

Synthetic approaches to the C11-C27 fragments of bryostatins

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Supplementary Data

Experimental for Schemes 1, 2, 3, 6, 7, 11 and 14

General experimental details

Flash column chromatography was performed using Merck silica gel (60H; 40-60 μ m, 230-240 mesh). Light petroleum refers to the fraction boiling between 40 and 60 °C and was redistilled. Tetrahydrofuran was dried over sodium-benzophenone and was distilled under nitrogen. Dichloromethane was dried over CaH₂ and was distilled. Ether refers to diethyl ether. Reactions under non-aqueous conditions were carried out under an atmosphere of nitrogen or argon.

Mass spectra used electron impact ionisation (EI⁺), chemical ionisation using ammonia (CI⁺), electrospray ionisation in the positive mode (ES⁺) and atmospheric pressure chemical ionisation in the positive or negative mode (APCI⁺ or APCI⁻). Low and high resolution mass spectra were recorded using a Micromass Trio 200 and a Kratos Concept IS spectrometer, respectively. Infra-red spectra were measured using a Genesis FTIR spectrometer on NaBr plates, either neat or as evaporated films. Nuclear magnetic resonance spectra were recorded using Varian Unity 500 (500 MHz), Varian INOVA 400 (400 MHz) and Varian Unity 300 (300 MHz) spectrometers. Coupling constants (*J*) are given in Hertz (Hz) and chemical shifts are relative to tetramethylsilane. Residual non-deuteriated solvent was used as the internal standard.

(6R)-4-[(Z)-2-tert-Butyldiphenylsilyloxyethylidene]-7-(4-methoxybenzyloxy)-6-triethylsilyloxyhept-1-ene (10).

Imidazole (8.14 g, 120 mmol) was added to the alcohol **9** (21.2 g, 39.9 mmol) in DCM (200 mL) and the mixture cooled to 0 °C before the dropwise addition of triethylsilyl chloride (8.0 mL, 48 mmol). After being allowed to warm to rt, the mixture was stirred for 2 h and saturated aqueous sodium bicarbonate (200 mL) was added. The aqueous layer was extracted with DCM (2 × 100 mL) and the organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (light petroleum then 50:1 light petroleum:ether) gave the *title compound 10* as a clear, colourless oil (25.7 g, ca. 100%), *R*_f = 0.60 (20:1 light petroleum:ether), [α]_D²⁸ -8.5 (c 4.7, CHCl₃) (Found: M⁺ + Na, 667.3599. C₃₉H₅₆O₄NaSi₂ requires M, 667.3609; ν_{\max} /cm⁻¹ 3071, 2954, 2876, 1613, 1512, 1461, 1428, 1248, 1110, 1006, 822, 739 and 703; δ_{H} (500 MHz, CDCl₃) 0.41 (6 H, q, *J* 8.1, 3 × SiCH₂), 0.80 (9 H, t, *J* 8.1, 3 × SiCH₂CH₃), 0.97 [9 H, s, SiC(CH₃)₃], 1.91 (1 H, dd, *J* 13.6, 7.2, 5-H), 2.07 (1 H, dd, *J* 13.6, 5.9, 5-H'), 2.67 (2 H, d, *J* 6.7, 3-H₂), 3.13 (2 H, d, *J* 5.0, 7-H₂), 3.70 (1 H, m, 6-H), 3.71 (3 H, m, OCH₃), 4.16 (1 H, dd, *J* 13.0, 5.9, 2'-H), 4.19 (1 H, dd, *J* 13.0, 6.7, 2'-H'), 4.25 and 4.28 (each 1 H, d,

J 11.8, ArHCH), 4.92-5.00 (2 H, m, 1-H₂), 5.42 (1 H, m, 1'-H), 5.67 (1 H, m, 2-H), 6.75 and 7.10 (each 2 H, d, *J* 7.9, ArH), 7.25-7.35 (6 H, m, ArH) and 7.57-7.64 (4 H, m, ArH); δ_{C} (125 MHz, CDCl₃) 4.9, 6.9, 19.2, 26.9, 35.9, 42.1, 55.3, 61.2, 70.5, 72.9, 74.0, 113.7, 116.3, 127.6, 128.1, 129.2, 129.5, 130.5, 134.0, 135.6, 136.0, 136.5 and 159.1; *m/z* (ES⁺) 667.5 (M⁺ + 23, 100%).

(2R)-4-[(Z)-2-tert-Butyldiphenylsilyloxyethylidene]-2-triethylsilyloxyhept-6-en-1-ol (11).

An aqueous pH 7 phosphate buffer (95 mL) was added to the PMB-ether **10** (12.7 g, 19.7 mmol) in DCM (95 mL) and then DDQ (5.40 g, 23.7 mmol) was added in one portion with vigorous stirring. The slurry was stirred at rt for 20 min, diluted with DCM (845 mL) and filtered through celite, washing the celite thoroughly with saturated aqueous sodium bicarbonate (845 mL). The aqueous layer was extracted with DCM (3 × 300 mL) and the organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (8.5:1 light petroleum:ether) gave the *title compound 11* as a clear, colourless oil (8.69 g, 84%), *R*_f = 0.69 (2:1 light petroleum:ether), [α]_D²⁸ -3.7 (c 14.6, CHCl₃) (Found: M⁺ + Na, 547.3029. C₃₁H₄₈O₃NaSi₂ requires M, 547.3034; ν_{\max} /cm⁻¹ 3468, 3072, 2956, 2877, 1637, 1472, 1463, 1428, 1390, 1240, 1112, 1056, 1006, 823, 739 and 702; δ_{H} (500 MHz, CDCl₃) 0.47 (6 H, q, *J* 8.0, 3 × SiCH₂), 0.83 (9 H, t, *J* 8.0, 3 × SiCH₂CH₃), 0.97 [9 H, s, SiC(CH₃)₃], 2.02 (1 H, dd, *J* 13.5, 5.9, 3-H), 2.09 (1 H, dd, *J* 13.5, 8.1, 3-H'), 2.13 (1 H, m, OH), 2.69 (2 H, d, *J* 6.9, 5-H₂), 3.24 (1 H, ddd, *J* 11.2, 6.5, 4.9, 1-H), 3.37 (1 H, ddd, *J* 11.2, 5.8, 4.3, 1-H'), 3.68 (1 H, m, 2-H), 4.12 (1 H, dd, *J* 12.7, 6.5, 2'-H), 4.18 (1 H, dd, *J* 12.7, 6.7, 2'-H'), 4.94-5.00 (2 H, m, 7-H₂), 5.42 (1 H, m, 1'-H), 5.68 (1 H, m, 6-H), 7.25-7.38 (6 H, m, ArH), 7.58-7.64 (4 H, m, ArH); δ_{C} (125 MHz, CDCl₃) 4.9, 6.9, 19.2, 26.8, 35.0, 42.2, 60.8, 65.7, 71.3, 116.6, 127.7, 127.9, 129.6, 133.7(2), 135.6, 136.3 and 136.4; *m/z* (ES⁺) 547.5 (M⁺ + 23, 100%).

1-Phenylsulfonyl-3-(4-methoxybenzyloxy)-2,2-dimethylpropane (15).

Tetra-*n*-butylammonium iodide (5%), sodium hydride (60% in oil, 1.22 g, 1.2 equiv.) and 4-methoxybenzyl chloride (4.69 g, 1.2 equiv.) were added to the alcohol **13**¹⁴ (6 g, 0.03 mol) in DMF (150 mL) at 0 °C and the reaction mixture was stirred at rt for 16 h. Ether (100 mL), aqueous sodium hydroxide (1 M, 300 mL) and more ether (100 mL) were added and the organic phase was washed with saturated aqueous sodium bicarbonate. The aqueous phases were extracted with ether (2 × 100 mL) and the organic extracts washed with brine, then dried (MgSO₄) and concentrated under reduced pressure. Chromatography (25:1 light petroleum:ether) of the residue gave the 4-methoxybenzyl ether **14** (8.72 g, 86%); δ_{H} (300 MHz, CDCl₃) 1.05 (6 H, s, 2 × 2-CH₃), 3.08 (2 H, s, 1-H₂), 3.31 (2 H, s, 3-H₂), 3.89 (3 H, s, OCH₃), 4.41 (2 H, s, ArCH₂), 6.91 (2 H, d, *J* 8.0, ArH), 7.20-7.35 (5 H, m, ArH) and 7.41 (2 H, d, *J* 7.3, ArH); δ_{C} (75 MHz, CDCl₃) 24.9, 36.8, 44.0, 55.5, 73.1, 77.0, 114.0, 125.8, 129.1, 129.3, 137.1, 138.6 and 159.3.

Oxone (46.1 g, 75 mmol) was added to the 4-methoxybenzyl ether **14** (8.5 g, 26.8 mmol) in MeOH, H₂O

and THF (1:1:1, 54 mL) at 0 °C. After 5 min, the white suspension was stirred at rt for 8 h then poured into water (400 mL). The mixture was extracted with DCM (3 × 125 mL) and the organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (3.5:1 light petroleum:ether) gave the *title compound 15* (9.8 g); δ_{H} (300 MHz, CDCl₃) 1.12 (6 H, s, 2 × 2-CH₃), 3.21 (2 H, s, 1-H₂), 3.31 (2 H, s, 3-H₂), 3.89 (3 H, s, OCH₃), 4.41 (2 H, s, ArCH₂), 6.91 and 7.26 (each 2 H, d, *J* 8, ArH), 7.50-7.70 (3 H, m, ArH) and 7.98 (2 H, d, *J* 7.3, ArH); δ_{C} (75 MHz, CDCl₃) 25.2, 36.8, 55.5, 63.2, 73.0, 77.9, 114.0, 127.8, 129.4(2), 130.8, 133.6, 142.2 and 159.4.

1-(Benzo[thiazol-2-ylsulfonyl]-3-(4-methoxybenzyloxy)-2,2-dimethylpropane (17).

3-(4-Methoxybenzyloxy)-2,2-dimethylpropan-1-ol (**16**) (39.1 g, 175 mmol) in THF (400 mL) was added to triphenylphosphine (68.3 g, 260 mmol) and 2-mercaptobenzothiazole (62.5 g, 374 mmol) in THF (1.6 L) and the solution cooled to 0 °C. Di-isopropylazodicarboxylate (51 mL, 260 mmol) was added and the reaction mixture warmed to rt. After stirring for 2.5 h, the solution was concentrated to *ca.* 400 mL under reduced pressure then diluted with ether (1 L) and water (1 L). The organic layer was washed with aqueous sodium hydroxide (1 M, 500 mL) and brine (500 mL) then dry loaded onto silica. Chromatography (2:1 light petroleum:ether then 1:2 light petroleum ether) afforded slightly impure 1-(benzo[thiazol-2-ylsulfonyl]-3-(4-methoxybenzyloxy)-2,2-dimethylpropane as an orange oil (69.8 g). Further chromatography (35:1 to 9:1 light petroleum:ether) of a sample gave 1-(benzo[thiazol-2-ylsulfonyl]-3-(4-methoxybenzyloxy)-2,2-dimethylpropane as a pale yellow oil, $R_{\text{f}} = 0.84$ (1:1 light petroleum:ether) (Found: M⁺ + H, 374.1251. C₂₀H₂₄O₂NS₂ requires M, 374.1243); $\nu_{\text{max}}/\text{cm}^{-1}$ 3062, 2958, 2859, 1612, 1512, 1460, 1427, 1303, 1248, 1174, 1094, 1036, 993 and 821; δ_{H} (300 MHz, CDCl₃) 0.99 (6 H, s, 2 × 2-CH₃), 3.18, (2 H, s, 1-H₂), 3.41 (2 H, s, 3-H₂), 3.71 (3 H, s, OCH₃), 4.35 (2 H, s, ArCH₂), 6.76 and 7.14 (each 2 H, d, *J* 8.5, ArH), 7.20 and 7.32 (each 1 H, m, ArH) and 7.65 and 7.77 (each 1 H, d, *J* 8.1, ArH); δ_{C} (CDCl₃, 75 MHz) 24.4, 36.5, 42.8, 55.3, 73.0, 77.2, 113.7, 120.9, 121.4, 124.1, 126.0, 129.1, 130.7, 135.2, 153.2, 159.1 and 168.2; m/z (ES⁺) 396.2 (M⁺ + 23, 89%) and 374.2 (M⁺ + 1, 100).

