Supporting Information

The Double Reduction of Cyclic Aromatic Sulfonamides: A Novel Method for the Synthesis of 2- and 3-Aryl Substituted Cyclic Amines

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General

Starting materials were purchased from commercial sources and were used without further purification. Anhydrous THF was distilled under nitrogen from the sodium-benzophenone ketyl radical, DCM was distilled from CaH₂. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were recorded using a Bruker AMX400 spectrometer. Infrared spectroscopy was performed on a Perkin-Elmer Paragon 1000 FTIR spectrometer. Optical rotation measurements were recorded using an Optical Activity, Polaar 2001 polarimeter at 589 nm and are quoted in units of 10⁻¹degcm²g⁻¹. Flash column chromatography, under moderate pressure was performed using silica gel – ICN 32-63, 60Å. Melting points were recorded on an Electrothermal IA9000 digital melting point apparatus and were uncorrected.

N,N-Diallyl-2-bromobenzenesulfonamide 4: At 0°C a mixture of 2-bromobenzenesulfonyl chloride **3** (4.86 g, 19.0 mmol, 1 eq.) and triethylamine (4.0 cm³, 28.7 mmol, 1.5 eq.) in DCM (75 cm³) was treated with diallylamine (1.5 cm³, 30.9 mmol, 1.1 eq.) in a dropwise fashion. Stirring was continued for 3 h during which time the reaction was warmed to room temperature. The solvent was removed under reduced pressure before Et₂O (100 cm³) and H₂O (100 cm³) were added. The resultant aqueous layer was further extracted with Et₂O (2 x 100 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* afforded the crude product, which was purified by flash column chromatography (Hex-EtOAc; 5:1) affording the product **4** (4.13 g, 85%) as a colourless liquid. *R*_f = 0.4 (Hex-EtOAc; 5:1); ν_{max} (neat/cm⁻¹) 3084, 2984, 2921, 2864, 1643, 1575, 1447, 1340, 1160; *m/z* (EI) 317 (M⁺, ⁸¹Br, 5%), 315 (M⁺, ⁷⁹Br, 5%), 221 (C₆H₄O₂S⁸¹Br⁺, 30%), 219 (C₆H₄O₂S⁷⁹Br⁺, 30%), 157 (C₆H₄Br⁺, 70%), 155 (C₆H₄Br⁺, 70%), 96 (100%); found 314.99254, C₁₂H₁₄NO₂SBr requires 314.99286 (-1.0 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 3.93 (d, *J*=6.5 Hz, 4H), 5.14-5.19 (m, 4H), 5.62-5.71 (m, 2H), 7.38 (dt, *J*=2.0, 7.75 Hz, 1H), 7.43 (dt, *J*=1.5, 7.75 Hz, 1H), 7.73 (dd, *J*=1.5, 7.75 Hz, 1H), 8.17 (dd, *J*=2.0, 7.75 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 49.4, 119.5, 120.8, 127.9, 132.7, 133.0, 133.9, 136.0, 140.0.

1-(2-Bromobenzenesulfonyl)-2,5-dihydro-1H-pyrrole 5: Under N₂, a degassed solution of the diallylsulfonamide **4** (1.08 g, 3.42 mmol, 1 eq.) in DCM (75 cm³) was treated with the Grubbs catalyst (28 mg, 0.034 mmol, 1 mol%). Stirring was continued at room temperature for 15 h before TLC analysis indicated consumption of the starting material. Silica (*ca.* 5 g) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 5:1) gave the dihydropyrrole **5** (1.02 g, 95%) as a colourless solid. *m.p.* 87-89°C; *R*_f = 0.3 (Hex-EtOAc; 5:1); ν_{max} (CH₂Cl₂/cm⁻¹) 3056, 2986, 2915, 2869, 1575, 1447, 1433,

1422, 1339, 1265, 1169; m/z (EI) 289 (M^+ , ^{81}Br , 20%), 287 (M^+ , ^{79}Br , 20%), 157 ($\text{C}_6\text{H}_4^{81}\text{Br}^+$, 60%), 155 ($\text{C}_6\text{H}_4^{79}\text{Br}^+$, 60%), 68 ($\text{C}_4\text{H}_6\text{N}^+$, 100%); found 286.96115 $\text{C}_{10}\text{H}_{10}\text{NO}_2\text{SBr}$ requires 286.96155 (-1.4 ppm); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ = 4.28 (s, 4H), 5.77 (s, 2H), 7.37 (dt, J =1.5, 7.5 Hz, 1H), 7.44 (dt, J =1.5, 7.5 Hz, 1H), 7.75 (dd, J =1.5, 7.5 Hz, 1H), 8.06 (dd, J =1.75, 7.5 Hz, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ = 54.9, 120.4, 125.3, 127.5, 131.6, 133.4, 135.7, 138.7; found C, 41.67; H, 3.46; N, 4.90%; $\text{C}_{10}\text{H}_{10}\text{NO}_2\text{SBr}$ requires C, 41.80; H, 3.45; N, 4.87%.

8-Thia-9-azatricyclo[7.2.1.0^{2,7}]dodeca-2(7),3,5,10-tetraene-8,8-dioxide 6:¹ Under N_2 , a mixture of the dihydropyrrole **5** (809 mg, 2.81 mmol, 1 eq.), $\text{Pd}(\text{OAc})_2$ (62 mg, 0.276 mmol, 10 mol%), PPh_3 (146 mg, 0.557 mmol, 20 mol%) and K_2CO_3 (773 mg, 5.597 mmol, 2 eq.) in DMF (30 cm^3) was heated to 110°C for 15 h. On cooling Et_2O (50 cm^3) and H_2O (50 cm^3) were added and the resultant aqueous layer was further extracted with Et_2O (2 x 50 cm^3) and the combined organic extracts were dried over MgSO_4 . Filtration followed by solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (Hex-EtOAc; 5:1) affording the Heck product **6** (701 mg, 87%) as a colourless solid. m.p. 138-140°C; R_f = 0.2 (Hex-EtOAc; 5:1); ν_{max} ($\text{CH}_2\text{Cl}_2/\text{cm}^{-1}$) 3056, 2989, 1593, 1470, 1447, 1339, 1266, 1169; m/z (EI) 207 M^+ , 10%), 143 (50%), 115 (100%); found 207.03543, $\text{C}_{10}\text{H}_9\text{NO}_2\text{S}$ requires 207.03540 (+1.0 ppm); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ = 3.30 (t, J =4.0 Hz, 1H), 4.05 (dd, J =4.0, 12.0 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 6.45 (d, J =4.0 Hz, 1H), 6.60 (t, J =4.0, 7.0 Hz, 1H), 7.13 (dd, J =1.5, 7.5 Hz, 1H), 7.38 (dt, J =1.5, 7.5 Hz, 1H), 7.46 (dt, J =1.5, 7.5 Hz, 1H), 7.71 (dd, J =1.5, 7.5 Hz, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) δ = 42.4, 63.2, 125.5, 127.5, 130.0, 131.7, 134.3, 134.8, 135.3, 139.8.

8-Thia-9-azatricyclo[7.2.1.0^{2,7}]dodeca-2(7),3,5-triene-8,8-dioxide 7: 10% w/w Pd/C (90 mg, 0.085 mmol, 10 mol%) was added to a solution of the alkene **6** (240 mg, 0.833 mmol, 1 eq.) in EtOH (40 cm^3). The mixture was degassed before stirring under a hydrogen atmosphere at room temperature for 15 h. Filtration through a celite[®] bed, solvent removal *in vacuo* and purification by flash column chromatography (Hex-EtOAc; 1:1) gave **7** (222 mg, 93%) as a colourless crystalline solid. m.p. 120-122°C (DCM). R_f = 0.4 (Hex:EtOAc; 1:1); ν_{max} ($\text{CH}_2\text{Cl}_2/\text{cm}^{-1}$) 3056, 2964, 2896, 1592, 1447, 1333, 1271, 1170; m/z (EI) 209 (M^+ , 50%), 117 (100%); found 209.05129 $\text{C}_{10}\text{H}_{11}\text{NO}_2\text{S}$ requires 209.05106 (+1.1 ppm); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ = 1.85-1.93 (m, 1H), 2.21-2.33 (m, 1H), 3.23 (dd, J =3.0, 13.0 Hz, 1H), 3.28 (dd, J =3.0, 6.5 Hz, 1H), 3.47-3.55 (m, 1H), 3.85-3.94 (m, 1H), 4.27 (dt, J =1.8, 13.0

(1) For the synthesis of cyclic sulfonamides following this route see: Grigg, R.; Sridharan, V.; York, M. *Tetrahedron Lett.* **1998**, 39, 4139; Grigg, R.; Santhakumar, V.; Sridharan, V. Stevenson, P.; Teasdale, A.; Thornton-Pett, M.; Worakun, T. *Tetrahedron* **1991**, 47, 9703.

Hz, 1H), 7.21 (dd, $J=1.5, 7.5$ Hz, 1H), 7.39 (dt, $J=1.5, 7.5$ Hz, 1H), 7.45 (dt, $J=1.5, 7.5$ Hz, 1H) 7.79 (dd, $J=1.5, 7.5$ Hz, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 33.2, 39.6, 46.7, 53.0, 126.3, 127.3, 128.6, 132.5, 135.7, 140.8; found C, 56.90; H, 5.33; N, 6.63%; $\text{C}_{10}\text{H}_{11}\text{NO}_2\text{S}$ requires C, 57.42; H, 5.26; N, 6.70%.

