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SUPPORTING INFORMATION

Studies on the Synthesis, Stability and Conformation of 2-(Arylsulfonyl)oxetane Fragments

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General Experimental Conditions:

All non-aqueous reactions were carried out under an inert atmosphere (argon) with oven-dried (160 ºC) or flame dried glassware using standard techniques. Anhydrous solvents were obtained by filtration through drying columns (THF, Et_2O, CH_2Cl_2, PhMe) or obtained from commercial suppliers and used without further purification (DMF).

Flash column chromatography was performed using 230-400 mesh silica, with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance (254 nm), aqueous potassium permanganate stain or PMA (phosphomolybdic acid).

Infrared spectra were recorded using a Perkin-Elmer spectrum 100 FT-IR Spectrometer and the absorbencies were reported in wavenumbers (cm^{-1}).

Nuclear magnetic resonance spectra were recorded on a Bruker AV 400 (400 MHz) or AV 500 (500 MHz) spectrometer. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant in Hz and assignment. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as an internal standard (^1H NMR spectra: $CDCl_3$: δ = 7.27 ppm, $(CD_3)_2CO$: δ = 2.05 ppm, CD_3OD: δ = 3.31 ppm, $(CD_3)_2SO$: δ = 2.50 ppm. ^{13}C NMR spectra: $CDCl_3$: δ = 77.00 ppm, $(CD_3)_2CO$: δ = 29.84, 206.26 ppm, CD_3OD: δ = 49.00 ppm, $(CD_3)_2SO$: δ = 39.52 ppm) or using chloroform with 1% tetramethylsilane as the internal standard. ^{13}C NMR spectra were recorded with complete proton decoupling. ^{19}F NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million referenced to the standard monofluorobenzene: −113.5 ppm. Assignments of ^1H and ^{13}C spectra were made by the analysis of δ/J values and COSY, HSQC and HMBC experiments as appropriate.

High resolution mass spectrometry were recorded on VG Platform II, Waters Xevo G2-S, VG Autospec or Thermofisher LTQ Orbitrap XL spectrometers. Melting points are uncorrected

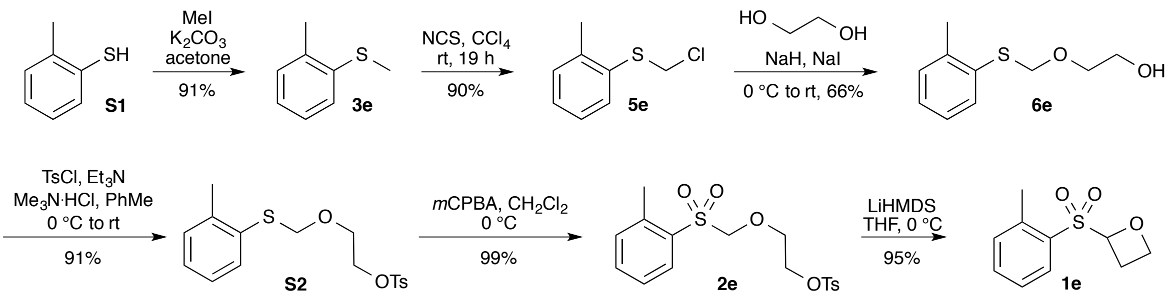
Reagents: For the preparation of a LiHMDS solution, hexamethyldisilazane was distilled over potassium hydroxide immediately before use. Unless otherwise stated *m*CPBA was dissolved in CH_2Cl_2, washed with a phosphate buffer (pH 7.5) and dried ($MgSO_4$) then the solvent removed under reduced pressure prior to use. All commercially available organometallic solutions were titrated against salicylaldehyde phenylhydrazone.[1] All other commercially available reagents were used without further purification.

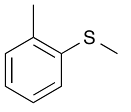
Preparation of a 0.61M solution of LiHMDS: A solution of HMDS (1.26 ml, 6.04 mmol) in THF (5.35 mL) was cooled to –78 ºC for 10 min then *n*BuLi (2.39 mL, 5.49 mmol, 2.3 M in hexane) was added dropwise. Solution stirred at –78 ºC for 30 min then warmed to 0 ºC for 30 min prior to use.

Compound Handling/Purification/Storage: All synthetic intermediates were stored under argon at –20 ºC for short periods of time. See full document for discussion of the stability of sulfonyl oxetanes.

For full experimental details and characterisation of compounds **1a-1d**, **8-12** and **13-16** see K. F. Morgan, I. A. Hollingsworth and J. A. Bull, *Chem. Commun.,* 2014, **50**, 5203–5205.

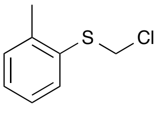
Synthesis of 2-(2-Methylbenzenesulfonyl)oxetane (1e)





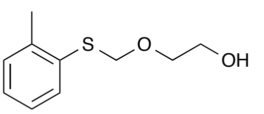
1-Methyl-2-(methylsulfanyl)benzene (3e)

Potassium carbonate (3.07 g, 22.21 mmol) was added to a solution of *o*-tolyl thiol (2.4 mL, 20.2 mmol) in acetone (25 mL) followed by MeI (1.3 mL, 21.20 mmol) and the reaction stirred at rt for 18 h. The reaction was filtered through celite and the solvent removed under reduced pressure. The crude material was dissolved in diethyl ether (30 mL) and washed with 1M NaOH (3 × 20 mL). The combined aqueous layers were extracted with ether (30 mL) then the combined organics were washed with brine (20 mL), dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to afford sulfide **3e** (2.66 g, 95%) as a yellow oil which was used without further purification. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.16 (3 H, m, 3 × Ar-H), 7.12–7.07 (1 H, m, Ar-H), 2.50 (3 H, s, CH_3), 2.38 (3 H, s, CH_3). The observed data (^1H) is consistent with that reported in the literature.[2]



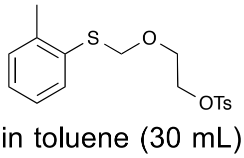
1-[(Chloromethyl)sulfanyl]-2-methylbenzene (5e)

N-Chlorosuccinimide (2.83 g, 21.19 mmol) was added portionwise to a solution of sulfide **3e** (2.66 g, 19.30 mmol) in dichloroethane (31.5 mL). The reaction was stirred at rt for 17 h then filtered through a short pad of silica, eluting with dichloromethane (50 mL) and the solvent removed under reduced pressure to afford chloromethyl sulfide **5e** as a yellow oil (3.03 g, 90%). Sulfide **5e** was taken on without further purification. R_f = 0.70 (40% EtOAc/hexane). IR (film)/cm^{-1} 3014, 3061, 1718, 1589, 1470, 1455, 1380, 1278, 1227, 1149, 1062, 1046, 908, 850, 739, 677. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61–7.57 (1 H, m, Ar-H), 7.30–7.25 (3 H, m, 3 × Ar-H), 5.00 (2 H, s, SCH_2Cl), 2.46 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0 (C_q), 132.5 (C_q), 130.5 (2 × Ar-C), 127.9 (Ar-C), 126.8 (Ar-C), 50.3 (SCH_2Cl), 20.5 (CH_3). HRMS (EI) *m/z* Calculated for $C_8H_9{}^{35}ClS$ [M]: 172.0113; Found: 172.0121 [M].



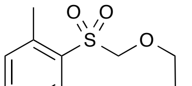
2-{[(2-Methylphenyl)sulfanyl]methoxy}ethan-1-ol (6e)

Sodium hydride (60% in mineral oil, 0.64 g, 16.00 mmol) was added to ethylene glycol (150 mL) at 0 ºC and stirred for 1 h. Sodium iodide (2.40 g, 16.01 mmol) was added followed by sulfide **5e** (2.51 g, 14.54 mmol). DMF (2 mL) was added to aid solubility. The resulting solution was stirred at 0 ºC for 1 h then warmed to rt for 18 h. H_2O (100 mL) was added and the product was extracted with ethyl acetate (10 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6e** (1.91 g, 66%) as a colourless oil. R_f = 0.19 (30% EtOAc/hexane). IR (film)/cm^{-1} 3389, 3058, 2928, 1589, 1470, 1456, 1379, 1308, 1265, 1094, 1047, 1016, 888, 824, 735, 696, 668. ^1H NMR (400 MHz, $CDCl_3$) δ 7.57–7.54 (1 H, m, Ar-H), 7.21–7.12 (3 H, m, 3 × Ar-H), 5.05 (2 H, s, SCH_2O), 3.80–3.70 (4 H, m, OCH_2CH_2OH), 2.41 (3 H, s, CH_3), 2.19 (1 H, br m, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1 (C_q), 134.8 (C_q), 130.1 (Ar-C), 129.8 (Ar-C), 126.7 (Ar-C), 126.6 (Ar-C), 75.5 (SCH_2O), 69.9 (OCH_2), 61.5 (OCH_2), 20.5 (CH_3). HRMS (NSI) *m/z* Calculated for $C_{10}H_{18}O_2NS^+$ $[M+NH_4]^+$: 216.1053; Found: 216.1054 $[M+NH_4]^+$.



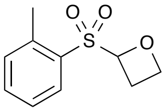
2-{[(2-Methylphenyl)sulfanyl]methoxy}ethyl-4-methylbenzene-1-sulfonate (S2)

Triethylamine (3.45 mL, 24.75 mmol) and trimethylamine hydrochloride (79 mg, 0.82 mmol) were added to a solution of sulfide **6e** (1.63 g, 8.22 mmol) in toluene (30 mL) at 0 ºC and stirred for 30 min. 4-Toluenesulfonyl chloride (3.14 g, 16.47 mmol) was added portionwise. The mixture was stirred at 0 ºC for 30 min then warmed to rt and stirred for a further 1 h 30 min. H_2O (75 mL) was added to the reaction and the product was extracted with EtOAc (5 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S2** (2.65 g, 91%) as a white solid; m.p. 46–47 ºC. R_f = 0.27 (20% EtOAc/hexane). IR (film)/cm^{-1} 2919, 2875, 1596, 1468, 1424, 1358, 1310, 1278, 1175, 1122, 1088, 1016, 922, 817, 780, 758, 696, 662. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (2 H, d, *J* = 8.3 Hz, 2 × Ts-H), 7.49–7.45 (1 H, m, Ar-H), 7.32 (2 H, d, *J* = 8.2 Hz, 2 × Ts-H), 7.19–7.12 (3 H, m, 3 × Ar-H), 4.95 (2 H, s, SCH_2O), 4.22–4.18 (2 H, m, $TsOCH_2$), 3.83–3.79 (2 H, m, SCH_2OCH_2), 2.45 (3 H, s, CH_3), 2.37 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8 (Ts-C_q), 137.9 (Ar-C_q), 134.7 (Ts-C_q), 132.8 (Ar-C_q), 130.0 (Ar-C), 129.7 (3 × Ar-C), 127.8 (2 × Ar-C), 126.7 (Ar-C), 126.6 (Ar-C), 75.4 (SCH_2O), 68.7 (OCH_2), 65.7 (OCH_2), 21.6 (CH_3), 20.5 (CH_3). HRMS (ES) *m/z* Calculated for $C_{17}H_{20}NaO_4S_2$ [M+Na]: 375.0701; Found: 375.0725 [M+Na].



1-Methyl-2-({2-[(4-methylbenzenesulfonyl)oxy]ethoxy}methanesulfonyl)benzene (2e)

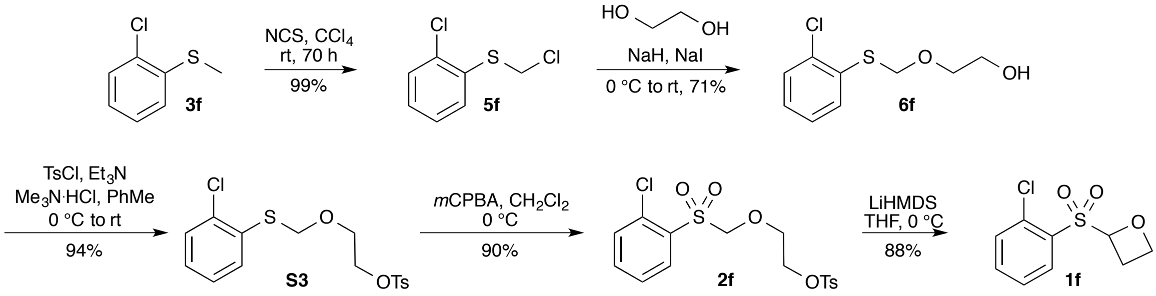
meta-Chloroperbenzoic acid (2.21 g, 12.81 mmol) was added to a solution of sulfide **S2** (1.55 g, 4.39 mmol) in dichloromethane (60 mL) at 0 ºC and the mixture stirred at 0 ºC for 1 h then stirred at rt for 3 h 45 min. The reaction was quenched with Na_2SO_3 (100 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic layers were washed with 1 M NaOH (2 × 15 mL) and sat. aq. NH_4Cl (25 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40 % EtOAc/hexane) afforded sulfone **2e** (1.67 g, 99%) as a white solid; m.p. 78–79 ºC. R_f = 0.17 (40% EtOAc/hexane). IR (film)/cm^{-1} 2925, 1597, 1574, 1457, 1428, 1372, 1357, 1319, 1289, 1247, 1235, 1189, 1120, 1096, 1080, 1058, 1047, 1021, 950, 844, 813, 806, 707. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (1 H, dd, *J* = 8.0, 1.3 Hz, Ar-H), 7.74 (2 H, d, *J* = 8.3 Hz, 2 × Ts-H), 7.58–7.53 (1 H, m, Ar-H), 7.41–7.31 (4 H, m, 2 × Ts-H + 2 × Ar-H), 4.57 (2 H, s, SCH_2O), 4.14–4.10 (2 H, m, OCH_2), 4.07–4.03 (2 H, m, OCH_2), 2.67 (3 H, s, CH_3), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0 (C_q), 138.8 (C_q), 135.3 (C_q), 134.2 (Ar-C), 132.8 (Ar-C), 132.7 (C_q), 131.1 (Ar-C), 129.9 (2 × Ts-C), 127.9 (2 × Ts-C), 126.7 (Ar-C), 86.0 (SCH_2O), 70.9 (OCH_2), 68.4 (OCH_2), 21.7 (CH_3), 20.5 (CH_3). HRMS (NSI) *m/z* Calculated for $C_{17}H_{24}NO_6S_2^+$ $[M+NH_4]^+$: 402.1040; Found: 402.1029 $[M+NH_4]^+$.

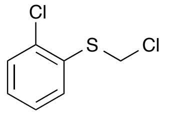


2-(2-Methylbenzenesulfonyl)oxetane (1e)

A solution of LiHMDS (0.61 M in THF, 3.52 mL, 2.15 mmol) was added dropwise to a solution of sulfone **2e** (0.75 g, 1.95 mmol) in THF (60 mL) at 0 ºC and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (30 mL) and extracted with CH_2Cl_2 (5 × 20 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded oxetane **1e** (0.39 g, 95%) as a colourless oil. R_f = 0.36 (40% EtOAc/hexane). IR (film)/cm^{-1} 2973, 2901, 1595, 1568, 1471, 1444, 1309, 1290, 1270, 1232, 1198, 1148, 1128, 1065, 1026, 936, 908, 840, 763, 716, 694, 665. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (1 H, dd, *J* = 7.6, 1.5 Hz, Ar-H), 7.56–7.51 (1 H, m, Ar-H), 7.41–7.32 (2 H, m, 2 × Ar-H), 5.46 (1 H, dd, *J* = 7.7, 5.5 Hz, OCHS), 4.88–4.80 (1 H, m, OCH*H*), 4.70–4.63 (1 H, m, OC*H*H), 3.22–3.07 (2 H, m, OCH_2CH_2), 2.72 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0 (C_q), 134.1 (Ar-C), 133.8 (C_q), 132.8 (Ar-C), 131.5 (Ar-C), 126.5 (Ar-C), 94.2 (OCHS), 71.6 (OCH_2), 22.4 (OCH_2CH_2), 20.9 (CH_3). HRMS (APCI) *m/z* Calculated for $C_{10}H_{13}O_3S^+$ $[M+H]^+$: 213.0580; Found: 213.0579 $[M+H]^+$.

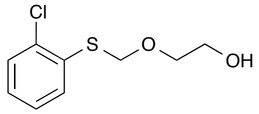
Synthesis of 2-((2-Chlorophenyl)sulfonyl)oxetane (1f)





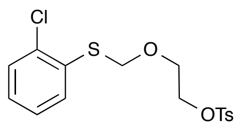
2-Chlorophenyl chloromethyl sulfide (5f)

N-Chlorosuccinimide (4.55 g, 34.11 mmol) was added portionwise to a solution of 2-chlorothioanisole (4.10 mL, 31.01 mmol) in dichloroethane (50 mL). The reaction was stirred at rt for 70 h then filtered through a short pad of silica, eluting with CH_2Cl_2 (50 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide **5f** (6.00 g, 99%) as a yellow oil, which was used without further purification. R_f = 0.10 (40% EtOAc/hexane). IR (film)/cm^{-1} 1576, 1452, 1432, 1226, 1117, 1035, 935, 851, 736, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar-H), 7.44 (1 H, dd, *J* = 7.8, 1.5 Hz, Ar-H), 7.32 (1 H, ddd, *J* = 9.1, 7.8, 1.5 Hz, Ar-H), 7.25 (1 H, ddd, *J* = 9.1, 7.8, 1.6 Hz, Ar-H), 5.02 (2 H, s, SCH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5 (C_q), 132.4 (C_q), 130.4 (Ar-C), 130.0 (Ar-C), 128.5 (Ar-C), 127.4 (Ar-C), 48.3 (SCH_2Cl). HRMS (EI) *m/z* Calculated $C_7H_6S^{35}Cl_2$ [M]: 191.9567; Found 191.9572 [M].



2-(((2-Chlorophenyl)thio)methoxy)ethanol (6f)

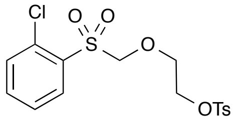
Sodium hydride (60% in mineral oil, 1.60 g, 40.11 mmol) was added to ethylene glycol (350 mL) at 0 ºC and stirred for 1 h 30 min. Sodium iodide (6.01 g, 40.10 mmol) was added followed by sulfide **5f** (6.88 g, 35.84 mmol). The resulting solution was stirred at 0 ºC for 2 h then warmed to rt for 17 h. H_2O (175 mL) was added and the product was extracted with ethyl acetate (10 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6f** (5.60 g, 71%) as a pale yellow oil. R_f = 0.42 (100% EtOAc). IR (film)/cm^{-1} 3380, 2927, 1575, 1454, 1431, 1309, 1253, 1100, 1055, 1033, 1018, 887, 824, 745, 656. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (1 H, dd, *J* = 7.8, 1.6 Hz, Ar-H), 7.38 (1 H, dd, *J* = 7.8, 1.5 Hz, Ar-H), 7.23 (1 H, ddd, *J* = 9.1, 7.8, 1.5 Hz, Ar-H), 7.16 (1 H, ddd, *J* = 9.1, 7.8, 1.6 Hz, Ar-H), 5.10 (2 H, s, SCH_2O), 3.75 (4 H, br s, OCH_2CH_2OH), 2.05 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.8 (C_q), 134.0 (C_q), 130.2 (Ar-C), 129.7 (Ar-C), 127.5 (Ar-C), 127.3 (Ar-C), 74.8 (SCH_2O), 70.0 (OCH_2), 61.5 (OCH_2). HRMS (EI) *m/z* Calculated for $C_9H_{15}NO_2S^{35}Cl$ [M+NH$_4$]: 236.0512; Found: 236.0521 [M+NH$_4$].



2-{[(2-Chlorophenyl)sulfanyl]methoxy}ethyl-4-methylbenzene-1-sulfonate (S3)

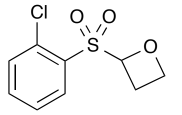
Triethylamine (9.59 mL, 68.80 mmol) and trimethylamine hydrochloride (0.22 g, 2.29 mmol) were added to a solution of sulfide **6f** (5.02 g, 22.93 mmol) in toluene (100 mL) at 0 ºC and stirred for 1 h. 4-Toluenesulfonyl chloride (8.74 g, 45.87 mmol) was added portionwise. The mixture was stirred at 0 ºC for 50 min then allowed to warm to rt and stirred for a further 1 h 30 min. H_2O (75 mL) was added to the reaction and the product was extracted with EtOAc (5 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S3** (8.03 g, 94%) as a white solid, m.p. = 40–42 ºC. R_f = 0.15 (20% EtOAc/hexane). IR (film)/cm^{-1} 3069, 2876, 1596, 1573, 1450, 1357, 1314, 1230, 1175, 1123, 1085, 1018, 924, 835, 759, 730, 661. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (2 H, d, *J* = 8.0 Hz, 2 × Ts-H), 7.55 (1 H, dd, *J* = 7.9, 1.7 Hz, Ar-H), 7.37 (1 H, dd, *J* = 7.9, 1.6 Hz, Ar-H), 7.32 (2 H, d, *J* = 8.0 Hz, 2 × Ts-H), 7.25–7.14 (2 H, m, 2 × Ar-H), 5.00 (2 H, s, SCH_2O), 4.23–4.18 (2 H, m, OCH_2CH_2), 3.80–3.80 (2 H, m, OCH_2CH_2), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9 (C_q), 134.6 (C_q), 133.8 (C_q), 132.9 (C_q), 130.3 (Ar-C), 129.8

(2 × Ts-C), 129.6 (Ar-C), 127.9 (2 × Ts-C), 127.5 (Ar-C), 127.4 (Ar-C), 74.6 (SCH_2O), 68.6 (OCH_2), 65.8 (OCH_2), 21.6 (CH_3). HRMS (ES) *m/z* Calculated $C_{18}H_{21}NO_4S_2{}^{35}Cl$ [M+H+CH_3CN]: 414.0601; Found: 414.0605 [M+H+CH_3CN].



2-(((2-Chlorophenyl)sulfonyl)methoxy)ethyl 4-methylbenzene sulfonate (2f)

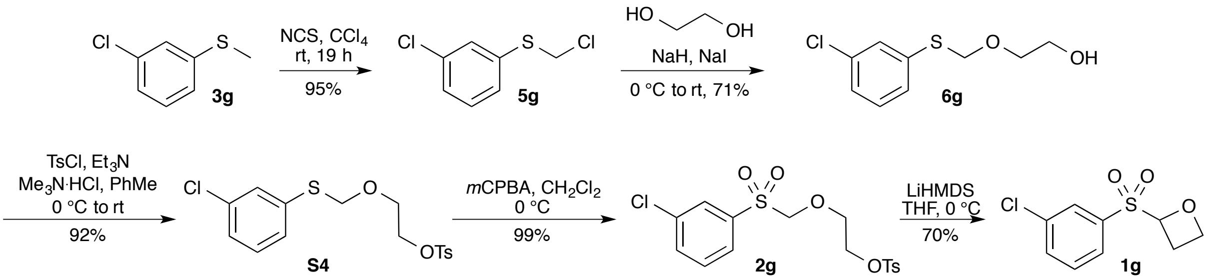
meta-Chloroperbenzoic acid (70%, 10.23 g, 41.52 mmol) was added to a solution of sulfide **S3** (5.16 g, 13.84 mmol) in dichloromethane (185 mL) at 0 °C and the mixture stirred at 0 °C for 2 h 30 min, then warmed to rt and stirred for a further 1 h. Another equivalent of *m*CPBA was added (3.30 g) and the reaction stirred at rt for 2 h. The reaction was quenched with sat. aq. Na_2SO_3 (50 mL) and extracted with dichloromethane (5 × 25 mL). The combined organic layers were washed with 1 M NaOH (2 × 20 mL) and sat. aq. NH_4Cl (20 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded sulfone **2f** (5.03 g, 90%) as a white solid; m.p = 113–114 °C. R_f = 0.16 (40% EtOAc/hexane). IR (film)/cm^{-1} 2996, 1597, 1575, 1429, 1373, 1358, 1325, 1296, 1250, 1190, 1175, 1126, 1093, 1036, 915, 844, 769, 728, 663. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (1 H, dd, *J* = 7.9, 1.6 Hz, Ar-H), 7.72 (2 H, d, *J* = 8.1 Hz, 2 × Ts-H), 7.64–7.55 (2 H, m, 2 × Ar-H), 7.52–7.47 (1 H, m, Ar-H), 7.33 (2 H, d, *J* = 8.1 Hz, 2 × Ts-H), 4.83 (2 H, s, SCH_2O), 4.11–4.07 (2 H, m, OCH_2CH_2), 4.06–4.03 (2 H, m, OCH_2CH_2), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0 (C_q), 135.3 (Ar-C), 134.6 (C_q), 132.9 (Ar-C), 132.9 (C_q), 132.6 (C_q), 131.8 (Ar-C), 129.9 (2 × Ts-C), 127.9 (2 × Ts-C), 127.6 (Ar-C), 84.7 (SCH_2O), 70.8 (OCH_2CH_2), 68.4 (OCH_2CH_2), 21.7 (CH_3). HRMS (ES) *m/z* Calculated $C_{16}H_{18}O_6S_2{}^{35}Cl$ [M+H]: 405.0233; Found 405.0237 [M+H].

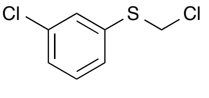


2-((2-Chlorophenyl)sulfonyl)oxetane (1f)

A solution of LiHMDS (0.61 M in THF, 4.45 mL, 2.71 mmol) was added dropwise to a solution of sulfone **2f** (1.00 g, 2.47 mmol) in THF (75 mL) at 0 °C and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (40 mL) and extracted with CH_2Cl_2 (5 × 20 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded oxetane **1f** (0.50 g, 88%) as a white solid; m.p = 70–71 °C. R_f = 0.24 (40% EtOAc/hexane). IR (film)/cm^{-1} 3065, 2918, 1574, 1435, 1311, 1274, 1146, 1107, 1066, 1028, 980, 894, 748, 710, 684. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (1 H, dd, *J* = 7.9, 1.5 Hz, Ar-H), 7.63–7.53 (2 H, m, 2 × Ar-H), 7.52–7.47 (1 H, m, Ar-H), 5.95 (1 H, dd, *J* = 8.1, 5.1 Hz, OCHS), 5.01–4.93 (1 H, m, OCH*H*), 4.71 (1 H, dt, *J* = 10.8, 5.5 Hz, O*C*HH), 3.32–3.15 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.2 (Ar-C), 133.5 (C_q), 133.4 (Ar-C), 133.2 (C_q), 131.9 (Ar-C), 127.4 (Ar-C), 92.9 (SCHO), 72.3 (OCH_2), 21.9 (OCH_2CH_2). HRMS (CI) *m/z* Calculated $C_9H_{10}O_3S{}^{35}Cl$ [M+H]: 233.0039; Found: 233.0043 [M+H].

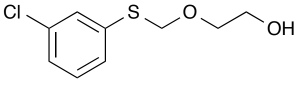
Synthesis of 2-(3-Chlorobenzenesulfonyl)oxetane (1g)





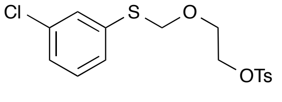
1-Chloro-3-[(choromethyl)sulfanyl]benzene (5g)

N-Chlorosuccinimide (1.00 g, 7.49 mmol) was added portionwise to a solution of 3-chlorothioanisole (0.90 mL, 6.81 mmol) in dichloroethane (10 mL). The reaction was stirred at rt for 17 h then filtered through a short pad of silica, eluting with CH_2Cl_2 (25 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide **5g** (1.24 g, 95%) as a pale yellow oil, which was used without further purification. R_f = 0.73 (40% EtOAc/hexane). IR (film)/cm^{-1} 1576, 1462, 1402, 1227, 1119, 1085, 852, 777, 720, 677. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.49 (1 H, m, Ar-H), 7.42–7.37 (1 H, m, Ar-H), 7.34–7.28 (2 H, m, 2 × Ar-H), 4.97 (2 H, s, SCH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.2 (C_q), 135.0 (C_q), 130.2 (Ar-C), 130.2 (Ar-C), 128.5 (Ar-C), 128.1 (Ar-C), 50.1 (SCH_2Cl).



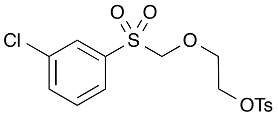
2-{[(3-Chlorophenyl)sulfanyl]methoxy}ethan-1-ol (6g)

Sodium hydride (60% in mineral oil, 0.27 g, 6.87 mmol) was added to ethylene glycol (55 mL) at 0 °C and stirred for 1 h 20 min. Sodium iodide (1.03 g, 6.87 mmol) was added followed by sulfide **5g** (1.20 g, 6.25 mmol). The resulting solution was stirred at 0 °C for 1 h then warmed to rt and stirred for a further 17 h. H_2O (30 mL) was added and the product was extracted with ethyl acetate (10 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6g** (0.97 g, 71%) as a colourless oil. R_f = 0.10 (30% EtOAc/hexane). IR (film)/cm^{-1} 3381 (OH), 2929, 1576, 1562, 1460, 1400, 1307, 1052, 1017, 886, 823, 773, 677. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (1 H, m, Ar-H), 7.35 (1 H, dt, *J* = 6.6, 2.0 Hz, Ar-H), 7.26–7.19 (2 H, m, 2 × Ar-H), 5.07 (2 H, s, SCH_2O), 3.83–3.73 (4 H, m, OCH_2CH_2OH), 1.87 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6 (C_q), 134.5 (C_q), 129.9 (Ar-C), 129.4 (Ar-C), 127.9 (Ar-C), 126.8 (Ar-C), 75.9 (SCH_2O), 69.9 (OCH_2), 61.4 (OCH_2). HRMS (CI) *m/z* Calculated $C_9H_{12}O_2S^{35}Cl$ [M+H]: 219.0247; Found: 219.0253 [M+H].



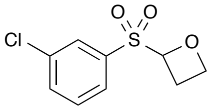
2-{[(3-Chlorophenyl)sulfanyl]methoxy}ethyl-4-methylbenzene-1-sulfonate (S4)

Triethylamine (1.65 mL, 11.83 mmol) and trimethylamine hydrochloride (38 mg, 0.39 mmol) were added to a solution of sulfide **6g** (0.86 g, 3.94 mmol) in toluene (18 mL) at 0 °C and stirred for 30 min. 4-Toluenesulfonyl chloride (1.50 g, 7.87 mmol) was added portionwise. The mixture was stirred at 0 °C for 20 min then allowed to warm to rt and stirred for a further 1 h 30 min. H_2O (20 mL) was added to the reaction and the product was extracted with EtOAc (5 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S4** (1.35 g, 92%) as a colourless oil. R_f = 0.15 (20% EtOAc/hexane). IR (film)/cm^{-1} 2921, 1576, 1453, 1431, 1251, 1117, 1034, 954, 907, 735, 658. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (2 H, d, *J* = 8.2 Hz, 2 × Ts-H), 7.40 (1 H, s, Ar-H), 7.33 (2 H, d, *J* = 8.2 Hz, 2 × Ts-H), 7.31–7.26 (1 H, m, Ar-H), 7.23–7.18 (2 H, m, 2 × Ar-H), 4.95 (2 H, s, SCH_2O), 4.24–4.18 (2 H, m, $TsOCH_2$), 3.84–3.78 (2 H, m, $CH_2OCH_2CH_2$), 2.44 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9 (C_q), 137.4 (C_q), 134.6 (C_q), 132.8 (C_q), 129.9 (Ar-C), 129.8 (2 × Ts-C), 129.4 (2 × Ar-C), 127.9 (2 × Ts-C), 126.9 (Ar-C), 75.8 (SCH_2O), 68.6 (OCH_2), 65.8 (OCH_2), 21.6 (CH_3). HRMS (APCI) *m/z* Calculated $C_{16}H_{21}{}^{35}ClNO_4S_2{}^+$ $[M+NH_4]^+$: 390.0595; Found: 390.0587 $[M+NH_4]^+$.



1-Chloro-3-({2-[(4-methylbenzenesulfonyl)oxy]ethoxy} methanesulfonyl)benzene (2g)

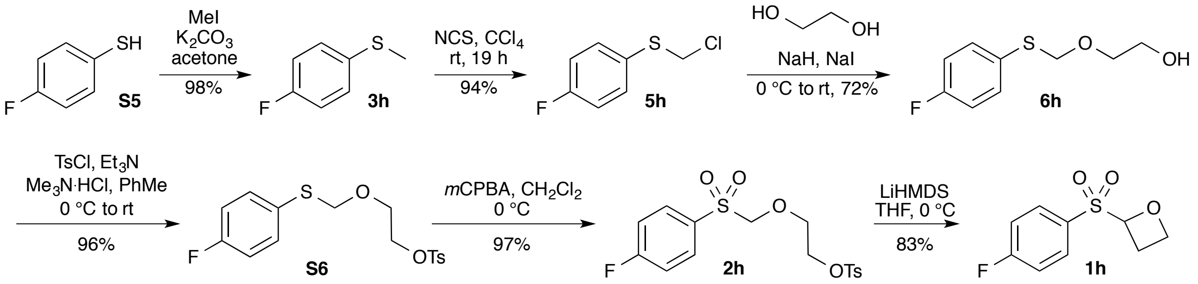
meta-Chloroperbenzoic acid (0.41 g, 2.38 mmol) was added to a solution of sulfide **S4** (0.29 g, 0.78 mmol) in dichloromethane (12 mL) at 0 ºC and the mixture stirred at 0 ºC for 2 h. The reaction was quenched with Na_2SO_3 (20 mL) and extracted with dichloromethane (5 × 10 mL). The combined organic layers were washed with 1 M NaOH (2 × 10 mL) and sat. aq. NH_4Cl (15 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded sulfone **2g** (0.32 g, 99%) as an off white solid; m.p. = 110–111 ºC. R_f = 0.30 (40% EtOAc/hexane). IR (film)/cm^{-1} 2956, 2256, 1598, 1458, 1416, 1356, 1327, 1294, 1175, 1153, 1096, 1020, 908, 814, 774, 727, 660. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (1 H, s, Ar-H), 7.81 (1 H, d, *J* = 7.8 Hz, Ar-H), 7.76 (2 H, d, *J* = 8.4 Hz, 2 × Ts-H), 7.66 (1 H, d, *J* = 7. 8 Hz, Ar-H), 7.53 (1 H, dd, *J* = 8.0, 7.8 Hz, Ar-H), 7.33 (2 H, d, *J* = 8.4 Hz, 2 × Ts-H), 4.54 (2 H, s, SCH_2O), 4.18–4.07 (4 H, m, OCH_2CH_2O), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1 (C_q), 138.6 (C_q), 135.5 (C_q), 134.4 (Ar-C), 132.6 (C_q), 130.6 (Ar-C), 129.9 (2 × Ts-C), 128.6 (Ar-C), 127.9 (2 × Ts-C), 127.1 (Ar-C), 86.1 (SCH_2O), 70.8 (OCH_2), 68.4 (OCH_2), 21.6 (CH_3). HRMS (ES) *m/z* Calculated $C_{16}H_{18}O_6S_2{}^{35}Cl$ [M+H]: 405.0233; Found: 405.0234 [M+H].

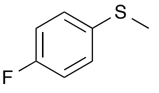


2-(3-Chlorobenzenesulfonyl)oxetane (1g)

A solution of LiHMDS (0.61 M in THF, 0.96 mL, 0.58 mmol) was added dropwise to a solution of sulfone **2g** (0.21 g, 0.52 mmol) in THF (16 mL) at 0 ºC and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with CH_2Cl_2 (5 × 15 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded oxetane **1g** (84 mg, 70%) as an off white solid; m.p. = 82–83 ºC. R_f = 0.26 (40% EtOAc/hexane). IR (film)/cm^{-1} 3090, 2912, 1579, 1460, 1439, 1409, 1312, 1263, 1232, 1148, 1119, 1075, 1026, 976, 928, 897, 797, 700, 662. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (1 H, t, *J* = 1.7 Hz, Ar-H), 7.87 (1 H, d, *J* = 7.7 Hz, Ar-H), 7.67 (1 H, d, *J* = 7.7 Hz, Ar-H), 7.53 (1 H, dd, *J* = 8.0, 7.6 Hz, Ar-H), 5.40 (1 H, dd, *J* = 7.3, 6.0 Hz, OCHS), 4.88–4.81 (1 H, m, OC*H*H), 4.71–4.64 (1 H, m, OCH*H*), 3.21–3.09 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1 (C_q), 135.5 (C_q), 134.4 (Ar-C), 130.4 (Ar-C), 129.4 (Ar-C), 127.5 (Ar-C), 94.1 (SCHO), 71.6 (OCH_2), 22.2 (OCH_2CH_2). HRMS (APCI) *m/z* Calculated $C_9H_{10}{}^{35}ClO_3S^+$ $[M+H]^+$: 233.0034; Found: 233.0032 $[M+H]^+$.

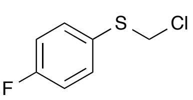
Synthesis of 2-((4-Fluorophenyl)sulfonyl)oxetane (1h)





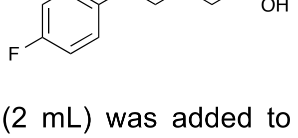
1-Fluoro-4-(methylsulfanyl)benzene (3h)

Potassium carbonate (11.84 g, 85.67 mmol) was added to a solution of 4-fluorobenzene thiol (10.00 g, 78.02 mmol) in acetone (100 mL) followed by MeI (5.10 mL, 81.92 mmol) and the reaction stirred at rt for 2 h 30 min. The reaction was filtered through celite and the solvent removed under reduced pressure. The crude material was dissolved in diethyl ether (50 mL) and washed with 5% NaOH (3 × 150 mL). The combined aqueous layers were extracted with ether (2 × 50 mL) then the combined organics were washed with brine (50 mL), dried ($MgSO_4$) and solvent removed under reduced pressure to afford sulfide **3h** (10.90 g, 98%) as a pale yellow oil which was used without further purification. R_f = 0.72 (40% EtOAc/hexane). IR (film)/cm^{-1} 2921, 1589, 1488, 1437, 1396, 1223, 1157, 1092, 1013, 968, 817, 723. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (2 H, m, 2 × Ar-H), 7.02 (2 H, dd, J = 8.7, 8.6 Hz, 2 × Ar-H), 2.48 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (C_q, d, J_{CF} = 244.1 Hz, Ar-C_q-F), 133.3 (C_q, d, J_{CF} = 3.1 Hz, Ar-C_q), 129.1 (d, J_{CF} = 7.9 Hz, 2 × Ar-C), 115.8 (d, J_{CF} = 21.5 Hz, 2 × Ar-C), 16.9 (CH_3). ^{19}F NMR (400 MHz, $CDCl_3$) δ –117.29 (Ar-F). HRMS (APCI) *m/z* Calculated $C_7H_8FS^+$ $[M+H]^+$: 143.0325; Found: 145.0322 $[M+H]^+$. The observed data (^{1}H) is consistent with that reported in the literature.[3]



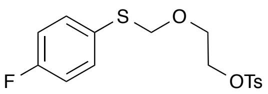
1-[(Chloromethyl)sulfany]-4-fluorobenzene (5h)

N-Chlorosuccinimide (10.33 g, 77.36 mmol) was added portionwise to a solution of sulfide **3h** (10.00 g, 70.33 mmol) in carbon tetrachloride (65 mL). The reaction was stirred at rt for 19 h then filtered through a short pad of silica, eluting with CH_2Cl_2 (40 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide **5h** (11.47 g, 94%) as a pale yellow oil, which was used without further purification. R_f = 0.74 (40% EtOAc/hexane). IR (film)/cm^{-1} 2985, 1734, 1590, 1491, 1226, 1173, 1157, 1091, 1044, 916, 826, 732. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.52 (2 H, m, 2 × Ar-H), 7.09 (2 H, dd, J = 8.7, 8.6 Hz, 2 × Ar-H), 4.90 (2 H, s, SCH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (C_q, d, J_{CF} = 249.5 Hz, Ar-C_q-F), 134.3 (d, J_{CF} = 7.8 Hz, 2 × Ar-C), 128.1 (C_q, d, J_{CF} = 2.7 Hz, Ar-C_q), 116.4 (d, J_{CF} = 22.1 Hz, 2 × Ar-C), 52.0 (SCH_2). ^{19}F NMR (400 MHz, $CDCl_3$) δ –112.57 (Ar-F). HRMS (APCI) *m/z* Calculated $C_7H_6{}^{35}ClFS^+$ $[M]^+$: 175.9857; Found: 175.9855 $[M]^+$. The observed data (^{1}H, ^{13}C, IR) is consistent with that reported in the literature.[4]

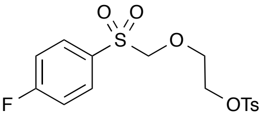


2-{[(4-Fluorophenyl)sulfanyl]methoxy}ethan-1-ol (6h)

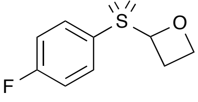
Sodium hydride (60% in mineral oil, 0.36 g, 9.00 mmol) was added to ethylene glycol (65 mL) at 0 °C and stirred for 1 h. Sodium iodide (1.35 g, 9.00 mmol) was added followed by sulfide **5h** (1.44 g, 8.18 mmol). DMF (2 mL) was added to aid solubility. The resulting solution was stirred at 0 °C for 45 min then warmed to rt and stirred for a further 16 h 30 min. H_2O (50 mL) was added and the product was extracted with ethyl acetate (10 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6h** (1.19 g, 72%) as a colourless oil. R_f = 0.16 (30% EtOAc/hexane). IR (film)/cm^{-1} 3379 (OH), 2927, 1589, 1489, 1458, 1397, 1308, 1219 (CF), 1087, 1053, 1013, 887, 823, 676. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.43 (2 H, m, 2 × Ar-H), 7.04–6.97 (2 H, m, 2 × Ar-H), 4.97 (2 H, s, SCH_2O), 3.79–3.71 (4 H, m, OCH_2CH_2OH), 2.11 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (C_q, d, J_{CF} = 247.7 Hz, Ar-C_q-F), 133.2 (d, J_{CF} = 8.5 Hz, 2 × Ar-C), 130.3 (C_q, d, J_{CF} = 2.8 Hz, Ar-C_q), 116.1 (d, J_{CF} = 21.2 Hz, 2 × Ar-C), 77.2 (SCH_2O), 69.8(OCH$_2$), 61.5 (OCH$_2$). ^{19}F NMR (400 MHz, CDCl$_3$) δ –114.53 (CF). HRMS (APCI) *m/z* Calculated $C_9H_{15}FNO_2S^+$ [M+NH$_4$]$^+$: 220.0802; Found: 220.0799 [M+NH$_4$]$^+$.



2-(((4-Fluorophenyl)thio)methoxy)ethyl 4-methylbenzenesulfonate (S6) Triethylamine (2.06 mL, 14.82 mmol) and trimethylamine hydrochloride (46 mg, 0.49 mmol) were added to a solution of sulfide **6h** (1.00 g, 4.94 mmol) in toluene (21 mL) at 0 ºC and stirred for 50 min. 4-Toluenesulfonyl chloride (1.88 g, 9.89 mmol) was added portionwise. The mixture was stirred at 0 ºC for 30 min then allowed to warm to rt and stirred for a further 1 h 30 min. H$_2$O (40 mL) was added to the reaction and the product was extracted with EtOAc (5 × 20 mL). The combined organic layers were dried (MgSO$_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S6** (1.71 g, 96%) as a colourless oil. R$_f$ = 0.22 (20% EtOAc/hexane). IR (film)/cm^{-1} 2977, 2910, 1588, 1485, 1458, 1433, 1355, 1307, 1216, 1169, 1120, 1020, 912, 806, 781, 662. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.79 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 7.45–7.39 (2 H, m, 2 × Ar-H), 7.33 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 7.01–6.95 (2 H, m, 2 × Ar-H), 4.88 (2 H, s, SCH$_2$O), 4.23–4.19 (2 H, m, OCH$_2$), 3.84–3.80 (2 H, m, OCH$_2$), 2.45 (3 H, s, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 162.3 (C$_q$, d, J_{CF} = 237.8 Hz, C$_q$), 144.9 (C$_q$), 133.3 (d, J_{CF} = 8.2 Hz, 2 × Ar-C), 132.9 (C$_q$), 130.0 (C$_q$), 129.8 (2 × Ts-C), 127.9 (2 × Ts-C), 116.1 (d, J_{CF} = 20.3 Hz, 2 × Ar-C), 70.7 (SCH$_2$O), 68.6 (O*C*H$_2$CH$_2$), 65.6 (OCH$_2$*C*H$_2$), 21.6 (CH$_3$). ^{19}F NMR (400 MHz, CDCl$_3$) δ –114.50 (CF). HRMS (NSI) *m/z* Calculated $C_{16}H_{21}FNO_4S_2^+$ [M+NH$_4$]$^+$: 374.0891; Found: 374.0891 [M+NH$_4$]$^+$.

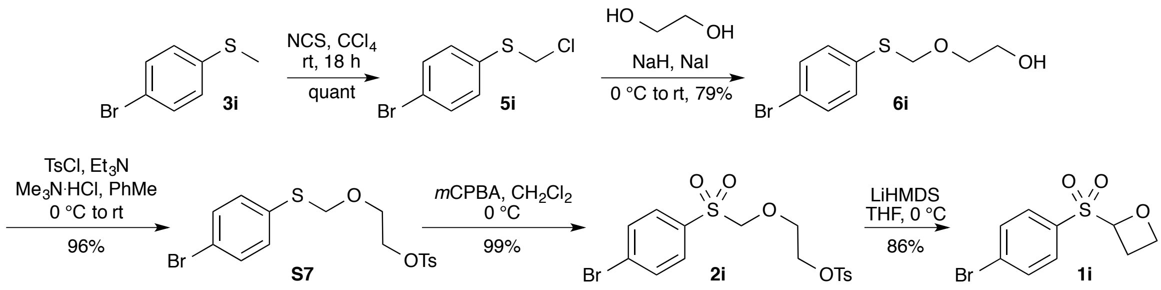


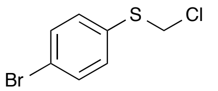
2-(((4-Fluorophenyl)sulfonyl)methoxy)ethyl 4-methylbenzenesulfonate (2h) *meta*-Chloroperbenzoic acid (70%, 2.07 g, 8.42 mmol) was added to a solution of sulfide **S6** (1.00 g, 2.80 mmol) in dichloromethane (38 mL) at 0 ºC and the mixture stirred at 0 ºC for 2 h then warmed to rt and stirred for a further 3 h. The reaction was quenched with sat. aq. Na$_2$SO$_3$ (20 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic layers were washed with 1 M NaOH (2 × 10 mL) and sat. aq. NH$_4$Cl (10 mL) then dried (MgSO$_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded sulfone **2h** (1.07 g, 97%) as a white solid; m.p = 73–74 ºC. R$_f$ = 0.25 (40% EtOAc/hexane). IR (film)/cm^{-1} 2947, 1590, 1494, 1459, 1359, 1322, 1289, 1230, 1175, 1134, 1078, 1018, 916, 835, 770, 703, 665. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96–7.90 (2 H, m, 2 × Ar-H), 7.76 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.34 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.27–7.21 (2 H, m, 2 × Ar-H), 4.52 (2 H, s, SCH$_2$O), 4.17–4.14 (2 H, m, OC*H$_2$*CH$_2$), 4.13–4.09 (2 H, m, OCH$_2$C*H$_2$*), 2.45 (3 H, s, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.2 (C$_q$, d, J_{CF} = 254.6 Hz, Ar-C$_q$-F), 145.1 (C$_q$), 132.7 (C$_q$, d J = 2.7 Hz, Ar-C$_q$), 132.5 (C$_q$), 131.8 (d, J_{CF} = 9.7 Hz, 2 × Ar-C), 129.9 (2 × Ts-C), 127.9 (2 × Ts-C), 116.6 (d, J_{CF} = 22.6, 2 × Ar-C), 86.0 (SCH$_2$O), 70.6 (OCH$_2$), 68.4 (OCH$_2$), 21.6 (CH$_3$). ^{19}F NMR (400 MHz, CDCl$_3$) δ –102.50 (CF). HRMS (ES) *m/z* Calculated for $C_{16}H_{18}O_6FS_2$ [M+H]: 389.0529; Found: 389.0521 [M+H].



2-((4-Fluorophenyl)sulfonyl)oxetane (1h) A solution of LiHMDS (0.61 M in THF, 2.32 mL, 1.42 mmol) was added dropwise to a solution of sulfone **2h** (0.50 g, 1.29 mmol) in THF (40 mL) at 0 ºC and stirred for 1 h 15 min. The reaction was quenched with sat. aq. NH$_4$Cl (40 mL) and extracted with CH$_2$Cl$_2$ (5 × 30 mL). The combined organics were dried (MgSO$_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded oxetane **1h** (0.23 g, 83%) as a white solid; m.p = 74–75 ºC. R$_f$ = 0.18 (20% EtOAc). IR (film)/cm^{-1} 2986, 2914, 1588, 1494, 1405, 1312, 1292, 1234, 1144, 1085, 1027, 982, 905, 846, 819, 723, 690. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.04–7.96 (2 H, m, 2 × Ar), 7.30–7.23 (2 H, m, 2 × Ar), 5.38 (1 H, dd, J = 7.8, 5.5 Hz, OCHS), 4.80 (1 H, ddd, J = 8.6, 7.7, 5.5 Hz, OCH*H*), 4.67 (1 H, ddd, J = 8.6, 6.2, 5.5 Hz, OC*H*H), 3.20–3.05 (2 H, m, OCH$_2$C*H$_2$*). ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.3 (C$_q$, d, J_{CF} = 253.8 Hz, C$_q$-F), 132.3 (d, J_{CF} = 9.9 Hz, 2 × Ar-C), 131.3 (C$_q$), 116.5 (d, J_{CF} = 22.8 Hz, 2 × Ar-C), 94.1 (OCHS), 71.4 (OCH$_2$), 22.3 (OCH$_2$*C*H$_2$). ^{19}F NMR (400 MHz, CDCl$_3$) δ –102.50 (CF). HRMS (CI) *m/z* Calculated for $C_9H_{10}O_3FS$ [M+H]: 217.0335; Found: 217.0339 [M+H].

