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Supporting Information

Sodium Bicyclo[1.1.1]pentanesulfinate: A Bench-Stable Precursor for Bicyclo[1.1.1]pentylsulfones and Bicyclo-[1.1.1]pentanesulfonamides

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Contents

1 General remarks

^{1}H-NMR spectra were recorded on BRUKER Avance AV 300 (300 MHz), BRUKER Avance 400 (400 MHz) and BRUKER Avance DRX 500 (500 MHz) spectrometers. Chemical shifts are given in parts per million (δ/ppm), downfield from tetramethylsilane (TMS) and are referenced to chloroform (δ = 7.26 ppm), dimethyl sulfoxide (δ = 2.50 ppm) or water (δ = 4.79 ppm) as internal standard. All coupling constants are absolute values and *J* values are expressed in Hertz (Hz). The description of signals include: s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, q = quartet, quin = quintet, sxt = sextet, sept = septet, m = multiplet. The spectra were analyzed according to first order.

^{13}C-NMR spectra were recorded on BRUKER Avance 400 (100 MHz) and BRUKER Avance DRX 500 (125 MHz) spectrometers. Chemical shifts are expressed in parts per million (δ/ppm) downfield from tetramethylsilane (TMS) and are referenced to chloroform (δ = 77.16 ppm) or dimethyl sulfoxide (δ = 39.52 ppm) as internal standard.

MS (EI) (electron impact mass spectrometry) / **MS (FAB)** (fast atom bombardment mass spectrometry): Finnigan MAT 95 (70 eV). The molecular fragments are quoted as the relation between mass and charge (*m/z*), the intensities as a percentage value relative to the intensity of the base signal (100%).

MS (ESI) (electrospray ionization mass spectrometry): ThermoFisher QExactive Plus (4 kV). The molecular fragments are quoted as the relation between mass and charge (*m/z*), the intensities as a percentage value relative to the intensity of the base signal (100%).

HRMS: HRMS data are recorded with the Finnigan MAT 95 (EI/FAB) or the ThermoFisher QExactive Plus (ESI).

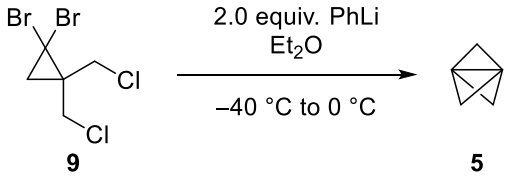
IR (infrared spectroscopy): ATR spectra were recorded by diamond crystal on Bruker ALPHA-IR.

Routine monitoring of reactions were performed using silica gel coated aluminium plates (Merck, silica gel 60, F_{254}) which were analyzed under UV-light at 254 nm and/or dipped into a solution of Seebach reagent (2.5% phosphor molybdic acid, 1.0% Cerium(IV) sulfate tetrahydrate and 6.0% sulfuric acid in H_2O, dipping solution) or potassium permanganate (1.5 g $KMnO_4$, 10 g K_2CO_3 and 1.25 mL 10% NaOH in 200 mL H_2O, dipping solution) and heated with a heat gun. Solvent mixtures are understood as v/v.

Solvents, reagents and chemicals were purchased from Sigma-Aldrich, Alfa Aesar, ABCR, Thermo Fisher Scientific, TCI and VWR and used without further purification unless stated otherwise.

2 Syntheses and characterizations

2.1 Synthesis of BCP-SO_2Na (**6**)



9 **5**

[1.1.1]Propellane was prepared according to a published procedure.[1] In a flame-dried round-bottomed flask that has been purged with argon 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane (**9**, 31.0 g, 94.0 mmol, 1.00 equiv.) was dissolved in Et_2O (130 mL) and cooled to –40 °C. 1.9 M PhLi solution (100 mL, 190 mmol, 2.02 equiv.) in Bu_2O was added dropwise under vigorous stirring (Figure 1 A). After complete addition, the mixture was warmed to 0 °C and stirred at this temperature for 2 h (Figure 1 B). The reaction flask was attached to an argon purged rotavap with dry ice condenser. The receiving flask, containing a magnetic stir bar, was cooled to –78 °C and the product was co-distilled with Et_2O (Figure 1 C). The water bath was set to 20 °C and the pressure was slowly reduced from 500 mbar to 20 mbar. A solution of **5** in Et_2O was obtained and used directly in the next reaction step.

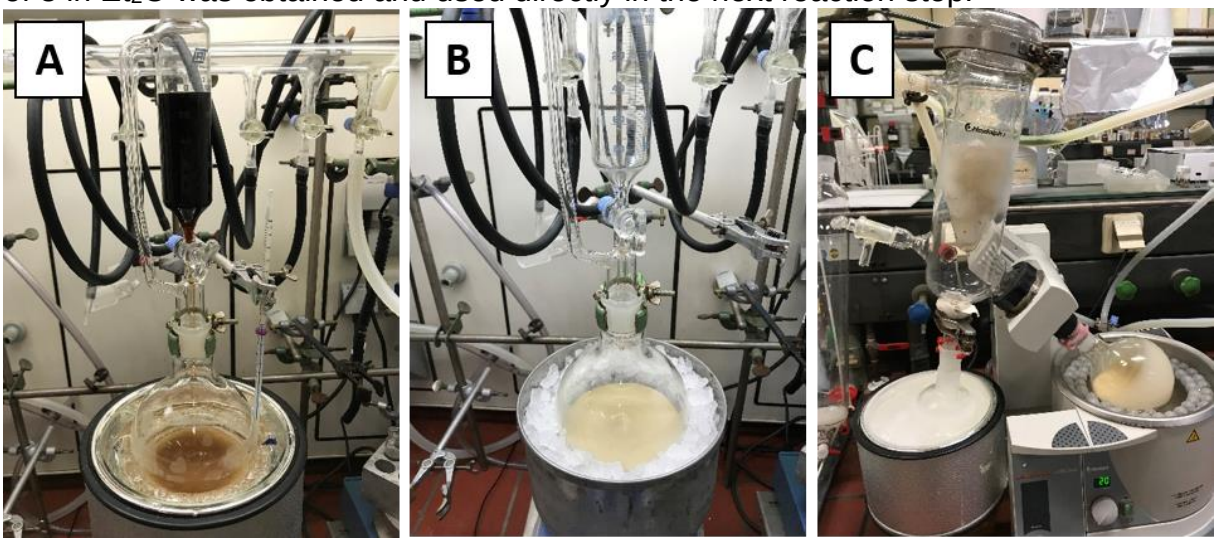
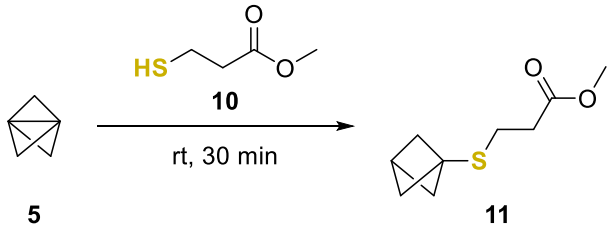


Figure 1. A, addition of PhLi to a solution of **9** at –40 °C. B, stirring at 0 °C for 2 h. C, co-distillation of **5** with Et_2O with a rotary evaporator.



5 **11**

Methyl 3-mercaptopropionate (**10**, 13.5 mL, 14.7 g, 122 mmol, 1.30 equiv.) was added to a solution of **5** in Et_2O (approx. 130 mL) under argon atmosphere and the mixture was stirred at room temperature for 30 min (Figure 2 A). The reaction mixture was poured into a separation funnel and the organic layer was washed with 150 mL of 1 M NaOH-solution (Figure 2 B). The organic layer was dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure to give **11** as a colorless liquid (13.8 g, 74.3 mmol, 79% from **9**).
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3H), 2.79 (t, J = 7.6 Hz, 2H), 2.73 (s, 1H), 2.60 (t, J = 7.6 Hz, 2H), 1.97 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.5, 53.9 (3C),

51.9, 44.4, 35.5, 28.9, 26.2 ppm; MS (EI, 20 °C): *m/z* (%) = 186 (0.5) $[M]^+$, 185 (1) $[M–H]^+$, 155 (5) $[M–CH_3O]^+$, 99 (100) $[C_5H_7S]^+$, 67 (48) $[C_5H_7]^+$; HRMS (EI, 20 °C): calc for $C_9H_{14}O_2{}^{32}S$ $[M–H]^+$: 185.0636; found 185.0637; IR (ATR): $\tilde{\nu}$ = 2976, 2908, 2874, 1737, 1435, 1354, 1299, 1285, 1245, 1207, 1171, 1154, 1139, 1018, 980, 931, 901, 823, 778, 741, 674, 445 cm^{-1}.

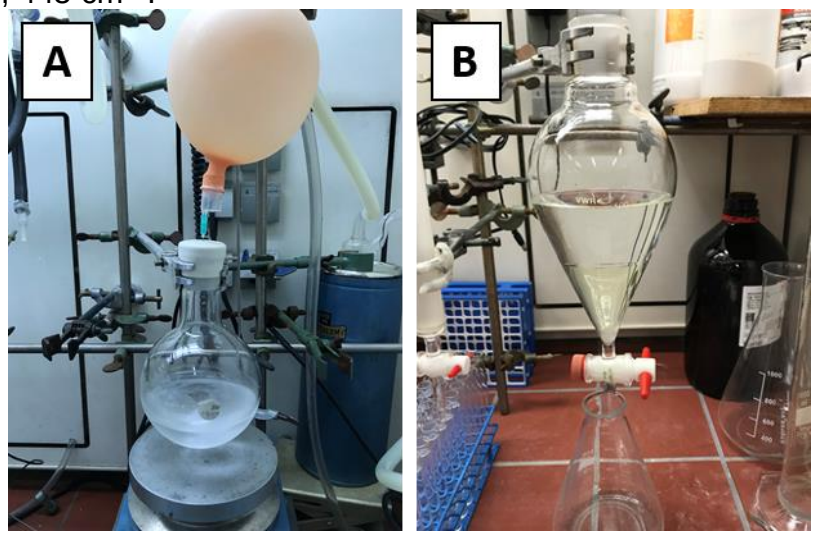
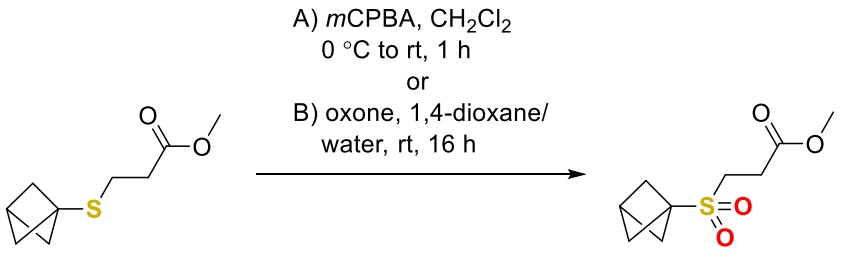


Figure 2. A, stirring of the propellane solution with **10**. B, only one washing step (NaOH-solution) for purification.



11 **12**

Method A: Sulfide **11** (13.8 g, 74.3 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (140 mL) and cooled to 0 °C in an ice bath. 3-Chlorobenzoic acid (43.6 g, 194 mmol, 2.62 equiv.) was added in portions (Figure 3 A) and the mixture was stirred for 1 h at room temperature after complete addition. The reaction mixture was poured into a beaker with 150 mL of sat. $Na_2S_2O_3$-solution. The precipitate was filtered off and washed with 50 mL of CH_2Cl_2 (Figure 3 B). The filtrate was poured into a separation funnel and the phases were separated. The organic layer was washed with 250 mL of 1 M NaOH-solution (Figure 3 C). The organic layer was collected and dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure to give **12** as a colorless oil (13.3 g, 60.9 mmol, 82%).

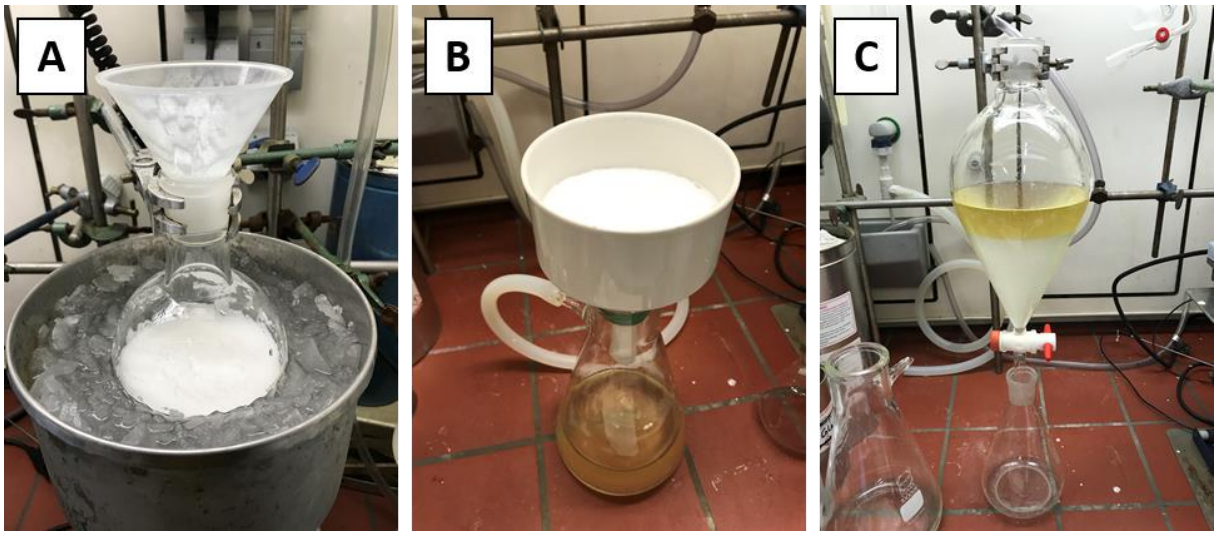
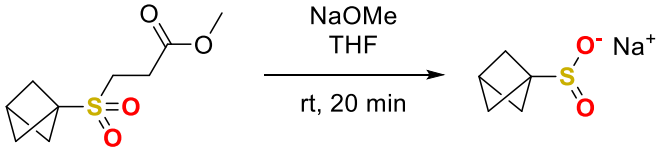


Figure 3. A, addition of *m*CPBA at 0 °C. B, filtration of the precipitated *m*-chlorobenzoic acid. C, washing the filtrate removes residual *m*-chlorobenzoic acid.

Method B: To a solution of sulfide **11** (4.39 g, 23.6 mmol, 1.00 equiv.) in 1,4-dioxane/water 1:1 (170 mL) potassium peroxymonosulfate (OXONE®) (29.0 g, 47.1 mmol, 2.00 equiv.) was added over 5 min. The reaction mixture was stirred at room temperature for 18 h. The solid was removed by filtration and washed with 50 mL of 1,4-dioxane. The filtrate was concentrated under reduced pressure to remove 1,4-dioxane. The aqueous phase was partitioned between 150 mL of $CH_2Cl_2$and 100 mL of sat. $NaHCO_3$-solution. The organic layer was collected and dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure to give **12** as a colorless oil (3.69 g, 16.9 mmol, 72%).
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3H), 3.28 – 3.21 (m, 2H), 2.88 – 2.82 (m, 2H), 2.79 (s, 1H), 2.27 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 171.1, 54.1, 52.6, 51.0, 45.1, 26.9, 26.2 ppm; MS (EI, 70 °C): *m/z* (%) = 219 (0.3) $[M+H]^+$, 135 (17) $[M–C_5H_7O]^+$, 88 (26) $[M–C_5H_7SO_2+H]^+$, 67 (100) $[C_5H_7]^+$; HRMS (EI, 70 °C): calc for $C_9H_{15}O_4{}^{32}S$ $[M+H]^+$: 219.0691; found 219.0690; IR (ATR): $\tilde{\nu}$ = 2996, 2976, 2956, 2922, 2887, 1737, 1438, 1364, 1302, 1251, 1210, 1173, 1140, 1106, 1057, 1018, 980, 941, 898, 877, 830, 782, 718, 704, 625, 605, 594, 545, 513, 477, 448, 397, 378 cm^{-1}.



12 **6**

The sulfone **12** (13.3 g, 60.9 mmol, 1.00 equiv.) was dissolved in tetrahydrofuran (130 mL) and stirred at room temperature. A 5.4 M solution of sodium methanolate in methanol (3.29 g, 11.3 mL, 60.9 mmol, 1.00 equiv.) was added and a pale yellow solid precipitated (Figure 4 A). After complete addition, the reaction mixture was stirred at room temperature for 20 min. The solvent and the formed acrylate were evaporated under reduced pressure (Figure 4 B) to give **6** as a pale yellow solid (9.38 g, 60.8 mmol, quant., Figure 4 C).
^{1}H-NMR (400 MHz, D_2O): δ = 2.68 (s, 1H), 1.88 (s, 6H) ppm; ^{13}C-NMR (100 MHz, D_2O): δ = 57.2, 47.2, 25.8 ppm; MS (ESI–): *m/z* (%) = 131 (100) $[M–Na]^–$; MS (ESI+): *m/z* (%) = 133 (100) $[M+2H]^+$; HRMS (ESI+): calc for $C_5H_9O_2{}^{32}S$ $[M+2H]^+$: 133.0318; found 133.0314; IR (ATR): $\tilde{\nu}$ = 2978, 2959, 2904, 2873, 1205, 1190, 1017, 990, 933, 898, 860, 779, 664, 584, 524, 477, 397 cm^{-1}.

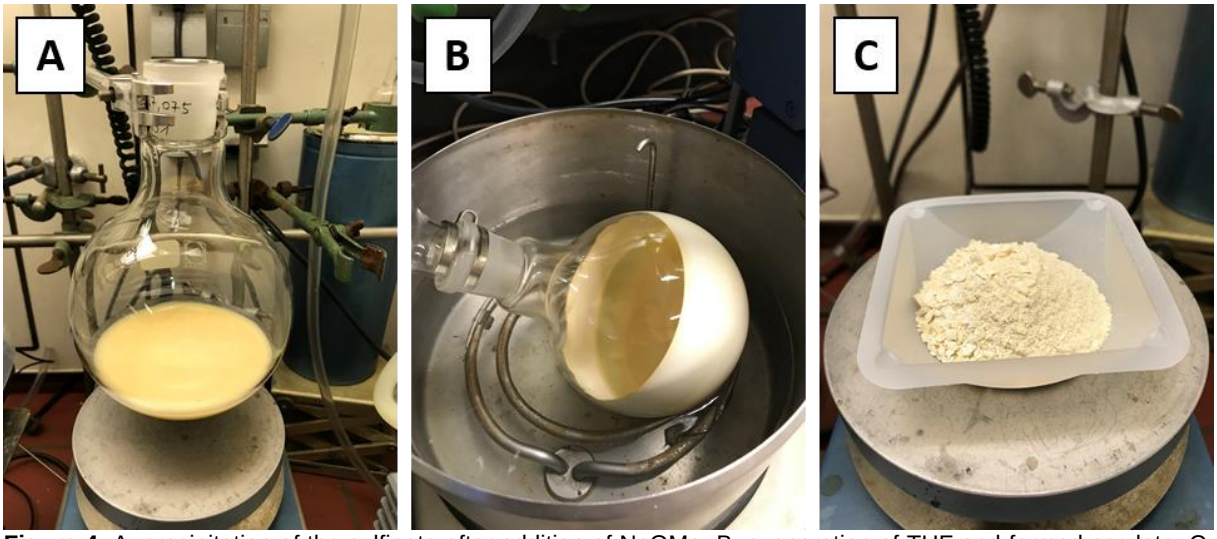


Figure 4. A, precipitation of the sulfinate after addition of NaOMe. B, evaporation of THF and formed acrylate. C, the final product.

