Total synthesis of 7-*des*-*O*-pivaloyl-7-*O*-benzylbryostatin 10

Anthony P. Green, Simon Hardy, Alan T. L. Lee and Eric J. Thomas

Supplementary data

Additional experimental

(3*S*,5*S*,7*S*,9*S*,11*S*,15*R*,16*EZ*)-7-Benzyloxy-3-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-18-(1,3-dithian-2-yl)-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8,18,18-tetramethyl-9-methoxyoctadec-16-ene (20).

Lithium hexamethyldisilazide (1.0 M in THF, 20 µL, 0.024 mmol) was added to the sulfone **19**[18] (9 mg, 0.024 mmol) in THF (241 µL) at −78 °C and the solution stirred for 30 min at −78 °C. The aldehyde **18** (15 mg, 0.015 mmol) in THF (0.2 mL) was added in one portion and the solution was allowed to warm to rt and stirred for 16 h. The reaction mixture was partitioned between ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:25 ether:light petroleum with 1% Et_3N) afforded the *title compound* **20** as a pale oil (13.5 mg, 78%), (*E*):(*Z*) = 2:1 (^{1}H NMR), R_f 0.65, 0.74 [(*Z*)- and (*E*)-isomers, 1:3 ether:light petroleum]; ν_{max}/cm^{-1} 2956, 2928, 2858, 1742, 1471, 1463, 1428, 1385, 1361, 1259, 1104, 1091, 882, 835, 802, 775 and 700. Repeated chromatography gave the (*E*)-isomer; δ_H (500 MHz, $CDCl_3$) −0.06 and −0.03 (each 3 H, s, $SiCH_3$), 0.77 [9 H, s, $SiC(CH_3)_3$], 0.94 (3 H, s, 8-CH_3), 0.94-1.07 [33 H, m, 8-CH_3′, 3 × $SiCH(CH_3)_2$, $SiC(CH_3)_3$], 1.14 and 1.15 (each 3 H, s, 18-CH_3), 1.27 (1 H, q, *J* 12.2, 6-H_{ax}), 1.49-1.63 (2 H, m, 2-H, 4-H), 1.65-1.75 (5 H, m, 2-H′, 4-H′, 10-H, 14-H_{ax}, 5′′-H), 1.90 (1 H, m, 12-Hax), 1.95-2.05 (2 H, m, 10-H′, 5′′-H′), 2.24 (1 H, d, *J* 12.9, 14-H_{eq}), 2.43 (1 H, d, *J* 13.6, 12-H_{eq}), 2.72-2.82 (4 H, m, 4′′-H_2, 6′′-H_2), 3.10 (3 H, s, 9-OCH_3), 3.44-3.53 (2 H, m, 5-H, 11-H), 3.59 (1 H, dd, *J* 11.5, 4.4, 7-H), 3.62-3.71 (3 H, m, 1-H_2, 15-H), 3.93 (1 H, s, 2′′-H), 3.94 (1 H, m, 3-H), 4.16-4.24 (2 H, m, 2′-H_2), 4.35 and 4.52 (each 1 H, d, *J* 11.7, PhHC*H*), 5.30 (1 H, t, *J* 6.2, 1′-H), 5.42 (1 H, dd, *J* 15.8, 5.7, 16-H), 5.70 (1 H, d, *J* 15.8, 17-H), 7.18 (1 H, m, ArH), 7.22-7.26 (4 H, m, ArH), 7.26-7.37 (6 H, m, ArH) and 7.56-7.61 (4 H, m, ArH); (*Z*)-isomer: 3.06 (3 H, s, 9-OCH_3), 3.99 (1 H, s, 2′′-H), 5.33 (1 H, dd, *J* 12.3, 9.1, 16-H) and 5.51 (1 H, d, *J* 12.3, 17-H); *m/z* (ES$^+$) 1196 (M^+ + 23, 27%).

(5*S*,7*R*,8*R*,2*E*)-5,8-Bis-*tert*-butyldimethylsilyloxy-3-benzyloxymethyl-1-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (22).

2,6-Lutidine (0.52 mL, 4.46 mmol) was added to the alcohol **21** (1.0 g, 1.41 mmol) in DCM (12 mL) and the solution cooled to 0 °C. *tert*-Butyldimethylsilyl trifluoromethylsulfonate (0.52 mL, 2.26 mmol) was added and the mixture stirred for 1 h. Water (10 mL) was added dropwise and the mixture allowed to warm to rt. Water (30 mL) and DCM (30 mL) were added and the aqueous layer was extracted with DCM (2 × 30 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 20:1 light petroleum:ether) gave the *title compound* **22** as a clear, colourless oil (1.03 g, 89%), R_f = 0.60 (20:1 light petroleum:ether), $[\alpha]_D^{22}$ –13.6 (*c* 6.1, $CHCl_3$) (Found: M^+ + Na, 847.5542. $C_{44}H_{88}O_6NaSi_4$ requires M, 847.5550); ν_{max}/ cm^{-1} 3066, 3031, 2953, 2893, 2863, 1464, 1381, 1252, 1102, 1059, 937 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 (9 H, s, 3 × $SiCH_3$), 0.04 (9 H, s, 3 × $SiCH_3$), 0.04 (3 H, s, $SiCH_3$), 0.81-0.97 (2 H, m, $SiCH_2$), 0.86 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 1.01 (3 H, d, *J* 6.3, 9-H_3), 1.03-1.16 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.39 (1 H, ddd, *J* 13.5, 10.2, 2.5, 6-H), 1.58 (1 H, m, 6-H′), 2.22 (1 H, dd, *J* 13.4, 8.4, 4-H), 2.36 (1 H, dd, *J* 13.4, 5.2, 4-H′), 3.44 (1 H, m, $SiCH_2CH$), 3.502 (1 H, m, 7-H), 3.67 (1 H, m, $SiCH_2CH$), 3.88-4.05 (4 H, m, 3-CH_2, 5-H, 8-H), 4.34 (2 H, d, *J* 5.7, 1-H_2), 4.45 (2 H, s, $PhCH_2$), 4.65 (2 H, s, OCH_2O), 5.69 (1 H, t, *J* 5.7, 2-H) and 7.23-7.35 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −3.3(2), −3.1, −2.4, 0.0, 13.4, 18.6, 19.4, 19.5, 19.6, 27.3, 27.4, 37.0, 39.2, 61.7, 66.6, 69.7, 70.4, 73.1, 75.7, 81.7, 97.5, 128.9, 129.2, 129.7, 132.3, 134.9 and 139.9; *m/z* (ES$^+$) 884.0 (75%) and 847.5 (M^+ + 23, 100).

(4*S*,6*R*,7*R*)-4,7-Bis-*tert*-butyldimethylsilyloxy-2-[(*E*)-2-tri-isopropylsilyloxyethylidene]-6-(2-trimethylsilylethoxymethoxy)octan-1-ol (23).

Finely chopped lithium wire (53 mg, 7.6 mmol) was added to naphthalene (1.75 g, 13.7 mmol) in THF (10 mL) and the resulting deep green mixture was stirred at rt for 2 h. An aliquot of this solution (5 mL) was added over 1 h to the benzyl ether **22** (0.90 g, 1.09 mmol) in THF (32 mL) at −20 °C. At this point the starting material had reacted (TLC) and solid NH_4Cl was added slowly with stirring until the brown colour of the solution had disappeared. The mixture was allowed to warm to rt over 20 min and ether (200 mL) and saturated aqueous $NaHCO_3$ were added. The aqueous layer was extracted with ether (100 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (20:1 then 10:1 light petroleum:ether) afforded the *title compound* **23** as a clear, colourless oil (0.705 g, 88%), R_f = 0.15 (10:1 light petroleum:ether) $[\alpha]_D^{34}$ +8.1 (*c* 6.4, $CHCl_3$) (Found: M^+ + Na, 757.5076. $C_{37}H_{82}O_6NaSi_4$ requires M, 757.5081); ν_{max}/cm^{-1} 3442, 2954, 2893, 2864, 1463, 1381, 1252, 1102, 1058, 937, 882 and 833; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.08 and 0.09 (each 3 H, s, $SiCH_3$), 0.77-0.99 [20 H, m, 2 × $SiC(CH_3)_3$, $SiCH_2$], 0.99-1.13 [24 H, m, 3 × $SiCH(CH_3)_2$, 8-H_3), 1.42 (1 H, ddd, *J* 14.2, 10.1, 4.1, 5-H), 1.62 (1 H, ddd, *J* 14.2, 7.6, 1.0, 5-H′), 2.26 (1 H, dd, *J* 13.8, 6.3, 3-H), 2.40 (1 H, dd, *J* 13.8, 5.0, 3-H′), 2.56 (1 H, br. t, *J* 6.0, OH), 3.45-3.55 (2 H, m, 6-H, HC*H*CH_2Si), 3.65 (1 H, ddd, *J* 10.1, 9.8, 5.7, HC*H*CH_2Si), 3.93-4.06 (4 H, m, 1-H_2, 4-H, 7-H), 4.28 (1 H, dd, *J* 13.2, 5.6, 2′-H), 4.32 (1 H, dd, *J* 13.2, 6.4, 2′-H′), 4.67 and 4.70 (each 1 H, d, *J* 6.9, OHC*H*O) and 5.69 (1 H, m, 1′-H); δ_C (125 MHz, $CDCl_3$) −3.3(2), −3.1, −2.6, 0.0, 13.4, 18.7, 19.5, 19.6, 27.3, 27.4, 37.0, 39.5, 61.7, 66.8, 69.3, 70.4, 70.9, 81.8, 97.3, 131.5

and 137.8; *m/z* (ES^+) 753.2 (M^+ + 18, 100%) and 735.7 (M^+ + 1, 83).

(5*S*,7*R*,8*R*,2*E*)-3-Bromomethyl-5,8-bis-*tert*-butyldimethylsilyloxy-1-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (24).

Carbon tetrabromide (2.83 g, 8.54 mmol) was added to triphenylphosphine (2.24 g, 8.54 mmol) in dry DCM (94 mL) at 0 °C. The solution was stirred for 1 min then transferred to a solution of the alcohol **23** (1.57 g, 2.13 mmol) in dry DCM (47 mL) at 0 °C. The mixture was stirred at 0 °C for 10 min and DCM (50 mL) and saturated aqueous $NaHCO_3$ (50 mL) were added. The aqueous layer was extracted with DCM (2 × 50 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (100:1 to 50:1 light petroleum:ether) gave the *title compound* **24** as a pale yellow oil (1.56 g, 92%), R_f = 0.23 (50:1 light petroleum:ether), $[\alpha]_D^{34}$ −2.1 (*c* 13.6, $CHCl_3$) (Found: M^+ + Na, 819.4237. $C_{37}H_{81}O_5{}^{79}BrNaSi_4$ requires M, 819.4237); ν_{max}/cm^{-1} 2954, 2893, 2863, 1464, 1381, 1252, 1102, 1057, 937 and 833; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.07 and 0.10 (each 3 H, s, $SiCH_3$), 0.80-0.98 (2 H, m, $SiCH_2$), 0.86 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 0.98-1.14 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.01 (3 H, d, *J* 6.3, 9-H_3), 1.34 (1 H, ddd, *J* 13.9, 10.1, 3.2, 6-H), 1.59 (1 H, ddd, *J* 13.9, 8.5, 1.0, 6-H′), 2.33 (1 H, dd, *J* 13.9, 7.9, 4-H), 2.45 (1 H, dd, *J* 13.9, 5.5, 4-H′), 3.44-3.54 (2 H, m, 7-H, HC*H*CH_2Si), 3.66 (1 H, ddd, *J* 11.4, 9.8, 5.4, HC*H*CH_2Si), 3.94 (1 H, m, 5-H), 3.98-4.06 (3 H, m, 3-CH_2, 8-H), 4.27 (1 H, dd, *J* 13.9, 5.4, 1-H), 4.30 (1 H, dd, *J* 13.9, 5.8, 1 H′), 4.68 and 4.71 (each 1 H, d, *J* 7.0, OHC*H*O) and 5.80 (1 H, m, 2-H); δ_C (125 MHz, $CDCl_3$) −3.3(2), −3.1, −2.5, 0.0, 13.4, 18.6, 19.4(2), 19.5, 19.6, 27.3, 27.4, 37.2, 38.6, 40.6, 61.9, 66.8, 69.6, 70.3, 81.7, 97.5, 134.7 and 135.5; *m/z* (ES^+) 857.8 (100%), 855.8 (90), 821.2 (M^+ + 23, 33) and 819.4 (M^+ + 23, 20).

(5*S*,7*R*,8*R*)-5,8-Bis-*tert*-butyldimethylsilyloxy-3-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-7-(2-trimethylsilyl-ethoxymethoxy)nonanenitrile (25).

