

ELECTRONIC SUPPLEMENTARY MATERIAL

Synthesis of the bis-spiroacetal moiety of the shellfish toxins spiroalides B and D using an iterative radical oxidative cyclization strategy

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Experimental

General

All reactions were carried out under an N₂ atmosphere using oven-dried glassware using standard syringe and septum techniques, unless otherwise stated. Diethyl ether and tetrahydrofuran were distilled from Na/benzophenone under N₂. Hexane, toluene, cyclohexane, CH₂Cl₂, and NEt₃ were distilled from CaH₂ under N₂. Butyllithium (1.6 M in hexane) was purchased from the Aldrich Chemical Co. Flash chromatography was performed using Riedel-de Hën or Merck 0.032-0.063 mm 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/sulphuric acid 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 ¹H nuclei and 75 MHz for ¹³C nuclei or on a Bruker DRX400 spectrometer operating at 400 MHz for ¹H nuclei and 100 MHz for ¹³C nuclei. ¹H NMR data is reported as chemical shift in δ ppm from tetramethylsilane as an internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances, br = broadening), integration and assignment. ¹³C NMR data is reported as follows: chemical shift in ppm from tetramethylsilane with the solvent as an internal indicator (CDCl₃ 77.0 ppm), multiplicity with respect to proton (deduced from DEPT experiments). Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined on a Perkin-Elmer 341 polarimeter.

(2S)-2-Benzyloxymethyloxirane **12**

To a mixture of (*R*)-(+)-glycidol (1.8 mL, 27.0 mmol) and benzyl bromide (6.4 mL, 54.0 mmol) at 0 °C was added tetrabutylammonium iodide (997 mg, 2.7 mmol). After stirring for 10 min NaH (713 mg, 29.7 mmol, 1.1 eq.) was added portion-wise. After 3 hours flash silica (20 g) was added and the solution filtered over through a Celite® pad and evaporated until dryness. Flash chromatography using hexane-ethyl acetate (95:5) as eluent afforded the title compound (3.20 g, 72%) as a colorless liquid for which the spectroscopic data agreed with the literature;ⁱ

$[\alpha]_{589}^{20}$ -3.0 (*c* = 0.37, CHCl₃); ν_{\max} (film)/cm⁻¹ 3060, 3030, 2860, 1495, 1455, 1385, 1335, 1255, 1206, 1095, 1025, 910, 860, 740, 700; δ_{H} (400 MHz; CDCl₃) 7.38–7.28 (m, 5H, ArH), 4.64 (d, 1H, *J* 11.8, CH₂Ph), 4.59 (d, 1H, *J* 11.8, CH₂Ph), 3.79 (dd, 1H, *J* 3.1 and 11.3, 1'-H_a), 3.46 (dd, 1H, *J* 5.6 and 11.3, 1'-H_b), 3.20 (dddd, 1H, *J* 2.8, 3.1, 4.1 and 5.6, 2-H), 2.81 (dd, 1H, *J* 4.1, *J* 5.1, 1-H_a) and 2.63 (dd, 1H, *J* 2.8 and 5.1, 1-H_b); δ_{C} (100 MHz; CDCl₃) 137.9 (C, C_{arom}), 128.4 (2 x CH, C_{arom}), 127.7 (3 x CH, C_{arom}), 73.3 (CH₂, CH₂Ph), 70.8 (CH₂, C-1'), 50.8 (CH, C-2), 44.3 and (CH₂, C-1).