2.2 Synthesis of sulfones 7

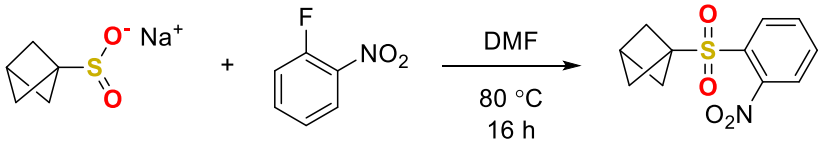
Sulfone **7a**

6 **13a** **7a**

BCP-SO_2Na (**6**, 142 mg, 0.921 mmol, 1.30 equiv.) and 1-fluoro-4-nitrobenzene (**13a**, 75 µL, 100 mg, 0.709 mmol, 1.00 equiv.) were mixed in a dry vial under argon atmosphere. DMF (1.0 mL) was added and the mixture was stirred at 80 °C for 3 d. The reaction mixture was cooled down to room temperature and purified by column chromatography (*c*Hex/EtOAc 5:1). The product was obtained as a colorless solid (172 mg, 0.679 mmol, 96%).

R_f (*c*Hex/EtOAc 5:1): 0.22; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.44–8.39 (m, 2H), 8.08–8.04 (m, 2H), 2.79 (s, 1H), 2.12 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.0, 142.9, 130.2, 124.4, 55.0, 50.8, 27.3 ppm; MS (EI, 130 °C): *m/z* (%) = 254 (0.1) $[M+H]^+$, 253 (0.1) $[M]^+$, 170 (3) $[M–C_5H_7–O]^+$, 67 (100) $[C_5H_7]^+$; HRMS (EI, 130 °C): calc for $C_{11}H_{11}O_4N^{32}S$ $[M]^+$: 253.0409; found 253.0407; IR (ATR): $\tilde{\nu}$ = 3003, 2919, 1524, 1349, 1296, 1285, 1210, 1194, 1170, 1126, 1078, 1014, 941, 881, 854, 778, 747, 732, 684, 619, 575, 548, 452, 407 cm^{-1}.
Crystallographic information of **7a** can be found in 3 Crystallographic Information.

Sulfone **7b**



6 **13b** **7b**

BCP-SO_2Na (**6**, 142 mg, 0.921 mmol, 1.30 equiv.) and 1-fluoro-2-nitrobenzene (**13b**, 100 mg, 0.709 mmol, 1.00 equiv.) were mixed in a dry vial under argon atmosphere. DMF (1.0 mL) was added and the mixture was stirred at 80 °C for 16 h. The reaction mixture was cooled down to room temperature and purified by column chromatography

(*c*Hex/EtOAc 5:1). The product was obtained as a colorless solid (176 mg, 0.695 mmol, 98%).

R_f (*c*Hex/EtOAc 5:1): 0.15; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.08–8.04 (m, 1H), 7.82–7.72 (m, 3H), 2.76 (s, 1H), 2.29 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.8, 134.9, 132.6, 132.2, 131.3, 124.5, 56.5, 52.0, 26.4 ppm; MS (FAB): *m/z* (%) = 254 (0.1) $[M+H]^+$, 253 (0.1) $[M]^+$, 170 (3) $[M–C_5H_7–O]^+$, 67 (100) $[C_5H_7]^+$; HRMS (FAB): calc for $C_{11}H_{11}O_4N^{32}S$ $[M]^+$: 253.0409; found 253.0407; IR (ATR): $\tilde{\nu}$ = 3094, 3003, 2972, 2918, 2885, 1589, 1536, 1438, 1371, 1309, 1207, 1170, 1137, 1103, 1055, 969, 945, 895, 877, 851, 773, 745, 721, 653, 611, 565, 533, 455, 384 cm^{-1}.
Crystallographic information of **7b** can be found in 3 Crystallographic Information.

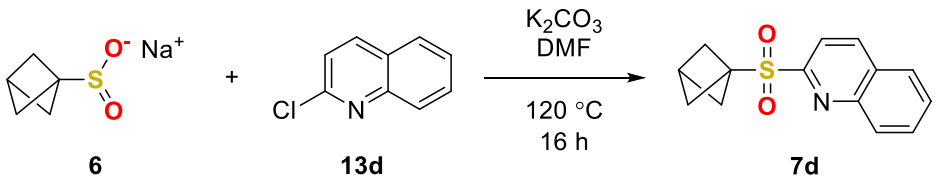
Sulfone **7c**

6 **13c** **7c**

BCP-SO_2Na (**6**, 128 mg, 0.828 mmol, 1.30 equiv.) and 3-fluoro-4-nitrophenol (**13c**, 100 mg, 0.637 mmol, 1.00 equiv.) were mixed in a dry vial under argon atmosphere. DMF (1.0 mL) was added and the mixture was stirred at 100 °C for 16 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (*c*Hex/EtOAc 2:1). The product was obtained as a colorless solid (128 mg, 0.475 mmol, 75%).

R_f (*c*Hex/EtOAc 2:1): 0.09; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 2.7 Hz, 1H), 7.19 (dd, *J* = 8.8, 2.7 Hz, 1H), 2.79 (s, 1H), 2.34 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 176.1, 160.0, 133.8, 128.1, 121.0, 119.0, 57.2, 52.6, 26.2 ppm; MS (FAB): *m/z* (%) = 270 (8) $[M+H]^+$, 186 (12) $[M–C_5H_7–O]^+$, 154 (100) [3-NBA], 137 (75) $[M–C_5H_7SO_2–H]^+$; HRMS (FAB): calc for $C_{11}H_{12}O_5N^{32}S$ $[M+H]^+$: 270.0436; found 270.0435; IR (ATR): $\tilde{\nu}$ = 3268, 3009, 2968, 2917, 1598, 1581, 1544, 1486, 1432, 1356, 1299, 1249, 1228, 1205, 1156, 1139, 1096, 1041, 939, 912, 875, 847, 839, 773, 745, 694, 629, 592, 560, 534, 517, 473, 435 cm^{-1}.
Crystallographic information of **7c** can be found in 3 Crystallographic Information.

Sulfone **7d**



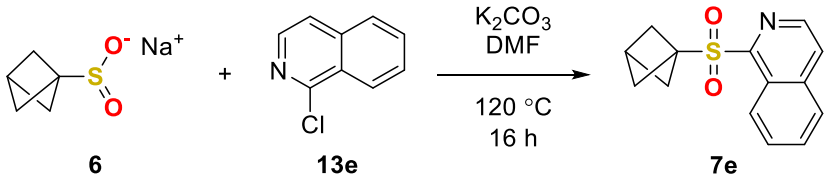
6 **13d** **7d**

BCP-SO_2Na (**6**, 123 mg, 0.795 mmol, 1.30 equiv.), 2-chloroquinoline (**13d**, 100 mg, 0.611 mmol, 1.00 equiv.) and potassium carbonate (127 mg, 0.917 mmol, 1.50 equiv.) were mixed in a dry vial under argon atmosphere. DMF (1.0 mL) was added and the mixture was stirred at 120 °C for 16 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (*c*Hex/EtOAc 10:1). The product was obtained as a colorless solid (46 mg, 0.177 mmol, 29%).

R_f (*c*Hex/EtOAc 5:1): 0.16; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.42 (dd, *J* = 8.5, 0.9 Hz, 1H), 8.28 (dt, *J* = 8.6, 1.0 Hz, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 7.94 (dd, *J* = 8.2, 1.4 Hz,

1H), 7.85 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.72 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 2.75 (s, 1H), 2.27 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 156.0, 147.5, 138.7, 131.2, 130.6, 129.4, 129.2, 128.0, 118.6, 54.5, 51.6, 27.7 ppm; MS (EI, 100 °C): *m/z* (%) = 259 (0.6) $[M]^+$, 258 (2) $[M–H]^+$,194 (73) $[M–C_5H_7+2H]^+$, 129 (100) $[M–C_5H_7SO_2+H]^+$, 128 (73) $[M–C_5H_7SO_2]^+$, 67 (18) $[C_5H_7]^+$; HRMS (EI, 100 °C): calc for $C_{14}H_{13}O_2N^{32}S$ $[M]^+$: 259.0667; found 259.0666; IR (ATR): $\tilde{\nu}$ = 3109, 2997, 2972, 2919, 2884, 1578, 1497, 1299, 1289, 1204, 1166, 1113, 1088, 878, 832, 766, 674, 649, 612, 588, 547, 520, 476, 445, 399, 388 cm^{-1}.

Sulfone **7e**



6 **13e** **7e**

BCP-SO_2Na (**6**, 123 mg, 0.795 mmol, 1.30 equiv.), 1-chloroisoquinoline (**13e**, 100 mg, 0.611 mmol, 1.00 equiv.) and potassium carbonate (127 mg, 0.917 mmol, 1.50 equiv.) were mixed in a dry vial under argon atmosphere. DMF (1.0 mL) was added and the mixture was stirred at 120 °C for 16 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (*c*Hex/EtOAc 10:1). The product was obtained as a colorless solid (65 mg, 0.251 mmol, 41%).

R_f (*c*Hex/EtOAc 5:1): 0.16; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.99 (dq, *J* = 8.5, 1.0 Hz, 1H), 8.57 (d, *J* = 5.5 Hz, 1H), 7.93 – 7.89 (m, 1H), 7.85 (dd, *J* = 5.5, 0.9 Hz, 1H), 7.77 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 2.74 (s, 1H), 2.29 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 155.3, 140.8, 137.6, 131.3, 129.3, 127.6, 125.4, 125.4, 55.4, 51.8, 27.6 ppm; MS (EI, 70 °C): *m/z* (%) = 259 (3) $[M]^+$, 194 (86) $[M–C_5H_7+2H]^+$, 129 (100) $[M–C_5H_7SO_2+H]^+$, 128 (62) $[M–C_5H_7SO_2]^+$, 67 (11) $[C_5H_7]^+$; HRMS (EI, 70 °C): calc for $C_{14}H_{13}O_2N^{32}S$ $[M]^+$: 259.0667; found 259.0666; IR (ATR): $\tilde{\nu}$ = 3009, 2966, 2918, 1622, 1584, 1557, 1496, 1453, 1373, 1292, 1204, 1160, 1108, 1095, 1020, 993, 949, 874, 840, 827, 786, 773, 748, 683, 656, 613, 569, 518, 462, 435, 408 cm^{-1}.

Sulfone **7f**

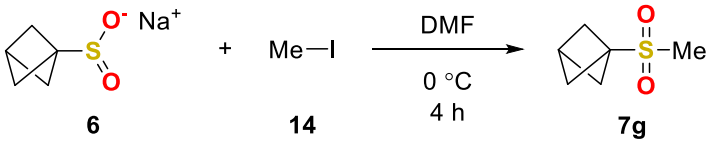
6 **13f** **7f**

BCP-SO_2Na (**6**, 80 mg, 0.518 mmol, 1.30 equiv.), 1-bromo-4-methoxybenzene (**13f**, 50 µL, 74.5 mg, 0.398 mmol, 1.00 equiv.), copper(I) iodide (7.6 mg, 40.0 µmol, 0.100 equiv.), L-proline (9.2 mg, 80.0 µmol, 0.200 equiv.) and potassium carbonate (55 mg, 0.398 mmol, 1.00 equiv.) were mixed in a dry vial under argon atmosphere. DMSO (1.0 mL) was added and the mixture was stirred at 110 °C for 22 h. The reaction mixture was cooled down and purified by column chromatography (*c*Hex/EtOAc 10:1 to 3:1). The product was obtained as a pale brown oil that slowly solidified (69 mg, 0.290 mmol, 73%).

R_f (*c*Hex/EtOAc 5:1): 0.21; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.80–7.75 (m, 2H), 7.04–6.99 (m, 2H), 3.89 (s, 3H), 2.71 (s, 1H), 2.06 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$):

δ = 163.8, 130.9, 128.5, 114.5, 55.8, 55.4, 50.5, 26.8 ppm; MS (EI, 60 °C): *m/z* (%) = 238 (12) $[M]^+$, 172 (36) $[M–C_5H_7+H]^+$, 155 (100) $[M–C_5H_7–O]^+$, 67 (55) $[C_5H_7]^+$; HRMS (EI, 70 °C): calc for $C_{12}H_{14}O_3{}^{32}S$ $[M]^+$: 238.0664; found 238.0664; IR (ATR): $\tilde{\nu}$ = 3009, 2966, 2918, 1622, 1584, 1557, 1496, 1453, 1373, 1292, 1204, 1160, 1108, 1095, 1020, 993, 949, 874, 840, 827, 786, 773, 748, 683, 656, 613, 569, 518, 462, 435, 408 cm^{-1}.

Sulfone **7g**



6 **14** **7g**

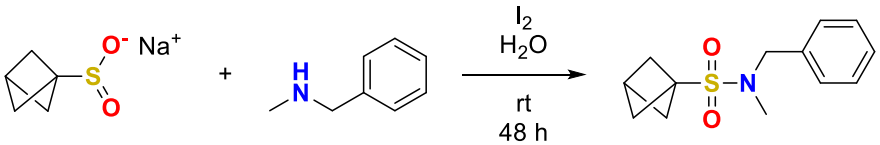
BCP-SO_2Na (**6**, 100 mg, 0.649 mmol, 1.00 equiv.) was dissolved in DMF (1.0 mL) and stirred at 0 °C (ice bath). A freshly prepared 0.5 M solution of iodomethane in DMF (1.95 mL, 138 mg, 0.973 mmol, 1.50 equiv.) was added dropwise and the reaction mixture was stirred for 4 h at 0 °C. The mixture was diluted with 2 mL of water and extracted with 15 mL of dichloromethane. The organic layer was collected and was dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure. The crude product was recrystallized from cyclohexane, dried under reduced pressure and the product was obtained as fine, colorless needles (57 mg, 0.390 mmol, 60%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.81 (s, 3H), 2.79 (s, 1H), 2.26 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 54.5, 50.7, 37.4, 26.4 ppm; MS (EI, 25 °C): *m/z* (%) = 147 (1) $[M+H]^+$, 67 (100) $[M–SO_2CH_3]^+$; HRMS (EI, 25 °C): calc for $C_6H_{11}O_2{}^{32}S$ $[M+H]^+$: 147.0480; found 147.0479; IR (ATR): $\tilde{\nu}$ = 3013, 2999, 2979, 2927, 2890, 1741, 1507, 1453, 1411, 1322, 1279, 1208, 1167, 1103, 969, 943, 875, 782, 749, 554, 540, 494 cm^{-1}.

Crystallographic information of **7g** can be found in 3 Crystallographic Information.

2.3 Synthesis of sulfonamides 8

Sulfonamide **8a**



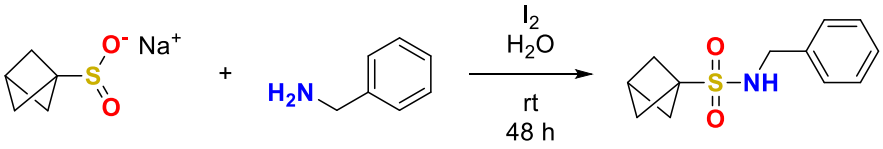
6 **15a** **8a**

BCP-SO_2Na (**6**, 100 mg, 0.649 mmol, 1.00 equiv.) was dissolved in water (1.00 mL). Benzyl(methyl)amine (**15a**, 126 µL, 118 mg, 973 µmol, 1.50 equiv.) was added, followed by iodine (165 mg, 649 µmol, 1.00 equiv.). The reaction mixture was stirred at room temperature for 48 h. The reaction mixture was poured into a separation funnel and diluted with CH_2Cl_2. The organic layer was washed successively with 10 mL of $Na_2S_2O_3$-solution. The aqueous layers were combined and reextracted with CH_2Cl_2. The organic layers were collected and dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (*c*Hex/EtOAc 10:1). The product was obtained as a colorless solid (40 mg, 0.159 mmol, 25%).

R_f (*c*Hex/EtOAc 5:1): 0.26; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5H), 4.37 (s, 2H), 2.81 (s, 3H), 2.73 (s, 1H), 2.28 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$):

δ = 136.4, 128.8, 128.4, 128.0, 54.3, 53.8, 52.1, 34.9, 27.7 ppm; MS (ESI+): *m/z* (%) = 252 (28) $[M+H]^+$, 188 (100) $[M–SO_2+H]^+$; HRMS (ESI+): calc for $C_{13}H_{18}NO_2{}^{32}S$ $[M+H]^+$: 252.1053; found 252.1050; IR (ATR): $\tilde{\nu}$ = 2979, 2918, 2885, 1494, 1455, 1373, 1313, 1211, 1197, 1181, 1145, 1113, 1075, 1000, 939, 902, 877, 779, 761, 727, 694, 613, 591, 554, 528, 490, 458 cm^{-1}.

Sulfonamide **8b**

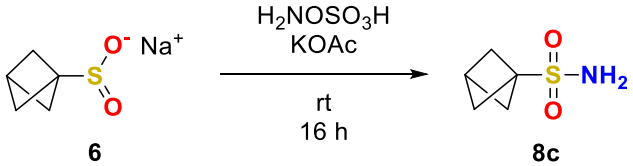


6 **15b** **8b**

BCP-SO_2Na (**6**, 100 mg, 0.649 mmol, 1.00 equiv.) was dissolved in water (1.0 mL). Benzylamine (**15b**, 92 µL, 90.4 mg, 0.843 mmol, 1.30 equiv.) was added, followed by iodine (165 mg, 649 µmol, 1.00 equiv.). The reaction mixture was stirred at room temperature for 48 h. The reaction mixture was poured into a separation funnel and diluted with CH_2Cl_2. The organic layer was washed with 10 mL of $Na_2S_2O_3$-solution. The aqueous layers were combined and reextracted with CH_2Cl_2. The organic layers were collected and dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (*c*Hex/EtOAc 10:1 to 5:1). The product was obtained as a colorless solid (38 mg, 0.160 mmol, 25%).

R_f (*c*Hex/EtOAc 5:1): 0.18; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.39–7.28 (m, 5H), 4.49 (bs, 1H), 4.31 (d, ^3J = 6.1 Hz, 2H), 2.68 (s, 1H), 2.17 (s, 6H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 137.5, 129.0, 128.1, 127.9, 54.3, 51.3, 47.6, 26.7 ppm; MS (ESI+): *m/z* (%) = 260 (9) $[M+Na]^+$, 238 (6) $[M+H]^+$, 174 (100) $[M–SO_2+H]^+$; HRMS (ESI+): calc for $C_{12}H_{16}NO_2{}^{32}S$ $[M+H]^+$: 238.0896; found 238.0894; IR (ATR): $\tilde{\nu}$ = 3286, 3247, 2978, 2918, 2880, 1494, 1452, 1439, 1431, 1302, 1211, 1183, 1146, 1120, 1082, 1062, 1051, 1026, 908, 878, 850, 829, 748, 724, 693, 662, 620, 588, 545, 527, 509, 452 cm^{-1}.
Crystallographic information of **8b** can be found in 3 Crystallographic Information.

