# Total synthesis of a 20-deoxybryostatin

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

## Supplementary data – Full experimental with compound characterisation

### General

Chromatography was performed using Merck silica gel (60H; 40-60μ, 230-240 mesh). Petrol refers to light petroleum which was redistilled before use and refers to the fraction boiling between 40 and 60 °C. Tetrahydrofuran was dried over sodium-benzophenone and was distilled prior to use. Dichloromethane was dried over $CaH_2$ and was distilled before use. Ether refers to diethyl ether. Reactions under non-aqueous conditions were carried out under an atmosphere of nitrogen or argon.

Low resolution mass spectra were recorded using a Micromass Trio 200 spectrometer and high resolution mass spectra on a Kratos Concept IS spectrometer. For high molecular weight compounds, peaks corresponding to the all-$^{12}C$ compounds are given. Infra-red spectra were measured using a Genesis FTIR spectrometer on NaBr plates, either neat or as evaporated films unless otherwise stated. Nuclear magnetic resonance spectra were recorded in deuteriated chloroform unless otherwise indicated on either a Bruker Avance 300 (300 MHz), Bruker Ultrashield 400 (400 MHz) or Bruker Ultrashield 500 (500 MHz) spectrometer. Coupling constants (*J*) are given in Hertz (Hz) and chemical shifts relative to tetramethylsilane.

### Dimethyl (4*S*)-4-benzyloxy-5-[(4*R*,6*S*)-6-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxan-4-yl]-3,3-dimethyl-2-oxopentylphosphonate 8

TBAF (1 M in THF, 12.87 mL, 12.87 mmol) was added to the *tert*-butyldiphenylsilyloxyphosphonate **7**[12] (7.8 g, 10.73 mmol) in THF (300 mL). The mixture stirred for 16 h then partitioned between EtOAc (300 mL) and saturated aqueous $NaHCO_3$ (300 mL). The aqueous phase was extracted with EtOAc (2 x 100 mL) and the organic extracts washed with brine (200 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (50→100% EtOAc/petrol, 1% $Et_3N$) afforded the *title compound* **8** as a colourless oil (5.4 g, 100%), $R_f$ 0.14 (EtOAc), $[\alpha]_D^{25}$ -4.9 (*c* 1.87, $CH_2Cl_2$) (Found: $M^+$ + Na, 509.2276. $C_{24}H_{39}O_8NaP$ requires *M*, 509.2275); $\nu_{max}$ (film)/cm$^{-1}$ 3419, 2955, 1703, 1455, 1380, 1259, 1223, 1096, 1029 and 805; $\delta_H$ (500 MHz; $C_6D_6$) 1.26 and 1.29 (each 3 H, s, 3-$CH_3$), 1.39 (1 H, m, 5'-H), 1.40 and 1.46 (each 3 H, s, 2'-$CH_3$), 1.51 (1 H, m, 5-H'), 1.60 (1 H, m, 1''-H), 1.64-1.73 (2 H, m, 5-$H_2$), 1.81 (1 H, m, 1''-H'), 2.77 (1 H, br s, OH), 3.23 (1 H, dd, *J* 21.5, 15.5, 1-H), 3.38 (1 H, dd, *J* 20.5, 15.5, 1-H'), 3.58 and 3.62 (each 3 H, d, *J* 11, $OCH_3$), 3.76 and 3.82 (each 1 H, m, 2''-H), 4.01 (1 H, m, 4-H), 4.07 (1 H, m, 6'-H), 4.17 (1 H, m, 4'-H), 4.67 and 4.78 (each 1 H, d, *J* 11.4, PhHC*H*), 7.21 (1 H, m, ArH), 7.27-7.32 (2 H, m, ArH) and 7.45 (2 H, d, *J* 7.6, ArH); $\delta_C$ (125 MHz; $C_6D_6$) 19.5, 19.8, 24.0, 24.2, 36.0 and 37.1 (d, $^1J_{C\text{-}P}$ 136.2), 37.3, 37.3, 38.0, 50.9 and 51.0 (d, $^2J_{C\text{-}P}$ 6.4), 51.1 and 51.2 ($^2J_{C\text{-}P}$ 6.4), 52.4 (d, $^3J_{C\text{-}P}$ 3.6), 58.7, 62.5, 64.2, 73.9, 80.1, 99.0, 126.1, 126.4, 127.3, 137.8, 205.2 and 205.2 (d, $^2J_{C\text{-}P}$ 7.0); *m/z* (ES) 509 ($M^+$ + 23, 100%).

### (*E*)-(2*S*,10*R*)-2-Benzyloxy-1-{(4*R*,6*S*)-6-(2-hydroxyethyl)-2,2-dimethyl[1,3]dioxan-4-yl}-11-(4-methoxybenzyloxy)-3,3-dimethyl-10-triethylsilyloxy-8-[(*Z*)-2-tri-*iso*propylsilyloxyethylidene]undec-5-en-4-one 9

Phosphonate **8** (2.9 g, 5.96 mmol) in THF (50.7 mL) was added to a suspension of $Ba(OH)_2.0.8H_2O$ (886 mg, 4.77 mmol, prepared by heating $Ba(OH)_2.8H_2O$ at 200 °C for 2 h) in THF (20.5 mL). The resulting mixture was stirred for 30 min before a solution of aldehyde **6**[12] (3.7 g, 6.56 mmol) in THF:$H_2O$ (40:1, 81.3 mL) was added over 10 min. After 16 h the mixture was filtered through a pad of Celite® and the solids washed with DCM (25 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (150 mL) and the aqueous phase extracted with DCM (2 x 100 mL). The organic extracts were washed with brine (100 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure to afford the *title compound* **9** as a pale yellow oil which was used immediately without purification, $R_f$ 0.24 (30% EtOAc/petrol) (Found: $M^+$ + Na, 947.5851. $C_{53}H_{88}O_9NaSi_2$ requires *M*, 947.5859); $\delta_H$ (400 MHz, $CHCl_3$) 0.48 (6 H, q, *J* 7.8, 3 x Si$CH_2$CH$_3$), 0.84 (9 H, t, *J* 7.8, 3 x SiCH$_2$C$H_3$), 0.93-1.02 [21 H, m, 3 x SiCH(C$H_3$)$_2$], 1.06 and 1.13 (each 3 H, s, 3-$CH_3$), 1.29 and 1.31 (each 3 H, s, 2'-$CH_3$), 1.40-1.51 (3 H, m, 1-$H_2$ and 6'-CH), 1.56-1.72 (4 H, m, 5'-$H_2$, 6'-CH' and OH), 2.08 (1 H, dd, *J* 13.6, 7.3, 9-H), 2.23 (1 H, dd, *J* 13.4, 5.3, 9-H'), 2.85 (2 H, d, *J* 7.1, 7-$H_2$), 3.20 (1 H, dd, *J* 9.6, 5.6, 11-H), 3.25 (1 H,

dd, *J*, 9.6, 5.2, 11-H'), 3.62-3.70 (2 H, m, 6'-$CH_2CH_2$), 3.72 (3 H, s, $OCH_3$), 3.78 (1 H, m, 10-H), 3.85 (1 H, m, 2-H), 3.92-4.02 (2 H, m, 4'-H and 6'-H), 4.14 (1 H, dd, *J* 13.1, 5.6, 8-CHC*H*), 4.21 (1 H, dd, *J* 12.9, 6.4, 8-CHC*H*'), 4.36 (2 H, s, $ArCH_2$), 4.51 (2 H, s, $PhCH_2$), 5.36 (1 H, t, *J* 6.0, 8-CH), 6.50 (1 H, d, *J* 15.1, 5-H), 6.76-6.87 (3 H, m, 6-H and ArH) and 7.13-7.28 (7 H, m, ArH); *m/z* (ES) 948 ($M^+$ + 23, 100%) and 943 ($M^+$ + 18, 70%).

**(*S*)-4-Benzyloxy-5-[(4*R*,6*S*)-6-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxan-4-yl]-1-{(2*S*,6*R*)-6-(4-methoxybenzyloxymethyl)-4-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]tetrahydropyran-2-yl}-3,3-dimethylpentan-2-one 11**

Pyridine (14.04 mL) was added to enone **9** in THF (144 mL). After cooling to 0 °C, HF-pyridine complex (7.08 mL) was added rapidly and the solution stirred for 25 min, followed by the rapid addition of saturated aqueous $NH_4Cl$ (200 mL) and warming to room temperature. The mixture was partitioned between ether (200 mL) and saturated aqueous $NH_4Cl$ (100 mL). The aqueous was extracted with ether (2 x 100 mL) and the organic extracts were washed with brine (200 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure to afford the diol **10** as a pale yellow oil. This was used immediately without further purification.[¶]

Potassium *tert*-butoxide in THF (1 M, 16.37 mL, 1.64 mmol) was added rapidly to diol **10** in THF (37.65 mL) at room temperature and the mixture stirred for precisely 5 min. Saturated aqueous $NH_4Cl$ (100 mL) and ether (100 mL) were added and the layers were separated. The aqueous phase was extracted with ether (2 x 100 mL) and the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (10→30% EtOAc/petrol) afforded the *title compound* **11** as a pale oil (2.37 g, 49% from phosphonate **8**), $R_f$ 0.13 (30% EtOAc/petrol), $[\alpha]_D^{25}$ +5.6 (*c* 2.35, $CHCl_3$) (Found: $M^+$ + Na, 833.4989. $C_{47}H_{74}O_9NaSi$ requires *M*, 833.4994); $\nu_{max}$ (film)/$cm^{-1}$ 3476, 2942, 2865, 1704, 1613, 1587, 1514, 1464, 1381, 1366, 1248, 1224, 1172, 1099, 1063, 1039 and 883; $\delta_H$ (400 MHz; $CDCl_3$) 0.95-1.03 [24 H, m, 3 x $SiCH(CH_3)_2$ and 3-$CH_3$], 1.15 (3 H, s, 3-$CH_3$'), 1.29 and 1.30 (each 3 H, s, 2"-$CH_3$), 1.30-1.55 (4 H, m, 5-$H_2$ and 5"-$H_2$), 1.56-1.68 (2 H, m, 6"-$CH_2$), 1.73 (1 H, t, *J* 12.6, 5'-$H_{ax}$), 1.82 (1 H, t, *J* 12.2, 3'-$H_{ax}$), 2.12 (1 H, d, *J* 13.1, 3'-$H_{eq}$), 2.37 (1 H, d, *J* 13.8, 5'-$H_{eq}$), 2.40 (1 H, br s, OH), 2.50 (1 H, dd, *J* 17.6, 6.5, 1-H), 2.93 (1 H, dd, *J* 17.6, 5.8, 1-H'), 3.30-3.38 (2 H, m, 6'-$CH_2$), 3.41 (1 H, m, 6'-H), 3.67 (2 H, m, 6"-$CH_2CH_2$), 3.73 (3 H, s, $OCH_3$), 3.79 (1 H, m, 2'-H), 3.87 (1 H, dd, *J* 9.8, 1.0, 4-H), 3.90-4.00 (2 H, m, 4"-H and 6"-H), 4.18 (2 H, d, *J* 6.3, 4'-CHC$H_2$), 4.39 (2 H, s, $ArCH_2$), 4.51 and 4.57 (each 1 H, d, *J* 11.3, PhHC*H*), 5.33 (1 H, t, *J* 6.2, 4'-CH), 6.79 (2 H, d, *J* 8.6, ArH) and 7.17-7.29 (7 H, m, ArH); $\delta_C$ (100 MHz; $CDCl_3$) 11.0, 17.0, 19.2, 19.9, 24.2, 24.3, 30.4, 36.5, 37.5, 38.0, 40.3, 44.0, 51.8, 54.2, 58.4, 60.3, 62.5, 65.9, 71.7, 71.9, 73.4, 73.9, 75.6, 79.4, 99.5, 112.7, 123.5, 126.1, 126.5, 127.4, 128.3, 129.3, 133.6, 137.6, 158.1 and 211.6; *m/z* (ES) 833 ($M^+$ + 23, 100%) and 828 ($M^+$ + 18, 17%).

**Prop-2-enyl {(4*R*,6*R*)-6-[(*S*)-2-benzyloxy-5-{(2*S*,6*R*)-6-(4-methoxybenzyloxymethyl)-4-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]tetrahydropyran-2-yl}-3,3-dimethyl-4-oxopentyl]-2,2-dimethyl-1,3-dioxan-4-yl}acetate 12**

To Dess-Martin periodinane (1.18 g, 2.77 mmol) and pyridine (2.24 mL, 27.74 mmol) in DCM (42.6 mL) was added the alcohol **11** (1.5 g, 1.85 mmol) in DCM (27.8 mL). After stirring for 1 h at rt, ether (100 mL), saturated aqueous $NaHCO_3$ (50 mL) and saturated aqueous $Na_2S_2O_3$ (50 mL) were added. After separation of the organic layer, the aqueous phase was extracted with ether (2 x 20 mL). The organic extracts were dried ($Na_2SO_4$), filtered and concentrated under reduced pressure to give a pale oil which was azeotroped with toluene to leave the corresponding aldehyde, $R_f$ 0.84 (30% EtOAc/petrol).

$NaClO_2$ (1.01 g, 11.12 mmol) and $NaH_2PO_4.2H_2O$ (2.89 g, 18.54 mmol) in $H_2O$ (14.8 mL) were added to the aldehyde, 2-methyl-2-butene (2M in THF, 18.5 mL) and *t*-butanol (27.8 mL) at room temperature. After 1 h, the reaction mixture was partitioned between brine (100 mL) and EtOAc (100 mL). After extraction of the aqueous phase with EtOAc (2 x 100 mL), the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure to give the corresponding acid as a pale oil, $R_f$ 0.27 (30% EtOAc/petrol).

Allyl bromide (0.481 mL, 5.56 mmol) was added to the acid and $NaHCO_3$ (312 mg, 3.71 mmol) in DMF (5.5 mL) and the reaction mixture was stirred at 70 °C for 16 h. After addition of saturated aqueous

[¶] During attempted chromatography of diol **10** using petrol/ethyl acetate with 1% triethylamine, cyclisation to a 2,6-*trans*-disubstituted tetrahydropyran the 2"-epimer of **11** was observed. Treatment of this with potassium *tert*-butoxide initiated epimerisation into the *cis*-isomer **11**.

