Supporting Information

A Convergent Total Synthesis of Hemibrevetoxin B.

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Experimental procedures, spectroscopic and analytical data for compounds 1 – 25.

General Information. All reactions were carried out under an inert atmosphere of dry nitrogen in oven or flame-dried glassware. Proton magnetic resonance spectra were recorded at 300, 400, and 500 MHz on Varian Gemini, Varian Unity Inova, and Varian VXR spectrometers, respectively. Carbon magnetic resonance spectra were recorded at 100 MHz on a Varian Unity Inova spectrometer. All chemical shifts were reported in δ units relative to tetramethylsilane. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter. Infrared spectra were recorded on Perkin-Elmer Paragon 1000 FT-IR spectrometer. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA). Mass spectral data were obtained by the Mass Spectrometry laboratory at the Florida State University. Melting points were determined on a 50-600 hot stage controller. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with silica Gel 60 F₂₅₄ (E. Merck no. 5715-7). Flash column chromatography was performed using 40-60 mm (400-230 mesh) silica gel (E. Merck no. 9385-9) as the stationary phase. Tetrahydrofuran (THF) and ether (Et₂O) were dried by refluxing over lithium aluminum hydride in a continuous still under an atmosphere of nitrogen. Dichloromethane (CH₂Cl₂), di-iso-propylamine, pyridine, triethylamine, and chlorotrimethylsilane (TMSCl) were refluxed over calcium hydride in a continuous still under an atmosphere of nitrogen. Chlorotriethylsilane (TESCl), and di-iso-propylethyl amine (Hunig's base) were distilled from calcium hydride under an inert atmosphere of dry nitrogen and stored over calcium hydride. 1,3-Dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU) and dimethyl sulfoxide (DMSO) were distilled under reduced pressure from calcium hydride and stored over calcium hydride. 1,1,1,3,3,3-Hexafluoro-isopropanol was distilled from Ba[OCH(CF₃)₂]₂ prior to use. Methanol was dried by refluxing over Mg(OMe)₂ in a continuous still under an atmosphere of nitrogen.

Preparation of 5R,6R-Bis-benzyloxy-5R-methyl-tetrahydro-pyran-3R,4R-diol (5). Benzyl β -D-arabinopyranoside (30.0 g, 124.8 mmol) was dissolved in a 5.5:1 mixture of dry acetone and 2,2-dimethoxypropane (1 L) and ($\pm$)-camphorsulfonic acid (1.44 g, 6.20 mmol, 0.05 eq) was added. The solution was stirred at room temperature for 1 h and neutralized by dropwise addition of saturated aqueous sodium bicarbonate to pH 8. The solvent was evaporated, and the residue was diluted with dichloromethane (800 ml) and washed with water (150 ml) and brine (100 ml). The organic solution was dried over anhydrous sodium sulfate, filtered, and evaporated. The product was dried in vacuo and utilized in the next step directly.

To a solution of oxalyl chloride in dichloromethane (2 M, 69 ml, 0.138 mol) was added dry dichloromethane (70 ml) and the mixture was cooled to -78°C under a nitrogen atmosphere. Dry dimethylsulfoxide (19.6 ml, 21.6 g, 0.276 mol) was added dropwise, and the mixture was stirred at -78°C for 25 min. A solution of the substrate (34.96 g, 0.125 mol) in dry dichloromethane (500 ml) was slowly added, and the mixture was stirred for 30 min. Triethylamine (57.7 ml, 41.9 g, 0.41 mol) was added dropwise, and the mixture was warmed to 0°C and stirred at this temperature for 20 min. Dilution with dichloromethane (500 ml), washing with 1M HCl (400 ml), water (250 ml), saturated sodium bicarbonate (250 ml), and brine (250 ml), drying over anhydrous sodium sulfate, filtration, and evaporation of the solvent afforded, after drying in vacuo, 34.7 g (124.8 mmol) of the crude ketone A (6R-Benzyloxy-2,2-dimethyl-dihydro-[1,3]dioxolo[4R,5R-c]pyran-7-one), which was used without further purification.

Cerium(III) chloride heptahydrate (141g, 0.378 mol, 3 eq) was refluxed with thionyl chloride (500 ml) for 2 h using a cold solution of sodium hydroxide as a hydrogen chloride trap. Excess thionyl chloride was distilled off, and the residual gray powder was dried at $140^{\circ}\text{C}/1\text{mm Hg}$ for 7 h. The anhydrous cerium trichloride was cooled to room temperature and dry cold THF (700 ml) was added while the mixture was stirred with a mechanical stirrer. The CeCl_3 suspension was stirred overnight. After cooling to -78°C , a solution of salt-free methyllithium in ether (1.4M, 270 ml, 0.378 mol) was slowly added to the vigorously stirring CeCl_3 -THF mixture, and the resultant bright yellow suspension was stirred for 1 h at -78°C . A solution of ketone A (34.7

g, 124.8 mmol) in dry THF (140 ml) was added, and the reaction mixture was warmed to -20°C and stirred at this temperature for 4 h. The reaction was quenched by careful portionwise addition of 188 ml of 3M aqueous sodium carbonate at -20°C (initially 5 ml, then, after the exothermic reaction subsided, 10 ml more, and, after 5 min, the remaining solution was added). The heterogeneous mixture was stirred for 30 min at room temperature and the solids were filtered off through a short pad of Celite. The solvent was evaporated and the residue was dried in vacuo to give 36.55 g (0.124 mol, 100%) of the crude product (6R-Benzylloxy-2,2,7R-trimethyl-tetrahydro-[1,3]dioxolo[4R,5R-c]pyran-7R-ol) as a yellow oil, which was directly submitted to the next step.

The tertiary alcohol was dissolved in dry DMF (210 ml) and cooled to 0°C under a nitrogen atmosphere. Sodium hydride (4.8 g, 0.20 mol, 1.6 eq) and imidazole (0.50 g) were added, and the mixture was stirred for 20 min. Benzyl bromide (17.0 ml, 24.4 g, 0.142 mol, 1.1 eq) was added and the reaction mixture was stirred for 1 h at room temperature (if the reagents or the solvent are of poor quality, addition of a greater excess of the reagents may be required). The reaction was quenched by a careful addition of water (200 ml), extracted with ethyl acetate (1 L), washed with water (2x100 ml) and brine (150 ml). The organic solution was dried over anhydrous sodium sulfate, filtered, and evaporated. The remaining oil was redissolved in methanol (1.4 L) and ($\pm$)-camphorsulfonic acid (1.44 g, 6.20 mmol, 0.05 eq) was added. After 1 h the solution was neutralized by addition of saturated aqueous sodium bicarbonate until pH 8 was reached. The solvent was evaporated and the residue was extracted with chloroform (1 L) and washed with water (150 ml) and brine (150 ml). The organic phase was dried over anhydrous NaSO_4 , filtered, and concentrated. The residue was recrystallized from ether – pentane (1:1, 800 ml) to give 33.15 g (96.2 mmol, 78%) of diol 5. An additional 5.50 g (15.4 mmol, 12%) of the product was isolated after column chromatography of the oil obtained by concentration of the mother-liquor, thus bringing the total yield of diol 5 to 38.65 g (112.2 mmol, 90% from benzyl β -D-arabinopyranoside).

$[\alpha]_{\text{D}}^{25} = -126.7^{\circ}$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3), $\delta(\text{ppm})$: 7.34 (m, 10H, Ph); 4.97 (s, 1H, H-1); 4.79 (d, $J=12.3$ Hz, 1 H, CH_2Ph); 4.55 (d, $J=12.3$ Hz, 1 H, CH_2Ph); 4.53 (d, $J=10.6$ Hz, 1 H, CH_2Ph); 4.48 (d, $J=10.6$ Hz, 1 H, CH_2Ph); 3.97 (d, 1H, $J=12.3$ Hz, H-5); 3.84 (d, 1H, $J=12.3$ Hz, H-5); 3.73 (bs, 1H, H-3); 3.71 (bs, 1H, H-4); 2.74 (bs, 2H, OH), 1.46 (s, 3H, Me); ^{13}C NMR (100 MHz, CDCl_3), $\delta(\text{ppm})$: 137.746; 137.119; 128.623; 128.499; 127.937;

127.739; 127.632; 98.163; 79.454; 69.826; 69.760; 69.512; 65.004; 64.517; IR (CHCl₃), ν (cm⁻¹): 3684, 3492, 3026, 3014, 2400, 1228, 1218, 1204, 1036; Calcd for C₂₀H₂₄O₅: C, 69.75; H 7.02. Found: C, 69.90; H, 7.04.

(2R,3R-Bis-benzyloxy-3R-methyl-5R-trityloxy-tetrahydro-pyran-4R-yloxy)-acetic acid tert-butyl ester. A mixture of diol 5 (0.80 g, 2.32 mmol), di-n-butyltin oxide (0.80 g, 3.48 mmol, 1.5 eq), and dry toluene (15 ml) was refluxed in a flask fitted with a Dean-Stark adapter for 1 h, cooled to room temperature, and the solvent was evaporated under reduced pressure. The residue was dissolved in dry DMF (15 ml) and treated with trityl bromide (1.50 g, 4.64 mmol, 2.0 eq) and tetra-n-butylammonium iodide (0.17 g, 0.464 mmol, 0.2 eq) under a nitrogen atmosphere at room temperature for 2 h. Ground sodium hydroxide (0.280 g, 7.0 mmol, 3.0 eq), water (0.30 ml), and ether (10 ml) were added and the stirring was continued for 1 h. The mixture was filtered through Celite and concentrated to give the product, which was purified by column chromatography (silica, 2% ethyl acetate – toluene) to give 1.35 g (2.30 mmol, 100%) of 2R,3R-Bis-benzyloxy-2R-methyl-6R-trityloxy-cyclohexanol.

$[\alpha]_D^{25} = -25.1$ (c 0.47, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 7.54 – 7.51 (m, Ph); 7.34 – 7.24 (m, Ph); 4.78 (d, J=11.6 Hz, 1H, PhCH₂1); 4.77 (s, 1H, H-1); 4.52 (d, J=12.2 Hz, 1H, PhCH₂2); 4.48 (d, J=11.6 Hz, 1H, PhCH₂1); 4.37 (d, J=12.2 Hz, 1H, PhCH₂2); 3.82 – 3.73 (m, 2H, H-5); 3.42 (dd, J₁=15.8 Hz, J₂=10.0 Hz, 1H, H-4); 3.03 (bs, 1H, H-3); 2.65 (bs, 1H, OH-3); 1.05 (s, 3H, Me); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): ; MW=586.72; IR (CHCl₃) ν (cm⁻¹): 3020, 1224, 1070; Calcd. for C₃₉H₃₈O₅: C, 79.84, H, 6.53; Found: C, 79.76, H, 6.58.

2R,3R-Bis-benzyloxy-2R-methyl-6R-trityloxy-cyclohexanol (0.300 g, 0.511 mmol) was dissolved in dry DMF (1 ml) under a nitrogen atmosphere and sodium hydride (24 mg, 1.0 mmol, 2 eq) was added at room temperature. After 30 min, tert-butyl bromoacetate (76 μ l, 100 mg, 0.52 mmol, 1.0 eq) was added, and the same portions of the reagents were added in 15 min intervals until TLC showed a complete consumption of the starting material (~2 h). The reaction mixture was diluted with ether (30 ml), and washed with water and brine. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated.

The residue was purified by column chromatography (silica, 4% ethyl acetate – hexanes) to give the title ester (0.360 g, 0.51 mmol, 100%).

$[\alpha]_D^{25} = -11.1^\circ$ (c 0.52, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 7.52 – 7.50 (m, Ph); 7.34 – 7.20 (m, Ph); 4.93 (s, 1H, H-1); 4.78 (d, $J=12.2$ Hz, 1H, PhCH_2 1); 4.56 (d, $J=12.2$ Hz, 1H, PhCH_2 2); 4.50 (d, $J=12.2$ Hz, 1H, PhCH_2 1); 4.43 (d, $J=12.2$ Hz, 1H, PhCH_2 2); 4.05 (AB, $J=15.4$ Hz, 2H, $\text{OCH}_2\text{CO}_2\text{Bu-t}$); 3.98 (7, $J=10.6$ Hz, 1H, H-5); 3.84 (ddd, $J_1=10.2$ Hz, $J_2=5.0$ Hz, $J_3=2.4$ Hz, 1H, H-4); 3.57 (dd, $J_1=10.6$ Hz, $J_2=5.0$ Hz, 1H, H-5); 2.63 (bs, 1H, H-3); 1.49 (s, 3H, Me); 1.45 (s, 9H, $\text{CO}_2\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 169.38; 144.31; 139.98; 138.02; 128.87; 128.18; 128.04; 127.98; 127.60; 127.38; 127.33; 126.77; 101.46; 87.19; 82.56; 80.81; 77.56; 77.21; 70.97; 70.89; 69.45; 68.48; 64.65; 63.39; 28.13; 28.00; 14.66; MW=715.27; IR (CHCl_3) ν (cm^{-1}): 3022, 1748, 1204, 1136, 1070; Calcd. for $\text{C}_{45}\text{H}_{48}\text{O}_7+0.8\text{H}_2\text{O}$: C, 75.56, H, 6.99; Found: C, 75.57, H, 7.12.

7R,8R-Dibenzyloxy-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one (6). A solution containing (2R,3R-Bis-benzyloxy-3R-methyl-5R-trityloxy-tetrahydro-pyran-4R-yloxy)-acetic acid tert-butyl ester (0.100 g, 0.143 mmol), sulfuric acid (0.10 ml, 0.20 g, 2.0 mmol, 1.4 eq), and dry acetonitrile (2.8 ml) was stirred at room temperature for 0.5 h. The mixture was diluted with ethyl acetate (35 ml) and washed with water (7 ml), saturated aqueous sodium bicarbonate (7 ml), and brine (7 ml), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (silica, 33% ethyl acetate – hexanes) to give pure lactone 6 (0.049 g, 0.127 mmol, 89% from diol 5).

$[\alpha]_D^{25} = -69.0^\circ$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 7.31 (m, 10H, Ph); 4.93 (s, 1H, H-1); 4.80 (d, $J=12.2$ Hz, 1H, CH_2Ph); 4.63 (dt, $J_d=4.8$ Hz, $J_t=3.5$ Hz, 1H, H-4); 4.59 (d, $J=11$ Hz, 1H, CH_2Ph); 4.56 (d, $J=12.2$ Hz, 1H, CH_2Ph); 4.52 (d, $J=17.4$ Hz, 1H, H-7); 4.47 (d, $J=11$ Hz, 1H, CH_2Ph); 4.21 (d, $J=17.4$ Hz, 1H, H-7); 4.08 (dd, $J_1=3.6$ Hz, $J_2=12.6$ Hz, 1H, H-5); 3.98 (d, $J=3.5$ Hz, 1H, H-3); 3.98 (dd, $J_1=4.9$ Hz, $J_2=12.5$ Hz, 1H, H-5); 1.46 (s, 3H, Me); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 166.932, 138.116, 137.026, 128.488,

128.290, 127.952, 127.762, 127.531, 127.365, 99.102, 77.428, 73.374, 70.394, 70.336, 64.680, 64.358, 61.996, 16.361; IR (CHCl₃), ν (cm⁻¹): 3026, 3014, 2926, 2400, 1756, 1520, 1454, 1424, 1272, 1226, 1204; Calcd for C₂₂H₂₄O₆: C, 68.74; H 6.29. Found: C, 68.57; H, 6.23.

2S-Allyl-7R,8R-dibenzyloxy-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one (7). Di-iso-propylamine (3.20 ml, 2.31 g, 22.8 mmol, 1.4 eq) was dissolved in dry THF (46 ml) and treated with n-butyllithium (2.60 M in hexanes, 7.65 ml, 19.9 mmol, 1.2 eq) at 0 °C under a nitrogen atmosphere for 15 min. The LDA solution was cooled to -78 °C and lactone 6 (6.37 g, 16.57 mmol) in dry THF (53 mmol) was added dropwise within 4 min. Allyl iodide (7.6 ml, 13.9 g, 83.0 mmol, 5 eq) was immediately added. The reaction mixture was stirred for 3.5 h at -78 °C, quenched with acetic acid (1.09 ml), and brought to room temperature. Dilution with ethyl acetate (300 ml) and washing with water (75 ml) and brine (75 ml), extraction of the combined aqueous layers with ethyl acetate (2x50 ml), drying over anhydrous sodium sulfate, filtration, and concentration gave a mixture of the allylated products, which was separated by column chromatography to afford 7 (5.781 g, 13.62 mmol, 83%) and its diastereomer (0.32 g, 0.75 mmol, 4.5%), along with the starting material (0.417 g, 1.08 mmol, 6.5%).

7: $[\alpha]_D^{25} = -75.5^\circ$ (c 1.1, CHCl₃); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 7.37 (d, J=7.6 Hz, 2H, Ph); 7.22 (t, J=7.6 Hz, 2H, Ph); 7.17 (t, J=7.6 Hz, 2H, Ph); 7.12 (d, J=7.6 Hz, 1H, Ph); 7.07 (t, J=7.6 Hz, 1H, Ph); 5.88 (qt, J_q=10.4 Hz, J_t=7.1 Hz, 1H, H-9); 5.12 (dq, J_d=17.0 Hz, J_q=1.5 Hz, 1H, HE-10); 5.05 (dt, J_d=10.3 Hz, J_t=0.9 Hz, 1H, HZ-10); 4.74 (s, 1H, H-1); 4.72 (dd, J₁=4.6 Hz, J₂=5.6 Hz, 1H, H-7); 4.45 (d, J=12.1 Hz, 1H, CH₂Ph); 4.34 (d, J=11.4 Hz, 1H, CH₂Ph); 4.18 (d, J=12.1 Hz, 1H, CH₂Ph); 4.14 (d, J=11.4 Hz, 1H, CH₂Ph); 3.95 (dt, J_d=3.9 Hz, J_t=2.5 Hz, 1H, H-4); 3.69 (dd, J₁=12.9 Hz, J₂=2.5 Hz, 1H, H-5); 3.60 (d, J=3.9 Hz, 1H, H-3); 3.48 (dd, J₁=12.9 Hz, J₂=2.4 Hz, 1H, H-5); 2.52 (m, 2H, H-8); 1.26 (s, 3H, Me); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 169.277, 137.827, 136.935, 132.691, 128.530, 128.249, 128.009, 127.712, 127.539, 127.481, 119.043, 98.268, 77.957, 73.622, 73.283, 69.857, 68.569, 64.729, 61.724, 38.432, 17.170; IR (CHCl₃), ν (cm⁻¹): 3026, 3014, 2400, 1744,

1520, 1454, 1418, 1380, 1226, 1204, 1042; Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.74; H, 6.57.

2R-Allyl-7R,8R-dibenzyloxy-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one (2-epi-7): $[\alpha]_D^{25} = -61.5^\circ$ (c 1.1, $CHCl_3$); 1H NMR (400 MHz, C_6D_6), δ (ppm): 7.39 (d, $J=7.4$ Hz, 2H, Ph); 7.23 (q, $J=7.5$ Hz, 4H, Ph); 7.12 (m, 3H, Ph); 7.07 (m, 1H, Ph); 5.85 (qt, $J_q=10.2$ Hz, $J_t=7.0$ Hz, 1H, H-9); 5.09 (dq, $J_d=17.3$ Hz, $J_q=1.8$ Hz, 1H, HE-10); 5.02 (dm, $J=10.2$ Hz, 1H, HZ-10); 4.79 (s, 1H, H-1); 4.69 (d, $J=12.2$ Hz, 1H, H-CH₂Ph); 4.39 (d, $J=11.5$ Hz, 1H, CH₂Ph); 4.33 (d, $J=12.2$ Hz, 1H, CH₂Ph); 4.24 (d, $J=11.5$ Hz, 1H, CH₂Ph); 3.89 (ddd, $J_1=2.8$ Hz, $J_2=5.1$ Hz, $J_3=8.6$ Hz, 1H, H-4); 3.76 (dd, $J_1=4.6$ Hz, $J_2=6.6$ Hz, 1H, H-7); 3.70 (dd, $J_1=5.0$ Hz, $J_2=11.6$ Hz, 1H, H_b-5); 3.63 (dd, $J_1=9.1$ Hz, $J_2=11.6$ Hz, 1H, H_a-5); 3.33 (d, $J=2.8$ Hz, 1H, H-3); 2.59 (m, 2H, H-8); 1.19 (s, 3H, Me); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm): 167.386, 139.867, 138.521, 133.765, 128.910, 128.835, 128.662, 128.315, 127.993, 127.952, 119.051, 101.043, 76.603, 76.025, 73.705, 73.399, 71.253, 64.779, 63.301, 36.838, 15.825; IR ($CHCl_3$), ν (cm^{-1}): 3684, 3026, 3014, 2400, 1748, 1520, 1456, 1418, 1228, 1202, 1138, 1082.

(7R,8R-Dibenzyloxy-8R-methyl-3-oxo-hexahydro-pyrano[3R,4R-b][1,4]dioxin-2S-yl)-acetaldehyde. Osmium tetroxide (0.04M in tert-butanol, 5.9 ml, 0.236 mmol, 0.07 eq) was added to a vigorously stirring mixture of lactone 7 (1.429 g, 3.37 mmol), ether (33.7 ml), water (3.4 ml), and saturated aqueous sodium bicarbonate (3.4 ml). After 5 min, ground sodium periodate (3.60 g, 16.8 mmol, 5 eq) was added and stirring was continued for 3.5 h. The reaction mixture was decanted into a separatory funnel. The remaining solids were

extracted with ethyl acetate (4x25 ml) and the combined organic solutions were washed with saturated aqueous sodium thiosulfate (2x15 ml), water (15 ml), and brine (15 ml). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated to furnish the aldehyde (1.406 g, 3.28 mmol, 97%), which required no further purification.

$[\alpha]_D^{25} = -63.1^\circ$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 9.66 (s, 1H, H-10); 7.31 (m, 10H, Ph); 5.00 (s, 1H, H-1); 4.90 (dt, $J_d=4.0$ Hz, $J_t=1.9$ Hz, 1H, H-4); 4.79 (t, $J=4.4$ Hz, 1H, H-8); 4.76 (d, $J=12.3$ Hz, 1H, CH_2Ph); 4.55 (d, $J=11.0$ Hz, 1H, CH_2Ph); 4.53 (d, $J=12.3$ Hz, 1H, CH_2Ph); 4.39 (d, $J=11.0$ Hz, 1H, CH_2Ph); 4.10 (dd, $J_1=13.2$ Hz, $J_2=1.6$ Hz, 1H, H-5); 4.06 (dd, $J_1=13.2$ Hz, $J_2=2.2$ Hz, 1H, H-5); 3.95 (d, $J=4.0$ Hz, 1H, H-3); 3.04 (dd, $J_1=18.5$ Hz, $J_2=5.0$ Hz, 1H, H-9); 2.97 (dd, $J_1=18.5$ Hz, $J_2=4.0$ Hz, 1H, H-9); 1.46 (s, 3H, Me); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 198.332, 169.690, 137.761, 136.836, 128.530, 128.298, 128.034, 127.762, 127.547, 127.316, 97.955, 78.155, 73.151, 69.741, 68.784, 67.941, 64.531, 61.633, 47.638, 17.212; IR (CHCl_3), $\nu(\text{cm}^{-1})$: 3034, 3024, 3016, 2922, 1732, 1498, 1454, 1384, 1256; Calcd for $\text{C}_{24}\text{H}_{26}\text{O}_7$: C, 67.59; H, 6.14. Found: C, 67.34; H, 6.14.

7R,8R-Dibenzyloxy-2S-(2-hydroxy-ethyl)-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one. Sodium cyanoborohydride (0.247 g, 3.93 mmol, 1.2 eq) was added to a solution of the previous aldehyde (1.40 g, 3.28 mmol) and acetic acid (0.68 ml, 0.713 g, 11.9 mmol, 3.6 eq) in dry THF (18.2 ml) at 0°C . After stirring for 20 min at room temperature, the reaction mixture was extracted with ethyl acetate (100 ml), washed with saturated aqueous ammonium chloride – concentrated ammonia mixture (9:1 v/v, 10 ml), water (10 ml), and brine (10 ml), dried over anhydrous sodium sulfate, filtered, and concentrated to furnish the unstable alcohol (1.406 g, 3.28 mmol, 97%), which was immediately utilized in the next step.

