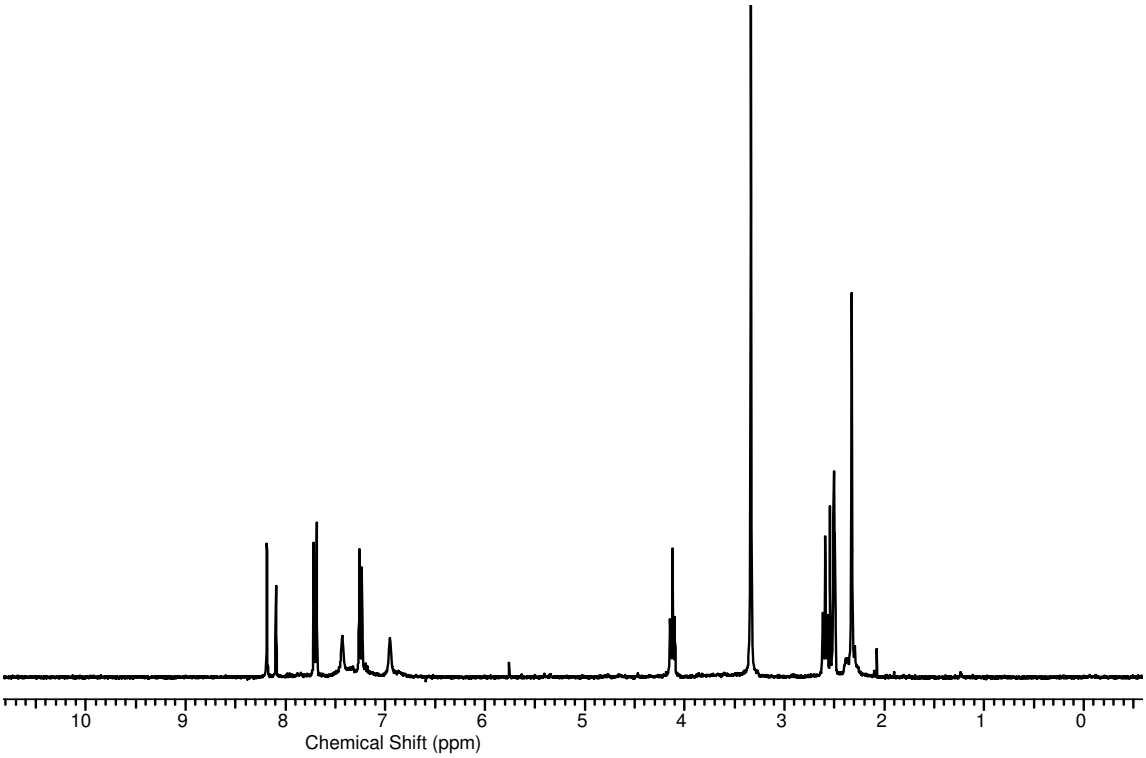


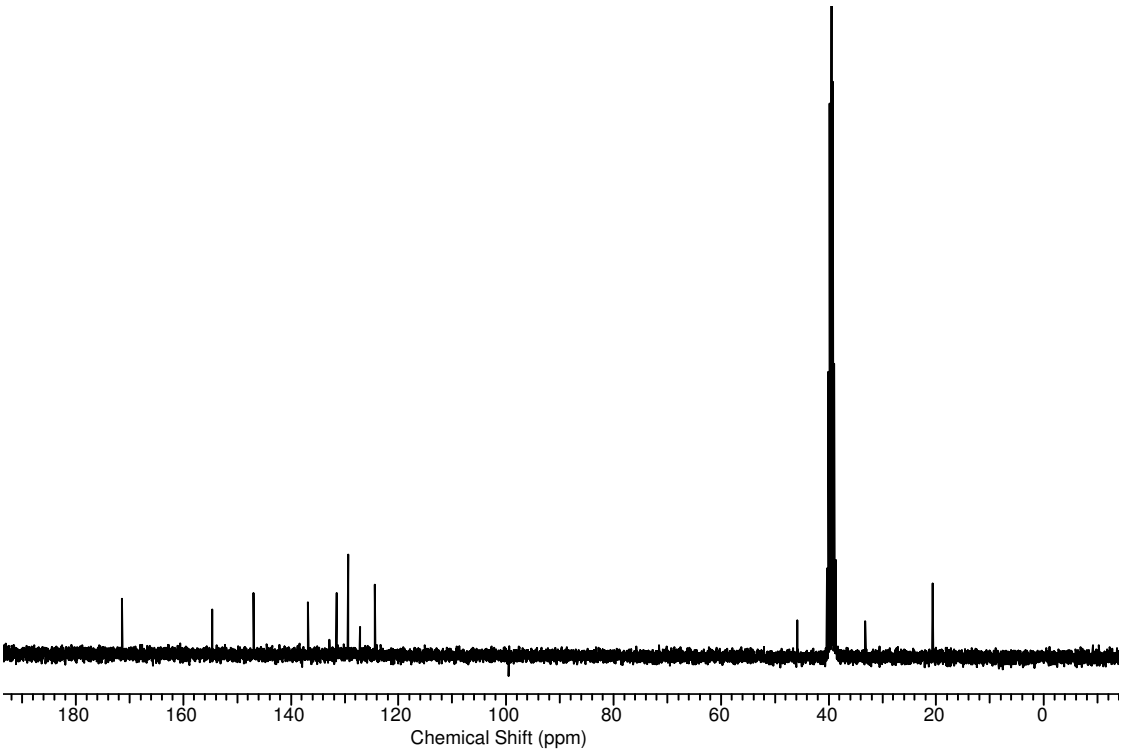


^{1}H NMR spectrum (d_6-DMSO) for compound 7(3,1,2)

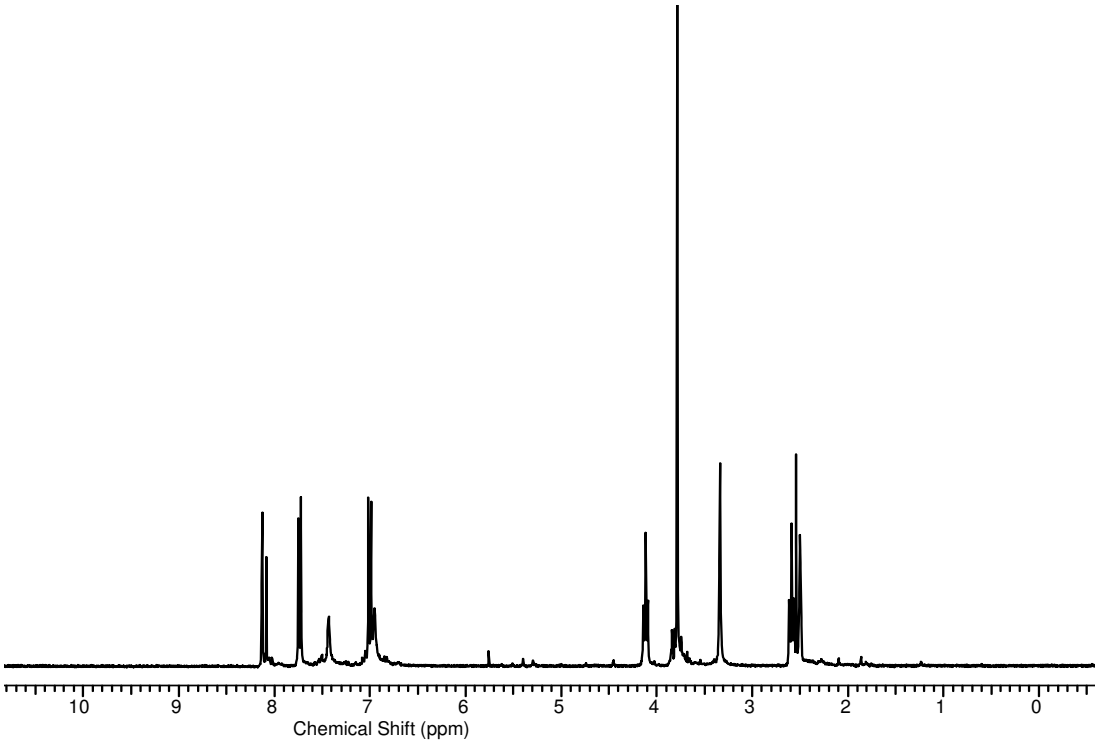


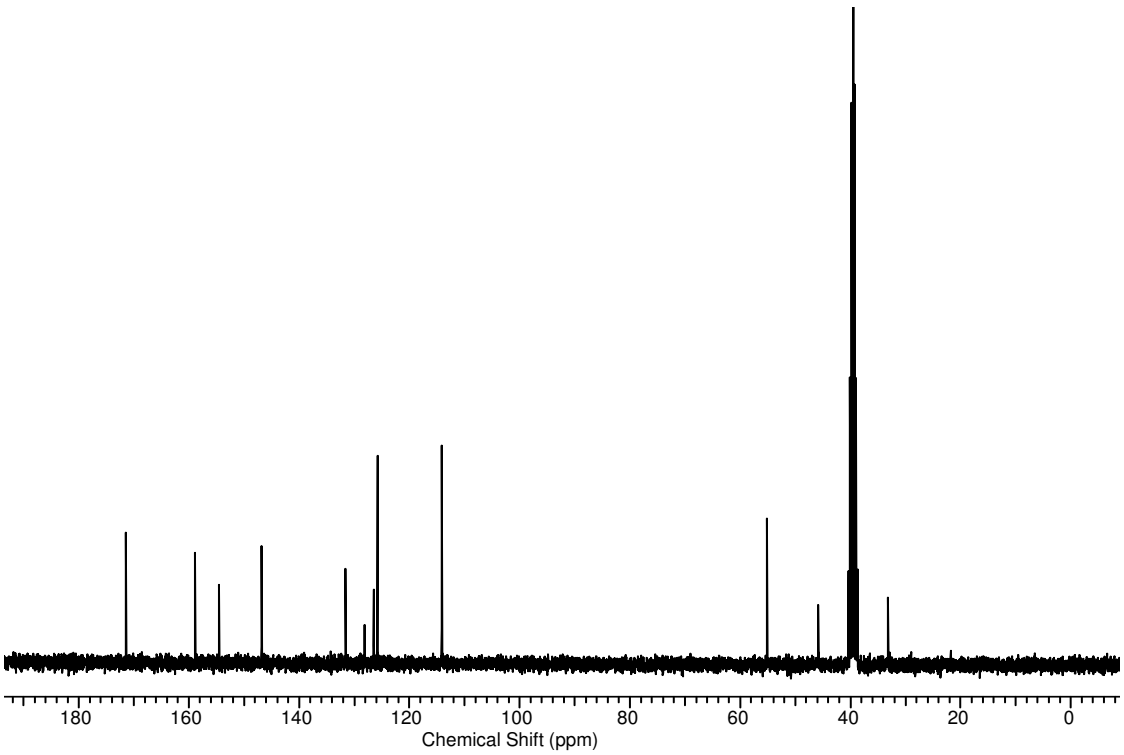
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(4,1,1)



