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Supporting Information

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Total Synthesis of (+)-Dactylolide througn an Efficient Sequential Peterson Olefination and Prins Cyclization Reaction

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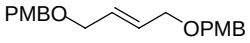
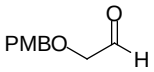
General Experimental Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded on Bruker Avance 300 at 300 MHz and 75 MHz, respectively, or at Bruker Avance 500 spectrometers at 500 MHz and 125 MHz if specified. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.27 ppm, C_6D_6 = 7.15 ppm, for ^{13}C NMR: $CDCl_3$ = 77.23. Data are reported as follows: (s = singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublets; dt = doublet of triplets; br = broad; a = apparent). High resolution and low resolution mass spectra were recorded on a VG 7070 spectrometer. Infrared (IR) spectra were collected on a Mattson Cygnus 100 spectrometer. Samples for IR were prepared as a thin film on a NaCl plate by dissolving the compound in CH_2Cl_2 and then evaporating the CH_2Cl_2. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. HPLC analysis was performed with an HP series 1100 instrument using either a Chiracel OD-H or CHIRAPAK AD column. Tetrahydrofuran and diethyl ether were dried by passage through an activated alumina column under positive N_2 pressure. Methylene chloride was distilled under N_2 from CaH_2. Analytical TLC was performed on E. Merck pre-coated (25 mm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash chromatography was done using ICN SiliTech 32-63 60 Å silica gel. Reagent grade ethyl acetate, diethyl ether, pentane and hexanes (commercial mixture) were purchased from EM Science and used as is for chromatography. All reactions were performed in oven or flame-dried glassware under a positive pressure of N_2 with magnetic stirring unless otherwise noted.

1-(((*E*)-4-(4-Methoxybenzyloxy)but-2-enyloxy)methyl)-4-methoxybenzene



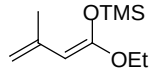
To a stirring suspension of sodium hydride (60% dispersion in mineral oil, 1.18 g, 31.1 mmol) under N_2 at 0 ºC in DMF (30 mL) was added but-2-ene-1,4-diol (1.21 g, 13.8 mmol). The reaction was stirred for 30 min and *p*-methoxybenzyl chloride (4.33 g, 27.7 mmol) was added. The reaction mixture was stirred for 18 h at room temperature, then was quenched by the addition of ice chips, and extracted into hexanes. The organic layer was dried ($MgSO_4$), filtered and concentrated. The resulting residue was purified by flash chromatography (20% EtOAc in hexanes) to afford the desired product (3.37 g, 74%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 6.5 Hz, 2H), 6.91 (d, *J* = 6.8 Hz, 2H), 5.80 (adt, *J* = 3.8, 1.0 Hz, 1H), 4.48 (s, 2H), 4.07 (dd, *J* = 3.8, 1.0 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 130.4, 129.7, 114.0, 72.0, 65.6, 55.5.

(4-Methoxybenzyloxy)acetaldehyde



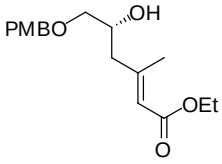
To a stirring solution of AD-mix-α (1.4 g/mmol substrate, 7.00 g) in *tert*-butyl alcohol (25 mL) and H_2O (25 mL) at 0 ºC was added bis *p*-methoxybenzyl ether (1.64 g, 5.00 mmol). The reaction mixture was warmed to room temperature and stirred for 18 h. The temperature was then decreased to 0 ºC and sodium sulfite (7.5 g) was added in bulk. The reaction mixture was allowed to stir for 1 h while warming to room temperature, then was extracted into CH_2Cl_2. The aqueous layer was washed with CH_2Cl_2 (2 x 25 mL) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated. The resulting residue was dissolved in CH_2Cl_2 (15 mL) and sodium periodate immobilized on silica gel (2.0 g/mmol substrate, 5.52 g) was added. The reaction mixture was stirred vigorously for 30 min, then was filtered. The filter cake was washed with CH_2Cl_2 (2 x 20 mL) and the filtrate was concentrated. The resulting residue was purified by vacuum distillation (bp 120 – 125 ºC, 2 mm Hg) to afford the desired product (1.44 g, 80%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.56 (s, 2H), 4.07 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.9, 156.0, 132.2, 129.8, 114.3, 73.6, 55.5.

((*Z*)-1-Ethoxy-3-methylbuta-1,3-dienyloxy)trimethylsilane (8)



To a solution of diisopropylamine (4.45 g, 44.0 mmol) in THF (50 mL) at 0 ºC under N_2 was added *n*-butyllithium (1.6M in hexanes, 27.5 mL, 44.0 mmol). The reaction mixture was stirred at 0 ºC for 30 min, then the temperature was decreased to -78 ºC. Ethyl 3,3-dimethylacrylate (5.12 g, 40.0 mmol) was added and the reaction mixture was stirred for 30 min. Trimethylsilyl chloride (6.52 g, 60.0 mmol) was added. The reaction mixture was stirred for an additional 20 min, then was allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in dry pentanes and filtered. The filtrate was concentrated and the resulting residue was purified by distillation (bp 63 – 75 ºC, 2 mm Hg) to afford the desired product (5.95 g, 74%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77 (d, *J* = 2.2 Hz, 1H), 4.52 (m, 1H), 4.23 (s, 1H), 3.80 (q, *J* = 6.9 Hz, 2H), 1.93 (s, 3H), 1.30 (t, *J* = 6.9 Hz, 3H), 0.25 (s, 9H); ^{13}C NMR (75

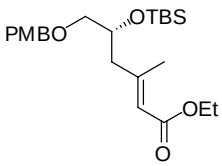
MHz, $CDCl_3$) δ 156.7, 140.7, 107.3, 81.1, 63.6, 23.9, 14.6, 0.7.



(*R*,*E*)-Ethyl 6-(4-methoxybenzyloxy)-5-hydroxy-3-methylhex-2-enoate (10)

