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Information

Metal-Free Sulfonylative Annulations of Alkyl Diiodides with Sulfur Dioxide: Synthesis of Cyclic Aliphatic Sulfones

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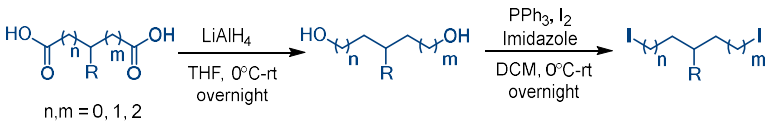
1. General information

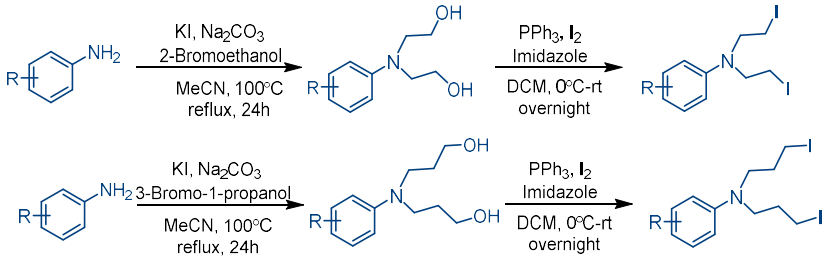
Unless otherwise noted, all reactions or reagents were obtained from commercial suppliers and used as received. Unless otherwise noted, all catalytic reactions were set up in an argon atmosphere glovebox (Vigor, SGI800-750TS-F). Unless otherwise noted, the substrates and reagents for catalytic reactions were degassed and stored in the glovebox. All work-up and purification procedures were carried out with reagent-grade solvents in air.
Thin Layer Chromatography analyses were performed on silica gel coated glass plates (0.25 mm) with fluorescence indicator UV254. For detection of spots, irradiation of UV light at 254 nm or staining reagent using phosphomolybdic acid solution was used. Flash column chromatography was conducted with silica gel 60 (particle size 230–400 mesh, Huanghai) at room temperature and under elevated pressure.
Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2030 instrument equipped with a Rtx-5 column (30 m × 0.25 mm) with dodecane as an internal standard. GC-MS analysis was conducted on an Agilent 5977B GC/MSD instrument equipped with a HP-5MS UI column (30 m × 0.25 mm). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at 400 MHz, 100 MHz and 376 MHz, respectively in $CDCl_3$ at room temperature. ^{1}H NMR was reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet), coupling constant (*J* values) in Hz and integration. Chemical shifts (δ) were reported with respect to the corresponding solvent residual peak at 7.26 ppm for $CDCl_3$ for ^{1}H NMR. ^{13}C NMR spectra (^{1}H-broadband decoupled) were reported in ppm using the central peak of $CDCl_3$ (77.16 ppm). High-resolution mass spectrometric measurements were provided by the Department of The State Key Laboratory of Biotherapy, Sichuan University. The molecular ion $[M+H]^+$ and $[M+Na]^+$ are given in m/z units.

2. General procedure for the synthesis of compounds 1a-1h.



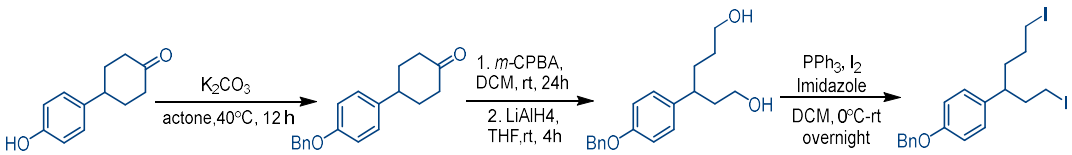
According to the reported methods with modified procedures [1-3]: Dioic acids (5.0 mmol, 1.0 equiv) was added in small portions, under a stream of argon, to a suspension of LAH (12.5 mmol, 2.5 equiv) in dry THF (50 ml) at 0 °C. The reaction was then warmed to room temperature and left to stir for 2 hours before being cooled to 0 °C and slowly quenched with water, a large amount of dichloromethane was added to dilute. Then filtered and the organic solution was dried with Na_2SO_4, filtered, and then gave the crude products diols. To the solution of the corresponding dialcohols (1.0 equiv) in DCM was added imidazole (2.0 equiv), PPh_3 (2.0 equiv). I_2 (2.0 equiv) were added over 20 minutes at 0 °C. The reaction mixture was allowed to stir overnight at room temperature. The suspension was washed with saturated Na_2SO_3 solution. The organic phase was dried over Na_2SO_4 and filtered, at which point silica gel was added. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded corresponding alkyl dihalides **1a-1h**.

3. General procedure for the synthesis of compounds 1i-1r, 1v-1ad, 1ag-1ah.



According to the reported methods with modified procedures [3, 4]: 2-Bromoethanol (or 3-Bromo-1-propanol) (3.6 equiv) and potassium iodide (3.6 equiv) were dissolved in anhydrous acetonitrile and stirred at room temperature for 15 minutes. Then added the solution of aniline (1.0 equiv) and sodium carbonate (4.0 equiv) in acetonitrile, and heated overnight in oil bath at 100 °C. After the reaction finished, cooled to room temperature, and then filtered. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded the corresponding diols. To the solution of the corresponding dialcohols (1.0 equiv) in DCM was added imidazole (2.0 equiv), PPh_3 (2.0 equiv). I_2 (2.0 equiv) were added over 20 minutes at 0 °C. The reaction mixture was allowed to stir overnight at room temperature. The suspension was washed with saturated Na_2SO_3 solution. The organic phase was dried over Na_2SO_4 and filtered, at which point silica gel was added. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded corresponding alkyl dihalides **1i-1r, 1v-1ad, 1ag-1ah**.

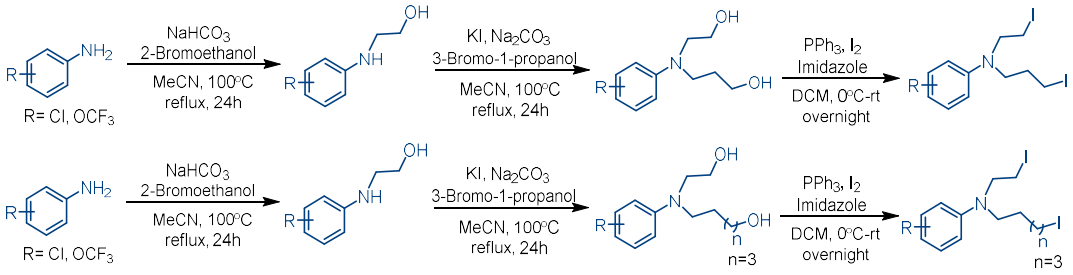
4. General procedure for the synthesis of compounds 1s.



According to the reported methods with modified procedures [3, 5]: A solution of phenol (1.0 equiv) in anhydrous acetone was cooled to 0 °C and potassium carbonate (2.2 equiv) was added, followed by a dropwise addition of benzyl bromide (1.5 equiv). The reaction mixture was then allowed to stir overnight at 40 °C. After 12 h, the reaction mixture was concentrated and the residue purified by column chromatography to afford 4-(4-(benzyloxy)phenyl)cyclohexan-1-one as a white amorphous solid; To a stirred solution of 4-(4-(benzyloxy)phenyl)cyclohexan-1-one (1.0 equiv) in dichloromethane, a solution of *m*-chloroperbenzoic acid (1.8 equiv) in dichloromethane was dropwise added. The reaction was stirred for 16 hours. Then the excess of *m*-chloroperbenzoic acid was quenched with saturated Na_2SO_3 aqueous solution. The organic layer was separated, washed with saturated $NaHCO_3$ aqueous solution, brine, dried over Na_2SO_4, filtered and concentrated under reduce pressure to afford crude 5-(4-(benzyloxy)phenyl)oxepan-2-one. According to a modified general procedure (2.0 equiv. of $LiAlH_4$), reduction of 5-(4-(benzyloxy)phenyl)oxepan-2-one (1.0 equiv) afforded pure product 3-(4-(benzyloxy)phenyl)hexane-1,6-diol as a colorless oil without further purification; To the solution of the corresponding 3-(4-(benzyloxy)phenyl)hexane-1,6-diol (1.0 equiv) in DCM was added imidazole (2.0 equiv), PPh_3 (2.0 equiv). I_2 (2.0 equiv) were added over 20 minutes at 0 °C. The reaction mixture was allowed to stir overnight at room temperature. The suspension

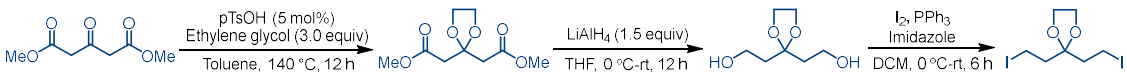
was washed with saturated Na_2SO_3 solution. The organic phase was dried over Na_2SO_4 and filtered, at which point silica gel was added. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded corresponding 1-(benzyloxy)-4-(1,6-diiodohexan-3-yl)benzene **1s**.

5. General procedure for the synthesis of compounds 1t, 1u, 1ae, 1af.



According to the reported methods with modified procedures [3,4]: 2-Bromoethanol (1.5 equiv) in anhydrous acetonitrile was added to the solution of aniline (1.0 equiv) and sodium carbonate (2.0 equiv) in acetonitrile and heated overnight in oil bath at 100 °C. After the reaction finished, cooled to room temperature, and then filtered. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded the corresponding 2-(phenylamino)ethan-1-ol; Corresponding 2-(phenylamino)ethan-1-ol (1.0 equiv) and potassium iodide (2.0 equiv) were dissolveded and stirred at room temperature for 15 minutes. Then added the solution of 3-Bromo-1-propanol or 5-bromopentan-1-ol (2.0 equiv) and sodium carbonate (4.0 equiv) in acetonitrile, and heated overnight in oil bath at 100 ℃. After the reaction finished, cooled to room temperature, and then filtered. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded the corresponding diols. To the solution of the corresponding dialcohols (1.0 equiv) in DCM was added imidazole (2.0 equiv), PPh_3 (2.0 equiv). I_2 (2.0 equiv) were added over 20 minutes at 0 °C. The reaction mixture was allowed to stir overnight at room temperature. The suspension was washed with saturated Na_2SO_3 solution. The organic phase was dried over Na_2SO_4 and filtered, at which point silica gel was added. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded corresponding alkyl dihalides **1t, 1u, 1ae, 1af.**

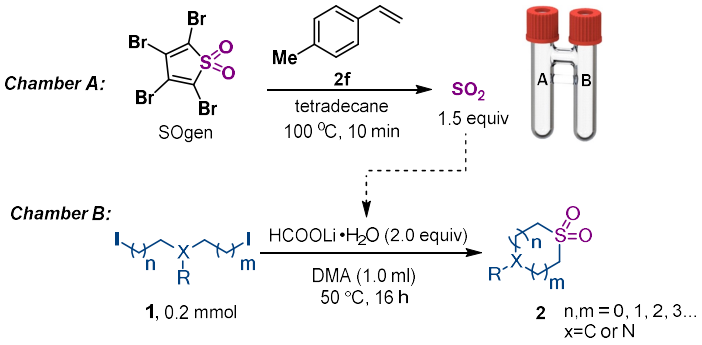
6. General procedure for the synthesis of compounds 1ai.



According to the reported methods with modified procedures [6]: To a mixture of diethyl 3-oxopentanedioate (1.0 equiv) and ethylene glycol (3.0 equiv) in toluene (100 mL) was added p-toluenesulfonic acid monohydrate (0.017 equiv). It was refluxed with Dean-Stark to remove water for 12 h. After being cooled to RT, it was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. Organic layer was washed with water, which was back-extracted with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4 and evaporated. The crude dimethyl 2,2'-(1,3-dioxolane-2,2-diyl)diacetate was obtained. To a suspension of $LiAlH_4$ (1.5 equiv) in anhydrous THF was added dimethyl 2,2'-(1,3-dioxolane-2,2-diyl)diacetate

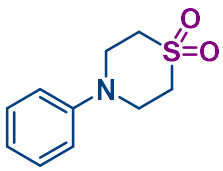
(5.54 g, 22.5 mmol) in anhydrous THF in an ice bath under nitrogen slowly. The reaction was allowed to warm up to RT and stirred for 3 h. It was quenched with water dropwisely on an ice bath, and filtered under suction. The solid was washed with DCM. The filtrate was evaporated, corresponding crude diols were obtained. the solution of the corresponding dialcohols (1.0 equiv) in DCM was added imidazole (2.0 equiv), PPh_3 (2.0 equiv). I_2 (2.0 equiv) were added over 20 minutes at 0 °C. The reaction mixture was allowed to stir overnight at room temperature. The suspension was washed with saturated Na_2SO_3 solution. The organic phase was dried over Na_2SO_4 and filtered, at which point silica gel was added. The mixture was concentrated under reduced pressure, and the residue was loaded onto a silica column. Flash chromatography afforded corresponding alkyl dihalides **1ai.**

7. General procedure for the synthesis of compounds 2a-2ai:



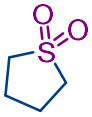
In the glovebox, Alkyl diiodides (0.2 mmol, 1.0 equiv), HCOOLi•H_2O (0.4 mmol, 2.0 equiv) were added to chamber B, followed by addition of DMA (1.0 mL). Tetrabromothiophene *S*,*S*-dioxides (0.33 mmol, 142 mg) in tetradecane (1.0 mL) was added to chamber A, followed by addition of 4-methylphenylene (0.3 mmol, 1.5 equiv, 40.0 μl). The two chamber system was sealed and removed out of the glovebox and chamber A was heated 10min at 100 °C in heat block, then the two chamber system was heated at 50 °C. After 16 hours, two chamber was cooled to room temperature. The mixture in chamber B was passed through a short silica gel pad with ethyl acetate. The filtrate was washed by ethyl acetate and H_2O (15 mL×3 times), dried by Na_2SO_4, then concentrated and the residue was purified by flash column chromatography to give the desired product.

8. Characterization data of compounds (2a-2ai):

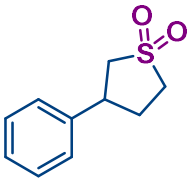


4-phenylthiomorpholine 1,1-dioxide (2a): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (40.1 mg, yield 95%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30-7.29 (m, 2H), 6.96-6.23 (m, 3H), 3.85 (t, *J* = 5.2 Hz, 4H), 3.12 (t, *J* = 5.2 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.6, 129.9, 121.2, 116.6, 50.6, 48.0; **HRMS** *m/z* calculated for

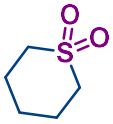
$C_{10}H_{13}NO_2S$ [M+Na]$^+$: 234.0559, found: 234.0565.



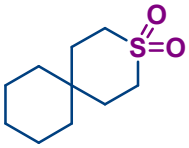
tetrahydrothiophene 1,1-dioxide (2b): Isolated as colorless oil using petroleum ether/ethyl acetate (3:1) as eluent (18.0 mg, yield 75%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.04-3.00 (m, 4H), 2.23-2.20 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 51.3, 22.9; **HRMS** *m/z* calculated for $C_4H_8O_2S$ [M]$^+$: 120.0245, found: 120.0239.



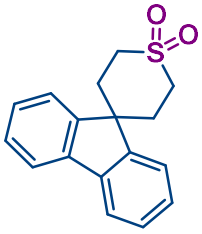
3-phenyltetrahydrothiophene 1,1-dioxide (2c): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (30.2 mg, yield 77%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.42-7.38 (m, 2H), 7.35-7.33 (m, 1H), 7.31-7.28 (m, 2H), 3.70-3.61 (m, 1H), 3.51 (dd, *J* = 12.8, 7.6 Hz, 1H), 3.43-3.37 (m, 1H), 3.25-3.12 (m, 2H), 2.62-2.55 (m, 1H), 2.40-2.29 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 139.6, 129.3, 128.0, 126.9, 57.7, 53.0, 41.9, 30.9; **HRMS** *m/z* calculated for $C_{10}H_{12}O_2S$ [M+Na]$^+$: 219.0450, found: 219.0456.



tetrahydro-2*H*-thiopyran 1,1-dioxide (2d): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (21.7 mg, yield 81%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 2.98 (t, *J* = 6.0 Hz, 4H), 2.13-2.07 (m, 4H), 1.66-1.60 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 52.3, 24.4, 24.0; **HRMS** *m/z* calculated for $C_5H_{10}O_2S$ [M+Na]$^+$: 157.0294 , found: 157.0291.

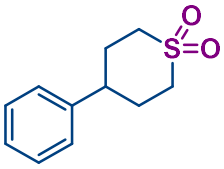


3-thiaspiro[5.5]undecane 3,3-dioxide (2e): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (37.2 mg, yield 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 2.93 (t, *J* = 6.4 Hz, 4H), 1.93 (t, *J* = 6.4 Hz, 4H), 1.44-1.38 (m, 10H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 47.2, 35.1, 33.9, 31.2, 26.3, 21.4; **HRMS** *m/z* calculated for $C_{10}H_{18}O_2S$ [M+H]$^+$: 203.1100, found: 203.1104.

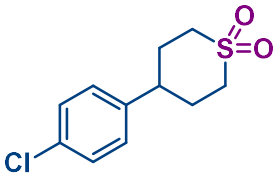


2',3',5',6'-tetrahydrospiro[fluorene-9,4'-thiopyran] 1',1'-dioxide (2f): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (47.2 mg, yield 83%). **^{1}H NMR**

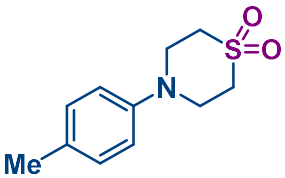
(400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.2 Hz, 2H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.44 (td, *J* = 7.2, 0.8 Hz, 2H), 7.37 (td, *J* = 7.2, 0.8 Hz, 2H), 3.47 (t, *J* = 6.4 Hz, 4H), 2.39 (t, *J* = 6.4 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.1, 139.8, 128.4, 127.9, 123.8, 120.8, 49.2, 47.6, 34.0; **HRMS** *m/z* calculated for $C_{17}H_{16}O_2S$ [M+Na]$^+$: 307.0763 , found: 307.0768 .



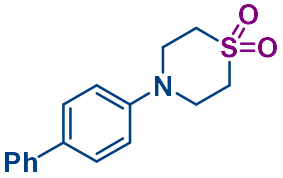
4-phenyltetrahydro-2*H*-thiopyran 1,1-dioxide (2g): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (35.3 mg, yield 84%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38-7.35 (m, 2H), 7.30-7.25 (m, 3H), 3.17 (dd, *J* = 8.8, 3.6 Hz, 4H), 2.85-2.77 (m, 1H), 2.47-2.39 (m, 2H), 2.26-2.23 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 143.4, 129.0, 127.3, 126.7, 51.7, 42.4, 31.6; **HRMS** *m/z* calculated for $C_{11}H_{14}O_2S$ [M+Na]$^+$: 233.0607, found: 233.0609.



4-(4-chlorophenyl)tetrahydro-2*H*-thiopyran 1,1-dioxide (2h): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (39.2 mg, yield 80%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 3.14 (t, *J* = 6.4 Hz, 4H), 2.77 (tt, *J* = 12.0, 2.8 Hz, 1H), 2.43-2.32 (m, 2H), 2.22-2.15 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 141.8, 133.1, 129.2, 128.1, 51.6, 41.8, 31.5; **HRMS** *m/z* calculated for $C_{11}H_{13}ClO_2S$ [M+ Na]$^+$: 267.0217, found: 267.0223.

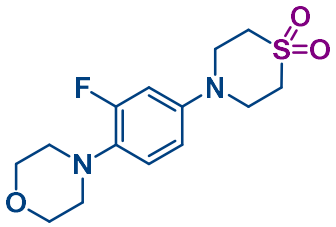


4-(*p*-tolyl)thiomorpholine 1,1-dioxide (2i): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (41.9 mg, yield 93%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 3.79 (t, *J* = 5.2 Hz, 4H), 3.11 (t, *J* = 5.6 Hz, 4H), 2.29 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 145.7, 130.9, 130.4, 117.0, 50.7, 48.4, 20.5; **HRMS** *m/z* calculated for $C_{11}H_{15}NO_2S$ [M+ Na]$^+$: 248.0716, found: 248.0714.

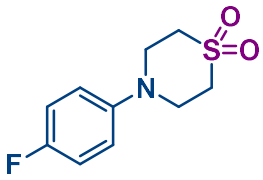


4-([1,1'-biphenyl]-4-yl)thiomorpholine 1,1-dioxide (2j): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (50.0 mg, yield 87%). **^{1}H NMR (400 MHz,**

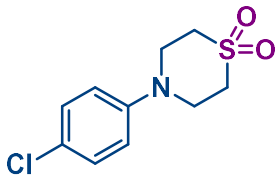
$CDCl_3$) δ 7.55 (d, *J* = 7.2 Hz, 4H), 7.45-7.41 (m, 2H), 7.34-7.30 (m, 1H), 6.99 (d, *J* = 4.8 Hz, 2H), 3.90 (t, *J* = 4.8 Hz, 4H), 3.14 (t, *J* = 4.8 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.8, 140.4, 133.8, 128.9, 128.5, 127.0, 126.7, 116.6, 50.6, 47.7; **HRMS** *m/z* calculated for $C_{16}H_{17}NO_2S$ $[M+Na]^+$: 310.0872, found: 310.0874.



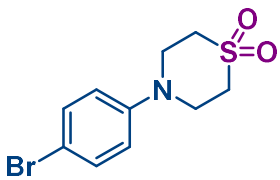
4-(3-fluoro-4-morpholinophenyl)thiomorpholine 1,1-dioxide (2k): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (55.3 mg, yield 88%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 6.93-6.88 (m, 1H), 6.68-6.60 (m, 2H), 3.85 (t, *J* = 5.2 Hz, 4H), 3.75 (t, *J* = 5.2 Hz, 4H), 3.08 (t, *J* = 4.8 Hz, 4H), 3.01 (t, *J* = 4.4 Hz, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -120.41; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.5 (d, $J_{C\text{-}F}$ = 245.0 Hz), 144.1 (d, $J_{C\text{-}F}$ = 8.0 Hz), 133.8 (d, $J_{C\text{-}F}$ = 4.0 Hz), 120.2 (d, $J_{C\text{-}F}$ = 2.0 Hz), 112.3 (d, $J_{C\text{-}F}$ = 3.0 Hz), 105.8 (d, $J_{C\text{-}F}$ = 24.0 Hz), 67.1, 51.4, 50.6, 48.2; **HRMS** *m/z* calculated for $C_{14}H_{19}FN_2O_3S$ $[M+Na]^+$: 337.0993, found: 337.1082.



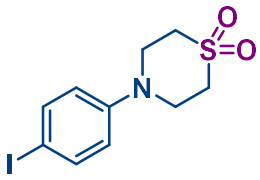
4-(4-fluorophenyl)thiomorpholine 1,1-dioxide (2l): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (42.2 mg, yield 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.03-6.98 (m, 2H), 6.93-6.89 (m, 2H), 3.73 (t, *J* = 5.6 Hz, 4H), 3.14 (t, *J* = 5.2 Hz, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -121.95; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.1 (d, $J_{C\text{-}F}$ = 240.0 Hz), 145.1 (d, $J_{C\text{-}F}$ = 3.0 Hz), 119.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 116.4 (d, $J_{C\text{-}F}$ = 22.0 Hz), 51.0, 49.3; **HRMS** *m/z* calculated for $C_{10}H_{12}FNO_2S$ $[M+Na]^+$: 252.0465, found: 252.0467.



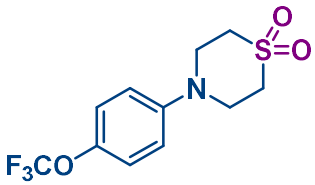
4-(4-chlorophenyl)thiomorpholine 1,1-dioxide (2m): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (42.3 mg, yield 86%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.83 (t, *J* = 5.6 Hz, 4H), 3.14 (t, *J* = 5.6 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.5, 129.8, 126.3, 118.0, 50.7, 48.2; **HRMS** *m/z* calculated for $C_{10}H_{12}ClNO_2S$ $[M+Na]^+$: 268.0169, found: 268.0174.



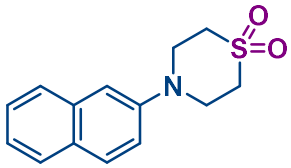
4-(4-bromophenyl)thiomorpholine 1,1-dioxide (2n): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (54.0 mg, yield 93%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.81 (t, *J* = 5.2 Hz, 4H), 3.10 (t, *J* = 5.2 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.0, 132.7, 118.3, 113.5, 50.6, 47.9; **HRMS** *m/z* calculated for $C_{10}H_{12}BrNO_2S$ $[M+Na]^+$: 311.9664, found: 311.9668.



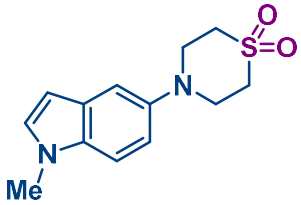
4-(4-iodophenyl)thiomorpholine 1,1-dioxide (2o): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (61.4 mg, yield 91%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 3.83 (t, *J* = 5.6 Hz, 4H), 3.10 (t, *J* = 5.6 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.4, 138.7, 118.5, 83.1, 50.6, 47.6; **HRMS** *m/z* calculated for $C_{10}H_{12}INO_2S$ $[M+Na]^+$: 359.9526, found: 359.9529.



4-(4-(trifluoromethoxy)phenyl)thiomorpholine 1,1-dioxide (2p): Isolated as white solid using petroleum ether/ethyl acetate (4:1) as eluent (54.9 mg, yield 93%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.16 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.82 (t, *J* = 5.2 Hz, 4H), 3.12 (t, *J* = 5.2 Hz, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -58.30; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.8, 143.2, 122.8, 120.7 (q, J_{C-F} = 255.0 Hz), 117.7, 50.7, 48.3; **HRMS** *m/z* calculated for $C_{11}H_{12}F_3NO_3S$ $[M+Na]^+$: 318.0382, found: 318.0385.

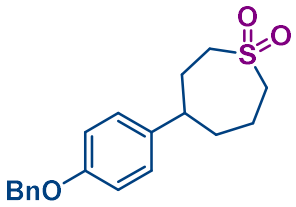


4-(naphthalen-2-yl)thiomorpholine 1,1-dioxide (2q): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (47.0 mg, yield 90%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.79 (d, *J* = 8.8 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.48-7.44 (m, 1H), 7.38-7.34 (m, 1H), 7.21 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.17 (d, *J* = 2.4 Hz, 1H), 3.94 (t, *J* = 6.4 Hz, 4H), 3.17 (t, *J* = 6.4 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 145.6, 134.5, 129.8, 129.0, 127.6, 127.0, 126.9, 124.4, 118.7, 111.7, 50.8, 48.2; **HRMS** *m/z* calculated for $C_{14}H_{15}NO_2S$ $[M+Na]^+$: 284.0716, found: 284.0721.

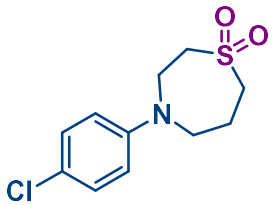


4-(1-methyl-1*H*-indol-5-yl)thiomorpholine 1,1-dioxide (2r): Isolated as white solid using

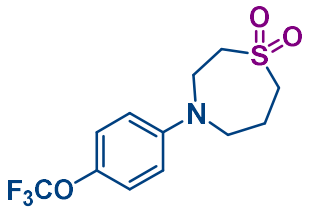
petroleum ether/ethyl acetate (2:1) as eluent (37.0 mg, yield 70%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31-7.25 (m, 2H), 7.08 (d, *J* = 3.2 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.44 (d, *J* = 2.8 Hz, 1H), 3.80 (s, 3H), 3.75 (t, *J* = 6.4 Hz, 4H), 3.22 (t, *J* = 6.4 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 143.0, 133.3, 130.0, 129.0, 115.4, 110.3, 110.0, 100.7, 51.5, 50.8, 33.1; **HRMS** *m/z* calculated for $C_{13}H_{16}N_2O_2S$ [M+Na]$^+$: 287.0825, found: 287.0826.