$NH_4Cl$ (100 mL) and ether (100 mL), extraction of the aqueous phase with ether (2 x 100 mL) followed by washing the organic extracts with brine (100 mL) and concentration under reduced pressure gave a yellow oil. Chromatography (5 → 15% EtOAc:petrol, 1% $Et_3N$) gave the *title compound* **12** as a pale oil (1.1 g, 70% from the alcohol **11**), $R_f$ 0.40 (30% EtOAc/petrol), $[\alpha]_D^{25}$ +2.2 (*c* 2.44, $CHCl_3$) (Found: $M^+$ + Na, 887.5094. $C_{50}H_{76}O_{10}NaSi$ requires *M*, 887.5100); $\nu_{max}$ (film)/$cm^{-1}$ 2942, 2866, 1740, 1706, 1613, 1514, 1464, 1381, 1367, 1248, 1224, 1171, 1101, 1066, 1038, 993, 882 and 820; $\delta_H$ (400 MHz; $CDCl_3$) 0.95-1.03 [24 H, m, 3 x $SiCH(CH_3)_2$ and 3"-$CH_3$], 1.14 (3 H, s, 3"-$CH_3$'), 1.27 and 1.28 (each 3 H, s, 2'-$CH_3$), 1.37 (1 H, ddd, *J* 14.6, 10.6, 1.5, 1"-H), 1.42-1.61 (3 H, m, 1"-H' and 5'-$H_2$), 1.73 (1 H, t, *J* 12.3, 5"'-$H_{ax}$), 1.82 (1 H, t, *J* 12.3, 3"'-$H_{ax}$), 2.11 (1 H, d, *J* 12.3, 3"'-$H_{eq}$), 2.36 (1 H, dd, *J* 15.4, 5.3, 2-H), 2.37 (1 H, m , 5"'-$H_{eq}$), 2.47 (1 H, dd, *J* 15.4, 8.3, 2-H'), 2.50 (1 H, dd, *J* 17.6, 6.6, 5"-H), 2.93 (1 H, dd, *J* 17.6, 5.8, 5"-H'), 3.29-3.38 (2 H, m, 6"'-$CH_2$), 3.41 (1 H, m, 6"'-H), 3.73 (3 H, s, $OCH_3$), 3.78 (1 H, m, 2"'-H), 3.88 (1 H, dd, *J* 9.8, 1.4, 2"-H), 3.95 (1 H, m, 6'-H), 4.18 (2 H, d, *J* 6.1, 4"'-CHC*H*$_2$), 4.19 (1 H, m, 4'-H), 4.39 (2 H, s, $ArCH_2$), 4.48-4.54 (3 H, m, PhHC*H* and OC*H*$_2$CH), 4.56 (1 H, d, *J* 11.4, PhHC*H*'), 5.15 (1 H, dq, *J* 10.4, 1.3, $OCH_2CHCHH$), 5.24 (1 H, dq, *J* 17.2, 1.5, $OCH_2CHCHH$'), 5.33 (1 H, t, *J* 6.3, 4"'-CH), 5.83 (1 H, ddt *J* 17.2, 10.6, 5.8, $OCH_2CHCH_2$), 6.79 (2 H, d, *J* 8.6, ArH), 7.17 (2 H, d, *J* 8.6, ArH) and 7.18-7.28 (5 H, m, ArH); $\delta_C$ (100 MHz; $CDCl_3$) 11.0, 17.0, 19.4, 19.7, 24.0, 24.1, 30.5, 37.1, 37.9, 39.7, 40.3, 44.0, 51.7, 54.2, 58.4, 62.3, 62.3, 64.1, 71.8, 71.9, 73.4, 73.8, 75.6, 79.4, 99.6, 112.7, 117.2, 123.5, 126.0, 126.4, 127.3, 128.3, 129.3, 131.0, 133.7, 137.7, 158.1, 169.5 and 211.6; *m/z* (ES) 904 ($M^+$ + 39, 100%) and 888 ($M^+$ + 23, 38%).

**Prop-2-enyl (3*R*,5*S*,7*S*,9*S*,11*S*,15*R*)-7-benzyloxy-5,9-epoxy-11,15-epoxy-3-hydroxy-13-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-16-(4-methoxybenzyloxy)-8,8-dimethylhexadecanoate 13**

Pyridinium toluene 4-sulfonate (32 mg, 0.127 mmol) was added to the ester **12** (1.1 g, 0.042 mmol) and trimethyl orthoformate (2.8 mL) in DCM (9.8 mL) and methanol (9.8 mL). The solution was stirred at room temperature for 1 h before partitioning between EtOAc (50 mL) and saturated aqueous $NaHCO_3$ (50 mL). The aqueous phase was extracted with EtOAc (2 x 50 mL) and the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (10 → 15% EtOAc:petrol) of the residue afforded the *title compound* **13** (700 mg, 66%) as a pale yellow oil, $R_f$ 0.70 (30% EtOAc/petrol), $[\alpha]_D^{25}$ +33.1 (*c* 2.56, $CHCl_3$) (Found: ($M^+$ + Na, 861.4940. $C_{48}H_{74}O_{10}NaSi$ requires *M*, 861.4943); $\nu_{max}$ (film)/$cm^{-1}$ 3494, 2945, 2863, 1737, 1733, 1615, 1514, 1463, 1362, 1259, 1171, 1096, 883, 802 and 684; $\delta_H$ (400 MHz; $CDCl_3$) 0.94 (3 H, s, 8-$CH_3$), 0.95-1.08 [24 H, m, 8-$CH_3$' and 3 x $SiCH(CH_3)_2$], 1.41 (1 H, q, *J* 12.1, 6-$H_{ax}$), 1.48-1.58 (2 H, m, 4-$H_2$), 1.64-1.72 (2 H, m, 10-H and 6-$H_{eq}$), 1.74 (1 H, t, *J* 12.4, 14-$H_{ax}$), 1.93 (1 H, t, *J* 12.5, 12-$H_{ax}$), 2.00 (1 H, dd, *J* 16.1, 6.1, 10-H'), 2.16 (1 H, d, *J* 13.1, 12-$H_{eq}$), 2.38 (1 H, d, *J* 13.4, 14-$H_{eq}$), 2.37-2.48 (2 H, m, 2-$H_2$), 3.14 (3 H, s, 9-$OCH_3$), 3.31 (1 H, d, *J* 3.8, 3-OH), 3.31-3.42 (2 H, m, 15-H and 16-H), 3.46 (1 H, dd, *J* 10.2, 5.0, 16-H'), 3.53 (1 H, m, 11-H), 3.64 (1 H, dd, *J* 11.4, 4.8, 7-H), 3.73 (3 H, s, $OCH_3$), 3.80 (1 H, m, 5-H), 4.18 (2 H, d, *J* 6.1, 13-CHC*H*$_2$), 4.28 (1 H, m, 3-H), 4.38 (1 H, d, *J* 11.6, PhHC*H*), 4.44 (2 H, s, $ArCH_2$), 4.48-4.59 (2 H, m, 1'-$H_2$ and PhHC*H*'), 5.17 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.25 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.29 (1 H, t, *J* 6.3, 13-CH), 5.84 (1 H, ddt *J* 17.2, 10.6, 5.8, 2'-H), 6.80 (1 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH) and 7.24-7.28 (3 H, m, ArH); $\delta_C$ (100 MHz; $CDCl_3$) 11.0, 15.9, 17.0, 17.0, 19.8, 30.5, 31.3, 38.3, 40.8, 40.8, 42.0, 42.2, 47.4, 54.2, 58.4, 63.7, 64.2, 64.4, 70.6, 71.9, 71.9, 73.9, 75.5, 77.7, 103.1, 112.7, 117.4, 122.9, 126.3, 126.3, 127.2, 128.1, 129.6, 130.9, 134.6, 138.3, 158.0 and 171.2; *m/z* (ES) 861 ($M^+$ + 23, 100%).

**Prop-2-enyl (3*R*,5*S*,7*S*,9*S*,11*S*,15*R*)-7-benzyloxy-3-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-13-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-16-(4-methoxybenzyloxy)-8,8-dimethylhexadecanoate 14**

To the 3-hydroxyhexadecanoate **13** (700 mg, 0.894 mmol) and 2,6-lutidine (1.04 mL, 8.94 mmol) in DCM (41.1 mL) at -78 °C was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (411 μL, 1.79 mmol) and 2,6-lutidine (1.04 mL, 8.94 mmol) in DCM (7.4 mL). The solution was stirred at -78 °C for 1 h before partitioning between ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with ether (3 x 10 mL), and the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (0→5% EtOAc:petrol) of the residue afforded the *title compound* **14** as a pale oil (666 mg, 84%), $R_f$ 0.65 (10% EtOAc/petrol), $[\alpha]_D^{24}$ +25.7 (*c* 2.13, $CH_2Cl_2$) (Found: $M^+$ + $NH_4$, 970.6257. $C_{54}H_{92}O_{10}NSi_2$ requires *M*, 970.6254); $\nu_{max}$ (film)/$cm^{-1}$ 2943, 2864, 1738, 1613, 1514, 1464, 1382, 1362, 1249, 1171, 1096, 883, 835, 776 and 682; $\delta_H$ (400 MHz; $CDCl_3$) -0.03 and 0.00 (each 3 H, s, $SiCH_3$), 0.79 [9 H, s, $SiC(CH_3)_3$], 0.93 (3 H, s, 8-$CH_3$), 0.95-1.05 [24 H, m, 8-$CH_3$' and 3 x $SiCH(CH_3)_2$], 1.30 (1 H, q,

*J* 12.1, 6-$H_{ax}$), 1.57 (1 H, dt, *J* 14.2, 4.9, 4-H), 1.65-1.79 (4 H, m, 4-H', 6-$H_{eq}$, 10-H and 14-$H_{ax}$), 1.87-1.98 (2 H, m, 10-H' and 12-$H_{ax}$), 2.20 (1 H, d, *J* 13.4, 12-$H_{eq}$), 2.37 (1 H, d, J 13.6, 14-$H_{eq}$), 2.41 (1 H, dd, *J* 14.9, 7.8, 2-H), 2.58 (1 H, dd, *J* 14.9, 4.3, 2-H'), 3.11 (3 H, s, 9-$OCH_3$), 3.31-3.46 (3 H, m, 15-H and 16-$H_2$), 3.46-3.55 (2 H, m, 5-H and 11-H), 3.59 (1 H, dd, *J* 11.6, 4.8, 7-H), 3.73 (3 H, s, $OCH_3$), 4.19 (2 H, d, *J* 6.1, 13-CHC*H*$_2$), 4.19 (1 H, m, 3-H), 4.38 (1 H, d, *J* 11.9, PhHC*H*), 4.44 (2 H, s, $ArCH_2$), 4.49 (2 H, m, 1'-$H_2$), 4.54 (1 H, d, *J* 11.9, PhHC*H*'), 5.15 (1 H, dq, *J* 10.3, 1.3, 3'-H), 5.24 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.31 (1 H, t, *J* 6.1, 13-CH), 5.84 (1 H, ddt *J* 17.2, 10.3, 5.8, 2'-H), 6.80 (1 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH) and 7.23-7.29 (3 H, m, ArH); $\delta_C$ (100 MHz; $CDCl_3$) -5.5, -5.3, 11.0, 15.8, 16.9, 17.0, 17.0, 19.9, 24.8, 30.5, 32.3, 38.1, 42.1, 42.3, 42.5, 43.5, 47.3, 54.2, 58.4, 65.1, 67.1, 70.7, 71.9, 72.0, 74.0, 75.6, 77.8, 103.2, 112.7, 117.2, 122.9, 126.3, 126.3, 127.2, 128.1, 129.5, 131.1, 134.6, 138.3, 158.1 and 170.2; *m/z* (ES) 976 ($M^+$ + 23, 64%) and 971 ($M^+$ + 18, 100%).

**Prop-2-enyl (3*R*,5*S*,7*S*,9*S*,11*S*,15*R*)-7-benzyloxy-3-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-16-hydroxy-13-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-8,8-dimethylhexadecanoate 15**

DDQ (107 mg, 0.472 mmol) was added to the PMB ether **14** (300 mg, 0.315 mmol) in DCM/methanol (9:1, 12.6 mL) at room temperature and the black slurry stirred at for 2 h before the addition of saturated aqueous $Na_2S_2O_3$ (50 mL) and saturated aqueous $NaHCO_3$ (50 mL). After stirring for an additional 10 min, DCM (100 mL) was added and the aqueous phase was extracted with DCM (2 x 50 mL). The organic extracts were washed with a mixture of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ (1:1, 100 mL) and brine (100 mL), then dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (5→10% EtOAc:petrol) of the residue afforded the *title compound* **15** as a pale oil (190 mg, 72%), $R_f$ 0.46 (10% EtOAc/petrol), $[\alpha]_D^{24}$ +29.3 (*c* 2.06, $CH_2Cl_2$) (Found: $M^+$ + Na, 855.5219. $C_{46}H_{80}O_9NaSi_2$ requires *M*, 855.5233); $\nu_{max}$ (film)/$cm^{-1}$ 3471, 2944, 2865, 1738, 1463, 1382, 1361, 1256, 1170, 1096, 882, 836, 776 and 681; $\delta_H$ (400 MHz; $C_6D_6$) 0.029 and 0.031 (each 3 H, s, $SiCH_3$), 0.86 [9 H, s, $SiC(CH_3)_3$], 0.95-1.03 [21 H, m, 3 x $SiCH(CH_3)_2$], 1.05 and 1.15 (each 3 H, s, 8-$CH_3$), 1.28 (1 H, q, *J* 12.1, 6-$H_{ax}$), 1.50-1.68 (4 H, m, 4-H, 6-$H_{eq}$, 12-$H_{ax}$ and 14-$H_{ax}$), 1.68-1.82 (2 H, m, 4-H' and 10-H), 1.95-2.09 (3 H, m, 10-H', 12-$H_{eq}$ and OH), 2.17 (1 H, d, *J* 13.4, 14-$H_{eq}$), 2.50 (1 H, dd, *J* 15.1, 7.8, 2-H), 2.61 (1 H, dd, *J* 15.1, 4.0, 2-H'), 3.05 (3 H, s, 9-$OCH_3$), 3.22 (1 H, m, 15-H), 3.31-3.43 (2 H, m, 16-$H_2$), 3.57-3.69 (3 H, m, 5-H, 7-H and 11-H), 4.12 (1 H, d, *J* 11.9, PhHC*H*), 4.14 (1 H, m, 13-CHC*H*H), 4.19 (1 H, dd, *J* 12.6, 6.3, 13-CHC*H*H'), 4.40 (1 H, d, *J* 11.9, PhHC*H*'), 4.33-4.44 (3 H, m, 1'-$H_2$ and 3-H), 4.87 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.03 (1 H, dq, *J* 17.2, 1.6, 3'-H'), 5.46 (1 H, t, *J* 6.1, 13-CH), 5.65 (1 H, ddt, J 17.2, 10.3, 5.8, 2'-H), 6.97 (1 H, t, *J* 7.3, ArH), 7.02-7.09 (2 H, m, ArH) and 7.18 (2 H, d, *J* 7.3, ArH); $\delta_C$ (100 MHz; $C_6D_6$) -5.4, 11.0, 15.8, 16.9, 16.9, 19.9, 24.7, 29.5, 32.3, 38.0, 42.0, 42.0, 42.6, 43.8, 47.1, 58.4, 63.7, 64.8, 65.0, 67.2, 70.3, 73.8, 76.6, 77.6, 103.1, 116.5, 123.4, 126.1, 126.2, 127.1, 131.4, 134.2, 138.5 and 169.6; *m/z* (ES) 856 ($M^+$ + 23, 56%), 851 ($M^+$ + 18, 20%) and 257 (100).

