Supporting Information

Solid-phase synthesis and chemical properties of 2-(2-amino/hydroxyethyl)-1-aryl-3, 4-dihydropyrazino [1, 2-b] indazol-2-iums

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Material and Methods

Solvents (ACS grade) were used without further purification. The following resins were used: Rink amide resin (100-200 mesh, 1% DVB, 0.75 mmol/g) and Wang resin (100-200 mesh, 1% DVB, 1.1 mmol/g). Syntheses were carried out on Domino Blocks in disposable polypropylene reaction vessels (Torviq, Niles, MI, www.torviq.com). Labquake Tube Rotator (Thermolyne, Dubuque, IA, www.barnsteadthermolyne.com) was used for gentle but efficient tumbling of resin slurry.

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 0.5 mL of MeOH.

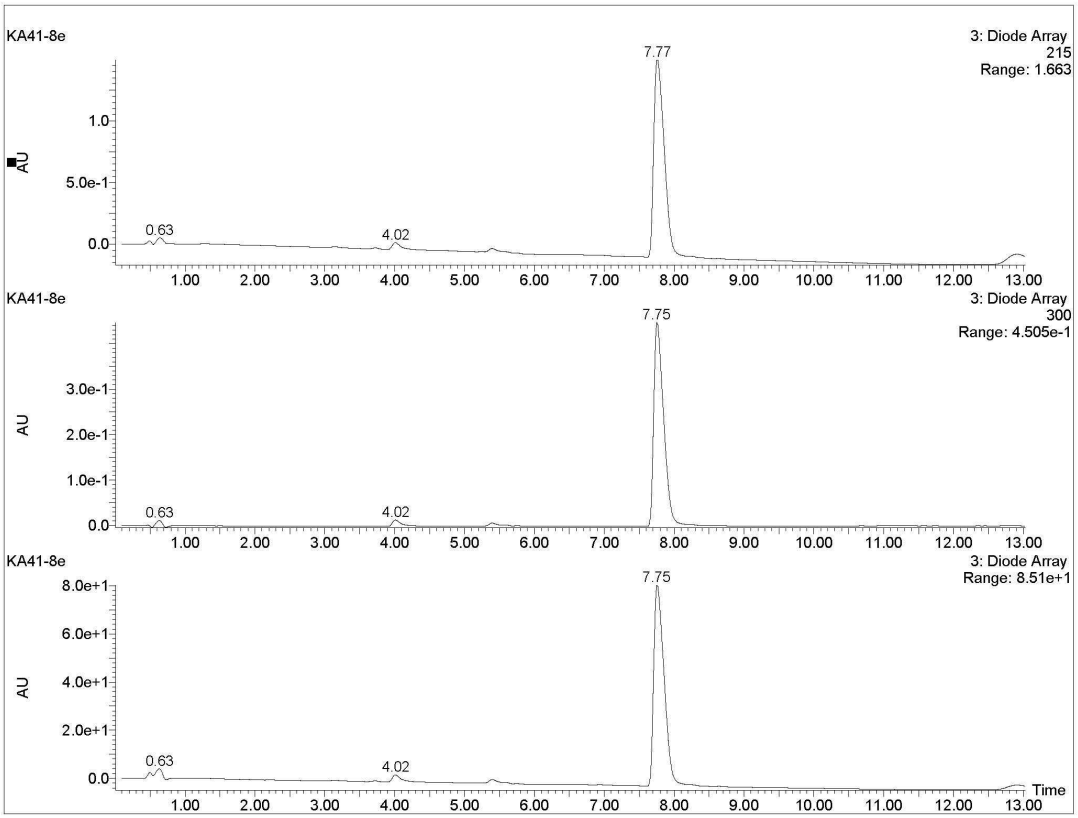
The LC/MS analyses were carried out on Waters ZQ instrument consisting of chromatography module Alliance HT, photodiode array detector 2996, and mass spectrometer Micromass ZQ, using a 3 x 50 mm Pro C18 YMC reverse phase column (Waters, Milford, MA, www.waters.com). Mobile phases: 10 mM ammonium acetate in HPLC grade water or TFA (0.1%) (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 SunFire Prep C18 OBD column 19 x 100 mm, 5 um particles (Waters, Milford, MA, www.waters.com), gradient elution using 10 mM aqueous ammonium acetate or 0.1 % TFA and acetonitrile or methanol, flow rate 15 mL/min.

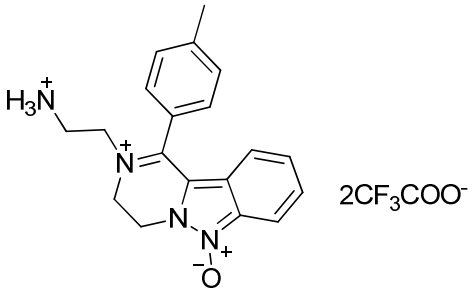
NMR $^{1}H/^{13}C$ spectra were obtained on a Varian Unity*Plus* (299.89, 500 and 600 MHz, ^{1}H) instrument. NMR spectra were recorded at ambient temperature (21 ^{o}C) in DMSO-d_6 solutions and referenced to the resonance signal of DMSO at δ = 2.50 ppm (^{1}H spectra) and δ = 39.51 ppm (^{13}C spectra). Chemical shifts, δ, are reported in ppm and coupling constants, *J,* in Hz. Acetate salts exhibited singlet at 1.7 – 1.9 ppm in the ^{1}H NMR spectrum two resonances at 173 and 23 ppm in ^{13}C spectrum. Trifuoroacetates exhibited typical quartets at 158 – 159 and 111 – 119 ppm in the ^{13}C spectrum.

Analytical data on individual compounds

LC traces of crude compound 1 reacted with Fmoc-OSu and cleaved from resin



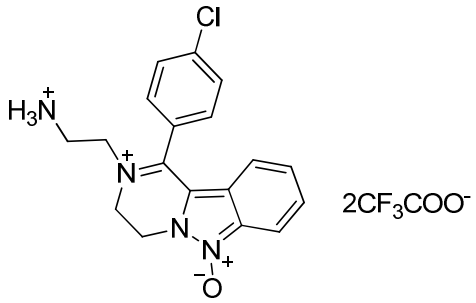
2-(2-Ammonioethyl)-1-*p*-tolyl-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(1,1)



Yield 22.1 mg (23 %). ESI-MS *m/z* = 321 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.18 (br. s., 3 H), 8.04 (d, *J* = 8.3 Hz, 1 H), 7.58 - 7.65 (m, 4 H), 7.46 - 7.58 (m, 2 H), 6.18 (d,

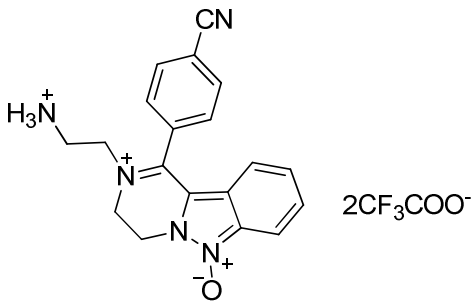
J = 8.0 Hz, 1 H), 4.83 - 4.97 (m, 2 H), 4.44 - 4.56 (m, 2 H), 3.95 (t, *J* = 6.4 Hz, 2 H, overlapped by water), 3.11 - 3.29 (m, 2 H), 2.51 (s, 3 H, overlapped by DMSO-d_6). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 155.7, 142.9, 132.6, 131.9, 130.5, 128.9, 128.2, 124.9, 123.3, 119.0, 115.0, 110.7, 50.4, 47.5, 40.6, 36.6, 21.3. HRMS (FAB) *m/z* calcd for $C_{19}H_{21}N_4O$+ [M]+ 321.1715, found 321.1737.

2-(2-Ammonioethyl)-1-(4-chlorophenyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(1,3)



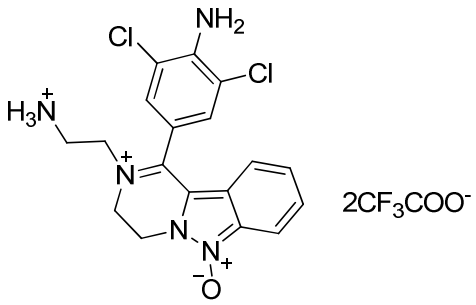
Yield 54.8 mg (59%). ESI-MS *m/z* = 341 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.20 (br. s., 3 H), 8.04 - 8.07 (m, 1 H), 7.86 - 7.90 (m, 2 H), 7.76 - 7.80 (m, 2 H), 7.57 - 7.61 (m, 1 H), 7.53 - 7.57 (m, 1 H), 6.24 - 6.28 (m, 1 H), 4.87 - 4.93 (m, 2 H), 4.48 - 4.53 (m, 2 H), 3.93 (t, *J* = 6.4 Hz, 2 H), 3.17 - 3.26 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 154.3, 137.7, 132.7, 132.2, 131.0, 130.3, 128.3, 126.5, 123.2, 118.9, 115.0, 110.6, 50.5, 47.5, 40.7, 36.6. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}ClN_4O$+ [M]+ 341.1164, found 341.1156.

2-(2-Ammonioethyl)-1-(4-cyanophenyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(1,4)



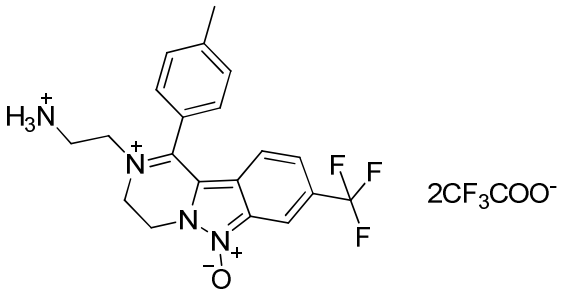
Yield 25.3 mg (28%). ESI-MS *m/z* = 332 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.26 - 8.31 (m, 2 H), 8.16 (br. t., 3 H), 8.07 (d, *J* = 8.6 Hz, 1 H), 7.93 - 7.98 (m, 2 H), 7.60 (ddd, *J* = 1.0, 7.2, 8.4 Hz, 1 H), 7.52 (ddd, *J* = 1.0, 7.2, 8.4 Hz, 1 H), 6.21 (d, *J* = 8.4 Hz, 1 H), 4.88 - 4.95 (m, 2 H), 4.47 - 4.56 (m, 2 H), 3.88 (t, *J* = 6.5 Hz, 2 H), 3.16 - 3.27 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 153.4, 134.1, 132.8, 132.5, 132.0, 130.1, 128.5, 123.1, 119.0, 118.1, 115.3, 115.1, 110.4, 50.6, 47.5, 40.9, 36.5. HRMS (FAB) *m/z* calcd for $C_{19}H_{18}N_5O$+ [M]+ 332.1506, found 332.1480.

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



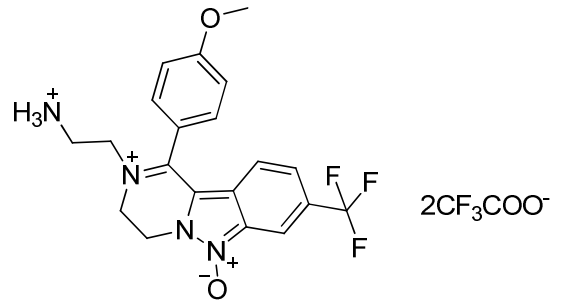
Yield 93.3 mg (99%). ESI-MS *m/z* = 390 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.06 - 8.13 (m, 3 H), 8.05 (dd, *J* = 2.5, 6.1 Hz, 1 H), 7.66 (s, 2 H), 7.58 - 7.62 (m, 2 H), 6.67 (br. s., 2 H), 6.65 (dd, *J* = 2.5, 6.3 Hz, 1 H), 4.79 - 4.85 (m, 2 H), 4.37 - 4.44 (m, 2 H), 4.04 (t, *J* = 6.2 Hz, 2 H), 3.18 - 3.26 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 153.4, 145.4, 132.5, 132.0, 129.7, 128.2, 123.2, 119.2, 118.3, 114.9, 114.1, 110.8, 50.3, 47.3, 40.6, 36.9. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}Cl_2N_5O$+ [M]+ 390.0883, found 390.0875.

2-(2-Ammonioethyl)-1-*p*-tolyl-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(2,1)



Yield 55.8 mg (82%). ESI-MS *m/z* = 389 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.50 (s, 1 H), 8.11 (br. s., 3 H), 7.81 (d, *J* = 8.8 Hz, 1 H), 7.59 - 7.65 (m, 4 H), 6.36 (d, *J* = 8.8 Hz, 1 H), 4.92 - 4.98 (m, 2 H), 4.50 - 4.56 (m, 2 H), 3.99 (t, *J* = 6.5 Hz, 2 H), 3.19 - 3.27 (m, 2 H), 2.52 (s, 3 H, overlapped by DMSO-d_6). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 157.0, 143.3, 131.7, 130.6, 129.1, 128.0, 127.8, 127.4, 124.5, 124.4 – 124.5 (m), 120.8, 113.6 - 113.7 (m), 110.6, 50.7, 47.7, 40.8, 36.5, 21.4. HRMS (FAB) *m/z* calcd for $C_{20}H_{20}F_3N_4O$+ [M]+ 389.1589, found 388.1586.

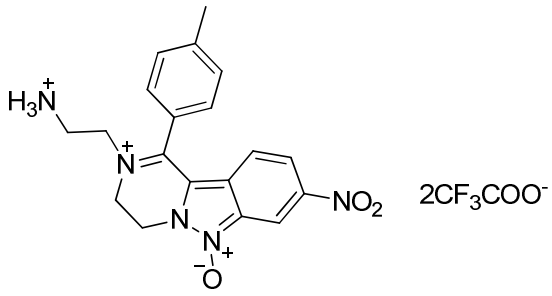
2-(2-Ammonioethyl)-1-(4-methoxyphenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(2,2)



Yield 43.7 mg (55%). ESI-MS *m/z* = 405 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.47 - 8.52 (m, 1 H), 8.16 (br. s., 3 H), 7.81 (dd, *J* = 1.5, 9.0 Hz, 1 H), 7.65 - 7.72 (m, 2 H), 7.31 - 7.38 (m, 2 H), 6.50 (d, *J* = 8.8 Hz, 1 H), 4.89 - 4.98 (m, 2 H), 4.47 - 4.57 (m, 2 H), 4.05 (t, *J* = 6.4 Hz, 2 H), 3.93 (s, 3 H), 3.17 - 3.30 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 162.8, 156.9, 131.6, 131.5, 129.6, 127.6, 127.1, 124.4, 121.0, 119.0, 115.5, 113.4 –

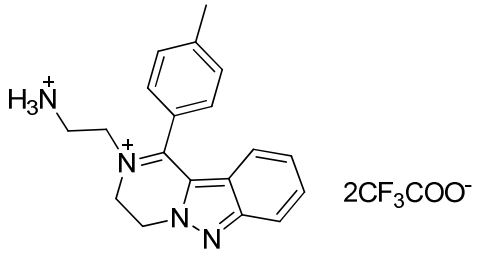
113.5 (m), 110.8, 55.7, 50.7, 47.6, 40.7, 36.6. HRMS (FAB) *m/z* calcd for $C_{20}H_{20}F_3N_4O_2$+ [M]+ 405.1538, found 405.1536.

2-(2-Ammonioethyl)-8-nitro-1-*p*-tolyl-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 7(3,1)



Yield 21.6 mg (33%). ESI-MS *m/z* = 366 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.83 (d, *J* = 1.4 Hz, 1 H), 8.21 (dd, *J* = 2.1, 9.3 Hz, 1 H), 8.16 (br. s., 3 H), 7.63 (s, 4 H), 6.34 (d, *J* = 9.1 Hz, 1 H), 4.92 - 5.03 (m, 2 H), 4.51 - 4.60 (m, 2 H), 4.02 (t, *J* = 6.4 Hz, 2 H), 3.17 - 3.31 (m, 2 H), 2.52 (s, 3 H, overlapped by DMSO-d_6). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 157.6, 146.2, 143.5, 131.5, 130.7, 129.0, 125.3, 124.9, 124.4, 120.5, 112.3, 110.8, 50.9, 47.8, 41.0, 36.5, 21.4. HRMS (FAB) *m/z* calcd for $C_{19}H_{20}N_5O_3$+ [M]+ 366.1566, found 366.1580.

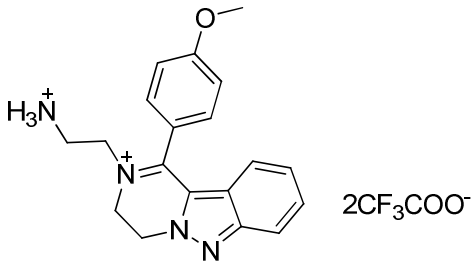
2-(2-Ammonioethyl)-1-*p*-tolyl-3,4-dihydropyrazino[1,2-*b*]indazol-2-ium 2,2,2-trifluoroacetate 8(1,1)



Yield 16 mg (56%). ESI-MS *m/z* = 305 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.32 (br. s., 3 H), 8.03 (d, *J*=8.8 Hz, 1 H), 7.65 (d, *J*=8.3 Hz, 2 H), 7.59 (d, *J*=8.0 Hz, 2 H), 7.44 -

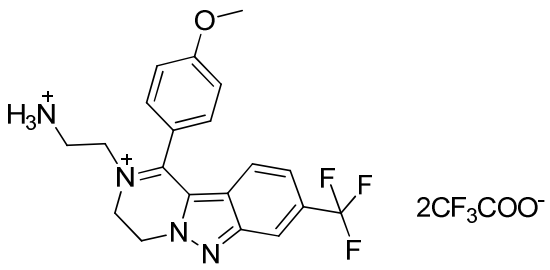
7.52 (m, 1 H), 7.26 - 7.33 (m, 1 H), 6.12 (d, *J*=8.3 Hz, 1 H), 5.11 - 5.25 (m, 2 H), 4.60 - 4.77 (m, 2 H), 4.15 (t, *J*=6.4 Hz, 2 H), 3.32 (br. s., 2 H), 2.50 (s, 3 H, overlapped by DMSO-d_6). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 164.1, 148.7, 143.1, 130.4, 128.5, 128.4, 127.7, 125.3, 124.9, 124.2, 119.9, 118.4, 51.6, 49.6, 46.8, 36.4, 21.3. HRMS (FAB) *m/z* calcd for $C_{19}H_{21}N_4$+ [M]+ 305.1761, found 305.1758

2-(2-Ammonioethyl)-1-(4-methoxyphenyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 2,2,2-trifluoroacetate 8(1,2)



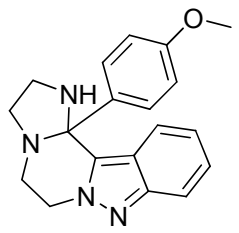
Yield 52.0 mg (76%). ESI-MS *m/z* = 321 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.22 (br. s., 3 H), 8.05 (d, *J* = 8.6 Hz, 1 H), 7.66 - 7.73 (m, 2 H), 7.50 (ddd, *J* = 1.0, 7.1, 8.5 Hz, 1 H), 7.30 - 7.38 (m, 3 H), 6.27 (d, *J* = 8.3 Hz, 1 H), 5.12 - 5.23 (m, 2 H), 4.61 - 4.72 (m, 2 H), 4.19 (t, *J* = 6.4 Hz, 2 H), 3.92 (s, 3 H), 3.24 - 3.42 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 163.9, 162.7, 148.6, 130.9, 128.4, 127.7, 125.4, 124.2, 119.8, 119.4, 118.5, 115.3, 55.7, 51.4, 49.5, 46.8, 36.4. HRMS (FAB) *m/z* calcd for $C_{19}H_{21}N_4O$+ [M]+ 321.1739, found 321.1727.

