2-Sulfinyl-Oxetanes: Synthesis, Stability and Reactivity

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General Experimental Conditions:

All non-aqueous reactions were carried out under an inert atmosphere (argon) with oven-dried (160 °C) or flame dried glassware using standard techniques. Anhydrous solvents were obtained by filtration through drying columns (THF, Et₂O, CH₂Cl₂, PhMe) or obtained from commercial suppliers and used without further purification (DMF). H₂O was distilled before use.

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: CDCl₃: δ = 7.27 ppm, (CD₃)₂CO: δ = 2.05 ppm, CD₃OD: δ = 3.31 ppm, (CD₃)₂SO: δ = 2.50 ppm. ¹³C NMR spectra: CDCl₃: δ = 77.00 ppm, (CD₃)₂CO: δ = 29.84, 206.26 ppm, CD₃OD: δ = 49.00 ppm, (CD₃)₂SO: δ = 39.52 ppm) or using chloroform with 1% tetramethylsilane as the internal standard.

¹⁹F 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 ¹³C 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 LDA or LiHMDS solutions, diisopropylamine or hexamethyldisilazane were distilled over potassium hydroxide immediately before use. Unless otherwise stated mCPBA was washed prior to use: dissolved in CH₂Cl₂, washed with a phosphate buffer (pH 7.5) and dried (MgSO₄) then the solvent removed under reduced pressure. 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 (1.27 ml, 6.0 mmol) in THF (5.38 mL) was cooled to −78 °C for 10 min then nBuLi (2.35 mL, 5.49 mmol, 2.3 M in hexane) was added dropwise. The solution was stirred at −78 °C for 30 min then warmed to 0 °C for 30 min prior to immediate use.

General Procedure for the preparation of a 1 M solution of LDA:
A solution of diisopropylamine (0.92 mL, 6.60 mmol) in THF (2.68 mL) was cooled to −78 °C for 10 min then nBuLi (2.40 mL, 6.00 mmol, 2.5 M in hexane) was added dropwise. Solution stirred at −78 °C for 1 h prior to use.

Compound Handling/Purification/Storage: All synthetic intermediates were stored under argon at −20 °C for short periods of time. Instability of sulfoxide compounds meant that in some cases appropriate molecular ions (HRMS) could not be obtained.

Sulfinyl-oxetane diastereoisomers: The relative configuration of the oxetane diastereoisomers was not assigned. For consistency, diastereoisomers are denoted A or B based on polarity, with compound A eluting first on flash chromatography.

Synthesis of 1-methyl-4-\{(2-\{(4-methylbenzenesulfonyl)oxy\}ethoxy)methanesulfinyl\}benzene (1a)

\[
\begin{align*}
\text{TsCl, Et}_3\text{N} & \quad \text{Me}_3\text{N}H\text{Cl}, \text{PhMe} \\
0^\circ \text{C} \rightarrow \text{rt, 83\%} & \quad \text{TsCl, Et}_3\text{N} \quad \text{Me}_3\text{N}H\text{Cl}, \text{PhMe} \\
\end{align*}
\]

2-\{\{(4-Methylphenyl)sulfanyl\}methoxy\}ethan-1-ol (4a)

Sodium hydride (60% in mineral oil, 2.57 g, 64.25 mmol) was added to ethylene glycol (400 mL) at 0°C and stirred for 1 h 15 min. Sodium iodide (9.62 g, 64.18 mmol) was added followed by a solution of chloromethylsulfide 3a (10.04 g, 58.37 mmol) in ethylene glycol (5 mL). The resulting solution was stirred at 0°C for 1 h then warmed to rt for 4 h. Water (300 mL) was added and the product was extracted with ethyl acetate (10 × 50 mL). The combined organic layers were dried (MgSO\(_4\)) for 4 h. Water (300 mL) was added and the product was extracted with ethyl acetate (10 × 50 mL). The combined organic layers were dried (MgSO\(_4\)) and the solvent removed under reduced pressure. Purification by flash chromatography (50% EtOAc/hexane) afforded alcohol 4a (9.60 g, 83%) as a yellow oil. \(R_f = 0.34\) (50% EtOAc/hexane). IR (film)/cm\(^{-1}\) 3449 (OH), 2926, 2872, 1734, 1493, 1461, 1373, 1250, 1052, 1017, 806, 734. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38 (2 H, d, \(J = 8.1\) Hz, 2 × Ar-H), 7.13 (2 H, d, \(J = 8.1\) Hz, 2 × Ar-H), 5.00 (2 H, s, SCH\(_2\)), 3.78–3.72 (4 H, m, OCH\(_2\)CH\(_2\)OH), 2.34 (3 H, s, CH\(_3\)), 1.94 (1 H, s, OH). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 137.2 (Ar-C\(_o\)), 131.5 (Ar-C\(_o\)), 131.1 (2 × Ar-C), 129.8 (2 × Ar-C), 77.0 (SCH\(_2\)), 69.7 (OCH\(_2\)), 61.7 (OCH\(_2\)), 21.1 (CH\(_3\)). HRMS (ESI) \(m/z\) Calculated for C\(_{10}\)H\(_{18}\)NaO\(_2\)S\(_2\)^\(^+\) \([\text{M}+\text{Na}]^+\): 221.0607; Found: 221.0607 [M+Na]^+^, \(\Delta 0\) ppm.

2-\{\{(4-Methylphenyl)sulfanyl\}methoxy\}ethyl-4-methylbenzene-1-sulfonate (5a)

Triethylamine (3.14 mL, 22.34 mmol) and trimethylamine hydrochloride (70 mg, 0.75 mmol) were added to a solution of alcohol 4a (1.50 g, 7.56 mmol) in toluene (10 mL) at 0°C and stirred for 10 min. A suspension of 4-toluenesulfonyl chloride (2.86 g, 15.00 mmol) in toluene (10 mL) was added dropwise. The mixture was stirred at 0°C for 30 min then allowed to warm to rt slowly over 40 min and stirred for a further 1 h 20 min. Water (100 mL) was added to the reaction and the product was extracted with EtOAc (4 × 50 mL). The combined organic layers were washed with H\(_2\)O (30 mL) and brine (50 mL) then dried (MgSO\(_4\)), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded tosylate 5a (2.52 g, 97%) as a yellow oil. \(R_f = 0.34\) (40% EtOAc/hexane). IR (film)/cm\(^{-1}\) 2984, 2891, 1734, 1596, 1499, 1362, 1237, 1175, 1095, 1011, 915, 807. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.79 (2 H, d, \(J = 8.2\) Hz, 2 × Ts-H), 7.34–7.30 (4 H, m, 2 × Ts-H + 2 × Tol-H), 7.10 (2 H, d, \(J = 8.2\) Hz, 2 × Tol-H), 4.90 (2 H, s, SCH\(_2\)), 4.22–4.18 (2 H, m, TsOCH\(_2\)), 3.83–3.78 (2 H, m, CH\(_3\)OCH\(_2\)), 2.45 (3 H, s, Ts-CH\(_3\)), 2.33 (3 H, s, Tol-CH\(_3\)). \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.8 (Ts-C\(_o\)), 137.1 (Tol-C\(_o\)), 132.9 (Ts-C\(_o\)), 131.4 (Tol-C\(_o\)), 131.0 (2 × Ar-C), 129.8 (2 × Ar-C), 129.7 (2 × Ar-C), 127.9 (2 × Ar-C), 76.8 (SCH\(_2\)), 68.7 (SCH\(_2\)OCH\(_2\)), 65.5 (TsOCH\(_2\)), 21.6 (Ts-CH\(_3\)), 21.0 (Tol-CH\(_3\)). HRMS (ESI) \(m/z\) Calculated for C\(_{17}\)H\(_{24}\)NO\(_2\)S\(_2\)^\(^+\) \([\text{M}+\text{NH}_4]^+\): 370.1141; Found: 370.1134 [M+NH\(_4\)]^+^, \(\Delta 1.9\) ppm.

1-Methyl-4-\{(2-\{(4-methylbenzenesulfonyl)oxy\}ethoxy)methanesulfinyl\} benzene (1a)

\text{meta-Chloroperbenzoic acid (70\%, 1.18 g, 4.80 mmol) was added to a solution of sulfide 5a (1.54 g, 4.37 mmol) in dichloromethane (20 mL) at 0°C and the mixture stirred at 0°C for 3 h. The reaction was quenched with sat. aq. Na\(_2\)SO\(_3\) (20 mL) and extracted with dichloromethane (7 × 20 mL). The combined organic layers were washed with 5% NaOH (3 × 10 mL) and sat. aq. NH\(_4\)Cl (50 mL) then dried (MgSO\(_4\)), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (60% EtOAc/hexane)
afforded a sample of sulfoxide 1a as pale yellow oil. Rf = 0.30 (60% EtOAc/hexane). IR (film)/cm⁻¹ 2970, 1599, 1496, 1355, 1189, 1175, 1142, 1096, 1004, 915, 810. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (2 H, d, J = 8.5 Hz, 2 × Ts-H), 7.48 (2 H, d, J = 8.2 Hz, 2 × Ar-H), 7.36–7.30 (4 H, m, 2 × Ts-H + 2 × Ar-H), 4.40 (1 H, d, J = 10.6 Hz, SCHHO), 4.35 (1 H, d, J = 10.6 Hz, SCHHO), 4.21–4.14 (2 H, m, OCH₂), 4.10–3.95 (2 H, m, OCH₂), 2.43 (3 H, s, CH₃), 2.40 (3 H, s, CH₃). This compound rapidly decomposed on isolation on each attempt and ¹³C NMR could not be obtained.
Synthesis of 2-(4-chlorobenzensulfinyl)oxetane (2b)

\[
\begin{align*}
\text{Sulfoxide (80 mL)} & \text{then dried (MgSO}_4\text{)}
\end{align*}
\]

by flash chromatography (70% EtOAc/hexane) afforded sulfoxide (80 mL) then dried (MgSO₄) dichloromethane (40% EtOAc/hexane) afforded tosylate then dried (MgSO₄) and the solvent removed under reduced pressure. Purification by flash chromatography (50% EtOAc/hexane) afforded alcohol (5.27 g, 74%) as a colourless oil. Rₚ = 0.31 (50% EtOAc/hexane). IR (film)/cm⁻¹: 3388 (OH), 2934, 2872, 1481, 1392, 1313, 1095, 1059, 1013, 816, 683. ¹H NMR (400 MHz, CDCl₃) δ 7.40 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 7.27 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 5.01 (2 H, s, SCH₂), 3.80–3.69 (4 H, m, OCH₂CH₂OH), 2.08 (1 H, s, OH). ¹³C NMR (100 MHz, CDCl₃) δ 133.9 (Ar-C₆), 133.0 (Ar-C₆), 131.6 (2 × Ar-C), 129.1 (2 × Ar-C), 76.4 (SCH₂O), 69.8 (OCH₂), 61.5 (OCH₂). HRMS (ESI) m/z Calculated for C₉H₇ClNaO₂S⁺ [M+Na]⁺: 241.0060; Found: 241.0060 [M+Na]⁺, Δ 0 ppm.