3-phenylpyrrolidine 8:² Under N_2 , at -78°C liquid NH_3 (250 cm^3) was treated with lithium shot (318 mg, 45.4 mmol, 19.5 eq.) in one portion. This mixture was stirred for 2 h before a solution of **7** (487 mg, 2.33 mmol, 1 eq.) in THF (15 cm^3) [washed with THF (5 cm^3)] was introduced in a dropwise fashion. Stirring was continued at -78°C for 4.5 h before solid NH_4Cl (ca. 7.5 g) was added portionwise. The reaction was warmed to room temperature over 16 h and the NH_3 was allowed to evaporate. EtOAc (100 cm^3) and H_2O (100 cm^3) were added to the residue, which was then basified to with 2 M NaOH solution (ca. 50 cm^3). The resultant aqueous layer was further extracted with EtOAc ($3 \times 50\text{ cm}^3$) and the combined organic extracts were dried over MgSO_4 . Filtration, followed by solvent removal under reduced pressure afforded the crude amine, which was purified by short-path distillation affording **8** (309 mg, 90%) as a colourless liquid. b.p. $150^\circ\text{C}/2\text{mmHg}$; R_f = 0.05 (EtOAc); ν_{max} (neat/ cm^{-1}) 3296, 3060, 3027, 2960, 2871, 1673, 1632, 1602, 1493, 1454, 1417; m/z (CI) 148 (M^+ , 100%), found 148.11225 $\text{C}_{10}\text{H}_{13}\text{N}\cdot\text{H}$ requires 148.11261 (-2.6 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 1.79–1.88 (m, 1H), 2.17–1.6 (m, 1H), 2.68 (s, 1H), 2.84 (dd, $J=8.0, 10.5$, 1H) 3.03–3.17 (m, 2H), 3.17–3.25 (m, 1H), 3.34 (dd, $J=7.5, 10.5$ Hz, 1H), 7.16–7.31 (m, 5H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 34.3, 45.4, 47.2, 55.0, 126.0, 127.0, 128.3, 144.0.

Optimised: 3-phenylpyrrolidine 8: Under N_2 , at -78°C liquid NH_3 (ca. 150 cm^3) was treated with lithium shot (34 mg, 4.86 mmol, 5 eq.). This mixture was stirred for 1 h before a solution of **7** (203 mg, 0.97 mmol, 1 eq.) in THF (10 cm^3) [washed with THF (5 cm^3)] was introduced in a dropwise fashion. Stirring was continued at -78°C for 0.5 h before solid NH_4Cl (ca. 5 g) was added portionwise. The reaction was warmed to room temperature over 16 h and the NH_3 was allowed to evaporate. EtOAc (25 cm^3) and H_2O (25 cm^3) were added to the residue, which was then basified with 1 M KOH solution (ca. 10 cm^3). The resultant aqueous layer was further extracted with EtOAc ($3 \times 25\text{ cm}^3$) and the combined organic extracts were dried over MgSO_4 . Filtration, followed by solvent removal under reduced pressure afforded the crude amine **8** (141 mg, 98%) as a viscous yellow liquid. Data as above.

(2) Reference: Sonesson, C.; Larhed, M.; Nyqvist, C.; Hallberg, A. *J. Org. Chem.* **1996**, *61*, 4756.

1-(4-Methylbenzenesulfonyl)-3-phenylpyrrolidine 9:² At 0°C, a solution of amine **8** (458 mg, 3.11 mmol, 1 eq.) and TEA (0.85 cm³, 6.10 mmol, 2 eq.) in DCM (10 cm³) was treated with TsCl (594 mg, 3.11 mmol, 1 eq.). The mixture was stirred for 15 h, during which time room temperature was reached. Silica (*ca.* 5 g) was added and the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography (Hex-EtOAc; 3:1) gave **9** (695 mg, 74%) as a colourless solid. m.p. 74°C (EtOAc-Hex); *R*_f = 0.3 (Hex-EtOAc; 3:1); ν_{max} (neat/cm⁻¹) 3547, 3062, 3030, 2973, 2884, 1598, 1496, 1454, 1344, 1162, 1092, 1030; *m/z* (CI) 302 (MH⁺, 100%); found 302.12223, C₁₇H₁₉NO₂S·H requires 302.12146 (+2.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.82-1.94 (m, 1H), 2.17-2.25 (m, 1H), 2.46 (s, 3H), 3.18-3.29 (m, 2H), 3.37 (ddd, *J*=7.0, 10.0 Hz, 1H), 3.54 (ddd, *J*=3.5, 8.5, 10.0 Hz, 1H), 3.70-3.78 (m, 1H), 7.11 (d, *J*=7.0 Hz, 2H), 7.18-7.30 (m, 3H), 7.35 (d, *J*=8.0 Hz, 2H), 7.77 (d, *J*=8.0 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 21.5, 32.9, 43.8, 47.8, 54.1, 126.9, 126.95, 127.6, 128.6, 129.7, 134.1, 140.7, 143.4; found C, 67.59; H, 6.55; N, 4.39%; C₁₇H₁₉NO₂S requires C, 67.77; H, 6.31; N, 4.65%.

1-(4-Methylbenzenesulfonyl)-3-cyclohexylpyrrolidine 11:³ Under argon at 0°C a mixture of ethylenediamine (20 cm³) and THF (10 cm³) was treated with lithium (200 mg, 28.6 mmol, 24 eq.). After 0.25 h the sulfonamide **7** (250 mg, 1.12 mmol, 1 eq.) was added in one portion and the mixture was stirred for 0.75 h. Solid NH₄Cl was added (*ca.* 10 g) and the mixture was stirred for 0.5 h before extraction with Et₂O (100 cm³) and 1 M NaOH (50 cm³). The resultant aqueous layer was further extracted with Et₂O (3 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal under reduced pressure gave crude 3-cyclohexenylpyrrolidine **10** as a mixture of regioisomers. This material (*ca.* 1.20 mmol) was dissolved in DCM (5 cm³) and TsCl (227 mg, 1.19 mmol, 0.95 eq.) and TEA (0.35 cm³, 2.51 mmol, 2 eq.) were added. After 2 h of stirring at room temperature silica (*ca.* 5 g) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1 → Hex-EtOAc 5:1) afforded the corresponding sulfonamide (205 mg, 55%) as a mixture of alkene regioisomers. This mixture (205 mg, 0.672 mmol) was dissolved in EtOH (10 cm³) and 5% w/w Pd/C (150 mg, 0.07 mmol, 10 mol%) was added. Stirring under a hydrogen atmosphere (1 atm.) for 15 h, filtration through a celite[®] bed, solvent removal *in vacuo* gave the *title compound* **11** (207 mg, 100%) as a colourless solid. m.p. 105-108°C (EtOAc); *R*_f = 0.1 (Hex-EtOAc; 9:1); ν_{max} (neat/cm⁻¹) 3055, 2928,

(3) Reference: Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1994**, *59*, 4576.

2853, 1450, 1430, 1342, 1266, 1162; m/z (CI) 308 (MH^+ , 100%), 152 (50%); found 308.16774, $C_{17}H_{25}NO_2S \cdot H$ requires 308.16843 (-2.5 ppm); 1H -NMR ($CDCl_3$, 400 MHz) δ = 0.82-0.95 (m, 2H), 0.98-1.07 (m, 1H), 1.09-1.23 (m, 2H), 1.32-1.44 (m, 1H), 1.55-1.75 (m, 6H), 1.70-1.80 (m, 1H), 1.88-1.98 (m, 1H), 2.45 (s, 3H), 2.79 (dd, app. t, $J=9.75$ Hz, 1H), 3.18 (ddd, app. dt, $J=7.0, 10.5$ Hz, 1H), 3.38 (ddd, app. dt, $J=2.25, 10.5$ Hz, 1H), 3.49 (dd, $J=7.5, 9.75$ Hz, 1H), 7.30 (d, $J=8.0$ Hz, 2H), 7.72 (d, $J=8.0$ Hz, 2H); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ = 21.5, 25.95, 26.0, 26.2, 29.6, 31.3, 31.9, 41.4, 45.1, 47.9, 51.9, 127.5, 129.6, 133.9, 143.2; found C, 66.23; H, 7.99; N, 4.51, $C_{17}H_{25}NO_2S$ requires C, 66.45; H, 8.14; N, 4.56.

2-Bromo-4,5-dimethoxybenzenesulfonylchloride 13:⁴ 4-Bromoveratrole **12** (4.0 cm^3 , 27.8 mmol) was added in a dropwise fashion over 20 min. to a well stirred flask containing chlorosulfonic acid (8 cm^3) cooled to 0°C. The black mixture was then stirred for a further 0.25 h before cautious addition to ice (*ca.* 150 cm^3). After the ice had melted DCM (100 cm^3) was added and the phases were separated. The aqueous phase was extracted with DCM (100 cm^3) and the combined organic phases were dried over $MgSO_4$. Filtration and solvent removal under reduced pressure gave the sulfonyl chloride **13** (7.17 g, 82%) as a white solid which was further purified by recrystallisation from Et_2O . m.p. 78°C (Et_2O); 1H -NMR ($CDCl_3$, 400 MHz) δ = 3.94 (s, 3H), 3.99 (s, 3H), 7.18 (s, 1H), 7.59 (s, 1H); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ = 56.5, 56.7, 112.5, 113.0, 117.7, 134.6, 147.8, 154.1.

N,N-Diallyl-2-bromo-4,5-dimethoxybenzenesulfonamide 14: A mixture of **13** (2.01 g, 6.37 mmol, 1 eq.) and triethylamine (1.8 cm^3 , 12.91 mmol, 2.0 eq.) in DCM (75 cm^3) was treated with diallylamine (0.86 cm^3 , 6.98 mmol, 1.1 eq.) in a dropwise fashion at 0°C. Stirring was continued for 15 h and the reaction gradually warmed to room temperature. The solvent was removed under reduced pressure and Et_2O (100 cm^3) and H_2O (100 cm^3) were added. The resultant aqueous layer was further extracted with Et_2O (2 x 100 cm^3) and the combined ethereal extracts were dried over $MgSO_4$. Filtration followed by solvent removal *in vacuo* afforded the crude product, which was purified by flash column chromatography (Hex- $EtOAc$; 5:1) affording the product **14** (2.08 g, 87%) as a colourless solid. m.p. 98°C ($EtOAc$); R_f = 0.2 (Hex- $EtOAc$; 5:1); ν_{max} ($CDCl_3/cm^{-1}$) 3055, 2993, 2846, 1583, 1498, 1440, 1364, 1325, 1265, 1210, 1152; m/z (CI) 378 (MH^+ , ^{81}Br , 100%), 376 (MH^+ , ^{79}Br , 100%); found 376.02145, $C_{14}H_{18}NO_4BrS \cdot H$ requires 376.02182 (-1.0 ppm); 1H -NMR ($CDCl_3$, 400 MHz) δ = 3.88 (d, $J=7.5$ Hz, 4H), 3.89 (s, 3H), 3.91 (s, 3H), 5.12-5.18 (m, 4H), 5.58-5.72 (m, 2H), 7.17 (s, 1H), 7.63 (s, 1H); ^{13}C -NMR ($CDCl_3$, 100 MHz) δ = 48.8, 56.3, 56.4, 111.7, 114.5, 117.3, 118.9, 130.9, 132.5, 147.5, 152.0; found C, 44.72; H, 4.73; N, 3.89%; $C_{14}H_{18}NO_4BrS$ requires C, 44.68; H, 4.79; N, 3.72%.