2-(2-Ammonioethyl)-1-(4-methoxyphenyl)-8-(trifluoromethyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 2,2,2-trifluoroacetate 8(2,2)



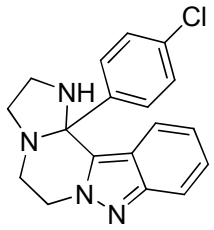
Yield 74.5 mg (97 %). ESI-MS *m/z* = 389 [M]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.55 - 8.60 (m, 1 H), 8.23 (br. s., 3 H), 7.68 - 7.76 (m, 2 H), 7.63 (dd, *J* = 1.2, 9.0 Hz, 1 H), 7.32 - 7.40 (m, 2 H), 6.47 (d, *J* = 8.8 Hz, 1 H), 5.20 - 5.31 (m, 2 H), 4.65 - 4.78 (m, 2 H), 4.25 (t, *J* = 5.9 Hz, 2 H), 3.95 (s, 3 H), 3.28 - 3.43 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 164.4, 163.0, 147.2, 131.3, 126.0, 125.4, 125.0, 123.7, 122.8, 120.6, 119.0, 118.1 - 118.4 (m), 115.4, 55.8, 51.7, 49.6, 47.1, 36.4. HRMS (FAB) *m/z* calcd for $C_{20}H_{20}F_3N_4O$+ [M]+ 389.1589, found 389.1570.

10c-(4-Methoxyphenyl)-1,2,3,4,5,10c-hexahydro-1,3a,5a,6-tetraaza-cyclopenta[c]fluorene 10(1,2)



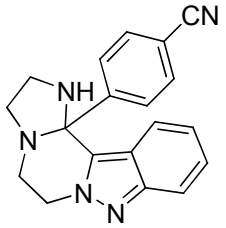
Yield 16.1 mg (69%). ESI-MS *m/z* = 321 [M+H]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.57 (d, *J*=8.8 Hz, 2 H), 7.51 (d, *J*=8.8 Hz, 1 H), 7.34 (d, *J*=8.3 Hz, 1 H), 7.14 (ddd, *J*=8.6, 6.6, 1.1 Hz, 1 H), 6.84 - 6.93 (m, 1 H), 6.83 (d, *J*=8.8 Hz, 2 H), 4.42 - 4.65 (m, 2 H), 3.70 (s, 3 H), 3.31 (ddd, *J*=12.5, 8.5, 4.1 Hz, 1 H), 3.04 - 3.18 (m, 2 H), 2.71 - 2.90 (m, 3 H), 2.50 (dt, *J*=3.6, 1.8 Hz, 1 H). ^{13}C NMR (125 MHz, DMSO-d_6) δ: 172.0, 158.5, 147.3, 135.5, 133.5, 128.4, 125.3, 120.8, 120.2, 118.9, 116.6, 113.1, 81.8, 54.9, 50.3, 47.2, 45.6, 44.2, 21.1. HRMS (FAB) *m/z* calcd for $C_{19}H_{21}N_4O$ [M + H]+ 321.1710, found 321.1695

10c-(4-Chlorophenyl)-1,2,3,4,5,10c-hexahydro-1,3a,5a,6-tetraaza-cyclopenta[c]fluorene 10(1,3)



Yield 17.1 mg (35%). ESI-MS *m/z* = 325 [M+H]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.66 - 7.73 (m, 2 H), 7.52 (d, *J* = 8.8 Hz, 1 H), 7.31 - 7.36 (m, 2 H), 7.27 (d, *J* = 8.6 Hz, 1 H), 7.12 - 7.18 (m, 1 H), 6.87 (dd, *J* = 6.8, 7.8 Hz, 1 H), 4.63 (ddd, *J* = 4.0, 9.8, 13.6 Hz, 1 H), 4.52 (dt, *J* = 3.5, 13.5 Hz, 1 H), 3.30 (ddd, *J* = 3.4, 9.6, 12.5 Hz, 2 H), 3.10 - 3.22 (m, 1 H), 2.87 (ddd, *J* = 3.9, 7.9, 11.3 Hz, 1 H), 2.67 - 2.83 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 147.4, 143.0, 132.6, 132.0, 129.2, 127.8, 125.5, 120.6, 120.3, 118.7, 116.7, 81.9, 50.7, 47.8, 46.1, 44.2. HRMS (FAB) *m/z* calcd for $C_{18}H_{18}ClN_4$ [M+H]+ 325.1209, found 325.1215.

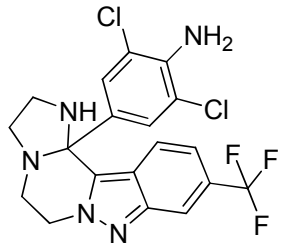
4-(2,3,4,5,-Tetrahydro-1H-1,3a,5a,6-tetraaza-cyclopenta[c]fluoren-10c-yl)-benzonitrile 10(1,4)



Yield 9.1 mg (11%). ESI-MS *m/z* = 316 [M+H]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.88 - 7.95 (m, 2 H), 7.74 - 7.80 (m, 2 H), 7.51 - 7.56 (m, 1 H), 7.23 (dd, *J* = 0.8, 8.4 Hz, 1 H), 7.15 (dd, *J* = 7.1, 8.3 Hz, 1 H), 6.84 - 6.91 (m, 1 H), 4.70 (ddd, *J* = 3.9, 10.0, 13.6 Hz, 1 H), 4.54 (dt, *J* = 3.3, 13.4 Hz, 1 H), 3.95 (br. s., 1 H), 3.27 - 3.34 (m, 1 H), 3.20 - 3.27 (m, 1 H), 3.16 (dt, *J* = 3.6, 12.1 Hz, 1 H), 2.86 - 2.94 (m, 1 H), 2.73 - 2.81 (m, 1 H), 2.63 - 2.72 (m, 1 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 149.6, 147.4, 132.0, 131.9, 128.2,

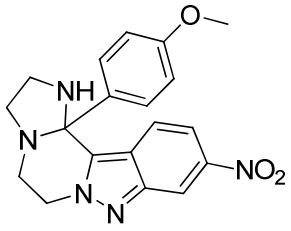
125.5, 120.8, 120.0, 118.8, 118.6, 116.8, 110.2, 82.1, 50.9, 48.0, 46.4, 44.3. HRMS (FAB) *m/z* calcd for $C_{19}H_{18}N_5$ [M+H]+ 316.1557, found 316.1562.

2,6-Dichloro-4-(8-trifluoromethyl-2,3,4,5-tetrahydro-1H-1,3a,5a,6-tetraaza-cyclopenta[c]fluorene-10c-yl)-phenylamine 10(2,5)



Yield 68.5 mg (68%). ESI-MS *m/z* = 442 $[M+H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.97 - 8.02 (m, 1 H), 7.54 (d, *J* = 8.4 Hz, 1 H), 7.48 (s, 2 H), 7.20 (d, *J* = 8.8 Hz, 1 H), 5.50 (s, 2 H), 4.72 (ddd, *J* = 4.2, 9.3, 13.7 Hz, 1 H), 4.57 (dt, *J* = 3.7, 13.7 Hz, 1 H), 3.87 (br. s., 1 H), 3.29 (ddd, *J* = 3.5, 9.3, 12.6 Hz, 1 H), 3.15 (dt, *J* = 4.0, 12.6 Hz, 1 H), 3.05 - 3.13 (m, 1 H), 2.75 - 2.91 (m, 3 H). ^{13}C NMR(126 MHz, DMSO-d_6) δ: 145.7, 140.5, 133.9, 132.1, 126.7, 125.7, 123.5, 122.2, 120.1, 117.6, 116.2 – 116.3 (m), 115.2 (q, *J* = 5.0 Hz), 81.2, 50.4, 47.7, 45.5, 44.1. HRMS (FAB) *m/z* calcd for $C_{19}H_{17}Cl_2F_3N_5$ $[M+H]^+$ 442.0808, found 442.0800.

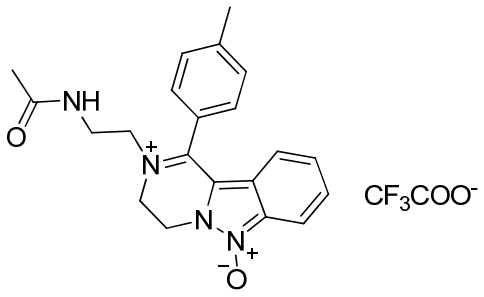
10c-(4-Methoxyphenyl)-8-nitro-1,2,3,4,5,10c-hexahydro-1,3a,5a,6-tetraaza-cyclopenta[c]fluorene 10(3,2)



Yield 53.9 mg (73%). ESI-MS *m/z* = 366 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.54 - 8.57 (m, 1 H), 7.67 - 7.71 (m, 1 H), 7.55 (d, *J* = 9.2 Hz, 1 H), 7.51 - 7.54 (m, 2 H), 6.81 -

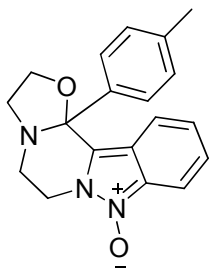
6.88 (m, 2 H), 4.61 - 4.71 (m, 2 H), 3.70 (s, 3 H), 3.34 (ddd, *J* = 5.1, 7.3, 12.7 Hz, 1 H), 3.16 (dt, *J* = 4.5, 12.8 Hz, 1 H), 3.03 - 3.12 (m, 1 H), 2.78 - 2.94 (m, 3 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 159.4, 146.5, 146.0, 136.1, 135.6, 129.0, 123.2, 122.3, 115.1, 114.9, 114.0, 82.2, 55.7, 50.7, 48.2, 45.6, 44.9. HRMS (FAB) *m/z* calcd for $C_{19}H_{20}N_5O_3$ [M+H]+ 366.1561, found 366.1551.

2-(2-Acetamidoethyl)-1-*p*-tolyl-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 21



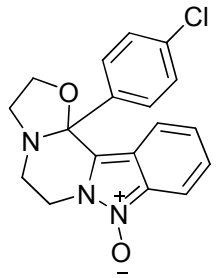
Yield 11.6 mg (53%). ESI-MS *m/z* = 363 [M]+. ^{1}H NMR (300MHz, DMSO-d_6) δ: 7.98 - 8.06 (m, 2 H), 7.44 - 7.62 (m, 6 H), 6.19 (d, *J* = 8.3 Hz, 1 H), 4.82 - 4.96 (m, 2 H), 4.50 (m, 2 H), 3.74 (m, 2 H), 3.35 - 3.47 (m, 2 H), 2.50 (s, 3 H, overlapped by DMSO-d_6), 1.76 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 169.8, 155.3, 142.7, 132.5, 131.6, 130.3, 129.0, 128.1, 125.2, 123.1, 118.9, 114.8, 110.4, 53.3, 47.5, 40.5, 36.6, 22.6, 21.3. HRMS (FAB) *m/z* calcd for $C_{21}H_{23}N_4O_2$+ [M]+ 363.1821, found 363.1824.

10c-*p*-Tolyl-2,3,4,5-tetrahydro-10cH-1-oxa-3a,5a,6-triaza-cyclopenta[c]fluorene 6-oxide 29(1,1)



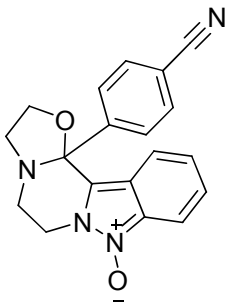
Yield 12.2 mg (64%). ESI-MS *m/z* = 322 [M+H]+. ^{1}H NMR (500 MHz, DMSO-d$_6$) δ: 8.02 (m, 1 H), 7.52 - 7.64 (m, 5 H), 7.48 (dd, *J* = 8.4, 1.0 Hz, 1 H), 6.19 (dt, *J* = 8.5, 0.9 Hz, 1 H), 4.82 - 4.90 (m, 2 H), 4.48 - 4.55 (m, 2 H), 3.74 - 3.80 (m, 2 H), 3.69 - 3.73 (m, 2 H), 2.51 (s, 3 H). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 156.2, 143.4, 133.1, 132.1, 130.9, 130.0, 128.6, 126.1, 123.7, 119.6, 115.5, 111.2, 58.7, 56.6, 48.6, 41.0, 22.0. HRMS (FAB) *m/z* calcd for $C_{19}H_{20}N_3O_2$ [M + H]+ 322.1550, found 322.1544

2-(4-chlorophenyl)-3-oxa-6,9,10-triazatetracyclo[7.7.0.0^{2,6}.0^{11,16}]hexadeca-1(16),10,12,14-tetraene 29(1,3)



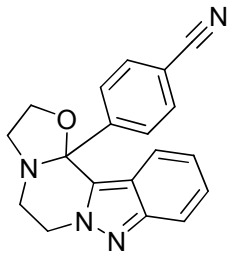
Yield 13.6 mg (67%) ESI-MS *m/z* = 342 [M+H]+. ^{1}H NMR (600 MHz, DMSO-d$_6$) δ: 7.55 - 7.60 (m, 2 H), 7.51 - 7.55 (m, 1 H), 7.36 - 7.42 (m, 2 H), 7.20 (ddd, *J*=8.8, 6.5, 0.9 Hz, 1 H), 7.09 (d, *J*=8.8 Hz, 1 H), 4.62 (ddd, *J*=13.6, 3.8, 3.7 Hz, 1 H), 4.30 (ddd, *J*=13.8, 9.7, 4.4 Hz, 1 H), 4.02 - 4.09 (m, 1 H), 3.95 (td, *J*=8.0, 3.7 Hz, 1 H), 3.31 - 3.36 (m, 2 H), 3.25 - 3.30 (m, 1 H), 3.22 (dddd, *J*=15.5, 7.7, 3.9, 3.7 Hz, 1 H), 2.95 (dt, *J*=11.7, 8.5 Hz, 1 H). ^{13}C NMR (151 MHz, DMSO-d$_6$) δ: 154.1, 137.5, 132.5, 131.8, 131.4, 130.0, 128.1, 127.1, 123.0, 118.9, 114.9, 110.4, 57.9, 56.2, 48.0, 40.4. HRMS (FAB) *m/z* calcd for $C_{18}H_{17}ClN_3O_2$ [M + H]$^+$ 342.1004, found 342.0981

2-(4-cyanophenyl)-3-oxa-6,9,10-triazatetracyclo[7.7.0.0^{2,6}.0^{11,16}]hexadeca-1(16),10,12,14-tetraene 29(1,4)



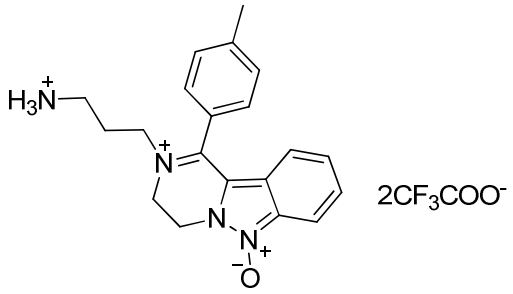
Yield 9.3 mg (47%), ESI-MS *m/z* = 333 [M+H]+. ^{1}H NMR (600 MHz, DMSO-d$_6$) δ: 7.81 - 7.84 (m, 2 H), 7.77 - 7.79 (m, 2 H), 7.54 (dt, *J*=8.9, 1.0 Hz, 1 H), 7.17 - 7.22 (m, 1 H), 7.04 - 7.08 (m, 1 H), 6.98 (ddd, 1 H), 4.64 (dt, *J*=13.6, 3.6 Hz, 1 H), 4.34 (ddd, 1 H), 4.06 - 4.12 (m, 1 H), 3.98 (td, *J*=8.1, 3.5 Hz, 1 H), 3.35 - 3.40 (m, 1 H), 3.24 - 3.30 (m, 2 H), 2.91 (ddd, *J*=12.1, 8.6, 8.4 Hz, 1 H). ^{13}C NMR (151 MHz, DMSO-d$_6$) δ: 147.4, 132.3, 127.9, 127.6, 125.9, 123.9, 119.1, 118.6, 115.3, 113.31, 112.4, 111.1, 94.4, 64.1, 50.3, 45.3, 41.2

4-(2,3,4,5-Tetrahydro-1-oxa-3a,5a,6-triaza-cyclopenta[c]fluoren-10c-yl)-benzonitrile 30(1,4)



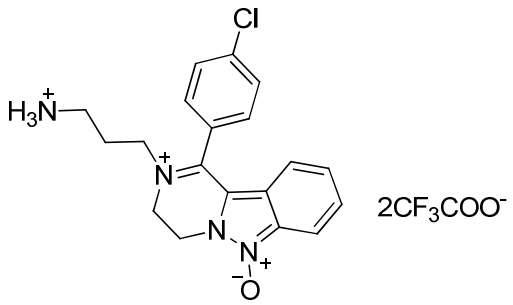
Yield 12 mg (63%). ESI-MS *m/z* = 317 [M+H]+. ^{1}H NMR (600 MHz, DMSO-d$_6$) δ: 7.75 (d, *J*=8.2 Hz, 2 H), 7.70 (d, *J*=8.2 Hz, 2 H), 7.50 (d, *J*=8.5 Hz, 1 H), 7.09 - 7.14 (m, 1 H), 7.03 (d, *J*=8.5 Hz, 1 H), 6.80 - 6.86 (m, 1 H), 4.65 - 4.73 (m, 1 H), 4.57 (dt, *J*=13.4, 3.0 Hz, 1 H), 4.00 - 4.09 (m, 1 H), 3.90 (td, *J*=8.0, 2.8 Hz, 1 H), 3.24 - 3.27 (m, 1 H), 3.17 - 3.26 (m, 2 H), 2.84 (dt, *J*=12.3, 9.0 Hz, 1 H). ^{13}C NMR (151 MHz, DMSO-d$_6$) δ: 147.8, 147.4, 132.2, 129.6, 127.5, 125.6, 121.5, 119.3, 118.7, 118.61, 117.1, 110.9, 95.1, 63.8, 50.7, 47.9, 46.5

2-(3-Ammoniopropyl)-1-*p*-tolyl-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 34(1,1)



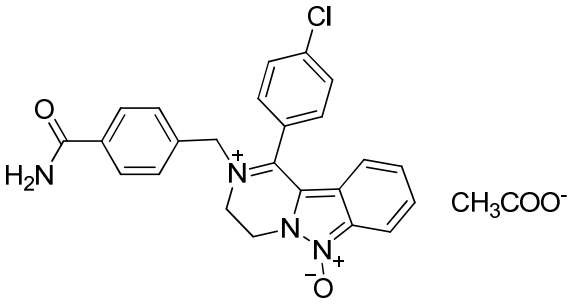
Yield 12 mg (57%). ESI-MS *m/z* = 335 [M]+. ^{1}H NMR (300 MHz, DMSO-d$_6$) δ: 7.92 - 8.06 (m, 4 H), 7.58 (s, 4 H), 7.43 - 7.55 (m, 2 H), 6.17 (d, *J* = 8.3 Hz, 1 H), 4.82 - 4.93 (m, 2 H), 4.41 - 4.56 (m, 2 H), 3.73 (t, *J* = 7.2 Hz, 2 H), 2.69 - 2.84 (m, 2 H), 2.50 (s, 3 H, overlapped by DMSO-d$_6$), 2.01 (t, *J* = 6.6 Hz, 2 H). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 155.1, 142.8, 132.4, 131.6, 130.4, 128.7, 128.1, 125.2, 123.1, 118.9, 114.8, 110.7, 51.0, 47.5, 40.4, 36.0, 25.8, 21.3. HRMS (FAB) *m/z* calcd for $C_{20}H_{23}N_4O$+ [M]+ 335.1866, found 335.1841.