(2S)-1-Benzyloxy-5-(trimethylsilyl)pent-4-yn-2-ol **13**

To a solution of trimethylsilyl acetylene (7.4 mL, 51.8 mmol) in dry toluene (150 mL) at 0 °C was added dropwise a solution of BuLi (1.6 M in hexane, 28.1 mL, 45.7 mmol). After stirring for 30 min the solution was cooled to -78 °C and epoxide **12** (5.0 g, 30.5 mmol) was added dropwise, followed by slow addition of Me₃Al (1.5 mL, 3.0 mmol). The solution was allowed to warm to room temperature overnight then 10% HCl was added (150 mL). After extraction with Et₂O (3 x 100 mL) and drying over MgSO₄ the solvent was removed at reduced pressure. Flash chromatography of the residue using using hexane-ethyl acetate (80:20) as eluent afforded the *title compound* (7.73 g, 98%) as a pale yellow liquid; $[\alpha]_{589}^{20}$ +17.0 (*c* = 0.27, CHCl₃); ν_{\max} (film)/cm⁻¹ 3430, 2960, 2175, 1454, 1420, 1365, 1250, 1205, 1115, 1030, 945, 840, 760, 700, 650; δ_{H} (400 MHz; CDCl₃) 7.30-7.19 (m, 5H, ArH); 4.60 (s, 2H, CH₂Ph); 3.87 (m, 1H, 2-H), 3.54 (dd, 1H, *J* 3.9 and 9.6, 1-H), 3.42 (dd, 1H, *J* 6.4 and 9.6, 1-H), 2.62 (d, 1H, *J* 4.6, 2-H), 2.44 (dd, 1H, *J* 4.6, 15.4, 3-H), 2.38 (dd, 1H, *J* 5.4 and 15.4, 3-H) and 0.08 (s, 9H, (CH₃)₃Si); δ_{C} (100 MHz; CDCl₃) 137.9 (C, C_{arom}), 128.4 (2 x CH, C_{arom}), 127.8 (CH, C_{arom}), 127.7 (CH, C_{arom}), 102.5 (C, C-5), 87.3 (C, C-4); 73.4 (CH₂, C-1), 72.7 (CH₂, CH₂Ph), 68.8 (CH, C-2), 25.0 (CH₂, C-3) and 0.10 (CH₃, (CH₃)₃Si); MS (EI) *m/z* (%) 280 (100, [M + NH₄]⁺), 263 (44, [M + H]⁺), 245 (5), 218 (11), 189 (19), 173 (59), 155 (8), 129 (8), 108 (28), 105 (25), 91 (98) and 70 (21); HRMS (CI) *m/z* 263.1465 (calcd for C₁₅H₂₃O₂Si 263.1467).

(2*S*,4*Z*)-1-(Benzyloxy)-5-(trimethylsilyl)pent-4-en-2-ol (*Z*)-14 and (2*S*,4*E*)-1-(Benzyloxy)-5-(trimethylsilyl)pent-4-en-2-ol (*E*)-14

To a solution of 1-benzyloxy-5-(trimethylsilyl)pent-4-yn-2-ol **13** (2 g, 7.62 mmol) in dry Et₂O (20 mL) at 0 °C was added drop-wise a solution of DIBALH (1 M in hexane, 22.9 mL, 22.9 mmol). The solution was allowed to warm to room temperature then heated under reflux for 24 hours. The cooled mixture was poured into a mixture of water-crushed ice 1:1 (30 mL) with vigorous stirring, followed by the addition of 1 M HCl (10 mL). After filtration through a Celite pad, the aqueous phase was extracted with Et₂O (3 x 30 mL) and the organic extracts dried (MgSO₄). Flash chromatography of the residue obtained after concentration of the solvent using hexane-ethyl acetate (95:5) as eluent afforded the title olefins (1.46 g, 72%) as a 92:8 *Z/E* mixture of diastereomers.

Spectroscopic data for (*Z*)-(**14**):