2-[[[(4-Chlorophenyl)sulfonyl]methoxy]ethan-1-ol (4b)¹

Sodium hydride (60% in mineral oil, 1.56 g, 39.01 mmol) was added to ethylene glycol (200 mL) at 0 °C and stirred for 30 min. Sodium iodide (5.83 g, 38.90 mmol) was added followed by chloromethyl sulfide (6.26 g, 32.42 mmol) using DMF (5 mL) to aid transfer. The resulting solution was stirred at 0 °C for 3 h then warmed to rt for 12 h. The reaction was quenched by the addition of sat. aq. NH₄Cl (200 mL) and the mixture extracted with EtOAc (4 × 75 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (50% EtOAc/hexane) afforded tosylate (5.39 g, 94%) as a colourless oil. Rₚ = 0.24 (20% EtOAc/hexane). IR (film)/cm⁻¹: 3247 (OH), 3153, 2922, 1655, 1511, 1170, 1059, 1021, 808, 756, 668, 559. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.38–7.31 (4 H, m, 2 × Ts-H + 2 × Ar-H), 7.26–7.20 (2 H, m, 2 × Ar-H), 4.92 (2 H, s, SCH₂O), 4.23–4.19 (2 H, m, TsOCH₂), 3.84–3.80 (2 H, m, CH₂OCH₂), 2.45 (3 H, s, CH₃). HRMS (ESI) m/z Calculated for C₉H₇ClNaO₂S⁺ [M+Na]⁺: 241.0060; Found: 241.0060 [M+Na]⁺, Δ 0 ppm.

2-[[[(4-Chlorophenyl)sulfonyl]methoxy]ethyl-4-methylbenzene-1-sulfonate (5b)¹

Triethylamine (6.19 mL, 44.04 mmol) and trimethylamine hydrochloride (141 mg, 1.48 mmol) were added to a solution of alcohol (3.24 g, 14.82 mmol) in toluene (40 mL) at 0 °C and stirred for 20 min. 4-Toluenesulfonfyl chloride (5.65 g, 29.64 mmol) was added portionwise. The mixture was stirred at 0 °C for 30 min then at rt for 2 h. The reaction was quenched by the addition of sat. aq. NaHCO₃ (200 mL) and the mixture extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with sat. aq. NH₄Cl (100 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded tosylate (5.39 g, 98%) as a colourless oil. Rₚ = 0.24 (20% EtOAc/hexane). IR (film)/cm⁻¹: 3240 (OH), 3168, 2927, 1656, 1511, 1170, 1059, 1021, 808, 756, 559. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.38–7.31 (4 H, m, 2 × Ts-H + 2 × Ar-H), 7.26–7.20 (2 H, m, 2 × Ar-H), 4.92 (2 H, s, SCH₂O), 4.23–4.19 (2 H, m, TsOCH₂), 3.84–3.80 (2 H, m, CH₂OCH₂), 2.45 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 144.9 (Ts-C₆), 133.7 (Ar-C₆), 133.0 (Ts-C₆), 132.8 (Ar-C₆), 131.7 (2 × Ar-C), 129.8 (2 × Ts-C), 129.0 (2 × Ar-C), 127.9 (2 × Ts-C), 76.3 (SCH₂O), 68.6 (SCH₂OCH₂), 65.6 (TsOCH₂), 21.7 (CH₃). HRMS (ESI) m/z Calculated for C₁₆H₁₅ClNaO₂S⁺ [M+Na]⁺: 390.0595; Found: 390.0595 [M+Na]⁺, Δ 0 ppm.

2-[[[(4-Chlorophenyl)sulfonyl]methoxy]ethyl-4-methylbenzenesulfonate (1b)

meta-Chloroperbenzoic acid (1.11 g, 6.43 mmol) was added slowly to a solution of sulfide (2.00 g, 5.36 mmol) in dichloromethane (50 mL) at 0 °C and the mixture stirred at 0 °C for 1 h then warmed to rt for 1 h. The reaction was quenched by the addition of sat. aq. Na₂SO₃ (80 mL) and NaHCO₃ (80 mL) then extracted with dichloromethane (4 × 40 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (80 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (70% EtOAc/hexane) afforded sulfoxide (1.95 g, 94%) as a colourless...
oil. R_f = 0.19 (70% EtOAc/hexane). IR (film)/cm⁻¹ 3060, 2954, 2932, 1597, 1475, 1452, 1391, 1353, 1244, 1174, 1086, 1010, 909, 815, 772, 740. ^1H NMR (400 MHz, CDCl₃) δ 7.76 (2 H, d, J = 8.5 Hz, 2 × Ts-H), 7.54 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 7.49 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 7.33 (2 H, d, J = 8.5 Hz, 2 × Ts-H), 4.45 (1 H, d, J = 10.5 Hz, SCH₂O), 4.38 (1 H, d, J = 10.5 Hz, SCH₂O), 4.18–4.16 (2 H, m, OCH₂), 4.10–3.89 (2 H, m, OCH₂), 2.44 (3 H, s, CH₃). ^13C NMR (100 MHz, CDCl₃) δ 145.1 (Ts-Cq), 138.9 (Ar-Cq), 137.6 (Ar-Cq), 132.5 (Ts-Cq), 129.9 (2 × Ts-C), 129.5 (2 × Ar-C), 127.8 (2 × Ts-C), 125.8 (2 × Ar-C), 91.7 (SCH₂O), 71.0 (OCH₂CH₂O), 68.5 (OCH₂CH₂O), 21.6 (CH₃). HRMS (ESI) m/z Calculated for C₁₆H₁₈ClO₃S₂^+ [M+H]^⁺: 389.0279; Found: Accurate mass could not be found due to compound degradation.

2-((4-Chlorobenzensulfinyl)oxetane (2b)
A solution of LiHMDS (1 M in THF, 0.16 mL, 0.16 mmol) was added dropwise to a solution of sulfoxide 1b (50 mg, 0.13 mmol) in THF (5 mL) at 0 ºC and stirred for 1 h. The reaction was quenched with sat. aq. NH₄Cl (10 mL) and extracted with CH₂Cl₂ (5 × 6 mL). The combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (70% EtOAc/hexane) afforded the oxetane as a mixture of two diastereoisomers 2b-A (10 mg, 36%) followed by 2b-B (12 mg, 44%) both as colourless oils.

Minor Diastereoisomer 2b-A: R_f = 0.30 (70% EtOAc/hexane). IR (film)/cm⁻¹ 3079, 2965, 2897, 1574, 1475, 1391, 1256, 1235, 1176, 1090, 1079, 1052, 975, 931, 913, 822, 741, 702. ^1H NMR (400 MHz, CDCl₃) δ 7.54–7.49 (4 H, m, 4 × Ar-H), 5.26 (1 H, dd, J = 7.6, 5.2 Hz, OCHS), 4.80 (1 H, ddd, J = 9.0, 6.8, 5.4 Hz, OCH₃), 3.26–3.18 (1 H, m, OCH₂CH₃), 2.73–2.63 (1 H, m, OCH₂CH₃). ^13C NMR (100 MHz, CDCl₃) δ 137.7 (Ar-Cq), 137.4 (Ar-Cq), 129.3 (2 × Ar-C), 126.5 (2 × Ar-C), 96.8 (OCH₃), 71.1 (OCH₂), 22.5 (OCH₂CH₂).

Major Diastereoisomer 2b-B: R_f = 0.13 (70% EtOAc/hexane). IR (film)/cm⁻¹ 3079, 2965, 2897, 1574, 1475, 1391, 1256, 1235, 1176, 1090, 1079, 1052, 975, 931, 913, 822, 741, 702. ^1H NMR (400 MHz, CDCl₃) δ 7.61 (2 H, dt, J = 8.4, 2.0 Hz, 2 × Ar-H), 7.51 (2 H, dt, J = 8.4, 2.0 Hz, 2 × Ar-H), 5.38 (1 H, dd, J = 7.4, 5.7 Hz, OCH₃), 4.65–4.55 (2 H, m, OCH₂), 3.07–3.98 (2 H, m, OCH₂CH₂). ^13C NMR (100 MHz, CDCl₃) δ 137.7 (Ar-Cq), 137.4 (Ar-Cq), 129.3 (2 × Ar-C), 126.5 (2 × Ar-C), 96.8 (OCH₃), 71.1 (OCH₂), 22.5 (OCH₂CH₂).
Synthesis of 2-(oxetan-2-ylsulfinyl)pyridine (2c)

2-c-{[Pyridin-2-ylsulfanyl]methoxy}ethan-1-ol (4c)

Sodium hydride (60% in mineral oil, 0.55 g, 13.78 mmol) was added to ethylene glycol (120 mL) at 0°C and stirred for 55 min. Sodium iodide (2.06 g, 13.78 mmol) was added followed by chloromethyl sulfide 3c (2.00 g, 12.53 mmol) using ethylene glycol (1 mL) to aid transfer. The resulting solution was stirred at 0°C for 25 min then warmed to rt for 19 h 20 min. Water (150 mL) was added to the reaction and the product was extracted with EtOAc (10 × 35 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography of the crude material (0–80% EtOAc/heptane) afforded alcohol 4c (1.46 g, 63%) as a colourless oil. R<sub>f</sub> = 0.59 (80% EtOAc/heptane). IR (film)/cm⁻¹: 3344 (OH), 2924, 1525, 1500, 1454, 1416, 1328, 1102, 1060, 908, 824, 758, 721, 678. ¹H NMR (400 MHz, CDCl₃) δ 8.46–8.44 (1 H, m, Py-H), 7.52 (1 H, ddd, J = 8.0, 7.3, 1.9 Hz, Py-H), 7.29 (1 H, ddd, J = 8.0, 1.0, 0.9 Hz, Py-H), 7.04 (1 H, ddd, J = 7.3, 5.0, 1.0 Hz, Py-H), 5.38 (2 H, s, SCH₂), 3.77–3.72 (4 H, m, OCH₂CH₂OH), 2.95 (1 H, br s, OH). ¹³C NMR (100 MHz, CDCl₃) δ 157.4 (Py-C), 149.5 (Py-C), 123.2 (Py-C), 120.4 (Py-C), 71.9 (SCH₂O), 70.5 (OCH₂), 61.6 (OCH₂). HRMS (ESI) m/z Calculated for C₁₇H₂₃NO₃S⁺ [M+H]⁺: 316.0891; Found: 316.0890 [M+H]⁺, Δ 0.0 ppm.