^1H NMR (400 MHz, CDCl_3), δ (ppm): 7.32 (m, 10H, Ph); 4.96 (s, 1H, H-1); 4.76 (d, $J=11.9$ Hz, 1H, CH_2Ph); 4.72 (dd, $J_1=6.8$ Hz, $J_2=5.3$ Hz, 1H, H-8); 4.66 (dt, $J_d=3.8$ Hz, $J_t=2.9$ Hz, 1H, H-4); 4.57 (d, $J=11.2$ Hz, 1H, CH_2Ph);

4.52 (d, $J=11.9$ Hz, 1H, CH₂Ph); 4.45 (d, $J=11.2$ Hz, 1H, CH₂Ph); 4.06 (dd, $J_1=13.0$ Hz, $J_2=2.8$ Hz, 1H, H-5); 4.04 (d, $J=3.5$ Hz, 1H, H-5); 4.01 (dd, $J_1=13.0$ Hz, $J_2=2.9$ Hz, 1H, H-3); 3.78 (m, 2H, H-10); 2.10 (m, 1H, H-9); 2.00 (dddd, $J_1=4.2$ Hz, $J_2=J_3=5.4$ Hz, $J_4=14.9$ Hz, 1H, H-10); 1.47 (s, 3H, Me).

7R,8R-Dibenzyloxy-2S-(2-iodo-ethyl)-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one (3). Iodine (1.75 g, 6.89 mmol, 2.1 eq) was added to a solution of the alcohol (1.41 g, 3.28 mmol), triphenylphosphine (1.72 g, 6.56 mmol, 2 eq), and 2,6-lutidine (1.53 ml, 1.41 g, 13.3 mmol, 4 eq) in dry dichloromethane (20 ml) at 0°C. The reaction mixture was stirred at room temperature for 4 h. The solution was diluted with dichloromethane (100 ml), washed with 1M aqueous hydrogen chloride (15 ml), water (15 ml), saturated aqueous sodium bicarbonate (15 ml), and brine (15 ml). The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. The resultant oil was purified by flash column chromatography to afford iodide 3 (1.553 g, 2.88 mmol, 83% from 7).

$[\alpha]_D^{25} = -64.6^\circ$ (c 1.1, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 7.32 (m, 10H, Ph); 4.97 (s, 1H, H-1); 4.76 (d, $J=11.9$ Hz, 1H, CH₂Ph); 4.66 (dd, $J_1=8.4$ Hz, $J_2=4.2$ Hz, 1H, H-8); 4.59 (dt, $J_d=4.0$ Hz, $J_t=2.2$ Hz, 1H, H-4); 4.54 (d, $J=11.1$ Hz, 1H, CH₂Ph); 4.53 (d, $J=11.9$ Hz, 1H, CH₂Ph); 4.45 (d, $J=11.1$ Hz, 1H, CH₂Ph); 4.05 (dd, $J_1=13.3$ Hz, $J_2=2.5$ Hz, 1H, H-5); 4.02 (dd, $J_1=13.2$ Hz, $J_2=2.0$ Hz, 1H, H-5); 3.98 (d, $J=4.0$ Hz, 1H, H-3); 3.27 (dd, $J_1=8.0$ Hz, $J_2=6.2$ Hz, 2H, H-10); 2.33 (dddd, $J_1=4.3$ Hz, $J_2=J_3=8.0$ Hz, $J_4=14.4$ Hz, 1H, H-9); 2.14 (dddd, $J_1=J_2=6.2$ Hz, $J_3=8.4$ Hz, $J_4=14.5$ Hz, 1H, H-9); 1.48 (s, 3H, Me); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 168.894, 137.744, 136.860, 128.563, 128.324, 128.076, 127.787, 127.597, 127.498, 98.329, 77.961, 73.602, 73.321, 69.961, 68.566, 64.784, 61.721, 37.448, 17.055, 0.584; IR (CHCl₃), ν (cm⁻¹): 3026, 3012, 1048, 718; Calcd for C₂₄H₂₇IO₆: C, 53.54; H 5.05. Found: C, 53.80; H, 5.17.

Ethyl 2-(trimethylstannylmethyl)acrylate. Tin dichloride dihydrate (3.34 g, 14.8 mmol, 1.1 eq) and acetic anhydride (2.8 ml) were stirred at room temperature under a nitrogen atmosphere for 1 h. The mixture was allowed to settle, and the white powder was washed with dry ether (4x10 ml). Ethyl 2-(bromomethyl)acrylate (2.6 g, 13.5 mmol), dry ether (5.6 ml), dry dichloromethane (5.6 ml), and lithium bromide (0.12 g, 1.4 mmol, 0.1 eq) were added and the resultant suspension was refluxed for 1.5 h. About 15 min after the reflux was initiated the suspension turned clear, and then, about 5 min later, murky again. The reaction mixture was evaporated, the residue was dissolved in chloroform, filtered, and evaporated. The crude oil was dissolved in dry THF (27 ml) and treated with a solution of methylmagnesium bromide (3M in ether, 13.2 ml, 39.7 mmol, 3 eq) under a nitrogen atmosphere at -78°C for 1 h and at room temperature for 30 min. The mixture was extracted with pentane (100 ml) and washed with saturated aqueous solution of ammonium chloride (50 ml) and brine (30 ml). After drying over anhydrous sodium sulfate, the solution was filtered the solvent was evaporated to give ethyl 2-(trimethylstannyl)acrylate (2.82 g, 10.2 mmol, 78%), which required no further purification.

^1H NMR (300 MHz, CDCl_3), δ (ppm): 5.82 (m, 1H, $\text{C}=\text{CH}_2$); 5.29 (m, 1H, $\text{C}=\text{CH}_2$); 4.18 (q, $J=7.4$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$); 1.97 (m, 2H, SnCH_2); 1.29 (t, $J=7.4$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$); 0.08 (t, $J=26$ Hz, 9H, SnMe_3).

2-(5S-Acetoxy-6R-acetoxymethyl-5,6-dihydro-2H-pyran-2R-ylmethyl)-acrylic acid ethyl ester (8) using ethyl 2-(trimethylstannylmethyl)acrylate. Tri-O-acetyl-D-glucal (9.7 g, 35.60 mmol) and ethyl 2-(trimethylstannylmethyl)acrylate (26.5 g, 95.8 mmol, 3 eq) were dissolved in dry acetonitrile (350 ml) under a nitrogen atmosphere. Boron trifluoride etherate (26.3 ml, 30.4 g, 0.214 mol, 6.0 eq) was added within about 5 min at -10°C , and the mixture was stirred for 15 min at this temperature. The reaction was quenched by a careful addition of a saturated aqueous solution of sodium bicarbonate (300 ml) and the mixture was extracted with dichloromethane. The organic layers were washed with water, saturated aqueous solution of sodium bicarbonate, and brine, dried over anhydrous sodium sulfate, filtered, and evaporated. The crude product was purified by column chromatography (silica gel, 35% ethyl acetate

– hexanes) to give pure ester 8 (11.6 g, 35.55 mmol, 100%, mixture of epimers at C-4 (97:3)) as a colorless oil.

$[\alpha]_D^{25} = +80.5$ (c 0.75, CHCl_3), ^1H NMR (400 MHz, CDCl_3), δ (ppm): 6.29 (d, $J=1.3$ Hz, 1H, H_E -10); 5.92 (ddd, $J_1=10.4$ Hz, $J_2=2.8$ Hz, $J_3=1.6$ Hz, 1H, H-5); 5.78 (ddd, $J_1=10.4$ Hz, $J_2=2.6$ Hz, $J_3=1.8$ Hz, 1H, H-6); 5.69 (d, $J=1.3$ Hz, 1H, H_Z -10); 5.17 (dd, $J_1=7.6$ Hz, $J_2=2.6$ Hz, 1H, H-7); 4.44 (ddd, $J_1=8.8$ Hz, $J_2=5.2$ Hz, $J_3=2.8$ Hz, 1H, H-4); 4.25-4.18 (m, 3H, H-9 and $\text{CO}_2\text{CH}_2\text{CH}_3$); 4.11 (dd, $J_1=11.6$ Hz, $J_2=3.3$ Hz, 1H, H-9); 3.94 (ddd, $J_1=7.6$ Hz, $J_2=6.4$ Hz, $J_3=3.2$ Hz, 1H, H-8); 2.66 (dd, $J_1=14.0$ Hz, $J_2=8.8$ Hz, 1H, H-3); 2.55 (dd, $J_1=14.0$ Hz, $J_2=5.2$ Hz, 1H, H-3); 2.08 (s, 3H, COCH_3); 2.08 (s, 3H, COCH_3); 1.30 (t, $J_1=7.2$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 170.82; 170.37; 166.72; 136.73; 132.45; 127.61; 124.30; 71.13; 68.92; 65.06; 63.04; 60.86; 35.19; 21.07; 20.80; 14.19; IR (CHCl_3) ν (cm^{-1}): 3026, 3014, 1740, 1708, 1630, 1210; Anal. Calcd. for $\text{C}_{16}\text{H}_{22}\text{O}_7$: C, 58.89, H, 6.79; Found: C, 58.86, H, 6.91.

2-(5S-Hydroxy-6R-hydroxymethyl-5,6-dihydro-2H-pyran-2R-ylmethyl)-acrylic acid ethyl ester. A freshly prepared solution of sodium methoxide in methanol (1M, 0.77 ml, 0.77 mmol, 0.05 eq) was added to a solution of 8 (5.0 g, 15.4 mmol) in dry methanol. The mixture was stirred at room temperature until TLC indicated completion of the reaction (typically 2 h). The reaction mixture was neutralized with dry ice, and the solvent was evaporated to give the desired diol as a brown oil (3.8 g), which was used without further purification.

$[\alpha]_D^{25} = +14.4$ (c 0.84, CH_3OH), ^1H NMR (400 MHz, C_6D_6), δ (ppm): 6.24 (d, $J=1.3$ Hz, 1H, H_E -10); 5.82 (ddd, $J_1=10.5$ Hz, $J_2=2.8$ Hz, $J_3=1.6$ Hz, 1H, H-5); 5.77 (ddd, $J_1=10.5$ Hz, $J_2=2.5$ Hz, $J_3=1.6$ Hz, 1H, H-6); 5.65 (d, $J=1.3$ Hz, 1H, H_Z -10); 4.36 (ddd, $J_1=8.8$ Hz, $J_2=5.2$ Hz, $J_3=2.8$ Hz, 1H, H-4); 4.20 (q, 2H, $J=7.2$ Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$); 4.08 (bs, 1H, H-7); 3.79 (bd, $J=12.0$ Hz, 1H, H-9); 3.72 (bd, $J=12.0$ Hz, 1H, H-9); 3.52 (ddd, $J_1=8.0$ Hz, $J_2=5.6$ Hz, $J_3=4.0$ Hz, 1H, H-8); 2.82 (bs, 1H, OH-7); 2.67 (dd, $J_1=14.0$ Hz, $J_2=8.8$ Hz, 1H, H-3); 2.57 (bs, 1H, OH-9); 2.49 (dd, $J_1=14.0$ Hz, $J_2=5.2$ Hz, 1H, H-3); 1.29 (t, $J=7.2$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 167.10; 137.30; 130.11; 129.07; 127.47; 72.83; 71.72; 63.93; 62.87; 60.95; 35.34; 14.12; IR (CHCl_3) ν (cm^{-1}):

3026, 3012, 1708, 1632, 1212; MW=245.87; Anal. Calcd. for C₁₂H₁₈O₅+0.2H₂O: C, 58.61, H, 7.54; Found: C, 58.79, H, 7.54.

2-(6R-Phenyl-hexahydro-1,3,5,7-tetraoxa-cyclopropa[a]naphthalen-2R-ylmethyl)-acrylic acid ethyl ester (9). The diol (3.73 g, 15.4 mmol), m-chloroperbenzoic acid (92% purity, 3.58 g, 1.24 eq) and sodium bicarbonate (2.6 g, 30.9 mmol, 2 eq) were stirred in dichloromethane (70 ml) at 0°C to room temperature for 72 h. Additional m-chloroperbenzoic acid (92% purity, 3.58 g, 1.24 eq) and sodium bicarbonate (2.6 g, 30.9 mmol, 2 eq) were added at 24 h intervals. The final reaction mixture was diluted with water (20 ml) and the highly water soluble product was extracted with dichloromethane (4x100 ml). The combined organic layers were washed with saturated aqueous sodium sulfite, and the combined aqueous layers were washed extracted with dichloromethane (20x100 ml). The organic layers were dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated to give the crude epoxide (3.65 g, 91.3 %).

$[\alpha]_D^{25} = +40.5$ (c 0.21, CH₃OH); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 6.28 (d, J=1.3 Hz, 1H, H_E-10); 5.70 (d, J=1.3 Hz, 1H, H_Z-10); 4.31 (ddd, J₁=8.8 Hz, J₂=5.2 Hz, J₃=2.8 Hz, 1H, H-4); 4.22 (q, 2H, J=7.2 Hz, CO₂CH₂CH₃); 3.92 (bd, J=8.0 Hz, 1H, H-7); 3.78 (dd, J₁=11.6 Hz, J₂=3.3 Hz, 1H, H-9); 3.66 (dd, J₁=11.6 Hz, J₂=5.6 Hz, 1H, H-9); 3.54-3.48 (m, 3H, H-5, H-6 and H-8); 2.79 (dd, J₁=14.0 Hz, J₂=8.8 Hz, 1H, H-3); 2.64 (dd, J₁=14.0 Hz, J₂=5.2 Hz, 1H, H-3); 1.31 (t, J=7.2 Hz, 3H, CO₂CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 166.87; 136.53; 128.06; 77.18; 70.35; 68.88; 66.42; 62.78; 60.94; 57.91; 54.93; 32.02; 14.17; IR (CHCl₃) ν (cm⁻¹): 3022, 3014, 1710, 1218; MW=258.27; Anal. Calcd. for C₁₂H₁₈O₆: C, 55.81, H, 7.02; Found: C, 55.84, H, 7.02.

A mixture of the epoxide (3.65 g, 14.1 mmol), benzaldehyde dimethyl acetal (8.5 ml, 8.62 g, 56.6 mmol, 4 eq), and (±)-camphorsulfonic acid (0.164 g, 0.71 mmol, 0.05 eq) was refluxed in dry acetonitrile (40 ml) for 1.5 h. The reaction mixture was cooled to room temperature and neutralized by addition of a saturated aqueous solution of sodium bicarbonate (80 ml). Extraction with ethyl acetate (3x100 ml), washing of the combined organic layers with saturated aqueous sodium bicarbonate (30 ml) and brine (30 ml),

drying over anhydrous sodium sulfate, filtration, and solvent evaporation followed by recrystallization of the solid residue (ethyl acetate – hexanes) gave 3.83 g of pure product. Recrystallization of the residue obtained by evaporation of the mother liquor gave an additional 0.42 g of the product, bringing the total yield of 9 to 4.25 g (83% from 8).

$[\alpha]_D^{25} = +67.8$ (c 0.55, CHCl_3); ^1H NMR (400 MHz, C_6D_6), δ (ppm): 7.65 – 7.62 (m, 2H, Ph); 7.20 – 7.11 (m, 3H, Ph); 6.20 (d, $J=1.6$ Hz, 1H, $\text{H}_\text{E}-10$); 5.33 (s, 1H, PhCH); 5.32 (q, $J=1.2$ Hz, 1H, $\text{H}_\text{Z}-10$); 4.21 (ddd, $J_1=8.9$ Hz, $J_2=5.3$ Hz, $J_3=3.3$ Hz, 1H, H-4); 4.08 (dd, $J_1=10.0$ Hz, $J_2=5.0$ Hz, 1H, $\text{H}_\text{E}-9$); 4.01 – 1.91 (m, 3H, H-8 and $\text{CO}_2\text{CH}_2\text{CH}_3$); 3.52 (dd, $J_1=9.0$ Hz, $J_2=1.0$ Hz, 1H, H-7); 3.42 (dd, $J_1=J_2=10.1$ Hz, 1H, $\text{H}_\text{A}-9$); 3.16 (bd, $J=4.5$ Hz, 1H, H-6); 2.85 (ddd, $J_1=13.9$ Hz, $J_2=9.1$ Hz, $J_3=0.7$ Hz, 1H, H-3); 2.80 (dd, $J_1=4.6$ Hz, $J_2=3.3$ Hz, 1H, H-5); 2.59 (ddd, $J_1=13.9$ Hz, $J_2=5.2$ Hz, $J_3=1.0$ Hz, 1H, H-3); 0.93 (t, $J=7.2$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 166.79; 137.26; 136.40; 129.22, 128.33; 128.13; 126.31; 102.68; 78.16; 77.21; 69.82; 69.20; 61.00; 60.87; 55.37; 51.88; 32.89; 14.20; IR (CHCl_3) ν (cm^{-1}): 3024, 3016, 1708, 1224, 1114; MW=346.47; Anal. Calcd. for $\text{C}_{19}\text{H}_{22}\text{O}_6$: C, 65.88, H, 6.40; Found: C, 65.66, H, 6.47.

6R-(2-Hydroxymethyl-allyl)-2R-phenyl-hexahydro-pyrano[3S,2R-d][1,3]dioxin-8S-ol (10). A solution of di-iso-butylaluminum hydride in toluene (1M, 4.9 ml, 4.9 mmol, 3 eq) was added dropwise to a solution of epoxide 9 (0.569 g, 1.64 mmol) in dry THF (16 ml) under a nitrogen atmosphere at -30°C . The reaction mixture was stirred at this temperature for 15 min, then LiAlH_4 (0.187 g, 4.93 mmol, 3 eq) was added in one portion. After stirring at -30°C for 30 min, 1M aqueous sulfuric acid was added carefully until pH was about 7 (about 2.2 ml of the acid). The resultant mixture was filtered through Celite, abundantly washed with ether and ethyl acetate, and the filtrate was evaporated. The residue was purified by flash column chromatography (silica gel, 50% ethyl acetate – hexanes) to give diol 10 (0.470 g, 1.53 mmol, 93%).

$[\alpha]_D^{25} = +69.5$ (c 0.84, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 7.50 – 7.48 (m, 2H, Ph); 7.40 – 7.37 (m, 3H, Ph); 5.63 (s, 1H, PhCH); 5.13 (q, $J=1.4$ Hz, 1H, $\text{H}_\text{Z}-10$); 5.00 (bs, 1H, $\text{H}_\text{E}-10$); 4.26 (dd, $J_1=10.4$ Hz, $J_2=5.1$ Hz, 1H, $\text{H}_\text{E}-$

9); 4.24 (ddd, $J_1=J_2=J_3=3.1$ Hz, 1H, H-6); 4.16 (ddd, $J_1=J_2=9.9$ Hz, $J_3=5.0$ Hz, 1H, H-8); 4.13 - 4.07 (m, 1H, H-4); 4.10 (d, $J=6.0$ Hz, 2H, H-1); 3.69 (dd, $J_1=J_2=10.1$ Hz, 1H, H_a-9); 3.61 (dd, $J_1=9.6$ Hz, $J_2=2.8$ Hz, 1H, H-7); 3.02 (dd, $J_1=14.7$ Hz, $J_2=9.5$ Hz, 1H, H-3); 2.52 (dd, $J_1=14.7$ Hz, $J_2=6.0$ Hz, 1H, H-3); 2.10 - 1.98 (m, 2H, H-5; ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 146.15; 137.27; 129.23; 128.34; 126.14; 113.36; 101.85; 79.94; 71.64; 69.66; 66.18; 65.42; 59.23; 36.95; 32.97; IR (CHCl_3) ν (cm^{-1}): 3018, 3014, 1210, 1100; MW=306.35; Anal. Calcd. for $\text{C}_{17}\text{H}_{22}\text{O}_5$: C, 66.65, H, 7.24; Found: C, 66.63, H, 7.32.

6R-(2,2-Dimethyl-[1,3]dioxan-5-ylmethyl)-8S-methoxymethoxy-2R-phenyl-hexahydro-pyrano[3R,2R-d][1,3]dioxine (11). Diol 10 (3.66 g, 11.95 mmol) was dissolved in dry THF (240 ml) and $\text{BH}_3\cdot\text{DMS}$ (2.0 M in THF, 17.9 ml, 35.5 mmol, 3 eq) was added at 0°C under a nitrogen atmosphere. The mixture was stirred and allowed to warm to room temperature for 3 h. A 1:1 mixture of ethanol and THF was added at 0°C , followed by phosphate buffer (pH 7.0, μ 0.3, 15 ml) and 30% aqueous hydrogen peroxide. After stirring at room temperature overnight, excess hydrogen peroxide was destroyed by addition of saturated aqueous sodium sulfite at 0°C (90 ml). The mixture was extracted with dichloromethane, washed with saturated aqueous sodium sulfite and brine, the organic phase was dried over anhydrous sodium sulfate, filtered, and the filtrate was evaporated. Flash column chromatography (silica gel, 100% ethyl acetate $\rightarrow$ 10% MeOH - ethyl acetate) afforded 4.75 g (99%) of the triol.

$[\alpha]_{\text{D}}^{25} = +69.3$ (c 0.31, CH_3OH); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 7.50 - 7.47 (m, 2H, Ph); 7.40 - 7.36 (m, 3H, Ph); 5.65 (s, 1H, PhCH); 4.28 (dd, $J_1=10.8$ Hz, $J_2=5.0$ Hz, 1H, H_e-9); 4.25 (ddd, $J_1=J_2=J_3=3.1$ Hz, 1H, H-6); 4.12 (ddd, $J_1=J_2=9.9$ Hz, $J_3=5.1$ Hz, 1H, H-8); 4.06 (ddd, $J_1=11.0$ Hz, $J_2=6.7$ Hz, $J_3=4.5$ Hz, 1H, H-4); 3.80 (ddd, $J_1=10.9$ Hz, $J_2=4.2$ Hz, $J_3=2.2$ Hz, 2H, H-1 and H-10); 3.71 (ddd, $J_1=10.6$ Hz, $J_2=6.3$ Hz, $J_3=2.4$ Hz, 2H, H-1 and H-10); 3.70 (dd, $J_1=J_2=10.2$ Hz, 1H, H_a-9); 3.62 (dd, $J_1=9.5$ Hz, $J_2=2.8$ Hz, 1H, H-7); 2.36 (ddd, $J_1=16.4$ Hz, $J_2=10.8$ Hz, $J_3=5.7$ Hz, 1H, H-3); 2.13 (ddd, $J_1=14.9$ Hz, $J_2=7.0$ Hz, $J_3=3.4$ Hz, 1H, H_e-5); 1.95 (ddd, $J_1=14.9$ Hz, $J_2=3.1$ Hz, $J_3=0.7$ Hz, 1H, H_a-5); 1.91 - 1.84 (m, 1H, H-2); 1.62 (ddd, $J_1=15.0$ Hz, $J_2=7.7$ Hz, $J_3=4.4$ Hz, 1H, H-3); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 137.33; 129.27; 128.36; 126.16;

101.92; 80.01; 77.21; 70.87; 69.70; 66.53; 65.42; 65.14; 59.15; 40.21; 34.05; 31.50; IR (CHCl₃) ν (cm⁻¹): 3022, 3014, 1210, 1102, MW=329.77; Anal. Calcd. for C₁₇H₂₄O₆+0.3H₂O: C, 61.91, H, 7.52; Found: C, 61.93, H, 7.45.

The triol (2.00 g, 6.2 mmol) was dissolved in a 1:1 mixture of dry acetone and 2,2-dimethoxypropane (31 ml) and treated with (±)-camphorsulfonic acid (72 mg, 0.31 mmol, 0.05 eq) at room temperature for 10 min. The reaction mixture was neutralized with saturated aqueous sodium bicarbonate (20 ml), evaporated, and extracted with ethyl acetate (3x70 ml). The combined organic layers were washed with saturated aqueous sodium bicarbonate (20 ml), water (20 ml), and brine (20 ml). Drying over anhydrous sodium sulfate, filtration, and the organic solvent evaporation afforded 2.23 g of the product, which was used without further purification.

$[\alpha]_D^{25} = +61.8$ (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 7.50 – 7.47 (m, 2H, Ph); 7.40 – 7.36 (m, 3H, Ph); 5.64 (s, 1H, PhCH); 4.29–4.23 (m, 2H, H-6 and H_e-9); 4.04 (ddd, J₁=J₂=10.0 Hz, J₃=5.2 Hz, 1H, H-8); 3.99–3.93 (m, 2H, H-1 and H-4); 3.89 (ddd, J₁=11.6 Hz, J₂=4.8 Hz, J₃=1.4 Hz, H-10); 3.70 (d, J₁=10.8 Hz, 1H, H_a-9); 3.67–3.59 (m, 3H, H-1, H-7 and H-10); 2.36 (ddd, J₁=17.6 Hz, J₂=11.2 Hz, J₃=6.4 Hz, 1H, H-3); 2.24 (s, 1H, OH-6); 2.11 (ddd, J₁=14.8 Hz, J₂=6.8 Hz, J₃=3.2 Hz, 1H, H_e-5); 2.03–1.94 (m, 1H, H-2); 1.88 (dd, J₁=14.8 Hz, J₂=3.0 Hz, 1H, H_a-5); 1.44 – 1.36 (m, 7H, H-3 and 2xCH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 137.26; 129.23; 128.34; 126.11; 101.85; 79.93; 77.18; 70.40; 69.64; 65.34; 65.21; 64.07; 58.95; 33.97; 32.25; 31.77; 27.20; 20.73; IR (CHCl₃) ν (cm⁻¹): 3016, 1214, 1102; MW=364.43; Anal. Calcd. for C₂₀H₂₈O₆: C, 65.91, H, 7.74; Found: C, 65.97, H, 7.85.