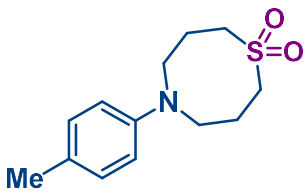
4-(4-(benzyloxy)phenyl)thiepane 1,1-dioxide (2s): Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (43.0 mg, yield 65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.33 (m, 5H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 5.05 (s, 2H), 3.30-3.24 (m, 4H), 2.89-2.82 (m, 1H), 2.22-2.16 (m, 4H), 2.01-1.97 (m, 1H), 1.89-1.82 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 157.6, 139.2, 137.1, 128.7, 128.1, 127.59, 127.55, 115.2, 70.2, 56.3, 54.4, 45.3, 36.1, 29.3, 21.5; **HRMS** *m/z* calculated for $C_{19}H_{22}O_3S$ [M+Na]$^+$: 353.1182, found: 353.1186.



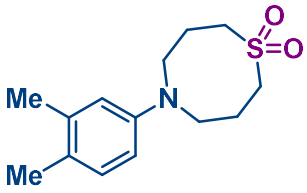
4-(4-chlorophenyl)-1,4-thiazepane 1,1-dioxide (2t): Isolated as pale yellow oil using petroleum ether/ethyl acetate (3:1) as eluent (28.1 mg, yield 54%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.21 (d, *J* = 9.2 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 3.81 (t, *J* = 5.6 Hz, 2H), 3.75 (t, *J* = 6.8 Hz, 2H), 3.31 (t, *J* = 5.6 Hz, 2H), 2.98 (t, *J* = 6.4 Hz, 2H), 2.25-2.18 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.6, 129.9, 122.6, 112.4, 54.6, 52.3, 48.3, 45.0, 19.7; **HRMS** *m/z* calculated for $C_{11}H_{14}ClNO_2S$ [M+Na]$^+$: 282.0326, found: 282.0329.



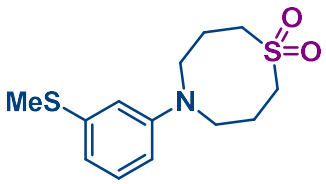
4-(4-(trifluoromethoxy)phenyl)-1,4-thiazepane 1,1-dioxide (2u): Isolated as colorless oil using petroleum ether/ethyl acetate (3:1) as eluent (32.2 mg, yield 52%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.13 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 9.2 Hz, 2H), 3.83 (t, *J* = 5.6. Hz, 2H), 3.77 (t, *J* = 6.8 Hz, 2H), 3.31 (t, *J* = 5.2 Hz, 2H), 2.99 (t, *J* = 6.4 Hz, 2H), 2.27-2.20 (m, 2H); **^{19}F NMR (376 MHz, $CDCl_3$)** -58.45; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.9, 140.7, 123.2, 120.8 (q, J_{C-F} = 254.0 Hz), 111.6, 54.7, 52.3, 48.4, 45.1, 19.8; **HRMS** *m/z* calculated for $C_{12}H_{14}F_3NO_3S$ [M+Na]$^+$: 332.0539, found: 332.0539.



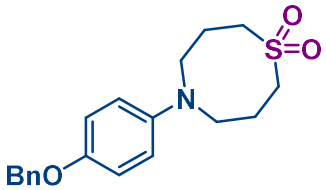
5-(*p*-tolyl)-1,5-thiazocane 1,1-dioxide (2v): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (25.3 mg, yield 50%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.08 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 3.43 (t, *J* = 6.4 Hz, 4H), 3.15 (t, *J* = 6.4 Hz, 4H), 2.32-2.27 (m, 7H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.8, 130.3, 127.9, 113.6, 53.5, 48.0, 22.9, 20.4; **HRMS** *m/z* calculated for $C_{13}H_{19}NO_2S$ $[M+Na]^+$: 276.1029, found: 276.1034.



5-(3,4-dimethylphenyl)-1,5-thiazocane 1,1-dioxide (2w): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (28.3 mg, yield 53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.02 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 2.8 Hz, 1H), 6.52 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.40 (t, *J* = 6.0 Hz, 4H), 3.14 (t, *J* = 5.6 Hz, 4H), 2.30-2.27 (m, 4H), 2.24 (s, 3H), 2.18 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.3, 137.8, 130.7, 126.7, 115.2, 111.1, 53.5, 47.9, 23.0, 20.6, 18.7; **HRMS** *m/z* calculated for $C_{14}H_{21}NO_2S$ $[M+Na]^+$: 290.1185, found: 290.1186.

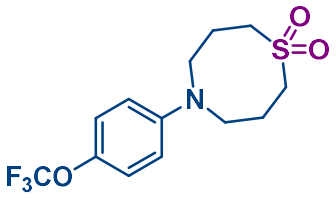


5-(3-(methylthio)phenyl)-1,5-thiazocane 1,1-dioxide (2x): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (22.8 mg, yield 40%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.20-7.16 (m, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 1H), 6.53 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.46 (t, *J* = 6.0 Hz, 4H), 3.13 (t, *J* = 5.6 Hz, 4H), 2.48 (s, 3H), 2.33-2.27 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.0, 140.0, 130.1, 116.2, 111.4, 110.3, 53.4, 48.0, 22.7, 16.0; **HRMS** *m/z* calculated for $C_{13}H_{19}NO_2S_2$: 308.0749, found: 308.0753.

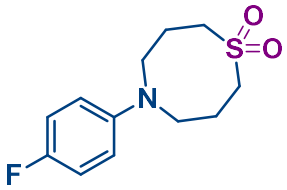


5-(4-(benzyloxy)phenyl)-1,5-thiazocane 1,1-dioxide (2y): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (29.7 mg, yield 43%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44-7.30 (m, 5H), 6.92 (d, *J* = 9.2 Hz, 2H), 6.72 (d, *J* = 9.2 Hz, 2H), 5.02 (s, 2H), 3.35 (t, *J* = 6.4 Hz, 4H), 3.15 (t, *J* = 6.4 Hz, 4H), 2.29-2.23 (m, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 152.0, 143.8, 137.5, 128.7, 128.0, 127.6, 116.3, 115.2, 70.8, 53.6, 48.3, 23.0;

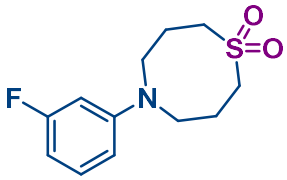
HRMS *m/z* calculated for $C_{19}H_{23}NO_3S$ [M+Na]$^+$: 368.1291, found: 368.1289.



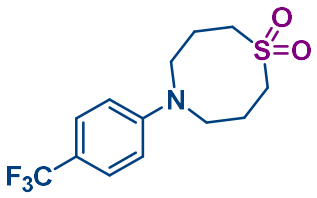
5-(4-(trifluoromethoxy)phenyl)-1,5-thiazocane 1,1-dioxide (2z): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (35.6 mg, yield 55%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 9.2 Hz, 2H), 3.47 (t, *J* = 6.0 Hz, 4H), 3.14 (t, *J* = 6.0 Hz, 4H), 2.33-2.27 (m, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -58.41; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.5, 141.1, 122.8, 120.8 (q, J_{C-F} = 254.0 Hz), 113.5, 53.6, 48.5, 22.8; **HRMS** *m/z* calculated for $C_{13}H_{16}F_3NO_3S$ [M+Na]$^+$: 346.0695, found: 346.0700.



5-(4-fluorophenyl)-1,5-thiazocane 1,1-dioxide (2aa): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (24.7 mg, yield 48%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.00-6.95 (m, 2H), 6.71-6.67 (m, 2H), 3.40 (t, *J* = 6.4 Hz, 4H), 3.15 (t, *J* = 5.6 Hz, 4H), 2.29-2.26 (m, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -126.73; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 156.3 (d, J_{C-F} = 236.0 Hz), 145.5 (d, J_{C-F} = 2.0 Hz), 116.2 (d, J_{C-F} = 22.0 Hz), 114.6 (d, J_{C-F} = 7.0 Hz), 53.6, 48.5, 22.9; **HRMS** *m/z* calculated for $C_{12}H_{16}FNO_2S$ [M+Na]$^+$: 280.0778, found: 280.0784.

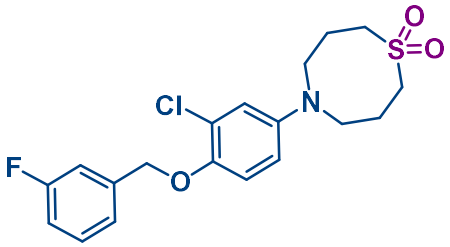


5-(3-fluorophenyl)-1,5-thiazocane 1,1-dioxide (2ab): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (26.8 mg, yield 52%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.22-7.16 (m, 1H), 6.50-6.46 (m, 2H), 6.40 (dt, *J* = 12.8, 2.4 Hz, 1H), 3.47 (t, *J* = 6.4 Hz, 4H), 3.13 (t, *J* = 6.4 Hz, 4H), 2.33-2.27 (m, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -111.46; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.3 (d, J_{C-F} = 242.0 Hz), 150.3 (d, J_{C-F} = 10.0 Hz), 130.8 (d, J_{C-F} = 10.0 Hz), 108.5 (d, J_{C-F} = 3.0 Hz), 104.7 (d, J_{C-F} = 21.0 Hz), 100.1 (d, J_{C-F} = 26.0 Hz), 53.5, 48.4, 22.6; **HRMS** *m/z* calculated for $C_{12}H_{16}FNO_2S$ [M+Na]$^+$: 280.0778, found: 280.0779.

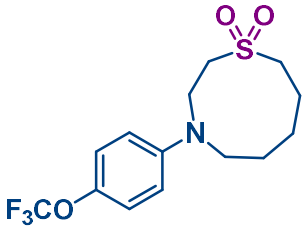


5-(4-(trifluoromethyl)phenyl)-1,5-thiazocane 1,1-dioxide (2ac): Isolated as white solid using petroleum ether/ethyl acetate (2:1) as eluent (25.2 mg, yield 41%). **^{1}H NMR (400**

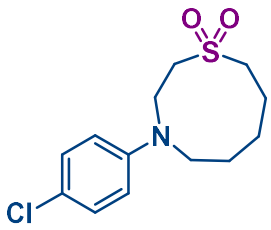
MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 3.55 (t, *J* = 6.0 Hz, 4H), 3.14 (t, *J* = 5.6 Hz, 4H), 2.55-2.30 (m, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -61.26; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 150.6, 127.1 (q, J_{C-F} = 4.0 Hz), 124.9 (q, J_{C-F} = 269.0 Hz), 119.7 (q, J_{C-F} = 32.0 Hz), 112.1, 53.6, 48.7, 22.6; **HRMS** *m/z* calculated for $C_{13}H_{16}F_3NO_2S$ $[M+Na]^+$: 330.0746, found: 330.0748.



5-(3-chloro-4-((3-fluorobenzyl)oxy)phenyl)-1,5-thiazocane 1,1-dioxide (2ad): Isolated as white solid using petroleum ether/ethyl acetate (1:1) as eluent (31.8 mg, yield 40%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.32 (m, 1H), 7.22-7.18 (m, 2H), 7.03-6.98 (m, 1H), 6.87 (d, *J* = 9.2 Hz, 1H), 6.80 (d, *J* = 3.2 Hz, 1H), 6.56 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.06 (s, 2H), 3.38 (t, *J* = 6.0 Hz, 4H), 3.15 (t, *J* = 6.0 Hz, 4H), 2.30-2.24 (m, 4H); **^{19}F NMR (376 MHz, $CDCl_3$)** -112.79; **^{13}C NMR (150 MHz, $CDCl_3$)** δ 163.1 (d, J_{C-F} = 246.0 Hz), 146.7, 144.5, 139.7 (d, J_{C-F} = 7.0 Hz), 130.2 (d, J_{C-F} = 7.5 Hz), 125.1, 122.7 (d, J_{C-F} = 3.0 Hz), 116.9, 115.7, 115.0 (d, J_{C-F} = 21.0 Hz), 114.3 (d, J_{C-F} = 21.0 Hz), 112.6, 71.4, 53.6, 48.4, 22.9; **HRMS** *m/z* calculated for $C_{19}H_{21}ClFNO_3S$ $[M+Na]^+$: 420.0807, found: 420.0813.

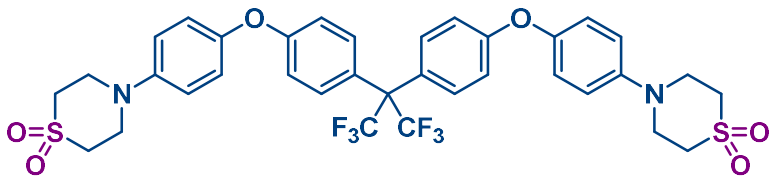


4-(4-(trifluoromethoxy)phenyl)-1,4-thiazonane 1,1-dioxide (2ae): Isolated as pale yellow oil using petroleum ether/ethyl acetate (2:1) as eluent (18.2 mg, yield 27%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.13 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 3.86-3.84 (m, 2H), 3.42 (t, *J* = 5.2 Hz, 2H), 3.33 (t, *J* = 5.2 Hz, 2H), 3.14 (t, *J* = 5.2 Hz, 2H), 1.96-1.87 (m, 4H), 1.78-1.73 (m, 2H); **^{19}F NMR (376 MHz, $CDCl_3$)** -58.38; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.3, 141.2, 122.8, 120.8 (q, J_{C-F} = 254.0 Hz), 113.8, 54.9, 54.8, 53.7, 48.1, 25.8, 25.3, 23.1; **HRMS** *m/z* calculated for $C_{14}H_{18}F_3NO_3S$ $[M+Na]^+$: 360.0852, found: 360.0855.

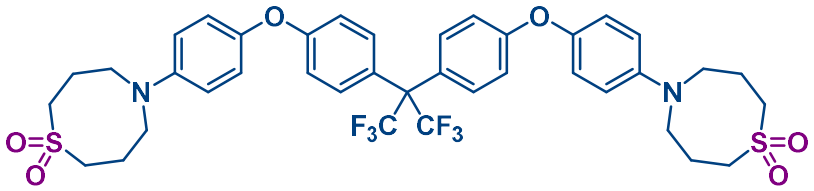


4-(4-chlorophenyl)-1,4-thiazonane 1,1-dioxide (2af): Isolated as pale yellow oil using petroleum ether/ethyl acetate (2:1) as eluent (13.2 mg, yield 23%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.22 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 9.2 Hz, 2H), 3.83 (t, *J* = 5.2 Hz, 2H), 3.41 (t, *J* = 5.2 Hz, 2H), 3.32 (t, *J* = 5.2 Hz, 2H), 3.13 (t, *J* = 5.2 Hz, 2H), 1.94-1.84 (m, 4H), 1.76-1.71 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.1, 129.6, 114.6, 54.9, 54.8, 53.5, 48.0,

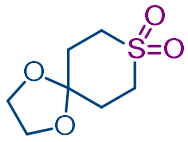
25.8, 25.3, 23.1; **HRMS** *m/z* calculated for $C_{13}H_{18}ClNO_2S$ $[M+H]^+$: 288.0820, found: 288.0824.



4,4'-((((perfluoropropane-2,2-diyl)bis(4,1-phenylene))bis(oxy))bis(4,1-phenylene))bis(thiomorpholine 1,1-dioxide) (2ag): Isolated as white solid using petroleum ether/ethyl acetate (1:1) as eluent (105.7 mg, yield 70%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (d, *J* = 8.8 Hz, 4H), 7.04 (d, *J* = 9.0 Hz, 4H), 6.96 (d, *J* = 9.0 Hz, 4H), 6.91 (d, *J* = 9.0 Hz, 4H), 3.80 (t, *J* = 5.2 Hz, 8H), 3.15 (t, *J* = 5.2 Hz, 8H); **^{19}F NMR (376 MHz, $CDCl_3$)** -64.11; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.8, 150.1, 145.1, 131.8, 127.3, 124.4 (q, J_{C-F} = 281.0 Hz), 121.7, 118.8, 116.9, 50.9, 48.9; **HRMS** *m/z* calculated for $C_{35}H_{32}F_6N_2O_6S_2$ $[M+Na]^+$: 777.1498, found: 777.1501.



5,5'-((((perfluoropropane-2,2-diyl)bis(4,1-phenylene))bis(oxy))bis(4,1-phenylene))bis(1,5-thiazocane 1,1-dioxide) (2ah): Isolated as pale yellow oil using ethyl acetate/petroleum ether (2:1) as eluent (64.9 mg, yield 40%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, *J* = 8.6 Hz, 4H), 7.00 (d, *J* = 8.8 Hz, 4H), 6.88 (d, *J* = 9.0 Hz, 4H), 6.74 (d, *J* = 9.0 Hz, 4H), 3.45 (t, *J* = 6.0 Hz, 8H), 3.17 (t, *J* = 5.2 Hz, 8H), 2.33-2.28 (m, 8H); **^{19}F NMR (376 MHz, $CDCl_3$)** -64.09; **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.4, 147.3, 146.0, 131.7, 126.8, 124.4 (q, J_{C-F} = 285.0 Hz), 122.0, 116.3, 114.4, 53.6, 48.4, 22.9; **HRMS** *m/z* calculated for $C_{39}H_{40}F_6N_2O_6S_2$ $[M+Na]^+$:833.2124, found: 833.2124.



1,4-dioxa-8-thiaspiro[4.5]decane 8,8-dioxide (2ai): Isolated as colorless oil using ethyl acetate/petroleum ether (3:1) as eluent (35.4 mg, yield 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.96 (s, 4H), 3.15 (t, *J* = 6.0 Hz, 4H), 2.20 (t, *J* = 6.0 Hz, 4H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 105.4, 65.0, 49.1, 32.9; **HRMS** *m/z* calculated for $C_7H_{12}O_4S$ $[M+Na]^+$:215.0349, found: 215.0349.

9. References

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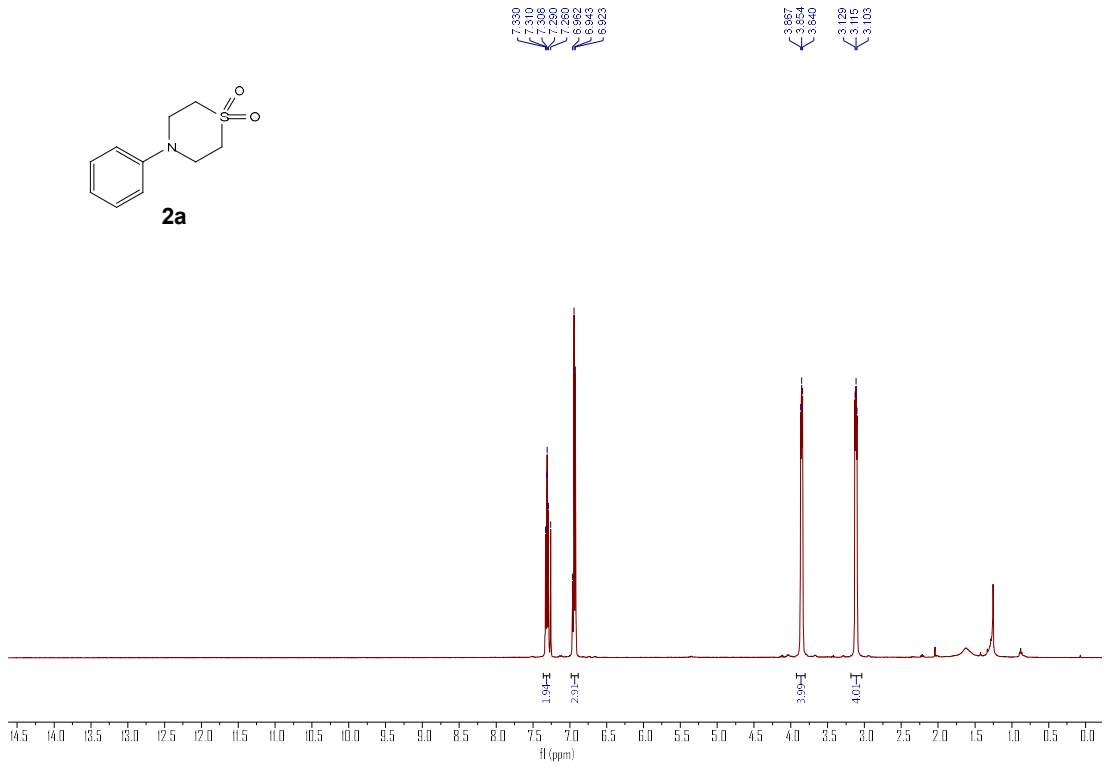
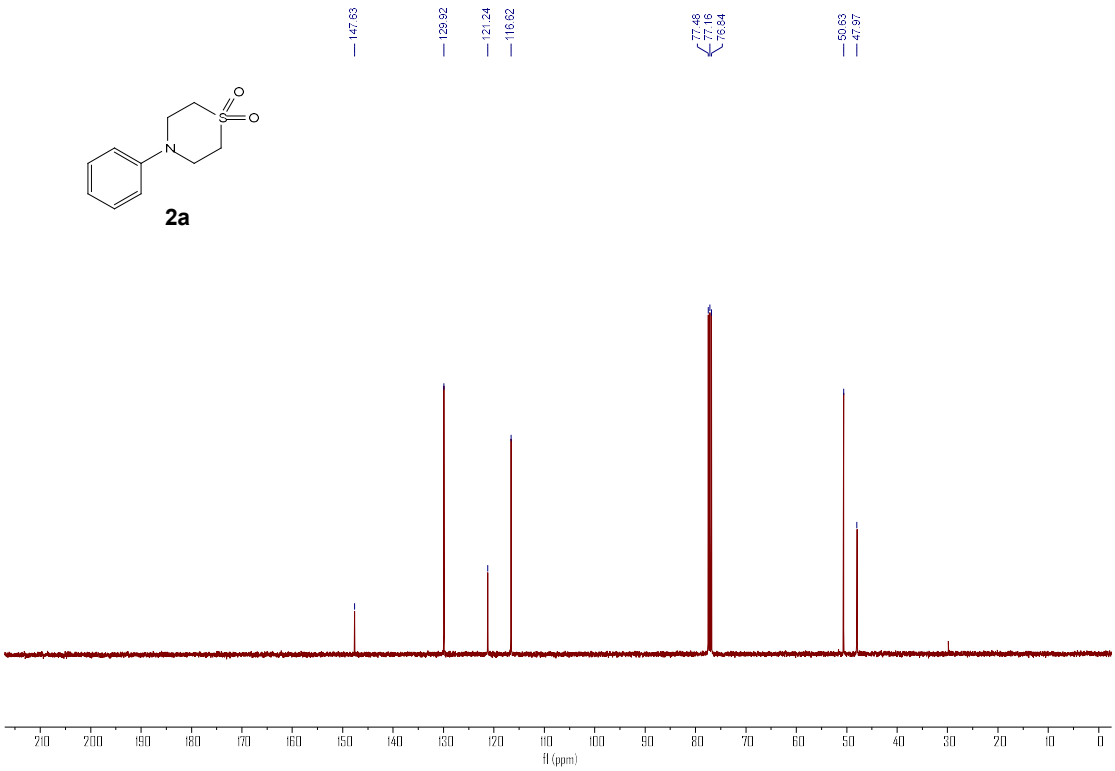
10. NMR Spectra



2a



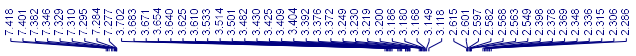
2a

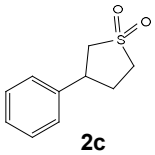
2b

7.260
3.039
3.020
3.003
2.232
2.223
2.214
2.204
2.195
f1 (ppm)

2b

77.46
77.16
76.84
51.27
22.90
f1 (ppm)





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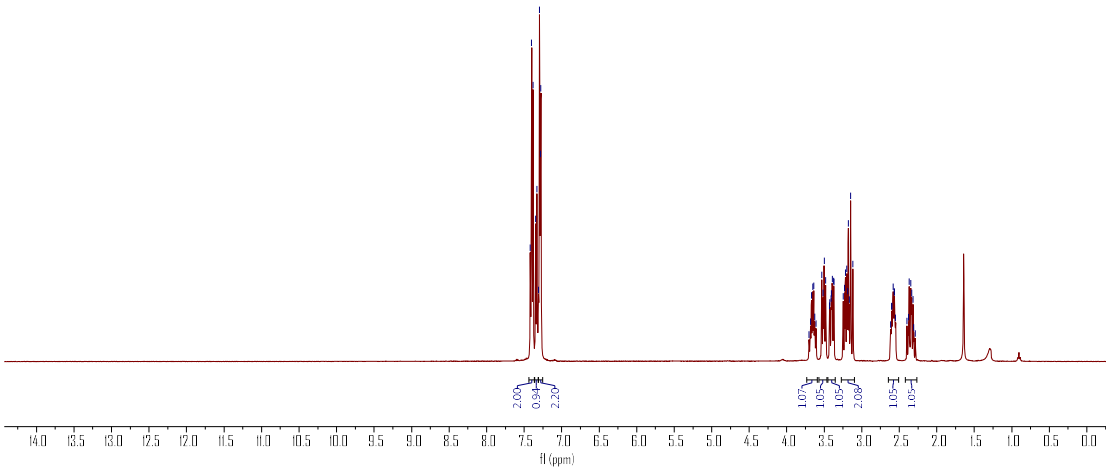

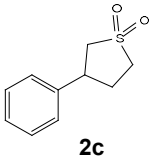

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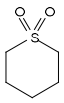

2d

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2.126
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2.097
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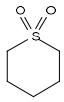
1.862
1.848
1.634
1.619
1.604
4.00
4.16
2.30
f1 (ppm)



2d

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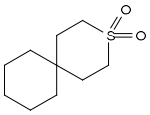
f1 (ppm)



2e

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4.25
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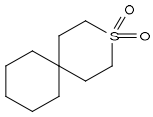
f1 (ppm)



