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Supporting Information

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Total Synthesis of Antascomicin B

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Supplementary Information – Experimental Procedures

General Details

Solvents: Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl; acetonitrile, benzene, dichloromethane and toluene from calcium hydride; and triethylamine from potassium hydroxide. Anhydrous *N,N*-dimethyl formamide, dimethylsulfoxide and pyridine were used as supplied. Petrol refers to petroleum ether b.p. 40-60 °C and ether to diethyl ether, which were distilled before use.

Reagents: All reactions were performed under an argon atmosphere unless otherwise stated. Reagents were used as supplied or purified using standard procedures as necessary.

Chromatography: Flash column chromatography was carried out using Merck Kieselgel 230-400 mesh under pressure unless otherwise indicated. Analytical thin layer chromatography was performed using precoated glass-backed plates (Merck Kiesekgel 60 F254) and visualised by ultra-violet radiation (254 nm), acidic ammonium molybdate (VI), or acidic potassium permanganate solutions as appropriate. Biotage flash chromatography refers to the use of a biotage FLASH 40i unit and cartridges pre-packed with KP-Sil™ silica (32-63 μm, 60 Å, 500-550 m^2/g silica).

Data Collection: Optical rotations were measured using an Optical Activity AA-1000 polarimeter and a Perkin Elmer Model 343 polarimeter; $[\alpha]_D$ values are reported in 10^{-1} deg cm^2 g^{-1}. Infra-red spectra were recorded as thin films between sodium chloride plates on a Perkin-Elmer FT-IR 1600 spectrometer or as thin films on a Perkin Elmer Spectrum One FT-IR spectrometer. ^{1}H NMR spectra were recorded on Bruker DPX-400 and Bruker DRX-600 spectrometers and are reported (based on appearance rather than interpretation) as follows: chemical shift δ/ppm (number of protons, multiplicity, coupling constant *J* /Hz, assignment). Non-integral proton numbers indicate isomeric

species, either rotamers or diastereomers. Residual protic solvent was used as the internal reference. ^{13}C NMR spectra were recorded at 100 MHz, 125 MHz and 150 MHz on Bruker DPX-400, Bruker DP-500 cryoprobe and Bruker DRX-600 spectrometers, respectively. The resonance of $CDCl_3$ (δ_C = 77.0 ppm, t) was used as an internal reference. Assignments were made using a range of NMR experiments; where full assignment was not capable of being made, as much data as possible is given, except in the cases where this approach was deemed to result in superfluous information. Therefore the final two compounds feature carbon data selected to be most relevant. Mass spectra were recorded on Bruker, Micromass, and Kratos spectrometers at the Department of Chemistry, University of Cambridge.

(2*R*,3*R*)-1,2-Bis-(benzyloxy)-3-methyl-pent-4-ene (9)

E-2-Butene (9 ml, excess) was added *via* cannula to a stirred suspension of KO^{t}Bu (4.90 g, 43.7 mmol) in THF (100 ml) at -78 °C, followed by the dropwise addition of ^{n}BuLi (30.0 ml, 1.45 M in hexanes, 43.5 mmol). The reaction suspension was warmed to -45 °C, stirred at this temperature for 10 min, and cooled to -78 °C. A solution of (+)-*B*-methoxydiisopinocampheylborane (15.80 g, 49.9 mmol) in ether (20 ml) was then added *via* cannula over 20 min. Stirring was continued for 10 min and boron trifluoride diethyl etherate (7.60 ml, 60.0 mmol) added, followed immediately by addition of a pre-cooled solution of benzyloxyacetaldehyde **8** (4.68 ml, 33.3 mmol) in ether (15 ml). After 17 h, t.l.c. (petrol:ether 1:1) indicated the absence of starting material (R_f 0.2). The reaction mixture was warmed to 0 °C, 2.5 M aqueous solution of NaOH (27 ml) and aqueous solution of hydrogen peroxide (7.50 ml, 66.1 mmol) were added, followed by refluxing for 1 h. The reaction mixture was cooled to room temperature, the organic phase separated and washed with Na_2SO_3 (150 ml). The aqueous layers were extracted with ethyl acetate (3 x 75 ml), and the combined organic layers dried ($MgSO_4$), filtered and

concentrated *in vacuo* to afford the crude *alcohol*, which was used without further purification.

Sodium hydride (2.90 g, 60% dispersion in mineral oil, 72.5 mmol) was washed with petrol (20 ml) and suspended in DMF (40 ml). A solution of the crude alcohol in DMF (35 ml) was added slowly to the stirred suspension *via* cannula. After stirring for 30 min, the mixture was cooled to 0 °C, benzyl bromide (8.90 ml, 74.8 mmol) was added and the reaction was allowed to warm to room temperature. After 20 h, t.l.c. (petrol:ether 1:1) indicated the absence of starting material (R_f 0.8). The mixture was cautiously poured onto crushed ice and the solvent removed (co-evaporation with toluene). The residue was dissolved in ether (400 ml), washed with water (2 x 200 ml) and brine (200 ml), and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo.* The residue was purified by flash chromatography (2% ether/petrol) to give olefin **9** (6.90 g, 70% over two steps) as a colourless oil; $[\alpha]_D^{30}$ +5.9 (*c* 1.05 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3065, 3030, 2965, 2868, 1496, 1454, 1366, 1206, 1098, 1028; δ_H ($(CD_3)_2O$, 400 MHz) 1.07 (3H, d, *J* 7.0, CH_3-27), 2.54 (1H, m, H-27), 3.53-3.65 (3H, m, H-25, H-25', H-26), 4.53 (2H, s, $PhCH_2O$), 4.59 (1H, d, *J* 11.8, 1/2 x $PhCH_2O$), 4.75 (1H, d, *J* 11.9, 1/2 x $PhCH_2O$), 5.01 (2H, m, H_a-29, H_b-29), 5.89 (1H, m, H-28), 7.24-7.39 (10H, m, 10 x ArCH); δ_C ($(CD_3)_2O$, 100 MHz) 16.0 (CH_3-27), 40.2 (C-27), 71.5 (C-25), 72.4 ($PhCH_2O$), 72.8 ($PhCH_2O$), 81.7 (C-26), 114.2 (C-29), 127.2, 127.3, 127.4, 127.5, 128.1, 128.2 (6 x ArCH), 138.9, 139.5 (2 x ArC), 140.5 (C-28); *m/z* ESI 319.1675 $[M+Na]^+$. $C_{20}H_{24}O_2Na$ requires 319.1668.

(2*R*,3*R*)-3,4-Dibenzyloxy-2-methylbutan-1-ol (10)

Alkene **9** (14.6 g, 49.4 mmol) was dissolved in DCM (600 ml) and cooled to -78°C. Ozone was bubbled through the solution for 30 min until a slightly blue colour appeared. The flow of ozone was stopped and subsequently oxygen was bubbled through the

solution for 10 min. The reaction mixture was warmed to rt and triphenylphosphine (39.3 g, 150 mmol) was added. After stirring the solution at rt for 6 h, the solvent was removed *in vacuo*. The residue was dissolved in methanol (500 ml) and cooled to 0°C before sodium borohydride (4.11 g, 109 mmol) was added. After stirring 1 h at 0°C, DCM (300 ml) and water (400 ml) were added. The aqueous layer was extracted with DCM (2 x 200 ml) and the combined organic phases were dried ($MgSO_4$), filtered through Celite® and the solvent removed *in vacuo*. Column chromatography (2% to 50% ether in petrol) yielded alcohol **10** (13.4 g, 90%) as a colourless oil. $[\alpha]_D^{30}$ +28.0 (*c* 0.90 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3423, 3087, 3062, 3029, 2961, 2874, 1496, 1453, 1365, 1207, 1097, 1028; δ_H ($(CD_3)_2O$, 400 MHz) 0.96 (3H, d, *J* 7.0, CH_3-27), 2.00 (1H, m, H-27), 3.53 (1H, dd, *J* 5.1, 9.9, H_a-25), 3.62-3.70 (3H, m, H_b-25, H-26, H_a-28), 3.74 (1H, dd, *J* 5.5, 12.8, H_b-28), 4.55 (3H, m, 3/2 x $PhCH_2O$), 4.75 (1H, d, *J* 11.7, 1/2 x $PhCH_2O$), 7.25-7.38 (10H, m, 10 x ArCH); δ_C ($(CD_3)_2O$, 100 MHz) 13.1 (CH_3-27), 38.0 (C-27), 64.0 (C-25), 71.1 (C-28), 72.1 ($PhCH_2O$), 72.9 ($PhCH_2O$), 80.8 (C-26), 127.2, 127.3, 127.5, 127.6, 128.1, 128.2 (6 x ArCH), 138.9, 139.5 (2 x ArC); *m/z* EI 300.1711 M^+. $C_{19}H_{24}O_3$ requires 300.1725.

(2*R*,3*S*)-1,2-Bis-(benzyloxy)-4-iodo-3-methyl-butane (11)

PPh_3 (16.68 g, 63.6 mmol), iodine (16.14 g, 63.6 mmol) and imidazole (4.33 g, 63.6 mmol) were added to a stirring solution of alcohol **10** (6.36 g, 21.2 mmol) in DCM (85 ml) at 0°C, and the reaction mixture was then heated to reflux at 40°C. After 2.5 h, t.l.c. (petrol:ether 3:2) indicated complete conversion of starting material (R_f 0.2) to a major product (R_f 0.8). The reaction mixture was cooled to 0°C, stirred for 1 h with a 1:1 mixture of saturated aqueous solutions of $NaHCO_3$ and $Na_2S_2O_3$ (80 ml) and diluted with DCM (50 ml) and water (50 ml). The layers were separated, the aqueous layer extracted with DCM (3 x 75 ml), and the combined organic layers washed with water (100 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was pre-adsorbed onto silica gel and purified by flash chromatography (5% ether/petrol) to give iodide **11** (7.82

g, 90%) as a colourless oil; $[\alpha]_D^{29}$ +32.1 (*c* 1.01 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3087, 3062, 3029, 2963, 2860, 2359, 1722, 1604, 1496, 1454, 1364, 1202, 1098; δ_H ($CDCl_3$, 400 MHz) 0.99 (3H, d, *J* 6.6, CH_3-27), 1.78 (1H, m, H-27), 3.35 (1H, dd, *J* 3.4, 9.5, H_a-28), 3.40 (1H, m, H-26), 3.52 (1H, dd, *J* 5.8, 9.5, H_b-28), 3.56 (1H, dd, *J* 4.5, 10.6, H_a-25), 3.69 (1H, dd, *J* 3.3, 10.6, H_b-25), 4.55 (3H, m, 3/2 x $PhCH_2O$), 4.72 (1H, d, *J* 11.2, 1/2 x $PhCH_2O$), 7.27-7.37 (10H, m, 10 x ArCH); δ_C ($CDCl_3$, 100 MHz) 15.8 (C-28), 17.6 (CH_3-27), 36.4 (C-27), 69.6 (C-25), 72.8 ($PhCH_2O$), 73.5 ($PhCH_2O$), 81.6 (C-26), 127.7, 127.7, 128.0, 128.4, 128.4 (6 x ArCH), 138.2, 138.6 (2 x ArC); *m/z* ESI 433.0622 $[M+Na]^+$. $C_{19}H_{23}O_2INa$ requires 433.0635.

2-Allylsulfanylpyridine

2-Mercaptopyridine (1.00 g, 9.00 mmol) was dissolved in 2-butanone (10 ml) and heated to reflux. Powdred sodium hydroxide (430 mg, 10.8 mmol) was added in small portions followed by allylbromide (1.09 g, 9.00 mmol, 0.76 ml) dropwise. The reaction mixture was stirred at 100°C for 3 h. After cooling the reaction mixture to 0°C, the white solid was filtered off and the solvent was removed *in vacuo*. The residue was taken up in hexane (10 ml) and 10% NaOH (10 ml). The layers were separated and the aqueous fraction was extracted with hexane (3 x 10 ml). The combined organic phases were passed through a plug of activated alumina (grade 1, 10 g) and eluted with hexane. After concentration *in vacuo*, 2-allylsulfanylpyridine was isolated as a colourless liquid; δ_H ($CDCl_3$, 400 MHz) 3.83 (2H, d, *J* 6.8, SCH_2), 5.09 (1H, d, *J* 9.9, *cis* $=CH_2$), 5.28 (1H, dd, *J* 17.0, 1.3, *trans* $=CH_2$), 5.96 (1H, ddd, *J* 17.0, 9.9, 6.8, $CH=CH_2$), 6.96 (1H, dd, *J* 5.6, 1.5, H-5), 7.15 (1H, d, *J* 8.1, H-3), 7.46 (1H, dd, *J* 8.1, 1.5, H-4), 8.41 (1H, d, *J* 4.4, H-6); δ_C ($CDCl_3$, 100 MHz) 33.9 (SCH_2), 117.5 ($CH=CH_2$), 119.5 (C-5), 122.3 (C-3), 133.9 ($CH=CH_2$), 135.9 (C-4), 149.4 (C-6), 158.2 (C-2).

(2*R*,3*R*,5*RS*)-1,2-Dibenzyloxy-3-methyl-5-pyridylsulfanylhept-6-ene (12) and (2*R*,3*R*,5*EZ*)-1,2-Dibenzyloxy-3-methyl-7-pyridylsulfanylhept-6-ene

t-BuLi (1.33 ml, 1.5 M in pentanes, 2.00 mmol) was added slowly to a solution of 2-allylsulfanyl pyridine (302 mg, 2.00 mmol) in THF (2 ml) at -78°C. After stirring for 10 min, a solution of iodide **11** (410 mg, 1.00 mmol) in THF was added slowly (0.1 ml/min). The solution was allowed to warm to rt over a period of 3 h. Saturated aqueous $NaHCO_3$ (2 ml), DCM (5 ml) and water (5 ml) were added. The layers were separated and the aqueous fraction was extracted with DCM (2 x 5 ml). The combined organic fractions were dried ($MgSO_4$), filtered through celite and concentrated *in vacuo*. Chromatographic purification (Biotage 40S, 3% ether in petrol) yielded pyridylsulfide **12** (350 mg, 81%) as an 85:15 epimeric mixture at C_{29}; ν_{max} (film)/cm^{-1} 2865, 1577, 1452, 1413, 1122, 1089, 733, 697; δ_H ($CDCl_3$, 400 MHz, major epimer) 1.00 (3H, d, *J* 6.9, CH_3-27), 1.62 (1H, m, H_a-28), 1.93 (1H, m, H_b-28), 2.16 (1H, m, H-27), 3.59 (1H, m, H-26), 3.61-3.68 (2H, m, H_a-25, H_b-25), 4.49 (1H, dd, *J* 7.0, 8.3, H-29), 4.53-4.56 (2H, m, C*H*$_2$Ph), 5.00 (1H, d, *J* 10.3, H_a-35), 5.18 (1H, d, *J* 17.0, H_b-35), 5.88 (1H, ddd, *J* 8.2, 10.3, 17.0, H-34), 6.96 (1H, dd, *J* 1.8, 5.3, ArH), 7.15 (1H, d, *J* 8.0, ArH), 7.25-7.37 (10H, m, 10 x PhH), 7.44 (1H, dd, *J* 1.5, 6.1, ArH), 8.40 (1H, d, *J* 4.2, ArH); δ_C ($CDCl_3$, 100 MHz, major epimer) 16.1 (CH_3-27), 32.9 (C-27), 36.7 (C-28), 45.8 (C-29), 71.3 (C-25), 72.4 (CH_2Ph), 73.4 (CH_2Ph), 82.0 (C-26), 115.1 (CH_2-34), 119.6, 123.2 (2 x ArC), 127.3, 127.5, 127.6, 127.7, 128.2, 128.3 (6 x PhH), 135.8 (ArCH), 138.5, 139.1 (2 x Ph), 139.3 (C-34), 149.4 (ArCH), 158.6 (ArC); *m/z* EI Found 433.2076, M^+. $C_{27}H_{31}NO_2S$ requires 433.2075. Further elution yielded the regioisomer pyridyl sulfide **12a** (61 mg, 14%) as a 70:30 *E/Z* mixture; ν_{max} (film)/cm^{-1} 2859, 1578, 1452, 1413, 1122, 1089, 734, 697; δ_H ($CDCl_3$, 400 MHz) 0.95 (3H, d, *J* 6.8, CH_3-27), 1.35 (1H, m, H_a-29), 1.67 (1H, m, H_a-28), 1.86 (1H, m, H_b-28), 2.17 (1H, m, H-27), 2.28 (1H, m, H_b-29), 3.47 (1H, m, H-26), 3.58-3.66 (2H, m, H_a-25, H_b-25), 4.55-4.58 (3H, m, 1.5 x C*H*$_2$Ph), 4.72 (1H, d, *J* 11.8, 0.5 x C*H*$_2$Ph), 5.87 (0.3H, dd, *J* 9.3, 0.3, H-34), 6.05 (0.7H, m, *J* 15.3, H-34), 6.56 (0.7 H, d, *J* 15.3, CH-34), 6.77 (0.3H, d, *J* 9.4, CH-34), 7.00 (1H, dd, *J* 1.2, 5.6, ArH), 7.16 (1H, d, *J* 8.1, ArH), 7.19-7.37 (10H, m, 10 x PhH), 7.50 (1H, dd, *J* 1.8, 6.5, ArH), 8.44 (1H, d, *J* 4.9, ArH); δ_C ($CDCl_3$, 100 MHz) 15.9 (CH_3-27), 27.9 (C-29), 31.8 (C-27), 35.1 (C-28), 71.6

(C-25), 72.9 (CH_2Ph), 73.7 (CH_2Ph), 82.8 (C-26), 119.4, (ArCH), 120.3 (CH-34), 122.6, (ArCH), 127.7, 127.9, 128.0, 128.1, 128.6, 128.7 (6 x PhH), 133.4 (C-34), 136.7 (ArCH), 138.9, 139.5 (2 x Ph), 150.1 (ArCH), 158.5 (ArC); *m/z* EI Found 433.2090, M^+. $C_{27}H_{31}NO_2S$ requires 433.2075.

(2'*EZ*, 5'*R*, 6'*R*)-Tributyl-(6,7-dibenzyloxy-5-methylhept-2-enyl)stannane (4)

Freshly distilled hexabutylditin (9.03 g, 15.6 mmol, 7.87 ml) was dissolved in THF (10 ml) at -30°C. *n*-Butyl lithium (6.22 ml, 2.5M in hexane, 13.6 mmol) was added slowly (0.5 ml/min). The solution was stirred for 30 min and then cooled to -78°C. After the addition of copper bromide (2.23 g, 15.6 mmol) stirring was continued at -78°C for 30 min. Subsequently, pyridyl sulfide **12** (1.69 g, 3.89 mmol) in THF/HMPA (4:1, 5 ml) was added slowly (0.1 ml/min). The solution was allowed to warm to -40°C and was stirred for a further 2 h at this temperature before being warmed to room temperature and quenched with pH 10 phosphate buffer solution (20 ml). DCM (50 ml) and water (50 ml) were added and the layers were separated. The aqueous layer was extracted with DCM (50 ml) and the combined organic fractions were dried ($MgSO_4$), filtered through celite and concentrated *in vacuo*. The residue was purified by column chromatography (2 to 10% ether in petrol) to give stannane **4** (2.19 g, 92%) as an inseparable *E/Z* (37:63) mixture. $[\alpha]_D^{31}$ +3.9 (c = 1.035 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 3495, 3085, 3064, 3030, 2956, 2924, 2854, 1496, 1454, 1376, 1097; δ_H ($CDCl_3$, 400 MHz) 0.88-1.00 (15H, m, 3 x $SnCH_2CH_2CH_2CH_3$), 1.01 (3H, d, *J* 7.0, CH_3-27), 1.34-1.43 (6H, m, 3 x $SnCH_2CH_2CH_2CH_3$), 1.54-1.64 (6H, m, 3 x $SnCH_2CH_2CH_2CH_3$), 1.78 (2H, d, *J* 8.3, CH_2-34), 1.81-1.99 (2H, m, H-27, H_a-28), 2.02 (1H, m, H_b-28), 3.51-3.58 (1H, m, H-26), 3.64-3.77 (2H, m, H_a-25, H_b-25), 4.62-4.68 (3H, m, CH_2Ph), 4.79 (1H, m, CH_2Ph),5.15 (0.37H, m, H-29_E), 5.28 (0.63H, m, H-29_Z), 5.55-5.72 (1H, m, H-34), 7.31-7.45 (10H, m, 10 x ArH); δ_C ($CDCl_3$, 100 MHz) 9.6 ($SnCH_2$), 9.8 ($SnCH_2$), 11.1 (CH_2-34_E), 14.2 ($SnCH_2CH_2CH_2CH_3$), 14.7 (CH_2-34_Z), 15.9, (CH_3-27_Z), 16.2 (CH_3-27_E), 27.8 ($SnCH_2$), 29.6 ($SnCH_2$),29.7 ($SnCH_2$), 30.3 (C-28_E), 36.2, 36.3, 36.3, (C-27_E, C-27_Z, C-28_Z), 71.7, 71.8 (C-25_E, C-25_Z), 72.9, 73.0 (2 x CH_2Ph), 82.7, 82.8 (C-26_E, C-26_Z), 123.0 (C-29_E), 124.3 (C-29_Z), 127.7, 127.8, 127.9, 128.0, 128.2, 128.3 (10 x ArCH), 129.8 (C-34_E),

131.3 (C-34_Z), 139.0, 139.1, 139.6, 139.7 (4 x ArC); *m/z* ESI 637.3048 $[M+Na]^+$. $C_{34}H_{54}O_2SnNa$ requires 637.3038.