2-c-{[Pyridin-2-ylsulfanyl]methoxy}ethyl-4-methylbenzene-1-sulfonate (5c)

Triethylamine (4.06 mL, 28.89 mmol) and trimethylamine hydrochloride (3.71 g, 0.97 mmol) were added to a solution of alcohol 4c (0.90 g, 4.86 mmol) in toluene (30 mL) at 0°C and stirred for 30 min. A solution of 4-toluenesulfonyl chloride (0.90 g, 4.86 mmol) was added to the reaction mixture and the product was extracted with EtOAc (7 × 30 mL). The combined organic layers were washed with H₂O (30 mL) and brine (30 mL) then dried (MgSO₄) and the solvent removed under reduced pressure. Purification by flash chromatography (0–40% EtOAc/heptane) afforded tosylate 5c (1.57 g, 95%) as a colourless oil. R<sub>f</sub> = 0.36 (40% EtOAc/heptane). IR (film)/cm⁻¹: 2924, 1610, 1533, 1494, 1453, 1419, 1353, 1281, 1216, 1172, 1119, 1032, 1009, 916, 816, 767, 680. ¹H NMR (400 MHz, CDCl₃) δ 8.43–8.41 (1 H, m, Py-H), 7.76 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.50 (1 H, ddd, J = 8.0, 7.4, 1.9 Hz, Py-H), 7.31 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.24 (1 H, d, J = 8.0 Hz, Py-H), 7.02 (1 H, ddd, J = 7.4, 4.9, 1.0 Hz, Py-H), 5.32 (2 H, s, SCH₂O), 4.18–4.16 (2 H, m, OCH₂CH₂), 3.79–3.76 (2 H, m, OCH₂CH₂), 2.42 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 157.2 (Py-C), 149.4 (Py-C), 144.7 (Ts-C), 136.4 (Py-C), 133.0 (Ts-C), 129.7 (2 × Ts-C), 127.8 (2 × Ts-C), 122.8 (Py-C), 120.3 (Py-C), 71.8 (SCH₂O), 68.7 (OCH₂CH₂), 66.2 (OCH₂CH₂), 21.5 (CH₃). HRMS (NSI) m/z Calculated for C₁₅H₁₉NO₃S₂⁺ [M+H]⁺: 340.0674; Found: 340.0674 [M+H]⁺, Δ 0.6 ppm.

2-c-{[4-Methylbenzenesulfonyl]oxy}jethoxy)methanesulfinyl)pyridine (1c)

Meta-Chloroperbenzoic acid (2.06 g, 11.93 mmol) was added portionwise to a solution of sulfide 5c (3.37 g, 9.93 mmol) in dichloromethane (150 mL) at 0°C and the mixture stirred whilst warming to rt for 2 h 30 min. The reaction was quenched with sat. aq. Na₂SO₃ (40 mL) and sat. aq. NaHCO₃ (40 mL) then extracted with dichloromethane (5 × 40 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (50 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography
(90–100% EtOAc/hexane) afforded sulfoxide 1c (2.54 g, 72%) as a yellow solid, m.p. = 81–83 °C. Rf = 0.30 (100% EtOAc). IR (film)/cm⁻¹ 1577, 1445, 1347, 1240, 1172, 1145, 1110, 1035, 1009, 947, 914, 805, 770, 664. ¹H NMR (400 MHz, CDCl₃) δ 8.62–8.59 (1 H, m, Py-H), 7.99–7.90 (2 H, m, Py-H), 7.75 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.38 (1 H, ddd, J = 7.0, 4.7, 1.8 Hz, Py-H), 7.32 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 4.85 (1 H, d, J = 10.8 Hz, SCHHO), 4.57 (1 H, d, J = 10.8 Hz, SCHHO), 4.17–3.99 (4 H, m, OCH₃S), 2.42 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 161.6 (Py-C₄), 149.6 (Py-C), 145.0 (Ts-C₂), 138.0 (Py-C), 132.7 (Ts-C₃), 129.8 (2 × Ts-C), 127.9 (2 × Ts-C), 124.7 (Py-C), 120.8 (Py-C), 91.1 (SCH₃O), 71.1 (OCH₂), 68.6 (OCH₂), 21.6 (CH₃). HRMS (ES) m/z Calculated for C₁₅H₁₇NNaO₅S₂ [M+Na]: 378.0446; Found: 378.0457 [M+Na], Δ 2.9 ppm.

2-(Oxetan-2-ylsulfinyl)pyridine (2c)
A solution of LDA (1 M in THF, 1.08 mL, 1.08 mmol) was added dropwise to a solution of sulfoxide 1c (0.26 g, 0.71 mmol) in THF (28 mL) at –78 °C and stirred for 15 min. The reaction flask was transferred to a –20 °C bath and stirred for a further 20 min. The reaction was quenched with sat. aq. NH₄Cl (50 mL) and extracted with CH₂Cl₂ (5 × 30 mL). The combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography afforded the oxetane as a mixture of two diastereoisomers 2c-A (50 mg, 38%) (20% EtOAc/hexane) followed by 2c-B (68 mg, 51%) (20% CH₂Cl₂/Et₂O) both as white solids.

Minor Diastereoisomer 2c-A: m.p. = 71–73 °C. Rf = 0.10 (20% CH₂Cl₂/Et₂O). IR (film)/cm⁻¹ 3502, 2970, 2912, 1575, 1449, 1421, 1240, 1088, 1053, 1009, 975, 915, 774, 739. ¹H NMR (400 MHz, CDCl₃) δ 8.61 (1 H, d, J = 4.7 Hz, Py-H), 8.04 (1 H, d, J = 7.8 Hz, Py-H), 7.94 (1 H, ddd, J = 7.8, 7.5, 1.7 Hz, Py-H), 7.37 (1 H, ddd, J = 7.5, 4.7, 1.1 Hz, Py-H), 5.78 (1 H, dd, J = 7.9, 5.6 Hz, OCHS), 4.82 (1 H, ddd, J = 8.8, 6.9, 5.4 Hz, OCHH), 4.65 (1 H, ddd, J = 8.4, 6.0, 5.4 Hz, OCHH), 3.39–3.28 (1 H, m, OCH₂CHH), 3.17–3.05 (1 H, m, OCH₂CHH). ¹³C NMR (100 MHz, CDCl₃) δ 161.0 (Py-C₄), 149.5 (Py-C), 137.7 (Py-C), 124.6 (Py-C), 121.4 (Py-C), 97.2 (OCHS), 71.4 (OCH₂), 22.7 (OCH₂CH₂). HRMS (ES) m/z Calculated for C₉H₁₃NO₂S [M+H]: 184.0432; Found: 184.0430 [M+H], Δ 1.1 ppm.

Major Diastereoisomer 2c-B: m.p. = 71–73 °C. Rf = 0.15 (20% CH₂Cl₂/Et₂O). IR (film)/cm⁻¹ 3398, 2956, 1573, 1564, 1447, 1418, 1332, 1222, 1113, 1083, 1042, 988, 764, 712. ¹H NMR (400 MHz, CDCl₃) δ 8.63–8.61 (1 H, d, J = 4.6 Hz, Py-H), 7.98–7.90 (2 H, m, 2 × Py-H), 7.38 (1 H, ddd, J = 6.8, 4.8, 2.2 Hz, Py-H), 5.82 (1 H, ddd, J = 7.4, 5.3 Hz, OCHS), 4.80 (1 H, ddd, J = 12.0, 6.8, 5.4 Hz, OCHH), 4.69 (1 H, ddd, J = 11.4, 6.0, 5.4 Hz, OCHH), 3.58–3.47 (1 H, m, OCH₂CHH), 3.22–3.12 (1 H, m, OCH₂CHH). ¹³C NMR (100 MHz, CDCl₃) δ 161.0 (Py-C₄), 149.7 (Py-C), 137.9 (Py-C), 124.6 (Py-C), 120.5 (Py-C), 100.0 (OCHS), 71.5 (OCH₂), 18.7 (OCH₂CH₂). HRMS (ES) m/z Calculated for C₉H₁₀NO₂S [M+H]: 184.0432; Found: 184.0430 [M+H], Δ 1.1 ppm.
Synthesis of 2-(2-chlorobenzenesulfinyl)oxetane (2d)

\[
\text{NaH, NaI} \quad 0^\circ \text{C to rt, 71%}
\]

2-((2-Chlorophenyl)thio)methoxyethanol (4d)\(^2\)

Sodium hydride (60% in mineral oil, 1.60 g, 40.01 mmol) was added to ethylene glycol (350 mL) at 0 °C and stirred for 1 h 30 min. Sodium iodide (6.01 g, 40.10 mmol) was added followed by chloromethylsulfide 3d (6.88 g, 35.63 mmol). The resulting solution was stirred at 0 °C for 2 h then warmed to rt for 17 h. Water (175 mL) was added and the product was extracted with ethyl acetate (10 × 30 mL). The combined organic layers were washed with sat. aq. NaHCO\(_x\) and the mixture for 1 h 45 min. The reaction was quenched with sat. aq. NaOH (129.6 (Ar-C)), 74.8 (SCH\(_2\)), 70.0 (OCH\(_2\)), 61.5 (OCH\(_2\)). HRMS (EI) \(m/z\) Calculated for C\(_9\)H\(_{15}\)NO\(_3\)S\(_3\)Cl [M+NH\(_4\)^+]: 236.0512; Found: 236.0521 [M+H+CH\(_3\)]: 236.0512; Found: 236.0521 [M+H+CH\(_3\)]: 236.0512.