Sodium cyanide (124 mg, 2.54 mmol) was added to the bromide **24** (1.56 g, 1.95 mmol) in DMF (20 mL) at 0 °C and the mixture was stirred at 0 °C for 3.5 h. Ether (250 mL) and water (150 mL) were added and the aqueous layer was extracted with ether (100 mL). The organic extracts were washed with water (2 × 50 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 20:1 light petroleum:ether) gave recovered bromide **24** (0.37 g, 24%) followed by the *title compound* **25** as a clear, colourless oil (1.03 g, 71%), R_f = 0.23 (10:1 light petroleum:ether), $[\alpha]_D^{32}$ −5.5 (*c* 2.9, $CHCl_3$) (Found: M^+ + Na, 766.5096. $C_{38}H_{81}O_5NNaSi_4$ requires M, 766.5084); ν_{max}/cm^{-1} 2954, 2929, 2862, 2361, 2252, 1463, 1381, 1252, 1103, 1058, 937 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.06 and 0.07 (each 3 H, s, $SiCH_3$), 0.83-0.98 (2 H, m, CH_2Si), 0.85 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 1.01 (3 H, d, *J* 6.3, 9-H_3), 1.02-1.12 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.34 (1 H, ddd, *J* 14.2, 10.1, 4.1, 6-H), 1.62 (1 H, ddd, *J* 14.2, 7.6, 1.9, 6-H′), 2.32 (2 H, d, *J* 6.0, 4-H_2), 3.15 (2 H, s, 2-H_2), 3.43-3.52 (2 H, m, 7-H, HC*H*CH_2Si), 3.66 (1 H, ddd, *J* 11.4, 9.5, 5.4, HC*H*CH_2Si), 3.93 (1 H, m, 5-H), 4.02 (1 H, dq, *J* 6.3, 5.7, 8-H) 4.27 (1 H, dd, *J* 13.2, 5.4, 2′-H), 4.30 (1 H, dd, *J* 13.2, 6.6, 2′-H′), 4.66 and 4.69 (each 1 H, d, *J* 7.0, OHC*H*O) and 5.78 (1 H, m, 1′-H); δ_C (125 MHz, $CDCl_3$) −3.3(2), −3.1, −2.6, 0.0, 13.4, 18.5, 19.2, 19.4, 19.5, 19.6, 27.3, 27.4(2), 36.9, 40.4, 61.6, 66.9, 70.2, 81.8, 97.4, 119.0, 128.1 and 133.7; *m/z* (ES^+) 802.3 (29%), 766.9 (M^+ + 23, 39) and 761.6 (M^+ + 18, 100).

Methyl (3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-3-hydroxy-2,2-dimethyl-5-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecanoate (27).

Di-isobutylaluminium hydride (1 M in heptane, 1.64 mL, 1.64 mmol) was added to the nitrile **25** (1.06 g, 1.42 mmol) in DCM (17.5 mL) at –78 °C and the mixture was stirred for 45 min before the dropwise addition of ethanol (7.3 mL). After stirring for 30 min, saturated aqueous NH_4Cl (100 mL) and ethyl acetate (100 mL) were added and the mixture stirred vigorously for 30 min before addition of saturated aqueous Rochelle's salt (100 mL) and further stirring for 2 h. The aqueous layer was extracted with ethyl acetate (2 × 100 mL) and the organic exracts were dried (Na_2SO_4) and concentrated under reduced pressure to leave the aldehyde **26** as a viscous, yellow oil (1.10 g) that was used directly in the next step, R_f = 0.23 (10:1 light petroleum:ether): δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03, 0.04 and 0.05(2) (each 3 H, s, $SiCH_3$), 0.80-0.95 (2 H, m, CH_2Si), 0.86 [18 H, s, 2 × $SiC(CH_3)_3$], 1.04 (3 H, d, *J* 7.0, 9-H_3), 0.98-1.15 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.38 (1 H, m, 6-H), 1.57 (1 H, dd, *J* 15.0, 7.9, 6-H′), 2.26 (2 H, d, *J* 8.0, 4-H_2), 3.09 (2 H, br. s, 2-H_2), 3.49 (1 H, m, HC*H*CH_2Si), 3.50 (1 H, m, 7-H), 3.65 (1 H, m, HC*H*CH_2Si), 3.90 (1 H, m, 5-H), 4.01 (1 H, pent, *J* 6.0, 8-H) 4.32 (2 H, d, *J* 7.0, 2′-H_2), 4.66 and 4.69 (each 1 H, d, *J* 7.0, OHC*H*O), 5.56 (1 H, t, *J* 7.0, 1′-H) and 9.61 (1 H, t, *J* 1.5, 1-H).

Lithium di-isopropylamide (1.7 M in THF, heptane, ethylbenzene, 0.92 mL, 1.56 mmol) was added to methyl 2-methylpropanoate (0.18 mL, 1.56 mmol) in THF (5.8 mL) at –78 °C and the mixture stirred for 70 min at −78 °C. A cooled solution of the aldehyde **26** (1.10 g, from 1.42 mmol nitrile **25**) in THF (5.83 mL) was added over 1 min and the mixture was stirred for 30 min, warmed to rt and stirred for a further 30 min. Ether and saturated aqueous $NaHCO_3$ (50 mL) were added and the aqueous layer was extracted with ether (2 × 50 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 10:1 light petroleum:ether) gave the *title compound* **27** as a pale yellow oil (0.63 g, 52% from nitrile **25**), as a 1:1 mixture of epimers (^1H and ^{13}C NMR), R_f = 0.17 and 0.20 (10:1 light petroleum:ether), $[\alpha]_D^{27}$ –10.2 (*c* 11.8, $CHCl_3$) (Found: M^+ + NH_4, 866.6214. $C_{43}H_{96}O_8NSi_4$ requires M, 866.6208); ν_{max}/cm^{-1} 3509, 2953, 2864, 1728, 1463, 1381, 1250, 1186, 1099, 1058, 936 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03, 0.04 and 0.06 (each 3 H, s, $SiCH_3$), 0.07 and 0.08 (each 1.5 H, s, $SiCH_3$), 0.86(2) and 0.87(2) [each 4.5 H, s, $SiC(CH_3)_3$], 0.88-0.98 (2 H, m, $SiCH_2$), 0.98-1.13 [24 H, m, 3 × $SiCH(CH_3)_2$, 11-H_3), 1.16, 1.17, 1.19 and 1.20 (each 1.5 H, s, 2-CH_3), 1.43 and 1.56 (each 1 H, m, 8-

H), 1.89 (0.5 H, dd, *J* 13.7, 11.0, 4-H), 1.98 (0.5 H, dd, *J* 13.6, 10.6, 4-H), 2.11-2.46 (4 H, m, 4-H', 6-H_2, OH), 3.44 (1 H, ddd, *J* 11.0, 9.7, 6.1, HC*H*CH_2Si), 3.53 (1 H, m, 9-H), 3.69 (1 H, m, HC*H*CH_2Si), 3.68(2) (each 1.5 H, s, CO_2CH_3), 3.79-3.93 (2 H, m, 3-H, 7-H), 4.05 (1 H, m, 10-H), 4.28 (1 H, dd, *J* 13.1, 5.7, 2'-H), 4.30 (1 H, dd, *J* 13.1, 6.2, 2'-H'), 4.67, 4.68, 4.69 and 4.71 (each 0.5 H, d, *J* 7.0 OHC*H*O) and 5.49 and 5.51 (each 0.5 H, t, *J* 5.7, 1'-H); δ_C (125 MHz, $CDCl_3$) −3.3(2), −3.0, −2.3(2), 0.0, 13.5, 18.5(2), 19.5(2), 19.6, 21.8, 22.2, 22.6, 23.1, 27.3, 27.4(2), 36.8, 36.9, 40.6, 41.1, 41.7, 41.9, 48.4, 48.5, 53.3, 61.7, 61.9, 66.7(2), 70.0, 70.2(2), 70.5, 74.9, 75.5, 81.8, 81.9, 97.6(2), 133.0, 133.1, 135.5, 135.7, 178.9 and 179.0; *m/z* (ES^+) 907.2 (100%) and 866.3 (M^+ + 18, 31).

Methyl (3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-3-triethylsilyloxy-2,2-dimethyl-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecanoate (28).

Imidazole (0.387 g, 5.69 mmol) and triethylsilyl chloride (0.65 mL, 3.88 mmol) were added to the alcohol **27** (0.525 g, 0.618 mmol) in DMF (14 mL) and the solution stirred at rt for 16 h. Ether (150 mL) and saturated aqueous $NaHCO_3$ (100 mL) were added and the organic layer was washed with water (2 × 100 mL) and brine (50 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (100:1 then 10:1 light petroleum:ether) gave the *title compound* **28** as a pale yellow oil (0.452 g, 76%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.58 and 0.60 (10:1 light petroleum:ether), $[\alpha]_D^{26}$ –13.3 (*c* 5.2, $CHCl_3$) (Found: M^+ + NH_4, 980.7081. $C_{49}H_{110}O_8NSi_5$ requires M, 980.7072); ν_{max}/cm^{-1} 2954, 2866, 1742, 1729, 1471, 1463, 1386, 1361, 1251, 1190, 1103, 1058, 937, 835 and 774; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03 (6 H, s, 2 × $SiCH_3$), 0.05(2), 0.07 and 0.09 (each 1.5 H, s, $SiCH_3$), 0.52 and 0.55 (each 3 H, q, *J* 7.9, 3 × $SiCH_2$), 0.81-0.95 (2 H, m, $SiCH_2$), 0.86(2), 0.87 and 0.88 [each 4.5 H, s, $SiC(CH_3)_3$], 0.90 and 0.91 (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.01 (3 H, d, *J* 6.2, 11-H_3), 1.03-1.14 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.09(2), 1.16, 1.17 (each 1.5 H, s, 2-CH_3), 1.39 and 1.42 (each 0.5 H, ddd, *J* 13.6, 10.5, 2.8, 8-H), 1.52 (1 H, m, 8-H'), 1.89-2.35 (4 H, m, 4-H_2, 6-H_2), 3.42 (1 H, td, *J* 10.4, 6.0, OHC*H*CH_2Si), 3.54 (1 H, m, 9-H), 3.64 (3 H, s, CO_2CH_3), 3.70 (1 H, td, *J* 10.4, 5.3, OHC*H*CH_2Si), 3.81 (1 H, m, 7-H), 4.07 (1 H, m, 10-H), 4.10 (0.5 H, dd, *J* 8.4, 3.3, 3-H), 4.13 (0.5 H, dd, *J* 8.9, 2.1, 3-H), 4.27 and 4.30 (each 1 H, dd, *J* 12.9, 5.7, 2'-H), 4.67 and 4.68 (each 0.5 H, d, *J* 7.6, OHC*H*O), 4.69 (1 H, s, OCH_2O) and 5.42 and 5.44 (each 0.5 H, t, *J* 5.7, 1'-H); δ_C (125 MHz, $CDCl_3$) −3.4, −3.3, −3.0(2), −2.3, −2.2, 0.0, 6.8, 6.9, 8.5, 13.4, 18.4(2), 19.5(2), 21.0, 22.3, 23.6, 27.3, 27.4, 36.7, 36.9, 41.0, 42.2, 42.8, 43.2, 49.9(2), 53.0, 53.1, 62.0, 62.1, 66.5, 66.6, 70.0, 70.1, 70.2, 70.3, 76.4, 76.9, 81.7, 81.8, 97.7, 132.4, 132.8, 134.6, 134.7 and 178.9; *m/z* (ES^+) 986.1 (M^+ + 23, 86%) and 981.5 (M^+ + 18, 100).

(3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecan-1-ol (29).

Di-isobutylaluminium hydride (1 M in heptane, 0.80 mL, 0.80 mmol) was added to methyl ester **28** (0.308 g, 0.320 mmol) in dry toluene (6 mL) at –78 °C and the solution stirred for 1.5 h before the addition of saturated aqueous Rochelle's salt. The mixture was allowed to warm to rt then stirred vigorously for 24 h. Ether (50 mL) and saturated aqueous Rochelle's salt (30 mL) were added and the aqueous layer extracted with ether (2 × 50 mL). The organic extracts were washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (15:1 then 10:1 light petroleum:ether) gave the *title compound* **29** as a clear, colourless oil (0.24 g, 80%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.19 (10:1 light petroleum:ether), $[\alpha]_D^{30}$ −16.2 (*c* 4.2, $CHCl_3$) (Found: M^+ + Na, 957.6673. $C_{48}H_{106}O_7NaSi_5$ requires M, 957.6677); ν_{max}/cm^{-1} 3504, 2956, 2866, 1464, 1380, 1251, 1100, 1058, 1014, 937, 859, 835 and 774; δ_H (500 MHz, $CDCl_3$) 0.00(2) [each 4.5 H, s, $Si(CH_3)_3$], 0.03 (6 H, s, 2 × $SiCH_3$), 0.04 and 0.05 (each 1.5 H, s, $SiCH_3$), 0.07 (3 H, s, $SiCH_3$), 0.58 and 0.60 (each 3 H, q, *J* 8.0, 3 × $SiCH_2$), 0.81-0.97 (2 H, m, $SiCH_2$), 0.86(2) and 0.87(2) [each 4.5 H, s, $SiC(CH_3)_3$], 0.93 (9 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 0.97-1.17 [30 H, m, 3 × $SiCH(CH_3)_2$, 2 × 2-CH_3, 11-H_3), 1.42 and 1.53 (each 1 H, m, 8-H), 1.98-2.41 (4 H, m, 4-H_2, 6-H_2), 3.00 (1 H, br. s, OH), 3.25 and 3.26 (each 0.5 H, d, *J* 10.8, 1-H), 3.43 (1 H, m, OHC*H*CH_2Si), 3.53 (1 H, m, 9-H), 3.65-3.75 (3 H, m, 1-H', 3-H, OHC*H*CH_2Si), 3.65 (1 H, m, 7-H), 4.04 (1 H, m, 10-H), 4.28 (1 H, dd, *J* 12.8, 6.1, 2'-H), 4.30 (1 H, dd, *J* 12.8, 5.3, 2'-H'), 4.64-4.71 (2 H, m, OCH_2O) and 5.45 (1 H, m, 1'-H); δ_C (125 MHz, $CDCl_3$) −3.4(2), −3.3(2), −2.9, −2.3, −2.2, 0.0, 6.7, 6.8, 8.5, 13.4, 18.4, 18.5, 19.5(3), 23.3, 23.5, 24.8, 25.0, 27.3, 27.4(2), 36.5, 37.0, 40.8, 40.9, 41.0, 42.3, 42.4, 42.8, 62.0(2), 66.6, 69.9, 70.1, 70.2(2), 71.6, 71.7, 80.2, 80.9, 81.5, 81.6, 97.6, 131.8, 132.6, 135.0 and 135.2; *m/z* (ES^+) 958.2 (M^+ + 23, 100%).

