Total Synthesis of (-)-Ulapualide A, a Novel *tris*-Oxazole Macrolide from Marine Nudibranchs, based on some Biosynthesis Speculation

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Electronic Supporting Information

Additional experimental procedures and data.

2-((*S*)-1-Amino-2-hydroxy-ethyl)-oxazole-4-carboxylic acid methyl ester hydrochloride (23). A solution of the known acetonide **21**[18] (4.6 g, 14 mmol) and 4 M hydrochloric acid in dioxane (20 ml) was stirred at room temperature for 12 h. The mixture was concentrated *in vacuo* and then azeotroped with toluene (2 x 10 ml) to leave the crude *amino alcohol* (3.2 g, 100%), which was used without further purification.

2-{2-Hydroxy-1-[(2-methyl-oxazole-4-carbonyl)-amino]-ethyl}-oxazole-4-carboxylic acid methyl ester (24). Oxalyl chloride (1.40 ml, 16.8 mmol) was added dropwise over 5 min to a stirred solution of 2-methyl-1,3-oxazole-4-carboxylic acid **22a**[18] (1.80 g, 14.0 mmol) in dry dichloromethane (52 ml) at 0 ^{o}C under a nitrogen atmosphere. The mixture was stirred at 0 ^{o}C for 5 min and then dimethylformamide (40 µl, 0.6 mmol) was added in one portion. The solution was allowed to warm to room temperature and then stirred until the mixture no longer effervesced. The mixture was concentrated *in vacuo* to leave the corresponding acid chloride **22b** as a yellow oil, which was used straight away.

A solution of **22b** in dry tetrahydrofuran (20 ml) was added dropwise over 15 min to a stirred solution of the amine **23** (3.2 g, 14.0 mmol) in dry tetrahydrofuran (120 ml) at 0 ^{o}C under a nitrogen atmosphere. The mixture was allowed to warm to room temperature and then stirred for 12 h. The mixture was concentrated *in vacuo* and

the residue was purified by chromatography on silica using ethyl acetate as eluent to give the *hydroxy amide* (3.6 g, 87%), which recrystallised from ethyl acetate-light petroleum (bp 40-60 ^{o}C) as colourless crystals, mp 146-148 ^{o}C: $[\alpha]_D^{22}$ –50.5 (*c* 0.19 in $CHCl_3$); ν_{max}(soln, $CHCl_3$)/cm^{-1} 1739 and 1673; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.48 (3H, s, CH_3CN), 3.92 (3H, s, CH_3O), 4.06 (1H, dd, *J* 11.6, 4.1 Hz C*H*H), 4.29 (1H, dd, *J* 11.6, 4.1 Hz, CH*H*), 5.50 (1H, app dt, *J* 8.5, 4.1 Hz, CONHC*H*), 7.74 (1H, d, *J* 8.5 Hz, NH), 8.13 (1H, s, C*H*CCONH), 8.21 (1H, s, $CHCCO_2Me$); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 13.8 (q), 48.7 (d), 52.4 (q), 63.3 (t), 133.3 (s), 135.4 (s), 141.5 (d), 144.6 (d), 160.8 (s), 161.4 (s), 161.7 (s), 162.8 (s); *m/z* (EI) 318.0702 (M^+ + Na), $C_{12}H_{13}N_3O_5$ + Na requires 318.0725.

Methyl 2-((*S*)-4,5-dihydro-2-(2-methyloxazol-4-yl)oxazol-4-yl) oxazole-4-carboxylate (27). (Diethylamino)sulphur trifluoride (57 µl, 0.43 mmol) was added dropwise over 1 min to a stirred solution of the amide **24** (100 mg, 0.39 mmol) in dry dichloromethane (3 ml) at –78 °C under a nitrogen atmosphere. The mixture was stirred at –78 °C for 2 h and then allowed to warm to room temperature and stirred for a further 10 min. The mixture was quenched with saturated sodium bicarbonate solution (5 ml) and the separated organic phase was then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^{o}C) (3:2) as eluent to give the *oxazoline* (92 mg, 99%), which recrystallised from ethyl acetate-light petroleum (bp 40-60 ^{o}C) as colourless crystals, mp 125-128 ^{o}C: $[\alpha]_D^{32}$ +97.1 (*c* 1.42 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1739, 1677 and 1586; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.47 (3H, s, CH_3CN), 3.86 (3H, s, CH_3O), 4.72 (1H, dd, *J* 10.4, 8.8 Hz, C*H*HO), 4.84 (1H, dd, *J* 8.8, 8.2 Hz, C*H*CH_2O), 5.51 (1H, dd, *J* 10.4, 8.2 Hz, CH*H*O), 8.05 (1H, s, C*H*$CCOCH_2$), 8.21 (1H, s, $CHCCO_2Me$); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 13.6 (q), 52.1 (q), 63.5 (d), 70.4 (t), 129.7 (s), 133.2 (s), 141.2 (d), 144.8 (d), 160.3 (s), 161.3 (s),

162.6 (s), 163.0 (s); *m/z* (EI) 278.0771 (M^+ + H), 300.0590 (M^+ + Na) $C_{12}H_{11}N_3O_5$ + H requires 278.0777.

(3'*S*, 2'*R*)-3-Benzyl-4-(5'-benzyloxy-3'-hydroxy-2'-methylpentanoyl)-oxazolidin-5-one (35). A solution of dibutylboron triflate (1.0 M in dichloromethane, 71 ml, 71 mmol) and triethylamine (11 ml, 77.3 mmol) was added sequentially to a stirred solution of the imide **34** (15 g, 64.4 mmol) in dry dichloromethane (125 ml) at –78 ^oC under a nitrogen atmosphere. The resulting pale yellow solution was stirred at –78 ^oC for 1 h, then at 0 ^oC for 30 min, and re-cooled to –78 ^oC. A solution of the aldehyde **33** (10.6 g, 64.4 mmol) in dry dichloromethane (54 ml) was added dropwise over 30 min to the mixture which was then stirred at –78 ^oC for 1.5 h. The mixture was allowed to warm to room temperature over 2 h, then quenched by the addition of pH 7 aqueous phosphate buffer solution (150 ml), followed by methanol (200 ml). After 30 min a premixed solution of methanol (330 ml) and a 30% aqueous hydrogen peroxide solution (160 ml) was added slowly keeping the temperature below 10 ^oC. The mixture was stirred at room temperature for 1 h and then concentrated *in vacuo* to remove the methanol and dichloromethane. The aqueous residue was extracted with diethyl ether (3 x 600 ml) and the combined organic extracts were then washed with 5% aqueous sodium bicarbonate solution (200 ml) and brine (400 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^oC) (1:5 to 2:5) as eluent to give the *alcohol* (36.6 g, 72%) as a colourless oil: $[\alpha]_D^{22}$ -52.7 (*c* 0.9 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3533, 1780 and 1688; (Found: C, 69.7; H, 6.9; N, 3.5; $C_{23}H_{27}NO_5$ requires C, 69.5; H, 6.9; N, 3.5%); ^1H NMR (360 MHz, $CDCl_3$) δ 1.30 (3H, d, *J* 7.1 Hz, CH_3), 1.71-1.80 (1H, m, C*H*HCHOH), 1.84-1.95 (1H, m, CH*H*CHOH), 2.79 (1H, dd, *J* 13.4, 9.4 Hz, CHC*H*HPh), 3.26 (1H, dd, *J* 13.4, 3.3 Hz, CHCH*H*Ph), 3.31-3.34 (1H, br, OH), 3.64-3.75 (2H, m, CH_2OBn) 3.84 (1H, dq, *J* 7.1, 3.8 Hz, CHCO), 4.14-4.23 (3H, m, CH_2OCO, C*H*OH), 4.52 (2H, s, OCH_2Ph), 4.69 (1H, dddd, *J* 12.7, 9.4, 7.0,

3.3 Hz, CHN), 7.20-7.23 (2H, m , ArH), 7.25-7.39 (8H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 11.2 (q), 33.7 (t), 37.7 (t), 42.6 (d), 55.2 (d), 66.1 (t), 68.3 (t), 70.4 (d), 73.2 (t), 127.4 (d), 127.7 (d), 128.2 (2d), 128.4 (2d), 128.9 (2d), 129.4 (2d), 135.1 (s), 138.1 (s), 153.1 (s), 176.6 (s); *m/z* (EI) 420.1761 (M^+ + Na), $C_{23}H_{27}NO_5$ + Na requires 420.1787.

(3*S*,4*R*)-1-Benzyloxy-5-(tert-butyldiphenylsilanyloxy)-4-methylpentan-3-ol (36b). A solution of lithium borohydride (2M in tetrahydrofuran, 63.8 ml, 128 mmol) was added dropwise over 10 min to a stirred solution of the imide 35 (20.2 g, 50.9 mmol) in dry tetrahydrofuran (300 ml) and dry methanol (5.2 ml, 128 mmol) at 0 ^{o}C under a nitrogen atmosphere. The solution was stirred for 2 h at 0 ^{o}C and then 1 M aqueous sodium hydroxide solution (300 ml) was added dropwise over 15 min. Ethyl acetate (200 ml) was added and the separated aqueous phase was extracted with ethyl acetate (2 x 200 ml). The combined organic extracts were washed with brine (200 ml), then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude diol 36a (11 g, 99%) as a colourless oil. The 1,3-diol was converted into the corresoponding acetonide, whose ^{1}H NMR data (*J* 2.6 Hz, between C_{32} and C_{33}) confirmed the *syn*-stereochemistry of **36a**.[49]

Imidazole (6.7 g, 98 mmol) and *tert*-butyldiphenylsilyl chloride (15.4 ml, 56 mmol) were added sequentially to a stirred solution of the crude diol **36a** (11 g, 50 mmol) in dry dimethylformamide (59 ml) at room temperature. The solution was stirred at room temperature overnight and then diluted with water (100 ml) and diethyl ether (200 ml). The organic extract was washed with water (3 x 60 ml) and brine (50 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^{o}C) (1:9) as eluent to give the *silyl ether* (23.7 g, 94%) as a colourless oil: $[\alpha]_D^{22}$ -0.9 (*c* 0.9

$CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3504; (Found: C, 75.4; H, 8.3; $C_{29}H_{38}O_3Si$ requires C, 75.3; H, 8.3%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.96 (3H, d, *J* 7.0 Hz, CH_3), 1.09 (9H, s, $(CH_3)_3C$), 1.68-1.94 (3H, m, C*H*$_2$CHOH, C*H*CH_3), 3.11-3.19 (1H, br, OH), 3.65-3.75 (4H, m, CH_2OSi, CH_2OBn), 4.05 (1H, app dt, *J* 9.5, 3.1 Hz, C*H*OH), 4.56 (2H, s, CH_2-Ph), 7.27-7.49 (11H, m, ArH), 7.66-7.74 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 10.9 (3q), 19.3 (s), 26.9 (q), 34.2 (t), 40.2 (d), 67.9 (t), 68.9 (t), 72.1 (d), 73.3 (t), 127.7 (d), 127.7 (2d), 127.8 (4d), 128.5 (2d), 129.8 (2d), 133.3 (s), 133.4 (s), 135.6 (2d), 135.7 (2d), 138.4 (s); *m/z* (EI) 463.2649 (M^+ + H), $C_{29}H_{38}O_3Si$ + H requires 463.2668.

(3*S*, 4*R*)-1-Benzyloxy-5-(*tert*-butyldiphenylsilanyloxy)-4-methyl-3-methoxypentane (36c). A solution of NaHMDS (1M in tetrahydrofuran, 49 ml, 49 mmol) was added dropwise over 10 min to a stirred solution of the alcohol **36b** (19 g, 41 mmol) in dry tetrahydrofuran (200 ml) at 0 ^{o}C under a nitrogen atmosphere. The solution was stirred at 0 ^{o}C for 10 min and then methyl iodide (11.8 ml, 189 mmol) was added dropwise over 15 min. The mixture was stirred at 0 ^{o}C for a further 1 h, then water (120 ml) and diethyl ether (400 ml) were added. The separated aqueous phase was extracted with diethyl ether (2 x 200 ml) and the combined organic extracts were then washed with brine (200 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:9) as eluent to give the *methyl ether* (17.5 g, 90%) as a colourless oil: $[\alpha]_D^{31}$ -5.33 (*c* 0.9 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932 and 2860; (Found: C, 75.8; H, 8.7; $C_{30}H_{40}O_3Si$ requires C, 75.6; H, 8.5%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.92 (3H, d, *J* 6.8 Hz, C*H*$_3$CH), 1.10 (9H, s, $(CH_3)_3C$), 1.77-1.84 (2H, m, C*H*$_2$CHOMe), 1.89 (1H, dddq, *J* 7.2, 6.8, 6.5, 3.7 Hz, C*H*CH_3), 3.35 (3H, s, CH_3O), 3.50-3.65 (3H, m, CHOMe, CH_2OBn), 3.62 (1H, dd, *J* 9.9, 6.5 Hz, C*H*HOSi), 3.74 (1H, dd, *J* 9.9, 7.2 Hz, CH*H*OSi), 4.52 (1H, d, *J* 12.2 Hz, C*H*HPh), 4.56 (1H, d, *J* 12.2

Hz, CH*H*Ph), 7.27-7.49 (11H, m, ArH), 7.66-7.74 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 11.3 (q), 19.6 (s), 27.0 (3q), 31.8 (t), 39.2 (d), 58.3 (q), 65.7 (t), 67.4 (t), 72.9 (t), 78.3 (d), 127.3 (d), 127.4 (2d), 127.6 (4d), 128.3 (2d), 129.5 (2d), 133.9 (2s), 135.5 (2d), 135.9 (2d), 138.5 (s); *m/z* (EI) 499.2624 (M^+ + Na), $C_{30}H_{40}O_3Si$ + Na requires 499.2644.

(3*S*,4*R*)-5-(*tert*-Butyldiphenylsilanyloxy)-3-methoxy-4-methylpentanal (37). Pearlman's catalyst[28] (670 mg) was added in one portion to a stirred solution of the benzyl ether **36c** (3 g, 6.3 mmol) in ethyl acetate (30 ml) at room temperature, and the apparatus was then evacuated prior to the introduction of hydrogen gas. The mixture was stirred at room temperature for 3 days under one atmosphere of hydrogen, then filtered through celite. The filter cake was washed with ethyl acetate (3 x 30 ml) and the combined washings were then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (2:1) as eluent to give the corresponding *alcohol* (2.2 g, 92%) as a colourless oil: $[\alpha]_D^{24}$ -12.0 (*c* 1.15 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3486 and 2931; (Found: C, 71.1; H, 9.1; $C_{23}H_{34}O_3Si$ requires C, 71.5; H, 8.9%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.94 (3H, d, *J* 7.2 Hz, C*H*$_3$CH), 1.07 (9H, s, $(CH_3)_3C$), 1.65-1.75 (2H, m, C*H*$_2$CHOMe), 1.87-1.97 (1H, m, C*H*CH_3), 3.34 (3H, s, CH_3O), 3.49 (1H, app dt, *J* 7.8, 4.5 Hz, CHOMe) 3.53 (1H, dd, *J* 10.0, 6.6 Hz, C*H*HOSi), 3.69 (1H, dd, *J* 10.0, 6.0 Hz, CH*H*OSi), 3.74 (2H, app dt, *J* 6.0, 2.3 Hz, C*H*$_2$OH), 7.37-7.46 (6H, m, ArH), 7.66-7.72 (4H, m, ArH); δ_C (90.6 MHz; $CDCl_3$) 12.4 (q), 19.4 (s), 27.0 (3q), 33.3 (t), 38.6 (d), 58.0 (q), 61.5 (t), 65.4 (t), 82.0 (d), 127.7 (4d), 129.7 (2d), 133.9 (2s), 135.6 (2d), 135.9 (2d); *m/z* (EI) 409.2216 (M^+ + Na), $C_{23}H_{34}O_3Si$ + Na requires 409.2175.

A solution of DMSO (1.8 ml, 26 mmol) in dry dichloromethane (10 ml) was added dropwise over 10 min to a stirred solution of oxalyl chloride (1.4 ml, 16 mmol) in dry

dichloromethane (20 ml) at –78 °C under a nitrogen atmosphere. The solution was stirred at –78 °C for 15 min and then a solution of the above alcohol (5 g, 13 mmol) in dry dichloromethane (20 ml) was added dropwise over 15 min. The mixture was stirred at –78 °C for 2 h and then triethylamine (8.8 ml, 65 mmol) was added dropwise over 15 min and the mixture was allowed to warm to room temperature. The mixture was diluted with water (400 ml) and the separated aqueous phase was then extracted with dichloromethane (3 x 300 ml). The combined dichloromethane extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:2) as eluent to give the *aldehyde* (4.8 g, 96%) as a colourless oil: $[\alpha]_D^{22}$ -13.8 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2732 and 1723; (Found: C, 71.8; H, 8.4; $C_{23}H_{32}O_3Si$ requires C, 71.8; H, 8.4%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.91 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 1.07 (9H, s, $(CH_3)_3C$), 1.85-1.91 (1H, m, C*H*CH_3), 2.55 (1H, ddd, *J* 16.3, 4.7, 2.1 Hz, C*H*HCHOMe), 2.69 (1H, ddd, *J* 16.3, 7.8, 2.1 Hz, CH*H*CHOMe), 3.34 (3H, s, CH_3O), 3.56 (1H, dd, *J* 10.2, 5.8 Hz, C*H*HOSi), 3.68 (1H, dd, *J* 10.2, 5.8 Hz, CH*H*OSi), 3.94 (1H, app dt, *J* 7.8, 4.7 Hz, CHOMe), 7.36-7.48 (6H, m, ArH), 7.62-7.74 (4H, m, ArH), 9.82 (1H, t, *J* 2.1 Hz, C*H*O); δ_C (90.6 MHz; $CDCl_3$) 11.6 (q), 19.2 (s), 27.0 (3q), 39.4 (d), 46.2 (t), 57.9 (q), 65.2 (t), 77.7 (d), 127.6 (4d), 129.8 (2d), 133.6 (2s), 135.5 (4d), 201.5 (d); *m/z* (EI) 407.1975 (M^+ + Na), $C_{23}H_{32}O_3Si$ + Na requires 407.2018.

(*R*)-3-((*E*)-5-(Benzyloxy)pent-2-enoyl)-4-benzyloxazolidin-2-one (40).[13,50] Oxalyl chloride (2.0 ml, 23 mmol) was added dropwise over 5 min to a stirred solution of (*E*)-5-(Benzyloxy)pent-2-enoic acid[50] (4.1 g, 20 mmol) in dry dichloromethane (20 ml) at 0 °C. The mixture was stirred at 0 °C for 5 min and then dimethylformamide (80 µl, 1.0 mmol) was added in one portion. The solution was allowed to warm to room temperature and then stirred until the mixture no longer effervesced. The mixture

was concentrated *in vacuo* to leave the crude *acid chloride* **39** (4.5 g, 99%) as a yellow oil.

n-Butyllithium (6.0 ml, 15 mmol) was added dropwise over 15 min to a stirred solution of (*R*)-4-benzyl-2-oxazolidinone (2.65 g, 15 mmol) in dry tetrahydrofuran (30 ml) at –78 ^{o}C under a nitrogen atmosphere. A solution of the acid chloride (4.5 g, 20 mmol) in dry tetrahydrofuran (10 ml) was added dropwise over 10 min at –78 ^{o}C and the resulting solution was stirred at –78 ^{o}C for 30 min, then at room temperature for 30 min. The mixture was quenched with 1 M aqueous potassium carbonate solution (10 ml) and then stirred at room temperature for 1 h. The solution was diluted with water (70 ml) and ethyl acetate (75 ml) and the separated aqueous phase was then extracted with ethyl acetate (2 x 75 ml). The combined organic extracts were washed with water (50 ml), dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-dichloromethane (1:25) as eluent to give the *imide* (5.8 g, 97%) as a colourless oil: $[\alpha]_D^{28}$ -49.3 (*c* 2.64 in $CHCl_3$) [lit[13] (for enantiomer) $[\alpha]_D$ +50.5 (*c* 2.6 in $CHCl_3$)]; ν_{max} (soln, $CHCl_3$)/cm^{-1} 2917, 2863, 1777, 1682 and 1637; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.64 (2H, dt, *J* 6.8, 6.5 Hz, C*H*$_2$CH$_2$OBn), 2.81 (1H, dd, *J* 13.4, 9.5 Hz, PhC*H*HCHN), 3.34 (1H, dd, *J* 13.4, 3.2 Hz, PhCH*H*CHN), 3.66 (2H, t, *J* 6.5 Hz, CH$_2$OBn), 4.12-4.24 (2H, m, OC*H*$_2$CHN), 4.56 (2H, s, C*H*$_2$OCH$_2$CH$_2$), 4.73 (1H, app ddd, *J* 9.5, 6.9, 3.2 Hz, CHN), 7.27 (1H, dd, *J* 22.4, 6.8 Hz, C*H*CHCO), 7.26-7.43 (11H, m, CHCO, ArH); ^{13}C NMR (90.6 MHz; $CDCl_3$) δ 33.1 (t), 37.8 (t), 55.2 (d), 66.1 (t), 68.3 (t), 73.0 (t), 121.8 (d), 127.3 (d), 127.6 (d), 127.7 (2d), 128.4 (2d), 128.9 (2d), 129.4 (2d), 135.3 (s), 138.1 (s), 148.4 (d), 153.4 (s), 164.7 (s); *m/z* (EI) 366.1704 (M^+ + H), 388.1522 (M^+ + Na), $C_{22}H_{23}NO_4$ + H requires 366.1705.