(2*S*,3*S*,5*R*,6*R*)-5,6-Dimethoxy-5,6-dimethyl[1,4]dioxane-2,3-dicarboxylic acid dimethyl ester (6)

Camphorsulfonic acid (4.65 g, 20.0 mmol) was added to a solution of dimethyl-*D*-tartrate (35,7 g, 200 mmol), butane-2,3-dione (20.7 g, 21.1 ml, 241 mmol) and trimethylorthoformate (63.7 g, 65.5 ml, 600 mmol) in methanol (700 ml) at rt. The solution was heated to reflux for 20 h and then cooled to rt before solid $NaHCO_3$ (34 g) was added and the mixture stirred for 1.5 h. After filtration the solvent was removed *in vacuo*. Two recrystallisations of the deep purple residue yielded the BDA protected diol **6** (39.4 g, 67%) as colourless crystals. m.p. 108-110 °C; $[\alpha]_D^{31}$ +147.9 (*c* 1.06, DCM); $\nu_{(max)}$ (Nujol)/cm^{-1} 2924, 2853, 1738, 1443, 1378, 1363, 1283, 1210, 1176, 1112, 1062, 1029, 1008, 982, 949, 899, 887, 858, 811, 746; δ_H ($CDCl_3$, 400 MHz) 4.54 (2H, s, H-2, H-3), 3.77 (6H, s, 2 x CO_2CH_3), 3.33 (6H, s, 2 x OCH_3), 1.36 (6H, s, 2 x CH_3); δ_C ($CDCl_3$, 100 MHz) 168.3 (2 x CO_2CH_3), 99.1 (C-2' and C-3'), 68.7 (C-2 and C-3), 52.4 (2 x CO_2CH_3), 48.3 (2 x OCH_3), 17.2 (2 x CH_3); *m/z* EI 261 $[M-OCH_3]^+$, (62), 218 (12), 203 (15), 189 (20), 144 (94), 114 (70), 101 (49), 85 (57), 73 (100), 49 (55); *m/z* EI 261.0976 $[M-OCH_3]^+$, $C_{11}H_{17}O_7$ requires 261.0974; Found: C 49.49 H 7.01, $C_{12}H_{20}O_8$ requires C 49.31 H 6.90%.

(2'*S*,3'*S*,5'*R*,6'*R*)-(3-Hydroxymethyl-5,6-dimethoxy-5,6-dimethyl[1,4]dioxan-2-yl)-methanol

A solution of diester **6** (38.9 g, 133 mmol) in THF (200 ml) was added *via cannula* to a solution of $LiAlH_4$ (370 ml, 1M in THF, 370 mmol) at 0°C. The solution was allowed to warm to rt and then stirred for 20 h before being cooled back to 0°C. Solid $Na_2SO_4.10H_2O$ (106 g) was added portionwise over 30 min followed by ether (300 ml) and the solution was stirred for 3 h. The solid was filtered off and washed with ether (300 ml) and ethyl acetate (500 ml). The solvent was removed *in vacuo* to give the *diol* (24.5

g, 78%) as colourless crystals. m.p. 122-123 °C; $[\alpha]_D^{30}$ +164.4 (*c* 0.82 in DCM); $\nu_{(max)}$ (Nujol)/cm^{-1} 3443, 3400, 2923, 2853, 1462, 1379, 1228, 1122, 1045; δ_H ($CDCl_3$, 400 MHz) 3.79-3.84 (2H, m, 2 x CH), 3.62-3.75 (4H, m, 2 x CH_2), 3.26 (6H, s, 2 x OCH_3), 2.23 (2H, t, *J* 6.4, 2 x OH), 1.31 (6H, s, 2 x CH_3); δ_C ($CDCl_3$, 100 MHz) 98.8 (C-2' and C-3'), 69.2 (C-2 and C-3), 62.2 (C-1 and C-4), 47.9 (2 x OCH_3), 17.5 (2 x CH_3); *m/z* APCI 254 $[MNH_4]^+$, (22), 222 (16), 190 (100), 173 (82); *m/z* APCI 254.1604 $[MNH_4]^+$, $C_{10}H_{24}O_6N$ requires 254.1603; Found: C 51.08 H 8.59, $C_{10}H_{20}O_6$ requires C 50.84 H 8.53%.

(2'*S*,3'*S*,5'*R*,6'*R*)-[3-(*tert*-Butyldimethylsilanyloxymethyl)-5,6-dimethoxy-5,6-dimethyl[1,4]dioxan-2-yl]-methanol (7)

Sodium hydride (2.62 g, 60% wt. dispersion in silicon oil, 109 mmol) was suspended in THF (150 ml) at rt. A solution of the diol derived from reduction of **6** (24.6 g, 104 mmol) in THF (120 ml) was added *via cannula*. After stirring for 30 min, a solution of TBSCl (16.2 g, 107 mmol) in THF (60 ml) was added and the reaction was stirred for 15 h. The mixture was diluted with ether (500 ml) and washed with saturated aqueous K_2CO_3 (400 ml). The organic layer was dried ($MgSO_4$), filtered through Celite® and concentrated *in vacuo*. Column chromatography (petrol/ether 1/1) gave alcohol **7** (31.3 g, 86%) as colourless crystals. m.p. 38 °C; $[\alpha]_D^{30}$ +112.5 (*c* 1.28, DCM); $\nu_{(max)}$ (Nujol)/cm^{-1} 3321, 2924, 2854, 1462, 1375, 1287, 1248, 1128, 1079, 1038; δ_H ($CDCl_3$, 400 MHz) 3.61-3.79 (6H, m, 2 x CH_2, 2 x CH), 3.26 (6H, s, 2 x OCH_3), 2.97-3.01 (1H, m, OH), 1.29 (3H, s, CH_3), 1.28 (3H, s, CH_3), 0.89 (9H, s, $SiC(CH_3)_3$), 0.09 (6H, s, 2 x $SiCH_3$); δ_C ($CDCl_3$, 100 MHz) 98.7 and 98.6 (C-2' and C-3'), 71.9 and 70.5 (C-2 and C-3), 63.9 and 62.6 (C-1 and C-4), 47.8 (2 x OCH_3), 25.7 ($SiC(CH_3)_3$), 18.1 ($SiC(CH_3)_3$), 17.4 (2 x CH_3), -5.6 (2 x $SiCH_3$); *m/z* APCI 368 $[MNH_4]^+$ (8), 336 (20), 304 (100), 287 (34), 132 (14), 117 (24), 92 (15); *m/z* APCI 368.2468 $[MNH_4]^+$, $C_{16}H_{38}O_6NSi$ requires 368.2468; Found: C 54.74 H 9.72, $C_{16}H_{34}O_6Si$ requires C 54.82 H 9.78%.

(2*S*,3*R*,5*S*,6*S*)-3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carbaldehyde (3)

A solution of DMSO (0.180 ml, 2.54 mmol) in DCM (2 ml) was added dropwise to a stirring solution of oxalyl chloride (0.200 ml, 2.29 mmol) in DCM (1 ml) at –78°C and stirred for 30 min before a solution of alcohol **7** (0.400 g, 1.14 mmol) in DCM (3 ml) was added *via* cannula. After 1.25 h, triethylamine (0.960 ml, 6.89 mmol) was added and the reaction mixture stirred for 30 min at –60°C and at room temperature for 1.5 h before the addition of water (2 ml). The reaction mixture was diluted with ether (100 ml), washed with saturated aqueous solution of NH_4Cl (50 ml) and brine (50 ml), and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo* to give crude aldehyde **3** (0.45 g) which was used in the subsequent step without further purification; δ_H (C_6D_6, 600 MHz) 0.17 (3H, s, $SiCH_3$), 0.19 (3H, s, $SiCH_3$), 1.07 (9H, s, $Me_2SiC(CH_3)_3$), 1.35 (3H, s, CH_3), 1.39 (3H, s, CH_3), 3.07 (3H, s, CH_3O), 3.13 (3H, s, CH_3O), 3.92-3.98 (3H, m, H-32, H_a-33, H_b-33), 4.27 (1H, dd, *J* 1.3 and 9.3, H-31), 9.65 (1H, d, *J* 1.3, H-30).

(1*S*,2*R*,2'*R*,3'*R*,5'*S*,6'*S*,2"*R*,3"*R*)-2-(3,4-Dibenzyloxy-2-methylbutyl)-1-[3-(*tert*-butyldimethylsilanyloxymethyl)-5,6-dimethoxy-5,6-dimethyl[1,4]dioxan-2-yl]-but-3-en-1-ol (13) and
(1*S*,2*S*,2'*R*,3'*R*,5'*S*,6'*S*,2"*R*,3"*R*)-2-(3,4-Dibenzyloxy-2-methylbutyl)-1-[3-(*tert*-butyldimethylsilanyloxymethyl)-5,6-dimethoxy-5,6-dimethyl[1,4]dioxan-2-yl]-but-3-en-1-ol (13a)

Zinc (II) iodide (3.58 g, 11.2 mmol) was dried under vacuum for 24 h at 150°C and then added to a solution of crude aldehyde **3** (3.55 g, 10.2 mmol) in DCM (50 ml) at -78°C. The mixture was stirred vigorously at this temperature for 1.5 h before a solution of stannane **4** (4.17 g, 6.8 mmol) in DCM (50 ml) was added *via* a syringe pump (0.5 ml/min). The solution was stirred for 24 h at -20°C, for 15 h at 0°C and finally for 3 h at rt. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (50 ml) and stirred for 15 min before being diluted with DCM (250 ml) and water (250 ml). The

layers were separated and the organic phase was washed with saturated NH_4Cl (200 ml). The combined aqueous phases were extracted with DCM (2 x 100 ml) and the combined organic fractions were dried ($MgSO_4$), filtered through Celite® and the solvent removed *in vacuo*. The residue was taken up in DCM/MeOH (2:1, 200 ml) and polymer supported ethylene diamine (6 g, 2.8 mmol/g, 16.8 mmol) was added. The mixture was shaken overnight and then filtered through a short pad of silica gel. Column chromatography (15 to 30% ether in petrol) gave alcohol **13** (3.48 g, 76%) as a colourless oil $[\alpha]_D^{26}$ +66.8 (*c* 1.12 in $CHCl_3$); n_{max} (film)/cm^{-1} 2927, 2857, 1463, 1373, 1252, 1207, 1129, 1039; δ_H ($CDCl_3$, 400 MHz) 0.06 (3H, s, $SiCH_3$), 0.07 (3H, s, $SiCH_3$), 0.89 (9H, s, $Me_2SiC(CH_3)_3$), 0.92 (3H, d, *J* 6.6, CH_3-27), 1.07 (1H, m, H_a-28), 1.24 (3H, s, CH_3), 1.26 (3H, s, CH_3), 1.92-1.98 (2H, m, H-27, H_b-28), 2.23 (1H, d, *J* 10.5, OH), 2.42 (1H, m, H-29), 3.18 (3H, s, CH_3O), 3.24 (3H, s, CH_3O), 3.41 (1H, t, *J* 9.9, H-30), 3.56-3.67 (4H, m, H_a-25, H_b-25, H-26, H_a-33), 3.71 (1H, dd, *J* 3.8 and 11.2, H_b-33), 3.88 (2H, m, H-31, H-32), 4.52 (1H, d, *J* 12.0, 0.5 x $PhCH_2O$), 4.58 (1H, d, *J* 11.6, 0.5 x $PhCH_2O$), 4.61 (1H, d, *J* 11.4, 0.5 x $PhCH_2O$), 4.67 (1H, d, *J* 12.0, 0.5 x $PhCH_2O$), 4.98 (1H, d, *J* 17.2, *E*-=CH_2), 5.06 (1H, d, *J* 10.3, *Z*-=CH_2), 5.50 (1H, dt, *J* 9.9 and 17.2, H-34), 7.23-7.38 (10H, m, 10 x ArCH); δ_C ($CDCl_3$, 100 MHz) –5.0 (2 x $SiCH_3$), 16.9 (CH_3-27), 18.0, 18.1 (2 x CH_3), 18.6 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 32.8 (C-27), 35.4 (C-28), 46.2 (C-29), 48.2, 48.9 (2 x CH_3O), 64.2 (C-33), 69.1, 69.3 (C-31, C-32), 71.3 (C-25), 72.3 ($PhCH_2O$), 72.8 (C-30), 73.7 ($PhCH_2O$), 81.3 (C-26), 98.8, 99.0 (2 x *BDA*-CO_2), 117.5 (=CH_2), 128.0, 128.6, 128.7 (6 x ArCH), 139.0 (ArC), 139.7 (C-34), 140.1 (ArC); *m/z* ESI 695.3937 $[M+Na]^+$. $C_{38}H_{60}O_8SiNa$ requires 695.3955. Further elution yielded epimeric alcohol **13a** (603 mg, 13%) as a colourless oil. $[\alpha]_D^{25}$ +73.4 (*c* 3.48 in $CHCl_3$); n_{max} (film)/cm^{-1} 2928, 2856, 1455, 1374, 1251, 1206, 1120, 1028; δ_H ($CDCl_3$, 600 MHz) 0.06 (3H, s, $SiCH_3$), 0.08 (3H, s, $SiCH_3$), 0.89 (9H, s, $Me_2SiC(CH_3)_3$), 0.90 (3H, d, *J* 6.3, CH_3-27), 1.25 (3H, s, CH_3), 1.28 (3H, s, CH_3), 1.37 (2H, m, H_a-28, H_b-28), 1.86 (1H, m, H-27), 2.51 (1H, m, H-29), 3.17 (3H, s, CH_3O), 3.24 (3H, s, CH_3O), 3.43-3.47 (2H, m, H-26, H-30), 3.57 (1H, dd, *J* 4.0 and 10.1, H_a-25), 3.59 (1H, dd, *J* 6.2 and 10.1, H_b-25), 3.69 (1H, dd, *J* 4.2 and 11.4, H_a-33), 3.74 (1H, dd, *J* 4.3 and 11.4, H_b-33), 3.87 (1H, d, *J* 9.9, H-31), 3.96 (1H, m, H-32), 4.52-4.55 (3H, m, 1.5 x $PhCH_2O$), 4.71 (1H, d, *J* 11.6, 0.5 x $PhCH_2O$), 5.13 (1H, dd, *J* 1.4 and 17.1, *E*-=CH_2), 5.18 (1H, dd, *J* 1.7 and 10.3, *Z*-=CH_2), 5.54 (1H, dt, *J* 9.9

and 17.1, H-34), 7.26-7.36 (10H, m, 10 x ArCH); δ_C ($CDCl_3$, 125 MHz) –5.4 ($SiCH_3$), -5.3 ($SiCH_3$), 15.3 (CH_3-27), 17.6 (2 x CH_3), 18.2 (Si*C*$(CH_3)_3$), 25.8, 25.9 (SiC(*C*$H_3)_3$), 32.0 (C-28) 32.5 (C-27), 44.6 (C-29), 47.7, 48.4 (2 x CH_3O), 63.6 (C-33), 68.7 (C-31), 69.2 (C-32), 71.5 (C-25), 72.2 (C-30), 72.8 ($PhCH_2O$), 73.4 ($PhCH_2O$), 83.1 (C-26), 98.5, 98.8 (2 x *BDA*-CO_2), 117.8 (=CH_2), 127.5, 127.6, 127.7, 128.2, 128.3 (6 x ArCH), 138.4 (ArC), 139.1 (ArC), 139.4 (C-34); *m/z* APCI 695.4 $[M+Na]^+$ (4), 609.3 (10), 517.3 (100); *m/z* ESI 695.3948 $[M+Na]^+$. $C_{38}H_{60}O_8SiNa$ requires 695.3955. (APCI).

(2*R*,3*R*,5*S*,6*S*,1'*S*,2'*R*,2''*R*,3''*R*)-{3-[2'-(3'',4''-Bis-benzyloxy-2''-methyl-butyl)-1'-methoxymethoxy-but-3'-enyl]-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-yl}-methanol (14)

Methoxymethyl chloride (1.45 ml, 19.1 mmol) was added dropwise *via* syringe pump over 1 h to a stirring solution of homoallylic alcohol **13** (2.568 g, 3.82 mmol) and diisopropylethylamine (3.33 ml, 19.1 mmol) in DCM (10 ml) at –5°C. After 20 h, t.l.c. (petrol:ether 1:1) indicated the complete conversion of starting material (R_f 0.3) to a major product (R_f 0.4). The reaction mixture was diluted with DCM (200 ml), washed with saturated aqueous solution of NH_4Cl (200 ml) and the layers separated. The aqueous layer was extracted with DCM (2 x 40 ml), and the combined organic layers dried ($MgSO_4$), filtered, concentrated *in vacuo*. The residue was dissolved in THF (19 ml), cooled to 0°C and a solution of TBAF in THF (19 ml, 1 M in THF, 19 mmol) added dropwise. After 1 1/2 h, t.l.c. (petrol:ether 3:7) indicated the formation of a major product (R_f 0.2). The reaction mixture was diluted with DCM (200 ml), washed with saturated aqueous solution of $NaHCO_3$ (200 ml) and the layers separated. The aqueous layer was extracted with DCM (2 x 40 ml), and the combined organic layers dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified twice by Biotage flash chromatography (petrol:ether 3:7) to give alcohol **14** (2.047 g, 89% over the two steps) as a colourless oil; $[\alpha]_D^{27}$ +101.7 (*c* 0.960 in $CHCl_3$); n_{max} (film)/cm^{-1} 3473, 2950, 1454,

1375, 1207, 1126, 1032; δ_H ($CDCl_3$, 400 MHz) 0.93 (3H, d, *J* 7.0, CH_3-27), 1.13 (1H, m, H_a-28), 1.28 (3H, s, CH_3), 1.30 (3H, s, CH_3), 1.76 (1H, m, H_b-28), 1.96 (1H, m, H-27), 2.40 (1H, t, *J* 7.6, OH), 2.67 (1H, m, H-29), 3.21 (3H, s, CH_3O), 3.23 (3H, s, CH_3O), 3.40 (3H, s, *MOM*-CH_3), 3.46 (1H, d, *J* 7.4, H-30), 3.55-3.65 (4H, m, H_a-25, H_b-25, H-26, H_a-33), 3.71 (1H, dd, *J* 3.5 and 11.8, H_b-33), 3.91 (1H, d, *J* 10.0, H-31), 4.01 (1H, m, H-32), 4.54 (2H, s, $PhCH_2O$), 4.59 (1H, d, *J* 12.0, 0.5 x $PhCH_2O$), 4.63-4.68 (3H, m, 0.5 x $PhCH_2O$, *MOM*-CH_2), 4.97 (1H, d, *J* 17.3, *E*-=CH_2), 5.06 (1H, dd, *J* 1.4 and 10.3, *Z*-=CH_2), 5.77 (1H, dt, *J* 9.7 and 17.2, H-34), 7.23-7.36 (10H, m, 10 x ArCH); δ_C ($CDCl_3$, 100 MHz) 16.5 (CH_3-27), 17.7 (2 x *BDA*-CH_3), 32.5 (C-27), 34.0 (C-28), 43.8 (C-29), 47.7, 48.8 (2 x *BDA*-CH_3O), 56.1 (*MOM*-CH_3), 62.3 (C-33), 68.6 (C-31), 68.9 (C-32), 70.9 (C-25), 72.0 ($PhCH_2O$), 73.3 ($PhCH_2O$), 79.6 (C-30), 80.9 (C-26), 97.3 (*MOM*-CH_2), 98.6, 99.1 (2 x *BDA*-CO_2), 116.4 (=CH_2), 127.3,127.4, 127.6, 127.7, 128.2, 128.3 (6 x ArCH), 138.5, 139.2 (2 x ArC), 139.7 (C-34); *m/z* APCI 620.7 $[M+NH_4]^+$ (100), 539.6 (36); *m/z* ESI 625.3340 $[M+Na]^+$. $C_{34}H_{50}O_9Na$ requires 625.3353.

(2*S*,3*R*,5*S*,6*S*,1'*S*,2'*R*,2''*R*,3''*R*)-3-[2'-(3'',4''-Bis-benzyloxy-2''-methyl-butyl)-1'-methoxymethoxy-but-3'-enyl]-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxane-2-carbaldehyde

A solution of DMSO (0.13 ml, 1.83 mmol) in DCM (1 ml) was added dropwise to a stirring solution of oxalyl chloride (0.15 ml, 1.72 mmol) in DCM (1 ml) at –78 °C and stirred for 30 min before a solution of alcohol **14** (0.34 g, 0.56 mmol) in DCM (1 ml) was added dropwise. After 1.75 h, triethylamine (0.47 ml, 3.37 mmol) was added and the reaction mixture stirred for 15 min at –60°C and at room temperature for 1.5 h before the addition of water (2 ml). The reaction mixture was diluted with DCM (100 ml), washed with saturated aqueous solution of NH_4Cl (50 ml), and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo* to give crude *aldehyde* which was used in the

subsequent step without further purification; δ_H ($CDCl_3$, 600 MHz) 0.92 (3H, d, *J* 7.0, CH_3-27), 1.11 (1H, m, H_a-28), 1.31 (3H, s, *BDA*-CH_3), 1.35 (3H, s, *BDA*-CH_3), 1.77 (1H, m, H_b-28), 1.94 (1H, m, H-27), 2.66 (1H, m, H-29), 3.20 (3H, s, *BDA*-CH_3O), 3.28 (3H, s, *BDA*-CH_3O), 3.37 (3H, s, *MOM*-CH_3), 3.55-3.59 (2H, m, H_a-25, H-26), 3.62 (1H, m, H_b-25), 3.73 (1H, d, *J* 8.2, H-30), 3.96 (1H, d, *J* 10.1, H-31), 4.42 (1H, d, *J* 10.1, H-32), 4.52 (1H, d, *J* 12.1, 0.5 x $PhCH_2O$), 4.55 (1H, d, *J* 12.1, 0.5 x $PhCH_2O$), 4.58 (1H, d, *J* 11.9, 0.5 x $PhCH_2O$), 4.63-4.66 (2H, m, 0.5 x $PhCH_2O$, 0.5 x *MOM*-CH_2), 4.72 (1H, d, *J* 6.7, 0.5 x *MOM*-CH_2), 4.98 (1H, d, *J* 17.0, *E*-=CH_2), 5.05 (1H, d, *J* 10.3, *Z*-=CH_2), 5.71 (1H, dt, *J* 9.7 and 17.3, H-34), 7.23-7.43 (10H, m, 10 x ArCH), 9.62 (1H, s, H-33).