(3*RS*,7*S*,9*R*,10*R*)-1-(Benzothiazol-2-ylsulfanyl)-7,10-bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecane (30).

2-Mercaptobenzothiazole (0.128 g, 0.763 mmol) and triphenylphosphine (0.198 g, 0.755 mmol) were added to the alcohol **29** (0.24 g, 0.254 mmol) in THF (3.6 mL) and the mixture stirred until homogeneous. Di-isopropyl azodicarboxylate (0.15 mL, 0.76 mmol) was added and the mixture stirred at rt for 24 h then concentrated under reduced pressure. The mixture was dissolved in the minimum of DCM and chromatography (100:1 then 50:1 light petroleum:ether) gave the *title compound* **30** as a viscous, clear, colourless oil (0.26 g, 93%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.57 and 0.60 (15:1 light petroleum:ether), $[\alpha]_D^{22}$ –8.4 (*c* 4.3, $CHCl_3$); ν_{max}/cm^{-1} 2955, 2866, 1463, 1429, 1385, 1250, 1100, 1058, 993, 937, 835, 774 and 754; δ_H (500 MHz, $CDCl_3$) 0.01 and 0.00 [each 4.5 H, s, $Si(CH_3)_3$], 0.02 and 0.04 (each 3 H, s, $SiCH_3$), 0.06, 0.07,

0.09 and 0.11 (each 1.5 H, s, $SiCH_3$), 0.61 and 0.62 (each 3 H, q, *J* 7.9, 3 × $SiCH_2$), 0.80-0.98 (2 H, m, $SiCH_2$), 0.85, 0.87, 0.88 and 0.89 [each 4.5 H, s, $SiC(CH_3)_3$], 0.95 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.02 and 1.03 (each 1.5 H, d, *J* 6.3, 11-H_3), 1.03-1.15 [27 H, m, 3 × $SiCH(CH_3)_2$, 2 × 2-CH_3], 1.45 and 1.54 (each 1 H, m, 8-H), 1.97 and 2.03 (each 0.5 H, dd, *J* 14.1, 9.3, 4-H), 2.13 (0.5 H, dd, *J* 13.1, 8.6, 6-H), 2.24 (1 H, m, 6-H_2), 2.29-2.40 (1.5 H, m, 4-H', 6-H'), 3.42 (1 H, m, OHC*H*CH_2Si), 3.45 and 3.48 (each 1 H, s, 1-H_2), 3.54 (1 H, m, 9-H), 3.69 (1 H, m, OHC*H*CH_2Si), 3.75 (1 H, m, 3-H), 3.87 (1 H, m, 7-H), 4.06 (1 H, m, 10-H), 4.30 (1 H, dd, *J* 12.6, 5.6, 2'-H), 4.32 (1 H, dd, *J* 12.6, 6.3, 2'-H'), 4.66 (1 H, s, OCH_2O), 4.68 and 4.70 (each 0.5 H, d, *J* 7.0, OHC*H*O), 5.48 (1 H, m, 1'-H), 7.28 and 7.40 (each 1 H, m, ArH) and 7.74 and 7.84 (each 1 H, d, *J* 8.1, ArH); δ_C (125 MHz, $CDCl_3$) −3.4, −3.3(3), −2.2, −2.1, 0.0, 6.9, 7.1, 8.7(2), 13.4, 18.4, 18.5, 19.4, 19.5(2), 24.0, 24.1, 25.3, 25.5, 27.3, 27.4(2), 36.5, 36.9, 41.0, 41.8(2), 42.1, 42.3, 42.9, 44.6, 62.0, 62.1, 66.6, 69.8, 70.0, 70.2, 70.3, 79.1, 81.6, 81.7, 97.6, 97.7, 122.3, 122.8, 125.5, 127.4, 132.0, 132.9, 134.9, 135.2, 136.5, 154.6 and 169.8; *m/z* (ES^+) 1143.7 (81%), 1107.4 (M^+ + 23, 100) and 1085.9 (M^+ + 1, 67).

(7*RS*,11*S*,13*R*,14*R*,4*E*)-11,14-Bis-*tert*-butyldimethylsilyloxy-6,6-dimethyl-7-triethylsilyloxy-9-[(*E*)-2-tri-isopropylsilyloxyethylidene]-13-(2-trimethylsilylethoxymethoxy)pentadec-4-ene (33).

Lithium hexamethyldisilazide (1.05 M in toluene, 26 µL, 0.027 mmol) was added to the sulfone **32** (azeotroped twice with benzene, 28 mg, 0.0247 mmol) in THF (0.25 mL) at −78 °C and the bright yellow solution was warmed to –60 °C, stirred for 30 min then cooled to –78 °C. A portion (0.16 mL, 0.124 mmol) of a solution of butanal (freshly distilled from calcium chloride, 0.11 mL) in THF (1.60 mL) was added dropwise and the solution was immediately allowed to warm to rt then stirred for 1 h. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous layer was extracted with ether (2 × 5 mL). The organic extracts were diluted (to 50 mL) with ether then washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (100:1 light petroleum:ether) gave the *title compound* **33** as a clear, colourless oil (21 mg, 85%), as a 1:1 mixture of epimers (^1H and ^{13}C NMR), a 4:1 mixture of (4*E*)- and (4*Z*)-isomers, R_f = 0.73 (30:1 light petroleum:ether) (Found: $M^+ + NH_4$, 990.7644. $C_{52}H_{116}O_6NSi_5$ requires M, 990.7643); ν_{max}/cm^{-1} 2954, 2927, 2863, 1471, 1463, 1382, 1360, 1250, 1098, 1058, 938, 882, 858, 835, 806, 773 and 737; δ_H (500 MHz, $CDCl_3$) (4*E*)-isomer: 0.00(2) [each 4.5 H, s, $Si(CH_3)_3$] 0.03 (6 H, s, 2 × $SiCH_3$), 0.04 (3 H, s, $SiCH_3$), 0.06 and 0.07 (each 1.5 H, s, $SiCH_3$), 0.50-0.61 (6 H, m, 3 × $SiCH_2$), 0.81-0.98 (11 H, m, 1-H_3, $SiCH_2$ 2 × 6-CH_3), 0.86(2), 0.87 and 0.88 [each 4.5 H, s, $SiC(CH_3)_3$], 0.92 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.01 and 1.02 (each 1.5 H, d, *J* 6.3, 15-H_3), 1.03-1.15 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.36 (2 H, pent, *J* 7.3, 2-H_2), 1.40-1.56 (2 H, m, 12-H_2), 1.82 (0.5 H, dd, *J* 13.8, 9.1, 8-H), 1.85 (0.5 H, dd, *J* 13.9, 8.8, 8-H), 1.93-2.00 (2 H, m, 3-H_2), 2.04 (0.5 H, dd, *J* 13.1, 8.5, 10-H), 2.10-2.24 (2 H, m, 8-H', 10-H, 10-H'), 2.27 (0.5 H, dd, *J* 13.2, 5.4, 10-H'), 3.42 (1 H, m, OHC*H*CH_2Si), 3.49-3.56 (2 H, m, 7-H, 13-H), 3.70(2) (each 0.5 H, ddd, *J* 11.1, 9.7, 5.5, OHC*H*CH_2Si), 3.81 (1 H, m, 11-H), 4.04 (1 H, m, 14-H), 4.23-4.33 (2 H, m, 2'-H_2), 4.66(2), 4.67 and 4.68 (each 0.5 H, d, *J* 6.9, OHC*H*O), 5.31 (1 H, dt, *J* 15.7, 6.7, 4-H), 5.39 (1 H, t, *J* 5.5, 1'-H) and 5.44 (1 H, dd, *J* 15.7, 1.4, 5-H); *m/z* (ES^+) 995.6 (M^+ + Na, 100%) and 917.8 (62).

(3*S*,5*R*,7*S*,9*S*,11*S*,15*R*)-7-Benzyloxy-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane-1,3-diyl methyl orthoformate (42a,b).

Pyridinium toluene *p*-sulfonate (1 mg, 0.0038 mmol) was added to the hydroxyacetonide **41** (31 mg, 0.038 mmol) and trimethyl orthoformate (83 µL) in DCM (291 µL) and methanol (291 µL) and the solution was stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:25 EtOAc:light petroleum) afforded the less polar epimer of the *title compound* **42a** as a pale oil (5 mg, 16%), R_f 0.62 (1:3 EtOAc:light petroleum) (Found: M^+ + Na, 849.4953. $C_{47}H_{74}O_{10}NaSi$ requires M, 849.4943); δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, 8-CH_3), 0.95-1.07 [24 H, m, 3 × $SiCH(CH_3)_2$, 8-CH_3'), 1.26 (1 H, m, 2-H_{ax}), 1.38 (1 H, m, 6-H_{ax}), 1.42-1.54 (2 H, m, 4-H_2), 1.61-1.83 (3 H, m, 14-H_{ax}, 10-H, 2-H_{eq}), 1.92 (1 H, t, *J* 12.2, 12-H_{ax}), 2.01 (1 H, dd, *J* 15.9, 4.3, 10-H'), 2.33-2.41 (2 H, m, 12-H_{eq}, 14-H_{eq}), 3.12 (3 H, s, 9-OCH_3), 3.22 (3 H, s, OCH_3), 3.36-3.46 (3 H, m, 15-H, 16-H_2), 3.50 (1 H, m, 11-H), 3.58-3.71 (2 H, m, 5-H, 1-H_{ax}), 3.63 (1 H, dd, *J* 11.6, 4.5, 7-H), 3.73 (3 H, s, $ArOCH_3$), 4.06 (1 H, m, 1-H_{eq}), 4.20 (2 H, m, 2'-H_2), 4.37 (1 H, d, *J* 11.7, PhHC*H*), 4.40 (1 H, m, 3-H), 4.45 (2 H, s, $ArCH_2$), 4.52 (1 H, d, *J* 11.7, PhHC*H*), 5.27 (1 H, s, MeOC*H*O_2), 5.31 (1 H, t, *J* 6.1, 1'-H), 6.80 (2 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH) and 7.26 (3 H, d, *J* 4.3, ArH); δ_C (100 MHz, $CDCl_3$) 11.0, 15.6, 17.0, 19.8, 30.6, 32.1, 37.8, 41.8, 42.4, 47.0, 51.8, 54.2, 57.1, 58.5, 62.8, 63.6, 70.6, 71.9, 72.0, 74.4, 75.7, 77.7, 102.8, 108.1, 112.7, 122.8, 126.2, 126.3, 127.2, 128.2, 129.5, 134.8, 138.3 and 158.1; *m/z* (ES^+) 849.6 (M^+ + 23, 100%) and 844.7 (M^+ + 18, 39). Further elution (1:25 to 1:10 EtOAc:light petroleum) afforded the more polar epimer of the *title compound* **44b** as a pale, yellow oil (5 mg, 16%), R_f 0.48 (1:3 EtOAc:light petroleum) (Found: M^+ + Na, 849.4957. $C_{47}H_{74}O_{10}NaSi$ requires *M*, 849.4943); δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, 8-CH_3), 0.95-1.07 [24 H, m, 3 × $SiCH(CH_3)_2$, 8-CH_3'), 1.18 (1 H, m, 6-H_{ax}), 1.28 (1 H, m, 2-H_{ax}), 1.52-1.63 (3 H, m, 4-H_2, 2-H_{eq}), 1.67-1.80 (3 H, m, 14-H_{ax}, 10-H, 6-H_{eq}), 1.95 (1 H, t, *J* 12.1, 12-H_{ax}), 2.00 (1 H, dd, *J* 16.0, 4.3, 10-H'), 2.27 (1 H, d, *J* 13.4, 12-H_{eq}), 2.36 (1 H, d, *J* 13.6, 14-H_{eq}), 3.10 (3 H, s, 9-OCH_3), 3.33-3.46 (3 H, m, 15-H, 16-H_2), 3.39 (3 H, s, OCH_3), 3.48 (1 H, m, 11-H), 3.62 (1 H, dd, *J* 11.6, 4.5, 7-H), 3.73 (3 H, s, $ArOCH_3$), 3.77 (1 H, t, *J* 11.6, 1-H_{ax}), 4.00 (1 H, m, 3-H), 4.06 (1 H, m, 1-H_{eq}), 4.17 (1 H, dd, *J* 12.9, 6.1, 2'-H), 4.22 (1 H, dd, *J* 12.6, 6.3, 2'-H'), 4.38 (1 H, d, *J* 11.7, PhHC*H*), 4.45 (2 H, s, $ArCH_2$), 4.52 (1 H, d, *J* 11.7, PhHC*H*), 5.04 (1 H, s, MeOC*H*O_2), 5.26 (1 H, t, *J* 6.3, 1'-H), 6.80 (2 H, d, *J* 8.8, ArH), 7.16-7.23 (4 H, m, ArH) and 7.26 (3 H, d, *J* 4.3, ArH); δ_C (100 MHz, $CDCl_3$) 11.0, 15.7, 17.0, 19.9, 29.6, 30.5, 31.8, 38.0, 41.1, 42.3, 42.5,

46.8, 52.1, 54.2, 58.4, 62.5, 63.8, 70.6, 71.9, 72.0, 74.4, 75.7, 77.7, 102.9, 111.2, 112.7, 123.0, 126.3, 126.4, 127.2, 128.2, 129.4, 134.6, 138.2 and 158.1; *m/z* (ES^+) 849.7 (M^+ + 23, 100%), 844.5 (M^+ + 18, 19).