To a solution of 6-bis[(4*R*)-4-phenyl-2-oxazolin-2-yl]pyridine (124 mg, 0.34 mmol) in CH_2Cl_2 (13 mL) was added $CuCl_2$ (45 mg, 0.34 mmol). The reaction mixture was stirred vigorously for 1 h to give a fluorescent green suspension. $AgSbF_6$ (232 mg, 0.675 mmol) in CH_2Cl_2 (10 mL) was added via cannula. The reaction mixture was wrapped in foil and stirred for 3 h. The resulting mixture was filtered directly into the reaction flask through and oven-dried glass pipet, tightly packed with cotton, to remove the white AgCl precipitate, yielding active catalyst (*R*,*R*)-[Cu(Ph-pybox)]$(SbF_6)_2$ as a clear blue solution. To the solution of active catalyst at -78 ºC was added (4-methoxybenzyloxy)acetaldehyde (2.25 g, 11.2 mmol) in CH_2Cl_2 (17 mL). Silyl ketene acetal (**8**) (2.69 g, 13.4 mmol) was added dropwise over 30 min The reaction was stirred at -78 ºC for 4 h, and then was filtered through a pad of silica (1.5 cm thick). The filtrate was concentrated, and the resulting residue was dissolved in THF (20 mL). HCl (1N) was added and the reaction mixture was allowed to stand for 20 min, then was diluted with ether (25 mL) and the two layers were separated. The organic layer was dried ($MgSO_4$) and concentrated. The resulting residue was purified by flash chromatography (40% EtOAc in hexanes) to afford the desired product (2.82 g, 82%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 8.6 Hz, 2H), 5.76 (s, 1H), 4.47 (s, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.04 (m, 1H), 3.83 (s, 3H), 3.51 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.37 (dd, *J* = 7.0, 2.3 Hz, 1H), 2.32 (m, 2H), 2.22 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 159.5, 155.9, 130.0, 129.6, 118.3, 114.0, 73.7, 73.3, 68.4, 59.8, 55.4, 44.8, 19.1, 14.5; $[\alpha]_D^{23}$ +1.48º (CH_2Cl_2, *c* = 1.20).

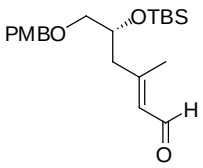
The ee was determined to be 95% by HPLC analysis using a Chirapak AD column. Conditions: Hexanes:*i*-PrOH 95:5, 1.0 mL/min.



(*R*, *E*)-Ethyl 5-(*tert*-butyldimethylsilanyloxy)-6-(4-methoxybenzyloxy)-3-methylhex-2-enoate

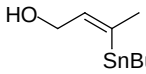
To a stirring solution of **10** (4.63 g, 15.0 mmol) in DMF was added imidazole (1.12 g, 16.5 mmol) followed by *tert*-butyldimethylsilyl chloride (2.49 g, 16.5 mmol). The reaction mixture was stirred for 18 h, then was quenched with ice chips and partitioned between water and hexanes. The organic layer was dried ($MgSO_4$) and concentrated. The resulting residue was purified by flash chromatography (20% EtOAc in hexanes) to afford the desired product (5.65 g, 89%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.70 (s, 1H), 4.45 (s, 2H), 4.15 (m, 2H), 3.98 (m, 1H), 3.81 (s, 3H), 3.38 (dd, *J* = 9.5, 5.3 Hz, 1H), 3.32 (dd, *J* = 9.5, 5.8 Hz, 1H), 2.42 (dd, *J* = 13.1, 4.4 Hz, 1H), 2.23 (dd, *J* = 13.1, 7.7 Hz, 1H), 2.18 (d, *J* = 1.2 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 159.2, 156.4, 130.4, 129.3, 118.6, 113.8, 74.2, 73.1, 69.9,

59.5, 55.3, 46.4, 25.8, 19.5, 18.2, 14.4, -4.4, -4.9; $[\alpha]_D^{23}$ +17.0º (MeOH, *c* = 1.17).



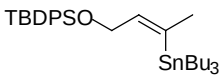
(*R*, *E*)-5-(*tert*-Butyldimethylsilanyloxy)-6-(4-methoxybenzyloxy)-3-methylhex-2-enal (6)

To a solution of lithium aluminum hydride (179 mg, 4.73 mmol) in Et_2O (15 mL) was added dropwise the TBS-protected ethyl ester (1.00 g, 2.36 mmol, in 5 mL Et_2O). The reaction mixture was stirred for 1 h, then was cooled to 0 ºC and quenched with a saturated solution of sodium potassium tartrate (10 mL). The reaction mixture was warmed to room temperature and stirred for 4 h. The two layers were separated. The water layer was washed with ether (2 x 15 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. The resulting residue (in 5 mL CH_2Cl_2) was added to a suspension of activated MnO_2 (2.00 g, 23.1 mmol) under N_2 in CH_2Cl_2 (10 mL). The reaction mixture was stirred for 18 h, and then was filtered through a pad of celite and concentrated. The resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to afford the desired product (720 mg, 80%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.00 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.93 (d, *J* = 8.1 Hz, 1H), 4.45 (s, 2H), 4.03 (m, 1H), 3.82 (s, 3H), 3.40 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.32 (dd, *J* = 9.4, 6.2 Hz, 1H), 2.51 (dd, *J* = 13.2, 4.3 Hz, 1H), 2.34 (dd, *J* = 13.2, 7.7 Hz, 1H), 2.20 (s, 3H), 0.87 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.1, 161.1, 159.4, 130.3, 130.1, 129.5, 114.0, 74.0, 73.2, 70.2, 55.4, 46.1, 26.0, 18.6, 18.26, -4.2, -4.6; $[\alpha]_D^{23}$ +3.40º (CH_2Cl_2, *c* = 1.42).



(*Z*)-3-Tributylstannanylbut-2-en-1-ol (11)

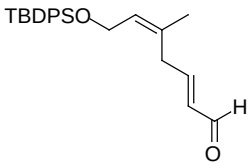
To a solution of 2-butyn-1-ol (4.00 g, 57.1 mmol) in THF (120 mL) at 0 ºC was added Red-Al® (65% wt solution in toluene, 17.8 g, 57.1 mmol) dropwise over 30 min. After the addition was complete the reaction mixture was warmed to room temperature and stirred for 3 h. Tri-*n*-butyltin chloride (37.2 g, 114 mmol) was added dropwise over a period of 10 min The reaction mixture was stirred for 18 h then was quenched with H_2O (20 mL). Saturated disodium tartrate (180 mL) was added and the mixture was stirred vigorously for 0.5 h. The two layers were separated and the water layer was extracted with Et_2O (100 mL). The combined organic layers were washed with 10% KF (80 mL) and brine (2 x 100 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting residue was purified by flash chromatography (gradient from hexanes to 10% EtOAc in hexanes) to afford the desired product (19.2 g, 93%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.28 (t, *J* = 6.7 Hz, $^3J_{\text{Sn-H } trans}$ = 123 Hz, 1H), 4.03 (t, *J* = 5.7 Hz, 2H), 1.96 (t, $^3J_{\text{Sn-H}}$ = 41 Hz, 3H), 1.55 – 1.27 (m, 12H), 0.92 (m, 15H).



