ELECTRONIC SUPPLEMENTARY MATERIAL

Synthesis of the ABC tricyclic fragment of the pectenotoxins via stereocontrolled cyclization of a $\gamma$-hydroxyepoxide appended to the AB spiroacetal unit.

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Experimental

General

All reactions were carried out under an N$_2$ atmosphere using oven-dried glassware using standard syringe and septum techniques, unless otherwise stated. Diethyl ether and tetrahydrofuran were distilled from Na/benzophenone under N$_2$. Hexane, CH$_2$Cl$_2$, and NEt$_3$ were distilled from CaH$_2$ under N$_2$. Butyllithium (1.6 M in hexane) was purchased from the Aldrich Chemical Co. Flash chromatography was performed using Riedel-de Häen or Merck 0.032-0.063mm silica gel and preparative layer chromatography with Merck silica gel 60 PF on glass plates, with the indicated solvents. Analytical TLC was performed with 0.20mm silica gel 60 aluminium-backed plates and analyzed using 365 nm ultraviolet irradiation followed by staining with either alkaline permanganate or vanillin solution. High resolution mass spectra were obtained using EI, CI and FAB techniques on a VG70-SE spectrometer. NMR spectra were recorded on either a Bruker DRX300 spectrometer operating at 300 MHz for $^1$H nuclei and 75 MHz for $^{13}$C nuclei or on a Bruker DRX400 spectrophotometer operating at 400 MHz for $^1$H nuclei and 100 MHz for $^{13}$C nuclei. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined on a Perkin-Elmer 341 polarimeter.
(2'R, 3'S, 4R, 5S)-(+)3-(7'-Benzyloxy-3'-hydroxy-2'-methylheptanoyl)-4-methyl-5-phenyloxazolidin-2-one (syn-adduct 17)

To a solution of (4'R, 5S)-(+)4-methyl-3-(1'-oxopropyl)-5-phenyloxazolidin-2-one (1.22 g, 5.2 mmol) in dry CH$_2$Cl$_2$ (40 mL) at 0 °C under N$_2$ was slowly added TiCl$_4$ (5.0 mL, 1 M solution in CH$_2$Cl$_2$, 5 mmol). The orange mixture was stirred at 0 °C for 5 min followed by the addition of (−)-sparteine (1.20 mL, 5.2 mmol) to form a dark red enolate. The mixture was stirred at 0 °C for 20 min then cooled to −78 °C. N-Methyl-2-pyrrolidone (0.50 mL, 5.2 mmol) was added and the mixture was stirred for 10 min followed by the addition of 5-benzyloxypentanal (1.18 g, 6.1 mmol) in dry CH$_2$Cl$_2$ (25 mL). The mixture was stirred at −78°C for 1 h, warmed to 0°C then stirred for 1 hr. During this time, the colour of the mixture changed from dark red to light brown. The reaction was quenched with 50% aqueous NH$_4$Cl (15 mL) and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 30 mL). The organic layers were combined, washed with brine (2 × 30 mL) and dried over Na$_2$SO$_4$. The solvent was evaporated to give a residual pale yellow oil. The crude product was purified by flash chromatography using hexane-ethyl acetate (4:1) to afford the title compound 17 (1.92 g, 90%) as a colourless oil; [α]$_D$ +7.7° (c=1.02, CH$_2$Cl$_2$); Found: MH$^+$, 426.2261, C$_{25}$H$_{32}$NO$_5$ requires 426.2281; ν$_{max}$ (film)/cm$^{-1}$ 3518 (OH), 1780s (OC=O), 1698m (NC=O), 1364m; δ$_H$ (300 MHz, CDCl$_3$) 0.87 (3H, d, J 6.6 Hz, 4-Me), 1.23 (3H, d, J 6.9 Hz, 2'-Me), 1.44-1.67 (6H, m, H-4', H-5', H-6'), 3.0 (1H, br, OH), 3.48 (2H, t, J 6.3 Hz, H-7'), 3.78 (1H, dq, J 3.0, 6.9 Hz, H-2'), 3.95 (1H, m, H-3'), 4.49 (2H, s, CH$_2$Ph), 4.76 (1H, pentet, J 6.6 Hz, H-4), 5.64 (1H, d, J 7.3 Hz, H-5), 7.26-7.40 (10H, m, 2 × Ph); δ$_C$ (75 MHz, CDCl$_3$) 10.2 (CH$_3$, Me), 14.2 (CH$_3$, Me), 20.8 (CH$_2$, C-5'), 29.4 (CH$_2$, C-4'), 33.6 (CH$_2$, C-6'), 42.2 (CH, C-2'), 54.6 (CH, C-4), 70.1 (CH$_2$, C-7'), 71.4 (CH, C-3'), 72.7 (CH$_2$, CH$_2$Ph), 78.7 (CH, C-5), 125.5 (CH, Ph), 127.3 (CH, p-Ph), 127.4 (CH, Ph), 128.5 (CH, Ph), 128.6 (CH, p-Ph), 133.0 (C, Ph), 138.5 (C, Ph), 152.5 (C, C-2), 176.9 (C, C-1'); m/z 426 (MH$^+$, 0.05%), 319 (MH-OCH$_2$Ph, 0.5%), 107 (OCH$_2$Ph, 56%), 91 (CH$_2$Ph, 100%).

