Stereoselective Synthesis of the C(1)-C(19) Fragment of Tetrafibricin

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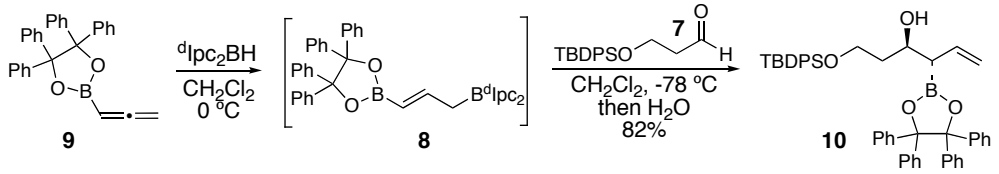
Supporting Information:

Experimental Procedures for The Synthesis of the C(1)-C(19) Fragment of Tetrafibricin

General Experimental Details. All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, diethyl ether, and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated otherwise, all reactions were conducted under an atmosphere of argon using flame-dried or oven-dried (140 °C) glassware. Four Å molecular sieves were dried under high vacuum at 180 ° for 12 h and activated by thorough flame-drying immediately prior to use. The term "concentrated under reduced pressure" refers to the removal of solvents and other volatile materials using a rotary evaporator while maintaining a water bath temperature below 40 °C, followed by residual solvent removal at high vacuum (<0.2 mbar).

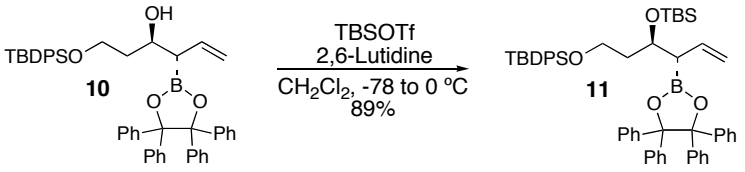
Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a commercial instrument at 400 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 MHz. The proton signal for residual non-deuterated solvent (δ 7.26 for $CHCl_3$) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the δ 77.0 resonance of $CHCl_3$. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as films on a FTIR instrument. Optical rotations were measured using a quartz cell with 1 mL capacity and a 10 cm path length. Mass spectra were recorded on a ZVG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester, UK).

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates pre-coated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid). Column chromatography was generally performed using Kieselgel 60 (230-400 mesh) silica gel, typically using a 50-100:1 weight ratio of silica gel to crude product.

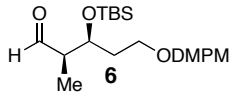


(3R,4S)-1-(*tert*-Butyl-diphenyl-silanyloxy)-4-(4,4,5,5-tetraphenyl-[1,3,2]dioxaborolan-2-yl)-hex-5-en-3-ol (10): Allene **9**[1] (4.6 g, 11.0 mmol) in CH_2Cl_2 (25 mL) was added via cannula to a suspension of (^{d}Ipc)$_2$BH[2] (3.2 g, 11.0 mmol) in CH_2Cl_2 (35 mL) at 0 °C. The suspension was stirred at 0 °C for 1 h and then warmed to 23 °C at which point it became homogeneous. The resulting mixture was cooled to –78 °C, and a solution of aldehyde **7**[3] (3.0 g, 9.5 mmol) in CH_2Cl_2 (2 mL) was added via a syringe pump over a period of 30 min. This mixture was stirred at –78 °C for 4 h, then was quenched by the addition of H_2O (30 mL) and allowed to warm to 23 °C. This mixture was stirred vigorously for 45

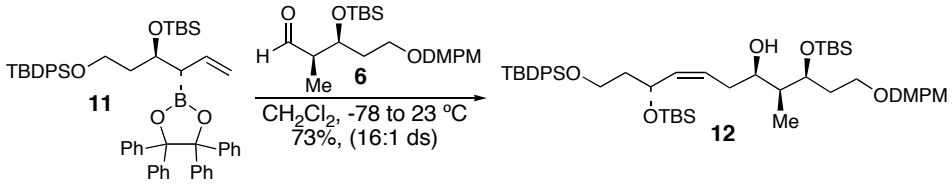
min, then the CH_2Cl_2 layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5:1 hexanes:ether) afforded allylboronate **10** (5.7 g, 82%) as a white gummy foam: $[\alpha]_D^{21.0}$ –12.9° (c 1.85, $CHCl_3$); ^{1}H NMR δ 7.70-7.68 (m, 4H), 7.45-7.35 (m, 6H), 7.18-7.14 (m, 8H), 7.09-7.02 (m, 12H), 6.17 (ddd, J = 17.2, 10.0, 10.0 Hz, 1H), 5.31 (dd, J = 17.2, 1.6 Hz, 1H), 5.27 (dd, J = 10.0, 1.6 Hz, 1H), 4.40 (m, 1H), 3.85 (m, 2H), 3.24 (d, J = 2.8, 1H), 2.60 (dd, J = 9.6, 6.8, 1H), 1.97-1.90 (m, 1H), 1.85-1.79 (m, 1 H), 1.07 (s, 9H); ^{13}C NMR δ 142.4, 142.3, 135.6, 135.5, 133.3, 133.2, 129.8, 128.6, 127.8, 127.2, 126.99, 126.97, 117.5, 96.1, 71.4, 63.2, 39.0 (bs), 37.8, 26.9, 19.1; IR (thin film, NaCl) 2930, 1446, 1359, 1111, 700 cm^{-1}; HRMS (ESI) 751.3397 m/z [calc M + Na^+ $C_{48}H_{49}BO_4SiNa$ 751.3391].



2-[(1S,2R)-2-(*tert*-Butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-1-vinyl-butyl]-4,4,5,5-tetraphenyl-[1,3,2]dioxaborolane (11): To a -78 °C solution of alcohol **10** (12.0 g, 16.5 mmol) in CH_2Cl_2 (60 mL) was added 2,6-lutidine (2.9 mL, 25.0 mmol) followed by a drop wise addition of neat TBS-OTf (4.4 mL, 19.0 mmol). This mixture was stirred at -78 °C for 2 h, then was warmed to 0 °C and stirred for 30 min. An aqueous solution of pH 7 buffer (75 mL) was added and the two-phase mixture was stirred to 23 °C. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (20:1 hexanes:ether) provided **11** (12.4 g, 89%) as a white sticky gum: $[\alpha]_D^{21.0}$ –28.7° (c 1.13, $CHCl_3$); ^{1}H NMR δ 7.74-7.70 (m, 4H), 7.47-7.35 (m, 6H), 7.28-7.25 (m, 4H), 7.18-7.04 (m, 16H), 6.04 (ddd, J = 17.2, 10.0, 10.0 Hz, 1H), 5.29 (dd, J = 17.2, 0.8 Hz, 1H), 5.20 (dd, 10.0, 1.6 Hz, 1H), 4.30 (m, 1H), 3.85 (d, J = 7.2 Hz, 1H), 3.83 (d, J = 7.6, 1H), 2.83 (dd, J = 9.6, 6.0 Hz, 1H), 2.17-2.09 (m, 1H), 2.05-2.02 (m, 1H), 1.16 (s, 9H), 0.94 (s, 9H), 0.19 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 143.0, 142.1, 136.4, 135.67, 135.65, 134.2, 134.1, 129.5, 128.8, 128.7, 127.7, 127.3, 127.2, 127.0, 126.8, 117.0, 96.2, 71.8, 61.2, 39.6, 38.3, 31.7, 27.0, 26.1, 19.3, 18.3, 14.2, -3.6, -3.9, -4.5; IR (thin film, NaCl) 2856, 1446, 1334, 1110, 1081, 700 cm^{-1}; HRMS (ESI) 865.4282 m/z [calc M + Na^+ $C_{54}H_{63}BO_4Si_2Na$ 865.4256].