2-(((2-Chlorophenyl)sulfinyl)methoxy)ethyl-4-methylbenzene-1-sulfonate (5d)\(^2\)

Triethylamine (9.59 mL, 68.24 mmol) and trimethylamine hydrochloride (0.22 g, 2.29 mmol) were added to a solution of alcohol 4d (5.02 g, 22.93 mmol) in toluene (100 mL) at 0 °C and stirred for 1 h. 4-Toluenesulfonfyl chloride (8.74 g, 45.87 mmol) was added portionwise. The mixture was stirred at 0 °C for 50 min then allowed to warm to rt and stirred for a further 1 h 30 min. Water (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 (30% EtOAc/hexane) afforded alcohol 4d (5.06 g, 94%) as a white solid; m.p. = 40–42 °C. \(R_f = 0.15\) (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\(_3\)) \(\delta\) 7.77 (2 H, d, \(J = 8.0 \text{ Hz, } 2 \times \text{ Ts-H}\)), 7.55 (1 H, dd, \(J = 7.9, 1.7 \text{ Hz, Ar-H}\)), 7.37 (1 H, dd, \(J = 7.9, 1.6 \text{ Hz, Ar-H}\)), 7.32 (2 H, d, \(J = 8.0 \text{ Hz, } 2 \times \text{ Ts-H}\)), 7.25–7.14 (2 H, m, \(2 \times \text{ Ar-H}\)), 5.00 (2 H, s, SCH\(_2\)), 4.23–4.18 (2 H, m, TsOCH\(_2\)), 3.80–3.80 (2 H, m, CH\(_2\)OCH\(_2\)), 2.43 (3 H, s, CH\(_3\)). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.9 (C\(_9\)), 134.6 (C\(_9\)), 133.8 (C\(_9\)), 132.9 (C\(_9\)), 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\(_2\)), 68.6 (OCH\(_2\)), 65.8 (OCH\(_2\)), 21.6 (CH\(_3\)). HRMS (ES) \(m/z\) Calculated C\(_{18}\)H\(_{17}\)NO\(_3\)S\(_3\)Cl [M+H+CH\(_3\)CN]: 414.0601; Found: 414.0605 [M+H+CH\(_3\)CN], \(\Delta 1.0 \text{ ppm.}\)

1-Chloro-2-(((4-methylbenzenesulfonyl)oxy)ethoxy)methane sulfanyl)benzene (1d)

\text{meta-Chloroperbenzoic acid (0.26 g, 1.51 mmol) was added portionwise to a solution of sulfide 5d (0.51 g, 1.37 mmol) in dichloromethane (20 mL) at 0 °C and the mixture for 1 h 45 min. The reaction was quenched with sat. aq. Na\(_2\)SO\(_3\) (20 mL) and sat. aq. NaHCO\(_3\) (20 mL) then extracted with dichloromethane (3 × 15 mL). The combined organic layers were washed with sat. aq. Na\(_2\)SO\(_3\) (2 × 10 mL) and sat. aq. NaHCO\(_3\) (10 mL) then dried (MgSO\(_4\)), filtered and the solvent removed under reduced pressure. Purification by flash}
chromatography (70% EtOAc/hexane) afforded sulfoxide 1d (0.51 g, 96%) as a colourless oil. Rf = 0.30 (70% EtOAc/hexane). IR (film)/cm⁻¹ 2953, 1598, 1448, 1355, 1175, 1095, 1018, 910, 814, 733, 661. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (1 H, dd, J = 7.6, 1.7 Hz, Ar-H), 7.89 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 7.55 (1 H, ddd, J = 9.0, 7.6, 1.3 Hz, Ar-H), 7.48 (1 H, ddd, J = 9.0, 7.9, 1.7 Hz, Ar-H), 7.41 (1 H, dd, J = 7.9, 1.3 Hz, Ar-H), 7.35 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 4.79 (1 H, d, J = 10.8 Hz, SCH₂O), 4.39 (1 H, d, J = 10.8 Hz, SCH≡O), 4.23–4.19 (2 H, m, OCH₂), 4.14–4.09 (2 H, m, OCH₂), 2.45 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 145.1 (C₁), 138.1 (C₂), 132.8 (C₃), 132.6 (C₄), 130.2 (Ar-C), 130.0 (2 × Ts-C), 129.9 (Ar-C), 128.2 (Ar-C), 128.1 (2 × Ts-C), 126.9 (Ar-C), 91.2 (SCH₂O), 71.2 (OCH₂), 68.8 (OCH₂), 21.8 (CH₃).

2-(2-Chlorobenzensulfinyl)oxetane (2d)

A solution of LiHMDS (1.0 M in THF, 0.94 mL, 0.94 mmol) was added dropwise to a solution of sulfoxide 1d (0.30 g, 0.78 mmol) in THF (30 mL) at 0 ºC and stirred for 1 h 15 min. The reaction was quenched with sat. aq. NH₄Cl (20 mL) and extracted with CH₂Cl₂ (5 × 15 mL). The combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded the sulfanyl oxetane as a mixture of two diastereoisomers 2d-A (12 mg, 6%) followed by 2d-B (62 mg, 37%) both as colourless oils.

Minor Diastereoisomer 2d-A: Rf = 0.22 (40% EtOAc/hexane). IR (film)/cm⁻¹ 2965, 1724, 1573, 1433, 1357, 1248, 1176, 1103, 1026, 914, 815, 752, 660. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (1 H, dd, J = 7.3, 1.8 Hz, Ar-H), 7.50 (1 H, ddd, J = 8.9, 7.3, 1.3 Hz, Ar-H), 7.44 (1 H, ddd, J = 8.9, 7.8, 1.8 Hz, Ar-H), 7.39 (1 H, dd, J = 7.8, 1.3 Hz, Ar-H), 5.79 (1 H, dd, J = 7.4, 5.3 Hz, OCHS), 4.81 (1 H, ddd, J = 8.9, 6.7, 5.3 Hz, OCH₂), 4.68 (1 H, ddd, J = 8.3, 6.1, 5.3 Hz, OCH₂), 3.27–3.18 (1 H, m, OCH₂CHH), 2.56–2.47 (1 H, m, OCH₂CHH). ¹³C NMR (100 MHz, CDCl₃) δ 136.9 (C₁), 132.2 (Ar-C), 130.3 (C₂), 129.8 (Ar-C), 127.9 (Ar-C), 126.4 (Ar-C), 97.5 (SCHO), 71.5 (OCH₂), 18.2 (OCH₂CH₂). HRMS (ES) m/z Calculated C₉H₁₀ClO₂S [M+H]: 217.0090; Found: 217.0104, [M+H], Δ 6.5 ppm.

Major Diastereoisomer 2d-B: Rf = 0.15 (40% EtOAc/hexane). IR (film)/cm⁻¹ 2965, 1724, 1573, 1433, 1357, 1248, 1176, 1103, 1026, 914, 815, 752, 660. ¹H NMR (400 MHz, CDCl₃) δ 7.92 (1 H, dd, J = 7.7, 1.7 Hz, Ar-H), 7.50 (1 H, ddd, J = 9.0, 7.7, 1.3 Hz, Ar-H), 7.43 (1 H, ddd, J = 9.0, 7.9, 1.7 Hz, Ar-H), 7.36 (1 H, dd, J = 7.9, 1.3 Hz, Ar-H), 5.75 (1 H, dd, J = 7.7, 5.5 Hz, OCHS), 4.79 (1 H, ddd, J = 8.8, 6.9, 5.2 Hz, OCH₂), 4.64 (1 H, ddd, J = 8.3, 5.9, 5.2 Hz, OCH₂), 3.31–3.23 (1 H, m, OCH₂CHH), 3.13–3.04 (1 H, m, OCH₂CHH). ¹³C NMR (100 MHz, CDCl₃) δ 136.8 (C₁), 132.1 (Ar-C), 129.9 (C₂), 129.5 (Ar-C), 128.0 (Ar-C), 127.5 (Ar-C), 94.5 (SCHO), 71.5 (OCH₂), 22.7 (OCH₂CH₂). HRMS (ES) m/z Calculated C₉H₁₀ClO₂S [M+H]: 217.0090; Found: 217.0104, [M+H], Δ 6.5 ppm.
Synthesis of 2-(3-chlorobenzenesulfinyl)oxetane (2e)

2-[(3-Chlorophenyl)sulfanyl]methoxy)ethan-1-ol (4e)

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 chloromethylsulfide 3e (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. Water (30 mL) was added and the product was extracted with ethyl acetate (10 × 15 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol 4e (0.97 g, 71%) as a colourless oil. Rₜ = 0.10 (30% EtOAc/hexane). IR (film)/cm⁻¹: 3381 (OH), 2929, 1576, 1562, 1460, 1400, 1307, 1052, 1017, 886, 823, 773, 677. ¹H NMR (400 MHz, CDCl₃) δ 7.49–7.46 (1 H, m, Ar-H), 7.35 (1 H, m, J = 1.9, 1.7 Hz, Ar-H), 7.26–7.19 (2 H, m, 2 × Ar-H), 5.07 (2 H, s, SCH₂O), 3.83–3.73 (4 H, m, OCH₂CH₂OH). ¹³C NMR (100 MHz, CDCl₃) δ 137.6 (C₂), 134.5 (C₂), 129.9 (A-C), 129.4 (A-C), 127.9 (A-C), 126.8 (A-C), 75.9 (SCH₂O), 69.9 (OCH₂), 61.4 (OCH₂). HRMS (CI) m/z Calculated C₁₈H₁₂O₂S²₃Cl [M+H]: 219.0247; Found: 219.0253 [M+H⁺], Δ 0.2 ppm.