(2'R, 3'S, 4R, 5S)-(+)3-(7'-Benzyloxy-3'-hydroxy-2'-methylheptanoyl)-4-methyl-5-phenyloxazolidin-2-thione (Evans syn-adduct 18), (2'S, 3'R, 4R, 5S)-(+)3-(7'-Benzyloxy-3'-hydroxy-2'-methylheptanoyl)-4-methyl-5-phenyloxazolidin-2-thione (non-Evans syn-adduct 19) and (2'S, 3'S, 4R, 5S)-(+)3-(7'-Benzyloxy-3'-hydroxy-2'-methylheptanoyl)-4-methyl-5-phenyloxazolidin-2-thione (anti-adduct 20)
To a solution of oxazolidinethione 15iii (120 mg, 0.48 mmol) in dry CH₂Cl₂ (2 mL) at 0 °C was slowly added neat TiCl₄ (0.053 mL, 0.48 mmol). The orange mixture was stirred at 0 °C for 5 min followed by the addition of (−)-sparteine (0.28 mL, 1.2 mmol) to form a dark red enolate. The red mixture was stirred at 0 °C for 20 min then cooled to −78 °C. 5-Benzylxypentanal ii (110 mg, 0.57 mmol) in dry CH₂Cl₂ (2 mL) was added slowly and the mixture was stirred at −78 °C for 1 h and then at 0 °C for 1 hr. The reaction was quenched with 50% aqueous NH₄Cl (5 mL) and warmed to room temperature. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The organic layers were combined, washed with brine (2 × 20 mL) and dried over MgSO₄. The solvent was evaporated to give the crude mixture which was purified by flash chromatography using hexane-ethyl acetate (4:1) to afford the Evans syn-isomer 18 (96 mg, 46%) as yellow oil together with the non-Evans syn-isomer 19 (43 mg, 20%) and anti-isomer 20 (20 mg, 10%); 18: [α]D +35.6° (c=0.82, CHCl₃); Found: MH⁺, 442.2062, C₂₅H₃₂NO₄S requires 442.2052; νmax (cm⁻¹) 3435br (OH), 1692s (C=O), 1377s; δH (300 MHz, CDCl₃) 0.94 (3H, d, J 6.6 Hz, Me), 1.23 (3H, d, J 7.0 Hz, Me), 1.45-1.71 (6H, m, H-4', H-5' and H-6'), 2.79 (1H, d, J 2.4 Hz, OH), 3.49 (2H, t, J 6.2 Hz, H-7'), 4.09 (1H, m, H-3'), 4.51 (2H, s, CH₂Ph), 4.81 (1H, dq, J 2.6, 7.0 Hz, H-3'), 5.00 (1H, pentet, J 6.6 Hz, H-4), 5.75 (1H, d, J 7.2 Hz, H-5), 7.25-7.43 (10H, m, 2 × Ph); δC (75 MHz, CDCl₃) 10.4 (CH₃, Me), 14.2 (CH₃, Me), 14.4 (CH₃, Me), 22.6 (CH₂, C-5'), 29.6 (CH₂, C-4'), 33.5 (CH₂, C-6'), 41.9 (CH, C-2'), 59.1 (CH, C-4), 70.2 (CH₂, C-7'), 71.2 (CH, C-3'), 72.9 (CH₂, CH₃Ph), 83.0 (CH, C-5), 125.8 (CH, Ph), 127.5 (CH, Ph), 127.6 (CH, Ph), 128.3 (CH, Ph), 128.7 (CH, Ph), 129.0 (CH, Ph), 132.2 (C, Ph), 138.5 (C, Ph), 178.2 (C, C-1'), 184.9 (C, C-2); m/z (CI) 442 (MH⁺, 1%), 250 (36%), 194 (45%), 91 (CH₂Ph, 43%), 85 (SCNCO, 100%).