(2*S*,3*S*,5*R*,6*R*,1'*S*,2'*R*,2''*R*,3''*R*)-5-[2'-(3'',4''-Bis-benzyloxy-2''-methyl-butyl)-1'-methoxymethoxy-but-3'-enyl]-2,3-dimethoxy-2,3-dimethyl-6-vinyl-[1,4]dioxane (2)

n-BuLi (1.0 ml, 1.6 M in hexanes, 1.6 mmol) was added to a solution of methyltriphenylphosphonium bromide (azeotroped once in toluene) (0.605 g, 1.69 mmol) in THF (4.3 ml) at 0 °C and stirred for 1 h. The resultant deep orange solution was added *via* cannula to a stirring solution of the crude aldehyde in THF (1.3 ml) at −78 °C and the reaction mixture allowed to warm slowly to room temperature. After 12 h, t.l.c. (petrol:ether 3:7) indicated the formation of a major product (R_f 0.7). The reaction mixture was quenched with water (5 ml), diluted with DCM (100 ml), washed with water (100 ml) and the layers separated. The aqueous layer was extracted with DCM (2 x 50 ml), and the combined organic layers dried ($MgSO_4$), filtered and concentrated *in vacuo.* The residue was purified by Biotage flash chromatography (petrol:ether 3:1) to give diene **2** (0.295 g, 87% over the two steps) as a colourless oil; $[\alpha]_D^{30}$ +93.3 (*c* 0.815 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2951, 1454, 1373, 1208, 1123, 1036; δ_H ($CDCl_3$, 400 MHz) 0.93 (3H, d, *J* 6.9, CH_3-27), 1.13 (1H, m, H_a-28), 1.29 (3H, s, *BDA*-CH_3), 1.32 (3H, s, *BDA*-CH_3), 1.74 (1H, m, H_b-28), 1.94 (1H, m, H-27), 2.63 (1H, m, H-29), 3.22 (3H, s, *BDA*-CH_3O),

3.25 (3H, s, *BDA*-CH_3O), 3.39 (1H, d, *J* 7.4, H-30), 3.42 (3H, s, *MOM*-CH_3), 3.54-3.64 (3H, m, H_a-25, H_b-25, H-26), 3.77 (1H, d, *J* 9.9, H-31), 4.38 (1H, dd, *J* 7.8 and 9.6, H-32), 4.55 (2H, s, $PhCH_2O$), 4.59 (1H, d, *J* 12.0, 0.5 x $PhCH_2O$), 4.65-4.70 (3H, m, 0.5 x $PhCH_2O$, *MOM*-CH_2), 4.97 (1H, d, *J* 17.3, *E*-=CH_2), 5.05 (1H, dd, *J* 1.3 and 10.3, *Z*-=CH_2), 5.29 (1H, dd, *J* 1.3 and 10.4, *Z*-=CH_2), 5.48 (1H, d, *J* 17.0, *E*-=CH_2), 5.72-5.83 (2H, m, H-33, H-34), 7.23-7.36 (10H, m, 10 x ArCH); δ_C ($CDCl_3$, 100 MHz) 16.5 (CH_3-27), 17.9 (2 x *BDA*-CH_3), 32.5 (C-27), 34.0 (C-28), 44.2 (C-29), 47.8, 48.8 (2 x *BDA*-CH_3O), 56.0 (*BDA*-CH_3), 70.4 (C-31, C-32), 70.9 (C-25), 72.0 ($PhCH_2O$), 73.3 ($PhCH_2O$), 79.5 (C-30), 81.0 (C-26), 97.6 (*MOM*-CH_2), 98.4, 99.1 (2 x *BDA*-CO_2), 116.4, 120.2 (2 x =CH_2), 127.3, 127.4, 127.5, 127.6, 128.2, 128.3 (6 x ArCH), 134.4 (C-33), 138.5, 139.2 (2 x ArC), 139.9 (C-34); *m/z* APCI 621.1 $[M+Na]^+$ (100), 616.3 (67). *m/z* ESI 621.3410 $[M+Na]^+$. $C_{35}H_{50}O_8Na$ requires 621.3403.

(7*E*,2*S*,3*S*,4a*R*,5*S*,6*R*,8a*R*,2'*R*,3'*R*)-6-(3',4'-Dibenzyloxy-2'-methyl-butyl)-2,3-dimethoxy-5-methoxymethoxy-2,3-dimethyl-2,3,4a,5,6,8a-hexahydro-benzo[1,4]dioxine

A solution of tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium dichloride (8.9 mg, 0.010 mmol) in toluene (2 ml) was added to a stirring solution of diene **2** (0.180 g, 0.30 mmol) in toluene (10 ml) and the reaction mixture heated to reflux. At 1 h intervals, a second, then a third portion of the catalyst (8.9 mg, 0.010 mmol) in toluene (2 ml) were added. After 1 h, t.l.c. (petrol:ether 1:1) indicated the complete conversion of starting material (R_f 0.4) to a major product (R_f 0.5). The reaction mixture was filtered through a short plug of silica (eluant : ether), concentrated *in vacuo* and the residue purified by flash chromatography (petrol:ether 7:3) to give the *cyclohexene* (0.153 g, 89%) as a colourless oil; $[\alpha]_D^{29}$ −24.9 (*c* 1.125 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2906, 2355,1454, 1371, 1204, 1117, 1036; δ_H (C_6D_6,

600 MHz) 1.10 (3H, d, *J* 6.9, CH_3-27), 1.29 (1H, m, H_a-28), 1.42 (3H, s, *BDA*-CH_3), 1.48 (3H, s, *BDA*-CH_3), 2.10 (1H, m, H_b-28), 2.18 (1H, m, H-27), 2.59 (1H, m, H-29), 3.18 (3H, s, *BDA*-OCH_3), 3.25 (3H, s, *BDA*-OCH_3), 3.39 (3H, s, *MOM*-CH_3), 3.65 (1H, m, H-26), 3.69-3.70 (2H, m, H_a-25, H_b-25), 3.75 (1H, dd, *J* 8.3 and 10.2, H-30), 4.12 (1H, t, *J* 9.7, H-31), 4.44 (1H, d, *J* 12.1, 0.5 x $PhCH_2O$), 4.47 (1H, d, *J* 12.2, 0.5 x $PhCH_2O$), 4.51 (1H, m, H-32), 4.63 (1H, d, *J* 11.9, 0.5 x $PhCH_2O$), 4.78 (1H, d, *J* 11.9, 0.5 x $PhCH_2O$),4.86 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 5.28 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 5.48 (1H, dt, *J* 2.6 and 10.1, H-33), 5.69 (1H, d, *J* 10.1, H-34), 7.17-7.47 (10H, m, 10 x ArCH); δ_C (C_6D_6, 150 MHz) 17.0 (CH_3-27), 17.8 (2 x *BDA*-CH_3), 33.3 (C-27), 36.4 (C-28), 42.6 (C-29), 47.1, 47.2 (2 x *BDA*-OCH_3), 55.8 (*MOM*-CH_3), 68.2 ($PhCH_2O$), 71.3 (C-25), 72.4 ($PhCH_2O$), 73.2 (C-32), 74.2 (C-31), 78.3 (C-30), 81.9 (C-26), 97.9 (*MOM*-CH_2), 99.7, 99.9 (2 x *BDA*-CO_2), 125.7 (C-34), 127.2,127.4, 127.5, 127.6, 128.2, 128.3 (6 x ArCH), 130.2 (C-33), 139.0, 139.6 (2 x ArC); *m/z* ESI 593.3104 $[M+Na]^+$. $C_{33}H_{46}O_8Na$ requires 593.3090.

(2*R*,3*R*,2'*S*,3'*S*,4a'*S*,5'*S*,6'*S*,8a'*R*)-4-(2',3'-Dimethoxy-5'-methoxymethoxy-2',3'-dimethyl-octahydro-benzo[1',4']dioxin-6'-yl)-3-methyl-butane-1,2-diol (15)

Palladium on carbon (36 mg) was added to a solution of cyclohexene (0.160 g, 0.281 mmol) in ethanol (3 ml) and purged three times with argon, before a hydrogen balloon was attached. After 5 h, t.l.c. (ethyl acetate) indicated the formation of a major product (R_f 0.2). The reaction mixture was filtered through Celite® (eluant : ethanol), concentrated *in vacuo* and the residue purified by flash chromatography (ethyl acetate) to give cyclohexane **15** (0.095 g, 86%) as a colourless oil; $[\alpha]_D^{25}$ +70.9 (*c* 0.860 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3438, 2946, 2327,1457, 1370, 1215, 1127, 1033; δ_H (C_6D_6, 600 MHz) 0.77 (1H, m, H-34), 0.87 (1H, m, H-28), 0.93 (3H, d, *J* 6.9, CH_3-27), 1.42 (3H, s, *BDA*-CH_3), 1.44-1.48 (4H, m, H_a-33, [including 1.46 (3H, s, *BDA*-CH_3)]), 1.61-1.67 (2H, m,

H-29, H_b-34), 1.75 (1H, dd, *J* 3.4 and 12.5, H_b-33), 1.87 (1H, m, H-27), 2.18 (1H, m, H_b-28), 2.59 (1H, br s, OH), 3.09 (1H, br s, OH), 3.21 (3H, s, *BDA*-OCH_3), 3.26-3.29 (4H, m, H-30, [including 3.28 (3H, s, *BDA*-OCH_3)]), 3.42 (3H, s, *MOM*-CH_3), 3.55-3.59 (2H, m, H_a-25, H-26), 3.65 (1H, dt, *J* 4.4 and 10.7, H-32), 3.73-3.78 (2H, m, H_b-25, H-31), 4.87 (1H, d, *J* 6.1, 0.5 x *MOM*-CH_2), 5.18 (1H, d, *J* 6.1, 0.5 x *MOM*-CH_2); δ_C (C_6D_6, 150 MHz) 17.1 (CH_3-27), 17.8 (2 x *BDA*-CH_3), 28.0 (C-34), 28.6 (C-33), 34.7 (C-27), 37.2 (C-28), 40.4 (C-29), 47.2, 47.3 (2 x *BDA*-OCH_3), 55.9 (*MOM*-CH_3), 64.2 (C-25), 69.1 (C-32), 76.2 (C-26), 76.9 (C-31), 81.3 (C-30), 98.5 (*MOM*-CH_2), 99.2, 99.3 (2 x *BDA*-CO_2); *m/z* APCI 415 $[M+Na]^+$, (5), 329 (32); *m/z* ESI 415.2300 $[M+Na]^+$. $C_{19}H_{36}O_8Na$ requires 415.2308.

(2*S*,3*S*,4a*S*,5*S*,6*S*,8a*R*,2'*R*,1''*R*)-2,3-Dimethoxy-5-methoxymethoxy-2,3-dimethyl-6-(2'-oxiranyl-propyl)-octahydro-benzo[1,4]dioxine (Fragment 2)

Sodium hydride (0.028 g, 0.70 mmol) was washed with petrol (2 x 5 ml), suspended in THF (1 ml) and cooled to 0 °C. A solution of cyclohexane **15** (0.110 g, 0.281 mmol) in THF (2 ml) was added dropwise. After 1 h, the suspension was cooled to −5°C, a solution of 2,4,6-triisopropylbenzenesulfonylimidazole (0.099 g, 0.30 mmol) in THF (1 ml) was added and the reaction mixture then allowed to warm to 0°C. After 1.5 h, t.l.c. (ethyl acetate) indicated the complete conversion of starting material (R_f 0.2) to a major product (R_f 0.6) and water was added (2 ml). The reaction mixture was diluted with DCM (20 ml), washed with water (40 ml) and the layers separated. The aqueous layer was extracted with DCM (2 x 20 ml), and the combined organic layers washed with brine (40 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo.* The residue was purified by flash chromatography (petrol:ether 6:4) to give epoxide **fragment 2** (0.086 g, 82%) as a colourless oil; $[\alpha]_D^{25}$ +40.3 (*c* 0.770 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3009, 2950, 1459, 1370, 1216, 1130, 1030; δ_H ($CDCl_3$, 600 MHz) 0.90 (1H, m, H_a-28), 0.96 (3H, d, *J* 7.0, CH_3-

27), 1.11 (1H, ddd, *J* 4.4, 9.8 and 13.9, H_a-34), 1.28 (3H, s, *BDA*-CH_3), 1.29 (3H, s, *BDA*-CH_3), 1.41-1.49 (2H, m, H-27, H_a-33), 1.69 (1H, m, H-29), 1.74 (1H, dd, *J* 3.3 and 12.8, H_b-33), 1.95-2.02 (2H, m, H_b-28, H_b-34), 2.44 (1H, dd, *J* 2.8 and 4.9, H_a-25), 2.67 (1H, m, H_b-25), 2.69 (1H, m, H-26), 3.19 (1H, t, *J* 9.4, H-30), 3.25 (3H, s, *BDA*-OCH_3), 3.26 (3H, s, *BDA*-OCH_3), 3.44 (3H, s, *MOM*-CH_3), 3.52-3.54 (2H, m, H-31, H-32), 4.74 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 5.01 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2); δ_C ($CDCl_3$, 150 MHz) 17.6 (CH_3-27), 17.7, 17.8 (2 x *BDA*-CH_3), 27.1 (C-28), 28.1 (C-33), 33.6 (C-27), 38.4 (C-34), 39.6 (C-29), 44.9 (C-25), 47.6, 47.8 (2 x *BDA*-OCH_3), 56.3 (*MOM*-CH_3), 56.8 (C-26), 69.2 (C-32), 76.6 (C-31), 80.4 (C-30), 98.2 (*MOM*-CH_2), 99.2 (2 x *BDA*-CO_2); *m/z* APCI 397 $[M+Na]^+$ (9), 343 (17), 302 (68); *m/z* ESI 397.2190 $[M+Na]^+$. $C_{19}H_{34}O_7Na$ requires 397.2202.

(5*R*)-6-(*tert*-Butyldimethylsilyloxy)-5-methylhex-1-ene

Allylmagnesium chloride (32 ml; 2 M solution in THF, 63 mmol) was added dropwise to a suspension of iodide **18** (10.0 g, 31.8 mmol) and copper (I) iodide (1.2 g, 6.3 mmol) in THF (100 ml) at -15°C over 15 min. The mixture was allowed to warm up to rt over 1 h and poured onto ice-water (300 ml), followed by extraction into ether (2 x 100 ml). The combined organic extracts were washed with H_2O (2 x 200 ml) and brine (200 ml), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography on silica gel (Biotage 40M; 0-10% ether-petrol) gave the *alkene* (6.22 g, 86%) as a colourless oil. $[\alpha]_D^{30}$ +2.2 (*c* 2.68 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 3078, 2954, 2929, 2856, 1641, 1472, 1463, 1388, 1361, 1255, 1095, 1029, 1006; δ_H ($CDCl_3$, 600 MHz) 0.04 (6H, s, 2 x $SiCH_3$), 0.88 (3H, d, *J* 6.7, CH_3-11), 0.89 (9H, s, $SiC(CH_3)_3$), 1.11-1.19 (1H, m, H_b-12), 1.46-1.54 (1H, m, H_a-12), 1.56-1.65 (1H, m, H-11), 1.99-2.15 (2H, m, H_a-13, H_b-13), 3.38 (1H, dd, *J* 9.7, 6.5, H-10), 3.45 (1H, dd, *J* 9.7, 5.9, H-10), 4.93 (1H, d, *J* 10.5, $=CH_2$), 5.00 (1H, d, *J* 17.1, $=CH_2$), 5.77-5.85 (1H, m, H-14); δ_C ($CDCl_3$, 100 MHz) -5.5 (2 x $SiCH_3$), 16.5 (CH_3-11), 18.3 ($SiC(CH_3)_3$), 25.9 ($SiC(CH_3)_3$), 31.2 (C-13), 32.4 (C-12), 35.2 (C-11), 68.1 (C-10), 114.0 ($=CH_2$), 139.2 (C-14); *m/z* EI 213 $[M-CH_3]^+$ (21), 205 (9), 171

(M-$C_4H_9^+$, 55), 115 (12), 75 (100); *m/z* EI Found: 171.1201 $[M-C_4H_9]^+$, $C_9H_{19}OSi$ requires 171.1205; Found: C 68.51 H 12.32, $C_{13}H_{28}OSi$ requires C 68.35 H 12.35%.

(4*R*)-5-(*tert*-Butyldimethylsilyloxy)-4-methylpentanal (19)

A solution of 6-(*tert*-Butyldimethylsilyloxy)-5-methylhex-1-ene (3.00 g, 13.1 mmol) in DCM (75 ml) was cooled to -78°C. Ozone was then bubbled through the solution for 15 min until a blue colour developed. The solution was flushed with oxygen then argon each for 5 min, and triphenylphosphine (7.67 g, 29.2 mmol) was added at -78°C. The mixture was warmed to rt over 30 min and then stirred at the same temperature for a further 4 h. The solvent was removed *in vacuo,* and petrol (100 ml) was added to the resulting thick slurry. The precipitate was removed by filtration and washed with petrol (2 × 50 ml). The filtrate and washings were concentrated *in vacuo* and purified by flash column chromatography (3-20% ether/petrol) to give the aldehyde **19** (2.67 g, 88%). $[\alpha]_D^{31}$ +6.3 (*c* 3.87 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 2956, 2930, 2858, 2713, 1728, 1472, 1463, 1389, 1361, 1255, 1094, 1006; δ_H ($CDCl_3$, 600 MHz) 0.03 (6H, s, 2 x $SiCH_3$), 0.87 (3H, s, CH_3), 0.89 (9H, s, $SiC(CH_3)_3$), 1.40-1.48 (1H, m, H-12), 1.57-1.67 (1H, m, H-11), 1.74-1.81 (1H, m, H_a-12), 2.40-2.52 (2H, m, H_a-13, H_b-13), 3.40-3.46 (2H, m, H_a-10, H_b-10), 9.77 (1H, t, *J* 1.8, H-14); δ_C ($CDCl_3$, 150 MHz) -5.5 (2 x $SiCH_3$), 16.4 (CH_3-11), 18.2 ($SiC(CH_3)_3$), 25.5 (C-3), 25.8 ($SiC(CH_3)_3$), 35.2 (C-11), 41.6 (C-13), 67.7 (C-10), 202.8 (C-14); *m/z* EI 173 $[M-C_4H_9]^+$ (17), 149 (11), 91 (100); *m/z* EI 173.0991 $[M-C_4H_9]^+$, $C_8H_{17}O_2Si$ requires 173.0998.

