A Formal [4+4] Complementary Ambiphile Pairing (CAP) Reaction: A New Cyclization Pathway for ortho-Quinone Methides

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Supporting Information

Contents

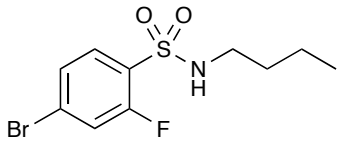
Experimental Section

General Methods. All reactions were carried out under argon in oven-dried or flame-dried glassware. THF and CH_2Cl_2 were purified by passage through a purification system (Solv-Tek) employing activated Al_2O_3. Flash column chromatography was performed with Merck silica gel (EM-9385-9, 230-400 mesh) or via the Biotage SP System with FLASH 12+ or FLASH 40+ cartridges. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5717, Merck). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise mentioned) on a 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).

General Procedure for preparation of α-fluorobenzene sulfonamide

To a vigorously stirred solution of amine (7.34 mmol, 2.0 equiv.) in CH_2Cl_2 (12.2 mL, 0.3 M) in a round bottom flask was added $NaHCO_3$ (3 equiv.) and H_2O (6.1 mL, 0.6 M). A solution of benzenesulfonyl chloride (1.0 g, 3.67 mmol) in CH_2Cl_2 (3.6 mL, 1 M) was added dropwise, and the reaction was stirred for 4-8 hours. Upon disappearance of sulfonyl chloride, 10% HCl (10 mL) was added and the reaction was stirred for 10 minutes. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), concentrated under reduced pressure and subjected to column chromatography (3:1, hexane:EtOAc) to afford the *o*-fluorobenzene sulfonamide.

4-bromo-*N*-butyl-2-fluorobenzenesulfonamide (1c)



Light yellow solid, 1.10 g (97%), mp 172-174 ºC.

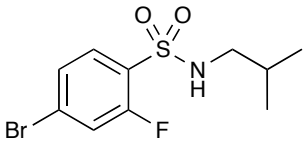
FTIR (thin film): 3261, 2923, 2850, 1577, 1560, 1448, 1369, 1326, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.73 (m, 1H), 7.44-7.37 (m, 2H), 4.91 (t, *J* = 5.9 Hz, 1H), 2.98 (dd, *J* = 13.4, 6.9 Hz, 2H), 1.49-1.41 (m, 2H), 1.29 (dq, *J* = 14.5, 7.3 Hz, 2H), 0.85 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (d, $J_{C\text{-}F}$ = 258.4 Hz), 131.4, 128.1 (d, $J_{C\text{-}F}$ = 9.1 Hz, 1H), 128.0 (d, $J_{C\text{-}F}$ = 3.8 Hz), 127.3 (d, $J_{C\text{-}F}$ = 13.8 Hz), 120.5 (d, $J_{C\text{-}F}$ = 24.4 Hz), 42.9, 31.5, 19.0, 13.4;

HRMS calculated for $C_{10}H_{12}FBrNO_2S$ $(M\text{-}H)^+$ 307.9756; found 307.9737 (TOF MS ES+).

4-bromo-2-fluoro-*N*-isobutylbenzenesulfonamide (1d)



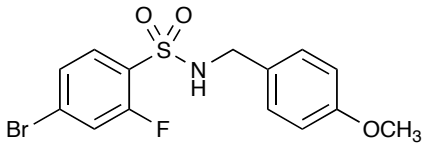
White Solid 1.3 g (92%), mp 149-150ºC.

FTIR (thin film): 3298, 2960, 2873, 1589, 1569, 1469, 1396, 1334, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.74 (m, 1H), 7.45-7.39 (m, 2H), 4.78 (t, *J* = 6.1 Hz, 1H), 2.79 (t, *J* = 6.6 Hz, 2H), 1.73 (dp, *J* = 13.4, 6.7 Hz, 1H), 0.89 (d, *J* = 6.7 Hz, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (d, $J_{C\text{-}F}$ = 258.2 Hz), 131.3, 128.1 (d, $J_{C\text{-}F}$ = 9.2 Hz), 127.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 127.3 (d, $J_{C\text{-}F}$ = 13.9 Hz), 120.6 (d, $J_{C\text{-}F}$ = 24.4 Hz), 50.6, 28.5, 19.7;
HRMS calculated for $C_{10}H_{12}FBrNO_2S$ $(M\text{-}H)^+$ 307.9756; found 307.9727 (TOF MS ES+).

4-bromo-2-fluoro-*N*-(4-methoxybenzyl)benzenesulfonamide (1e)



White Solid 1.30 g (96%), mp 107-108 ºC.

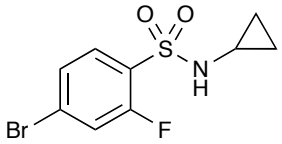
FTIR (thin film): 3270, 2931, 1589, 1492, 1357, 1348, 1321, 1251, 1226, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.39 (ddd, *J* = 8.4, 1.8, 0.6 Hz, 1H), 7.31 (dd, *J* = 9.5, 1.8 Hz, 1H), 7.10-7.05 (m, 2H), 6.78-6.73 (m, 2H), 5.02 (t, *J* = 6.0 Hz, 1H), 4.13 (d, *J* = 6.1 Hz, 2H), 3.77 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 158.3 (d, $J_{C\text{-}F}$ = 258.2), 131.3, 129.3, 128.1 (d, $J_{C\text{-}F}$ = 9.3 Hz), 127.8 (d, $J_{C\text{-}F}$ = 3.7 Hz), 127.6, 127.5 (d, $J_{C\text{-}F}$ = 13.1 Hz), 120.5 (d, $J_{C\text{-}F}$ = 24.4 Hz), 114.0, 55.3, 47.0;

HRMS calculated for $C_{14}H_{12}FBrNO_3S$ $(M\text{-}H)^+$ 371.9705; found 371.9699 (TOF MS ES+).

4-bromo-*N*-cyclopropyl-2-fluorobenzenesulfonamide (1f)



White Solid 1.01 g (94%), mp 88-89 ºC.

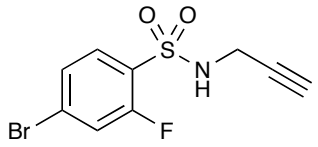
FTIR (thin film): 3286, 3093, 3020 1589, 1568, 1469, 1400, 1349, 1330, 1137 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.8 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.46 (ddd, *J* = 8.4, 1.8, 0.7 Hz, 1H), 7.41 (dd, *J* = 9.4, 1.8 Hz, 1H), 5.28 (d, *J* = 14.1 Hz, 1H), 2.26 (ttd, *J* = 6.7, 3.5, 1.3 Hz, 1H), 0.68-0.63 (m, 2H), 0.60 (tdd, *J* = 7.6, 5.9, 1.6 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4 (d, $^1J_{C\text{-}F}$ = 259.2 Hz), 131.8, 128.5 (d, $J_{C\text{-}F}$ = 9.2 Hz), 128.0 (d, $J_{C\text{-}F}$ = 3.8 Hz), 126.8 (d, $J_{C\text{-}F}$ = 13.7 Hz), 120.6 (d, $J_{C\text{-}F}$ = 24.4 Hz), 24.2, 6.1;

HRMS calculated for $C_9H_9FNO_2SNa$ $(M\text{-}H)^+$ 291.9443; found 291.9436 (TOF MS ES+).

4-bromo-2-fluoro-*N*-(prop-2-ynyl)benzenesulfonamide (1g)



White Solid 1.02g (88%), mp 104-105 ºC.

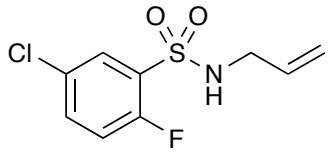
FTIR (thin film): 3248, 2128, 1598, 1571, 1460, 1400, 1361, 1332, 1161 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.77 (m, 1H), 7.45 (ddd, *J* = 8.3, 1.8, 0.6, 1H), 7.42 (dd, J= 9.4, 1.8, 1H), 4.99 (t, *J* = 5.9, 1H), 3.93 (dd, *J* = 6.2, 2.5, 2H), 2.06 (t, *J* = 2.5, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7 (d, $J_{C\text{-}F}$ = 258.6 Hz), 131.2, 128.61 (d, $J_{C\text{-}F}$ = 9.3 Hz), 127.9 (d, $J_{C\text{-}F}$ = 3.7 Hz), 127.2 (d, $J_{C\text{-}F}$ = 13.8 Hz), 120.5 (d, $J_{C\text{-}F}$ = 24.3 Hz), 77.1, 73.1, 32.9;

HRMS calculated for $C_9H_6FNO_2S$ $(M\text{-}H)^+$ 289.9287; found 289.9281 (TOF MS ES+).

***N*-allyl-5-chloro-2-fluorobenzenesulfonamide (1h)**



White Solid 0.82 g (89 %), mp 81-82 ºC.

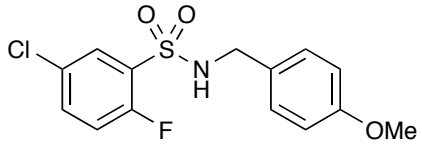
FTIR (thin film): 3292, 3095, 3076, 1649, 1596, 1467, 1429, 1334, 1255, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 6.1, 2.7 Hz, 1H), 7.53 (ddd, *J* = 8.8, 4.3, 2.7 Hz, 1H), 7.17 (t, *J* = 9.1 Hz, 1H), 5.73 (ddt, *J* = 16.1, 10.3, 5.9 Hz, 1H), 5.20 (ddd, *J* = 17.1, 2.6, 1.5 Hz, 1H), 5.13 (dd, *J* = 10.2. 1.2 Hz, 1H), 4.81 (s, 1H), 3.69 (t, *J* = 6.0 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2 (d, $J_{C\text{-}F}$ = 254.0 Hz), 134.7 (d, $J_{C\text{-}F}$ = 8.6 Hz), 132.4, 130.0, 129.9 (d, $J_{C\text{-}F}$ = 3.6 Hz), 129.7 (d, $J_{C\text{-}F}$ = 15.4 Hz), 118.3 (d, $J_{C\text{-}F}$ = 23.3 Hz), 118.2, 45.8;

HRMS calculated for $C_9H_8ClFNO_2S$ $(M\text{-}H)^+$ 247.9948; found 247.9941 (TOF MS ES+).

5-chloro-2-fluoro-*N*-(4-methoxybenzyl)benzenesulfonamide (1i)



White Solid 1.05 g (87%), mp 41-42 ºC.

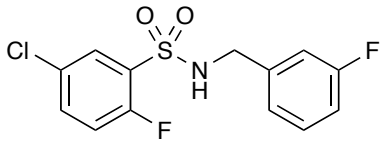
FTIR (thin film): 3299, 3097, 1616, 1593, 1471, 1467, 1388, 1338, 1166 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 2.7, 6.1 Hz, 1H), 7.45 (ddd, *J* = 2.7, 4.2, 8.8 Hz, 1H), 7.11-7.05 (m, 3H), 6.76-6.71 (m, 2H), 5.23 (t, *J* = 6.0 Hz, 1H), 4.15 (d, *J* = 6.1 Hz, 2H), 3.75 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 157.0 (d, $J_{C\text{-}F}$ = 254.0 Hz), 134.3 (d, $J_{C\text{-}F}$ = 8.6 Hz), 129.8, 129.7 (d, $J_{C\text{-}F}$ = 12.5 Hz), 129.6, 129.3, 127.4, 118. 1 (d, $J_{C\text{-}F}$ = 23.2 Hz), 113.9, 55.2, 46.9;

HRMS calculated for $C_{14}H_{12}ClFNO_3S$ $(M\text{-}H)^+$ 328.0210; found 328.0220 (TOF MS ES+).

5-chloro-2-fluoro-*N*-(3-fluorobenzyl)benzenesulfonamide (1j)



White Solid 0.96 g (81%), mp 81-82 ºC.

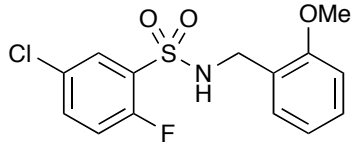
FTIR (thin film): 3298, 2941, 2358, 1602, 1494, 1467, 1340, 1310, 1166 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 6.1, 2.7 Hz, 1H), 7.51-7.46 (m, 1H), 7.25-7.21 (m, 1H), 7.13-7.09 (m, 1H), 6.99 (dd, *J* = 11.5, 3.9 Hz, 1H), 6.95-6.89 (m, 2H), 5.23 (t, *J* = 6.1 Hz, 1H), 4.23 (d, *J* = 6.3 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.71 (d, $J_{C\text{-}F}$ = 247.1 Hz), 157.02 (d, $J_{C\text{-}F}$ = 254.1 Hz), 138.1 (d, $J_{C\text{-}F}$ = 7.2 Hz), 134.65 (d, $J_{C\text{-}F}$ = 8.6 Hz), 130.20 (d, $J_{C\text{-}F}$ = 8.2 Hz), 129.8, 129.8, 129.5 (d, $J_{C\text{-}F}$ = 15.4 Hz), 123.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 118.24 (d, $J_{C\text{-}F}$ = 23.1 Hz) 46.7 (d, $J_{C\text{-}F}$ = 1.5 Hz).

HRMS calculated for $C_{13}H_9ClF_2NO_2S$ $(M\text{-}H)^+$ 316.0011; found 316.0013 (TOF MS ES+).

5-chloro-2-fluoro-*N*-(2-methoxybenzyl)benzenesulfonamide (1k)



White Solid 1.10 g (90%), mp 99-101 ºC.

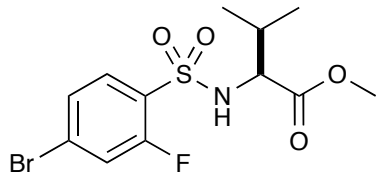
FTIR (thin film): 3298, 2941, 2358, 1602, 1494, 1467, 1340, 1310, 1166 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 6.1, 2.7 Hz, 1H), 7.31 (ddd, *J* = 8.8, 4.3, 2.7 Hz, 1H), 7.12 (td, *J* = 8.1, 1.7 Hz, 1H), 6.92 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.87-6.82 (m, 1H), 6.71 (td, *J* = 7.4, 0.9 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 5.59 (t, *J* = 6.3 Hz, 1H), 4.25 (d, *J* = 6.5 Hz, 2H), 3.78 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1, 157.0 (d, $J_{C\text{-}F}$ = 252.7 Hz), 134.0 (d, $J_{C\text{-}F}$ Hz, = 8.6), 130.0, 129.9 (d, $J_{C\text{-}F}$ = 15.7 Hz), 129.7, 129.5, 129.4 (d, $J_{C\text{-}F}$ = 3.6 Hz), 122.9, 120.2, 117.6 (d, *J* = 23.3 Hz), 109.8, 55.0, 44.6.

HRMS calculated for $C_{14}H_{12}ClFNO_3S$ $(M\text{-}H)^+$ 328.0210; found 328.0217 (TOF MS ES+).

(*S*)-methyl 2-(4-bromo-2-fluorophenylsulfonamido)-3-methylbutanoate (1-l)



White Solid 1.24 g (92 %), mp 71-72 ºC.

$[\alpha]_D^{20}$ + 53.8 (*c* = 0.52, $CHCl_3$)

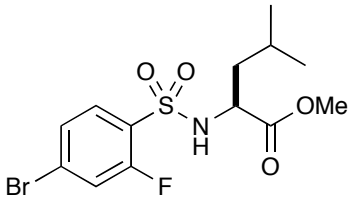
FTIR (thin film): 3288, 2968, 1739, 1589, 1569, 1471, 1398, 1350, 1172 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.68 (m, 1H), 7.41-7.37 (m, 2H), 5.39 (d, *J* = 9.9 Hz, 1H), 3.87 (dd, *J* = 5.0, 9.9 Hz, 1H), 3.53 (s, 3H), 2.15-2.05 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ δ 171.4 (s, 1H), 158.6 (d, $J_{C\text{-}F}$ = 259.8, Hz), 130.9, 128.4 (d, $J_{C\text{-}F}$ = 9.2 Hz), 127.7(d, $J_{C\text{-}F}$ = 3.8 Hz), 127.2 (d, $J_{C\text{-}F}$ = 14.1 Hz), 120.5 ($J_{C\text{-}F}$ = 24.4 Hz), 61.3, 52.3, 31.4, 18.9, 17.3;

HRMS calculated for $C_{12}H_{14}FBrNO_4S$ $(M\text{-}H)^+$ 365.9811; found 365.9800 (TOF MS ES+).

(*S*)-methyl 2-(4-bromo-2-fluorophenylsulfonamido)-4-methylpentanoate (1m)



White Solid 1.31g (94%), mp 82-83 ºC.

FTIR (thin film): 3282, 3093, 2956, 1743, 1589, 1569, 1471, 1398, 1350, 1170 cm^{-1}

$[\alpha]_D^{20}$ + 35.0 (*c* = 0.60, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.69 (m, 1H), 7.40 (ddd, *J* = 9.6, 5.3, 1.1 Hz, 2H), 5.32 (d, *J* = 9.9 Hz, 1H), 4.06 (dt, *J* = 9.7, 7.4 Hz, 1H), 3.51 (s, 3H), 1.85-1.74 (m, 1H), 1.54 (t, *J* = 7.2 Hz, 2H), 0.91 (dd, *J* = 6.6, 4.0 Hz, 6H);

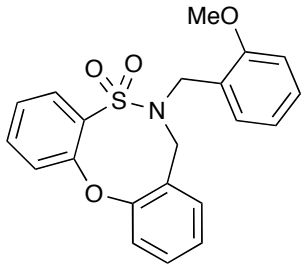
^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 158.7 ($J_{C\text{-}F}$ = 259.6 Hz), 130.9, 128.4 ($J_{C\text{-}F}$, *J* = 9.2 Hz), 127.7 ($J_{C\text{-}F}$, *J* = 3.8 Hz), 127.2 ($J_{C\text{-}F}$, *J* = 14.1 Hz), 120.5 (d, *J* = 24.3 Hz), 54.6, 52.4, 42.1, 24.3, 22.7, 21.3;

HRMS calculated for $C_{13}H_{14}FBrNO_4S$ $(M\text{-}H)^+$ 379.9967; found 379.9959 (TOF MS ES+).

General procedure for [4+4] reaction

A flame-dried vial was charged with the sulfonamide (0.090 g, 0.29 mmol), *o*-silyloxy benzyl acetate (0.165 g, 0.584 mmol), THF (0.5 M, 0.58 mL) and TBAF (0.88 mmol, 0.88 mL). The vial was quickly sealed and stirred for 30 minutes under *mW* irradiation at 100 ºC. Upon completion of the reaction, the mixture was concentrated under reduced pressure and subjected to column chromatography (6:1 hexane:EtOAc) to afford the product as a white solid.

6-(2-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2a)



White solid, 92 mg (71%), mp 173-174 ºC.

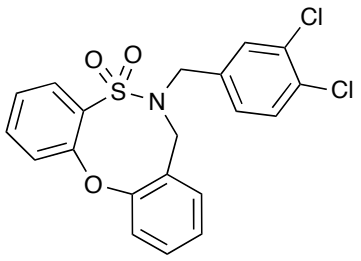
FTIR (thin film): 3064, 2926, 2358, 2341, 1610, 1581, 1478, 1452, 1353, 1340 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.62 (tdd, *J* = 9.1, 8.2, 1.4 Hz, 3H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.39 (td, *J* = 7.8, 1.7 Hz, 1H), 7.29 (td, *J* = 7.6, 1.1 Hz, 2H), 7.13 (td, *J* = 7.4, 1.0 Hz, 1H), 7.04 (td, *J* = 7.5, 0.9 Hz, 1H), 6.99 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.57 (dd, *J* = 15.2, 1.3 Hz, 1H), 4.10 (d, *J* = 16.0 Hz, 1H), 3.81 (d, *J* = 15.2 Hz, 1H), 3.73 (d, *J* = 16.0 Hz, 1H), 3.68 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3, 157.1, 155.5, 134.4, 134.3, 131.7, 130.4, 130.3, 130.2, 129.2, 128.8, 125.2, 124.1, 123.6, 122.2, 120.8, 110.1, 55.0, 47.6, 42.8;

HRMS calculated for $C_{21}H_{19}BrNO_4S$ $(M+Na)^+$ 404.0933; found 404.0927 (TOF MS ES+).

6-(3,4-dichlorobenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2b)



White solid, 91mg, (73%), mp 134-136 ºC.