19: [α]D +53.6° (c=1.2, CHCl₃); Found: MH⁺, 442.2043, C₂₅H₃₂NO₄S requires 442.2052; νmax (cm⁻¹) 3432br (OH), 1698s (C=O), 1375s; δH (300 MHz, CDCl₃) 0.92 (3H, d, J 6.6 Hz, Me), 1.26 (3H, d, J 6.9 Hz, Me), 1.44-1.68 (6H, m, H4', H-5' and H-6'), 2.91 (1H, d, J 21Hz, OH), 3.50 (2H, t, J 6.2 Hz, H-7'), 4.05 (1H, m, H-3'), 4.51 (2H, s, CH₃Ph), 4.68 (1H, dq, J 2.8, 6.9 Hz, H-2'), 5.00 (1H, pentet, J 6.6 Hz, H-4), 5.75 (1H, d, J 7.2 Hz, H-5), 7.25-7.43 (10H, m, 2 × Ph); δC (75 MHz, CDCl₃) 10.1 (CH₃, Me), 14.0 (CH₃, Me), 22.7 (CH₂, C-5'), 29.6 (CH₂, C-4'), 33.8 (CH₂, C-6'), 42.1 (CH, C-2'), 59.0 (CH, C-4), 70.2 (CH₂, C-7'), 71.4 (CH, C-3'), 72.9 (CH₂, CH₃Ph), 83.1 (CH, C-5), 125.8 (CH, Ph), 127.5 (CH, Ph), 127.6 (CH, Ph), 128.3 (CH, Ph), 128.7 (CH, Ph), 129.0 (CH, Ph), 132.3 (C, Ph), 138.6 (C, Ph), 178.3 (C, C-2'), 184.8 (C, C-2); m/z (CI) 442 (MH⁺, 1.5%), 427 (MH-CH₃, 2%), 250 (38%), 194 (100%), 178 (87%), 91 (CH₂Ph, 84%), 84 (SCNCO, 99%).

20: [α]D +1.86° (c=1.05, CHCl₃); Found: MH⁺, 442.2045, C₂₅H₃₂NO₄S requires 442.2052; νmax (cm⁻¹) 3436br (OH), 1680s (C=O); δH (300 MHz, CDCl₃) 0.95 (3H, d, J 6.6 Hz, Me), 1.15 (3H,
d, J 6.9 Hz, Me), 1.22-1.70 (6H, m, H-4', H-5' and H-6'), 2.85 (1H, d, J 9.3 Hz, OH), 3.49 (2H, t, J 6.1 Hz, H-7'), 3.74 (1H, q, J 7.6 Hz, H-3'), 4.51 (2H, s, CH₂Ph), 4.89 (1H, pentet, J 6.9 Hz, H-2'), 5.02 (1H, pentet, J 6.6 Hz, H-4), 5.75 (1H, d, J 7.1 Hz, H-5), 7.25-7.44 (10H, m, 2 × Ph); δC (75 MHz, CDCl₃) 14.1 (CH₃, Me), 14.9 (CH₃, Me), 22.2 (CH₂, C-5'), 29.6 (CH₂, C-4'), 34.6 (CH₂, C-6'), 43.1 (CH, C-2'), 59.3 (CH, C-4), 70.2 (CH₂, C-7'), 72.9 (CH, C-3'), 72.9 (CH₂, CH₂Ph) 83.2 (CH, C-5), 125.8 (CH, Ph), 127.6 (CH, Ph), 127.7 (CH, Ph), 128.3 (CH, Ph), 128.7 (CH, Ph), 129.0 (CH, Ph), 132.1 (C, Ph), 138.5 (C, Ph), 177.5 (C, C-1'), 185.6 (C, C-2); m/z (Cl) 442 (MH⁺, 0.2%), 194 (63%), 91(CH₂Ph, 100%), 85 (SCNCO, 99%).