A cooled solution of ammonium molybdate tetrahydrate (46.1 g, 39.7 mmol) in aqueous hydrogen peroxide (30%, 207 mL) was added to the sulfide (56.5 g from 141 mmol alcohol **16**) in ethanol (1.07 L) at 0 °C maintaining a temperature of <10 °C during the addition. The solution was stirred at 0 °C for 1 h, before warming to rt and stirring for 19 h. This addition was repeated twice at 24 h intervals, before the addition of ethyl acetate (460 mL). The solution was cooled to 0 °C before the careful addition of saturated aqueous sodium bisulfite (250 mL). The organic layer was washed with saturated aqueous sodium bisulfite (5 × 250 mL) and aqueous sodium bisulfite was added to the aqueous washes until a negative peroxide test was obtained. After extraction of the aqueous washings with ethyl acetate (3 × 500 mL), concentration of the organic extracts under reduced

pressure to *ca.* 100 mL gave a crystalline solid, which was filtered off and washed with ice-cold ethanol (20 mL) to give the *title compound 17* as a white, granular solid (45.7 g, 80% from alcohol **16**), $R_{\text{f}} = 0.57$ (1:1 light petroleum:ether), m.p. 78.3-79.5 °C (Found: M⁺ + Na, 428.0964. C₂₀H₂₃O₄NNaS₂ requires M, 428.0961); $\nu_{\text{max}}/\text{cm}^{-1}$ 3065, 2964, 2863, 1701, 1612, 1512, 1472, 1327, 1248, 1150, 1094, 1034, 853 and 822; δ_{H} (300 MHz, CDCl₃) 1.25 (6 H, s, 2 × 2-CH₃), 3.37 (2 H, s, 1-H₂), 3.68 (2 H, s, 3-H₂), 3.81 (3 H, s, OCH₃), 4.41 (2 H, s, ArCH₂), 6.86 and 7.22 (each 2 H, d, *J* 8.5, ArH), 7.55-7.68 (2 H, m, ArH) and 8.01 and 8.22 (each 1 H, d, *J* 7.6, ArH); δ_{C} (CDCl₃, 75 MHz) 25.0, 36.7, 55.3, 61.5, 72.9, 77.6, 113.7, 122.4, 125.4, 127.6, 127.9, 129.2, 130.4, 136.8, 152.7, 159.1 and 167.9; m/z (ES⁺) 428.3 (M⁺ + 23, 100%) and 406.3 (M⁺ + 1, 9).

(7E)-(6R)-9,9-Dimethyl-4-[(Z)-2-tert-butylidiphenylsilyloxyethylidene]-6-triethylsilyloxy-10-(4-methoxybenzyloxy)deca-1,7-diene (18).

Pyridine (0.18 ml, 2.22 mmol) and the Dess-Martin periodinane (0.167 g, 0.394 mmol) were added to the alcohol **11** (0.107 g, 0.189 mmol) in DCM (1.3 mL) and the mixture was stirred at rt for 3 h. Ether (10 mL) and a mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium bisulfite (1:1, 10 mL) were added and the aqueous layer was extracted with ether (2 × 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure to give the aldehyde **12**, a yellow oil (0.13 g), used without purification.

Lithium hexamethyldisilazide (1.0 M in toluene, 0.42 mL, 0.42 mmol) was added to the sulfone **17** (0.154 g, 0.381 mmol) in THF (4.0 mL) at -78 °C and the solution was stirred at -78 °C for 20 min. The aldehyde **12** (0.224 g from 0.204 g, 0.389 mmol of the alcohol **11**) in THF (1.0 mL) was added and the solution was allowed to warm to rt. After 1.5 h, the mixture was partitioned between ether (30 mL) and saturated aqueous sodium bicarbonate (30 mL), and the aqueous layer was extracted with ether (2 × 30 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (50:1 light petroleum:ether) gave the *title compound 18* containing *ca.* 20% of its (7Z)-isomer, as a pale yellow oil (0.178 g, 65%), $R_{\text{f}} = 0.67$ (1:1 light petroleum:ether), $[\alpha]_{\text{D}}^{26} +3.6$ (*c* 14.4, CHCl₃) (Found: M⁺ + Na, 735.4236. C₄₄H₆₄O₄NaSi₂ requires M, 735.4235); $\nu_{\text{max}}/\text{cm}^{-1}$ 3071, 2956, 2874, 1615, 1588, 1514, 1463, 1428, 1361, 1247, 1111, 1055, 1006, 823, 740 and 702; δ_{H} (300 MHz, CDCl₃) (7E)-isomer **18** 0.38 (6 H, q, *J* 7.9, 3 × SiCH₂), 0.77 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 0.85 and 0.86 (each 3 H, s, 9-CH₃), 0.96 [9 H, s, SiC(CH₃)₃], 1.89 and 2.01 (each 1 H, dd, *J* 13.2, 6.8, 5-H), 2.65 (2 H, d, *J* 7.0, 3-H₂), 2.99 (2 H, s, 10-H₂), 3.72 (3 H, s, OCH₃), 3.91 (1 H, m, 6-H), 4.15 (2 H, d, *J* 6.1, 2'-H₂), 4.30 (2 H, s, ArCH₂), 4.88-4.99 (2 H, m, 1-H₂), 5.15 (1 H, dd, *J* 15.7, 7.2, 7-H), 5.33-5.45 (2 H, m, 8-H, 1'-H), 5.65 (1 H, m, 2-H), 6.78 and 7.14 (each 2 H, d, *J* 8.6, ArH), 7.22-7.38 (6 H, m, ArH) and 7.54-7.65 (4 H, m, ArH); (7Z)-isomer 3.00 (2 H, s, 10-H₂) and 4.32 (2 H, s, ArCH₂); δ_{C} (75 MHz, CDCl₃) (7E)-isomer **18** 4.8, 6.9, 19.2, 24.4, 26.9, 37.1, 40.0, 42.5, 55.3, 61.4, 72.9, 73.2, 79.1, 113.7, 116.2, 127.6, 127.9, 128.9, 129.5, 129.9, 131.0, 134.0, 135.6, 135.8, 136.6, 137.6 and 159.0; m/z (ES⁺)

735.5 ($M^+ + 23$, 100%), 730.5 ($M^+ + 18$, 20) and 581.5 (13).

n-Butyllithium (1.6 M in THF, 95 μ L) was added to the sulfone **15** (45 mg) in THF (1.5 mL) at -78°C and the solution stirred for 10 min. The aldehyde **12** (from 75 mg alcohol **11**, 0.138 mmol) in THF (1 mL) was added and the mixture stirred at -78°C for 10 min. Ether (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added and the aqueous phase was extracted with ether (2×10 mL). The organic extracts were washed with brine, dried (MgSO_4) and concentrated under reduced pressure. Chromatography (8:1 light petroleum:ether) of the residue gave the adducts (75 mg, 60%). These adducts (155 mg, 0.178 mmol) in THF (2.0 mL) were added to a freshly prepared solution of SmI_2 (1.067 mmol, 6 equiv) and hexamethylphosphoric triamide (4.27 mmol, 24 equiv.) in THF (10 mL) and the mixture stirred for 1 h. Saturated aqueous ammonium chloride (15 mL) and ether (15 mL) were added and the aqueous layer was extracted with ether (2×15 mL). The organic extracts were washed with brine, dried (MgSO_4) and concentrated under reduced pressure. Chromatography (19:1 light petroleum:ether) gave the diene **18** (19 mg, 15%).

(3E,5R)-7-[2-(Z)-tert-Butyldiphenylsilyloxyethylidene]-2,2-dimethyl-5-triethylsilyloxydeca-3,9-dienal (19).

An aqueous pH7 phosphate buffer (13.5 mL) was added to the PMB-ether **18** (1.99 g, 2.78 mmol) in DCM (13.5 mL) and the mixture stirred rapidly whilst DDQ (0.760 g, 3.35 mmol) was added. The slurry was stirred for 20 min, DCM (120 mL) was added and the mixture filtered through celite, washing the celite thoroughly with saturated aqueous sodium bicarbonate (190 mL). The aqueous layer was extracted with DCM (3×200 mL) and the organic extracts were dried (Na_2SO_4) then concentrated under reduced pressure to give (3E,5R)-7-[2-(Z)-tert-butyldiphenylsilyloxyethylidene]-2,2-dimethyl-5-triethylsilyloxy-deca-3,9-dienol (2.1 g), $R_f = 0.53$ (1:1 ether:light petroleum).

Pyridine (2.55 mL, 31.5 mmol) and then the Dess-Martin periodinane (2.41 g, 5.68 mmol) were added to this alcohol (2.1 g from 2.78 mmol **18**) in DCM (20 mL). After 1.5 h, the mixture was partitioned between ether (100 mL) and a mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium bisulfite (3:2, 100 mL). The aqueous layer was extracted with ether (2×100 mL) and the organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (100:1 then 50:1 light petroleum:ether) of the residue gave the *title compound* **19** as a pale yellow oil (1.32 g, 80% from **18**), $R_f = 0.69$ (2:1 ether:light petroleum), $[\alpha]_D^{26} +8.7$ (c 9.0, CHCl_3) (Found: $M^+ + \text{Na}$, 613.3504. $\text{C}_{36}\text{H}_{54}\text{O}_3\text{NaSi}_2$ requires M , 613.3504); $\nu_{\text{max}}/\text{cm}^{-1}$ 3072, 2956, 2933, 2875, 1732, 1463, 1428, 1390, 1362, 1261, 1237, 1112, 1057, 1007, 913, 823 and 739; δ_{H} (400 MHz, CDCl_3) 0.39 (6 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.78 (9 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 0.97 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 1.00 and 1.01 (each 3 H, s, 2- CH_3), 1.89 (1 H, dd, J 13.2, 6.7, 6-H), 2.02 (1 H, dd, J 13.2, 7.1, 6-H'), 2.66 (2 H, d, J 6.9, 8- H_2), 3.98 (1 H, m, 5-H), 4.12 (2 H, d, J 6.3, 2'- H_2), 4.90-5.06 (2 H, m, 10- H_2), 5.31 (1 H, dd, J 15.7, 6.5, 4-H), 5.33 (1 H, d, J 15.7, 3-H), 5.42 (1 H, t, J 6.3, 1'-H), 5.66 (1 H, ddt, J 16.9, 10.2, 6.9, 9-H), 7.26-

7.38 (6 H, m, ArH), 1.97-2.03 (4 H, m, ArH) and 9.17 (1 H, s, 1-H); δ_{C} (100 MHz, CDCl_3) 3.6, 5.7, 18.1, 20.1, 20.2, 25.8, 38.6, 41.4, 47.1, 60.1, 71.2, 115.4, 126.6, 127.2, 128.5, 129.7, 132.8, 133.5, 134.3, 134.6, 135.3 and 201.3; m/z (ES^+) 613 ($M^+ + 23$, 100%) and 608 ($M^+ + 1$, 26).

