Electronic Supplementary Material (ESI) for Chemical Communications

Intramolecular Monomer-on-Monomer (MoM) Mitsunobu Cyclization for the Synthesis of Benzofused Thiadiazepine-dioxides

Pradip K. Maity,[a] Quirin M. Kainz,[b] Saqib Faisal,[a,c] Alan Rolfe,[a] Thiwanka. B. Samarakoon,[a] Fatima Z. Basha,[c] Oliver Reiser,*[b] and Paul R. Hanson*[a]

[a] *Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, KS, 66045 and The University of Kansas Center for Chemical Methodologies and Library Development (KU-CMLD), 2034 Becker Drive, Delbert M. Shankel Structural Biology Center, Lawrence, KS, 66047; E-mail: phanson@ku.edu*

[b] *Institute for Organic Chemistry, University of Regensburg, Universitätsstr. 31, D-93053 Regensburg, Germany; E-mail: Oliver.Reiser@chemie.uni-regensburg.de*

[c] *H. E. J. Research Institute of Chemistry, International Center for Chemical and Biological Science, University of Karachi, Karachi, Pakistan.*

phanson@ku.edu

Table of contents

General Experimental Section	S2
General experiment Methods **A**–**C**	S3
General experiment Methods **D**–**E**	S4
Experimental data for compounds **2a–2n**	S5–S11
Experimental data for compounds **3a–3n**	S12–S18
^{1}H NMR and ^{13}C NMR spectra	S19–46
References	n/a

Experimental Section

General procedures and reagents: All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon atmosphere using standard gastight syringes, canullas and septa. CH_2Cl_2 and toluene were purified by passage through a Solv-Tek (www.solvtek.com) purification system employing activated Al_2O_3 and degassed with argon. Flash column chromatography was performed with SiO_2 (Sorbent Technologies 30930M-25, Silica Gel 60 Å, 40-63 μm). Thin layer chromatography was performed on silica gel 60F 254 plates. Visualization of TLC spots was effected using $KMnO_4$ stain. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise mentioned) on a Bruker DRX-400 spectrometer operating at 400 MHz, and 100 MHz respectively as well as Bruker DRX-500 spectrometer operating at 500 MHz, and 125 MHz, respectively and calibrated to the solvent peak. High-resolution mass spectrometry (HRMS) was recorded on a LCT Premier Spectrometer (Micromass UK Limited) operating on ESI (MeOH). The nanoparticles were analyzed by scanning electron microscopy (Hitachi S-2700 equipped with a quartz PCI digital capture) and FTIR Perkin Elmer Spectrum 100 FT-IR spectrometer. All other commercially available compounds were used as received. metathesis catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh; cat-**B**] was provided by Materia Inc. and used without further purification. Deuterated solvents were purchased from Cambridge Isotope laboratories.

General Procedure A: Synthesis of the benzofused sulfonamides.

To a 25 mL round-bottom flask was added sulfonyl chloride (1 equiv) followed by CH_2Cl_2 (0.4 M), amine (2.0 equiv) and a solution of $NaHCO_3$ (3.0 equiv) in H_2O (0.8 M). The reaction was stirred at room temperature for 12 h, after which time the reaction mixture was quenched with H_2O (30 mL) and extracted with CH_2Cl_2 (3x30 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated *in vacuo* and purification by column chromatography eluting with hexanes/EtOAc 4:1.

General Procedure B: Synthesis of 2a–2n via S_NAr.

To a microwave vial was added sulfonamide (1 equiv) under argon atmosphere followed by the addition of dry DMSO (0.8 M), amine (1.5 equiv) and Cs_2CO_3 (3.0 equiv). The mixture was heated in the microwave at 120 °C for 60 mins, after which time the mixture was quenched with H_2O (30 mL), and extracted with EtOAc (2x30 mL). The combined organic layer separated, washed with H_2O (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Thereafter, the crude mixture was purified by column chromatography eluting with hexanes/EtOAc 3:1.

General Procedure C: Intramolecular monomer-on-monomer (MoM) Mitsunobu reaction utilizing [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh, cat-B] [Sequestration Method A].

To a round-bottom under argon atmosphere was added benzenesulfonamide alcohol **2c**–**2f** (1 equiv) in dry THF (0.1 M). The reaction was cooled to 0 ºC, stirred for 15 min, after which Nb-TPP (3 equiv) and Nb-BEAD (3 equiv) were added to the reaction mixture and stirred at room temperature for 2-12 hrs (TLC monitoring). The reaction was concentrated and resolvated in degassed CH_2Cl_2 (0.1 M), cat-**B** (0.05 equiv) [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh, cat-**B**] was added and reaction heated at 50 ºC for 30 mins to 1 hr (TLC monitoring). Upon completion, the reaction was cooled to room temperature, quenched with ethyl vinyl ether (4 equiv) and stirred for an additional 30 mins. After such time was added Na_2CO_3 (10 equiv) followed by dropwise addition of tetrakis(hydroxymethyl) phosphonium chloride (THPC) 80% in water (10 equiv) while stirring and was refluxed for 4 h. The reaction mixture was cooled to room temperature, extracted with dichloromethane (2x20 mL), washed with water and brine. The organic layer was dried over $MgSO_4$, filtered through a celite plug and concentrated in *vacuo*. The resulting solution was filtered through a plug of silica, eluting with 2:1-Hexane/EtOAc. The resulting eluent was then concentrated *in vacuo* to yield the desired products in good to excellent yields and purities.

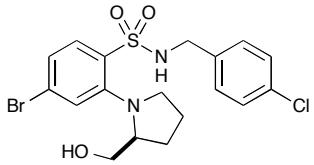
General Procedure D: Intramolecular monomer-on-monomer (MoM) Mitsunobu reaction utilizing catalyst-armed Nb-tagged Co/C magnetic nanoparticles [Sequestration Method B].

To a round-bottom flask under argon atmosphere was added benzenesulfonamide alcohol **2g**–**2j** (2.92 x 10^{-4} mol, 1 equiv) solvated in dry THF (0.1 M). The reaction was cooled to 0 °C, stirred for 20 minutes, after which was added Nb-TPP (3.0 equiv.) and Nb-BEAD (3.0 equiv.) and the reaction warmed to room temperature and stirred for 2–12 h (TLC monitoring). Upon completion of the reaction, the solvent was removed, the crude mixture was dissolved in degassed CH_2Cl_2 (0.1 M) and added to a pressure tube containing a mixture of Co/C-Np (3 mol %) and Grubbs catalyst [3 mol %, $(IMesH_2)(PCy_3)$-$(Cl)_2Ru$=CHPh, cat-**B**] in dry degassed CH_2Cl_2 (0.05 M), that had been sonicated at 60 °C for 30 min. After additional sonication for 1–5 h at 60 ºC (TLC monitoring), a neodymium-based magnet was attached to the side of the tube and the crude reaction mixture was decanted, filtered through a silica SPE and concentrated *in vacuo*, yielding the desired products in good purities.

General Procedure E: Intramolecular monomer-on-monomer (MoM) Mitsunobu reaction utilizing catalyst-armed Nb-tagged silica particles [Sequestration Method C].

Into a 1-dram vial was added benzenesulfonamide alcohol **2k**–**2l** (1.28 x 10^{-4} mol, 1 equiv), dry THF (0.1 mL) and Nb-TPP (2.04 10^{-4} mol, 1.6 equiv) under an argon atmosphere. After stirring for 5 mins, a solution of Nb-BEAD (2.04 10^{-4} mol, 1.6 equiv) in dry THF (0.16 mL) was added dropwise and the reaction was stirred at room temperature for 2–12 h (TLC monitoring). After evaporation of the solvent, Nb-tagged silica (6.12 10^{-4} mol, 3 mol %) was added followed by the addition of a solution of cat-**B** [3 mol %, $(IMesH_2)(PCy_3)$-$(Cl)_2Ru$=CHPh] in dry Ar degassed CH_2Cl_2 (2 mL). The reaction was heated at 50 ºC for 30 mins (TLC monitoring), after which the crude reaction was diluted with EtOAc, filtered through a silica SPE washing the SPE and residual Si-ROMP gel with EtOAc, concentrated, yielding the desired products in good purities.

(*S*)-4-Bromo-*N*-(4-chlorobenzyl)-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzene-sulfonamide (2a).



Utilizing general procedure **B**, **2a** (0.186 g, 0.405 mmol, 51%) was isolated as a brown thick liquid.

$[\alpha]_D^{20}$ = –28.6 ° (c = 0.99, $CHCl_3$);

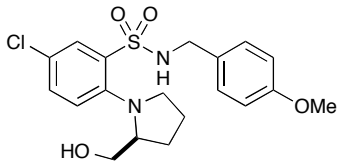
FTIR (neat, cm^{-1}): 3502, 3204, 2947, 2874, 1574, 1553, 1454, 1389, 1161, 1086, 1014;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 1.7 Hz, 1H), 7.32 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.17–7.11 (m, 4H), 6.91 (t, *J* = 6.4 Hz, 1H), 3.99 (dd, *J* = 14.4, 7.1 Hz, 1H), 3.76 (dd, *J* = 14.4, 5.8 Hz, 1H), 3.60–3.50 (m, 2H), 3.39 (s, 2H), 2.75 (dt, *J* = 10.3, 7.0 Hz, 1H), 2.10 (s, 1H), 2.02–1.93 (m, 1H), 1.83–1.71 (m, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.3, 136.7, 135.8, 133.3, 131.1, 129.2, 128.6, 128.3, 128.2, 127.9, 64.7, 62.3, 58.4, 46.9, 26.5, 24.1;

HRMS calculated for $C_{18}H_{20}BrClN_2NaO_3S$ $(M+Na)^+$ 480.9964; found 480.9965 (TOF MS);

(*S*)-5-Chloro-2-(2-(hydroxymethyl)pyrrolidin-1-yl)-*N*-(4-methoxybenzyl) benzenesulfonamide (2b).



Utilizing general procedure **B**, **2b** (0.915 g, 2.22 mmol, 47%) was isolated as a brown thick liquid.

$[\alpha]_D^{20}$ = +27.2 ° (c = 1.05, $CHCl_3$);

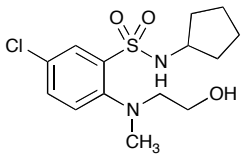
FTIR (neat, cm^{-1}): 3511, 2952, 1610, 1512, 1458, 1319, 1249, 1161, 1031;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (t, *J* = 4.6 Hz, 1H), 7.50 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.83–6.79 (m, 2H), 6.67 (t, *J* = 5.7 Hz, 1H), 4.11 (dd, *J* = 13.7, 6.2 Hz, 1H), 3.99–3.92 (m, 1H), 3.81 (s, 3H), 3.61–3.56 (m, 1H), 3.50 (ddd, *J* = 16.2, 10.2, 4.8 Hz, 1H), 3.46–3.42 (m, 2H), 2.84–2.73 (m, 1H), 2.17 (t, *J* = 5.4 Hz, 1H), 2.08–1.98 (m, 2H), 1.88–1.82 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.1, 148.6, 139.4, 133.6, 130.7, 129.6, 129.3, 128.8, 126.5, 113.9, 65.4, 62.3, 58.3, 55.3, 47.4, 26.5, 24.1;

HRMS calculated for $C_{19}H_{23}ClN_2NaO_4S$ $(M+Na)^+$ 433.0965; found 433.0970 (TOF MS);

5-Chloro-*N*-cyclopentyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2c).



Utilizing general procedure **B**, **2c** (0.210 g, 0.631 mmol, 58%) was isolated as a white solid.

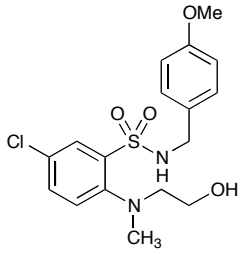
FTIR (neat, cm^{-1}): 3498, 2956, 1558, 1506, 1471, 1456, 1323, 1157, 1058;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.5 Hz, 1H), 7.54 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 6.61 (d, *J* = 6.6 Hz, 1H), 3.85 (dd, *J* = 10.2, 5.1 Hz, 2H), 3.52 (m, 1H), 3.16–3.03 (m, 2H), 2.77 (s, 3H), 2.56 (t, *J* = 5.1 Hz, 1H), 1.75–1.69 (m, 2H), 1.66–1.56 (m, 2H), 1.50–1.44 (m, 2H), 1.43–1.33 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.9, 138.7, 133.5, 130.9, 129.7, 125.8, 59.8, 59.1, 55.5, 41.8, 32.9, 23.1;

HRMS calculated for $C_{14}H_{21}ClN_2NaO_3S$ $(M+Na)^+$ 355.0859; found 355.0857 (TOF MS ES+).

5-Chloro-2-((2-hydroxyethyl)(methyl)amino)-*N*-(4-methoxybenzyl) benzenesulfonamide (2d).



Utilizing general procedure **B**, **2d** (0.196 g, 0.51 mmol, 55%) was isolated as a colourless thick liquid.

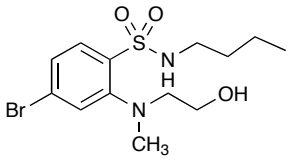
FTIR (neat, cm^{-1}): 3521, 3182, 2358, 1575, 1552, 1454, 1323, 1159, 1137, 1074;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.48 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.25 (d, *J* = 6.3 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 7.13–7.02 (m, 2H), 6.80–6.71 (m, 2H), 4.04 (d, *J* = 6.3 Hz, 2H), 3.77–3.74 (m, 5H), 3.01–2.95 (m, 2H), 2.60 (s, 3H), 2.42 (t, *J* = 4.6 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 150.8, 138.4, 133.4, 130.9, 129.7, 129.6, 128.6, 125.8, 113.7, 59.2, 59.0, 55.3, 47.3, 42.6;

HRMS calculated for $C_{17}H_{21}ClN_2NaO_4S$ $(M+Na)^+$ 407.0808; found 407.0806 (TOF MS ES+).

4-Bromo-*N*-butyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2e).



Utilizing general procedure **B**, **2e** (0.166 g, 0.454 mmol, 56%) was isolated as a brown solid.

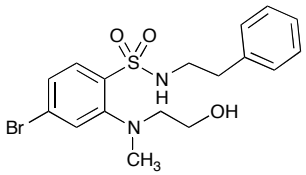
FTIR (neat, cm^{-1}): 3301, 2958, 1583, 1454, 1406, 1319, 1159, 1130, 1081;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.83 (t, *J* = 4.9 Hz, 1H), 3.87–3.79 (m, 2H), 3.14–3.05 (m, 2H), 2.95 (t, *J* = 7.1 Hz, 1H), 2.75 (s, 5H), 1.51–1.40 (m, 2H), 1.33–1.24 (m, 2H), 0.85 (t, *J* = 7.5 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 155.7, 129.4, 129.2, 123.9, 122.0, 121.6, 52.2, 48.5, 42.8, 31.4, 30.8, 19.6, 13.5;

HRMS calculated for $C_{13}H_{21}BrN_2NaO_3S$ $(M+Na)^+$ 387.0354; found 387.0323 (TOF MS ES+);

4-Bromo-2-((2-hydroxyethyl)(methyl)amino)-*N*-phenethylbenzenesulfonamide (2f).



Utilizing general procedure **B**, **2f** (0.282 g, 0.682 mmol, 49%) was isolated as a brown thick liquid.

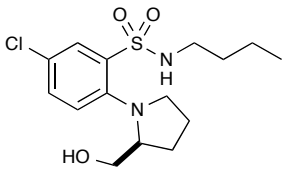
FTIR (neat, cm^{-1}): 3496, 3197, 1573, 1454, 1386, 1321, 1159, 1074;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.84 (m, 1H), 7.45–7.43 (m, 2H), 7.29–7.19 (m, 3H), 7.13–7.11 (m, 2H), 6.94 (t, *J* = 6.3 Hz, 1H), 3.71 (t, *J* = 4.9 Hz, 2H), 3.06–2.97 (m, 4H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.56 (s, 3H), 2.35 (brs, 1H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 153.5, 138.5, 135.3, 131.3, 128.9, 128.9, 128.7, 128.7, 128.6, 128.1, 127.8, 126.6, 59.5, 59.0, 44.9, 42.1, 36.2;

HRMS calculated for $C_{17}H_{21}BrN_2NaO_3S$ $(M+Na)^+$ 435.0354; found 435.0338 (TOF MS).

(*S*)-N-Butyl-5-chloro-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzenesulfonamide (2g).



Utilizing general procedure **B**, **2g** (0.311 g, 0.898 mmol, 48%) was isolated as a yellow oil.

$[\alpha]_D^{20} = +28.4$ ° (c = 1.1, $CHCl_3$);

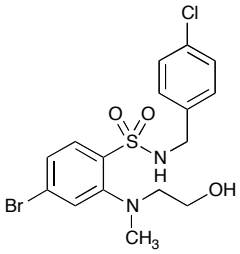
FTIR (neat, cm^{-1}): 3502, 3215, 2959, 2872, 1464, 1319, 1163, 1105, 895;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, *J* = 2.5 Hz, 1H), 7.49 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 6.16 (t, *J* = 6.2 Hz, 1H), 3.60–3.49 (m, 2H), 3.47 (t, *J* = 4.0 Hz, 2H), 2.89–2.78 (m, 4H), 2.10-2.02 (m, 1H), 1.95–1.87 (m, 3H), 1.51–1.43 (m, 2H), 1.36–1.26 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 148.6, 139.3, 133.7, 130.8, 129.6, 126.8, 65.8, 62.3, 58.5, 43.6, 32.0, 26.5, 24.3, 19.8, 13.7;

HRMS calculated for $C_{15}H_{24}ClN_2O_3S$ $(M+H)^+$ 347.1196; found 347.1190 (TOF MS).

4-Bromo-*N*-(4-chlorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2h).



Utilizing general procedure **B**, **2a** (0.220 g, 0.507 mmol, 49%) was isolated as a white solid.

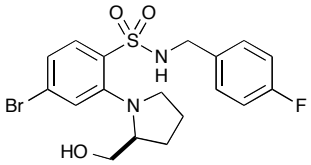
FTIR (neat, cm^{-1}): 3475, 3132, 1575, 1524, 1384, 1327, 1245, 1154, 1074.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.48–7.42 (m, 2H), 7.37 (t, *J* = 6.5 Hz, 1H), 7.24–7.20 (m, 2H), 7.15 (d, *J* = 8.5 Hz, 2H), 3.96 (d, *J* = 6.5 Hz, 2H), 3.79 (dd, *J* = 9.8, 4.6 Hz, 2H), 3.09–3.02 (m, 2H), 2.67 (s, 3H), 2.19 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 135.6, 135.4, 133.4, 131.3, 129.4, 128.7, 128.5, 128.0, 127.9, 59.1, 59.0, 46.9, 42.7;

HRMS calculated for $C_{16}H_{18}BrClN_2O_3S$ $(M+H)^+$ 432.9988; found 432.9966 (TOF MS ES+).

(*S*)-4-Bromo-*N*-(4-fluorobenzyl)-2-(2-(hydroxymethyl)pyrrolidin-1-yl) benzenesulfonamide (2i).



Utilizing general procedure **B**, **2i** (0.368 g, 0.831 mmol, 43%) was isolated as a brown thick liquid.

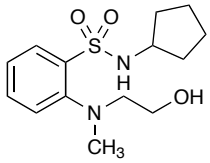
FTIR (neat, cm^{-1}): 3502, 3209, 2947, 1573, 1552, 1510, 1456, 1388, 1321, 1220, 1161;

^{1}H NMR (400 MHz, CDCl3): δ 7.84 (d, *J* = 8.4 Hz, 1H), 7.47–7.36 (m, 2H), 7.26–7.21 (m, 2H), 6.99–6.90 (m, 2H), 6.87 (t, *J* = 6.4 Hz, 1H), 4.08 (dd, *J* = 14.2, 7.0 Hz, 1H), 3.87 (dd, *J* = 14.2, 5.9 Hz, 1H), 3.64–3.57 (m, 2H), 3.49–3.44 (m, 2H), 2.87–2.76 (m, 1H), 2.15 (t, *J* = 5.3 Hz, 1H), 2.09–1.97 (m, 1H), 1.89–1.80 (m, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.2, 161.2, 151.3, 136.7, 133.0, 132.9, 131.1, 129.5, 129.5, 128.4, 128.3, 127.9, 115.4, 115.3, 64.9, 62.4, 58.4, 46.9, 26.5, 24.2;

HRMS calculated for $C_{19}H_{21}BrFN_2O_3S$ $(M+H)^+$ 443.0440; found 443.0403 (TOF MS).

***N*-Cyclopentyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2j).**



Utilizing general procedure **B**, **2j** (0.130 g, 0.434 mmol, 42%) was isolated as a white solid.

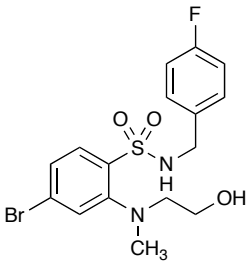
FTIR (neat, cm^{-1}): 3489, 3120, 2958, 1574, 1532, 1453, 1396, 1332, 1255, 1064;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.59 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.30 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.53 (brs, 1H), 3.84 (dd, *J* = 10.2, 5.1 Hz, 2H), 3.54–3.45 (m, 1H), 3.18–3.09 (m, 2H), 2.84–2.76 (m, 4H), 1.76–1.57 (m, 4H), 1.50–1.32 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.4, 137.1, 133.6, 129.8, 125.4, 124.3, 60.1, 59.2, 55.5, 41.8, 33.0, 23.1;

HRMS calculated for $C_{14}H_{22}N_2NaO_3S$ $(M+Na)^+$ 321.1249; found 321.1254 (TOF MS ES+).

4-Bromo-*N*-(4-fluorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2k).



Utilizing general procedure **B**, **2k** (0.150 g, 0.360 mmol, 52%) was isolated as a white solid.

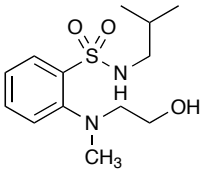
FTIR (neat, cm^{-1}): 3494, 2958, 1571, 1523, 1453, 1386, 1342, 1321, 1259, 1060;

^{1}H NMR (400 MHz, CDCl3): δ 7.87 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.41 (d, *J* = 1.8 Hz, 1H), 7.34–7.29 (m, 1H), 7.16 (dd, *J* = 8.5, 5.4 Hz, 2H), 6.94–6.89 (m, 2H), 3.96 (d, *J* = 6.4 Hz, 2H), 3.77 (brs, 2H), 3.04–3.01 (m, 2H), 2.64 (s, 3H), 2.28–2.16 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.2, 161.2, 153.5, 135.7, 132.6, 131.2, 129.9, 129.8, 128.6, 128.1, 128.0, 127.8, 115.3, 115.1, 59.2, 46.8, 42.6;

HRMS calculated for $C_{16}H_{18}BrFN_2NaO_3S$ $(M+Na)^+$ 439.0103; found 439.0071 (TOF MS).

2-((2-Hydroxyethyl)(methyl)amino)-*N*-isobutylbenzenesulfonamide (2l).



Utilizing general procedure **B**, **2l** (0.201 g, 0.701 mmol, 54%) was isolated as a white solid.

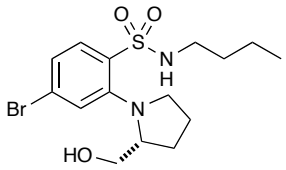
FTIR (neat): 3501, 3296, 2958, 2358, 1558, 1521, 1473, 1419, 1319, 1163, 1068 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.59 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.42 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.33 (dt, *J* = 7.9, 1.1 Hz, 1H), 6.65 (t, *J* = 6.2 Hz, 1H), 3.82 (q, *J* = 4.6 Hz, 2H), 3.12 (t, *J* = 4.6 Hz, 2H), 2.79 (s, 3H), 2.71 (brs, 1H), 2.57 (t, *J* = 6.7 Hz, 2H), 1.82–1.76 (m, 1H), 0.91 (d, *J* = 6.7 Hz, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.2, 135.9, 133.7, 130.2, 125.5, 124.3, 60.3, 59.2, 50.8, 42.1, 28.7, 20.1;

HRMS calculated for $C_{13}H_{22}N_2NaO_3S$ $(M+Na)^+$ 309.1249; found 309.1234 (TOF MS ES+).

(*R*)-4-Bromo-*N*-butyl-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzenesulfonamide (2m).



Utilizing general procedure **B**, **2m** (0.111 g, 0.284 mmol, 44%) was isolated as a brown thick liquid.

$[\alpha]_D^{20} = +3.4$ ° (c = 1.0, $CHCl_3$);

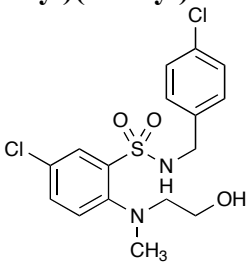
FTIR (neat, cm^{-1}): 3498, 3220, 2956, 1573, 1529, 1388, 1319, 1163, 1083;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.4 Hz, 1H), 7.49 (s, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 6.09 (s, 1H), 3.61–3.56 (m, 2H), 3.50 (s, 2H), 2.93–2.76 (m, 4H), 2.09–2.04 (m, 1H), 1.93 (s, 3H), 1.53–1.42 (m, 2H), 1.34–1.27 (m, 3H), 0.87 (t, *J* = 6.5 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.3, 136.8, 131.1, 128.8, 128.4, 127.8, 65.7, 62.4, 58.4, 43.5, 32.0, 26.5, 24.4, 19.8, 13.7;

HRMS calculated for $C_{15}H_{23}BrN_2NaO_3S$ $(M+Na)^+$ 413.0510; found 413.0519 (TOF MS).

5-Chloro-*N*-(4-chlorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2n).



Utilizing general procedure **B**, **2n** (0.180 g, 0.462 mmol, 46%) was isolated as a brown solid.

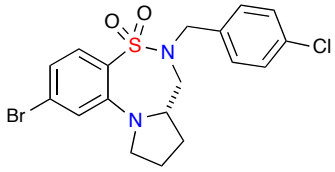
FTIR (neat, cm^{-1}): 3502, 2358, 2331, 1490, 1471, 1325, 1161;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.51 (dt, *J* = 8.1, 4.1 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.22–7.14 (m, 4H), 4.01 (d, *J* = 6.5 Hz, 2H), 3.78 (m, 2H), 3.05–2.99 (m, 2H), 2.64 (s, 3H), 2.32 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.8, 138.2, 135.3, 133.6, 133.4, 131.1, 129.7, 129.5, 128.5, 125.9, 59.1, 59.0, 46.9, 42.9;

HRMS calculated for $C_{16}H_{18}Cl_2N_2NaO_3S$ $(M+Na)^+$ 411.0313; found 411.0310 (TOF MS ES+).