(2S, 3S)-(+)-7-Benzyloxy-2-methylheptane-1,3-diol 21

To a solution of syn-adduct 17 (310 mg, 0.73 mmol) in dry THF (4 mL) at 0 °C was added LiBH₄ (23 mg, 1.1 mmol) and the reaction mixture was stirred at room temperature for 5 min. Water (2 mL) was added and the mixture concentrated under reduced pressure. The residue was extracted with ethyl acetate (3 × 5 mL), dried over MgSO₄ and the solvent evaporated under reduced pressure. The crude product was purified by flash chromatography using hexane-ethyl acetate (3:2) as eluent to afford the title compound 21 (160 mg, 87%) as a yellow oil; [α]D +11.5° (c=0.8, CHCl₃); Found: MH⁺, 253.1804, C₁₅H₂₆O₃ requires 253.1803; νmax (film)/cm⁻¹ 3390 (br, OH); δH (300 MHz, CDCl₃) 0.89 (3H, d, J 7.1 Hz, Me), 1.26 (1H, m, H-2), 1.41-1.67 (6H, m, H-4, H-5, H-6), 2.50 (2H, br, OH), 3.49 (2H, t, J 6.3 Hz, H-7), 3.68 (2H, d, J 5.4 Hz, H-1), 3.81 (1H, m, H-3), 4.50 (2H, s, CH₂Ph), 7.26-7.39 (5H, m, Ph); δC (75 MHz, CDCl₃) 10.1 (CH₃, Me), 22.9 (CH₂, C-5), 29.6 (CH₂, C-4), 33.7 (CH₂, C-6), 39.1 (CH, C-2), 67.1 (CH₂, C-1), 70.3 (CH₂, C-7), 72.9 (CH₂, CH₂Ph), 74.3 (CH, C-3), 127.5 (CH, p-Ph), 127.6 (CH, Ph), 128.3 (CH, Ph), 138.5 (C, Ph); m/z (Cl) 253 (MH⁺, 72%), 235 (MH-H₂O, 37%), 217 (MH-H₂O-H₂O, 28%), 145 (M-OCH₂Ph, 27%), 91 (CH₂Ph, 100%).

(2S, 3S)-(–)-7-Benzyloxy-1-tert-butyldiphenylsilyloxy-2-methylheptan-3-ol 22

To a solution of tert-butyldiphenylsilyl chloride (0.20 mL, 0.77 mmol) and imidazole (81 mg, 1.2 mmol) in dry dichloromethane (5 mL) at 0 °C was added a solution of diol 21 (150 mg, 0.60 mmol) in dry dichloromethane (5 mL). The reaction mixture was stirred at room temperature overnight. The mixture was diluted with dichloromethane (20 mL), washed with saturated solution of NaHCO₃ (1 × 5 mL), brine (2 × 5 mL) and dried over MgSO₄. The solvent was
evaporated under reduced pressure to give the crude product which was purified by flash chromatography using hexane-ethyl acetate (9:1) as eluent to afford the title compound 22 (220 mg, 77%) as a colourless oil; \([\alpha]_D -3.0^\circ\) (c=0.73, CHCl3); Found: MH+, 491.2982, C31H43O3Si requires 491.3007; \(\nu_{\text{max}}\) (film)/cm\(^{-1}\) 3479br (OH), 1265s (Si-O-C); \(\delta_H\) (300 MHz, CDCl3) 0.89 (3H, d, \(J\ 7.1\ Hz\), Me), 1.06 (9H, s, \(\text{tBu}\)), 1.25-1.66 (7H, m, H-2, H-4, H-5, H-6), 2.74 (1H, br, OH), 3.49 (2H, t, \(J\ 6.4\ Hz\), H-7), 3.67 (1H, dd, \(J \ 5.9, 10.0\ Hz\), H-1A), 3.75 (1H, dd, \(J\ 4.3, 10.0\ Hz\), H-1B), 3.86 (1H, m, H-3), 4.50 (2H, s, \(CH_2\)Ph), 7.25-7.44 (11H, m, Ph), 7.64-7.69 (4H, m, Ph); \(\delta_C\) (75 MHz, CDCl3) 10.2 (CH3, Me), 19.2 (C, \(\text{tBu}\)), 22.9 (CH2, C-5), 26.9 (CH3, \(\text{tBu}\)), 29.8 (CH2, C-4), 34.0 (CH2, C-6), 39.1 (CH, C-2), 68.7 (CH2, C-1), 70.4 (CH2, C-7), 72.9 (CH2, \(CH_2\)Ph), 74.1 (CH, C-3), 127.5 (CH, p-Ph), 127.6 (CH, Ph), 127.8 (CH, Ph), 128.3 (CH, Ph), 129.78 (CH, p-Ph), 129.82 (CH, p-Ph), 133.0 (C, Ph), 133.1 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 138.7 (C, Ph); \(m/z\) (CI) 491 (MH+, 23%), 196 (100%), 91 (CH2Ph, 81%).

