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SUPPORTING INFORMATION

Title: Optically Active γ-Hydroxy Sulfone Julia Reagents for the Synthesis of Peptidyl Olefin Peptidomimetics
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Experimental procedures

General

Anhydrous solvents were dried and freshly distilled (THF, DME, ether and toluene from sodium/benzophenone, DMF from molecular sieves, and CH_2Cl_2 from $CaCl_2$).

Chromatography refers to flash column chromatography, carried out on silica gel 60 (230-400 mesh ASTM, E. Merck), using analytical grade solvents. TLC was performed on E. Merck 0.2 mm percolated silica gel F-254 plates. Compounds were detected by UV light (254 nm) and/or by staining with vanillin, or phosphomolybdic acid.

^1H and ^{13}C NMR spectra were recorded at 600 or 300 MHz and 150 or 75 MHz, respectively, in $CDCl_3$, unless otherwise indicated. Chemical shifts are reported in ppm relative to TMS in $CDCl_3$ or relative to solvent resonance in other solvents. Most ^1H NMR assignments were supported by 2D homonuclear COSY and NOSEY experiments. ^{13}C NMR assignments were supported by DEPT or 2D heteronuclear COSY **(**HMQC**)** and heteronuclear multiple bond connectivity (HMBC) experiments. Mass spectra were recorded in DCI mode with methane as the reagent gas.

HPLC was carried out on CHIRALCEL$_R$ OD-H 250x10 mm or CHIRA GROM 250x2 mm chiral columns, at flow rates of 1mL/min and 0.3 mL/min, respectively.

Synthesis

Diols 1b-e. A three-necked round bottomed flask equipped with a pressure equalizing addition funnel, reflux condenser and drying tube was flushed with Ar and $LiAlH_4$ (5.7 g, 0.15 mol) was added. The flask was loaded dropwise with dry THF (100 mL). Diethyl alkyl melonate (0.1 mol) in dry THF (50 mL) was added dropwise over 1 h at r.t., via the pressure equalizing addition funnel, and the reaction mixture was refluxed for 3 days. The mixture was cooled to 0°C and quenched by 0.5M HCl (50 mL). The white suspension was diluted with water (100 mL) and its pH was adjusted to 7 with concentrated HCl. The aqueous solution was extracted with CH_2Cl_2 (3x300 mL). The volume of the combined organic layers was partially reduced to 100 mL under vacuum and washed with sat. $NaHCO_3$ and sat. NaCl solutions. The organic layer was dried over $MgSO_4$, filtered and evaporated to dryness. The aqueous solution was further extracted in a continueous extraction apparatus for 5 days, to give some more clean product.

2-(Hydroxymethyl) butanol (**1b**). 95% yield. ^1H NMR: δ 3.79 (dd, J=10.8, 3.9 Hz, 2H); 3.63 (dd, J=10.8, 7.5 Hz, 2H); 3.49 (bs, 2H, OH); 1.67 (quint.t, J=7.0, 4.2 Hz); 1.29 (quint, J=7.2 Hz, 2H); 0.94 (t, J=7.5 Hz, 3H). ^{13}C NMR: δ 64.7; 43.8; 20.6; 11.6. MS: *m/z* 105 (MH^+); 103; 86. HRMS: *m/z* for $C_5H_{13}O_2$ (MH^+): calcd. 105.0916, found 105.0895.

2-Hydroxymethyl-3-methyl butanol (**1c**). 94% yield. ^{1}H NMR: δ 3.83 (dd, J=10.8, 3.9 Hz, 2H); 3.75 (obscured, 2H); 3.73 (dd, J=10.8, 8.1 Hz, 2H); 1.72 (octet, J=6.8 Hz, 1H); 1.53 (qt, J=7.6, 3.8 Hz, 1H); 0.93 (d, J=6.6 Hz, 6H). ^{13}C NMR: δ 64.2; 47.9; 26.4; 20.3. MS: *m/z* 119 (MH^+, 7); 101 (9); 83 (16). HRMS: *m/z* for $C_6H_{15}O_2$ (MH^+): calcd. 119.1072, found 119.1071.

2-Hydroxymethyl-4-methyl pentanol (**1d**). 92% yield. ^{1}H NMR: δ 4.24 (bs, 2H); 3.65 (dd, J=10.5, 3.9 Hz, 2H); 3.49 (dd, J=10.5, 7.5 Hz, 2H); 1.80 (quint.t, J=7.4, 3.6 Hz, 1H); 1.62 (nonet, J=6.7 Hz, 1H); 1.07 (t, J=7.2 Hz, 2H); 0.90 (d, J=6.6 Hz, 6H). ^{13}C NMR: δ 65.3; 39.6; 36.9; 25.3; 22.8. MS: *m/z* 133 (MH^+, 10); 115 (10); 97 (52). HRMS: *m/z* for $C_7H_{17}O_2$ (MH^+): calcd. 133.1229, found 133.1232.