2-(3-Ammoniopropyl)-1-(4-chlorophenyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide 2,2,2-trifluoroacetate 34(1,3)



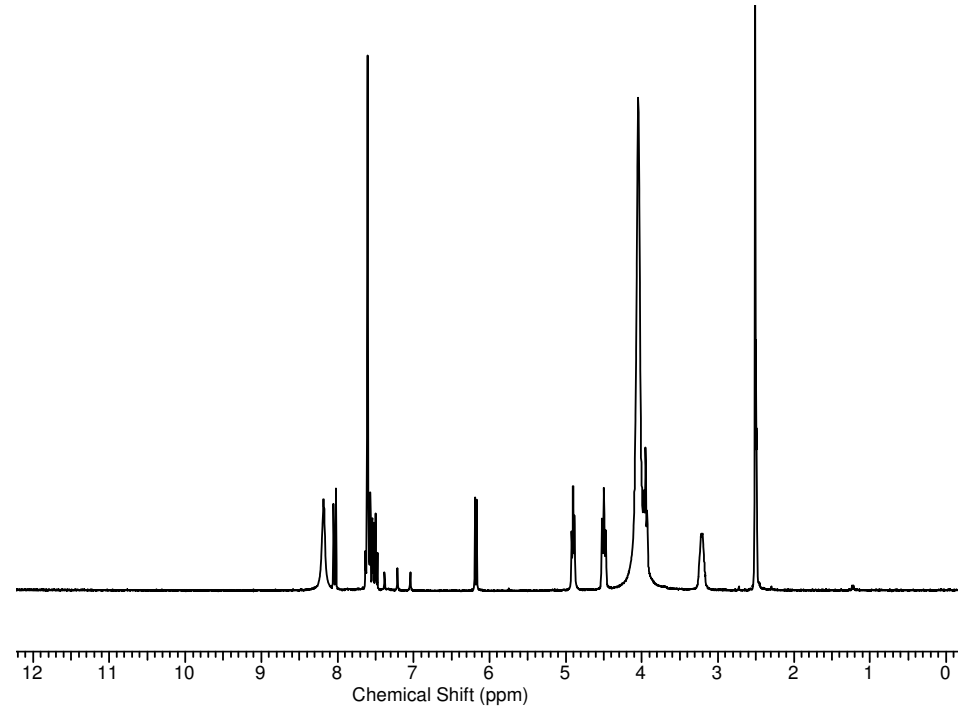
Yield 15 mg (63%). ESI-MS *m/z* = 355 [M]+. ^{1}H NMR (300 MHz, DMSO-d$_6$) δ: 8.04 (d, *J*=7.7 Hz, 1 H), 7.84 - 7.92 (m, 5 H), 7.74 (d, *J*=8.6 Hz, 2 H), 7.48 - 7.64 (m, 2 H), 6.26 (d, *J*=7.5 Hz, 1 H), 4.79 - 4.95 (m, 2 H), 4.40 - 4.55 (m, 2 H), 3.71 (t, *J*=7.5 Hz, 2 H), 2.70 - 2.90 (m, 2 H), 1.89 - 2.11 (m, 2 H). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ: 153.8, 137.6, 132.5, 131.9, 130.8, 130.3, 128.2, 126.8, 123.0, 118.9, 114.9, 110.7, 51.1, 47.6, 40.7, 36.0, 25.8. HRMS (FAB) *m/z* calcd for $C_{19}H_{20}ClN_4O$+ [M]+ 355.1320, found 355.1309.

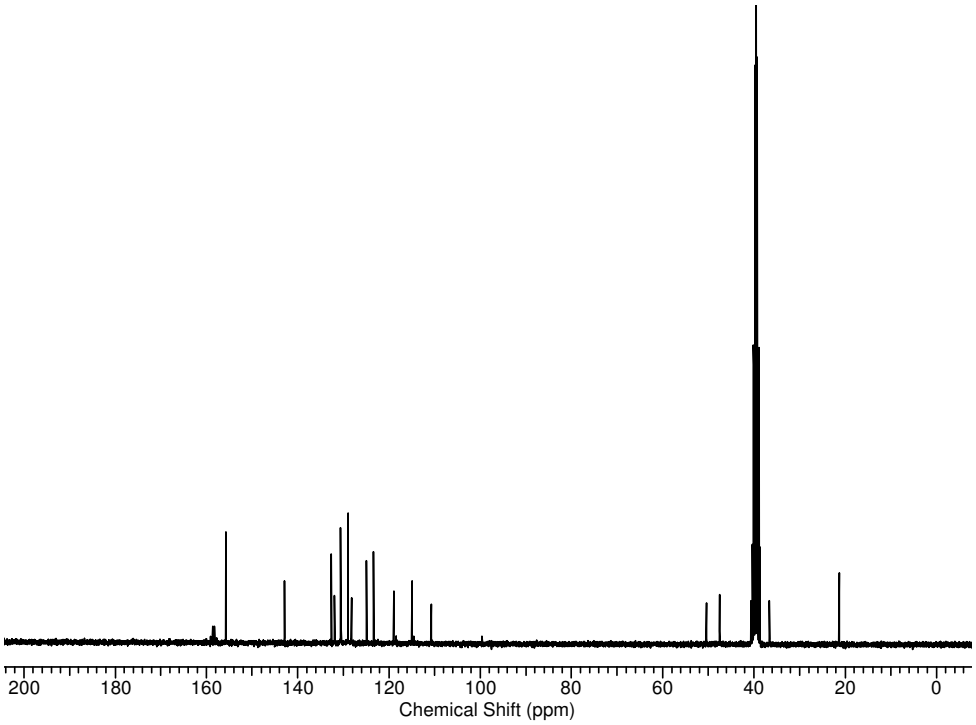
2-(4-Carbamoylbenzyl)-1-(4-chlorophenyl)-3,4-dihydropyrazino[1,2-*b*]indazole-2-ium 6-oxide acetate 40(1,3)



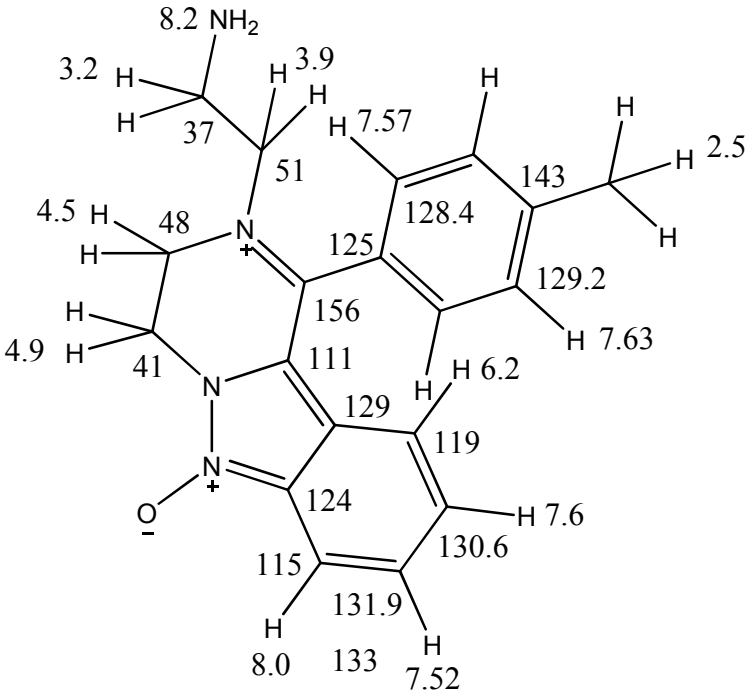
Yield 67.0 mg (83%). ESI-MS *m/z* = 431 [M]+. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.08 (d, *J* = 8.4 Hz, 1 H), 8.06 (br. s., 1 H), 7.88 - 7.92 (m, 2 H), 7.85 - 7.88 (m, 2 H), 7.78 - 7.83 (m, 2 H), 7.55 - 7.64 (m, 2 H), 7.47 – 7.51 (m, 2 H), 7.46 (br. s., 1 H), 6.33 (dd, *J* = 1.0, 8.2 Hz, 1 H), 4.98 (s, 2 H), 4.75 - 4.82 (m, 2 H), 4.33 - 4.42 (m, 2 H). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 167.2, 153.8, 137.7, 136.9, 134.2, 132.7, 132.1, 130.8, 130.3, 128.4, 128.1, 127.4, 126.9, 123.4, 119.1, 115.0, 110.9, 56.3, 47.9, 41.0. HRMS (FAB) *m/z* calcd for $C_{24}H_{20}ClN_4O_2$+ [M]+ 431.1269, found 431.1243.

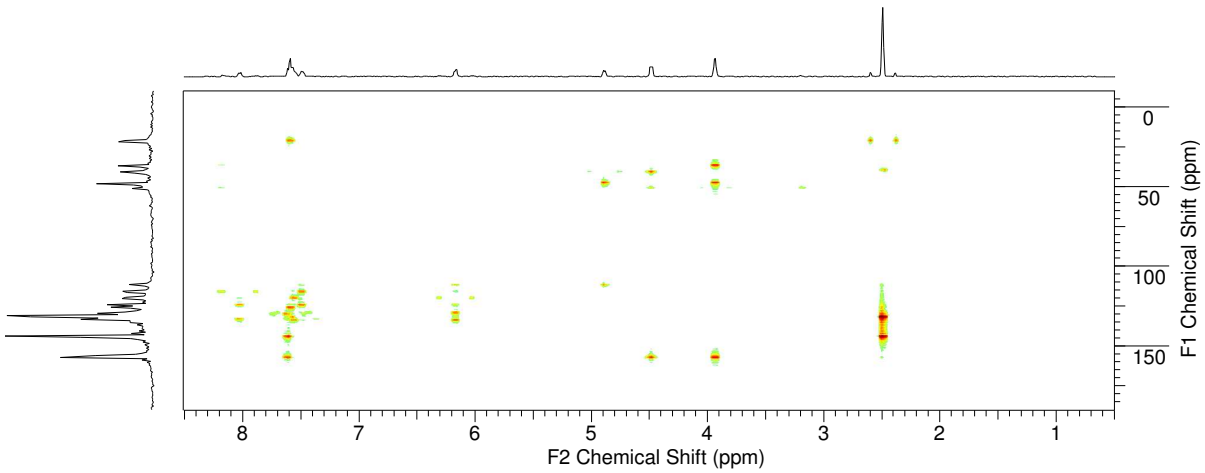
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,1)



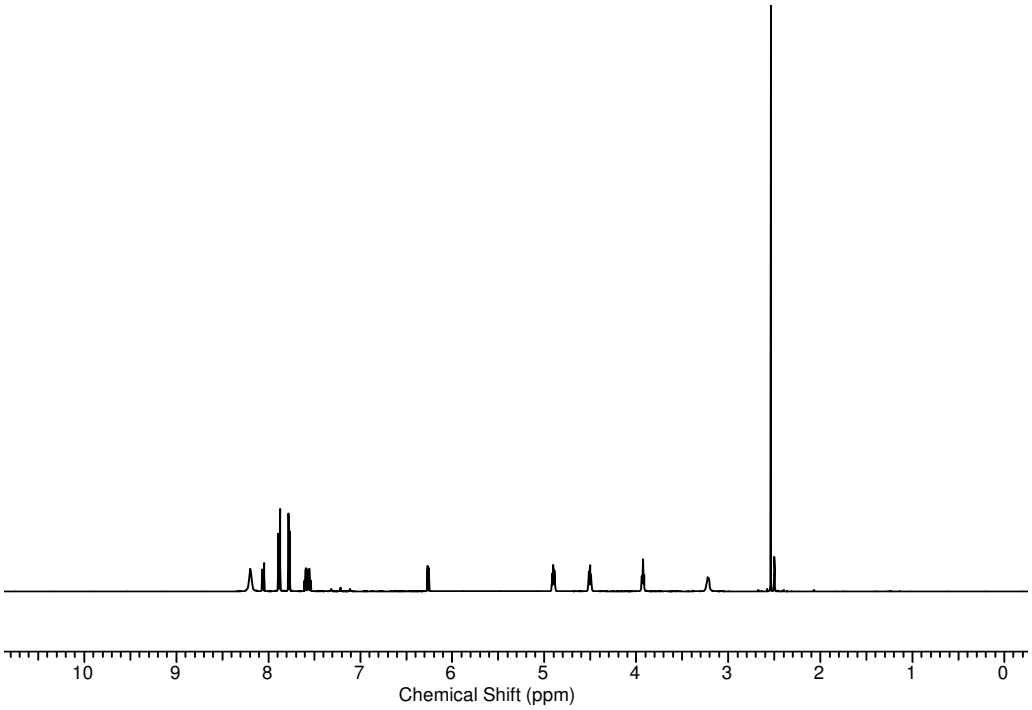


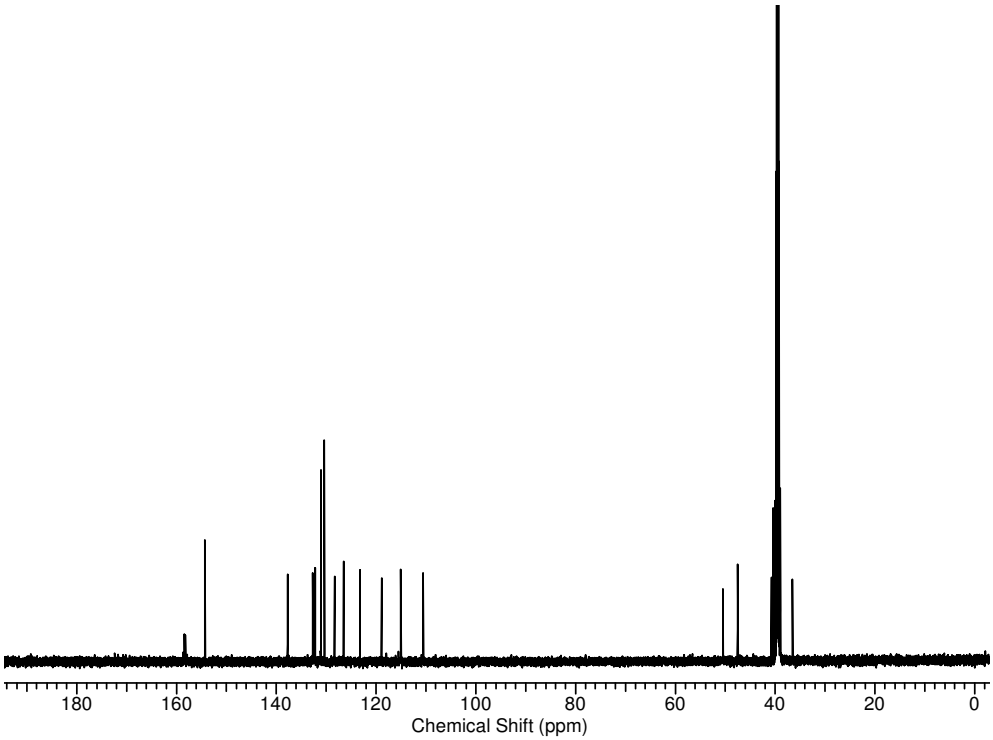
Chemical shifts and gHMBC NMR spectrum (d_6-DMSO) for compound 7(1,1)



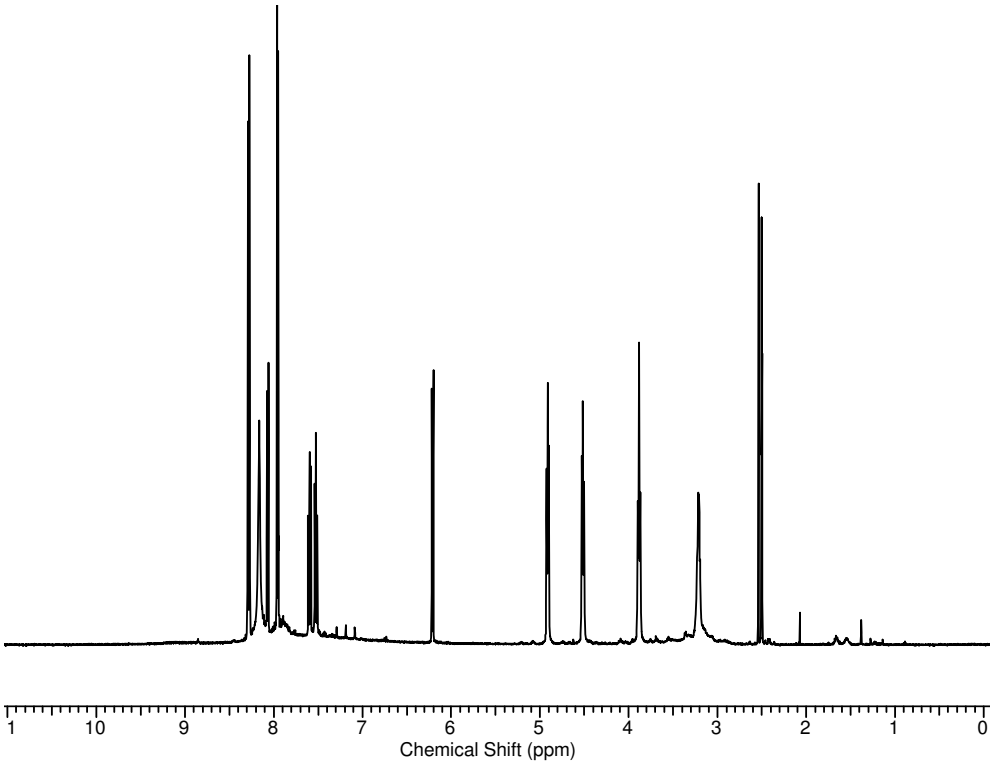


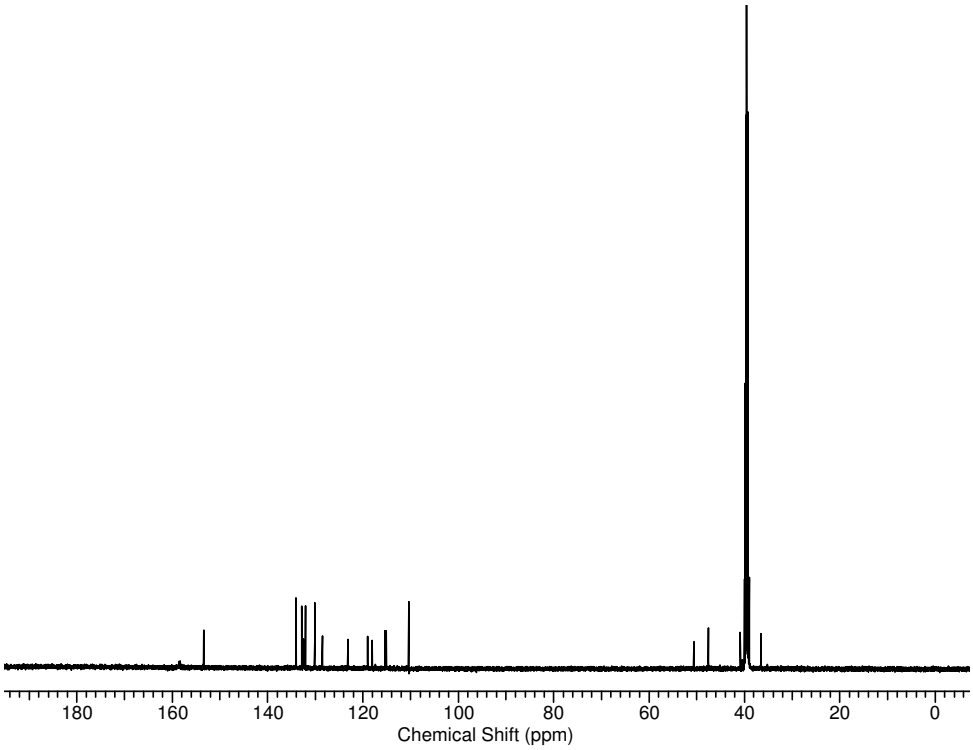
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,3)