$[\alpha]_{589}^{20} +3$ (c = 0.16, CHCl₃); ν_{\max} (film)/cm⁻¹ 3435, 3030, 2950, 2860, 1605, 1495, 1455, 1410, 1365, 1250, 1095, 860, 830, 765, 740, 700, 605; δ_{H} (400 MHz; CDCl₃) 7.40-7.27 (m, 5H, ArH), 6.34 (td, 1H, *J* 7.3 and 14.4, 4-H), 5.66 (d, 1H, *J* 14.4, 5-H), 4.57 (s, 2H, CH₂Ph), 3.90 (m, 1H, 2-H), 3.53 (dd, 1H, *J* 3.3 and 9.4, 1-H_a), 3.39 (dd, 1H, *J* 7.5 and 9.4, 1-H_b), 2.27-2.43 (m, 2H, 3-H), 0.15 (s, 9H, (CH₃)₃Si); δ_{C} (100.6 MHz; CDCl₃) 143.6 (CH, C-4), 137.8 (C, C_{arom}), 132.1 (CH, C-5); 128.3 (3 x CH, C_{arom}), 127.6 (2 x CH C_{arom}), 74.6 (CH₂, CH₂Ph), 74.0 (CH₂, CH₂Ph), 70.1 (CH, C-2), 37.1 (CH₂, C-3) and -1.73 (CH₃, (CH₃)₃Si); MS (CI) *m/z* (%) 282 (93, [M + NH₄]⁺), 265 (13, [M + H]⁺), 249 (4), 157 (28), 108 (82), 91 (100) and 73 (12); HRMS (CI): *m/z* 265.1626 (calcd for C₁₅H₂₅O₂Si 265.1624).

Spectroscopic data for (*E*)-(**14**):

δ_{H} (400 MHz; CDCl₃) 7.36-7.27 (m, 5H, ArH), 6.05 (td, 1H, *J* 6.7 and 18.5, 4-H), 5.70 (td, 1H, *J* 1.3 and 18.5, 5-H), 4.57 (s, 2H, CH₂Ph), 3.90 (m, 1H, 2-H), 3.50 (dd, 1H, *J* 6.2 and 9.4, 1-H_a), 3.33 (dd, 1H, *J* 7.9 and 9.4, 1-H_b), 2.26-2.34 (m, 2H, 3-H) and 0.05 (s, 9H, (CH₃)₃Si); δ_{H} (100 MHz, CDCl₃) 142.0 (CH, C-4), 138.0 (C, C_{arom}), 133.9 (CH, C-5), 128.4 (2 x CH, C_{arom}), 127.7 (2 x CH, C_{arom}), 126.5 (CH, C_{arom}), 74.7, 73.3 (2 x CH₂, C-1, CH₂Ph), 69.6 (CH, C-2), 40.8 (CH₂, C-3) and -1.68 (CH₃, (CH₃)₃Si).

(2*S*,6*S*)-(2-[(Benzyloxy)methyl]-6-(2-bromoethyl)-3,6-dihydro-2*H*-pyran) *cis*-10 and (2*S*,6*R*)-(2-[(Benzyloxy)methyl]-6-(2-bromoethyl)-3,6-dihydro-2*H*-pyran) *anti*-10

To a solution of (*Z*)-olefin **14** (2.0 g, 7.6 mmol) and 2-(2-bromoethyl)-1,3-dioxolane **15** (906 μ L, 7.56 mmol) in dry dichloromethane (40 mL) was added InCl_3 (1.7g, 7.6 mmol). After 48 hours at room temperature the mixture was diluted with dichloromethane (20 mL) and water was added (50 mL). The organic phase was extracted with brine (40 mL) then dried over MgSO_4 . Flash chromatography of the residue obtained after removal of the solvent at reduced pressure using hexane-ethyl acetate (95:5) as eluent afforded the *title compound* **10** (1.71 g, 73%) of as a 77:23 mixture of *cis/trans* diastereomers as a colourless liquid.