(3*S*,5*R*,7*S*,9*S*,11*S*,15*R*)-7-Benzyloxy-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane-1,3-diol (43) and (3*S*,5*R*,7*S*,9*S*,11*S*,15*R*)-7-Benzyloxy-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-1,3-di-*O*-isopropylidene-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane (44).

Pyridinium toluene *p*-sulfonate (0.15 mg, 0.0006 mmol) was added to the hydroxyacetonide **41** (5 mg, 0.0062 mmol) in DCM (47 µL) and methanol (47 µL) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:10 EtOAc:light petroleum) afforded the *title compound* **44** as a colourless oil (1 mg, 20%), R_f 0.84 (1:3 EtOAc:light petroleum) (Found: M^+ + Na, 847.5158. $C_{48}H_{76}O_9NaSi$ requires *M*, 847.5151); ν_{max}/cm^{-1} 2959, 2864, 1612, 1514, 1463, 1455, 1379, 1367, 1260, 1171, 1099, 970, 882, 870 and 803; δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, 8-CH_3), 0.95-1.05 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.15 (3 H, s, 8-CH_3'), 1.22 (1 H, m, 6-H_{ax}), 1.29 (3 H, s, CCH_3), 1.32 (1 H, m, 2-H_{ax}), 1.35 (3 H, s, CCH_3'), 1.43-1.56 (3 H, m, 4-H_2, 2-H_{eq}), 1.67-1.79 (3 H, m, 14-H_{ax}, 10-H, 6-H_{eq}), 1.93 (1 H, t, *J* 12.4, 12-H_{ax}), 1.99 (1 H, dd, *J* 15.4, 4.2, 10-H'), 2.35 (2 H, m, 12-H_{eq}, 14-H_{eq}), 3.09 (3 H, s, 9-OCH_3), 3.34-3.45 (3 H, m, 15-H, 16-H_2), 3.48 (1 H, m, 11-H), 3.62 (1 H, dd, *J* 11.4, 4.3, 7-H), 3.69 (1 H, m, 5-H), 3.73 (3 H, s, ArOCH_3), 3.75 (1 H, m, 1-H_{ax}), 3.92 (1 H, td, *J* 11.7, 2.4, 1-H_{eq}), 4.13 (1 H, t, *J* 9.9, 3-H), 4.20 (2 H, m, 2'-H_2), 4.37 (1 H, d, *J* 11.7, PhHC*H*), 4.45 (2 H, s, ArCH_2), 4.52 (1 H, d, *J* 11.7, PhHC*H*), 5.27 (1 H, t, *J* 6.4, 1'-H), 6.80 (2 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH), and 7.26 (3 H, d, *J* 4.5, ArH); *m/z* (ES^+) 847 (M^+ + 23, 100%). Further elution (1:10 to 1:5 EtOAc:light petroleum) afforded the *title compound* **43** as a pale oil (2 mg, 41%), R_f 0.27 (30% EtOAc/light petroleum) (Found: M^+ + Na, 807.4838. $C_{45}H_{72}O_9NaSi$ requires M, 807.4838); ν_{max}/cm^{-1} 3436, 2959, 2864, 1612, 1586, 1514, 1463, 1455, 1379, 1367, 1260, 1171, 1099, 882, 870 and 803; δ_H (400 MHz, $CDCl_3$) 0.91-1.08 [27 H, m, 2 × 8-CH_3, 3 × $SiCH(CH_3)_2$], 1.43-1.59 (2 H, m, 6-H_{ax}, 2-H), 1.59-1.72 (5 H, m, 2-H', 4-H_2, 6-H_{eq}, 10-H), 1.77 (1 H, dd, *J* 13.5, 12.5, 14-H_{ax}), 1.95 (1 H, t, *J* 12.2, 12-H_{ax}), 2.05 (1 H, dd, *J* 15.7, 7.0, 10-H'), 2.14 (1 H, d, *J* 13.6, 12-H_{eq}), 2.37 (1 H, d, *J* 13.9, 14-H_{eq}), 2.82 (1 H, t, *J* 4.8, 1-OH), 3.13 (3 H, s, 9-OCH_3), 3.37 (1 H, m, 15-H), 3.41 (1 H, dd, *J* 9.8, 4.1, 16-H), 3.46 (1 H, dd, *J* 10.1, 4.8, 16-H'), 3.50 (1 H, br. s, 3-OH), 3.59 (1 H, m, 11-H), 3.67 (1 H, dd, *J* 11.5, 4.8, 7-H), 3.7-3.77 (2 H, m, 1-H_2), 3.73 (3 H, s, ArOCH_3), 3.82 (1 H, m, 5-H), 4.16 (1 H, m, 3-H), 4.19 (2 H, d, *J* 6.1, 2'-H_2), 4.40 (1 H, d, *J* 11.8, PhHC*H*), 4.44 (2 H, s, ArCH_2), 4.54 (1 H, d, *J* 11.8, PhHC*H*), 5.32 (1 H, t, *J* 6.1, 1'-H), 6.80 (2 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH), and 7.27 (3 H, d, *J* 4.3, ArH); *m/z* (ES^+) 807 (M^+ + 23, 100%).

(3*RS*,7*S*,9*R*,10*R*)-1-(2-Benzothiazolylsulfonyl)-10-*tert*-butyldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecan-3-ol (57).

Chromium(II) chloride (95 mg, 0.77 mmol) was heated to 180 °C under reduced pressure in a round bottomed flask for 45 min. The flask was purged with N_2 and allowed to cool to rt Tetrahydrofuran (90 µL) was added followed by the bromide **56** (42 mg, 0.069 mmol) and the aldehyde **52**[18] (74 mg, 0.26 mmol) in THF (0.16 mL). The resulting dark red mixture was stirred at rt for 15 h, diluted with ether (5 mL) and filtered through a short pad of silica, washing the silica thoroughly with ether (10 mL). Water and saturated aqueous sodium bisulfite (1:1) were added and aqueous phase was extracted with ether (2 × 5 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 5:1 light petroleum:ether) gave recovered bromide **56** (4 mg, 10%) followed by the *title compound* **57** (34 mg, 63%) as a colourless, viscous oil, a 1:1 mixture of epimers (^1H and ^{13}C NMR), R_f = 0.48 and 0.52 (1:1 light petroleum:ether), $[\alpha]_D^{31}$ −4.5 (*c* 14.2, $CHCl_3$) (Found: M^+ + NH_4, 833.4469. $C_{39}H_{77}O_7N_2S_2Si_3$ requires M, 833.4475); ν_{max}/cm^{-1} 3564, 2954, 2927, 2873, 1645, 1557, 1471, 1377, 1330, 1250, 1149, 1103, 1056, 1032, 833 and 760; δ_H (400 MHz, $CDCl_3$) 0.00(2) [each 4.5 H, s, $Si(CH_3)_3$], 0.04 (1.5 H, s, $SiCH_3$), 0.05 (4.5 H, s, 2 × $SiCH_3$), 0.59 and 0.60 (each 3 H, q, *J* 7.9, 3 × $SiCH_2$), 0.81-0.98 (2 H, m, $SiCH_2$), 0.87(2) [each 4.5 H, s, $SiC(CH_3)_3$], 0.94 and 0.95 (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.05 and 1.06 (each 1.5 H, d, *J* 6.3, 11-H_3), 1.19(2), 1.35 and 1.36 (each 1.5 H, s, 2-CH_3), 1.50-1.70 (2 H, m, 8-H_2), 1.95 (0.5 H, dd, *J* 13.7, 11.0, 4-H), 2.00 (0.5 H, dd, *J* 13.7, 10.9, 4-H), 2.19-2.39 (3 H, m, 4-H', 6-H_2), 2.41 and 2.55 (each 0.5 H, d, *J* 3.0, OH), 3.43-3.63 (3 H, m, OHC*H*CH_2Si, 1-H, 9-H), 3.63-3.75 (2 H, m, OHC*H*CH_2Si, 3-H), 3.80 and 3.81 (each 0.5 H, d, *J* 14.2, 1-H'), 3.93-4.06 (2 H, m, 7-H, 10-H), 4.67-4.75 (2 H, m, OCH_2O), 4.92 (0.5 H, s, 5-CH), 4.94-4.99 (1.5 H, m, 5-CH', 5-CH_2), 7.58, 7.63, 8.01 and 8.21 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3 −3.2, 0.0, 6.7, 6.8, 8.5(2), 18.7, 19.5, 19.6(2), 23.8, 25.6, 27.3, 37.2, 37.3, 39.8, 40.2, 41.3, 41.4, 45.8, 45.9, 63.2, 66.7, 66.8, 70.0, 70.7, 76.0, 76.2, 81.4, 81.5, 97.2, 97.3, 117.6, 123.8, 126.9, 129.0, 129.4, 138.2, 145.0, 145.2, 154.1 and 169.3; *m/z* (ES^+) 838.6 (M^+ + 23, 100%) and 834.0 (M^+ + 18, 4). Unreacted aldehyde **52** (16 mg, 22%) was also recovered.

(7*S*,9*R*,10*R*)-1-(2-Benzothiazolylsulfonyl)-10-*tert*-butyldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecan-3-one (58).

Sodium hydrogen carbonate (21 mg, 0.25 mmol) and Dess Martin periodinane (30 mg, 0.070 mmol) were added to the alcohol **57** (13 mg, 0.015 mmol) in DCM (1 mL) and the suspension stirred at rt for 1 h. Ether (10 mL) was added and the solution washed with saturated aqueous sodium bisulfite (2 × 10 mL), saturated aqueous sodium hydrogen carbonate (2 × 10 mL), water (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to yield the *title compound* **58** as a pale yellow,

viscous oil (13 mg, *ca*. 100%), R_f = 0.50 (1:1 light petroleum:ether), $[\alpha]_D^{30}$ −8.8 (*c* 5.0, $CHCl_3$) (Found: M^+ + Na, 836.3863. $C_{39}H_{71}O_7NNaS_2Si_3$ requires M, 836.3872); ν_{max}/cm^{-1} 2955, 2932, 2876, 1713, 1471, 1375, 1332, 1250, 1151, 1101, 1054 and 835; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04(2) (each 3 H, s, $SiCH_3$), 0.58 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.82-0.99 (2 H, m, $SiCH_2$), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.05 (3 H, d, *J* 6.3, 11-H_3), 1.46 and 1.47 (each 3 H, s, 2-CH_3), 1.50-1.64 (2 H, m, 8-H_2), 2.21 (1 H, dd, *J* 14.2, 7.5, 6-H), 2.35 (1 H, dd, *J* 14.2, 5.1, 6-H'), 3.37 (2 H, s, 4-H_2), 3.47 (1 H, ddd, *J* 11.1, 9.6, 6.0, OHC*H*CH_2Si), 3.54 (1 H, ddd, *J* 9.3, 4.3, 2.6, 9-H), 3.68 (1 H, ddd, *J* 11.3, 9.6, 5.6, OHC*H*CH_2Si), 3.92-4.05 (2 H, m, 7-H, 10-H), 3.93 and 3.94 (each 1 H, d, *J* 14.4, 1-H), 4.70 and 4.71 (each 1 H, d, *J* 7.1, OHC*H*O), 4.87 and 5.00 (each 1 H, s, 5-CH), 7.58 and 7.62 (each 1 H, m, ArH) and 8.00 and 8.20 (each 1 H, d, *J* 8.0, ArH); δ_C (100 MHz, $CDCl_3$) −3.3(2), 0.0, 6.7, 8.5, 18.8, 19.5, 19.6, 26.2, 26.4, 27.3, 37.4, 45.9, 46.2, 48.7, 63.8, 66.7, 70.0, 70.7, 81.5, 97.4, 118.6, 123.8, 126.9, 129.0, 129.4, 138.2, 141.2, 153.9, 168.9 and 210.8; *m/z* (ES^+) 836.3 (M^+ + 23, 100%) and 832.2 (M^+ +18, 50).