(4) Levi, A. A.; Smiles, S. *J. Chem. Soc.* **1931**, 520.

1-(2-Bromo-4,5-dimethoxybenzenesulfonyl)-2,5-dihydro-1H-pyrrole 15: Under N₂, a degassed solution of the diallylsulfonamide **14** (2.14 g, 5.69 mmol, 1 eq.) in DCM (100 cm³) was treated with the Grubbs catalyst (100 mg, 0.118 mmol, 2 mol%). Stirring was continued at room temperature for 24 h before silica (*ca.* 10 g) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 5:1) gave the dihydropyrrole **15** (1.65 g, 83%) as a colourless solid. m.p. 140°C (EtOAc-Hex); *R*_f = 0.15 (Hex-EtOAc; 5:1); ν_{max} (CDCl₃/cm⁻¹) 3148, 2973, 2896, 1641, 1465, 1380; *m/z* (CI) 350 (MH⁺, ⁸¹Br, 100%), 348 (MH⁺, ⁷⁹Br, 100%); found 347.98977, C₁₂H₁₄NO₄BrS·H requires 347.99051 (-2.3 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 3.92 (s, 3H), 3.94 (s, 3H), 4.26 (s, 4H), 5.77 (s, 2H), 7.16 (s, 1H), 7.59 (s, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 54.7, 56.4, 56.45, 111.8, 114.3, 117.5, 125.3, 130.0, 147.7, 152.1; found C, 41.34; H, 3.90; N, 4.08%; C₁₂H₁₄NO₄BrS requires C, 41.38; H, 4.02; N, 4.02%.

1-(2-Bromo-4,5-dimethoxybenzenesulfonyl)-2,5-dihydro-1H-pyrrole 15: A mixture of **13** (997 mg, 3.52 mmol, 1.05 eq.) and triethylamine (0.73 cm³, 5.24 mmol, 1.55 eq.) in DCM (50 cm³) was treated with 3-pyrroline (0.26 cm³, 3.39 mmol, 1 eq.) in a dropwise fashion at 0°C. Stirring was continued for 15 h and the reaction was warmed to room temperature before the solvent was removed under reduced pressure and Et₂O (100 cm³) and H₂O (100 cm³) were added. The aqueous layer was then further extracted with Et₂O (2 x 100 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* afforded the crude product, which was purified by flash column chromatography **15** (Hex-EtOAc; 5:1) affording the product (1.14 g, 93%) as a colourless solid. Data as above.

4,5-Dimethoxy-8-thia-9-azatricyclo[7.2.1.0^{2,7}]dodeca-2(7),3,5,10-tetraene-8,8-dioxide 16: Under N₂, a mixture of the dihydropyrrole **15** (420 mg, 1.21 mmol, 1 eq.), Pd(OAc)₂ (27 mg, 0.12 mmol, 10 mol%), PPh₃ (63 mg, 0.24 mmol, 20 mol%) and K₂CO₃ (333 mg, 2.41 mmol, 2 eq.) in DMF (10 cm³) was heated to 110°C for 18 h. The reaction mixture was cooled and Et₂O (50 cm³) and H₂O (50 cm³) were added. The resultant aqueous layer was further extracted with Et₂O (2 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (Hex-EtOAc; 5:1) affording the Heck product **16** (195 mg, 61%) as a colourless solid. m.p. 182-186°C; *R*_f = 0.2 (Hex-EtOAc; 1:1); ν_{max} (CHCl₃/cm⁻¹) 3055, 2987, 2853, 1639, 1506, 1422, 1336, 1266, 1150; *m/z* (CI) 285 (MNH₄⁺, 100%), 268 (MH⁺, 80%); found 268.06436, C₁₂H₁₃NO₄S·H requires 268.06433 (+0.1 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 3.23 (t, *J*=3.75 Hz, 1H), 3.88 (s, 3H), 3.93 (s, 3H), 4.05 (dd, *J*=3.75, 11.75 Hz, 1H), 4.48 (d, *J*=11.75 Hz, 1H),

6.42 (d, $J=3.75$ Hz, 1H), 6.62 (d, $J=3.75$ Hz, 1H), 6.63 (s, 1H), 7.12 (s, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 42.0, 56.1, 56.2, 63.5, 108.2, 109.2, 125.2, 133.4, 134.0, 135.5, 149.7, 151.0.

4,5-Dimethoxy-8-thia-9-azatricyclo[7.2.1.0^{2,7}]dodeca-2(7),3,5-triene-8,8-dioxide

17: 5% w/w Pd/C (500 mg, 0.235 mmol, 10 mol%) was added to a solution of the alkene **16** (560 mg, 2.10 mmol, 1 eq.) in EtOH (20 cm³). The mixture was degassed before stirring under a hydrogen atmosphere at room temperature for 15 h. Filtration through a celite[®] bed, washing with EtOAc (50 cm³) and solvent removal *in vacuo* and purification by flash column chromatography (Hex-EtOAc; 1:1) gave **17** (448 mg, 79%) as a colourless solid. m.p. 195-197°C (DCM-Hex); R_f = 0.25 (Hex-EtOAc; 1:1); ν_{max} ($\text{CDCl}_3/\text{cm}^{-1}$) 3110, 3055, 2934, 2868, 1506, 1443, 1402, 1325, 1224, 1166, 1141; m/z (CI) 287 (MNH_4^+ , 70%), 270 (MH^+ , 100%); found 270.07946, $\text{C}_{12}\text{H}_{15}\text{NO}_4\text{S}\cdot\text{H}$ requires 270.07999 (-2.2 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 1.86-1.99 (m, 1H), 2.20-2.32 (m, 1H), 3.16-3.24 (m, 2H), 3.51 (ddd, $J=4.0$, 10.5, 14.25 Hz, 1H), 3.87 (ddd, $J=7.5$, 14.25 Hz, 1H), 3.91 (s, 3H), 3.93 (s, 3H), 4.25 (d, $J=12.5$ Hz, 1H), 6.56 (s, 1H), 7.20 (s, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 33.1, 39.4, 46.9, 56.1, 56.2, 57.3, 107.6, 109.0, 126.5, 134.3, 148.9, 152.1; found C, 53.30; H, 5.58; N, 5.30%; $\text{C}_{12}\text{H}_{15}\text{NO}_4\text{S}$ requires C, 53.53; H, 5.58; N, 5.20%.

1-(4-Methylbenzenesulfonyl)-3-(3,4-dimethoxyphenyl)pyrrolidine 18 and 1-(4-methylbenzenesulfonyl)-3-(4-methoxyphenyl)pyrrolidine 19: Under N_2 , at -78°C liquid NH_3 (*ca.* 100 cm³) was treated with lithium shot (30 mg, 4.29 mmol, 5.7 eq.). This mixture was stirred for 1 h before a solution of **17** (212 mg, 0.749 mmol, 1 eq.) in THF (10 cm³) [washed with THF (5 cm³)] was introduced in a dropwise fashion. Stirring was continued at -78°C for 0.5 h before solid NH_4Cl (*ca.* 5 g) was added portionwise. The reaction was warmed to room temperature over 16 h and the NH_3 was allowed to evaporate. EtOAc (25 cm³) and H_2O (25 cm³) were added to the residue, which was then basified with 1 M KOH solution (*ca.* 10 cm³). The resultant aqueous layer was further extracted with EtOAc (3 x 25 cm³) and the combined organic extracts were dried over MgSO_4 . Filtration, followed by solvent removal under reduced pressure afforded a viscous yellow liquid. At 0°C , a solution of the pyrrolidines (*ca.* 0.749 mmol) and TEA (0.21 cm³, 1.51 mmol, 2 eq.) in DCM (10 cm³) was treated with TsCl (143 mg, 0.75 mmol, 1 eq.). The mixture was stirred for 5 h, during which time room temperature was reached. Silica (*ca.* 5 g) was added and the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography (Hex-EtOAc; 4:1) gave initially **19** (90 mg, 36%) as a

colourless solid. m.p. 66-69°C (Hex-EtOAc); $R_f = 0.15$ (Hex-EtOAc; 4:1); $\nu_{\max}$ (CDCl₃/cm⁻¹) 3055, 2952, 2928, 1509, 1456, 1333, 1246, 1158; m/z (CI) 349 (MNH₄⁺, 10%), 332 (MH⁺, 100%); found 332.13189, C₁₈H₂₁NO₃S·H requires 332.13202 (-0.4 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.78-1.89 (m, 1H), 2.15-2.23 (m, 1H), 2.47 (s, 3H), 3.13-3.25 (m, 2H), 3.32-3.40 (m, 1H), 3.51-3.57 (m, 1H), 3.68-3.75 (m, 1H), 3.80 (s, 3H), 6.83 (d, $J=8.5$ Hz, 2H), 7.05 (d, $J=8.5$ Hz, 2H), 7.37 (d, $J=8.5$ Hz, 2H), 7.78 (d, $J=8.5$ Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 21.5, 33.0, 43.1, 47.8, 54.2, 55.2, 113.9, 127.5, 127.9, 129.7, 132.5, 133.8, 143.4, 158.4; found C, 65.12; H, 6.40; N, 4.03%; C₁₈H₂₂NO₃S requires C, 65.06; H, 6.63; N, 4.22%.

