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Supporting Information

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The Use of Vinyl Sulfonium Salts in the Stereocontrolled Asymmetric Synthesis of Epoxide- and Aziridine-Fused Heterocycles: Application to the Synthesis of (-)-Balanol

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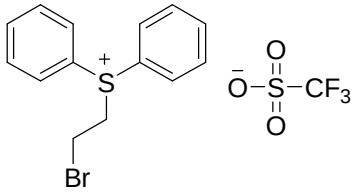
Contents

General Directions

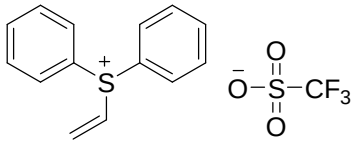
Reactions requiring anhydrous conditions were performed in vacuum oven-dried glassware under an argon atmosphere. Reaction mixtures were stirred magnetically. Air- and moisture-sensitive liquids and solutions were transferred *via* syringe or cannula into the reaction vessels through rubber septa. Chromatography: Flash chromatography was performed on silica gel (Merck Kiesegel 60, 230-400 mesh) unless otherwise stated. TLC was performed on aluminium backed silica plates ($60F_{254}$, 0.2 mm) which were developed using standard visualising agents: UV fluorescence (254 and 366 nm), phosphomolybdic acid/?, anisaldehyde/?, permanganate/?. Melting points were determined on a Kofler hot stage. Optical rotations were measured using a Perkin-Elmer 241 MC polarimeter. $[\alpha]_D$ values are given in angular degrees per g/cm^3. Infrared spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer. Only selected absorbencies (υ_{max}) are reported. ^{1}H NMR spectra were recorded at 270 or 400 MHz on Jeol Delta GX/270 or Jeol Delta GX/400 instruments, respectively. Chemical shifts (δ_H) are quoted in parts per million (ppm), referenced to TMS, *J* values are given in Hz. ^{13}C NMR spectra were recorded at 101 MHz on a Jeol Delta GX/400 instrument. Chemical shifts (δ_C) are quoted in parts per million (ppm), referenced to the appropriate residual solvent peak and are assigned as s, d, t, q for C, CH, CH_2, CH_3. Low resolution mass spectra (*m/z*) were recorded on a Micromass Analytical Autospec spectrometer with only molecular ions $\mathbf{M}^+$ and major peaks being reported with intensities quoted as percentages of the base peak. High-resolution mass spectra were recorded on a Micromass Analytical Autospec spectrometer. All chiral HPLC was carried out using an Agilent 1100 series HPLC with multiple wave length UV detection in the range of 200-280 nm with a mobile phase of iso-propyl alcohol/hexane pumped at 1 mL/min though an OD, OD-H, or OJ type chiral HPLC column at 23 °C. All chemicals were purchased from Aldrich, Fluka or Lancaster. Anhydrous THF, CH_2Cl_2, hexanes, Et_2O, acetonitrile and toluene were obtained from a purification column composed of activated alumina (A-2). For toluene a supported copper catalyst (Q-5 reagent) is also employed. Other anhydrous solvents were used as obtained from Aldrich.

(2-Bromoethyl)(diphenyl)sulfonium trifluoromethanesulfonate,[1] 19



2-Bromoethyl trifluoromethanesulfonate (3.58 g, 13.9 mmol) was dissolved in anhydrous DCM (20 mL) and treated with diphenyl sulfide (2.59 g, 13.9 mmol) drop-wise over 5 minutes at room temperature under nitrogen with stirring. The reaction mixture was then stirred for 7 days at 45 °C under reflux and nitrogen after which time the DCM was removed under reduced pressure and anhydrous diethyl ether (18 mL) was added to the resulting residue. The reaction mixture was then stirred for 1 hour to precipitate the reaction product which was isolated by filtration as an off white solid. This solid was then re-dissolved in the minimum amount of DCM (~10 mL) and the DCM solution was added slowly and drop-wise to rapidly stirred diethyl ether (~200 mL). The resulting precipitate was then isolated by filtration, and was washed with diethyl ether (4 × 20 mL) to give the product as a white solid (3.67 g, 60%). Mp 89-90 °C; R_f (MeOH-DCM, 10:90) 0.20; δ_H (400 MHz; $CDCl_3$) 3.68 (2 H, t, *J* 6.0, Br-CH_2), 4.86 (2 H, t, *J* 6.0, S^+-CH_2), 7.60-7.80 (6 H, m, ArH), 8.01-8.12 (4 H, m, ArH), [lit.,[1] δ_H (400 MHz; $CDCl_3$) 3.72 (2 H, t, *J* 5.8), 4.94 (2 H, t, *J* 5.8), 7.7-7.8 (6 H, m), 8.1-8.15 (4 H, m)]; δ_c (100.5 MHz; $CDCl_3$) 23.8 (t), 48.3 (t), 120.6 (q, *J* 320), 122.9 (d), 131.2 (d), 131.9 (d), 135.3 (s), [lit,.[1] δ_c ($CDCl_3$) 24.0, 48.6, 122.7, 131.1, 132.0, 135.4].

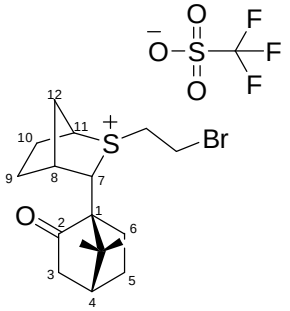
Diphenylvinylsulfonium trifluoromethanesulfonate[1] 1



Using an improved procedure based on a method of Jimenez and co-workers[1], a suspension of (2-bromoethyl)(diphenyl)sulfonium trifluoromethanesulfonate **19** (3.58 g, 8.08 mmol) and silver (I) oxide (2.81 g, 12.12 mmol) in deionised water (7 mL) and THF (7 mL) was stirred for 18 hours at room temperature under nitrogen. The reaction mixture was then filtered through Celite then the filtrate concentrated under reduced pressure to remove the majority of the water. The yellow residue was

dissolved in DCM (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The yellow residue was then dissolved in the minimum amount of DCM and loaded onto a 4 cm silica plug with a diameter of 5-7 cm topped with sand (2-3 cm) to avoid disturbing the silica pad. DCM was then passed through the silica plug to elute the bright yellow layer of impurities (100-200 mL). The product (a pale yellow band on the silica) was then eluted from the silica with an excess of 10% MeOH in DCM (~250 mL) to give the desired product as a pale yellow oil (2.75 g, 94%) after concentration under reduced pressure. R_f (MeOH-DCM, 20:80) 0.30; δ_H (400 MHz; $CDCl_3$) 6.57 (1 H, dd, *J* 16.0, 2.0, *trans*-H*H*C=CH), 6.69 (1 H, dd, *J* 9.0, 2.0, *cis*-*H*HC=CH), 7.51 (1 H, dd, *J* 16.0, 9.0, H_2C=C*H*), 7.64-7.75 (6 H, m, ArH), 7.86-7.90 (4 H, m, ArH), [lit.,[1] δ_H (400 MHz; $CDCl_3$) 6.46 (1 H, dd, *J* 10.6, 1.4), 6.70 (1 H, dd, *J* 6.0, 1.4), 7.54 (1 H, dd, *J* 10.6, 6.0), 7.65-7.75 (6 H, m), 7.8-7.85 (4 H, m)]; δ_c (100.5 MHz; $CDCl_3$) 123.3 (d), 125.4 (s), 130.5 (d), 131.6 (d), 134.6 (d), 138.1 (t), [lit.,1 δ_c ($CDCl_3$) 123.4, 125.0, 130.6, 131.7, 134.8, 137.9].

