Total Synthesis of (-)-Dictyostatin

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SUPPORTING INFORMATION

General Experimental Procedures.

^1H and ^{13}C NMR spectra were recorded at 25 °C on Varian Inova spectrometers at the indicated frequencies using CDCl_3 as the solvent unless otherwise indicated. Inverse detect spectra were obtained with a Varian 3mm PFG indirect detect probe with $j_{\text{N}^1\text{H}} = 8.3$ Hz and $^1J_{\text{CH}} = 130$ Hz. Coupling constants are reported in hertz, Hz. All non-aqueous reactions were run in flame-dried glassware under a dry N_2 atmosphere. Toluene, THF, CH_2Cl_2 , and Et_2O were obtained from Aldrich (Pure-Pac) and further dried by passage through activated alumina as described by Bergman and Grubbs.¹ All flash chromatography was performed with normal phase silica gel (Sorbent Technologies, 32-63 μm particle size, 60 Å pore size), following the general protocol of Still.²

Diisopropyl-{1-[2-(4-methoxy-benzyloxy)-1-methyl-ethyl]-allyloxy}-prop-1-ynyl-silane, **6**

To a stirred solution of oxazolidinone **5** (5.00 g, 17.30 mmol, 1.0 eq) in DMF (35 mL) was added imidazole (2.94 g, 43.35 mmol, 2.5 eq) and bromo(diisopropyl)propynyl silane (4.84 g, 20.76 mmol, 1.2 eq) and the reaction was warmed to rt. The reaction was stirred for 1 h and was then diluted with water (100 mL) and Et_2O (100 mL). The organic phase was dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% Et_2O /hexanes) to yield the intermediate silyl ether (7.40 g, 97%) as an oil.

^1H NMR (500 MHz, CDCl_3): δ 7.36 (t, $J = 7$ Hz, 2H), 7.30 (m, 1H), 7.25 (d, $J = 7$ Hz, 2H), 5.93 (m, 1H), 5.25 (dt, $J = 1.5, 17$ Hz, 1H), 5.15 (dt, $J = 1, 10.5$ Hz, 1H), 4.63 (m, 1H), 4.17 (m, 3H), 4.03 (m, 1H), 3.32 (dd, $J = 3, 13.5$ Hz, 1H), 2.80 (dd, $J = 9.5, 13$ Hz, 1H), 1.92 (s, 3H), 1.27 (d, $J = 7$ Hz, 3H), 1.01-1.08 (m, 12H), 0.96 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.77, 153.45, 139.03, 135.70, 129.71 (2C), 129.16 (2C), 127.53, 116.19, 105.31, 78.95, 76.38, 66.18, 55.96, 44.46, 38.01, 17.54, 17.43, 17.21, 17.04, 13.92, 13.35, 12.67, 5.01.

To a stirred solution of the intermediate silyl ether (5.00 g, 11.30 mmol, 1.0 eq) in THF (68 mL) at 0 °C was added a 1M solution of LiBH_4 in THF (45.20 mL, 4.0 eq). The reaction was stirred for 6h and was then quenched with saturated NH_4Cl . The organic phase was separated and then washed with water and saturated aqueous NaCl , dried over MgSO_4 , and concentrated *in vacuo*. The crude product was purified

¹ a) Alaimo, P. J.; Peters, D.W.; Arnold, J.; Bergman, R.G. *J. Chem. Educ.* **2001** 78 64. b) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R.K.; Timmers, F. J. *Organometallics* **1996**, 15, 151.

² Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, 43, 2923.

by flash chromatography (10% EtOAc/hexanes) to yield the intermediate alcohol (2.40 g, 78%) as an oil.

¹H NMR (400 MHz, CDCl₃): δ 5.87 (m, 1H), 5.24 (dt, *J* = 2, 17.2 Hz, 1H), 5.17 (dt, *J* = 1.6, 10.4 Hz, 1H), 4.52 (m, 1H), 3.66 (t, *J* = 10.8 Hz, 1H), 3.47 (m, 1H), 2.85 (b, 1H), 1.96 (m, 1H), 1.94 (s, 3H), 1.00 - 1.07 (m, 12H), 0.91 (m, 2H), 0.77 (d, *J* = 6.8 Hz, 3H); **¹³C NMR** (400 MHz, CDCl₃): 138.53, 115.46, 105.55, 79.18, 75.84, 65.16, 41.29, 17.57, 17.40, 17.34 (2C), 13.86, 13.17, 11.09, 4.97.

