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 °C under a nitrogen atmosphere. The mixture was stirred at 0 °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 °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 °C) as colourless crystals, mp 146-148 °C: \([\alpha]_D^{22} -50.5\) (c 0.19 in CHCl₃); \(\nu_{\text{max}}\) (soln, CHCl₃)/cm\(^{-1}\) 1739 and 1673; \(^1\)H NMR (360 MHz, CDCl₃) \(\delta\) 2.48 (3H, s, CH₃CN), 3.92 (3H, s, CH₃O), 4.06 (1H, dd, \(J\) 11.6, 4.1 Hz CHH), 4.29 (1H, dd, \(J\) 11.6, 4.1 Hz, CHH), 5.50 (1H, app dt, \(J\) 8.5, 4.1 Hz, CONHCH), 7.74 (1H, d, \(J\) 8.5 Hz, NH), 8.13 (1H, s, CHCONH), 8.21 (1H, s, CHCCO₂Me); \(^{13}\)C NMR (90.6 MHz, CDCl₃) \(\delta\) 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), C₁₂H₁₃N₃O₅ + 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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (3:2) as eluent to give the oxazoline (92 mg, 99%), which recrystallised from ethyl acetate-light petroleum (bp 40-60 °C) as colourless crystals, mp 125-128 °C: \([\alpha]_D^{32} +97.1\) (c 1.42 in CHCl₃); \(\nu_{\text{max}}\) (soln, CHCl₃)/cm\(^{-1}\) 1739, 1677 and 1586; \(^1\)H NMR (360 MHz, CDCl₃) \(\delta\) 2.47 (3H, s, CH₃CN), 3.86 (3H, s, CH₃O), 4.72 (1H, dd, \(J\) 10.4, 8.8 Hz, CHHO), 4.84 (1H, dd, \(J\) 8.8, 8.2 Hz, CHCH₂O), 5.51 (1H, dd, \(J\) 10.4, 8.2 Hz, CHHO), 8.05 (1H, s, CHCCOCH₂), 8.21 (1H, s, CHCCO₂Me); \(^{13}\)C NMR (90.6 MHz, CDCl₃) \(\delta\) 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 (El) 278.0771 (M+ + H), 300.0590 (M+ + Na) C12H11N3O5 + H requires 278.0777.

(3'S, 2'R)-3-Benzyl-4-(5'-benzylxyloxy-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 °C under a nitrogen atmosphere. The resulting pale yellow solution was stirred at –78 °C for 1 h, then at 0 °C for 30 min, and re-cooled to –78 °C. 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 °C 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 °C. 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 (MgSO4) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:5 to 2:5) as eluent to give the alcohol (36.6 g, 72%) as a colourless oil: [α]D22 -52.7 (c 0.9 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 3533, 1780 and 1688; (Found: C, 69.7; H, 6.9; N, 3.5; C23H27NO5 requires C, 69.5; H, 6.9; N, 3.5%); ¹H NMR (360 MHz, CDCl3) δ 1.30 (3H, d, J 7.1 Hz, CH₃), 1.71-1.80 (1H, m, CHCHOH), 1.84-1.95 (1H, m, CHCHOH), 2.79 (1H, dd, J 13.4, 9.4 Hz, CHCHPh), 3.26 (1H, dd, J 13.4, 3.3 Hz, CHCHPh), 3.31-3.34 (1H, br, OH), 3.64-3.75 (2H, m, CH₂OBn) 3.84 (1H, dq, J 7.1, 3.8 Hz, CHCO), 4.14-4.23 (3H, m, CH₂OCO, CHOH), 4.52 (2H, s, OCH₂Ph), 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$_3$) $\delta$ 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.

(3S,4R)-1-Benzylxoy-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 °C under a nitrogen atmosphere. The solution was stirred for 2 h at 0 °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 $\text{in vacuo}$ to leave the crude diol 36a (11 g, 99%) as a colourless oil. The 1,3-diol was converted into the corresponding 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 $\text{in vacuo}$. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °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
CHCl₃); νₓₐₓₚ (soln, CHCl₃)/cm⁻¹ 3504; (Found: C, 75.4; H, 8.3; C₂₉H₃₆O₃Si requires C, 75.3; H, 8.3%); ¹H NMR (360 MHz, CDCl₃) δ 0.96 (3H, d, J 7.0 Hz, CH₃), 1.09 (9H, s, (CH₃)₃C), 1.68-1.94 (3H, m, CH₂CHOH, CHCH₃), 3.11-3.19 (1H, br, OH), 3.65-3.75 (4H, m, CH₂OSi, CH₂OBn), 4.05 (1H, app dt, J 9.5, 3.1 Hz, CHOH), 4.56 (2H, s, CH₂Ph), 7.27-7.49 (11H, m, ArH), 7.66-7.74 (4H, m, ArH); ¹³C NMR (90.6 MHz, CDCl₃) 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), C₂₉H₃₆O₃Si + H requires 463.2668.

(3S, 4R)-1-Benzyloxy-5-(tert-butyldiphenylsilylanoxy)-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 °C under a nitrogen atmosphere. The solution was stirred at 0 °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 °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 (MgSO₄) 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 methyl ether (17.5 g, 90%) as a colourless oil: [α]D³¹ -5.33 (c 0.9 in CHCl₃); νₓₐₓₚ (soln, CHCl₃)/cm⁻¹ 2932 and 2860; (Found: C, 75.8; H, 8.7; C₃₀H₄₀O₃Si requires C, 75.6; H, 8.5%); ¹H NMR (360 MHz, CDCl₃) δ 0.92 (3H, d, J 6.8 Hz, CH₃CH), 1.10 (9H, s, (CH₃)₃C), 1.77-1.84 (2H, m, CH₂CHOMe), 1.89 (1H, ddddq, J 7.2, 6.8, 6.5, 3.7 Hz, CHCH₃), 3.35 (3H, s, CH₃O), 3.50-3.65 (3H, m, CHOMe, CH₂OBn), 3.62 (1H, dd, J 9.9, 6.5 Hz, CHHOSi), 3.74 (1H, dd, J 9.9, 7.2 Hz, CHHOSi), 4.52 (1H, d, J 12.2 Hz, CHHPh), 4.56 (1H, d, J 12.2
Hz, CHHPh), 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$_3$Si + Na requires 499.2644.

(3S,4R)-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 °C) (2:1) as eluent to give the corresponding alcohol (2.2 g, 92%) as a colourless oil: [α]$_D^{24}$ -12.0 (c 1.15 in CHCl$_3$); $\nu_{\text{max}}$ (soln, CHCl$_3$)/cm$^{-1}$ 3486 and 2931; (Found: C, 71.1; H, 9.1; C$_{23}$H$_{34}$O$_3$Si requires C, 71.5; H, 8.9%); $^1$H NMR (360 MHz, CDCl$_3$) δ 0.94 (3H, d, J 7.2 Hz, CH$_3$CH), 1.07 (9H, s, (CH$_3$)$_3$C), 1.65-1.75 (2H, m, CH$_2$CHOMe), 1.87-1.97 (1H, m, CH$_3$CH$_2$), 3.34 (3H, s, CH$_3$O), 3.49 (1H, app dt, J 7.8, 4.5 Hz, CHOMe) 3.53 (1H, dd, J 10.0, 6.6 Hz, CHHOSi), 3.69 (1H, dd, J 10.0, 6.0 Hz, CHHOSi), 3.74 (2H, app dt, J 6.0, 2.3 Hz, CH$_2$OH), 7.37-7.46 (6H, m, ArH), 7.66-7.72 (4H, m, ArH); $\delta_{C}$ (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$_3$Si + 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 (MgSO₄) 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: [α]D²² -13.8 (c 1.0 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 2732 and 1723; (Found: C, 71.8; H, 8.4; C₂₃H₃₂O₃Si requires C, 71.8; H, 8.4%); ¹H NMR (360 MHz, CDCl₃) δ 0.91 (3H, d, J 6.9 Hz, CH₃CH), 1.07 (9H, s, (CH₃)₃C), 1.85-1.91 (1H, m, CHCH₂), 2.55 (1H, ddd, J 16.3, 4.7, 2.1 Hz, CHHCHOME), 2.69 (1H, ddd, J 16.3, 7.8, 2.1 Hz, CHHCHOME), 3.34 (3H, s, CH₂O), 3.56 (1H, dd, J 10.2, 5.8 Hz, CHHOSi), 3.68 (1H, dd, J 10.2, 5.8 Hz, CHHOSi), 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, CHO); δC (90.6 MHz; CDCl₃) 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), C₂₃H₃₂O₃Si + Na requires 407.2018.

(R)-3-((E)-5-(Benzyloxy)pent-2-enoyl)-4-benzyloxazolidin-2-one (40).³⁵ Oxalyl chloride (2.0 ml, 23 mmol) was added dropwise over 5 min to a stirred solution of (E)-5-(Benzyloxy)pent-2-enolic acid (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 °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 °C and the resulting solution was stirred at –78 °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 (MgSO₄) 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: [α]D²⁸ -49.3 (c 2.64 in CHCl₃) [lit¹³ (for enantiomer) [α]D +50.5 (c 2.6 in CHCl₃)]; νmax (soln, CHCl₃)/cm⁻¹ 2917, 2863, 1777, 1682 and 1637; ¹H NMR (360 MHz, CDCl₃) δ 2.64 (2H, dt, J 6.8, 6.5 Hz, CH₂CH₂OBn), 2.81 (1H, dd, J 13.4, 9.5 Hz, PhCHCH₂CH₂OBn), 3.34 (1H, dd, J 13.4, 3.2 Hz, PhCHCH₂CH₂OBn), 3.66 (2H, t, J 6.5 Hz, CH₂OBn), 4.12-4.24 (2H, m, OC₆H₄CH₂), 4.56 (2H, s, CH₂OCH₂CH₂), 4.73 (1H, app ddd, J 9.5, 6.9, 3.2 Hz, CHN), 7.27 (1H, dd, J 22.4, 6.8 Hz, CHCHCO), 7.26-7.43 (11H, m, CHCO, ArH); ¹³C NMR (90.6 MHz; CDCl₃) 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), C₂₂H₂₃NO₄ + H requires 366.1705.
(4'R,2'R,1S,3S,4R)-4'-Benzy1-3'(5'-benzyloxy-2''-[5-(tert-butylidiphenylsianyloxy)-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 °C under a nitrogen atmosphere. The resulting pale yellow solution was stirred at −78 °C for 30 min, then at 0 °C for 30 min and re-cooled to −78 °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 °C for 3 h. The mixture was allowed to warm to 0 °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 °C for 20 min and then a 30% aqueous hydrogen peroxide solution (7.4 ml) was added slowly keeping the temperature below 10 °C. The mixture was stirred at 0 °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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °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: [α]D28 +4.9 (c 0.7 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 3523, 2930, 2858, 1781 and 1693; ¹H NMR (500 MHz, CDCl3, Z-isomer) δ 1.02 (3H, d, J 7.1 Hz, CH₃CHCH₂OSi), 1.14 (9H, s, (CH₃)₃C), 1.54-1.66 (1H, m, CHHCHOMe), 1.66-1.79 (1H, m, CHHCHOMe), 1.81-1.94 (1H, br OH), 1.95-2.12 (1H, m, CHCH₃), 2.80 (1H, dd, J 13.7, 9.6 Hz, ArCHCH₂N), 3.31 (1H, dd, J 13.7, 3.8 Hz, ArCHHCHN), 3.43 (3H, s, OCH₃), 3.64 (1H, dd, J 13.1, 6.6 Hz, CHHOSi) 3.67-3.73 (1H, m, CHOMe), 3.77 (1H, dd, J 13.1, 5.6 Hz, CHHOSi), 4.12-4.23 (2H, m, OCH₂CHN), 4.23-4.35 (3H, m, CHO, CH₂OBn), 4.60 (2H, s, OCH₂Ar), 4.70-4.79 (1H, m, CHN), 5.01 (1H, dd, J 10.2, 4.8 Hz, CHCHOH), 5.86 (1H, dd, J 10.5, 10.2 Hz,
CHCH₂OBn), 6.09 (1H, dt, J 12.2, 10.5 Hz, CHCH₂OBn), 7.19-7.27 (2H, m, ArH), 7.30-7.53 (14H, m, ArH), 7.70-7.81 (4H, m, ArH); ¹H NMR (500 MHz, CDCl₃, E-isomer) δ 1.00 (3H, d, J 7.1 Hz, CH₃CH₂OSi), 1.14 (9H, s, (CH₃)₃C), 1.54-1.66 (1H, m, CHHCHOMe), 1.66-1.79 (1H, m, CHHCHOMe), 1.81-1.94 (1H, br OH), 1.95-2.12 (1H, m, CHCH₂), 2.76 (1H, dd, J 13.7, 9.6 Hz, ArCHHCHN), 3.26 (1H, dd, J 13.7, 3.5 Hz, ArCHHCHN), 3.42 (3H, s, OCH₃), 3.62 (1H, dd, J 13.1, 6.5 Hz, CHHOSi) 3.67-3.73 (1H, m, CHOMe), 3.76 (1H, dd, J 13.1, 5.1 Hz, CHHOSi), 4.12-4.23 (4H, m, OCH₂CHN, CH₂OBn), 4.26-4.35 (1H, m, CHOH), 4.59 (2H, s, OCH₂Ar), 4.63 (1H, dd, J 7.8, 3.8 Hz, CHCHOH), 4.70-4.79 (1H, m, CHN), 5.97-6.06 (2H, m, CHCH₂OBn), 7.19-7.27 (2H, m, ArH), 7.30-7.53 (14H, m, ArH), 7.70-7.81 (4H, m, ArH); ¹³C NMR (90.6 MHz, CDCl₃) 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), C₄₅H₅₅NO₇Si + Na requires 772.3646.