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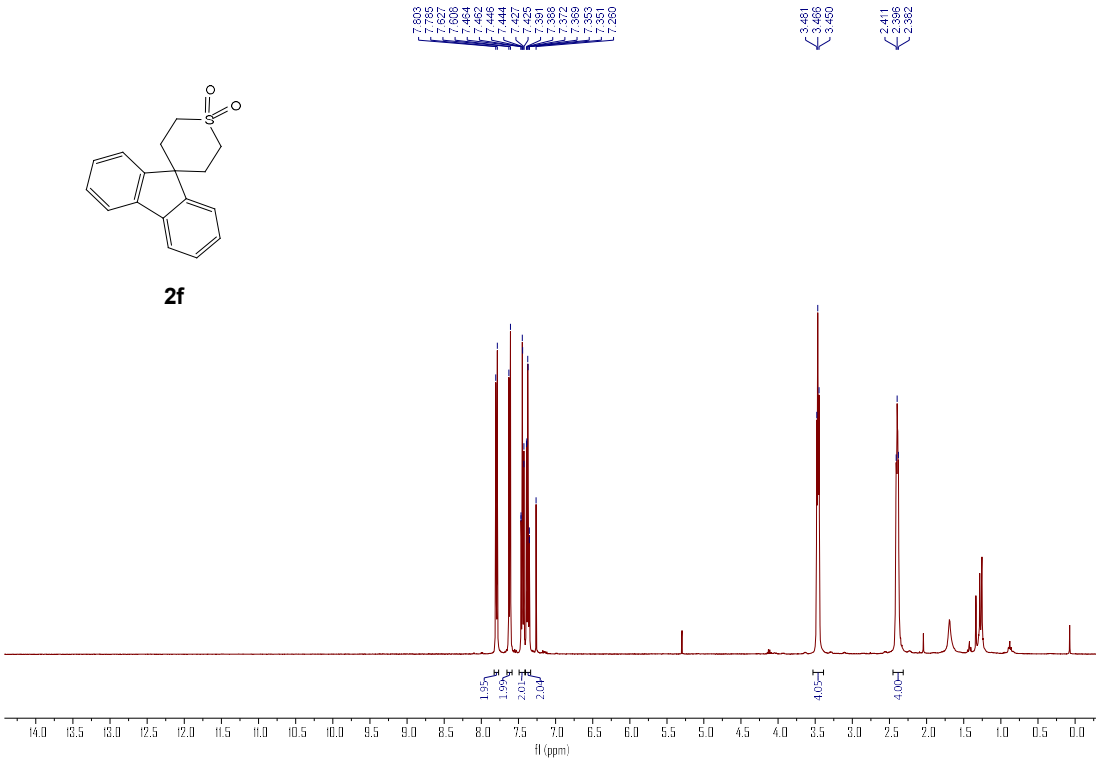
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7.425
7.391
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7.372
7.369
7.353
7.351
7.260
3.481
3.466
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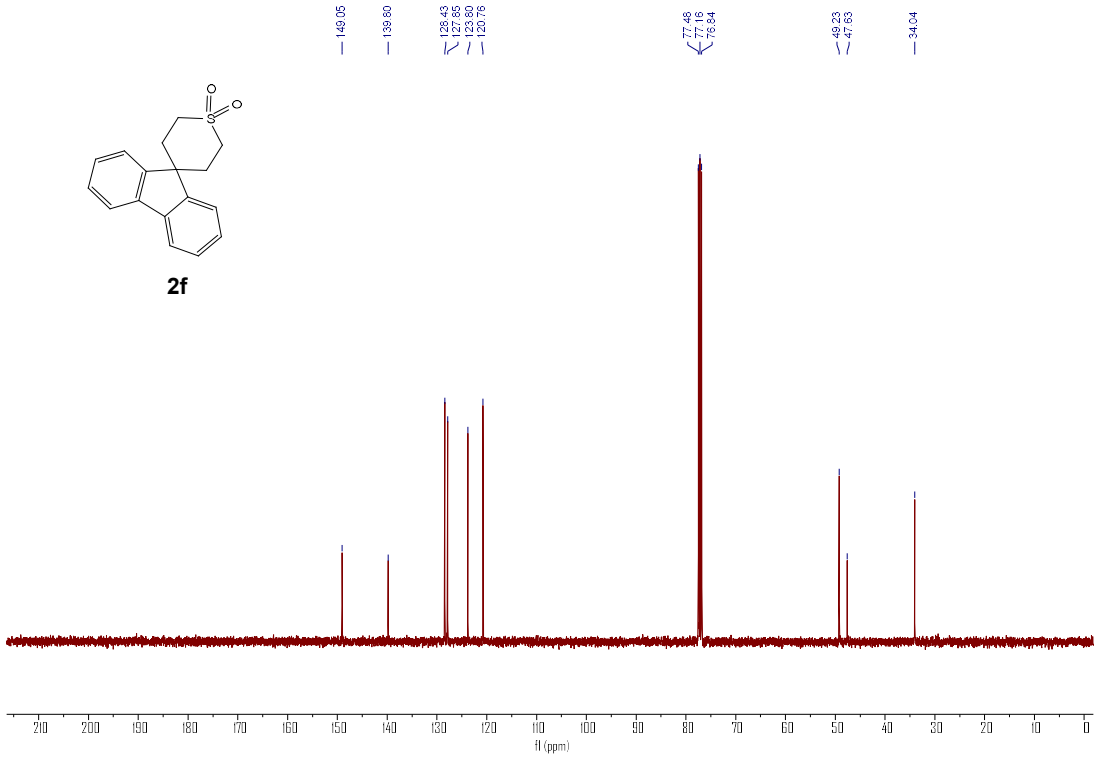
2.04
4.05
4.00
f1 (ppm)

2f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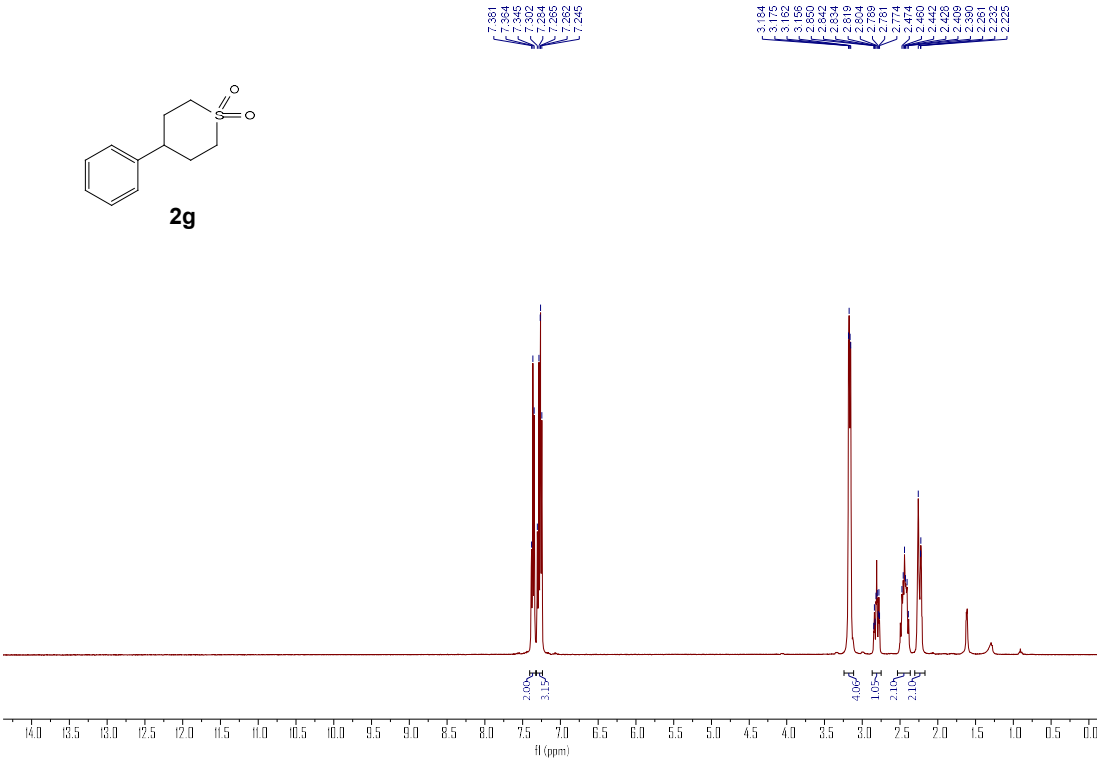
77.16
76.84
49.23
47.63
34.04
f1 (ppm)

2f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2.460
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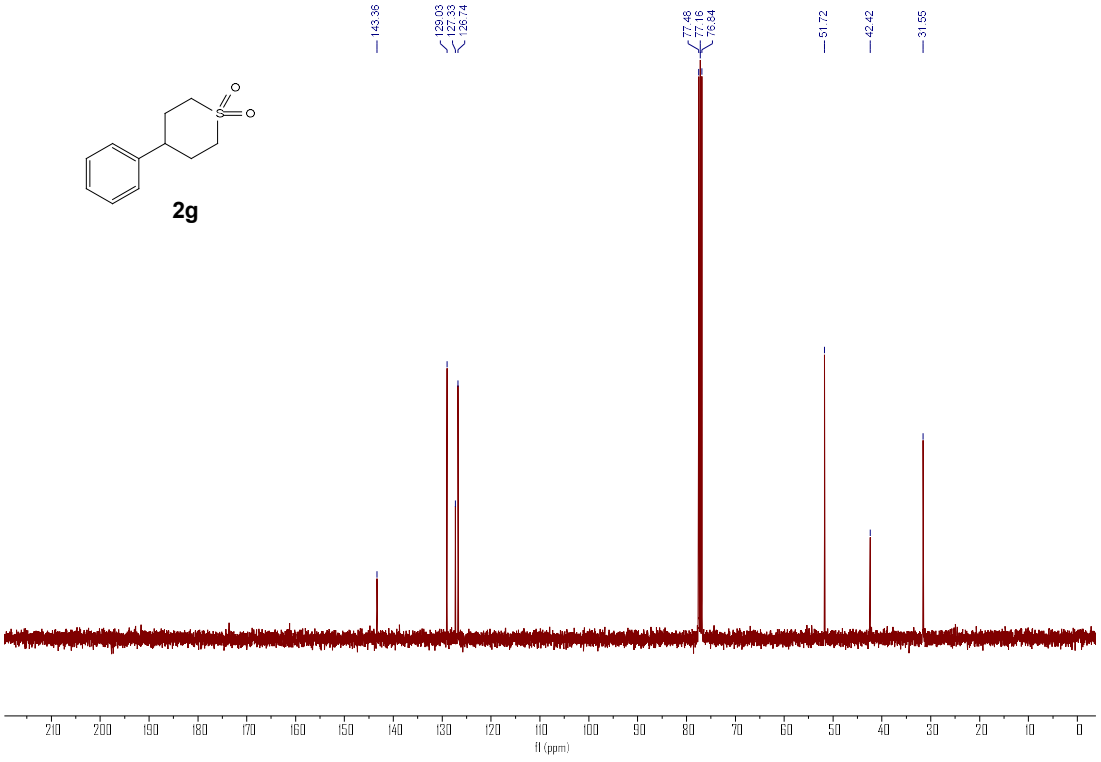
2.10
2.10
f1 (ppm)

2g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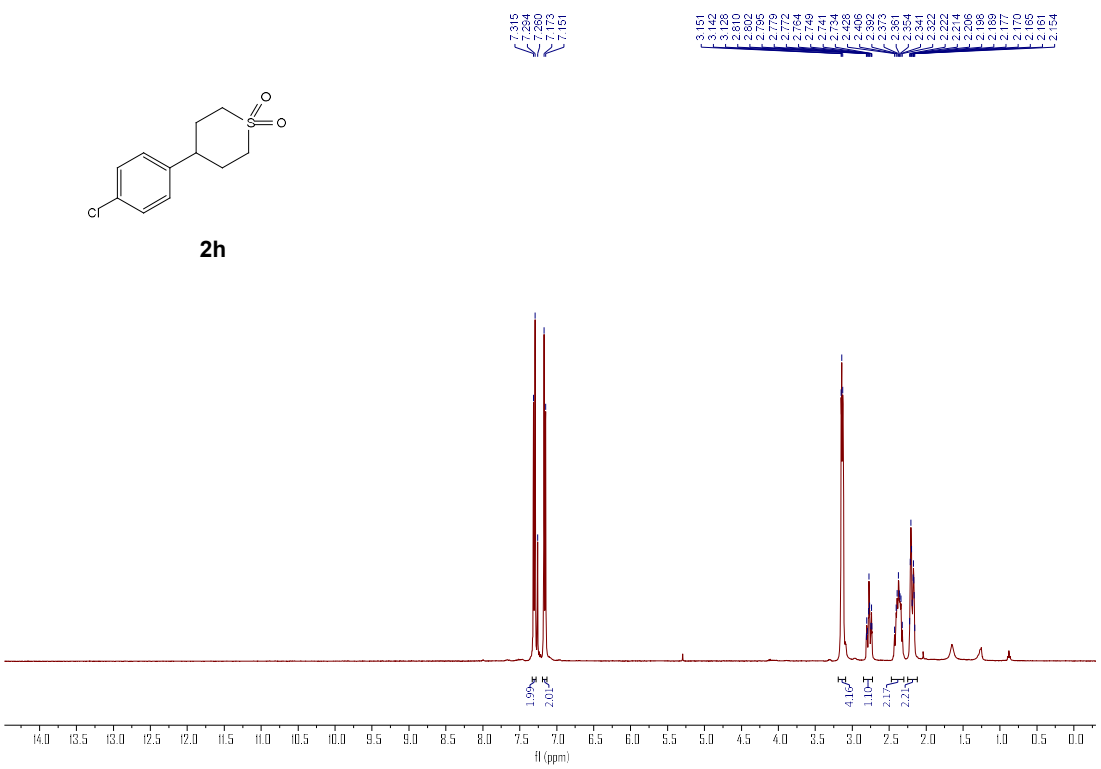
2g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2.764
2.749
2.741
2.734
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2.354
2.341
2.332
2.222
2.214
2.206
2.196
2.189
2.177
2.170
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2.154
Cl
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1.10
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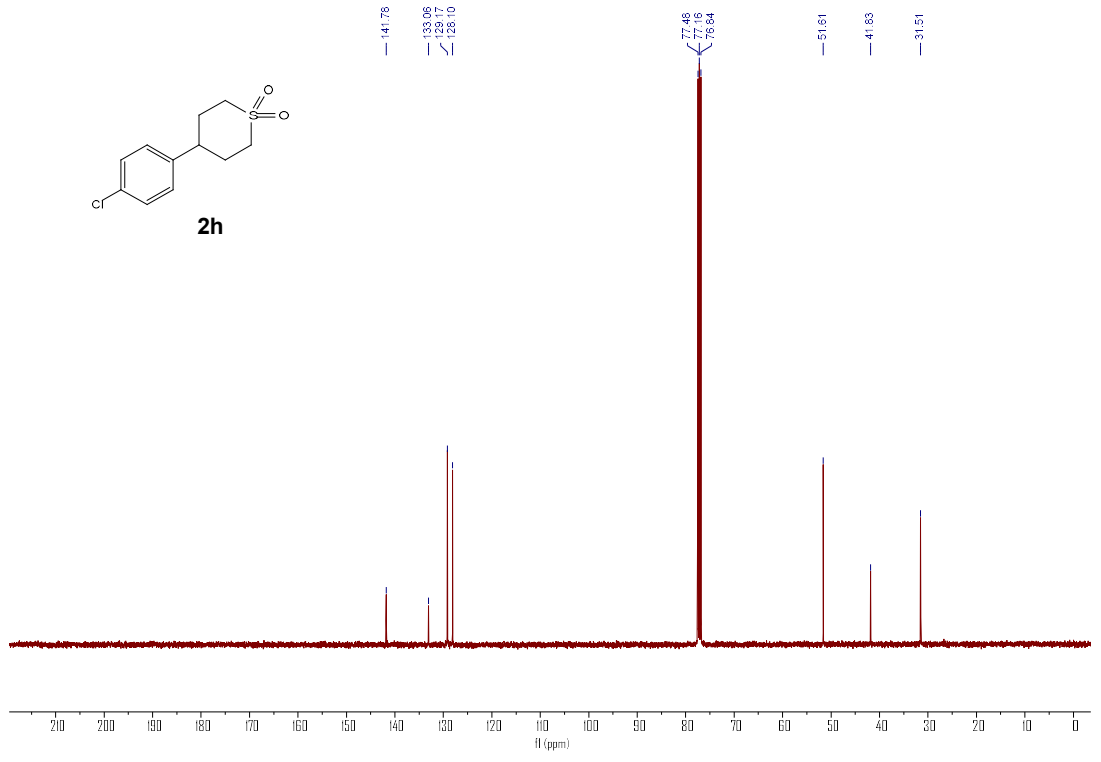
2.21
f1 (ppm)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Cl
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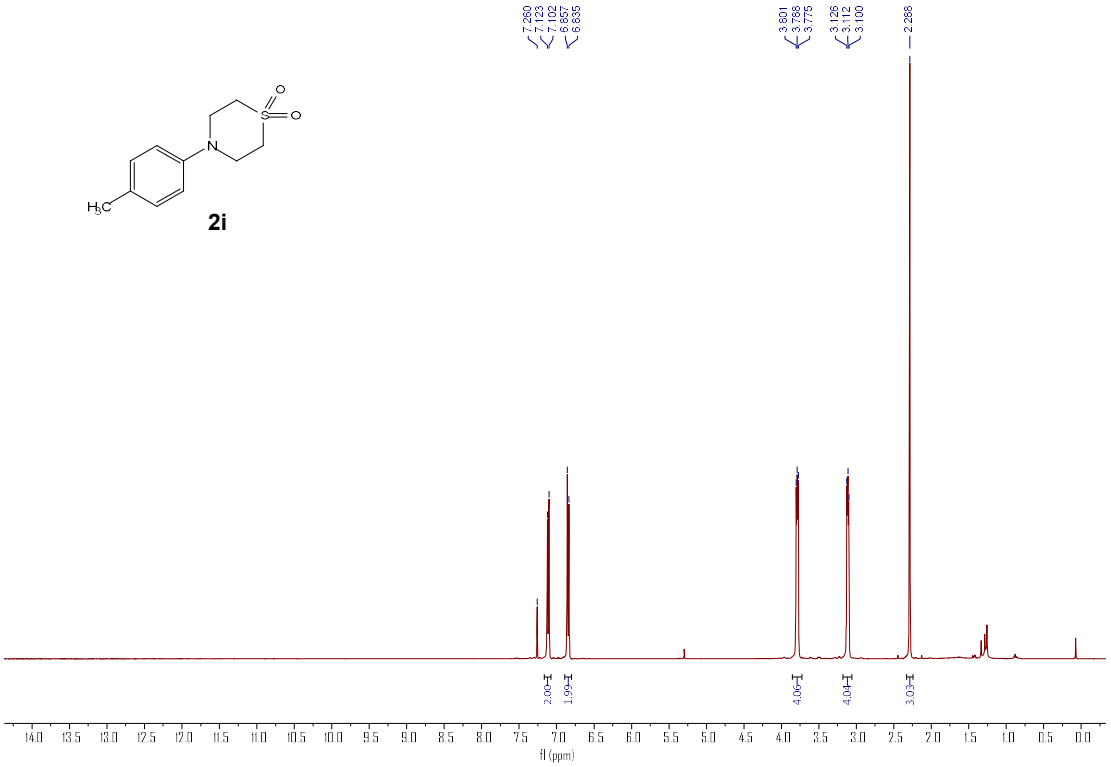
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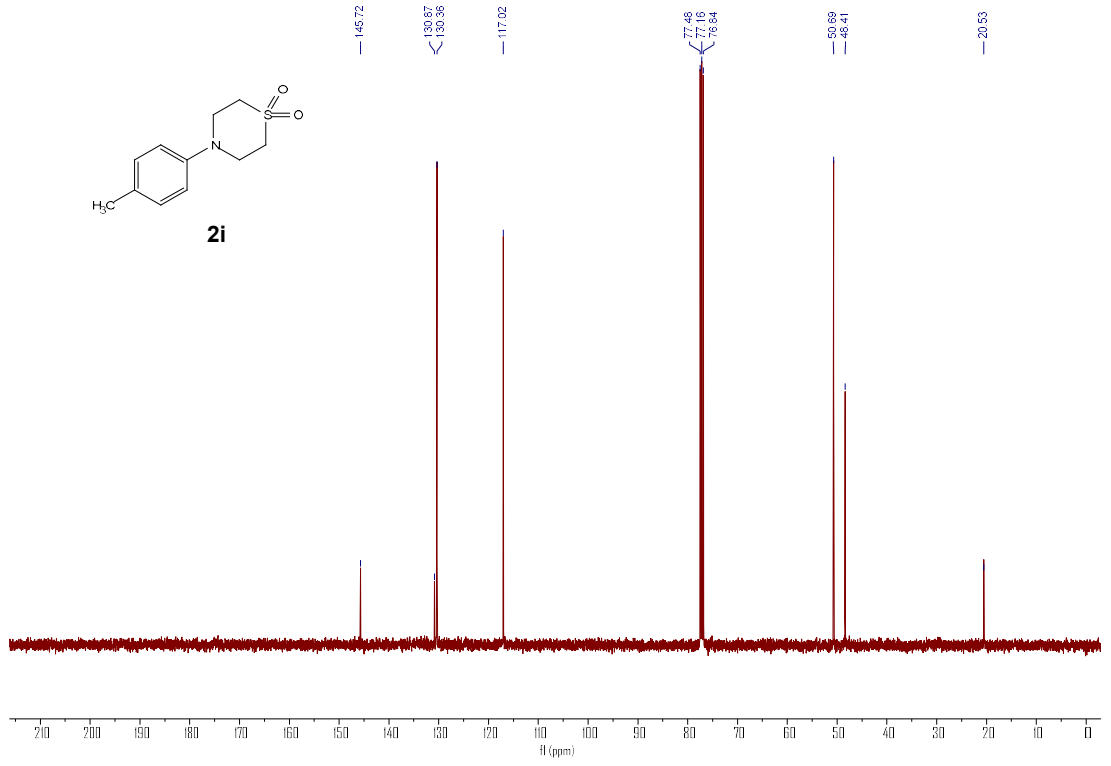
f1 (ppm)

2i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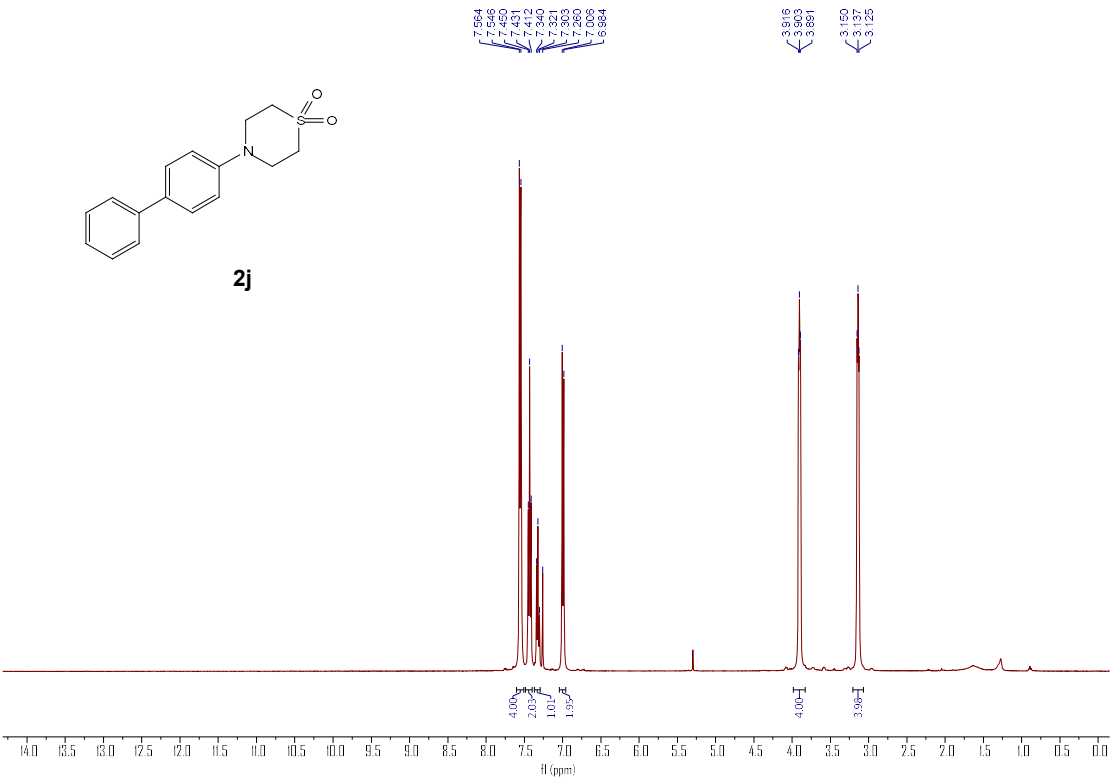
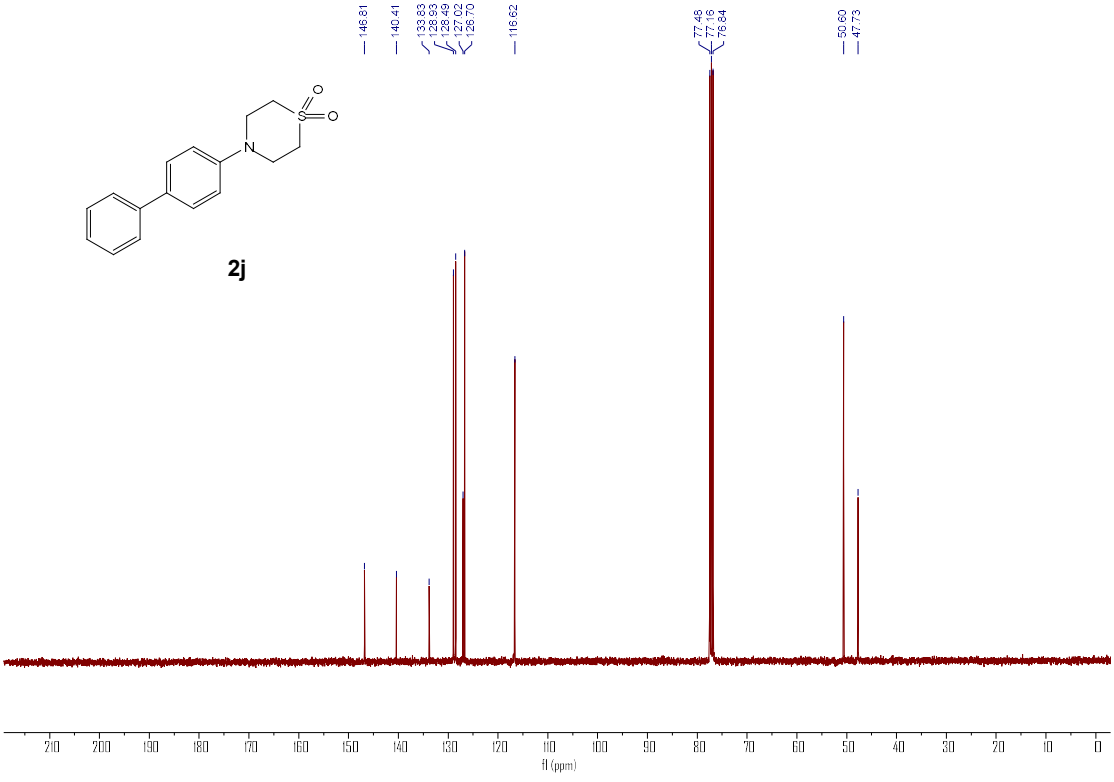
130.36
117.02
77.48
77.16
76.84
50.69
48.41
20.53
f1 (ppm)