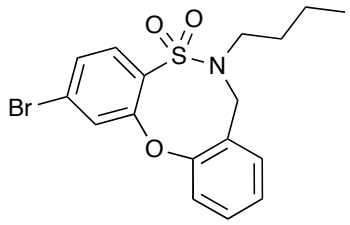
FTIR (thin film): 3071, 2358, 2341, 1577, 1488, 1460, 1400, 1338, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.63 (dtd, *J* = 9.9, 8.2, 1.4 Hz, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 11.8, 5.0 Hz, 2H), 7.39 (d, *J* = 1.5 Hz, 1H), 7.30 (td, *J* = 7.7, 1.3 Hz, 1H), 7.20 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.18-7.14 (m, 1H), 7.00 (dd, *J* = 7.4, 1.6 Hz, 1H), 5.56 (dd, *J* = 15.3, 1.2 Hz, 1H), 4.35 (d, *J* = 15.2 Hz, 1H), 3.68 (d, *J* = 15.3 Hz, 1H), 3.19 (d, *J* = 15.2 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 155.3, 135.7, 134.7, 133.9, 132.9, 132.1, 131.3, 130.7, 130.6, 130.4, 130.1, 129.5, 127.6, 125.6, 125.4, 124.1, 122.5, 47.6, 47.2;

HRMS calculated for $C_{12}H_{14}FBrNO_4S$ $(M-H)^+$ 365.9811; found 365.9800 (TOF MS ES+).

2-bromo-6-butyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2c)



White solid, 103 mg (90%), mp 171-172 ºC.

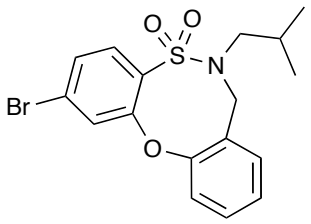
FTIR (thin film): 3261, 2923, 2850, 2356, 2339, 1470, 1396, 1332, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 1.8 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.42 (dq, *J* = 5.1, 2.0 Hz, 2H), 7.24-7.18 (m, 2H), 5.55 (d, *J* = 15.3 Hz, 1H), 3.96 (t, *J* = 17.7 Hz, 1H), 3.00-2.92 (m, 1H), 2.28-2.22 (m, 1H), 1.64-1.48 (m, 3H), 1.39-1.31 (m, 1H), 1.29-1.19 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 155.6, 133.4, 131.5, 131.3, 130.5, 130.1, 128.5, 127.6, 127.5, 125.9, 122.2, 47.3, 44.5, 29.5, 19.6, 13.7;

HRMS calculated for $C_{16}H_{14}BrNNaO_3S$ (M+Na) 401.9775; found 401.9773 (TOF MS ES+).

2-bromo-6-isobutyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2d)



White Solid, 104 mg (91%), mp 125-126 ºC.

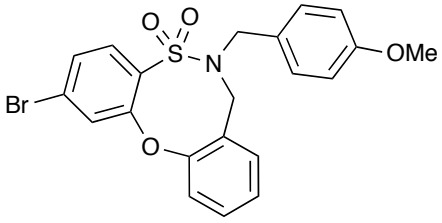
FTIR (thin film): 3061, 2923, 2850, 2356, 2339, 1470, 1396, 1332, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 11.3, 5.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.44-7.40 (m, 2H), 7.22-7.18 (m, 2H), 5.59 (dd, *J* = 15.3, 1.2 Hz, 1H), 3.92 (d, *J* = 15.3 Hz, 1H), 2.66-2.59 (m, 1H), 2.09-2.04 (m, 1H), 2.04-1.97 (m, 1H), 0.98 (d, *J* = 6.6, 3H), 0.82 (d, *J* = 6.5 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 155.6, 133.2, 131.6, 131.4, 130.5, 129.7, 128.5, 127.7, 127.5, 125.9, 122.2, 51.7, 47.6, 26.0, 20.2, 19.5;

HRMS calculated for $C_{16}H_{14}BrNNaO_3S$ (M+Na) 401.9775; found 401.9772 (TOF MS ES+).

2-bromo-6-(4-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2e)



Colorless oil, 101 mg (82%).

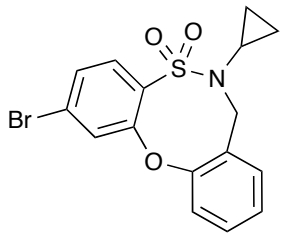
FTIR (thin film): 3087, 2997, 2931, 2442, 2393, 1569, 1400, 1388, 1338, 1161 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 1.8 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.44 (ddd, *J* = 7.2, 4.4, 1.6 Hz, 2H), 7.24-7.18 (m, 3H), 7.02 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.93-6.88 (m, 2H), 5.45 (d, *J* = 15.2 Hz, 1H), 4.39 (d, *J* = 14.5 Hz, 1H), 3.83 (s, 3H), 3.70 (d, *J* = 15.3 Hz, 1H), 3.12 (d Hz, *J* = 14.5, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 159.0, 155.7, 133.5, 131.7, 131.3, 130.6, 129.9, 129.7, 128.6, 127.8, 127.5, 126.7, 125.8, 122.3, 114.08, 77.25, 55.3, 48.0, 46.6;

HRMS calculated for $C_{21}H_{18}BrNO_4SNa$ $(M+Na)^+$ 482.0038; found 482.0050 (TOF MS ES+).

2-bromo-6-cyclopropyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2f)



White Solid, 104 mg (81%), mp 175-176 ºC.

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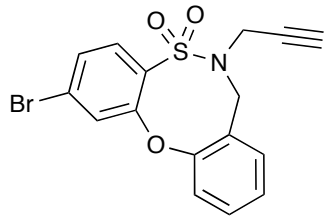
FTIR (thin film): 3280, 3071, 3020, 2350, 2335, 1400, 1359, 1330 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.58-7.51 (m, 2H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.31 (td, *J* = 7.7, 1.6 Hz, 1H), 7.26-7.20 (m, 2H), 7.10 (td, *J* = 7.4, 1.1 Hz, 1H), 5.52 (d, *J* = 14.8 Hz, 1H), 3.87 (d, *J* = 14.8 Hz, 1H), 1.28-1.22 (m, 2H), 0.63-0.56 (m, 2H), 0.41-0.33 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 155.4, 134.6, 133.1, 131.7, 131.3, 130.2, 130.1, 125.6, 125.3, 124.1, 122.1, 50.9, 27.7, 10.2, 5.2;

HRMS calculated for $C_{17}H_{18}BrNNaO_3$ (M+Na) 418.0088; found 418.0083 (TOF MS ES+).

2-bromo-6-(prop-2-yn-1-yl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2g)



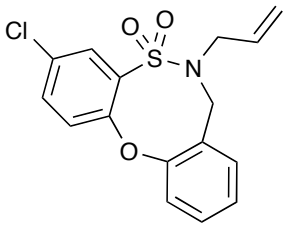
White Solid, 118 mg (94%), mp 140-141 ºC.

FTIR (thin film): 3092, 3089, 2354, 2334, 2123, 1569, 1452, 1390, 1352, 1344, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.1, 6.9 Hz, 2H), 7.48 (d, *J* = 7.0 Hz, 1H), 7.44 (ddt, *J* = 2.1, 4.2, 8.3 Hz, 2H), 7.36 (dd, *J* = 1.6, 7.4 Hz, 1H), 7.23 (td, *J* = 1.2, 7.4 Hz, 1H), 5.60 (d, *J* = 15.4 Hz, 1H), 4.20 (d, *J* = 15.3 Hz, 1H), 3.98 (ddd, *J* = 1.3, 2.5, 17.3 Hz, 1H), 3.26 (dd, *J* = 2.5, 17.3 Hz, 1H), 2.15 (t, *J* = 2. Hz, 5, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 155.6, 133.1, 131.6, 131.3, 130.8, 129.3, 128.7, 128.1, 127.6, 126.0, 121.8, 76.2, 73.9, 48.1, 35.8;
HRMS calculated for $C_{16}H_{12}BrNNaO_3S$ (M+Na) 399.9619; found 339.9618 (TOF MS ES+).

6-allyl-3-chloro-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2h)



White Solid, 87 mg (95%), mp 138-140 ºC.

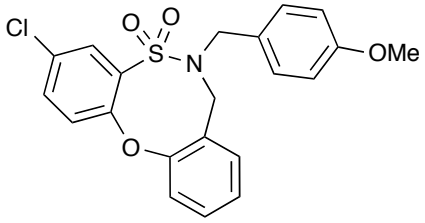
FTIR (thin film): 3082, 2974, 2358, 2341, 1604, 1577, 1452, 1386, 1342, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 2.5 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.52 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.39 (dt, *J* = 8.1, 3.7 Hz, 1H), 7.18 (dd, *J* = 5.0, 0.8 Hz, 2H), 5.74 (dddd, *J* = 17.1, 10.1, 8.5, 3.8 Hz, 1H), 5.52 (dd, *J* = 15.2, 1.5 Hz, 1H), 5.26 (d, *J* = 10.1 Hz, 1H), 5.18 (ddt, *J* = 17.1, 2.1, 1.1 Hz, 1H), 3.95 (d, *J* = 15.2 Hz, 1H), 3.81 (ddq, *J* = 15.3, 3.7, 1.8 Hz, 1H), 2.83 (dd, *J* = 15.2, 8.5 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 153.8, 135.7, 134.1, 132.2, 131.5, 130.8, 130.5, 130.1, 129.9, 125.7, 125.4, 122.2, 119.3, 47.8, 47.1.

HRMS calculated for $C_{16}H_{15}ClNO_3S$ $(M+H)^+$ 336.0461; found 336.0468 (TOF MS ES+).

3-chloro-6-(4-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide



White Solid, 92 mg (87%), mp 138-139 ºC.

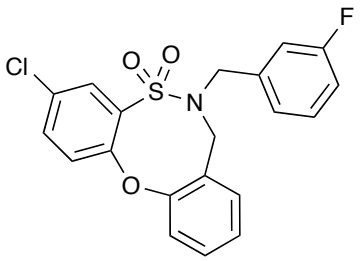
FTIR (thin film): 3072, 2933, 2835, 2358, 2331, 1610, 1512, 1358, 1338, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.5 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.55-7.48 (m, 2H), 7.41 (td, *J* = 7.9, 1.7 Hz, 1H), 7.24-7.17 (m, 3H), 7.03 (dd, *J* = 7.4, 1.6 Hz, 1H), 6.92-6.87 (m, 2H), 5.45 (d, *J* = 16.1 Hz, 1H), 4.42 (d, *J* = 14.5 Hz, 1H), 3.83 (s, 3H), 3.70 (t, *J* = 10.2 Hz, 1H), 3.17 (d, *J* = 14.5 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 159.0 153.8, 135.8, 134.1, 131.6, 130.8, 130.5, 130.1, 129.9, 129.8, 126.6, 125.7, 125.4, 122.2, 114.1, 55.3, 48.1, 46.6;

HRMS calculated for $C_{21}H_{18}ClNO_4SNa$ $(M+Na)^+$ 438.0543; found 438.0540 (TOF MS ES+).

3-chloro-6-(3-fluorobenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide



White Solid, 118 mg (87%), mp 158-160 ºC.

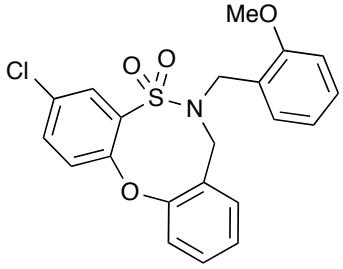
FTIR (thin film): 3078, 2929, 2358, 2341, 1591, 1487, 1452, 1353, 1340, 133, 1163 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.5 Hz, 1H), 7.61-7.58 (m, 1H), 7.55 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.51 (t, *J* = 6.6 Hz, 1H), 7.44-7.40 (m, 1H), 7.35 (dd, *J* = 13.7, 7.7 Hz, 1H), 7.20 (td, *J* = 7.4, 1.0 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.07-7.00 (m, 3H), 5.56-5.47 (m, 1H), 4.43 (d, *J* = 15.0 Hz, 1H), 3.71 (d, *J* = 15.3 Hz, 1H), 3.24 (d, *J* = 15.0 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 162.1, 159.0, 153.9, 137.6, 137.6, 135.6, 134.3, 131.5, 130.9, 130.7, 130.4, 130.3, 130.1, 130.0, 129.5, 125.8, 125.4, 123.9, 123.8, 122.3, 115.3, 115.2, 115.1, 115.0, 48.2, 48.1, 47.0.

HRMS calculated for $C_{20}H_{15}ClFNO_3SNa$ $(M+Na)^+$ 426.0343; found 426.0340 (TOF MS ES+).

3-chloro-6-(2-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2k)



White Solid, 73 mg (91%), mp 170-171 ºC.

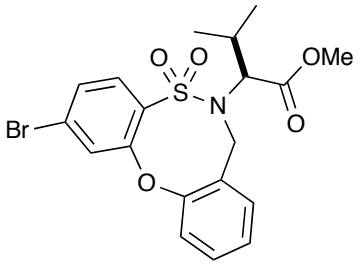
FTIR (thin film): 3072, 2939, 2356, 2339, 1464, 1386, 1330, 1164 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.54 (dd, *J* = 2.6, 8.7 Hz, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.39 (td, *J* = 1.7, 7.8 Hz, 1H), 7.30 (tt, *J* = 3.2, 6.4 Hz, 1H), 7.16-7.11 (m, 1H), 7.04 (td, *J* = 0.9, 7.5 Hz, 1H), 7.00 (dd, *J* = 1.6, 7.5 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.53 (dd, *J* = 1.3, 15.2 Hz, 1H), 4.15-4.08 (m, 1H), 3.79 (dd, *J* = 15.5, 32.4 Hz, 2H), 3.69 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 157.1, 154.0, 136.0, 134.0, 131.9, 130.7, 130.4, 130.2, 130.1, 129.3, 128.9, 125.4, 125.4, 123.3, 122.1, 120.9, 110.2, 55.0, 47.6, 43.0;

HRMS calculated for $C_{21}H_{18}ClNO_4SNa$ $(M+Na)^+$ 438.0543; found 438.0545 (TOF MS ES+).

Methyl 2-(2-bromo-5,5-dioxidodibenzo[b,g][1,4,5]oxathiazocin-6(7H)-yl)-3-methylbutanoate 2-l



White Solid, 108 mg (94%) mp 165-166 ºC.

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FTIR (thin film): 2954, 2360, 2330, 1741, 1569, 1488, 1452, 1388, 1342, 1166 cm^{-1}

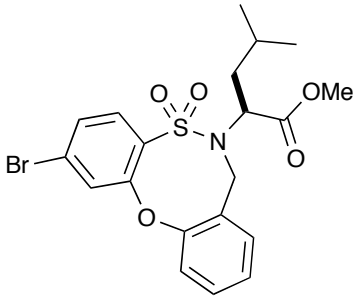
$[\alpha]_D^{20}$ + 5.75 (*c* = 1.49, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.1, 5.1 Hz, 2H), 7.48-7.43 (m, 2H), 7.36 (dd, *J* = 8.4, 4.9 Hz, 1H), 7.16 (d, *J* = 4.3 Hz, 2H), 5.58 (d, *J* = 15.9 Hz, 1H), 3.96 (d, *J* = 10.9 Hz, 1H), 3.85 (d, *J* = 15.9 Hz, 1H), 2.46 (qd, *J* = 13.1, 6.6 Hz, 1H), 2.28 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.3 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 158.9, 155.4, 135.4, 132.3, 130.4, 130.3, 129.8, 128.2, 126.9, 126.4, 125.4, 121.7, 63.2, 50.7, 45.0, 25.5, 20.2, 18.7.

HRMS calculated for $C_{19}H_{20}BrNO_5SNa$ $(M+Na)^+$ 476.0143; found 476.0133 (TOF MS ES+).

methyl 2-(2-bromo-5,5-dioxidodibenzo[b,g][1,4,5]oxathiazocin-6(7H)-yl)-4-methylpentanoate (2m)



White Solid, 108 mg (77%), mp 160-161 ºC.

FTIR (thin film): 2960, 2354, 2334, 1745, 1569, 1470, 1356, 1334, 1166 cm^{-1}

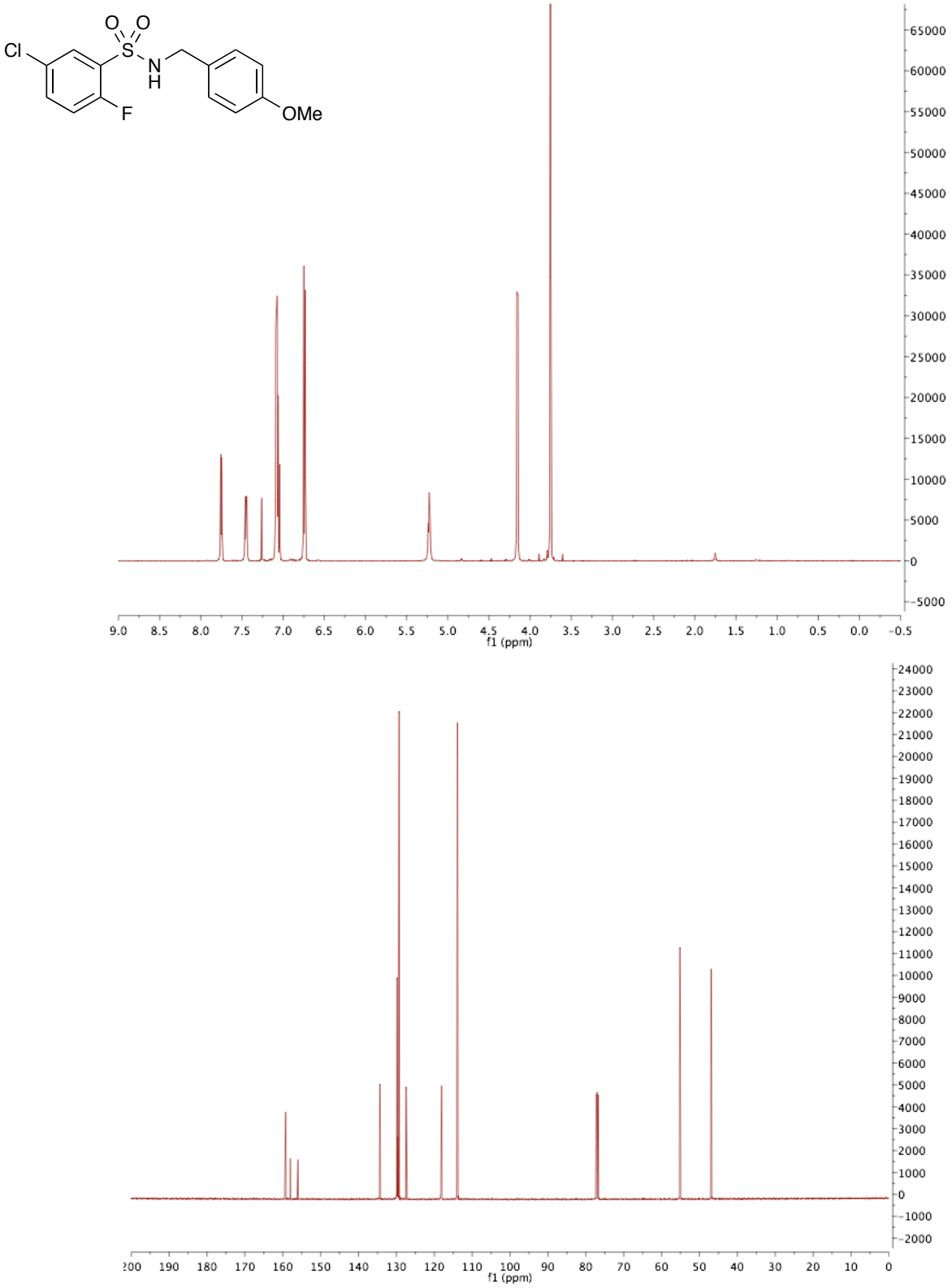
$[\alpha]_D^{20}$ -4.12 (*c* = 3.01, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79-7.75 (m, 2H), 7.48 (d, *J* = 8.1Hz, 1H), 7.43 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.39-7.34 (m, 1H), 7.14 (d, *J* = 4.3 Hz, 2H), 5.59 (d, *J* = 15.8, 1H), 4.52 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.93 (d, *J* = 15.8 Hz, 1H), 2.40 (s, 3H), 1.88 (ddd, *J* = 14.4, 10.0, 4.5 Hz, 1H), 1.77 (ddd, *J* = 14.5, 9.2, 5.5 Hz, 1H), 1.72-1.63 (m, 1H), 0.99 (dd, *J* = 13.3, 6.5 Hz, 6H);

