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SUPPORTING INFORMATION

Total Synthesis of Macrodiolide Ionophores Aplasmomycin and Boromycin via Double Ring Contraction

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(2*S*,3*R*)-(-)-1,2-Epoxy-3-butanol (18). **A. From 19 via Kinetic Resolution.** To a solution of titanium tetraisopropoxide (5.94 mL, 20.0 mmol) in methylene chloride (200 mL) at -20 °C was added (-)-diethyl (D)-tartrate and the mixture was stirred for 5 min. To this solution was added **19** (1.79 mL, 20.0 mmol) followed by a solution of *tert*-butyl hydroperoxide (3.6 mL, 40 mmol) in methylene chloride (11 mL) and the mixture was stored at -20 °C for 48 h. To the solution was added dimethyl sulfide (5.9 mL, 80 mmol) and the mixture was stirred at -20 °C for 10 h. The solution was diluted with ether (20 mL), saturated aqueous sodium sulfate (8 mL) was added and the mixture was stirred vigorously at room temperature for 2 h. The resulting suspension was filtered through Celite and the filtrate was concentrated by distillative removal of the solvent. The residure was chromatographed on silica (25 g, pentane:ether 1:1 to 1:2) to give **18** (457 mg, 52%) as a colourless oil: $[\alpha]_D^{20}$ -16.3 (*c* 0.97 MeOH); IR (neat) 3400, 1240 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.23 (d, *J* = 6.8 Hz, 3H), 2.30 (s, 1H, exchanged with D_2O), 2.78 (d, *J* = 3.2 Hz, 2H), 3.00 (q, *J* = 3.2 Hz, 1H), 3.96 (dq, *J* = 6.8, 3.2 Hz, 1H); HRMS (EI) calcd for $C_4H_8O_2$ *m/z* 88.0524, found 88.0526.

B. From (2*R*,3*R*)-(-)-Dihydroxybutyric Acid. To a solution of cyclopentanone (10.0 g, 0.12 mmol) in benzene (150 mL) was added (2*R*,3*R*)-dihydroxybutyric acid (12.0 g, 0.10 mmol) and *p*-toluenesilfonic acid (100 mg) and the mixture was heated at 80 °C for 10 h. The cooled mixture was decanted from a small quantity of a brown residue and the solvent was removed under reduced pressure to give virtually pure **20** (17.7 g, 95%) as a viscous oil. This material was used without further purification in the next reaction.

To a suspension of lithium aluminium hydride (3.8 g, 0.10 mol) in tetrahydrofuran (200 mL) at 0 °C was added a solution of **20** (17.7 g, 0.095 mol) and the suspension was refluxed for 1 h. To the cooled mixture (0 °C) was added carefully ethyl acetate (5 mL) followed by water (4 mL)

and aqueous sodium hydroxide (15%, 4 mL). The mixture was diluted with a further quantity of water (12 mL) and the resulting precipitate was filtered off. The filtered solid was washed thoroughly with ether (3 x 50 mL) and the combined filtrate was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give **21** (11.7 g, 72%) as a colourless oil which was used in the next reaction without further purification.

To a stirred solution of **21** (11.7 g, 0.068 mol) in pyridine (150 mL) at 0 °C was added *p*-toluenesulfonyl chloride (25.0 g, 0.14 mol) in several portions and the mixture was stored at -20 °C for 24 h. The mixture was poured on to ice (400 g) and the solution was extracted after warming to room temperature with ether (3 x 150 mL). The combined extract was washed with saturated aqueous copper sulfate, water and brine and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to leave an oil which was crystallized from a mixture of methylene chloride and carbon tetrachloride at 0 °C to give **22** (18.1 g, 81%) as colourless needles: mp 41-43 °C; $[\alpha]_D^{20}$ -20.9 (*c* 0.35 MeOH); IR (neat) 1360, 1180, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, *J* = 6.9 Hz, 3H), 1.70 (m, 8H), 2.42 (s, 3H), 3.97 (m, 4H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.83 (d, *J* = 7.2 Hz, 2H); HRMS (EI) calcd for $C_{16}H_{22}O_5S$ *m/z* 326.1188, found 326.1184.

To a solution of **22** (13.3 g, 41.0 mmol) in methanol (150 mL) at room temperature was added *p*-toluenesulfonic acid and the mixture was stirred for 10 h. Solid potassium carbonate was added, the suspension was filtered through Celite and the filtrate was concentrated under reduced pressure to leave a pale pink coloured oil. The oil was crystallized from a mixture of methylene chloride and carbon tetrachloride to give **23** (7.49 g, 70%) as prisms: mp 69-71 °C; $[\alpha]_D^{20}$ -14.2 (*c* 1.1 H_2O); IR (neat) 3550, 1600, 1350 cm^{-1}; IR (neat) 3550, 1600, 1350 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (d, *J* = 6.6 Hz, 3H), 2.45 (s, 3H), 2.80 (br s, 2H, exchanged with D_2O), 3.82

(m, 2H), 4.15 (d, *J* = 2.2 Hz, 1H), 4.21 (s, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 7.8 Hz, 2H).

To a solution of **23** (1.02 g, 3.81 mmol) in tetrahydrofuran (20 mL) containing dimethyl sulfoxide (2 drops) at room temperature was added sodium hydride (50 % suspension in mineral oil, 184 mg, 3.83 mmol) and the suspension was stirred for 8 h. The mixture was filtered through Celite and the filtrate was concentrated to leave a brown oil which was vacuum distilled (50 °C, 12 mm Hg) to give **18 (**0.24 g, 71%) as a colourless oil: $[\alpha]_D^{20}$ -17.9 (*c* 1.2, MeOH), identical with material prepared by method A.

(5*S*,6*R*)-1-Tetrahydropyranyloxy-2-heptyn-5,6-diol (25). To a solution of **24** (4.31 g, 30.8 mmol) in tetrahydrofuran (25 mL) at -78 °C was added *n*-butyllithium (1.6M in hexane, 19.3 mL, 30.8 mmol). The mixture was warmed to -20 °C, stirred for 20 min and cooled to -78 °C before addition to a solution of **18** (1.36 g, 15.4 mmol) in tetrahydrofuran (25 mL) at -78 °C. The mixture was allowed to warm to room temperature, stirred for 24 h and diluted with ether (30 mL). The solution was washed with brine, the aqueous washings were extracted with ether (2 x 20 mL) and the combined extract was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 1:1 to 1:3) to give **25** (2.56 g, 73%) as a pale yellow oil: IR (neat) 3400, 2950, 2870 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, *J* = 6.9 Hz, 3H), 1.60 (m, 6H), 2.45 (dt, *J* = 6.4, 1.8 Hz, 2H), 3.57 (br s, 1H), 3.77 (m, 2H), 4.29 (d, *J* = 1.8 Hz, 2H), 4.91 (br s, 1H); HRMS (EI) calcd for $C_{12}H_{20}O_4$ *m/z* 228.1362, found 228.1359.

(2*Z*,5*S*,6*R*)-1-Tetrahydropyranyloxy-2-hepten-5,6-diol (26). A suspension of palladium on barium sulfate (10%, 99 mg) in methanol (100 mL) was stirred under a hydrogen atmosphere at room temperature for 20 min before a solution of **25** (2.45 g, 10.7 mmol) and quinoline (25 mg) in methanol (25 mL) was added. The suspension was stirred for 3 h and was filtered through

Celite. The filtrate was concentrated and the residual oil was dissolved in ether (100 mL) and filtered. The filtrate was concentrated to dryness to leave virtually pure **26** (2.30 g, 93%) as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (d, *J* = 6.6 Hz, 3H), 1.66 (m, 6H), 2.30 (m, 2H), 3.48 (br s, 2H, exchanged with D_2O), 3.74 (m, 2H), 4.22 (m, 2H), 4.71 (m, 1H), 5.76 (m, 2H). This material was used immediately in the next reaction.

(2*Z*,5*S*,6*R*)-5,6-*O*-Isopropylidene-2-hepten-1,5,6-triol (27). To a solution of **26** (2.30 g, 10.0 mmol) in methanol (25 mL) at room temperature was added *p*-toluenesulfonic acid (190 mg, 1.0 mmol) and the mixture was stirred for 1 h. The solution was concentrated under vacuum, the residue was dissolved in a mixture of benzene (50 mL) and acetone (50 mL) and the solution was refluxed with distillation of volatiles. After 1 h, the collected distillate (75 mL) was discarded, the mixture was cooled to room temperature and solid sodium bicarbonate was added. The suspension was filtered, the filtrate was concentrated under reduced pressure and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 3:1 to 1:3) to give **27** (1.37 g, 74%) as a colourless oil: $[\alpha]_D^{20}$ -22.5 (*c* 4.9 $CHCl_3$); IR (neat) 3430, 1380, 1220, 1080 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.7 Hz, 3H), 1.28 (s, 3H), 1.44 (s, 3H), 2.31 (dd, *J* = 14.2, 6.8 Hz, 2H), 4.20 (m, 4H), 4.99 (br s, 1H, exchanged with D_2O), 5.73 (m, 2H); HRMS (EI) calcd for $C_{10}H_{18}O_3$ *m/z* 186.1256, found 186.1258.

(2*Z*,5*S*,6*R*)-1-Chloro-5,6-*O*-isopropylidene-2-hepten-5,6-diol (28). To a solution of *N*-chlorosuccinimide (970 mg, 7.20 mmol) in methylene chloride (35 mL) at -20 °C was added dimethyl sulfide (0.62 mL, 9.00 mmol) and the solution was stirred for 10 min, during which a white precipitate formed. To this stirred suspension was added a solution of **27** (1.23 g, 6.60 mmol) in methylene chloride (10 mL), the mixture was warmed to 0 °C and was stirred for 1 h. Saturated aqueous sodium chloride (50 mL) was added and the mixture was extracted with ether

(200 mL). The extract was dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure and the residue was chromatographed on silica (20 g, hexanes:ethyl acetate 1:1) to give **28** (970 mg, 72%) as a colourless oil: $[\alpha]_D^{22}$ -1.6 (*c* 2.1 $CHCl_3$); IR (neat) 1660, 1450, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (d, *J* = 6.8 Hz, 3H), 1.46 (s, 3H), 1.55 (s, 3H), 2.42 (m, 2H), 4.31 (m, 4H), 5.79 (m, 2H); HRMS (CI) calcd for $C_{10}H_{17}{}^{35}ClO_2$ *m/z* 204.0917, found 204.0920.

(3*Z*,6*S*,7*R*)-1-Phenylsulfonyl-6,7-*O*-isopropylidene-3-octen-6,7-diol (29). To a solution of methyl phenyl sulfone (967 mg, 6.20 mmol) in tetrahydrofuran (20 mL) at -78 °C was added *n*-butyllithium (1.6M in hexane, 3.87 mL, 6.20 mmol). The solution was allowed to warm to 0 °C, stirred for 30 min, then was cooled to -78 °C before copper(I) iodide (1.18 g, 6.20 mmol) was added. The mixture was warmed to -20 °C and stirred for 1 h at this temperature. To this solution was added a solution of **28** (553 mg, 2.71 mmol) in tetrahydrofuran (10 mL) and the mixture was allowed to warm to room temperature and was stirred for 24 h. The mixture was poured into saturated aqueous ammonium chloride (50 mL) and was extracted with ethyl acetate (2 x 100 mL). The combined extract was washed with aqueous sodium thiosulfate (2%) and with saturated aqueous ammonium chloride, and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (20 g, hexanes:ethyl acetate 1:1) to give **29** (508 mg, 58%) as a colourless oil; IR (neat) 1580, 1440, 1300 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (d, *J* = 6.9 Hz, 3H), 1.32 (s, 3H), 1.43 (s, 3H), 2.35 (m, 4H), 3.14 (m, 2H), 4.18 (m, 2H), 5.53 (m, 2H), 7.65 (m, 3H), 7.93 (m, 2H); HRMS (EI) calcd for $C_{17}H_{24}O_4S$ *m/z* 324.1395, found 324.1388.