Further elution gave **18** (75 mg, 28%) as a tan coloured viscous oil. $R_f = 0.1$ (Hex-EtOAc; 4:1); $\nu_{\max}$ (CDCl₃/cm⁻¹) 3055, 2940, 2835, 1597, 1517, 1460, 1421, 1336, 1254, 1237, 1158; m/z (CI) 379 (MNH₄⁺, 50%), 362 (MH⁺, 100%); found 362.14213, C₁₉H₂₃NO₄S·H requires 362.14261 (-1.5 ppm); ¹H-NMR (CDCl₃, 100 MHz) δ = 1.81-1.93 (m, 1H), 2.15-2.23 (m, 1H), 2.46 (s, 3H), 3.15-3.24 (m, 2H), 3.31-3.37 (m, 1H), 3.53-3.59 (m, 1H), 3.66-3.75 (m, 1H), 3.85 (s, 3H), 3.87 (s, 3H), 6.65 (s, 1H), 6.66 (d, $J=8.0$ Hz, 1H), 6.78 (d, $J=8.0$ Hz, 1H), 7.35 (d, $J=8.25$ Hz, 2H), 7.76 (d, $J=8.25$ Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 21.5, 33.0, 43.4, 47.8, 54.1, 55.8, 55.85, 110.1, 111.1, 118.8, 127.5, 129.6, 133.1, 133.9, 143.4, 147.9, 148.9.

1-(2-Bromobenzenesulfonyl)pyrrolidin-2-one 21: At 0°C, under nitrogen a 1.6 M solution of ⁿBuLi in hexanes (13.5 cm³, 21.6 mmol, 1.1 eq.) was added dropwise to a solution of freshly distilled 2-pyrrolidinone **20** (1.78 cm³, 23.4 mmol, 1.2 eq.) in THF (250 cm³). The mixture was stirred for 0.5 h before the sulfonylchloride **3** (5.0 g, 19.6 mmol, 1.0 eq.) was added in one portion. Stirring was maintained for 1 h at 0°C before a saturated aqueous solution of NH₄Cl (50 cm³) and EtOAc (75 cm³) were added. The resultant aqueous layer was further extracted with EtOAc (3 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* and purification by recrystallisation from hot EtOAc gave the product **21** (4.43 g, 74%) as a colourless microcrystalline solid. m.p. 170-172°C (EtOAc); $R_f = 0.3$ (Hex-EtOAc; 1:1); $\nu_{\max}$ (CDCl₃/cm⁻¹) 3440, 3053, 2985, 1734, 1420, 1352, 1266, 1173; m/z (CI) 323 (MNH₄⁺, ⁸¹Br, 70%), 321 (MNH₄⁺, ⁷⁹Br, 70%), 306 (MH⁺, ⁸¹Br, 45%), 304 (MH⁺, ⁷⁹Br, 45%); found 303.96446, C₁₀H₁₀NO₃SBr·H requires 303.96432 (+0.5 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 2.19 (pent, $J=7.5$ Hz, 2H), 2.48 (t, $J=7.5$ Hz, 2H), 4.17 (t, $J=7.5$ Hz, 2H), 7.45 (dt, $J=1.75, 8.0$ Hz, 1H), 7.52 (dt, $J=1.25, 8.0$ Hz, 1H), 7.72 (dd, $J=1.25, 8.0$ Hz, 1H), 8.33 (dd, $J=1.75, 8.0$ Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 18.7, 32.0, 47.6, 119.9, 127.7, 134.0, 134.7, 135.1, 137.7, 173.2; found C, 39.80; H, 3.21; N, 4.49%; C₁₀H₁₀NO₃SBr requires C, 39.47; H, 3.29; N, 4.61%.

1-(2-Bromobenzenesulfonyl)pyrrolidin-2-ol 22: Under N₂, at -78°C, a stirred solution of the *N*-sulfonamide **21** (7.63 g, 25.1 mmol, 1 eq.) in CH₂Cl₂ (140 cm³) was treated dropwise with a 1 M solution of Dibal in hexane (31.0 cm³, 31.0 mmol, 1.25 eq.). The mixture was stirred at -78°C to -40°C for 1 h. Methanol (25 cm³) was added and the mixture was warmed to room temperature before pouring into an aqueous solution of Rochelle's salt (100 cm³) and DCM (100 cm³) and partitioning for 1 h. The phases were separated and the aqueous phase was further extracted with DCM (2 x 100 cm³). The combined organic phases were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* and purification by flash column chromatography (Hex-EtOAc; 1:1) afforded the product **22** (6.34 g, 83%) as a colourless viscous liquid. *R*_f = 0.3 (Hex-EtOAc; 1:1); *ν*_{max} (neat/cm⁻¹) 3499, 3353, 3089, 2978, 2879, 1574, 1446, 1427, 1329, 1158; *m/z* (CI) 325 (MNH₄⁺, ⁸¹Br, 5%), 323 (MNH₄⁺, ⁷⁹Br, 5%), 307 (M-H₂O+NH₄⁺, ⁸¹Br, 10%), 305 (M-H₂O+NH₄⁺, ⁷⁹Br, 10%), 290 (M-H₂O+H⁺, ⁸¹Br, 100%), 288 (M-H₂O+H⁺, ⁷⁹Br, 100%); found 323.00530, C₁₀H₁₂O₃NS⁷⁹Br requires 323.00650 (-3.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) *δ* = 1.97-2.01 (m, 3-H₂, 4H), 3.24 (m, 1H), 3.64 (m, 1H), 5.70 (m, 1H), 7.44 (m, 2H), 7.75 (dd, *J*=1.5, 7.75 Hz, 1H), 8.13 (dd, *J*=1.75, 7.75 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) *δ* = 23.1, 33.8, 47.1, 84.4, 127.7, 131.9, 133.7, 135.7, 139.9, 150.1.

1-(2-Bromobenzenesulfonyl)-2,3-dihydro-1H-pyrrole 23: A solution of citric acid monohydrate (1.07 g, 5.1 mmol, 0.25 eq.) and **22** (6.20 g, 20.3 mmol, 1 eq.) in toluene (125 cm³) was heated under reflux with constant removal of water for 6 h (Dean-Stark apparatus). On cooling a saturated aqueous solution of NaHCO₃ (75 cm³) was added and the resultant aqueous layer was further extracted with EtOAc (2 x 25 cm³). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 2:1) gave **23** (4.84 g, 83%) as a white solid. m.p. 70-72°C; *R*_f = 0.3 (Hex-EtOAc; 2:1); *ν*_{max} (CH₂Cl₂/cm⁻¹) 3092, 2975, 2948, 2861, 1615, 1574, 1447, 1422, 1352, 1172; *m/z* (CI) 290 (MH⁺, ⁸¹Br, 100%), 288 (MH⁺, ⁷⁹Br, 100%); found 287.96931, C₁₀H₁₀NO₂SBr-H requires 287.96939 (-0.3 ppm); ¹H-NMR (CDCl₃, 400 MHz) *δ* = 2.64 (m, 2H), 3.65 (t, *J*=9.0 Hz, 2H), 5.08 (m, 1H), 6.56 (m, 1H), 7.42 (m, 2H), 7.75 (dd, *J*=1.5, 7.75 Hz, 1H), 8.01 (dd, *J*=1.75, 7.75 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) *δ* = 29.6, 47.0, 87.1, 91.3, 108.6, 127.6, 130.8, 132.1, 133.6, 135.7; found C, 41.62; H, 3.54; N, 4.82%; C₁₀H₁₀NO₂SBr requires C, 41.68; H, 3.50; N, 4.86%.

2,3-Dihydropyrrolo[1,2-*b*][1,2]benzisothiazole-5,5-dioxide 24: Under N₂, a mixture of **23** (1.00 g, 3.50 mmol, 1 eq.), Pd(OAc)₂ (78 mg, 0.35 mmol, 10 mol%), PPh₃ (182 mg, 0.70 mmol, 20 mol%) and K₂CO₃ (961 mg, 6.95 mmol, 2 eq.) in DMF (40 cm³) were heated at 110°C for 16 h. On cooling Et₂O (50 cm³) and H₂O (50 cm³) were added and the resultant aqueous layer was further extracted with Et₂O (2 x 50 cm³). The combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal gave the crude product, which was purified by flash column chromatography (Hex-EtOAc; 1:1) affording **24** (460 mg, 67%) as a colourless solid. m.p. 110-115°C; *R*_f = 0.3 (Hex-EtOAc; 1:1); $\nu_{\max}$ (CH₂Cl₂/cm⁻¹) 3565, 3062, 2984, 2856, 1597, 1467, 1308, 1171; *m/z* (EI) 207 (M⁺, 90%), 143 (50%), 115 (100%); found 207.03481, C₁₀H₉NO₂S requires 207.03539 (-2.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 3.10 (m, 2H), 3.78 (m, 2H), 5.57 (t, *J*=3.0 Hz, 1H), 7.38-7.80 (m, 4H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 34.0, 43.2, 122.1, 122.7, 127.0, 130.1, 132.8, 139.4, 141.1; found C, 57.63; H, 4.69; N, 6.59%; C₁₀H₉NO₂S requires C, 57.97; H, 4.38; N, 6.76%.