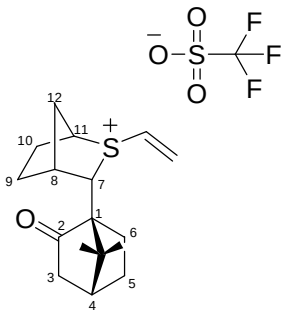
2-(2-Bromo-ethyl)-3-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-yl)-2-thionia-bicyclo[2.2.1]heptane; trifluoro-methanesulfonate 20



(1R)-7,7-Dimethyl-1-[(3S)-2-thiabicyclo[2.2.1]hept-3-yl]bicyclo[2.2.1]heptan-2-one (1.0 g, 4.0 mmol)[2] **7** was dissolved in anhydrous DCM (7.6 mL) and treated with a solution of 2-bromoethyl trifluoromethanesulfonate (2.34 g, 9.1 mmol) in anhydrous DCM (5 mL) drop-wise over 20 minutes at room temperature under nitrogen. The reaction mixture was then stirred for a further 48 hours, then the DCM was removed under reduced pressure and diethyl ether (25 mL) was added to the residue and stirred vigorously for 10 minutes, then filtered and the precipitate washed with excess diethyl ether (100 mL) to give the product as a white solid (1.98 g, 97%) after removal of solvent under vacuum. Mp 149-150 °C; $[\alpha]_D^{20}$ +8 (*c*. 1, $CHCl_3$); R_f (MeOH-DCM, 5:95) 0.20; n_{max} (film)/cm^{-1} 2964 (CH), 1735 (C=O), 1248 (SO_2), 1148 (SO_2); δ_H (400

MHz; $CDCl_3$) 1.13 (3 H, s, CH_3), 1.21 (3 H, s, CH_3), 1.40-1.50 (1 H, m, C*H*H), 1.60-1.75 (3 H, m, C^9H_2, C*H*H), 2.01 (1 H, d, *J* 18.5, C^3HH), 2.09-2.35 (6 H, m, C^4H, $C^{10}H_2$, $C^{12}H_2$, C*H*H), 2.57-2.68 (2 H, m, C^3HH, C*H*H), 3.16 (1 H, br.s, C^8H), 3.71-3.91 (3 H, m, S^+CHHCH_2Br), 3.98 (1 H, ddd, *J* 14.5, 8.5, 4.5, S^+CHHCH_2Br), 4.49 (1 H, d, *J* 2.5, C^7H), 4.53 (1 H, d, *J* 5.0, $C^{11}H$); δ_c (100.5 MHz; $CDCl_3$) 19.4 (q), 21.9 (q), 24.4 (t), 26.2 (t), 26.7 (t), 26.8 (t), 33.3 (t), 41.9 (d), 42.9 (t), 44.1 (d), 45.1 (t), 47.2 (d), 50.0 (t), 59.7 (d), 60.3 (s), 120.6 (q, CF_3), 215.3 (s); *m/z* (ESI) 357 and 359 (M^+, 100%), 277 (M^+-Br, 15%); HRMS (ESI) cacld for $C_{17}H_{26}BrOS$ 357.0882, found 357.0889; Elemental analysis required %C 42.61, %H 5.16, found %C 42.57, %H 4.95.

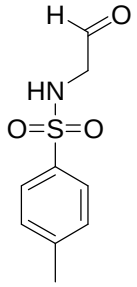
3-(7,7-Dimethyl-2-oxo-bicyclo[2.2.1]hept-1-yl)-2-vinyl-2-thionia-bicyclo[2.2.1]heptane; trifluoro-methanesulfonate 6



A suspension of 2-(2-Bromo-ethyl)-3-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-yl)-2-thionia-bicyclo[2.2.1]heptane; trifluoro-methanesulfonate **20** (1.87 g, 3.69 mmol) and silver (I) oxide (0.873 g, 3.76 mmol) in deionised water (25 mL) and DCM (5 mL) was stirred for 72 hours at room temperature under nitrogen, then filtered through Celite and concentrated under reduced pressure. The residue was then partitioned between water (15 mL) and DCM (15 mL) and the aqueous extracted with DCM (3 × 15 mL), the combined organics washed with brine and dried ($MgSO_4$). Diethyl ether (25 mL) was added to the residue and stirred vigorously for 10 minutes, then filtered and washed with excess diethyl ether (100 mL) to give the product as a white solid (2.16 g, 80%) after removal of solvent under vacuum. Mp 135-136 °C; $[\alpha]_D^{20}$ +28 (*c*. 1, $CHCl_3$); R_f (MeOH-DCM, 5:95) 0.20; n_{max} (film)/cm^{-1} 2931, 1737 (C=O), 1256 (SO_2), 1152 (SO_2), 1029; δ_H (400 MHz; $CDCl_3$) 1.12 (3 H, s, CH_3), 1.21 (3 H, s, CH_3), 1.39-1.47 (1 H, m, C*H*H), 1.58-1.76 (3 H, m, 3 × C*H*H), 2.00 (1 H, d, *J* 18.5, C^3HH), 2.05-2.34 (6 H, m, C^4H, 5 × C*H*H), 2.61 (1 H, ddd, *J* 18.5, 5.0, 2.5, C^3HH),

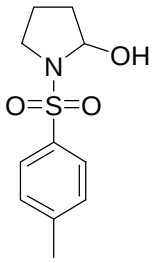
2.77(1 H, d, *J* 12.5, $C^{12}HH$), 3.25 (1 H, br. s, $C^{8}H$), 4.32 (1 H, d, *J* 5.5, $C^{11}H$), 4.47 (1 H, dd, *J* 3.5, 1.5, $C^{7}H$), 6.37 (2 H, m) 7.07 (1 H, dd, *J* 15.5, 9.5); δ_c (100.5 MHz; $CDCl_3$) 19.5 (q), 21.8 (q), 24.3 (t), 26.7 (t), 26.8 (t), 33.1 (t), 41.7 (t), 42.9 (d), 44.0 (t), 44.8 (d), 50.1 (s), 60.6 (d), 62.6 (s), 71.2 (d), 125.6 (d), 136.6 (t), 215.2 (s). *m/z* (ESI) 227 (M^+, 100%), 217 (M^+-60, 40%). HRMS (ESI) C17H25OS calcd 277.1621, found 277.1626. Elemental analysis required %C 50.69, %H 5.91, found %C 50.60, %H 5.82.

_N_1-(2-oxoethyl)-4-methyl-1-benzenesulfonamide, 21



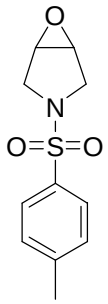
A solution of *N*-allyl-4-methyl-1-benzenesulfonamide[3] (1 g, 4.74 mmol) was dissolved in a mixture of anhydrous methanol (4.6 mL) and anhydrous DCM (46 mL) then treated with ozone at − 78 °C with stirring until the solution maintained a blue colouration. The solution was then degassed with nitrogen and treated with zinc (0.55 g, 8.41 mmol) and concentrated acetic acid (0.91 mL) then stirred for 3 hours at − 78 °C then allowed to warm to room temperature and stirred for a further 18 hours under nitrogen. The reaction mixture was then filtered through Celite and concentrated under reduced pressure to give the product as a white gummy solid (0.97 g, 96%) which was used without further purification.

1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinol,[4] 4



A solution of 1-(toluene-4-sulfonyl)-pyrrolidin-2-one[4] (4.78 g, 20.0 mmol) was dissolved in anhydrous DCM (100 mL) and cooled to - 78 °C under argon with stirring. The reaction mixture was then treated with neat DIBAL (4 mL, 22.0 mmol) drop-wise over 10 minutes then stirred for 1 hour at - 78 °C followed by 1 hour at room temperature. The reaction was then cooled to - 78 °C and quenched with MeOH (15 mL) and allowed to slowly warm to room temperature. The reaction mixture was poured onto an aqueous solution of Rochelles salts (100 mL) and extracted with DCM (3 × 50 mL). The combined organics were then washed with brine (1 × 50 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the pure desired product as a white waxy solid (4.69 g, 98%). Mp 59-61 °C; R_f (EtOAc-pet., 20:80) 0.15; δ_H (400 MHz; $CDCl_3$) 1.68-1.81 (2H, m), 1.87-1.95 (1H, m), 2.04-2.16 (1H, m), 2.43 (3H, s), 3.06 (1H, td, *J* 10.0, 6.5), 3.16 (1H, dd, *J* 3.0, 1.0), 3.56 (1H, ddd, *J* 10.0, 8.0, 2.5), 5.44 (1H, m), 7.32 (2H, d, *J* 8.5), 7.74 (2H, d, *J* 8.5), [lit.,[4] δ_H (300 MHz; $CDCl_3$) 1.63-1.79 (2 H, m), 1.80-1.92 (1H, m), 1.96-2.15 (1 H, m), 2.39 (3 H, s, CH_3-tosyl), 3.03 (1 H, ddd, *J* 9.5, 9.5, 6.5), 3.42 (1 H, s, -OH), 3.52 (1 H, ddd, *J* 9.5, 9.5, 2.5), 5.42 (1 H, m), 7.32 (2 H, d, *J* 8.3), 7.75 (2 H, d, *J* 8.3)]; δ_c (100.5 MHz; $CDCl_3$) 21.5 (q), 23.0 (t), 33.9 (t), 47.5 (t), 83.9 (d), 127.1 (d), 127.5 (d), 129.8 (s), 143.6 (s), [lit.,[4] δ_c (75 MHz; $CDCl_3$) 21.5, 23.1, 33.7, 47.8, 83.9, 127.4, 129.7, 135.5, 143.4].