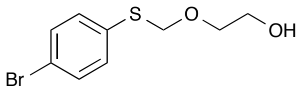
Synthesis of 2-(4-Bromobenzenesulfonyl)oxetane (1i)





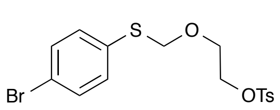
1-Bromo-4-[(chloromethyl)sulfanyl]benzene (5i)

N-Chlorosuccinimide (3.75 g, 28.11 mmol) was added portionwise to a solution of 4-bromothioanisole (5.19 g, 25.55 mmol) in dichloroethene (40 mL). The reaction was stirred at rt for 18 h then filtered through a short pad of silica, eluting with dichloroethene (20 mL) and the solvent removed under reduced pressure to afford chloromethyl sulfide **5i** as a yellow oil (6.03 g, quant). Product was taken on without further purification. R_f = 0.65 (40% EtOAc/hexane). IR (film)/cm^{-1} 1636, 1565, 1472, 1386, 1334, 1226, 1175, 1144, 1090, 1067, 1007, 906, 854, 808, 731, 715. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (2 H, d, *J* = 8.6 Hz, 2 × Ar-H), 7.39 (2 H, d, *J* = 8.6 Hz, 2 × Ar-H), 4.94 (2 H, s, SCH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1 (C_q), 132.5 (2 × Ar-C), 132.3 (2 × Ar-C), 122.3 (C_q), 50.6 (SCH_2Cl). HRMS (APCI) *m/z* Calculated for $C_7H_6{}^{80}Br^{35}ClS^+$ $[M]^+$: 237.9033; Found: 237.9031 $[M]^+$.



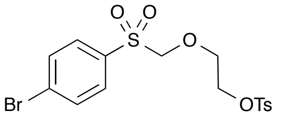
2-{[(4-Bromophenyl)sulfanyl]methoxy}ethan-1-ol (6i)

Sodium hydride (60% in mineral oil, 1.03 g, 25.70 mmol) was added to ethylene glycol (200 mL) at 0 ºC and stirred for 1 h. Sodium iodide (3.85 g, 25.70 mmol) was added followed by sulfide **5i** (5.51 g, 23.36 mmol). DMF (2 mL) added to aid solubility. The resulting solution was stirred at 0 ºC for 30 min then warmed to rt for 18 h. H_2O (100 mL) was added and the product was extracted with ethyl acetate (10 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6i** (4.83 g, 79%) as a pale yellow oil. R_f = 0.14 (30% EtOAc/hexane). IR (film)/cm^{-1} 3348, 2926, 1473, 1426, 1387, 1308, 1263, 1105, 1087, 1052, 1019, 1006, 940, 915, 887, 727, 674. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (2 H, d, *J* = 8.4 Hz, 2 × Ar-H), 7.35 (2 H, d, *J* = 8.4 Hz, 2 × Ar-H), 5.03 (2 H, s, SCH_2O), 3.79–3.72 (4 H, m, OCH_2CH_2), 1.85 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.7 (C_q), 132.0 (2 × Ar-C), 131.8 (2 × Ar-C), 121.0 (C_q), 76.3 (SCH_2O), 69.8 (OCH_2), 61.6 (OCH_2). HRMS (APCI) *m/z* Calculated for $C_9H_{15}{}^{79}BrNO_2S^+$ $[M+NH_4]^+$: 280.0001; Found: 280.0000 $[M+NH_4]^+$.



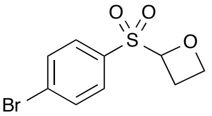
2-{[(4-Bromophenyl)sulfanyl]methoxy}ethyl-4-methylbenzenesulfonate (S7)

Triethylamine (6.59 mL, 47.28 mmol) and trimethylamine hydrochloride (0.15 g, 1.57 mmol) were added to a solution of sulfide **6i** (4.12 g, 15.73 mmol) in toluene (55 mL) at 0 ºC and stirred for 30 min. 4-Toluenesulfonyl chloride (6.01 g, 31.52 mmol) was added portionwise. The mixture was stirred at 0 ºC for 30 min then warmed to rt and stirred for a further 1 h 30 min. H_2O (100 mL) was added to the reaction and the product was extracted with EtOAc (5 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S7** (6.31 g, 96%) as a white solid, m.p. = 54–55 ºC. R_f = 0.19 (20% EtOAc/hexane). IR (film)/cm^{-1} 1598, 1473, 1368, 1346, 1297, 1280, 1191, 1171, 1120, 1099, 1085, 1015, 1006, 949, 923, 809, 784, 725, 796, 680, 661. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (2 H, d, *J* = 8.3 Hz, 2 × Ar-H), 7.38 (2 H, d, *J* = 8.5 Hz, 2 × Ar-H), 7.33 (2 H, d, *J* = 8.3 Hz, 2 × Ar-H), 7.28 (2 H, d, *J* = 8.5 Hz, 2 × Ar-H), 4.92 (2 H, s, SCH_2O), 4.23–4.19 (2 H, m, OCH_2), 3.84–3.80 (2 H, m, OCH_2), 2.46 (3 H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9 (C_q), 134.5 (C_q), 132.9 (C_q), 132.0 (2 × Ar-C), 131.8 (2 × Ar-C), 129.8 (2 × Ts-C), 127.9 (2 × Ts-C), 121.0 (C_q), 76.1 (SCH_2O), 68.5 (OCH_2), 65.7 (OCH_2), 21.7 (CH_3). HRMS (ESI) *m/z* Calculated for $C_{16}H_{17}O_4{}^{79}BrNaS_2$ [M+Na]: 438.9644; Found: 438.9622 [M+Na].



1-Bromo-4-({2-[(4-methylbenzenesulfonyl)oxy]ethoxy}methane sulfonyl)benzene (2i)

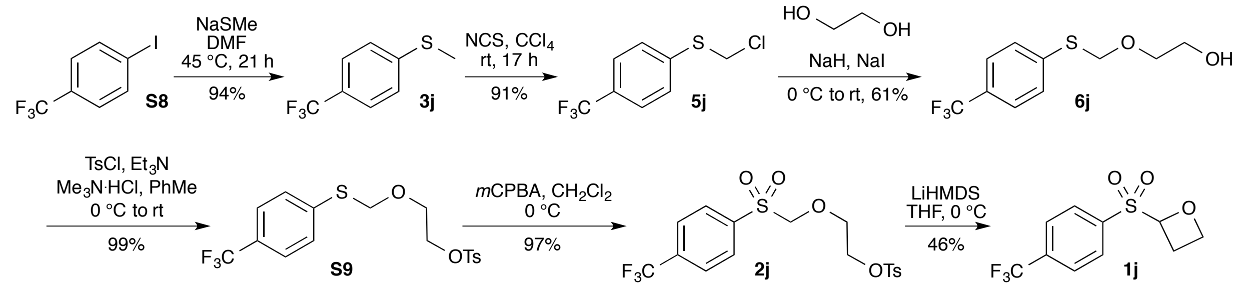
meta-Chloroperbenzoic acid (3.85 g, 22.31 mmol) was added to a solution of sulfide **S7** (3.10 g, 7.45 mmol) in dichloromethane (100 mL) at 0 ºC and the mixture stirred at 0 ºC for 3 h. The reaction was quenched with Na_2SO_3 (75 mL) and extracted with dichloromethane (5 × 30 mL). The combined organic layers were washed with 1 M NaOH (2 × 25 mL) and sat. aq. NH_4Cl (25 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (50 % EtOAc/hexane) afforded sulfone **2i** (3.34 g, 99%) as a white solid; m.p. = 88–89 ºC. R_f = 0.42 (50% EtOAc/hexane). IR (film)/cm^{-1} 3099, 2953, 1574, 1458, 1358, 1323, 1290, 1247, 1175, 1135, 1107, 1078, 1008, 949, 916, 815, 715, 665. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–7.73 (4 H, m, 4 × Ar-H), 7.70 (2 H, d, J = 8.7 Hz, 2 × Ar-H), 7.35 (2 H, d, J = 8.0 Hz, 2 × Ar-H), 4.52 (2 H, s, SCH_2O), 4.18–4.13 (2 H, m, $TsOCH_2$), 4.12–4.08 (2 H, m, OCH_2), 2.46 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1 (C_q), 135.8 (C_q), 132.6 (C_q), 132.6 (2 × Ts-C), 130.4 (2 × Ts-C), 129.9 (2 × Ar-C), 129.8 (C_q), 127.9 (2 × Ar-C), 86.0 (SCH_2O), 70.6 (OCH_2), 68.3 (OCH_2), 21.7 (CH_3). HRMS (ES) *m/z* Calculated for $C_{16}H_{17}{}^{79}BrNaO_6S_2$ [M+Na]: 470.9548; Found: 470.9576 [M+Na].

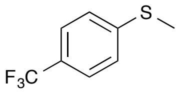


2-(4-Bromobenzenesulfonyl)oxetane (1i)

A solution of LiHMDS (0.61 M in THF, 4.03 mL, 2.46 mmol) was added dropwise to a solution of sulfone **2i** (1.01 g, 2.25 mmol) in THF (70 mL) at 0 ºC and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (30 mL) and extracted with CH_2Cl_2 (5 × 20 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded oxetane **1i** (0.54 g, 86%) as a white solid; m.p. = 99–100 ºC. R_f = 0.38 (40% EtOAc/hexane). IR (film)/cm^{-1} 3089, 2979, 2929, 2909, 1571, 1468, 1441, 1387, 1313, 1272, 1246, 1175, 1144, 1109, 1084, 1067, 1059, 1029, 1007, 975, 953, 939, 895, 843, 818, 769, 707, 681. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 7.73 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 5.37 (1 H, dd, J = 7.7, 5.5 Hz, OC*H*S), 4.85–4.77 (1 H, m, OCH*H*), 4.70–4.63 (1 H, m, OC*H*H), 3.20–3.05 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3 (C_q), 132.5 (2 × Ar-C), 131.0 (2 × Ar-C), 129.9 (C_q), 94.1 (OCHS), 71.6 (OCH_2), 22.3 (OCH_2CH_2). HRMS (NSI) *m/z* Calculated for $C_9H_9{}^{79}BrNaO_3S^+$ $[M+Na]^+$: 298.9348; Found: 298.9349 $[M+Na]^+$.

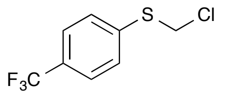
Synthesis of 2-[4-(Trifluoromethyl)benzenesulfonyl]oxetane (1j)





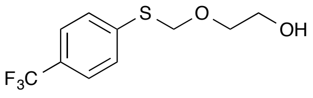
1-(Methylsulfanyl)-4-(trifluoromethyl)benzene (3j)

4-Iodobenzo-trifluoride (1.08 mL, 7.35 mmol) was added to a solution of sodium thiomethoxide (0.57 g, 8.08 mmol) in DMF (18 mL) and the resulting solution was heated at 45 °C for 21 h. The reaction was quenched with sat. aq. NaCl (10 mL) and extracted with Et_2O (6 × 10 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (100% hexane) afforded methyl sulfide **3j** (1.32 g, 94%) as a white solid. R_f 0.65 (100% hexane). IR (film)/cm^{-1} 2926, 1605, 1436, 1404, 1322, 1196, 1157, 1091, 1011, 949, 817, 779, 725, 698. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (2 H, d, J = 8.2 Hz, 2 × Ar-H), 7.31 (2 H, d, J = 8.2 Hz, 2 × Ar-H), 2.52 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8 (C$_q$), 126.7 (C$_q$, q, J_{CF} = 31.8 Hz, *C*-CF_3), 125.6 (4 × Ar-C), 124.2 (C$_q$, q, J_{CF} = 270.5 Hz, CF_3), 15.0 (CH_3). ^{19}F NMR (400 MHz, $CDCl_3$) δ –62.33 (CF_3). HRMS (EI) *m/z* Calculated for $C_8H_7F_3S$ [M]: 192.0221; Found: 192.0228 [M]. The observed data (^{1}H and ^{13}C) is consistent with that reported in the literature.[5]



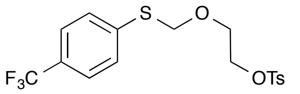
1-[(Chloromethyl)sulfanyl]-4-(trifluoromethyl)benzene (5j)

N-Chlorosuccinimide (0.53 g, 3.97 mmol) was added portionwise to a solution of *p*-trifluoromethyl methyl sulfide **3j** (0.73 g, 3.81 mmol) in dichloroethane (8 mL). The reaction was stirred at rt for 17 h then filtered through a short pad of silica, eluting with CH_2Cl_2 (15 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide **5j** (0.78 g, 91%) as a pale yellow oil. R_f 0.27 (10% Et_2O/hexane). IR (film)/cm^{-1} 1607, 1500, 1405, 1321, 1228, 1165, 1119, 1094, 1061, 1013, 824, 734, 700. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 7.58 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 5.03 (2 H, s, SCH_2Cl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5 (C$_q$), 129.3 (C$_q$, q, J_{CF} = 32.1 Hz, *C*-CF_3), 129.0 (2 × Ar-C), 125.9 (q, J_{CF} = 3.1 Hz, 2 × Ar-C), 123.9 (C$_q$, q, J_{CF} = 272.9 Hz, CF_3), 48.8 (SCH_2Cl). ^{19}F NMR (400 MHz, $CDCl_3$) δ –62.66 (CF_3). HRMS (EI) *m/z* Calculated for $C_8H_6{}^{35}ClF_3S$ [M]: 225.9831; Found: 225.9831 [M].



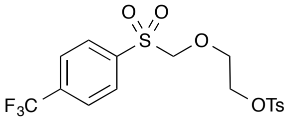
2-({[4-(Trifluoromethyl)phenyl]sulfanyl}methoxy)ethan-1-ol (6j)

Sodium hydride (60% in mineral oil, 76 mg, 1.95 mmol) was added to ethylene glycol (16 mL) at 0 °C and stirred for 40 min. Sodium iodide (0.29 g, 1.95 mmol) was added followed by sulfide **5j** (0.40 g, 1.77 mmol). The resulting solution was stirred at 0 °C for 2 h then warmed to rt for 15 h. H_2O (20 mL) was added and the product was extracted with ethyl acetate (10 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6j** (0.28 g, 61%) as a pale yellow oil. R_f = 0.10 (30% EtOAc/hexane). IR (film)/cm^{-1} 2927, 2296, 1607, 1403, 1321, 1162, 1060, 1013, 888, 825, 779, 677. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.52 (4 H, m, 4 × Ar-H), 5.12 (2 H, s, SCH_2O), 3.83–3.75 (4 H, m, OCH_2CH_2OH), 2.03 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0 (C$_q$), 128.7 (2 × Ar-C), 128.2 (C$_q$, q, J_{CF} = 32.9 Hz, *C*-CF_3), 125.5 (q, J_{CF} = 3.3 Hz, 2 × Ar-C), 123.9 (C$_q$, q, J_{CF} = 272.0 Hz, CF_3), 75.0 (SCH_2O), 69.9 (OCH_2), 61.2 (OCH_2). ^{19}F NMR (400 MHz, $CDCl_3$) δ –62.57 (CF_3). HRMS (CI) *m/z* Calculated $C_{10}H_{15}NF_3O_2S$ $[M+NH_4]^+$: 270.0770; Found: 270.0770 $[M+NH_4]^+$.



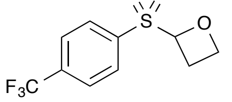
2-({[4-(Trifluoromethyl)phenyl]sulfanyl}methoxy)ethyl-4-methylbenzene-1-sulfonate (S9)

Triethylamine (0.33 mL, 2.37 mmol) and trimethylamine hydrochloride (7 mg, 0.07 mmol) were added to a solution of sulfide **6j** (0.20 g, 0.79 mmol) in toluene (4 mL) at 0 ºC and stirred for 30 min. 4-Toluenesulfonyl chloride (0.31 g, 1.61 mmol) was added portionwise. The mixture was stirred at 0 ºC for 20 min then allowed to warm to rt and stirred for a further 1 h 30 min. H_2O (20 mL) was added to the reaction and the product was extracted with EtOAc (5 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S9** (0.32 g, 99%) as an off white solid; m.p. = 70–71 ºC. R_f = 0.15 (20% EtOAc/hexane). IR (film)/cm^{-1} 2926, 1603, 1317, 1161, 1097, 1083, 1028, 996, 909, 826, 811, 759, 683. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.52–7.48 (4 H, m, 4 × Ar-H), 7.33 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 5.02 (2 H, s, SCH_2O), 4.26–4.29 (2 H, m, $TsOCH_2$), 3.86–3.81 (2 H, m, $CH_2OC\textit{H}_2CH_2$), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9 (C_q), 140.7 (C_q), 132.9 (C_q), 129.8 (2 x Ts-C), 129.0 (2 × Ar-C), 128.5 (C_q, q, J_{CF} = 32.1 Hz, *C*-CF_3), 127.9 (2 x Ts-C), 125.6 (q, J_{CF} = 3.5 Hz, 2 × Ar-C), 124.0 (C_q, q, J_{CF} = 272.6 Hz, CF_3), 75.1 (SCH_2O), 68.5 (OCH_2), 65.8 (OCH_2), 21.6 (CH_3). ^{19}F NMR (400 MHz, $CDCl_3$) δ –62.5 (CF_3). HRMS (APCI) *m/z* Calculated $C_{17}H_{21}F_3NO_4S_2^+$ $[M+NH_4]^+$: 424.0859; Found: 424.0854 $[M+NH_4]^+$.



1-({2-[(4-Methylbenzenesulfonyl)oxy]ethoxy}methanesulfonyl)-4-(trifluoromethyl)benzene (2j)

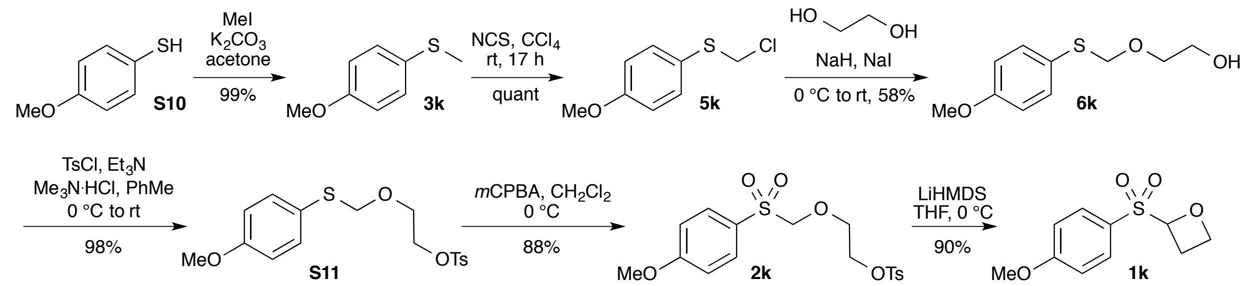
meta-Chloroperbenzoic acid (0.12 g, 0.72 mmol) was added to a solution of sulfide **S9** (95 mg, 0.24 mmol) in dichloromethane (4 mL) at 0 ºC and the mixture stirred at 0 ºC for 2 h. The reaction was quenched with Na_2SO_3 (10 mL) and extracted with dichloromethane (5 × 10 mL). The combined organic layers were washed with 1 M NaOH (2 × 10 mL) and sat. aq. NH_4Cl (15 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded sulfone **2j** (99 mg, 97%) as a white solid; m.p. = 86–87 ºC. R_f = 0.26 (40% EtOAc/hexane). IR (film)/cm^{-1} 2927, 1598, 1453, 1403, 1357, 1320, 1295, 1172, 1129, 1083, 1060, 1016, 915, 842, 815, 755, 695, 662. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (2 H, d, J = 8.2 Hz, 2 × Ar-H), 7.83 (2 H, d, J = 8.2 Hz, 2 × Ar-H), 7.77 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.34 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 4.57 (2 H, s, SCH_2O), 4.20–4.09 (4 H, m, OCH_2CH_2O), 2.45 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, (C_q), 140.4 (C_q), 135.8 (C_q, q, J_{CF} = 32.0 Hz, Ar-C_q), 132.6 (C_q), 129.9 (2 x Ts-C), 129.6 (2 × Ar-C), 127.9 (2 x Ts-C), 126.3 (q, J_{CF} = 3.5 Hz, 2 × Ar-C), 123.1 (C_q, q, J_{CF} = 263.9 Hz, CF_3), 85.9 (SCH_2O), 70.7 (OCH_2), 68.3 (OCH_2), 21.6 (CH_3). ^{19}F NMR (400 MHz, $CDCl_3$) δ –63.2 (CF_3). HRMS (ES) *m/z* Calculated $C_{17}H_{16}O_6F_3NaS_2$ [M+Na]: 461.0316; Found 461.0328 [M+Na].

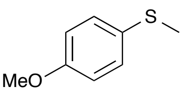


2-[4-(Trifluoromethyl)benzenesulfonyl]oxetane (1j)

A solution of LiHMDS (0.61 M in THF, 0.15 mL, 0.09 mmol) was added dropwise to a solution of sulfone **2j** (37 mg, 0.08 mmol) in THF (3 mL) at 0 ºC and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (20 mL) and extracted with CH_2Cl_2 (5 × 10 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded oxetane **1j** (10 mg, 46%) as a white solid. R_f = 0.24 (20% EtOAc/hexane). IR (film)/cm^{-1} 2977, 2907, 1403, 1319, 1130, 1107, 1061, 1029, 984, 909, 844, 787, 715, 679. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (2 H, d, J = 8.0 Hz, 2 × Ar-H), 7.86 (2 H, d, J = 8.0 Hz, 2 × Ar-H), 5.41 (1 H, dd, J = 6.7, 6.0 Hz, OCHS), 4.90–4.82 (1 H, m, $OCH\textit{H}$), 4.73–4.65 (1 H, m, $OC\textit{H}H$), 3.22–3.11 (2 H, m, $OCH_2C\textit{H}_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 (C_q), 135.9 (C_q, q, J_{CF} = 33.0 Hz, *C*-CF_3), 130.1 (2 × Ar-C), 126.2 (q, J_{CF} = 3.6 Hz, 2 × Ar-C), 123.1 (C_q, q, J_{CF} = 272.6 Hz, CF_3), 94.1 (OCHS), 71.7 (OCH_2), 22.1 ($OCH_2\textit{C}H_2$). ^{19}F NMR (400 MHz, $CDCl_3$) δ –63.3 (CF_3). HRMS (ASAP) *m/z* Calculated for $C_{10}H_{10}F_3O_3S$ [M+H]: 267.0303; Found: 267.0303 [M+H].

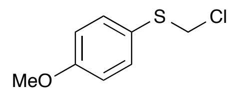
Synthesis of 2-((4-Methoxyphenyl)sulfonyl)oxetane (1k)





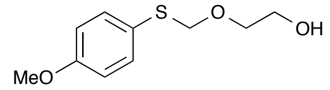
1-Methoxy-4-(methylthio)-benzene (3k)

Potassium carbonate (5.42 g, 39.23 mmol) was added to a solution of 4-methoxythiophenol (5.00 g, 4.39 mL, 35.66 mmol) in acetone (45 mL) followed by MeI (2.33 mL, 37.43 mmol) and the reaction stirred at rt for 70 h. The reaction was filtered through celite and the solvent removed under reduced pressure. The crude material was dissolved in diethyl ether (30 mL) and washed with 1M NaOH (3 × 25 mL). The combined aqueous layers were extracted with ether (20 mL) then the combined organics were washed with brine (20 mL), dried ($MgSO_4$) and solvent removed under reduced pressure to afford sulfide **3k** (5.45 g, 99%) as a yellow oil which was used without further purification. R_f = 0.43 (40% EtOAc/hexane). IR (film)/cm^{-1} 2919, 2834, 1592, 1492, 1462, 1438, 1282, 1238, 1175, 1105, 1029, 967, 818. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (2 H, d, *J* = 8.7 Hz, 2 × Ar-H), 6.87 (2 H, d, *J* = 8.7 Hz, 2 × Ar-H), 3.80 (3 H, s, OCH_3), 2.46 (3 H, s, SCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (C_q), 130.2 (2 × Ar-C), 128.7 (C_q), 114.6 (2 × Ar-C), 55.3 (OCH_3), 18.1 (CH_3). The observed data (^{1}H) is consistent with that reported in the literature.[6]



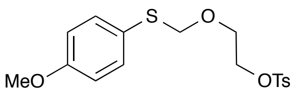
4-(Chloromethyl)thioanisole (5k)

N-Chlorosuccinimide (5.10 g, 38.13 mmol) was added portionwise to a solution of sulfide **3k** (5.34 g, 34.66 mmol) in dichloroethane (55 mL). The reaction was stirred at rt for 16 h 30 min then filtered through a short pad of silica, eluting with CH_2Cl_2 (40 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide **5k** (6.52 g, quant) as a pale yellow oil, which was used without further purification. R_f = 0.45 (40% EtOAc/hexane). IR (film)/cm^{-1} 2836, 1723, 1589, 1492, 1462, 1288, 1245, 1172, 1138, 1026, 823, 716. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (2 H, d, *J* = 8.9 Hz, 2 × Ar), 7.51 (2 H, d, *J* = 8.9 Hz, 2 × Ar), 5.46 (2 H, s, SCH_2Cl), 4.42 (3 H, s, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2 (C_q), 134.7 (2 × Ar-C), 123.3 (C_q), 114.7 (2 × Ar-C), 55.3 (OCH_3), 53.0 (SCH_2Cl). HRMS (CI) *m/z* Calculated for $C_8H_9{}^{35}ClOS^+$ $[M]^+$: 188.0057; Found: 188.0052 $[M]^+$. The observed data (^{1}H) is consistent with that reported in the literature.[7]



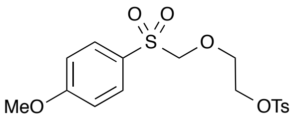
2-(((4-Methoxyphenyl)thio)methoxy)ethanol (6k)

Sodium hydride (60% in mineral oil, 1.40 g, 35.09 mmol) was added to ethylene glycol (300 mL) at 0 ºC and stirred for 1 h 30 min. Sodium iodide (5.26 g, 35.09 mmol) was added followed by sulfide **5k** (6.00 g, 31.90 mmol). The resulting solution was stirred at 0 ºC for 2 h then warmed to rt for 16 h. H_2O (150 mL) was added and the product was extracted with ethyl acetate (10 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol **6k** (3.95 g, 58%) as a colourless oil. R_f = 0.10 (30% EtOAc/hexane) IR (film)/cm^{-1} 3403, 2937, 1591, 1493, 1461, 1440, 1284, 1240, 1174, 1053, 1025, 887, 822, 676. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (2 H, d, *J* = 8.7 Hz, 2 × Ar-H), 6.86 (2 H, d, *J* = 8.7 Hz, 2 × Ar-H), 4.93 (2 H, s, SCH_2O), 3.80 (3 H, s, OCH_3), 3.78–3.71 (4 H, m, OCH_2CH_2OH), 2.07 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C_q), 133.8 (2 × Ar-C), 125.4 (C_q), 114.6 (2 × Ar-C), 77.8 (SCH_2O), 69.7 (OCH_2), 61.6 (OCH_2), 55.3 (OCH_3). HRMS (EI) *m/z* Calculated for $C_{10}H_{14}O_3S$ [M]: 214.0664; Found: 214.0665 [M].



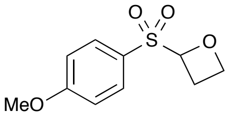
2-(((4-Methoxyphenyl)thio)methoxy)ethyl 4-methylbenzene sulfonate (S11)

Triethylamine (6.82 mL, 48.93 mmol) and trimethylamine hydrochloride (0.15 g, 1.63 mmol) were added to a solution of sulfide **6k** (3.53 g, 16.47 mmol) in toluene (70 mL) at 0 ºC and stirred for 1 h. 4-Toluenesulfonyl chloride (6.22 g, 32.63 mmol) was added portionwise. The mixture was stirred at 0 ºC for 50 min then allowed to warm to rt and stirred for a further 1 h 30 min. H_2O (75 mL) was added to the reaction and the product was extracted with EtOAc (5 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate **S11** (5.93 g, 98%) as a yellow oil. R_f = 0.23 (20% EtOAc/hexane). IR (film)/cm^{-1} 2954, 1595, 1493, 1353, 1286, 1245, 1172, 1095, 1003, 912, 814, 771, 661. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (2 H, d, *J* = 7.9 Hz, 2 × Ts-H), 7.37 (2 H, d, *J* = 8.9 Hz, 2 × Ar-H), 7.31 (2 H, d, *J* = 7.9 Hz, 2 × Ts-H), 6.82 (2 H, d, *J* = 8.7 Hz, 2 × Ar-H), 4.81 (2 H, s, SCH_2O), 4.21–4.17 (2 H, m, OCH_2CH_2), 3.82–3.76 (5 H, m, OCH_3 + OCH_2CH_2), 2.43 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C_q), 144.8 (C_q), 133.8 (2 × Ar-C), 132.9 (C_q), 129.8 (2 × Ts-C), 128.0 (2 × Ts-C), 125.3 (C_q), 114.6 (2 × Ar-C), 77.7 (SCH_2O), 68.7 (OCH_2CH_2), 65.5 (OCH_2CH_2), 55.3 (OCH_3), 21.6 (CH_3).



2-(((4-Methoxyphenyl)sulfonyl)methoxy)ethyl 4-methyl benzenesulfonate (2k)

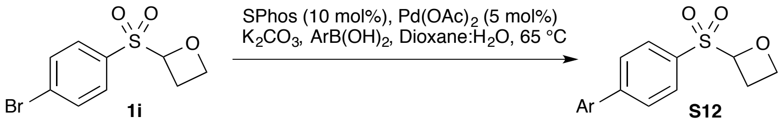
meta-Chloroperbenzoic acid (5.62 g, 32.57 mmol) was added to a solution of sulfide **S11** (4.00 g, 10.86 mmol) in dichloromethane (150 mL) at 0 ºC and the mixture stirred at 0 ºC for 2 h. Then warmed to rt and stirred for a further 3 h. The reaction was quenched with sat. aq. Na_2SO_3 (30 mL) and extracted with dichloromethane (5 × 25 mL). The combined organic layers were washed with 1 M NaOH (2 × 20 mL) and sat. aq. NH_4Cl (15 mL) then dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded sulfone **2k** (3.81 g, 88%) as a white solid; m.p. = 85–87 ºC. R_f = 0.12 (40% EtOAc/hexane). IR (film)/cm^{-1} 3013, 2981, 1594, 1498, 1456, 1287, 1255, 1174, 1135, 1081, 1009, 994, 957, 815, 755, 658. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2 H, d, *J* = 9.2 Hz, 2 × Ar-H), 7.77 (2 H, d, *J* = 7.8 Hz, 2 × Ts-H), 7.34 (2 H, d, *J* = 7.8 Hz, 2 × Ts-H), 7.04 (2 H, d, *J* = 9.2 Hz, 2 × Ar-H), 4.48 (2 H, s, SCH_2O), 4.17–4.13 (2 H, m, OCH_2CH_2), 4.09–4.06 (2 H, m, OCH_2CH_2), 3.90 (3 H, s, OCH_3), 2.46 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (C_q), 145.0 (C_q), 132.7 (C_q), 131.1 (2 × Ar-C), 129.9 (2 × Ts-C), 128.2 (C_q), 127.9 (2 × Ts-C), 114.6 (2 × Ar-C), 86.2 (SCH_2O), 70.5 (OCH_2CH_2), 68.5 (OCH_2CH_2), 55.7 (OCH_3), 21.6 (CH_3). HRMS (ES) *m/z* Calculated for $C_{17}H_{21}O_7S_2$ [M+H]: 401.0729; Found: 401.0724. [M+H].



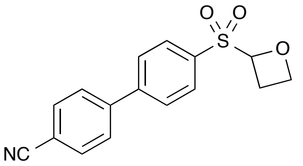
2-((4-Methoxyphenyl)sulfonyl)oxetane (1k)

A solution of LiHMDS (0.61 M in THF, 3.38 mL, 2.06 mmol) was added dropwise to a solution of sulfone **2k** (0.75 g, 1.87 mmol) in THF (58 mL) at 0 ºC and stirred for 1 h 30 min. The reaction was quenched with sat. aq. NH_4Cl (40 mL) and extracted with CH_2Cl_2 (5 × 25 mL). The combined organics were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded oxetane **1k** (0.40 g, 95%) as a white solid; m.p = 65–66 ºC. R_f = 0.12 (40% EtOAc/hexane). IR (film)/cm^{-1} 2973, 2929, 1594, 1497, 1448, 1302, 1262, 1136, 1090, 1058, 1027, 976, 896, 828, 801, 726, 696. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (2 H, d, *J* = 9.7 Hz, 2 × Ar-H), 7.02 (2 H, d, *J* = 9.7 Hz, 2 × Ar-H), 5.33 (1 H, dd, *J* = 7.8, 5.5 Hz, OCHS), 4.74–4.67 (1 H, m, OCH*H*), 4.61 (1 H, dt, *J* = 8.3, 5.7 Hz, OC*H*H), 3.87 (3 H, s, OCH_3), 3.13–2.97 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3 (C_q), 131.7 (2 × Ar-C), 126.4 (C_q), 114.5 (2 × Ar-C), 94.0 (SCHO), 71.2 (OCH_2), 55.7 (OCH_3), 22.5 (OCH_2CH_2). HRMS (APCI) *m/z* Calculated for $C_{10}H_{16}NO_4S^+$ $[M+NH_4]^+$: 246.0795; Found: 246.0793 $[M+NH_4]^+$.

Preparation of Oxetane 17 and 18 by Suzuki Cross-coupling of Oxetane 1i

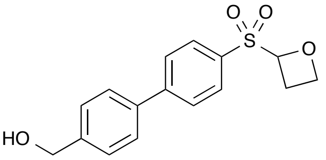


Conditions related to those reported by Buchwald were employed, using the S-Phos ligand.[8]



4-[4-(Oxetane-2-sulfonyl)phenyl]benzonitrile (17)

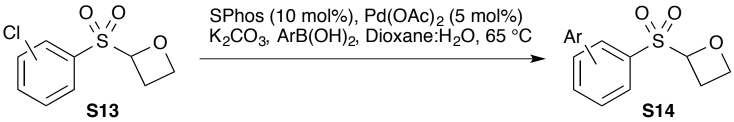
A flask was charged with Pd(OAc)$_2$ (2 mg, 0.009 mmol), S-Phos (7 mg, 0.017 mmol), K_2CO_3 (47 mg, 0.36 mmol), 4-cyanophenylboronic acid (35 mg, 0.24 mmol) and 2-(4-bromobenzenesulfonyl) oxetane **1i** (51 mg, 0.18 mmol) then flushed with Ar. The mixture was dissolved in dioxane:water (4:1, 1.6 mL) and heated to 65 °C for 15 h. The crude mixture was filtered through celite and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded oxetane **17** (43 mg, 78%) as a white solid; m.p. 156–157 °C. R_f = 0.36 (30% EtOAc/hexane). IR (film)/cm^{-1} 2976, 2915, 2222, 1592, 1392, 1323, 1310, 1274, 1151, 1091, 1031, 981, 905, 873, 821, 734, 675. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (2 H, d, *J* = 8.1 Hz, 2 × Ar-H), 7.81–7.76 (4 H, m, 4 × Ar-H), 7.72 (2 H, d, *J* = 8.3 Hz, 2 × Ar-H), 5.43 (1 H, dd, *J* = 6.7, 6.4 Hz, OCHS), 4.90–4.83 (1 H, m, OC*H*H), 4.72–4.65 (1 H, m, OCH*H*), 3.20–2.13 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1 (C_q), 143.5 (C_q), 135.4 (C_q), 132.9 (2 × Ar-C), 130.3 (2 × Ar-C), 128.1 (2 × Ar-C), 128.0 (2 × Ar-C), 118.4 (CN), 112.5 (C_q), 94.2 (SCHO), 71.7 (OCH_2), 22.3 (OCH_2CH_2). HRMS (ES) *m/z* Calculated $C_{16}H_{14}NO_3S$ [M+H]: 300.0694; Found: 300.0708 [M+H].



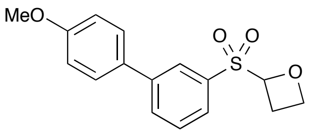
{4-[4-Oxetane-2-sulfonyl)phenyl]phenyl}methanol (18)

A flask was charged with Pd(OAc)$_2$ (2 mg, 0.009 mmol), S-Phos (7 mg, 0.017 mmol), K_2CO_3 (47 mg, 0.36 mmol) 4-(hydroxymethyl)phenylboronic acid (36 mg, 0.24 mmol) and 2-(4-bromobenzenesulfonyl)oxetane **1i** (50 mg, 0.18 mmol) then flushed with Ar. The mixture was dissolved in dioxane:water (4:1, 1.6 mL) and heated to 65 °C for 15 h. The crude mixture was filtered through celite and the solvent removed under reduced pressure. Purification by flash chromatography (40–100% EtOAc/hexane) afforded oxetane **18** (41 mg, 75%) as a white solid; m.p. 136–137 °C. R_f = 0.06 (40% EtOAc/hexane). IR (film)/cm^{-1} 3505 (OH), 2913, 1593, 1392, 1302, 1272, 1146, 1025, 978, 901, 804, 756, 688. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (2 H, d, *J* = 8.5 Hz, 2 × Ar-H), 7.76 (2 H, d, *J* = 8.5 Hz, 2 × Ar-H), 7.60 (2 H, d, *J* = 8.1 Hz, 2 × Ar-H), 7.49 (2 H, d, *J* = 8.1 Hz, 2 × Ar-H), 5.42 (1 H, dd, *J* = 7.0, 6.3 Hz, OCHS), 4.86–4.79 (1 H, m, OC*H*H), 4.77 (2 H, s, C*H*$_2$OH), 4.70–4.64 (1 H, m, OCH*H*), 3.19–2.09 (2 H, m, OCH_2CH_2), 1.99 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8 (C_q), 141.6 (C_q), 138.3 (C_q), 133.7 (C_q), 130.0 (2 × Ar-C), 127.7 (2 × Ar-C), 127.6 (2 × Ar-C), 127.5 (2 × Ar-C), 94.1 (SCHO), 71.5 (OCH_2), 64.8 (CH_2OH), 22.4 (OCH_2CH_2). HRMS (ES) *m/z* Calculated $C_{18}H_{19}NO_4S$ [M+CH_3CN+Na]: 368.0932; Found: 368.0936 [M+CH_3CN+Na].

Preparation of Oxetanes 19 and 20 by Suzuki Cross-coupling of Oxetanes 1g and 1f

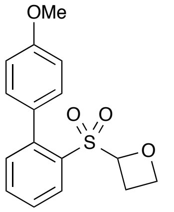


Conditions related to those reported by Buchwald were employed, using the S-Phos ligand.[8]



2-[3-(4-Methoxyphenyl)benzenesulfonyl]oxetane (19)

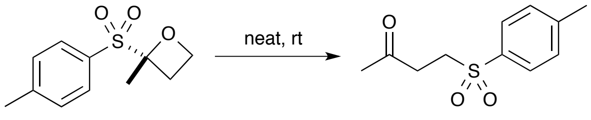
A flask was charged with $Pd(OAc)_2$ (2 mg, 0.01 mmol), S-Phos (9 mg, 0.021 mmol), K_2CO_3 (58 mg, 0.42 mmol), 4-methoxyphenylboronic acid (41 mg, 0.28 mmol) and 2-(3-chlorobenzenesulfonyl)oxetane **1g** (50 mg, 0.21 mmol) then flushed with Ar. The mixture was dissolved in dioxane:water (4:1, 1.9 mL) and heated to 65 ºC for 20 h. The crude mixture was filtered through celite and the solvent removed under reduced pressure. The residue was partitioned between EtOAc (20 mL) and H_2O (10 mL). The aqueous layer was extracted with EtOAc (2 × 15 mL) and the combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded oxetane **19** (71 mg, 95%) as a white solid; m.p. 67–68 ºC. R_f = 0.24 (20% EtOAc/hexane). IR (film)/cm^{-1} 2966, 2898, 1607, 1518, 1470, 1431, 1304, 1256, 1184, 1148, 1020, 983, 904, 833, 794, 771, 699. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.13 (1 H, m, Ar-H), 7.90 (1 H, ddd, *J* = 7.9, 1.7, 1.0 Hz, Ar-H), 7.86 (1 H, ddd, *J* = 7.8, 1.7, 1.0 Hz, Ar-H), 7.62 (1 H, dd, *J* = 7.9, 7.7 Hz, Ar-H), 7.56 (2 H, d, *J* = 8.9 Hz, 2 × Ar-H), 7.01 (2 H, d, *J* = 8.9 Hz, 2 × Ar-H), 5.43 (1 H, dd, *J* = 6.8, 6.6 Hz, OCHS), 4.86–4.79 (1 H, m, OC*H*H), 4.70–4.64 (1 H, m, OCH*H*), 3.87 (3 H, s, OCH_3), 3.18–3.11 (2 H, m, OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (C_q), 142.2 (C_q), 135.9 (C_q), 132.3 (Ar-C), 131.4 (C_q), 129.6 (Ar-C), 128.4 (2 × Ar-C), 127.4 (Ar-C + Ar-C), 114.5 (2 × Ar-C), 94.1 (SCHO), 71.5 (OCH_2), 55.4 (OCH_3), 22.4 (OCH_2CH_2). HRMS (ES) *m/z* Calculated $C_{18}H_{19}NNaO_4S$ [M+CH_3CN+Na]: 368.0932; Found: 368.0748 [M+CH_3CN+Na].



2-[2-(4-Methoxyphenyl)benzenesulfonyl]oxetane (20)

A flask was charged with $Pd(OAc)_2$ (2 mg, 0.01 mmol), S-Phos (9 mg, 0.021 mmol), K_2CO_3 (58 mg, 0.42 mmol), 4-methoxyphenylboronic acid (41 mg, 0.28 mmol) and 2-((2-chlorophenyl)sulfonyl) oxetane **1f** (53 mg, 0.22 mmol) then flushed with Ar. The mixture was dissolved in dioxane:water (4:1, 1.9 mL) and heated to 65 ºC for 20 h. The crude mixture was filtered through celite and the solvent removed under reduced pressure. The residue was partitioned between EtOAc (20 mL) and H_2O (10 mL). The aqueous layer was extracted with EtOAc (2 × 15 mL) and the combined organic layers were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (10% EtOAc/hexane) afforded oxetane **20** (24 mg, 34%) as a white solid; m.p. 109–110 ºC. R_f = 0.13 (10% EtOAc/hexane). IR (film)/cm^{-1} 2968, 1609, 1516, 1465, 1442, 1309, 1244, 1147, 982, 906, 834, 755, 693. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (1 H, dd, *J* = 7.9, 1.4 Hz, Ar-H), 7.63 (1 H, ddd, *J* = 8.9, 7.4, 1.4 Hz, Ar-H), 7.55 (1 H, ddd, *J* = 8.9, 7.7, 1.4 Hz, Ar-H), 7.38–7.32 (3 H, m, 3 × Ar-H), 6.96 (2 H, d, *J* = 8.9 Hz, 2 × Ar-H), 4.86 (1 H, dd, *J* = 8.2, 5.0 Hz, OCHS), 4.85–4.79 (1 H, m, OC*H*H), 4.54 (1 H, dt, *J* = 8.7, 5.5 Hz, OCH*H*), 3.88 (3 H, s, OCH_3), 3.10–3.00 (1 H, m, OCH_2C*H*H), 2.94–2.83 (1 H, m, OCH_2CH*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5 (C_q), 142.4 (C_q), 134.7 (C_q), 133.4 (Ar-C), 132.9 (Ar-C), 131.2 (2 × Ar-C), 130.8 (Ar-C), 130.6 (C_q), 127.7 (Ar-C), 113.1 (2 × Ar-C), 93.0 (SCHO), 71.8 (OCH_2), 55.2 (OCH_3), 21.7 (OCH_2CH_2). HRMS (ES) *m/z* Calculated $C_{18}H_{19}NNaO_4S$ [M+CH_3CN+Na]: 368.0932; Found: 368.0948 [M+CH_3CN+Na].

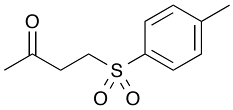
Rearrangement of alkylated oxetane 8 when stored at room temperature



8

21

Alkylated oxetane **8** was left to stand at room temperature for 24 h. Analysis of the rearranged product showed the formation of β-sulfonyl ketone **21** exclusively.

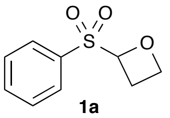


4-(4-Methylbenzenesulfonyl)butan-2-one (21)

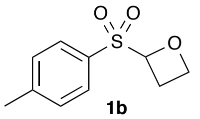
Oxetane **8** was left to stand at room temperature for 24 h affording β-sulfonyl ketone **21** in a quantitative yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (2 H, d, *J* = 8.4 Hz, 2 × Ar-H), 7.38 (2 H, d, *J* = 8.4 Hz, 2 × Ar-H), 3.36 (2 H, dd, *J* = 7.8, 7.1 Hz, SO_2CH_2), 2.93 (2 H, dd, *J* = 7.8, 7.1 Hz, $COCH_2$), 2.47 (3 H, s, Ar-CH_3), 2.19 (3 H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7 (C=O), 144.9 (C_q), 136.1 (C_q), 130.0 (2 × Ar-C), 128.0 (2 × Ar-C), 50.7 (SO_2CH_2), 36.0 ($COCH_2$), 29.8 (CH_3), 21.6 (Ar-CH_3). The observed data (^{1}H) is consistent with that reported in the literature.[9]

Studies into the stability of 2-sulfonyl oxetanes 1a-d, 1h, 1k, 13 and 16

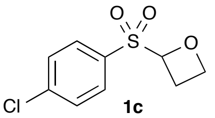
The solution stability of the compounds shown below was assessed by incubating the compound (10 μM) at pH 1, 4, 6, 8 and 10 in buffers containing 5% v/v 2-methoxyethanol at 70 ºC for 15 hours. Analysis was performed at regular intervals by LC-UV-MS to obtain half-lives at 70 ºC. Half-lives at 25 ºC were then predicted using a reduction in rate of a factor of 2 per 10 degree reduction in temperature which was regarded as the worst case scenario.



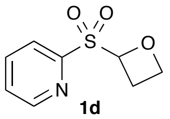
1a



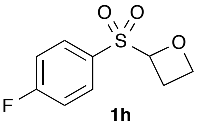
1b



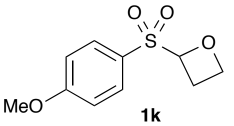
1c



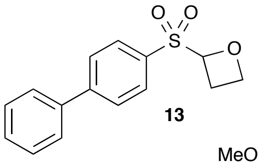
1d



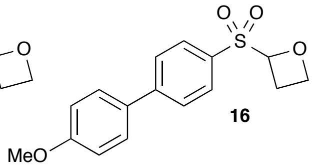
1h



1k



13



16

The measured half-lives at 70 ºC and predicted half-lives at 25 ºC are reported in the tables below.

2-(Phenylsulfonyl)oxetane (**1a)**

pH	Measured half-life at 70 ºC/days	Predicted half-life at 25 ºC/days
1	0.18	4.0
4	0.22	5.0
6	0.23	5.3
8	0.23	5.3
10	0.16	3.7

2-(4-Methylbenzenesulfonyl)oxetane (**1b**)

pH	Measured half-life at 70 ºC/days	Predicted half-life at 25 ºC/days
1	0.31	10.2
4	0.45	9.9
6	0.44	9.9
8	0.40	9.1
10	0.41	9.2

2-(4-Chlorobenzenesulfonyl)oxetane (**1c**)

pH	Measured half-life at 70 ºC/days	Predicted half-life at 25 ºC/days
1	0.09	2.0
4	0.12	2.7
6	0.11	2.4
8	0.10	2.2
10	0.16	3.5

2-(Oxetane-2-sulfonyl)pyridine (**1d**)

No results were possible for **1d** as the compound was not detected by UV or mass spec.