(*S*)-2-Bromo-6-(4-chlorobenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*] pyrrolo[2,1-*d*][1,2,5]thiadiazepine 5,5-dioxide (3a).



Utilizing general procedure **C**, **3a** (0.086 g, 0.195 mmol, 85%) was isolated as a brown thick liquid.

$[\alpha]_D^{20}$ =–65.6 ° (c = 1.0, $CHCl_3$);

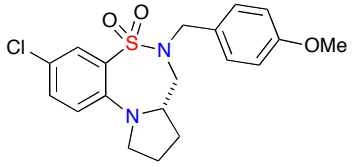
FTIR (neat, cm^{-1}): 2961, 2937, 1578, 1539, 1467, 1410, 1338, 1155, 1095;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.5 Hz, 1H), 7.33–7.28 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.04 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.96 (s, 1H), 4.40–4.22 (m, 3H), 3.40–3.29 (m, 3H), 2.86 (brs, 1H), 2.14–1.99 (m, 2H), 1.98–1.83 (m, 1H), 1.63–1.60 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 146.6, 134.5, 133.8, 130.8, 129.7 (2C), 128.8 (2C), 127.6, 127.1, 121.9, 118.5, 59.6, 54.3, 53.2, 51.2, 29.7, 23.5;

HRMS calculated for $C_{18}H_{19}BrClN_2O_2S$ $(M+H)^+$ 441.0039; found 441.0040 (TOF MS);

(*S*)-3-Chloro-6-(4-methoxybenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5]thiadiazepine 5,5-dioxide (3b).



Utilizing general procedure **C**, **3b** (0.101 g, 0.257 mmol, 88%) was isolated as a brown thick liquid.

$[\alpha]_D^{20}$ =–106.5 ° (c = 1.05, $CHCl_3$);

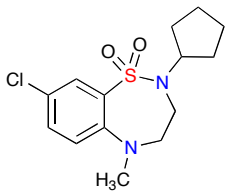
FTIR (neat, cm^{-1}): 2952, 1733, 1591, 1512, 1471, 1338, 1245, 1153, 1058;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* = 2.4 Hz, 1H), 7.31 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.89–6.85 (m, 2H), 6.79 (brs, 1H), 4.27 (brs, 2H), 3.82 (s, 3H), 3.33–3.28 (m, 4H), 3.04 (brs, 1H), 2.15–2.02 (m, 2H), 2.01–1.91 (m, 1H), 1.63–1.58 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.4, 144.3, 132.6, 129.8 (2C), 129.4, 128.9, 127.7, 123.8, 116.9, 114.0 (2C), 59.3, 55.3, 53.6, 53.1, 51.3, 29.8, 23.6;

HRMS calculated for $C_{19}H_{21}ClN_2NaO_3S$ $(M+Na)^+$ 415.0859; found 415.0864 (TOF MS);

8-Chloro-2-cyclopentyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5] thiadiazepine 1,1-dioxide (3c).



Utilizing general procedure **C**, **3c** (0.054 g, 0.172 mmol, 81%) was isolated as a brown solid.

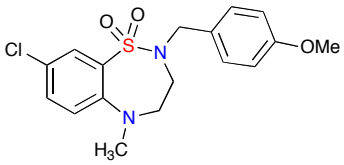
FTIR (neat, cm^{-1}): 2952, 1733, 1716, 1558, 1490, 1394, 1323, 1151, 1054;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 2.6 Hz, 1H), 7.32–7.27 (m, 1H), 6.83 (d, *J* = 8.9 Hz, 1H), 4.24–4.14 (m, 1H), 3.63–3.56 (m, 2H), 3.51–3.44 (m, 2H), 3.06 (s, 3H), 1.77–1.74 (m, 2H), 1.66–1.61 (m, 2H), 1.57–1.41 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.7, 132.4, 132.2, 128.6, 124.3, 117.7, 59.5, 54.3, 44.3, 41.7, 29.5, 22.8;

HRMS calculated for $C_{14}H_{19}ClN_2O_2S$ $(M+H)^+$ 315.0934; found 315.0949 (TOF MS ES+).

8-Chloro-2-(4-methoxybenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5] thiadiazepine 1,1-dioxide (3d).



Utilizing general procedure **C**, **3d** (0.087 g, 0.237 mmol, 83%) was isolated as colorless oil.

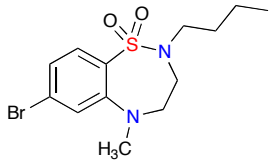
FTIR (neat, cm^{-1}): 2952, 1733, 1591, 1512, 1471, 1338, 1245, 1153, 1058;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 2.6 Hz, 1H), 7.40 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.27–7.23 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.91–6.86 (m, 2H), 4.19 (s, 2H), 3.82 (s, 3H), 3.43–3.37 (m, 2H), 3.32–3.25 (m, 2H), 3.03 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.4, 147.2, 132.9, 131.9, 129.8, 129.4, 127.4, 125.8, 119.5, 114.1, 55.3, 51.5, 51.3, 46.9, 42.6.

HRMS calculated for $C_{17}H_{20}ClN_2O_3S$ $(M+H)^+$ 367.8703; found 367.8732 (TOF MS ES+);

7-Bromo-2-butyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3e).



Utilizing general procedure **C**, **3e** (0.05 g, 0.144 mmol, 80%) was isolated as a colorless thick liquid.

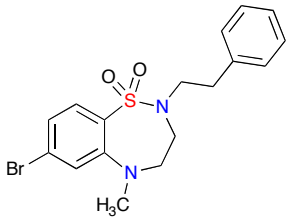
FTIR (neat, cm^{-1}): 2956, 1577, 1542, 1481, 1373, 1326, 1153, 1093;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3 Hz, 1H), 7.15–7.10 (m, 2H), 3.54–3.47 (m, 2H), 3.36–3.31 (m, 2H), 3.06 (s, 3H), 2.99 (t, *J* = 7.2 Hz, 2H), 1.61–1.51 (m, 2H), 1.38–1.31 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 148.5, 130.2, 128.5, 126.4, 122.4, 119.9, 75.7, 51.2, 47.4, 41.5, 29.7, 18.7, 12.7;

HRMS calculated for $C_{13}H_{19}BrN_2NaO_2S$ $(M+Na)^+$ 369.0248; found 369.0251 (TOF MS ES+).

7-Bromo-5-methyl-2-phenethyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3f).



Utilizing general procedure **C**, **3f** (0.046 g, 0.116 mmol, 98%) was isolated as a colorless thick liquid.

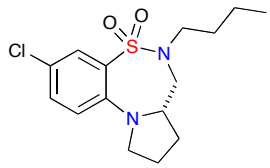
FTIR (neat, cm^{-1}): 2925, 1577, 1541, 1481, 1436, 1328, 1153, 1091;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.72 (m, 1H), 7.34–7.27 (m, 2H), 7.24–7.18 (m, 3H), 7.14–7.10 (m, 2H), 3.42–3.40 (m, 2H), 3.34–3.28 (m, 2H), 3.26–3.20 (m, 2H), 3.03 (s, 3H), 2.95–2.91 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 149.5, 138.3, 131.2, 129.4, 128.9, 128.6, 127.5, 126.6, 123.4, 120.9, 52.5, 51.1, 49.8, 42.4, 36.2;

HRMS calculated for $C_{17}H_{19}BrN_2NaO_2S$ $(M+Na)^+$ 417.0248; found 417.0247 (TOF MS).

(*S*)-6-Butyl-3-chloro-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5] thiadiazepine 5,5-dioxide (3g).



Utilizing general procedure **C**, **3a** (0.085 g, 0.260 mmol, 89%) was isolated as a yellow oil.

$[\alpha]_D^{20} = -120.0$ ° (c = 0.6, $CHCl_3$);

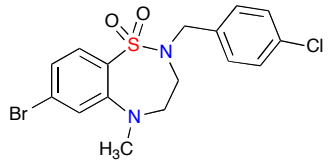
FTIR (neat, cm^{-1}): 2957, 2932, 2872, 1591, 1472, 1396, 1337, 1150, 1057, 808;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 2.5 Hz, 1H), 7.30–7.24 (m, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 4.19 (bs, 1H), 3.54–3.40 (m, 1H), 3.40–3.25 (m, 2H), 3.09 (bs, 3H), 2.18–1.94 (m, 3H), 1.72–1.65 (m, 1H), 1.59–1.48 (m, 2H), 1.33 (dq, *J* = 15.0, 7.3 Hz, 2H), 0.90 (t, *J* = 7.3 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 144.3, 132.5, 129.1, 123.9, 117.0, 59.2, 55.1, 51.4, 49.8, 30.8, 29.8, 23.6, 19.7, 13.7;

HRMS calculated for $C_{15}H_{22}ClN_2O_2S$ $(M+H)^+$ 329.1091; found 329.1096 (TOF MS).

7-Bromo-2-(4-chlorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3h).



Utilizing general procedure **C**, **3a** (0.099 g, 0.239 mmol, 82%) was isolated as a yellow oil.

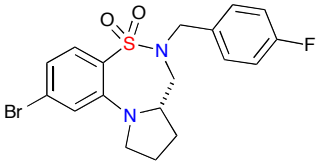
FTIR (neat, cm^{-1}): 2947, 2883, 1578, 1489, 1327, 1277, 1155, 1092, 976;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80–7.75 (m, 1H), 7.33–7.29 (m, 2H), 7.27–7.24 (m, 2H), 7.16–7.14 (m, 2H), 4.19 (s, 2H), 3.37 (s, 4H), 3.03 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 149.5, 134.3, 133.9, 131.1, 129.7, 129.3, 128.9, 127.8, 123.6, 121.0, 51.9, 51.6, 47.5, 42.4, 29.7;

HRMS calculated for $C_{16}H_{17}BrClN_2O_2S$ $(M+H)^+$ 414.9882; found 414.9870 (TOF MS).

(*S*)-2-bromo-6-(4-fluorobenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5] thiadiazepine 5,5-dioxide (3i).



Utilizing general procedure **C**, **3i** (0.100 g, 0.235 mmol, 81%) was isolated as a colourless thick liquid.

$[\alpha]_D^{20} = -60.2$ ° (c = 1.05, $CHCl_3$);

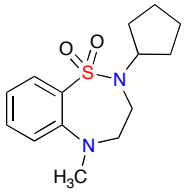
FTIR (neat, cm^{-1}): 2957, 2872, 1578, 1508, 1468, 1412, 1337, 1221, 1155, 781;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.5 Hz, 1H), 7.28–7.23 (m, 2H), 7.06–6.98 (m, 3H), 6.95 (s, 1H), 4.50–4.15 (m, 3H), 3.40–3.25 (m, 3H), 2.95 (brs, 1H), 2.03 (dt, *J* = 6.5, 5.7 Hz, 2H), 1.98–1.86 (m, 1H), 1.61 (dd, *J* = 11.4, 6.4 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.6, 161.6, 146.7, 131.8, 130.9, 130.2, 130.1, 127.7, 122.0, 118.6, 115.7, 115.6, 59.8, 54.2, 53.3, 51.3, 29.9, 23.6;

HRMS calculated for $C_{18}H_{19}BrFN_2O_2S$ $(M+H)^+$ 425.0335; found 425.0331 (TOF MS).

2-Cyclopentyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3j).



Utilizing general procedure **D**, **3j** (0.065 g, 0.23 mol, 79%) was isolated as a yellow oil.

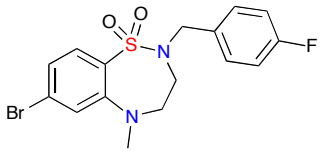
FTIR (neat, cm^{-1}): 2953, 2872, 1593, 1491, 1321, 1148, 754, 588.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.34 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 6.93–6.86 (m, 2H), 4.16 (ddd, *J* = 17.3, 9.2, 7.8 Hz, 1H), 3.61–3.54 (m, 2H), 3.49–3.43 (m, 2H), 3.05 (s, 3H), 1.77–1.69 (m, 2H), 1.66–1.57 (m, 2H), 1.52–1.43 (m, 4H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 148.2, 132.5, 131.4, 129.1, 119.4, 116.5, 59.6, 54.4, 44.5, 41.7, 29.7, 22.9;

HRMS calculated for $C_{14}H_{21}N_2O_2S$ $(M+H)^+$ 281.1323; found 281.1313 (TOF MS).

7-Bromo-2-(4-fluorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3k).



Utilizing general procedure **E**, **3k** (0.044 g, 0.11 mmol, 86%) was isolated as a clear oil.

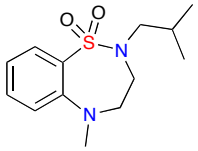
FTIR (neat, cm^{-1}): 1577, 1467, 1409, 1321, 1155;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79–7.77 (d, J = 8.6 Hz, 1H), 7.30–7.27 (m, 2H), 7.15 (dt, J = 4.7, 1.8 Hz, 2H), 7.04–7.00 (m, 2H), 4.19 (s, 2H), 3.37 (s, 4H), 3.02 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.5 (d, $^1J_{C\text{-}F}$ = 244.2 Hz), 149.5, 131.4, 131.1, 130.0 (d, $^2J_{C\text{-}F}$ = 10.2 Hz), 129.3, 127.7, 123.5, 121.0, 115.6 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 51.4, 47.3, 42.4;

HRMS calculated for $C_{16}H_{16}BrFN_2NaO_2S$ $(M+Na)^+$ 420.9998; found 420.9987 (TOF MS ES+).

2-Isobutyl-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3l).



Utilizing general procedure **E**, **3l** (0.028 g, 0.105 mmol, 82%) was isolated as a light yellow oil.

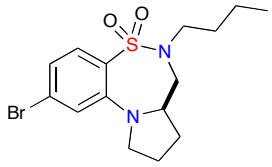
FTIR (neat, cm^{-1}): 1577, 1467, 1409, 1321, 1155;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (dd, J = 7.9, 1.6 Hz, 1H), 7.41 (ddd, J = 8.6, 7.3, 1.7 Hz, 1H), 7.04 (d, J = 8.3 Hz, 1H), 7.02–6.99 (m, 1H), 3.50 (t, J = 7.8 Hz, 2H), 3.29–3.25 (m, 2H), 3.06 (s, 3H), 2.74 (d, J = 7.4 Hz, 2H), 1.90 (dq, J = 13.8, 6.9 Hz, 1H), 0.94 (d, J = 6.7 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 148.6, 132.9, 130.7, 130.1, 120.6, 118.1, 55.5, 52.0, 49.4, 42.6, 27.9, 20.0;

HRMS calculated for $C_{13}H_{21}N_2O_2S$ $(M+H)^+$ 269.1324; found 269.1326 (TOF MS ES+).

(*R*)-2-Bromo-6-butyl-6,7,7a,8,9,10-hexahydrobenzo[f]pyrrolo[2,1-d][1,2,5] thiadiazepine 5,5-dioxide (3m).



Utilizing general procedure **E**, **3m** (0.038 g, 0.102 mmol, 80%) was isolated as a light yellow oil.

$[\alpha]_D^{20}$ = +69.0 (*c* = 1.5, $CHCl_3$);

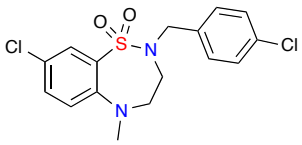
FTIR (neat, cm^{-1}): 1577, 1467, 1409, 1321, 1155;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.4 Hz, 1H), 7.01 (dd, *J* = 8.4, 1.3 Hz, 1H), 6.96 (s, 1H), 3.48 (dd, *J* = 14.0, 6.9 Hz, 1H), 3.37 (dd, *J* = 9.9, 4.9 Hz, 1H), 3.31 (dt, *J* = 14.5, 7.4 Hz, 1H), 3.15–2.99 (m, 3H), 2.14–1.97 (m, 4H), 1.70 (dd, *J* = 11.9, 4.6 Hz, 1H), 1.59–1.50 (m, 2H), 1.37–1.27 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 146.6, 130.9, 127.3, 121.8, 118.5, 55.2, 51.2, 30.8, 29.8, 23.5, 19.7, 13.7;

HRMS calculated for $C_{15}H_{22}BrN_2O_2S$ $(M+H)^+$ 373.0585; found 373.0585 (TOF MS ES+).

8-Chloro-2-(4-chlorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3n).



Utilizing general procedure **E**, **3n** (0.040 g, 0.107 mmol, 84%) was isolated as a light yellow oil.

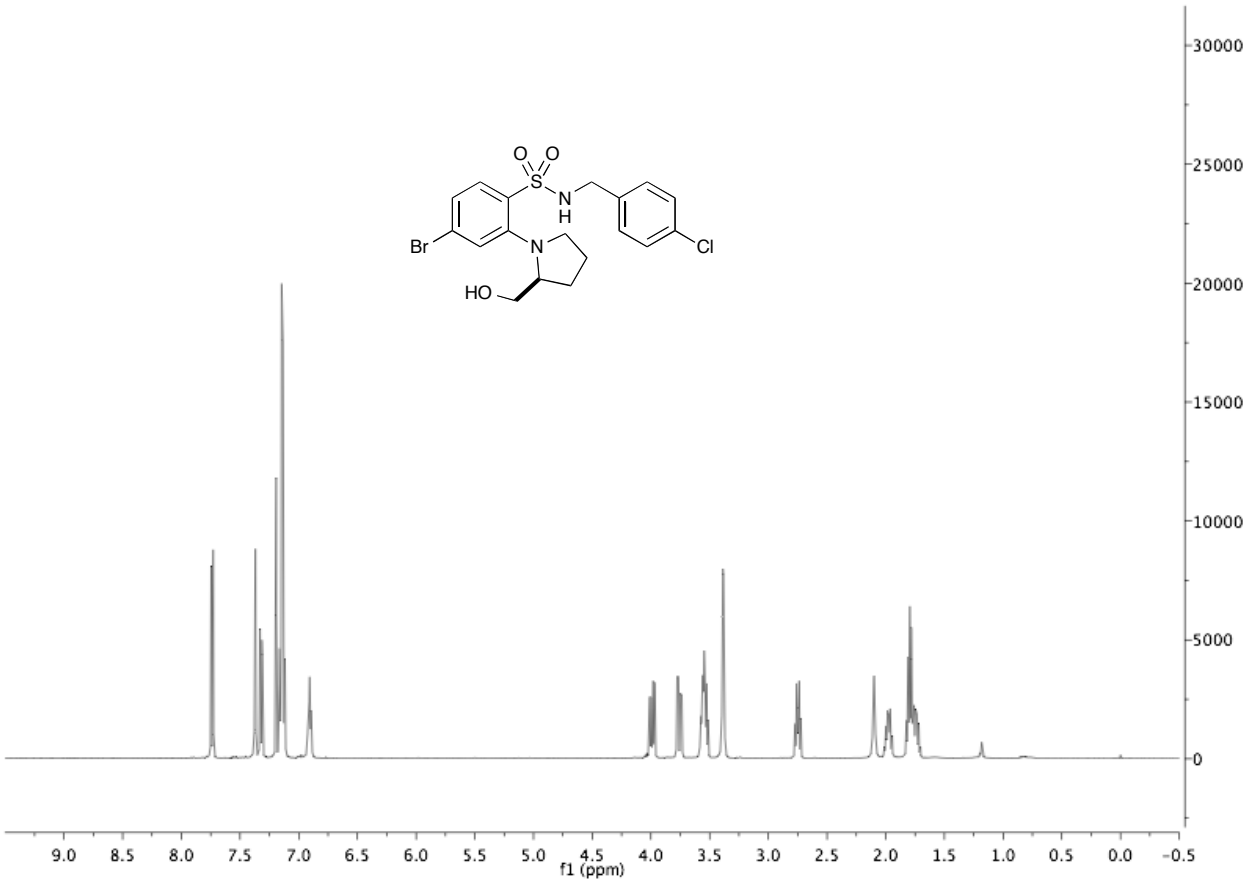
FTIR (neat, cm^{-1}): 1577, 1467, 1409, 1321, 1155;

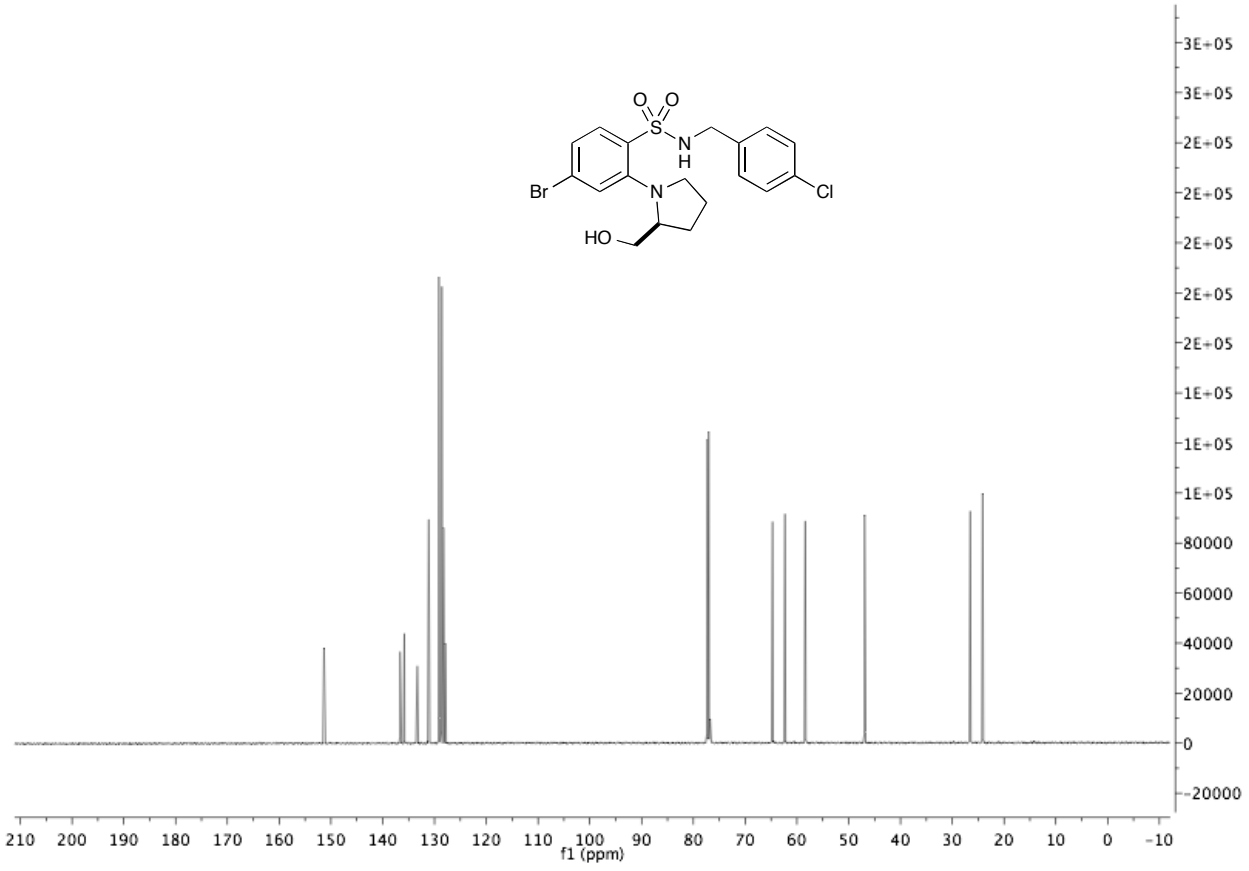
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 2.6 Hz, 1H), 7.38 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 1H), 4.19 (s, 2H), 3.38 (m, 2H), 3.32–3.28 (m, 2H), 3.02 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$): δ 147.2, 134.2, 133.9, 133.1, 131.7, 129.7, 129.4, 128.9, 125.8, 119.5, 51.6, 50.8, 46.5, 43.1;

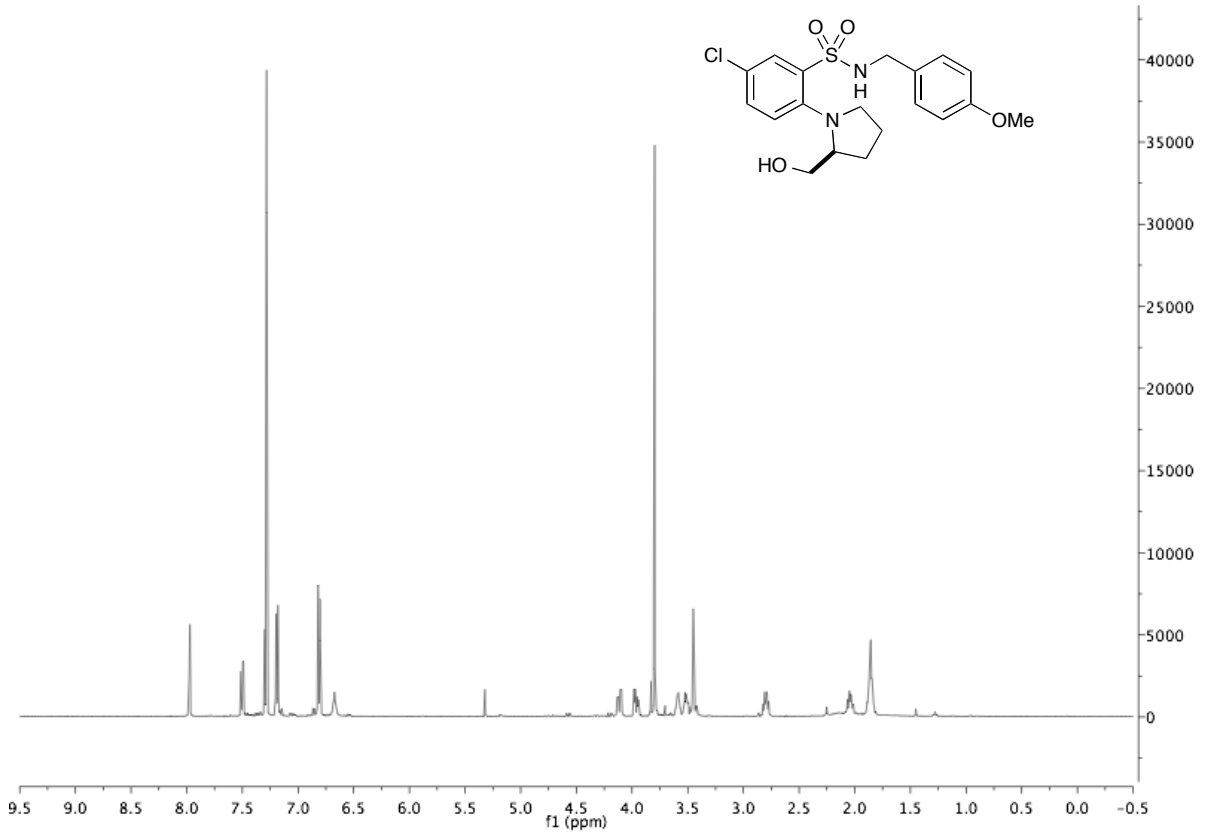
HRMS calculated for $C_{16}H_{17}Cl_2N_2O_2S$ $(M+H)^+$ 371.0388; found 371.0396 (TOF MS ES+).