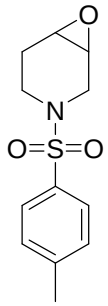
3-[(4-methylphenyl)sulfonyl]tetrahydro-1a*H*-oxireno[2,3-*c*]pyrrole, 2



*N*1-(2-oxoethyl)-4-methyl-1-benzenesulfonamide **21** (0.052 g, 0.244 mmol) was dissolved in THF (1.5 mL) and stirred at 0 °C under nitrogen then treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.074 g, 0.488 mmol) and stirred for 10 minutes. The reaction mixture was then treated with a solution of diphenylvinylsulfonium trifluoromethanesulfonate **1** (0.106 g, 0.293 mmol) in THF (2 mL) drop-wise over 15 minutes then stirred for 4 hours at room temperature. The reaction was quenched with water (15 mL) and extracted with DCM (3 × 15 mL), then the combined organics

were washed with brine (1 × 20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was then purified by flash chromatography, eluting with 20% EtOAc-pet. ether followed by 50% EtOAc-pet. ether to give the product as a white solid (0.047 g, 81%) after concentration under reduced pressure. Mp 147-148 °C (from EtOAc-hexane), [lit.,[6] mp 149-150, EtOAc-hexane]; R_f(EtOAc-pet. ether, 1:1) 0.30; n_{max} (film)/cm^{-1} 2932 (CH ep),1328 (SO_2), 1156 (SO_2); δ_H (400 MHz; $CDCl_3$) 2.42 (3 H, s, CH_3), 3.36 (2 H, d, *J* 12.5, 2 × NCH*H*), 3.58 (2 H, s, 2 × CH), 3.69 (2 H, d, *J* 12.5, 2 × NC*H*H), 7.31 (2 H, d, *J* 8.5, ArH), 7.67 (2 H, d, *J* 8.5, ArH), [lit.,[6] δ_H (400 MHz; $CDCl_3$) 2.42 (3 H, s), 3.36 (2 H, d, *J* 12.4), 3.58 (2 H, s), 3.70 (2 H, d, *J* 12.4), 7.31 (2 H, d, *J* 8.1), 7.66 (2 H, d, *J* 8.1)]; δ_c (100.5 MHz; $CDCl_3$) 21.5 (q), 48.7 (t), 55.1 (d), 127.5 (d), 129.6 (d), 134.9 (s), 143.5 (s). *m/z* (EI) 239 (11%, M^+), 155 (21%, $M^+ - C_4H_6NO$), 91 (100%, $PhCH_2$).

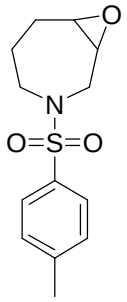
Racemic-3-[(4-methylphenyl)sulfonyl]perhydrooxireno[2,3-*c*]pyridine, 3



*N*1-(3-oxopropyl)-4-methyl-1-benzenesulfonamide[5] (0.1 g, 0.441 mmol) was dissolved in THF (2 mL) and stirred at 0 °C under nitrogen then treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.074 g, 0.487 mmol) and stirred for 10 minutes. The reaction mixture was then treated with a solution of diphenyl vinyl sulfonium trifluoromethanesulfonate **1** (0.191 g, 0.529 mmol) in THF (4 mL) drop-wise over 15 minutes then stirred for 4 hours at room temperature. The reaction was quenched with water (15 mL) and extracted with DCM (3 × 15 mL), then combined organics washed with brine (1 × 20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was then purified by flash chromatography, eluting with DCM followed by 1% MeOH-DCM to give the product as a white solid (0.069 g, 62%) after concentration under reduced pressure. Mp 141 °C (from EtOAc/Hex.) [lit.,[6] mp 140.5-142 °C]; R_f(DCM) 0.15; n_{max} (film)/cm^{-1} 1339 (SO_2), 1160 (SO_2); δ_H (400 MHz; $CDCl_3$) 2.10 (2 H, m, NCH_2CH_2CH), 2.43 (3 H, s, CH_3), 2.56 (1 H, m,

NC*H*HCH$_2$), 3.09 (1 H, d, *J* 13.5, NC*H*HCH(O)), 3.27 (2 H, m, NCH$_2$C*H*(O), NCH$_2$CH$_2$C*H*(O)), 3.36 (1 H, dtd, *J* 11.5, 4.5, 1.5, NCH*H*CH$_2$), 3.85, (1 H, ddd, *J* 13.5, 4.0, 1.5, NCH*H*CH(O)), 7.3 (2 H, d, *J* 8.5, ArH), 7.62 (2 H, d, *J* 8.5, ArH), [lit.,[6] δ_H (400 MHz; $CDCl_3$) 2.11 (2 H, m), 2.43 (3 H, s), 2.55 (1 H, m), 3.09 (1 H, d, *J* 13.7), 3.28 (2 H, m), 3.37 (1 H, m), 3.85 (1 H, ddd, *J* 13.7, 4.1, 1.1), 7.32 (2 H, d, *J* 8.3), 7.62 (2 H, d, *J* 8.3)]; δ_C (100.5 MHz; $CDCl_3$) 21.5 (q), 25.2 (t), 39.2 (t), 44.1 (t), 49.8 (d), 50.4 (d), 127.6 (d), 129.8 (d), 132.8 (s), 143.7 (s); *m*/*z* (CI) 254 (100%, MH^+).

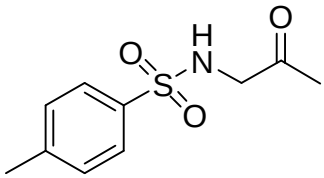
3-[(4-methylphenyl)sulfonyl]perhydrooxireno[2,3-*c*]azepine 5



1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinol **4** (0.1 g, 0.415 mmol) was dissolved in CH_2Cl_2 (1.62 mL) and stirred at 0 °C under nitrogen then treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.124 g, 0.829 mmol) and stirred for 10 minutes. The reaction mixture was then treated with a solution of diphenyl vinyl sulfonium trifluoromethanesulfonate **1** (0.180 g, 0.498 mmol) in CH_2Cl_2 (3.25 mL) drop-wise over 15 minutes then stirred for 4 hours at room temperature. The reaction was quenched with water (15 mL) and extracted with DCM (3 × 15 mL), then the combined organics were washed with brine (1 × 20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was then purified by flash chromatography, eluting with 20% EtOAc-pet. ether to give the product as a white solid (0.075 g, 62%) after concentration under reduced pressure. Mp 77-78 °C (from toluene-pentane) [lit.,[7] 77-78 °C, toluene-pentane]; R_f(EtOAc-pet. ether, 1:1) 0.40; n_{max} (film)/cm^{-1} 2922 (CH st), 1331 (SO_2), 1155 (SO_2); δ_H (400 MHz; $CDCl_3$) 1.67 (2 H, m, NCH$_2$C*H*$_2$), 1.84 (1 H, m,NCH$_2$CH$_2$C*H*H), 2.12 (1 H, m, NCH$_2$CH$_2$CH*H*), 2.42 (3 H, s, CH_3), 2.95 (1 H, ddd, *J* 13.0, 7.0, 3.5, NC*H*HCH$_2$), 3.11 (1 H, dt, *J* 6.0, 4.0, NCH$_2$CH(O)C*H*), 3.15 (1 H, dd, *J* 15.0, 6.0, NC*H*HCH(O)), 3.24 (1 H, dt, *J* 6.0, 4.0,

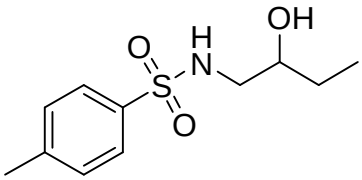
$NCH_2CH(O)$), 3.44 (1 H, dddd, *J* 13.0, 7.0, 5.0, 1.0, $NCHHCH_2$), 3.96 (1 H, ddd, *J* 15.0, 4.5, 1.0, $NCHHCH(O)$), 7.3 (2 H, d, *J* 8.5, ArH), 7.67 (2 H, d, *J* 8.5, ArH), [lit.,[7] δ_H (300 MHz; C_6D_6) 1.12-1.51 (4 H, m), 1.92 (3 H, s), 2.49 (1 H, td, *J* 12.0, 4.5), 2.58 (1 H, td, *J* 4.0, 5.0), 2.80 (1 H, dd, *J* 14.0, 6.0), 2.91 (1 H, td, *J* 6.0, 4.0), 3.18 (1 H, dtd, *J* 12.0, 4.0, 1.0) 3.65 (1 H, ddd, *J* 14.0, 4.0, 1.0), 6.80 and 7.63 (4 H, AA'BB', J_{AB} 8.0]; δ_c (100.5 MHz; $CDCl_3$) 21.5 (q), 24.0 (t), 27.7 (t), 48.2 (t), 50.8 (t), 54.3 (d), 55.0 (d), 127.1 (d), 129.7 (d), 136.6 (s), 143.3 (s).