2-((4-Fluorophenyl)sulfonyl)oxetane **(1h)**

pH	Measured half-life at 70 °C/days	Predicted half-life at 25 °C/days
1	0.09	2.0
4	0.12	2.7
6	0.11	2.4
8	0.10	2.2
10	0.16	3.5

2-((4-Methoxyphenyl)sulfonyl)oxetane **(1k)**

pH	Measured half-life at 70 °C/days	Predicted half-life at 25 °C/days
1	0.28	6.3
4	0.50	11.2
6	0.51	11.5
8	0.49	11.1
10	0.44	10.0

2-([1,1'-Biphenyl]-4-ylsulfonyl)oxetane **(13)**

pH	Measured half-life at 70 °C/days	Predicted half-life at 25 °C/days
1	0.17	3.9
4	0.21	4.7
6	0.21	4.7
8	0.20	4.6
10	0.20	4.6

2-([4'-Methoxybiphenyl]-4-ylsulfonyl)oxetane **(16)**

pH	Measured half-life at 70 °C/days	Predicted half-life at 25 °C/days
1	0.20	4.6
4	0.25	5.7
6	0.25	5.7
8	0.31	7.1
10	0.23	5.3

Although the mass spec data is not conclusive for every compound as to what the sulfonyl oxetane is degrading to; it is believed that the oxetane is being hydrolysed to the parent sulfonic acid (as shown below for **1c**) as the product gives rise to a [M-H]$^-$ signal 41 mass units less than the parent:

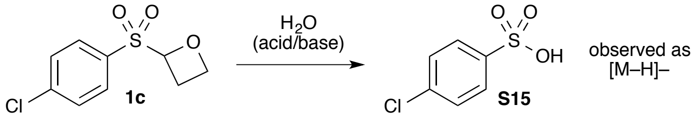
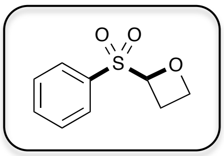


Figure S1: Hydrolysis of oxetane **1c** to the sulfonic acid **S15**.

Conformational Analysis of 2-(Phenylsulfonyl)oxetane 1a

The conformational profiles of a selected variety of 2-sulfonyl oxetane fragments were investigated using computational methods. The dihedral angle around the oxetane-C-S bond was varied in 10 degree increments between 0 and 360 degrees. A relaxed coordinate scan was performed using the Gaussian 09 suite of programmes; DFT B3LYP/6-31G9(d,p) with implicit solvation in water. The data produced is shown below for 2-(phenylsulfonyl)oxetane **1a**. See full text for discussion.



Dihedral Angle	E	ΔE	ΔE kcal/mol
0	-972.754568	0.00469	**2.94301721**
10	-972.754568	0.00469	**2.94301721**
20	-972.7557	0.003558	**2.232677022**
30	-972.756845	0.002413	**1.514179217**
40	-972.758057	0.001201	**0.753638309**
50	-972.758939	0.000319	**0.200175371**
60	-972.759258	0	**0**
70	-972.759012	0.000246	**0.154367214**
80	-972.758215	0.001043	**0.654491887**
90	-972.757211	0.002047	**1.284510923**
100	-972.756156	0.003102	**1.946532918**
110	-972.755245	0.004013	**2.518193617**
120	-972.754657	0.004601	**2.887168909**
130	-972.754667	0.004591	**2.880893819**
140	-972.75514	0.004118	**2.584082062**
150	-972.755989	0.003269	**2.051326921**
160	-972.756848	0.00241	**1.51229669**
170	-972.757443	0.001815	**1.138928835**
180	-972.757654	0.001604	**1.006524436**
190	-972.757387	0.001871	**1.174069339**
200	-972.756656	0.002602	**1.632778418**
210	-972.75548	0.003778	**2.370729002**
220	-972.754212	0.005046	**3.166410414**
230	-972.75328	0.005978	**3.751248802**
240	-972.75289	0.006368	**3.995977312**
250	-972.75323	0.006028	**3.782624252**
260	-972.754014	0.005244	**3.290657196**
270	-972.755174	0.004084	**2.562746756**
280	-972.75651	0.002748	**1.724394732**
290	-972.757712	0.001546	**0.970128914**
300	-972.758355	0.000903	**0.566640627**
310	-972.758284	0.000974	**0.611193766**
320	-972.757531	0.001727	**1.083708043**
330	-972.756482	0.002776	**1.741964984**
340	-972.755445	0.003813	**2.392691817**
350	-972.754775	0.004483	**2.813122847**
360	-972.7545682	0.00468977	**2.942872883**

Conformational Analysis of 2-(Oxetan-2-ylsulfonyl)pyridine 1d

The same analysis was performed on 2-(oxetan-2-ylsulfonyl)pyridine. There were two possible low energy orientations of the pyridyl group, A and B, figure S2. Analysis was performed on both possible conformations.

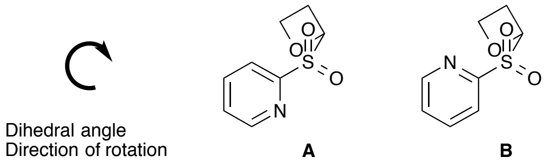
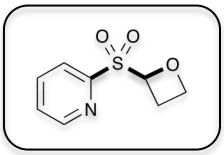


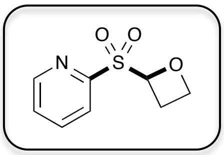
Figure S2: Two conformations of the pyridyl group at dihedral angle = 0.

Conformation **A**



Dihedral Angle	E	ΔE	ΔE kcal/mol
0	-988.788739	0.005239	**3.287519651**
10	-988.789386	0.004592	**2.881521328**
20	-988.790482	0.003496	**2.193771464**
30	-988.791742	0.002236	**1.403110124**
40	-988.792943	0.001035	**0.649471815**
50	-988.793736	0.000242	**0.151857178**
60	-988.793978	0	**0**
70	-988.793753	0.000225	**0.141189525**
80	-988.793206	0.000772	**0.484436948**
90	-988.792405	0.001573	**0.987071657**
100	-988.791484	0.002494	**1.565007446**
110	-988.790557	0.003421	**2.146708289**
120	-988.789848	0.00413	**2.59161217**
130	-988.789646	0.004332	**2.718368988**
140	-988.789937	0.004041	**2.535763869**
150	-988.790607	0.003371	**2.115332839**
160	-988.79135	0.002628	**1.649093652**
170	-988.791843	0.002135	**1.339731715**
180	-988.791965	0.002013	**1.263175617**
190	-988.791692	0.002286	**1.434485574**
200	-988.790918	0.00306	**1.92017754**
210	-988.789674	0.004304	**2.700798736**
220	-988.788381	0.005597	**3.512167873**
230	-988.787533	0.006445	**4.044295505**
240	-988.787326	0.006652	**4.174189868**
250	-988.787888	0.00609	**3.82152981**
260	-988.788887	0.005091	**3.194648319**
270	-988.789992	0.003986	**2.501250874**
280	-988.790892	0.003086	**1.936492774**
290	-988.791318	0.00266	**1.66917394**
300	-988.791244	0.002734	**1.715609606**
310	-988.790864	0.003114	**1.954063026**
320	-988.790124	0.003854	**2.418419686**
330	-988.789395	0.004583	**2.875873747**
340	-988.788831	0.005147	**3.229788823**
350	-988.788572	0.005406	**3.392313654**
360	-988.7887392	0.00523877	**3.287375324**

Conformation **B**



Dihedral Angle	E	ΔE	ΔE kcal/mol
0	-988.789444	0.003058	**1.918922522**
10	-988.789444	0.003058	**1.918922522**
20	-988.789416	0.003086	**1.936492774**
30	-988.790042	0.00246	**1.54367214**
40	-988.790891	0.001611	**1.010916999**
50	-988.791643	0.000859	**0.539030231**
60	-988.791643	0.000859	**0.539030231**
70	-988.792142	0.00036	**0.22590324**
80	-988.791934	0.000568	**0.356425112**
90	-988.7915	0.001002	**0.628764018**
100	-988.790891	0.001611	**1.010916999**
110	-988.790228	0.002274	**1.426955466**
120	-988.789824	0.002678	**1.680469102**
130	-988.789871	0.002631	**1.650976179**
140	-988.790359	0.002143	**1.344751787**
150	-988.791104	0.001398	**0.877257582**
160	-988.791834	0.000668	**0.419176012**
170	-988.792334	0.000168	**0.105421512**
180	-988.792455	0.000168	**0.105421512**
190	-988.79212	0.000382	**0.239708438**
200	-988.791414	0.001088	**0.682729792**
210	-988.790312	0.00219	**1.37424471**
220	-988.789046	0.003456	**2.168671104**
230	-988.787909	0.004593	**2.882148837**
240	-988.787282	0.00522	**3.27559698**
250	-988.787355	0.005147	**3.229788823**
260	-988.788026	0.004476	**2.808730284**
270	-988.78912	0.003382	**2.122235438**
280	-988.790283	0.002219	**1.392442471**
290	-988.791379	0.001123	**0.704692607**
300	-988.792164	0.000338	**0.212098042**
310	-988.792502	0	**0**
320	-988.792264	0.000238	**0.149347142**
330	-988.791682	0.00082	**0.51455738**
340	-988.790797	0.001705	**1.069902845**
350	-988.789975	0.002527	**1.585715243**
360	-988.7894445	0.0030575	**1.918608768**

Conformational Analysis of 2-(2-Methylbenzenesulfonyl)oxetane 1e

There were two possible low energy orientations of the tolyl group; both orientations were investigated; figure S3.

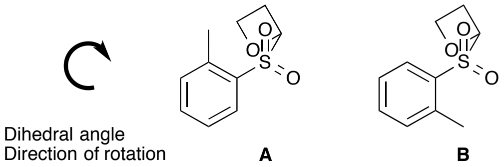
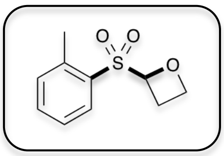


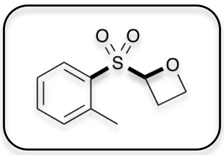
Figure S3: Orientations of the tolyl ring at dihedral angle = 0.

Conformation **A**

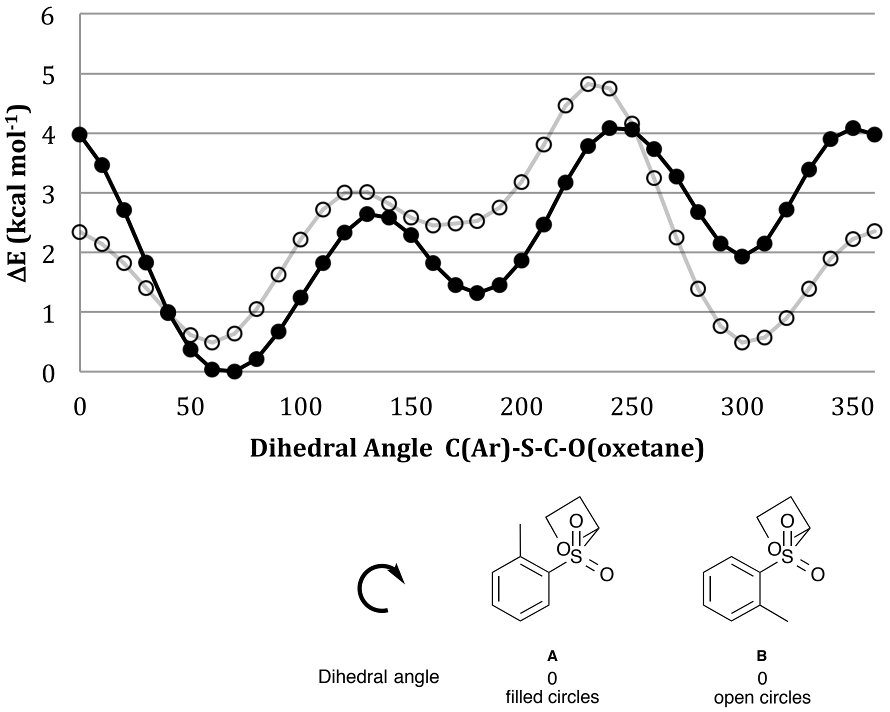


Dihedral Angle	E	ΔE	ΔE kcal/mol
0	-1012.07044	0.00633	**3.97213197**
10	-1012.07125	0.00552	**3.46384968**
20	-1012.07245	0.00432	**2.71083888**
30	-1012.07385	0.00292	**1.83232628**
40	-1012.07517	0.0016	**1.0040144**
50	-1012.07619	0.00058	**0.36395522**
60	-1012.07672	5E-05	**0.03137545**
70	-1012.07677	0	**0**
80	-1012.07644	0.00033	**0.20707797**
90	-1012.07571	0.00106	**0.66515954**
100	-1012.0748	0.00197	**1.23619273**
110	-1012.07388	0.00289	**1.81350101**
120	-1012.07305	0.00372	**2.33433348**
130	-1012.07255	0.00422	**2.64808798**
140	-1012.07266	0.00411	**2.57906199**
150	-1012.07312	0.00365	**2.29040785**
160	-1012.07388	0.00289	**1.81350101**
170	-1012.07446	0.00231	**1.44954579**
180	-1012.07468	0.00209	**1.31149381**
190	-1012.07445	0.00232	**1.45582088**
200	-1012.07381	0.00296	**1.85742664**
210	-1012.07284	0.00393	**2.46611037**
220	-1012.07171	0.00506	**3.17519554**
230	-1012.07075	0.00602	**3.77760418**
240	-1012.07027	0.0065	**4.0788085**
250	-1012.0703	0.00647	**4.05998323**
260	-1012.07083	0.00594	**3.72740346**
270	-1012.07157	0.0052	**3.2630468**
280	-1012.07251	0.00426	**2.67318834**
290	-1012.07335	0.00342	**2.14608078**
300	-1012.0737	0.00307	**1.92645263**
310	-1012.07335	0.00342	**2.14608078**
320	-1012.07244	0.00433	**2.71711397**
330	-1012.07138	0.00539	**3.38227351**
340	-1012.07056	0.00621	**3.89683089**
350	-1012.07026	0.00651	**4.08508359**
360	-1012.070436	0.00633441	**3.974899285**

Conformation **B**



Dihedral Angle	E	ΔE	ΔE kcal/mol
0	-1012.07304	0.00296	**1.85742664**
10	-1012.07336	0.00264	**1.65662376**
20	-1012.07387	0.00213	**1.33659417**
30	-1012.07454	0.00146	**0.91616314**
40	-1012.0752	0.0008	**0.5020072**
50	-1012.07579	0.00021	**0.13177689**
60	-1012.076	0	**0**
70	-1012.07576	0.00024	**0.15060216**
80	-1012.0751	0.0009	**0.5647581**
90	-1012.07418	0.00182	**1.14206638**
100	-1012.07324	0.00276	**1.73192484**
110	-1012.07244	0.00356	**2.23393204**
120	-1012.07199	0.00401	**2.51631109**
130	-1012.07197	0.00403	**2.52886127**
140	-1012.07229	0.00371	**2.32805839**
150	-1012.07266	0.00334	**2.09588006**
160	-1012.07287	0.00313	**1.96410317**
170	-1012.07282	0.00318	**1.99547862**
180	-1012.07274	0.00326	**2.04567934**
190	-1012.07238	0.00362	**2.27158258**
200	-1012.0717	0.0043	**2.6982887**
210	-1012.0707	0.0053	**3.3257977**
220	-1012.06967	0.00633	**3.97213197**
230	-1012.06909	0.00691	**4.33608719**
240	-1012.06921	0.00679	**4.26078611**
250	-1012.07015	0.00585	**3.67092765**
260	-1012.0716	0.0044	**2.7610396**
270	-1012.07319	0.00281	**1.76330029**
280	-1012.07456	0.00144	**0.90361296**
290	-1012.07555	0.00045	**0.28237905**
300	-1012.07599	1E-05	**0.00627509**
310	-1012.07585	0.00015	**0.09412635**
320	-1012.07534	0.00066	**0.41415594**
330	-1012.07456	0.00144	**0.90361296**
340	-1012.07376	0.00224	**1.40562016**
350	-1012.07323	0.00277	**1.73819993**
360	-1012.07301	0.00298995	**1.876220535**



Figures S4: Graphical representation of the results from the conformational analysis of 2-(2-methylbenzenesulfonyl)oxetane **1e**.

Orientation A had a lowest energy conformation with a dihedral angle of 70 degrees whilst orientation B had a preferred conformation with a dihedral angle of 60 degrees. Orientation A had the lowest overall energy conformation, figure S5, suggesting this would be the preferred conformation. This conformation was expected to be higher in energy due to potential steric interactions, however it appears to adopt a favourable intramolecular Van der Waals interaction between the oxetane oxygen and a proton on the benzyl CH_3, therefore lowing the energy.

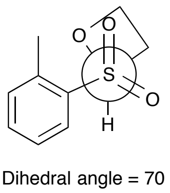
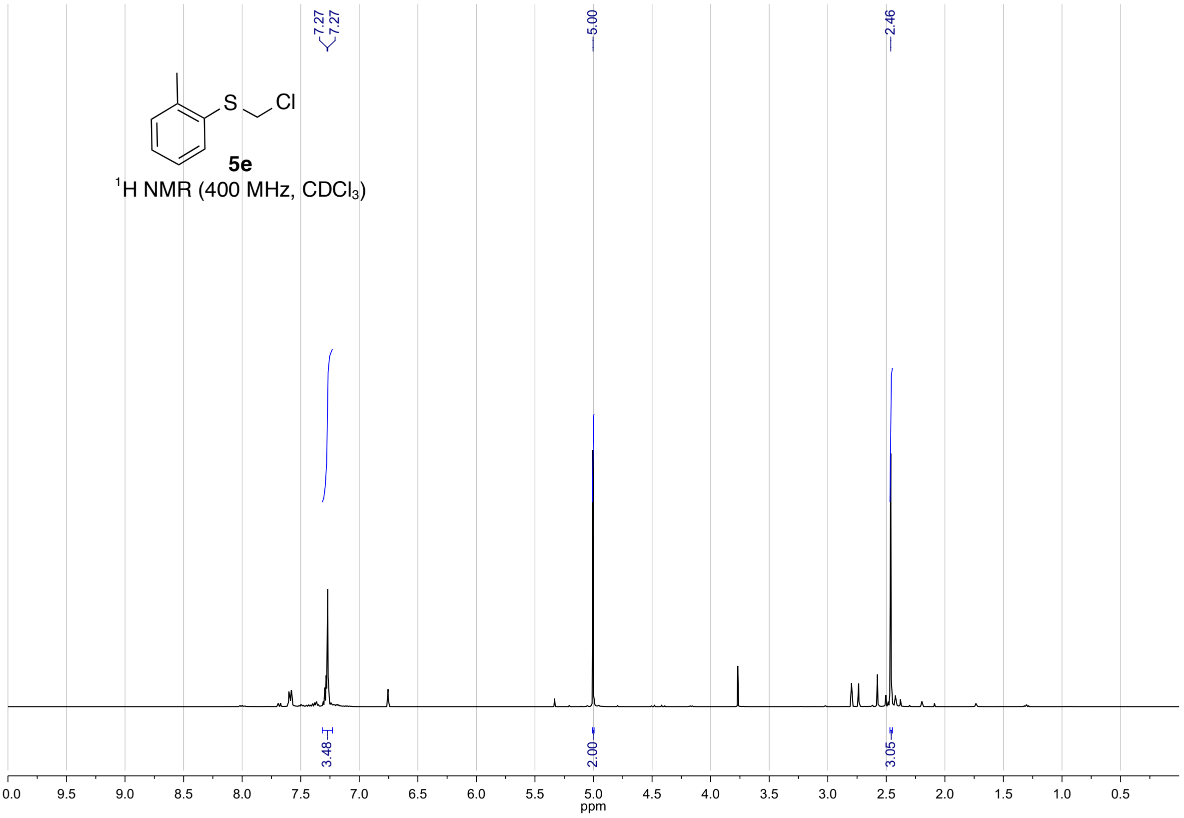


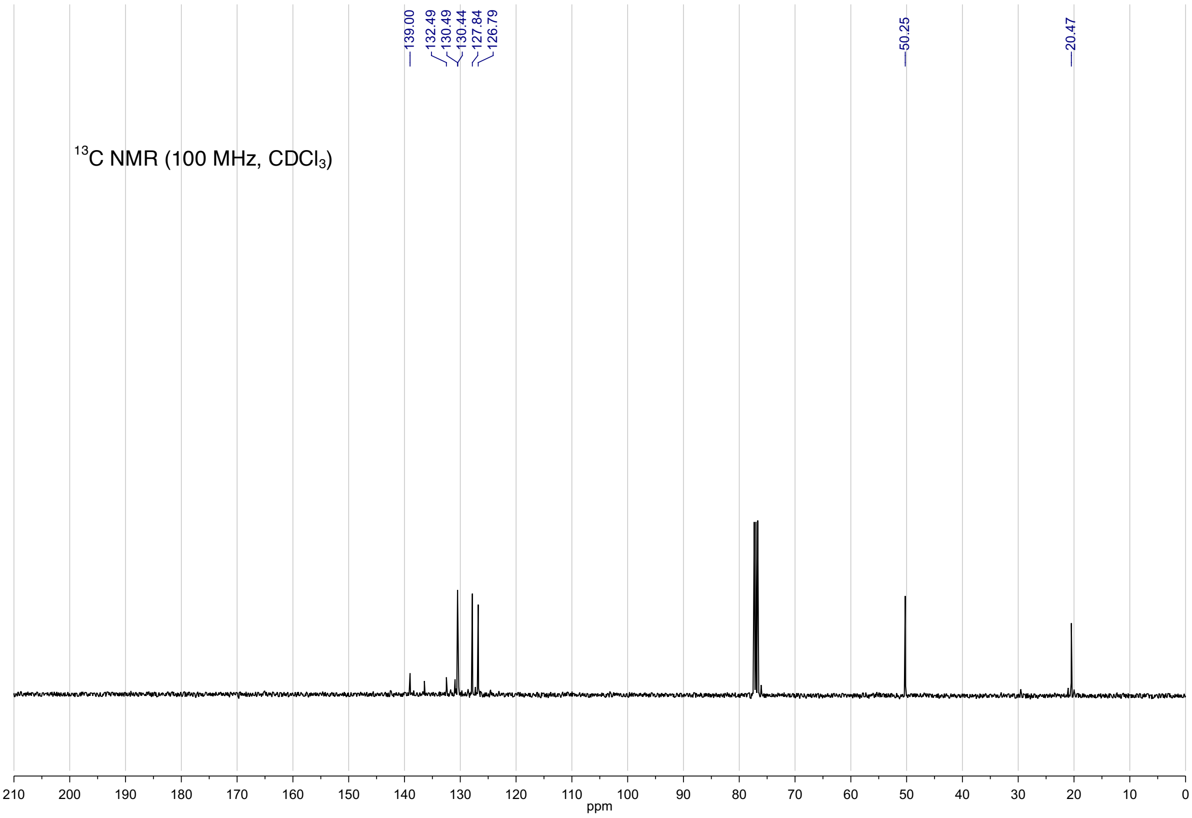
Figure S5: Lowest overall energy conformation

^{1}H and ^{13}C NMR spectra of selected compounds

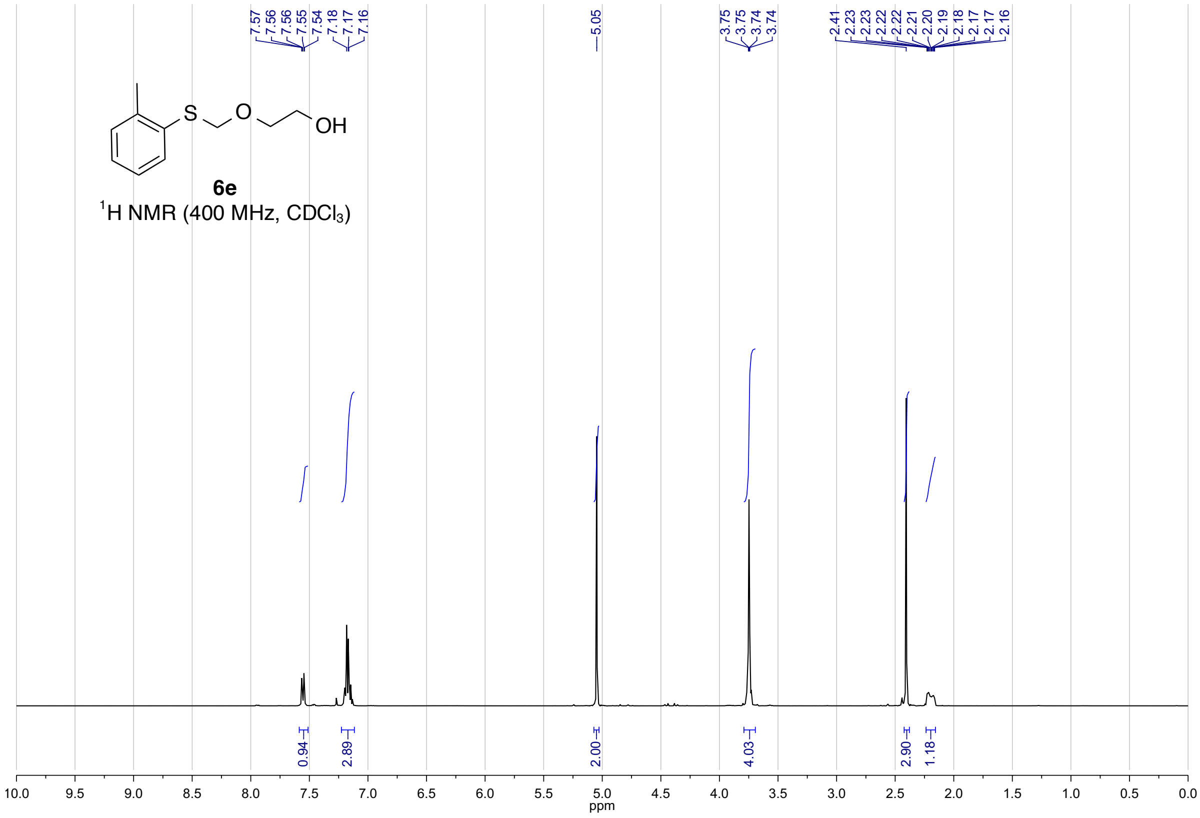


5e

^{1}H NMR (400 MHz, $CDCl_3$)

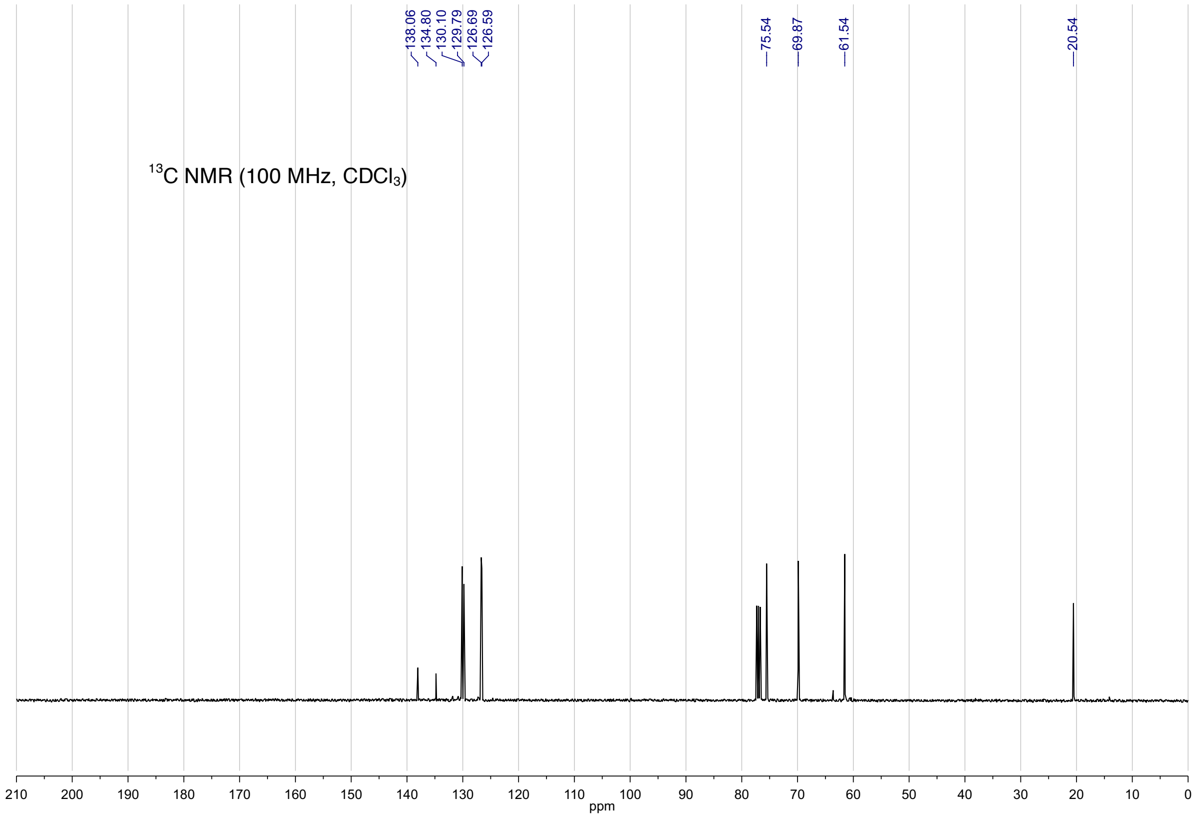


^{13}C NMR (100 MHz, $CDCl_3$)

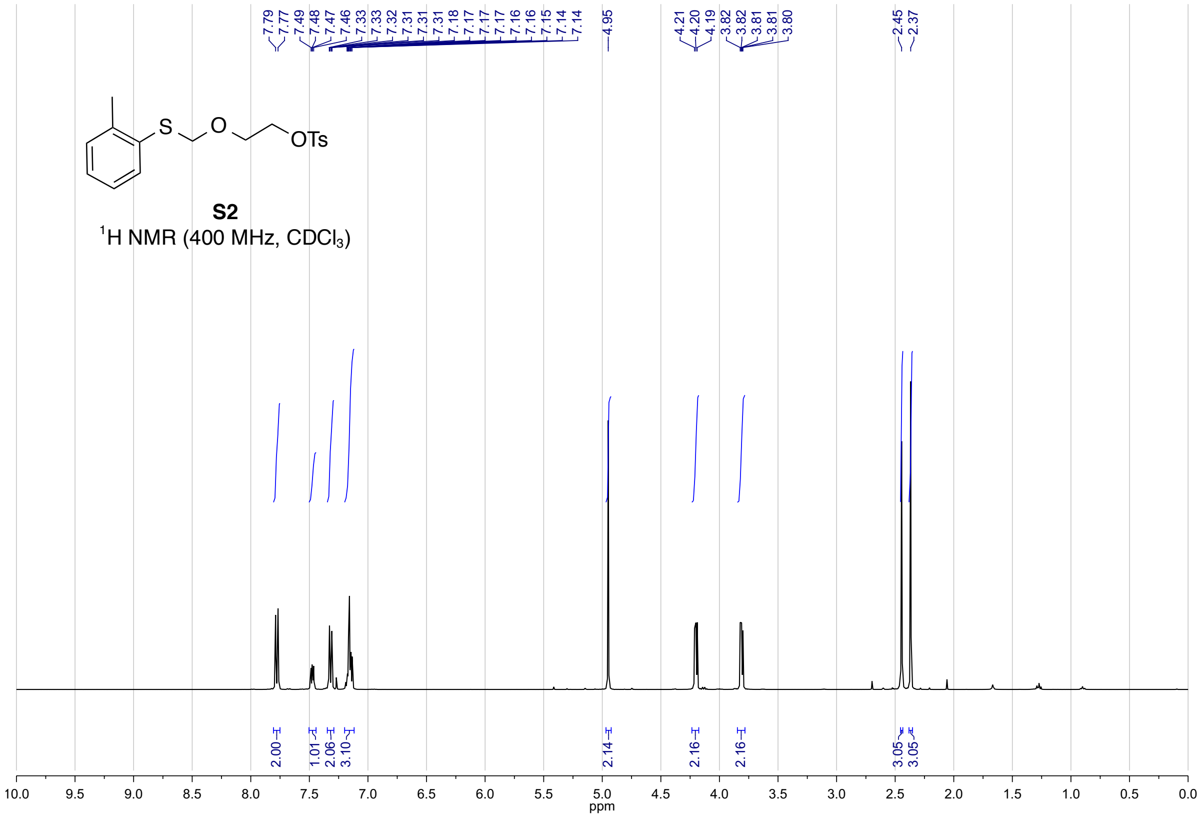


6e

^{1}H NMR (400 MHz, $CDCl_3$)

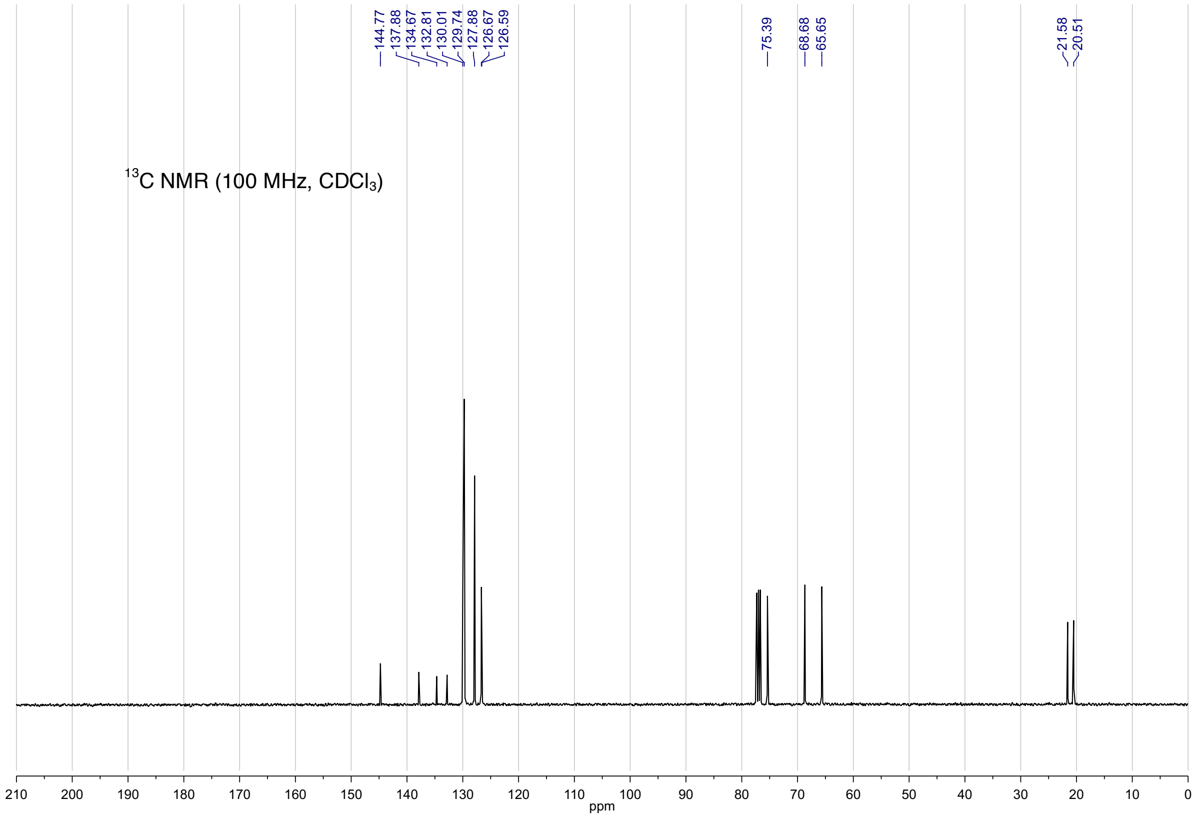


^{13}C NMR (100 MHz, $CDCl_3$)

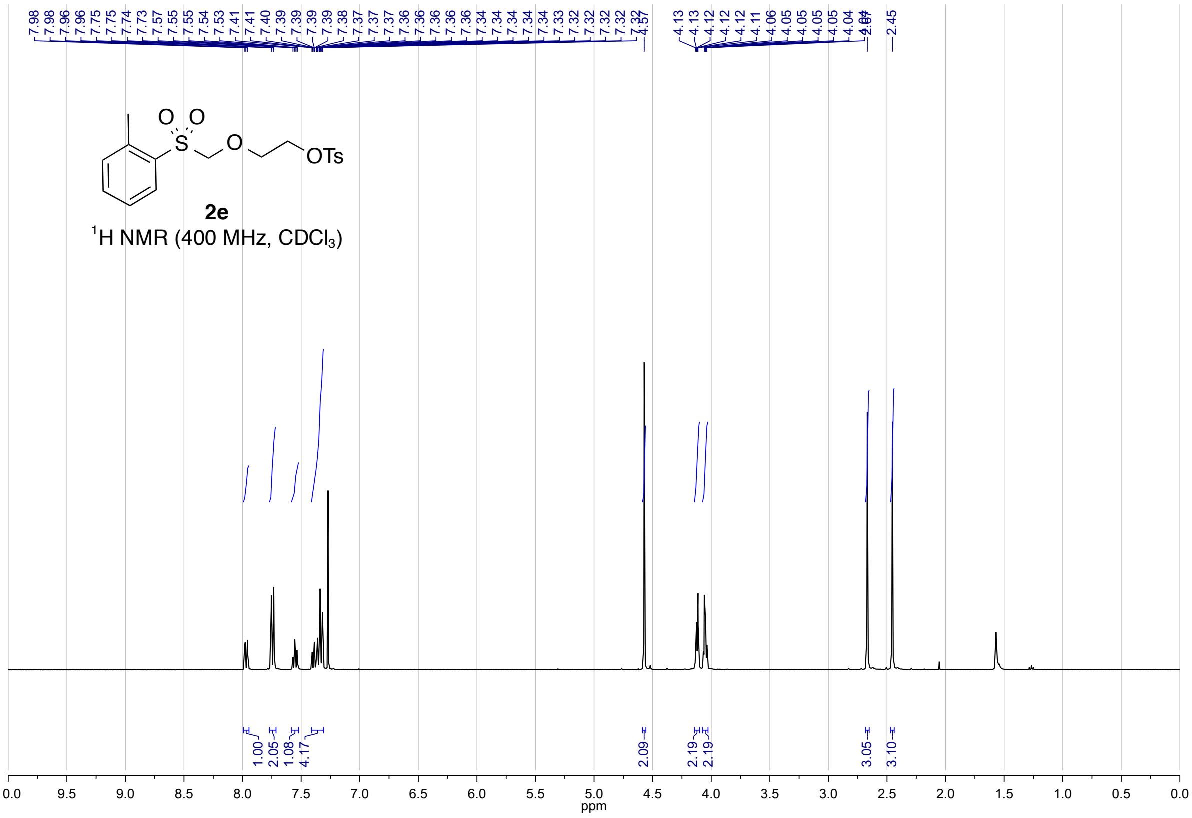


S2

^{1}H NMR (400 MHz, CDCl$_3$)



^{13}C NMR (100 MHz, CDCl$_3$)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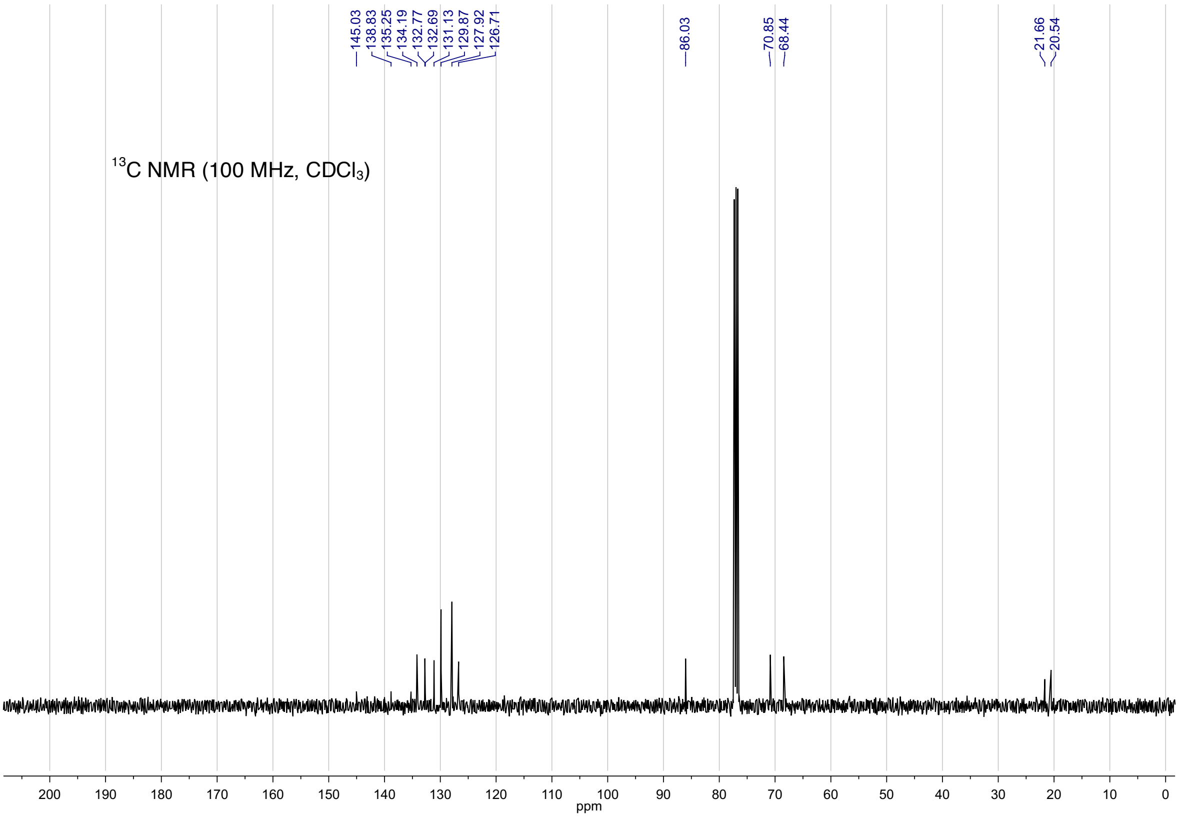
7.98
7.96
7.96
7.75
7.75
7.74
7.73
7.57
7.55
7.55
7.54
7.53
7.41
7.40
7.39
7.39
7.39
7.39
7.38
7.37
7.37
7.36
7.36
7.36
7.36
7.34
7.34
7.34
7.34
7.33
7.32
7.32
7.32
7.32
4.57
4.13
4.13
4.12
4.12
4.12
4.11
4.06
4.05
4.05
4.05
4.05
4.04
2.67
2.45
O
O
S
O
OTs
2e
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
2.05
1.08
4.17
2.09
2.19
2.19
3.05
3.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
ppm
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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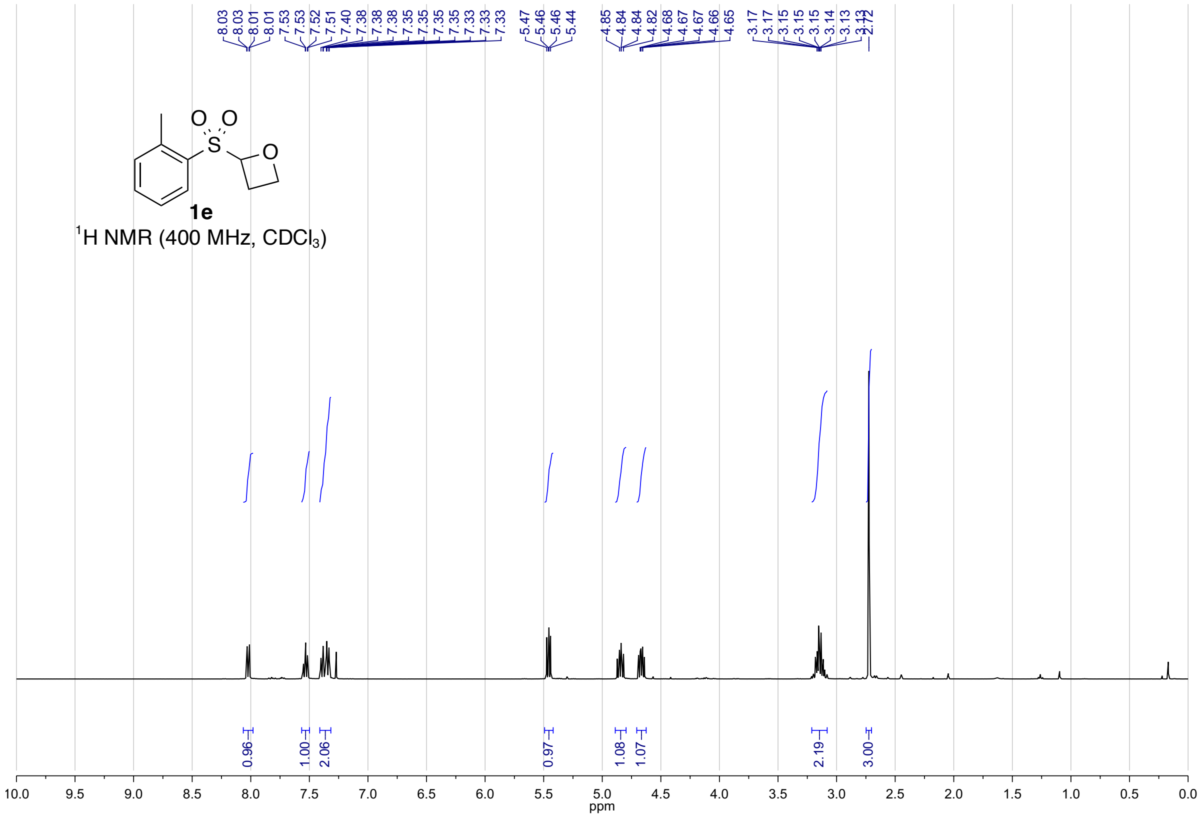
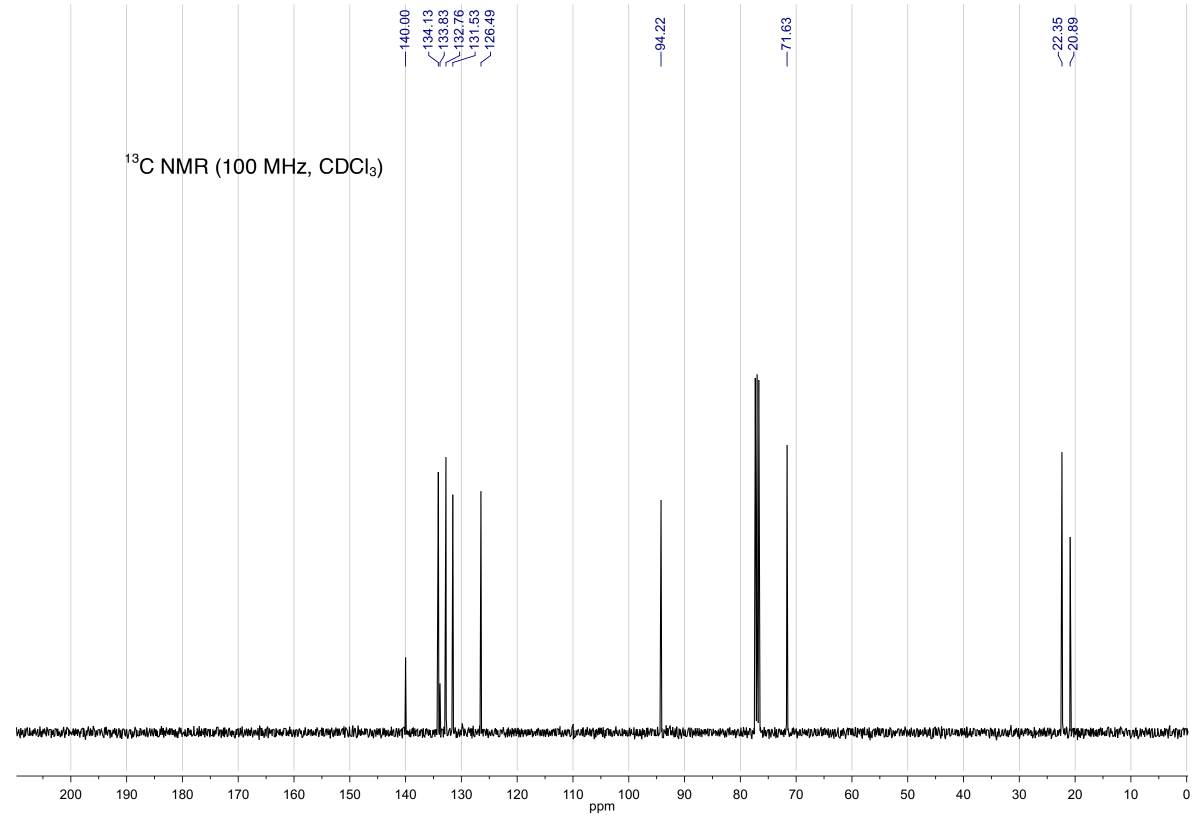
138.83
135.25
134.19
132.77
132.69
131.13
129.87
127.92
126.71
86.03
70.85
68.44
21.66
20.54
^{13}C NMR (100 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
ppm
90
80
70
60
50
40
30
20
10
0