The alcohol (2.23 g, 6.2 mmol) was dissolved in a 1:1 v/v mixture of dichloromethane and Hunig's base (20.6 ml), the solution was cooled to 0 °C, and methoxymethyl chloride (2.35 ml, 31 mmol, 5 eq) was added. The reaction mixture was allowed to warm up to room temperature for 12 h, neutralized by addition of 1 M aqueous hydrogen chloride (27 ml), and extracted with ethyl acetate (3x50 ml). The combined ethyl acetate extracts were washed with brine and saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and concentrated. This afforded 2.59 g (~100%) of 11, which required no further purification.

$[\alpha]_D^{25} = +58.4$ (c 0.83, CHCl₃); ¹H NMR (500 MHz, CDCl₃), δ (ppm): 7.47 – 7.45 (m, 2H, Ph); 7.37 – 7.33 (m, 3H, Ph); 5.55 (s, 1H, PhCH); 4.80 (d, J=6.6 Hz, 1H, OCH₂OCH₃); 4.72 (d, J=6.6 Hz, 1H, OCH₂OCH₃); 4.24 (dd, J₁=10.3 Hz, J₂=5.2 Hz, 1H, H_e-9); 4.21 (ddd, J₁=J₂=J₃=3.0 Hz, 1H, H-6); 4.04 (ddd, J₁=J₂=9.9 Hz, J₃=5.1 Hz, 1H, H-8); 4.01 – 3.95 (m, 2H, H-1 and H-4); 3.88 (ddd, J₁=11.6

Hz, $J_2=4.5$ Hz, $J_3=1.2$ Hz, 1H, H-10); 3.67 – 3.60 (m, 4H, H-1, H-7, H_a-9, and H-10); 3.37 (s, 3H, OCH₂OCH₃); 2.30 (ddd, $J_1=17.3$ Hz, $J_2=11.1$ Hz, $J_3=6.2$ Hz, 1H, H-3); 2.11 (ddd, $J_1=14.7$ Hz, $J_2=7.0$ Hz, $J_3=3.2$ Hz, 1H, H_e-5); 1.95 (m, 1H, H-2); 1.85 (dd, $J_1=14.8$ Hz, $J_2=3.3$ Hz, 1H, H_a-5); 1.43 (s, 3H, CH₃); 1.41 (s, 3H, CH₃); 1.43 – 1.38 (m, 1H, H-3); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 137.60; 128.92; 128.18; 126.06; 101.81; 96.03; 80.11; 77.18; 70.50; 69.77; 69.36; 65.26; 63.94; 59.47; 55.47; 33.79; 32.20; 31.44; 26.75; 21.17; IR (CHCl₃) ν (cm⁻¹): 3026, 3014, 1214, 1106, 1030; MW=408.49; Anal. Calcd. for C₂₂H₃₂O₇: C, 64.49, H, 7.90; Found: C, 64.69, H, 7.96.

Trifluoro-methanesulfonic acid 6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-ylmethyl ester (12). Dry ammonia (~125 ml) was condensed into a 300 ml round-bottomed flask and lithium (1.2 g, 173 mmol, 28 eq), cut into small pieces, was added. After stirring for 1 h at -78 °C, a solution of 11 (2.59 g, 6.2 mmol) in dry THF (12.5 ml) was added to the dark blue solution. The reaction mixture was stirred at -78 °C for 1 h, then quenched with solid ammonium chloride until the blue color disappeared. The mixture was diluted with ether (75 ml) and ammonia was allowed to evaporate overnight. The residue was diluted with ether, filtered, evaporated, and the residue was purified by flash column chromatography (silica gel, 10% methanol – ethyl acetate) to give 1.83 g (5.68 mmol, 92% over 3 steps) of the diol (11-1).

$[\alpha]_D^{25} = +18.7$ (c 0.83, CH₃OH); ¹H NMR (500 MHz, CDCl₃), δ (ppm): 4.71 (AB, $J=6.9$ Hz, 2H, OCH₂OCH₃); 3.97 (ddd, $J_1=11.6$ Hz, $J_2=4.4$ Hz, $J_3=1.3$ Hz, 1H, H-1); 3.92 (ddd, $J_1=7.6$ Hz, $J_2=J_3=3.8$ Hz, 1H, H-6); 3.90 (ddd, $J_1=11.3$ Hz, $J_2=4.5$ Hz, $J_3=1.2$ Hz, 1H, H-10); 3.86 – 3.83 (m, 1H, H-4); 3.82 – 3.71 (m, 3H, H-7; H-10); 3.66 – 3.59 (m, 3H, H-1, H-9); 3.41 (s, 3H, OCH₂OCH₃); 2.57 (bs, 2H, OH); 1.97 – 1.80 (m, 3H, H-3, H_e-5, and H_a-5); 1.43 (ddd, $J_1=14.0$ Hz, $J_2=7.1$ Hz, $J_3=3.4$ Hz, 1H, H-3); 1.41 (s, 3H, CH₃); 1.40 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 124.79; 95.97; 74.46; 73.42; 68.64; 67.40; 65.16; 63.89; 62.00; 55.86; 33.30; 33.07; 31.77; 25.79; 22.14; IR (CHCl₃) ν (cm⁻¹): 3024, 3014, 1224, 1150, 1036; MW=322.18; Anal. Calcd. for C₁₅H₂₈O₇ · 0.1H₂O: C, 55.91, H, 8.82; Found: C, 55.76, H 8.89.

A solution of the diol (1.83 g, 5.68 mmol) and 2,6-lutidine (3.3 ml, 3.04 g, 28.6mmol, 5 eq) in dry dichloromethane (57 ml) was cooled to -78°C , and trifluoro-methanesulfonic anhydride (0.96 ml, 1.61 g, 5.71 mmol, 1.00 eq) was added. The reaction mixture was stirred at -78°C for 30 min. Triethylsilyl trifluoromethanesulfonate (1.94 ml, 2.27 g, 8.58 mmol, 1.5 eq) was added at -78°C and the mixture was warmed to 0°C and stirred for 30 min. The solution was diluted with dichloromethane and saturated aqueous sodium bicarbonate (12 ml) was added at 0°C . The mixture was extracted with dichloromethane (3x50 ml) and the combined organic layers were washed with saturated aqueous sodium bicarbonate (10 ml), water (10 ml), and brine (10 ml). After drying over anhydrous sodium sulfate and filtration, the solvent was evaporated and the residue was quickly submitted to flash column chromatography (25% ethyl acetate – hexanes) to give 3.45 g of the product containing 2,6-lutidine. The labile product must be immediately utilized in the next step to avoid an extensive decomposition.

^1H NMR (400 MHz, C_6D_6), $\delta(\text{ppm})$: 4.55 (d, $J=6.7$ Hz, 1H, OCH_2OCH_3); 4.47 (d, $J=6.7$ Hz, 1H, OCH_2OCH_3); 4.27 (dd, $J_1=10.7$ Hz, $J_2=5.8$ Hz, 1H, H-9); 4.23 (dd, $J_1=10.7$ Hz, $J_2=3.8$ Hz, 1H, H-9); 4.00 (ddd, $J_1=5.8$ Hz, $J_2=J_3=3.8$ Hz, 1H, H-8); 3.91 (ddd, $J_1=10.6$ Hz, $J_2=3.2$ Hz, $J_3=1.0$ Hz, 1H, H-1); 3.82 (ddd, $J_1=11.5$ Hz, $J_2=4.0$ Hz, $J_3=0.9$ Hz, 1H, H-10); 3.58 (ddd, $J_1=6.6$ Hz, $J_2=J_3=3.3$ Hz, 1H, H-6); 3.56 – 3.43 (m, 4H, H-1, H-4, H-7, and H-10); 3.16 (s, 3H, OCH_2OCH_3); 1.86 – 1.72 (m, 2H, H-2 and H-3); 1.61 (ddd, $J_1=13.6$ Hz, $J_2=6.7$ Hz, $J_3=5.3$ Hz, 1H, H_a -5); 1.45 (s, 3H, CH_3); 1.42(ddd, $J_1=13.7$ Hz, $J_2=5.0$ Hz, $J_3=3.5$ Hz, 1H, H_e -5); 1.40 (s, 3H, CH_3); 1.33 (ddd, $J_1=13.8$ Hz, $J_2=7.0$ Hz, $J_3=3.5$ Hz, 1H, H-3); 0.96 (t, $J=8.0$ Hz, 9H, TES); 0.56 (qd, $J_q=8.0$ Hz, $J_d=1.8$ Hz, 6H, TES).

2R-But-2-ynyl-6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-tetrahydro-pyran-3R-yloxy]-triethyl-silane (13). Propyne (5-6 ml) was condensed into a dry 100 ml round-bottomed flask, containing a stirring bar, and dissolved in dry THF (10 ml) at -78°C under a N_2 atmosphere. n-BuLi (2.5 M in hexanes [in order to achieve optimal yields it is essential to use a higher concentration of n-BuLi to keep the fraction of hexanes in

the reaction mixture as low as possible], 3.5 ml, 8.6 mmol, 1.5 eq) was added dropwise at -78°C , which resulted in a gel-like slurry. The mixture was stirred for 15 min, then dry, freshly distilled (from calcium hydride) DMPU (3.5 ml) was added followed by a solution of the freshly prepared substrate (12 from the previous step) in dry THF (5ml, + 2x5 ml rinse). The reaction mixture was stirred at -78°C for 4 h, at -50°C to -40°C for 45 min. Careful temperature control is imperative for success of the reaction. The dry ice bath was removed and the reaction was quenched by addition of pH 7.00 aqueous phosphate buffer (m=0.3, 10 ml), diluted with hexanes (50ml), washed with water (20 ml) and brine (20 ml), and the organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. The product was immediately purified by flash column chromatography (silica, 25% EtOAc-hexanes) to give 2.06 g (4.51 mmol, 79% over two steps) of desired alkyne 13.

$[\alpha]_{\text{D}}^{25} = +7.9$ (c 0.61, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 4.68 (s, 1H, OCH_2OCH_3); 3.95 (ddd, $J_1=11.8$ Hz, $J_2=4.6$ Hz, $J_3=1.0$ Hz, 1H, H-1); 3.91 – 3.84 (m, 3H, H-7, H-8, and H-13); 3.82 (ddd, $J_1=8.6$ Hz, $J_2=3.8$ Hz, $J_3=3.0$ Hz, 1H, H-6); 3.68 (dddd, $J_1=13.8$ Hz, $J_2=J_3=J_4=3.8$ Hz, 1H, H-4); 3.58 (dt, $J_{\text{d}}=11.6$ Hz, $J_{\text{t}}=8.6$ Hz, 2H, H-1 and H-13); 3.37 (s, 3H, OCH_2OCH_3); 2.43 (ddq, $J_{\text{d1}}=16.7$ Hz, $J_{\text{d2}}=6.8$ Hz, $J_{\text{q}}=2.5$ Hz, 1H, H-9); 2.35 (ddq, $J_{\text{d1}}=16.6$ Hz, $J_{\text{d2}}=6.8$ Hz, $J_{\text{q}}=2.5$ Hz, 1H, H-9); 2.09 – 1.99 (m, 1H, H-2); 1.82 (ddd, $J_1=12.9$ Hz, $J_2=J_3=8.1$ Hz, 1H, $\text{H}_{\text{a}}-5$); 1.79 (t, $J=2.5$ Hz, 3H, H-12); 1.75 – 1.67 (m, 2H, H-3 and $\text{H}_{\text{e}}-5$); 1.40 (s, 3H, CH_3); 1.38 (s, 3H, CH_3); 1.37 (ddd, $J_1=14.4$ Hz, $J_2=8.1$ Hz, $J_3=3.4$ Hz, 1H, H-3); 0.96 (t, $J=7.6$ Hz, 9H, TES); 0.63 (q, $J_{\text{q}}=7.6$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 97.68; 94.97; 78.09; 75.00; 74.87; 72.21; 69.34; 68.40; 65.37; 64.05; 55.50; 33.78; 32.94; 31.42; 26.55; 21.40; 21.00; 6.85; 4.95; 3.48; IR (CHCl_3) ν (cm^{-1}): 3022, 3014, 1212, 1104, 1038; MW=456.69; Anal. Calcd. for $\text{C}_{24}\text{H}_{44}\text{OSi}$: C, 63.12, H, 9.71; Found: C, 63.07, H, 9.81.

5-[6R-[3-(Dimethyl-phenyl-silanyl)-but-2E-enyl]-4S-methoxymethoxy-5R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-ylmethyl]-2,2-dimethyl-[1,3]dioxane. To a mixture of CuCN (1.79 g, 20.0 mmol, 2.5 eq.) and dry THF (5 ml) was added PhMe_2SiLi (prepared according to Fleming's protocol, 0.9 M in THF, 44.4 ml, 40.0 mmol, 5.0 eq) at 0°C under a nitrogen atmosphere. The

resultant red mixture was stirred at 0°C for 20 min, then cooled down to -78°C. A solution of alkyne 13 (3.65 g, 8.0 mmol) in dry ether (40 ml) was added, and the mixture was stirred at -78°C for 2 h and at 0°C for 15 min. A saturated aqueous NH₄Cl-concentrated NH₃ (9:1 v/v, 20 ml) was added to quench the reaction, the mixture was stirred at 0°C for 10 min, then extracted with ethyl acetate (2x50 ml). Organic layers were washed with saturated aqueous NH₄Cl-concentrated NH₃ (9:1 v/v) (20 ml) and brine (20 ml), dried over anhydrous Na₂SO₄, filtered, and concentrated. Column chromatography (silica, 20% EtOAc – hexanes) gave 4.50 g (7.59 mmol, 95%) of the pure product.

$[\alpha]_D^{25} = +9.9$ (c 0.9, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 7.40 (m, 2H, Ph); 7.24 (m, 3H, Ph); 5.70 (t, J=6.6 Hz, 1H, H-10); 4.57 (d, J=6.7 Hz, 1H, OCH₂OCH₃); 4.53 (d, J=6.7 Hz, 1H, OCH₂OCH₃); 3.81 (dd, J₁=11.6 Hz, J₂=4.3 Hz, 1H, H-1); 3.77 – 3.70 (m, 3H, H-6, H-8, and H-13); 3.59 – 3.50 (m, 1H, H-4); 3.55 (dd, J₁=J₂=3.0 Hz, 1H, H-7); 3.45 (dt, J_d=11.7 Hz, J_t=7.4 Hz, 2H, H-1 and H-13); 3.24 (s, 3H, OCH₂OCH₃); 2.37 (ddd, J₁=14.0 Hz, J₂=J₃=7.0 Hz, 1H, H-9); 2.19 (ddd, J₁=14.4 Hz, J₂=J₃=7.2 Hz, 1H, H-9); 1.89 – 1.82 (m, 1H, H-2); 1.71 (dt, J_d=12.5 Hz, J_t=9.8 Hz, 1H, H_a-5); 1.59 – 1.54 (m, 1H, H_e-5); 1.57 (bs, 3H, H-12); 1.50 (ddd, J₁=14.3 Hz, J₂=9.2 Hz, J₃=4.3 Hz, 1H, H-3); 1.32 (ddd, J₁=14.3 Hz, J₂=8.6 Hz, J₃=3.3 Hz, 1H, H-3); 1.30 (s, 3H, CH₃); 1.29 (s, 3H, CH₃); 0.85 (t, J=7.8 Hz, 9H, TES); 0.61 (q, J_q=7.8 Hz, 6H, TES); 0.24 (s, 6H, Si(CH₃)₂); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 138.27; 136.91; 136.55; 133.97; 128.89; 127.71; 97.74; 94.41; 77.23; 71.76; 69.78; 67.62; 65.37; 63.82; 55.40; 34.41; 32.79; 31.16; 29.46; 25.97; 22.01; 15.09; 6.91; 4.98; -3.59; -3.64; IR (CHCl₃) ν (cm⁻¹): 3024, 3014, 1214, 1110, 1036; MW=592.95; Anal. Calcd. for C₃₂H₅₆O₆Si₂: C, 64.82, H, 9.52; Found: C, 64.97, H, 9.39.

[6-R(2,2-Dimethyl-[1,3]dioxan-5-ylmethyl)-2R-(3-iodo-but-2E-enyl)-4S-methoxymethoxy-tetrahydro-pyran-3R-yloxy]-triethyl-silane 4. Vinylsilane 13-1 (4.19 g, 7.07 mmol) was dissolved in hexafluoroisopropanol (22 ml) and 2,6-lutidine (0.33 ml, 0.30 g, 2.82 mmol, 0.40 eq) was added. The solution was cooled to 0 °C and N-iodosuccinimide (2.39 g, 10.6 mmol, 1.5 eq) was added in one portion. After stirring for 90 sec, the reaction mixture was poured into a separatory funnel containing dichloromethane (150 ml) and saturated aqueous

sodium sulfite (30 ml). The organic layer was washed with saturated aqueous sodium bicarbonate (20 ml) and brine (20 ml). The combined aqueous layers were extracted with dichloromethane (2x20 ml). The combined organic layers were dried over sodium sulfate, filtered, and evaporated. The residue was purified by flash column chromatography to yield 3.89 g (6.65 mmol, 94%) of the pure product.

$[\alpha]_D^{25} = +11.7$ (c 0.4, CHCl_3); ^1H NMR (400 MHz, CDCl_3), δ (ppm): 6.16 (tq, $J_t=7.3$ Hz, $J_q=1.4$ Hz, 1H, H-10); 4.67 (AB, $J=6.7$ Hz, 2H, OCH_2OCH_3); 3.98 (dd, $J_1=11.5$ Hz, $J_2=4.3$ Hz, 1H, H-1); 3.89 (dd, $J_1=11.6$ Hz, $J_2=4.2$ Hz, 1H, H-13); 3.83 – 3.77 (m, 2H, H-6 and H-8); 3.68 – 3.63 (m, 1H, H-4); 3.61 (dd, $J_1=J_2=3.1$ Hz, 1H, H-7); 3.58 (dt, $J_d=11.8$ Hz, $J_t=8.0$ Hz, 2H, H-1 and H-13); 3.37 (s, 3H, OCH_2OCH_3); 2.37 (d, $J=1.4$ Hz, 3H, H-12); 2.31 (ddd, $J_1=14.8$ Hz, $J_2=J_3=7.4$ Hz, 1H, H-9); 2.19 (ddd, $J_1=14.8$ Hz, $J_2=J_3=7.5$ Hz, 1H, H-9); 1.96 – 1.88 (m, 1H, H-2); 1.83 (ddd, $J_1=12.8$ Hz, $J_2=J_3=8.5$ Hz, 1H, H_a -5); 1.73 – 1.64 (m, 2H, H-3 and H-5); 1.50 (ddd, $J_1=14.2$ Hz, $J_2=8.3$ Hz, $J_3=3.8$ Hz, 1H, H-3); 1.41 (s, 3H, CH_3); 1.40 (s, 3H, CH_3); 0.96 (t, $J_t=7.8$ Hz, 9H, TES); 0.61 (q, $J_q=7.6$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 137.03; 97.82; 94.79; 75.46; 72.08; 70.11; 68.21; 65.37; 63.74; 55.53; 34.01; 32.81; 31.60; 31.42; 27.74; 25.49; 22.55; 6.86; 5.01; IR (CHCl_3) ν (cm^{-1}): 3024, 3014, 1208, 1110, 1036.

7R,8R-Dibenzyloxy-2S-{5-[6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-yl]-3-methyl-pent-3E-enyl}-8R-methyl-tetrahydro-pyrano[3R,4R-b][1,4]dioxin-3-one (15). Lithium (0.238 g, 34.3 mmol, 5 eq), cleaned by successive dipping in hexanes, methanol, and ether, and cut into small pieces was stirred with naphthalene (4.82 g, 37.6 mmol, 5 eq) and dry THF (13.5 ml) in a 40 ml test tube, using a glass coated stirring bar, under a N_2 atmosphere at room temperature for 5 h. The characteristic green color usually appeared within 20 min, otherwise the reaction could be initiated ultrasonically. A solution of zinc chloride in THF (1.01 M, 17.3 ml, 17.4 mmol, 2.5 eq) was then added slowly dropwise during a 10 min period, while the reaction vessel was kept in a 25°C water bath. After stirring at room temperature for 15 min, the Rieke zinc

suspension was centrifuged. The THF solution was removed with a syringe, then freshly distilled dry THF (14 ml) was added. To the stirring suspension of Rieke zinc was added a solution of iodide 3 (4.05 g, 7.52 mmol) in dry THF (7.0 ml) at 0°C, and stirring was continued at room temperature until TLC showed that the alkyl iodide was consumed (about 20 min). The solution of the organozinc reagent was centrifuged again, and the resultant clear dark brown liquid was transferred via cannula to a mixture of iodoalkene 4 (3.89 g, 6.65 mmol), Pd(dppf)Cl₂ (0.25 g, 0.342 mmol, 5 mol%), and dry THF (10 ml) at -30°C. The orange suspension was warmed to room temperature, when it became dark green and clear, and was stirred for 6 h, after which it turned dark red. The solution was poured into a separatory funnel containing EtOAc (100 ml) and water (50 ml), the aqueous layer was extracted with EtOAc (3x25 ml), and the combined organic layers were washed with brine (35 ml). After drying over Na₂SO₄, the organic solution was filtered, evaporated, and the residue was subjected to column chromatography (silica, 10% to 40% EtOAc-hexanes) to give 3.74 g (4.30 mmol, 65%) of pure 15 as a brownish oil, along with starting iodoalkene 4 (0.58 g, 0.99 mmol, 15%) and a homocoupling by-product (0.213 g, 0.232 mmol, 7%).

15: $[\alpha]_D^{25} = -38.0^\circ$ (c 1.3, CHCl₃); ¹H NMR (500 MHz, C₆D₆), δ (ppm): 7.40 (d, J=7.5 Hz, 2H, Ph); 7.25 (t, J=7.5 Hz, 2H, Ph); 7.19 - 7.09 (m, 6H, Ph); 5.27 (t, J=7.0 Hz, 1H, H-10); 4.79 (s, 1H, H-16); 4.70 (dd, J₁=7.3 Hz, J₂=4.1 Hz, 1H, H-14); 4.59 (s, 2H, OCH₂OCH₃); 4.51 (d, J=12.1 Hz, 1H, PhCH₂1); 4.41 (d, J=11.4 Hz, PhCH₂2); 4.23 (d, J=12.1 Hz, 1H, PhCH₂1); 4.21 (d, J=11.4 Hz, PhCH₂2); 4.03 (ddd, J₁=J₂=J₃=3.0 Hz, 1H, H-19); 3.97 (ddd, J₁=7.8 Hz, J₂=J₃=2.0 Hz, 1H, H-8); 3.93 (dd, J₁=11.4 Hz, J₂=4.4 Hz, 1H, H-1); 3.85 (dd, J₁=11.5 Hz, J₂=4.3 Hz, 1H, H-21); 3.80 (ddd, J₁=10.5 Hz, J₂=J₃=3.4 Hz, 1H, H-6); 3.78 - 3.76 (m, 2H, H-7 and H-18); 3.72 (dd, J₁=12.2 Hz, J₂=2.9 Hz, 1H, H-20); 3.57 (dd, J₁=12.2 Hz, J₂=2.8 Hz, 1H, H-20); 3.48 (dd, J₁=11.4 Hz, J₂=8.8 Hz, 1H, H-21); 3.44 (dd, J₁=11.6 Hz, J₂=9.0 Hz, 1H, H-1); 3.36 (dddd, J₁=J₂=9.9 Hz, J₃=J₄=2.7 Hz, 1H, H-4); 3.23 (s, 3H, OCH₂OCH₃); 2.32 - 2.22 (m, 2H); 2.19 - 1.97 (m, 5H); 1.92 - 1.99 (ddd, J₁=J₂=J₃=10.9 Hz, 1H, H_a-5); 1.54 (s, 3H, CH₃); 1.51 - 1.46 (m, 1H, H_e-5); 1.49 (s, 3H, CH₃); 1.39 (ddd, J₁=14.9 Hz, J₂=9.5 Hz, J₃=6.0 Hz, 1H, H-3); 1.36 (s, 3H, CH₃); 1.14 (ddd, J₁=14.8 Hz, J₂=7.7 Hz, J₃=2.8 Hz, 1H, H-3); 1.08 (t, J=7.8 Hz, 9H, TES); 0.70 (dq, J_q=7.8 Hz, J_d=2.8 Hz, 6H, TES); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 169.85; 137.96; 136.98; 136.23; 128.52; 128.24; 127.99; 127.72; 127.49; 127.37; 120.93; 98.46; 97.72; 94.36; 77.87; 77.22; 73.37; 73.30; 71.76; 69.93; 69.63; 68.42; 67.60; 65.37; 64.66; 63.95; 61.84; 55.42; 34.75; 34.49; 32.74; 32.59; 31.31; 28.81; 26.23; 21.77;

16.99; 16.25; 6.89; 4.99; IR (ν , cm^{-1}): 3024, 3014, 2954, 1742, 1602, 1456, 1382, 1260, 1218, 1142, 1038, 910; Calcd for $\text{C}_{48}\text{H}_{72}\text{O}_{12}\text{Si}$: C, 66.33; H, 8.35. Found: C, 66.13; H, 8.40.