4-Methyl-N-(2-oxo-propyl)-benzenesulfonamide,[8] 8a



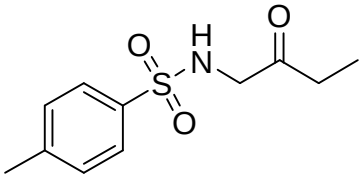
A solution of oxalyl chloride (1.14 mL, 13.1 mmol) in CH_2Cl_2 (6 mL) was cooled to - 78 °C under argon and treated with anhydrous dimethylsulfoxide (3.1 mL, 43.7 mmol) in CH_2Cl_2 (2 mL) drop-wise over 10 minutes. The solution was then stirred for 30 minutes and treated with a solution of *N*-(2-hydroxy-propyl)-4-methyl-benzenesulfonamide[9] (2.0 g, 8.73 mmol) in CH_2Cl_2 (8 mL) drop-wise over 10 minutes then stirred for a further 50 minutes at - 78 C°. The reaction mixture was then allowed to warm to 0 °C over 30 minutes then made acidic with saturated aqueous citric acid solution (100 mL) and extracted with ether-EtOAc (1:1, 100 mL). The organic layer was then washed sequentially with H_2O (2 × 100 mL), 5% aqueous sodium bicarbonate solution (1 × 100 mL), brine (1 × 100 mL) and finally dried ($MgSO_4$). The crude yellow oil was then purified by flash chromatography, eluting with 40% EtOAc/Pet. to give the desired ketone as a white solid (0.848 g, 43%). Mp 96-98 °C (from EtOAc/Hex.); δ_H (400 MHz; $CDCl_3$) 2.04 (3 H, s, $CH_3C=O$), 2.35 (3 H, s, CH_3Ar), 3.77 (2 H, d, *J* 5.0, $NHCH_2C=O$), 5.26 (1 H, br.t, *J* 5.0, NH), 7.25 (2 H, d, *J* 8.0, Ar*H*), 7.66 (2 H, d, *J* 8.0, Ar*H*). Elemental analysis required %C 54.75, %H 6.27, %N 5.80 found %C 54.68, %H 6.18, %N 5.90.

***N*-(2-Hydroxy-butyl)-4-methyl-benzenesulfonamide, 22**



Following a procedure by Ohno and co-workers[5] 1-amino-2-butanol (1.0 g, 11.20 mmol) was dissolved in $CHCl_3$ (2 mL) and treated with Et_3N (3.15 mL, 22.40 mmol) at 0 °C under argon with stirring. A solution of *p*-toluenesulfonyl chloride (2.35 g, 12.30 mmol) in $CHCl_3$ (4 mL) was then added and the reaction mixture was stirred for 18 hours at room temperature. The $CHCl_3$ was then removed under reduced pressure and the residue dissolved in CH_2Cl_2 (20 mL) and washed with 10% aqueous citric acid solution (2 × 20 mL), saturated aqueous sodium bicarbonate solution (2 × 20 mL), brine (1 × 20 mL) and dried (MgSO4). The product was isolated as a pure white solid (2.43 g, 89%), after concentration under reduced pressure. R_f(EtOAc-pet. ether, 1:1) 0.25; n_{max} (film)/cm^{-1} 1154 (SO_2), 1320 (SO_2), 2927 (NH), 2974 (NH), 3278 (OH); δ_H (400 MHz; $CDCl_3$) 0.82 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$), 1.34 (2 H, quin. *J* 7.5, CH$_3$C*H*$_2$-), 2.34 (3 H, s, C*H*$_3$Ar-), 2.61 (1 H, d, *J* 5.0, -OH), 2.70 (1 H, ddd, *J* 13.0, 8.0, 5.0, N-C*H*H-), 2.97 (1 H, ddd, *J* 13.0, 8.0, 3.0, N-CH*H*-), 3.54 (1 H, br. m, NCH$_2$C*H*(OH)-), 5.39 (1 H, br. t, *J* 8.0, N*H*), 7.21 (2 H, d, *J* 8.0, ArH), 7.69 (2 H, d, *J* 8.0, ArH); δ_C (100.5 MHz; $CDCl_3$) 9.8, 21.6, 27.6, 48.4, 71.9, 127.15, 129.8, 136.7, 143.6.

4-Methyl-*N*-(2-oxo-butyl)-benzenesulfonamide, 8b



A solution of *N*-(2-hydroxy-butyl)-4-methyl-benzenesulfonamide **22** (1.07 g, 4.40 mmol) was dissolved anhydrous dimethylsulfoxide (10 mL) and treated with Et_3N (2.16 mL, 15.40 mmol) and pyridine.SO_3 complex (2.45 g, 15.40 mmol) at room temperature under argon and stirred for 3 hours. The reaction mixture was then poured onto saturated aqueous sodium bicarbonate solution (100 mL) and EtOAc (100 mL) and the organics washed with saturated aqueous sodium bicarbonate solution (2 × 100 mL), 10% aqueous citric acid solution (2 × 100 mL), brine (1 × 100 mL) and dried ($MgSO_4$). The crude product of high purity (0.71 g, 67%) was

isolated after concentration under reduced pressure. The crude product was then re-crystallised from ether/hexane with cooling and evaporation of the ether to give the product as fine white crystals (0.43 g, 41%). Mp 90-92 °C (from EtOAc/Hex); R_f(EtOAc-pet. ether, 1:1) 0.40; n_{max} (film)/cm^{-1} 1161 (SO_2), 1323 (SO_2), 1716 (C=O), 3277 (NH); δ_H (400 MHz; $CDCl_3$) 1.01 (3 H, t, *J* 7.5, -CH_2CH_3), 2.34 (2 H, q, *J* 7.5, (CO)CH_2CH_3), 2.40 (3 H, s, CH_3Ar), 3.83 (2 H, d, *J* 4.5, NHCH_2(CO)), 5.31 (1 H, t, *J* 4.5, N*H*), 7.29 (2 H, d, *J* 8.0, Ar*H*), 7.72 (2 H, d, *J* 8.0, Ar*H*); δ_C (100.5 MHz; $CDCl_3$) 7.4, 21.50, 33.4, 51.0, 76.7, 77.0, 127.2, 129.8, 143.8, 205.0; *m/z* (CI) 242 (MH^+, 100%), 224 (M^+- OH 10%), 155 ($C_7H_7SO_2$, 28%), 86 (M^+- $C_7H_7SO_2$, 15%); HRMS (CI) cacld for $C_{11}H_{16}NO_3S$ [MH^+] 242.9851, found 242.0850.

General Procedures for the epoxy-annulation reaction of a-amino ketones, ß-amino aldehydes and ß-amino ketones.

Method A.

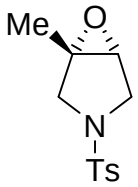
A solution of amino-ketone (0.132 mmol) in anhydrous CH_2Cl_2 (1 mL) and treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.264 mmol) at 0 °C under argon with stirring. The reaction mixture was then treated with a solution of diphenyl vinyl sulfonium salt **1** (0.158 mmol) in CH_2Cl_2 (0.5 mL) and stirred for 2-4 hours until complete consumption of starting material was detected by HPLC or TLC. The reaction mixture was then quenched with 10% aqueous citric acid solution (10 mL) and the aqueous was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organics washed with brine (1 × 10 mL) and dried ($MgSO_4$). The crude reaction mixture was then purified by flash chromatography, eluting with 20-30% EtOAc/Pet. Ether to give the desired product after concentration under reduced pressure.

Method B.

A solution of amino-ketone or –aldehyde in CH_2Cl_2 and cooled to - 20 °C by means of a ice/acetone/dry ice bath, under argon with stirring. The reaction mixture was then treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (mmol) followed by a solution of chiral vinyl sulfonium salt **6** drop-wise over 10 minutes to ensure the reaction temperature is maintained at - 20 °C. The reaction mixture was then placed in the freezer at - 20 °C for 2-5 days until complete consumption of starting material is

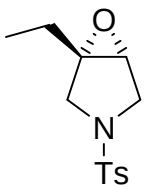
detected by HPLC or TLC, after which time the reaction was quenched with 10% aqueous citric acid solution (10 mL) and the aqueous was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organics washed with brine (1 × 10 mL) and dried ($MgSO_4$). The crude reaction mixture was then purified by flash chromatography, eluting with 20-30% EtOAc/Pet. Ether to give the desired product after concentration under reduced pressure. Enantiomeric excess was then determined by chiral HPLC.