To a stirred solution of the intermediate alcohol (2.40 g, 8.80 mmol, 1.0 eq) in CH₂Cl₂ (35 mL) was added PMB-trichloroacetimidate (2.24 g, 7.92 mmol, 0.9 eq) and the solution was cooled to -10 °C. CSA (0.184 g, 0.792 mmol, 0.1 eq) was then added and the reaction warmed to rt. The reaction was stirred for 10 h and was then quenched with saturated NaHCO₃, the layers were separated, and the organic layer was dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% Et₂O/hexanes) to yield **6** (2.80 g, 82%) as an oil.

¹H NMR (500 MHz, CDCl₃): δ 7.31 (d, *J* = 9 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.84 (m, 1H), 5.22 (dt, *J* = 1.5, 17.5 Hz, 1H), 5.11 (dt, *J* = 1.8, 10.5 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 4.46 (m, 1H), 4.42 (d, *J* = 11.5 Hz, 1H), 3.83 (s, 3H), 3.61 (dd, *J* = 6, 9 Hz, 1H), 3.28 (dd, *J* = 7.5, 9 Hz, 1H), 1.96 (m, 1H), 1.904 (s, 1H), 1.0-1.1 (m, 14H), 0.95 (d, *J* = 7 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.24, 139.69, 131.21, 129.38 (2C), 114.81, 113.91 (2C), 104.64, 79.44, 79.54, 72.84, 72.66, 55.50, 40.30, 17.68, 17.57, 17.49, 13.89, 13.40, 12.09, 5.02 (2C); [α]_D -17.7 (*c* 0.5, CHCl₃); **IR** (thin film): 2989, 2120, 1247, 1066, 985, 911 cm⁻¹; **HRMS** (ESI): calculated for C₂₃H₃₆O₃SiNa⁺ 411.2325, found 411.2323.

3-Ethylidene-2,2-diisopropyl-5-[2-(4-methoxy-benzyloxy)-1-methyl-ethyl]-4-methyl-[1,2]oxasilolane, **7**

To a solution of Ti(*i*-PrO)₃Cl (0.503 g, 1.93 mmol, 3.0 eq) in Et₂O (6.40 mL) at -40 °C was added (siloxy)enyne **6** (0.25 g, 0.64 mmol, 1.0 eq) and a 2M solution of *i*-PrMgCl (1.93 mL, 3.86 mmol, 6.0 eq) via syringe pump over 2h. The reaction was stirred an additional 6h, quenched with saturated NH₄Cl (25 mL), and stirred with EtOAc (50 mL) for 1h. The mixture was filtered through Celite, the layers were separated, and the organic phase dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (40% CH₂Cl₂/hexanes) to yield siloxane **7** (0.162 g, 65%) as an oil.

¹H NMR (500 MHz, CDCl₃): δ 7.30 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.12 (qd, *J* = 3, 6 Hz, 1H), 4.75 (m, 1H), 4.48 (m, 1H), 3.83 (s, 3H), 3.59 (dd, *J* = 7.5, 9 Hz, 1H), 3.55 (dd, *J* = 2, 10 Hz, 1H), 3.43 (dd, *J* = 6.5, 8.5 Hz, 1H), 2.30 (m, 1H), 2.00 (m, 1H), 1.80 (dd, *J* = 2.5, 6.5 Hz, 3H), 1.07-1.16 (m, 5H), 1.03 (d, *J* = 7 Hz, 6H), 0.99 (d, *J* = 6.5 Hz, 6H), 0.91 (d, *J* = 6.5 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.21, 142.83, 131.82, 131.27, 129.36 (2C), 113.92, 83.24, 74.30, 73.01, 55.49, 42.24, 36.37, 20.79, 18.26, 17.83, 17.74, 17.65, 14.79, 13.52, 12.95, 9.86; [α]_D -21.1 (*c* 0.5, CHCl₃); **IR** (thin film): 2948, 1610, 1508, 1037, 832 cm⁻¹; **HRMS** (ESI) calculated for C₂₃H₃₈O₃SiNa⁺ 413.2482, found 413.2488.

Acrylic acid 1-[2-(4-methoxy-benzyloxy)-1-methyl-ethyl]-2-methyl-pent-3-enyl ester, **8**

To a stirred solution of siloxane **7** (0.162 g, 0.416 mmol, 1.0 eq) in DMF (2.10 mL) was added TBAF•H₂O (0.33 g, 1.25 mmol, 3.0 eq) and the reaction was heated to 75 °C for 6h. The reaction was cooled to rt and diluted with Et₂O and water. The organic phase was separated, dried over MgSO₄, filtered through a plug of silica with EtOAc, and concentrated *in vacuo*. This material was used directly in the next step.