Spectroscopic data for *cis*-10:

$[\alpha]_{589}^{20}$ -31 ($c = 0.22$, CHCl_3); ν_{max} (film)/ cm^{-1} 3030, 2925, 2855, 1495, 1455, 1365, 1345, 1255, 1205, 1190, 1130, 1090, 1030, 950, 909, 735, 700; δ_{H} (400 MHz; CDCl_3) 7.36-7.27 (m, 5H, ArH), 5.86 (m, 1H, 5-H), 5.63 (tdd, 1H, J 1.4, 2.7 and 10.2, 4-H), 4.66 (d, 1H, J 12.2, CH_2Ph), 4.61 (d, 1H, J 12.2, CH_2Ph), 4.34 (brm, 1H, 6-H), 3.84 (tdd, 1H, J 3.9, 5.9 and 10.1, 2-H), 3.61-3.46 (m, 4H, 1'-H, 2''-H) and 2.13-1.91 (m, 4H, 1''-H, 3-H); δ_{C} (100 MHz; CDCl_3) 138.3 (C, C_{arom}), 129.1 (CH, C-4), 128.3 (2 x CH, C_{arom}), 127.6 (2 x CH, C_{arom}), 127.5 (CH, C_{arom}), 125.2 (CH, C-5), 73.4 (CH_2 , CH_2Ph), 73.3 (CH, C-2), 73.0 (CH_2 , C-1'), 72.7 (CH, C-6), 38.7 (CH_2 , C-1''), 29.6 (CH_2 , C-2'') and 27.6 (CH_2 , C-3); MS (EI) m/z (%) 312 (3, $[\text{M}(\text{C}_{15}\text{H}_{19}^{81}\text{BrO}_2)^+]$), 310 (3, $[\text{M}(\text{C}_{15}\text{H}_{19}^{79}\text{BrO}_2)^+]$), 221 (11), 219 (11), 137 (5), 135 (5), 91 (100), 81 (33, $[\text{Br}^+]$), 79 (11, $[\text{Br}^+]$); HRMS (CI) m/z 310.0564 (calcd for $\text{C}_{15}\text{H}_{19}^{79}\text{BrO}_2$ 310.0568), 312.0539 (calcd for $\text{C}_{15}\text{H}_{19}^{81}\text{BrO}_2$ 312.0548).

Spectroscopic data for *trans*-10:

δ_{H} (400 MHz; CDCl_3) 7.27-7.38 (m, 5H, ArH), 5.87 (m, 1H, 5-H), 5.69 (bd, 1H, J 10.6, 4-H), 4.62 (d, 1H, J 12.1, CH_2Ph), 4.58 (d, 1H, J 12.1, CH_2Ph), 4.41 (brd, 1H, J 9.8, 6-H), 3.87 (td, 1H, J 4.3 and 13.3, 2-H), 3.45-3.64 (m, 4H, 1'-H, 2''-H) and 1.87-2.30 (m, 4H, 1''-H, 3-H); δ_{C} (100 MHz; CDCl_3) 138.3 (C, C_{arom}), 128.6 (CH, C-4), 128.4 (2 x CH, C_{arom}), 127.6 (3 x CH, C_{arom}), 124.4 (CH, C-5), 73.5 (CH_2 , C-1'), 72.6 (CH_2 , CH_2Ph), 70.6 (CH, C-6), 67.2 (CH, C-2), 36.6 (CH_2 , C-1''), 30.0 (CH_2 , C-3) and 27.1 (CH_2 , C-2'').