1(S), 5(R)-1-Methyl-3-(toluene-4-sulfonyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane 9a



Mp 94-96 °C; $[\alpha]_D^{20}$ +16 (*c*. 1, CH_2Cl_2); R_f(MeOH-CH_2Cl_2, 1:99) 0.45; n_{max} (film)/cm^{-1} 1158 (SO_2), 1340 (SO_2), 2875 (CH), 2933 (CH); δ_H (400 MHz; $CDCl_3$); 1.37 (3 H, s, C*H*$_3$C(O)-), 2.35 (3 H, s, C*H*$_3$Ar), 3.19 (1 H, d, *J* 11.9, NC*H*H-), 3.27-3.35 (2 H, m, NC*H*H-, -C*H*(O)), 3.49 (1 H, d, *J* 11.9, NCH*H*-), 3.59 (1 H, d, *J* 12.2, NCH*H*-), 7.22 (2 H, d, *J* 8.0, Ar*H*), 7.60 (2 H, d, *J* 8.0, Ar*H*); δ_C (100.5 MHz; $CDCl_3$) 15.3, 21.6, 49.3, 51.8, 60.8, 63.1, 127.5, 129.7, 135.0, 143.6; Chiral HPLC (OD-H col., 1 mL/min, 23 °C, 4% IPA/Hex) major at 36.39 min., minor at 42.80 min., 97% e.e.; *m/z* (CI) 254 (MH^+, 100%), 236 (M^+- OH 10%), 155 ($C_7H_7SO_2$, 11%), 98 (M^+- $C_7H_7SO_2$, 6%); HRMS (CI) cacld for $C_{12}H_{16}NO_3S$ [MH^+] 254.0851, found 254.0849. Elemental analysis required %C 56.90, %H 5.97, %N 5.53 found %C 56.96, %H 5.83, %N 5.53.

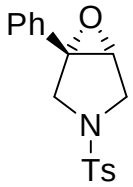
1(S), 5(R)-1-Ethyl-3-(toluene-4-sulfonyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane 9b



Mp 79-81 °C; $[\alpha]_D^{20}$ +24 (*c*. 1, CH_2Cl_2); R_f(EtOAc-pet., 3:7) 0.30; n_{max} (film)/cm^{-1} 1158 (SO_2), 1339 (SO_2), 2877 (CH), 2938 (CH), 2972 (CH); δ_H (400 MHz; $CDCl_3$) 0.84 (3 H, t, *J* 7.5, C*H*$_3$CH$_2$-), 1.63 (1 H, sextet, *J* 7.5, CH$_3$C*H*H-), 1.76 (1 H, sextet, *J* 7.5, CH$_3$CH*H*-), 2.36 (3 H, s, C*H*$_3$Ar), 3.21 (1 H, d, *J* 12.0, NC*H*H-), 3.29 (1H, dd, *J* 12.0, 1.5, NCH*H*-), 3.32 (1 H, br.s, C*H*(O)-), 3.50 (1 H, d, *J* 12.0, NC*H*H-), 3.58 (1 H,

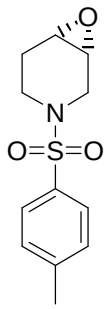
d, *J* 12.0, NCH*H*-), 7.22 (2 H, d, *J* 8.0, Ar*H*), 7.59 (2 H, d, *J* 8.0, Ar*H*); δ_C (100.5 MHz; $CDCl_3$) 9.0, 21.49, 22.1, 49.0, 50.5, 59.0, 67.1, 127.4, 129.5, 134.8, 143.4; Chiral HPLC (OD-H col., 1 mL/min, 23 °C, 3% IPA/Hex) major (shown) at 37.85 min., minor at 44.24 min., 99% e.e.; *m/z* (CI) 268 (MH^+, 100%), 250 (M^+- OH 33%), 155 ($C_7H_7SO_2$, 16%), 112 (M^+- $C_7H_7SO_2$, 10%); HRMS (CI) cacld for $C_{13}H_{18}NO_3S$ [MH^+] 268.1007, found 268.1005. Elemental analysis required %C 58.40, %H 6.41, %N 5.24 found %C 58.58, %H 6.27, %N 5.40.

1(S), 5(R)-1-Phenyl-3-(toluene-4-sulfonyl)-6-oxa-3-aza-bicyclo[3.1.0]hexane, 9c



Mp 77-80 °C; $[\alpha]_D^{20}$ +68 (*c*. 1, CH_2Cl_2); R_f(EtOAc-pet., 2:8) 0.25; n_{max} (film)/cm^{-1} 1158 (SO_2), 1340 (SO_2), 2875 (CH), 2928 (CH); δ_H (400 MHz; $CDCl_3$) 2.35 (3 H, s, C*H*$_3$Ar), 3.47 (1 H, dd, *J* 12.0, 1.0, NC*H*HCH(O)-), 3.61 (1 H, d, *J* 1.0, C*H*(O)-), 3.73 (1 H, d, *J* 12.0, NCH*H*CH(O)-), 3.80 (1 H, d, *J* 12.0, NC*H*HC(Ph)-), 3.84 (1 H, d, *J* 12.0, NCH*H*C(Ph)), 7.13-7.30 (7 H, m, Ar*H*), 7.63 (2 H, d, *J* 8.0, Ar*H*); δ_C (100.5 MHz; $CDCl_3$) 21.6, 49.4, 50.1, 63.2, 65.8, 122.6, 126.0, 127.0, 127.5, 128.7, 128.8, 129.2, 129.7, 131.0; Chiral HPLC (OD-H col., 1 mL/min, 23 °C, 5% IPA/Hex) major (shown) at 45.60 min., minor at 56.56 min., 92 % e.e.; *m/z* (CI) 316 (MH^+, 100%), 298 (M^+- OH, 55%), 160 (M^+- $C_7H_7SO_2$, 46%), 155 ($C_7H_7SO_2$, 8%); HRMS (CI) cacld for $C_{17}H_{18}NO_3S$ [MH^+] 316.1007, found 316.1004.

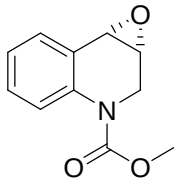
1(R), 6(S)-3-(Toluene-4-sulfonyl)-7-oxa-3-aza-bicyclo[4.1.0]heptane, 3



Mp 138-139 °C (from EtOAc/Hex.); $[\alpha]_D^{20}$ −16 (*c*. 1, $CHCl_3$); R_f (DCM) 0.15; n_{max} (film)/cm^{-1} 1339 (SO_2), 1160 (SO_2); δ_H (400 MHz; $CDCl_3$) 2.10 (2 H, m,

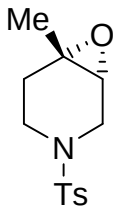
NCH_2CH_2CH), 2.43 (3 H, s, CH_3), 2.56 (1 H, m, $NCHHCH_2$), 3.09 (1 H, d, *J* 13.5, $NCHHCH(O)$), 3.27 (2 H, m, $NCH_2CH(O)$, $NCH_2CH_2CH(O)$, 3.36 (1 H, dtd, *J* 11.5, 4.5, 1.5, $NCHHCH_2$), 3.85, (1 H, ddd, *J* 13.5, 4.0, 1.5, $NCHHCH(O)$), 7.3 (2 H, d, *J* 8.5, ArH), 7.62 (2 H, d, *J* 8.5, ArH), [lit.,[6] δ_H (400 MHz; $CDCl_3$) 2.11 (2 H, m), 2.43 (3 H, s), 2.55 (1 H, m), 3.09 (1 H, d, *J* 13.7), 3.28 (2 H, m), 3.37 (1 H, m), 3.85 (1 H, ddd, *J* 13.7, 4.1, 1.1), 7.32 (2 H, d, *J* 8.3), 7.62 (2 H, d, *J* 8.3)]; δ_C (100.5 MHz; $CDCl_3$) 21.5 (q), 25.3 (t), 39.2 (t), 44.2 (t), 49.8 (d), 50.4 (d), 127.6 (d), 129.8 (d), 132.8 (s), 143.7 (s); *m*/*z* (CI) 254 (100%, MH^+). Chiral HPLC (OJ col., 1 mL/min, 23 °C, 15% IPA/Hex) major (shown) at 35.90 min., minor at 41.42 min., 98 % e.e.

3-(Toluene-4-sulfonyl)-1a,2,3,7b-tetrahydro-1-oxa-3-aza-cyclopropa-[a]-naphthalene, 11b



R_f (EtOAc-Pet., 30:70) 0.30; n_{max} (film)/cm^{-1} 1250, 1440, 1702, 2923, 2954; δ_H (400 MHz; $CDCl_3$) 3.10 (brd, 1H, J14.0, NCH*H*), 3.75 (s, 1H, OCH_3), 3.87 (d, 1H, J4.3, ArC*H*(O)), 3.90 (dd, 1H, J4.3, 2.0, ArCH(O)C*H*), 4.88 (brdd, 1H, J14.0, 2.0, NC*H*H), 7.15 (td, 1H, J7.5, 1.2, CCHC*H*), 7.32 (td, 1H, J7.5, 1.5, CCHC*H*), 7.39 (dd, 2H, J7.5, 1.5, 2 × CC*H*); δ_c (100.5 MHz; $CDCl_3$) 41.5, 51.0, 53.3, 58.7, 125.0, 125.8, 126.3, 128.8, 129.4, 137.1, 156.2; *m/z* (ESI) 228.06 (M^++Na, 100%), 206.1 (MH^+, 15%); HRMS $C_{11}H_{11}NO_3Na$ 228.0631, found 228.0636. Chiral HPLC (OJ col., 1 mL/min, 23 °C, 10% IPA/Hex) major (shown) at 35.53 min., minor at 84.59 min., 87% e.e.