2-[(3*RS*,7*S*,9*R*,10*R*)-3,10-Bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecanyl-1-sulfonyl]benzothiazole (59).

2,6-Lutidine (45 µL, 0.386 mmol) was added to the alcohol **57** (98 mg, 0.120 mmol) in DCM (1 mL) and the solution cooled to 0 °C. *tert*-Butyldimethylsilyl triflate (44 µL, 0.192 mmol) was added and the solution stirred for 2 h at rt. Additional 2,6-lutidine (45 µL, 0.386 mmol) and *tert*-butyldimethylsilyl triflate (44 µL, 0.192 mmol) were added and the mixture stirred for a further 30 min. The mixture was partitioned between DCM (10 mL) and water (10 mL) and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (20:1 light petroleum:ether) gave the *title compound* **59** as a clear, colourless oil (93 mg, 86%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.68 (2:1 light petroleum:ether), $[\alpha]_D^{31}$ −3.1 (*c* 15.6, $CHCl_3$) (Found: M^+ + NH_4, 947.5349. $C_{45}H_{91}O_7N_2S_2Si_4$ requires M, 947.5339); ν_{max}/cm^{-1} 2954, 2927, 2876, 2857, 1645, 1471, 1377, 1331, 1250, 1150, 1102, 1072, 938, 835 and 775; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.01-0.06 (12 H, overlapping s, 4 × $SiCH_3$), 0.58 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.81-0.98 (2 H, m, $SiCH_2$), 0.86(3) and 0.87 [each 4.5 H, s, $SiC(CH_3)_3$], 0.93 and 0.94 (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.03 and 1.04 (each 1.5 H, d, *J* 6.3, 11'-H_3), 1.22, 1.23, 1.24 and 1.26 (each 1.5 H, s, 2'-CH_3), 1.45-1.61 (2 H, m, 8'-H_2), 1.97 (0.5 H, dd, *J* 12.5, 7.3, 4'-H), 2.00 (0.5 H, dd, *J* 11.8, 6.6, 4'-H), 2.11 (0.5 H, dd, *J* 8.2, 2.8, 6'-H), 2.15 (0.5 H, dd, *J* 8.4, 3.0, 6'-H), 2.26-2.42 (2 H, m, 4'-H', 6'-H'), 3.46 (1 H, m, OHC*H*CH_2Si), 3.52-3.73 (3.5 H, m, OHC*H*CH_2Si, 1'-H, 3'-H, 9'-H), 3.77 and 3.78 (each 0.5 H, d *J* 14.4, 1'-H or 1'-H'), 3.78 (0.5 H, d, *J* 14.4, 1'-H'), 3.95 (1 H, m, 7'-H), 4.04 (1 H, m, 10'-H), 4.65-4.70 (1.5 H, m, OCH_2O), 4.71 (0.5 H, d, *J* 7.0, OHC*H*O), 4.85-4.90 (1.5 H, m, 5'-CH_2, 5'-CH), 4.91 (0.5 H, s, 5'-CH') and 7.56, 7.62, 8.00 and 8.19 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3 −3.2, −2.9, −2.7, −1.8, −1.7, 0.0, 6.8, 6.9, 8.5, 18.6, 18.7, 19.5(2), 19.6, 19.7, 19.8, 24.4, 24.5, 26.1, 26.3, 27.3, 27.6(2), 37.0, 37.3, 41.8, 42.1, 42.2, 46.8, 47.3, 62.2, 62.3, 66.7, 69.7, 70.0, 70.6(2), 79.3, 79.5, 81.4, 97.4, 97.5, 116.4, 117.0, 123.8, 126.9, 128.9, 129.3, 138.1, 144.3, 144.6, 154.1 and 169.5(2); *m/z* (ES^+) 990.3 (22%), 952.7 (M^+ + 23, 100) and 948.2 (M^+ + 18, 19).

(2*R*,3*R*,5*S*,9*RS*)-11-(2-Benzothiazolylsulfonyl)-2,9-bis-*tert*-butyldimethylsilyloxy-10,10-dimethyl-7-methylene-3-(2-trimethylsilylethoxymethoxy)undecan-5-ol (60).

An aliquot (20 µL, 0.0056 mmol) of a solution of PPTS (0.28 g, 1.11 mmol) in methanol (4 mL) was added to the triethylsilyl ether **59** (74 mg, 0.082 mmol) in THF-methanol (2:3, 0.52 mL). The mixture was stirred at rt for 24 h then partitioned between ether (5 mL) and saturated aqueous sodium hydrogen carbonate (5 mL). The aqueous layer was extracted with ether (2 × 5 mL) and the organic extracts were washed with brine (5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (10:1 to 2:1 light petroleum:ether) gave recovered silyl ether **59** (8 mg, 11%) followed by the *title compound* **60** as a clear, colourless oil (49 mg, 73%), R_f = 0.39 (2:1 light petroleum:ether), $[\alpha]_D^{30}$ +14.5 (*c* 6.6, $CHCl_3$) (Found: M^+ + Na, 838.4040. $C_{39}H_{73}O_7NNaS_2Si_3$ requires M, 838.4028); ν_{max}/cm^{-1} 3463, 3068, 2953, 2928, 2893, 2856, 1645, 1472, 1388, 1329, 1250, 1150, 1085, 1057, 1023, 938, 835 and 775; δ_H (400 MHz, $CDCl_3$) 0.00-0.04 [15 H, m, $Si(CH_3)_3$, 2 × $SiCH_3$), 0.06 and 0.07(3) (each 1.5 H, s, $SiCH_3$), 0.82-0.99 (2 H, m, $SiCH_2$), 0.86(2) and 0.88(2) [each 4.5 H, s, $SiC(CH_3)_3$], 1.10 (3 H, d, *J* 6.3, 1-H_3), 1.23, 1.24 and 1.25(2) (each 1.5 H, s, 10-CH_3), 1.50-1.62 (2 H, m, 4-H_2), 1.99-2.34 (3 H, m, 6-H_2, 8-H), 2.45 (0.5 H, dd, *J* 10.6, 3.8, 8-H'), 2.49 (0.5 H, dd, *J* 10.1, 3.5, 8-H'), 3.51-3.70 (5 H, m, 3-H, OH, OCH_2CH_2Si, 11-H), 3.74 (1 H, m, 9-H), 3.77(2) (each 0.5 H, d, *J* 14.5, 11-H'), 3.82-3.95 (2 H, m, 2-H, 5-H), 4.70(2) (each 0.5 H, d, *J* 6.7, OHC*H*O), 4.75 (1 H, d, *J* 6.7, OHC*H*O), 4.89-4.93 (1.5 H, m, 7-CH, 7-CH_2), 4.94 (0.5 H, s, 7-CH') and 7.58, 7.63, 8.01 and 8.20 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3(2), −2.8, −2.7, −1.7(2), 0.0, 19.5, 19.6, 19.7, 20.0, 20.1, 24.6, 24.7, 26.1, 27.3(2), 27.6, 39.1(2), 41.7, 41.8, 42.3(2), 45.7(2), 62.3, 62.4, 67.2(2), 67.3, 67.6, 68.0, 72.3(2), 79.2(2), 81.5, 97.5, 97.6, 116.4, 116.5, 123.8, 126.9, 129.0, 129.3, 138.2, 145.1, 145.3, 154.1 and 169.5; *m/z* (ES^+) 838.3 (M^+ + 23, 100%), 833.7 (M^+ + 18, 43), 748.6 (22), 533.5 (39) and 435.6 (50).

(2*R*,3*R*,5*S*,9*RS*)-11-(2-Benzothiazolylsulfonyl)-2,9-bis-*tert*-butyldimethylsilyloxy-10,10-dimethyl-7-methylene-3-(2-trimethylsilylethoxymethoxy)undecan-5-yl acrylate (61).

Di-isopropylethylamine (0.11 ml, 0.63 mmol) was added to the alcohol **60** (49 mg, 0.06 mmol) in DCM (1.1 mL) and the solution cooled to 0 °C. Acryloyl chloride (25 µL, 0.31 mmol) was added dropwise, and the mixture stirred at rt for 1 h then partitioned between DCM (5 mL) and brine (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL) and the organic extracts were washed with saturated aqueous sodium hydrogen carbonate (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of

the residue (10:1 to 2:1 light petroleum:ether) gave the *title compound* **61** as a clear, colourless gum (52 mg, 100%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.50 (2:1 light petroleum:ether), $[\alpha]_D^{31}$ −13 (*c* 9.7, $CHCl_3$) (Found: M^+ + Na, 892.4126. $C_{42}H_{75}O_8NNaS_2Si_3$ requires M, 892.4134); ν_{max}/cm^{-1} 2951, 2925, 2853, 1716, 1636, 1470, 1328, 1248, 1197, 1171, 1148, 1101, 1055, 1024 and 835; δ_H (400 MHz, $CDCl_3$) −0.03 to 0.05 [21 H, m, $Si(CH_3)_3$, 4 × CH_3], 0.78-0.97 (2 H, m, $SiCH_2$), 0.86(2) and 0.87(2) [each 4.5 H, s, $SiC(CH_3)_3$], 1.06 (3 H, d, *J* 6.3, 1'-H_3), 1.23, 1.24, 1.26 and 1.27 (each 1.5 H, s, 10'-CH_3), 1.56 and 1.59 (each 0.5 H, ddd, *J* 14.8, 4.4, 2.0, 4'-H), 1.84 (0.5 H, ddd, *J* 14.8, 10.8, 1.2, 4'-H'), 1.89 (0.5 H, ddd, *J* 14.6, 10.5, 1.3, 4'-H'), 2.00 (0.5 H, dd, *J* 15.1, 7.3, 8'-H), 2.05 (0.5 H, dd, *J* 15.1, 7.0, 8'-H), 2.21 (0.5 H, dd, *J* 13.1, 7.2, 6'-H), 2.27 (0.5 H, dd, *J* 14.1, 5.4, 6'-H), 2.37 (0.5 H, dd, *J* 14.1, 7.8, 6'-H'), 2.41-2.51 (1.5 H, m, 6'-H', 8'-H'), 3.36 (1 H, m, 3'-H), 3.45 (1 H, m, OHC*H*CH_2Si), 3.57-3.70 (2.5 H, m, OHC*H*CH_2Si, 11'-H, 9'-H), 3.71-3.82 (1.5 H, m, 11'-H', 9'-H), 4.03 (1 H, m, 2'-H), 4.55, 4.59 and 4.67(2) (each 0.5 H, d, *J* 7.1, OHC*H*O), 4.88 (0.5 H, s, 7'-CH), 4.90 (1.5 H, s, 7'-CH, 7'-CH'), 5.16 and 5.25 (each 0.5 H, m, 5'-H), 5.77 and 5.78 (each 0.5 H, dd, *J* 10.4, 1.5, 3-H), 6.04(2) (each 0.5 H, dd, *J* 17.3, 10.4, 2-H), 6.33 and 6.34 (each 0.5 H, d, *J* 17.3, 1.5, 3-H') and 7.57, 7.63, 8.01 and 8.20 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.4, −3.2, −2.7, −1.7(2), 0.0, 18.3, 19.5, 19.7, 19.8, 24.6(2), 26.1, 26.2, 27.3, 27.6(2), 34.0, 34.6, 40.9, 41.3, 42.3(2), 43.6(2), 62.3, 66.6, 66.7, 70.0, 70.8, 70.9, 79.2, 79.3, 80.1, 80.4, 97.6, 97.7, 117.7, 118.0, 123.8, 126.9, 128.9, 129.3, 130.1, 132.0(2), 138.2(2), 143.3, 143.4, 154.1, 167.1 and 169.5(2); *m/z* (ES^+) 892.6 (M^+ + 23, 100%).

(6*S*)-4-[(2*RS*)-4-(2-Benzothiazolylsulfonyl)-2-*tert*-butyldimethylsilyloxy-3,3-dimethylbutyl]-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-5,6-dihydropyran-2-one (62).