(4*R*,5*S*)-3-[(2'*R*,3'*S*,6'*R*)-7'-*tert*-Butyldimethylsilyloxy-3'-hydroxy-2',5'-dimethyl-1'-heptanoyl]-4-methyl-5-phenyl-2-oxazolidinone (21)

A solution of dibutylboron triflate (1.0 M in DCM, 39 ml, 39 mmol) was added to a solution of the oxazolidinone **20** (8.25 g, 35.4 mmol) in DCM (80 ml) dropwise at 0°C. After stirring for 5 min, triethylamine (5.92 ml, 42.4 mmol) was added at 0°C dropwise. The mixture was stirred at 0°C for 30 min, then cooled to -80°C. A solution of **19** in DCM (100 ml) was added using a cannula at -80°C dropwise. The mixture was stirred at

the same temperature for 60 h. Phosphate buffer (50 ml, pH 7.2) was added followed by methanol (400 ml) and an aqueous solution of hydrogen peroxide (50 ml, 30 wt%). The mixture was stirred at rt for 6 h, diluted with H_2O (300 ml), and extracted with DCM (2 x 100 ml). The combined organic fractions were washed with H_2O (2 x 100 ml) and brine (100 ml), dried, filtered and concentrated *in vacuo*. Recrystallisation of the crude product from petrol-ether gave an isomerically pure **21** (12.03 g) as colourless needles. From the mother liquor, another crop of **21** (also isomerically pure) was obtained after chromatography on silica gel (Biotage 40M; 25-50% ether/petrol), and recrystallisation as above (2.07 g, in total 94%). m.p. 98-99 °C; $[\alpha]_D^{30}$ -14.6 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (Nujol)/cm^{-1} 3472, 2923, 2854, 1784, 1688, 1460, 1375, 1342, 1248, 1192, 1153, 1120, 1090, 1072, 1030; δ_H ($CDCl_3$, 600 MHz, major isomer) 0.04 (6H, s, 2 x $SiCH_3$), 0.86-0.93 (15H, m, CH_3, CH_3-11, [including 0.90 (9H, s, $SiC(CH_3)_3$)]), 1.08-1.17 (1H, m, H-12), 1.24 (3H, d, *J* 7.1, CH_3-15), 1.46-1.66 (4H, m, H-11, H-12, H_a-13, H_b-13), 2.92 (1H, d, *J* 2.8, OH), 3.38 (1H, dd, *J* 9.8, 6.4, H_b-10), 3.48 (1H, dd, *J* 9.8, 5.5, H_a-10), 3.78 (1H, qd, *J* 7.0, 2.5, H-15), 3.91-3.97 (1H, m, H-14), 4.77-4.83 (1H, m, NC*H*Me), 5.68 (1H, d, *J* 7.3, OC*H*Ph), 7.29-7.33 (2H, m, 2 x PhH), 7.36-7.45 (3H, m, 3 x PhH); δ_C ($CDCl_3$, 150 MHz) -5.4 (2 x $SiCH_3$), 10.0 (CH_3-15), 16.7 and 14.3 (CH_3 and CH_3-11), 18.3 (Si*C*$(CH_3)_3$), 25.9 (SiC(*C*$H_3)_3$), 31.3 (C-13), 29.5 (C-12), 35.7 (C-11), 42.0 (C-15), 54.7 (NCHMe), 68.1 (C-10), 71.9 (C-14), 78.9 (OCHPh), 125.6, 128.7 and 128.8 (5 x PhCH), 133.1 (PhC), 152.5 (NCO_2), 177.4 (C-16); *m/z* LSIMS 464 $[MH]^+$ (100), 406 (20), 314 (80), 270 (18), 178 (51); *m/z* LSIMS 464.2833 $[MH]^+$, $C_{25}H_{42}NO_5Si$ requires 464.2832; Found: C 64.41 H 8.72 N 2.98, $C_{25}H_{41}NO_5Si$ requires C 64.76 H 8.91 N 3.02%.

(4*R*,5*S*)-3-[(2'*R*,3'*S*,6'*R*)-3',7'-bis(*tert*-Butyldimethylsilyloxy)-2',5'-dimethyl-1'-heptanoyl]-4-methyl-5-phenyl-2-oxazolidinone

tert-Butyldimethylsilyl Chloride (6.85 g, 45.5 mmol) was added to a solution of the alcohol **21** (14.05 g, 30.3 mmol) and imidazole (4.13 g, 61 mmol) in DMF (35 ml). The mixture was stirred at 40 °C for 2 days. A solution of $NaHCO_3$ (50 ml) was added and the mixture was extracted with ether (2 x 100 ml). The combined organic extract was

washed with H_2O (2 x 100 ml), a solution of $NaHCO_3$ (100 ml) and brine (100 ml), dried, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel (6% ether/petrol) to give the *bis-TBS ether* as a colourless oil (17.43 g, 99%). $[\alpha]_D^{30}$ +2.0 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 1782, 1706, 1472, 1462; δ_H ($CDCl_3$, 600 MHz) 0.038 (3H, s, $SiCH_3$), 0.043 (6H, s. 2 x $SiCH_3$), 0.06 (3H, s, $SiCH_3$), 0.90 (24H, m, 2 x $SiC(CH_3)_3$, CH_3-11, CH_3), 1.14-1.05 (1H, m, H_b-12), 1.17 (3H, d, *J* 6.8, CH_3-15), 1.65-1.42 (4H, m, H-11, H_a-12, H_a-13, H_b-13), 3.38 (1H, dd, *J* 9.8, 6.6, H_b-10), 3.47 (1H, dd, *J* 9.7, 5.7, H_a-10), 3.87 (1H, qd, *J* 6.7, 4.9, H-15), 4.02 (1H, q, *J* 5.4, H-14), 4.70 (1H, quintet, *J* 6.7, NC*H*Me), 5.60 (1H, d, *J* 7.0, OC*H*Ph), 7.31 (2H, d, *J* 7.4, 2 x ArH), 7.37 (1H, t, *J* 7.3, ArH), 7.42 (2H, t, *J* 7.4, 2 x ArH); δ_C ($CDCl_3$, 150 MHz) –5.4, -5.3, -4.9, -4.1 (4 x $SiCH_3$), 11.2 (CH_3-15), 14.2 (CH_3), 16.7 (CH_3-11), 18.1, 18.3 (2 x Si*C*$(CH_3)_3$), 25.9, 26.0 (2 x -SiC(*C*$H_3)_3$), 28.4 (C-12), 33.0 (C-13), 36.1 (C-11), 42.9 (C-15), 55.3 (NCHMe), 68.2 (C-10), 73.2 (C-14), 78.8 (OCHPh), 125.6 (ArCH), 128.7, 128.7 (ArCH), 133.3 (ArC), 152.6 (NCO_2), 175.1 (C-15); *m/z* ESI 600.3511 $[M+Na]^+$, $C_{31}H_{55}NNaO_5Si_2$ requires 600.3525.

(3*S*,4*S*,7*R*)-3,7-Bis-(*tert*-butyldimethylsilanyloxy)-2,6-dimethylheptanethioic acid *S*-ethyl ester (22)

A solution of *n*-BuLi in hexanes (1.6 M, 1.95 ml, 6.28 mmol) was added dropwise to a solution of ethanethiol (0.26 ml, 3.5 mmol) in THF (5 ml) at -78°C. After stirring at the same temperature for 15 min, a solution of the TBS-protected **21** (1.00 g, 1.73 mmol) in THF (10 ml) was added using a cannula. The mixture was stirred at -78°C for 20 min and at -15°C for 1 h. A solution of $NaHCO_3$ (20 ml) was added. The mixture was diluted with H_2O (50 ml) and extracted with ether (2 x 20 ml). The combined extract was washed with a 10% aqueous solution of NaOH (20 ml), H_2O (2 x 20 ml) and brine (20 ml), dried, filtered and concentrated *in vacuo*. Purification by flash column chromatography (25% $CHCl_3$-hexane) gave the thioester **22** (772 mg, 96%) as a colourless oil. $[\alpha]_D^{30}$ -15.7 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 1684, 1472, 1463; δ_H ($CDCl_3$, 600 MHz) 0.15 (3H, s, $SiCH_3$), 0.25 (6H, s, 2 x $SiCH_3$), 0.37 (3H, s, $SiCH_3$), 0.86 (3H, d, *J* 6.8, CH_3-11), 0.86 (9H, s, $SiC(CH_3)_3$), 0.88 (9H, s, $SiC(CH_3)_3$), 1.08-1.00

(1H, m, H_b-12), 1.15 (3H, d, *J* 6.9, CH_3-15), 1.23 (3H, t, *J* 7.4, SCH_2CH_3), 1.59-1.40 (4H, m, H-11, H_a-12, H_a-13, H_b-13), 2.70 (1H, qd, *J* 6.8, 5.6, H-15), 2.84 (2H, q, *J* 7.4, SCH_2CH_3), 3.36 (1H, dd, *J* 9.7, 6.3, H_b-10),), 3.42 (1H, dd, *J* 9.7, 5.9, H_a-10), 3.98 (1H, q, *J* 5.3, H-14); δ_C ($CDCl_3$, 150 MHz) –5.4, -4.7, -4.2 (4 x $SiCH_3$), 12.2 (CH_3-15), 14.6 (SCH_2CH_3), 16.7 (CH_3-11), 18.1, 18.3 (2 x $SiC(CH_3)_3$), 23.0 (SCH_2CH_3), 25.9, 26.0 (2 x $SiC(CH_3)_3$), 28.2 (C-12), 32.6 (C-13), 36.0 (C-11), 53.0 (C-15), 68.2 (C-10), 73.7 (C-14), 202.3 (C-16); *m/z* ESI 485.2899 $[M+Na]^+$, $C_{23}H_{50}O_3NaSSi_2$ requires 485.2917.

(2*R*,3*S*,6*R*)-3,7-Di(*tert*-butyldimethylsilyloxy)-2,6-dimethylheptanal (16)

A suspension of the thioester **22** (770 mg, 1.66 mmol) and 10% Pd-C (100 mg) in acetone (7 ml) was degassed under an atmosphere of argon. Triethylsilane (0.80 ml, 5.0 mmol) was added at rt. The mixture was stirred at the same temperature for 30 min and filtered through a Celite® pad. The catalyst was washed with acetone (x 5). The filtrate and the washings were combined and concentrated *in vacuo*. The crude product was purified by flash column chromatography (17-33% DCM in petrol) to give the aldehyde **16** (659 mg, 99%) as a colourless oil. $[\alpha]_D^{28}$ -20.0 (*c* 1.10 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 2955, 2930, 2857, 1728, 1472, 1463, 1389, 1351, 1255, 1097, 1032, 1006; δ_H ($CDCl_3$, 600 MHz) 0.03 (9H, s, 3 x $SiCH_3$), 0.07 (3H, s, $SiCH_3$), 0.86 (9H, s, $SiC(CH_3)_3$), 0.88 (3H, d, *J* 6.7, CH_3-11), 0.89 (9H, s, $SiC(CH_3)_3$), 0.95-1.03 (1H, m, H_b-12), 1.06 (3H, d, *J* 6.9, CH_3-15), 1.41-1.62 (4H, m, H-11, H_a-12, H_a-13, H_b-13), 2.42-2.48 (1H, m, H-15), 3.40 (2H, d, *J* 5.9, H_a-10, H_b-10), 4.07-4.12 (1H, m, H-14), 9.76 (1H, s, H-16); δ_C ($CDCl_3$, 150 MHz) -5.4, -4.7, and -4.2 (4 x $SiCH_3$) 7.4 (CH_3-15), 16.6 (CH_3-11), 18.0 and 18.3 (2 x $SiC(CH_3)_3$), 25.7 and 25.9 (2 x $SiC(CH_3)_3$), 29.1 (C-12), 31.9 (C-13), 35.7 (C-11), 51.0 (C-15), 68.0 (C-10), 72.3 (C-14), 205.3 (C-16); *m/z* EI 387 $[M-CH_3]^+$ (5), 345 (21), 287 (71), 253 (19), 213 (60), 185 (25), 171 (28), 159 (23), 147 (25), 119 (47), 115 (47), 91 (75), 81 (37), 75 (100); *m/z* EI 402.2995 $[M]^+$, $C_{21}H_{46}O_3Si_2$ requires 402.2985; Found: C 63.12 H 11.40, $C_{21}H_{46}O_3Si_2$ requires C 62.62 H 11.51%.

(2*R*)-3-(4-Methoxybenzyloxy)-2-methylpropan-1-ol (23)

Amberlite IR-120 (H^+ form, 200 g) was added to a solution of the THP ether of **23** (32.57 g, 0.111 mol) in methanol (300 ml). The mixture was stirred at rt for 6 h. The resin was removed by filtration and the filtrate was concentrated *in vacuo*. Purification by flash column chromatography (50-66% ether/petrol) gave the alcohol **23** (16.44 g, 70%) as a colourless oil. $[\alpha]_D^{31}$ +15.3 (*c* 1.31 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 3414, 2957, 2872, 1613, 1586, 1513, 1464, 1362, 1302, 1248, 1173, 1091, 1036; δ_H ($CDCl_3$, 600 MHz) 0.87 (3H, d, *J* 7.0, CH_3-23), 2.01-2.10 (1H, m, H-25), 2.58 (1H, broad s, OH), 3.37-3.42 (1H, m, H_b-22), 3.52 (1H, dd, *J* 9.1, 4.7, H_a-22), 3.55-3.65 (2H, m, H_a-24, H_b-24), 3.81 (3H, s, OCH_3), 4.44 (1H, d, *J* 11.6, 0.5 x CH_2Ar), 4.46 (1H, d, *J* 11.6, 0.5 x CH_2Ar), 6.86-6.90 (2H, m, 2 x ArH), 7.23-7.27 (2H, m, 2 x ArH); δ_C ($CDCl_3$, 150 MHz) 13.4 (CH_3-23), 35.5 (C-25), 55.2 (OCH_3), 67.7 (C-22 or C-24), 73.0 (OCH_2Ar), 75.0 (C-22 or C-24), 113.8, 129.2 (4 x ArCH), 130.1 (ArC), 159.2 (ArC); *m/z* EI 210 M^+ (18), 137 (81), 121 ($CH_2C_6H_4OCH_3^+$, 100), 107 (20), 91 (15), 78 (42); *m/z* EI 210.1259 M^+, $C_{12}H_{18}O_3$ requires 210.1256; Found: C 68.32 H 8.72, $C_{12}H_{18}O_3$ requires C 68.55 H 8.63%.

(2*R*)-3-(4-Methoxybenzyloxy)-2-methylpropan-1-al

DMSO (2.02 ml, 28.5 mmol) was added to a solution of oxalyl chloride (1.25 ml, 14.3 mmol) in DCM (20 ml) at -78°C dropwise over 10 min. After stirring at the same temperature for 15 min, a solution of the alcohol **23** (1.50 g, 7.13 mmol) in DCM (15 ml) was added dropwise. The mixture was stirred at -78°C for 2 h. Triethylamine (6.0 ml, 43 mmol) was added dropwise at the same temperature. After stirring at -78°C for 10 min, the mixture was allowed to warm up to 5°C and stirred at the same temperature for 1 h and then at rt for 30 min. 0.1 M aq. HCl (20 ml) was added and the aqueous layer was extracted with DCM (2 x 20 ml). The combined organic layers were washed with H_2O (2 x 50 ml), dried, filtered and concentrated *in vacuo*. Flash column chromatography (10-25% ether in petrol) yielded the *aldehyde* as a colourless oil (1.44 g, 97%). $[\alpha]_D^{30}$ 24.0 (*c* 1.00, $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 1721, 1612, 1586, 1512; δ_H ($CDCl_3$, 600 MHz) 1.11 (3H, d, *J* 7.1, CH_3-23), 2.60-2.68 (1H, m, H-23), 3.61 (1H, dd, *J* 9.4, 5.3, H_b-24), 3.65 (1H, dd, *J* 9.4, 6.8, H_a-24), 3.80 (3H, s, -OCH_3), 4.45 (2H, s, -OCH_2Ar), 6.88 (2H, d, *J* 8.6, 2 x ArH), 7.23 (2H, d, *J* 8.6, 2 x ArH), 9.71 (1H, d, *J* 1.6, H-27); δ_C ($CDCl_3$, 100

MHz) 10.7 (CH_3-23), 46.7 (C-23), 55.2 (OCH_3), 69.8 (C-24), 72.9 (OCH_2Ar), 113.8 (2 x ArCH), 129.2 (2 x ArCH), 130.0 (ArC), 159.3 (ArC), 203.8 (C-22); *m/z* ESI 231.0984 $[M+Na]^+$, $C_{22}H_{42}NaO_3$ requires 231.0997.

(2*E*,4*R*)- and (2*Z*,4*R*)-5-(4-Methoxybenzyloxy)-4-methylpentan-2-enoate ethyl ester (24)

(Ethoxycarbonylmethylene)triphenylphosphorane (22.1 g, 63.4 mmol) was added portionwise to a solution of 3-(4-methoxybenzyloxy)-2-methylpropan-1-al (11.5 g, 55.2 mmol) in DCM (300 ml) at 0°C. The mixture was stirred at rt for 2 days and concentrated to dryness. The residual oil was diluted with petrol (200 ml). The resulting precipitate was filtered off and washed with petrol several times. The filtrate and the washings were combined and concentrated *in vacuo*. Flash column chromatography (10-50% ether in petrol) yielded *cis*-**24** (0.11g, 0.7%) and *trans*-**24** (14.99 g, 98%) as colourless oils, respectively.

cis-**24**: $[\alpha]_D^{29}$ -44.8 (*c* 2.05 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 1716, 1643, 1612, 1586, 1512; δ_H ($CDCl_3$, 400 MHz) 1.05 (3H, d, *J* 6.8, CH_3-23), 1.28 (3H, t, *J* 7.1, OCH_2CH_3), 3.35 (2H, d, *J* 9.7, H-24), 3.80 (3H, s, OCH_3), 3.78-3.90 (1H, m, H-23), 4.17 (2H, q, *J* 7.1, OCH_2CH_3), 4.43 (1H, d, *J* 11.8, OCH_2Ar), 4.46 (1H, d, *J* 11.8, OCH_2Ar), 5.78 (1H, d, *J* 11.5, H-21), 6.10 (1H, dd, *J* 11.5, 9.8, H-22), 6.87 (2H, d, *J* 8.6, 2 x ArH), 7.23 (2H, d, *J* 8.6, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 14.20 (OCH_2CH_3), 16.78 (CH_3-23), 33.15 (C-23), 55.19 (OCH_3), 59.79 (OCH_2CH_3), 72.37 (OCH_2Ar), 74.25 (C-19), 113.68 (2 x ArCH), 119.73 (C-20), 129.08 (2 x ArCH), 130.58 (ArC), 152.63 (C-22), 159.08 (ArC), 166.13 (C-20); *m/z* ESI 301.1410 $[M+Na]^+$, $C_{16}H_{22}NaO_4$ requires 301.1411.

trans-**24**: $[\alpha]_D^{29}$ +11.9 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 1714, 1652, 1612, 1586, 1512; δ_H ($CDCl_3$, 400 MHz) 1.08 (3H, d, *J* 6.8, CH_3-23), 1.28 (3H, t, *J* 7.1, -OCH_2CH_3), 2.64 (1H, d sept, *J* 1.1, 6.6, H-23), 3.35 (1H, dd, *J* 9.1, 6.3, H_b-24), 3.38 (1H, dd, *J* 9.1, 6.9, H_a-24), 3.80 (3H, s, -OCH_3), 4.18 (2H, q, *J* 7.1, -OCH_2CH_3), 4.44 (2H, s, OCH_2Ar), 5.85 (1H, dd, *J* 15.8, 1.1, H-21), 6.87 (2H, d, *J* 8.6, 2 x ArH), 6.94 (1H, dd, *J* 15.8, 7.0, H-22), 7.24 (2H, d, *J* 8.5, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 14.2 (OCH_2CH_3), 16.0 (CH_3-23), 36.7 (C-23), 55.2 (OCH_3), 60.1 (OCH_2CH_3), 72.7 (OCH_2Ar), 73.6 (C-24), 113.7 (2 x

ArCH), 120.9 (C-21), 129.1 (2 x ArCH), 130.3 (ArC), 151.1 (C-22), 159.2 (ArC), 166.6 (C-20); *m/z* ESI 301.1410 $[M+Na]^+$, $C_{16}H_{22}NaO_4$ requires 301.1410.

(2*E*,4*R*)-5-(4-Methoxybenzyloxy)-4-methyl-2-penten-1-ol (25)

A solution of DIBAL-H (80 ml, 1.5 M in toluene, 120 mmol) was added dropwise to a solution of the *trans*-**24** (15.0 g, 53.9 mmol) in toluene (200 ml) at -78°C over 20 min. The mixture was stirred at the same temperature for 1.5 h. 1 N HCl solution (300 ml) was added and the aqueous layer was extracted with ether (100 ml). The combined organic layers were washed with H_2O (2 x 200 ml) and brine (100 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography (33-50% ether in petrol) gave the alcohol **25** as a colourless oil (11.82 g, 93%). $[\alpha]_D^{27}$ +9.4 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 3375, 1612, 1586, 1513; δ_H ($CDCl_3$, 400 MHz) 1.02 (3H, d, *J* 6.8, CH_3-23), 1.82 (1H, s, OH), 2.49 (1H, septet, *J* 6.6, H-23), 3.27 (1H, dd, *J* 9.3, 6.7, H_b-24), 3.33 (1H, dd, *J* 9.2, 6.7, H_a-24), 3.80 (3H, s, OCH_3), 4.07 (2H, broad s, H_a-20, H_b-20), 4.45 (2H, s, OCH_2Ar), 5.64 (1H, dd, *J* 15.7, 5.7, H-22), 5.67 (1H, dd, *J* 15.7, 5.1, H-21), 6.87 (2H, d, *J* 8.7, 2 x ArH), 7.25 (2H, d, *J* 8.6, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 16.9 (CH_3-23), 36.4 (C-23), 55.2 (OCH_3), 63.6 (C-20), 72.6 (OCH_2Ar), 74.7 (C-24), 113.7 (2 x ArCH), 128.8 (C-21), 129.1 (2 x ArCH), 130.5 (ArC), 135.2 (C-22), 159.1 (ArC); *m/z* ESI 259.1305 $[M+Na]^+$, $C_{14}H_{20}NaO_3$ requires 259.1290.