1,2,3,9b-Tetrahydropyrrolo[1,2-*b*][1,2]benzisothiazole-5,5-dioxide 25: A mixture of 10% Pd/C (219 mg, 0.20 mmol, 10 mol%) and **24** (432 mg, 2.00 mmol, 1 eq.) in EtOH (20 cm³) was stirred under a hydrogen atmosphere at room temperature for 15 h. Filtration through celite[®] and washing with ethanol (3 x 20 cm³), solvent removal *in vacuo* followed by flash column chromatography (Hex-EtOAc; 1:1) gave **25** (380 mg, 87%) as viscous colourless oil which gradually solidified on standing. An analytical sample of **25** was obtained on recrystallisation from EtOAc-Hex. m.p. 48-50°C (EtOAc-Hex); *R*_f = 0.3 (Hex-EtOAc; 1:1); $\nu_{\max}$ (CH₂Cl₂/cm⁻¹) 3515, 3090, 2978, 2850, 1469, 1453, 1310, 1178, 1165; *m/z* (CI) 227 (MNH₄⁺, 20%), 210 (M⁺, 100%); found 210.05943, C₁₀H₁₁NO₂S·H requires 210.0588 (+2.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.83-2.04 (m, 3H), 2.40-2.48 (m, 1H), 3.37 (ddd, *J*=6.5, 11.0 Hz, 1H), 3.81 (ddd, *J*=6.5, 11.0 Hz, 1H), 4.98 (dd, *J*=5.5, 7.5 Hz, 1H), 7.36 (dd, *J*=1.0, 7.5 Hz, 1H), 7.50 (t, *J*=7.5 Hz, 1H), 7.60 (dd, *J*=1.0, 7.5 Hz, 1H), 7.74 (d, *J*=7.5 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 26.7, 32.8, 48.6, 65.4, 121.9, 124.7, 129.7, 133.5, 136.7, 140.4; found C, 57.34; H, 5.34; N, 6.62%; C₁₀H₁₁NO₂S requires C, 57.42; H, 5.30; N, 6.70%.

4-Phenylbutylamine: Under N₂, at -78°C a mixture of lithium (200 mg, 28.60 mmol, 17 eq.) in liquid NH₃ (100 cm³) was treated with **25** (350 mg, 1.67 mmol, 1 eq.) in THF (15 cm³, washed 5 cm³) and stirred for 3 h. NH₄Cl (9 g) was added and the NH₃

was allowed to evaporate overnight. EtOAc (50 cm³) and H₂O (50 cm³) were added and the mixture was basified with 2 M NaOH solution (ca. 35 cm³). The resultant aqueous layer was further extracted with EtOAc (2 x 50 cm³). The combined organic extracts were dried over MgSO₄, filtered and the solvent removed *in vacuo* affording 4-phenylbutylamine (219 mg, 88%) as a yellow oil. *R*_f = 0.05 (EtOAc); ν_{max} (neat/cm⁻¹) 3364, 3061, 3025, 2931, 2856, 1664, 1602, 1495, 1452; *m/z* (CI) 150 (MH⁺, 100%); found 150.12820, C₁₀H₁₅N·H requires 150.12827 (-0.5 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.27 (s(br), 2H), 1.47 (pent, *J*=7.5 Hz, 2H), 1.65 (pent, *J*=7.5 Hz, 2H), 2.62 (t, *J*=7.5 Hz, 2H), 2.71 (t, *J*=7.5 Hz, 2H), 7.15-7.19 (m, 3H), 7.25-7.29 (m, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 28.7, 33.4, 35.7, 42.1, 125.6, 128.2, 128.3, 142.4.

1-(4-Methylbenzenesulfonyl)-4-phenylbutylamine 26: A mixture of 4-phenylbutylamine (201 mg, 1.35 mmol, 1. eq.) and TEA (0.3 cm³, 2.15 mmol, 1.6 eq.) in DCM (5 cm³) was treated with TsCl (257 mg, 1.35 mmol, 1 eq.) for 15 h. Silica (ca. 5 g) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 5:1) gave **26** (335 mg, 82%) as a colourless solid. m.p. 55°C; *R*_f = 0.2 (Hex-EtOAc; 5:1); ν_{max} (neat/cm⁻¹) 3290, 3054, 2986, 2940, 1599, 1495, 1452, 1420, 1328, 1265, 1161, 1094; *m/z* (CI) 321 (MNH₄⁺, 40%), 304 (MH⁺, 100%); found 304.13795, C₁₇H₂₁NO₂S·H requires 304.13712 (+3.0 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.42-1.52 (m, 2H), 1.54-1.62 (m, 2H), 2.41 (s, 3H), 2.53 (t, *J*=7.5 Hz, 2H), 2.94 (q, *J*=6.5 Hz, 2H), 4.75 (t, *J*=6.5 Hz, 1H), 7.08 (d, *J*=7.25 Hz, 2H), 7.15 (t, *J*=7.25 Hz, 1H), 7.23 (t, *J*=7.25 Hz, 2H), 7.27 (d, *J*=8.0 Hz, 2H), 7.73 (d, *J*=8.0 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 21.4, 28.1, 29.0, 35.2, 43.0, 125.8, 127.0, 128.25, 128.3, 129.6, 137.0, 141.8, 143.2.

2-Phenyl-1-(4-methylbenzenesulfonyl)pyrrolidine 27:⁵ Under N₂, at -78°C liquid NH₃ (ca. 100 cm³) was treated with Li (25 mg, 3.57 mmol, 5 eq.). The dark blue solution was stirred for 1h before a solution of the sulfonamide **25** (150 mg, 0.718 mmol, 1 eq.) in THF (5 cm³ + 1 cm³ washing) was added. The reaction was stirred for approximately 5 min before the colour of the solution cleared. Solid NH₄Cl (ca. 3 g) was added and the reaction was warmed to room temperature and the NH₃ allowed to evaporate. EtOAc (40 cm³) and H₂O (40 cm³) were added and the mixture was basified with 1 M NaOH solution (pH 10). The resultant aqueous layer was further extracted with EtOAc (3 x 40 cm³). The combined organic extracts were dried over Na₂SO₄ and the mixture was filtered and the solvent removed under reduced pressure. At room temperature the crude 2-phenylpyrrolidine (ca. 0.718 mmol, 1 eq.) was dissolved in CHCl₃ (5 cm³) and treated with TsCl (135 mg, 0.708 mmol, 0.99 eq.) and TEA (0.15 cm³, 1.08 mmol, 1.5 eq.). Stirring was continued for 3 h before silica (ca. 5 g) was added and the solvent removed under reduced pressure. Purification by flash

(5) Reference: Schlummer, B.; Hartwig, J. F. *Org. Lett.* **2002**, 4, 1471

column chromatography (Hex-EtOAc; 5:1) afforded the *title compound 27* (165 mg, 76%) as a colourless solid. m.p = 104°C (EtOAc-Hex); R_f = 0.3 (Hex-EtOAc; 3:1); $\nu_{\max}$ (CDCl₃/cm⁻¹) 3054, 2986, 1600, 1422, 1346, 1265, 1161; m/z (CI) 319 (MNH₄⁺, 20%), 302 (MH⁺, 100%); found 302.12223, C₁₇H₁₉NO₂S·H requires 302.12146 (+2.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.62-1.73 (m, 1H), 1.79-1.92 (m, 2H), 1.95-2.03 (m, 1H), 2.43 (s, 3H), 3.40-3.47 (m, 1H), 3.60-3.67 (m, 1H), 4.81 (dd, J =4.0, 8.0 Hz, 1H), 7.22-7.34 (m, 7H), 7.69 (d, J =8.0 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 21.5, 23.9, 35.7, 49.3, 63.2, 126.1, 127.1, 127.4, 128.3, 129.5, 135.0, 143.0, 143.2; found C, 67.51; H, 6.37; N, 4.67%; C₁₇H₁₉NO₂S requires C, 67.77; H, 6.35; N, 4.65%.

1-(2-Bromobenzenesulfonyl)piperidin-2-one 29: Under nitrogen a 2.5 M solution of ⁿBuLi in hexanes (4.8 cm³, 12.0 mmol, 1.34 eq.) was added dropwise to a solution of freshly distilled 2-pyrrolidinone **28** (1.18 g, 11.9 mmol, 1.33 eq.) in THF (60 cm³) at 0°C. The mixture was stirred for 0.5 h before solid 2-bromobenzenesulfonylchloride (2.28 g, 8.93 mmol, 1.0 eq.) was added in one portion. Stirring was maintained for 1 h at 0°C before a saturated aqueous solution of NH₄Cl (50 cm³) and EtOAc (50 cm³) were added. The resultant aqueous layer was further extracted with EtOAc (3 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* and purification by recrystallisation from EtOAc-Hex gave the product **29** (1.22 g, 43%) as a colourless crystalline solid. m.p = 136°C; R_f = 0.3 (Hex-EtOAc; 5:1); $\nu_{\max}$ (CH₂Cl₂/cm⁻¹) 3057, 2959, 2880, 1692, 1572, 1449, 1350, 1265, 1177, 1155; m/z (CI) 337 (MNH₄⁺, ⁸¹Br, 30%), 335 (MNH₄⁺, ⁷⁹Br, 30%), 320 (MH⁺, ⁸¹Br, 100%), 318 (MH⁺, ⁷⁹Br, 100%); found 317.98016, C₁₁H₁₂N⁷⁹BrO₃S·H requires 317.97995 (+0.7 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.72-1.80 (m, 2H), 1.87-1.95 (m, 2H), 2.37 (t, J =6.75 Hz, 2H), 3.97 (t, J =6.0 Hz, 2H), 7.35 (dt, J =1.5, 7.5 Hz, 1H), 7.43 (dt, J =1.0, 7.5, 1H), 7.63 (dd, J =1.5, 7.5 Hz, 1H), 8.27 (dd, J =1.0, 7.5 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 20.2, 22.8, 33.6, 46.5, 119.1, 127.6, 133.7, 134.2, 134.8, 139.0, 170.0; found C, 41.27; H, 3.68; N, 4.19%; C₁₁H₁₂NO₃SBr requires C, 41.51; H, 3.77; N, 4.40%.