((*Z*)-3-(Tributylstannyl)but-2-enyloxy)(*tert*-butyl)diphenylsilane

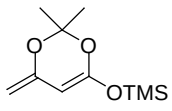
To a stirring solution of **11** (6.00 g, 16.61 mmol) in anhydrous DMF (120 ml) was added imidazole (1.36 g, 19.9 mmol) followed by *tert*-

butyldiphenylsilyl chloride (5.48 g, 19.9 mmol). The reaction mixture was stirred for 3 h, then was quenched with ice chips and partitioned between water and hexanes. The organic layer was dried ($MgSO_4$) and concentrated. The resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to afford the desired product (8.70 g, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (m, 4H), 7.41 (m, 6H), 6.26 (tq, J = 6.5, 1.5 Hz, $^3J_{\text{Sn-H, }trans}$ 127 Hz, 1H), 4.07 (d, J = 6.3 Hz, 2H), 1.94 (d, J = 0.97 Hz, $^3J_{\text{Sn-H}}$ = 41 Hz, 3H), 1.44 – 1.21 (m, 12H), 1.06 (s, 9H), 0.83 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 139.7, 135.7, 134.0, 129.6, 127.7, 66.6, 29.2, 27.4, 26.9, 13.8, 10.0; IR (neat) 3069, 2952, 2923, 2850, 1949, 1890, 1818, 1461, 1425, 1374, 1112, 1083, 1047, 821, 741, 698; HRMS (EI): calcd for $C_{24}H_{43}OSiSn$ (M-C_4H_9) 543.2105, found 543.2078.



(2*E*,5*Z*)-7-(*tert*-Butyldiphenylsilanyloxy)-5-methylhepta-2,5-dienal (13)

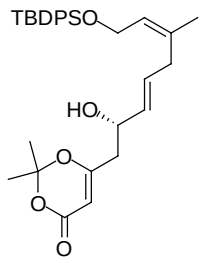
A solution of the TBDPS-protected tin compound (6.00 g, 10.0 mmol), (*E*)-4-bromo-1,1-dimethoxy-but-2-ene (1.82 g, 10.0 mmol), bis(acetonitrile)dichloropalladium(II) (130 mg, 0.50 mmol) and triphenylphosphine (66 mg, 0.25 mmol) in $CHCl_3$ (40 ml, passed through a short basic alumina column prior to the reaction) was stirred at 65 °C for 22 h. After the reaction mixture was cooled to room temperature, a mixture of HCOOH/CH_2Cl_2 (27.0 mL, 1:2) was added. The suspension was stirred for another 1 h at room temperature, diluted with Et_2O (60 ml) and poured into a separatory funnel containing saturated NH_4Cl solution (60 ml). The two layers were separated and the aqueous layer was extracted with Et_2O (60 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography (5% EtOAc in hexanes) to give the aldehyde (2.95 g, 80%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.45 (d, J = 7.8 Hz, 1H), 7.71 (m, 4H), 7.42 (m, 6H), 6.61 (dt, J = 15.5, 6.6 Hz, 1H), 6.01 (ddt, J = 15.5, 7.8, 1.5 Hz, 1H), 5.60 (t, J = 5.9 Hz, 1H), 4.19 (d, J = 6.4 Hz, 2H), 2.86 (d, J = 3.6 Hz, 2H), 1.72 (d, J = 1.2 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 155.2, 135.8, 134.0, 133.7, 133.0, 129.9, 127.8, 60.8, 35.7, 27.0, 23.6, 19.4; IR (neat) 3061, 2960, 2923, 2865, 1687, 1469, 1425, 1389, 1112, 1047, 974, 814, 698; HRMS (EI): *m*/*z* calcd for $C_{20}H_{21}O_2Si$ (M-C_4H_9) 321.1311, found 321.1307.



(2,2-Dimethyl-6-methylene-6*H*-[1,3]dioxin-4-yloxy)trimethylsilane

To a stirring solution of anhydrous diisopropylamine (2.22 g, 22.0 mmol) in THF (20 mL) at 0 ºC was added *n*-butyllithium (1.6 M in hexanes, 13.8 ml, 22.0 mmol) dropwise over 15 min The reaction mixture was stirred at 0 ºC for 30 min, then the temperature was decreased to -78 ºC. 2,2,6-Trimethyl-[1,3]dioxin-4-one (2.84 g, 20.0 mmol) was added dropwise over 10 min and the resulting bright orange suspension was stirred at -78 ºC for 60 min. Chlorotrimethylsilane (2.61 g, 24.0 mmol, freshly distilled) was added over 10 min and the reaction mixture was stirred for an additional 30 min at -78 ºC, then was warmed to room temperature. The reaction mixture was then filtered through a pad

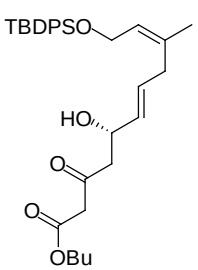
of oven dried anhydrous Na_2SO_4 and concentrated. The resulting residue was purified by Kugelrohr distillation (65 ºC at 0.2 mm Hg, temperature must not exceed 65 ºC in order to avoid decomposition) to afford the desired product as a bright orange liquid (3.76 g, 88%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.65 (s, 1H), 4.08 (s, 1H), 3.89 (s, 1H), 1.56 (s, 6H), 0.26 (s, 9H).



6-[(*S*,3*E*,6*Z*)-8-(*tert*-Butyldiphenylsilanyloxy)-2-hydroxy-6-methylocta-3,6-dienyl]-2,2-dimethyl-[1,3]dioxin-4-one (16)

To a stirring solution of bis-phosphoramide **15** (51 mg, 60 μmol) and aldehyde **13** (2.27 g, 6.00 mmol) in CH_2Cl_2 (21 mL) at -78 ºC was added silicon tetrachloride (0.76 mL, 6.6 mmol). Silyl ketene acetal **14** (1.41 g, 6.60 mmol) in CH_2Cl_2 (5 mL) was added dropwise via syringe pump over 5 h. The reaction mixture was stirred at -78 ºC for 18 h, then was transferred via cannula to a stirring room temperature solution of 1M KH_2PO_4 (60 mL). The resulting biphasic mixture was allowed to warm to room temperature before filtration through a pad of celite. The filtrate was washed with 10% KF (40 mL) and the organic layer was dried ($MgSO_4$), filtered and concentrated. The resulting residue was purified by flash chromatography (30% EtOAc in hexanes) to afford the desired product (2.08 g, 67%, 83% based on recovered aldehyde **13**) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 4H), 7.42 (m, 6H), 5.55–5.53 (m, 3H), 5.28 (s, 1H), 4.31 (m, 1H), 4.19 (d, *J* = 6.4 Hz, 2H), 2.59 (d, *J* = 6.3 Hz, 2H), 2.37 (d, *J* = 3.7 Hz, 1H), 2.34 (d, *J* = 1.8 Hz, 1H), 1.67 (m, 9H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 160.9, 135.9, 135.9, 135.1, 134.4, 132.6, 130.3, 129.8, 127.9, 125.2, 106.1, 95.6, 69.7, 61.0, 41.9, 35.2, 27.2, 25.6, 25.2, 23.5, 19.4; IR (neat) 3454, 3069, 3047, 2996, 2923, 2850, 1723, 1629, 1425, 1367, 1280, 1200, 1098, 952, 901, 814, 734, 705 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{27}H_{31}O_5Si$ (M-C_4H_9) 463.1941, found 463.1941. $[\alpha]_D^{23}$ = -9.14º ($CHCl_3$, *c* 1.01)