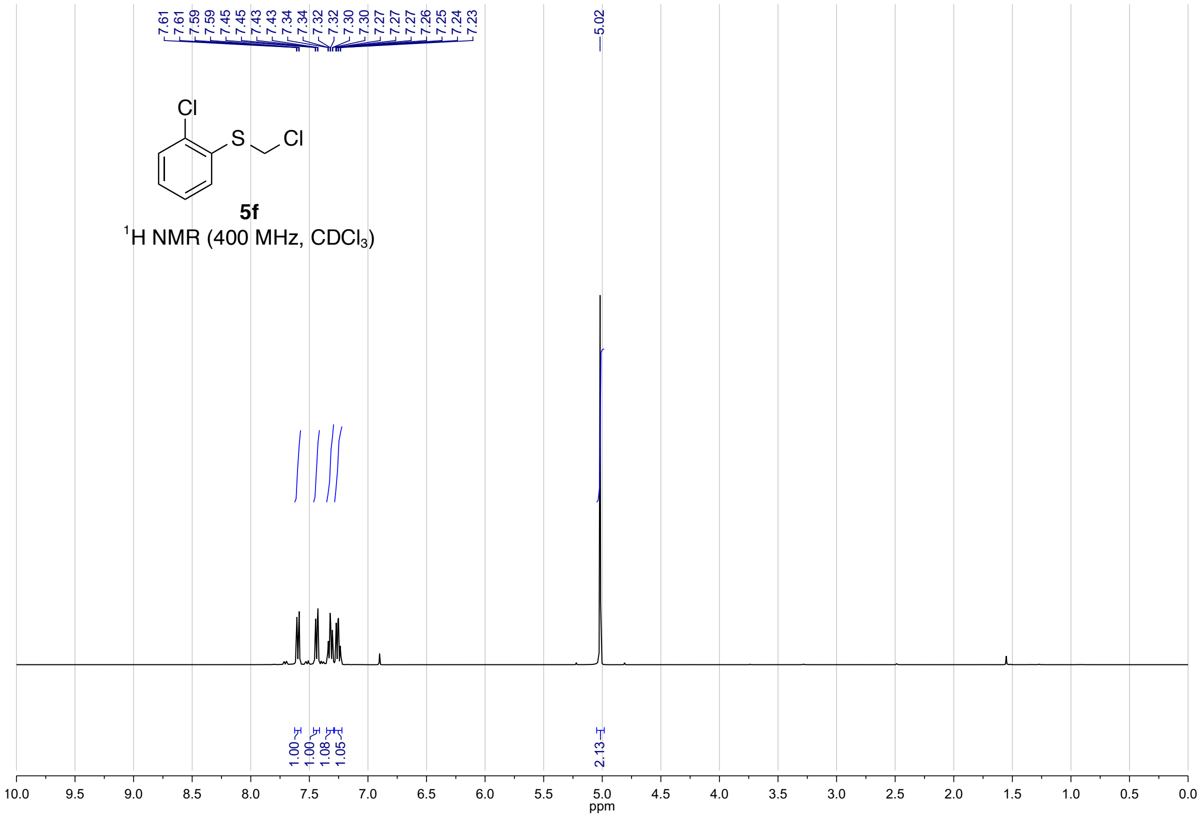


1e

^{1}H NMR (400 MHz, CDCl$_3$)



^{13}C NMR (100 MHz, CDCl$_3$)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7.61
7.59
7.59
7.45
7.45
7.43
7.43
7.34
7.34
7.32
7.32
7.30
7.30
7.27
7.27
7.27
7.26
7.25
7.24
7.23
5.02
Cl
S
Cl
5f
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.00
1.08
1.05
2.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
2.5
2.0
1.5
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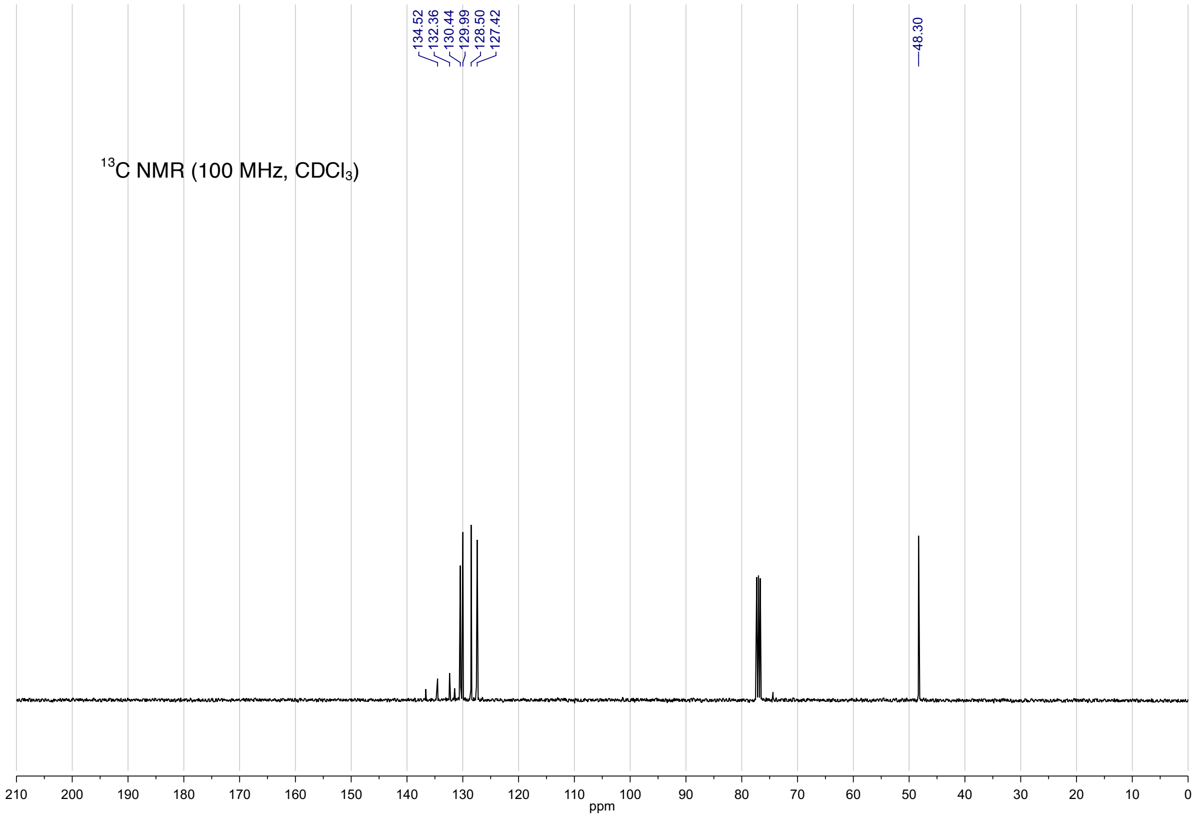
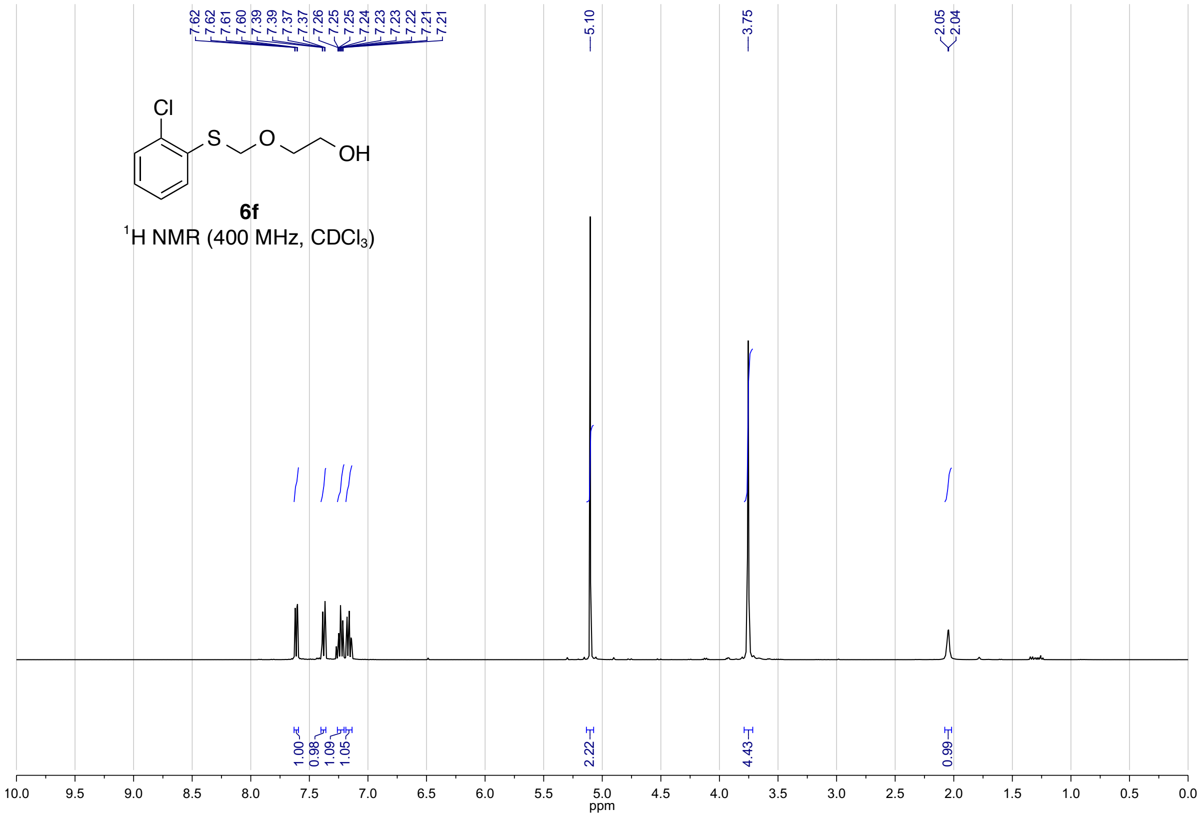
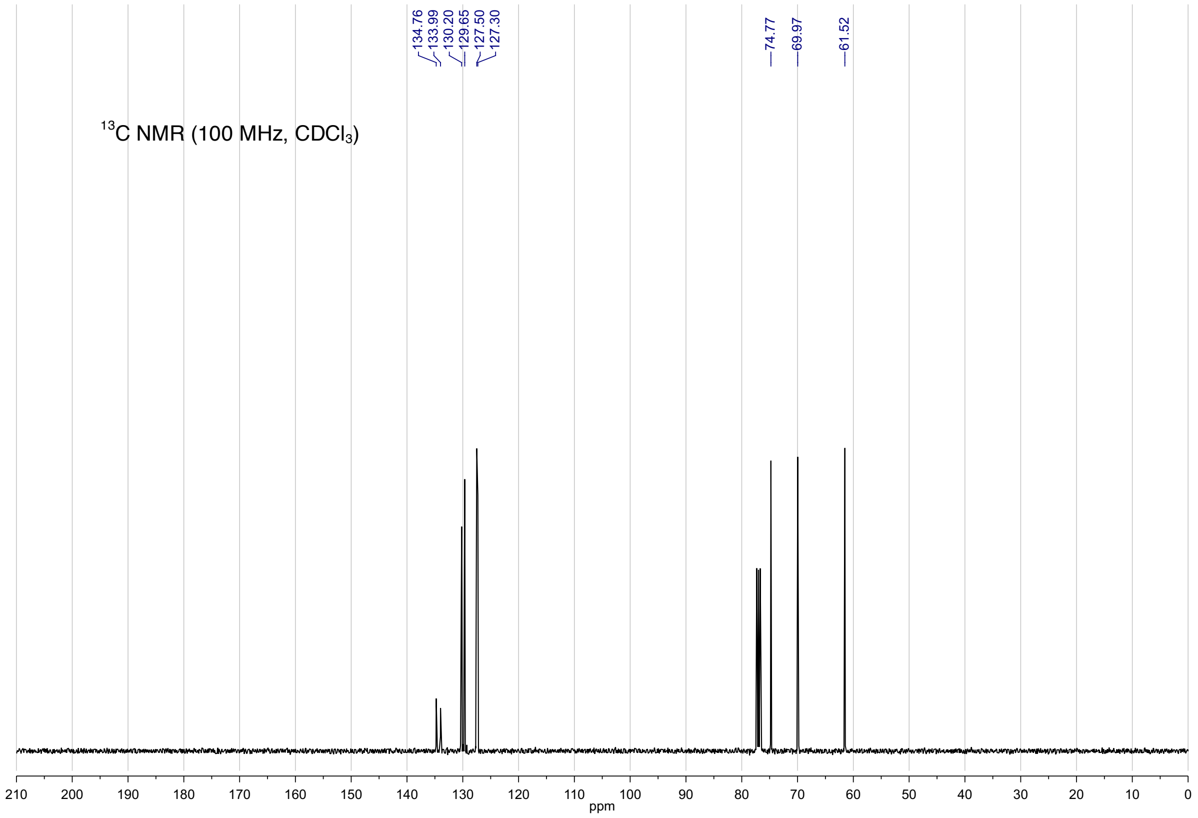
0.5
0.0
ppm


134.52
132.36
130.44
129.99
128.50
127.42
48.30
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

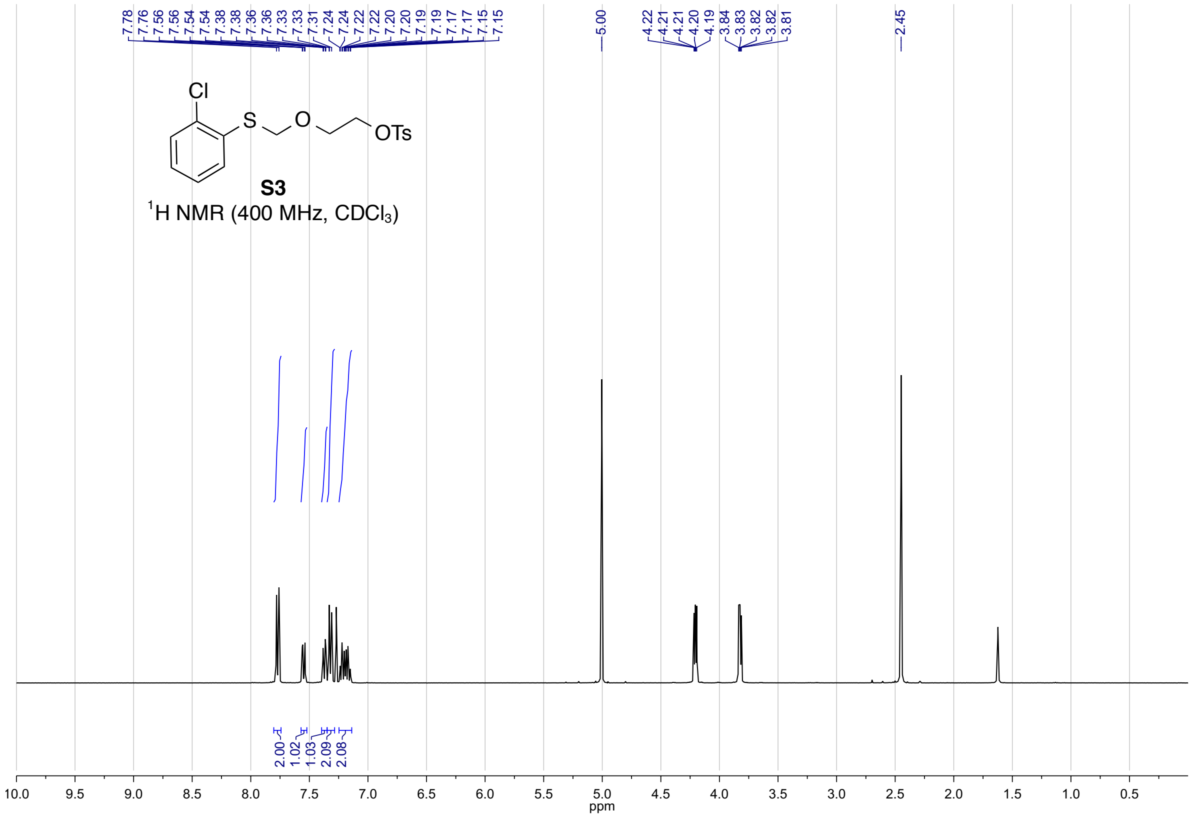


6f

^{1}H NMR (400 MHz, CDCl$_3$)



^{13}C NMR (100 MHz, CDCl$_3$)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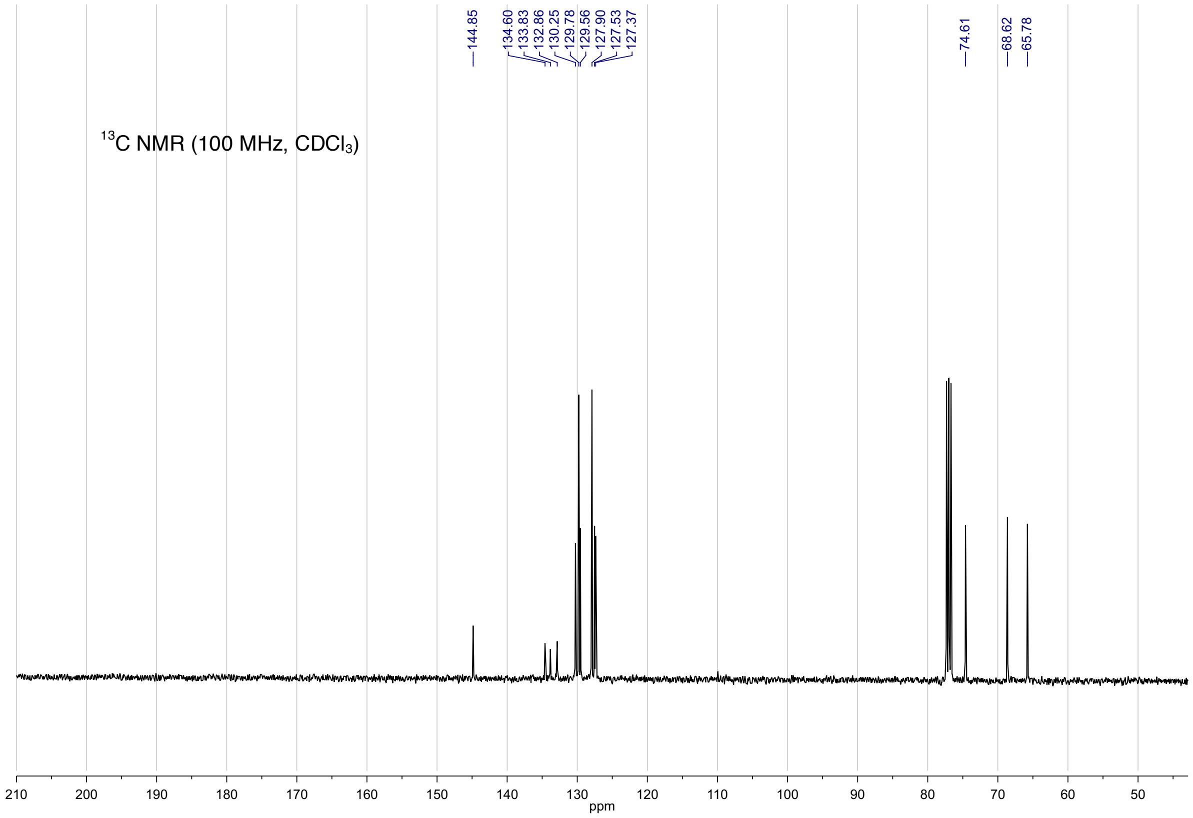
7.56
7.54
7.54
7.38
7.38
7.36
7.36
7.33
7.33
7.31
7.24
7.24
7.22
7.22
7.20
7.20
7.19
7.19
7.17
7.17
7.15
7.15
5.00
4.22
4.21
4.21
4.20
4.19
3.84
3.83
3.82
3.82
3.81
2.45
Cl
S
O
OTs
S3
¹H NMR (400 MHz, CDCl₃)
2.00
1.02
1.03
2.09
2.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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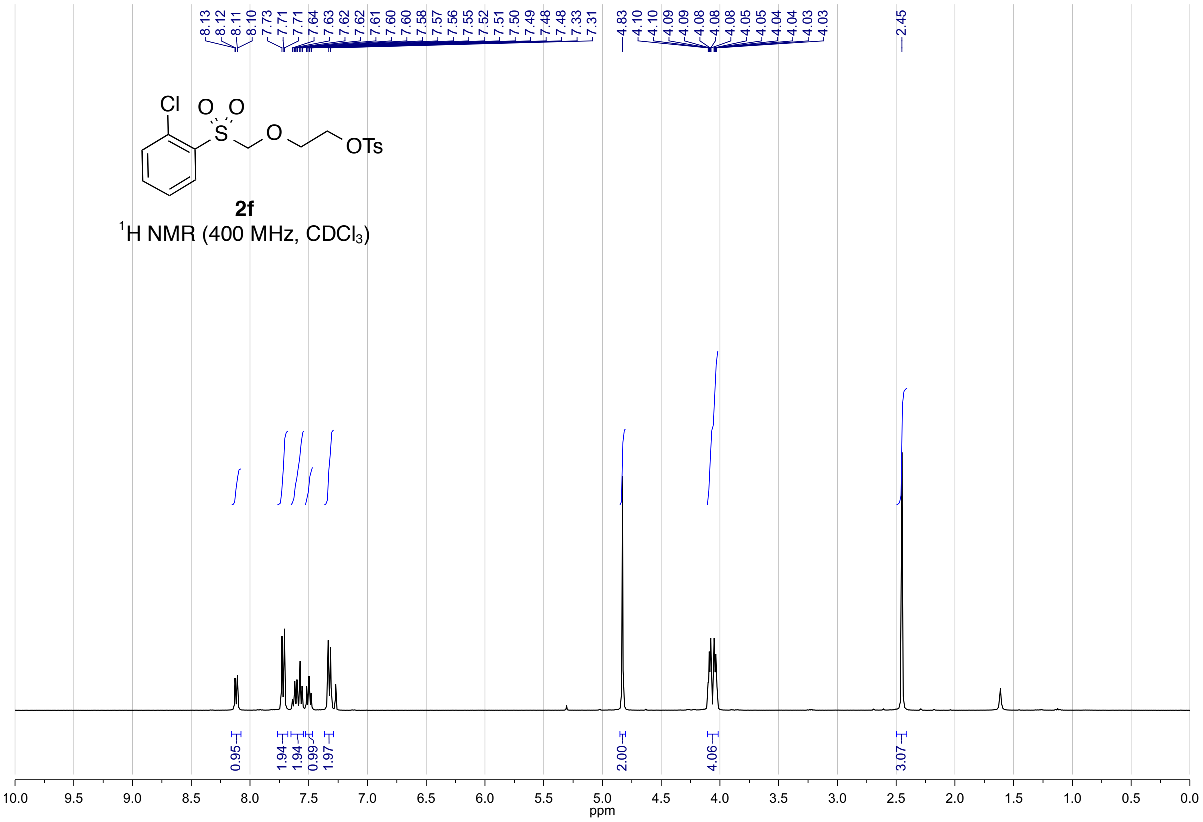
133.83
132.86
130.25
129.78
129.56
127.90
127.53
127.37
74.61
68.62
65.78
¹³C NMR (100 MHz, CDCl₃)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm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8.11
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7.73
7.71
7.71
7.64
7.63
7.62
7.62
7.61
7.60
7.60
7.58
7.57
7.56
7.55
7.52
7.51
7.50
7.49
7.48
7.48
7.33
7.31
4.83
4.10
4.10
4.09
4.09
4.08
4.08
4.08
4.05
4.05
4.04
4.04
4.03
4.03
2.45
Cl
O
O
S
O
OTs
2f
¹H NMR (400 MHz, CDCl₃)
0.95
1.94
1.94
0.99
1.97
2.00
4.06
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
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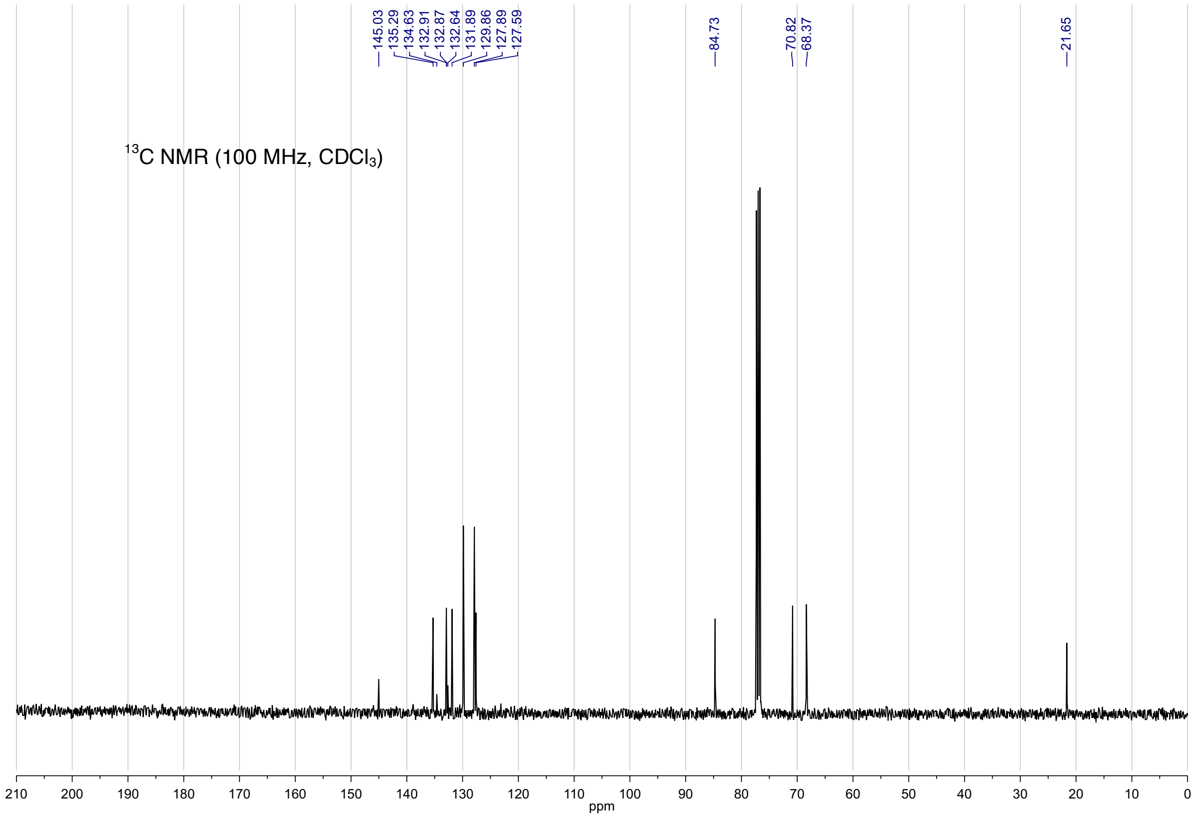
2.0
1.5
1.0
0.5
0.0
ppm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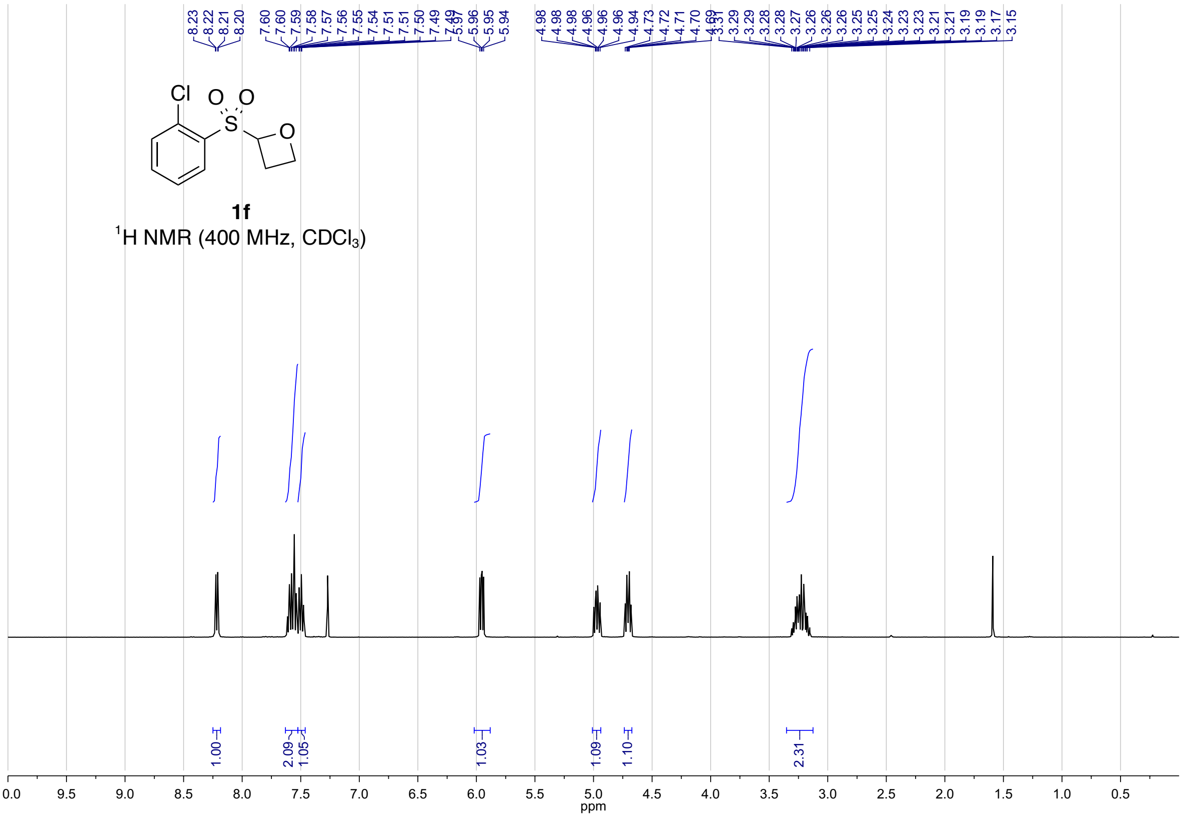
132.87
132.64
131.89
129.86
127.89
127.59
84.73
70.82
68.37
21.65
¹³C NMR (100 MHz, CDCl₃)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.60
7.59
7.58
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7.56
7.55
7.54
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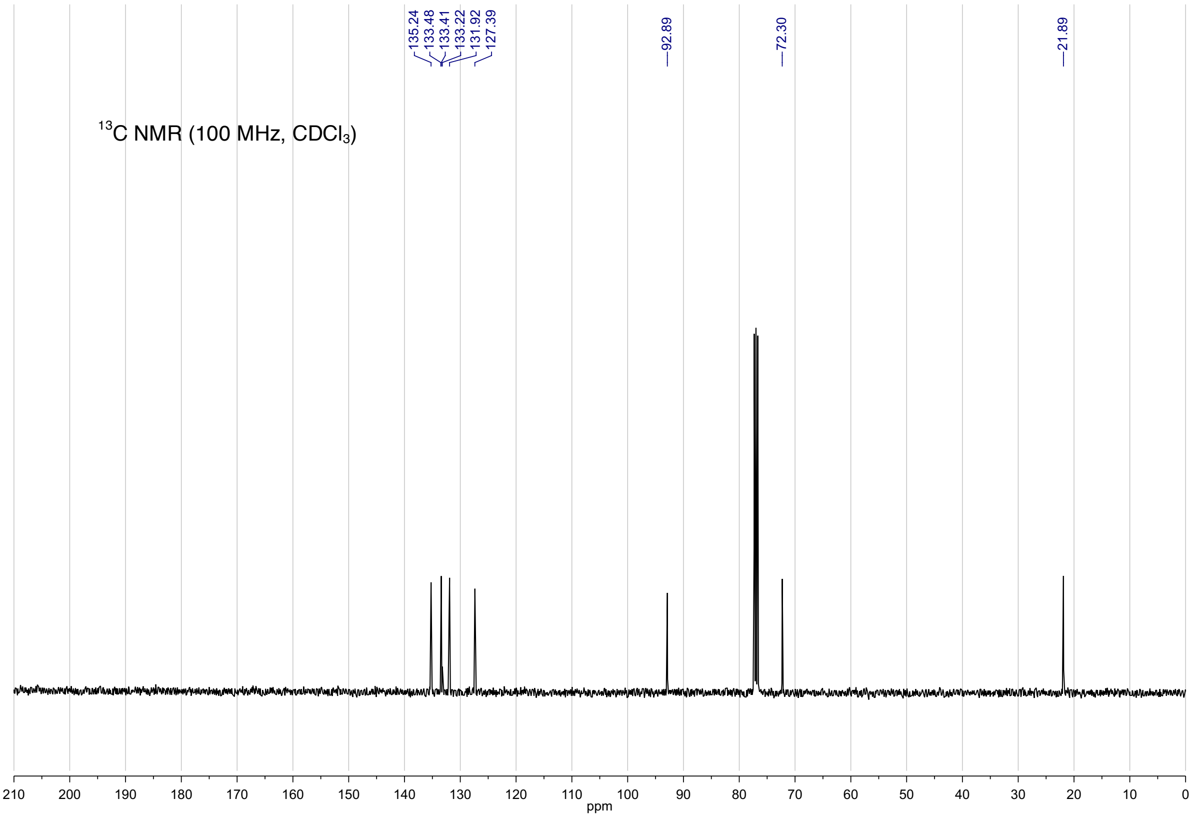
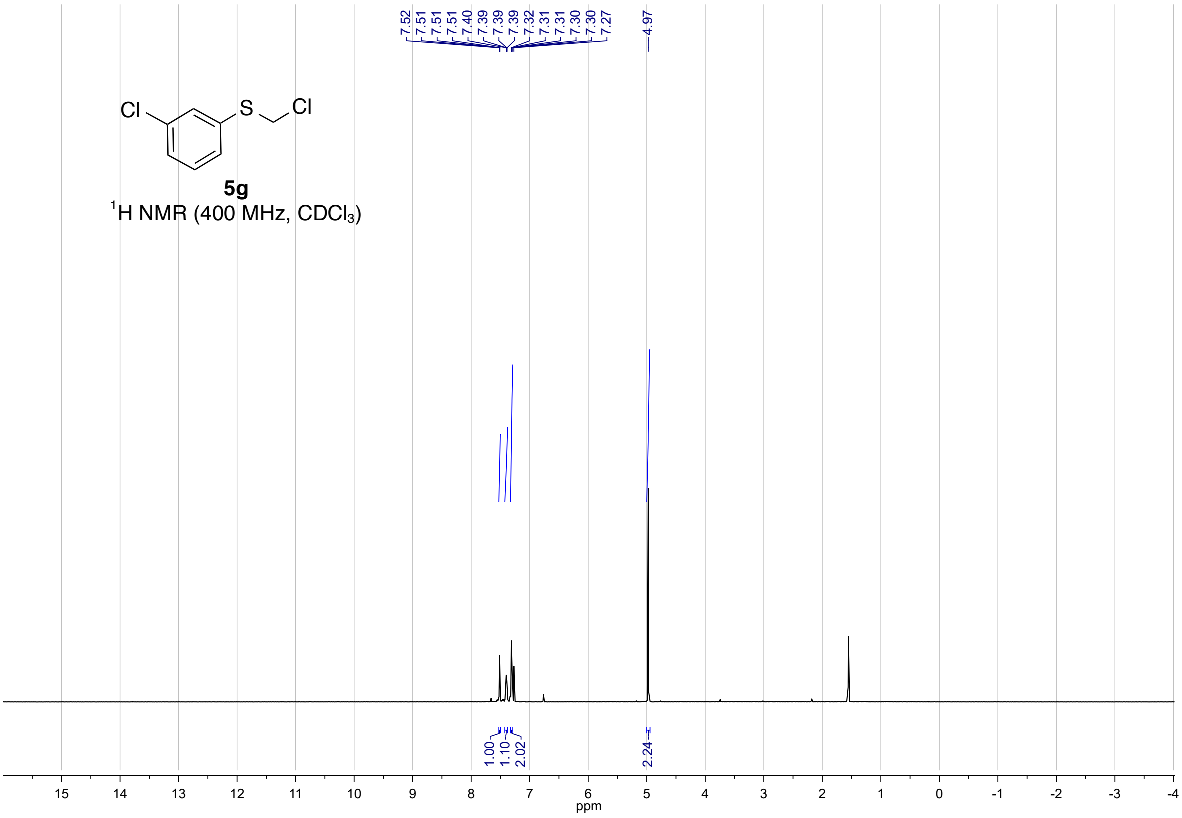
7.51
7.50
7.49
7.49
5.97
5.96
5.95
5.94
4.98
4.98
4.98
4.96
4.96
4.96
4.94
4.73
4.72
4.71
4.70
4.69
3.31
3.29
3.29
3.28
3.28
3.27
3.26
3.26
3.26
3.25
3.25
3.24
3.23
3.23
3.21
3.21
3.19
3.17
3.15
Cl
O
O
S
O
1f
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
2.09
1.05
1.03
1.09
1.10
2.31
10.0
9.5
9.0
8.5
8.0
7.5
7.0
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
ppm


135.24
133.48
133.41
133.22
131.92
127.39
92.89
72.30
21.89
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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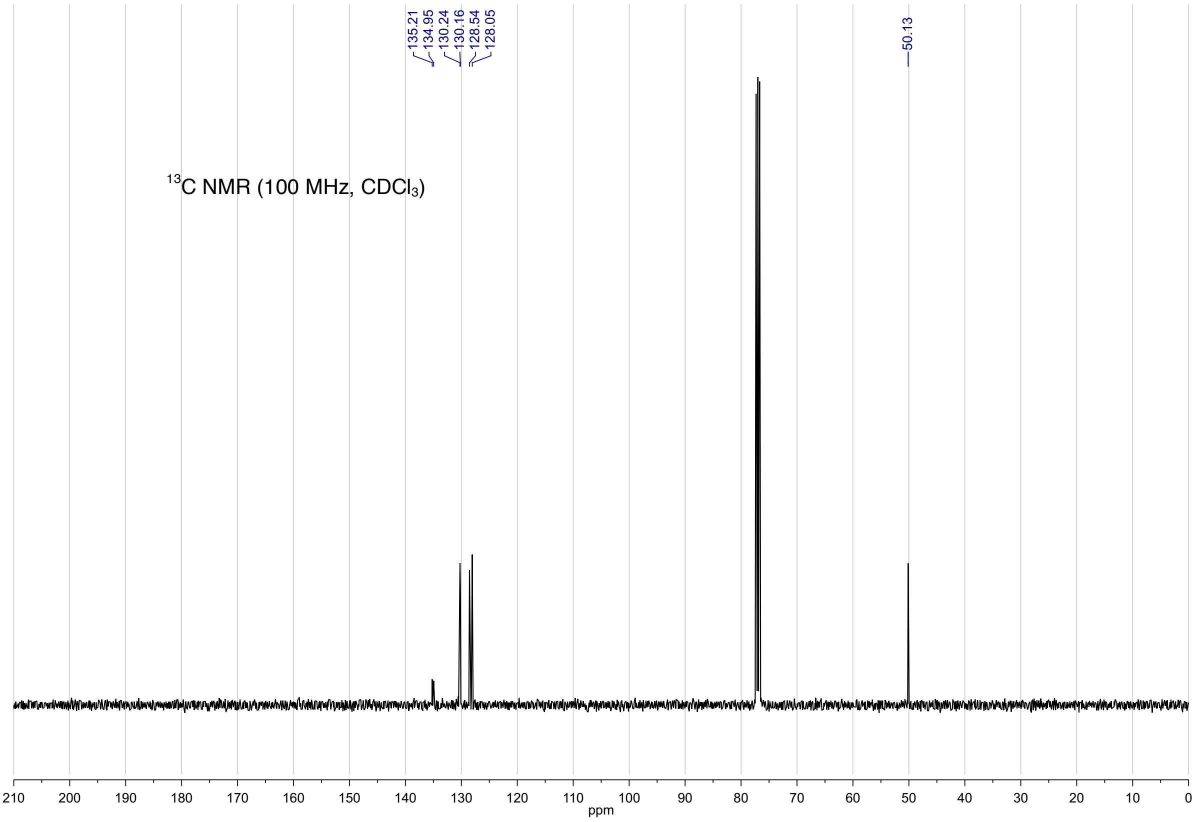
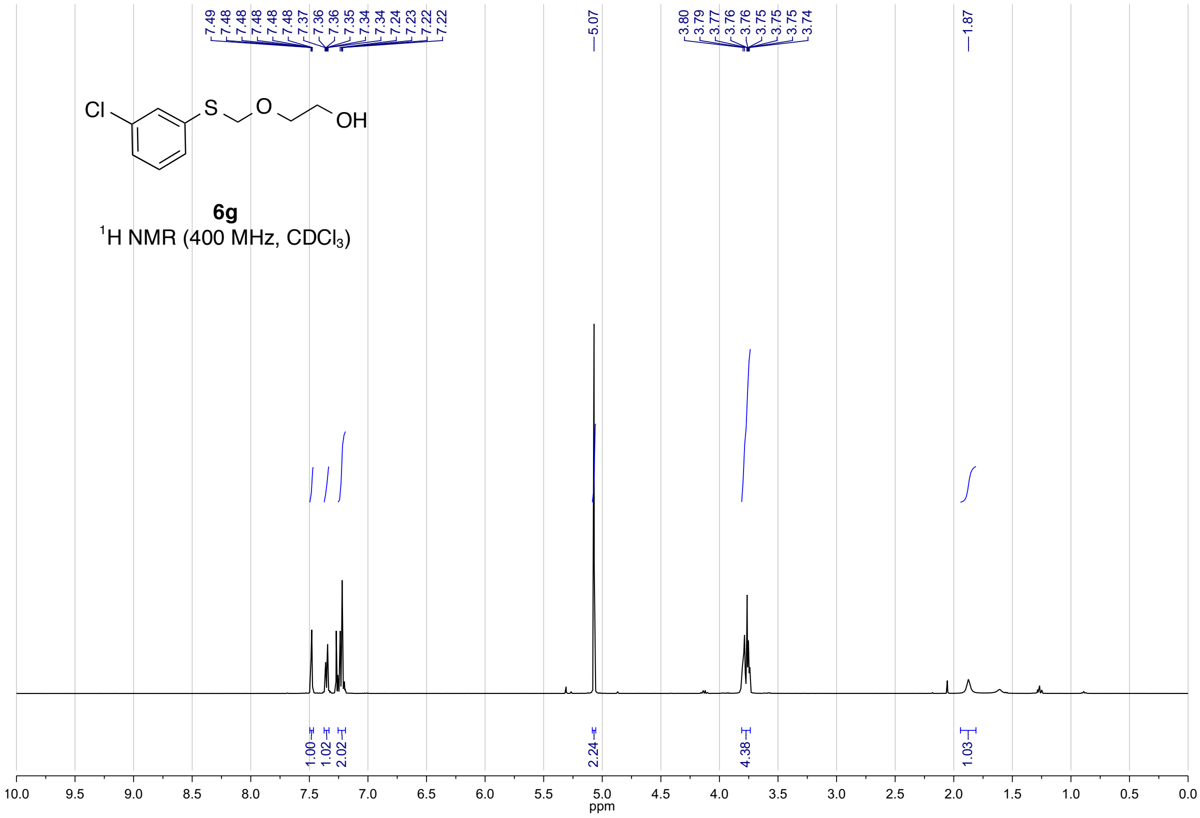
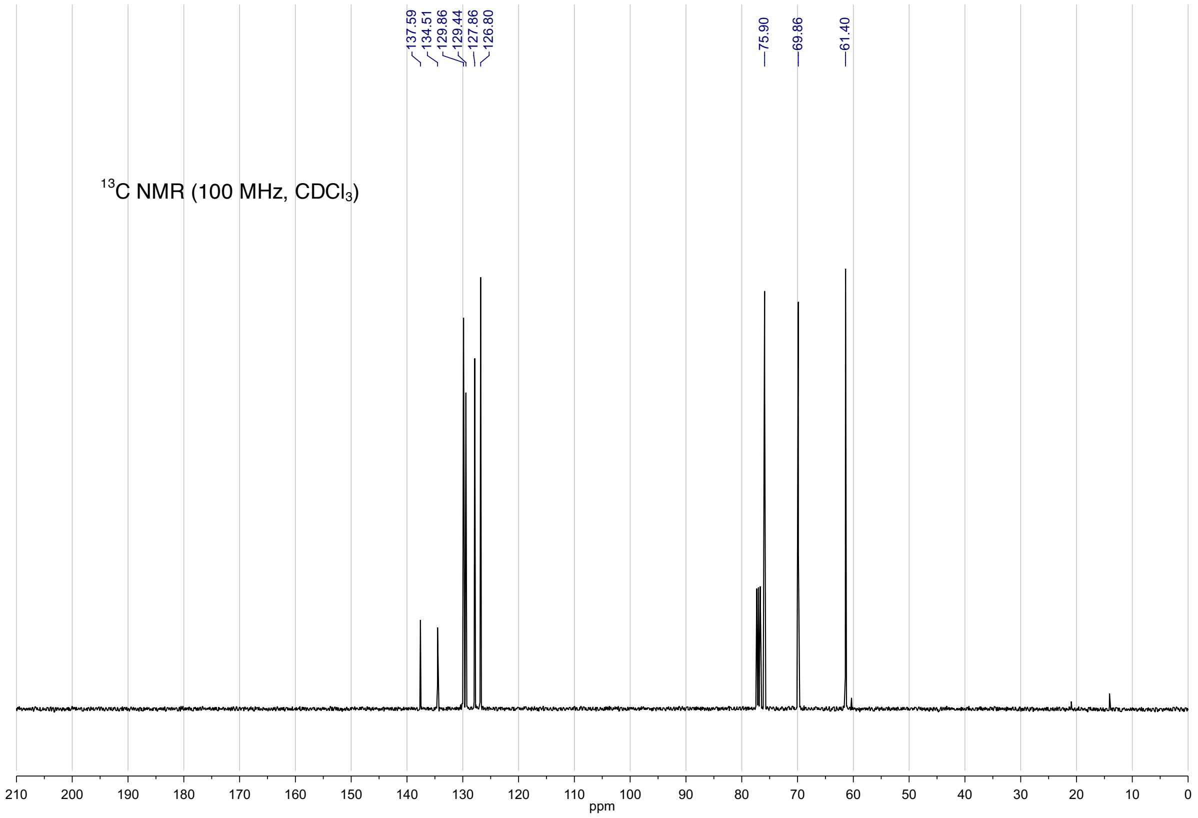
7.51
7.51
7.40
7.39
7.39
7.39
7.32
7.31
7.31
7.30
7.30
7.27
4.97
Cl
S
Cl
5g
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.10
2.02
2.24
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
ppm


135.21
134.95
130.24
130.16
128.54
128.05
50.13
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