Sulfonamide **8c**



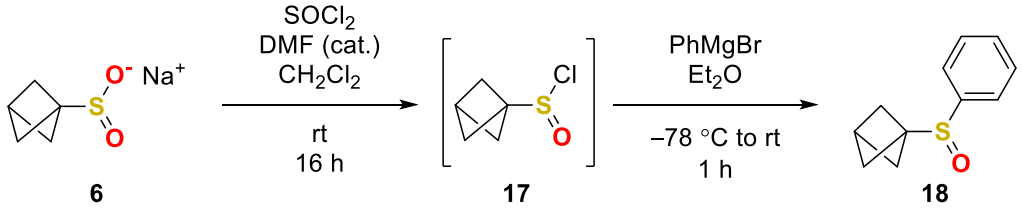
6 **8c**

BCP-SO_2Na (1.00 g, 6.50 mmol, 1.00 equiv.) was dissolved in water (30 mL) and hydroxylamine-O-sulfonic acid (1.47 g, 13.0 mmol, 2.00 equiv.) and potassium acetate (637 mg, 6.50 mmol, 1.00 equiv.) were added. The reaction mixture was stirred at room temperature for 18 h. Subsequently, the solution was basified with 4 M NaOH-solution and extracted with ethyl acetate (3x 50 mL). The organic layers were collected and dried by the addition of Na_2SO_4. The mixture was filtered through a glass funnel and the solvent was evaporated under reduced pressure. The product was obtained as a white solid (821 mg, 5.58 mmol, 86%).

^{1}H-NMR (500 MHz, DMSO-d_6): δ = 6.76 (bs, 2H), 2.67 (s, 1H), 2.04 (s, 6H) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 54.4, 50.0, 25.2 ppm; MS (ESI+): *m/z* (%) = 170 (100) $[M+Na]^+$; HRMS (ESI+): calc for $C_5H_9NO_2{}^{32}S$ $[M+Na]^+$: 170.0246; found

170.0246; IR (ATR): $\tilde{\nu}$ = 3302, 3218, 3002, 2975, 2922, 2885, 2853, 1738, 1459, 1295, 1208, 1200, 1170, 1111, 1074, 945, 921, 877, 721, 673, 628, 581, 548, 499, 453 cm^{-1}.

2.4 Synthesis of sulfoxide 18



6 **17** **18**

BCP-SO_2Na (**6**, 154 mg, 1.00 mmol, 1.00 equiv.) was suspended in dichloromethane (1.5 mL) and stirred at room temperature. Thionyl chloride (109 µL, 179 mg, 1.5 mmol, 1.50 equiv.) was added, followed by catalytic DMF (8 µL, 7.55 mg, 0.100 mmol, 0.10 equiv.) and the reaction mixture was stirred at room temperature for 16 h. The crude solution was used directly in the next step.
The crude solution of the sulfinyl chloride (**17**, 0.5 mL) was cooled down to –78 °C (dry ice/acetone bath) and 1 M phenylmagnesium bromide solution in tetrahydrofuran (834 µL, 151 mg, 0.834 mmol, 2.50 equiv.) was added. The reaction mixture was allowed to warm to room temperature over 1 h. The reaction was quenched by careful addition of 1 mL of sat. NH_4Cl-solution, extracted with CH_2Cl_2 (2x 10 mL), dried by the addition of Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (*c*Hex/EtOAc 98:2 to 65:35). The product was obtained as a colorless oil (38 mg, 0.198 mmol, 59%).

R_f (*c*Hex/EtOAc 5:1): 0.18; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.53–7.47 (m, 5H, Ar-H), 2.81 (s, 1H, C*H*), 1.88 (s, 6H, 3 × CH_2) ppm.

The analytical data is in accordance with the literature.[2]

3 Crystallographic Information

Crystal Structure Determinations of 7a, 7b, 7c, 7g, 8b

The single-crystal X-ray diffraction studies were carried out on a Bruker D8 Venture diffractometer with PhotonII detector at 123(2) K using Cu-Kα radiation (λ = 1.54178 Å). Dual space methods (SHELXT) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **A71**, 3-8] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2) [G. M. Sheldrick, *Acta Crystallogr.* 2015, **C71**, 3-8]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(N, O, C3 and C23) free). Semi-empirical absorption corrections were applied.

7a: colorless crystals, $C_{11}H_{11}NO_4S$, M_r = 253.27, crystal size 0.16 × 0.08 × 0.06 mm, triclinic, space group *P-1* (No. 2), a = 7.3339(3) Å, b = 7.9774(3) Å, c = 10.7533(4) Å, α = 68.613(1)°, β = 76.287(1)°, γ = 85.342(1)°, V = 569.10(4) Å^3, Z = 2, ρ = 1.478 Mg/m^{-3}, μ(Cu-Kα) = 2.59 mm^{-1}, F(000) = 264, $2\theta_{max}$ = 144.2°, 11823 reflections, of which 2222 were independent (R_{int} = 0.027), 157 parameters, 1 restraint, R_1 = 0.033 (for 2186 I > 2σ(I)), wR_2 = 0.087 (all data), S = 1.06, largest diff. peak / hole = 0.37 / -0.36 e Å^{-3}.

7b: colorless crystals, $C_{11}H_{11}NO_4S$, M_r = 253.27, crystal size 0.30 × 0.25 × 0.20 mm, monoclinic, space group $P2_1/n$ (No. 14), a = 9.7936(3) Å, b = 8.6615(3) Å, c = 13.9543(4) Å, β = 102.614(1)°, V = 1155.13(6) Å^3, Z = 4, ρ = 1.456 Mg/m^{-3}, μ(Cu-Kα) = 2.55 mm^{-1}, F(000) = 528, $2\theta_{max}$ = 144.4°, 11641 reflections, of which 2246 were independent (R_{int} = 0.023), 157 parameters, 1 restraint, R_1 = 0.029 (for 2237 I > 2σ(I)), wR_2 = 0.070 (all data), S = 1.05, largest diff. peak / hole = 0.31 / -0.36 e Å^{-3}.

7c: colorless crystals, $C_{11}H_{11}NO_5S$, M_r = 269.27, crystal size 0.08 × 0.04 × 0.01 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 8.3279(4) Å, b = 9.6745(5) Å, c = 14.8135(8) Å, β = 105.753(2)°, V = 1148.67(10) Å^3, Z = 4, ρ = 1.557 Mg/m^{-3}, μ(Cu-Kα) = 2.67 mm^{-1}, F(000) = 560, $2\theta_{max}$ = 144.4°, 9976 reflections, of which 2251 were independent (R_{int} = 0.040), 169 parameters, 2 restraints, R_1 = 0.036 (for 2029 I > 2σ(I)), wR_2 = 0.093 (all data), S = 1.04, largest diff. peak / hole = 0.60 / -0.31 e Å^{-3}.

7g: colorless crystals, $C_6H_{10}O_2S$, M_r = 146.20, crystal size 0.18 × 0.06 × 0.02 mm, monoclinic, space group $P2_1/c$ (No. 14), a = 5.2606(5) Å, b = 13.1057(14) Å, c = 10.3357(11) Å, β = 97.507(4)°, V = 706.48(13) Å^3, Z = 4, ρ = 1.375 Mg/m^{-3}, μ(Cu-Kα) = 3.47 mm^{-1}, F(000) = 312, $2\theta_{max}$ = 144.2°, 6055 reflections, of which 1392 were independent (R_{int} = 0.036), 86 parameters, 1 restraint, R_1 = 0.032 (for 1361 I > 2σ(I)), wR_2 = 0.084 (all data), S = 1.06, largest diff. peak / hole = 0.29 / -0.36 e Å^{-3}.

8b: colorless crystals, $C_{12}H_{15}NO_2S$, M_r = 237.31, crystal size 0.24 × 0.08 × 0.02 mm, monoclinic, space group $P2_1/n$ (No. 14), a = 5.7746(2) Å, b = 17.6889(5) Å, c = 23.1791(7) Å, β = 96.793(2)°, V = 2351.04(13) Å^3, Z = 8, ρ = 1.341 Mg/m^{-3}, μ(Cu-Kα) = 2.33 mm^{-1}, F(000) = 1008, $2\theta_{max}$ = 144.0°, 23913 reflections, of which 4548 were independent (R_{int} = 0.062), 301 parameters, 4 restraints, R_1 = 0.061 (for 3714 I > 2σ(I)), wR_2 = 0.148 (all data), S = 1.11, largest diff. peak / hole = 0.52 / -0.44 e Å^{-3}.

CCDC 1959595 (**7a**), 1959596 (**7b**), 1959597 (**7c**), 1959598 (**7g**), and 1959599 (**8b**) contain the supplementary crystallographic data for this paper. These data can be

obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

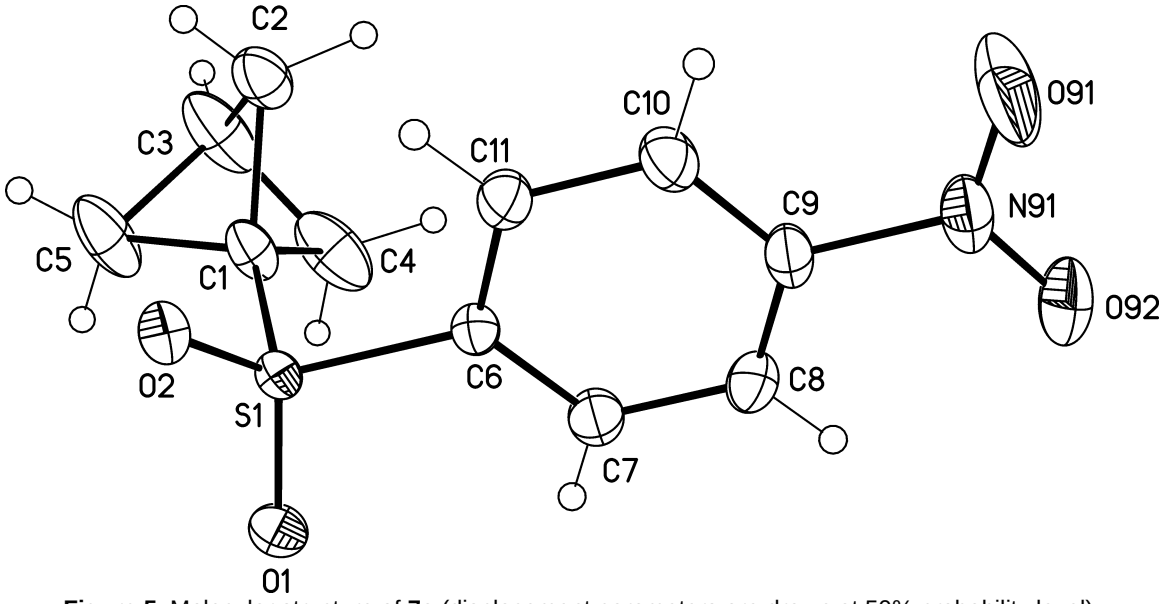


Figure 5. Molecular structure of **7a** (displacement parameters are drawn at 50% probability level).

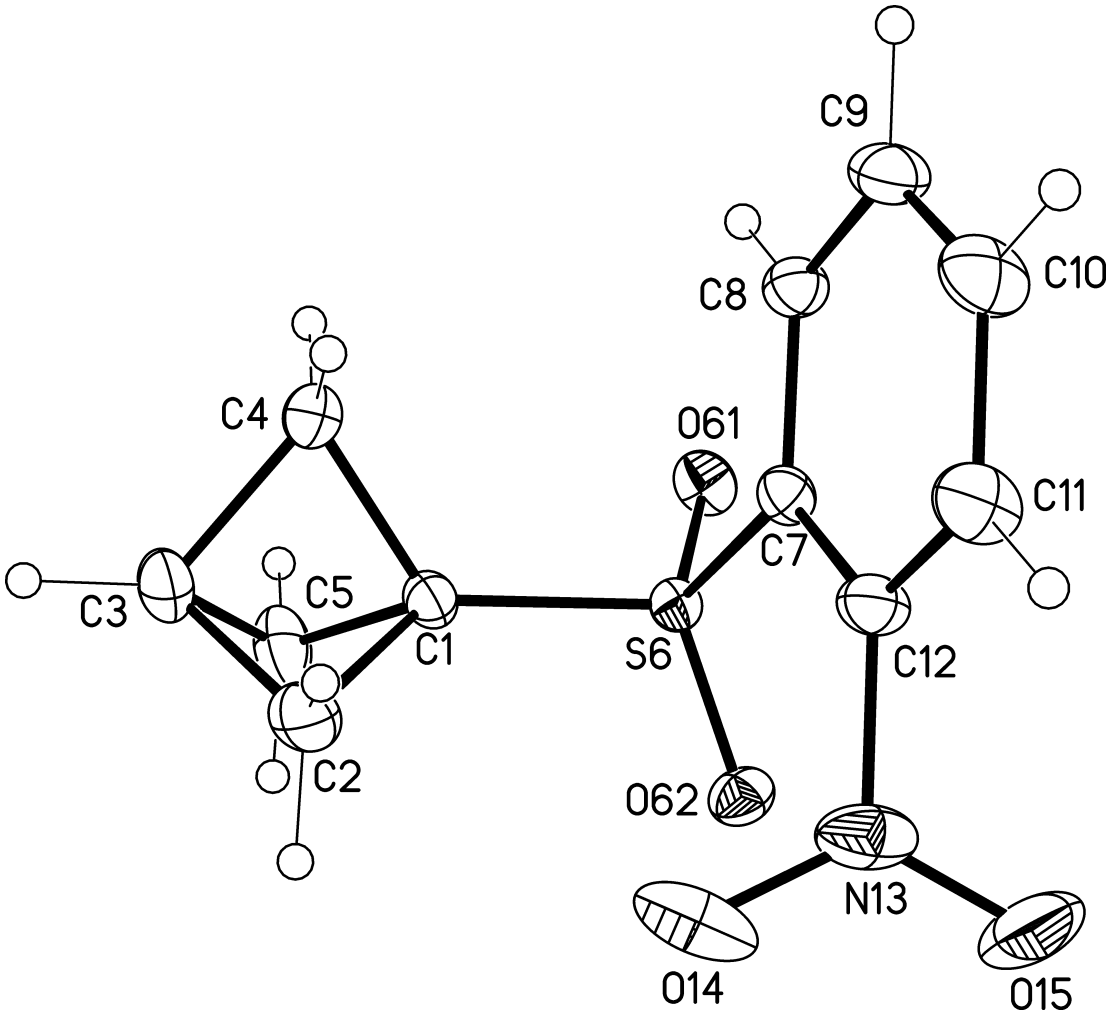


Figure 6. Molecular structure of **7b** (displacement parameters are drawn at 50% probability level).

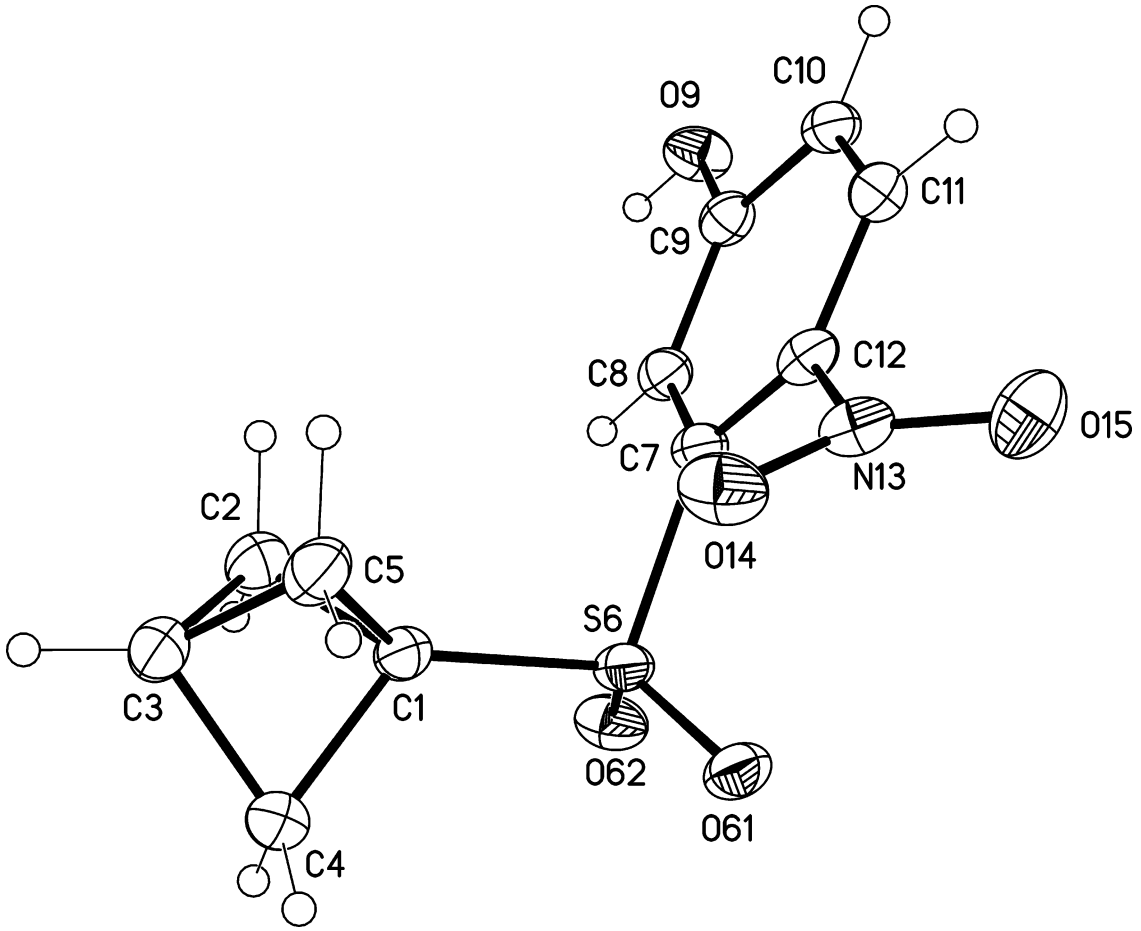


Figure 7. Molecular structure of **7c** (displacement parameters are drawn at 50% probability level).