(5*S*,6*R*)-5,6-*O*-Isopropylidene-2-heptyn-1,5,6-triol (30). To a solution of **25** (200 mg, 0.87 mmol) in benzene (3 mL) at room temperature were added methanol (1 mL), 2,2-

dimethoxypropane (1 mL) and *p*-toluenesulfonic acid (7 mg) and the mixture was stirred for 18 h. Solid sodium carbonate (2 g) was added, the suspension was stirred for 5 min and then filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 1:2) to give **30** (107 mg, 68%) as a colourless oil: $[\alpha]_D^{26}$ -38.1 (*c* 3.2 $CHCl_3$); IR ($CHCl_3$) 3450, 2200, 1460, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.9 Hz, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 2.33 (m, 3H), 4.26 (m, 4H); HRMS (EI) calcd for $C_{10}H_{16}O_3$ *m/z* 184.1099, found 184.1103.

(2*E*,5*S*,6*R*)-5,6-*O*-Isopropylidene-2-hepten-1,5,6-triol (31). To a suspension of lithium aluminium hydride (12 mg, 0.31 mmol) in tetrahydrofuran (5 mL) at room temperature was added aluminium trichloride (1 mg) followed by a solution of **30** (48 mg, 0.26 mmol) in tetrahydrofuran (1 mL). The mixture was refluxed for 3 h, cooled to 0 °C and ethyl acetate (15 μL) was added. The mixture was allowed to warm to room temperature and water (12 μL) followed by aqueous sodium hydroxide (15%, 12 μL) were added. The suspension was filtered and the filtrate was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave virtually pure **31** (42 mg, 88%) as a colourless oil: $[\alpha]_D^{23}$ -58.8 (*c* 1.2 $CHCl_3$); IR ($CHCl_3$) 3500, 1440, 1380, 1085 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, *J* = 6.9 Hz, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 1.70 (br s, 1H, exchanged with D_2O), 2.24 (m, 2H), 4.26 (m, 4H), 5.71 (m, 2H). This material was used immediately for the next reaction.

(2*E*,5*S*,6*R*)-1-Chloro-5,6-*O*-isopropylidene-2-hepten-5,6-diol (32). To a solution of *N*-chlorosuccinimide (33 mg, 0.25 mmol) in methylene chloride (5 mL) at -20 °C was added dimethyl sulfide (22 μL, 0.30 mmol) and the solution was stirred for 10 min, during which a white precipitate formed. To the stirred suspension was added a solution of **31** (42 mg, 0.23 mmol) in methylene chloride (5 mL), the mixture was allowed to warm to 0 °C and was stirred

for 1 h. Saturated aqueous sodium chloride (10 mL) was added and the mixture was extracted with ether (50 mL). The extract was washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (8 g, hexanes:ethyl acetate 1:2) to give **32** (42 mg, 91%) as a colourless oil: $[\alpha]_D^{20}$ -28.2 (*c* 0.5 $CHCl_3$); IR ($CHCl_3$) 1660, 1450, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (d, *J* = 6.8 Hz, 3H), 1.33 (s, 3H), 1.45 (s, 3H), 2.26 (m, 2H), 4.01 (m, 2H), 4.06 (dt, *J* = 14.0, 6.6 Hz, 1H), 4.28 (dt, *J* = 14.0, 6.7 Hz, 1H), 5.76 (m, 2H); HRMS (CI) calcd for $C_{10}H_{17}ClO_2$ *m/z* 204.0917, found 204.0920.

(3*E*,6*S*,7*R*)-6,7-*O*-Isopropylidene-1-phenylsulfonyl-3-octen-6,7-diol (33). To a solution of methyl phenyl sulfone (45 mg, 0.29 mmol) in tetrahydrofuran (3 mL) at -78°C was added *n*-butyllithium (186 μL, 1.55M in hexane, 186 μL, 0.29 mmol), the solution was allowed to warm to 0 °C and was stirred for 30 min before being cooled to -78 °C. To this solution was added anhydrous copper(I) iodide (55 mg, 0.29 mmol), the mixture was stirred at -20 °C for 1 h and a solution of **32** (38 mg, 0.19 mmol) in tetrahydrofuran (3 mL) was added. The mixture was warmed to room temperature, stirred for 24 h, poured into saturated aqueous ammonium chloride (10 mL) and extracted with ethyl acetate (2 x 30 mL). The combined extract was washed with aqueous sodium thiosulfate (2%) and with saturated aqueous ammonium chloride, and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (5 g, hexanes:ethyl acetate 1:1) to give **33** (52 mg, 86%) as a colourless oil: IR ($CHCl_3$) 1580, 1440, 1305 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.9 Hz, 3H), 1.31 (s, 3H), 1.42 (s, 3H), 2.11 (m, 2H), 2.43 (m, 2H), 3.16 (m, 2H), 4.09 (m, 2H), 5.45 (m, 2H), 7.54 (m, 3H), 7.86 (m, 2H); HRMS (EI) calcd for $C_{17}H_{24}O_4S$ *m/z* 324.1395, found 324.1389.

(3*Z*,6*S*,7*R*)-1-Phenylsulfonyl-3-octen-6,7-diol (34). To a solution of **29** (85 mg, 0.26 mmol) in methanol (2 mL) at room temperature was added *p*-toluenesulfonic acid (5 mg, 0.03 mmol) and the mixture was stirred for 8 h. Solid sodium carbonate (10 mg) was added, the suspension was filtered through Celite and the filtrate was concentrated to leave a residue that was chromatographed on silica (12 g, hexanes:ethyl acetate 1:3) to give **34** (65 mg, 87%) as a colourless oil: $[\alpha]_D^{22}$ -7.3 (*c* 6.0 $CHCl_3$); IR (neat) 3400, 1470, 1440, 1310 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.9 Hz, 3H), 2.36 (m, 6H), 3.19 (t, *J* = 8.2 Hz, 2H), 3.66 (m, 2H), 5.51 (m, 2H), 7.54 (m, 3H), 7.86 (m, 2H); HRMS (FAB) calcd for $C_{14}H_{20}O_4S$ *m/z* 284.1082, found 284.1078.

(3*E*,6*S*,7*R*)-1-Phenylsulfonyl-3-octen-6,7-diol (35). To a solution of **33** (62 mg, 0.19 mmol) in methanol (5 mL) was added *p*-toluenesulfonic acid (10 mg) and the mixture was stirred for 12 h. Solid sodium carbonate (15 mg) was added and the suspension was filtered through Celite which was washed with methanol. The combined filtrate was concentrated under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 1:3) to give **35** (41 mg, 67%) as a colourless oil: IR ($CHCl_3$) 3500, 1605, 1440, 1295 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (d, *J* = 6.8 Hz, 3H), 1.93 (br s, 1H), 2.35 (m, 5H), 3.16 (t, *J* = 8.4 Hz, 2H), 3.72 (m, 2H), 5.48 (m, 2H), 7.56 (m, 3H), 7.88 (m, 2H); HRMS (FAB) calcd for $C_{14}H_{20}O_4S$ *m/z* 284.1082, found 284.1089.

(2*R*,3*S*,5*S*)-3-Hydroxy-2-methyl-5-(1*E*-3-phenylsulfonyl-1-propenyl)tetrahydrofuran (36) and (*2R*,3*S*,5*R*)-3-Hydroxy-2-methyl-5-(1*E*-3-phenylsulfonyl-1-propenyl)tetrahydrofuran (37). A. From 34. To a solution of **34** (502 mg, 1.76 mmol) in methylene chloride (50 mL) at -78 °C was added phenylselenyl chloride (404 mg, 2.11 mmol) in one portion and the mixture was stirred until all of the solid had dissolved (3 h). The mixture was diluted with methylene

chloride (150 mL) and the solution was washed with aqueous potassium bicarbonate (10%) and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (50 g, hexanes:ethyl acetate 1:1) to give a stereoisomeric mixture of phenyselenyl tetrahydrofurans (715 mg, 93%) which was subjected to the next reaction without further purification.

To a solution of the mixture of phenylselenyl tetrahydrofurans obtained above (715 mg, 1.62 mmol) in tetrahydrofuran (50 mL) at 0 °C was added hydrogen peroxide (1N in tetrahydrofuran, 2.73 mL, 2.73 mmol) and the mixture was allowed to warm to room temperature. The solution was stirred for 5 h and diluted with ether (50 mL), and the solution was washed with aqueous potassium bicarbonate (10%), aqueous sodium thiosulfate (10%) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (50 g, hexanes:ethyl acetate 1:2) to give a mixture of **36** and **37** (1:1.4, 422 mg, 92%) as a colourless oil.

B. From 35. To a solution of **35** (30.0 mg, 0.11 mmol) in methylene chloride (5 mL) at -78 °C was added phenylselenyl chloride (25.0 mg, 0.13 mmol) in one portion and the mixture was stirred until all the solid had dissolved (2 h). The solution was diluted with methylene chloride (10 mL) and was washed with aqueous potassium bicarbonate (10%) and brine, and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (8 g, hexanes:ethyl acetate 1:1) to give a stereoisomeric mixture of phenylselenyl tetrahydrofurans which was taken on to the next reaction.

To a solution of the mixture of phenylselenyl tetrahydrofurans obtained above in tetrahydrofuran (5 mL) at 0 °C was added hydrogen peroxide (1N in tetrahydrofuran, 150 μL, 0.15 mmol) and the mixture was allowed to warm to room temperature. The solution was stirred for 3 h and

diluted with ether (10 mL), and the solution was washed with aqueous potassium bicarbonate (10%), aqueous sodium thiosulfate (10%) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (7 g, hexanes:ethyl acetate 1:3) to give a mixture of **36** and **37** (1.4:1, 26.5 mg, 89%) as a colourless oil.

(2*R*,3*S*,5*S*)-3-*tert*-Butyldimethylsilyloxy-2-methyl-5-(1*E*-3-phenylsulfonyl-1-propenyl)tetrahydrofuran (38) and (2*R*,3*S*,5*R*)-3-*tert*-Butyldimethylsilyloxy-2-methyl-5-(1*E*-3-phenylsulfonyl-1-propenyl)tetrahydrofuran (39). To a solution of *tert*-butyldimethylsilyl chloride (377 mg, 2.50 mmol) in *N*,*N*-dimethylformamide (15 mL) at room temperature was added imidazole (358 mg, 6.17 mmol) and the mixture was stirred for 10 min. To this solution was added a solution of a mixture of **36** and **37** (470 mg, 1.67 mmol) in *N*,*N*-dimethylformamide (5 mL) and the mixture was stirred at room temperature for 18 h. The mixture was diluted with ether (30 mL) and the ethereal solution was washed with aqueous copper sulfate (10%) and water. The aqueous washings were extracted with ether (2 x 20 mL) and the combined extract was washed with brine and dried over anhydrous sodium sulfate. The solvent and volatiles were removed under vacuum and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 2:1) to give a mixture of **38** and **39** (581 mg, 88%) as a colourless oil. The mixture was separated by high-performance liquid chromatography (μ-Porasil, hexanes:ethyl acetate 1:3) to give **38** and **39**.

38: R_t 7.2 min; IR (neat) 1450, 1430, 1300, 1235 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.92 (s, 9H), 1.13 (d, *J* = 6.7 Hz, 3H), 1.46 (ddd, *J* = 13.4, 7.1, 6.7 Hz, 1H), 2.25 (ddd, *J* = 13.3, 7.0, 6.7 Hz, 1H), 3.78 (m, 4H), 4.41 (m, 2H), 5.60 (m, 2H), 7.43 (m, 3H), 7.82 (m, 2H); HRMS (CI) calcd for $C_{16}H_{23}O_4SSi$ (M^+-C_4H_9) *m/z* 339.1086, found 339.1088.