2-Benzyl-1,3-propanediol (**1e**). 97% yield. ^{1}H NMR: δ 7.29-7.13 (m, 5H); 3.72 (dd, J=10.8, 3.9 Hz, 2H); 3.59 (dd, J=10.8, 6.9 Hz, 2H); 3.41 (s, 2H); 2.56 (d, J=7.5 Hz, 2H); 2.00 (quint.t, J=7.4, 3.7 Hz, 1H). ^{13}C NMR: δ 139.9; 129.1; 128.5; 126.2; 64.9; 43.9; 34.3. MS: *m/z* 167 (MH^+, 0.2); 148 (65); 130 (32); 104 (20); 91 (71). HRMS: *m/z* for $C_{10}H_{15}O_2$ (MH^+): calcd. 167.1072, found 167.1063; for $C_{10}H_{12}O$ (M^+-H_2O): calcd. 148.0888, found 148.0880.

Diacetate 2a-e. AcCl (2.6 mL, 36 mmol) was added dropwise to a stirred solution of 2-alkyl-1,3-propanediol **1a-e** (12 mmol) in $CHCl_3$ (15 mL). After stirring at r.t. for 24 h, water (30 mL) was added and the solution was extracted with CH_2Cl_2 (3x40 mL). The combined organic layers were washed with saturated $NaHCO_3$ and saturated NaCl solutions, dried over $MgSO_4$, filtered and concentrated to give the clean product as a yellow oil.

2-(Acetoxymethyl) propyl acetate (**2a**). 94% yield. ^{1}H NMR: δ 4.01 (d, J=6.0 Hz, 4H); 2.17 (octet, J=6.3 Hz, 1H); 2.07 (s, 6H); 0.99 (d, J=6.9 Hz, 3H). ^{13}C NMR: δ 171.2; 66.0; 32.4; 21.0; 14.0. MS: m/z 175 (MH^+, 12); 133 (22); 115 (100). HRMS: *m/z* for $C_8H_{15}O_4$ (MH^+): calcd. 175.0970, found 175.0970; for $C_6H_{11}O_2$ (MH^+-CH_3CO_2H): calcd. 115.0759, found 115.0708.

2-(Acetoxymethyl) butyl acetate (**2b**). 88% yield. ^{1}H NMR: δ 4.03 (dd, J=11.1, 5.4 Hz, 2H); 3.98 (dd, J=11.1, 6.3 Hz, 2H); 1.99 (s, 6H); 1.86 (ttt, J=7.2, 6.3, 5.4 Hz, 1H); 1.35 (quint, J=7.4 Hz, 2H); 0.90 (t, J=7.5 Hz, 3H). ^{13}C NMR**:** δ 171.1; 64.0; 38.8; 21.1; 20.9; 11.2. MS: *m/z* 189 (MH^+, 9); 129 (100); 103 (16); 86 (53). HRMS: *m/z* for $C_9H_{17}O_4$ (MH^+): calcd. 189.1127, found 189.1165; for $C_7H_{13}O_2$ (MH^+-CH_3CO_2H): calcd. 129.0916, found 129.0894.

2-Acetoxymethyl-3-methyl butyl acetate (**2c**). 87% yield. ^{1}H NMR: δ 4.18 (dd, J=11.1, 4.5 Hz, 2H); 4.06 (dd, J=11.1, 6.3 Hz, 2H); 2.06 (s, 6H); 1.81 (m, 2H); 0.97 (d, J=6.0 Hz, 6H). ^{13}C NMR: δ 171.2; 63.0; 43.0; 26.9; 21.0; 20.0. MS: *m/z* 203 (MH$^+$); 143 (8); 114 (15). HRMS: *m/z* for $C_{10}H_{19}O_4$ (MH$^+$): calcd. 203.1283, found 203.1268.

2-Acetoxymethyl-4-methyl pentyl acetate (**2d**). 90% yield. ^{1}H NMR: δ 4.08 (dd, J=11.1, 5.1 Hz, 2); 4.01 (dd, J=11.1, 6.3 Hz, 2H); 2.08 (obscured, 1H); 2.06 (s, 6H); 1.67 (nonet, J=6.7 Hz, 1H); 1.22 (t, J=7.2 Hz, 2H); 0.91 (d, J=6.6 Hz, 6H). ^{13}C NMR: δ 170.7; 64.3; 37.3; 34.9; 25.0; 22.5; 20.6. MS: *m/z* 217 (MH$^+$, 3); 216 (M$^+$, 3); 173 (6); 157 (40); 114. HRMS: *m/z* for $C_{11}H_{21}O_4$ (MH$^+$): calcd. 217.1440, found 217.1474; for $C_9H_{17}O_2$ (MH$^+$-CH_3CO_2H): calcd. 157.1229, found 157.1232.