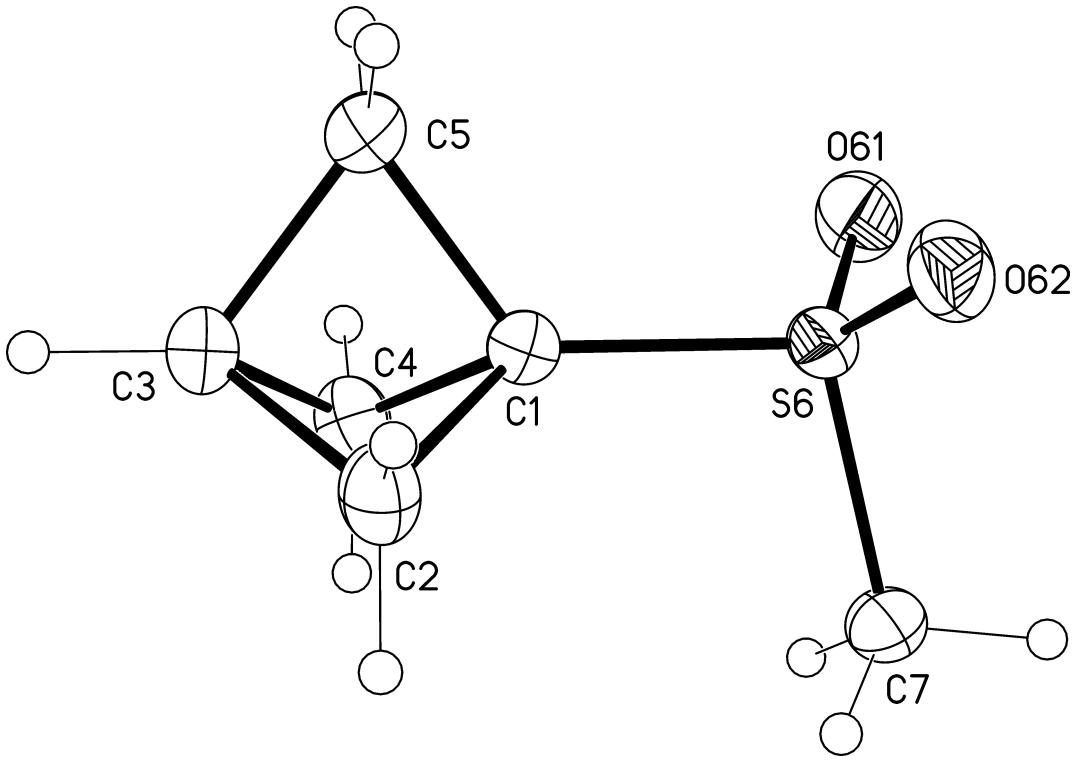


Figure 8. Molecular structure of **7g** (displacement parameters are drawn at 50% probability level).

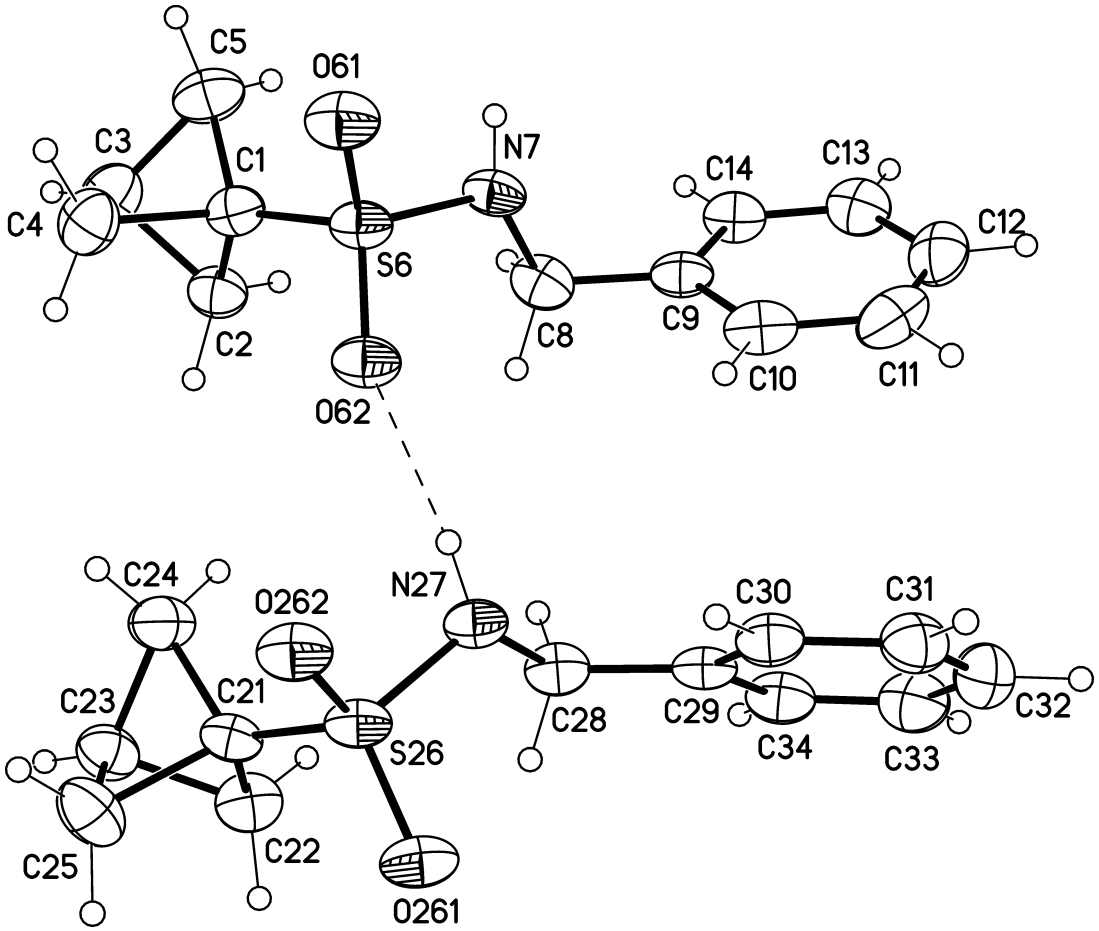
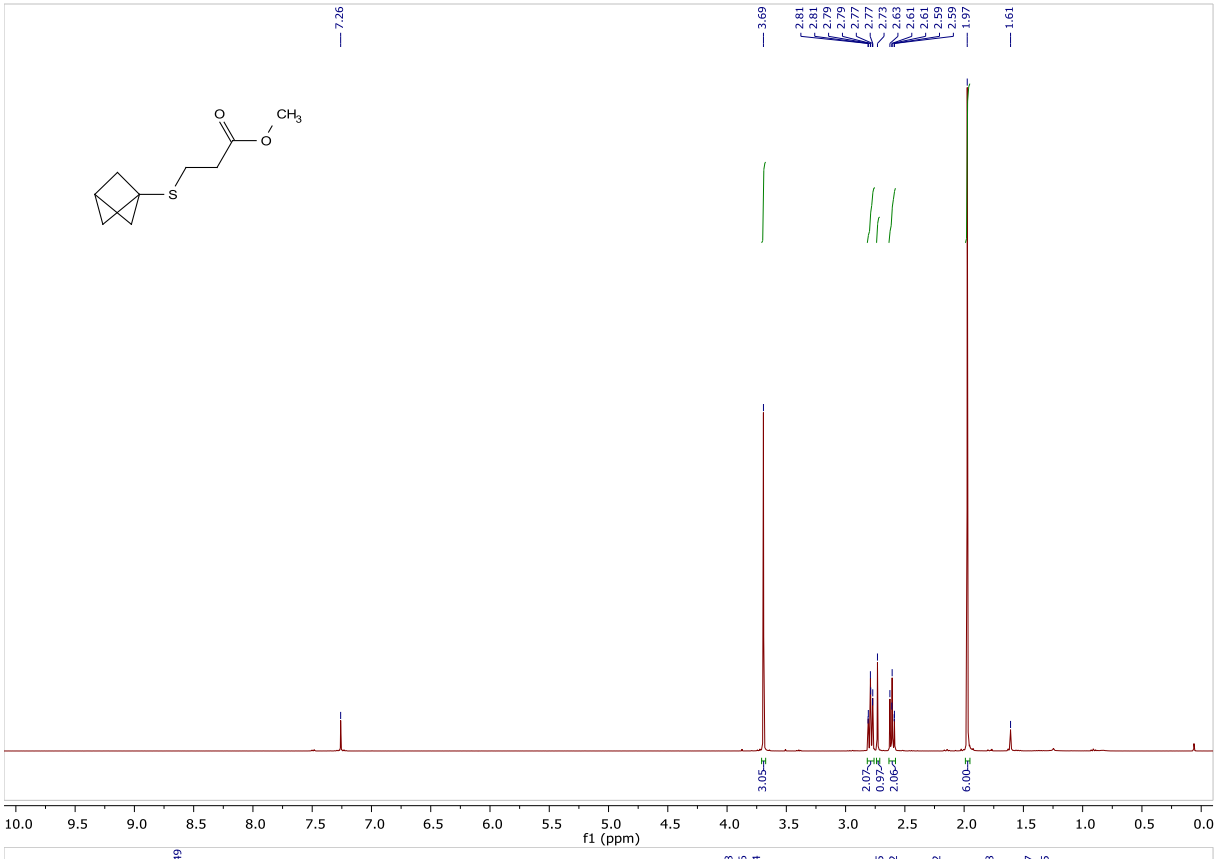
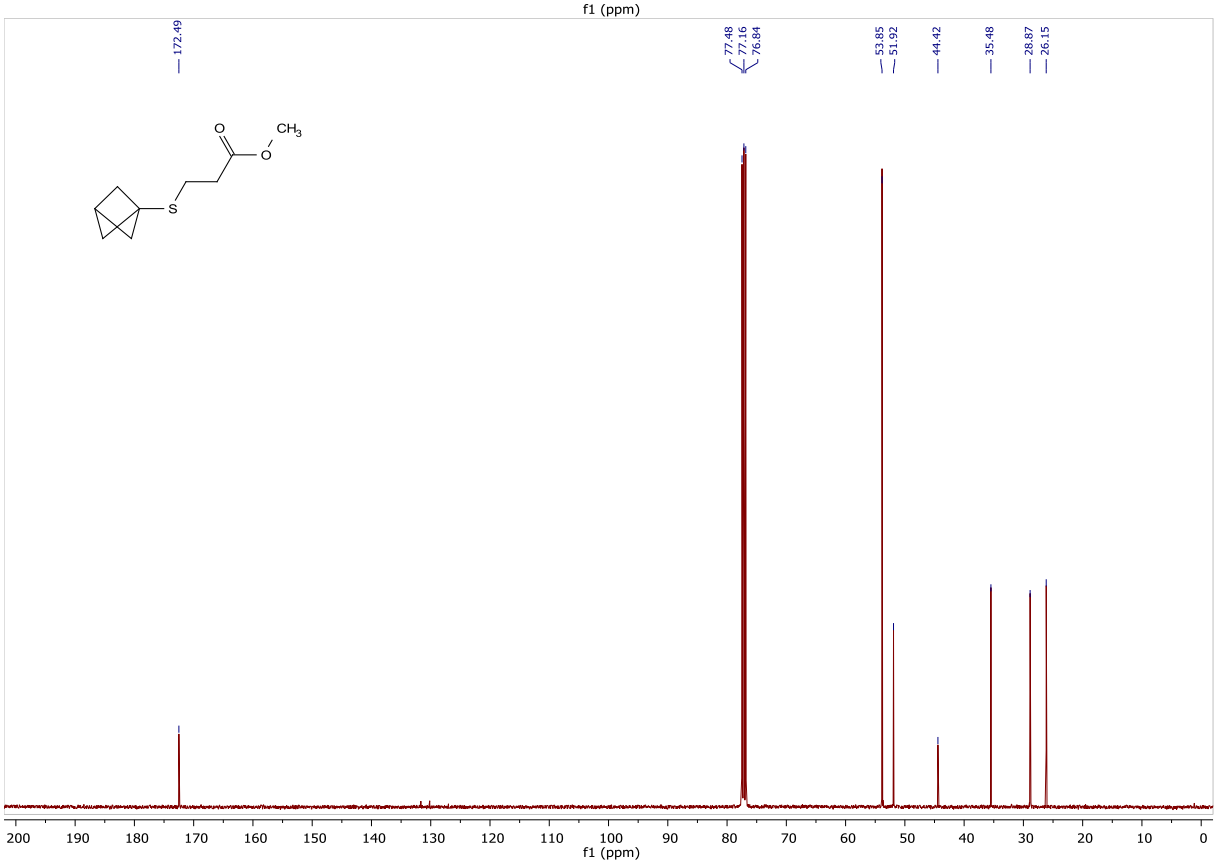


Figure 9. Molecular structure of **8b** (both crystallographic independent molecules are shown, displacement parameters are drawn at 50% probability level).

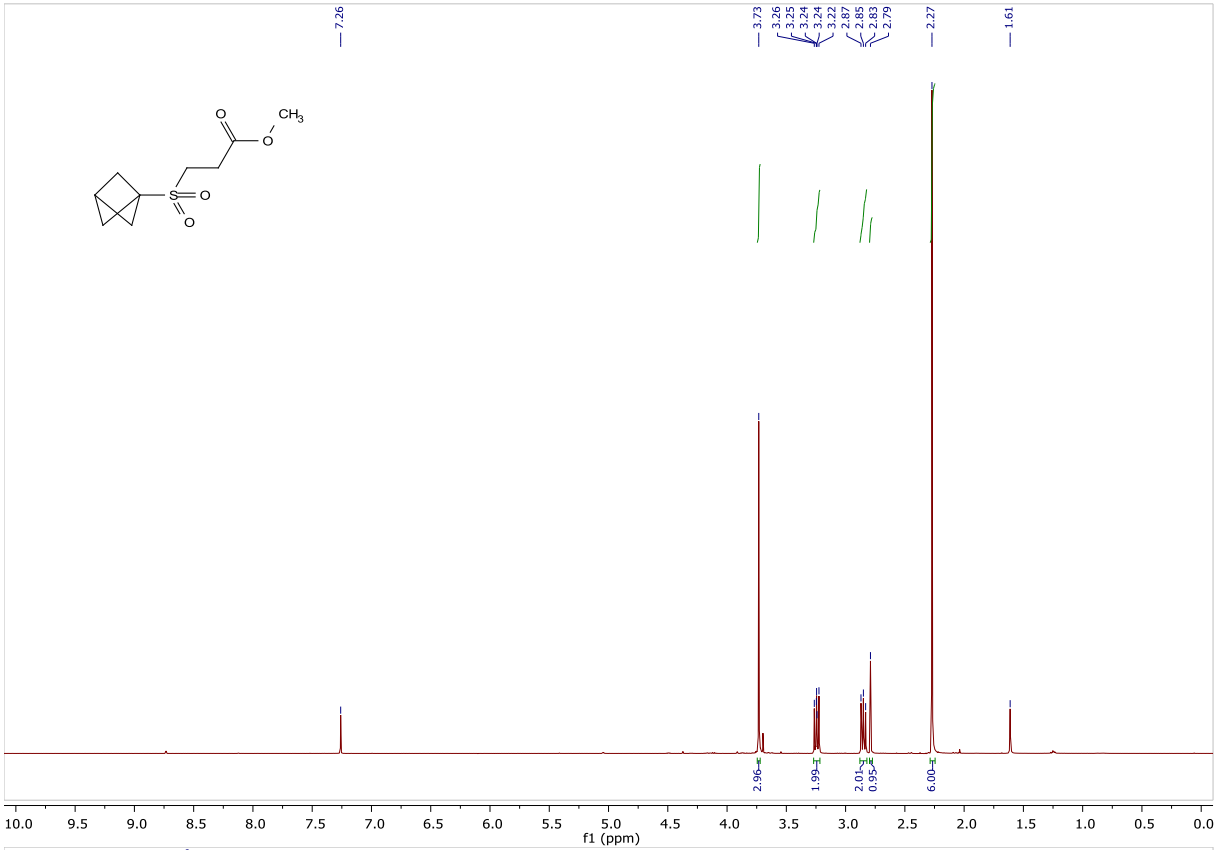
4 NMR spectra

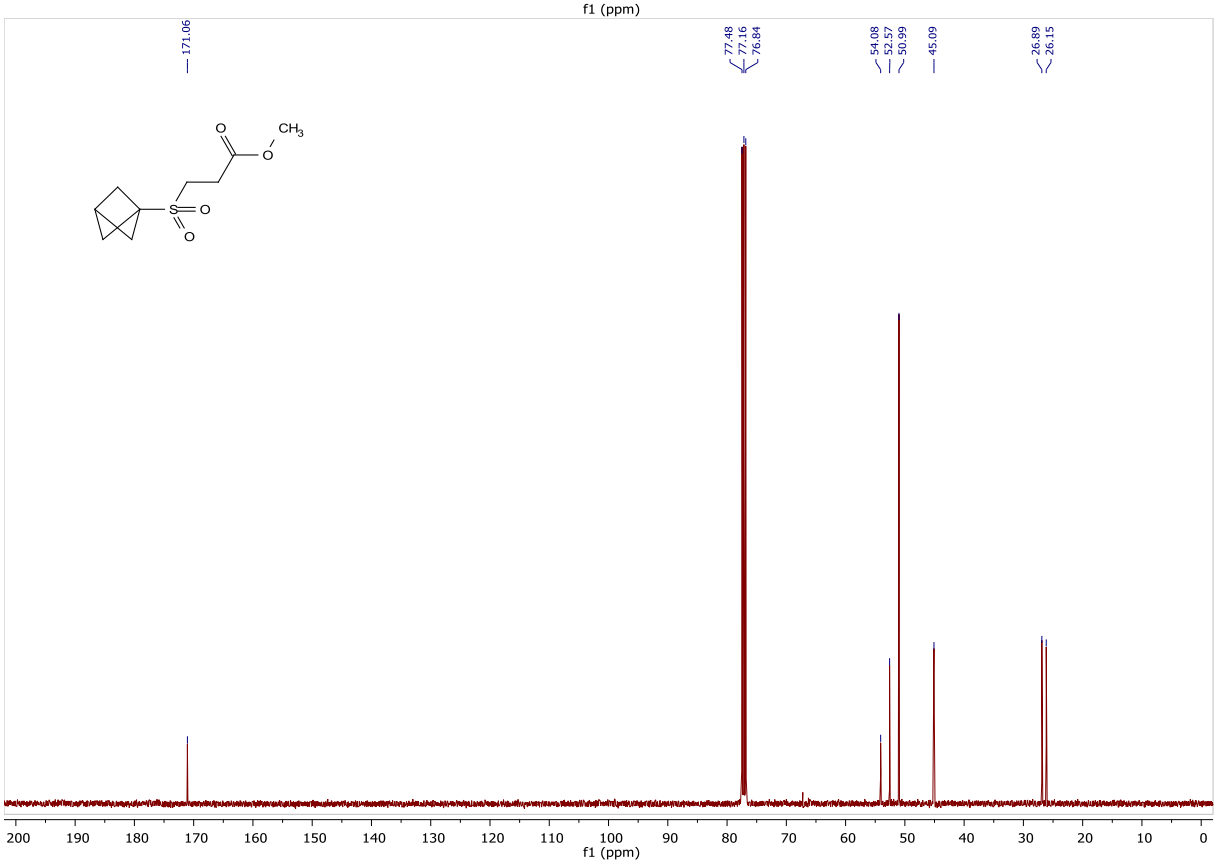
11





12


7.26
3.73
3.26
3.25
3.24
3.24
3.22
2.87
2.85
2.83
2.79
2.27
1.61
2.96
1.99
2.01
0.95
6.00
f1 (ppm)