39: R_t 6.4 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.89 (s, 9H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.61 (ddd, *J* = 13.1, 8.8, 6.8 Hz, 1H), 1.82 (ddd, *J* = 13.2, 6.7, 2.9 Hz, 1H), 3.76 (m, 4H), 4.44 (m, 2H), 5.58 (m, 2H), 7.41 (m, 3H), 7.70 (m, 2H); HRMS (CI) calcd for $C_{16}H_{23}O_4SSi$ (M^+-C_4H_9) *m/z* 339.1086, found 339.1093.

cis- and trans-2,6,6-Trimethyl-6-formyl-5-hydroxyhexanoic Acid δ-Lactone (43). To a solution of lithium diisopropylamide, prepared from diisopropylamine (3.00 g, 29.6 mmol) and *n*-butyllithium (1.5M in hexane, 19.0 mL, 28.5 mmol), in tetrahydrofuran (20 mL) at -78 °C was added tiglic acid (1.30 g, 13.0 mmol). The mixture was stirred for 30 min, then was warmed to room temperature and stirred for 1 h. To this yellow solution at -78 °C was added dropwise a solution of **40 (**1.71 g, 12.0 mmol) in tetrahydrofuran (29 mL) and the mixture was allowed to warm to room temperature. The solution was stirred for 18 h and was poured into a mixture of saturated aqueous ammonium chloride (20 mL) and ether (20 mL). The separated ethereal layer was extracted with saturated aqueous sodium bicarbonate (3 x 10 mL) and the extract was acidified to pH 2 with hydrochloric acid (3M). The aqueous solution was extracted with ether (3 x 30 mL), the combined extract was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure to give virtually pure **41** (2.61 g, 88%) as a colourless oil.
To a solution of **41** (2.61 g, 10.6 mmol) obtained above in methanol (100 .mL) was added palladium-on-carbon (0.26 g) and the suspension was stirred under an atmosphere of hydrogen for 24 h. The suspension was filtered through a pad of Celite and the filtrate was concentrated under vacuum to leave a residue (2.40 g) which was dissolved in benzene (75 mL). To this solution was added benzoic acid (12 mg) and the mixture was refluxed under a Soxhlet extractor containing molecular sieves (4A) for 24 h. The solution was washed with saturated aqueous sodium carbonate and brine and was dried over anhydrous sodium sulfate. The solvent was

removed under reduced pressure to give **42** (1.96 g, 80%) as a 1:1 mixture of cis and trans isomers as a colourless oil: IR (neat) 1740, 1460, 1380, 1180, 1080 cm^{-1}.

A solution of titanium tetrachloride (0.52 mL, 4.70 mmol) and acetyl chloride 0.34 mL, 4.70 mmol) in methylene chloride (5 mL) was stirred at 0 °C for 10 min. To this solution was added a solution of **42** (1.01 g, 4.35 mmol) in methylene chloride (10 mL) and the mixture was stirred for 20 min. Water (1 mL) was added followed by solid sodium bicarbonate (2 g) and the suspension was stirred at 0 °C for 2 h. The suspension was extracted with methylene chloride (2 x 50 mL), the extract was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The residue was chromatographed on silica (15 g, hexanes:ethyl acetate 1:1) to give **43** (670 mg, 82%, 1:1 mixture of cis and trans isomers) as a colourless oil: IR (neat) 1735, 1715, 1460, 1380 cm^{-1}; HRMS (EI) cacld for $C_{10}H_{16}O_3$ *m/z* 184.1099, found 184.1103.

Methyl cis- and trans-2,6,6-Trimethyl-5-hydroxyheptan-1,7-dioate δ-Lactone (47). To a solution of sodium periodate (12.2 g, 57 mmol) in a mixture of water (69 mL) and carbon tetrachloride (48 mL) at room temperature was added ruthenium(III) chloride trihydrate (284 mg, 1.10 mmol) followed by a solution of **43** (2.50 g, 13.5 mmol) in acetonitrile (24 mL). The mixture was stirred for 4 h and was diluted with ether (50 mL). The layers were separated, the aqueous layer was extracted with ether (2 x 30 mL) and the combined extract was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 2:1 containing 4% acetic acid) to give **46** (2.13 g, 78%, mixture of stereoisomers) as a colourless amorphous solid**:** IR (KBr) 2900, 1710, 1460, 1360 cm^{-1}. This material was used immediately in the next reaction.

To a solution of **46** obtained above (2.13 g, 10.6 mmol) in ether (10 mL) at 0 °C was added dropwise a solution of diazomethane in ether until a yellow colour persisted. Acetic acid (6

drops) was added to destroy excess diazomethane and the solvent was removed under vacuum to give a mixture of cis and trans **47** (2.01 g, 88%) as a colourless oil: IR (neat) 1725, 1460, 1360, 1270 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{18}O_4$ *m/z* 214.1205, found 214.1211.

Methyl (2'*R*,3'*R*,10'*R*)-2-Methyl-2,7'-[2',3',10'-trimethyl-1',4',10'-trioxaspiro-(4',5')-decyl]propionate (48). **A. From 61**. A solution of **61** (121 mg, 0.57 mmol), (2*R*,3*R*)-butane-2,3-diol (86 mg, 0.96 mmol) and *p*-toluenesulfonic acid (10 mg) in benzene (20 mL) was refluxed in a Dean-Stark apparatus with azeotropic removal of water for 24 h. The solution was evaporated to dryness and the residue was chromatographed on silica (15 g, hexanes;ethyl acetate 2:1) to give **48** (97 mg, 57%) as a colourless oil: $[\alpha]_D^{20}$ +0.88 (*c* 2.5 $CHCl_3$); IR (neat) 2985, 2960, 1740, 1470, 1375, 1365, 1270, 1255, 1145, 1115, 1060, 1030, 1015, 1010, 970 cm^{-1}; ^{1}H NMR(400 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.6 Hz, 3H), 1.07 (s, 3H), 1.14 (s, 3H), 1.22 (d, *J* = 5.9 Hz, 3H), 1.23 (d, *J* = 6.0 Hz, 3H), 1.42 (m, 3H), 1.73 (dq, *J* = 8.6, 3.2 Hz, 1H), 1.82 (pent, *J* = 6.0 Hz, 1H), 3.61 (s, 3H), 3.77 (dq, *J* = 8.2, 6.0 Hz, 1H), 3.94 (dd, *J* = 11.1, 2.4 Hz, 1H); HRMS (EI) calcd for $C_{15}H_{26}O_5$ *m/z* 286.1780, found 286.1776.

B. From cis- and trans-47. To a solution of cis and trans **47** (267 mg, 1.25 mmol) in benzene (20 mL) was added (2*R*,3*R*)-butane-2,3-diol (162 mg, 1.80 mmol), camphorsulfonic acid (20 mg) and 4A molecular sieves and the mixture was heated at 80 °C for 18 h. The cooled mixture was diluted with ether (100 mL) and filtered, and the filtrate was washed with saturated aqueous sodium bicarbonate and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the residue was chromatographed on silica (20 g, hexanes:ethyl acetate 4:1 to 1:1) to give a mixture of **48** and **49** (3.7:1, 284 mg, 80%).

(2'*R*,3'*R*,10'*R*)-3-Methyl-1-phenylsulfonyl-3,7'-[2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4',5')-decyl]butan-2-one (51). To a solution of methyl phenyl sulfone (3.12 g, 20 mmol) in

tetrahydrofuran at 0 °C was added slowly *n*-butyllithium (1.27M in hexane, 0.32 mL, 40.6 mmol). The solution was allowed to warm to room temperature over 2 h then was cooled to 0 °C before adding a solution of the mixture of **48** and **49** (2.86 g, 10 mmol) in tetrahydrofuran (8 mL). The mixture was stirred at room temperature for 18 h and diluted with ethyl acetate (20 mL), and the reaction was quenched by addition of water. The separated organic layer was washed with water and brine, and was dried over ahhydrous magnesium sulfate. Removal of the solvent under vacuum left a semi-solid which was chromatographed on silica (50 g, hexanes:ethyl:acetate 5:1) to give **51** (2.87 g, 89% based on **48**) as a colourless solid which was crystallized from methanol as needles: mp 96-98 °C; $[\alpha]_D^{20}$ +2.5 (*c* 2.0 $CHCl_3$); IR (KBr) 1715, 1440, 1360, 1300 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.6 Hz, 3H), 1.09 (s, 3H), 1.10 (s, 3H), 1.21 (d, *J* = 6.1 Hz, 3H), 1.24 (d, *J* = 6.1 Hz, 3H), 1.40 (m, 2H), 1.68 (m, 3H), 3.60 (m, 1H), 3.71 (m, 2H), 4.35 (d, *J* = 15.9 Hz, 1H), 4.53 (d, *J* = 15.9 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 2H), 7.64 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.95 (dd, *J* = 7.2, 2.1 Hz, 2H); HRMS (EI) calcd for $C_{21}H_{30}O_6S$ *m/z* 410.1763, found 410.1769. There was also isolated **52** (32 mg) as an oil.

(2*RS*,5*R*)-2-(3-methyl-3-butenyl)-5-methylcyclohexanone 55. To a suspension of copper(I) bromide (11.8 g, 82 mmol) in tetrahydrofuran (50 mL) at -23 °C was added dropwise vinylmagnesium bromide (1.0M solution in tetrahydrofuran, 164 mL, 164 mmol). The mixture was stirred at -23 °C for 30 min and a solution of (*R*)-pulegone (**53**, 10.0 g, 65.6 mmol) in tetrahydrofuran (20 mL) was added. The mixture was stirred at -20 °C for 4 h and the reaction was quenched by addition of saturated aqueous ammonium chloride. The mixture was diluted with ether (80 mL), the organic phase was separated and the aqueous phase was extracted with ether (2 x 50 mL). The combined extract was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was dissolved in ethanol (150 mL) to which

were added water (20 mL) and solid potassium hyroxide (17.5 g), and the mixture was heated at reflux for 3 h. The mixture was concentrated under reduced pressure to remove ethanol, and the remaining aqueous solution was with ether (50 mL). The ethereal extract was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum to leave a residue which was chromatographed on silica (200 g, hexanes:ethyl acetate 50:1 to 10:1) to give **55** (9.59 g, 80%) as a colourless oil: $[\alpha]_D^{20}$ -32.0 (*c* 8.4 $CHCl_3$); IR (neat) 2960, 2930, 2870, 2850, 1720, 1470, 1455, 1450, 1415, 1380, 1360, 1335, 1320, 1270, 1230, 1190, 1175, 1120, 1100, 1090, 1040, 1005, 980, 905, 730 $cm^{-1;}$ ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, *J* = 6.2 Hz, 3H), 1.04 (s, 3H), 1.06 (s, 3H), 1.19-1.40 (m, 2H), 1.70-2.23 (m, 6H), 4.85 (ddd, *J* = 11.5, 9.6, 1.4 Hz, 2H), 5.90 (dd, *J* = 11.5, 9.5, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 23.5, 25.2, 28.8, 34.5, 36.2, 37.7, 52.2, 58.5, 110.8, 147.2, 211.2; HRMS (EI) calcd for $C_{12}H_{20}O$ *m/z* 180.1514, found 180.1519.

Methyl (1*S*,4*R*)-2-(4-Methyl-2-oxocyclohexyl)-2-methylpropionate (54). A. From 55. To a vigorously stirred mixture of sodium metaperiodate (68 mg, 3.19 mmol) and ruthenium trichloride trihydrate (5.0 mg, 0.02 mmol) in acetonitrile (2 mL), carbon tetrachloride (2 mL) and water (3 mL) at room temperature was added **55** (140 mg, 0.77 mmol). The mixture was stirred for 5 h and diluted with ethyl acetate (25 mL), and the organic layer was separated. The aqueous layer and solid material was extracted with ethyl acetate (3 x 10 mL) and the combined extract was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, the residue was taken up into ethyl acetate (15 mL) and the solution was filtered through a pad of Celite which was washed with ethyl acetate. The combined filtrate was concentrated under reduced pressure and the resulting crude carboxylic acid was dissolved in ether (20 mL) at 0 °C to which was added an ethereal solution of diazomethane until gas

evolution ceased and the solution had turned yellow. The mixture was concentrated under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 9:1 to 3:1) to give **54** (125 mg, 77%) as a colourless oil: IR (neat) 2970, 2950, 2925, 2880, 1730, 1710, 1475, 1460, 1450, 1430, 1385, 1370, 1300, 1270, 1245, 1235, 1205, 1190, 1155, 1135, 1120, 1095, 910, 905, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, *J* = 6.2 Hz, 3H), 1.07 (s, 3H), 1.10 (s, 3H), 1.31 (dq, *J* = 10.4, 2.8 Hz, 1H), 1.44 (dq, *J* = 10.3, 2.6 Hz, 1H), 1.75 (m, 1H), 1.86-2.03 (m, 3H), 2.27 (dt, *J* = 13.0, 2.4 Hz, 1H), 2.71 (dd, *J* = 13.1, 4.8 Hz, 1H), 3.57 (s, 3H); HRMS (EI) calcd for $C_{12}H_{20}O_3$ *m/z* 212.1412, found 212.1408.