(4R,5S,7S,8R)-1-Benzzyloxy-9-(tert-butyldiphenylsilanyloxy)-7-methoxy-4,8-dimethylnon-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 °C. The solution was stirred at 0 °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 (Na₂SO₄) and concentrated in vacuo. The residue was purified by
chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:1 to 2:1) as eluent to give (2R,3S,5S,6R)-2-(3'-benzyloxyprop-1'eny1)-7-(tert-butylidiphenylsilanyloxy)-5-methoxy-6-methyl-heptane-1,3-diol (3.7 g, 99%) as a colourless oil and a mixture of E/Z isomers: [α]D28 -4.9 (c 0.77 in CHCl3); νmax (soln, CHCl3)/cm-1 3458, 2931, 2856 and 1602; (Found: C, 72.8; H, 8.35; C35H48O5Si requires C, 73.1; H, 8.1%); 1H NMR (500 MHz, CDCl3, Z-isomer) δ 1.03 (3H, d, J 6.7 Hz, CH3CHCH2OSi), 1.11 (9H, s, (CH3)3C), 1.45-1.64 (1H, m, CHHCHOMe), 1.65-1.74 (1H, m, CHHCHOMe), 1.90-2.03 (1H, m, CHCH3), 2.56 (1H, app dt, J 9.5, 5.3 Hz, CHCHOH), 2.59-2.70 (1H, br, CHOH), 3.10-3.20 (1H, br, CH2OH), 3.39 (3H, s, OCH3), 3.54-3.62 (2H, m, CHOME, CHHOSi), 3.61-3.75 (1H, m, CHHOSi), 3.67 (1H, dd, J 10.6, 5.9 Hz, CHHOH), 3.75 (1H, dd, J 10.6, 5.9 Hz, CHHOH), 4.00-4.10 (1H, m, CHOH), 4.06 (1H, dd, J 11.6, 6.8 Hz, CHHOBn), 4.12 (1H, dd, J 11.6, 7.0 Hz, CHHOBn), 4.54 (2H, s, CH2Ar), 5.71 (1H, dd, J 10.7, 9.5 Hz, CHCH2OBn), 5.93 (1H, ddd, J 10.7, 7.0, 6.8 Hz, CHCH2OBn), 7.26-7.56 (11H, m, ArH), 7.66-7.83 (4H, m, ArH); 1H NMR (500 MHz, CDCl3, E-isomer) δ 1.03 (3H, d, J 6.6 Hz, CH3CHCH2OSi), 1.11 (9H, s, (CH3)3C), 1.45-1.54 (1H, m, CHHCHOMe), 1.65-1.74 (1H, m, CHHCHOMe), 1.90-2.03 (2H, m, CHCH3, OH), 2.20-2.32 (1H, m, CHCHOH), 3.39 (3H, s, OCH3), 3.53-3.62 (2H, m, CHOME, CHHOSi), 3.61-3.75 (3H, m, CH2OH CHHOSi), 4.00-4.10 (3H, m, CHOH, CH2OBn), 4.55 (2H, s, CH2Ar), 5.75-5.79 (1H, m, CHCH2OBn), 5.84 (1H, dd, J 16.8, 6.5 Hz, CHCHCH2OBn), 7.26-7.56 (11H, m, ArH), 7.66-7.83 (4H, m, ArH); 13C NMR (90.6 MHz, CDCl3) 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), C35H48O5Si + 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 °C under a nitrogen atmosphere. The solution was allowed to warm to -20 °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 (\(\text{Na}_2\text{SO}_4\)) and concentrated \textit{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 °C. The solution was stirred for 3 h at 0 °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 (\(\text{Na}_2\text{SO}_4\)) and concentrated \textit{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 secondary \textit{alcohol} (3.12 g, 85%) as a colourless oil and a mixture of E/Z isomers: \([\alpha]_D^{31} -7.5 (c 1.4 \text{ in CHCl}_3)\); (Found: C, 74.7; H, 8.8; \(\text{C}_{35}\text{H}_{48}\text{O}_4\text{Si}\) requires C, 74.9; H, 8.6%); \(\nu_{\text{max}}\) (soln, CHCl\(_3\))/cm\(^{-1}\) 3453, 2931 and 1602; \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\), Z-isomer) \(\delta\) 0.97 (3H, d, \(J\ 6.8\) Hz, CH\(_3\)CHCH(OH)), 0.99 (3H, d, \(J\ 6.6\) Hz, CH\(_3\)CHCH\(_2\)OSi), 1.08 (9H, s, (CH\(_3\))\(_3\)C), 1.45-1.62 (2H, m, CH\(_2\)CHOMe), 1.90-1.97 (1H, m, CHCH\(_2\)OSi), 2.41 (1H, app dq, \(J\ 16.4, 6.4\) Hz, CHCHOH), 2.53 (1H, d, \(J\ 3.4\) Hz, OH), 3.36 (3H, s, OCH\(_3\)), 3.51-3.61 (3H, m, CHOMe, CHHOSi, CHO), 3.68 (1H dd, \(J\ 9.9, 5.4\) Hz, CHHOSi), 4.07 (1H, dd, \(J\ 3.3, 1.3\) Hz, CHHOBn), 4.08 (1H, dd, \(J\)
3.9, 1.3 Hz, CHHOBr), 4.52 (2H, s, CH2Ar), 5.51 (1H, app t, J 10.6 Hz,
CHCHCH2OBn), 5.71-5.76 (1H, ddd, J 10.6, 3.9, 3.3 Hz, CHCH2OBn), 7.46-7.49
(11H, m, ArH), 7.62-7.75 (4H, m, ArH); 1H NMR (500 MHz, CDCl3, E-isomer) δ 0.99
(3H, d, J 6.6 Hz, CH3CH2CH2OSi), 1.03 (3H, d, J 6.8 Hz, CH3CHCHOH), 1.08 (9H, s,
(CH3)3C), 1.54-1.62 (2H, m, CH2CHOMe), 1.90-1.97 (1H, m, CH2CH2OSi), 2.20 (1H,
ddq, J 6.6, 6.7, 6.8 Hz, CHCHOH), 2.35 (1H, d, J 3.5 Hz, OH), 3.37 (3H, s, OCH3),
3.51-3.59 (2H, m, CHOMe, CHHOSi), 3.61-3.66 (1H, m, CHO), 3.68 (1H dd, J 9.9,
5.4 Hz, CHHOSi), 4.01 (2H, d, J 4.6 Hz, CH2OBn), 4.52 (2H, s, CH2Ar), 5.63-5.71
(2H, m, CHCHCH2OBn), 7.46-7.49 (11H, m, ArH), 7.62-7.75 (4H, m, ArH); 13C NMR
(90.6 MHz, CDCl3) 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 (El) 561.3410 (M+ + H), 578.3675 (M+ + NH4),
583.3225 (M+ + Na), C35H48O4Si + H requires 561.3400.

(2R,3S,5S,6R)-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 °C under a nitrogen atmosphere. The solution was stirred at 0
°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
(Na2SO4) and concentrated in vacuo. The residue was purified by chromatography
on silica using diethyl ether-light petroleum (bp 40-60 °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$_3$); $\nu_{\max}$ (soln, CHCl$_3$)/cm$^{-1}$ 2930 and 2858; $^1$H NMR (500 MHz, CDCl$_3$, Z-isomer) $\delta$ 0.06 (3H, s, CH$_3$Si), 0.09 (3H, s, CH$_3$Si), 0.89 (3H, d, J 7.0 Hz, CH$_3$CHCH$_2$OSi), 0.91 (9H, s, (CH$_3$)$_3$Si(CH$_3$)$_2$), 0.99 (3H, d, J 6.8 Hz, CH$_3$CHCHOSi), 1.08 (9H, s, (CH$_3$)$_3$Si(Ph)$_2$), 1.42-1.52 (2H, m, CH$_2$CHOMe), 1.85-1.97 (1H, m, CHCH$_2$OSi), 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, CHCH$_2$OBn), 5.59-5.66 (1H, m, CHCH$_2$OBn), 7.25-7.46 (10H, m, ArH), 7.65-7.71 (5H, m, ArH); $^1$H NMR (500 MHz, CDCl$_3$, E-isomer) $\delta$ 0.06 (3H, s, CH$_3$Si), 0.09 (3H, s, CH$_3$Si), 0.87 (3H, d, J 6.8 Hz, CH$_3$CHCH$_2$OSi), 0.92 (9H, s, (CH$_3$)$_3$Si(CH$_3$)$_2$), 1.03 (3H, d, J 6.8 Hz, CH$_3$CHCHOSi), 1.08 (9H, s, (CH$_3$)$_3$Si(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, CHHCHO), 1.85-1.97 (1H, m, CHCH$_2$OSi), 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$_2$OBn), 4.49 (1H, s, CH$_2$Ar), 5.59 (1H, m, CHCH$_2$OBn), 5.69 (1H, dd, J 15.6, 7.3 Hz, CHCH$_2$OBn), 7.25-7.46 (10H, m, ArH), 7.65-7.71 (5H, m, ArH); $^{13}$C NMR (90.6 MHz, CDCl$_3$) $\delta$ -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$_4$Si$_2$ + 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 °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 °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) (1:9) as eluent to give the corresponding aldehyde (3.49 g, 93%) as a colourless oil: $[\alpha]_D^{22} +6.7$ (c 1.8 in CHCl₃); $\nu_{\text{max}}$ (soln, CHCl₃)/cm⁻¹ 2717 and 1722; $^1$H NMR (360 MHz, CDCl₃) δ 0.10 (3H, s, CH₃Si), 0.12 (3H, s, CH₃Si), 0.89 (3H, d, J 6.5 Hz, CH₃CHCH₂OSi), 0.91 (9H, s, (CH₃)₃CSi(CH₃)₂), 1.06 (9H, s, (CH₃)₃CSi(Ph)₂), 1.12 (3H, d, J 7.0 Hz, CH₂CHCC=O), 1.56 (1H, ddd, J 14.3, 8.5, 5.2 Hz, CHHCHOMe) 1.65 (1H, ddd, J 14.3, 7.5, 5.1 Hz, CHHCHOMe), 1.94 (1H, dddq, J 6.5, 6.5, 3.3 Hz, CHCH₂OSi), 2.56 (1H, dddq, J 7.0, 3.3, 1.7 Hz, CHCHO), 3.29 (3H, s, OCH₃), 3.49-3.53 (1H, m, CHOMe), 3.54 (1H dd, J 9.9, 6.5 Hz, CHHOSi), 3.70 (1H dd, J 9.9, 6.5 Hz, CHHOSi), 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, CH=O); $^{13}$C NMR (90.6 MHz, CDCl₃) 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), C₃₂H₅₂O₄Si₂ + H requires 557.3482.