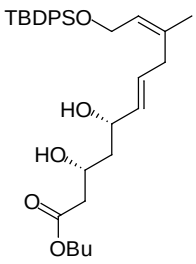
The ee was determined to be 93% by HPLC analysis using a chiracel OD-H column. Conditions: Hexanes:*i*-PrOH 95:5, 0.90 mL/min. Retention time: minor 13.9, major 15.6



(*S*,6*E*,9*Z*)-11-(*tert*-Butyldiphenylsilanyloxy)-5-hydroxy-9-methyl-3-oxoundeca-6,9-dienoic acid butyl ester

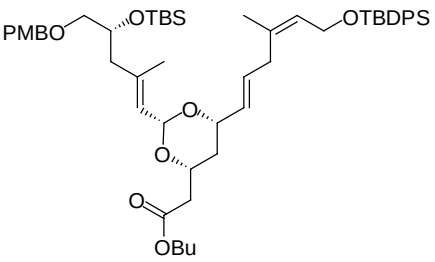
16 (0.62 g, 1.19 mmol) in anhydrous 1-butanol (23 mL, degassed by passing a stream of N_2 through for 2h prior to reaction) was immersed into a preheated oil bath (140 ºC) and allowed to reflux for 1h. Upon cooling to room temperature and concentrating under reduced pressure, the resulting residue was purified by flash chromatography (20% EtOAc in hexanes) to afford the desired product (0.47 g, 74%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 4H), 7.42 (m, 6H), 5.49-5.34 (m, 3H), 4.49 (m, 1H), 4.20 (d, *J* = 6.4 Hz, 2H), 4.14 (t, *J* = 6.7 Hz, 2H), 3.45 (s, 2H), 2.68-2.57 (m, 4H), 1.68 (s, 3H), 1.62 (m, 2H), 1.36 (m, 2H), 1.05 (s, 9H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 167.1, 135.8, 135.2, 134.1, 131.8, 129.8, 129.4, 127.8, 125.9, 68.3, 65.6, 60.8, 50.1, 49.8, 35.1, 30.6, 27.0, 23.5, 19.3, 19.2, 13.8; IR (neat) 3476, 3127, 3061, 2945, 1956, 1890, 1818, 1738, 1650, 1465, 1419, 1306,

1111, 973, 825, 784, 743, 702, 609 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{32}H_{44}O_5Si$ (M^+) 536.2958, found 536.2936; $[\alpha]_D^{23}$ -9.87º ($CHCl_3$, *c* 1.07).



(3*R*,5*S*,6*E*,9*Z*)-11-(*tert*-Butyldiphenylsilanyloxy)-3,5-dihydroxy-9-methylundeca-6,9-dienoic acid butyl ester (7)

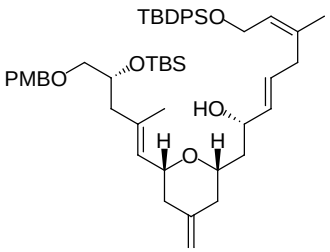
To a stirring solution of the β-hydroxy keto ester (1.08 g, 2.02 mmol) in THF (15 mL) at -78 ºC was added diethylmethoxyborane (0.22 g, 2.2 mmol). The reaction mixture was stirred for 30 min, then $NaBH_4$ (0.45 g, 12.14 mmol) was added in bulk. The reaction mixture was stirred at -78 ºC for 18 h before being quenched with saturated NH_4Cl (5 mL). The reaction mixture was warmed to room temperature, diluted with Et_2O and acidified to pH 1 by the addition of 1N HCl. The two layers were separated and the aqueous layer was washed with Et_2O (3 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The resulting residue was azeotroped with MeOH (3 x 25 mL) and purified by flash chromatography (50% EtOAc in hexanes) to afford the desired product (0.90 g, 83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 4H), 7.41 (m, 6H), 5.44 (m, 3H), 4.29 (m, 2H), 4.21 (d, *J* = 5.5 Hz, 2H), 4.12 (t, *J* = 6.6 Hz, 2H), 2.57 (d, *J* = 6.0 Hz, 2H), 2.47 (d, *J* = 3.6 Hz, 1H), 2.45 (d, *J* = 0.88 Hz, 1H), 1.68 (s, 3H), 1.65-1.50 (m, 4H), 1.35 (m, 2H), 1.05 (s, 9H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 135.8, 135.5, 134.1, 133.4, 129.7, 128.7, 127.7, 125.8, 72.7, 68.5, 64.8, 60.8, 42.8, 41.8, 35.1, 30.7, 27.0, 23.6, 19.3, 19.3, 13.9; IR (neat) 3403, 3069, 3040, 2734, 1963, 1890, 1818, 1730, 1672, 1592, 1425, 1258, 1112, 814 cm^{-1}; HRMS (EI): *m/z* calcd for $C_{28}H_{35}O_4Si$ ($M–C_4H_9$, H_2O) 463.2305, found 463.2311; $[\alpha]_D^{23}$ = -8.57º ($CHCl_3$, *c* 1.08).



{2-((4*R*,6*S*)-[(*R*,*E*)-4-(*tert*-Butyldimethylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methylpent-1-enyl]-6-[(1*E*,4*Z*)-6-(*tert*-butyldiphenylsilanyloxy)-4-methylhexa-1,4-dienyl]-[1,3]dioxan-4-yl)}acetic acid butyl ester (17)

To a stirring solution of **7** (310 mg, 0.58 mmol) in anhydrous DMF (4.5 mL) was added imidazole (200 mg, 2.92 mmol). The reaction mixture was stirred for 5 min and chlorotrimethylsilane (140 mg, 1.28 mmol) was added, followed by 4-dimethylaminopyridine (4 mg). The reaction mixture was stirred for 18h, then quenched with ice chips. The reaction mixture was extracted into hexanes, and the water layer was washed with hexanes (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The resulting residue was dissolved in CH_2Cl_2 (4.5 mL) and the temperature was decreased to -78 ºC. **6** (220 mg, 0.583 mmol) and TMSOTf (13 mg, 0.058 mmol) were added, then the reaction mixture was stirred for 45 min and quenched with pyridine (6 mg, 0.073 mmol). The solution was warmed to room temperature and washed with saturated $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash

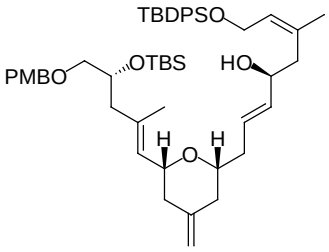
chromatography (5% EtOAc in hexanes) to afford the desired acetal (438 mg, 83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (m, 4H), 7.41 (m, 6H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.51-5.42 (m, 3H), 5.33 (d, *J* = 5.9 Hz, 1H), 5.23 (d, *J* = 6.1 Hz, 1H), 4.44 (s, 2H), 4.20 (d, *J* = 6.3 Hz, 2H), 4.09 (t, *J* = 6.6 Hz, 4H), 3.94 (m, 1H), 3.80 (s, 3H), 3.36 (d, *J* = 5.3 Hz, 2H), 2.66 (dd, *J* = 15.7, 7.0 Hz, 1H), 2.59 (d, *J* = 6.1 Hz, 2H), 2.43 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.26 (dd, *J* = 13.5, 5.3 Hz, 1H), 2.14 (dd, *J* = 13.5, 6.9 Hz, 1H), 1.73 (s, 3H), 1.67 (s, 3H), 1.61 (m, 4H), 1.34 (m, 2H), 1.05 (s, 9H), 0.93 (t, *J* = 7.6 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 159.2, 139.4, 135.8, 135.4, 134.1, 130.8, 130.7, 129.7, 129.4, 127.8, 125.7, 125.3, 113.8, 98.4, 76.4, 74.5, 73.1, 72.8, 70.5, 64.7, 60.8, 55.4, 44.8, 41.1, 36.6, 35.2, 31.8, 30.8, 27.0, 26.1, 23.5, 22.8, 19.3, 18.3, 18.2, 13.9, -4.3, -4.6; IR (neat) 3061, 2952, 2923, 2850, 1730, 1672, 1607, 1505, 1469, 1381, 1301, 1250, 1120, 1032, 996, 836, 785, 698 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{53}H_{78}O_8Si_2Na$ (M + Na) 921.5133, found 921.5137; $[\alpha]_D^{23}$ = -4.25º ($CHCl_3$, *c* 1.00).



(2*S*,3*E*,6*Z*)-1-((2*S*,6*R*)-{6-(*R*,*E*)-[4-(*tert*-Butyldimethylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methylpent-1-enyl]-4-methylenetetrahydropyran-2-yl})-8-(*tert*-butyldiphenylsilanyloxy)-6-methylocta-3,6-dien-2-ol (18)

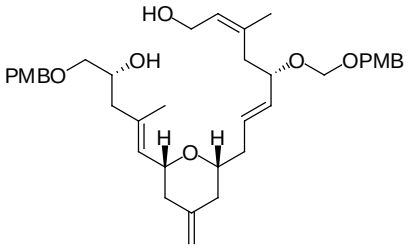
$CeCl_3$ (1.56 g, 6.34 mmol) was dried with vigorous stirring under vacuum (0.2 mm Hg) at 150 ºC for 2 h, then cooled to room temperature, flushed with N_2 and suspended in THF (9.5 mL). The suspension was sonicated for 2 h, then transferred to a -78 ºC cold bath. Trimethylsilylmethylmagnesium chloride (1.0 M in Et_2O, 6.34 mL, 6.34 mmol) was added over 20 min to form a pale yellow suspension, which was stirred for 1 h. **17** (341 mg, 0.380 mmol) in THF (1.0 mL) was added dropwise, and the reaction mixture was allowed to gradually warm to room temperature while stirring for 18h. The temperature was then decreased to -78 ºC and the reaction was quenched by the dropwise addition of EtOAc (3.4 mL). After stirring for 20 min, the reaction mixture was warmed to room temperature. Saturated $NaHCO_3$ (15 mL) was added and the mixture was diluted with Et_2O (20 mL). The two layers were separated and the aqueous layer was washed with Et_2O (2 x 30 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was dissolved in CH_2Cl_2 (17.0 mL), then anhydrous $MgSO_4$ (180 mg, 0.79 mmol) was added. After 5 min, pyridinium triflate (113 mg, 0.493 mmol, azeotropically dried with benzene) was added. The white suspension was stirred for 1.5 h, then quenched with saturated $NaHCO_3$. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography (10% - 20% EtOAc in hexanes) to afford the desired product (239 mg, 75%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 1.4 Hz, 2H), 7.68 (d, *J* = 1.5 Hz, 2H), 7.40 (m, 6H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.46 (m, 2H), 5.38 (dd, *J* = 15.6, 6.2 Hz, 1H), 5.22 (d, *J* = 7.5 Hz, 1H), 4.73 (s, 2H), 4.45 (s, 2H), 4.24 (ddd, *J* = 9.2, 6.2, 2.2 Hz, 1H),

4.20 (d, *J* = 6.4 Hz, 2H), 4.00 (ddd, *J* = 11.0, 7.8, 2.5 Hz, 1H), 3.95 (m, 1H), 3.80 (s, 3H), 3.53 (m, 1H), 3.32 (d, *J* = 5.2 Hz, 2H), 2.57 (d, *J* = 6.0 Hz, 2H), 2.26 (dd, *J* = 13.5, 6.3 Hz, 1H), 2.20 (s, 1H), 2.13 (m, 3H), 2.00 (m, 2H), 1.69 (s, 3H), 1.68 (s, 3H), 1.06 (s, 9H), 0.88 (s, 9H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 143.8, 137.0, 135.7, 135.7, 134.0, 133.6, 130.7, 129.7, 129.4, 128.0, 127.7, 125.5, 113.8, 109.2, 78.8, 75.7, 74.0, 73.0, 72.2, 70.8, 60.8, 55.4, 44.8, 43.4, 40.9, 40.6, 35.1, 27.0, 26.0, 23.5, 19.3, 18.3, 18.0, -4.3, -4.5; IR (neat) 3476, 3076, 2930, 2894, 2850, 1672, 1614, 1585, 1512, 1469, 1425, 1352, 1287, 1250, 1105, 1040, 843, 770, 698 cm $^{-1}$; HRMS (ESI): *m/z* calcd for $C_{51}H_{74}O_6Si_2Na$ (M + Na) 861.4922, found 861.4961; $[\alpha]_D^{23}$ = +0.79º ($CHCl_3$, *c* 1.01).



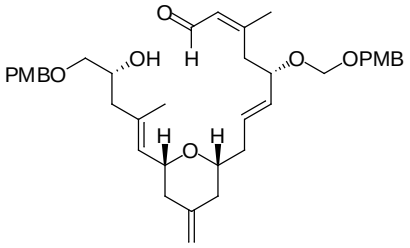
(2*E*,4*S*,6*Z*)-1-((2*R*,6*R*)-{6-(*R*,*E*)-[4-(*tert*-Butyldimethylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methylpent-1-enyl]-4-methylenetetrahydropyran-2-yl})-8-(*tert*-butyldiphenylsilanyloxy)-6-methylocta-2,6-dien-4-ol (19)