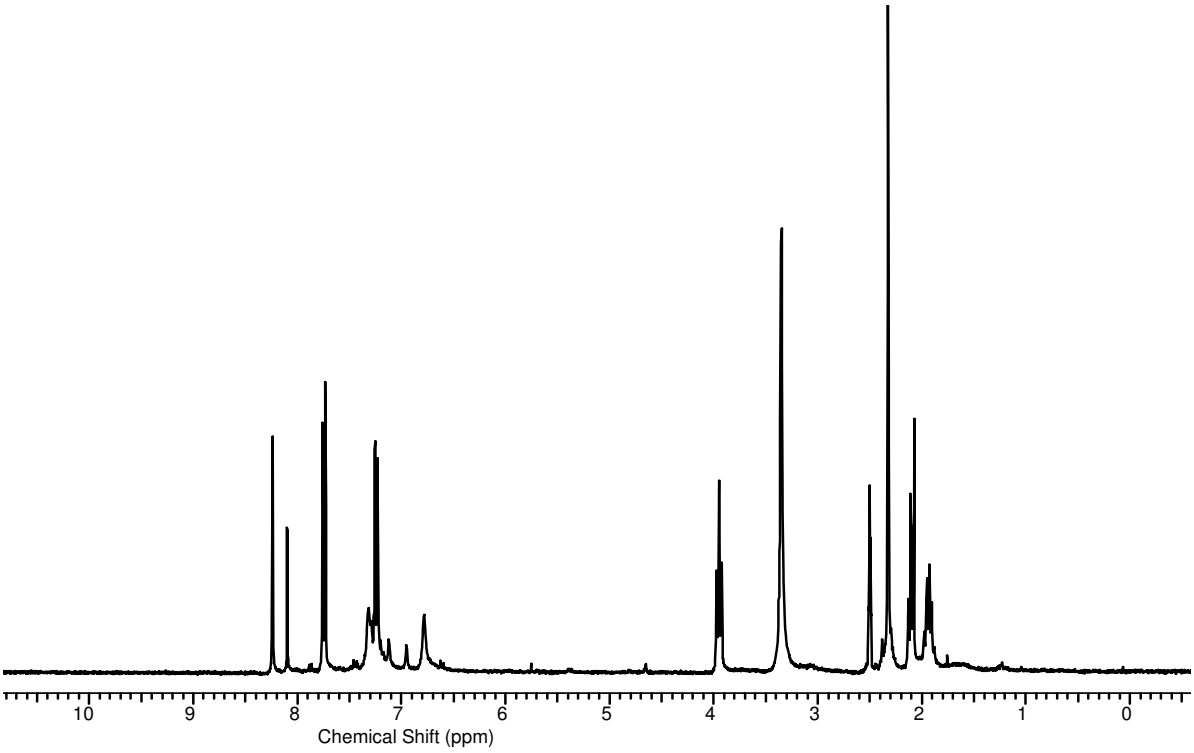


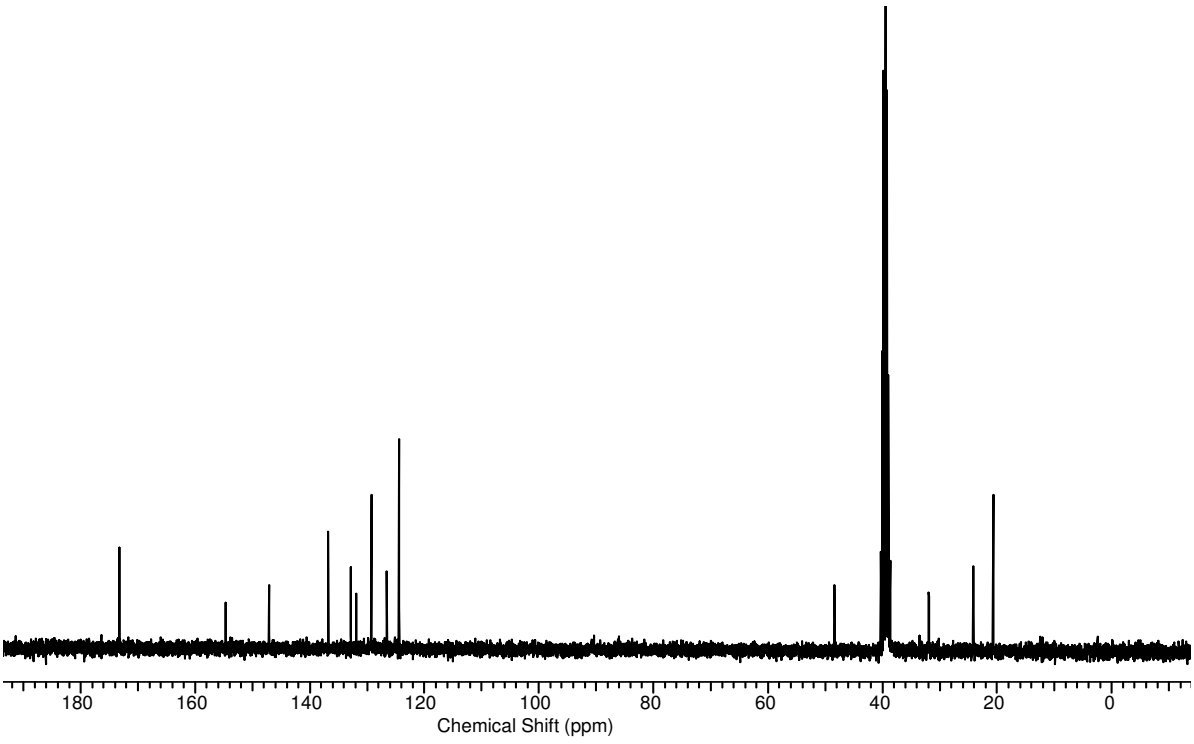
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(4,2,1)



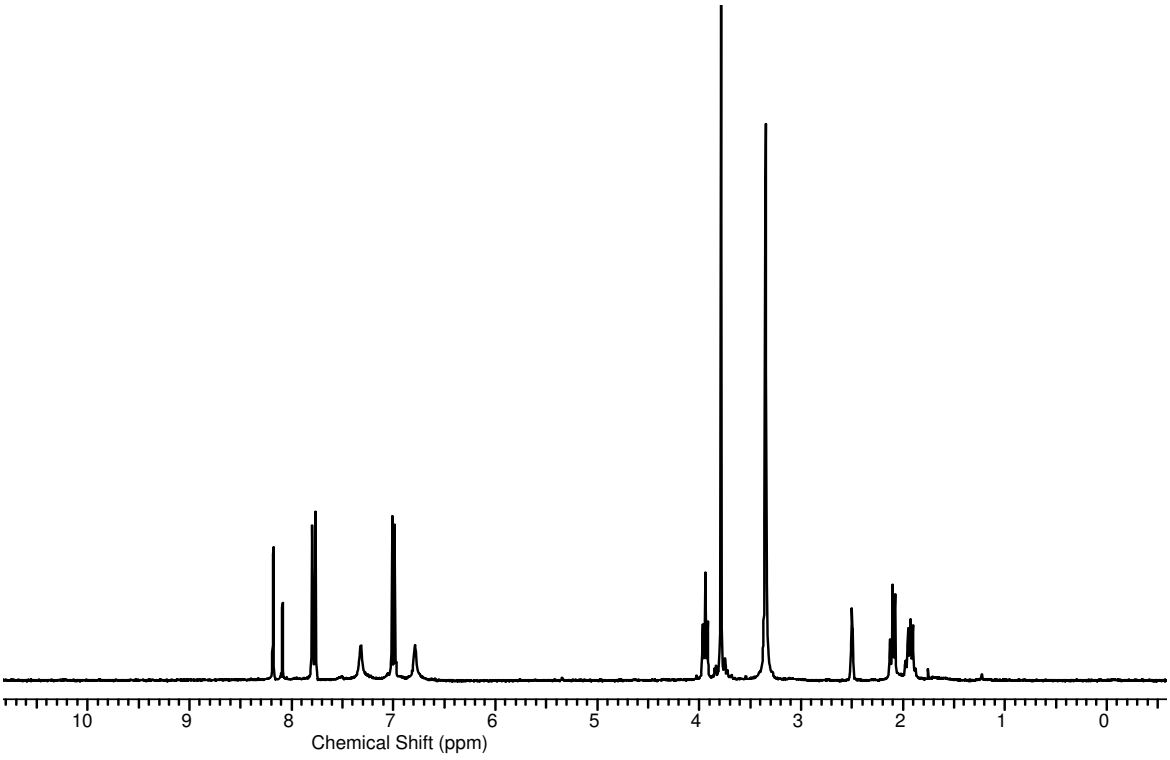


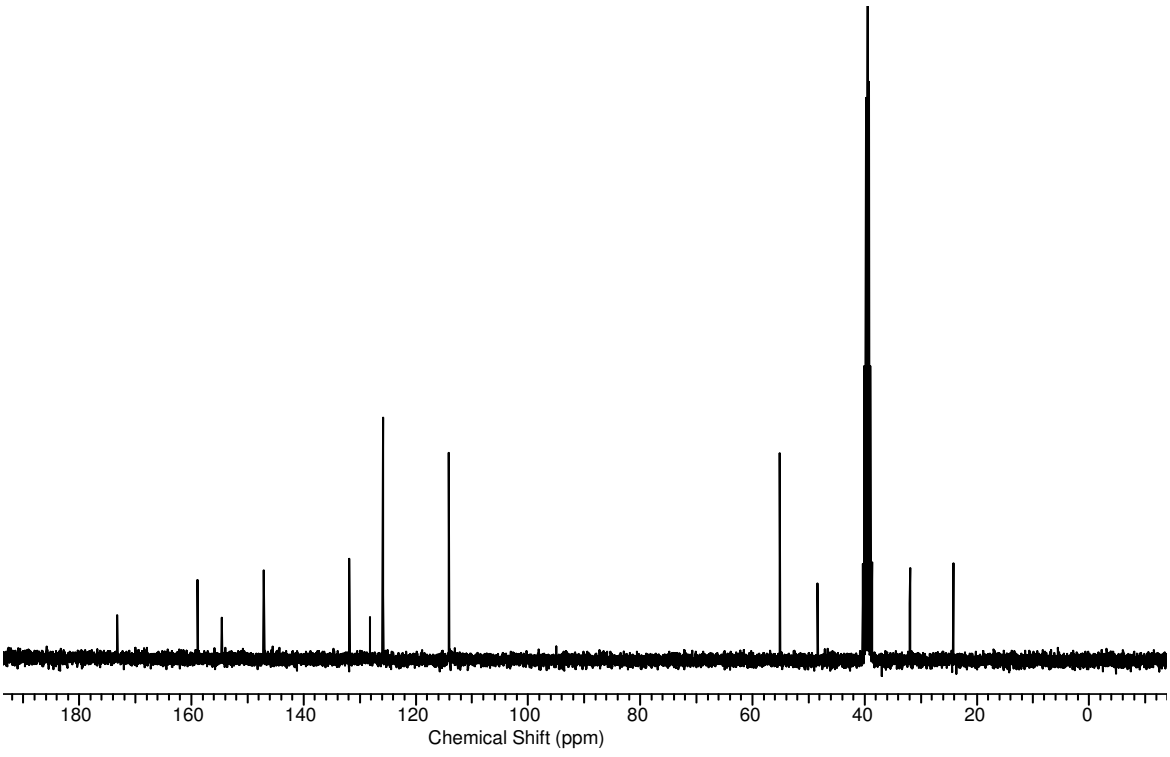
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(6,1,1)