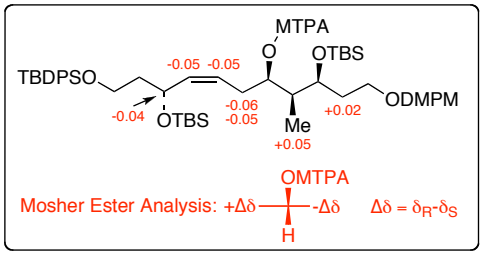


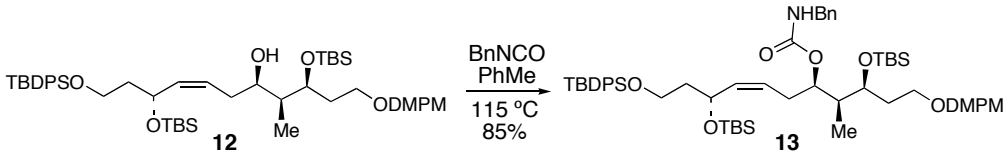
(2R,3S)-3-(*tert*-Butyl-dimethyl-silanyloxy)-5-(3,4-dimethoxy-benzyloxy)-2-methyl-pentanal (6) was prepared following the protocol reported for the synthesis of ***ent*-6**[4]: $[\alpha]_D^{21.0}$ –35.03 (c 2.04, $CHCl_3$); ^{1}H NMR δ 9.78 (s, 1H), 6.88-6.82 (m, 3H), 4.44 (d, J = 11.6, 1H), 4.38 (d, J = 11.6, 1H), 4.30 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.50 (dd, J = 6.4, 6.4 Hz, 2H), 2.48 (m, 1H), 1.84-1.74 (m, 2H), 1.06 (d, J = 7.2 Hz), 0.86 (s, 9H), 0.069 (s, 3H, 0.042 (s, 3H); ^{13}C NMR δ 204.90, 204.88, 148.9, 148.5, 130.7, 120.1, 110.9, 110.8, 72.8, 69.2, 66.2, 55.8, 55.7, 51.4, 34.4, 25.6, 17.9, 7.8, -4.6, -4.7; IR (thin film, NaCl) 1725, 1517, 1260, 1030 cm^{-1}; HRMS (ESI) 419.2226 m/z [calc M + Na^+ $C_{21}H_{36}O_5SiNa$ 419.2230].



(Z)-(3S,4S,5R,9R)-3,9-Bis-(*tert*-butyl-dimethyl-silanyloxy)-11-(*tert*-butyl-diphenyl-silanyloxy)-1-(3,4-dimethoxy-benzyloxy)-4-methyl-undec-7-en-5-ol (12). To a -78 °C solution of allylboronate **11** (2.5 g, 3.0 mmol) in CH_2Cl_2 (18 mL) was added aldehyde **6**[4] (1.5 g, 3.8 mmol) in CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at -78 °C for 0.5 h prior to being allowed to warm to 23 °C and was stirred for 3 d. Neat ethanolamine (0.27 mL, 4.5 mmol) was then added and the resulting mixture was stirred for 18 h, during which time a white precipitate formed. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with brine (50 mL). The aqueous layer was then extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5:1 hexanes:ethyl acetate) afforded homoallylic alcohol **12** (2.0 g, 77%) as a pale-yellow gum: $[\alpha]_D^{21.0}$ 17.3° (c 1.03, $CHCl_3$); ^{1}H NMR δ 7.69-7.65 (m, 4H), 7.42-7.35 (m, 6H), 6.86 (m, 3H), 5.48 (dd, J = 10.8, 8.8 Hz, 1H), 5.34 (ddd, 11.2, 7.2, 7.2 Hz, 1H), 4.73 (ddd, J = 8.4, 8.4, 5.2 Hz, 1H), 4.43 (d, J = 11.6 Hz, 1H), 4.40 (d, J = 11.6 Hz, 1H), 3.97 (ddd, J = 6.0, 6.0, 3.2 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.84-3.76 (m, 2H), 3.72-3.67 (m, 1H), 3.47-3.43 (m, 2H), 2.46 (d, J = 2.8 Hz, 1H), 2.28 (d, J = 7.2 Hz, 1H), 2.25 (d, J = 7.2 Hz, 1 H), 1.88 (d, J = 6.8 Hz, 1H), 1.85 (d, J = 6.4, 1H), 1.75-1.56 (m, 3H), 1.58 (s, 9H), 1.06 (m, 12H), 0.90 (s, 9H), 0.101 (s, 3H), 0.096 (s, 3H), 0.029 (s, 3H), 0.020 (s, 3H); ^{13}C NMR δ 149.0, 148.6, 136.3, 135.6, 134.0, 133.9, 130.9, 129.6, 127.64, 127.62, 125.2, 120.1, 110.94, 110.91, 74.5, 73.6, 73.0, 66.9, 65.8, 60.4, 55.9, 55.8, 41.3, 40.7, 34.4, 34.0, 26.9, 25.90, 25.88, 19.2, 18.2, 18.0, 7.1, -4.0, -4.2, -4.4, -4.8; IR (thin film, NaCl) 2930, 1516, 1463, 1256, 1087 cm^{-1}; HRMS (ESI) 887.5131 m/z [calc M + Na^+ $C_{49}H_{80}O_7Si_3Na$ 887.5110].

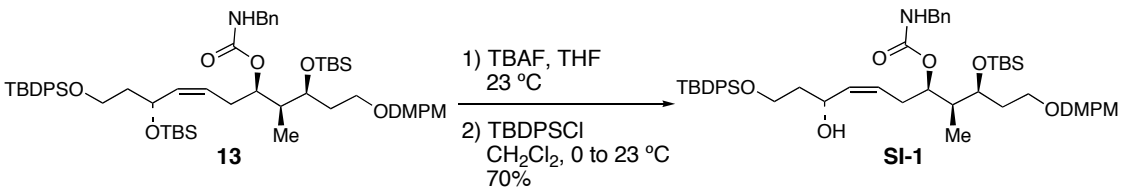
The absolute configuration of the C(13)-hydroxyl group of **12** was assigned by ^{1}H NMR analysis of the diastereomeric R- and S-Mosher (MTPA) esters[5]:





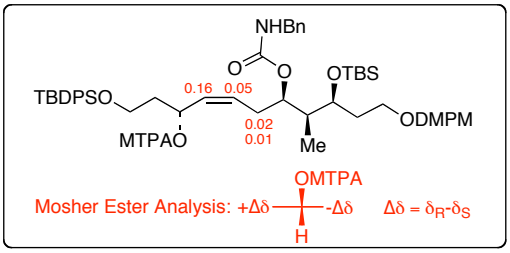
Benzyl-carbamic acid (Z)-(1R,5R)-5-(*tert*-butyl-dimethyl-silanyloxy)-1-[(1S,2S)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(3,4-dimethoxy-benzyloxy)-1-methyl-butyl]-7-(*tert*-butyl-diphenyl-silanyloxy)-hept-3-enyl ester (13). To a stirred mixture of alcohol **12** (3.7 g, 4.3 mmol) in toluene (5 mL) in a sealed tube equipped with a stir bar was added neat benzyl isocyanate (0.8 mL, 6.4 mmol). The sealed tube was then placed in a pre-heated oil bath at 115 °C and stirred for 24 h. The reaction mixture was stirred at 23 °C for 15 min, then was transferred to a round bottom flask and concentrated under reduced pressure. Purification of the crude product by flash chromatography (1.5:1 hexanes:ether) afforded benzyl carbamate **13** (3.0 g, 85%) as a clear colorless gum: $[\alpha]_D^{21.0}$ –14.5° (c 1.32, $CHCl_3$); ^{1}H NMR δ 7.66-7.62 (m, 4H), 7.43-7.18 (m, 11H), 6.89-6.81 (m, 3H), 5.42 (dd, J = 10.8, 8.4 Hz, 1H), 5.28 (m, 1H), 5.12 (dd, J = 10.8, 6.4 Hz, 1H), 4.74 (t, J = 12.0 Hz, 1H), 4.71 (m, 1H), 4.44 (d, J = 11.6 Hz, 1H), 4.39 (d, J = 11.6 Hz, 1H), 4.29 (d, J = 6.0 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.80-3.75 (m, 2H), 3.66-3.61 (m, 1H), 3.51-3.44 (m, 2H), 2.46-2.32 (m, 2H), 1.86-1.51 (m, 6H), 1.05 (s, 9H), 0.91-0.89 (m, 12H), 0.86 (s, 9H), 0.041 (s, 3H), 0.028 (s, 3H), 0.020 (s, 3H), 0.011 (s, 3H); ^{13}C NMR δ 156.2, 149.0, 148.5, 138.7, 136.3, 135.58, 135.55, 134.05, 133.9, 131.2, 129.58, 129.57, 128.6, 127.6, 127.4, 124.4, 120.2, 111.1, 110.9, 73.4, 72.8, 71.4, 66.9, 65.7, 60.4, 55.9, 55.8, 44.9, 41.8, 41.3, 33.2, 32.2, 29.7, 26.9, 25.93, 25.85, 19.2, 18.13, 18.06, 10.9, -4.0, -4.21, -4.24, -4.5; IR (thin film, NaCl) 2930, 1722, 1515, 1471, 1257, 1087 cm^{-1}; HRMS (ESI) 1020.5637 m/z [calc M + Na^+ $C_{57}H_{87}NO_8Si_3Na$ 1020.5637].

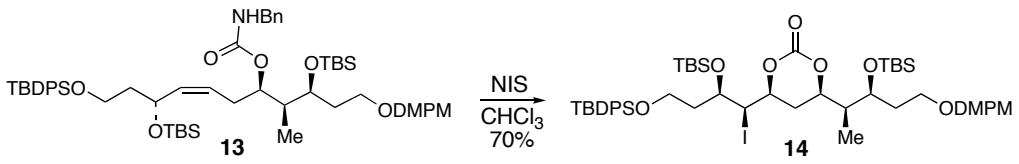
The absolute configuration of the C(17)-hydroxyl group was assigned by ^{1}H NMR analysis of the R- and S-Mosher ester (MTPA) derivatives of intermediate SI-1, prepared as summarized below:[5]



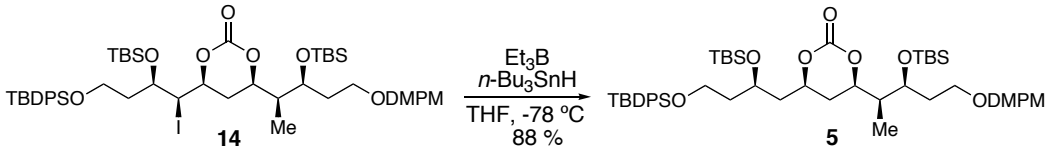
Benzyl-carbamic acid (Z)-(1R,5R)-1-[(1S,2S)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(3,4-dimethoxy-benzyloxy)-1-methyl-butyl]-7-(*tert*-butyl-diphenyl-silanyloxy)-5-hydroxy-hept-3-enyl ester (SI-1): To a 0 °C stirred solution of **13** (100 mg, 0.1 mmol) in THF (1 mL) was added 1.0 M solution of TBAF in THF (0.11 mL, 0.1 mmol). The mixture was allowed to warm to 23 °C and stir for 16 h. Purification of the crude product by column chromatography (10% MeOH/CH_2Cl_2) afforded the corresponding diol (60 mg, 93%) as a clear gum.

To a stirred 23 °C solution of the above diol (60 mg) in CH_2Cl_2 (1 mL) were added Et_3N (14 μL, 0.1 mmol), TBDPSCl (26 μL, 0.1 mmol) and DMAP (1 mg, 0.009 mmol). After being stirred for 24 h, the reaction was quenched by adding a sat. aqueous solution of ammonium chloride. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (2:1, hexanes:ethyl acetate) afforded alcohol **SI-1** (60 mg, 70%) as a clear pale-yellow gum: $[\alpha]_D^{21.0}$ –7.9° (c 1.23, $CHCl_3$); ^{1}H NMR δ 7.69-7.66 (m, 4H), 7.45-7.36 (m, 6H), 7.29-7.21 (m, 5H), 6.89-6.81 (m, 3H), 5.54 (dd, J = 10.8, 8.4 Hz, 1H), 5.44 (m, 1H), 5.07 (dd (J = 11.6, 6.0 Hz, 1H), 4.93 (t, J = 6.0 Hz, 1H), 4.70 (m, 1H), 4.44 (d, J = 11.6 Hz, 1H), 4.38 (d, J = 11.6 Hz, 1H), 4.32 (d, J = 6.0 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.84-3.78 (m, 3H), 3.49-3.45 (m, 2H), 2.97 (bs, 1H), 2.49-2.35 (m, 2H), 1.80-1.61 (m, 6H), 1.06 (s, 9H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.044 (s, 3H), 0.039 (s, 3H); ^{13}C NMR δ 156.3, 149.0, 148.5, 138.7, 135.59, 135.55, 134.9, 133.3, 133.1, 131.1, 129.84, 129.8, 128.6, 127.79, 127.78, 127.4, 126.5, 120.3, 111.1, 110.9, 73.8, 72.8, 71.1, 66.8, 66.7, 62.4, 55.9, 55.8, 45.0, 41.4, 39.0, 33.5, 31.6, 26.9, 25.9, 19.1, 18.1, 10.5, -4.3, -4.4; IR (thin film, NaCl) 2931, 2857, 1716, 1515, 1258, 1111, 702 cm^{-1}; HRMS (ESI) 906.4759 m/z [calc M + Na^+ $C_{51}H_{73}NO_8Si_2Na$ 906.4722].