To a stirring solution of **18** (430 mg, 0.51 mmol) in THF (10 mL) at 0 ºC were added phenylselenocyanate (93 mg, 0.51 mmol) and tri-*n*-butylphosphine (104 mg, 0.51 mmol). The reaction mixture was stirred at room temperature for 3 h, then concentrated. The resulting residue was purified by flash chromatography (50% - 80% CH_2Cl_2 in hexanes) to yield the desired selenide. The selenide was dissolved in CH_2Cl_2 (7 mL) and the temperature was decreased to -30 ºC. Pyridine (2.3 mL) was added, followed by 30% H_2O_2 (3.3 mL), and the reaction mixture was stirred for 1 h, then quenched with saturated $Na_2S_2O_3$ (15 mL). The reaction mixture was warmed up to room temperature and extracted into Et_2O (15 mL). The aqueous layer was washed with Et_2O (2 x 15 mL) and the combined organic layer was washed with 10% HCl (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography (5% - 20% EtOAc in hexanes) to afford the desired product (0.266 g, 62%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (at, *J* = 7.1 Hz, 4H), 7.44 (m, 6H), 7.28 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 5.72 (dt, *J* = 15.3, 4.1 Hz, 1H), 5.63 (t, *J* = 6.5 Hz, 1H), 5.54 (dd, *J* = 15.3, 6.4 Hz, 1H), 5.29 (d, *J* = 7.5 Hz, 1H), 4.75 (s, 2H), 4.48 (s, 2H), 4.23 (m, 1H), 4.16 (m, 1H), 3.98 (m, 2H), 3.84 (s, 3H), 3.38 (d, *J* = 5.2 Hz, 2H), 3.34 (m, 1H), 2.37 (m, 4H), 2.23 (m, 2H), 2.14 (m, 2H), 2.06 (m, 2H), 1.93 (m, 1H), 1.80 (s, 3H), 1.72 (s, 3H), 1.65 (s, 1H), 1.11 (s, 9H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 144.6, 136.0, 135.6, 133.6, 130.6, 129.6, 129.2, 128.6, 127.7, 127.4, 127.2, 113.6, 108.8, 77.9, 75.8, 74.1, 73.1, 70.5, 70.2, 60.0, 55.2, 45.2, 41.0, 40.7, 40.2, 39.4, 26.8, 25.9, 23.9, 19.1, 18.4, 18.0, -4.2, -4.5; IR (neat) 3461, 3083, 2923, 2894, 2850, 1650, 1607, 1505, 1469, 1425, 1360, 1250, 1120, 836, 770, 741, 705 cm $^{-1}$; HRMS (ESI): *m/z* calcd for $C_{51}H_{74}O_6Si_2Na$ (M + Na) 861.4922, found 861.4948; $[\alpha]_D^{23}$ = -2.32º (PhH, *c* 1.82).



(*S*,2*Z*,6*E*)-5-((4-Methoxybenzyloxy)methoxy)-8-((2*R*,6*R*)-6-((*R*,*E*)-5-(4-methoxybenzyloxy)-4-hydroxy-2-methylpent-1-enyl)tetrahydro-4-methylene-2*H*-pyran-2-yl)-3-methylocta-2,6-dien-1-ol

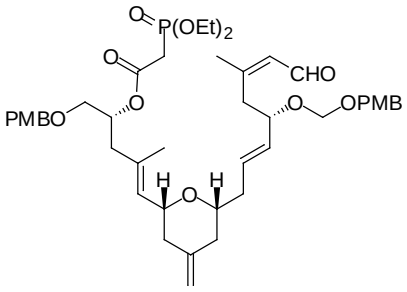
Under nitrogen, a solution of **19** (176 mg, 0.210 mmol, azeotropically dried with benzene) in CH_2Cl_2 (2.0 ml) at room temperature was treated with 4-dimethylaminopyridine (0.051 g, 0.42 mmol), anhydrous diisopropylethylamine (0.22 mL, 1.26 mmol) and 4-methoxybenzyloxymethyl chloride (196 mg, 1.05 mmol). After 1.5 h, anhydrous diisopropylethylamine (6.0 equiv) and 4-methoxybenzyloxymethyl chloride (5.0 equiv) were added. After another 1.5 h, anhydrous diisopropylethylamine (4.0 equiv) was added followed by 4-methoxybenzyloxymethyl chloride (3.0 equiv). After the reaction mixture was stirred for further 3 h, TLC showed the complete consumption of the starting material **19**. The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with 10% HCl (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography (10% - 15% EtOAc in Hexane) gave the desired product as a colorless oil. The resulting product was dissolved in anhydrous THF (6.0 mL) and cooled to 0 °C. Pyridine (0.50 mL) was added followed by dropwise addition of HF·pyridine (0.50 mL). The reaction mixture was warmed up to room temperature and stirred for 7 h, then quenched by dropwise addition of saturated $NaHCO_3$ at 0 °C. The mixture was extracted with EtOAc (3 x 10 mL). The organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The resulting residue was azeotroped with benzene to remove the excess pyridine and purified by flash chromatography (50% - 70% EtOAc in hexanes) to give the desired diol (102 mg, 80%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.70 (m, *2*H), 5.40 (dd, *J* = 15.5, 8.1 Hz, 1H), 5.29 (d, *J* = 7.6, 1H), 4.74 (m, 3H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.60 (d, *J* = 11.1 Hz, 1H), 4.49 (s, 2H), 4.39 (d, *J* = 11.3 Hz, 1H), 4.19 (m, 1H), 4.12 (m, 1H), 4.04-3.88 (m, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.44 (dd, *J* = 9.5, 3.8 Hz, 1H), 3.35 (dd, *J* = 9.5, 6.8 Hz, 2H), 2.68 (br s, 2H), 2.56 (dd, *J* = 13.4, 8.7 Hz, 1H), 2.36 (dd, *J* = 14.5, 8.2 Hz, 1H), 2.74 (m, 1H), 2.22-2.16 (m, 4H), 2.12 (m, 1H), 2.04-1.89 (m, 2H), 1.81 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 144.4, 136.8, 135.8, 132.0, 130.8, 130.4, 130.0, 129.8, 129.6, 128.8, 127.4, 114.1, 109.0, 91.1, 77.9, 75.8, 74.3, 73.9, 73.3, 69.4, 68.6, 58.5, 55.5, 44.0, 40.9, 40.4, 39.3, 38.6, 24.2, 17.3; IR (neat) 3418, 3070, 2927, 2854, 1651, 1612, 1586, 1513, 1463, 1442, 1379, 1360, 1302, 1247, 1173, 1092, 1032, 819; HRMS (ESI): *m*/*z* calcd for $C_{38}H_{52}O_8Na$ (M + Na) 659.3560, found 659.3547; $[\alpha]_D^{23}$ = -69.1° (PhH, *c* 0.75).



