Palladium-Catalysed Aminosulfonylation of Aryl-, Alkenyl- and Heteroaryl Halides: Scope of the Three-Component Synthesis of *N*-Aminosulfonamides

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Electronic Supporting Information

Experimental

General considerations

Chemicals were purchased from Sigma Aldrich, Alfa Aesar, TCI UK or Acros and used without further purification with the exception of DABCO which was sublimed (50 ^{o}C, 1 mbar) prior to use. Anhydrous (where stated), HPLC grade solvents were purchased from Sigma Aldrich, Fisher Scientific or Rathburn and used directly without further purification with the exception of 1,4-dioxane which was distilled from calcium hydride onto 4 Å molecular sieves which had been activated by heating under vacuum (0.1 mbar) at >200 ^{o}C for 12 hrs. 'Petrol' refers to the fraction of light petroleum ether boiling in the range 40-60 ^{o}C. Cesium carbonate was dried prior to use in a vacuum drying pistol (120 ^{o}C, 10 mbar) for 18 hrs.

Reactions were performed with continuous magnetic stirring, under an atmosphere of nitrogen, unless otherwise stated, using standard Schlenk techniques and all glassware was dried in an oven (>200 ^{o}C, overnight) and allowed to cool under a flow of nitrogen (passed through a Drierite® filled tube) prior to use. Flash column chromatography was performed using Apollo scientific silica gel 60 (particle size 0.040-0.063 nm) with the indicated eluents. Thin Layer Chromatography (TLC) analysis was carried out on Merck Kieselgel 60 PF254 pre-coated aluminium backed sheets and visualised either by UV fluorescence (254 nm) and/or by staining with potassium permanganate ($KMnO_4$).

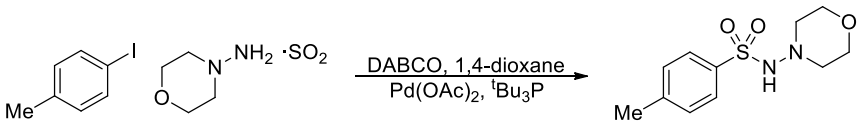
NMR spectra were recorded at ambient temperature on either Brüker DPX200 (200 MHz), DPX400 (400 MHz) or AVC500 (500 MHz) spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) and referenced relative to the residual solvent peak(s) (as specified). Coupling constants (*J*) are given in Hertz (Hz) and rounded to the nearest 0.1 Hz. Assignments were made on the basis of chemical shifts, coupling constants, COSY, HSQC and comparison with spectra of related compounds. Signal multiplicities are denoted as: s, singlet; d, doublet; t, triplet; q, quartet; quin., quintet; m, multiplet; br., broad; app., apparent.

Melting points were measured using a Leica Gallen III hot-stage microscope. Low resolution mass spectra were recorded on a Fisons Platform spectrometer (ESI). High resolution mass spectra were measured by the internal service at the University of Oxford using a Bruker Daltronics microTOF spectrometer. *m/z* ratio values are reported in Daltons; high resolution values are calculated to four decimal places from the molecular formula, all found within a tolerance of 5 ppm. Infrared spectra were determined neat using a Bruker Tensor 27 FT spectrometer with an internal range of 600-4000 cm^{-1}.

Data for compounds not included below can be found in our earlier Communicaiton.[1]

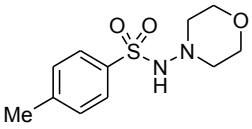
N-Aminosulfonamides

General procedure for the formation of *N*-morpholinosulfonamides using 4-aminomorpholine-sulfur dioxide complex, 8, exemplified by the preparation of 4-methyl-*N*-morpholinobenzenesulfonamide, 4a



A glass reaction tube was charged with 4-iodotoluene (50 mg, 0.23 mmol), 4-aminomorpholine-sulfur dioxide complex **8** (57 mg, 0.34 mmol), 1,4-diazabicyclo[2.2.2]octane (DABCO) (28 mg, 0.25 mmol), palladium(II) acetate (5 mg, 23 μmol) and tri-*tert*-butylphosphonium tetrafluoroborate (13 mg, 46 μmol) and sealed under N_2. 1,4-Dioxane (1.6 mL) was added and the tube heated at 70 °C with stirring for 16 hrs. After cooling, the reaction mixture was filtered through Celite. The Celite pad was washed sequentially with CH_2Cl_2 (10 mL) and Et_2O (5 mL) and the combined organic extracts concentrated *in vacuo*. Purification by flash column chromatography (50–100% Et_2O in petrol) afforded the *N-aminosulfonamide* **4a** as colourless crystals (54 mg, 92%). Data for all compounds made by this method is either previously reported in our communication[1] or reported below, made by the DABSO method.

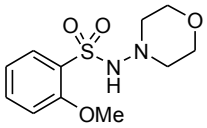
General procedure (A) for the formation of *N*-aminosulfonamides using DABCO·$(SO_2)_2$ complex, 1 (0.6 equivalents), and DABCO (0.5 equivalents), exemplified by the preparation of 4-methyl-*N*-morpholinobenzenesulfonamide, 4a



A glass reaction tube was charged with 4-iodotoluene (50 mg, 0.23 mmol), 4-aminomorpholine (33 μl, 0.34 mmol), DABCO·$(SO_2)_2$ complex **1** (33 mg, 0.14 mmol), 1,4-diazabicyclo[2.2.2]octane (13 mg, 0.11 mmol), palladium(II) acetate (5 mg, 23 μmol) and tri-*tert*-butylphosphonium tetrafluoroborate (13 mg, 46 μmol) and sealed under N_2. 1,4-Dioxane (1.6 mL) was added and the tube heated at 70 °C for 16 hrs. After cooling, the reaction mixture was filtered through Celite. The Celite pad was washed sequentially with CH_2Cl_2 (10 mL) and Et_2O (5 mL) and the combined organic extracts concentrated *in vacuo*. Purification by flash column chromatography (50–100% Et_2O in petrol) afforded the *N*-

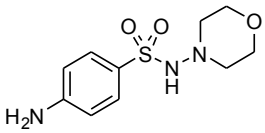
aminosulfonamide **4a** as colourless crystals (54 mg, 92%). Data previously reported in communication.[1]

General procedure (B) for the formation of *N*-aminosulfonamides using DABCO·$(SO_2)_2$ complex, 1 (1.1 equivalents), exemplified by the preparation of 2-methoxy-*N*-morpholinobenzenesulfonamide (Table 2, Entry 7)



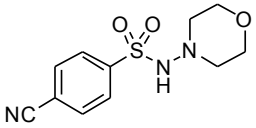
A glass reaction tube was charged with 2-iodoanisole (50 mg, 0.21 mmol), 4-aminomorpholine (31 µl, 0.32 mmol), DABCO·$(SO_2)_2$ complex **1** (57 mg, 0.24 mmol), palladium(II) acetate (5 mg, 21 µmol) and tri-*tert*-butylphosphonium tetrafluoroborate (12 mg, 42 µmol) and sealed under N_2. 1,4-Dioxane (1.6 mL) was added and the tube heated at 70 °C for 16 hrs. After cooling, the reaction mixture was filtered through Celite. The Celite pad was washed sequentially with CH_2Cl_2 (10 mL) and Et_2O (5 mL) and the combined organic extracts concentrated *in vacuo*. Purification by flash column chromatography (50–100% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (44 mg, 76%). Data previously reported in communication.[1]

4-Amino-*N*-morpholinobenzenesulfonamide (Table 2, Entry 9)



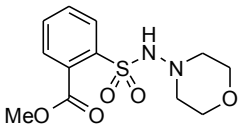
The general procedure A was followed with the use of 4-iodoaniline (50 mg, 0.23 mmol). Flash column chromatography (100% Et_2O) afforded the *N-aminosulfonamide* as colourless crystals (52 mg, 88%); mp 159-160 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (2H, d, *J* 8.6, Ar-*H*), 6.69 (2H, d, *J* 8.6, Ar-*H*), 5.17 (1H, s, N*H*), 4.16 (2H, br. s, NH_2), 3.62 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$), 2.63 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 130.3, 126.6, 113.8, 66.7, 56.8; IR υ_{max} (neat)/cm^{-1} 3478, 3374, 3148, 1632, 1594, 1501, 1314 (SO_2), 1143 (SO_2), 1099; LRMS (ESI) *m/z* 280 (35%, $[M+Na]^+$), 537 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 280.0718 $[M+Na]^+$, $C_{21}H_{22}N_2O_3SNa$ requires *m/z* 280.0726.

4-Cyano-*N*-morpholinobenzenesulfonamide (Table 2, Entry 11)



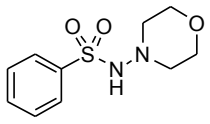
The general procedure B was followed with the use of 4-iodobenzonitrile (50 mg, 0.22 mmol). Flash column chromatography (50–100% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (25 mg, 43%); mp 185-186 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (1H, s, N*H*), 8.08 (2H, d, *J* 8.4, Ar-*H*), 8.01 (2H, d, *J* 8.4, Ar-*H*), 3.45 (4H, t, *J* 4.4, ($NCH_2CH_2O)_2$), 2.50 – 2.47 (4H, m, ($NCH_2CH_2O)_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.9, 132.6, 128.7, 117.2, 116.9, 66.5, 56.9; IR υ_{max} (neat)/cm^{-1} 3194, 2960, 2923, 2853, 2233 (CN), 1459, 1338 (SO_2), 1264, 1165 (SO_2), 1110, 1090; LRMS (ESI) *m/z* 266 (100%, $[M-H]^-$); HRMS (ESI) found *m/z* 266.0610 $[M-H]^-$, $C_{11}H_{12}N_3O_3S$ requires 266.0605.

Methyl 2-(*N*-morpholinosulfamoyl)benzoate (Table 2, Entry 13)



The general procedure B was followed with the use of 2-iodomethylbenzoate (50 mg, 0.19 mmol). Flash column chromatography (25–50% EtOAc in petrol) afforded the *N-aminosulfonamide* as a yellow oil (20 mg, 39%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 – 8.20 (1H, m, Ar-*H*), 7.78 – 7.76 (1H, m, Ar-*H*), 7.69 – 7.66 (2H, m, Ar-*H*), 6.77 (1H, s, N*H*), 3.99 (3H, s, *Me*), 3.58 (4H, t, *J* 4.5, ($NCH_2CH_2O)_2$), 2.68 (4H, t, *J* 4.5, ($NCH_2CH_2O)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 137.7, 132.8, 131.6, 131.2, 131.1, 130.1, 66.5, 56.4, 53.5; IR υ_{max} (neat)/cm^{-1} 3240, 2961, 2855, 1723 (CO), 1436, 1340 (SO_2), 1297, 1263, 1171 (SO_2), 1112, 1061; LRMS (ESI) *m/z* 323 (90%, $[M+Na]^+$), 623 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 323.0678 $[M+Na]^+$, $C_{12}H_{16}N_2O_5SNa$ requires *m/z* 323.0672.

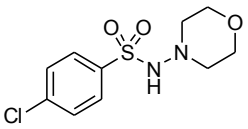
***N*-Morpholinobenzenesulfonamide (Table 2, Entry 15)**



The general procedure B was followed with the use of iodobenzene (50 mg, 0.25 mmol). Flash column chromatography (50–100% Et_2O in hexane) afforded the *N-aminosulfonamide* as colourless crystals (46 mg, 77%); mp 121-122 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ

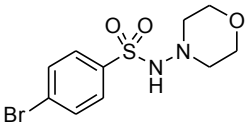
8.00 – 7.97 (2H, m, Ar-*H*), 7.64 – 7.60 (1H, m, Ar-*H*), 7.56 – 7.52 (2H, m, Ar-*H*), 5.43 (1H, s, N*H*), 3.61 (4H, t, *J* 4.5, (NCH_2CH_2O)$_2$), 2.62 (4H, t, *J* 4.5, (NCH_2CH_2O)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 133.2, 128.8, 128.1, 66.6, 56.8; IR υ_{max} (neat)/cm^{-1} 3213, 2963, 2858, 1448, 1362, 1327 (SO_2), 1264, 1164 (SO_2), 1110; LRMS (ESI) *m/z* 265 (60%, $[M+Na]^+$), 507 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 265.0618 $[M+Na]^+$, $C_{10}H_{14}N_2O_3SNa$ requires *m/z* 265.0617.

4-Chloro-*N*-morpholinobenzenesulfonamide (Table 2, Entry 17)



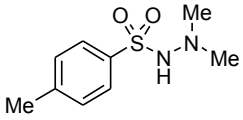
The general procedure B was followed with the use of 1-chloro-4-iodobenzene (50 mg, 0.21 mmol). Flash column chromatography (50–75% Et_2O in petrol) afforded the *N-aminosulfonamide* **XX** as colourless crystals (49 mg, 84%); mp 174-175 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (2H, d, *J* 8.6, Ar-*H*), 7.51 (2H, d, *J* 8.6, Ar-*H*), 5.58 (1H, s, N*H*), 3.62 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$), 2.65 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 137.1, 129.6, 129.2, 66.6, 56.8; IR υ_{max} (neat)/cm^{-1} 3190, 2975, 2856, 1336 (SO_2), 1164 (SO_2), 1111; LRMS (ESI) *m/z* 277, 279 (20%, 10%, $[M+H]^+$), 299, 301 (70%, 40%, $[M+Na]^+$), 331 (30%, $[M+Na+MeOH]^+$), 577 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 299.0228, 301.0198 $[M+Na]^+$, $C_{10}H_{13}ClN_2O_3SNa$ requires *m/z* 299.0228, 301.0198.

4-Bromo-*N*-morpholinobenzenesulfonamide (Table 2, Entry 18)



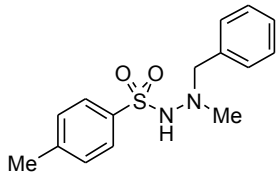
The general procedure B was followed with the use of 1-bromo-4-iodobenzene (65 mg, 0.23 mmol). Flash column chromatography (50–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (57 mg, 77%); mp 170-171 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* 8.6, Ar-*H*), 7.67 (2H, d, *J* 8.6, Ar-*H*), 5.60 (1H, s, N*H*), 3.63 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$), 2.65 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 132.2, 129.7, 128.3, 66.6, 56.8; IR υ_{max} (neat)/cm^{-1} 3195, 2970, 2858, 1338 (SO_2), 1165 (SO_2), 1112; LRMS (ESI) *m/z* 321, 323 (20%, $[M+H]^+$), 342, 344 (45%, $[M+Na]^+$), 663, 665, 667 (80%, 100%, 90%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 342.9729, 344.9706 $[M+Na]^+$, $C_{10}H_{13}BrN_2O_3SNa$ requires *m/z* 342.9722, 344.9702.

_N'_,_N'_,4-Trimethylbenzenesulfonohydrazide (Table 3, Entry 4)



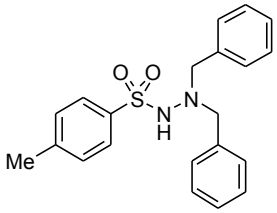
The general procedure A was followed with the use of 1,1-dimethylhydrazine (21 mg, 0.34 mmol). Flash column chromatography (25–50% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (32 mg, 65%); mp 76-77 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* 8.1, Ar-*H*), 7.32 (2H, d, *J* 8.1, Ar-*H*), 5.14 (1H, br. s, N*H*), 2.45 (3H, s, Ar-*Me*), 2.40 (6H, s, N*Me*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 135.8, 129.5, 128.2, 48.5, 21.6; IR υ_{max} (neat)/cm^{-1} 3258, 2919, 1596, 1458, 1394, 1325 (SO_2), 1156 (SO_2), 1092, 1036; LRMS (ESI) *m/z* 237 (70%, $[M+Na]^+$), 269 (30%, $[M+Na+MeOH]^+$), 451 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 237.0670 $[M+Na]^+$, $C_9H_{14}N_2O_2SNa$ requires *m/z* 237.0668.

_N'_-Benzyl-_N'_,4-dimethylbenzenesulfonohydrazide (Table 3, Entry 5)



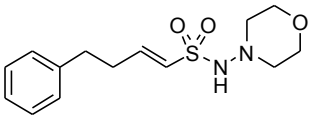
The general procedure A was followed with the use of 1-benzyl-1-methylhydrazine (47 mg, 0.34 mmol). Flash column chromatography (11:8:1 petrol:Et_2O:Et_3N) afforded the *N-aminosulfonamide* as yellow crystals (53 mg, 80%); mp 84-85 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* 8.2, Ar-*H*), 7.29 – 7.25 (5H, m, Ar-*H*), 7.16 – 7.14 (2H, m, Ar-*H*), 5.51 (1H, s, N*H*), 3.71 (2H, s, NC*H*$_2$Ph), 2.43 (3H, s, Ar-*Me*), 2.32 (3H, s, NHN*Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 135.7, 135.2, 129.6, 129.4, 128.3, 128.2, 127.7, 64.5, 44.8, 21.6; IR υ_{max} (neat)/cm^{-1} 3236, 1597, 1493, 1452, 1399, 1328 (SO_2), 1162 (SO_2), 1091; LRMS (ESI) *m/z* 291 (20%, $[M+H]^+$), 313 (80%, $[M+Na]^+$), 603 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 313.0972 $[M+Na]^+$, $C_{15}H_{18}N_2O_2SNa$ requires *m/z* 313.0981.

_N'_,_N'_-Dibenzyl-4-methylbenzenesulfonohydrazide (Table 3, Entry 6)



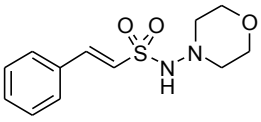
The general procedure A was followed with the use of 4-iodotoluene (350 mg, 1.61 mmol), 1,1-dibenzylhydrazine (511 mg, 2.41 mmol), DABCO-$(SO_2)_2$ complex (231 mg, 0.96 mmol), DABCO (90 mg, 0.80 mmol), palladium(II) acetate (36 mg, 0.16 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (93 mg, 0.32 mmol) and 1,4-dioxane (11 mL). Flash column chromatography (13:6:1 petrol:Et_2O:Et_3N) afforded the *N-aminosulfonamide* **XX** as pale yellow crystals (499 mg, 85%); mp 123-124 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (2H, d, *J* 8.3, Ar-*H*), 7.28 – 7.26 (6H, m, Ar-*H*), 7.19 – 7.16 (6H, m, Ar-*H*), 5.53 (1H, s, N*H*), 3.73 (4H, s, N(CH_2Ph)$_2$), 2.41 (3H, s, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 135.4, 134.9, 129.8, 129.4, 128.4, 128.2, 127.6, 59.7, 21.6; IR υ_{max} (neat)/cm^{-1} 3203, 1738, 1598, 1427, 1325 (SO_2), 1157 (SO_2), 1091; LRMS (ESI) *m/z* 367 (80%, $[M+H]^+$), 389 (60%, $[M+Na]^+$), 755 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 389.1280 $[M+Na]^+$, $C_{21}H_{22}N_2O_2SNa$ requires *m/z* 389.1294.

(_E_)-_N_-Morpholino-4-phenylbut-1-ene-1-sulfonamide (Table 4, Entry 1)



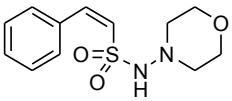
The general procedure B was followed with the use of (*E*)-(4-iodobut-3-enyl)benzene[2] (50 mg, 0.19 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (35 mg, 60%); mp 95-97 °C (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (2H, m, Ar-*H*), 7.24 – 7.17 (3H, m, Ar-*H*), 6.92 (1H, dt, *J* 15.2, 6.7, CH_2CHCH), 6.26 (1H, dt, *J* 15.2, 1.5, CH_2CHCH), 5.13 (1H, br. s, N*H*), 3.67 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$), 2.84 (2H, t, *J* 7.4, CCH_2CH_2CH), 2.72 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$), 2.67 – 2.59 (2H, m, CCH_2CH_2CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 139.9, 128.6, 128.3, 127.2, 126.4, 66.6, 57.2, 33.7, 32.6; IR υ_{max} (neat)/cm^{-1} 3210, 3060, 2960, 2856, 2284, 1960, 1714, 1632, 1496, 1361 (SO_2), 1278, 1149 (SO_2), 1072, 1011; LRMS (ESI) *m/z* 297 (20%, $[M+H]^+$), 319 (80%, $[M+Na]^+$), 615 (100%, $[2M+Na]^+$), 911 (10%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 319.1091 $[M+Na]^+$, $C_{14}H_{20}N_2O_3SNa$ requires *m/z* 319.1087.

(*E*)-*N*-Morpholino-2-phenylethenesulfonamide (Table 4, Entry 3)



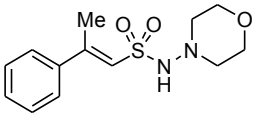
The general procedure B was followed with the use of (*E*)-(2-iodovinyl)benzene[3] (50 mg, 0.22 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (31 mg, 53%); mp 159-161 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, d, *J* 15.5, CHC*H*SO_2), 7.56 – 7.40 (5H, m, Ar-*H*), 6.81 (1H, d, *J* 15.5, C*H*CHSO_2), 5.31 (1H, br. s, N*H*), 3.73 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$), 2.88 (4H, t, *J* 4.6, (NCH_2CH_2O)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 132.5, 131.1, 129.2, 128.3, 123.5, 66.6, 57.4; IR υ_{max} (neat)/cm^{-1} 3175, 2851, 1457, 1370, 1327 (SO_2), 1263, 1137 (SO_2), 1108; LRMS (ESI) *m/z* 269 (15%, $[M+H]^+$), 291 (55%, $[M+Na]^+$), 323 (15%, $[M+Na+MeOH]^+$), 559 (100%, $[2M+Na]^+$), 827 (20%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 291.0772 $[M+Na]^+$, $C_9H_{14}N_2O_2SNa$ requires *m/z* 291.0774.

(*Z*)-*N*-Morpholino-2-phenylethenesulfonamide (Table 4, Entry 4)



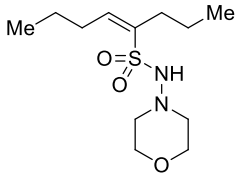
The general procedure B was followed with the use of (*Z*)-(2-iodovinyl)benzene[3] (>20:1, *Z*:*E*) (50 mg, 0.22 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded an inseparable mixture (3.5:1, *Z*:*E*) of *Z N-aminosulfonamide* and *E N-aminosulfonamide* as a yellow oil (30 mg, 51%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (2H, m, Ar-*H*, *Z*), 7.62 (0.3H, d, *J* 15.5, CHC*H*SO_2, *E*), 7.54 – 7.33 (4.5H, m, Ar-*H*, *Z* and *E*), 7.09 (1H, d, *J* 12.2, CHC*H*SO_2, *Z*), 6.81 (0.3H, d, *J* 15.5, C*H*CHSO_2, *E*), 6.48 (1H, d, *J* 12.2, C*H*CHSO_2, Z), 5.51 (0.3H, s, N*H*, *E*), 5.48 (1H, s, N*H*, *Z*), 3.75 – 3.65 (5.2H, m, (NCH_2CH_2O)$_2$, *Z* and *E*), 2.87 (1.2H, t, *J* 4.6, (NCH_2CH_2O)$_2$, *E*), 2.78 (4H, t, *J* 4.5, (NCH_2CH_2O)$_2$, *Z*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7 (*E*), 141.3 (*Z*), 132.5 (*E*), 131.1 (*E*), 130.4 (*Z*), 130.1 (*Z*), 129.2 (*E*), 128.3 (*E* and *Z*) (2H), 126.9 (*Z*), 123.5 (*E* and *Z*) (2H), 66.6 (*E*), 66.5 (*Z*), 57.4 (*E*), 57.1 (*Z*); LRMS (ESI) *m/z* 269 (15%, $[M+H]^+$), 291 (55%, $[M+Na]^+$), 323 (15%, $[M+Na+MeOH]^+$), 559 (100%, $[2M+Na]^+$), 827 (20%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 291.0772 $[M+Na]^+$, $C_9H_{14}N_2O_2SNa$ requires *m/z* 291.0774.

(*E*)-*N*-Morpholino-2-phenylprop-1-ene-1-sulfonamide (Table 4, Entry 6)



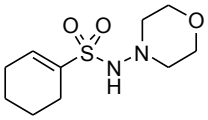
The general procedure B was followed with the use of (*E*)-(1-iodoprop-1-en-2-yl)benzene[3] (50 mg, 0.20 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (50 mg, 86%); mp 117-118 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (5H, m, Ar-*H*), 6.54 (1H, d, *J* 1.2, C*H*), 5.43 (1H, s, N*H*), 3.75 (4H, t, *J* 4.5, ($NCH_2CH_2O)_2$), 2.89 (4H, t, *J* 4.5, ($NCH_2CH_2O)_2$), 2.59 (3H, d, *J* 1.2, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 140.3, 129.8, 128.8, 126.3, 124.1, 66.7, 57.3, 17.9; IR υ_{max} (neat)/cm^{-1} 3226, 2830, 1608, 1309 (SO_2), 1263, 1140 (SO_2), 1106; LRMS (ESI) *m/z* 283 (10%, $[M+H]^+$), 305 (15%, $[M+Na]^+$), 587 (100%, $[2M+Na]^+$), 869 (30%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 305.0928 $[M+Na]^+$, $C_{13}H_{18}N_2O_3SNa$ requires *m/z* 305.0930.

(*Z*)-*N*-Morpholinooct-4-ene-4-sulfonamide (Table 4, Entry 7)



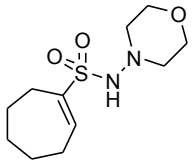
The general procedure B was followed with the use of (*Z*)-4-iodooct-4-ene[4] (50 mg, 0.21 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (33 mg, 57%); mp 73-75 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (1H, t, *J* 7.6, C*H*), 5.09 (1H, br. s, N*H*), 3.70 (4H, t, *J* 4.5, ($NCH_2CH_2O)_2$), 2.81 (4H, t, *J* 4.5($NCH_2CH_2O)_2$), 2.34 (2H, app. t, *J* 8.0, $CHCCH_2$), 2.21 (2H, app. q, *J* 7.4, CH_2CHCCH_2), 1.67 – 1.46 (4H, m, 2 x CH_2), 1.00 – 0.94 (6H, m, 2 x *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 137.7, 66.7, 57.3, 30.5, 29.0, 22.8, 21.8, 14.1, 13.8; IR υ_{max} (neat)/cm^{-1} 3205, 2957, 2872, 1455, 1323 (SO_2), 1279, 1170, 1138 (SO_2), 1108, 1074; LRMS (ESI) *m/z* 277 (25%, $[M+H]^+$), 299 (85%, $[M+Na]^+$), 331 (20%, $[M+Na+MeOH]^+$), 575 (100%, $[2M+Na]^+$), 851 (15%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 299.1400 $[M+Na]^+$, $C_{12}H_{24}N_2O_3SNa$ requires *m/z* 299.1400.

_N_-Morpholinocyclohex-1-ene-1-sulfonamide (Table 4, Entry 8)



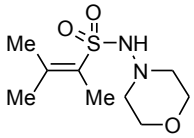
The general procedure B was followed with the use of 1-iodocyclohex-1-ene[3] (50 mg, 0.24 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (47 mg, 79%); mp 120-122 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 – 6.94 (1H, m, C*H*), 5.13 (1H, br. s, N*H*), 3.72 (4H, t, *J* 4.6, $(NCH_2CH_2O)_2$), 2.82 (4H, t, *J* 4.6, $(NCH_2CH_2O)_2$), 2.40 – 2.34 (2H, m, CH_2), 2.32 – 2.25 (2H, m, CH_2), 1.76 – 1.69 (2H, m, CH_2), 1.67 – 1.60 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 136.5, 66.6, 57.3, 25.5, 23.7, 22.1, 20.9; IR υ_{max} (neat)/cm^{-1} 3196, 1438, 1319 (SO_2), 1263, 1143 (SO_2), 1108, 1052; LRMS (ESI) *m/z* 247 (10%, $[M+H]^+$), 269 (85%, $[M+Na]^+$), 301 (25%, $[M+Na+MeOH]^+$), 515 (100%, $[2M+Na]^+$), 761 (10%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 269.0930 $[M+Na]^+$, $C_{10}H_{18}N_2O_3SNa$ requires *m/z* 269.0930.

_N_-Morpholinocyclohept-1-ene-1-sulfonamide (Table 4, Entry 9)



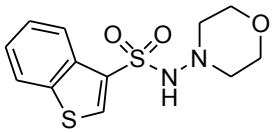
The general procedure B was followed with the use of 1-iodocyclohept-1-ene[2] (50 mg, 0.23 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (52 mg, 89%); mp 109-110 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (1H, t, *J* 6.5, C*H*), 5.09 (1H, br. s, N*H*), 3.73 (4H, t, *J* 4.6, $(NCH_2CH_2O)_2$), 2.84 (4H, t, *J* 4.6, $(NCH_2CH_2O)_2$), 2.58 – 2.54 (2H, m, CH_2), 2.40 – 2.34 (2H, m, CH_2), 1.83 – 1.77 (2H, m, CH_2), 1.66 – 1.56 (4H, m, 2 x CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 141.3, 66.6, 57.6, 31.4, 28.6, 28.0, 26.5, 25.5; IR υ_{max} (neat)/cm^{-1} 3168, 2919, 2849, 1645, 1455, 1299 (SO_2), 1157, 1140 (SO_2), 1114; LRMS (ESI) *m/z* 261 (15%, $[M+H]^+$), 283 (45%, $[M+Na]^+$), 543 (100%, $[2M+Na]^+$), 803 (25%, $[3M+Na]^+$); HRMS (ESI) found *m/z* 283.1088 $[M+Na]^+$, $C_{11}H_{20}N_2O_3SNa$ requires *m/z* 283.1087.