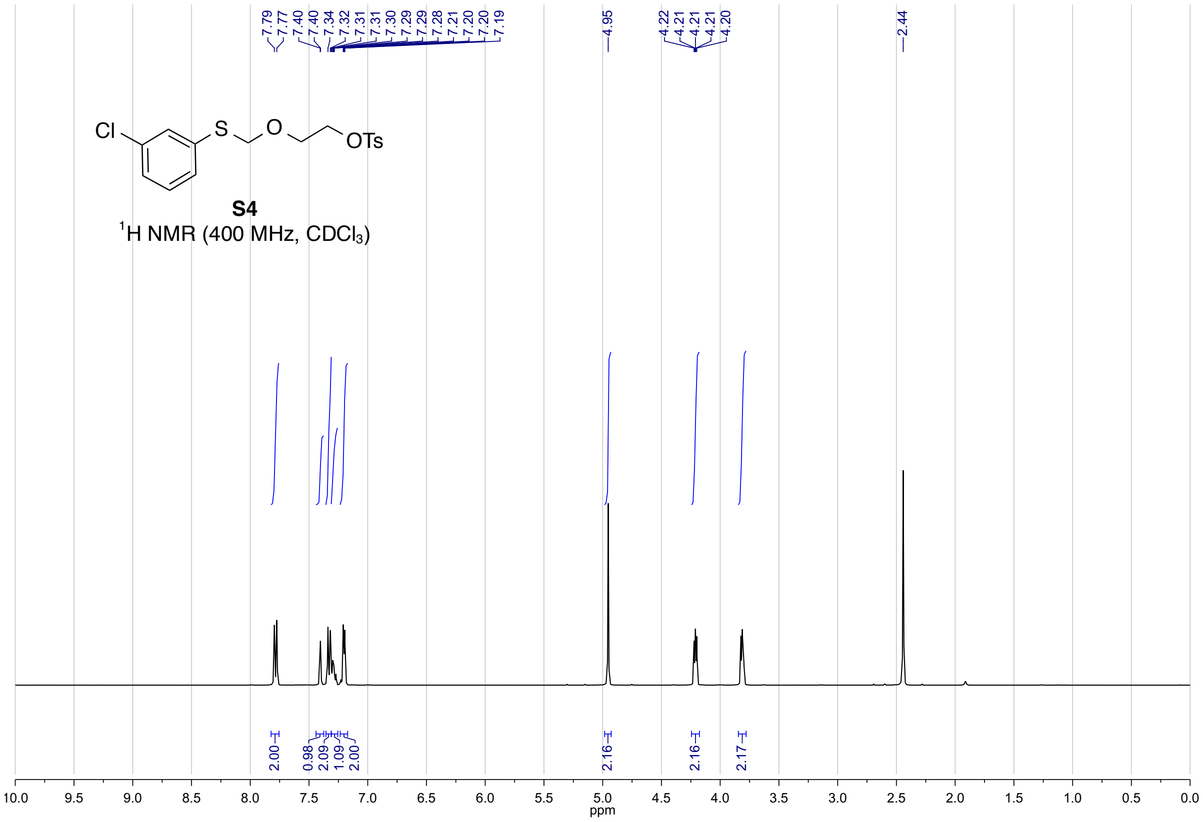


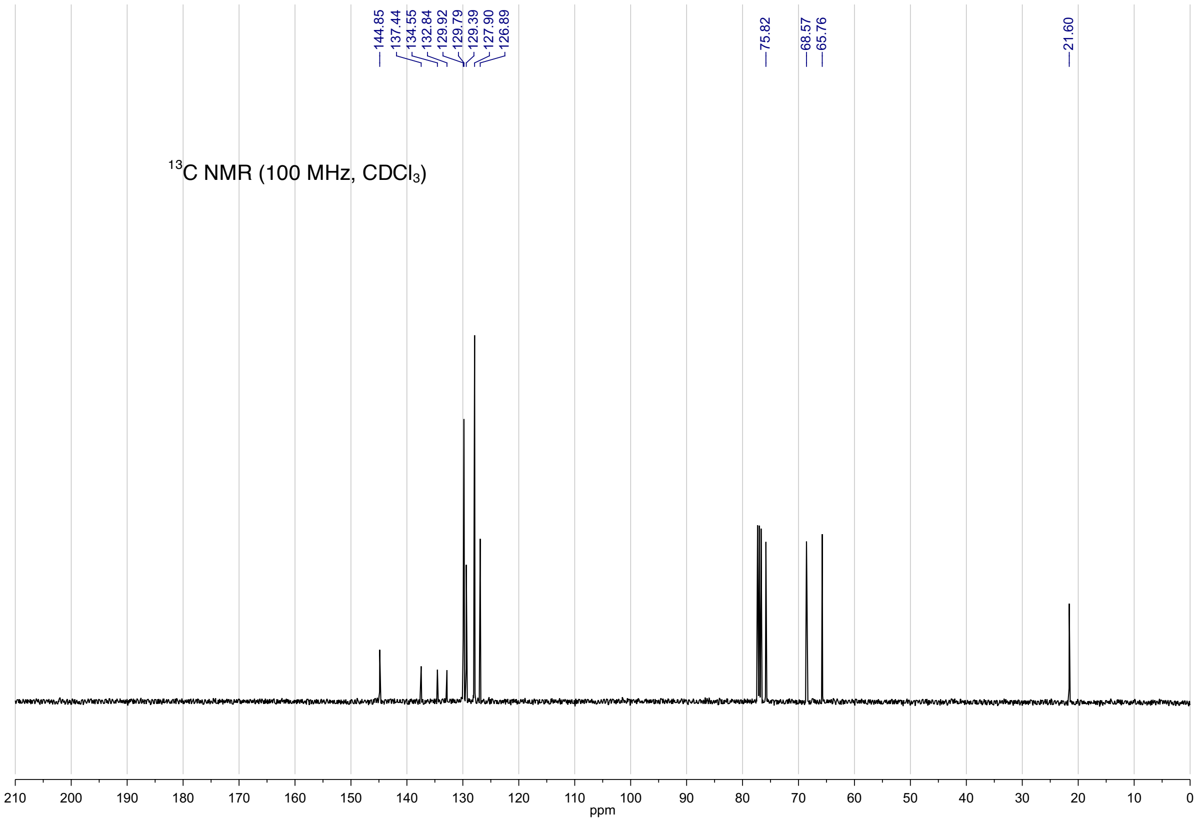
6g

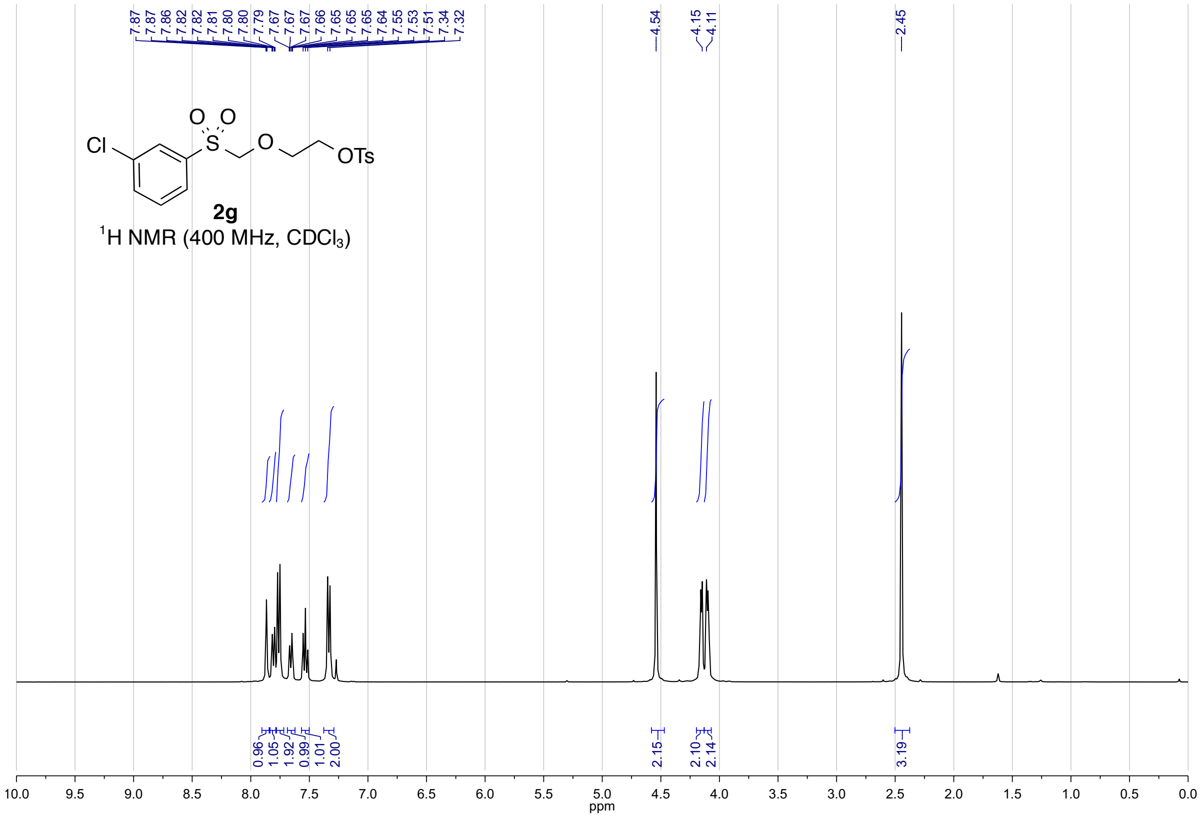
^{1}H NMR (400 MHz, CDCl$_3$)



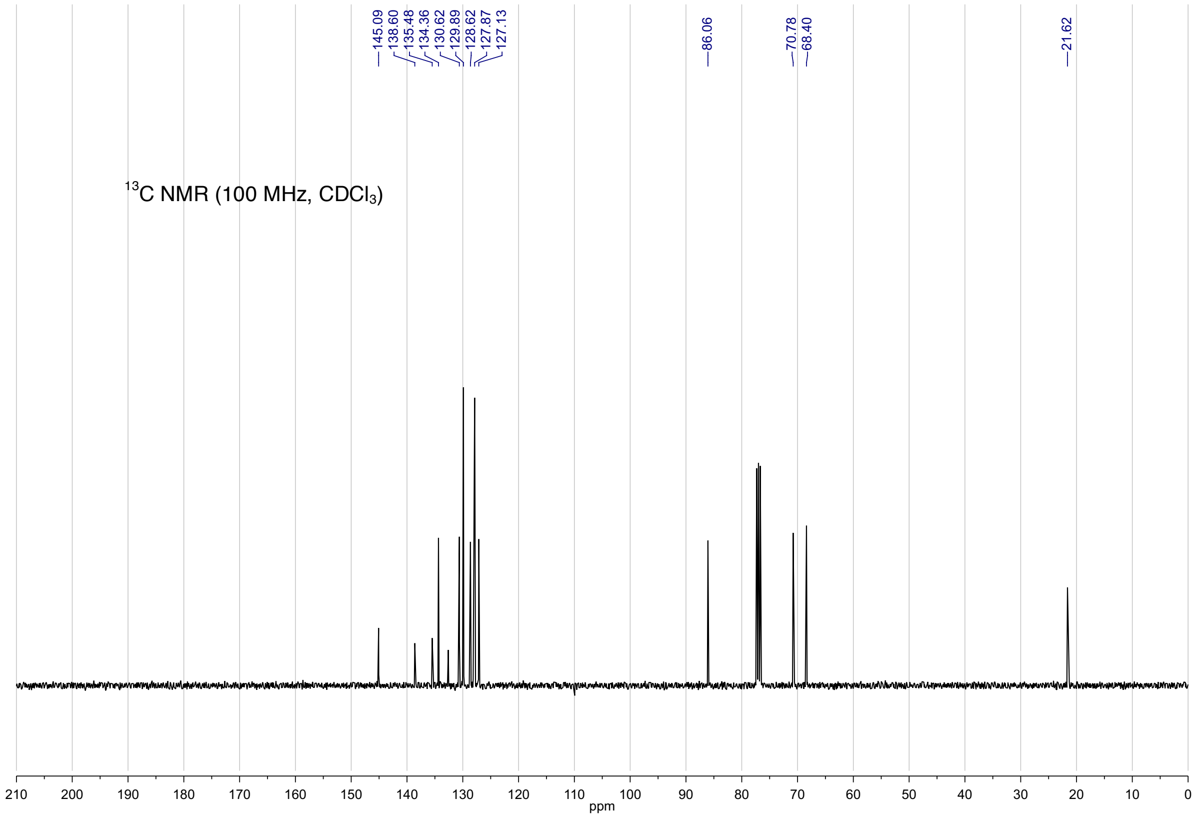
^{13}C NMR (100 MHz, CDCl$_3$)

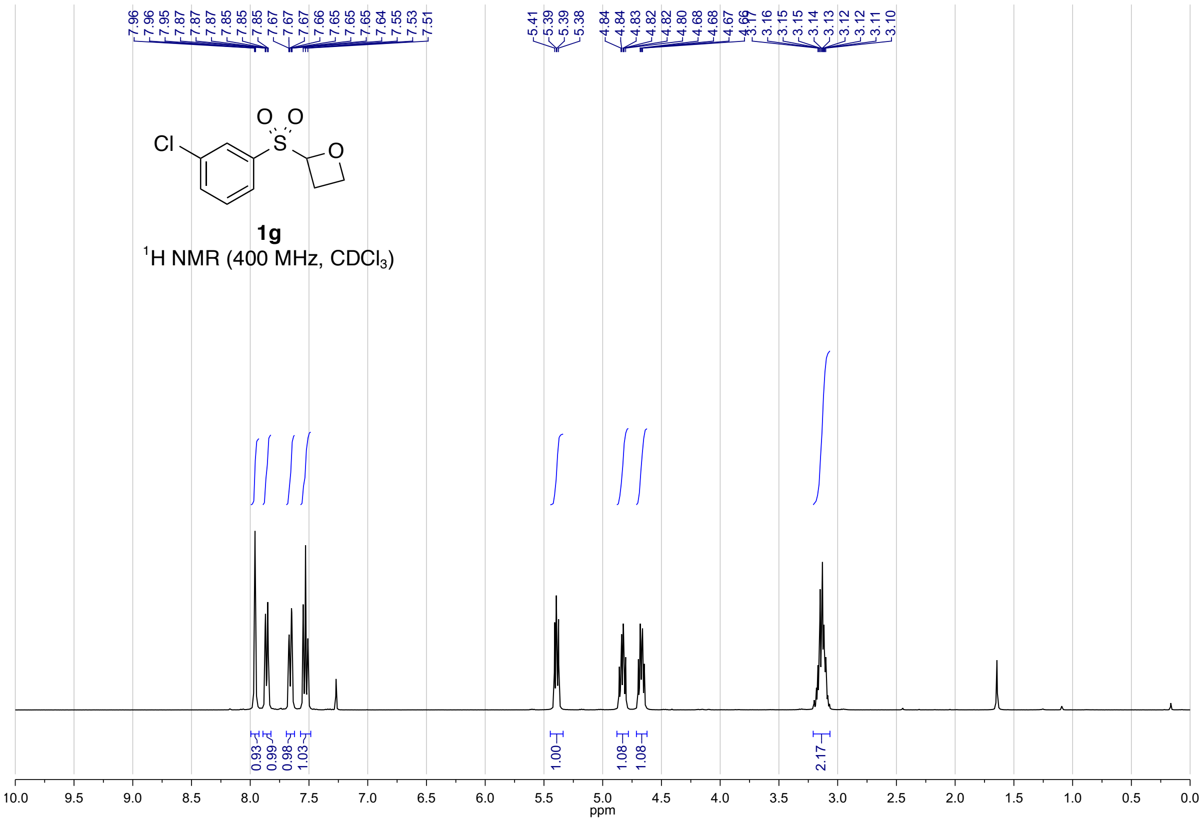

7.79
7.77
7.40
7.40
7.34
7.32
7.31
7.31
7.30
7.29
7.29
7.28
7.21
7.20
7.20
7.19
4.95
4.22
4.21
4.21
4.21
4.20
2.44
Cl
S
O
OTs
S4
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
0.98
2.09
1.09
2.00
2.16
2.16
2.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


144.85
137.44
134.55
132.84
129.92
129.79
129.39
127.90
126.89
75.82
68.57
65.76
21.60
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


2g

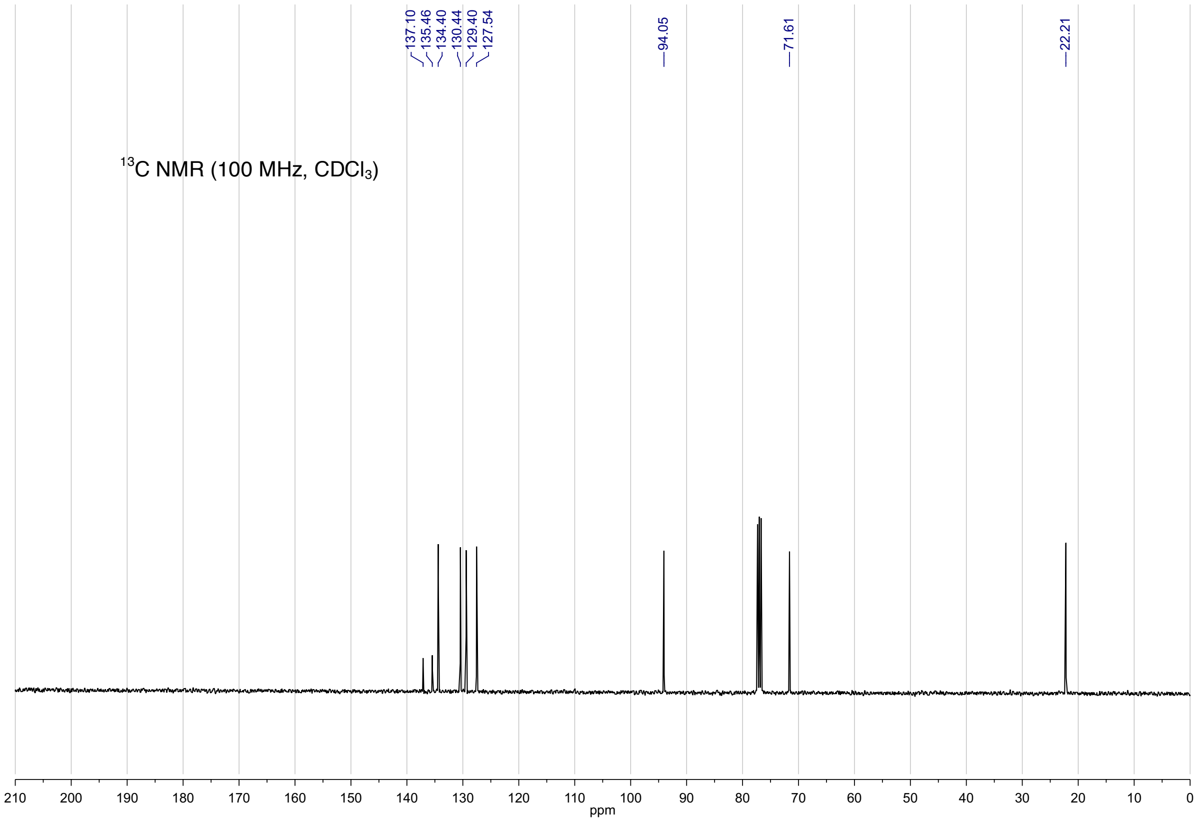
^{1}H NMR (400 MHz, CDCl$_3$)


^{13}C NMR (100 MHz, CDCl$_3$)

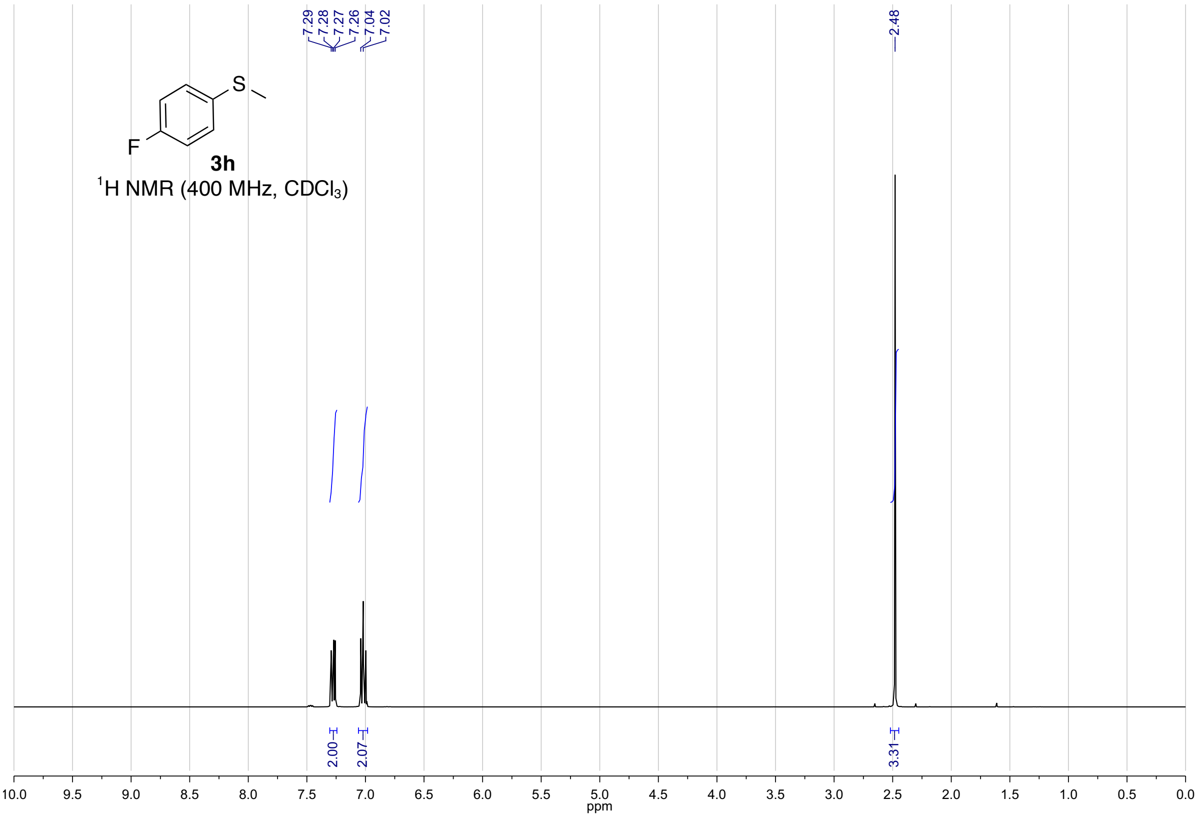


1g

^{1}H NMR (400 MHz, CDCl$_3$)



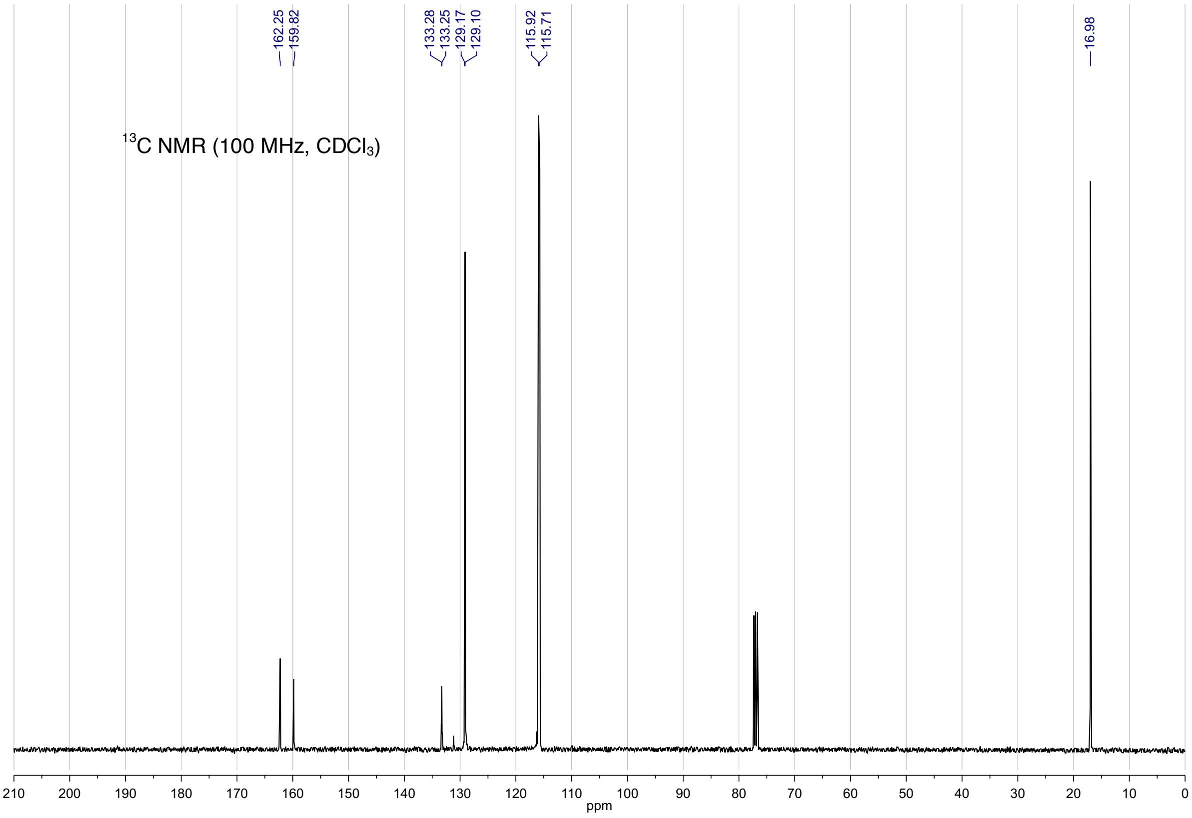
^{13}C NMR (100 MHz, CDCl$_3$)

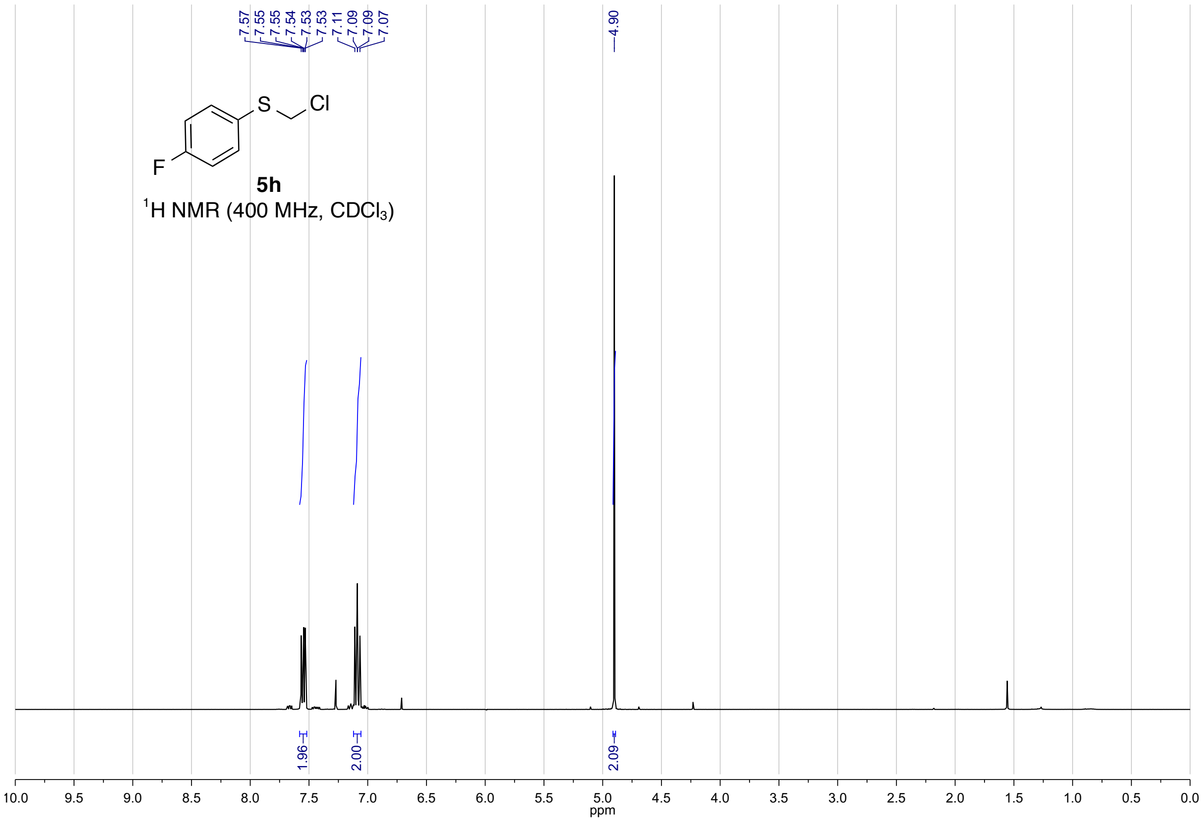


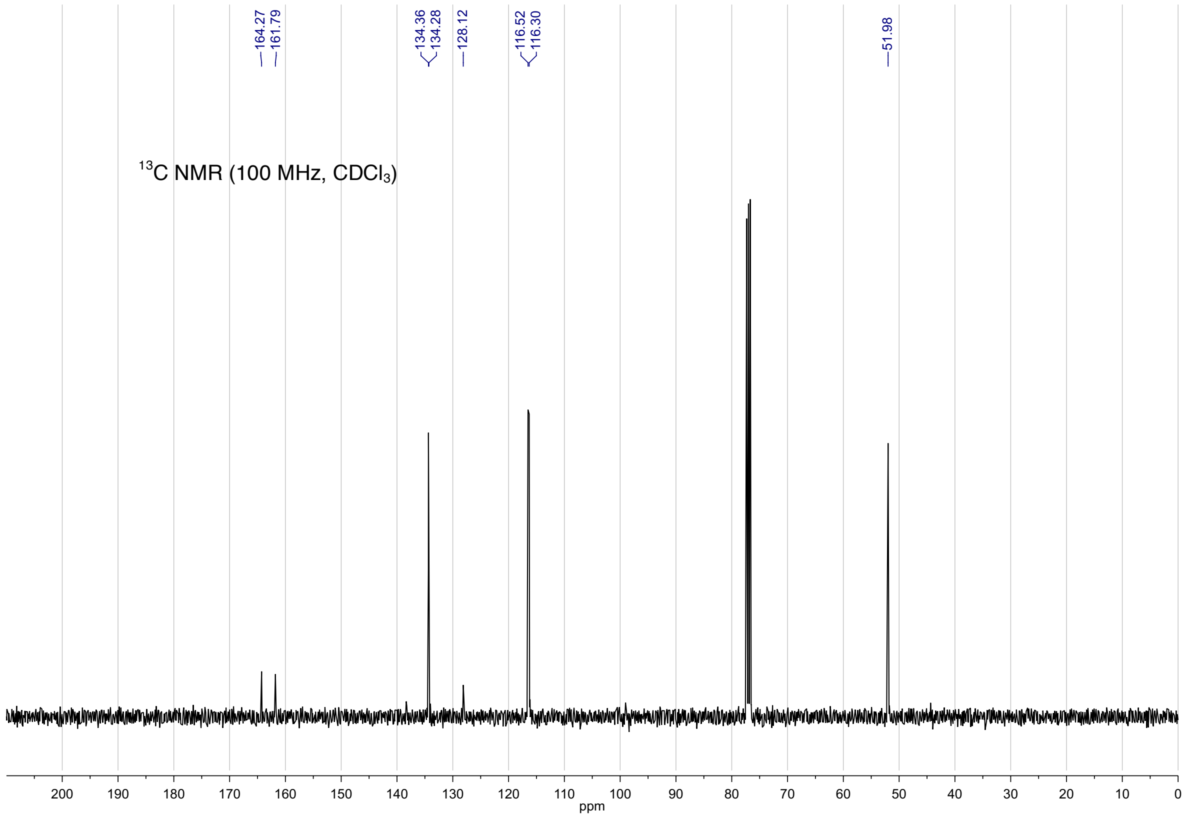
3h

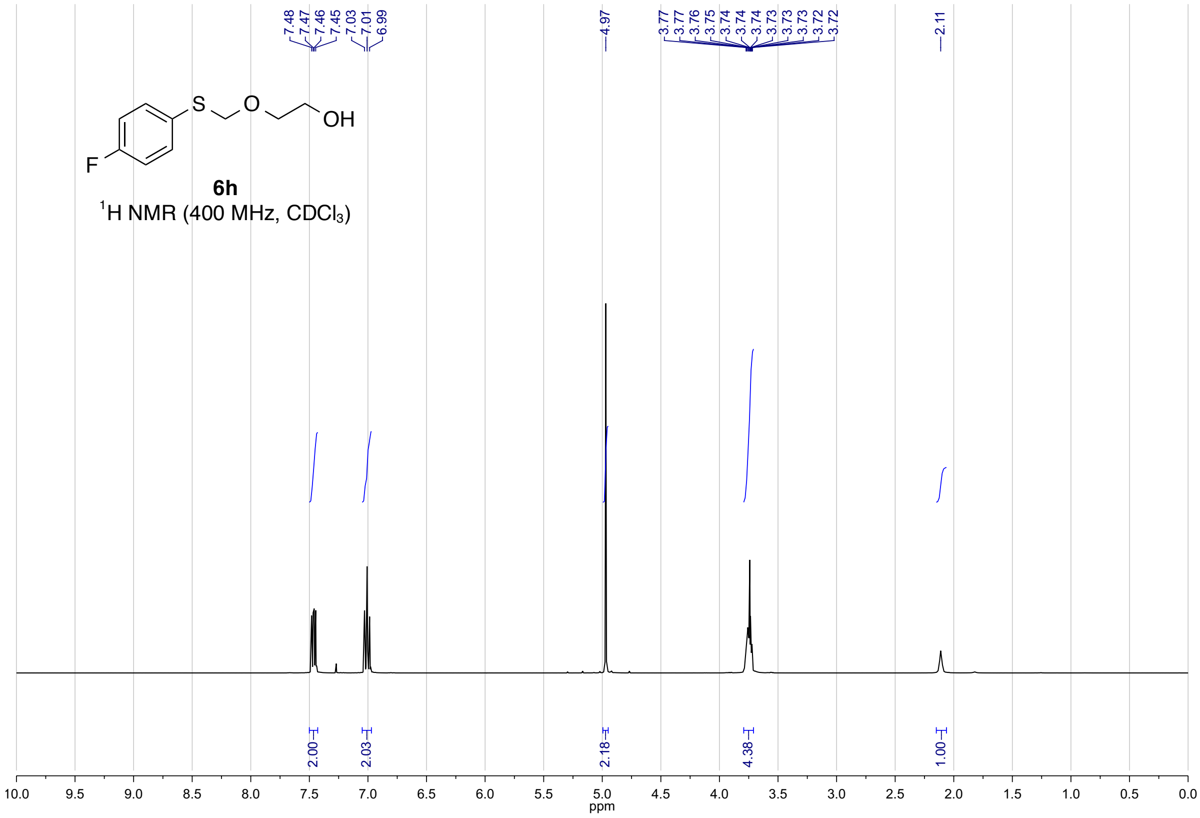
^{1}H NMR (400 MHz, CDCl$_3$)

^{13}C NMR (100 MHz, CDCl$_3$)



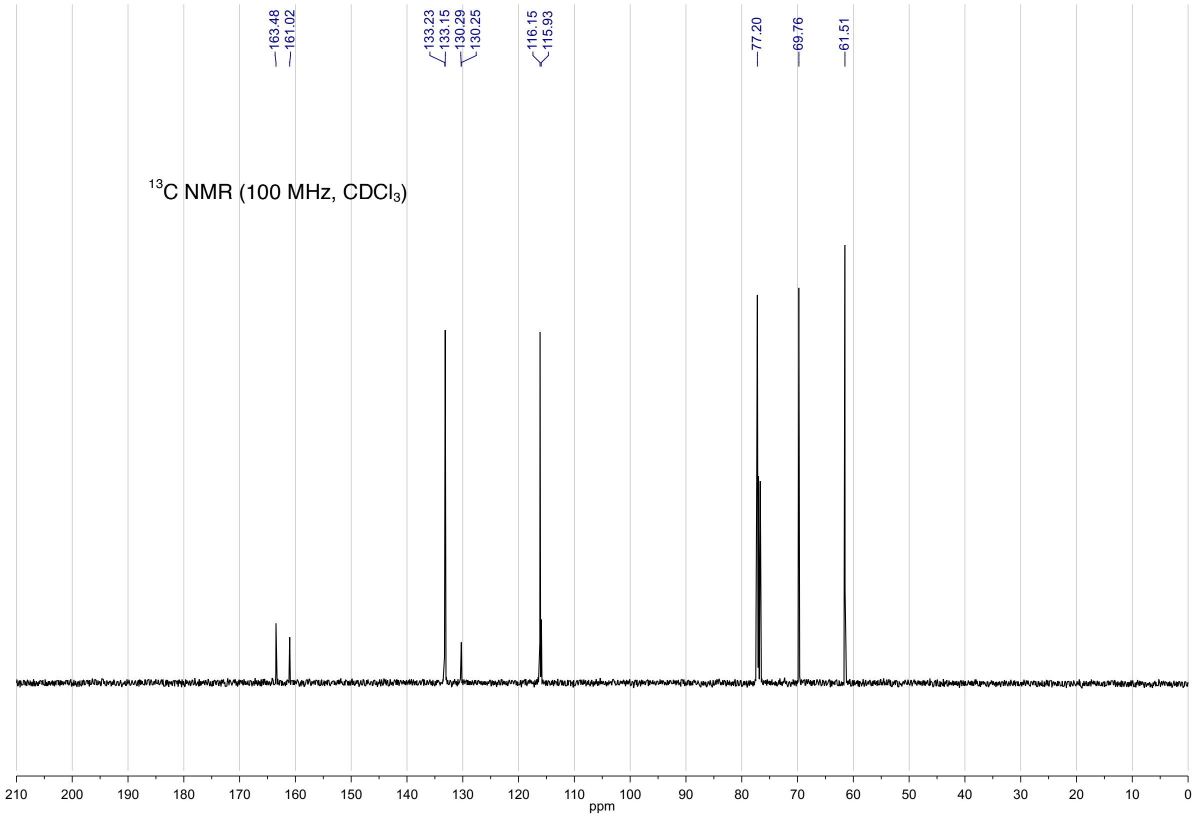

7.57
7.55
7.55
7.54
7.53
7.53
7.11
7.09
7.09
7.07
4.90
S
Cl
F
5h
^{1}H NMR (400 MHz, CDCl$_3$)
1.96
2.00
2.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


164.27
161.79
134.36
134.28
128.12
116.52
116.30
51.98
^{13}C NMR (100 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

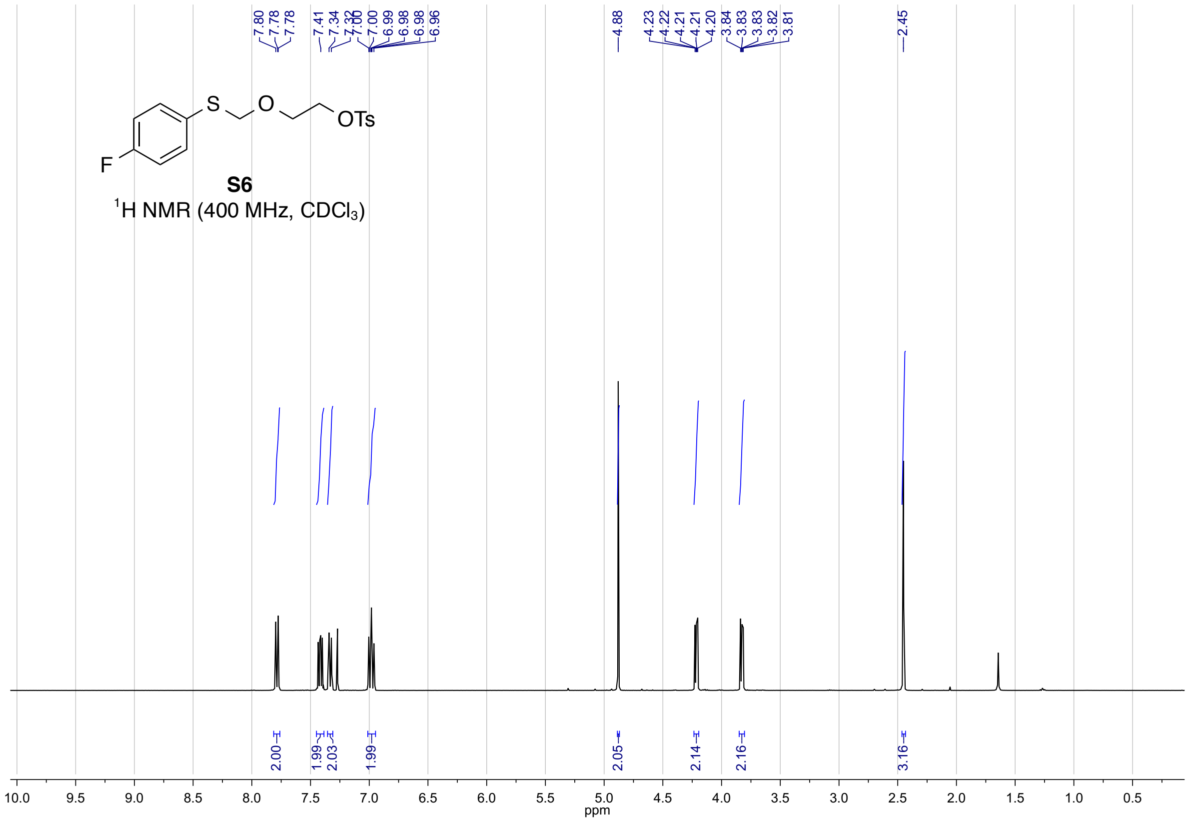


6h

^{1}H NMR (400 MHz, CDCl$_3$)

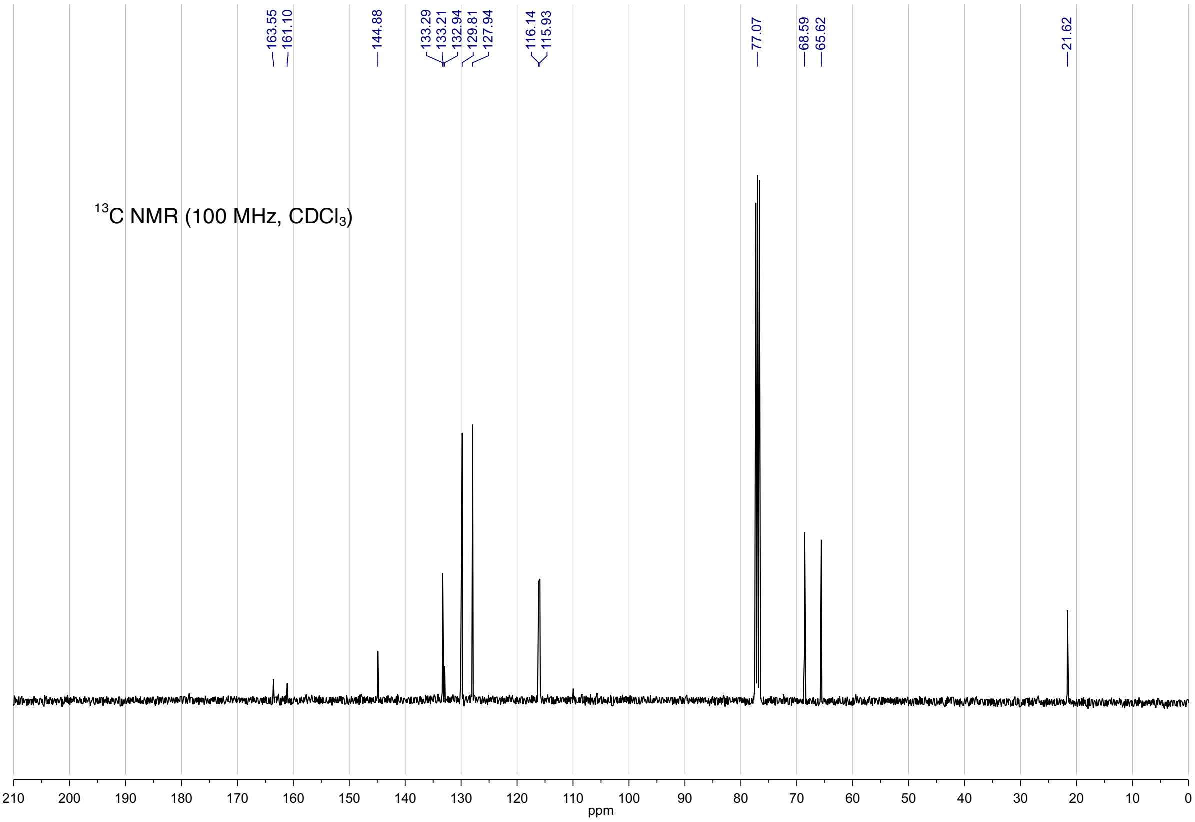


^{13}C NMR (100 MHz, CDCl$_3$)

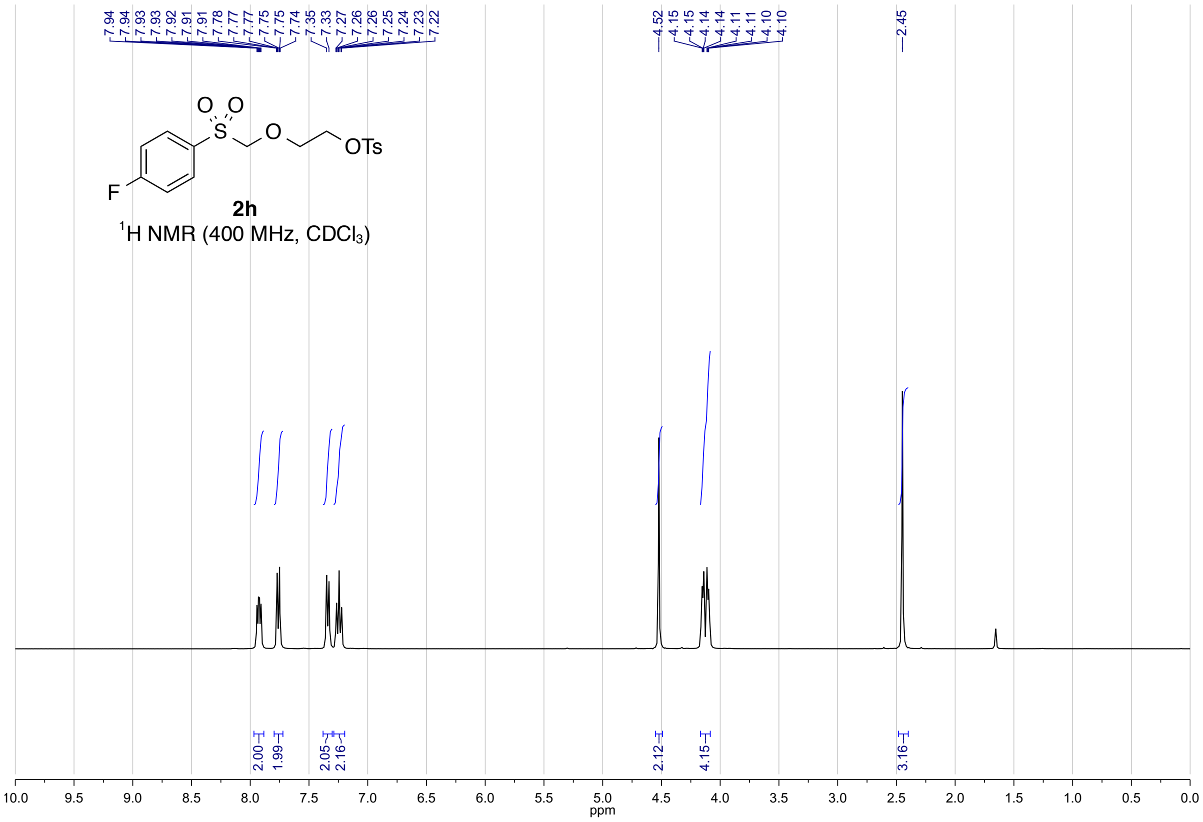


S6

^{1}H NMR (400 MHz, CDCl$_3$)

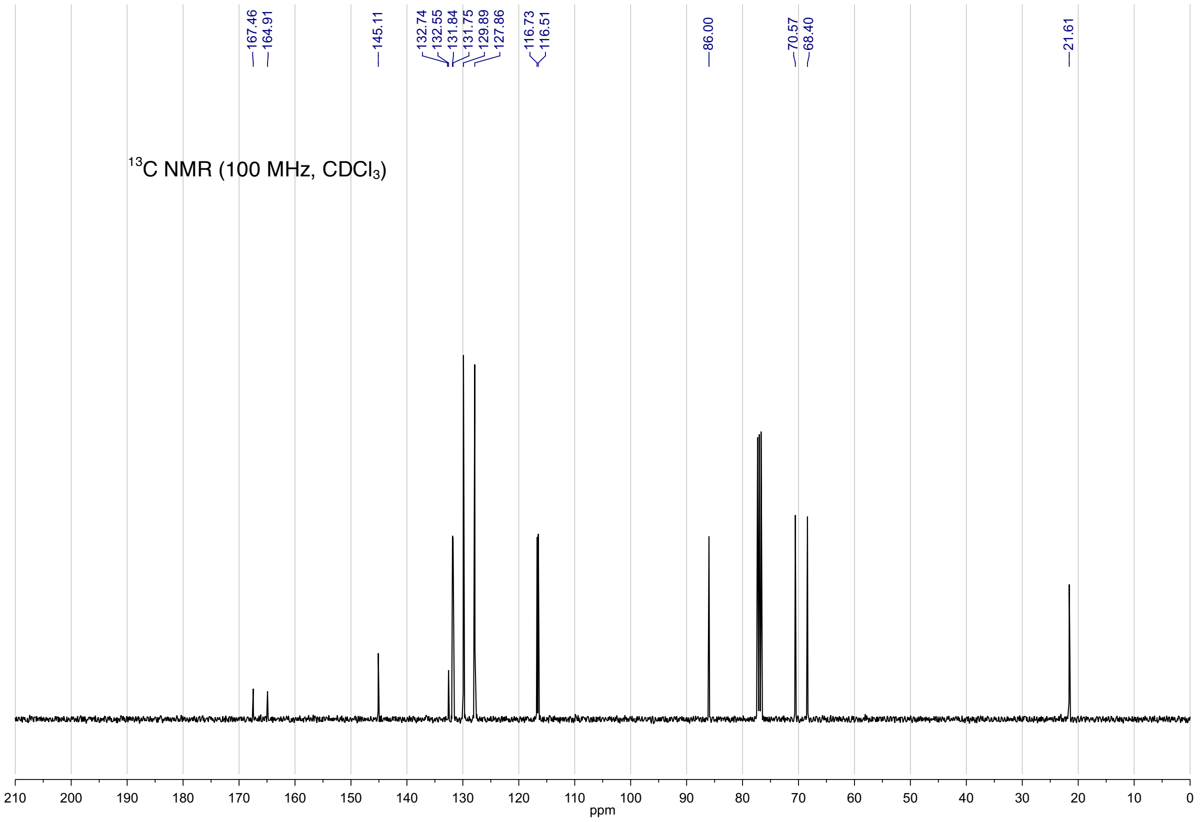


^{13}C NMR (100 MHz, CDCl$_3$)