171.06
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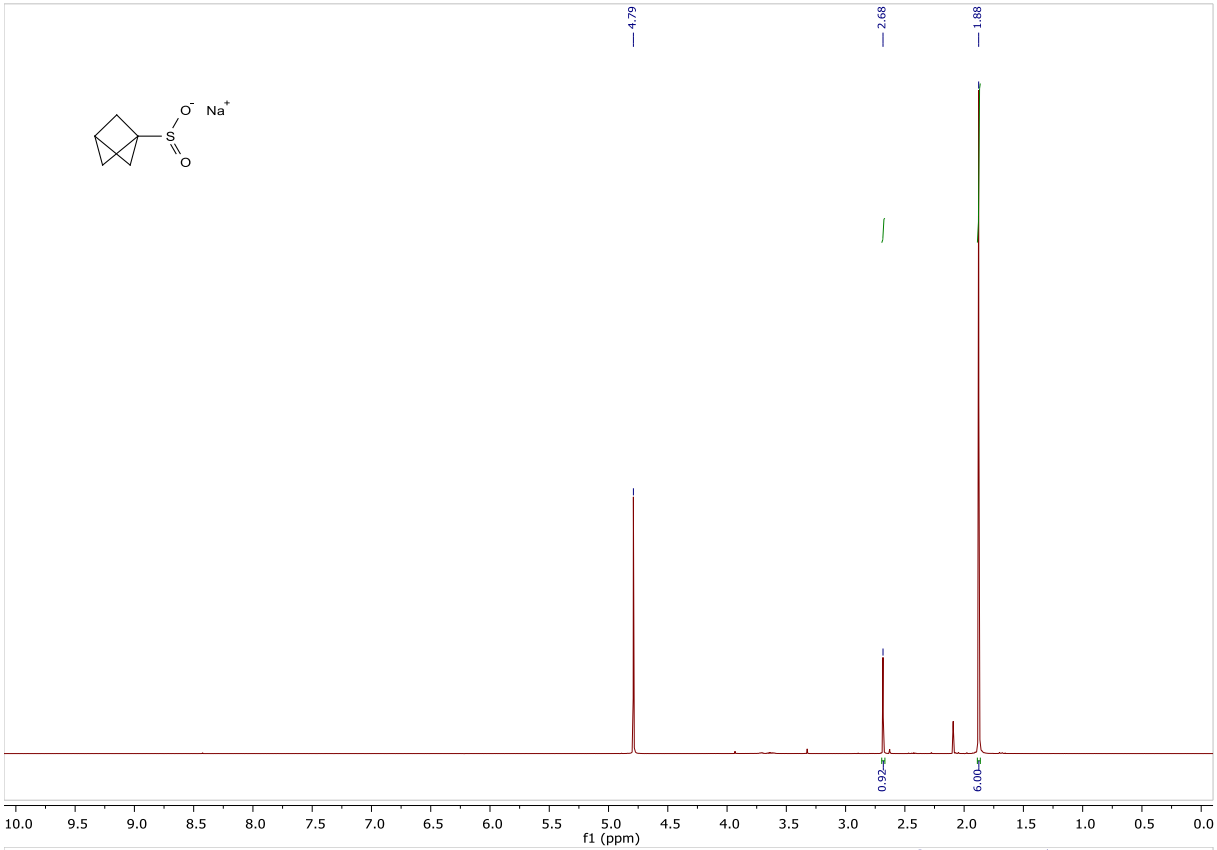
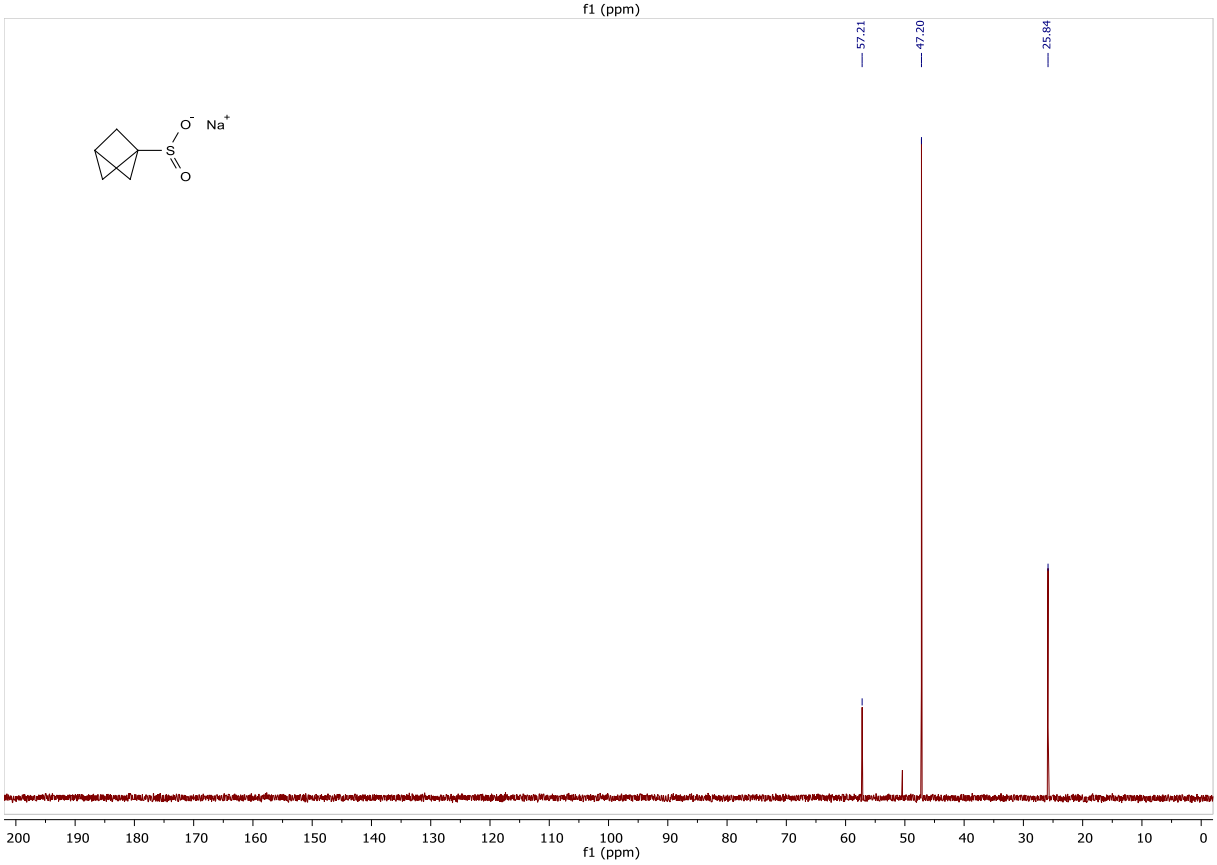
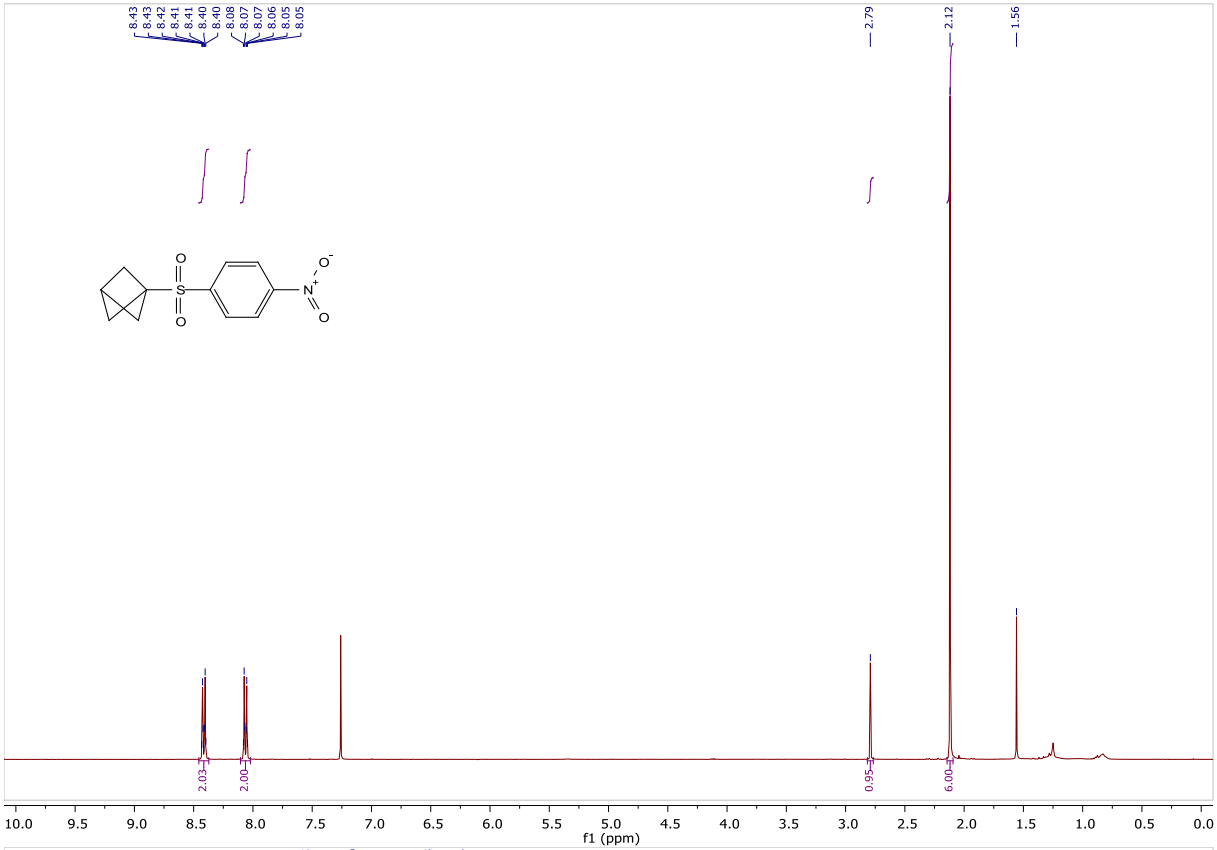
77.16
76.84
54.08
52.57
50.99
45.09
26.89
26.15
f1 (ppm)

6


4.79
2.68
1.88
O⁻ Na⁺
S
O
0.92
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


57.21
47.20
25.84
O⁻ Na⁺
S
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

7a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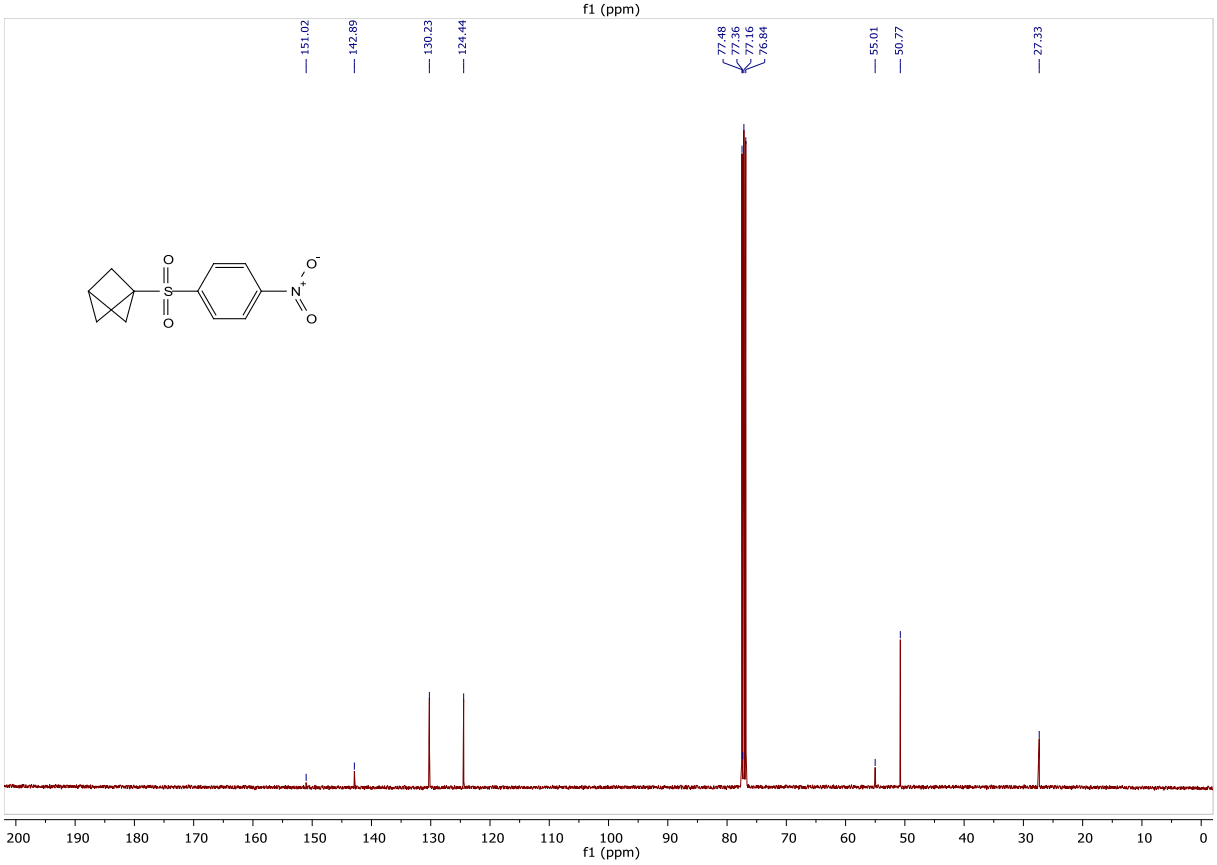
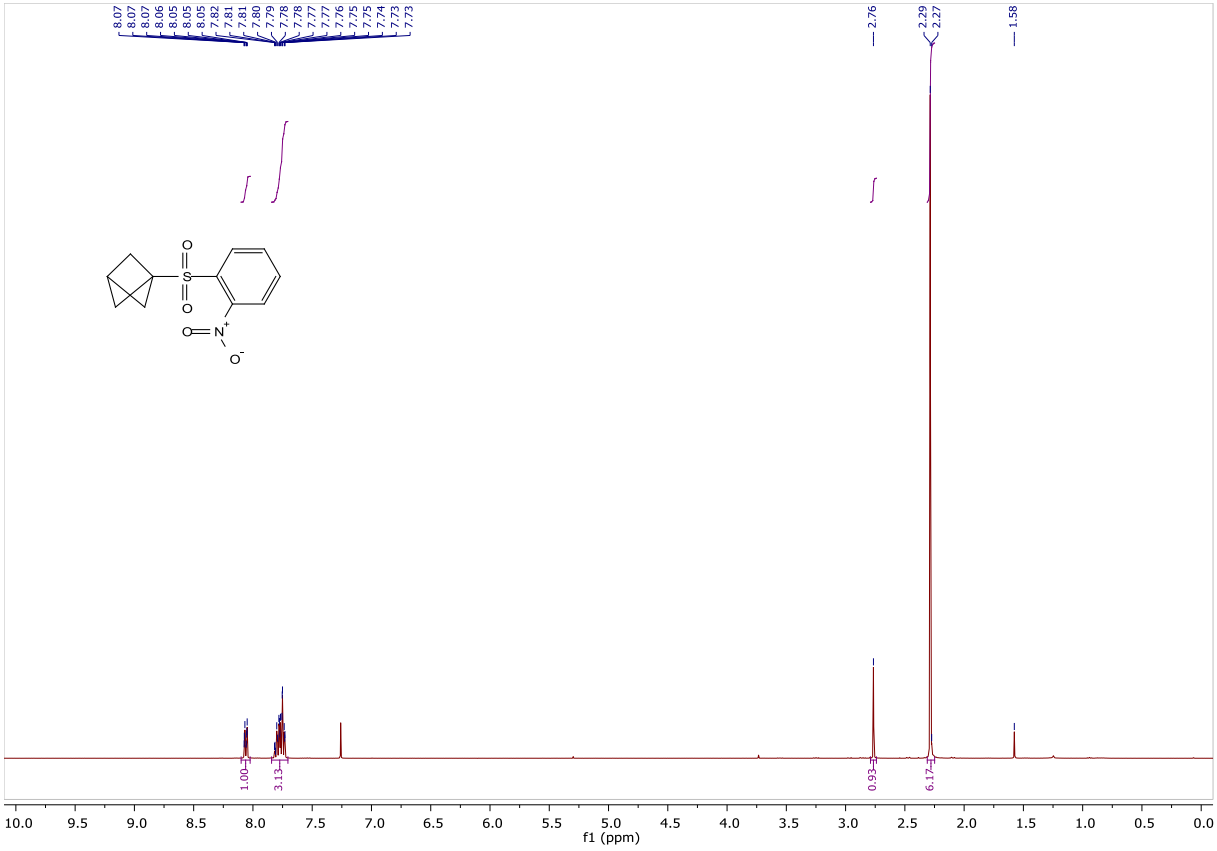
8.43
8.42
8.41
8.41
8.40
8.40
8.08
8.07
8.07
8.06
8.05
8.05
2.79
2.12
1.56
2.03
2.00
0.95
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


151.02
142.89
130.23
124.44
77.48
77.36
77.16
76.84
55.01
50.77
27.33
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

7b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8.07
8.07
8.06
8.05
8.05
8.05
7.82
7.81
7.81
7.80
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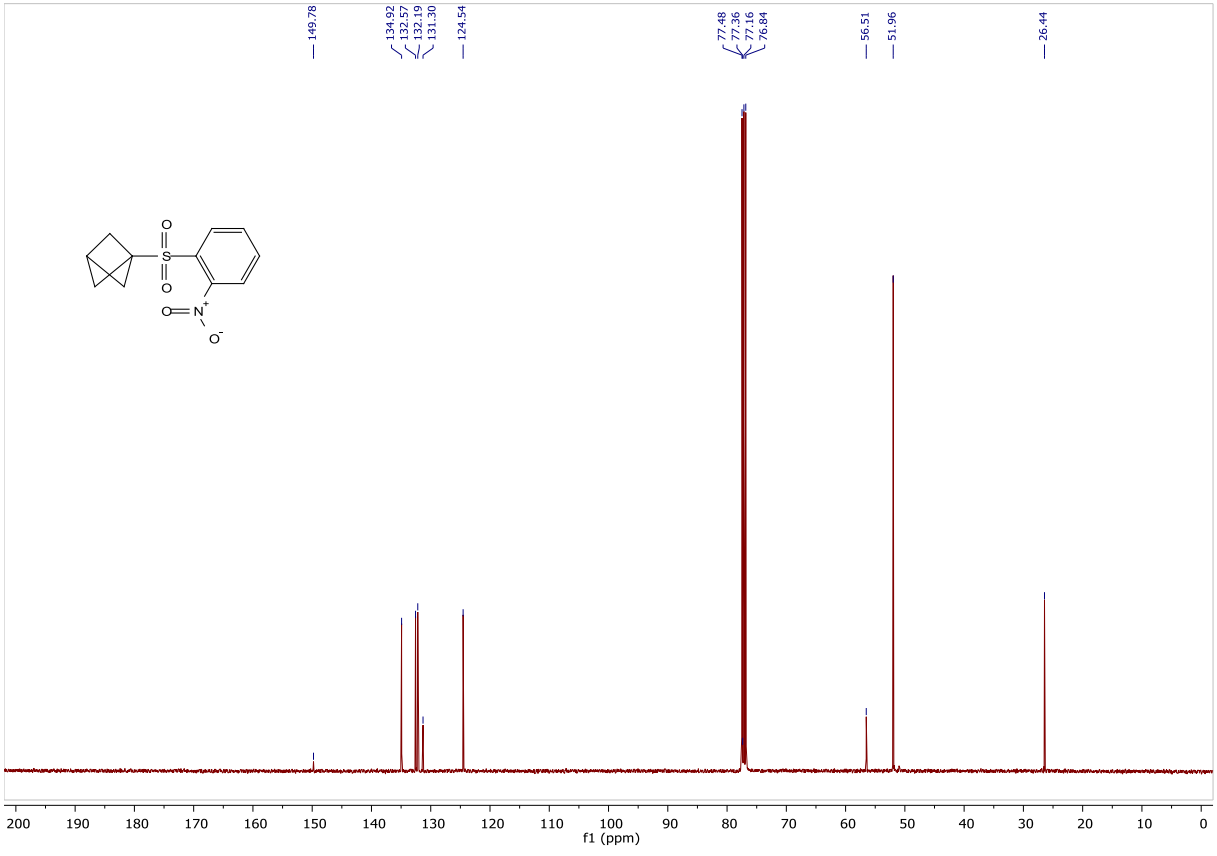
7.78
7.77
7.77
7.76
7.75
7.75
7.74
7.73
7.73
2.76
2.29
2.27
1.58
1.00
3.13
0.93
6.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