**(4*S*,6*R*,7*R*)-2-Benzyloxymethyl-7-*tert*-butyldimethylsilyloxy-4-triethylsilyloxy-6-(2-trimethylsilylethoxy)-methoxyoct-1-ene 17**

Imidazole (86 mg, 1.26 mmol) and chlorotriethylsilane (0.106 mL, 0.62 mmol) were added to the alcohol **16**[13] (250 mg, 0.48 mmol) in DCM (3.4 mL). The solution was stirred at room temperature for 60 min before the addition of DCM (30 mL) and saturated aqueous $NaHCO_3$ (30 mL). After separation of the organic layer, the aqueous phase was extracted with DCM (2 x 30 mL). The organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Chromatography (35 : 1 petrol : ether) afforded the *title compound* **17** (298 mg, 98%) as a colourless oil, $R_f$ = 0.55 (19 : 1, petrol : ether), $[\alpha]_D^{26}$ -1.5 (*c* 3.8, $CHCl_3$) (Found: $M^+$ + Na, 661.4116. $C_{34}H_{66}O_5Si_3Na$ requires *M*, 661.4116); $\nu_{max}$ (film)/$cm^{-1}$ 2954, 2929, 2876, 2858, 1649, 1462, 1377, 1250, 1102, 1071, 1057, 1033, 1017, 859, 835, 774, 740 and 696; $\delta_H$ (400 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 x $SiCH_3$), 0.58 (6 H, q, *J* 7.8, 3 x $SiCH_2CH_3$), 0.83-0.99 (2 H, m, $OCH_2CH_2Si$), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (9 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.05 (3 H, d, *J* 6.3, 8-$H_3$), 1.53 (1 H, ddd, *J* 14.2, 9.1, 3.5, 5-H), 1.59 (1 H, ddd, *J* 14.3, 8.1, 2.5, 5-H'), 2.22 (1 H, dd, *J* 13.9, 7.8, 3-H), 2.38 (1 H, dd, *J* 13.9, 4.8, 3-H'), 3.48 (1 H, ddd, *J* 11.1, 9.6, 6.1, OC*H*HCH$_2$Si), 3.56 (1 H, ddd, *J* 9.1, 4.5, 2.8, 6-H), 3.67 (1 H, ddd, *J* 11.4, 9.6, 5.6, OCH*H*'CH$_2$Si), 3.93 (1 H, d, *J* 12.6, 2-CH), 3.96-4.04 (3 H, m, 2-CH', 4-H and 7-H), 4.47 (2 H, s, $PhCH_2$), 4.68 (2 H, s, $OCH_2O$), 4.97 (1 H, s, 1-H), 5.11 (1 H, m, 1-H') and 7.22-7.35 (5 H, m, Ar-H); $\delta_C$ (125 MHz) -3.3, -3.2, 0.0, 6.7, 8.5, 18.8, 19.6, 19.6, 27.3, 37.4, 43.8, 66.7, 69.6, 70.8, 73.4, 74.8, 81.5, 97.4, 115.6, 128.9, 129.1, 129.7, 139.9 and 144.4; *m/z* (ES) 697 (34%), 661 ($M^+$ + 23, 100) and 656 ($M^+$ + 18, 32).

**(4*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-2-methylene-4-triethylsilyloxy-6-(2-trimethylsilylethoxy)-methoxyoctan-1-ol 18**

Lithium (864 mg, 123.2 mmol) was added to naphthalene (28.0 g, 218.4 mmol) in THF (160 mL) and the mixture stirred vigorously at room temperature for 2 h. The resulting dark green solution was added dropwise to the benzyl ether **17** (6.14 g, 9.62 mmol) in THF (276 mL) at -25 °C until consumption of the starting material was observed by TLC. Water was added dropwise and the mixture partitioned between ether (300 mL) and saturated aqueous $NaHCO_3$ (400 mL). The aqueous phase was extracted with ether (2 x 300 mL) and the organic extracts were dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography (7 : 1 petrol : ether) of the residue afforded the *title compound* **18** (5.13 g, 97%) as a colourless oil, $R_f$ = 0.21 (4 : 1, petrol:ether), $[\alpha]_D^{29}$ +6.9 (*c* 2.0, $CHCl_3$) (Found: $M^+$ + Na, 571.3632. $C_{27}H_{60}O_5Si_3Na$ requires *M*, 571.3646); $\nu_{max}$ (film)/$cm^{-1}$ 3444, 2954, 2928, 2878, 2858, 1651, 1472, 1463, 1414, 1378, 1250, 1148, 1102, 1057, 1034, 938, 899, 860, 835, 811, 775, 744 and 726; $\delta_H$ (400 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 x $SiCH_3$), 0.62 (6 H, q, *J* 7.8, 3 x $SiCH_2CH_3$), 0.83-0.99 (2 H, m, $OCH_2CH_2Si$), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.95 (9 H, t, *J* 7.9, 3 x $SiCH_2CH_3$)$_3$, 1.06 (3 H, d, *J* 6.3, 8-$H_3$), 1.59 (1 H, ddd, *J* 14.3, 8.6, 5.4, 5-H), 1.66 (1 H, ddd, *J* 14.4, 7.1, 3.8, 5-H'), 2.32 (1 H, dd, *J* 13.9, 5.8, 3-H), 2.39 (1 H, dd, *J* 14.0, 4.5, 3-H'), 3.01 (1 H, t, *J* 6.1, OH), 3.47-3.55 (2 H, m, $OCHHCH_2Si$ and 6-H), 3.64 (1 H, ddd, *J* 11.3, 9.6, 5.8, $OCHH'CH_2Si$), 3.98 (1 H, qd, *J* 6.3, 4.5, 7-H), 4.02 (2 H, d, *J* 6.1, 1-$H_2$), 4.06 (1 H, m, 4-H), 4.69 (2 H, s, $OCH_2O$), 4.91 (1 H, s, 2-CH) and 5.09 (1 H, m, 2-CH'); $\delta_C$ (75 MHz) -3.3, -3.2, 0.0, 6.5, 8.4, 18.9, 19.5, 19.6, 27.3, 37.2, 44.1, 66.8, 68.1, 70.6, 71.0, 81.1, 96.9, 115.9 and 147.1; *m/z* (ES) 608 (68%), 571 ($M^+$ + 23, 42), 549 ($M^+$ + 1, 100) and 431 (19).

**(4*S*,6*R*,7*R*)-2-Bromomethyl-7-*tert*-butyldimethylsilyloxy-4-triethylsilyloxy-6-(2-trimethylsilylethoxy)-methoxyoct-1-ene 19**

Carbon tetrabromide (909 mg, 2.74 mmol) was added to the alcohol **18** (503 mg, 0.91 mmol), triphenylphosphine (759 mg, 2.90 mmol) and triethylamine (1.30 mL, 9.36 mmol) in DCM (35.0 mL) at 0 °C and the solution stirred at this temperature for 20 min before adding DCM (30 mL), saturated aqueous $NaHCO_3$ (30 mL) and saturated aqueous $Na_2S_2O_3$ (30 mL). The aqueous phase was extracted with DCM (2 x 40 mL) and the organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography (40 : 1 petrol : ether) of the residue afforded the *title compound* **19** (526 mg, 95%) as a colourless oil, $R_f$ = 0.15 (60 : 1 petrol : ether), $[\alpha]_D^{24}$ +0.8, (*c* 2.0, $CHCl_3$) (Found: $M^+$ + Na, 633.2802. $C_{27}H_{59}O_4{}^{79}BrSi_3Na$ requires *M*, 633.2802); $\nu_{max}$ (film)/ $cm^{-1}$ 2954, 2929, 2877, 2858, 1638, 1472, 1463, 1377, 1250, 1148, 1102, 1057, 1034, 938, 910, 859, 835, 775, 745 and 726; $\delta_H$ (400 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 x $SiCH_3$), 0.61 (6 H, q, *J* 7.8, 3 x $SiCH_2CH_3$), 0.83-0.99 (2 H, m, $OCH_2CH_2Si$), 0.86 [9 H, s, $SiC(CH_3)_3$], 0.95 (9 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.04 (3 H, d, *J* 6.3, 8-$H_3$), 1.47 (1 H, ddd, *J* 14.2, 9.6, 4.0, 5-H), 1.61 (1 H, ddd, *J* 14.4, 8.3, 2.5, 5-H'), 2.38 (1 H, dd, *J* 14.1, 7.3, 3-H), 2.49 (1 H, dd, *J* 14.1, 4.8, 3-H'), 3.50 (1 H, ddd, *J* 11.1, 9.6, 5.8, $OCHHCH_2Si$), 3.54 (1 H, ddd, *J* 9.6, 4.5, 2.5, 6-H), 3.66 (1 H, ddd, *J* 11.4, 9.6, 5.5, $CHH'CH_2Si$), 3.96-4.03 (2 H, m, 4-H and 7-H), 3.98 and 4.02 (each 1 H, d, *J* 9.8, 2-CH), 4.71 (2 H, s, $OCH_2O$), 4.99 (1 H, m, 1-H) and 5.21 (1 H, s, 1-H'); $\delta_C$ (100 MHz) -3.3, -3.2, 0.0, 6.6, 8.5, 18.8, 19.5, 19.6, 27.3, 37.4, 38.9, 43.3, 66.8, 69.6, 70.7, 81.4, 97.3, 119.4 and 144.1; *m/z* (ES) 635 ($M^+$ + 23, 87%) and 633 ($M^+$ + 23, 100).

**(4*S*,6*R*,7*R*)-2-Bromomethyl-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxyoct-1-en-4-ol 20**

Pyridinium toluene 4-sulfonate (21 mg, 0.082 mmol) was added to the triethylsilyl ether **19** (526 mg, 0.860 mmol) in a mixture of THF (14.0 mL), methanol (14.0 mL) and trimethyl orthoformate (1.4 mL, 12.8 mmol) and the solution stirred at room temperature for 3 h. The reaction mixture was then partitioned between ether (60 mL) and saturated aqueous $NaHCO_3$ (60 mL). The aqueous phase was extracted with ether (3 x 50 mL) and the organic extracts were dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography (5 : 1 petrol : ether) of the residue afforded the *title compound* **20** (405 mg, 95%) as a colourless oil, $R_f$ = 0.28 (4 : 1 petrol : ether), $[\alpha]_D^{26}$ +34.7 (*c* 1.2, $CHCl_3$) (Found: $M^+$ + Na, 519.1927. $C_{21}H_{45}O_4{}^{79}BrSi_2Na$ requires *M*, 519.1937); $\nu_{max}$ (film)/$cm^{-1}$ 3467, 2953, 2929, 2896, 2857, 1641, 1377, 1250, 1210, 1151, 1102, 1056, 1031, 938, 860, 832 and 775; $\delta_H$ (400 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.06 and 0.07 (each 3 H, s, $SiCH_3$), 0.88 [9 H, s, $SiC(CH_3)_3$], 0.93 (2 H, dd, *J* 9.4, 8.0, $OCH_2CH_2Si$), 1.10 (3 H, d, *J* 6.3, 8-$H_3$), 1.54 (1 H, ddd, *J* 14.4, 8.6, 3.3, 5-H), 1.60 (1 H, ddd, *J* 14.4, 9.1, 5.0, 5-H'), 2.33-2.43 (2 H, m, 3-$H_2$), 3.55 (1 H, td, *J* 9.5, 8.0, $CHHCH_2Si$),

3.59 (1 H, dt, *J* 8.7, 5.4, 6-H), 3.69 (1 H, td, *J* 9.6, 7.8, CH*H*'$CH_2$Si), 3.73 (1 H, d, *J* 3.2, OH), 3.83 (1 H, qn, *J* 6.0, 7-H), 3.97 (1 H, m, 4-H), 4.04 and 4.05 (each 1 H, dd, *J* 10.1, 0.8, 2-CH), 4.70 and 4.76 (each 1 H, d, *J* 6.8, OC*H*HO), 5.05 (1 H, m, 1-H) and 5.24 (1 H, s, 1-H'); $\delta_C$ (100 MHz) -3.3, -3.3, 0.0, 19.5, 19.6, 20.3, 27.3, 38.5, 39.4, 42.6, 67.5, 67.5, 72.5, 81.7, 97.7, 118.8 and 144.7; *m/z* (ES) 558 (25%), 556 (30%), 521 ($M^+$ + 23, 75), 519 ($M^+$ + 23, 100), 499 ($M^+$ + 1, 22) and 497 ($M^+$ + 1, 23).

**(4*S*,6*R*,7*R*)-2-Bromomethyl-7-*tert*-butyldimethylsilyloxy-6-(2-trimethylsilylethoxy)methoxyoct-1-en-4-yl acrylate 21**

*N*,*N*-Di*iso*propylethylamine (0.51mL, 2.87 mmol) and acryloyl chloride (0.116 mL, 1.39 mmol) were added to the alcohol **20** (405 mg, 0.82 mmol) in DCM (5.5 mL) at 0°C and the solution stirred at this temperature for 40 min. The reaction mixture was then partitioned between DCM (40 mL) and saturated aqueous $NaHCO_3$ (400 mL). The aqueous phase was extracted with DCM (2 x 40mL) and the organic extracts were dried ($MgSO_4$), then filtered and concentrated under reduced pressure. Chromatography (10 : 1 petrol : ether) of the residue afforded the *title compound* **21** (435 mg, 97%) as a colourless oil, $R_f$ = 0.68 (4 : 1 petrol : ether), $[\alpha]_D^{27}$ -0.7 (*c* 1.2, $CHCl_3$) (Found: $M^+$ + Na, 573.2053. $C_{24}H_{47}O_5{}^{79}BrSi_2Na$ requires *M*, 573.2038); $\nu_{max}$ (film)/ $cm^{-1}$ 2953, 2928, 2858, 2893, 1724, 1638, 1405, 1296, 1270, 1250, 1192, 1103, 1056, 985, 860, 835, 809 and 776; $\delta_H$ (500 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02 and 0.03 (each 3 H, s, $SiCH_3$), 0.84 (1 H, ddd, *J* 13.6, 11.4, 5.0, $OCH_2CH$*H*Si), 0.86 [9 H, s, $SiC(CH_3)_3$], 0.95 (1 H, ddd, *J* 13.9, 12.0, 6.0, $OCH_2CH$*H*Si), 1.06 (3 H, d, *J* 6.3, 8'-$H_3$), 1.58 (1 H, ddd, *J* 14.2, 10.4, 1.9, 5'-H), 1.92 (1 H, dd, *J* 14.2, 10.4, 5'-H'), 2.46 (1 H, dd, *J* 14.5, 8.2, 3'-H), 2.58 (1 H, dd, *J* 14.5, 4.7, 3'-H'), 3.36 (1 H, dd, *J* 10.1, 4.4, 6'-H), 3.49 (1 H, ddd, *J* 11.3, 10.1, 5.9, OC*H*H$CH_2$Si), 3.66 (1 H, ddd, *J* 11.7, 9.8, 5.4, OCH*H*$CH_2$Si), 3.95 (1 H, d, *J* 10.4, 2'-CH), 4.01 (1 H, qd, *J* 6.2, 4.7, 7'-H), 4.07 (1 H, d, *J* 10.4, 2'-CH'), 4.60 and 4.70 (each 1 H, d, *J* 7.1, OCH*H*O), 4.99 and 5.20 (each 1 H, s, 1'-H), 5.27 (1 H, m, 4'-H), 5.79 (1 H, d, *J* 10.5, 3-H), 6.05 (1 H, dd, J 17.3, 10.4, 2-H) and 6.35 (1 H, d, *J* 17.3, 3-H'); $\delta_C$ (125 MHz) -3.4, -3.2, 0.0, 18.3, 19.5, 19.5, 27.3, 34.7, 37.9, 40.8, 66.8, 70.0, 70.5, 80.3, 97.6, 119.8, 130.0, 132.2, 143.0 and 167.2; *m/z* (ES) 575 ([$M^+$ + 23, 84%), 573 ($M^+$ + 23, 100), 570 ($M^+$ + 18, 68) and 568 ($M^+$ + 18, 61).