(4S,5R,6S,8S,9R)-6-(tert-Butyldimethylsilyloxy)-10-(tert-butyldiphenylsilyloxy)-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 °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$_2$SO$_4$) 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$_3$); $\nu_{\text{max}}$ (soln, CHCl$_3$)/cm$^{-1}$ 3464 and 1641; (Found: C, 69.9; H, 9.7; C$_{35}$H$_{58}$O$_4$Si$_2$ requires C, 70.2; H, 9.8%); $^1$H NMR (360 MHz, CDCl$_3$) $\delta$ 0.11 (3H, s, CH$_3$Si), 0.12 (3H, s, CH$_3$Si), 0.85 (3H, d, $J$ 7.0 Hz, CH$_3$CHCH$_2$OSi), 0.91 (9H, s, (CH$_3$)$_3$CSi(CH$_3$)$_2$), 1.04 (3H, d, $J$ 7.2 Hz, CH$_3$CHCHOH), 1.07 (9H, s, (CH$_3$)$_3$CSi(Ph)$_2$), 1.57-1.65 (1H, m, CH$_3$CHCHOH), 1.68 (1H, ddd, $J$ 14.0, 7.3, 5.2 Hz, CHHCHOME), 1.81 (1H, dddq, $J$ 7.8, 7.0, 6.1, 2.4 Hz, CHCH$_2$OSi), 2.00 (1H ddd, $J$ 14.0, 8.6, 6.6 Hz, CHHCHOME), 2.08 (1H, ddd, $J$ 14.1, 6.5, 1.5 Hz, CHH=), 2.33 (1H, ddd, $J$ 14.1, 7.4, 6.5 Hz, CHHC=), 3.28 (3H, s, OCH$_3$), 3.39 (1H, ddd, $J$ 7.3, 6.6, 2.4 Hz CHOME), 3.51 (1H, ddd, $J$ 9.9, 6.1 Hz, CHHOSi), 3.68 (1H, dd, $J$ 9.9, 7.8 Hz, CHHOSi), 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, CHOH), 5.02 (1H, dd $J$ 10.2, 1.4 Hz, CHH=), 5.10 (1H, dd $J$ 17.1, 1.4 Hz, CHH=), 5.80 (1H, app ddt, $J$ 17.1, 10.2, 6.5 Hz, CH$_2$=CH), 7.36-7.47 (6H, m, ArH), 7.64-7.70 (4H, m, ArH); $^{13}$C NMR (90.6 MHz, CDCl$_3$) $\delta$ -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), C₃₅H₅₆O₄Si₂ + 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 ¹³C NMR spectrum,⁵⁰ ie ketal carbon δ 100.6 ppm and gem-methyl carbons δ 23.9 and 25.0 ppm.

(4S,5R,6S,8S,9R)-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 (MgSO₄) 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: [α]D²⁷ -12.5 (c 1.1 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 2930 and 2857; (Found: C, 70.3; H, 9.9; C₃₅H₆₀O₄Si₂ requires C, 70.5; H, 9.9%); ¹H NMR (360 MHz, CDCl₃) δ 0.04 (3H, s, CH₃Si), 0.05 (3H, s, CH₃Si), 0.88 (9H, s, (CH₃)₃CSi(CH₃)₂), 0.91 (3H, d, J 7.0 Hz, CH₃CHCH₂OSi), 0.92 (3H, d, J 6.9 Hz, CH₃CHCHOTBS), 1.06 (9H, s, (CH₃)₃CSi(Ph)₂), 1.28-1.48 (2H, m, CH₂CHOSi), 1.82 (1H, ddq, J 7.6, 6.9, 3.9 Hz, =CHCH₂CHCH₃), 1.96-2.07 (1H, m, CH₂CHCH₃) 2.22-2.41 (2H, m, =CHCH₂), 2.94 (1H, ddd, J 7.6, 5.8, 5.2 Hz, =CHCH₂CHOMe), 3.29 (3H, s, OCH₃), 3.31 (3H, s, =CHCH₂CHOMe), 3.31 (3H, s, =CHCH₂CHOMe).
OCH₃), 3.42 (1H, ddd, J 9.9, 3.6, 2.4 Hz CH₂ CHCHOMe), 3.60 (1H, dd, J 9.9, 6.8 Hz, CHHOSi), 3.72 (1H, dd, J 9.9, 5.6 Hz, CHHOSi), 3.89 (1H, ddd, J 9.5, 3.9, 1.7 Hz, CHOTBS), 5.06-5.14 (2H, m, CH₂=), 5.84 (1H, dddd, J 16.9, 10.5, 7.6, 6.5 Hz, CH₂=CH), 7.36-7.45 (6H, m, ArH), 7.66-7.71 (4H, m, ArH); ¹³C NMR (90.6 MHz, CDCl₃) 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), C₃₆H₆₀O₄Si₂ + H requires 613.4108.

(3S, 4R, 5S, 7S, 8R)-5-tert-Butyldimethylsilanyloxy)-9- (tert-butylidiphenylsilanyloxy)-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 ºC) (1:9 then 1:5) as eluent, and was obtained as an oil (94%) which showed, [α]D₂² - 12.2 (c 0.6 in CHCl₃); νmax (soln, CHCl₃, cm⁻¹) 1721;
¹H NMR (360 MHz, CDCl₃) δ 0.05 (3H, SiMe), 0.08 (3 H, SiMe), 0.89 (9H, CMe₃), 0.92 (3H, d, J 7.0 Hz, CH₃ CH), 0.97 (3H, d, J 6.9Hz, CH₂CH), 1.07 (9H, CMe₃), 1.32 - 1.5 (2H, m, CH₂CHOSi), 1.84 (1H, app. qd, J 6.9 and 3.7 Hz, CH₃CH.CHOTBS), 1.94 – 2.05 (1H, m, CHCH₂OSi), 2.57 – 2.69 (2H, m, CH₂CO), 3.29 (3H, CH₃) 3.31 (3H, OMe), 3.36 – 3.46 (2H, m, 2 x CHOMe), 3.55 (1 H, dd, J 9.9 and 6.6 Hz, CHHOSi), 3.68 (1H, dd, J 9.9 and 6.6 Hz, CHHOSi), 3.86 (1H, app, dt, J 9.2 and 2.8 Hz, CHOTBS), 7.37 – 7.44 (6H, m, ArH), 7.66 – 7.70 (4H, m, ArH), 9.81 (1H, t, J 2.3 Hz, CH=O). ¹³C NMR (90 MHz, CDCl₃) 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), C₃₆H₆₀O₆Si₂ Na requires 669. 3983.
2-[(E)-(4S, 5R, 6S, 8S, 9S)-6-(tert-Butyl-dimethylsilyloxy)]
-10-(tert-butyl-diphenylsilyloxy)-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 [α]D22 - 25.0 (c
1.03 in CHCl3); νmax (soln, CHCl3, cm⁻¹) 1726; Found: C, 67.6; H, 8.6; N, 1.5; C₄₄H₆₉O₇NSi₂ requires C, 67.7; H, 8.9; N, 1.8%; ¹H NMR (360 Mz, CDCl₃) δ = 0.03 (3H, SiMe),
0.01 (3H, SiMe), 0.86 (9H, CMe₃), 0.92 (3H, d, J 7.0 Hz, CH₃ CH CH₂), 0.95 (3H, d, J 6.8 Hz, CH₃ CH), 1.07 (9H, CMe₃), 1.25 – 1.34 (1H, m, CHCH.CHOSi), 1.4 – 1.48 (1H, m,
CHH.CHOSi), 1.59 (9H, CMe₃), 1.75 – 1.83 (1H, m, CH₃ CH), 1.97 – 2.08 (1H, m,
CHCH.OSi), 2.42 – 2.51 (1H, m, = CH.CH(H), 2.54 – 2.63 (1H, m, = CHCHH), 3.02 (1H,
app. dt, J 7.5 and 4.8 Hz, = CH.CH₂CH₂), 3.31 (6H, 2 x OMe), 3.35 – 3.42 (1H, m, CH₂
CH CH CH₂O Me), 3.57 (1H, dd, J 9.9 and 6.7 Hz, CHH.OSi), 3.68 (1H, dd, J 9.9 and 5.5 Hz,
CHH OSi), 3.88 (1H, dd, J 8.5 and 3.3 Hz, CHOTBS), 6.41 (1H, d, J 16.2 Hz, CH = CH
CH₂), 6.66 (1H, ddd, J 16.2, 8.1 and 6.6 Hz, = CHCH₂), 7.35 – 7.45 (6H, m, ArH), 7.65 –
7.74 (4H, m, ArH), 8.01 (1H, OCH=) ¹³C NMR (90 MHz, CDCl₃), - 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%, C₄₄H₇₀O₇NSi₂ requires 780.4691.