An aliquot (60 µL, 0.0028 mmol, 6 mol%) of a solution of Grubbs II catalyst (8 mg, 0.0094 mmol) in DCE (0.20 mL) was added to the acrylate **61** (42 mg, 0.048 mmol) in DCE (0.36 mL) and the solution degassed (freeze-thaw × 3) then heated under reflux. Four further aliquots of the Grubbs II solution (30 µL, 0.0014 mmol, 3 mol%) were added every 2 h, and the reaction mixture was then stirred under reflux for 16 h. After cooling to rt, the mixture was concentrated under reduced pressure and chromatography of the residue (20:1 to 2:1 light petroleum:ether) gave unreacted acrylate **61** (16 mg, 39%) followed by the *title compound* **62** as a clear, pale brown gum (20 mg, 52%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.33 (2:1 light petroleum:ether), $[\alpha]_D^{28}$ −27.2 (*c* 6.9, $CHCl_3$) (Found: M^+ + NH_4, 859.4267. $C_{40}H_{75}O_8N_2S_2Si_3$ requires M, 859.4267); ν_{max}/cm^{-1} 2953, 2924, 2853, 1718, 1472, 1387, 1328, 1250, 1148, 1103, 1056, 1027, 937, 857 and 836; δ_H (400 MHz, $CDCl_3$) 0.00(2) [each 4.5 H, s, $Si(CH_3)_3$], 0.01 and 0.04 (each 1.5 H, s, $SiCH_3$), 0.07 (6 H, s, 2 × $SiCH_3$), 0.09 and 0.11 (each 1.5 H, s, $SiCH_3$), 0.82-0.98 (2 H, m, $SiCH_2$), 0.88(2) and 0.89(2) [each 4.5 H, s, $SiC(CH_3)_3$], 1.10(2) (each 1.5 H, d, *J* 6.3, 4''-H_3), 1.21-1.27 (6 H, overlapping s, 2 × 3'-CH_3), 1.64 and 2.07 (each 1 H, m, 1''-H), 2.26-2.48 (3 H, 1'-H, 5-H_2), 2.65 (1 H, m, 1'-H'), 3.51 (1 H, m, OHC*H*CH_2Si), 3.59-3.68 (2 H, m, OHC*H*CH_2Si, 4'-H), 3.70 and 3.71 (each 0.5 H, d, *J* 14.6, 4'-H'), 3.78 (1 H, m, 2''-H), 3.96 (0.5 H, dd, *J* 6.3, 4.1, 2'-H), 3.99-4.09 (1.5 H, m, 2'-H, 3''-H), 4.60 (1 H, m, 6-H), 4.70 and 4.71 (each 0.5 H, d, *J* 7.0, OHC*H*O), 4.72 (1 H, s, OCH_2O), 5.88 (1 H, s, 3-H) and 7.59, 7.66, 8.03 and 8.21 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3, −2.8(2), −1.9, 0.0, 18.7, 18.8, 19.5(2), 19.6, 19.7, 24.7, 25.0, 25.7(2), 27.3, 27.4(2), 31.1, 35.7, 35.9, 36.0, 37.0, 42.5, 42.6, 42.9, 62.2, 66.9, 67.3, 70.3, 70.4, 75.4, 75.6, 77.0(2), 79.2, 97.4(2), 119.5, 120.2, 123.8, 126.9, 129.0, 129.1, 129.5, 129.9, 138.1, 154.0, 158.8, 159.0, 165.9, 166.0, 169.0 and 169.1; *m/z* (ES^+) 864.5 (M^+ + 23, 100%) and 859.3 (M^+ + 18, 2).

(2*E*)-(5*S*,7*R*,8*R*)-3-[(2*RS*)-4-(2-Benzothiazolylsulfonyl)-2-*tert*-butyldimethylsilyloxy-3,3-dimethylbutyl]-8-*tert*-butyl-dimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene-1,5-diol (63).

Cerium(III) chloride heptahydrate (44 mg, 0.12 mmol) was added to the lactone **62** (20 mg, 0.0233 mmol) in methanol (0.29 mL) and THF (0.09 mL) at 0 °C. After the solid had dissolved, sodium borohydride (4 mg, 0.11 mmol) was added and the solution was stirred at rt for 2 h. Five further portions of cerium trichloride and sodium borohydride were then added every 2 h. Dichloromethane was added the mixture added to silica gel with chromatography (20:1 to 1:2 light petroleum:ether) giving the *title compound* **63** as a colourless gum (16 mg, 83%), a 1:1 mixture of epimers (^{1}H and ^{13}C NMR), R_f = 0.42 and 0.45 (1:2 light petroleum:ether), $[\alpha]_D^{25}$ −1.6 (*c* 8.8, $CHCl_3$) (Found: M^+ + Na, 868.4113. $C_{40}H_{75}O_8NNaS_2Si_3$ requires M, 868.4134); ν_{max}/cm^{-1} 3420, 2951, 2928, 2857, 1472, 1328, 1250, 1149, 1084, 1058, 1024, 937, 856, 835 and 775; δ_H (400 MHz, $CDCl_3$) −0.09 and −0.03 (each 1.5 H, s, $SiCH_3$), 0.00(2) [each 4.5 H, s, $Si(CH_3)_3$], 0.01 and 0.04 (each 1.5 H, s, $SiCH_3$), 0.07 (3 H, s, $SiCH_3$), 0.07 and 0.08 (each 1.5 H, s, $SiCH_3$), 0.83-0.94 (2 H, m, $SiCH_2$), 0.86 and 0.87 [each 4.5 H, s, $SiC(CH_3)_3$], 0.88 [9 H, s, $SiC(CH_3)_3$], 1.11(2) (each 1.5 H, d, *J* 6.3, 9-H_3), 1.23, 1.24(2), 1.27 (each 1.5 H, s, 3'-CH_3), 1.50-1.73 (2 H, m, 6-H_2), 1.95-2.10 (2 H, m, 1'-H, 4-H), 2.40-2.58 (2 H, m, 1'-H', 4-H'), 2.79 (2 H, br. s, 2 × OH), 3.46-3.91 (9 H, m, 1-H, 5-H, 7-H, 8-H, 2'-H, O*C*$H_2$$CH_2$Si, 4'-$H_2$), 4.15 (1 H, m, 1-H'), 4.70(2) (each 0.5 H, d, *J* 6.5, OHC*H*O), 4.75 (1 H, d, *J* 6.5, OHC*H*O), 5.82 (1 H, m, 2-H), 7.58, 7.64, 8.02 and 8.21 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3(2), −2.7, −2.3, −1.9, −1.6, 0.0, 16.7, 19.5, 19.7, 19.8, 20.2, 20.3, 23.8, 25.1, 25.5, 25.9, 26.2, 27.3, 27.6(2), 38.5, 40.0, 40.1, 40.7, 41.8, 42.3(2), 58.8, 59.0, 62.5, 62.6, 66.1, 66.4, 67.3, 72.6, 72.7, 80.1, 81.7, 81.9, 97.6, 97.7, 123.8, 126.9, 129.0, 129.4, 129.9, 130.4, 132.0, 138.1, 139.4, 141.1, 154.1(2), 169.4 and 169.5; *m/z* (ES^+) 869.0 (M^+ + 23, 100%) and 846.0 (M^+ + 1, 5).

(*E*)-(5*S*,7*R*,8*R*)-3-[(2*RS*)-4-(Benzothiazol-2-yl)sulfonyl-3,3-dimethyl-2-triethylsilyloxybutyl]-1,5,8-tris-*tert*-butyldimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (91).

tert-Butyldimethylsilyl trifluoromethanesulfonate (81 µL, 0.354 mmol) was added to the diol **69** (100 mg, 0.118 mmol) and 2,6-lutidine (137 µL, 1.18 mmol) in DCM (945 µL) at −78

°C and the solution stirred at −78 °C for 2 h. Ether (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) were added and the aqueous phase was extracted with ether (3 × 20 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:10 ether:light petroleum) afforded the *title compound* **91** as a colourless oil (120 mg, 96%), R_f 0.48 (1:10 ether:light petroleum), $[\alpha]_D^{25}$ −9.9 (*c* 2.01, $CHCl_3$); ν_{max}/cm^{-1} 2929, 2956, 2882, 2857, 1472, 1463, 1331, 1251, 1151, 1101, 1058, 835, 775 and 729. δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02-0.06 (18 H, overlapping s, 6 × $SiCH_3$), 0.54 (2.8 H, q, *J* 7.8, 3 × $SiCH_2$), 0.56 (3.2 H, q, *J* 7.6, 3 × $SiCH_2$), 0.84-0.87 [27 H, overlapping s, 3 × $SiC(CH_3)_3$], 0.80-0.98 (2 H, m, $SiCH_2$), 0.98 (4.8 H, t, *J* 8.1, 3 × $SiCH_2CH_3$), 0.90 (4.2 H, t, *J* 8.1, 3 × $SiCH_2CH_3$), 1.01 (1.4 H, d, *J* 6.3, 9-H_3), 1.02 (1.6 H, d, *J* 6.3, 9-H_3), 1.22 and 1.26 (each 1.4 H, s, 3'-CH_3), 1.24 and 1.29 (each 1.6 H, s, 3'-CH_3), 1.41 and 1.54 (each 1 H, m, 6-H), 1.82 (0.53 H, dd, *J* 13.9, 9.3, 1'-H), 1.88 (0.47 H, dd, *J* 14.1, 8.6, 1'-H), 2.08 (0.47 H, dd, *J* 13.1, 8.1, 4-H), 2.14-2.36 (2.53 H, m, 1'-H', 4-H', 4-H_2), 3.42 (1 H, m, OHC*H*CH_2Si), 3.52 (1 H, m, 7-H), 3.53 (0.53 H, d, *J* 14.4, 4'-H), 3.56 (0.47 H, d, *J* 14.4, 4'-H), 3.60 (0.53, dd, *J* 9.3, 1.8, 2'-H), 3.64 (0.47, dd, *J* 8.6, 2.8, 2'-H), 3.70 (1 H, m, OHC*H*CH_2Si), 3.75 (0.53 H, d, *J* 14.4, 4'-H'), 3.75 (0.47 H, d, *J* 14.4, 4'-H'), 3.84 (1 H, m, 5-H), 4.05 (1 H, m, 8-H), 4.13-4.25 (2 H, m, 1-H_2), 4.63-4.71 (2 H, m, OCH_2O), 5.38 (0.53 H, t, *J* 6.1, 2-H), 5.40 (0.47 H, t, *J* 5.8, 2-H), 7.54-7.64 (2 H, m, ArH) and 8.00 and 8.19 (each 1 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.9, −3.4, −3.3(2), −2.9, −2.3, −2.2, 0.0, 6.8, 6.9, 8.6, 18.4, 18.5, 19.4(2), 19.5, 19.7, 24.6, 24.7, 26.2, 26.3, 27.3, 27.4, 36.4, 37.1, 40.8, 41.6, 41.8, 42.0(2), 42.6, 61.6, 61.7, 62.1, 62.2, 66.6, 69.8, 70.1, 70.2(2), 78.6, 80.3, 80.9, 81.5, 81.7, 97.6(2), 123.8, 126.9, 128.9, 129.3, 132.0, 132.7, 134.9, 135.0, 138.2, 154.1 and 169.5(2); *m/z* (ES^+) 1097 (M^+ + 23, 100%).

(6*RS*,10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*E*)-2-*tert*-butyldimethylsilyloxyethylidene]-6-triethylsilyloxy-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-ene (92).

Lithium hexamethyldisilazide (1.0 M in THF, 133 µL, 0.134 mmol) was added to the sulfone **91** (120 mg, 0.112 mmol) in THF (5.7 mL) at −78 °C and the yellow solution was stirred at −60 °C for 30 min then cooled to −78 °C. 2-Methylpropanal (42 µL, 0.465 mmol) in THF (1.14 mL) was added and the solution was stirred for 1 h at −78 °C and at rt for 20 min. Ether (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) were added and the aqueous phase was extracted with Et_2O (2 × 20 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:20 ether:light petroleum) afforded the *title compound* **92** as a colourless oil (54 mg, 52%), R_f 0.24 (1:20 ether:light petroleum), $[\alpha]_D^{25}$ −14.8 (*c* 2.69, $CHCl_3$); ν_{max}/cm^{-1} 2956, 2928, 2883, 2858, 1472, 1463, 1382, 1361, 1258, 1099, 1058, 938, 835, 808, 774 and 737; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03-0.07 (18 H, overlapping s, 6 × $SiCH_3$), 0.54 (2.82 H, q, *J* 7.9, 3 × $SiCH_2$), 0.55 (3.18 H, q, *J* 7.6, 3 × $SiCH_2$), 0.80-0.98 [50 H, m, 1-H_3 or 2-CH_3, 2 × 5-CH_3, 14-H_3, 3 × $SiCH_2CH_3$, 3 × $SiC(CH_3)_3$, $SiCH_2$), 1.02 (3 H, d, *J* 6.3, 1-H_3 or 2-CH_3), 1.42 and 1.51 (each 1 H, m, 11-H), 1.83 (1 H, m, 7-H), 2.04 (0.47 H, dd, *J* 12.9, 8.5, 9-H), 2.15-2.30 (2.5 H, m, 2-H, 9-H', 9-H_2), 3.42 (1 H, m, OHC*H*CH_2Si), 3.47-3.57 (2 H, m, 6-H, 12-H), 3.70 (1 H, m, OHC*H*CH_2Si), 3.81 (1 H, m, 10-H), 4.05 (1 H, m, 13-H), 4.15-4.24 (2 H, m, 2'-H_2), 4.64-4.70 (2 H, m, OCH_2O), 5.25 (0.47 H, dd, *J* 15.6, 7.0, 3-H), 5.27 (0.53 H, dd, *J* 15.6, 6.8, 3-H), 5.36 (1 H, m, 1'-H), 5.38 (0.53 H, d, *J* 15.8, 4-H) and 5.39 (0.47 H, d, *J* 15.8, 4-H); δ_C (100 MHz, $CDCl_3$) −3.9, −3.4, −3.3(2), −3.0, −2.9, −2.3, −2.2, 0.0, 2.5, 6.9, 7.0, 8.7, 18.5, 18.6, 19.5(2), 19.8, 24.2, 24.3, 24.4, 24.5, 26.5, 26.7, 27.3(2), 27.4(2), 32.7, 32.8, 36.5, 37.0, 41.3, 42.5, 42.6, 42.7, 42.9, 61.8, 61.9, 66.5, 69.8, 70.1, 70.3, 70.4, 78.6, 79.8, 80.8, 81.7(2), 97.6, 97.7, 131.0, 131.6, 135.8(2), 135.9 and 136.2(2); *m/z* (ES^+) 954 (M^+ + 23, 100%).