**(2*R*,3*R*,5*S*,9*RS*)-11-Benzothiazol-2-ylsulfonyl-2-*tert*-butyldimethylsilyloxy-10,10-dimethyl-7-methylene-9-triethylsilyloxy-3-(2-trimethylsilylethoxy)methoxyundecan-5-yl acrylate 24**

Activated zinc powder (11.1 mg, 0.172 mmol) was added to a vigorously stirred solution of bismuth(III) iodide (89 mg, 0.151 mmol) in THF (0.5 mL) and the resulting orange/grey suspension was stirred vigorously at room temperature for 75 min resulting in the formation of a black suspension. Solid $NaHCO_3$ (38 mg, 0.455 mmol) was added in one portion, followed by the addition of the bromide **21** (50 mg, 0.091 mmol) and aldehyde **22**[12] (80 mg, 0.282 mmol) in THF (0.35 mL). The mixture was heated under reflux for 4.5 h before being diluted with ether (5 mL) and filtered through celite. The filter cake was washed with ether (2 x 5 mL) and saturated aqueous $NaHCO_3$ (5 mL) and water (10 mL) was added to the washings. The aqueous phase was extracted with ether (3 x 10 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3 : 1 petrol : ether) of the residue afforded the homoallyllic alcohol **23** together with the excess of aldehyde **22**. This mixture was used without further purification, $R_f$ = 0.25 (3 : 1 petrol : ether).

Imidazole (60 mg, 0.88 mmol) and chlorotriethylsilane (0.067 mL, 0.40 mmol) were added to the homoallylic alcohol **23** in DCM (0.5 mL). The solution was stirred at room temperature for 90 min before ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added. The aqueous phase was extracted with ether (3 x 10 mL), and the organic extracts were dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography (9 : 1 petrol : ether) of the residue afforded the *title compound* **24** (48 mg, 61%), a colourless oil, a 55:45 mixture of epimers, $R_f$ = 0.19 (9 : 1 petrol : ether), $[\alpha]_D^{28}$ -10.1 (*c* 1.0, $CHCl_3$) (Found: $M^+$ + Na, 892.4117. $C_{42}H_{75}O_8NS_2Si_3Na$ requires *M*, 892.4140); $\nu_{max}$ (film)/$cm^{-1}$ 2954, 2924, 2874, 1722, 1471, 1404, 1330, 1250, 1195, 1150, 1102, 1055, 1034, 856, 835, 761 and 729; $\delta_H$ (400 MHz) 0.00 [4.95 H, s, $Si(CH_3)_3$], 0.00 [4.05 H, s, $Si(CH_3)_3$], 0.02 and 0.04 (each 1.35 H, s, $SiCH_3$), 0.03 and 0.04 (each 1.65 H, s, $SiCH_3$), 0.55 (3.3 H, q, *J* 8.1, 3 x $SiCH_2CH_3$), 0.56 (2.7 H, q, *J* 8.0, 3 x $SiCH_2CH_3$), 0.78-0.98 (2 H, m, $OCH_2CH_2Si$), 0.87 [4.05 H, s, $SiC(CH_3)_3$], 0.87 [4.95 H, s, $SiC(CH_3)_3$], 0.90 (4.95 H, t, *J* 8.1, 3 x $SiCH_2CH_3$), 0.91 (4.05 H, t, *J* 8.1, 3 x $SiCH_2CH_3$), 1.06 (1.65 H, d, *J* 6.3, 1'-$H_3$), 1.07 (1.35 H, d, *J* 6.3, 1'-$H_3$), 1.23 (1.35 H, s, 10'-$CH_3$), 1.27 (3 H, s, 10'-$CH_3$'), 1.29 (1.65 H, s, 10'-$CH_3$), 1.59 (1 H, m, 4'-H), 1.80-2.01 (2 H, m, 4'-H' and 8'-H), 2.18-2.48 (3 H, m, 6'-$H_2$ and 8'-H'), 3.35 (0.45 H, ddd, *J* 10.9, 4.3, 1.1, 3'-H), 3.38 (0.55 H, ddd, 10.9,

4.5, 1.0, 3'-H), 3.40-3.49 (1 H, m, OC*H*HCH$_2$Si), 3.57 (1 H, d, *J* 14.1, 11'-H), 3.60-3.72 (2 H, m, OCH*H*CH$_2$Si and 9'-H), 3.75 (0.45 H, d, *J* 14.4, 11'-H'), 3.77 (0.55 H, d, *J* 14.4, 11'-H'), 4.02 (1 H, qd, *J* 6.3, 4.5, 2'-H), 4.55 (0.55 H, d, *J* 7.1, OC*H*HO), 4.60 (0.45 H, d, *J* 7.1, OC*H*HO), 4.67 (0.55 H, d, *J* 7.1, OCH*H*O), 4.67 (0.45 H, d, *J* 7.1, OCH*H*O), 4.88 (1.45 H, s, 7'-CH$_2$ and 7'-CH), 4.90 (0.55 H, s, 7'-CH'), 5.15 (0.55 H, m, 5'-H), 5.25 (0.45 H, m, 5'-H), 5.77 (0.45 H, dd, *J* 10.3, 1.5, 3-H), 5.78 (0.55 H, dd, *J* 10.5, 1.5, 3-H), 6.04 (0.45 H, dd, *J* 17.4, 10.3, 2-H), 6.04 (0.55 H, dd, *J* 17.2, 10.3, 2-H), 6.34 (1 H, dd, *J* 17.4, 1.5, 3-H'), 7.55-7.65 (2 H, m, ArH), 7.98-8.02 (1 H, m, ArH) and 8.19-8.23 (1 H, m, ArH); $\delta_C$ (100 MHz) -3.4, -3.2, 0.0, 7.0, 8.6, 18.3, 19.5, 19.5, 24.7, 24.8, 26.2, 27.3, 33.9, 34.7, 40.7, 41.0, 42.1, 42.2, 43.3, 43.4, 62.2, 66.7, 66.7, 70.0, 70.1, 70.8, 71.0, 80.0, 80.1, 80.2, 80.4, 97.6, 97.7, 117.7, 118.0, 123.8, 126.9, 129.0, 129.0, 129.3, 130.1, 130.1, 132.0, 138.2, 138.2, 143.1, 143.3, 154.1, 167.1, 169.5 and 169.5; *m/z* (ES) 892 ($M^+$ + 23, 37%), 887 ($M^+$ + 18, 100), 468 (29) and 331 (37).

**(*S*)-4-[(*RS*)-4-Benzothiazol-2-ylsulfonyl-3,3-dimethyl-2-triethylsilyloxybutyl]-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(2-trimethylsilylethoxy)methoxybutyl]-5,6-dihydropyran-2-one 25**

A de-gassed solution of Grubbs' 2$^{nd}$ generation catalyst (2.6 mg, 3.1 μmol) was added *via* a syringe pump over 20 h to a de-gassed solution heated under reflux of the acrylate **24** (50 mg, 0.058 mmol) in DCE (0.45 mL). The reaction mixture was allowed to cool to room temperature and was concentrated under reduced pressure. Chromatography (3 : 1 petrol : ether) of the residue afforded the *title compound* **25** (44 mg, 90%), a pale red oil, a 55:45 mixture of epimers, $R_f$ = 0.13 (3 : 1 petrol : ether), $[\alpha]_D^{28}$ -28.2 (*c* 1.0, $CHCl_3$) (Found: $M^+$ + $NH_4$, 864.3814. $C_{40}H_{71}O_8NS_2Si_3Na$ requires *M*, 864.3827); $\nu_{max}$ (film)/cm$^{-1}$ 2954, 2935, 2879, 1716, 1643, 1471, 1328, 1250, 1150, 1101, 1056, 1029, 858, 836, 761 and 730; $\delta_H$ (400 MHz) 0.00 [4.05 H, s, Si(CH$_3$)$_3$], 0.00 [4.95 H, s, Si(CH$_3$)$_3$], 0.06-0.07 (6 H, m, 2 x SiCH$_3$), 0.53-0.67 (6 H, 3 x m, SiC*H*$_2$CH$_3$), 0.82-0.99 (2 H, m, OCH$_2$C*H*$_2$Si), 0.87 [4.95 H, s, SiC(CH$_3$)$_3$], 0.87 [4.05 H, s, SiC(CH$_3$)$_3$], 0.94 (4.05 H, t, *J* 8.1, 3 x SiCH$_2$C*H*$_3$), 0.94 (4.95 H, t, *J* 8.1, 3 x SiCH$_2$C*H*$_3$), 1.10 (1.65 H, d, *J* 6.3, 4''-H$_3$), 1.10 (1.35 H, d, *J* 6.3, 4''-H$_3$), 1.24 (4.35 H, s, 3'-CH$_3$ and 2 x 3'-CH$_3$), 1.26 (1.65 H, s, 3'-CH$_3$'), 1.63 (1 H, m, 1''-H), 2.05 (0.55 H, ddd, *J* 9.3, 7.1, 2.3, 1''-H'), 2.08 (0.45 H, ddd, *J* 9.6, 7.1, 2.3, 1''-H'), 2.24-2.46 (3 H, m, 1'-H and 5-H$_2$), 2.59 (1 H, m, 1'-H'), 3.46-3.54 (1 H, m, OC*H*HCH$_2$Si), 3.58 (0.45 H, d, *J* 14.4, 4'-H), 3.59 (0.55 H, d, *J* 14.4, 4'-H), 3.65 (1 H, m, OCH*H*CH$_2$Si), 3.70 (0.45 H, d, *J* 14.4, 4'-H'), 3.71 (0.55 H, d, *J* 14.4, 4'-H'), 3.77 (1 H, m, 2''-H), 3.96 (0.45 H, dd, *J* 7.6, 3.3, 2'-H), 4.00 (0.55 H, dd, *J* 7.1, 4.0, 2'-H), 4.04 (1 H, qd, *J* 6.3, 4.8, 3''-H), 4.59 (1 H, m, 6-H), 4.69-4.73 (2 H, m, OCH$_2$O), 5.86 (1 H, s, 3-H), 7.57-7.67 (2 H, m, ArH), 8.02 (1 H, m, ArH) and 8.19-8.23 (1 H, m, ArH); $\delta_C$ (100 MHz) -3.3, -3.3, 0.0, 7.0, 8.5, 8.6, 18.7, 18.8, 19.5, 19.5, 25.0, 25.2, 25.7, 25.7, 27.3, 31.1, 35.7, 35.9, 36.0, 42.2, 42.4, 42.5, 42.7, 62.2, 66.9, 66.9, 70.3, 70.4, 75.5, 75.6, 77.6, 77.9, 79.2, 79.4, 97.4, 97.5, 119.6, 120.1, 123.9, 126.9, 129.2, 129.5, 138.1, 154.0, 158.8, 159.0, 165.9, 166.0, 169.0 and 169.1; *m/z* (ES) 1297 (35%), 1283 (23%), 901 (69), 864 ($M^+$ + 23, 100) and 859 ($M^+$ + 18, 81), 454 (23) and 441 (37).

**(*E*)-(5*S*,7*R*,8*R*)-3-[(*RS*)-4-Benzothiazol-2-ylsulfonyl-3,3-dimethyl-2-triethylsilyloxybutyl]-8-*tert*-butyldimethylsilyloxy-7-(2-trimethylsilylethoxy)methoxynon-2-ene-1,5-diol 26**

A solution of the lactone **25** (20 mg, 0.0233 mmol) in methanol (0.29 mL) and THF (0.09 mL) was cooled to 0 $^oC$ before the addition of cerium(III) chloride heptahydrate (44 mg, 0.12 mmol). After dissolution of the solid, sodium borohydride (4 mg, 0.11 mmol) was added and the solution was warmed to rt and stirred for 7.5 h. After each 1.5 h interval, further cerium(III) chloride and sodium borohydride were added. The reaction mixture was then partitioned between ether (10 mL) and water (10 mL), and the aqueous phase was extracted with ether (2 x 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (2 : 1 petrol : ether then 1 : 1 petrol : ether) of the residue afforded unreacted starting material (5 mg, 25%) followed by the *title compound* **26** (15 mg, 75%), a colourless oil, a 58 : 42 mixture of diastereomers, $R_f$ = 0.24 (1 : 1 petrol : ether); $[\alpha]_D^{28}$ +27.9 (*c* 0.9, $CHCl_3$) (Found: $M^+$ + Na, 868.4146. $C_{40}H_{75}O_8NS_2Si_3Na$ requires *M*, 868.4140); $\nu_{max}$ (film)/cm$^{-1}$ 3391, 2953, 2925, 2873, 1472, 1329, 1250, 1150, 1097, 1055, 1009, 856, 832, 761, 729 and 634; $\delta_H$ (400 MHz) 0.00 [3.78 H, s, Si(CH$_3$)$_3$], 0.00 [5.22 H, s, Si(CH$_3$)$_3$], 0.07 (3 H, s, SiCH$_3$), 0.07 (1.26 H, s, SiCH$_3$'), 0.08 (1.74 H, s, SiCH$_3$'), 0.47-0.59 (6 H, m, 3 x SiC*H*$_2$CH$_3$), 0.82-0.95 (2 H, m, OCH$_2$C*H*$_2$Si), 0.88 [3.78 H, s, SiC(CH$_3$)$_3$], 0.88 [5.22 H, s, SiC(CH$_3$)$_3$], 0.91 (3.78 H, t, *J* 8.1, 3 x SiCH$_2$C*H*$_3$), 0.92 (5.22 H, t, *J* 8.1, 3 x SiCH$_2$C*H*$_3$), 1.11 (3 H, d, *J* 6.3, 9-H$_3$), 1.24 (1.26 H, s, 3'-CH$_3$), 1.24 (1.74 H, s, 3'-CH$_3$), 1.26 (3 H, s, 3'-CH$_3$'), 1.55 (1 H, m, 6-H), 1.67 (1 H, m, 6-H'), 1.91-2.09 (2 H, m, 1'-H and 4-H), 2.35-2.59 (2 H, m, 1'-H' and 4-H'), 3.45-3.91 (9 H, m, 1-H, 5-H, 7-H, 8-H, 2'-H, OC*H*$_2$CH$_2$Si and 4'-H$_2$), 3.95 (2 H, br s, 2 x OH), 4.15 (1 H, m, 1-H'), 4.70 (1 H, d, *J* 6.6, OC*H*HO), 4.75 (0.58

H, d, *J* 6.6, OCH*H*O), 4.75 (0.42 H, d, *J* 6.6, OCH*H*O), 5.81 (1 H, t, *J* 7.8, 2-H), 7.56-7.66 (2 H, m, ArH), 8.01 (1 H, m, ArH) and 8.21 (1 H, m, ArH); $\delta_C$ (100 MHz) -3.3, -3.3, 0.0, 6.9, 7.1, 8.6, 19.4, 19.5, 19.5, 20.3, 20.4, 25.1, 25.4, 26.0, 26.1, 27.3, 38.4, 40.0, 40.3, 40.7, 41.5, 41.6, 42.2, 42.2, 58.8, 59.0, 62.4, 62.5, 66.1, 66.5, 67.3, 67.4, 72.7, 72.8, 79.4, 81.0, 81.8, 82.1, 97.7, 97.8, 123.8, 123.9, 126.9, 129.1, 129.1, 129.4, 129.4, 130.3, 132.0, 138.2, 139.4, 141.1, 154.1, 154.1, 169.4 and 169.5; *m/z* (ES) 868 ($M^+$ + 23, 100), 863 ($M^+$ + 18, 10), 846 ($M^+$ + 1, 8), 456 (7) and 443 (7).