3-Methyl-*N*-morpholinobut-2-ene-2-sulfonamide (Table 4, Entry 10)



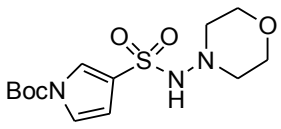
The general procedure B was followed with the use of 2-iodo-3-methylbut-2-ene[5] (50 mg, 0.26 mmol). Flash column chromatography (25–75% Et_2O in petrol) afforded the *N-aminosulfonamide* as colourless crystals (43 mg, 72%); mp 132-133 ^oC (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (1H, br. s, N*H*), 3.71 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$), 2.81 (4H, t, *J* 4.6, ($NCH_2CH_2O)_2$), 2.25 (3H, app. d, *J* 2.7, *Me*CSO_2), 2.07 (3H, app. t, *J* 1.0, *Me*$CCSO_2$), 1.92 (3H, app. d, *J* 0.8, *Me*$CCSO_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 128.8, 66.8, 57.0, 24.3, 22.8, 16.6; IR υ_{max} (neat)/cm^{-1} 3174, 2960, 2920, 2863, 1653, 1457, 1319 (SO_2), 1260, 1151 (SO_2), 1106; LRMS (ESI) *m/z* 235 (5%, $[M+H]^+$), 257 (80%, $[M+Na]^+$), 289 (30%, $[M+Na+MeOH]^+$), 491 (100%, $[2M+Na]^+$), ; HRMS (ESI) found *m/z* 257.0932 $[M+Na]^+$, $C_9H_{18}N_2O_3SNa$ requires *m/z* 257.0930.

***N*-(Morpholin-4-yl)-1-benzothiophene-3-sulfonamide (Table 5, Entry 2)**



The general procedure B was followed with the use of 3-iodo-1-benzothiophene[5] (62 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* as a white solid (53 mg, 73%); mp 142-144 °C (CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, s, C=C*H*S), 8.37-8.32 (1H, m, Ar-*H*), 7.95-7.88 (1H, m, Ar-*H*), 7.57-7.44 (2H, m, 2 × Ar-*H*), 5.68 (1H, s, N*H*), 3.55 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$), 2.60 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 136.2, 133.8, 132.3, 125.8, 125.7, 123.8, 122.9, 66.5, 56.9; IR ν_{max} (neat)/cm^{-1} 3242, 2963, 2857, 2361, 1336 (SO_2), 1158 (SO_2); LRMS (ESI^+) *m/z* 619 (100%, $[2M + Na]^+$) 321 (69%, $[M + Na]^+$); HRMS (ESI^+) found *m/z* 321.0335 $[M + Na]^+$, $C_{12}H_{14}N_2NaO_3S_2^+$ requires *m/z* 321.0344.

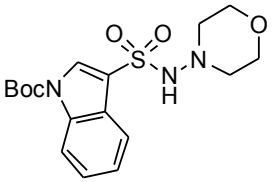
***tert*-Butyl 3-(morpholin-4-ylsulfamoyl)-1*H*-pyrrole-1-carboxylate (Table 5, Entry 3)**



The general procedure B was followed with the use of *tert*-butyl 3-iodo-pyrrole-1-carboxylate[6] (70 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded

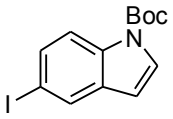
the *N-aminosulfonamide* as a white solid (16 mg, 20%); mp 130-132 ºC (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.81 (1H, m, C=C*H*N), 7.30-7.28 (1H, m, CH=C*H*N), 6.55 (1H, dd, *J* 3.5, 2.0, C*H*=CHN), 5.47 (1H, s, N*H*), 3.68 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 2.75 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 1.63 (9H, s, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 125.3, 124.2, 121.5, 110.5, 86.0, 66.6, 57.0, 27.9; IR ν_{max} (neat)/cm^{-1} 3227, 2979, 2925, 2857, 1755 (CO), 1334 (SO_2), 1154 (SO_2); LRMS (ESI$^+$) *m/z* 686 (100%, [2M + Na]$^+$); HRMS (ESI$^+$) found *m/z* 354.1094 [M + Na]$^+$, $C_{13}H_{21}N_3NaO_5S^+$ requires *m/z* 354.1095.

tert-Butyl 3-(morpholin-4-ylsulfamoyl)-1*H*-indole-1-carboxylate (Table 5, Entry 4)



The general procedure B was followed with the use of *tert*-butyl 3-iodo-1*H*-indole-1-carboxylate[7] (92 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* as a white solid (44 mg, 48%); mp 149-153 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (1H, s, C=C*H*N) overlapping 8.23 (1H, app d, *J* 9.5, Ar-*H*), 8.02-7.95 (1H, m, Ar-*H*), 7.48-7.35 (2H, m, 2 × Ar-*H*), 5.71 (1H, s, N*H*), 3.60 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 2.69 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 1.70 (9H, s, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 135.5, 131.3, 126.0, 125.1, 124.2, 120.7, 118.7, 115.5, 85.8, 66.5, 57.0, 28.1; IR ν_{max} (neat)/cm^{-1} 3161, 2976, 2957, 2360, 1748 (CO), 1341 (SO_2), 1146 (SO_2); LRMS (ESI$^+$) *m/z* 785 (100%, [2M + Na]$^+$), 404 (48%, [M + Na]$^+$), 382 (18%, [M + H]$^+$); HRMS (ESI$^+$) found *m/z* 404.1244 [M + Na]$^+$, $C_{17}H_{23}N_3NaO_5S^+$ requires *m/z* 404.1251.

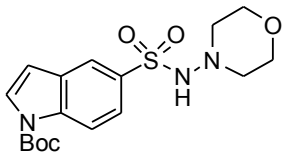
tert-Butyl 5-iodo-1*H*-indole-1-carboxylate



Di-*tert*-butyldicarbonate (1.55 g, 7.11 mmol), NEt_3 (2.7 mL, 19.4 mmol) and 4-dimethylaminopyridine (79 mg, 0.65 mmol) were added to a solution of 5-iodoindole (1.57 g, 6.46 mmol) in CH_2Cl_2 (30 mL). The reaction mixture was stirred at rt for 1 h and then washed twice with sodium metabisulphite (5% aq solution), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (5% ethyl acetate in petrol) afforded the titled *iodide* as a light orange solid (1.41 g, 63%); mp 45-46 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (1H, d, *J* 8.5, Ar*H*) overlapping 7.90 (1H, d, *J* 2.0, Ar*H*), 7.59 (1H, dd, *J* 8.5,

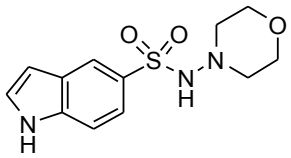
2.0, Ar*H*) overlapping 7.56 (1H, d, *J* 3.5, CH=C*H*N), 6.49 (1H, d, *J* 3.5, C*H*=CHN), 1.68 (9H, s, 3 × *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 134.5, 132.9, 132.6, 129.7, 126.7, 117.0, 106.2, 86.7, 84.1, 28.2; IR ν_{max} (neat)/cm^{-1} 3115, 2979, 2933, 1731 (CO); *m/z* (FI$^+$) $C_{13}H_{14}INO_2^+$ ([M]$^+$) requires 343.0096; found 343.0092.

tert-Butyl 5-(morpholin-4-ylsulfamoyl)-1*H*-indole-1-carboxylate (Table 5, Entry 5)



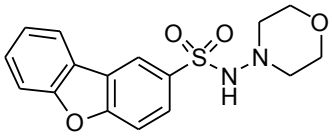
The general procedure B was followed with the use of *tert*-butyl 5-iodo-1*H*-indole-1-carboxylate (82 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* as an off-white solid (75 mg, 81%); mp 167-170 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (1H, app d, *J* 9.0, Ar-*H*), 8.23 (1H, app d, *J* 1.5, Ar-*H*), 7.90 (1H, app dd, *J* 9.0, 1.5, Ar-*H*), 7.72 (1H, d, *J* 3.5, CH=C*H*N), 6.69 (1H, d, *J* 3.5, C*H*=CHN), 5.56 (1H, s, N*H*), 3.58 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 2.61 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 1.69 (9H, s, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 137.5, 132.6, 130.2, 128.1, 123.6, 122.0, 115.4, 107.5, 84.8, 66.6, 56.7, 28.1; IR ν_{max} (neat)/cm^{-1} 3211, 2977, 2858, 1740 (CO), 1335 (SO_2), 1156 (SO_2); LRMS (ESI$^-$) *m/z* 380 (100%, [M – H]$^-$); HRMS (ESI$^+$) found *m/z* 404.1245 [M + Na]$^+$, $C_{17}H_{23}N_3NaO_5S^+$ requires *m/z* 404.1251.

1*H*-indole-5-sulfonamide, *N*-4-morpholinyl (Table 5, Entry 6)



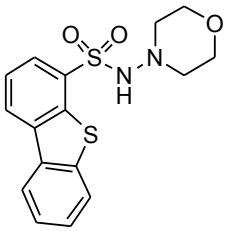
The general procedure B was followed with the use of 5-iodo-1*H*-indole (58 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* as a white solid (50 mg, 74%); mp 143-145 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (1H, br. s, N(indole)*H*), 8.33 (1H, app br. d, *J* 1.0, Ar-*H*), 7.79 (1H, app dd, *J* 8.5, 1.0, Ar-*H*), 7.49 (1H, app d, *J* 8.5, Ar-*H*), 7.37 (1H, app t, *J* 3.0, CH=C*H*N), 6.71 (1H, app dt, *J* 3.0, 1.0, C*H*=CHN), 5.25 (1H, br. s, N*H*), 3.59 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O), 2.59 (4H, app t, *J* 4.5, N(CH_2CH_2)$_2$O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 129.3, 127.3, 126.7, 122.4, 121.2, 111.5, 104.0, 66.6, 56.7; IR ν_{max} (neat)/cm^{-1} 3356, 3224, 2858, 1326 (SO_2), 1151 (SO_2); LRMS (ESI$^-$) *m/z* 280 (100%, [M – H]$^-$); HRMS (ESI$^+$) found *m/z* 304.0725 [M + Na]$^+$, $C_{12}H_{15}N_3NaO_3S^+$ requires *m/z* 304.0726.

_N_-(Morpholin-4-yl)dibenzo[*b,d*]furan-2-sulfonamide (Table 5, Entry 7)



The general procedure B was followed with the use of 3-iododibenzofuran (71 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* as a white solid (71 mg, 89%); mp 197-199 °C (decomp.) (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (1H, app d, *J* 2.0, Ar-*H*), 8.10 (1H, app dd, *J* 8.5, 2.0, Ar-*H*), 8.05-8.00 (1H, m, Ar-*H*), 7.69 (1H, app d, *J* 8.5, Ar-*H*), 7.67-7.62 (1H, m, Ar-*H*), 7.57 (1H, app td, *J* 7.5, 1.5, Ar-*H*), 7.44 (1H, app t, *J* 7.5, Ar-*H*), 5.50 (1H, s, N*H*), 3.60 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$), 2.65 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 157.0, 133.1, 128.6, 127.2, 124.8, 123.8, 123.1, 121.7, 121.2, 112.10, 112.08, 66.6, 56.8; IR ν_{max} (neat)/cm^{-1} 3196, 2962, 2917, 2859, 1324 (SO_2), 1159 (SO_2); LRMS (ESI$^+$) *m/z* 687 (100%, $[2M + Na]^+$), 355 (77%, $[M + Na]^+$); HRMS (ESI$^+$) found *m/z* 355.0707 $[M + Na]^+$, $C_{16}H_{16}N_2NaO_4S^+$ requires *m/z* 355.0723.

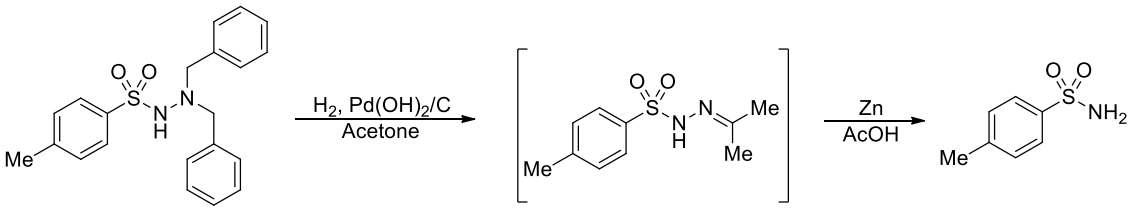
_N_-(Morpholin-4-yl)dibenzo[*b,d*]thiophene-4-sulfonamide (Table 5, Entry 8)



The general procedure B was followed with the use of 4-iododibenzothiophene (74 mg, 0.24 mmol). Flash chromatography (25—100% Et_2O in petrol) afforded the *N-aminosulfonamide* **XX** as a white solid (77 mg, 92%); mp 169-172 °C (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (1H, app dd, *J* 8.0, 1.0, Ar-*H*), 8.23-8.19 (1H, m, Ar-*H*), 8.17 (1H, app dd, *J* 7.5, 1.0, Ar-*H*), 7.95-7.91 (1H, m, Ar-*H*), 7.64 (1H, app t, *J* 7.5, Ar-*H*), 7.60-7.51 (2H, m, Ar-*H*), 5.70 (1H, s, N*H*), 3.51 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$), 2.54 (4H, app t, *J* 4.5, $N(CH_2CH_2)_2O$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 137.6(4), 137.6(0), 134.0, 132.3, 128.7, 127.9, 126.0, 125.0, 124.3, 122.7, 121.8, 66.5, 56.7; IR ν_{max} (neat)/cm^{-1} 3218, 2964, 2922, 2858, 1335 (SO_2), 1142 (SO_2); LRMS (ESI$^-$) *m/z* 347 (100%, $[M - H]^-$); HRMS (ESI$^+$) found *m/z* 371.0490 $[M + Na]^+$, $C_{16}H_{16}N_2NaO_3S_2^+$ requires *m/z* 371.0495.

N-N Bond Cleavage

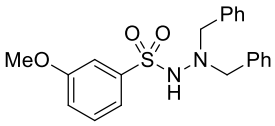
General procedure (C) for the formation of unsubstituted sulfonamides from the corresponding dibenzyl-*N*-aminosulfonamide, exemplified by the preparation of tosylamine



A glass reaction tube was charged with recrystallised *N*',*N*'-dibenzyl-4-methylbenzenesulfonohydrazide **4b** (293 mg, 0.80 mmol) and Pearlman's catalyst ($Pd(OH)_2$ on carbon, 20 wt% Pd, ~60% moisture, 140 mg, 0.08 mmol). Acetone (2 mL) was added and the reaction mixture degassed with N_2. The tube was flushed with H_2 gas and left stirring under a balloon of H_2 atmosphere for 16 hrs. The reaction flask was purged with N_2, the suspension filtered through Celite and the Celite pad washed with CH_2Cl_2 (5 mL). The filtrate was concentrated *in vacuo* affording *tosyl hydrazone* **9** (180 mg, 100%) as analytically pure white crystals; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* 8.0, Ar-*H*), 7.31 (2H, d, *J* 8.0, Ar-*H*), 2.43 (3H, s, Ar-*Me*), 1.94 (3H, s, NC*Me*), 1.80 (3H, s, NC*Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 144.0, 135.4, 129.5, 128.0, 25.3, 21.6, 16.8; IR υ_{max} (neat)/cm^{-1} 3225, 1655, 1597, 1389, 1330 (SO_2), 1158 (SO_2), 1086; LRMS (ESI) *m/z* 227 (65%, $[M+H]^+$), 249 (95%, $[M+Na]^+$), 281 (40%, $[M+Na+MeOH]^+$), 475 (100%, $[2M+Na]^+$); HRMS (ESI) found *m/z* 249.0668 $[M+Na]^+$, $C_{10}H_{14}N_2O_2SNa$ requires *m/z* 249.0668.

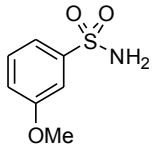
The *N*-*N* bond cleavage was carried out in accordance with a similar literature procedure.[8] The crude sulfonyl hydrazone (180 mg, 0.80 mmol) was dissolved in acetic acid (5 mL) and zinc dust (1.31 g, 25 mmol) added under N_2. The resulting suspension was stirred at 25 ^{o}C for 1 hr. CH_2Cl_2 (10mL) was added to the reaction mixture, sonicated for 1 min and filtered through Celite, the zinc residue being washed with further CH_2Cl_2 (5 mL). The organic solution was washed with water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* affording analytically pure tosyl amine **10a** (114 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (2H, d, *J* 8.3, Ar-*H*), 7.31 (2H, d, *J* 8.3, Ar-*H*), 4.95 (2H, br. s, N*H*$_2$), 2.44 (3H, s, *Me*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 139.0, 129.7, 126.4, 21.5; LRMS (ESI) *m/z* 194 (100%, $[M+Na]^+$), 226 (80%, $[M+Na+MeOH]^+$). Data was consistent with a commercially available sample.

_N'_,_N'_-Dibenzyl-3-methoxybenzenesulfonohydrazide (Scheme 4)



The general procedure B was followed with the use of 3-iodoanisole (350 mg, 1.50 mmol) and 1,1-dibenzylhydrazine (476 mg, 2.24 mmol). Flash column chromatography (11:8:1 petrol:Et_2O:Et_3N) afforded the *N-aminosulfonamide* as a pale yellow oil (450 mg, 79%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (1H, d, *J* 7.7, Ar-*H*), 7.34 – 7.25 (8H, m, Ar-*H*), 7.20 – 7.18 (4H, m, Ar-*H*), 7.04 (1H, dd, *J* 8.2, 2.1, Ar-H), 5.59 (1H, s, N*H*), 3.80 (3H, s, O*Me*), 3.75 (4H, s, N(CH_2Ph)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 139.5, 134.9, 129.7, 129.6, 128.4, 127.7, 120.6, 119.7, 112.4, 59.9, 55.4; IR υ_{max} (neat)/cm^{-1} 1598, 1478, 1315 (SO_2), 1240, 1150 (SO_2), 1022; LRMS (ESI) *m/z* 405 (15%, [M+Na]$^+$), 787 (100%, [2M+Na]$^+$); HRMS (ESI) found *m/z* 405.1227 [M+Na]$^+$, $C_{21}H_{22}N_2O_3SNa$ requires *m/z* 405.1243.

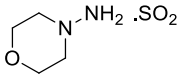
3-Methoxybenzenesulfonamide (10b, Scheme 4)



The general procedure C was followed using re-crystallised *N'*,*N'*-dibenzyl-3-methoxybenzenesulfonohydrazide (120 mg, 0.31 mmol) to first afford the *hydrazone* as a white solid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.57 – 7.38 (3H, m, Ar-*H*), 7.16 – 7.10 (1H, m, Ar-*H*), 3.87 (3H, s, O*Me*), 1.96 (3H, s, NC*Me*), 1.80 (3H, s, NC*Me*); LRMS (ESI) *m/z* 210 (100%, [M+Na]$^+$). Zinc in acetic acid reduction afforded unsubstituted sulfonamide **10b** as colourless crystals (46 mg, 80%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.48 (1H, t, *J* 7.9, Ar-*H*), 7.41 – 7.35 (4H, m, Ar-*H* incl. NH_2), 7.16 (1H, dd, *J* 8.2, 2.4, Ar-*H*), 3.82 (3H, s, O*Me*); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.2, 145.4, 130.1, 117.6 (2C), 110.8, 55.5; LRMS (ESI) *m/z* 186 (100%, [M-H]$^-$). HRMS (ESI) *m/z* 210.0192 [M+Na]$^+$, $C_7H_9NO_3SNa$ requires 210.0195. Data consistent with literature.[9]

Sulfur dioxide complexes

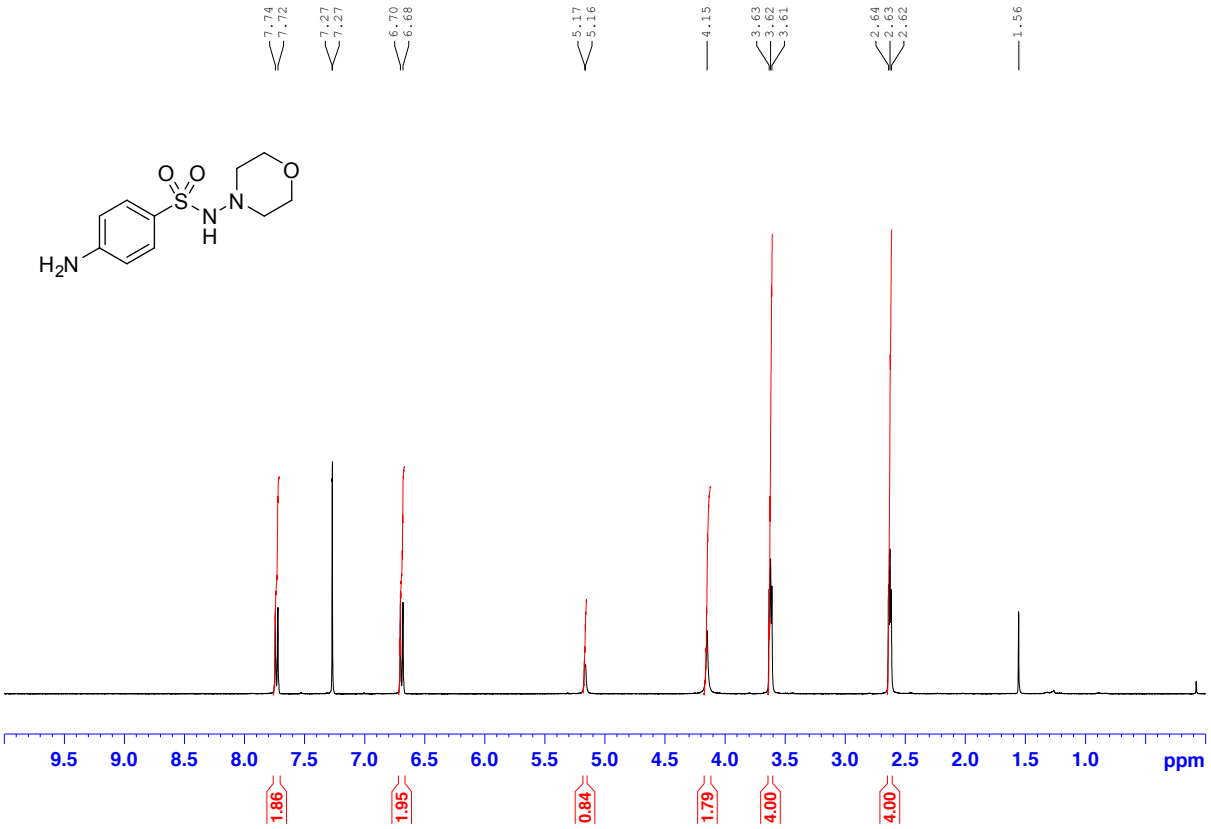
4-Aminomorpholine-sulfur dioxide complex, 8

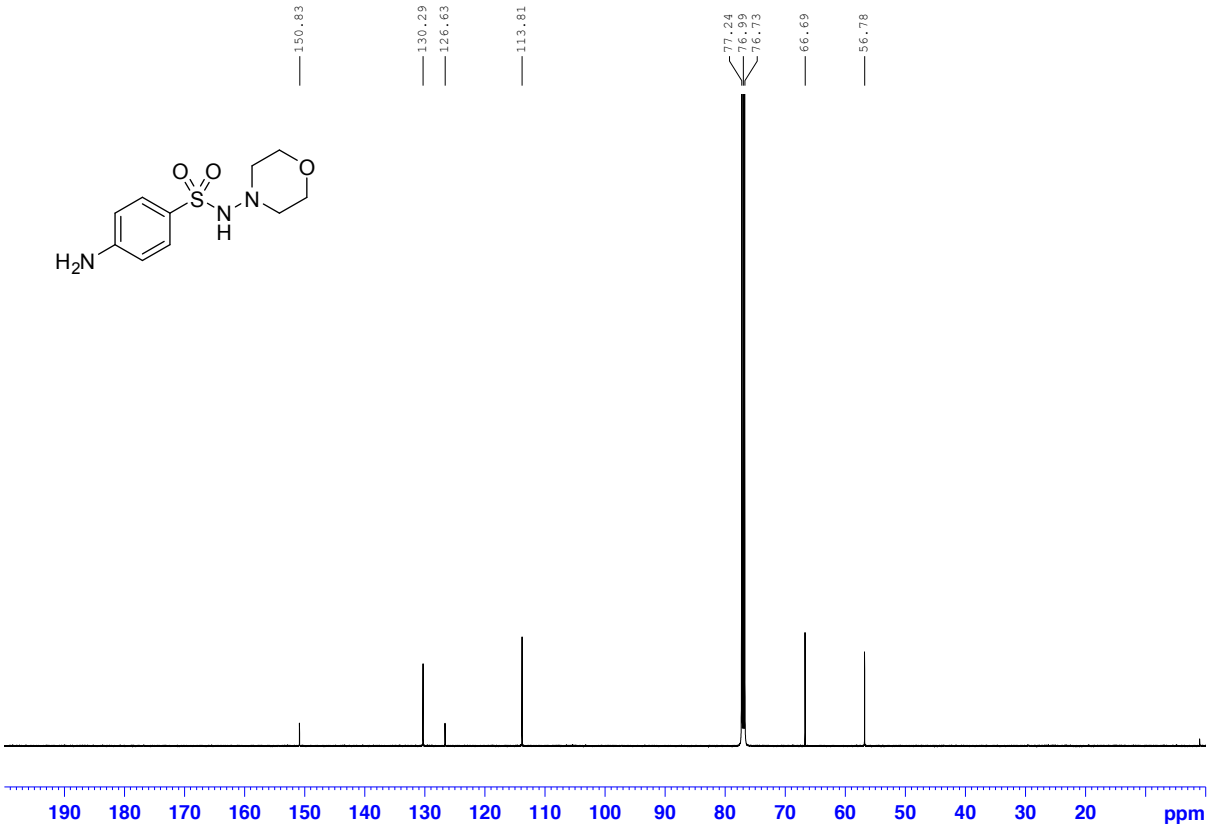


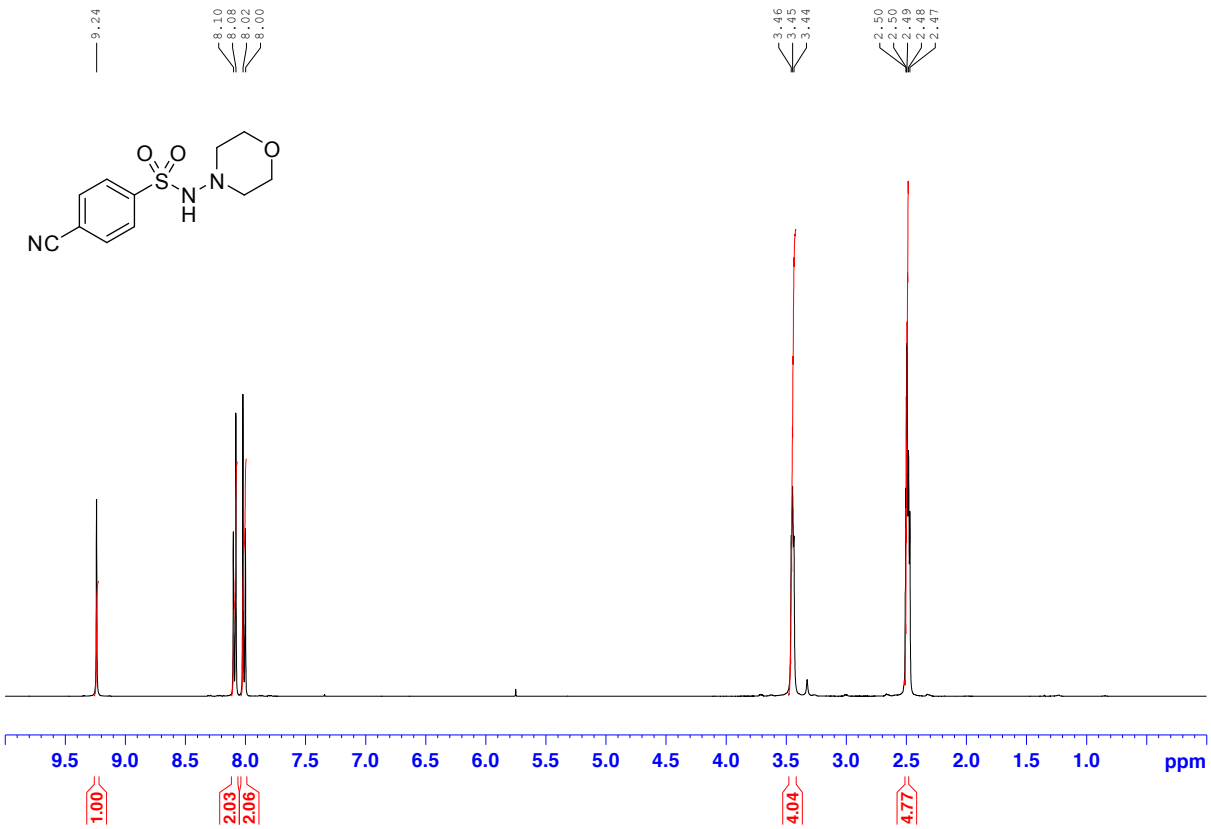
The general procedure as described for DABSO in our communication[1] was followed with the use of distilled 4-aminomorpholine (1.00 mL, 10.4 mmol) affording *complex* **8** as a white powder (1.65 g, 96%). Elemental analysis found 29.01% C, 6.15% H, 16.82% N, 19.08% S; $C_4H_{10}N_2O_3S$ requires 28.91% C, 6.06% H, 16.86% N, 19.29% S; ^{1}H NMR (400 MHz, MeOD-d$_4$) δ 3.80 (4H, br. s, (NCH$_2$C*H*$_2$O)$_2$), 2.99 (4H, br. s, (NC*H*$_2$CH$_2$O)$_2$); ^{13}C NMR (100 MHz, MeOD-d$_4$) δ 66.5, 56.0; IR υ_{max} (neat)/cm^{-1} 2869, 2600 (br.), 2173, 1630, 1595, 1468, 1299 (SO_2), 1200, 1104 (SO_2). DSC analysis for both this complex and DABSO are attached. For this complex the first 'event' occurs around 95 ^{o}C (melting) but for DABSO this occurs around 220 ^{o}C (decomposition).