2-(Benzyl)-1,3-propanediol diacetate (**2e**). 96% yield. ^{1}H NMR: δ 7.30-7.12 (m, 5H); 4.07 (dd, J=11.1, 5.4 Hz, 2H); 4.00 (dd, J=11.1, 6.0 Hz, 2H); 2.68 (d, J=7.5 Hz, 2H); 2.31 (ttt, J=7.4, 6.0, 5.3 Hz, 1H); 2.03 (s, 6H). ^{13}C NMR: δ 170.8; 138.7; 128.9; 128.5; 126.4; 63.7; 39.1; 34.5; 20.8. MS: *m/z* 251 (MH$^+$, 0.9); 190 (33); 131 (39); 117 (28); 104 (12); 91 (44). HRMS: *m/z* for $C_{14}H_{19}O_4$ (MH$^+$): calcd. 251.1283, found 251.1272.

Monoacetate **3a-e**. Enzymatic (chiral) synthesis.

To a stirred suspension of diester **2a-e** (0.1-1 g) in aqueous solution containing 40 mM NaCl, 5mM $CaCl_2$, 0.07% BSA at pH 7.5 (2-5 mL) at 37°C, was added the enzyme lipase (from *Pseudomonas Cepacia*, 50u/mg, 12.5-40 mg). The pH of the suspension was kept constant by the continuous addition of 0.2M aqueous NaOH using an automatic titrator. The reaction was monitored by TLC (hexane: EtOAc 3:1) and NMR spectroscopy. When the desired degree of conversion was reached, the reaction was quenched by the addition of ether (8 mL) and the layers were separated. The aqueous layer was further extracted with ether (3x15 mL) and the combined extracts were washed with saturated NaCl solution, dried over $MgSO_4$ and concentrated to give a mixture of diester starting material, the monoester product and diol, which was separated by chromatography (hexane: EtOAc 3:1) to give the optically active monoester product as a yellow oil. The compounds were characterized by chiral HPLC analysis.

Monoacetate **3a-e**. Chemical (racemic) synthesis.

AcCl (0.75 mL, 10.6 mmol) was slowly added via a syringe to a solution of 2-alkyl-1,3-propanediol **1a-e** (10.6 mol) in $CHCl_3$ (8 mL) and the solution was stirred at r.t. for 30 min. Then, the mixture was diluted with water (75 mL) and extracted with CH_2Cl_2 (3x100 mL). The combined organic layers were washed with sat. $NaHCO_3$ and sat. NaCl solutions, dried over $MgSO_4$, filtered and evaporated to dryness.

Chromatography (hexane: EtOAc 4:1) separated the desired monoacetate **3a-e** (major product) from the diacetate **2a-e** (minor product) and some diol **1a-e** starting material.

2-(Acetoxymethyl) propanol (**3a**). 28% yield. ^{1}H NMR: δ 4.08 (dd, J=11.1, 5.7 Hz, 1H); 4.03 (dd, J=11.1, 6.9 Hz, 1H); 3.56 (dd, J=11.1, 5.4 Hz, 1H); 3.52 (dd, J=11.1, 5.7 Hz, 1H); 2.21 (quint.q, J=6.9, 5.5 Hz, 1H); 2.07 (s, 3H,); 1.06 (d, J=6.9 Hz, 3H). ^{13}C NMR: δ 171.0; 65.9; 47.3; 35.1; 20.9; 14.8. MS: *m/z* 133 (MH$^+$, 20); 115 (34); 73 (60). HRMS: *m/z* for $C_6H_{13}O_3$ (MH$^+$): calcd. 133.0865, found 133.0867.

2-(Acetoxymethyl) butanol (**3b**). 36% yield. ^{1}H NMR: δ 4.07 (dd, J=11.1, 5.1 Hz, 1H); 4.01 (dd, J=11.1, 6.3 Hz, 1H); 3.51 (dd, J=11.1, 4.8 Hz, 1H); 3.44 (dd, J=11.1, 6.3 Hz, 1H); 2.81 (bs, 1H); 1.98 (s, 3H); 1.64 (ttt, J=6.9, 6.3, 5.1 Hz, 1H); 1.32 (dqd, J=13.8, 7.8, 6.9 Hz, 1H); 1.27 (dqd, J=13.8, 7.8, 6.9 Hz, 1H); 0.87 (t, J=7.5 Hz, 3H). ^{13}C NMR: δ 171.7; 64.4; 62.1; 41.9; 20.8; 20.6; 11.3. MS: *m/z* 147 (MH$^+$, 100); 129 (73); 103 (15); 87 (43); 69 (73). HRMS: *m/z* for $C_7H_{15}O_3$ (MH$^+$): calcd. 147.1021, found 147.1033; for $C_7H_{13}O_2$ (MH$^+$-H_2O): calcd. 129.0916, found 129.0931.