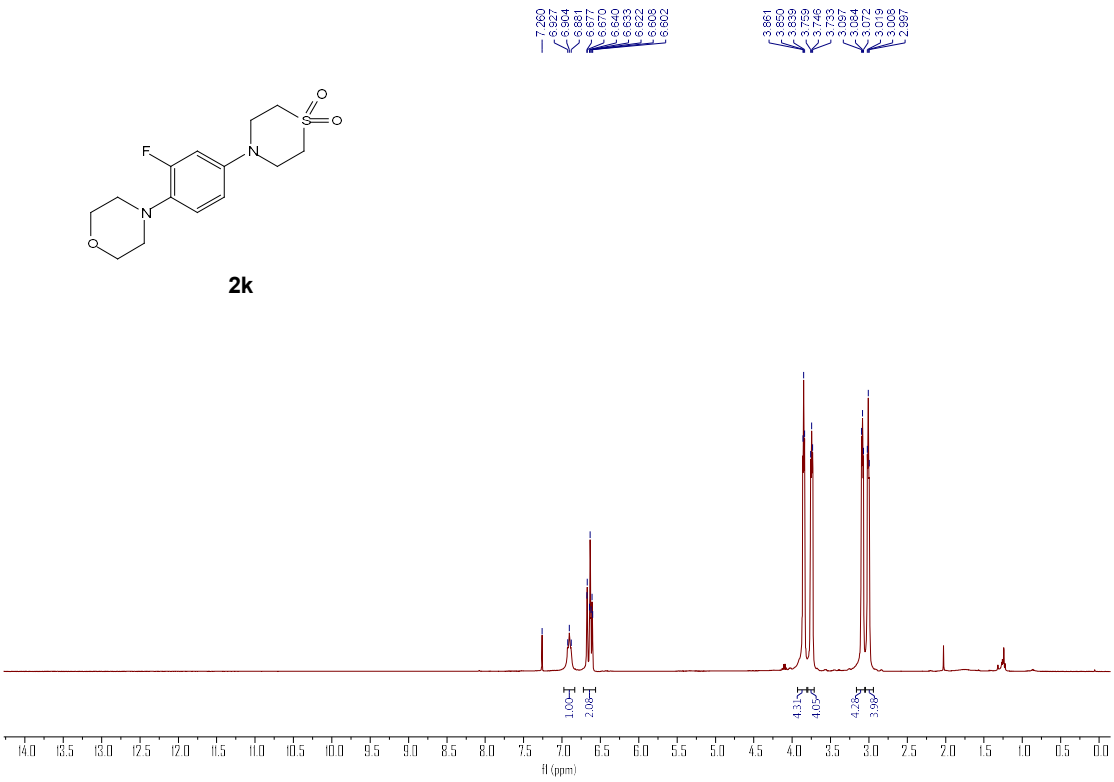
2i


7.564
7.546
7.450
7.431
7.412
7.340
7.321
7.303
7.260
7.006
6.984
3.916
3.903
3.891
3.150
3.137
3.125
4.00
2.03
1.01
1.95
4.00
3.98
f1 (ppm)

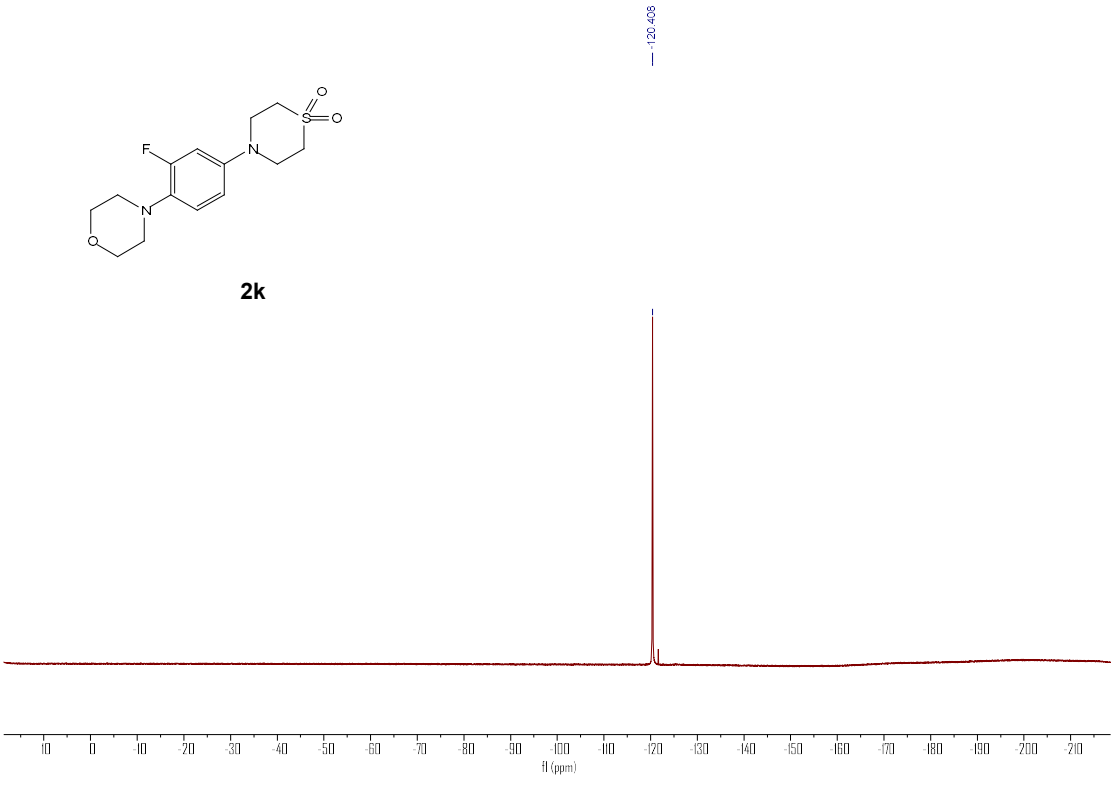
2j


146.81
140.41
133.83
128.93
128.49
127.02
126.70
116.62
77.48
77.16
76.84
50.60
47.73
f1 (ppm)

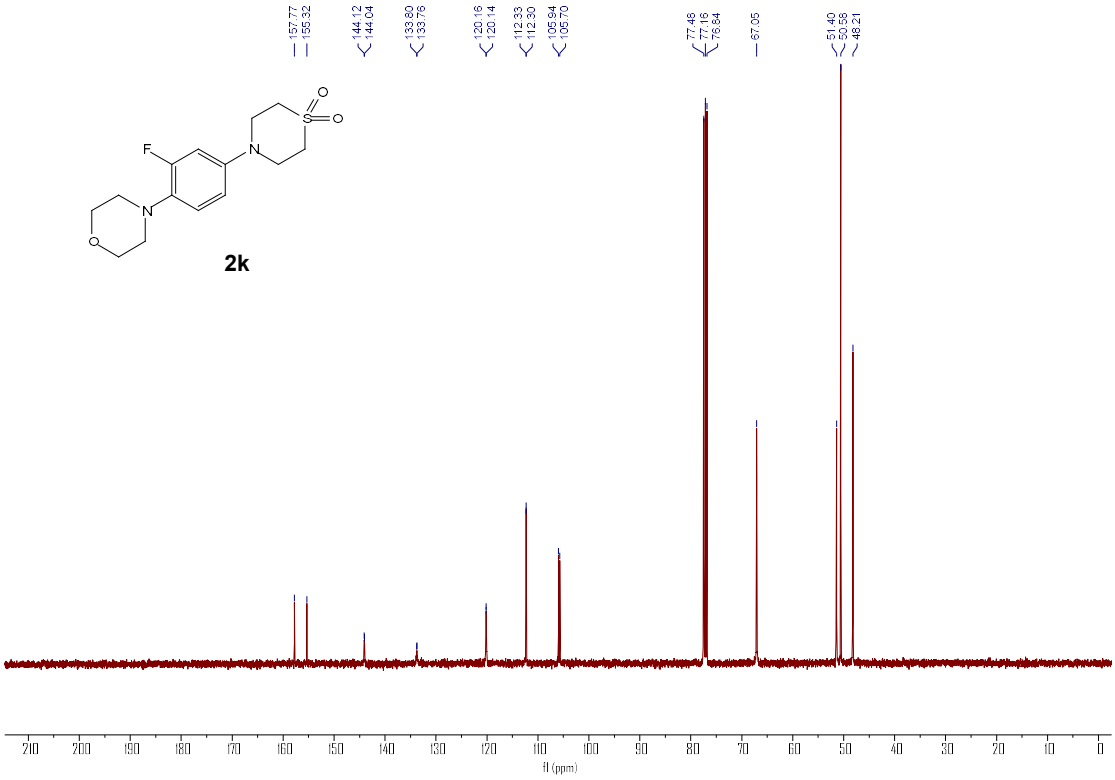
2j


7.260
6.927
6.904
6.881
6.677
6.670
6.640
6.633
6.622
6.608
6.602
3.861
3.850
3.839
3.759
3.746
3.733
3.087
3.084
3.072
3.019
3.008
2.997
1.00
2.06
4.31
4.05
4.26
3.98
f1 (ppm)

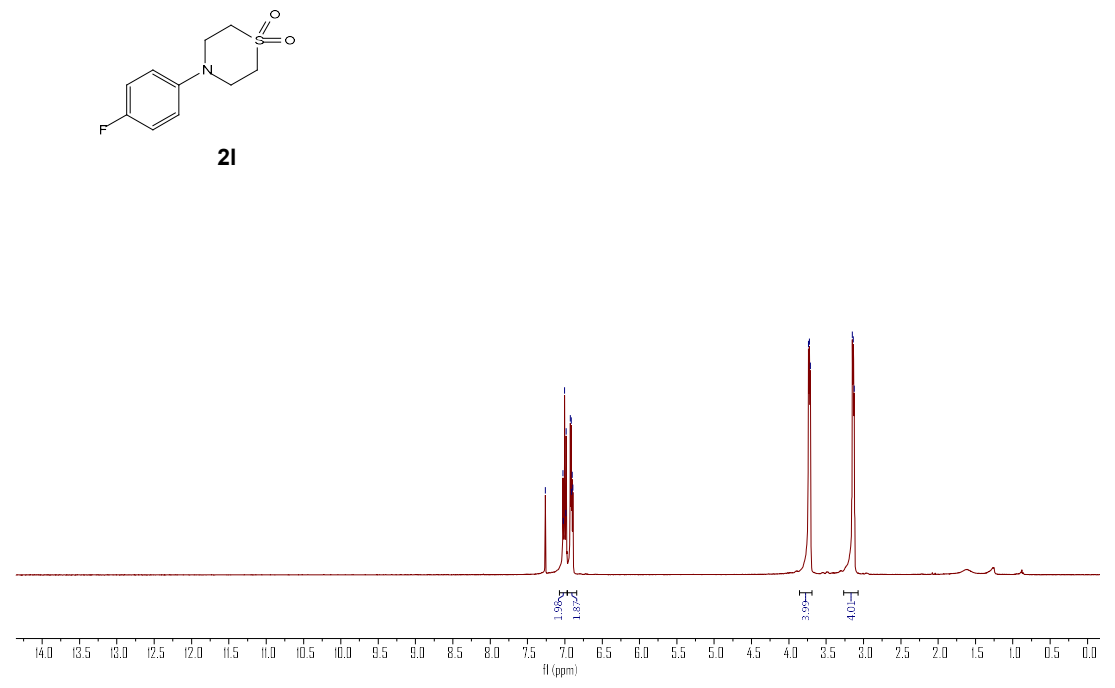
2k


-120.408
f1 (ppm)

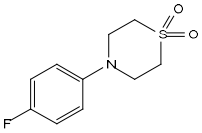
2k


157.77
155.32
144.12
144.04
133.80
133.76
120.16
120.14
112.33
112.30
105.94
105.70
77.48
77.16
76.84
67.05
51.40
50.58
48.21
F
N
O
S
O
O
N
O
f1 (ppm)

2k

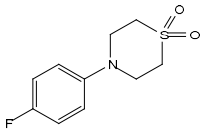

7.260
7.025
7.019
7.002
6.987
6.982
6.926
6.915
6.909
6.903
6.892
3.737
3.725
3.711
3.149
3.136
3.123
S
O
O
N
F
1.98
1.87
3.99
4.01
f1 (ppm)

2l



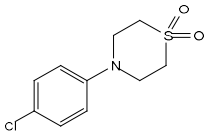
2l

-121.95
f1 (ppm)



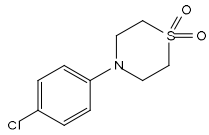
2l

159.32
156.92
145.11
145.08
119.30
119.22
116.49
116.27
77.48
77.16
76.84
50.99
49.32
f1 (ppm)



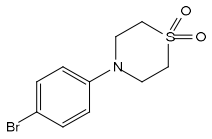
2m

7.296
7.274
8.906
8.894
3.847
3.834
3.820
3.156
3.144
3.132
2.16
1.93
4.00
3.93
f1 (ppm)



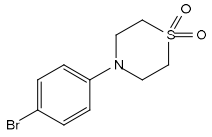
2m

146.54
129.81
126.34
118.03
77.48
77.16
76.84
50.66
48.15
f1 (ppm)


O
S
O
N
Br

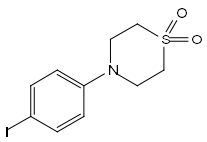
2n

7.405
7.383
7.260
6.808
6.786
3.825
3.812
3.799
3.112
3.089
3.067
2.00
2.00
3.96
4.01
f1 (ppm)


O
S
O
N
Br

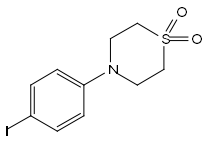
2n

146.95
132.73
118.27
113.45
77.48
77.16
76.84
50.63
47.89
f1 (ppm)



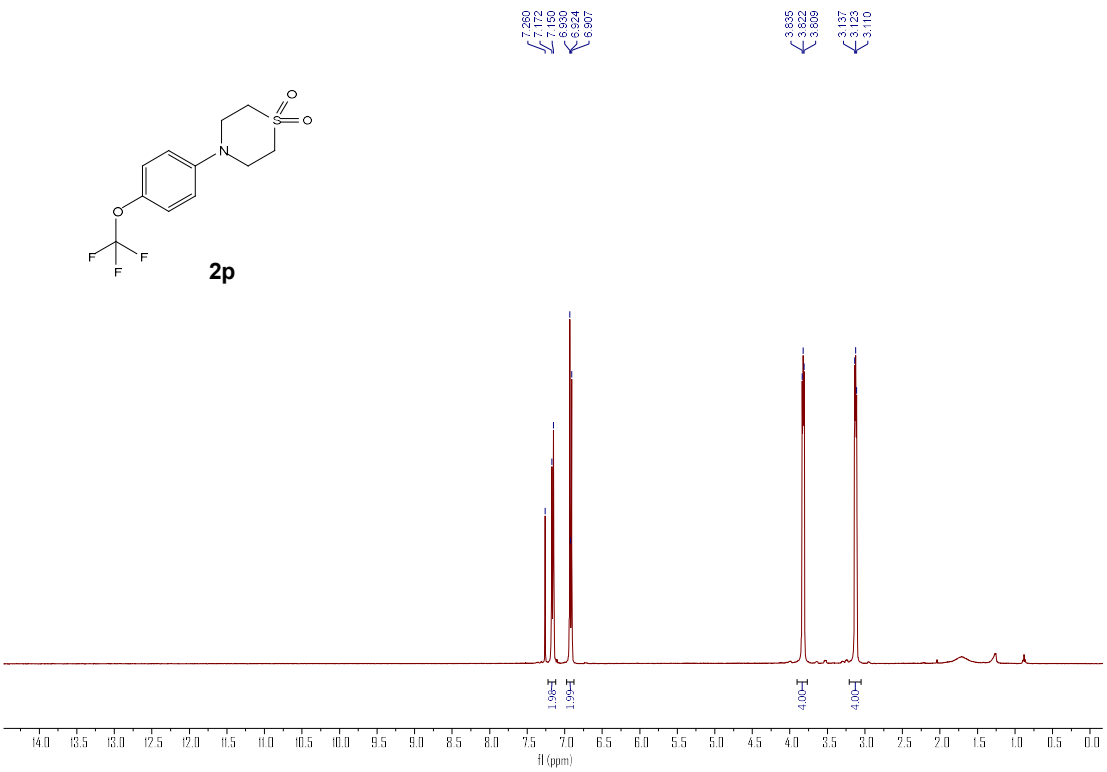
2o

7.584
7.562
7.260
6.707
6.684
3.838
3.825
3.811
3.110
3.096
3.084
1.98
2.00
3.99
3.97
f1 (ppm)

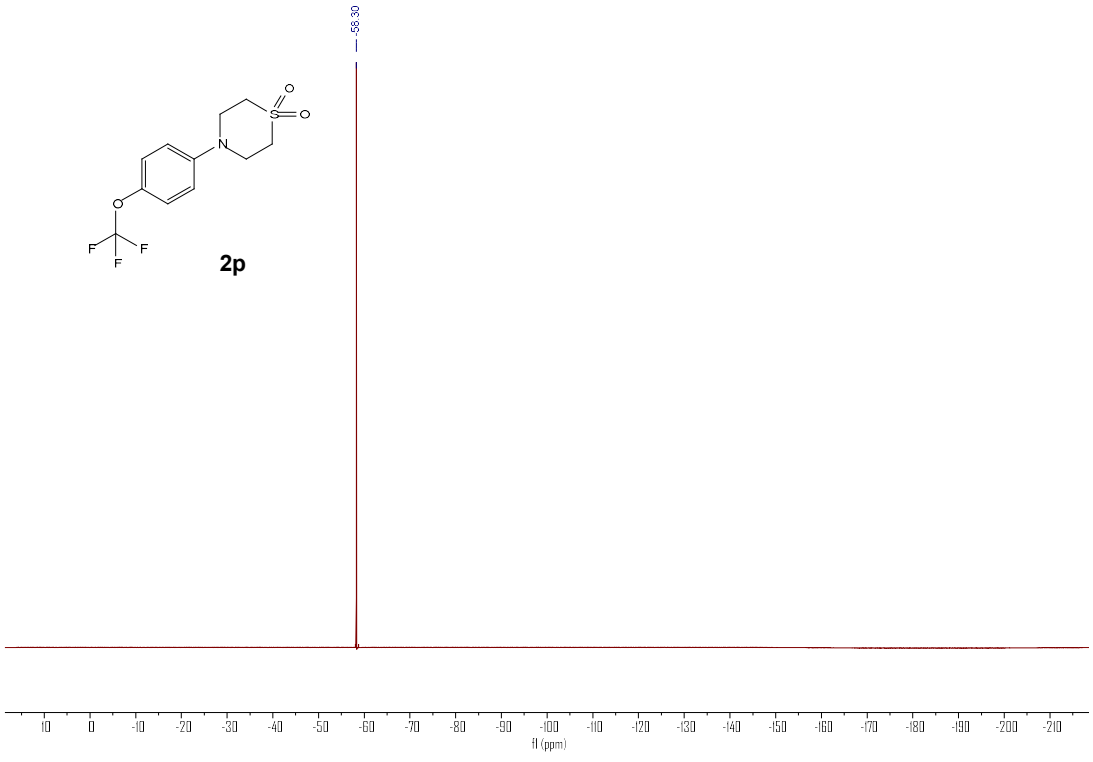


2o

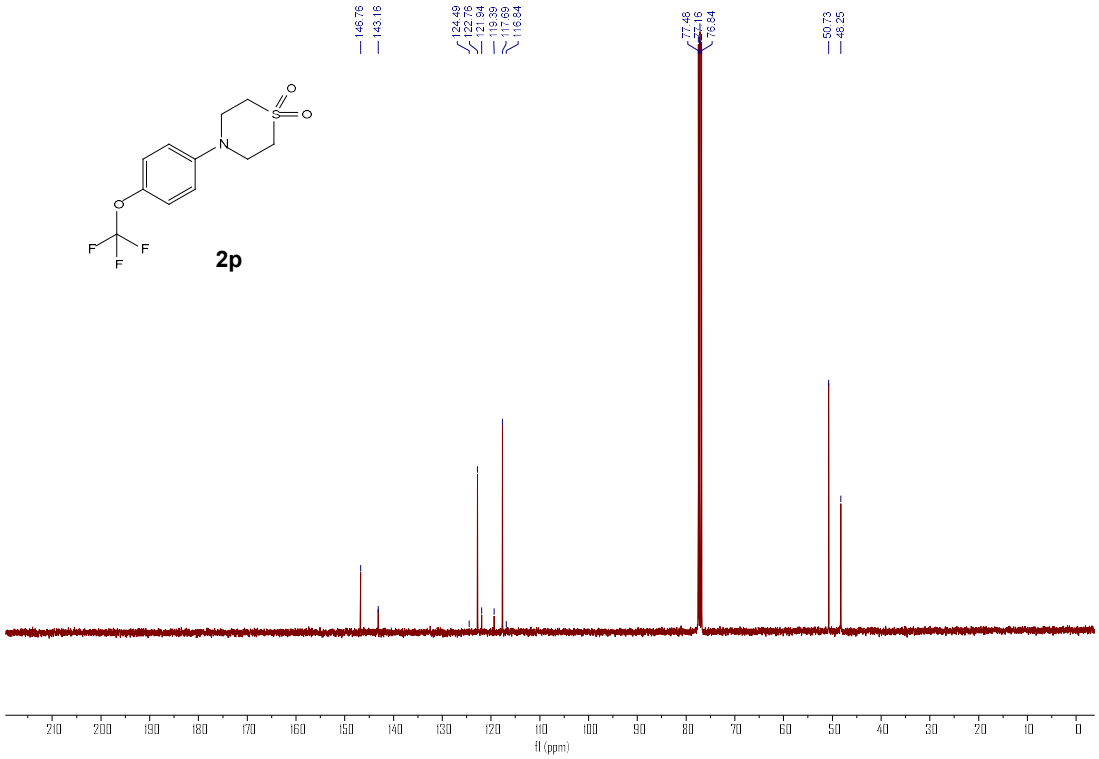
147.41
138.65
118.51
83.05
77.48
77.16
76.84
50.56
47.60
f1 (ppm)


7.280
7.172
7.150
6.930
6.924
6.907
3.835
3.822
3.809
3.137
3.123
3.110
1.98
1.99
4.00
4.00
f1 (ppm)

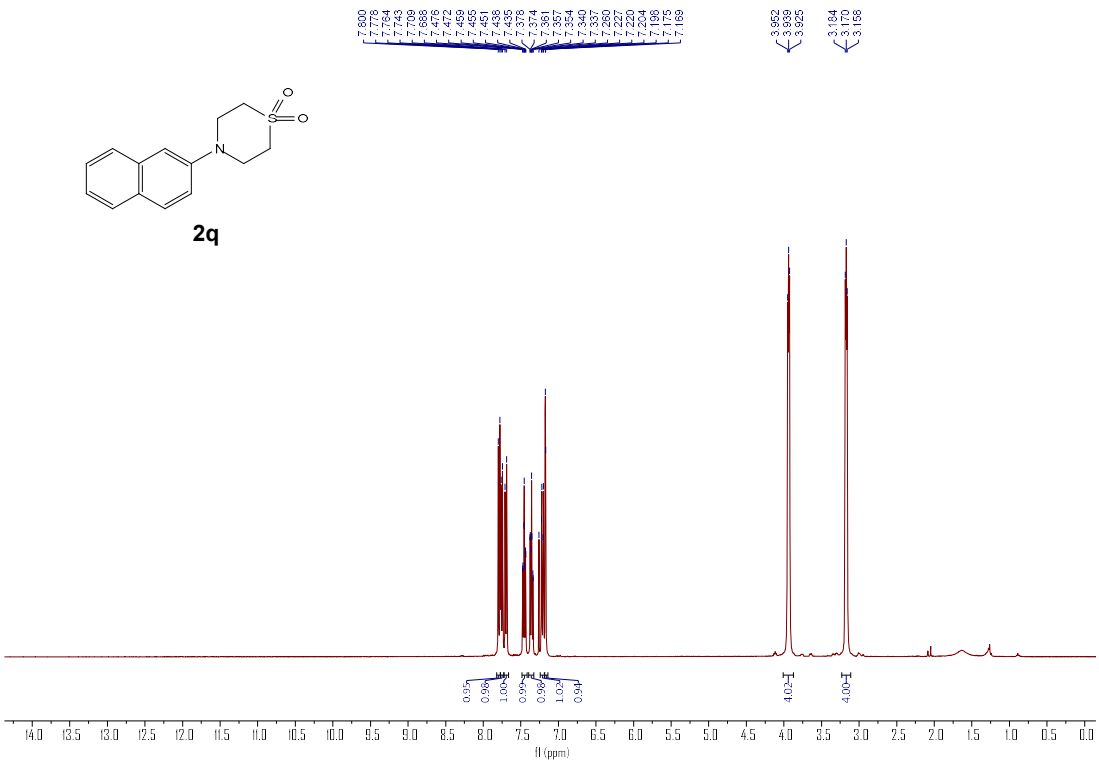
2p


-58.30
f1 (ppm)

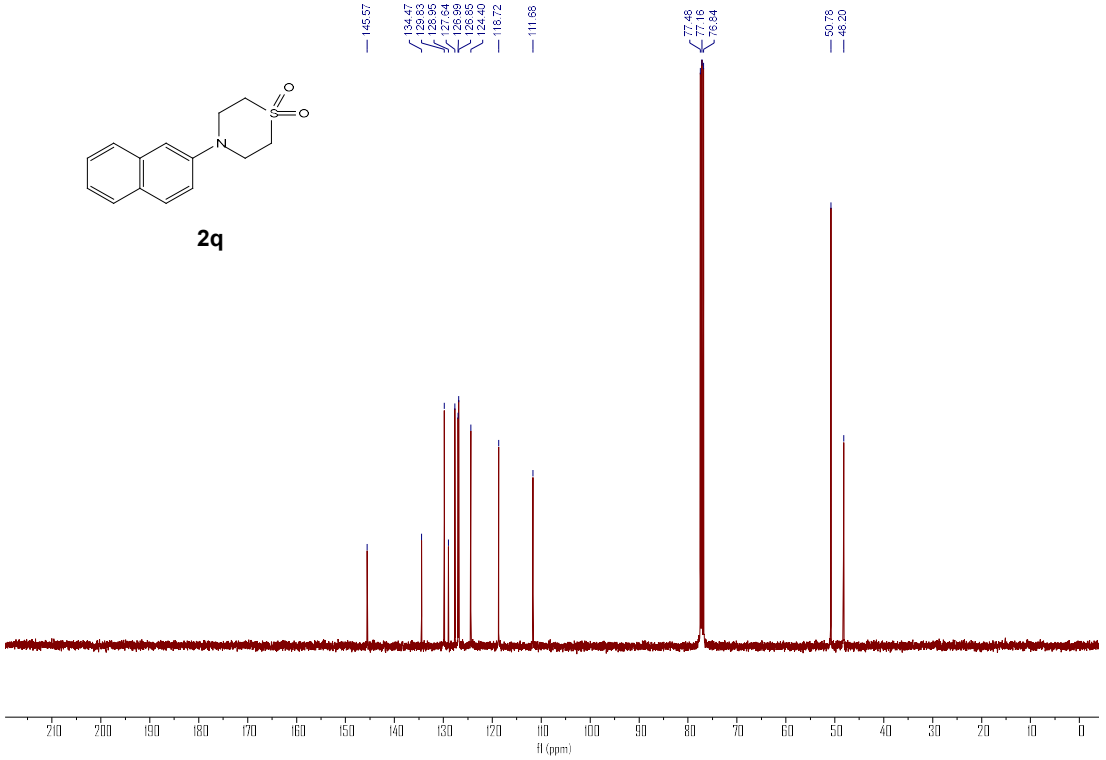
2p


146.76
143.16
124.49
122.78
121.94
119.39
117.69
116.84
77.46
77.16
76.84
50.73
48.25
f1 (ppm)