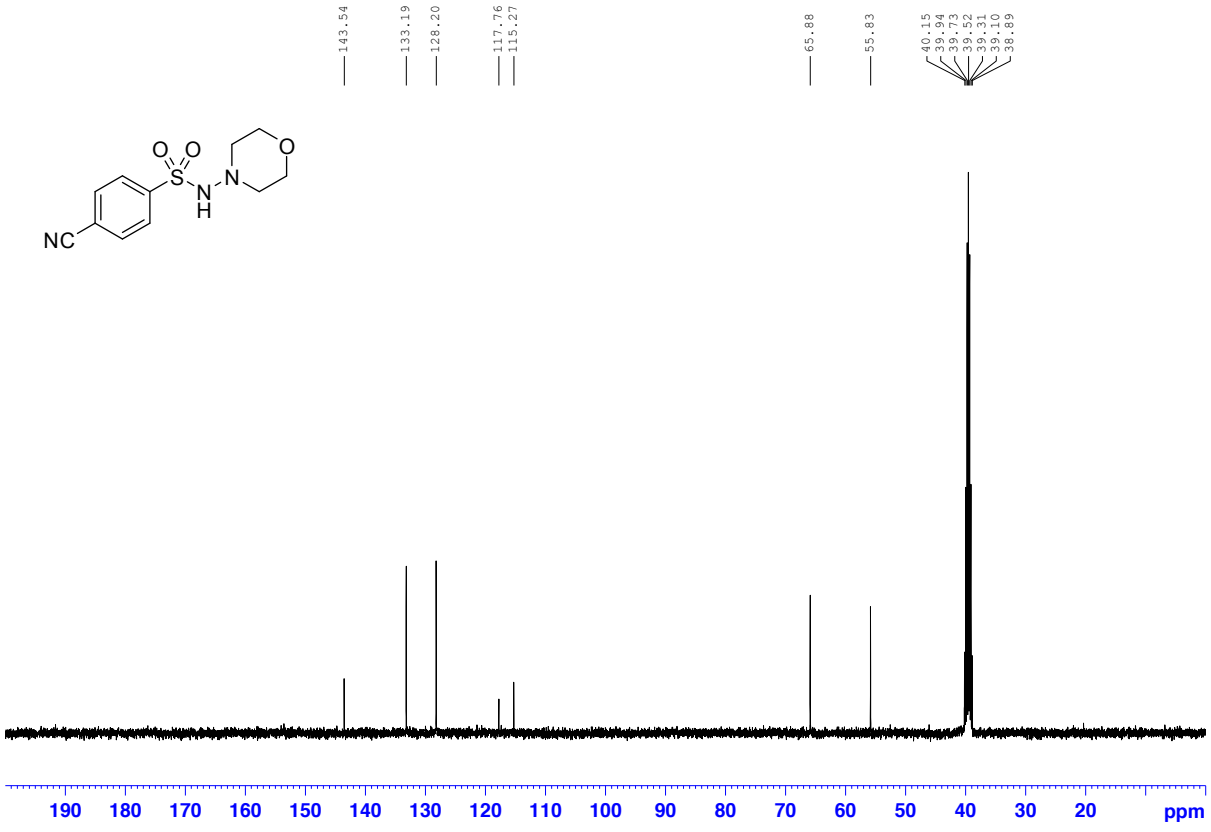
References

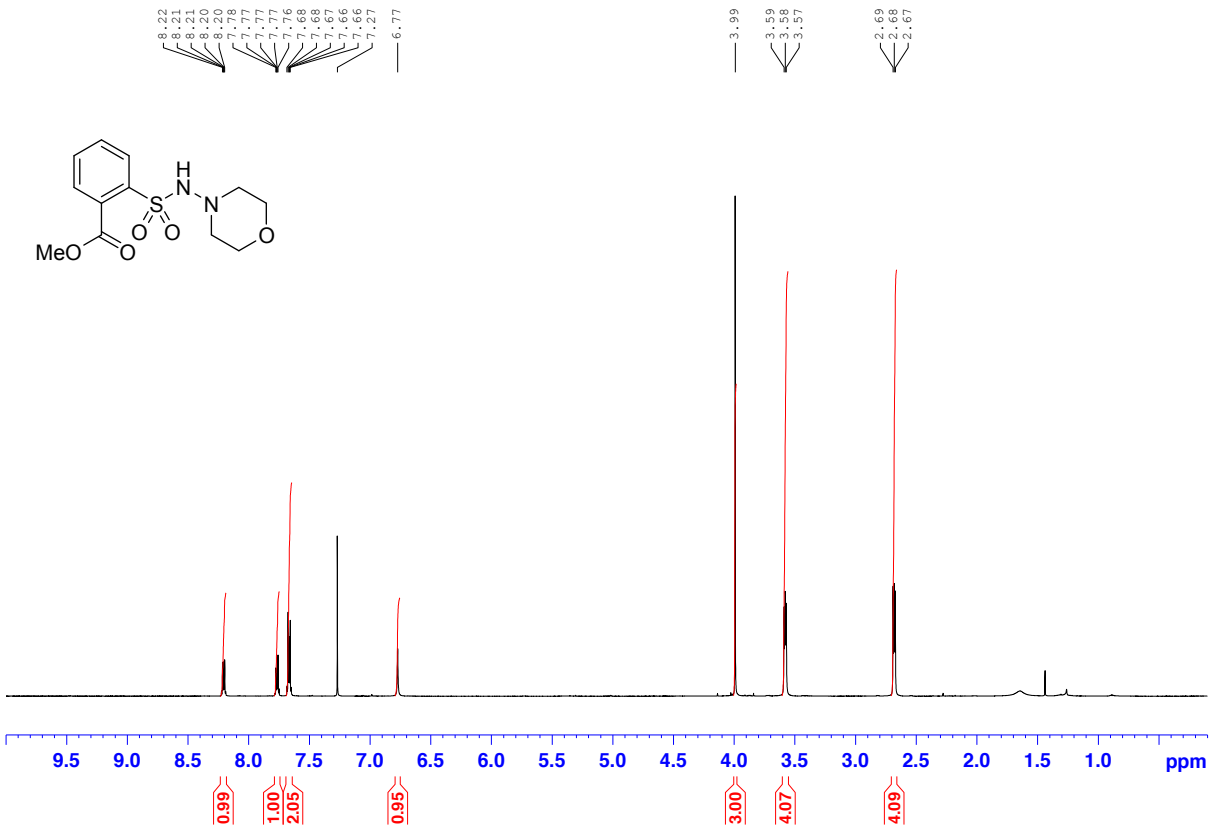
1. B. Nguyen, E. J. Emmett and M. C. Willis, *J. Am. Chem. Soc.*, 2010, **132**, 16372.
2. L. L. W. Cheung and A. K. Yudin, *Org. Lett.*, 2009, **11**, 1281.
3. J. J. Mousseau, J. A. Bull and A. B. Charette, *Angew. Chem. Int. Edit.*, 2010, **49**, 1115.
4. S.-i. Kawaguchi and A. Ogawa, *Org. Lett.*, 2010, **12**, 1893.
5. A. Klapars and S. L. Buchwald, *J. Am. Chem. Soc.*, 2002, **124**, 14844.
6. J. C. Conrad, J. Kong, B. N. Laforteza and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2009, **131**, 11640.
7. C. l. Mothes, S. Lavielle and P. Karoyan, *J. Org. Chem.*, 2008, **73**, 6706.
8. W. Y. Chan and C. Berthelette, *Tetrahedron Lett.*, 2002, **43**, 4537.
9. K. L. Lobb, P. A. Hipskind, J. A. Aikins, E. Alvarez, Y.-Y. Cheung, E. L. Considine, A. De Dios, G. L. Durst, R. Ferritto, C. S. Grossman, D. D. Giera, B. A. Hollister, Z. Huang, P. W. Iversen, K. L. Law, T. Li, H.-S. Lin, B. Lopez, J. E. Lopez, L. M. M. Cabrejas, D. J. McCann, V. Molero, J. E. Reilly, M. E. Richett, C. Shih, B. Teicher, J. H. Wikel, W. T. White and M. M. Mader, *J. Med. Chem.*, 2004, **47**, 5367.