(4'*R*,2''*R*,1*S*,3*S*,4*R*)-4'-Benzyl-3'-{5''-benzyloxy-2''-[5-(*tert*-butyldiphenylsianyloxy)-1-hydroxy-3-methoxy-4-methylpentyl]-pent-3''-enoyl}-oxazolidin-2'-one (41). Dibutylborontriflate (1.0 M in dichloromethane, 14.8 ml, 14.8 mmol) and triethylamine (2.6 ml, 18.7 mmol) were added sequentially to a stirred solution of the imide **40** (4.75 g, 13.6 mmol) in dry dichloromethane (102 ml) at –78 ^{o}C under a nitrogen atmosphere. The resulting pale yellow solution was stirred at –78 ^{o}C for 30 min, then at 0 ^{o}C for 30 min and re-cooled to –78 ^{o}C. A solution of the aldehyde 37 (5.26 g, 13.6 mmol) in dry dichloromethane (34 ml) was added dropwise over 30 min to the mixture which was then stirred at –78 ^{o}C for 3 h. The mixture was allowed to warm to 0 ^{o}C over 1 h, then quenched by the addition of sodium acetate (1.5 g, 18.3 mmol) in methanol (140 ml) and water (14.2 ml). The mixture was stirred at 0 ^{o}C for 20 min and then a 30% aqueous hydrogen peroxide solution (7.4 ml) was added slowly keeping the temperature below 10 ^{o}C. The mixture was stirred at 0 ^{o}C for 30 min and then diluted with water (170 ml). The separated aqueous phase was extracted with dichloromethane (3 x 340 ml). The combined organic extracts were washed with brine (100 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:4 to 1:1) as eluent to give the alcohol (4.38 g, 58%) as a colourless oil and a mixture of *E*/*Z* isomers: $[\alpha]_D^{28}$ +4.9 (*c* 0.7 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3523, 2930, 2858, 1781 and 1693; ^{1}H NMR (500 MHz, $CDCl_3$, *Z*-isomer) δ 1.02 (3H, d, *J* 7.1 Hz, C*H*$_3$CHCH$_2$OSi), 1.14 (9H, s, (CH$_3$)$_3$C), 1.54-1.66 (1H, m, C*H*HCHOMe), 1.66-1.79 (1H, m, CH*H*CHOMe), 1.81-1.94 (1H, br OH), 1.95-2.12 (1H, m, C*H*CH$_3$), 2.80 (1H, dd, *J* 13.7, 9.6 Hz, ArC*H*HCHN), 3.31 (1H, dd, *J* 13.7, 3.8 Hz, ArCH*H*CHN), 3.43 (3H, s, OCH$_3$), 3.64 (1H, dd, *J* 13.1, 6.6 Hz, C*H*HOSi) 3.67-3.73 (1H, m, CHOMe), 3.77 (1H, dd, *J* 13.1, 5.6 Hz, CH*H*OSi), 4.12-4.23 (2H, m, OC*H*$_2$CHN), 4.23-4.35 (3H, m, C*H*OH, CH$_2$OBn), 4.60 (2H, s, OCH$_2$Ar), 4.70-4.79 (1H, m, CHN), 5.01 (1H, dd, *J* 10.2, 4.8 Hz, C*H*CHOH), 5.86 (1H, dd, *J* 10.5, 10.2 Hz,

C*H*CHCH$_2$OBn), 6.09 (1H, dt, *J* 12.2, 10.5 Hz, C*H*CH$_2$OBn), 7.19-7.27 (2H, m, ArH), 7.30-7.53 (14H, m, ArH), 7.70-7.81 (4H, m, ArH); ^{1}H NMR (500 MHz, $CDCl_3$, *E*-isomer) δ 1.00 (3H, d, *J* 7.1 Hz, C*H*$_3$CHCH$_2$OSi), 1.14 (9H, s, $(CH_3)_3C$), 1.54-1.66 (1H, m, C*H*HCHOMe), 1.66-1.79 (1H, m, CH*H*CHOMe), 1.81-1.94 (1H, br OH), 1.95-2.12 (1H, m, C*H*CH$_3$), 2.76 (1H, dd, *J* 13.7, 9.6 Hz, ArC*H*HCHN), 3.26 (1H, dd, *J* 13.7, 3.5 Hz, ArCH*H*CHN), 3.42 (3H, s, OCH_3), 3.62 (1H, dd, *J* 13.1, 6.5 Hz, C*H*HOSi) 3.67-3.73 (1H, m, CHOMe), 3.76 (1H, dd, *J* 13.1, 5.1 Hz, CH*H*OSi), 4.12-4.23 (4H, m, OC*H*$_2$CHN, CH$_2$OBn), 4.26-4.35 (1H, m, C*H*OH), 4.59 (2H, s, OCH$_2$Ar), 4.63 (1H, dd, *J* 7.8, 3.8 Hz, C*H*CHOH), 4.70-4.79 (1H, m, CHN), 5.97-6.06 (2H, m, C*H*C*H*CH$_2$OBn), 7.19-7.27 (2H, m, ArH), 7.30-7.53 (14H, m, ArH), 7.70-7.81 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 12.4 (q), 12.5 (q), 19.3 (2s), 27.0 (6q), 36.0 (t), 36.1 (t), 37.5 (t), 37.6 (t), 38.9 (d), 39.0 (d), 48.2 (d), 51.4 (d), 55.1 (d), 55.2 (d), 58.6 (2q), 65.5 (2t), 66.0 (2t), 66.7 (t), 69.1 (d), 69.6 (d), 70.2 (t), 72.0 (t), 72.8 (t), 79.1 (d), 79.2 (d), 126.1 (d), 126.4 (d), 127.4 (2d), 127.7 (8d), 127.8 (2d), 127.9 (2d), 128.4 (4d), 129.0 (4d), 129.4 (4d), 129.5 (2d), 129.6 (2d), 132.8 (2d), 133.3 (2d), 133.9 (4s), 135.0 (2s), 135.6 (4d), 136.1 (4d), 138.2 (2s), 152.8 (s), 153.0 (s), 173.6 (s), 174.1 (s); *m/z* (EI) 772.3639 (M^+ + Na), $C_{45}H_{55}NO_7Si$ + Na requires 772.3646.

(4*R*,5*S*,7*S*,8*R*)-1-Benzyloxy-9-(*tert*-butyldiphenylsilanyloxy)-7-methoxy-4,8-dimethlnon-2-en-5-ol (42). Lithium borohydride (2M in tetrahydrofuran, 8.5 ml, 17.0 mmol) was added dropwise over 10 min to a stirred solution of the imide **41** (4.86 g, 6.5 mmol) in dry tetrahydrofuran (60 ml) and dry methanol (0.66 ml, 16.3 mmol) at 0 ^{o}C. The solution was stirred at 0 ^{o}C for 1 h and then 1 M aqueous sodium hydroxide solution (11 ml) was added dropwise over 15 min. Ethyl acetate (50 ml) and water (30 ml) were added and the separated aqueous phase was then extracted with ethyl acetate (3 x 50 ml). The combined organic extracts were washed with brine (30 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by

chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1 to 2:1) as eluent to give *(2R,3S,5S,6R)-2-(3'-benzyloxyprop-1'enyl)-7-(tert-butyldiphenylsilanyloxy)-5-methoxy-6-methyl-heptane-1,3-diol* (3.7 g, 99%) as a colourless oil and a mixture of *E*/*Z* isomers: $[\alpha]_D^{28}$ -4.9 (*c* 0.77 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3458, 2931, 2856 and 1602; (Found: C, 72.8; H, 8.35; $C_{35}H_{48}O_5Si$ requires C, 73.1; H, 8.1%); ^{1}H NMR (500 MHz, $CDCl_3$, *Z*-isomer) δ 1.03 (3H, d, *J* 6.7 Hz, C*H*$_3$CHCH$_2$OSi), 1.11 (9H, s, (CH$_3$)$_3$C), 1.45-1.64 (1H, m, C*H*HCHOMe), 1.65-1.74 (1H, m, CH*H*CHOMe),1.90-2.03 (1H, m, C*H*CH$_3$), 2.56 (1H, app dt, *J* 9.5, 5.3 Hz, C*H*CHOH), 2.59-2.70 (1H, br, CHO*H*), 3.10-3.20 (1H, br, CH$_2$O*H*), 3.39 (3H, s, OCH$_3$), 3.54-3.62 (2H, m, C*H*OMe, C*H*HOSi), 3.61-3.75 (1H, m, CH*H*OSi), 3.67 (1H, dd, *J* 10.6, 5.9 Hz, C*H*HOH), 3.75 (1H, dd, *J* 10.6, 5.9 Hz, CH*H*OH), 4.00-4.10 (1H, m, C*H*OH), 4.06 (1H, dd, *J* 11.6, 6.8 Hz, C*H*HOBn), 4.12 (1H, dd, *J* 11.6, 7.0 Hz, CH*H*OBn), 4.54 (2H, s, CH$_2$Ar), 5.71 (1H, dd, *J* 10.7, 9.5 Hz, C*H*CHCH$_2$OBn), 5.93 (1H, ddd, *J* 10.7, 7.0, 6.8 Hz, C*H*CH$_2$OBn), 7.26-7.56 (11H, m, ArH), 7.66-7.83 (4H, m, ArH); ^{1}H NMR (500 MHz, $CDCl_3$, *E*-isomer) δ 1.03 (3H, d, *J* 6.6 Hz, C*H*$_3$CHCH$_2$OSi), 1.11 (9H, s, (CH$_3$)$_3$C), 1.45-1.54 (1H, m, C*H*HCHOMe), 1.65-1.74 (1H, m, CH*H*CHOMe),1.90-2.03 (2H, m, C*H*CH$_3$, OH), 2.20-2.32 (1H, m, C*H*CHOH), 3.39 (3H, s, OCH$_3$), 3.53-3.62 (2H, m, CHOMe, C*H*HOSi), 3.61-3.75 (3H, m, CH$_2$OH CH*H*OSi), 4.00-4.10 (3H, m, C*H*OH, CH$_2$OBn), 4.55 (2H, s, CH$_2$Ar), 5.75-5.79 (1H, m, C*H*CH$_2$OBn), 5.84 (1H, dd, *J* 16.8, 6.5 Hz, C*H*CHCH$_2$OBn), 7.26-7.56 (11H, m, ArH), 7.66-7.83 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 12.3 (q), 12.4 (q), 19.2 (2s), 26.9 (6q), 37.5 (t), 37.6 (t), 38.9 (d), 39.0 (d), 48.1 (d), 51.3 (d), 58.5 (2q), 64.6 (t), 65.4 (t), 65.9 (2t), 66.6 (t), 69.0 (d), 69.6 (d), 70.2 (t), 72.0 (t), 72.7 (t), 79.0 (d), 79.1 (d), 127.6 (8d), 127.7 (2d), 127.8 (4d), 128.4 (4d), 129.7 (4d), 130.0 (d), 130.4 (2d), 130.7 (d), 133.7 (2s), 133.8 (2s) 135.5 (4d), 135.6 (4d), 138.0 (s), 138.2 (s); *m/z* (EI) 577.3334 (M^+ + H), 599.3160 (M^+ + Na), $C_{35}H_{48}O_5Si$ + H requires 577.3349.

N,N-Diisopropylethylamine (2.5 ml, 14.1 mmol), and methanesulfonyl chloride (0.5 ml, 6.5 mmol) were added sequentially to a stirred solution of the above 1,3-diol (3.8 g, 6.5 mmol) in dry dichloromethane (80 ml) at -40 ^{o}C under a nitrogen atmosphere. The solution was allowed to warm to -20 ^{o}C over 1 h, then quenched with 1 M aqueous potassium carbonate solution (128 ml) and stirred at room temperature for 10 min. The separated aqueous phase was extracted with dichloromethane (3 x 100 ml) and the combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to leave the corresponding *methanesulfonate* of the primary alcohol as an oil, which was used without further purification.

Lithium borohydride (2M in tetrahydrofuran, 11.3 ml, 22.6 mmol) was added dropwise over 10 min to a stirred solution of the mesylate (4.25 g, 6.5 mmol) in dry tetrahydrofuran (115 ml) and dry methanol (0.91 ml, 22.6 mmol) at 0 ^{o}C. The solution was stirred for 3 h at 0 ^{o}C and then 1 M aqueous sodium hydroxide solution (120 ml) was added dropwise over 15 min. Ethyl acetate (20 ml) was added and the separated aqueous phase was extracted with ethyl acetate (3 x 50 ml). The combined organic extracts were washed with water (50 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1 to 1:0) as eluent to give the secondary *alcohol* (3.12 g, 85%) as a colourless oil and a mixture of *E*/*Z* isomers: $[\alpha]_D^{31}$ -7.5 (*c* 1.4 in $CHCl_3$); (Found: C, 74.7; H, 8.8; $C_{35}H_{48}O_4Si$ requires C, 74.9; H, 8.6%); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3453, 2931 and 1602; ^{1}H NMR (500 MHz, $CDCl_3$, *Z*-isomer) δ 0.97 (3H, d, *J* 6.8 Hz, C*H*$_3$CHCHOH), 0.99 (3H, d, *J* 6.6 Hz, C*H*$_3$CHCH$_2$OSi), 1.08 (9H, s, $(CH_3)_3C$), 1.45-1.62 (2H, m, C*H*$_2$CHOMe), 1.90-1.97 (1H, m, C*H*CH$_2$OSi), 2.41 (1H, app dq, *J* 16.4, 6.4 Hz, C*H*CHOH), 2.53 (1H, d, *J* 3.4 Hz, OH), 3.36 (3H, s, OCH_3), 3.51-3.61 (3H, m, CHOMe, C*H*HOSi, C*H*OH), 3.68 (1H dd, *J* 9.9, 5.4 Hz, CH*H*OSi), 4.07 (1H, dd, *J* 3.3, 1.3 Hz, C*H*HOBn), 4.08 (1H, dd, *J*

3.9, 1.3 Hz, CH*H*OBn), 4.52 (2H, s, CH_2Ar), 5.51 (1H, app t, *J* 10.6 Hz, C*H*CHCH$_2$OBn), 5.71-5.76 (1H, ddd, *J* 10.6, 3.9, 3.3 Hz, C*H*CH$_2$OBn), 7.46-7.49 (11H, m, ArH), 7.62-7.75 (4H, m, ArH); ^{1}H NMR (500 MHz, $CDCl_3$, *E*-isomer) δ 0.99 (3H, d, *J* 6.6 Hz, C*H*$_3$CHCH$_2$OSi), 1.03 (3H, d, *J* 6.8 Hz, C*H*$_3$CHCHOH), 1.08 (9H, s, $(CH_3)_3C$), 1.54-1.62 (2H, m, C*H*$_2$CHOMe), 1.90-1.97 (1H, m, C*H*CH$_2$OSi), 2.20 (1H, ddq, *J* 6.6, 6.7, 6.8 Hz, C*H*CHOH), 2.35 (1H, d, *J* 3.5 Hz, OH), 3.37 (3H, s, OCH_3), 3.51-3.59 (2H, m, CHOMe, C*H*HOSi), 3.61-3.66 (1H, m, C*H*OH), 3.68 (1H dd, *J* 9.9, 5.4 Hz, CH*H*OSi), 4.01 (2H, d, *J* 4.6 Hz, CH_2OBn), 4.52 (2H, s, CH_2Ar), 5.63-5.71 (2H, m, C*H*C*H*CH$_2$OBn), 7.46-7.49 (11H, m, ArH), 7.62-7.75 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 12.7 (q), 12.8 (q), 16.6 (q), 17.2 (q), 19.4 (2s), 27.0 (6q), 35.4 (t), 35.5 (t), 39.0 (d), 39.1 (d), 43.2 (2d), 58.5 (q), 58.6 (q), 65.6 (2t), 66.0 (t), 70.9 (2t), 72.1 (2d), 72.4 (t), 80.0 (2d), 127.4 (2d), 127.6 (2d), 127.7 (8d), 127.7 (2d), 127.8 (4d), 128.4 (4d), 133.8 (2s), 133.9 (2s), 135.5 (4d), 135.6 (4d), 135.9 (2d), 136.0 (2d), 138.3 (s), 138.4 (s); *m/z* (EI) 561.3410 (M^+ + H), 578.3675 (M^+ + NH_4), 583.3225 (M^+ + Na), $C_{35}H_{48}O_4Si$ + H requires 561.3400.

(2*R*,3*S*,5*S*,6*R*)-3-(*tert*-Butyldimethylsilanyloxy)-7-(*tert*-butyldiphenylsilanyloxy)-5-methoxy-2,6-dimethylheptanol (43). *tert*-Butyldimethylsilyltrifluoromethane sulfonate (1.6 ml, 6.8 mmol) was added dropwise over 5 min to a stirred solution of the alcohol **42** (3.12 g, 5.6 mmol) and 2,6-lutidine (1.6 ml, 13.4 mmol) in dry dichloromethane at 0 ^{o}C under a nitrogen atmosphere. The solution was stirred at 0 ^{o}C for 1 h, then allowed to warm to room temperature and stirred for a further 1 h. Methanol (2.3 ml) was added followed by dichloromethane (10 ml) and the separated organic phase was washed with water (2 x 75 ml) and brine (30 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:10) as eluent to give the corresponding *bis-silyl ether* (3.21 g, 85%) as a colourless oil and a mixture of *E*/*Z*

isomers: $[\alpha]_D^{31}$ -7.6 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2930 and 2858; ^1H NMR (500 MHz, $CDCl_3$, *Z*-isomer) δ 0.06 (3H, s, CH_3Si), 0.09 (3H, s, CH_3Si), 0.89 (3H, d, *J* 7.0 Hz, CH_3CHCH_2OSi), 0.91 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 0.99 (3H, d, *J* 6.8 Hz, $CH_3CHCHOSi$), 1.08 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.42-1.52 (2H, m, CH_2CHOMe), 1.85-1.97 (1H, m, $CHCH_2OSi$), 2.54-2.61 (1H, m, $CHCHOSi$), 3.22 (3H, s, OCH_3), 3.38 (1H, ddd, *J* 7.8, 5.6, 3.3 Hz, CHOMe), 3.53 (1H dd, *J* 9.8, 6.9 Hz, $CHHOSi$), 3.66 (1H, ddd, *J* 7.8, 4.9, 3.3 Hz, $CHOSi$), 3.70 (1H dd, *J* 9.8, 6.7 Hz, $CHHOSi$), 4.03 (1H, app ddd, *J* 12.0, 5.8, 1.1 Hz, $CHHOBn$), 4.10 (1H, app ddd, *J* 12.0, 7.1, 1.1 Hz, $CHHOBn$), 4.45 (1H, d, *J* 12.0 Hz, $CHHAr$), 4.47 (1H, d, *J* 12.0 Hz, $CHHAr$), 5.55 (1H, dd, *J* 11.0, 9.8 Hz, $CHCHCH_2OBn$), 5.59-5.66 (1H, m, $CHCH_2OBn$), 7.25-7.46 (10H, m, ArH), 7.65-7.71 (5H, m, ArH); ^1H NMR (500 MHz, $CDCl_3$, *E*-isomer) δ 0.06 (3H, s, CH_3Si), 0.09 (3H, s, CH_3Si), 0.87 (3H, d, *J* 7.0 Hz, CH_3CHCH_2OSi), 0.92 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 1.03 (3H, d, *J* 6.8 Hz, $CH_3CHCHOSi$), 1.08 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.47 (1H, ddd, *J* 13.9, 8.0, 5.3 Hz, $CHHCHOMe$), 1.54 (1H, ddd, *J* 13.9, 7.9, 5.1 Hz, $CHHCHOMe$), 1.85-1.97 (1H, m, $CHCH_2OSi$), 2.40 (1H, ddq, *J* 7.3, 6.8, 3.2 Hz, $CHCHOSi$), 3.26 (3H, s, OCH_3), 3.48 (1H, ddd, *J* 7.9, 5.3, 3.3 Hz, $CHOMe$), 3.54 (1H dd, *J* 9.8, 6.9 Hz, $CHHOSi$), 3.71 (1H dd, *J* 9.8, 6.7 Hz, $CHHOSi$), 3.74 (1H, ddd, *J* 8.0, 5.1, 3.2 Hz, $CHOSi$), 3.99 (1H, d, *J* 5.9 Hz, CH_2OBn), 4.49 (1H, s, CH_2Ar), 5.59 (1H, m, $CHCH_2OBn$), 5.69 (1H, dd, *J* 15.6, 7.3 Hz, $CHCHCH_2OBn$), 7.25-7.46 (10H, m, ArH), 7.65-7.71 (5H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.2 (2q), -4.1 (2q), 11.6 (q), 11.9 (q), 15.3 (q), 16.3 (q), 18.2 (2s), 19.4 (2s), 26.1 (6q), 27.0 (6q), 34.8 (t), 35.3 (t), 37.8 (d), 38.1 (d), 42.0 (2d), 57.1 (q), 57.3 (q), 51.9 (2d), 65.4 (t), 66.2 (t), 71.0 (t), 72.2 (t), 72.7 (t), 72.8 (t), 78.0 (d), 78.5 (d), 126.7 (d), 126.8 (d), 127.6 (2d), 127.7 (8d), 127.8 (d), 127.9 (d), 128.4 (4d), 129.6 (4d), 134.0 (2s), 134.1 (2s), 135.0 (2d), 135.6 (4d), 135.7 (4d), 136.2 (2d), 138.4 (s), 138.5 (s); *m/z* (EI) 692.4534 ($M^+ + NH_4$), 697.4092 (M^+ + Na), $C_{41}H_{62}O_4Si_2$ + Na requires 697.4084.