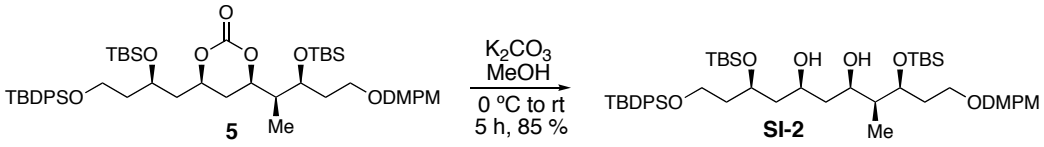


(4S,6R)-4-[(1R,2R)-2-(*tert*-Butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-1-iodo-butyl]-6-[(1S,2S)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(3,4-dimethoxy-benzyloxy)-1-methyl-butyl]-[1,3]dioxan-2-one (14): To a 0 °C stirred solution of carbamate **13** (300 mg, 0.3 mmol) in $CHCl_3$ (2.0 mL) was added NIS (74 mg, 0.33 mmol). The reaction flask was covered with aluminum foil and the mixture stirred at 23 °C. After 24 h, 0.5 equiv of NIS (33 mg, 0.15 mmol) was added and the mixture was stirred for another 24 h. At this point, an additional 0.4 equiv (27 mg, 0.12 mmol) of NIS was added and stirring was continued. The resulting bright orange reaction mixture was placed in an ice bath (0 °C), quenched by adding an aqueous solution (3 mL) of sodium bicarbonate (5%) and sodium thiosulfate (20%). This two-phase mixture was stirred until the organic layer became a clear pale-yellow color. The organic layer was then removed and the aqueous layer extracted with $CHCl_3$ (3 x 5 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash chromatography (1.5:1, hexanes:ether) provided iodo carbonate **14** (220 mg, 70%) as a clear gum: $[\alpha]_D^{21.0}$ 7.2° (c 2.0, $CHCl_3$); ^{1}H NMR δ 7.68-7.65 (m, 4H), 7.45-7.37 (m, 6H), 6.88-6.82 (m, 3H), 4.67-4.62 (m, 1H), 4.42 (d, J = 11.6 Hz, 1H), 4.36 (d, J = 11.6 Hz, 1H), 4.35 (m, 1H), 4.19 (m, 1H), 4.14 (dd, J = 11.2, 4.0 Hz, 1H), 3.89 (s, 3H), 3.88 (m, 4H), 3.70 (m, 2H), 3.47 (m, 2H), 2.28 (m, 1H), 2.04-1.63 (m, 6H), 1.06 (s, 3H), 1.01 (d, J = 7.2 Hz, 3H), 0.86 (s, 9H), 0.85 (s, 9H), 0.07 (s, 3H), 0.053 (s, 3H), 0.049 (s, 3H), 0.024 (s, 3H); ^{13}C NMR δ 149.0, 148.7, 148.6, 135.7, 135.6, 133.7, 133.3, 130.9, 129.8, 129.7, 128.6, 127.8, 127.7, 127.4, 120.2, 111.1, 110.9, 77.8, 75.7, 72.9, 71.3, 70.6, 66.4, 60.0, 56.0, 55.9, 43.3, 40.7, 36.5, 33.0, 32.8, 29.7, 26.9, 25.9, 25.8, 19.2, 18.02, 18.00, 10.0, -4.3, -4.38, -4.44; IR (thin film, NaCl) 2929, 1763, 1516, 1257, 1111, 836 cm^{-1}; HRMS (ESI) 1057.3964 m/z [calc M + Na^+ $C_{50}H_{79}IO_9Si_3Na$ 1057.3974].



(4S,6R)-4-[(R)-2-(*tert*-Butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-butyl]-6-[(1S,2S)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(3,4-dimethoxy-benzyloxy)-1-methyl-butyl]-[1,3]dioxan-2-one (5): To a stirred –78 °C solution of iodo carbonate **14** (615 mg, 0.59 mmol) in THF (6 mL) were added neat $(n\text{-Bu})_3SnH$ (310 μL, 1.18 mmol), followed by a 1.0 N solution of Et_3B in hexanes (180 μL, 0.18 mmol). The reaction mixture was stirred at –78 °C for 4 h, then was quenched by adding SiO_2 (1g) and allowed to warm to 23 °C. Purification of the resulting heterogeneous mixture by flash

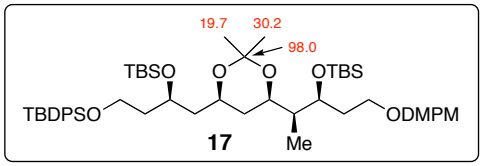
chromatography (3:1, hexanes-ethyl acetate) provided cyclic carbonate **5** (480 mg, 88%) as a clear colorless gum: $[\alpha]_D^{21.0}$ –6.4° (c 2.2, $CHCl_3$); ^{1}H NMR δ 7.66-7.03 (m, 4H), 7.45-7.35 (m, 6H), 6.87-6.81 (m, 3H), 4.60 (ddd, J = 12.0, 3.2, 3.2 Hz, 1H), 4.50 (m, 1H), 4.43 (d, J = 11.6 Hz, 1H), 4.38 (d, J = 11.6 Hz, 1H), 4.10 (m, 1H), 3.91 (m, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.73 (t, J = 6.4 Hz, 2H), 3.48 (m, 2H), 1.99 (ddd, J = 14.0, 2.4, 2.4 Hz, 1H), 1.94-1.86 (m, 2H), 1.80-1.62 (m, 6H), 1.05 (s, 9H), 1.00 (d, J = 7.2 Hz, 3H), 0.87 (s, 9H), 0.84 (s, 9H), 0.057 (s, 3H), 0.023 (s, 3H), 0.021 (s, 3H), 0.015 (s, 3H); ^{13}C NMR δ 149.4, 149.0, 148.6, 135.6, 133.72, 133.69, 131.0, 129.71, 129.68, 127.71, 127.70, 120.2, 111.1, 110.9, 78.7, 75.6, 72.9, 70.7, 66.5, 65.8, 60.5, 55.9, 55.8, 43.2, 42.5, 39.2, 33.1, 32.7, 26.9, 25.9, 25.8, 19.2, 18.0, 17.9, 10.0, -4.3, -4.4, -4.5; IR (thin film, NaCl) 2930, 1753, 1516, 1463, 1257, 1111, 836 cm^{-1}; HRMS (ESI) 931.4990 m/z [calc M + Na^+ $C_{50}H_{80}O_9Si_3Na$ 931.5008].

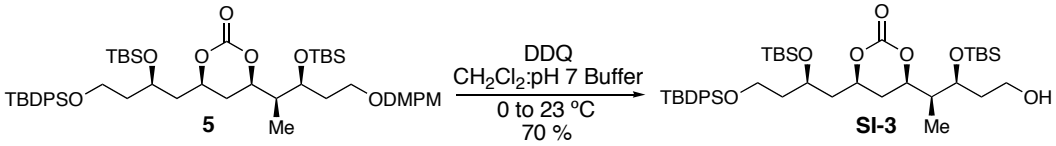


Assignment of the C(13)-C(15) *syn*-Relationship in 5 via the Rychnovsky Method via (3S,4S,5R,7S,9R)-3,9-Bis-(*tert*-butyl-dimethyl-silanyloxy)-11-(*tert*-butyl-diphenyl-silanyloxy)-1-(3,4-dimethoxy-benzyloxy)-4-methyl-undecane-5,7-diol (SI-2): To a stirred 23 °C solution of cyclic carbonate **5** (35 mg, 0.038 mmol) in MeOH (2 mL) was added K_2CO_3 (12 mg, 0.090 mmol). After being stirred at 23 °C for 5 h the reaction mixture was concentrated under reduced pressure. Purification of the residue by flash chromatography (2:1, hexanes:ethyl acetate) afforded diol **SI-2** (27 mg, 85%) as a clear gum: ^{1}H NMR δ 7.66-7.64 (m, 4H), 7.44-7.34 (m, 6H), 6.86-6.80 (m, 3H), 4.42 (s, 2H), 4.14-4.07 (m, 1H), 4.05-4.01 (m, 1H), 3.97-3.91 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.72 (t, J = 6.4 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 1.91-1.75 (m, 5H), 1.65-1.42 (m, 5H), 1.04 (s, 9H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.85 (s, 9H), 0.073 (s, 9H), 0.042 (s, 3H); ^{13}C NMR δ 149.0, 148.6, 135.54, 135.53, 133.76, 133.75, 131.0, 129.6, 127.6, 120.1, 111.0, 110.9, 73.9, 73.6, 72.9, 71.1, 69.4, 66.8, 60.6, 55.9, 55.8, 44.2, 42.5, 42.0, 40.3, 34.2, 26.9, 25.9, 25.8, 19.1, 18.0 17.9, 8.4, -4.0, -4.3, -4.4, -4.6; HRMS (ESI) 905.5208 m/z [calc M + Na^+ $C_{49}H_{82}O_8Si_3Na$ 905.5215].