B. From 56. A solution of **56** (556 mg, 3.11 mmol) in methanol (8 mL) containing dilute sulfuric acid (3.4 mL) was refluxed for 6 h and poured into ice-water (100 mL). The solution was extracted with ether (4 x 40 mL) and the combined extract was washed with water, saturated aqueous sodium bicarbonate and brine. The organic solution was dried over anhydrous magnesium sulfate and concentrated under reduced pressure, and the residue was chromatographed on silica (15 g, hexanes:ethyl acetate 3:1) to give **54** (627 mg, 95%) identical with material prepared from **55**.

Methyl (3*S*,5*R*)-3-Hydroxy-2,2,6-trimethyl-1,8-octandioate ε-Lactone (57). To a solution of hydrogen peroxide (30%, 1.60 g, 14.1 mmol) in methylene chloride (12 mL) at 0 °C was added trifluoroacetic anhydride (10.8 mL, 76.4 mmol) and the solution was stirred for 10 min. To this solution at 0 °C was added a solution of **54** (1.01 g, 4.71 mmol) in methylene chloride (5 mL) and the mixture was allowed to warm to room temperature and was stirred for 4 h. The mixture was poured into ether (20 mL) containing solid sodium bicarbonate and the suspension was stirred for 30 min and then filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 5:1 to 1:1) to give **57**

(790 mg, 74%) as a colourless oil: IR (neat) 2970, 2900, 1750, 1730, 1475, 1465, 1400, 1380, 1360, 1335, 1300, 1280, 1235, 1200, 1160, 1145, 1130, 1110, 1080, 1040, 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.00 (d, *J* = 6.6 Hz, 3H), 1.14 (s, 3H), 1.21 (s, 3H), 1.29 (dq, *J* = 11.8, 4.4 Hz, 1H), 1.54 (dq, *J* = 11.8, 4.3 Hz, 1H), 1.74 (dt, *J* = 15.1, 3.8 Hz, 1H), 1.80 (m, 1H), 1.89 (m, 1H), 2.44 (dt, *J* = 13.3, 1.8 Hz, 1H), 2.57 (dd, *J* = 13.3, 12.1 Hz, 1H), 3.65 (s, 3H), 4.47 (d, *J* = 8.9 Hz, 1H); HRMS (EI) calcd for $C_{12}H_{20}O_4$ *m/z* 228.1362, found 228.1356.

Methyl (3*S*,6*R*)-3-Hydroxy-8,8-diphenyl-2,2,6-trimethyl-7-octenoate (58). To a solution of **57** (336 mg, 1.47 mmol) in tetrahydrofuran (9 mL) at 0 °C was added phenylmagnesium bromide (3.1M in ether, 1 mL) and the mixture was stirred vigorously for 1 h. The mixture was diluted with ether (100 mL) and the ethereal solution was washed with saturated aqueous ammonium chloride and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to leave crude dihydroxy ester (551 mg) which was immediately subjected to dehydration.

To a solution of the crude material obtained above in benzene (50 mL) was added pyridinium *p*-toluenesulfonate (20 mg) and the solution was refluxed for 4 h. The solution was evaporated to dryness under vacuum and the residue was chromatographed on silica (30 g, hexanes:ethyl acetate 9:1) to give pure **58** (294 mg, 55%) as a pale yellow oil. This material was taken forward immediately to acetate **59**.

Methyl (3*S*,6*R*)-3-Acetoxy-8,8-diphenyl-2,2,6-trimethyl-7-octenoate (59). To a solution of **58** (135 mg, 0.37 mmol) in methylene chloride (10 mL) at room temperature was added 4-(dimethylamino)pyridine (10 mg), pyridine (200 μL) and acetic anhydride (260 μL). The mixture was stirred for 18 h, saturated aqueous sodium bicarbonate (20 mL) was added and the mixture was stirred for 30 min. The two-phase mixture was separated, the (upper) aqueous

phase was extracted with ether and the combined organic phase was washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the crude residue (147 mg) was chromatographed on silica (30 g, hexanes:ethyl acetate 9:1) to give **59 (**99.2 mg, 66%) as a pale yellow oil: $[\alpha]_D^{20}$ -2.0 (*c* 5.2 $CHCl_3$); IR (neat) 2950, 1740, 1495, 1470, 1455, 1390, 1370, 1275, 1235, 1145, 1025, 1000, 985, 765, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.01 (d, *J* = 6.7 Hz, 3H), 1.16 (s, 3H), 1.17 (s, 3H), 1.29 (m, 2H), 1.50 (q, *J* = 6.8 Hz, 1H), 2.05 (s, 3H), 2.26 (m, 1H), 2.26 (m, 1H), 3.62 (s, 3H), 5.11 (dd, *J* = 8.8, 1.5 Hz, 1H), 5.81 (d, *J* = 12.2 Hz, 1H), 7.10-7.42 (m, 10H); HRMS (EI) calcd for $C_{26}H_{32}O_4$ *m/z* 408.2301, found 408.2297.

(3*S*,6*R*)-3-Acetoxy-2,2,6-trimethyl-1,7-heptandioic Acid Mono Methyl Ester (60). To a mixture of ruthenium trichloride hydrate (385 mg) and sodium metaperiodate (74 g) in acetonitrile (155 mL), carbon tetrachloride (155 mL) and water (230 mL) at room temperature was added **59** (31.0 g, 80.0 mmol) and the mixture was stirred vigorously for 4 h. Methylene chloride (300 mL) was added, the layers were separated and the aqueous (upper) layer was extracted with methylene chloride (3 x 200 mL). The combined extract was concentrated under reduced pressure and the residue was dissolved in ether (300 mL). The ethereal solution was with saturated aqueous sodium bicarbonate (6 x 150 mL) and the extract was acidified to pH 2 concentrated hydrochloric acid. The aqueous solution was extracted with ethyl acetate (4 x 200 mL) and the extract was dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure left a residue which was chromatographed on silica (50 g, hexanes:ethyl acetate 1:1) to give **60** (16.6 g, 78%) as a colourless viscous oil: $[\alpha]_D^{20}$ -0.30 (*c* 3.7 $CHCl_3$); IR (neat) 3300 (br), 2980, 1745, 1740, 1720, 1695, 1465, 1435, 1390, 1375, 1270, 1235, 1175, 1145, 1060, 1025 cm^{-1}; ^1H NMR (400 MHz) δ 1.14 (s, 6H), 1.16 (d, *J* = 6.6 Hz, 3H), 1.41 (m, 1H), 1.52 (m,

2H), 1.65 (m, 1H), 2.09 (s, 3H), 2.49 (pent, *J* = 6.3 Hz, 1H), 3.68 (s, 3H), 5.22 (dd, *J* = 10.6, 2.8 Hz, 1H); HRMS (CI) calcd for $C_{13}H_{22}O_6$ *m/z* 274.1416, found 274.1420.

Methyl (3*S*,6*R*)-3-Hydroxy-2,2,6-trimethyl-1-heptanoate-7-carboxylic Acid δ-Lactone (61). To a solution of **60** (16.6 g, 60.6 mmol) in methanol (400 mL) was added anhydrous potassium carbonate (8.4 g) and the mixture was refluxed for 16 h. The solvent was removed under reduced pressure and the residue was dissolved in chloroform (200 mL) to which was added hydrochloric acid (1N, 200 mL). The acidic solution was stirred at room temperature for 48 h, the phases were separated and the aqueous (upper) phase was extracted with methylene chloride (3 x 100 mL). The combined extract was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to leave a residue that was chromatographed on silica (50 g, :ethyl acetate 2:1 to 1:2) to give **61** (13.5 g, 87%) as a colourless oil: $[\alpha]_D^{20}$ +3.9 (*c* 3.4 $CHCl_3$); IR (neat) 2990, 2980, 2900, 1740, 1730, 1460, 1380, 1270, 1250, 1190, 1180, 1150, 1125, 1085, 1040, 1020, 995 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.23 (s, 3H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.50 (dq, *J* = 12.2, 2.8 Hz, 1H), 1.62 (dq, *J* = 12.2, 2.8 Hz, 1H), 1.79 (m, 1H), 1.99 (m, 1H), 2.37 (dq, *J* = 13.3, 6.8 Hz, 1H), 3.66 (s, 3H), 4.50 (dd, *J* = 11.3, 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 20.2, 20.8, 23.9, 28.1, 36.2, 46.3, 52.1, 85.0, 173.4, 175.5; HRMS (EI) calcd for $C_{11}H_{18}O_4$ *m/z* 214.1205, found 214.1208.

(9*S*,10*R*,6*Z*)-2-Methyl-9,10-*O*-isopropylidene-4-phenylsulfonyl-[(2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4',5')-decyl]undecen-3-one (62). To a solution of **51** (1.50 g, 3.66 mmol) and potassium iodide (1.10 g, 6.6 mmol) in a mixture of dimethyl sulfoxide (30 mL) and tetrahydrofuran (12 mL) at 0 °C was added *n*-butyllithium (1.6M in hexane, 2.4 mL, 3.84 mmol) and the mixture was stirred for 1 h. The solution was warmed to room temperature and a solution of **28** (912 mg, 4.43 mmol) in tetrahydrofuran (12 mL) was added slowly. The mixture

was warmed to 40 °C, stirred for 24 h and diluted with ether (100 mL). Aqueous potassium hydroxide (0.5%, 100 mL) was added, the layers were separated and the aqueous layer was extracted with ether 100 mL). The combined extract was washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give **62** (2.45 g, 97%) as a mixture of two stereoisomers. The mixture was carried forward to the next reaction without further purification.

(9*S*,10*R*,6*Z*)-2-Methyl-9,10-*O*-isopropylidene-[(2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4'.6'-trioxaspiro-(4',5')-decyl]undecen-3-one (63). To a solution of **62** (2.45 g, 4.24 mmol) in a mixture of tetrahydrofuran (200 mL) and water (20 mL) was added aluminium amalgam, prepared from aluminium foil (13 g) and aqueous mercuric chloride (2%, 700 mL), and the mixture was refluxed for 2 h. The mixture was cooled to room temperature and diluted with ethyl acetate (100 mL), and the suspension was filtered through Celite which was washed thoroughly with ethyl acetate (5 x 100 mL). The combined filtrate was concentrated under reduced pressure and the residue was chromatographed on silica (50 g, pentane:ether 3:1) to give **63** (1.57 g, 84%) as a colourless oil: $[\alpha]_D^{20}$ +2.9 (*c* 1.9 $CHCl_3$); IR (neat) 2980, 2935, 1705, 1485, 1460, 1255, 1215, 1175, 1140, 1085, 1055, 1030, 1015, 975, 945, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.8 Hz, 3H), 1.06 (s, 3H), 1.14 (s, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 1.57 (m, 2H), 1.75 (m, 2H), 2.28 (m, 5H), 2.60 (t, *J* = 5.7 Hz, 2H), 3.63 (m, 1H), 3.73 (q, *J* = 5.9 Hz, 1H), 3.92 (d, *J* = 11.6 Hz, 1H), 4.06 (m, 1H), 4.37 (pent, *J* = 6.6 Hz, 1H), 5.45 (t, *J* = 5.8 Hz, 1H), 5.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 15.4, 16.6, 17.5, 18.8 19.5, 21.5, 21.7, 24.8, 25.6, 26.9, 27.2, 28.1, 28.4, 29.3, 36.2, 38.4, 50.2, 73.5, 77.8, 79.0, 80.3, 125.9, 130.6, 214.1; HRMS calcd for $C_{25}H_{42}O_6$ *m/z* 438.2981, found 438.2977.