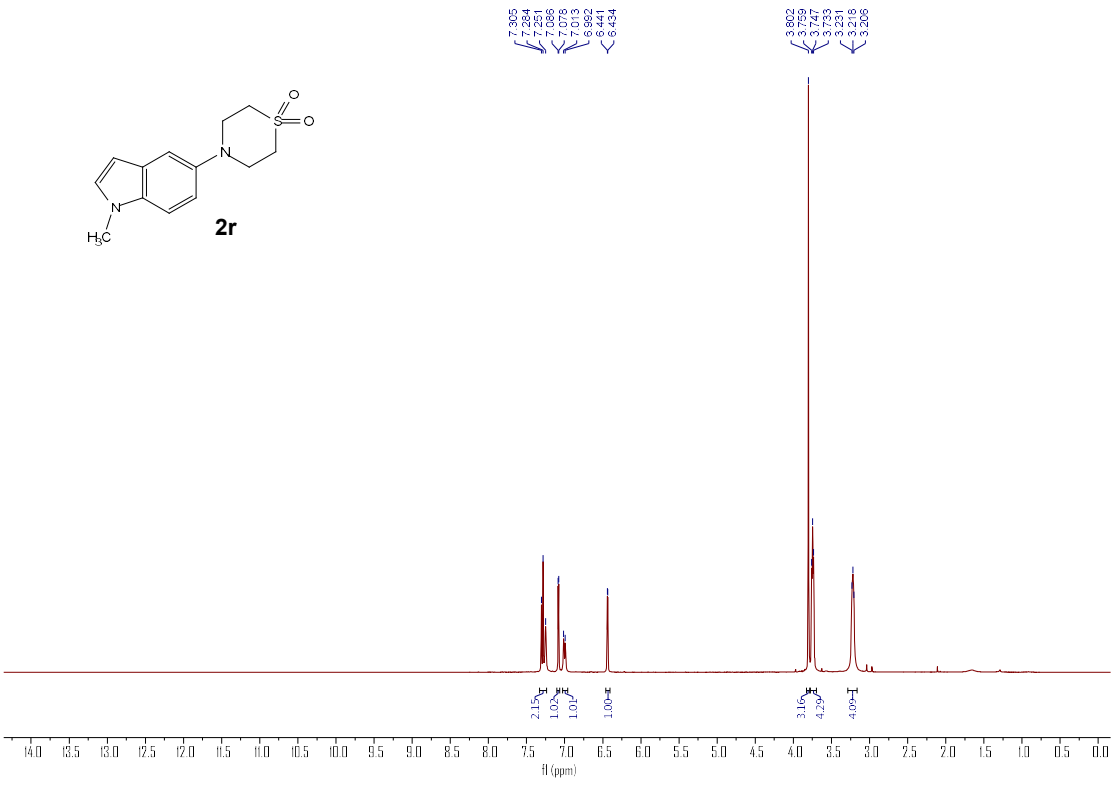
2p


7.800
7.778
7.764
7.744
7.709
7.688
7.476
7.472
7.459
7.455
7.451
7.438
7.435
7.376
7.374
7.361
7.357
7.354
7.340
7.337
7.260
7.227
7.220
7.204
7.196
7.175
7.169
3.952
3.939
3.925
3.184
3.170
3.156
0.95
0.98
1.00
0.99
0.98
1.03
0.94
4.02
4.00
f1 (ppm)

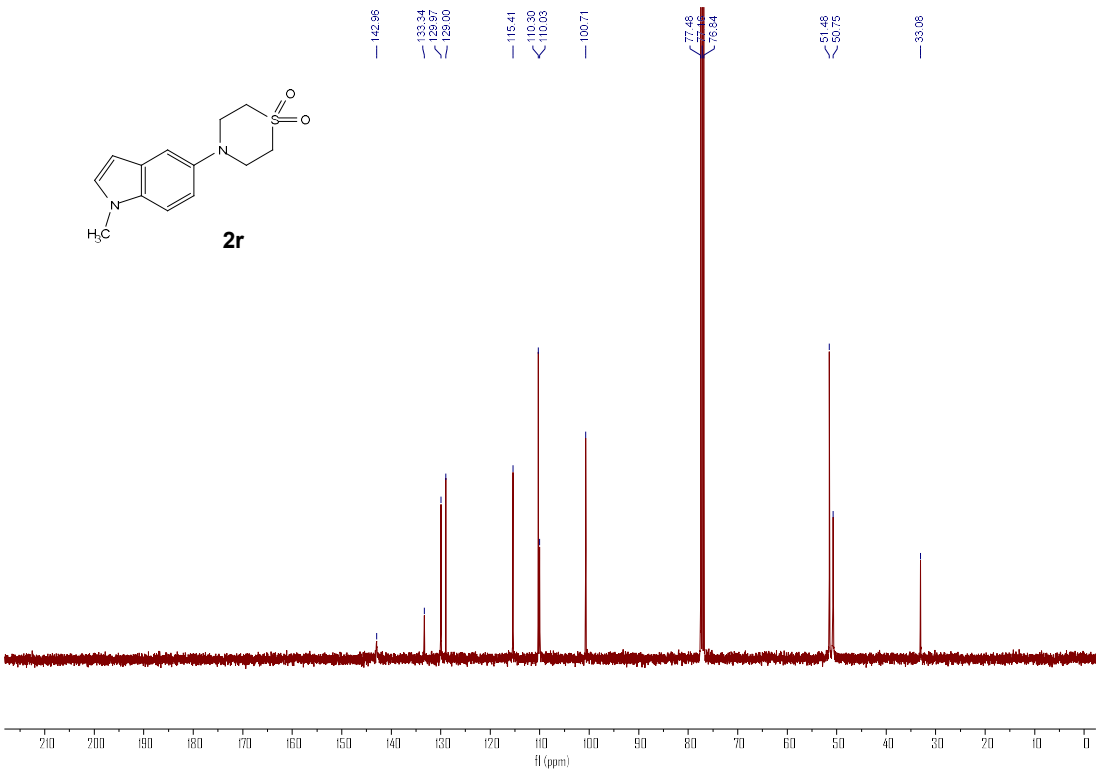
2q


145.57
134.47
129.83
128.95
127.64
126.89
126.85
124.40
118.72
111.68
77.48
77.16
76.84
50.78
48.20
f1 (ppm)

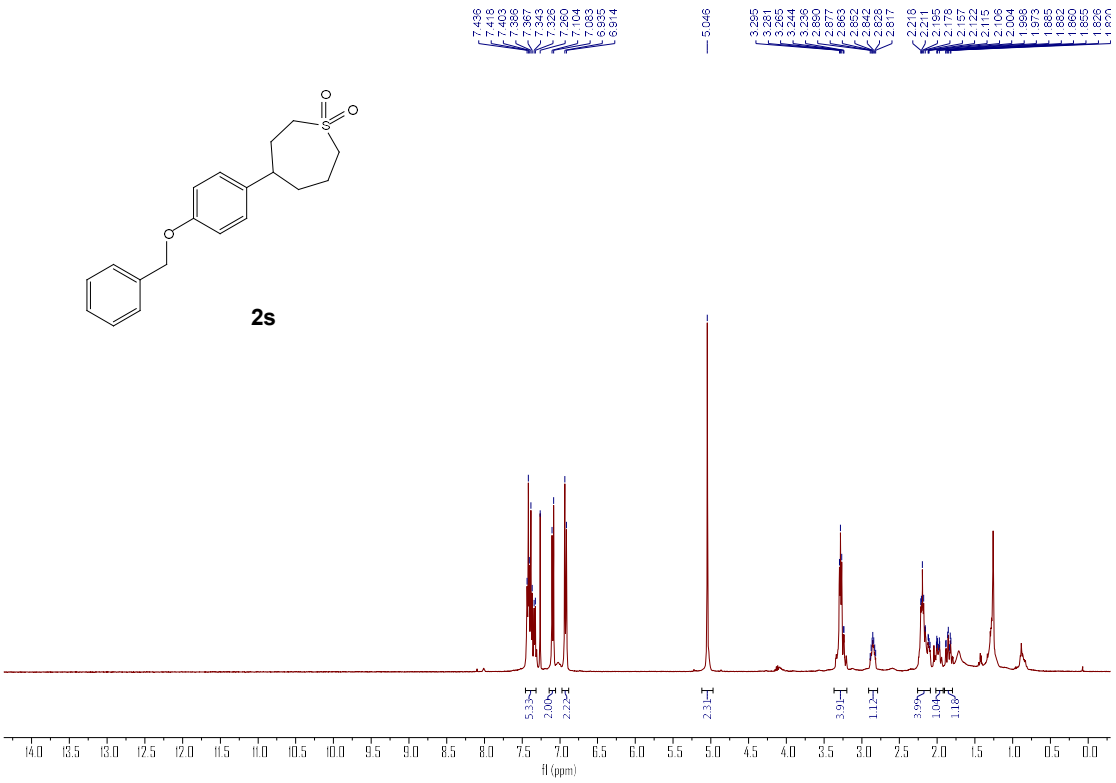
2q


7.305
7.284
7.251
7.086
7.078
7.073
6.892
6.441
6.434
3.802
3.759
3.747
3.733
3.231
3.218
3.206
2.15
1.02
1.01
1.00
3.16
4.29
4.00
f1 (ppm)

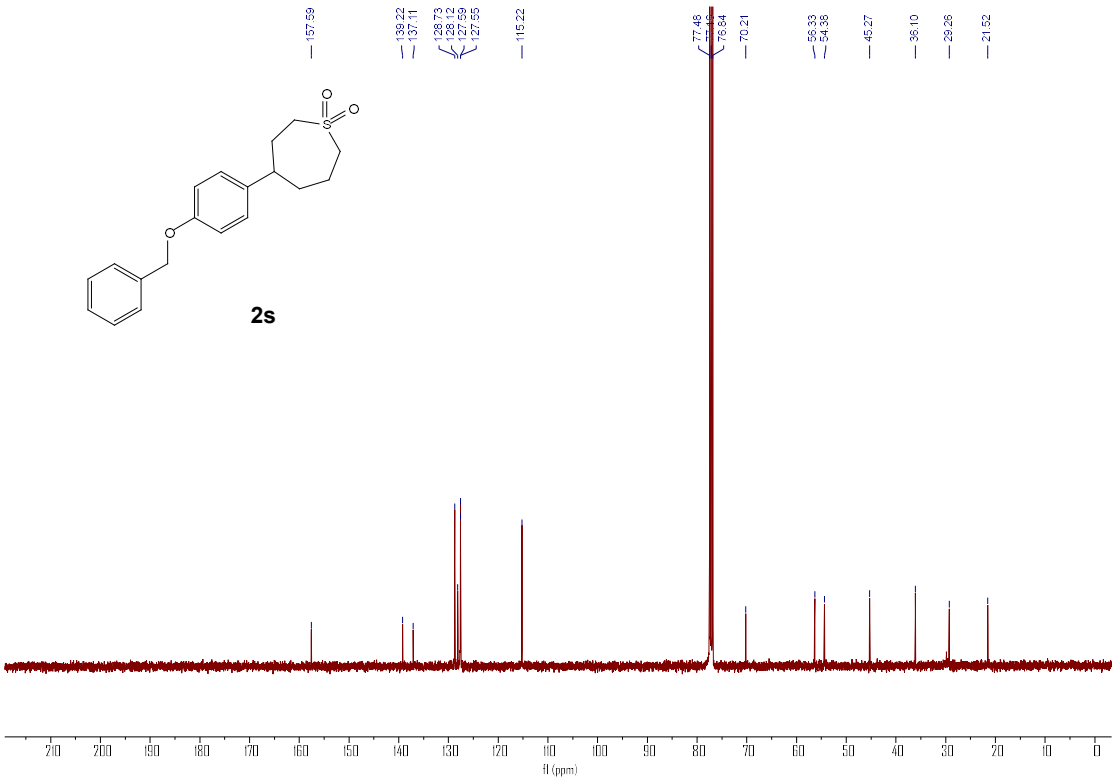
2r


142.96
133.34
129.97
129.00
115.41
110.30
110.03
100.71
77.48
77.16
76.84
51.48
50.75
33.08
f1 (ppm)

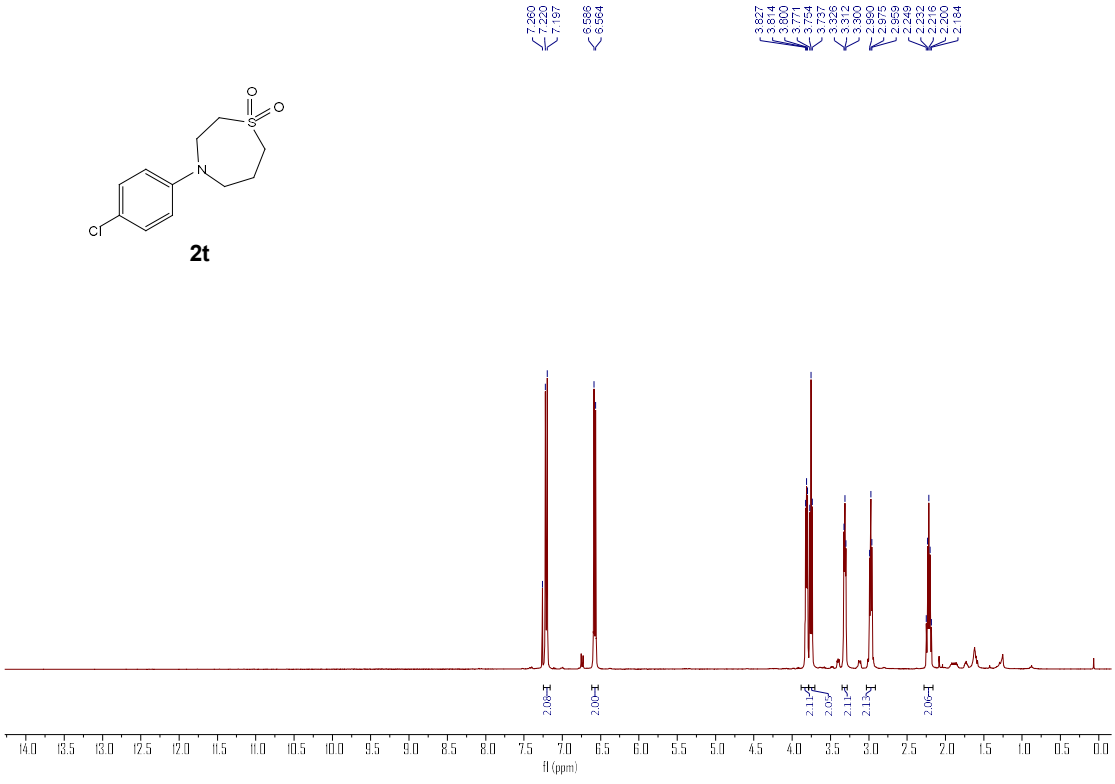
2r


7.436
7.418
7.403
7.386
7.367
7.343
7.326
7.260
7.104
7.083
6.935
6.914
5.046
3.295
3.281
3.265
3.244
3.236
2.880
2.877
2.863
2.852
2.842
2.828
2.817
2.218
2.211
2.195
2.178
2.157
2.122
2.115
2.108
2.004
1.966
1.875
1.885
1.882
1.860
1.855
1.826
1.691
5.33
2.00
2.22
2.31
3.91
1.12
3.99
1.04
1.10
f1 (ppm)

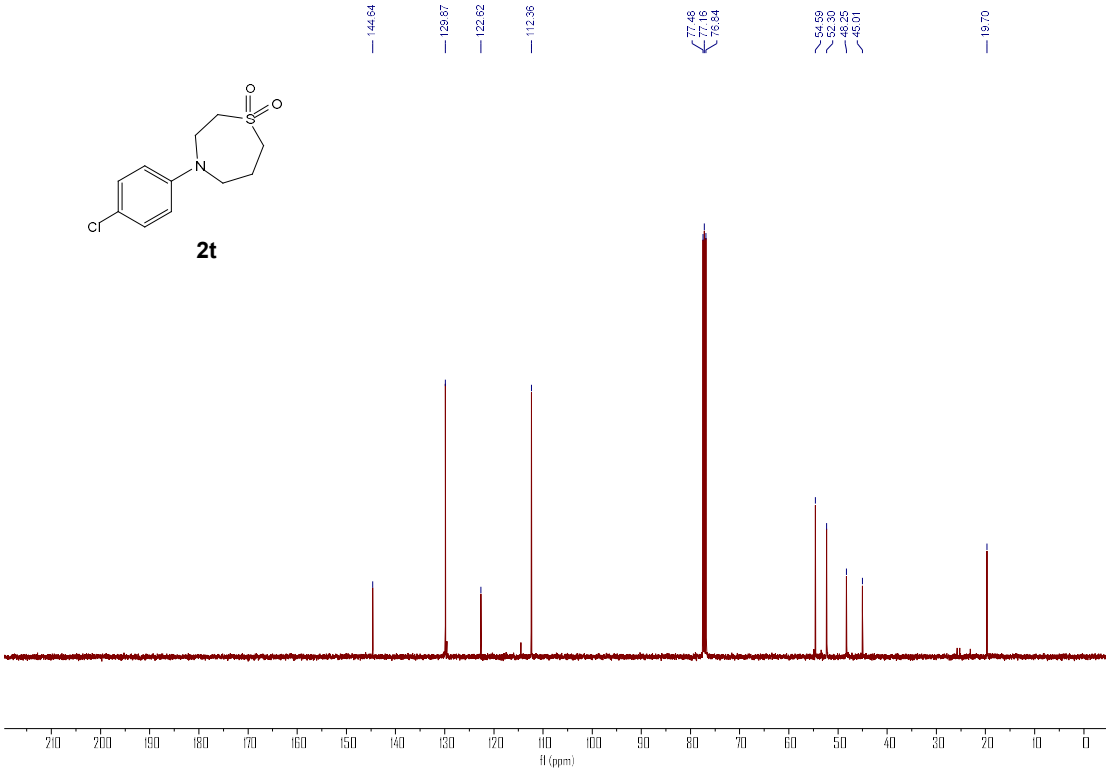
2s


157.59
138.22
137.11
128.73
128.42
127.59
127.55
115.22
77.48
77.16
76.84
70.21
56.33
54.38
45.27
36.10
29.26
21.52
f1 (ppm)

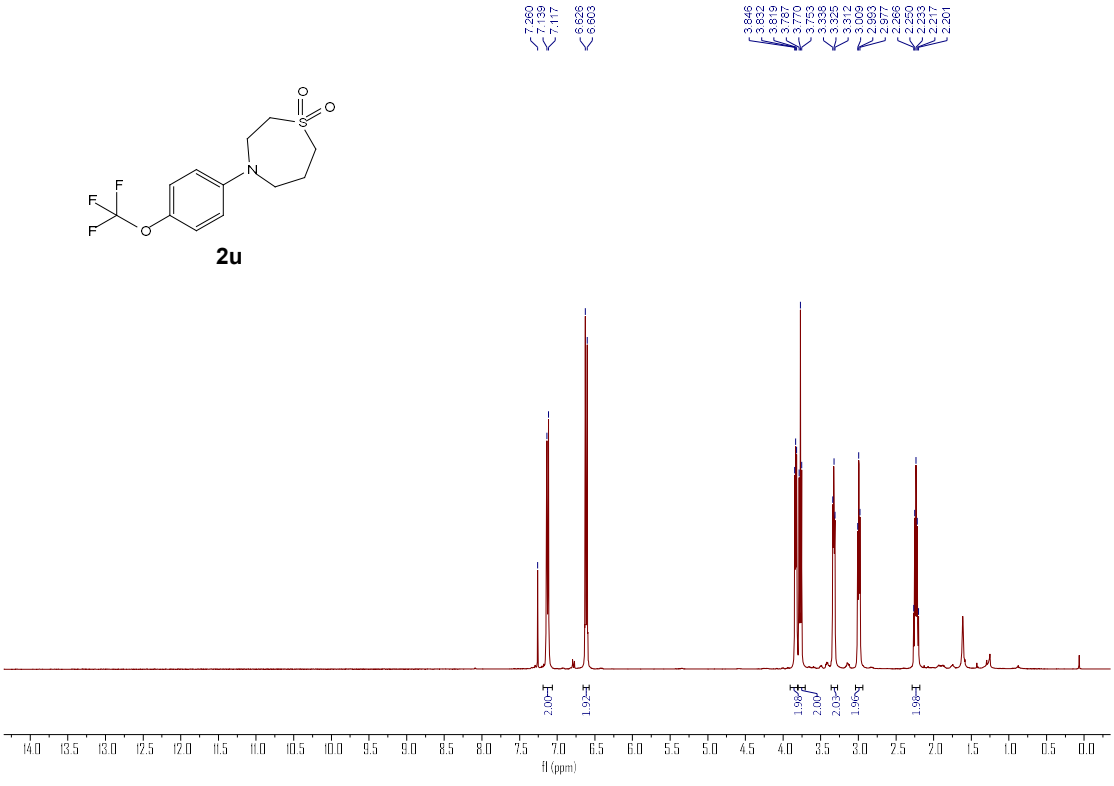
2s


7.260
7.220
7.197
6.586
6.564
3.827
3.814
3.800
3.771
3.754
3.737
3.326
3.312
3.300
3.286
2.975
2.869
2.249
2.232
2.216
2.200
2.184
2.08
2.00
2.11
2.09
2.11
2.13
2.06
f1 (ppm)

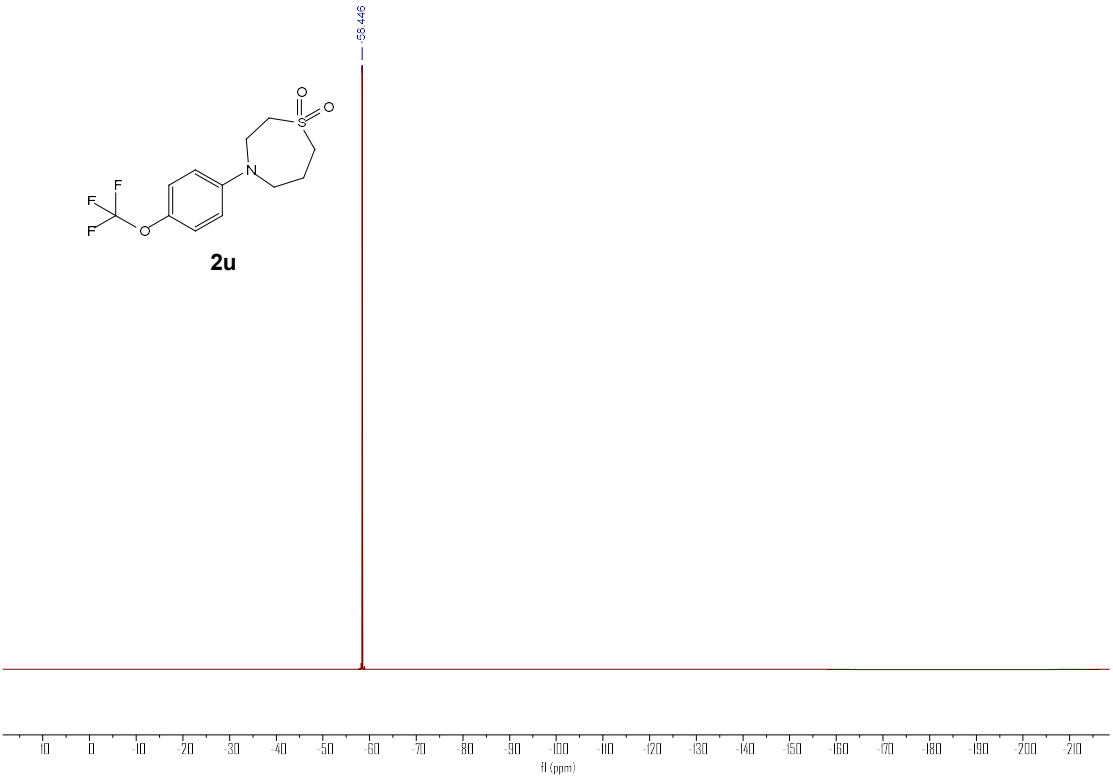
2t

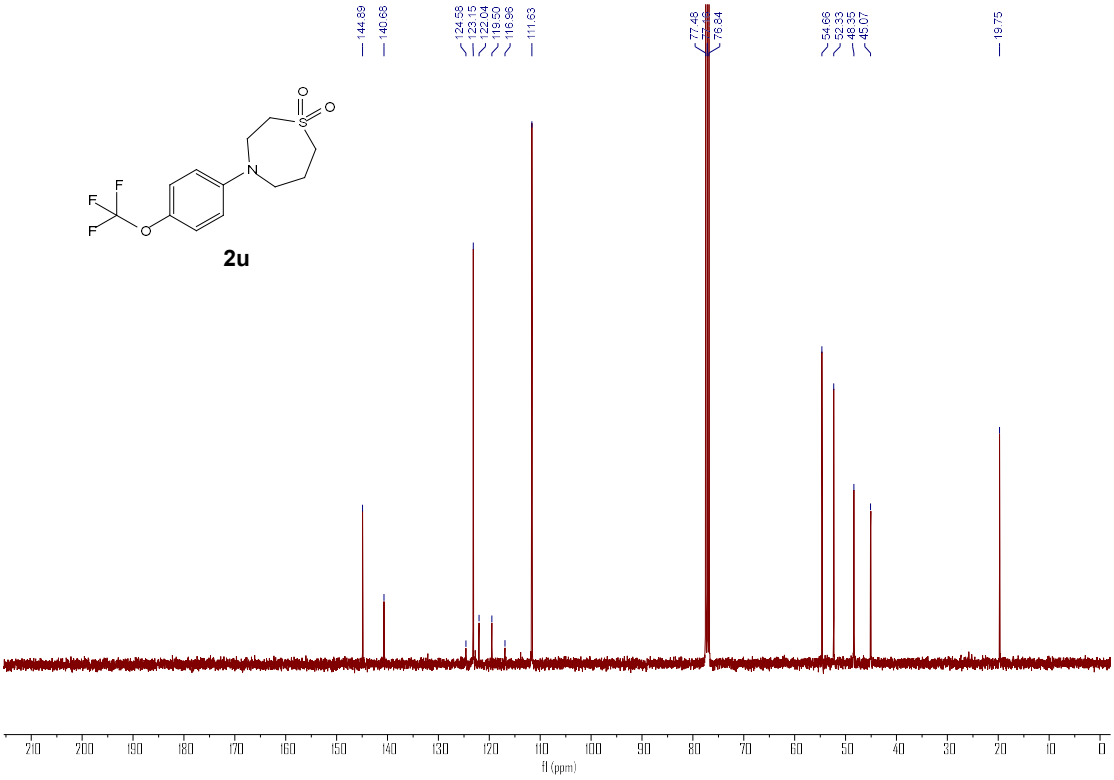

144.64
129.67
122.62
112.36
77.48
77.16
76.84
54.59
52.30
46.25
45.01
19.70
Cl
f1 (ppm)

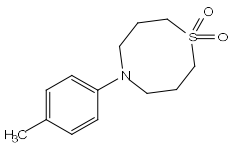
2t


7.260
7.139
7.117
6.626
6.603
3.846
3.832
3.819
3.807
3.770
3.753
3.338
3.325
3.312
3.009
2.993
2.977
2.266
2.250
2.233
2.217
2.201
F
F
F
O
N
S
O
O
2.00
1.92
1.98
2.00
2.03
1.96
1.98
f1 (ppm)

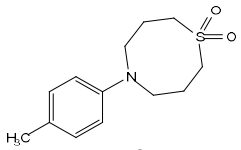
2u


-58.446
2u
f1 (ppm)