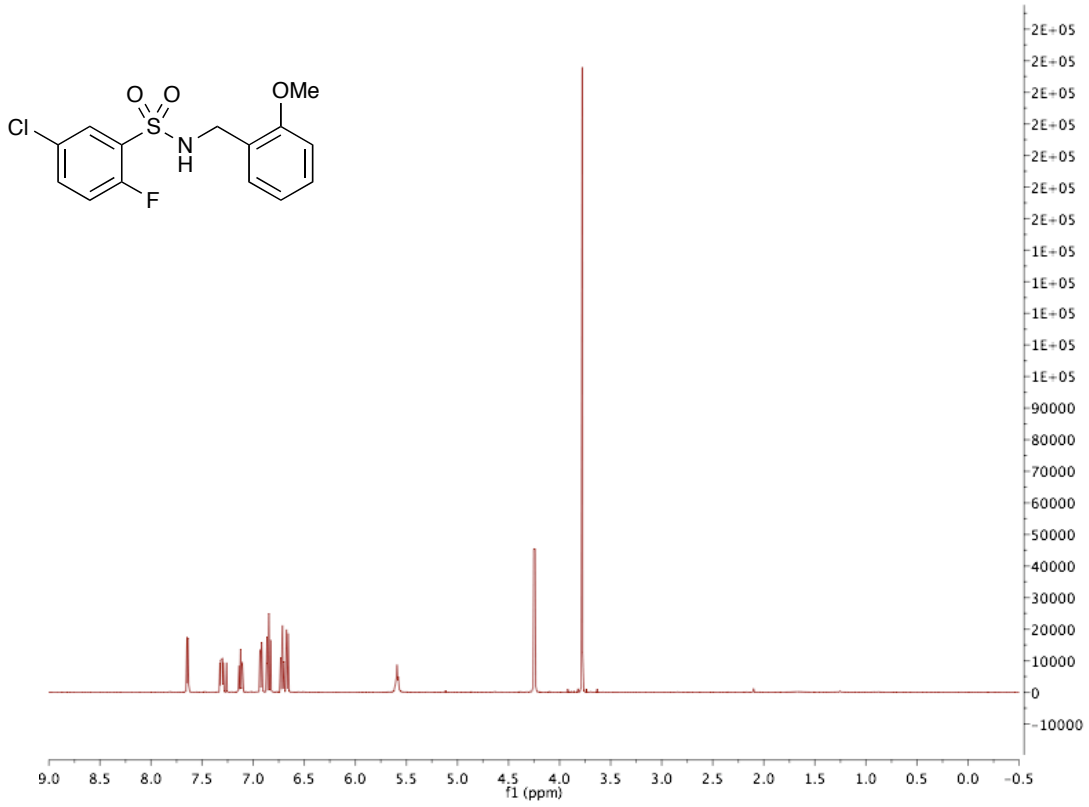
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.60, 158.9, 155.2, 135.9, 131.2, 130.4, 130.1, 128.3, 126.8, 126.8, 125.6, 121.5, 56.0, 51.0, 44.4, 36.4, 23.9, 23.2, 21.3;

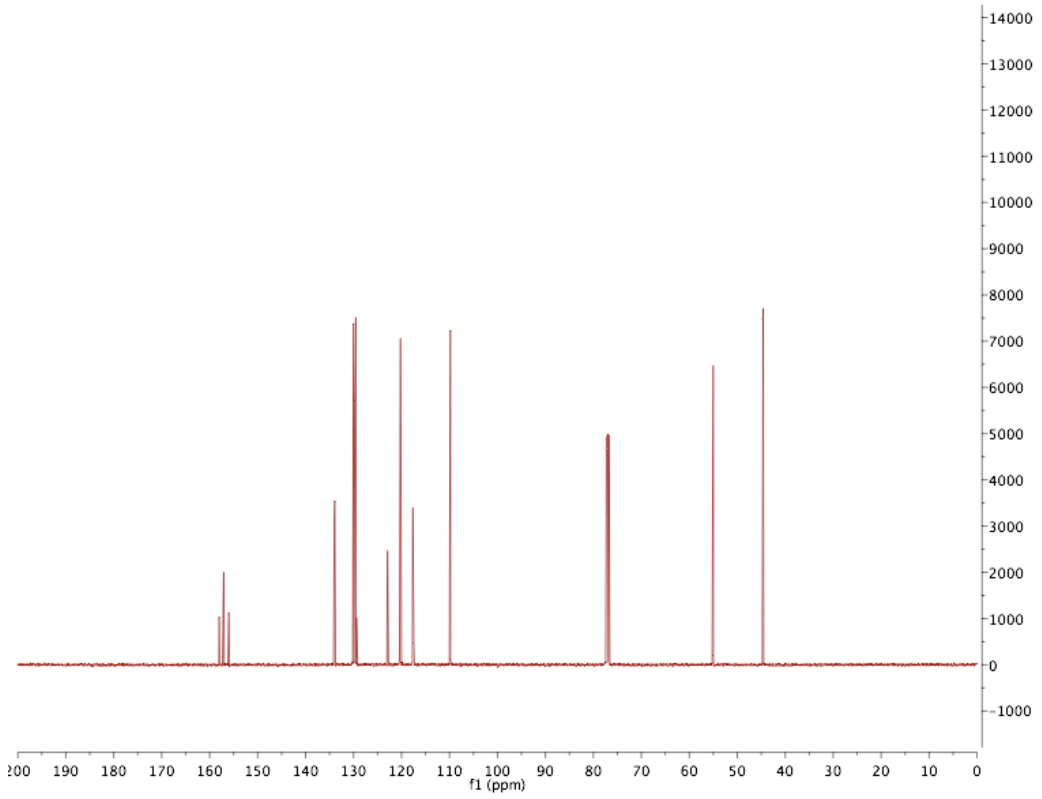
HRMS calculated for $C_{20}H_{22}BrNO_5SNa$ $(M+Na)^+$ 490.0300; found 490.0300 (TOF MS ES+).

5-chloro-2-fluoro-*N*-(4-methoxybenzyl)benzenesulfonamide (1i)

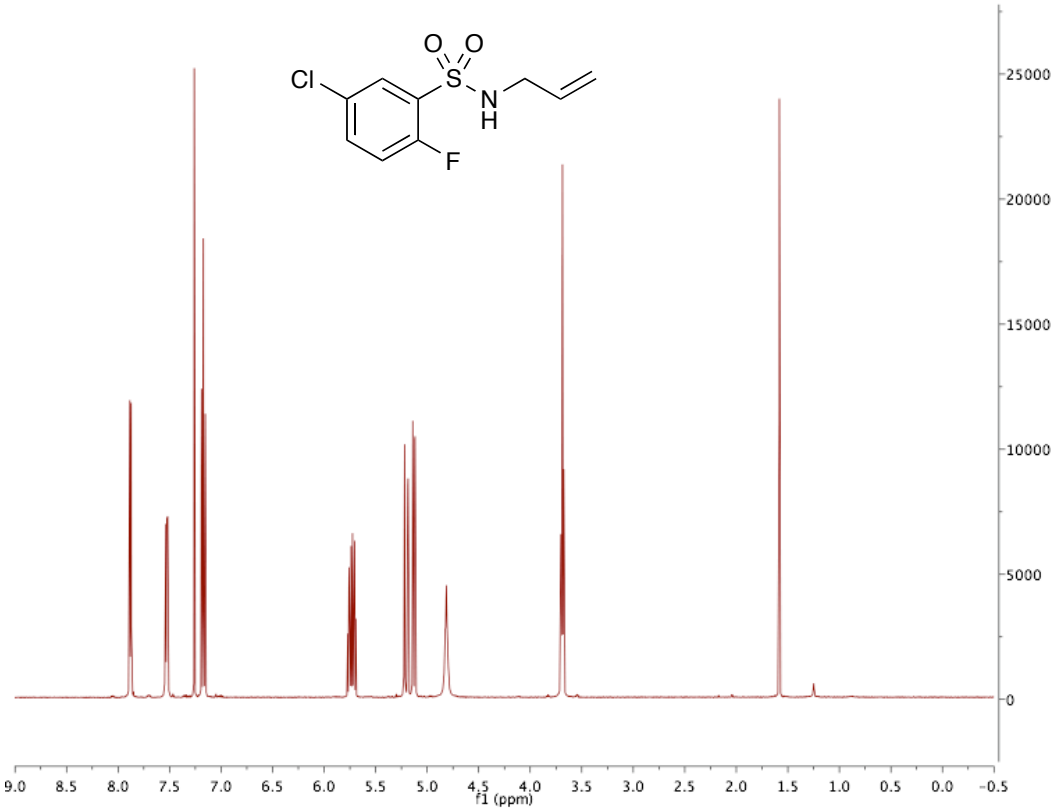


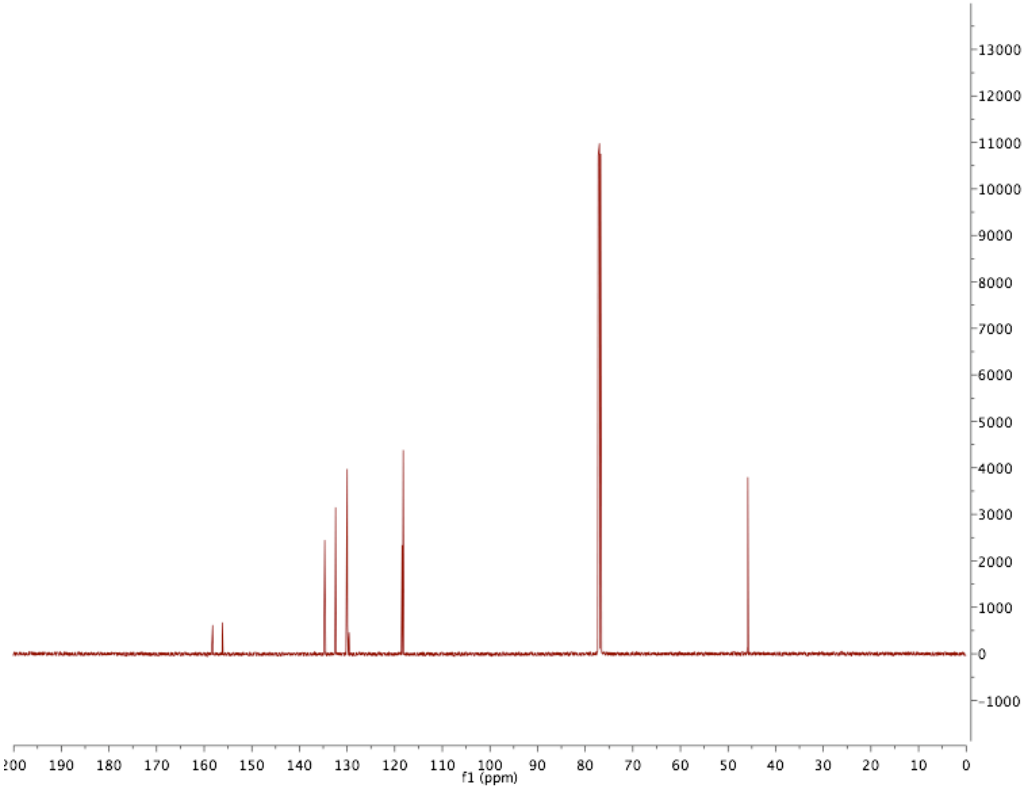
5-chloro-2-fluoro-*N*-(2-methoxybenzyl)benzenesulfonamide (1k)



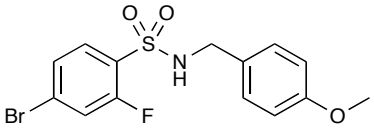


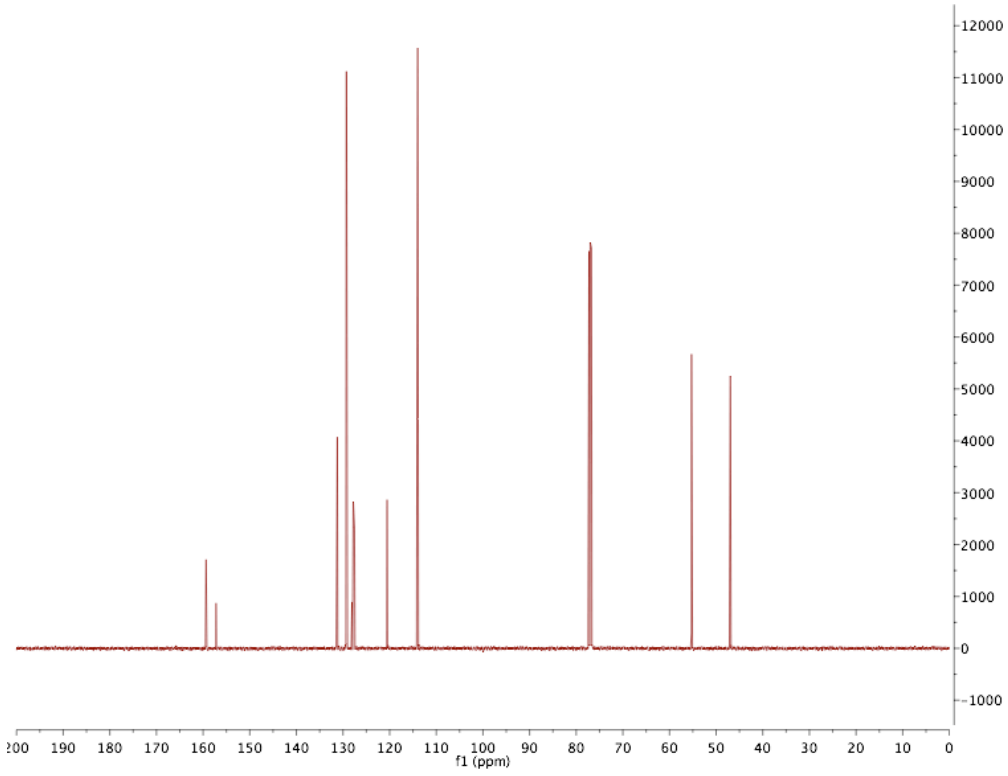
***N*-allyl-5-chloro-2-fluorobenzenesulfonamide (1h)**



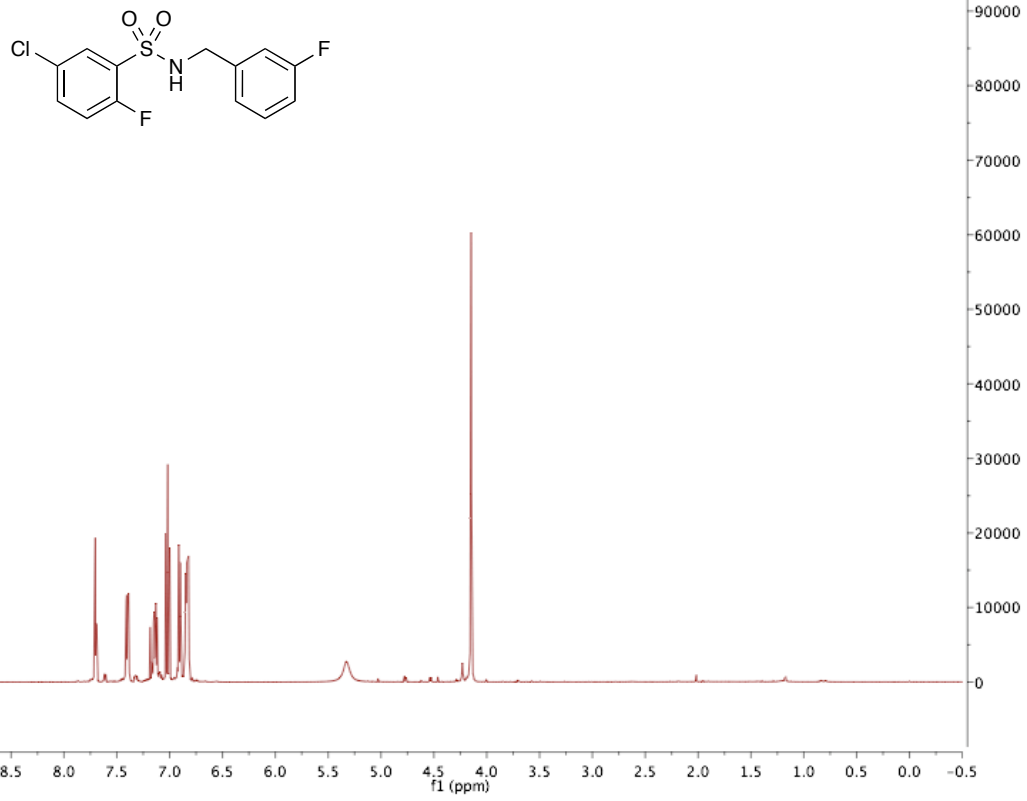


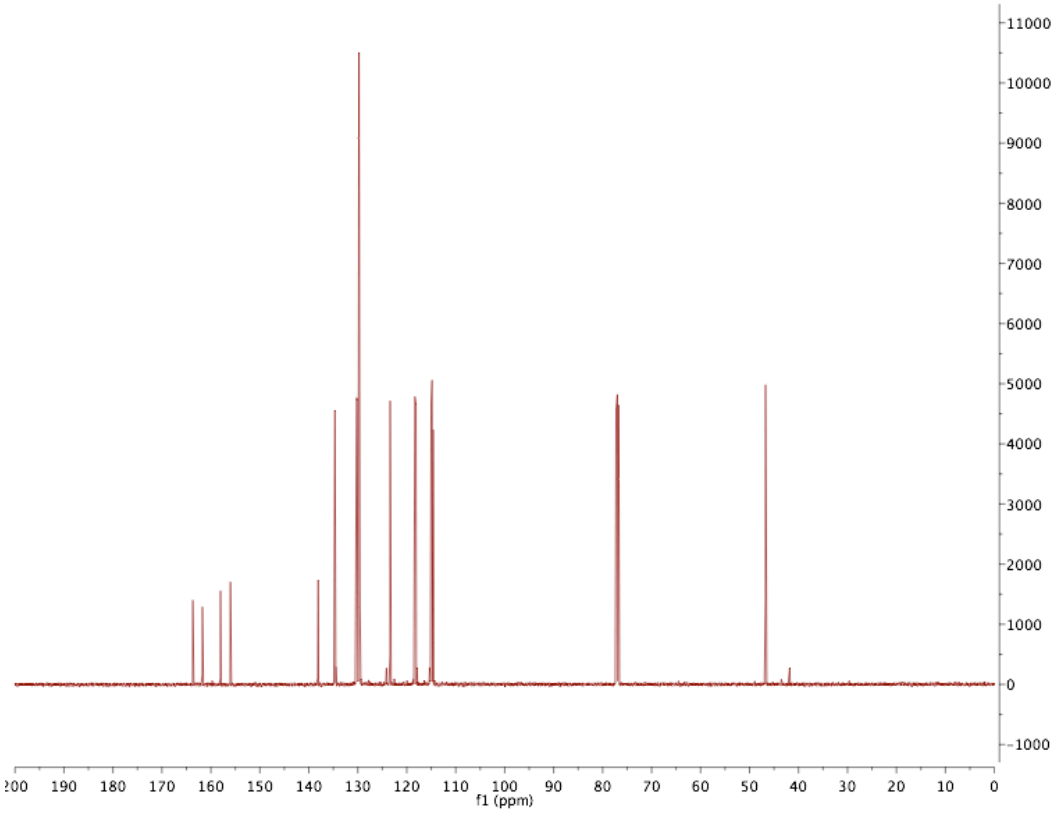
4-bromo-2-fluoro-*N*-(4-methoxybenzyl)benzenesulfonamide (1e)