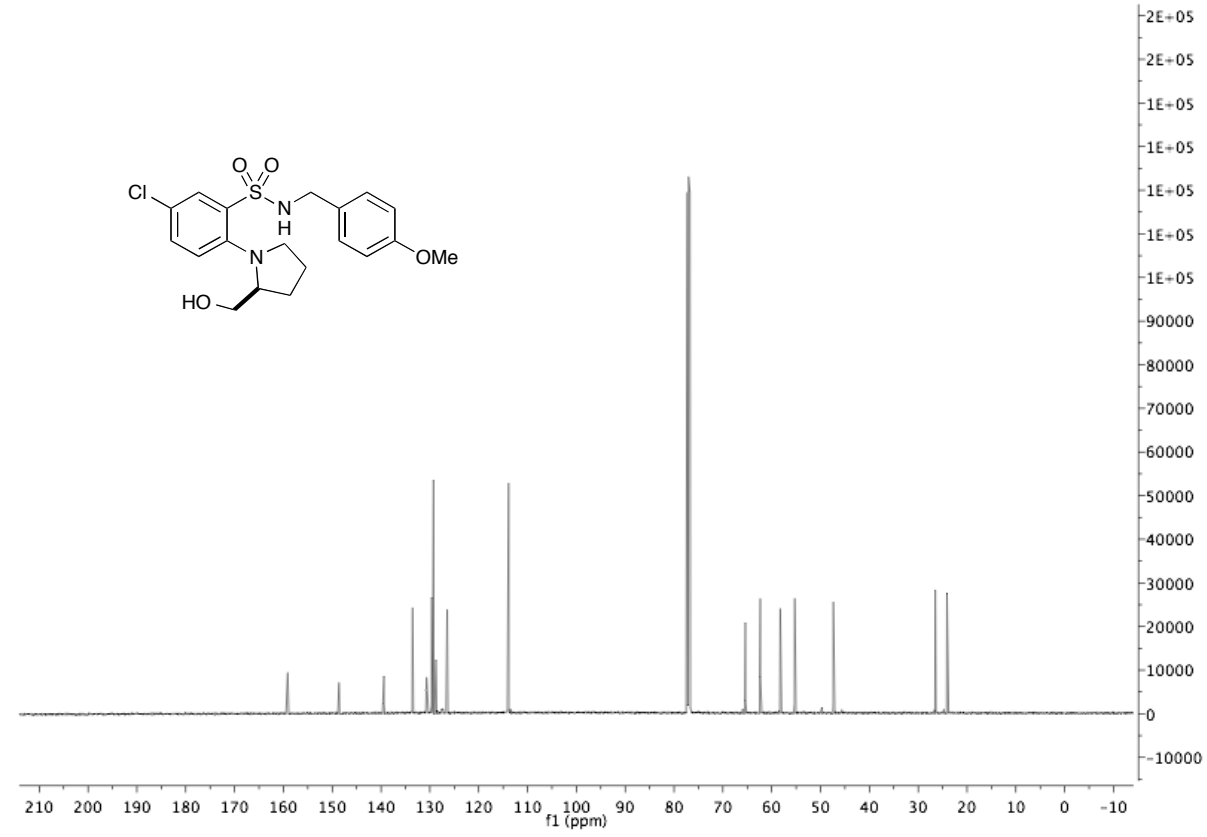
(*S*)-4-Bromo-*N*-(4-chlorobenzyl)-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzene-sulfonamide (2a).



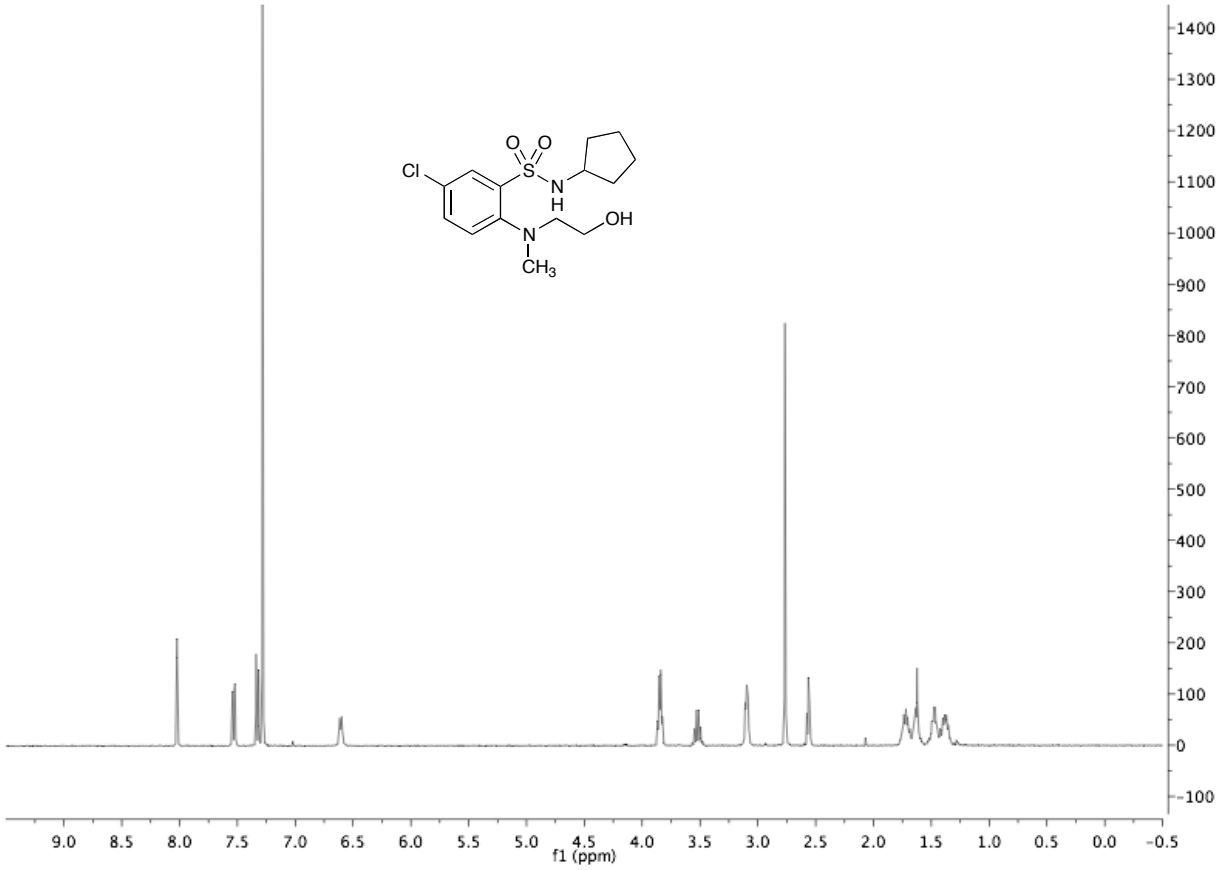


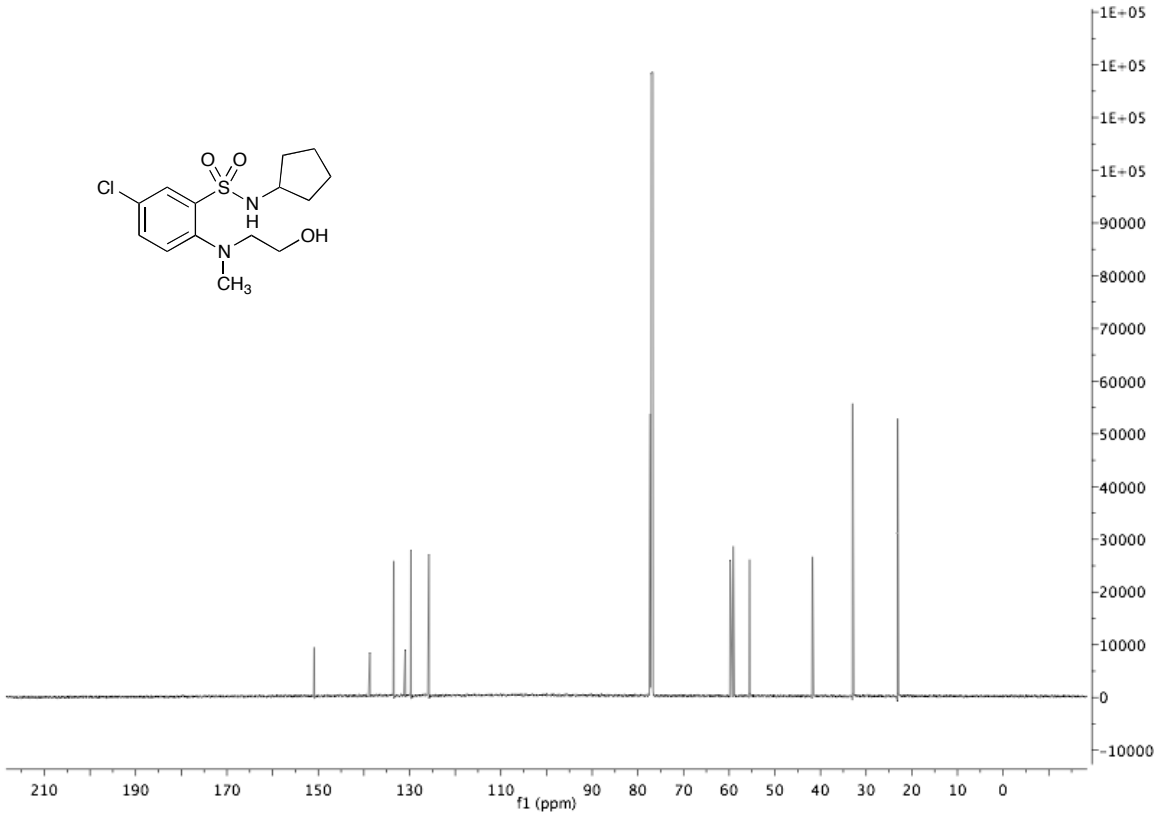
(*S*)-5-Chloro-2-(2-(hydroxymethyl)pyrrolidin-1-yl)-*N*-(4-methoxybenzyl) benzenesulfonamide (2b).



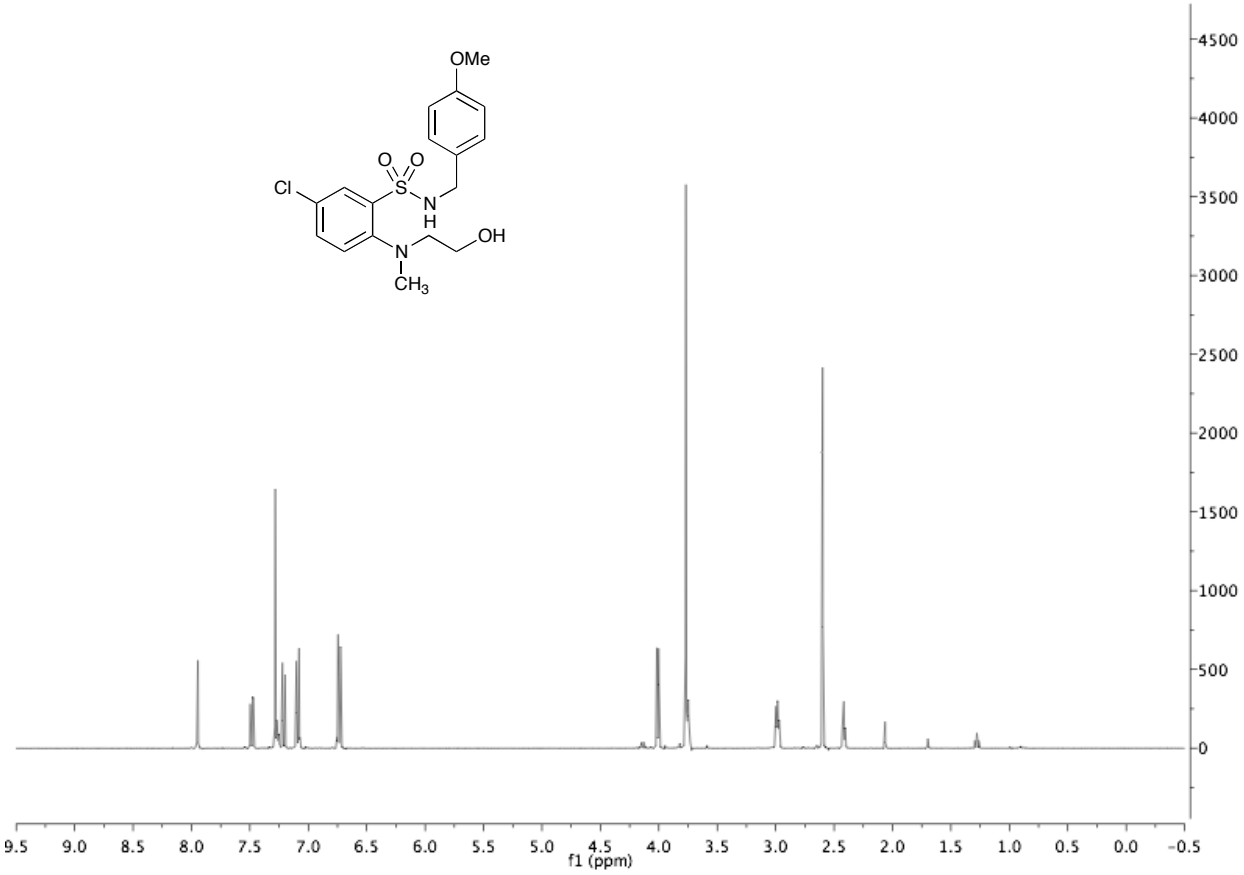


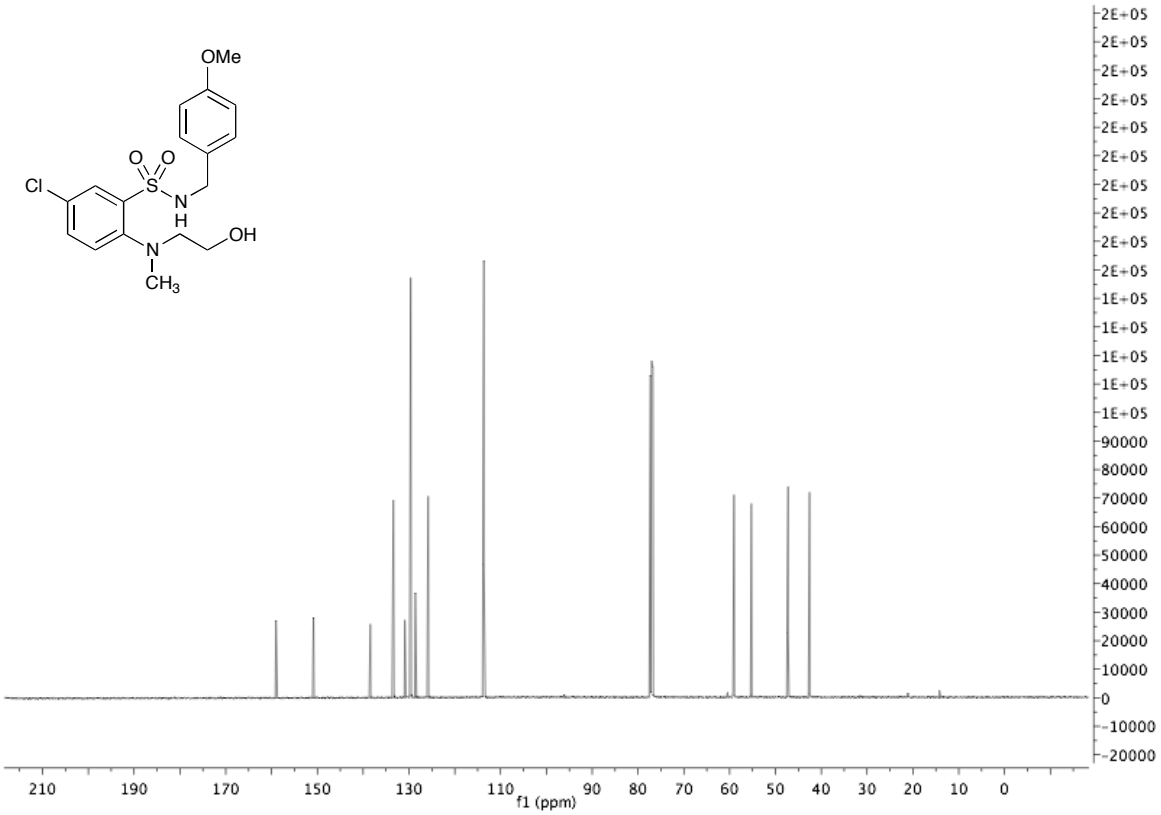
5-Chloro-*N*-cyclopentyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2c).



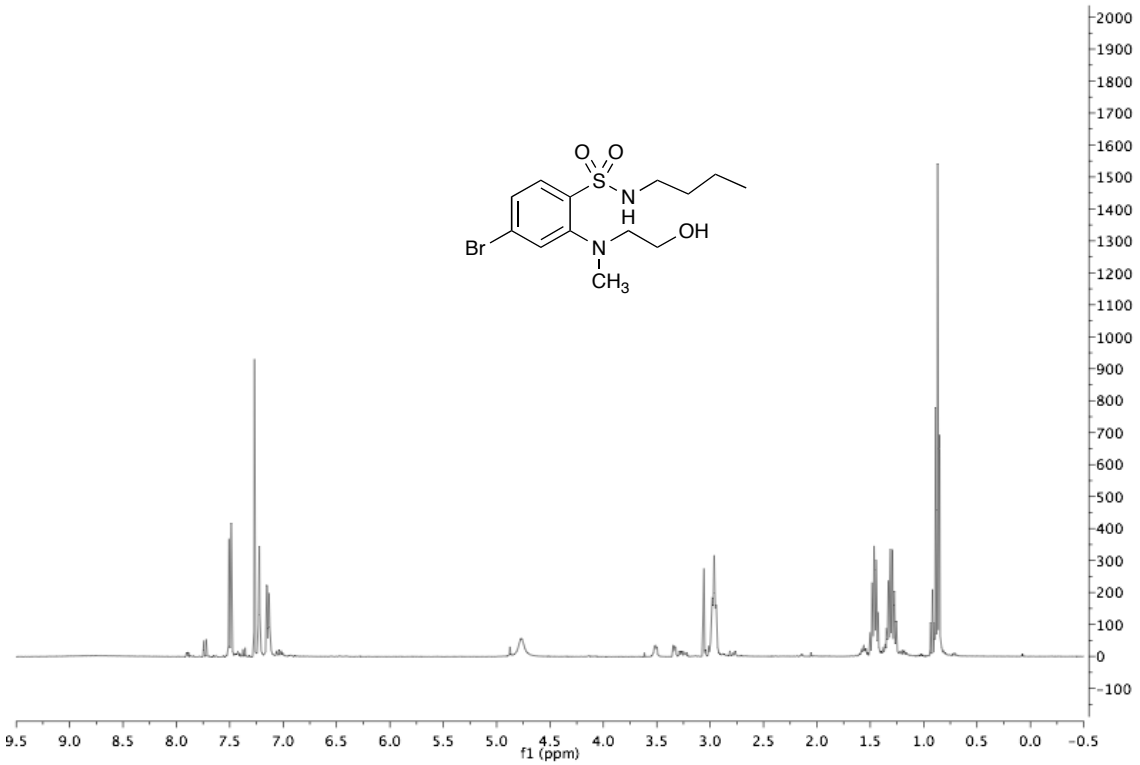


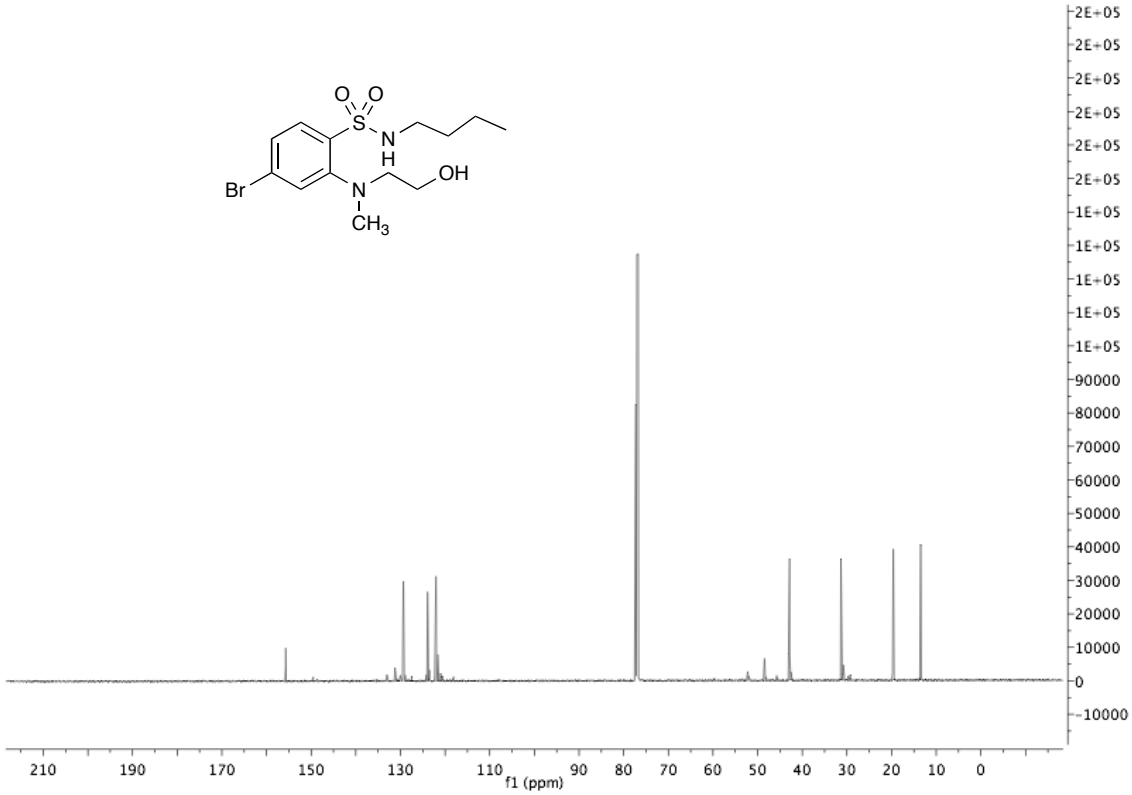
5-Chloro-2-((2-hydroxyethyl)(methyl)amino)-*N*-(4-methoxybenzyl) benzenesulfonamide (2d).



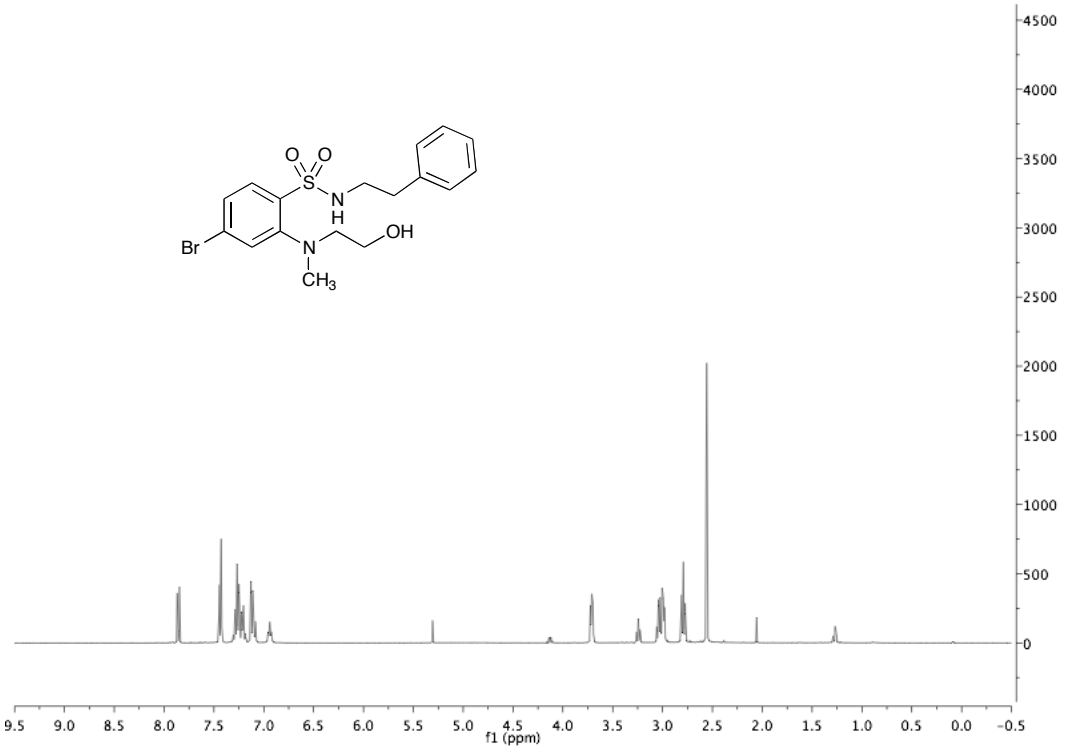


4-Bromo-*N*-butyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2e).