2-[(E)-(4S, 5R, 6S, 8S, 9S)-10-(tert-Butyl-diphenylsilyloxy)]
-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 CHCl₃); \([\nu]_{\text{max}}\) (soln, CHCl₃, cm⁻¹) 3464, 2971, 2880, 1725;
\(^1\)H NMR (360 MHz, CDCl₃) δ 0.88 (3H, d, J 7.0 Hz, CH₃), 0.94 (3H, d, J 7.0 Hz, CH₃),
1.49 (1H, ddd, J 14.0, 9.7 and 2.3 Hz, CH,H,CHOH), 1.59 (9H, CMe₃), 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, CH,CHOH),
2.14 – 2.27 (2H, m, CH₂ CHMeOH), 2.43 (1H, dddd, J 14.4, 7.7, 6.1 and 1.2 Hz,
CH,H,CH=), 2.65 (1H, app. dtd, J 14.4, 7.1, and 1.3 Hz, CHH,CH=), 2.98 (1H, brs, OH),
3.42 (3H, OMe), 3.44 (3H, OMe), 3.52 – 3.73 (4H, m, CH₂OH and 2 x CHOMe), 3.80
(1H, t, J 8.0 Hz, CH₂CHOH), 6.39 (1H, d, J 16.0 Hz, CH₂CH=CH), 6.78 (1H, app. dt, J
16.0 and 7.5 Hz, CH₂CH=), 8.01 (1H, OCH=); \(^{13}\)C NMR (90 MHz, CDCl₃) 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), C₂₂H₃₇O₇NNa 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 petroleum (bp 40 – 60 °C) as eluent,
and was obtained as an oil, which showed, \([\alpha]_D^{22} – 7.8\) (c 1.03 in CHCl₃); \([\nu]_{\text{max}}\) (soln,
CHCl₃, cm⁻¹) 3468, 2962, 2877, 1725; \(^1\)H NMR (500 MHz, CDCl₃) δ 0.98 (3H, d, J 6.9 Hz, CH₂CHCH₂), 1.06 (9H, CMe₃), 1.49 (1H, ddd,
J 14.0, 9.1 and 2.2 Hz, CH,H,CHOH), 1.57 (9H, CMe₃), 1.6 (1H, ddd, J 14.0, 9.1 and 2.2
Hz, CHH,CHOH), 1.68 (1H, app. qd, J 7.1 and 2.4 Hz, CH₃CH,CHOH), 1.96 (1H, app.
sp, J 6.2, CH CH₂ OSi), 2.38 (1H, app. dt, J 14.4 and 7.0 Hz, CHH.CH=), 2.62 (1H, app.
dtd, J 14.4, 6.9 and 1.1 Hz, CHH. CH=), 3.33 (3H, OMe), 3.36 (3H, OMe), 3.56 (1H, dd,
J 10.2 and 6.7 Hz, CHH. OSi), 3.56 – 3.61 (2H, m, CHCH₂CHOH), 3.63 (1H, td, J 6.7
and 2.4 Hz, = CH.CH₂CH), 3.69 (1H, dd, J 10.0 and 5.5 Hz, CHH.OSi), 3.74 (1H, brt, J
8.3 Hz, $\text{CH}_2\text{OH}$), 6.39 (1H, d, $J = 16.1$ Hz, $\text{CH} = \text{CH}_2\text{CH}_2$), 6.78 (1H, app, dt, $J = 16.1$ and 7.5 Hz, = $\text{CH}_2\text{CH}_2$), 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$_7$NSi requires 666.3836.

($4\text{S}, 5\text{R}, 6\text{S}, 8\text{S}, 9\text{R})$-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 °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$_3$); $\nu_{\text{max}}$ (soln, CHCl$_3$)/cm$^{-1}$ 3468; (Found: C, 73.0; H, 9.7; C$_{30}$H$_{46}$O$_4$Si, C, 72.3; H, 9.2%). $^1$H NMR (360 MHz, CDCl$_3$) $\delta$ 0.88 (3H, d, $J = 7.1$ Hz, $\text{CH}_3\text{CHCHOH}$), 0.97 (3H, d, $J = 6.9$ Hz, $\text{CH}_3\text{CHCH}_2\text{OSi}$), 1.07 (9H, s, (CH$_3$)$_3$C), 1.52 (1H, ddd, $J = 14.2$, 9.3, 3.3 Hz, CHFCHOH), 1.63 (1H, ddd, $J = 14.2$, 9.0, 2.6 Hz, CHHCHOH), 1.71 (1H, ddq, $J = 7.1$, 7.0, 4.5 Hz, =CHCH$_2$CHCH$_2$CH$_3$), 1.90-1.99 (1H, m, CH$_3$CHCH$_2$OSi), 2.20 (1H, ddd, $J = 14.1$, 7.3, 7.2 Hz, =CHCHH), 2.47 (1H, ddd, $J = 14.1$, 6.8, 6.7 Hz, =CHCHH), 3.38 (3H, s, OCH$_3$), 3.39 (3H, s, OCH$_3$), 3.55-3.61 (2H, m, CHHOSi, =CHCH$_2$CHOME), 3.63 (1H, ddd, $J = 9.0$, 4.5, 3.3 Hz, CHOH), 3.75 (1H, dd, $J = 10.0$, 5.6 Hz, CHHOSi), 3.73-3.81 (1H, m, CH$_2$CHCHOME), 5.03-5.09 (1H, m, CHH=), 5.13 (1H, dd, $J = 17.2$, 1.6 Hz, CHH=), 5.79 (1H, app ddt, $J = 13.6$, 7.3, 6.7 Hz, CH$_2$=CH), 7.36-7.47 (6H, m, ArH), 7.67-7.72 (4H, m, ArH); $^{13}$C NMR (90.6 MHz, CDCl$_3$) $\delta$ 11.5 (q), 12.6 (q), 19.4 (s), 27.0 (3q), 27.1 (3q), 28.3 (q), 31.2 (s), 32.2 (s), 33.2 (s), 34.4 (d), 36.5 (d), 38.6 (d), 40.1 (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).
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) C30H46O4Si + H requires 499.3244.

(4S,5R,6S,8S,9R)-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 (Na2SO4) and concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (0:1 to 1:5) as eluent to give the methoxymethyl ether (850 mg, 95%) as a colourless oil: [α]D23 -15.7 (c 0.92 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 2931, 1639 and 1088; (Found: C, 70.6; H, 9.3; C32H50O5Si requires C, 70.8; H, 9.3%); ¹H NMR (360 MHz, CDCl3) δ 0.91 (3H, d, J 6.2 Hz, CH3CHCH2OSi), 0.94 (3H, d, J 6.3 Hz, CH3CHCHOCH2OMe), 1.06 (9H, s, (CH3)3C), 1.42-1.52 (2H, m, CH2CHOCH2OMe), 1.85-2.00 (2H, m, =CHCH2CHCH2OMe), 2.33 (2H app dd, J 7.1, 6.1 Hz, =CHCH2), 3.10 (1H, ddd, J 11.3, 6.1, 5.7 Hz =CHCH2CHOME), 3.36 (3H, s, OCH3), 3.38 (3H, s, OCH3), 3.39 (3H, s, OCH3), 3.45-3.56 (1H, m, CH2CHCHOMe), 3.58 (1H, dd, J 10.0, 6.6 Hz, CHHOSi), 3.69 (1H, dd, J 10.0, 6.1 Hz, CHHOSi), 3.73-3.79 (1H, m, CH2=CH2), 4.61 (1H, d, J 6.8 Hz, OCHHOMe), 4.69 (1H, d, J 6.8 Hz, OCHHOMe), 5.05-5.15 (2H, m, CH2=), 5.84 (1H, dddd, J 17.3, 10.1, 7.1, 4.2 Hz, CH2=CH), 7.35-7.47 (6H, m, ArH), 7.65-7.71 (4H, m, ArH); ¹³C NMR (90.6 MHz,
\[ \text{CDCl}_3 \delta 9.2 \text{ (q), 12.3 (q), 19.4 (s), 27.0 (3q), 33.8 (t), 35.0 (t), 39.0 (d), 39.7 (d), 55.9 (q), 57.3 (q), 58.2 (q), 65.4 (t), 77.1 (d), 79.0 (d), 81.7 (d), 96.4 (t), 117.3 (t), 127.7 (4d), 129.6 (2d), 133.9 (s), 134.0 (s), 134.6 (d), 135.7 (4d); \text{m/z} (\text{EI}) 565.3315 \text{ (M}^+ + \text{Na)} \text{ C}_{32}\text{H}_{50}\text{O}_5\text{Si} + \text{Na requires 565.3325.} \]

\((3S,4R,5S,7S,8R)-9-(\text{tert-Butyldiphenylsilanyloxy})-1,1,3,7\text{-tremamethoxy-5-methoxymethoxy-4,8-dimethylnonanane (49b).} \)

A solution of the alkene 48b (2.6 g, 4.8 mmol) in dry dichloromethane (85 ml) was ozonised at \(-78^\circ\text{C}\) 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 \(-78^\circ\text{C}\) for 15 min. The solution was allowed to warm to room temperature over 1 h and then concentrated \textit{in vacuo}. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 \(^\circ\text{C}\)) (1:5 to 3:2) as eluent to give \((3S,4R,5S,7S,8R)-9-(\text{tert-Butyldiphenylsilanyloxy})-3,7\text{-dimethoxy-5-methoxymethoxy-4,8-dimethylnonanal (2.6 g, 99%) as a colourless oil: [\alpha]_D^{22} -19.1 (c 1.83 \text{ in CHCl}_3); \nu_{\max} (\text{soln, CHCl}_3)/\text{cm}^{-1} 2728 \text{ and 1723; } \text{\textsuperscript{1}H NMR (360 MHz, CDCl}_3 \delta 0.93 (3H, d, J 6.0 \text{ Hz, CH}_3\text{CHCH}_2\text{OSi}), 0.95 (3H, d, J 6.1 \text{ Hz, CH}_3\text{CHOCH}_2\text{OMe}), 1.06 (9H, s, (CH}_3)_3\text{C), 1.44-1.55 (2H, m, CH}_2\text{CHOCH}_2\text{OMe), 1.87-2.01 (2H, m, O=CHCH}_2\text{CHCH}_3, CHCH}_2\text{OSi), 2.61 (1H, ddd, J 16.3, 5.1, 2.1 \text{ Hz, CHHC=O) 2.69 (1H, ddd, J 16.3, 6.6, 2.1 Hz, CHHC=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, CHCH}_2\text{C=O), 3.58 (1H, dd, J 9.9, 6.5 Hz, CHHOSi), 3.64 (3H, m, CHHOSi, CHOCH}_2\text{OMe, CH}_2\text{CHCHOMe), 4.65 (1H, d, J 6.8 Hz, OCHHOMe), 4.69 (1H, d, J 6.8 Hz, OCHHOMe), 7.35-7.47 (6H, m, ArH), 7.65-7.74 (4H, m, ArH), 9.83 (1H, t, J 2.1 Hz, CH=O); } \text{\textsuperscript{13}C NMR (90.6 MHz, CDCl}_3 \delta 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} \]
$p$-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$_2$SO$_4$) and then concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (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 °C) as colourless crystals, mp 25-28 °C: $[\alpha]_D^{22}$ -19.4 (c 1.03 in CHCl$_3$); $\nu_{\text{max}}$ (soln, CHCl$_3$)/cm$^{-1}$ 2932 and 2858; (Found: C, 67.4; H, 9.5; C$_{33}$H$_{54}$O$_7$Si requires C, 67.1; H, 9.2%); $^1$H NMR (360 MHz, CDCl$_3$) $\delta$ 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$_3$)$_3$C), 1.46-1.52 (2H, m, CH$_2$CHOCH$_2$OMe), 1.81 (2H, app ddd, $J$ 5.8, 5.7, 1.5 Hz, CH$_2$CH(OMe)$_2$), 1.86-2.02 (2H, m, CHCHOCH$_2$OMe, CHCH$_2$OSi), 2.22 (1H, ddd, $J$ 12.3, 5.7, 5.6 Hz, CHCH$_2$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, CHCHCH$_2$OSi), 3.57 (1H, dd, $J$ 10.0, 6.6 Hz, CHHOSi), 3.71 (1H, dd, $J$ 10.0, 6.2 Hz, CHHOSi), 3.73-3.79 (1H, m, CHOCH$_2$OMe), 4.54 (1H, t, $J$ 5.8 Hz, CH(OMe)$_2$), 4.64 (1H, d, $J$ 6.8 Hz, OCHHOMe), 4.71 (1H, d, $J$ 6.8 Hz, OCHHOMe), 7.35-7.46 (6H, m, ArH), 7.65-7.74 (4H, m, ArH); $^{13}$C NMR (90.6 MHz, CDCl$_3$) $\delta$ 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 (El) 613.3542 (M$^+$ + Na) C$_{33}$H$_{54}$O$_7$Si + Na requires 613.3537.
The absolute stereochemistry of the acetal was determined by X-ray crystallographic analysis.\textsuperscript{26}

\((3S,4R,5S,7S,8R)\)-1,1,3,7-Tetrormethoxy-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 \textit{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\(_3\)); \(\nu_{\text{max}}\) (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\(_3\)) \(\delta\) 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, CHHCHOCH\(_2\)OMe), 1.57 (1H, ddd, \(J\) 14.6, 10.0, 1.7 Hz, CHHCHOCH\(_2\)OMe), 1.79 (2H, app t, \(J\) 6.0 Hz CH\(_2\)CH(OMe)\(_2\)), 1.82-1.93 (1H, m, CHCHOCH\(_2\)OMe), 2.20-2.34 (1H, m, CHCH\(_2\)OH) 2.96-3.01 (1H, br, OH), 3.17-3.25 (1H, m, C\(_{17}\)H\(_{36}\)O\(_7\)), 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, CHCHCH\(_2\)OH), 3.49 (1H, dd, \(J\) 10.8, 5.0 Hz, CHHOH), 3.68 (1H, dd, \(J\) 10.8, 9.0 Hz, CHHOH), 3.76 (1H, ddd, \(J\) 10.0, 4.4, 1.7 Hz CHOCH\(_2\)OMe), 4.51 (1H, t, \(J\) 6.0 Hz, CH(OMe)\(_2\)), 4.58 (1H, d, \(J\) 6.8 Hz, OCHHOMe), 4.67 (1H, d, \(J\) 6.8 Hz, OCHHOMe); \(^{13}\)C NMR (90.6 MHz, CDCl\(_3\)) \(\delta\) 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); \(m/z\) (El) 375.2353 (M\(^{+}\) + Na) C\(_{17}\)H\(_{36}\)O\(_7\) + Na requires 375.2359.