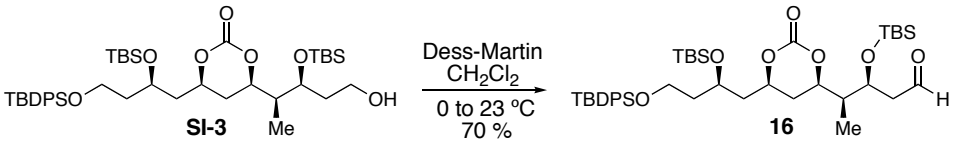
To a 23 °C stirred solution of diol **SI-2** (25 mg, 0.03 mmol) in CH_2Cl_2 (1 mL) was added 2,2-dimethoxypropane (17 μL, 0.14 mmol) followed by a catalytic amount of CSA. The reaction mixture was stirred at 23 °C for 14 h then was concentrated under reduced pressure. Purification of the resulting residue by column chromatography provided 1,3-acetonide **17** having ^{13}C NMR data consistent with the indicated 1,3-*syn* stereochemistry[6]: $[\alpha]_D^{21.0}$ –2.10 (c 2.75, $CHCl_3$); ^{1}H NMR δ 7.67-7.64 (m, 4H), 7.44-7.43 (m, 6H), 6.89-6.82 (m, 3H), 4.43 (d, J = 11.6 Hz, 1H), 4.40 (d, J = 11.6 Hz, 1H), 4.09-4.03 (m, 1H), 3.99-3.93 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.84-3.80 (m, 1H), 3.76-3.70 (m, 2H), 3.48-3.43 (m, 2H),

1.86-1.65 (m, 5H), 1.53-1.43 (m, 4H), 1.38 (s, 3H), 1.31 (s, 3H), 1.05 (s, 9H), 0.89 (d, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.84 (s, 9H), 0.035 (s, 6H), 0.024 (s, 3H), 0.007 (s, 3H); ^{13}C NMR δ 149.0, 148.5, 135.5, 134.05, 133.99, 131.1, 129.52, 129.5, 127.58, 127.57, 120.2, 111.03, 110.90, 98.0, 72.9, 70.9, 68.5, 67.3, 66.0, 65.9, 60.8, 55.9, 55.8, 44.4, 43.4, 39.8, 35.9, 33.7, 30.2, 26.9, 25.88, 25.87, 19.7, 19.2, 18.1, 18.0, 10.0, -4.27, -4.34, -4.37, -4.55; IR (thin film, NaCl) 2931, 1516, 1463, 1258, 1111, 835 cm^{-1}; HRMS (ESI) 945.5523 m/z [calc M + Na$^+$ $C_{52}H_{86}O_8Si_3Na$ 955.5528].

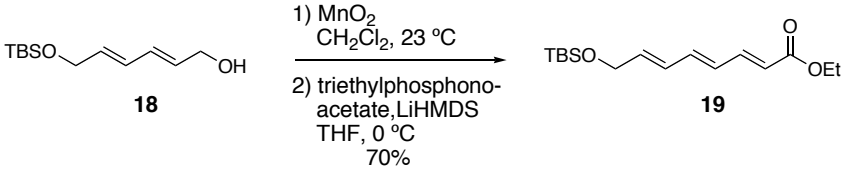




(4S,6R)-4-[(R)-2-(*tert*-Butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-butyl]-6-[(1S,2S)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-hydroxy-1-methyl-butyl]-[1,3]dioxan-2-one (SI-3): To a stirred, heterogeneous 0 °C solution of carbonate **5** (265 mg, 0.29 mmol) in CH_2Cl_2 and pH 7 buffer (7 mL:0.7 mL) was added DDQ in 3 portions (10 min intervals). The resulting heterogeneous reaction mixture was stirred at 0 °C for 0.5 h prior to warming to 23 °C. After being stirred for 0.5 h the reaction was quenched by the addition of a saturated aqueous sodium bicarbonate solution. The organic layer was removed and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over anhydrous sodium sulfate filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (twice; 4:3, hexanes:ether) provided alcohol **SI-3** (200 mg, 70%) as a clear gum: $[\alpha]_D^{21.0}$ –11.6° (c 1.09, $CHCl_3$); ^{1}H NMR δ 7.66-7.63 (m, 4H), 7.43-7.35 (m, 6H), 4.63 (ddd, J = 11.6, 3.2, 3.2 Hz, 1H), 4.56-4.50 (m, 1H), 4.11 (dddd, J = 5.6, 5.6, 5.6, 5.6 Hz, 1H), 3.91 (ddd, J = 8.0, 4.0, 4.0 Hz, 1H), 3.75-3.68 (m, 4H), 2.0 (ddd, J = 14.4, 3.2, 3.2 Hz, 1H), 1.96-1.89 (m, 1H), 1.86-1.67 (m, 8H), 1.05 (s, 9H), 1.00 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.84 (s, 9H), 0.10 (s, 3H), 0.050 (s, 3H), 0.031 (s, 3H), 0.021 (s, 3H); ^{13}C NMR δ 149.4, 135.6, 133.70, 133.67, 129.71, 129.69, 127.7, 78.3, 75.7, 71.6, 65.8, 60.5, 59.7, 43.1, 42.4, 39.2, 35.2, 32.6, 26.9, 25.9, 25.8, 19.2, 17.98, 17.95, 10.13, -4.3, -4.50, -4.54; IR (thin film, NaCl) 2930, 1748, 1472, 1252, 1112, 836 cm^{-1}; HRMS (ESI) 781.4325 m/z [calc M + Na$^+$ $C_{41}H_{70}O_7Si_3Na$ 781.4327].



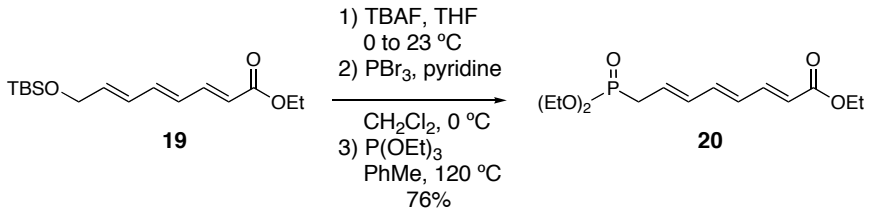
(3S,4S)-3-(*tert*-Butyl-dimethyl-silanyloxy)-4-{(4R,6S)-6-[(R)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-butyl]-2-oxo-[1,3]dioxan-4-yl}-pentanal (16): To a 0 °C stirred solution of intermediate **SI-3** (140 mg, 0.18 mmol) in CH_2Cl_2 (3 mL) was added the Dess-Martin periodinane reagent[7] in three portions at 10 min intervals. The resulting heterogeneous reaction mixture was warmed to 23 °C and stirred for 1 h. It was then quenched with a 10% sodium bicarbonate aqueous solution (2 mL), the organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (5:1, hexanes:ethyl acetate) furnished sensitive aldehyde **16** (91 mg, 70 %) as a clear gum: $[\alpha]_D^{21}$ –14.2° (c 1.22, $CHCl_3$); ^{1}H NMR δ 9.80 (t, J = 1.6 Hz, 1H), 7.66-7.64 (m, 4H), 7.46-7.40 (m, 4H), 4.72 (ddd, J = 12.0, 3.2, 3.2 Hz, 1H), 4.56 (m, 1H), 4.28 (ddd, J = 7.2, 4.4, 4.4 Hz, 1H), 4.11 (dddd, J = 6.0, 6.0, 6.0, 6.0 Hz, 1H), 3.73 (t, J = 7.2 Hz, 3H), 2.78-2.66 (m, 2H), 1.96-1.68 (m, 8H), 1.05 (s, 9H), 0.98 (d, J = 7.2 Hz, 3H), 0.086 (s, 9H), 0.085 (s, 9H), 0.059 (s, 6H), 0.034 (s, 3H), 0.025 (s, 3H); ^{13}C NMR δ 201.4, 149.2, 135.6, 133.7, 133.6, 129.73, 129.71, 127.72, 127.71, 75.7, 69.0, 65.7, 60.4, 47.6, 43.5, 42.3, 39.2, 32.3, 26.9, 25.81, 25.77, 19.2, 18.0, 9.7, -4.24, -4.49, -4.52, -4.59; IR (thin film, NaCl) 2930, 1755, 1472, 1253, 1112, 836 cm^{-1}; HRMS (ESI) 779.4179 m/z [calc M + Na^+ $C_{41}H_{68}O_7Si_3Na$ 779.4171].