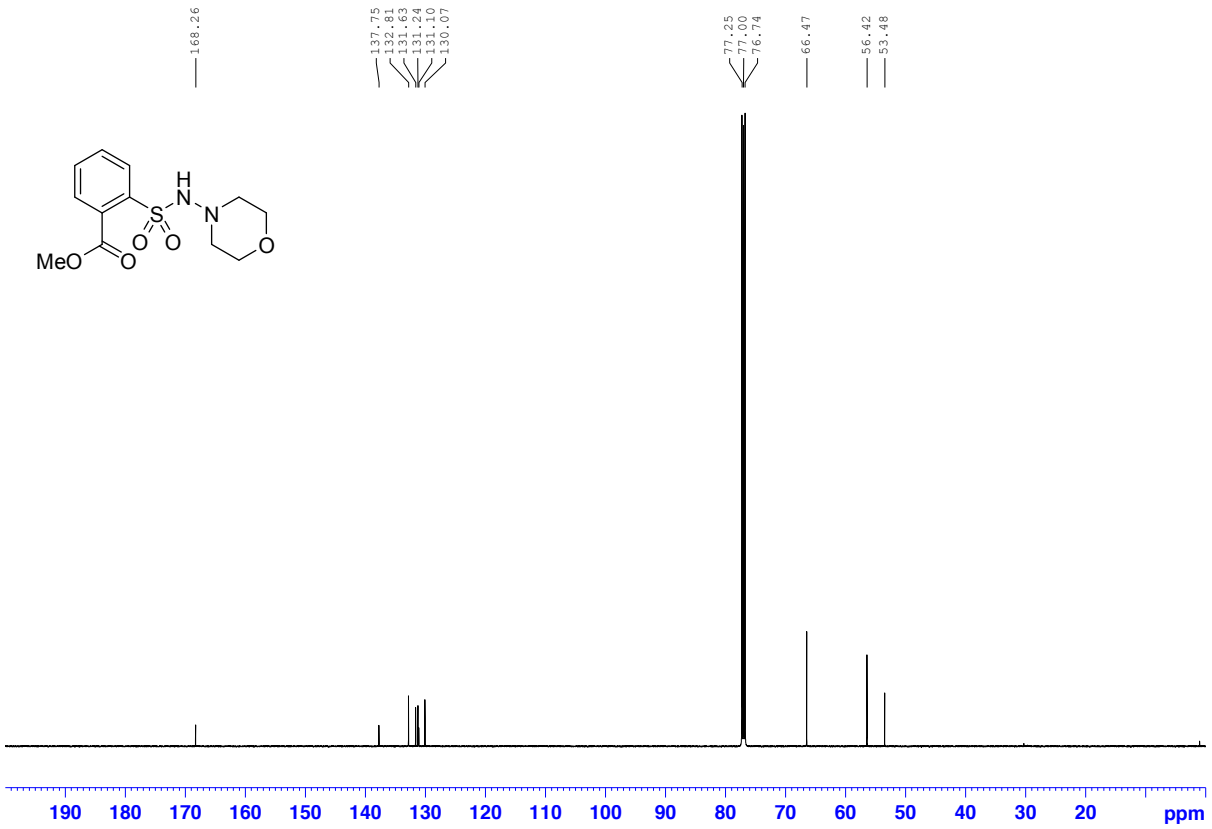


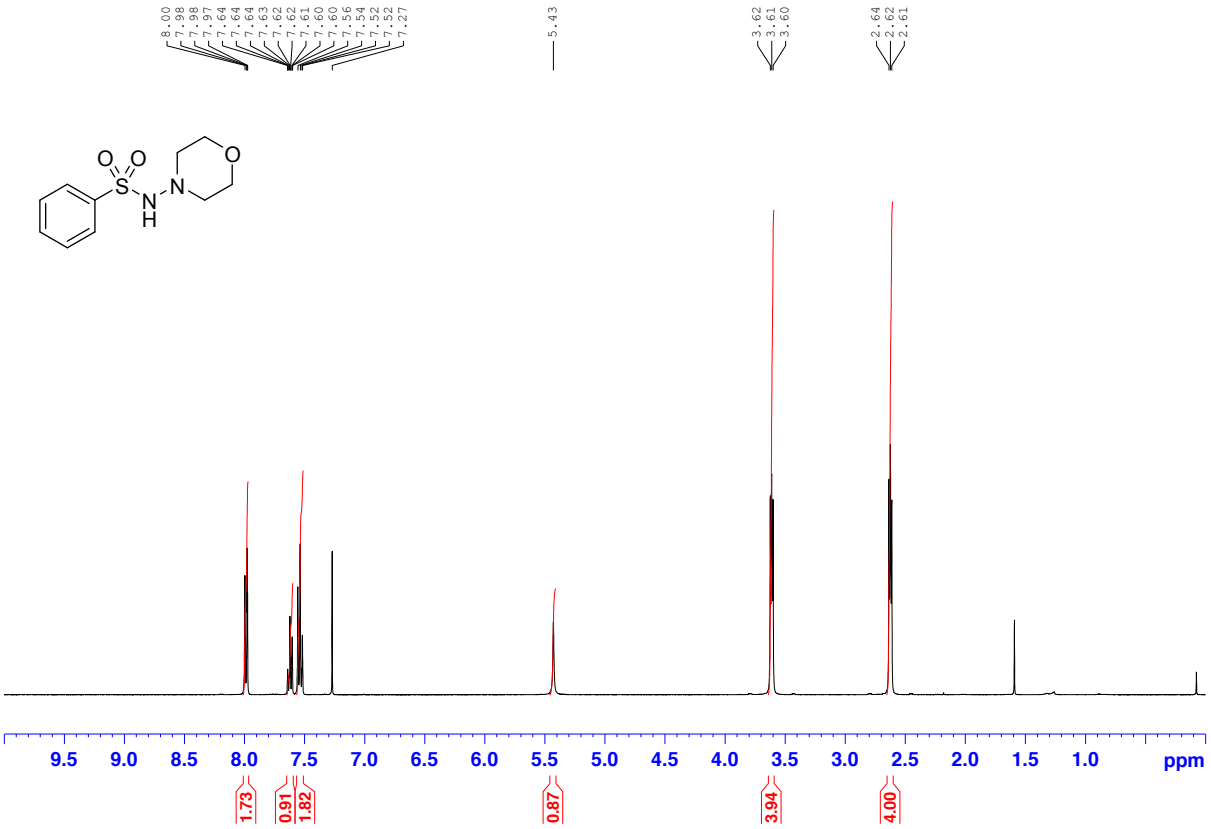


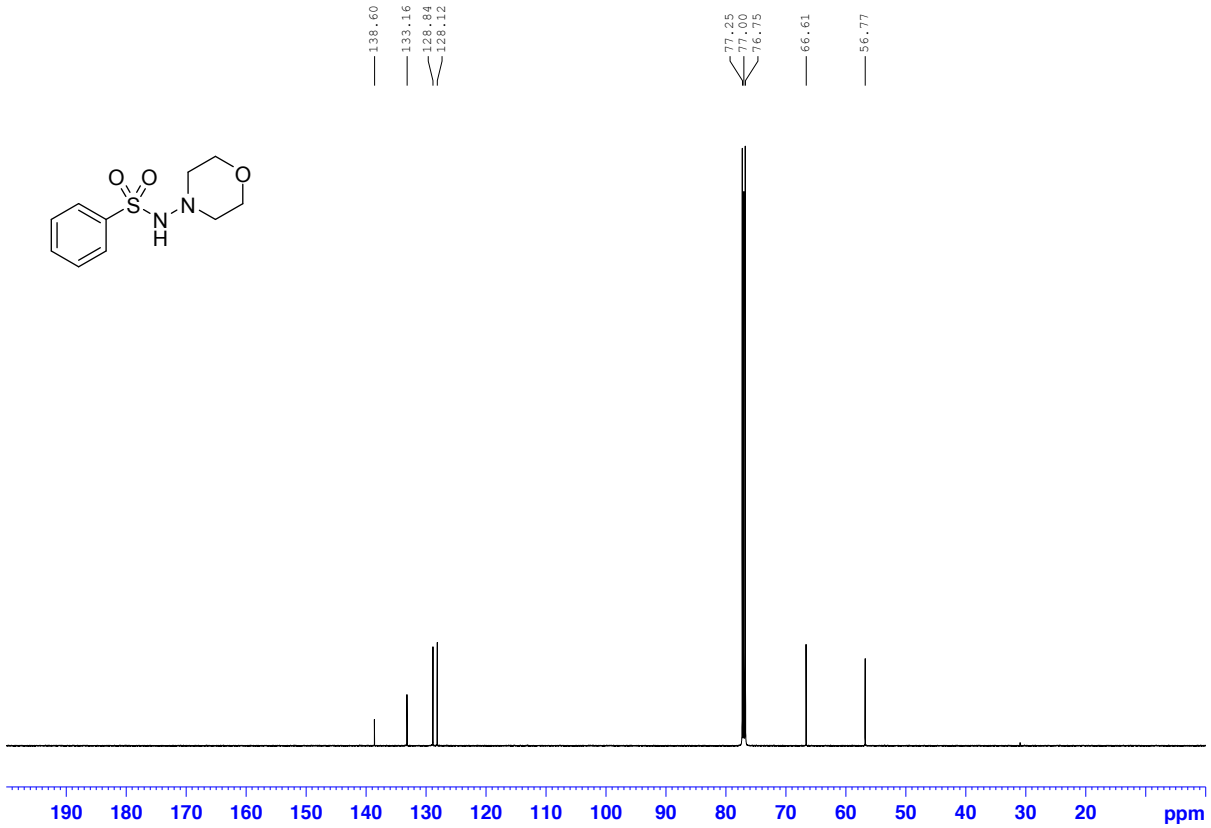


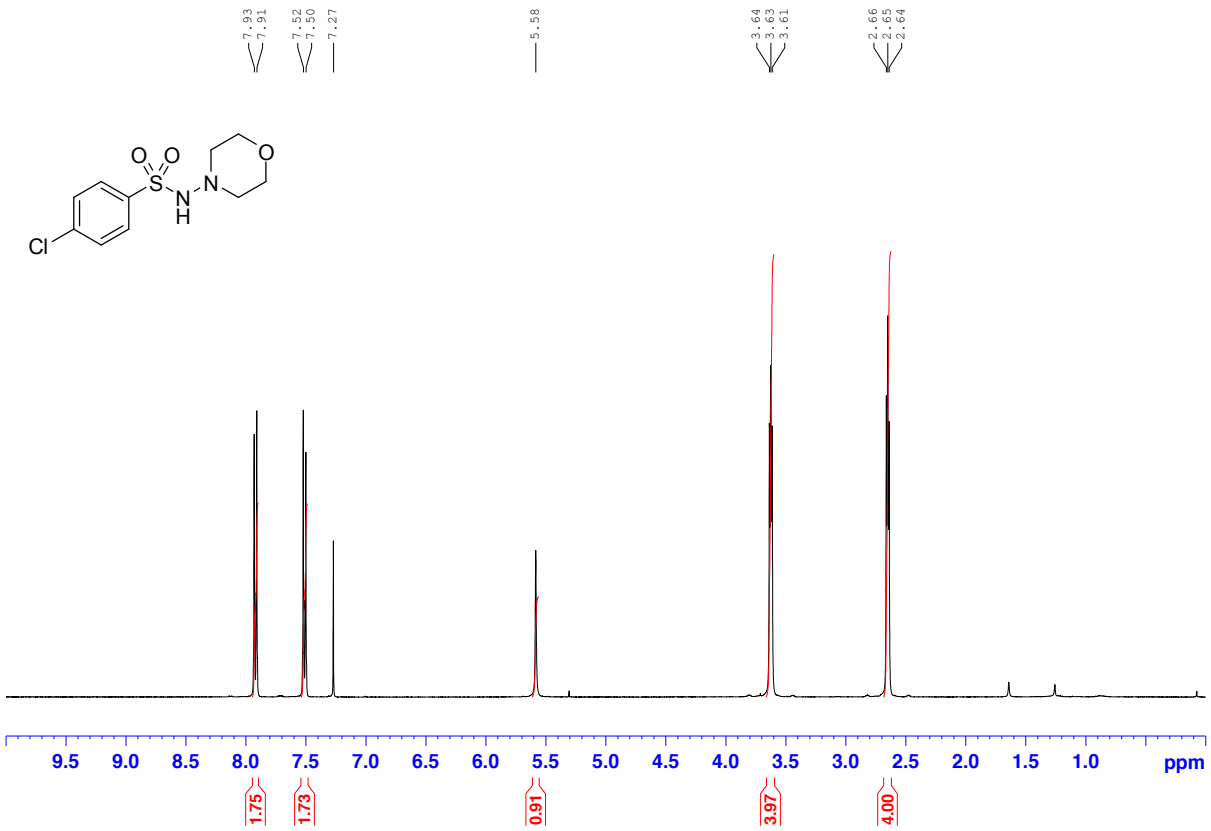


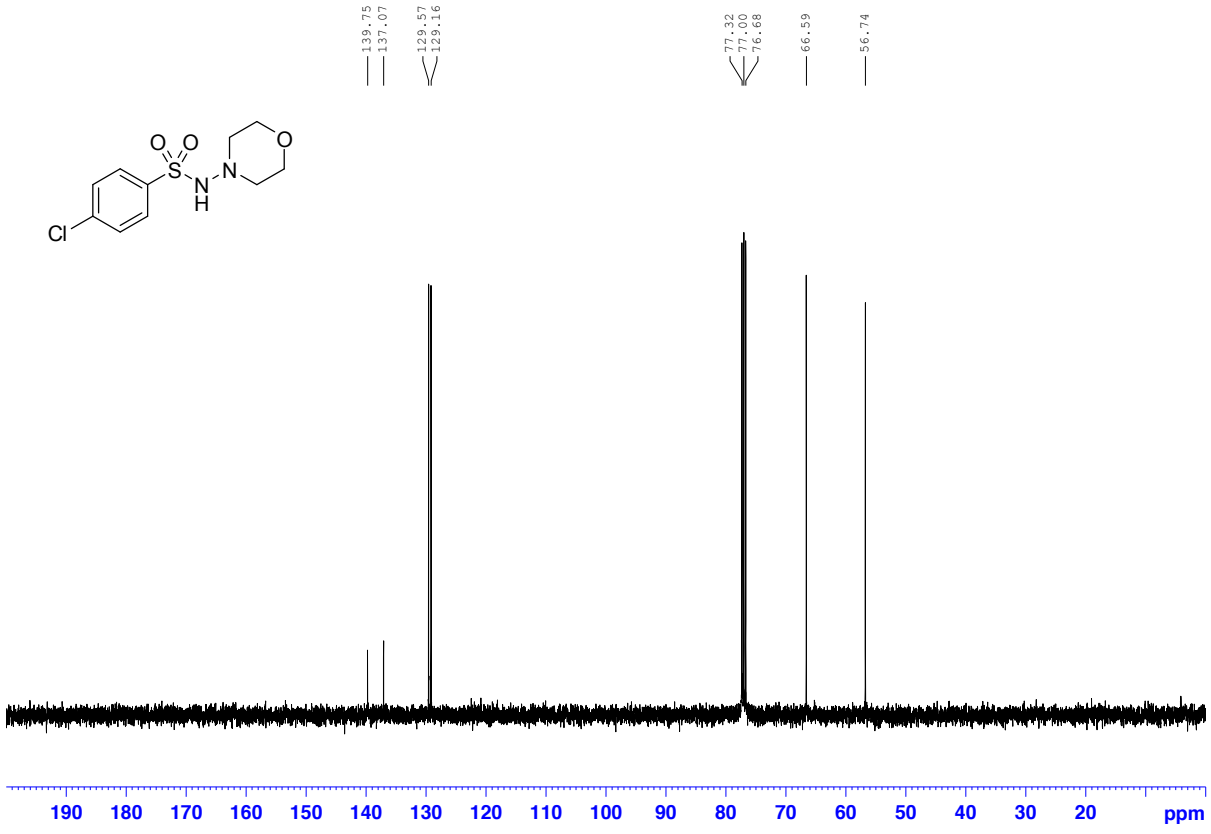


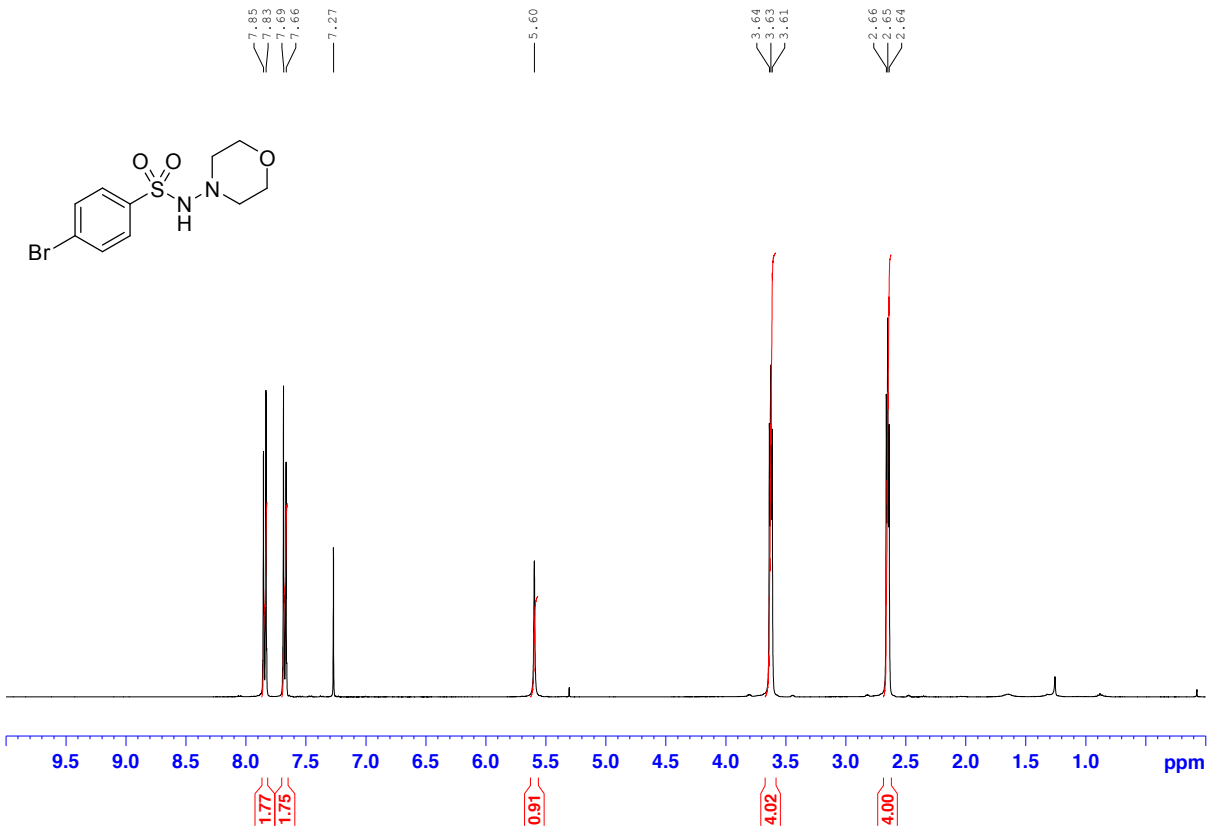


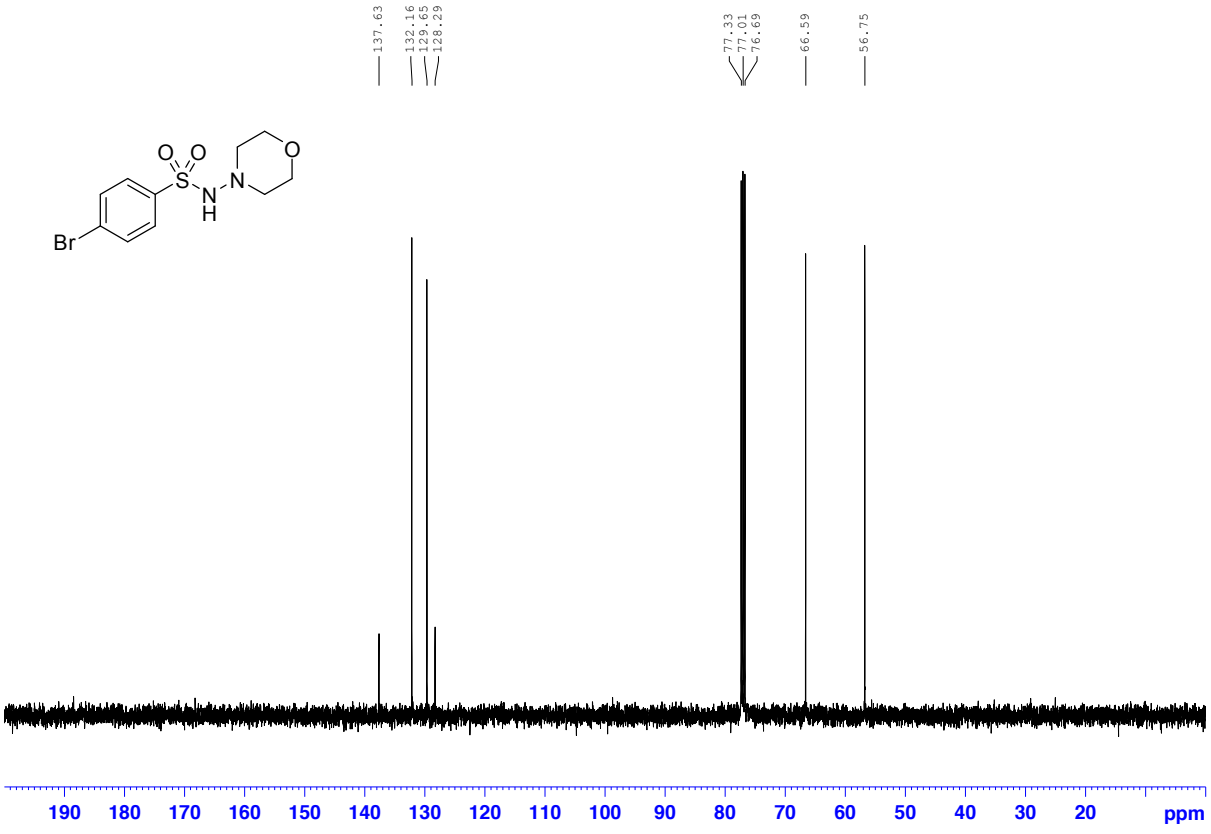


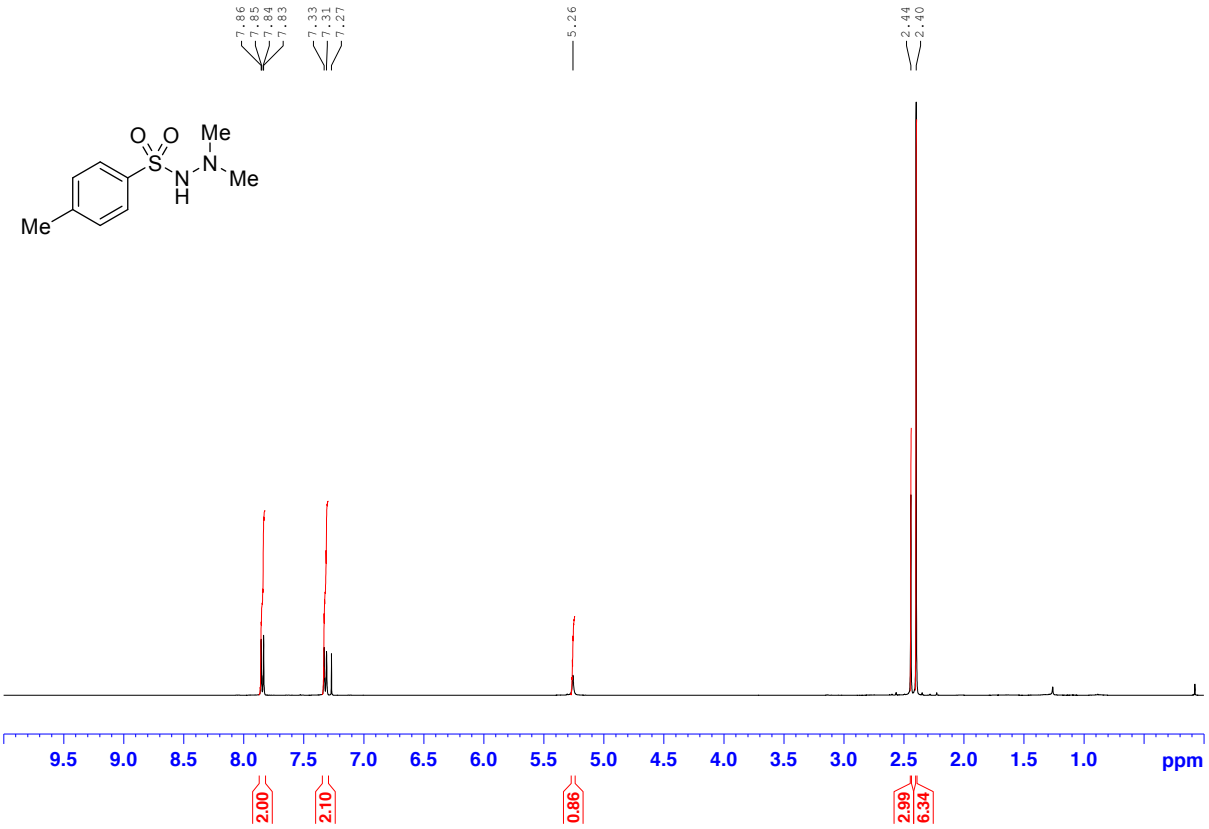


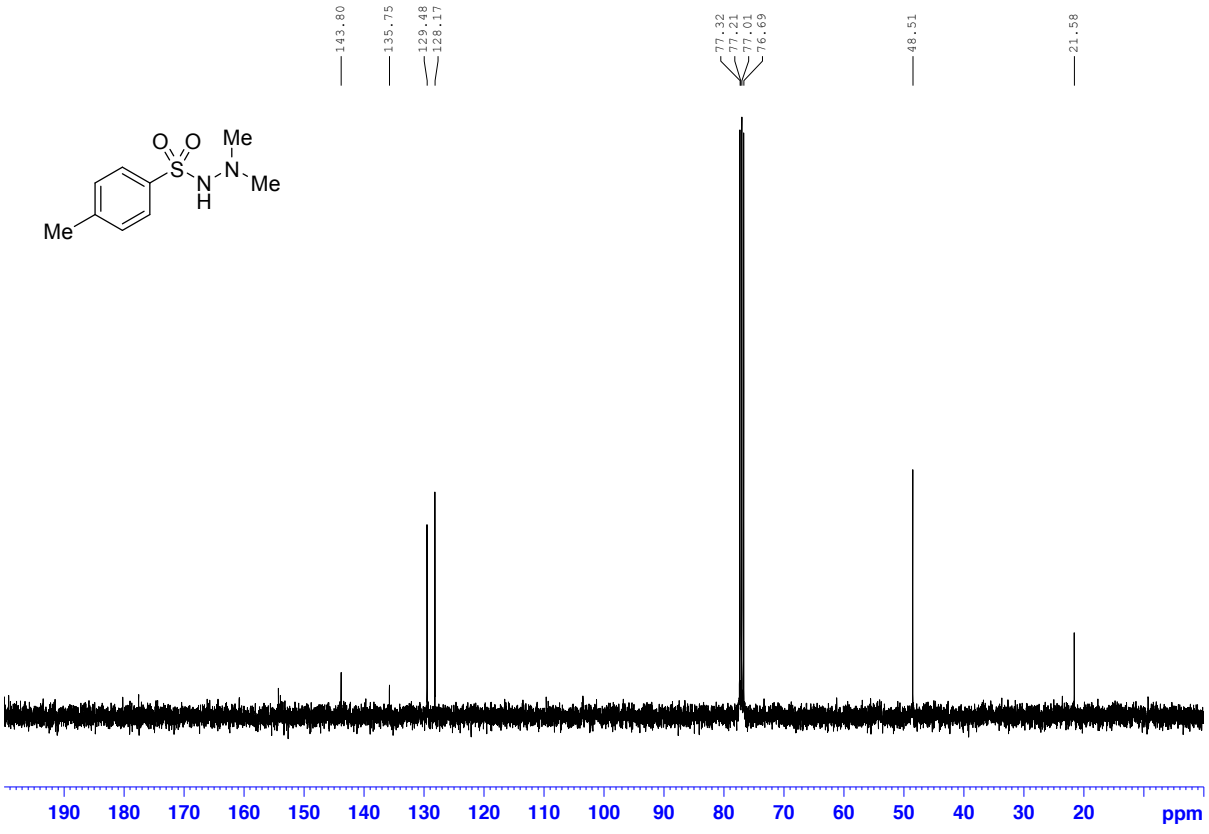


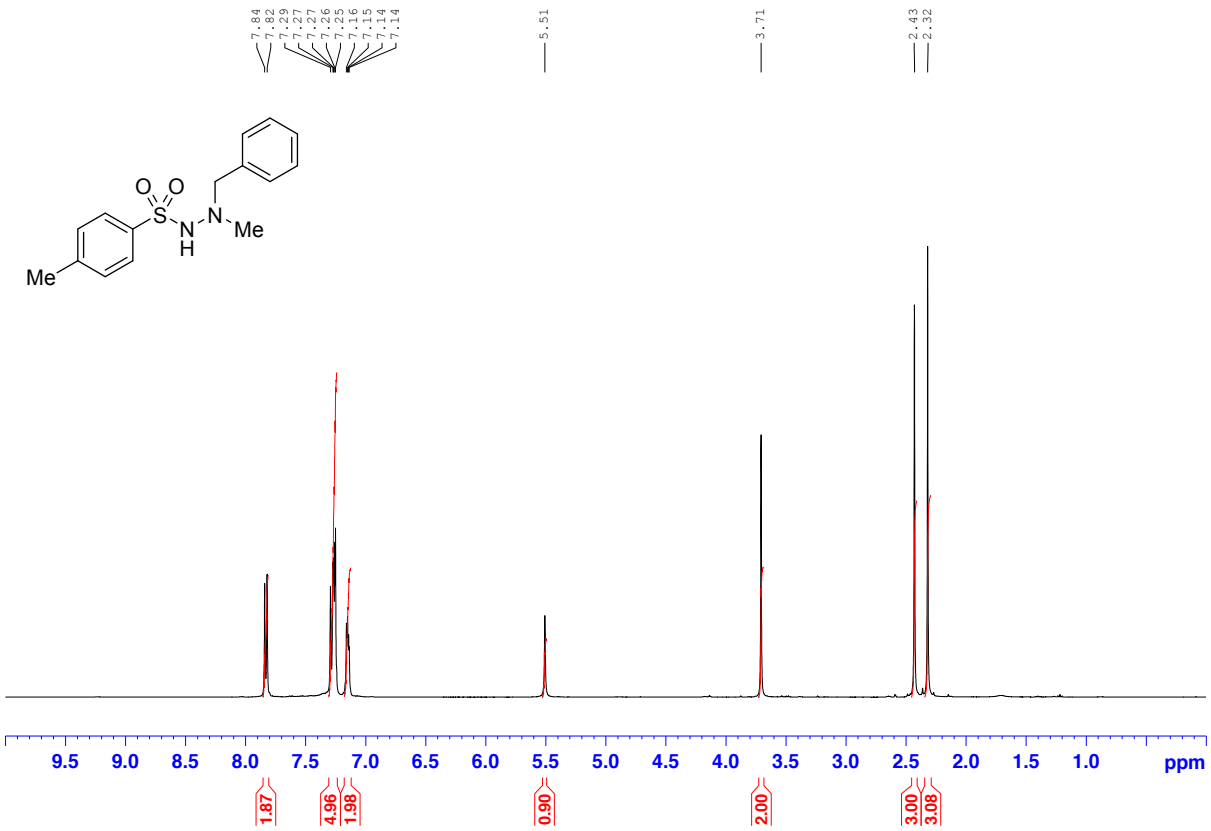


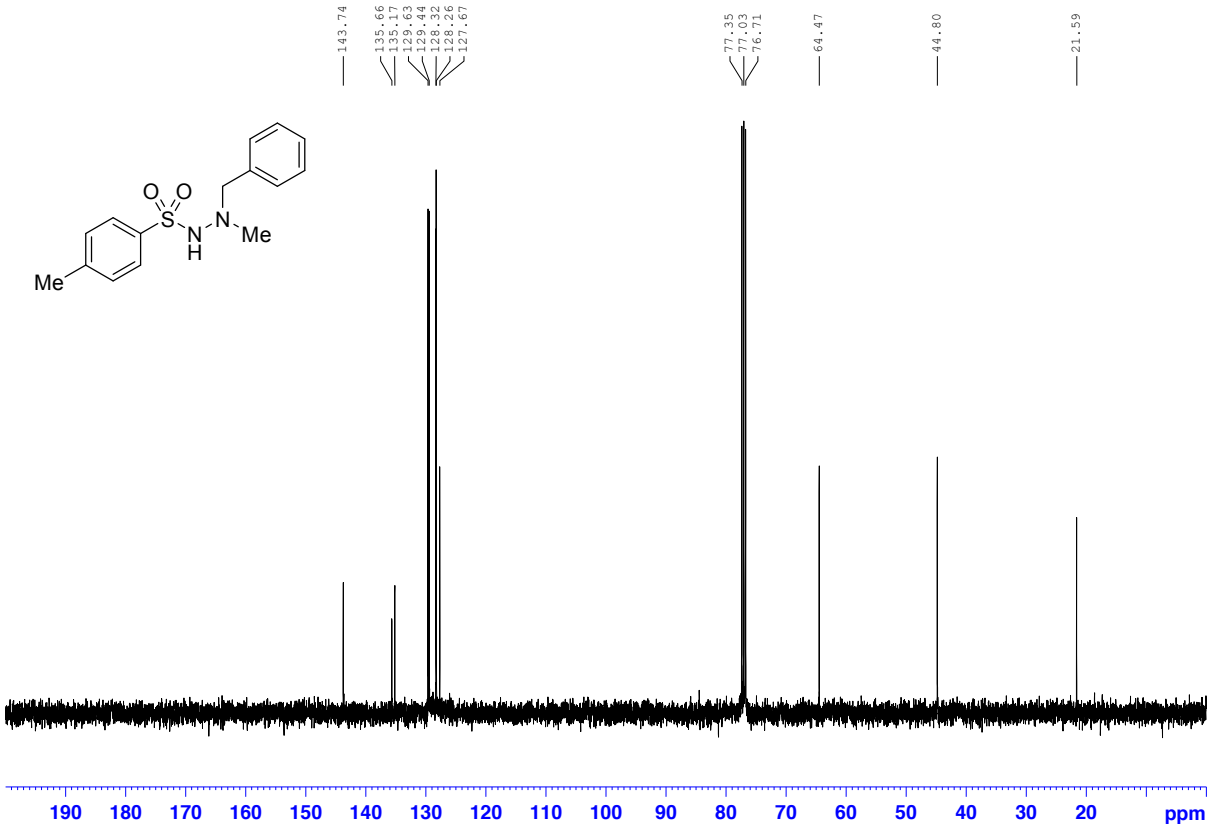