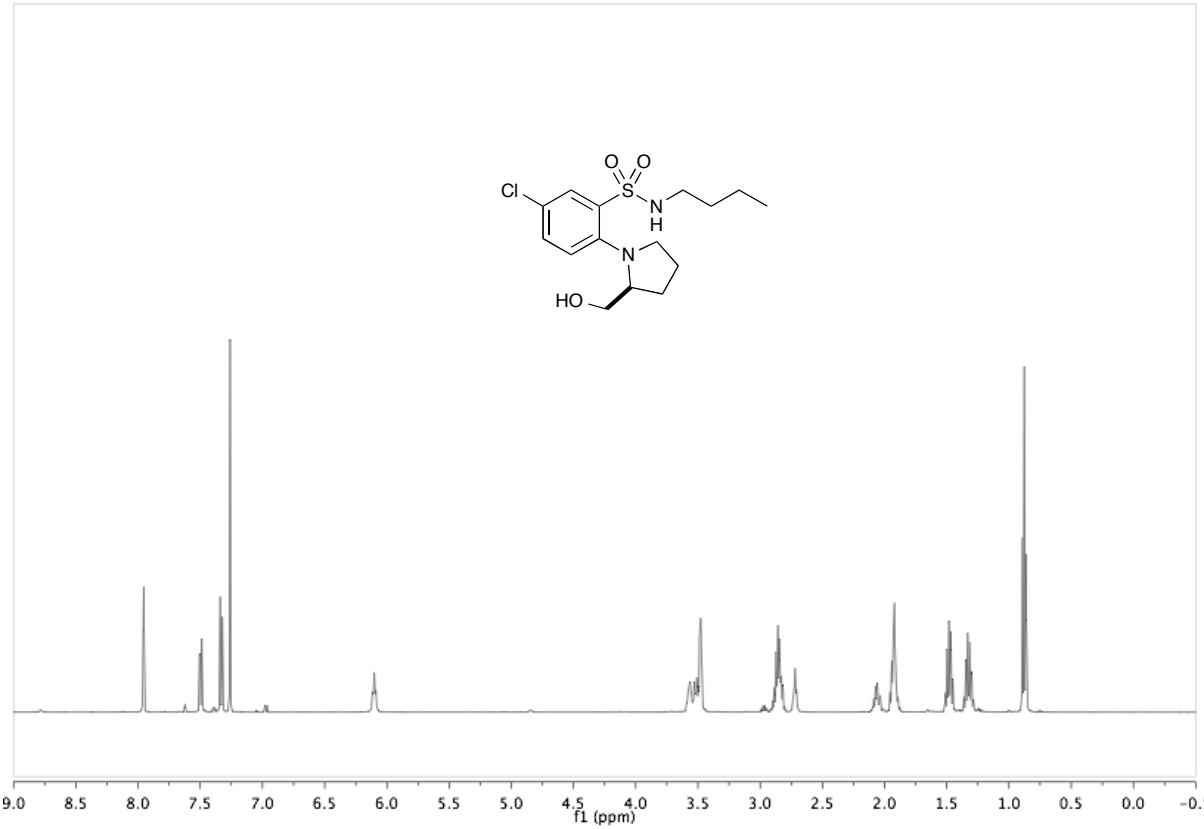


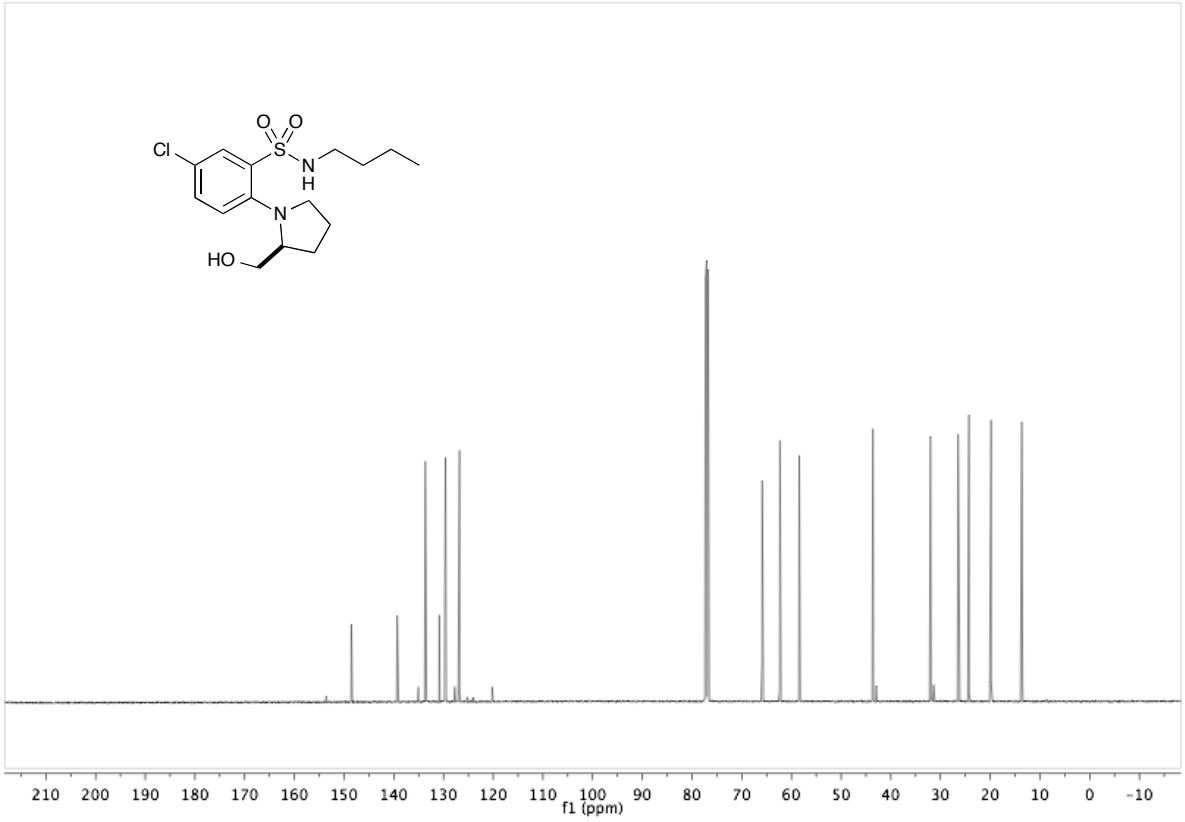


4-Bromo-2-((2-hydroxyethyl)(methyl)amino)-*N*-phenethylbenzenesulfonamide (2f).

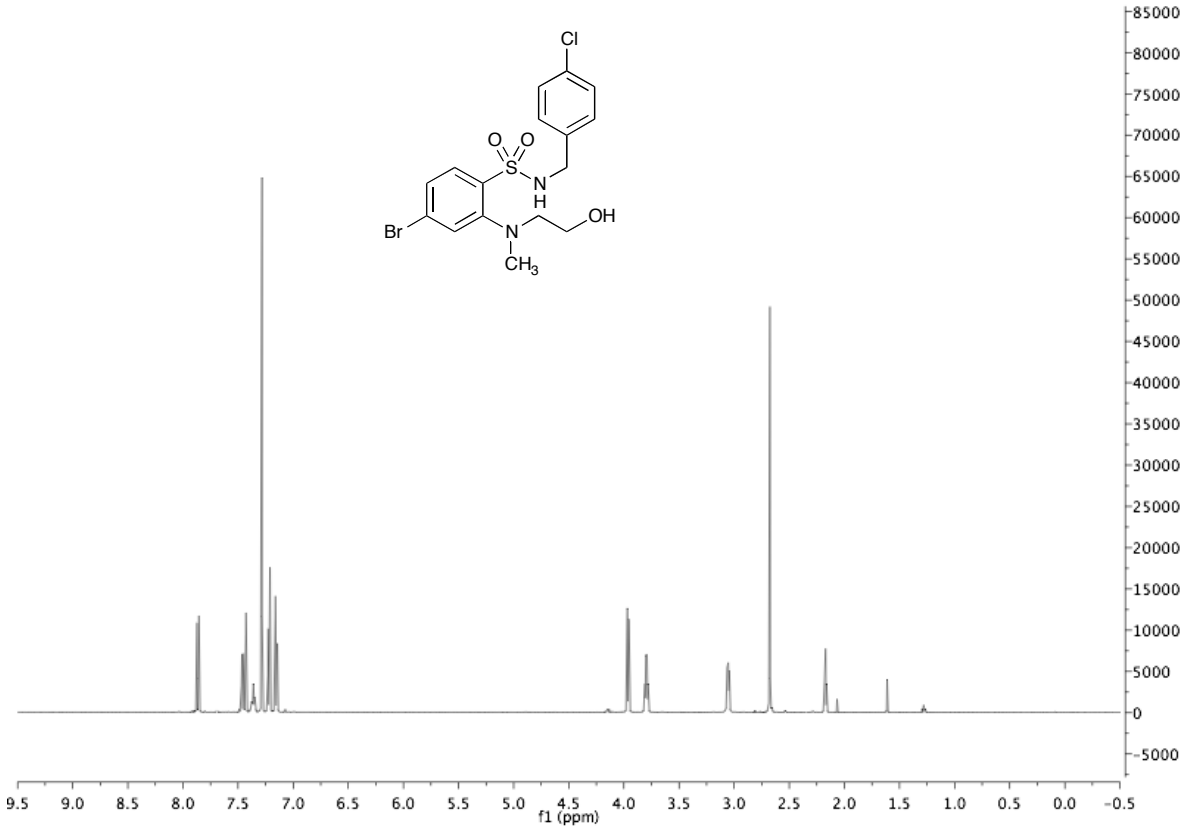


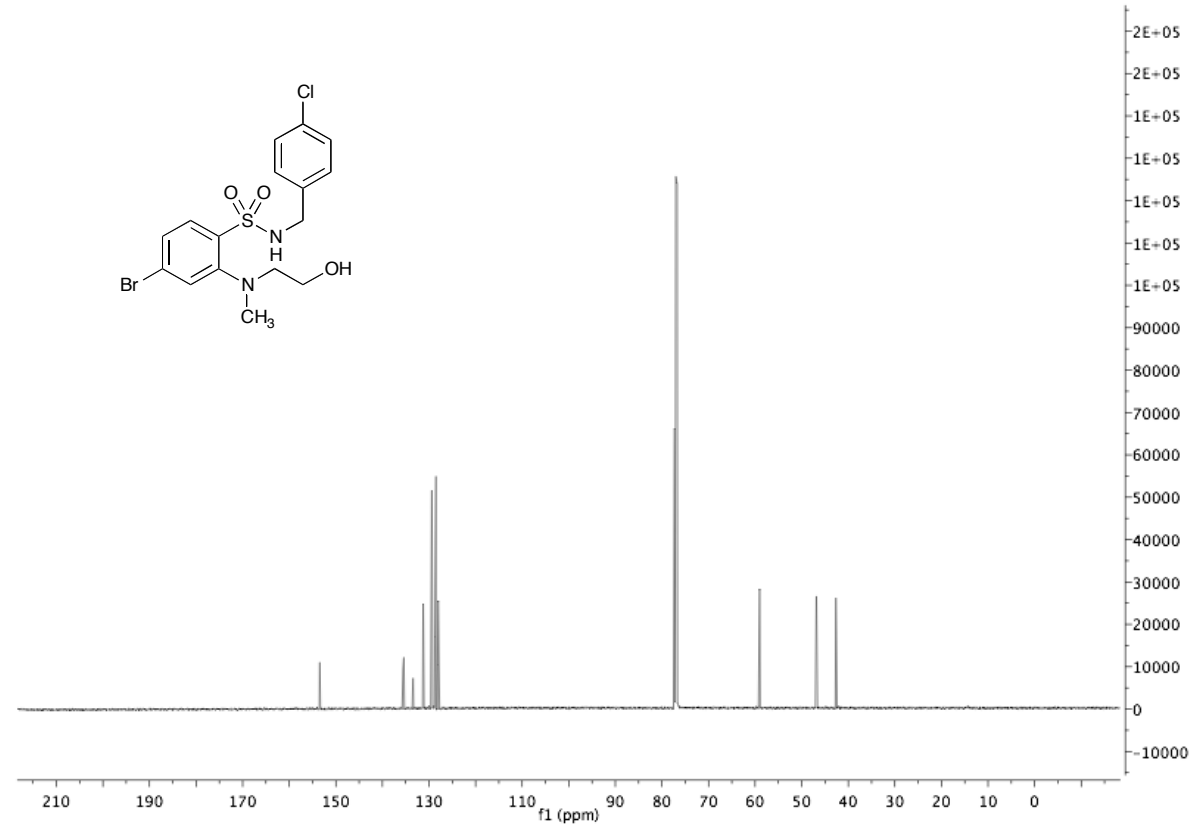
(*S*)-N-Butyl-5-chloro-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzenesulfonamide (2g).



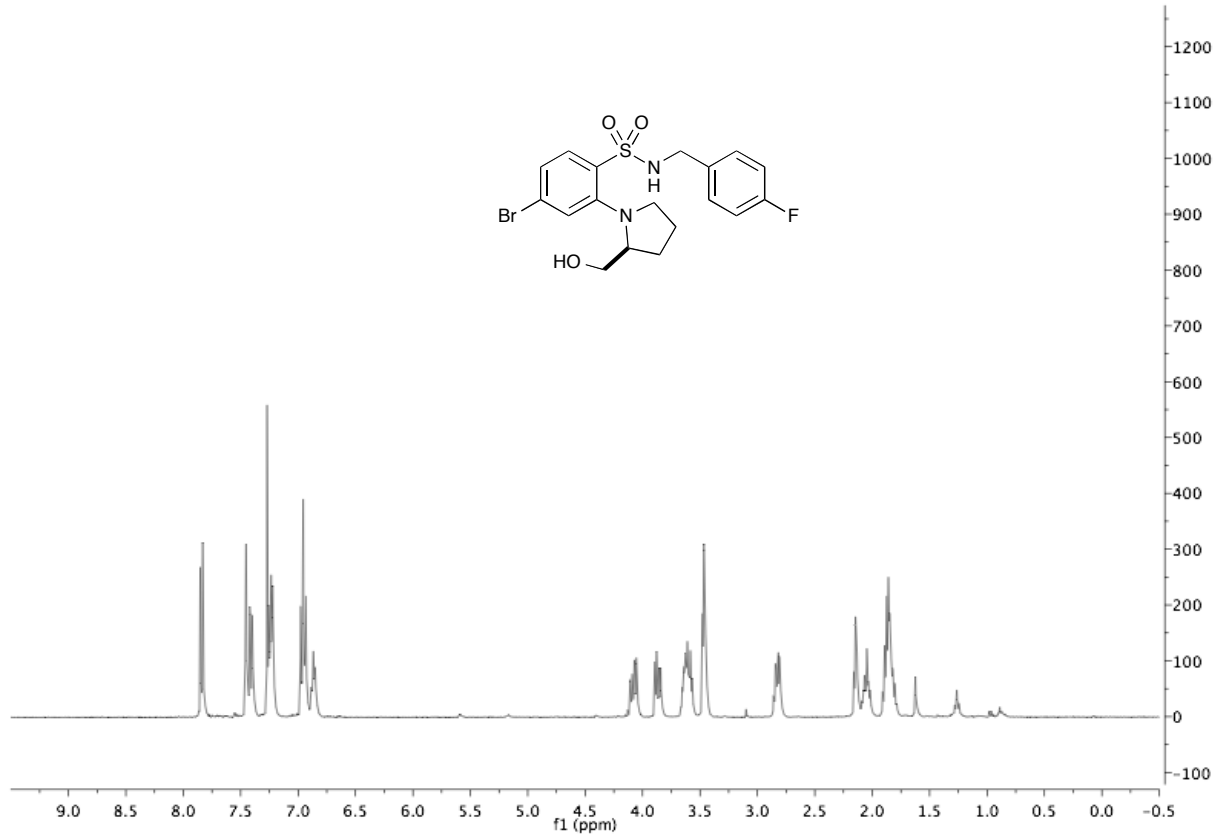


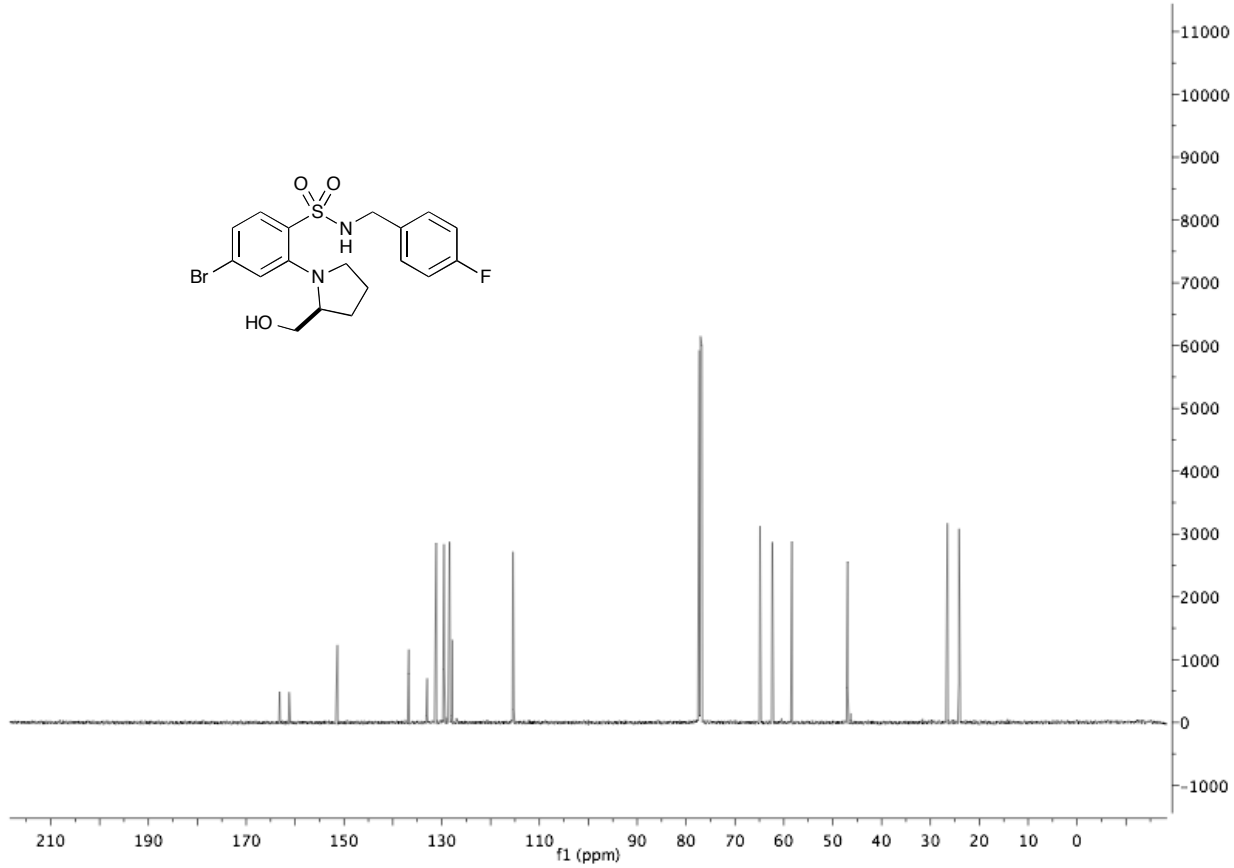
4-Bromo-*N*-(4-chlorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2h).



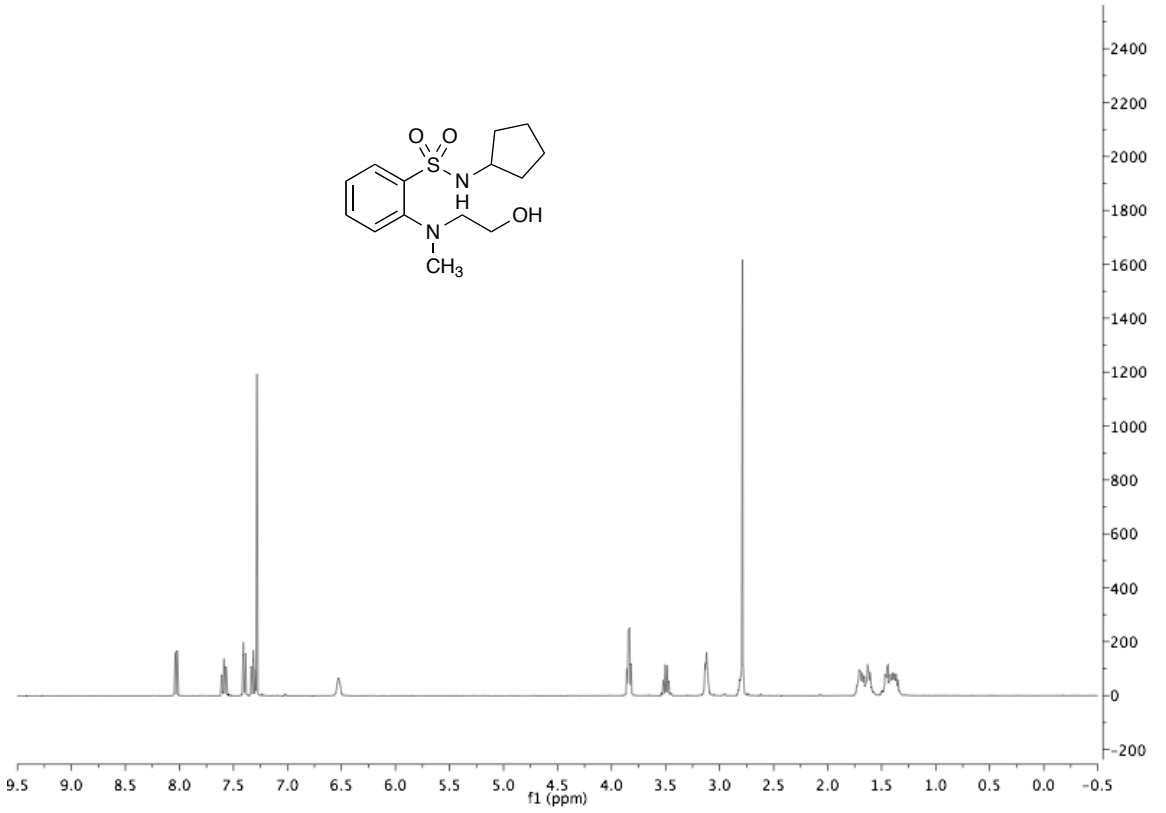


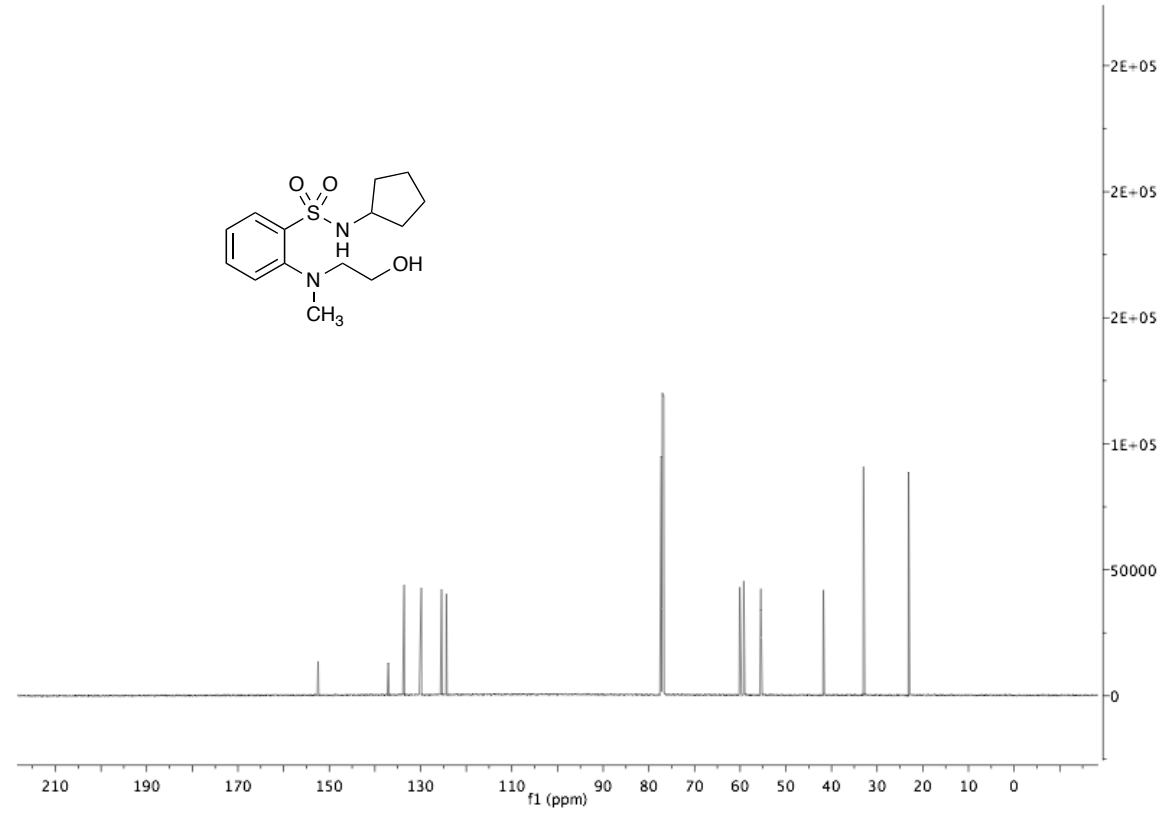
(*S*)-4-Bromo-*N*-(4-fluorobenzyl)-2-(2-(hydroxymethyl)pyrrolidin-1-yl) benzenesulfonamide (2i).