(2*E*,4*R*)-1-Bromo-5-(4-methoxybenzyloxy)-4-methyl-2-pentene (26)

Triphenylphosphine (7.46 g, 28.9 mmol) was added in one portion to a solution of the alcohol (5.70 g, 24.1 mmol) and carbon tetrabromide (9.60g, 28.9 mmol) in DCM (200 ml) at 0°C. The mixture was stirred at the same temperature for 30 min. MeOH (0.3 ml) was added and after 30 min, the solvent was removed by evaporation. The residual syrup was chromatographed (0-50% ether in petrol) to give the bromide **26** as a colourless oil (6.85 g, 95%). $[\alpha]_D^{27}$ +8.2 (*c* 1.07 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 1655, 1612, 1586, 1512; δ_H ($CDCl_3$, 400 MHz) 1.04 (3H, d, *J* 6.8, CH_3-23), 2.53 (1H, septet, *J* 6.4, H-23), 3.30 (1H, dd, *J* 9.2, 6.5, H_b-20), 3.34 (1H, dd, *J* 9.2, 6.8, H_a-20), 3.81 (3H, s, OCH_3), 3.92-4.00

(2H, m, H_a-24, H_b-24), 4.45 (2H, s, OCH_2Ar), 5.69-5.78 (2H, m, H-22 and 21), 6.89 (2H, d, *J* 8.7, 2 x ArH), 7.26 (2H, d, *J* 8.6, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 16.6 (CH_3-23), 33.3 (C-20), 36.4 (C-23), 55.2 (OCH_3), 72.6 (OCH_2Ar), 74.4 (C-24), 113.7 (2 x ArCH), 126.0 (C-21), 129.1 (2 x ArCH), 130.5 (ArC), 138.7 (C-22), 159.1 (ArC); *m/z* ESI 321.0461 $[M+Na]^+$, $C_{14}H_{19}BrNaO_2$ requires 321.0462.

(3*E*,2*R*)-1-(4-Methoxybenzyloxy)-2-Methyl-8-(trimethylsilyloxy)-oct-3-en-7-yne (27)

A solution of 1-trimethylsilyl-1-propyne (3.90 g, 34.7 mmol) in THF (50 ml) was added to a solution of *n*-BuLi (1.6 M in hexanes, 21.7 ml, 34.7 mmol) in THF (250 ml) at -15°C dropwise over 20 min. After stirring at the same temperature for 2 min, the mixture was cooled to -78°C. A solution of the bromide **26** (8.00 g, 26.7 mmol) in THF (50 ml) was added dropwise at -78°C over 20 min. The mixture was stirred at the same temperature for 1 h. Phosphate buffer (200 ml, pH 7.2) was added and the mixture was extracted with petrol (2 x 200 ml). The combined organic extract was washed with H_2O (2 x 200 ml) and brine (100 ml), dried over ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was purified by chromatography (Biotage 40M; 2.5-50% ether/petrol) to give the TMS acetylene **27** (7.80 g, 88%) as a colourless oil. $[\alpha]_D^{28}$ -3.2 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 2174, 1613, 1587, 1512; δ_H ($CDCl_3$, 400 MHz) 0.15 (9H, s, 3 x $SiCH_3$), 1.02 (3H, d, *J* 6.8, CH_3-23), 2.17-2.23 (2H, m, H_a-20, H_b-20), 2.24-2.28 (2H, m, H_a-19, H_b-19), 2.46 (1H, septet, *J* 6.7, H-23), 3.24 (1H, dd, *J* 9.1, 7.2, H_b-24), 3.34 (1H, dd, *J* 9.1, 6.3, H_a-24), 3.81 (3H, s, OCH_3), 4.43 (1H, d, *J* 11.8, OCH_2Ar), 4.46 (1H, d, *J* 11.8, OCH_2Ar), 5.44 (1H, dd, *J* 15.5, 6.9, H-22), 5.50 (1H, dt, *J* 15.4, 6.9, H-21), 6.88 (2H, d, *J* 8.6, 2 x ArH), 7.26 (2H, d, *J* 8.6, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 0.1 (3 x $SiCH_3$), 17.2 (CH_3-23), 20.2 (C-19), 31.8 (C-20), 36.8 (C-23), 55.2 (OCH_3), 72.5 (OCH_2Ar), 75.1 (C-24), 84.7 (C-17), 107.0 (C-18), 113.7 (2 x ArCH), 128.9 (C-21), 129.1 (2 x ArCH), 130.7 (ArC), 134.2 (C-22), 159.1 (ArC); *m/z* ESI 353.1907 $[M+Na]^+$, $C_{20}H_{30}NaO_2Si$ requires 353.1890.

4'-Methoxybenzyl (3*E*,2*R*)-2-Methyloct-3-en-7-ynyl Ether (17)

A 10% aqueous solution of NaOH (5 ml) was added to a solution of the TMS acetylene **27** (7.80 g, 23.6 mmol) in MeOH (200 ml). The mixture was stirred at rt for 2 days, concentrated *in vacuo* to ca. 1/4 in volume, diluted with H_2O (200 ml), and then extracted with ether (2 x 200 ml). The combined organic extracts were washed with H_2O (2 x 100 ml) and brine (100 ml), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was purified by chromatography (Biotage 40M; 6% ether/petrol) to give the terminal acetylene **17** (6.02 g, 99%) as a colourless oil. $[\alpha]_D^{28}$ -2.8 (*c* 1.00 in $CHCl_3$); $\nu_{(max)}$ (film)/cm^{-1} 2174, 1613, 1587, 1512; δ_H ($CDCl_3$, 600 MHz) 1.03 (3H, d, *J* 6.8, CH_3-23), 1.97 (1H, s, H-17), 2.28-2.19 (4H, m, H_a-19, H_b-19, H_a-20, H_b-20), 2.47 (1H, septet, *J* 6.7, H-23), 3.26 (1H, dd, *J* 9.1, 7.0, H_b-24), 3.34 (1H, dd, *J* 9.1, 6.4, H_a-24), 3.80 (3H, s, OCH_3), 4.44 (1H, d, *J* 12.0, OCH_2Ar), 4.46 (1H, d, *J* 12.0, OCH_2Ar), 5.46 (1H, dd, *J* 15.5, 6.8, H-22), 5.53 (1H, dt, *J* 15.4, 6.2, H-21), 6.89 (2H, d, *J* 8.7, 2 x ArH), 7.27 (2H, d, *J* 8.6, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) 17.1 (CH_3-23), 18.7 (C-19), 31.6 (C-20), 36.6 (C-23), 55.1 (OCH_3), 68.4 (C-18), 72.3 (OCH_2Ar), 75.0 (C-24), 84.0 (C-17), 113.6 (2 x ArCH), 127.7 (C-21), 129.0 (2 x ArCH), 130.7 (ArC), 134.3 (C-3), 159.0 (ArC); *m/z* ESI 281.1512 $[M+Na]^+$, $C_{17}H_{22}NaO_2$ requires 281.1517.

(8*E*,12*E*,2*R*,5*S*,6*S*,7*R*,14*R*)- and (8*E*,12*E*,2*R*,5*S*,6*S*,7*S*,14*R*)-1,5-Bis(*tert*-butyldimethylsilyloxy)-15-(4-methoxybenzyloxy)-2,6,14-trimethylpentadeca-8,12-dien-7-ol (28)

A solution of the terminal acetylene **17** (834 mg, 3.23 mmol; azeotroped with toluene before use) in DCM (7 ml) was added to a suspension of dicyclopentadienylzirconocene hydride chloride (prepared according to the literature (see below); 916 mg, 3.55 mmol) in DCM (15 ml) at -15°C. The mixture was stirred at rt for 20 min and cooled to 0°C; the mixture turned pale yellow within 5 min. A solution of the aldehyde **16** (1.00 g, 2.48 mmol; azeotroped once with toluene before use) in DCM (7 ml) was added to the solution followed by a solution of silver perchlorate in toluene (20g/l, 1.3 ml, 0.12 mmol). The mixture was stirred at 0°C ~ rt for 3 h giving a dark brown solution. H_2O (0.1 ml) was added. The mixture was stirred at rt for 10 min, dried ($MgSO_4$) and passed through a Flosiril® pad. The precipitate was washed with ether (500 ml). The filtrate and

washings were concentrated *in vacuo* and the residual oil was purified by flash chromatography (Biotage 40M; 10-33% ether/petrol), to give 7*S*-**28** (less polar; 778 mg, 47%) and 7*R*-**28** (more polar; 813mg, 49%) each as a colourless oil. The 400 MHz ^{1}H-NMR of the crude product showed the ratio of the two isomers to be 1 : 1.

Preparation of dicyclopentadienylzirconocene hydride chloride[*] all the transfers *via* a cannula or filtrations were driven by a positive pressure of argon: In a 100-ml vessel fitted with a glass scinter, dicyclopentadienylzirconocene dichloride (1.50 g, 51.3 mmol) was dissolved in THF (70 ml) with slight heating. While this solution was still warm, a solution of lithium aluminium hydride in THF (1.0 M, 14.1 ml, 14.1 mmol) was added dropwise, over a 20-min period. The resulting reddish suspension was stirred in dark at rt for 1.5 hr. The solvent was removed by positive pressure of argon. The precipitate was washed with THF (5 x 10 ml), DCM (2 x 15 ml), and ether (4 x 10 ml), and dried under a flow of argon, and then *in vacuo* overnight to give a colourless powder (11.0 g, 42.6 mmol, 83%). The reagent thus obtained was stored in a dark bottle in a glove box and used within two weeks.

7*S*-28 $[\alpha]_D^{31}$ -4.2 (*c* 0.77 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 3475, 2955, 2856, 1613, 1587, 1514, 1471, 1462, 1387, 1360, 1302, 1249, 1172, 1092, 1037, 1005; δ_H ($CDCl_3$, 600 MHz) 0.04 (6H, s, 2 x $SiCH_3$), 0.08 (3H, s, $SiCH_3$), 0.11 (3H, s, $SiCH_3$), 0.74 (3H, d, *J* 7.1, CH_3-23), 0.84-1.03 (25H, m, H_b-12, CH_3-11, [including 0.99 (3H, d, *J* 6.7, CH_3-23) 0.90 (9H, s, $SiC(CH_3)_3$) 0.89 (9H, s, $SiC(CH_3)_3$)]), 1.47-1.62 (4H, m, H-11, H_a-12, H_a-13, H_b-13), 1.66-1.74 (1H, m, H-15), 2.04-2.15 (4H, m, H_a-19, H_b-19, H_a-20, H_a-20), 2.39-2.47 (1H, m, H-23), 3.19-3.25 (1H, m, H_b-24), 3.29-3.35 (1H, m, H_a-24), 3.38 (1H, dd, *J* 9.7, 5.9, H_b-10), 3.44 (1H, dd, *J* 9.7, 5.6, H_a-10), 3.78-3.84 (4H, m, H-14 [including 3.80 (3H, s, OCH_3)]), 3.90 (1H, broad s, OH), 3.97 (1H, apparent t, *J* 8.4, H-16), 4.43 (1H, d, *J* 11.9, OCH_2Ar), 4.44 (1H, d, *J* 11.9, OCH_2Ar), 5.33-5.49 (3H, m, $J_{\text{alkenyl Hs}}$ 15.4, H-17, H-21, and H-22), 5.59-5.67 (1H, m, $J_{\text{alkenyl Hs}}$ 15.2, H-18), 6.87 (2H, d, *J* 8.5, 2 ArH), 7.25 (2H, d, *J* 8.5, 2 ArH); δ_C ($CDCl_3$, 100 MHz) -4.4 and -5.4 (4 x $SiCH_3$), 13.1 (CH_3-15), 16.8 (CH_3-11), 17.3 (CH_3-23), 18.3 and 18.0 (2 x $SiC(CH_3)_3$), 25.9 (2 x

[*] S. L. Buchwald, S. J. LaMaire, R. B. Nielsen, B. T. Watson, S. M. King, *Tetrahedron Lett*., 1987, **28**, 3895-3898.

SiC(CH_3)$_3$), 29.4 (C-13), 30.2 (C-12), 32.4 and 32.3 (C-19 and C-20), 35.9 (C-11), 36.8 (C-23), 42.9 (C-15), 55.2 (OCH_3), 68.1 (C-10), 72.5 (OCH_2Ar), 75.2 (C-24), 75.7 (C-19), 76.9 (C-14), 113.7 (2 x ArCH), 129.1 (2 x ArCH), 129.3 (C-21), 130.8 (ArC), 132.3 (C-18), 132.7 (C-17), 133.2 (C-22), 159.1 (ArC); *m/z* ES 685 $[M+Na]^+$ (100), 669 (9), 576 (11); *m/z* ES 685.4713 $[M+Na]^+$, $C_{38}H_{70}O_5Si_2Na$ requires 685.4659; Found: C 69.07 H 10.60, $C_{38}H_{70}O_5Si_2$ requires C 68.83 H 10.64%.

7*R*-28 $[\alpha]_D^{29}$ +18.5 (*c* 1.17 in DCM); $\nu_{(max)}$ (film)/cm^{-1} 3456, 2956, 2931, 2856, 1614, 1587, 1514, 1471, 1387, 1360, 1302, 1250, 1172, 1094, 1038, 1006; δ_H ($CDCl_3$, 600 MHz) 0.04 (6H, s, 2 x $SiCH_3$), 0.09 (6H, s, 2 x $SiCH_3$), 0.86-1.01 (28H, m, H_a-12, CH_3-11, CH_3-15, [including 1.00 (3H, d, *J* 6.7, CH_3-23), 0.90 (9H, s, SiC(CH_3)$_3$), 0.89 (9H, s, SiC(CH_3)$_3$)]), 1.30-1.38 (1H, m, H_a-12), 1.42-1.63 (4H, m, H-11, H_a-13, H_b-13, H-15), 2.06-2.13 (4H, m, H_a-19, H_b-19, H_a-20, H_b-20), 2.39-2.47 (1H, m, H-23), 2.78 (1H, broad s, OH), 3.20-3.25 (1H, m, H_b-24), 3.32 (1H, dd, *J* 9.0, 6.4, H_a-24), 3.39 (2H, d, *J* 6.1, H_a-10, H_b-10), 3.80 (3H, s, OCH_3), 3.82-3.86 (1H, m, H-14), 4.20-4.25 (1H, m, H-16), 4.43 (1H, d, *J* 11.9, OCH_2Ar), 4.44 (1H, d, *J* 11.9, OCH_2Ar), 5.37 (1H, dd, *J* 15.4, 7.0, H-22), 5.44-5.50 (2H, m, H-17 and H-21), 5.64-5.72 (1H, m, $J_{\text{alkenyl Hs}}$ 15.3, H-18), 6.85-6.89 (2H, m, 2 x ArH), 7.24-7.28 (2H, m, 2 x ArH); δ_C ($CDCl_3$, 100 MHz) −5.4, -5.3, -4.5 and −3.6 (4 x $SiCH_3$), 5.8 (CH_3-15), 16.5 (CH_3-11), 17.3 (CH_3-23), 18.0 and 18.3 (2 x Si*C*(CH_3)$_3$), 25.9 and 26.0 (2 x SiC(*C*H_3)$_3$), 28.7 (C-12), 32.1 (C-13), 32.4 (C-19 and C-20), 35.8 (C-11), 36.8 (C-23), 40.6 (C-15), 55.3 (OCH_3), 68.1 (C-10), 72.5 (OCH_2Ar), 75.2 (C-24), 75.7 (C-19), 77.2 (C-14), 113.7 (2 x ArCH), 129.1 (2 x ArCH), 129.4 (C-17 or C-21), 130.8 and 130.9 (ArC, C-18), 131.9 (C-17 or C-21), 133.1 (C-22), 159.0 (ArC); *m/z* ES 685.4656 $[MNa]^+$, $C_{38}H_{70}O_5Si_2Na$ requires 685.4659; Found: C 69.02 H 10.55, $C_{38}H_{70}O_5Si_2$ requires C 68.83 H 10.64%.

(3*E*,7*E*,2*R*,9*R*,11*S*,14*R*)-9,11,15-Tri-(*tert*-butyldimethylsilanyloxy)-1-(*para*-methoxybenzyloxy)-2,10,14-trimethylpentadeca-3,7-diene (Fragment 3)

TBSCl (1.05 g, 6.97 mmol) was added to a stirring solution of alcohol **28** (1.98 g, 2.99 mmol) and imidazole (0.688 g, 9.82 mmol) in DMF (4.5 ml). After 20h, t.l.c indicated the

complete conversion of starting material to a major product. The reaction mixture was added to a saturated aqueous solution of $NaHCO_3$ (30 ml) and extracted with ether (2 x 50 ml). The combined organic layers were washed with water (3 x 50 ml), saturated aqueous $NaHCO_3$ (50 ml) and brine (50 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (4 to 6% ether in petrol) to give protected tetrol **fragment 3** (2.25 g, 97%) as a colourless oil; $[\alpha]_D^{25}$ +4.50 (*c* 1.00 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2954, 2928, 2856, 1614, 1514, 1472, 1462, 1360, 1302, 1248, 1087, 1038; δ_H ($CDCl_3$, 400 MHz) –0.01 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$), 0.035 (3H, s, $SiCH_3$), 0.04 (6H, s, 2 x $SiCH_3$), 0.82–1.07 (37H, m, CH_3-15, H_a-12, [including 0.87 (3H, d, *J* 6.8, CH_3-11), 0.88 (9H, s, $SiC(CH_3)_3$), 0.89 (9H, s, $SiC(CH_3)_3$), 0.90 (9H, s, $SiC(CH_3)_3$), 1.01 (3H, d, *J* 6.7, CH_3-23)]), 1.25–1.63 (5H, m, H-11, H_b-12, H_a-13, H_b-13, H-15), 2.03 (4H, m, H_a-19, H_b-19, H_a-20, H_b-20), 2.44 (1H, m, H-23), 3.22 (1H, dd, *J* 7.6, 8.8, H_a-24), 3.34 (1H, dd, *J* 6.5, 8.8, H_b-24), 3.36 (1H, dd, *J* 6.2, 8.0, H_a-10), 3.43 (1H, dd, *J* 6.2, 9.7, H_b-10), 3.65 (1H, dt, *J* 4.8, 6.0, H-14), 3.81 (3H, s, OCH_3), 4.45 (2H, d, *J* 1.6, OCH_2Ar), 5.39 (2H, dd, *J* 7.2, 15.5, H-17, H-22), 5.44 - 5.59 (2H, m, H-18, H-21), 6.88 (2H, d, *J* 8.6, 2 x ArCH), 7.26 (2H, d, *J* 8.6, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) –5.4, -4.7, -4.4, -3.6 (6 x $SiCH_3$), 9.3 (CH_3-15), 16.6 (CH_3-11), 17.3 (CH_3-23), 18.17, 18.21, 18.3 (3 x $SiC(CH_3)_3$), 25.96, 25.99 (3 x $SiC(CH_3)_3$), 28.6 (C-12), 32.2 (C-13), 32.4, 32.5 (C-19, C-20), 36.0 (C-11), 36.8 (C-23), 43.6 (C-15), 55.2 (OCH_3), 68.3 (C-10), 72.5 (OCH_2Ar), 72.7 (C-14), 75.0 (C-16), 75.2 (C-23), 113.7 (ArCH), 129.1 (ArCH), 129.4 (C-21), 130.7 (ArC), 131.0 (C-18), 133.0 (C-22), 133.4 (C-17), 159.0 (ArC); *m/z* ESI Found 799.5516, $[M+Na]^+$. $C_{44}H_{84}O_5Si_3Na$ requires 799.5524.

(3*E*,7*E*,2*R*,9*R*,10*R*,11*S*,14*R*)-9,11,15-Tri-(*tert*-butyldimethylsilanyloxy)-2,10,14-trimethylpentadeca-3,7-diene-1-ol

DDQ (1.02 g, 4.47 mmol) was added to a vigorously stirred emulsion of tetrol **fragment 3** (2.90 g, 3.73 mmol) in DCM (28 ml) and water (7 ml) at 0°C. After 3.5 h, t.l.c. indicated complete conversion of the starting material to a major product. The reaction

mixture was diluted with DCM (100 ml), washed with saturated aqueous $NaHCO_3$ (250 ml) and extracted with DCM (2 x 50 ml). The combined organic layers were washed with brine (250 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude *deprotected alcohol* (2.90 g) contaminated with some *para*-methoxybenzaldehyde. This mixture was used in the subsequent step without further purification.