**(2*R*,3*R*,5*S*,9*RS*)-11-Benzothiazol-2-ylsulfonyl-2-*tert*-butyldimethylsilyloxy-10,10-dimethyl-9-triethylsilyloxy-7-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-3-(2-trimethylsilylethoxy)methoxyundecan-5-ol 27**

Imidazole (18 mg, 0.26 mmol) and tri*iso*propylsilyl chloride (0.026 mL, 0.12 mmol) were added to the diol **26** (50 mg, 0.059 mmol) in DCM (0.5 mL). The solution was stirred at rt for 12 h before partitioning between ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with ether (3 x 10 mL), and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (6 : 1 petrol : ether) of the residue afforded the *title compound* **27** (51 mg, 86%), a colourless oil, a 58:42 mixture of epimers, $R_f$ = 0.33 (4 : 1 petrol : ether), $[\alpha]_D^{28}$ +1.5 (*c* 0.8, $CHCl_3$) (Found: $M^+$ + Na, 1024.5477. $C_{49}H_{95}O_8NS_2Si_4Na$ requires *M*, 1024.5474); $\nu_{max}$ (film)/$cm^{-1}$ 3468, 2951, 2868, 1471, 1331, 1250, 1150, 1098, 1057, 1013, 856, 835, 776, 762, 730, 686 and 637; $\delta_H$ (500 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.06 (1.74 H, s, $SiCH_3$), 0.06 (1.26 H, s, $SiCH_3$), 0.07 (3 H, s, $SiCH_3$'), 0.56 (2.52 H, q, *J* 7.9, 3 x $SiCH_2CH_3$), 0.56 (3.48 H, q, *J* 7.9, 3 x $SiCH_2CH_3$), 0.85-0.97 (2 H, m, $OCH_2CH_2Si$), 0.88 [5.22 H, s, $SiC(CH_3)_3$], 0.88 [3.78 H, s, $SiC(CH_3)_3$], 0.91 (9 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.02-1.13 [24 H, m, 1-$H_3$ and 3 x $SiCH(CH_3)_2$], 1.24 and 1.27 (each 1.26 H, s, 10-$CH_3$), 1.25 and 1.27 (each 1.74 H, s, 10-$CH_3$), 1.44-1.62 (2 H, m, 4-$H_2$), 1.91 (0.58 H, dd, *J* 13.9, 8.5, 8-H), 1.95 (0.42 H, dd, *J* 14.1, 8.5, 8-H), 2.07 (0.42 H, dd, *J* 13.6, 4.4, 6-H), 2.19 (0.58 H, dd, *J* 13.6, 6.0, 6-H), 2.25 (0.58 H, dd, *J* 13.6, 7.3, 6-H'), 2.35 (0.42 H, dd, *J* 13.6, 8.2, 6-H'), 2.43 (0.42 H, d, *J* 14.2, 8-H'), 2.48 (0.58 H, d, *J* 13.9, 8-H'), 3.49-3.76 (6 H, m, 3-H, 5-OH, 9-H, 11-H and $OCH_2CH_2Si$ ), 3.75 (1 H, d, *J* 14.2, 11-H'), 3.80 (1 H, m, 5-H), 3.86 (0.58 H, qn, *J* 6, 2-H), 3.90 (0.42 H, qn, *J* 6, 2-H), 4.18-4.30 (2 H, m, 2'-$H_2$), 4.69 (0.58 H, d, *J* 6.8, OC*H*HO), 4.70 (0.42 H, d, *J* 6.6, OC*H*HO), 4.72 (0.42 H, d, *J* 6.6, OCH*H*O), 4.73 (0.58 H, d, *J* 6.6, OCH*H*O), 5.51 (0.58 H, t, *J* 6.2, 1'-H), 5.56 (0.42 H, t, *J* 6.3, 1'-H), 7.55-7.65 (2 H, m, ArH), 8.00 (1 H, m, ArH) and 8.21 (1 H, m, ArH); $\delta_C$ (125 MHz) -3.3, -3.3, 0.0, 7.0, 8.6, 13.4, 19.5, 19.5, 19.8, 20.0, 24.9, 24.9, 26.1, 26.2, 27.3, 27.3, 39.0, 39.0, 40.1, 41.9, 42.0, 42.1, 42.1, 61.3, 61.5, 62.3, 62.3, 66.9, 67.1, 67.5, 68.1, 72.0, 72.2, 80.2, 80.4, 81.4, 81.4, 97.7, 123.8, 126.9, 129.0, 129.3, 131.8, 132.0, 136.7, 136.9, 138.2, 154.1 and 169.5; *m/z* (ES) 1025 ($M^+$ + 23, 100), 710 (38), 578 (78), 466 (23), 446 (29) and 398 (55).

**2-[(3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-(*tert*-butyldimethylsilyloxy)-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-tri*iso*propylsilyloxyethylidene]-9-(2-trimethylsilylethoxy)methoxyundecanylsulfonyl]benzothiazole 4[13]**

2,6-Lutidine (23 μL, 0.196 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (22 μL, 0.098 mmol) were added to the undecanol **27** (49 mg, 0.049 mmol) in DCM (0.5 mL). The solution was stirred at rt for 2 h then partitioned between ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with ether (3 x 10 mL), and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (20 : 1 petrol : ether) of the residue afforded the *title compound* **4** (51 mg, 93%), a colourless oil, a 58:42 mixture of epimers, $R_f$ = 0.35 (9 : 1, petrol : ether), $[\alpha]_D^{28}$ –13.3 (*c* 1.1, $CHCl_3$); $\nu_{max}$ (film)/$cm^{-1}$ 2954, 2865, 1472, 1463, 1331, 1250, 1151, 1101, 1058, 856, 835, 774, 759 and 729; $\delta_H$ (500 MHz) 0.00 [9 H, s, $Si(CH_3)_3$], 0.01-0.07 (12 H, overlapping s, 4 x $SiCH_3$), 0.55 (3.48 H, q, *J* 8.1, 3 x $SiCH_2CH_3$), 0.57 (2.52 H, q, *J* 8.1, 3 x $SiCH_2CH_3$), 0.80-0.98 (2 H, m, $OCH_2CH_2Si$), 0.84 [7.56 H, s, 2 x $SiC(CH_3)_3$], 0.86 [10.44 H, s, 2 x $SiC(CH_3)_3$], 0.89 (5.22 H, t, *J* 8.0, 3 x $SiCH_2CH_3$), 0.90 (3.78 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.00 (1.26 H, d, *J* 6.3, 11'-$H_3$), 1.01 (1.74 H, d, *J* 6.3, 11'-$H_3$), 1.01-1.13 [21 H, m, 3 x $SiCH(CH_3)_2$],1.23 and 1.27 (each 1.26 H, s, 2'-$CH_3$), 1.24 and 1.29 (each 1.74 H, s, 2'-$CH_3$), 1.40 (1 H, m, 8'-H), 1.53 (1 H, m, 8'-H'), 1.82 (0.58 H, dd, *J* 14, 9.2, 4'-H), 1.88 (0.42 H, dd, *J* 14.2, 8.5, 4'-H), 2.07 (0.42 H, dd, *J* 13.0, 8.3, 6'-H), 2.15-2.24 (1.16 H, m, 6'-$H_2$), 2.28 (0.42 H, dd, *J* 12.9, 5.4, 6'-H'), 2.29-2.35 (1 H, m, 4'-H'), 3.43 (1 H, m, OC*H*H$CH_2Si$), 3.49-3.58 (2 H, m, 1'-H and 9'-H), 3.60 (0.58 H, d, *J* 9.0, 3'-H), 3.64 (0.42 H, dd, *J* 8.5, 2.5, 3'-H), 3.66-3.73 (1 H, m, OCH*H*$CH_2Si$), 3.75 (0.58 H, d, *J* 14.2, 1'-H'), 3.75 (0.42 H, d, *J* 14.2, 1'-H'), 3.77-3.88 (1 H, m, 7'-H), 4.06 (1 H, m, 10'-H), 4.23-4.32 (2 H, m, 2"-$H_2$), 4.63-4.71 (2 H, m, $OCH_2O$), 5.41 (0.58 H, t, *J* 5.7, 1"-H), 5.43 (0.42 H, t, *J* 5.7, 1"-H), 7.54-7.64 (2 H, m, ArH), 8.00 (1 H, m, ArH) and 8.19 (1 H, m, ArH); $\delta_C$ (125 MHz) -3.4, -3.4, -3.3, -3.3, -2.9, -2.3, -2.1, 0.0, 6.9, 7.0, 8.6, 13.4, 18.3, 18.5, 19.5, 19.5, 19.6, 24.7, 24.7, 26.2, 26.4, 27.3, 27.4, 27.4, 36.4, 36.9, 40.9, 41.6, 41.8, 42.0, 42.1, 42.8, 62.0, 62.1, 62.1, 62.2, 66.6, 66.6, 69.8,

70.0, 70.1, 70.2, 80.3, 81.0, 81.6, 81.7, 97.6, 97.7, 123.8, 126.9, 126.9, 129.0, 129.3, 132.4, 133.2, 134.4, 134.6, 138.2, 154.1, 169.5 and 169.5; *m/z* (ES) 1139 ($M^+$ + 23, 95), 1134 ($M^+$ + 18, 100), 629 (25) and 590 (24).

**(2*R*,3*R*,5*S*,9*RS*)-11-(Benzothiazol-2-ylsulfonyl)-2,5-bis-(*tert*-butyldimethylsilyloxy)-10,10-dimethyl-9-triethylsilyloxy-7-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]undecan-3-ol 28**

$K_2CO_3$ (155 mg, 1.12 mmol), *n*-butanethiol (0.102 mL, 0.95 mmol) and $MgBr_2.OEt_2$ (243 mg, 0.85 mmol) were added to the SEM-ether **4** (125 mg, 0.112 mmol) in $Et_2O$ (2.5 mL). The mixture was stirred vigorously at rt for 1 h before partitioning between ether (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The aqueous phase was extracted with ether (2 x 20 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (50 : 1 then 9 : 1 petrol : ethyl acetate) of the residue afforded the *title compound* **28** (106 mg, 96%), a colourless oil, a 50:50 mixture of epimers, $R_f$ = 0.31 (4 : 1 petrol : ethyl acetate), $[\alpha]_D^{24}$ +4.2 (*c* 2.1, $CHCl_3$) (Found: $M^+$ + Na, 1008.5555. $C_{49}H_{95}O_7NS_2Si_4Na$ requires *M*, 1008.5519); $\nu_{max}$ (film)/$cm^{-1}$ 3565, 2946, 2864, 1471, 1463, 1331, 1257, 1151, 1084, 1006, 836, 776 and 729; $\delta_H$ (500 MHz, $C_6D_6$) 0.00, 0.02, 0.03, 0.04, 3 x 0.26, 0.28 (each 1.5 H, s, $SiCH_3$), 0.69-0.77 (6 H, m, 3 x $SiCH_2CH_3$), 0.90, 0.91, 1.02, 1.05 [each 4.5 H, s, $SiC(CH_3)_3$], 1.06 (9 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.10-1.19 [24 H, m, 3 x $SiCH(CH_3)_2$ and 1-$H_3$], 1.33, 1.33, 1.35, 1.44 (each 1.5 H, s, 10-$CH_3$)$_2$), 1.55 (1 H, m, 4-H), 1.77 (1 H, m, 4-H'), 1.93 (0.5 H, dd, *J* 13.9, 9.5, 8-H), 2.10 (0.5 H, dd, *J* 13.9, 8.8, 8-H), 2.45-2.55 (2.5 H, m, 6-H, 8-H' and 3-OH), 2.56 (0.5 H, dd, *J* 13.6, 6.0, 6-H), 2.60 (0.5 H, dd, *J* 13.6, 8.8, 6-H'), 2.69 (0.5 H, dd, *J* 13.2, 6.3, 6-H'), 3.57 (1 H, m, 2-H), 3.68 and 3.73 (each 0.5 H, d, *J* 14.2, 11-H), 3.77 (1 H, m, 3-H), 3.92 (0.5 H, d, *J* 14.2, 11-H'), 3.99 (1 H, m, 9-H), 4.07 (0.5 H, d, *J* 14.2, 11-H'), 4.39 (1 H, m, 5-H), 4.49 (0.5 H, dd, *J* 12.6, 5.4, 7-CHC*H*H), 4.54 (1 H, m, 2 x 7-CHC*H*H), 4.60 (0.5 H, dd, *J* 12.6, 6.3, 7-CHCH*H*), 5.68 (0.5 H, t, *J* 5.8, 7-CH), 5.73 (0.5 H, t, *J* 5.8, 7-CH), 6.88 (1 H, m, ArH), 7.01-7.08 (2 H, m, ArH) and 7.96-8.01 (1 H, m, ArH); $\delta_C$ (100 MHz, $CDCl_3$) -5.8, -5.7, -5.2, -5.2, -5.1, 4.5, 4.5, 6.2, 11.0, 17.0, 17.0, 18.9, 18.9, 22.3, 22.3, 23.7, 23.8, 24.8, 24.9, 38.2, 39.1, 39.4, 39.4, 39.5, 39.6, 39.7, 59.4, 59.5, 59.8, 59.9, 67.7, 67.9, 70.9, 71.1, 71.1, 78.0, 78.3, 121.3, 124.4, 126.5, 126.9, 130.0, 130.4, 132.4, 132.5, 135.7, 135.8, 151.7, 167.0 and 167.1; *m/z* (ES) 1008 ($M^+$ + 23, 100%).