The homocoupling byproduct: ^1H NMR (500 MHz, C_6D_6), δ (ppm): 5.71 (t, $J=7.1$ Hz, 1H, H-10); 4.60 (s, 2H, $\text{CH}_3\text{OCH}_2\text{O}$); 4.06 (ddd, $J_1=J_2=7.5$ Hz, $J_3=2.3$ Hz, 1H, H-8); 3.93 (dd, $J_1=11.5$ Hz, $J_2=4.2$ Hz, 1H, H_e -1); 3.85 (ddd, $J_1=11.7$ Hz, $J_2=4.4$ Hz, $J_3=1.1$ Hz, 1H, H_e -13); 3.82 (ddd, $J_1=10.7$ Hz, $J_2=J_3=3.6$ Hz, 1H, H-6); 3.79 (dd, $J_1=J_2=2.4$ Hz, 1H, H-7); 3.49 (dd, $J_1=11.5$ Hz, $J_2=9.3$ Hz, 1H, H_a -1); 3.45 (dd, $J_1=11.5$ Hz, $J_2=9.3$ Hz, 1H, H_a -13); 3.39 (tm, $J=9.3$ Hz, 1H, H-4); 3.25 (s, 3H, $\text{CH}_3\text{OCH}_2\text{O}$); 2.31 (t, $J=7.3$ Hz, 2H, H-9); 2.16 – 2.06 (m, 1H); 1.92 (s, 3H, Me-12); 1.51 (s, 3H, Me); 1.37 (s, 3H, Me); 1.43 – 1.27 (m, 3H); 1.09 (t, $J=8.0$ Hz, 9H, TES); 0.70 (qd, $J_q=8.0$; $J_d=2.6$ Hz, 6H, TES).

2S-(2R,3R-Bis-benzyloxy-5R-hydroxy-3R-methyl-tetrahydro-pyran-4R-yloxy)-7-[6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethylsilanyloxy)-tetrahydro-pyran-2R-yl]-5-methyl-hept-5E-enoic acid. A solution of lactone 15 (3.00 g, 3.45 mmol) in a mixture of THF (29.0 ml) and water (14.0 ml) was cooled to 0 °C in an ice bath and lithium hydroxide monohydrate (0.290 g, 6.90 mmol, 2 eq) was added. The reaction mixture was stirred at 0 °C for 20 min, then extracted with ethyl acetate (3x30 ml). The aqueous layer was acidified with 1 M HCl (7 ml) and extracted with ethyl acetate (3x30 ml) again. The combined organic layers were washed with brine, which was acidified with 1 ml of 1 M hydrogen chloride, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated. After drying of the

residue in vacuo, 3.05 g (3.45 mmol, 100%) of the carboxylic acid were obtained.

$[\alpha]_D^{25} = -57.7^\circ$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, C_6D_6), δ (ppm): 7.35 (d, $J=7.6$ Hz, 2H, Ph); 7.23 (d, $J=7.6$ Hz, 2H, Ph); 7.19 - 7.15 (m, 4H, Ph); 7.12 - 7.06 (m, 2H, Ph); 5.40 (t, $J=6.7$ Hz, 1H, H-10); 4.81 (s, 1H, H-16); 4.68 (d, $J=11.2$ Hz, 1H, PhCH_2 1); 4.62 - 4.57 (m, 3H, OCH_2OCH_3 , PhCH_2 2); 4.53 (d, $J=11.2$ Hz, 1H, PhCH_2 1); 4.36 (dd, $J_1=6.4$ Hz, $J_2=5.1$ Hz, 1H, H-14); 4.31 (d, $J=12.1$ Hz, 1H, PhCH_2 2); 3.99 (ddd, $J_1=8.6$ Hz, $J_2=6.5$ Hz, $J_3=2.0$ Hz, 1H, H-8); 3.93 (ddd, $J_1=11.6$ Hz, $J_2=4.7$ Hz, $J_3=1.2$ Hz, 1H, H-1); 3.87 - 3.76 (m, 6H, H-6, H-7, H-18, H-19, H-20, H-21); 3.66 (d, $J=11.4$ Hz, 1H, H-20); 3.45 - 3.39 (m, 2H, H-1 and H-21); 3.35 (dddd, $J_1=J_2=9.9$ Hz, $J_3=J_4=2.6$ Hz, 1H, H-4); 3.23 (s, 3H, OCH_2OCH_3); 2.43 (t, $J=7.4$ Hz, 2H, H-12); 2.26 - 2.05 (m, 3H); 1.91 (ddd, $J_1=12.0$ Hz, $J_2=J_3=10.6$ Hz, 1H, H_a -5); 1.58 (bs, 3H, CH_3); 1.55 (s, 3H, CH_3); 1.52 (s, 3H, CH_3); 1.46 (dm, $J_d=12.0$ Hz, 1H, H_e -5); 1.35 (ddd, $J_1=14.5$ Hz, $J_2=9.9$ Hz, $J_3=6.1$ Hz, 1H, H-3); 1.32 (s, 3H, CH_3); 1.08 (t, $J=8.0$ Hz, 9H, TES); 1.00 (ddd, $J_1=14.5$ Hz, $J_2=7.6$ Hz, $J_3=2.6$ Hz, 1H, H-3); 0.70 (dq, $J_q=8.0$ Hz, $J_d=1.8$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 174.02; 138.25; 137.20; 136.33; 128.48; 127.96; 127.92; 127.65; 120.83; 100.32; 98.07; 94.49; 78.84; 77.75; 71.91; 70.10; 69.71; 67.67; 66.45; 66.30; 65.38; 64.82; 64.28; 55.42; 34.74; 34.49; 32.99; 31.63; 31.53; 28.64; 27.03; 20.91; 16.66; 16.35; 6.87; 5.04; IR (ν , cm^{-1}): 3676, 3618, 3024, 3016, 2360, 1226, 1218, 1204, 1046, 796; Calcd for $\text{C}_{48}\text{H}_{74}\text{O}_{13}\text{Si}$: C, 64.98; H, 8.41. Found: C, 65.21; H, 8.53.

3S-(2R,3R-Bis-benzyloxy-5-hydroxyR-3R-methyl-tetrahydro-pyran-4R-yloxy)-6S-{2-[6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethylsilanyloxy)-tetrahydro-pyran-2R-yl]-1R-iodo-ethyl}-6S-methyl-tetrahydro-pyran-2-one (16). The crude acid (15-1) (3.05 g, 3.45 mmol) was dissolved in dry dichloromethane (25 ml). 2,6-Lutidine (0.58 ml, 0.534 g, 4.98 mmol, 1.5 eq) and N-iodosuccinimide (1.80 g, 8.00 mmol, 2.3 eq) were added at 0 °C under

a N₂ atmosphere, and the stirred solution was allowed to warm to room temperature for 3.5 h. The reaction mixture was extracted with CH₂Cl₂, washed with 1 M HCl (7 ml), saturated aqueous Na₂S₂O₃ (10 ml), water, brine, and saturated aqueous sodium bicarbonate. Drying over anhydrous Na₂SO₄ followed by filtration, concentration, and column chromatography (silica, 50% EtOAc – hexanes) afforded iodolactones epi-16 (0.382 g, 0.377 mmol, 11%) and 16 (2.57 g, 2.53 mmol, 74%).

$[\alpha]_D^{25} = -50.7^\circ$ (c 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃), δ (ppm): 7.37 – 7.30 (m, 10H, Ph); 4.79 (s, 1H, H-16); 4.73 (d, J=12.3 Hz, 1H, PhCH₂1); 4.72 (d, J=11.0 Hz, 1H, PhCH₂2); 4.69 (AB, J=6.9 Hz, 2H, OCH₂OCH₃); 4.60 (d, J=11.0 Hz, 1H, PhCH₂2); 4.52 (d, J=12.2 Hz, 1H, PhCH₂1); 4.35 (bd, J=10.6 Hz, 1H, OH-19); 4.32 (d, J=11.7 Hz, 1H, H-10); 4.18 (d, J=5.8 Hz, 1H, H-14); 4.08 (d, J=3.1 Hz, 1H, H-18); 4.05 (ddd, J₁=10.9 Hz, J₂=4.4 Hz, J₃=1.7 Hz, 1H, H-8); 4.02 (bd, J=10.6 Hz, H-19); 3.93 (dd, J₁=11.5 Hz, J₂=4.5 Hz, 1H, H-1); 3.91 (d, J=12.0 Hz, 1H, H-20); 3.85 (dd, J₁=11.5 Hz, J₂=4.3 Hz, 1H, H-21); 3.83 (dd, J₁=12.0 Hz, J₂=2.1 Hz, 1H, H-20); 3.79 (ddd, J₁=8.3 Hz, J₂=J₃=3.3 Hz, 1H, H-6); 3.65 (ddd, J₁=12.1 Hz, J₂=8.2 Hz, J₃=4.2 Hz, 1H, H-4); 3.62 – 3.58 (m, 2H, H-1 and H-7); 3.55 (dd, J₁=11.5 Hz, J₂=8.3 Hz, 1H, H-21); 3.38 (s, 3H, OCH₂OCH₃); 2.57 – 2.51 (m, 1H, H-12); 2.19 – 2.14 (m, 3H, H-9, H-13, and H-13); 1.98 – 1.92 (m, 2H, H-2 and H-12); 1.89 – 1.81 (m, 2H, H-5 and H-9); 1.74 (ddd, J₁=13.0 Hz, J₂=J₃=3.9 Hz, 1H, H-5); 1.68 (ddd, J₁=14.2 Hz, J₂=8.2 Hz, J₃=6.0 Hz, 1H, H-3); 1.56 (s, 3H, CH₃); 1.48 (s, 3H, CH₃); 1.49 – 1.44 (m, 1H, H-3); 1.36 (s, 3H, CH₃); 1.34 (s, 3H, CH₃); 0.98 (t, J=8.0 Hz, 9H, TES); 0.63 (q, J=8.0 Hz, 6H, TES); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 169.15; 138.48; 137.19; 132.15; 132.05; 131.92; 128.55; 128.46; 127.88; 127.83; 127.57; 127.50; 99.92; 97.73; 94.92; 85.43; 79.00; 77.21; 72.52; 71.41; 69.22; 68.17; 66.31; 65.66; 65.35; 64.85; 64.11; 55.58; 34.87; 33.87; 32.54; 31.29; 30.95; 29.56; 26.06; 24.88; 22.91; 21.89; 17.15; 6.91; 4.98; IR (ν , cm⁻¹): 3618, 3020, 3016, 2976, 1684, 1654, 1558, 1216, 1212, 1046, 878; Calcd for C₄₈H₇₃IO₁₃Si+1.3H₂O: C, 55.62; H, 7.35. Found C, 55.63; H, 7.21.

Epi-16: $[\alpha]_D^{25} = -58.0^\circ$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3), δ (ppm): 7.3 - 7.28 (m, 10H, Ph); 4.81 (s, 1H, H-16); 4.75 (d, $J=12.3$ Hz, 1H, PhCH_2 1); 4.71 (d, $J=11.2$ Hz, 1H, PhCH_2 2); 4.65 (s, 2H, OCH_2OCH_3); 4.61 (d, $J=11.2$ Hz, 1H, PhCH_2 2); 4.53 (d, $J=12.2$ Hz, 1H, PhCH_2 1); 4.39 (d, $J=10.8$ Hz, 1H, OH-19); 4.15 (d, $J=3.4$ Hz, 1H, H-18); 4.11 (dd, $J_1=9.6$ Hz, $J_2=5.8$ Hz, 1H, H-14); 4.05 (dd, $J_1=9.6$ Hz, $J_2=3.0$ Hz, 1H, H-10); 4.00 (ddd, $J_1=7.0$ Hz, $J_2=J_3=2.5$ Hz, 1H, H-8); 3.97 (m, 1H, H-19); 3.94 (dd, $J_1=11.7$ Hz, $J_2=4.7$ Hz, 1H, H-1); 3.91 (d, $J=12.0$ Hz, 1H, H-20); 3.89 (dd, $J_1=11.6$ Hz, $J_2=4.4$ Hz, 1H, H-21); 3.85 (dd, $J_1=12.0$ Hz, $J_2=2.0$ Hz, 1H, H-20); 3.72 (ddd, $J_1=10.7$ Hz, $J_2=3.4$ Hz, $J_3=2.7$ Hz, 1H, H-6); 3.65 (dd, $J_1=J_2=2.6$ Hz, 1H, H-7); 3.63 - 3.57 (m, 3H, H-1, H-4, and H-21); (s, 3H, OCH_2OCH_3); 2.34 (ddd, $J_1=15.0$ Hz, $J_2=7.7$ Hz, $J_3=2.8$ Hz, 1H, H-9); 2.28 - 2.10 (m, 3H); 2.07 - 2.01 (m, 2H); 1.85 (ddd, $J_1=12.3$ Hz, $J_2=J_3=10.5$ Hz, 1H, H_a -5); 1.65 (ddd, $J_1=12.3$ Hz, $J_2=J_3=3.5$ Hz, 1H, H_e -5); 1.60 (s, 3H, CH_3); 1.56 (ddd, $J_1=14.2$ Hz, $J_2=8.4$ Hz, $J_3=6.3$ Hz, 1H, H-3); 1.50 (s, 3H, CH_3); 1.43 - 1.39 (m, 1H, H-3); 1.42 (s, 3H, CH_3); 1.41 (s, 3H, CH_3); 0.98 (t, $J=7.8$ Hz, 9H, TES); 0.64 (q, $J=7.8$ Hz, 6H, TES); IR (u, cm^{-1}): 3618, 3016, 2976, 1718, 1684, 1602, 1226, 1216, 1046, 796.

3S-[2R,3R-Bis-benzyloxy-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydropyran-4-yloxy]-6R-{2R-[6-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-

methoxymethoxy-3R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-yl]-1R-iodo-ethyl}-6S-methyl-tetrahydro-pyran-2-one. Triisopropylsilyl trifluoromethanesulfonate (2.05 ml, 2.34 g, 7.63 mmol, 3 eq) was added to a solution of lactone 16 (2.57 g, 2.53 mmol) and 2,6-lutidine (1.20 ml, 1.10 g, 10.3 mmol, 4 eq) in dry tert-butyl acetate (13 ml) at -78°C under a nitrogen atmosphere. After 15 min, TLC showed completion of the reaction and the reaction mixture was extracted with ethyl acetate (100 ml), washed with 1 M hydrogen chloride (15 ml), water (25 ml), and brine (15 ml). The organic phase was dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated. The residue was purified by column chromatography (silica, 20 % ethyl acetate – hexanes) to give 16-1 (2.72 g, 2.32 mmol, 92%).

$[\alpha]_{\text{D}}^{25} = -29.1^{\circ}$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, C_6D_6), δ (ppm): 7.60 (d, $J=7.4$ Hz, 2H, Ph); 7.49 (d, $J=7.4$ Hz, 2H, Ph); 7.29 (t, $J=7.4$ Hz, 2H, Ph); 7.21 (t, $J=7.4$ Hz, 2H, Ph); 7.12 (m, 2H, Ph); 5.46 (s, 1H, H-16); 5.08 (d, $J=11.8$ Hz, 1H, PhCH_2 1); 5.03 (d, $J=12.2$ Hz, 1H, PhCH_2 2); 4.87 (d, $J=12.1$ Hz, 1H, PhCH_2 2); 4.82 (d, $J=11.8$ Hz, 1H, PhCH_2 1); 4.80 (dd, $J_1=8.3$ Hz, $J_2=6.2$ Hz, 1H, H-14); 4.59 (d, $J=6.8$ Hz, 1H, OCH_2OCH_3); 4.54 (d, $J=6.8$ Hz, 1H, OCH_2OCH_3); 4.53 (d, $J=10.9$ Hz, 1H, H-10); 4.36 (bs, 1H, H-18); 3.31 (dddd, $J_1=11.5$ Hz, $J_2=J_3=3.1$ Hz, 1H, H-8); 4.20 (ddd, $J_1=9.9$, $J_2=4.5$ Hz, $J_3=1.9$ Hz, 1H, H-19); 4.15 (dd, $J_1=11.6$ Hz, $J_2=4.6$ Hz, 1H, H-1); 4.06 (dd, $J_1=J_2=10.2$ Hz, 1H, H-20); 3.96 (dd, $J_1=11.3$ Hz, $J_2=4.4$ Hz, 1H, H-21); 3.86 (dd, $J_1=10.5$ Hz, $J_2=4.6$ Hz, 1H, H-20); 3.79 (ddd, $J_1=9.1$ Hz, $J_2=J_3=3.2$ Hz, 1H, H-6); 3.65 (dd, $J_1=J_2=3.2$ Hz, 1H, H-7); 3.61 (dd, $J_1=11.7$ Hz, $J_2=9.2$ Hz, 1H, H-1); 3.54 (ddd, $J_1=12.1$ Hz, $J_2=8.0$ Hz, $J_3=3.6$ Hz, 1H, H-4); 3.47 (dd, $J_1=11.3$ Hz, $J_2=9.1$ Hz, 1H, H-21); 3.21 (s, 3H, OCH_2OCH_3); 2.47 (ddd, $J_1=14.1$ Hz, $J_2=11.9$ Hz, $J_3=10.9$ Hz, 1H, H-9); 2.40 (ddd, $J_1=14.3$ Hz, $J_2=7.5$ Hz, $J_3=4.2$ Hz, 1H, H-12); 2.14 - 2.05 (m, 2H, H-13 and H-2); 1.98 - 1.91 (m, 1H, H-13); 1.85 (ddd, $J_1=12.2$ Hz, $J_2=J_3=8.4$ Hz, 1H, H-3); 1.76 (ddd, $J_1=14.1$ Hz, $J_2=11.9$ Hz, $J_3=2.6$ Hz, 1H, H-9); 1.68 - 1.61 (m, 1H, H-12); 1.55 - 1.48 (m, 2H); 1.50 (s, 3H, CH_3); 1.45 (s, 3H, CH_3); 1.36 (s, 3H, CH_3); 1.25 (s, 3H, CH_3); 1.09 (t, $J=7.8$ Hz, TES); 1.06-1.05 (m, 21H, TIPS); 0.70 (q, $J=7.8$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 169.69; 140.39; 128.23; 127.99; 127.59; 127.39; 126.71; 101.47; 97.60; 94.98; 84.55; 82.03; 77.85; 77.21; 74.57; 73.33; 72.72; 71.21; 69.11; 68.30; 65.50; 64.72; 64.45; 64.08; 55.54; 40.04; 34.54; 33.84; 32.54; 31.59; 26.25; 23.03; 21.90; 18.13; 18.06; 15.53; 12.34; 6.91; 5.02; IR (ν , cm^{-1}): 3618, 3446, 3024, 3016, 2976, 2360, 1558, 1540, 1508, 1456, 1394, 1240, 1226, 1216, 1206, 1046, 796; Calcd for $\text{C}_{57}\text{H}_{93}\text{IO}_{13}\text{Si}_2$: C, 58.54; H, 8.02. Found C, 58.49; H, 8.10.

2S-[2R,3R-Bis-benzyloxy-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydro-pyran-4R-yloxy]-4S-{3-[6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-ylmethyl]-2S-methyl-oxiranyl}-butyric acid methyl ester (17). The triisopropylsilyl ether from the previous step (2.72 g, 2.32 mmol) was dissolved in dry dichloromethane (30 ml) and treated with a freshly prepared solution of sodium methoxide (2.0M in MeOH, 1.25 ml, 2.50 mmol, 1.08 eq) at -30°C for 20 – 25 min. It is imperative to use sodium methoxide with a higher concentration to ensure a clean reaction and facile extractive work-up. The reaction mixture was diluted with CH_2Cl_2 (100 ml) and washed with saturated aqueous ammonium chloride and water. The combined aqueous layers were extracted with CH_2Cl_2 , and the combined organic layers were washed with brine and saturated aqueous NaHCO_3 . Drying over anhydrous sodium sulfate, filtration, and solvent evaporation afforded 2.60 g of epoxide 17.

$[\alpha]_{\text{D}}^{25} = -28.9^{\circ}$ (c 1.2, CHCl_3); ^1H NMR (500 MHz, C_6D_6), δ (ppm): 7.45 (d, $J=7.8$ Hz, 2H, Ph); 7.37 (d, $J=7.8$ Hz, 2H, Ph); 7.24 (t, $J=7.8$ Hz, 2H, Ph); 7.18 – 7.08 (m, 4H, Ph); 5.35 (s, 1H, H-16); 4.95 (d, $J=11.9$ Hz, 1H, PhCH_2 1); 4.91 (d, $J=12.2$ Hz, 1H, PhCH_2 2); 4.74 (d, $J=12.2$ Hz, 1H, PhCH_2 2); 4.61 (t, $J=6.4$ Hz, 1H, H-14); 4.56 (d, $J=11.9$ Hz, 1H, PhCH_2 1); 4.56 (s, 2H, OCH_2OCH_3); 4.20 (ddd, $J_1=10.0$ Hz, $J_2=4.9$ Hz, $J_3=2.2$ Hz, 1H, H-19); 4.08 (dd, $J_1=J_2=10.2$ Hz, 1H, H-20); 4.10 – 4.07 (m, 1H, H-8); 4.05 (bs, 1H, H-18); 3.97 – 3.93 (m, 2H, H-1 and H-21); 3.86 (dd, $J_1=10.4$ Hz, $J_2=4.8$ Hz, 1H, H-20); 3.72 – 3.69 (m, 2H, H-6 and H-7); 3.59 (dd, $J_1=11.6$ Hz, $J_2=7.7$ Hz, 1H, H-1); 3.48 (dd, $J_1=11.7$ Hz, $J_2=7.7$ Hz, 1H, H-21); 3.49 – 3.44 (m, 1H, H-4); 3.22 (s, 3H, CO_2Me); 3.20 (s, 3H, OCH_2OCH_3); 2.82 (t, $J=5.8$ Hz, 1H, H-10); 2.14 – 2.03 (m, 3H); 1.97 – 1.88 (m, 2H); 1.79 – 1.70 (m, 2H); 1.51 – 1.46 (m, 3H); 1.49 (s, 3H, CH_3); 1.41 (s, 3H, CH_3); 1.40 (s, 3H, CH_3); 1.36 (ddd, $J_1=14.1$ Hz, $J_2=8.0$ Hz, $J_3=3.2$ Hz, 1H, H-3); 1.17 (s, 3H, CH_3); 1.11 – 1.07 (m, 30H, TIPS, TES); 0.71 (dq, $J_{\text{d}}=2.4$ Hz, $J_{\text{q}}=7.8$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 172.62; 140.23; 138.00; 128.25; 127.98; 127.74; 127.49; 127.02; 126.77; 101.39; 97.78; 94.65; 83.87; 80.12; 77.77; 75.75; 71.99; 71.17; 70.55; 68.92; 67.73; 65.38; 64.78; 64.68; 63.83; 60.37; 59.52; 55.50; 51.09; 34.54; 33.96; 32.74;

31.13; 29.26; 25.38; 22.68; 18.13; 18.06; 16.89; 15.24; 12.27; 6.89; 5.02; IR (ν , cm^{-1}): 3444, 3018, 2950, 1604, 1222, 1212, 1130, 786; Calcd for $\text{C}_{58}\text{H}_{96}\text{O}_{14}\text{Si}_2$: C, 64.89; H, 9.01. Found C, 64.93; H, 9.05.