¹H NMR (500 MHz, CDCl₃): δ 7.28 (d, *J* = 8 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.57 (m, 1H), 5.38 (ddd, *J* = 1.5, 8.5, 15 Hz, 1H), 4.47 (m, 2H), 3.83 (s, 3H), 3.56 (dd, *J* = 6, 9 Hz, 1H), 3.46 (m, 2H), 2.22 (m, 1H), 1.98 (m, 1H), 1.72 (dd, *J* = 1.5, 6 Hz, 3H), 0.95 (d, *J* = 7 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.35, 134.63, 130.73, 129.43 (2C), 126.89, 113.97 (2C), 75.82, 74.72, 73.19, 55.45, 41.15, 35.16, 18.31, 17.30, 10.02.

To a stirred mixture of the intermediate alcohol in CH₂Cl₂ (2.10 mL) at 0°C was added *i*-Pr₂NEt (0.108 g, 0.832 mmol, 2.0 eq), DMAP (0.001 g, 0.042 mmol, 0.1 eq) and acryloyl chloride (0.056 g, 0.624 mmol, 1.5 eq) and the reaction was warmed to rt. The reaction was stirred for 6h and was then quenched with saturated aq. NaHCO₃. The layers were separated and the organic phase was dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography to yield **8** (0.131 g, 95% over 2 steps) as an oil.

¹H NMR (400 MHz, CDCl₃): δ 7.25 (d, *J* = 8.4, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.36 (dd, *J* = 2, 17.2 Hz, 1H), 6.09 (dd, *J* = 10, 17.2 Hz, 1H), 5.79 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.33 (m, 2H), 4.97 (dd, *J* = 4.8, 7.2 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 3.80 (s, 3H), 3.31 (dd, *J* = 6, 8.8 Hz, 1H), 3.24 (dd, *J* = 6.8, 8.8 Hz, 1H), 2.38 (m, 1H), 2.09 (m, 1H), 1.59 (d, *J* = 6 Hz, 3H), 0.95 (d, *J* = 5.2 Hz, 3H), 0.93 (d, *J* = 5.2 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 166.08, 159.31, 132.91, 130.80, 130.39, 129.51 (2C), 129.04, 126.17, 113.94 (2C), 77.43, 73.07, 72.77, 55.50, 39.71, 35.34, 18.13, 17.82, 11.89; [α]_D -4.5 (*c* 0.5, CHCl₃); **IR** (thin film): 2990, 2930, 2810, 1715, 1634, 1527, 1262, 974, 905 cm⁻¹; **HRMS** (ESI) calculated for C₂₀H₂₈O₄Na⁺ 355.1879, found 355.1890.

1-(4-Methoxy-benzyloxy)-2,4-dimethyl-octa-5,7-dien-3-ol, **9**

To a stirred solution of the diene **8** (0.131 g, 0.395 mmol, 1.0 eq) in toluene (8.00 mL) was added Grubbs 2nd generation catalyst (0.0335 g, 0.0395 mmol, 0.1 eq) and the reaction was warmed to 60 °C. The reaction was stirred for 3 h and was then cooled to -78 °C and a 1M solution of DIBAL-H in toluene (0.395 mL, 0.395 mmol, 1.0 eq) was added over 30 min via syringe pump. The reaction was stirred an additional 15 min, then quenched with saturated Na₂SO₄ (25 mL). The mixture was stirred with EtOAc (50 mL) 1 h, and was then filtered through Celite, and the layers were separated. The

organic phase was dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude material was used without further purification.

^1H NMR (500 MHz, CDCl_3): δ 7.26 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.67 (dt, J = 10.5, 16.5 Hz, 1H), 6.04 (t, J = 11 Hz, 1H), 5.55 (t, J = 10 Hz, 1H), 5.22 (d, J = 17 Hz, 1H), 5.12 (d, J = 10.5 Hz, 1H), 4.58 (d, J = 11 Hz, 1H), 4.46 (d, J = 11 Hz, 1H), 3.80 (s, 3H), 3.61 (dd, J = 7, 11 Hz, 1H), 3.53 (dd, J = 5, 10.5 Hz, 1H), 3.41 (dd, J = 4, 6 Hz, 1H), 3.00 (dt, J = 6, 10 Hz, 1H), 1.97 (m, 1H), 1.03 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 7 Hz, 3H).