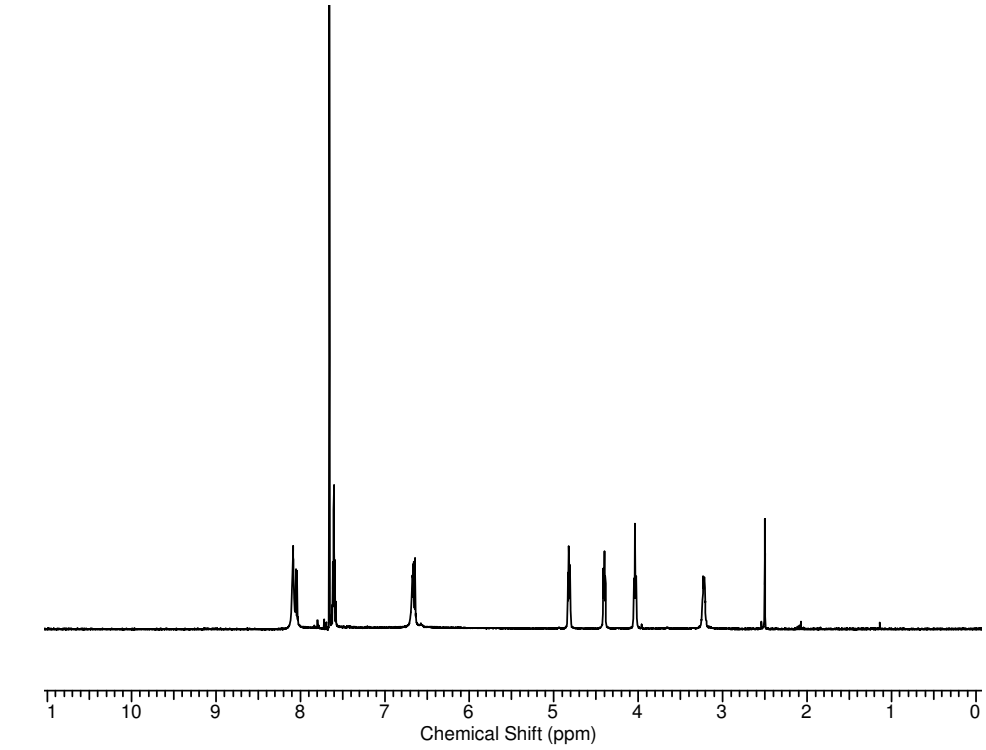


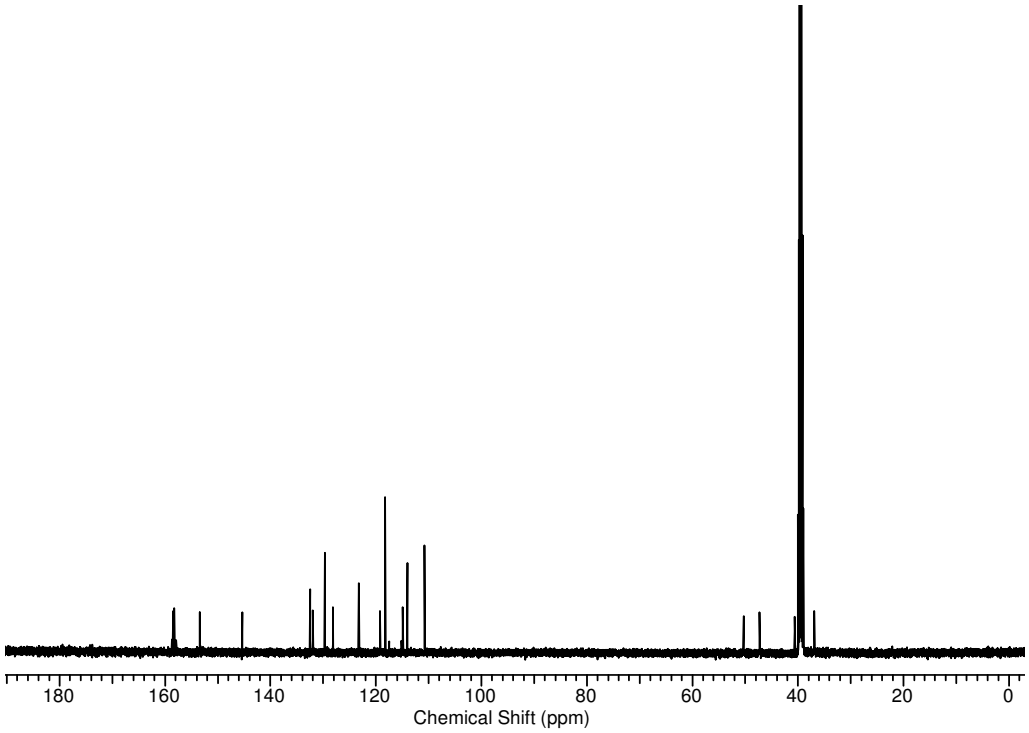
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,4)



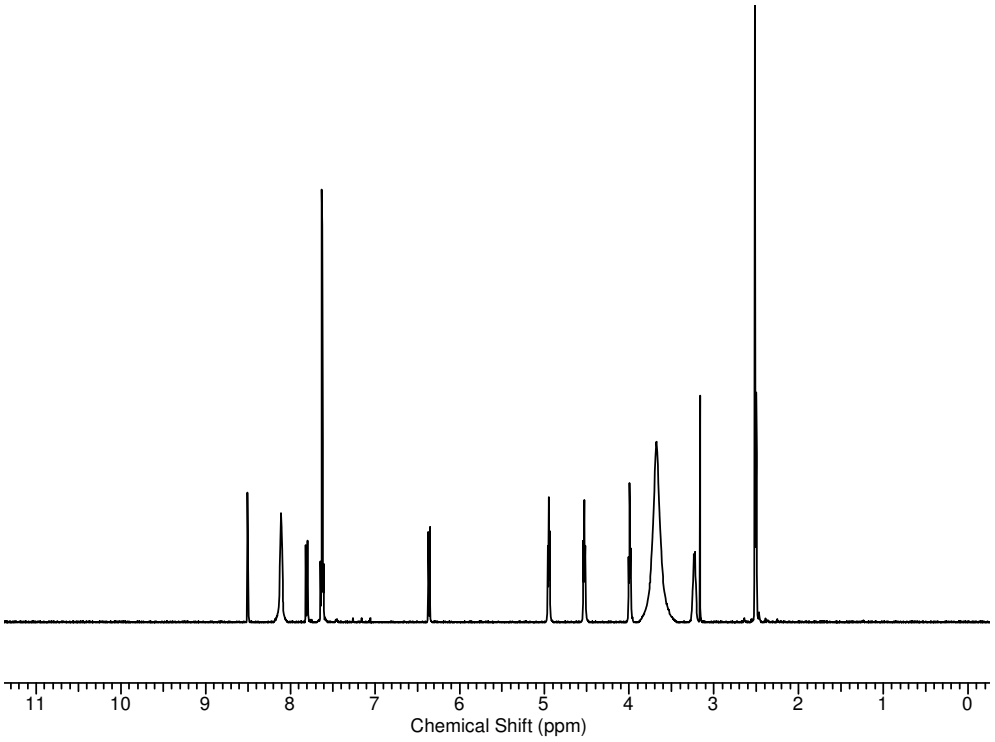


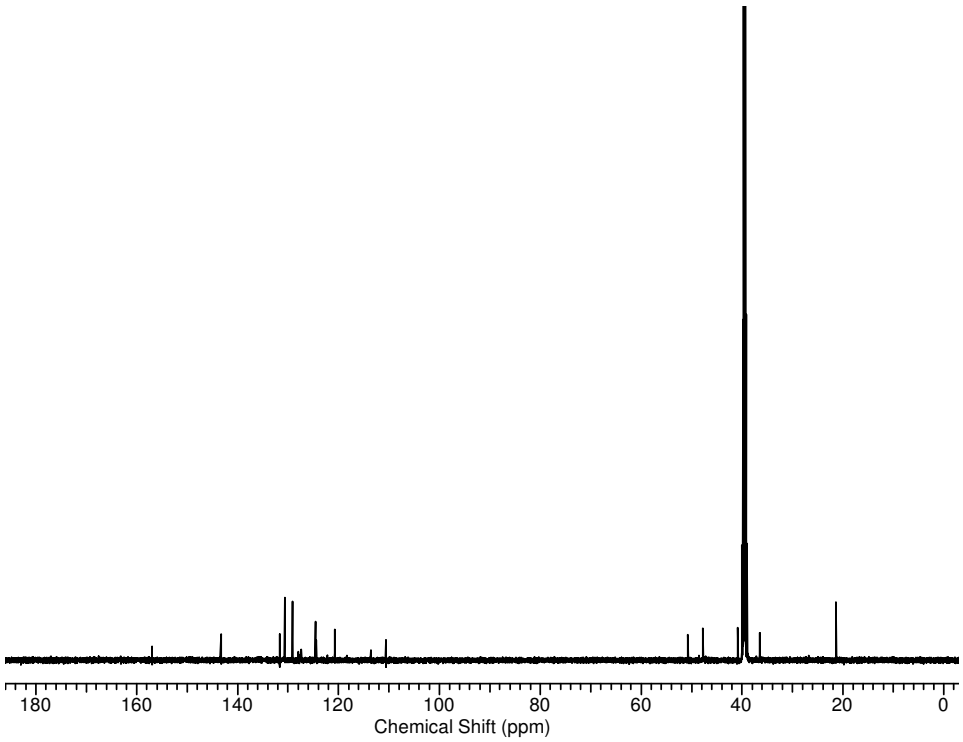
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(1,5)



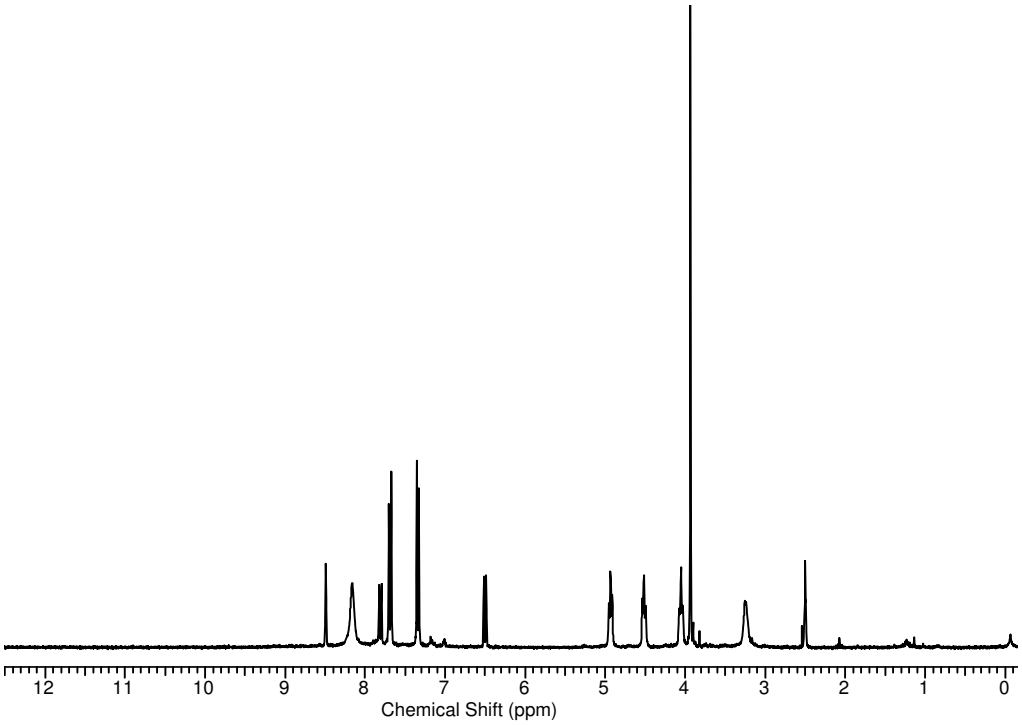


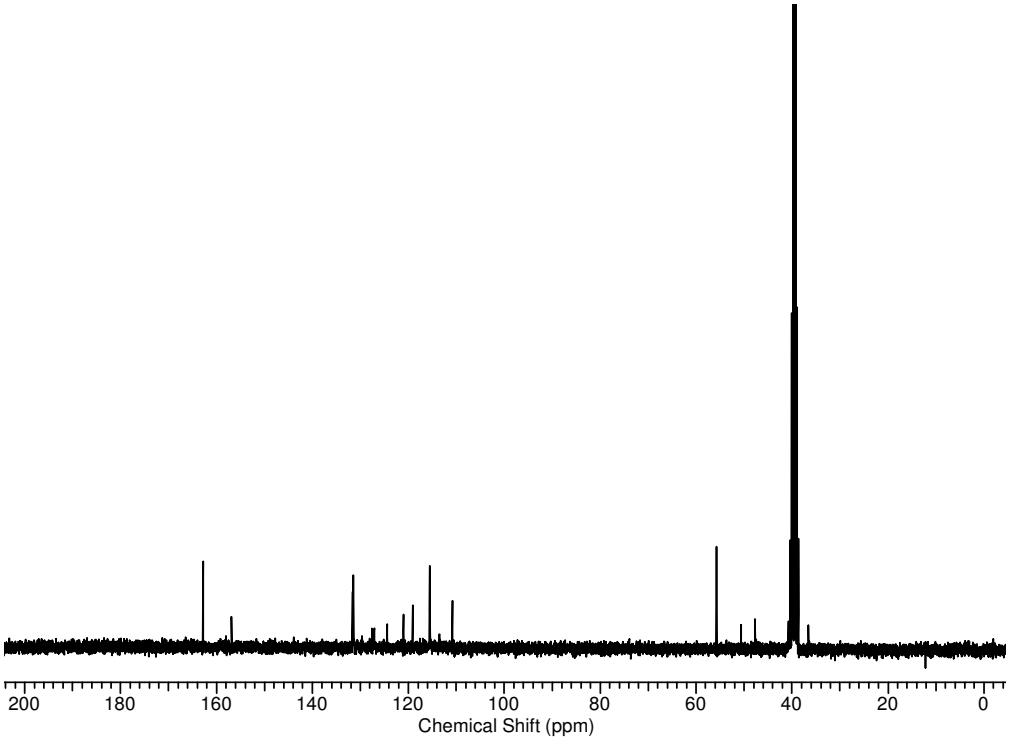
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(2,1)



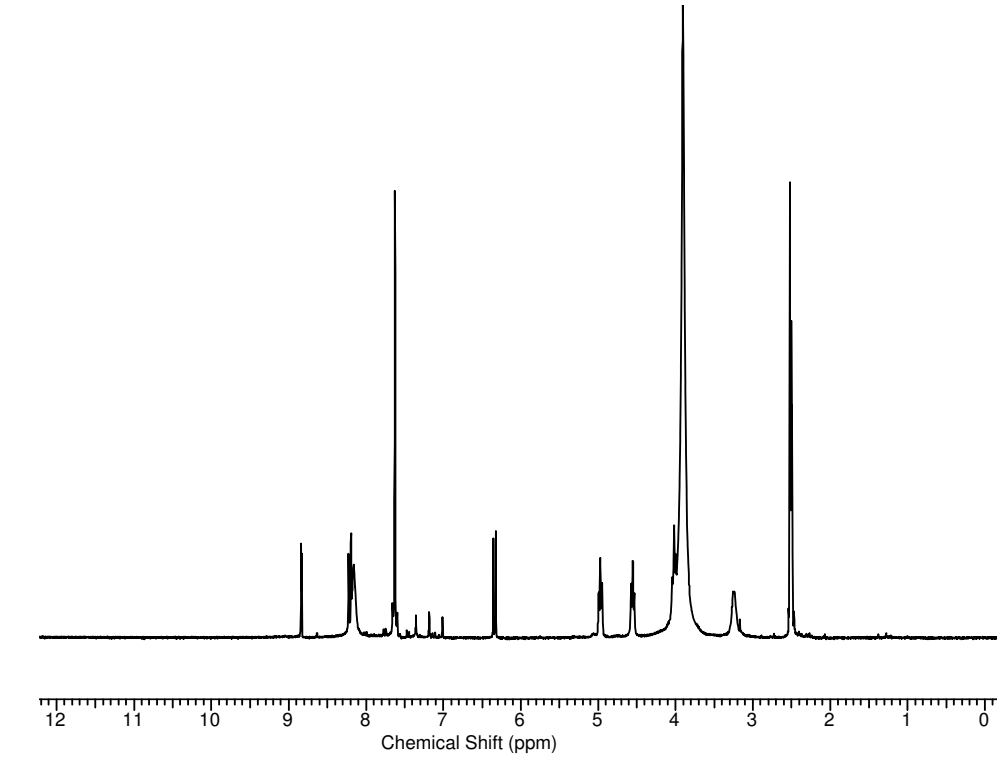


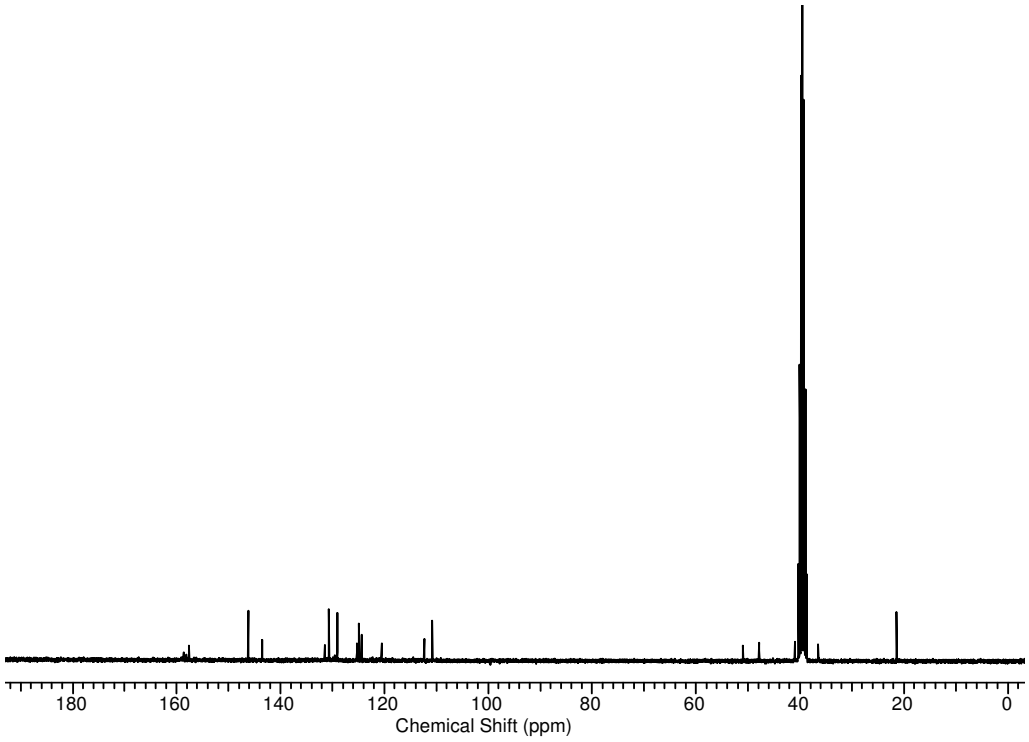
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(2,2)