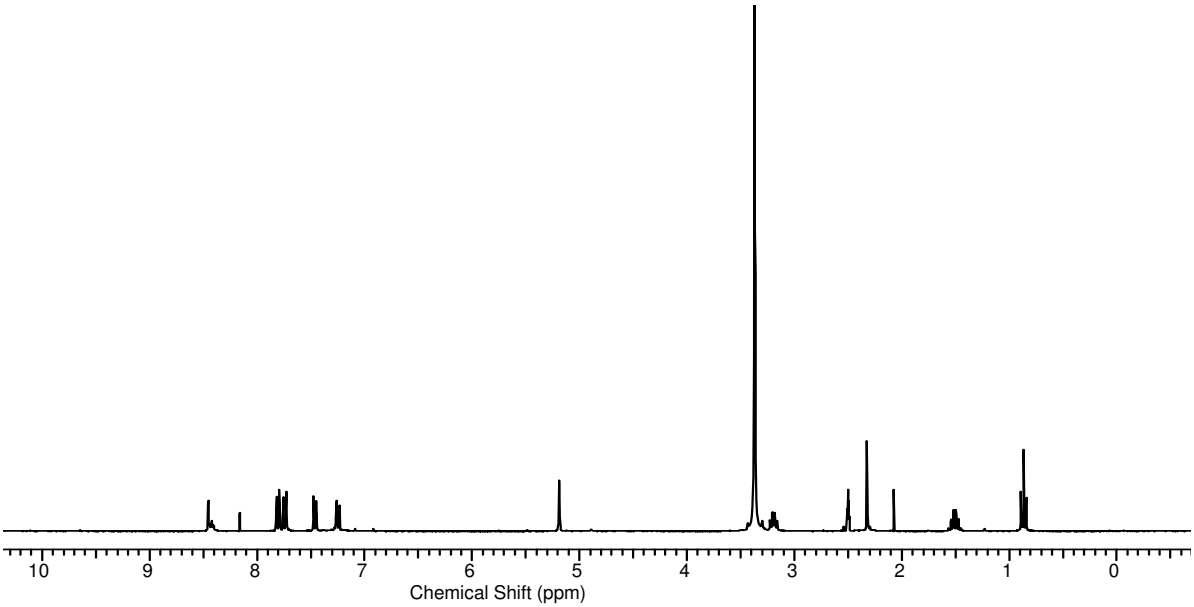


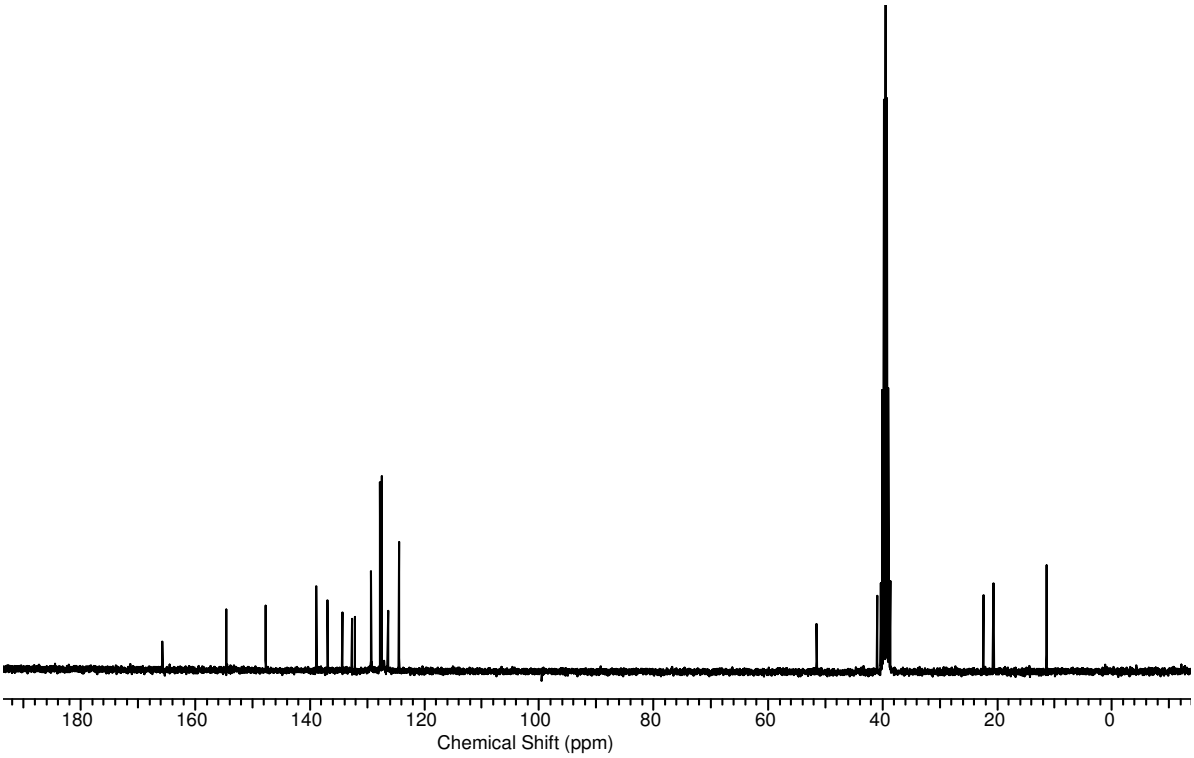
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(6,2,1)



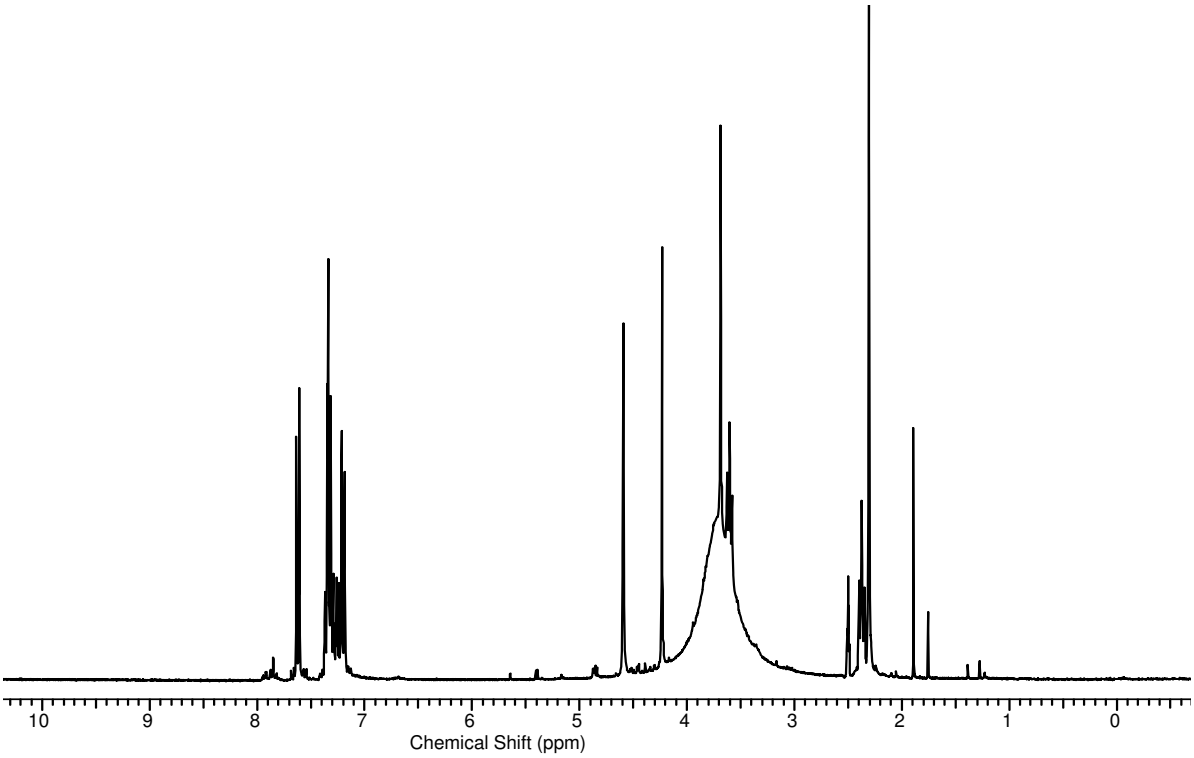


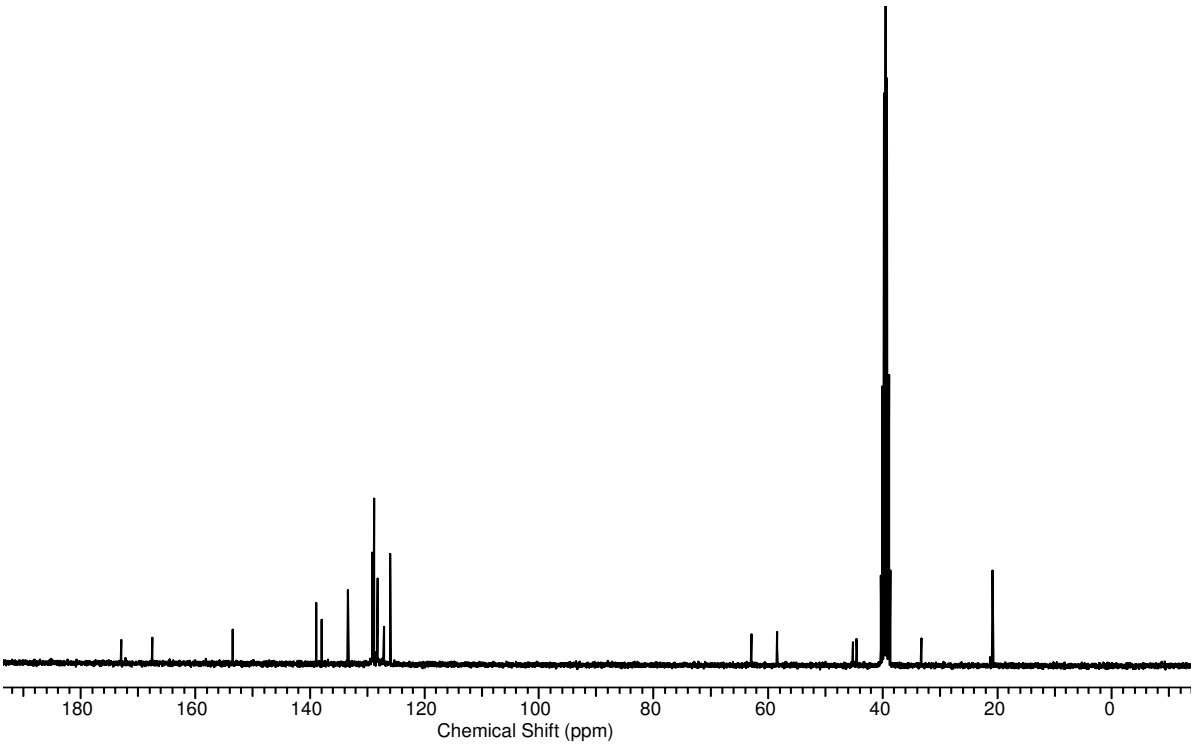
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(7,1,1)