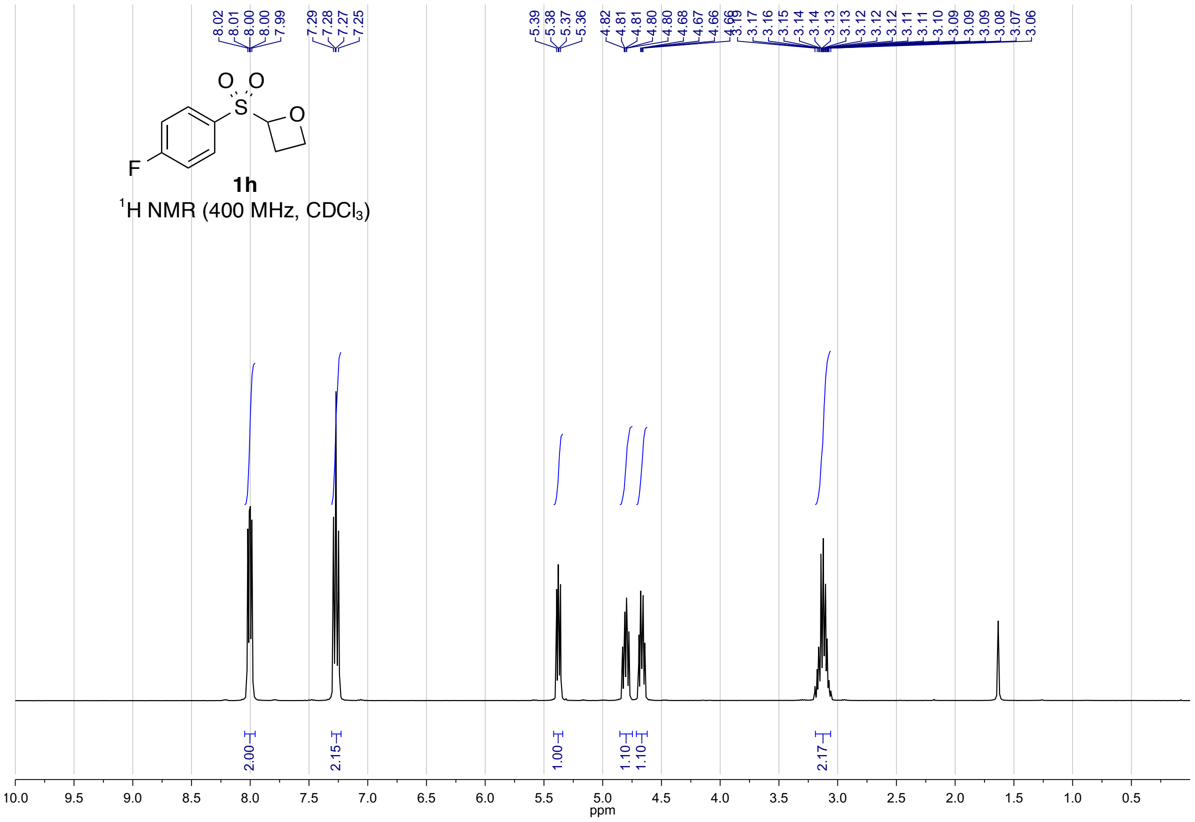


2h

^{1}H NMR (400 MHz, CDCl$_3$)

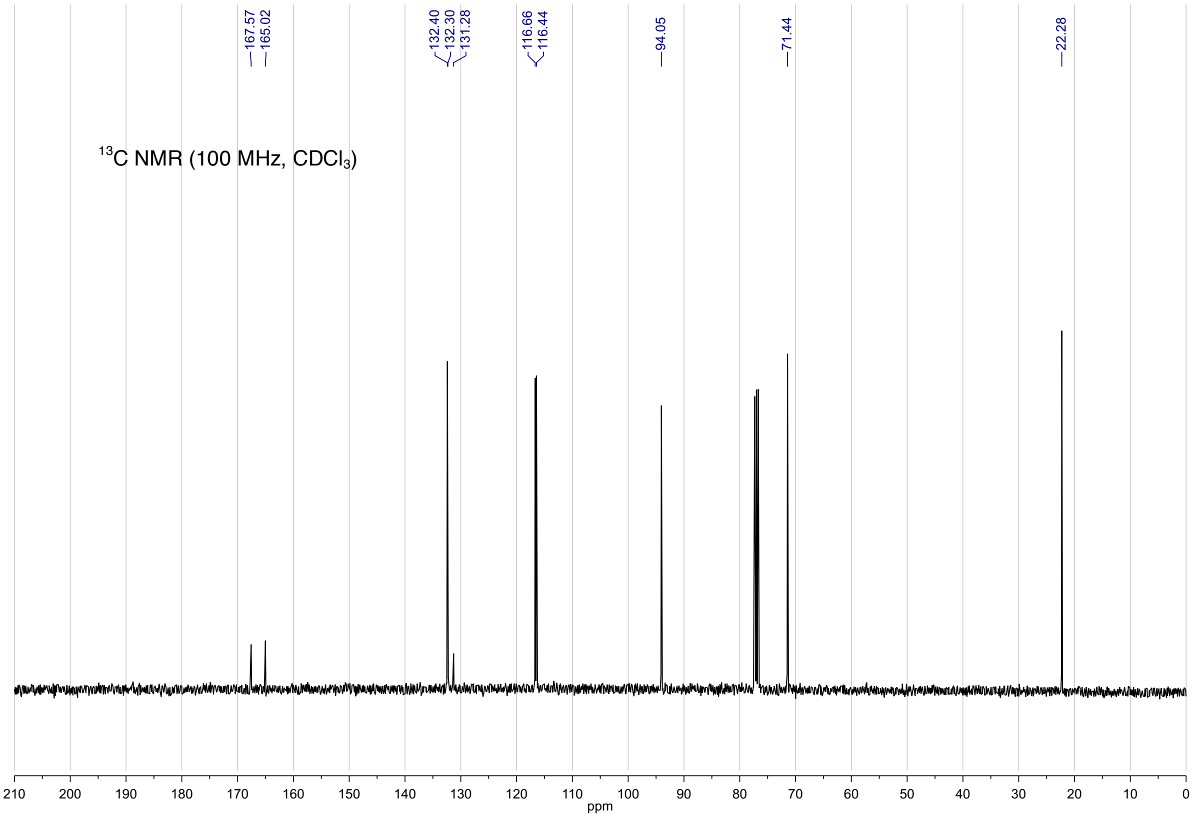


^{13}C NMR (100 MHz, CDCl$_3$)

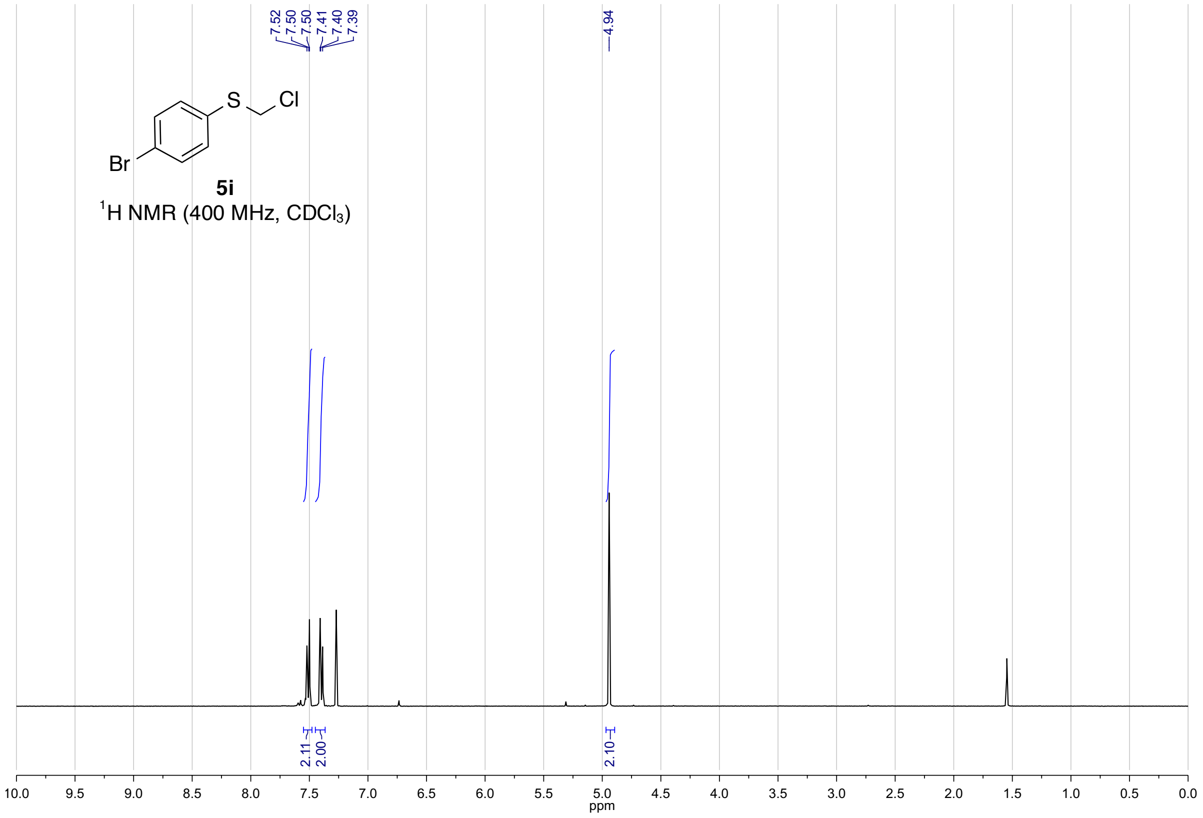


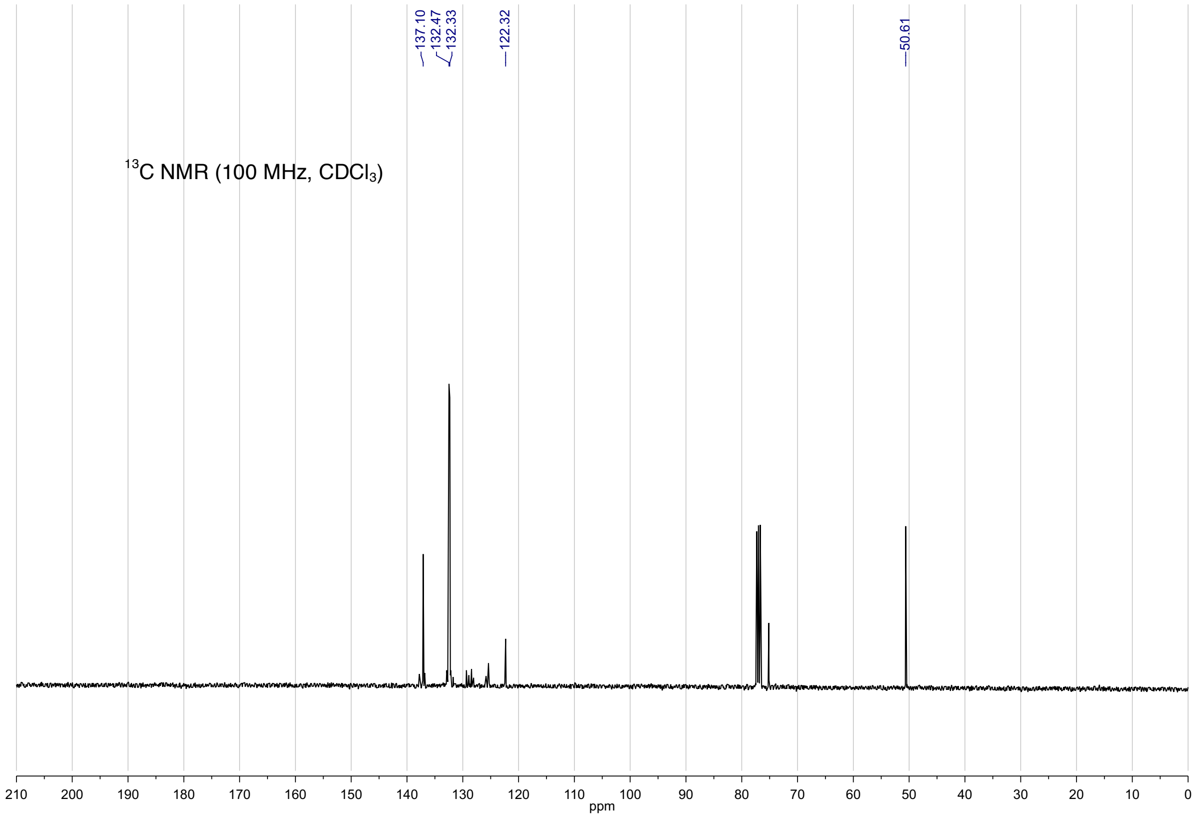
1h

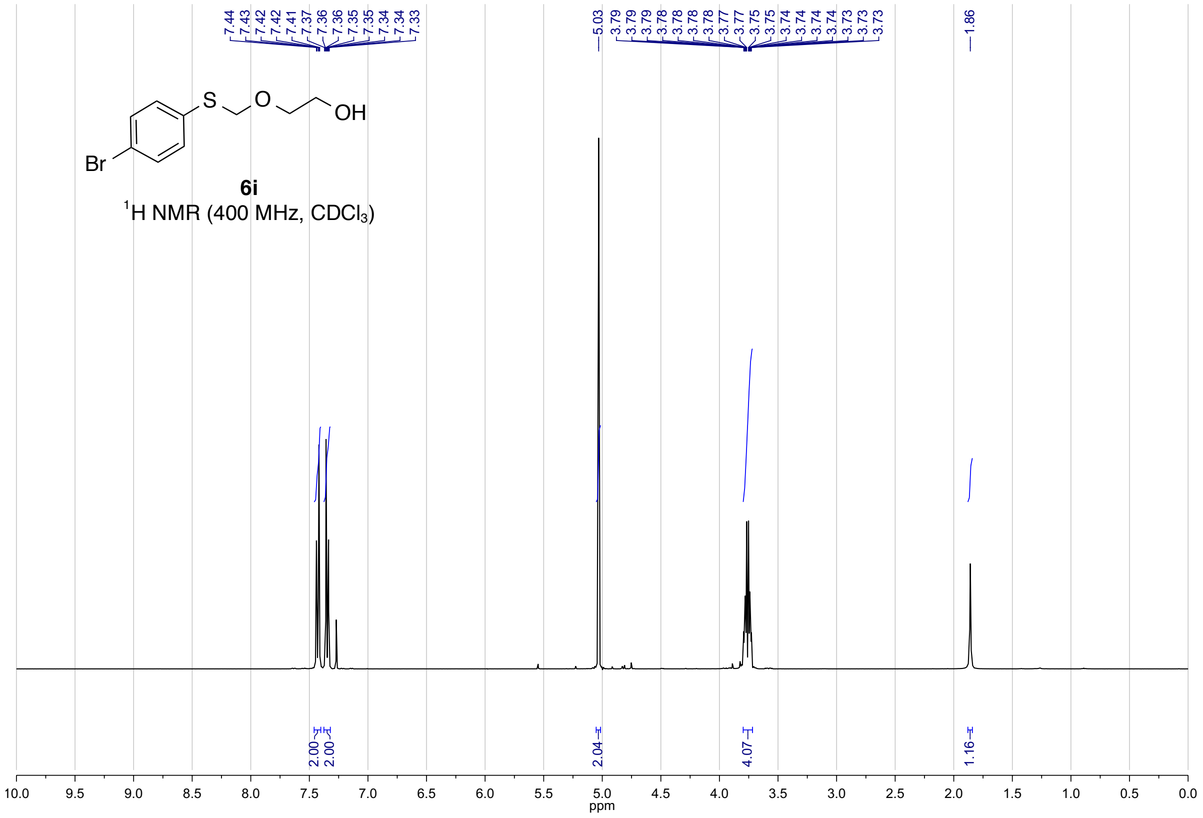
^{1}H NMR (400 MHz, CDCl$_3$)

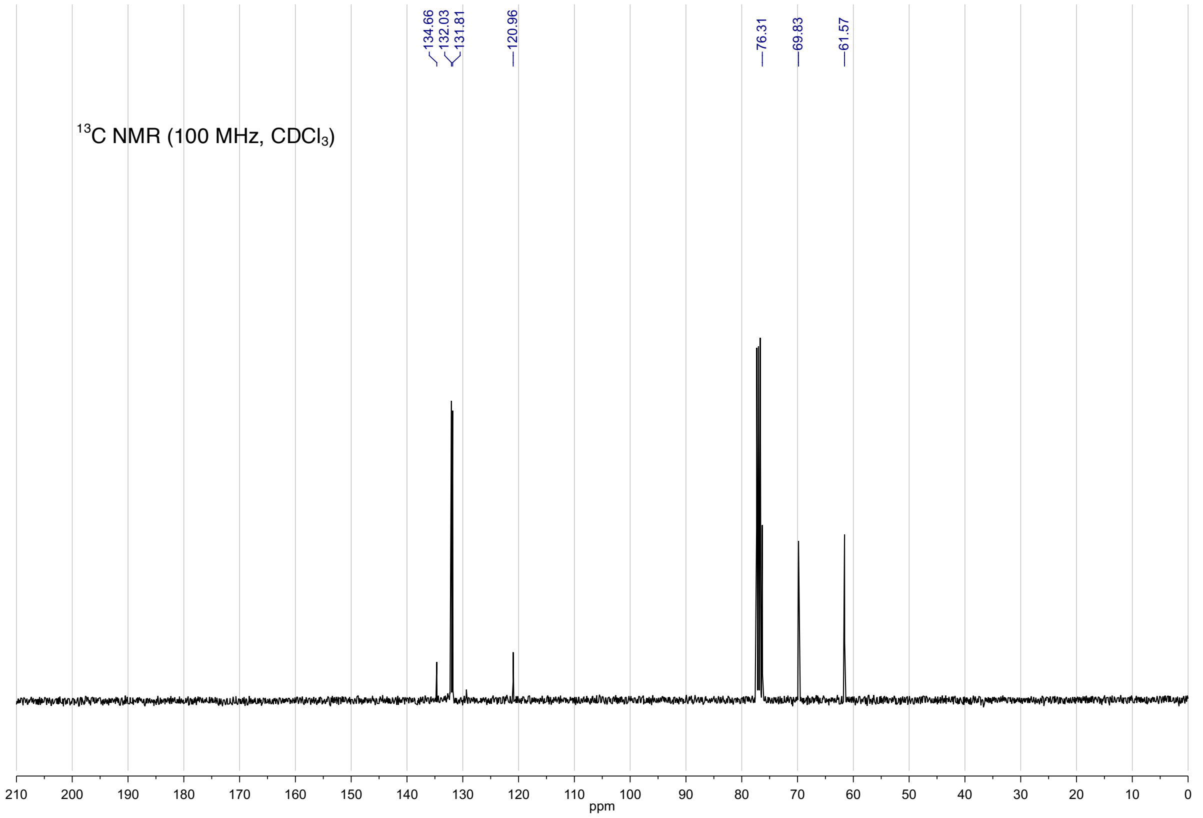


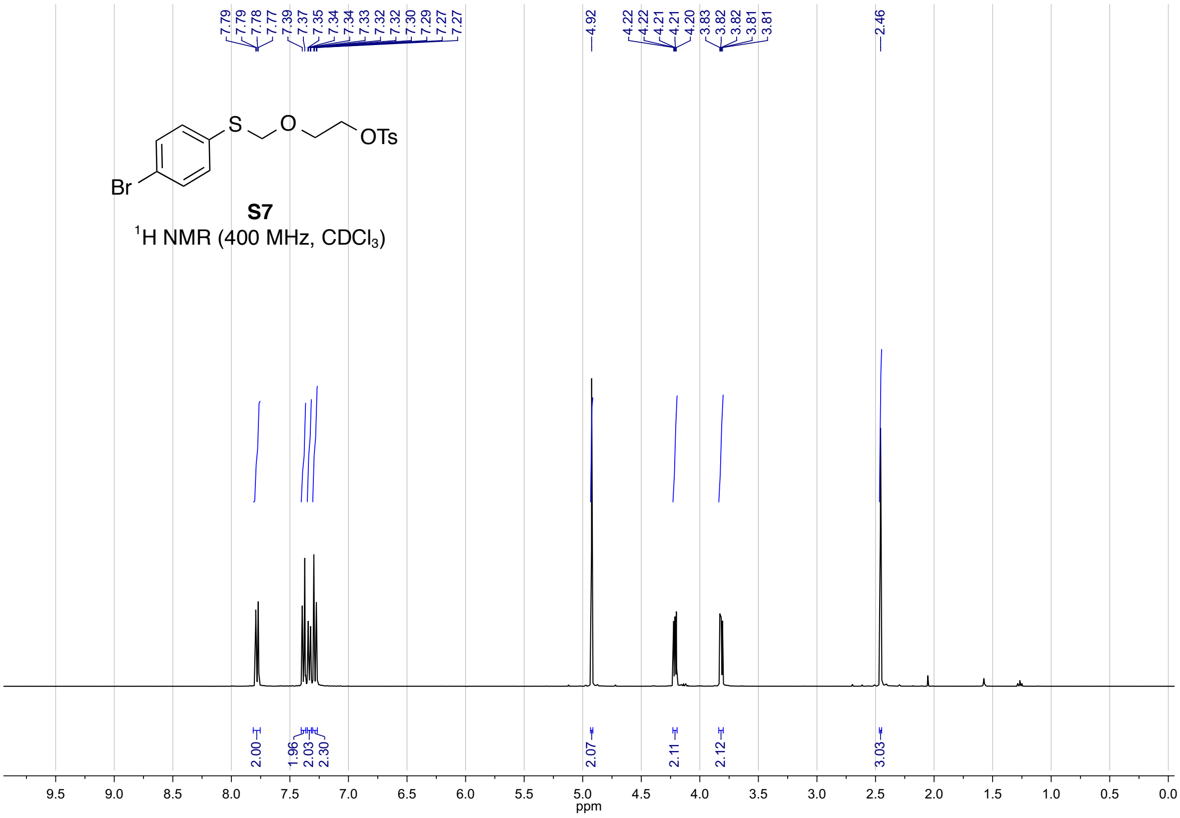
^{13}C NMR (100 MHz, CDCl$_3$)


7.52
7.50
7.50
7.41
7.40
7.39
4.94
S
Cl
Br
5i
^{1}H NMR (400 MHz, CDCl$_3$)
2.11
2.00
2.10
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
ppm


137.10
132.47
132.33
122.32
50.61
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

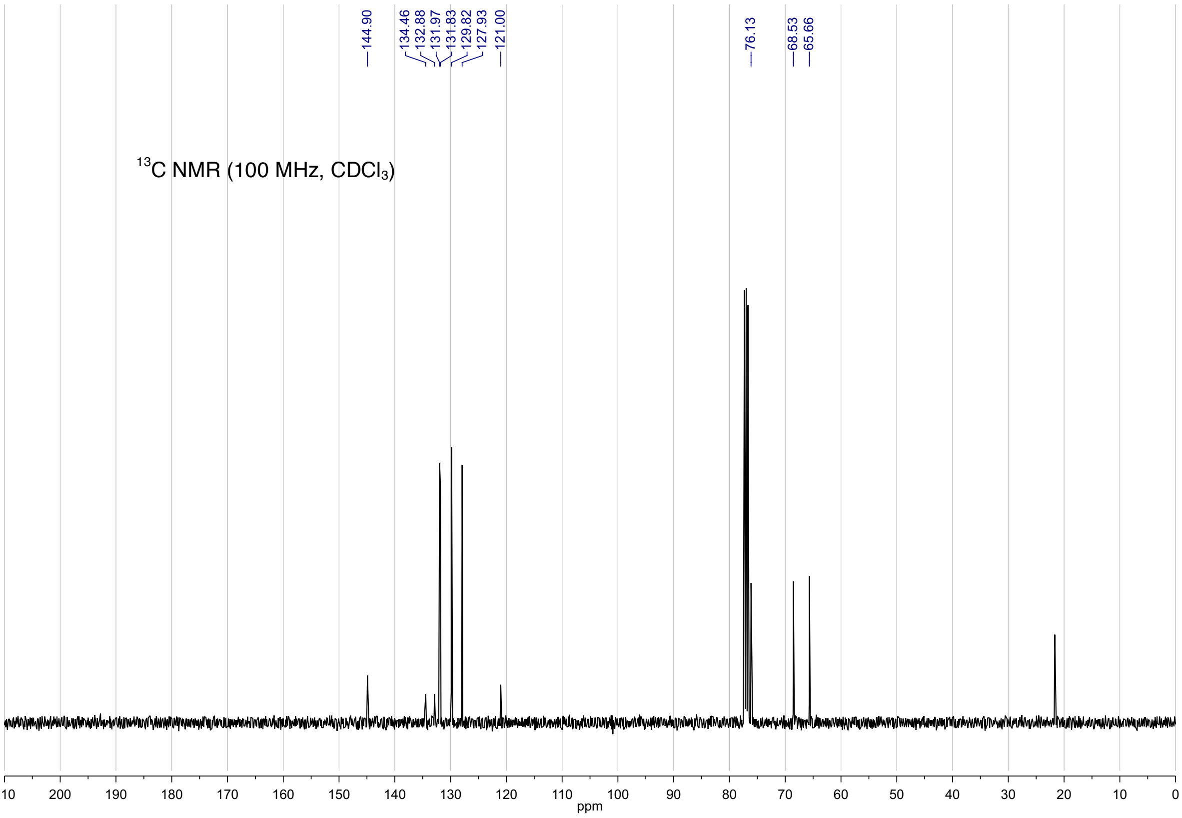

7.44
7.43
7.42
7.42
7.41
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
5.03
3.79
3.79
3.79
3.78
3.78
3.78
3.78
3.77
3.77
3.75
3.75
3.74
3.74
3.74
3.74
3.73
3.73
3.73
1.86
S
O
OH
Br
6i
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
2.00
2.04
4.07
1.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


134.66
132.03
131.81
120.96
76.31
69.83
61.57
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

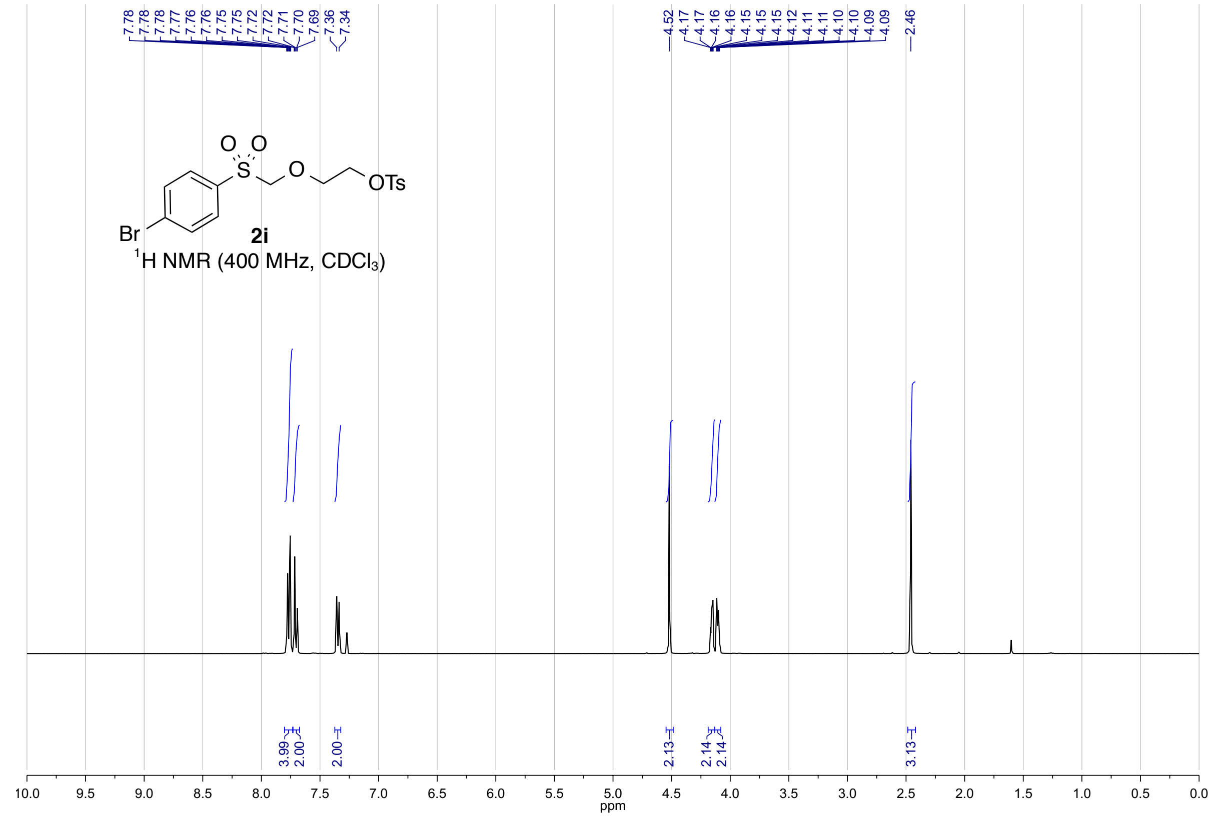


S7

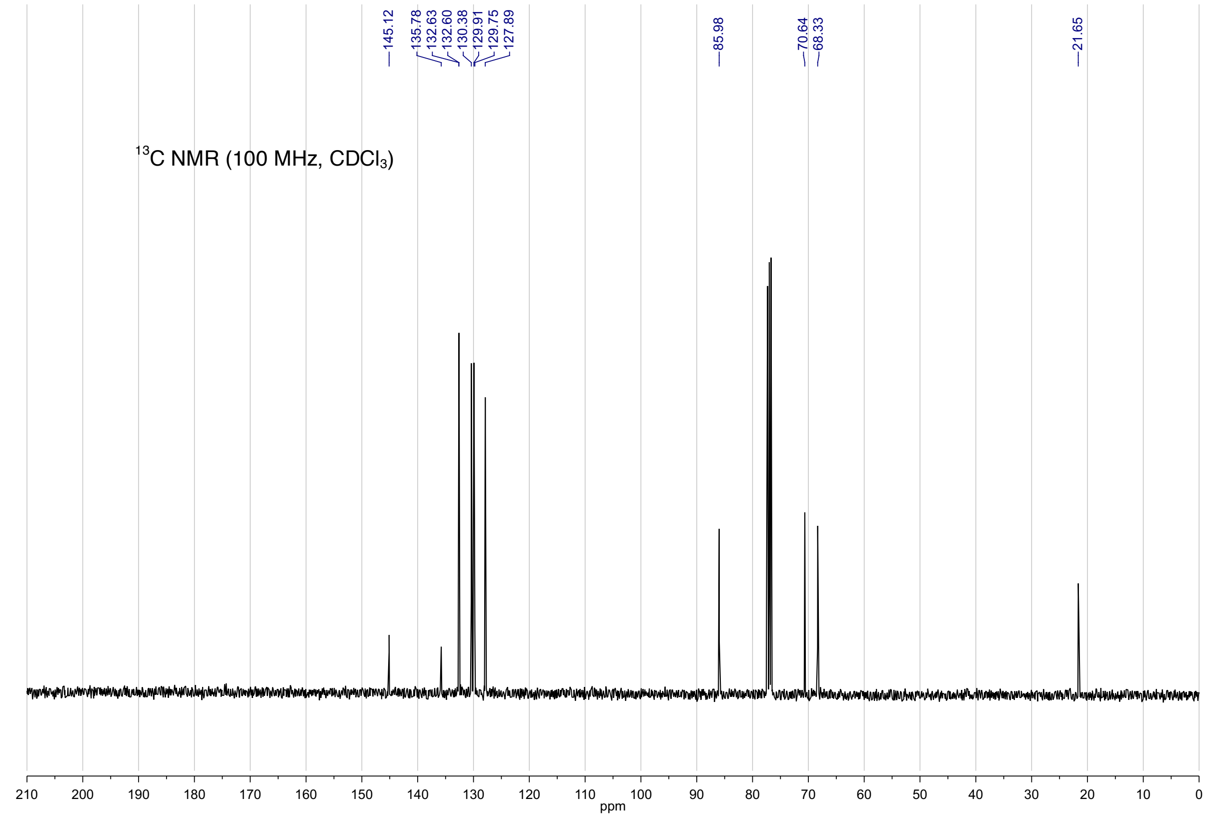
^{1}H NMR (400 MHz, CDCl$_3$)

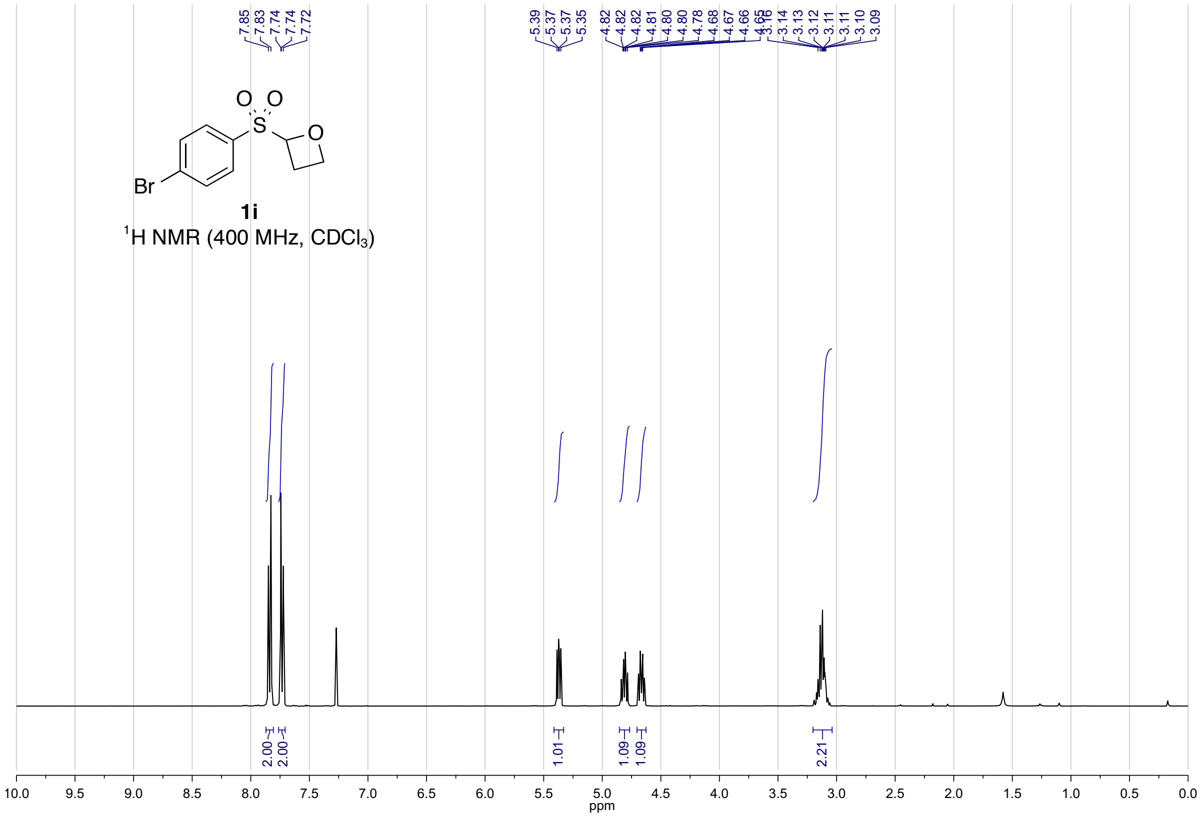


^{13}C NMR (100 MHz, CDCl$_3$)


2i

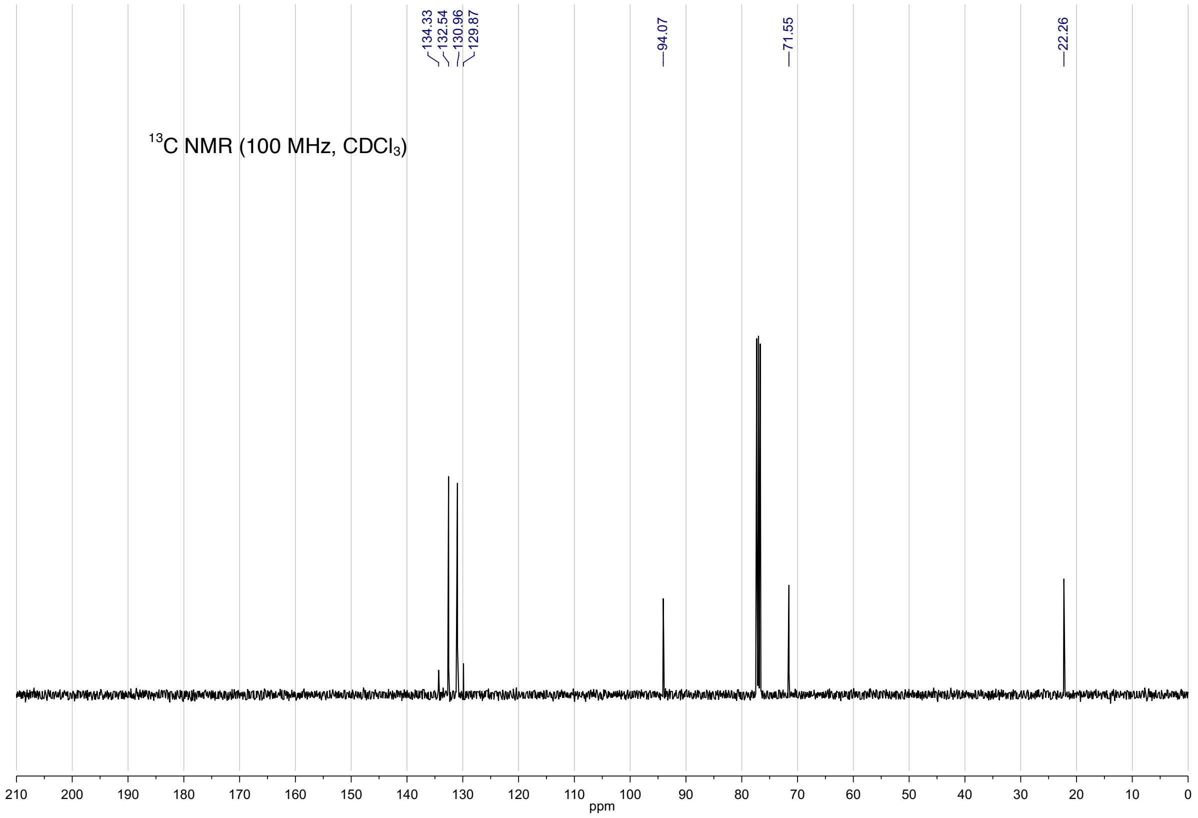
^{1}H NMR (400 MHz, CDCl$_3$)


^{13}C NMR (100 MHz, CDCl$_3$)

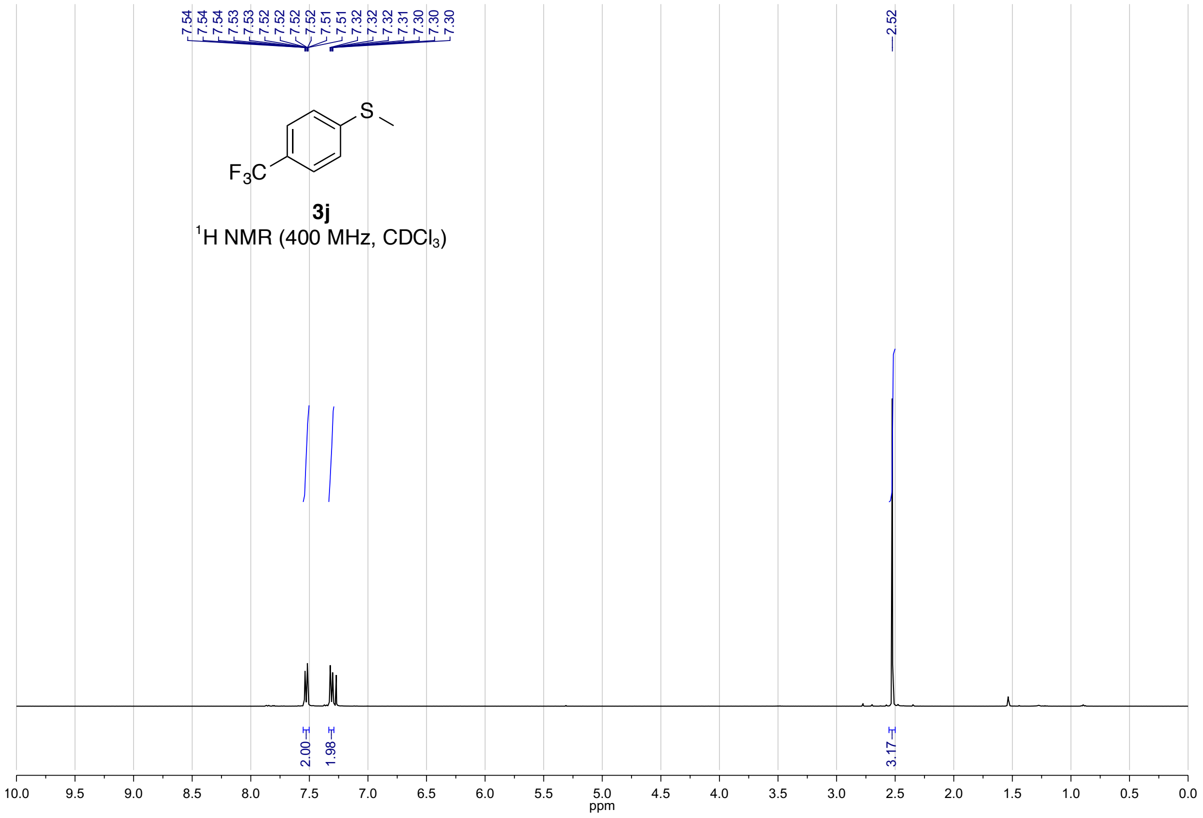


1i

^{1}H NMR (400 MHz, CDCl$_3$)

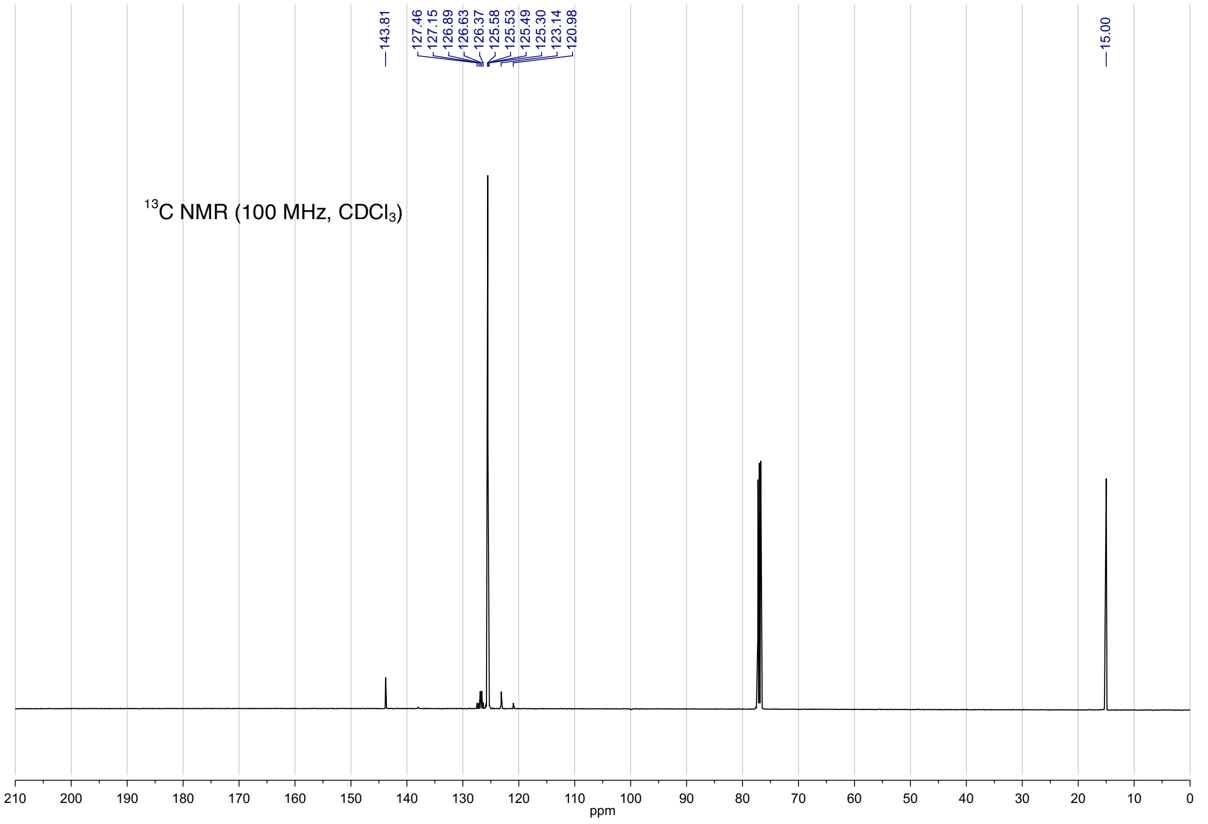


^{13}C NMR (100 MHz, CDCl$_3$)

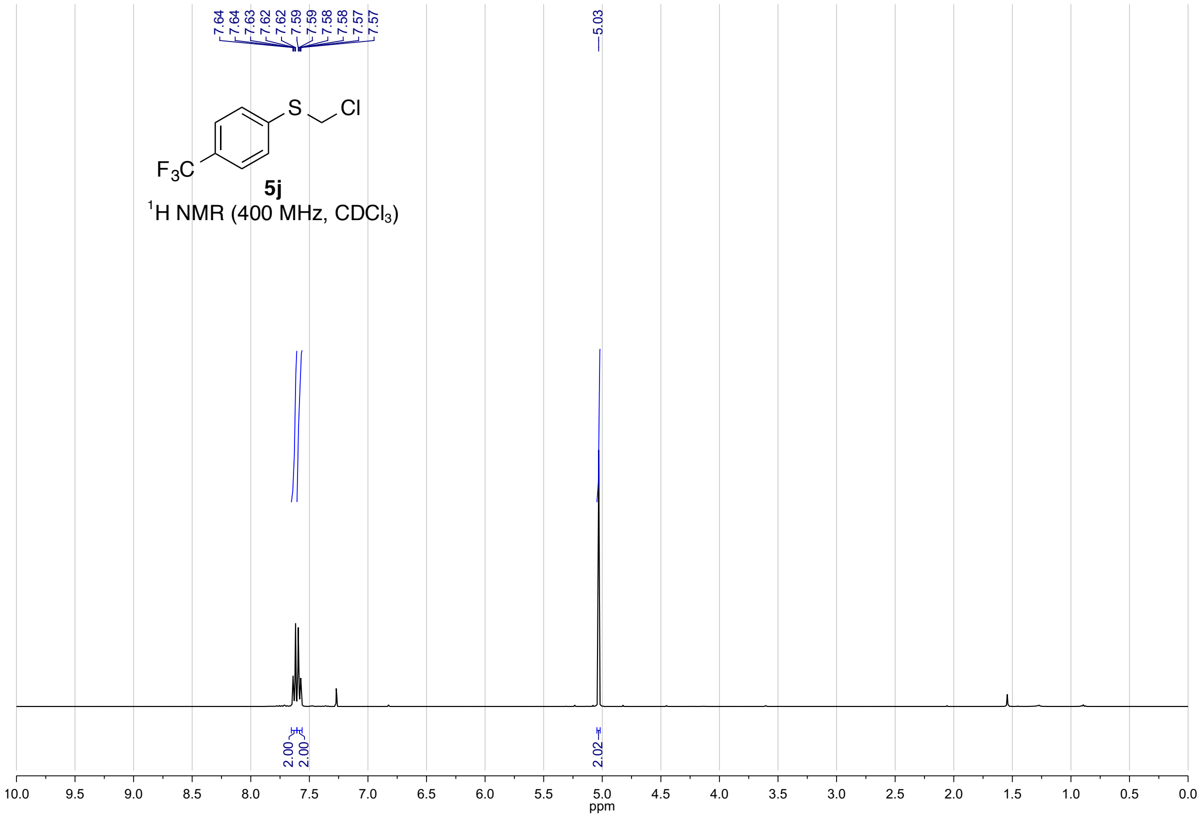


3j

^{1}H NMR (400 MHz, $CDCl_3$)

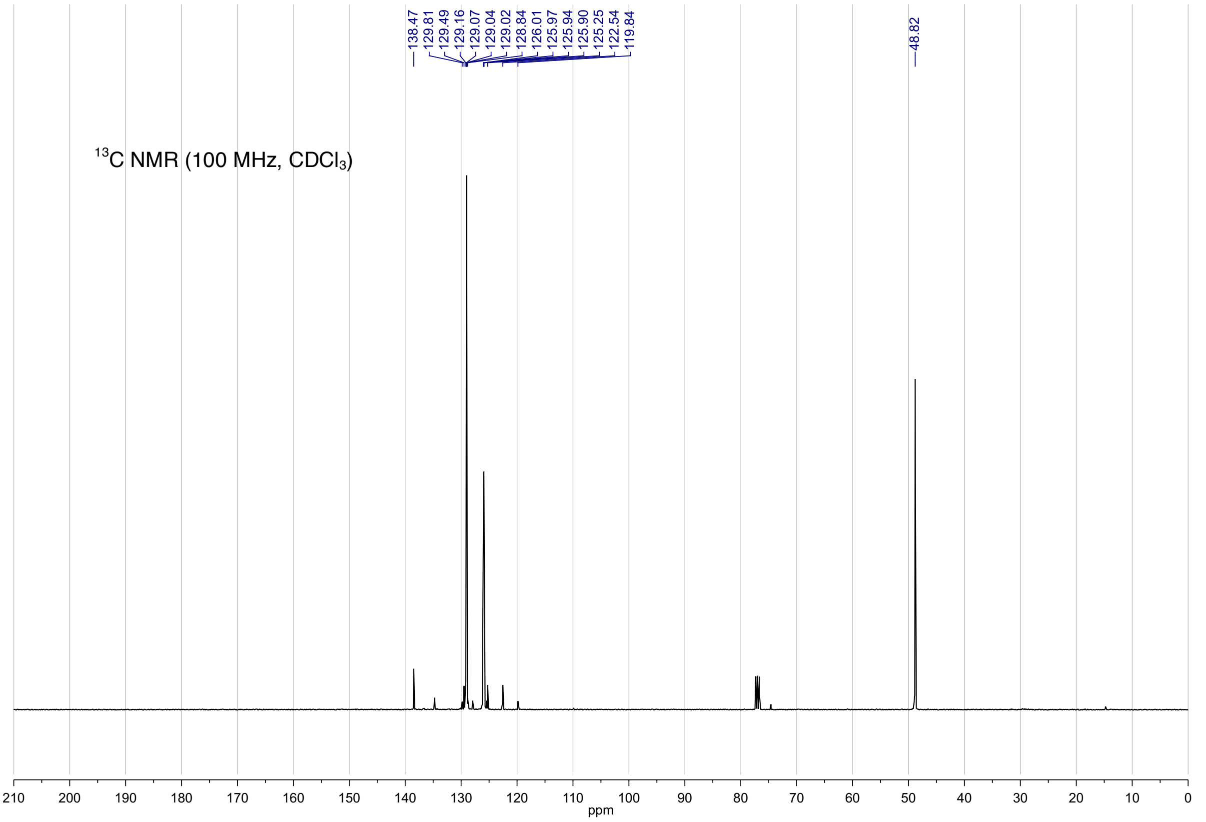


^{13}C NMR (100 MHz, $CDCl_3$)