149.78
134.92
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132.19
131.30
124.54
77.48
77.36
77.16
76.84
56.51
51.96
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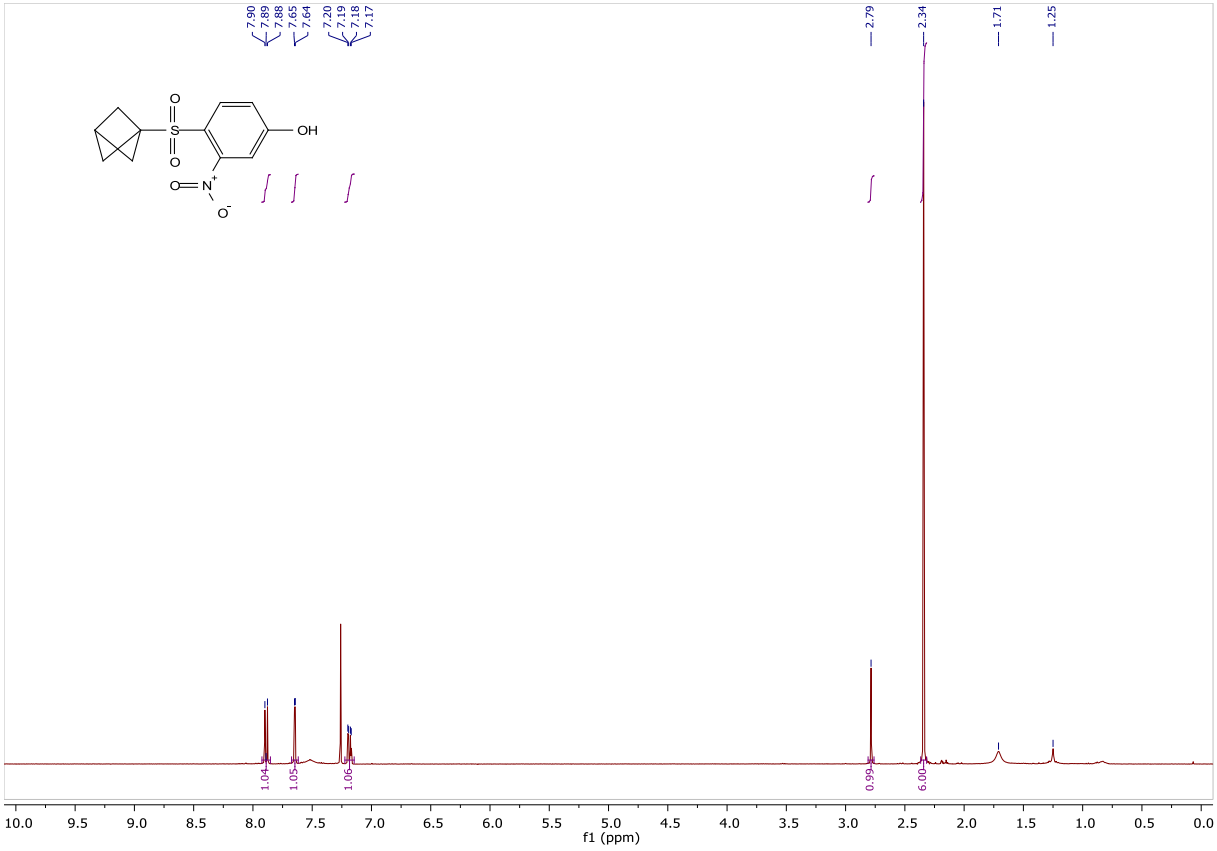
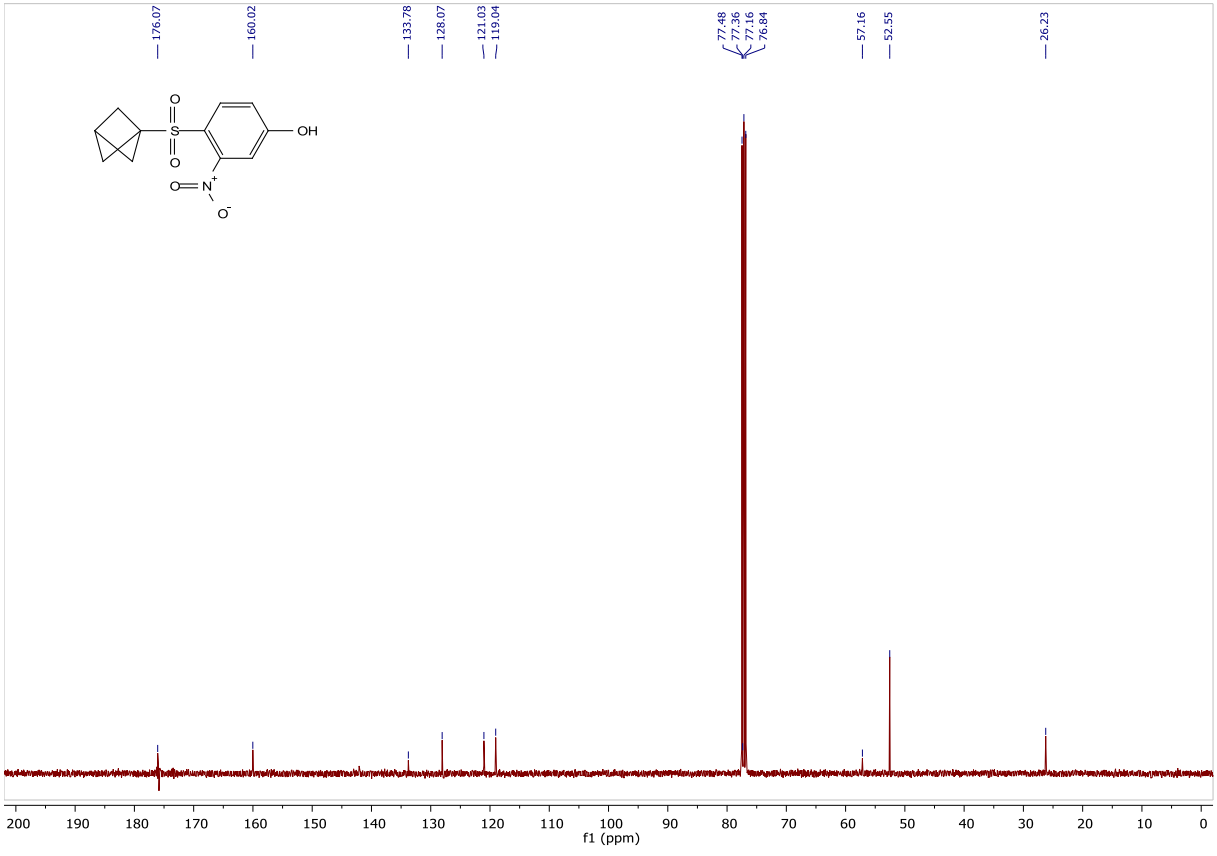
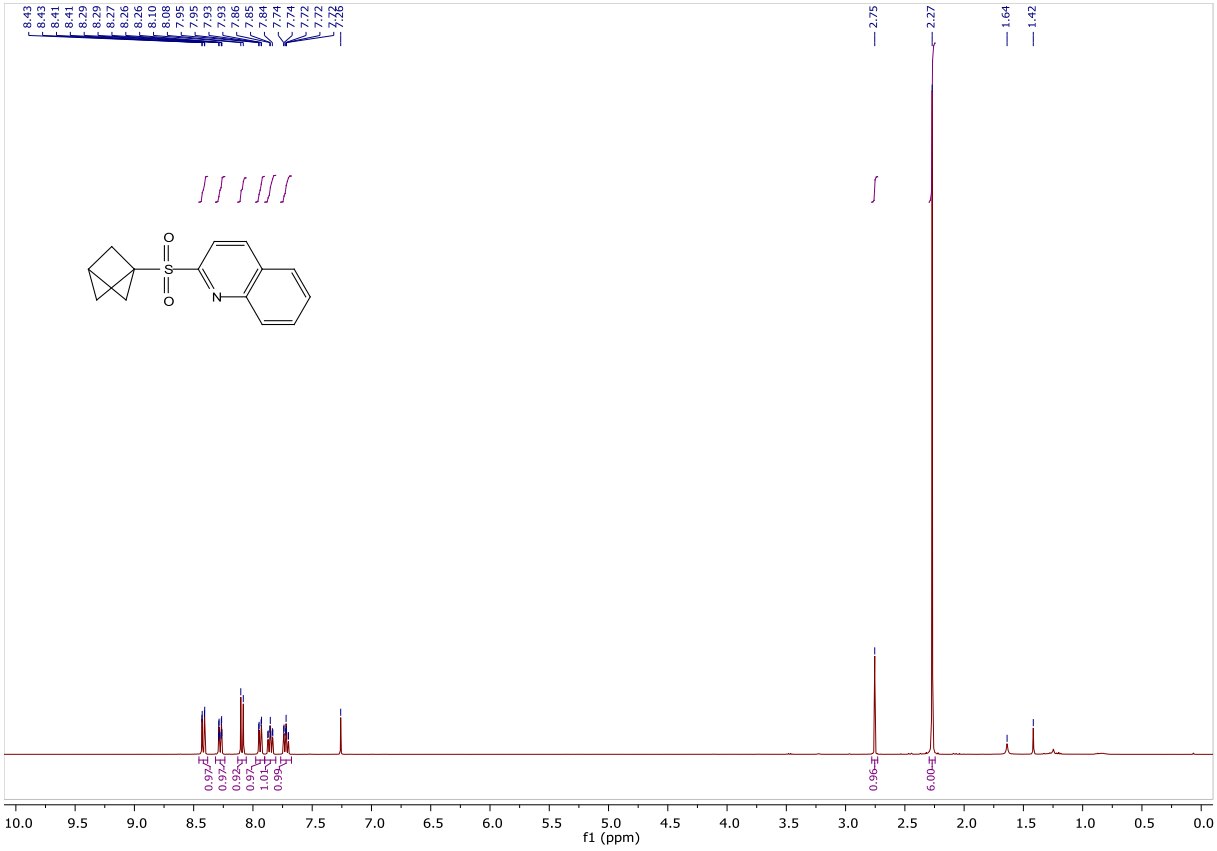
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

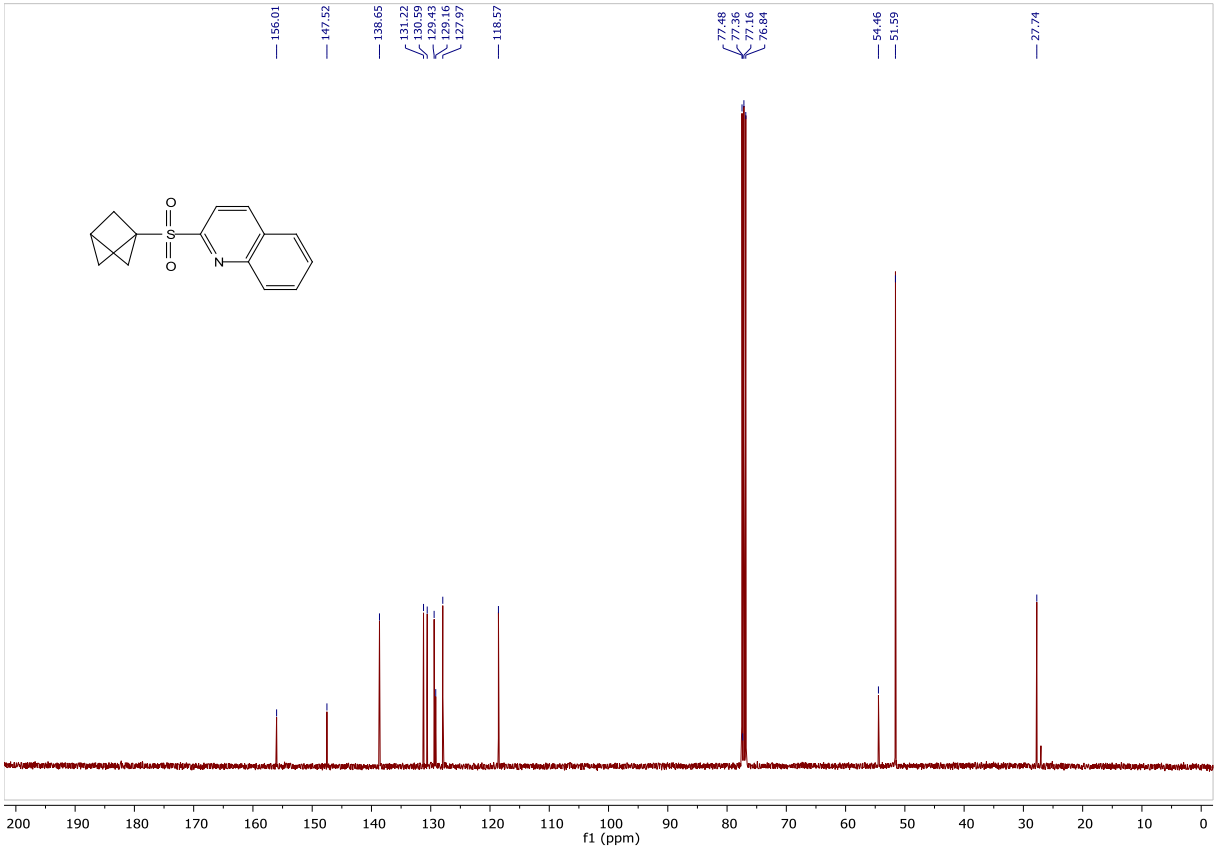
7c


7.90
7.89
7.88
7.65
7.64
7.20
7.19
7.18
7.17
2.79
2.34
1.71
1.25
OH
1.04
1.05
1.06
0.99
6.00
f1 (ppm)

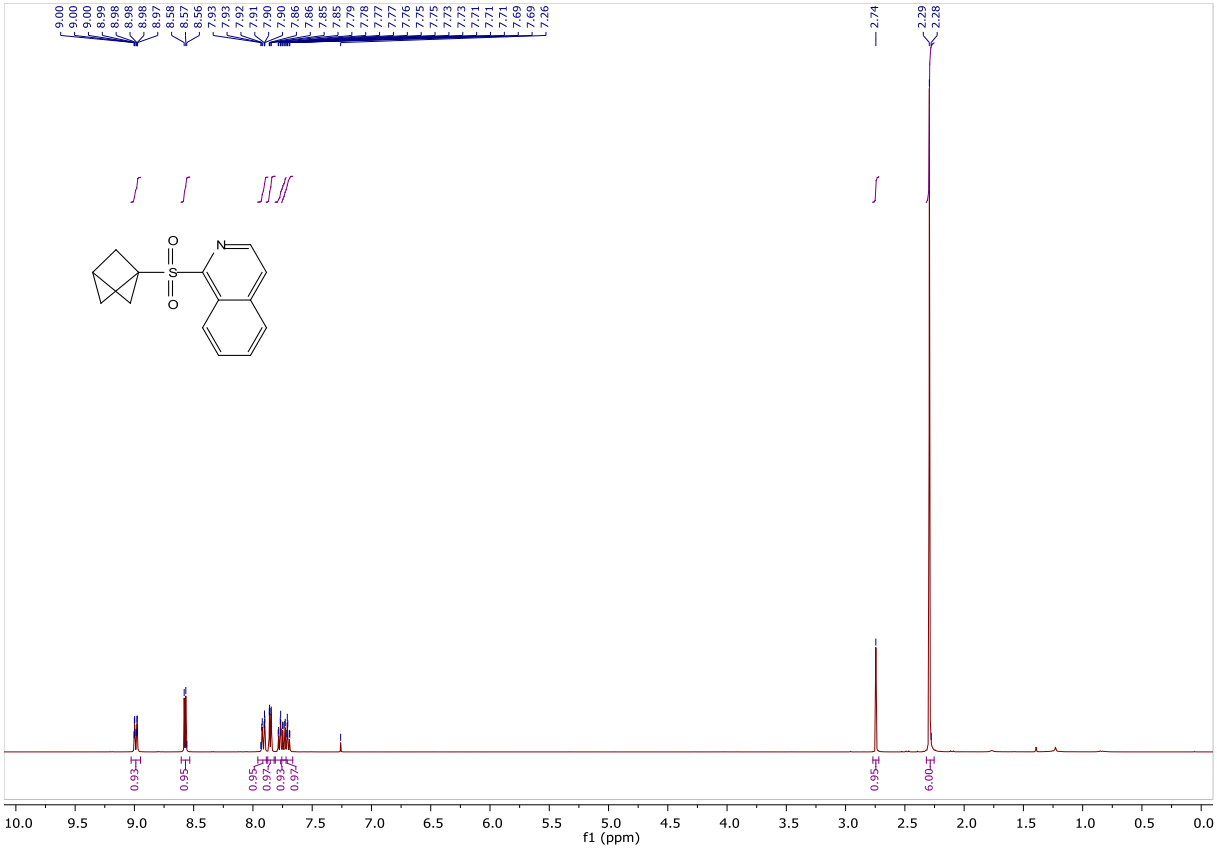

176.07
160.02
133.78
128.07
121.03
119.04
77.48
77.36
77.16
76.84
57.16
52.55
26.23
OH
f1 (ppm)