(3*S*,9*S*,10*R*,6*Z*)-3-Hydroxy-2-methyl-9,10-*O*-isopropylidene-[2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4',5')-decyl]undecene (64) and (3*R*,9*S*,10*R*,6*Z*)-3-Hydroxy-2-methyl-9,10-*O*-isopropylidene-[(2'*R,3'R*,10'*R*)-2',3',10'-trimethyl-1',4',6-trioxaspiro-(4',5')-decyl]undecene (65). To a solution of **63** (98 mg, 0.23 mmol) in tetrahydrofuran (10 mL) at 0 °C was added L-Selectride (1.0M in tetrahydrofuran, 1.2 mL, 1.2 mmol) and the mixture was stirred for 3 h. Excess hydride was destroyed by careful addition of water (0.8 mL) to the cold (0 °C) mixture followed by aqueous sodium hydroxide (3M, 0.8 mL). Aqueous hydrogen peroxide (30%, 0.8 mL) was added and the mixture was stirred at 45 °C for 30 min. The cooled mixture was diluted with ether (70 mL) and the ethereal solution was washed with saturated aqueous ammonium chloride, water and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give an inseparable mixture of **64** and **65** (95 mg,, 96%, 3.5:1) which was subjected without purification to the next reaction.

(3*S*,9*S*,10*R*,6*Z*)-3-Acetoxy-2-methyl-9,10-*O*-isopropylidene-[(2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4',5')-decyl]undecene (66) and (3*R*,9*S*,10*R*,6*Z*)-3-Acetoxy-2-methyl-9,10-*O*-isopropylidene-[(2'*R,3'*R,10'*R*)-2'.3',10'-trimethyl-1',4',6'-trioxaspiro-(4'5')-decyl]undecene (67). To a mixture of **64** and **65** (95 mg, 0.26 mmol) in methylene chloride (6 mL) at room temperature was added acetic anhydride (1 mL), pyridine (1 mL) and 4-(dimethylamino)pyridine (30 mg) and the solution was stirred for 18 h. The mixture was diluted with ether (15 mL) and the ethereal solution was washed with water and brine, and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (10 g, hexanes;ether 6:1) to give **66** (81 mg, 75%) as a colourless oil; $[\alpha]_D^{20}$ +4.9 (*c* 4.1 $CHCl_3$); IR (neat) 2975, 2910, 1735, 1455, 1375, 1245, 1220, 1120, 1090, 1075, 1035, 975 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 3H), 0.86 (d, *J* = 6.7

Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 1.25 (s, 3H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.33 (d, *J* = 7.0 Hz, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 1.52-1.78 (m, 8H), 2.16 (s, 3H), 2.25 (m, 1H), 3.47 (*J* = 7.0 Hz, 1H), 3.50 (m, 1H), 3.63 (pent, *J* = 6.2 Hz, 1H), 3.88 (m, 1H), 4.03 (m, 1H), 4.11 (q, *J* = 7.0 Hz, 1H), 4.26 (pent, *J* = 5.5 Hz, 1H), 4.99 (m, 1H), 5.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 15.4, 16.7, 18.8, 19.2, 19.7, 21.1, 24.4, 24.6, 25.7, 27.3, 28.1, 28.4, 29.5, 29.9, 36.3, 40.4, 73.6, 76.7, 77.7, 80.3, 107.3, 121.1, 125.7, 171.6; HRMS (CI) calcd for $C_{27}H_{46}O_7$ *m/z* 482.3244, found 482.3239.

There was also obtained **67** (23 mg, 21%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (s, 3H), 0.89 (s, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.34 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.42 (s, 3H), 1.55-1.82 (m, 6H), 2.02 (m, 2H), 2.08 (s, 3H), 2.16 (m, 1H), 2.22 (m, 2H), 3.57 (d, *J* = 9.8 Hz, 1H), 3.66 (pent, *J* = 7.8 Hz, 1H), 3.85 (dt, *J* = 10.2, 3.6 Hz, 1H), 4.06 (m, 1H), 4.29 (pent, *J* = 7.6 Hz, 1H), 5.06 (dd, *J* = 11.8, 6.6 Hz, 1H), 5.45 (m, 2H); HRMS (CI) calcd for $C_{27}H_{46}O_7$ *m/z* 482.3244, found 482.3250.

(2*R*,5*S*,7S,10*Z*)-5,7,13,14-Tetrahydroxy-2,6,6-trimethylpentadecenoic Acid δ-Lactone (71). To a suspension of lithium aluminium hydride (403 mg) in tetrahydrofuran (25 mL) at 0 °C was added dropwise a solution of **64** (380 mg, 0.79 mmol) in tetrahydrofuran (7 mL) and the suspension was allowed to warm to room temperature with stirring. After 2 h, the mixture was cooled to 0 °C and diluted with ether (50 mL). Excess hydride was destroyed by addition of water (400 μL), after which aqueous sodium hydroxide (3N, 400 μL) and water (1.2 mL) were added. The mixture was stirred at room temperature for 2 h, during which the gray suspension turned to a white precipitate. Magnesium sulfate (0.5 g) was added, the suspension was stirred for 1 h and filtered, and the collected solid was washed with ethyl acetate (100 mL). The combined filtrate was concentrated under reduced pressure to give virtually pure **66** (347 mg,

99%) as a colourless oil. This material was used without further purification in the next reaction.

To a solution of **66** (347 mg, 0.79 mmol) in tetrahydrofuran (40 mL) and water (10 mL) at room temperature was added *p*-toluenesulfonic acid and the solution was stirred for 16 h. To this mixture containing **72** was added aqueous sodium hydroxide (3N, 5 mL), and the solution was stirred for 2 h and acidified to pH 2 with hydrochloric acid (5%, *ca* 10 mL). The mixture was stirred at room temperature for 3 h, diluted with chloroform (80 mL) and stirred for 48 h. The phases were separated, the (lower) aqueous phase was extracted with methylene chloride (4 x 30 mL) and the combined extract was washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (30 g, hexanes;ethyl acetate 1:2) to give **71** (245 mg, 94%) as a polar viscous oil identical with material obtained from **69**.

(2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-5-Hydroxy-7,13,14-triacetoxy-2,6,6-trimethylpentadecenoic Acid δ-Lactone (73). To a solution of **71 (**32.8 mg, 0.10 mmol) in methylene chloride (6 mL) at room temperature were added acetic anhydride (1.0 mL), 4-(dimethylamino)pyridine (32 mg) and pyridine (0.5 mL) and the solution was stirred for 23 h. The mixture was diluted with ether (15 mL) and the ethereal solution was washed with saturated aqueous sodium bicarbonate and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 3:1 to 1:1) to give **73** (31.1 mg, 69%) as a colourless oil: $[\alpha]_D^{20}$ +14.2 (*c* 4.1 $CHCl_3$); IR ($CHCl_3$) 1710, 1360, 1240 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 6H), 1.20 (d, *J* = 6.9 Hz, 3H). 1.27 (d, *J* = 6.9 Hz, 3H), 1.35-2.55 (m, 11H), 2.03 (s, 3H), 2.04 (s, 3H), 2.06 (s, 3H), 4.06 (m, 1H), 4.81-5.16 (m, 3H), 5.32 (m, 2H); HRMS (EI) calcd for $C_{24}H_{38}O_8$ *m/z* 454.2567, found 454.2572.

(9*S*,10*R*,6*E*)-2-Methyl-9,10-*O*-isopropylidene-[(2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4'5')-decyl]undecen-3-one (74). To a solution of **51** (177 mg, 0.43 mmol) and potassium iodide (143 mg, 0.86 mmol) in dry dimethyl sulfoxide (10 mL) at room temperature was added *n*-butyllithium (1.39M solution in hexane, 0.35 mL) and the mixture was stirred for 1.5 h. To the pale yellow solution was added a solution of **32** (107 mg, 0.52 mmol) in tetrahydrofuran (6 mL) and the mixture was stirred at 40 °C for 24 h. The mixture was diluted with ether (15 mL), aqueous potassium hydroxide (0.5%, 15 mL) was added and the mixture was stirred for 30 min. The ethereal layer was separated, the aqueous layer was extracted with ether (3 x 10 mL) and the combined extract was dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (20 g, hexanes;ethyl acetate 3:1) to give a keto sulfone (213 g, 86%) as a mixture of two diastereomers. To a solution of the mixture of keto sulfones (213 mg, 0.37 mmol) obtained above in tetrahydrofuran (25 mL) and water (2.5 mL) was added aluminium amalgam, prepared from aluminium foil (870 mg) and an aqueous solution of mercuric chloride (2%, 25 mL). The mixture was heated at 75 °C for 80 min, then was cooled and diluted with ether (20 mL). The ethereal solution was washed with saturated aqueous sodium bicarbonate and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (20 g, hexanes:ethyl acetate 3:1) to give **74** (113 mg, 70%) as a colourless oil: $[\alpha]_D^{20}$ +0.1 (*c* 40.8 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.9 Hz, 3H), 1.05 (s, 3H), 1.13 (d, *J* = 6.8 Hz, 3H), 1.14 (s, 3H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.36 (s, 3H), 1.49 (s, 3H), 1.75 (m, 2H), 2.10 (m, 2H), 2.24 (m, 5H), 2.60 (dt, *J* = 11.6, 6.6 Hz, 2H), 3.63 (m, 1H), 3.73 (m, 1H), 3.92 (dd, *J* = 12.8, 2.7 Hz, 1H), 4.04 (m, 1H), 4.21 (pent, *J* = 7.2 Hz, 1H), 5.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$ δ 14.7, 15.1, 16.3, 18.5,

19.2, 21.3, 24.5, 25.4, 26.7, 28.1, 29.2, 33.1, 36.2, 38.6, 50.9, 73.3, 76.9, 77.4, 79.8, 80.2, 106.9, 120.8, 125.9, 131.8, 170.2; HRMS (EI) calcd for $C_{25}H_{42}O_6$ *m/z* 438.2981, found 438.2984.

(3*R*,9*S*,10*R*,6*E*)-3-Acetoxy-2-methyl-9,10-*O*-isopropylidene-[(2'*R*,3'*R*,10'*R*)-2',3',10'-trimethyl-1',4',6'-trioxaspiro-(4',5')-decyl]undecene (76). To a stirred slurry of lithium aluminium hydride (1.1 mg, 0.027 mmol) in ether (1 mL) at -110 °C was added dropwise a solution of **74** (10.0 mg, 0.023 mmol) in ether (1 mL) and the mixture was stirred for 30 min. Methanol (2 mL) was added, the mixture was allowed to warm to room temperature and five drops of water were added. The mixture was passed through a pad of anhydrous magnesium sulfate and the filtrate was evaporated under reduced pressure to leave crude **75** (9.5 mg) which was used without further purification for the next reaction.

To a solution of crude **75** obtained above in methylene chloride (2 mL) at room temperature was added acetic anhydride (120 μL, 1.3 mmol), pyridine (150 μL) and a catalytic quantity of 4-(dimethylamino)pyridine and the solution was stirred for 8 h. The mixture was diluted with ether (5 mL) and the solution was washed successively with saturated aqueous copper sulfate, saturated aqueous sodium bicarbonate and brine. The solution was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to leave a residue which was chromatographed on silica (5 g, hexanes:ethyl acetate 10:1) to give **76** (8.7 mg, 78%) as a colourless oil: $[\alpha]_D^{20}$ +1.2 (*c* 5.2 $CHCl_3$); IR ($CHCl_3$) 3010, 2910, 1735, 1475, 1460, 1380, 1260, 1250, 1120, 1090, 1020, 990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 3H), 0.92 (s, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.25-1.40 (m, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.35 (s, 3H), 1.37 (d, *J* = 6.8 Hz, 3H), 1.45 (s, 3H), 1.56 (m, 2H), 1.72 (m, 2H), 1.81 (m, 1H), 1.98 (m, 2H), 2.06 (s, 3H), 2.11 (m, 1H), 2.21 (m, 1H), 3.48 (dd, *J* = 12.6, 1.8 Hz, 1H), 3.63 (pent, *J* = 7.0 Hz, 1H), 4.06 (dt, *J* = 9.2, 6.8 Hz, 1H), 4.24 (pent, *J* = 7.1 Hz, 1H), 5.07 (dd, *J* = 9.4, 1.6 Hz,

1H), 5.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 15.0, 16.2, 18.3, 18.4, 19.2, 20.7, 24.8, 25.1, 28.1, 28.8, 29.2, 29.3, 33.0, 36.0, 39.9, 73.1, 76.8, 77.1, 79.9, 107.0, 121.6, 125.6, 130.8, 170.1; HRMS (EI) calcd for $C_{27}H_{46}O_7$ *m/z* 482.3244, found 482.3239. There was also isolated a small quantity of the (*S*) acetate (0.4 mg).