2-Acetoxymethyl-3-methyl butanol (**3c**). 32% yield. ^{1}H NMR: δ 4.25 (dd, J=11.1, 4.8 Hz, 1H); 4.13 (dd, J=11.1, 6.3 Hz, 1H); 3.68 (dd, J=11.1, 4.8 Hz, 1H); 3.57 (dd, J=11.1, 6.6 Hz, 1H); 3.03 (bs, 1H); 2.07 (s, 3H); 1.81 (octet, J=6.9 Hz, 1H); 1.61 (qt, J=6.6, 4.8 Hz, 1H); 0.96 (d, J=6.9 Hz, 3H); 0.95 (d, J=6.9 Hz, 3H). ^{13}C NMR: δ 171.6; 63.4; 60.9; 46.1; 26.3; 20.9; 20.2; 19.8. MS: *m/z* 161 (MH$^+$); 143; 101. HRMS: *m/z* for $C_8H_{17}O_3$ (MH$^+$): calcd. 161.1178, found 161.1174.

2-Acetoxymethyl-4-methyl pentanol (**3d**). 41% yield. ^{1}H NMR: δ 4.13 (dd, J=11.1, 4.5 Hz, 1H); 4.01 (dd, J=11.1, 6.3 Hz, 1H); 3.54 (dd, J=11.1, 4.5 Hz, 1H); 3.44 (dd, J=11.1, 6.3 Hz, 1H); 2.56 (bs, 1H); 2.02 (s, 3H); 1.84 (quint.t, J=6.8, 4.5 Hz, 1H); 1.62 (nonet, J=6.8 Hz, 1H); 1.17 (dt, J=14.1, 7.2 Hz, 1H); 1.08 (dt, J=14.1, 7.2 Hz, 1H); 0.86 (d, J=6.6 Hz, 6H). ^{13}C NMR: δ 171.8; 64.9; 62.8; 38.1; 37.1; 25.2; 22.8; 22.7; 21.0. MS: *m/z* 174 (M$^+$); 157 (100); 114 (15). HRMS: *m/z* for $C_9H_{17}O_2$ (MH$^+$-H_2O): calcd. 157.1229, found 157.1253.

2-Benzyl-1,3-propanediol monoacetate (**3e**). 47% yield. ^{1}H NMR: δ 7.32-7.16 (m, 5H); 4.14 (dd, J=11.4, 5.0 Hz, 1H); 4.06 (dd, J=11.4, 6.3 Hz, 1H); 3.58 (dd, J=11.1, 4.8 Hz, 1H); 3.49 (dd, J=11.1, 6.0 Hz, 1H); 2.69 (dd, J=13.8, 7.5 Hz, 1H); 2.61 (dd, J=13.8, 6.3 Hz, 1H); 2.59 (s, 1H); 2.13 (dqt, J=7.5, 6.2, 5.0 Hz, 1H); 2.05 (s, 3H). ^{13}C NMR: δ 171.6; 139.4; 129.0; 128.4; 126.1; 64.0; 61.8; 42.3; 34.2; 20.8. MS: *m/z*

208 (M^+); 190 (5); 148 (56); 130 (55); 117 (100); 91 (30). HRMS: *m/z* for $C_{12}H_{17}O_3$ (MH^+): calc. 209.1178, found 209.1175.

(3-Acetoxy-2-benzyl-propoxy) *tert*-butyl dimethyl silane (**4**). 2-(Benzyl)-1,3-propanediol monoacetate **3e** (5.7 g, 27.2 mmol) in dry DMF (20 mL) was added to a solution of imidazole (2.7 g, 39.5 mmol) and *t*-butylchlorodimethylsilane (6.0 g, 39.5 mmol) in dry DMF (60 mL). After stirring overnight at r.t., the mixture was diluted with ether (100 mL) and water (50 mL) and the layers were separated. The aqueous phase was further extracted with CH_2Cl_2 (3x75 mL) and the combined organic layers were washed with water and brine, dried over $MgSO_4$ and filtered. Evaporation of the solvent afforded the clean product as a yellow oil (8.72 g, 99% yield). ^1H NMR: δ 7.35-7.19 (m, 5H); 4.10 (d, J=6.0 Hz, 2H); 3.62 (dd, J=9.9, 4.8 Hz, 1H); 3.55 (dd, J=9.9, 5.1 Hz, 1H); 2.75 (dd, J=13.7, 7.7 Hz, 1H); 2.64 (dd, J=13.7, 7.1 Hz, 1H); 2.14 (septet, J=6.1 Hz, 1H); 2.06 (s, 3H); 0.95 (s, 9H); 0.07 (s, 6H). ^{13}C NMR: δ 171.0; 139.8; 129.1; 128.4; 126.1; 64.3; 61.8; 42.2; 34.2; 25.9; 20.9; 18.3; -5.5; -5.6. HRMS: *m/z* for $C_{18}H_{31}O_3Si$ (MH^+): calc. 323.2042, found 323.2082.