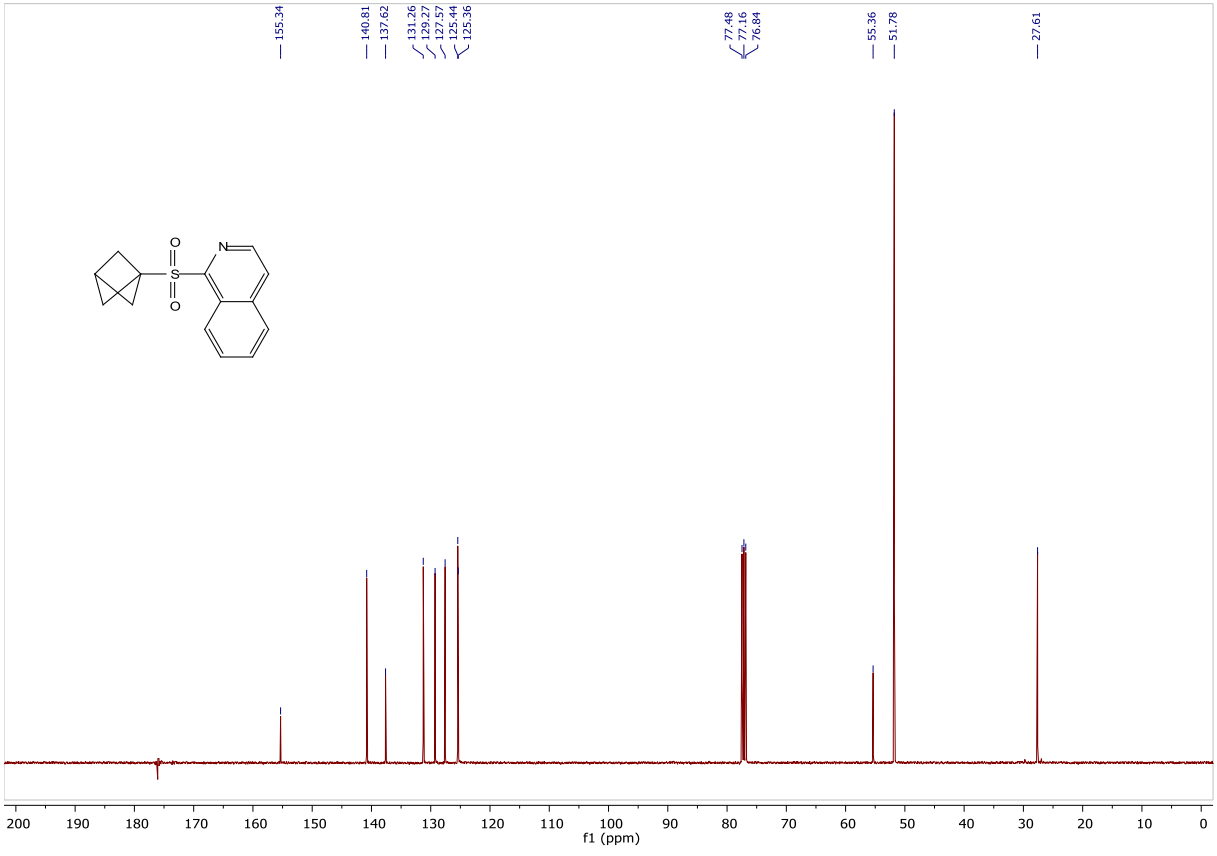
7d


8.43
8.43
8.41
8.41
8.29
8.29
8.27
8.26
8.26
8.10
8.08
7.95
7.95
7.93
7.93
7.86
7.85
7.84
7.74
7.74
7.72
7.72
7.26
2.75
2.27
1.64
1.42
0.97
0.97
0.92
0.92
1.01
0.99
0.96
6.00
f1 (ppm)

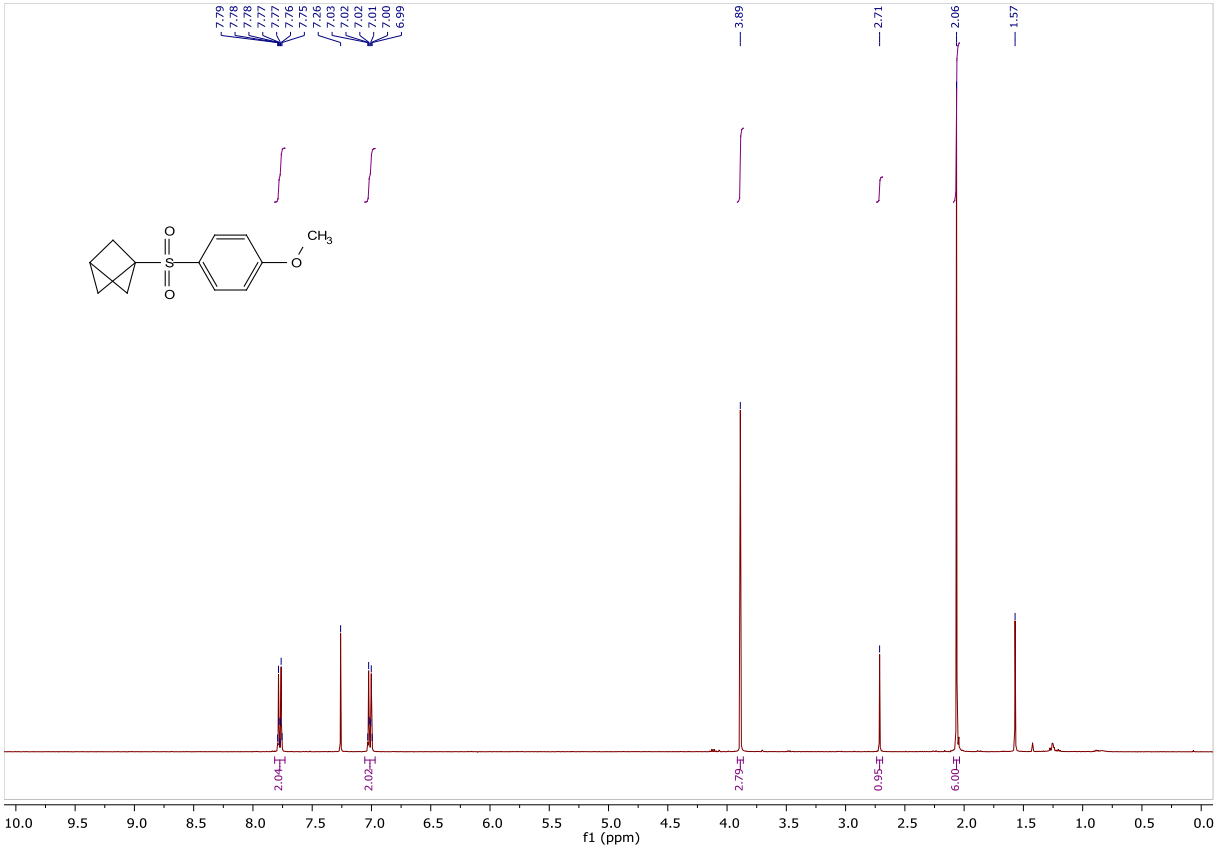

156.01
147.52
138.65
131.22
130.59
129.43
129.16
127.97
118.57
77.48
77.36
77.16
76.84
54.46
51.59
27.74
f1 (ppm)

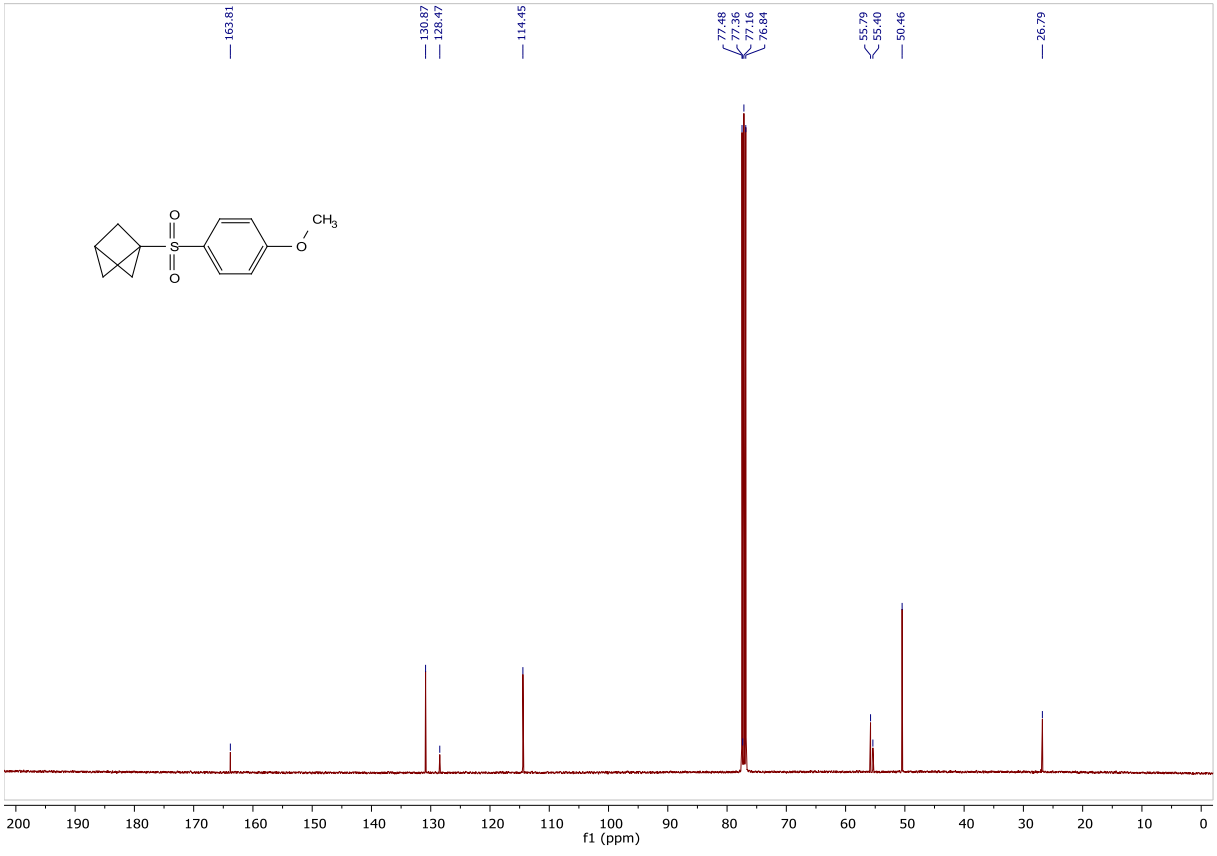
7e


9.00
9.00
9.00
8.99
8.98
8.98
8.98
8.97
8.58
8.57
8.56
7.93
7.93
7.92
7.91
7.90
7.90
7.86
7.86
7.85
7.85
7.79
7.78
7.77
7.77
7.76
7.75
7.75
7.73
7.73
7.71
7.71
7.71
7.69
7.69
7.69
7.26
2.74
2.29
2.28
O
S
O
N
0.93
0.95
0.95
0.97
0.93
0.97
0.95
6.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

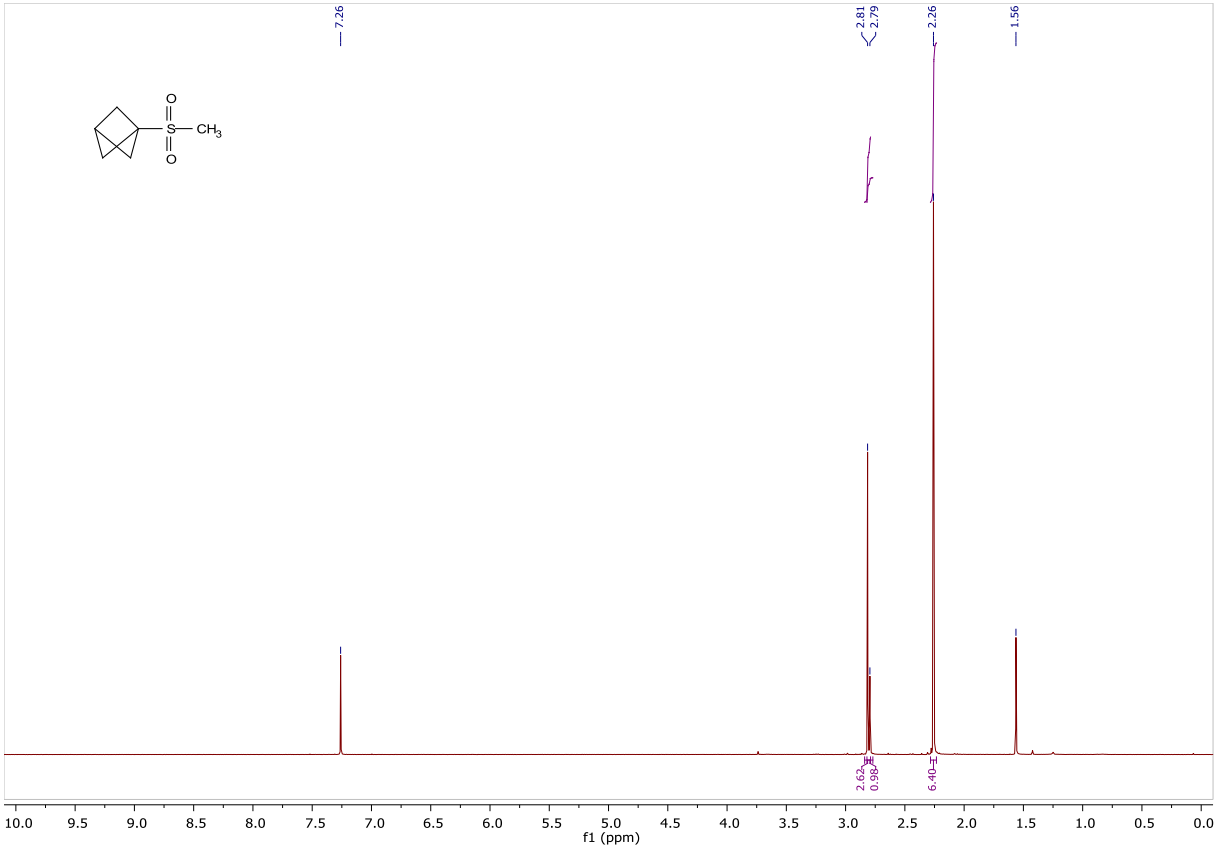

155.34
140.81
137.62
131.26
129.27
127.57
125.44
125.36
77.48
77.16
76.84
55.36
51.78
27.61
O
S
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

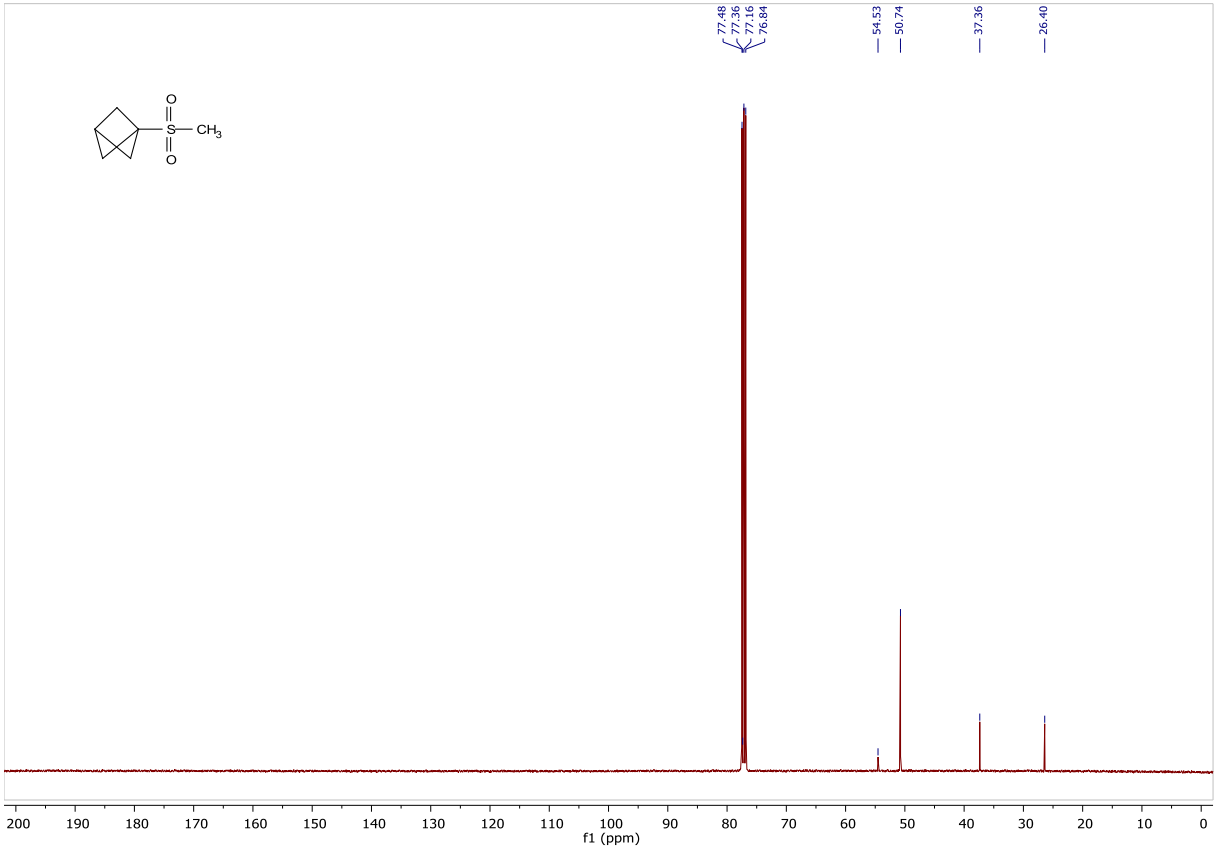
7f


7.79
7.78
7.78
7.77
7.77
7.76
7.75
7.26
7.03
7.02
7.02
7.01
7.00
6.99
3.89
2.71
2.06
1.57
O
S
O
O
CH3
2.04
2.02
2.79
0.95
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

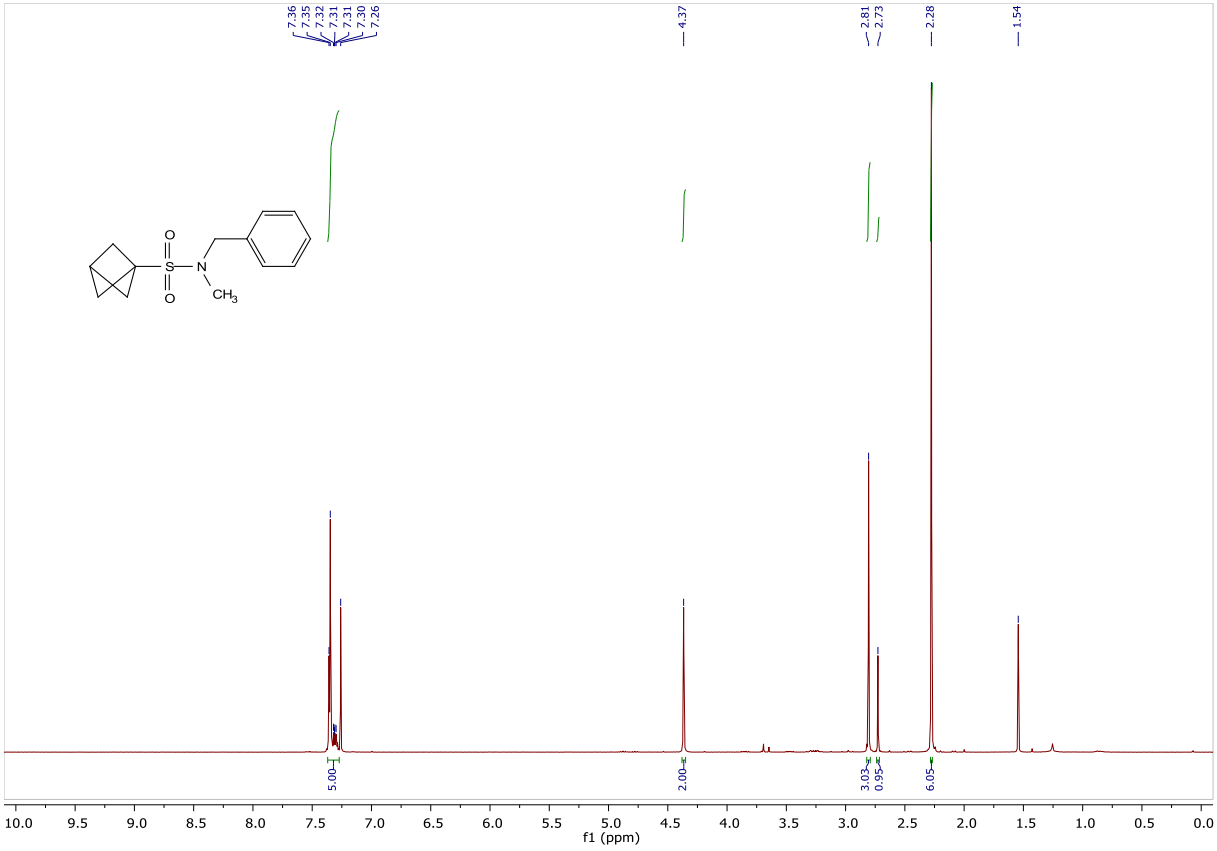

163.81
130.87
128.47
114.45
77.48
77.36
77.16
76.84
55.79
55.40
50.46
26.79
O
S
O
O
CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