2S-[2R,3R-Bis-benzyloxy-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydro-pyran-4R-yloxy]-4-{3S-[6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-3R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-ylmethyl]-2S-methyl-oxiranyl}-butyraldehyde. Lithium aluminum hydride (0.265 g, 6.98 mmol, 3 eq) was added to a solution of 17 (crude from previous step, ~2.32 mmol) in dry THF (25 ml) at -78°C under a nitrogen atmosphere. The reaction mixture was stirred at -78°C for 45 min, warmed to -30°C , and quenched by careful addition of water (0.265 ml) while vigorously stirring. The dry ice-acetone bath was removed and 3M aqueous sodium hydroxide (0.265 ml) was added followed by water (0.795 ml). After stirring for 1 h at room temperature, the mixture was filtered and the solvent was evaporated to give the primary alcohol (2.61 g), which was used in the next step directly.

$[\alpha]_D^{25} = -34.0^\circ$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, C_6D_6), δ (ppm): 7.37 (d, $J=7.4$ Hz, 2H, Ph); 7.28 (d, $J=7.4$ Hz, 2H, Ph); 7.23 (t, $J=7.4$ Hz, 2H, Ph); 7.14 (t, $J=7.4$ Hz, 3H, Ph); 7.07 (t, $J=7.4$ Hz, 1H, Ph); 5.13 (s, 1H, H-16); 4.92 (d, $J=11.2$ Hz, 1H, PhCH_2 1); 4.89 (d, $J=12.1$ Hz, 1H, PhCH_2 2); 4.64 (d, $J=11.2$ Hz, 1H, PhCH_2 1); 4.57 (AB, $J=7.0$ Hz, 2H, OCH_2OCH_3); 4.35 (d, $J=12.1$ Hz, 1H, PhCH_2 2); 4.17 (ddd, $J_1=10.5$ Hz, $J_2=5.1$ Hz, $J_3=2.3$ Hz, 1H, H-19); 4.10 (ddd, $J_1=8.8$ Hz, $J_2=5.7$ Hz, $J_3=2.4$ Hz, 1H, H-8); 4.05 (dd, $J_1=J_2=10.5$ Hz, 1H, H-20); 3.96 (dd, $J_1=8.6$ Hz, $J_2=4.2$ Hz, 1H, H-1); 3.94 (bs, 1H, H-18); 3.92 (dd, $J_1=7.8$ Hz, $J_2=4.2$ Hz, 1H, H-21); 3.87 (m, 3H, H-20, H-19, and H-19); 3.73 (d, $J=2.4$ Hz, 1H, H-7); 3.71 (ddd, $J_1=10.2$ Hz, $J_2=3.9$ Hz, $J_3=2.9$ Hz, 1H, H-6); 3.57 (dd, $J_1=11.7$ Hz, $J_2=8.6$ Hz, 1H, H-1); 3.51 (dddd, $J_1=J_2=7.2$ Hz, $J_3=J_4=5.3$ Hz, 1H, H-14); 3.47 (dd, $J_1=11.6$ Hz, $J_2=7.8$ Hz, 1H, H-21); 3.46 (m, 1H, H-4); 3.23 (s, 3H, OCH_2OCH_3); 2.85 (t, $J=6.0$ Hz, 1H, H-10); 2.08 (m, 2H); 1.91 (dt, $J_d=12.2$ Hz, $J_t=10.2$ Hz, 1H, H-5); 1.81 (m, 3H); 1.65 (m, 1H); 1.49 (s, 3H, CH_3); 1.46 (m, 3H); 1.39 (s, 3H, CH_3); 1.37 (s, 3H, CH_3); 1.30 (ddd, $J_1=14.1$ Hz, $J_2=7.8$

Hz, $J_3=3.2$ Hz, 1H, H-3); 1.09 (m, 30H, TIPS, TES); 0.70 (dq, $J_d=2.8$ Hz, $J_q=7.6$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), $\delta(\text{ppm})$: 138.66; 137.53; 128.33; 127.88; 127.69; 127.59; 101.92; 97.72; 94.56; 83.08; 81.45; 77.28; 77.18; 75.88; 71.90; 71.18; 70.44; 69.00; 67.68; 66.67; 65.33; 64.61; 63.80; 63.04; 60.48; 59.95; 55.45; 34.67; 34.53; 32.69; 31.12; 29.60; 27.58; 25.45; 22.51; 18.11; 18.03; 12.26; 6.84; 5.00; 3.33; IR (ν , cm^{-1}): 3944, 3754, 3692, 3054, 3020, 2986, 2686, 2410, 2306, 1422, 1262, 1216; Calcd for $\text{C}_{57}\text{H}_{96}\text{O}_{13}\text{Si}_2$: C, 65.48; H 9.25. Found C, 65.59; H, 9.38.

To a solution of oxalyl chloride (2.0M in CH_2Cl_2 , 1.74 ml, 3.48 mmol) in dry dichloromethane (4.0 ml) was added dry dimethylsulfoxide (0.496 ml, 0.546 g, 7.00 mmol) at -78°C under nitrogen. After stirring for 20 min, a solution of the crude substrate (2.6 g, 2.32 mmol) in dry dichloromethane (16 ml) was added dropwise, and stirring was continued for 25 min. Dry di-isopropylethylamine (1.82 ml, 1.35 g, 10.4 mmol) was added at this point, the mixture was stirred for 10 min, then warmed to 0°C and stirred for an additional 15 min. After dilution with dichloromethane, the mixture was washed with 1M HCl (12 ml) and water (25 ml). The combined aqueous layers were extracted with CH_2Cl_2 (2x30 ml). The combined organic layers were washed with saturated aqueous NaHCO_3 , dried over anhydrous Na_2SO_4 , filtered, and concentrated to furnish 2.45 g (~100%) of the aldehyde, which was used without purification.

$[\alpha]_{\text{D}}^{25} = -35.9^\circ$ (c 1.7, CHCl_3); ^1H NMR (500 MHz, C_6D_6), $\delta(\text{ppm})$: 9.78 (d, $J=3.2$ Hz, 1H, H-15); 7.37 (d, $J=7.4$ Hz, 2H, Ph); 7.34 (d, $J=7.4$ Hz, 2H, Ph); 7.28 (d, $J=7.4$ Hz, 2H, Ph); 7.23 (t, $J=7.4$ Hz, 3H, Ph); 7.10 (t, $J=7.4$ Hz, 1H, Ph); 5.16 (s, 1H, H-16); 4.93 (d, $J=12.1$ Hz, 1H, PhCH_21); 4.77 (d, $J=11.9$ Hz, 1H, PhCH_22); 4.63 (d, $J=11.9$ Hz, 1H, PhCH_22); 4.56 (AB, $J=6.8$ Hz, 2H, OCH_2OCH_3); 4.51 (d, $J=12.1$ Hz, 1H, PhCH_21); 4.15 (ddd, $J_1=10.5$ Hz, $J_2=5.3$ Hz, $J_3=2.0$ Hz, 1H, H-19); 4.09 (m, 2H, H-14 and H-8); 3.97 (dd, $J_1=J_2=10.5$ Hz, 1H, H-20); 3.95 (m, 2H, H-1 and H-21); 3.86 (dd, $J_1=10.7$ Hz, $J_2=5.4$ Hz, 1H, H-20); 3.74 (d, $J=2.0$ Hz, 1H, H-18); 3.70 (m, 2H, H-6 and H-7); 3.59 (dd, $J_1=11.9$ Hz, $J_2=8.2$ Hz, 1H, H-1); 3.48 (dd, $J_1=11.5$ Hz, $J_2=8.1$ Hz, 1H, H-21); 3.46 (m, 1H, H-4); 3.22 (s, 3H, OCH_2OCH_3); 2.78 (t, $J=5.9$ Hz, 1H, H-10); 2.05 (m, 1H); 1.9 (m, 3H); 1.80-1.62 (m, 4H); 1.50 (bs, 6H, CH_3); 1.40 (s, 3H, CH_3); 1.34 (s, 3H, CH_3); 1.08 (m, 30H, TIPS, TES); 0.70 (dq, $J_d=2.8$ Hz, $J_q=7.6$ Hz, 6H, TES); ^{13}C NMR (100 MHz, CDCl_3), $\delta(\text{ppm})$: 204.86; 139.39; 137.62; 128.36; 128.20; 127.91; 127.72; 127.39; 127.19; 101.75; 97.77; 94.66; 86.24; 85.59; 77.50; 75.65; 72.00; 71.15; 70.56; 68.52; 67.79; 65.67; 65.36; 64.74; 63.82; 60.33; 59.40; 55.49; 34.48; 33.35; 32.71; 31.18; 29.62; 26.83; 25.41; 22.63; 18.13;

18.05; 16.87; 14.63; 12.26; 6.88; 5.02; IR (ν , cm^{-1}): 3056, 3050, 1278, 1216, 780; Calcd for $\text{C}_{57}\text{H}_{94}\text{O}_{13}\text{Si}_2$: C, 65.61; H, 9.08. Found C, 65.75; H, 8.92.

5-[6R-(3-{3S-[2R,3R-Bis-benzyloxy-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydro-pyran-4R-yloxy]-hex-4Z-enyl}-3S-methyl-oxiranylmethyl)-4S-methoxymethoxy-5R-(triethyl-silanyloxy)-tetrahydro-pyran-2R-ylmethyl]-2,2-dimethyl-[1,3]dioxane. To a suspension of dry ethyltriphenylphosphonium bromide (2.16 g, 5.81 mmol, 2.5 eq) in dry THF (3.0 ml) was added sodium hexamethyldisilazide (1.0 M in THF, 4.7 ml, 4.7 mmol, 2 eq) at 0 °C. The orange mixture was stirred for 30 min. The solution of the Wittig reagent was transferred via cannula to a mixture of crude aldehyde 17-1 (2.6 g, ~2.32 mmol), dry tetrahydrofuran (2.0 ml) and dry freshly distilled DMPU (4.0 ml) at -78 °C and, after stirring for 30 min, the reaction mixture was stirred at 0 °C to room temperature for 1 h. The mixture was extracted with ethyl acetate (45 ml), washed with saturated aqueous ammonium chloride (10 ml), water (10 ml), and brine (10 ml), dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated. The residue was purified by column chromatography (silica, 25% to 60% ethyl acetate – hexanes) to give alkene 17-2 (1.76 g, 1.67 mmol, 72% from 16-1), along with deprotected epoxy alcohol 2 (0.390 g, 0.414 mmol, 18%).

$[\alpha]_{\text{D}}^{25} = -26.5^{\circ}$ (c 1.25, CHCl_3); ^1H NMR (500 MHz, C_6D_6), δ (ppm): 7.51 (d, $J=7.4$ Hz, 2H, Ph); 7.35 (d, $J=7.4$ Hz, 2H, Ph); 7.28 (t, $J=7.4$ Hz, 2H, Ph); 7.15 (t, $J=7.4$ Hz, 3H, Ph); 7.08 (t, $J=7.4$ Hz, 1H, Ph); 5.66 (tq, $J_{\text{t}}=10.0$ Hz, $J_{\text{q}}=1.7$ Hz, 1H, H-15); 5.50 (dq, $J_{\text{d}}=11.3$ Hz, $J_{\text{q}}=7.2$ Hz, 1H, H-16); 5.15 (s, 1H, C-18); 4.93 (d, $J=11.9$ Hz, 1H, PhCH_2 1); 4.83 (d, $J=12.0$ Hz, 1H, PhCH_2 2); 4.81 (dt, $J_{\text{d}}=7.7$ Hz, $J_{\text{t}}=6.4$ Hz, 1H, H-14); 4.72 (d, $J=12.1$ Hz, 1H, PhCH_2 2); 4.56 (s, 2H, OCH_2OCH_3); 4.50 (d, $J=11.9$ Hz, 1H, PhCH_2 1); 4.23 (ddd, $J_1=9.7$ Hz, $J_2=4.7$ Hz, $J_3=2.0$ Hz, 1H, H-21); 4.10 (m, 1H, H-8); 4.08 (dd, $J_1=J_2=10.0$ Hz, 1H, H-22); 3.92 (m, 4H, H-1, H-20, H-22, H-23); 3.74 (dd, $J_1=J_2=2.5$ Hz, 1H, H-7); 3.71 (ddd, $J_1=10.7$ Hz, $J_2=4.0$ Hz, $J_3=3.0$ Hz, 1H, H-6); 3.58 (dd, $J_1=11.7$ Hz, $J_2=7.9$ Hz, 1H, H-1); 3.46 (dd, $J_1=11.7$ Hz, $J_2=8.0$ Hz, 1H, H-23); 3.44 (m, 1H, H-4); 3.22 (s, 3H, OCH_2OCH_3); 2.82 (t, $J=6.0$ Hz, 1H, H-10); 2.06 (m, 2H); 1.9

(m, 2H); 1.82-1.64 (m, 3H); 1.58 (dd, $J_1=7.2$ Hz, $J_2=1.7$ Hz, 3H, H-17); 1.50-1.42 (m, 3H); 1.47 (s, 3H, CH₃); 1.44 (s, 3H, CH₃); 1.38 (s, 3H, CH₃); 1.32 (ddd, $J_1=14.1$ Hz, $J_2=8.0$ Hz, $J_3=3.4$ Hz, 1H, H-3); 1.10 (m, 30H, TIPS, TES); 0.71 (dq, $J_d=2.8$ Hz, $J_q=7.6$ Hz, 6H, TES); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 140.30; 138.17; 133.33; 128.20; 127.97; 127.56; 127.39; 126.79; 126.69; 125.81; 124.79; 101.60; 97.75; 94.57; 79.44; 76.86; 76.02; 75.83; 71.88; 71.05; 70.43; 69.53; 67.73; 64.87; 64.47; 60.56; 60.10; 55.47; 34.62; 32.71; 31.14; 29.64; 25.33; 22.63; 18.21; 18.11; 16.98; 15.70; 13.60; 12.46; 10.26; 6.88; 5.02; IR (ν , cm⁻¹): 3690, 3444, 3054, 3020, 2986, 2306, 1654, 1638, 1422, 1258, 1216, 1156; Calcd for C₅₉H₉₈O₁₂Si₂: C, 67.13; H, 9.36. Found C, 67.35; H, 9.43.

2R-(3S-{3S-[2R,3R-Bis-benzyloxy-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydro-pyran-4R-yloxy]-hex-4Z-enyl}-3S-methyl-oxiranylmethyl)-6R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-tetrahydro-pyran-3R-ol (2). The alkene from previous step (0.500 g, 0.474 mmol) was dissolved in acetonitrile (5.5 ml) and pyridine (2.0 ml, 25.9 mmol), and aqueous hydrogen fluoride (6M, 2.0 ml, 12.0 mmol) was added. After stirring at 25°C for 7 h, the mixture was diluted with ethyl acetate (40 ml), washed with 1M aqueous hydrogen chloride (14 ml) and water (5 ml). The combined aqueous layers were extracted with ethyl acetate (3x5 ml), and the combined organic layers were washed with brine (3 ml) and saturated aqueous sodium bicarbonate (10 ml). The organic solution was dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was subjected to column chromatography (silica, 50 to 70% EtOAc – hexanes) which gave epoxy alcohol 2 (0.415 g, 0.441 mmol, 94 %), along with a small amount of the starting material (20 mg, 19 mmol, 4%).

$[\alpha]_D^{25} = -19.5^\circ$ (c 1.1, CHCl₃); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 7.51 (d, $J=7.6$ Hz, 2H, Ph); 7.34 (d, $J=7.6$ Hz, 2H, Ph); 7.28 (t, $J=7.6$ Hz, 2H, Ph); 7.15 (t, $J=7.6$ Hz, 3H, Ph); 7.08 (t, $J=7.6$ Hz, 1H, Ph); 5.67 (tq, $J_t=10.0$ Hz, $J_q=1.5$ Hz, 1H, H-15); 5.50 (dq, $J_d=11.1$ Hz, $J_q=7.0$ Hz, 1H, H-16); 5.16 (s, 1H, C-18); 4.92 (d, $J=11.7$ Hz, 1H, PhCH₂1); 4.84 (d, $J=12.1$ Hz, 1H, PhCH₂2); 4.81 (dt, $J_d=8.8$ Hz, $J_t=6.5$ Hz, 1H, H-14); 4.77 (d, $J=12.1$ Hz, 1H, PhCH₂2); 4.49 (d,

$J=11.7$ Hz, 1H, PhCH_2); 4.42 (AB, $J=6.7$ Hz, 2H, OCH_2OCH_3); 4.23 (ddd, $J_1=9.8$ Hz, $J_2=4.8$ Hz, $J_3=2.3$ Hz, 1H, H-21); 4.09 (dd, $J_1=J_2=9.8$ Hz, 1H, H-22); 4.08 (m, 1H, H-8); 3.98 (dd, $J_1=11.5$ Hz, $J_2=4.2$ Hz, 1H, H-1); 3.94-3.88 (m, 3H, H-23, H-20, H-22); 3.65-3.58 (m, 2H, H-6, H-7); 3.58 (dd, $J_1=11.7$ Hz, $J_2=7.6$ Hz, 1H, H-1); 3.53 (dd, $J_1=11.7$ Hz, $J_2=7.6$ Hz, 1H, H-23); 3.47 (tt, $J_1=9.1$ Hz, $J_2=3.8$ Hz, 1H, H-4); 3.11 (s, 3H, OCH_2OCH_3); 2.86 (t, $J=5.8$ Hz, 1H, H-10); 2.41 (d, $J=4.2$ Hz, 1H, OH-7); 2.10-1.98 (m, 2H); 1.89 (ddd, $J_1=J_2=11.7$ Hz, $J_3=4.5$ Hz, 1H, H-21); 1.80-1.70 (m, 2H); 1.68-1.56 (m, 3H); 1.57 (dd, $J_1=7.0$ Hz, $J_2=1.5$ Hz, 1H, H-17); 1.50 (m, 1H); 1.48 (s, 3H, CH_3); 1.44 (s, 3H, CH_3); 1.41 (s, 3H, CH_3); 1.33 (ddd, $J_1=14.2$ Hz, $J_2=7.8$ Hz, $J_3=3.4$ Hz, 1H, H-3); 1.17 (s, 3H, CH_3); 1.11 (m, 21H, TIPS); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 140.28; 138.15; 133.31; 128.20; 127.97; 127.58; 127.39; 126.79; 126.69; 125.81; 124.79; 111.00; 101.56; 97.81; 95.13; 79.44; 76.86; 75.81; 74.12; 73.85; 72.47; 71.05; 69.67; 69.53; 69.07; 67.32; 66.49; 65.34; 64.47; 63.75; 60.60; 60.21; 56.89; 55.71; 41.61; 34.56; 34.31; 33.39; 32.85; 31.63; 31.18; 29.78; 29.35; 28.15; 25.08; 23.76; 22.89; 20.63; 18.21; 18.11; 17.02; 16.96; 15.70; 14.38; 13.60; 13.23; 12.46; IR (ν , cm^{-1}): 3056, 3050, 2944, 1278, 1258, 1216, 1068, 780; Calcd for $\text{C}_{57}\text{H}_{96}\text{O}_{13}\text{Si}_2$: C, 65.48; H 9.25. Found C, 65.59; H, 9.38; Calcd for $\text{C}_{53}\text{H}_{84}\text{O}_{12}\text{Si}$: C, 67.63; H, 8.99. Found C, 67.27; H, 9.05.

{5R,6R-Dibenzyloxy-4-[2R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-5Ra-methyl-9S-(1S-phenylselenanyl-ethyl)-dodecahydro-1,5,10-trioxa-cyclohepta[b]naphthalen-8S-yloxy]-5R-methyl-tetrahydro-pyran-3R-yloxy}-triisopropyl-silane (18). A solution of epoxy alcohol 2 (1.75 g, 1.86 mmol) in hexafluoro-iso-propanol (20 ml), freshly distilled from $\text{Ba}[\text{OCH}(\text{CF}_3)_2]_2$, was cooled to 0°C under a nitrogen atmosphere. N-Phenylselenenyl-phthalimide (1.40 g, 4.65 mmol, 2.5 eq) was added, and the reaction mixture was stirred at 0°C for 80 min. The mixture was diluted with chloroform (80 ml), washed with 5M aqueous KOH (3x15 ml), and a brine-water mixture (1:1, 20 ml). The combined aqueous layers were extracted with CHCl_3 (30 ml), and the combined chloroform extracts were dried over anhydrous NaSO_4 , filtered, and evaporated. The residue was purified by column chromatography

(silica, 33% ethyl acetate – hexanes) to give tricyclic ether 18 (1.69 g, 1.54 mmol, 83%).

$[\alpha]_D^{25} = -16.4^\circ$ (c 0.5, CHCl_3); ^1H NMR (400 MHz, C_6D_6), δ (ppm): 7.48-7.15 (m, 12H, Ph); 6.99-6.96 (m, 3H, Ph); 5.12 (s, 1H, H-17); 4.93 (d, $J=11.8$ Hz, 1H, PhCH_2 1); 4.88 (d, $J=6.4$ Hz, 1H, OCH_2OCH_3); 4.79 (d, $J=12.0$ Hz, 1H, PhCH_2 2); 4.69 (d, $J=6.4$ Hz, 1H, OCH_2OCH_3); 4.68 (d, $J=12.0$ Hz, 1H, PhCH_2 2); 4.50 (d, $J=11.8$ Hz, 1H, PhCH_2 1); 4.40 (dd, $J_1=2.3$ Hz, $J_2=1.0$ Hz, 1H, H-15); 4.23 (bd, $J=5.5$ Hz, 1H, H-14); 4.17 (ddd, $J_1=10.2$ Hz, $J_2=5.1$ Hz, $J_3=2.1$ Hz, 1H, H-20); 4.00-3.90 (m, 4H, H-1, H-21, H-22, H-6); 3.87 (bs, 1H, H-19); 3.85-3.80 (m, 3H, H-8, H-10, H-21); 3.74-3.67 (m, 1H, H-4); 3.54 (dd, $J_1=9.1$ Hz, $J_2=4.6$ Hz, 1H, H-1); 3.51 (dd, $J_1=9.1$ Hz, $J_2=4.6$ Hz, 1H, H-22); 3.37 (dq, $J_q=6.9$ Hz, $J_d=2.5$ Hz, 1H, H-16); 3.29 (dd, $J_1=9.6$ Hz, $J_2=2.6$ Hz, 1H, H-7); 3.29 (s, 3H, OCH_2OCH_3); 2.43 (t, $J=13.1$ Hz, 1H, H-12); 2.38-2.31 (m, 1H, H-13); 2.25 (ddd, $J_1=16.8$ Hz, $J_2=10.7$ Hz, $J_3=6.1$ Hz, 1H, H-3); 2.13 (t, $J=14.2$ Hz, 1H, H-13); 2.04 (dd, $J_1=11.9$ Hz, $J_2=4.9$ Hz, 1H, H_e -9); 2.08-2.02 (m, 1H, H-2); 1.77 (ddd, $J_1=J_2=J_3=11.9$ Hz, 1H, H_a -9); 1.64 (ddd, $J_1=14.4$ Hz, $J_2=6.7$ Hz, $J_3=3.1$ Hz, 1H, H-5); 1.53-1.44 (m, 1H, H-5); 1.51 (s, 3H, CH_3); 1.45 (d, $J=6.9$ Hz, 3H, Me-25); 1.38 (s, 3H, CH_3); 1.37 (s, 3H, CH_3); 1.37 (s, 3H, CH_3); 1.28-1.19 (m, 1H, H-3); 1.08-1.06 (m, 21H, TIPS); ^{13}C NMR (100 MHz, C_6D_6), δ (ppm): 140.70; 138.92; 133.98; 133.90; 131.67; 129.59; 129.41; 129.13; 129.06; 128.65; 128.53; 128.42; 128.30; 128.17; 128.00; 127.94; 127.29; 123.45; 103.05; 98.25; 97.11; 88.52; 88.37; 86.44; 86.29; 79.14; 78.13; 78.10; 73.51; 71.74; 70.01; 69.76; 66.67; 65.83; 65.55; 64.75; 64.11; 55.56; 46.37; 37.011; 34.68; 34.07; 32.98; 32.55; 27.81; 21.70; 21.39; 19.39; 18.76; 18.68; 18.35; 16.17; 15.41; 13.51; 13.36; 13.10; 12.98; IR (ν , cm^{-1}): 3022, 3010, 2946, 1740, 1222, 1210, 1198, 1096, 1064, 800. Calcd for $\text{C}_{59}\text{H}_{88}\text{O}_{112}\text{SeSi}$: C, 64.63; H 8.09. Found: C, 64.72; H, 8.03.