To a stirred solution of methyltriphenylphosphonium bromide (0.423 g, 1.185 mmol, 3.0 eq) in THF (3.00 mL) at 0 °C was added a 1.6 M solution of butyllithium in hexanes (0.74 mL, 1.185 mmol, 3.0 eq) and the solution was stirred for 5 min. The solution was then cooled to -78 °C and the intermediate lactol was added as a solution in THF (0.21 mL). The reaction mixture was warmed to 0 °C for 1 h and was then quenched with 1/2 saturated NH_4Cl (25 mL). The mixture was extracted with EtOAc (3 x 25 mL), and the combined organic extracts dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% EtOAc/hexanes) to yield **9** (0.098 g, 85% over 3 steps) as an oil.

^1H NMR (500 MHz, CDCl_3): δ 7.28 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 6.65 (dt, J = 10.5, 17 Hz, 1H), 6.14 (t, J = 11 Hz, 1H), 5.40 (t, J = 10.5 Hz, 1H), 5.25 (d, J = 17 Hz, 1H), 5.15 (d, J = 10 Hz, 1H), 4.48 (d, J = 11.5 Hz, 1H), 4.45 (d, J = 11.5 Hz, 1H), 3.83 (s, 3H), 3.52-3.58 (m, 2H), 3.49 (dd, J = 5, 9 Hz, 1H), 2.80 (m, 1H), 2.00 (m, 1H), 0.99 (d, J = 7 Hz, 3H), 0.97 (d, J = 7 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): 159.39, 135.68, 132.48, 130.59, 129.50 (3C), 118.28, 113.99 (2C), 76.55, 74.64, 73.22, 55.51, 36.06, 35.30, 17.49, 10.18; **$[\alpha]_D$** -18.8 (*c* 0.5, CHCl_3); **IR** (thin film): 2989, 2853, 2721, 1613, 1524, 1253, 1037 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{18}\text{H}_{26}\text{O}_3\text{Na}^+$ 313.1774, found 313.1774.

2-(4-Methoxy-phenyl)-5-methyl-4-(1-methyl-penta-2,4-dienyl)-[1,3]dioxane, **10**

To a stirred solution of diene alcohol **9** (98 mg, 0.336 mmol, 1.0 eq) in CH_2Cl_2 (3.40 mL) at 0 ° over freshly activated 4 Å MS was added DDQ (76 mg, 0.336 mmol, 1.0 eq). The reaction was stirred for 30 min and was then quenched with pH = 7 buffer (25 mL). The mixture was extracted with CH_2Cl_2 (3 x 25 mL), and the combined organic extracts were dried with MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% Et_2O /hexanes) to provide **10** (73 mg, 78 %) as an oil.

^1H NMR (500 MHz, CDCl_3): δ 7.40 (d, J = 9 Hz, 2H), 6.87 (d, J = 9 Hz, 2H), 6.70 (dt, J = 10.8, 16.5 Hz, 1H), 6.07 (t, J = 11 Hz, 1H), 5.45 (s, 1H), 5.39 (t, J = 10 Hz, 1H), 5.21 (d, J = 17 Hz, 1H), 5.12 (d, J = 10 Hz, 1H), 4.07 (m, 2H), 3.81 (s, 3H), 3.61 (dd, J = 2, 9 Hz, 2H), 2.90 (m, 1H), 1.73 (m, 1H), 1.22 (d, J = 7 Hz, 3H), 0.99 (d, J = 6.5 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl_3): 159.87, 135.97, 133.27, 129.86, 127.43 (2C), 117.26, 113.61, 101.51, 83.56, 74.08, 55.50, 34.33, 30.25, 29.94, 16.24, 11.33; **$[\alpha]_D$** -28.4 (*c* 0.5, CHCl_3); **IR** (thin film): 2955, 2927, 2853, 1617, 1518, 1459, 1382, 1157, 1101 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{18}\text{H}_{24}\text{O}_3\text{Na}^+$ 311.1617, found 311.1613.