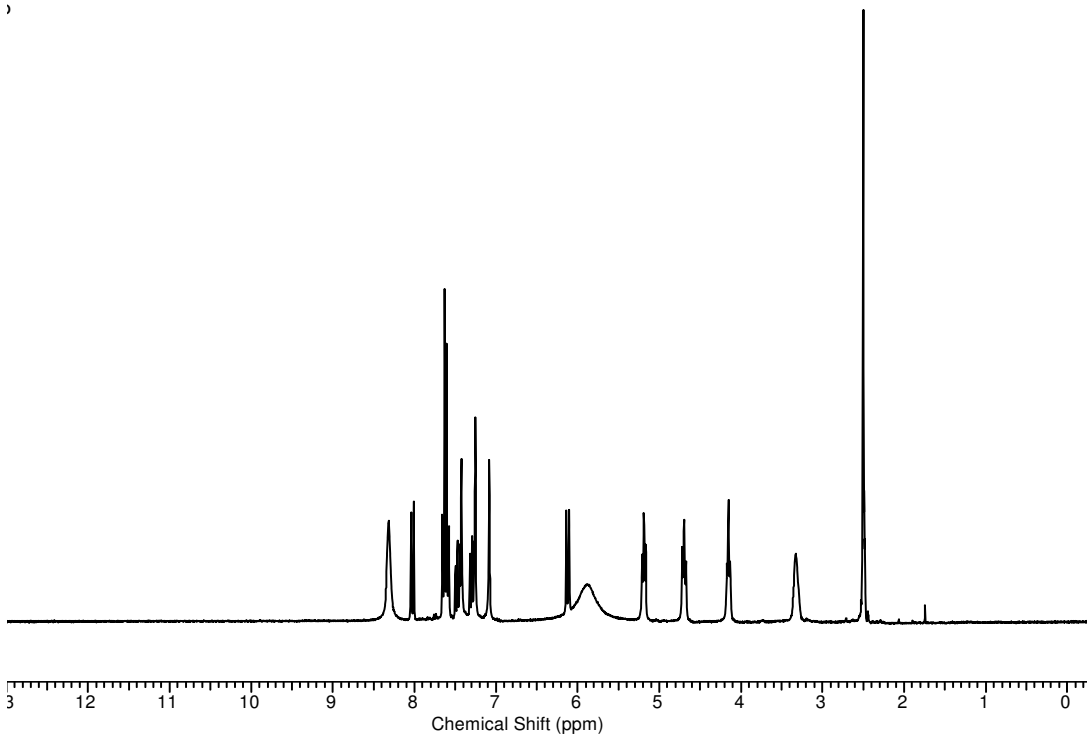


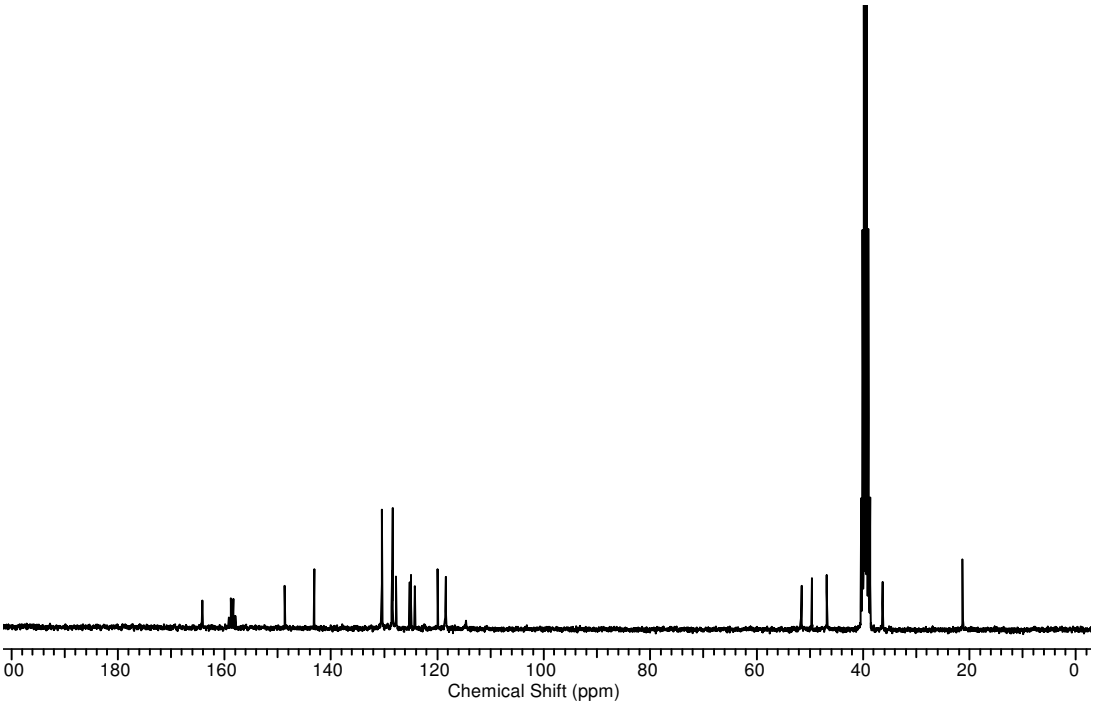
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 7(3,1)



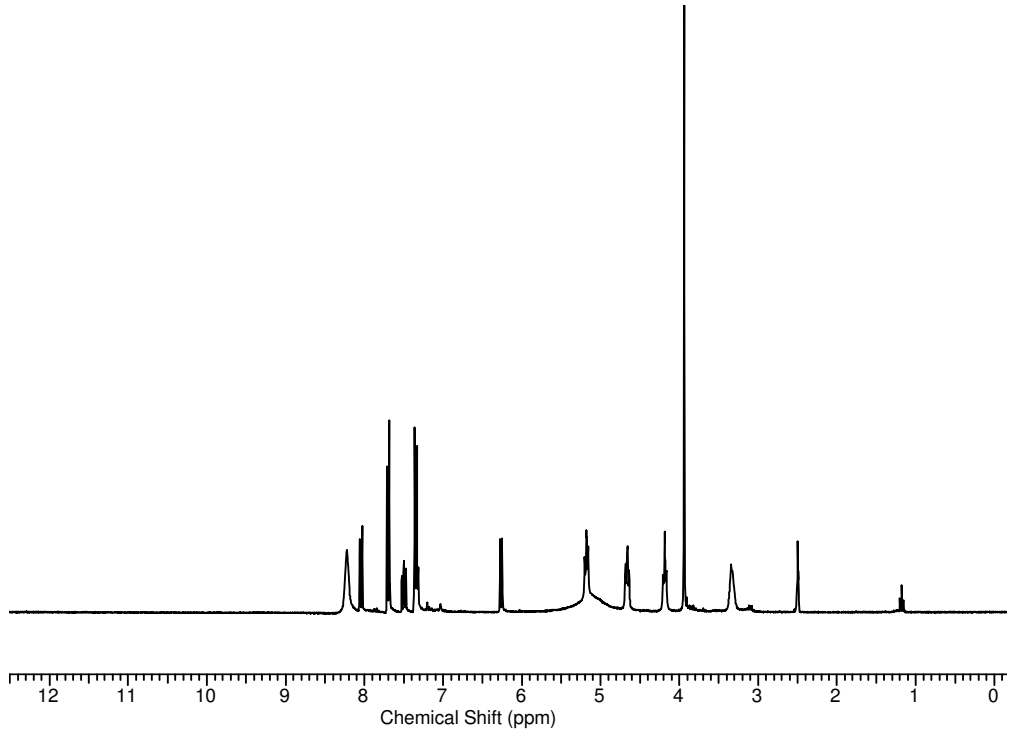


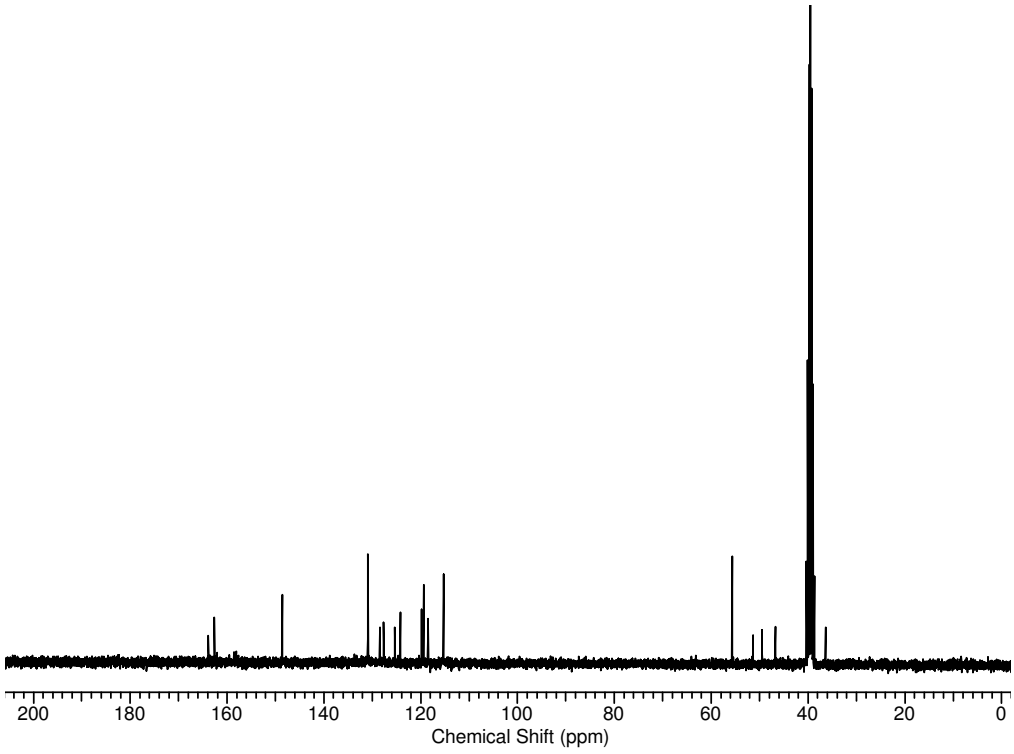
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,1)



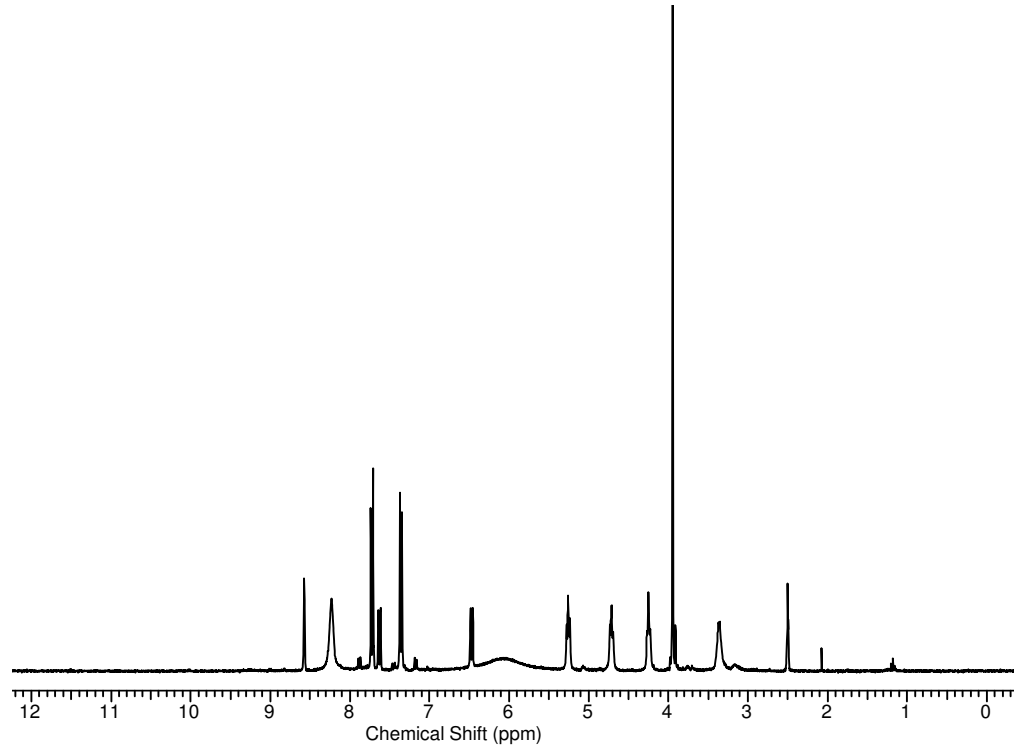


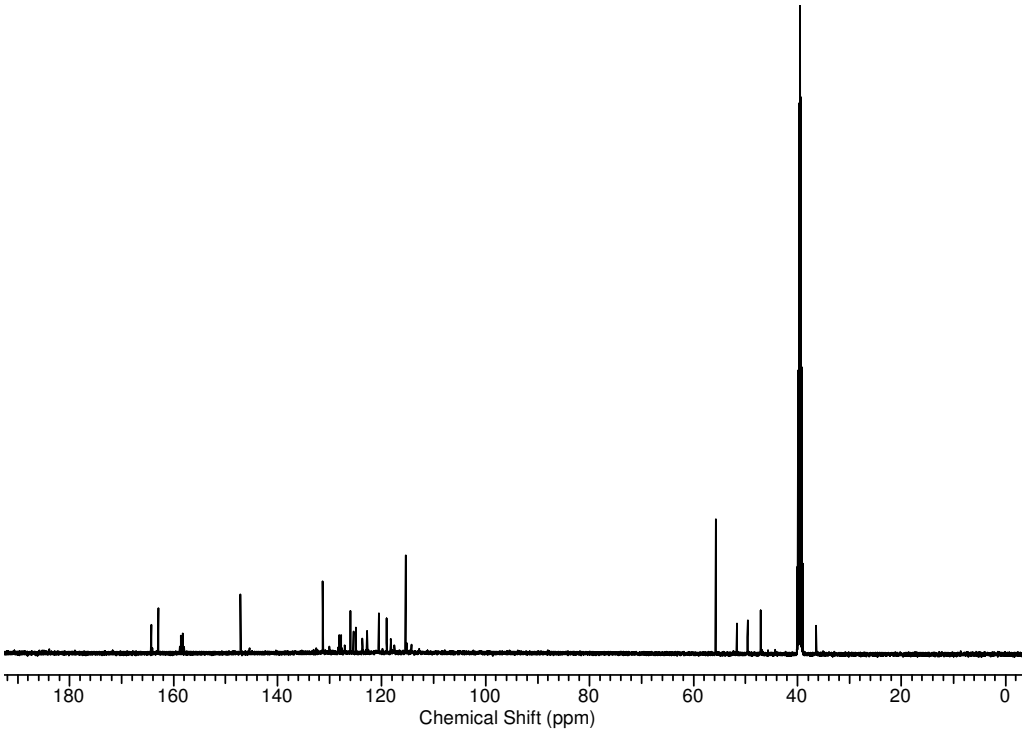
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(1,2)