(*S*,2*Z*,6*E*)-5-((4-Methoxybenzyloxy)methoxy)-8-((2*R*,6*R*)-6-((*R*,*E*)-5-(4-methoxybenzyloxy)-4-hydroxy-2-methylpent-1-enyl)tetrahydro-4-methylene-2*H*-pyran-2-yl)-3-methylocta-2,6-dienal (20)

A solution of the diol (102 mg, 160 μmol) in CH_2Cl_2 (3.6

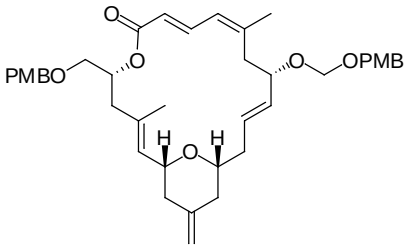
ml) at room temperature was treated with TEMPO (2.5 mg, 16 μmol) followed by bis(acetoxy)iodobenzene (103 mg, 320 μmol). The mixture was stirred for 1.7 h and diluted with CH_2Cl_2 (5.0 ml). A saturated $Na_2S_2O_3$/$NaHCO_3$ solution (1:1, 16.0 ml) was added and the biphasic mixture was separated after stirring for 20 min The aqueous layer was extracted with CH_2Cl_2 (3 x 15 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. Gradient flash chromatography (50% - 70% EtOAc in hexanes) gave the aldehyde (89.1 mg, 87%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.94 (d, *J* = 8.1 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.98 (d, *J* = 8.0 Hz, 1H), 5.74 (m, 1H), 5.39 (dd, *J* = 15.5, 8.1 Hz, 1H), 5.28 (d, *J* = 7.5, 1H), 4.73 (m, 3H), 4.61 (d, *J* = 7.0 Hz, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.49 (s, 2H), 4.37 (d, *J* = 11.4 Hz, 1H), 4.27 (m, 1H), 3.96 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.45 (dd, *J* = 9.5, 3.4 Hz, 1H), 3.32 (m, 2H), 2.99 (dd, *J* = 13.2, 8.4 Hz, 1H), 2.58 (dd, *J* = 13.2, 4.8 Hz, 1H), 2.37 (m, 2H), 2.30-2.10 (m, 4H), 2.03 (s, 3H), 1.92 (m, 2H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.5, 159.7, 159.6, 144.4, 135.6, 131.4, 131.3, 130.5, 130.4, 130.0, 129.7, 129.6, 128.8, 114.1, 109.0, 91.3, 75.8, 75.1, 73.9, 73.3, 69.5, 68.7, 55.5, 43.8, 40.9, 40.3, 39.3, 39.2, 26.2, 17.4; IR (neat) 3472, 2936, 2894, 1674, 1612, 1586, 1514, 1463, 1442, 1396, 1302, 1248, 1209, 1175, 1093, 1032, 893, 848, 820; HRMS (ESI): *m*/*z* calcd for $C_{38}H_{50}O_8Na$ (M + Na) 657.3403, found 657.3384; $[\alpha]_D^{23}$ = -54.1° (PhH, *c* 0.53).



(Diethoxyphosphoryl)acetic acid (*R*)-4-((2*R*,6*R*)-{6-((2*E*,4*S*,6*Z*)- [4-(4-methoxybenzyloxymethoxy)-6-methyl-8-oxoocta-2,6-dienyl])-4-methylenetetrahydropyran-2-yl})-1-(4-methoxybenzyloxymethyl)-[(*E*)-3-methylbut-3-en]yl ester

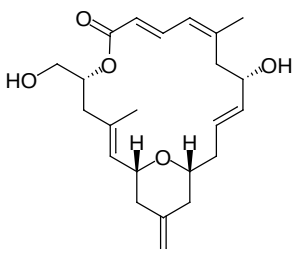
To a solution of aldehyde **20** (89 mg, 140 μmol, azeotropically dried with benzene) and diethylphosphonoacetic acid (54 mg, 280 μmol) in CH_2Cl_2 (5.0 mL) at room temperature were added 4-dimethylaminopyridine (17 mg, 140 μmol) and 1,3-dicyclohexylcarbodiimide (87 mg, 420 μmol, dissolved in 1.0 mL of CH_2Cl_2). The resulting cloudy reaction mixture was stirred for 15 min and concentrated in vacuo. The white residue was taken up in hexanes/Et_2O (1:1, 6.0 ml) and filtered through a pad of celite. The filtrate was concentrated in vacuo. Gradient flash chromatography (70% - 80% EtOAc in hexanes) gave the corresponding phosphonoester (109 mg, 95%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (d, *J* = 8.0 Hz, 1H), 7.31-7.24 (m, 4H), 6.91 (m, 4H), 6.02 (d, *J* = 7.9 Hz, 1H), 5.77 (m, 1H), 5.43 (dd, *J* = 15.4, 8.1 Hz, 1H), 5.28 (d, *J* = 7.8 Hz, 1H), 5.21 (m, 1H), 4.76 (m, 3H), 4.65 (d, *J* = 7.0 Hz, 1H), 4.56 (d, *J* = 11.3 Hz, 1H), 4.51 (s, 1H), 4.48 (s, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.30 (m, 1H), 4.19 (m, 4H), 3.98 (m, 1H), 3.84 (s, 6H), 3.53 (d, *J* = 4.4 Hz, 2H), 3.34 (m, 1H), 3.06 (s, 1H), 3.03 (m, 1H), 2.99 (s, 1H), 2.61 (dd, *J* = 13.2, 4.6 Hz, 1H), 2.44-2.34 (m, 3H), 2.29 (m, 1H), 2.22-2.11 (m, 2H), 2.06 (s, 3H), 1.93 (m, 2H), 1.74 (s, 3H), 1.36 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.4, 165.5 (*J* = 5.6 Hz, 1C), 159.6, 159.5, 144.2, 134.2, 131.5, 131.2, 130.4, 130.2, 130.0, 129.7, 129.5, 129.4, 114.1,

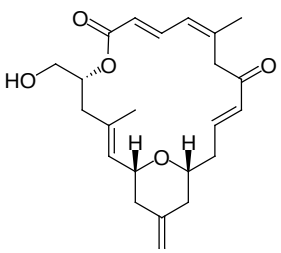
114.0, 109.1, 91.3, 75.6, 75.0, 73.0, 72.7, 70.1, 69.4, 62.8 (*J* = 6.4 Hz, 2C), 55.4, 40.9, 40.7, 40.1, 39.2, 39.2, 34.6 (*J* = 133.6 Hz, 1C), 26.1, 17.2, 16.5 (*J* = 6.0 Hz, 2C); IR (neat) 2980, 2934, 2856, 1736, 1703, 1675, 1612, 1586, 1514, 1444, 1367, 1302, 1249, 1175, 1162, 1096, 1028, 971, 892, 820; HRMS (ESI): *m*/*z* calcd for $C_{44}H_{61}O_{12}PNa$ (M + Na) 835.3798, found 835.3779; $[\alpha]_D^{23}$ = -36.1° (PhH, *c* 1.45).