3-[(4-Methoxybenzyl)oxy]propanal **17**

To a solution of oxalyl chloride (1.4 mL, 16.2 mmol) in dichloromethane (15 mL) at $-78\text{ }^{\circ}\text{C}$ was added dropwise a solution of dimethyl sulfoxide (1.9 mL, 27.0 mmol) in dichloromethane (6 mL). After 30 minutes, a solution of 3-[(4-methoxybenzyl)oxy]-1-propanol **16**ⁱⁱ (1 g, 6.0 mmol) in dichloromethane (1 mL) was added dropwise. After stirring for 1 hour at $-78\text{ }^{\circ}\text{C}$, Et_3N (6.7 mL, 48.1 mmol) was added dropwise and the solution allowed to warm to room temperature. After 30 minutes, 1 M HCl (30 mL) was added and the aqueous phase extracted with dichloromethane (2 x 50 mL). The organic extracts were washed with sat. NaHCO_3 and dried over MgSO_4 . Flash chromatography of the residue obtained after removal of the solvent at reduced pressure using hexane-ethyl acetate (80:20) as eluent afforded the title aldehyde **17**ⁱⁱⁱ (949 mg, 96%) as a colorless oil; ν_{max} (film)/ cm^{-1} 2905, 2835, 1725, 1615, 1585, 1515, 1465, 1360, 1300, 1245, 1175, 1090, 1035, 820, 760; δ_{H} (400 MHz; CDCl_3) 9.78 (t, 1H, J 1.9, 1-H), 7.25 (d, 2H, J 8.5, ArH), 6.88 (d, 2H, J 8.5, ArH), 4.46 (s, 2H, CH_2Ar), 3.80 (s, 3H, CH_3OAr), 3.78 (t, 2H, J 6.2, 3-H) and 2.67 (dt, 2H, J 1.9 and 6.2, 2-H); δ_{C} (100 MHz; CDCl_3) 201.2 (C, C-1), 159.2 (C, C_{arom}), 129.9 (C, C_{arom}), 129.3 (2 x CH, C_{arom}), 113.8 (2 x CH, C_{arom}), 72.9 (CH_2 , CH_2Ar), 63.5 (CH_2 , C-3), 55.2 (CH_3 , CH_3OAr) and 43.8 (CH_2 , C-2); MS (EI) m/z (%) 194 (16, $[\text{M}]^+$), 137 (78, $[\text{OPMBn}]^+$), 121 (100, $[\text{PMBn}]^+$), 109 (17) and 77 (16); HRMS (EI) m/z 194.0939 (calcd for $\text{C}_{11}\text{H}_{14}\text{O}_3$ 194.0943).

(+)-(3*R*,4*R*)-1-[(4-Methoxybenzyl)oxy]-4-methylhex-5-en-3-ol **18**

(*Z*)-butene (5 mL) was condensed and transferred to a mixture of $t\text{BuOK}$ (1.4 g, 11.3 mmol) in dry THF (24 mL). BuLi (7.1 mL, 11.3 mmol) was added dropwise and the yellow solution allowed to warm to $-45\text{ }^{\circ}\text{C}$ for 15 minutes. After cooling to $-78\text{ }^{\circ}\text{C}$, a solution of (-)- $\text{B}(\text{Ipc})_2\text{B}(\text{OMe})$ (3.90 g, 12.4 mmol) in THF (22 mL) was added dropwise to afford a colourless solution. After 45 minutes, $\text{BF}_3\cdot\text{OEt}_2$ (1.8 mL, 13.2 mmol) was added, followed immediately by a solution of 3-[(4-methoxybenzyl)oxy]propanal **17** (2.0 g, 10.3 mmol) in THF (28 mL). After 2 hours at $-78\text{ }^{\circ}\text{C}$, a solution of 1 M NaOH (12 mL) in water (2 mL) was added and the mixture heated under reflux for 1 hour. The aqueous phase was extracted with EtOAc (3 x 80 mL) and the organic extracts were dried over MgSO_4 . Flash chromatography of the residue obtained after removal of the solvent at reduced pressure using hexane-ethyl acetate (80:20) as eluent afforded the *title product* (1.90 g, 72%) as a single diastereomer and as a colourless liquid; $[\alpha]_{589}^{20} + 7.5$ ($c = 0.12$, CHCl_3); ν_{max} (film)/ cm^{-1} 3450, 2960, 2870, 1615, 1515, 1465, 1365,