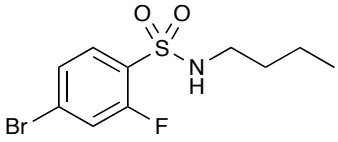


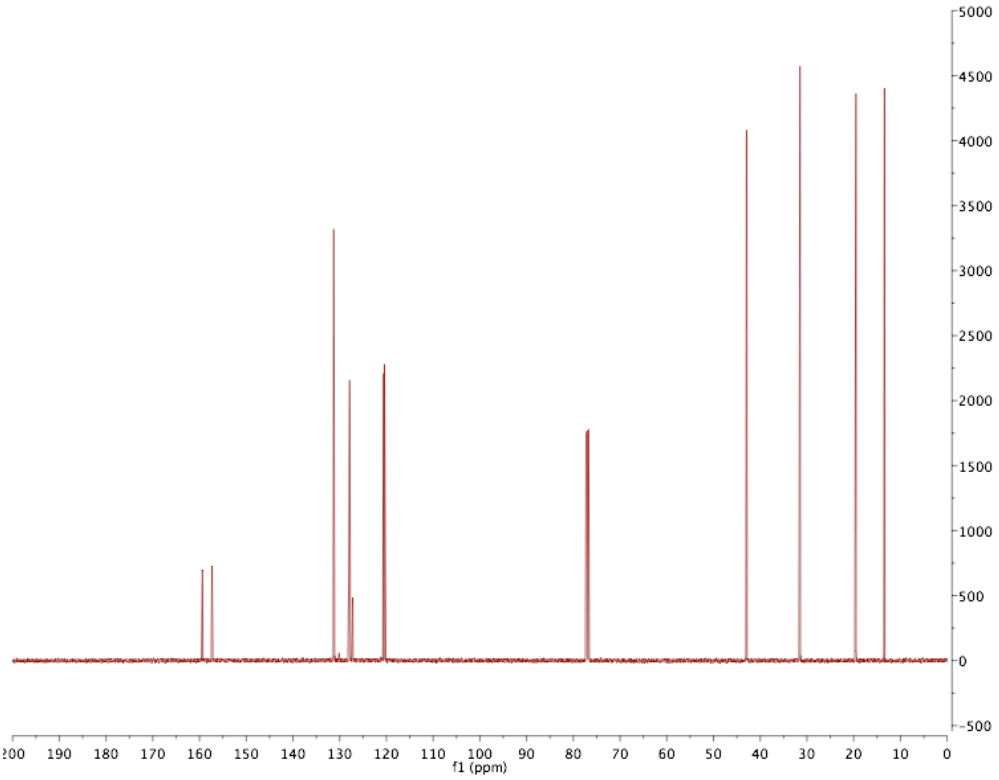
5-chloro-2-fluoro-*N*-(3-fluorobenzyl)benzenesulfonamide (1j)



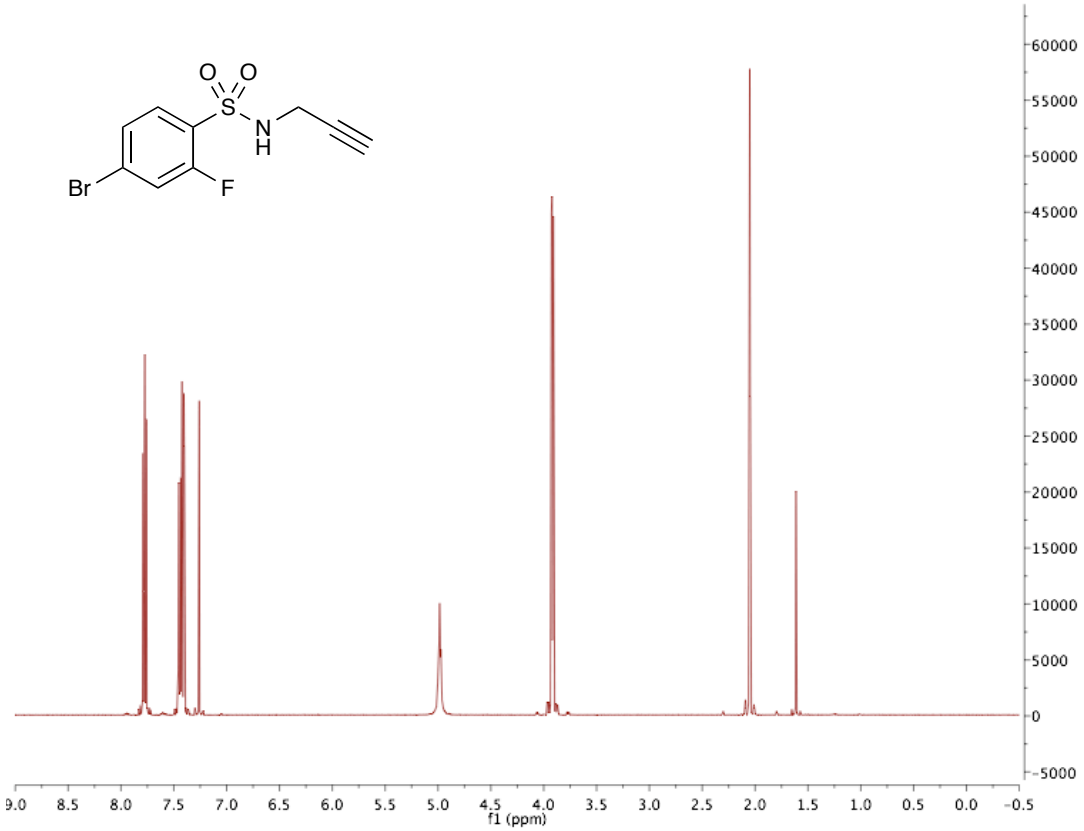


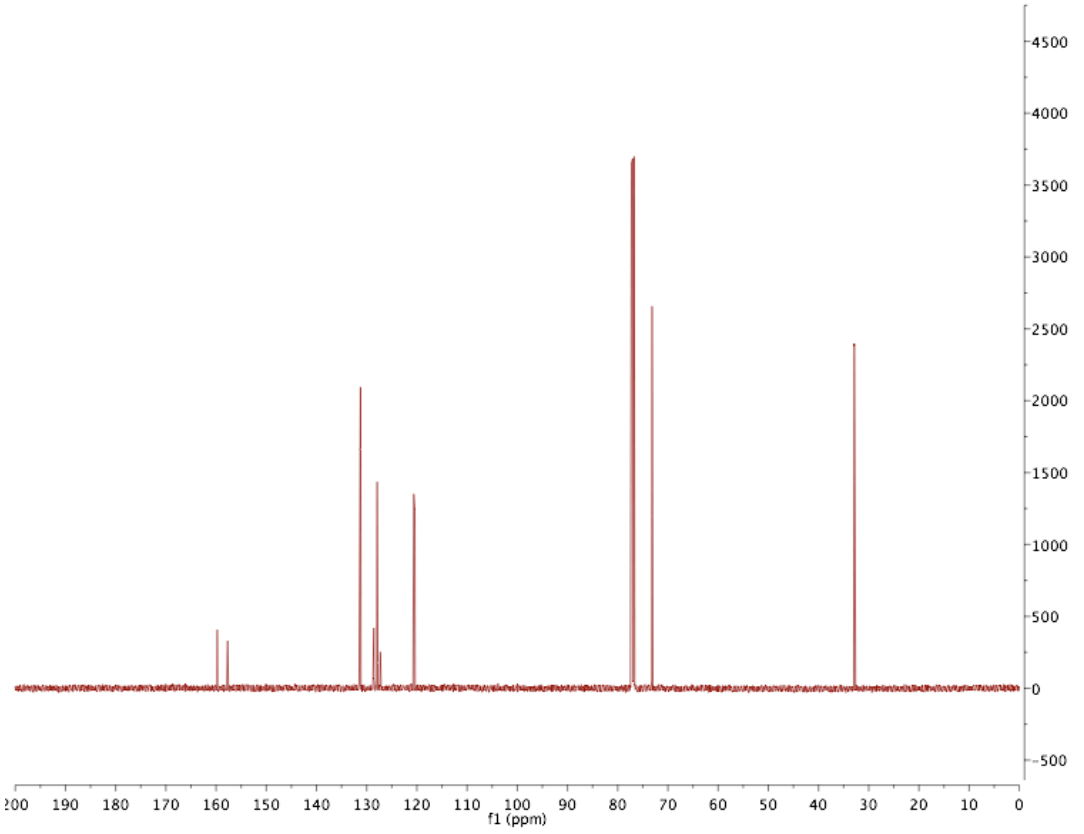
4-bromo-*N*-butyl-2-fluorobenzenesulfonamide (1c)



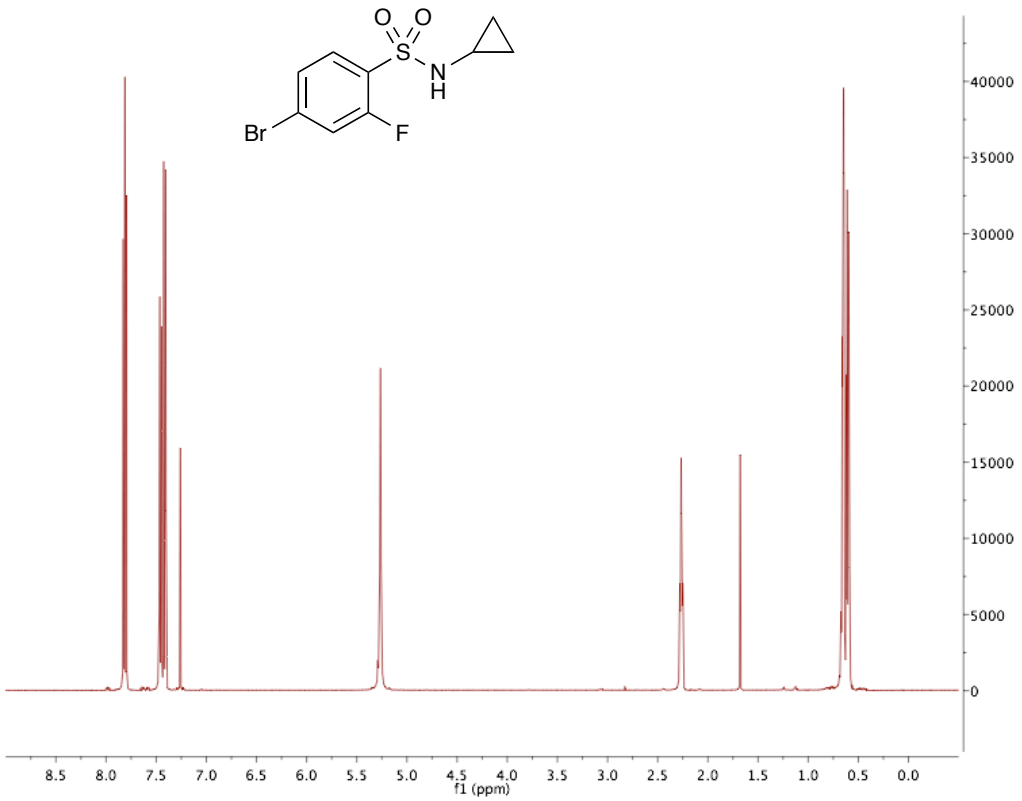


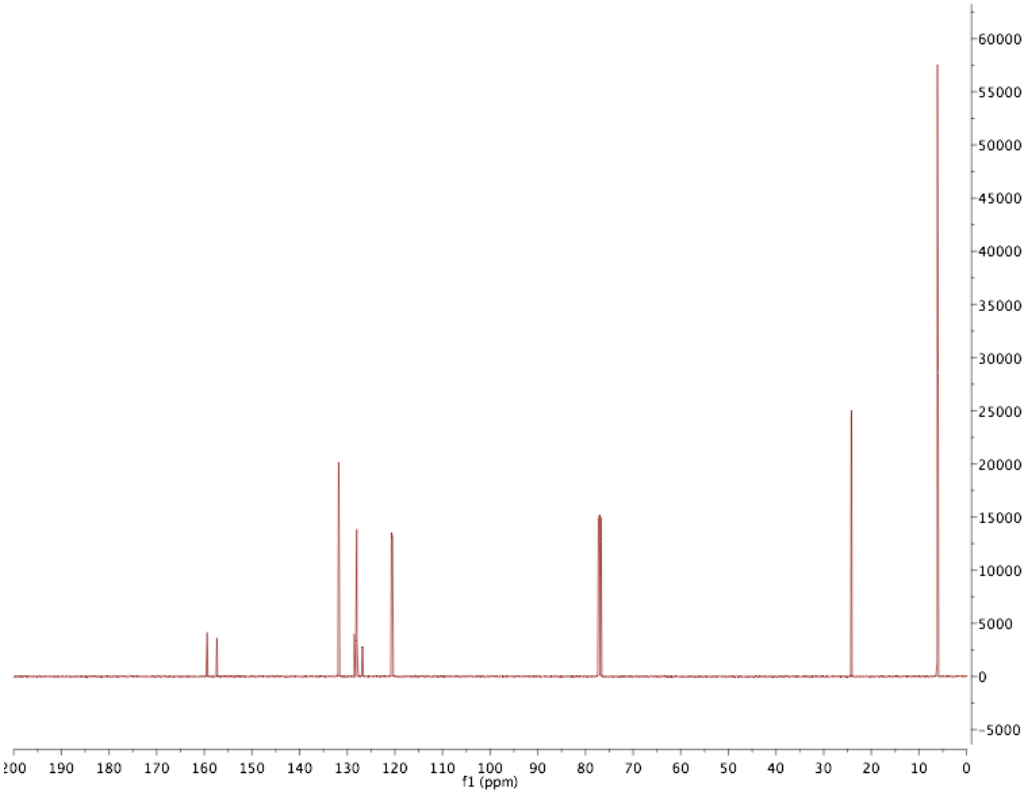
4-bromo-2-fluoro-*N*-(prop-2-ynyl)benzenesulfonamide (1g)



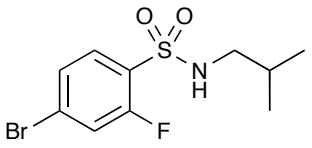


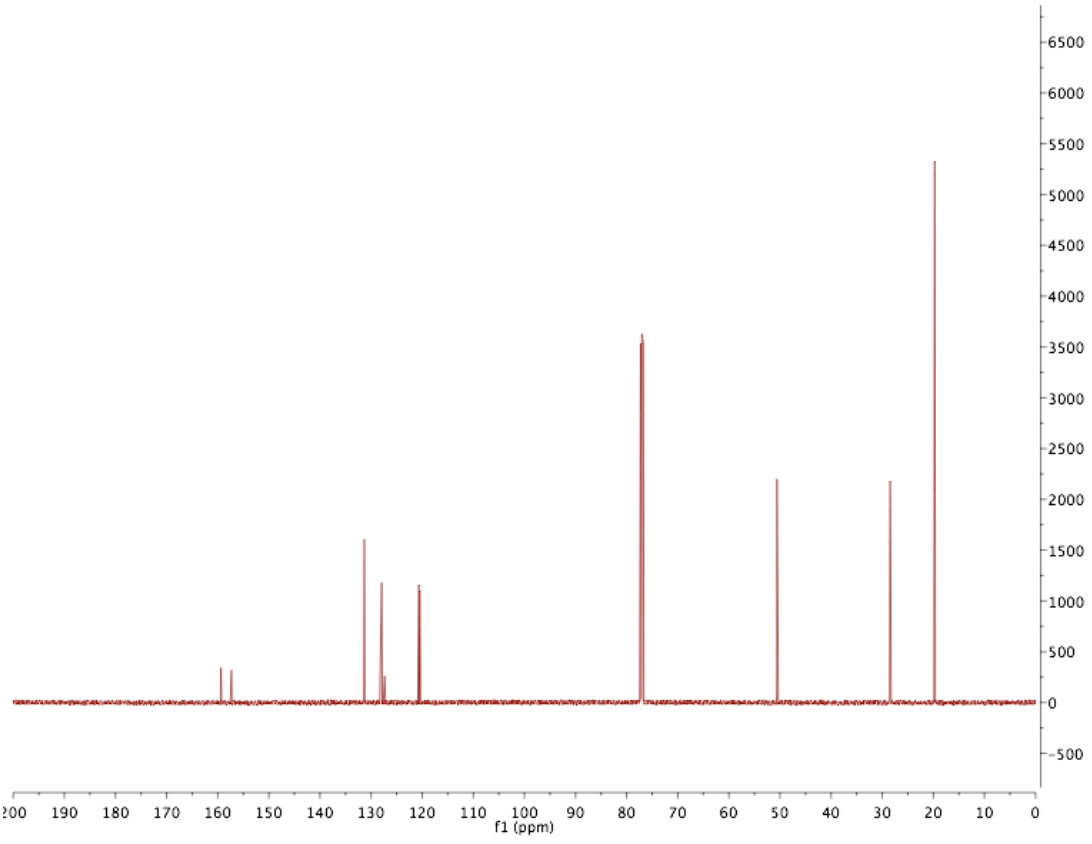
4-bromo-*N*-cyclopropyl-2-fluorobenzenesulfonamide (1f)



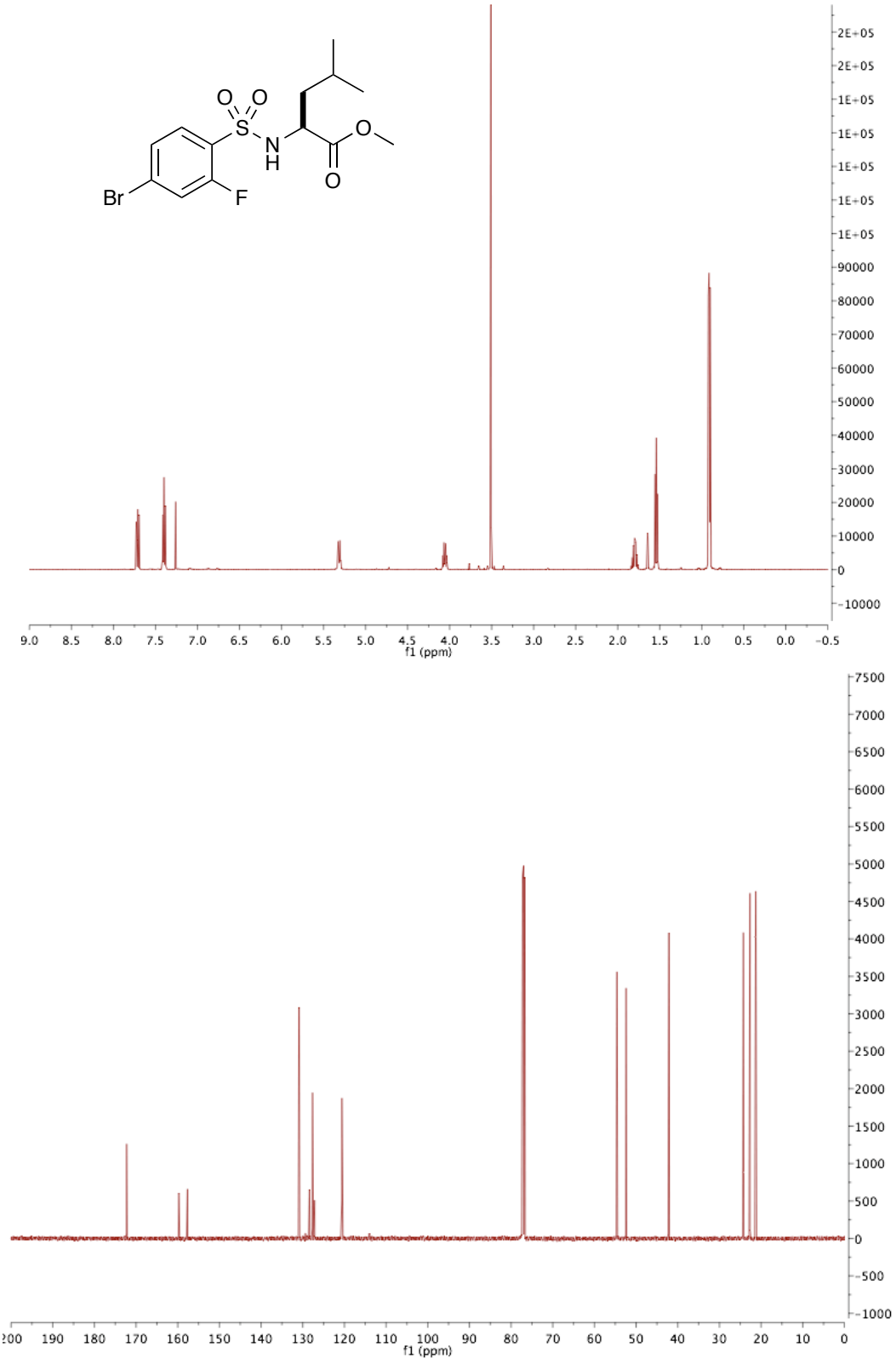


4-bromo-2-fluoro-*N*-isobutylbenzenesulfonamide (1d)