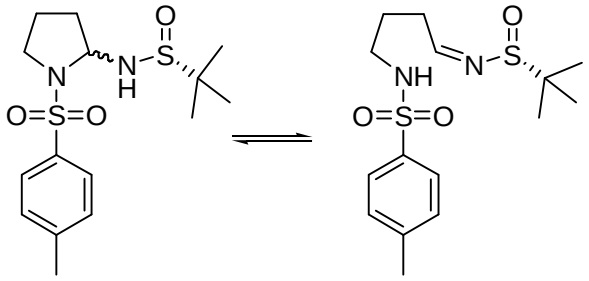
1(R), 6(S)-6-Methyl-3-(toluene-4-sulfonyl)-7-oxa-3-aza-bicyclo[4.1.0]heptane, 11c



Mp 95-97 °C (from EtOAc/Hex.); $[\alpha]_D^{20}$ +24 (*c*. 1, CH_2Cl_2); R_f(EtOAc-pet., 4:6) 0.30; n_{max} (film)/cm^{-1} 1160 (SO_2), 1338 (SO_2), 2866 (CH), 2922 (CH) ;δ_H (400 MHz; $CDCl_3$) 1.26 (3 H, s, $CH_3C(O)$-), 1.88 (1 H, dt, *J* 14.50, 3.0, NCH_2CHH-), 1.97 (1 H,

ddd, *J* 14.50, 11.0, 5.0, $NCH_2CH\mathit{H}$-), 2.34 (3 H, s, $C\mathit{H}_3Ar$), 2.40 (1 H, dd, *J* 11.50, 3.50, $NC\mathit{H}HCH_2$-), 2.89 (1 H, d, *J* 13.50, $NC\mathit{H}HCH(O)$-), 3.03 (1 H, d, *J* 4.5, $C\mathit{H}(O)$-), 3.37 (1 H, m, $NCH\mathit{H}CH_2$-), 3.82 (1 H, ddd, *J* 13.50, 4.5, 1.5, $NCH\mathit{H}CH(O)$-), 7.24 (2 H, d, *J* 8.0, Ar*H*), 7.56 (2 H, d, *J* 8.0, Ar*H*); δ_C (100.5 MHz; $CDCl_3$) 21.6, 22.4, 30.4, 40.1, 44.4, 56.6, 56.7, 127.6, 129.7, 133.7, 143.6. *m/z* (CI) 268 (MH^+, 100%), 250 (M^+- 18 45%), 155 ($C_7H_7SO_2$, 8%), 112 (M^+- $C_7H_7SO_2$, 21%). HRMS (CI) cacld for $C_{13}H_{18}NO_3S$ [MH^+] 268.1007, found 268.1006. Elemental analysis required %C 58.40, %H 6.41, %N 5.24 found %C 59.00, %H 6.74, %N 4.84. Chiral HPLC (OD col., 1 mL/min, 23 °C, 15% IPA/Hex) major (shown) at 9.37 min., minor at 10.74 min., 86% e.e.

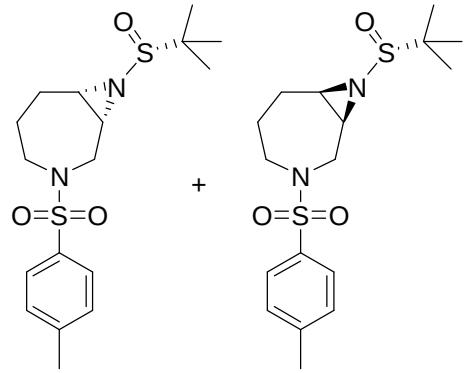
N2-1-[(4-methylphenyl)sulfonyl]tetrahydro-1H-2-pyrrolyl-2-methyl-2-propanesulfinamide, 14



A stirred solution of 1-[(4-methylphenyl)sulfonyl]-2-pyrrolidinol **4** (0.50 g, 2.08 mmol) in anhydrous DCM (35 mL) was treated with $Ti(OEt)_4$ (~20% solution in ethanol, 4.77 mL, 4.15 mmol) under argon at room temperature. The solution was then treated with (±)-2-methyl-2-propanesulfinamide (0.28 g, 2.280 mmol) in one portion and the reaction mixture was then heated at reflux for 7 hours under argon then allowed to cool to room temperature before quenching with an equal volume of brine (~40 ml). The resulting slurry was then filtered through Celite, washing with an excess of DCM (300 mL) and the filtrate partitioned between brine and DCM. The aqueous was extracted with DCM (3 × 75 mL) and the combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was then purified by flash chromatography using triethylamine deactivated silica, eluting with 50% EtOAc/pet.ether followed by 100% EtOAc to give the product as a clear gum (0.68 g, 95%) after concentration under reduced pressure. R_f (EtOAc-pet., 50:50) 1.1/0.15/0.30; ν_{max} (film)/cm^{-1} 1033 (S=O), 1091 (S=O), 1155 (SO_2), 1335 (SO_2),

1597 (HC=N), 2870 (NH) 2925 (NH), 2957 (NH); Open form; 1.15 (3H , s) 1.81 (2H, dq, *J* 14.2, 7.1, NCH_2CH_2), 2.42 (3H, s, CH_3), 2.53 (2H, td, *J* 7.1, 4.0, CH_2C=N), 3.00 (2H, m, NCH_2), 4.74 (1H, t, *J* 6.3, N*H*), 7.29 (2H, d, *J* 8.0, ArH) 7.72 (2H, d, *J* 8.0, ArH), 8.01(1H, t, *J* 4.0); Two Diastereomers; 1.22 (3H, s, CH_3), 1.23 (3H, s, CH_3), 1.70-2.20 (4H, m, 2 × NCH_2CH_2), 2.41 (6H, s, 2 × CH_3), 3.11 (2H, m, 2× NCH*H*), 3.42 (1H, ddd, *J* 11.3, 6.2, 2.5, NC*H*H), 3.59 (1H, ddd, *J* 10.3, 7.5, 3.1, NC*H*H), 3.89 (1H, d, *J* 6.7, N*H*), 4.16 (1H, d, *J* 1.7, N*H*), 5.05 (dt, 1H, *J* 6.3, 2.4), 5.18 (td, 1H, *J* 6.8, 2.6, TsNC*H*NH), 7.27-7.33 (4H, d, J8.0, ArH), 7.70-7.80 (4H, d, *J* 8.0, ArH); δ_c (100.5 MHz; $CDCl_3$) 14.2, 21.0, 21.6, 21.6, 22.4, 22.5, 22.6, 23.2, 23.5, 25.28, 32.2, 33.1, 34.0, 42.6, 48.1, 48.6, 55.9, 56.3, 56.7, 60.4, 70.6, 72.8, 127.1, 127.5, 127.6, 129.7, 129.8, 129.9, 137.2, 143.3, 143.8, 144.0, 168.4; m/z (ESI) 711.23 ($2M^+$ + Na, 100%), 367.11 (M^+ + Na, 25%), 345.13 (MH^+, 23%); HRMS $C_{15}H_{24}N_2O_3S_2Na$ 367.1121, found 367.1115.

1-(tert-butylsulfinyl)-3-[(4-methylphenyl)sulfonyl]perhydroazireno[2,3-c]-azepine, 15

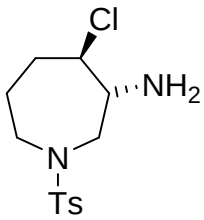


Major, **15a** Minor, **15b**

A stirred solution of *N*2-1-[(4-methylphenyl)sulfonyl]tetrahydro-1H-2-pyrrolyl-2-methyl-2-propanesulfinamide **14** (1.49 g, 4.34 mmol) in DMF (240 mL) was cooled to 0°C under argon and treated with sodium hydride (60% in mineral oil, 0.21 g, 5.21 mmol) in one portion and stirred for 5 minutes. The reaction mixture was then treated with a solution of diphenylvinyl sulfonium salt **1** (1.57 g, 4.34 mmol) in DMF (60 mL) added drop wise over 20 minutes. The reaction mixture was stirred for 4 hours at 0°C, then quenched with saturated sodium bicarbonate solution (100 mL) and water