(2*R*,5*S*,7*R*,13*S*,14*R*,10*E*)-7-Acetoxy-5,13,14-trihydroxy-2,6,6-trimethylpentadecenoic Acid δ-Lactone (78). To a solution of **76** (40.0 mg, 0.083 mmol) in a mixture of tetrahydrofuran (10 mL) and water (2 mL) at room temperature was added *p*-toluenesulfonic acid (20.0 mg, 0.105 mmol) and the solution was stirred for 18 h. A solution of sodium hydroxide (8.1 mg, 0.205 mmol) in water (0.5 mL) was added, the mixture was stirred for 30 min and then was acidified to pH 3 with dilute hydrochloric acid (5%, 1.0 mL). The mixture was stirred for 20 h and was poured into chloroform (15 mL), and the biphasic mixture was stirred vigorously at room temperature for 24 h. The organic layer was separated, the aqueous phase was extracted with chloroform (3 x 10 mL) and the combined extract was washed with saturated aqueous sodium bicarbonate and brine. The organic solution was dried over anhydrous magnesium sulfate, the solvent was removed under reduced pressure and the residue was chromatographed on silica (6 g, hexanes:ethyl acetate 2:1 to 1:3) to give **78** (23.2 mg, 76%) as a colourless oil: $[\alpha]_D^{24}$ +5.4 (*c* 0.82 $CHCl_3$); IR ($CHCl_3$) 3500 (br), 2925, 2910, 2875, 1725, 1715, 1460, 1450, 1375, 1370, 1210, 1085, 1045, 1010, 975 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 3H), 0.92 (s, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.54 (dq, *J* = 8.8, 2.4 Hz, 1H), 1.65 (m, 5H), 1.91 (m, 2H), 2.07 (m, 2H), 2.09 (s, 3H), 2.18 (m, 2H), 2.39 (pent, *J* = 6.2 Hz, 1H), 3.59 (dt, *J* = 9.6, 6.3 Hz, 1H), 3.86 (m, 1H), 4.17 (dd, *J* = 12.7, 3.2 Hz, 1H), 5.17 (dd, *J* = 10.4, 2.5 Hz, 1H), 5.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.1, 17.2, 18.7, 19.0, 20.9, 23.9, 28.4, 28.7, 28.8, 35.0,

36.2, 41.2, 69.7, 74.4, 76.4, 85.3, 127.5, 132.2, 170.8, 174.1; HRMS (CI) calcd for $C_{20}H_{34}O_6$ *m/z* 370.2355, found 370.2362.

(2*R*,5*S*,7*R*,9*E*)-7-Acetoxy-5-hydroxy-10-[(2'*R*,3'*S*,5'*R*)-2-methyl-3-(*tert*-butyldimethylsilyloxytetrahydrofuranyl]-2,6,6-trimethyldecenoic Acid δ-Lactone (81). To a solution of **78** (228 mg, 0.61 mmol) in dry carbon tetrachloride (30 mL) at 70 °C was added phenylselenyl chloride (177 mg, 0.92 mmol) in one portion and the mixture was stirred for 5 min. The cooled mixture was diluted with ether (20 mL) and the solution was washed with saturated aqueous sodium bicarbonate and brine. The solution was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to leave a stereoisomeric mixture of phenylselenyl tetrahydrofuranols (304 mg, 90%) which was used immediately for the next reaction.

To a solution of the selenides (304 mg, 0.57 mmol) obtained above in tetrahydrofuran (45 mL) at 0 °C was added aqueous hydrogen peroxide (30%, 784 μL, 6.9 mmol). The mixture was stirred for 2 h at 0 °C, then was warmed to room temperature and was stirred for a further 4 h. Dimethyl sulfide (8 mL) was added, the mixture was stirred for 14 h and was diluted with chloroform (20 mL). The solution was washed with saturated aqueous sodium bicarbonate and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (15 g, hexanes:ethyl acetate 1:2) to give a mixture of **79** and **80** (175 mg, 84%) as a colourless oil.

To a solution of the mixture of **79** and **80** (56.0 mg, 0.15 mmol) obtained above and 2,6-lutidine (45 μL, 0.39 mmol) in methylene chloride (5 mL) at -23 °C was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (46 μL, 0.20 mmol) and the mixture was stirred for 15 min. The mixture was diluted with ether (10 mL) and the solution was washed with saturated aqueous

sodium bicarbonate and brine. The solvent was removed under reduced pressure and the residue was chromatographed on silica (8 g, hexanes:ethyl acetate 2:1 to 1:1) to give **81** (30.1 mg, 42%) as a colourless oil: $[\alpha]_D^{20}$ +3.5 (*c* 1.1 $CHCl_3$); IR ($CHCl_3$) 2930, 2880, 1725, 1720, 1370, 1250, 1195, 1085, 1020, 830, 800, 770, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.01 (s, 3H), 0.83 (s, 9H), 0.85 (s, 3H), 0.99 (s, 3H), 1.12 (d, *J* = 6.1 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.40 (m, 1H), 1.49 (m, 3H), 1.96 (s, 3H), 1.99 (m, 1H), 2.15 (m, 2H), 2.34 (m, 2H), 3.71 (pent, *J* = 6.6 Hz, 1H), 3.79 (q, *J* = 6.5 Hz, 1H), 4.10 (dd, *J* = 11.4, 2.9 Hz, 1H), 4.31 (q, *J* = 7.6 Hz, 1H), 4.95 (dd, *J* = 10.3, 2.7 Hz, 1H), 5.45 (ddd, *J* = 15.4, 8.1, 3.6 Hz, 1H), 5.57 (dd, *J* = 15.4, 8.0 Hz, 1H); HRMS (CI) calcd for $C_{26}H_{46}O_6Si$ *m/z* 482.3064, found 482.3055. There was also isolated *tert*-butyldimethylsilyl ether **82** (35.0 mg, 48%).

(2*R*,5*S*,7*R*)-7-Acetoxy-5-hydroxy-10-[(2'*R*,3'*S*,5'*R*)-3-acetoxy-2-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoic Acid δ-Lactone (83). From 79 and 80. To a solution of the mixture of **79** and **80** (6.0 mg, 0.015 mmol) obtained above in ethyl acetate (5 mL) was added palladium-on-carbon (25 mg) and the suspension was stirred under an atmosphere of hydrogen for 20 h. The suspension was filtered and the filtrate was evaporated under reduced pressure to leave a residual oil which was dissolved in methylene chloride (5 mL). To this solution at room temperature was added acetic anhydride (20 μL, 0.22 mmol), pyridine (20 μL) and a trace amount of 4-(dimethylamino)pyridine, and the mixture was stirred for 30 min. The mixture was diluted with ether (10 mL) and the solution was washed with saturated aqueous copper sulfate and brine. The solution was dried over anhydrous magnesium sulfate, the solvent was removed under reduced pressure and the residue was chromatographed on silica (2 g, hexanes:ethyl acetate 3:1 to 1:1) to give **83** (2.9 mg, 93 % from **79**) as a colourless oil: $[\alpha]_D^{20}$ +30.6 (*c* 1.7 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (s, 3H), 1.01 (s, 3H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.27

(d, *J* = 6.6 Hz, 3H), 1.32 (m, 2H), 1.45 (m, 2H), 1.58 (m, 6H), 1.99 (m, 2H), 2.04 (s, 3H), 2.06 (s, 3H), 2.39 (pent, *J* = 6.5 Hz, 1H), 2.44 (dt, *J* = 10.2, 6.6 Hz, 1H), 4.05 (m, 1H), 4.13 (dd, *J* = 8.7, 2.2 Hz, 1H), 4.32 (m, 1H), 5.00 (dd, *J* = 10.2, 2.5 Hz, 1H); HRMS (EI) calcd for $C_{22}H_{36}O_7$ *m/z* 412.2461, found 412.2456.

From 70. To a solution of **70** (5.5 mg, 0.017 mmol) in methylene chloride (5 mL) at room temperature were added acetic anhydride (12 μL, 0.13 mmol), pyridine (210 μL) and 4-(dimethylamino)pyridine (12 mg, 0.10 mmol), and the mixture was stirred for 21 h. The mixture was diluted with chloroform (30 mL) and the solution was washed with saturated aqueous sodium bicarbonate, dilute hydrochloric acid (2%) and brine, and was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 2:1 to 3:2 to give **83** (3.9 mg, 56%) identical with material prepared from **79** and **80**.

(2*R*,5*S*,7*R*,10*R*)-7-Acetoxy-10-bromo-5-hydroxy-10-[(2'*R*,3'*S*,5'*R*)-3-hydroxy-2-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoic Acid δ-Lactone (84). To a solution of **78** (10.0 mg, 0.027 mmol) in ether (2 mL) at -110 °C was added a solution of *N*-bromosuccinimide (8.0 mg, 0.045 mmol) in a mixture of ether and acetonitrile (5:1, 1 mL) and the solution was stirred for 4 h. The mixture was allowed to warm slowly to room temperature and was concentrated under reduced pressure. The residue was chromatographed on silica (8 g, hexanes:ethyl acetate 3:2) to give **84** (6.3 mg, 52%) as a colourless oil: $[\alpha]_D^{20}$ +33.8 (*c* 2.4 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 3H), 1.03 (s, 3H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.48 (dq, *J* = 10.7, 3.5 Hz, 1H), 1.62 (m, 2H), 1.81 (m, 2H), 1.96 (dq, *J* = 12.8, 4.8 Hz, 1H), 2.01 (m, 3H), 2.10 (s, 3H), 2.29 (br s, 1H), 2.42 (m, 2H), 3.95 (m, 2H), 4.06 (m, 1H), 4.16 (dt, *J* = 10.6, 3.4 Hz, 2H), 5.01 (dd, *J* = 10.4, 3.6 Hz, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 17.3, 18.5, 18.7, 19.2, 21.0, 23.9, 27.1, 28.6, 31.0, 36.3, 38.7, 41.3, 59.6, 75.9, 77.3, 80.0, 81.9, 85.5, 171.0, 172.1; HRMS (FAB) calcd for $C_{20}H_{33}{}^{79}BrO_6$ *m/z* 448.1461, found 448.1455.

(2*R*,5*S*,7*R*)-7-Acetoxy-5-hydroxy-10-[(2'*R*,3'*S*,5'*R*)-3-hydroxy-2-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoic Acid δ-Lactone (85). To a solution of **84** (50.8 mg, 0.113 mmol) in dry benzene (1 mL) was added AIBN (3 mg) and tri-*n*-butylstannane (37 μL, 0.138 mmol) and the mixture was refluxed for 2 h. The mixture was concentrated under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 1:1) to give **85** (41.5 mg, 99%) as a colourless oil: $[\alpha]_D{}^{20}$ +19.3 (*c* 1.7 $CHCl_3$); IR ($CHCl_3$) 2970, 2935, 2875, 1732, 1460, 1374, 1328, 1243, 1184, 1088, 1044, 1021, 978, 954, 909, 897, 872, 821, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (s, 3H), 1.00 (s, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.30 (m, 1H), 1.46-1.58 (m, 10H), 1.78 (d, *J* = 5.5 Hz, 1H), 2.01 (m, 2H), 2.05 (s, 3H), 2.35 (m, 1H), 3.87 (q, *J* = 6.6 Hz, 1H), 3.95 (dq, *J* = 12.1, 6.7 Hz, 1H), 4.12 (dd, *J* = 10.2, 3.6 Hz, 1H), 4.99 (dd, *J* = 9.4, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 18.3, 18.7, 19.2, 21.0, 22.4, 24.0, 28.6, 29.3, 36.2, 36.3, 40.3, 41.3, 76.4, 77.2, 80.3, 85.5, 99.9, 170.7, 174.1; HRMS (EI) calcd for $C_{20}H_{34}O_6$ *m/z* 370.2355, found 370.2352.