1-(2-Bromobenzenesulfonyl)-1,2,3,4-tetrahydropyridine 31: Under N₂, at -78°C, a stirred solution of the **29** (409 mg, 1.29 mmol, 1 eq.) in CH₂Cl₂ (25 cm³) was treated dropwise with a 1 M solution of Dibal in hexane (1.8 cm³, 1.80 mmol, 1.4 eq.). The mixture was stirred at -78°C to -40°C for 3 h. Methanol (25 cm³) was added and the

mixture was warmed to room temperature before pouring into an aqueous solution of Rochelle's salt (100 cm³) and DCM (100 cm³) and partitioning for 1 h. The phases were separated and the aqueous phase was further extracted with DCM (2 x 100 cm³). The combined organic phases were dried over MgSO₄. Filtration followed by solvent removal *in vacuo* afforded the crude hemiaminal **30** as a viscous liquid. The crude material was directly dissolved in toluene (50 cm³) and citric acid monohydrate (67 mg, 0.32 mmol, 0.25 eq.) was added and the mixture heated to reflux with constant removal of water for 7 h (Dean-Stark apparatus). On cooling a saturated aqueous solution of NaHCO₃ (50 cm³) was added and the resultant aqueous layer was further extracted with EtOAc (2 x 25 cm³). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1) gave **31** (353 mg, 91%) as a colourless waxy solid. m.p = 62°C; *R*_f = 0.15 (Hex-EtOAc; 9:1); ν_{max} (CHCl₃/cm⁻¹) 3088, 3064, 2944, 2874, 1649, 1574, 1448, 1332, 1161; *m/z* (CI) 304 (MH⁺, ⁸¹Br, 100%), 302 (MH⁺, ⁷⁹Br, 100%); found 301.98453, C₁₁H₁₂N⁷⁹BrO₂S·H requires 301.98505 (-1.9 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.82 (pent, *J*=5.25 Hz, 2H), 2.01-2.08 (m, 2H), 3.48 (t, *J*=5.25 Hz, 2H), 4.96 (dt, *J*=4.0, 8.0 Hz, 1H), 6.74 (dt, *J*=1.5, 8.0 Hz, 1H), 7.37 (m, 2H), 7.77 (dd, *J*=1.5, 7.5 Hz, 1H), 8.12 (dd, *J*=1.75, 8.0 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 20.9, 21.4, 43.9, 106.4, 120.2, 125.0, 127.6, 132.0, 133.7, 135.8, 138.1.

7,8-Dihydro-6H-9-thia-8a-azafluorene-9,9-dioxide 32: Under N₂, a mixture of **31** (281 mg, 0.93 mmol, 1 eq.), Pd(OAc)₂ (21 mg, 0.09 mmol, 10 mol%), PPh₃ (49 mg, 0.19 mmol, 20 mol%) and K₂CO₃ (257 mg, 1.86 mmol, 2 eq.) in DMF (10 cm³) were heated at 110°C for 2.5 h. On cooling Et₂O (30 cm³) and H₂O (30 cm³) were added and the resultant aqueous layer was further extracted with Et₂O (2 x 25 cm³). The combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal gave the crude product, which was purified by flash column chromatography (Hex-EtOAc; 3:1) affording **32** (177 mg, 86%) as a colourless solid. m.p = 140°C; *R*_f = 0.3 (Hex-EtOAc; 3:1); ν_{max} (CHCl₃/cm⁻¹) 3054, 2986, 1471, 1421, 1305, 1265; *m/z* (CI) 239 (MNH₄⁺, 10%), 222 (MH⁺, 100%); found 222.05925, C₁₁H₁₁NO₂S·H requires 222.05887 (+1.8 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 2.09 (pent, *J*=5.0 Hz, 2H), 2.34 (q, *J*=5.0 Hz, 2H), 3.62 (t, *J*=5.0 Hz, 2H), 5.68 (t, *J*=5.0 Hz, 1H), 7.51-7.66 (m, 3H), 7.82 (d, *J*=7.5 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 20.7, 21.1, 38.1, 100.9, 120.6, 121.0, 129.6, 130.2, 131.1, 131.9, 132.7.

5,6,7,8-Tetrahydro-4bH-9-thia-8a-azafluorene-9,9-dioxide 33: A mixture of 5% Pd/C (150 mg, 0.071 mmol, 10 mol%) and **32** (163 mg, 0.737 mmol, 1 eq.) in EtOH (15 cm³) was stirred under a hydrogen atmosphere at room temperature for 18 h. The

mixture was filtered through celite[®] and washed with ethanol (3 x 20 cm³). Solvent removal *in vacuo* followed by flash column chromatography (Hex-EtOAc; 3:1) gave **33** (160 mg, 98%) as a colourless solid. m.p = 92-94°C; *R*_f = 0.3 (Hex-EtOAc; 3:1); ν_{max} (CHCl₃/cm⁻¹) 3057, 2949, 2859, 1444, 1266, 1168, 1131; *m/z* (CI) 241 (MNH₄⁺, 60%), 224 (MH⁺, 100%); found 224.07478, C₁₁H₁₃NO₂S·H requires 224.07452 (+1.2 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.45-1.87 (m, 4H), 2.05 (dd, *J*=2.75, 13.0 Hz, 1H), 2.32 (dd, *J*=2.5, 12.5 Hz, 1H), 3.05 (ddd, app. dt, *J*=3.25, 12.5 Hz, 1H), 3.84-3.92 (m, 1H), 4.23 (dd, *J*=3.0, 11.5 Hz, 1H), 7.38 (d, *J*=7.5 Hz, 1H), 7.52 (t, *J*=7.5 Hz, 1H), 7.60 (d, *J*=7.5 Hz, 1H), 7.80 (d, *J*=7.5 Hz, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 23.4, 23.9, 30.0, 39.9, 58.5, 121.1, 122.9, 129.0, 132.5, 135.0, 138.5; found C, 58.95; H, 5.75; N, 6.14%; C₁₁H₁₃NO₂S requires C, 59.19; H, 5.83; N, 6.28%.

2-Phenyl-1-(toluene-4-sulfonyl)piperidine 34:⁵ Under N₂, at -78°C liquid NH₃ (*ca.* 100 cm³) was treated with Li (25 mg, 3.57 mmol, 5 eq.). The dark blue solution was stirred for 1h before a solution of the sulfonamide **33** (105 mg, 0.471 mmol, 1 eq.) in THF (5 cm³ + 5 cm³ washing) was added. The reaction was stirred for approximately 10 min before solid NH₄Cl (*ca.* 5 g) was added and the reaction was warmed to room temperature and the NH₃ allowed to evaporate. EtOAc (50 cm³) and H₂O (50 cm³) were added and the mixture was basified with 1 M NaOH solution (pH 12). The resultant aqueous layer was further extracted with EtOAc (3 x 50 cm³). The combined organic extracts were dried over MgSO₄ and the mixture was filtered and the solvent removed under reduced pressure. At room temperature the crude 2-phenylpiperidine (*ca.* 0.471 mmol, 1 eq.) was dissolved in CHCl₃ (5 cm³) and treated with TsCl (90 mg, 0.472 mmol, 1.0 eq.) and TEA (0.13 cm³, 0.933 mmol, 2 eq.). Stirring was continued for 5 h before silica (*ca.* 5 g) was added and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded **34** (104 mg, 70%) as a colourless fluffy solid. m.p = 120°C (EtOAc-Hex); *R*_f = 0.2 (Hex-EtOAc; 9:1); ν_{max} (CHCl₃/cm⁻¹) 3054, 2986, 2947, 1422, 1260, 1155; *m/z* (CI) 316 (MH⁺, 100%); found 316.13750, C₁₈H₂₁NO₂S·H requires 316.13712 (+1.2 ppm); ¹³C-NMR (CDCl₃, 100 MHz) δ = 1.26-1.55 (m, 5H), 1.62-1.74 (m, 1H), 2.21-2.26 (m, 1H), 2.48 (s, 3H), 3.03 (ddd, app. dt, *J*=3.0, 13.0 Hz, 1H), 3.87 (d, *J*=13.0 Hz, 1H), 7.23-7.37 (m, 7H), 7.78 (d, *J*=8.0 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 18.9, 21.5, 24.3, 27.2, 41.8, 55.2, 126.8, 126.95, 127.0, 128.6, 129.7, 138.7, 138.8, 142.9; found C, 68.48; H, 6.66; N, 4.41%; C₁₈H₂₁NO₂S requires C, 68.57; H, 6.66; N, 4.44%.

5S-(tert-Butyldiphenylsilanyloxymethyl)pyrrolidin-2-one 36:⁶ A solution of **35** (5.17 g, 44.91 mmol, 1 eq.) and TBDPSCl (14.6 cm³, 56.14 mmol, 1.25 eq.) in dry DCM (500 cm³) was treated with TEA (9.5 cm³, 68.16 mmol, 1.5 eq.) and stirred for

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5 days at room temperature. Saturated NH_4Cl (500 cm^3) was added and the resultant aqueous layer was extracted with DCM (500 cm^3). The combined organic extracts were dried over MgSO_4 , filtered and the solvent removed under reduced pressure. The crude material was purified by flash column chromatography (Hex-EtOAc; 5:1 $\rightarrow$ Hex-EtOAc; 1:1) affording **36** (7.30 g, 46%) as a clear viscous oil. $R_f = 0.15$ (Hex-EtOAc; 1:1); ν_{max} ($\text{CDCl}_3/\text{cm}^{-1}$) 3431, 3054, 2985, 2895, 2860, 1701, 1697, 1428, 1266, 1113; m/z (CI) 354 (MH^+ , 100%); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) $\delta = 1.08$ (s, 9H), 1.70-1.80 (m, 1H), 2.12-2.21 (m, 1H), 2.28-2.43 (m, 2H), 3.54 (dd, $J=7.5$, 10.5 Hz, 1H), 3.65 (dd, $J=3.5$, 10.5 Hz, 1H), 3.77-3.87 (m, 1H), 6.02 (s(br), 1H), 7.38-7.49 (m, 6H), 7.67 (d, $J=7.0$ Hz, 4H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) $\delta = 19.1$, 22.7, 26.7, 29.7, 55.7, 67.4, 127.8, 129.9, 132.9, 135.45, 135.5, 177.9.