1305, 1250, 1175, 1090, 1085, 1000, 915, 820, 735; δ_{H} (400 MHz; CDCl_3) 7.26 (d, 2H, J 8.6, ArH), 6.88 (d, 2H, J 8.6, ArH), 5.79 (ddd, 1H, J 7.6, 10.4 and 17.3, 5-H), 5.03-5.08 (m, 2H, 6-H), 4.46 (s, 2H, CH_2Ar), 3.81 (s, 3H, CH_3OAr), 3.59-3.73 (m, 3H, 1-H, 3-H), 2.90 (d, 1H, J 3.2, OH), 2.18-2.34 (m, 1H, 4-H), 1.64-1.82 (m, 2H, 2-H) and 1.06 (d, 3H, J 6.9, CH_3); δ_{C} (100 MHz; CDCl_3) 152.7 (C, C_{arom}), 141.0 (CH, C-5), 130.0 (CH, C_{arom}), 129.3 (2 x CH, C_{arom}), 114.9 (CH, C-6), 113.8 (2 x CH, C_{arom}), 74.6 (CH, C-3), 73.0 (CH_2 , CH_2Ar), 69.2 (CH_2 , C-1), 55.3 (CH_3 , CH_3OAr), 43.8 (CH, C-4), 33.5 (CH_2 , C-2) and 15.0 (CH_3 , CH_3); MS (EI) m/z (%) 250 (1, $[\text{M}]^+$), 232 (0.5, $[\text{M}-\text{H}_2\text{O}]^+$), 194 (2), 137 (22, $[\text{OPMBn}]^+$) and 121 (100); HRMS (EI) m/z 250.1567 (calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$ 250.1569).

Conversion to a Mosher ester derivative established the enantiomeric excess to be 97%.

(+)-(3*R*,4*R*)-1-[(4-Methoxybenzyl)oxy]-4-methyl-3-(*tert*-butyldiphenylsilyloxy)-5-hexene 19

To a solution of alcohol **18** (1.8 g, 7.2 mmol) and imidazole (2.2 g, 31.7 mmol) in DMF (15 mL) was added dropwise *tert*-butyldiphenylsilyl chloride (5.6 mL, 21.6 mmol). The mixture was stirred overnight at 100 °C then the DMF was evaporated under reduced pressure. The residue was taken up in Et_2O (200 mL), washed with brine (3 x 40 mL) and the organic layer dried over MgSO_4 . Flash chromatography using hexane-ethyl acetate (100:0 \rightarrow 95:5 \rightarrow 9:1) as eluent afforded the *title product* (3.48 g, 99%) as a colourless oil;

$[\alpha]_{589}^{20} + 11$ ($c = 0.21$, CHCl_3); ν_{max} (film)/ cm^{-1} 2965, 1790, 1750, 1610, 1515, 1465, 1305, 1265, 1250, 1175, 1100, 1060, 1035, 930, 820; δ_{H} (400 MHz; CDCl_3) 7.67-7.69 (m, 4H, PhSi), 7.32-7.45 (m, 6H, PhSi), 7.11 (d, 2H, J 8.7, ArH), 6.84 (d, 2H, J 8.7, ArH), 5.98 (ddd, 1H, J 6.4, 10.6 and 17.2, 5-H), 5.01 (td, J 1.7, 1.7 and 10.6, 6- H_a), 4.97 (td, J 1.7, 1.7 and 17.2, 6- H_b), 4.18 (s, 2H, CH_2Ph), 3.81 (m, 3H, CH_3OAr), 3.79-3.85 (m, 1H, 3-H), 3.37 (td, 1H, J 7.0, J 9.2, 1- H_a), 3.25 (td, 1H, J 7.0 and 9.2, 1- H_b), 2.28-2.38 (m, 1H, 4-H), 1.71 (q, 2H, J 7.0, 2-H), 1.06 (s, 9H, $(\text{CH}_3)_3\text{CSi}$) and 0.90 (d, 3H, J 7.0, CH_3); δ_{C} (100 MHz; CDCl_3) 159.0 (C, C_{arom}), 140.7 (CH, C-5), 136.0 (4 x CH, C_{arom}), 134.5, 134.1 (2 x C, C_{arom}), 130.7 (C, C_{arom}), 129.5 (2 x CH, C_{arom}), 129.4 (2 x CH, C_{arom}), 127.4 (4 x CH, C_{arom}), 114.2 (CH_2 , C-6), 113.6 (2 x CH, C_{arom}), 74.6 (CH, C-3), 72.3 (CH_2 , CH_2Ph), 67.0 (CH_2 , C-1), 55.2 (CH_3 , CH_3OAr), 42.4 (CH, C-4), 33.5 (CH_2 , C-2), 27.1 (CH_3 , $(\text{CH}_3)_3\text{CSi}$), 19.6 (C, $(\text{CH}_3)_3\text{CSi}$) and 14.5 (CH_3 , CH_3); MS (CI) m/z (%) 489 (1, $[\text{M} + \text{H}]^+$), 433 (2, $[\text{M}-t\text{Bu}]^+$), 352 (2), 336 (2), 216 (5), 199 (5), 137 (14, $[\text{OPMBn}]^+$) and 121 (100); HRMS (CI) m/z 489.2825 (calcd for $\text{C}_{31}\text{H}_{41}\text{O}_3\text{Si}$ 489.2825).