(6*RS*,10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*Z*)-2-hydroxyethylidene]-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-en-6-ol (93).

Pyridinium toluene 4-sulfonate (1.5 mg, 0.027 mmol) was added to the alkene **92** (54 mg) in DCM/methanol (1:1, 884 µL) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with EtOAc (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (1:5 to 1:1 ether:light petroleum) afforded the *title compound* **93** as a pale oil (20 mg, 50%), R_f 0.33 (3:2 ether:light petroleum), $[\alpha]_D^{25}$ −9.6 (*c* 2.03, $CHCl_3$) (Found: M^+ + Na, 725.5007. $C_{37}H_{78}O_6NaSi_3$ requires M, 725.4999); ν_{max}/cm^{-1} 3349, 2954, 2925, 2858, 1470, 1464, 1377, 1359, 1274, 1251, 1101, 1056, 1033, 835, 770 and 750; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 and 0.05 (each 6 H, s, 2 × $SiCH_3$), 0.87 [18 H, s, 2 × $SiC(CH_3)_3$], 0.85-1.05 [2 H, m, $SiCH_2$), 0.97 (6 H, d, *J* 6.3, 2 × $CHCH_3$), 1.00 (6 H, s, 2 × 5-CH_3), 1.03 and 1.04 (each 1.5 H, d, *J* 5.5, 14-H_3), 1.42-1.92 (4 H, m, 7-H, 11-H_2, OH), 2.15 (1 H, m, 9-H), 2.21-2.38 (3.45 H, m, 2-H, 7-H', 9-H', OH), 2.51 (0.55 H, m, 9-H'), 3.36 (1 H, m, 6-H), 3.42-3.57 (2 H, m, 12-H, OHC*H*CH_2Si), 3.68 (1 H, m, OHC*H*CH_2Si), 3.89 (1 H, m, 10-H), 4.01-4.09 (2 H, m, 2'-H, 13-H), 4.20 (1 H, m, 2'-H'), 4.65-4.71 (2 H, m, OCH_2O), 5.32-5.42 (2 H, m, 3-H, 4-H), 5.59 (0.45 H, t, *J* 6.9, 1'-H) and 5.63 (0.55 H, t, *J* 6.9, 1'-H); δ_C (100 MHz, $CDCl_3$) −3.3(2), −3.0, −2.9, −2.4(2), 0.0, 18.6, 19.5(2), 19.6, 24.3(2), 24.5, 24.7, 25.0, 25.1, 27.4(2), 32.8(2), 37.2, 37.3, 40.5, 40.7, 41.0, 41.6, 41.7, 60.3, 60.4, 66.8, 66.9, 70.3, 70.4(2), 70.8, 77.2, 77.7, 78.7, 81.6, 81.9, 97.2, 97.3, 130.2, 130.9, 135.0, 135.1, 137.7, 137.9, 140.1 and 140.2; *m/z* (ES^+) 726 (M^+ + 23, 100%) and 721 (M^+ + 18, 20).

Methyl (5*RS*,2*Z*,7*E*)-3-[(2S,4*R*,5*R*)-2,5-bis-*tert*-butyldimethylsilyloxy-4-(2-trimethylsilylethoxymethoxy)hexyl)]-5-hydroxy-6,6,9-trimethyldeca-2,7-dienoate (95).

Manganese(IV) dioxide (74 mg, 0.854 mmol) was added to the diol **93** (20 mg, 0.0284 mmol) in DCM (568 µL) and the mixture was stirred at rt for 4 h then filtered through Celite. The filter cake was washed with DCM (10 mL) and the filtrate

was concentrated under reduced pressure to give the corresponding aldehyde as a pale oil, R_f 0.56 (1:1 ether:light petroleum); δ_H (500 MHz, $CDCl_3$) 5.3 (1 H, d, *J* 16.0, 7-H), 5.42 (1 H, dd, *J* 16.0, 6.3, 8-H), 6.0 (1 H, d, *J* 6.5, 2-H), and 9.99 (1 H, d, *J* 6.5, 1-H).

Sodium chlorite (30 mg, 0.342 mmol) and $NaH_2PO_4.2H_2O$ (88 mg, 0.568 mmol) in H_2O (554 µL) were added to this aldehyde and 2-methyl-2-butene (2 M in THF, 568 µL, 1.14 mmol) in *t*-butanol (426 µL) and the mixture stirred at rt for 2 h. Brine (10 mL) and EtOAc (10 mL) were added and the aqueous phase extracted with EtOAc (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the acid **94** as a pale oil, R_f 0.81 (1:1 ether:light petroleum).

A solution of the acid **94** in methanol (966 µL) and toluene (484 µL) was cooled to 0 °C and (trimethylsilyl)diazomethane (2 M in hexanes, 42 µL, 0.0854 mmol) was added dropwise. After stirring for 1 h at 0 °C, acetic acid (2-3 drops) was added and the reaction mixture was partitioned between saturated aqueous $NaHCO_3$ (10 mL) and DCM (10 mL). The aqueous phase was extracted with DCM (2 × 10 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:20 ether:light petroleum) afforded the *title compound* **95** as a pale oil (16 mg, 77%), R_f 0.12 (1:10 ether:light petroleum), $[\alpha]_D^{25}$ −39.5 (*c* 1.60, $CHCl_3$) (Found: M^+ + Na, 753.4930. $C_{38}H_{78}O_7NaSi_3$ requires M, 753.4948); ν_{max}/cm^{-1} 3487, 2955, 2928, 2856, 1719, 1641, 1663, 1470, 1463, 1432, 1378, 1359, 1250, 1101, 1056, 832 and 775; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.01-0.07 (12 H, overlapping s, 4 × $SiCH_3$), 0.81-0.99 [2 H, m, $SiCH_2$), 0.88 [18 H, s, 2 × $SiC(CH_3)_3$], 0.97 (6 H, d, *J* 6.3, 10-H_3, 9-CH_3), 1.00 (6 H, s, 2 × 6-CH_3), 1.01-1.06 (3 H, m, 6'-H_3), 1.41 and 1.49 (each 0.5 H, m, 3'-H), 1.60-1.82 (2 H, m, OH, 3'-H'), 1.96 (0.55 H, dd, *J* 13.6, 10.6, 4-H), 2.06 (0.45 H, dd, *J* 13.9, 10.3, 4-H), 2.27 (1 H, m, 9-H), 2.33-2.43 (1 H, m, 1'-H and 4-H'), 2.50 (0.55 H, d, *J* 13.6, 4-H'), 2.84 (0.45, dd, *J* 12.4, 7.3, 1'-H), 2.97 (0.45, dd, *J* 12.4, 7.3, 1'-H'), 3.30 (0.55 H, dd, *J* 12.4, 6.1, 1'-H'), 3.40 (1 H, m, 5-H), 3.44 (1 H, m, OHC*H*CH_2Si), 3.56 (1 H, m, 4'-H), 3.65 (3 H, s, CO_2CH_3), 3.69 (1 H, m, OHC*H*CH_2Si), 3.99-4.10 (2 H, m, 2'-H, 5'-H), 4.67-4.74 (1.54 H, m, OCH_2O, OHC*H*O), 4.78 (0.46 H, d, *J* 7.1, OHC*H*O), 5.33 (0.46 H, d, *J* 16.1, 7-H), 5.34 (0.54 H, d, *J* 15.9, 7-H), 5.34 (0.54 H, dd, *J* 15.9, 6.3, 8-H), 5.41 (0.46 H, dd, *J* 15.9, 6.3, 8-H) and 5.77 (1 H, s, 2-H). δ_C (100 MHz, $CDCl_3$) −3.3(2), −3.1, −3.0, −2.6, −2.3, 0.0, 18.5, 18.7, 19.4, 19.5(2), 19.6, 24.2, 24.3, 24.5, 24.8, 25.2, 27.4(3), 27.5, 32.8(2), 37.7, 38.0, 41.4, 41.8, 42.0, 42.5, 43.3, 43.8, 52.3, 66.6, 70.6, 71.0, 72.3, 77.4, 81.7, 82.0, 97.5, 97.7, 120.0, 120.3, 134.7(2), 138.4, 160.6, 161.4 and 167.7(2); *m/z* (ES^+) 753 (M^+ + 23, 100%) and 749 (M^+ + 18, 93).

Methyl (2*E*,7*E*)-3-[(2S,4*R*,5*R*)-2,5-bis-*tert*-butyldimethylsilyloxy-4-(2-trimethylsilylethoxymethoxy)hexyl]-6,6,9-trimethyl-5-oxodeca-2,7-dienoate (96).

A solution of the Dess-Martin periodinane (50 mg, 0.118 mmol) and pyridine (95 µL, 1.18 mmol) in DCM (5.21 mL) was stirred for 5 min. An aliquot (4.79 mL, 0.109 mmol) was added to the alcohol **95** (16 mg, 21.9 µmol) and the solution stirred for 2 h at rt. Dichloromethane (10 mL), saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:30 ether:light petroleum) afforded the *title compound* **96** as a pale oil (13 mg, 81%), R_f 0.27 (1:10 ether:light petroleum), $[\alpha]_D^{25}$ −53.1 (*c* 1.40, $CHCl_3$) (Found: M^+ + Na, 751.4801. $C_{38}H_{76}O_7NaSi_3$ requires M, 751.4792); ν_{max}/cm^{-1} 2956, 2930, 2858, 1721, 1645, 1464, 1378, 1251, 1142, 1101, 1049, 937, 835 and 775; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.01 (3 H, s, $SiCH_3$), 0.04 (9 H, s, 3 × $SiCH_3$), 0.85 (1 H, m, HC*H*Si), 0.86 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 0.94 (1 H, m, HC*H*Si), 0.98 (6 H, d, *J* 6.9, 10-H_3, 9-CH_3), 1.03 (3 H, d, *J* 6.3, 6'-H_3), 1.18 and 1.19 (each 3 H, s, 6-CH_3), 1.37 (1 H, ddd, *J* 14.8, 9.5, 5.4, 3'-H), 1.74 (1 H, ddd, *J* 14.2, 6.9, 1.0, 3'-H'), 2.29 (1 H, oct, *J* 6.6, 9-H), 2.56 (1 H, dd, *J* 12.6, 7.3, 1'-H), 3.05 (1 H, dd, *J* 12.6, 5.7, 1'-H'), 3.26 (1 H, d, *J* 16.4, 4-H), 3.45 (1 H, m, OHC*H*CH_2Si), 3.48 (1 H, d, *J* 16.0, 4-H'), 3.54 (1 H, ddd, *J* 9.5, 4.1, 1.3, 4'-H), 3.65 (3 H, s, CO_2CH_3), 3.69 (1 H, ddd, *J* 11.4, 9.8, 5.4, OHC*H*CH_2Si), 3.99-4.08 (2 H, m, 2'-H, 5'-H), 4.69 and 4.75 (each 1 H, d, *J* 6.9, OHC*H*O), 5.40 (1 H, d, *J* 15.8, 7-H), 5.51 (1 H, dd, *J* 15.8, 6.6, 8-H) and 5.62 (1 H, s, 2-H); δ_C (100 MHz, $CDCl_3$) −3.3, −3.0, −2.6, 0.0, 18.5, 19.4, 19.6, 23.9, 25.4, 25.5, 27.4, 27.5, 32.7, 38.1, 42.1, 49.5, 51.7, 52.3, 66.6, 70.6, 72.2, 81.9, 97.7, 121.6, 132.2, 139.7, 156.9, 167.4 and 211.0; *m/z* (ES^+) 751 (M^+ + 23, 100%) and 746 (M^+ + 18, 9).

(6*S*)-6-[(2*R*,3*R*)-3-Hydroxy-2-(2-trimethylsilylethoxymethoxy)butyl]-4-[(*EZ*)-methoxycarbonylmethylene]-2-[(*E*)-2,5-dimethylhex-3-en-2-yl]-5,6-dihydropyran (97).