(2E,4E,6E)-8-(*tert*-Butyl-dimethyl-silanyloxy)-octa-2,4,6-trienoic acid ethyl ester (19): To a 23 °C solution of alcohol **18**[8] (3.0 g, 13.1 mmol) in CH_2Cl_2 (400 mL) was added activated MnO_2 (6 g, 69 mmol). This mixture was stirred for 5 h at ambient temperature. The black solid was removed by filtration through a short plug of Celite with CH_2Cl_2. The filtrate was concentrated under reduced pressure, and the crude aldehyde was used in the next step without purification.

A solution of triethyl phosphonoacetate (2.9 mL, 14.8 mmol) in THF (5 mL) was added via a syringe pump over 0.5 h to a 0 °C stirred suspension of 95 % NaH (330 mg, 13.7 mmol) in THF (40 mL). This mixture was stirred at 0 °C for 0.5 h during time became a homogeneous mixture. A solution of the crude aldehyde from above in THF (5 mL) was then added drop wise via a syringe pump over a period of 0.5 h. The mixture was allowed to warm to 23 °C and stirred for 2 h. At this point, a saturated aqueous ammonium chloride solution was added (50 mL) and stirred for 10 min. The organic layer was separated

and the aqueous phase extracted with Et_2O (4 x 50 mL). The combined organic extracts were washed with water (2 x 40 mL), brine (3 x 20 mL) dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography (5 % ether-hexanes) furnished trienoate **19** (2.7 g, 70 %; two steps): ^{1}H NMR δ 7.30 (dd, J = 15.6, 11.6 Hz, 1H), 6.56 (dd, J = 14.8, 10.8 Hz, 1H), 6.38-6.31 (m, 1H), 6.28 (dd, J = 14.8, 11.2 Hz, 1H), 5.97 (ddd, 15.2, 4.8, 4.8 Hz, 1H), 5.87 (d, J = 15.2 Hz, 1H), 4.27 (m, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR δ 167.1, 144.5, 140.1, 137.7, 129.3, 128.6, 120.8, 63.2, 60.2, 25.9, 18.4, 14.3, -5.3; IR (thin film, NaCl) 1713, 1620, 1256, 1119, 837 cm^{-1}; HRMS (ESI) 297.1876 m/z [calc M + H$^+$ $C_{16}H_{29}O_3Si$ 297.1886].

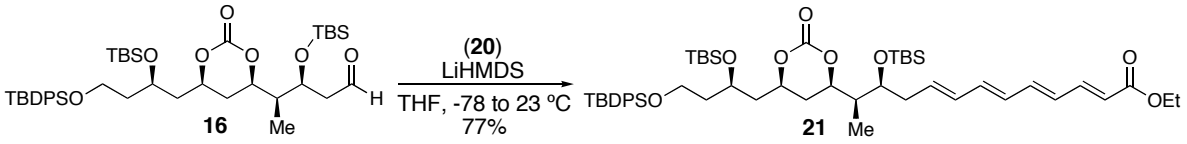


(2E,4E,6E)-8-(Diethoxy-phosphoryl)-octa-2,4,6-trienoic acid ethyl ester (20): To a stirred 0 °C solution of **19** (2.0 g, 6.7 mmol) in THF (30 mL) was added drop wise a 1.0 N solution of TBAF in THF (8.1 mL, 8.1 mmol). The mixture was stirred at 0 °C for 1 h, then was diluted with ethyl acetate (50 mL), washed with water (2 x 30 mL) and brine (30 mL). The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (1:1, hexanes:ethyl acetate) provided the corresponding alcohol (1.2 g, 6.6 mmol) as a pale waxy gum.

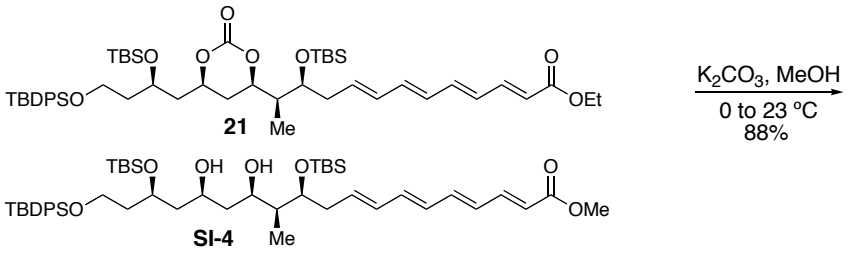
To a 0 °C stirred solution of the above alcohol (775 mg, 4.3 mmol) in CH_2Cl_2 (14 mL) was added pyridine (40 μL) followed by neat PBr_3 (0.61 ml, 6.5 mmol). While being stirred at 0 °C for 10 min, a white precipitate formed. The resulting reaction mixture was then quenched with water (20 mL) and extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with water (20 mL), saturated sodium bicarbonate solution (30 mL), brine (40 mL). The organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The waxy allylic bromide was employed in the next step without purification.[9]

To a 23 °C stirred solution of the above crude allylic bromide in toluene (25 mL) in a flask equipped with a reflux condenser was added neat $P(OEt)_3$. and heated to 121 °C for 12 h. It was then cooled to 23 °C, diluted with ethyl acetate (25 mL), washed with water (2 x 30 mL) and brine (30 mL). The organic phase was dried over anhydrous sulfate, filtered and concentrated under reduced pressure.[9] Purification of the residue by column chromatography (5 % MeOH/ CH_2Cl_2) provided phosphonate **20** (1.0 g, 76 % over three steps) as a pale-orange wax: ^{1}H NMR δ 7.27 (dd, J = 15.2, 11.6 Hz, 1H), 6.52 (dd,

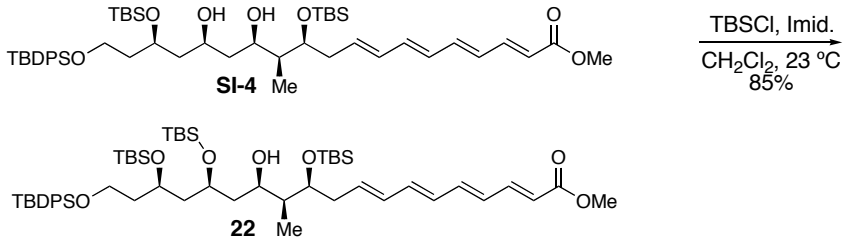
J = 15.6, 10.8 Hz, 1H), 6.29-6.22 (m, 2H), 5.86 (d, J = 15.2 Hz, 1H), 5.87-5.81 (m, 1H), 4.18 (q, J = 6.8 Hz, 2H), 4.09 (m, 4H), 2.68 (dd, J = 23.6, 8.4 Hz, 2H), 1.30 (t, J = 7.2 Hz, 6H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 167.0, 144.1 (app d), 139.6 (app d), 134.3 (app d), 129.7 (app d), 127.2 (app d), 121.3 (app d), 62.1 (app d), 60.3, 31.9, 30.5, 16.5, 16.4, 14.3; IR (thin film, NaCl) 1707, 1618, 1234, 1134, 1024 cm^{-1}; HRMS (ESI) 303.1358 m/z [calc M + H$^+$ $C_{14}H_{24}O_5P$ 303.1361].