1-(2-Bromobenzenesulfonyl)-5S-(tert-butyl diphenylsilanyloxymethyl)pyrrolidin-2-one 37: Under nitrogen at 0°C a 2.5 M solution of $^n\text{BuLi}$ in hexanes (1.5 cm^3 , 3.75 mmol, 1.05 eq.) was added dropwise to a solution of **36** (1.31 g, 3.71 mmol, 1.05 eq.) in THF (40 cm^3). The mixture was stirred for 0.5 h before 2-bromobenzenesulfonylchloride **3** (0.90 g, 3.52 mmol, 1.0 eq.) was added in one portion. Stirring was maintained for 1 h at 0°C before a saturated aqueous solution of NH_4Cl (50 cm^3) and EtOAc (75 cm^3) were added. The resultant aqueous layer was further extracted with EtOAc ($3 \times 50\text{ cm}^3$) and the combined organic extracts were dried over MgSO_4 . Filtration followed by solvent removal *in vacuo* and purification flash column chromatography (Hex-EtOAc; 5:1 $\rightarrow$ Hex-EtOAc; 2:1) gave the product **37** (1.58 g, 74%) as a colourless viscous oil. $R_f = 0.2$ (Hex-EtOAc; 5:1); $[\alpha]_D^{25} +12.0$ ($c = 1.0$, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3020, 2961, 2858, 1738, 1655, 1428, 1357, 1174, 1112; m/z (ES^+) 596 (MNa^+ , ^{81}Br , 100%), 594 (MNa^+ , ^{79}Br , 100%); found 596.0705, $\text{C}_{27}\text{H}_{30}\text{NO}_4^{81}\text{BrSSi-Na}$ requires 596.0725 (-3.4 ppm); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) $\delta = 1.12$ (s, 9H), 2.15-2.22 (m, 1H), 2.28-2.40 (m, 2H), 2.73-2.85 (m, 1H), 3.92 (dd, $J=2.5$, 10.5 Hz, 1H), 4.12 (dd, $J=4.5$, 10.5 Hz, 1H), 4.70-4.76 (m, 1H), 7.41-7.50 (m, 7H), 7.55 (t, $J=7.5$ Hz, 1H), 7.68-7.80 (m, 5H), 8.41 (dd, $J=1.5$, 8.0 Hz, 1H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) $\delta = 19.2$, 22.5, 26.8, 31.4, 61.7, 66.3, 119.8, 127.7, 127.8, 127.85, 129.85, 129.9, 132.2, 133.0, 134.2, 134.6, 135.0, 135.5, 135.8, 137.8, 173.9.

1-(2-Bromobenzenesulfonyl)-2S-(tert-butyl diphenylsilanyloxymethyl)-2,3-dihydro-1H-pyrrole 38: Under N_2 , at -78°C a stirred solution of **37** (1.584 g, 2.77 mmol, 1 eq.) in CH_2Cl_2 (40 cm^3) was treated dropwise with a 1 M solution of Dibal in hexane (4.15 cm^3 , 4.15 mmol, 1.5 eq.). The mixture was stirred at -78°C to -20°C for 2 h. Methanol (10 cm^3) was added and the mixture was warmed to room

temperature before pouring into a saturated aqueous solution of Rochelle's salt (50 cm³) and partitioning for 1 h. The phases were separated and the aqueous phase was further extracted with DCM (3 x 50 cm³). The combined organic phases were dried over MgSO₄, filtered and the solvent removed *in vacuo*. The residue was dissolved in toluene (30 cm³) and citric acid monohydrate (140 mg, 0.67 mmol, 0.25 eq.) was added and the mixture was heated to reflux with constant removal of water for 5 h (Dean-Stark apparatus). On cooling silica (*ca.* 5 g) was added and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 5:1) gave the unstable **38** (1.09 g, 71%) as a colourless viscous oil. *R*_f = 0.25 (Hex-EtOAc; 5:1); ν_{max} (CH₂Cl₂/cm⁻¹) 3071, 2931, 2858, 1622, 1428, 1360, 1323, 1173, 1113; *m/z* (ES⁺) 580 (MNa⁺, ⁸¹Br, 100%), 578 (MNa⁺, ⁷⁹Br, 100%); found 580.0757, C₂₇H₃₀NO₄⁸¹BrSSi·Na requires 580.0776 (-3.3 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.09 (s, 9H), 2.72-2.76 (m, 2H), 3.73 (dd, *J*=7.5, 10.5 Hz, 1H), 3.80 (dd, *J*=4.0, 10.5 Hz, 1H), 4.17-4.23 (m, 1H), 5.09 (dt, *J*=2.5, 4.5 Hz, 1H), 6.49 (dt, *J*=2.0, 4.5 Hz, 1H), 7.32-7.49 (m, 8H), 7.58-7.65 (m, 4H), 7.65-7.69 (m, 1H), 7.87-7.90 (m, 1H); ¹³C-NMR (CDCl₃, 100 MHz) δ = 19.2, 26.8, 33.2, 60.6, 65.0, 109.6, 120.3, 127.5, 127.7, 129.7, 130.4, 131.6, 133.2, 133.4, 135.5, 135.55, 135.6, 135.8, 138.2. NB. **38** is unstable in CDCl₃ and is used as quickly as possible.

3S-(tert-Butyldiphenylsilyloxymethyl)-1,2,3,9bS-tetrahydrobenzo[d]pyrrolo[1,2-b] isothiazole-5,5-dioxide *anti*-41 and 3S-(tert-Butyldiphenylsilyloxymethyl)-1,2,3,9bR-tetrahydrobenzo[d]pyrrolo[1,2-b]isothiazole-5,5-dioxide *syn*-41: Under N₂, a mixture of **38** (1.00 g, 1.80 mmol, 1 eq.), Pd(OAc)₂ (40 mg, 0.18 mmol, 10 mol%), PPh₃ (94 mg, 0.36 mmol, 20 mol%) and K₂CO₃ (500 mg, 3.62 mmol, 2 eq.) in DMF (30 cm³) were heated at 110°C for 16 h. On cooling Et₂O (50 cm³) and H₂O (50 cm³) were added and the resultant aqueous layer was further extracted with Et₂O (2 x 50 cm³). The combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal gave the crude product, which was purified by flash column chromatography (Hex-EtOAc; 5:1) affording an inseparable mixture of **39** and **40** (564 mg, 66%) as a viscous oil [**39**:**40**; 8:1, judged by ¹H-NMR spectroscopy]. *R*_f = 0.2 (Hex-EtOAc; 5:1). This mixture of regioisomeric alkenes (564 mg, 1.19 mmol, 1 eq.) was dissolved in EtOH (25 cm³) and 5% Pd/C (219 mg, 0.2 mmol, 10 mol%), was added before stirring under a hydrogen atmosphere at room temperature for 15 h. Filtration through celite[®] and washing with ethanol (3 x 20 cm³), solvent removal *in vacuo* followed by flash column chromatography (Hex-EtOAc; 5:1) gave **41** (510 mg, 90%) as an inseparable mixture of diastereomers [*anti*-**41**:*syn*-**41**; 3:1, judged by nOe experiments]. Further purification by careful flash column chromatography (Hex-DCM; 1:1) allowed the partial separation of the diastereomers, thus an analytical sample of *anti*-**41** was obtained as a colourless viscous oil. *R*_f = 0.3 (Hex-EtOAc; 5:1), 0.2 (Hex-DCM; 1:1); [α]_D²⁵ -44.2 (*c* = 2.0, CHCl₃); ν_{max} (CHCl₃/cm⁻¹) 3020, 2963, 2933, 2860, 1641, 1428, 1307, 1265, 1215, 1113; *m/z* (ES⁺) 516 (MK⁺, 20%), 500 (MNa⁺, 100%); found 500.1692, C₂₇H₃₁NO₃SSi·Na requires 500.1692 (+0.1 ppm); ¹H-NMR (CDCl₃, 400 MHz) δ = 1.11 (s, 9H), 1.81-1.92 (m, 1H), 1.98-2.15 (m, 2H), 2.43-2.52 (m, 1H), 3.73 (dd, *J*=6.5, 10.25 Hz, 1H), 3.85 (dd, *J*=5.25, 10.25 Hz, 1H), 4.27 (ddd, *J*=6.5,

12.6 Hz, 1H), 5.02 (dd, app. t, $J=7.0$ Hz, 1H), 7.36 (d, $J=7.5$ Hz, 1H), 7.39-7.47 (m, 6H), 7.53 (t, $J=7.5$ Hz, 1H), 7.62 (dt, $J=1.0$, 7.5 Hz, 1H), 7.71-7.79 (m, 5H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 19.2, 26.8, 29.1, 32.0, 61.4, 65.7, 66.7, 121.6, 123.7, 127.7, 129.3, 129.7, 133.0, 133.2, 134.8, 135.6, 135.7.

Further elution gave the minor diastereomer *syn*-**41** as a viscous oil. R_f = 0.3 (Hex-EtOAc; 5:1), 0.2 (Hex-DCM; 1:1); $[\alpha]_D^{25}$ -8.0 (c = 1.0, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3020, 2963, 2860, 1641, 1428, 1307, 1215, 1171, 1113; m/z (ES^+) 516 (MK^+ , 10%), 500 (MNa^+ , 100%); found 500.1671, $\text{C}_{27}\text{H}_{31}\text{NO}_3\text{SSi}\cdot\text{Na}$ requires 500.1692 (-4.1 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 0.98 (s, 9H), 1.86-2.08 (m, 1H), 2.21-2.35 (m, 2H), 2.37-2.45 (m, 1H), 3.86-4.09 (m, 3H), 4.97 (dd, app. t, $J=8.25$ Hz, 1H), 7.33-7.45 (m, 7H), 7.47 (t, $J=7.75$ Hz, 1H), 7.52-7.61 (m, 5H), 7.69 (d, $J=7.5$ Hz, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 19.0, 26.7, 29.7, 31.7, 62.0, 62.1, 64.5, 120.6, 123.5, 127.6, 128.8, 129.6, 132.3, 132.9, 135.5, 135.6, 139.0.

The separated diastereoisomers were both subjected to nOe measurements. Thus, irradiation of *syn*-**41** at 4.97 ppm gave an enhancement at 2.30 ppm which in turn on irradiation gave an enhancement at 4.05 ppm and *vice versa*. No similar enhancements were observed for *anti*-**41**.