2-[(3-Chlorophenyl)sulfanyl]methoxy)ethyl-4-methylbenzene-1-sulfonate (5e)

Triethylamine (1.66 mL, 11.83 mmol) and trimethylamine hydrochloride (38 mg, 0.39 mmol) were added to a solution of alcohol 4e (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. Water (20 mL) was added to the reaction and the product was extracted with EtOAc (5 × 15 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate 5e (1.35 g, 92%) as a colourless oil. Rₜ = 0.15 (20% EtOAc/hexane). IR (film)/cm⁻¹: 2921, 1576, 1431, 1251, 1117, 1034, 954, 907, 735, 658. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (2 H, d, J = 8.2 Hz, 2 × Ts-H), 7.40 (1 H, br 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, SCH₂O), 4.24–4.18 (2 H, m, TsOCH₂), 3.84–3.78 (2 H, m, CH₂OCH₂), 2.44 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 144.9 (Ts-C₂), 137.4 (A-C₂), 134.6 (A-C₂), 132.8 (Ts-C₂), 129.9 (A-C), 129.8 (2 × Ts-C), 129.4 (2 × Ar-C), 127.9 (2 × Ts-C), 126.9 (A-C), 75.8 (SCH₂O), 68.6 (OCH₂), 65.8 (OCH₂), 21.6 (CH₃). HRMS (APCI) m/z Calculated C₁₈H₁₂O₂S³Cl [M+NH₄⁺]: 390.0595; Found: 390.0587 [M+NH₄⁺], Δ 0.2 ppm.

1-Chloro-3-[(2-[(4-methylbenzenesulfonyl)oxy]ethyl)oxy]methane sulfinyl]benzene (1e)

meta-Chloroperbenzoic acid (0.36 g, 2.09 mmol) was added to a solution of sulfide 4e (0.71 g, 1.91 mmol) in dichloromethane (28 mL) at 0 °C and the mixture stirred at 0 °C for 2 h. The reaction was quenched with sat. aq. Na₂SO₃ (25 mL) and extracted with dichloromethane (5 × 20 mL). The combined organic layers were washed with 1 M NaOH (2 × 10 mL) and sat. aq. NH₄Cl (15 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (70% EtOAc/hexane) afforded sulfoxide 1e (0.50 g, 68%) as a white solid, m.p. = 81–82 °C. Rₜ = 0.30 (70%
EtOAc/hexane). IR (film)/cm⁻¹ 3060, 2957, 1597, 1588, 1457, 1406, 1352, 1249, 1186, 1172, 1121, 1041, 1015, 937, 915, 887, 775, 664. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 7.63–7.60 (1 H, m, Ar-H), 7.51–7.44 (3 H, m, 3 × Ar-H). 7.34 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 4.49 (1 H, d, J = 10.6 Hz, SCHHO), 4.39 (1 H, d, J = 10.6 Hz, SCHHO), 4.23–3.99 (4 H, m, OCH₂CH₂O), 2.44 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 145.1 (Ts-C₅), 142.6 (Ar-C₆), 132.6 (Ts-C₇), 131.5 (Ar-C₇), 130.5 (Ar-C₈), 129.9 (2 × Ts-C₉), 127.9 (2 × Ts-C₉), 124.3 (Ar-C₈), 122.5 (Ar-C₇), 92.1 (SCH₂O), 71.1 (OCH₂), 68.8 (OCH₂), 21.6 (CH₃). HRMS (ES) m/z Calculated C₁₇H₁₈O₅S₂Cl [M+H]: 389.0324; Found 389.0300 [M+H], Δ 1.1 ppm.

Major Diastereoisomer 2e-A: m.p. = 65–66 °C. Rf = 0.17 (50% EtOAc/hexane). IR (film)/cm⁻¹ 3025, 2970, 2937, 1756, 1738, 1438, 1336, 1228, 1217, 1208, 914, 650. ¹H NMR (400 MHz, CDCl₃) δ 7.60–7.58 (1 H, m, Ar-H), 7.49–7.41 (3 H, m, 3 × Ar-H), 5.31 (1 H, dd, J = 7.5, 5.0 Hz, OCHS), 4.81 (1 H, ddd, J = 8.8, 6.7, 5.4 Hz, OCHH), 4.68 (1 H, ddd, J = 8.5, 6.2, 5.4 Hz, OCHH), 3.28–3.16 (1 H, m, OCH₂CHH), 2.74–2.62 (1 H, m, OCH₂CHH). ¹³C NMR (100 MHz, CDCl₃) δ 141.3 (C₃), 135.7 (C₄), 131.4 (Ar-C₅), 130.4 (Ar-C₅), 124.2 (Ar-C₆), 122.2 (Ar-C₆), 99.9 (SCHO), 71.3 (OCH₂), 19.5 (OCH₂CH₂). HRMS (ES) m/z Calculated C₉H₁₀O₅ClOS²⁺ [M+H]⁺: 217.0085; Found: 217.0079, [M+H]⁺, Δ 1.2 ppm.

Minor Diastereoisomer 2e-B: m.p. = 65–66 °C. Rf = 0.09 (50% EtOAc/hexane). IR (film)/cm⁻¹ 3025, 2970, 2937, 1756, 1738, 1438, 1336, 1228, 1217, 1208, 914, 650. ¹H NMR (400 MHz, CDCl₃) δ 7.69–7.67 (1 H, m, Ar-H), 7.55–7.44 (3 H, m, 3 × Ar-H), 5.42 (1 H, dd, J = 7.6, 5.6 Hz, OCHS), 4.67–4.59 (2 H, m, OCH₂), 3.10–2.99 (2 H, m, OCH₂CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 141.1 (C₃), 135.5 (C₄), 131.5 (Ar-C₅), 130.2 (Ar-C₅), 125.2 (Ar-C₆), 123.2 (Ar-C₆), 97.0 (SCHO), 71.2 (OCH₂), 22.6 (OCH₂CH₂). HRMS (ES) m/z Calculated C₉H₁₀O₅ClOS²⁺ [M+H]⁺: 217.0085; Found: 217.0079, [M+H]⁺, Δ 2.8 ppm.
Synthesis of 2-[4-(trifluoromethyl)benzenesulfinyloxy]ethane-1-ol (4f)²

2-[(4-[4-(trifluoromethyl)phenyl]sulfanyl)methoxy]ethanol-1-ol (4f)²

Sodium hydride (60% in mineral oil, 76 mg, 1.92 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 chloromethyl sulfide 3f (0.40 g, 1.77 mmol). The resulting solution was stirred at 0 °C for 2 h then warmed to rt for 15 h. Water (20 mL) was added and the product was extracted with ethyl acetate (10 × 10 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded alcohol 4f (0.28 g, 61%) as a pale yellow oil. Rₚ = 0.10 (30% EtOAc/hexane). IR (film)/cm⁻¹ 2927, 2296, 1607, 1403, 1321, 1162, 1060, 1013, 888, 825, 779, 677. ¹H NMR (400 MHz, CDCl₃) δ 7.59–7.52 (4 H, m, 4 × Ar-H), 5.12 (2 H, s, SCH₂O), 3.83–3.75 (4 H, m, OCH₂CH₂OH), 2.03 (1 H, br s, OH). ¹³C NMR (100 MHz, CDCl₃) δ 141.0 (Ar-C₆), 128.7 (2 × Ar-C), 128.2 (C₆q, J_CF = 32.9 Hz, C-CF₃), 125.5 (q, J_CF = 3.3 Hz, 2 × Ar-C), 123.9 (C₆q, J_CF = 272.0 Hz, CF₃), 75.0 (SCH₂O), 69.9 (OCH₂), 61.2 (OCH₃). ¹⁹F NMR (400 MHz, CDCl₃) δ −62.57 (CF₃). HRMS (CI) m/z Calculated C₁₉H₁₅NF₃O₇S [M+Na⁺]⁺: 270.0770; Found: 270.0770 [M+Na⁺]⁺, Δ 0 ppm.

2-[(4-[4-(trifluoromethyl)phenyl]sulfanyl)methoxy]ethyl-4-methylbenzene-1-sulfonate (5f)²

Triethylamine (0.33 mL, 2.37 mmol) and trimethylamine hydrochloride (7 mg, 0.07 mmol) were added to a solution of alcohol 4f (0.20 g, 0.79 mmol) in toluene (4 mL) at 0 °C and stirred for 30 min. 4-Toluenesulfonfyl chloride (0.31 g, 1.61 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. Water (20 mL) was added to the reaction and the product was extracted with EtOAc (5 × 10 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/hexane) afforded tosylate 5f (0.32 g, 99%) as an off white solid; m.p. = 70–71 °C. Rₚ = 0.15 (20% EtOAc/hexane). IR (film)/cm⁻¹ 2926, 2063, 1317, 1161, 1097, 1083, 1028, 996, 909, 826, 811, 759, 683. ¹H NMR (400 MHz, CDCl₃) 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, SCH₂O), 4.26–4.29 (2 H, m, TsOCH₂), 3.86–3.81 (2 H, m, CH₂OCH₂), 2.45 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 144.9 (Ts-C₆), 140.7 (Ar-C₆), 132.9 (Ts-C₆), 129.8 (2 × Ts-C), 129.0 (2 × Ar-C), 128.5 (C₆q, J_CF = 32.1 Hz, C-CF₃), 127.9 (2 × Ts-C), 125.6 (q, J_CF = 3.5 Hz, 2 × Ar-C), 124.0 (C₆q, J_CF = 272.6 Hz, CF₃), 75.1 (SCH₂O), 68.5 (OCH₂), 65.8 (OCH₂), 21.6 (CH₃). ¹⁹F NMR (400 MHz, CDCl₃) δ −62.5 (CF₃). HRMS (APCI) m/z Calculated C₁₉H₁₅NF₃O₇S [M+Na⁺]⁺: 424.0859; Found: 424.0854 [M+Na⁺]⁺, Δ 1.2 ppm.