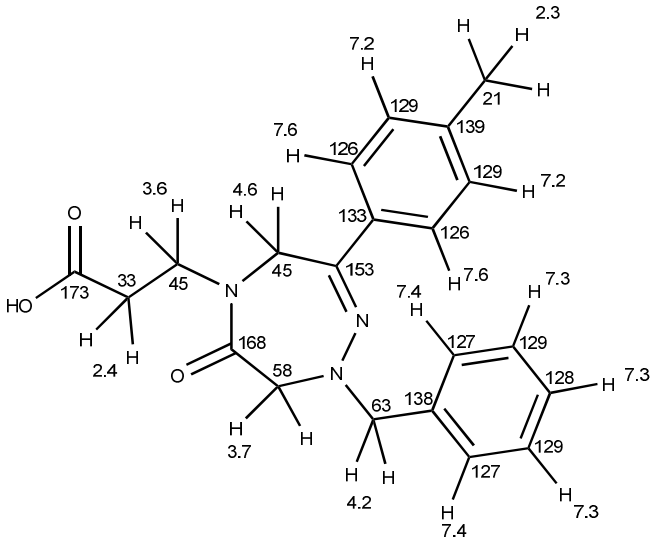


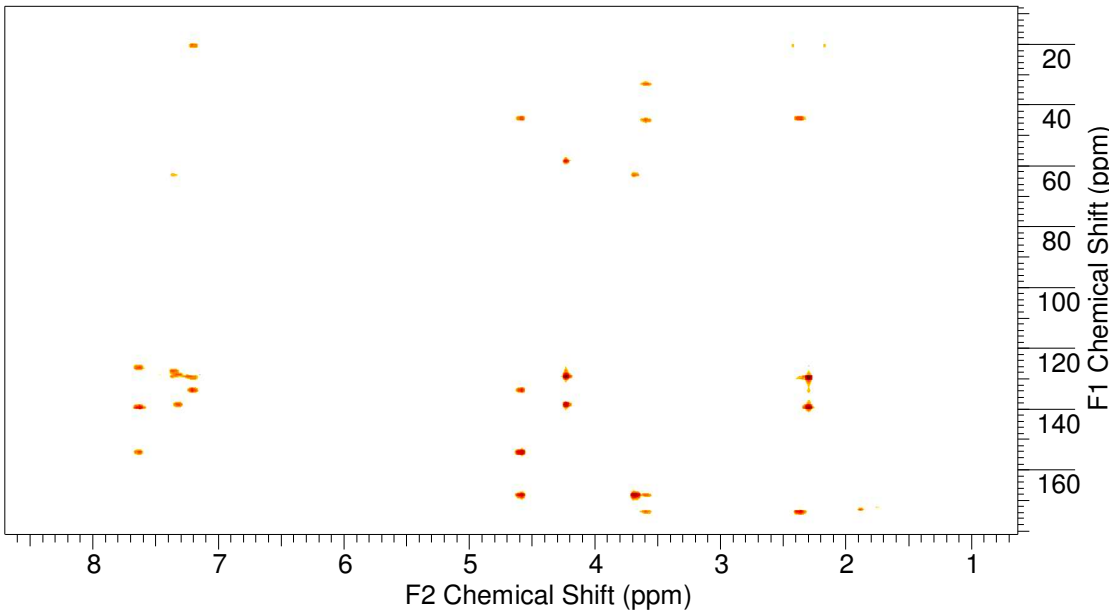
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 9(1,1,1)



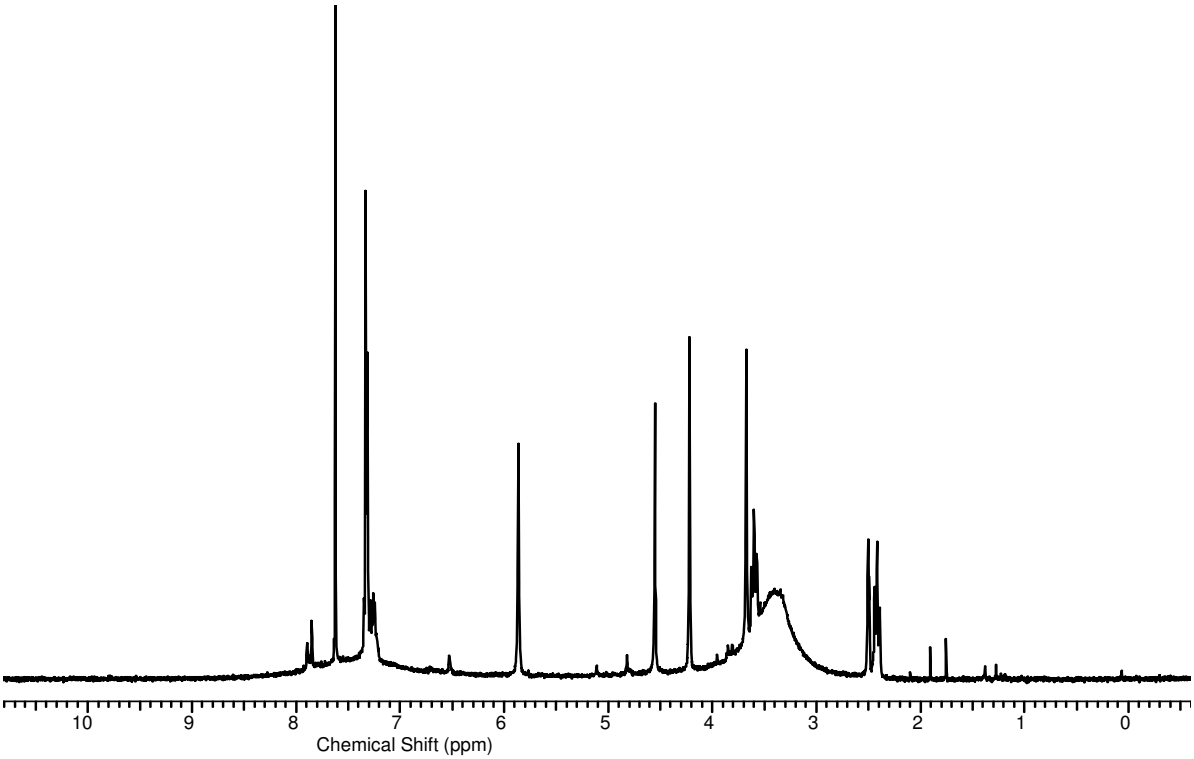


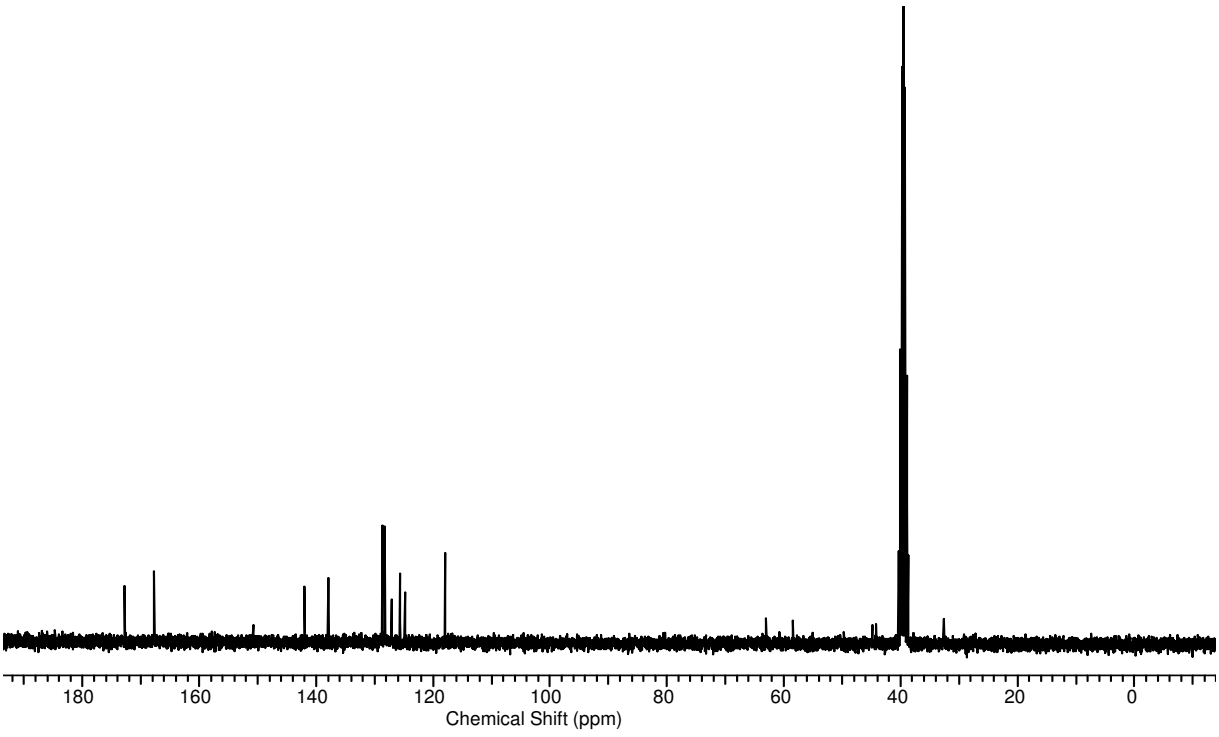
Chemical shifts and gHMBC NMR spectrum (d_6-DMSO) for compound 9(1,1,1)