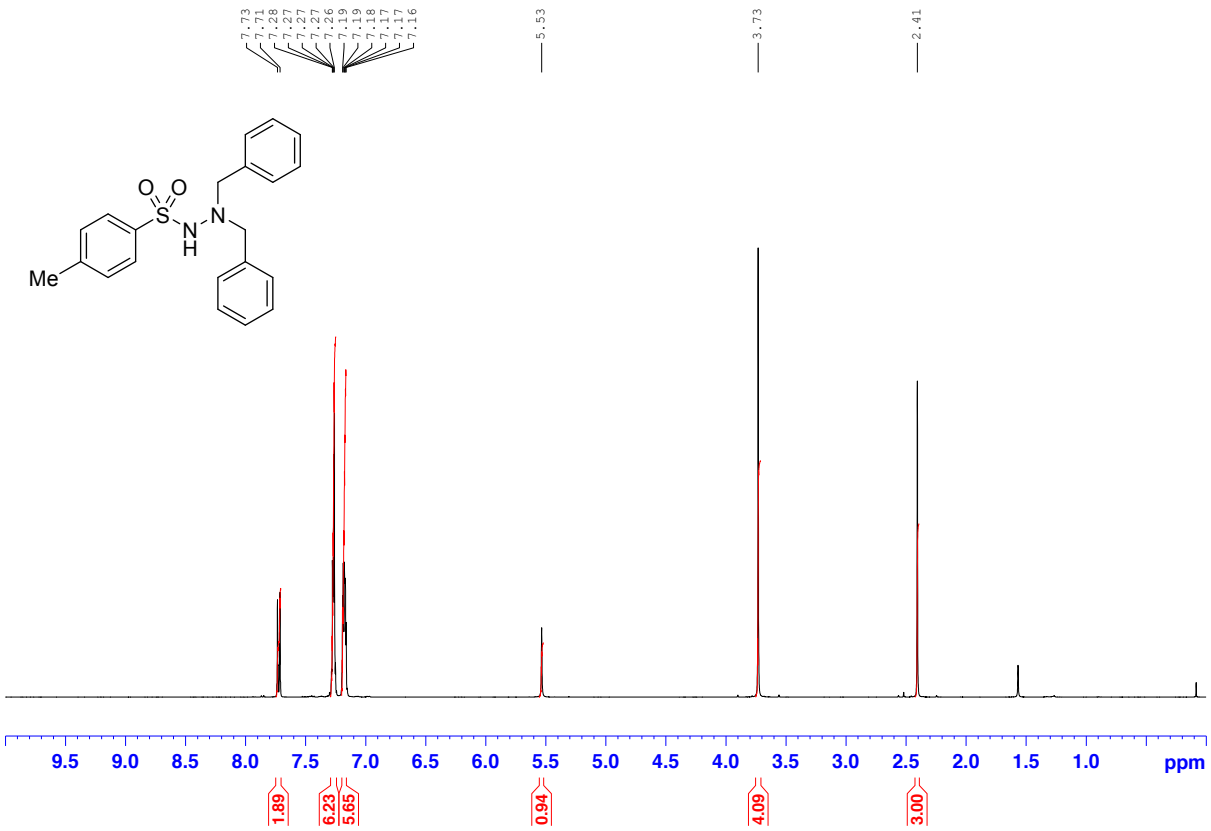


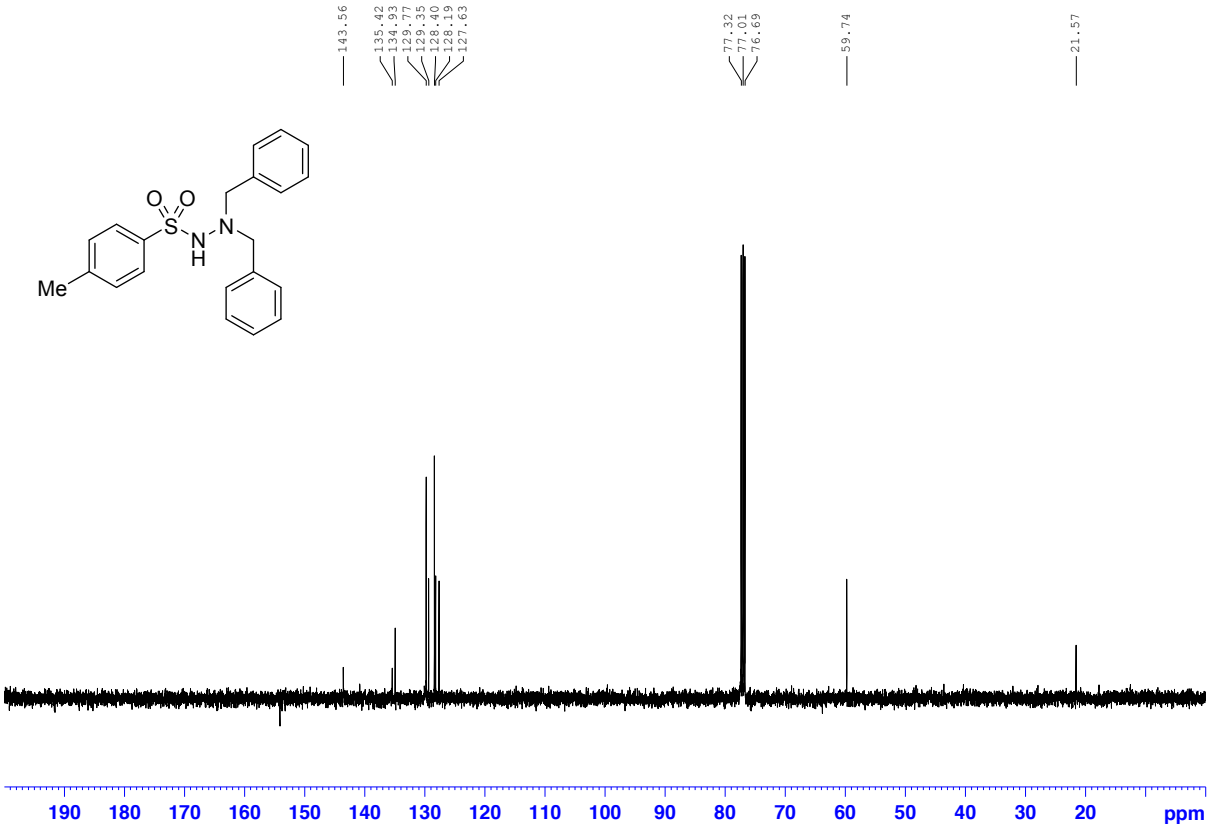


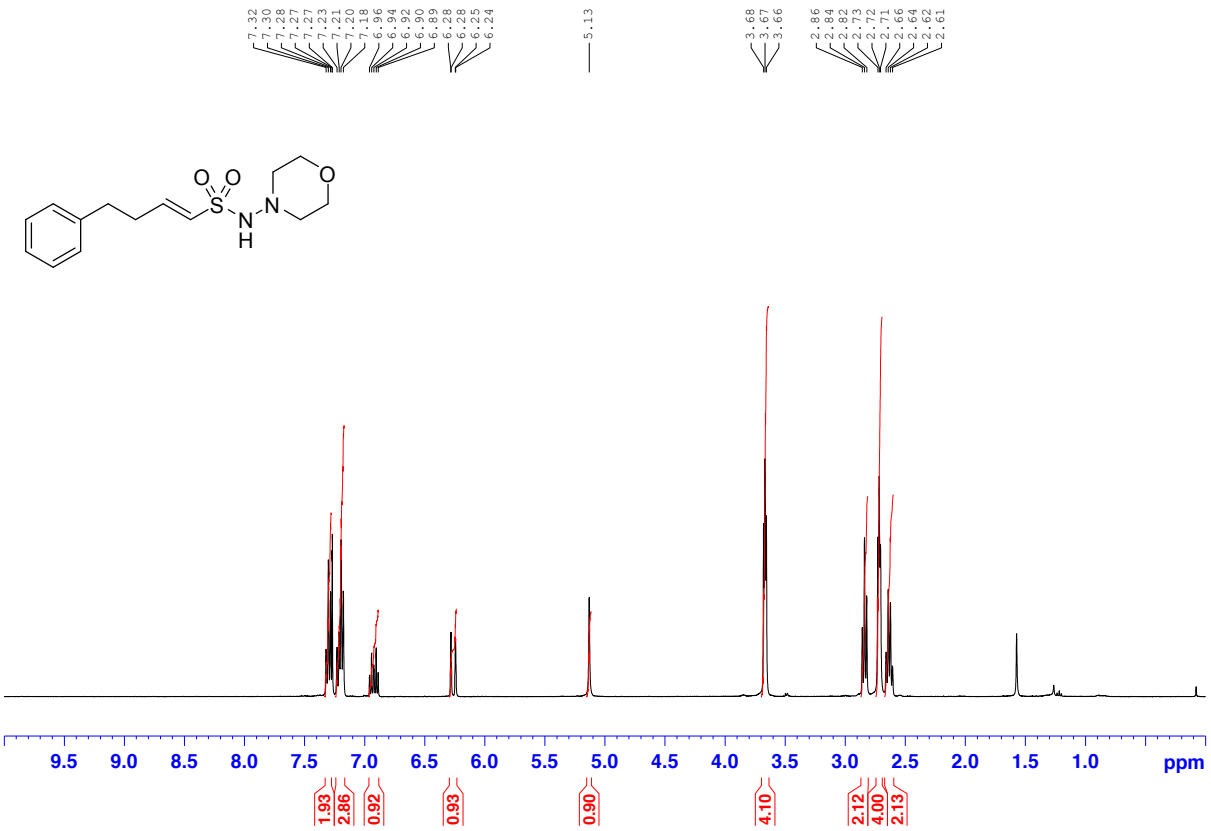


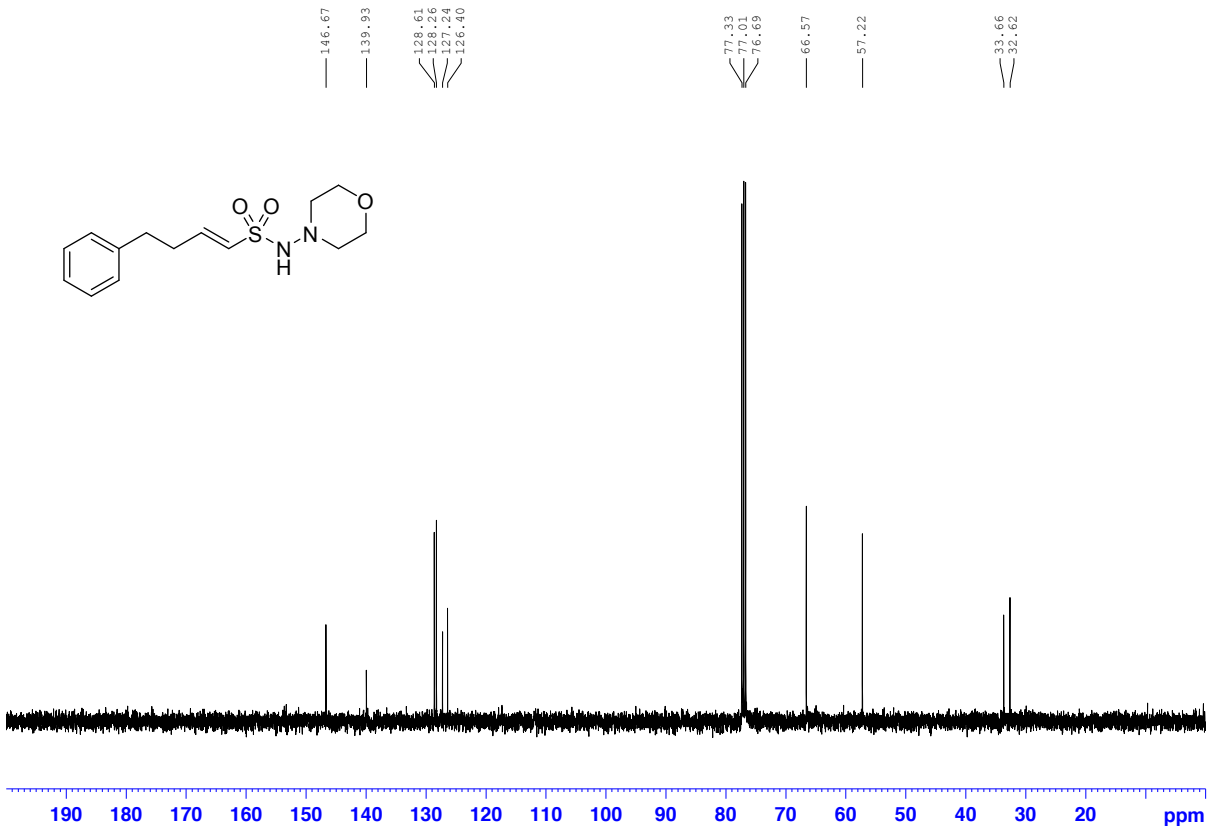


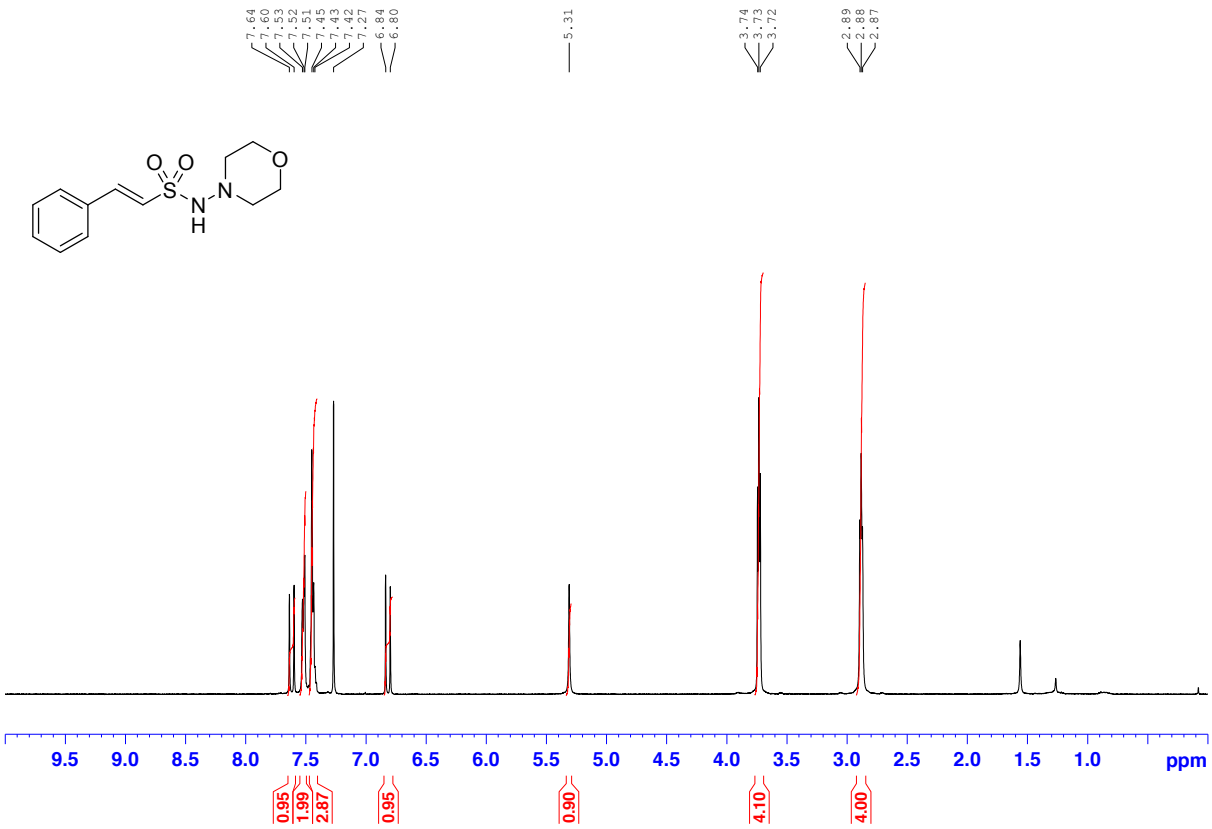


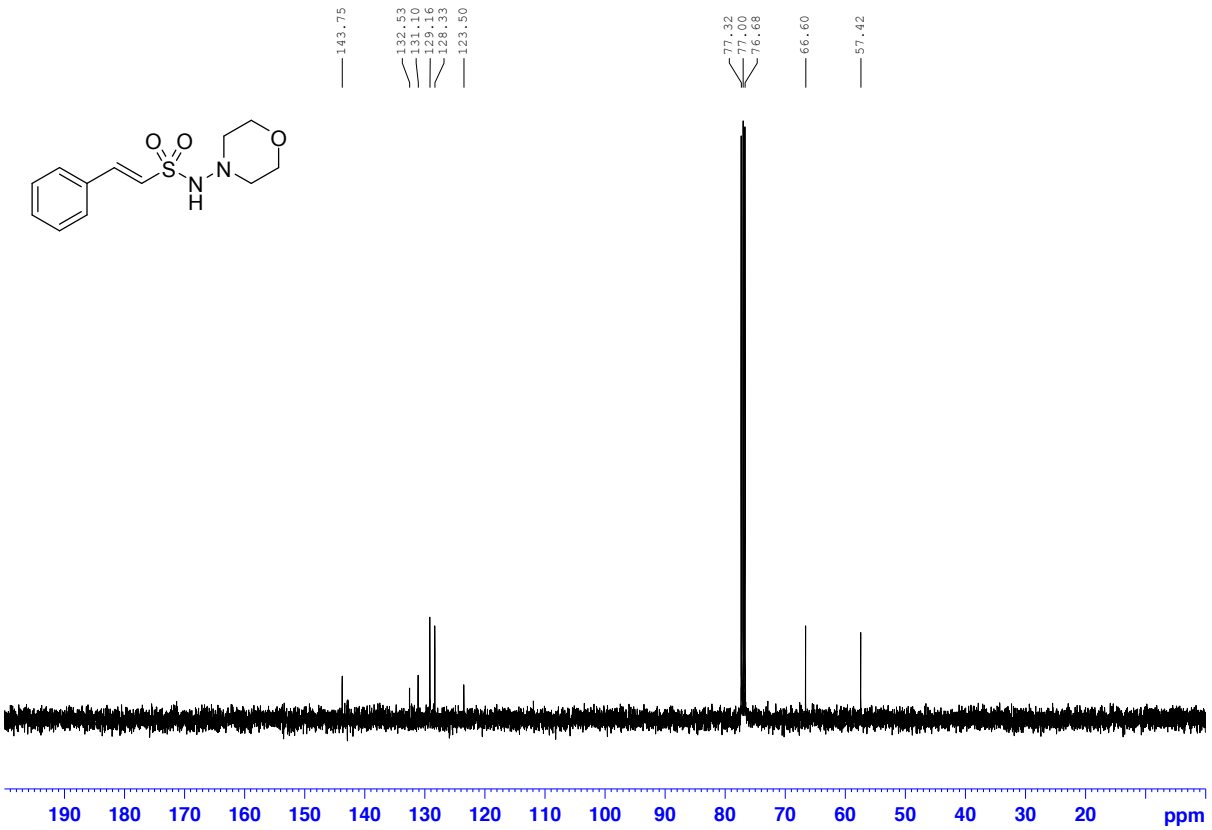


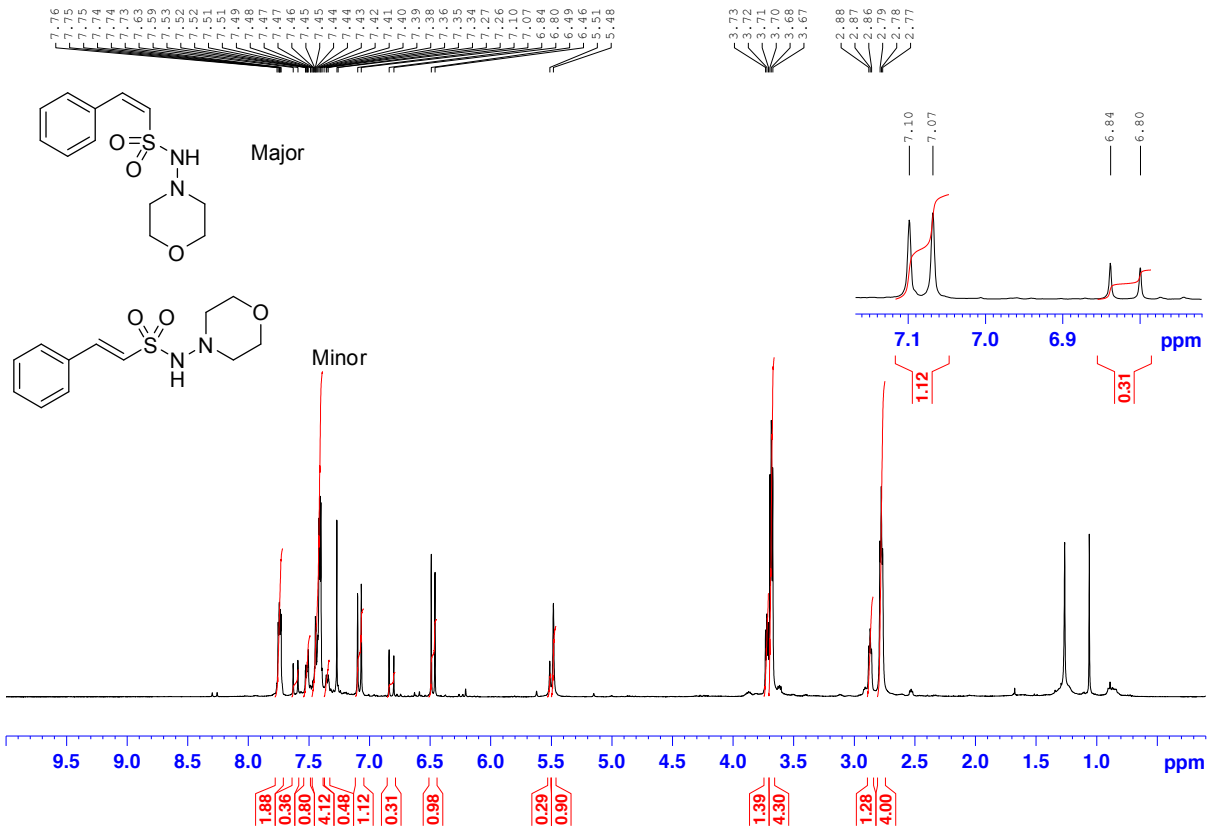


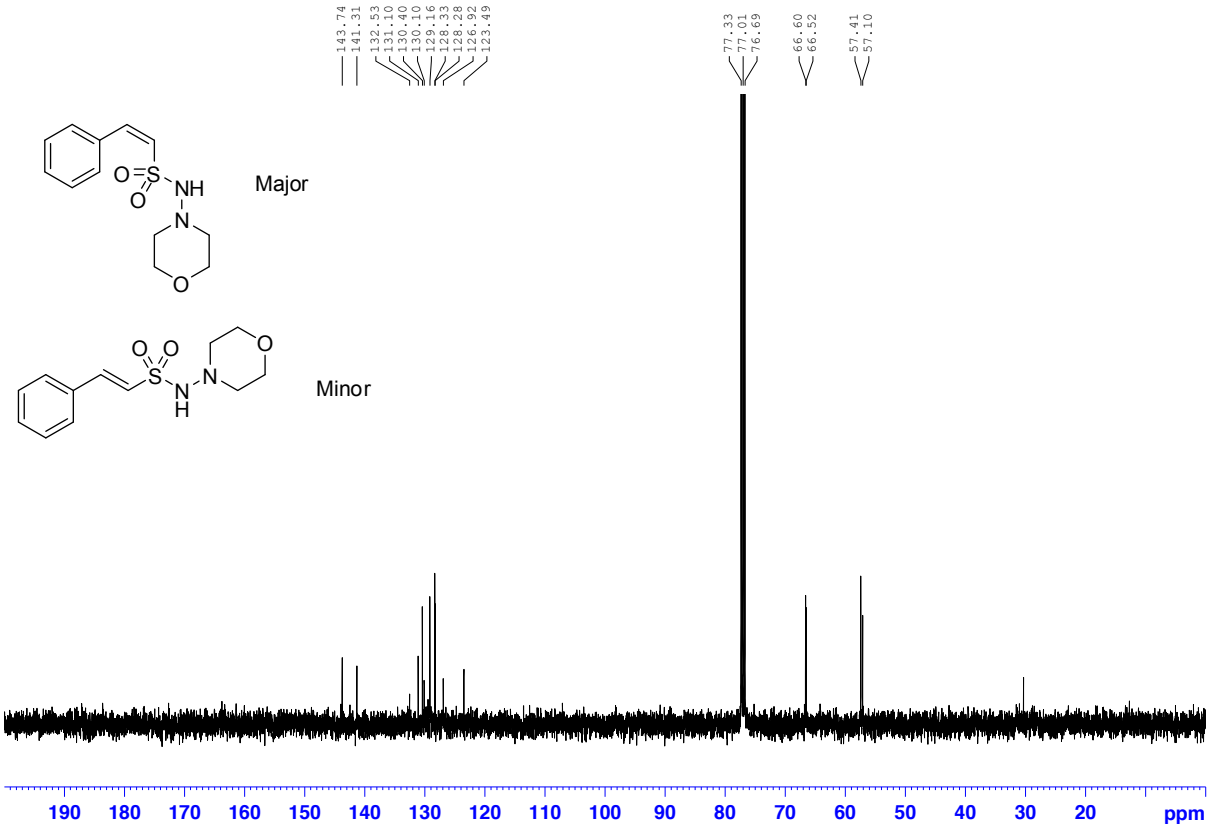


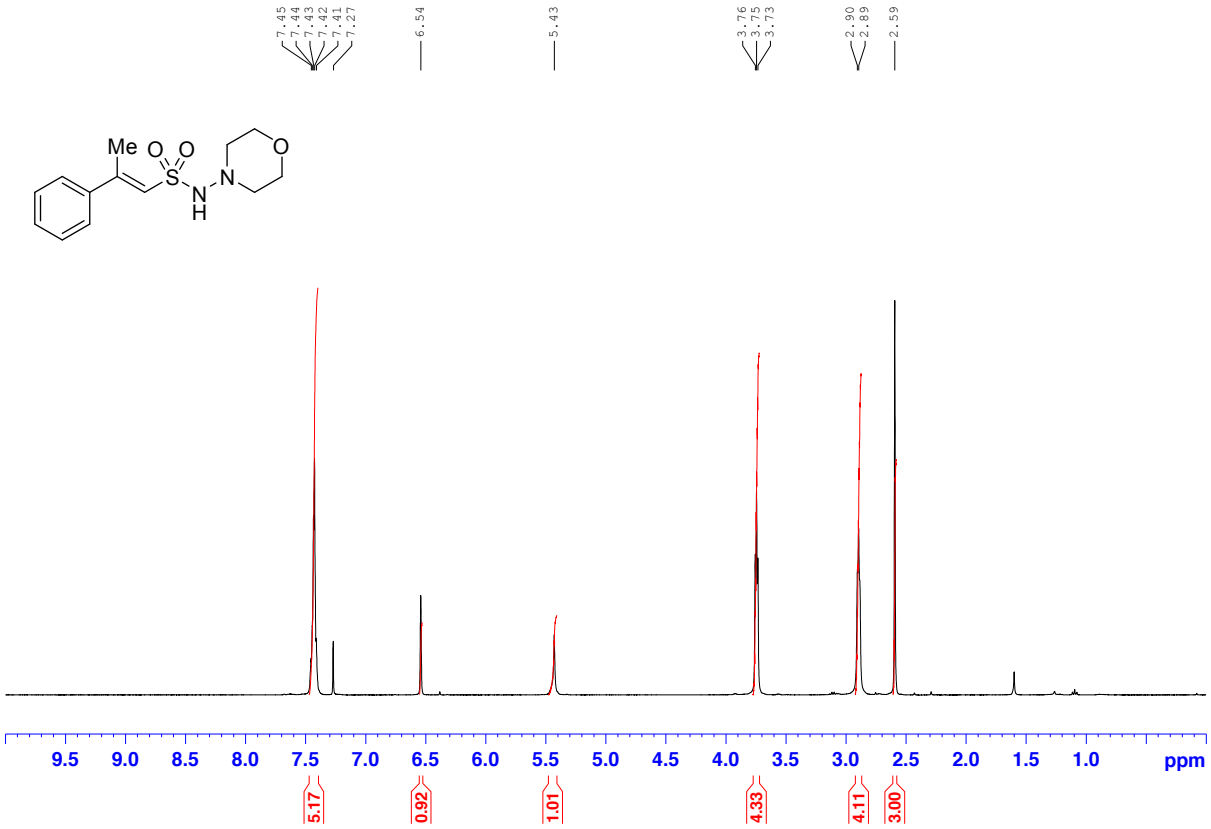


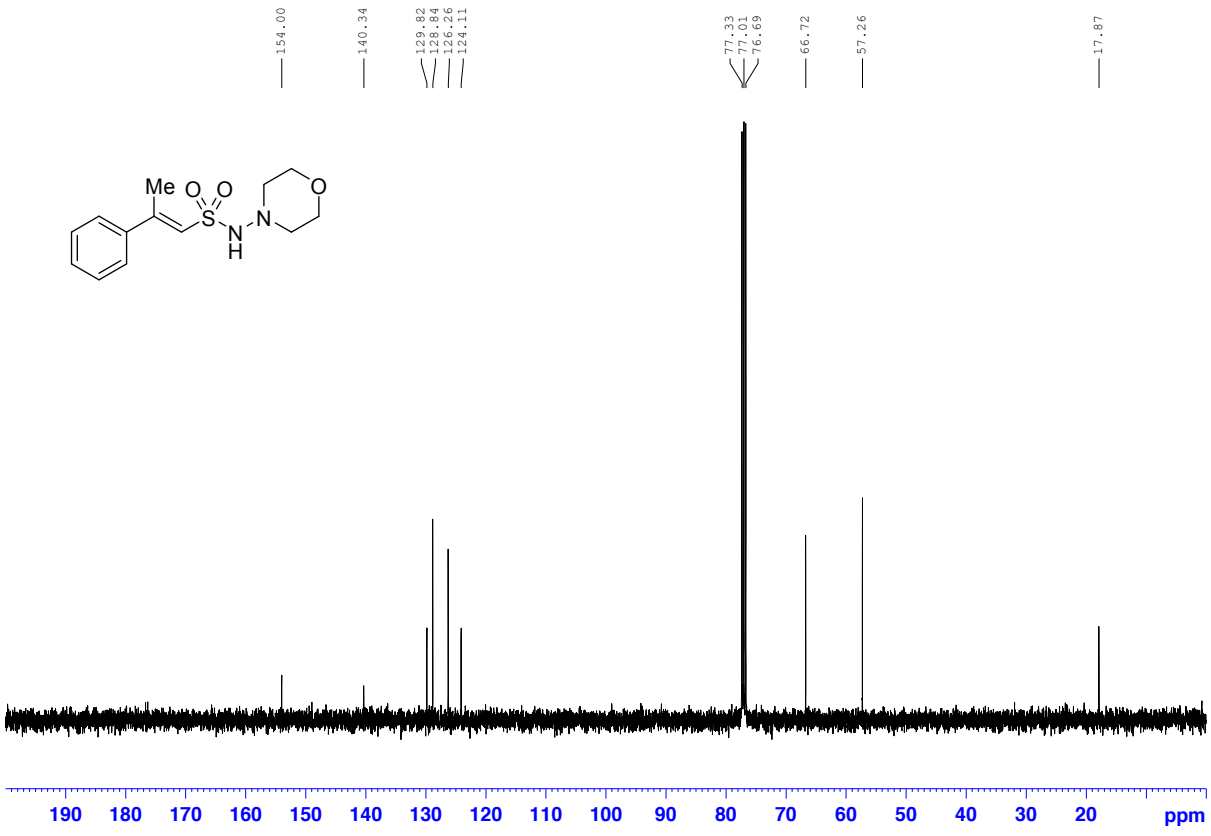


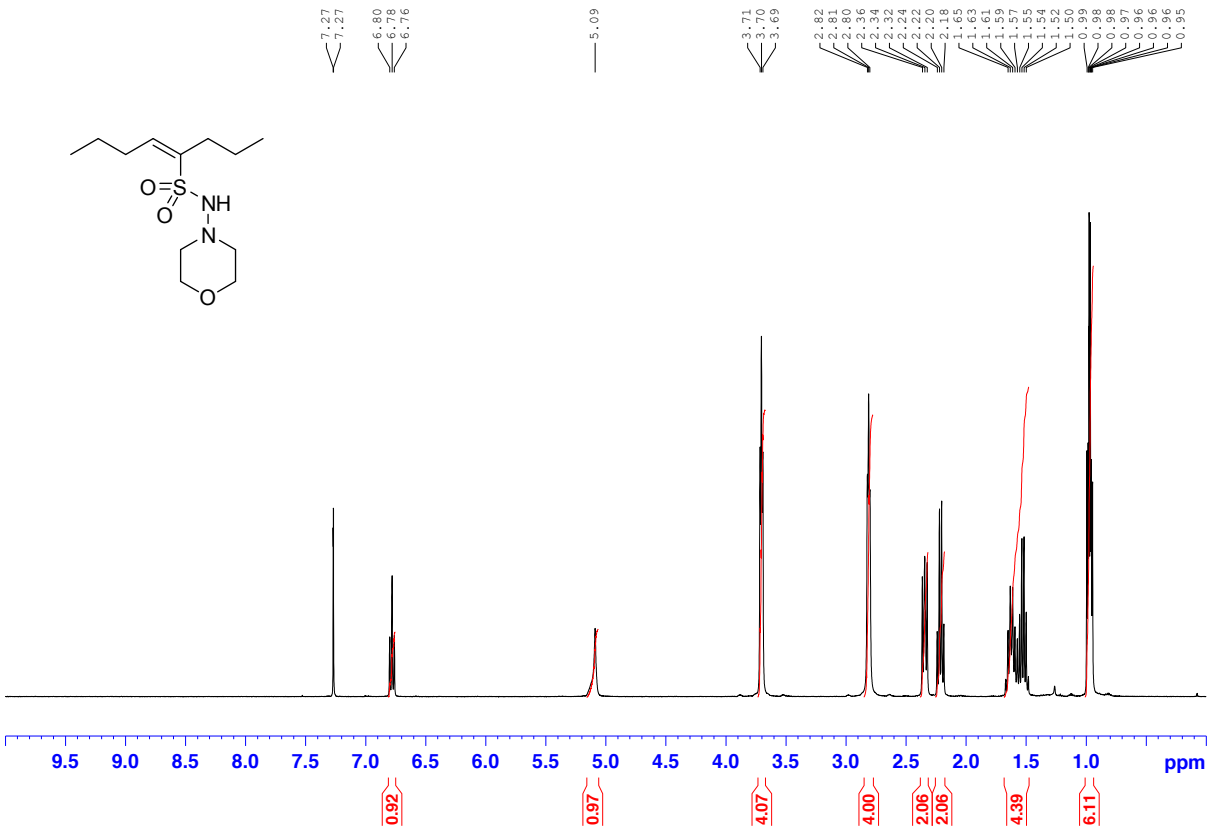