**2-[(3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-trimethylsilyloxyundecan-1-ylsulfonyl]benzothiazole 29**

Triethylamine (0.30 mL, 2.15 mmol) and chlorotrimethylsilane (0.068 mL, 0.537 mmol) were added to the alcohol **28** (106 mg, 0.107 mmol) in DCM (2.14 mL) at 0 °C. The solution was allowed to warm to rt and was stirred for 3 h before partitioning between ethyl acetate (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The aqueous phase was extracted with ethyl acetate (2 x 20 mL) and the organic extracts were dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography (1% $NEt_3$ in petrol) of the residue afforded the *title compound* **29** (115 mg, 100%), a colourless oil, a 50 : 50 mixure of epimers, $R_f$ = 0.45 (4 : 1, petrol : ethyl acetate), $[\alpha]_D^{24}$ +8.7 (*c* 2.4, $CHCl_3$) (Found: $M^+$ + Na, 1080.5933. $C_{52}H_{103}O_7NS_2Si_5Na$ requires *M*, 1080.5915); $\nu_{max}$ (film)/$cm^{-1}$ 2956, 2865, 1473, 1464, 1331, 1251, 1151, 1093, 1062, 1006, 837 and 775; $\delta_H$ (500 MHz, $C_6D_6$) -0.02, 0.00, 0.02, 0.04, 0.125, 0.13, 0.14, 0.15 (each 1.5 H, s, $SiCH_3$), 0.10 and 0.12 [each 4.5 H, s, $Si(CH_3)_3$], 0.61 (6 H, q, *J* 7.9, 3 x $SiCH_2CH_3$), 0.88, 0.91, 0.925, 0.935 [each 4.5 H, s, $SiC(CH_3)_3$], 0.94 and 0.95 (each 4.5 H, t, *J* 7.9, 3 x $SiCH_2CH_3$), 1.02-1.10 [22.5 H, m, 3 x $SiCH(CH_3)_2$ and 11'-$H_3$), 1.12 (1.5 H, d, *J* 6.3, 11'-$H_3$), 1.22, 1.24, 1.27, 1.37 (each 1.5 H, s, 2'-$CH_3$), 1.54-1.82 (2.5 H, m, 8'-$H_2$ and 4'-H), 1.93 (0.5 H, dd, *J* 14.2, 8.5, 4'-H), 2.31 (0.5 H, dd, *J* 12.9, 8.8, 6'-H), 2.32-2.38 (1 H, m, 4'-H'), 2.42 (1 H, d, *J* 7.3, 6'-H), 2.49 (0.5 H, dd, *J* 12.9, 5.5, 6'-H'), 3.56 and 3.66 (each 0.5 H, d, *J* 14.5, 1'-H), 3.77 (0.5 H, dd, *J* 8.5, 2.5, 3'-H), 3.79-3.98 (3.5 H, m, 1'-H', 3'-H, 9'-H and 10'-H), 4.00 and 4.05 (each 0.5 H, m, 7'-H), 4.37-4.51 (2 H, m, 5'-CHC$H_2$), 5.52 and 5.58 (each 0.5 H, t, *J* 5.7, 5'-CH), 6.81 (1 H, m, ArH), 6.93-7.00 (2 H, m, ArH) and 7.85 (1 H, m, ArH); $\delta_C$ (100 MHz, $C_6D_6$) -5.5, -5.5, -4.8, -4.2, -4.1, 0.0, 0.1, 4.9, 5.0, 6.5, 11.3, 15.7, 16.0, 17.2, 17.3, 17.3, 17.3, 22.4, 22.7, 23.7, 24.1, 25.1, 25.2, 25.3, 36.1, 37.0, 39.1, 39.5, 39.7, 39.8, 39.8, 40.9, 59.7, 59.9, 60.1, 60.2, 68.1, 68.5, 69.8, 70.0, 71.9, 72.0, 77.5, 78.1, 121.3, 124.2, 124.2, 126.2, 126.4, 130.2, 131.2, 132.7, 132.8, 135.8, 135.8, 152.0, 168.5 and 168.5; *m/z* (ES) 1080 ($M^+$ + 23, 100%).

**Prop-2-enyl (3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-25-hydroxy-13,21-bis-[(*Z*)-2-tri*iso*propylsilyloxyethyl-idene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enoate 32**

$SO_3$.py complex (146 mg, 0.912 mmol) was added to the tetrahydropyranylmethanol **15** (190 mg, 0.228 mmol), DMSO (162 μL, 2.28 mmol) and DIPEA (278 μL, 1.60 mmol) in DCM (2.28 mL) at room temperature. The mixture was stirred for 1 h and partitioned between saturated aqueous $NaHCO_3$ (20 mL) and DCM (20 mL). The aqueous phase was extracted with DCM (2 x 20 mL) and the organic extracts were washed with brine (20 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure. The residue was passed through a short silica column (20% EtOAc:petrol, 1% $Et_3N$) to afforded the aldehyde **30** (190 mg) as a pale oil $R_f$ 0.50 (streak) (30% EtOAc/petrol); $\delta_H$ (400 MHz; $C_6D_6$) 0.27 (6 H, s, 2 x $SiCH_3$), 1.11 [9 H, s, $SiC(CH_3)_3$], 1.17-1.30 [21 H, m, 3 x $SiCH(CH_3)_2$], 1.32 and 1.40 (each 3 H, s, 8-$CH_3$), 1.57 (1 H, q, *J* 12.1, 6-$H_{ax}$), 1.78-2.04 (6 H, m, 4-$H_2$, 6-$H_{eq}$, 10-H, 12-$H_{ax}$, and 14-$H_{ax}$), 2.30-2.40 (2 H, m, 10-H' and 12-$H_{eq}$), 2.72 (1 H, dd, *J* 15.1, 7.3, 2-H), 2.78 (1 H, dd, J 15.1, 4.8, 2-H'), 2.87 (1 H, d, *J* 12.9, 14-$H_{eq}$), 3.28 (3 H, s, 9-$OCH_3$), 3.69 (1 H, dd, *J* 11.9, 2.8, 15-H), 3.82-3.91 (2 H, m, 5-H and 11-H), 3.92 (1 H, dd, *J* 11.6, 4.5, 7-H), 4.32-4.45 (3 H, m, PhHC*H* and 13-CHC$H_2$), 4.57 (1 H, d, *J* 11.6, PhHC*H*'),4.60-4.68 (3 H, m, 1'-$H_2$ and 3-H), 5.13 (1 H, dq, *J* 10.4, 1.2, 3'-H), 5.28 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.73 (1 H, t, *J* 6.3, 13-CH), 5.90 (1 H, ddt, *J* 17.2, 10.5, 5.7, 2'-H), 7.22 (1 H, m, ArH), 7.28-7.33 (2 H, m, ArH), 7.44 (2 H, d, *J* 7.3, ArH) and 9.71 (1 H, s, 16-H).

LiHMDS (1.0 M in THF, 343 μL, 0.343 mmol) was added dropwise to the sulfone **29** (363 mg, 0.343 mmol) in THF (3.5 mL) at -78 °C and the yellow solution stirred at -60 °C for 30 min. The reaction mixture was cooled to -78 °C before addition of a solution of the aldehyde **30** (190 mg, 0.229 mmol) in THF (2.34 mL). The solution was stirred for 1 h, allowed to warm to rt and stirred for a further 20 min. The mixture was then partitioned between EtOAc (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The aqueous phase was extracted with EtOAc (2 x 20 mL) and the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure to give the alkene **31** containing the excess of sulfone **29** (combined mass 390 mg); $\delta_H$ (400 MHz; $C_6D_6$) peaks attributed to the alkene 0.00 and 0.04 (each 3 H, s, $SiCH_3$), 0.07 (6 H, s, 2 x $SiCH_3$), 0.13 and 0.15 (each 3 H, s, $SiCH_3$), 0.29-0.32 (9 H, m, 3 x $SiCH_3$), 0.75-0.85 (6 H, m, 3 x $SiCH_2CH_3$), 1.02-1.03 [18 H, m, 2 x $SiC(CH_3)_3$], 1.08 [9 H, s, $SiC(CH_3)_3$], 1.11-1.38 (63 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$, 3 x $SiCH_2CH_3$, 6 x $SiCH(CH_3)_2$], 1.49 (1 H, q, *J* 12.3, 6-$H_{ax}$), 1.70-2.80 (17 H, m, 2-$H_2$, 4-$H_2$, 6-$H_{eq}$, 10-$H_2$, 12-$H_2$, 14-$H_2$, 20-$H_2$, 22-$H_2$, and 24-$H_2$), 3.15 (3 H, s, 9-$OCH_3$), 3.60-3.78 (4 H, m, 5-H, 7-H, 11-H and 25-H), 3.80-3.89 (2 H, m, 15-H and 26-H), 3.94 (1 H, dd, *J* 9.6, 3.9, 19-H), 4.05 (1 H, m, 23-H), 4.17 (1 H, d, *J* 11.6, PhHC*H*), 4.26-4.53 (8 H, m, 1'-$H_2$, 3-H, PhHC*H*', 13- and 21-CHC$H_2$), 4.93 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.09 (1H, dq, *J* 17.2, 1.5, 3'-H'), 5.58 (1 H, dd, *J* 16.0, 5.4, 16-H), 5.58-5.65 (2 H, m, 13- and 21-CH), 5.72 (1 H, ddt, *J* 17.2, 10.6, 5.7, 2'-H), 5.96 (0.6 H, d, *J* 16.0, 17-H), 6.05 (0.4 H, d, *J* 16.0, 17-H), 6.99 (1 H, t, *J*, 7.3, ArH), 7.04-7.10 (2 H, m, ArH) and 7.19-7.25 (2 H, m, ArH).

Pyridinium toluene 4-sulfonate (7 mg, 0.027 mmol) was added to the mixture of alkene **31** and sulfone **29** (390 mg) and trimethyl orthoformate (594 μL) in DCM/methanol (1:1, 4.18 mL). The solution was stirred at room temperature for 1 h before partitioning between DCM (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The aqueous phase was extracted with EtOAc (2 x 20 mL) and the organic extracts were dried ($Na_2SO_4$) then concentrated under reduced pressure. Chromatography (0→2% EtOAc:petrol, 1% $Et_3N$) of the residue afforded the *title compound* **32** (220 mg, 60% over 3 steps), as a pale yellow oil, a 3 : 2 mixture of epimers $R_f$ 0.21 (6 % EtOAc/petrol), $[\alpha]_D^{24}$ +20.4 (*c* 2.05, $CH_2Cl_2$); $\nu_{max}$ (film)/$cm^{-1}$ 3561, 2952, 2865, 1741, 1463, 1382, 1359, 1256, 1088, 1005, 882, 836 and 776; $\delta_H$ (500 MHz; $C_6D_6$) -0.01, 0.00, 0.01 and 0.03 (each 1.5 H, s, $SiCH_3$), 0.14 (6 H, s, 2 x $SiCH_3$), 0.26 and 0.27 (each 3 H, s, $SiCH_3$), 0.70-0.79 (6 H, m, 3 x $SiCH_2CH_3$), 0.90, 0.97 and 1.03 [each 9 H, s, $SiC(CH_3)_3$], 1.05-1.36 [66 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$, 3 x $SiCH_2CH_3$ and 6 x $SiCH(CH_3)$], 1.40-1.58 (2 H, m, 6-H and 24-H), 1.67-2.74 (17 H, m, 2-$H_2$, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-$H_2$, 20-$H_2$, 22-$H_2$, 24-H' and OH), 3.22 (1.8 H, s, $OCH_3$), 3.23 (1.2 H, s, $OCH_3$), 3.55 (1 H, m, 26-H), 3.67-3.85 (5 H, m, 5-H, 7-H, 11-H, 19-H and 25-H), 3.91 (1 H, m, 15-H), 4.25 (1 H, d, *J* 11.7, PhHC*H*), 4.31-4.58 (9 H, m, 1'-$H_2$, 3-H, PhHC*H*', 23-H, 13-CHC$H_2$ and 21-CHC$H_2$), 5.01 (1 H, d, *J* 10.4, 0.6, 3'-H), 5.16 (1 H, dd, *J* 17.3, 1.3, 3'-H'), 5.57-5.74 (3 H, m, 16-H, 13-CH and 21-CH), 5.79 (1 H, m, 2'-H), 6.02 (0.6 H, d, *J* 15.8, 17-H), 6.07 (0.4, d, *J* 15.8, 17-H), 7.06 (1 H, m, ArH), 7.12-7.18 (2 H, m, ArH) and 7.27 (2 H, d, *J* 7.6, ArH); $\delta_C$ (100 MHz; $C_6D_6$) -6.1, -6.1, -5.8, -5.7, -5.5, -5.5, -5.5, -5.2, -5.1, 4.7, 4.8, 6.3, 11.0, 11.1, 12.9, 15.6, 16.7, 16.8, 16.9, 17.0, 18.7, 18.8, 19.9, 21.3, 22.4, 22.6, 22.7, 22.9, 23.2, 24.6, 24.7, 24.9, 24.9, 32.4, 34.4, 34.7, 37.8, 38.2, 38.6, 39.1, 39.3, 39.8, 40.0, 40.4, 40.4, 40.5, 40.8, 42.3, 42.6, 42.7, 43.8, 47.0, 58.5, 59.6, 59.7, 63.7, 65.2, 67.3, 67.6, 67.9, 70.3, 70.9, 70.9, 71.1, 71.3, 74.0, 76.8, 77.4, 77.6, 78.2, 103.3, 116.6, 122.8, 122.9, 126.1, 126.2, 127.1, 127.2, 127.3, 127.3, 127.5, 127.6, 127.8, 129.1, 129.4, 129.7, 131.4, 133.8, 134.0, 135.2, 135.3, 136.7, 137.0, 138.5, 169.5 and 169.5; *m/z* (ES) 1624 ($M^+$ + 23, 100%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-13,21-bis-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide 34**

$Pd(PPh_3)_4$ (16 mg, 10 mol%) was added to the allyl ester **32** (220 mg, 0.137 mmol) and morpholine (120 μL, 1.37 mmol) in THF (3.43 mL) at room temperature. The mixture was stirred for 16 h then partitioned between pH 4.6 acetate buffer (20 mL) and DCM (20 mL). The aqueous phase was extracted with DCM (2 x 20 mL) and the organic extracts dried ($Na_2SO_4$) then concentrated under reduced pressure to leave the hydroxy-acid **33**, as a pale yellow oil, a 60 : 40 mixture of epimers, $R_f$ 0.11 (6% EtOAc/petrol); $\delta_H$ (500 MHz; $C_6D_6$) -0.02-0.05 (6 H, m, 2 x $SiCH_3$), 0.15 and 0.17 (each 3 H, s, $SiCH_3$), 0.24-0.30 (6 H, m, 2 x $SiCH_3$), 0.70-0.79 (6 H, m, 3 x $SiCH_2CH_3$), 0.90 [9 H, s, $SiC(CH_3)_3$], 0.98 and 1.03 (each 9 H, s, 2 x $SiC(CH_3)_3$], 1.05-1.35 [66 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$, 3 x $SiCH_2CH_3$ and 6 x $SiCH(CH_3)_2$], 1.40-1.55 (2 H, m, 6-H and 24-H), 1.68-2.82 (17 H, m, 2-$H_2$, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-$H_2$, 20-$H_2$, 22-$H_2$, 24-H and 25-OH), 3.18 (1.2 H, s, 9-$OCH_3$), 3.20 (1.8 H, s, 9-$OCH_3$), 3.31 (1 H, m, 19-H), 3.57 (1 H, m, 26-H), 3.71-3.87 (5 H, m, 5-H, 7-H, 11-H and 25-H), 3.98 (1 H, m, 15-H), 4.21 (1 H, d, *J* 11.6, PhHC*H*), 4.24-4.58 (7 H, m, 3-H, PhHC*H*', 23-H, 13- and 21-CHC$H_2$), 5.61-5.76 (3 H, m, 16-H, 13- and 21-CH), 6.05 (1 H, m, 17-H), 7.06 (1 H, m, ArH), 7.11-7.18 (2 H, m, ArH) and 7.27 (2 H, d, *J* 7.3, ArH).