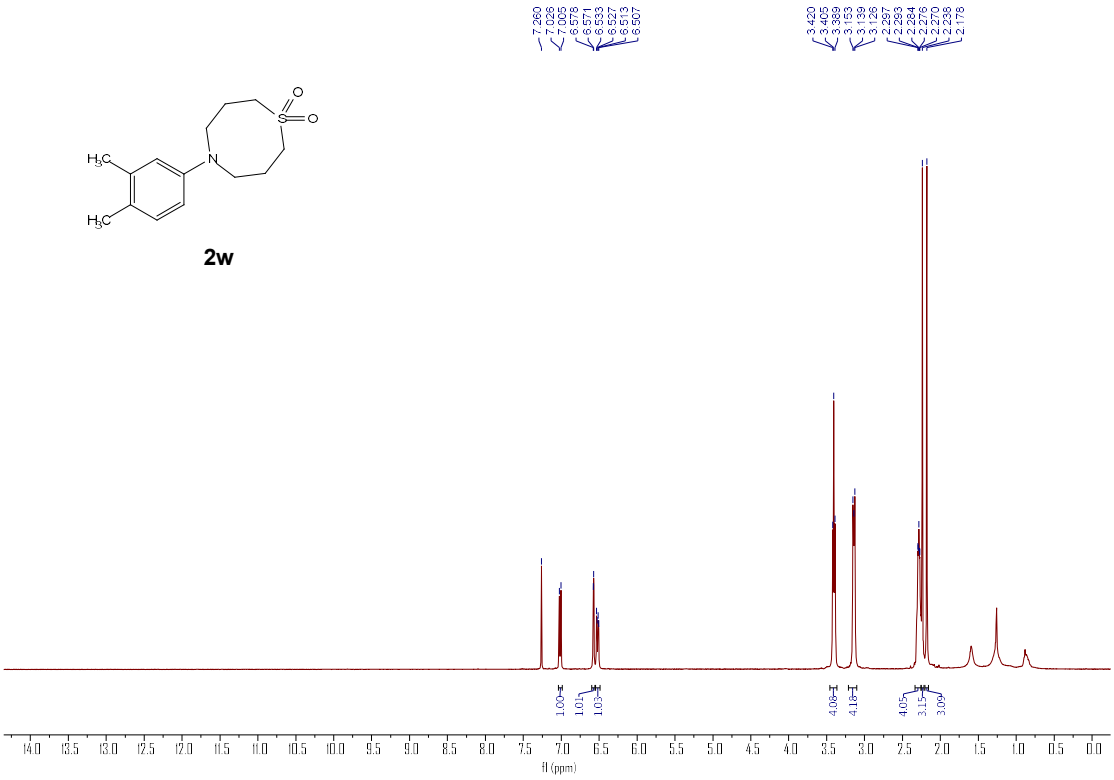

144.89
140.68
124.58
123.15
122.04
119.50
116.96
111.63
77.48
77.16
76.84
54.66
52.33
48.35
45.07
19.75
2u
f1 (ppm)



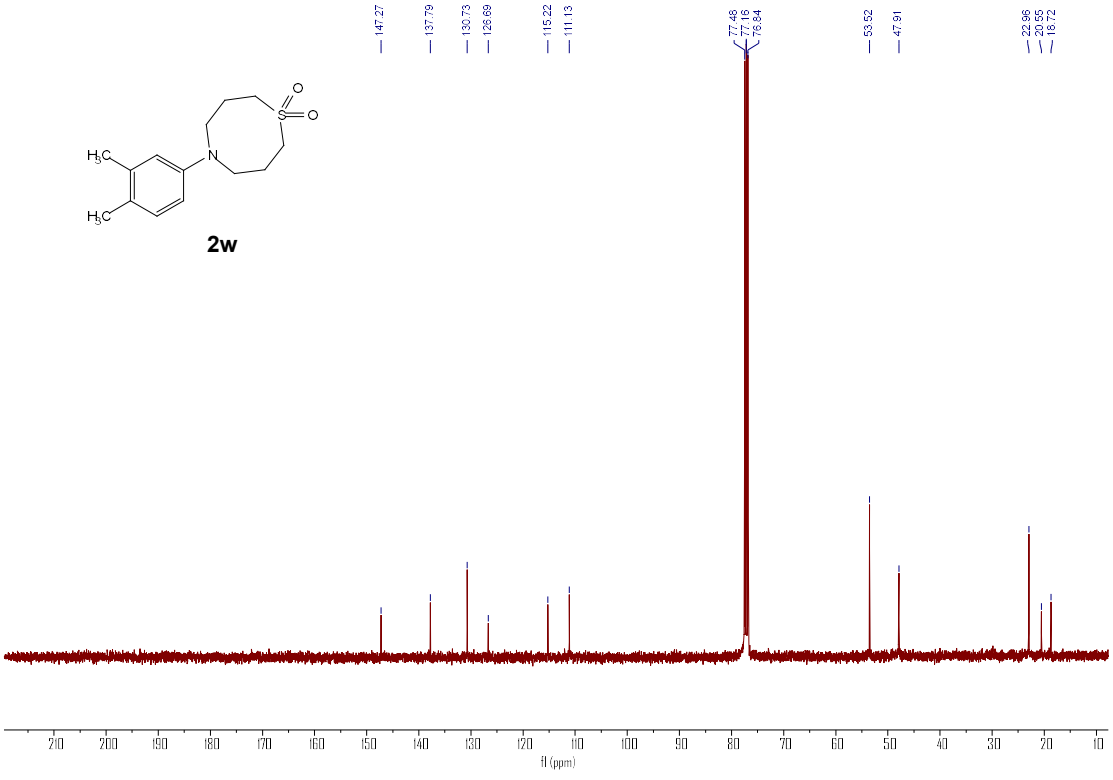
2v



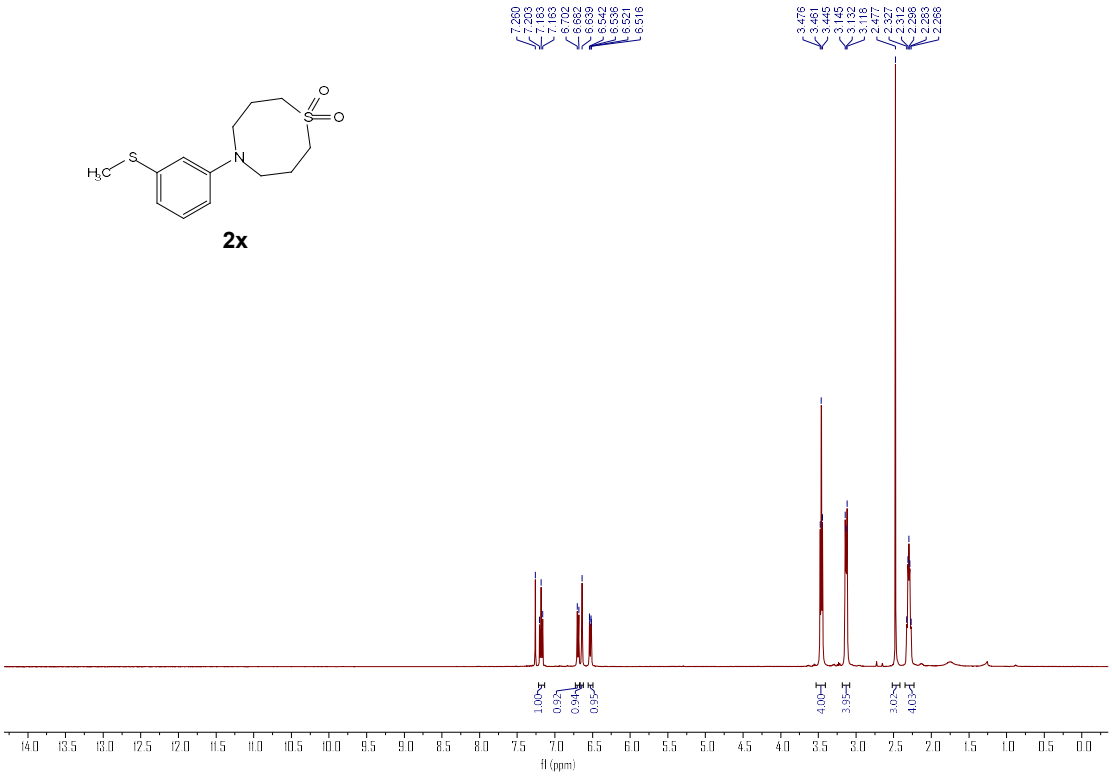
2v


7.260
7.028
7.005
6.578
6.571
6.533
6.527
6.513
6.507
3.420
3.405
3.389
3.153
3.139
3.126
2.297
2.283
2.264
2.256
2.270
2.238
2.176
1.00
1.01
1.03
4.08
4.18
4.05
3.15
3.09
f1 (ppm)

2w


147.27
137.79
130.73
126.69
115.22
111.13
77.48
77.16
76.84
53.52
47.91
22.96
20.55
18.72
f1 (ppm)

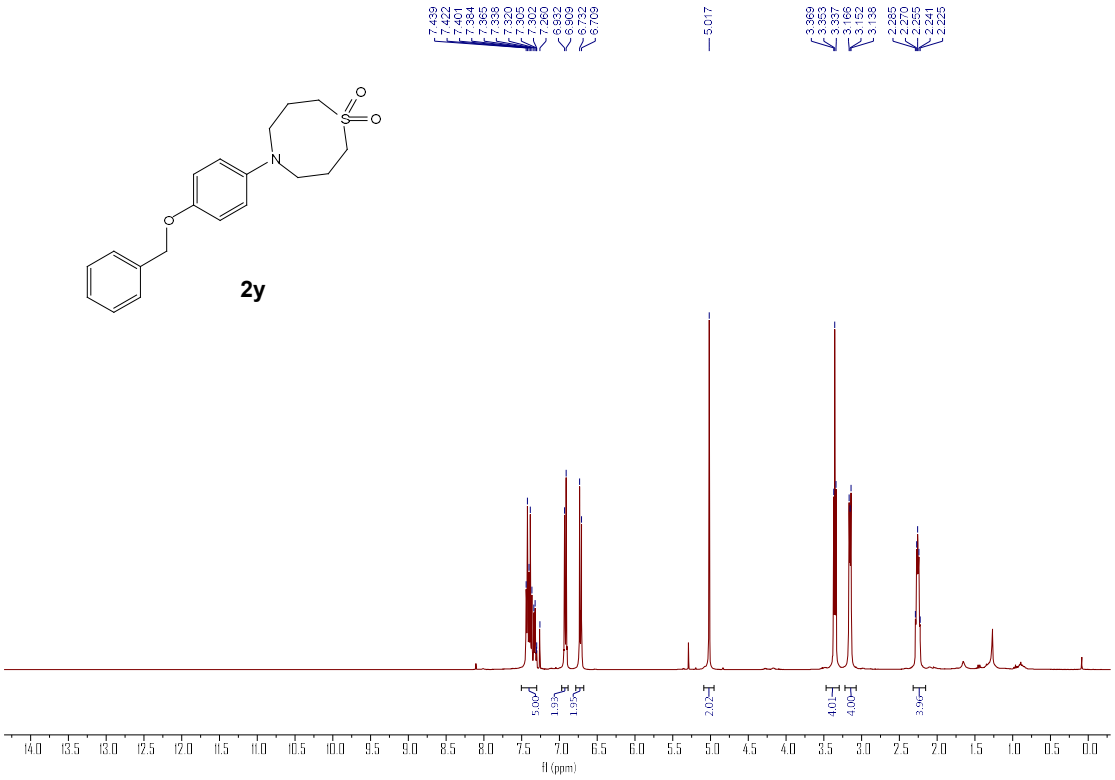
2w

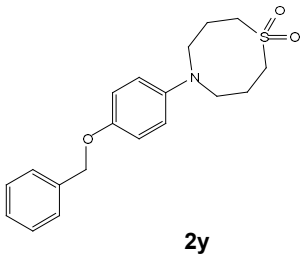

7.280
7.203
7.183
7.163
6.702
6.682
6.639
6.542
6.536
6.521
6.516
3.476
3.461
3.445
3.145
3.132
3.118
2.477
2.327
2.312
2.296
2.283
2.268
1.00
0.92
0.94
0.95
4.00
3.95
3.02
4.03
f1 (ppm)

2x

149.00
140.02
130.11
116.15
111.41
110.28
77.46
77.16
76.84
53.41
48.04
22.73
16.02
f1 (ppm)

2x

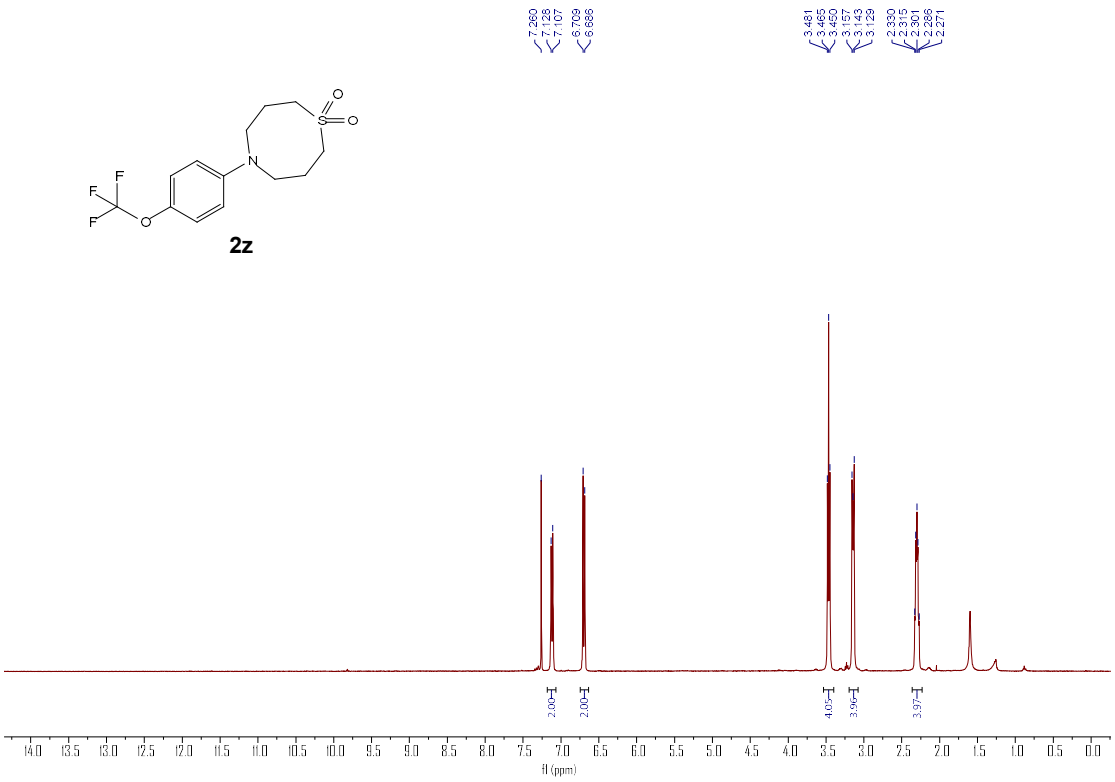

7.439
7.422
7.401
7.384
7.365
7.338
7.320
7.305
7.302
7.260
6.932
6.909
6.732
6.709
5.017
3.369
3.353
3.337
3.166
3.152
3.138
2.285
2.270
2.255
2.241
2.225
5.00
1.93
1.95
2.02
4.01
4.00
3.96
f1 (ppm)



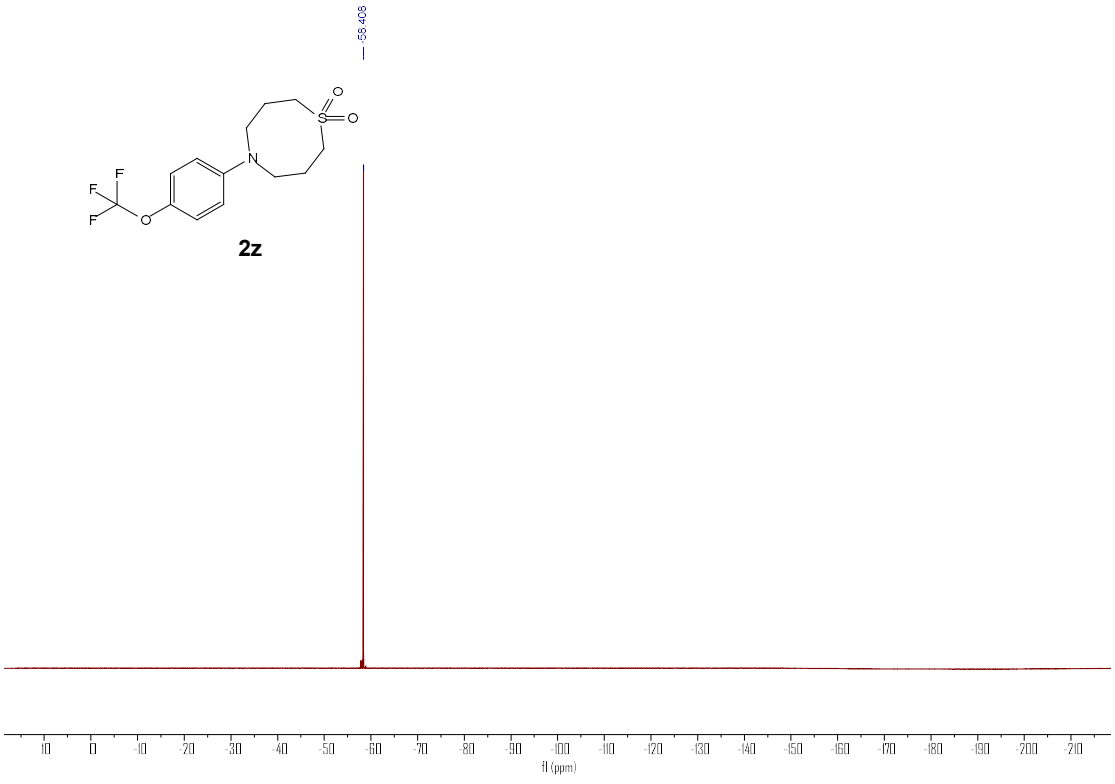
2y

151.97
143.81
137.45
128.66
128.59
127.55
116.29
115.21
77.48
77.16
76.84
70.77
53.60
48.27
23.04
f1 (ppm)

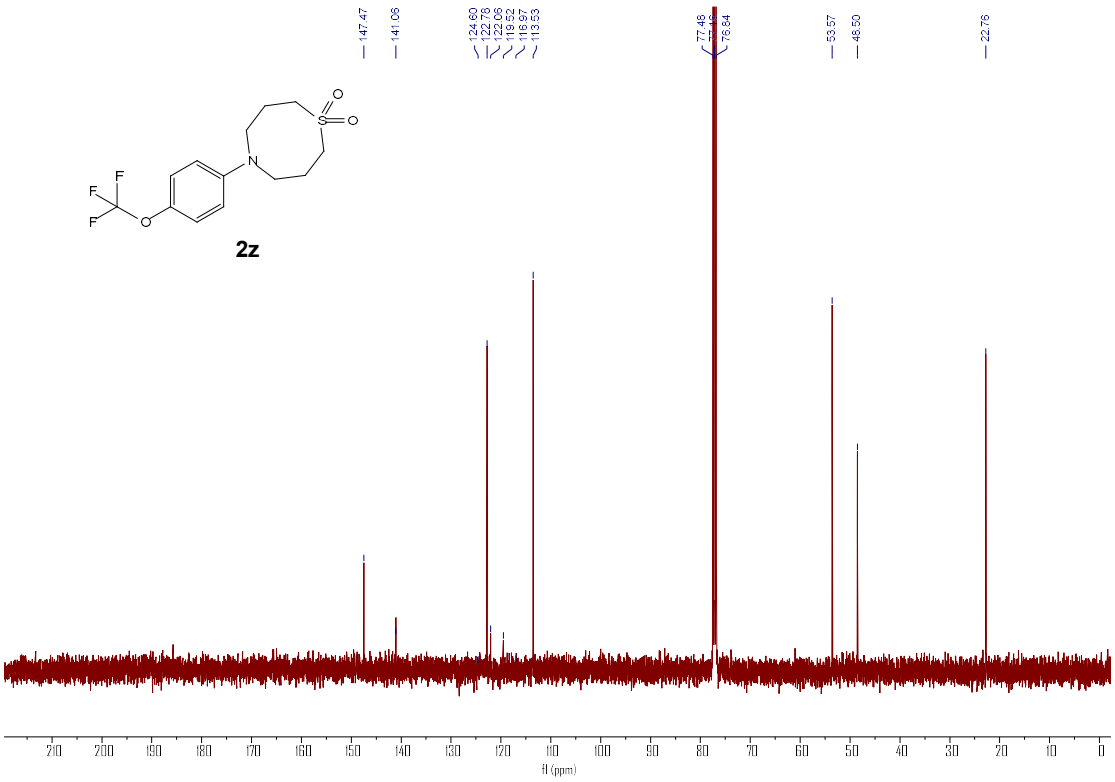
2y


7.260
7.128
7.107
6.709
6.686
3.481
3.465
3.450
3.157
3.143
3.129
2.330
2.315
2.301
2.286
2.271
2.00
2.00
4.05
3.96
3.97
f1 (ppm)

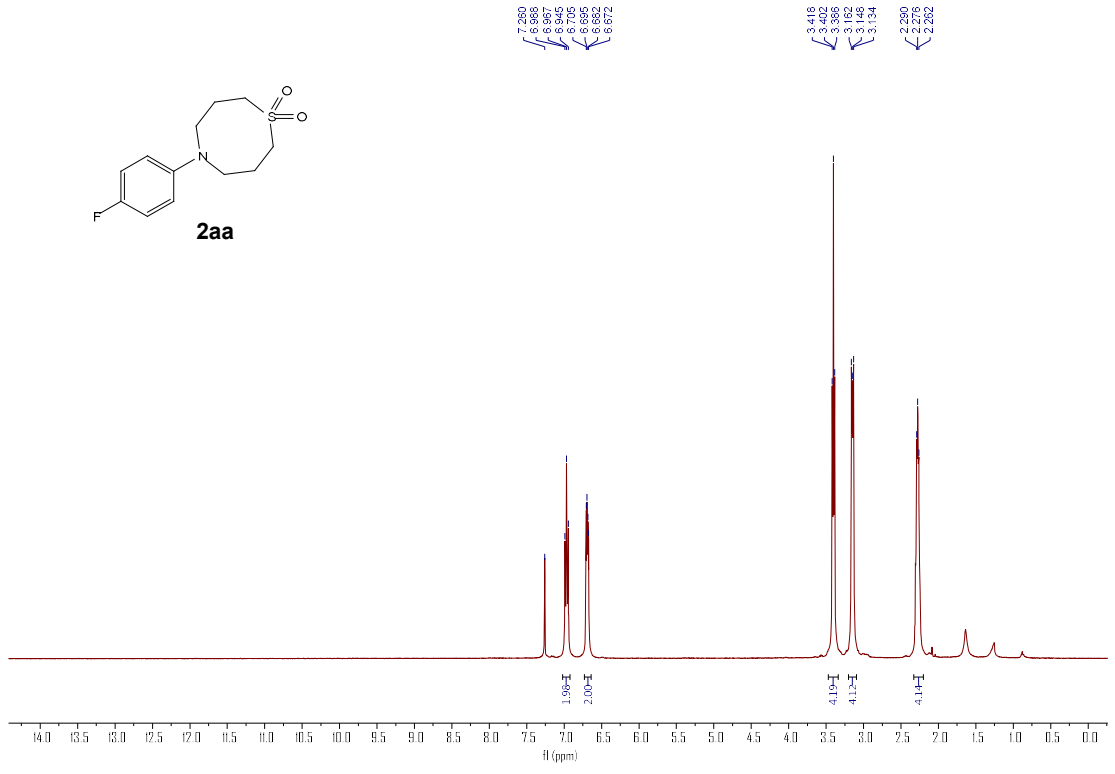
2z


-58.408
f1 (ppm)

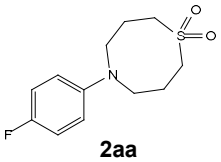
2z


147.47
141.06
124.60
122.78
122.06
119.52
118.97
113.53
77.46
76.84
53.57
46.50
22.78
F
F
F
O
N
S
O
O
f1 (ppm)

2z

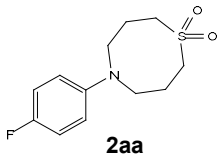

7.280
6.966
6.957
6.945
6.705
6.695
6.682
6.672
3.418
3.402
3.386
3.162
3.148
3.134
2.290
2.276
2.262
F
N
S
O
O
1.96
2.00
4.19
4.12
4.14
f1 (ppm)

2aa



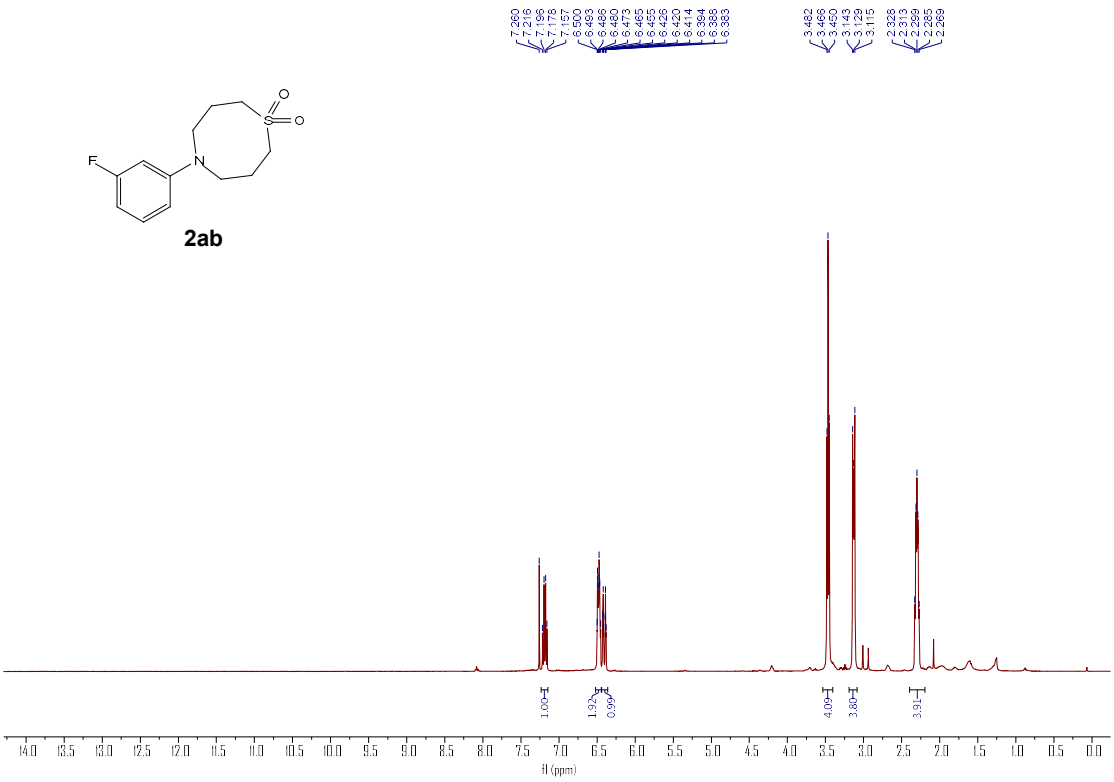
2aa

-126.725
f1 (ppm)