(1'*R*,2'*R*)-2-Hydroxy-1-methylpropyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-5,7-Di(*tert*-butyldimethylsilyloxy)-13,14-*O*-isopropylidene-2,6,6-trimethylpentadecenoate (96). To a stirred suspension of lithium aluminium hydride (403 mg, 10.6 mmol) in tetrahydrofuran (25 mL) at 0 °C was added dropwise a solution of **66** (380 mg, 0.79 mmol) in tetrahydrofuran (7 mL) and the mixture was stirred for 2 h. The mixture aws diluted with ether (40 mL) and excess hydride was destroyed by careful addition of water (400 μL). To this mixture was added aqueous sodium hydroxide (3N, 400 μL) and water (1.2 mL) and the gray suspension was stirred

at room temperature for 2 h, during which the suspension turned white. To this mixture was added magnesium sulfate (5 g), and the suspension was stirred for 1 h and was filtered. The collected solid was washed with ethyl acetate (100 mL) and the combined filtrate was concentrated under reduced pressure to give crude **64** (378 mg) which was used without further purification for the next reaction.

To a solution of crude **64** obtained above in tetrahydrofuran (40 mL) and water (10 mL) at room temperature was added *p*-toluenesulfonic acid (75 mg) and the mixture was stirred for 18 h. Saturated aqueous sodium bicarbonate (80 mL) was added and the solution was extracted with methylene chloride (4 x 50 mL). The combined extract was washed with brine and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (25 g, hexanes:ethyl acetate 1:2) to give **96** (306 mg, 85% from **66**) as a colourless viscous oil: IR (neat) 3450, 3445, 2975, 1730, 1455, 1375, 1245, 1215, 1175, 1080, 915, 880 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 3H),1.18 (d, *J* = 6.8 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.25 (m, 6H), 1.31 (s, 3H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.43 (s, 3H), 1.56 (m, 5H), 1.94 (m, 1H), 2.16 (m, 2H), 2.31 (m, 2H), 2.52 (m, 1H), 3.49 (m, 3H), 3.73 (pent, *J* = 8.8 Hz, 2H), 4.08 (m, 1H), 4.27 (q, *J* = 7.2 Hz, 1H), 4.75 (pent, *J* = 8.8 Hz, 1H), 5.47 (m, 1H), 5.51 (m, 1H); HRMS (FAB) calcd for $C_{25}H_{46}O_7$ *m/z* 458.3244, found 458.3247.

(1'*R*,2'*R*)-2-*tert*-Butyldimethylsilyloxy-1-methylpropyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-5,7-Di(*tert*-butyldimethylsilyloxy)-13,14-*O*-isopropylidene-2,6,6-trimethylpentadecenoate (97). To a solution of **96** (23.0 mg, 0.05 mmol) and 2,6-lutidine (250 μL) in methylene chloride (2 mL) at room temperature was added *tert*-butyldimethylsilyl triflate (230 μL) and the mixture was stirred for 18 h. The mixture was diluted with ether (40 mL) and the solution was washed with hydrochloric acid (1N, 2 x 10 mL), saturated aqueous sodium bicarbonate (2 x 10 mL) and brine

(20 mL). The solution was dried over anhydrous magnesium sulfate, the solvent was removed under reduced pressure and the residue was chromatographed on silica (10 g, hexanes:ethyl acetate 3:1) to give **97** (37.3 mg, 93%) as a colourless oil: $[\alpha]_D^{20}$ -20.6 (*c* 4.0 $CHCl_3$); IR (neat) 1735, 1470, 1410, 1320, 1105, 1075, 960, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 15H), 0.80 (s, 6H), 0.89 (s, 9H), 0.90 (s, 9H), 0.91 (s, 9H), 1.09 (d, *J* = 7.1 Hz, 3H), 1.14 (d, *J* = 7.2 Hz, 3H), 1.16 (m, 6H), 1.31 (m, 5H), 1.33 (s, 3H), 1.45 (s, 3H), 1.60 (s, 3H), 1.90 (m, 2H), 2.32 (m, 4H), 3.48 (m, 2H), 3.83 (pent, *J* = 6.6 Hz, 1H), 4.07 (dt, *J* = 10.6, 4.5 Hz, 1H), 4.24 (pent, *J* = 6.8 Hz, 1H), 4.81 (dt, *J* = 10.5, 4.7 Hz, 1H), 5.45 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ -4.8, -4.7, -3.6, -3.5, -3.2, 14.0, 15.5, 17.4, 17.7, 18.0, 18.1, 18.5, 18.6, 20.3, 20.4, 25.4, 25.5, 25.7, 25.8, 26.2, 27.1, 27.3, 28.3, 28.5, 30.0, 30.6, 31.8, 32.8, 40.5, 44.3, 44.4, 68.8, 73.1, 73.6, 77.4, 77.6, 77.8, 107.4, 107.5, 107.7, 124.5, 125.3, 131.9; HRMS (FAB) calcd for $C_{43}H_{88}O_7Si_3$ *m/z* 800.5838, found 800.5848.

(2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-5,7-Di(*tert*-butyldimethylsilyloxy)-13,14-*O*-isopropylidene-2,6,6-trimethylpentadecenoic Acid (98). To a solution of **97** (37.3 mg, 0.048 mmol) in a mixture of tetrahydrofuran (4 mL) and methanol (2 mL) was added aqueous sodium hydroxide (3N, 1 mL) and the mixture was refluxed for 18 h. The solution was cooled to 0 °C, acidified with hydrochloric acid (1N, 20 mL) and extracted with methylene chloride (5 x 10 mL). The combined extract was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to give virtually pure **98** (28.2 mg, 98%) as a colourless viscous oil: IR (neat) 3200 (br), 1735, 1470, 1255, 1075, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 12H), 0.83 (s, 6H), 0.89 (s, 9H), 0.90 (s, 9H), 1.16 (d, *J* = 7.0 Hz, 3H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.37 (s,), 1.48 (s, 3H), 1.57 (br s, 1H), 1.88 (m, 3H), 2.18 (m, 1H), 2.29 (m, 2H), 2.38 (m, 1H), 3.48 (m, 3H), 4.15 (dt, *J* = 10.6, 6.2 Hz, 1H), 4.27 (pent, *J* = 6.6 Hz, 1H), 5.46 (m, 2H). This material

was used without further purification for the next reaction.

Methyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-5,7-Di(*tert*-butyldimethylsilyloxy)-13,14-*O*-isopropylidene-2,6,6-trimethylpentadecenoate (99). To a solution of **98** (28.2 mg, 0.046 mmol) in ether (4 mL) at 0 °C was added an ethereal solution of diazomethane (1 mL) until the solution turned yellow. The mixture was allowed to warm to room temperature and was stirred for 2 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica (5 g, hexanes;ethyl acetate 9:1) to give **99** (27.5 mg, 95%) as a colourless oil: $[\alpha]_D^{20}$ -27.8 (*c* 14.2 $CHCl_3$); IR (neat) 1735, 1470, 1255, 1075, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 12H), 0.81 (s, 6H), 0.90 (s, 9H), 0.91 (s, 9H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.32 (s, 3H), 1.43 (s, 3H), 1.88 (m, 4H), 2.15-2.39 (m, 6H), 3.48 (m, 3H), 3.65 (s, 3H), 4.08 (dt, *J* = 10.8, 6.8 Hz, 1H), 4.25 (pent, *J* = 7.1 Hz, 1H), 5.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -3.7, -3.6, -3.5, -3.4, -3.2, 15.5, 17.1, 17.7, 18.4, 20.4, 25.5, 25.8, 26.1, 27.1, 28.3, 28.5, 30.5, 31.4, 31.7, 32.6, 33.0, 33.3, 39.8, 44.4, 51.4, 73.5, 73.7, 81.8, 107.3, 124.5, 125.3, 131.8, 176.8; HRMS (FAB) calcd for $C_{34}H_{68}O_6Si_2$ *m/z* 628.4554, found 628.4449.

Methyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-13,14-Dihydroxy-5,7-di(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylpentadecenoate (100). To a solution of **99** (19.6 mg, 0.031 mmol) in methanol (4 mL) was added *p*-toluenesulfonic acid and the mixture was refluxed for 5 h. The mixture was diluted with ethyl acetate (40 mL) and the solution was washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (8 g, hexanes:ethyl acetate 3:1) to give **100** (8.7 mg, 48%) as a colourless oil: IR (neat) 3465, 1735, 1465, 1440, 1380, 1365, 1255, 1070, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (m, 12H), 0.83 (s, 6H), 0.90 (s, 9H), 0.91 (s, 9H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.41 (m, 4H), 1.61 (br s, 2H, exchanged with D_2O),

1.74-2.33 (m, 6H), 2.42 (m, 1H), 3.45 (m, 2H), 3.59 (m, 1H), 3.68 (s, 3H), 3.86 (m, 1H), 5.45 (m, 1H), 5.57 (m, 1H); HRMS (FAB) calcd for $C_{31}H_{64}O_6Si_2$ *m/z* 588.4241, found 588.4236.

Methyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-13-Hydroxy-5,7,14-tri(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylpentadecenoate (101). To a solution of **100** (16.0 mg, 0.027 mmol) and 2,6-lutidine (8.2 μL) in methylene chloride (2 mL) at -78 °C was added *tert*-butyldimethylsilyl triflate (8.2 μL) and the mixture was stirred at this temperature for 1 h. To this solution at -78 °C was added ether (60 mL) and the solution was washed with hydrochloric acid (1N, 10 mL), saturated aqueous sodium bicarbonate (10 mL) and brine. The ethereal solution was dried over anhydrous magnesium sulfate, the solvent was removed under reduced pressure and the residue was chromatographed on silica (5 g, hexanes:ethyl acetate 92:8) to give **101** (13.5 mg, 71%) as a colourless oil: $[\alpha]_D^{20}$ –22.5 (*c* 13.4 $CHCl_3$); IR (neat) 2930, 1740, 1470, 1435, 1255, 1195, 1075, 1005, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (m, 18H), 0.82 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 0.90 (s, 9H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.35 (m, 6H), 1.87 (m, 2H), 2.16 (m, 3H), 2.48 (m, 1H), 3.43 (m, 2H), 3.52 (m, 1H), 3.63 (s, 3H), 3.72 (m, 1H), 5.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.5, -3.6. -3.5, -3.4, -3.3, 17.0, 17.3, 17.5, 18.0, 18.4, 18.5, 20.1, 20.3, 20.6, 25.3, 25.4, 25.8, 25.9. 26.1, 26.2, 30.2, 30.3, 30.6, 31.4, 31.7, 32.9, 35.6, 39.8, 44.3, 51.4, 70.9, 74.9, 77.4, 125.6, 132.1, 176.8; HRMS (FAB) calcd for $C_{37}H_{78}O_6Si_3$ *m/z* 702.5106, found 702.5113.