1-[(2-[4-Methylbenzenesulfonyl]oxy]ethoxy)methanesulfenyl)-4-(trifluoromethyl)benzene (1f)

Meta-Chloroperbenzoic acid (79 mg, 0.46 mmol) was added to a solution of sulfide 5f (0.17 g, 0.42 mmol) in dichloromethane (6 mL) at 0 °C and the mixture stirred at 0 °C for 2 h 15 min. The reaction was quenched with sat. aq. Na₂SO₃ (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. NH₄Cl (10 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (70% EtOAc/hexane)
afforded sulfoxide 1f (0.12 g, 66%) as a colourless oil. Rf = 0.21 (70% EtOAc/hexane). IR (film)/cm⁻¹ 2914, 1599, 1452, 1404, 1359, 1322, 1170, 1102, 1037, 946, 811, 659. ¹H NMR (400 MHz, CDCl₃) δ 7.83–7.70 (6 H, m, 4 × Ar-H + 2 × Ts-H), 7.34 (2 H, d, J = 8.3 Hz, 2 × Ts-H), 4.53 (1 H, d, J = 10.4 Hz, SCH₂), 4.44 (1 H, d, J = 10.4 Hz, SCH₂), 4.22–4.00 (4 H, m, OCH₂CH₂O), 2.44 (3 H, s, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 145.2 (Ts-CHq), 133.6 (Ar-CHq), 132.6 (Ts-CHq), 131.9 (C(q, q, JCF = 31.2 Hz, C-CH₃), 129.9 (2 × Ts-C), 127.9 (2 × Ts-C), 126.3 (q, JCF = 3.6 Hz, 2 × Ar-C), 124.9 (2 × Ar-C), 123.5 (C(q, q, JCF = 248.9 Hz, C-F₃), 99.9 (C(q, q, JCF = 32.3 Hz, C-CH₃)), 71.4 (OCH₂), 19.8 (OCH₂CH₂). ¹⁹F NMR (400 MHz, CDCl₃) δ –62.5 (CF₃). HRMS (ES) m/z Calculated C₁₇H₁₇O₅F₃NaS₂ [M+Na]: 445.0367; Found 445.0373 [M+Na], Δ 1.3 ppm.

2-[4-(Trifluoromethyl)benzenesulfinyl]oxetane (2f)

A solution of LiHMDS (1 M in THF, 0.21 mL, 0.21 mmol) was added dropwise to a solution of sulfoxide 1f (74 mg, 0.17 mmol) in THF (7 mL) at 0 °C and stirred for 1 h 45 min. The reaction was quenched with sat. aq. NH₄Cl (20 mL) and extracted with CH₂Cl₂ (5 × 10 mL). The combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (50% EtOAc/hexane) afforded oxetane 2f (6 mg, 13%) as a colourless oil. Only one diastereoisomer isolated. Rf = 0.22 (50% EtOAc/hexane). IR (film)/cm⁻¹ 2929, 1730, 1605, 1402, 1321, 1169, 1128, 1102, 1061, 1014, 952, 836, 698, 666. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (2 H, d, J = 7.7 Hz, 2 × Ar), 7.72 (2 H, d, J = 7.7 Hz, 2 × Ar), 5.32 (1 H, dd, J = 7.4, 5.2 Hz, SCH₂), 4.84 (1 H, ddd, J = 8.8, 6.8, 5.4 Hz, OCHH), 4.70 (1 H, ddd, J = 8.8, 6.2, 5.4 Hz, OCHH), 3.28–3.18 (1 H, m, OCH₂CH₂), 2.75–2.64 (1 H, m, OCH₂CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 143.7 (Ar-C(q)), 133.2 (C(q, q, JCF = 32.3 Hz, C-CF₃)), 126.2 (q, JCF = 4.2 Hz, 2 × Ar-C), 124.7 (2 × Ar-C), 123.5 (q, JCF = 274.4 Hz, CF₃), 99.9 (OCH₃), 71.4 (OCH₂), 19.8 (OCH₂CH₂). ¹⁹F NMR (400 MHz, CDCl₃) δ –62.5 (CF₃). HRMS (EI) m/z Calculated C₁₀H₉F₃O₂S [M]: 250.0275; Found 250.0287 [M], Δ 4.8 ppm.
Synthesis of 4-(oxetane-2-sulfanyl)benzonitrile (2g)

![Chemical Structure](image)

\[ \text{3g} \rightarrow \text{4g} \rightarrow \text{5g} \rightarrow \text{1g} \rightarrow \text{2g} \]

4-4-[(Chloromethyl)sulfanyl]benzonitrile (3g)
N-Chlorosuccinimide (2.46 g, 18.42 mmol) was added portionwise to a solution of 4-(methylthio)benzonitrile (2.50 g, 16.75 mmol) in dichloromethane (25 mL). The reaction was stirred at rt for 1 h then filtered through a short pad of silica, eluting with dichloromethane (50 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide 3g (3.00 g, 97%) as an off white solid, which was used without further purification; m.p. = 146–147 °C. Rr = 0.51 (40% EtOAc/hexane). IR (film)/cm⁻¹: 3034, 2224 (CN), 1590, 1486, 1403, 1224, 1140, 1123, 1085, 1016, 975, 888, 822, 778, 760, 680. The observed data (¹H and ¹³C) is consistent with that reported in the literature.³

4-4-[(2-Hydroxyethoxy)methyl]sulfanyl]benzonitrile (4g)
Potassium t-butoxide (1.01 g, 9.00 mmol) was added to a solution of ethylene glycol (4.6 mL, 82.50 mmol) in DMF (67 mL) at 0 °C and stirred for 1 h. Potassium iodide (1.49 g, 8.98 mmol) was added followed by chloromethylsulfide 3g (1.50 g, 8.17 mmol). DMF (2 mL) was added to aid solubility. The resulting solution was stirred at 0 °C for 1 h then warmed to rt for 14 h. Water (100 mL) was added and the product was extracted with ethyl acetate (7 × 20 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded alcohol 4g (0.76 g, 44%) as a colourless oil. Rr = 0.09 (40% EtOAc/hexane). IR (film)/cm⁻¹: 3411 (OH), 2925, 2226 (CN), 1592, 1457, 1432, 1402, 1316, 1303, 1273, 1181, 1106, 1058, 1016, 975, 888, 822, 778, 760, 680. ¹H NMR (400 MHz, CDCl₃) δ 7.67–7.65 (2 H, d, J = 8.7 Hz, 2 × Ar-H), 7.55–7.52 (2 H, d, J = 8.6 Hz, 2 × Ar-H), 5.16 (2 H, s, SCH₂Cl). ¹³C NMR (100 MHz, CDCl₃) δ 140.6 (Ar-C), 132.6 (2 × Ar-C), 128.4 (2 × Ar-C), 118.4 (CN), 110.5 (Ar-C₃), 47.8 (SCH₂Cl). HRMS (EI) m/z Calculated for C₆H₅NS₂Cl [M]: 218.9909; Found: 218.9908 [M], Δ 0.5 ppm.

2-4-[(4-Cyanophenyl)sulfanyl]methoxethyl-4-methylbenzene-1-sulfonate (5g)
Triethylamine (2.52 mL, 17.93 mmol) and trimethylamine hydrochloride (57 mg, 0.60 mmol) were added to a solution of alcohol 4g (1.26 g, 6.03 mmol) in toluene (20 mL) at 0 °C and stirred for 30 min. 4-Toluenesulfonyl chloride (2.30 g, 12.06 mmol) was added portionwise. The mixture was stirred at 0 °C for 35 min then allowed to warm to rt slowly and stirred for a further 3 h. Water (75 mL) was added to the reaction and the product was extracted with EtOAc (4 × 25 mL). The combined organic layers were washed with brine (25 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (30% EtOAc/hexane) afforded tosylate 5g (1.79 g, 82%) as an off white solid; m.p. = 86–87 °C. Rr = 0.18 (30% EtOAc/hexane). IR (film)/cm⁻¹: 2221 (CN), 1590, 1487, 1430, 1317, 1292, 1240, 1188, 1171, 1118, 1081, 1029, 995, 907, 822, 761, 683. ¹H NMR (400 MHz,
CDCl$_3$ δ 7.77 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 7.54–7.46 (4 H, m, 4 × Ar-H), 7.34 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 5.04 (2 H, s, SCH$_2$O), 4.24–4.20 (2 H, m, TsOCH$_2$), 3.85–3.82 (2 H, m, CH$_2$OCH$_2$), 2.46 (3 H, s, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.0 (Ts$_2$C$_x$), 143.0 (Ar$_x$C$_y$), 132.8 (Ts$_2$C$_y$), 132.3 (2 × Ar$_y$C$_z$), 129.8 (2 × Ts-C), 128.5 (2 × Ar-C), 127.9 (2 × Ts-C), 118.6 (CN), 109.5 (Ar$_y$C$_z$), 74.5 (SCH$_2$O), 68.4 (OCH$_2$), 65.9 (OCH$_2$), 21.7 (CH$_3$). HRMS (NSI) m/z Calculated for C$_{17}$H$_{21}$N$_2$O$_4$S$_2^+$ [M+Na$^+$]$^+$: 381.0937; Found: 381.0940 [M+Na$^+$]$^+$, Δ 0.8 ppm.