\((3S,4R,5S,7S,8R)\)-1,1,3,7-Tetrormethoxy-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 °C) (1:1) as eluent to give the aldehyde (410 mg, 78%) as a colourless oil: [α]D24 -82.3 (c 3.0 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 2718 and 1721; ¹H NMR (360 MHz, CDCl3) δ 0.91 (3H, d, J 7.0 Hz, CH₃CHCHOCH₂OMe), 1.08 (3H, d, J 7.1 Hz, CH₃CH=O), 1.48 (1H, ddd, J 14.6, 10.0, 2.7 Hz, CHHCHOCH₂OMe), 1.59 (1H, ddd, J 14.6, 10.2, 2.0 Hz, CHHCHOCH₂OMe), 1.79 (2H, m, CH₂CH(OMe)₂), 1.90 (1H, ddq, J 7.0, 4.8, 2.4 Hz, CHHCHOCH₂OMe), 2.65 (1H, ddq, J 7.1, 3.5, 0.8 Hz, CHC=O), 3.19-3.29 (1H, m, CH₂CH(OMe)₂), 3.34 (3H, s, OCH₃), 3.36 (3H, s, OCH₃), 3.37 (3H, s, OCH₃), 3.95 (3H, s, OCH₃), 3.43 (3H, s, OCH₃), 3.78-3.85 (2H, m, CHOCH₂OMe, CHCH₂OMe), 4.51 (1H, t, J 5.7 Hz, CH(OMe)₂), 4.62 (1H, d, J 6.8 Hz, OCH(OMe)₆), 4.70 (1H, d, J 6.8 Hz, OCHHOMe), 9.84 (1H, d, J 0.8 Hz, CH=O); ¹³C NMR (90.6 MHz, CDCl₃) 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 (El) 373.2197 (M⁺ + Na) C₁₇H₃₄O₇ + Na requires 373.2202.

(E)-(3R,4R,5R,9S,10S,12S,13R,14S)-1-Benzylxy-4-(tert-butyl-dimethyl-silyloxy)-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 °C in vacuo overnight. A solution of the β-keto phosphonate 51¹³ (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 (MgSO₄) 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 enone (362 mg, 68%) as a colourless oil: \([\alpha]D^{22}_{22} -68.4 (c 1.0 \text{ in CHCl}_3); \nu_{\text{max}} (\text{soln, CHCl}_3)/\text{cm}^{-1} 1690, 1663 \text{ and } 1622;\) (Found: C, 65.6; H, 9.9; C₃₉H₇₀O₉Si requires C, 65.9; H, 9.9%); \(^1\text{H NMR} (400 \text{ MHz, CDCl}_3) \delta -0.08 (3\text{H, s, CH}_3\text{Si}), 0.05 (3\text{H, s, CH}_3\text{Si}), 0.83 (9\text{H, s, (CH}_3)_3\text{C}), 0.88 (3\text{H, d, } J 6.8 \text{ Hz, CH}_3-13), 0.93 (3\text{H, d, } J 7.2 \text{ Hz, CH}_3-3), 1.00 (3\text{H, d, } J 7.2 \text{ Hz, CH}_3-5), 1.07 (3\text{H, d, } J 6.8 \text{ Hz, CH}_3-9), 1.35-1.55 (2\text{H, m, H-11}), 1.76 (2\text{H, app t, } J 6.0 \text{ Hz, H-2}), 1.80-1.90 (4\text{H, m, H-13, H-15, H-3}), 2.64-2.75 (1\text{H, m, H-9}), 3.04 (1\text{H, dq, } J 8.0, 7.2 \text{ Hz, H-5}), 3.18 (1\text{H, ddd, } J 11.4, 6.3, 6.2 \text{ Hz, H-14}), 3.31 (3\text{H, s, OCH}_3-16), 3.32 (3\text{H, s, OCH}_3-16), 3.33 (3\text{H, s, OCH}_3-14), 3.37-3.42 (1\text{H, m, H-10}), 3.38 (3\text{H, s, OCH}_3-10), 3.39 (3\text{H, s, CH}_2\text{OCH}_3), 3.42-3.59 (2\text{H, m, H-1}), 3.72-3.79 (1\text{H, m, H-12}), 3.91 (1\text{H, dd, } J 8.0, 2.2 \text{ Hz, H-4}), 4.45 (1\text{H, d, } J 11.9 \text{ Hz, CHHAr}), 4.49 (1\text{H, dd, } J 5.5, 2.0 \text{ Hz, H-16}), 4.51 (1\text{H, d, } J 11.9 \text{ Hz, CHHAr}), 4.59 (1\text{H, d, } J 6.7 \text{ Hz, CHOME}), 4.66 (1\text{H, d, } J 6.7 \text{ Hz, CHOME}), 6.15 (1\text{H, dd, } J 16.0, 1.4 \text{ Hz, H-7}), 6.90 (1\text{H, dd, } J 16.0, 6.5 \text{ Hz, H-8}), 7.24-7.35 (5\text{H, m, ArH}); \(^{13}\text{C NMR} (100 \text{ MHz, CDCl}_3) \delta -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⁺ + NH₄). C₃₉H₇₀O₉Si + Na requires 734.4687.
(3R,4R,5R,9S,10S,12S,13R,14S)-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 °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\(_3\)); \(\nu_{\text{max}}\) (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\(_3\)) \(\delta\) -0.07 (3H, s, CH\(_3\)Si), 0.06 (3H, s, CH\(_3\)Si), 0.83 (3H, d, J 6.8 Hz, CH\(_3\)-9), 0.84 (9H, s, (CH\(_3\))\(_3\)C), 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, CH\(_2\)H-2), 1.32-1.44 (2H, m, H-13, CHH H-11), 1.50 (1H, ddt, J 14.3, 8.5, 6.1 Hz, CHH H-8), 1.66 (1H, ddt, J 14.3, 5.2, 3.9 Hz, CHH H-8), 1.71-1.90 (6H, m, H-15, H-9, CHH H-11, H-3, CHH H-2), 2.10-2.36 (1H, br, OH), 2.47 (1H, ddd, J 18.1, 9.8, 5.2 Hz, CHH H-7), 2.56 (1H, ddd, J 18.1, 9.8, 6.1 Hz, CHH 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\(_2\)OCH\(_3\)), 3.56 (1H, dt, J 10.5, 6.8 Hz, CHH H-1), 3.66-3.79 (2H, m, H-12, CHH 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, CH\(_2\)OMe), 4.66 (1H, d, J 6.8 Hz, CH\(_2\)OMe); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) -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),...
(3R,4R,5R,9S,10S,12S,13R,14S)-4-(tert-Butyl-dimethyl-silyloxy)-1-(tert-butyl-diphenyl-silyloxy)-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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:1) as eluent to give the silyl ether (667 mg, 93%) as a colourless oil: [α]D26 -32.0 (c 1.02 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 2931, 2886 and 1712; (Found: C, 67.0; H, 9.9; C₄₈H₈₄O₉Si₂ requires C, 66.9; H, 9.8%); ¹H NMR (400 MHz, CDCl₃) δ -0.07 (3H, s, CH₃Si), 0.04 (3H, s, CH₅Si), 0.85 (9H, s, (CH₃)₃CSi(CH₃)₂), 0.87 (3H, d, J 7.2 Hz, CH₃-9), 0.88 (3H, d, J 7.0 Hz, CH₃-13), 0.94 (3H, d, J 6.9 Hz, CH₃-3), 0.95 (3H, d, J 7.1 Hz, CH₃-5), 1.05 (9H, s, (CH₃)₃CSi(Ph)₂), 1.19-1.49 (4H, m, CH₂H H-11, H-9, CH₂H H-8, CH₂H H-2), 1.71-1.85 (5H, m, H-15, H-13, H-3, CH₂H H-2), 1.86-1.95 (2H, m, CH₂H H-11, CH₂H 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, OCH₃-16), 3.34 (3H, s, OCH₂-16), 3.37 (3H, s, OCH₃-10), 3.38 (3H, s, OCH₃-14), 3.41 (3H, s, CH₂OCH₃), 3.64 (1H, ddd, J 10.0, 8.8, 5.6 Hz, CH₂H H-1), 3.70-3.82 (2H, m, H-12, CH₂H 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, CH₂OMe), 4.70 (1H, d, J 6.7 Hz, CH₂OMe), 7.35-7.47 (6H, m, ArH), 7.65-7.70 (4H, m, ArH); ¹³C
NMR (100 MHz, CDCl$_3$) $\delta$ -4.4 (q), -4.2 (q), 9.5 (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$_9$Si$_2$Na requires 883.5573.

(3S,4R,5S,7S,8S,12R,13R,14R)-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$_2$SO$_4$) 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$_3$); $\nu_{\text{max}}$ (soln, CHCl$_3$)/cm$^{-1}$ 2932, 2885, 2733, 1721 and 1712; $^1$H NMR (360 MHz, CDCl$_3$) $\delta$ -0.07 (3H, s, CH$_3$Si), 0.04 (3H, s, CH$_3$Si), 0.82-0.89 (6H, m, CH$_3$-8, CH$_3$-4), 0.85 (9H, s, (CH$_3)_3$CSi(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$_3)_3$CSi(Ph)$_2$), 1.39-1.48 (3H, m, CH$_3$H H-6, H-15), 1.73-1.97 (6H, m, H-4, CH$_3$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, CH$_3$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$_2$OCH$_3$), 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, CH$_3$HOMe), 4.69
(1H, d, J 6.8 Hz, CHOMe), 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$_3$) $\delta$ -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 (El) 837.5104 (M$^+$ + Na), 832.5550 (M$^+$ + NH$_4$) C$_{46}$H$_{78}$O$_8$Si$_2$ + Na requires 837.5133.