2-Benzyl-3-hydroxypropoxy *tert*-butyl dimethyl silane (**5**). Sodium carbonate (12 g) was added to a stirred solution of acetate **4** (8.7 g, 27.0 mmol) in dry MeOH (500 mL). The suspension was stirred vigorously at r.t. for 1.5 h, when TLC (hexane: EtOAc 5:1) indicated full consumption of the starting material. The reaction mixture was filtered off to remove the sodium carbonate and repeatedly washed with methanol and ether. The filtrate was evaporated to dryness and the residue was dissolved in ether. The ether phase was washed with acidic water (pH 2.5, 3x80 mL) until the pH of the aqueous layer was neutral. Then the ether phase was washed with sat. NaCl solution, dried over $MgSO_4$, filtered and evaporated to give the desired product as a yellow oil (6.97 g, 92% yield). ^1H NMR: δ 7.35-7.16 (m, 5H); 3.77 (dd, J=9.9, 4.2 Hz, 1H); 3.75 (dd, J=10.7, 3.8 Hz, 1H); 3.65 (dd, J=10.7, 6.5 Hz, 1H); 3.65 (dd, J=9.9, 6.3 Hz, 1H); 2.93 (bs, 1H); 2.68 (dd, J=13.5, 7.8 Hz, 1H); 2.63 (dd, J=13.5, 5.4 Hz, 1H); 2.02 (ttt, J=7.5, 6.5, 3.9 Hz, 1H); 0.95 (s, 9H); 0.09 (s, 3H); 0.09 (s, 3H). ^{13}C NMR: δ 140.2; 129.1; 128.4; 126.0; 65.6; 65.2; 44.2; 34.2; 25.9; 18.2; -5.5. MS: *m/z* 269 (MH^+); 131 (100); 117 (10); 105 (21); 91 (46). HRMS: *m/z* for $C_{15}H_{29}O_2Si$ (MH^+): calcd. 269.1937, found 269.1936.

2-Benzyl-3-(*t*-butyl dimethyl silyloxy) propyl methane sulfonate (**6**). A solution of alcohol **5** (1.2 g, 4.3 mmol) and Et_3N (0.9 mL, 6.4 mmol) in dry CH_2Cl_2 (7 mL), under argon atmosphere was cooled to 0°C. The solution was stirred for 30 min, followed by slow addition (10 min) of MsCl (0.5 mL, 6.6 mmol) in dry CH_2Cl_2 (1.5 mL). Stirring was continued at 0°C under argon atmosphere for 3 h. The solution turned yellow. Ether was added, and the solution was washed with 1N HC1, saturated $NaHCO_3$ and saturated NaCl solutions. The organic phase was dried over $MgSO_4$, filtered and concentrated to give the clean product (1.51 g, 98% yield). ^{1}H NMR :δ 7.31-7.16 (m, 5H); 4.21 (dd, J=9.6, 5.1 Hz, 1H); 4.17 (dd, J=9.6, 6 Hz, 1H); 3.63 (dd, J=10.2, 4.5 Hz, 1H); 3.53 (dd, J=10.2, 6 Hz, 1H); 2.93 (s, 3H); 2.70 (dd, J=13.7, 7.8 Hz, 1H); 2.64 (dd, J=13.7, 7.2 Hz, 1H); 2.16 (tquint, J=7.5, 5.4 Hz, 1H); 0.91 (s, 9H); 0.04 (s, 6H). **^{13}C** NMR :δ 138.9; 129.1; 128.5; 126.3; 69.4; 61.1; 42.7; 36.8; 33.5; 25.9; 18.2; -5.5. HRMS *m/z* for $C_{17}H_{31}O_4SiS$ (MH$^+$): calc. 359.1712, found 359.1721.