Methyl (2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-13-Acetoxy-5,7,14-tri(*tert*-butyldimethylsilyloxy)-2,6,6-trimethypentadecenoate (102). To a solution of **101** (5.6 mg, 0.008 mmol) in methylene chloride (1 mL) at room temperature was added 4-(dimethylamino)pyridine (10 mg), pyridine (100 μL) and acetic anhydride (100 μL) and the mixture was stirred for 4 h. The solution was diluted with ether (30 mL) and was washed with hydrochloric acid (1N, 10 mL), saturated

aqueous sodium bicarbonate (10 mL) and brine, and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (5 g, hexanes:ethyl acetate 95:5) to give **102** (5.4 mg, 92%) as a colourless oil: IR (neat) 1740, 1475, 1435, 1375, 1215, 1190, 1025, 955, 875 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.07 (m, 18H), 0.83 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 0.90 (s, 9H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.22-1.43 (m, 4H), 1.58 (s, 3H), 1.88 (m, 2H), 2.04 (s, 3H), 2.20-2.36 (m, 2H), 3.49 (m, 2H), 3.66 (s, 3H), 3.87 (m, 1H), 4.79 (m, 1H), 5.34 (m, 1H), 5.40 (m, 1H); HRMS (FAB) calcd for $C_{39}H_{80}O_7Si_3$ *m/z* 744.5212, found 744.5217.

(2*R*,5*S*,7*S*,13*S*,14*R*,10*Z*)-13-Hydroxy-5,7,14-tri(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylpentadecenoic Acid (103). To a solution of **101** (14.3 mg, 0.02 mmol) in a mixture of tetrahydrofuran (4 mL) and water (2 mL) was added aqueous sodium hydroxide (3N, 1 mL) and the mixture was refluxed for 1.5 h. The solution was cooled to 0 °C, acidified to pH 3 with hydrochloric acid (1N, 4 mL) and was extracted with methylene chloride (5 x 10 mL). The combined extract was washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (8 g, hexanes:ethyl acetate 3:1) to give **103** (13.4 mg, 96%) as a colourless oil: $[\alpha]_D^{20}$ -8.4 (*c* 12.4 $CHCl_3$); IR (neat) 2955 (br),1710, 1470, 1460, 1255, 1070, 1005, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (m, 18H), 0.85 (s, 6H), 0.91 (m, 27H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.38 (m, 6H), 1.81 (m, 1H), 1.96 (pent, *J* = 7.2 Hz, 1H), 2.14 (m, 4H), 2.42 (m. 1H), 3.44 (m, 2H), 3.60 (q, *J* = 4.8 Hz, 1H), 3.83 (m, 1H), 5.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.5, -4.3, -3.7, -3.5, -3.2, 16.8, 17.2, 17.3, 18.0, 18.1, 18.5, 20.5, 20.6, 25.3, 25.7, 25.8, 25.9, 26.2, 29.3, 29.9, 30.7, 30.9, 32.7, 39.2, 39.4, 44.2, 44.3, 70.7, 71.1, 75.2, 75.8, 126.0, 132.4, 180.6; HRMS (FAB) calcd for $C_{36}H_{76}O_6Si_3$ *m/z* 688.4950, found 688.4947.

(2*R*,5*S*,7*R*)-5,7-Di(*tert*-butyldimethylsilyloxy)-10-[(2'*R*,3'*S*,5'*R*)-2'-methyl-3'-*tert*-butyldimethylsilyloxy-5-tetrahydrofuranyl]-2,6,6-trimethyldecanoic Acid (104). To a solution of **85** (23.4 mg, 0.063 mmol) in methanol (5 mL) at 0 °C was added aqueous sodium hydroxide (10%, 2 mL) and the mixture was stirred for 10 min at this temperature, then was warmed to room tempaerature and stirred for 24 h. The solution was brought to pH 7 with hydrochloric acid (1N, 5 mL) and was evaporated to dryness under vacuum for 12 h. The resultant viscous residue was suspended in methylene chloride (2 mL) at 0 °C to which were added 2,6-lutidine (300 μL) followed by *tert*-butyldimethylsilyl triflate (300 μL). The mixture was allowed to warm to room temperature and was stirred for 3 h. The solution was diluted with ether (40 mL), the ethereal solution was washed with water (3 x 10 mL) and brine and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to leave a residue which was dissolved in a mixture of hexane (3 mL) and ethyl acetate (1 mL). To this solution at room temperature was added *p*-toluenesulfonic acid (10 mg) and the mixture was stirred for 18 h. The mixture was filtered through a short pad of Celite and the filtrate was concentrated to leave a residue which was chromatographed on silica (10 g, hexanes:ethyl acetate 96:4 to 5:1) to give **104** (34.0 mg, 78%) as a colourless oil: $[\alpha]_D^{20}$ +14.0 (*c* 29.2 $CHCl_3$); IR (neat) 2955 (br), 1710, 1470, 1465, 1360, 1255, 1110, 1095, 870, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (m, 18H), 0.75 (s, 3H), 0.82 (s, 3H), 0.89 (m, 27H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.38 (m, 6H), 1.60 (m, 4H), 1.88 (m, 1H), 2.22 (dt, *J* = 12.4, 7.8 Hz, 2H), 2.42 (q, *J* = 6.8 Hz, 1H), 3.54 (m, 2H), 3.77 (pent, *J* = 6.6 Hz, 1H), 3.84 (q, *J* = 6.7 Hz, 1H), 3.99 (pent, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.8, -4.6, -3.9, -3.8, -3.3, -3.2, 16.9, 18.0, 18.4, 18.5, 18.6, 18.7, 21.6, 24.0, 25.7, 25.8, 26.1, 26.2, 30.7, 31.4, 33.3, 37.2, 39.8,

40.9, 44.1, 77.0, 77.1, 77.7, 78.2, 79.5, 181.6; HRMS (FAB) calcd for $C_{36}H_{76}O_6Si_3$ *m/z* 688.4950, found 688.4944.

(2*R*,5*S*,7*R*)-5,7-Di(*tert*-butyldimethylsilyloxy)-10-[(2'*R*,3'*S*,5'*R*)-3'-hydroxy-2'-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoic Acid (105). To a solution of **104** (23.6 mg, 0.034 mmol) in tetrahydrofuran (4,5 mL) at room temperature was added tetra-*n*-butylammonium fluoride (1M in tetrahydrofuran, 115 μL) and the mixture was stirred for 3 h. The mixture was diluted with ethyl acetate (60 mL), the solution was washed with brine and was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica (12 g, hexanes:ethyl acetate 1:1) to give **105** (18.2 mg, 93%) as a colourless oil: $[\alpha]_D^{20}$ +4.3 (*c* 15.2 $CHCl_3$); IR (neat) 2955 (br), 1710, 1470, 1385, 1255, 1080, 1005, 805 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.03 (s, 3H), 0.04 (s, 6H), 0.72 (s, 3H), 0.83 (s, 3H), 0.89 (s, 9H), 0.90 (s, 9H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.19 (d *J* = 6.8 Hz, 3H), 1.39 (m, 6H), 1.66 (m, 4H), 1.85 (m, 2H), 2.40 (dt, *J* = 11.6, 6.9 Hz, 2H), 2.89 (br s, 2H), 3.53 (dt, *J* = 8.2, 5.5 Hz, 2H), 3.98 (m, 1H), 4.03 (pent, *J* = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.0, -3.9, -3.3, -3.2. 13.7, 17.0, 18.3, 18.4, 18.5, 18.8, 20.3, 21.8, 24.1, 24.3, 25.3, 26.2, 26.3, 30.7, 31.5, 33.3, 37.2, 39.9, 40.4, 44.1, 77.1, 77.2, 77.4, 77.8, 80.5, 181.0; HRMS (FAB) calcd for $C_{30}H_{62}O_6Si_2$ *m/z* 574.4085, found 574.4088.

2-Trimethylsilylethoxycarbonylmethyl (2*R*,5*S*,7*R*)-5,7-Di(*tert*-butyldimethylsilyloxy)-10-[(2'*R*,3'*S*,5'*R*)-3'-hydroxy-2'-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoate (106). To a solution of **105** (17.2 mg, 0.03 mmol) in acetone (5 mL) was added potassium carbonate (4 mg) followed by 2-trimethylsilylethyl α-bromoacetate (40 μL) and the mixture was refluxed for 3 h. The mixture was cooled to room temperature and filtered through Celite which was washed with ether (10 mL). The filtrate was concentrated and the residue was chromatographed on silica (6

g, hexanes:ethyl acetate 10:1) to give **106** (18.5 mg, 85%) as a colourless oil;$[\alpha]_D^{20}$ 1.4 (*c* 46 $CHCl_3$); IR (neat) 1745, 1470, 1385, 1250, 1150, 1005, 940, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (m, 21H), 0.74 (s, 3H), 0.84 (s, 3H), 0.90 (s, 18H), 1.19 (d, *J* = 6.5 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.29 (m, 6H), 1.52 (m, 4H), 1.61 (s, 2H), 1.90 (m, 1H), 2.02 (br s, 1H), 2.39 (dt, *J* = 10.4, 7.1 Hz, 1H), 2.49 (q, *J* = 6.9 Hz, 1H), 3.52 (m, 2H), 3.88 (dt, *J* = 7.2, 3.6 Hz, 1H), 3.98 (dt, *J* = 10.4, 6.8 Hz, 2H), 4.24 (m, 2H), 4.58 (ABq, *J* = 15.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -3.9, -3.8, -3.3, -3.2, -1.6 (x 3), 14.1, 17.1, 17.3, 18.3, 18.4, 18.5, 18.9, 21.3, 22.6, 24.2, 26.1, 26.2, 26.3, 30.7, 31.4, 31.5, 33.3, 37.3, 39.8, 40.6, 44.1, 60.6, 63.7, 76.7, 76.8, 77.0, 80.2, 167.9, 175.8; HRMS (FAB) calcd for $C_{37}H_{76}O_8Si_3$ *m/z* 732.4848, found 732.4841.

2-Trimethylsilylethoxycarbonylmethyl (2*R*,5*S*,7*R*)-5,7-Di(*tert*-butyldimethylsilyloxy)-10-[(2'*R*,3'*S*,5'*R*)- 3'-bromoacetoxy-2'-methyltetrahydrofuranyl]-2,6,6-trimethyldecanoate (107). To a solution of **106** (3.3 mg, 0.005 mmol) in methylene chloride at 0 °C was added 4-(dimethylamino)pyridine (2 mg) pyridine (10 μL) and α-bromoacetyl bromide (10 μL). The mixture was stirred for 30 min, during which the solution turned cloudy and a precipitate was formed. The suspension was diluted with ether (40 mL) and filtered, and the filtrate was washed with saturated aqueous sodium bicarbonate (10 mL), hydrochloric acid (1N, 2 x 10 mL) and brine. The filtrate was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to leave a residue which was chromatographed on silica (5g, hexanes:ethyl acetate 92:8) to give **107** (3.4 mg, 89%) as a colourless oil: $[\alpha]_D^{20}$ +1.8 (*c* 24.5 $CHCl_3$); IR (neat) 1760, 1745, 1475, 1275, 1250, 1150, 1095, 1005, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (m, 21H), 0.70 (s, 3H), 0.79 (s, 3H), 0.84 (s, 9H), 0.85 (s, 9H), 0.97 (m, 2H), 1.16 (d, *J* = 7.0 Hz, 3H), 1.18 (d, *J* = 7.1 Hz, 3H), 1.36-1.47 (m, 7H), 1.66 (m, 3H), 1.91 (m, 1H), 2.43 (pent, *J* = 7.2 Hz, 2H), 3.51 (m, 2H), 3.78 (s, 2H), 4.08 (pent, *J* = 6.6 Hz, 2H), 4.13

(dq, *J* = 6.6, 2.6 Hz, 2H), 4.52 (ABq, *J* = 15.8 Hz, 2H), 4.93 (pent, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.0, -3.9, -3.4, -3.3, -1.6 (x 3) , 17.0, 17.2, 18.3, 18.4, 18.6, 21.3, 24.1, 25.4, 25.6 (x 2), 25.8, 26.1, 30.6, 31.3, 33.2, 34.3, 36.5, 36.8, 39.7, 44.0, 60.5, 63.5, 77.0, 77.1, 77.3, 77.5, 78.4, 81.5, 166.9, 167.7, 175.6; HRMS (FAB) calcd for $C_{39}H_{77}{}^{79}BrO_9Si_3$ *m/z* 852.4059, found 852.4066.