A solution of the above alkene *bis*-silyl ether (4.5 g, 6.7 mmol) in dry dichloromethane (120 ml) was ozonised at –78 ^{o}C until the solution turned blue. Oxygen was then bubbled through the solution for 10 min to remove any excess of ozone. Triphenylphosphine (1.9 g, 7.3 mmol) was added in one portion under a nitrogen atmosphere and the solution was stirred at –78 ^{o}C for 15 min. The solution was allowed to warm to room temperature over 1 h and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:9) as eluent to give the corresponding *aldehyde* (3.49 g, 93%) as a colourless oil: $[\alpha]_D^{22}$ +6.7 (*c* 1.8 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2717 and 1722; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.10 (3H, s, CH_3Si), 0.12 (3H, s, CH_3Si), 0.89 (3H, d, *J* 6.5 Hz, C*H*$_3$CHCH$_2$OSi), 0.91 (9H, s, (C*H*$_3$)$_3$CSi(CH$_3$)$_2$), 1.06 (9H, s, (CH$_3$)$_3$CSi(Ph)$_2$), 1.12 (3H, d, *J* 7.0 Hz, C*H*$_3$CHCC=O), 1.56 (1H, ddd, *J* 14.3, 8.5, 5.2 Hz, C*H*HCHOMe) 1.65 (1H, ddd, *J* 14.3, 7.5, 5.1 Hz, CH*H*CHOMe), 1.94 (1H, dddq, *J* 6.5, 6.5, 6.5, 3.3 Hz, C*H*CH$_2$OSi), 2.56 (1H, ddq, *J* 7.0, 3.3, 1.7 Hz, C*H*CHO), 3.29 (3H, s, OCH$_3$), 3.49-3.53 (1H, m, CHOMe), 3.54 (1H dd, *J* 9.9, 6.5 Hz, C*H*HOSi), 3.70 (1H dd, *J* 9.9, 6.5 Hz, CH*H*OSi), 4.15 (1H, ddd, *J* 8.5, 5.1, 3.3 Hz, CHOTBS), 7.35-7.46 (6H, m, ArH), 7.66-7.72 (4H, m, ArH), 9.75 (1H, d, *J* 1.7 Hz, C*H*=O); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.5 (q), -4.4 (q), 9.7, (q), 11.8 (q), 18.0 (s), 19.2 (s), 25.8 (3q), 26.8 (3q), 36.3 (t), 37.8 (d), 51.9 (d), 57.0 (q), 64.9 (t), 70.6 (d), 78.2 (d), 127.7 (4d), 129.6 (d), 129.7 (d), 133.7 (2s), 135.6 (2d), 135.7 (2d), 204.1 (d); *m/z* (EI) 557.3477 (M^+ + H), $C_{32}H_{52}O_4Si_2$ + H requires 557.3482.

(4*S*,5*R*,6*S*,8*S*,9*R*)-6-(*tert*-Butyldimethylsilanyloxy)-10-(*tert*-butyldiphenylsilanyloxy)-8-methoxy-5,9-dimethyldec-1-en-4-ol (44a). A solution of allylmagnesium bromide (1.0 M in diethyl ether, 2.65 ml, 2.65 mmol) was added dropwise over 2 min to a stirred solution of (-)-*B*-chlorodiisopinocamphenylborane (885 mg, 2.76 mmol) in dry diethyl ether (3 ml) at –78 ^{o}C under an argon

atmosphere. The solution was stirred at –78 °C for 1 h and then allowed to warm to room temperature and stirred for an additional 1 h. The solution was re-cooled to –78 °C and then a solution of the aldehyde **43** (1.23 g, 2.21 mmol) in dry diethyl ether (6 ml) was added dropwise over 15 min. The solution was stirred at –78 °C for 5 h and then quenched by slow addition of 3 M aqueous sodium hydroxide solution (2.0 ml) and a 30% aqueous hydrogen peroxide solution (0.78 ml). The mixture was stirred at room temperature overnight and then diluted with diethyl ether (50 ml). The separated organic phase was washed with water (2 x 20 ml) and brine (25 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:9) as eluent to give the *alcohol* (1.42 g, 91%) as a colourless oil: $[\alpha]_D^{27}$ +8.4 (*c* 2.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3464 and 1641; (Found: C, 69.9; H, 9.7; $C_{35}H_{58}O_4Si_2$ requires C, 70.2; H, 9.8%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.11 (3H, s, CH_3Si), 0.12 (3H, s, CH_3Si), 0.85 (3H, d, *J* 7.0 Hz, C*H*$_3$CHCH$_2$OSi), 0.91 (9H, s, (C*H*$_3$)$_3$CSi(CH$_3$)$_2$), 1.04 (3H, d, *J* 7.2 Hz, C*H*$_3$CHCHOH), 1.07 (9H, s, (CH$_3$)$_3$CSi(Ph)$_2$), 1.57-1.65 (1H, m, CH$_3$C*H*CHOH), 1.68 (1H, ddd, *J* 14.0, 7.3, 5.2 Hz, C*H*HCHOMe), 1.81 (1H, dddq, *J* 7.8, 7.0, 6.1, 2.4 Hz, C*H*CH$_2$OSi), 2.00 (1H ddd, *J* 14.0, 8.6, 6.6 Hz, CH*H*CHOMe), 2.08 (1H, ddd, *J* 14.1, 6.5, 1.5 Hz, C*H*HC=), 2.33 (1H, ddd, *J* 14.1, 7.4, 6.5 Hz, CH*H*C=), 3.28 (3H, s, OCH_3), 3.39 (1H, ddd, *J* 7.3, 6.6, 2.4 Hz CHOMe), 3.51 (1H, dd, *J* 9.9, 6.1 Hz, C*H*HOSi), 3.68 (1H, dd, *J* 9.9, 7.8 Hz, CH*H*OSi), 3.69-3.72 (1H, br, OH), 3.80 (1H, ddd, *J* 8.6, 5.2, 1.6 Hz, CHOTBS), 4.17 (1H, ddd, *J* 7.4, 5.6, 1.5 Hz, C*H*OH), 5.02 (1H, dd *J* 10.2, 1.4 Hz, C*H*H=), 5.10 (1H, dd *J* 17.1, 1.4 Hz, CH*H*=), 5.80 (1H, app ddt, *J* 17.1, 10.2, 6.5 Hz, CH$_2$=C*H*), 7.36-7.47 (6H, m, ArH), 7.64-7.70 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.7 (q), -4.4 (q), 10.7 (q), 11.2 (q), 17.9 (s), 19.2 (s), 25.8 (3q), 26.9 (3q), 35.4 (t), 37.8 (d), 38.3 (d), 39.3 (t), 57.2 (q), 65.1 (t), 70.1 (d), 76.6 (d), 77.6 (d), 116.9 (t), 127.6 (4d), 129.6 (2d), 133.7 (2s), 135.4 (d),

135.5 (2d), 135.6 (2d); *m/z* (EI) 599.3915 (M^+ + H), $C_{35}H_{58}O_4Si_2$ + H requires 599.3952.

The *anti*-relationship between the diol functionalities at C28 and C30 in **44a** was established by conversion into the corresponding acetonide and examination of relative chemical shifts in the ^{13}C NMR spectrum,[50] *ie* ketal carbon δ 100.6 ppm and *gem*-methyl carbons δ 23.9 and 25.0 ppm.

(4*S*,5*R*,6*S*,8*S*,9*R*)-6-(*tert*-Butyldimethylsilanyloxy)-10-*tert*-butyldiphenylsilanyloxy-4,8-dimethoxy-5,9-dimethyldec-1-ene (44b). NaHMDS (1M in tetrahydrofuran, 3.3 ml, 3.3 mmol) was added dropwise over 15 min to a stirred solution of the alcohol **44a** (1.5 g, 2.5 mmol) in dry tetrahydrofuran (30 ml) at -15 °C under a nitrogen atmosphere. The solution was stirred at -15 °C for 30 min and then methyl iodide (0.8 ml, 12.5 mmol) was added dropwise over 15 min. The mixture was stirred at -10 °C for 1 h, and then water (50 ml) and diethyl ether (100 ml) were added. The separated aqueous phase was extracted with diethyl ether (3 x 100 ml) and the combined organic extracts were then washed with brine (25 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:20 to 1:5) as eluent to give the *methyl ether* (1.4 g, 91%) as a colourless oil: $[\alpha]_D^{27}$ -12.5 (*c* 1.1 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2930 and 2857; (Found: C, 70.3; H, 9.9; $C_{36}H_{60}O_4Si_2$ requires C, 70.5; H, 9.9%); ^1H NMR (360 MHz, $CDCl_3$) δ 0.04 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si), 0.88 (9H, s, $(CH_3)_3CSi(CH_3)_2$) 0.91 (3H, d, *J* 7.0 Hz, CH_3CHCH_2OSi), 0.92 (3H, d, *J* 6.9 Hz, $CH_3CHCHOTBS$), 1.06 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.28-1.48 (2H, m, CH_2CHOSi), 1.82 (1H, ddq, *J* 7.6, 6.9, 3.9 Hz, $=CHCH_2CHCHCH_3$), 1.96-2.07 (1H, m, CH_2CHCH_3) 2.22-2.41 (2H, m, $=CHCH_2$), 2.94 (1H, ddd, *J* 7.6, 5.8, 5.2 Hz, $=CHCH_2CHOMe$), 3.29 (3H, s, OCH_3), 3.31 (3H, s,

OCH_3), 3.42 (1H, ddd, *J* 9.9, 3.6, 2.4 Hz $CH_2CHCHOMe$), 3.60 (1H, dd, *J* 9.9, 6.8 Hz, C*H*HOSi), 3.72 (1H, dd, *J* 9.9, 5.6 Hz, CH*H*OSi), 3.89 (1H, ddd, *J* 9.5, 3.9, 1.7 Hz, CHOTBS), 5.06-5.14 (2H, m, CH_2=), 5.84 (1H, dddd, *J* 16.9, 10.5, 7.6, 6.5 Hz, CH_2=C*H*), 7.36-7.45 (6H, m, ArH), 7.66-7.71 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.6 (q), -3.9 (q), 8.8 (q), 12.6 (q), 18.1 (s), 19.3 (s), 26.0 (3q), 26.9 (3q), 34.0 (t), 34.8 (t), 37.9 (d), 42.4 (d), 57.3 (q), 57.5 (q), 65.0 (t), 70.2 (d), 79.5 (d), 82.6 (d), 117.2 (t), 127.6 (4d), 129.5 (2d), 133.9 (s), 134.0 (s), 135.6 (d), 135.6 (4d); *m/z* (EI) 613.4120 (M^+ + H), $C_{36}H_{60}O_4Si_2$ + H requires 613.4108.

(3*S*, 4*R*, 5*S*, 7*S*, 8*R*)-5-*tert*-Butyldimethylsilanyloxy)-9-(*tert*-butyldiphenylsilanyloxy)-3,7-dimethoxy-4,8-dimethylnonanal (45). The aldehyde was prepared from the alkene **44b**, according to the procedure described for the synthesis of **49a** from **48b**. It was purified by chromatography on silica, using diethyl ether-light petroleum (bp 40-60 °C) (1:9 then 1:5) as eluent, and was obtained as an oil (94%) which showed, $[\alpha]_D^{22}$ - 12.2 (c 0.6 in $CHCl_3$); ν_{max} (soln, $CHCl_3$, cm^{-1}) 1721; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.05 (3H, SiMe), 0.08 (3 H, SiMe), 0.89 (9H, CMe_3), 0.92 (3H, d, J 7.0 Hz, C*H*$_3$ CH), 0.97 (3H, d, *J* 6.9Hz, C*H*$_3$CH), 1.07 (9H, CMe_3), 1.32 - 1.5 (2H, m, C*H*$_2$CHOSi), 1.84 (1H, app. qd, *J* 6.9 and 3.7 Hz, CH_3C*H*.CHOTBS), 1.94 – 2.05 (1H, m, C*H*CH_2OSi), 2.57 – 2.69 (2H, m, C*H*$_2$CO), 3.29 (3H, CH_3) 3.31 (3H, OMe), 3.36 – 3.46 (2H, m, 2 x C*H*OMe), 3.55 (1 H, dd, *J* 9.9 and 6.6 Hz, C*H*HOSi), 3.68 (1H, dd, *J* 9.9 and 6.6 Hz, CH*H*OSi), 3.86 (1H, app, dt, *J* 9.2 and 2.8 Hz, C*H*OTBS), 7.37 – 7.44 (6H, m, ArH), 7.66 – 7.70 (4H, m, ArH), 9.81 (1H, t, *J* 2.3 Hz, C*H*=O). ^{13}C NMR (90 MHz, $CDCl_3$) δ – 4.5 (q), - 4.0 (q), 9.8 (q), 12.6 (q), 18.1 (s), 19.4 (s), 26.0 (q), 27.0 (q), 34.5 (t), 37.8 (d), 43.6 (d), 46.0 (t), 57.6 (q), 57.9 (q), 65.0 (d), 70.3 (d), 79.1 (d), 79.4 (d), 127.7 (d), 129.6 (d), 129.7 (d), 134.0 (2 x s), 135.7 (2 x d), 201.8 (d), *m/z* (ESI) 669. 3922 (M^+ + Na), C_{36} H_{62} O_6 Si_2 Na requires 669. 3983.

2-[(*E*)-(4*S*, 5*R*, 6*S*, 8*S*, 9*S*)-6-(*tert*-Butyl-dimethylsilanyloxy)

-10-(*tert*-butyl-diphenylsilanyloxy)-4, 8-dimethoxy – 5, 9-dimethyl-dec

-1-enyl]-oxazole-4-carboxylic acid *tert*-butyl ester (47a). The vinyloxazole was prepared from the phosphonium salt **46b**, and the aldehyde **45**, according to the procedure described for the synthesis of **55a** from **46a** and the aldehyde **54**. It was purified by chromatography on silica, using diethyl ether-light petroleum (bp 40 – 60 °C) (1:9, then 1:5) as eluent, and was obtained as an oil (91%) which showed $[\alpha]_D^{22}$ - 25.0 (c 1.03 in $CHCl_3$); ν_{max} (soln, $CHCl_3$, cm^{-1}) 1726; Found: C, 67.6; H, 8.6; N, 1.5; C_{44} H_{69} O_7 NSi_2 requires C, 67.7; H, 8.9; N, 1.8%; ^{1}H NMR (360 Mz, $CDCl_3$) δ – 0.03 (3H, SiMe), 0.01 (3H, SiMe), 0.86 (9H, CMe_3), 0.92 (3H, d, *J* 7.0 Hz, C*H*$_3$ CH CH_2), 0.95 (3H, d, *J* 6.8 Hz, C*H*$_3$ CH), 1.07 (9H, CMe_3), 1.25 – 1.34 (1H, m, C*H*CH.CHOSi), 1.4 – 1.48 (1H, m, CH*H*.CHOSi), 1.59 (9H, CMe_3), 1.75 – 1.83 (1H, m, CH_3 C*H*), 1.97 – 2.08 (1H, m, C*H*CH.OSi), 2.42 – 2.51 (1H, m, = CH.C*H*H), 2.54 – 2.63 (1H, m, = CHCH*H*), 3.02 (1H, app. dt, *J* 7.5 and 4.8 Hz, = CH.CH_2C*H*), 3.31 (6H, 2 x OMe), 3.35 – 3.42 (1H, m, CH_2 CH C*H* OMe), 3.57 (1H, dd, *J* 9.9 and 6.7 Hz, C*H*H.OSi), 3.68 (1H, dd, *J* 9.9 and 5.5 Hz, CH*H* OSi), 3.88 (1H, dd, *J* 8.5 and 3.3 Hz, CHOTBS), 6.41 (1H, d, *J* 16.2 Hz, C*H* = CH CH_2), 6.66 (1H, ddd, *J* 16.2, 8.1 and 6.6 Hz, = C*H*CH_2), 7.35 – 7.45 (6H, m, ArH), 7.65 – 7.74 (4H, m, ArH), 8.01 (1H, OC*H*=) ^{13}C NMR (90 MHz, $CDCl_3$), - 4.6 (q), - 4.1 (q), 9.3 (q), 12.6 (q), 17.9 (s), 19.2 (s), 25.8 (q), 26.9 (q), 28.1 (q), 33.8 (t), 34.0 (t), 37.5 (d), 43.0 (d), 57.5 (q), 64.7 (t), 69.7 (d), 79.5 (d), 81.9 (s), 82.3 (d), 118.2 (d), 127.5 (d), 129.4 (d), 129.5 (d), 133.8 (s), 133.9 (s), 135.3 (s), 135.5 (d), 135.6 (d), 137.8 (d), 142.4 (d), 160.5 (s), 161.2 (s); *m/z* (ESI) 780.4680 (M^+ + H,100%, $C_{44}H_{70}O_7NSi_2$ requires 780.4691.

2-[(*E*)-(4*S*, 5*R*, 6*S*, 8*S*, 9*S*)-10-(*tert*-Butyl-diphenylsilanyloxy)

-6-hydroxy-4, 8-dimethoxy – 5, 9-dimethyl-dec-1-enyl]-oxazole-4-carboxylic acid, *tert*-butyl ester (47b). The *bis*-silyl ether **47a** was first converted into the corresponding 1,5-diol by treatment with HF-pyridine complex and pyridine in THF, using the procedure described for the synthesis of **55b** from **55a**. The diol was purified by chromatography

on silica, using first 1:1 diethyl ether-light petroleum (bp 40-60 °C), next diethyl ether, and then methanol-diethyl ether (1:9) as eluents, and was obtained as an oil (91%) which showed, $[\alpha]_D^{22}$ – 15.9 (c 0.98 in $CHCl_3$); ν_{max} (soln, $CHCl_3$, cm^{-1}) 3464, 2971, 2880, 1725; ^1H NMR (360 MHz, $CDCl_3$) δ 0.88 (3H, d, *J* 7.0 Hz, CH_3), 0.94 (3H, d, *J* 7.0 Hz, CH_3), 1.49 (1H, ddd, *J* 14.0, 9.7 and 2.3 Hz, C*H*H.CHOH), 1.59 (9H, CMe_3), 1.69 (1H, ddd, *J* 14.0, 9.6 and 2.3 Hz, CH*H*.CHOH), 1.80 (1H, app. qd, *J* 7.2 and 2.7 Hz, C*H*.CHOH), 2.14 – 2.27 (2H, m, CH_2 C*H*MeOH), 2.43 (1H, dddd, *J* 14.4, 7.7, 6.1 and 1.2 Hz, C*H*H.CH=), 2.65 (1H, app. dtd, *J* 14.4, 7.1, and 1.3 Hz, CH*H.*CH=), 2.98 (1H, brs, OH), 3.42 (3H, OMe), 3.44 (3H, OMe), 3.52 – 3.73 (4H, m, CH_2OH and 2 x CHOMe), 3.80 (1H, t, *J* 8.0 Hz, CH_2C*H*OH), 6.39 (1H, d, *J* 16.0 Hz, CH_2CH=C*H*), 6.78 (1H, app. dt, *J* 16.0 and 7.5 Hz, CH_2C*H*=), 8.01 (1H, OC*H*=); ^{13}C NMR (90 MHz, $CDCl_3$) 11.8 (q), 12.7 (q), 28.1 (q), 33.6 (t), 35.5 (t) 36.3 (d), 40.0 (d), 57.5 (q), 58.0 (q), 65.5 (t), 71.0 (d), 81.6 (d), 82.1 (s), 82.8 (d), 117.9 (d), 135.2 (s), 138.0 (d), 142.5 (d), 160.4 (s), 161.1 (s). *m/z* (ESI) 450.2462 (M^+ + Na), $C_{22}H_{37}O_7NNa$ requires 450.2468.

The above 1,5 diol was next treated with TBDPS-Cl and imidazole in DMF at 0 °C, using the procedure described for the deprotection of **53a** to **53b**. It was purified by chromatography on silica, using diethyl ether-light pretroleum (bp 40 – 60 °C) as eluent, and was obtained as an oil, which showed, $[\alpha]_D^{22}$ – 7.8 (c 1.03 in $CHCl_3$); ν_{max} (soln, $CHCl_3$, cm^{-1}) 3468, 2962, 2877, 1725; ^1H NMR (500 MHz, $CDCl_3$) δ 0.85 (3H, d, *J* 7.0 Hz, C*H*$_3$ CH.CHOH), 0.98 (3H, d, *J* 6.9 Hz, C*H*$_3$CHCH$_2$), 1.06 (9H, CMe_3), 1.49 (1H, ddd, *J* 14.0, 9.1 and 2.2 Hz, CH*H*.CHOH), 1.57 (9H, CMe_3), 1.6 (1H, ddd, *J* 14.0, 9.1 and 2.2 Hz, CH*H*.CHOH), 1.68 (1H, app, qd, *J* 7.1 and 2.4 Hz, CH_3C*H*.CHOH), 1.96 (1H, app. sp, *J* 6.2, C*H* CH_2 OSi), 2.38 (1H, app, dt, *J* 14.4 and 7.0 Hz, C*H*H.CH=), 2.62 (1H, app, dtd, *J* 14.4, 6.9 and 1.1 Hz, CH*H.* CH=), 3.33 (3H, OMe), 3.36 (3H, OMe), 3.56 (1H, dd, *J* 10.2 and 6.7 Hz, C*H*H. OSi), 3.56 – 3.61 (2H, m, C*H*CH_2CHOH), 3.63 (1H, td, *J* 6.7 and 2.4 Hz, = CH.CH_2C*H*), 3.69 (1H, dd, *J* 10.0 and 5.5 Hz, CH*H.*OSi), 3.74 (1H, brt, *J*

8.3 Hz, C*H* OH), 6.39 (1H, d, *J* 16.1 Hz, C*H* = CH.CH_2), 6.78 (1H, app, dt, *J* 16.1 and 7.5 Hz, = C*H*CH_2), 7.34 – 7.42 (6H, m, ArH), 7.64 – 7.68 (4H, m, ArH), 8.0 (1H, OCH=). ^{13}C NMR (90 Mz, $CDCl_3$), 11.0 (q), 12.6 (q), 19.1 (s), 26.7 (q), 28.0 (q), 34.0 (t), 36.3 (t), 38.6 (d), 40.5 (d), 57.5 (q), 58.1 (q), 65.2 (t), 70.8 (d), 79.5 (d), 81.6 (d), 81.8 (s), 117.1 (d), 127.4 (d), 129.4 (d), 133.6 (2 x s), 135.2 (s), 135.4 (d), 138.1 (d), 142.4 (d), 160.3 (s), 161.1 (s). *m/z* (ESI) 666.3803 (M^++ H), $C_{38}H_{58}O_7NSi$ requires 666.3836.