2-Benzyl-3-(*t*-butyl dimethyl silyloxy) propyl (1-phenyl-1*H*-tetrazol-5-yl) sulfide (**7**)._-1Phenyl-1*H*-tetrazol-5-thiol (2.46 g, 13.8 mmol) was dissolved in dry THF (29 mL). NaH (60% in mineral oil, 0.54 g) was added slowly and the white suspension was stirred at r.t. for 15 min. A solution of mesylate **6** (1.5 g, 4.2 mmol), in dry THF (6 mL), was added and the mixture was stirred overnight at 50°C. The mixture was cooled to r.t., diluted with CH_2Cl_2 (30 mL) and washed with 10% NaOH solution (50 mL). The aqueous phase was re-extracted with CH_2Cl_2 (3x50 mL) and the volume of the combined organic phase was partially reduced to 50 mL under vacuum. The organic layer was washed with saturated NaCl solution, dried over $MgSO_4$, filtered and evaporated to provide a yellow oil, which was chromatographed (hexane: EtOAc 5:1) to give the clean product (1.34 g, 73% yield). ^{1}H NMR :δ 7.59-7.50 (m, 5H); 7.30-7.16 (m, 5H); 3.64 (dd, J=10.2, 3.9 Hz, 1H); 3.52 (dd, J=13.0, 6.4 Hz, 1H); 3.50 (dd, J=10.2, 4.5 Hz, 1H); 3.47 (dd, J=13.0, 6.8 Hz, 1H); 2.78 (d, J=7.2 Hz, 2H); 2.30 (ttt, J=7.8, 6.6, 4.3 Hz, 1H); 0.90 (s, 9H); 0.01 (s, 3H); 0.01 (s, 3H). **^{13}C** NMR :δ 154.7; 139.5; 133.9; 130.2; 129.9; 129.3; 128.5; 126.3; 124.0; 62.7; 42.3; 36.6; 35.3; 26.0; 18.3; -5.40; -5.44. HRMS *m/z* for $C_{23}H_{33}N_4OSiS$ (MH$^+$): calc. 441.2144, found 441.2130.

2-Benzyl-3-(*t*-butyl dimethyl silyloxy) propyl (1-phenyl-1*H*-tetrazol-5-yl) sulfone (**8**). m-CPBA 75% (1.68 g, 9.7 mmol) was added to a stirred solution of sulfide **7** (1.34 g, 3.0 mmol) in dry CH_2Cl_2 (24 mL) at 0°C. The ice bath was removed and the reaction mixture was allowed to proceed at r.t. overnight. CH_2Cl_2 (10 mL) was added and the mixture was washed with saturated $Na_2S_2O_5$/10% NaOH solution (1:1, 30 mL). The layers were separated and the aqueous phase was further extracted with CH_2Cl_2 (3x30 mL)**.** The combined organic layers were washed with saturated $NaHCO_3$ and saturated NaCl solutions., dried over $MgSO_4$, filtered and concentrated to give a yellow oil (1.43 g, 98% yield), which was crystallized from hexane: EtOAc 3:1 to afford white crystalline product. ^{1} H NMR :δ 7.47-7.60 (m, 5H); 7.13-7.28 (m, 5H); 3.96 (dd, J=14.9, 6.9 Hz, 1H); 3.74 (dd, J=10.2, 3.9 Hz, 1H);); 3.63 (dd, J=14.9, 5.1 Hz, 1H); 3.53 (dd, J=10.2, 3.2 Hz, 1H); 2.91 (dd, J=13.5, 6.2 Hz, 1H); 2.84 (dd, J=13.5, 8.7 Hz, 1H); 2.62 (dtq, J=8.7, 6.6, 4 Hz, 1H); 0.91 (s, 9H); 0.04 (s, 6H). **^{13}C** NMR :δ 153.8; 138.3; 133.0; 131.3; 129.6; 128.5; 126.6; 125.2; 62.0; 56.4; 37.5; 36.7; 25.9; 18.2; -5.6; HRMS *m/z* for $C_{23}H_{33}N_4O_3SiS$ (MH$^+$): calc. 473.2043, found 473.2019.

3-Acetoxy-2-benzyl-1-propyl methanesulfonate (**9**). This compound was prepared from alcohol **3e** according to the procedure described for mesylate **6**, in 100% yield. ^{1}H NMR: δ 7.33-7.16 (m, 5H); 4.20 (dd, J=9.8, 5.0 Hz, 1H); 4.14 (dd, J=9.8, 5.6 Hz, 1H); 4.13 (dd, J=11.4, 5.1 Hz, 1H); 4.02 (dd, J=11.4, 6.6 Hz, 1H); 2.97 (s, 3H); 2.74 (dd, J=14.3, 7.9 Hz, 1H); 2.70 (dd, J=14.3, 7.2 Hz, 1H); 2.39 (qq, J=7.2, 5.2 Hz, 1H); 2.06 (s, 3H). ^{13}C NMR: δ 170.7; 137.9; 128.9; 128.6; 126.6; 68.6; 62.8; 39.5; 37.0; 33.8; 20.7. MS: *m/z* 287 (MH^+, 1.4); 226 (3); 190 (18); 130 (100); 91 (4). HRMS: *m/z* for $C_{13}H_{19}O_5S$ (MH^+): calcd. 287.0953, found 287.0957; for $C_{11}H_{14}O_3S$ (M^+-CH_3CO_2H): calcd. 226.0630, found 226.0623.