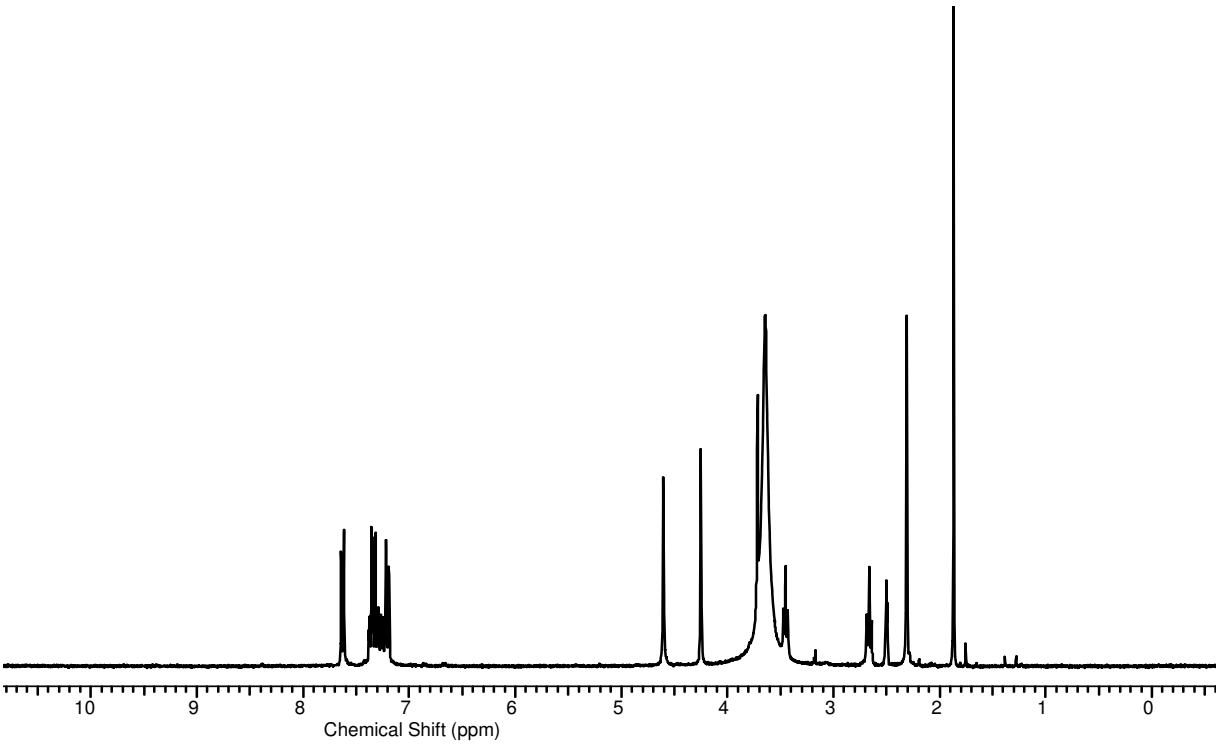


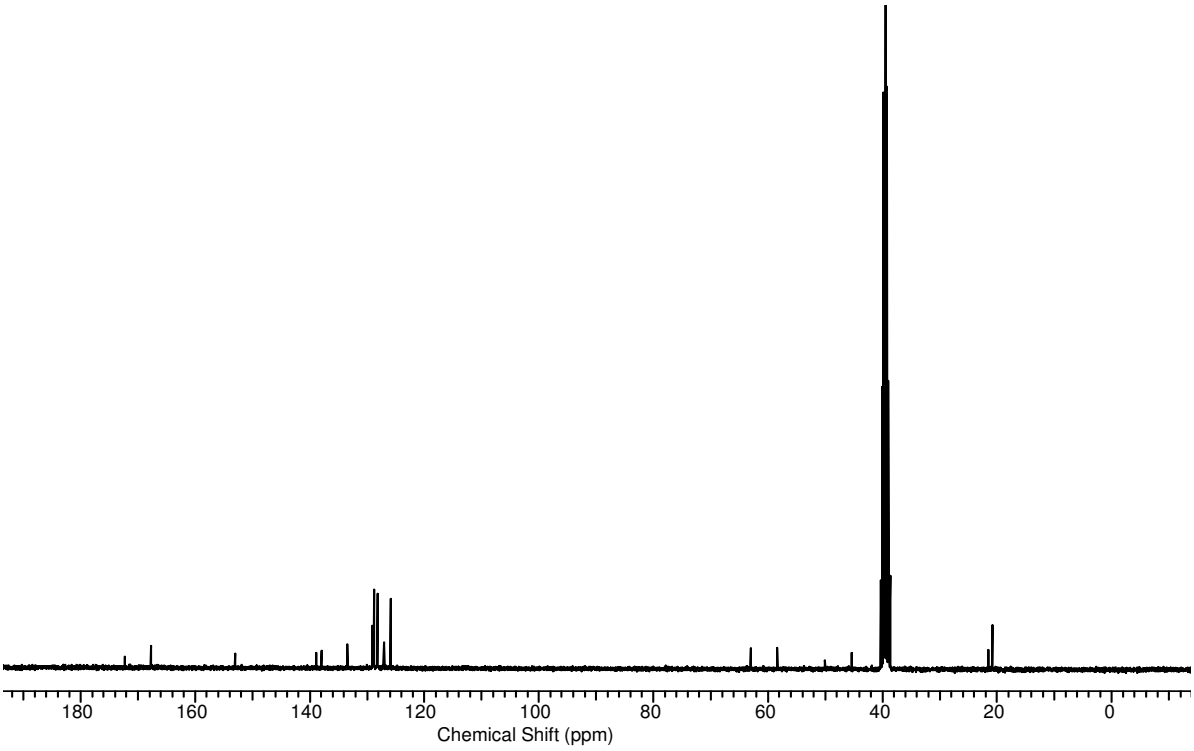
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 9(1,4,1)



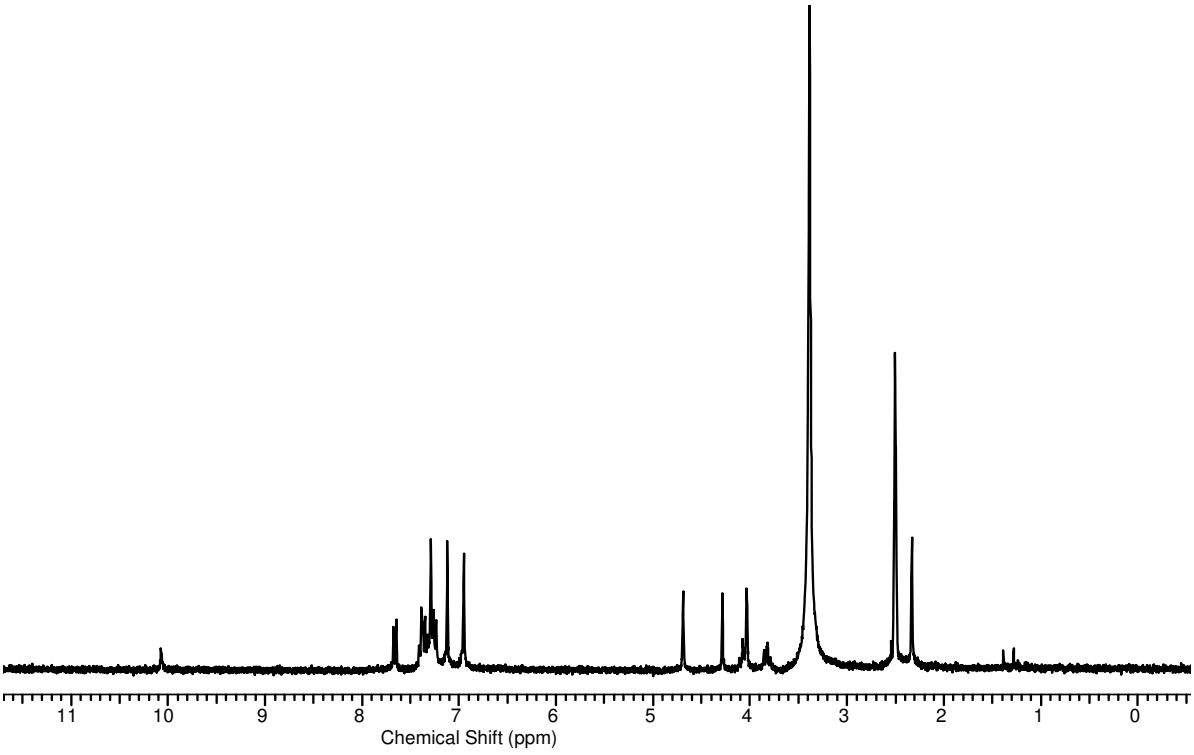


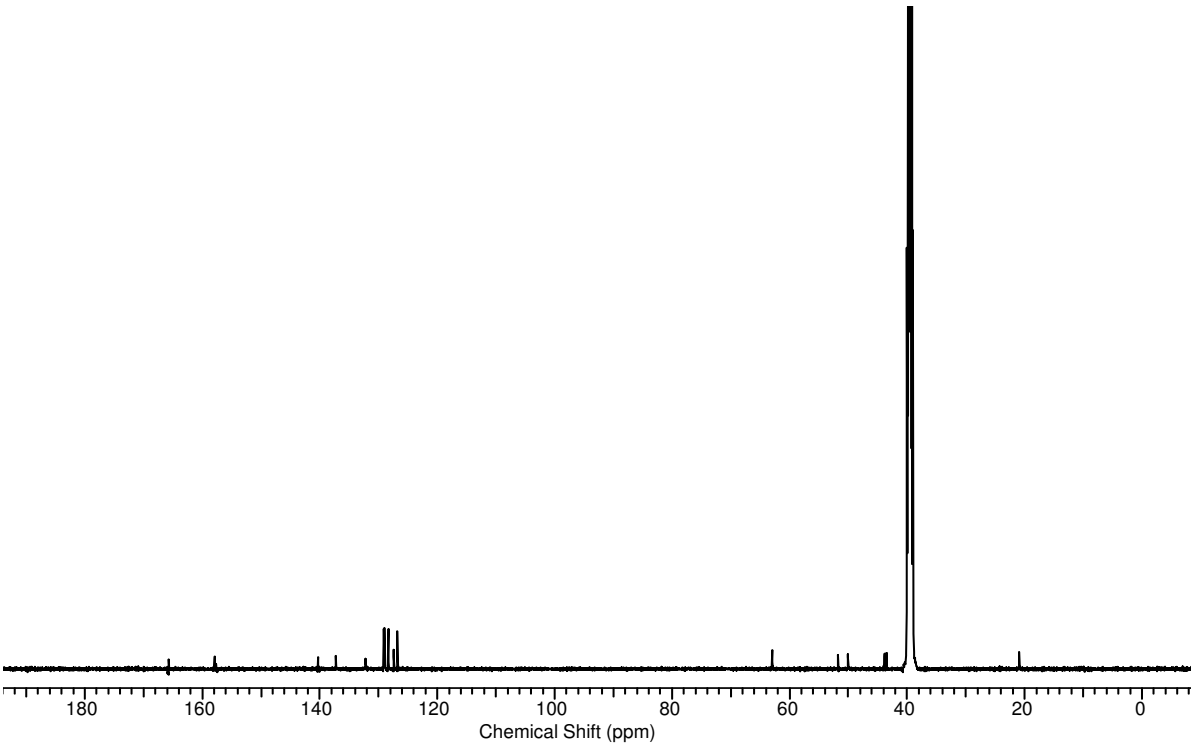
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 9(3,1,1)