$Et_3N$ in THF (0.1 M, 13.8 mL, 1.376 mmol) was added to this *seco*-acid **33** in THF (3.45 mL) at 0 °C followed by 2,4,6-trichlorobenzoyl chloride in THF (0.1 M, 6.88 mL, 0.688 mmol). The mixture was stirred at room temperature for 16 h then diluted with toluene/THF (3:1, 75 mL) and added *via* syringe-pump to a stirred solution of DMAP (336 mg) in toluene (92 mL) at 40 °C over 12 h. The residual contents of the syringe were rinsed into the reaction flask with toluene (29 mL) and stirring continued for an additional 2 h. The reaction mixture was cooled to room temperature and washed with saturated aqueous $NaHCO_3$ (2 x 50 mL) and brine (100 mL). The organic phase was dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (0→2% EtOAc/petrol) of the residue gave the *title compound* **34** (180 mg, 85%) as a pale yellow oil, 50 : 50 mixture of epimers, $R_f$ 0.29 (6% EtOAc/petrol), $[\alpha]_D^{24}$ 20.2 (*c*, 2.33, $CH_2Cl_2$); $\nu_{max}$ (film)/$cm^{-1}$ 2956, 2864, 1734, 1463, 1381, 1361, 1255, 1088, 1013, 1005, 882, 836, 775 and 736; $\delta_H$ (500 MHz; $C_6D_6$) 0.04, 0.05, 0.09 and 0.10 (each 1.5 H, s, $SiCH_3$), 0.13 and 0.14 (each 3 H, s, 2 x $SiCH_3$), 0.22, 0.23, 0.25 and 0.26 (each 1.5 H, s, $SiCH_3$), 0.63 (6 H, m, 3 x $SiCH_2CH_3$), 0.92 [18 H, s, 2 x $SiC(CH_3)_3$], 0.95-1.17 [75 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$, 3 x $SiCH_2CH_3$, $SiC(CH_3)_3$ and 6 x $SiCH(CH_3)_2$], 1.36 (1 H, m, 6-H), 1.56-2.46 (14 H, m, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-H, 20-$H_2$, 22-$H_2$ and 24-$H_2$), 2.52 (1 H, dd, *J* 16.1, 7.6, 2-H), 2.60 (1 H, d, *J*, 13.6, 14-H'), 2.78 (1 H, dd, *J* 16.1, 3.2, 2-H'), 3.19 (2.1 H, s, $OCH_3$), 3.20 (0.9 H, s, $OCH_3$), 3.64 (1 H, m, 19-H), 3.68-3.80 (4 H, m, 5-H, 7-H, 11-H and 15-H), 3.94 (1 H, m, 23-H), 4.07 (1 H, m, 26-H), 4.14 (1 H, d, *J* 12.0, PhHC*H*), 4.16-4.50 (6 H, m, 3-H, PhHC*H*', 13-CHC$H_2$ and 21-CHC$H_2$), 5.12 (0.3 H, m, 25-H), and 5.17 (0.7 H, m, 25-H), 5.47-5.60 (3 H, m, 16-H, 13-CH and 21-CH), 5.75 (0.3 H, d, *J* 15.9, 17-H), 5.92 (0.7 H, d, *J* 16.0, 17-H), 6.99 (1 H, m, ArH), 7.08 (2 H, t, *J*, 7.6, ArH) and 7.21 (2 H, d, *J* 7.3, ArH); $\delta_C$ (100 MHz; $C_6D_6$) -5.9, -5.8, -5.7, -5.6, -5.5 (2), -5.3, -5.2, -5.1, 4.6 (2), 4.7, 6.2, 9.8, 11.0, 11.1, 16.5, 16.6, 16.7, 16.9, 17.0, 17.1, 19.7, 19.8, 21.7, 22.0, 22.8, 24.6, 24.8 (2), 24.9, 25.0, 25.1, 26.0, 27.9, 28.8, 29.4, 32.6, 32.8, 33.8, 34.2, 34.6, 34.9, 37.8, 38.5, 39.0, 39.1, 39.2, 39.5, 40.3, 40.5, 41.1, 41.2, 42.0, 42.1, 42.6, 44.6, 44.8, 47.9, 48.0, 58.4, 59.7, 59.8, 65.2, 65.5, 66.6, 67.1 (2), 67.2 (2), 67.9, 70.2, 70.3, 73.5, 73.6 (2), 76.1, 76.2, 77.1, 78.3, 80.1, 102.8, 102.9, 123.1, 126.1 (2), 126.2 (2), 127.1, 127.1 (2), 127.3, 127.4, 127.4, 127.5, 127.7, 127.8, 128.3, 128.5, 129.4, 129.9, 132.0, 132.7, 132.9, 133.5, 134.3, 134.9, 135.9, 137.0, 137.9, 135.5, 169.6 and 167.7; *m/z* (ES) 1566 ($M^+$ + 23, 8%) and 413 (100%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-13,21-bis-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide 35**

Pyridinium toluene 4-sulfonate (PPTS) (0.65 mg, 10 mol%) in DCM/methanol (1:1, 394 μL), taken from PPTS (6.5 mg) in DCM (1.97 mL) and methanol (1.97 mL), and trimethyl orthoformate (56 μL) were added to the triethylsilyl ether **34** (40 mg, 0.026 mmol). The solution was stirred at room temperature for 48 h before partitioning between DCM (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with DCM (2 x 10 mL) and the organic extracts dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (2→6% EtOAc:petrol, 1% $Et_3N$) of the residue afforded the *title compound* **35** (20 mg, 54%) as a pale oil, a 50 : 50 mixture of epimers, $R_f$ 0.36 and 0.29 (10% EtOAc/petrol), $[\alpha]_D^{24}$ 26.7 (c, 1.42, $CH_2Cl_2$); $\nu_{max}$ (film)/$cm^{-1}$ 3564, 2957, 2864, 1738, 1658, 1463, 1382, 1362, 1259, 1091, 882, 835, 806, 776

and 682; $\delta_H$ (500 MHz; $C_6D_6$) 0.09 (3 H, s, $SiCH_3$), 0.12 and 0.12 (each 1.5 H, s, $SiCH_3$), 0.15-0.18 (9 H, overlapping s, 3 x $SiCH_3$), 0.21 and 0.24 (each 1.5 H, s, $SiCH_3$), 0.91-1.22 [84 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$, 3 x $SiC(CH_3)_3$ and 6 x $SiCH(CH_3)_2$], 1.41 (1 H, m, 6-H), 1.58-2.68 (17 H, m, 2-H, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-$H_2$, 19-OH, 20-$H_2$, 22-$H_2$ and 24-$H_2$), 2.81 (1 H, m, 2-H'), 3.19 and 3.21 (each 1.5 H, s, $OCH_3$), 3.31 (0.5 H, d, *J* 11.0, 19-H), 3.38 (0.5 H, d, *J* 10.4, 19-H), 3.70-3.85 (4 H, m, 5-H, 7-H, 11-H and 15-H), 4.00 (1 H, m, 23-H), 4.07 and 4.11 (each 0.5 H, m, 26-H), 4.18 (1 H, d, *J* 11.7, PhHC*H*), 4.25-4.54 (7 H, m, 3-H, PhHC*H*', 13-CHC$H_2$ and 21-CHC$H_2$), 5.14 (0.5 H, dd, *J* 9.4, 3.2, 25-H), 5.19 (0.5 H, dd, *J* 9.7, 3.7, 25-H), 5.49 (0.5 H, dd, *J* 15.8, 5.7, 16-H), 5.49-5.55 (1 H, m, 13-CH or 21-CH), 5.55 (0.5 H, dd, *J* 15.8, 5.0, 16-H), 5.63 (1 H, m, 13-CH or 21-CH), 5.86 (0.5 H, d, *J* 16.0, 17-H), 5.96 (0.5 H, d, *J* 15.8, 17-H), 7.02 (1 H, m, ArH), 7.11 (2 H, t, *J*, 7.5, ArH) and 7.24 (2 H, d, *J* 7.6, ArH); $\delta_C$ (100 MHz; $C_6D_6$) -6.0, -5.9 (3), -5.6 (2), -5.5, -5.3, -5.2, -5.1, -5.0, 11.0 (4), 12.9, 16.5, 16.6, 16.7, 17.0, 19.7, 20.8, 21.3, 21.7, 22.1 (2), 24.0, 24.7 (2), 24.8 (2), 24.9, 28.8, 32.8, 33.0, 34.1, 34.4 (2), 34.7, 38.6, 39.1 (3), 39.2 (2), 39.3, 39.8, 41.1, 42.0, 42.4, 42.7, 44.9, 45.0, 47.9 (2), 51.9, 58.3, 58.4, 59.3, 59.4, 64.9, 65.0, 66.7 (2), 66.9, 67.0, 68.0 (2), 68.3, 70.2, 72.8, 73.3, 73.4, 73.5, 74.7, 76.1, 76.2, 76.8, 77.1, 102.8 (2), 123.1 (2), 126.0 (2), 126.1 (2), 127.1, 127.3 (2), 128.2, 128.6, 129.4, 129.9, 134.2, 134.4, 134.8, 135.0, 137.1, 137.3, 138.5, 169.7 and 169.9; *m/z* (ES) 1453 ($M^+$ + 23, 67%) and 413 (100%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-13,21-bis-[(*Z*)-2-tri*iso*propylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide 36**

TPAP (0.25 mg, 5 mol%) was added to the alcohol **35** (20 mg, 0.014 mmol), NMO (8 mg, 0.07 mmol) and 4Å molecular sieves (32 mg) in DCM (322 μL). After stirring for 4 h additional NMO (8 mg, 0.07 mmol) and TPAP (0.25 mg) were added and the mixture stirred for a further 2 h. After addition of saturated aqueous $Na_2S_2O_3$ (5 mL) and saturated aqueous $NaHCO_3$ (5 mL) with stirring for a further 10 min, the mixture was partitioned with DCM (10 mL). The aqueous phase was extracted with DCM (2 x 10 mL) and the organic extracts were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (5→10% EtOAc:petrol) of the residue afforded the *title compound* **36** (10 mg, 50%) as a pale oil, $R_f$ 48 (10% EtOAc/petrol), $[\alpha]_D^{24}$ 12.5 (*c*, 1.60, $CH_2Cl_2$) (Found: $M^+$ + $NH_4$, 1445.0001. $C_{79}H_{150}O_{12}NSi_5$ requires *M*, 1444.9999); $\nu_{max}$ (film)/$cm^{-1}$ 2929, 1733, 1716, 1470, 1463, 1380, 1361, 1259, 1091, 881, 835, 807, 776 and 683; $\delta_H$ (400 MHz; $C_6D_6$) 0.19 (6 H, s, 2 x $SiCH_3$), 0.26, 0.27, 0.30 and 0.33 (each 3 H, s, $SiCH_3$), 1.04, 1.05 and 1.09 [each 9 H, s, $SiC(CH_3)_3$], 1.00-1.38 [57 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$ and 6 x $SiCH(CH_3)_2$], 1.49 (1 H, q, *J* 12.1, 6-$H_{eq}$), 1.75-2.11 (8 H, m, 4-$H_2$, 6-$H_{ax}$, 10-H, 12-$H_{ax}$, 14-$H_{ax}$, 24-$H_2$), 2.15 (1 H, d, *J* 13.1, 12-$H_{eq}$), 2.26 (1 H, dd, *J* 16.5, 6.6, 10-H'), 2.55-2.70 (3 H, m, 2-H, 14-$H_{eq}$ and 22-H), 2.81 (1 H, dd, *J* 13.5, 4.5, 22-H'), 2.94 (1 H, dd, *J* 15.6, 3.7, 2-H'), 3.25 (2 H, m, 20-$H_2$), 3.29 (3 H, s, $OCH_3$), 3.76-3.90 (4 H, m, 5-H, 7-H, 11-H and 15-H), 4.09 (1 H, m, 23-H), 4.23 (1 H, m, 26-H), 4.27 (1 H, d, *J* 11.9, PhHC*H*), 4.35-4.58 (6 H, m, 3-H, PhHC*H*' 13-CHC$H_2$ and 21-CHC$H_2$), 5.29 (1 H, m, 25-H), 5.58-5.65 (3-H, m, 16-H, 13-CH and 21-CH), 6.03 (1 H, dd, *J* 15.9, 1.26, 17-H), 7.11 (1 H, t, *J* 7.3, ArH), 7.21 (2 H, t, *J* 7.6, ArH) and 7.34 (2 H, d, *J* 7.3, ArH); $\delta_C$ (100 MHz; $C_6D_6$) -5.9, -5.8, -5.7 (2C), -5.2 (2C), 11.0, 11.1, 16.5, 16.9 (2C), 17.0, 20.0, 22.8, 23.0, 24.8 (2C), 25.0, 30.1, 32.9, 34.0, 34.3, 39.1, 39.3, 41.1, 42.0, 42.6, 44.1, 44.8, 47.7, 48.9, 58.4, 59.4, 65.5, 66.9, 67.2, 67.3, 70.2, 73.2, 73.6, 75.7, 77.1, 102.9, 123.3, 126.1, 126.2, 127.1, 129.5, 130.1, 131.6, 134.1, 134.7, 138.5, 169.6 and 207.7; *m/z* (ES) 1445 ($M^+$ + 18, 100%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-13,21-bis-[(*Z*)-2-hydroxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide 37**

TBAF-AcOH in THF [280 μL, 0.28 mmol; from TBAF in THF (1 M, 1 mL) and AcOH (57 μL] was added to the bis-tri-*iso*propylsilyl ether **35** (20 mg, 0.014 mmol) in THF (0.68 mL). The solution was stirred at room temperature for 40 h before partitioning between DCM (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The aqueous phase was extracted with DCM (2 x 10 mL) and the organic extracts dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography (0→40% EtOAc:pentane, 1% $Et_3N$) of the residue afforded the title *compound* **37** (8 mg, 53%) as a pale oil, a 55 : 45 mixture of epimers, $R_f$ 0.24 and 0.17 (50% EtOAc/petrol), $[\alpha]_D^{24}$ 33 (*c*, 1.7, $CH_2Cl_2$) (Found: $M^+$ + $NH_4$, 1134.7533. $C_{61}H_{112}NO_{12}Si_3$ requires *M*, 1134.7487); $\nu_{max}$ (film)/$cm^{-1}$ 3401, 2955, 2929, 2856, 1737, 1732, 1471, 1463, 1380, 1361, 1258, 1091, 1005, 836, 810, 776; $\delta_H$ (500 MHz; $C_6D_6$) 0.00-0.25 (18 H, overlapping s, 6 x $SiCH_3$), 0.87-1.28 [42 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-

$CH_3$ and 3 x $SiC(CH_3)_3$], 1.35 (1 H, m, 6-H), 1.59-2.56 (17 H, m, 2-H, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-$H_2$, 19-OH, 20-$H_2$, 22-$H_2$ and 24-$H_2$), 2.80 (1 H, m, 2-H'), 3.17 (1.35 H, s, 9-$OCH_3$), 3.19 (1.65 H, s, 9-$OCH_3$), 3.24 (1 H, m, 19-H), 3.61-4.11 (10 H, m, 5-H, 7-H, 11-H, 15-H, 23-H, 26-H, 13-CHC*H*$_2$ and 21-CHC*H*$_2$), 4.16 and 4.35 (each 0.45 H, d, *J* 11.7, PhHC*H*), 4.17 and 4.36 (each 0.55 H, d, *J* 11.7, Ph*H*CH), 4.47 (0.55 H, m, 3-H), 4.53 (0.45 H, m, 3-H), 4.97 (0.55 H, m, 25-H), 5.10 (0.45 H, m, 25-H), 5.29 (1 H, t, *J* 6.7, 13- or 21-CH), 5.33-5.52 (2 H, m, 16-H and 13- or 21-CH), 5.80 (0.45 H, d, *J* 16.0, 17-H), 5.88 (0.55 H, d, *J* 16.0, 17-H), 7.00 (1 H, m, ArH), 7.08 (2 H, m, ArH) and 7.21 (2 H, m, ArH); *m/z* (ES) 1135 ($M^+$ + 18, 6%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-9-methoxy-13,21-bis-[(*Z*)-methoxycarbonylmethylidene]-8,8,18,18-tetramethylheptacos-16-enolide 38**