(1*R*,2*E*,5*R*,8*E*,10*Z*,13*S*,14*E*,17*R*)-13-((4-Methoxybenzyloxy)methoxy)-5-((4-methoxybenzyloxy)methyl)-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraen-7-one (21)

To a solution of the phosphonoester (40 mg, 50 μmol, azeotropically dried with benzene) in THF (10.0 mL) at -78 °C was added dropwise sodium hexamethyldisilylamide (0.05 mol/L, 1.2 mL). The pale yellow reaction mixture was stirred at -78 °C for 10 min, then at 0 °C for 1.5 h. Saturated NH_4Cl solution (5.0 mL) was added and the mixture was poured into water (4.0 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography (25% EtOAc in hexanes) produced the macrocycle (24 mg, 73%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 15.1, 11.7 Hz, 1H), 7.25 (m, 4H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.04 (d, *J* = 12.1 Hz, 1H), 5.78 (d, *J* = 15.0 Hz, 1H), 5.60 (ddd, *J* = 15.1, 7.9, 4.6 Hz, 1H), 5.38 (dd, *J* = 15.6, 8.5 Hz, 1H), 5.27 (m, 2H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.72 (s, 2H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.45 (d, *J* = 11.3 Hz, 1H), 4.17 (m, 1H), 3.92 (m, 1H), 3.81 (s, 6H), 3.58 (dd, *J* = 10.3, 5.2 Hz, 1H), 3.51 (dd, *J* = 10.2, 5.6 Hz, 1H), 3.31 (m, 1H), 2.60 (d, *J* = 5.1 Hz, 2H), 2.35 (m, 2H), 2.28-1.90 (m, 6H), 2.00 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 159.5, 159.5, 147.3, 144.9, 140.3, 133.0, 132.3, 130.6, 130.3, 130.1, 130.0, 129.7, 129.5, 126.0, 120.1, 114.1, 114.0, 108.7, 91.6, 75.9, 73.1, 71.4, 69.6, 69.5, 55.5, 55.5, 41.8, 41.1, 40.9, 39.0, 38.5, 26.0, 16.7; IR (neat) 2934, 2856, 2837, 1706, 1635, 1612, 1514, 1463, 1442, 1365, 1302, 1248, 1171, 1091, 1034, 973, 888, 819; HRMS (ESI): *m*/*z* calcd for $C_{40}H_{50}O_8Na$ (M + Na) 681.3403, found 681.3419; $[\alpha]_D^{23}$ = -89.8° (PhH, *c* 0.70).

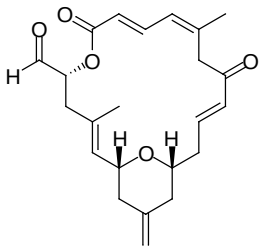




(1*R*,2*E*,5*R*,8*E*,10*Z*,13*S*,14*E*,17*R*)-13-Hydroxy-5-(hydroxymethyl)-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraen-7-one and (1*R*,2*E*,5*R*,8*E*,10*Z*,14*E*,17*R*)-5-(Hydroxymethyl)-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraene-7,13-dione

To a solution of **21** (6 mg, 9 μmol) in CH_2Cl_2 (0.5 mL) at room temperature was added pH 7 buffer (1 drop) followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (12 mg, 55 μmol, freshly recrystallized from benzene). The greenish mixture was stirred at room temperature for 6 h, then quenched with saturated $NaHCO_3$ (3.0 ml). The mixture was extracted with CH_2Cl_2 (3 x 10 mL) and the combined extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. Gradient flash chromatography (30% - 60% EtOAc in hexanes) gave the C(7) alcohol (2.2 mg, 63%) and C(7) ketone (0.5 mg, 14%) as colorless oils. C(7) alcohol: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 15.2, 11.6 Hz, 1H), 6.08 (d, *J* = 11.6 Hz, 1H), 5.78 (d, *J* = 15.1 Hz, 1H), 5.64 (m, 2H), 5.30 (d, *J* = 7.7 Hz, 1H), 5.17 (m, 1H), 4.74 (s, 2H), 4.24 (m, 1H), 3.93 (ddd, 10.6, 2.4, 2.4 Hz, 1H), 3.74 (d, *J* = 4.6 Hz, 2H), 3.33 (m, 1H), 2.56 (m, 2H), 2.41 (dd, *J* = 14.2, 9.6 Hz, 1H), 2.32-2.27 (m, 2H), 2.24-2.14 (m, 4H), 2.05-1.90 (m, 1H), 2.00 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 147.8, 144.7, 141.0, 133.8, 133.6, 129.9, 129.1, 125.9, 119.6, 108.9, 75.8, 72.8, 72.6, 65.6, 41.4, 41.0, 40.8, 40.4, 38.8, 29.9, 25.7, 16.8; IR (neat) 3422, 2924, 2852, 1701, 1686, 1632, 1439, 1378, 1359, 1264, 1157, 1047, 974, 888; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{32}O_5Na$ (M + Na) 411.2147, found 411.2142; $[\alpha]_D^{23}$ = -49.0° (PhH, *c* 0.20).

(+)-Dactylolide (1)



A solution of the mixture of the C(7) alcohol and C(7) ketone (3.1 mg, 8.0 μmol) in CH_2Cl_2 (1.0 mL) at room temperature was treated with $NaHCO_3$ powder (9 mg, 110 μmol) followed by Dess-Martin periodinane (20 mg, 48 μmol). The white suspension was stirred for 1 h and then quenched with saturated $NaHCO_3$/$Na_2S_2O_3$ (1:1, 4 mL). After stirred for 30 min, the biphasic mixture was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (20% - 50% EtOAc in hexanes) to give (+)-**1** as a white solid (2.4 mg, 77%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.64 (dd, *J* = 15.1, 11.6 Hz, 1H), 6.86 (ddd, *J* = 16.0, 8.7, 5.9 Hz, 1H), 6.17 (d, *J* = 11.6 Hz, 1H), 6.01 (d, *J* = 16.6 Hz, 1H), 5.98 (d, *J* = 15.2 Hz, 1H), 5.33 (dd, *J* = 11.4, 2.4 Hz, 1H), 5.25 (d, *J* = 8.0 Hz, 1H), 4.76 (br s, 2H), 4.00-3.95 (m, 1H), 3.96 (d, *J* = 14.1 Hz, 1H), 3.33 (dddd, *J* = 11.3, 9.4, 2.4, 2.4 Hz, 1H), 3.24 (d, *J* = 14.3 Hz, 1 H), 2.55 (d, *J* = 13.9 Hz, 1H), 2.39-2.28 (m, 3H), 2.18 (d, *J* = 13.3 Hz, 1H), 2.12 (d, *J* = 13.4 Hz, 1H), 1.99-1.94 (m, 1H), 1.97 (t, *J* = 12.3 Hz, 1H), 1.87 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 197.6, 166.5, 146.2, 144.2, 143.7, 140.6, 131.7, 131.2, 130.7, 125.8, 120.0, 109.5, 76.7, 76.0, 75.6, 45.1, 41.0, 40.7, 39.9, 39.8, 24.3, 16.2; IR (neat) 2924, 2852, 1720, 1668, 1636, 1434, 1356, 1280, 1145, 1085, 1050, 978, 890; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{28}O_5Na$ (M + Na) 407.1834, found 407.1831; $[\alpha]_D^{23}$ = +163° (MeOH, *c* 0.29).