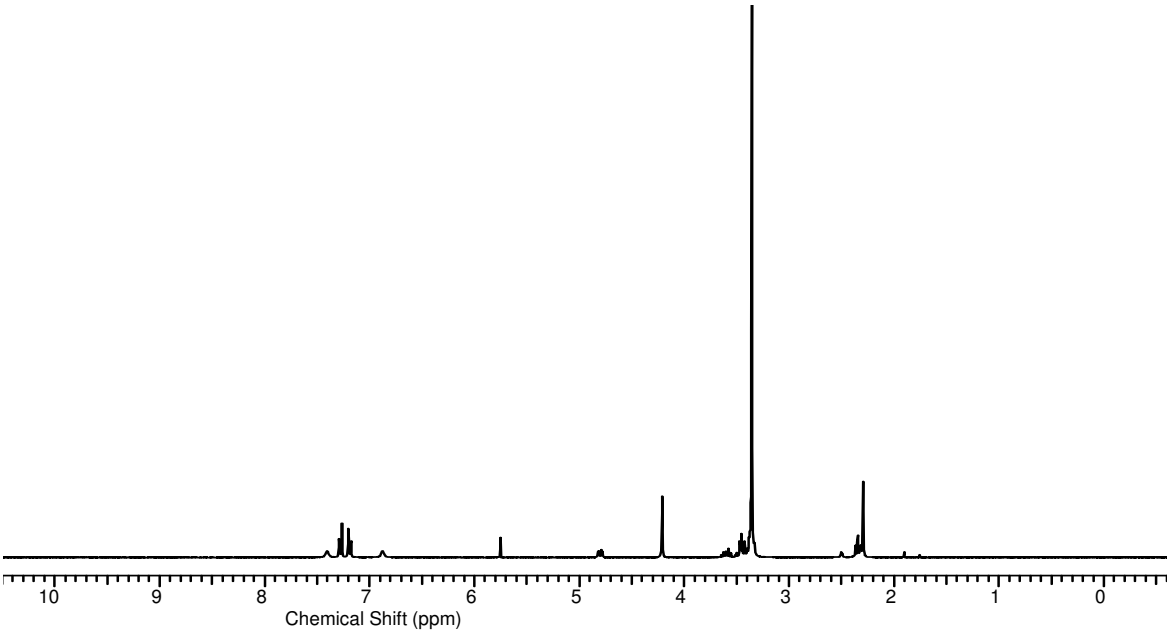


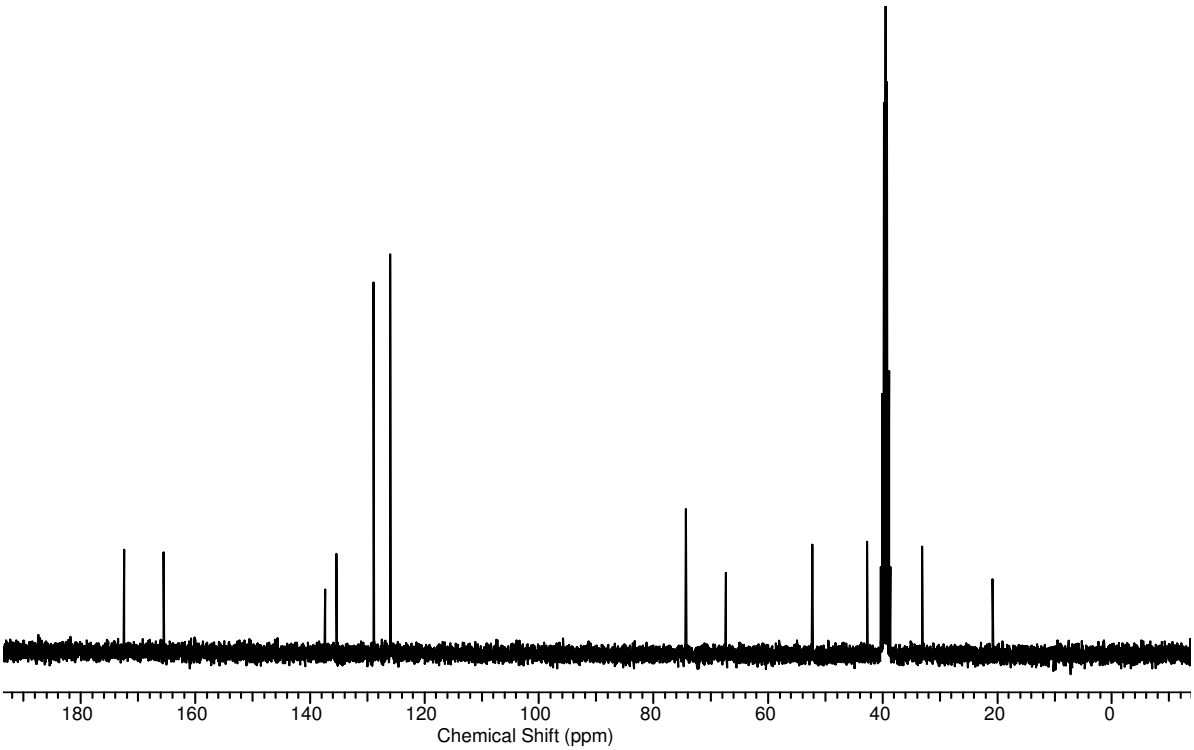
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 13(10,1,1)



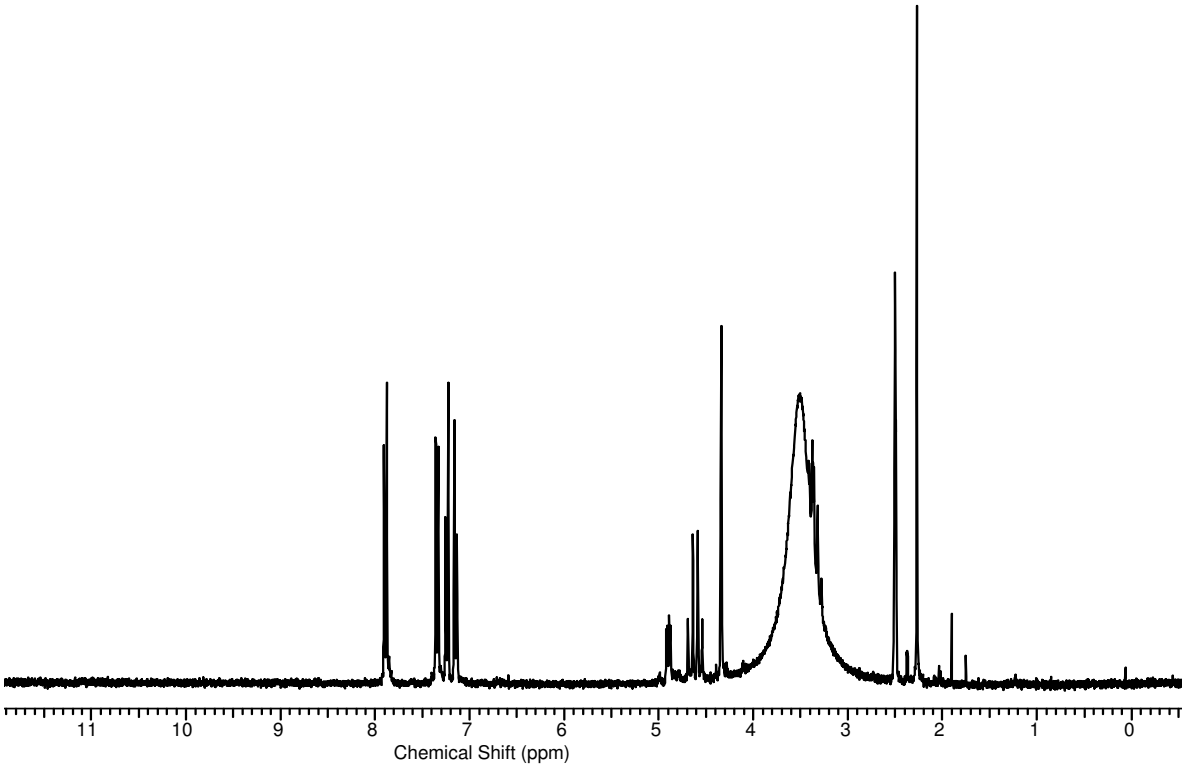


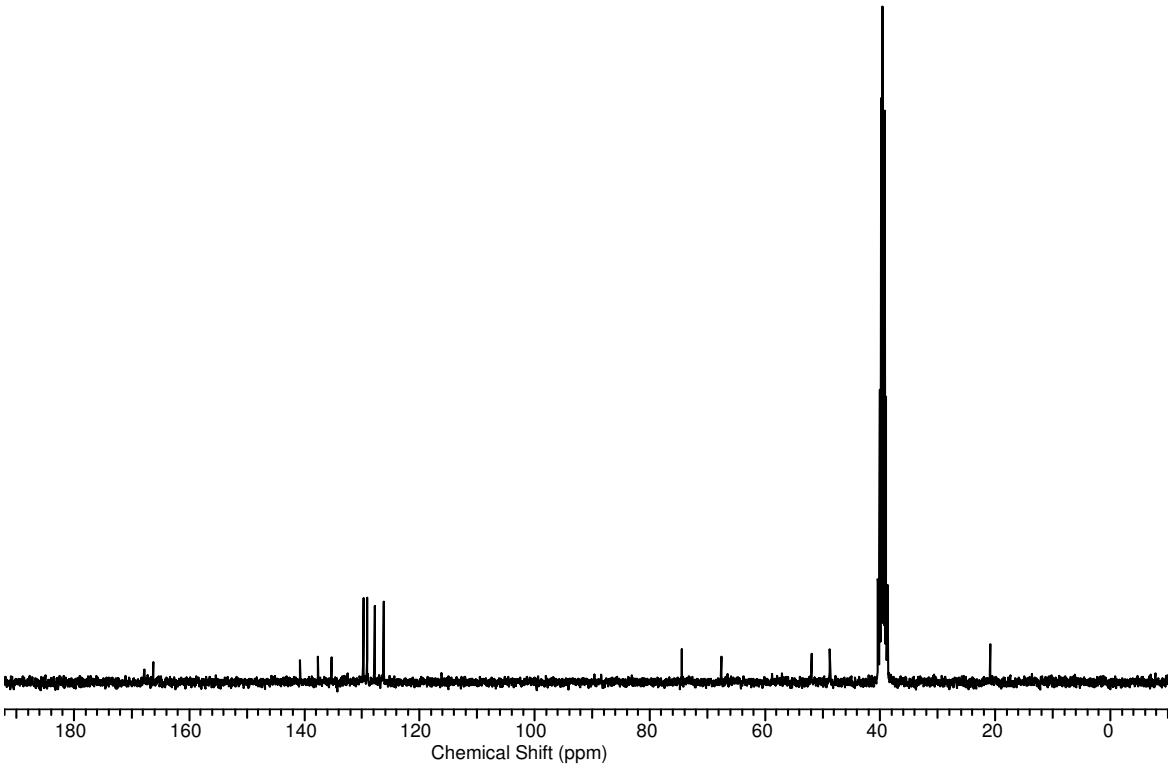
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 15(4,1,1)



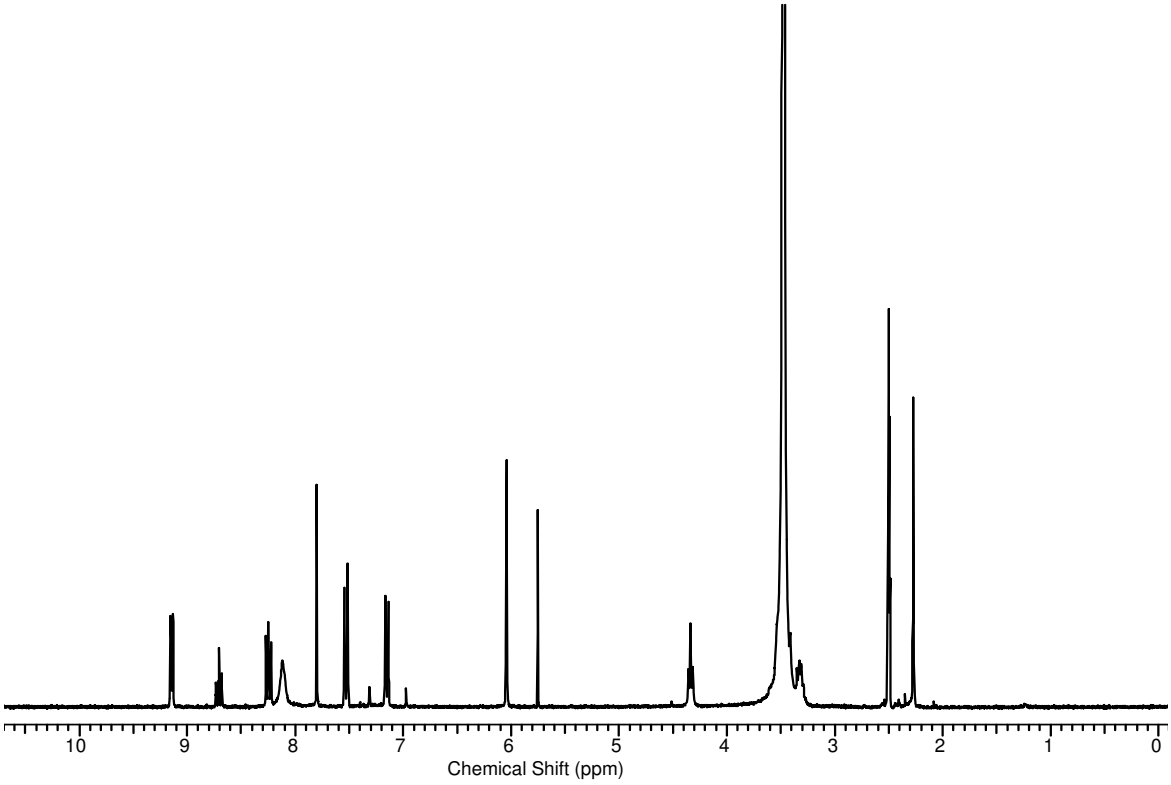


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 15(8,1,1)