(2E,4E,6E,8E)-(11S,12S)-11-(*tert*-Butyl-dimethyl-silanyloxy)-12-{(4R,6S)-6-[(R)-2-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-diphenyl-silanyloxy)-butyl]-2-oxo-[1,3]dioxan-4-yl}-trideca-2,4,6,8-tetraenoic acid ethyl ester (21): To a stirred –78 °C solution of phosphonate **20** (76 mg, 0.24 mmol) in THF (25 mL) was added dropwise a 0.2 N solution of LHMDS in THF (1.0 mL, 0.20 mmol). The resulting bright orange-red reaction mixture was stirred at –78 °C for 15 min prior to the dropwise addition of aldehyde **16** (120 mg, 0.16 mmol) in THF (15 mL). This mixture was stirring at –78 °C for 15 min, then was placed in an ice bath and stirred for 15 min. The reaction mixture was quenched by adding a saturated aqueous ammonium chloride solution (20 mL), the organic phase was extracted with ether (2 x 30 mL), and washed with brine (10 mL). The organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated. Purification of the resulting residue by flash column chromatography (6:1, hexanes:ethyl acetate) provided intermediate **21** (112 mg, 77%) as a pale-yellow gummy foam: $[\alpha]_D^{21.0}$ –16.4° (c 1.06, $CHCl_3$); ^{1}H NMR δ 7.66-7.63 (m, 4H), 7.45-7.33 (m, 6H), 7.31 (dd, J = 15.2, 11.2 Hz, 1H), 6.56 (dd, J = 14.8, 10.8 Hz, 1H), 6.35 (dd, J = 14.8, 10.4 Hz, 1H), 6.28 (dd, J = 14.8, 11.6 Hz, 1H), 6.20 (dd, J = 14.8, 10.8 Hz, 1H), 6.12 (dd, J = 14.8, 7.2 Hz, 1H), 5.86 (d, J = 15.2 Hz, 1H), 5.75 (ddd, J = 15.2, 7.6, 7.6 Hz, 1H), 4.54-4.49 (m, 2H), 4.20 (q, J = 7.2 Hz, 2H), 4.11 (m, 1H), 3.77 (dd, 10.8, 6.0 Hz, 1H), 3.73 (t, J = 6.0 Hz, 2H), 2.45-2.30 (m, 2H), 2.0 (ddd, J = 14.4, 2.8, 2.8 Hz, 1H), 1.91 (m, 1H), 1.81-1.64 (m, 5H), 1.30 (t = 7.2 Hz, 3H), 1.05 (s, 9H), 1.01 (d, J = 6.8 Hz, 3H), 0.87 (s, 9H), 0.84 (s, 9H), 0.07-0.02 (m, 12H); ^{13}C NMR δ 167.2, 149.4, 144.4, 140.6, 136.8, 135.6, 133.68, 133.65, 133.59, 132.8, 130.6, 129.7, 129.6, 127.7, 120.5, 79.0, 75.8, 65.8, 60.4, 60.3, 42.7, 42.4, 39.2, 37.6, 32.3, 26.9, 25.83, 25.82, 19.2, 18.03, 17.95, 14.3, 9.6, -4.0, -4.46, -4.51, -4.55; IR (thin film, NaCl) 2930, 1755, 1709, 1597, 1254, 1112, 836 cm^{-1}; HRMS (ESI) 905.5220 m/z [calc M + H$^+$ $C_{51}H_{81}O_8Si_3$ 905.5239].

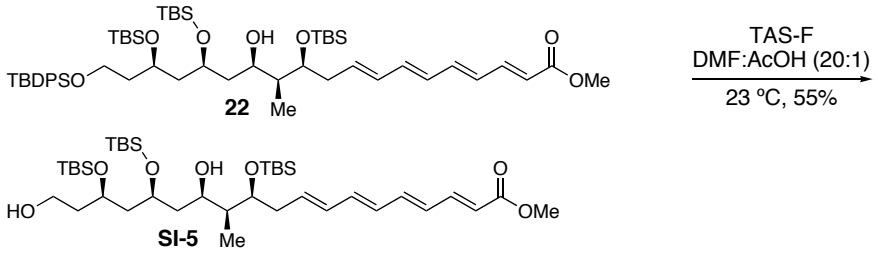


(2E,4E,6E,8E)-(11S,12S,13R,15S,17R)-11,17-Bis-(*tert*-butyl-dimethyl-silanyloxy)-19-(*tert*-butyl-diphenyl-silanyloxy)-13,15-dihydroxy-12-methyl-nonadeca-2,4,6,8-tetraenoic acid methyl ester (SI-4): To a stirred 23 °C solution of carbonate **21** (45 mg, 0.050 mmol) in MeOH (1 mL) was added K_2CO_3 (17 mg, 0.13 mmol). This mixture was stirred at 23 °C for 5 h, then was concentrated under reduced pressure. Purification of the residue by flash chromatography (2:1, hexanes:ether) afforded diol **SI-4** (38 mg, 88%) as a clear yellow gum: $[\alpha]_D^{21.0}$ –8.3° (c 0.94, $CHCl_3$); ^{1}H NMR δ 7.66-7.63 (m, 4H), 7.44-7.35 (m, 6H), 7.32 (dd, J = 15.2, 11.6 Hz, 1H), 6.56 (dd, J = 14.8, 11.2 Hz, 1H), 6.36 (dd, J = 14.8, 10.4 Hz, 1H), 6.31 (dd, 14.8, 11.6 Hz, 1H), 6.20 (dd, J = 14.4, 10.8 Hz, 1H), 6.17 (dd, 14.8, 11.2 Hz, 1H), 5.84 (d, J = 15.6 Hz, 1H), 5.77 (ddd, J = 14.8, 7.6, 7.6 Hz, 1H), 4.10 (m, 1H), 4.00-3.85 (m, 4H), 3.76-3.67 (m, 5H), 3.58 (bs, 1H), 2.43-2.39 (m, 2H), 1.85-1.38 (m, 7H), 1.04 (s, 9H), 0.92 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.09-0.05 (m, 12H); ^{13}C NMR δ 167.6, 144.7, 140.9, 137.3, 135.57, 135.56, 134.0, 133.74, 133.71, 132.5, 130.2, 129.7, 129.5, 127.7, 119.9, 75.7, 74.1, 71.3, 69.6, 60.6, 51.5, 44.1, 42.0, 41.9, 40.4, 38.4, 26.9, 25.9, 25.8, 19.2, 18.1, 17.1, 7.6, -3.8, -4.2, -4.5, -4.6; IR (thin film, NaCl) 2930, 1717, 1596, 1428, 1256, 1111, 1006, 836 cm^{-1}; HRMS (ESI) 865.5280 m/z [calc M + H^+ $C_{49}H_{81}O_7Si_3$ 865.5290].