2-[(E)-(4S,5R,6S,8S,9S,13R,14R,15R)-14-(tert-Butyl-dimethyl-silyloxy)-17-(tert-butyl-diphenyl-silyloxy)-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 tert-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$_2$SO$_4$) and 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 oxazole (471 mg, 75%) as a colourless oil: $[\alpha]_D^{30}$ -26.7 (c 1.43 in CHCl$_3$); $\nu_{max}$ (soln, CHCl$_3$)/cm$^{-1}$ 2932, 2885, 1714, 1712, 1663 and 1575; (Found: C, 67.2; H, 9.3; N, 1.5 C$_{56}$H$_{89}$NO$_{10}$Si$_2$ requires C, 67.4; H, 9.2; N,
1.4%); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ -0.07 (3H, s, CH$_3$Si), 0.04 (3H, s, CH$_3$Si), 0.85 (9H, s, (CH$_3$)$_3$CSi(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$_3$)$_3$CSi(Ph)$_2$), 1.16-1.47 (4H, m, CH$_2$H H-7, H-9, CHH H-10, CHH H-16), 1.58 (9H, s, (CH$_3$)$_3$CO), 1.70-1.95 (5H, m, H-5, CHH H-7, CHH H-10, H-15, CHH 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$_2$OCH$_3$), 3.64 (1H, ddd, J 10.1, 8.8, 5.6 Hz, CHH H-17), 3.69-3.78 (3H, m, H-6, CHH H-17), 3.84 (1H, dd, J 8.0, 2.5 Hz, H-14), 4.59 (1H, d, J 6.7 Hz, CHHOMe), 4.64 (1H, d, J 6.7 Hz, CHHOMe), 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$_3$) $\delta$ -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 (El) 1002.5894 (M$^+$ + Na), 980.6043 (M$^+$ + H) C$_{55}$H$_{90}$NO$_{10}$Si$_2$ + Na requires 980.6103.


Dimethylboron bromide (2.5 M in dichloromethane, 600 $\mu$L, 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 °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 (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 (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:4 to 1:1) as eluent to give the *alcohol* (370 mg, 79%) as a colourless oil: [α]D°<sup>30</sup> - 23.4 (c 1.37 in CHCl₃); ν<sub>max</sub> (soln, CHCl₃)/cm<sup>-1</sup> 3480, 2932, 2885, 1714, 1713 and 1665; <sup>1</sup>H NMR (400 MHz, CDCl₃) δ -0.08 (3H, s, CH₃Si), 0.04 (3H, s, CH₂Si), 0.84 (9H, s, (CH₃)₂CSi(CH₃)₂), 0.87 (3H, d, J 7.0 Hz, CH₃-9), 0.88 (3H, d, J 7.3 Hz, CH₃-5), 0.91 (3H, d, J 7.1 Hz, CH₃-15), 0.95 (3H, d, J 7.0 Hz, CH₃-13), 1.05 (9H, s, (CH₃)₂CSi(Ph)₂), 1.18-1.40 (3H, m, CH₂H H-7, CH₂H H-10, CH₂H H-16), 1.51-1.66 (1H, m, CHH H-7) 1.58 (9H, s, (CH₃)₃CO), 1.68-1.93 (5H, m, H-5, H-9, CHH H-10, H-15, CHH H-16), 2.35-2.48 (1H, m, CHH H-3), 2.51 (1H, app dd, J 8.3, 2.7 Hz, CHH H-11), 2.56 (1H, app dd, J 8.3, 2.5 Hz, CHH H-11), 2.59-2.70 (1H, m, CHH 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, OCH₃-8), 3.41 (3H, s, OCH₃-4), 3.58-3.69 (3H, m, H-4, CHH H-17, OH), 3.69-3.82 (2H, m, H-6, CHH 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'); <sup>13</sup>C NMR (100 MHz, CDCl₃) 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), C₅₃H₈₅NO₉Si₂ + 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 °C 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 °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 °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: [α]D +22.7 (c 1.47 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 3625, 3429 and 1722; ¹H NMR (360 MHz, CDCl3) δ 1.49-1.73 (4H, m, CH₂CH₂CH₂OH), 2.45 (1H, dd, J 16.2, 7.3 Hz, CH/HCO₂Me), 2.50 (1H, dd, J 16.2, 5.2 Hz, CH/HCO₂Me), 3.00-3.20 (1H, br, OH), 3.64 (2H, app tt, J 7.0, 6.0 Hz, CH₂OH), 3.69 (3H, s, CH₃O), 3.75-3.90 (1H, br, OH), 4.04 (1H, app ddt, J 7.3, 5.2, 4.2 Hz, CHO); ¹³C NMR (90.6 MHz, CDCl3) δ 28.9 (t), 33.6 (t), 41.3 (t), 51.9 (d), 62.6 (t), 68.0 (q), 173.4 (s); m/z (El) 297.1482 (M⁺ + Na), C₁₃H₂₆O₄Si + 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 °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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:5) as eluent to give the primary alcohol silyl ether (13.6 g, 83%) as a colourless oil: [α]D₂² +9.4 (c 1.19 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 3607 and 1727; (Found: C, 56.2; H, 10.1; C₁₃H₂₆O₄Si requires C, 56.5; H, 10.2%); ¹H NMR (360 MHz, CDCl₃) δ 0.04 (6H, s, CH₃Si), 0.86 (9H, s, (CH₃)₃C), 1.44-1.69 (4H, m, CH₂CH₂CH₂O), 2.42 (1H, dd, J 16.0, 7.5 Hz, CHHC=O), 2.44 (1H, dd, J 16.0, 5.0 Hz, CHHC=O) 3.45 (1H, d, J 2.8 Hz, OH), 3.63 (2H, t, J 5.8 Hz, CH₂O), 3.69 (3H, s, OCH₃), 3.80-4.03 (1H, m, CH₂OSi), 3.95-4.03 (1H, m, OH); ¹³C NMR (90.6 MHz, CDCl₃) 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) C₁₃H₂₆O₄Si + 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 (MgSO₄) 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 silyl ether (23.7 g, 94%) as a colourless oil: [α]D₂² +19.7 (c 1.42 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 1732; (Found: C, 67.5; H, 8.9; C₂₉H₄₆O₄Si₂ requires C, 67.7; H, 9.0%); ¹H NMR (360 MHz, CDCl₃) δ 0.05 (3H, s, CH₃Si), 0.06 (3H, s, CH₃Si), 0.92 (9H, s, (CH₃)₃CSi(CH₃)₂), 1.11 (9H, s, (CH₃)₃CSi(Ph)₂), 1.47-1.62 (4H, m, CH₂CH₂CH₂O), 2.51 (1H, dd, J 14.8, 5.8 Hz, CHHC=O), 2.59 (1H, dd, J 14.8, 7.0 Hz, CHHC=O), 3.43-3.54 (2H, m, CH₂OSi), 3.60 (3H, s, OCH₃), 4.03 (1H, app pentet, J 5.8 Hz, CHOTBDPS), 7.41-7.48 (6H, m, ArH), 7.72-7.77 (4H, m, ArH); ¹³C 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$_{26}$O$_4$Si + 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 °C under a nitrogen atmosphere. The solution was stirred at 0 °C 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 °C) (1:4) as eluent to give the alcohol (17.5 g, 97%) as a colourless oil: [α]$_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$_4$Si$_2$ requires C, 69.0; H, 8.1%); $^1$H NMR (360 MHz, CDCl$_3$) δ 1.08 (9H, s, (CH$_3$)$_3$C), 1.45-1.61 (4H, m, CH$_2$CH$_2$CH$_2$O), 2.49 (1H, dd, $J$ 14.9, 6.1 Hz, CH=O), 2.57 (1H, dd, $J$ 14.9, 6.7 Hz, CH=CH=O), 3.43-3.48 (2H, m, CH$_2$OH), 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$_4$Si + 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 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 20 min and then imidazole (2.8 g, 40.6 mmol) was added in one portion. The mixture was stirred at 0 °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 °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 °C) (1:9) as eluent to give the iodide (8.7 g, 86%) as a colourless oil: [α]_D^22 +27.7 (c 2.21 in CHCl₃); ν_max (soln, CHCl₃)/cm⁻¹ 1732 and 611; (Found: C, 54.2; H, 6.1; C₂₃H₃₁IO₃Si₂ requires C, 54.1; H, 6.1%); ¹H NMR (360 MHz, CDCl₃) δ 1.07 (9H, s, (CH₃)₃C), 1.54-1.63 (2H, m, C₆H₂CH₂I), 1.81 (2H, app dt, J 15.0, 7.3 Hz, C₆H₂CH₂CH₂I), 2.42 (1H, dd, J 14.9, 6.0 Hz, CHH₂C=O), 2.54 (1H, dd, J 14.9, 6.6 Hz, CHH₂C=O), 2.90-3.01 (2H, m, CH₂I), 3.56 (3H, s, OCH₃), 4.24 (1H, app pentet, J 6.0 Hz, CHOTBDPS), 7.35-7.49 (6H, m, ArH), 7.63-7.74 (4H, m, ArH); ¹³C NMR (90.6 MHz, CDCl₃) 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 (Cl) 453.0373 (M⁺ - Bu), C₂₃H₂₁IO₃Si - Bu requires 453.0383.

Methyl (3S)-6-(benzyloxy)-3-hydroxyhexanoate (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 °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 °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 °C) (1:1 to 1:0) as eluent to give the alcohol (424 mg, 84%) as a colourless oil; 

\[ \alpha \]D \text{25} +9.8 (c 1.0 in CHCl3) \text{[lit34]} \[ \alpha \]D \text{22} +23.7 (c 1.0 in CHCl3); \nu_{max} (soln, CHCl3)/cm⁻¹ 3417, 2953, 2863 and 1725; \text{H NMR} (360 MHz; CDCl3) \delta 1.50-1.68 (2H, m, CH₂CH₂CH₂OBn), 1.68-1.86 (2H, m, CH₂CH₂OBn), 2.44 (1H, dd, J 16.4, 8.3 Hz CHHCO₂Me), 2.52 (1H, dd, J 16.4, 4.2 Hz, CHHCO₂Me), 3.15-3.39 (1H, br, OH), 3.52 (2H, t, J 6.1, CH₂OBn), 3.71 (3H, s, CH₃O), 4.05 (1H, app septet, J 4.2, CHOH), 4.51 (2H, s, CH₂Ph), 7.25-7.38 (5H, m, ArH); \text{C NMR} (90.6 MHz; CDCl3) \delta 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 (El) 275.1261 (M⁺ + Na), C₁₄H₂₀O₄ + 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
(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\textsuperscript{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\textsubscript{4}) and concentrated in vacuo to leave the alcohol (14.6 g, 90%) as a colourless oil: [α\textsubscript{D}]+22 –26.0 (c 1.38 in CHCl\textsubscript{3}); ν\textsubscript{max} (soln, CHCl\textsubscript{3})/cm\textsuperscript{–1} 3624 and 1685; (Found: C, 61.9; H, 9.95; N, 5.0; C\textsubscript{14}H\textsubscript{27}NO\textsubscript{4} requires C, 61.5; H, 10.0; N, 5.1%); \textsuperscript{1}H NMR (360 MHz; C\textsubscript{6}D\textsubscript{6}, 333K) δ 0.83 (3H, d, J 7.2 Hz, CH\textsubscript{3}CH), 1.22-1.41 (2H, m, CH\textsubscript{2}CH\textsubscript{2}OH), 1.38 (9H, s, (CH\textsubscript{3})\textsubscript{3}C), 1.51 (3 H, s, CH\textsubscript{3}CN), 1.62-1.79 (1H, m, CHCH\textsubscript{3}), 1.73 (3H, s, CH\textsubscript{3}CN), 2.09-2.21 (1H, br, OH), 3.39-3.49 (1H, m, CHHCHN), 3.49-3.57 (1H, m, CHHCHN) 3.58-3.65 (2H, m, CH\textsubscript{2}OH), 3.69-3.88 (1H, m, CHN); \textsuperscript{13}C NMR (90.6 MHz; C\textsubscript{6}D\textsubscript{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\textsuperscript{+} + Na), C\textsubscript{14}H\textsubscript{27}NO\textsubscript{4} + Na requires 296.1838.
(R)-4-((S)-3-Benzylxoy-1-methyl-propyl)-2,2-dimethyl-oxazolidine-3-carboxylic acid tert-butyl ester (61c). Sodium hydrdride (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 °C under a nitrogen atmosphere. The solution was stirred at 0 °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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:9) as eluent to give the corresponding benzyl ether (13 g, 78%) as a colourless oil: [α]D₂₂ –25.8 (c 1.25 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 1682; (Found: C, 69.5; H, 9.0; N, 3.8; C₂₁H₃₃NO₄ requires C, 69.4; H, 9.2; N, 3.9%); ¹H NMR (360 MHz; C₆D₆, 333 K) δ 0.94 (3H, d, J 6.8, CH₃), 1.33-1.46 (1H, m, CHCH₂O), 1.51 (9 H, s, (CH₃)₃C), 1.59 (3H, s, CH₂CN), 1.77 (3H, s, CH₃CN), 1.92 (1H, ddt, J 13.7, 7.2, 3.6 Hz, CHH₂CH₂O), 2.26-2.37 (1H, m, CHCH₃), 3.32-3.45 (2H, m, CH₂OBn), 3.66-3.95 (3H, m, OCH₂CH₃N), 4.41 (1H, d, J 12.2 Hz, OCH₂Ph), 4.47 (1H, d, J 12.2 Hz, OCH₂Ph), 7.12 (5H, m ArH); ¹³C NMR (90.6 MHz; C₆D₆, 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), C₂₁H₃₃NO₄ + Na requires 386.241.