(-)-(3R,4R)-4-[tert-Butyl(diphenyl)silyl]oxy-6-[(4-methoxybenzyl)oxy]-3-methyl-1-hexanol 20

To a solution of alkene **19** (3.3 g, 6.8 mmol) in dry THF (100 mL) was added BH₃·DMS (1.3 mL, 13.5 mmol) dropwise. After stirring for 6 hours at room temperature MeOH was slowly added followed by 1 M NaOH (30 mL) and 30% hydrogen peroxide (2.7 mL, 23.6 mmol). The solution was left to stir for 3 hours at room temperature the water (30 mL) was added, the separated and the aqueous layer extracted with Et₂O (2 x 100 mL). The combined organic extracts were washed with brine (100 mL) and dried over MgSO₄. Flash chromatography (SiO₂, using hexane-diethyl ether 70:30) afforded the *title compound* (2.7 g, 78%) as a colourless oil.

$[\alpha]_{589}^{20}$ -7 (c = 0.43, CHCl₃) ν_{\max} (film)/cm⁻¹ 3400, 2930, 2860, 1610, 1590, 1515, 1460, 1430, 1360, 1300, 1250, 1175, 1110, 1040, 1005, 820, 740, 705, 610; δ_{H} (400 MHz; CDCl₃) 7.34-7.69 (m, 10H, PhSi), 7.10 (d, 2H, *J* 8.7, ArH), 6.84 (d, 2H, *J* 8.7, ArH), 4.19 (d, 1H, *J* 11.6, CH₂Ar); 4.16 (d, 1H, *J* 11.6, CH₂Ar), 3.82 (ddd, 1H, *J* 2.8, 5.2 and 8.3, 4-H), 3.80 (s, 3H, CH₃OPh), 3.57 (td, 1H, *J* 6.1 and 9.8, 1-H_a), 3.46 (td, 1H, *J* 6.6 and 9.8, 1-H_b), 3.35 (ddd, 1H, *J* 5.9, 7.2 and 9.1, 6-H_a), 3.22 (td, 1H, *J* 7.0 and 9.1, 6-H_b), 1.66-1.83 (m, 4H, 2-H, 3-H, 5-H), 1.38-1.44 (m, 1H, 2-H), 1.06 (s, 9H, (CH₃)₃CSi) and 0.82 (d, 3H, *J* 6.8, CH₃); δ_{C} (100 MHz; CDCl₃) 159.0 (C, C_{arom}), 136.0 (4 x CH, PhSi), 134.4 (C, PhSi), 134.0 (C, PhSi), 130.5 (C, C_{arom}), 129.7 (2 x CH, C_{arom}), 129.5 (2 x CH, PhSi), 129.1 (2 x CH, C_{arom}), 127.5 (4 x CH, PhSi), 113.6 (2 x CH, C_{arom}), 74.4 (CH, C-4), 72.3 (CH₂, CH₂Ph), 67.3 (CH₂, C-6), 61.5 (CH₂, C-1), 55.3 (CH₃, CH₃OPh), 35.2 (CH, C-3), 35.1 (CH₂, C-2), 33.0 (CH₂, C-5), 27.1 (3 x CH₃, (CH₃)₃CSi), 19.5 (C, (CH₃)₃CSi) and 15.3 (CH₃, CH₃); MS (CI) *m/z* (%) 507 (1, [M + H]⁺), 433 (1), 255 (2), 199 (11), 137 (4, [OPMBn]⁺) and 121 (100); HRMS (CI) *m/z* 507.2921 (calcd for C₃₁H₄₃O₄Si 507.2931).