[4-(4-Methoxy-benzyloxy)-3,5-dimethyl-2-oxo-nona-6,8-dienyl]-phosphonic-acid dimethyl ester, 4

To a solution of PMP-acetal **10** (0.073 g, 0.252 mmol, 1.0 eq) in CH_2Cl_2 (2.50 mL) at 0 °C was added DIBAL-H (0.1075 g, 0.756 mmol, 3.0 eq). The reaction was stirred 3 h and was then quenched with saturated Na_2SO_4 (25 mL). EtOAc (50 mL) was then added and the mixture stirred for 1 h, then filtered through Celite, and the layers were separated. The organic phase was dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was used without further purification.

^1H NMR (500 MHz, CDCl_3): δ 7.25 (d, J = 9 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.66 (dt, J = 10.5, 17 Hz, 1H), 6.03 (t, J = 11 Hz, 1H), 5.54 (t, J = 10.5 Hz, 1H), 5.21 (d, J = 17.5 Hz, 1H), 5.11 (t, J = 10 Hz, 1H), 4.57 (d, J = 10.5 Hz, 1H), 4.45 (d, J = 10.5 Hz, 1H), 3.79 (s, 3H), 3.60 (dd, J = 7, 10.5 Hz, 1H), 3.53 (dd, J = 5, 10.5 Hz, 1H), 3.40 (dd, J = 4, 5.5 Hz, 1H), 2.99 (dt, J = 7, 10, Hz, 1H), 1.96 (m, 1H), 1.02 (d, J = 7 Hz, 3H), 0.95 (d, J = 7 Hz, 3H).

To a solution of the intermediate alcohol in CH_2Cl_2 (2.50 mL) at 0 °C was added Dess-Martin periodinane (0.16 g, 0.378 mmol, 1.5 eq). The solution was stirred for 45 min and was then quenched with Na_2SO_3 -doped saturated NaHCO_3 solution. The mixture was stirred vigorously for 30 min (until the organic layer was clear) and then the two layers were separated. The organic phase was washed with water, dried over MgSO_4 , filtered, and concentrated to yield the intermediate aldehyde as a pale yellow oil that was used immediately in the next step.

^1H NMR (500 MHz, CDCl_3): δ 9.72 (d, J = 1 Hz, 1H), 7.25 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 6.5 Hz, 2H), 6.58 (dt, J = 10.5, 17 Hz, 1H), 6.07 (t, J = 11 Hz, 1H), 5.47 (t, J = 10 Hz, 1H), 5.24 (d, J = 16.5 Hz, 1H), 5.15 (d, J = 10 Hz, 1H), 4.50 (m, 2H), 3.83 (s, 3H), 3.73 (t, J = 5 Hz, 1H), 2.99 (m, 1H), 2.62 (m, 1H), 1.19 (d, J = 7 Hz, 3H), 1.09 (d, J = 7 Hz, 3H).

To a solution of (dimethyl)methylphosphonate (94 mg, 0.756 mmol, 3.0 eq) in THF (1.50 mL) at -78 °C was added a 1.6 M solution of butyllithium in hexanes (470 μL , 0.756 mmol, 3.0 eq). The reaction was stirred for 30 min and then the aldehyde obtained above was added as a solution in THF (0.50 mL). The reaction mixture was stirred for 30 min, warmed to 0 °C for 15 min, and was then quenched with saturated NH_4Cl solution. The mixture was extracted with EtOAc and the combined organic extracts dried over MgSO_4 , filtered, and concentrated *in vacuo* to yield the intermediate β -hydroxy phosphonate. This material was dissolved in CH_2Cl_2 (2.50 mL), cooled to 0 °C and Dess-Martin periodinane (0.16 g, 0.378 mmol, 1.5 eq) was added. The reaction was warmed to rt, stirred for 1 h and was then quenched with Na_2SO_3 -doped saturated NaHCO_3 solution (25 mL) and EtOAc (25 mL). The mixture was stirred vigorously for 30 min (until the organic layer was clear) and then the two layers were separated. The organic phase was dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (50-100% EtOAc/hexanes) to yield β -ketophosphonate **4** (62 mg, 60 % over 4 steps).