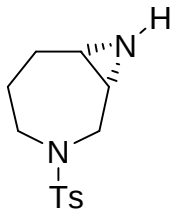
(100 mL) and stirred for a further 18 hours under argon. The reaction mixture was diluted with diethyl ether (500 mL) and the aqueous layer separated. The organic layer was then washed with water (5 × 200 mL) and brine (1 × 100 mL) then dried ($MgSO_4$). The initial aqueous extraction was then re-extracted with diethyl ether (500 mL) which was in turn re-extracted with water (5 × 200 mL) and brine (1 × 100 mL) then dried ($MgSO_4$). The two organic fractions were then combined and purified by flash chromatography, eluting with 80% Et_2O/pet.ether to give the *major aziridine diastereomer* as a clear oil (0.83 g, 51%) and the *minor aziridine* diastereomer as a white solid (0.28 g, 17%) after concentration under reduced pressure. The minor diastereomer was recrystalised (EtOAc/Hexane) and the absolute stereochemistry confirmed by X-ray crystallography. Major diastereomer **15a***;* $[\alpha]_D^{20}$ - 116 (*c.* 1, CH_2Cl_2); R_f (EtOAc-pet., 50:50) 0.30; ν_{max} (film)/cm^{-1} 1074 (S=O), 1156 (SO_2), 1332 (SO_2); δ_H (400 MHz; $CDCl_3$) 1.20 (9 H, s, CC*H*$_3$), 1.75 (3 H, m, NCH$_2$C*H*$_2$C*H*H-), 2.06 (1 H, m, NCH$_2$CH$_2$CH*H*-), 2.39 (3 H, s, ArC*H*$_3$), 2.47 (1 H, td, *J* 7.0, 3.9, NCH$_2$C*H*(N)C), 2.83 (1 H, dt, *J* 7.0, 4.2, NCH$_2$CH(N)C*H*-), 3.06 (1 H, ddd, *J* 12.0, 7.2, 2.9, NCH*H*CH$_2$-), 3.22 (1 H, ddd, *J* 12.0, 6.8, 2.8, NC*H*HCH$_2$-), 3.30 (1 H, dd, *J* 14.9, 7.0, NCH*H*CH(N)C), 3.79 (1 H, dd, *J* 14.9, 3.9, NC*H*HCH(N)C), 7.26 (2 H, d, *J* 8.2, ArH), 7.64 (2 H, d, *J* 8.2, ArH); δ_c (100.5 MHz; $CDCl_3$) 21.9, 22.9, 26.9, 27.6, 33.2, 36.8, 49.2, 51.8, 56.7, 127.3, 130.1, 137.4, 143.6; m/z (ESI)763.23 ($2M^+$ + Na, 90%), 393.13 (M^+ + Na, 100%), 371.15 (MH^+, 65%); HRMS $C_{17}H_{26}N_2O_3S_2Na$ 393.1277, found 393.1267. Minor diastereomer **15b**; Mp 127-129 °C (from EtOAc/Hex.); $[\alpha]_D^{20}$ - 34 (*c.* 0.35, CH_2Cl_2); R_f(EtOAc-pet., 50:50) 0.32; ν_{max} (film)/cm^{-1} 1074 (S=O), 1156 (SO_2), 1332 (SO_2); δ_H (400 MHz; $CDCl_3$) 1.25 (9H, s, CC*H*$_3$), 1.78 (2H, m, NCH$_2$C*H*$_2$), 1.94 (2H, m, NCH$_2$CH$_2$C*H*$_2$), 2.35 (1H, ddd, *J* 7.5, 5.9, 4.1, NCH$_2$CH(N)C*H*), 2.40 (3H, s, ArC*H*$_3$), 2.95 (2 H, m, NCH$_2$C*H*(N), NCH*H*CH$_2$), 3.23 (1H, ddd, *J* 13.7, 7.9, 2.5, NC*H*HCH$_2$), 3.53 (1H, dd, *J* 14.7, 6.2, NCH*H*CH(N)), 3.59 (1H, dd, *J* 14.7, 3.5, NC*H*HCH(N)), 7.28 (2H, d, *J* 8.2, ArH), 7.64 (2H, d, *J* 8.2, ArH); δ_c (100.5 MHz; $CDCl_3$) 21.45, 22.49, 25.69, 27.65, 32.92, 36.13, 48.08, 51.40, 56.50, 126.95, 129.73, 144.00, 149.01. *m/z* (CI) 371 (MH^+, 20%), 315 (MH^+- ^{t}Bu, 100%); HRMS (CI) cacld for $C_{17}H_{27}N_2O_3S_2$ [MH^+] 371.1463, found 371.1463.

4-chloro-1-[(4-methylphenyl)sulfonyl]-3-azepanamine, 16



A solution of 1-(tert-butylsulfinyl)-3-[(4-methylphenyl)sulfonyl]perhydroazireno[2,3-c]azepine **15** (80.0 mg, 0.216 mmol) in dioxane (4 mL) was treated with ethereal HCl (2M solution in diethyl ether, 0.324 mL, 0.648 mmol) drop wise under argon and stirred for 20 minutes. The reaction mixture was then diluted with aqueous HCl (5 M, 4 mL) solution and washed with diethyl ether (3 × 5 mL). The acidic aqueous layer was then basified with 32% aqueous NaOH (4 mL) solution and extracted with diethyl ether (3 × 10 mL). This organic layer was then dried ($MgSO_4$) to give the desired *product* (50.0 mg, 77%) after concentration under reduced pressure. Mp 119-122 °C (from EtOAc/Hex.); R_f (EtOAc) 0.15; ν_{max} (film)/cm^{-1} 1154 (SO_2), 1331 (SO_2), 2863 (NH_2), 2924 (NH_2); δ_H (400 MHz; $CDCl_3$) 1.69 (brm, 3H, N*H*$_2$, NCH$_2$C*H*H), 2.01 (m, 2H, NCH$_2$CH*H*, CClC*H*$_2$), 2.22 (tdd, 1H, *J* 2.2Hz, *J* 9.2, 14.6), 2.43 (s, 3H), 3.16 (m, 3H, C*H*NH$_2$), 3.29 (ddd, 1H, *J* 5.5, 6.6, 12.1), 3.38 (dd, 1H, *J* 12.2, 1.74), 3.84 (m, 1H, C*H*Cl), 7.31 (d, 2H, *J* 8.0), 7.67 (d, 2H, *J* 8.0); δ_c (100.5 MHz; $CDCl_3$) 21.5, 23.5, 31.2, 47.5, 49.1, 58.4, 91.4, 127.1, 129.8, 135.5, 143.6; *m/z* (ESI) 303.1 (MH^+ 100%), 305.1 (MH^+, 33%), 286.1 (MH^+-NH_2, 20%), 288.1 (MH^+-NH_2, 6.6%); HRMS $C_{13}H_{19}ClN_2O_2SH$ 303.0929. found 303.0928.

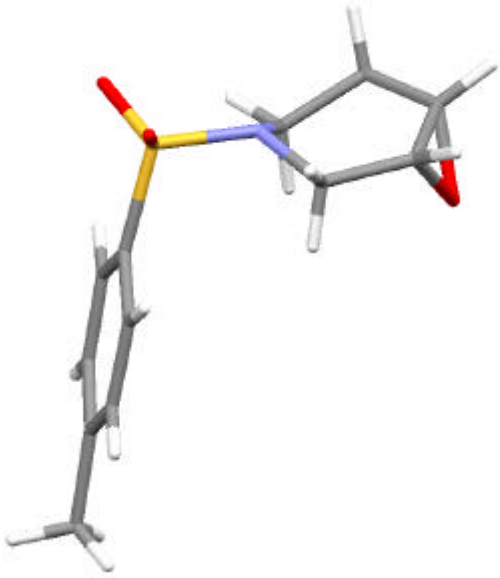
3-[(4-methylphenyl)sulfonyl]perhydroazireno[2,3-*c*]azepine,[7] 17