(2S, 3S)-(+)\-7-\text{Benzyloxy-1-\textit{tert}-butyldiphenylsilyloxy-3-\textit{tert}-butyldimethylsilyloxy-2-methylheptane} 23

To a mixture of 2,6-lutidine (0.09 mL, 0.8 mmol), 4-(dimethylamino)pyridine (49 mg, 0.4 mmol) and \textit{tert}-butyldimethylsilyl trifluoromethanesulfonate (0.12 mL, 0.5 mmol) in dry DMF (5 mL) at 0 °C was added a solution of alcohol 22 (217 mg, 0.4 mmol) in dry DMF (10 mL). The mixture was stirred at room temperature overnight then the solvent was evaporated under reduced pressure. The residue was diluted with Et2O (20 mL), washed with brine (2 \times 10 mL), water (2 \times 10 mL) and dried over Na2SO4. Removal of the solvent by evaporation under reduced pressure yielded the crude product that was purified by flash chromatography using hexane-ethyl acetate (95:5) as eluent to afford the title compound 23 (230 mg, 95%) as a colourless oil; \([\alpha]_D +1.8^\circ\) (c = 1.025, CHCl3); Found: MH+, 605.3846, C37H57O3Si2 requires 605.3846; \(\nu_{\text{max}}\) (cm\(^{-1}\)) 1252s (Si-O-C); \(\delta_H\) (300 MHz, CDCl3) –0.02 (3H, s, \(\text{Me}_2\text{tBuSi}\)), 0.01 (3H, s, \(\text{Me}_2\text{tBuSi}\)), 0.81 (3H, d, \(J\ 7.1\ Hz\), Me), 0.84 (9H, s, \(\text{Me}_2\text{tBuSi}\)), 1.05 (9H, s, \(\text{tBuPh}_2\)Si), 1.25-1.41 (6H, m, H-4, H-5, H-6), 1.58 (1H, m, H-2), 3.45 (2H, t, \(J\ 6.5\ Hz\), H-7), 3.48 (1H, dd, \(J\ 6.7, 9.8\ Hz\), H-1A), 3.61 (1H, dd, \(J\ 6.7, 9.8\ Hz\), H-1B), 3.81 (1H, dt, \(J\ 3.0, 6.2\ Hz\), H-3), 4.49 (2H, s, \(CH_2\)Ph), 7.2-7.4 (11H, m, Ph), 7.6-7.7 (4H, m, Ph); \(\delta_C\) (75 MHz, CDCl3) –4.6 (CH3, \(\text{Me}_2\text{BuSi}\)), –4.1 (CH3, \(\text{Me}_2\text{BuSi}\)), 10.6 (CH3, Me), 18.1 (C, \(\text{tBuMe}_2\)Si), 19.3 (C, \(\text{tBuPh}_2\)Si), 22.4 (CH2, C-5), 25.9 (CH3, \(\text{tBuMe}_2\)Si), 26.9 (CH3, \(\text{tBuPh}_2\)Si), 29.9 (CH2, C-4), 34.4 (CH2, C-6), 39.9 (CH, C-2), 66.3 (CH2, C-1), 70.4 (CH2, C-7), 72.0 (CH, C-3), 72.9 (CH2, \(CH_2\)Ph), 127.6
A mixture of (2S, 3S)-(−)-7-benzyloxy-1-tert-butylidiphenylsilyloxy-2-methylheptane 23 (0.441 g, 0.73 mmol) and 10% palladium on carbon (catalytic amount) in methanol (10 mL) was stirred under a hydrogen atmosphere overnight. The mixture was filtered through Celite® and the solvent evaporated under reduced pressure. The crude product was purified by flash chromatography using hexane-ethyl acetate (95:5) as eluent to give the title compound 24 (0.37 g, 99%) as a colourless oil; [α]D +3.1° (c=0.88, CHCl3); Found: MH+, 515.3383, C30H51O3Si2 requires 515.3377; νmax (cm−1) 3369br (OH), 1252s (Si-O-C); δH (300 MHz, CDCl3) −0.02 (3H, s, Me2tBuSi), 0.02 (3H, s, Me2tBuSi), 0.84 (12H, s, Me2tBuSi and Me), 1.05 (9H, s, 'BuPh2Si), 1.04-1.60 (6H, m, H-2, H-3, H-4), 1.74 (1H, m, H-6), 3.47 (1H, dd, J 6.7, 9.8 Hz, H-7A), 3.59-3.64 (2H, m, H-7B, H-1), 3.81 (1H, td, J 6.2, 3.2 Hz, H-5), 7.33-7.42 (6H, m, Ph), 7.63-7.68 (4H, m, Ph); δC (75MHz, CDCl3) −4.6 (CH3, Me2tBuSi), −4.1 (CH3, Me2tBuSi), 10.7 (CH3, Me), 18.1 (C, 'BuMe2Si), 19.3 (C, 'BuPh2Si), 25.9 (CH3, 'BuMe2Si), 26.9 (CH3, 'BuPh2Si), 29.7 (CH2, 29.7) (CH2, C-4), 32.9 (CH2, C-3), 34.3 (CH2, 29.9 (CH, C-6), 63.0 (CH2, C-1), 66.2 (CH2, C-7), 72.0 (CH, C-5), 127.6 (CH, Ph), 129.5 (CH, Ph), 134.07 (C, Ph), 135.6 (CH, Ph); m/z (CI) 515 (MH+, 1%), 325 (65%), 109 (100%).