(4*S*,5*R*,6*S*,8*S*,9*R*)-10-(*tert*-Butyldiphenylsilanyloxy)-4,8-dimethoxy-5,9-dimethyldec-1-en-6-ol (48a). Pyridinium *p*-toluenesulphonate (246 mg, 1.0 mmol) was added in one portion to a stirred solution of the *bis*-silyl ether **44b** (2.0 g, 3.3 mmol) in dry ethanol (30 ml) and the mixture was heated under reflux in a nitrogen atmosphere for 9 h. The mixture was cooled to room temperature, and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:20) as eluent to give the *alcohol* (1.25 g, 77%) as a colourless oil: $[\alpha]_D^{22}$ -7.7 (*c* 0.92 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3468; (Found: C, 73.0; H, 9.7; $C_{30}H_{46}O_4Si$, C, 72.3; H, 9.2%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (3H, d, *J* 7.1 Hz, C*H*$_3$CHCHOH), 0.97 (3H, d, *J* 6.9 Hz, C*H*$_3$CHCH_2OSi), 1.07 (9H, s, $(CH_3)_3C$), 1.52 (1H, ddd, *J* 14.2, 9.3, 3.3 Hz, C*H*HCHOH), 1.63 (1H, ddd, *J* 14.2, 9.0, 2.6 Hz, CH*H*CHOH), 1.71 (1H, ddq, *J* 7.1, 7.0, 4.5 Hz, =CHCH_2CHC*H*CH_3), 1.90-1.99 (1H, m, CH_3C*H*CH_2OSi), 2.20 (1H, ddd, *J* 14.1, 7.3, 7.2 Hz, =CHC*H*H), 2.47 (1H, ddd, *J* 14.1, 6.8, 6.7 Hz, =CHCH*H*), 3.38 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 3.55-3.61 (2H, m, C*H*HOSi, =CHCH_2C*H*OMe), 3.63 (1H, ddd, *J* 9.0, 4.5, 3.3 Hz, C*H*OH), 3.73 (1H, dd, *J* 10.0, 5.6 Hz, CH*H*OSi), 3.73-3.81 (1H, m, CH_2CHC*H*OMe), 5.03-5.09 (1H, m, C*H*H=), 5.13 (1H, dd, *J* 17.2, 1.6 Hz, CH*H*=), 5.79 (1H, app ddt, *J* 13.6, 7.3, 6.7 Hz, CH_2=C*H*), 7.36-7.47 (6H, m, ArH), 7.67-7.72 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 11.5 (q), 12.6 (q), 19.4 (s), 27.0 (3q),

34.8 (t), 37.1 (t), 39.0 (d), 39.9 (d), 57.5 (q), 58.5 (q), 65.5 (t), 71.4 (d), 79.6 (d), 82.6 (d), 117.0 (t), 127.7 (4d), 129.6 (2d), 133.9 (2s), 135.3 (d), 135.7 (4d); *m/z* (EI) 499.3277 (M^+ + H), 521.3044 (M^+ + Na) $C_{30}H_{46}O_4Si$ + H requires 499.3244.

(4*S*,5*R*,6*S*,8*S*,9*R*)-10-(*tert*-Butyldiphenylsilanyloxy)-4,8-dimethoxy-5,9-dimethyldec-1-en-6-ol (48b). Methoxymethyl chloride (0.6 ml, 8.3 mmol) was added dropwise over 5 min to a stirred solution of the alcohol **48a** (0.83 g, 1.7 mmol) and diisopropylethylamine (2.8 ml, 16.6 mmol) in dry dichloromethane (50 ml) at room temperature under a nitrogen atmosphere, and the mixture was then heated under reflux for 1 h. The solution was cooled to room temperature, and another portion of diisopropylethylamine (2.8 ml, 16.6 mmol) and methoxymethyl chloride (0.6 ml, 8.3 mmol) were added and the mixture was heated under reflux for a further 1 h. The solution was diluted with dichloromethane (100 ml), then washed with water (2 x 50 ml), brine (50 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (0:1 to 1:5) as eluent to give the methoxymethyl ether (850 mg, 95%) as a colourless oil: $[\alpha]_D^{23}$ -15.7 (*c* 0.92 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2931, 1639 and 1088; (Found: C, 70.6; H, 9.3; $C_{32}H_{50}O_5Si$ requires C, 70.8; H, 9.3%); ^1H NMR (360 MHz, $CDCl_3$) δ 0.91 (3H, d, *J* 6.2 Hz, C*H*$_3$CHCH$_2$OSi), 0.94 (3H, d, *J* 6.3 Hz, C*H*$_3$CHCHOCH$_2$OMe), 1.06 (9H, s, $(CH_3)_3C$), 1.42-1.52 (2H, m, C*H*$_2$CHOCH$_2$OMe), 1.85-2.00 (2H, m, =CHCH$_2$CHC*H*CH$_3$, C*H*CH$_2$OSi), 2.33 (2H app dd, *J* 7.1, 6.1 Hz, =CHC*H*$_2$), 3.10 (1H, ddd, *J* 11.3, 6.1, 5.7 Hz =CHCH$_2$C*H*OMe), 3.36 (3H, s, OCH_3), 3.38 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 3.45-3.56 (1H, m, CH$_2$CHC*H*OMe), 3.58 (1H, dd, *J* 10.0, 6.6 Hz, C*H*HOSi), 3.69 (1H, dd, *J* 10.0, 6.1 Hz, CH*H*OSi), 3.73-3.79 (1H, m, C*H*OCH$_2$OMe), 4.61 (1H, d, *J* 6.8 Hz, OC*H*HOMe), 4.69 (1H, d, *J* 6.8 Hz, OCH*H*OMe), 5.05-5.15 (2H, m, C*H*$_2$=), 5.84 (1H, dddd, *J* 17.3, 10.1, 7.1, 4.2 Hz, CH$_2$=C*H*), 7.35-7.47 (6H, m, ArH), 7.65-7.71 (4H, m, ArH); ^{13}C NMR (90.6 MHz,

$CDCl_3$) δ 9.2 (q), 12.3 (q), 19.4 (s), 27.0 (3q), 33.8 (t), 35.0 (t), 39.0 (d), 39.7 (d), 55.9 (q), 57.3 (q), 58.2 (q), 65.4 (t), 77.1 (d), 79.0 (d), 81.7 (d), 96.4 (t), 117.3 (t), 127.7 (4d), 129.6 (2d), 133.9 (s), 134.0 (s), 134.6 (d), 135.7 (4d); *m/z* (EI) 565.3315 (M^+ + Na) $C_{32}H_{50}O_5Si$ + Na requires 565.3325.

(3*S*,4*R*,5*S*,7*S*,8*R*)-9-(*tert*-Butyldiphenylsilanyloxy)-1,1,3,7-tetramethoxy-5-methoxymethoxy-4,8-dimethylnonanane (49b). A solution of the alkene **48b** (2.6 g, 4.8 mmol) in dry dichloromethane (85 ml) was ozonised at –78 °C until the solution turned blue. Oxygen was then bubbled through the solution for 10 min to remove any excess of ozone. Triphenylphosphine (1.6 g, 6.1 mmol) was added in one portion under a nitrogen atmosphere and the solution was then stirred at –78 °C for 15 min. The solution was allowed to warm to room temperature over 1 h and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:5 to 3:2) as eluent to give *(3S,4R,5S,7S,8R)-9-(tert-butyldiphenylsilanyloxy)-3,7-dimethoxy-5-methoxymethoxy-4,8-dimethylnonanal* (2.6 g, 99%) as a colourless oil: $[\alpha]_D^{22}$ -19.1 (*c* 1.83 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2728 and 1723; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.93 (3H, d, *J* 6.0 Hz, C*H*$_3$CHCH$_2$OSi), 0.95 (3H, d, *J* 6.1 Hz, C*H*$_3$CHCHOCH$_2$OMe), 1.06 (9H, s, $(CH_3)_3$C), 1.44-1.55 (2H, m, C*H*$_2$CHOCH$_2$OMe), 1.87-2.01 (2H, m, O=CHCH$_2$CHC*H*CH$_3$, C*H*CH$_2$OSi), 2.61 (1H, ddd, *J* 16.3, 5.1, 2.1 Hz, C*H*HC=O) 2.69 (1H, ddd, *J* 16.3, 6.6, 2.1 Hz, CH*H*C=O), 3.32 (3H, s, OCH_3), 3.34 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 3.45-3.54 (1H, m, C*H*CH$_2$C=O), 3.58 (1H, dd, *J* 9.9, 6.5 Hz, C*H*HOSi), 3.64 (3H, m, CH*H*OSi, C*H*OCH$_2$OMe, CH$_2$CHC*H*OMe), 4.65 (1H, d, *J* 6.8 Hz, OC*H*HOMe), 4.69 (1H, d, *J* 6.8 Hz, OCH*H*OMe), 7.35-7.47 (6H, m, ArH), 7.65-7.74 (4H, m, ArH), 9.83 (1H, t, *J* 2.1 Hz, CH=O); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 9.8 (q), 12.3 (q), 19.3 (s), 26.9 (3q), 34.0 (t), 38.7 (d), 41.5 (d), 46.2 (t), 55.9 (q), 57.7 (q), 58.1 (q), 65.2 (t), 77.3 (d), 77.7 (d), 78.9 (d), 96.7 (t), 127.7 (4d), 129.6 (2d), 133.9

(s), 134.0 (s), 135.6 (2d), 135.7 (2d) 201.5 (d); *m/z* (EI) 567.3081 (M^+ + Na) $C_{31}H_{48}O_6Si$ + Na requires 567.3118.

p-Toluenesulfonic acid (12 mg, 0.06 mmol) was added in one portion to a stirred solution of the above aldehyde (780 mg, 1.4 mmol) in a mixture of trimethylorthoformate (32 ml) and dry methanol (22 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 1 h and then quenched with saturated aqueous sodium bicarbonate solution (5 ml). The separated organic phase was dried (Na_2SO_4) and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:1) as eluent to give the acetal (0.7 g, 89%) as a colourless oil, which crystallised from diethyl ether-light petroleum (bp 40-60 ^oC) as colourless crystals, mp 25-28 ^oC: $[\alpha]_D^{22}$ -19.4 (*c* 1.03 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932 and 2858; (Found: C, 67.4; H, 9.5; $C_{33}H_{54}O_7Si$ requires C, 67.1; H, 9.2%); ^1H NMR (360 MHz, $CDCl_3$) δ 0.93 (3H, d, *J* 7.0 Hz, CH_3), 0.94 (3H, d, *J* 7.0 Hz, CH_3), 1.06 (9H, s, $(CH_3)_3C$), 1.46-1.52 (2H, m, C*H*$_2$CHOCH$_2$OMe), 1.81 (2H, app ddd, *J* 5.8, 5.7, 1.5 Hz, C*H*$_2$CH(OMe)$_2$), 1.86-2.02 (2H, m, C*H*CHOCH$_2$OMe, C*H*CH$_2$OSi), 3.22 (1H, ddd, *J* 12.3, 5.7, 5.6 Hz, C*H*CH$_2$CH(OMe)$_2$), 3.29 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 3.34 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 3.40 (3H, s, OCH_3), 3.48-3.54 (1H, m, C*H*CHCH$_2$OSi), 3.57 (1H, dd, *J* 10.0, 6.6 Hz, C*H*HOSi), 3.71 (1H, dd, *J* 10.0, 6.2 Hz, CH*H*OSi), 3.73-3.79 (1H, m, C*H*OCH$_2$OMe), 4.54 (1H, t, *J* 5.8 Hz, C*H*(OMe)$_2$), 4.64 (1H, d, *J* 6.8 Hz, OC*H*HOMe), 4.71 (1H, d, *J* 6.8 Hz, OCH*H*OMe), 7.35-7.46 (6H, m, ArH), 7.65-7.74 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 9.5 (q), 12.3 (q), 19.3 (s), 26.9 (3q), 33.8 (t), 35.1 (t) 38.9 (d), 41.2 (d), 52.0 (q), 53.2 (q), 55.9 (q), 58.1 (q), 58.1 (q), 65.4 (t), 77.6 (d), 78.7 (d), 79.4 (d), 96.5 (t), 102.1 (d), 127.7 (4d), 129.6 (2d), 133.9 (s), 134.0 (s), 135.6 (2d), 135.7 (2d); *m/z* (EI) 613.3542 (M^+ + Na) $C_{33}H_{54}O_7Si$ + Na requires 613.3537.

The absolute stereochemistry of the acetal was determined by X-ray crystallographic analysis.[26]

(3*S*,4*R*,5*S*,7*S*,8*R*)-1,1,3,7-Tetrmethoxy-5-methoxymethoxy-4,8-dimethylnonan-9-ol (50a). Tetrabutylammonium fluoride (850 mg, 2.7 mmol) was added in one portion to a stirred solution of the silyl ether **49b** (1.1 g, 1.8 mmol) in dry tetrahydrofuran (20 ml) at room temperature. The mixture was stirred at room temperature for 12 h and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-dichloromethane (3:1) as eluent to give the alcohol (630 mg, 99%) as a colourless oil: $[\alpha]_D^{23}$ -44.1 (*c* 1.2 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3485; (Found: C, 57.9; H, 10.3; $C_{17}H_{36}O_7$ requires C, 57.9; H, 10.3%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.80 (3H, d, *J* 7.1 Hz, CH_3), 0.92 (3H, d, *J* 7.0 Hz, CH_3), 1.46 (1H, ddd, *J* 14.6, 10.0, 2.2 Hz, C*H*HCHOCH$_2$OMe), 1.57 (1H, ddd, *J* 14.6, 10.0, 1.7 Hz, CH*H*CHOCH$_2$OMe), 1.79 (2H, app t, *J* 6.0 Hz C*H*$_2$CH(OMe)$_2$), 1.82-1.93 (1H, m, C*H*CHOCH$_2$OMe), 2.20-2.34 (1H, m, C*H*CH$_2$OH) 2.96-3.01 (1H, br, OH), 3.17-3.25 (1H, m, C*H*CH$_2$CH(OMe)$_2$), 3.30 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.34 (3H, s, OCH_3), 3.38 (3H, s, OCH_3), 3.41 (3H, s, OCH_3), 3.44-3.47 (1H, m, C*H*CHCH$_2$OH), 3.49 (1H, dd, *J* 10.8, 5.0 Hz, C*H*HOH), 3.68 (1H, dd, *J* 10.8, 9.0 Hz, CH*H*OH), 3.76 (1H, ddd, *J* 10.0, 4.4, 1.7 Hz C*H*OCH$_2$OMe), 4.51 (1H, t, *J* 6.0 Hz, C*H*(OMe)$_2$), 4.58 (1H, d, *J* 6.8 Hz, OC*H*HOMe), 4.67 (1H, d, *J* 6.8 Hz, OCH*H*OMe); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 9.3 (q), 13.0 (q), 31.4 (t), 35.0 (t), 35.4 (d), 41.1 (d) 52.2 (q), 53.2 (q), 55.8 (q), 57.6 (q), 58.1 (q), 65.7 (t), 76.8 (d), 79.3 (d), 82.2 (d), 96.5 (t), 102.1 (d); *m/z* (EI) 375.2353 (M^+ + Na) $C_{17}H_{36}O_7$ + Na requires 375.2359.

(3*S*,4*R*,5*S*,7*S*,8*R*)-1,1,3,7-Tetrmethoxy-5-methoxymethoxy-4,8-dimethylnonanal (50b). 4-Methylmorpholine *N*-oxide (406 mg, 3.0 mmol) was added in one portion to

a stirred mixture of the alcohol **50a** (519 mg, 1.5 mmol) and molecular sieves (2.5 g) in dry dichloromethane (46 ml) at room temperature. The mixture was stirred at room temperature for 10 min and then TPAP (53 mg, 0.15 mmol) was added in one portion and the mixture was stirred at room temperature for 1h. The solution was diluted with diethyl ether (400 ml) and then filtered through celite. The filter cake was washed with diethyl ether (2 x 100 ml) and the combined diethyl ether extracts were concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1) as eluent to give the aldehyde (410 mg, 78%) as a colourless oil: $[\alpha]_D^{24}$ -82.3 (*c* 3.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2718 and 1721; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.91 (3H, d, *J* 7.0 Hz, C*H*$_3$CHCHOCH$_2$OMe), 1.08 (3H, d, *J* 7.1 Hz, C*H*$_3$CH=O), 1.48 (1H, ddd, *J* 14.6, 10.0, 2.7 Hz, C*H*HCHOCH$_2$OMe), 1.59 (1H, ddd, *J* 14.6, 10.2, 2.0 Hz, CH*H*CHOCH$_2$OMe), 1.79 (2H, m, C*H*$_2$CH(OMe)$_2$), 1.90 (1H, ddq, *J* 7.0, 4.8, 2.4 Hz, C*H*CHOCH$_2$OMe), 2.65 (1H, ddq, *J* 7.1, 3.5, 0.8 Hz, CHC=O), 3.19-3.29 (1H, m, C*H*CH$_2$CH(OMe)$_2$), 3.34 (3H, s, OCH$_3$), 3.36 (3H, s, OCH$_3$), 3.37 (3H, s, OCH$_3$), 3.95 (3H, s, OCH$_3$), 3.43 (3H, s, OCH$_3$), 3.78-3.85 (2H, m, C*H*OCH$_2$OMe, C*H*CHC=O), 4.51 (1H, t, *J* 5.7 Hz, CH(OMe)$_2$), 4.62 (1H, d, *J* 6.8 Hz, OC*H*HOMe), 4.70 (1H, d, *J* 6.8 Hz, OCH*H*OMe), 9.84 (1H, d, *J* 0.8 Hz, CH=O); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 8.5 (q), 9.2 (q), 34.6 (t), 35.0 (t), 40.9 (d), 49.5 (d) 52.3 (q), 53.2 (q), 55.9 (q), 57.8 (q), 58.0 (q), 77.4 (d), 78.1 (d), 79.2 (d), 96.6 (t), 102.2 (d), 204.8 (d); *m/z* (EI) 373.2197 (M^+ + Na) $C_{17}H_{34}O_7$ + Na requires 373.2202.

(*E*)-(3*R*,4*R*,5*R*,9*S*,10*S*,12*S*,13*R*,14*S*)-1-Benzyloxy-4-(*tert*-butyl-dimethyl-silanyloxy)-10,14,16,16-tetramethoxy-12-methoxymethoxy-3,5,9,13-tetramethyl-hexadec-7-en-6-one (52). Barium hydroxide octahydrate (161 mg, 0.93 mmol) was pre-dried by heating at 140 ^{o}C *in vacuo* overnight. A solution of the *β*-keto phosphonate **51**[13] (368 mg, 0.75 mmol) in dry tetrahydrofuran (15 ml) was added at

room temperature under a nitrogen atmosphere and the solution was stirred for 30 min. A solution of the aldehyde **50b** (392 mg, 1.12 mmol) in tetrahydrofuran (30 ml) and water (0.6 ml) was added in one portion and the mixture was then stirred at room temperature for 5 h. The mixture was diluted with dichloromethane (250 ml) and saturated aqueous sodium bicarbonate solution (100 ml) and the separated aqueous phase was then extracted with dichloromethane (2 x 150 ml). The combined dichloromethane extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:2) as eluent to give the *enone* (362 mg, 68%) as a colourless oil: $[\alpha]_D^{22}$ -68.4 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1690, 1663 and 1622; (Found: C, 65.6; H, 9.9; $C_{39}H_{70}O_9Si$ requires C, 65.9; H, 9.9%); ^1H NMR (400 MHz, $CDCl_3$) δ -0.08 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si), 0.83 (9H, s, $(CH_3)_3C$), 0.88 (3H, d, *J* 6.8 Hz, CH_3-13), 0.93 (3H, d, *J* 7.2 Hz, CH_3-3), 1.00 (3H, d, *J* 7.2 Hz, CH_3-5), 1.07 (3H, d, *J* 6.8 Hz, CH_3-9), 1.35-1.55 (2H, m, H-11), 1.76 (2H, app t, *J* 6.0 Hz, H-2), 1.80-1.90 (4H, m H-13, H-15, H-3), 2.64-2.75 (1H, m, H-9), 3.04 (1H, dq, *J* 8.0, 7.2 Hz, H-5), 3.18 (1H, ddd, *J* 11.4, 6.3, 6.2 Hz, H-14), 3.31 (3H, s, OCH_3-16), 3.32 (3H, s, OCH_3-16), 3.33 (3H, s, OCH_3-14), 3.37-3.42 (1H, m, H-10), 3.38 (3H, s, OCH_3-10), 3.39 (3H, s, CH_2OCH_3), 3.42-3.59 (2H, m, H-1), 3.72-3.79 (1H, m, H-12), 3.91 (1H, dd, *J* 8.0, 2.2 Hz, H-4), 4.45 (1H, d, *J* 11.9 Hz, C*H*HAr), 4.49 (1H, dd, *J* 5.5, 2.0 Hz, H-16), 4.51 (1H, d, *J* 11.9 Hz, CH*H*Ar), 4.59 (1H, d, *J* 6.7 Hz, C*H*HOMe), 4.66 (1H, d, *J* 6.7 Hz, CH*H*OMe), 6.15 (1H, dd, *J* 16.0, 1.4 Hz, H-7), 6.90 (1H, dd, *J* 16.0, 6.5 Hz, H-8), 7.24-7.35 (5H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.4 (q), -4.1 (q), 9.3 (q), 14.2 (q), 14.5 (q), 16.9 (q), 18.4 (s), 26.2 (3q), 30.7 (t), 33.2 (d), 33.5 (t), 35.0 (t), 38.5 (d), 41.2 (d), 48.1 (d), 52.1 (q), 53.2 (q), 55.8 (q), 57.6 (q), 58.0 (q), 68.9 (t), 73.0 (t), 77.4 (d), 78.3 (d), 79.1 (d), 81.1 (d), 96.6 (t), 102.1 (d), 127.5 (d), 127.6 (2d), 128.3 (2d), 130.2 (d), 138.6 (s), 148.5 (d), 203.3 (s); *m/z* (EI) 734.4725 (M^+ + Na), 728.5137 (M^+ + NH_4) $C_{39}H_{70}O_9Si$ + Na requires 734.4687.