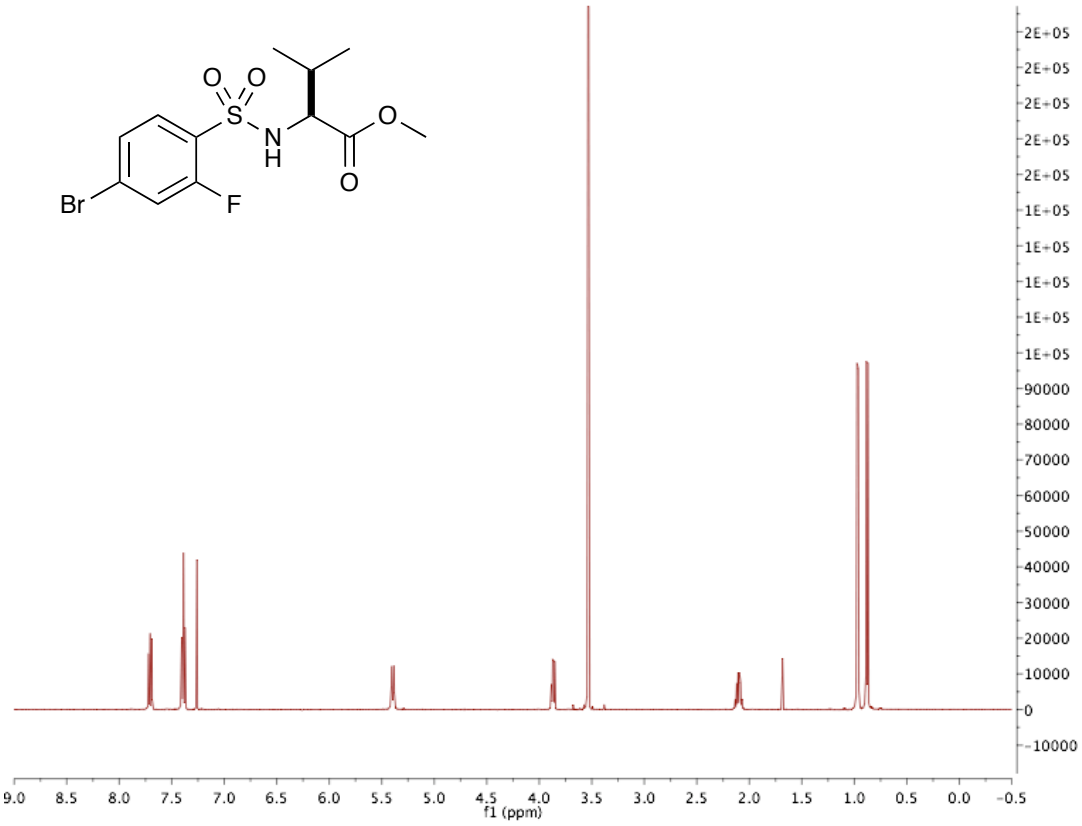


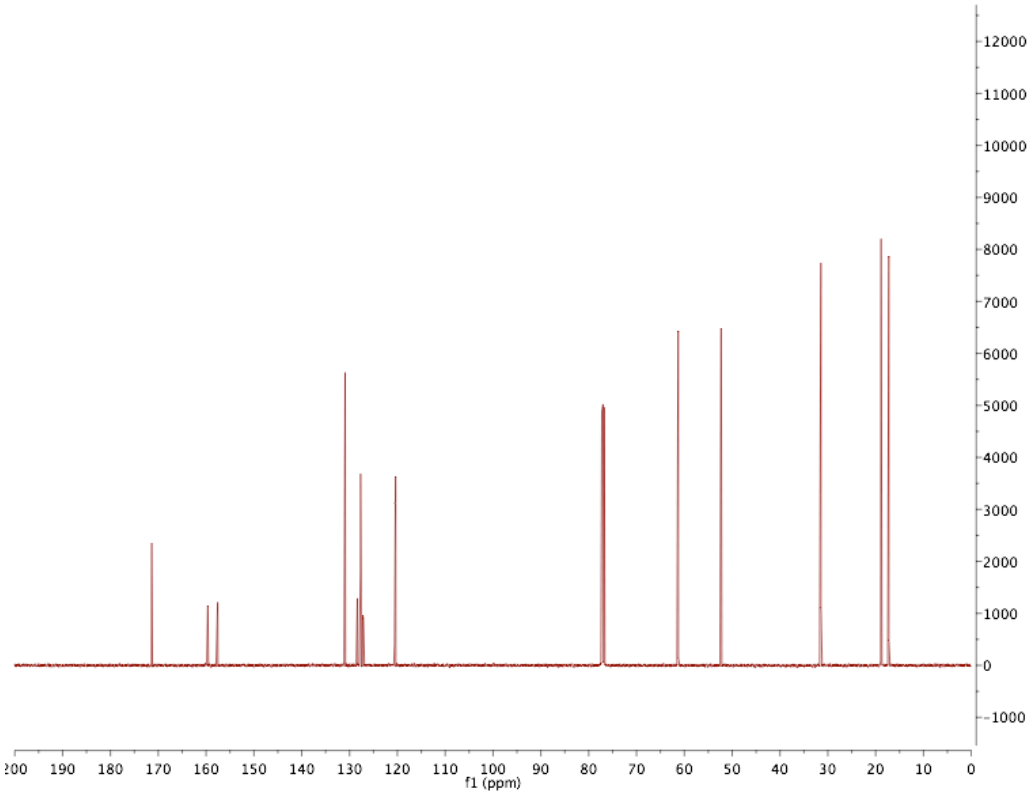


(*S*)-methyl 2-(4-bromo-2-fluorophenylsulfonamido)-4-methylpentanoate (1m)

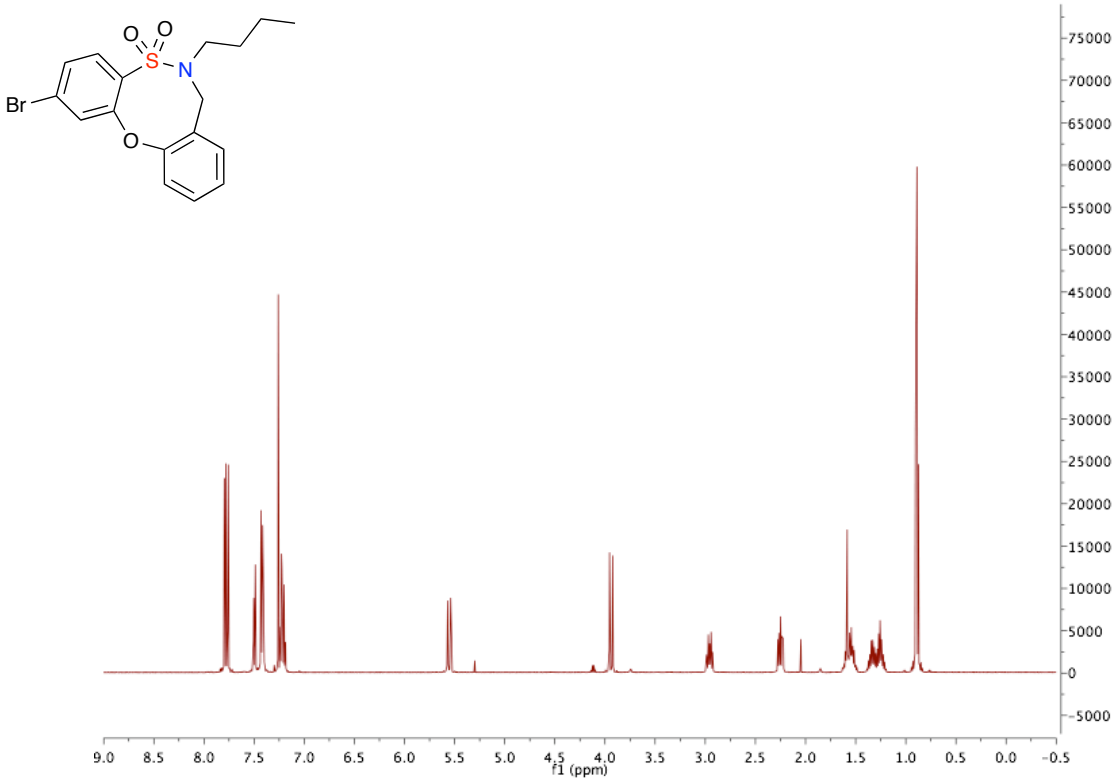


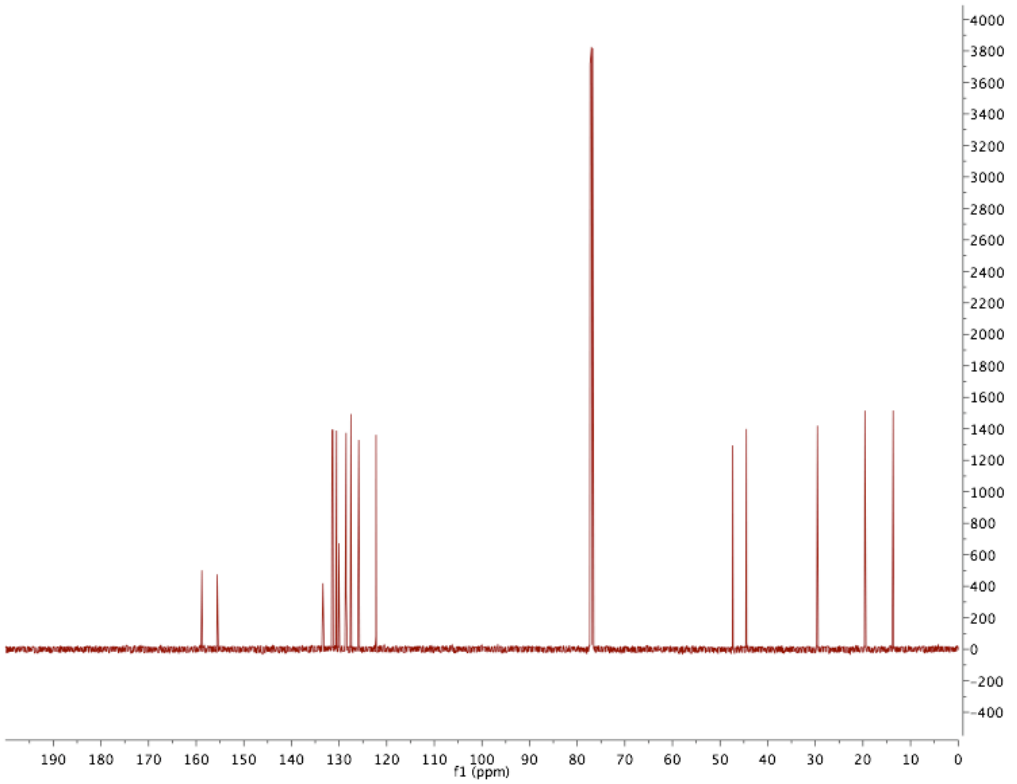
(*S*)-methyl 2-(4-bromo-2-fluorophenylsulfonamido)-3-methylbutanoate (1-l)



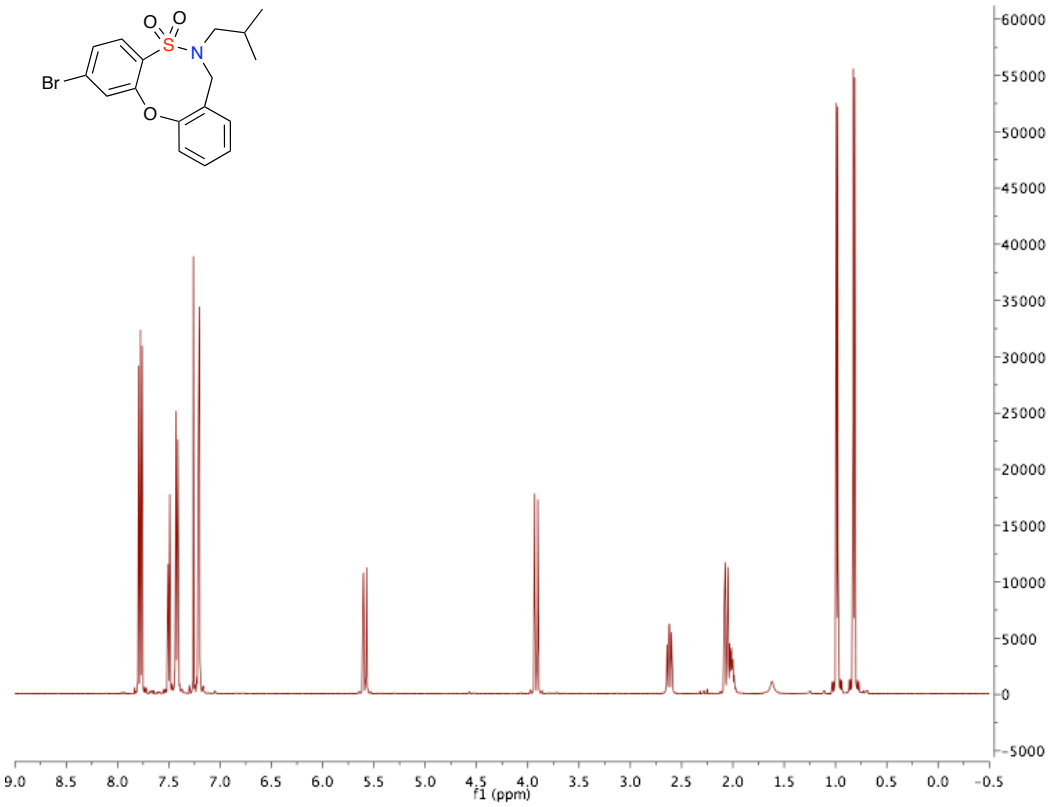


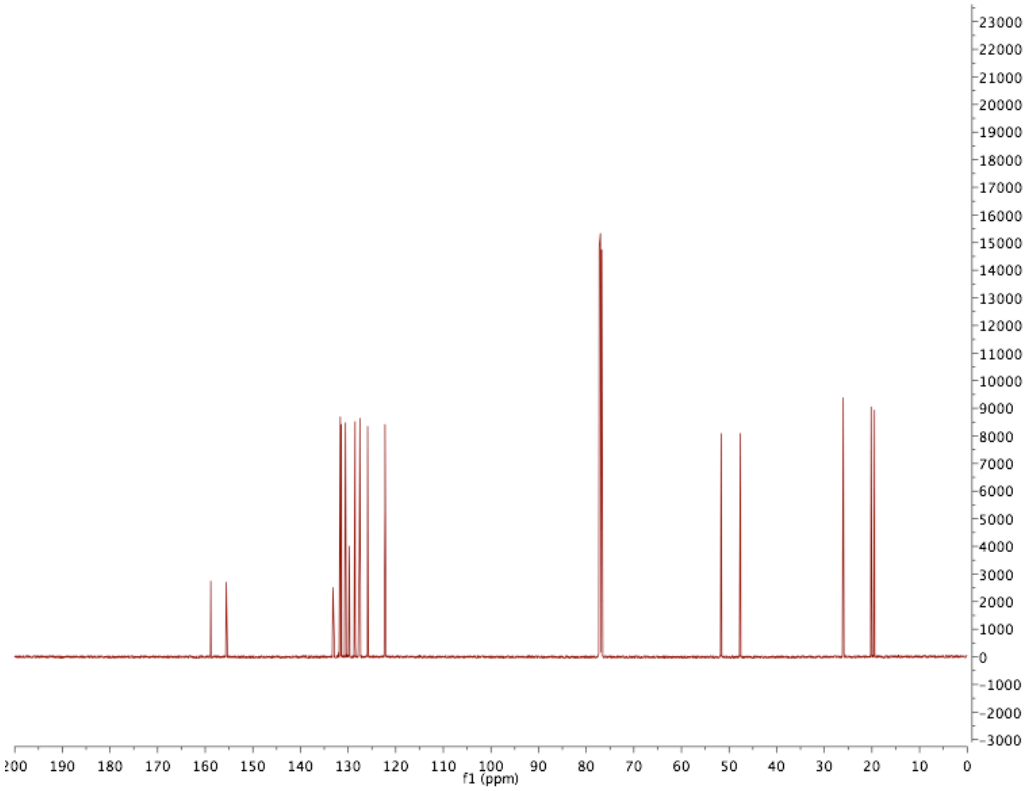
2-bromo-6-butyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2c)



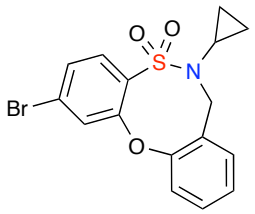


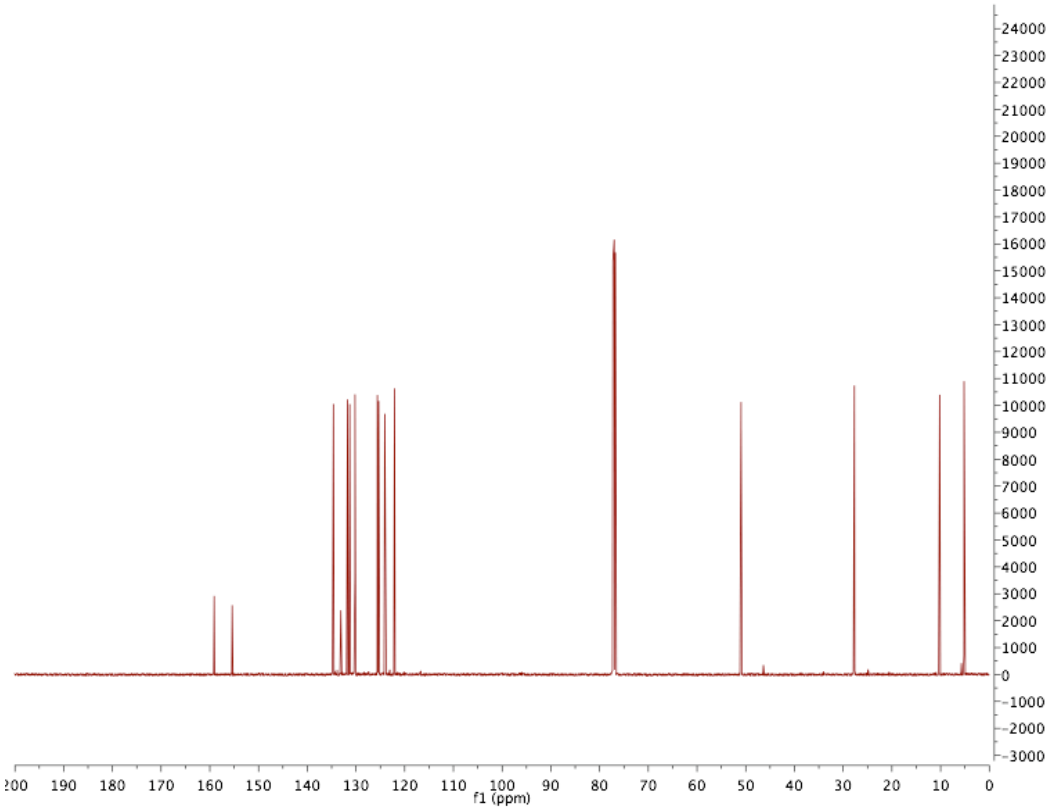
2-bromo-6-isobutyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine-5,5-dioxide (2d)



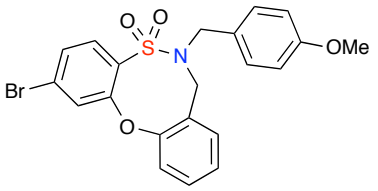


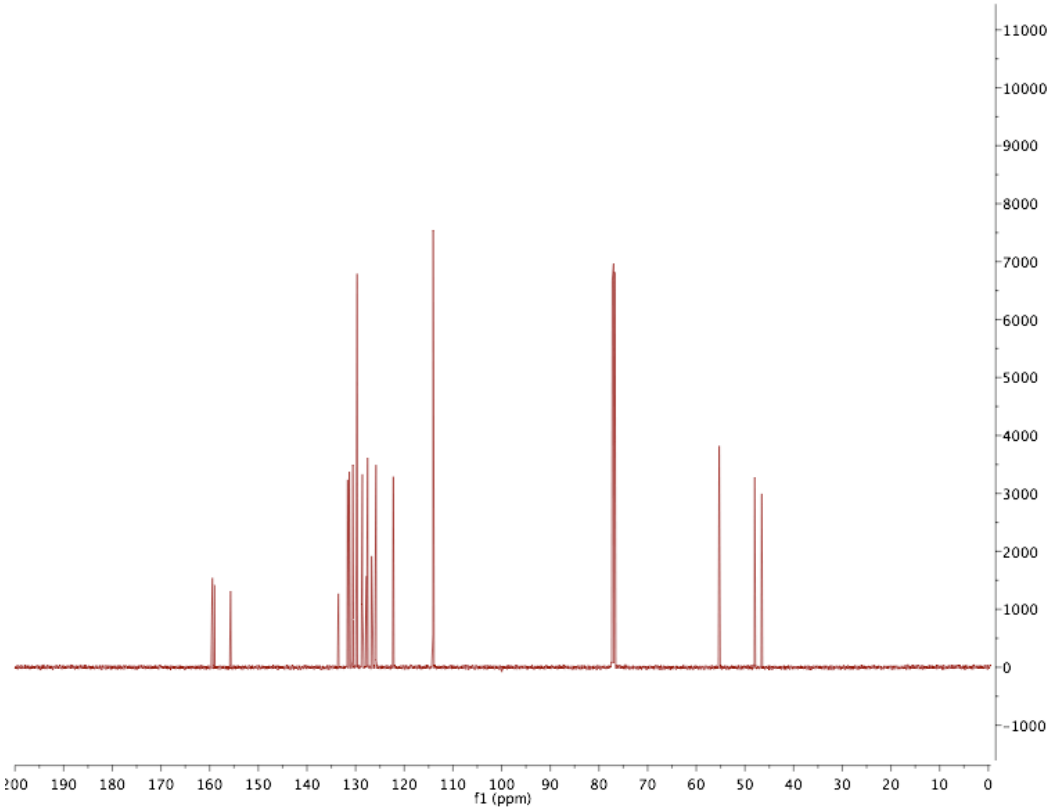
2-bromo-6-cyclopropyl-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2f)