(+)-(3R,4R)-4-[tert-Butyl(diphenyl)silyl]oxy-6-[(4-methoxybenzyl)oxy]-3-methylhexanal 11

To a solution of alcohol **20** (1.2 g, 2.36 mmol) in dichloromethane (30 mL) is added pyridine (572 mL, 7.08 mmol) followed by Dess-Martin periodinane (2.01 g, 4.73 mmol). After stirring for 2 hours at room temperature the mixture was diluted with dichloromethane (50 mL) and sat. Na₂S₂O₃ (50 mL) was added. The organic layer was washed with brine (100 mL) and dried over MgSO₄. Flash chromatography of the residue obtained after removal of the solvent at reduced pressure using hexane-diethyl ether (90:10) as eluent afforded the *title compound* (1.60 g, 84%) as a colourless oil; $[\alpha]_{589}^{20}$ +10 (c = 0.23, CHCl₃); ν_{\max} (film)/cm⁻¹ 2930, 2860, 1725, 1615, 1515,

1460, 1430, 1360, 1300, 1250, 1175, 1110, 1040, 935, 820, 740, 705, 615; δ_{H} (400 MHz; CDCl_3) 9.51 (t, 1H, J 1.7, 1-H), 7.65-7.67 (m, 4H, PhSi), 7.34-7.45 (m, 6H, PhSi), 7.11 (d, 2H, J 8.5, ArH), 6.84 (d, 2H, J 8.5, ArH), 4.21 (d, 1H, J 11.9, CH_2Ar), 4.18 (d, 1H, J 11.9, CH_2Ar), 3.86 (ddd, 1H, J 2.5, 5.0 and 7.3, 4-H), 3.81 (s, 3H, CH_3OPh), 3.36 (ddd, 1H, J 5.9, 7.0 and 9.1, 6- H_a), 3.26 (td, 1H, J 7.0 and 9.1, 6- H_b), 2.62 (m, 1H, 2- H_a), 2.15-2.24 (m, 2H, 2- H_b , 3-H), 1.63-1.79 (m, 2H, 5-H), 1.06 (s, 9H, $(\text{CH}_3)_3\text{CSi}$) and 0.84 (d, 3H, J 6.4, CH_3); δ_{C} (100 MHz; CDCl_3) 202.6 (CH, C-1), 159.1 (C, C_{arom}), 135.9 (4 x CH, PhSi), 134.2 (C, PhSi), 133.8 (C, PhSi), 130.5 (C, C_{arom}), 129.8 (2 x CH, PhSi), 129.6 (CH, C_{arom}), 129.1 (2 x CH, C_{arom}), 127.6 (CH, PhSi), 127.5 (4 x CH, PhSi), 113.7 (2 x CH, C_{arom}), 73.8 (CH, C-4), 72.4 (CH_2 , CH_2Ar), 67.0 (CH_2 , C-6), 55.2 (CH_3 , CH_3OAr), 46.5 (CH_2 , C-2), 33.0 (CH_2 and CH, C-5 and C-3), 27.1 (3 x CH_3 , $(\text{CH}_3)_3\text{CSi}$), 19.5 (C, $(\text{CH}_3)_3\text{CSi}$) and 14.9 (CH_3 , CH_3); MS (CI) m/z (%) 522 (2, $[\text{M} + \text{NH}_4]^+$), 367 (12), 216 (3), 196 (4), 137 (9), 121 (100), 111 (8); HRMS (CI) m/z 522.3037 ($\text{M} + \text{NH}_4^+$) (calcd for $\text{C}_{31}\text{H}_{40}\text{O}_4\text{SiNH}_4$ 522.3034).

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