(3*R*,4*R*,5*R*,9*S*,10*S*,12*S*,13*R*,14*S*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-1-hydroxy-10,14,16,16-tetramethoxy-12-methoxymethoxy-3,5,9,13-tetramethyl-hexadecan-6-one (53a). Pearlman's catalyst[28] (102 mg) was added in one portion to a stirred solution of the benzyl ether **52** (512 mg, 0.72 mmol) in ethyl acetate (20 ml) at room temperature, and the apparatus was then evacuated prior to the introduction of hydrogen gas. The mixture was stirred at room temperature for 2 days under one atmosphere of hydrogen, then filtered through celite. The filter cake was washed with ethyl acetate (3 x 30 ml) and the combined organic washings were then concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (2:1 to 1:0) as eluent to give the *alcohol* (433 mg, 96%) as a colourless oil: $[\alpha]_D^{22}$ -48.4 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3621 and 1713; (Found: C, 61.6; H, 10.7; $C_{32}H_{66}O_9Si$ requires C, 61.7; H, 10.7%); ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.07 (3H, s, CH_3Si), 0.06 (3H, s, CH_3Si), 0.83 (3H, d, *J* 6.8 Hz, CH_3-9), 0.84 (9H, s, $(CH_3)_3C$), 0.90 (3H, d, *J* 7.0 Hz, CH_3-13), 0.94 (3H, d, *J* 7.0 Hz, CH_3-3), 0.95 (3H, d, *J* 7.0 Hz, CH_3-5), 1.18-1.30 (1H, m, C*H*H H-2), 1.32-1.44 (2H, m, H-13, C*H*H H-11), 1.50 (1H, ddt, *J* 14.3, 8.5, 6.1 Hz, C*H*H H-8), 1.66 (1H, ddt, *J* 14.3, 5.2, 3.9 Hz, CH*H* H-8), 1.71-1.90 (6H, m, H-15, H-9, CH*H* H-11, H-3, CH*H* H-2), 2.10-2.36 (1H, br, OH), 2.47 (1H, ddd, *J* 18.1, 9.8, 5.2 Hz, C*H*H H-7), 2.56 (1H, ddd, *J* 18.1, 9.8, 6.1 Hz, C*H*H H-7), 2.84 (1H, dq, *J* 8.3, 7.0 Hz, H-5), 3.18-3.27 (2H, m, H-14, H-10), 3.29 (3H, s, OCH_3-16), 3.31 (3H, s, OCH_3-16), 3.32 (3H, s, OCH_3-10), 3.34 (3H, s, OCH_3-14), 3.37 (3H, s, CH_2OCH_3), 3.56 (1H, dt, *J* 10.5, 6.8 Hz, C*H*H H-1), 3.66-3.79 (2H, m, H-12, CH*H* H-1), 3.88 (1H, dd, *J* 8.3, 2.5 Hz, H-4), 4.51 (1H, t, *J* 5.7 Hz, H-16), 4.59 (1H, d, *J* 6.8 Hz, C*H*HOMe), 4.66 (1H, d, *J* 6.8 Hz, CH*H*OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.3 (q), -4.2 (q), 9.5 (q), 14.1 (q), 15.6 (q), 16.7 (q), 18.4 (s), 24.6 (t), 26.2 (3q), 32.1 (t), 33.2 (d), 33.8 (t), 34.0 (d), 35.0 (t), 41.3 (d), 42.5 (t), 50.1 (d), 52.0 (q), 53.2 (q), 55.8 (q), 57.4 (q), 58.1 (q), 60.2 (t), 76.8 (d),

78.2 (d), 79.3 (d), 81.9 (d), 96.6 (t), 102.1 (d), 213.8 (s); *m/z* (EI) 645.4343 (M^+ + Na), 640.4790 (M^+ + NH_4) $C_{32}H_{66}O_9Si$ + Na requires 645.4374.

(3*R*,4*R*,5*R*,9*S*,10*S*,12*S*,13*R*,14*S*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-1-(*tert*-butyl-diphenyl-silanyloxy)-10,14,16,16-tetramethoxy-12-methoxymethoxy-3,5,9,13-tetramethyl-hexadecan-6-one (53b). Imidazole (167 mg, 2.45 mmol) and *tert*-butyldiphenylsilyl chloride (540 µl, 2.5 mmol) were added sequentially to a stirred solution of the alcohol **53a** in dry dimethylformamide (10 ml) at room temperature under a nitrogen atmosphere. The solution was stirred at room temperature overnight and then diluted with water (80 ml) and ethyl acetate (160 ml). The separated aqueous phase was extracted with ethyl acetate (3 x 160 ml) and the combined organic extracts were then washed with water (160 ml) and brine (160 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^oC) (1:1) as eluent to give the *silyl ether* (667 mg, 93%) as a colourless oil: $[\alpha]_D^{26}$ -32.0 (*c* 1.02 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2931, 2886 and 1712; (Found: C, 67.0; H, 9.9; $C_{48}H_{84}O_9Si_2$ requires C, 66.9; H, 9.8%); ^1H NMR (400 MHz, $CDCl_3$) δ -0.07 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.85 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 0.87 (3H, d, *J* 7.2 Hz, CH_3-9), 0.88 (3H, d, *J* 7.0 Hz, CH_3-13), 0.94 (3H, d, *J* 6.9 Hz, CH_3-3), 0.95 (3H, d, *J* 7.1 Hz, CH_3-5), 1.05 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.19-1.49 (4H, m, C*H*H H-11, H-9, C*H*H H-8, C*H*H H-2), 1.71-1.85 (5H, m, H-15, H-13, H-3, CH*H* H-2), 1.86-1.95 (2H, m, CH*H* H-11, CH*H* H-8), 2.53 (2H, app dt, *J* 9.1, 5.6 Hz, H-7), 2.77 (1H, dq, *J* 8.1, 7.1 Hz, H-5), 3.24 (2H, m, H-14, H-10), 3.32 (3H, s, OCH_3-16), 3.34 (3H, s, OCH_3-16), 3.37 (3H, s, OCH_3-10), 3.38 (3H, s, OCH_3-14), 3.41 (3H, s, CH_2OCH_3), 3.64 (1H, ddd, *J* 10.0, 8.8, 5.6 Hz, C*H*H H-1), 3.70-3.82 (2H, m, H-12, CH*H* H-1), 3.84 (1H, dd, *J* 8.1, 2.5 Hz, H-4), 4.54 (1H, t, *J* 5.7 Hz, H-16), 4.63 (1H, d, *J* 6.7 Hz, C*H*HOMe), 4.70 (1H, d, *J* 6.7 Hz, CH*H*OMe), 7.35-7.47 (6H, m, ArH), 7.65-7.70 (4H, m, ArH); ^{13}C

NMR (100 MHz, $CDCl_3$) δ -4.4 (q), -4.2 (q), 9.5 (q), 14.1 (q), 15.7 (q), 16.2 (q), 18.4 (s), 19.2 (s), 24.8 (t), 26.2 (3q), 26.9 (3q), 32.3 (t), 33.0 (d), 33.8 (t), 34.2 (d), 35.1 (t), 41.4 (d), 42.4 (t), 50.1 (d), 52.1 (q), 53.2 (q), 55.8 (q), 57.4 (q), 58.1 (q), 60.2 (t), 77.7 (d), 78.6 (d), 79.3 (d), 81.9 (d), 96.7 (t), 102.2 (d), 127.7 (4d), 129.6 (2d), 134.0 (2s), 135.6 (4d), 214.0 (s); *m/z* (EI) 883.5552 (M^+ + Na), 878.5998 (M^+ + NH_4) $C_{48}H_{84}O_9Si_2Na$ requires 883.5573.

(3*S*,4*R*,5*S*,7*S*,8*S*,12*R*,13*R*,14*R*)-13-(*tert*-Butyl-dimethyl-silanyloxy)-16-(*tert*-butyl-diphenyl-silanyloxy)-3,7-dimethoxy-5-methoxymethoxy-4,8,12,14-tetramethyl-11-oxo-hexadecanal (54). Dimethylboron bromide (2.5 M in dichloromethane, 511 µl, 1.28 mmol) was added dropwise over 10 min to a stirred solution of the acetal **53b** (550 mg, 0.64 mmol) in dry diethyl ether (15 ml) at –78 °C under a nitrogen atmosphere. The solution was stirred at –78 °C for 1 h and then quenched by careful addition of a mixture of saturated aqueous sodium bicarbonate solution (30 ml) and tetrahydrofuran (30 ml). The separated aqueous phase was extracted with diethyl ether (3 x 200 ml) and the combined organic extracts were then washed with saturated aqueous sodium bicarbonate solution (50 ml) and brine (50 ml), dried (Na_2SO_4) and concentrated *in vacuo* to leave the *aldehyde* (510 mg, 98%) as a colourless oil: $[\alpha]_D^{25}$ -30.5 (*c* 1.32 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932, 2885, 2733, 1721 and 1712; ^1H NMR (360 MHz, $CDCl_3$) δ -0.07 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.82-0.89 (6H, m, CH_3-8, CH_3-4), 0.85 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 0.95 (3H, d, *J* 7.0 Hz, CH_3-14), 0.96 (3H, d, *J* 7.0 Hz, CH_3-12), 1.05 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.39-1.48 (3H, m, C*H*H H-6, H-15), 1.73-1.97 (6H, m, H-4, CH*H* H-6, H-8, H-9, H-14), 2.48-2.58 (2H, m, H-2), 2.53 (2H, ddd, *J* 16.4, 5.3, 2.1 Hz, H-10), 2.70 (1H, ddd, *J* 16.4, 6.5, 2.6 Hz, C*H*H H-10), 2.77 (1H, dq, *J* 8.1, 7.0 Hz, H-12), 3.20-3.29 (1H, m, H-7), 3.36 (6H, s, OCH_3-3, OCH_3-7), 3.41 (3H, s, CH_2OCH_3), 3.57-3.80 (4H, m, H-3, H-5, H-16), 3.84 (1H, dd, *J* 8.1, 2.4 Hz, H-13), 4.64 (1H, d, *J* 6.8 Hz, C*H*HOMe), 4.69

(1H, d, *J* 6.8 Hz, CH*H*OMe), 7.32-7.47 (6H, m, ArH), 7.62-7.72 (4H, m, ArH), 9.85 (1H, t, *J* 2.2 Hz, H-1); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.4 (q), -4.2 (q), 9.8 (q), 14.1 (q), 15.7 (q), 16.2 (q), 18.4 (s), 19.2 (s), 24.5 (t), 26.2 (3q), 26.9 (3q), 32.3 (t), 33.0 (d), 33.8 (t), 33.9 (d), 41.7 (d), 42.5 (t), 46.2 (t), 50.0 (d), 55.9 (q), 57.4 (q), 57.7 (q), 62.1 (t), 77.3 (d), 77.7 (d), 78.6 (d), 81.9 (d), 96.8 (t), 127.7 (4d), 129.6 (2d), 134.0 (2s), 135.6 (4d), 201.6 (d), 214.1 (s); *m/z* (EI) 837.5104 (M^+ + Na), 832.5550 (M^+ + NH_4) $C_{46}H_{78}O_8Si_2$ + Na requires 837.5133.

2-[(*E*)-(4*S*,5*R*,6*S*,8*S*,9*S*,13*R*,14*R*,15*R*)-14-(*tert*-Butyl-dimethyl-silanyloxy)-17-(*tert*-butyl-diphenyl-silanyloxy)-4,8-dimethoxy-6-methoxymethoxy-5,9,13,15-tetramethyl-12-oxo-heptadec-1-enyl]-oxazole-4-carboxylic acid *tert*-butyl ester (55a). Tri-*n*-butylphosphine (0.8 ml, 3.2 mmol) was added dropwise over 5 min to a stirred solution of the *t*-butyl 2-(bromomethyl)oxazole-4-carboxylate **46a**[25] (201 mg, 0.77 mmol) in dry dimethylformamide (13 ml) at room temperature under a nitrogen atmosphere. The solution was stirred at room temperature for 1 h and then a solution of the aldehyde **54** (521 mg, 0.64 mmol) in dry dimethylformamide (7 ml) was added in one portion, 1,8-Diazabicyclo[5.4.0]undec-7-ene (5.9 ml, 39 mmol) was then added dropwise over 5 min. The mixture was stirred for 2.5 h at room temperature and then diluted with saturated aqueous ammonium chloride solution (50 ml) and ethyl acetate (100 ml). The separated aqueous phase was extracted with ethyl acetate (2 x 100 ml) and the combined organic extracts were then washed with water (50 ml) and brine (50 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:2) as eluent to give the *oxazole* (471 mg, 75%) as a colourless oil: $[\alpha]_D^{30}$ -26.7 (*c* 1.43 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932, 2885, 1714, 1712, 1663 and 1575; (Found: C, 67.2; H, 9.3; N, 1.5 $C_{55}H_{89}NO_{10}Si_2$ requires C, 67.4; H, 9.2; N,

1.4%); ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.07 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.85 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 0.86 (3H, d, *J* 7.1 Hz, CH_3-9), 0.87 (3H, d, *J* 7.0 Hz, CH_3-5), 0.94 (3H, d, *J* 6.5 Hz, CH_3-15), 0.96 (3H, d, *J* 7.1 Hz, CH_3-13), 1.05 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.16-1.47 (4H, m, C*H*H H-7, H-9, C*H*H H-10, C*H*H H-16), 1.58 (9H, s, $(CH_3)_3CO$), 1.70-1.95 (5H, m, H-5, CH*H* H-7, CH*H* H-10, H-15, CH*H* H-16), 2.49-2.58 (4H, m, H-3, H-11), 2.77 (1H, dq, *J* 8.0, 7.1 Hz, H-13), 3.21-3.28 (2H, m, H-4, H-8), 3.36 (3H, s, OCH_3-8), 3.37 (3H, s, OCH_3-4), 3.38 (3H, s, CH_2OCH_3), 3.64 (1H, ddd, *J* 10.1, 8.8, 5.6 Hz, C*H*H H-17), 3.69-3.78 (3H, m, H-6, CH*H* H-17), 3.84 (1H, dd, *J* 8.0, 2.5 Hz, H-14), 4.59 (1H, d, *J* 6.7 Hz, C*H*HOMe), 4.64 (1H, d, *J* 6.7 Hz, CH*H*OMe), 6.41 (1H, d, *J* 16.1 Hz, H-1), 6.83 (1H, dt, *J* 16.1, 7.7 Hz, H-2), 7.33-7.47 (6H, m, ArH), 7.63-7.71 (4H, m, ArH), 8.01 (1H, s, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.4 (q), -4.1 (q), 9.5 (q), 14.1 (q), 15.7 (q), 16.2 (q), 18.4 (s), 19.2 (s), 24.5 (t), 26.2 (3q), 26.9 (3q), 28.3 (3q), 32.1 (t), 33.1 (d), 33.8 (t), 34.0 (d), 34.2 (t), 40.5 (d), 42.5 (t), 50.1 (d), 55.8 (q), 57.5 (q), 57.5 (q), 62.2 (t), 77.0 (d), 78.6 (d), 81.3 (d), 82.0 (d), 82.1 (s), 96.7 (t), 118.2 (d), 127.7 (4d), 129.6 (2d), 134.0 (2s), 135.4 (s), 135.6 (d), 137.9 (4d), 142.6 (d), 160.6 (s), 161.4 (s), 214.0 (s); *m/z* (EI) 1002.5894 (M^+ + Na), 980.6043 (M^+ + H) $C_{55}H_{90}NO_{10}Si_2$ + Na requires 980.6103.

2-[(*E*)-(4*S*,5*S*,6*S*,8*S*,9*S*,13*R*,14*R*,15*R*)-14-(*tert*-Butyl-dimethyl-silanyloxy)-17-(*tert*-butyl-diphenyl-silanyloxy)-6-hydroxy-4,8-dimethoxy-5,9,13,15-tetramethyl-12-oxo-heptadec-1-enyl]-oxazole-4-carboxylic acid *tert*-butyl ester (55b). Dimethylboron bromide (2.5 M in dichloromethane, 600 µl, 1.5 mmol) was added dropwise over 10 min to a stirred solution of the methoxy methyl ether **55a** (488 mg, 0.5 mmol) in dry dichloromethane (42 ml) at –78 ^{o}C under a nitrogen atmosphere. The solution was stirred at –78 ^{o}C for 1 h and then quenched by careful addition of a mixture of saturated aqueous sodium bicarbonate solution (15 ml) and tetrahydrofuran (15 ml). The separated aqueous phase was extracted with

dichloromethane (2 x 60 ml) and the combined organic extracts were then washed with brine (50 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:4 to 1:1) as eluent to give the *alcohol* (370 mg, 79%) as a colourless oil: $[\alpha]_D^{30}$ -23.4 (*c* 1.37 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3480, 2932, 2885, 1714, 1713 and 1665; ^1H NMR (400 MHz, $CDCl_3$) δ -0.08 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.84 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 0.87 (3H, d, *J* 7.0 Hz, CH_3-9), 0.88 (3H, d, *J* 7.3 Hz, CH_3-5), 0.91 (3H, d, *J* 7.1 Hz, CH_3-15), 0.95 (3H, d, *J* 7.0 Hz, CH_3-13), 1.05 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.18-1.40 (3H, m, C*H*H H-7, C*H*H H-10, C*H*H H-16), 1.51-1.66 (1H, m, CH*H* H-7) 1.58 (9H, s, $(CH_3)_3CO$), 1.68-1.93 (5H, m, H-5, H-9, CH*H* H-10, H-15, CH*H* H-16), 2.35-2.48 (1H, m, C*H*H H-3), 2.51 (1H, app dd, *J* 8.3, 2.7 Hz, C*H*H H-11), 2.56 (1H, app dd, *J* 8.3, 2.5 Hz, CH*H* H-11), 2.59-2.70 (1H, m, CH*H* H-3), 2.77 (1H, dq, *J* 8.1, 7.0 Hz, H-13) 3.33-3.41 (1H, m, H-8), 3.38 (3H, s, OCH_3-8), 3.41 (3H, s, OCH_3-4), 3.58-3.69 (3H, m, H-4, C*H*H H-17, OH), 3.69-3.82 (2H, m, H-6, CH*H* H-17), 3.84 (1H, dd, *J* 8.1, 2.5 Hz, H-14), 6.41 (1H, d, *J* 16.1 Hz, H-1), 6.80 (1H, dt, *J* 16.1, 7.5 Hz, H-2), 7.34-7.46 (6H, m, ArH), 7.63-7.69 (4H, m, ArH), 8.02 (1H, s, H-5'); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.4 (q), -4.2 (q), 11.6 (q), 14.1 (q), 15.6 (q), 16.2 (q), 18.4 (s), 19.2 (s), 24.9 (t), 26.2 (3q), 26.9 (3q), 28.3 (3q), 33.0 (d), 33.8 (t), 34.1 (t), 34.5 (d), 35.5 (t), 40.2 (d), 42.2 (t), 50.0 (d), 57.8 (q), 57.9 (q), 62.1 (t), 71.1 (d), 78.6 (d), 82.2 (s), 82.3 (d), 82.4 (d), 118.0 (d), 127.7 (4d), 129.6 (2d), 134.0 (2s), 135.4 (s), 135.6 (4d), 138.4 (d), 142.6 (d), 160.5 (s), 161.3 (s), 213.9 (s); *m/z* (EI) 936.5755 (M^+ + H), 958.5591 (M^+ + Na), $C_{53}H_{85}NO_9Si_2$ + H requires 936.5841.