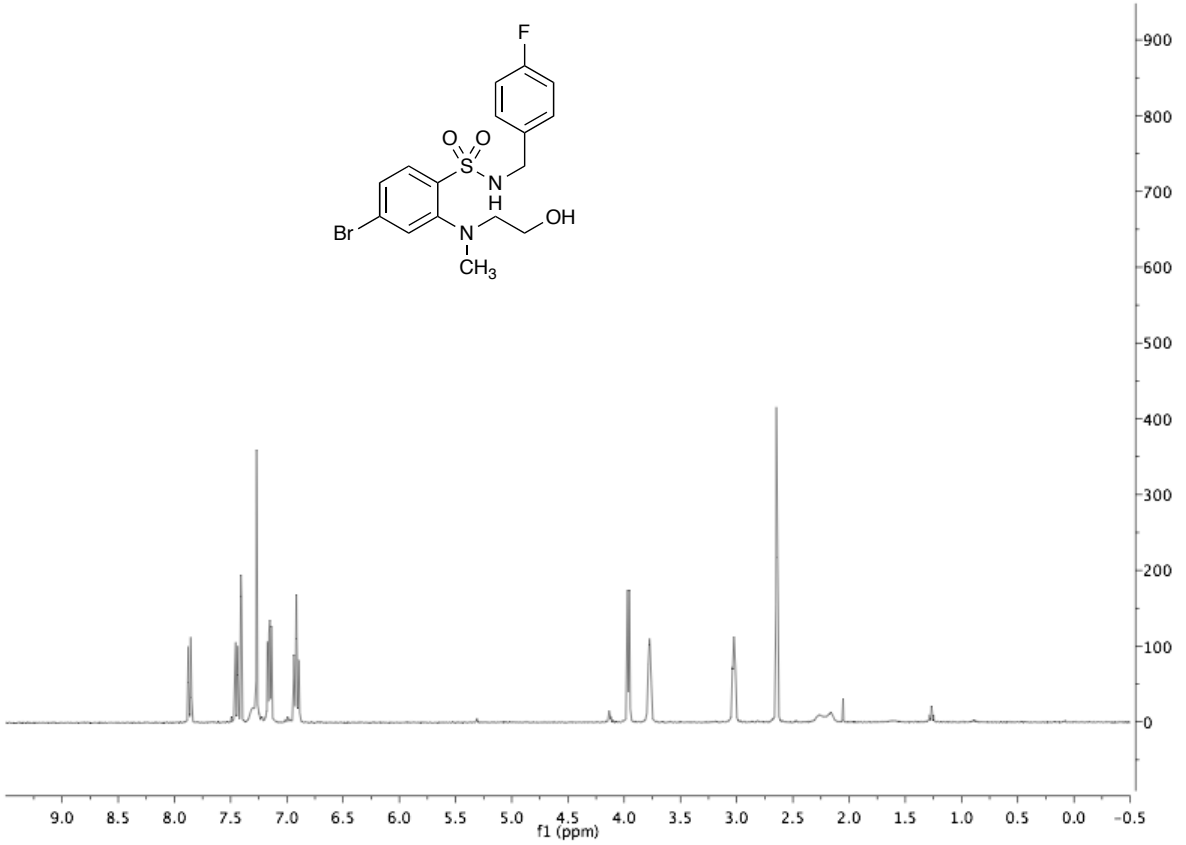


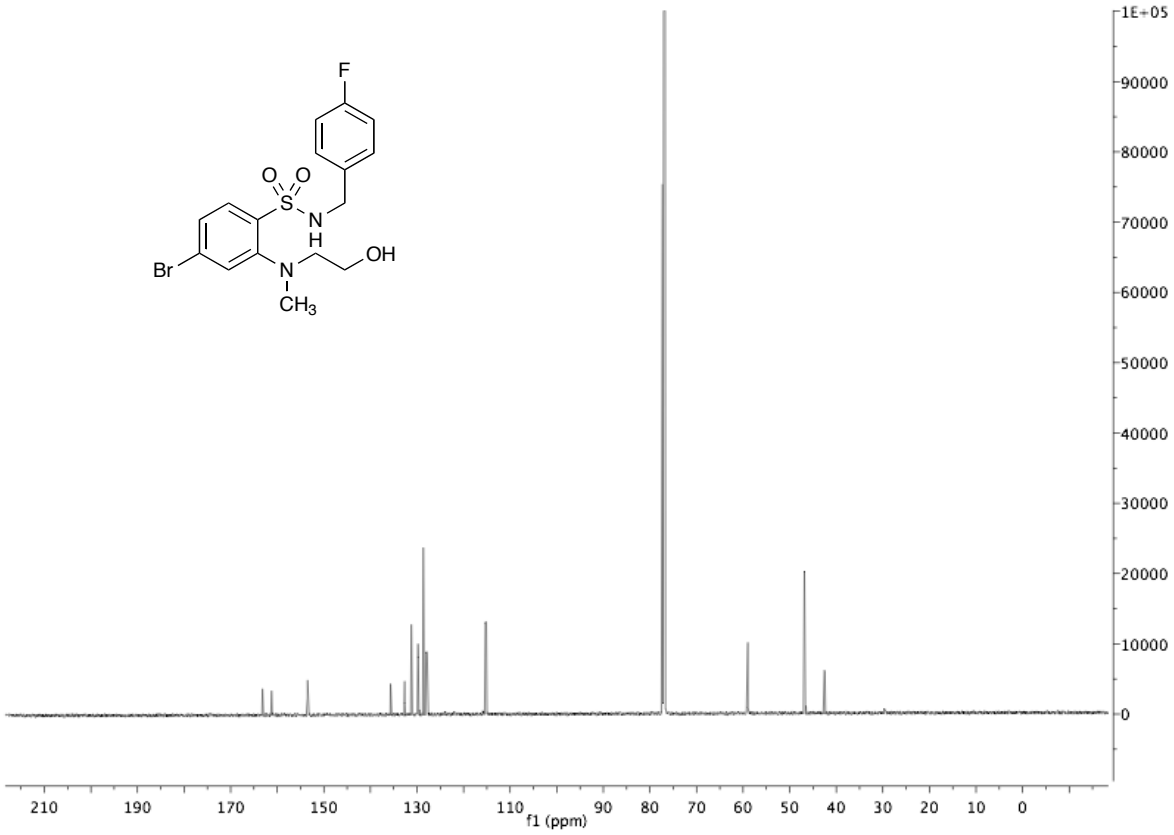
_N_-Cyclopentyl-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2j).



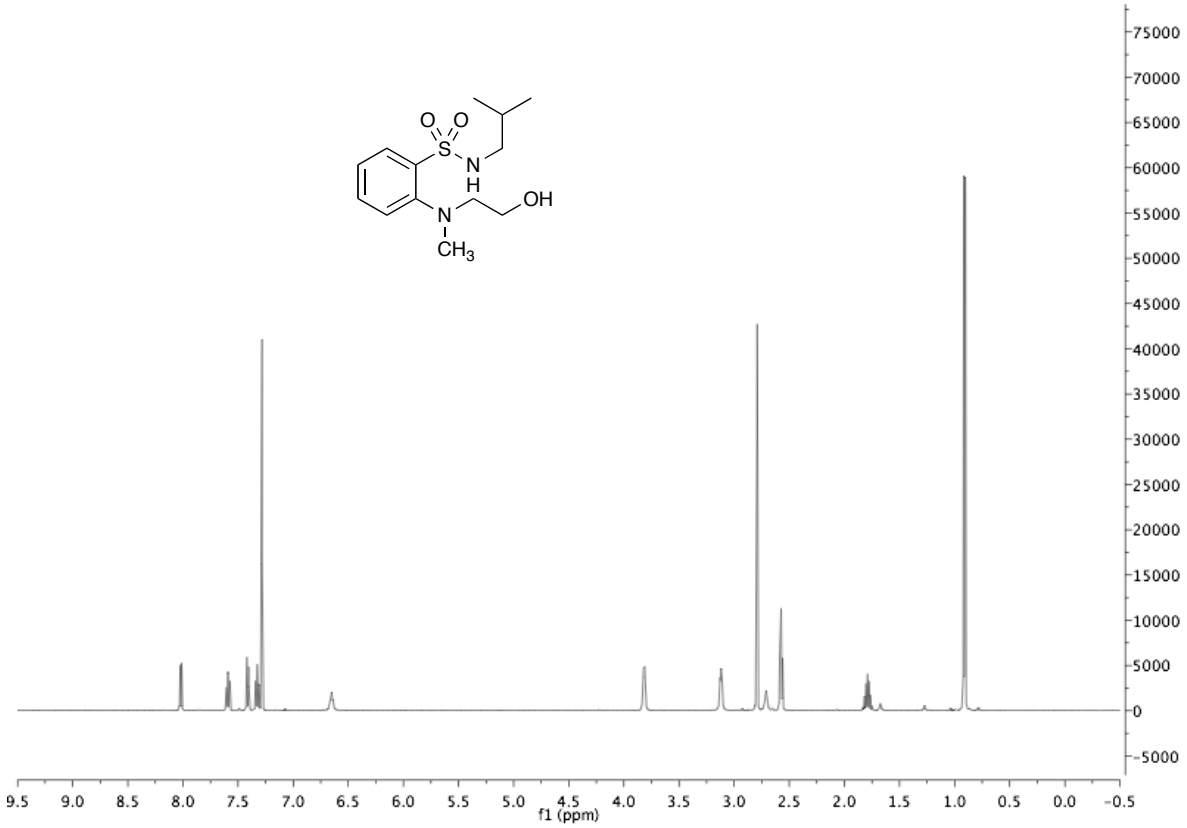


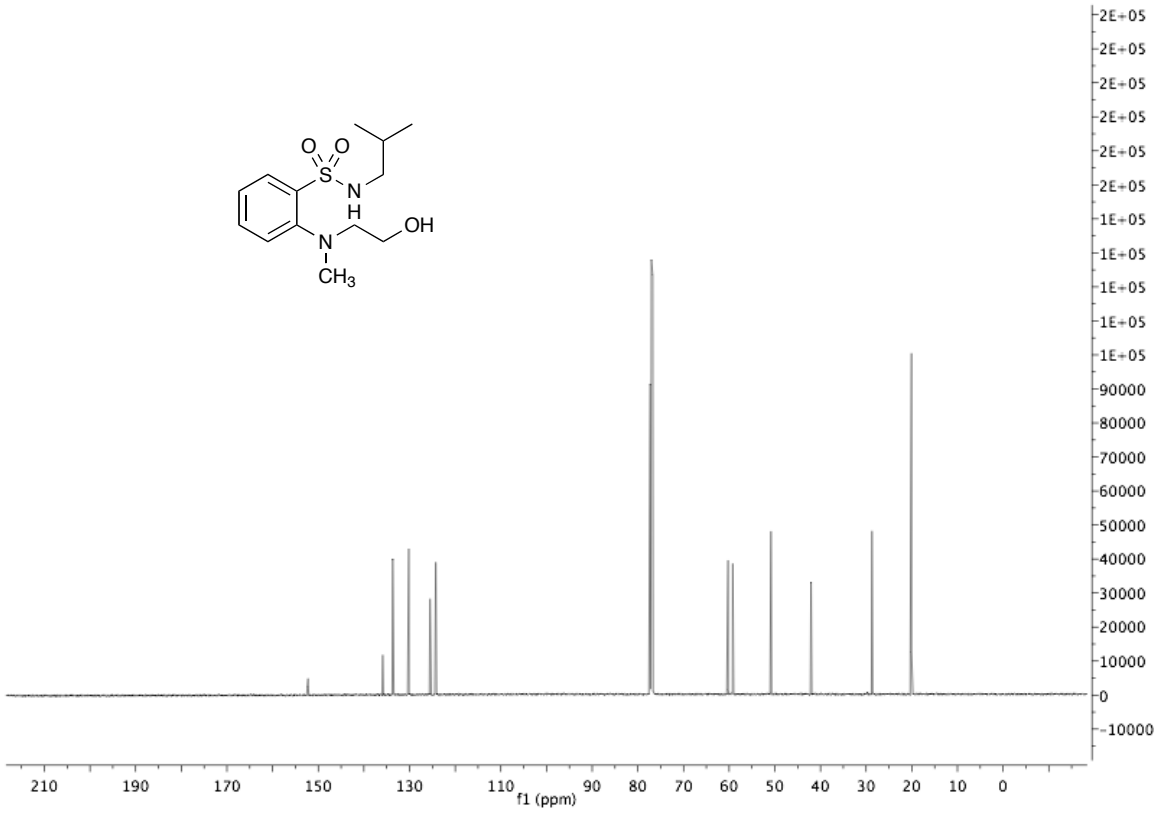
4-Bromo-*N*-(4-fluorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2K).



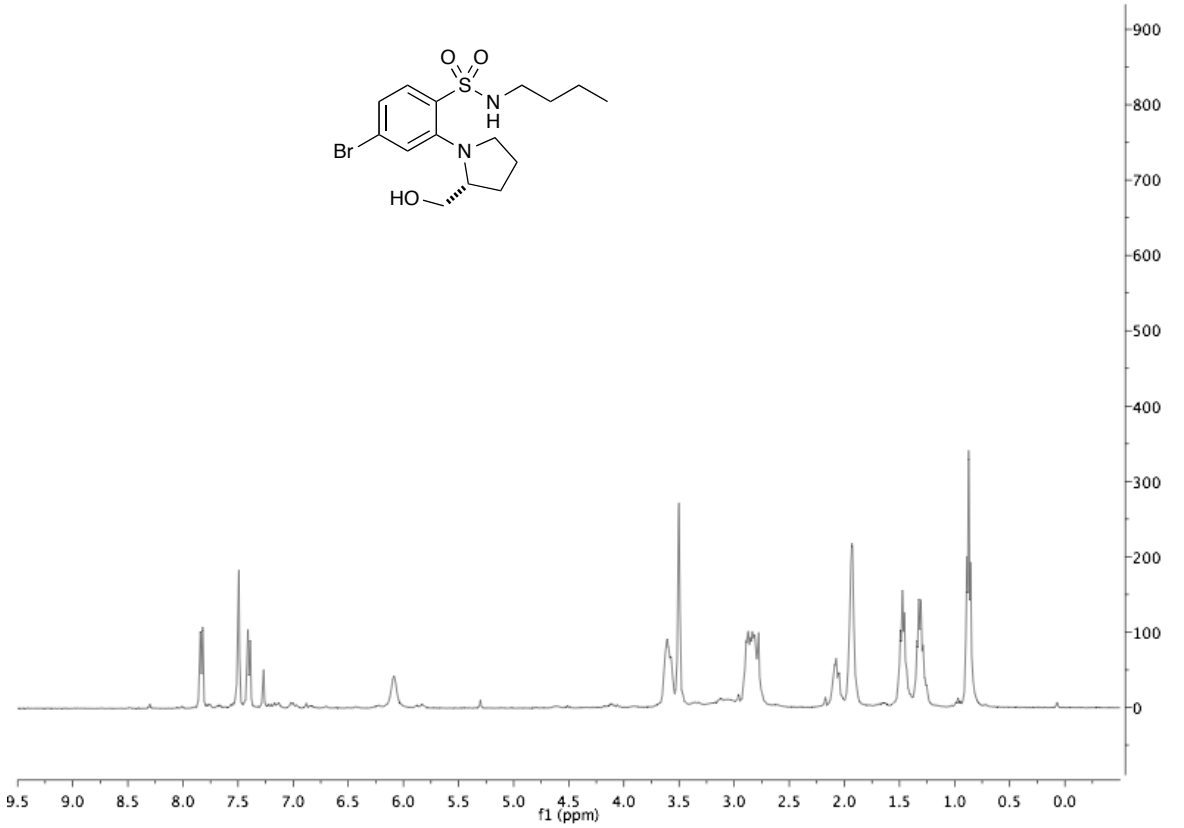


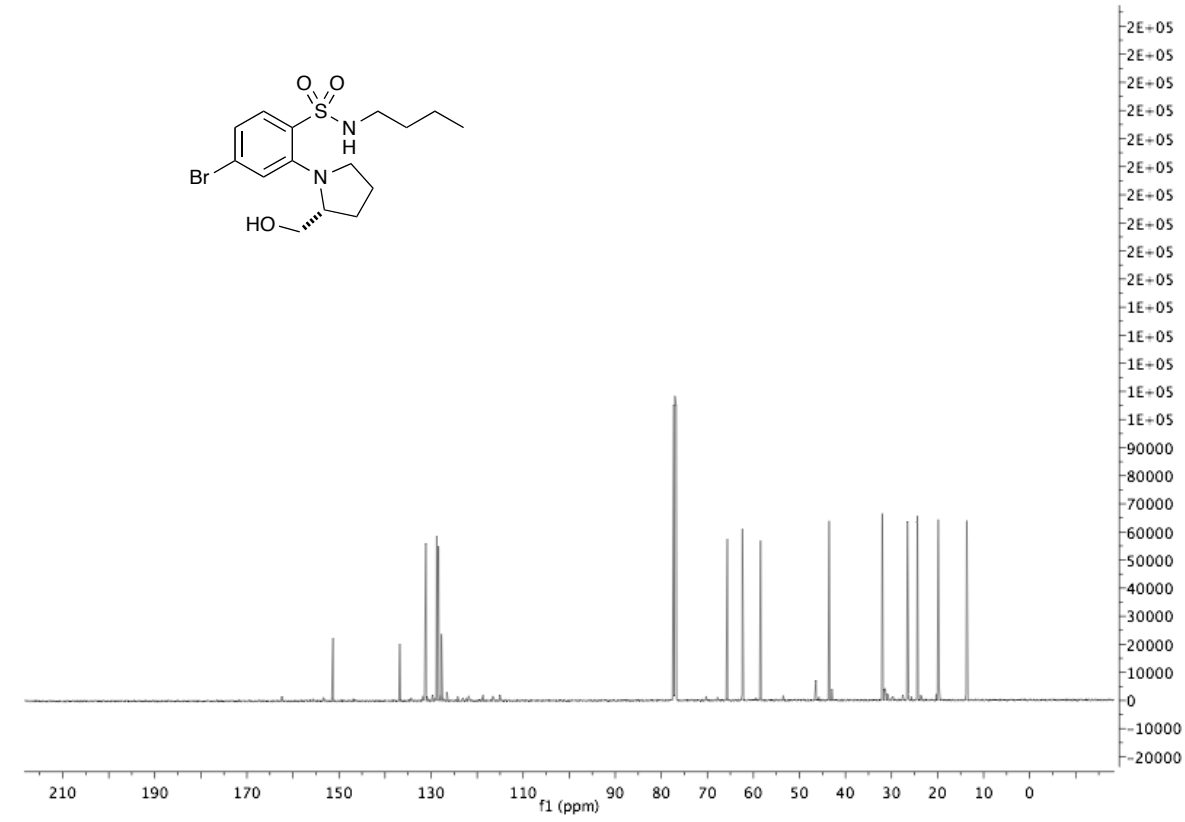
2-((2-Hydroxyethyl)(methyl)amino)-*N*-isobutylbenzenesulfonamide (2l).



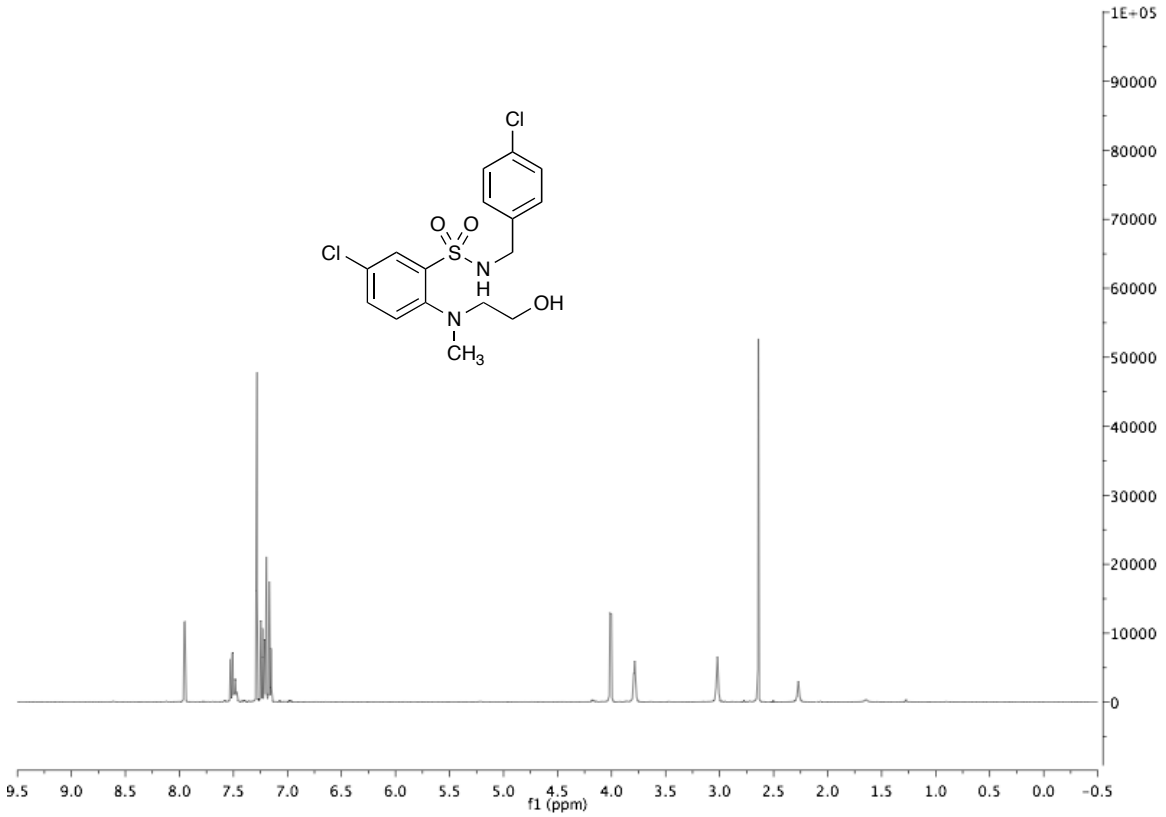


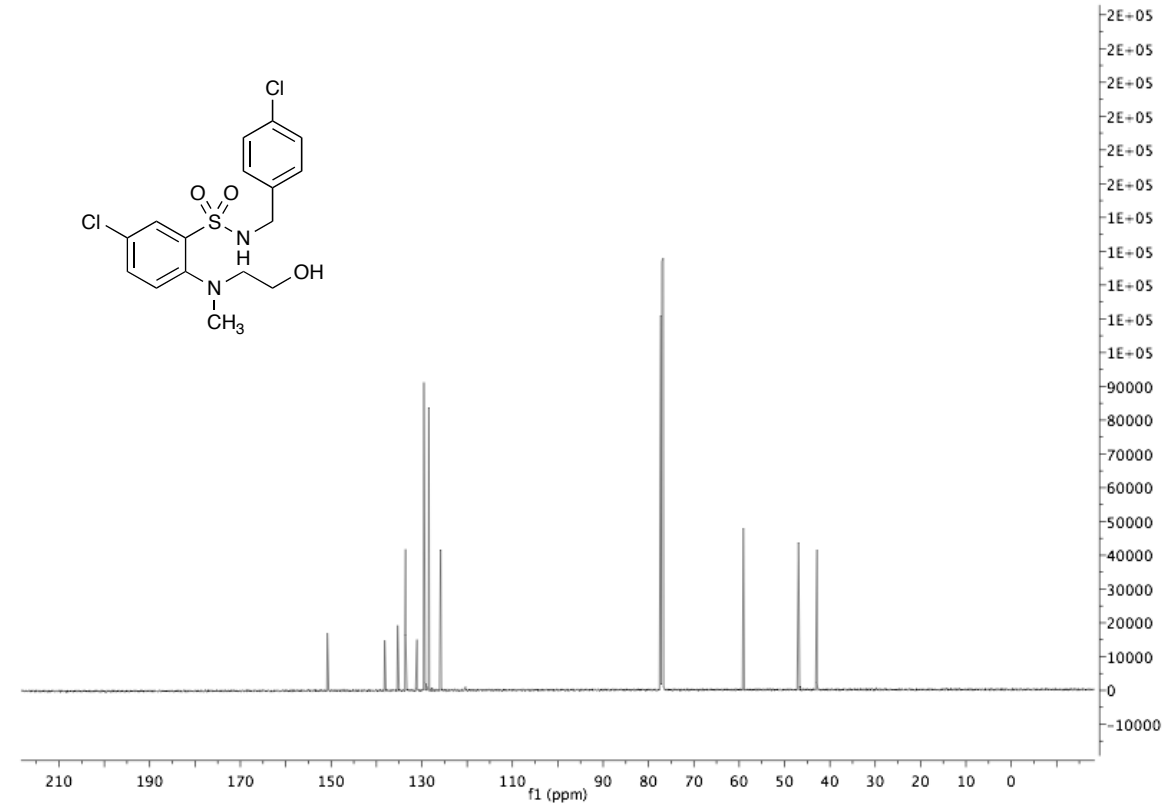
(*R*)-4-Bromo-*N*-butyl-2-(2-(hydroxymethyl)pyrrolidin-1-yl)benzenesulfonamide (2m).



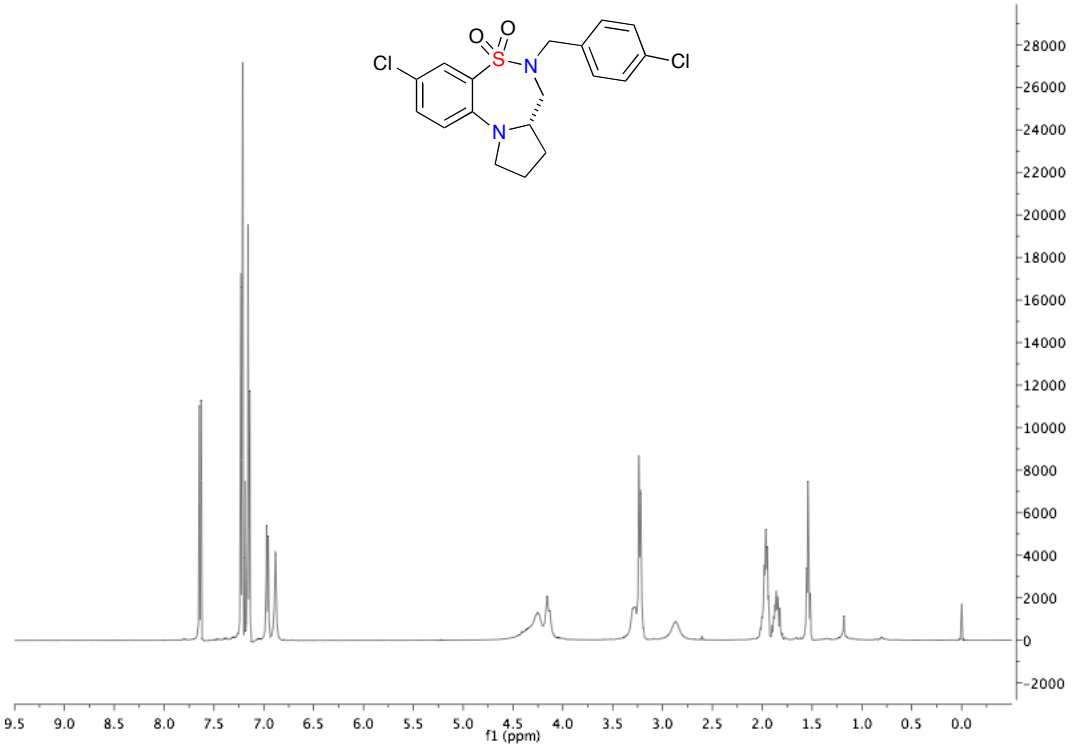


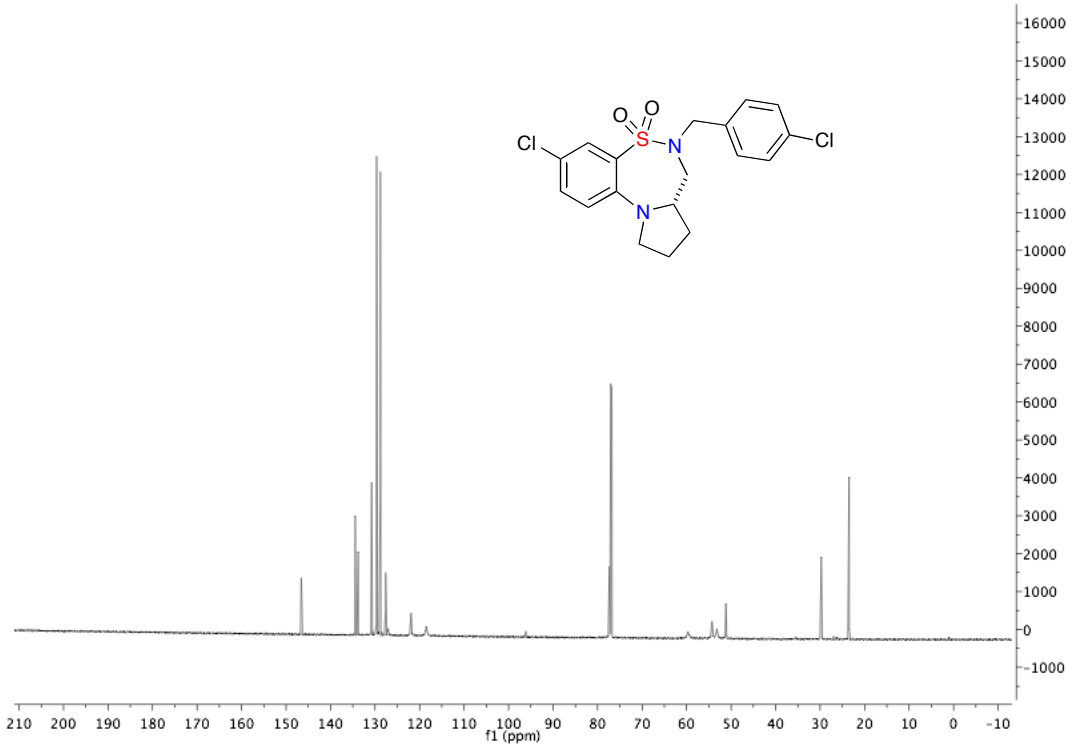
5-Chloro-*N*-(4-chlorobenzyl)-2-((2-hydroxyethyl)(methyl)amino)benzenesulfonamide (2n).