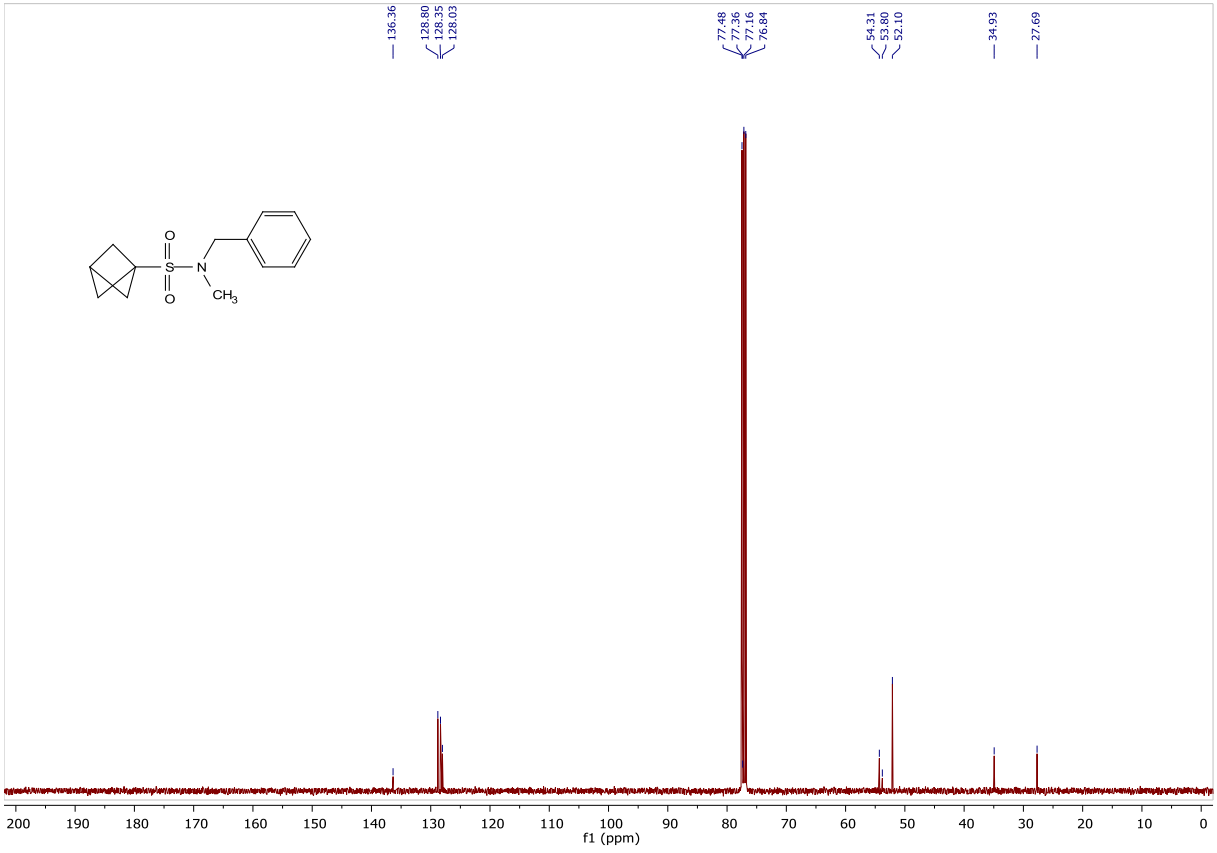
7g


7.26
2.81
2.79
2.26
1.56
2.62
0.98
6.40
f1 (ppm)

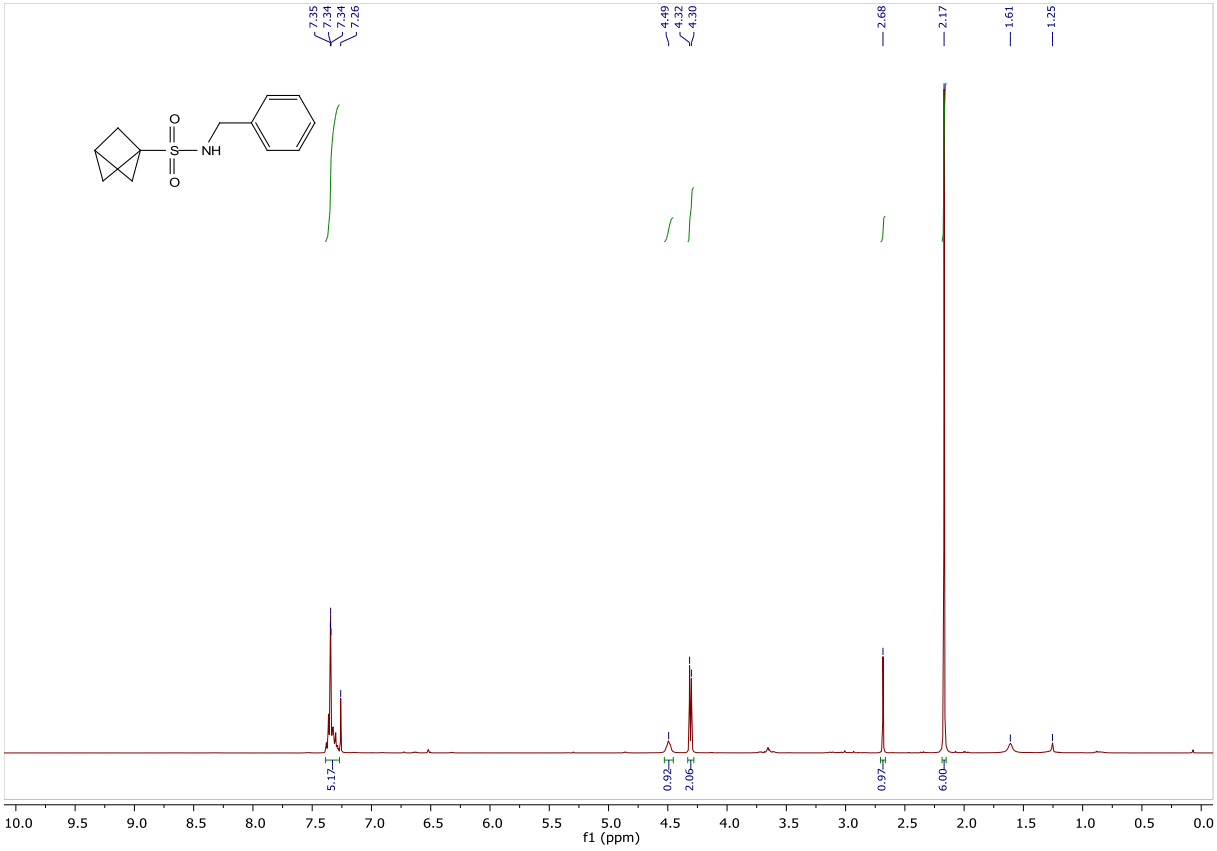

77.48
77.36
77.16
76.84
54.53
50.74
37.36
26.40
f1 (ppm)

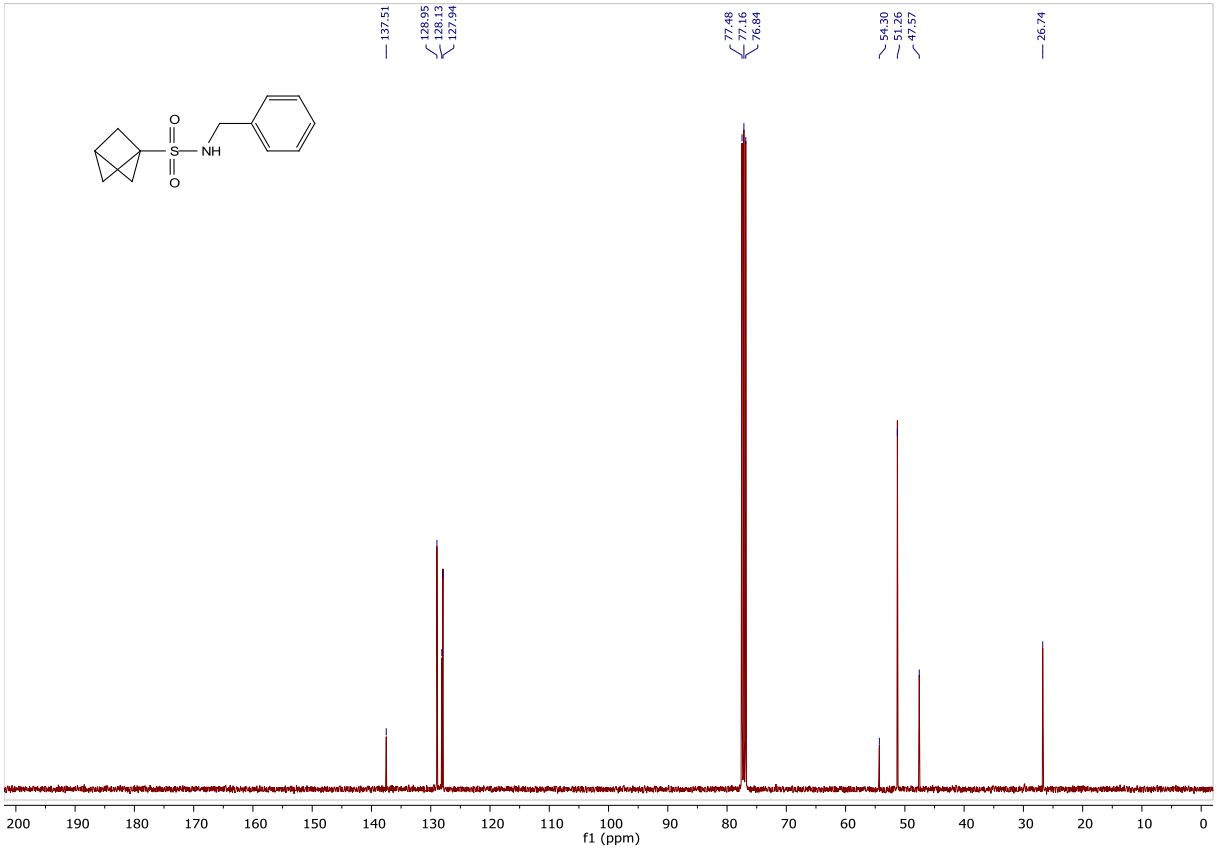
8a


7.36
7.35
7.32
7.31
7.31
7.30
7.26
4.37
2.81
2.73
2.28
1.54
5.00
2.00
3.03
0.95
6.05
f1 (ppm)

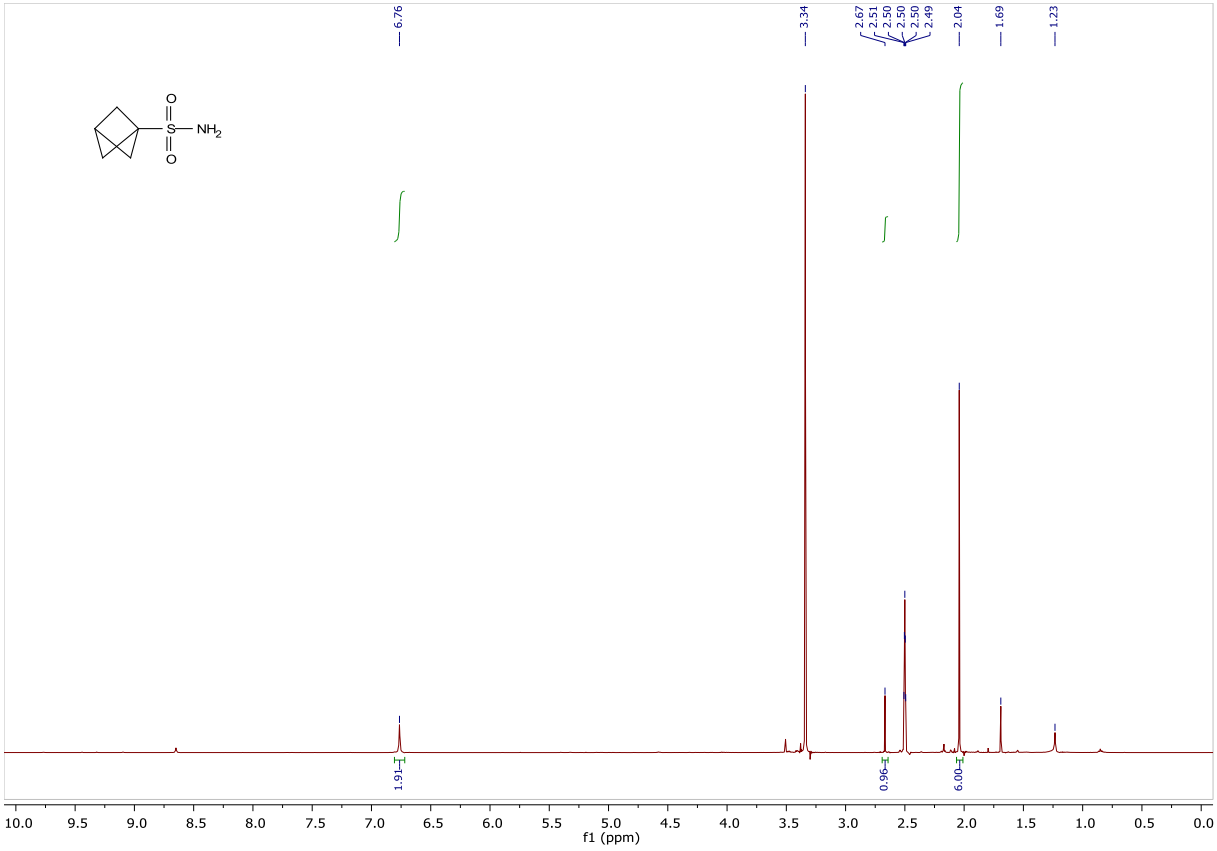

136.36
128.80
128.35
128.03
77.48
77.36
77.16
76.84
54.31
53.80
52.10
34.93
27.69
f1 (ppm)

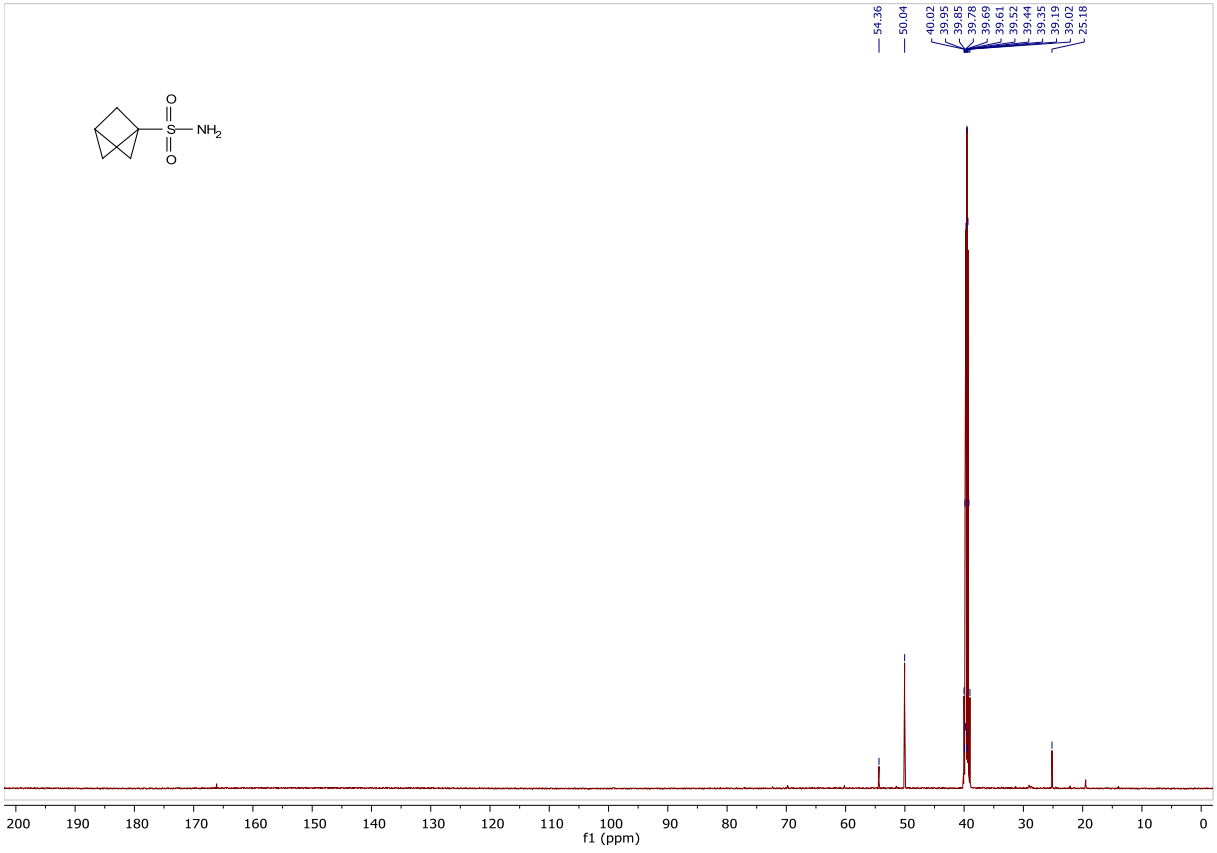
8b


7.35
7.34
7.34
7.26
4.49
4.32
4.30
2.68
2.17
1.61
1.25
O
S
NH
O
5.17
0.92
2.06
0.97
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


137.51
128.95
128.13
127.94
77.48
77.16
76.84
54.30
51.26
47.57
26.74
O
S
NH
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

8c


6.76
3.34
2.67
2.51
2.50
2.50
2.50
2.49
2.04
1.69
1.23
1.91
0.96
6.00
f1 (ppm)


54.36
50.04
40.02
39.95
39.85
39.78
39.69
39.61
39.52
39.44
39.35
39.19
39.02
25.18
f1 (ppm)

5 References

[1] R. Gianatassio, J. M. Lopchuk, J. Wang, C.-M. Pan, L. R. Malins, L. Prieto, T. A. Brandt, M. R. Collins, G. M. Gallego, N. W. Sach, et al., *Science* **2016**, *351*, 241–246.

[2] R. M. Bär, S. Kirschner, S. Bräse, *Chem. – Eur. J.* **2018**, *24*, 1373–1382.