Manganese(IV) oxide (233 mg, 2.68 mmol) was added to the alcohol **37** (5 mg, 0.0045 mmol) in DCM (894 µL) and the reaction mixture was stirred at r.t. for 1 h then filtered through a pad of Celite®. The filter cake was washed with DCM (10 mL) and the filtrate was concentrated under reduced pressure to give the 13,21-bis-formylmethylidene lactone as a pale oil, $R_f$ 0.43 and 0.29 (25% EtOAc/petrol). $NaClO_2$ (4.9 mg, 0.054 mmol) and $NaH_2PO_4.2H_2O$ (14 mg, 0.090 mmol) in $H_2O$ (72 µL) were added to this bis-aldehyde and 2-methyl-2-butene (2 M in THF, 90 µL, 0.180 mmol) in *t*-butanol (135 µL) at r.t. After 1 h, the reaction mixture was partitioned between brine (10 mL) and EtOAc (10 mL) and the aqueous phase was extracted with EtOAc (2 x 10 mL). The organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure to leave the bis-acid as a pale oil, $R_f$ 0.13 (25% EtOAc/petrol). A solution of this bis-acid in methanol (148 µL) and toluene (74 µL) was cooled to 0 °C and (trimethylsilyl)diazomethane (2 M in hexanes, 6.5 µL, 0.0131 mmol) was added dropwise. After stirring for 1 h at 0 °C, the reaction mixture was partitioned between saturated aqueous $NaHCO_3$ (10 mL) and DCM (10 mL). The aqueous phase was extracted with DCM (2 x 10 mL) and the organic extracts were dried ($Na_2SO_4$) and concentrated under reduced pressure. Chromatography of the residue (0→6% EtOAc:pentane, 1% $Et_3N$) afforded the *title compound* **38** (2 mg, 40%) as a pale yellow oil, a 70 : 30 mixture of epimers, $R_f$ 0.38 (25% EtOAc/petrol), $[\alpha]_D^{24}$ 31 (*c*, 0.26, $CH_2Cl_2$); $\nu_{max}$ (film)/$cm^{-1}$ 3523, 2953, 2928, 2855, 1719, 1653, 1647, 1472, 1462, 1437, 1378, 1361, 1257, 1173, 1150, 1091, 836, 809, 776; $\delta_H$ (500 MHz; $C_6D_6$) 0.17-0.35 (18 H, overlapping s, 6 x $SiCH_3$), 1.03-1.11 [27 H, overlapping s, 3 x $SiC(CH_3)_3$], 1.22-1.30 (15 H, m, 27-$H_3$, 2 x 8-$CH_3$, 2 x 18-$CH_3$), 1.48 (1 H, m, 6-H), 1.65-2.40 (15 H, m, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 14-H, 19-OH, 20-$H_2$, 22-$H_2$ and 24-$H_2$), 2.56 (0.7 H, dd, *J* 16.4 and 7.1, 2-H), 2.62 (0.3 H, dd, *J* 16.7 and 7.8, 2-H), 2.79 (0.7 H, dd, *J* 16.4 and 3.8, 2-H'), 2.88 (0.3 H, dd, *J* 16.7 and 3.5, 2-H'), 3.07 (1 H, dd, *J* 12.3, 6.0, 14-H'), 3.23 (1 H, m, 19-H), 3.24 (2.1 H, s, 9-$OCH_3$), 3.29 (0.9 H, s, 9-$OCH_3$), 3.42-3.45 (6 H, overlapping s, 2 x $CO_2CH_3$), 3.58 (1 H, m), 3.71-3.90 (3 H, m), 4.15 (1 H, m, 26-H), 4.23 – 4.39 (2 H, m, 23-H, PhHC*H*), 4.46-4.59 (2 H, m, 3-H and PhHC*H*), 5.31 (0.7 H, m, 25-H), 5.36 (0.3 H, m, 25-H), 5.51 (1 H, dd, *J* 15.8 and 5.5, 16-H), 5.77 (1 H, br. s, 13-CH or 21-CH), 5.81 (0.3 H, d, *J* 15.4, 17-H), 5.90 (0.7 H, d, *J* 15.9, 17-H), 5.93-5.97 (1 H, m, 13-CH or 21-CH), 7.12 (1 H, m, ArH), 7.21 (2 H, m, ArH) and 7.35 (2 H, m, ArH); *m/z* (ES) 1196 ($M^+$ + 23, 18 %) and 1212 ($M^+$ + 39, 7 %).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-9-methoxy-13,21-bis-[(*Z*)-methoxycarbonylmethylidene]-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide 39**

Dess-Martin periodinane (10 mg, 23.6 µmol) and pyridine (19.2 µL, 0.236 mmol) in DCM (1.04 mL) was stirred for 5 min. An aliquot (373 µL, 8.5 µmol) was added to alcohol **38** (2 mg, 1.70 µmol). After stirring for 2 h at r.t. the reaction mixture was partitioned between DCM (10 mL) and a mixture of saturated aqueous $NaHCO_3$ (5 mL) and saturated aqueous $Na_2S_2O_3$ (5 mL). After separation of the organic layer, the aqueous phase was extracted with DCM (2 x 10 mL). The organic extracts were dried ($Na_2SO_4$), filtered and concentrated under reduced pressure to give the *title compound* **39** (~1.5 mg) as a pale oil that was azeotroped with toluene and used immediately,[¶] $R_f$ 0.60 (25% EtOAc/petrol) (Found: $M^+$ + Na, 1193.6759. $C_{63}H_{106}O_{14}Si_3Na$ requires *M*, 1193.6783); $\nu_{max}$ (film)/$cm^{-1}$ 2959, 2927, 2853, 1723, 1651, 1470, 1460, 1432, 1377, 1359, 1259, 1093, 1018, 799; $\delta_H$ (400 MHz; $C_6D_6$) 0.12-0.25 (18 H, m, 6 x $SiCH_3$), 0.97, 0.98 and 1.00 [each 9 H, s, $Si(CH_3)_3$], 1.09-1.30 (15 H, m, 27-$H_3$, 28-$H_3$, 29-$H_3$, 32-$H_3$ and 33-$H_3$), 1.40 (1 H, m, 6-H), 1.60-

[¶] This ketone decomposed to give a mixture of products that were not identified during attempted chromatography using ethyl acetate/pentane (1 : 4) containing 1% triethylamine.

2.25 (10 H, m, 4-$H_2$, 6-H', 10-$H_2$, 12-$H_2$, 22-H and 24-$H_2$), 2.60 (1 H, dd, *J* 16.1 and 7.5, 2-H), 2.81-2.91 (2 H, m, 2-H and 14-$H_{ax}$), 3.15 (1-H, d, *J* 17.2, 20-H), 3.24 (3 H, s, 9-$OCH_3$), 3.31 and 3.38 (each 3 H, s, $CO_2CH_3$), 3.38 (1 H, m, 20-H'), 3.67-3.81 (5 H, m, 5-H, 7-H, 11-H, 15-H and 22-H'), 4.14 (1 H, m, 26-H), 4.18-4.30 (3 H, m, 14-$H_{eq}$, 23-H and Ph*H*CH), 4.42 (1 H, d, *J* 11.9, PhHC*H*), 4.47 (1 H, m, 3-H), 5.24 (1 H, m, 25-H), 5.49 (1 H, dd, *J* 15.9 and 4.8, 16-H), 5.72 and 5.78 (each 3 H, s, 13-CH or 21-CH), 5.86 (1 H, dd, *J* 15.7 and 1.1, 17-H), 7.06 (1 H, m, ArH), 7.16 (2 H, m, 2 x ArH), 7.29 (2 H, m, 2 x ArH); *m/z* (ES) 1194 ($M^+$ + 23, 31%).

**25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*R*,23*S*,25*R*,26*R*,16*E*)-7-Benzyloxy-5,9-epoxy-11,15-epoxy-19,23-epoxy-3,9,19,26-tetrahydroxy-13,21-bis-[(*Z*)-methoxycarbonylmethylidene]-8,8,18,18-tetramethylheptacos-16-enolide 40**

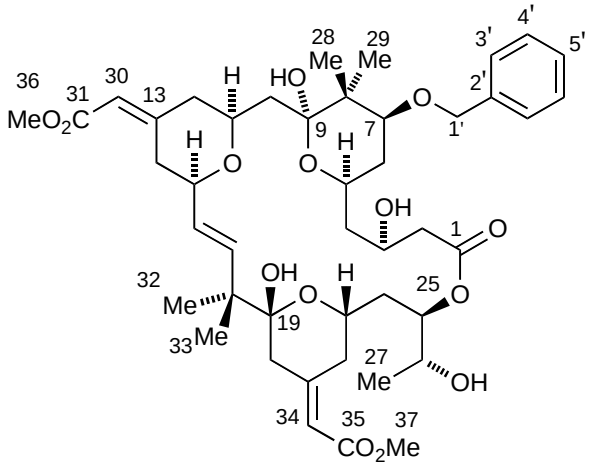
Pyridine (50 µL, 0.618 mmol) was added to the keto bis-ester **39** in THF (376 µL) and the mixture cooled to 0 °C. HF-pyridine (70:30, 18 µL, 0.693 mmol) was added and the mixture stirred at r.t. After 24 h, the mixture was cooled to 0 °C and pyridine (40 µL, 0.497 mmol) was added followed by aqueous hydrogen fluoride (48 % in $H_2O$, 18 µL, 0.497 mmol). The mixture was stirred for 24 h before partitioning between saturated aqueous $NaHCO_3$ (10 mL) and EtOAc (10 mL). After separation of the phases, the aqueous phase was extracted with EtOAc (2 x 10 mL), and the organic extracts were dried ($Na_2SO_4$) then concentrated under reduced pressure. Chromatography on silica (neutralised with aqueous potassium bicarbonate and oven dried) using 20→50% EtOAc:pentane as eluent afforded the *title compound* **40** (*ca.* 0.5 mg; 50% from **38**), as a white solid, $R_f$ 0.73 (80% EtOAc/petrol) (Found: $M^+$ + Na, 837.4030. $C_{44}H_{62}O_{14}Na$ requires *M*, 837.4032); $\nu_{max}$ (film)/$cm^{-1}$ 3459, 3354, 2929, 2853, 1716, 1652, 1436, 1381, 1362, 1279, 1261, 1246, 1230, 1153, 1076, 858, 801, 736, 700; $\delta_H$ (500 MHz; $C_6D_6$) see Table; $\delta_C$ (100 MHz; $C_6D_6$) see Table; *m/z* (ES) 837 ($M^+$ + 23, 100%) and 834 ($M^+$ + 18, 25%).

**Table $^{1}$H and $^{13}$C NMR data for the 20-deoxybryostatin 40 in benzene-$d_6$**

| Position | $^{1}$H (500 MHz) | $^{13}$C (100 MHz) |
|---|---|---|
| 1 | - | 172.9* |
| 2a | 2.18 (1 H, dd, *J* 12.0 and 1.6 Hz) | 42.7 |
| 2b | 2.43 (1 H, t, *J* 12.0 Hz) | - |
| 3 | 4.10 (1 H, br t, *J* 11.9 Hz) | 68.9 |
| 3-OH | 4.47 (1 H, d, *J* 12.3 Hz) | - |
| 4a | 0.99 (1 H, m) | 40.5 |
| 4b | 1.64 (1 H, m) | - |
| 5 | 3.79 (1 H, m) | 66.5 |
| $6_{ax}$ | 1.18 (1 H, m) | 33.7 |
| $6_{eq}$ | 1.33 (1 H, m) | - |
| 7 | 3.53 (1 H, *J* 11.5 and 4.5 Hz) | 78.1 |
| 8 | - | 42.8 |
| 9 | - | 102.3 |
| 9-OH | 2.14 (1 H, s) | - |
| 10a | 1.42 (1 H, d, *J* 15.1 Hz) | 43.0 |
| 10b | 2.10 (1 H, dd, *J* 15.1, 7.3 Hz) | - |
| 11 | 3.76 (1 H, m) | 72.1 |
| $12_{ax}$ | 1.62 (1 H, m) | 44.7 |
| $12_{eq}$ | 1.88 (1 H, br t, *J* 12.4 Hz) | - |
| 13 | - | 157.1 |
| $14_{ax}$ | 2.05 (1 H, br t, *J* 12.6 Hz) | 37.6 |
| $14_{eq}$ | 4.21 (1 H, d, *J* 12.9 Hz) | - |
| 15 | 4.55 (1 H, br t, *J* 9.9 Hz) | 80.1 |
| 16 | 5.63 (1 H, dd, *J* 15.9 and 8.4 Hz) | 131.2 |
| 17 | 6.24 (1 H, d, *J* 15.8 Hz) | 139.1 |
| 18 | - | 45.4 |
| 19 | - | 102.0 |
| 19-OH | 5.44 (1 H, s) | - |
| 20a | 2.21 (2 H, s) | 40.8 |
| 20b | - | - |
| 21 | - | 157.9 |
| $22_{ax}$ | 1.73 (1 H, m) | 36.7 |
| $22_{eq}$ | 4.39 (1 H, m) | - |
| 23 | 4.33 (1 H, br t, *J* 11.5 Hz) | 65.5 |
| 24a | 1.55 (1 H, ddd, *J* 14.5, 11.0 and 2.5 Hz) | 36.6 |
| 24b | 1.73 (1 H, m) | - |

| | | |
|---|---|---|
| 25 | 5.23 (1 H, ddd, *J* 11.8, 5.7 and 2.5 Hz) | 74.3 |
| 26 | 3.66 (1 H, br s) | 70.5 |
| 26-OH | 1.77 (1 H, br s) | - |
| 27 | 1.00 (3 H, d, *J* 6.6 Hz) | 20.0 |
| 28 (or 29) | 0.99 (3 H, s) | 17.1 |
| 29 (or 28) | 1.10 (3 H, s) | 24.9 |
| 30 | 5.76 (1 H, s) | 115.3 |
| 31 (or 35) | - | 166.8 |
| 32 (or 33) | 1.09 (3 H, s) | 20.8 |
| 33 (or 32) | 1.11 (3 H, s) | 21.9 |
| 34 | 5.90 (1 H, s) | 116.7 |
| 35 (or 31) | - | 167.2 |
| 36 (or 37) | 3.32 (3 H, s) | 51.1 |
| 37 (or 36) | 3.36 (3 H, s) | 50.8 |
| 1'a | 4.17 (1 H, d, *J* 11.7 Hz) | 71.7 |
| 1'b | 4.38 (1 H, d, *J* 11.7 Hz) | - |
| 2' | - | 139.9 |
| 3' | 7.30 (2 H, d, *J* 7.6 Hz) | 127.9 |
| 4' | 7.20 (2 H, t, *J* 7.6 Hz) | 128.0 |
| 5' | 7.12 (1 H, t, *J* 7.1 Hz) | 128.9 |

*HMBC correlation with 2b-H




**The 20-deoxybryostatin 40 showing the numbering system used**