{5R,6R-Dibenzyloxy-4R-[2R-(2,2-dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-5Ra-methyl-9R-vinyl-dodecahydro-1,5,10-trioxacyclohepta[b]naphthalen-8S-yloxy]-5R-methyl-tetrahydro-pyran-3R-yloxy}-triisopropyl-silane (19). Hydrogen peroxide (30% aqueous, 4.4 ml) was added

to a mixture of **7** (1.69 g, 1.54 mmol), sodium bicarbonate (1.30 g, 15.4 mmol, 10 eq), and THF (47 ml) at 0 °C. After stirring at 0 °C for 10 min, the mixture was heated to reflux for 1 h. After cooling to 25 °C, the reaction mixture was diluted with CH₂Cl₂ (250 ml), washed with water (40 ml) and brine (40 ml). The combined aqueous layers were extracted with CH₂Cl₂ (2x30 ml), and the combined organic layers were dried over anhydrous NaSO₄ and filtered. Solvent evaporation followed by column chromatography of the residue (silica, 10% EtOAc – toluene) afforded 1.32 g (1.41 mmol, 91%) of the desired product.

$[\alpha]_D^{25} = -31.9^\circ$ (c 0.42, CHCl₃); ¹H NMR (500 MHz, C₆D₆), δ (ppm): 7.48 (d, J=7.6 Hz, 2H, Ph); 7.42 (d, J=7.6 Hz, 2H, Ph); 7.33 (t, J=7.6 Hz, 2H, Ph); 7.27 (t, J=7.6 Hz, 2H, Ph); 5.63 (ddd, J₁=17.2 Hz, J₂=10.6 Hz, J₃=4.7 Hz, 1H, H-16); 5.39 (dt, J_d=17.1 Hz, J_t=1.5 Hz, 1H, H_c-24); 5.04 (d, J=11.5 Hz, 1H, PhCH₂1); 4.98 (dt, J_d=10.6 Hz, J_t=1.6 Hz, 1H, H_t-24); 4.92 (bd, J=3.5 Hz, 1H, H-15); 4.91 (d, J=6.4 Hz, 1H, OCH₂OCH₃); 4.82 (d, J=11.9 Hz, 1H, PhCH₂2); 4.77 (d, J=11.9 Hz, 1H, PhCH₂2); 4.74 (d, J=6.4 Hz, 1H, OCH₂OCH₃); 4.66 (d, J=11.5 Hz, 1H, PhCH₂1); 4.24 (dd, J₁=12.0 Hz, J₂=4.5 Hz, 1H, H-10); 4.15 (ddd, J₁=10.3 Hz, J₂=5.0 Hz, J₃=1.6 Hz, 1H, H-20); 4.02 (d, J=7.0 Hz, 1H, H-14); 3.99 (dd, J₁=J₂=10.4 Hz, 1H, H-21); 3.98 (m, 1H, H-6); 3.91 (dd, J₁=11.7 Hz, J₂=4.5 Hz, 1H, H-1); 3.86 (dd, J₁=11.7 Hz, J₂=4.5 Hz, 1H, H-22); 3.84 (dd, J₁=10.5 Hz, J₂=5.0 Hz, 1H, H-21); 3.83 (ddd, J₁=J₂=11.5 Hz, J₃=4.7 Hz, 1H, H-8); 3.77 (bs, 1H, H-19); 3.68 (dddd, J₁=J₂=J₃=J₄=5.4 Hz, 1H, H-4); 3.48 (m, 2H, H-1 and H-22); 3.29 (s, 3H, OCH₂OCH₃); 3.27 (dd, J₁=9.5 Hz, J₂=2.7 Hz, 1H, H-7); 2.44 (dd, J₁=J₂=13.1 Hz, 1H, H-12); 2.21 (ddd, J₁=14.4 Hz, J₂=10.7 Hz, J₃=6.2 Hz, 1H, H-3); 2.07-1.97 (m, 3H); 1.76 (ddd, J₁=J₂=J₃=11.8 Hz, 1H, H-9); 1.74-1.62 (m, 3H); 1.49 (s, 3H, CH₃); 1.46 (m, 1H); 1.39 (s, 3H, CH₃); 1.35 (s, 3H, CH₃); 1.32 (s, 3H, CH₃); 1.23 (ddd, J₁=14.4 Hz, J₂=7.7 Hz, J₃=4.8 Hz, 1H, H-3); 1.04 (m, 18 H, TIPS); 0.97 (m, 3H, TIPS); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 139.70; 137.84; 137.77; 128.41; 128.34; 127.73; 127.70; 127.24; 127.20; 127.15; 114.50; 102.58; 97.72; 96.37; 85.24; 84.55; 82.32; 77.64; 77.54; 75.13; 72.39; 71.58; 71.07; 69.77; 68.54; 65.69; 65.21; 65.06; 64.27; 63.36; 55.25; 35.37; 33.96; 33.19; 32.15; 31.77; 27.19; 23.09; 20.77; 18.11; 18.01; 15.62; 14.66; 12.31; IR (ν , cm⁻¹): 3624, 3014, 2976, 1390, 1210, 1060, 878; Calcd for C₅₃H₈₂O₁₂Si: C, 67.77; H, 8.80. Found: C, 67.61; H, 8.81.

4R-[2R-(2,2-Dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-5Ra-methyl-9R-vinyl-dodecahydro-1,5,10-trioxa-cyclohepta[b]naphthalen-8S-yloxy]-3R-methyl-5R-(triisopropyl-silanyloxy)-tetrahydro-pyran-2,3R-diol (20). A solution of lithium in ammonia was prepared by stirring lithium (0.14 g, 20.2 mmol) [cleaned by successive dipping in hexanes, methanol, and ether and cut into small pieces] and liquid ammonia (~60 ml) at about -45°C for 1.5 h. Using a stainless steel cannula, the blue liquid was added in small portions to a solution of 19 (1.245 g, 1.325 mmol) and ethyl allyl ether (0.52 ml, 0.395 g, 4.59 mmol, 3.5 eq) in dry THF (21 ml) at -78°C under a nitrogen atmosphere. After addition of each portion, the mixture was stirred for ~ 1 min and analyzed by TLC. When about 10-15% of the starting material remained the reaction was quenched by addition of excess solid ammonium chloride, diluted with ether, and ammonia was allowed to evaporate at room temperature. More ether was added and the mixture was filtered. The solvent was evaporated and the products were separated by flash column chromatography (silica, 60 to 75 to 100% ethyl acetate – hexanes) to give 20 (0.440 g, 0.595 mmol, 45%), monodeprotected 20, and 20 (0.258 g, 0.304 mmol, 23 % combined), along with the starting material (0.370 g, 0.394 mmol, 30%). The mono-debenzylated products and the starting material were combined and resubjected to the same reaction conditions, providing, after four more cycles, a total of 0.770 g (1.01 mmol, 77%) of lactol 20.

$[\alpha]_{\text{D}}^{25} = -11.5^{\circ}$ (c 1.2, CHCl_3); ^1H NMR (500 MHz, C_6D_6), (mixture of anomers ~ 3:1) major anomer δ (ppm): 5.81 (ddd, $J_1=17.2$ Hz, $J_2=10.7$ Hz, $J_3=5.2$ Hz, 1H, H-16); 5.43 (dt, $J_d=17.2$ Hz, $J_t=1.5$ Hz, 1H, H_c-24); 5.04 (dt, $J_d=10.6$ Hz, $J_t=1.7$ Hz, 1H, H_t-24); 4.86 (d, $J=6.2$ Hz, OCH_2OCH_3); 4.86 (bs, 1H, H-17); 4.70 (d, $J=6.2$ Hz, 1H, OCH_2OCH_3); 4.06-3.82 (m, 8H); 3.74-3.67 (m, 2H); 3.59 (dd, $J_1=11.5$ Hz, $J_2=8.8$ Hz, 1H, H-1); 3.54-3.48 (m, 2H); 3.29 (s, 3H, OCH_2OCH_3); 3.27 (dd, $J_1=9.6$ Hz, $J_2=2.7$ Hz, 1H, H-7); 2.34-2.12 (m, 14H); 2.00-1.92 (m, 1H); 1.90-1.78 (m, 2H); 1.49 (s, 3H, CH_3); 1.39 (s, 3H, CH_3); 1.37 (s, 3H, CH_3); 1.30 (s, 3H, CH_3); 1.18 (ddd, $J_1=14.6$ Hz, $J_2=6.9$ Hz, $J_3=4.4$ Hz,

1H, H-3); 1.09 (m, TIPS); 1.03 (m, TIPS); minor anomer δ (ppm): 5.77 (ddd, $J_1=17.2$ Hz, $J_2=10.7$ Hz, $J_3=5.2$ Hz, 1H, H-16); 5.41 (dt, $J_d=17.2$ Hz, $J_t=1.5$ Hz, 1H, H_c-24); 5.06 (dt, $J_d=10.6$ Hz, $J_t=1.7$ Hz, 1H, H_t-24); 4.92 (d, $J=6.2$ Hz, OCH₂OCH₃); 4.75 (d, $J=6.2$ Hz, 1H, OCH₂OCH₃); 3.60 (dd, $J_1=11.5$ Hz, $J_2=8.8$ Hz, 1H, H-1); 3.31 (s, 3H, OCH₂OCH₃); 3.25 (dd, $J_1=9.6$ Hz, $J_2=2.7$ Hz, 1H, H-7); 1.48 (s, 3H, CH₃); 1.39 (s, 3H, CH₃); 1.29 (s, 3H, CH₃); 1.23 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 137.69; 137.51; 129.53; 127.60; 115.97; 115.54; 114.60; 97.77; 97.61; 96.22; 83.18; 77.87; 77.56; 77.15; 72.49; 72.41; 70.61; 70.29; 70.21; 68.49; 68.31; 66.20; 65.84; 65.37; 65.27; 64.27; 63.28; 63.11; 60.37; 55.37; 40.95; 35.52; 34.53; 34.13; 33.24; 32.73; 32.46; 31.57; 30.89; 27.01; 24.72; 24.29; 21.03; 18.80; 18.13; 18.01; 17.75; 17.61; 17.55; 17.00; 15.50; 15.25; 14.20; 14.00; 12.89; 12.76; 12.45; IR (ν , cm⁻¹): 3444, 3024, 3016, 2946, 1372, 1220, 1208; Calcd for C₃₉H₇₀O₁₂Si: C, 61.71; H, 9.30. Found: C, 61.93; H, 9.25.

3R-[2R-(2,2-Dimethyl-[1,3]dioxan-5-ylmethyl)-4S-methoxymethoxy-5Ra-methyl-9R-vinyl-dodecahydro-1,5,10-trioxo-cyclohepta[b]naphthalen-8S-yloxy]-4S-methyl-hex-5-ene-1,2R,4S-triol (21). Lactol 20 (0.215 g, 0.283 mmol) was dissolved in dry THF (1.9 ml), and trimethylsilylmethyl magnesium chloride (1.5M in THF, 1.9 ml, 2.85 mmol, 10 eq) was added. The reaction mixture was brought to reflux for 1 h, cooled to room temperature, diluted with ether (5 ml), and poured into a separatory funnel containing ethyl acetate (25 ml) and saturated aqueous ammonium chloride (10 ml). The organic phase was washed with water (10 ml) and saturated aqueous sodium bicarbonate (10 ml), dried over anhydrous sodium sulfate, filtered, and evaporated. Flash column chromatography (silica, 50 to 75% ethyl acetate – hexanes) afforded the corresponding silanol (0.223 g, 0.263 mmol, 93%).

$[\alpha]_D^{25} = +9.5^\circ$ (c 0.9, CHCl₃); ¹H NMR (500 MHz, C₆D₆), δ (ppm): 5.83 (ddd, $J_1=17.2$ Hz, $J_2=10.7$ Hz, $J_3=5.2$ Hz, 1H, H-16); 5.47 (dt, $J_d=17.2$ Hz, $J_t=1.5$ Hz, 1H, H_c-21); 5.08 (dt, $J_d=10.7$ Hz, $J_t=1.6$ Hz, 1H, H_t-21); 4.77 (d, $J=6.5$ Hz, 1H, OCH₂OCH₃); 4.66 (d, $J=6.5$ Hz, 1H, OCH₂OCH₃); 4.63 (dq, $J_d=5.2$ Hz, $J_q=1.5$ Hz, 1H,

H-15); 4.26 (bd, $J=6.5$ Hz, 1H, H-14); 4.24 (dd, $J_1=8.0$ Hz, $J_2=3.9$ Hz, 1H, H-21); 4.13 (dd, $J_1=11.1$ Hz, $J_2=7.5$ Hz, 1H, H-21); 4.08 (ddd, $J_1=12.2$ Hz, $J_2=3.6$ Hz, $J_3=2.6$ Hz, 1H, H-17); 3.99 (dd, $J_1=12.0$ Hz, $J_2=4.6$ Hz, 1H, H-10); 3.97 - 3.94 (m, 2H, H-1 and H-6); 3.89 (ddd, $J_1=11.4$ Hz, $J_2=9.9$ Hz, $J_3=4.8$ Hz, 1H, H-8); 3.83 (bs, 1H, H-19); 3.83 (dd, $J_1=11.4$ Hz, $J_2=4.4$ Hz, 1H, H-23); 3.71 - 3.66 (m, 2H, H-4 and H-20); 3.57 (dd, $J_1=11.3$ Hz, $J_2=8.5$ Hz, 1H, H-1); 3.50 (dd, $J_1=11.5$ Hz, $J_2=8.6$ Hz, 1H, H-23); 3.28 (s, 3H, OCH₂OCH₃); 3.27 (dd, $J_1=9.7$ Hz, $J_2=2.9$ Hz, 1H, H-7); 2.49 (dd, $J_1=3.8$ Hz, $J_2=1.6$ Hz, 1H, OH-17); 2.32 - 2.21 (m, 3H, H_e-9); 2.11 (m, 1H, H-13); 1.90 (m, 1H, H-2); 1.86 (ddd, $J_1=J_2=J_3=11.9$ Hz, 1H, H_a-9); 1.71 - 1.65 (m, 2H, H-13 and H-14); 1.61 (ddd, $J_1=14.7$ Hz, $J_2=7.0$ Hz, $J_3=3.3$ Hz, 1H, H_a-5); 1.49 (m, 1H, H_e-5); 1.48 (s, 3H, CH₃); 1.39 (s, 3H, CH₃); 1.30 (s, 3H, CH₃); 1.28 (s, 3H, CH₃); 1.19 (ddd, $J_1=14.1$ Hz, $J_2=6.6$ Hz, $J_3=4.5$ Hz, 1H, H-3); 0.81 (dd, $J_1=14.3$ Hz, $J_2=12.4$ Hz, 1H, H-22); 0.62 (bd, $J=14.3$ Hz, 1H, H-22); 0.25 (s, 9H, TMS); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 137.53; 115.62; 97.82; 96.15; 87.08; 84.98; 83.54; 78.57; 77.44; 77.23; 74.04; 72.24; 71.56; 70.80; 70.14; 65.25; 64.28; 63.25; 63.09; 55.42; 35.36; 33.86; 33.32; 32.41; 31.63; 26.97; 21.10; 20.50; 18.07; 15.55; 12.42; -0.73; IR (ν , cm⁻¹): 3620, 3016, 2948, 1458, 1384, 1216, 1208, 1060, 882; Calcd for C₄₃H₈₂O₁₂Si₂: C, 60.96; H 9.75. Found C, 60.79; H, 9.73.

A solution of potassium tert-butoxide in THF (1.0M, 1.5 ml, 1.50 mmol, 5.5 eq) was added to a solution of the silanol from the previous step (0.232 g, 0.274 mmol) in dry THF (1.40 ml) at room temperature under a nitrogen atmosphere. The resulting orange-brown mixture was stirred at room temperature for 1 h, then a THF solution of tetra-*n*-butyl-ammonium fluoride (1.0M, 1.75 ml, 1.75 mmol, 6.4 eq) was added. Stirring was continued for an additional 1.5 h. The mixture was diluted with ether (25 ml) and water (10 ml), the aqueous layer was separated and extracted with ethyl acetate (4x15 ml). Combined organic layers were washed with brine (10 ml), dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was purified by column chromatography (silica, 70 to 100% ethyl acetate – hexanes to 1.5 % methanol – ethyl acetate) to give diene 21 (0.152 g, 0.253 mmol, 92%).

$[\alpha]_D^{25} = +11.7^\circ$ (c 1.0, CHCl₃); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 5.87 (dd, $J_1=17.2$ Hz, $J_2=10.6$ Hz, 1H, H-17); 5.76 (ddd, $J_1=17.2$ Hz, $J_2=10.6$ Hz, $J_3=4.7$ Hz, 1H, H-16); 5.44 (dt, $J_d=17.2$ Hz, $J_t=1.8$ Hz, 1H, H_c-26); 5.35 (dd, $J_1=17.2$ Hz, $J_2=1.5$ Hz, 1H, H_c-27); 5.06 (m, 2H, H_c-26, H_t-27); 4.82 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.69 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.50 (dq, $J_d=4.5$ Hz, $J_q=1.5$ Hz, 1H, H-15); 3.97 (dd, $J_1=11.5$ Hz, $J_2=4.5$ Hz, 1H, H-1); 3.95 - 3.77 (m, 6H, H-10, H-14, H-20, H-21, H-21, H-23); 3.81 (ddd, $J_1=11.6$ Hz, $J_2=10.0$ Hz, $J_3=4.7$ Hz, 1H,

H-8); 3.68 (ddd, $J_1=11.0$ Hz, $J_2=6.5$ Hz, $J_3=4.4$ Hz, 1H, H-4); 3.63 (ddd, $J_1=J_2=J_3=5.4$ Hz, 1H, H-6); 3.56 (dd, $J_1=11.5$ Hz, $J_2=8.9$ Hz, 1H, H-1); 3.49 (dd, $J_1=11.5$ Hz, $J_2=9.0$ Hz, 1H, H-23); 3.41 (m, 1H, H-19); 3.28 (s, 3H, OCH₂OCH₃); 3.25 (dd, $J_1=9.7$ Hz, $J_2=2.7$ Hz, 1H, H-7); 2.26 (ddd, $J_1=14.4$ Hz, $J_2=10.9$ Hz, $J_3=6.5$ Hz, 1H, H-3); 2.23 - 2.14 (m, 2H); 1.95 (m, 1H, H-2); 1.87 (m, 1H); 1.83 (ddd, $J_1=J_2=J_3=11.9$ Hz, 1H, H_a-9); 1.66 - 1.55 (m, 3H); 1.49 (s, 3H, CH₃); 1.47 (dd, $J_1=14.4$ Hz, $J_2=3.3$ Hz, 1H, H_e-5); 1.37 (s, 3H, CH₃); 1.27 (s, 3H, CH₃); 1.26 (s, 3H, CH₃); 1.12 (ddd, $J_1=14.5$ Hz, $J_2=6.8$ Hz, $J_3=4.3$ Hz, 1H, H-3); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 142.77; 137.43; 115.68; 114.01; 97.78; 96.28; 84.36; 84.09; 83.08; 77.23; 76.86; 75.58; 72.67; 72.37; 70.94; 70.20; 65.27; 64.28; 63.23; 63.13; 55.42; 35.28; 34.06; 33.13; 32.45; 31.61; 27.03; 24.78; 23.30; 21.01; 15.55; IR (ν , cm⁻¹): 3620, 3024, 1384, 1236, 1210, 1204, 1062, 790; Calcd for C₃₁H₅₂O₁₁Si+0.5H₂O: C, 61.06; H 8.76. Found C, 61.16; H, 8.62.

Pentacyclic triol (22). The ruthenium catalyst (35 mg, 41 mmol, 10 mol%) was added to a solution of diene 21 (0.246 g, 0.409 mmol) in dry benzene (13.6 ml), freshly distilled from sodium-benzophenone. The reaction mixture was heated to reflux for 30 min. The mixture was cooled to room temperature, diluted with dichloromethane (50 ml), and 2.3 ml of a solution of tris-(hydroxymethyl)phosphine (0.54 g, 4.35 mmol) and triethylamine (1.0 ml, 0.726 g, 7.17 mmol) in dichloromethane (3.8 ml) were added. After stirring for 25 min, the mixture was washed with water (20 ml), the aqueous phase was extracted with dichloromethane (2x15 ml), and combined aqueous layers were dried over anhydrous sodium sulfate, filtered, and evaporated. The remaining oil was purified by flash column chromatography (silica, 0 to 3% methanol – ethyl acetate) to give 0.200 g (0.349 mmol, 85%) of tetracyclic ether 22.

$[\alpha]_D^{25} = +12.8^\circ$ (c 1.0, CHCl₃); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 5.64 (s, 2H, H-16 and H-17);* 4.76 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.62 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.04 (ddd, $J_1=11.4$ Hz, $J_2=4.6$ Hz, $J_3=1.4$ Hz, 1H, H-1); 3.94 (ddd, $J_1=J_2=J_3=2.8$ Hz, 1H, H-6); 3.89 (ddd, $J_1=11.3$ Hz, $J_2=4.5$ Hz, $J_3=1.2$ Hz, 1H, H-22); 3.87 - 3.64 (m, 6H, H-4, H-8, H-15, H-20, H-21, H-21); 3.61 (dd, $J_1=11.4$ Hz, $J_2=8.9$ Hz, 1H, H-1); 3.53 (dd, $J_1=11.5$ Hz, $J_2=8.9$ Hz, 1H, H-22); 3.55 (d, $J=9.2$ Hz, 1H, H-19); 3.35 (ddd, $J_1=8.8$ Hz, $J_2=J_3=6.5$ Hz, 1H, H-14); 3.25 (s,

3H, OCH₂OCH₃); 3.25 - 3.21 (m, 1H, H-10); 3.20 (dd, $J_1=9.3$ Hz, $J_2=1.9$ Hz, 1H, H-7); 2.29 (ddd, $J_1=14.6$ Hz, $J_2=11.2$ Hz, $J_3=6.4$ Hz, 1H, H-3); 2.10 (ddd, $J_1=11.8$ Hz, $J_2=J_3=4.7$ Hz, 1H, H_e-9); 2.03 (m, 1H, H-2); 1.89 - 1.75 (m, 4H); 1.68 - 1.58 (m, 3H); 1.60 (s, 3H, CH₃); 1.45 (m, 1H, H-5); 1.43 (s, 3H, CH₃); 1.39 (s, 3H, CH₃); 1.14 (s, 3H, CH₃); 1.14 (m, 1H, H-3); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 137.88; 131.02; 97.82; 96.03; 86.20; 83.60; 82.92; 80.92; 77.21; 72.70; 72.20; 70.84; 70.22; 65.31; 64.10; 63.46; 55.36; 37.75; 33.92; 32.56; 32.33; 31.51; 30.25; 26.87; 21.59; 21.16; 17.30; IR (ν , cm⁻¹): 3024, 3014, 2950, 1454, 1374, 1222, 1208, 1104, 792; Calcd for C₂₉H₄₆O₁₁: C, 60.82; H 8.45. Found C, 60.54; H, 8.39.

Conjugated amide. Ground sodium periodate (0.314 g, 1.47 mmol, 5 eq) was added to a mixture of 22 (0.168 g, 0.293 mmol), THF (3.2 ml), tert-butanol (0.50 ml), and saturated aqueous sodium bicarbonate (0.50 ml). The reaction mixture was vigorously stirred for 10 min, then extracted with ethyl acetate, washed with water and brine. After drying over anhydrous sodium sulfate, the ethyl acetate extracts were filtered and evaporated. The crude aldehyde was dissolved in 1 ml of dry THF under a nitrogen atmosphere. A solution of the sodium salt of (N-methyl-N-methoxycarbamoyl)methylphosphonate [obtained by stirring sodium hydride (21 mg, 0.85 mmol, 2.9 eq) and (N-methyl-N-methoxycarbamoyl)methylphosphonate (0.181 ml, 0.211 g, 0.879 mmol, 3 eq) in dry THF (3.2 ml) at 0 to 25°C under N₂ for 30 min] was added at 0°C, and the reaction mixture was stirred at room temperature for 30 min. Dilution with ethyl acetate (20 ml) and washing with water (5 ml) and brine (5 ml) followed by drying over anhydrous sodium sulfate, filtration, and evaporation gave the crude product, which was subjected to flash column chromatography (silica, 100% ethyl acetate) to give the pure conjugated amide as a 10:1 mixture of E and Z isomers (0.171 g, 0.273 mmol, 93%).