Pyridine (64 µL, 0.796 mmol) was added to the ketoester **96** (13 mg, 0.0179 mmol) in THF (284 µL) and HF-pyridine (70:30, 23 µL, 0.893 mmol) was added at 0 °C. The mixture was stirred at rt for 72 h and saturated aqueous $NaHCO_3$ (10 mL) and EtOAc (10 mL) were added. The aqueous phase was extracted with EtOAc (2 × 10 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (pentane to 1:20 EtOAc:pentane with 1% Et_3N) afforded the lactone **98** as a colourless oil (0.5 mg, 6%), R_f 0.72 (1:5 ether:light petroleum); ν_{max}/cm^{-1} 3445, 2959, 2926, 1713, 1464, 1379, 1260, 1147, 1098, 1029, 978, 938, 861, 836 and 800; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.92 and 0.93 (each 3 H, d, *J* 6.3, 6'-CH_3 or 7'-H_3), 0.98 (2 H, m, $SiCH_2$), 1.05 and 1.06 (each 3 H, s, 3'-CH_3), 1.15 (3 H, d, *J* 6.3, 4"-H_3), 1.41 (1 H, m, 1"-H), 1.74 (1 H, ddd, *J* 14.2, 10.1, 2.2, 1''-H'), 1.85-1.94 (2 H, m, 5-H_2), 2.14 (1 H, oct, *J* 6.7, 6'-H), 2.80 and 2.86 (each 1 H, d, *J* 16.4, 1'-H), 3.39 (1 H, d, *J* 2.9, 3"-OH), 3.51 (1 H, dt, *J* 9.8, 6.9, OHC*H*CH_2Si), 3.68-3.75 (2 H, m, 3"-H, OHC*H*CH_2Si), 3.78 (1 H, m, 2"-H), 4.62 and 4.68 (each 1 H, d, *J* 6.9, OHC*H*O), 4.68 (1 H, m, 6-H), 5.25 (1 H, dd, *J* 15.8, 0.6, 4'-H), 5.37 (1 H, dd, *J* 15.8, 6.9, 5'-H and 5.79 (1 H, s, 3-H); *m/z* (ES^+) 491 (M^+ + 23, 100%) and 486 (M^+ + 18, 16). Further elution (1:20 to

1:10 EtOAc:pentane with 1% Et_3N) afforded the *title compound* **97** as a colourless oil (7 mg, 93%), (*E*):(*Z*) = 44:56 (^{1}H NMR), R_f 0.35 (1:5 ether:light petroleum), $[\alpha]_D^{25}$ +28.5 (*c* 0.70, $CHCl_3$) (Found: M^+ + Na, 505.2955. $C_{26}H_{46}O_6NaSi$ requires M, 505.2956); ν_{max}/cm^{-1} 3462, 2960, 2926, 1708, 1609, 1434, 1376, 1317, 1261, 1213, 1153, 1095, 1056, 1023, 861, 836 and 801; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, 3 × $Si(CH_3)_3$], 0.91-0.99 (2 H, m, CH_2Si), 0.95-1.00 (6 H, m, 5'-CH_3, 6'-H_3), 1.14 and 1.15 (each 1.5 H, d, *J* 6.3, 4''-H_3), 1.17 and 1.21 (each 3 H, s, 1'-H_3, 2'-CH_3), 1.56 (0.5 H, ddd, *J* 14.4, 10.6, 2.0, 1''-H), 1.62 (0.5 H, ddd, *J* 14.6, 10.3, 2.0, 1''-H), 1.81 and 1.85 (each 0.5 H, m, 1''-H'), 2.20-2.50 (2.5 H, 5-H, 5-H', 5'-H), 3.50 (0.5 H, m, 5-H'), 3.50-3.58 (2 H, m, 2''-H, OHC*H*CH_2Si), 3.64 (1 H, m, 3''-H), 3.65 and 3.68 (each 1.5 H, s, CO_2CH_3), 3.77 (1 H, m, OHC*H*CH_2Si), 3.68 (1 H, br. d, *J* 6.6, OH), 4.07 and 4.18 (each 0.5 H, m, 6-H), 4.68(2), 4.79 and 4.80 (each 0.5 H, d, *J* 7.0, OHC*H*O), 5.20 (0.5 H, s, 3-H), 5.35-5.47 (2 H, m, 3'-H, 4'-H), 5.36 and 5.43 (each 0.5 H, s, 4-CH) and 6.79 (0.5 H, s, 3-H); δ_C (100 MHz, $CDCl_3$) 0.0, 19.6, 20.3, 24.1, 27.2, 27.4(2), 31.2, 32.6, 33.0, 38.1, 38.4, 38.6, 42.5, 42.6, 52.2, 67.6, 67.7, 71.6, 74.3, 74.4, 85.6, 98.1, 98.4, 102.1, 109.2, 109.6, 134.5, 134.6, 136.7, 136.8, 149.8, 151.8, 169.3, 171.3 and 171.8; *m/z* (ES^+) 505 (M^+ + 23, 100%).

(10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*Z*)-(2-*tert*-butyldimethylsilyloxyethylidene)]-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-en-6-one (100).

Imidazole (4 mg, 0.0626 mmol) and tert-butyldimethylsilyl chloride (5 mg, 0.0312 mmol) were added to the diol **93** (20 mg, 0.0284 mmol) in DCM (284 µL) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and water (10 mL) were added and the aqueous phase extracted with DCM (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue through a short plug of silica (1:10 ether:pentane) gave the alcohol **99** as a pale oil (20 mg, 87%); δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02-0.07 (18 H, m, 6 × $SiCH_3$), 0.80-0.98 [29 H, m, CH_2Si, 3 × $SiC(CH_3)_3$], 0.96 (6 H, d, *J* 6.8, 1-H_3, 2-CH_3), 0.98-1.01 (6 H, overlapping s, 2 × 5-CH_3), 1.02 and 1.02 (each 1.5 H, d, *J* 6.1, 14-H_3), 1.43 and 1.54 (each 1 H, m, 11-H), 1.73 (0.5 H, d, *J* 2.8, 6-OH), 1.79 (0.5 H, dd, *J* 13.9, 10.9, 7-H), 1.85 (0.5 H, d, *J* 3.3, 6-OH), 1.87 (0.5 H, dd, *J* 13.9, 10.9, 7-H), 2.10-2.40 (4 H, m, 2-H, 7-H', 9-H_2), 3.34 (1 H, dd, *J* 10.6, 2.0, 6-H), 3.44 (1 H, m, OHC*H*CH_2Si), 3.52 (1 H, m, 12-H), 3.69 (1 H, m, OHC*H*CH_2Si), 3.85 (1 H, m, 10-H), 4.04 (1 H, m, 13-H), 4.19 (1 H, dd, *J* 12.9, 5.6, 8-CHC*H*), 4.24 (1 H, m, 8-CHC*H*), 4.65-4.71, m, OCH_2O), 5.32-5.41 (2 H, m, 3-H, 4-H) and 5.44 (1 H, t, *J* 6.1, 8-CH); *m/z* (ES^+) 816 (M^+, 100%).

The Dess-Martin periodinane (56 mg, 0.132 mmol) was added to the alcohol **99** (20 mg, 0.024 mmol) and $NaHCO_3$ (48 mg, 5.71 mmol) in DCM (4.8 mL) and the reaction mixture stirred for 2 h at rt. Dichloromethane (10 mL) and a mixture of saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL) were added and the aqueous phase extracted with DCM (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give a pale, yellow oil. Chromatography of the residue (light petroleum to 1:30 ether:light petroleum) afforded the *title compound* **100** as a pale oil (18 mg, 90%), R_f 0.17 (1:20 EtOAc:light petroleum); δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.11(2), 0.14, 0.18, 0.25 and 0.27 (each 3 H, s, $SiCH_3$), 0.92 (1 H, m, HC*H*Si), 0.94 (6 H, d, *J* 6.8, 1-H_3, 2-CH_3), 0.99, 1.00 and 1.04 [each 9 H, s, $SiC(CH_3)_3$], 1.16 and 1.17 (each 3 H, s, 5-CH_3), 1.23 (1 H, m, HC*H*Si), 1.28 (3 H, d, *J* 6.3, 14-H_3), 1.78 (1 H, ddd, *J* 13.6, 10.1, 3.0, 11-H), 1.92 (1 H, ddd, *J* 14.1, 8.8, 1.3, 11-H'), 2.18 (1 H, m, 2-H), 2.61 (1 H, dd, *J* 13.6, 8.1, 9-H), 2.73 (1 H, dd, *J* 13.6, 5.6, 9-H'), 3.23 and 3.28 (each 1 H, d, *J* 16.5, 7-H), 3.51 (1 H, dt, *J* 9.8, 6.3, OHC*H*CH_2Si), 3.78-3.91 (2 H, m, 12-H, OHC*H*CH_2Si), 4.24 (1 H, m, 10-H), 4.29-4.37 (2 H, m, 13-H, 8-CHC*H*), 4.40 (1 H, dd, *J* 12.9, 6.3, 8-CHC*H*), 4.81 and 4.89 (each 1 H, d, *J* 6.8, OHC*H*O), 5.39-5.47 (2 H, m, 3-H, 4-H) and 5.58 (1 H, t, *J* 6.1, 8-CH); δ_C (100 MHz, C_6D_6) −3.6, −3.2, −2.9, −2.2, 0.0, 2.7, 15.6, 18.8, 19.6, 19.7(2), 19.8, 23.9, 24.0, 25.7, 27.5(2), 27.6, 32.9, 37.5, 41.4, 47.2, 51.7, 61.8, 66.9, 70.5, 70.8, 82.1, 98.0, 129.5, 133.3, 134.1, 138.7 and 210.8; *m/z* (ES^+) 839 (M^+ + 23, 15%).

(10*S*,12*R*,13*R*,3*E*,7*E*)- and (10*S*,12*R*,13*R*,3*E*,7*Z*)-8-Ethenyl-10,13-dihydroxy-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)-tetradeca-3,7-dien-6-one (101) and (102).

Tetra-*n*-butylammonium fluoride (1 M in THF, 18 µL, 0.018 mmol) was added to the ketone **100** (5 mg, 0.0061 mmol) in THF (515 µL) and the mixture was stirred at rt for 16 h. Ethyl acetate (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase extracted with EtOAc (2 × 10 mL). The organic extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography (light petroleum to 1:10 EtOAc:light petroleum with 1% Et_3N) afforded the (7*E*)-isomer of the *title compound* **101** as a colourless oil (1 mg, 37%), R_f 0.43 (1:3 EtOAc:light petroleum) (Found: M^+ + Na, 477.3017. $C_{25}H_{46}O_5NaSi$ requires M, 477.3007); ν_{max}/ cm^{-1} 3444, 2956, 2920, 2855, 1716, 1608, 1463, 1379, 1260, 1096, 1055, 1029, 860, 836 and 802; δ_H (400 MHz, $CDCl_3$) 0.05 [9 H, s, $Si(CH_3)_3$], 0.86-0.97 (2 H, m, CH_2Si), 0.93 (6 H, d, *J* 6.8, 1-H_3, 2-CH_3), 1.04 and 1.06 (each 3 H, s, 5-CH_3), 1.09 (3 H, d, *J* 6.3, 14-H_3), 1.51 (1 H, m, 11-H), 1.56 (1 H, ddd, *J* 7.3, 4.0, 1.5, 11-H'), 2.06 (1 H, dt, *J* 16.7, 2.8, 9-H), 2.24 (1 H, m, 2-H), 2.33 (1 H, d, *J* 17.1, 9-H'), 3.44-3.62 (3 H, m, 12-H, 13-H, OHC*H*CH_2Si), 3.69 (1 H, m, OHC*H*CH_2Si), 4.44 (1 H, m, 10-H), 4.70 and 4.76 (each 1 H, d, *J* 6.8, OHC*H*O), 4.94 (1 H, d, *J* 10.6, 2'-H), 5.05 (1 H, d, *J* 17.4, 2'-H'), 5.44 (1 H, dd, *J* 16.1, 7.1, 3-H), 5.57 (1 H, s, 7-H), 5.57 (1 H, d, *J* 16.0, 0.8, 4-H) and 6.30 (1 H, dd, *J* 17.5, 10.7, 1'-H); *m/z* (ES^+) 477 (M^+ + 23, 100%). Further elution (1:10 to 1:5 EtOAc:light petroleum with 1% Et_3N) afforded the (7*Z*)-isomer of the *title compound* **102** as a colourless oil (1 mg, 37%), R_f 0.27 (1:3 EtOAc:light petroleum) (Found: M^+ + Na, 477.2986. $C_{25}H_{46}O_5NaSi$ requires M, 477.3007); ν_{max}/cm^{-1} 3400, 2960, 2916, 2848, 1681, 1571, 1462, 1378, 1260, 1096, 1055, 1021, 860, 835 and 799; δ_H (400 MHz, $CDCl_3$) 0.06 [9 H, s, $Si(CH_3)_3$], 0.72-0.94 (2 H, m, CH_2Si), 0.91 (6 H, d, *J* 6.6, 1-H_3, 2-CH_3), 1.08 (3 H, d, *J* 6.3, 14-H_3), 1.13 and 1.14 (each 3 H, s, 5-CH_3), 1.45-1.61 (2 H, m, 11-H_2), 2.22 (1 H, oct, *J* 6.6, 2-H),

2.33 (1 H, dd, *J* 13.6, 8.3, 9-H), 2.46 (1 H, dd, *J* 13.4, 4.3, 9-H'), 2.69 and 3.02 (each 1 H, br. s, OH), 3.49 (1 H, ddd, *J* 9.6, 6.6, 3.5, OHC*H*CH_2Si), 3.54-3.64 (3 H, m, 12-H, 13-H, OHC*H*CH_2Si), 3.87 (1 H, m, 10-H), 4.68 and 4.73 (each 1 H, d, *J* 6.9, OHC*H*O), 5.37 (1 H, d, *J* 15.7, 4-H), 5.37 (1 H, m, 2'-H), 5.44 (1 H, dd, *J* 15.7, 6.1, 3-H), 5.53 (1 H, d, *J* 17.7, 2'-H'), 6.23 (1 H, s, 7-H) and 7.49 (1 H, ddd, *J* 17.7, 11.1, 0.8, 1'-H); *m/z* (ES^+) 477 (M^+ + 23, 100%).