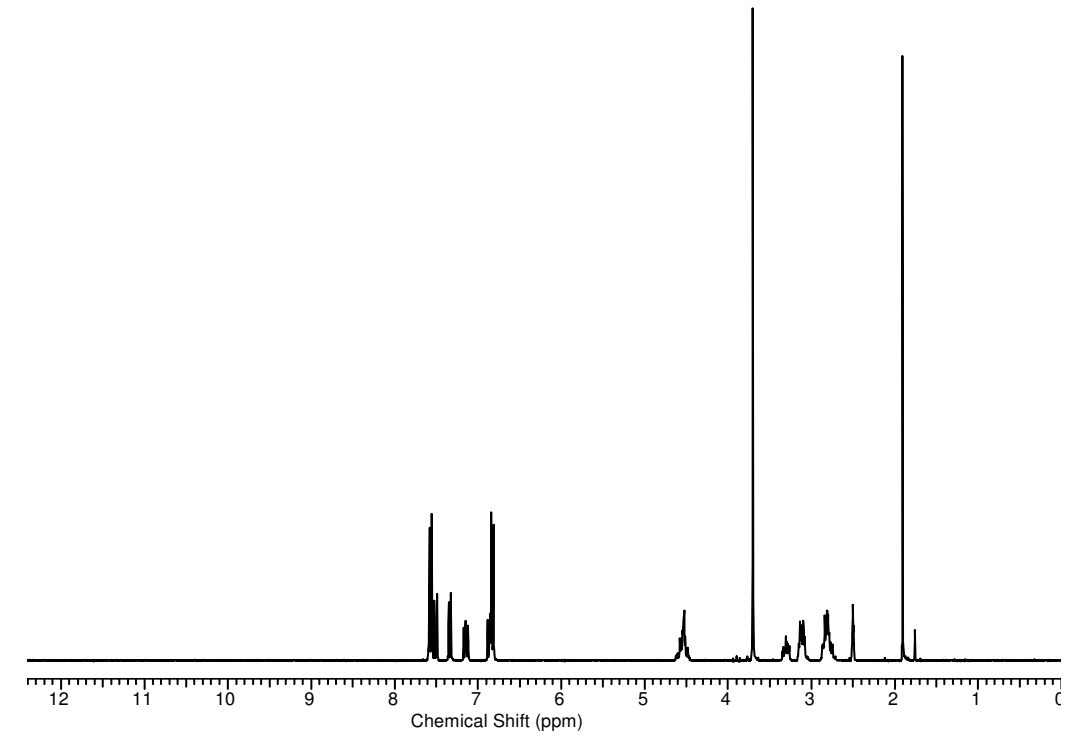


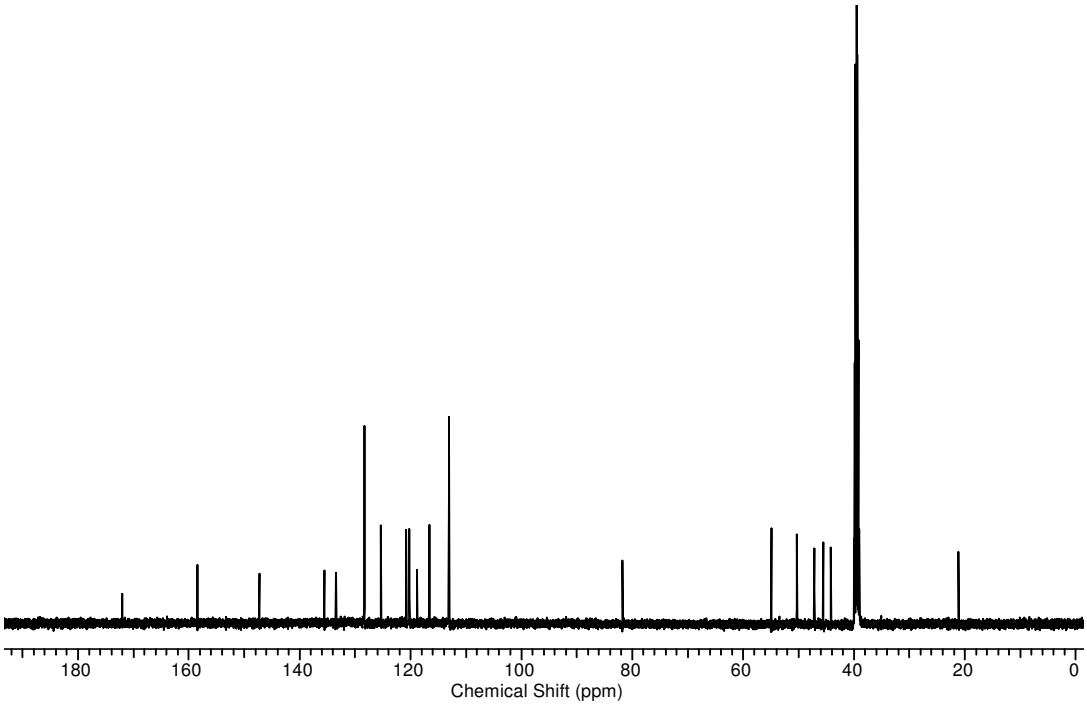
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 8(2,2)



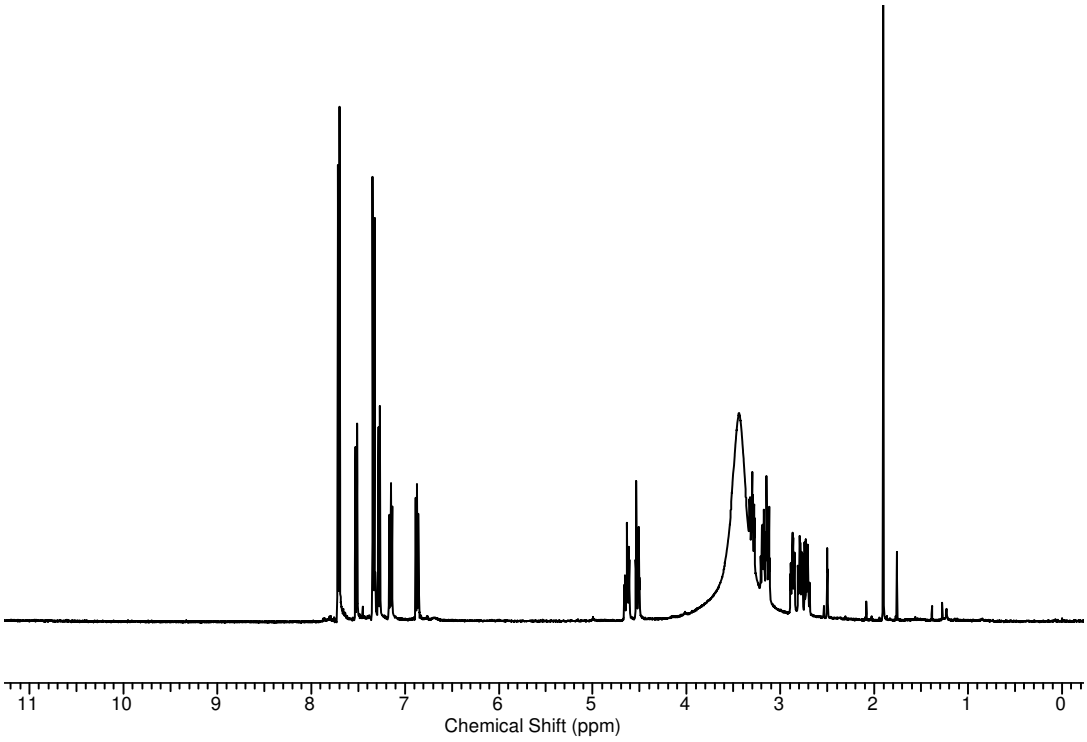


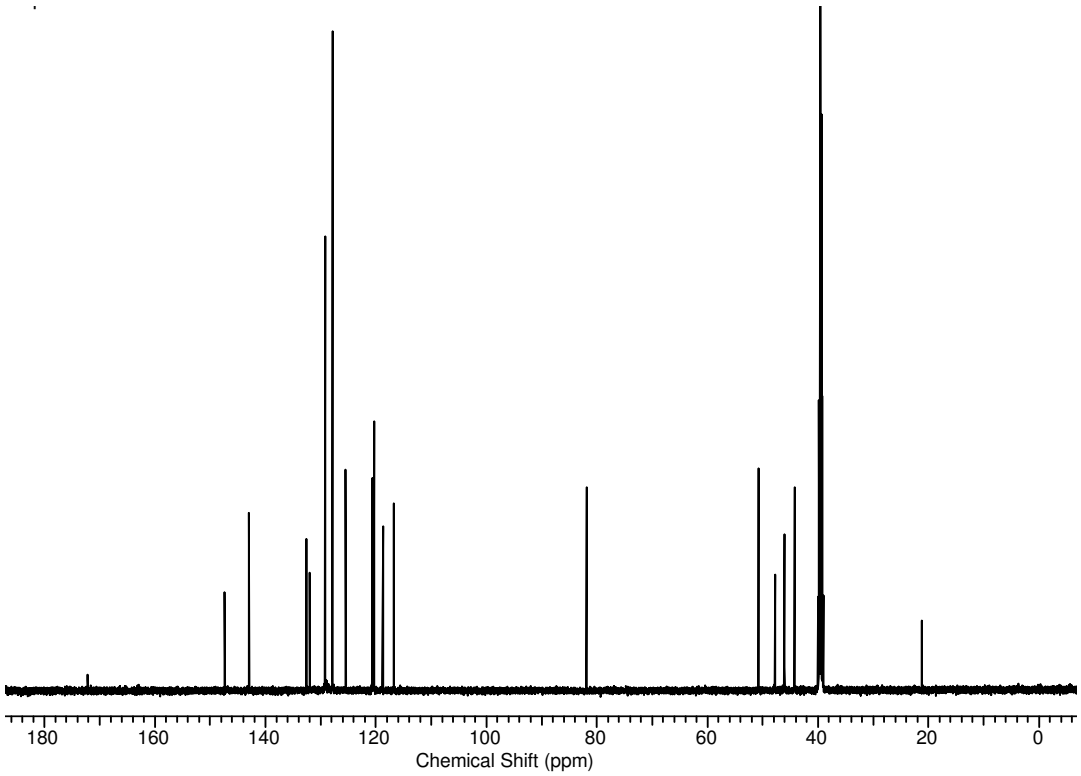
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(1,2)



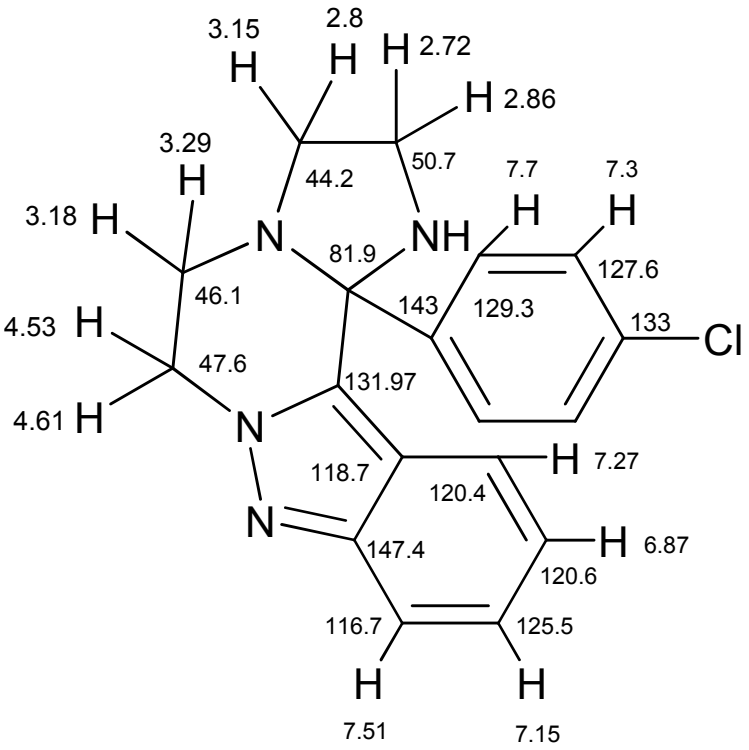


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(1,3)

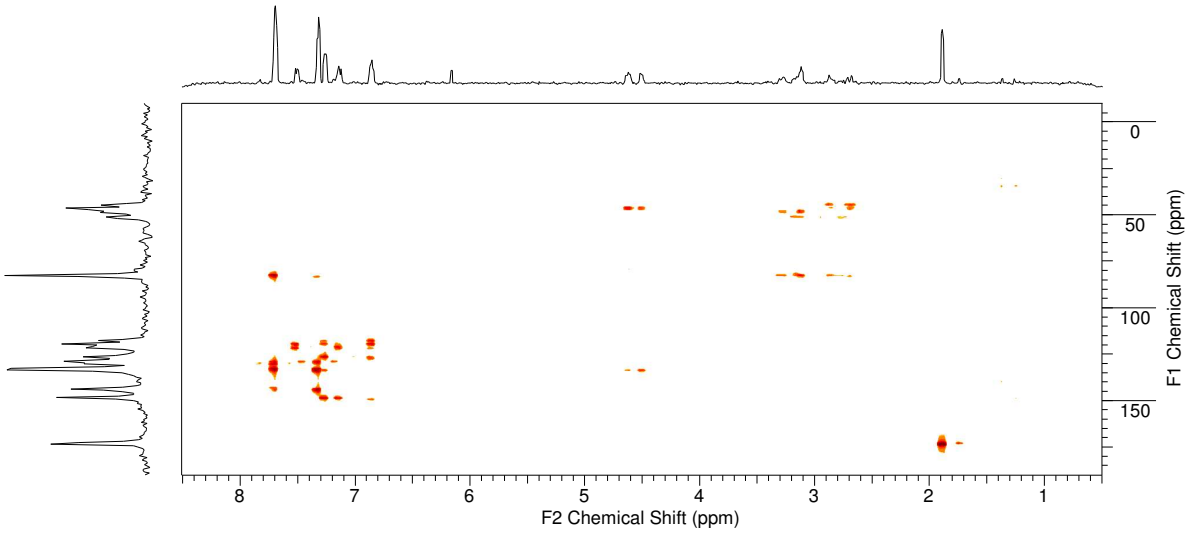




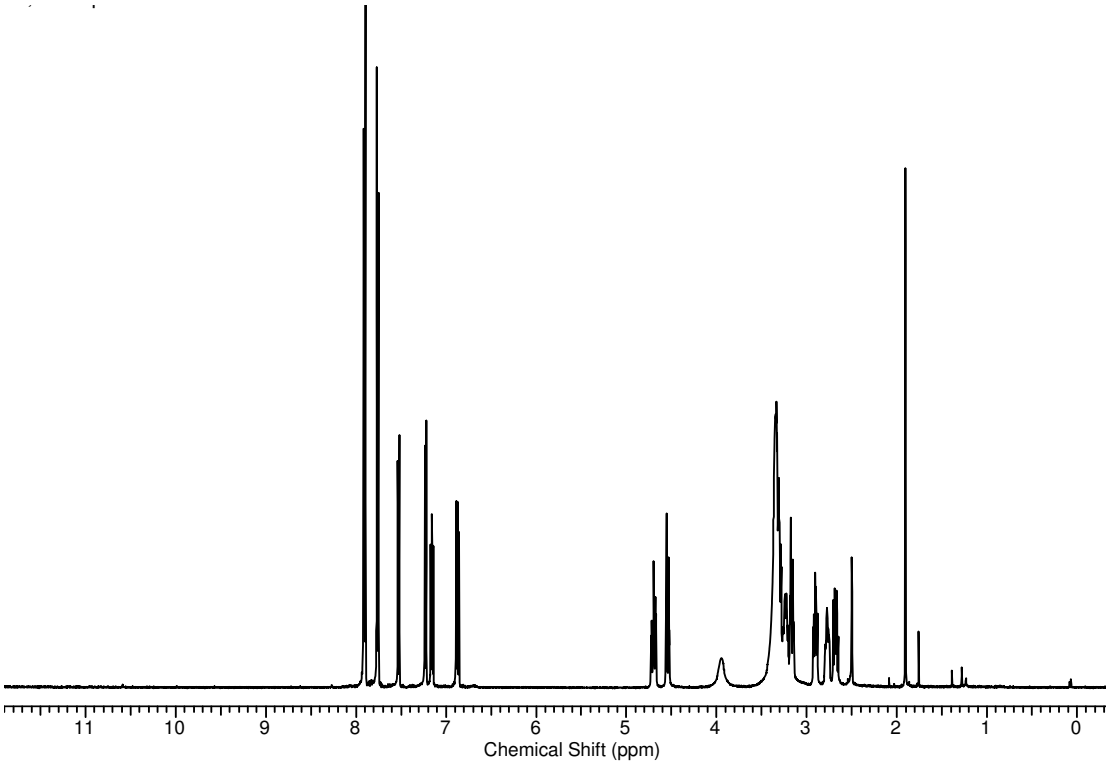
Chemical shifts and gHMBC NMR spectrum (d_6-DMSO) for compound 10(1,3)

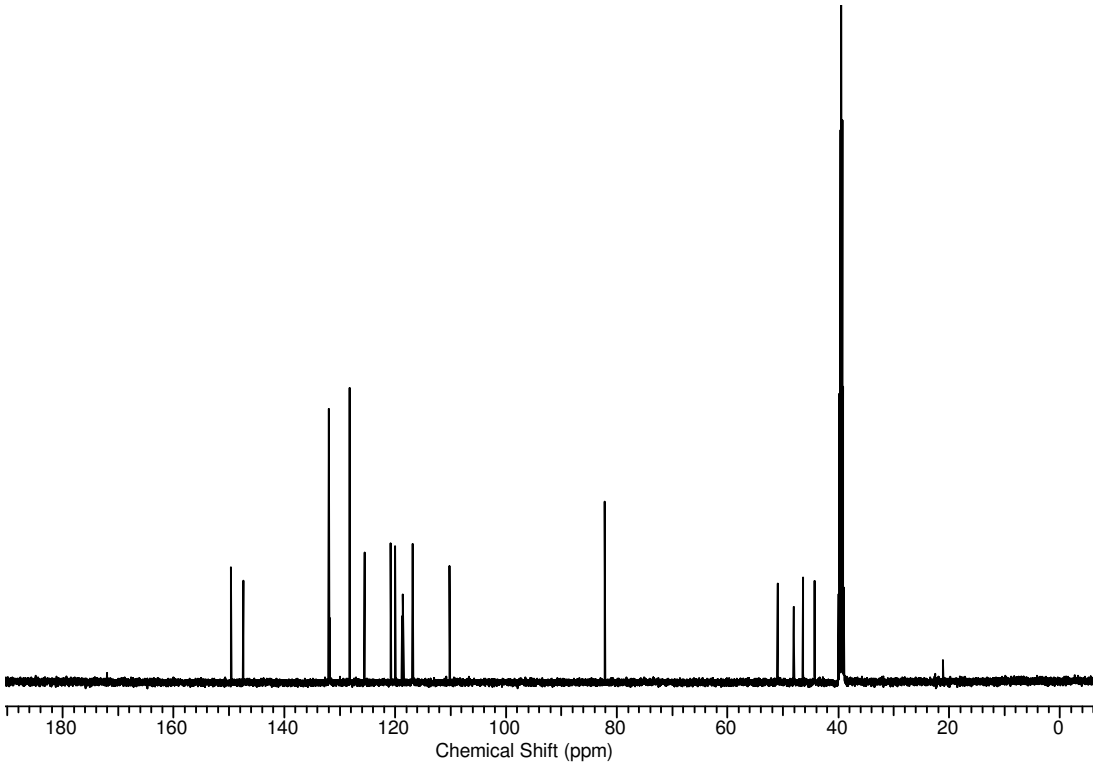


HMBC spectrum

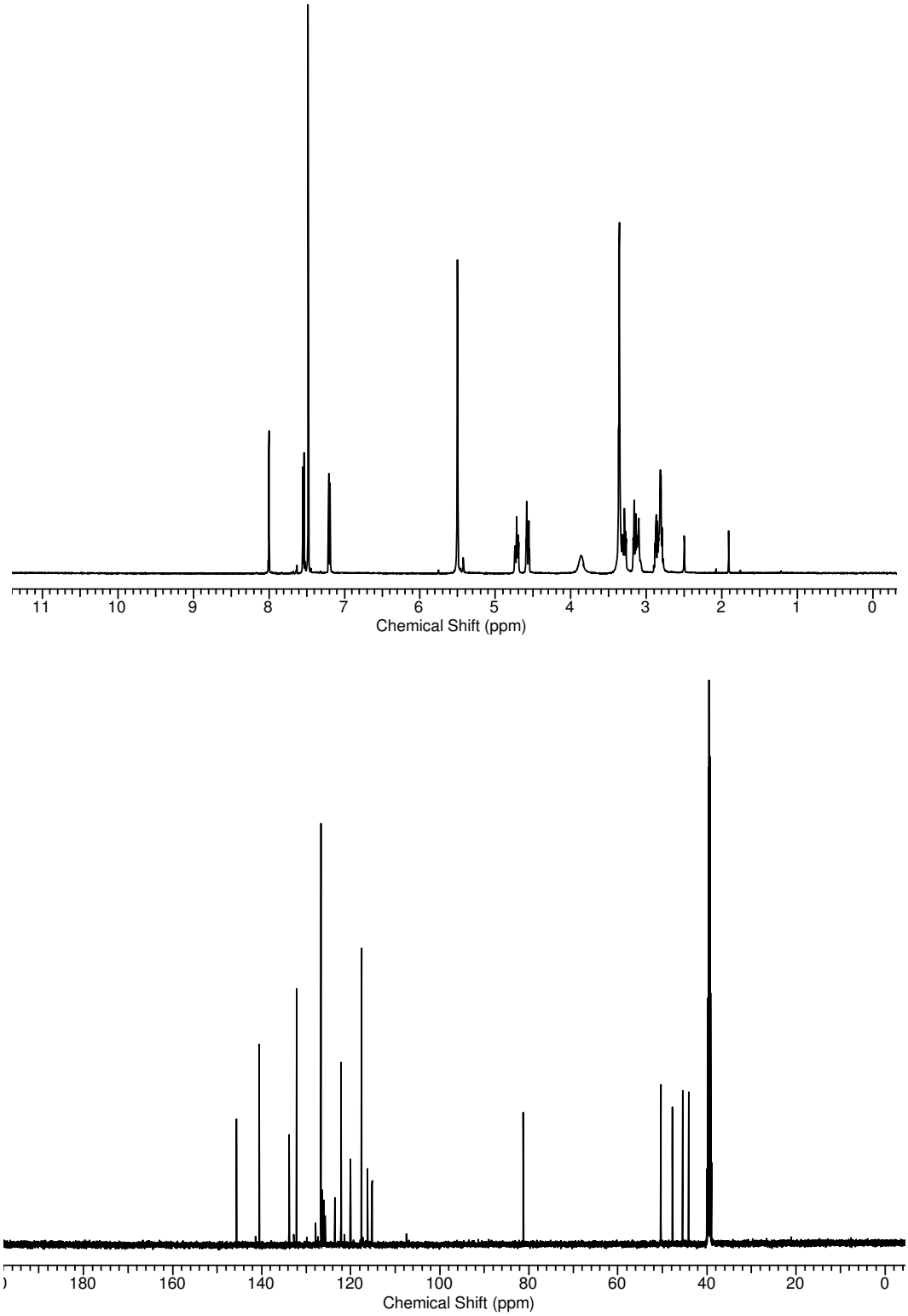


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(1,4)