(4E)-(2RS,6R)-2-tert-Butyldimethylsilyloxy-8-[(Z)-2-tert-butyldiphenylsilyloxyethylidene]-3,3-dimethyl-6-triethylsilyloxyundeca-4,10-dienenitrile (20).

tert-Butyldimethylsilyl cyanide (86 mg, 0.61 mmol) and then zinc iodide (18 mg, 0.056 mmol) were added to the aldehyde **19** (0.279 g, 0.472 mmol) in DCM (4.6 mL) and the mixture was stirred at rt for 1 h. More *tert*-butyldimethylsilyl cyanide (66 mg, 0.47 mmol) and zinc iodide (13 mg, 0.041 mmol) were added and after a further 3 h, the mixture was partitioned between saturated aqueous sodium bicarbonate (40 mL) and ether (40 mL). The aqueous layer was extracted with ether (2×40 mL) and the organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (50:1 light petroleum:ether) gave the *title compound* **20** as a pale yellow oil (0.23 g, 66%), a 50:50 mixture of 2-epimers, $R_f = 0.47$ (10:1 light petroleum:ether), $[\alpha]_D^{28} -7.2$ (c 6.4, CHCl_3) (Found: $M^+ + \text{Na}$, 754.4471. $\text{C}_{43}\text{H}_{69}\text{O}_3\text{NNaSi}_3$ requires M , 754.4477); $\nu_{\text{max}}/\text{cm}^{-1}$ 2955, 2858, 2351, 2324, 1638, 1471, 1428, 1413, 1388, 1363, 1256, 1110, 1056, 1005, 977 and 837; δ_{H} (500 MHz, CDCl_3) 0.00 (3 H, s, SiCH_3), 0.09 (3 H, s, SiCH_3), 0.39 (6 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.77 (9 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 0.82 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.93, 0.94, 0.95, 0.96 (each 1.5 H, s, 3- CH_3), 0.96 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 1.86 (0.5 H, dd, J 13.3, 6.4, 7-H), 1.87 (0.5 H, dd, J 13.3, 6.2, 7-H), 2.00 (0.5 H, dd, J 13.3, 7.1, 7-H'), 2.01 (0.5 H, dd, J 13.3, 7.2, 7-H'), 2.66 (2 H, d, J 6.6, 9- H_2), 3.87 (1 H, s, 2-H), 3.97 (1 H, m, 6-H), 4.14 (2 H, d, J 6.3, 2'- H_2), 4.90-5.00 (2 H, m, 11- H_2), 5.31 (0.5 H, dd, J 15.7, 6.2, 5-H), 5.31 (0.5 H, dd, J 15.7, 6.5, 5-H), 5.41 (1 H, m, 1'-H), 5.43 and 5.47 (each 0.5 H, d, J 15.7, 4-H), 5.66 (1 H, m, 10-H), 7.25-7.36 (6 H, m, ArH) and 7.56-7.62 (4 H, m, ArH); δ_{C} (100 MHz, CDCl_3) -6.5 , -6.3 , 3.7, 5.8(2), 17.1, 18.1, 21.2, 21.5, 21.8, 22.0, 24.5, 25.8, 38.7, 38.8, 39.6, 39.7, 41.3, 41.4, 60.2, 69.3, 69.4, 71.1, 71.4, 115.3, 117.8(2), 126.6, 127.2, 128.5, 131.7, 132.0, 132.1, 132.4, 132.9, 134.3(2), 134.6 and 135.4; m/z (ES^+) 755.0 ($M^+ + 23$, 100%) and 382.5 (22).

(4E)-(2RS,6R)-2-Benzyl-2-tert-butyldimethylsilyloxy-8-[(Z)-2-tert-butyldiphenylsilyloxyethylidene]-3,3-dimethyl-6-triethylsilyloxyundeca-4,10-dienenitrile (21).

Hexamethylphosphoric triamide (46 μ L, 0.26 mmol) was added to the silylated cyanohydrin **20** (75 mg, 0.10 mmol) in THF (0.4 mL) and the solution was cooled to -78°C before the dropwise addition of lithium diisopropylamide (1.5 M in THF/heptane/ethylbenzene, 89 μ L, 13 mmol). The reaction mixture was stirred at -78°C for 1 h, benzyl bromide (61 μ L, 0.51 mmol) was added, and the solution stirred at -78°C for 1 h then at rt for 1 h. Ether (10 mL) and saturated aqueous sodium bicarbonate were added and the aqueous layer was extracted with ether (2×10 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (light petroleum to 50:1 light

petroleum:ether) gave the *title compound 21* as a pale yellow oil (69 mg, 83%), a 45:55 mixture of 2-epimers, $R_f = 0.657$ (10:1 light petroleum:ether), $[\alpha]_D^{30} +3.6$ (c 5.0, CHCl₃) (Found: M⁺ + NH₄, 844.4960. C₅₀H₇₅O₃NNaSi₃ requires M, 844.4947); $\nu_{\max}/\text{cm}^{-1}$ 3071, 2959, 2929, 2856, 1471, 1464, 1429, 1390, 1361, 1262, 1112, 1055, 1016, 940, 830, 803, 781, 742 and 701; δ_H (400 MHz, CDCl₃) -0.92 (1.7 H, s, SiCH₃), -0.91 (1.3 H, s, SiCH₃), 0.04 (3 H, s, SiCH₃), 0.37-0.49 (6 H, m, 3 × SiCH₂), 0.74-0.85 [18 H, m, Si(C(CH₃)₃, 3 × SiCH₂CH₃), 0.95 [5 H, s, SiC(CH₃)₃], 0.95 [4 H, s, SiC(CH₃)₃], 1.04 (1.3 H, s, 3-CH₃), 1.07 (3.4 H, s, 2 × 3-CH₃), 1.09 (1.3 H, s, 3-CH₃'), 1.96 and 2.06 (each 1 H, m, 7-H), 2.62-2.74 (3 H, m, 9-H₂, 2-CH), 2.78 (0.5 H, d, J 13.7, 2-CH'), 2.80 (0.5 H, d, J 13.7, 2-CH'), 4.07 (1 H, m, 6-H), 4.11-4.22 (2 H, m, 2'-H₂), 4.91-5.03 (2 H, m, 11-H₂), 5.33 (1 H, dd, J 15.7, 6.6, 5-H), 5.41 (1 H, m, 1'-H), 5.61-5.75 (2 H, m, 4-H, 10-H), 7.14-7.39 (11 H, m, ArH) and 7.54-7.63 (4 H, m, ArH); δ_C (100 MHz, CDCl₃) -6.3(2), -3.8, 3.8, 5.8, 17.6, 18.1, 25.0, 25.8, 38.7, 41.3, 41.4, 41.7, 44.0(2), 60.2, 71.4, 71.5, 78.3(2), 115.4(2), 118.8, 126.3, 126.6, 127.2, 127.4, 128.5, 130.6, 131.8, 131.9, 132.3, 132.4, 132.8(2), 134.1(2), 134.5 and 135.3; m/z (ES⁺) 844.3 (M⁺ + 23, 57%), 840.4 (M⁺ + 1, 25), 568.2 (47) and 549.2 (100).

3-(Benzothiazol-2-ylsulfonyl)-2,2-dimethylpropan-1-ol (22).

An aqueous pH 7.2 phosphate buffer (58 mL) was added to the PMB ether **17** (4.99 g, 12.3 mmol) in DCM (58 mL) and the mixture was stirred rapidly whilst DDQ (8.40 g, 37.0 mmol) was added in one portion. The slurry was stirred for 30 min, DCM (100 mL) was added, and the mixture filtered through celite. The filter cake was washed with saturated aqueous sodium bicarbonate (100 mL) and DCM (2 × 100 mL). The aqueous layer was extracted with DCM (4 × 40 mL), and the organic extracts were washed with saturated aqueous sodium bisulfite (2 × 100 mL) and saturated aqueous sodium bicarbonate (2 × 100 mL), dried (MgSO₄) and concentrated under reduced pressure. Chromatography (2:1 then 1:2 light petroleum:ether) of the residue gave the *title compound 22* as a clear, colourless oil (3.51 g, ca. 100%), $R_f = 0.57$ (1:1 light petroleum:ether) (Found: M⁺ + Na, 308.0389. C₁₂H₁₅O₃NNaS₂ requires M, 308.0386); $\nu_{\max}/\text{cm}^{-1}$ 3417, 3066, 2966, 2878, 1555, 1472, 1421, 1325, 1237, 1147, 1051, 1024, 854 and 762; δ_H (CDCl₃, 300 MHz) 1.23 (6 H, s, 2 × 2-CH₃), 2.58 (1 H, t, J 6.5, OH), 3.61, (2 H, s, 3-H₂), 3.66 (2 H, d, J 6.5, 1-H₂), 7.56-7.71 (2 H, m, ArH), 8.03 (1 H, d, J 7.5, ArH) and 8.23 (1 H, d, J 8.0, ArH); δ_C (75 MHz, CDCl₃) 25.1, 38.1, 61.2, 69.9, 122.4, 125.4, 127.8, 128.1, 136.7, 152.6 and 167.4; m/z (ES⁺) 308.0 (M⁺ + 23, 100%).

3-(Benzothiazol-2-ylsulfonyl)-2,2-dimethylpropanal (23).

Dimethyl sulfoxide (3.00 mL, 42.3 mmol) was added to oxalyl chloride (1.90 mL, 21.8 mmol) in DCM (130 mL) at -78 °C and the solution stirred for 1 h. The alcohol **22** (5.00 g, 17.5 mmol) in DCM (90 mL) was added and, after stirring for 1 h at -78 °C, triethylamine (12 mL, 86 mmol) was added. The solution was stirred at -78 °C for 1 h before warming to rt and stirring for 30 min. Water (90 mL) was added and the aqueous layer was extracted with ether (3 × 200 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure.

Chromatography (1:1 light petroleum:ether) of the residue gave the *title compound 23* as a pale yellow oil (4.61 g, 93%) (Found: M⁺ + H, 284.0405. C₁₂H₁₄O₃NS₂ requires M, 284.0410); $\nu_{\max}/\text{cm}^{-1}$ 3066, 2974, 2927, 1731, 1555, 1471, 1329, 1150, 1124, 1024 and 855; δ_H (CDCl₃, 300 MHz) 1.33 (6 H, s, 2 × 2-CH₃), 3.79 (2 H, s, 3-H₂), 7.49-7.63 (2 H, m, ArH), 7.95 (1 H, d, J 7.5, ArH), 8.15 (1 H, d, J 8.0, ArH) and 9.46 (1 H, s, 1-H); δ_C (75 MHz, CDCl₃) 22.0, 45.3, 60.1, 122.4, 125.5, 127.8, 128.2, 136.8, 152.5, 166.8 and 201.3; m/z (ES⁺) 306.1 (M⁺ + 23, 100%) and 284.1 (M⁺ + 1, 26).

2-[2-(Benzothiazol-2-ylsulfonyl)-1,1-dimethylethyl]-1,3-dithiane (24).