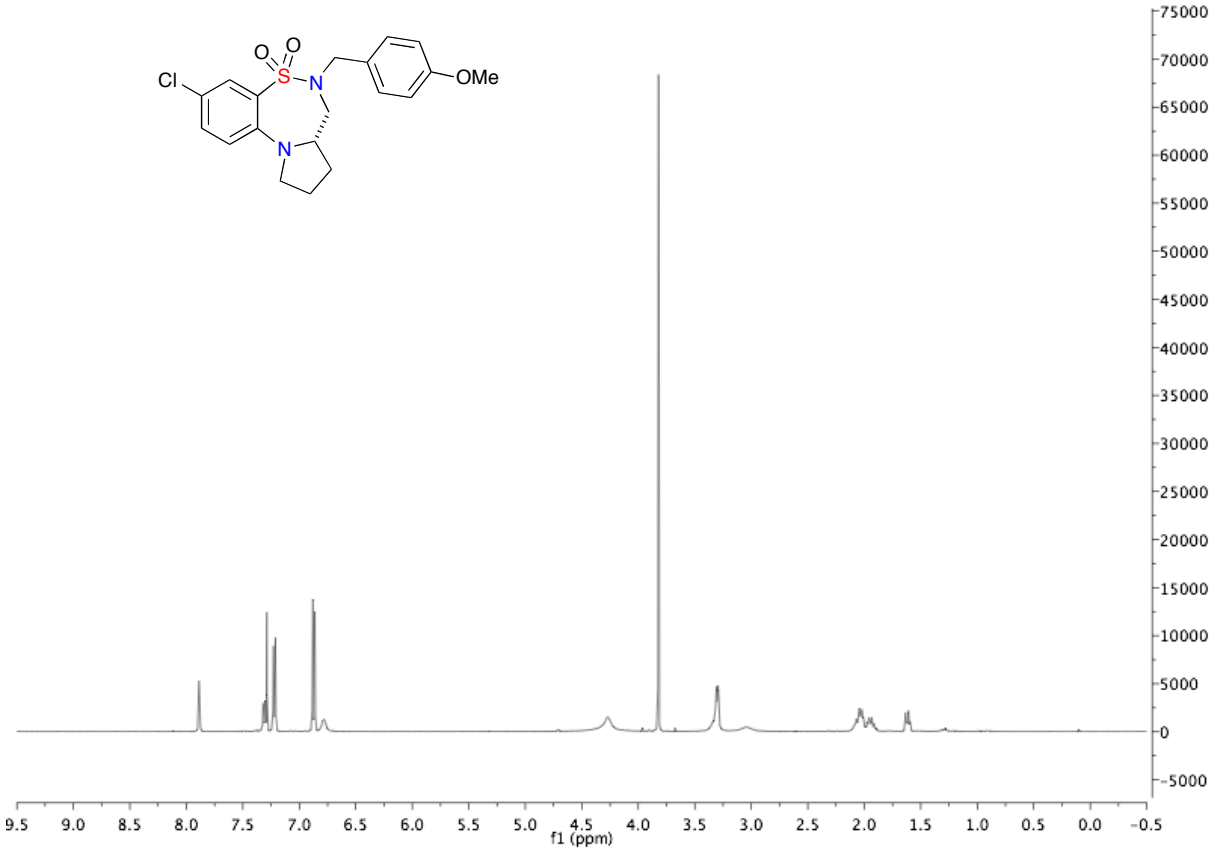


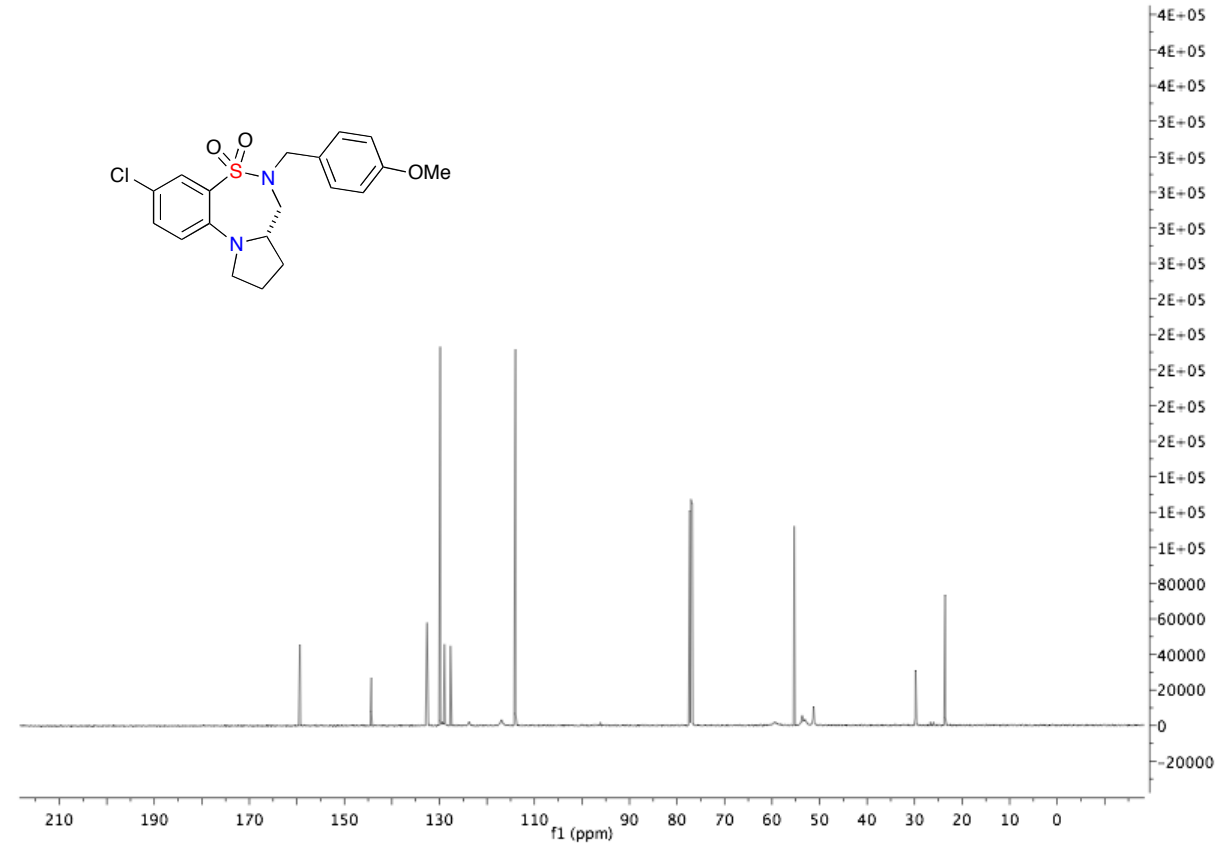
(*S*)-2-Bromo-6-(4-chlorobenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*] pyrrolo[2,1-*d*][1,2,5]thiadiazepine 5,5-dioxide (3a).



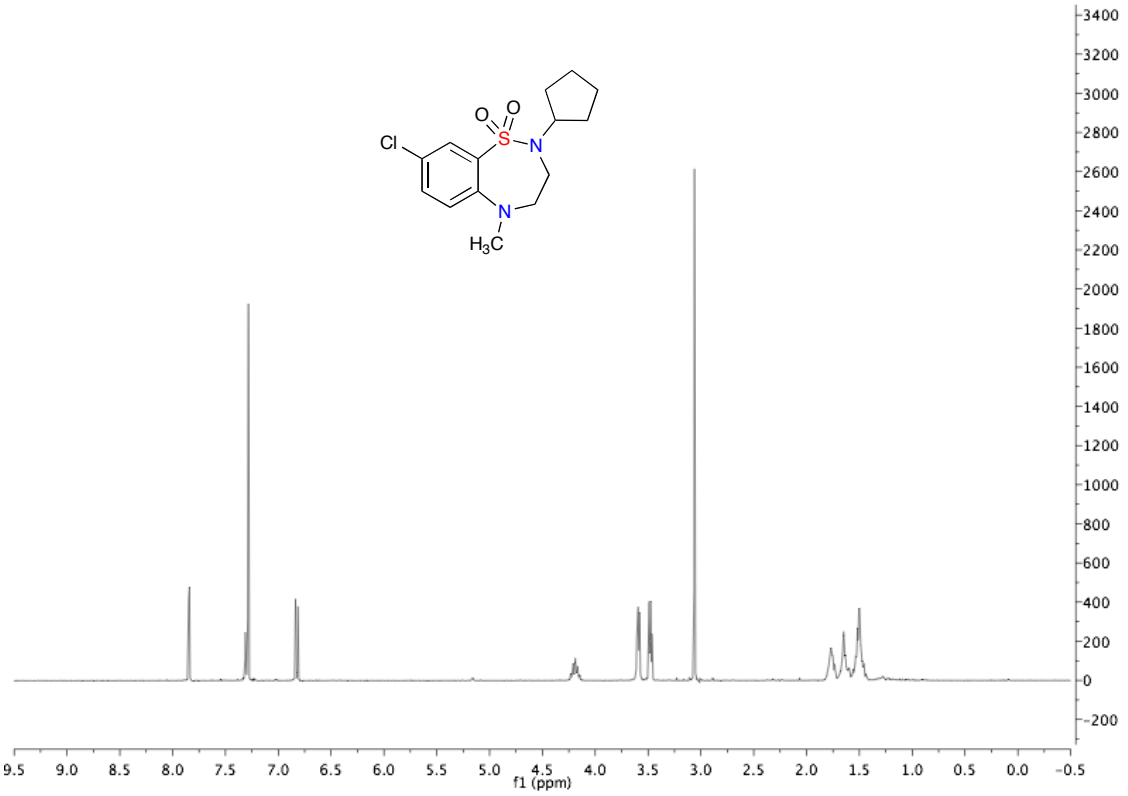


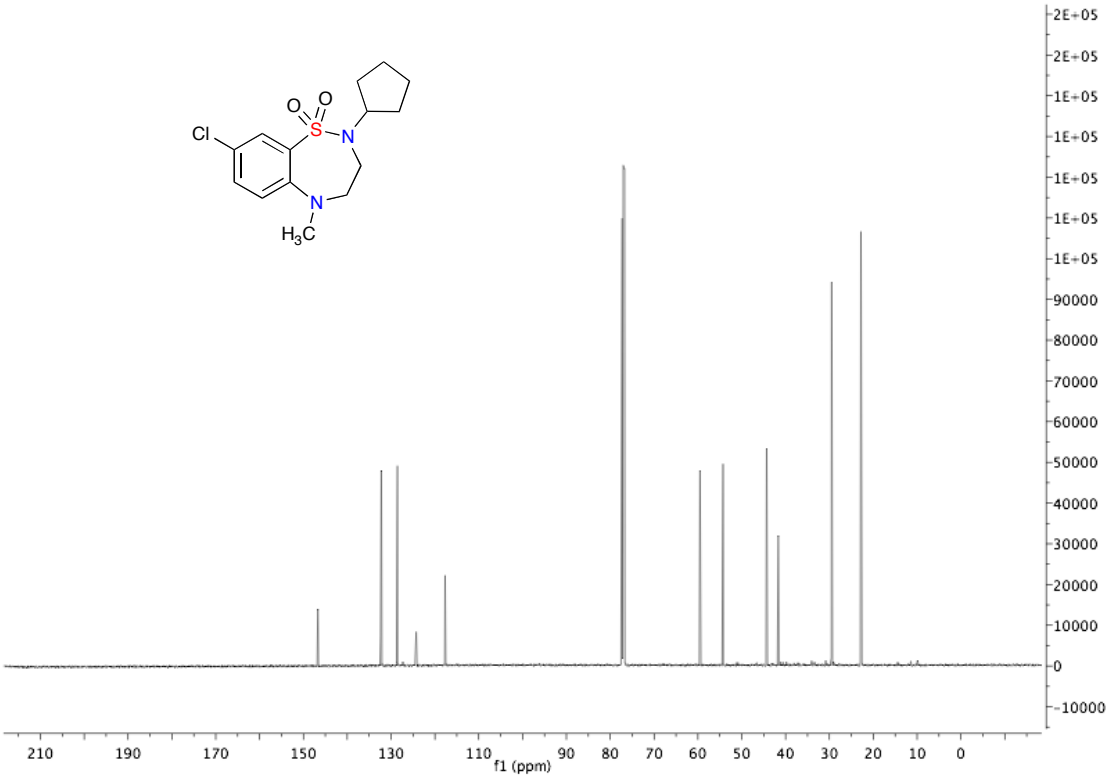
(*S*)-3-Chloro-6-(4-methoxybenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5]thiadiazepine 5,5-dioxide (3b).



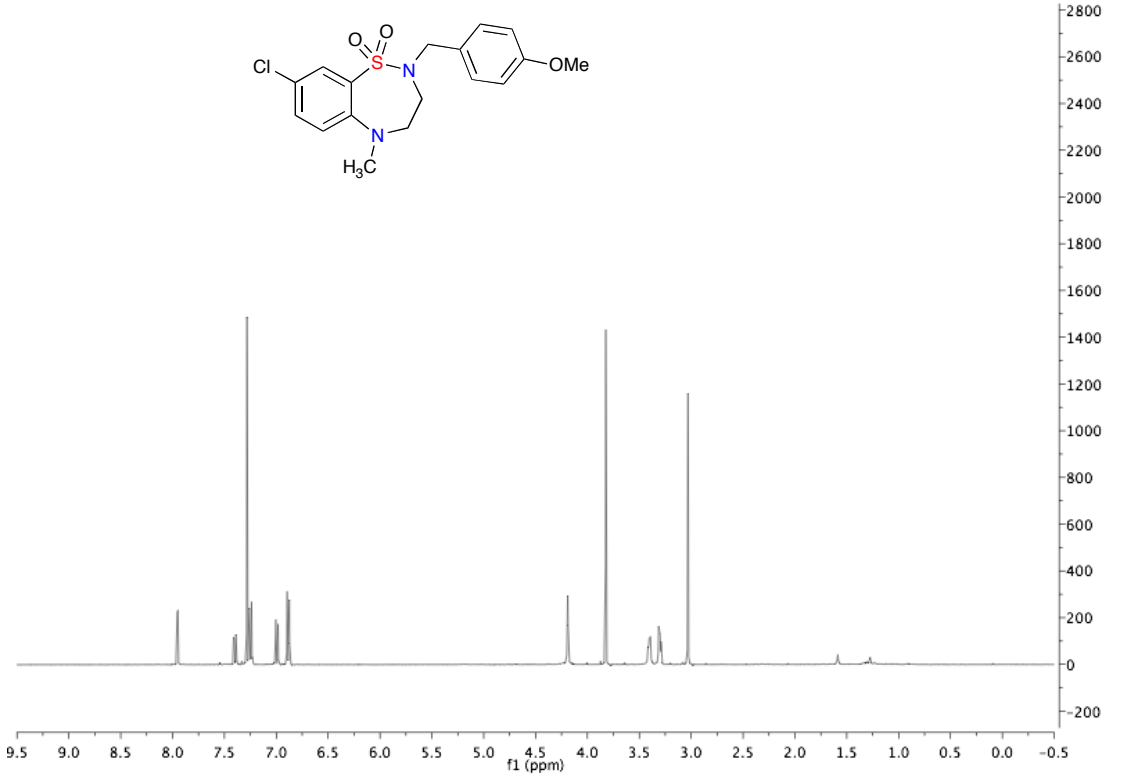


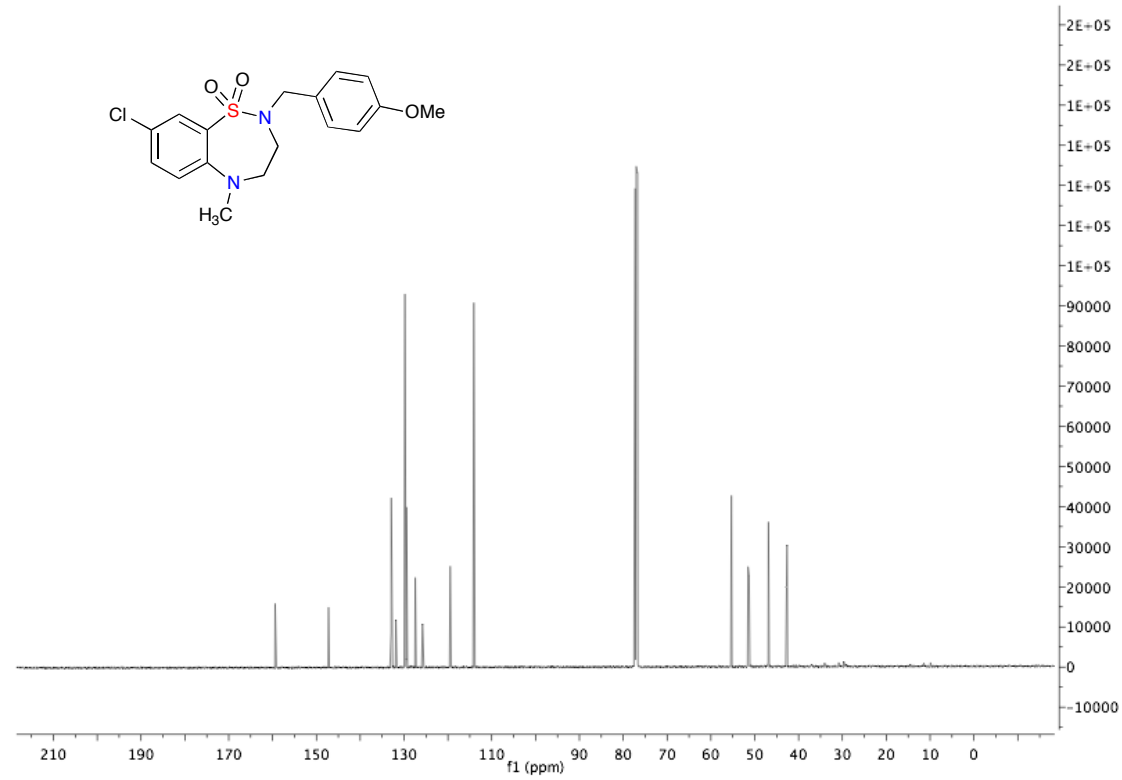
8-Chloro-2-cyclopentyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5] thiadiazepine 1,1-dioxide (3c).



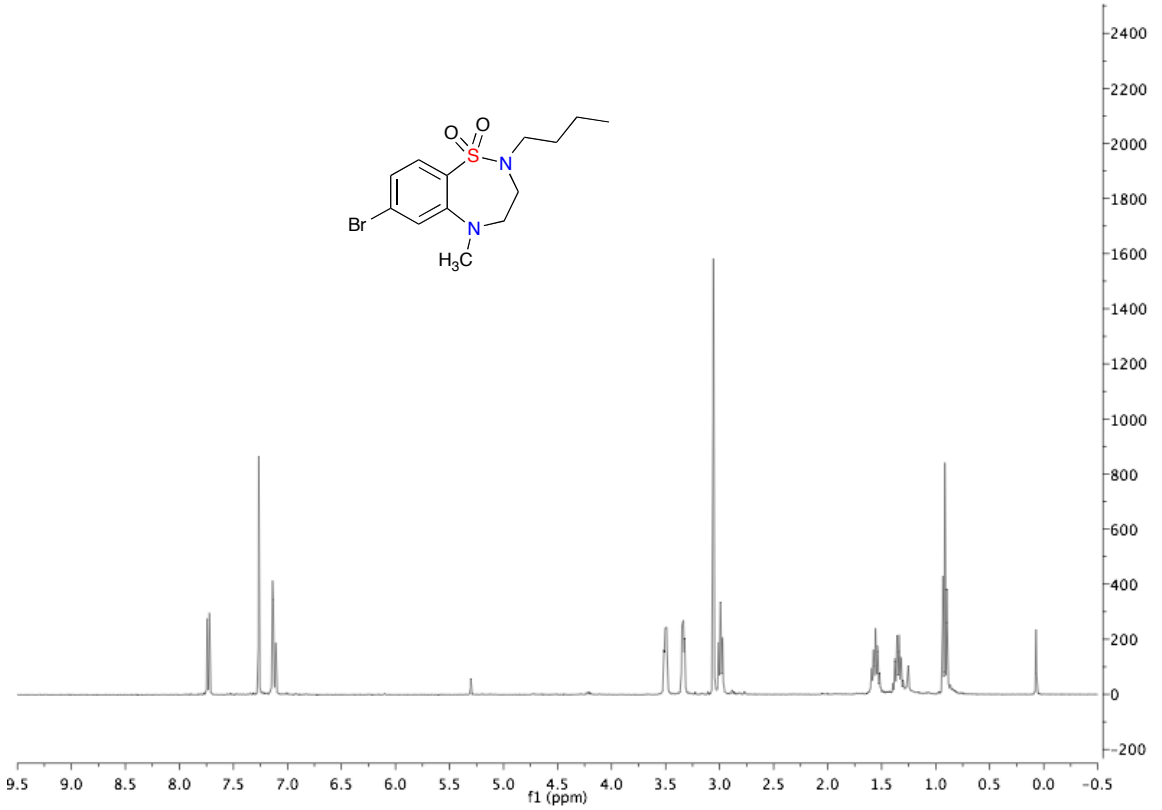


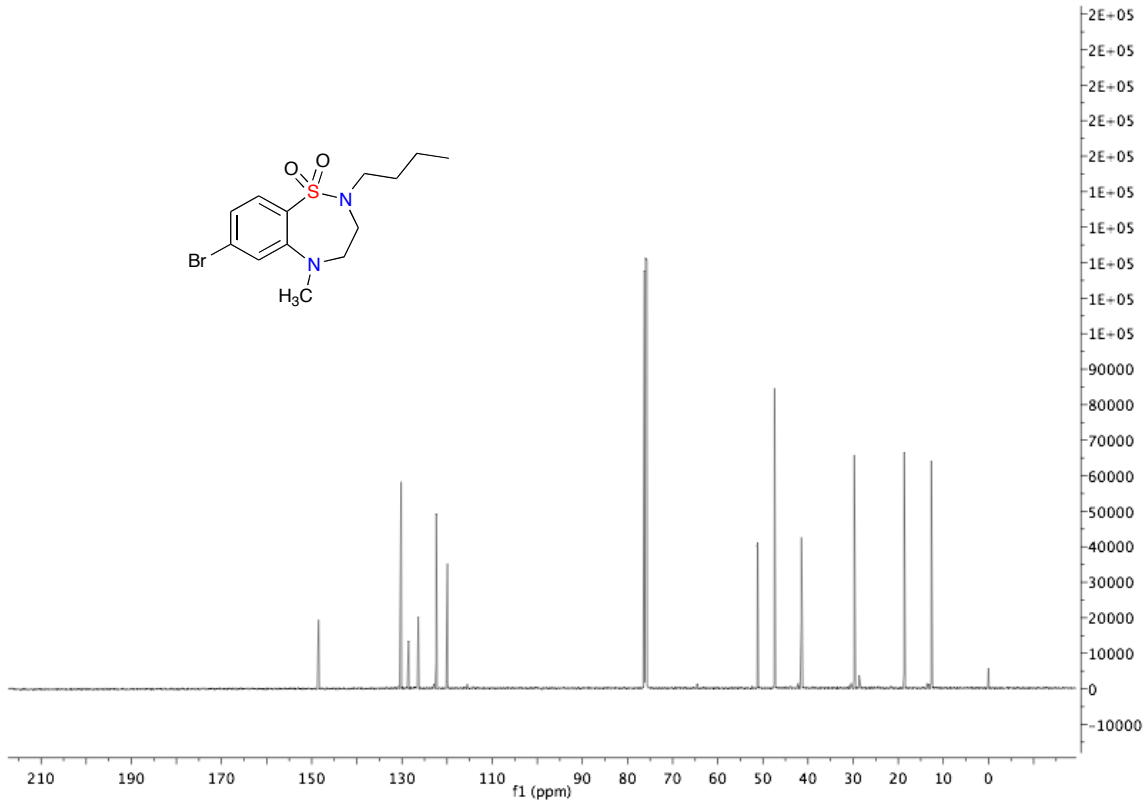
8-Chloro-2-(4-methoxybenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5] thiadiazepine 1,1-dioxide (3d).