A solution of 1-(tert-butylsulfinyl)-3-[(4-methylphenyl)sulfonyl] perhydroazireno-[2,3-c]azepine **16** (0.108 g, 0.292 mmol) in dioxane (5 mL) was treated with ethereal HCl (2M solution in diethyl ether, 0.438 mL, 0.875 mmol) drop wise under argon and stirred for 20 minutes. The reaction mixture was the treated with saturated aqueous ammonia solution (5 mL) and stirred for a further 36 hours at room temperature under argon. The reaction mixture was then saturated with solid sodium chloride with stirring then quenched with brine and extracted with DCM (3 × 10 mL). The

combined organics were concentrated under reduced pressure and purified by flash chromatography, eluting with 3% MeOH/Et_2O to give the product as a white crystalline solid (quant) after concentration under reduced pressure. Mp 155-157 °C (from EtOAc/Hex.) [lit.,[7] Mp 154-155 °C]; $[\alpha]_D^{20}$ - 5 (*c*. 0.8, CH_2Cl_2); R_f (MeOH-Et_2O., 3:97) 0.15; δ_H (400 MHz; $CDCl_3$) 0.80-1.00 (1 H, ,br.s NH), 1.23-1.36 (1 H, m, NCH_2CH_2CH*H*-), 1.64-1.85 (2 H, m, NCH_2C*H*$_2$-), 2.15-2.30 (2 H, m, $NCH_2CH(NH)C$*H*- + NCH_2CH_2C*H*H-), 2.41-2.48 (2 H, br.m, NCH_2C*H*(NH) + NCH*H*CH(NH)), 2.42 (3 H, s, $ArCH_3$), 2.53-2.68 (1 H, br.m, NCH*H*CH_2-), 3.73 (1 H, br.m, NC*H*HCH_2-), 4.15 (1 H, br.m, NC*H*HCH(NH)), 7.29 (2 H, d, *J* 8.0, Ar*H*), 7.66 (2 H, d, *J* 8.0, Ar*H*); [lit.[7] δ_H (400 MHz; $CDCl_3$) 1.10 (1 H, br., N*H*) 1.30-1.40 (1 H, m), 1.60-1.85 (2 H, m), 2.15-2.30 (2 H, m), 2.41 (3 H, s), 2.45 (1 H, m), 2.50-2.64 (2 H, m), 3.73 (1 H, br.m), 4.15 (1 H, br.m) 7.28 and 7.65 (4 H, AA'BB', *J* 8.5)] δ_c (100.5 MHz; $CDCl_3$) 21.4, 27.0, 29.4, 33.0, 33.5, 51.5, 52.2, 126.9, 129.6, 136.4, 143.1; [lit. (75 MHz; $CDCl_3$) 21.5, 27.0, 29.5, 33.0, 33.6, 51.6, 52.3, 127.0, 129.7, 136.4, 143.2]. *m/z* (CI) 267 (MH^+, 85%), 250 (M^+- NH_2, 100%), 155 ($C_7H_7SO_2$, 17%), 111 (M^+- $C_7H_7SO_2$, 51%); HRMS (CI) cacld for $C_{13}H_{19}N_2O_2S$ [MH^+] 267.1167, found 267.1156.

Structure Report for **3** (from method B)

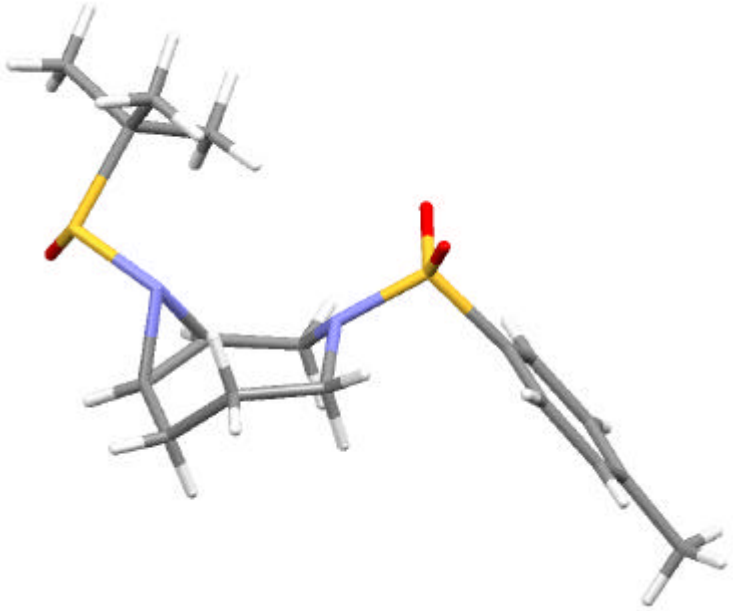


A single crystal of **3** (from method B) was coated in perfluoropolyether oil and mounted on a glass fibre. X-ray measurements were made using a Bruker SMART CCD area-detector diffractometer with Mo -K_α radiation (λ = 0.71073:0 Å).[1] Intensities were integrated[2] from several series of exposures, each exposure covering 0.3° in ω, and the total data set being almost a sphere. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.[3] The structure was solved by direct methods and refined by least squares on weighted F^2 values for all reflections (see Table 1).[4] All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. The positions of the methyl hydrogen atoms were assigned by a rotating group refinement with fixed idealised C-H or O-H distances. All other hydrogen atoms were constrained to ideal geometries. All hydrogen atoms were assigned isotropic displacement parameters equal to 1.5 times (methyl hydrogen atoms) or 1.2 times (all other hydrogen atoms) that of their parent atom. Refinement proceeded smoothly to give the residuals shown in Table 1. Complex neutral-atom scattering factors were used.[5]

Table 1. Crystal data and structure refinement for **3**.

Identification code	cmg1a	
Empirical formula	$C_{12}H_{15}NO_3S$	
Formula weight	253.31	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 6.064(5) Å	a = 90°
	b = 12.196(9) Å	b = 90°
	c = 16.417(12) Å	g = 90°
Volume	1214.0(16) Å^3	
Z	4	
Density (calculated)	1.386 Mg/m^3	
Absorption coefficient	0.262 mm^{-1}	
F(000)	536	
Crystal size	0.10 x 0.10 x 0.05 mm	
θ range for data collection	2.48 to 27.58°	
Index ranges	-7<=h<=7, -15<=k<=15, -16<=l<=21	
Reflections collected	7081	
Independent reflections	2681 [R_{int} = 0.1728]	
Completeness to q = 27.58°	95.2 %	
Absorption correction	multi-scan	
Max. and min. transmission	0.990 and 0.772	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2681 / 0 / 155	
Goodness-of-fit on F^2	S = 0.998	
R indices [for 1332 reflections with $I>2s(I)$]	R_1 = 0.0833, wR_2 = 0.1384	
R indices (for all 2681 data)	R_1 = 0.1780, wR_2 = 0.1705	
Weighting scheme	$w^{-1} = s^2(F_o^2) + (aP)^2$,	
	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$	
	a = 0.0556	
Absolute structure (Flack) parameter	0.17(19)	
Largest diff. peak and hole	0.449 and -0.478 eÅ^{-3}	

Structure Report for **15** (Minor Diastereomer)



A single crystal of **15b** was coated in perfluoropolyether oil and mounted on a glass fibre. X-ray measurements were made using a Bruker SMART Apex CCD area-detector diffractometer with Mo-K_a radiation (l = 0.71073 Å).[1] Intensities were integrated[2] from several series of exposures, each exposure covering 0.3° in *w*, and the total data set being almost a hemisphere. Absorption corrections were applied, based on multiple and symmetry-equivalent measurements.[3] The structure was solved by direct methods and refined by least squares on weighted F^2 values for all reflections (see Table 1).[4] All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. The positions of the methyl hydrogen atoms were assigned by a rotating group refinement with fixed, idealised C-H distances. All other hydrogen atoms were constrained to ideal geometries. All hydrogen atoms were assigned isotropic displacement parameters equal to 1.5 times (methyl hydrogen atoms) or 1.2 times (all other hydrogen atoms) that of their parent atom. Refinement proceeded smoothly to give the residuals shown in Table 1. Complex neutral-atom scattering factors were used.[5]

References

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2. *SAINT integration software version 7.06A*, Bruker AXS Inc., Madison,WI, 1997-2003.
3. G. M. Sheldrick. *SADABS version 2.05*, University of Göttingen: Germany, 2003.
4. *SHELXTL program system version 6.14*, Bruker-AXS Inc., Madison, WI, 2000-2003.
5. *International Tables for Crystallography*, Kluwer, Dordrecht, 1992, vol. C.

Table 1. Crystal data and structure refinement for **17**.

Identification code	mattusad	
Empirical formula	$C_{17}H_{26}N_2O_3S_2$	
Formula weight	370.52	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 6.1051(12) Å	a = 90°
	b = 13.389(3) Å	b = 90°
	c = 22.618(5) Å	g = 90°
Volume	1848.8(7) Å^3	
Z	4	
Density (calculated)	1.331 Mg/m^3	
Absorption coefficient	0.306 mm^{-1}	
F(000)	792	
Crystal size	0.16 x 0.10 x 0.04 mm	
q range for data collection	1.80 to 27.48°	
Index ranges	-7<=h<=7, -17<=k<=13, -28<=l<=29	
Reflections collected	13094	
Independent reflections	4231 [R_{int} = 0.0849]	
Completeness to q = 27.48°	100.0 %	
Absorption correction	multi-scan	
Max. and min. transmission	0.990000 and 0.592342	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4231 / 0 / 222	
Goodness-of-fit on F^2	S = 1.086	
R indices [for 3451reflections with I>2s(I)]	R_1 = 0.0652, wR_2 = 0.1341	
R indices (for all 4231 data)	wR_2 = 0.1502	
Weighting scheme	w^{-1} = $s^2(F_o^2)$ + (aP)^2,	
	where P = [max(F_o^2, 0) + 2F_c^2]/3	
	a = 0.0687	
Absolute structure (Flack) parameter	-0.11(12)	
Largest diff. peak and hole	0.485 and -0.362 eÅ^{-3}	

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