Propane-1,3-dithiol (3.2 mL, 32 mmol) was added to the aldehyde **23** (6.00 g, 21.2 mmol) in DCM (200 mL) and the solution cooled to 0 °C. Boron trifluoride diethyl etherate (6.6 mL, 53 mmol) was added and the mixture was stirred at 0 °C for 30 min and then at rt for 40 min. Aqueous sodium hydroxide (1 M, 200 mL) was added and the aqueous layer was extracted with ether (3 × 50 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (5:1 then 2:1 light petroleum:ether) of the residue gave the *title compound 24* as colourless needles (6.09 g, 77%), $R_f = 0.50$ (4:1 ether:light petroleum), m.p. 85.6-86.3°C (Found: M⁺ + Na, 396.0200. C₁₅H₁₉O₂NNaS₄ requires M, 396.0191); $\nu_{\max}/\text{cm}^{-1}$ 3062, 2972, 2936, 2902, 1556, 1471, 1422, 1392, 1328, 1273, 1148, 1086, 1023, 905 and 854; δ_H (500 MHz, CDCl₃) 1.37 (6 H, s, 2 × CH₃), 1.71 and 2.03 (each 1 H, m, 5-H), 2.79-2.90 (4 H, m, 4-H₂, 6-H₂), 3.80 (2 H, s, 2'-H), 4.41 (1 H, s, 2-H), 7.50-7.60 (2 H, m, ArH), 7.94 (1 H, d, J 8.0, ArH) and 8.16 (1 H, d, J 8.2, ArH); δ_C (125 MHz, CDCl₃) 25.6, 25.8, 31.3, 40.3, 59.7, 62.0, 122.4, 125.6, 127.7, 128.1, 136.8, 152.6 and 167.5; m/z (ES⁺) 396.0 (M⁺ + 23, 100%) and 374.0 (M⁺ + 1, 13).

2-{{(2E,4R)-6-[(Z)-2-tert-Butyldiphenylsilyloxyethylidene]-1,1-dimethyl-4-triethylsilyloxynona-2,8-dien-1-yl}}-1,3-dithiane (25).

Lithium hexamethyldisilazide (1.0 M in toluene, 0.21 mL) was added to the sulfone **24** (74 mg, 0.20 mmol) in THF (2 mL) at -78 °C, and the solution stirred at -78 °C for 20 min before the addition of the aldehyde **12** (0.111 g prepared from 0.196 mmol of the alcohol **11**) in THF (1.3 mL). The mixture was immediately allowed to warm to rt. After stirring for 1.5 h, ether (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added, and the aqueous layer was extracted with ether (2 × 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (100:1 then 50:1 light petroleum:ether) of the residue gave the *title compound 25* as a clear, colourless oil (74 mg, 55%), $R_f = 0.43$ (8.5:1.0 light petroleum:ether), $[\alpha]_D^{28} -0.7$ (c 5.5, CHCl₃) (Found: M⁺ + NH₄, 698.3917. C₃₉H₆₄O₂NS₂Si₂ requires M, 698.3912); $\nu_{\max}/\text{cm}^{-1}$ 3072, 2959, 2932, 2875, 1636, 1463, 1428, 1385, 1363, 1261, 1112, 1058, 1008, 823, 798, 740 and 702; δ_H (400 MHz, CDCl₃) 0.42 (6 H, q, J 7.9, 3 × SiCH₂), 0.79 (9 H, t, J 7.9, 3 × SiCH₂CH₃), 0.97 [9 H, s, SiC(CH₃)₃], 1.03 and 1.05 (each 3 H, s, 1'-CH₃), 1.70 and 1.97 (each 1 H, m, 5-H), 1.91 (1 H, dd, J 13.3, 6.6, 5'-H), 2.03 (1 H, dd, J 13.3, 6.8, 5'-H'), 2.69

(2 H, d, *J* 6.9, 7'-H₂), 2.70-2.80 (4 H, m, 4-H₂, 6-H₂), 3.85 (1 H, s, 2-H), 3.96 (1 H, m, 4'-H), 4.17 (2 H, d, *J* 6.2, 2''-H₂), 4.92-5.01 (2 H, m, 9'-H₂), 5.20 (1 H, dd, *J* 15.7, 7.0, 3'-H), 5.40 (1 H, t, *J* 6.2, 1''-H), 5.49 (1 H, d, *J* 15.7, 2'-H), 5.68 (1 H, m, 8'-H), 7.26-7.38 (6 H, m, ArH) and 7.57-7.65 (4 H, m, ArH); δ_c (100 MHz, CDCl₃) 3.7, 5.8, 18.1, 24.1, 24.3, 25.0, 25.8, 30.2, 38.9, 39.4, 41.4, 59.8, 60.3, 71.8, 115.2, 126.6, 126.9, 128.5, 129.8, 133.0, 134.6, 134.7, 135.5 and 135.6; *m/z* (ES⁺) 698.6 (M⁺ + 18, 100%).

2-[(2E,6Z,4R)-1,1-Dimethyl-6-(2-hydroxyethyl)-4-triethylsilyloxy-8-triisopropylsilyloxyocta-2,6-dien-1-yl]-1,3-dithiane (40).

Ammonia (*ca.* 10 mL) was condensed into a stirred, 50 mL, 3-necked round bottomed flask at -78 °C. The BOM-ether **36** (0.105 g, 0.145 mmol) in THF (3.0 mL) was added followed by ethanol (40 μ L, 0.69 mmol). Finely chopped sodium (*ca.* 1 mg pieces) were added until a deep blue colour persisted, and then the mixture was stirred at -78 °C for 5 min. Solid NH₄Cl was added until the blue colour disappeared and the mixture was diluted with ether (5 mL) and allowed to warm to rt over 2 h. Water (20 mL) and ether (30 mL) were added and the aqueous layer was extracted with ether (2 \times 20 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (5:1 to 2:1 light petroleum:ether) of the residue gave recovered starting material **36** (31 mg, 30%) and then the *title compound 40* as a clear, colourless oil (43 mg, 49%), *R_f* = 0.50 (1:1 light petroleum:ether), [α]_D²⁶ +3.0 (*c* 8.6, CHCl₃) (Found: M⁺ + Na, 625.3563. C₃₁H₆₂O₃NS₂Si₂ requires M, 625.3571); ν_{\max} /cm⁻¹ 3426, 2945, 2865, 1464, 1411, 1386, 1365, 1243, 1063, 1011, 972, 882 and 744; δ_H (500 MHz, CDCl₃) 0.51 (6 H, q, *J* 7.9, 3 \times SiCH₂), 0.86 (9 H, t, *J* 7.9, 3 \times SiCH₂CH₃), 0.97-1.07 [21 H, m, 3 \times SiCH(CH₃)₂], 1.12 and 1.13 (each 3 H, s, 1'-CH₃), 1.71 (1 H, m, 5-H), 1.84 (1 H, br. s, OH), 1.99 (1 H, m, 5-H'), 2.17 (1 H, dd, *J* 13.4, 6.4, 5'-H), 2.23 (1 H, dd, *J* 13.4, 6.8, 5'-H'), 2.23-2.31 (2 H, m, 1''-H₂), 2.73-2.84 (4 H, m, 4-H₂, 6-H₂), 3.57-3.70 (2 H, m, 2''-H₂), 3.91 (1 H, s, 2-H), 4.07-4.14 (1 H, m, 4'-H), 4.23 (2 H, d, *J* 6.2, 8'-H₂), 5.32 (1 H, dd, *J* 15.7, 7.4, 3'-H), 5.44 (1 H, t, *J* 6.2, 7'-H) and 5.58 (1 H, d, *J* 15.7, 2'-H); δ_c (75 MHz, CDCl₃) 5.1, 7.1, 12.3, 18.3, 24.9, 26.0, 26.2, 31.5(2), 40.4, 40.8, 41.2, 60.7, 60.9(2), 73.8, 130.7, 131.1, 133.5 and 137.5; *m/z* (ES⁺) 625.5 (M⁺ + 23, 100%).

Lithium (0.11 g) was added to naphthalene (4 mL) in THF (20 mL) and the mixture stirred at rt for 2 h then an aliquot (1.6 mL) added to the BOM-ether **36** (0.095 g, 0.13 mmol) in THF (4 mL) at -20 °C over 1 h. Work-up as above gave the alcohol **40** (41 mg, 71% with 2-phenylethanol).

(2EZ,6E)-(5R)-3-(2-Benzyloxymethoxyethyl)-8-(1,3-dithian-2-yl)-8-methyl-5-triethylsilyloxynona-2,6-dienal (41).

An aqueous pH7 phosphate buffer (0.66 mL) was added to the TIPS ether **36** (0.10 g, 0.138 mmol) in DCM (0.66 mL) and the biphasic mixture was stirred rapidly at rt whilst DDQ (0.195 g, 0.858 mmol) was added in one portion. After 1 h, saturated aqueous sodium bicarbonate (20 mL) and ether (20 mL) were added and the organic layer was washed with a mixture of saturated aqueous sodium

bicarbonate and saturated aqueous sodium bisulfite (10 mL), dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (5:1 to 2:1 light petroleum:ether) of the residue gave unreacted starting material **36** (38 mg, 38%) followed by the *title compound 41* as a clear, colourless oil (33 mg, 43 %), a 3:1 mixture of diastereoisomers, *R_f* = 0.27 (5:1 light petroleum:ether), [α]_D²⁹ -3.0 (*c* 6.6, CHCl₃) (Found: M⁺ + NH₄⁺ 582.3111. C₃₀H₅₂O₄NS₂Si requires M, 582.3102); ν_{\max} /cm⁻¹ 2955, 2874, 1674, 1456, 1422, 1385, 1362, 1277, 1239, 1162, 1107, 1063, 1043, 975 and 744; δ_H (400 MHz, CDCl₃) 0.45-0.54 (6 H, m, 3 \times SiCH₂), 0.84 (6.75 H, t, *J* 7.9, 3 \times SiCH₂CH₃), 0.85 (2.25 H, t, *J* 7.9, 3 \times SiCH₂CH₃), 1.12 (3 H, s, 8-CH₃), 1.13 (0.75 H, s, 9-H₃), 1.13 (2.25 H, s, 9-H₃), 1.69 and 1.99 (each 1 H, m, 5''-H), 2.33 (0.25 H, ddd, *J* 13.2, 5.6, 0.8, 4-H), 2.41 (0.25 H, ddd, *J* 13.2, 7.1, 0.7, 4-H'), 2.50 (1.5 H, td, *J* 6.5, 1.0, 1'-H₂), 2.60 (0.75 H, dd, *J* 13.1, 4.8, 4-H), 2.74-2.86 (5.25 H, m, 4-H', 4''-H₂, 6''-H₂, 1'-H₂), 3.66 (0.5 H, t, *J* 6.5, 2'-H₂), 3.68 (1.5 H, t, *J* 6.5, 2'-H₂), 3.90 (0.25 H, s, 2''-H), 3.91 (0.75 H, s, 2''-H), 4.23 (1 H, m, 5-H), 4.49 (0.5 H, s, PhCH₂), 4.52 (1.5 H, s, PhCH₂), 4.66 (0.5 H, s, OCH₂O), 4.68 (1.5 H, s, OCH₂O), 5.34 (0.25 H, dd, *J* 15.7, 7.3, 6-H), 5.38 (0.75 H, dd, *J* 15.7, 7.3, 6-H), 5.62 (0.25 H, m, 7-H), 5.66 (0.75 H, dd, *J* 15.7, 0.7, 7-H), 5.92 (1 H, m, 2-H), 7.20-7.32 (5 H, m, ArH) and 9.87 (1 H, d, *J* 8.0, 1-H); *m/z* (ES⁺) 587.4 (M⁺ + 23, 100%), 582.5 (M⁺ + 18, 36) and 497.5 (25).

(4R,6R,7R)- and (4S,6R,7R)-2-Benzyloxymethyl-7-tert-butylidimethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)oct-1-en-4-ols (43) and (44).