4-[[2-[[4-Methylbenzenesulfonyl]oxy]ethoxy]methanesulfinyl] benzonitrile (1g)

meta-Chloroperbenzoic acid (0.26 g, 1.51 mmol) was added to a solution of sulfide 5g (0.50 g, 1.38 mmol) in dichloromethane (20 mL) at 0°C and the mixture stirred at 0°C for 2 h 30 min. The reaction was quenched with sat. aq. Na$_2$SO$_3$ (30 mL) and extracted with dichloromethane (5 × 15 mL). The combined organic layers were washed with 1 M NaOH (2 × 15 mL) and sat. aq. NH$_4$Cl (15 mL) then dried (MgSO$_4$), filtered, and the solvent removed under reduced pressure. Purification by flash chromatography (70% EtOAc/hexane) afforded sulfoxide 1g (0.47 g, 90%) as pale yellow solid, m.p. = 85–87 °C. R$_f$ = 0.20 (70% EtOAc/hexane). IR (film)/cm$^{-1}$ 2929, 2231, 1596, 1487, 1445, 1397, 1351, 1309, 1295, 1247, 1189, 1120, 1080, 1042, 939, 834, 811, 775, 719, 704, 663. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.86–7.73 (6 H, m, 4 × Ar-H + 2 × Ts-H), 7.37 (2 H, d, J = 8.4 Hz, 2 × Ts-H), 4.56 (1 H, d, J = 10.6 Hz, SCH$_2$O), 4.47 (1 H, d, J = 10.6 Hz, SCH$_2$O), 4.24–4.03 (4 H, m, OCH$_2$CH$_2$O), 2.47 (3 H, s, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.6 (Ar$_x$C$_y$), 145.2 (Ts$_2$C$_y$), 132.9 (2 × Ar$_y$C$_z$), 132.9 (Ar$_x$C$_y$), 130.0 (2 × Ts-C), 127.9 (2 × Ts-C), 125.2 (2 × Ar-C), 117.7 (CN), 115.2 (Ar$_x$C$_y$), 91.4 (SCH$_2$O), 71.4 (OCH$_2$), 68.5 (OCH$_2$), 21.7 (CH$_3$). HRMS (ES) m/z Calculated for C$_{17}$H$_{18}$NO$_5$S$_2^+$ [M+H]$^+$: 380.0621; Found: 380.0624 [M+H]$^+$, Δ 0.8 ppm.

Minor Diastereoisomer 2g-A: R$_r$ = 0.45 (70% EtOAc/pentane). IR (film)/cm$^{-1}$ 3090, 2967, 2881, 2229, 1731, 1589, 1483, 1397, 1338, 1245, 1147, 1104, 1073, 1015, 953, 828, 778, 715, 663. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.82 (2 H, d, J = 8.5 Hz, 2 × Ar-H), 7.72 (2 H, d, J = 8.5 Hz, 2 × Ar-H), 5.31 (1 H, dd, J = 7.3, 5.0 Hz, OCH$_3$), 4.84 (1 H, dd, J = 8.8, 7.0, 5.5 Hz, OCH$_2$), 4.71 (1 H, dd, J = 8.5, 5.9, 5.5 Hz, OCH$_2$), 3.25–3.15 (1 H, m, OCH$_2$CH$_2$H), 2.78–2.68 (1 H, m, OCH$_2$CH$_2$H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.2 (C$_x$), 132.8 (2 × Ar-C), 124.9 (2 × Ar-C), 117.6 (CN), 115.0 (C$_y$), 99.9 (OCH$_3$), 71.5 (OCH$_2$), 20.1 (OCH$_2$CH$_2$). HRMS (ASAP) m/z Calculated for C$_{10}$H$_{10}$NO$_2$S [M+H]: 208.0432; Found: 208.0432 [M], Δ 0 ppm.

Major Diastereoisomer 2g-B: R$_r$ = 0.13 (70% EtOAc/pentane). IR (film)/cm$^{-1}$ 3090, 2967, 2881, 2229, 1731, 1589, 1483, 1397, 1338, 1245, 1177, 1144, 1073, 1015, 953, 828, 778, 715, 663. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 (2 H, d, J = 8.3 Hz, 2 × Ar-H), 7.78 (2 H, d, J = 8.3 Hz, 2 × Ar-H), 5.44 (1 H, dd, J = 7.6, 5.4 Hz, OCH$_3$), 4.66–4.60 (2 H, m, OCH$_2$), 3.18–3.02 (2 H, m, OCH$_2$CH$_2$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.9 (C$_x$), 132.5 (2 × Ar-C), 125.8 (2 × Ar-C), 117.8 (CN), 115.0 (C$_y$), 97.1 (OCH$_3$), 71.5 (OCH$_2$), 22.7 (OCH$_2$CH$_2$). HRMS (ASAP) m/z Calculated for C$_{10}$H$_{10}$NO$_2$S [M+H]: 208.0432; Found: 208.0432 [M], Δ 0 ppm.
Synthesis of 2-[[4-nitrophenyl)sulfanyl]methoxy]ethyl-4-methylbenzene-1-sulfonate (5h)

1-[[Chloromethyl)sulfanyl]-4-nitrobenzene (3h)

N-Chlorosuccinimide (2.17 g, 16.25 mmol) was added portionwise to a solution of 4-nitrothioanisole (2.50 g, 14.78 mmol) in dichloroethane (25 mL). The reaction was stirred at rt for 17 h then filtered through a short pad of silica, eluting with dichloromethane (25 mL). The solvent was removed under reduced pressure to afford chloromethyl sulfide 82k (3.04 g, quant) as a pale yellow solid. m.p. = 58–59 °C (lit m.p. 63–64 °C). IR (film)/cm−1: 3098, 3022, 2964, 2829, 1593, 1575, 1500 (NO), 1454, 1345 (NO), 1332, 1280, 1188, 1172, 1103, 1085, 1013, 946, 852, 837, 810, 781, 739, 682, 655, 623, 594, 553, 525, 508, 477, 450, 428, 403, 385, 367, 347, 326, 309, 295, 286, 238, 1504, 1454, 1345, 1332, 1280, 1188, 1172, 1103, 1085, 1013, 946, 852, 837, 810, 781, 739, 682.

1H NMR (400 MHz, CDCl3) δ 8.23 (2 H, d, J = 9.0 Hz, 2 × Ar-H), 7.57 (2 H, d, J = 9.0 Hz, 2 × Ar-H), 5.07 (2 H, s, SCH₂Cl). 13C NMR (100 MHz, CDCl3) δ 142.7 (C₆), 141.3 (C₆), 127.5 (2 × Ar-C), 123.9 (2 × Ar-C), 47.1 (SCH₂Cl). HRMS (Cl) m/z Calculated for C₆H₅ClNO₂S: [M+H]+: 203.9881; Found: 203.9879 [M+H]+, Δ 0.1 ppm. The observed data (1H) was consistent with that reported in the literature.

2-[[4-Nitrophenyl)sulfanyl]methoxy]ethan-1-ol (4h)

Sodium hydride (60% in mineral oil, 0.11 g, 2.70 mmol) was added to ethylene glycol (25 mL) at 0 °C and stirred for 1 h 30 min. Sodium iodide (0.41 g, 2.71 mmol) was added followed by chloromethyl sulfoxide 3h (0.50 g, 2.46 mmol). DMF (1 mL) was added to aid solubility. The resulting solution was stirred at 0 °C for 30 min then warmed to rt for 15 h 30 min. Water (50 mL) was added and the product was extracted with ethyl acetate (10 × 30 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (50% EtOAc/hexane) afforded alcohol 4h (0.22 g, 39%) as a pale yellow solid. m.p. = 40–41 °C. Rr = 0.15 (50% EtOAc/hexane). IR (film)/cm−1: 3292, 2932, 1595, 1578, 1510 (NO), 1479, 1338 (NO), 1109, 1080, 1062, 888, 853, 742, 683. 1H NMR (400 MHz, CDCl₃) δ 8.14 (2 H, d, J = 8.9 Hz, 2 × Ar-H), 7.57 (2 H, d, J = 8.9 Hz, 2 × Ar-H), 5.18 (2 H, s, SCH₂O). 13C NMR (100 MHz, CDCl₃) δ 146.0 (C₆), 145.8 (C₆), 127.8 (2 × Ar-C), 124.0 (2 × Ar-C), 74.5 (SCH₂O), 70.2 (OCH₂), 61.5 (OCH₃). HRMS (APCI) m/z Calculated for C₆H₅NO₃S⁺ [M+NH₄]⁺: 247.0747; Found: 247.0749 [M+NH₄]⁺, Δ 0.8 ppm.

2-[[4-Nitrophenyl)sulfanyl]methoxy]ethyl-4-methylbenzene-1-sulfonate (5h)

Triethylamine (0.24 mL, 1.71 mmol) and trimethylamine hydrochloride (6 mg, 0.06 mmol) were added to a solution of alcohol 4h (0.13 g, 0.57 mmol) in toluene (2 mL) at 0 °C and stirred for 30 min. 4-Toluenesulfonyl chloride (0.22 g, 1.15 mmol) was added portionwise to the mixture. The mixture was stirred at 0 °C for 30 min then allowed to warm to rt slowly over 30 min and stirred for a further 1 h 30 min. Water (20 mL) was added to the reaction and the product was extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with brine (25 mL) and H₂O (20 mL) then dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (40% EtOAc/hexane) afforded tosylate 5h (0.19 g, 90%) as a white solid. m.p. = 82–83 °C. Rr = 0.29 (40% EtOAc/hexane). IR (film)/cm−1: 2925, 1593, 1577, 1505 (NO), 1454, 1345 (NO), 1332, 1280, 1188, 1172, 1103, 1085, 1013, 946, 852, 837, 810, 781, 739, 682. 1H NMR (400 MHz, CDCl₃) δ 8.09 (2 H, d, J = 8.7 Hz, 2 × Ar-H), 7.78 (2 H, d, J = 8.2 Hz, 2 × Ts-H), 7.50 (2 H, d, J = 8.7 Hz, 2 × Ar-H), 7.34 (2 H, d, J =...
8.2 Hz, 2 × Ts-H), 5.08 (2 H, s, SCH2O), 4.25–4.21 (2 H, m, TsOCH2), 3.88–3.84 (2 H, m, CH2OCH2), 2.46 (3 H, s, CH3). 13C NMR (100 MHz, CDCl3) δ 145.9 (Ar-Cq), 145.6 (Ar-Cq), 145.1 (Ts-Cq), 132.8 (Ts-Cq), 129.8 (2 × Ts-C), 128.0 (2 × Ts-C), 127.9 (2 × Ar-C), 123.9 (2 × Ar-C), 74.3 (SCH2O), 68.3 (TsOCH2), 66.0 (CH2OCH2), 21.6 (CH3). HRMS (NSI) m/z Calculated for C16H21N2O6S2 [M+NH4]+: 401.0836; Found: 401.0834 [M+NH4]+, Δ 0.5 ppm.
Sulfoxide-magnesium exchange on oxetane 2e to give 6