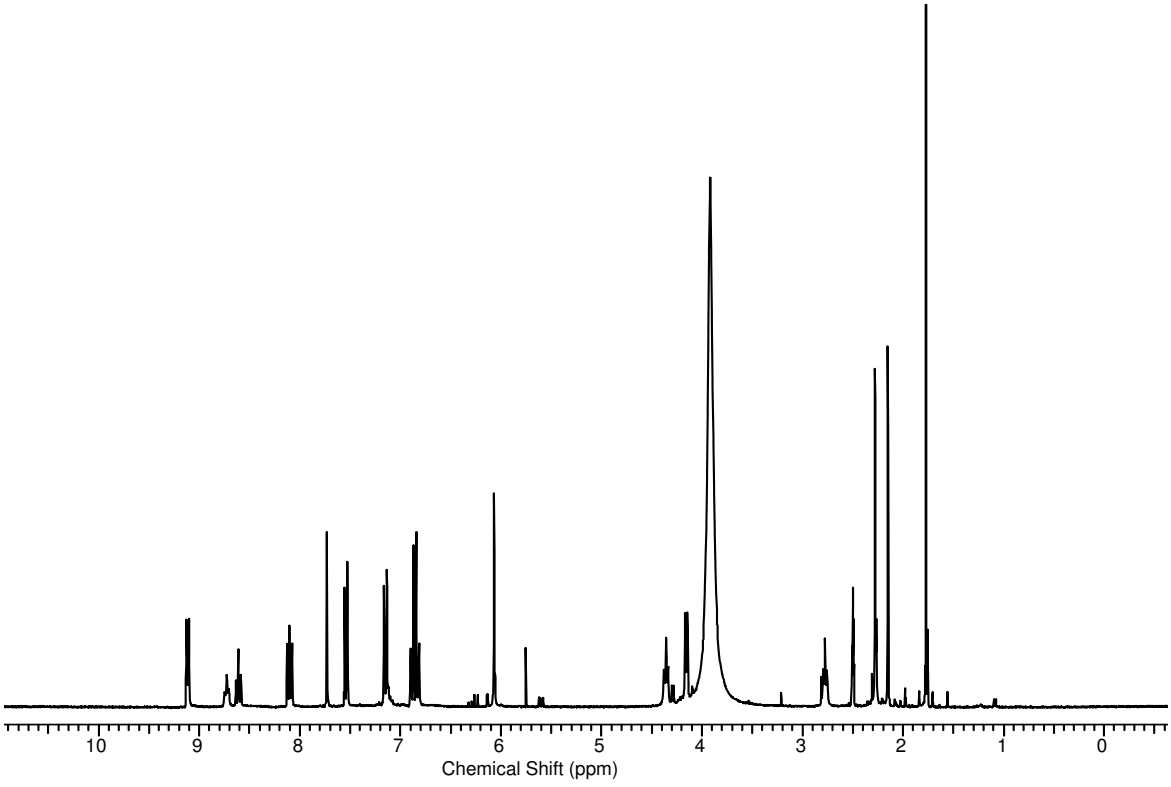


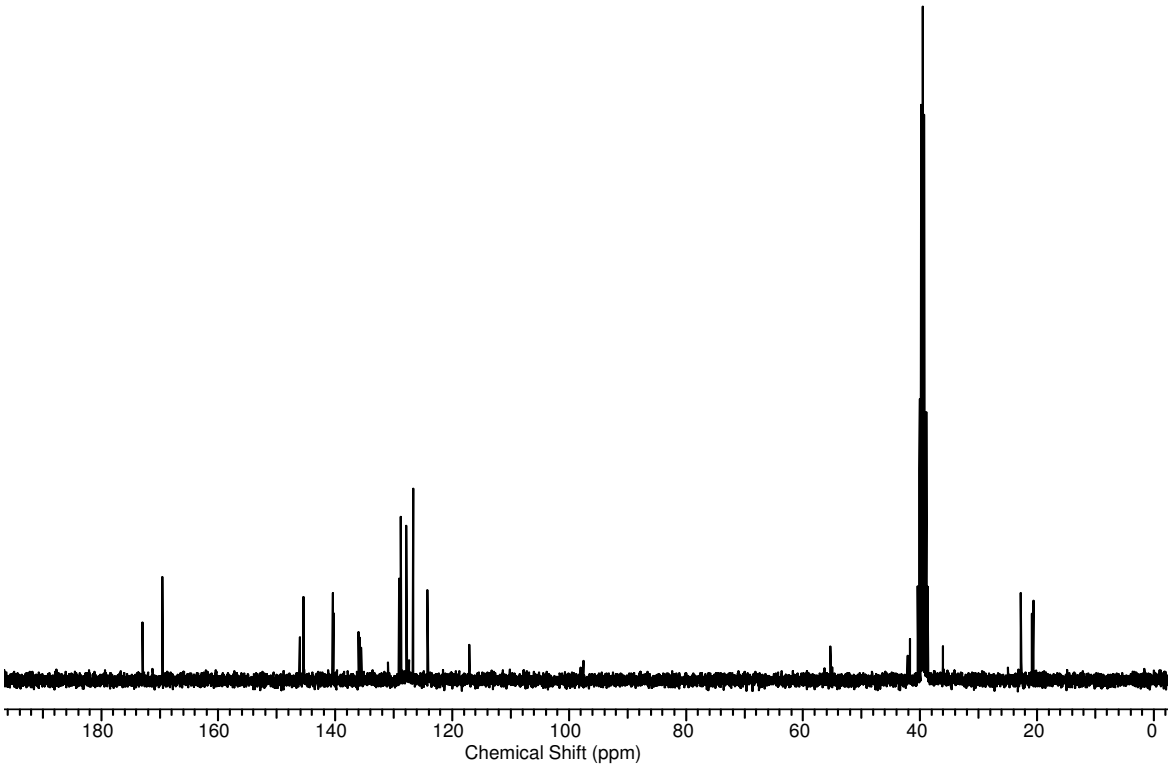


^{1}H NMR spectrum (d_6-DMSO) for compound 19(3,1,4)

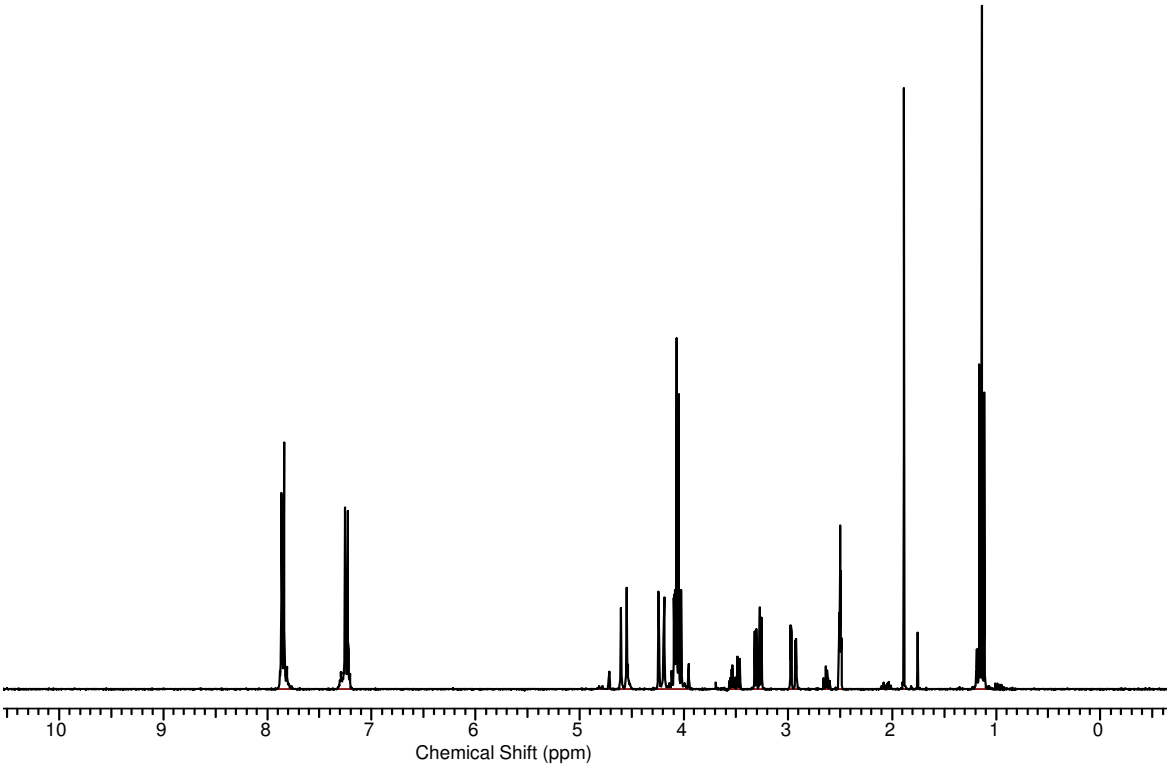


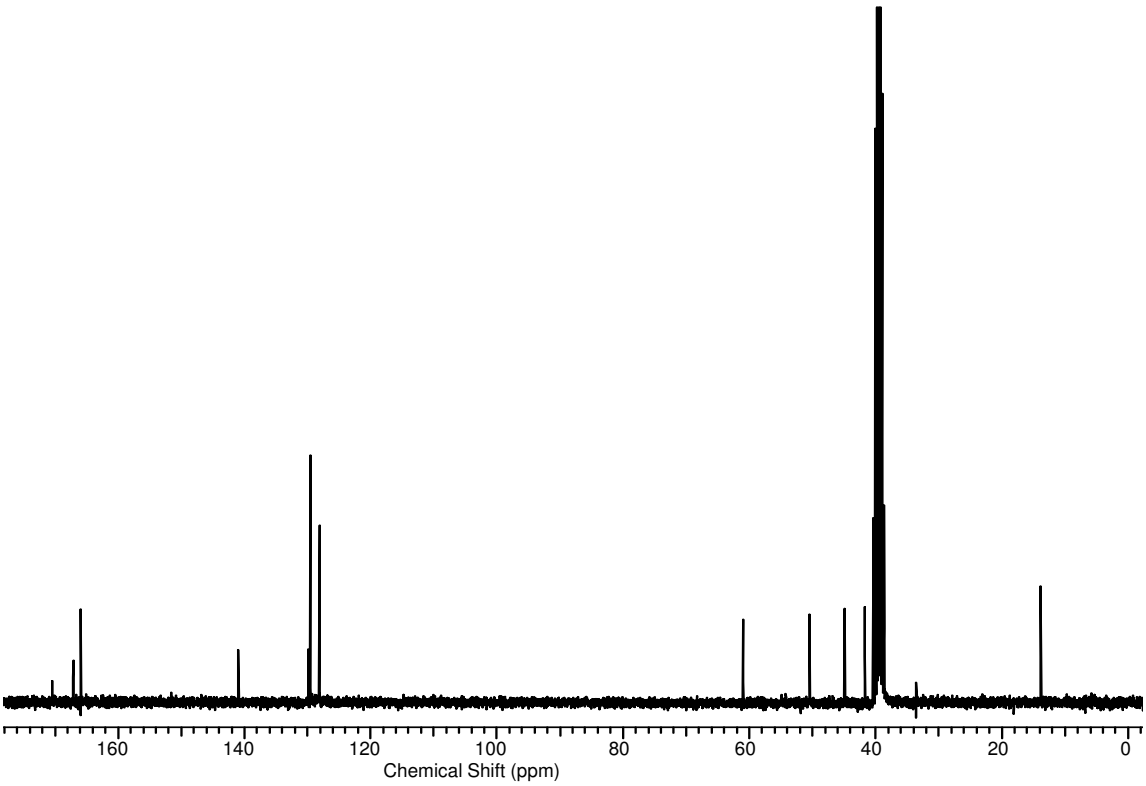
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 19(5,1,4)