3-Acetoxy-2-benzyl propyl phenyl sulfide (**10**). Thiophenol (1.26 ml, 12.3 mmol) was dissolved in dry THF (24 mL). NaH (60% in mineral oil, 0.29 g) was added slowly and the white suspension was stirred at r.t. for 15 min. A solution of mesylate **9** (1.0 g, 3.5 mmol), in dry THF (5 mL), was added and the mixture was stirred overnight at 50°C. The mixture was cooled to r.t., diluted with CH_2Cl_2 (50 mL) and washed with 10% NaOH solution (100 mL). The aqueous phase was re-extracted with CH_2Cl_2 (3x100 mL) and the volume of the combined organic phase was partially reduced to 100 mL under vacuum. The organic layer was washed with saturated NaCl solution, dried over $MgSO_4$, filtered and evaporated to provide yellow oil (1.3 g). It was crystallized from hexane: EtOAc 9:1 to give a white crystalline solid (0.58 g, 55% yield). To improve the yield, the filtrate was evaporated and chromatographed (hexane: EtOAc 9:1) to give some more clean product (0.25 g, 23% yield). The total yield of the product was 78%. ^{1}H NMR: δ 7.27-7.10 (m, 10H); 4.14 (dd, J=11.1, 5.1 Hz, 1H); 4.05 (dd, J=11.1, 5.4 Hz, 1H); 2.94 (d, J=6.6 Hz, 2H); 2.81 (dd, J=13.8, 7.2 Hz, 1H); 2.72 (dd, J=13.8, 7.5 Hz, 1H); 2.21 (ttt, J=7.2, 6.6, 5.3 Hz, 1H); 2.02 (s, 3H). ^{13}C NMR: δ 171.0; 139.1 136.4; 129.3; 129.2; 129.0; 128.6; 126.5; 126.1; 65.3; 39.7; 37.0; 34.9; 21.0. MS: *m/z* 300 (M^+, 48); 191 (9); 149 (45); 110 (47); 91 (94). HRMS: *m/z* for $C_{18}H_{20}O_2S$ (M^+): calcd. 300.1184, found 300.1189.

3-Acetoxy-2-benzyl propyl phenyl sulfone (**11**). m-CPBA 75% (0.28 g, 1.6 mmol) was added to a stirred solution of sulfide **10** (0.15 g, 0.5 mmol) in dry CH_2Cl_2 (4 mL) at 0°C. The ice bath was removed and the reaction mixture was allowed to proceed at r.t. for 3 h. CH_2Cl_2 (10 mL) was added and the mixture was washed with saturated $Na_2S_2O_5$/10% NaOH solution (1:1, 10 mL). The layers were separated and the aqueous phase was further extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were washed with saturated $NaHCO_3$ and saturated NaCl solutions., dried over $MgSO_4$, filtered and concentrated to give a yellow oil (0.17 g), which was purified by chromatography (hexane: EtOAc 4:1) to afford the clean product (0.13 g, 76% yield). ^{1}H NMR: δ 7.84 (d, J=7.8 Hz, 2H); 7.64 (tt, J=7.5, 1.4 Hz, 1H); 7.53 (tt, J=7.5, 1.4 Hz, 2H); 7.27-7.03 (m, 5H); 4.12 (dd, J=11.3, 5.0 Hz, 1H); 4.03 (dd, J=11.3, 5.0 Hz, 1H); 3.23 (dd, J=14.6, 6.5 Hz, 1H); 3.09 (dd, J=14.6, 5.6 Hz, 1H); 2.83 (dd, J=13.8, 7.2 Hz, 1H); 2.74 (dd, J=13.8, 7.5 Hz, 1H); 2.54 (tdq, J=7.4, 6.5, 5.1 Hz, 1H); 2.01 (s, 3H). ^{13}C NMR: δ 170.7; 139.4; 137.7; 133.8; 129.4; 129.1; 128.7; 127.9; 126.7; 64.8; 56.3; 37.2; 35.1; 20.8. MS: *m/z* 333 (MH^+, 2); 273 (5); 131 (100); 117 (10); 91 (30). HRMS: *m/z* for $C_{18}H_{21}O_4S$ (MH^+): calcd. 333.1161, found 333.1139.