(3*E*,7*E*,2*R*,9*R*,10*R*,11*S*,14*R*)-9,11,15-Tri-(*tert*-butyldimethylsilanyloxy)-2,10,14-trimethyl-1-phenylsulfanylpentadeca-3,7-diene

Tributylphosphine (3.06 ml, 12.3 mmol) was added to a solution of diphenyldisulfide (2.44 g, 11.2 mmol) in pyridine (10 ml) and heated to 80°C. After 15 min, the solution was added in one portion to a stirring solution of crude deprotected fragment 3 (2.90 g) in pyridine (7 ml) at room temperature. After 3.5 h, t.l.c. indicated the complete conversion of starting material to a major product. The reaction mixture was diluted with ether (200 ml) and washed with saturated aqueous $NaHCO_3$ (2 x 100 ml) and subsequently with saturated aqueous NH_4Cl (2 x 100 ml). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (0 to 1% ether in petrol) to give the *sulfide* (2.14 g, 77% over the steps) as a colourless oil; $[\alpha]_D^{25}$ +18.6 (*c* 1.02 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2954, 2928, 2856, 1586, 1472, 1462, 1439, 1389, 1361, 1250, 1087, 1026; δ_H ($CDCl_3$, 400 MHz) 0.02 (3H, s, $SiCH_3$), 0.04 (3H, s, $SiCH_3$), 0.05 (3H, s, $SiCH_3$), 0.06 (9H, s, 3 x $SiCH_3$), 0.86 – 1.10 (34H, m, CH_3-11, CH_3-15, H_a-12, [including 0.91 (9H, s, $SiC(CH_3)_3$), 0.917 (9H, s, $SiC(CH_3)_3$), 0.921 (9H, s, $SiC(CH_3)_3$)]), 1.14 (3H, d, *J* 6.7, CH_3-23), 1.27-1.63 (5H, m, H-11, H_b-12, H_a-13, H_b-13, H-15), 2.04-2.16 (4H, m, H_a-19, H_b-19, H_a-20, H_b-20), 2.42 (1H, m, H-23), 2.83 (1H, dd, *J* 7.3, 12.5, H_a-24), 2.97 (1H, dd, *J* 6.6, 12.5, H_b-24), 3.38 (1H, dd, *J* 6.4, 9.7, H_a-10), 3.44 (1H, dd, *J* 5.9, 9.7, H_b-10), 3.68 (1H, dt, *J* 4.8, 5.9, H-14), 4.06 (1H, dd, *J* 7.2, 7.2, H-16), 5.42 (2H, dd, *J* 7.2, 15.5, H-17, H-22), 5.46 - 5.62 (2H, m, H-18, H-21), 7.16 (1H, t, *J* 7.5, ArCH), 7.28 (2H, dd, *J* 7.5, 7.5, 2 x ArCH), 7.34 (2H, d, *J* 7.5, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) –5.3, -4.7, -4.4, -3.61, -3.58 (6 x $SiCH_3$), 9.4 (CH_3-15), 16.7 (CH_3-11), 18.18, 18.22, 18.3 (3 x $SiC(CH_3)_3$), 19.9 (CH_3-23), 25.98, 26.00, 26.02 (3

x SiC(CH_3)$_3$), 28.7 (C-12), 32.27 (C-13), 32.30, 32.4 (C-19, C-20), 36.0 (C-11), 36.4 (C-23), 41.0 (C-24), 43.7 (C-15), 68.3 (C-10), 72.8 (C-14), 75.0 (C-16), 125.6 (ArCH), 128.8 (2 x ArCH), 129.0 (2 x ArCH), 129.5 (C-21), 130.9 (C-17), 133.5 (C-18), 134.3 (C-22), 137.3 (ArC); *m/z* ESI Found 771.5057, $[M+Na]^+$. $C_{42}H_{80}O_3SSi_3Na$ requires 771.5034.

(3*E*,7*E*,2*R*,9*R*,10*R*,11*S*,14*R*)-1-Benzenesulfonyl-9,11,15-tri-(*tert*-butyldimethyl-silanyloxy)-2,10,14-trimethylpentadeca-3,7-diene (29)

An aqueous solution of hydrogen peroxide (0.945 ml, 27.5 wt% in water, 8.58 mmol) was added dropwise to a solution of 9,11,15-Tri-(*tert*-butyldimethylsilanyloxy)-2,10,14-trimethyl-1-phenylsulfanylpentadeca-3,7-diene (1.07 g, 1.43 mmol) and diphenyl-diselenide (0.446 g, 1.43 mmol) in ether (6 ml) at -10°C and the resulting mixture was allowed to warm slowly to room temperature. After 24 h, a second portion of aqueous hydrogen peroxide (0.945 ml, 27.5 wt% in water, 8.58 mmol) was added. After a further 5 h, t.l.c. indicated the complete conversion of the starting material to a major product. The reaction mixture was diluted with ether (200 ml) and washed with saturated aqueous $NaHCO_3$ (100 ml) and subsequently with saturated aqueous $Na_2S_2O_3$ (100 ml). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol/ether 4/1) to give sulfone **29** (1.02 g, 91%) as a colourless oil; $[\alpha]_D^{25}$ +8.02 (*c* 0.855 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2955, 2928, 2856, 1472, 1462, 1447, 1306, 1250, 1149, 1085, 1030; δ_H ($CDCl_3$, 400 MHz) -0.04 (3H, s, $SiCH_3$), -0.01 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$), 0.02 (9H, s, 3 x $SiCH_3$), 0.82 – 1.05 (34H, m, CH_3-15, H_a-12, [including 0.85 (3H, d, *J* 3.8, CH_3-11), 0.87 (9H, s, SiC(CH_3)$_3$), 0.877 (9H, s, SiC(CH_3)$_3$), 0.880 (9H, s, SiC(CH_3)$_3$)]), 1.14 (3H, d, *J* 6.8, CH_3-23), 1.23-1.57 (5H, m, H-11, H_b-12, H_a-13, H_b-13, H-15), 1.90-2.05 (4H, m, H_a-19, H_b-19, H_a-20, H_b-20), 3.01 (1H, dd, *J* 7.0, 14.1, H_a-24), 3.12 (1H, dd, *J* 6.2, 14.1, H_b-24), 3.35 (1H, dd, *J* 6.3, 9.7, H_a-10), 3.40 (1H, dd, *J* 6.0, 9.7, H_b-10), 3.63 (1H, m, H-14), 4.01 (1H, dd, *J* 7.2, 7.2, H-16), 5.25 (1H, dd, *J* 7.7, 15.1, H-22),5.36 (1H, dd, *J* 7.2, 15.1, H-17), 5.43 (1H, dt, *J* 5.2, 15.1, H-21), 5.47 (1H, dt, *J* 6.0, 15.1, H-18), 7.50-7.56 (2H, m, 2 x ArCH),

7.57-7.65 (1H, m, ArCH), 7.85-7.92 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) −5.4, -4.7, -4.4, -3.7, -3.6 (6 x $SiCH_3$), 9.3 (CH_3-15), 16.6 (CH_3-11), 18.12, 18.14, 18.3 (3 x $SiC(CH_3)_3$), 20.6 (CH_3-23), 25.93, 25.96 (3 x $SiC(CH_3)_3$), 28.6 (C-12), 31.9 (C-20), 32.0 (C-23), 32.1 (C-19), 32.2 (C-13), 35.9 (C-11), 43.7 (C-15), 62.4 (C-24), 68.2 (C-10), 72.7 (C-14), 74.8 (C-16), 127.9 (2 x ArCH), 129.1 (2 x ArCH), 130.0 (C-21), 130.5 (C-18), 132.7 (C-22), 133.4 (ArCH), 133.6 (C-17), 140.3 (ArC); *m/z* ESI Found 803.4903, $[M+Na]^+$. $C_{42}H_{80}O_5SSi_3Na$ requires 803.4932.

(7*E*,11*E*,2*R*,3*S*,5*RS*,6*R*,13*R*,14*R*,15*S*,18*R*,2'*S*,3'*S*,4a'*S*,5'*S*,6'*S*,8a'*R*)-5-Benzenesulfonyl-13,15,19-tris-(*tert*-butyldimethylsilanyloxy)-1-(2',3'-dimethoxy-5'-methoxymethoxy-2',3'-dimethyloctahydrobenzo[1',4']dioxin-6'-yl)-2,6,14,18-tetramethylnonadeca-7,11-dien-3-ol

A solution of *n*-BuLi (2.95 ml, 1.6 M in hexane, 4.72 mmol) was added dropwise to a stirring solution of sulfone **29** (1.84 g, 2.35 mmol) in THF (6 ml) at -78°C. The reaction mixture was stirred for 30 min, before boron trifluoride diethyletherate (0.26 ml, 2.05 mmol) was added dropwise. After a further 5 min, a solution of **fragment 2** (0.695 g, 1.86 mmol) in THF (4ml) was added dropwise. Stirring continued for a further 1.5 h at -78°C before the reaction was quenched with saturated aqueous NH_4Cl (20 ml), diluted with ether (150 ml) and the layers were separated. The aqueous layer was extracted with ether (100 ml) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol/ether 4/1 to 3/7) to give sulfone **29** (333 mg, 18%) as a coluorless oil; data identical to that previously described. Further elution yielded the *coupled sulfone* (1.37 g, 63%) as a colourless oil; $[\alpha]_D^{25}$ +29.0 (*c* 0.935 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2955, 2928, 2856, 1447, 1472, 1462, 1388, 1361, 1306, 1250, 1149, 1086, 1030, 1005; δ_H ($CDCl_3$, 400 MHz) -0.07 (3H, s, $SiCH_3$), -0.03 (3H, s, $SiCH_3$), -0.01 (3H, s, $SiCH_3$), 0.00 (3H, s, $SiCH_3$), 0.01 (6H, s, 2 x $SiCH_3$), 0.77-0.89 (37H, m, CH_3-11, CH_3-15, CH_3-27, H_a-28, [including 0.85 (9H, s, $SiC(CH_3)_3$), 0.86 (9H, s, $SiC(CH_3)_3$), 0.87 (9H, s, $SiC(CH_3)_3$)]), 0.90-1.10 (5H, m, H_a-12, H_a-34, [including 1.05 (3H, d, *J* 6.8, CH_3-23)]), 1.20-1.56 (14H,

m, H-11, H_b-12, H_a-13, H_b-13, H-15, H_a-25, H-29, H_a-33, [including 1.259 (3H, s, *BDA*-CH_3), 1.263 (3H, s, *BDA*-CH_3)]), 1.61 (1H, m, H-27), 1.67-1.83 (2H, m, H_b-33, H_b-34), 1.86-2.07 (5H, m, H_a-19, H_b-19, H_a-20, H_b-20, [including 1.93 (1H, ddd, *J* 4.4, 5.9, 14.3, H_b-28)]), 2.13 (1H, ddd, *J* 2.0, 9.3, 15.0, H_b-25), 2.24 (1H, brs, OH), 2.64-2.75 (1H, m, H-23), 3.13 (1H, dd, *J* 9.4, 9.4, H-30), 3.22 (3H, s, *BDA*-OCH_3), 3.24 (3H, s, *BDA*-OCH_3), 3.30-3.43 (6H, m, H_a-10, H_b-10, H-26, [including 3.37 (3H, s, *MOM*-CH_3)]), 3.44-3.56 (3H, m, H-24, H-31, H-32), 3.61 (1H, dt, *J* 4.9, 5.9, H-14), 3.99 (1H, dd, *J* 6.9, 6.9, H-16), 4.73 (1H, d, *J* 6.2, 0.5 x *MOM*-CH_2), 4.95 (1H, d, *J* 6.2, 0.5 x *MOM*-CH_2), 5.22-5.50 (4H, m, H-17, H-18, H-21, H-22), 7.48-7.56 (2H, m, 2 x ArCH), 7.57-7.60 (1H, m, ArCH), 7.84-7.92 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) –5.4, -4.7, -4.4, -3.70, -3.67 (6 x $SiCH_3$), 9.3 (CH_3-15), 13.9 (CH_3-23), 16.6 (CH_3-11), 16.9 (CH_3-27), 17.70, 17.77 (2 x *BDA*-CH_3), 18.10, 18.12, 18.3 (3 x Si*C*$(CH_3)_3$), 25.93, 25.96 (3 x SiC(*C*$H_3)_3$), 28.0 (C-25), 28.2, 28.3 (C-33, C-34), 28.6 (C-12), 32.1 (C-13), 32.2, 32.3 (C-19, C-20), 35.4 (C-23), 35.9 (C-11), 37.2 (C-28), 38.5 (C-27), 40.2 (C-29), 43.7 (C-15), 47.6, 47.8 (2 x *BDA*-OCH_3), 56.1 (*MOM*-CH_3), 62.3 (C-24), 68.2 (C-10), 69.0 (C-32), 72.7 (C-14), 73.2 (C-26), 74.7 (C-16), 76.5 (C-31), 81.5 (C-30), 98.3 (*MOM*-CH_2), 99.16, 99.19 (2 x *BDA*-CO_2), 128.4 (2 x ArCH), 129.1 (2 x ArCH), 130.4 (C-21), 130.5 (C-18), 132.2 (C-22), 133.4 (ArCH), 133.5 (C-17), 139.6 (ArC); *m/z* ESI Found 1177.7302 $[M+Na]^+$. $C_{61}H_{114}O_{12}SSi_3Na$ requires 1177.7231. Further elution yielded the *epimeric sulfone* (486 mg, 23%) as a colourless oil; $[\alpha]_D^{25}$ +45.6 (*c* 1.30 in $CHCl_3$); δ_H ($CDCl_3$, 400 MHz) -0.03 (3H, s, $SiCH_3$), -0.01 (3H, s, $SiCH_3$), 0.02 (12H, s, 4 x $SiCH_3$), 0.80-1.10 (42H, m, CH_3-11, CH_3-15, CH_3-27, H_a-12, H_a-28, H_a-34, [including 0.86 (9H, s, $SiC(CH_3)_3$), 0.87 (18H, s, 2 x $SiC(CH_3)_3$), 1.05 (3H, d, *J* 7.1, CH_3-23)]), 1.20-1.56 (14H, m, H-11, H_b-12, H_a-13, H_b-13, H-15, H_a-25, H-29, H_a-33, [including 1.24 (6H, s, 2 x *BDA*-CH_3)]), 1.67-2.10 (9H, m, H_a-19, H_b-19, H_a-20, H_b-20, H_b-25, H-27, H_b-33, H_b-34), 2.68-2.84 (1H, m, H-23), 3.18 (1H, dd, *J* 9.6, 9.6, H-30), 3.22 (6H, s, 2 x *BDA*-OCH_3), 3.30-3.55 (9H, m, H_a-10, H_b-10, H-24, H-26, H-31, H-32, [including 3.36 (3H, s, *MOM*-CH_3)]), 3.63 (1H, m, H-14), 4.01 (1H, dd, *J* 7.2, 7.2, H-16), 4.69 (1H, d, *J* 6.1, 0.5 x *MOM*-CH_2), 4.94 (1H, d, *J* 6.1, 0.5 x *MOM*-CH_2), 5.30-5.60 (4H, m, H-18, H-21, [including 5.37 (1H, dd, *J* 7.2, 15.5, H-17), 5.56 (1H, dd, *J* 6.5, 15.5, H-22)]), 7.47-7.56 (2H, m, 2 x ArCH), 7.56-7.65 (1H, m, ArCH), 7.84-7.93 (2H, m, 2 x ArCH); δ_C ($CDCl_3$,

150 MHz) –5.4, -4.7, -4.4, -3.7, -3.6 (6 x $SiCH_3$), 9.3 (CH_3-15), 16.5 (CH_3-11), 16.6 (CH_3-27), 17.68, 17.74 (2 x *BDA*-CH_3), 18.10, 18.13, 18.3 (3 x Si*C*$(CH_3)_3$), 18.6 (CH_3-23), 25.91, 25.95 (3 x SiC(CH_3)$_3$), 28.1 (C-25), 28.15, 28.22 (C-33, C-34), 28.6 (C-12), 32.1 (C-13), 32.2, 32.4 (C-19, C-20), 35.1 (C-23), 35.9 (C-11), 37.1 (C-28), 38.1 (C-27), 40.2 (C-29), 43.7 (C-15), 47.5, 47.8 (2 x *BDA*-OCH_3), 56.1 (*MOM*-CH_3), 66.5 (C-24), 68.2 (C-10), 68.9 (C-32), 72.7 (C-14), 74.0 (C-26), 74.8 (C-16), 76.6 (C-31), 81.4 (C-30), 98.4 (*MOM*-CH_2), 99.15, 99.20 (2 x *BDA*-CO_2), 128.8 (2 x ArCH), 129.0 (2 x ArCH), 129.9 (C-21), 130.6 (C-18), 131.3 (C-22), 133.4 (ArCH), 133.5 (C-17), 138.6 (ArC); *m/z* ESI Found 1177.7313 $[M+Na]^+$. $C_{61}H_{114}O_{12}SSi_3Na$ requires 1177.7231.

(7*E*,11*E*,2*R*,3*S*,6*R*,13*S*,14*R*,15*S*,18*R*,2'*S*,3'*S*,4a'*S*,5'*S*,6'*S*,8a'*R*)-13,15,19-tris-(*tert*-butyldimethylsilanyloxy)-1-(2',3'-dimethoxy-5'-methoxymethoxy-2',3'-dimethyl-octahydrobenzo[1',4']dioxin-6'-yl)-2,6,14,18-tetramethylnonadeca-7,11-dien-3-ol (30)

The THF used in the reaction was degassed by bubbling argon through the reaction mixture with sonication for 15 min before use. A suspension of lithium (48.5 mg, 30wt% in mineral oil, 0.48 mmol) and 4,4'-di-*tert*-butylbiphenyl (55.9 g, 0.21 mmol) in THF (0.7 ml) was sonicated for 15 min until a dark blue colour appeared. The reaction mixture was cooled to -78°C and a solution of epimeric sulfones (162 mg, 0.14 mmol) in THF (0.7 ml) was added. The dark blue colour faded and reappeared after 1 h. The reaction mixture was quenched cautiously with water (3 ml) and allowed to warm to room temperature. The mixture was diluted with DCM (50 ml) and brine (20 ml). The aqueous layer was extracted with DCM (20 ml) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol/ether 3/2) to give alcohol **30** (126 mg, 88%) as a colourless oil; $[\alpha]_D^{25}$ +19.2 (*c* 1.00 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2952, 2928, 2856, 1471 1462, 1368, 1251, 1215, 1120, 1090, 1005; δ_H ($CDCl_3$, 400 MHz) -0.04 (3H, s, $SiCH_3$), -0.02 (3H, s, $SiCH_3$), -0.004 (3H, s, $SiCH_3$), 0.004 (9H, s, 3 x $SiCH_3$), 0.80-1.07 (39H, m, CH_3-11, CH_3-15, CH_3-27, H_a-12, H_a-28, H_a-34, [including 0.85 (9H, s, SiC(CH_3)$_3$), 0.86 (18H, s, 2

x $SiC(CH_3)_3$)]), 1.20-1.55 (17H, m, H-11, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, [including 1.25 (6H, s, 2 x *BDA*-CH_3)]), 1.58-1.77 (2H, m, H-27, H_b-33), 1.76-2.15 (7H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23, H_b-34, [including 1.94 (1H, ddd, *J* 3.2, 7.0, 14.0, H_b-28)]), 3.13-3.25 (7H, m, H-30, [including 3.21 (3H, s, *BDA*-OCH_3), 3.22 (3H, s, *BDA*-OCH_3)]), 3.27-3.43 (6H, m, H_b-10, H-26, [including 3.33 (1H, dd, *J* 6.4, 9.7, H_a-10), 3.39 (3H, s, *MOM*-CH_3)]), 3.43-3.54 (2H, m, H-31, H-32), 3.63 (1H, m, H-14), 4.00 (1H, dd, *J* 7.1, 7.1, H-16), 4.71 (1H, d, *J* 6.3, 0.5 x *MOM*-CH_2), 4.97 (1H, d, *J* 6.3, 0.5 x *MOM*-CH_2), 5.23-5.42 (3H, m, H-17, H-21, H-22), 5.50 (1H, dt, *J* 5.3, 15.4, H-18); δ_C ($CDCl_3$, 150 MHz) –5.4, -4.7, -4.4, -3.70, -3.66 (6 x $SiCH_3$), 9.3 (CH_3-15), 16.6 (CH_3-11), 17.3 (CH_3-27), 17.69, 17.74 (2 x *BDA*-CH_3), 18.10, 18.13, 18.3 (3 x $SiC(CH_3)_3$), 20.6 (CH_3-23), 25.90, 25.92, 25.94 (3 x $SiC(CH_3)_3$), 28.1, 28.2, (C-33, C-34), 28.6 (C-12), 31.0 (C-24), 32.2 (C-13), 32.4, 32.6 (C-19, C-20), 33.3 (C-25), 35.9 (C-11), 36.7 (C-23), 37.1 (C-28), 37.7 (C-27), 40.6 (C-29), 43.7 (C-15), 47.6, 47.7 (2 x *BDA*-OCH_3), 56.2 (*MOM*-CH_3), 68.2 (C-10), 69.0 (C-32), 72.7 (C-14), 74.9 (C-16), 76.58 (C-26), 76.62 (C-31), 81.0 (C-30), 98.3 (*MOM*-CH_2), 99.14, 99.15 (2 x *BDA*-CO_2), 127.8 (C-21), 131.0 (C-18), 133.3 (C-17), 136.6 (C-22); *m/z* ESI Found 1014.7168 $[M+Na]^+$. $C_{55}H_{110}O_{10}Si_3Na$ requires 1014.7407.