(5,5-Dioxo-2,3*S*,5,9*bR*-tetrahydro-1*H*-5 λ^6 -benzo[d]pyrrolo[1,2-*b*]isothiazol-3-yl)methanol *syn*-42 and (5,5-Dioxo-2,3*S*,5,9*bS*-tetrahydro-1*H*-5 λ^6 -benzo[d]pyrrolo[1,2-*b*]isothiazol-3-yl)methanol *anti*-42: A mixture of *syn*-**41** and *anti*-**41** (370 mg, 0.78 mmol, 1 eq.) in THF (25 cm^3) was treated with a 1 M solution of TBAF in THF (0.8 cm^3 , 0.80 mmol, 1 eq.) in a dropwise fashion. The mixture was stirred for 1.5 h before silica (*ca.* 5 g) was added and the solvent removed *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 1:1) initially gave *syn*-**42** (58 mg, 31%) as a colourless viscous oil. R_f = 0.2 (Hex-EtOAc; 1:1); $[\alpha]_D^{25}$ +24.0 (c = 1.0, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3441, 3020, 2931, 1630, 1472, 1290, 1217, 1160, 1158; m/z (CI) 257 (MNH_4^+ , 100%), 240 (MH^+ , 50%); found 240.06957, $\text{C}_{11}\text{H}_{13}\text{NO}_3\text{S}\cdot\text{H}$ requires 240.06943 (+0.6 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 1.88-1.97 (m, 1H), 2.22-2.44 (m, 3H), 2.71 (s(br), 1H), 3.80 (dd, $J=4.0$, 12.75 Hz, 1H), 4.06-4.10 (m, 1H), 4.28 (dd, $J=3.0$, 12.75 Hz, 1H), 4.94 (dd, $J=6.0$, 9.0 Hz, 1H), 7.39 (d, $J=7.5$ Hz, 1H), 7.54 (t, $J=7.5$ Hz, 1H), 7.62 (dt, $J=1.0$, 7.5 Hz, 1H), 7.75 (dd, $J=1.0$, 7.5 Hz, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 29.9, 32.0, 62.5, 62.55, 65.7, 121.0, 123.6, 129.2, 132.8, 138.0, 138.8.

Further elution gave *anti*-**42** (110 mg, 59%) as a colourless viscous oil. R_f = 0.15 (Hex-EtOAc; 1:1); $[\alpha]_D^{25}$ -66.0 (c = 1.0, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3425, 3020, 2960, 1639, 1303, 1215, 1170; m/z (CI) 257 (MNH_4^+ , 100%), 240 (MH^+ , 70%); found 240.06934, $\text{C}_{11}\text{H}_{13}\text{NO}_3\text{S}\cdot\text{H}$ requires 240.06943 (-0.4 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 1.79-1.89 (m, 1H), 2.05 (s(br), 1H), 2.03-2.21 (m, 2H), 2.48-2.55 (m, 1H), 3.65 (dd, $J=6.0$, 11.5 Hz, 1H), 3.86 (dd, $J=4.0$, 11.5 Hz, 1H), 4.17-4.24 (m, 1H), 5.07 (dd, app. t, $J=7.25$ Hz, 1H), 7.38 (dd, $J=1.0$, 7.5 Hz, 1H), 7.55 (t, $J=7.5$ Hz, 1H), 7.63

(dt, $J=1.0, 7.5$ Hz, 1H), 7.79 (d, $J=7.5$ Hz, 1H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 29.1, 32.4, 61.9, 64.9, 66.0, 121.8, 123.8, 129.5, 133.3, 135.5, 139.2.

The separated diastereoisomers were both subjected to nOe measurements. Irradiation of *syn*-**42** at 4.94 ppm gave an enhancement at 4.08 ppm and *vice versa*. No similar enhancements were observed for *anti*-**42**.

[5*S*-Phenyl-1-(toluene-4-sulfonyl)pyrrolidin-2*S*-yl]methanol **44:** Under N_2 , at -78°C liquid NH_3 (*ca.* 100 cm^3) was treated with Li (21 mg, 3.09 mmol, 6 eq.). The dark blue solution was stirred for 1 h before a solution of *anti*-**42** (123 mg, 0.515 mmol, 1 eq.) in THF (5 cm^3 + 5 cm^3 washing) was added. The reaction was stirred for approximately 5 min before solid NH_4Cl (*ca.* 3 g) was added and the reaction was warmed to room temperature and the NH_3 allowed to evaporate. Et_2O (50 cm^3) and H_2O (50 cm^3) were added and the mixture was basified with 1 M NaOH solution (pH 10). The resultant aqueous layer was further extracted with Et_2O (3 x 50 cm^3). The combined organic extracts were dried over MgSO_4 before filtration and solvent removal under reduced pressure. At room temperature the crude amine *anti*-**43** (*ca.* 0.515 mmol, 1 eq.) was dissolved in CH_2Cl_2 (5 cm^3) and treated with TsCl (97 mg, 0.509 mmol, 0.99 eq.) and TEA (0.14 cm^3 , 1.00 mmol, 1.95 eq.). Stirring was continued for 15 h before silica (*ca.* 5 g) was added and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 1:1) afforded *anti*-**44** (75 mg, 44%) isolated as a colourless solid. R_f = 0.4 (Hex-EtOAc; 1:1), 0.4 (Hex-DCM; 1:4); $[\alpha]_{\text{D}}^{25}$ -17.0 (c = 1.0, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3424, 3020, 2958, 1637, 1331, 1216, 1156, 1098; m/z (CI) 349 (MNH_4^+ , 50%), 332 (MH^+ , 100%); found 332.13220, $\text{C}_{18}\text{H}_{21}\text{NO}_3\cdot\text{H}$ requires 332.13205 (+0.5 ppm); ^1H -NMR (CDCl_3 , 400 MHz) δ = 1.73-1.80 (m, 1H), 1.98-2.07 (m, 1H), 2.27-2.42 (m, 1H), 2.37 (s, 3H), 2.43-2.49 (m, 1H), 2.70 (s(br), 1H), 3.90 (dd, $J=3.0, 11.75$ Hz, 1H), 3.97 (dd, $J=3.0, 11.75$ Hz, 1H), 4.00-4.07 (m, 1H), 5.06 (d, $J=8.5$ Hz, 1H), 6.95 (d, $J=7.5$ Hz, 2H), 7.06 (d, $J=8.0$ Hz, 2H), 7.11 (t, $J=7.5$ Hz, 2H), 7.18 (t, $J=7.5$ Hz, 1H), 7.26 (d, $J=8.0$ Hz, 2H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ = 21.4, 28.7, 33.5, 62.6, 65.4, 65.7, 126.9, 127.0, 127.1, 128.1, 129.0, 137.4, 141.7, 142.8; found C, 64.93; H, 6.35; N, 4.13%; $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}$ requires C, 65.26; H, 6.34; N, 4.23%.

[5*R*-Phenyl-1-(toluene-4-sulfonyl)pyrrolidin-2*S*-yl]methanol **44:**⁷ As described above a solution of the sulfonamide *syn*-**42** (104 mg, 0.435 mmol, 1 eq.) in THF (5 cm^3 + 5 cm^3 washing) was added to a preformed solution of lithium (19 mg, 2.71 mmol, 6.2 eq.) in liquid ammonia (*ca.* 100 cm^3). The resultant crude amine *syn*-**43** (*ca.* 0.435 mmol, 1 eq.) in CHCl_3 (5 cm^3) was treated with TsCl (82 mg, 0.430 mmol, 0.99 eq.) and TEA (0.12 cm^3 , 0.860 mmol, 2 eq.). Purification by flash column

(7) Reference: Gallagher, T.; Jones, S. W.; Mahon, M. F.; Molloy, K. C. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2193.

chromatography (Hex-EtOAc; 1:1) afforded *syn*-**44** (66 mg, 46%) as a colourless crystalline solid. Crystal suitable for X-ray structure analysis were grown in EtOAc. m.p. 108°C (EtOAc); $R_f = 0.4$ (Hex-EtOAc; 1:1); $[\alpha]_D^{25} +86.0$ ($c = 1.0$, CHCl_3); ν_{max} ($\text{CHCl}_3/\text{cm}^{-1}$) 3423, 3020, 2960, 1641, 1216, 1150, 1045; m/z (CI) 349 (MNH_4^+ , 20%), 332 (MH^+ , 100%); found 332.13220, $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}\cdot\text{H}$ requires 332.13205 (+0.5 ppm); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) $\delta = 1.64$ -1.75 (m, 2H), 1.80-1.96 (m, 2H), 2.43 (s, 3H), 3.53 (s(br), 1H), 3.73-3.77 (m, 1H), 3.81-3.92 (m, 2H), 4.79 (dd, app. t, $J=7.0$ Hz, 1H), 7.26 (t, $J=7.25$ Hz, 1H), 7.31-7.37 (m, 4H), 7.41(d, $J=7.5$ Hz, 2H), 7.75 (d, $J=8.5$ Hz, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz) $\delta = 21.5$, 27.4, 33.7, 63.5, 65.3, 65.8, 126.1, 127.1, 127.7, 128.4, 129.8, 134.0, 142.1, 144.0; found C, 64.97; H, 6.25; N, 4.34%; $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}$ requires C, 65.26; H, 6.34; N, 4.23%.

X-ray Structure of *syn*-[5*R*-Phenyl-1-(toluene-4-sulfonyl)pyrrolidin-2*S*-yl]methanol **44:**

$\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}$ $M = 331.42$, orthorhombic spacegroup $P2_12_12_1$, $a = 7.8668(2)$ Å, $b = 13.3346(17)$ Å, $c = 16.4644(4)$ Å, $\beta = 90.000(3)^\circ$, $U = 1727.13(5)$ Å³, $T = 150$ K, $Z = 4$, $\mu(\text{Mo}, \text{K}\alpha) = 0.200$ mm⁻¹, 17039 measured reflections, 4186 unique ($R_{\text{int}} = 0.0219$). The final wR^2 was 0.1086 (all data), Flack = -0.01(5),⁸ CCDC reference number: 247297.

(8) See Flack, H. D. *Acta Cryst.* **1983**, *A39*, 876

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BMI/224 NH
carbon, ly CDCl₃ (C: w) smr 25

BM1223_Tosyl
carbon,lv CDCl3 {C:lv} smr 24

P. Evans
BM11229
carbon, lvs CDCl₃ (C¹³), w/ san 23