(S)-4-((1S,2S)-4-Benzoyloxy-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 °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 (MgSO₄) 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 °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 (MgSO₄) 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: [α]D$_{23}$ –42.3 (c 1.50 in CHCl₃); ν$_{max}$ (soln, CHCl₃)/cm$^{-1}$ 3626, 3425, 1698 and 1674; (Found: C, 63.8; H, 8.5; N, 6.3; C$_{24}$H$_{38}$N$_2$O$_6$ requires C, 64.0; H, 8.5; N, 6.2%); $^1$H NMR (360 MHz; C$_6$D$_6$, 333 K) δ 1.02 (3H, d, $J$, 6.9 Hz, C$_{3}$H), 1.50 (9H, s, (CH$_3$)$_3$C), 1.54 (3H, s, CCH$_3$), 1.52-1.60 (1H, m, CHHCH$_2$O), 1.81 (3H, s, CCH$_3$), 1.93 (1H, ddt, $J$ 13.2, 6.6, 0.8 Hz, CHHCH$_2$O), 2.11-2.16 (1H, m, CHCH$_3$), 3.49-3.60 (3H, m, CH$_2$OBn, OH), 3.65-3.78 (2H, m, CH$_2$OH), 3.94 (1H, dd, $J$ 8.2, 5.2 Hz, CHHCHNBOc), 4.16 (1H, ddd, $J$ 14.0, 5.2, 5.1 Hz, NCHCH$_2$OH), 4.32 (1H, br d, $J$ 8.2 Hz, CHHCHNBOc), 4.37-4.41 (1H, m, CHNBoc), 4.43 (1H, d, $J$ 12.2 Hz CHHPh), 4.46 (1H, d, $J$ 12.2 Hz, CHHPh), 6.75-6.95 (1H, br, NH), 7.11-7.40 (5H, m, ArH); $^{13}$C NMR (90.6 MHz; C$_6$D$_6$, 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), C₂₄H₃₈N₂O₆ + Na requires 473.2628.

(S)-4-((S)-3-Benzylloxy-1-methyl-propyl)-2',2''-dimethyl-4',5'-dihydro-
[2,4']bioloxazol-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 (MgSO₄) 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: [α]D²₂ –117.5 (c 0.81 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 3690, 2716, 1731 and 1682; ¹H NMR (360 MHz; CDCl₃, 318 K, rotamers) δ 0.85 (2H, d, J 7.0 Hz, CH₃CH), 1.00 (1H, d, J 7.0 Hz, CH₂CH) 1.40-1.55 (13H, m, CH₃, (CH₃)₃C), CHHCH₂OBn), 1.62-1.85 (4H, m, CH₃ and CHHCH₂OBn), 2.50 (1H, app dq, J 7.0, 3.2 Hz, CHCH₃), 3.43 (0.3H, ddd, J 8.3, 3.2 Hz, CH₂OBn), 3.47-3.60 (1H, m, CH₂OBn), 3.65 (0.7H, ddd, 9.8, 7.0, 5.2 Hz, CH₂OBn), 4.06 (1H, dd, J 15.7, 8.6 Hz, CHHCHN), 4.15-4.33 (1H, m, CHC=O), 4.34-4.59 (3H, m, CHHCHN, CH₂Ph), 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); ¹³C NMR (90.6 MHz; CDCl₃, 318 K, major rotamer) δ 14.4 (q), 24.0 (q), 27.0 (q), 28.2 (3q), 29.9 (d), 33.3
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 °C 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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:9 to 1:1) as eluent to give the oxazole (4.7 g, 72%) as a waxy colourless solid, mp 64-68 °C: [α]D₂₂ −41.8 (c 0.31 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 1698 and 1573; (Found: C, 66.8; H, 8.1; N, 6.7; C₂₅H₄₀N₂O₇ requires C, 67.0; H, 8.0; N, 6.5%); ¹H NMR (360 MHz; C₆D₆, 333 K) δ 1.30 (3H, d, J₆.8 Hz, C₃H), 1.47 (9H, s, (CH₃)₃C), 1.71 (3H, s, CCH₃), 1.90 (1H, app dt, J 13.6, 6.7 Hz, CHHCH₂O), 2.00 (3H, s, CCH₃), 2.16 (1H, ddt, J 13.6, 6.2, 1.1 Hz, CHHCH₂O), 3.01 (1H, ddq, J 6.8, 6.7, 6.6 Hz, CHCH₃), 3.46-3.57 (2H, m, CH₂OBn), 3.88 (1H, dd, J 8.8, 6.6 Hz, CHHCHN), 3.99 (1H, dd, J 8.8, 3.4 Hz, CHHCHN), 4.45 (2H, s, CH₂Ar), 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); ¹³C NMR (90.6 MHz; C₆D₆, 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⁺
(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 °C: [α]D 22 -73.4 (c 0.61 in CHCl3); νmax (soln, CHCl3)/cm⁻¹
3690, 1699 and 1602; (Found: C, 59.8; H, 8.3; N, 8.3; C17H28N2O5 requires C, 60.0;
H, 8.3; N, 8.2%); 1H NMR (360 MHz; C6D6, 333 K) δ 1.26 (3H, d, J 6.9, C(CH3)), 1.44
(9H, s, (CH3)3C), 1.65 (3H, s, CCH3), 1.79 (1H, app dt, J 13.3, 6.8 Hz, CHCH2O),
1.91-2.01 (1H, m, CHHCH2O), 1.92 (3H, s, CCH3), 2.79-2.90 (1H, br, OH), 2.94 (1H,
ddq, J 6.8, 6.7, 6.6 Hz, CHCH3), 3.69 (2H, t, J 6.3 Hz, CH2OH), 3.93 (1H, dd, J 8.7,
6.5 Hz, CHHCHN), 4.02 (1H, dd, J 8.7, 2.8 Hz, CHHCHN), 4.90-5.08 (1H, m, CHN),
7.15 (1H, s, CHCN); 13C NMR (90.6 MHz; C6D6, 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 (El) 363.1901 (M⁺ + Na), 285.1517 (M⁺ – Bu +
2H), C17H28N2O5 + 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 °C under a nitrogen atmosphere. The solution was
stirred at –78 °C 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 °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 (MgSO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using diethyl ether-light petroleum (bp 40-60 °C) (1:1) as eluent to give the aldehyde (3.5 g, 87%) as a colourless oil: [α]D²² -69.4 (c 1.90 in CHCl₃); νmax (soln, CHCl₃)/cm⁻¹ 2727, 1722 and 1698; ¹H NMR (360 MHz; C₆D₆, 333 K) δ 1.05 (3H, d, J 6.9 Hz, CH₃CH), 1.35 (9H, s, (CH₃)₃C), 1.59 (3H, s, CCH₃), 1.89 (3H, s, CCH₃), 2.11 (1H, ddd, J 16.8, 6.9, 1.7 Hz, CHHCHO), 2.46 (1H, ddd, J 16.8, 6.9, 1.7 Hz, CHHCHO) 3.04 (1H, ddq, J 6.9, 6.8, 6.7 Hz, CHCH₃), 3.75 (1H, dd, J 8.9, 6.5 Hz, CHHCHN), 3.86 (1H, dd, J 8.9, 3.0 Hz, CHHCHN), 4.68-5.10 (1H, m, CHN), 6.85 (1H, s, CHCN), 9.42 (1H, t, J 1.7 Hz, CHO); ¹³C NMR (90.6 MHz; C₆D₆, 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 (Cl) 339.1911 (M⁺ + H), 393.1779 (M⁺ + Na + MeOH), 283.1110 (M⁺ – Bu + 2H), 239.1414 (M⁺ – Boc + 2H) C₁₇H₂₆N₂O₅ + H requires 339.1920.

(L)-4-{[(1S,7S)-7-(tert-Butyl-diphenyl-silanyloxy)-8-carboxy-1-methyl-3-oxo-octyl]-2',2'-dimethyl-4',5'-dihydro-[2,4']bioazolyl-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 (MgSO₄) 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 °C) as colourless crystals, mp 23-25 °C: \([\alpha]_D^{29} -22.1 \text{ (c 1.46 in CHCl}_3\); \(\nu_{\text{max}}\) (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\(_2\)O\(_8\)Si requires C, 66.3; H, 7.7; N, 4.0%); \(^1\)H NMR (400 MHz; C\(_6\)D\(_6\), 333 K) \(\delta\) 1.16 (3H, d, \(J 6.8\) Hz, CHCH\(_3\)), 1.18 (9H, s, \((\text{CH}_3)_3\text{Si}\)), 1.37 (9H, s, \((\text{CH}_3)_3\text{CO}\)), 1.47-1.55 (4H, m, CH\(_2\)CH\(_2\)CHOSi), 1.58-1.62 (3H, br, CH\(_3\)C), 1.84-1.96 (5H, m, CH\(_2\)COCH\(_2\)CHCH\(_3\), CH\(_3\)C), 2.17-2.25 (1H, m, CHHCHCH\(_3\)), 2.47 (1H, dd, \(J 15.1, 6.1\) Hz, CHHCO\(_2\)H), 2.58 (1H, dd, \(J 15.1, 6.2\) Hz, CHHCO\(_2\)H), 2.61 (1H, dd, \(J 16.7, 6.2\) Hz, CHHCHCH\(_3\)), 3.26 (1H, ddq, \(J 6.8, 6.7, 6.6\) Hz, CHCH\(_3\)), 3.87 (1H, dd, \(J 8.8, 6.5\) Hz, CHHCHN), 3.93 (1H, dd, \(J 8.8, 3.0\) Hz, CHHCHN), 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\(_6\)D\(_6\), 333 K) \(\delta\) 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); \(m/z\) (El) 707.3686 (M\(^+\) + H), 729.3521 (M\(^+\) + Na), C\(_{39}\)H\(_{54}\)N\(_2\)O\(_8\)Si + H requires 707.3728.