(5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-Piperidine-1,2-dicarboxylic acid 2-{11”,13”,17”-tris-(*tert*-butyldimethylsilanyloxy)-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyloctahydrobenzo[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-4”,12”,16”-trimethylheptadeca-5”,9”-dienyl} ester 1-(9’*H*-fluoren-9’-ylmethyl) ester

DCC (0.25 ml, 1.0 M in DCM, 0.25 mmol), followed by DMAP (3.06 mg, 0.025 mmol) was added to a solution of alcohol **30** (126 mg, 0.124 mmol) and *N*-Fmoc pipecolic acid (87.0 mg, 0.248 mmol) in DCM (0.6 ml) at -5°C. The reaction mixture was allowed to warm to 0°C over 3h before t.l.c. indicated the complete conversion of starting material to a major product. The reaction mixture was diluted with DCM (25 ml), washed with saturated aqueous NH_4Cl (25 ml) and the layers were separated. The aqueous layer was

extracted with DCM (25 ml). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol/ether 3/2) to yield *the ester* (164 mg, 98%) as a colourless oil; $[\alpha]_D^{25}$ +5.84 (*c* 1.10 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2929, 2856, 1729, 1705, 1450, 1360, 1336, 1251, 1214, 1164, 1120, 1089, 1030; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.03 (9H, s, 3 x $SiCH_3$), 0.77-0.99 (42H, m, CH_3-11, CH_3-15, H_a-12, H_a-28, H_a-34, [including 0.80 (3H, d, *J* 5.7, CH_3-27), 0.88 (9H, s, $SiC(CH_3)_3$), 0.886 (9H, s, $SiC(CH_3)_3$), 0.890 (9H, s, $SiC(CH_3)_3$), 0.95 (3H, d, *J* 6.7, CH_3-23)]), 1.20-1.60 (19H, m, H_a-4, H_a-5, H-11, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, [including 1.29 (6H, s, 2 x *BDA*-CH_3)]), 1.64-1.80 (5H, m, H_a-3, H_b-4, H_b-5, H_b-33, H_b-34), 1.82-2.11 (7H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23, H-27, H_b-28), 2.25-2.35 (1H, m, H_a-3), 2.95-3.08 (0.3H, m, H_a-6), 3.09-3.20 (1.7H, m, H_a-6, H-30), 3.25 (3H, s, *BDA*-OCH_3), 3.26 (3H, s, *BDA*-OCH_3), 3.31-3.45 (5H, m, H_b-10, [including 3.35 (1H, dd, *J* 6.5, 9.7, H_a-10), 3.40 (3H, s, *MOM*-CH_3)]), 3.45-3.55 (2H, m, H-31, H-32), 3.64 (1H, m, H-14), 3.98-4.49 (5H, m, H_b-6, *Fmoc*C*H*CH_2, [including 4.02 (1H, dd, *J* 4.0, 7.0, H-16)]), 4.69 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 4.82-4.90 (1.3H, m, H-2, H-26), 4.92-5.01 (1.7H, H-2, [including 4.97 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.16-5.43 (3H, m, H-17, H-21, H-22), 5.45-5.57 (1H, m, H-18), 7.27-7.34 (2H, m, 2 x ArCH), 7.35-7.43 (2H, m, 2 x ArCH), 7.49-7.64 (2H, m, 2 x ArCH), 7.71-7.84 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) –5.4, -4.7, -4.4, -3.65, -3.61 (6 x $SiCH_3$), 9.3 (CH_3-15), 15.7 and 15.9 (CH_3-27), 16.6 (CH_3-11), 17.7, 17.8 (2 x *BDA*-CH_3), 18.1, 18.2, 18.3 (3 x Si*C*$(CH_3)_3$), 20.4 and 20.6 (CH_3-23), 20.7 and 20.8 (C-34), 24.6 and 24.8 (CH_2), 25.9, 26.0 (3 x SiC(CH_3)$_3$), 26.8 (CH_2), 27.1 (CH_2), 28.2, (C-33), 28.6 (C-12), 29.7 (CH_2), 32.2 (C-13), 32.35 and 32.42, 32.6 (C-19, C-20), 33.8 and 33.9 (C-27), 35.9 (CH_2), 36.0 (C-11), 36.5 and 36.6 (C-23), 39.7 (C-29), 41.9 (C-6), 43.6 (C-15), 47.2 (*Fmoc*-*C*HCH_2), 47.6, 47.8 (2 x *BDA*-OCH_3), 54.5 and 54.9 (C-2), 56.3 (*MOM*-CH_3), 67.7 and 67.8 (*Fmoc*-CH*C*H_2), 68.3 (C-10), 69.0 (C-32), 72.7 (C-14), 74.8 (C-16), 76.6 (C-31), 78.2 (C-26), 80.5 (C-30), 98.1 (*MOM*-CH_2), 99.15, 99.18 (2 x *BDA*-CO_2), 119.9 (2 x ArCH), 125.1 (2 x ArCH), 127.0 (2 x ArCH), 127.6 (2 x ArCH), 128.2 (C-21), 130.9 and 131.0 (C-18), 133.3 (C-17), 136.0 and 136.1 (C-22), 141.2 and 141.3 (2 x ArC), 143.9 and 144.1 (2 x ArC), 155.8 and 156.3

(C-9), 171.25 and 171.35 (C-1); *m/z* ESI Found 1370.8583 $[M+Na]^+$. $C_{76}H_{129}NO_{13}Si_3Na$ requires 1370.8664.

(5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-Piperidine-1,2-dicarboxylic acid 2-{11”,13”,bis-(*tert*-butyldimethylsilanyloxy)-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyloctahydrobenzo-[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-17”-hydroxy-4”,12”,16”-trimethylheptadeca-5”,9”-dienyl} ester 1-(9’*H*-fluoren-9’-ylmethyl) ester (31a) and (5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-Piperidine-1,2-dicarboxylic acid 2-{13”(*tert*-butyldimethylsilanyloxy)-11”,17”-dihydroxy-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyloctahydrobenzo-[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-4”,12”,16”-trimethylheptadeca-5”,9”-dienyl} ester 1-(9’*H*-fluoren-9’-ylmethyl) ester (31b)

CSA (1 mg, 0.004 mmol) was added to a stirring solution of ester **31** (29 mg, 0.02 mmol) in DCM-MeOH (1:1, 1 ml) at -15°C. The resulting solution was stirred for 6 h, maintaining a temperature between –20 and –10°C. The reaction was diluted with DCM (5 ml) and saturated aqueous $NaHCO_3$ (5 ml) was added. The layers were separated and the aqueous fraction was extracted with DCM (2 x 5 ml). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give a white solid. The crude product was purified by flash column chromatography (10-50% ether/petrol) to give the alcohol **31a** (19 mg, 70%) as a white solid; $[\alpha]_D^{25}$ +7.31 (*c* 0.752 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3485, 2951, 2928, 2856, 1732, 1701, 1450, 1360, 1336, 1321, 1251, 1214, 1164, 1120, 1092, 1030; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), -0.01 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$), 0.77-1.09 (33H, m, CH_3-15, H_a-12, H_a-28, H_a-34, [including 0.81 (3H, d, *J* 5.1, CH_3-27), 0.88 (9H, s, $SiC(CH_3)_3$), 0.89 (9H, s, $SiC(CH_3)_3$), 0.91 (3H, d, *J* 6.8, CH_3-11), 0.95 (3H, d, *J* 6.7, CH_3-23)]), 1.20-1.61 (19H, m, H_a-4, H_a-5, H-11, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, [including 1.28 (6H, s, 2 x *BDA*-CH_3)]), 1.62-1.80 (5H, m, H_a-3, H_b-4, H_b-5, H_b-33, H_b-34), 1.82-2.15 (7H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23, H-27, H_b-28), 2.22-2.35 (1H, m, H_b-3),

2.94-3.08 (0.4H, m, H_a-6), 3.09-3.18 (1.6H, m, H_a-6, H-30), 3.24 (3H, s, *BDA*-OCH_3), 3.26 (3H, s, *BDA*-OCH_3), 3.37-3.44 (4H, m, H_a-10, [including 3.38 (3H, s, *MOM*-CH_3)]), 3.44-3.55 (3H, m, H_b-10, H-31, H-32), 3.66 (1H, m, H-14), 4.00-4.52 (5H, m, H_b-6, *Fmoc*C*H*CH_2, [including 4.03 (1H, dd, *J* 7.1, 7.1, H-16)]), 4.69 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 4.77-4.92 (1.4H, m, H-2, H-26), 4.93-5.02 (1.6H, H-2, [including 4.97 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.13-5.43 (3H, m, H-17, H-21, H-22), 5.45-5.60 (1H, m, H-18), 7.24-7.35 (2H, m, 2 x ArCH), 7.35-7.44 (2H, m, 2 x ArCH), 7.48-7.65 (2H, m, 2 x ArCH), 7.71-7.81 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) -4.7, -4.4, -3.64, -3.61 (4 x $SiCH_3$), 9.4 (CH_3-15), 15.8 and 16.0 (CH_3-27), 16.5 (CH_3-11), 17.7, 17.8 (2 x *BDA*-CH_3), 18.16, 18.19 (2 x Si*C*$(CH_3)_3$), 20.4 and 20.6 (CH_3-23), 20.5 and 20.8 (C-34), 24.6 and 24.9 (CH_2), 25.96, 25.97 (2 x SiC(CH_3)$_3$), 26.8 and 27.1 (CH_2), 27.2 (CH_2), 28.2, (C-33), 28.7 (C-12), 29.7 (CH_2), 32.2 (C-13), 32.4, 32.6 (C-19, C-20), 33.5 (CH_2), 33.9 (C-27), 35.9 (CH_2), 36.0 (C-11), 36.5 and 36.6 (C-23), 39.8 (C-29), 41.9 (C-6), 43.8 (C-15), 47.2 (*Fmoc*-*C*HCH_2), 47.6, 47.8 (2 x *BDA*-OCH_3), 54.5 and 54.9 (C-2), 56.3 (*MOM*-CH_3), 67.7 and 67.8 (*Fmoc*-CH*C*H_2), 68.3 (C-10), 69.1 (C-32), 72.7 (C-14), 74.9 (C-16), 76.6 (C-31), 78.3 (C-26), 80.6 (C-30), 98.1 (*MOM*-CH_2), 99.19, 99.23 (2 x *BDA*-CO_2), 119.9 (2 x ArCH), 125.1 (2 x ArCH), 127.0 (2 x ArCH), 127.6 (2 x ArCH), 128.1 and 128.2 (C-21), 131.1 (C-18), 133.3 (C-17), 135.8 and 136.2 (C-22), 141.3 (2 x ArC), 144.0 and 144.1 (2 x ArC), 155.9 and 156.3 (C-9), 171.27 and 171.34 (C-1); *m/z* ESI Found 1239.6096 $[M+Na]^+$. $C_{70}H_{114}NO_{12}Si_2Na$ requires 1239.6310. Further elution yielded the bis-deprotected alcohol **31b** (5 mg, 25%) as a white solid; $[\alpha]_D^{25}$ +12.6 (*c* 0.792 in $CHCl_3$); δ_H ($CDCl_3$, 600 MHz) 0.07 (6H, s, 2 x $SiCH_3$), 0.76-1.06 (23H, m, CH_3-11, CH_3-15, H_a-28, H_a-34, [including 0.79 (3H, d, *J* 5.9, CH_3-27), 0.88 (9H, s, SiC$(CH_3)_3$), 0.93 (3H, d, *J* 6.8, CH_3-23)]), 1.15-1.77 (23H, m, H_a-4, H_b-4, H_a-5, H_b-5, H_a-12, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, H_b-33, H_b-34, [including 1.26 (6H, s, 2 x *BDA*-CH_3)]), 1.80-2.11 (7H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23, H-27, H_b-28), 2.21-2.32 (1H, m, H_b-3), 2.92-3.05 (0.4H, m, H_a-6), 3.06-3.18 (1.6H, m, H_a-6, H-30), 3.22 (3H, s, *BDA*-OCH_3), 3.24 (3H, s, *BDA*-OCH_3), 3.35-3.50 (7H, m, H_a-10, H_b-10, H-31, H-32, [including 3.38 (3H, s, *MOM*-CH_3)]), 3.81 (1H, m, H-14), 3.98-4.48 (5H, m, H_b-6, H-16, *Fmoc*C*H*CH_2), 4.67 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 4.78-4.88 (1.4H, m, H-2, H-26), 4.90-4.98 (1.6H, H-2, [including 4.95 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.12-

5.48 (3H, m, H-17, H-21, H-22), 5.56-5.71 (1H, m, H-18), 7.23-7.32 (2H, m, 2 x ArCH), 7.32-7.40 (2H, m, 2 x ArCH), 7.47-7.62 (2H, m, 2 x ArCH), 7.69-7.76 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) -4.5, -3.6 (2 x $SiCH_3$), 6.3 (CH_3-15), 16.0 (CH_3-27), 16.5 (CH_3-11), 17.7, 17.8 (2 x *BDA*-CH_3), 18.0, ($SiC(CH_3)_3$), 20.5 and 20.7 (CH_3-23), 20.7 and 20.8 (C-34), 24.6 and 24.8 (CH_2), 25.9, ($SiC(CH_3)_3$), 26.8 and 27.1 (CH_2), 27.2 (CH_2), 28.2, (CH_2), 28.8 (C-12), 32.2 (C-13), 32.3, 32.5 (C-19, C-20), 33.4 and 33.5 (CH_2), 33.9 (C-27), 35.87 (C-11), 35.89 (CH_2), 36.46 and 36.54 (C-23), 39.8 (C-29), 41.0 (C-15), 41.8 and 41.9 (C-6), 47.2 (*Fmoc*-$CHCH_2$), 47.6, 47.8 (2 x *BDA*-OCH_3), 54.5 and 54.9 (C-2), 56.3 (*MOM*-CH_3), 67.7 and 67.8 (*Fmoc*-$CHCH_2$), 68.0 (C-10), 69.0 (C-32), 72.3 (C-14), 75.3 (C-16), 76.6 (C-31), 78.3 and 78.4 (C-26), 80.6 (C-30), 98.1 (*MOM*-CH_2), 99.17, 99.21 (2 x *BDA*-CO_2), 119.9 (2 x ArCH), 125.1 (2 x ArCH), 127.0 (2 x ArCH), 127.6 (2 x ArCH), 128.1 (C-21), 130.9 (C-18), 132.1 (C-17), 136.1 and 136.2 (C-22), 141.3 (2 x ArC), 143.9 (2 x ArC), 155.9 and 156.3 (C-9), 171.3 (C-1); *m/z* APCI 1121 $[M+H]^+$.

(5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-Piperidine-1,2-dicarboxylic acid 2-{11”,13”,17”-tris-(*tert*-butyldimethylsilanyloxy)-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyloctahydro-benzo[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-4”,12”,16”-trimethylheptadeca-5”,9”-dienyl} ester 1-(9’*H*-fluoren-9’-ylmethyl) ester

TBSCl (770 mg, 5.11 mmol) was added to a stirring solution of diol **31b** (572 mg, 0.51 mmol) and imidazole (418 mg, 6.13 mmol) in DMF (7 ml). After 2 h, t.l.c. indicated the complete conversion of starting material to a major product. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (10 ml) and extracted with ether (2 x 20 ml). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo.* The residue was purified by flash column chromatography (petrol/ether 4/1) to give *the ester* (639 mg, 93%) as a colourless oil; data identical to that described previously.

(5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-Piperidine-1,2-dicarboxylic acid 2-{11”,13”-bis-(*tert*-butyldimethylsilanyloxy)-16”-carboxy-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyl-octahydrobenzo[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-4”,12”,16”-trimethyl-heptadeca-5”,9”-dienyl} ester 1-(9’*H*-fluoren-9’-ylmethyl) ester

TPAP (5.4 mg, 0.016 mmol) and NMO (109 mg, 0.93 mmol) were added to a solution of alcohol **31a** (328 mg, 0.31 mmol) in DCM (2 ml). After stirring for 15 min the reaction mixture was filtered through a short plug of silica, eluted with ether and concentrated *in vacuo*. The residue was dissolved in *tert*-butanol/2-methyl-2-butene (5:1, 6 ml) and a solution of sodium dihydrogenphosphate (228 mg, 1.90 mmol) and sodium chlorite (228 mg, 2.29 mmol) in water (1.8 ml) was added dropwise. After stirring for 1 h, the reaction was diluted with water (5 ml), extracted with DCM (3 x 15 ml) and the combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petrol/ether 1/1) to give *the carboxylic acid* (283 mg, 85%) as a colourless oil; $[\alpha]_D^{25}$ +4.64 (*c* 1.51 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2929, 2856, 1731, 1649, 1446, 1368, 1250, 1212, 1119, 1028; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), 0.02 (6H, s, 2 x s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$), 0.77-0.97 (29H, m, CH_3-15, H_a-28, H_a-34, [including 0.82 (3H, d, *J* 5.9, CH_3-27), 0.87 (9H, s, $SiC(CH_3)_3$), 0.89 (9H, s, $SiC(CH_3)_3$), 0.95 (3H, d, *J* 6.8, CH_3-23)]), 1.09-1.57 (20H, m, H_a-4, H_a-5, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, [including 1.17 (3H, d, *J* 7.0, CH_3-11), 1.28 (6H, s, 2 x *BDA*-CH_3)]), 1.59-1.80 (6H, m, H_a-3, H_b-4, H_b-5, H_b-12, H_b-33, H_b-34), 1.82-2.12 (7H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23, H-27, H_b-28), 2.20-2.33 (1H, m, H_b-3), 2.39 (1H, m, H-11) 2.94-3.07 (0.4 H, m, H_a-6), 3.10-3.20 (1.6H, m, H_a-6, H-30), 3.24 (3H, s, *BDA*-OCH_3), 3.25 (3H, s, *BDA*-OCH_3), 3.40 (3H, s, *MOM*-CH_3), 3.44-3.50 (2H, m, H-31, H-32), 3.67 (1H, m, H-14), 4.00-4.11 (1.6H, m, H_a-6 [including 4.05 (1H, dd, *J* 6.7, 6.7, H-16)]), 4.31-4.51 (3.4H, m, H_b-6, *Fmoc*-C*H*CH_2), 4.70 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 4.77-4.90 (1.4H, m, H-2, H-26), 4.92-5.03 (1.6H, m, H-2, [including 4.98 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.14-5.45 (3H, m, H-17, H-21, H-22), 5.45-5.58 (1H, m, H-18), 7.24-7.33 (2H, m, 2 x ArCH), 7.34-7.42 (2H, m, 2 x ArCH), 7.48-7.65 (2H, m, 2 x ArCH), 7.70-7.77 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) -4.8, -4.5, -3.9, -

3.7 (4 x $SiCH_3$), 9.4 (CH_3-15), 15.9 (CH_3-27), 16.8 (CH_3-11), 17.6, 17.7 (2 x *BDA*-CH_3), 18.0, 18.1 (2 x Si*C*$(CH_3)_3$), 20.4 and 20.5 (CH_3-23), 20.6 and 20.7 (C-34), 25.87, 25.88 (2 x SiC(CH_3)$_3$), 26.7 and 27.0 (CH_2), 27.1 (CH_2), 28.1, (C-33), 28.9 (C-12), 32.2 (C-13), 32.3, 32.5 (C-19, C-20), 33.4 and 33.5 (CH_2), 33.8 (C-27), 35.8 (CH_2), 36.4 and 36.5 (C-23), 39.3 (C-11), 39.7 (C-29), 41.7 and 41.8 (C-6), 43.9 (C-15), 47.2 (*Fmoc*-*C*HCH_2), 47.6, 47.8 (2 x *BDA*-OCH_3), 54.5 and 54.9 (C-2), 56.2 (*MOM*-CH_3), 67.7 (*Fmoc*-CH*C*H_2), 69.0 (C-32), 72.4 (C-14), 74.5 (C-16), 76.5 (C-31), 78.4 (C-26), 80.5 (C-30), 98.0 (*MOM*-CH_2), 99.11, 99.14 (2 x *BDA*-CO_2), 119.8 (2 x ArCH), 125.0 (2 x ArCH), 128.0 (C-21), 128.1 (C-18), 133.2 (C-17), 136.0 and 136.2 (C-22), 141.2 (2 x ArC), 143.9 (2 x ArC), 155.8 and 156.3 (C-9), 171.2 (C-1), 181.6 (C-10); *m/z* ESI Found 1270.7486 $[M+Na]^+$. $C_{70}H_{113}NO_{14}Si_2Na$ requires 1270.7597.