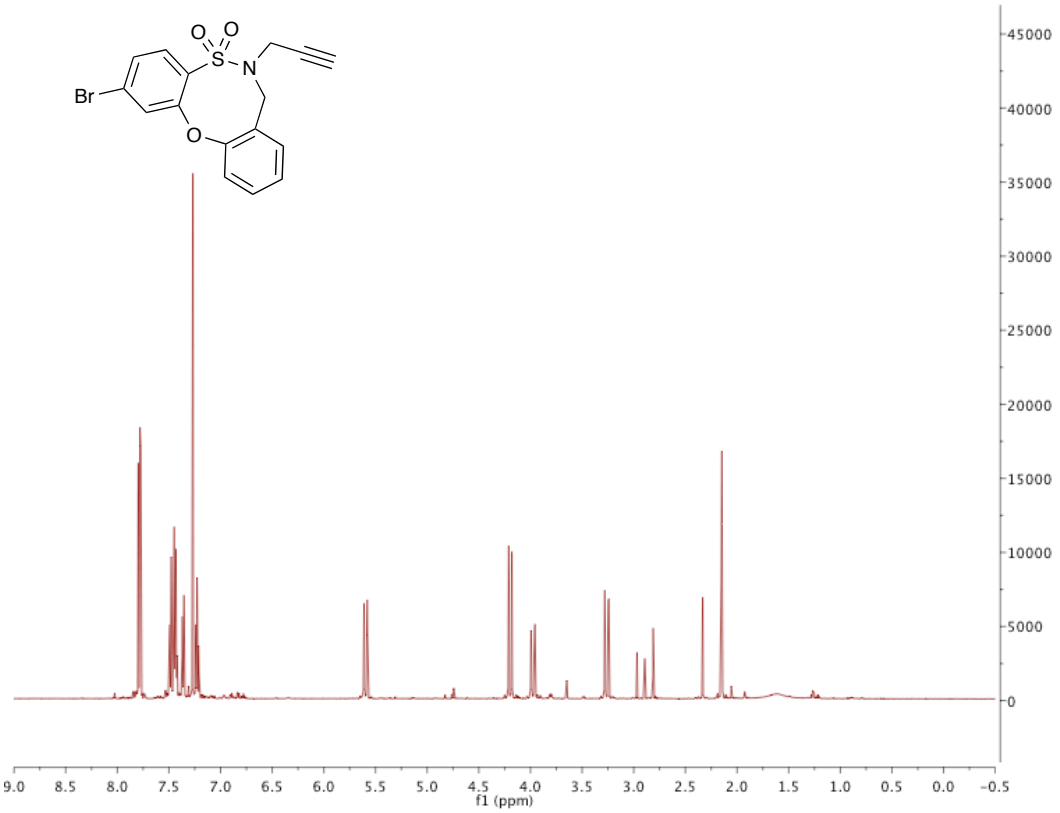


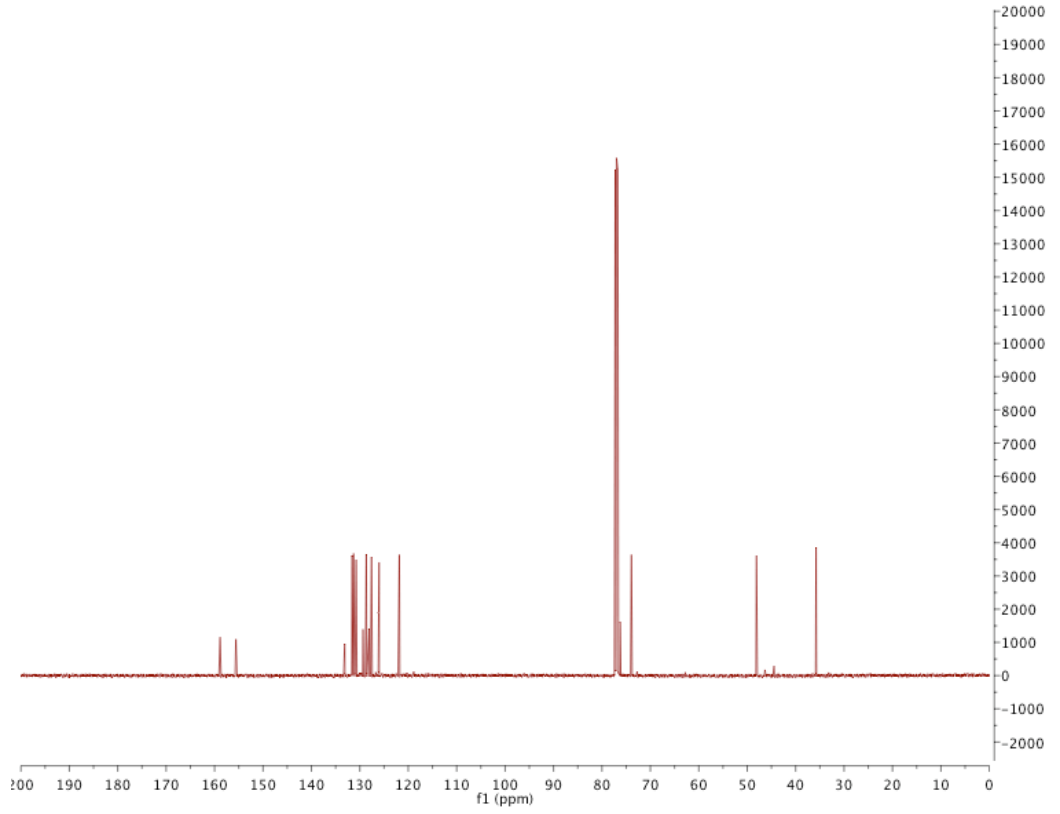
2-bromo-6-(4-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2e)



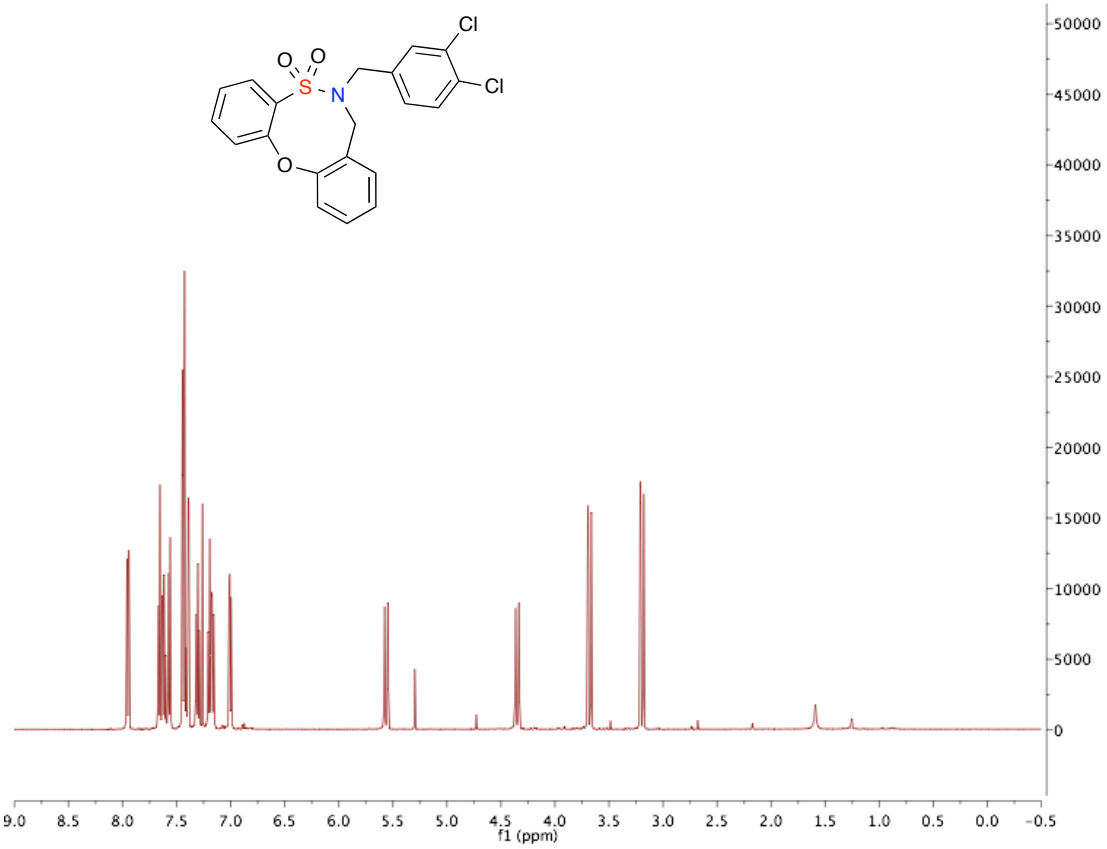


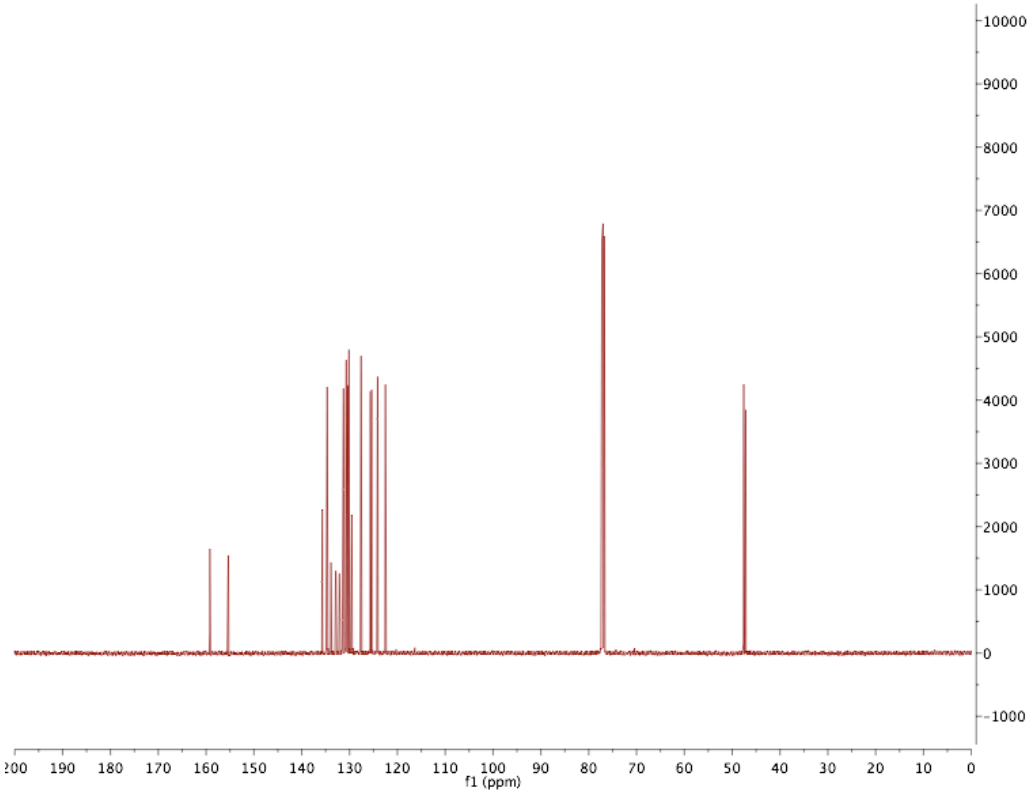
2-bromo-6-(prop-2-yn-1-yl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2g)



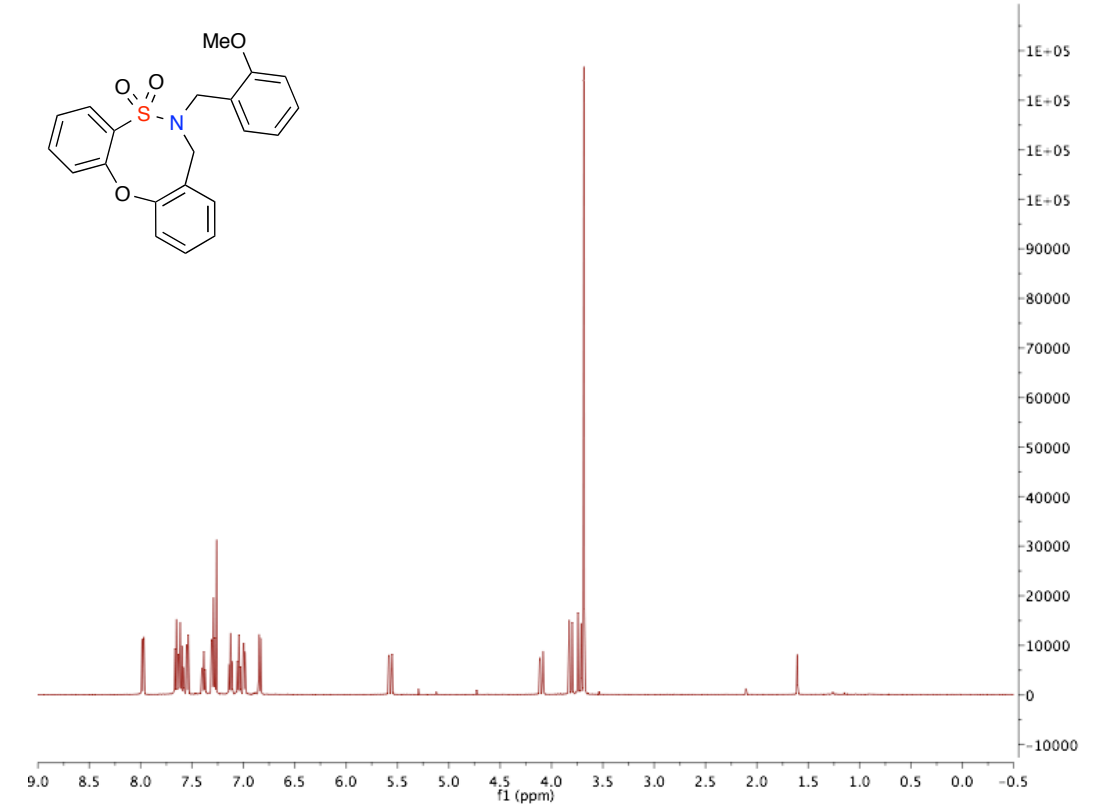


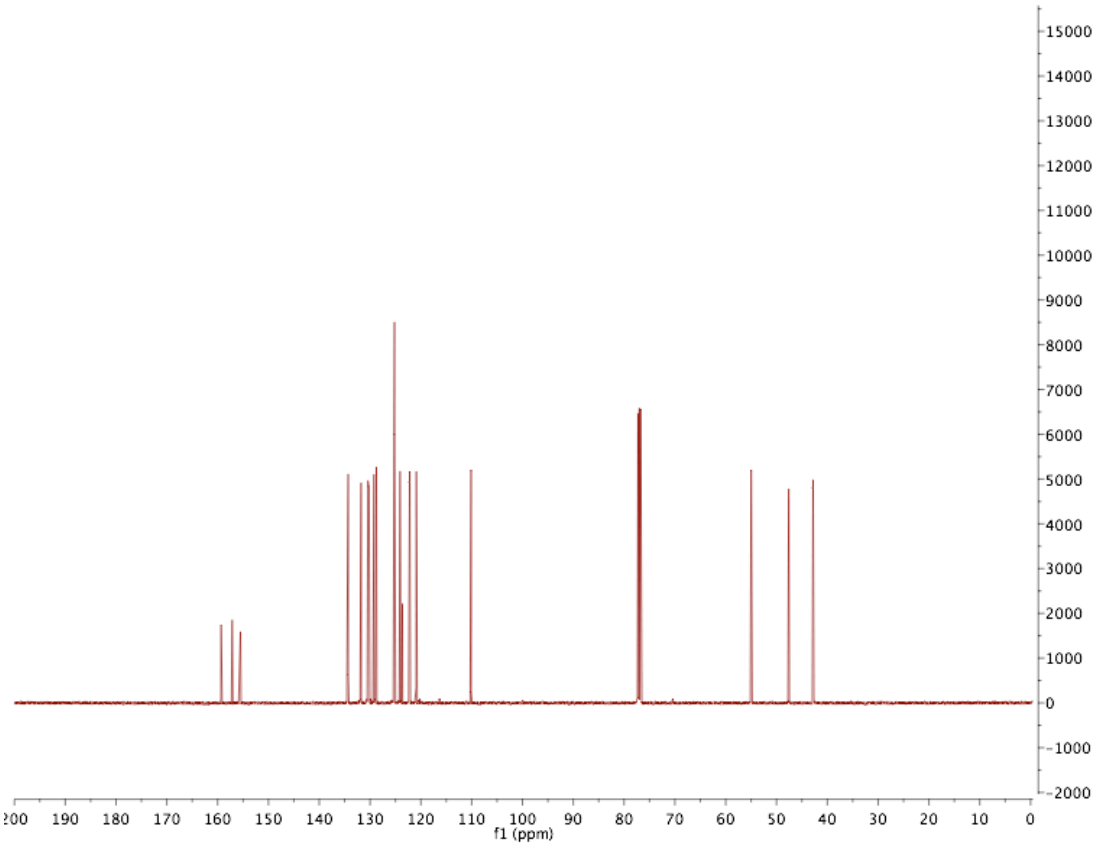
6-(3,4-dichlorobenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2b)