Indium powder (4.20 g, 36.6 mmol) was added to a the aldehyde **42** (3.29 g, 9.06 mmol) and 2-benzyloxymethyl-3-bromoprop-1-ene (4.37 g, 18.13 mmol) in THF (150 mL) and water (50 mL) and the mixture stirred vigorously at rt for 45 h. Ether (300 mL) and saturated aqueous NaHCO₃ (300 mL) were added and the aqueous phase was extracted with ether (2 \times 250 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (15:1 to 4:1 light petroleum:ether) gave the (4S)-epimer of the *title compound 44* (2.16 g, 45%) as a clear, colourless oil, *R_f* = 0.31 (4:1 light petroleum:ether), [α]_D²⁶ +20.8 (*c* 2.1, CHCl₃) (Found: M⁺ + Na, 547.3236. C₂₈H₅₂O₅Si₂Na requires M, 547.3245); ν_{\max} /cm⁻¹ 3467, 2953, 2930, 2894, 2858, 1650, 1461, 1378, 1251, 1102, 1057, 1029, 859, 835 and 776; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.06 and 0.07 (each 3 H, s, SiCH₃), 0.88 [9 H, s, SiC(CH₃)₃], 0.91-0.95 (2 H, m, CH₂Si), 1.10 (3 H, d, *J* 6.3, 8-H₃), 1.57 (2 H, m, 5-H₂), 2.25 (1 H, dd, *J* 14.2, 4.8, 3-H), 2.29 (1 H, dd, *J* 14.2, 7.5, 3-H'), 3.54-3.68 (4 H, m, OCH₂CH₂Si, 6-H, OH), 3.87 (1 H, pent, *J* 6.0, 7-H), 3.95 (1 H, m, 4-H), 3.97 and 4.02 (each 1 H, d, *J* 12.5, 2-CH), 4.48 and 4.51 (each 1 H, d, *J* 12.0, PhHCH), 4.70 and 4.75 (each 1 H, d, *J* 6.6, OHCHO), 5.04 and 5.15 (each 1 H, s, 1-H) and 7.25-7.34 (5 H, m, ArH); δ_c (125 MHz, CDCl₃) -3.3, 0.0, 19.5, 19.6, 20.0, 27.3, 39.1, 43.2, 67.2, 67.8, 72.2, 73.5, 74.8, 81.5, 97.6, 116.0, 129.0, 129.2, 129.8, 139.7 and 144.9; *m/z* (ES⁺) 583.3 (41 %) and 547.2 (M⁺ + 23, 100). The second fraction was the (4R)-epimer of the *title compound 43* (2.06 g, 43%), *R_f* = 0.45 (2:1 light petroleum:ether), [α]_D²⁹ +7.7 (*c* 2.5, CHCl₃)

(Found: $M^+ + H$, 525.3430. $C_{28}H_{53}O_5Si_2$ requires M , 525.3426); ν_{max}/cm^{-1} 3464, 2953, 2933, 2887, 2857, 1376, 1250, 1102, 1056, 1030, 861, 835, 775 and 696; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 and 0.05 (each 3 H, s, $SiCH_3$), 0.86 [9 H, s, $SiC(CH_3)_3$], 0.86-0.95 (2 H, m, CH_2Si), 1.08 (3 H, d, J 6.3, 8- H_3), 1.55 (1 H, dt, J 14.5, 8.6, 5-H), 1.83 (1 H, dt, J 14.5, 3.8, 5- H'), 2.25 (1 H, dd, J 14.5, 7.3, 3-H), 2.30 (1 H, dd, J 14.5, 5.3, 3- H'), 3.41 (1 H, br. s, OH), 3.57-3.64 (3 H, m, OCH_2CH_2Si , 6-H), 3.93-3.98 (3 H, m, 2-CH, 4-H, 7-H), 4.01 (1 H, d, J 12.3, 2- CH'), 4.50 (2 H, s, $PhCH_2$), 4.70 and 4.73 (each 1 H, d, J 6.9, OHCHO), 5.03 and 5.15 (each 1 H, s, 1-H) and 7.26-7.36 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) -3.4, -3.2, 0.0, 18.9, 19.5, 19.6, 27.4, 37.2, 43.3, 67.1, 70.6(2), 73.5, 74.8, 82.8, 96.6, 116.4, 129.0, 129.2, 129.8, 139.6 and 144.5; m/z (ES^+) 583.8 (54%), 542.5 ($M^+ + 18$, 100) and 525.6 ($M^+ + 1$, 60).

An excess of 2-benzyloxymethylprop-2-enyl magnesium chloride and the aldehyde **42** (290 mg, 0.80 mmol) in ether (4.5 mL) at rt, after chromatography (15:1 to 4:1 light petroleum:ether), gave the (4*S*)-epimer **44** (147 mg, 36%) followed by the (4*R*)-epimer **43** (215 mg, 53%).

Di-isopropylazo dicarboxylate (6.64 mL, 33.7 mmol) was added dropwise to the (4*R*)-alcohol **43** (10.40 g, 19.8 mmol), PPh_3 (8.85 g, 33.7 mmol) and 4-nitrobenzoic acid (5.64 g, 33.7 mmol) in THF (156 mL) at 0 °C and the solution stirred for 10 min before warming to rt and stirring for 12 h. After concentration under reduced pressure, chromatography of the residue (20:1 light petroleum:ether) gave the 4-nitrobenzoate of the (4*S*)-alcohol **44** (12.29 g, 92%) as a pale yellow oil, R_f = 0.52 (5:1 light petroleum:ether), $[\alpha]_D^{29}$ -10.7 (c 3.0, $CHCl_3$) (Found: $M^+ + NH_4$, 691.3795. $C_{35}H_{59}O_8N_2Si_2$ requires M , 691.3804); ν_{max}/cm^{-1} 2953, 2928, 2892, 2860, 1724, 1608, 1529, 1349, 1273, 1250, 1102, 1029, 836, 776 and 719; δ_H (500 MHz, $CDCl_3$) -0.04 and 0.02 (each 3 H, s, $SiCH_3$), 0.00 [9 H, s, $Si(CH_3)_3$], 0.78-0.95 (2 H, m, CH_2Si), 0.85 [9 H, s, $SiC(CH_3)_3$], 1.09 (3 H, d, J 6.3, 8- H_3), 1.71 (1 H, ddd, J 14.8, 10.7, 1.9, 5-H), 2.05 (1 H, ddd, J 14.8, 10.4, 1.3, 5- H'), 2.52 (1 H, dd, J 14.5, 5.7, 3-H), 2.55 (1 H, dd, J 14.5, 6.9, 3- H'), 3.43 (1 H, ddd, J 10.5, 4.4, 1.2, 6-H), 3.49 and 3.64 (each 1 H, ddd, J 11.5, 9.5, 5.5, OHCHCH $_2Si$), 3.97 (1 H, d, J 12.6, 2-CH), 4.01 (1 H, qd, J 6.3, 4.7, 7-H), 4.07 (1 H, d, J 12.6, 2- CH'), 4.45 and 4.49 (each 1 H, d, J 11.8, PhHCH), 4.61 and 4.68 (1 H, d, J 7.3, OHCHO), 5.01 (1 H, s, 1-H), 5.11 (1 H, d, J 1.3, 1- H'), 5.50 (1 H, m, 4-H), 7.26-7.34 (5 H, m, ArH) and 8.15 and 8.24 (each 2 H, m, ArH); δ_C (125 MHz, $CDCl_3$) -3.5, -3.2, 0.0, 18.3, 19.5, 27.3, 34.7, 40.5, 66.8, 70.0, 72.9, 73.5, 74.3, 80.3, 97.5, 116.9, 124.9, 129.0, 129.8, 132.1, 137.3, 139.7, 143.2, 151.9 and 165.6; m/z (ES^+) 691.9 ($M^+ + 18$, 100%).

Potassium carbonate (930 mg, 6.73 mmol) was added to the 4-nitrobenzoate of the (4*S*)-alcohol **44** (50 mg, 0.074 mmol) in methanol (1.9 mL) at 0 °C and the suspension stirred for 3 h. Water (15 mL) and DCM (15 mL) were added and the aqueous layer was extracted with DCM (2 × 15 mL) The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the (4*S*)-alcohol **44** (35 mg, 90 %) as a colourless oil.

Dicyclohexyl carbodi-imide (39 mg, 0.19 mmol), (*R*)-(-)-acetylmandelic acid (27 mg, 0.14 mmol) and DMAP (1.2 mg, 9.5 μ mol) were added to the (4*S*)-alcohol **44** (50 mg, 0.095 mmol) in THF (0.5 mL) at 0 °C and the mixture stirred for 5 min at 0 °C and at rt for 2 h. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the (*R*)-acetylmandelate of the alcohol **44** (54 mg, 81 %) as a colourless oil, R_f = 0.28 (5:1 light petroleum:ether), $[\alpha]_D^{26}$ -39.0 (c 3.7, $CHCl_3$) (Found: $M^+ + Na$, 723.3717. $C_{38}H_{60}O_8Si_2Na$ requires M , 723.3719); ν_{max}/cm^{-1} 2952, 2933, 2892, 2858, 1748, 1373, 1235, 1210, 1179, 1102, 1054, 1033 and 835; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.08 and 0.11 (each 3 H, s, $SiCH_3$), 0.84 (1 H, ddd, J 13.8, 11.3, 5.4, HC HSi), 0.92 [9 H, s, $SiC(CH_3)_3$], 0.94 (1 H, ddd, J 13.8, 11.6, 5.9, HC HSi), 1.06 (3 H, d, J 6.3, 8- H_3), 1.54 (1 H, ddd, J 14.6, 10.9, 2.3, 5-H), 1.87 (1 H, ddd, J 14.6, 10.6, 1.5, 5- H'), 2.14 [3 H, s, C(O) CH_3], 2.16 (1 H, dd, J 14.4, 7.5, 3-H), 2.20 (1 H, dd, J 14.4, 5.3, 3- H'), 3.40-3.49 (2 H, m, 6-H, OHCHCH $_2Si$), 3.67 (1 H, ddd, J 11.6, 9.6, 5.4, OHCHCH $_2Si$), 3.69 and 3.82 (each 1 H, d, J 12.9, 2-CH), 4.08 (1 H, qd, J 6.3, 4.5, 7-H), 4.33 and 4.34 (each 1 H, d, J 11.9, PhHCH), 4.43 (1 H, s, 1-H), 4.59 and 4.64 (each 1 H, d, J 6.8, OHCHO), 5.11 (1 H, m, 1- H'), 5.25 (1 H, m, 4-H), 5.78 (1 H, s, 2'-H) and 7.22-7.41 (10 H, m, ArH); δ_C (100 MHz, $CDCl_3$) -3.4, -3.2, 0.0, 18.3, 19.5(2), 22.1, 27.3, 34.4, 40.3, 66.6, 70.0, 72.0, 73.3, 73.9, 76.0, 80.4, 97.9, 116.5, 128.9, 129.1, 129.2, 129.7, 130.1, 130.6, 135.3, 139.8, 142.2, 169.9 and 171.4; m/z (ES^+) 724 ($M^+ + 23$, 100%) and 719 ($M^+ + 18$, 83).