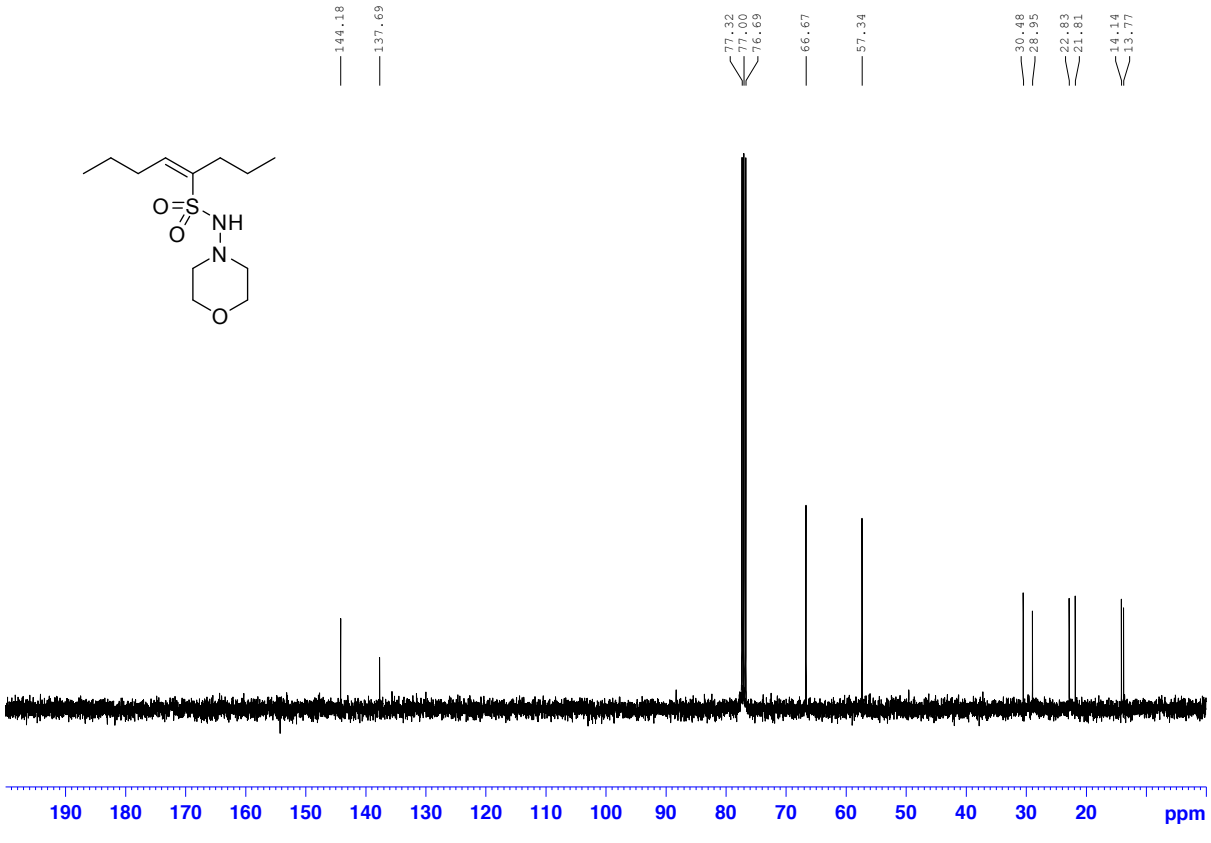


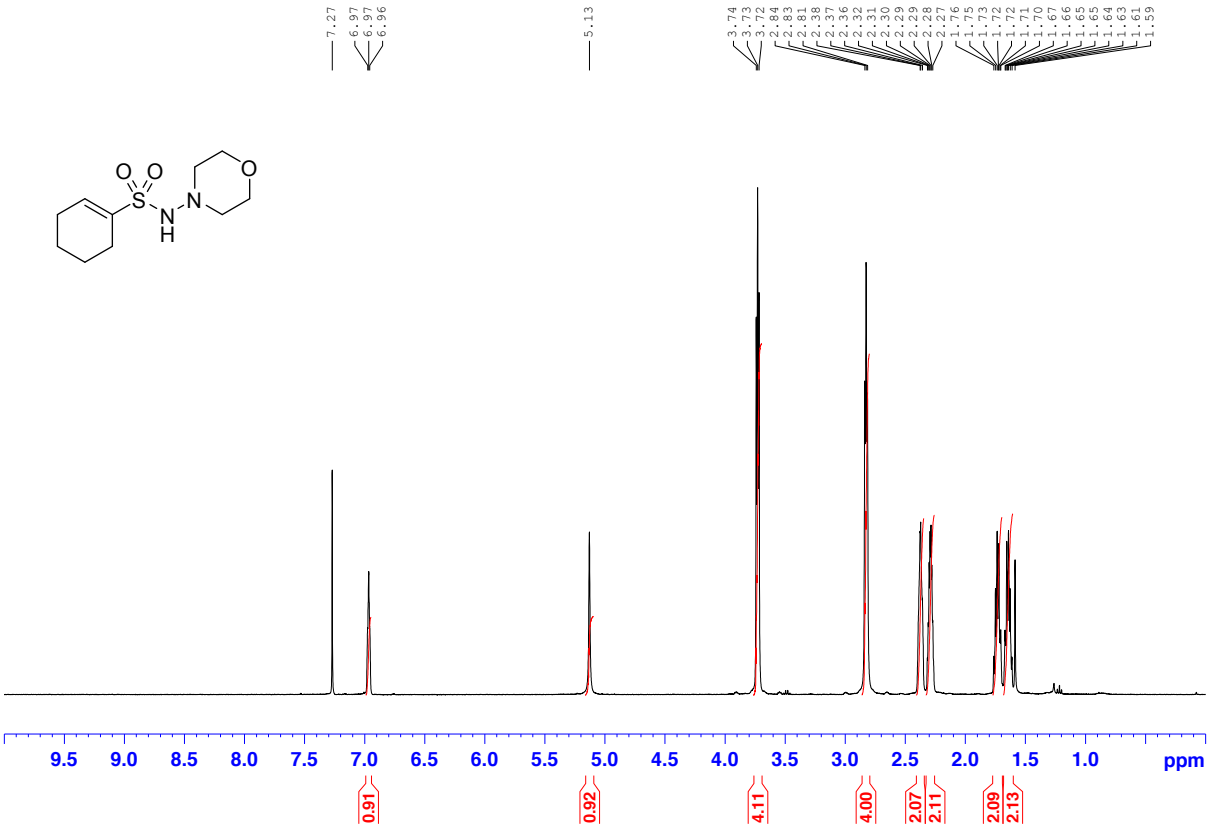


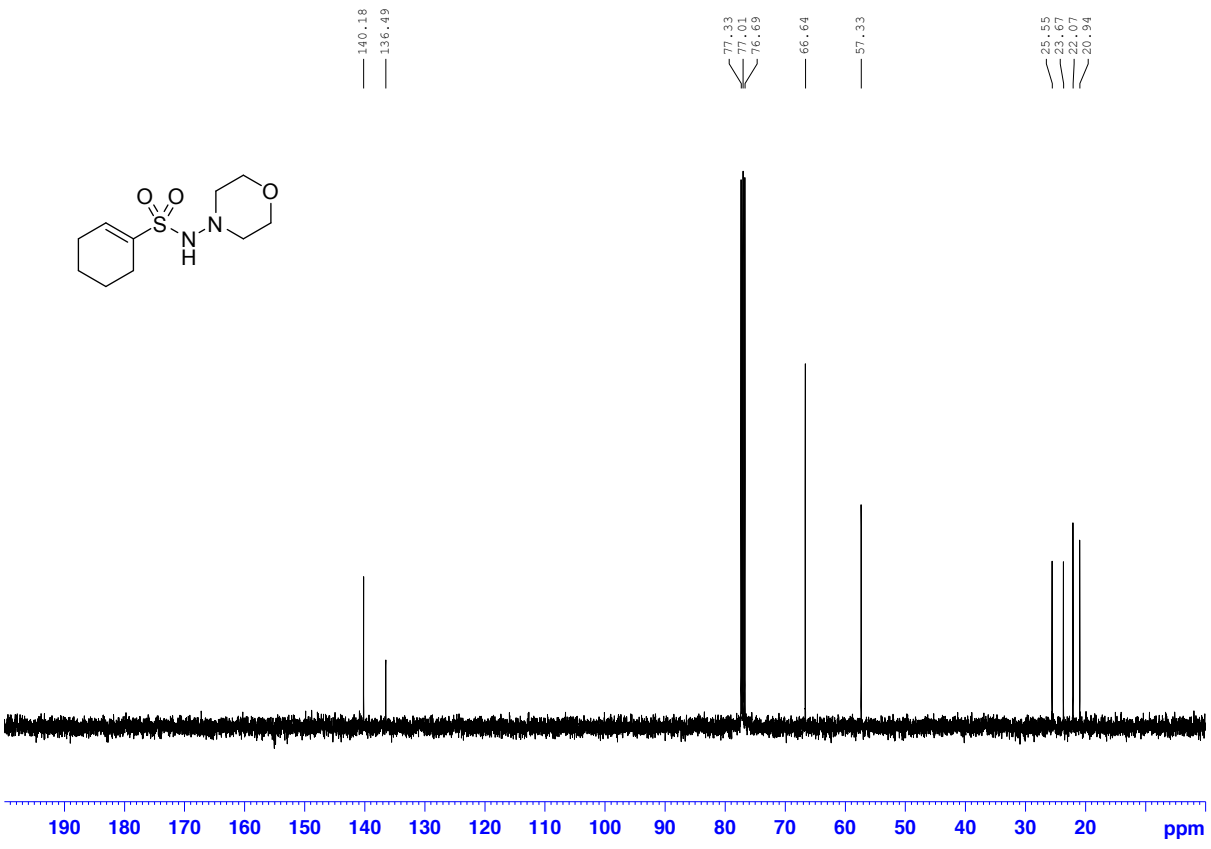


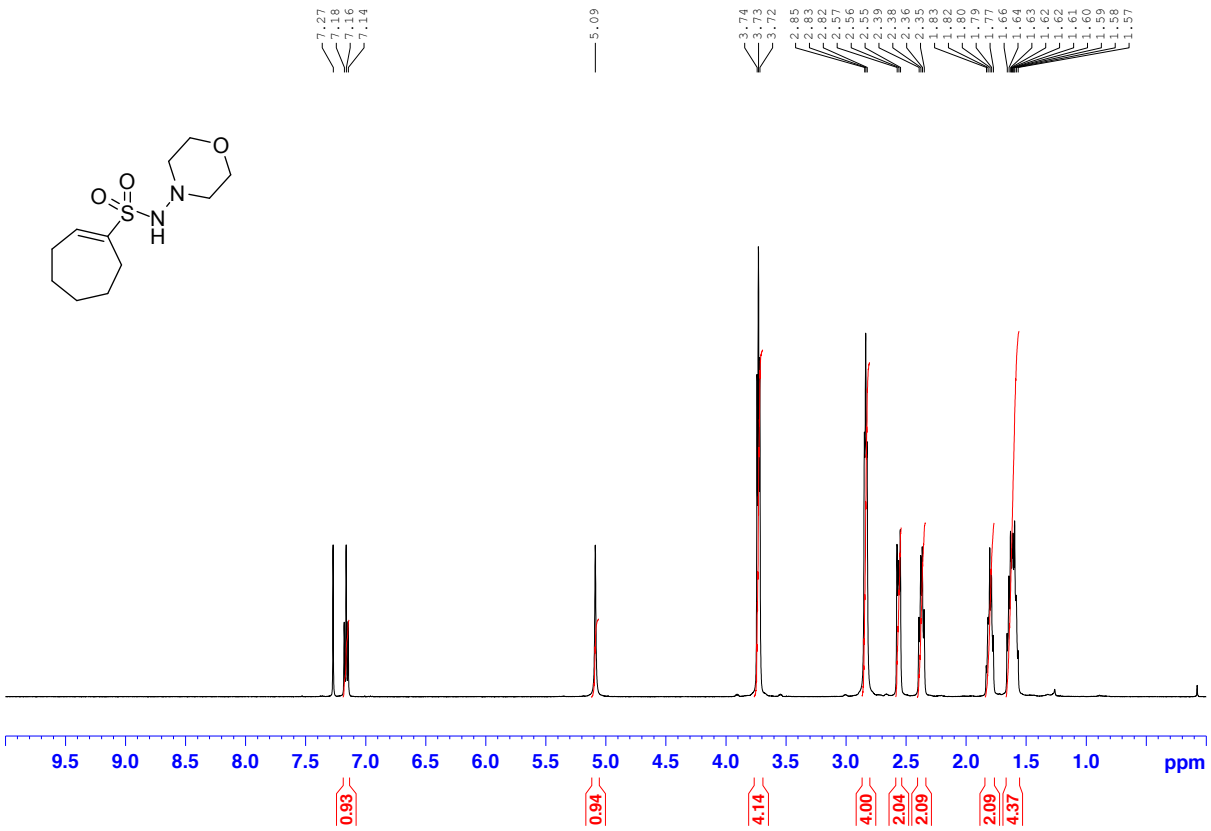


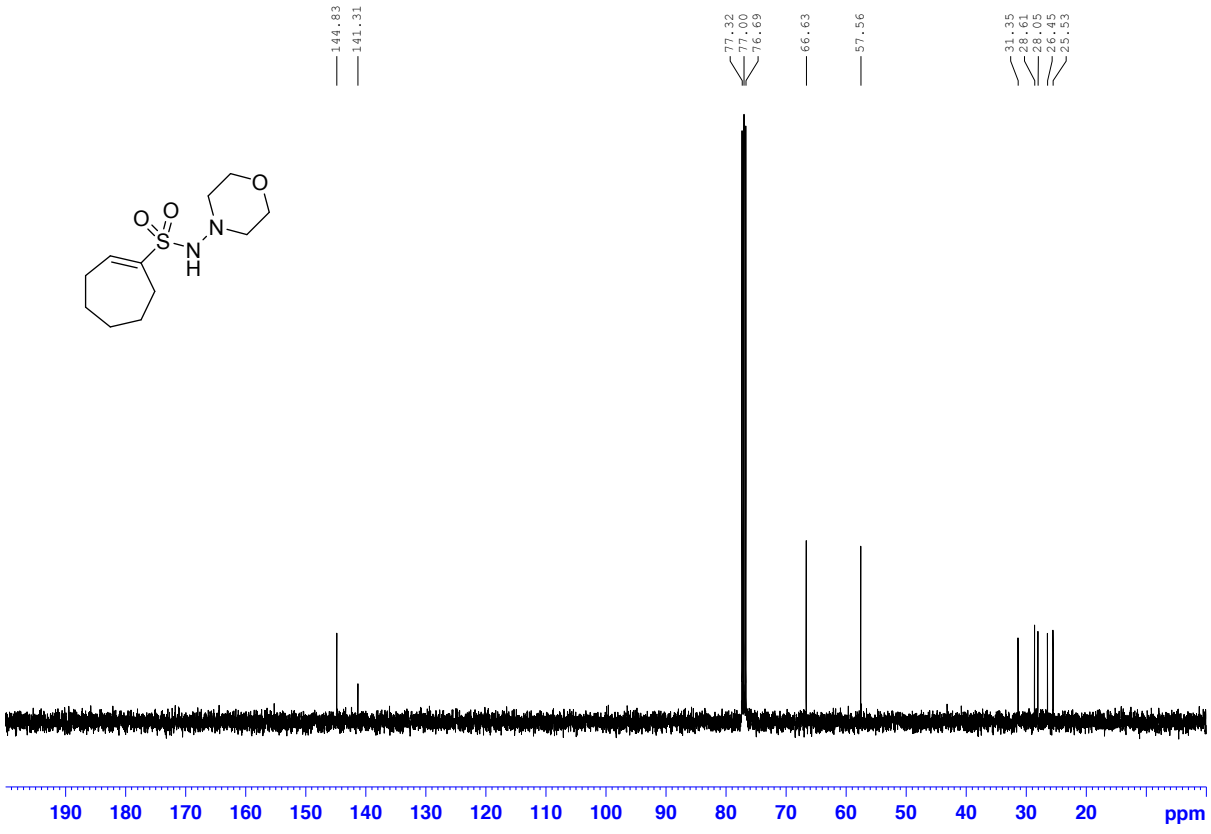


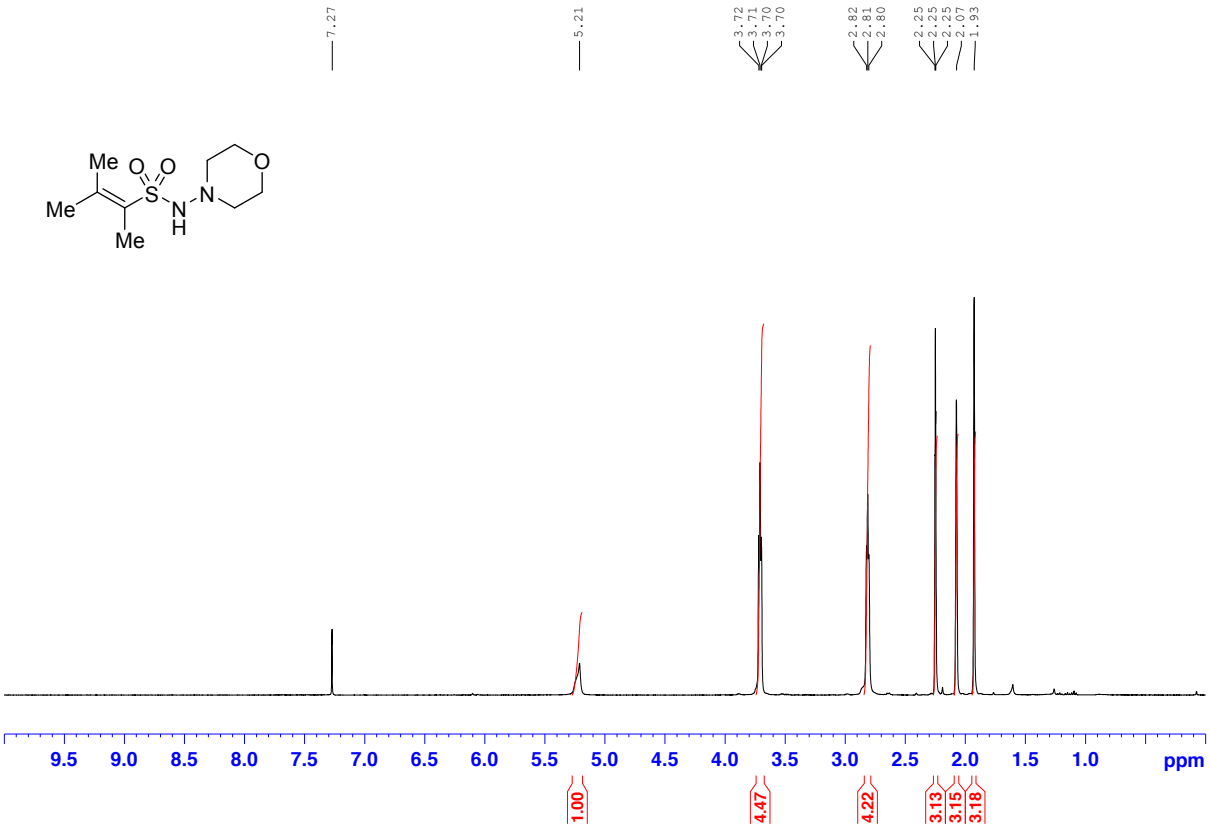


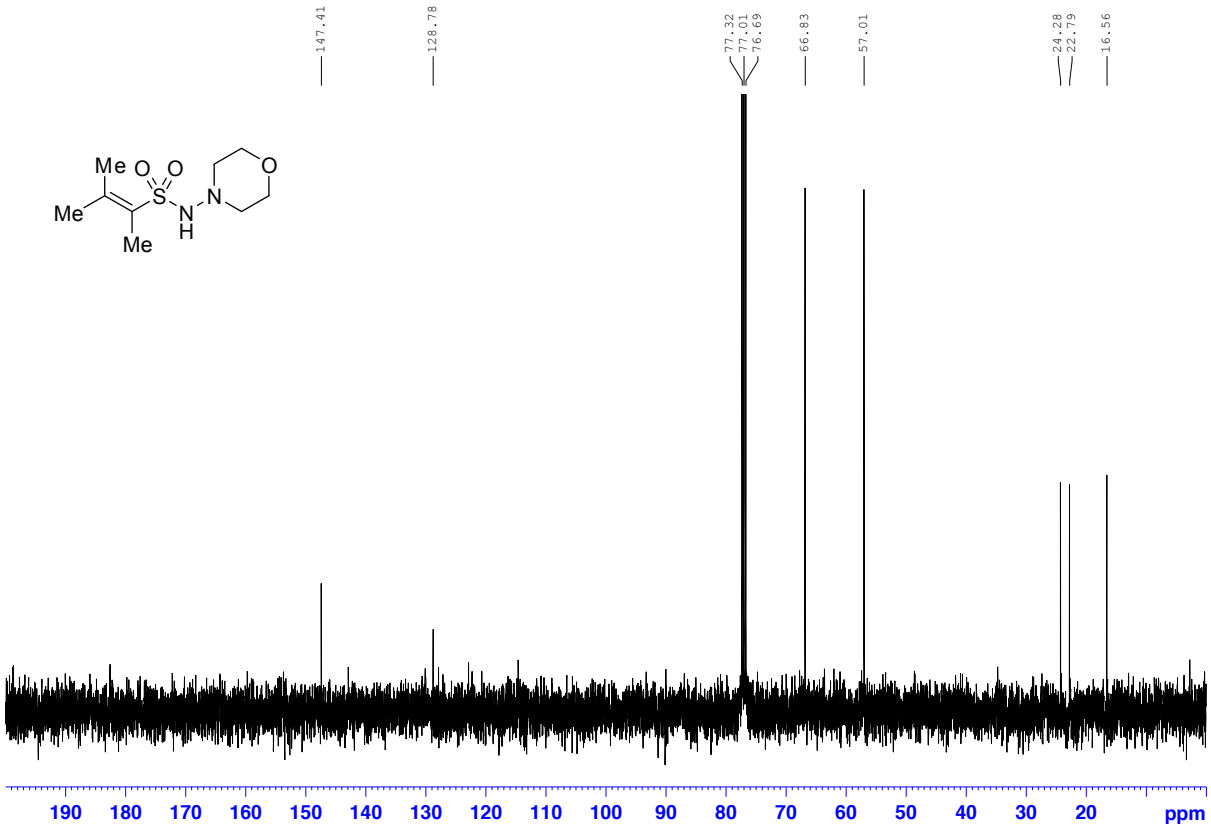


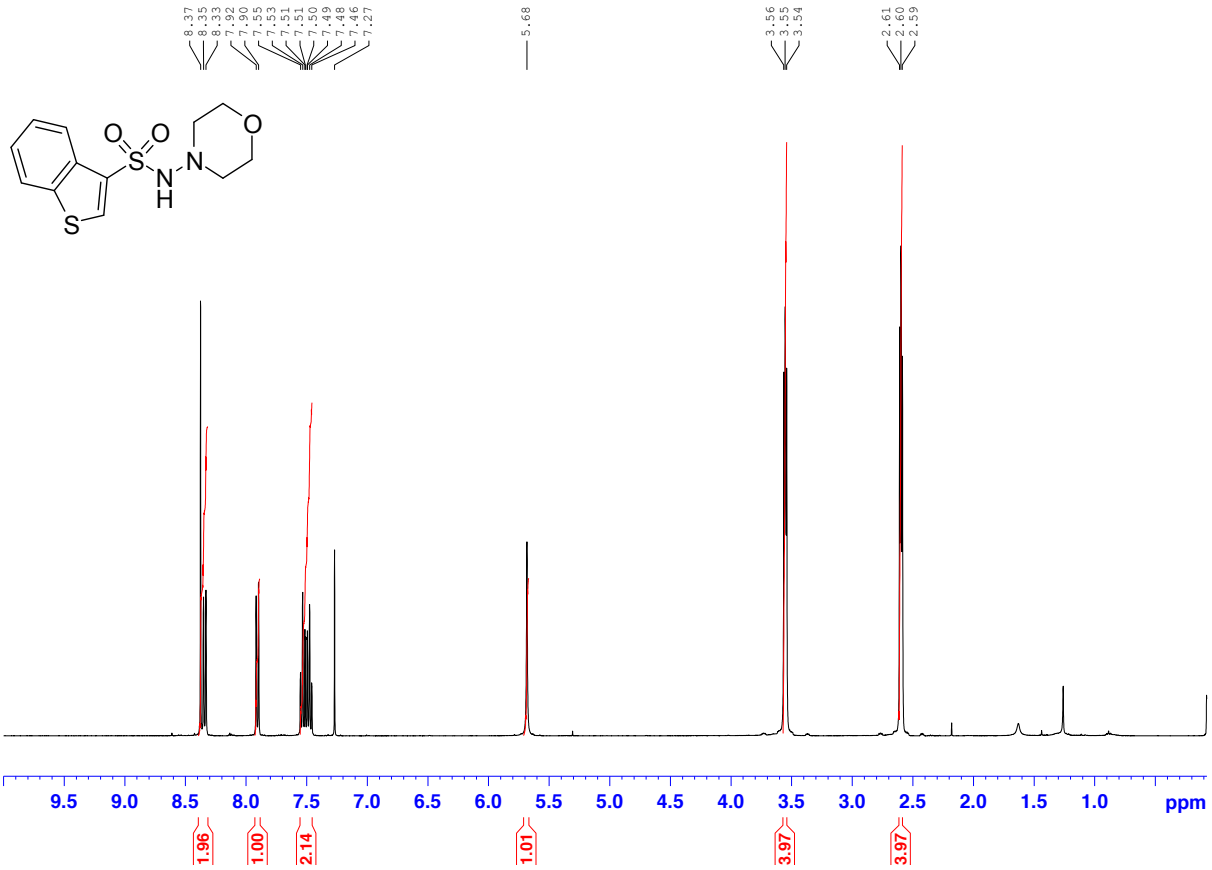


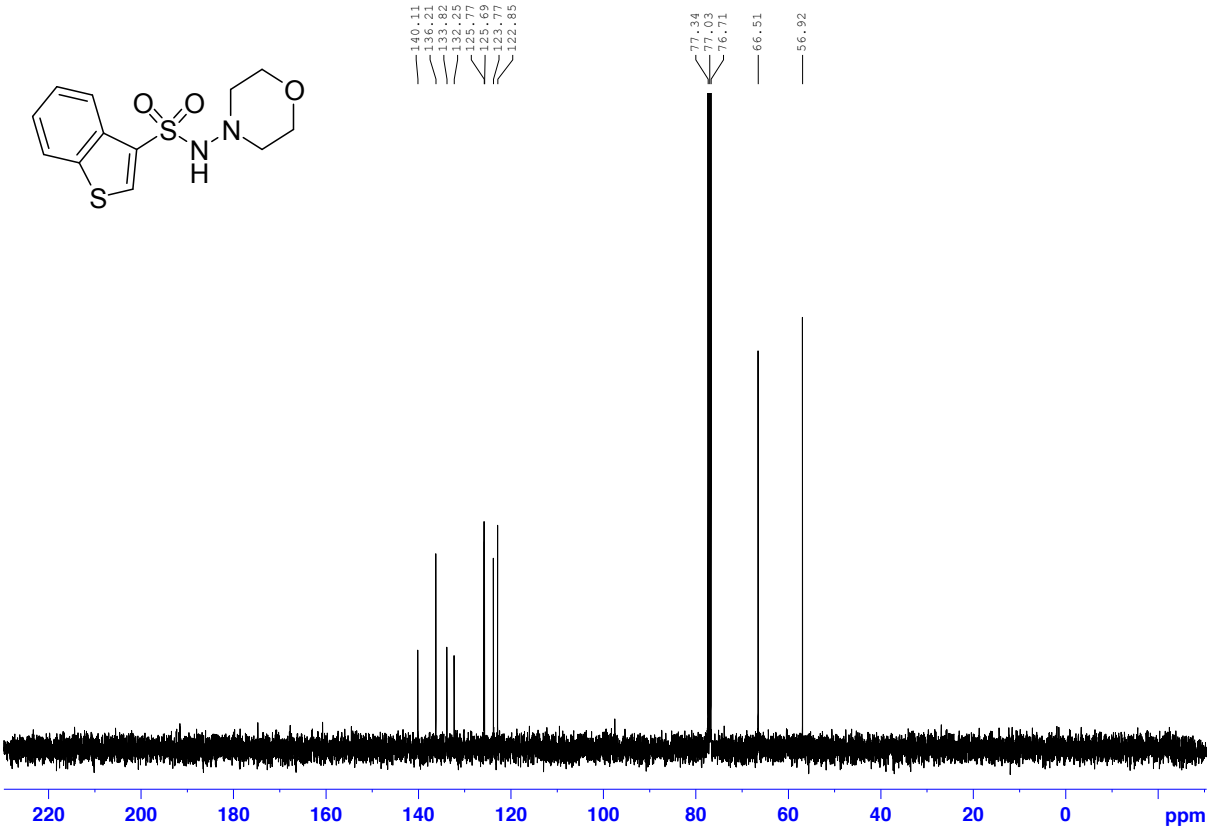


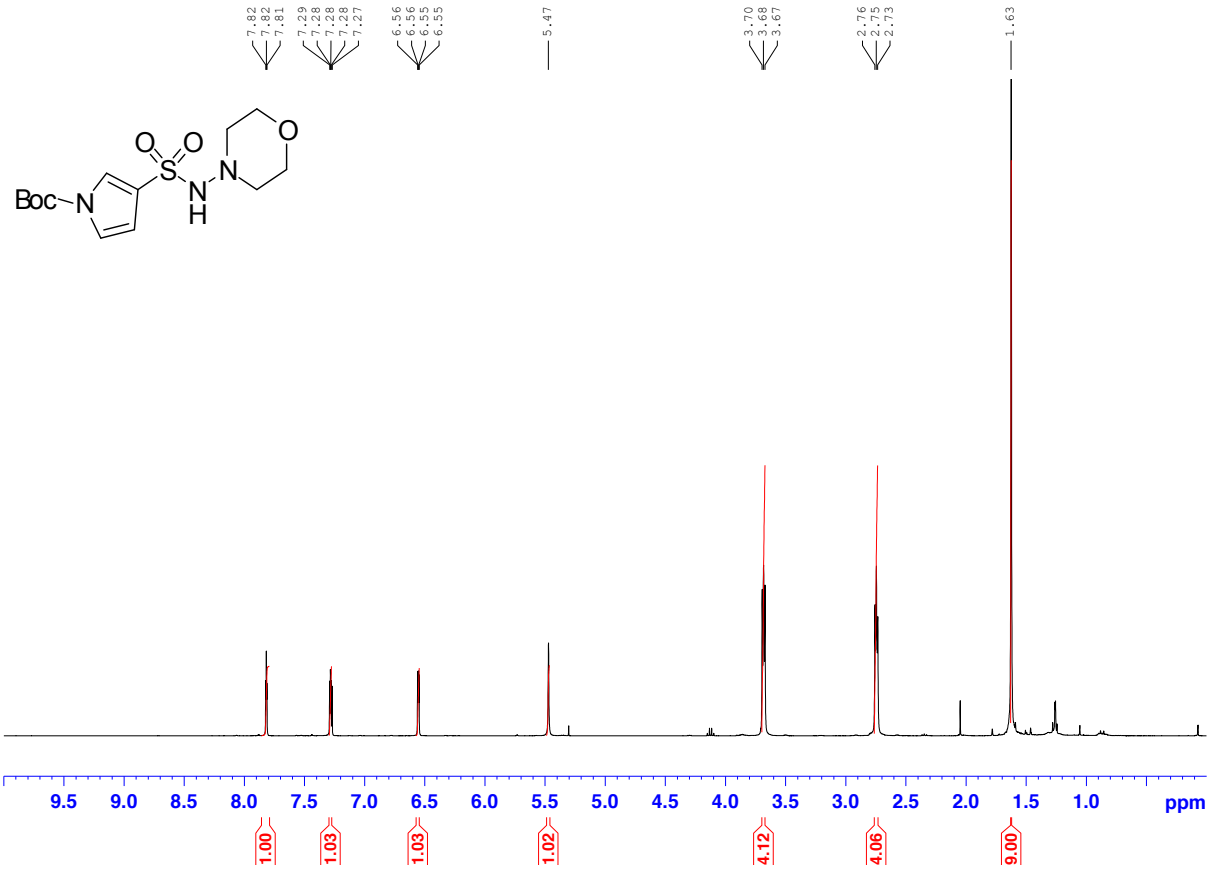


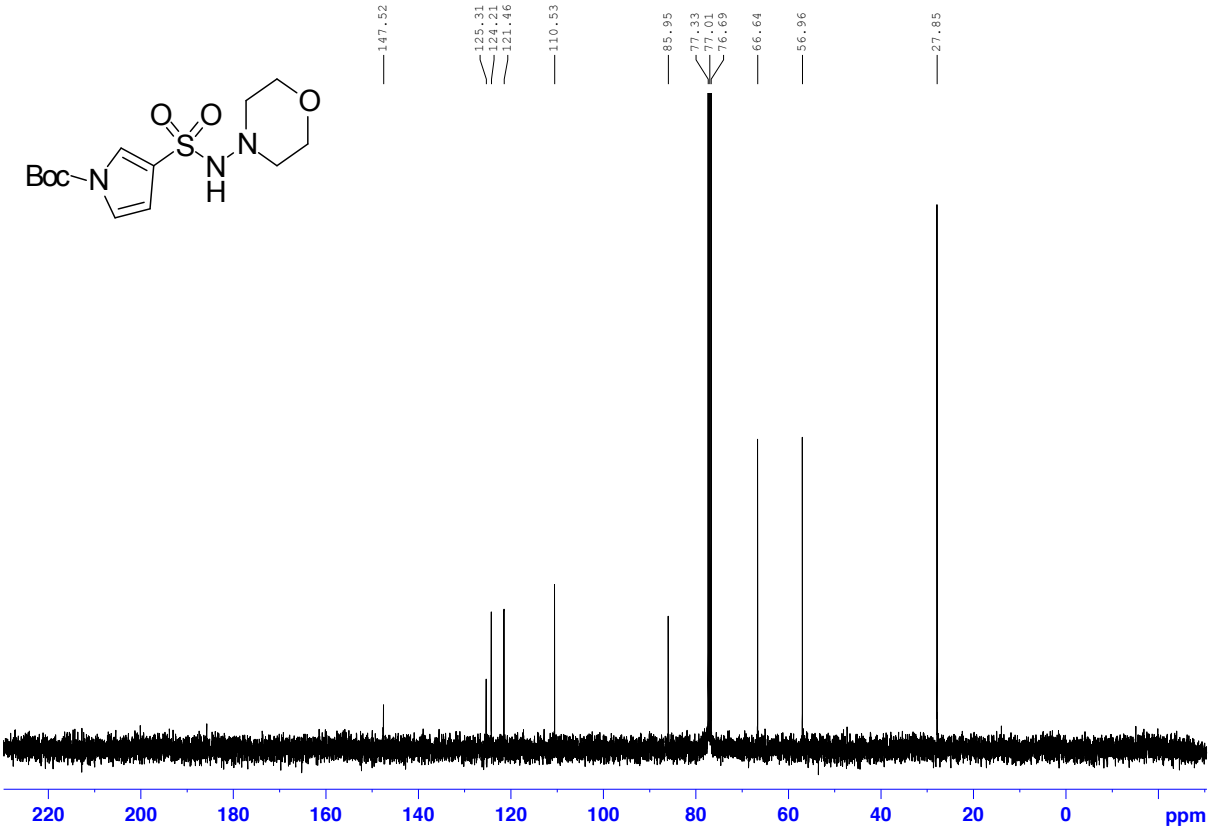