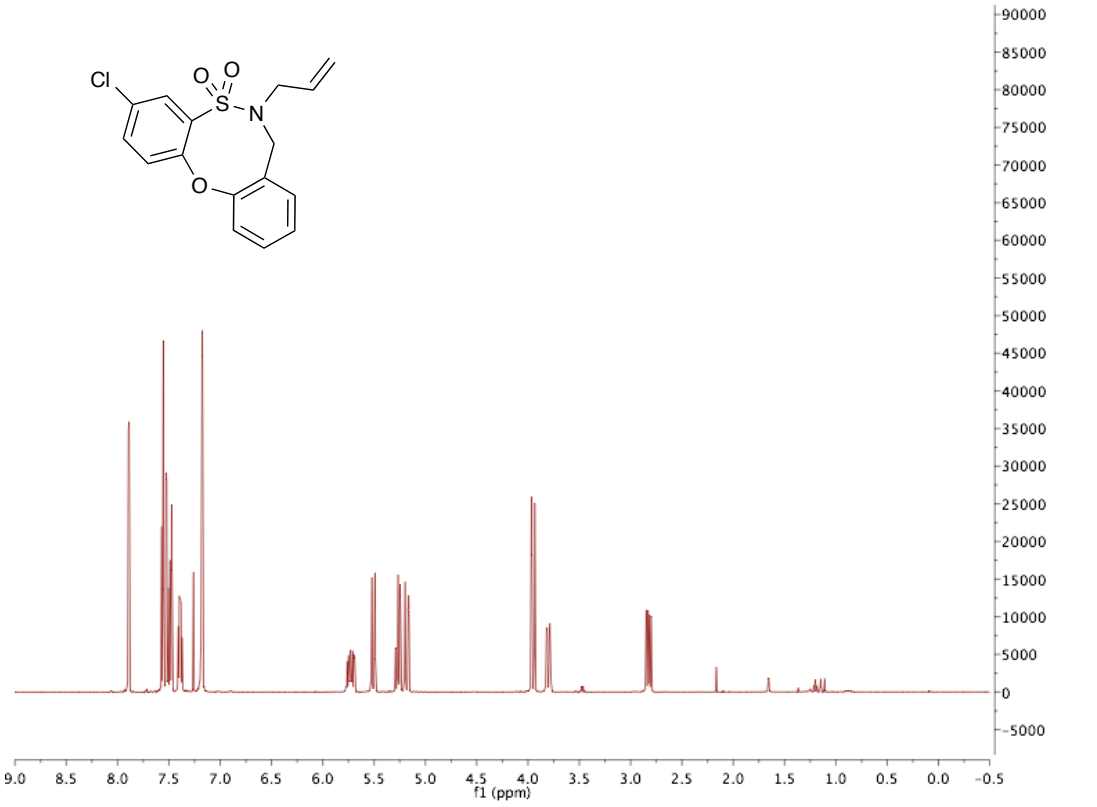


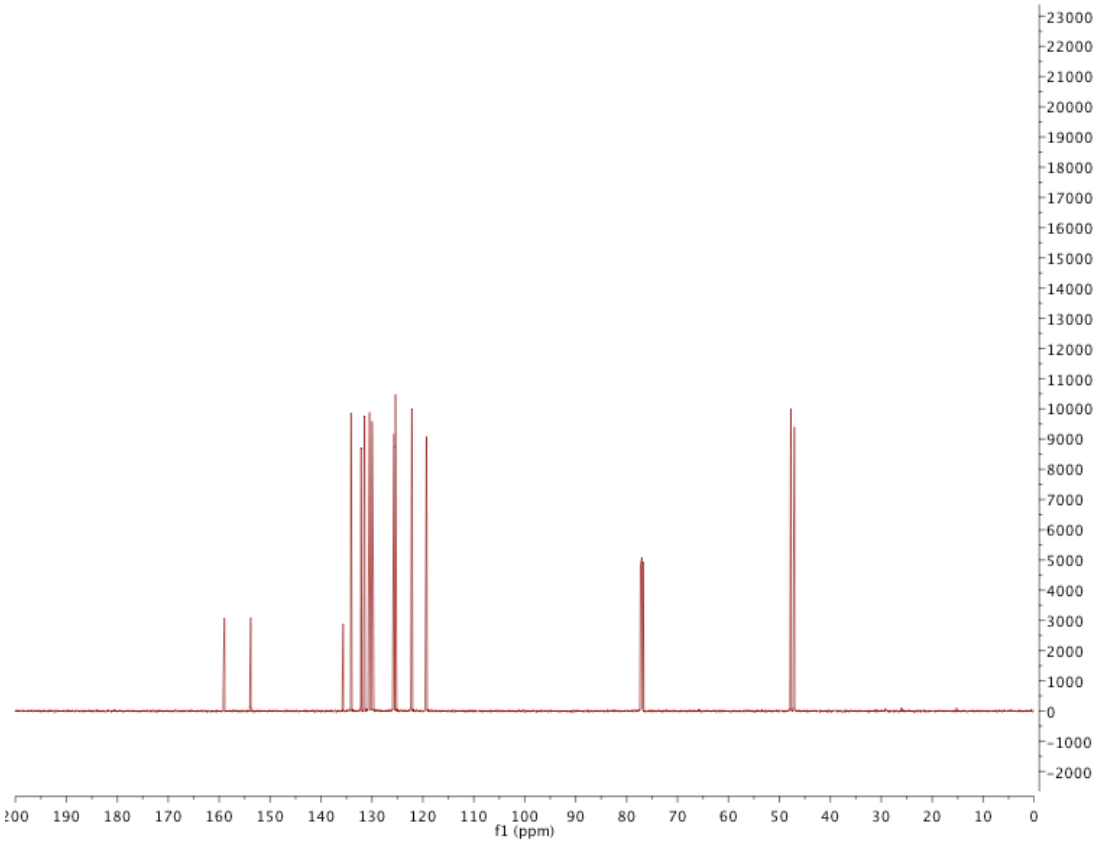
6-(2-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2a)



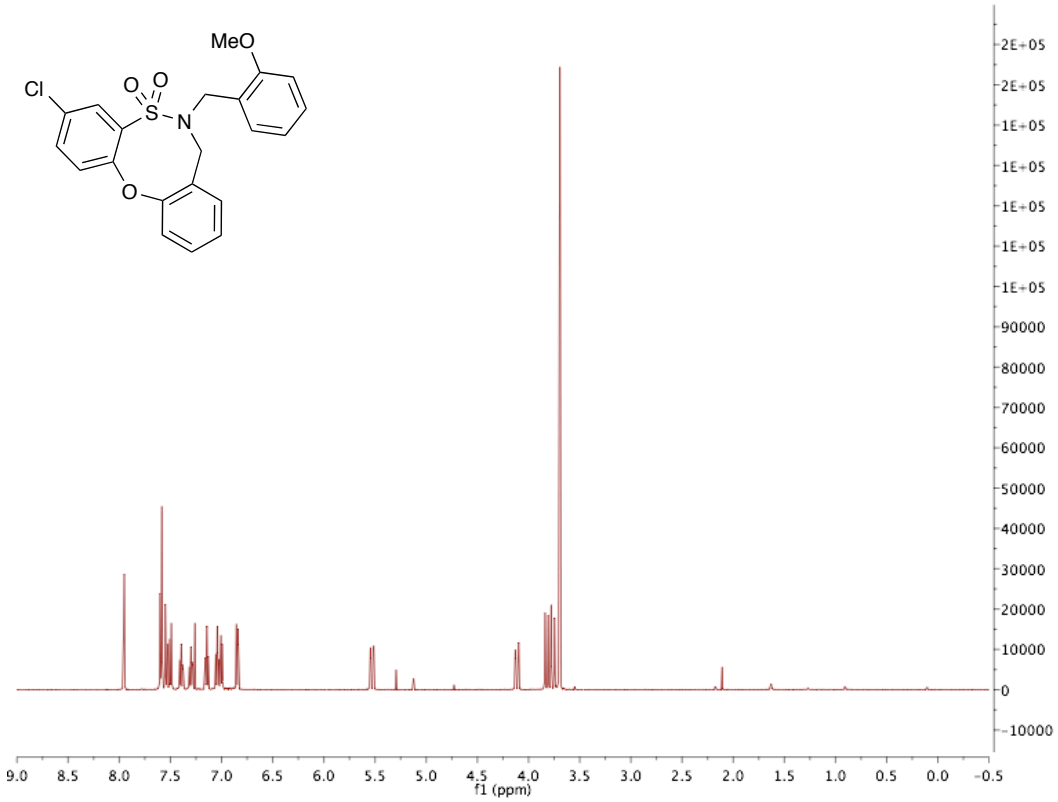


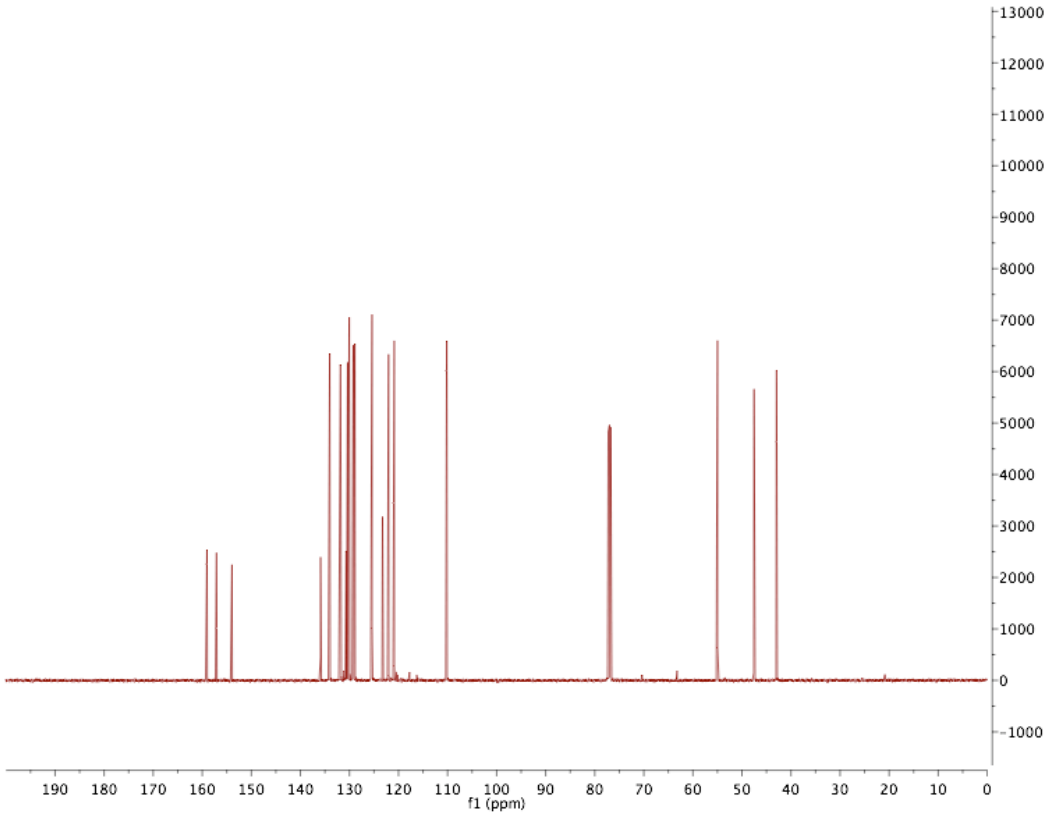
6-allyl-3-chloro-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2h



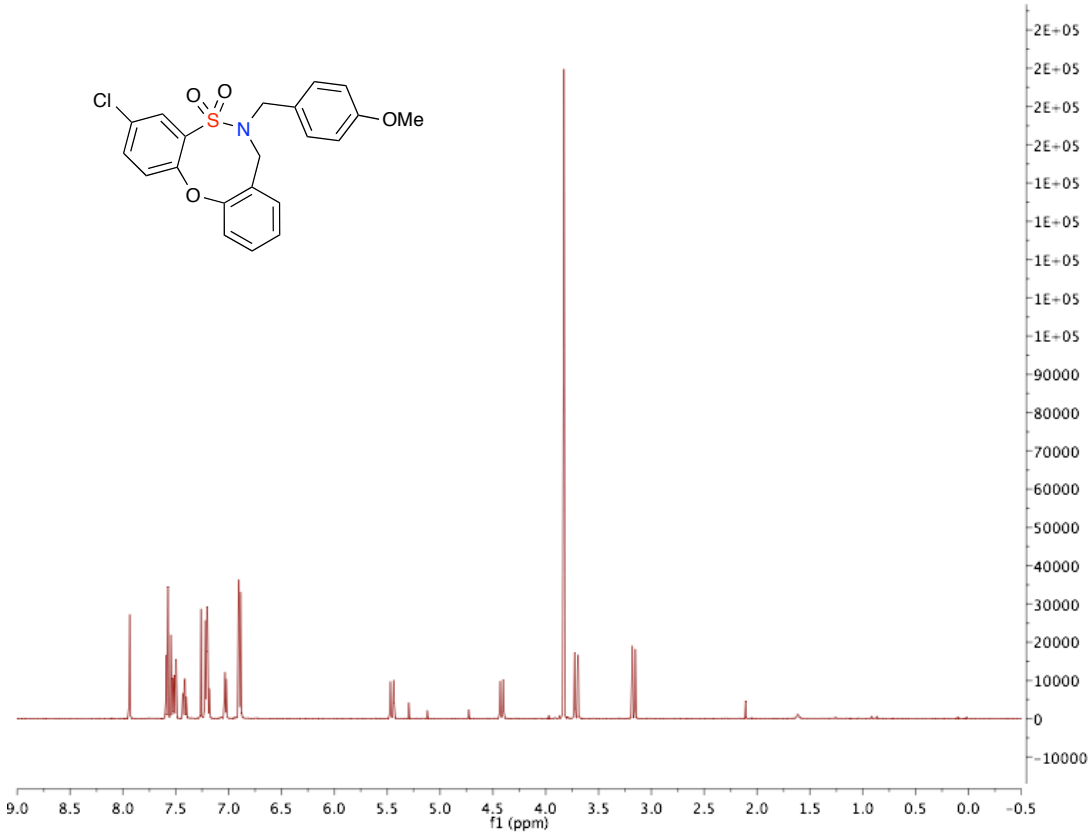


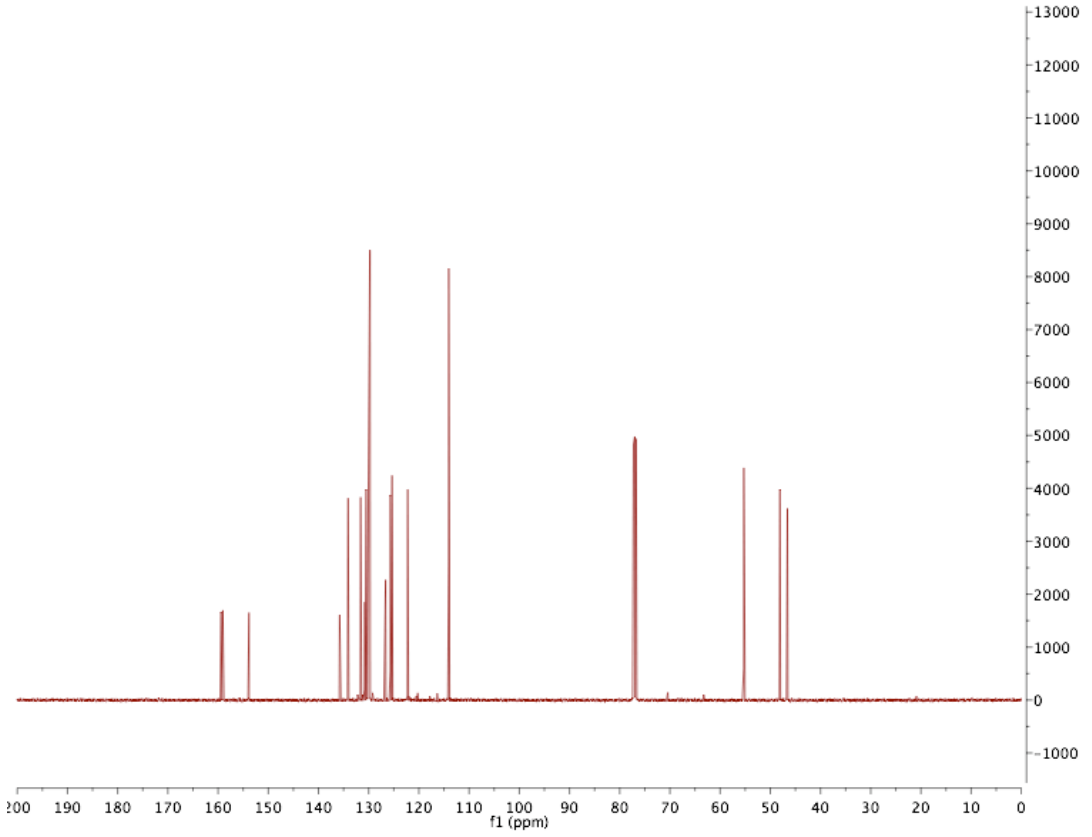
3-chloro-6-(2-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2k)



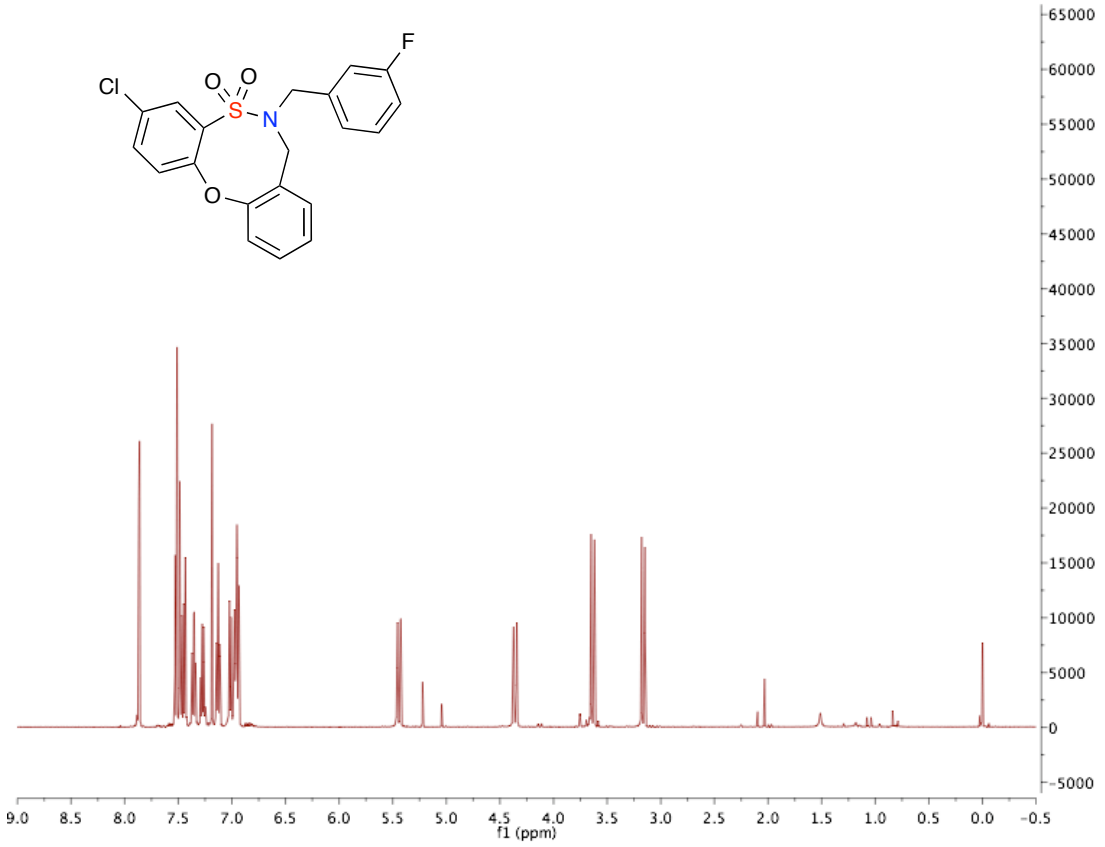


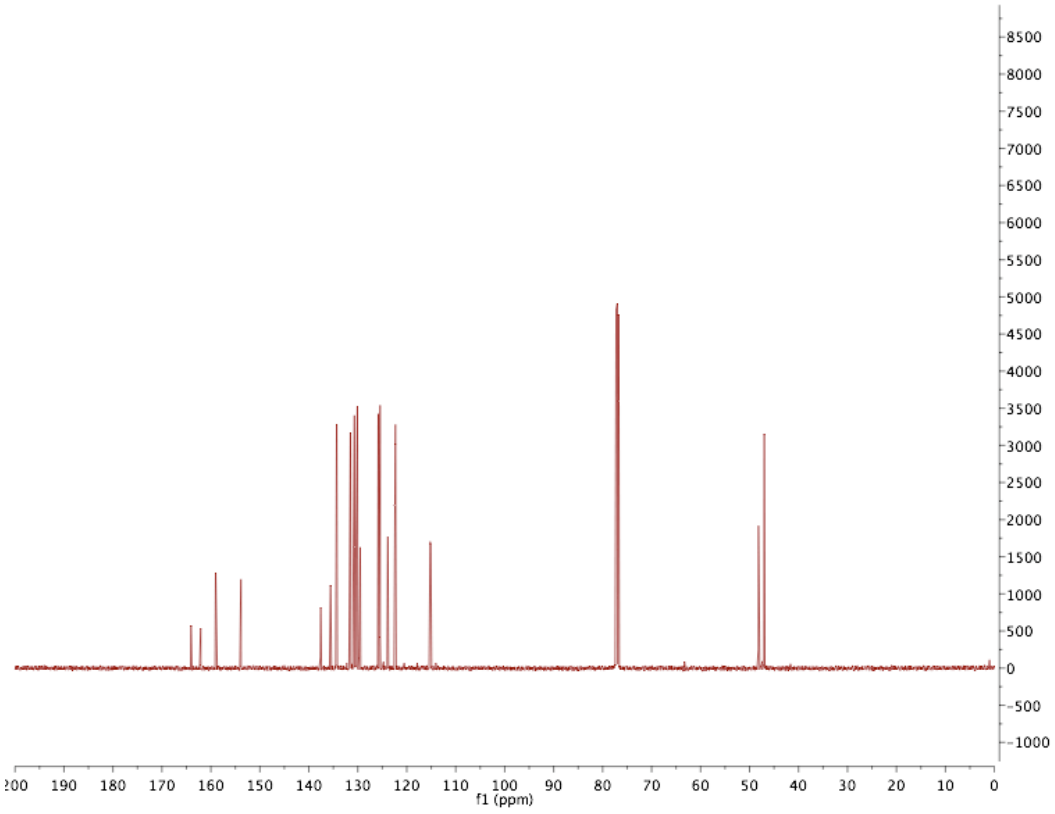
3-chloro-6-(4-methoxybenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2i)