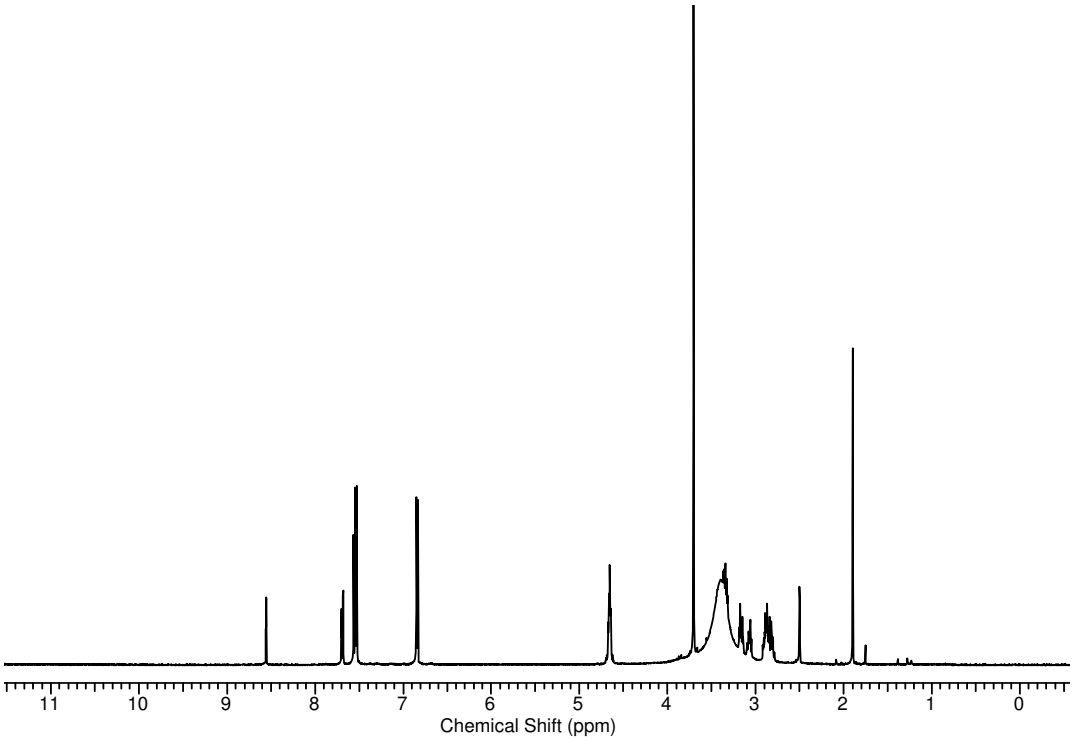


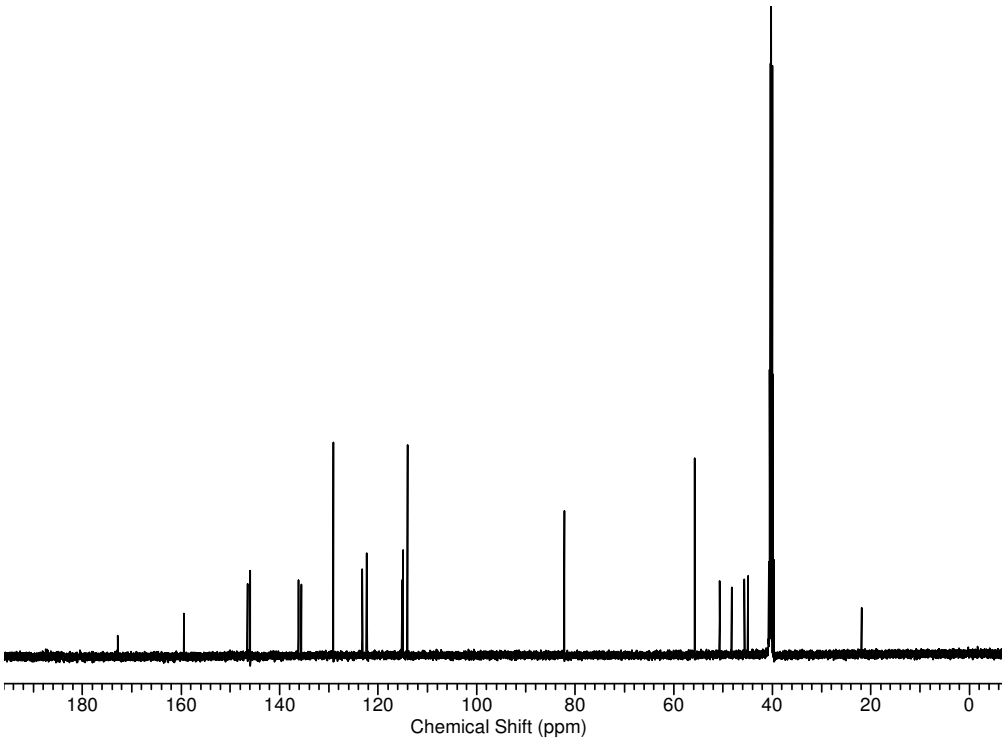


^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(2,5)

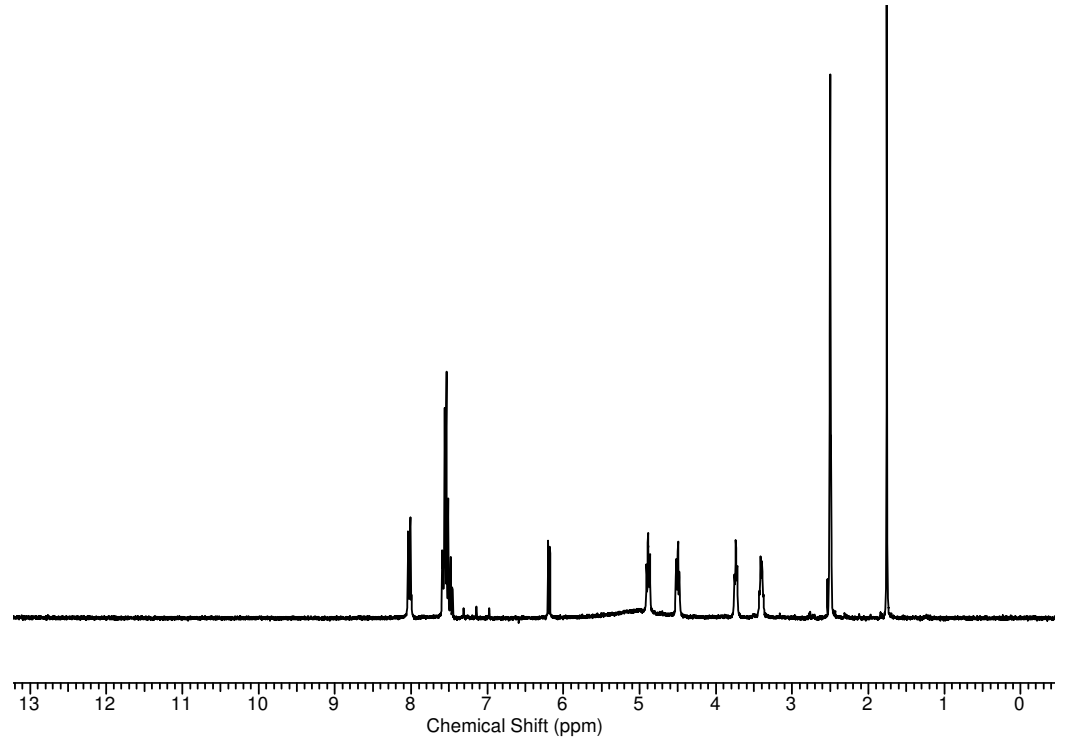


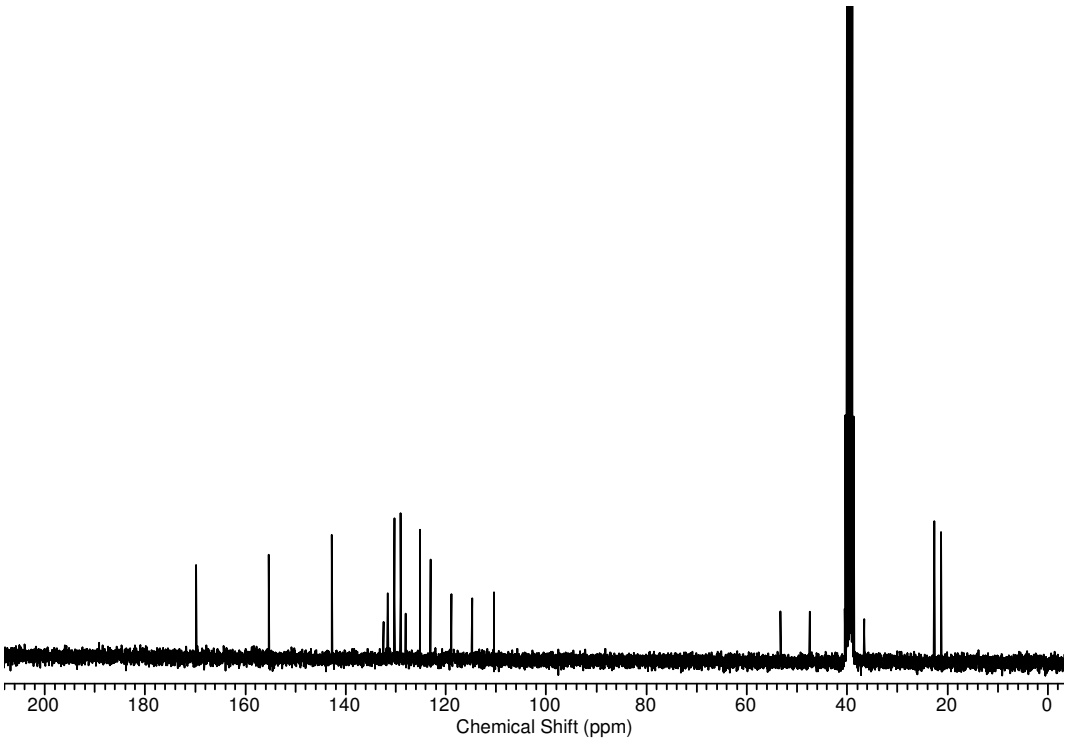
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 10(3,2)



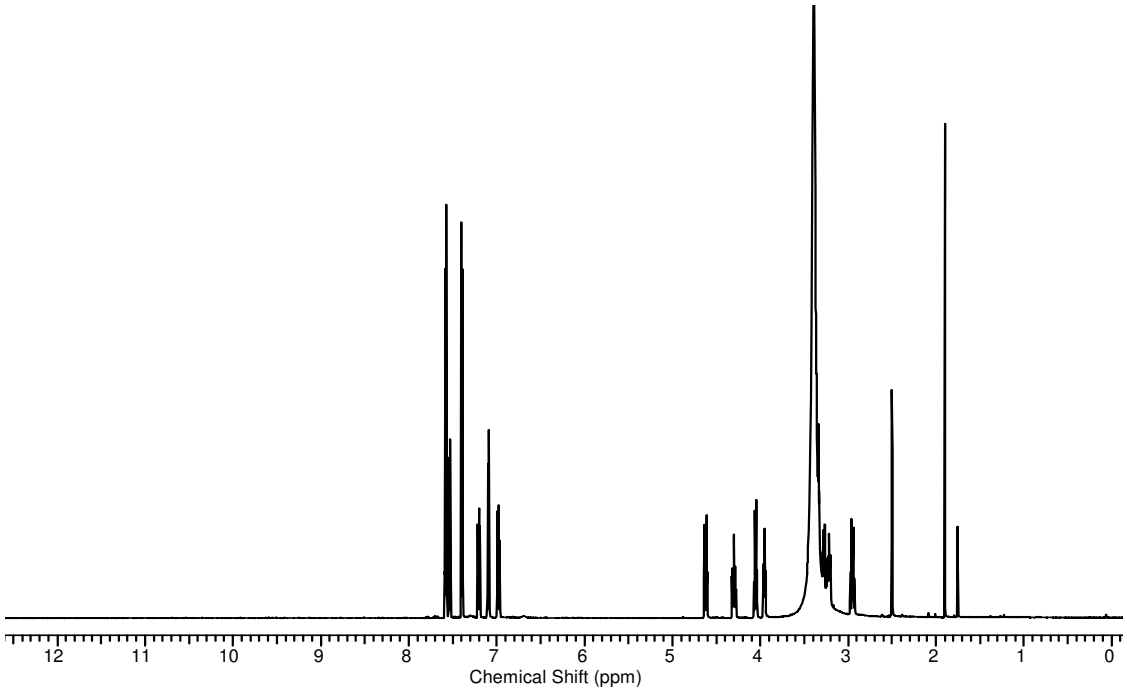


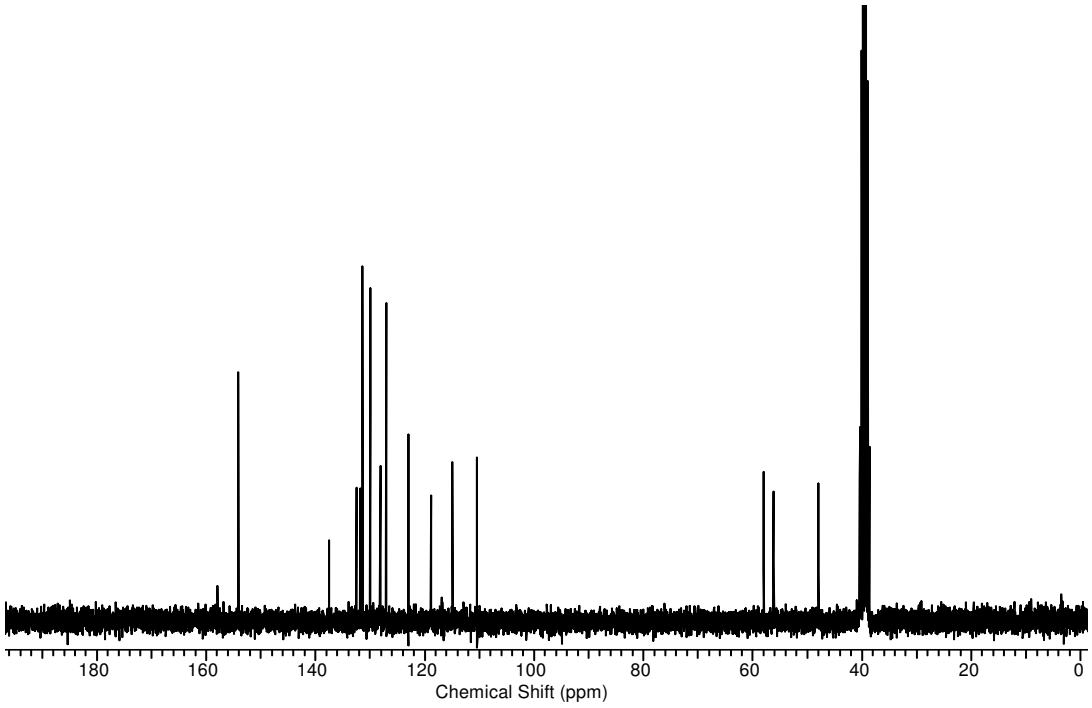
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 21