(*S*)-3,6-Dihydroxy-hexanoic acid methyl ester (57a). Benzene ruthenium chloride dimer (398 mg, 0.8 mmol) was added to a stirred suspension of (*S*)-BINAP (1.12 g, 1.8 mmol) in dry dimethylformamide (13 ml), and the mixture was heated at 100 ^oC for 10 min under an argon atmosphere. The mixture was cooled to room

temperature and the solvent was removed under reduced pressure (5 mmHg). The residue was heated at 60 ^{o}C under reduced pressure (5 mmHg) for 3 h to leave the chiral catalyst as a solid. A solution of the β-Keto ester **56a** (19.3 g, 70 mmol) in dry methanol (100 ml) was added to the catalyst under an argon atmosphere and the mixture was degassed with four freeze-pump-thaw cycles. The mixture was transferred to a high pressure hydrogenation vessel under an argon atmosphere and the apparatus was purged with hydrogen by pressurising to 20 atm and depressurising to 5 atm. Finally, the apparatus was pressurised with hydrogen to 80 atm and the mixture was stirred at room temperature for 4 days. The pressurised hydrogen was released and the mixture was concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1 to 1:0), followed by methanol-diethyl ether (1:20) as eluent to give the *1,4-diol* (9.9 g, 87%) as a colourless oil: $[\alpha]_D^{22}$ +22.7 (*c* 1.47 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3625, 3429 and 1722; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.49-1.73 (4H, m, C*H*$_2$C*H*$_2$CH$_2$OH), 2.45 (1H, dd, *J* 16.2, 7.3 Hz, C*H*HCO$_2$Me), 2.50 (1H, dd, *J* 16.2, 5.2 Hz, CH*H*CO$_2$Me), 3.00-3.20 (1H, br, OH), 3.64 (2H, app tt, *J* 7.0, 6.0 Hz, C*H*$_2$OH), 3.69 (3H, s, CH_3O), 3.75-3.90 (1H, br, OH), 4.04 (1H, app ddt, J 7.3, 5.2, 4.2 Hz, C*H*OH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 28.9 (t), 33.6 (t), 41.3 (t), 51.9 (d), 62.6 (t), 68.0 (q), 173.4 (s); *m/z* (EI) 297.1482 (M^+ + Na), $C_{13}H_{26}O_4Si$ + Na requires 297.1498.

(*S*)-6-(*tert*-Butyl-dimethyl-silanyloxy)-3-(*tert*-butyl-diphenyl-silanyloxy)-hexanoic acid methyl ester (58a). Imidazole (8 g, 118 mmol) and *tert*-butyldimethylsilyl chloride (8.9 g, 59 mmol) were added sequentially to a stirred solution of the diol **57a** (9.6 g, 59 mmol) in dry dimethylformamide (60 ml) at 0 ^{o}C under a nitrogen atmosphere. The solution was allowed to warm to room temperature and then stirred overnight. The mixture was diluted with diethyl ether (400 ml) and water (70 ml) and the separated organic phase was washed with water

(4 x 70 ml) and brine (140 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:5) as eluent to give the primary alcohol *silyl ether* (13.6 g, 83%) as a colourless oil: $[\alpha]_D^{22}$ +9.4 (*c* 1.19 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3607 and 1727; (Found: C, 56.2; H, 10.1; $C_{13}H_{28}O_4Si$ requires C, 56.5; H, 10.2%); ^1H NMR (360 MHz, $CDCl_3$) δ 0.04 (6H, s, CH_3Si), 0.86 (9H, s, $(CH_3)_3C$), 1.44-1.69 (4H, m, C*H*$_2$C*H*$_2$CH$_2$O), 2.42 (1H, dd, *J* 16.0, 7.5 Hz, C*H*HC=O), 2.44 (1H, dd, *J* 16.0, 5.0 Hz, CH*H*C=O) 3.45 (1H, d, *J* 2.8 Hz, OH), 3.63 (2H, t, *J* 5.8 Hz, CH_2O), 3.69 (3H, s, OCH_3), 3.95-4.03 (1H, m, C*H*OH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -5.3 (2q), 18.3 (s), 26.0 (3q), 28.9 (t), 33.7 (t), 41.4 (t), 51.7 (d), 63.2 (t), 67.9 (q), 173.2 (s); *m/z* (EI) 277.1811 (M^+ + H), 299.1634 (M^+ + Na) $C_{13}H_{28}O_4Si$ + H requires 277.1835.

Imidazole (6.7 g, 98 mmol) and *tert*-butyldiphenylsilyl chloride (16.5 ml, 63 mmol) were added sequentially to a stirred solution of the above secondary alcohol (13.5 g, 49 mmol) in dry dimethylformamide (85 ml) at room temperature under a nitrogen atmosphere. The solution was stirred at room temperature overnight and then diluted with water (90 ml) and diethyl ether (280 ml). The organic extract was washed with water (4 x 70 ml) and brine (120 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:9) as eluent to give the *silyl ether* (23.7 g, 94%) as a colourless oil: $[\alpha]_D^{22}$ +19.7 (*c* 1.42 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1732; (Found: C, 67.5; H, 8.9; $C_{29}H_{46}O_4Si_2$ requires C, 67.7; H, 9.0%); ^1H NMR (360 MHz, $CDCl_3$) δ 0.05 (3H, s, CH_3Si), 0.06 (3H, s, CH_3Si), 0.92 (9H, s, $(CH_3)_3CSi(CH_3)_2$), 1.11 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.47-1.62 (4H, m, C*H*$_2$C*H*$_2$CH$_2$O), 2.51 (1H, dd, *J* 14.8, 5.8 Hz, C*H*HC=O), 2.59 (1H, dd, *J* 14.8, 7.0 Hz, CH*H*C=O), 3.43-3.54 (2H, m, CH_2OSi), 3.60 (3H, s, OCH_3), 4.03 (1H, app pentet, *J* 5.8 Hz, CHOTBDPS), 7.41-7.48 (6H, m, ArH), 7.72-7.77 (4H, m, ArH); ^{13}C NMR (90.6 MHz,

$CDCl_3$) δ -5.3 (2q), 18.4 (s), 19.4 (s), 26.0 (3q), 27.0 (3q), 28.1 (t), 35.5 (t), 41.9 (t), 51.4 (q), 63.0 (t), 70.4 (d), 127.5 (2d), 127.6 (2d), 129.6 (d), 129.7 (d), 134.1 (s), 134.1 (s), 135.9 (2d) 136.0 (2d) 172.0 (s); *m/z* (EI) 277.1811 (M^+ + H), 299.1634 (M^+ + Na) $C_{13}H_{28}O_4Si$ + H requires 277.1835.

(*S*)-3-(*tert*-Butyl-diphenyl-silanyloxy)-6-hydroxy-hexanoic acid methyl ester (58b). 10-Camphorsulfonic acid (2.1 g, 9.1 mmol) was added in one portion to a stirred solution of the *bis*-silyl ether **58a** (23.3 g, 45.0 mmol) in dry dichloromethane (135 ml) and dry methanol (135 ml) at 0 ^oC under a nitrogen atmosphere. The solution was stirred at 0 ^oC for 30 min and then at room temperature for 20 min. The solution was diluted with dichloromethane (300 ml) and saturated aqueous ammonium chloride solution (230 ml) and the separated aqueous phase was then extracted with dichloromethane (2 x 300 ml). The combined organic extracts were washed with water (150 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:4) as eluent to give the *alcohol* (17.5 g, 97%) as a colourless oil: $[\alpha]_D^{22}$ +18.6 (*c* 1.14 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3622 and 1732; (Found: C, 68.9; H, 8.1; $C_{23}H_{32}O_4Si_2$ requires C, 69.0; H, 8.1%); ^1H NMR (360 MHz, $CDCl_3$) δ 1.08 (9H, s, $(CH_3)_3C$), 1.45-1.61 (4H, m, $CH_2CH_2CH_2O$), 2.49 (1H, dd, *J* 14.9, 6.1 Hz, C*H*HC=O), 2.57 (1H, dd, *J* 14.9, 6.7 Hz, CH*H*C=O), 3.43-3.48 (2H, m, CH_2OH), 3.59 (3H, s, OCH_3), 4.28 (1H, app pentet, *J* 5.6 Hz, CHOTBDPS), 7.40-7.49 (6H, m, ArH), 7.68-7.75 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 19.4 (s), 27.0 (3q), 27.8 (t), 33.2 (t), 41.7 (t), 51.5 (d), 62.7 (t), 70.0 (q), 127.6 (2d), 127.7 (2d), 129.8 (d), 129.8 (d), 133.9 (s), 133.9 (s), 136.0 (2d), 136.1 (2d), 171.9 (s); *m/z* (EI) 423.1933 (M^+ + Na), $C_{23}H_{32}O_4Si$ + Na requires 423.1968.

(*S*)-3-(*tert*-Butyl-diphenyl-silanyloxy)-6-iodo-hexanoic acid methyl ester (59). Triphenylphosphine (6.3 g, 24 mmol) was added to a stirred solution of iodine (6.1 g, 24 mmol) in dry dichloromethane (210 ml) at 0 ^{o}C under a nitrogen atmosphere. The solution was stirred at 0 ^{o}C for 20 min and then imidazole (2.8 g, 40.6 mmol) was added in one portion. The mixture was stirred at 0 ^{o}C for 20 min and then a solution of the alcohol **58b** (8 g, 20 mmol) in dry dichloromethane (40 ml) was added dropwise over 5 min. The mixture was stirred at 0 ^{o}C for 90 min, and then concentrated *in vacuo*. The residue was purified by flash chromatography on silica eluting with diethyl ether, and finally chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:9) as eluent to give the *iodide* (8.7 g, 86%) as a colourless oil: $[\alpha]_D^{22}$ +27.7 (*c* 2.21 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1732 and 611; (Found: C, 54.2; H, 6.1; $C_{23}H_{31}IO_3Si_2$ requires C, 54.1; H, 6.1%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.07 (9H, s, $(CH_3)_3C$), 1.54-1.63 (2H, m, C*H*$_2$CH$_2$I), 1.81 (2H, app dt, *J* 15.0, 7.3 Hz, C*H*$_2$CH$_2$CH$_2$I), 2.42 (1H, dd, *J* 14.9, 6.0 Hz, C*H*HC=O), 2.54 (1H, dd, *J* 14.9, 6.6 Hz, CH*H*C=O), 2.90-3.01 (2H, m, CH_2I), 3.56 (3H, s, OCH_3), 4.24 (1H, app pentet, *J* 6.0 Hz, CHOTBDPS), 7.35-7.49 (6H, m, ArH), 7.63-7.74 (4H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 6.5 (t), 19.4 (s), 27.0 (q), 28.9 (t), 37.9 (t), 41.9 (t), 51.6 (d), 69.3 (q), 127.7 (2d), 127.7 (2d), 129.8 (d), 129.9 (d), 133.8 (s), 133.8 (s), 136.0 (2d), 136.1 (2d), 171.6 (s); *m/z* (CI) 453.0373 (M^+ - Bu), $C_{23}H_{21}IO_3Si$ - Bu requires 453.0383.

Methyl (3*S*)-6-(benzyloxy)-3hydroxyhexanoate (57b). Benzene ruthenium chloride dimer (11.5 mg, 0.02 mmol) was added to a stirred suspension of (*S*)-BINAP (32.5 mg, 0.05 mmol) in dry dimethylformamide (0.5 ml), and the mixture was heated at 100 ^{o}C for 10 min under an argon atmosphere. The mixture was cooled to room temperature and the solvent was then removed under reduced pressure (5 mmHg).

The residue was heated at 60 ^{o}C under reduced pressure (5 mmHg) for 3 h to leave the chiral catalyst as a solid. A solution of the ester **56b** (0.5 g, 2 mmol) in dry methanol (10 ml) was added to the catalyst under an argon atmosphere and the mixture was degassed with four freeze-pump-thaw cycles. The mixture was transferred to a high pressure hydrogenation vessel under an argon atmosphere and the apparatus was purged with hydrogen by pressurising to 20 atm and depressurising to 5 atm. Finally, the apparatus was pressurised with hydrogen to 80 atm and the mixture was stirred at room temperature for 4 days. The pressurised hydrogen was released and the mixture was concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1 to 1:0) as eluent to give the alcohol (424 mg, 84%) as a colourless oil; $[\alpha]_D^{25}$ +9.8 (*c* 1.0 in $CHCl_3$) [lit[34] $[\alpha]_D^{22}$ +23.7 (*c* 1.0 in $CHCl_3$)]; ν_{max} (soln, $CHCl_3$)/cm^{-1} 3417, 2953, 2863 and 1725; ^{1}H NMR (360 MHz; $CDCl_3$) δ 1.50-1.68 (2H, m, C*H*$_2$CH$_2$CH$_2$OBn), 1.68-1.86 (2H, m, C*H*$_2$CH$_2$OBn), 2.44 (1H, dd, *J* 16.4, 8.3 Hz C*H*HCO$_2$Me), 2.52 (1H, dd, *J* 16.4, 4.2 Hz, CH*H*CO$_2$Me), 3.15-3.39 (1H, br, OH), 3.52 (2H, t, *J* 6.1, CH$_2$OBn), 3.71 (3H, s, CH$_3$O), 4.05 (1H, app septet, *J* 4.2, C*H*OH), 4.51 (2H, s, CH$_2$Ph), 7.25-7.38 (5H, m, ArH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 26.0 (t), 33.8 (t), 41.4 (t), 51.8 (q), 67.9 (d), 70.2 (t), 73.0 (t), 127.7 (d), 128.2 (2d), 128.5 (2d), 138.3 (s), 173.3 (s); *m/z* (EI) 275.1261 (M^+ + Na), $C_{14}H_{20}O_4$ + Na requires 275.1259

(*S*)-3,6-Dihydroxy-hexanoic acid methyl ester (57a). 10% Palladium on carbon (35 mg) was added in one portion to a solution of the benzyl ether **57b** (354 mg, 1.01 mmol) in methanol (10 ml) at room temperature, and the apparatus was then evacuated prior to the introduction of hydrogen gas. The mixture was stirred at room temperature for 3 days under one atmosphere of hydrogen, then filtered through celite. The filter cake was washed with ethyl acetate (3 x 30 ml) and the combined washings were then concentrated *in vacuo* to leave the *1,4-diol* (273 mg, 99%) as a

colourless oil; $[\alpha]_D^{22}$ +21.9 (*c* 1.48 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3625, 3429 and 1722; ^1H NMR (360 MHz, $CDCl_3$) δ 1.49-1.73 (4H, m, C*H*$_2$C*H*$_2$CH$_2$OH), 2.45 (1H, dd, *J* 16.2, 7.3 Hz, C*H*HCO$_2$Me), 2.50 (1H, dd, *J* 16.2, 5.2 Hz, CH*H*CO$_2$Me), 3.00-3.20 (1H, br, OH), 3.64 (2H, app tt, *J* 7.0, 6.0 Hz, C*H*$_2$OH), 3.69 (3H, s, CH_3O), 3.75-3.90 (1H, br, OH), 4.04 (1H, app ddt, J 7.3, 5.2, 4.2 Hz, C*H*OH); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 28.9 (t), 33.6 (t), 41.3 (t), 51.9 (d), 62.6 (t), 68.0 (q), 173.4 (s); *m/z* (EI) 297.1482 (M^+ + Na), $C_{13}H_{26}O_4Si$ + Na requires 297.1498.

(*R*)-4-((*S*)-3-Hydroxy-1-methyl-propyl)-2,2-dimethyl-oxazolidine-3-carboxylic acid *tert*-butyl ester (61b). A solution of DIBAL-H (1 M in hexane, 174 ml, 174 mmol) was added dropwise over 30 min to a stirred solution of the ester **61a**[35] (18.3 g, 58 mmol) in dry tetrahydrofuran (318 ml), at –78 °C under a nitrogen atmosphere. The solution was stirred at –78 °C for 1 h and then allowed to warm to room temperature and stirred for a further 1 h. Saturated aqueous Rochelle's salt solution (530 ml) was added and the mixture was stirred for a further 1 h. Diethyl ether (800 ml) was added and the separated aqueous phase was then extracted with diethyl ether (2 x 500 ml). The combined organic extracts were washed with brine (300 ml), then dried ($MgSO_4$) and concentrated *in vacuo* to leave the *alcohol* (14.6 g, 90%) as a colourless oil: $[\alpha]_D^{25}$ –26.0 (*c* 1.38 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3624 and 1685; (Found: C, 61.9; H, 9.95; N, 5.0; $C_{14}H_{27}NO_4$ requires C, 61.5; H, 10.0; N, 5.1%); ^1H NMR (360 MHz; C_6D_6, 333K) δ 0.83 (3H, d, *J* 7.2 Hz, C*H*$_3$CH), 1.22-1.41 (2H, m, C*H*$_2$CH$_2$OH), 1.38 (9H, s, $(CH_3)_3C$), 1.51 (3 H, s, CH_3CN), 1.62-1.79 (1H, m, C*H*CH_3), 1.73 (3H, s, CH_3CN), 2.09-2.21 (1H, br, OH), 3.39-3.49 (1H, m, C*H*HCHN), 3.49-3.57 (1H, m, CH*H*CHN) 3.58-3.65 (2H, m, C*H*$_2$OH), 3.69-3.88 (1H, m, CHN); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 16.6 (q), 23.6 (q), 27.0 (q), 28.5 (3q), 33.1 (d), 35.3 (t), 61.1 (t), 62.2 (d), 65.3 (t), 79.4 (s), 94.2 (s), 153.0 (s); *m/z* (EI) 296.1809 (M^+ + Na), $C_{14}H_{27}NO_4$ + Na requires 296.1838.

(*R*)-4-((*S*)-3-Benzyloxy-1-methyl-propyl)-2,2-dimethyl-oxazolidine-3-carboxylic acid *tert*-butyl ester (61c). Sodium hydride (60 % dispersion in oil, 3.5 g, 87 mmol) was added portion wise over 30 min to a stirred solution of the alcohol **61b** (12.4 g, 46 mmol) in dry tetrahydrofuran (286 ml) at 0 ^{o}C under a nitrogen atmosphere. The solution was stirred at 0 ^{o}C for 1 h and then benzyl bromide (20.2 ml, 170 mmol) was added dropwise over 15 min, TBAI (510 mg, 1.4 mmol) was added in one portion and the mixture was then allowed to warm to room temperature overnight. Water (100 ml) was added carefully followed by diethyl ether (200 ml). The separated aqueous phase was extracted with diethyl ether (2 x 200 ml) and the combined organic extracts were then washed with brine (200 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^{o}C) (1:9) as eluent to give the corresponding *benzyl ether* (13 g, 78%) as a colourless oil: $[\alpha]_D^{22}$ –25.8 (*c* 1.25 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1682; (Found: C, 69.5; H, 9.0; N, 3.8; $C_{21}H_{33}NO_4$ requires C, 69.4; H, 9.2; N, 3.9%); ^{1}H NMR (360 MHz; C_6D_6, 333 K) δ 0.94 (3H, d, *J* 6.8, C*H*$_3$CH), 1.33-1.46 (1H, m, C*H*HCH$_2$O), 1.51 (9 H, s, $(CH_3)_3C$), 1.59 (3H, s, CH_3CN), 1.77 (3H, s, CH_3CN), 1.92 (1H, ddt, *J* 13.7, 7.2, 3.6 Hz, CH*H*CH$_2$O), 2.26-2.37 (1H, m, C*H*CH$_3$), 3.32-3.45 (2H, m, CH$_2$OBn), 3.66-3.95 (3H, m, OC*H*$_2$C*H*N), 4.41 (1H, d, *J* 12.2 Hz, OC*H*HPh), 4.47 (1H, d, *J* 12.2 Hz, OCH*H*Ph), 7.12 (5H, m ArH); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 16.6 (q), 23.8 (q), 27.0 (q), 28.5 (3q), 32.6 (t), 33.2 (d), 62.2 (d), 65.1 (t), 69.0 (t), 73.0 (t), 79.2 (s), 94.2 (s), 127.5 (d), 127.7 (2d), 128.5 (2d), 139.5 (s), 152.8 (s); *m/z* (EI) 386.2307 (M^+ + Na), 264.1913 (M^+ – Boc + 2H), $C_{21}H_{33}NO_4$ + Na requires 386.241.