$[\alpha]_D^{25} = -1.7^\circ$ (c 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃), δ (ppm): 7.07 (dd, $J_1=15.5$ Hz, $J_2=4.1$ Hz, 1H, H-20); 6.68 (d, $J=15.5$ Hz, 1H, H-21); 5.70 (dd, $J_1=12.9$ Hz, $J_2=1.8$ Hz, 1H, H-16); 5.57 (dd, $J_1=12.9$ Hz, $J_2=1.8$ Hz, 1H, H-17); 4.72 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.66 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.16 (dd,

$J_1=4.0$ Hz, $J_2=1.8$ Hz, 1H, H-19); 4.08 (ddd, $J_1=9.4$ Hz, $J_2=J_3=2.2$ Hz, 1H, H-15); 4.00 (q, $J=2.5$ Hz, 1H, H-6); 3.99 (dd, $J_1=11.5$ Hz, $J_2=4.7$ Hz, 1H, H-1); 3.91 (ddd, $J_1=10.9$ Hz, $J_2=6.5$ Hz, $J_3=4.6$ Hz, 1H, H-4); 3.88 (dd, $J_1=11.4$ Hz, $J_2=4.6$ Hz, 1H, H-23); 3.72 (s, 3H, NOME); 3.67 (ddd, $J_1=J_2=10.9$ Hz, $J_3=4.9$ Hz, 1H, H-8); 3.63 (dd, $J_1=11.5$ Hz, $J_2=9.2$ Hz, 1H, H-1); 3.62 (dd, $J_1=11.4$ Hz, $J_2=10.0$ Hz, 1H, H-23); 3.47 (m, 1H, H-14); 3.44 (dd, $J_1=12.3$ Hz, $J_2=4.4$ Hz, 1H, H-10); 3.38 (s, 3H, OCH₂OCH₃); 3.28 (dd, $J_1=9.7$ Hz, $J_2=2.5$ Hz, 1H, H-7); 3.26 (s, 3H, NMe); 2.18 (ddd, $J_1=17.4$ Hz, $J_2=11.3$ Hz, $J_3=6.4$ Hz, 1H, H-3); 2.07 - 1.92 (m, 5H); 1.79 - 1.73 (m, 2H); 1.64 (ddd, $J_1=J_2=J_3=11.8$ Hz, 1H, H_a-9); 1.44 (s, 3H, CH₃); 1.41 (s, 3H, CH₃); 1.34 (ddd, $J_1=14.7$ Hz, $J_2=7.4$ Hz, $J_3=4.0$ Hz, 1H, H-3); 1.21 (s, 6H, 2CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 166.56; 143.36; 137.84; 131.65; 128.34; 120.17; 97.82; 96.09; 86.01; 85.81; 83.85; 80.86; 77.21; 75.48; 72.76; 70.84; 70.24; 65.32; 64.10; 63.48; 61.77; 55.38; 37.83; 33.96; 32.58; 32.35; 31.53; 30.58; 26.85; 21.94; 21.18; 17.36; IR (ν , cm⁻¹): 3024, 3012, 2360, 1622, 1374, 1224, 1218, 1210, 1204, 1108, 798.

Saturated amide. Palladium hydroxide (20% on activated carbon, 10 mg), the diene from the previous step (22.9 mg, 36.6 mmol), and ethyl acetate (0.40 ml) were stirred under an atmosphere of hydrogen for 20 h. The reaction mixture was filtered through a short pad of Celite and the solvent was evaporated. The residue was purified by column chromatography (silica, 0 to 5% MeOH - EtOAc) to furnish the desired product (21.0 mg, 33.3 mmol, 91%).

$[\alpha]_D^{25} = +24.3^\circ$ (c 1.0, CHCl₃); ¹H NMR (500 MHz, C₆D₆), δ (ppm): 4.79 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.62 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.05 (ddd, $J_1=11.5$ Hz, $J_2=4.7$ Hz, $J_3=1.3$ Hz, 1H, H-1); 3.95 (ddd, $J_1=J_2=J_3=2.8$ Hz, 1H, H-6); 3.88 (ddd, $J_1=11.4$ Hz, $J_2=4.6$ Hz, $J_3=1.3$ Hz, 1H, H-23); 3.83 (ddd, $J_1=11.4$ Hz, $J_2=9.9$ Hz, $J_3=4.9$ Hz, 1H, H-8); 3.69 (ddd, $J_1=11.0$ Hz, $J_2=6.7$ Hz, $J_3=4.3$ Hz, 1H, H-4); 3.62 (dd, $J_1=11.4$ Hz, $J_2=8.7$ Hz, 1H, H-1); 3.54 (dd, $J_1=11.4$ Hz, $J_2=8.7$ Hz, 1H, H-23); 3.46 (bq, $J=7.7$ Hz, H-14 or 15); 3.25 (s, 3H, NOCH₃); 3.18 (dd, $J_1=10.1$ Hz, $J_2=3.3$ Hz, 1H, H-7); 3.17 (m, 1H, H-14 or 15); 3.11 (dd, $J_1=12.1$ Hz, $J_2=4.1$ Hz, 1H, H-10); 3.08 (s, 3H, OCH₂OCH₃); 2.89 (s, 3H, NCH₃); 2.56 (m, 2H, H-21); 2.30 (ddd, $J_1=17.5$ Hz, $J_2=11.1$ Hz, $J_3=6.5$ Hz, 1H, H-3);

2.20 – 2.14 (m, 3H); 2.03 – 1.94 (m, 2H); 1.86 – 1.58 (m, 8H); 1.51 (s, 3H, CH₃); 1.47 (dd, $J_1=14.6$ Hz, $J_2=3.2$ Hz, 1H, H_e-5); 1.39 (s, 3H, CH₃); 1.18 (ddd, $J_1=14.6$ Hz, $J_2=7.0$ Hz, $J_3=4.2$ Hz, 1H, H-3); 1.15 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 173.89; 97.80; 95.99; 87.56; 85.97; 84.80; 82.12; 77.42; 77.23; 74.49; 72.39; 70.67; 70.18; 65.31; 64.12; 63.42; 61.21; 55.34; 38.00; 37.57; 33.86; 32.91; 32.37; 31.49; 29.51; 28.95; 26.89; 25.69; 24.79; 23.30; 21.12; 16.21; IR (ν , cm⁻¹): 3012, 2940, 1650, 1462, 1384, 1230, 1224, 1208, 1202, 1148, 1094, 1064, 910; Calcd for C₃₂H₅₅NO₁₁+1.0H₂O: C, 59.32; H 8.87. Found C, 59.08; H, 8.60.

Trimethylsilyl ether. Chlorotrimethylsilane (46 μ l, 0.367 mmol, 3 eq) was added to a solution of the tertiary alcohol (27) (77 mg, 0.122 mmol), triethylamine (68 μ l, 0.488 mmol, 4 eq), and DMAP (1.5 mg, 0.012 mmol, 0.1 eq) in dry dichloromethane (1.22 ml) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred for 12 h, then diluted with dichloromethane (15 ml) and washed with water (3 ml) and brine (3 ml). Drying over anhydrous sodium sulfate, filtration, and evaporation of the solvent gave the crude product, which was subjected to flash column chromatography (silica, 50% ethyl acetate – hexanes) to give pure product (78 mg, 0.111 mmol, 91%).

$[\alpha]_D^{25} = +19.3^\circ$ (c 1.5, CHCl₃); ¹H NMR (400 MHz, C₆D₆), δ (ppm): 4.80 (d, $J=6.5$ Hz, 1H, OCH₂OCH₃); 4.63 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.04 (ddd, $J_1=11.5$ Hz, $J_2=4.5$ Hz, $J_3=1.3$ Hz, 1H, H-1); 3.95 (ddd, $J_1=J_2=J_3=2.9$ Hz, 1H, H-6); 3.87 (ddd, $J_1=11.5$ Hz, $J_2=4.7$ Hz, $J_3=1.3$ Hz, 1H, H-1); 3.85 (ddd, $J_1=11.4$ Hz, $J_2=9.9$ Hz, $J_3=4.8$ Hz, 1H, H-8); 3.69 (ddd, $J_1=11.0$ Hz, $J_2=6.7$ Hz, $J_3=4.5$ Hz, 1H, H-4); 3.62 (dd, $J_1=11.5$ Hz, $J_2=9.8$ Hz, 1H, H-1); 3.54 (dd, $J_1=11.4$ Hz, $J_2=8.7$ Hz, 1H, H-23); 3.55 – 3.49 (m, 1H, H-14 or 15); 3.45 (dd, $J_1=10.6$ Hz, $J_2=2.1$ Hz, 1H, H-19); 3.26 (s, 3H, NOME); 3.21 (ddd, $J_1=J_2=8.5$ Hz, $J_3=4.5$ Hz, 1H, H-15 or 14); 3.18 (dd, $J_1=9.8$ Hz, $J_2=2.8$ Hz, 1H, H-7); 3.14 (dd, $J_1=12.2$ Hz, $J_2=4.1$ Hz, 1H, H-10); 3.11 (s, 3H, OCH₂OCH₃); 2.91 (s, 3H, NMe); 2.66 (ddd, $J_1=14.9$ Hz, $J_2=9.1$ Hz, $J_3=5.0$ Hz, 1H, H-21); 2.53 (ddd, $J_1=15.1$ Hz, $J_2=J_3=7.9$ Hz, 1H, H-21); 2.31 (ddd, $J_1=17.8$ Hz, $J_2=10.9$ Hz, $J_3=6.5$ Hz, 1H, H-3); 2.25 – 2.17 (m, 3H, H_e-9 and

H-20); 2.08 – 1.96 (m, 2H, H-13 or 16 and H-2); 1.93 – 1.74 (m, 6H, (H_a-9)); 1.68 – 1.59 (m, 2H, (H-5)); 1.50 (s, 3H, CH₃); 1.47 (dd, J₁=14.7 Hz, J₂=3.1 Hz, 1H, H_e-5); 1.39 (s, 3H, CH₃); 1.20 (ddd, J₁=18.1 Hz, J₂=7.2 Hz, J₃=4.4 Hz, 1H, H-3); 1.17 (s, 3H, CH₃); 1.16 (s, 3H, CH₃); 0.14 (s, 9H, TMS); ¹³C NMR (100 MHz, CDCl₃), δ(ppm): 174.82; 128.30; 98.25; 96.81; 88.77; 86.57; 85.33; 82.89; 78.41; 78.11; 73.52; 71.31; 70.60; 65.81; 64.74; 64.14; 61.02; 55.54; 38.45; 38.37; 34.72; 34.07; 33.43; 32.62; 32.45; 30.27; 29.78; 27.50; 26.61; 24.41; 21.98; 16.67; 3.03; IR (ν, cm⁻¹): 3014, 2950, 1654, 1522, 1476, 1422, 1208, 1104, 1062, 1030; Calcd for C₃₅H₆₃NO₁₁Si: C, 59.89; H 9.05. Found C, 60.00; H, 9.13.

Aldehyde 23. Di-iso-butylaluminum hydride (1M in toluene, 0.16 ml, 0.16 mmol, 1.5 eq) was added to a solution of the Weinreb amide (77 mg, 0.109 mmol) in dry THF (2.0 ml) at -78°C under a nitrogen atmosphere. The reaction mixture was stirred for 45 min, and then transferred via cannula to a vigorously stirring mixture of ethyl acetate (12 ml) and 23% aqueous Rochelle's salt (12 ml). After stirring for 30 min, the layers were separated, the aqueous solution was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to give aldehyde 23 (67 mg, 0.104 mmol, 96%).

[α]_D²⁵ = +27.5° (c 1.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃), δ(ppm): 9.74 (t, J=2.0 Hz, 1H, H-22); 4.69 (d, J=6.6 Hz, 1H, OCH₂OCH₃); 4.63 (d, J=6.6 Hz, 1H, OCH₂OCH₃); 3.99 – 3.95 (m, 2H, H-1 and H-4); 3.91 – 3.83 (m, 2H, H-8 and H-23); 3.35 (s, 3H, OCH₂OCH₃); 3.34 – 3.28 (m, 2H, H-14 and H-19); 3.24 – 3.15 (m, 3H, H-4, H-10, and H-15); 2.54 – 2.38 (m, 2H, H-21); 2.17 (ddd, J₁=17.2 Hz, J₂=10.9 Hz, J₃=6.2 Hz, 1H, H-3); 2.10 – 2.05 (m, 1H, H-2); 2.00 – 1.62 (m, H); 1.55 (ddd, J₁=J₂=J₃=11.9 Hz, 1H, H_a-9); 1.42 (s, 3H, CH₃); 1.39 (s, 3H, CH₃); 1.30 (ddd, J₁=14.7 Hz, J₂=7.3 Hz, J₃=4.3 Hz, 1H, H_a-5); 1.17 (s, 3H, CH₃); 1.13 (s, 3H, CH₃); 0.08 (s, 9H, TMS); ¹³C NMR (100 MHz, CDCl₃), δ(ppm): 203.01; 97.78; 96.01; 88.20; 85.76; 84.59; 82.28; 72.34; 70.67; 70.16; 65.31; 64.16; 63.42; 55.34; 41.81; 37.44; 37.15; 33.84; 32.91; 32.35; 31.51; 29.69; 29.26;

28.78; 26.99; 23.75; 23.32; 21.03; 16.04; 15.12; 14.19; 2.50; Calcd for $C_{33}H_{58}O_{10}Si$: C, 61.65; H 9.09. Found C, 61.32; H, 8.80.

Conjugated diene 24. A solution of 23 (0.202 g, 0.314 mmol) and ethylene (E)- γ -trimethylsilylallyl boronate (87 mg, 0.473 mmol, 1.5 eq) in dry dichloromethane (3.2 ml) was stirred at room temperature under a nitrogen atmosphere for 1 h, diluted with dichloromethane, washed with water and saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude mixture of products was dissolved in dry THF (3.4 ml) and treated with a tetrahydrofuran solution of potassium tert-butoxide (1.0M, 1.6 ml, 1.60 mmol, 5 eq) at room temperature under a nitrogen atmosphere for 1 h. The reaction mixture was extracted with ethyl acetate (25 ml), washed with saturated aqueous ammonium chloride (5 ml), water (10 ml), and brine (5 ml). The organic solution was dried over anhydrous sodium sulfate, filtered, and concentrated. The resultant oil was purified by flash column chromatography (silica, 50% ethyl acetate – hexanes) to give pure 24 (0.174 g, 0.261 mmol, 83%) as a 15:1 mixture of Z and E isomers.

$[\alpha]_D^{25} = +22.5^\circ$ (c 1.5, $CHCl_3$); 1H NMR (400 MHz, C_6D_6), δ (ppm): 6.76 (dtd, $J_{d1}=16.7$ Hz, $J_t=10.5$ Hz, $J_{d2}=0.8$ Hz, 1H, H-24); 6.06 (t, $J=10.6$ Hz, 1H, H-23); 5.49 (dt, $J_d=10.6$ Hz, $J_t=7.8$ Hz, 1H, H-22); 5.15 (dd, $J_1=16.9$ Hz, $J_2=1.8$ Hz, 1H, H_c-25); 5.05 (bd, $J=10.3$ Hz, 1H, H_t-25); 4.81 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.64 (d, $J=6.4$ Hz, 1H, OCH₂OCH₃); 4.04 (ddd, $J_1=11.6$ Hz, $J_2=4.5$ Hz, $J_3=1.3$ Hz, 1H, H-1); 3.97 (ddd, $J_1=11.6$ Hz, $J_2=4.6$ Hz, $J_3=1.2$ Hz, 1H, H-26); 3.85 (ddd, $J_1=14.8$ Hz, $J_2=10.0$ Hz, $J_3=4.7$ Hz, 1H, H-8); 3.70 (ddd, $J_1=11.1$ Hz, $J_2=6.5$ Hz, $J_3=4.4$ Hz, 1H, H-4); 3.62 (dd, $J_1=11.6$ Hz, $J_2=8.9$ Hz, 1H, H-1); 3.54 (dd, $J_1=11.4$ Hz, $J_2=8.7$ Hz, 1H, H-26); 3.44 (dt, $J_d=8.3$ Hz, $J_t=7.7$ Hz, 1H, H-14 or 15); 3.35 (dd, $J_1=10.4$ Hz, $J_2=1.0$ Hz, 1H, H-19); 3.26 (s, 3H, OCH₂OCH₃); 3.21 – 3.16 (m, 1H, H-15 or 14); 3.19 (dd, $J_1=10.0$ Hz, $J_2=2.8$ Hz, 1H, H-7); 3.13 (dd, $J_1=12.1$ Hz, $J_2=4.2$ Hz, 1H, H-10); 2.36 (q, $J=7.6$ Hz, 2H, H-21); 2.31 (ddd, $J_1=17.4$ Hz, $J_2=10.9$ Hz, $J_3=6.6$ Hz, 1H, H-3); 2.19 (dt, $J_d=10.9$ Hz, $J_t=5.0$ Hz, 1H, H_e-9); 2.08 – 1.94 (m, 2H); 1.90 – 1.58 (m, 10H); 1.50 (s, 3H, CH₃); 1.48

(dd, $J_1=14.8$ Hz, $J_2=2.8$ Hz, 1H, H-5); 1.39 (s, 3H, CH₃); 1.19 (ddd, $J_1=16.5$ Hz, $J_2=7.3$ Hz, $J_3=4.3$ Hz, 1H, H-3); 1.16 (s, 3H, CH₃); 1.12 (s, 3H, CH₃); 0.12 (s, 9H, TMS); ¹³C NMR (100 MHz, C₆D₆), δ (ppm): 133.42; 133.06; 130.51; 128.30; 117.57; 98.26; 96.83; 88.30; 86.64; 85.45; 82.89; 78.31; 78.11; 73.52; 71.31; 70.62; 65.81; 64.75; 64.16; 55.56; 38.41; 38.30; 34.73; 34.09; 33.46; 32.47; 30.97; 30.39; 29.71; 27.50; 25.62; 24.49; 22.00; 16.76; 3.01; IR (ν , cm⁻¹): 3024, 3012, 1374, 1226, 1064, 796.

Triol 25. A solution of 24 (0.137 g, 0.205 mmol) in THF (20 ml) containing 1.0M aqueous hydrogen chloride (1.0 ml) was stirred at room temperature for 15 min. The mixture was extracted with ethyl acetate, washed with saturated aqueous sodium bicarbonate (5 ml) and brine (5 ml). The combined aqueous layers were extracted with ethyl acetate (3x10 ml), and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated to give triol 25 (0.114 g, 0.205 mmol, 100%), which required no further purification.

$[\alpha]_D^{25} = +21.3^\circ$ (c 1.0, CHCl₃); ¹H NMR (400 MHz, CHCl₃), δ (ppm): 6.65 (dddd, $J_1=16.9$ Hz, $J_2=J_3=10.6$ Hz, $J_4=1.0$ Hz, 1H, H-24); 6.04 (t, $J=11.0$ Hz, 1H, H-23); 5.45 (dt, $J_d=10.4$ Hz, $J_t=7.9$ Hz, 1H, H-22); 5.20 (dd, $J_1=16.8$ Hz, $J_2=1.2$ Hz, 1H, H_c-25); 5.10 (bd, $J=10.3$ Hz, 1H, H_t-25); 4.71 (d, $J=6.5$ Hz, 1H, OCH₂OCH₃); 4.65 (d, $J=6.5$ Hz, 1H, OCH₂OCH₃); 4.03 – 3.98 (m, 1H, H-4); 3.99 (ddd, $J_1=J_2=J_3=2.9$ Hz, 1H, H-6); 3.79 – 3.71 (m, 4H, H-1, H-14 or 15, H-19, H-26); 3.69 (ddd, $J_1=J_2=10.8$ Hz, $J_3=6.1$ Hz, 1H, H-8); 3.36 (s, 3H, OCH₂OCH₃); 3.34 – 3.20 (m, 5H, H-1, H-26, H-15 or 14, H-7, and H-10); 2.35 – 2.26 (m, 3H, H-3 and H-21); 2.20 – 2.13 (m, 1H); 2.05 – 1.70 (m, 10H); 1.58 (ddd, $J_1=J_2=J_3=11.6$ Hz, 1H, H_a-9); 1.46 (ddd, $J_1=15.3$ Hz, $J_2=6.9$ Hz, $J_3=3.9$ Hz, 1H, H-3); 1.18 (s, 3H, CH₃); 1.11 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃), δ (ppm): 132.44; 132.09; 129.74; 117.26; 96.05; 86.98; 85.97; 84.98; 81.93; 77.23; 74.53; 72.34; 70.78; 70.61; 66.22; 65.27; 63.56; 55.38; 40.95; 38.25; 37.59; 34.23; 32.91; 31.61; 30.23; 29.59; 28.87; 24.72; 23.47; 16.35; IR (ν , cm⁻¹): 684, 3024, 2400, 1524, 1476, 1422, 1204, 1094, 1032, 928; Calcd for C₃₀H₅₀O₉+0.5H₂O: C, 63.92; H 9.11. Found C, 63.85; H, 8.87.

Hemibrevetoxin B. A mixture of triol 25 (21 mg, 37.9 μmol), di-n-butyltin oxide (25 mg, 0.100 mmol, 2.6 eq), and dry methanol (1.8 ml) was stirred at room temperature under a nitrogen atmosphere for 6 h. Methanol was evaporated, and the residue was treated with dry dichloromethane (1.0 ml) and recrystallized p-toluenesulfonyl chloride (18 mg, 94.5 mmol, 2.5 eq) at room temperature under a nitrogen atmosphere for 1.5 h, at which point TLC showed consumption of the starting material and formation of two new products. After dilution with dichloromethane (15 ml), the mixture was washed with water (5 ml) and brine (5 ml), dried with anhydrous sodium sulfate, filtered, and evaporated. Flash column chromatography (silica, 75 to 100% ethyl acetate – hexanes) afforded an equimolar mixture of the diastereomeric tosylates (26 mg, 36.6 μmol , 97%).

Dry dimethylsulfoxide (12 μl , 13.2 mg, 0.169 mmol, 4 eq) was added to a solution of oxalyl chloride (2M in CH_2Cl_2 , 40 μl , 80 μmol , 2 eq) in dry dichloromethane (0.30 ml) under a nitrogen atmosphere at -78°C . After 20 min a solution of the tosylates (26 mg, 36.6 mmol) in dry dichloromethane (0.40 ml) was added, followed, after stirring for 20 min, by triethylamine (55 μl , 39.9 mg, 0.395 mmol, 11 eq). The reaction mixture was brought to 0°C and stirred for 30 min. Dichloromethane (15 ml) was added, and the resultant solution was washed with a mixture of 1M aqueous hydrogen chloride and water (1:2, 3 ml), water (3 ml), saturated aqueous sodium bicarbonate (3 ml), and brine (3 ml). The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. Flash chromatography (silica, 50% ethyl acetate – hexanes) of the residue afforded 17 mg (31.8 μmol , 84%) of the aldehyde (28).

$[\alpha]_{\text{D}}^{25} = +45.4$ (c 0.5, CHCl_3); ^1H NMR (500 MHz, CD_2Cl_2), δ (ppm): 9.51 (s, 1H, H-1); 6.68 (ddd, $J_1=17.0$ Hz, $J_2=J_3=10.8$ Hz, 1H, H-24); 6.35 (bs, 1H, H_E-28); 6.08 (bs, 1H, H_Z-28); 6.04 (t, $J=10.8$ Hz, 1H, H-23); 5.47 (ddd, $J_1=10.9$ Hz, $J_2=J_3=7.7$ Hz, 1H, H-22); 5.20 (dd, $J_1=17.0$ Hz, $J_2=1.7$ Hz, 1H, H_Z-25); 5.10 (bd, $J=10.1$ Hz, 1H, H_E-25); 4.70 (d, $J=6.5$ Hz, 1H, OCH_2OCH_3); 4.66 (d, $J=6.5$ Hz, 1H, OCH_2OCH_3); 3.96 (ddd, $J_1=J_2=J_3=3.0$ Hz, 1H, H-6); 3.92 (ddd, $J_1=10.5$ Hz, $J_2=6.7$ Hz, $J_3=4.9$ Hz, 1H, H-4); 3.77 (ddd, $J_1=J_2=10.7$ Hz, $J_3=4.9$ Hz, 1H, H-8); 3.34 (s, 3H, OCH_2OCH_3); 3.34 – 3.31 (m, 2H, H-14 and H-15); 3.26 (dd, $J_1=12.1$ Hz, $J_2=4.2$ Hz, 1H, H-10); 3.22 (dd, $J_1=10.0$ Hz, $J_2=2.7$ Hz, 1H, H-7); 3.19 (dd, $J_1=10.9$ Hz, $J_2=1.4$ Hz, 1H, H-19); 3.15 (dd, $J_1=14.4$ Hz, $J_2=10.5$ Hz, 1H, H-3); 2.42 (dd, $J_1=14.4$ Hz, $J_2=4.8$ Hz, 1H, H-3); 2.31 (q, $J=7.3$ Hz, 2H, H-21); 2.19

— 2.13 (m, 1H, H-13); 1.95 (ddd, $J_1=14.6$ Hz, $J_2=6.9$ Hz, $J_3=3.1$ Hz, 1H, H_e-5); 1.90 — 1.68 (m, 4 H); 1.58 (dddd, $J_1=13.5$ Hz, $J_2=J_3=8.1$ Hz, $J_2=1.7$ Hz, 1H, H-20); 1.46 (ddd, $J_1=J_2=J_3=11.8$ Hz, 1H, H_a-9); 1.43 — 1.36 (m, 1H, H-20); 1.16 (s, 3H, Me-27); 1.07 (s, 3H, Me-26); ^{13}C NMR (100 MHz, CD_2Cl_2), $\delta(\text{ppm})$: 195.06; 148.60; 136.51; 133.26; 132.78; 130.07; 117.47; 96.52; 87.32; 86.48; 85.40; 82.53; 77.97; 74.83; 72.92; 71.20; 71.15; 63.89; 55.71; 38.73; 38.17; 33.96; 33.50; 31.73; 30.82; 30.13; 29.42; 25.29; 23.84; 16.64; IR (ν , cm^{-1}): 3684, 3024, 2978, 2434, 2400, 1522, 1476, 1422, 1220, 1036, 928.