2-(Propane-2-sulfanyl)oxetane (6)

iPrMgCl (2 M in Et₂O, 0.13 mL, 0.26 mmol) was added dropwise to a solution of 2-(3-chlorobenzensulfinyl)oxetane 2e (28 mg, 0.13 mmol) in THF (1.5 mL) at −78 °C and stirred for 5 min. The reaction was quenched with sat. aq. NH₄Cl (10 mL) and extracted with CH₂Cl₂ (5 × 10 mL). The combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (100% EtOAc) afforded oxetane 6 (16 mg, 86%) as a colourless oil. Rf = 0.14 (100% EtOAc). IR (film)/cm⁻¹: 2967, 1646, 1471, 1368, 1241, 1051, 1009, 976, 916, 764. ¹H NMR (400 MHz, CDCl₃) δ 5.57 (1 H, dd, J = 8.1, 6.0 Hz, SCHO), 4.84–4.77 (1 H, m, OCH₂H), 4.76–4.70 (1 H, m, OC₃H), 3.30–3.22 (1 H, m, OCH₂CH₂H), 3.19 (1 H, sept, J = 7.0 Hz, (SC₃H₂)₂), 3.06–2.95 (1 H, m, OCH₂CH₂H), 1.42 (3 H, d, J = 7.0 Hz, CH₃), 1.14 (3 H, d, J = 7.0 Hz, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 91.3 (SCHO), 71.6 (OCH₂), 46.0 (SCH(CH₃)₂), 22.2 (OCH₂CH₂), 16.7 (CH₃), 15.9 (CH₃).

Sulfoxide-magnesium exchange on oxetane 2c to give 7

2-(Oxetan-2-yl)pyridine (7)

iPrMgCl·LiCl (1.3 M in THF, 0.35 mL, 0.46 mmol) was added dropwise to a solution of 2-(oxetan-2-ylsulfinyl)pyridine 2c (41 mg, 0.23 mmol) in THF (4.5 mL) at −78 °C and stirred for 5 min. 3-Pentanone (75 µL, 0.69 mmol) was added and the reaction stirred at −78 °C for a further 5 min. Reaction quenched with sat. aq. NH₄Cl (10 mL) and extracted with CH₂Cl₂ (5 × 10 mL). Combined organics were dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (100% EtOAc) afforded oxetane 7 (18 mg, 60%) as a colourless oil. Rf = 0.48 (100% EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 8.60 (1 H, d, J = 4.7 Hz, Py-H), 7.78 (1 H, ddd, J = 9.4, 7.7, 1.6 Hz, Py-H), 7.62 (1 H, d, J = 7.7 Hz, Py-H), 7.23 (1 H, dd, J = 7.2, 4.7 Hz, Py-H), 5.87 (1 H, t, J = 7.5 Hz, OCHPy), 4.91–4.85 (1 H, m, OCHH), 4.72 (1 H, dt, J = 9.2, 5.9 Hz, OCHH), 3.19–3.08 (1 H, m, OCH₂CH₂H), 2.80–2.69 (1 H, m, OCH₂CH₂H). ¹³C NMR (100 MHz, CDCl₃) δ 162.4 (C₃), 149.3 (Py-C), 136.8 (Py-C), 122.5 (Py-C), 119.8 (Py-C), 83.0 (OCHPy), 69.0 (OCH₂), 28.9 (OCH₂CH₂).
Formation of sulfonyl-oxetanes 8d and 8g

2-((2-Chlorophenyl)sulfonyl)oxetane (8d)
meta-Chloroperbenzoic acid (25.9 mg, 0.15 mmol) was added portionwise to a solution of sulfide 2d-B (21.7 mg, 0.10 mmol) in dichloromethane (1.0 mL) at 0°C and the mixture stirred for 1 h at 0°C followed by 1 h at rt. The reaction was quenched with sat. aq. Na₂SO₃ (1.0 mL) and extracted with dichloromethane (5 × 3 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (20% EtOAc/pentane) afforded sulfone 8d (21.2 mg, 91%) as a colourless oil.

1H NMR (400 MHz, CDCl₃) δ 8.20 (dd, J = 7.9, 1.7 Hz, 1H, Ar-H), 7.61-7.51 (m, 2H, 2 × Ar-H), 7.48 (ddd, J = 7.9, 7.0, 1.5 Hz, 1H, Ar-H), 5.94 (dd, J = 7.9, 5.0 Hz, 1H, OCHS), 4.95 (ddd, J = 8.5, 7.6, 5.5 Hz, 1H, OCHH), 4.69 (dt, J = 8.5, 5.5 Hz, 1H, OCHH), 3.30-3.13 (m, 2H, OCH₂C₂H₂). All other data was consistent with that previously reported in the literature.

4-(Oxetan-2-ylsulfonyl)benzonitrile (8g)
meta-Chloroperbenzoic acid (19.9 mg, 0.12 mmol) was added portionwise to a solution of sulfide 2g-B (15.9 mg, 0.077 mmol) in dichloromethane (0.8 mL) at 0°C and the mixture stirred for 1 h at 0°C. The reaction was quenched with sat. aq. Na₂SO₃ (1.0 mL) and extracted with dichloromethane (5 × 3 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. Purification by flash chromatography (70% Et₂O/pentane) afforded sulfone 8g (10.8 mg, 63%) as a colourless oil. Rᵣ = 0.26 (70% Et₂O/pentane). IR (film)/cm⁻¹: 3095, 2977, 2905, 2235, 1443, 1396, 1322, 1285, 1150, 1086, 1031, 983, 908, 842, 726, 689. 1H NMR (400 MHz, CDCl₃) δ 8.14-8.04 (m, 2H, 2 × Ar-H), 7.91-7.83 (m, 2H, 2 × Ar-H), 5.39 (dd, J = 7.3, 5.8 Hz, 1H, OCHS), 4.86 (app. td, J = 8.0, 5.5 Hz, 1H, OCHH), 4.72-4.65 (m, 1H, OCHH), 3.25-3.07 (m, 2H, OCH₂CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 139.8 (C₃), 132.9 (2 × Ar-C), 130.2 (2 × Ar-C), 118.1 (CN), 117.1 (C₄), 94.2 (OCHS), 71.9 (OCH₂), 22.1 (OCH₂CH₂). HRMS (NSI) m/z Calculated for C₁₀H₉NaO₃NS⁺ [M+Na⁺]: 246.0195; Found: 246.0197 [M+Na⁺], Δ 0.7 ppm.
References

$^1$H and $^{13}$C NMR spectra of selected compounds
3a

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

3a

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
2a

$^1$H NMR (400 MHz, CDCl$_3$)
4b

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

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^{1}$H NMR (400 MHz, CDCl$_3$)

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

5b

Cl

5b

H NMR (400 MHz, CDCl$_3$)
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^H NMR (400 MHz, CDCl\textsubscript{3})

^13\text{C} NMR (100 MHz, CDCl\textsubscript{3})
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2b-A (minor)
$^1$H NMR (400 MHz, CDCl$_3$)

13C NMR (100 MHz, CDCl$_3$)
2b-B major

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

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$, 1% SiMe$_4$)

$^{13}$C NMR (100 MHz, CDCl$_3$, 1% SiMe$_4$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
2c-A minor

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

2c-A

$^{13}$C NMR (100 MHz, CDCl$_3$)
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2c-B major

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

13C NMR (100 MHz, CDCl$_3$)
**1H NMR (400 MHz, CDCl$_3$)**

- Chemical shifts and peak assignments are shown.

**13C NMR (100 MHz, CDCl$_3$)**

- Chemical shifts are indicated with corresponding peak heights.

The images depict spectral data for compounds 4d, showing various chemical shifts and peak intensities in the 1H and 13C NMR spectra.
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H NMR (400 MHz, CDCl₃)

13C NMR (100 MHz, CDCl₃)
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$\text{38}$

$\text{0.0}$

$\text{0.5}$

$\text{1.0}$

$\text{1.5}$

$\text{2.0}$

$\text{2.5}$

$\text{3.0}$

$\text{3.5}$

$\text{4.0}$

$\text{4.5}$

$\text{5.0}$

$\text{5.5}$

$\text{6.0}$

$\text{6.5}$

$\text{7.0}$

$\text{7.5}$

$\text{8.0}$

$\text{8.5}$

$\text{9.0}$

$\text{9.5}$

$\text{10.0}$

$\text{ppm}$

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

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

$\text{1d}$

$\text{Cl}$

$\text{O}$

$\text{O}$

$\text{Ts}$

$\text{H NMR (400 MHz, CDCl}_3\text{)}$

$\text{13C NMR (100 MHz, CDCl}_3\text{)}$
2d-A minor

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

2d-A

$^{13}$C NMR (100 MHz, CDCl$_3$)
2d-B major

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

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^13$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
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2e-A major
$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)
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$^{1}$H NMR (400 MHz, CDCl$_3$)

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

2e-B minor

1H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
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$^{1}$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)
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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^13$C NMR (100 MHz, CDCl$_3$)
$1g$

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

$12$C NMR (100 MHz, CDCl$_3$)
2g-A minor

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

2g-A

$^{13}$C NMR (100 MHz, CDCl$_3$)
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$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
\hspace{1cm} 

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

$^{13}$C NMR (100 MHz, CDCl$_3$)
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$^1$H NMR (400 MHz, CDCl$_3$)

$^1^3$C NMR (100 MHz, CDCl$_3$)
$\text{Cl} \quad \text{O} \quad \text{O}$

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

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