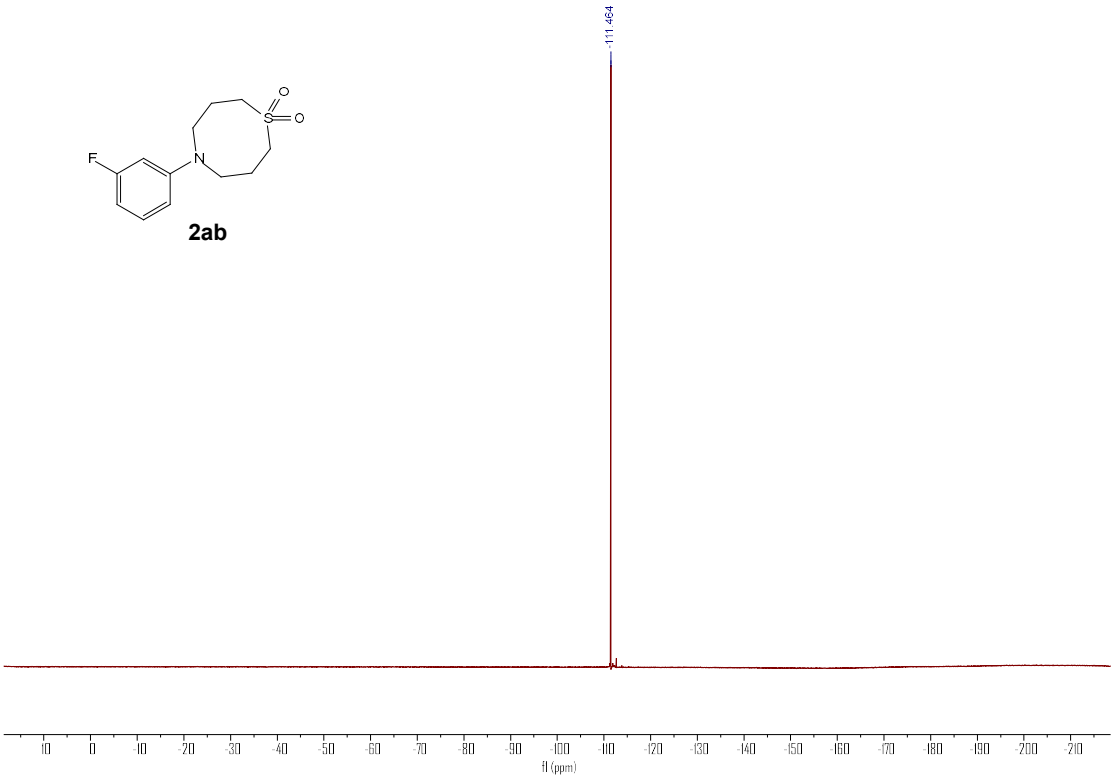


2aa

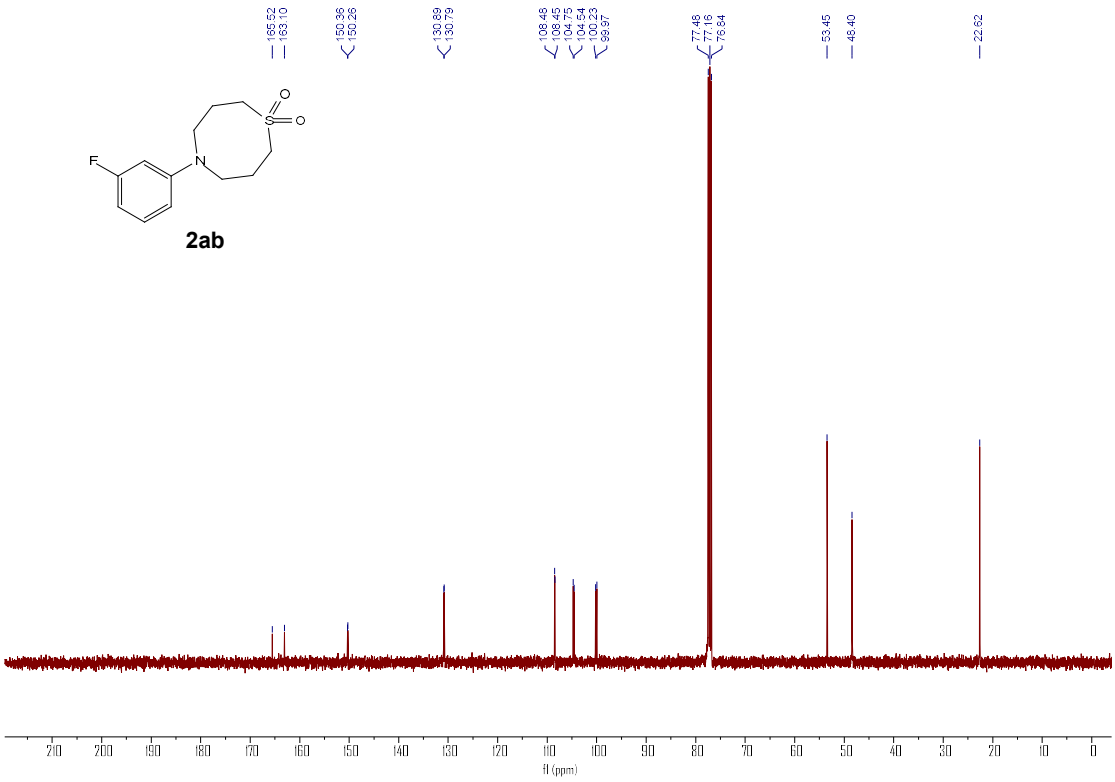
157.46
155.10
145.55
145.53
116.27
116.05
114.62
114.55
77.48
77.16
76.84
53.60
48.50
22.92
f1 (ppm)


7.260
7.216
7.196
7.178
7.157
6.500
6.493
6.486
6.480
6.473
6.465
6.455
6.426
6.420
6.414
6.394
6.384
6.383
3.482
3.466
3.450
3.143
3.129
3.115
2.328
2.313
2.299
2.285
2.269
1.00
1.92
0.99
4.09
3.80
3.91
f1 (ppm)

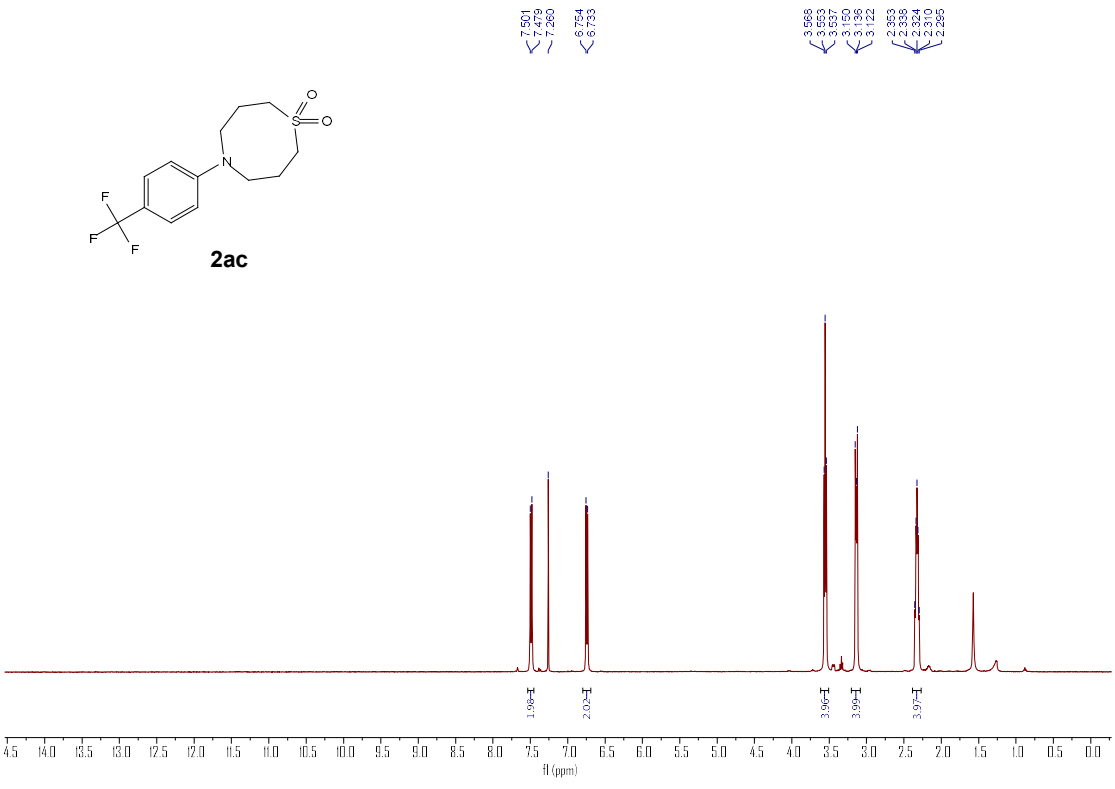
2ab


-111.464
f1 (ppm)

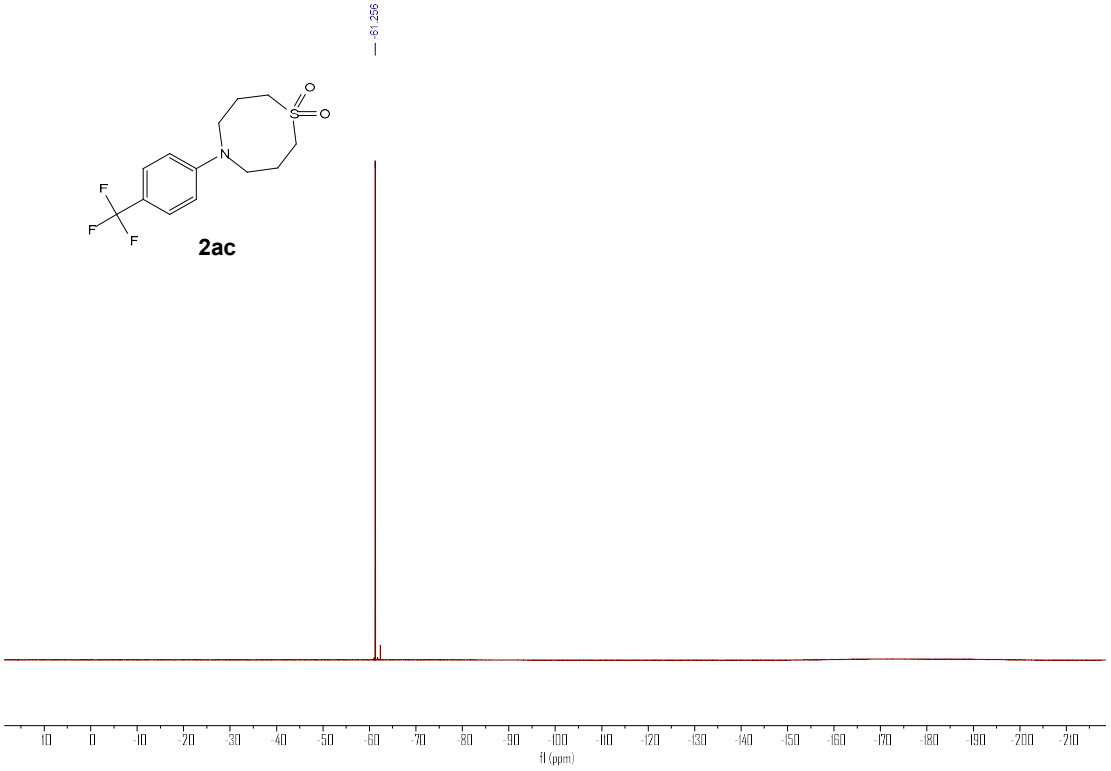
2ab

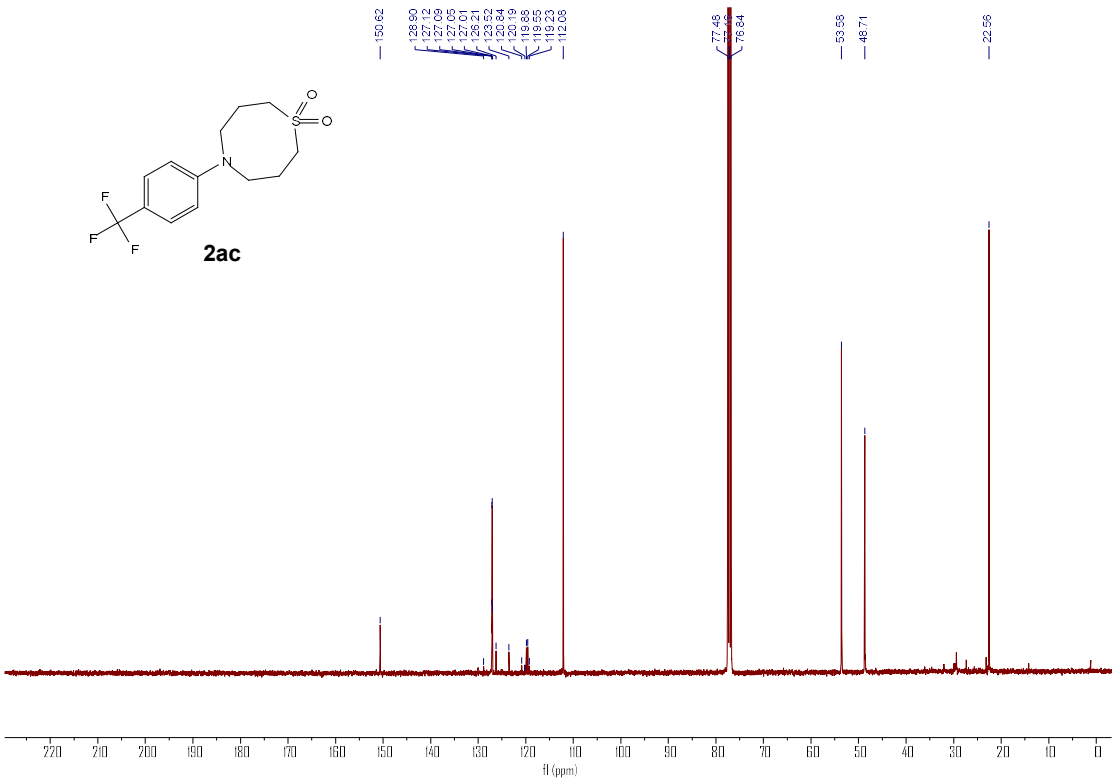

165.52
163.10
150.36
150.28
130.89
130.79
108.48
108.45
104.75
104.54
100.23
99.97
77.48
77.16
76.84
53.45
46.40
22.62
f1 (ppm)

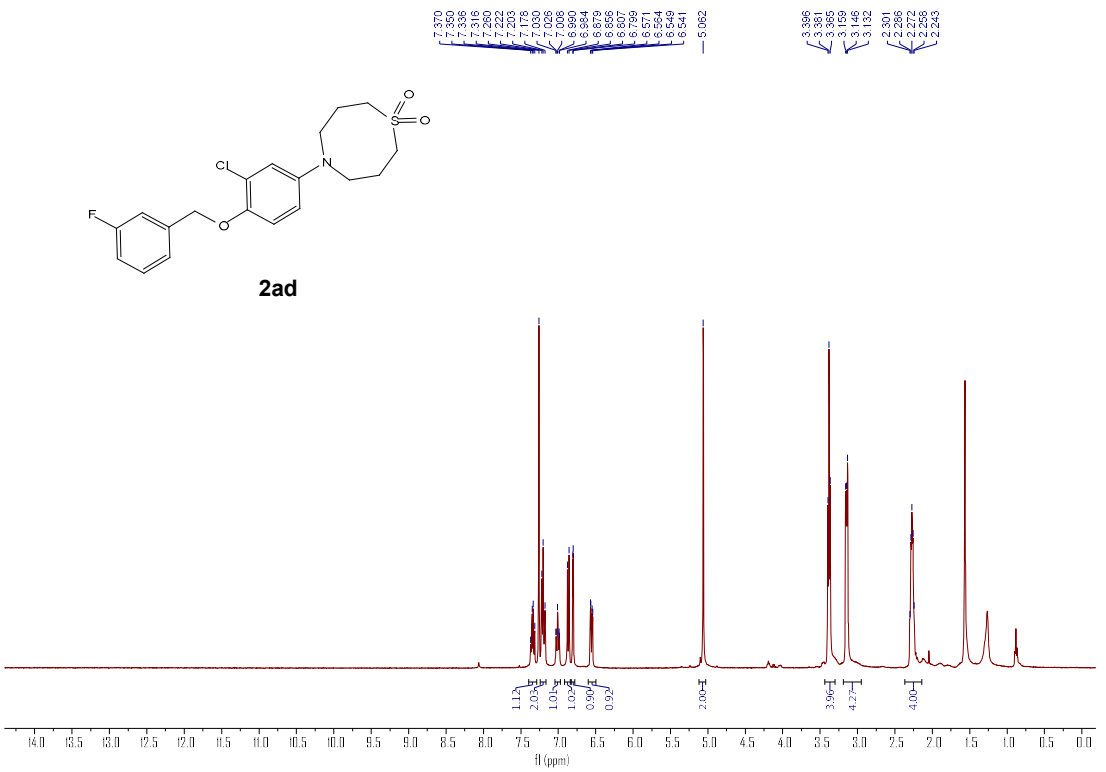
2ab


7.501
7.479
7.260
6.754
6.733
3.568
3.553
3.537
3.150
3.136
3.122
2.353
2.338
2.324
2.310
2.295
1.00
2.02
3.96
3.99
3.97
f1 (ppm)

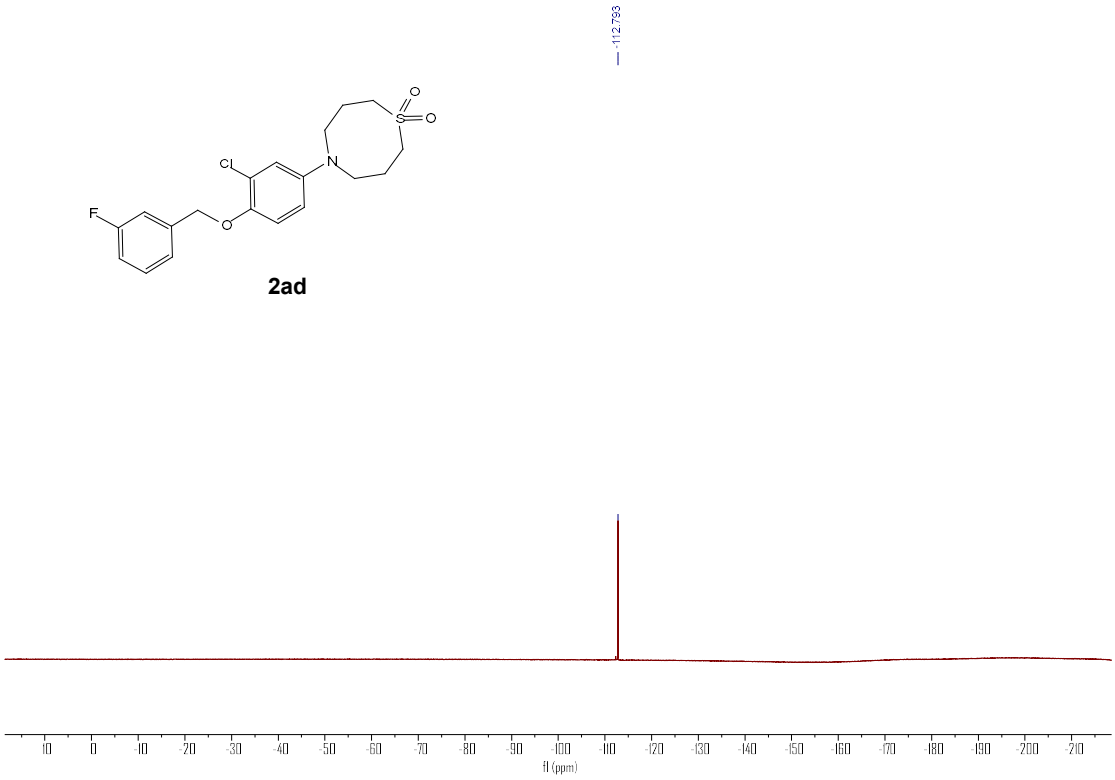
2ac


-61.256
2ac
f1 (ppm)

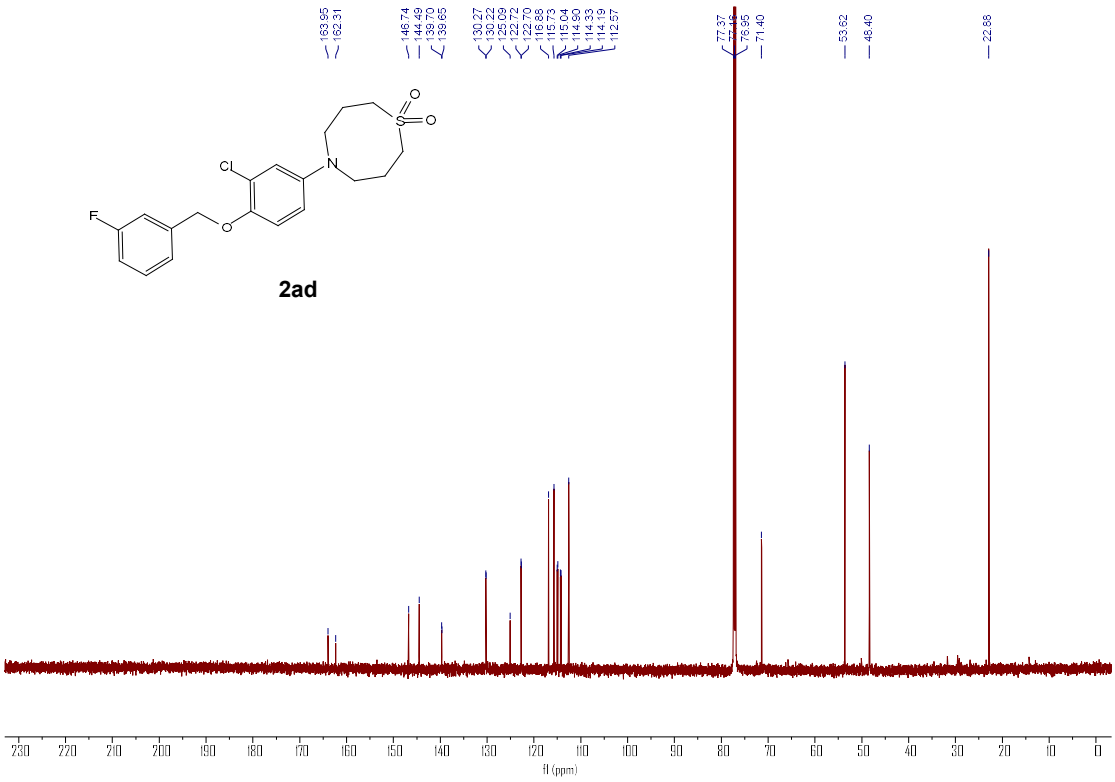

150.62
128.90
127.12
127.09
127.05
127.01
126.21
123.52
120.84
120.19
119.88
119.55
119.23
112.08
77.46
77.25
76.84
53.58
48.71
22.56
2ac
f1 (ppm)


7.370
7.350
7.338
7.316
7.260
7.222
7.203
7.178
7.030
7.028
7.008
6.990
6.934
6.879
6.855
6.807
6.799
6.571
6.564
6.549
6.541
5.062
3.396
3.381
3.385
3.159
3.146
3.132
2.301
2.288
2.272
2.256
2.243
Cl
F
O
N
S
O
O
1.12
2.03
1.01
1.02
0.90
0.92
2.00
3.96
4.27
4.00
f1 (ppm)

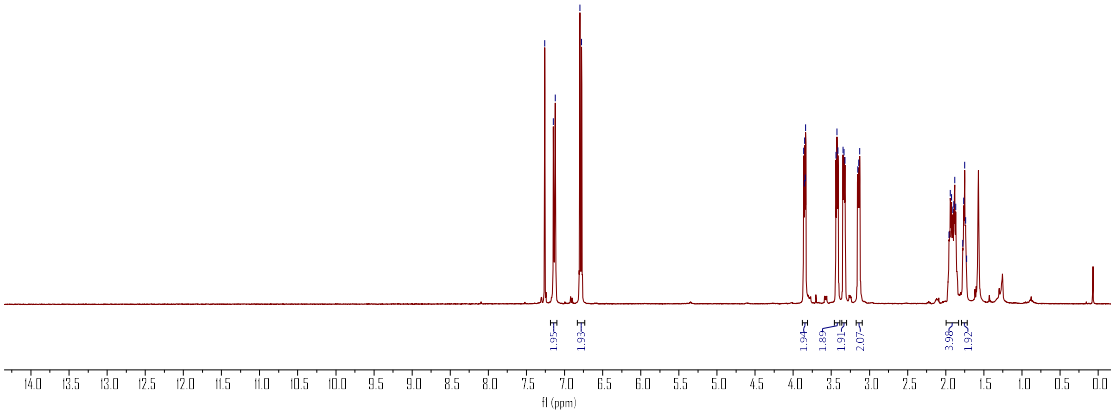
2ad


-112.793
Cl
F
O
N
S
O
O
f1 (ppm)

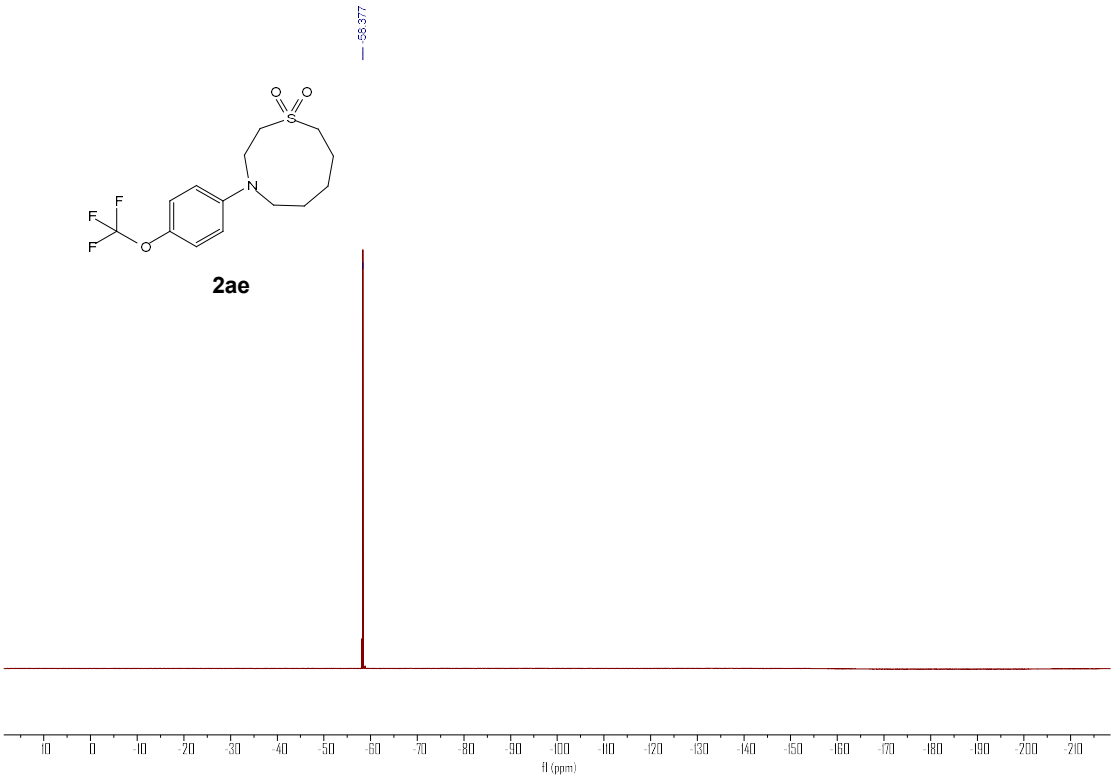
2ad

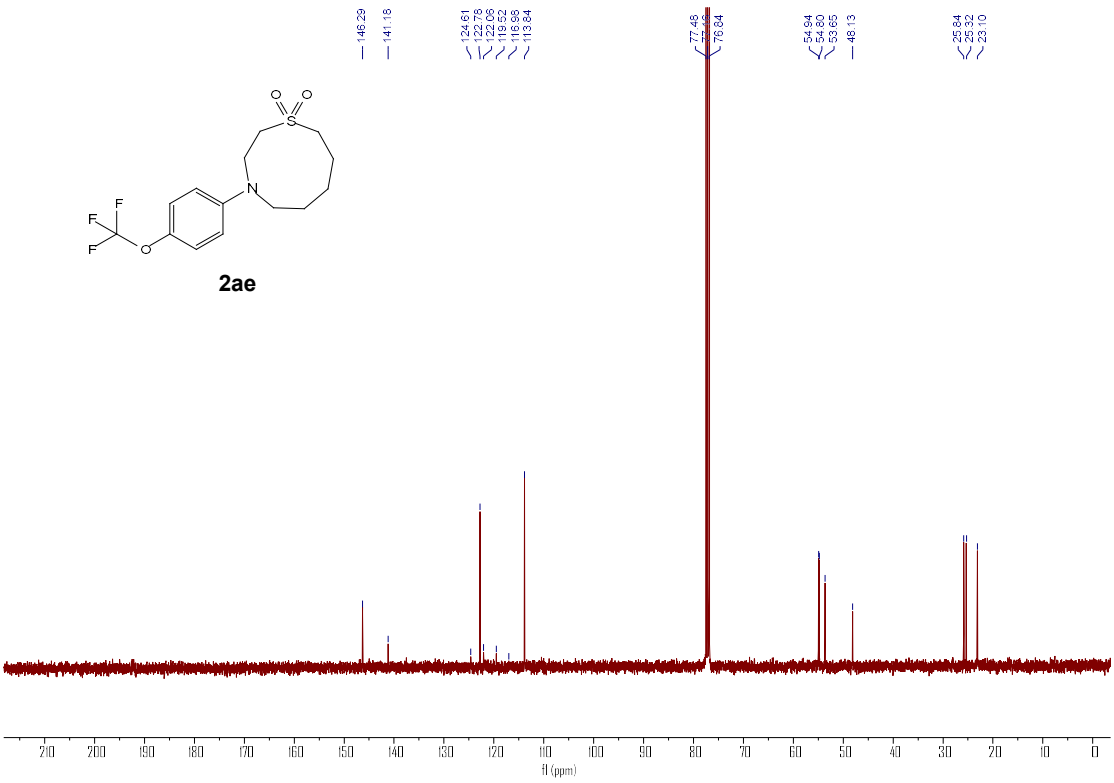

163.95
162.31
146.74
144.49
139.70
139.65
130.27
130.22
125.09
122.72
122.70
116.88
115.73
115.04
114.90
114.33
114.19
112.57
77.37
77.16
76.95
71.40
53.62
46.40
22.88
f1 (ppm)
7.260
7.145
7.124
6.799
6.776
3.862
3.855
3.849
3.842
3.835
3.437
3.424
3.412
3.347
3.334
3.321
3.155
3.142
3.127
1.955
1.938
1.925
1.907
1.894
1.882
1.867
1.775
1.763
1.751
1.739
1.727