The aldehyde (16 mg, 29.9 μmol) was refluxed in a solution of lithium tetrafluoroborate in aqueous acetonitrile (1.5 ml) [prepared by dissolving LiBF_4 (64 mg, 0.68 mmol) and water (80 μl) in acetonitrile (2.0 ml)] for 60 min. The reaction mixture was cooled to room temperature, diluted with dichloromethane (15 ml), washed with water (3 ml), saturated aqueous sodium bicarbonate (3 ml), and brine (3 ml). The organic solution was dried over anhydrous sodium sulfate, filtered, and concentrated. Flash chromatography (silica, 50% ethyl acetate — hexanes) furnished hemibrevetoxin B (12 mg, 24.5 μmol , 82%).

$[\alpha]_{\text{D}}^{25} = +114.2$ (c 0.3, CHCl_3); ^1H NMR (400 MHz, CD_2Cl_2), $\delta(\text{ppm})$: 9.51 (s, 1H, H-1); 6.68 (dddd, $J_1=17.0$ Hz, $J_2=11.0$ Hz, $J_3=10.3$ Hz, $J_4=0.9$ Hz, 1H, H-24); 6.37 (bs, 1H, H_E-28); 6.09 (bs, 1H, H_Z-28); 6.04 (t, $J=11.4$ Hz, 1H, H-23); 5.47 (ddd, $J_1=10.9$ Hz, $J_2=J_3=7.7$ Hz, 1H, H-22); 5.20 (dd, $J_1=17.0$ Hz, $J_2=1.9$ Hz, 1H, H_Z-25); 5.10 (bd, $J=9.5$ Hz, 1H, H_E-25); 4.00 (ddd, $J_1=J_2=J_3=3.1$ Hz, 1H, H-6); 3.91 (ddd, $J_1=10.7$ Hz, $J_2=J_3=5.7$ Hz, 1H, H-4); 3.75 (ddd, $J_1=11.6$ Hz, $J_2=10.0$ Hz, $J_3=4.6$ Hz, 1H, H-8); 3.34 — 3.31 (m, 2H, H-14 and H-15); 3.26 (dd, $J_1=12.0$ Hz, $J_2=4.3$ Hz, 1H, H-10); 3.21 (dd, $J_1=10.9$ Hz, $J_2=1.4$ Hz, 1H, H-19); 3.20 (dd, $J_1=10.4$ Hz, $J_2=2.6$ Hz, 1H, H-7); 3.15 (dd, $J_1=14.5$ Hz, $J_2=10.1$ Hz, 1H, H-3); 2.46 (dd, $J_1=14.5$ Hz, $J_2=5.4$ Hz, 1H, H-3); 2.32 (q, $J=7.3$ Hz, 2H, H-21); 2.28 (bs, 1H, OH-6); 2.21 — 2.14 (m, 1H, H-13); 1.94 (ddd, $J_1=14.9$ Hz, $J_2=7.2$ Hz, $J_3=3.7$ Hz, 1H, H_e-5); 1.90 — 1.68 (m, 7 H); 1.58 (dddd, $J_1=13.5$ Hz, $J_2=J_3=8.1$ Hz, $J_2=1.7$ Hz, 1H, H-20); 1.53 (m, H-20); 1.50 (ddd, $J_1=J_2=J_3=11.8$ Hz, 1H, H_a-9); 1.45 — 1.37 (m, 1H, H-20); 1.18 (s, 3H, Me-27); 1.07 (s, 3H, Me-26); ^{13}C NMR (100 MHz, CD_2Cl_2), $\delta(\text{ppm})$: 195.14; 148.54; 136.65; 133.26; 132.78; 130.08; 117.49; 87.29; 86.43; 85.59; 82.71; 78.52; 74.84; 72.61; 71.19; 66.81; 63.09; 38.75; 38.08; 34.05; 33.34; 32.06; 30.83; 30.15; 29.41; 25.29; 23.91; 17.15; IR (ν , cm^{-1}): 3624–3200, 2930, 1670; Calcd for $\text{C}_{28}\text{H}_{42}\text{O}_7$: C, 68.54; H 8.63. Found C, 68.20; H, 8.89.

Tables of NOE data for selected intermediates.

Table 1. NOE Data for 7.

Proton	δ (ppm)	NOE (%)
H-3	3.60	H-4 (9.2); H _a -5 (1.3); Me (4.9)
H _a -5	3.48	H-4 (10.1); H _b -5 (31); H-3 (2.6)
H-8	2.52	H-9 (3.3); H-10 (1.7); H-7 (8.2)
Me	1.26	H-1 (1.8); H-3 (3.5); H-7 (1.1)

Table 2. NOE Data for epi-7.

Proton	δ (ppm)	NOE (%)
H-1	4.79	H _a -5 (4.3)
H-4	3.89	H _b -5 (6.2); H-3 (8.3); Me (7.7)
H-7	3.76	H-3 (4.8)
H _b -5	3.70	H _a -5 (2.8); H-4 (7.7)

Table 3. NOE data for ester 8.

Proton	δ (ppm)	NOE (%)
H-3	2.66	H-3 (26); H-8 (8.6)
H-3	2.55	H-3 (29); H-4 (4.1); H-5 (4.1)
H-4	4.44	H-3 (1.9); H-5 (4.1)
H-8	3.94	H-3 (3.9%); H-9 (2.0); H-9 (2.5)
H-7	5.17	H-6 (3.9); H-9 (3.8); H-9 (2.1)
H-9	4.11	H-9 (17); H-7 (2.3)

Table 4. NOE data for epoxide 9.

Proton	δ (ppm)	NOE (%)
H-4	4.21	H-5 (6.5); H-3 (2.0)
H-7	3.52	H-11 (12.9); H-4 (1.5); H-9 _a (1.2); H-6 (4.6)
H-6	3.16	H-5 (8.7); H-7 (3.7)
H-8	3.95	H-3 (3.3)
H-11	5.33	H-7 (3.4); H-9 _a (1.7)

Table 5. NOE data for diol 10.

Proton	δ (ppm)	NOE (%)
H-3	3.02	H-3 (21); H-8 (8.0)
H-3	2.52	H-3 (19.9); H-8 (3.5)
H-7	3.61	H-5 _a (3.4); H-9 _a (1.5); H-6 (4.0)
H-8	4.16	H-3 (5.4); H-3 (2.3)
H-11	5.63	H-7 (5.5); H-9 _a (9.9)

Table 6. NOE data for diol 11 .

Proton	δ (ppm)	NOE (%)
MeOCH ₂ O-	4.71	H-6 (4.5)
H _e -1	3.97	H _a -1 (13.8); H-3 (2.6)
H-6	3.92	MeOCH ₂ O- (3.5); H-9 (8.8); H _e -5 (4.4)
H-4	3.84	H-9 (4.1); H _e -5 (3.0); H-3 (2.5); H-3 (1.9)
H-9	3.64	H-6 (10.0); H-4 (4.1); OH (0.5);
H-3	1.43	H-4 (2.3); H-1 (2.0); H-3 (19.1)

Table 7. NOE data for 13 .

Proton	δ (ppm)	NOE (%)
H-9	2.37	H-10 (3.4); H-6 (8.2); H-8 (1.8); H-4 (6.0); H-9 (18.8); H-12 (3.3)
H-9	2.19	H-10 (3.9); H-6 (2.7); H-8 (3.2); H-4 (2.8); H-9 (14.6); H-12 (0.2)
H-10	5.70	H-6 (2.2); H-8 (3.0); H-4 (1.7); H-9 (0.9); H-9 (1.4); SiMe ₂ (5.8)
Me-12	1.57	H-9 (4.9); H-9 (6.2); SiMe ₂ (4.3)
H-4	3.58	H-6 (6.7); H-9 (3.9); H-9 (4.5); H _e -5 (3.1)
H-6	3.55	H-8 (4.0); H-6 (3.3)
H _a -5	1.71	H _e -5 (19.1); H-3 (6.4); H-3 (1.9)

Table 8. NOE Data for 15.

Proton	δ (ppm)	NOE (%)
H-10	5.27	H-9 (3.0); H-12 (3.3)
H-16	4.79	PhCH ₂ 2 (6.4); PhCH ₂ 1 (8.4); H-20 (3.8)
H-14	4.70	H-12 (5.1); H-13 (4.4)
H-19	4.03	H-18 (4.7); H-20 (7.1); H-20 (4.8);
H-8	3.97	H-10 (4.4); H-7 (4.5); H-9 and 9 (3.7); H-3 (3.1)
H _e -21	3.85	H _a -21 (22.1); H-2 (3.2); Me (3.1)
H-6	3.80	MeOCH ₂ O- (2.4); H-4 (3.7); H-9 (4.1)
H-20	3.57	H-19 (4.8); H-20 (21.9)
H _a -21	3.48	H _e -21 (18.4); Me (4.2)
H-4	3.36	H-6 (3.9); H-9 and 9 (5.4); H _e -5 (2.7); H-3 (2.0)
H _a -5	1.92	H _e -5 (12.8); H-3 (1.8)
Me-22	1.54	H-9 (1.0); H-9 (1.4)
Me	1.36	H _a -1 and H _a -20 (2.6)

Table 9. NOE Data for 16.

Proton	δ (ppm)	NOE (%)
H-16	4.79	Bn2 (5.4); Bn1 (5.8)
CH ₃ OCH ₂ O-	4.69	H-6 (1.7); H-7 (0.7); CH ₃ OCH ₂ O- (1.9)
OH-19	4.35	H-20 (0.7)
H-10	4.32	H-8 (1.4); H-12 (1.1); H-9 (2.1); H-12 (0.6)
H-14	4.18	H-19 (6.4); H-13 (4.0); H-12 (0.9)
H-8	4.05	H-7 (2.3); H-9 (0.8); H-9 (1.4); H-3 (1.2)
H-19	4.02	H-14 (3.9)
H _e -1	3.93	H _a -1 (17.2); H-2 (3.5)
H _e -21	3.83	H _a -21 (17.4); H-2 (4.6)
H-6	3.79	CH ₃ OCH ₂ O- (2.7); H-7 (2.2)
H-4	3.65	H-6 (2.2); H-9 (2.7); H-5 (2.4); H-3 (1.4)
H _a -21	3.55	H _e -21 (15.1); Me-1.36 (2.6)
H-12	2.54	H-10 (2.6); H-13 (2.6); H-12 (14.1)
H-13		H-14 (3.5); Me-1.56 (1.3)
H-5	1.74	H-6 (3.5); H-4 (6.1); H-5 (3.9)
Me	1.56	H-13 (1.9); H-12 (2.0); H-9 (0.7); H-10 (0.3); H-14 (0.3)
H-3	1.68	H-8 (7.3); H-4 (4.3); H-1 (5.5); H-3 (12.9)
Me	1.48	H-16 (1.9); Bn2 (1.6); Bn2 (1.6); H-18 (2.1);
Me	1.34	H _e -1 (0.7); H _e -21 (0.7)

Table 10. NOE Data for epi-16.

Proton	δ (ppm)	NOE (%)
H-7	3.65	H-10 (2.8); H-8 (2.9); H-9 (0.9)
H-14	4.11	H-19 (1.6); H-13 (3.0)
H-9	2.34	H-10 (2.0); H-8 (1.2); H-6 (4.6); H-7 (4.0); H-9 (16.2); Me-1.60 (2.0)
Me	1.60	H-10 (0.8); H-9 (0.7); H-12 (0.7); H-13 (1.1)
Me	1.49	Bn2 (2.0); Bn1 (1.8); H-19 (2.4)
Me	1.41&1.42	H-1 (2.4); H-21 (3.2); H-2 (1.4)

Table 11. NOE Data for 16 .

Proton	δ (ppm)	NOE (%)
H-16	5.46	Bn1 (2.0); Bn1 (6.6); H-20 (4.0)
H-14	4.80	H-18 (7.6); H _a -13 (0.9); H _b -13 (1.1); H-12 (1.0)
CH ₃ OCH ₂ O-	4.59	H-6 (2.3); H-7 (0.7); CH ₃ OCH ₂ O- (2.8)
H-10	4.53	H-8 (3.3); H-9 (3.0); H-12 (3.1)
H-18	4.36	H-16 (0.5); Bn1 (1.2); Bn2 (1.4); H-14 (6.9); H-19 (4.5); Me-23 (3.4)
H-8	4.31	H-10 (0.9); H-7 (3.9); H-9 (1.6)
H-19	4.20	H-18 (4.0); Me-23 (6.4)
H-20	4.06	H-16 (7.4); H-20 (17.0)
H-20	3.86	H-19 (3.8); H-20 (14.8)
H-6	3.79	MOM (3.8); H-7 (5.3); H-4 (1.9); H-9 (2.5)
H-7	3.65	H-8 (3.7); H-6 (2.8); H-9 (1.8)
H-4	3.54	H-6 (2.1); H-9 (2.4); H-2 (2.5); H _e -5 (3.2);
H-9	2.47	H-10 (1.9); H-6 (4.6); H-7 (1.2); H-4 (4.3); H-9 (24.1)
H _a -12	2.40	H-10 (2.1); H _b -13 (1.8); H _b -12 (17.9)
H-9	1.76	H-10 (1.5); H-8 (6.0); H-7 (4.4); H-9 (12.7); Me-22 (3.3)
H _b -12	1.64	H-14 (1.8); H _a -12 (18.9); Me-22 (2.0)
Me-23	1.45	H-16 (0.5); Bn1 (0.9); Bn2 (1.5); H-18 (1.8); H-19 (2.9)
Me-22	1.25	H-14 (0.5); H-10 (0.5); H-9 (0.7); H-9 (1.1); H _b -13 (0.7); H _e -12 (1.1)

Table 12. NOE Data for 17.

Proton	δ (ppm)	NOE (%)
H-16	5.35	Bn1 (2.6); Bn2 (1.4); Bn1 (5.8); H-20 (4.4)
H-14	4.61	H-18 (8.0); H-13 (4.8)
H-19	4.20	H-18 (9.8); Me-23 (6.6)
H-20	3.86	H-19 (5.8); H-20 (16.4); TIPS (4.6)
H _a -1	3.59	H _e -1 (18.4); H-3 (3.7); Me (2.5)
H _a -1	3.48	H _e -21 (21.4)
H-10	2.82	H-8 (3.5); H-12 (3.0); H-12 (3.1)
Me-22	1.49	H-8 (0.7); H-9 (3.4); H-12 (2.8)
Me-23	1.41	Bn1 (0.9); Bn2 (0.6); H-19 (1.5); H-18 (0.8)

Table 13. NOE Data for 17 .

Proton	δ (ppm)	NOE (%)
H-15	5.66	H-16 (7.5)
H-16	5.50	H-15 (6.2); Me-17 (5.4)
Me-17	1.58	H-16 (2.5); H-14 (1.6)

Table 14. NOE Data for 18.

Proton	δ (ppm)	NOE (%)
H-17	5.12	Bn1 (0.8); Bn2 (0.6); Bn1 (5.3); H-21 (4.2); Me-25 (0.7)
H-15	4.40	H-1 (1.2); H-14 (0.5); H-10 (9.0); H-16 (6.2); Me-24 (2.0)
H-14	4.23	H-15 (2.2); H-19 (9.0); H-16 (6.1); H _a -13 (2.8); H _b -13 (2.0); TIPS (3.0)
H-20	4.17	H-19 (8.7); Me-25 (7.6)
H-21	3.95	H-17 (4.4); Bn2 (5.7); H-21 (7.3)
H-19	3.87	H-20 (4.0); H-14 (5.8); Me-25 (2.6)
H-10	3.84	H-15 (7.9); H _a -12 (3.0); H _e -9 (2.8)
H-8	3.83	H-3 (5.0); H _e -6 (2.8)
H-4	3.71	H-2 (2.9); H _a -5 (3.2)
H _a -22	3.51	H _e -22 (22.3); Me _e (4.3)
H-16	3.37	H-15 (4.0); H-14 (4.2); Me-24 (6.1)
H-7	3.29	H-6 (5.8); Me-23 (5.5); H _a -9 (1.9); H _a -5 (2.1)
H _a -12	2.43	H-10 (4.8); H _b -12 (16.6)
H _a -13	2.34	H-14 (4.8); H _b -13 (12.0); H _b -12 (3.9)
H-3	2.25	H-8 (4.3); H-3 (17.5)
H _b -13	2.13	H-14 (2.9); H _a -13 (13.1); Me-23 (5.1)
H _a -9	1.77	H-7 (2.3); H _a -12 (8.7); H _e -9 (9.7); Me-23 (3.6)
H _a -5	1.64	H-6 (5.9); H-4 (7.8); H-7 (3.7); Me-23 (11.5)
Me-25	1.38	H-17 (0.3); Bn2 (0.9); Bn2 (1.5); H-20 (2.1); H-19 (1.1);
Me-23	1.37	H-7 (1.7); H _b -13 (1.0); H _a -9 (1.7)

22-1

Table 15. NOE Data for the unsturated amide 22-1.

Proton	δ (ppm)	NOE (%)
H-20	7.07	H-19 (3.3); Me-25 (1.6)
H-21	6.68	H-19 (2.0); NOME (3.5)
H-17	5.70	H-16 (5.5);
H-16	5.57	H-17 (8.3); H-15 (2.9)
H-19	4.16	H-20 (8.9); H-21 (6.3); H-14 (15.5)
H-15	4.08	H-16 (3.9); H-10 (10.5); H-13 (1.5); Me-25 (1.4)
H-6	4.00	MOM (2.0); h-7 (2.9); H-5 (3.6)
H-14	3.47	H-19 (10.9); Me-24 (1.2); H-13 (0.9)
H-10	3.44	H-15 (15.1); H-8 (2.0); H-12 (10.3)
H-7	3.28	H-6 (3.3); Me-24 (3.5)
H-3	2.18	H-8 (11.4); H-3 (14.1)
H _a -9	1.64	H-7 (5.3); Me-24 (6.0); H _e -9 (7.5)
H-3	1.34	H-4 (6.9); H-3 (14.8)
Me-24 and Me-25	1.21	H-20 (1.1); H-21 (0.4); H-17 (0.7); H-15 (0.5);
		H-7 (1.6); H-12 (0.7); H _a -9 (1.0)

22-2

Table 16. NOE Data for amide 22-2.

Proton	δ (ppm)	NOE (%)
H _e -1	4.05	H _a -1 (22.1); H-2 (4.6); Me (1.3)
H-6	3.95	MeOCH ₂ O (3.1); MeOCH ₂ O (0.4); H-7 (4.1); H-5 (1.9)
H _a -23	3.88	H _e -23 (18.4); H-2 (3.6); Me (0.4)
H-8	3.83	H-10 (2.1); H-3 (3.4); H _e -9 (2.3)
H _e -1	3.62	H _e -1 (20.3); Me (3.5)
H _e -23	3.54	H _e -23 (15.4); Me (2.6)
H-14	3.46	H-12 (2.8); Me-24 (2.9)
H-19	3.39	H-14 (4.0); H-21 (1.9); H-16 (2.7); H-17 (2.2)
H-7	3.18	H-6 (2.9); H _a -9 (2.6); Me-24 (2.7)
H-10	3.11	H-8 (2.2); H _e -9 (1.3);
H-3	2.30	H-8 (10.2); H-3 (20.3)
H-3	1.18	H-4 (1.6); H-3 (6.0)

25-1

Table 17. NOE Data for aldehyde 25-1.

Proton	δ (ppm)	NOE (%)
H-1	9.51	H _Z -28 (7.1)
H-24	6.68	H-23 (1.4); H _E -25 (5.8); H-21 (3.9)
H _E -28	6.35	H _Z -28 (26.0); H-4 (1.1); H-8 (0.7); H-3 (0.7); H-3' (0.6)

H _Z -28	6.08	H-1 (14.3); H _E -28 (23.9)
H-23	6.04	H-22 (6.2); H _Z -25 (3.2)
H-22	5.47	H-23 (9.5); H-21 (2.2); H-19 (0.5)
H _Z -25	5.20	H-23 (6.3); H _E -25 (19.1)
H _E -25	5.10	H-24 (6.3); H _Z -25 (18.8)
MeOCH ₂ O	4.70	H-6 (4.6); MeO (3.5)
MeOCH ₂ O	4.66	H-6 (1.7); MeO (3.7)
H-6	3.96	MeOCH ₂ O (4.5); MeO (0.5); H-7 (3.2); H _E -5 (2.9); H _a -5 (2.0);
H-4	3.92	H-1 (0.6); H _E -28 (1.0); H-3 (2.7); H _E -5 (3.4)
H-8	3.77	H _E -28 (1.4); H-10 (7.2); H-7 (7.8); H _E -9 (4.8)
H-14 & 15	3.25	H-10 (1.2); H-19 (3.9); H-13 (1.5); H-12&13 (3.0); H-16&17 (1.6); Me-27 (1.4)
H-10	3.26	H-8 (6.9); H _E -9&12 (9.5)
H-7	3.22	H-6 (6.7); Me-27 (7.4)
H-3	3.15	H _E -28 (1.8); H-8 (10.4); H-3 (24.2)
H-3	2.42	H _E -28 (1.8); H-4 (6.7); H-3 (25.5)
H-21	2.31	H-24 (5.6); H-22 (3.4); H-19 (1.4); H-20 (0.9)
H-13	2.16	H-14 or 15 (4.4); H-13 (20.6)
H _E -5	1.95	H-4 (9.1); H-6 (9.1);
H-20	1.58	H-22 (3.0); H-19 (4.5); H-21 (2.4); H-20 (12.2); Me-26 (7.1)
H _a -9	1.46	H-7 (7.8); Me-27 (3.2); H _E -9 (21.5)
Me-27	1.16	H-14 (1.6); H-7 (4.9); H-13 (0.5); H _a -9 (3.3)
Me-26	1.07	H-17 (0.8); H-17 (1.6); H-20 (1.6)

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum of in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

400 MHz ¹H NMR Spectrum in CDCl₃

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

400 MHz ¹H NMR in C₆D₆

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in C_6D_6

400 MHz ¹H NMR Spectrum in CDCl₃

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

400 MHz ¹H NMR Spectrum in CDCl₃

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

300 MHz ^1H NMR Spectrum in CDCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ¹³C NMR Spectrum in CDCl₃

400 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl₃

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in C_6D_6

500 MHz ¹H NMR Spectrum in C₆D₆

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl₃

500 MHz ^1H NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ¹H NMR Spectrum in C₆D₆

100 MHz ¹³C NMR Spectrum in CDCl₃

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl₃

FT IR Spectrum in CHCl₃

500 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

500 MHz ^1H NMR Spectrum in C_6D_6

FT IR Spectrum in CHCl₃

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in C_6D_6

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

500 MHz ¹H NMR Spectrum in C₆D₆

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ¹H NMR Spectrum in C₆D₆

100 MHz ¹³C NMR Spectrum in CDCl₃

FT IR Spectrum in CHCl_3

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl₃

500 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

400 MHz ^1H NMR Spectrum in C_6D_6

100 MHz ^{13}C NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

500 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

500 MHz ^1H NMR Spectrum in CDCl_3

100 MHz ^{13}C NMR Spectrum in CDCl_3

FT IR Spectrum in CHCl_3

500 MHz ^1H NMR Spectrum in CD_2Cl_2

100 MHz ^{13}C NMR Spectrum in CD_2Cl_2

FT IR Spectrum in CHCl₃

500 MHz ¹H NMR Spectrum of Hemibrevetoxin B in CD₂Cl₂

100 MHz ^{13}C NMR Spectrum of Hemibrevetoxin B in CD_2Cl_2

FT IR Spectrum of Hemibrevetoxin B in CHCl₃