Following this procedure, (*S*)-(+)-acetylmandelic acid (27 mg, 0.14 mmol) and the (4*S*)-alcohol **44** (50 mg, 0.095 mmol), after chromatography, gave the (*S*)-acetylmandelate of the alcohol **44** (52 mg, 78%) as a colourless oil, R_f = 0.28 (5:1 light petroleum:ether), $[\alpha]_D^{26}$ +26.8 (c 5.2, $CHCl_3$) (Found: $M^+ + Na$, 723.3723. $C_{38}H_{60}O_8Si_2Na$ requires M , 723.3719); ν_{max}/cm^{-1} 2954, 2929, 2894, 2856, 1747, 1374, 1249, 1232, 1210, 1178, 1102, 1054, 1030, 860 and 835; δ_H (400 MHz, $CDCl_3$) -0.07 and -0.03 (each 3 H, s, $SiCH_3$), 0.00 [9 H, s, $Si(CH_3)_3$], 0.81 (1 H, ddd, J 13.9, 11.1, 5.6, HC HSi), 0.84 [9 H, s, $SiC(CH_3)_3$], 0.88 (1 H, m, HC HSi), 0.94 (3 H, d, J 6.3, 8- H_3), 1.56 (1 H, ddd, J 14.6, 10.9, 2.8, 5-H), 1.71 (1 H, ddd, J 14.8, 10.6, 2.3, 5- H'), 2.16 [3 H, s, C(O) CH_3], 2.38 (1 H, dd, J 14.2, 6.2, 3-H), 2.45 (1 H, dd, J 14.1, 6.3, 3- H'), 2.92 (1 H, ddd, J 10.8, 4.8, 2.1, 6-H), 3.38 (1 H, ddd, J 11.0, 9.6, 6.1, OHCHCH $_2Si$), 3.55 (1 H, ddd, J 11.1, 9.6, 5.5, OHCHCH $_2Si$), 3.80 (1 H, qd, J 6.3, 4.8, 7-H), 3.95 and 4.02 (each 1 H, d, J 13.1, 2-CH), 4.16 and 4.37 (each 1 H, d, J 6.8, OHCHO), 4.47 and 4.48 (each 1 H, d, J 11.9, PhHCH), 4.99 (1 H, s, 1-H), 5.13 (1 H, m, 1- H'), 5.17 (1 H, m, 4-H), 5.86 (1 H, s, 2'-H) and 7.24-7.46 (10 H, m, ArH); δ_C (100 MHz, $CDCl_3$) -3.4, -3.3, 0.0, 18.7, 19.3, 19.4, 22.2, 27.3, 34.3, 40.1, 66.6, 70.5, 72.8, 73.4, 74.3, 76.0, 80.2, 97.5, 116.5, 128.9, 129.1, 129.2, 129.7, 130.2, 130.7, 135.5, 139.9, 142.7, 169.8 and 171.4; m/z (ES^+) 723.7 ($M^+ + 23$, 100%).

(4*S*,6*R*,7*R*)-2-Benzyloxymethyl-7-*tert*-butyldimethylsilyloxy-6-(2-

trimethylsilylethoxymethoxy)oct-1-en-4-yl acrylate (45).

N,N-Di-isopropylethylamine (0.84 mmol, 0.15 mL) and acryloyl chloride (0.42 mmol, 0.035 mL) were added to the alcohol **44** (200 mg, 0.38 mmol) in DCM (2.5 mL) at 0 °C and the solution stirred for 5 h. Dichloromethane (12 mL) and brine (10 mL) were added and the aqueous phase extracted with DCM (2 × 10 mL). The organic phase was dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the *title compound* **45** (213 mg, 97%) as a colourless oil, *R*_f = 0.64 (4:1 light petroleum:ether), [α]_D²⁶ –12.8 (*c* 2.2, CHCl₃) (Found: *M*⁺ + Na, 601.3350. C₃₁H₅₄O₆Si₂Na requires *M*, 601.3351); *v*_{max}/cm⁻¹ 3067, 3033, 2954, 2930, 2892, 2858, 1723, 1406, 1251, 1195, 1103, 1053, 1028, 860, 835 and 776; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.02 and 0.03 (each 3 H, s, SiCH₃), 0.84 (1 H, ddd, *J* 13.9, 11.6, 5.3, HCHSi), 0.87 [9 H, s, SiC(CH₃)₃], 0.94 (1 H, ddd, *J* 13.6, 11.7, 5.9, HCHSi), 1.06 (3 H, d, *J* 6.3, 8-H₃), 1.60 (1 H, ddd, *J* 14.5, 10.5, 1.9, 5-H), 1.85 (1 H, ddd, *J* 14.5, 10.4, 0.9, 5-H'), 2.38 (1 H, dd, *J* 14.5, 5.7, 3-H), 2.42 (1 H, dd, *J* 14.3, 6.9, 3-H'), 3.36 (1 H, ddd, *J* 10.2, 4.4, 0.8, 6-H), 3.47 (1 H, ddd, *J* 11.0, 9.6, 6.0, OHCHCH₂Si), 3.65 (1 H, ddd, *J* 11.7, 9.8, 5.4, OHCHCH₂Si), 3.94 (1 H, d, *J* 12.8, 2-CH), 4.01 (1 H, qd, *J* 6.3, 4.7, 7-H), 4.03 (1 H, d, *J* 12.4, 2-CH'), 4.45 and 4.48 (each 1 H, d, *J* 12.0, PhHCH), 4.59 and 4.67 (each 1 H, d, *J* 6.9, OHCHO), 4.98 and 5.11 (each 1 H, s, 1-H), 5.28 (1 H, m, 4-H), 5.76 (1 H, dd, *J* 10.4, 1.3, 3'-H), 6.04 (1 H, dd, *J* 17.3, 10.4, 2-H'), 6.33 (1 H, dd, *J* 17.3, 1.3, 3'-H') and 7.24-7.34 (5 H, m, ArH); δ_C (125 MHz, CDCl₃) –3.4, –3.2, 0.0, 18.3, 19.5, 19.5, 27.3, 34.6, 40.5, 66.7, 70.1, 71.0, 73.5, 74.4, 80.4, 97.6, 116.4, 128.9, 129.1, 129.8, 130.2, 131.9, 139.8, 143.3 and 167.1; *m/z* (ES⁺) 601.5 (*M*⁺ + 23, 100%) and 596.1 (*M*⁺ + 18, 11).

(6S)-4-Benzyloxymethyl-6-[(2R,3R)-3-tert-butylidimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-5,6-dihydropyran-2-one (46).

A de-gassed solution of Grubbs II catalyst^{27,28a} (1.11 g, 1.31 mmol) in DCE (67 mL) was added via a syringe pump over 24 h to a de-gassed solution of the acrylate **45** (14.78 g, 25.5 mmol) in DCE (192 mL) heated under reflux. After heating under reflux for a further 2 h, the mixture was cooled to rt and concentrated under reduced pressure. Chromatography of the residue (3:1 light petroleum:ether) gave the *title compound* **46** (11.24 g, 80%) as a pale red oil, *R*_f = 0.11 (4:1 light petroleum:ether); [α]_D²⁶ –29.9 (*c* 2.8, CHCl₃) (Found: *M*⁺ + Na, 573.3042. C₂₉H₅₀O₆Si₂Na requires *M*, 573.3038); *v*_{max}/cm⁻¹ 3032, 2954, 2930, 2892, 2858, 1724, 1250, 1148, 1104, 1054, 1031, 859, 835 and 777; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.07 (6 H, s, 2 × SiCH₃), 0.85-0.96 (2 H, m, CH₂Si), 0.88 [9 H, s, SiC(CH₃)₃], 1.10 (3 H, d, *J* 6.3, 4'-H₃), 1.62 (1 H, ddd, *J* 14.0, 10.4, 3.2, 1'-H), 2.07 (1 H, ddd, *J* 14.5, 9.8, 2.2, 1'-H'), 2.30 (2 H, d, *J* 7.3, 5-H₂), 3.52 and 3.63 (each 1 H, td, *J* 10.4, 6.2, OHCHCH₂Si), 3.78 (1 H, ddd, *J* 10.4, 4.7, 2.5, 2'-H), 4.01 (1 H, pent, *J* 6.2, 3'-H), 4.07 and 4.11 (each 1 H, d, *J* 15.3, 4-CH), 4.54 and 4.57 (each 1 H, d, *J* 12.0, PhHCH), 4.61 (1 H, m, 6-H), 4.72 (2 H, s, OCH₂O), 6.07 (1 H, s, 3-H) and 7.29-7.38 (5 H, m, ArH); δ_C

(125 MHz, CDCl₃) –3.3, 0.0, 18.8, 19.5, 19.6, 27.3, 32.4, 35.9, 66.9, 70.4, 72.0, 74.3, 75.7, 79.1, 97.3, 117.1, 129.1, 129.5, 130.0, 138.7, 157.6 and 166.1; *m/z* (ES⁺) 573.5 (*M*⁺ + 23, 100%).

(2E)-(5S,7R,8R)-3-Benzyloxymethyl-8-tert-butylidimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene-1,5-diol (47).

Cerium(III) chloride heptahydrate (405 mg, 1.09 mmol) and sodium borohydride (41 mg, 1.09 mmol) were added to a the lactone **46** (250 mg, 0.46 mmol) in methanol (2.1 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. Additional cerium(III) chloride heptahydrate (202 mg, 0.54 mmol) and sodium borohydride (20 mg, 0.53 mmol) were added and this process was repeated hourly until the reaction was complete (TLC). Methanol (20 mL) was added followed by silica. The mixture was dried under reduced pressure to give a fine white powder that was loaded directly onto a silica gel column. Chromatography (ether) gave the *title compound* **47** (248 mg, 98%) as a colourless oil, *R*_f = 0.19 (1:1 light petroleum:ether); [α]_D²⁹ +28.4 (*c* 1.1, CHCl₃) (Found: *M*⁺ + Na, 577.3346. C₂₉H₅₄O₆Si₂Na requires *M*, 577.3351); *v*_{max}/cm⁻¹ 3399, 2953, 2928, 2893, 2856, 1250, 1150, 1101, 1057, 1028, 860, 835 and 775; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.07 and 0.08 (each 3 H, s, SiCH₃), 0.88 [9 H, s, SiC(CH₃)₃], 0.88-0.92 (2 H, m, CH₂Si), 1.11 (3 H, d, *J* 6.3, 9-H₃), 1.56 (1 H, ddd, *J* 14.0, 8.9, 1.7, 6-H), 1.66 (1 H, ddd, *J* 14.2, 10.4, 5.0, 6-H'), 2.19 (1 H, dd, *J* 13.7, 1.5, 4-H), 2.52 (1 H, dd, *J* 13.5, 10.3, 4-H'), 3.51-3.68 (4 H, m, OCH₂CH₂Si, 7-H, OH), 3.81-3.88 (2 H, m, 5-H, 8-H), 3.89-3.95 (2 H, m, 3-CH, 1-H), 4.07 (1 H, d, *J* 11.7, 3-CH'), 4.23 (1 H, dd, *J* 12.0, 8.4, 1-H'), 4.43 and 4.50 (each 1 H, d, *J* 11.8, PhHCH), 4.53 (1 H, br. s, OH), 4.70 and 4.75 (each 1 H, d, *J* 6.6, OHCHO), 6.01 (1 H, t, *J* 7.7, 2-H) and 7.26-7.36 (5 H, m, ArH); δ_C (125 MHz, CDCl₃) –3.3, 0.0, 19.4, 19.5, 20.2, 27.2, 36.9, 40.0, 58.7, 66.5, 67.4, 72.6, 73.3, 75.6, 81.9, 97.7, 129.1, 129.2, 129.9, 131.1, 139.5 and 139.7; *m/z* (ES⁺) 577.2 (*M*⁺ + 23, 100%).

(2E)-(5S,7R,8R)-3-Benzyloxymethyl-8-tert-butylidimethylsilyloxy-1,5-bis-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (48).