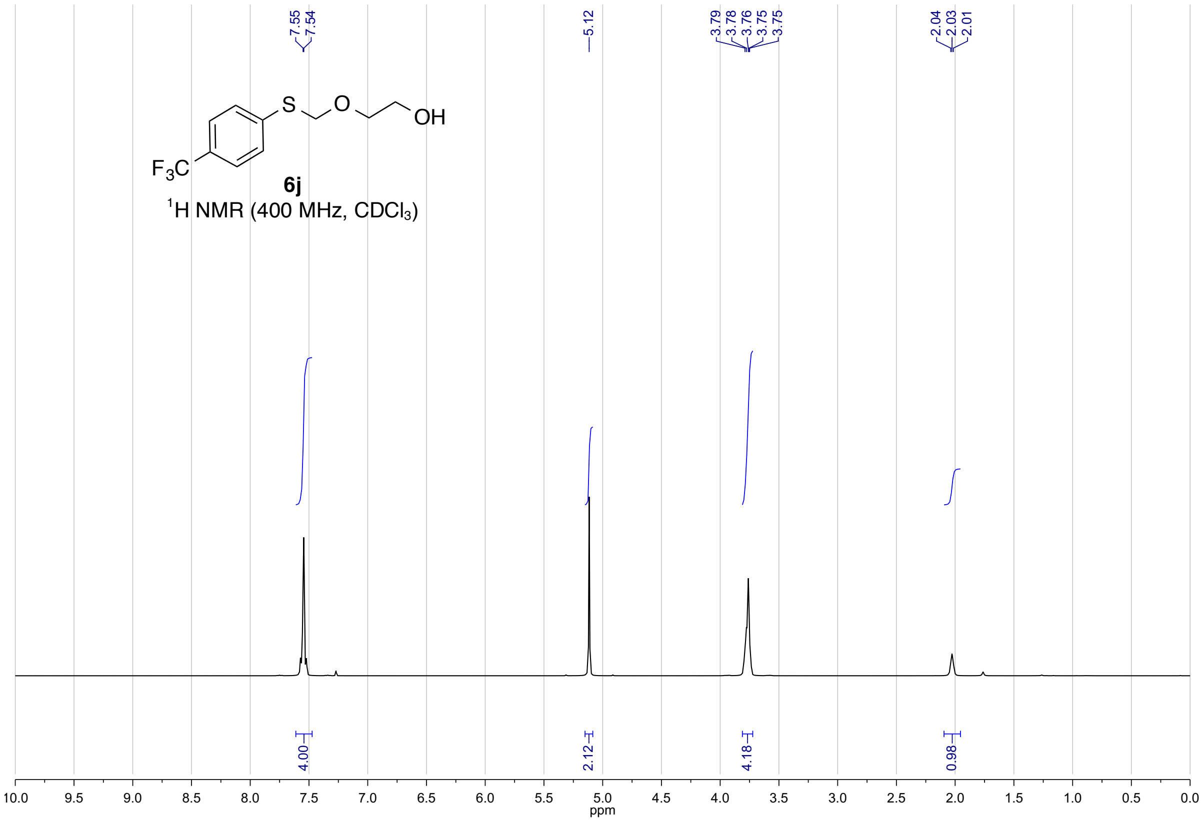


5j

^{1}H NMR (400 MHz, $CDCl_3$)

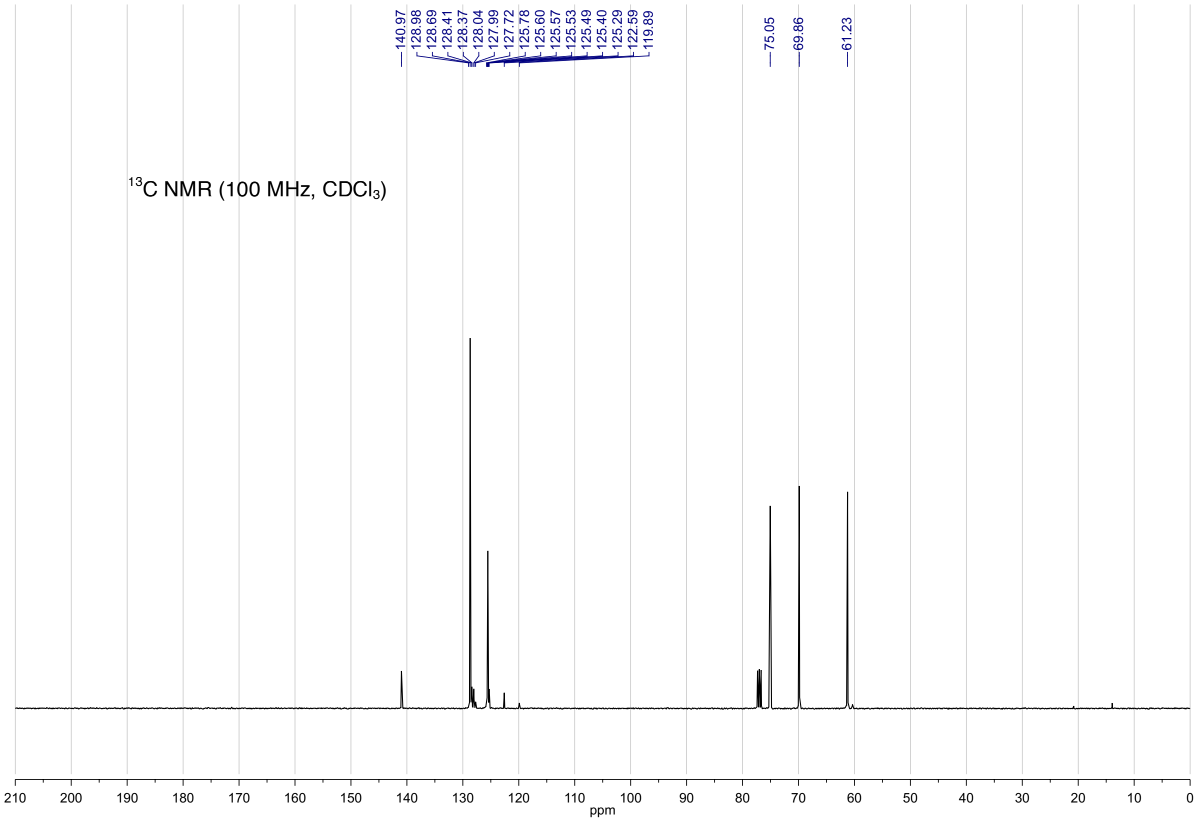


^{13}C NMR (100 MHz, $CDCl_3$)

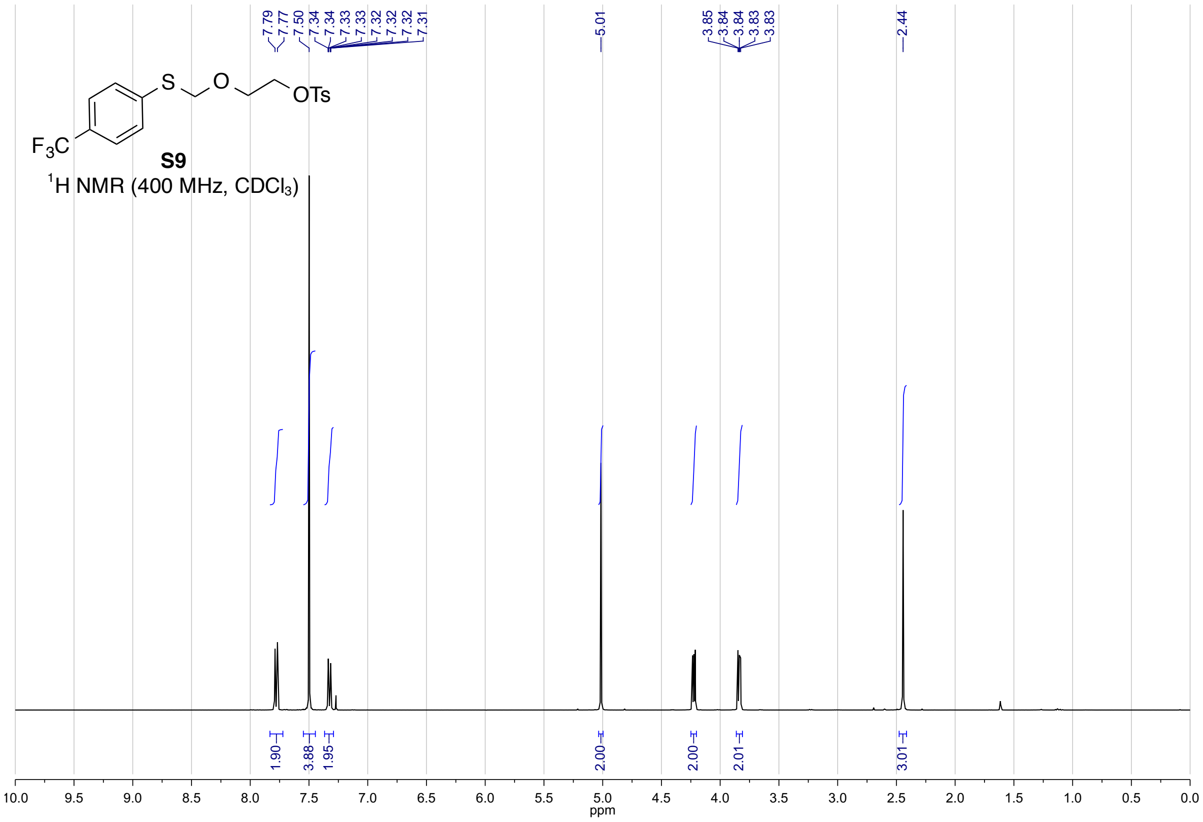


6j

^{1}H NMR (400 MHz, CDCl$_3$)

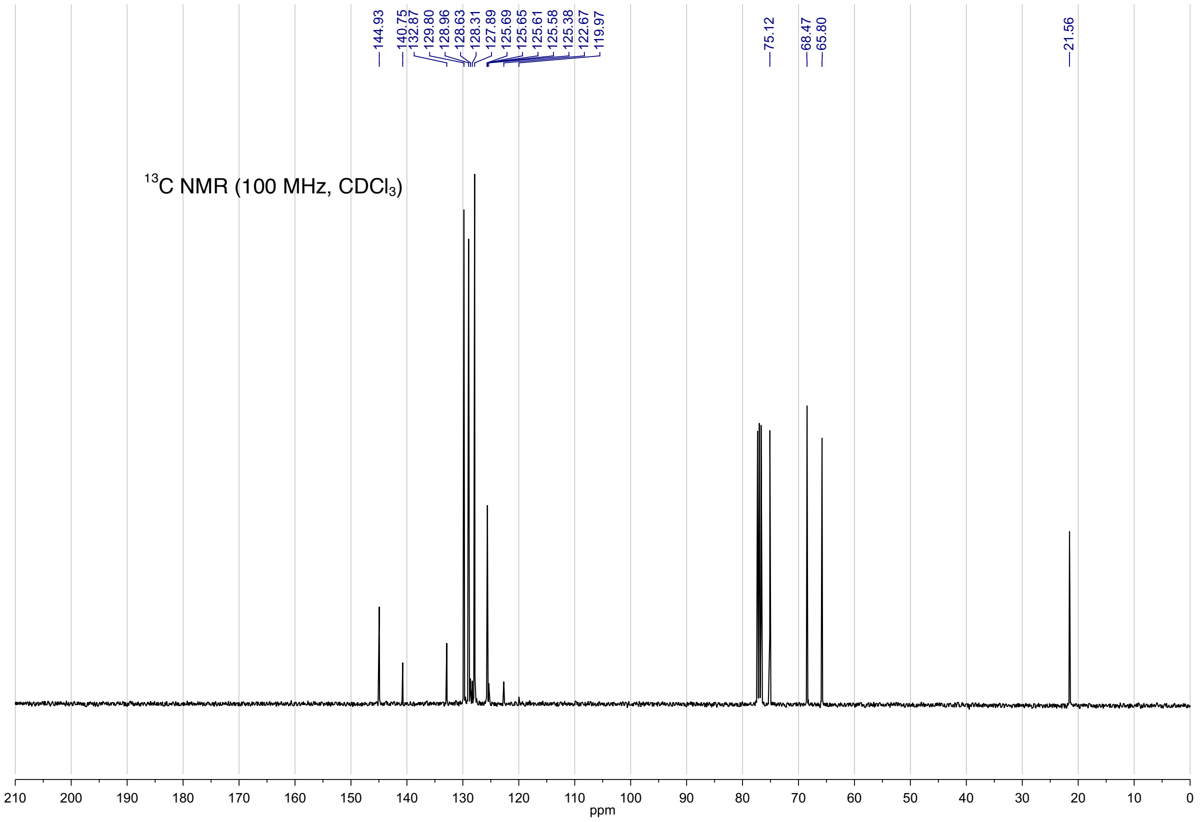


^{13}C NMR (100 MHz, CDCl$_3$)

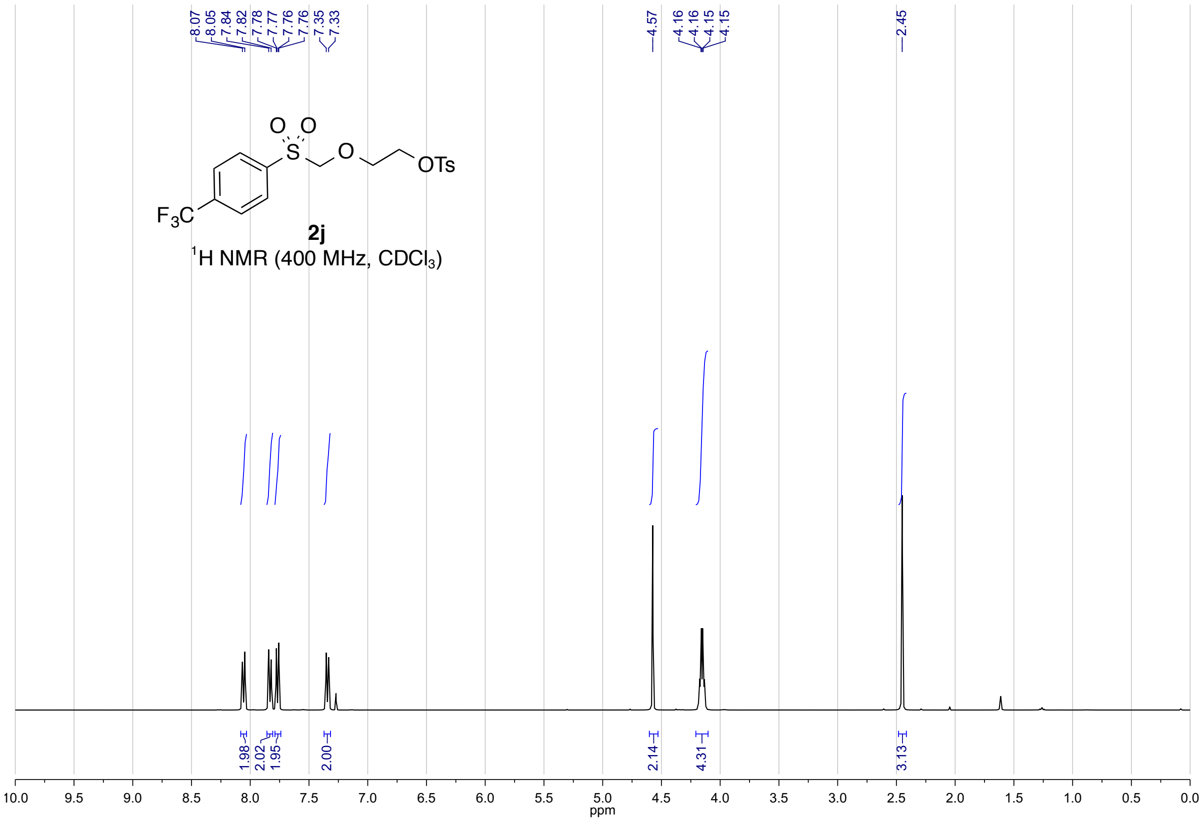


S9

^{1}H NMR (400 MHz, $CDCl_3$)

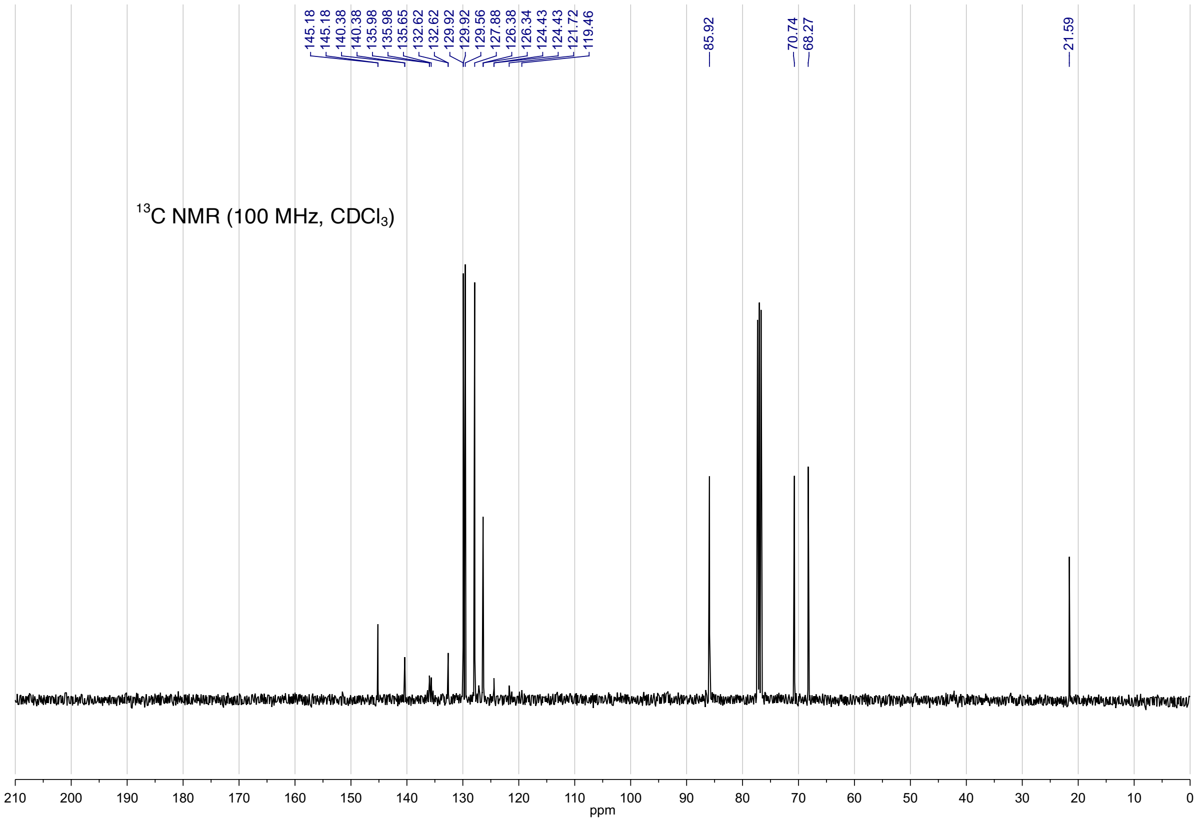


^{13}C NMR (100 MHz, $CDCl_3$)

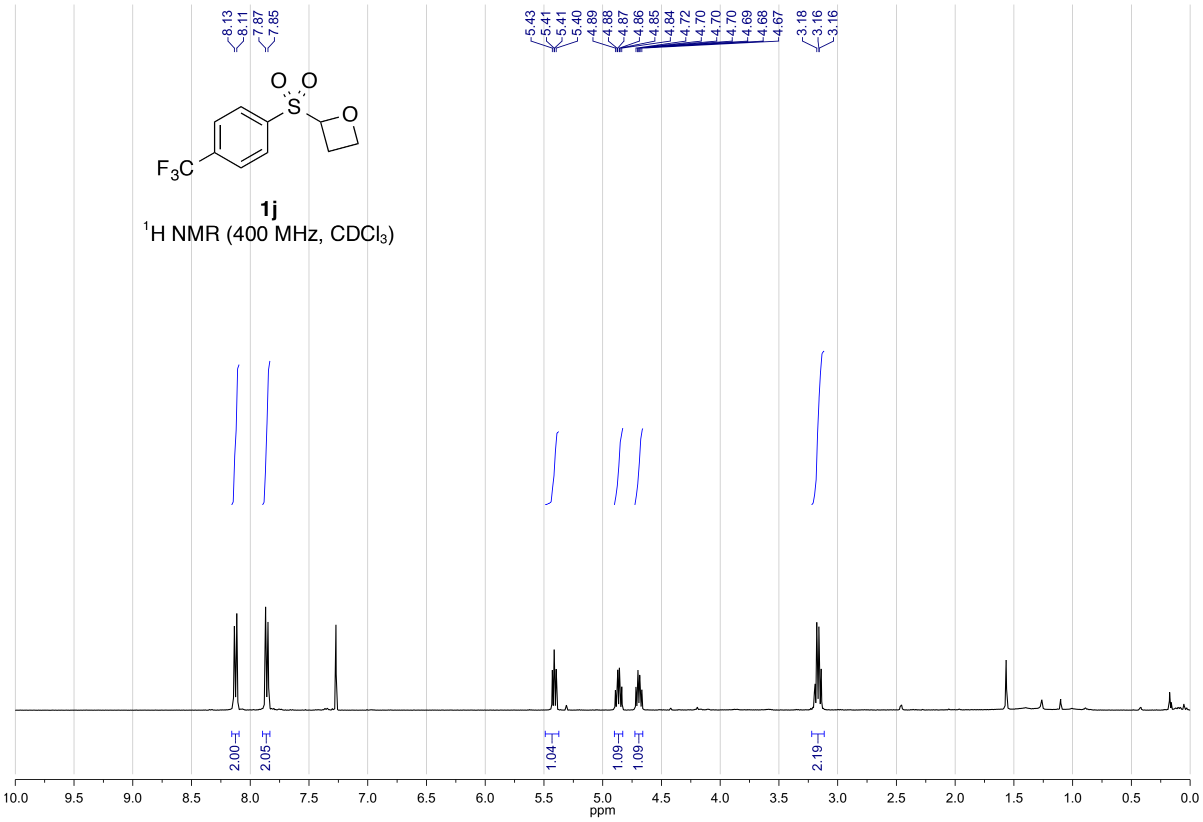


2j

^{1}H NMR (400 MHz, CDCl$_3$)

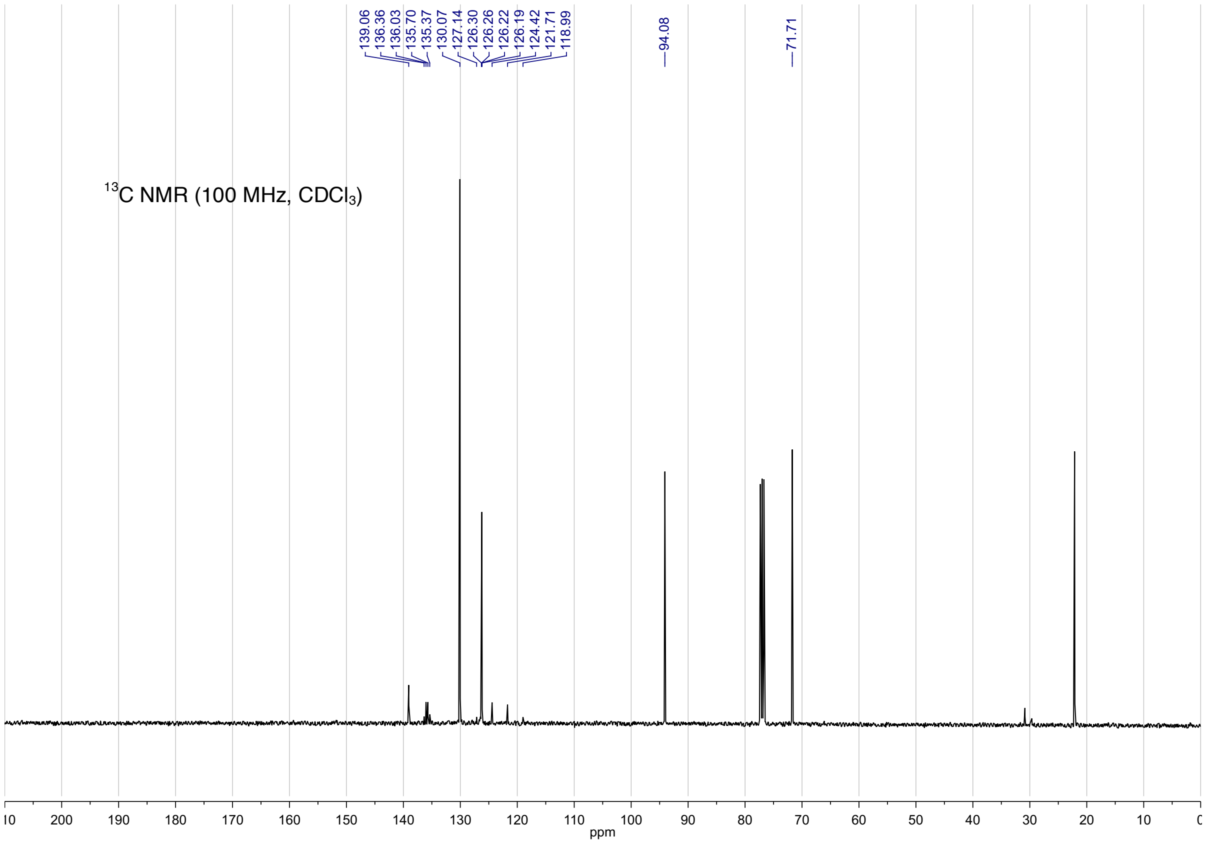


^{13}C NMR (100 MHz, CDCl$_3$)

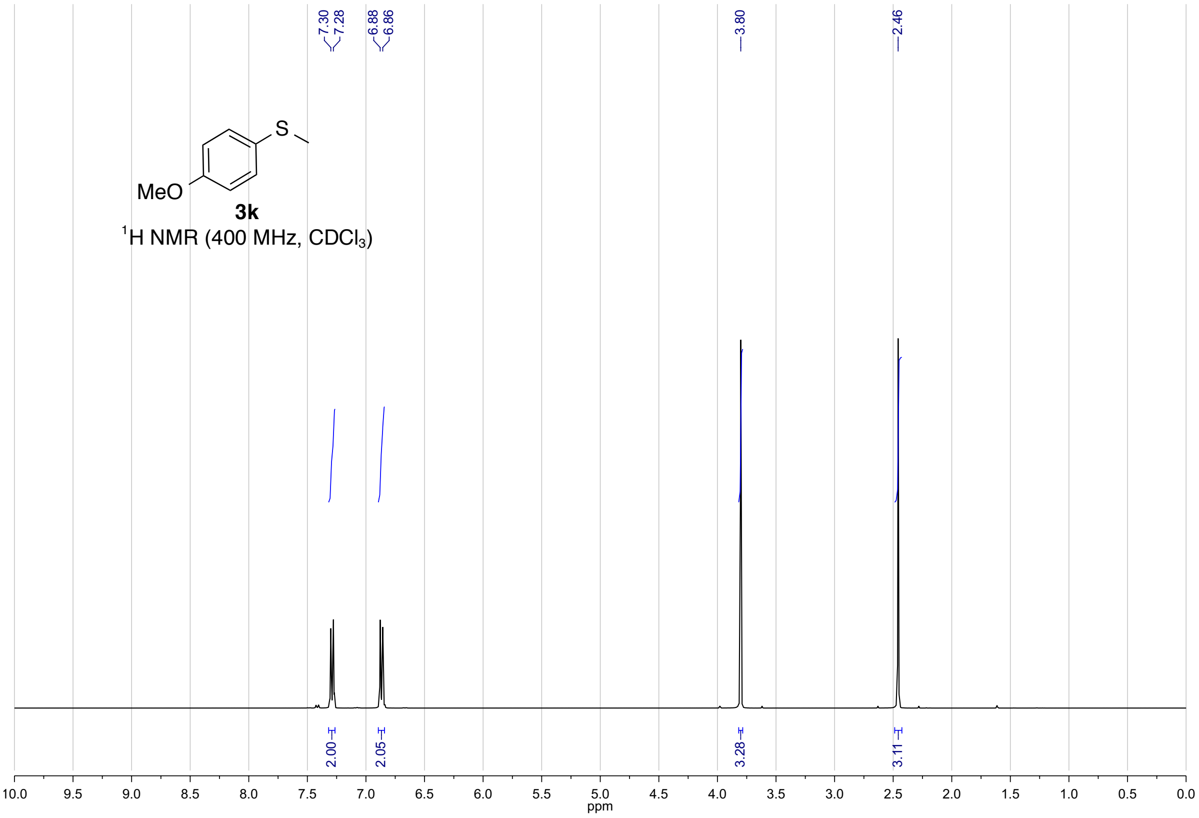


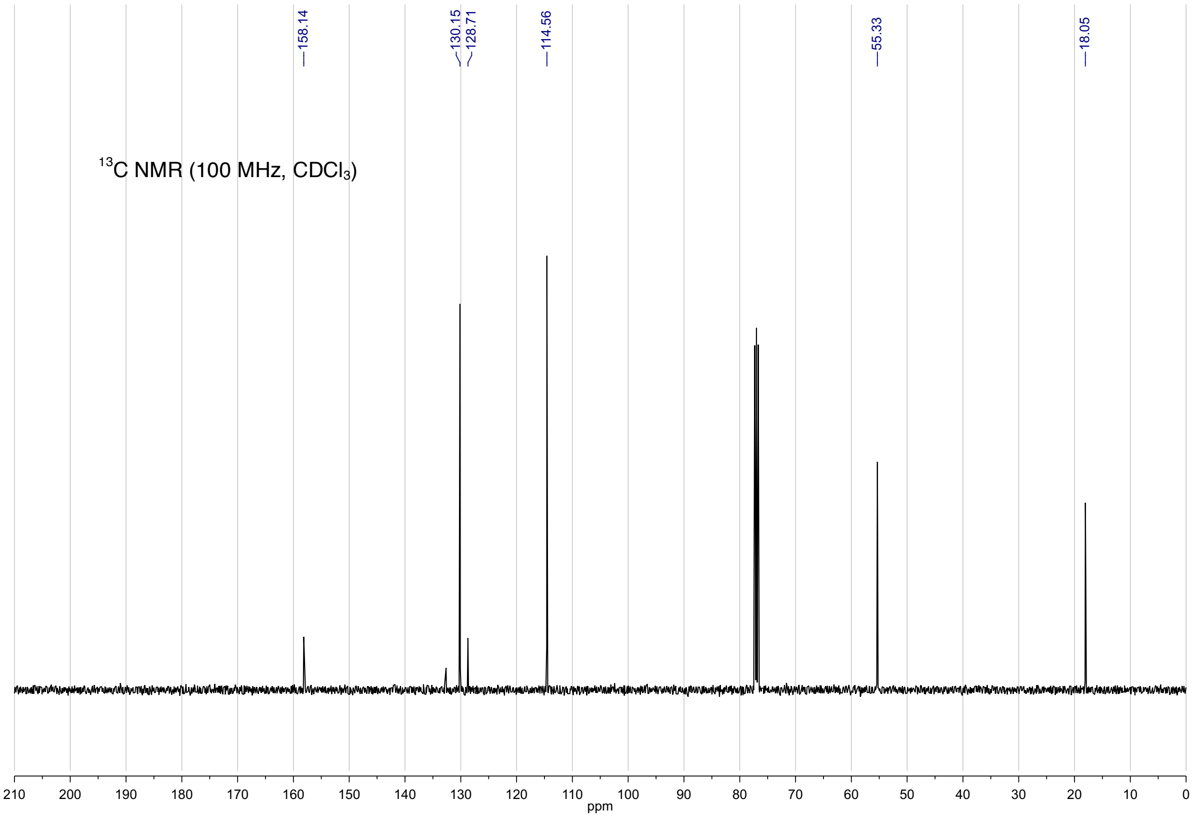
1j

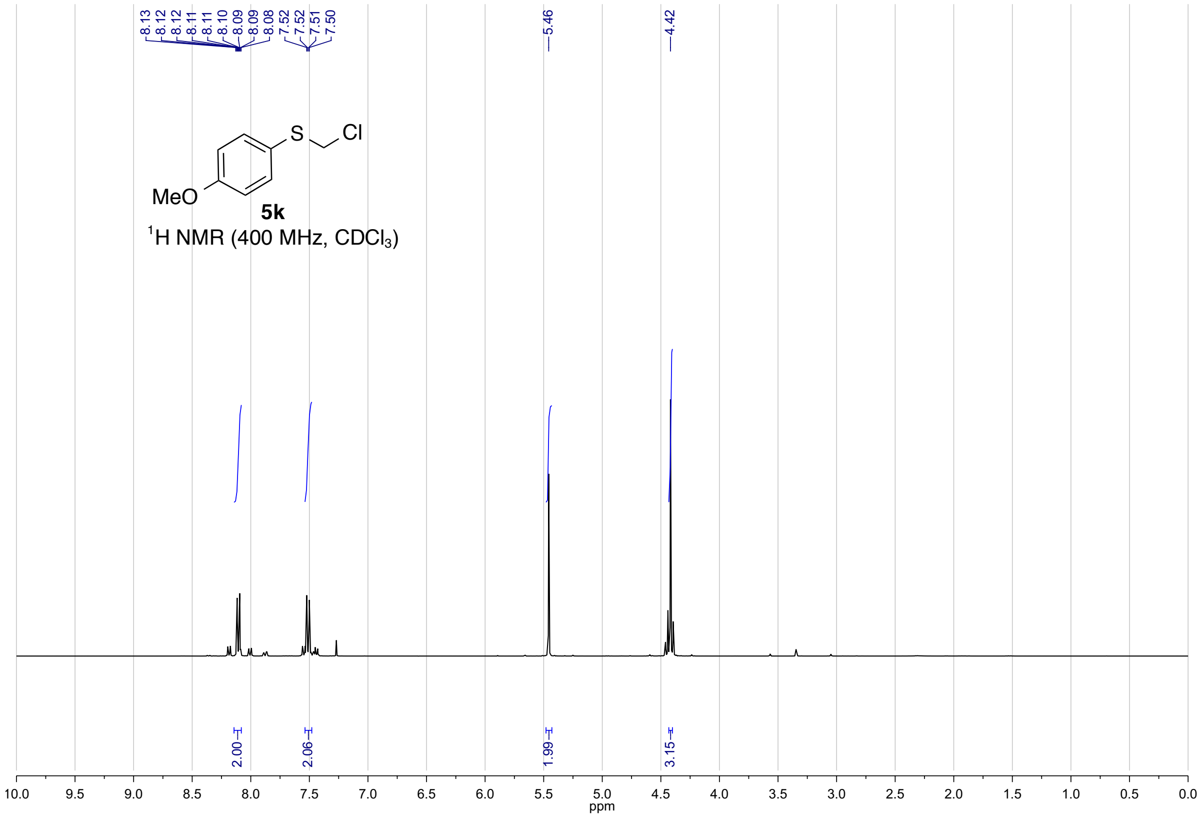
^{1}H NMR (400 MHz, CDCl$_3$)

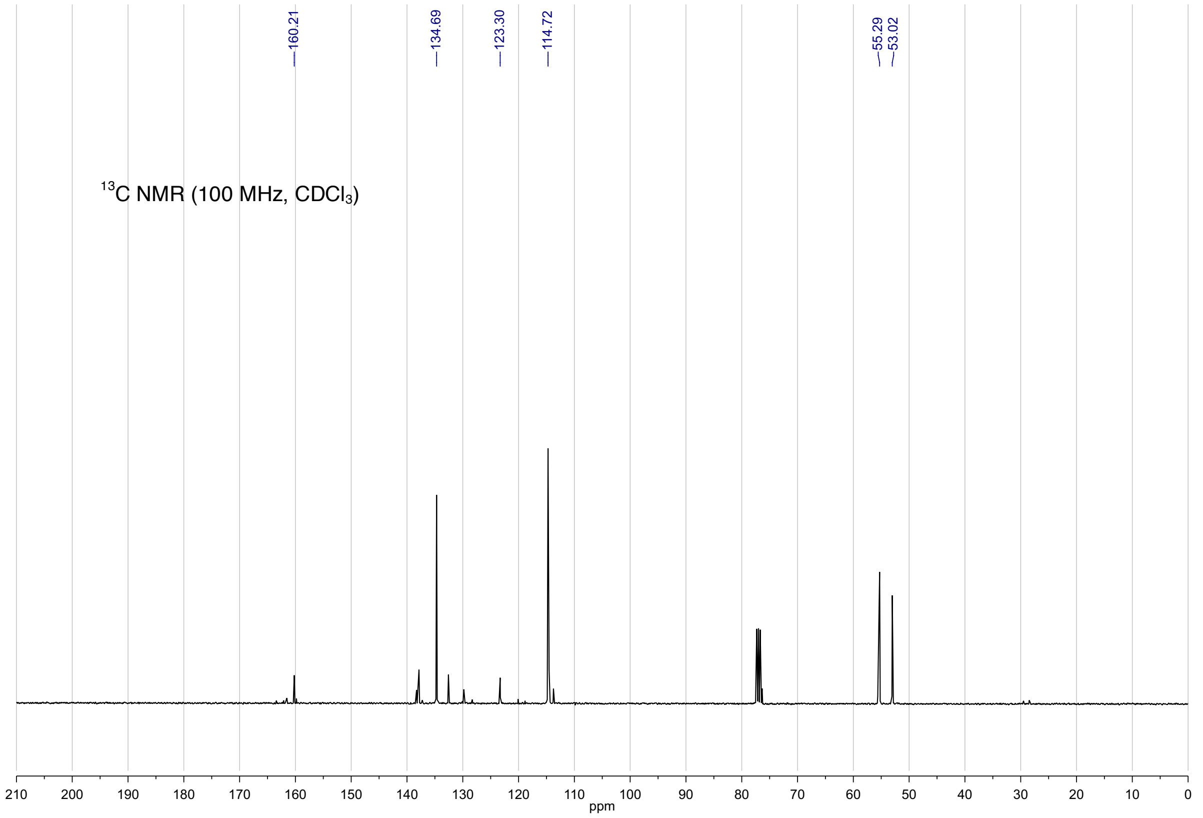


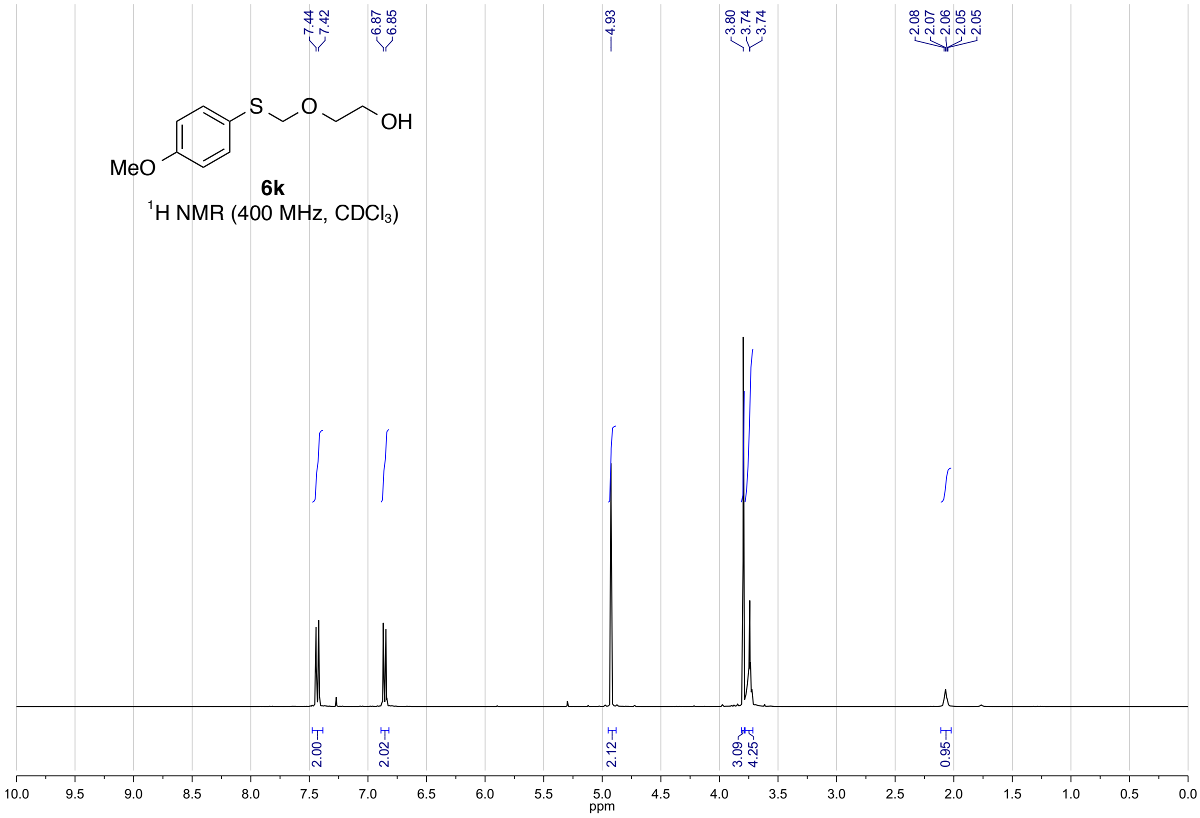
^{13}C NMR (100 MHz, CDCl$_3$)


7.30
7.28
6.88
6.86
3.80
2.46
S
MeO
3k
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
2.05
3.28
3.11
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
ppm


158.14
130.15
128.71
114.56
55.33
18.05
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

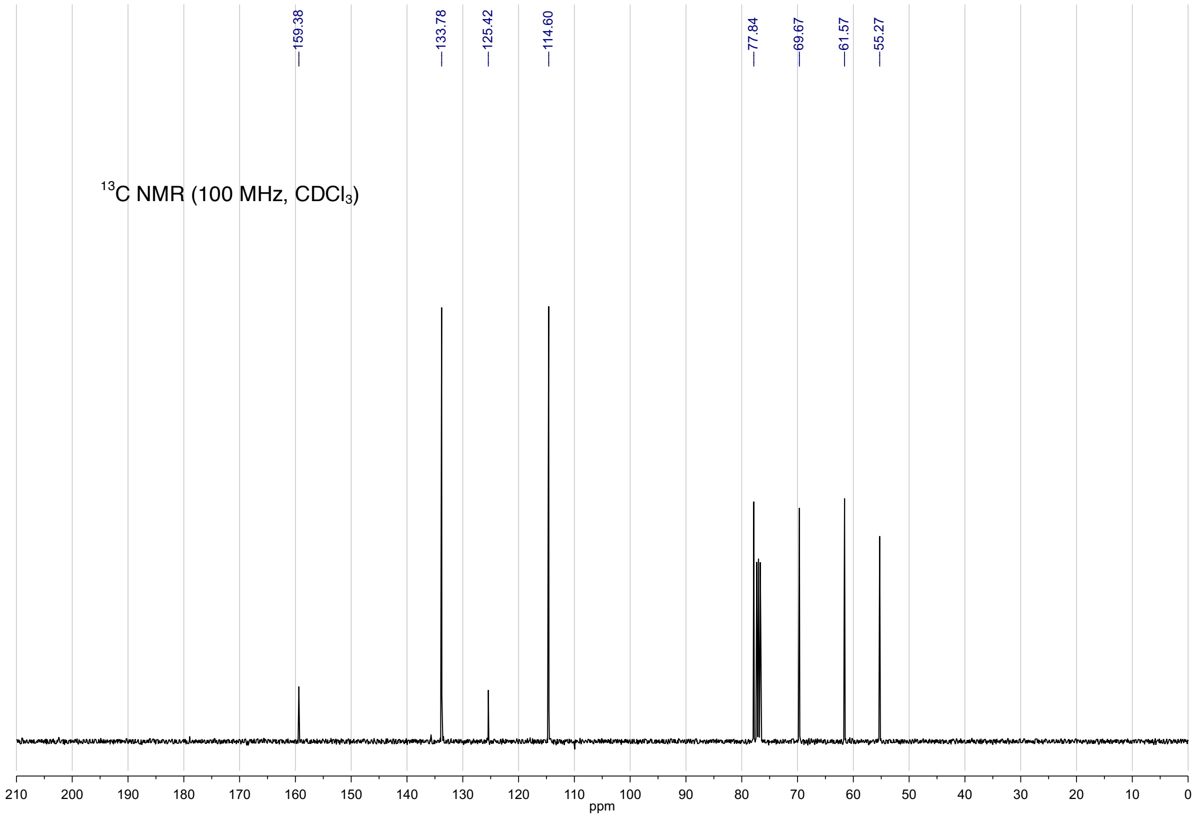

8.13
8.12
8.12
8.11
8.11
8.10
8.09
8.09
8.08
7.52
7.52
7.51
7.50
5.46
4.42
S
Cl
MeO
5k
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
2.06
1.99
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


160.21
134.69
123.30
114.72
55.29
53.02
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