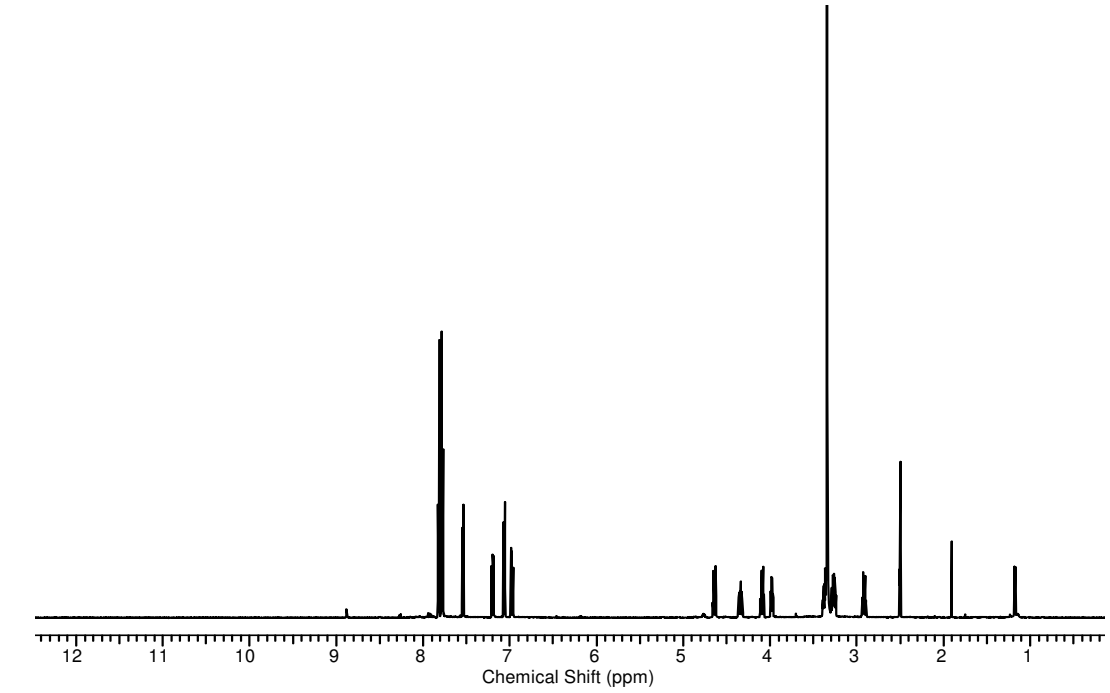


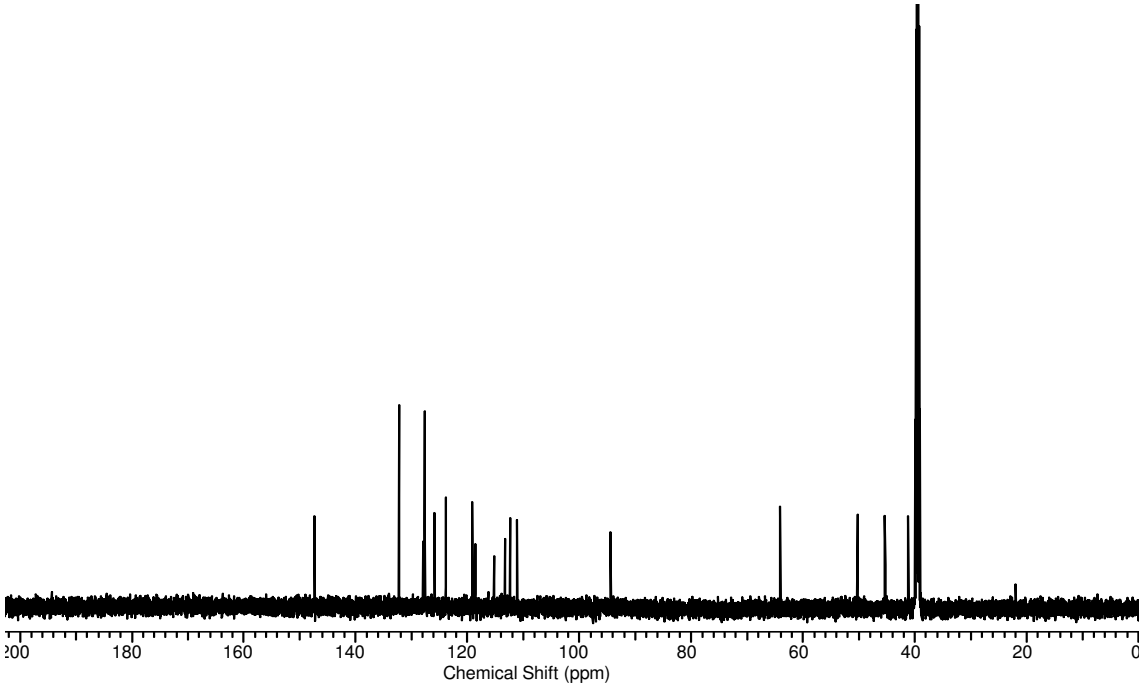
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 29(1,3)xxx



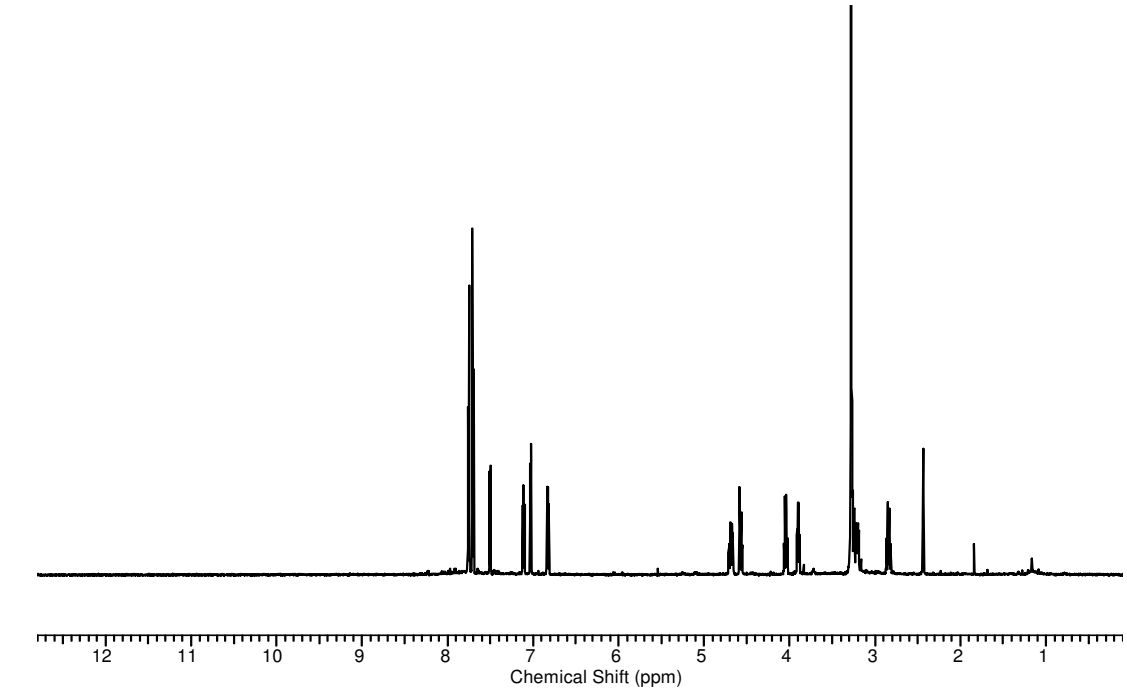


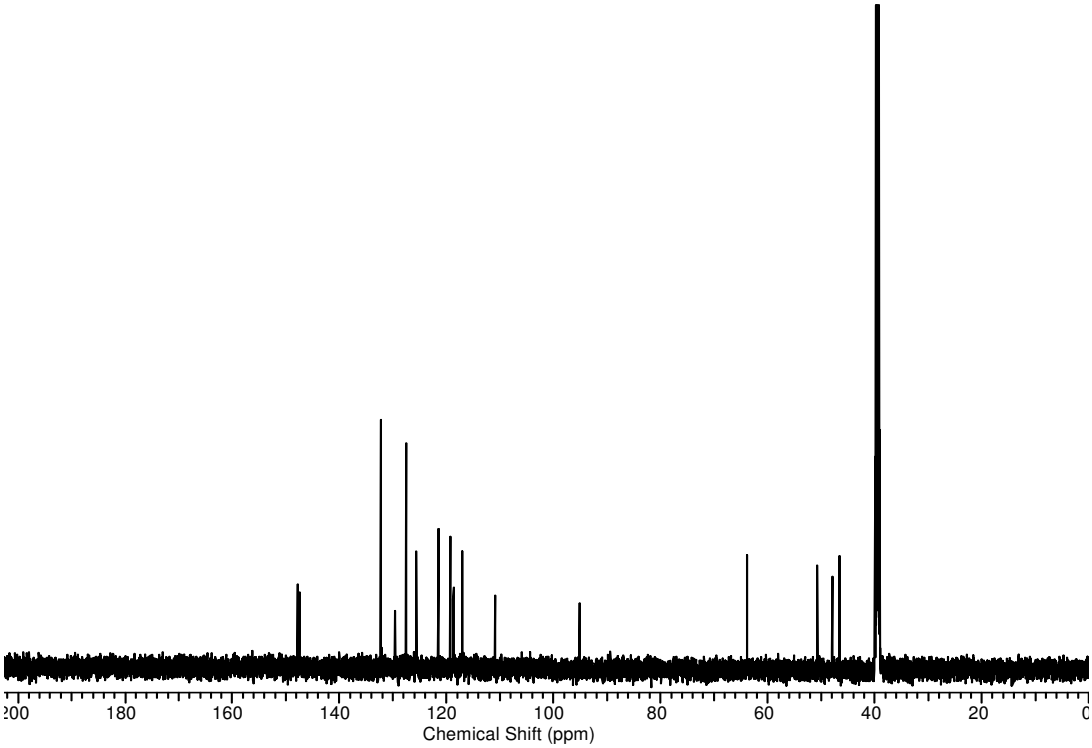
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 29(1,4)



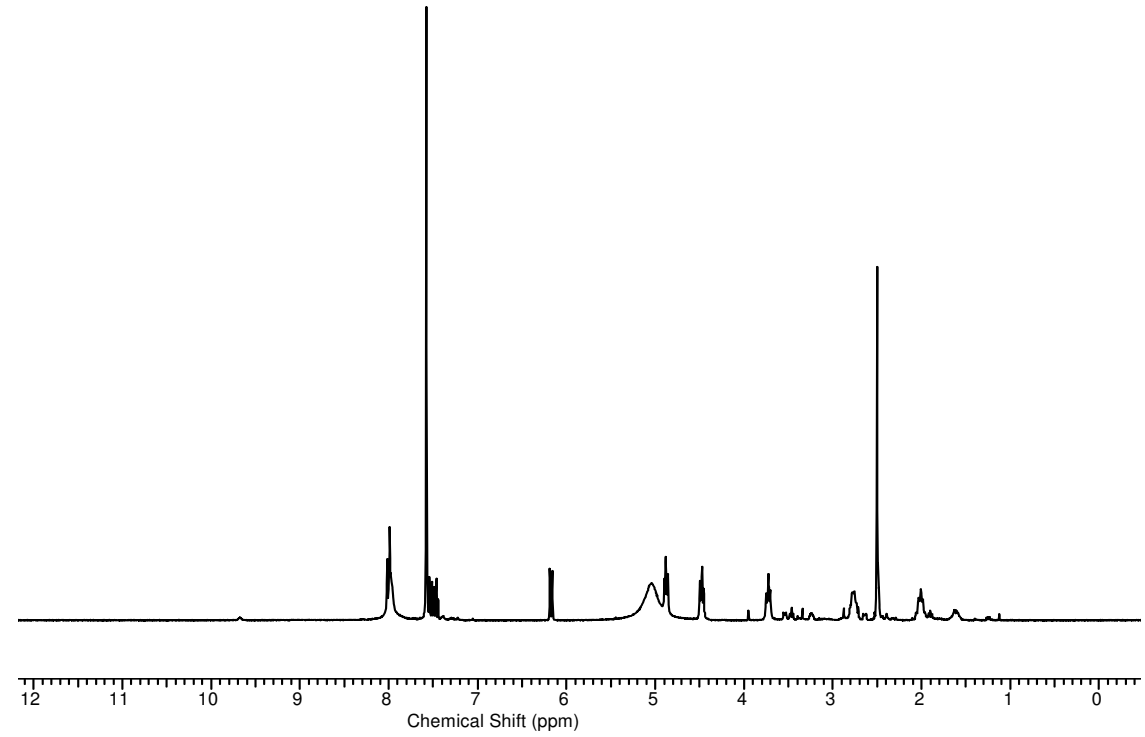


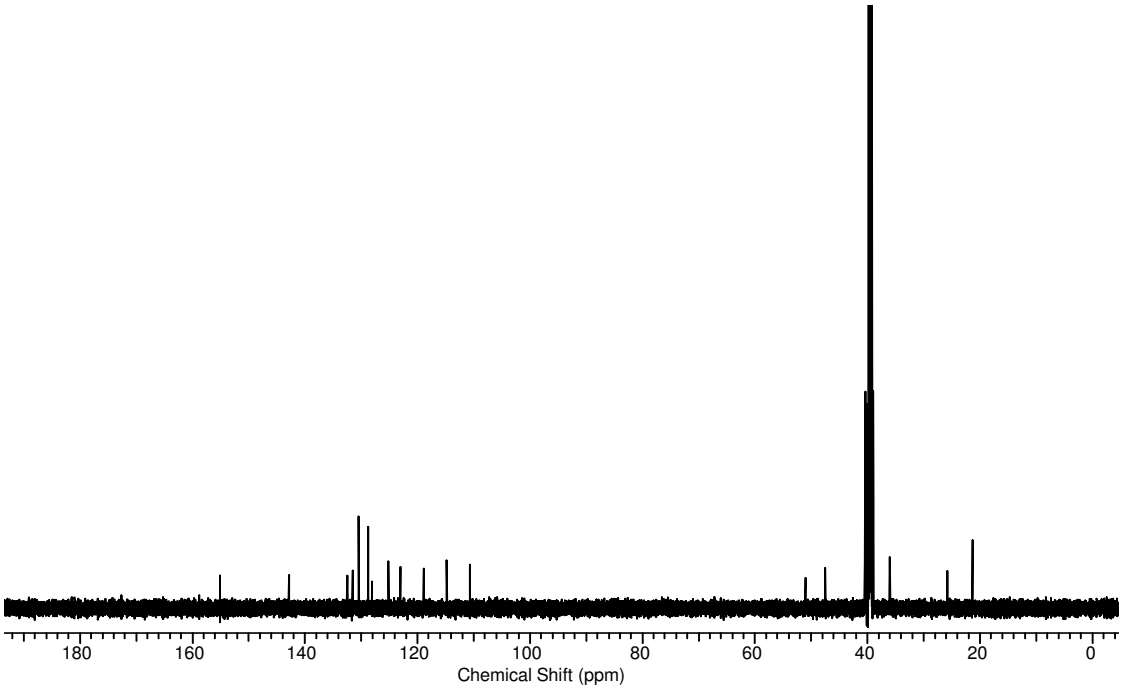
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 30(1,4)



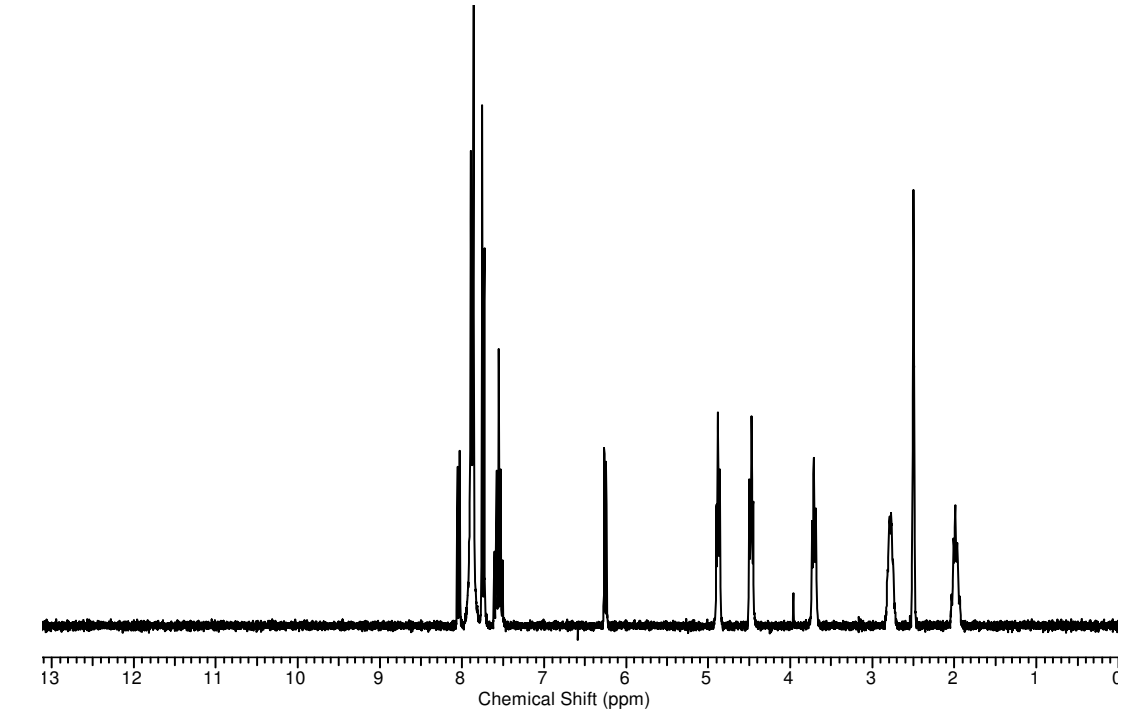


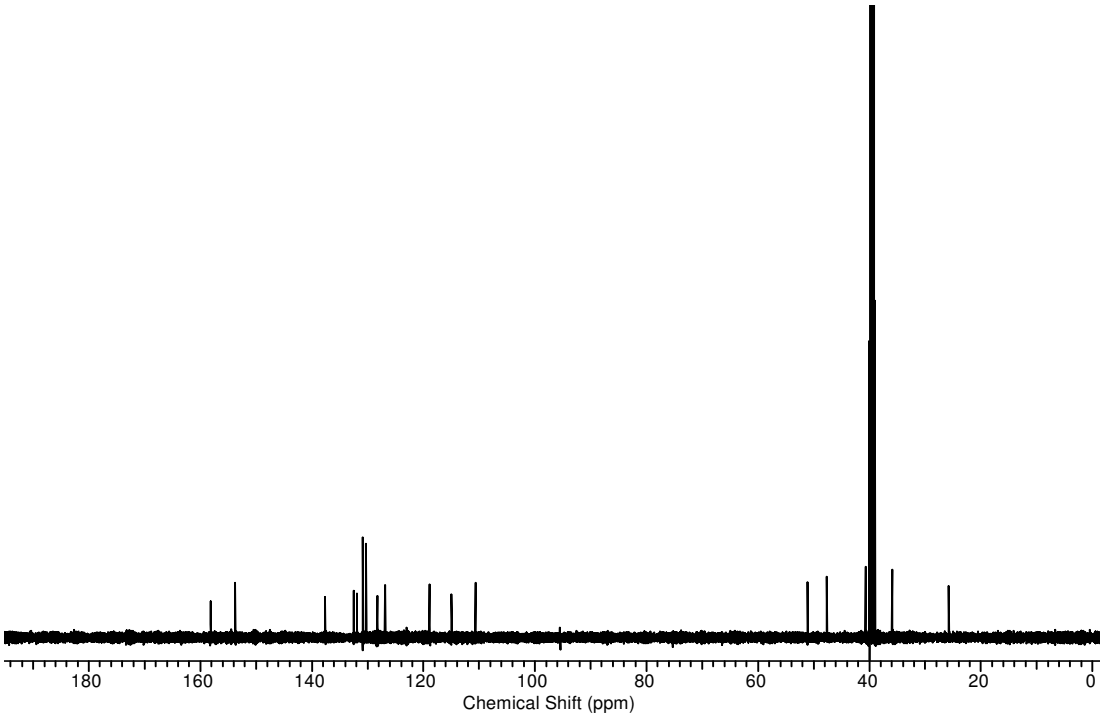
^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 34(1,1)





^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 34(1,3)





^{1}H and ^{13}C NMR spectra (d_6-DMSO) for compound 40(1,3)