2-Benzyl-3-hydroxy propyl phenyl sulfone (**12**). This compound was prepared from acetate **11** according to the procedure described for alcohol **5**, in 95% yield. ^{1}H NMR: δ 7.81 (d, J=7.8 Hz, 2H); 7.56 (t, J=7.5 Hz, 1H); 7.47 (t, J=7.8 Hz, 2H); 7.25-7.02 (m, 5H); 3.76 (dd, J=11.1, 4.5 Hz, 1H); 3.57 (dd, J=11.1, 5.1 Hz, 1H); 3.33 (dd, J=14.4, 7.2 Hz, 1H); 3.03 (dd, J=14.4, 5.4 Hz, 1H); 2.77 (dd, J=13.8, 7.8 Hz, 1H); 2.76 (obscured, 1H); 2.72 (dd, J=13.8, 7.2 Hz, 1H); 2.37 (qq, J=7.3, 4.8 Hz, 1H). ^{13}C NMR: δ 139.3; 138.4; 133.6; 129.3; 129.1; 128.5; 127.6; 126.4; 62.9; 56.1; 37.8; 36.1. MS: *m/z* 291 (MH^+, 13); 273 (13); 131 (100); 117 (26); 104 (6); 91 (43). HRMS: *m/z* for $C_{16}H_{19}O_3S$ (MH^+): calcd. 291.1055, found 291.1058.

2-Benzyl-3-(*tert*-butyl dimethyl silanyloxy) propyl phenyl sulfone (**13**). This compound was prepared from alcohol **12** according to the procedure described for **4**, in 84% yield. ^{1}H NMR: δ 7.85 (d, J=7.8 Hz, 2H); 7.65 (t, J=7.8 Hz, 1H); 7.53 (t, J=7.8 Hz, 2H); 7.30-7.06 (m, 5H); 3.65 (dd, J=9.9, 4.2 Hz, 1H); 3.50 (dd, J=9.9, 4.2 Hz, 1H); 3.37 (dd, J=14.4, 6.6 Hz, 1H); 3.01 (dd, J=14.4, 5.1 Hz, 1H); 2.80 (dd, J=13.8, 6.6 Hz, 1H); 2.76 (dd, J=13.8, 7.5 Hz, 1H); 2.33 (qq, J=6.9, 4.8 Hz, 1H); 0.89 (s, 9H); 0.02 (s, 3H); 0.01 (s, 3H). ^{13}C NMR: δ 139.8; 138.8; 133.6; 129.3; 129.2; 128.5; 127.9; 126.4; 62.8; 56.2; 38.0; 36.9; 25.9; 18.2; -5.5. MS: *m/z* 405 (MH^+, 2); 347 (100); 131 (42); 91 (42). HRMS: *m/z* for $C_{22}H_{33}O_3SiS$ (MH^+): calcd. 405.1920, found 405.1952.

N-trityl-5-amino-2-benzyl-1-(*t*-butyldimethylsilyloxy)-3-hexene (**14**). LiHMDS 1M (0.23 mL, 0.23 mmol) was slowly added to a stirring solution of sulfone **8** (110 mg, 0.23 mmol) in dry THF (1 mL) under Ar atmosphere at -78ºC. After 20 min, a solution of *N*-trityl-alaninal (104 mg, 0.33 mmol) in dry THF (1 mL) was added slowly. After 3 h at -78ºC, the reaction mixture was further stirred at r.t. for 15h. Ether (50 mL) and water (35 mL) were added and the organic phase was washed with brine (30 mL), dried over $MgSO_4$, filtered and evaporated to yield a 1:1 *E:Z* mixture of the product (88 mg, 68% yield). Chromatography (hexane: EtOAc 19:1), afforded the clean *E* isomer as a clear oil. ^{1}H NMR: δ 7.08-7.82 (m, 20H); 5.28 (ddd, J=15.8, 7.7, 0.9 Hz, 1H); 5.13 (dd, J=15.8, 6.2 Hz, 1H); 3.40 (dd, J=9.9, 5.4 Hz, 1H); 3.35 (dd, J=9.9, 6.3 Hz, 1H); 2.97 (bquint, J=6.1 Hz, 1H); 2.76 (dd, J=13.5, 6.3 Hz, 1H); 2.42 (dd, J=13.5, 7.2 Hz); 2.27 (bsex, J=6.6 Hz, 1H); 0.88 (s, 9H); 0.57 (d, J=6.0 Hz, 3H); 0.06 (s, 6H). ^{13}C NMR: δ 147.04; 144.57; 140.57; 137.11-125.61; 128.96; 128.32; 71.46; 65.32; 50.46; 46.07; 37.52; 25.94; 23.38; 18.29; -5.31; -5.36. HRMS: *m/z* for $C_{33}H_{46}NOSi$ (MH^+): calc. 500.3349, found 500.3305.