2,6-Lutidine (0.134 mL, 1.15 mmol) and tri-isopropylsilyl trifluoromethanesulfonate (0.215 mL, 0.80 mmol) were added to the diol **47** (139 mg, 0.25 mmol) in DCM (0.2 mL) at 0 °C and the solution stirred at rt for 2 h. Dichloromethane (15 mL) and saturated aqueous NaHCO₃ (15 mL) were added and the aqueous phase was extracted with DCM (2 × 15 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (50:1 light petroleum:ether) gave the *title compound* **48** (178 mg, 82%) as a colourless oil, *R*_f = 0.32 (20:1 light petroleum:ether), [α]_D²⁸ –10.8 (*c* 1.0, CHCl₃) (Found: *M*⁺ + Na, 889.6028. C₄₇H₉₄O₆Si₄Na requires *M*, 889.6020); *v*_{max}/cm⁻¹ 2943, 2892, 2863, 1462, 1382, 1250, 1100, 1058, 1014, 882, 859, 835, 775 and 681; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.03 and 0.04 (each 3 H, s, SiCH₃), 0.84 (1 H, ddd, *J* 13.9, 11.2, 5.3, HCHSi), 0.87 [9 H, s, SiC(CH₃)₃], 0.93 (1 H, ddd, *J* 13.9, 11.6, 6.1, HCHSi), 1.02 (3 H, d, *J* 6.3, 9-H₃), 1.02-1.15 [42 H, m, 6 × SiCH(CH₃)₂],

1.43 (1 H, ddd, J 13.6, 10.3, 3.3, 6-H), 1.55 (1 H, ddd, J 13.9, 8.8, 1.5, 6-H'), 2.27 (1 H, dd, J 13.1, 9.1, 4-H), 2.45 (1 H, dd, J 13.1, 4.9, 4-H'), 3.41 (1 H, ddd, J 11.1, 9.6, 6.1, OHCHCH₂Si), 3.62 (1 H, ddd, J 10.1, 4.3, 1.5, 7-H), 3.68 (1 H, ddd, J 11.4, 9.6, 5.3, OHCHCH₂Si), 3.91 and 4.00 (each 1 H, d, J 12.2, 3-CH), 4.06 (1 H, qd, J 6.3, 4.5, 8-H), 4.12 (1 H, m, 5-H), 4.33 (1 H, dd, J 13.1, 5.8, 1-H), 4.37 (1 H, dd, J 13.1, 6.1, 1-H'), 4.44 (2 H, s, PhCH₂), 4.66 and 4.67 (each 1 H, d, J 7.1, OHCHO), 5.70 (1 H, t, J 5.8, 2-H) and 7.23-7.34 (5 H, m, ArH); δ_c (100 MHz, CDCl₃) -3.3, 0.0, 13.4, 14.5, 18.5, 19.5(2), 19.6, 19.8, 27.3, 37.0, 39.5, 61.7, 66.6, 70.0, 70.4, 73.1, 75.7, 81.8, 97.8, 128.8, 129.1, 129.7, 132.4, 135.0 and 139.9; m/z (ES⁺) 889.5 (M⁺ + 23, 100%).

(4S,6R,7R)-7-tert-Butyldimethylsilyloxy-4-tri-isopropylsilyloxy-2-[(E)-2-tri-isopropylsilyloxyethylidene]-6-(2-trimethylsilylethoxymethoxy)octan-1-ol (49).

Lithium (48 mg, 6.92 mmol) was added to naphthalene (1.31 g, 10.2 mmol) in THF (17 mL) and the mixture stirred vigorously at rt for 1 h then added dropwise to the benzyl ether **48** (890 mg, 1.03 mmol) in THF (8.6 mL) at -30 °C until the reaction was complete (TLC). Water, ether (50 mL) and saturated aqueous NaHCO₃ (50 mL) were added and the aqueous phase was extracted with ether (2 × 50 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the *title compound* **49** (617 mg, 77%) as a colourless oil, R_f = 0.35 (4:1 light petroleum:ether), $[\alpha]_D^{28}$ +5.5 (c 0.8, CHCl₃) (Found: M⁺ + Na, 799.5552. C₄₀H₈₈O₆Si₄Na requires M, 799.5550); ν_{max}/cm^{-1} 3442, 2944, 2866, 1462, 1382, 1250, 1102, 1058, 882, 835 and 775; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.03(2) (each 3 H, s, SiCH₃), 0.86 (1 H, m, HCCHSi), 0.86 [9 H, s, SiC(CH₃)₃], 0.93 (1 H, ddd, J 13.8, 11.4, 6.0, HCCHSi), 1.01-1.13 [45 H, m, 8-H₃, 6 × SiCH(CH₃)₂], 1.56 (1 H, ddd, J 14.8, 9.9, 5.5, 5-H), 1.64 (1 H, ddd, J 14.4, 6.1, 2.9, 5-H'), 2.33 (1 H, dd, J 13.6, 6.6, 3-H), 2.49 (1 H, dd, J 13.6, 4.8, 3-H'), 2.78 (1 H, t, J 5.8, OH), 3.48 (1 H, ddd, J 11.1, 9.6, 6.1, OHCHCH₂Si), 3.57 (1 H, ddd, J 9.8, 4.5, 2.9, 6-H), 3.64 (1 H, ddd, J 11.4, 9.6, 5.6, OHCHCH₂Si), 3.99 (1 H, qd, J 6.3, 4.6, 7-H), 4.00-4.06 (2 H, m, 1-H₂), 4.13 (1 H, pent, J 5.8, 4-H), 4.31 (1 H, dd, J 13.9, 5.8, 2'-H), 4.33 (1 H, dd, J 13.9, 6.1, 2'-H'), 4.66 and 4.69 (each 1 H, d, J 7.1, OHCHO) and 5.71 (1 H, t, J 6.0, 1'-H); δ_c (100 MHz, CDCl₃) -3.3(2), 0.0, 13.5, 14.3, 18.7, 19.5, 19.7(2), 27.3, 36.8, 39.8, 61.8, 66.9, 69.4, 70.6, 71.5, 82.0, 97.2, 131.8 and 137.8; m/z (ES⁺) 800 (M⁺ + 23, 100%).

(2E)-(5S,7R,8R)-3-Bromomethyl-8-tert-butylidimethylsilyloxy-1,5-bis-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (50).

Triethylamine (0.11 mL, 0.79 mmol) and methanesulfonyl chloride (38 μ L, 0.49 mmol) was added to the alcohol **49** (300 mg, 0.39 mmol) in THF (2.0 mL) at 0 °C and the solution stirred at 0 °C for 1 h. Anhydrous lithium bromide (134 mg, 1.54 mmol) in THF (2.0 mL) was added and the mixture stirred for 1 h at 0 °C. Saturated aqueous NaHCO₃ (30 mL) and light petroleum (30 mL) were added and the aqueous phase was extracted with light petroleum (2 × 30 mL). The organic extracts were dried

(MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (30:1 light petroleum:ether) gave the *title compound* **50** (300 mg, 93%) as a colourless oil, R_f = 0.41 (30:1 light petroleum:ether); $[\alpha]_D^{28}$ -10.9 (c 1.0, CHCl₃) (Found: M⁺ + Na, 861.4680. C₄₀H₈₇O₅⁷⁹BrSi₄Na requires M, 861.4712); ν_{max}/cm^{-1} 2946, 2867, 1464, 1381, 1251, 1101, 1057, 882, 835 and 776; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.03(2) (each 3 H, s, SiCH₃), 0.85 (1 H, m, HCCHSi), 0.86 [9 H, s, SiC(CH₃)₃], 0.94 (1 H, ddd, J 13.9, 11.6, 6.1, HCCHSi), 1.02 (3 H, d, J 6.3, 9-H₃), 1.02-1.13 [42 H, m, 6 × SiCH(CH₃)₂], 1.40 (1 H, ddd, J 14.4, 10.3, 4.3, 6-H), 1.62 (1 H, ddd, J 14.4, 7.8, 2.0, 6-H'), 2.37 (1 H, dd, J 13.9, 8.1, 4-H), 2.53 (1 H, dd, J 13.9, 5.6, 4-H'), 3.45 (1 H, ddd, J 11.4, 9.6, 6.1, OHCHCH₂Si), 3.59 (1 H, ddd, J 10.1, 4.3, 1.8, 7-H), 3.67 (1 H, ddd, J 11.6, 9.6, 5.6, OHCHCH₂Si), 4.01 and 4.02 (each 1 H, d, J 10.1, 3-CH), 4.04 (1 H, qd, J 6.3, 4.5, 8-H), 4.10 (1 H, m, 5-H), 4.30 (2 H, d, J 5.6, 1-H₂), 4.70 and 4.71 (each 1 H, d, J 7.1, OHCHO) and 5.81 (1 H, t, J 5.8, 2-H); δ_c (100 MHz, CDCl₃) -3.3(2), 0.0, 13.4, 14.5, 58.6, 19.4, 19.5, 19.6, 19.8, 27.3, 37.3, 38.9, 40.5, 61.9, 66.8, 70.3, 70.4, 82.0, 97.6, 134.8 and 135.7; m/z (ES⁺) 863 (M⁺ + 23, 93%), 861 (M⁺ + 23, 100), 858 (M⁺ + 18, 54) and 856 (M⁺ + 18, 39).

(4S,7S,9R,10R)-1-Benzyloxy-4,10-bis-tert-butylidimethylsilyloxy-7-triethylsilyloxy-5-[(E)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecane (71).

2,6-Lutidine (0.055 mL, 0.47 mmol) and *tert*-butyldimethylsilyl triflate (0.054 mL, 0.24 mmol) were added to the alcohol **61** (40 mg, 0.039 mmol) in DCM (0.35 mL) and the solution stirred at rt for 14 h. Dichloromethane (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (65:1 light petroleum:ether) gave the *title compound* **71** (41 mg, 92%) as a colourless oil, R_f = 0.61 (19:1 light petroleum:ether), $[\alpha]_D^{20}$ -10.1 (c 1.4, CHCl₃); ν_{max}/cm^{-1} 2954, 2933, 2864, 1473, 1463, 1378, 1250, 1099, 1058, 1011, 885, 836 and 776; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.02 (3 H, s, SiCH₃), 0.04 (6 H, s, 2 × SiCH₃), 0.11 (3 H, s, SiCH₃), 0.55-0.67 (6 H, m, 3 × SiCH₂), 0.85 (1 H, m, HCCHSi), 0.87 and 0.92 [each 9 H, s, 2 × SiC(CH₃)₃], 0.93 (1 H, m, HCCHSi), 0.95 (9 H, t, J 7.9, 3 × SiCH₂CH₃), 0.99 (3 H, d, J 6.2, 11-H₃), 1.03-1.13 [21 H, m, 3 × SiCH(CH₃)₂], 1.28 and 1.30 (each 3 H, s, 2-CH₃), 1.39-1.49 (2 H, m, 8-H₂), 1.74-1.89 (2 H, m, SCH₂CH₂), 2.36 (1 H, t, J 12.6, 6-H), 2.54-2.90 (4 H, m, 2 × SCH₂), 3.04 (1 H, d, J 12.9, 6-H'), 3.39 (1 H, ddd, J 11.0, 9.7, 6.0, OHCHCH₂Si), 3.61 (1 H, m, 9-H), 3.68 (1 H, d, J 8.4, 1-H), 3.70 (1 H, ddd, J 11.5, 9.7, 5.4, OHCHCH₂Si), 3.85 (1 H, d, J 8.6, 1-H'), 4.09 (1 H, m, 7-H), 4.13 (1 H, qd, J 6.3, 4.4, 10-H), 4.29 (1 H, dd, J 12.9, 5.4, 2'-H), 4.34 (1 H, dd, J 12.7, 6.6, 2'-H'), 4.48 and 4.53 (each 1 H, d, J 12.2, PhHCH), 4.56 (1 H, s, 4-H), 4.66 and 4.69 (each 1 H, d, J 6.8, OHCHO), 6.14 (1 H, m, 1'-H and, 7.22-7.32 (5 H, m, ArH); δ_c (125 MHz CDCl₃) -3.7, -3.3, -0.6, 0.0, 7.2, 8.6, 13.4, 18.5, 19.5(2), 20.2, 22.4, 24.0, 27.3, 27.8, 28.3, 36.1, 43.2, 50.5, 62.2, 66.6, 69.0, 69.9, 71.9, 74.8, 77.3,

77.9, 81.9, 97.9, 128.5, 128.6, 129.6, 134.2, 137.8 and 140.8; *m/z* (ES⁺) 1151.8 (M⁺ + 23, 100%).