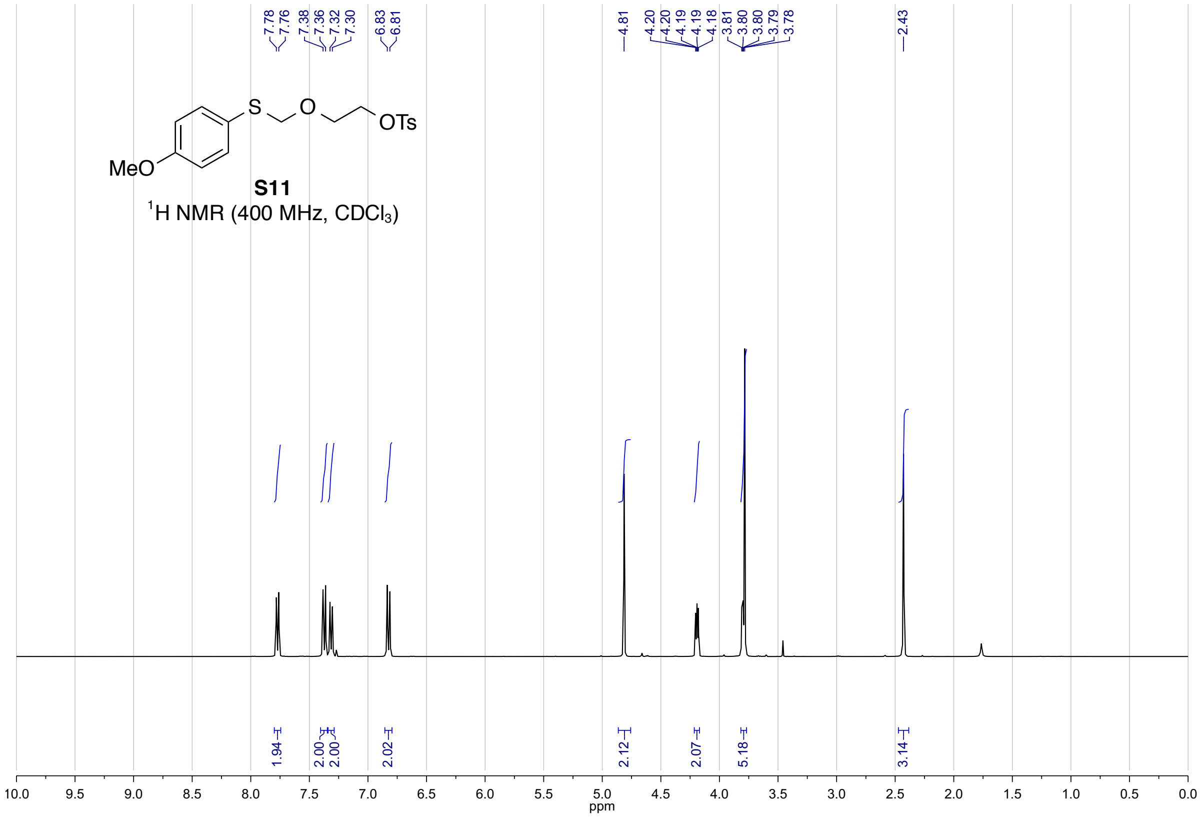


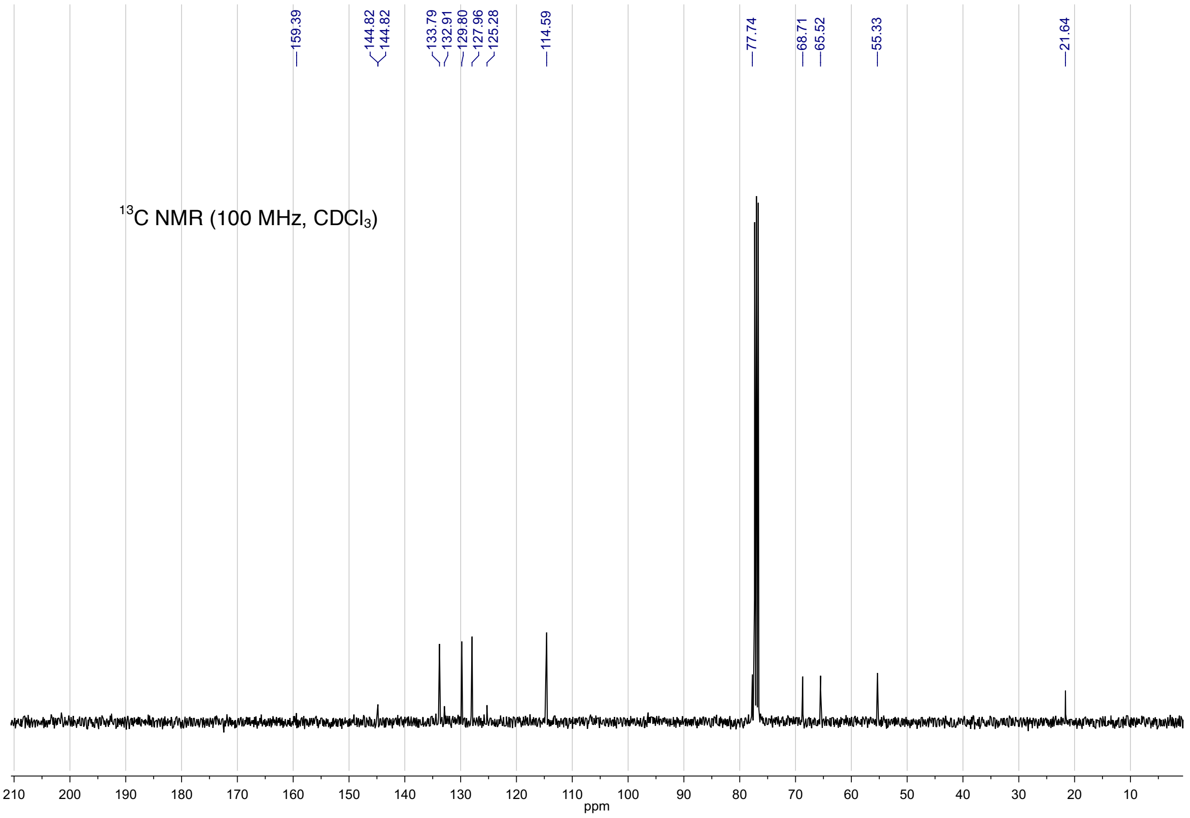
6k

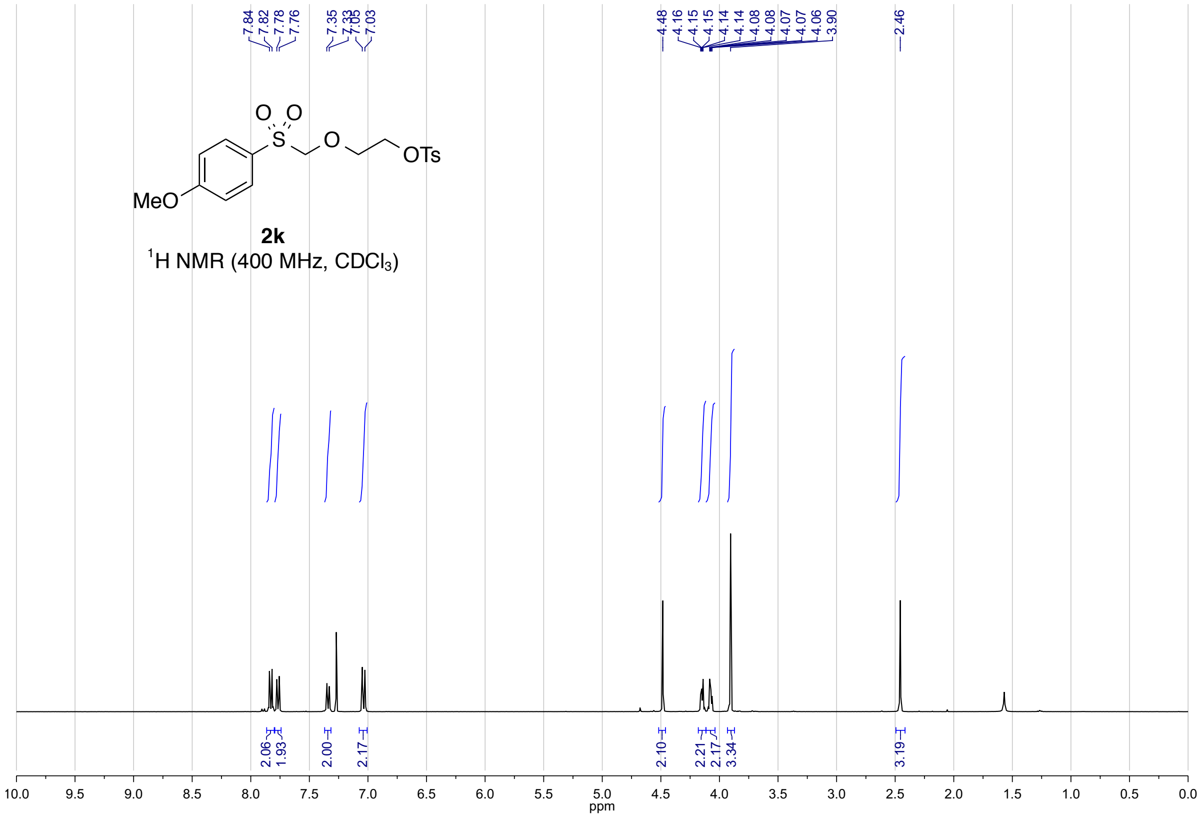
^{1}H NMR (400 MHz, CDCl$_3$)

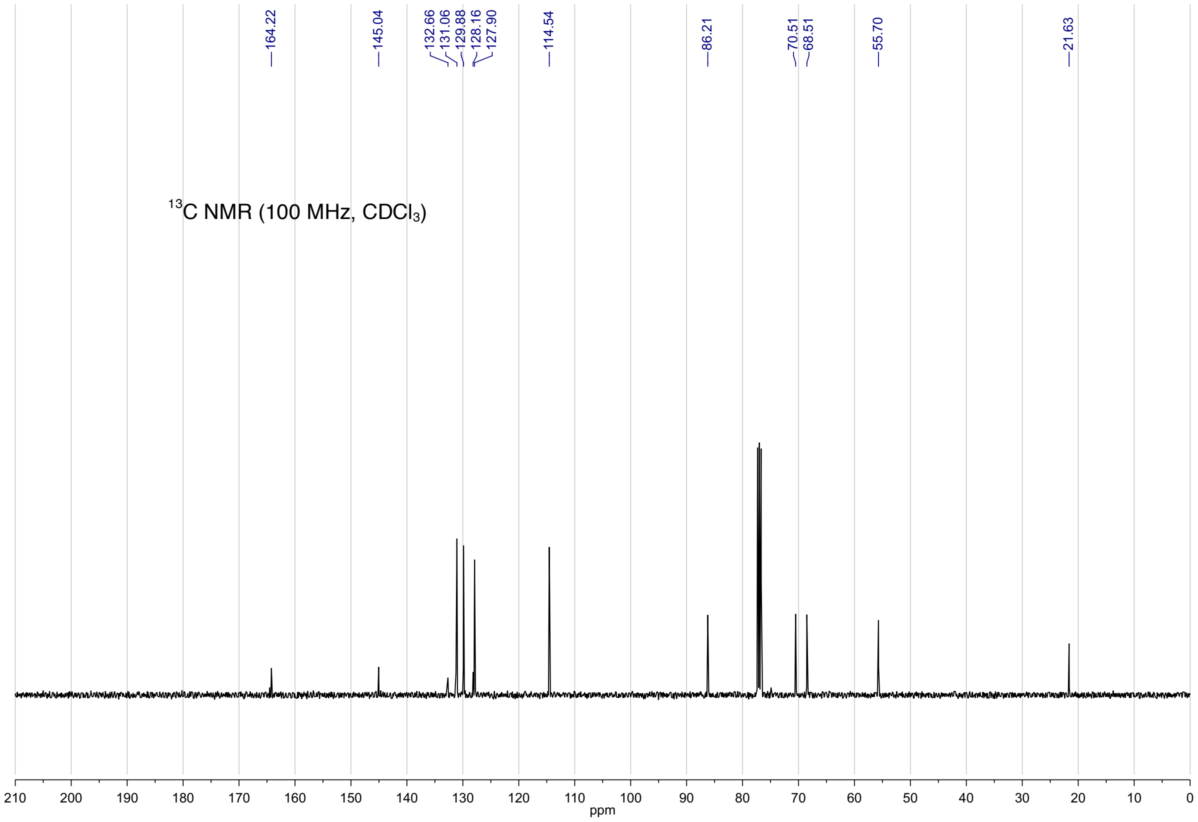


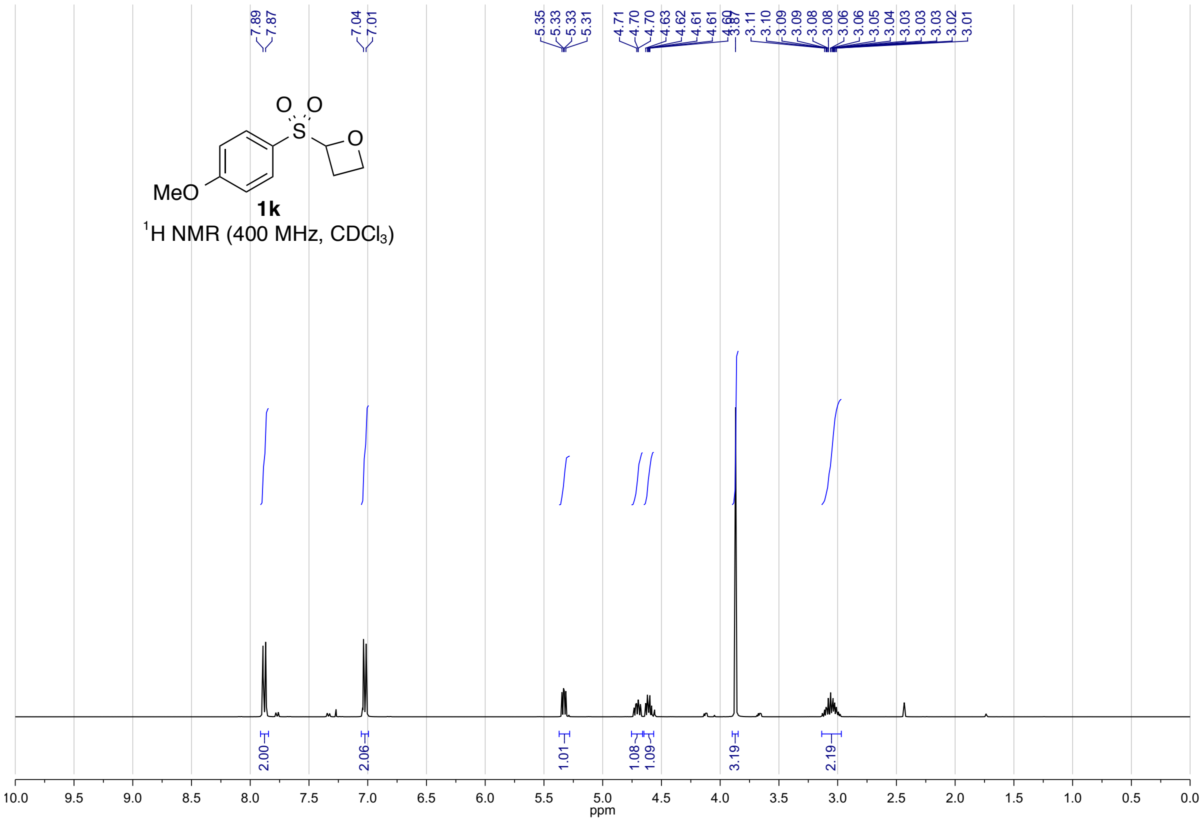
^{13}C NMR (100 MHz, CDCl$_3$)


7.78
7.76
7.38
7.36
7.32
7.30
6.83
6.81
4.81
4.20
4.20
4.19
4.19
4.18
3.81
3.80
3.80
3.79
3.78
2.43
S
O
OTs
MeO
S11
^{1}H NMR (400 MHz, CDCl$_3$)
1.94
2.00
2.00
2.02
2.12
2.07
5.18
3.14
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
ppm


159.39
144.82
144.82
133.79
132.91
129.80
127.96
125.28
114.59
77.74
68.71
65.52
55.33
21.64
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

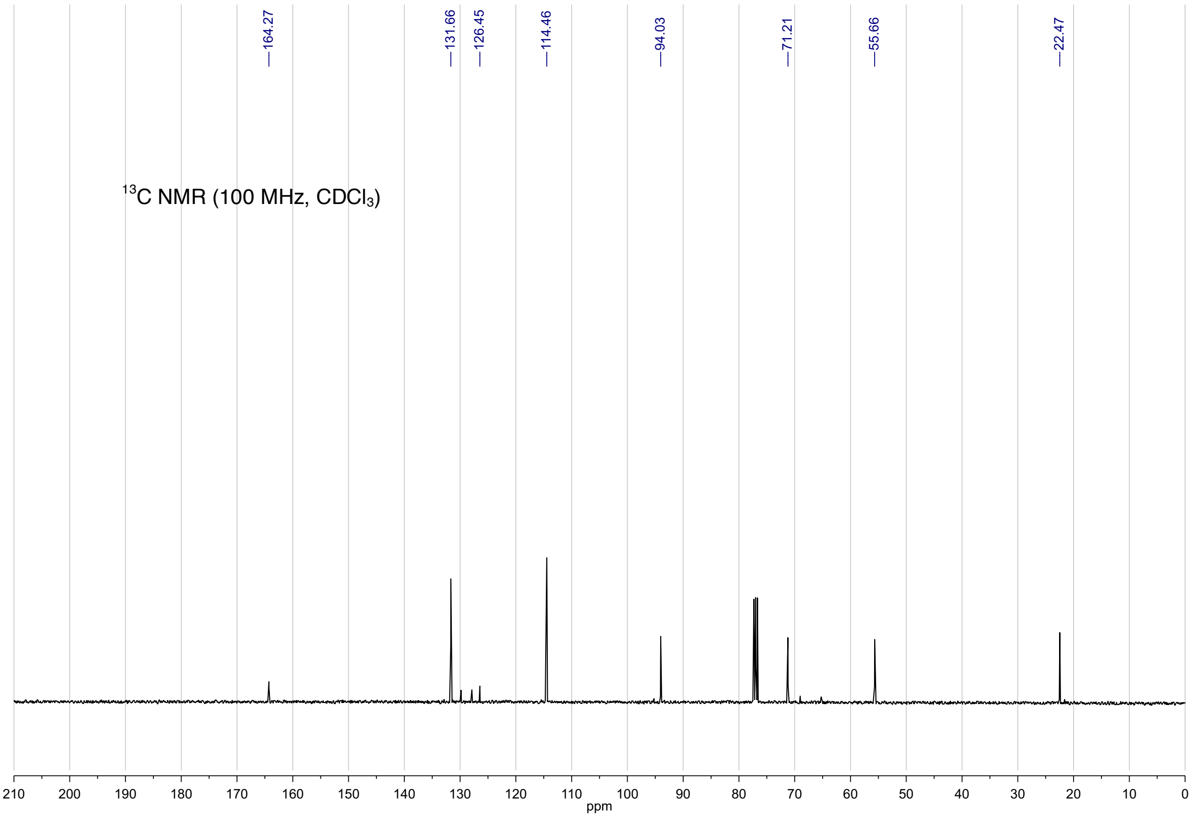

7.84
7.82
7.78
7.76
7.35
7.33
7.05
7.03
4.48
4.16
4.15
4.15
4.14
4.14
4.08
4.08
4.07
4.07
4.06
3.90
2.46
MeO
O
O
S
O
OTs
2k
^{1}H NMR (400 MHz, CDCl$_3$)
2.06
1.93
2.00
2.17
2.10
2.21
2.17
3.34
3.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


164.22
145.04
132.66
131.06
129.88
128.16
127.90
114.54
86.21
70.51
68.51
55.70
21.63
^{13}C NMR (100 MHz, CDCl$_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

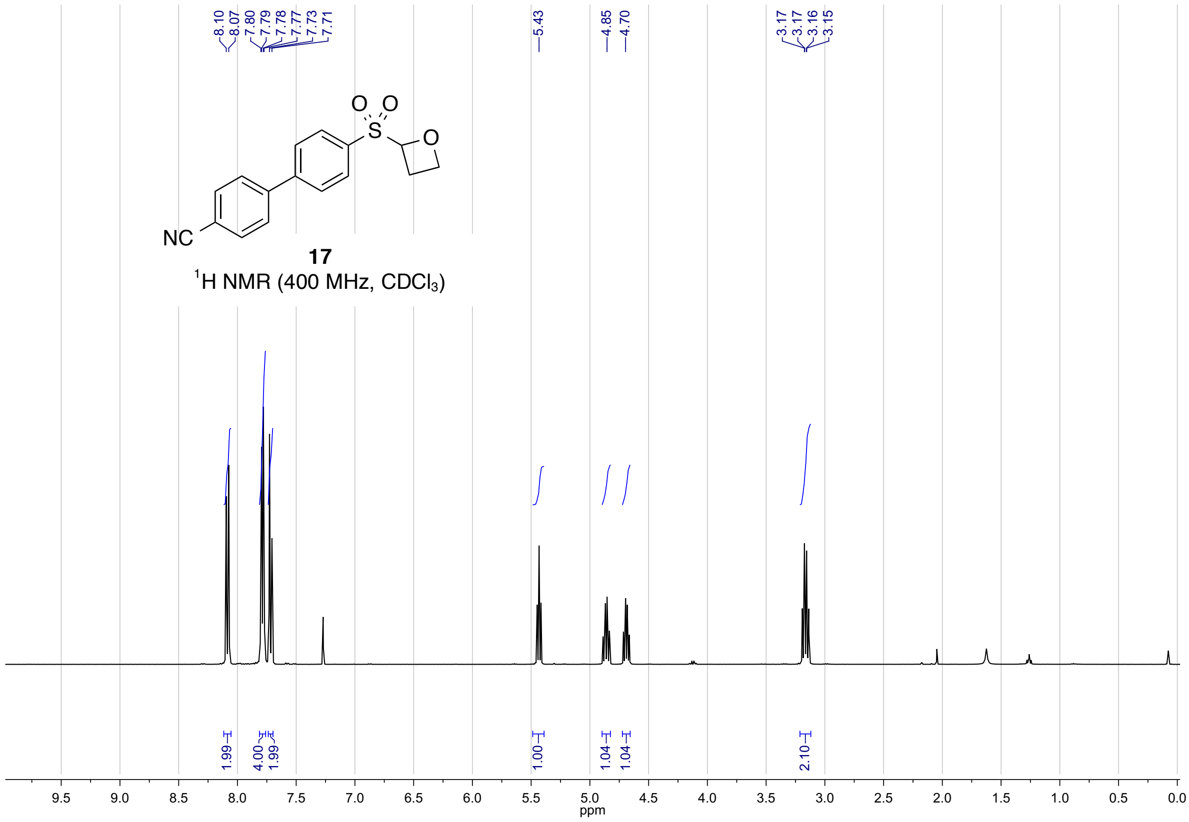


1k

^{1}H NMR (400 MHz, CDCl$_3$)

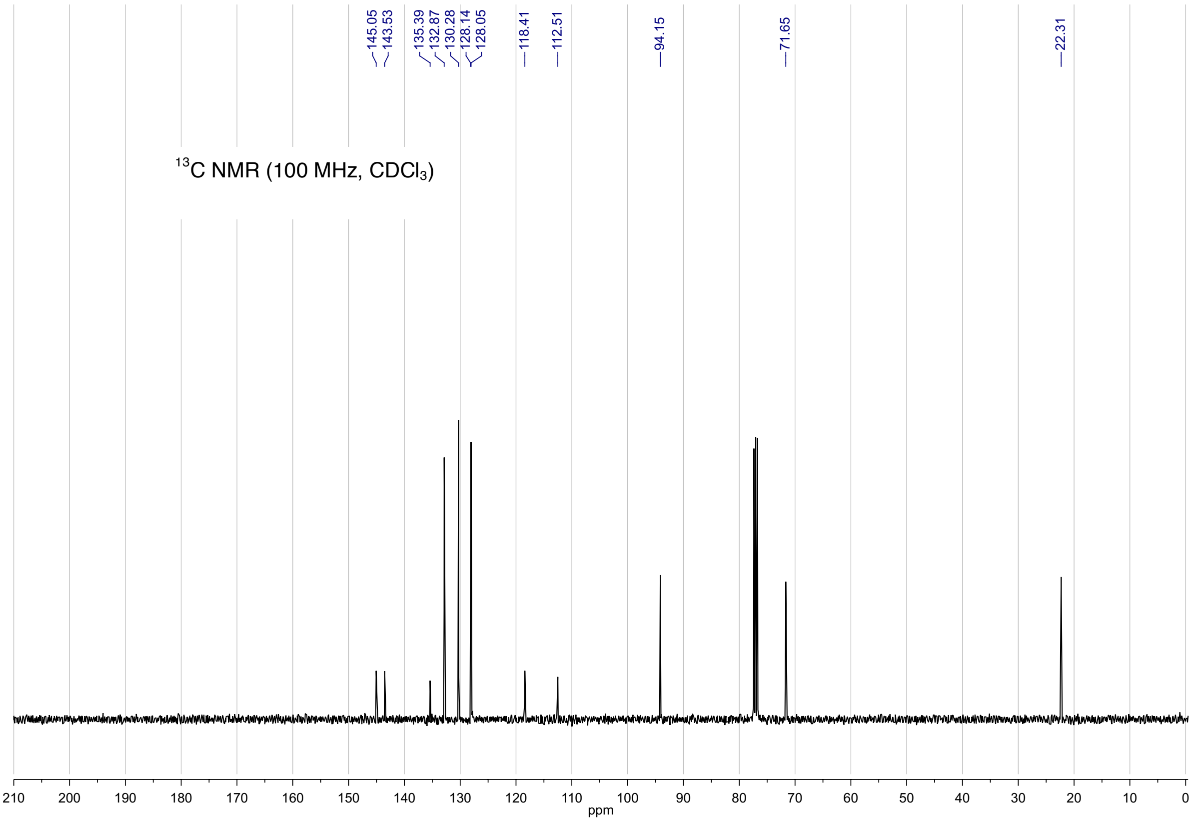


^{13}C NMR (100 MHz, CDCl$_3$)

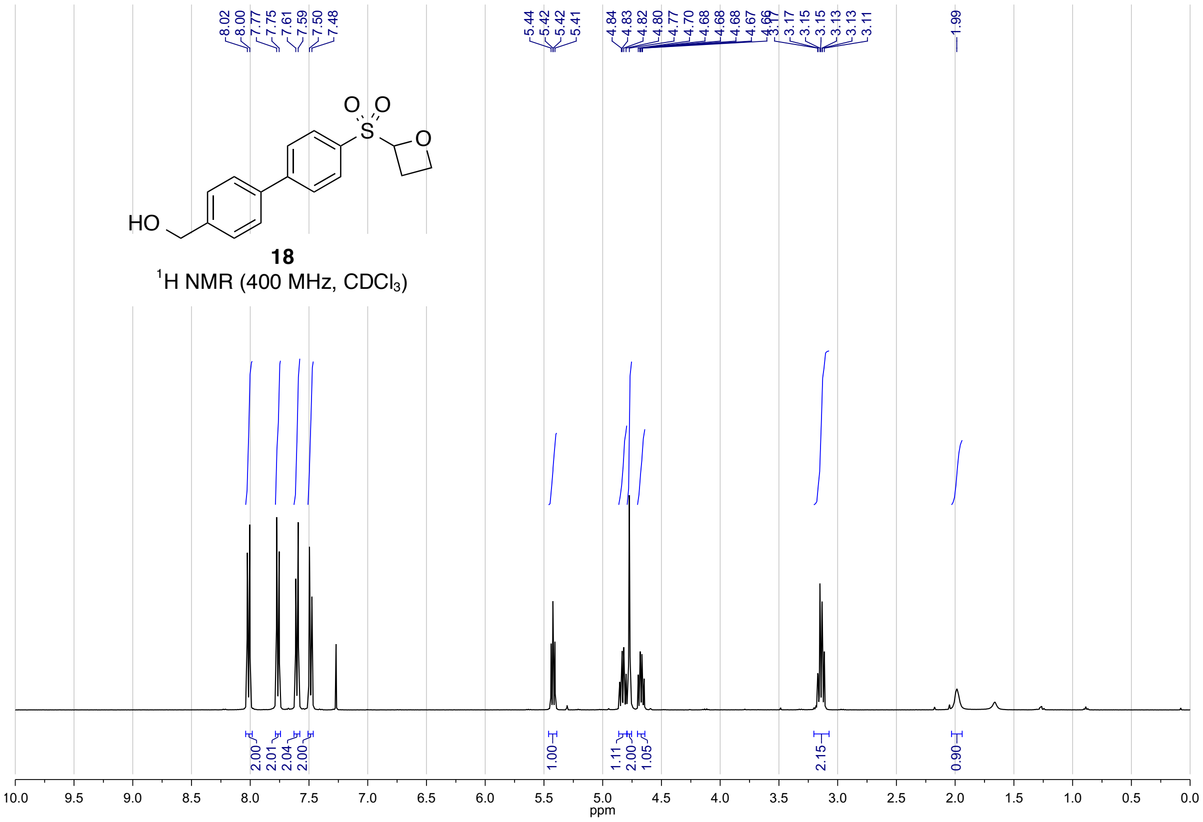


17

^{1}H NMR (400 MHz, $CDCl_3$)

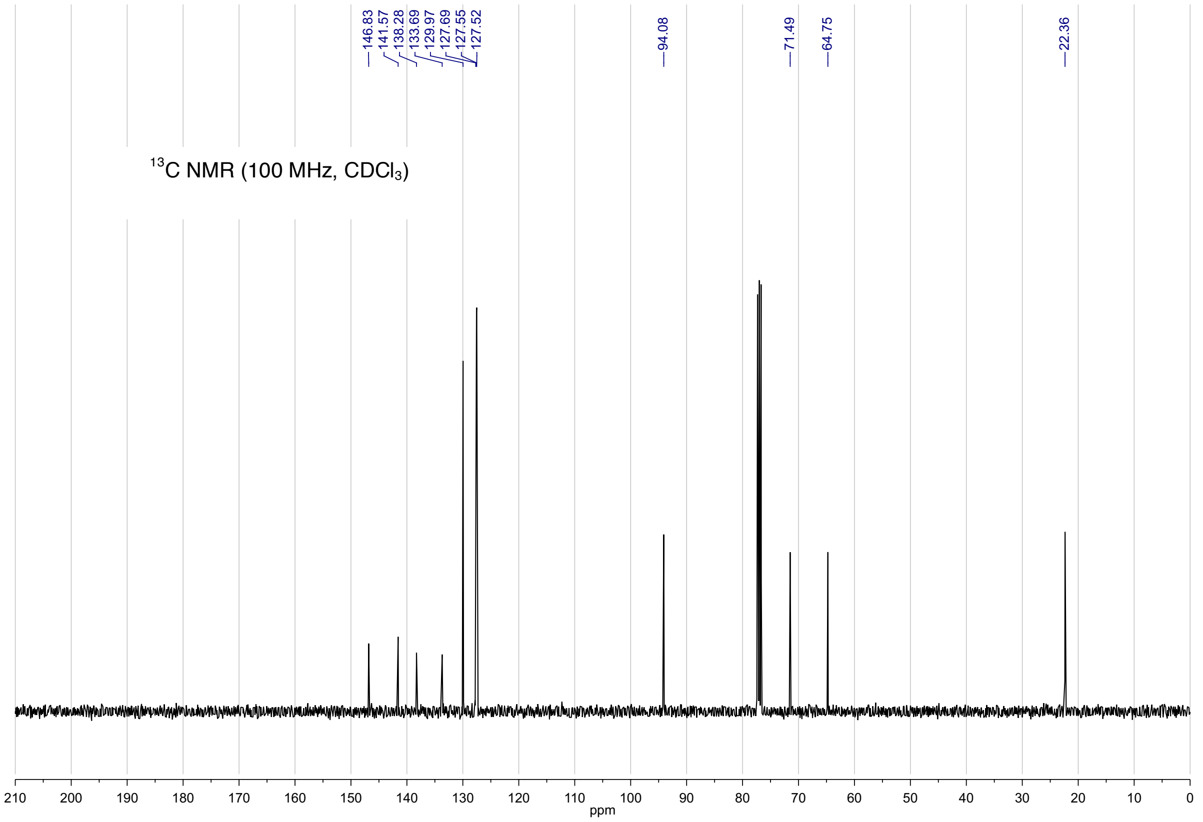


^{13}C NMR (100 MHz, $CDCl_3$)

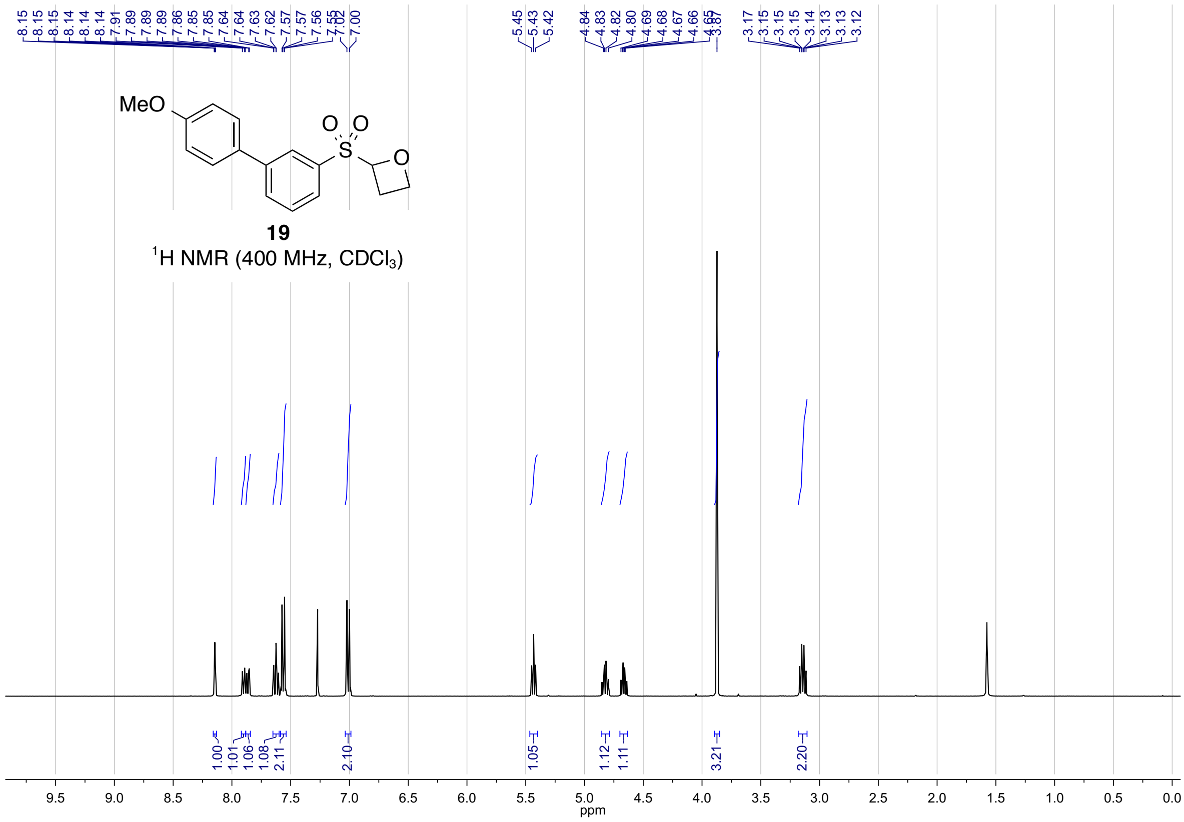


18

^{1}H NMR (400 MHz, CDCl$_3$)

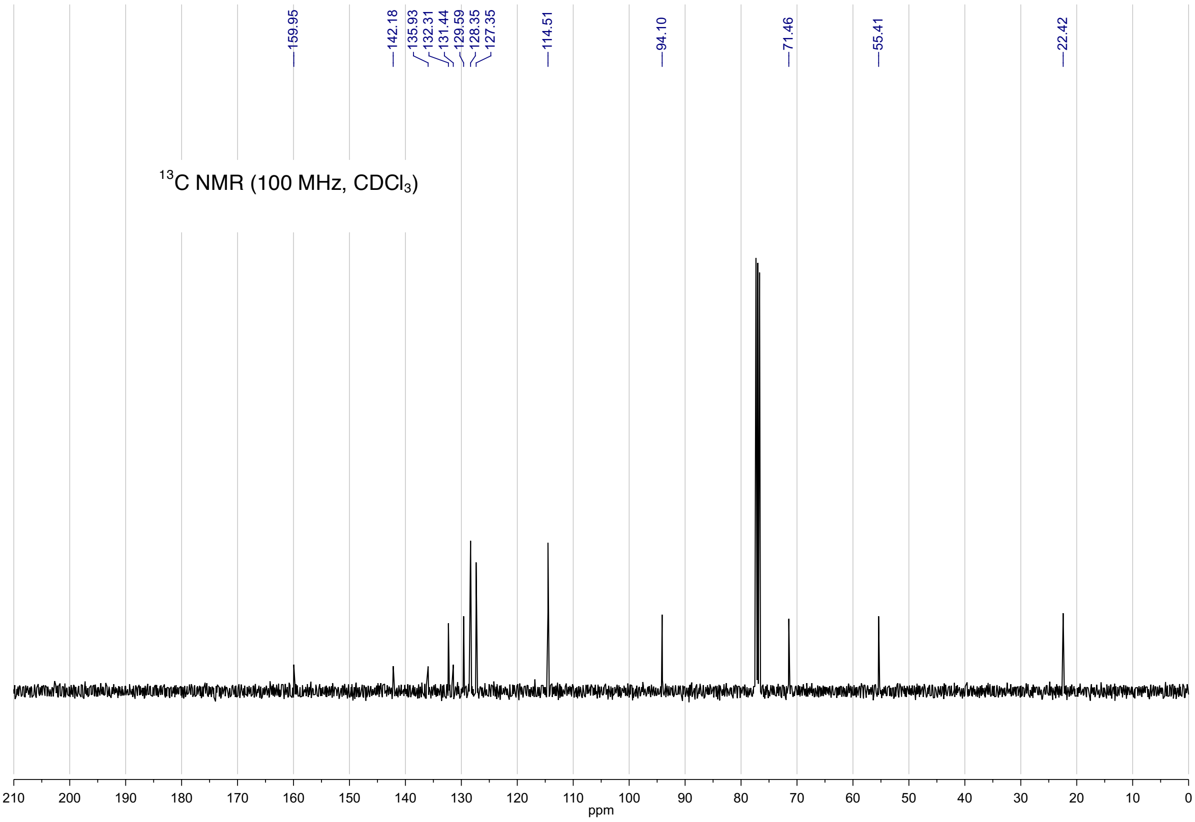


^{13}C NMR (100 MHz, CDCl$_3$)

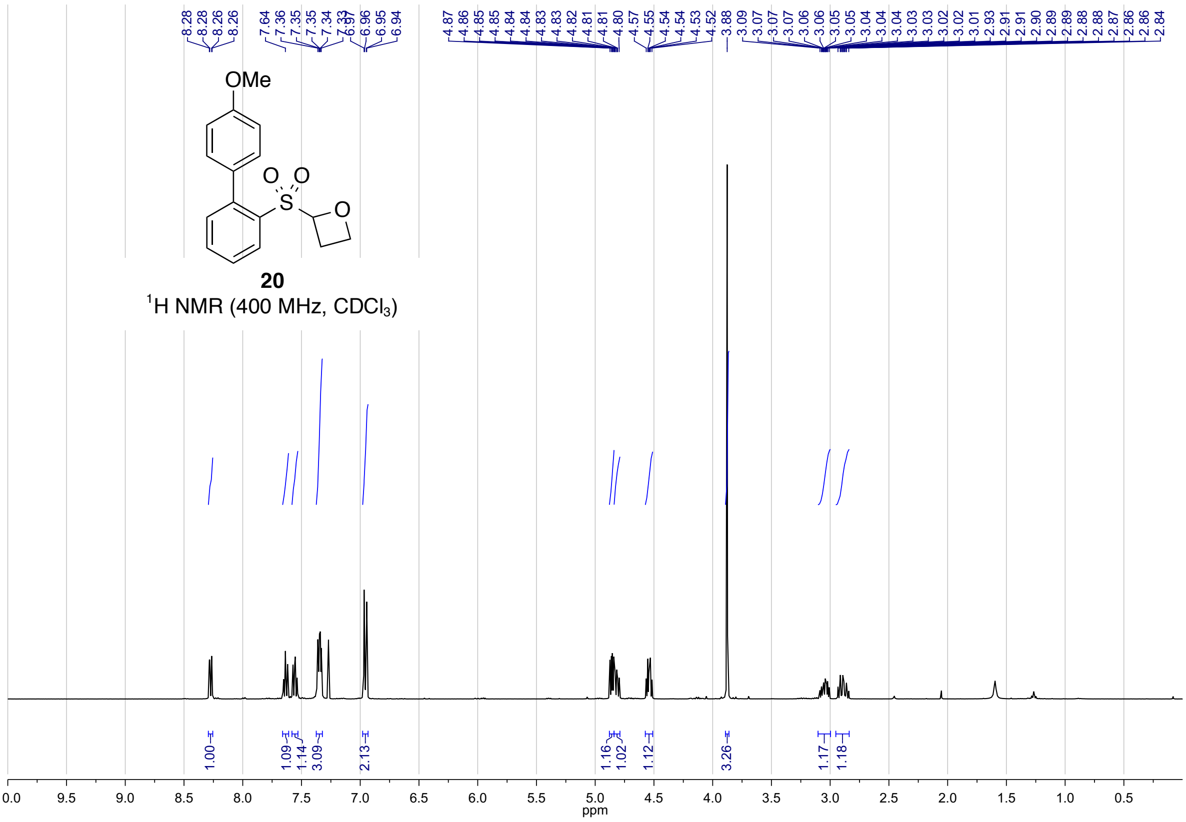


19

^{1}H NMR (400 MHz, CDCl$_3$)

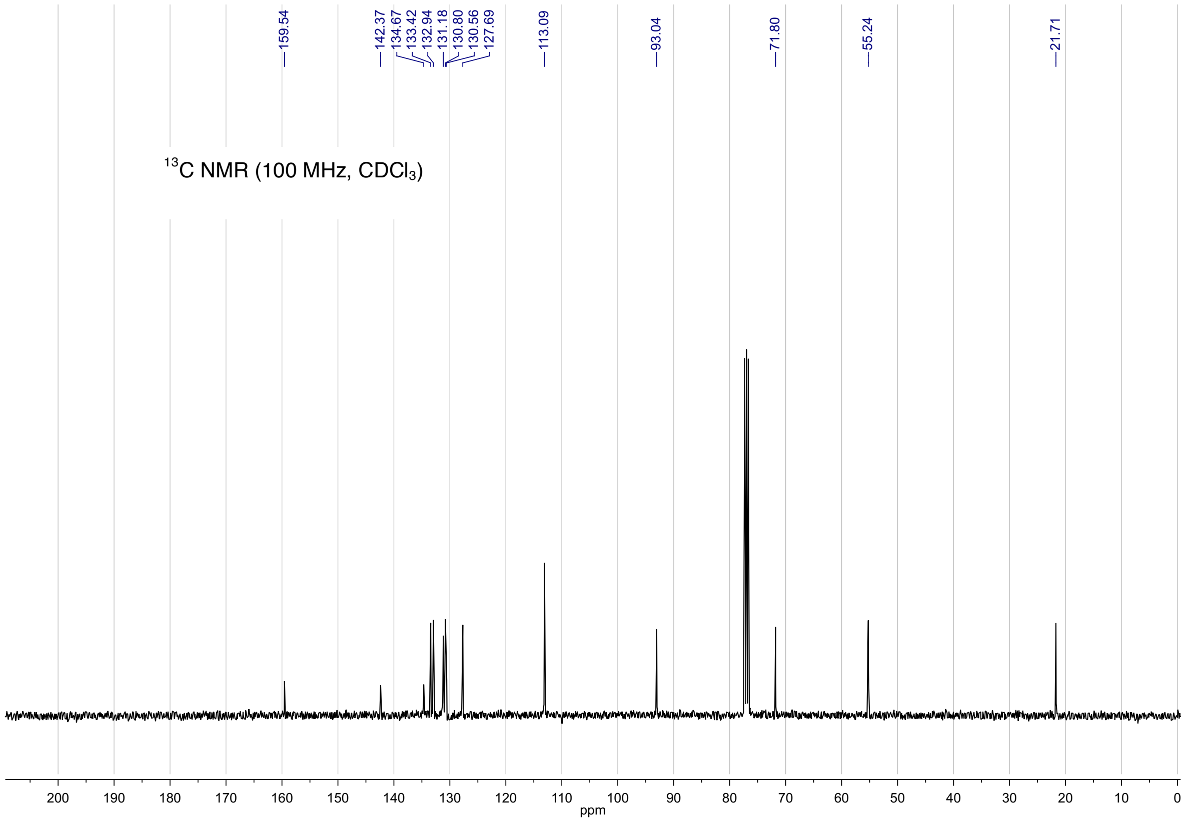


^{13}C NMR (100 MHz, CDCl$_3$)

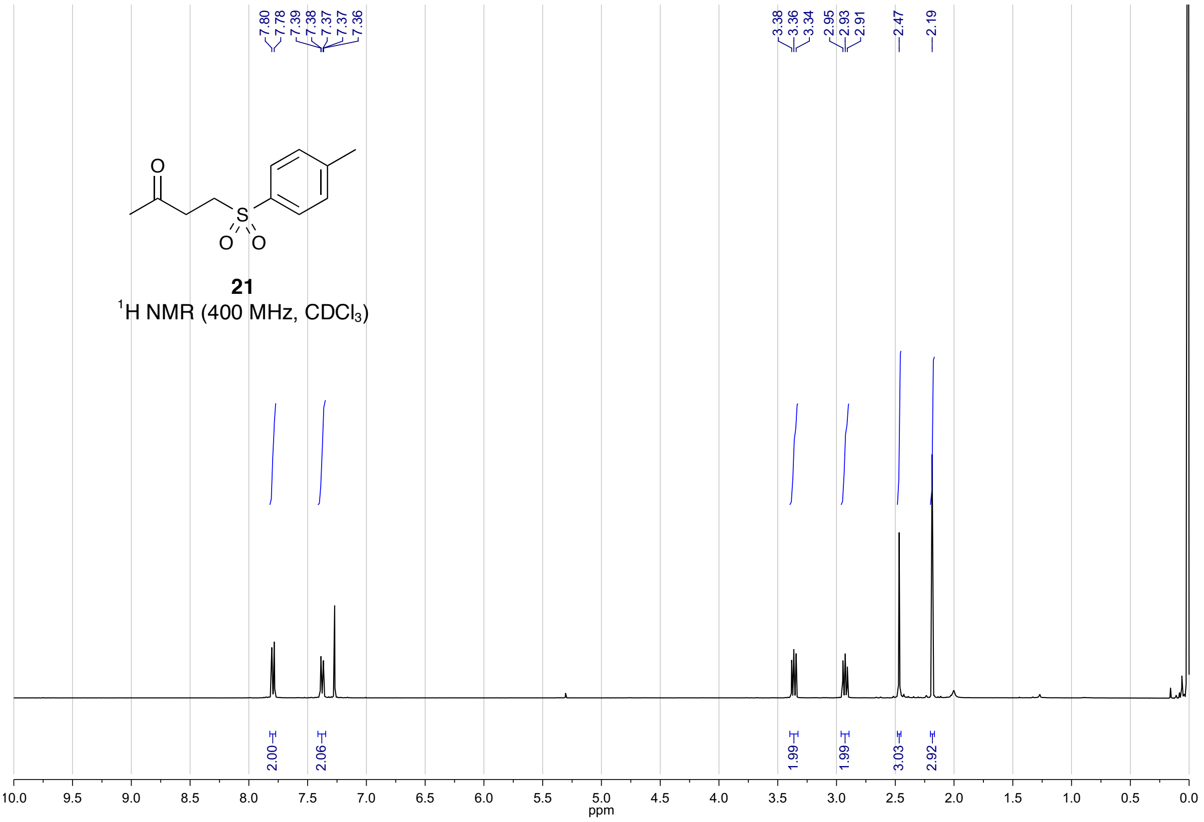


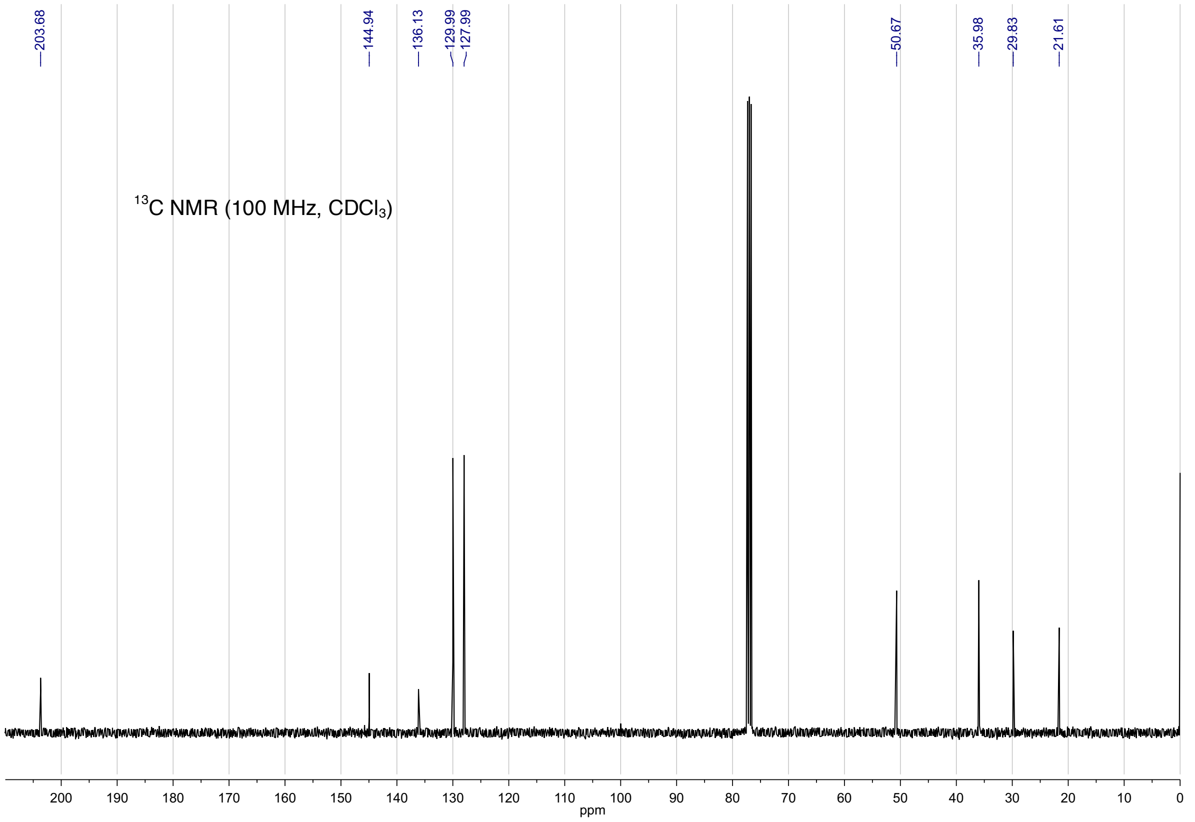
20

^{1}H NMR (400 MHz, CDCl$_3$)



^{13}C NMR (100 MHz, CDCl$_3$)


7.80
7.78
7.39
7.38
7.37
7.37
7.36
3.38
3.36
3.34
2.95
2.93
2.91
2.47
2.19
O
S
O
O
21
^{1}H NMR (400 MHz, $CDCl_3$)
2.00
2.06
1.99
1.99
3.03
2.92
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
ppm


203.68
144.94
136.13
129.99
127.99
50.67
35.98
29.83
21.61
^{13}C NMR (100 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

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