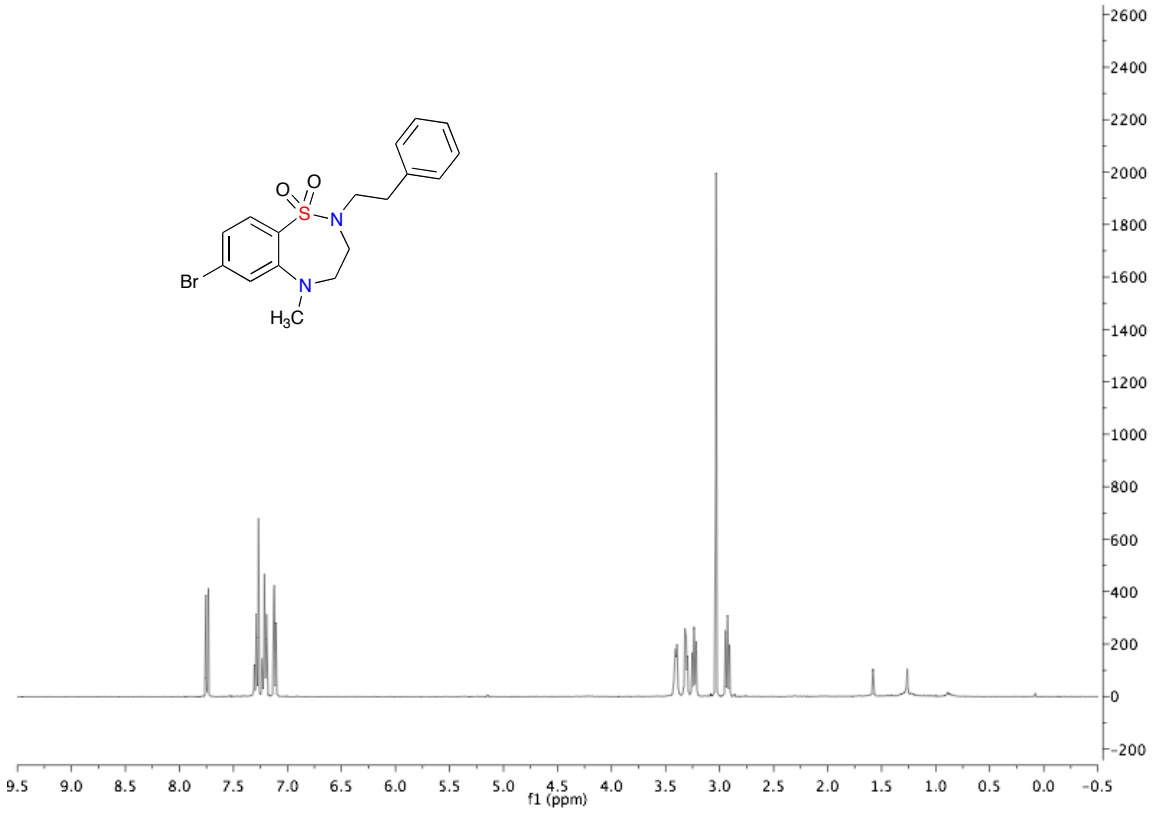


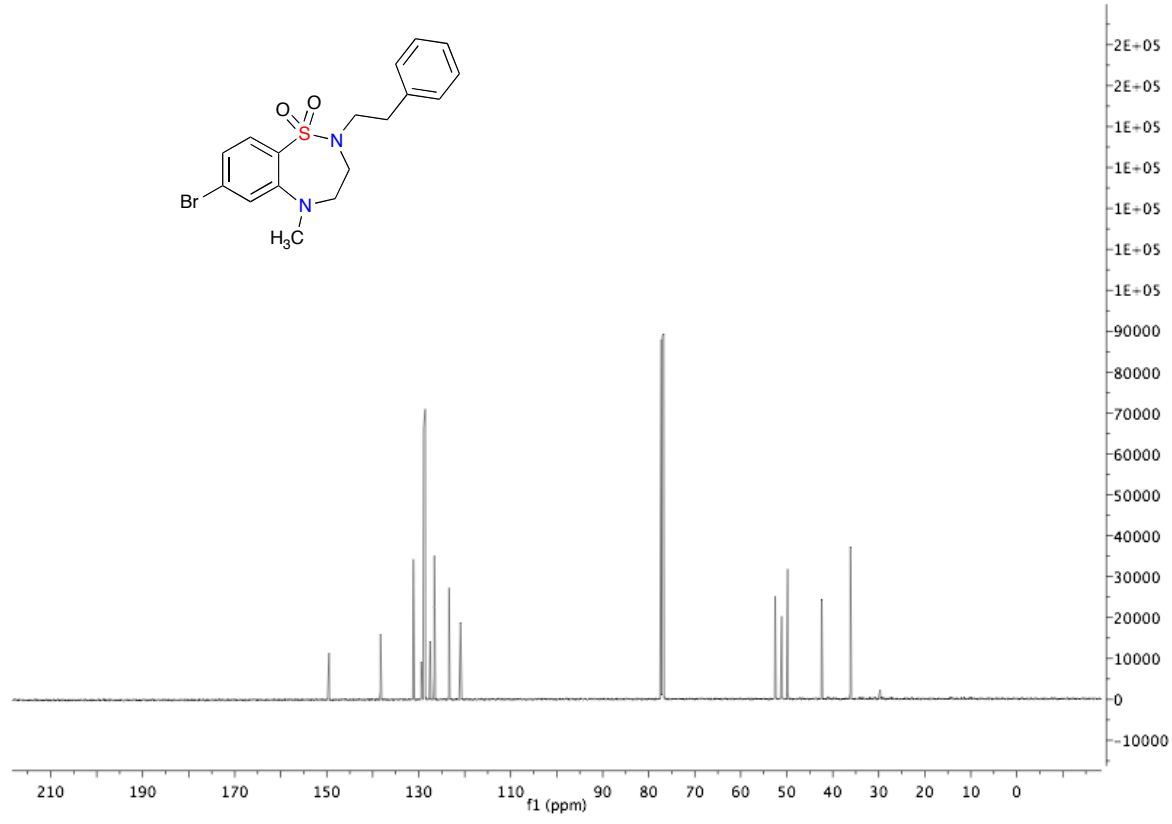
7-Bromo-2-butyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3e).



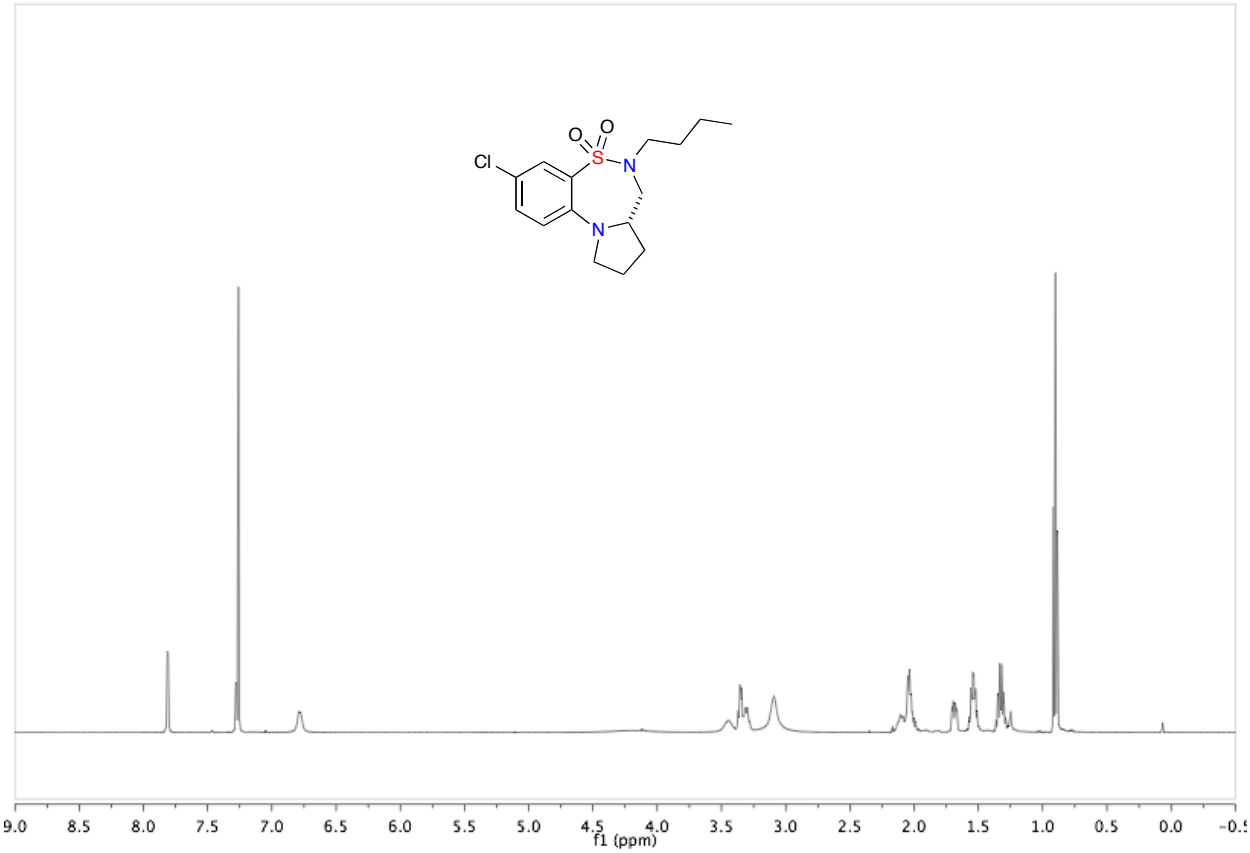


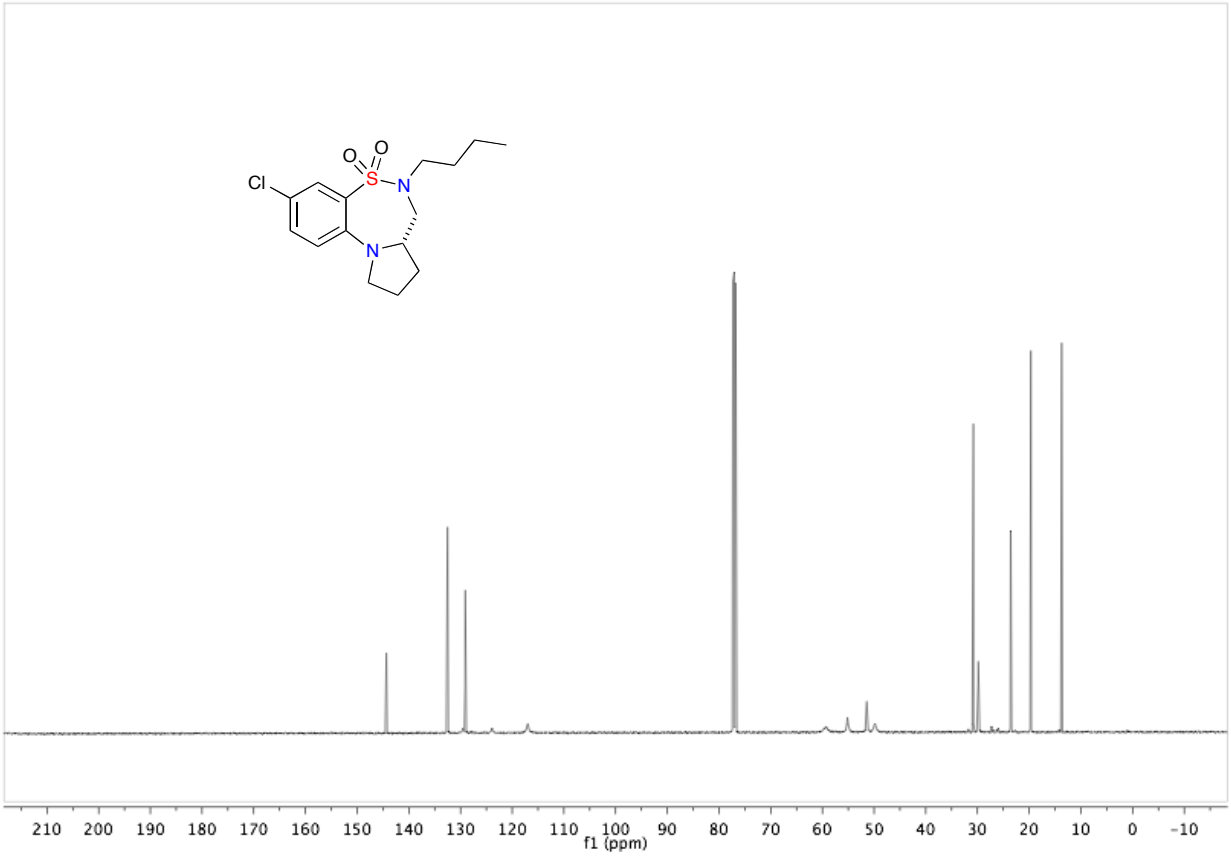
7-Bromo-5-methyl-2-phenethyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3f).



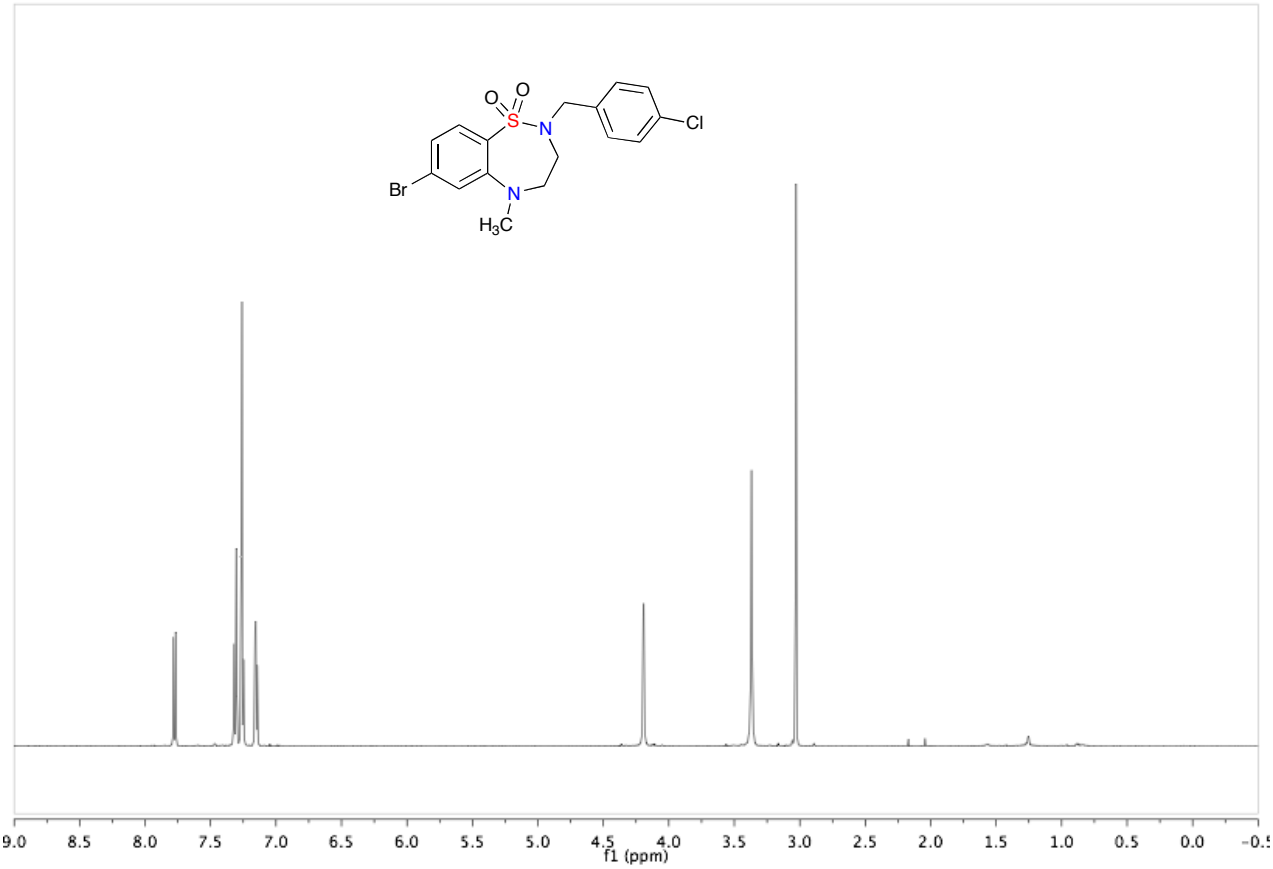


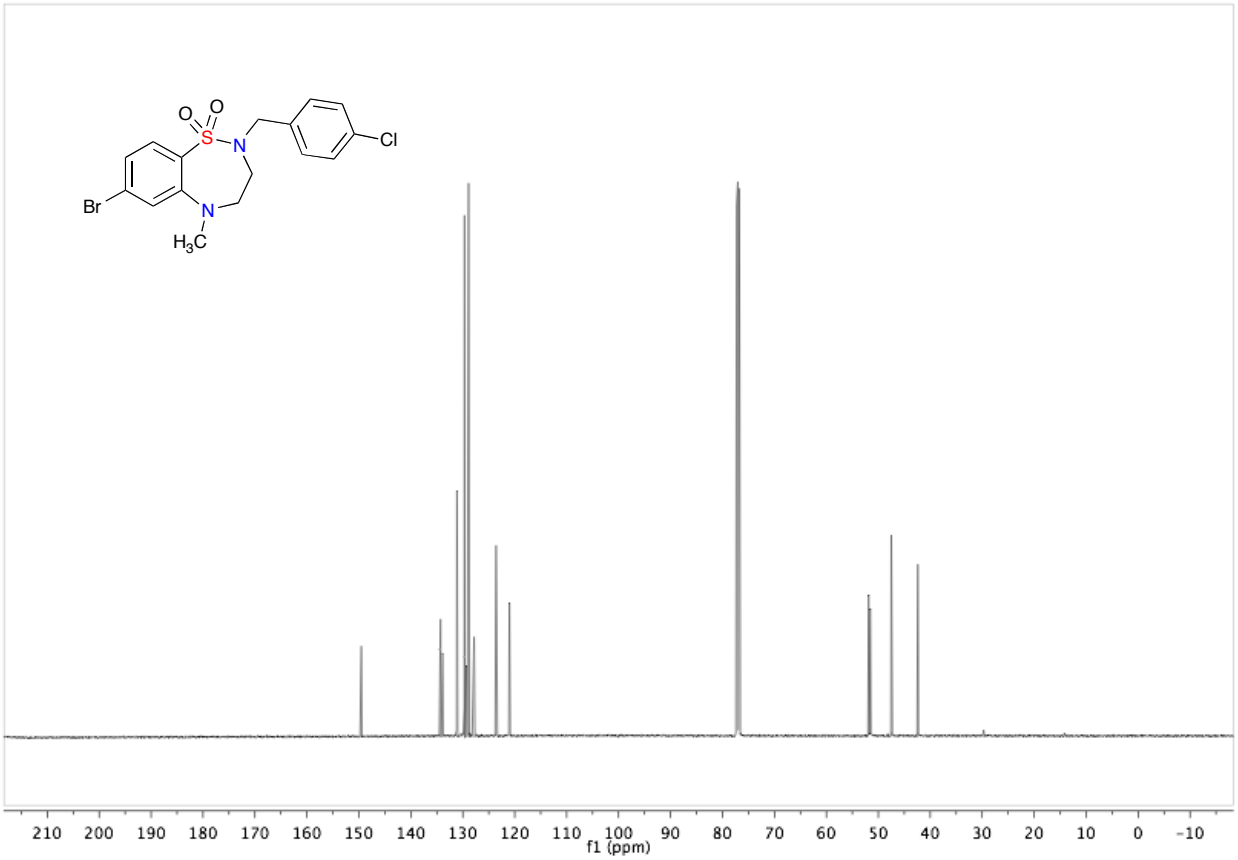
(*S*)-6-Butyl-3-chloro-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5] thiadiazepine 5,5-dioxide (3g).



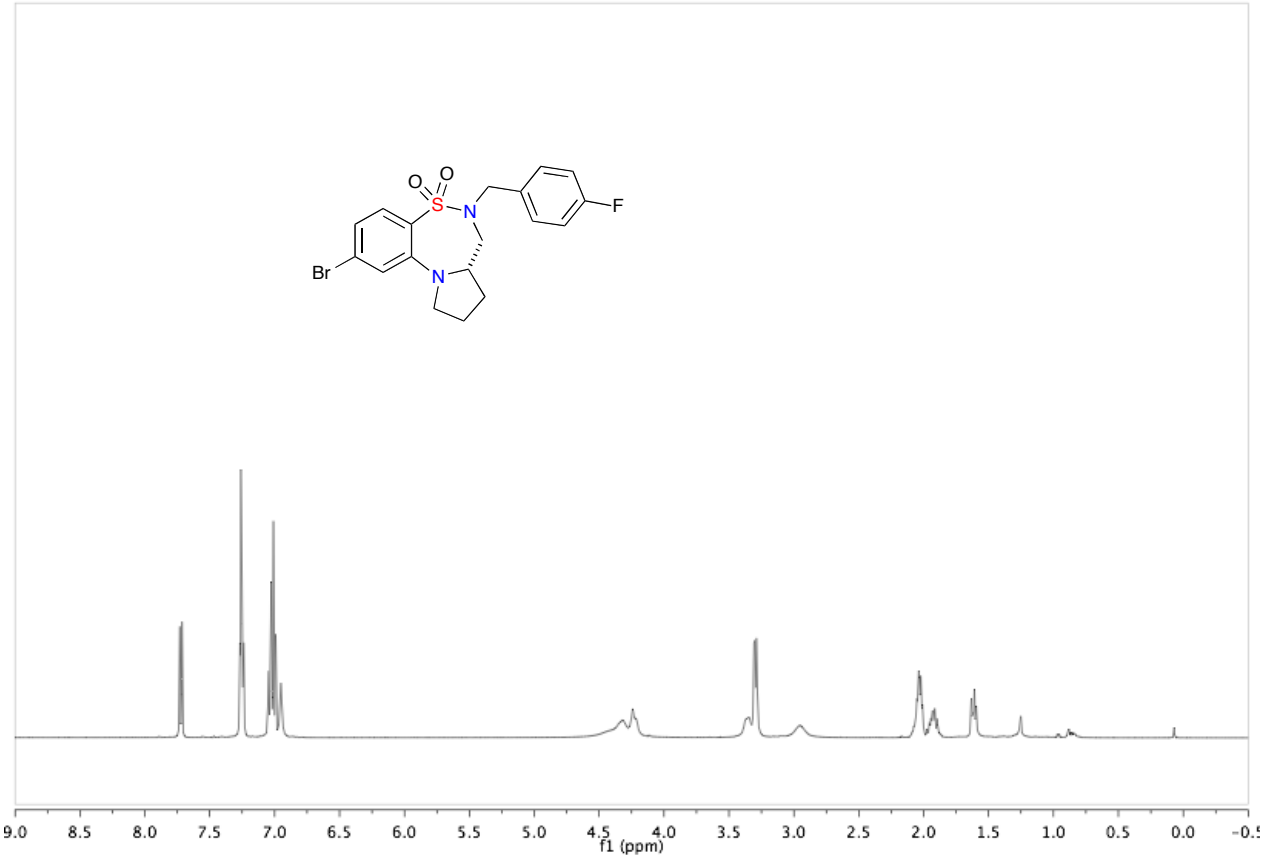


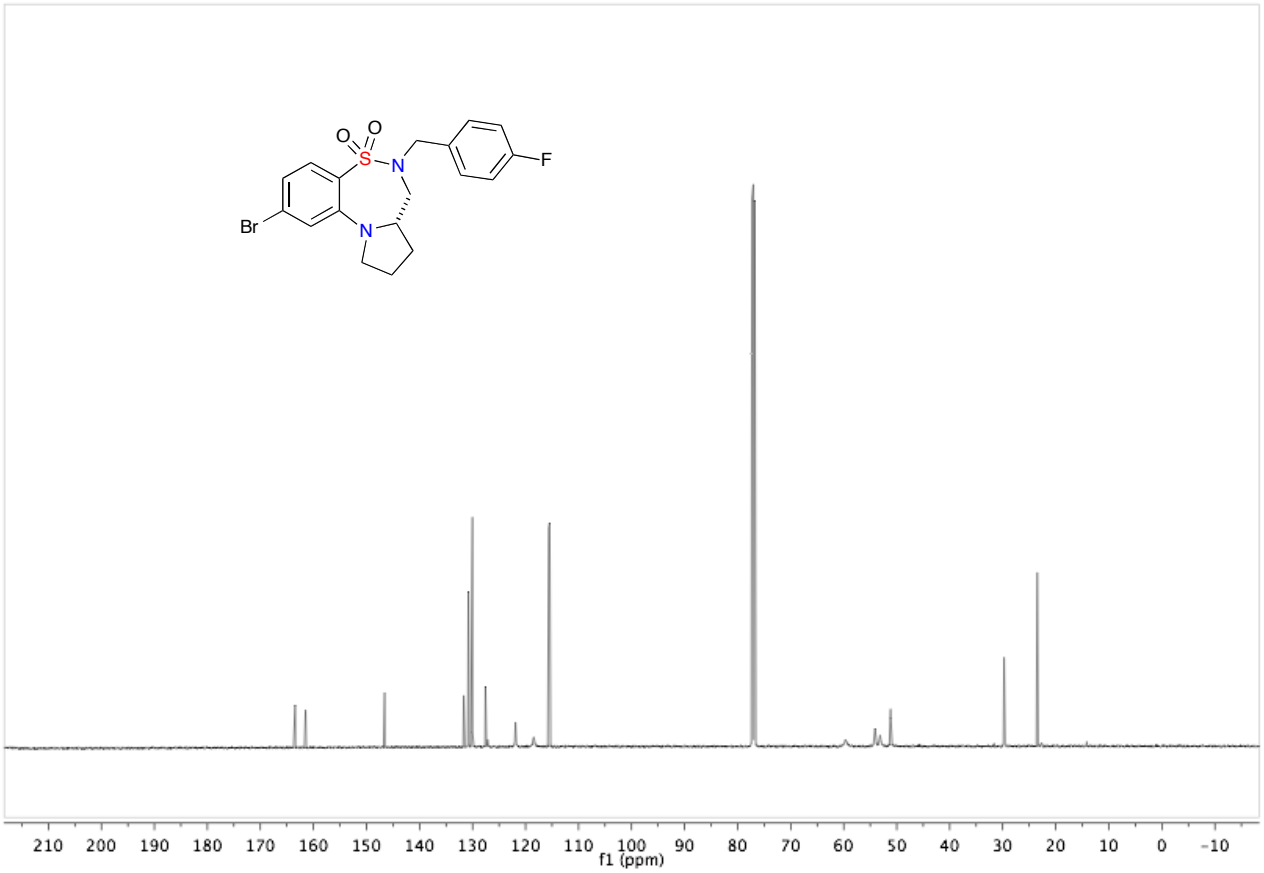
7-Bromo-2-(4-chlorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3h).