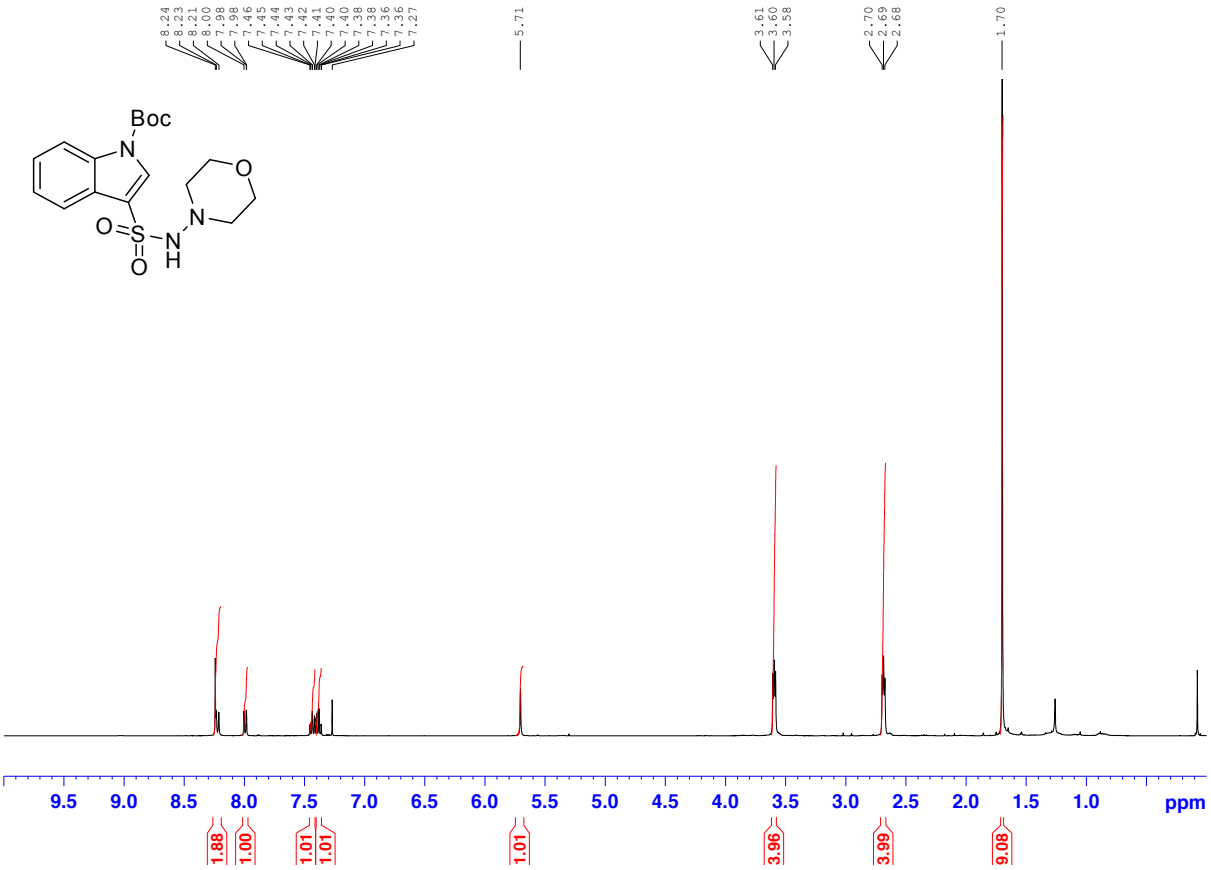


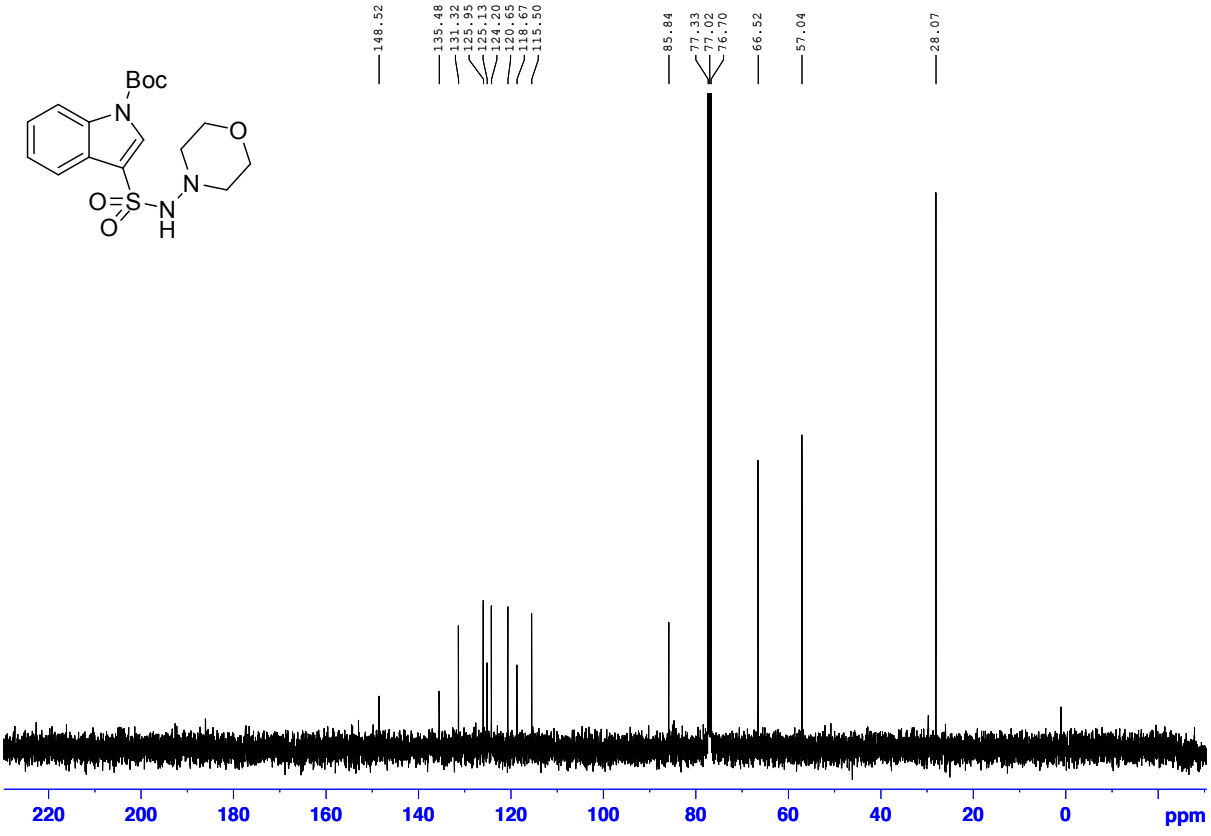


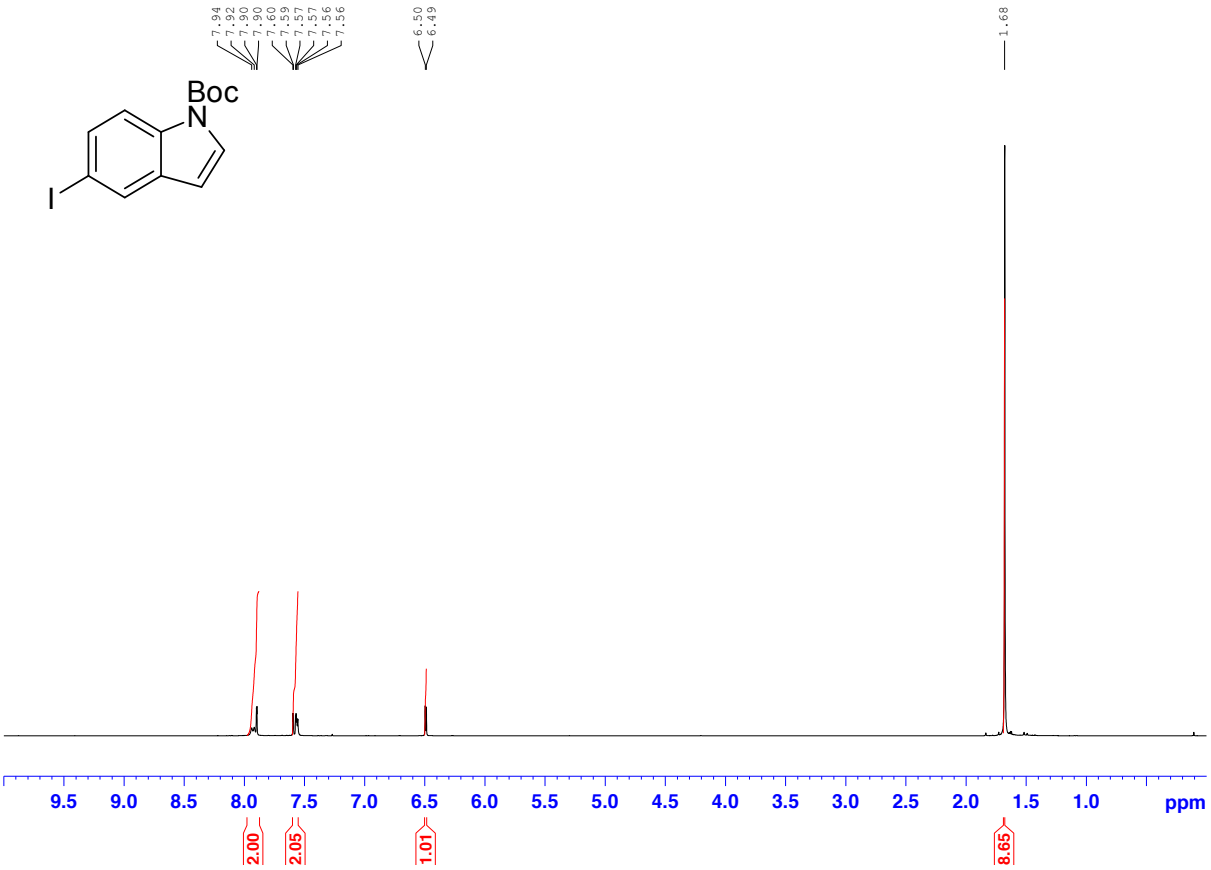


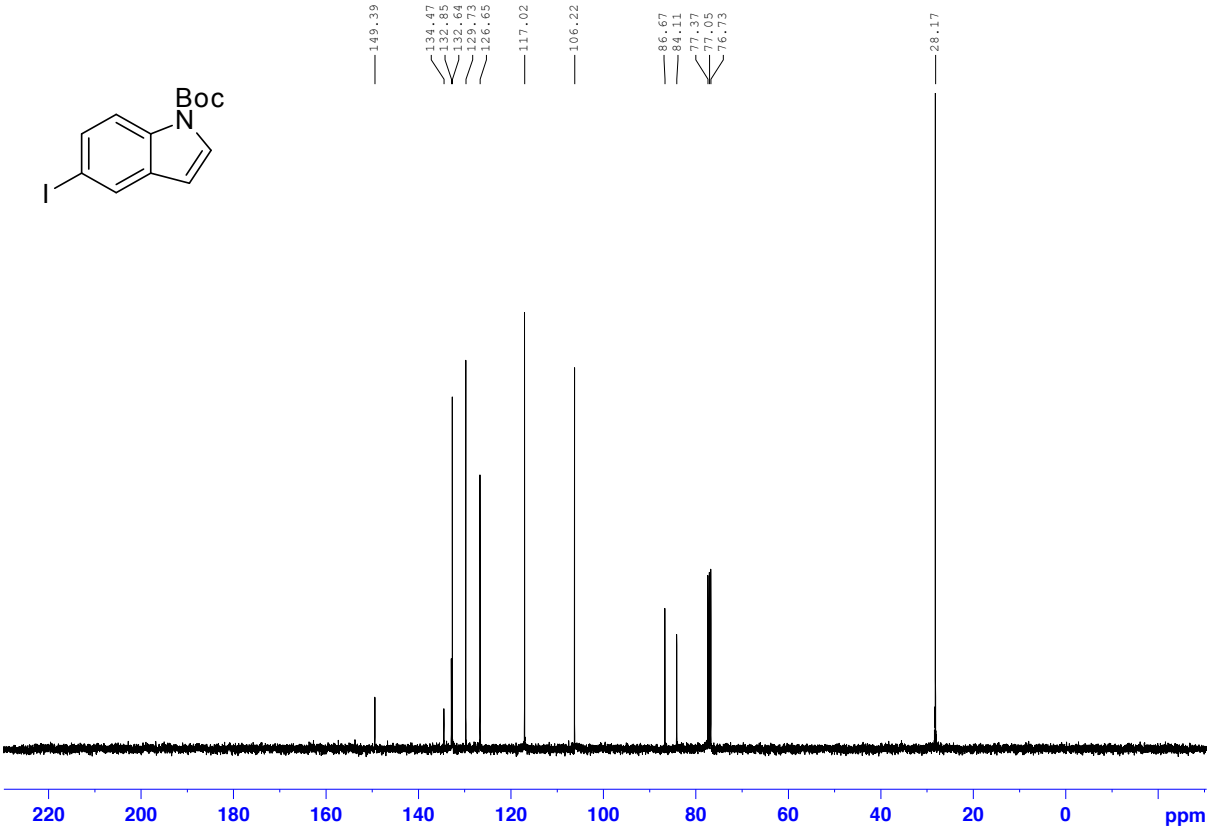


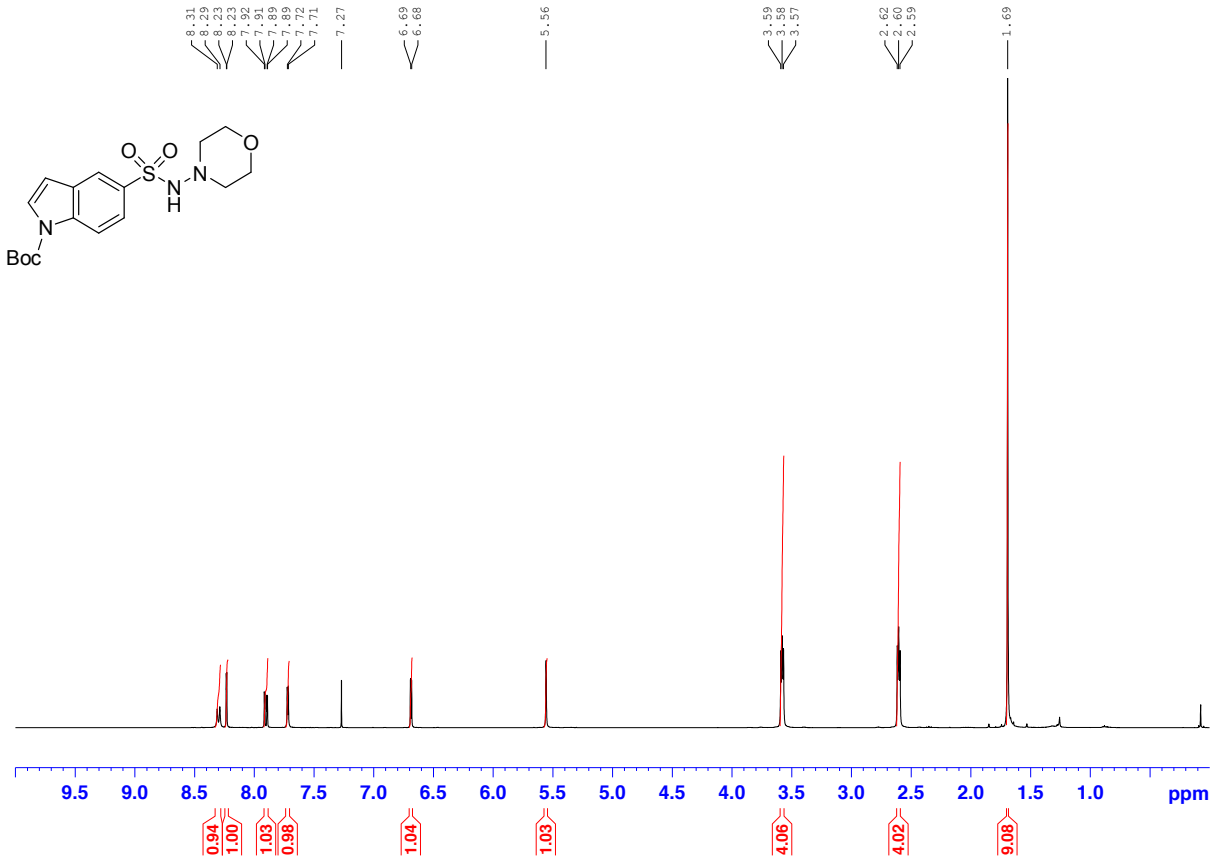


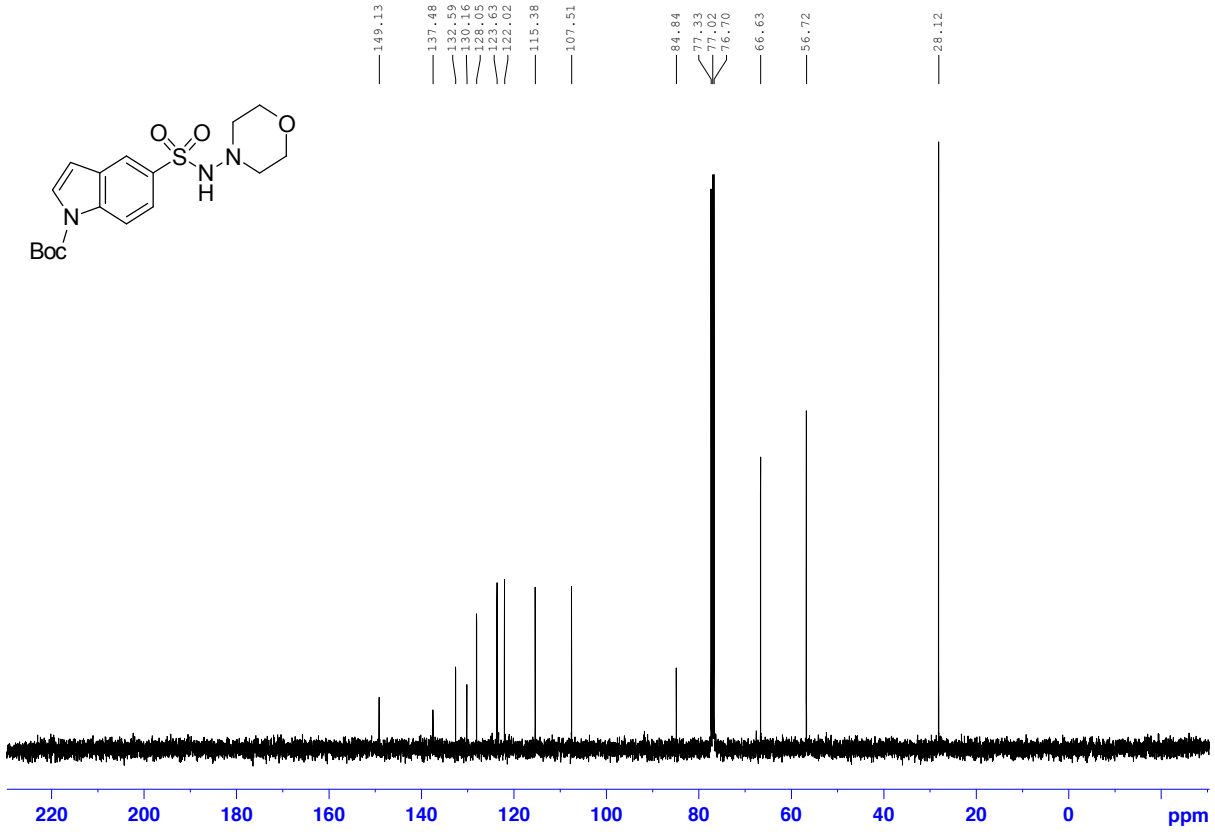


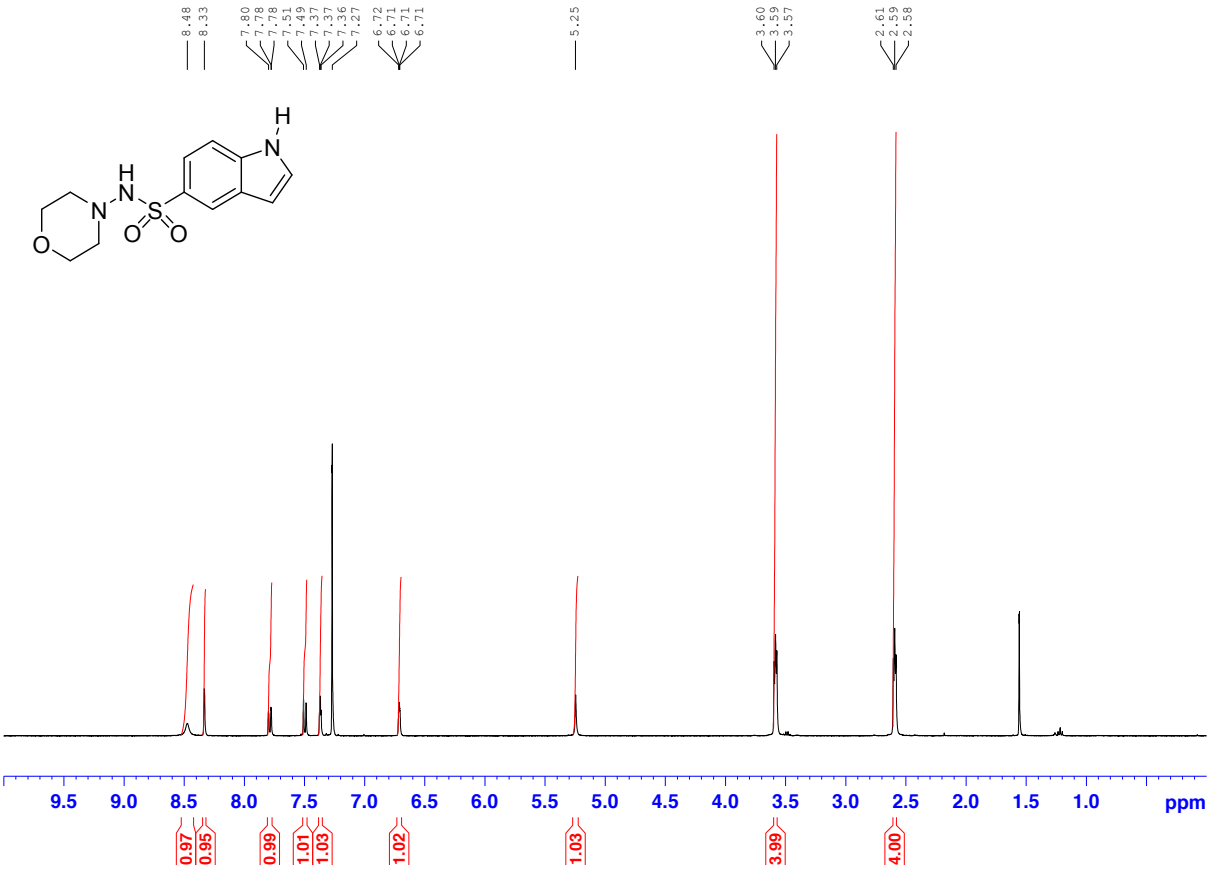


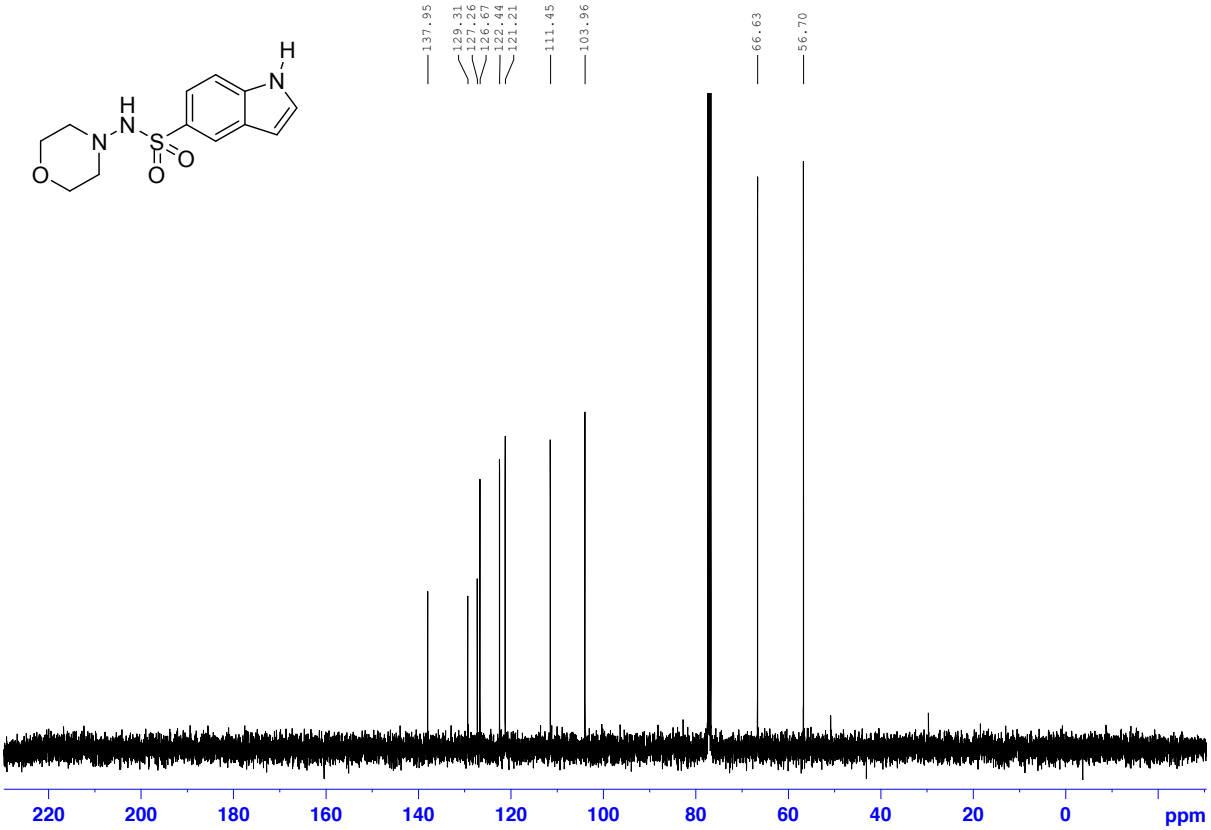


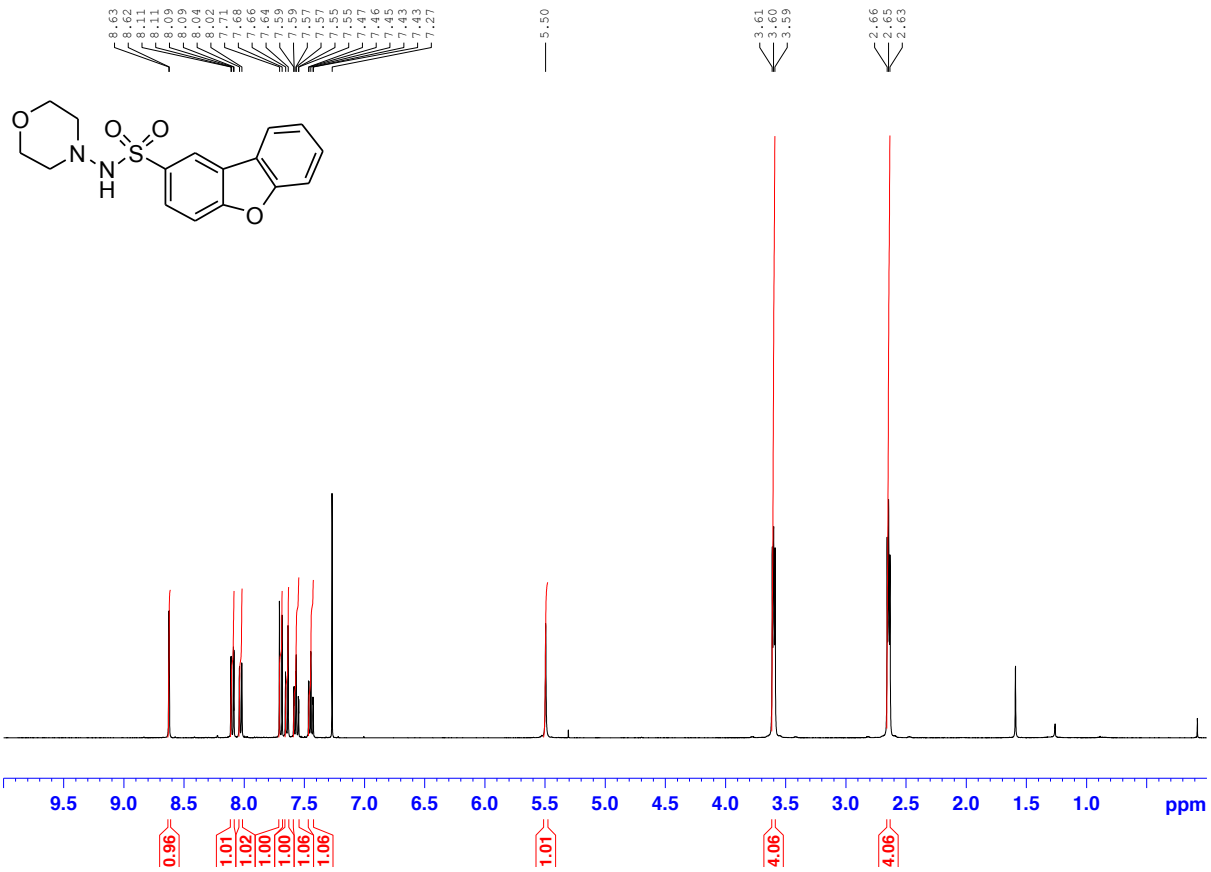


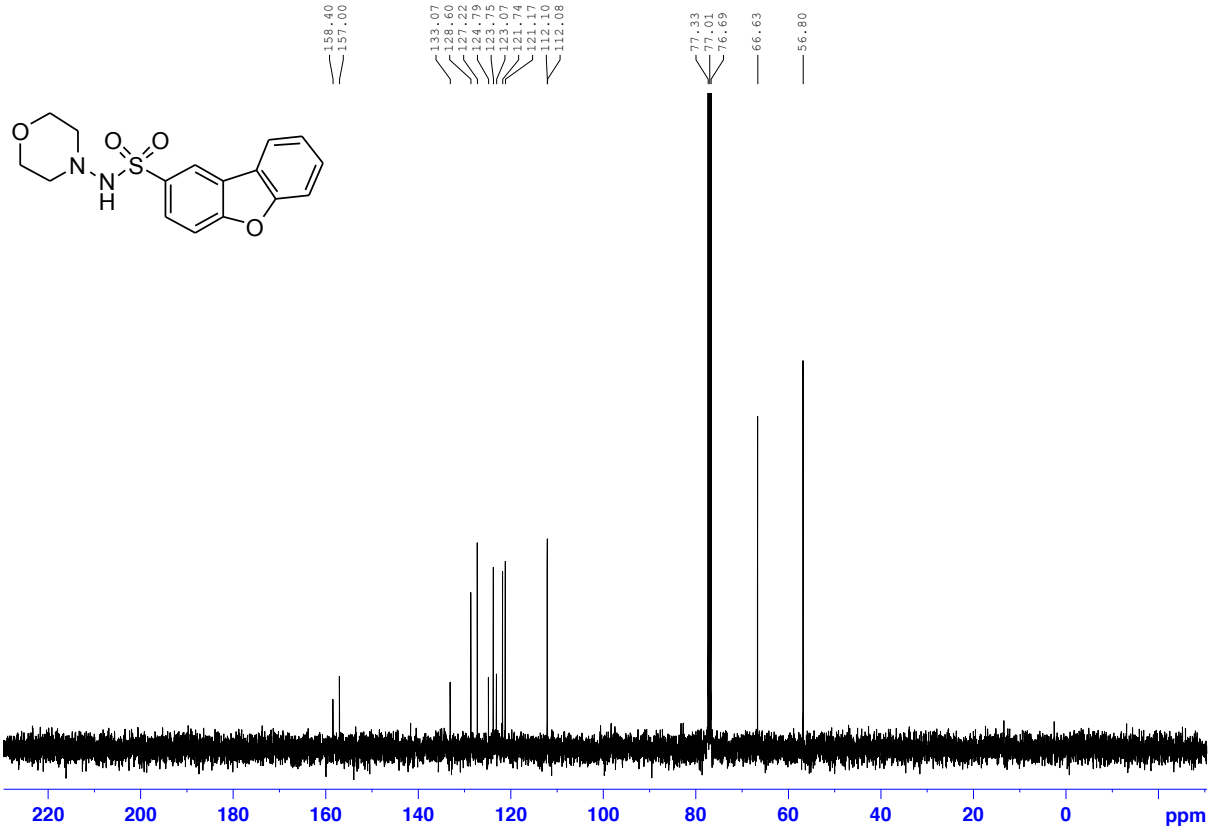


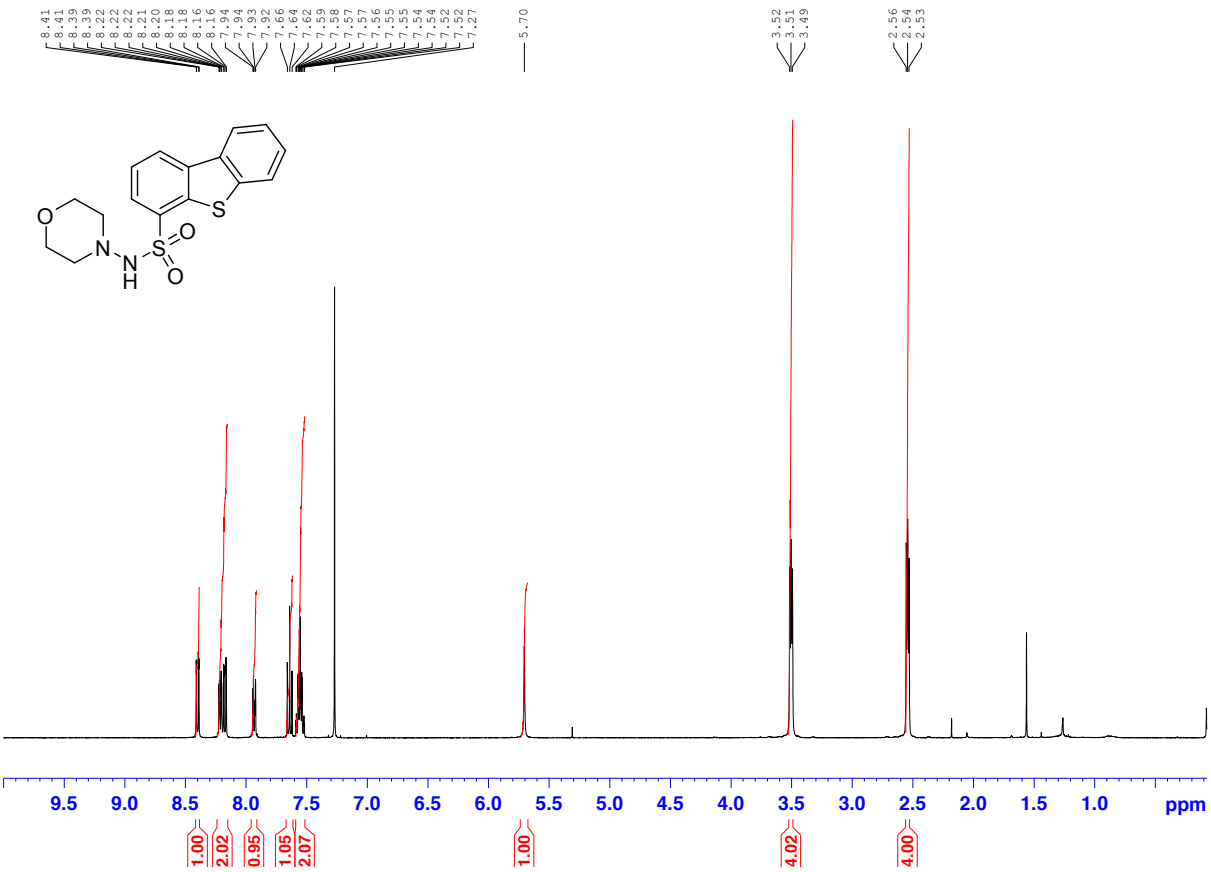


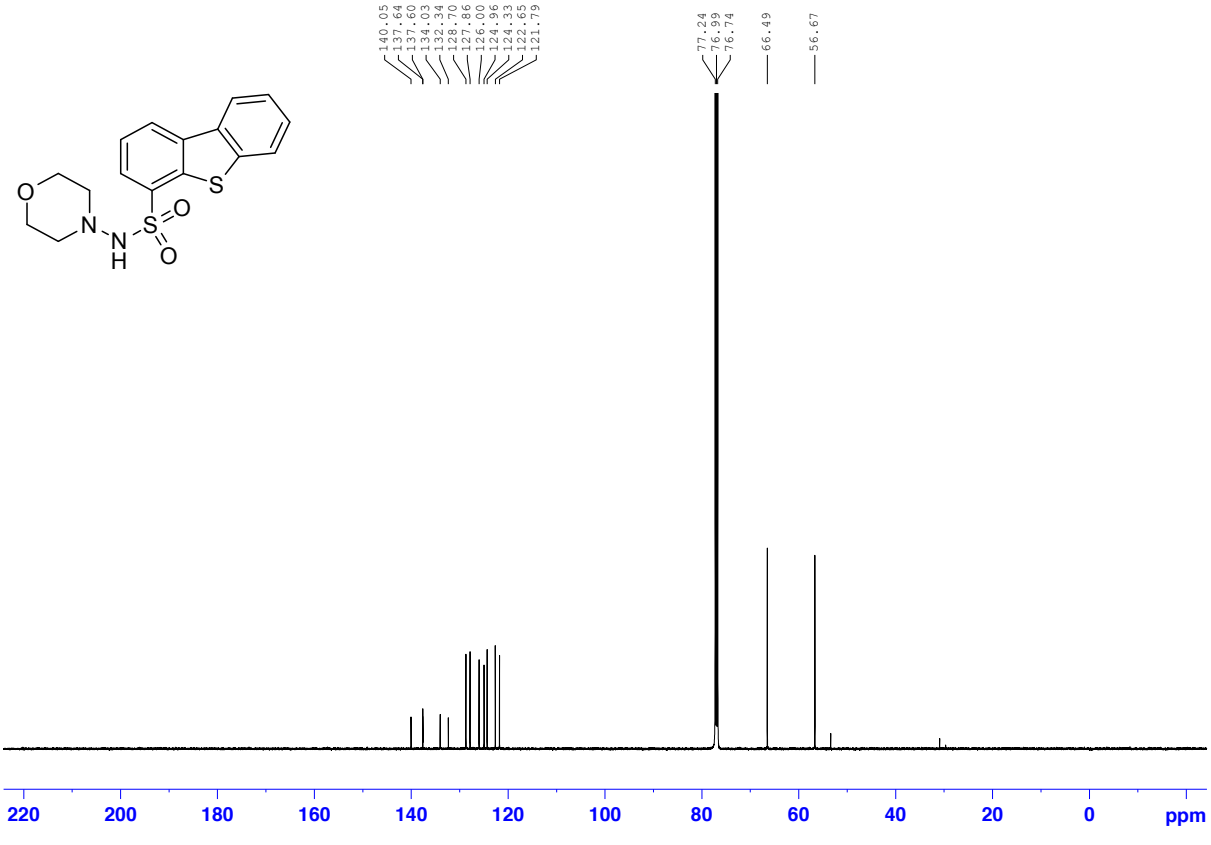