(*S*)-4-((1*S*,2*S*)-4-Benzyloxy-1-hydroxymethyl-2-methyl-butylcarbamoyl)-2,2-dimethyl-oxazolidine-3-carboxylic acid *tert*-butyl ester (63). 12 M Hydrochloric acid (126 ml) was added dropwise over 5 min to a stirred solution of the acetonide

61c (20 g, 56 mmol) in dioxane (320 ml) at room temperature. The mixture was stirred overnight, then diluted with water (100 ml) and carefully basified to pH 14 with 10 M aqueous sodium hydroxide solution at 0 ^{o}C. The mixture was concentrated *in vacuo* and the residual aqueous phase was extracted with diethyl ether (3 x 400 ml). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo* to leave the crude *amino alcohol* **62**, which was used straightaway. Triethylamine (9.8 ml, 70 mmol), Garner's acid (12.5 g, 51 mmol), HOBt (6.9 g, 51 mmol), and EDC (9.8 g, 51 mmol) were added sequentially to a solution of the crude amino alcohol in dry tetrahydrofuran (510 ml) at 0 ^{o}C, under a nitrogen atmosphere. The solution was allowed to warm to room temperature and stirred overnight. Water (250 ml) and diethyl ether (500 ml) were added and the separated aqueous phase was extracted with diethyl ether (2 x 500 ml). The combined organic extracts were washed with brine (300 ml), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether as eluent to give the *amide* (20 g, 79%) as a colourless oil: $[\alpha]_D^{23}$ –42.3 (*c* 1.50 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3626, 3425, 1698 and 1674; (Found: C, 63.8; H, 8.5; N, 6.3; $C_{24}H_{38}N_2O_6$ requires C, 64.0; H, 8.5; N, 6.2%); ^{1}H NMR (360 MHz; C_6D_6, 333 K) δ 1.02 (3H, d, *J*, 6.9 Hz, C*H*$_3$CH), 1.50 (9H, s, $(CH_3)_3C$), 1.54 (3H, s, CCH_3), 1.52-1.60 (1H, m, C*H*HCH$_2$O), 1.81 (3H, s, CCH_3), 1.93 (1H, ddt, *J* 13.2, 6.6, 0.8 Hz, CH*H*CH$_2$O), 2.11-2.16 (1H, m, C*H*CH$_3$), 3.49-3.60 (3H, m, CH_2OBn, OH), 3.65-3.78 (2H, m, C*H*$_2$OH), 3.94 (1H, dd, *J* 8.2, 5.2 Hz, C*H*HCHNBoc), 4.16 (1H, ddd, *J* 14.0, 5.2, 5.1 Hz, NC*H*CH$_2$OH), 4.32 (1H, br d, *J* 8.2 Hz, CH*H*CHNBoc), 4.37-4.41 (1H, m, CHNBoc), 4.43 (1H, d, *J* 12.2 Hz C*H*HPh), 4.46 (1H, d, *J* 12.2 Hz, CH*H*Ph), 6.75-6.95 (1H, br, NH), 7.11-7.40 (5H, m, ArH); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 15.1 (q), 23.7 (q), 26.4 (q), 28.0 (3q), 31.4 (d), 33.7 (t), 54.9 (d), 60.1 (d), 63.0 (t), 66.3 (t), 68.2 (t), 72.7 (t), 80.5 (s), 94.5 (s), 127.2 (d), 127.4 (2d), 128.1 (2d), 139.0 (s), 152.4 (s), 171 (s); *m/z* (EI) 395.2117

(M^+ – Bu + 2H), 351.1478 (M^+– Boc + 2H), 473.2584 (M^+ + Na), $C_{24}H_{38}N_2O_6$ + Na requires 473.2628.

(*S*)-4-((*S*)-3-Benzyloxy-1-methyl-propyl)-2',2'-dimethyl-4',5'-dihydro-[2,4']bioxazolyl-3'-carboxylic acid *tert*-butyl ester (64). A solution of DMSO (2.7 ml, 38.2 mmol) in dry dichloromethane (15 ml) was added dropwise over 10 min to a stirred solution of oxalyl chloride (2.0 ml, 22.5 mmol) in dry dichloromethane (93 ml) at –78 °C under a nitrogen atmosphere. The solution was stirred at –78 °C for 15 min and then a solution of the alcohol **63** (6.75 g, 15 mmol) in dry dichloromethane (23 ml) was added dropwise over 15 min. The mixture was stirred at –78 °C for 1.5 h, then triethylamine (12.0 ml, 85.5 mmol) was added dropwise over 15 min. The mixture was allowed to warm to room temperature, and then diluted with water (80 ml). The separated aqueous phase was extracted with dichloromethane (2 x 150 ml) and the combined dichloromethane extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:1 to 1:0) as eluent to give the corresponding *aldehyde* (6.54 g, 97%) as a colourless oil: $[\alpha]_D^{22}$ –117.5 (*c* 0.81 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3690, 2716, 1731 and 1682; ^{1}H NMR (360 MHz; $CDCl_3$, 318 K, rotamers) δ 0.85 (2H, d, *J* 7.0 Hz, C*H*$_3$CH), 1.00 (1H, d, *J* 7.0 Hz, C*H*$_3$CH) 1.40-1.55 (13H, m, CH_3, $(CH_3)_3C$), C*H*HCH_2OBn), 1.62-1.85 (4H, m, CH_3 and CH*H*CH_2OBn), 2.50 (1H, app dq, *J* 7.0, 3.2 Hz, C*H*CH_3), 3.43 (0.3H, ddd, *J* 18.2, 9.0, 4.5 Hz, CH_2OBn), 3.47-3.60 (1H, m, CH_2OBn), 3.65 (0.7H, ddd, 9.8, 7.0, 5.2 Hz, CH_2OBn), 4.06 (1H, dd, *J* 15.7, 8.6 Hz, C*H*HCHN), 4.15-4.33 (1H, m, CHC=O), 4.34-4.59 (3H, m, CH*H*CHN, CH_2Ph), 4.65 (1H, dd, *J* 8.3, 3.2 Hz, CHNBoc), 6.75-7.20 (1H, m, NH), 7.27-7.37 (5H, m, ArH), 9.54-9.58 (1H, m, CHO); ^{13}C NMR (90.6 MHz; $CDCl_3$, 318 K, major rotamer) δ 14.4 (q), 24.0 (q), 27.0 (q), 28.2 (3q), 29.9 (d), 33.3

(t), 60.4 (d), 61.5 (d), 65.8 (t), 67.4 (t), 72.9 (t), 81.3 (s), 94.7 (s), 127.7 (d), 127.8 (2d), 128.4 (2d), 138.4 (s), 153.3 (s), 171 (s), 199.2 (d); *m/z* (EI) 503.2692 (M^+ + Na + MeOH), 349.2305 (M^+ + 2H - Boc), $C_{25}H_{40}N_2O_7$ + Na requires 503.2733.

Triphenylphosphine (5.9 g, 22.5 mmol), 1,2-dibromotetrachloroethane (7.3 g, 22.5 mmol) and 2,6-di-*tert*-butylpyridine (6.7 ml, 30 mmol) were added sequentially to a stirred solution of the above aldehyde (6.7 g, 15 mmol) in dry dichloromethane (107 ml) at 0 ^oC under a nitrogen atmosphere. The solution was allowed to warm to room temperature overnight and then a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (11.2 ml, 75 mmol) in dry acetonitrile (107 ml) was added dropwise over 5 min. The solution was stirred at room temperature for 5 h, then water (85 ml) and diethyl ether (170 ml) were added. The separated aqueous phase was extracted with diethyl ether (3 x 170 ml) and the combined organic extracts were then washed with brine (175 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:9 to 1:1) as eluent to give the *oxazole* (4.7 g, 72%) as a waxy colourless solid, mp 64-68 ^oC: $[\alpha]_D^{22}$ -41.8 (*c* 0.31 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 1698 and 1573; (Found: C, 66.8; H, 8.1; N, 6.7; $C_{24}H_{34}N_2O_5$ requires C, 67.0; H, 8.0; N, 6.5%); ^1H NMR (360 MHz; C_6D_6, 333 K) δ 1.30 (3H, d, *J* 6.8 Hz, C*H*$_3$CH), 1.47 (9H, s, $(CH_3)_3C$), 1.71 (3H, s, CCH_3), 1.90 (1H, app dt, *J* 13.6, 6.7 Hz, C*H*HCH$_2$O), 2.00 (3H, s, CCH_3), 2.16 (1H, ddt, *J* 13.6, 6.2, 1.1 Hz, CH*H*CH$_2$O), 3.01 (1H, ddq, *J* 6.8, 6.7, 6.6 Hz, C*H*CH$_3$), 3.46-3.57 (2H, m, CH_2OBn), 3.88 (1H, dd, *J* 8.8, 6.6 Hz, C*H*HCHN), 3.99 (1H, dd, *J* 8.8, 3.4 Hz, CH*H*CHN), 4.45 (2H, s, CH_2Ar), 4.92-5.06 (1H, m, CHN), 7.04 (1H, d, *J* 0.6 Hz, CHCN), 7.19-7.24 (1H, m, ArH), 7.27-7.37 (2H, m, ArH), 7.39-7.40 (2H, m, ArH); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 20.1 (q), 25.2 (q), 26.1 (q), 28.7 (3q), 29.1 (d), 36.6 (t), 56.1 (d), 67.9 (t), 68.8 (t), 73.4 (t), 80.1 (s), 95.3 (s), 127.5 (d), 128.0 (2d), 128.8 (2d), 135.5 (d), 139.9 (s), 146.8 (s), 152.0 (s), 163.8 (s); *m/z* (EI) 431.2528 (M^+

+ H), 453.2035 (M^+ + Na), 375.1760 (M^+ – Bu + 2H) $C_{24}H_{34}N_2O_5$ + H requires 431.2546.

(*S*)-2',2'-Dimethyl-4-((*S*)-1-methyl-3-oxo-propyl)-4',5'-dihydro-[2,4']bioxazolyl-3'-carboxylic acid *tert*-butyl ester (65). 10% Palladium on carbon (4.6 g) was added to a solution of the benzyl ether **64** (9.25 g, 21.5 mmol) in ethyl acetate (165 ml) at room temperature, and the apparatus was then evacuated prior to the introduction of hydrogen gas. The mixture was stirred at room temperature for 3 days under one atmosphere of hydrogen, then filtered through celite. The filter cake was washed with ethyl acetate (2 x 100 ml) and the combined organic washings were then concentrated *in vacuo* to leave the corresponding *alcohol* (7.1 g, 98%) as a waxy colourless solid mp 54-57 ^oC: $[\alpha]_D^{22}$ -73.4 (*c* 0.61 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3690, 1699 and 1602; (Found: C, 59.8; H, 8.3; N, 8.3; $C_{17}H_{28}N_2O_5$ requires C, 60.0; H, 8.3; N, 8.2%); ^1H NMR (360 MHz; C_6D_6, 333 K) δ 1.26 (3H, d, *J* 6.9, C*H*$_3$CH), 1.44 (9H, s, $(CH_3)_3C$), 1.65 (3H, s, CCH_3), 1.79 (1H, app dt, *J* 13.3, 6.8 Hz, C*H*HCH$_2$O), 1.91-2.01 (1H, m, CH*H*CH$_2$O), 1.92 (3H, s, CCH_3), 2.79-2.90 (1H, br, OH), 2.94 (1H, ddq, *J* 6.8, 6.7, 6.6 Hz, C*H*CH$_3$), 3.69 (2H, t, *J* 6.3 Hz, C*H*$_2$OH), 3.93 (1H, dd, *J* 8.7, 6.5 Hz, C*H*HCHN), 4.02 (1H, dd, *J* 8.7, 2.8 Hz, CH*H*CHN), 4.90-5.08 (1H, m, CHN), 7.15 (1H, s, CHCN); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 20.0 (q), 25.0 (q), 26.0 (q), 28.7 (3q), 29.3 (d), 36.8 (t), 56.1 (d), 61.0 (t), 67.9 (t), 80.2 (s), 95.6 (s), 133.6 (d), 146.8 (s), 152.0 (s), 163.9 (s); *m/z* (EI) 363.1901 (M^+ + Na), 285.1517 (M^+ – Bu + 2H), $C_{17}H_{28}N_2O_5$ + Na requires 363.1896.

A solution of DMSO (2.1 ml, 29.5 mmol) in dry dichloromethane (8 ml) was added dropwise over 10 min to a stirred solution of oxalyl chloride (1.6 ml, 17.8 mmol) in dry dichloromethane (82 ml) at –78 ^oC under a nitrogen atmosphere. The solution was stirred at –78 ^oC for 15 min and then a solution of the above alcohol (4 g, 11.8 mmol)

in dry dichloromethane (16 ml) was added dropwise over 15 min. The mixture was stirred at –78 ^{o}C for 1.5 h, then triethylamine (9.4 ml, 67.3 mmol) was added dropwise over 15 min. The mixture was allowed to warm to room temperature, then diluted with water (80 ml). The separated aqueous phase was extracted with dichloromethane (2 x 180 ml) and the combined dichloromethane extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^{o}C) (1:1) as eluent to give the *aldehyde* (3.5 g, 87%) as a colourless oil: $[\alpha]_D^{22}$ -69.4 (*c* 1.90 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2727, 1722 and 1698; ^{1}H NMR (360 MHz; C_6D_6, 333 K) δ 1.05 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 1.35 (9H, s, $(CH_3)_3C$), 1.59 (3H, s, CCH_3), 1.89 (3H, s, CCH_3), 2.11 (1H, ddd, *J* 16.8, 6.9, 1.7 Hz, C*H*HCHO), 2.46 (1H, ddd, *J* 16.8, 6.9, 1.7 Hz, CH*H*CHO) 3.04 (1H, ddq, *J* 6.9, 6.8, 6.7 Hz, C*H*CH_3), 3.75 (1H, dd, *J* 8.9, 6.5 Hz, C*H*HCHN), 3.86 (1H, dd, *J* 8.9, 3.0 Hz, CH*H*CHN), 4.68-5.10 (1H, m, CHN), 6.85 (1H, s, CHCN), 9.42 (1H, t, *J* 1.7 Hz, CHO); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 19.7 (q), 25.1 (q), 26.0 (q), 26.9 (d), 28.7 (3q), 49.9 (t), 56.1 (d), 67.9 (t), 80.2 (s), 95.6 (s), 133.7 (d), 145.6 (s), 152.0 (s), 164.0 (s), 199.8 (d); *m/z* (CI) 339.1911 (M^+ + H), 393.1779 (M^+ + Na + MeOH), 283.1110 (M^+ – Bu + 2H), 239.1414 (M^+ – Boc + 2H) $C_{17}H_{26}N_2O_5$ + H requires 339.1920.

(*S*)-4-[(1*S*,7*S*)-7-(*tert*-Butyl-diphenyl-silanyloxy)-8-carboxy-1-methyl-3-oxo-octyl]-2',2'-dimethyl-4',5'-dihydro-[2,4']bioxazolyl-3'-carboxylic acid *tert*-butyl ester (67b). Lithium hydroxide (116 mg, 2.8 mmol) was added in one portion to a stirred solution of the ester **67a** (220 mg, 0.3 mmol) in methanol (6.4 ml) and water (1.4 ml) at room temperature. The solution was stirred overnight at room temperature, then acidified with 2 M hydrochloric acid and saturated with sodium chloride. The mixture was extracted with diethyl ether (5 x 20 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave the

acid (186 mg, 88%) as a colourless oil. The oil crystallised from diethyl ether, light petroleum (bp 40-60 ^{o}C) as colourless crystals, mp 23-25 ^{o}C: $[\alpha]_D^{29}$ -22.1 (*c* 1.46 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3209, 2932, 2859, 1749 and 1702; (Found: C, 65.9; H, 7.7; N, 3.9; $C_{39}H_{54}N_2O_8Si$ requires C, 66.3; H, 7.7; N, 4.0%); ^{1}H NMR (400 MHz; C_6D_6, 333 K) δ 1.16 (3H, d, *J* 6.8 Hz, CHC*H*$_3$), 1.18 (9H, s, $(CH_3)_3CSi$), 1.37 (9H, s, $(CH_3)_3CO$), 1.47-1.55 (4H, m, C*H*$_2$C*H*$_2$CHOSi), 1.58-1.62 (3H, br, CH_3C), 1.84-1.96 (5H, m, C*H*$_2$COCH$_2$CHCH$_3$, C*H*$_3$C), 2.17-2.25 (1H, m, C*H*HCHCH$_3$), 2.47 (1H, dd, *J* 15.1, 6.1 Hz, C*H*HCO$_2$H), 2.58 (1H, dd, *J* 15.1, 6.2 Hz, CH*H*CO$_2$H), 2.61 (1H, dd, *J* 16.7, 6.2 Hz, CH*H*CHCH$_3$), 3.26 (1H, ddq, *J* 6.8, 6.7, 6.6 Hz, C*H*CH$_3$), 3.87 (1H, dd, *J* 8.8, 6.5 Hz, C*H*HCHN), 3.93 (1H, dd, *J* 8.8, 3.0 Hz, CH*H*CHN), 4.33-4.39 (1H, m, CHOSi), 4.90-4.96 (1H, m, CHN), 6.97 (1H, s, CHCN), 7.26-7.29 (6H, m, ArH), 7.79-7.81 (4H, m, ArH), 10.04-10.46 (1H, br, OH); ^{13}C NMR (90.6 MHz; C_6D_6, 333 K) δ 19.4 (t), 19.7 (q), 19.7 (s), 24.8 (q), 25.7 (q), 27.4 (3q), 27.4 (d), 28.5 (3q), 36.9 (t), 42.1 (t), 42.8 (t), 48.6 (t), 55.8 (d), 67.7 (t), 70.7 (d), 80.1 (s), 95.4 (s), 128.0 (4d), 130.0 (2d), 133.5 (d), 134.4 (s), 134.6 (s), 136.3 (4d), 145.7 (s), 151,7 (s), 163.7 (s), 175.9 (s), 207.4 (s); *m/z* (EI) 707.3686 (M^+ + H), 729.3521 (M^+ + Na), $C_{39}H_{54}N_2O_8Si$ + H requires 707.3728.

(3*R*,4*R*,5*R*)-[4-(*tert*-Butyldimethylsilanyloxy)-7-(*tert*-butyldiphenylsilanyloxy)–3, 5-dimethyl-2-oxoheptyl]-phosphonic acid, dimethyl ester (74). Palladium on charcoal (53 mg, 10%) was added, in one portion, to a stirred solution of the benzyl ether **51** (51 mg, 0.082 mmol) in dry methanol at room temperature. The mixture was stirred at room temperature for 12h under an atmosphere of hydrogen and then filtered through celite, eluting with ethyl acetate. The combined organic washings were concentrated in vacuo to leave the corresponding primary alcohol as an oil. Imidazole (23 mg, 0.34 mmol) and TBDPSCl (43 µl, 0.17 mmol) were added to a stirred solution of the alcohol in DMF (500

μl), and the mixture was then stirred overnight at room temperature. Water (2 ml) and diethyl ether (10 ml) were added and the separated organic phase was washed with water (3 x 2 ml) and brine (2 ml), then dried and concentrated in vacuo. The residue was purified by chromatography on silica, using diethyl ether-light petroleum (1:1 to 1:4) as eluent, to give the *silyl ether* (32 mg) as an oil, $[\alpha]_D^{22}$ – 58.5 (c 0.40 in $CHCl_3$); ν_{max} (soln, $CHCl_3$, cm^{-1}) 1714; ^1H NMR (500 MHz, $CDCl_3$) δ 0.04 (3H, SiMe), 0.12 (3H, SiMe), 0.94 (9H, CMe_3), 0.97 (3H, d, *J* 6.9 Hz, C*H*$_3$ CH), 1.12 (3H, d, *J* 6.2 Hz, C*H*$_3$ CH C=O), 1.13 (9H, CMe_3), 1.37 – 1.44 (1H, m), 1.84 – 1.91 (1H, m), 1.96 – 2.04 (1H, m), 3.10 (1H, dd, *J* 22.1 and 14.0 Hz, C*H*H.P=O), 3.13 (1H, app, qn, *J* 7.1 Hz, CH_3C*H*.C=O), 3.44 (1H, dd, *J* 22.2 and 14.0 Hz, CH*H*.P=O), 3.71 (1H, ddd, *J* 9.5, 9.1 and 5.4 Hz, C*H*HOSi), 3.78 – 3.83 (2H, m), 3.85, d, *J* 2.9 Hz, OMe), 3.87 (3H, d, *J* 2.4 Hz, OMe), 7.45 – 7.54 (6H, m. ArH), 7.72 – 7.77 (4H, m, ArH); ^{13}C NMR (125 MHz, $CDCl_3$), -4.4 (q), -4.3 (q), 14.2 (q), 15.4 (q), 18.3 (s), 19.2 (s), 26.1 (q), 26.9 (q), 34.2 (d), 34.5 (t), 43.2 (CH_2, d, $J_{c\text{-}p}$ 509 Hz), 50.1 (d), 52.9 (CH_3, d, $J_{c\text{-}p}$ 24.9 Hz), 53.0 (CH_3, d, $J_{c\text{-}p}$ 25.2 Hz), 62.0 (t), 79.9 (d), 127.7 (d), 129.6 (d), 133.9 (s), 135.6 (d), 205.8 (C, d, $J_{c\text{-}p}$ 24.5 Hz). *m/z* (ESI) 635.3380 (M^+ + H), $C_{33}H_{55}O_6PSi_2$ requires 635.3353.