(4S,7S,9R,10R)-1-Benzoyloxy-4,10-bis-tert-butyltrimethylsilyloxy-5-[(E)-2-triisopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilyloxyethoxymethoxy)-3,3-(1,3-dithiopropyl)undecan-7-ol (72).

Pyridinium toluene 4-sulfonate (3.6 mg, 0.014 mmol) was added to the triethylsilyl ether **71** (155 mg, 0.137 mmol) in THF (2.4 mL), methanol (2.4 mL) and trimethyl orthoformate (0.24 mL, 2.19 mmol) and the solution was stirred at rt for 12 h. Ether (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase extracted with ether (3 × 20 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (16:1 light petroleum:ether) gave the *title compound* **72** (128 mg, 92%) as a viscous colourless oil, *R*_f = 0.14 (19:1 light petroleum:ether), [α]_D²⁰ −22.9 (c 1.1, CHCl₃); *v*_{max}/cm^{−1} 3437, 2951, 2929, 2895, 2862, 1463, 1251, 1060, 886, 835 and 776; δ_H (500 MHz, CDCl₃) −0.01 (3 H, s, SiCH₃) 0.00 [9 H, s, Si(CH₃)₃], 0.07 (9 H, s, 3 × SiCH₃), 0.85-0.94 (2 H, m, CH₂Si), 0.88 and 0.93 [each 9 H, s, SiC(CH₃)₃], 1.02-1.11 [21 H, m, SiCH(CH₃)₂], 1.10 (3 H, d, *J* 6.2, 11-H₃), 1.28 and 1.29 (each 3 H, s, 2-CH₃), 1.51-1.64 (2 H, m, 8-H₂), 1.73-1.83 (2 H, m, SCH₂CH₂), 2.32 (1 H, dd, *J* 14.4, 3.0, 6-H), 2.47 (1 H, m, 6'-H), 2.58-2.87 (3 H, m, 3 × SHCH), 2.99 (1 H, m, SHCH), 3.52-3.64 (5 H, m 1-H, 9-H, OCH₂CH₂Si, OH), 3.80-3.90 (3 H, m, 1-H', 7-H, 10-H), 4.25 (1 H, dd, *J* 12.3, 5.7, 2'-H), 4.30 (1 H, dd, *J* 12.3, 7.3, 2'-H'), 4.49 and 4.53 (each 1 H, d, *J* 12.3, PhHCH), 4.69 (2 H, s, OCH₂O), 4.92 (1 H, s, 4-H), 6.12 (1 H, t, 1'-H) and 7.20-7.34 (5 H, m, ArH); δ_C (125 MHz, CDCl₃) −3.4, −3.3, −0.6, 0.0, 13.5, 19.5, 19.6, 19.7, 20.0(2), 22.6, 23.3, 23.8, 27.1, 27.3, 27.7, 28.3, 40.0, 42.3, 50.2, 61.5, 66.5, 70.6, 71.2, 72.4, 74.7, 77.6, 78.9, 81.3, 97.1, 128.6(2), 129.6, 131.6, 140.9 and 141.0; *m/z* (ES⁺) 1038 (M⁺ + 23, 100%).

(2S,3S,6S)-2-(2-Benzoyloxy-1,1-dimethylethyl)-6-[(2R,3R)-3-tert-butyltrimethylsilyloxy-2-(trimethylsilyloxyethoxymethoxy)butyl]-3-tert-butyltrimethylsilyloxy-2-methoxy-4-[(E)-2-triisopropylsilyloxyethylidene]tetrahydropyran (73)

2,6-Lutidine (0.27 mL, 2.3 mmol) and Hg(ClO₄)₂·3H₂O (273 mg, 0.68 mmol) were added to the dithiane **72** (341 mg, 0.34 mmol) in THF (5.5 mL) and MeOH (5.5 mL) at 0 °C and the mixture stirred at 0 °C for 10 min and at rt for 8 h. The white suspension was filtered through celite and the filtrate partitioned between ether (30 mL) and saturated aqueous NaHCO₃ (30 mL). The aqueous phase was extracted with ether (2 × 30 mL) and the organic extracts dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (50:1 light petroleum:ether) gave the *title compound* **73** (277 mg, 88%) as a colourless oil, *R*_f = 0.34 (15:1 light petroleum:ether), [α]_D²⁴ −32.0 (c 0.5, DCM) (Found: M⁺ + Na, 961.6243. C₅₀H₉₈O₈Si₄Na requires M, 961.6231); *v*_{max}/cm^{−1} 2954, 2894, 2864, 1471, 1463, 1380, 1361, 1251, 1148, 1102, 1058, 883, 859, 835 and 775; δ_H (400 MHz, C₆D₆) 0.00 [9 H, s, Si(CH₃)₃], 0.15, 0.16, 0.17 and 0.23 (each 3 H, s, SiCH₃), 0.91-1.01 (2 H, m, CH₂Si), 1.01 and

1.03 [each 9 H, SiC(CH₃)₃], 1.05-1.15 [21 H, m, 3 × SiCH(CH₃)₂], 1.31 (3 H, d, *J* 6.0, 4'''-H₃), 1.52 (6 H, s, 2 × 1'-CH₃), 1.68 (1 H, t, *J* 12.6, 1'''-H), 2.13 (1 H, dd, *J* 13.1, 10.6, 1'''-H'), 2.26 (1 H, dd, *J* 13.5, 3.0, 5-H), 2.33 (1 H, t, *J* 12.7, 5-H'), 3.38 (3 H, s, 2-OCH₃), 3.47 (1 H, m, OHCHCH₂Si), 3.75 (1 H, br. s, 2'-H), 3.82 (1 H, m, OHCHCH₂Si), 4.03-4.21 (3 H, m, 6-H, 2'-H', 2'''-H), 4.28 (1 H, dd, *J* 12.6, 5.7, 2''-H), 4.30-4.38 (3 H, m, 3-H, 2''-H', 3'''-H), 4.60 and 4.63 (each 1 H, d, *J* 12.3, PhHCH), 4.74 and 4.91 (each 1 H, d, *J* 6.8, OHCHO), 5.75 (1 H, m, 1''-H), 7.10 (1 H, t, *J* 7.4, ArH) and 7.21 (2 H, t, *J* 7.5, ArH) and 7.44 (2 H, d, *J* 7.5, ArH); δ_C (100 MHz, C₆D₆) −4.4, −4.2, −4.0, −3.4, −0.9, 12.7, 17.6, 18.7(2), 18.8, 19.0, 21.9, 22.5, 26.6, 26.7, 31.9, 36.3, 46.7, 52.3, 60.1, 65.9, 68.7, 69.8, 73.9, 76.3, 76.9, 80.1, 97.2, 104.2, 127.0, 127.8, 127.9, 128.9, 137.2 and 140.4; *m/z* (ES⁺) 962 (M⁺ + 23, 100%).

(6R,9RS,13S,15R,16R)-1-Benzoyloxymethoxy-7,7-dimethyl-5,9-bis-triethylsilyloxy-13,16-bis-tert-butyltrimethylsilyloxy-11-[(E)-2-triisopropylsilyloxyethylidene]-3-[(Z)-2-triisopropylsilyloxyethylidene]-15-(2-trimethylsilyloxyethoxymethoxy)heptadec-6-ene (88).

Lithium hexamethyldisilazide (1 M, 28 μL, 0.028 mmol) was added to the sulfone **87** (26 mg, 0.023 mmol) in THF (0.23 mL) at −78 °C and the mixture stirred at −60 °C for 30 min. After cooling to −78 °C, the aldehyde **35** (13 mg from the alcohol **34** (13 mg, 0.023 mmol) in THF (0.2 mL) was added and the mixture stirred at −78 °C for 20 min. After allowing the solution to warm to rt, ether (5 mL) and saturated aqueous sodium hydrogen carbonate (5 mL) were added. The aqueous layer was extracted with ether (2 × 5 mL) and the organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (15:1 light petroleum:ether) gave the *title compound* **88** (18 mg, 53%), as a colourless oil, a 60:40 mixture of epimers, *R*_f = 0.35 (15:1 light petroleum:ether); *v*_{max}/cm^{−1} 2951, 2866, 1463, 1382, 1250, 1101, 1058, 1011, 937, 882, 835, 774 and 741; δ_H (500 MHz, CDCl₃) −0.01 [9 H, s, Si(CH₃)₃], 0.02 (6 H, s, 2 × SiCH₃), 0.03 and 0.05 (each 3 H, s, SiCH₃), 0.50-0.60 (12 H, m, 6 × SiCH₂), 0.80-1.00 (2 H, m, CH₂Si), 0.87 [24 H, overlapping s, 2 × 8-CH₃, 2 × SiC(CH₃)₃], 0.92 (18 H, t, *J* 7.9, 6 × SiCH₂CH₃), 1.04 (3 H, d, *J* 6.3, 17-H₃), 1.04-1.12 [42 H, m, 6 × Si(CH(CH₃)₂)], 1.35-1.42 (3 H, m), 1.90 (1 H, m), 2.01-2.37 (6 H, m), 3.40 (1 H, m, OHCHCH₂Si), 3.48-3.54 (2 H, m, 5-H, 9-H), 3.60-3.72 (3 H, m, 1-H₂, OHCHCH₂Si), 3.79 (1 H, m, 13-H), 4.05 (1 H, m, 16-H), 4.12 (1 H, m, 15-H), 4.22-4.32 (4 H, m, 2'-H₂, 2''-H₂), 4.57 (2 H, s, PhCH₂), 4.65 and 4.66 (each 1 H, d, *J* 6.9, OHCHO), 4.77 (2 H, s, OCH₂O), 5.30 (1 H, m, 6-H), 5.35 and 5.54 (each 1 H, m, 1'-H or 1''-H), 5.67 (0.4 H, d, *J* 15.4, 7-H), 5.71 (0.6 H, d, *J* 15.4, 7-H) and 7.26-7.36 (5 H, m, ArH); δ_C (125 MHz, CDCl₃) −3.5, −3.2, −2.5, 0.0, 6.5, 7.5, 8.4, 8.5, 13.4, 13.5, 18.4(2), 19.5(2), 19.6, 25.5, 25.7, 26.3, 27.2, 27.3, 27.4(2), 36.6, 36.9, 39.1, 41.4, 42.0, 42.1, 42.6, 42.9, 61.9, 62.1, 62.2, 66.5, 68.2, 70.0, 70.1, 70.2, 70.7, 74.4, 74.9, 79.9, 81.1, 81.6(2), 96.0, 97.7, 116.6, 129.1, 129.3, 129.8, 130.7, 131.7(2), 132.3, 135.0, 135.1, 135.3, 135.6, 137.7, 138.5 and 139.4; *m/z* (ES⁺) 1489.0 (M⁺ + 23, 100%).