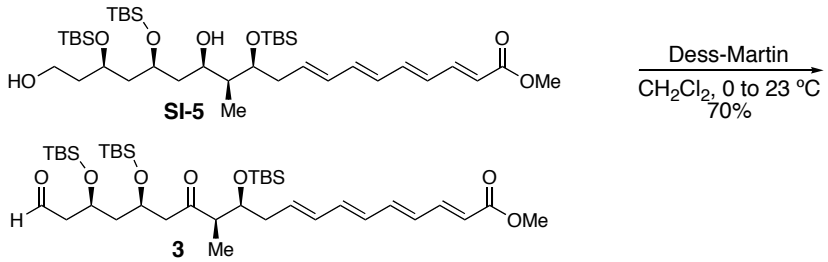


(2E,4E,6E,8E)-(11S,12S,13R,15S,17R)-11,15,17-Tris-(*tert*-butyl-dimethyl-silanyloxy)-19-(*tert*-butyl-diphenyl-silanyloxy)-13-hydroxy-12-methyl-nonadeca-2,4,6,8-tetraenoic acid methyl ester (22): To a 23 °C stirred solution of diol **SI-4** (33 mg, 0.038 mmol) in CH_2Cl_2 (1 mL) was added imidazole (36 mg, 0.53 mmol) followed by TBSCl (41 mg, 0.27 mmol). This mixture was stirred at 23 °C for 18 h, then was directly purified by flash chromatography (11:1, hexanes:ether) providing **22** as the major product (32 mg, 85%, 10:1 mixture of regioisomers) as a clear colorless gum. Major regioisomer **22**: $[\alpha]_D^{21.0}$ –1.3° (c 1.0, $CHCl_3$); ^{1}H NMR δ 7.67-7.64 (m, 4H), 7.44-7.35 (m, 6H), 7.32 (dd, J = 15.2, 11.2 Hz, 1H), 6.55 (dd, J = 14.8, 11.2 Hz, 1H), 6.36 (dd, J = 14.8, 10.4 Hz, 1H), 6.28 (dd, J = 14.8, 11.6

Hz, 1H), 6.21-6.10 (m, 2H), 5.91-5.81 (m, 1H), 5.86 (d, J = 15.2 Hz, 1H), 4.03-3.81 (m, 4H), 3.75 (s, 3H), 3.68 (dd, J = 6.4, 6.4 Hz, 2H), 3.18 (s, 1H), 2.48-2.40 (m, 2H), 1.81-1.45 (m, 7H), 1.04 (s, 9H), 0.92-0.89 (m, 21H), 0.82 (s, 9H), 0.11-0.07 (m, 12H), -0.01 (s, 3H), -0.03 (s, 3H); ^{13}C NMR δ 167.6, 144.8, 141.1, 137.6, 135.5, 134.4, 133.80, 133.76, 132.3, 130.0, 129.62, 129.60, 129.3, 127.67, 127.65, 119.7, 75.0, 71.2, 70.4, 66.9, 60.6, 51.5, 46.0, 42.6, 40.9, 38.3, 27.0, 25.93, 25.91, 25.86, 19.2, 18.1, 18.0, 17.9, 8.4, -3.9, -4.0, -4.27, -4.28, -4.48, -4.49; IR (thin film, NaCl) 2930, 1719, 1597, 1472, 1257, 1111, 1006, 836 cm^{-1}; HRMS (ESI) 979.6132 m/z [calc M + H$^+$ $C_{55}H_{95}O_7Si_4$ 979.6155].



(2E,4E,6E,8E)-(11S,12S,13R,15S,17R)-11,15,17-Tris-(*tert*-butyl-dimethyl-silanyloxy)-13,19-dihydroxy-12-methyl-nonadeca-2,4,6,8-tetraenoic acid methyl ester (SI-5). To a stirred 0 °C solution of **22** (26 mg, 0.027 mmol) in DMF (0.5 mL) was added acetic acid (25 μL), followed by a solution of 0.5 N TAS-F in DMF (60 μL, 0.029 mmol).[10] The resulting reaction mixture was allowed to warm slowly to 23 °C and then stirred for 48 h. Purification of the reaction mixture by flash chromatography afforded diol **SI-5** (11 mg, 55%) as a pale yellow clear gum: $[\alpha]_D^{21.0}$ 3.6° (c 0.80, $CHCl_3$); ^{1}H NMR δ 7.32 (dd, J = 15.2, 11.2 Hz, 1H), 6.55 (dd, J = 14.8, 10.8 Hz, 1H), 6.36 (dd, J = 14.8, 10.8 Hz, 1H), 6.32 (dd, J = 14.8, 11.6 Hz, 1H), 6.21 (dd, J = 14.8, 10.8 Hz, 1H), 6.14 (dd, J = 15.2, 10.8 Hz, 1H), 5.86 (d, J = 15.2 Hz, 1H), 5.74 (ddd, J = 14.8, 7.2, 7.2 Hz, 1H), 4.05-3.99 (m, 1H), 3.96-3.77 (m, 5H), 3.76-3.70 (m, 2H), 2.99 (bs, 1H), 2.51 (bm, 1H), 2.41 (d, J = 7.2 Hz, 1H), 2.37 (d, J = 7.2 Hz, 1H), 1.87-1.63 (m, 6H), 1.52-1.46 (m, 2H), 0.92-0.88 (m, 30H), 0.12-0.05 (m, 18H); ^{13}C NMR δ 167.6, 144.7, 140.9, 137.2, 133.5, 132.5, 130.4, 129.6, 119.9, 76.3, 71.5, 68.9, 68.8, 59.8, 51.5, 44.0, 42.5, 41.8, 38.5, 38.1, 25.86, 25.84, 18.0, 17.9, 7.0, -3.85, -4.3, -4.4, -4.5, -4.6; IR (thin film, NaCl) 2929, 1718, 1597, 1256, 1005, 836 cm^{-1}; HRMS (ESI) 741.4975 m/z [calc M + H$^+$ $C_{39}H_{76}O_7Si_3$ 741.4977].



(2E,4E,6E,8E)-(11S,12R,15R,17S)-11,15,17-Tris-(*tert*-butyl-dimethyl-silanyloxy)-12-methyl-13,19-dioxo-nonadeca-2,4,6,8-tetraenoic acid methyl ester (3). To a 0 °C stirred solution of diol **SI-5** (7 mg, 0.009 mmol) in CH_2Cl_2 (0.5 mL) was added Dess-Martin periodinane (9 mg, 0.022 mmol) in 4 portions. The mixture was stirred at 23 °C for 36 h, then was purified by flash chromatography (9:1, hexanes:ethyl acetate) giving keto aldehyde **3** (5 mg, 70%) as a pale yellow gum: $[\alpha]_D^{21.0}$ –17.2° (c 0.40, $CHCl_3$); ^{1}H NMR δ 9.75 (t, J = 2.4 Hz, 1H), 7.28 (dd, J = 14.8, 11.2 Hz, 1H), 6.51 (dd, J =14.8, 10.8 Hz, 1H), 6.31 (dd, J = 14.4, 10.4 Hz, 1H), 6.25 (dd, J = 13.2, 9.6 Hz, 1H), 6.15 (dd, 15.2, 11.2 Hz, 1H), 6.04 (dd, J = 15.2, 10.8 Hz, 1H), 5.82 (d, J = 15.2 Hz, 1H), 5.73 (ddd J = 15.2, 7.6, 7.6 Hz, 1H), 4.24-4.14 (m, 2H), 3.92 (ddd, 5.6, 5.6, 5.6 Hz, 1H), 3.69 (m, 3 H), 2.69-2.43 (m, 5H), 2.33-2.24 (m, 1H), 2.16-2.09 (m, 1H), 1.71-1.53 (m, 2H), 0.99 (d, J = 6.8 Hz, 3H), 0.84-0.80 (m, 27H), 0.030-(-0.066)(m, 18H); ^{13}C NMR δ 211.0, 201.7, 167.6, 144.7, 140.8, 137.0, 133.6, 132.9, 130.5, 129.7, 120.0, 72.8, 65.6, 65.4, 52.4, 51.5, 50.8, 50.6, 45.9, 38.8, 25.85, 25.80, 25.78, 18.07, 17.92, 17.86, 12.2, -4.21, -4.36, -4.51, -4.53, -4.56, -4.62; IR (thin film, NaCl) 2857, 1717, 1598, 1256, 1126, 1006, 836 cm^{-1}; HRMS (ESI) 737.4650 m/z [calc M + H$^+$ $C_{39}H_{73}O_7Si_3$ 737.4664].

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