The *bis*-Oxazole Ester (77). 2,4,6-Trichlorobenzoyl chloride (70 μl, 0.45 mmol) was added dropwise over 5 min to a stirred solution of the acid 55b (319 mg, 0.45 mmol) and triethylamine (63 μl, 0.45 mmol) in dry toluene (8 ml) at 0 ^oC under a nitrogen atmosphere. The solution was allowed to warm to room temperature and stirred at this temperature for 6 h. A solution of the alcohol 67b (352 mg, 0.38 mmol) and DMAP (93 mg, 0.76 mmol) in dry toluene (4 ml) was added dropwise over 2 min at room temperature and this mixture was stirred at room temperature overnight. Water (35 ml) was added and the separated aqueous phase was then extracted with ethyl acetate (3 x 70 ml). The combined organic extracts were washed with brine (35 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 ^oC) (1:1) as

eluent to give the *ester* (572 mg, 93%) as a colourless oil. The oil crystallised from diethyl ether-light petroleum (bp 40-60 °C) as colourless crystals, mp 25-27 °C: $[\alpha]_D^{29}$ –27.7 (*c* 1.01 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932, 2858, 1702 and 1703; (Found: C, 67.8; H, 8.6; N, 2.2; $C_{92}H_{137}N_3O_{16}Si_3$ requires C, 68.0; H, 8.5; N, 2.6%); ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.08 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.79 (3H, d, *J* 6.8 Hz, CH_3-29), 0.84 (9H, s, (CH_3)$_3$CSi(CH_3)$_2$), 0.86 (3H, d, *J* 7.0 Hz, CH_3-39), 0.87 (3H, d, *J* 7.0 Hz, CH_3-33), 0.94 (3H, d, *J* 7.0 Hz, CH_3-37), 1.02 (9H, s, (CH_3)$_3$CSi(Ph)$_2$), 1.05 (9H, s, (CH_3)$_3$CSi(Ph)$_2$), 1.19 (3H, d, *J* 6.5 Hz, CH_3-9), 1.28 (9H, s, (CH_3)$_3$COOC-17), 1.40-1.56 (5H, m, H-4, H-31 C*H*H H-40), 1.49 (3H, s, CH_3CN), 1.58 (9H, s, (CH_3)$_3$COOCN), 1.65-1.83 (7H, m, H-5, H-29, H-33, H-34, CH*H* H-40), 1.73 (3H, s, CH_3CN), 1.84-1.91 (1H, m, H-39), 2.15 (2H, t, *J* 6.2 Hz, H-6), 2.32-2.59 (7H, m, H-2, H-8, H-27, C*H*H H-35), 2.67-2.80 (2H, m, CH*H* H35, H-37), 2.81-2.88 (1H, m, H-32), 3.14 (1H, app dd, *J* 10.9, 5.1 Hz, H-28), 3.21-3.26 (1H, m, H-9), 3.24 (3H, s, CH_3OC-32), 3.26 (3H, s, CH_3OC-28), 3.63 (1H, ddd, *J* 10.6, 8.8, 5.6 Hz, C*H*H H-41), 3.74 (1H, ddd, *J* 10.6, 6.6, 4.5 Hz, CH*H* H-41), 3.83 (1H, dd, *J* 8.1, 2.5 Hz, H-38), 4.00-4.13 (1H, m, C*H*H H-19), 4.14-4.26 (2H, m, CH*H* H-19, H-3), 4.92-5.16 (2H, m, H-15, H-30), 6.39 (1H, d, *J* 16.0 Hz, H-25), 6.77 (1H, dt, *J* 16.0, 7.6 Hz, H-26), 7.29 (1H, s, H-14), 7.32-7.45 (12H, m, ArH), 7.63-7.73 (8H, m, ArH), 8.00 (1H, s, H-24); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ -4.4 (q), -4.2 (q), 9.4 (q), 14.1 (q), 14.3 (q), 15.7 (q), 16.2 (q), 18.4 (s), 18.7 (t), 19.2 (s), 19.3 (s), 19.4 (q), 24.4 (t), 25.1 (3q), 26.2 (3q), 26.8 (3q), 26.9 (3q), 27.0 (3q), 28.2 (d), 28.2 (q), 31.4 (t), 33.0 (d), 33.7 (t), 34.1 (d), 35.0 (t), 36.0 (t), 40.2 (d), 41.7 (t), 42.4 (t), 42.9 (t), 48.3 (t), 50.0 (d), 55.3 (d), 57.8 (q), 57.9 (q), 62.1 (t), 67.5 (t), 69.6 (d), 72.9 (d), 78.5 (d), 80.1 (s), 80.8 (d), 81.9 (s), 82.0 (d), 95.0 (s), 118.2 (d), 127.6 (8d), 129.6 (2d), 129.7 (2d), 133.2 (d), 133.8 (2s), 133.9 (2s), 135.3 (s), 135.6 (4d), 135.8 (2d), 135.9 (2d), 137.8 (d), 142.6 (d), 145.1 (s), 151.3 (s), 160.6 (s), 161.3 (s), 162.8 (s), 170.5 (s), 208.6 (s), 213.8 (s); *m/z* (EI) 1624.9326 (M^+ + H), 1646.9240 (M^+ + Na), $C_{92}H_{137}N_3O_{16}Si_3$ + H requires 1624.9385.

The C38 Alcohol (81a). Trimethylsilyl triflurormethanesulphonate (57 µl, 0.03 mmol), was added dropwise over 5 min to a stirred solution of the TBS ether **76** (142 mg, 0.01 mmol) in dry dichloromethane (15 ml) at -78 ^{o}C under a nitrogen atmosphere. The mixture was stirred at –78 ^{o}C for 1 h, diluted with dichloromethane (200 ml) and then quenched with a premixed solution of saturated aqueous sodium bicarbonate solution (10 ml) and tetrahydrofuran (10 ml). The solution was allowed to warm to room temperature and stirred for 20 min. The separated organic phase was dried (Na_2SO_4) and then concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^{o}C) (1:4 to 3:2) as eluent to give the *alcohol* (111 mg, 85%), as a colourless foam: $[\alpha]_D^{23}$ –12.8 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3622, 2931, 2858 and 1708; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (3H, d, *J* 6.7 Hz, CH_3-33), 0.83 (3H, d, *J* 6.9 Hz CH_3-29), 0.92 (3H, d, *J* 6.8 Hz, CH_3-39), 1.03 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.06 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.07 (3H, d, *J* 7.4 Hz, CH_3-37), 1.28 (3H, d, *J* 7.0 Hz, CH_3-9), 1.35-1.63 (5H, m, C*H*H H-4, H-31, C*H*H H-34, C*H*H H-40), 1.66-1.82 (6H, m, CH*H* H-4, H-5, H-33, CH*H* H-34, CH*H* H-40), 1.82-1.95 (2H, m, H-29, H-39), 2.18-2.33 (3H, m, H-6, OH), 2.39 (1H, dd, *J* 16.5, 5.4 Hz, C*H*H H-8), 2.42-2.51 (1H, m, C*H*H H-27), 2.50-2.64 (4H, m, H-2, H-35), 2.64-2.69 (1H, m CH*H* H-27), 2.76 (1H, dq, *J* 7.4, 7.3 Hz, H-37), 2.87-2.97 (1H, m, H-32), 3.14 (1H, dd, *J* 16.5, 7.9 Hz, CH*H* H-8), 3.18-3.24 (1H, m, H-28), 3.27 (3H, s, CH_3OC-32), 3.31 (3H, s, CH_3OC-28), 3.40 (1H, ddq, *J* 7.9, 7.0, 5.4 Hz, H-9), 3.52-3.61 (1H, m, H-38), 3.66 (1H, ddd, *J* 10.4, 8.2, 5.5 Hz C*H*H H-41), 3.77 (1H, ddd, *J* 10.4, 5.5, 5.4 Hz, CH*H* H-41), 4.29 (1H, dddd, *J* 5.2, 5.1, 5.0, 4.9 Hz, H-3), 5.11 (1H, ddd, *J* 9.5, 6.3, 1.3 Hz, H-30), 6.35 (1H, d, *J* 15.5 Hz, H-25), 7.09 (1H, ddd, *J* 15.5, 8.4, 6.2 Hz, H-26), 7.30-7.47 (13H, m, ArH, H-14), 7.64-7.75 (8H, m, ArH), 8.05 (2H, s, H-19, H-24); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 8.8 (q), 14.2 (q), 15.8 (q), 17.0 (q), 19.2 (s), 19.4 (t), 19.4 (s), 19.8 (q), 24.7 (t), 26.9 (3q), 27.1 (3q), 27.1 (d)

31.3 (t), 32.0 (d), 32.8 (t), 33.1 (t), 34.1 (d), 36.2 (t), 39.2 (d), 41.2 (t), 41.5 (t), 44.0 (t), 47.6 (t), 48.8 (d), 57.4 (q), 58.0 (q), 61.8 (t), 69.8 (d), 72.9 (d), 78.0 (d), 80.6 (d), 81.8 (d), 117.3 (d), 127.6 (4d), 127.7 (4d), 129.6 (2d), 129.7 (2d), 130.5 (s), 131.8 (s), 133.5 (d), 133.7 (2s), 134.2 (2s), 135.6 (4d), 135.9 (2d), 136.0 (2d), 137.1 (d), 137.7 (d), 138.9 (d), 146.5 (s), 154.2 (s), 156.5 (s), 162.4 (s), 170.6 (s), 210.5 (s), 216.1 (s); *m/z* (EI) 1298.6392 (M^+ + Na), $C_{74}H_{97}N_3O_{12}Si_2$ + Na requires 1298.6508.

The C38 Acetate (81b). Acetic anhydride (2.2ml) was added dropwise over 5 min to a stirred solution of the alcohol **81a** (100 mg, 0.075 mmol) and DMAP (11 mg, 0.09 mmol) in dry dichloromethane (5.5 ml) and dry pyridine (5.5 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 12 h, and then diluted with dichloromethane (100 ml) and water (25 ml). The separated organic phase was washed with water (2 x 25 ml), saturated aqueous copper sulphate solution (2 x 25 ml) and brine (25 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^oC) (1:2 to 2:1) as eluent to give the *acetate* (87 mg, 84%), as a colourless foam: $[\alpha]_D^{24}$ –14.0 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2931, 2858 and 1731; ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (3H, d, *J* 6.7 Hz, CH_3-33), 0.82 (3H, d, *J* 6.8 Hz CH_3-29), 0.83 (3H, d, *J* 6.8 Hz, CH_3-39), 1.03 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.06 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.00-1.08 (3H, m, CH_3-37), 1.28 (3H, d, *J* 6.9 Hz, CH_3-9), 1.37-1.61 (5H, m, C*H*H H-4, H-31, C*H*H H-34, C*H*H H-40), 1.64-1.83 (6H, m, CH*H* H-4, H-5, H-33, CH*H* H-34, CH*H* H-40), 1.85-1.93 (1H, m, H-29), 1.95 (3H, s, CH_3CO), 1.98-2.04 (1H, m, H-39), 2.20-2.37 (2H, m, H-6), 2.38 (1H, dd, *J* 16.5, 5.8 Hz, C*H*H H-8), 2.43-2.52 (2H, m, C*H*H H-27, C*H*H H-35), 2.56 (1H, dd, *J* 5.2, 4.6 Hz, C*H*H H-2), 2.57 (1H, dd, *J* 5.2, 4.5 Hz, CH*H* H-2), 2.62 (1H, ddd, *J* 5.1, 2.5, 2.0 Hz, CH*H* H-35), 2.64-2.69 (1H, m CH*H* H-27), 2.80-2.88 (1H, m, H-37), 2.88-2.97 (1H, m, H-32), 3.14 (1H, dd, *J* 16.5, 7.8 Hz, CH*H* H-8), 3.20 (1H, ddd, *J* 8.4, 4.6, 4.5 Hz, H-28), 3.27

(3H, s, CH_3OC-32), 3.31 (3H, s, CH_3OC-28), 3.40 (1H, ddq, *J* 7.8, 6.9, 5.8 Hz, H-9), 3.64 (1H, ddd, *J* 10.4, 9.3, 5.3 Hz C*H*H H-41), 3.75 (1H, ddd, *J* 10.4, 6.7, 4.2 Hz, CH*H* H-41), 4.30 (1H, dddd, *J* 4.5, 4.6, 4.7, 4.8 Hz, H-3), 5.07-5.20 (1H, m, H-30), 5.12 (1H, dd, *J* 9.0, 3.2 Hz, H-38), 6.35 (1H, d, *J* 15.5 Hz, H-25), 7.09 (1H, ddd, *J* 15.5, 8.6, 6.2 Hz, H-26), 7.30-7.47 (13H, m, ArH, H-14), 7.64-7.75 (8H, m, ArH), 8.05 (2H, s, H-19, H-24); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 8.8 (q), 13.4 (q), 15.7 (q), 16.6 (q), 19.2 (s), 19.4 (s), 19.4 (t), 19.8 (q), 20.9 (q), 24.8 (t), 26.9 (3q), 27.1 (3q), 27.1 (d), 30.4 (d), 31.4 (t), 32.8 (t), 33.1 (t), 34.2 (d), 36.2 (t), 39.3 (d), 40.0 (t), 41.5 (t), 44.1 (t), 47.6 (t), 48.2 (d), 57.4 (q), 58.0 (q), 61.5 (t), 69.8 (d), 72.8 (d), 78.5 (d), 80.6 (d), 81.8 (d), 117.3 (d), 127.6 (4d), 127.7 (4d), 129.6 (2d), 129.7 (2d), 130.6 (s), 131.8 (s), 133.5 (d), 133.8 (2s), 134.2 (2s), 135.6 (4d), 135.9 (2d), 136.0 (2d), 137.0 (d), 137.3 (d), 138.9 (d), 146.5 (s), 154.2 (s), 156.5 (s), 162.4 (s), 170.1 (s), 170.6 (s), 210.5 (s), 212.0 (s); *m/z* (EI) 1340.6567 (M^+ + Na), $C_{76}H_{99}N_3O_{13}Si_2$ + Na requires 1340.6614.

The C41 Primary Alcohol (82a). A 70% solution of hydrogen fluoride in pyridine (405 µl) was added dropwise over 5 min to a stirred solution of the TBDPS ether **81b** (52 mg, 0.039 mmol) in dry dichloromethane (2.2 ml) and dry pyridine (2.2 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 1.5 h, and then diluted with ethyl acetate (22 ml) and quenched by the careful addition of saturated aqueous sodium bicarbonate solution (9 ml). The separated organic phase was washed with water (2 x 5 ml), saturated aqueous copper sulphate solution (2 x 5 ml) and brine (5 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^oC) (1:2 to 1:0) as eluent to give the *alcohol* (26 mg, 61%), as a colourless foam: $[\alpha]_D^{27}$ –15.0 (*c* 1.0 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 3624, 2932, 2858 and 1731; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (3H, d, *J* 6.8 Hz, CH_3-33), 0.83 (3H, d, *J* 6.9 Hz CH_3-29), 0.93 (3H, d, *J* 6.9 Hz, CH_3-39), 1.02

(9H, s, $(CH_3)_3CSi(Ph)_2$), 1.07 (3H, d, *J* 7.1 Hz, CH_3-37), 1.28 (3H, d, *J* 6.9 Hz, CH_3-9), 1.34-1.61 (5H, m, C*H*H H-4, H-31, C*H*H H-34, C*H*H H-40), 1.65-1.81 (6H, m, CH*H* H-4, H-5, H-33, CH*H* H-34, CH*H* H-40), 1.88 (1H, ddq, *J* 6.9, 4.9, 4.2 Hz, H-29), 1.99 (3H, s, CH_3CO), 1.92-2.08 (1H, m, H-39), 2.21-2.39 (2H, m, H-6), 2.39 (1H, dd, *J* 16.6, 5.5 Hz, C*H*H H-8), 2.43-2.53 (2H, m, C*H*H H-27, C*H*H H-35), 2.56 (1H, dd, *J* 5.8, 4.3 Hz, C*H*H H-2), 2.57 (1H, dd, *J* 5.8, 4.4 Hz, CH*H* H-2), 2.59-2.63 (1H, m, CH*H* H-35), 2.64-2.69 (1H, m CH*H* H-27), 2.86-2.96 (2H, m, H-32, H-37), 3.12 (1H, dd, *J* 16.6, 7.9 Hz, CH*H* H-8), 3.20 (1H, ddd, *J* 8.2, 4.2, 4.1 Hz, H-28), 3.26 (3H, s, CH_3OC-32), 3.31 (3H, s, CH_3OC-28), 3.38 (1H, ddq, *J* 7.9, 6.9, 5.5 Hz, H-9), 3.63 (1H, ddd, *J* 10.8, 7.9, 6.4 Hz C*H*H H-41), 3.77 (1H, ddd, *J* 10.8, 6.8, 5.3 Hz, CH*H* H-41), 4.28 (1H, dddd, *J* 4.3, 4.4, 4.5, 4.6 Hz, H-3), 5.06-5.11 (1H, m, H-30), 5.12 (1H, dd, *J* 8.6, 4.0 Hz, H-38), 6.35 (1H, d, *J* 15.5 Hz, H-25), 7.08 (1H, ddd, *J* 15.5, 8.6, 6.0 Hz, H-26), 7.30-7.43 (7H, m, ArH, H-14), 7.65-7.74 (4H, m, ArH), 8.05 (2H, s, H-19, H-24); ^{13}C NMR (90.6 MHz, $CDCl_3$) δ 8.8 (q), 13.4 (q), 15.7 (q), 16.5 (q), 19.4 (s), 19.4 (t), 19.8 (q), 21.0 (q), 24.9 (t), 27.1 (3q), 27.1 (d), 31.0 (d), 31.5 (t), 33.1 (t), 33.4 (t), 34.3 (d), 36.2 (t), 39.3 (d), 40.1 (t), 41.5 (t), 44.0 (t), 47.6 (t), 48.1 (d), 57.4 (q), 58.0 (q), 60.5 (t), 69.8 (d), 72.9 (d), 78.3 (d), 80.6 (d), 81.7 (d), 117.3 (d), 127.6 (4d), 129.6 (2d), 130.6 (s), 131.8 (s), 133.5 (d), 134.2 (2s), 135.9 (2d), 136.0 (2d), 137.1 (d), 137.4 (d), 138.9 (d), 146.5 (s), 154.2 (s), 156.5 (s), 162.4 (s), 170.2 (s), 170.6 (s), 210.6 (s), 211.9 (s); *m/z* (EI) 1102.5478 (M^+ + Na), $C_{60}H_{81}N_3O_{13}Si$ + Na requires 1102.5436.

The C41 Aldehyde (82b). Dess-Martin periodinane (5 mg, 0.012 mmol) was added in one portion to a stirred solution of the alcohol **82a** (8 mg, 0.007 mmol) in dichloromethane (2 ml) at room temperature. The mixture was stirred at room temperature for 1.5 h, and then diluted with diethyl ether (10 ml) and quenched by the addition of a mixture of saturated aqueous sodium bicarbonate solution (2.5 ml) and saturated aqueous sodium thiosulphate solution (2.5 ml). The mixture was

stirred at room temperature for 20 min and the separated organic phase was washed with brine (5 ml), then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 ^oC) (1:2 to 1:0) as eluent to give the *aldehyde* (6.4 mg, 80%), as a colourless oil: $[\alpha]_D^{27}$ –13.8 (*c* 0.64 in $CHCl_3$); ν_{max} (soln, $CHCl_3$)/cm^{-1} 2932, 2398 and 1726; ^1H NMR (500 MHz, $CDCl_3$) δ 0.78 (3H, d, *J* 6.8 Hz, CH_3-33), 0.83 (3H, d, *J* 7.0 Hz CH_3-29), 0.98 (3H, d, *J* 6.9 Hz, CH_3-39), 1.02 (9H, s, $(CH_3)_3CSi(Ph)_2$), 1.10 (3H, d, *J* 7.1 Hz, CH_3-37), 1.19-1.26 (1H, m, C*H*H H-34), 1.28 (3H, d, *J* 7.0 Hz, CH_3-9), 1.40-1.48 (2H, m, H-4), 1.42 (1H, ddd, *J*, 11.2, 9.9, 1.0 Hz, C*H*H H-31), 1.53 (1H, ddd, *J*, 15.7, 11.2, 2.0 Hz, C*H*H H-31), 1.68-1.79 (4H, m, H-5, H-33, CH*H* H-34), 1.83-1.89 (1H, m, H-29), 2.00 (3H, s, CH_3CO), 2.20-2.39 (2H, m, H-6), 2.31 (1H, dd, *J* 8.7, 1.9 Hz, C*H*H H-40), 2.38 (1H, dd, *J* 16.7, 5.8 Hz, C*H*H H-8), 2.42-2.54 (5H, m, C*H*H H-27, H-35, H-39, CH*H* H-40), 2.54 (1H, dd, *J* 15.5, 5.6 Hz, C*H*H H-2), 2.59 (1H, dd, *J* 15.5, 5.3 Hz, CH*H* H-2), 2.61-2.67 (1H, m CH*H* H-27), 2.80 (1H, dq, *J* 7.8, 7.1 Hz, H-37), 2.88-2.92 (1H, m, H-32), 3.15 (1H, dd, *J* 16.7, 7.6 Hz, CH*H* H-8), 3.19-3.23 (1H, m, H-28), 3.26 (3H, s, CH_3OC-32), 3.31 (3H, s, CH_3OC-28), 3.38 (1H, ddq, *J* 7.6, 7.0, 5.8 Hz, H-9), 4.29 (1H, dddd, *J* 5.3, 5.4, 5.5, 5.6 Hz, H-3), 5.07-5.12 (1H, m, H-30), 5.10 (1H, dd, *J* 7.8, 4.6 Hz, H-38), 6.35 (1H, d, *J* 16.0 Hz, H-25), 7.08 (1H, ddd, *J* 16.0, 9.4, 6.2 Hz, H-26), 7.31-7.42 (7H, m, ArH, H-14), 7.67-7.74 (4H, m, ArH), 8.06 (2H, s, H-19, H-24), 9.8 (1H, app t, *J* 1.9 Hz, H-41); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.8 (q), 13.2 (q), 15.8 (q), 17.8 (q), 19.4 (s), 19.5 (t), 19.7 (q), 20.9 (q), 24.8 (t), 27.1 (d), 27.1 (3q), 29.5 (d), 31.5 (t), 33.1 (t), 34.1 (d), 36.3 (t), 39.3 (d), 40.0 (t), 41.5 (t), 44.1 (t), 46.0 (t), 47.6 (t), 48.5 (d), 57.5 (q), 58.0 (q), 69.7 (d), 72.8 (d), 77.6 (d), 80.4 (d), 81.7 (d), 117.2 (d), 127.6 (4d), 129.6 (2d), 130.6 (s), 131.8 (s), 133.5 (d), 134.1 (s), 134.2 (s), 135.9 (2d), 136.0 (2d), 137.0 (d), 137.3 (d), 138.9 (d), 146.5 (s), 154.2 (s), 156.5 (s), 162.4 (s), 170.0 (s), 170.5 (s), 201.2 (d), 210.5 (s), 211.2 (s); *m/z* (EI) 1100.5260 (M^+ + Na), $C_{60}H_{79}N_3O_{13}Si$ + Na requires 1100.5280.