(5”*E*,9”*E*,2*S*,1”*S*,4”*S*,11”*R*,12”*R*,13”*S*,16”*R*,1’”*R*,2””*S*,3””*S*,4a””*S*,5””*S*,6””*S*,8a””*R*)-1-[(2’-Hydroxyphenoxy)acetyl]piperidine-2-carboxylic acid 11”,13”-bis-(*tert*-butyldimethylsilanyloxy)-16”-carboxy-1”-[2”’-(2””,3””-dimethoxy-5””-methoxymethoxy-2””,3””-dimethyloctahydrobenzo[1””,4””]dioxin-6””-yl)-1”’-methylethyl]-4”,12”-dimethylheptadeca-5”,9”-dienyl ester (32)

Piperidine (0.15 ml) was added dropwise to a solution of carboxylic acid (121 mg, 0.10 mmol) in DMF (0.6 ml). The resulting solution was stirred for 5 min, then concentrated *in vacuo*. The residue was dissolved in DCM (3ml) and 1,4-benzodioxan-2-one (73 mg, 0.49 mmol) was added. After 1 h at 0°C and 2 h at rt, the solution was concentrated *in vacuo* and the residue purified by flash column chromatography (petrol/ether 3/7) to yield the deprotected compound **32** (85 mg, 76%) as a colourless oil; $[\alpha]_D^{25}$ –0.88 (*c* 1.34 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2931, 2856, 1731, 1706, 1647, 1497, 1461, 1376, 1250, 1215, 1118, 1030; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), 0.01 (6H, s, 2 x s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.78-0.98 (28H, m, CH_3-15, H_a-28, [including 0.83 (3H, d, *J* 5.9, CH_3-27), 0.87 (9H, s, SiC(CH_3)$_3$), 0.88 (9H, s, SiC(CH_3)$_3$), 0.94 (3H, d, *J* 6.7, CH_3-23)]), 1.10-1.80 (27H, m, H_a-3, H_a-4, H_b-4 H_a-5, H_b-5, H_a-12, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-29, H_a-33, H_b-33, H_a-34, [including 1.11 (3H, d, *J* 6.4, CH_3-11), 1.28

(6H, s, 2 x *BDA*-CH_3)]), 1.85-1.95 (3H, m, H-27, H_b-28, H_b-34), 1.95-2.13 (5H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23,), 2.20-2.32 (1H, m, H_b-3), 2.39 (1H, m, H-11) 3.11 (1H, m, H-30), 3.20-3.34 (7H, m, H_a-6, [including 3.24 (3H, s, *BDA*-OCH_3), 3.25 (3H, s, *BDA*-OCH_3)]), 3.35-3.55 (6H, m, H-31, H-32, H_b-6, [including 3.39 (3H, s, *MOM*-CH_3)]), 3.66 (1H, dt, *J* 4.4, 5.2 H-14), 4.04 (1H, dd, *J* 6.8, 6.8, H-16), 4.61-4.88 (4H, m, H_a-9, H_b-9, H-26, [including 4.69 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 4.97 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 5.18-5.44 (4H, m, H-2, H-17, H-21, H-22), 5.45-5.58 (1H, m, H-18), 6.72-6.82 (1H, m, ArCH), 6.90-7.00 (3H, m, 3 x ArCH); δ_C ($CDCl_3$, 150 MHz) -4.8, -4.4, -3.8, -3.6 (4 x $SiCH_3$), 9.5 (CH_3-15), 16.2 (CH_3-27), 16.9 (CH_3-11), 17.7, 17.8 (2 x *BDA*-CH_3), 18.1, 18.2 (2 x $SiC(CH_3)_3$), 20.5 (CH_3-23), 20.7 (C-34), 24.9 (C-3), 25.9 (2 x $SiC(CH_3)_3$), 26.4 (CH_2), 27.2 (CH_2), 28.2, (CH_2), 29.0 (CH_2), 29.6 (C-12), 32.3, 32.5 (C-19, C-20), 33.4 (C-24), 34.0 (C-27), 35.7 (C-28), 36.5 (C-23), 39.4 (C-11), 40.0 (C-29), 42.1 (C-6), 43.9 (C-15), 47.6, 47.8 (2 x *BDA*-OCH_3), 52.6 (C-2), 56.3 (*MOM*-CH_3), 69.0 (C-32), 71.5 (C-9), 72.4 (C-14), 74.6 (C-16), 76.6 (C-31), 79.0 (C-26), 80.7 (C-30), 98.1 (*MOM*-CH_2), 99.20, 99.22 (2 x *BDA*-CO_2), 117.3, 119.5, 119.8, 125.0 (4 x ArCH), 128.2 (C-21), 131.0 (C-18), 133.3 (C-17), 136.2 (C-22), 147.5, 149.6 (2 x ArC), 170.2, 170.3 (C-1, C-8), 181.2 (C-10); *m/z* ESI Found 1198.7354 $[M+Na]^+$. $C_{63}H_{109}NO_{15}Si_2Na$ requires 1198.7233.

(5*E*,7*Z*,9*E*,19*E*,23*E*,13*R*,16*S*,17*R*,18*S*,25*S*,28*S*,31*S*,1'*R*,2"*S*,3"*S*,4a"*S*,5"*S*,6"*S*,8a"*R*)-16,18-Bis-(*tert*-butyldimethylsilanyloxy)-13,17,25-trimethyl-28-[2'-(2",3"-dimethoxy-5"-methoxymethoxy-2",3"-dimethyloctahydrobenzo[1",4"]dioxin-6"-yl)-1-methyl-ethyl]-4,11,29-trioxa-1-azatricyclo[29.4.0.0]pentatriaconta-5,7,9,19,23-pentaene-2,12,30-trione (34)

EDCI (5 mg, 0.02 mmol) was added to a solution of hydroxyphenoxyacetylated acid **33** (10 mg, 0.01 mmol)in DCM (8 ml) followed by DMAP (0.1 mg) at 0°C. The resulting solution was stirred overnight at rt before being quenched by the addition of saturated aqueous NH_4Cl (10 ml). The aqueous layer was extracted with DCM (3 x 10 ml). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. The

resulting oil was purified by column chromatography (ether/petrol 1/1) to give macrolactone **34** (7 mg, 70%) as a clear oil; $[\alpha]_D^{25}$ –10.9 (*c* 1.10 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2930, 2856, 1759, 1731, 1500, 1459, 1376, 1250, 1215, 1117, 1030; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$), 0.05 (3H, s, $SiCH_3$), 0.63-0.96 (28H, m, CH_3-15, H_a-28, [including 0.63 (3H, d, *J* 5.8, CH_3-27), 0.87 (9H, s, $SiC(CH_3)_3$), 0.90 (9H, s, $SiC(CH_3)_3$), 0.92 (3H, d, *J* 6.7, CH_3-11)]), 1.15-1.86 (26H, m, H_a-3, H_a-4, H_b-4 H_a-5, H_b-5, H_a-12, H_b-12, H_a-13, H_b-13, H-15, H_a-24, H_b-24, H_a-25, H_b-25, H-27, H-29, H_a-33, H_b-33, H_a-34, H_b-34, [including 1.28 (6H, s, 2 x *BDA*-CH_3)]), 1.86-2.18 (5H, m, H_a-19, H_b-19, H_a-20, H_b-20, H-23,), 2.20-2.30 (1H, m, H_b-3), 2.62 (1H, m, H-11) 3.11 (1H, m, H-30), 3.20-3.30 (7H, m, H_a-6, [including 3.24 (3H, s, *BDA*-OCH_3), 3.25 (3H, s, *BDA*-OCH_3)]), 3.39 (3H, s, *MOM*-CH_3), 3.43-3.57 (2H, m, H-31, H-32), 3.68-3.80 (1H, m, H-14), 3.87-4.00 (2H, m, H_b-6 H-16), 4.68 (1H, d, *J* 6.4, 0.5 x *MOM*-CH_2), 4.73 (2H, s, H_a-9, H_b-9), 4.76-4.89 (1H, m, H-26), 4.96 (1H, d, *J* 6.4, 0.5 x *MOM*-CH_2), 5.18-5.45 (4H, m, H-2, H-17, H-21, H-22), 5.46-5.60 (1H, m, H-18), 6.90-7.05 (2H, m, 2 x ArCH), 7.08-7.20 (2H, m, 2 x ArCH); δ_C ($CDCl_3$, 150 MHz) -4.7, -4.4, -3.8, -3.4 (4 x $SiCH_3$), 8.9 (CH_3-15), 16.0 (CH_3-27), 17.1 (CH_3-11), 17.7, 17.8 (2 x *BDA*-CH_3), 18.1, 18.2 (2 x $SiC(CH_3)_3$), 20.7 (CH_3-23), 20.9 (CH_3-34), 25.5 (CH_2), 25.9 (2 x $SiC(CH_3)_3$), 26.5 (CH_2), 27.2 (CH_2), 28.2, (CH_2), 29.2 (C-12), 31.9 (CH_2), 32.92, 32.94, 33.0 (C-19, C-20, CH_2), 33.4 (C-27), 36.08 (C-23), 36.13 (C-28), 39.6 (C-11), 39.8 (C-29), 43.2 (C-15), 43.4 (C-6), 47.6, 47.8 (2 x *BDA*-OCH_3), 52.4 (C-2), 56.3 (*MOM*-CH_3), 69.1 (C-9), 71.7 (C-32), 75.4 (C-14), 76.6 (C-16), 77.2 (C-31), 78.0 (C-26), 80.5 (C-30), 98.1 (*MOM*-CH_2), 99.17, 99.21 (2 x *BDA*-CO_2), 113.9, 123.0, 125.5, 126.6 (4 x ArCH), 128.0 (C-21), 131.4 (C-18), 134.0 (C-17), 136.5 (C-22), 139.7, 149.9 (2 x ArC), 167.3 (C-8), 170.6 (C-1), 174.2 (C-10); *m/z* ESI Found 1180.7089 $[M+Na]^+$. $C_{63}H_{107}NO_{14}Si_2Na$ requires 1180.7128.

(14*E*,18*E*,6*RS*,8*R*,11*S*,12*R*,13*S*,20*S*,23*S*,25a*S*,1”*R*,2”’*S*,3”’*S*,4a”’*S*,5”’*S*,6”’*S*,8a”’*R*)-11,13-bis-(*tert*-Butyldimethylsilanyloxy)-6-(2’-hydroxyphenoxy)-8,12,20-trimethyl-23-[1”-methyl-2”-(2”’,3”’-dimethoxy-5”’-methoxymethoxy-2”’,3”’-dimethyl-octahydro[1”’,4”’]dioxin-6”’-yl)ethyl]-1,3,4,8,9,10,11,12,13,16,17,22,23,25a-hexadecahydro-2*H*-24-oxa-4a-azabenzocyclotricosene-5,7,25-trione (35)

The reaction was performed in a glove box and all equipment was dried in a dessicator with phosphorus pentoxide overnight. LHMDS (7 µl, 1M in THF, 7 µmol) was added to a stirring solution of macrolactone **34** (4 mg, 4 µmol) at -78°C. The reaction mixture was wwarmed to -15°C for 5 min, then cooled back to -78°C, quenched by the addition of brine (0.5 ml) and allowed to warm to room temperature. The reaction mixture was diluted with ether (1 ml), washed with brine (1 ml) and the layers separated. The aqueous layer was extracted with ether (3 x 1 ml). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a yellow oil, which was purified by column chromatography to yield the diastereomeric Dieckmann cyclisation products **35** (3 mg, 75%) as a colourless oil. ν_{max} (film)/cm^{-1} 2929, 2856, 1763, 1643, 1495, 1461, 1376, 1250, 1198, 1164, 1131, 1030; δ_H ($CDCl_3$, 600 MHz) -0.02 (3H, s, $SiCH_3$), -0.01 (6H, s, 2 x $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.78-2.10 (62H, m, 4 x CH_3, 11 x CH_2, 4 x CH, [including 0.86 (9H, s, $SiC(CH_3)_3$), 0.88 (9H, s, $SiC(CH_3)_3$), 1.28 (6H, s, 2 x *BDA*-CH_3)]), 2.20-2.46 (2H, m), 2.78-3.05 (1H, m), 3.12-3.35 (4H, m, [including 3.23 (3H, s, *BDA*-OCH_3), 3.24 (3H, s, *BDA*-OCH_3)]), 3.38-3.75 (5H, m, [including 3.39 (3H, s, *MOM*-CH_3)]), 3.67-3.75 (1H, m, H-14), 4.01-4.26 (2H, m, H_b-6 H-16), 4.63-5.02 (5H, m, [including 4.72 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 5.00 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.15-5.57 (5H, m, H-2, H-17, H-18, H-21, H-22), 6.75-6.84 (1H, m, ArH), 6.85-7.01 (3H, m, ArH); δ_C ($CDCl_3$, 150 MHz) –4.6, -3.7, -3.4 (4 x $SiCH_3$), 9.5 (CH_3-15), 14.1 (CH_3-27), 16.2 (CH_3-11), 17.7 (2 x *BDA*-CH_3), 18.1, 18.2 (2 x $SiC(CH_3)_3$), 21.4 (CH_2), 23.3 (CH_3-23), 25.4 (CH2), 25.9 (2 x $SiC(CH_3)_3$), 26.1, 27.1, 28.2, 29.7, 30.3, 32.5, (6 x CH_2), 33.4 (C-23), 34.2 (CH_2), 36.2 (C-28), 39.1 (C-11), 41.4 (C-29), 42.0 (C-15), 43.7 (C-6), 47.6, 47.8 (2 x *BDA*-OCH_3), 51.6 (C-2), 56.3 (*MOM*-CH_3), 66.6 (C-31), 69.0 (C-32), 71.7 (C-14), 74.6 (C-16), 76.8 (C-26), 81.1 (C-30), 83.8 (C-9), 99.2 (*MOM*-CH_2), 102.8 (2 x *BDA*-CO_2), 120.1, 121.3, 125.5, (4xArCH), 127.8 (C-21), 131.2 (C-18), 134.0 (C-17),

135.8 (C-22), 166.5 (C-8), 169.9 (C-1), 175.3 (C-10); *m/z* ESI 1086.6704 $[M+Na]^+$. $C_{57}H_{101}NO_{13}Si_2Na$ requires 1086.6693.

(14*E*,18*E*,8*R*,11*S*,12*R*,13*S*,20*S*,23*S*,25a*S*,1'*R*,2"*S*,3"*S*,4a"*S*,5"*S*,6"*S*,8a"*R*)-11,13-bis-(*tert*-Butyldimethylsilanyloxy)-8,12,20-trimethyl-23-[1'-methyl-2'-(2",3"-dimethoxy-5"-methoxymethoxy-2",3"-dimethyl-octahydro[1",4"]dioxin-6"-yl)ethyl]-1,3,4,8,9,10,11,12,13,16,17,20,21,22,23,25a-hexadecahydro-2*H*-24-oxa-4a-azabenzocyclotricosene-5,6,7,25-tetraone (36)

Dess-Martin periodinane (9 mg, 0.02 mmol) was added to a solution of Dieckmann cyclisation products **35** (4mg, 0.003 mmol) in pyridine (1 drop) and DCM (1 ml), which was open to the atmosphere. After 6 h, a 1:1 mixture of saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ (2 ml) was added and the mixture was stirred vigourously for 15 min until colourless. The reaction mixture was diluted with ether (5 ml) and washed with a 1:1 mixture of saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ (5 ml). The aqueous layer was extracted with ether (2 x 5 ml) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo.* The residue was purified by column chromatography (5-50% ether in petrol) to give the tricarbonyl **36** (2 mg, 54%) as a colourless oil; $[\alpha]_D^{25}$ – 30.1 (*c* 0.10 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2929, 2856, 1822, 1729, 1646, 1455, 1374, 1251, 1211, 1118; δ_H ($CDCl_3$, 600 MHz) -0.05 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$), 0.07 (6H, s, 2 x $SiCH_3$), 0.73-1.10 (28H, m, CH_3-11, CH_3-15, CH_3-27, H_a-28, [including 0.86 (9H, s, $SiC(CH_3)_3$), 0.87 (9H, s, $SiC(CH_3)_3$)]), 1.15-2.06 (34H, m, CH_3-23, H_a-3, 10 x CH_2, 4 x CH, [including 1.28 (6H, s, 2 x *BDA*-CH_3)]), 2.27-2.45 (2H, m, H_b-3, H-11), 3.07-3.20 (2H, m, H_a-6, H-30), 3.24 (3H, s, *BDA*-OCH_3), 3.25 (3H, s, *BDA*-OCH_3), 3.38 (3H, s, *MOM*-CH_3), 3.45-3.52 (2H, m, H-31, H-32), 3.62-3.73 (1H, m, H-14), 3.82-4.15 (2H, m, H_b-6 H-16), 4.65 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2), 4.70-5.00 (4H, m, H_a-9, H_b-9, H-26, [including 4.95 (1H, d, *J* 6.5, 0.5 x *MOM*-CH_2)]), 5.06-5.70 (5H, m, H-2, H-17, H-18, H-21, H-22); δ_C ($CDCl_3$, 150 MHz) –4.5, -3.7, -3.6 (4 x $SiCH_3$), 9.2 (CH_3-15), 15.6 (CH_3-27), 16.6 (CH_3-11), 17.76, 17.82 (2 x *BDA*-CH_3), 18.1, 18.2 (2 x $SiC(CH_3)_3$), 21.0 (CH_2), 22.7 (CH_3-23), 25.4 (CH2), 25.87, 25.89 (2 x $SiC(CH_3)_3$), 26.9, 27.5, 28.2, 29.7, 31.7,

32.6, 32.7 (7 x CH_2), 33.0 (C-23), 35.9 (C-28), 39.5 (C-11), 40.1 (C-29), 43.2 (C-15), 44.0 (C-6), 47.6, 47.8 (2 x *BDA*-OCH_3), 51.8 (C-2), 56.3 (*MOM*-CH_3), 66.0 (C-31), 69.0 (C-32), 71.5 (C-14), 74.9 (C-16), 78.3 (C-26), 80.6 (C-30), 99.2 (*MOM*-CH_2), 102.9 (2 x *BDA*-CO_2), 127.8 (C-21), 131.2 (C-18), 134.0 (C-17), 136.2 (C-22), 140.4, 149.8 (2 x ArC), 165.4 (C-8), 169.4 (C-1), 185.7, 201.4 (C-9, C-10); *m/z* ESI 1086.6704 $[M+Na]^+$. $C_{57}H_{101}NO_{13}Si_2Na$ requires 1086.6693.

Antascomicin B

Tricarbonyl compound **36** (11 mg, 0.01 mmol) was dissolved in HF.py/pyridine/THF (1 : 1 : 8, 1 ml) in an eppendorf tube. The resulting solution was stirred at rt for 3 days. Ethoxytrimethylsilane (0.2 ml) was added and the reaction stirred for a further 1 h before being concentrated *in vacuo*.

The residue was taken up in DCM (0.5 ml) and pyridine (0.05 ml) and DMP (2 mg) were added. The reaction was stirred for 40 min, before being quenched by the addition of saturated aqueous $NaHCO_3$ (1 ml) and saturated aqueous $Na_2S_2O_3$ (1 ml) and stirred for 10 min until colourless. The aqueous fraction was extracted with DCM (4 x 2 ml) and the combined organic fractions were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the crude *BDA and MOM protected Antascomicin B* as a pale yellow oil. This was immediately dissolved in TFA/water (1 : 9, 1 ml) and stirred for 10 mins at rt, before being concentrated *in vacuo*. The residue was purified by column chromatography (0 to 80% ethyl acetate in ether) to give **Antascomicin B** (1.2 mg, 13% over 3 steps) as a white solid.

All analytical data were consistent with those from a natural sample donated by Novartis. δ_H ($CDCl_3$, 600 MHz) 0.90 (3H, d, *J* 7, CH_3-11), 0.92 (3H, d, *J* 7, CH_3-11), 0.95 (3H, d, *J* 7, CH_3-27), 0.97 (3H, d, *J* 7, CH_3-27), 1.00 (3H, d, *J* 7, CH_3-23), 1.03 (3H, d, *J* 7, CH_3-23), 1.06 (3H, d, *J* 7, CH_3-15), 1.13 (3H, d, *J* 7, CH_3-15), 1.15-2.05 (20H, m), 2.07-2.42 (6H, m), 2.70 (1H, dq, *J* 4,7, H-15), 2.95, (2H, m, H-15, H-30), 2.99 (1H, m, H-30), 3.15 (1H, m, H-32), 3.21-3.25 (2H, m, H-6, H-32), 3.35 (1H, m, H-6), 3.40 (1H, m, H-31), 3.51 (1H, m, H-31), 3.53 (1H, m, H-6), 4.21 (1H, d, *J* 5, H-2), 4.23 (1H, t, *J* 11, H-14),

4.39 (1H, m, H-2), 4.61 (1H, m, H-14), 4.84 (1H, m, H-26), 4.94 (1H, dt, *J* 8,4 H-26), 5.14 (1H, dd, *J* 15, 8, H-22), 5.16 (1H, dd, *J* 15, 9, H-22), 5.28 (1H, m, H-21), 5.43 (1H, m, H-21), 6.02 (1H, d, *J* 15, H-17), 6.39 (1H, d, *J* 15, H-17), 6.78 (1H, m, H-18), 6.82 (1H, m, H-18); δ_H (DMSO, 700 MHz) 0.71 (3H, d, *J* 7, CH_3-11), 0.84-1.96 (28H, m, [including 0.86 (3H, d, *J* 7, CH_3-27), 0.95 (3H, d, *J* 7, CH_3-23), 1.08 (3H, d, *J* 7, CH_3-15)], 2.07-2.36 (6H, m), 2.73 (1H, dt, *J* 5, 9, H-30), 2.89 (1H, dt, *J* 4, 9, H-31), 3.03 (1H, q, *J* 7, H-15), 3.12-3.18 (2H, m, H_a-6, H-32), 3.54 (1H, d, *J* 13, H_b-6), 3.90 (1H, t, *J* 11, H-14), 4.91 (1H, dt, *J* 9, 4, H-26), 4.98 (1H, d, *J* 5, H-2), 5.20 (1H, dd, *J* 9, 15, H-22), 5.44 (1H, m, H-21), 5.98 (1H, d, *J* 16, H-17), 6.97 (1H, m, H-18); δ_C (DMSO, 175 MHz) 15.7 (CH_3-11), 15.9 (CH_3-15), 16.7 (CH_3-27), 21.2 (C-4), 21.5 (CH_3-23), 24.6 (C-5), 26.5 (C-12), 26.7 (C-25), 26.8 (C-3), 27.2 (C-34), 28.9 (C-13), 31.4 (C-20), 31.5 (C-19), 32.3 (C-33), 33.6 (C-24), 34.1 (C-27), 35.1 (C-11), 36.2 (C-28), 38.0 (C-23), 40.3 (C-29), 44.0 (C-6), 45.5 (C-15), 51.8 (C-2), 71.1 (C-14), 72.4 (C-32), 77.2 (C-30), 79.2 (C-26), 80.1 (C-31), 127.6 (C-21), 131.6 (C-17), 137.5 (C-22), 147.9 (C-18); *m/z* ESI 698.3913 $[M+Na]^+$. $C_{37}H_{57}NO_{10}Na$ requires 698.8499. MSMS on $[M+Na]^+$ gives 543 (16), 525 (44), 513 (15), 497 (57), 320 (21), 209 (34); hplc (C13 reverse phase column; 50-80% isopropanol in 10% TFA/water over 25 min; 10µl injection) retention times 10.8, 12.8, 15.4 min.