\((3R,4R,5R)-[4-(\text{tert-Butyldimethylsilanyloxy})-7-(\text{tert-butyldiphenylsilanyloxy})-3,5-\text{dimethyl-2-oxoheptyl}]\text{-phosphonic acid, dimethyl ester (74).}\) 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 TBDPSCI (43 \(\mu\)l, 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, [α]D$^2$2 – 58.5 (c 0.40 in CHCl$_3$); ν$_{max}$ (soln, CHCl$_3$, cm$^{-1}$) 1714; $^1$H 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, CH$_3$CH), 1.12 (3H, d, J 6.2 Hz, CH$_3$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, CHH.P=O), 3.13 (1H, app, qn, J 7.1 Hz, CH$_2$CH.C=O), 3.44 (1H, dd, J 22.2 and 14.0 Hz, CHH.P=O), 3.71 (1H, ddd, J 9.5, 9.1 and 5.4 Hz, CHHOSi), 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$_{c-p}$ 509 Hz), 50.1 (d), 52.9 (CH$_3$, d, J$_{c-p}$ 24.9 Hz), 53.0 (CH$_3$, d, J$_{c-p}$ 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$_{c-p}$ 24.5 Hz). m/z (ESI) 635.3380 (M$^+$ + H), C$_{33}$H$_{55}$O$_6$PSi$_2$ 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$_2$SO$_4$) 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: [α]_D^{29} –27.7 (c 1.01 in CHCl₃); ν_max (soln, CHCl₃)/cm⁻¹ 2932, 2858, 1702 and 1703; (Found: C, 67.8; H, 8.6; N, 2.2; C₉₂H₁₃₇N₃O₁₆Si₃ requires C, 68.0; H, 8.5; N, 2.6%). ¹H NMR (400 MHz, CDCl₃) δ -0.08 (3H, s, CH₃Si), 0.04 (3H, s, CH₃Si), 0.79 (3H, d, J 6.8 Hz, CH₃-29), 0.84 (9H, s, (CH₃)₂CSi(CH₃)₂), 0.86 (3H, d, J 7.0 Hz, CH₃-39), 0.87 (3H, d, J 7.0 Hz, CH₃-33), 0.94 (3H, d, J 7.0 Hz, CH₃-37), 1.02 (9H, s, (CH₃)₂CSi(Ph)₂), 1.05 (9H, s, (CH₃)₂CSi(Ph)₂), 1.19 (3H, d, J 6.5 Hz, CH₃-9), 1.28 (9H, s, (CH₃)₂COOC-17), 1.40-1.56 (5H, m, H-4, H-31 CH/H H-40), 1.49 (3H, s, CH₃CN), 1.58 (9H, s, (CH₃)₃COOCN), 1.65-1.83 (7H, m, H-5, H-29, H-33, H-34, CHH H-40), 1.73 (3H, s, CH₃CN), 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, CHH H-35), 2.67-2.80 (2H, m, CHH 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, CH₂OC-32), 3.26 (3H, s, CH₂OC-28), 3.63 (1H, ddd, J 10.6, 8.8, 5.6 Hz, CH/H H-41), 3.74 (1H, ddd, J 10.6, 6.6, 4.5 Hz, CHH H-41), 3.83 (1H, dd, J 8.1, 2.5 Hz, H-38), 4.00-4.13 (1H, m, CHH H-19), 4.14-4.26 (2H, m, CHH 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); ¹³C NMR (90.6 MHz, CDCl₃) 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), C₉₂H₁₃₇N₃O₁₆Si₃ + H requires 1624.9385.
The C38 Alcohol (81a). Trimethylsilyl trifluoromethanesulphonate (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 °C under a nitrogen atmosphere. The mixture was stirred at -78 °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 (Na2SO4) and then concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:4 to 3:2) as eluent to give the alcohol (111 mg, 85%), as a colourless foam: [α]D23 –12.8 (c 1.0 in CHCl3); νmax (soln, CHCl3)/cm⁻¹ 3622, 2931, 2858 and 1708; ¹H NMR (400 MHz, CDCl3) δ 0.78 (3H, d, J 6.7 Hz, CH₃-33), 0.83 (3H, d, J 6.9 Hz CH₃-29), 0.92 (3H, d, J 6.8 Hz, CH₃-39), 1.03 (9H, s, (CH₃)₃CSi(Ph)₂), 1.06 (9H, s, (CH₃)₃CSi(Ph)₂), 1.07 (3H, d, J 7.4 Hz, CH₃-37), 1.28 (3H, d, J 7.0 Hz, CH₃-9), 1.35-1.63 (5H, m, CHH H-4, H-31, CHH H-34, CHH H-40), 1.66-1.82 (6H, m, CHH H-4, H-5, H-33, CHH H-34, CHH 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, CHH H-8), 2.42-2.51 (1H, m, CHH H-27), 2.50-2.64 (4H, m, H-2, H-35), 2.64-2.69 (1H, m CHH 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, CHH H-8), 3.18-3.24 (1H, m, H-28), 3.27 (3H, s, CH₃OC-32), 3.31 (3H, s, CH₃OC-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 CHH H-41), 3.77 (1H, ddd, J 10.4, 5.5, 5.4 Hz, CHH 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); ¹³C NMR (90.6 MHz, CDCl₃) 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)
The C38 Acetate (81b). Acetic anhydride (2.2 ml) 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 (Na₂SO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:2 to 2:1) as eluent to give the acetate (87 mg, 84%), as a colourless foam: [α]D$_{24}^{24}$ = −14.0 (c 1.0 in CHCl₃); ν$_{max}$ (soln, CHCl₃)/cm⁻¹ 2931, 2858 and 1731; ¹H NMR (400 MHz, CDCl₃) δ 0.78 (3H, d, J 6.7 Hz, CH₃-33), 0.82 (3H, d, J 6.8 Hz CH₃-29), 0.83 (3H, d, J 6.8 Hz, CH₃-39), 1.03 (9H, s, (CH₃)$_3$CSi(Ph)$_2$), 1.06 (9H, s, (CH₃)$_3$CSi(Ph)$_2$), 1.00-1.08 (3H, m, CH₃-37), 1.28 (3H, d, J 6.9 Hz, CH₃-9), 1.37-1.61 (5H, m, CHH H-4, H-31, CHH H-34, CHH H-40), 1.64-1.83 (6H, m, CHH H-4, H-5, H-33, CHH H-34, CHH H-40), 1.85-1.93 (1H, m, H-29), 1.95 (3H, s, CH₃CO), 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, CHH H-8), 2.43-2.52 (2H, m, CHH H-27, CHH H-35), 2.56 (1H, dd, J 5.2, 4.6 Hz, CHH H-2), 2.57 (1H, dd, J 5.2, 4.5 Hz, CHH H-2), 2.62 (1H, ddd, J 5.1, 2.5, 2.0 Hz, CHH H-35), 2.64-2.69 (1H, m CHH 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, CHH H-8), 3.20 (1H, ddd, J 8.4, 4.6, 4.5 Hz, H-28), 3.27
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 (Na2SO4) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:2 to 1:0) as eluent to give the alcohol (26 mg, 61%), as a colourless foam: [α]D27 −15.0 (c 1.0 in CHCl3); ν max (soln, CHCl3)/cm⁻¹ 3624, 2932, 2858 and 1731; ¹H NMR (400 MHz, CDCl3) δ 0.78 (3H, d, J 6.8 Hz, CH3-33), 0.83 (3H, d, J 6.9 Hz CH3-29), 0.93 (3H, d, J 6.9 Hz, CH3-39), 1.02
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 (Na₂SO₄) and concentrated in vacuo. The residue was purified by chromatography on silica using ethyl acetate-light petroleum (bp 40-60 °C) (1:2 to 1:0) as eluent to give the aldehyde (6.4 mg, 80%), as a colourless oil: 

\[ [\alpha]_D^{27} -13.8 \text{ (c 0.64 in CHCl}_3); \nu_{\text{max}} \text{ (soln, CHCl}_3)/\text{cm}^{-1} 2932, 2398 and 1726; 1^H \text{ NMR (500 MHz, CDCl}_3 \delta 0.78 \text{ (3H, d, } J 6.8 \text{ Hz, CH}_3\text{-33), 0.83 \text{ (3H, d, } J 7.0 \text{ Hz CH}_3\text{-29), 0.98 \text{ (3H, d, } J 6.9 \text{ Hz, CH}_3\text{-39), 1.02 \text{ (9H, s, (CH}_3\text{)_3CSi(Ph)}_2), 1.10 \text{ (3H, d, } J 7.1 \text{ Hz, CH}_3\text{-37), 1.19-1.26 \text{ (1H, m, CH}_2\text{H H-34), 1.28 \text{ (3H, d, } J 7.0 \text{ Hz, CH}_3\text{-9), 1.40-1.48 \text{ (2H, m, H-4), 1.42 \text{ (1H, ddd, J 11.2, 9.9, 1.0 Hz, CH}_2\text{H H-31), 1.53 \text{ (1H, ddd, J 15.7, 11.2, 2.0 Hz, CH}_2\text{H H-31), 1.68-1.79 \text{ (4H, m, H-5, H-33, CH}_2\text{H H-34), 1.83-1.89 \text{ (1H, m, H-29), 2.00 \text{ (3H, s, CH}_3\text{CO), 2.20-2.39 \text{ (2H, m, H-6), 2.31 \text{ (1H, dd, J 8.7, 1.9 Hz, CH}_2\text{H H-40), 2.38 \text{ (1H, dd, J 16.7, 5.8 Hz, CH}_2\text{H H-8), 2.42-2.54 \text{ (5H, m, CH}_2\text{H H-27, H-35, H-39, CH}_2\text{H H-40), 2.54 \text{ (1H, dd, J 15.5, 5.6 Hz, CH}_2\text{H H-2), 2.59 \text{ (1H, dd, J 15.5, 5.3 Hz, CH}_2\text{H H-2), 2.61-2.67 \text{ (1H, m CH}_2\text{H H-27), 2.80 \text{ (1H, dq, J 7.8, 7.1 Hz, H-37), 2.88-2.92 \text{ (1H, m, H-32), 3.15 \text{ (1H, dd, J 16.7, 7.6 Hz, CH}_2\text{H H-8), 3.19-3.23 \text{ (1H, m, H-28), 3.26 \text{ (3H, s, CH}_3\text{OC-32), 3.31 \text{ (3H, s, CH}_3\text{OC-28), 3.38 \text{ (1H, ddq, J 7.6, 7.0, 5.8 Hz, H-9), 4.29 \text{ (1H, dddd, J 5.3, 5.4, 5.5, 5.6 Hz, H-3), 5.07-5.12 \text{ (1H, m, H-30), 5.10 \text{ (1H, dd, J 7.8, 4.6 Hz, H-38), 6.35 \text{ (1H, d, J 16.0 Hz, H-25), 7.08 \text{ (1H, ddd, J 16.0, 9.4, 6.2 Hz, H-26), 7.31-7.42 \text{ (7H, m, ArH, H-14), 7.67-7.74 \text{ (4H, m, ArH), 8.06 \text{ (2H, s, H-19, H-24), 9.8 \text{ (1H, app t, J 1.9 Hz, H-41); }^{13}\text{C NMR (125 MHz, CDCl}_3 \delta 8.8 \text{ (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.}