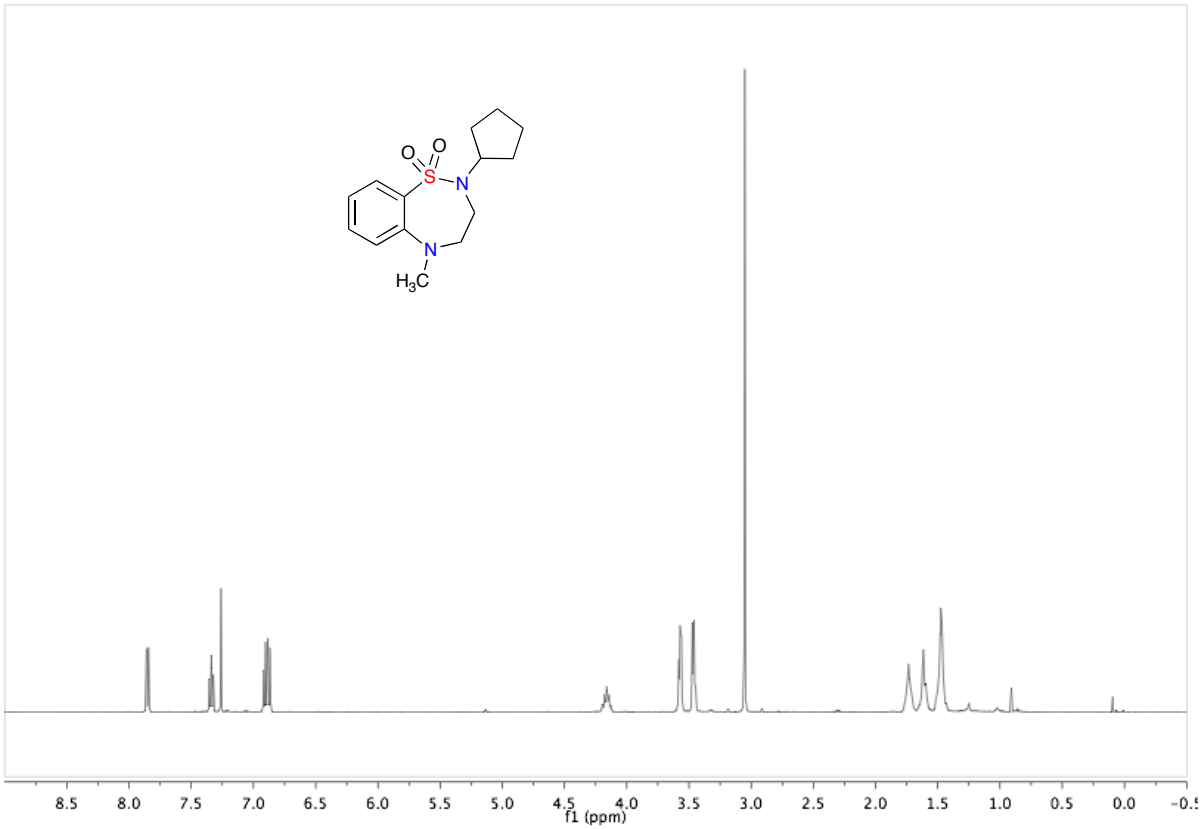


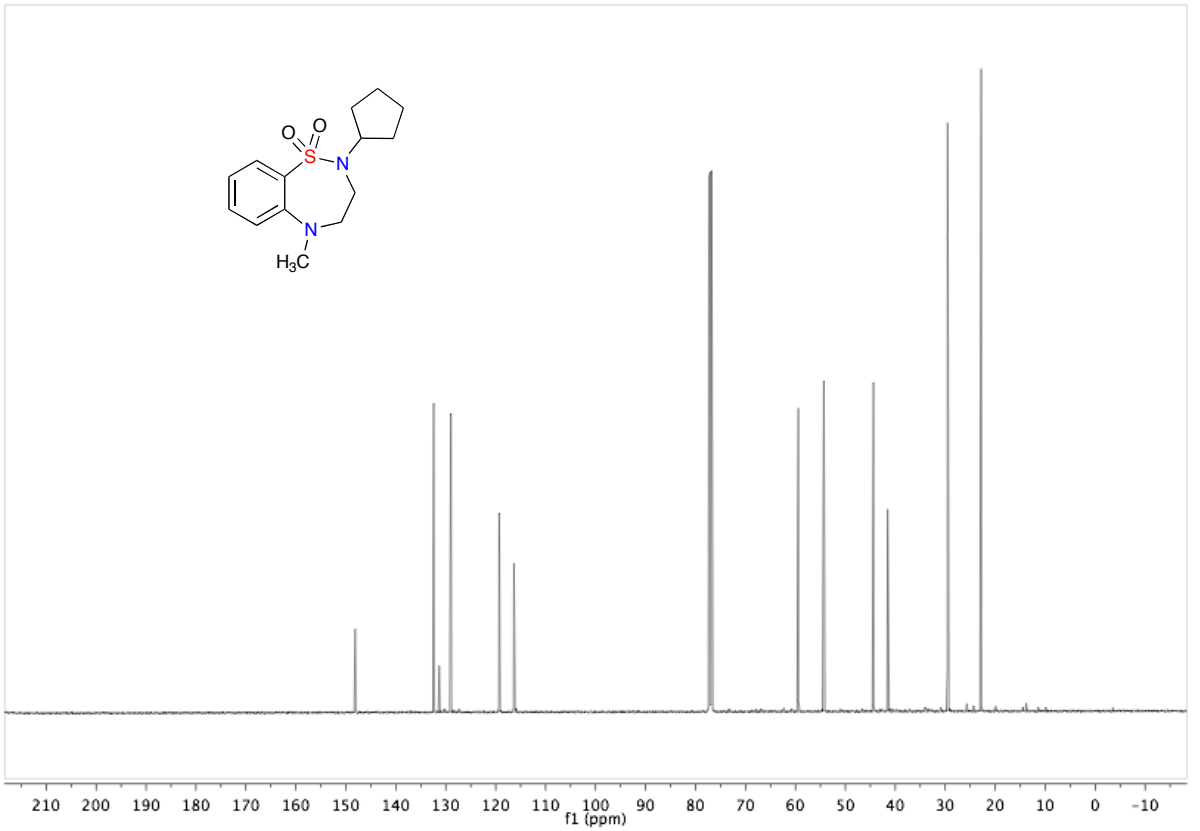
(*S*)-2-bromo-6-(4-fluorobenzyl)-6,7,7a,8,9,10-hexahydrobenzo[*f*]pyrrolo[2,1-*d*][1,2,5] thiadiazepine 5,5-dioxide (3i).



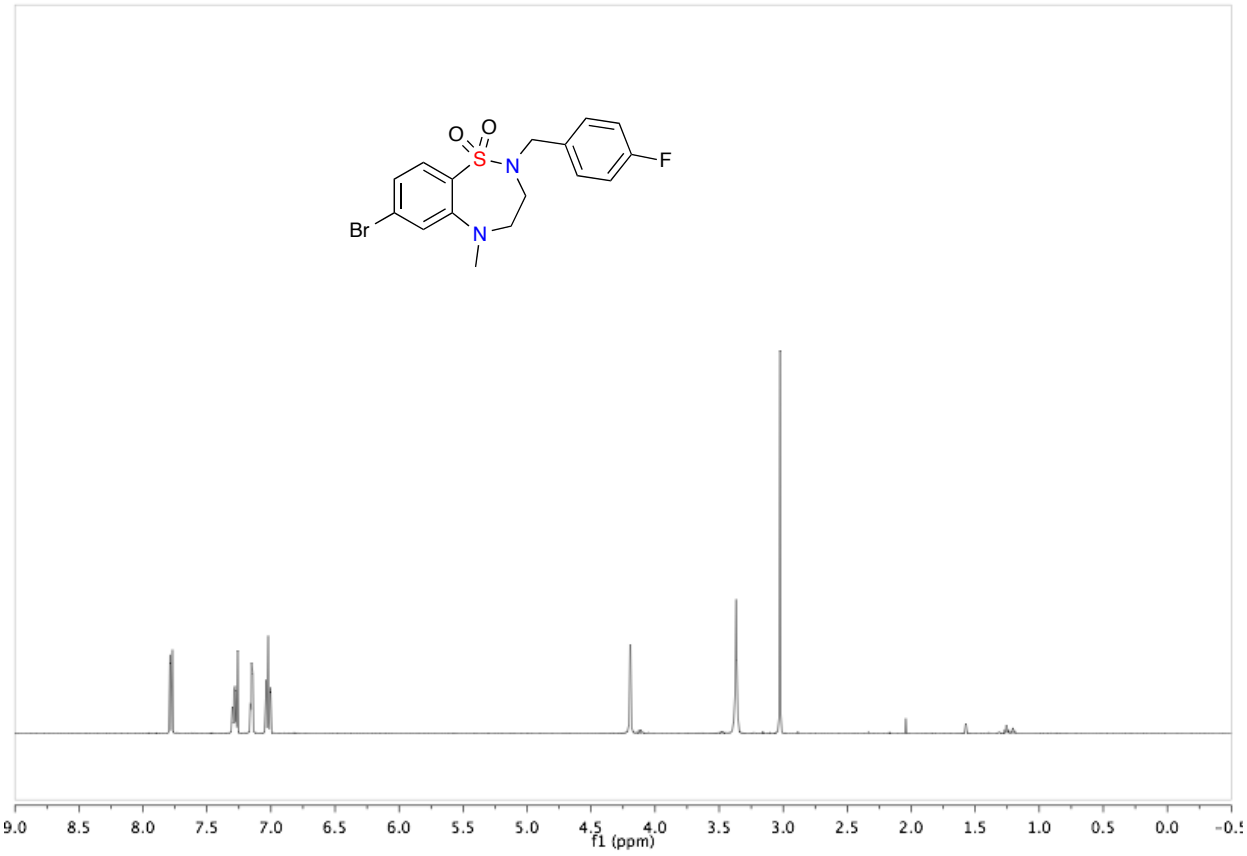


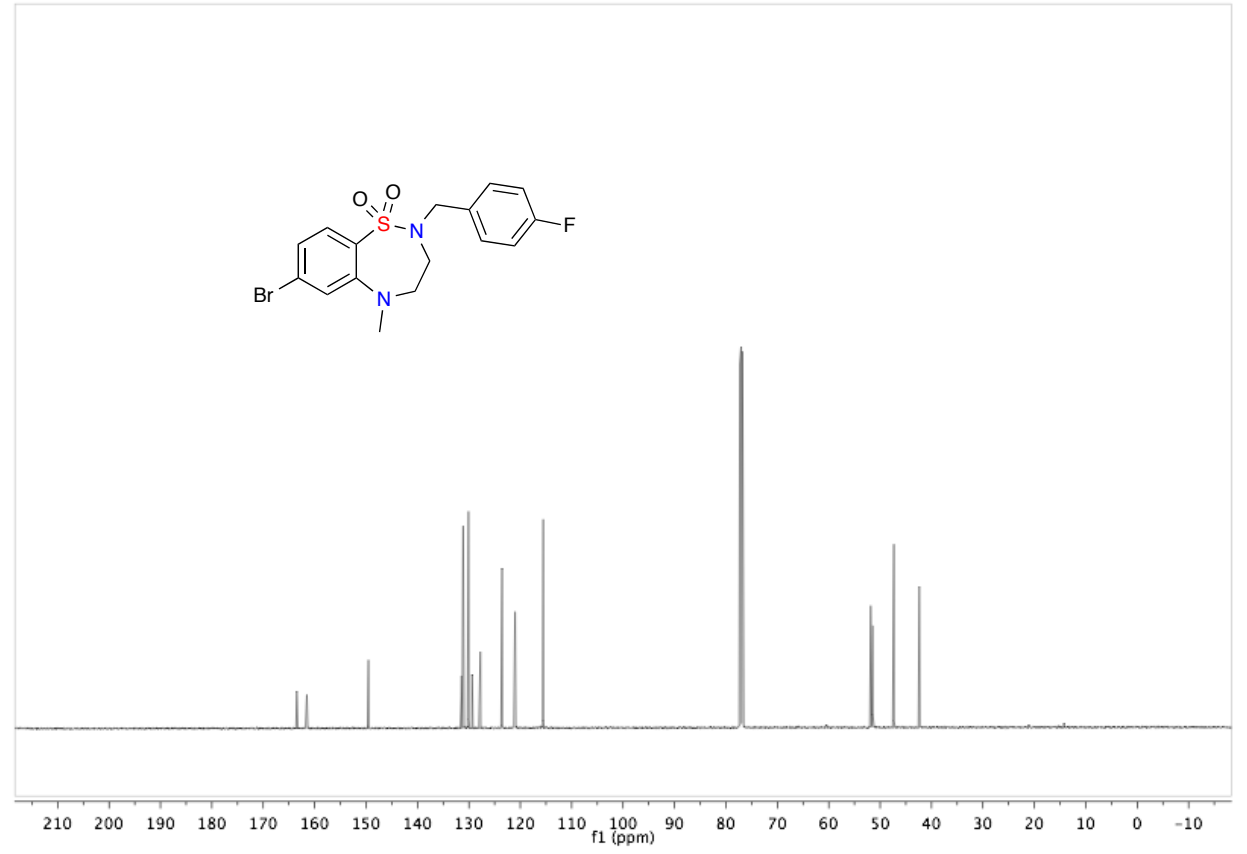
2-Cyclopentyl-5-methyl-2,3,4,5-tetrahydrobenzo[*f*][1,2,5]thiadiazepine 1,1-dioxide (3j).



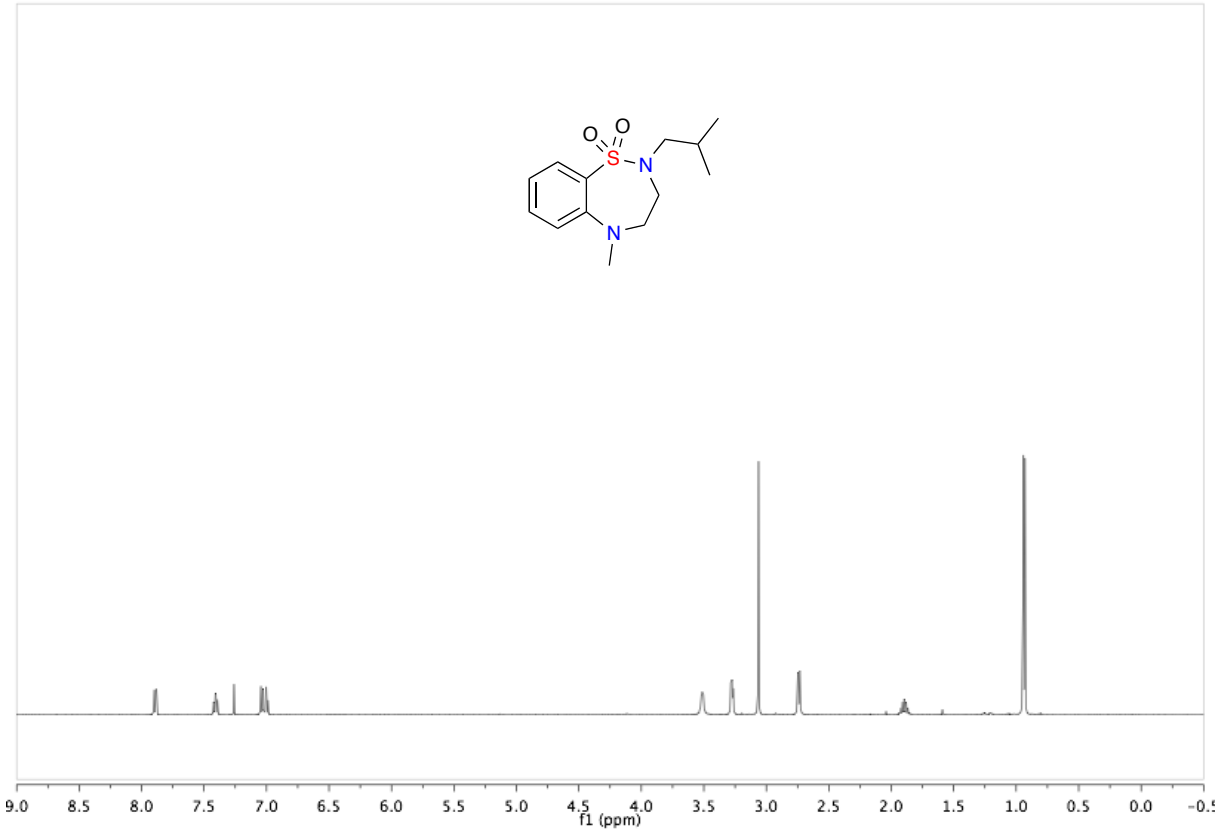


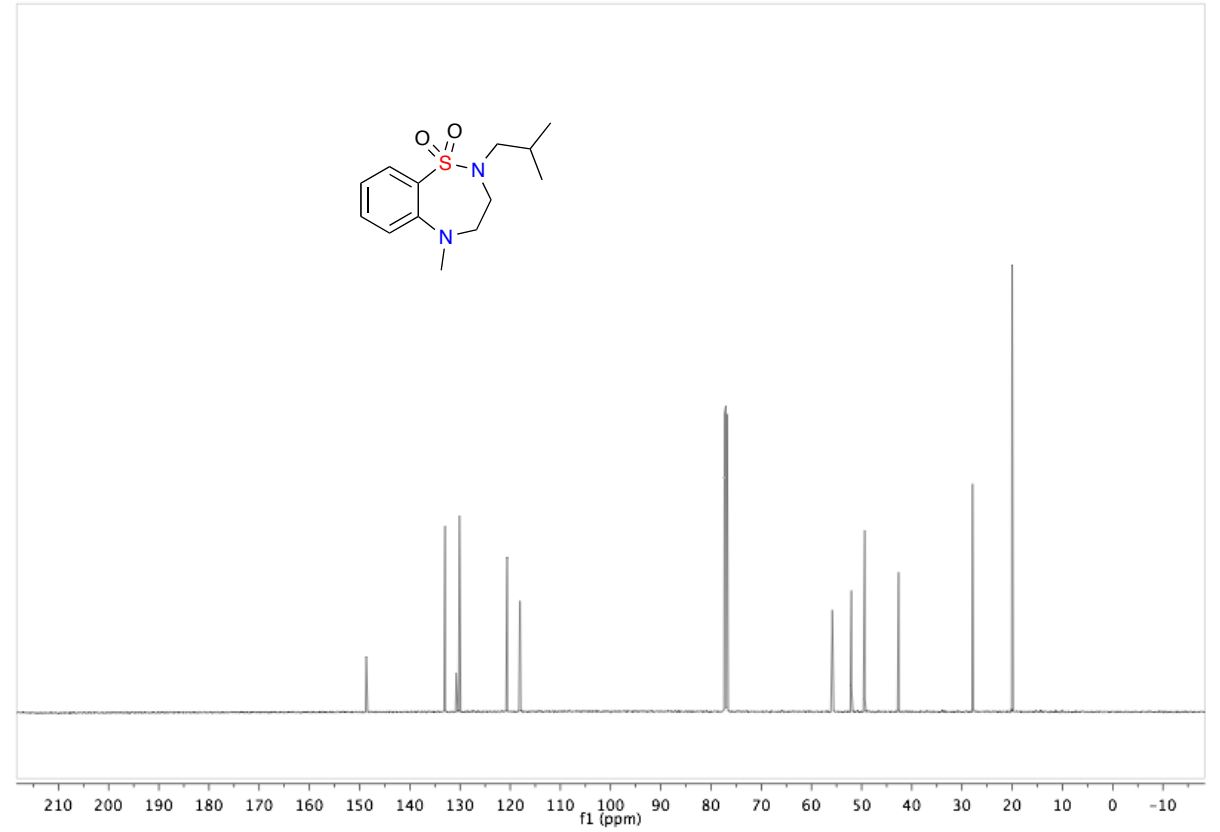
7-Bromo-2-(4-fluorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3k).



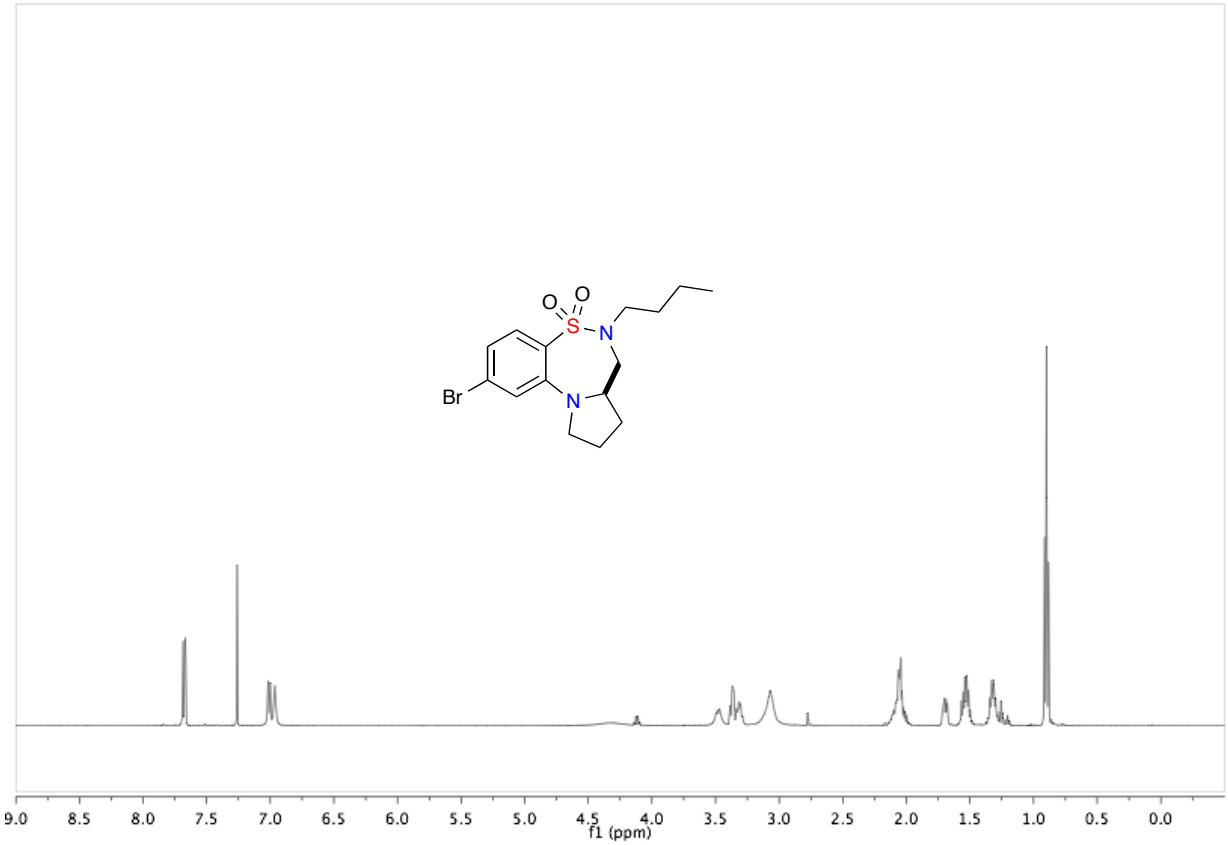


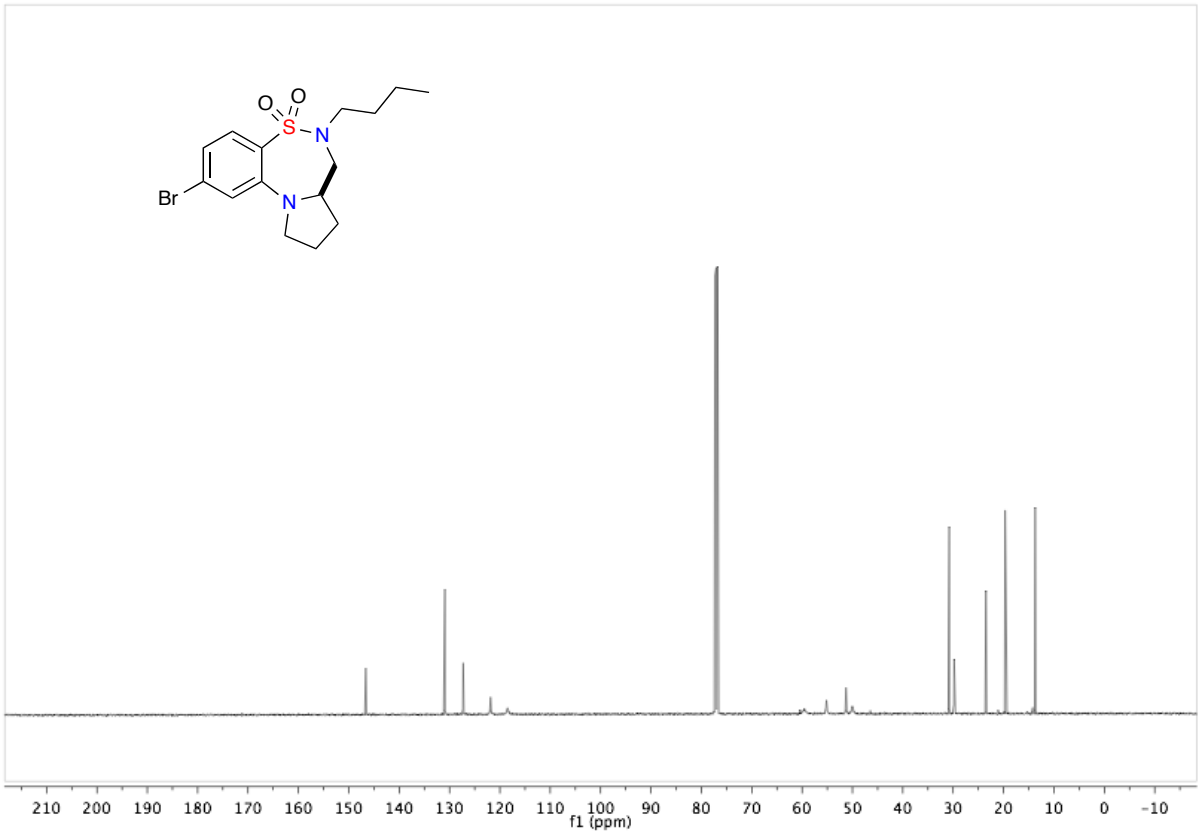
2-Isobutyl-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3l).





(*R*)-2-Bromo-6-butyl-6,7,7a,8,9,10-hexahydrobenzo[f]pyrrolo[2,1-d][1,2,5]thiadiazepine 5,5-dioxide (3m).





8-Chloro-2-(4-chlorobenzyl)-5-methyl-2,3,4,5-tetrahydrobenzo[f][1,2,5]thiadiazepine 1,1-dioxide (3n).