A mixture of alcohol 24 (0.643 g, 1.25 mmol), pyridinium chlorochromate (0.40 g, 1.87 mmol) and potassium carbonate (0.5 g) in dry dichloromethane (20 mL) was stirred at room temperature. After 3 h, the mixture was filtered through a pad of Celite® and silica gel. The solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography using hexane-ethyl acetate (95:5) as eluent to afford the title compound 12 (0.63 g, 99%) as a colourless oil, [α]D +1.7° (c = 1.39, CHCl3); Found: MH+, 513.3230, C30H49O3Si2 requires 513.3230; νmax (cm−1) 1727s (C=O), 1252s (Si-O-C); δH (300 MHz, CDCl3) −0.01 (3H, s, Me2tBuSi), 0.02 (3H, s, Me2tBuSi), 0.81 (3H, s, Me), 0.84 (9H, s,
Me$_2$'BuSi), 1.05 (9H, s, 'BuPh$_2$Si), 1.35-1.60 (4H, m, H-3, H-4), 1.74 (1H, m, H-6), 2.38 (2H, td, J 7.2, 1.7 Hz, H-2), 3.47 (1H, dd, J 6.6, 9.9 Hz, H-7A), 3.62 (1H, dd, J 6.6, 9.9 Hz, H-7B), 3.81 (1H, td, J 3.4, 5.9 Hz, H-5), 7.33-7.44 (6H, m, Ph), 7.62-7.67 (4H, m, Ph), 9.73 (1H, t, J 1.7 Hz, H-1); δc (75 MHz, CDCl$_3$) –4.6 (CH$_3$, Me$_2$'BuSi), –4.2 (CH$_3$, Me$_2$'BuSi), 10.9 (CH$_3$, Me), 18.1 (C, Me$_2$'BuSi), 18.4 (CH$_2$, C-3), 19.2 (C, 'BuPh$_2$Si), 25.9 (CH$_3$, 'BuMe$_2$Si), 26.9 (CH$_3$, 'BuPh$_2$Si), 34.0 (CH$_2$, C-4), 40.0 (CH, C-6), 43.9 (CH$_2$, C-2), 66.0 (CH$_2$, C-7), 71.9 (CH, C-5), 127.58 (CH, Ph), 127.60 (CH, Ph), 129.52 (CH, Ph), 129.54 (CH, Ph), 134.0 (C, Ph), 135.6 (CH, Ph), 202.4 (CH, C-1); m/z 513 (MH$^+$, 27%), 455 (M-'Bu, 54%), 381 (M-'BuMe$_2$SiO, 100).