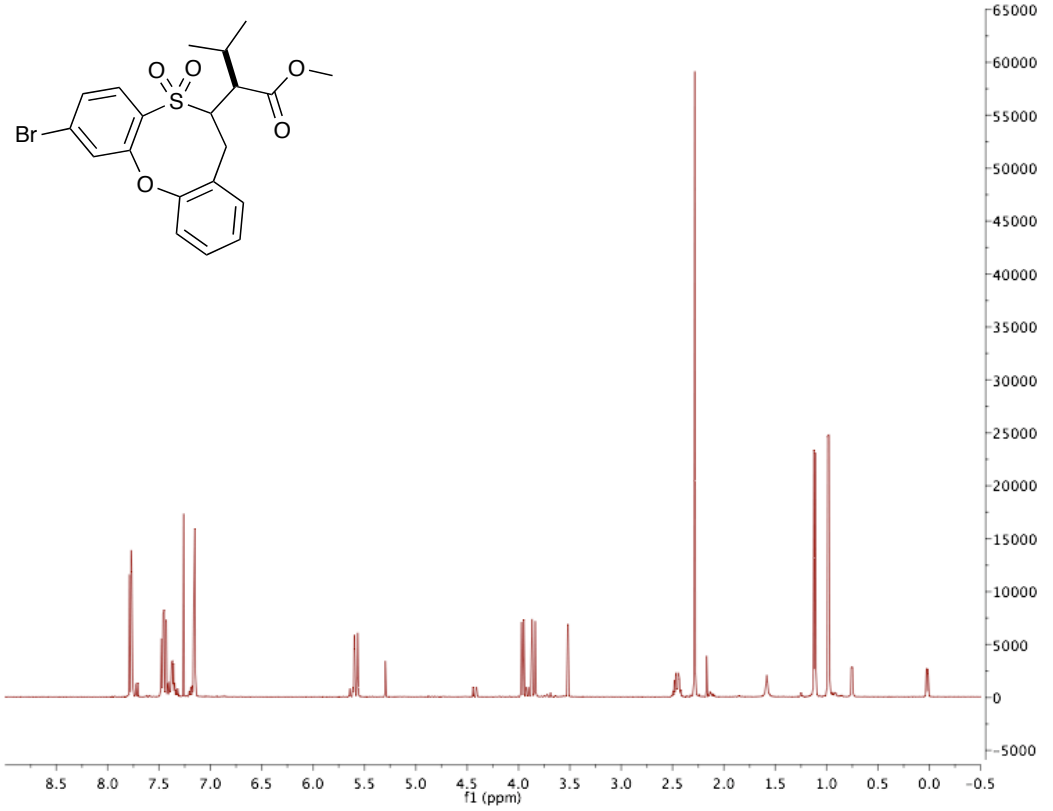


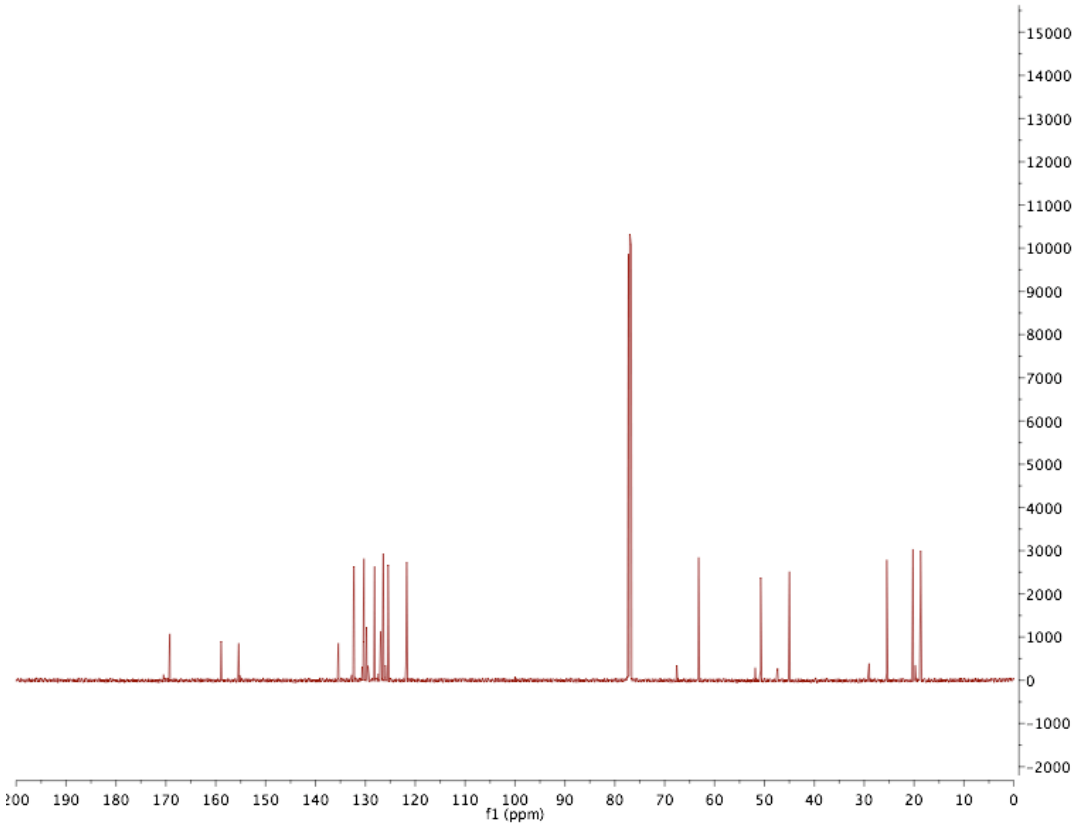
3-chloro-6-(3-fluorobenzyl)-6,7-dihydrodibenzo[b,g][1,4,5]oxathiazocine 5,5-dioxide (2j)



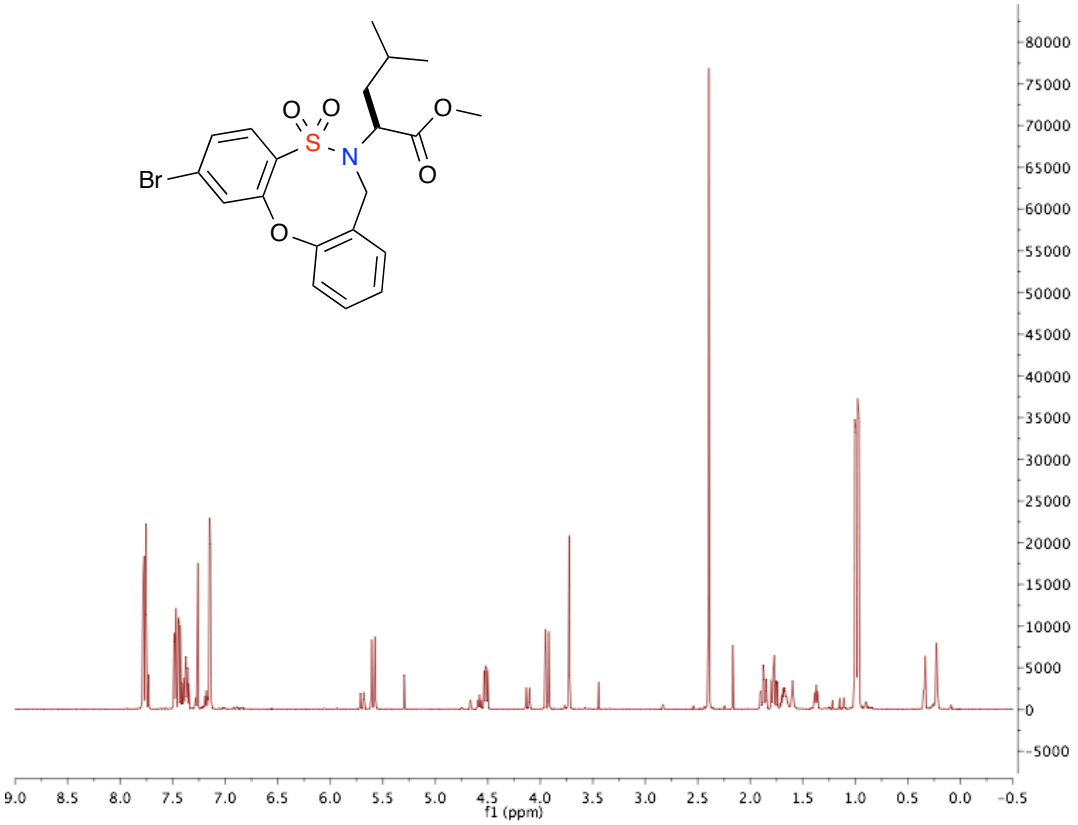


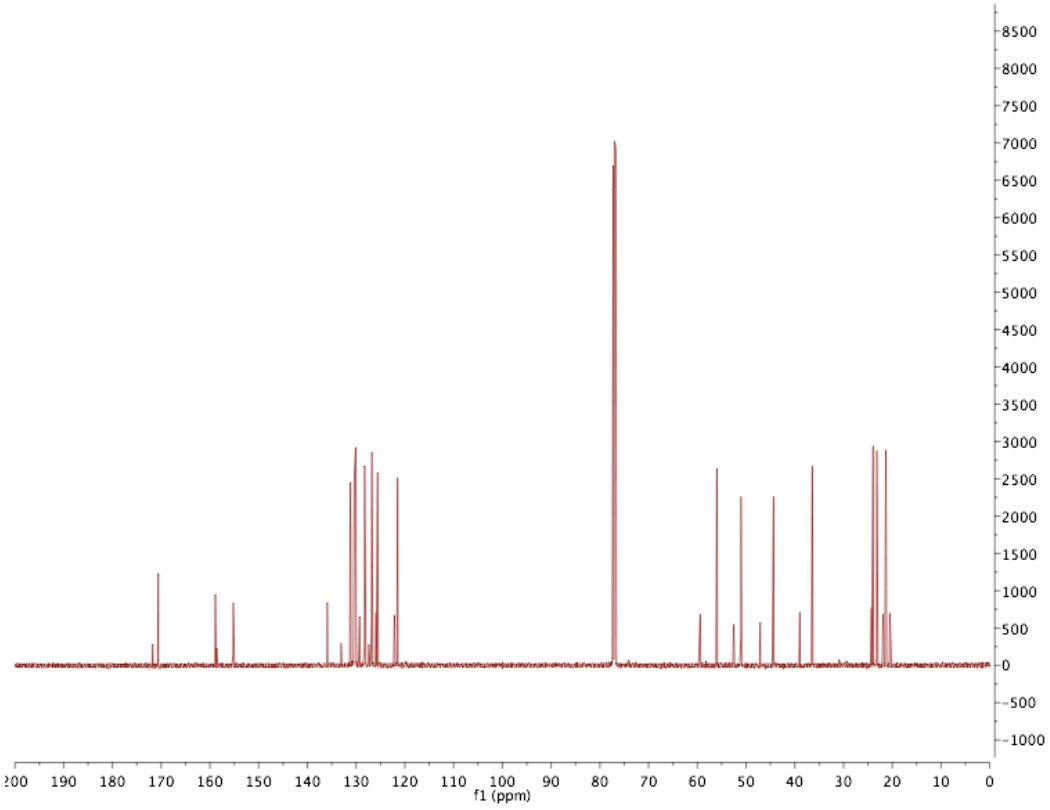
Methyl 2-(2-bromo-5,5-dioxidodibenzo[b,g][1,4,5]oxathiazocin-6(7H)-yl)-3-methylbutanoate 2-l

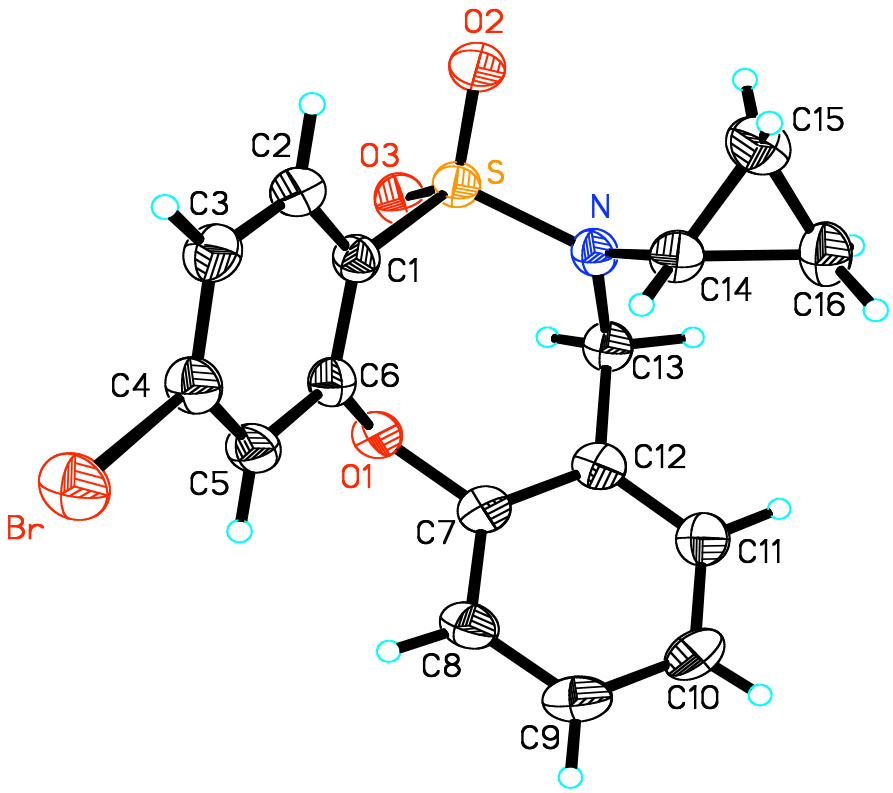




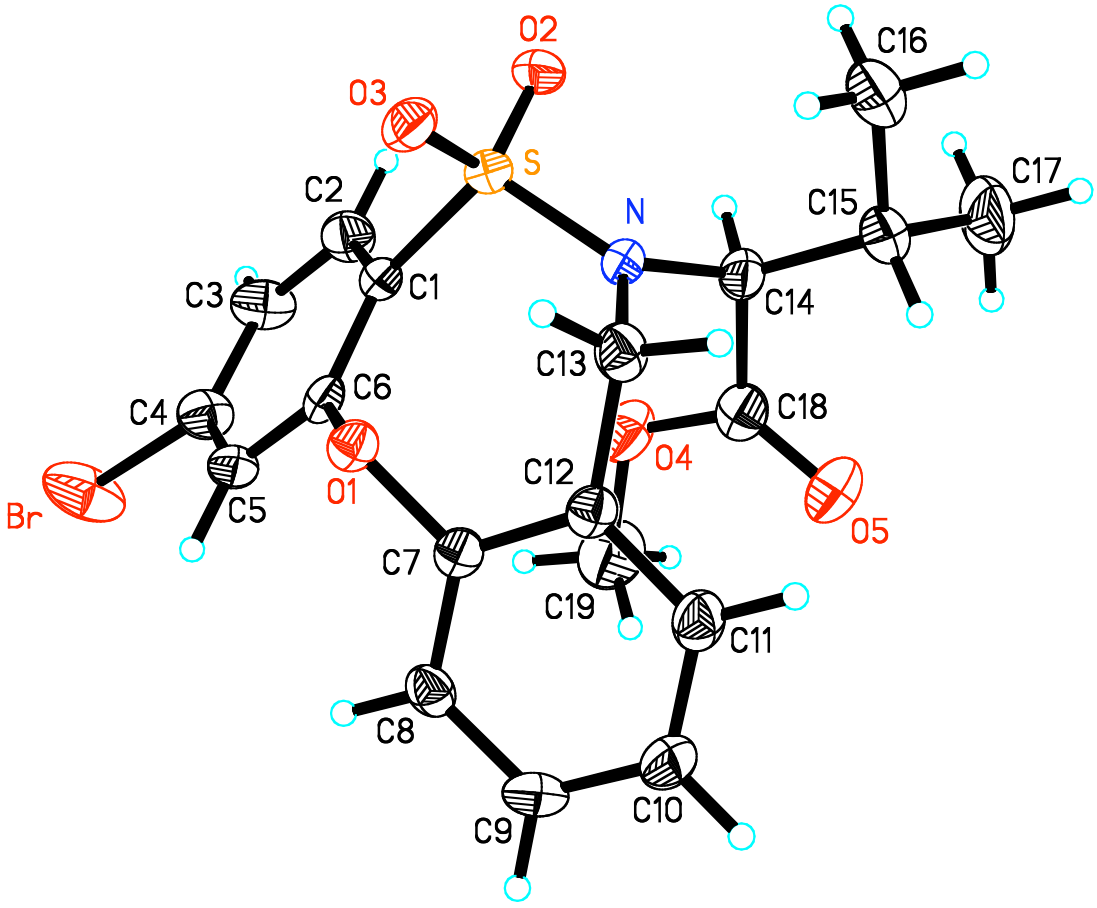
methyl 2-(2-bromo-5,5-dioxidodibenzo[b,g][1,4,5]oxathiazocin-6(7H)-yl)-4-methylpentanoate (2m)



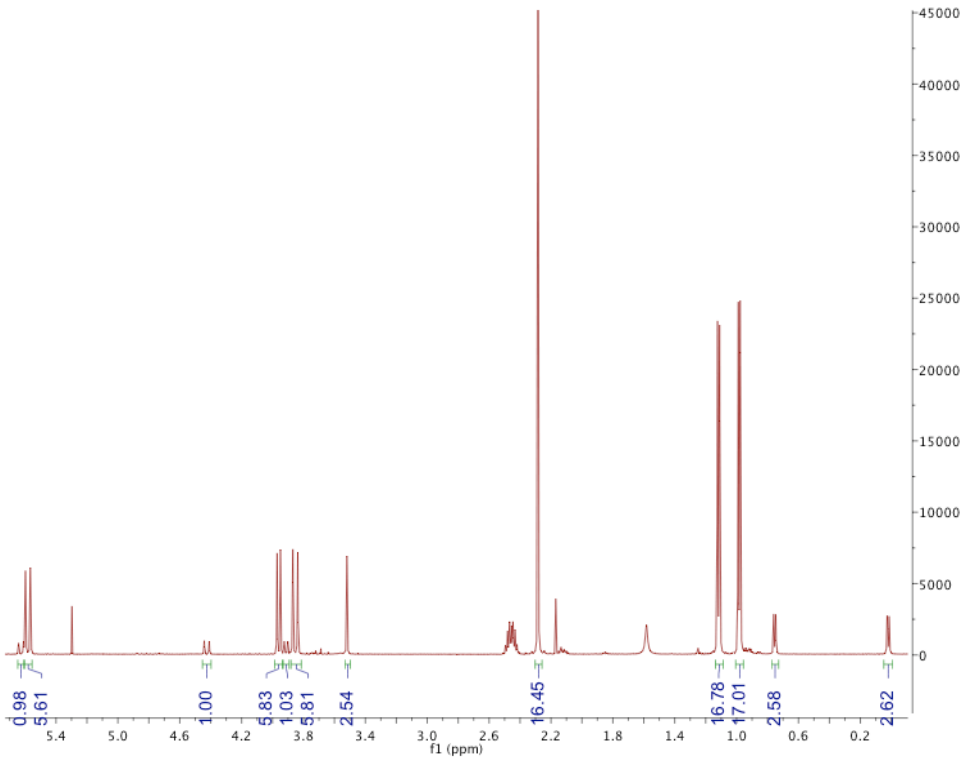




Thermal ellipsoid diagram of compound 2f at 50% probability level.



Thermal ellipsoid diagram of compound 2-l at 50% probability level.



	Chemical Shift (δ)	Multiplicity	J (Hz)	Rel. Intensity
minor-**2l**	5.63	d	16.0	1.0
major-**2l**	**5.58**	**d**	**15.9**	**5.82**
minor-**2l**	4.43	d	16.0	1.0
major-**2l**	**3.85**	**d**	**15.9**	**5.96**
major-**2l**	**3.96**	**d**	**10.9**	**5.95**
minor-**2l**	3.91	d	11.3	1.0
minor-**2l**	3.52	s	na	2.6
major-**2l**	**2.28**	**s**	**na**	**17.2**
major-**2l**	**1.1, 0.98**	**d, d**	**6.3, 6.4**	**16.8, 17.0**
minor-**2l**	0.75, 0.02	d, d	6.5, 6.6	2.6, 2.6

Table 3: Selected ^{1}H NMR (500 MHz, $CDCl_3$) comparison data for rotomer presence Major product NMR peak values are bolded