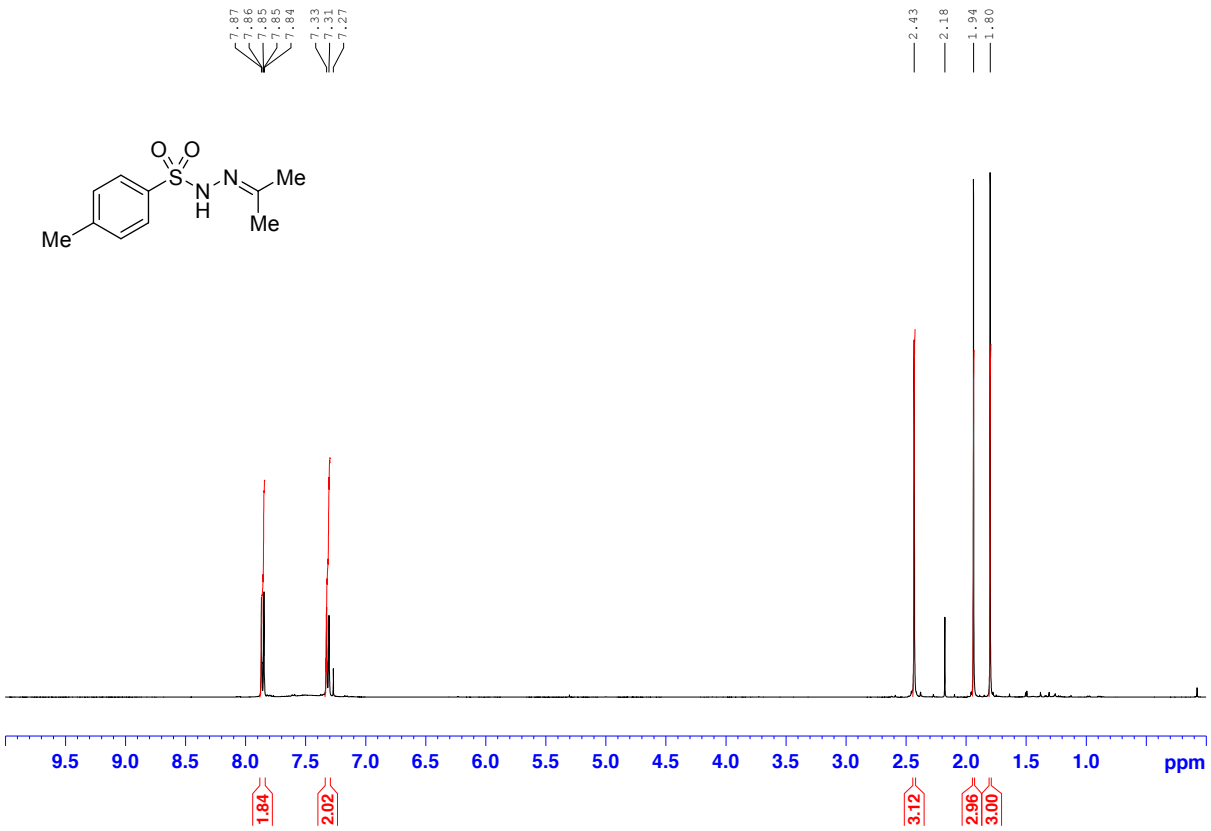


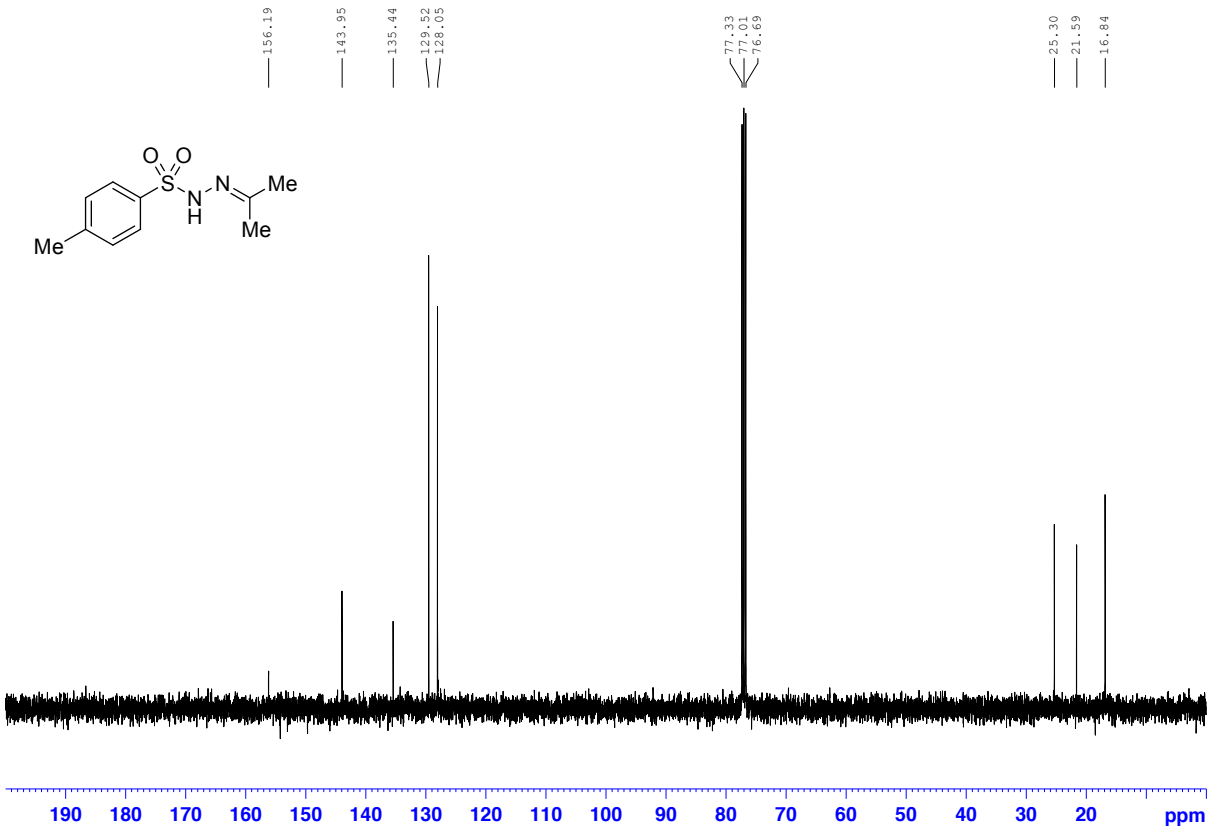


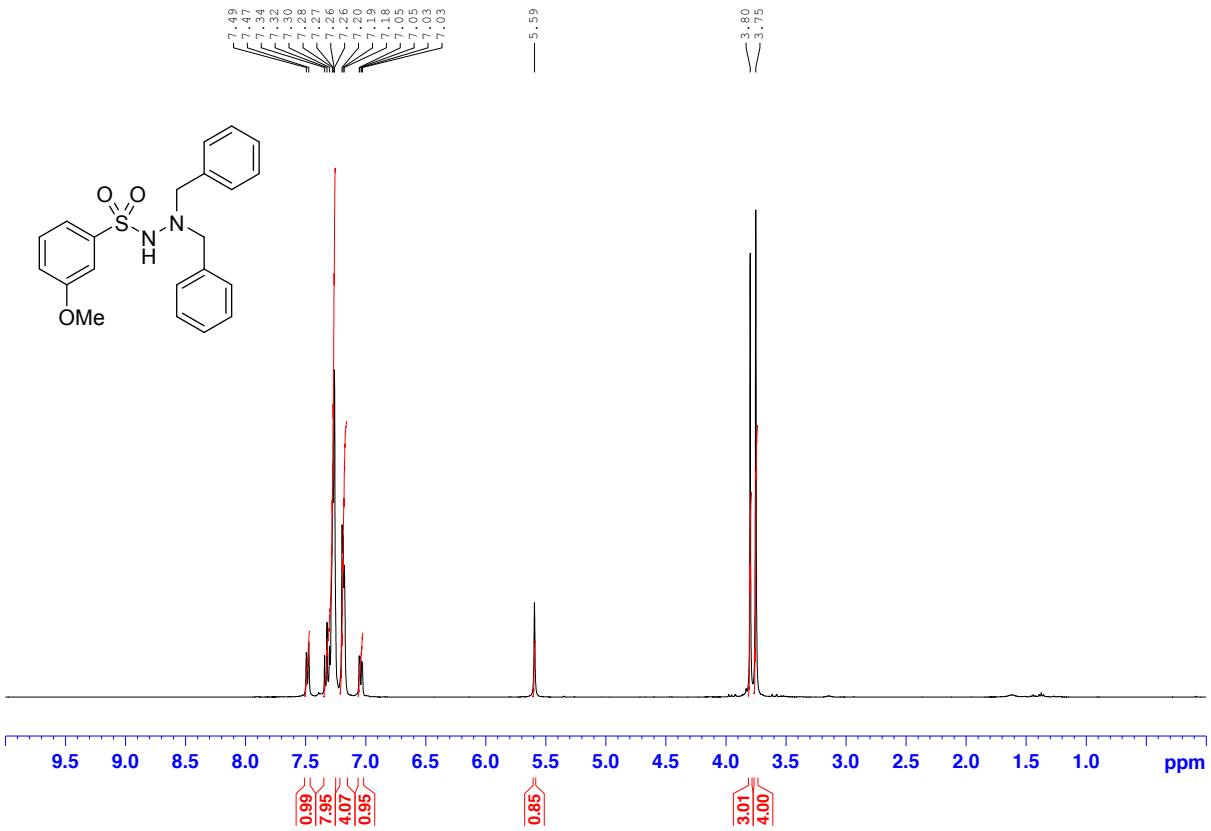


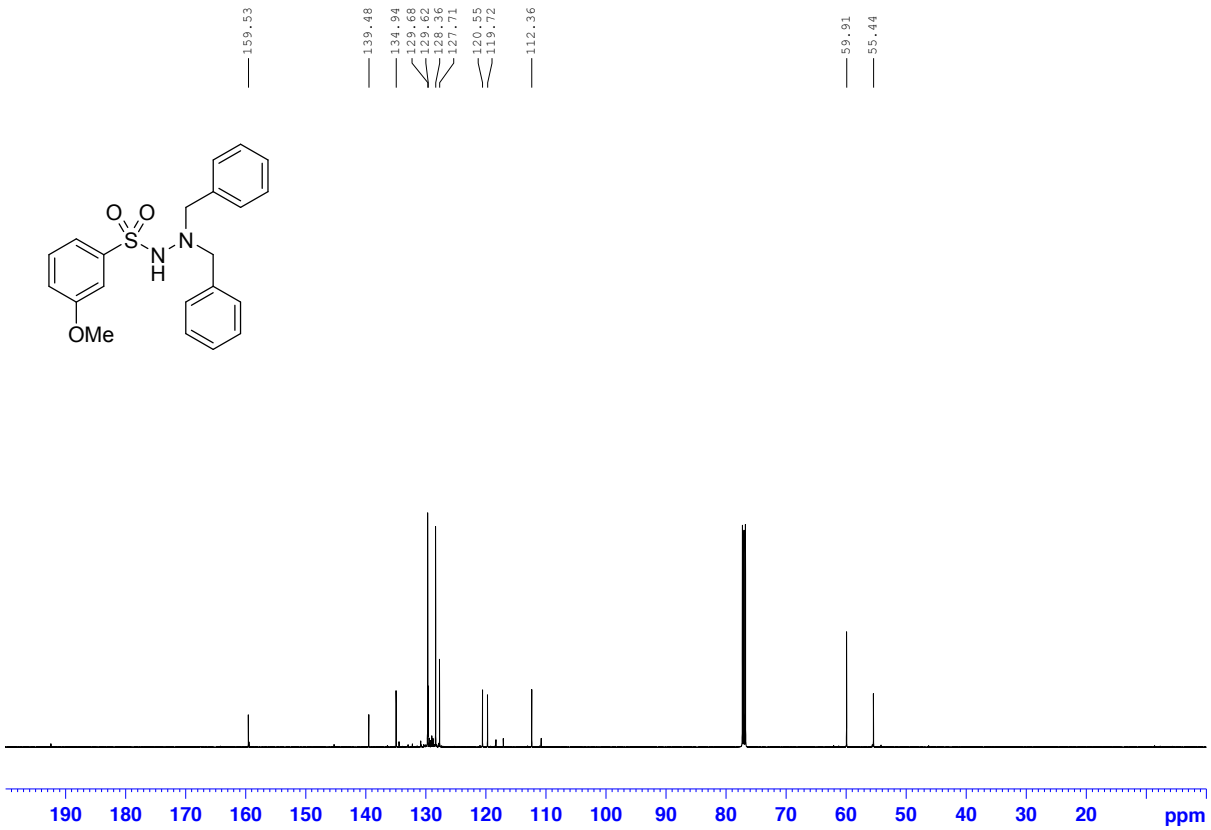


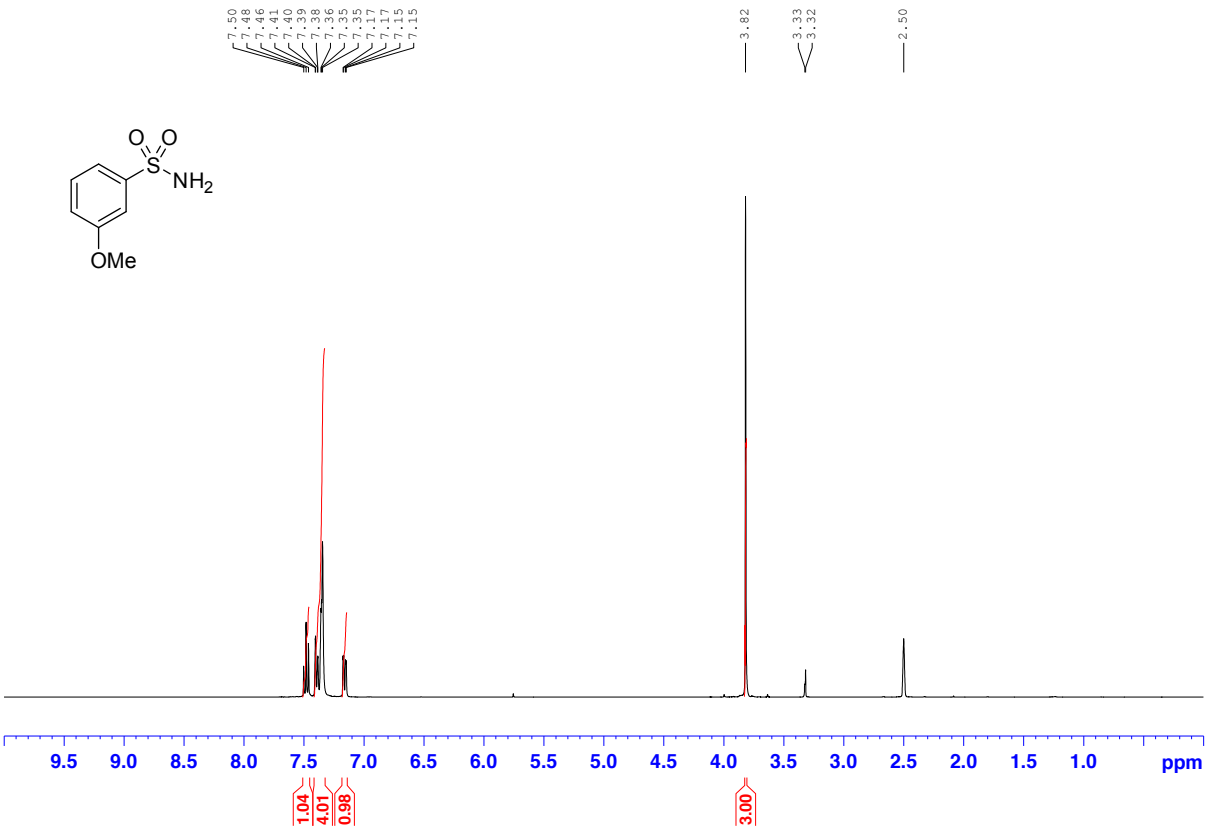


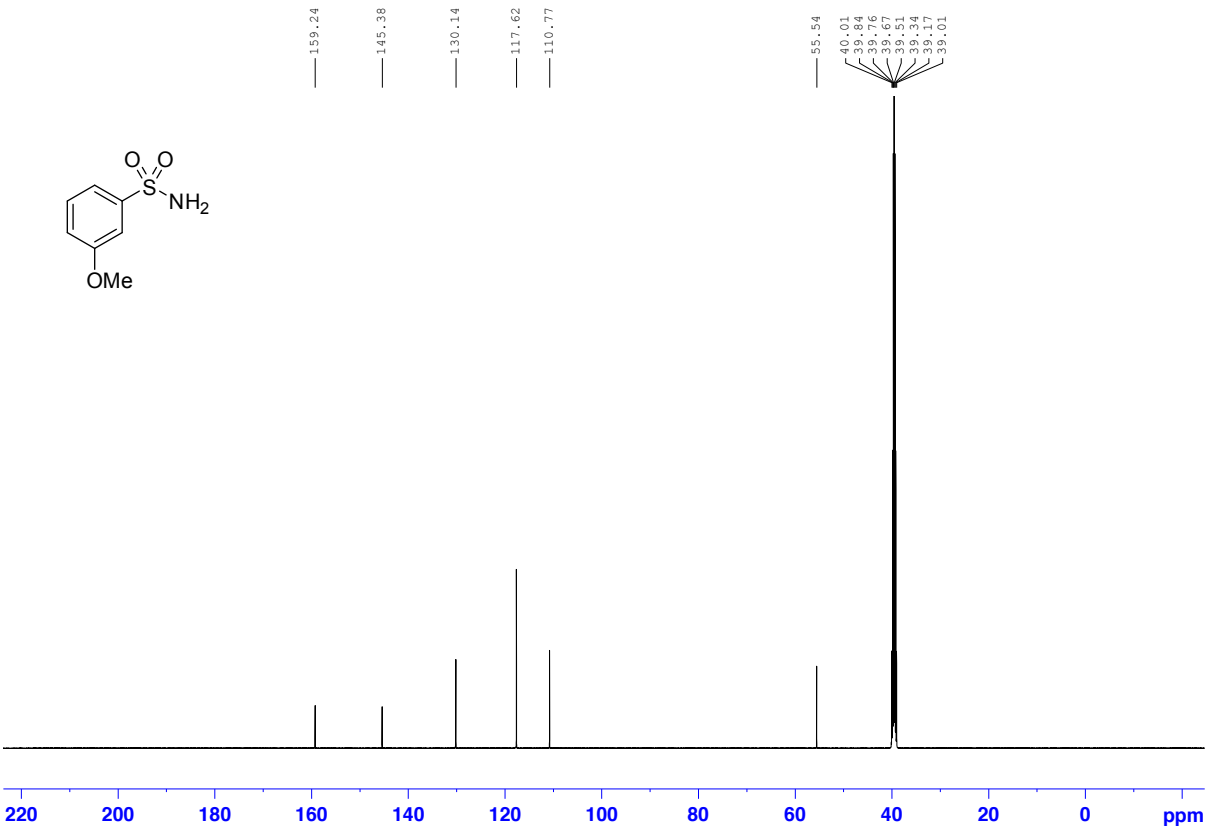


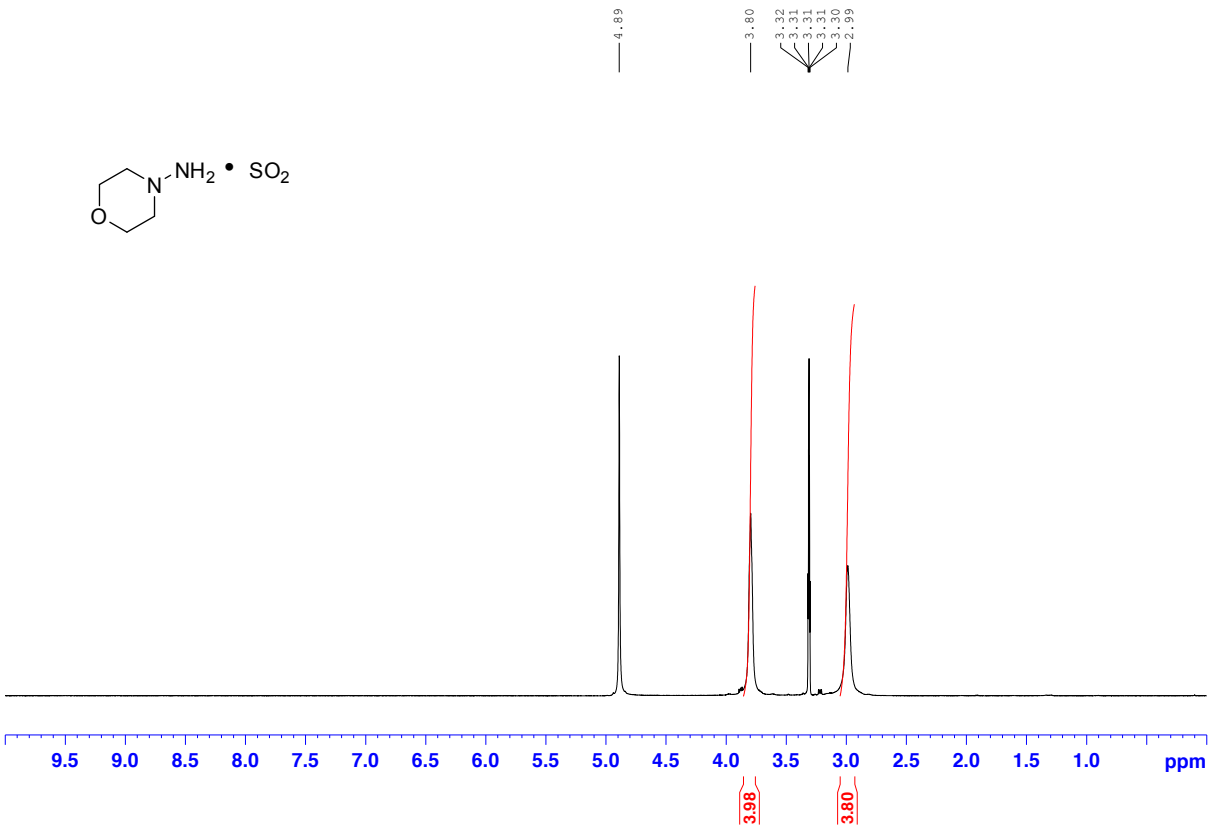


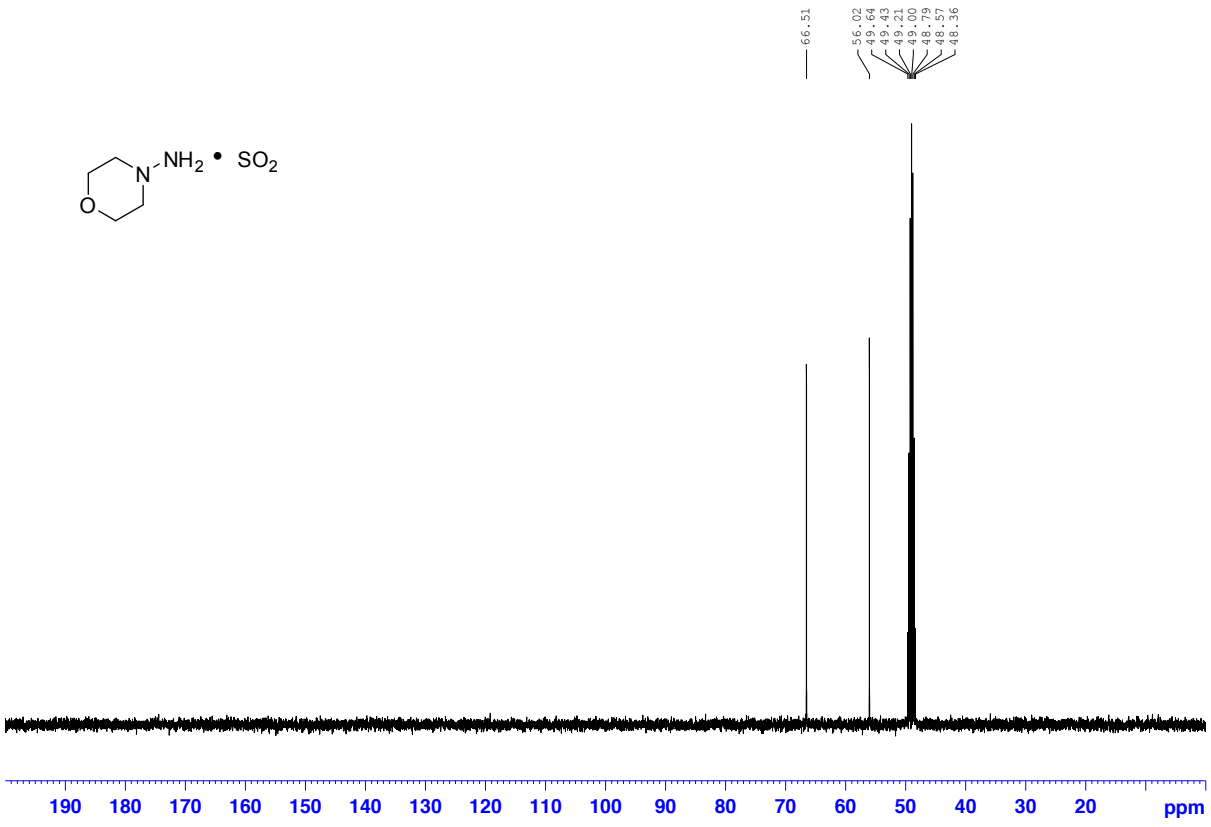




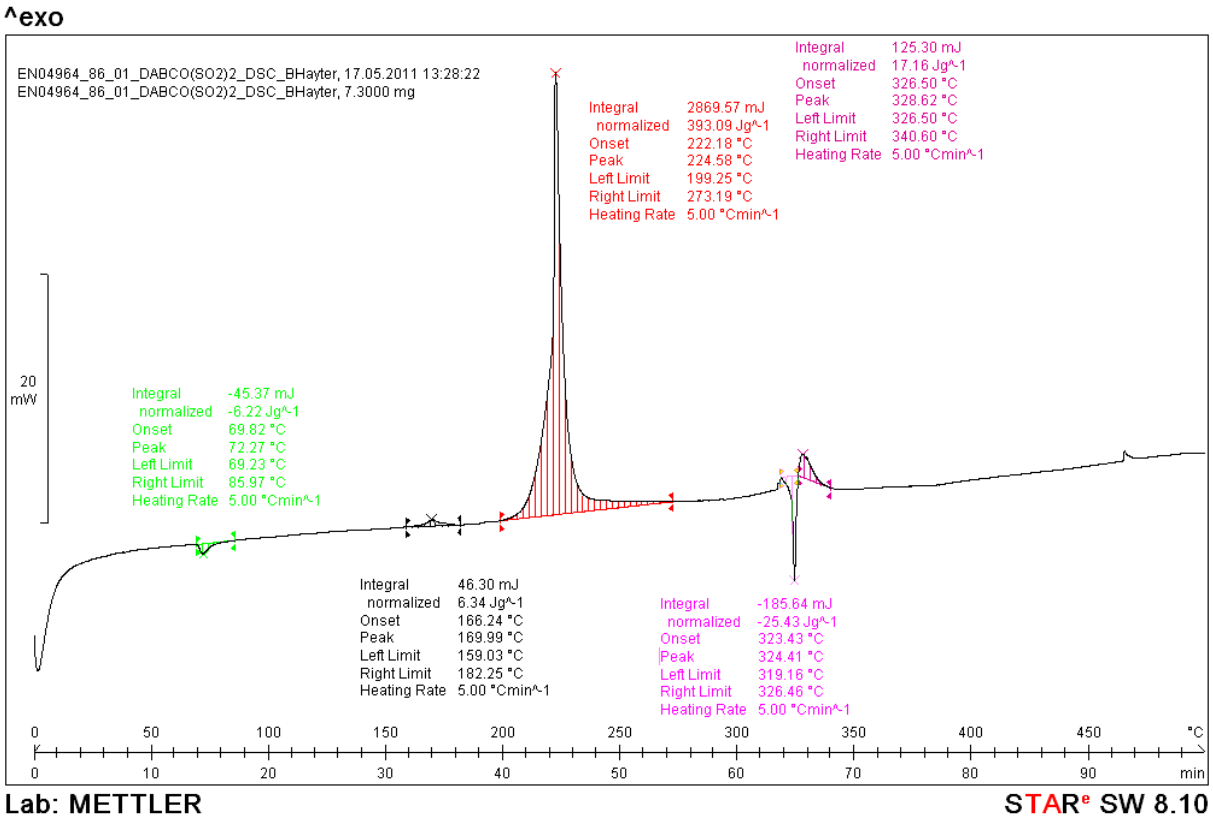








DABCO-$(SO_2)_2$ DSC



4-Aminomorpholine sulfur dioxide complex DSC