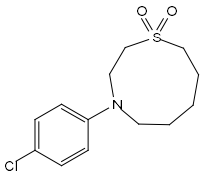
2ad


1.95
1.93
1.94
1.85
1.91
2.07
3.98
1.92
f1 (ppm)

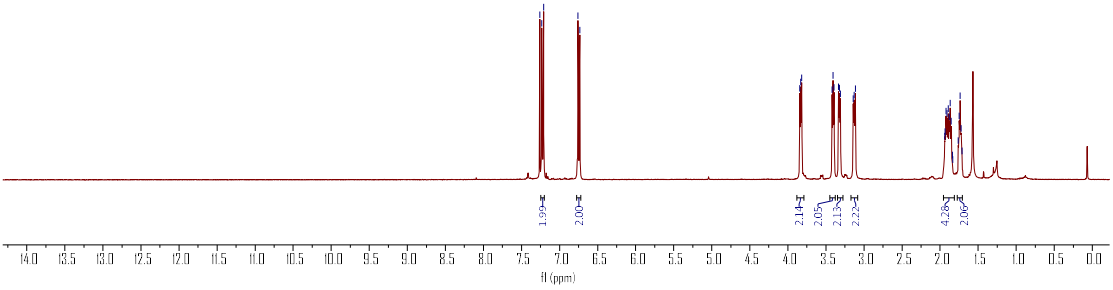
2ae

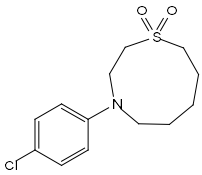

-58.377
2ae
f1 (ppm)


146.29
141.18
124.61
122.78
122.06
119.52
116.96
113.84
77.48
77.16
76.84
54.94
54.80
53.65
48.13
25.84
25.32
23.10
2ae
f1 (ppm)

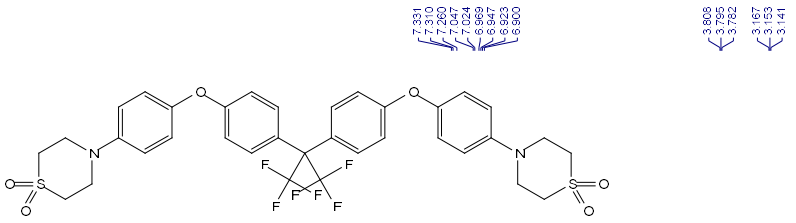


2af

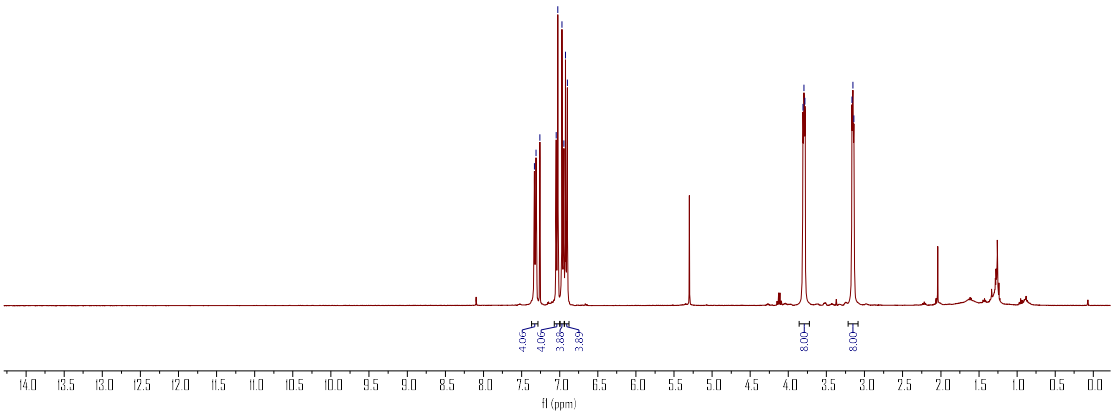


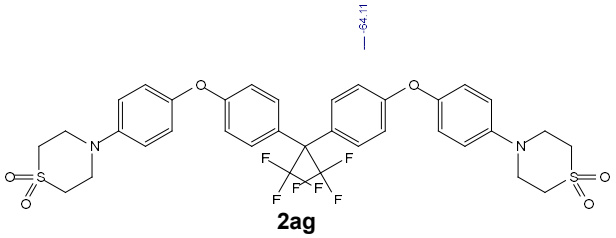


2af

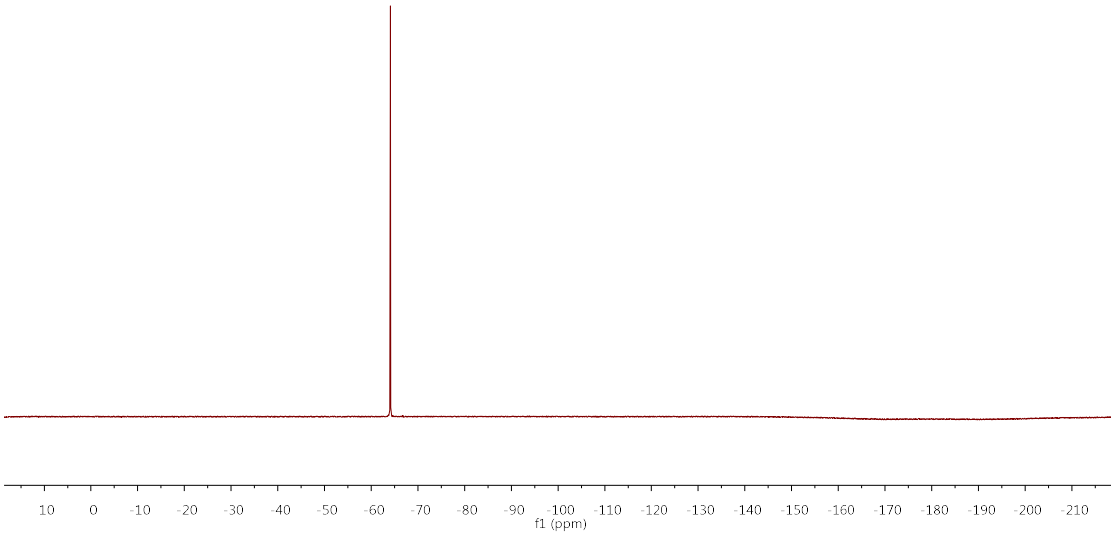


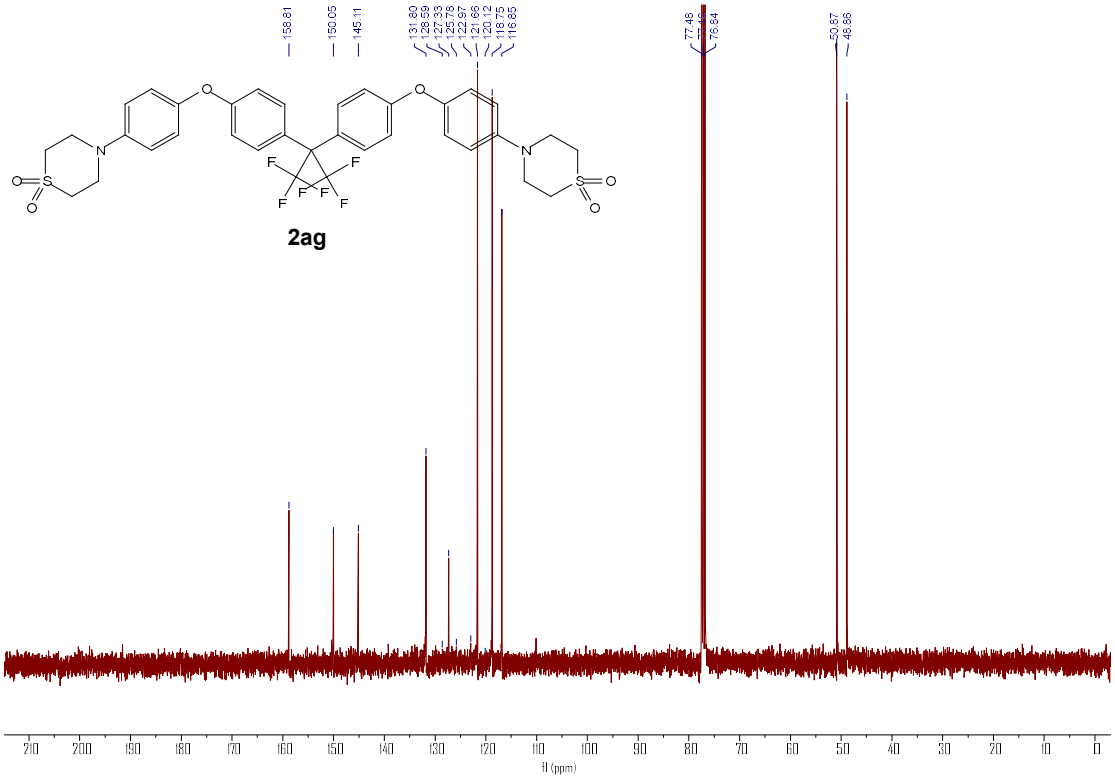
2ag



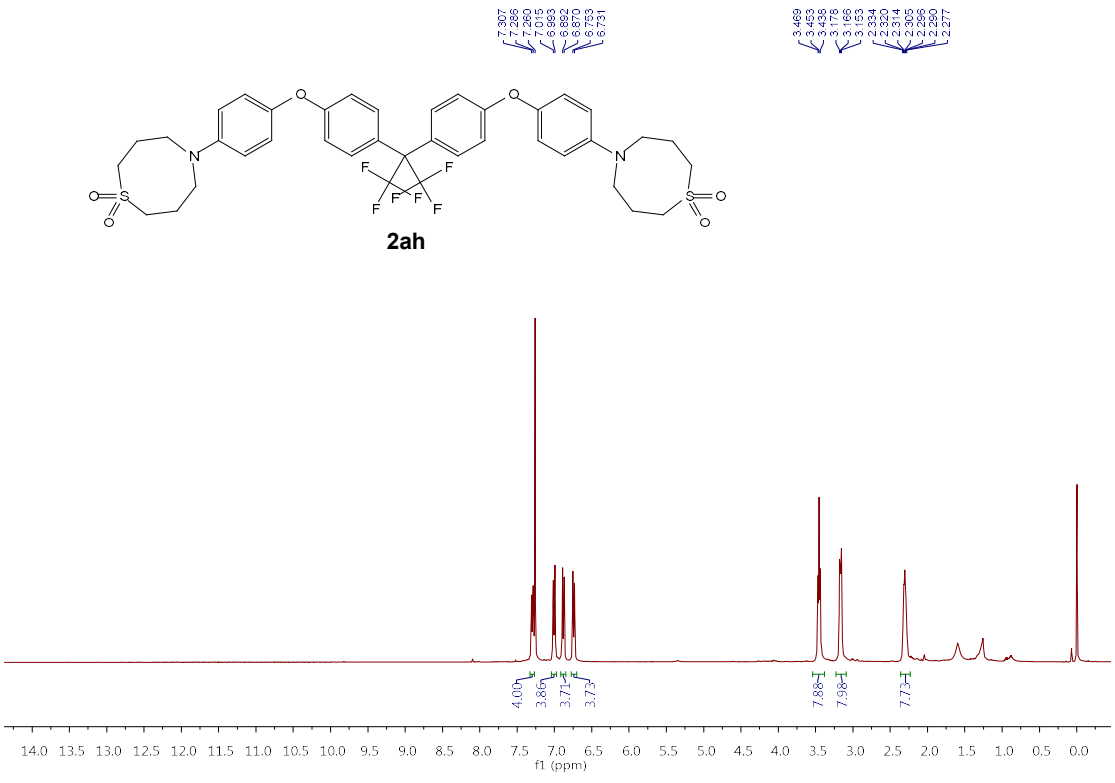


2ag

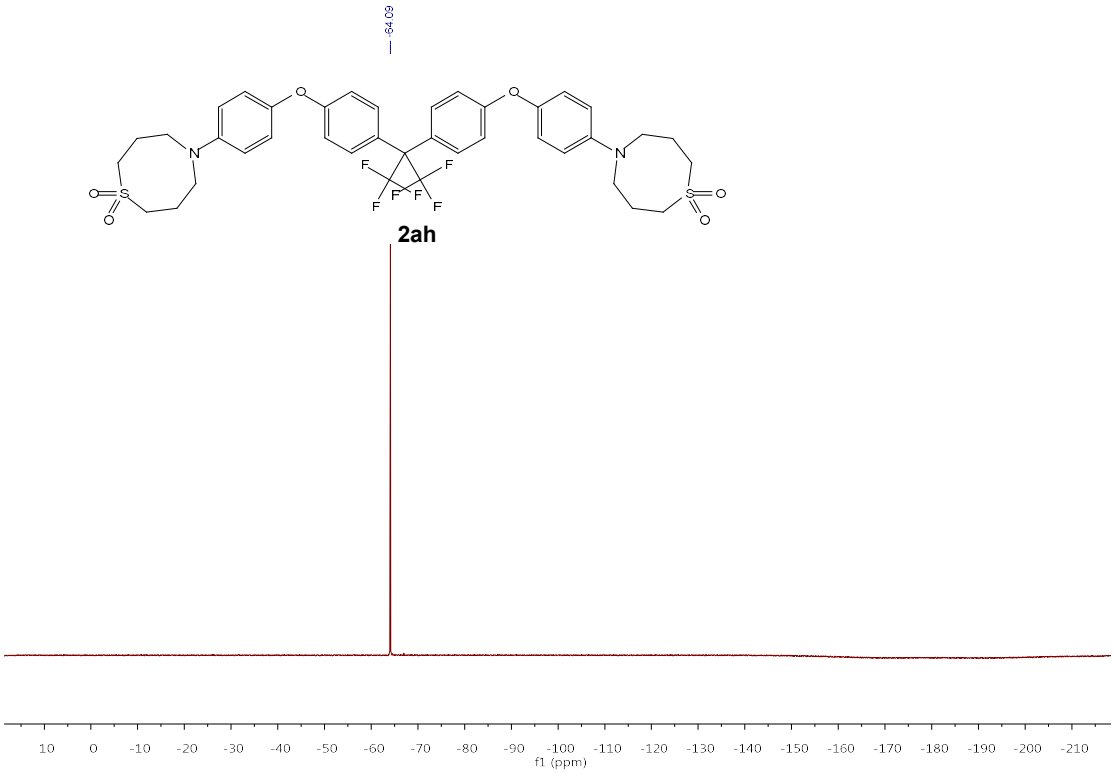


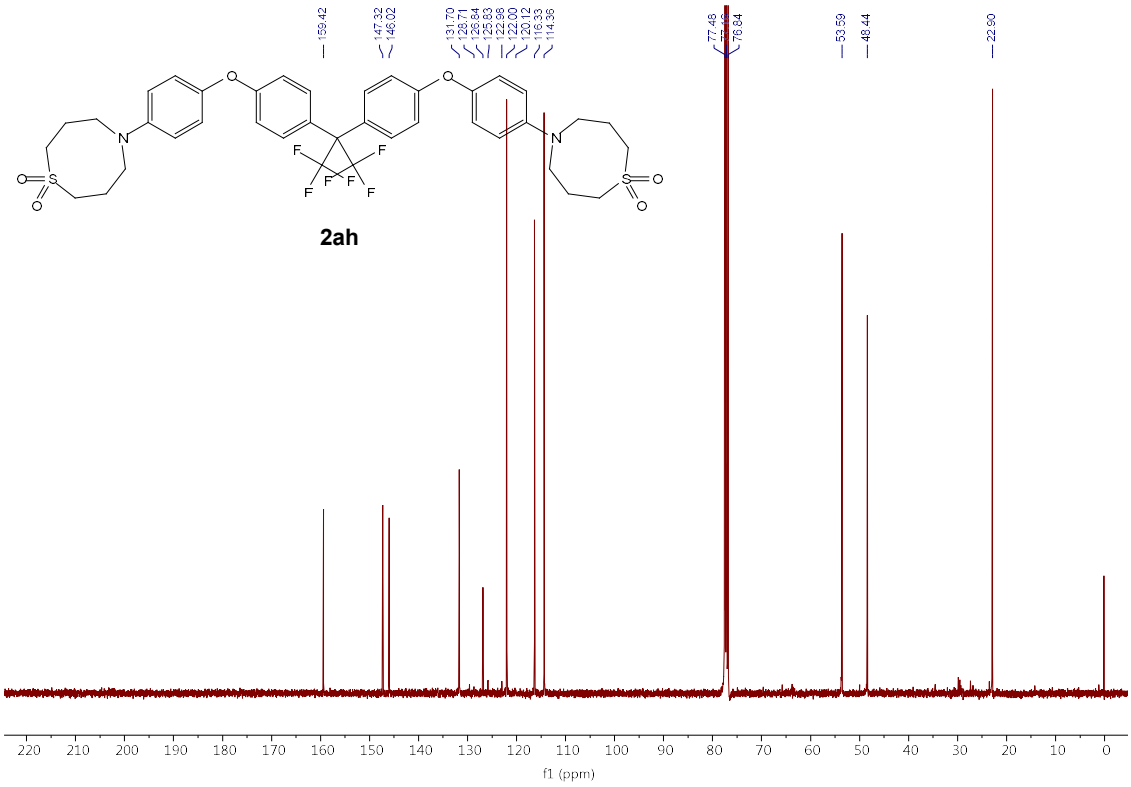

158.81
150.05
145.11
131.80
129.59
127.33
125.78
123.97
121.66
120.12
118.75
116.85
77.48
77.16
76.84
50.87
46.86
f1 (ppm)

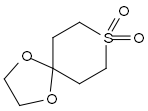
2ag


7.307
7.286
7.260
7.015
6.983
6.882
6.870
6.753
6.731
3.469
3.453
3.438
3.178
3.166
3.153
2.334
2.320
2.314
2.305
2.296
2.290
2.277
4.00
3.86
3.71
3.73
7.88
7.98
7.73
f1 (ppm)

2ah

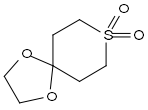

-64.09
2ah
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


159.42
147.32
146.02
131.70
128.71
126.64
125.83
122.98
122.00
120.12
116.33
114.36
77.48
76.84
53.59
48.44
22.90
2ah
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



2ai

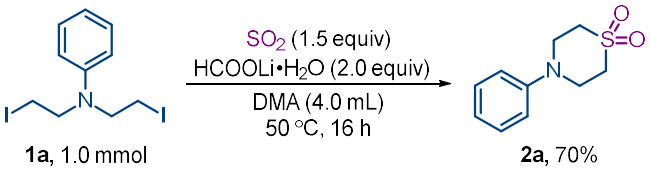
7.260
3.986
3.164
3.149
3.133
2.216
2.200
2.186
3.93
3.97
4.02
f1 (ppm)



2ai

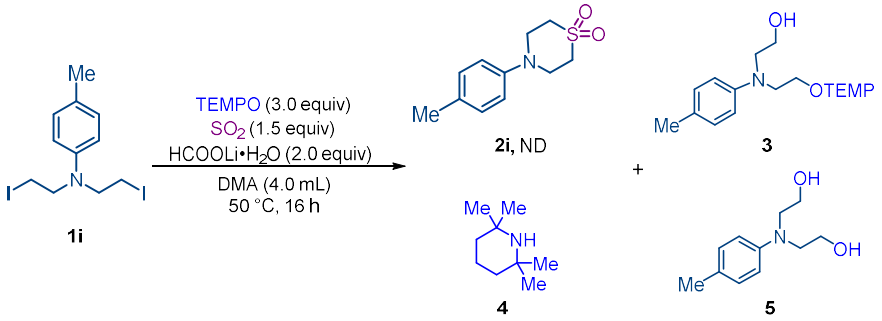
105.36
77.48
77.16
76.84
65.01
49.06
32.90
f1 (ppm)

11. 1.0 mmol scale synthesis of compound 2a



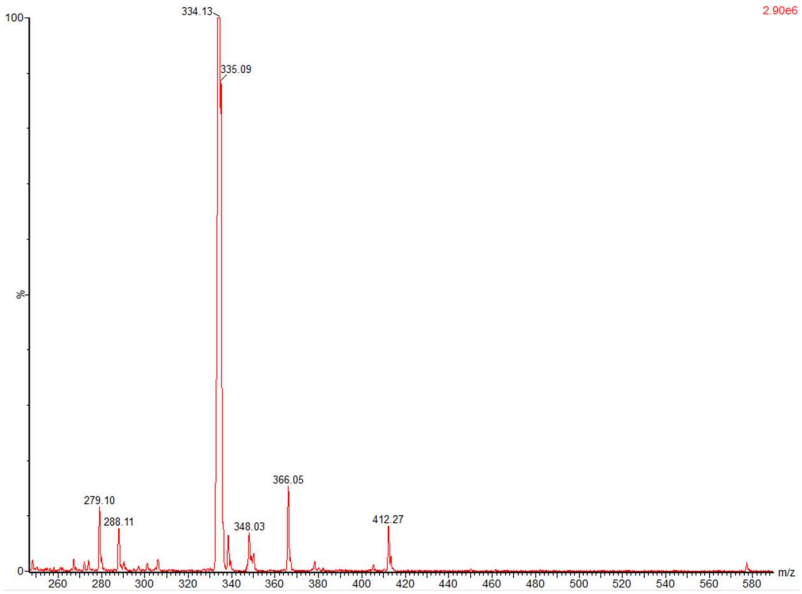
In the glovebox, **1a** (1.0 mmol, 1.0 equiv), $HCOOLi•H_2O$ (2.0 mmol, 2.0 equiv) were added to chamber B, followed by addition of DMA (4.0 mL). Tetrabromothiophene *S*,*S*-dioxides (1.65 mmol, 712 mg) in tetradecane (4.0 mL) was added to chamber A, followed by addition of 4-methylphenylene (1.5 mmol, 1.5 equiv, 198 μl). The two chamber system was sealed and removed out of the glovebox and chamber A was heated 10min at 100 °C in heat block, then the two chamber system was heated at 50 °C. After 16 hours, two chamber was cooled to room temperature. The mixture in chamber B was passed through a short silica gel pad with ethyl acetate. The filtrate was washed by ethyl acetate and H_2O (15 mL×3 times), dried by Na_2SO_4, then concentrated and the residue was purified by flash column chromatography to give the desired product **2a**. Isolated as white solid using petroleum ether/ethyl acetate (3:1) as eluent (148 mg, yield 70%)

12. Radical trapping experiment



3, **4** and **5** were detected by LC-MS

In the glovebox, **1i** (0.2 mmol, 1.0 equiv), $HCOOLi•H_2O$ (0.4 mmol, 2.0 equiv), TEMPO (0.6 mmol, 3.0 equiv) were added to chamber B, followed by addition of DMA (1.0 mL). Tetrabromothiophene *S*,*S*-dioxides (0.33 mmol, 142 mg) in tetradecane (1.0 mL) was added to chamber A, followed by addition of 4-methylphenylene (0.3 mmol, 1.5 equiv, 40.0 μl). The two chamber system was sealed and removed out of the glovebox and chamber A was heated 10min at 100 °C in heat block, then the two chamber system was heated at 50 °C. After 16 hours, two chamber was cooled to room temperature. The mixture in chamber B was passed through a short silica gel pad with ethyl acetate. The mixture was detected by LCMS.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335.09
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m/z
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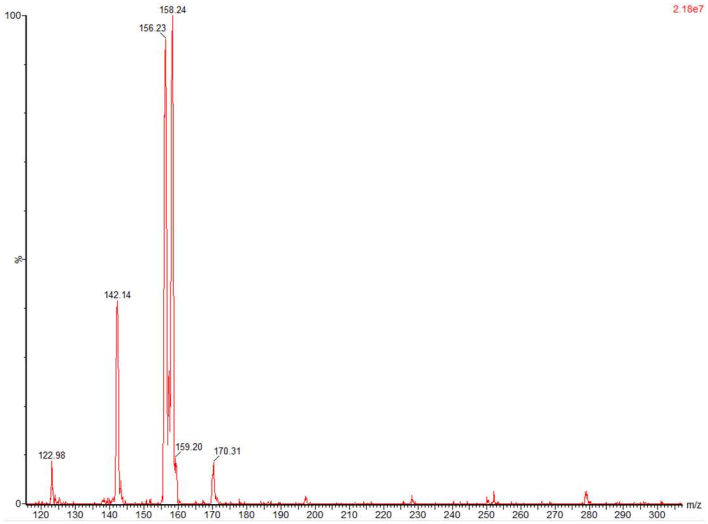
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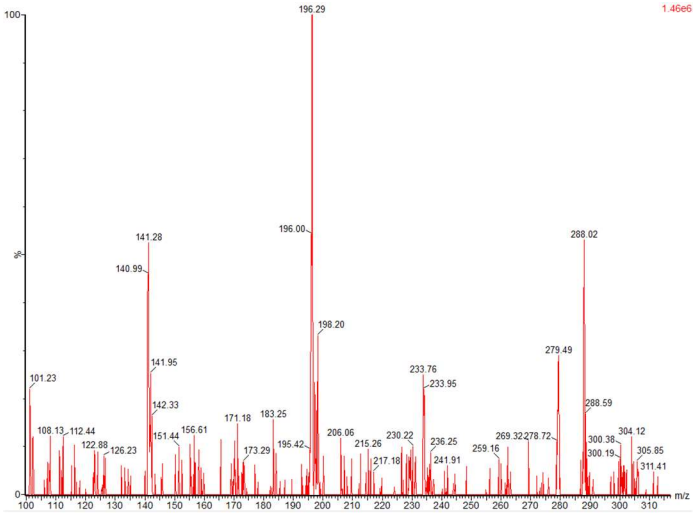
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101.23
142.33
288.59
108.13
112.44
151.44
156.61
171.18
183.25
206.06
215.26
230.22
236.25
269.32
278.72
304.12
122.88
126.23
173.29
195.42
217.18
241.91
259.16
300.38
300.19
305.85
311.41
m/z
100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310