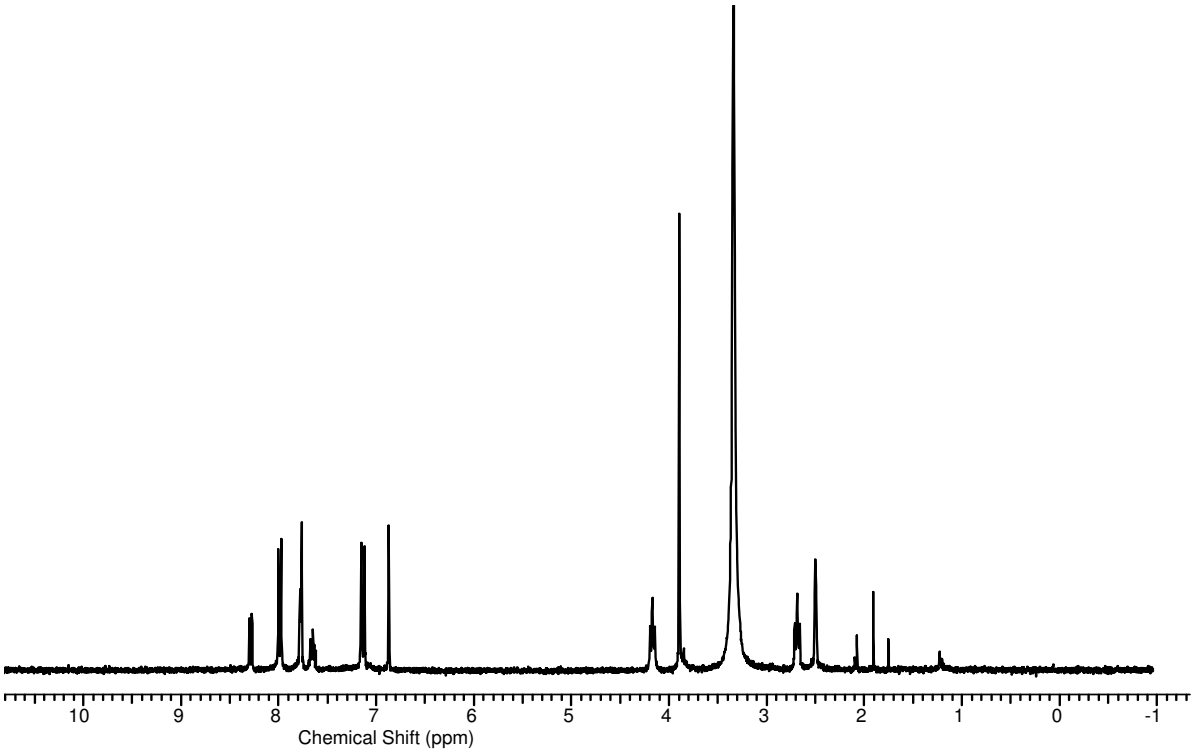


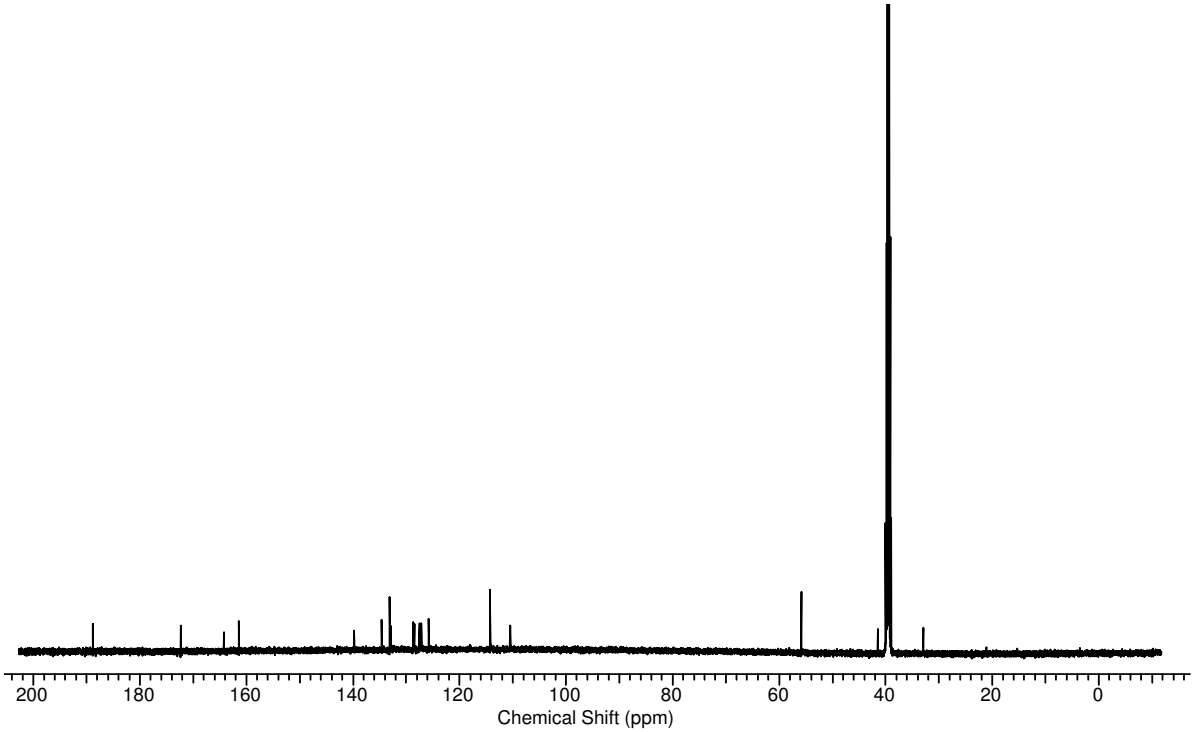
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 21(8,4,1)



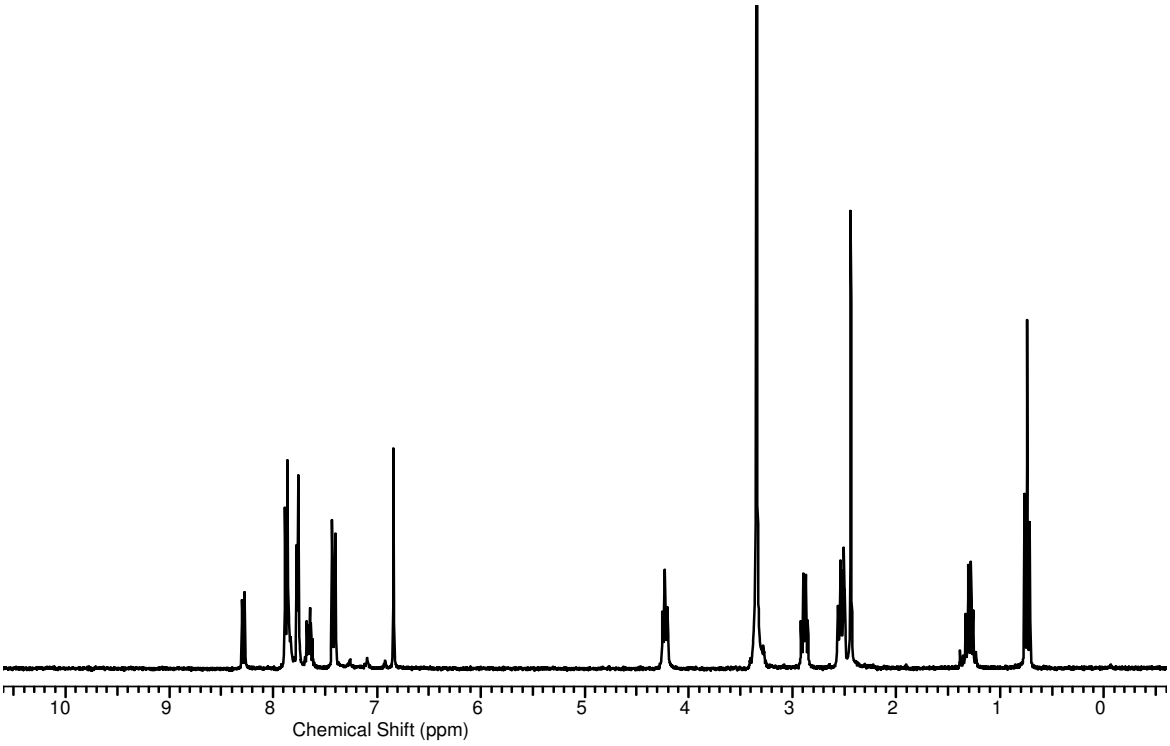


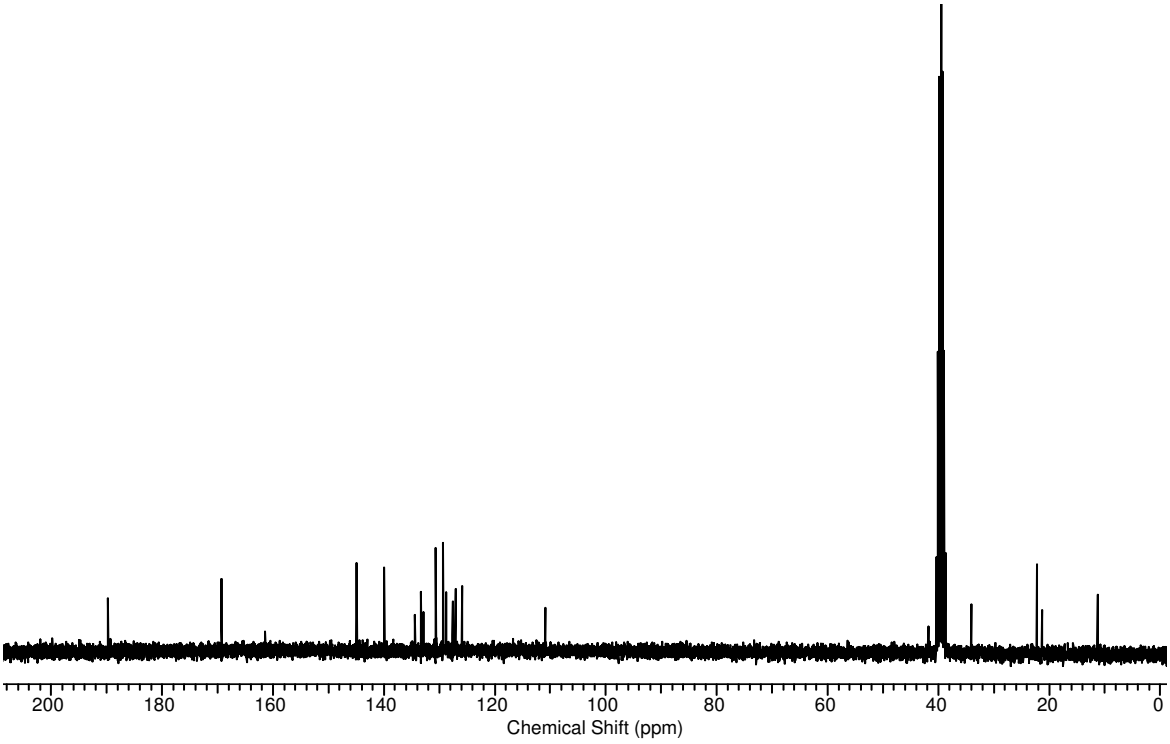
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 23(1,2,5)





^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 23(9,1,5)





^{1}H NMR spectrum (d_6-DMSO) for compound 24(10,1,5)