(S)-(–)-[4-Benzyloxy-3-(tert-butyldimethylsilyloxy)butane]-1-sulfonylbenzene 13

To a solution of methyl phenyl sulfone (0.22 g, 1.39 mmol) in dry THF (6 mL) at –78 °C was added BuLi (0.96 mL, 1.6 M solution in hexane, 1.53 mmol) and the light brown solution was stirred at –78 °C for 10 min then at room temperature for 30 min. Hexamethylphosphoramidite (0.53 mL, 3.06 mmol) and a solution of epoxide 25iv (0.2 g, 1.22 mmol) in dry THF (2 mL) were added at room temperature. The resultant clear bright yellow solution was stirred for 1.5 hr, then cooled to 0 °C. A premixed solution of tert-butyldimethylsilyl trifluoromethanesulfonate (0.35 mL, 1.53 mmol) and 2,6-lutidine (0.24 mL, 2.09 mmol) in dry THF (2 mL, 2 × 1 mL wash) was added to the reaction mixture via cannula. A white precipitate formed that disappeared after 15 min. The mixture was stirred at 0 °C for 2.5 h then quenched with saturated NH$_4$Cl solution (3 mL). The organic phase was separated and the aqueous layer was extracted with Et$_2$O (3 × 10 mL). The combined organic layers were washed with brine (2 × 20 mL) and dried over MgSO$_4$. The solvent was evaporated under reduced pressure and the crude mixture was purified by flash chromatography using hexane-ethyl acetate (95:5) as eluent to afford the title compound 13 (0.58 g, 97%) as a yellow oil; [α]$_D$ –14.2° (c=1.6, CHCl$_3$; Found: M$^+$, 434.1943, C$_{22}$H$_{34}$O$_4$SSi requires 434.1947; ν$_{\text{max}}$ (cm$^{-1}$) 1447m, 1307s (SO$_2$Ph), 1255s (Si-O-C), 1146s (SO$_2$Ph); δ$_{\mathrm{H}}$ (400 MHz, CDCl$_3$) –0.012 (3H, s, Me$_2$'BuSi), 0.02 (3H, s, Me$_2$'BuSi), 0.82 (9H, s, 'Bu), 1.84-1.96 (2H, m, H-2), 3.17 (2H, m, H-1), 3.23 (1H, dd, J 6.6, 9.5 Hz, H-4A), 3.36 (1H, dd, J 5.2, 9.5 Hz, H-4B), 3.91 (1H, m, H-3), 4.43 and 4.48 (2H, AB, J$_{AB}$ 11.9 Hz, CH$_2$Ph), 7.23-7.35 (5H, m, CH$_2$Ph), 7.55 (2H, m, SO$_2$Ph), 7.63 (1H, m, SO$_2$Ph), 7.89 (2H, m, SO$_2$Ph); δc (75 MHz, CDCl$_3$) –4.99 (CH$_3$, Me$_2$'BuSi), –4.6 (CH$_3$, Me$_2$'BuSi), 18.0 (C, Me$_2$'BuSi), 25.7 (CH$_3$, Me$_2$'BuSi), 27.8 (CH$_2$, C-2), 52.1 (CH$_2$, C-1), 69.1 (CH, C-3), 73.31 (CH$_2$, C-4 or CH$_2$Ph), 73.38 (CH$_2$, CH$_2$Ph or C-4), 127.6 (CH, Ph), 127.7 (CH, Ph), 128.1 (CH, Ph).
(Ph), 128.4 (CH, Ph), 129.2 (CH, Ph), 133.6 (CH, Ph), 137.9 (C, Ph), 139.0 (C, Ph); m/z 434
(M+, 0.3%), 171 (10%), 143 (18%), 91 (CH$_2$Ph, 100%).

References