^1H NMR (500 MHz, CDCl_3): δ 7.28 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.52 (dt, J = 10.5, 16.5 Hz, 1H), 6.04 (t, J = 11 Hz, 1H), 5.53 (t, J = 10.5 Hz, 1H), 5.23 (d, J = 16.5 Hz, 1H), 5.14 (d, J = 10 Hz, 1H), 4.58 (d, J = 10.5 Hz, 1H), 4.54 (d, J = 11 Hz, 1H), 3.82 (s, 3H), 3.79 (d, J = 10 Hz, 3H),

3.76 (d, $J = 10$ Hz, 3H), 3.60 (dd, $J = 4, 6.5$ Hz, 1H), 3.33 (dd, $J = 14, 22$ Hz, 1H), 2.94-3.04 (m, 2H), 2.83 (m, 1H), 1.22 (d, $J = 7$ Hz, 3H), 1.09 (d, $J = 7$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 205.04, 159.43, 133.74, 132.28, 130.63, 130.15, 129.73 (2C), 118.43, 113.93 (2C), 83.80, 74.53, 55.50, 53.26 (d, $J = 6.1$ Hz, 1C), 53.07 (d, $J = 6.7$ Hz, 1C), 50.81, 41.17 (d, $J = 129.25$ Hz, 1C), 36.01, 19.22, 13.02; $[\alpha]_D -3.8$ (c 0.5, CHCl_3); IR (thin film): 2959, 1711, 1574, 1248 cm^{-1} ; HRMS (ESI) calculated for $\text{C}_{21}\text{H}_{31}\text{O}_6\text{PNa}^+$ 433.1750, found 433.1756.

Ethynyl-diisopropyl-[5-(4-methoxy-benzyloxy)-2,4-dimethyl-1-vinyl-pentyloxy]-silane, **12**

To a stirred solution of allylic alcohol **11** (5.00 g, 17.96 mmol, 1 eq) in DMF (72.00 mL) at 0 °C was added imidazole (2.445 g, 35.92 mmol, 2.0 eq) then bromo(diisopropyl)ethynyl silane (4.74 g, 21.552 mmol, 1.2 eq) and the reaction mixture was allowed to warm to rt. The mixture was stirred for 6 h then poured into a separatory funnel containing Et_2O (150 mL) and water (150 mL). The layers were separated and the organic phase dried with MgSO_4 , filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% Et_2O /hexanes) to yield **12** (7.35 g, 95%) as a clear oil.

^1H NMR (500 MHz, CDCl_3): δ 7.30 (d, $J = 8.5$ Hz, 2H), 6.91 (d, $J = 9$ Hz, 2H), 5.84 (m, 1H), 5.21 (dt, $J = 1.5, 17$ Hz, 1H), 5.14 (dt, $J = 1.5, 10$ Hz, 1H), 4.48 (d, $J = 11.5$ Hz, 1H), 4.44 (d, $J = 12$ Hz, 1H), 4.42 (m, 1H), 3.84 (s, 3H), 4.43 (dd, $J = 5, 9.5$ Hz, 1H), 3.25 (t, $J = 8.5$ Hz, 1H), 2.41 (s, 1H), 1.94 (m, 1H), 1.76 (m, 1H), 1.58 (m, 1H), 1.07-1.12 (m, 14H), 1.03 (m, 1H), 1.01 (d, $J = 6.5$ Hz, 3H), 0.92 (d, $J = 7$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.22, 139.20, 131.22, 129.29 (2C), 115.43, 113.90 (2C), 94.91, 85.62, 78.86, 75.68, 72.81, 55.46, 37.15, 36.66, 31.21, 18.98, 17.56, 17.45, 17.36, 17.33, 15.74, 13.71, 13.17; $[\alpha]_D -5.2$ (c 0.5, CHCl_3); IR (thin film): 2989, 2857, 2127, 1608, 1513, 1098, 987, 912 cm^{-1} ; HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{40}\text{O}_3\text{SiNa}^+$ 439.2638, found 439.2654.

2,2-Diisopropyl-5-[4-(4-methoxy-benzyloxy)-1,3-dimethyl-butyl]-4-methyl-3-methylene-[1,2]oxasilolane, **13**

To a stirred solution of $\text{Ti}(\text{i-PrO})_3\text{Cl}$ (0.495 g, 1.8 mmol, 3.0 eq) in Et_2O (5.80 mL) at -40 °C was added (siloxy)enyne **12** (0.25 g, 0.6 mmol, 1.0 eq) followed by the slow addition of a 2M solution of $i\text{-PrMgCl}$ (1.8 mL, 3.6 mmol, 6.0 eq) over 2h. The reaction mixture was stirred for an additional 6h and was then quenched with the addition of saturated NH_4Cl (50 mL) and EtOAc (50 mL). The resulting solution was stirred for 1h, filtered through Celite, and the layers were separated. The organic phase was dried with MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (40% CH_2Cl_2 /hexanes) to yield **13** (0.183 g, 73%) as a clear oil.

¹H NMR (500 MHz, CDCl₃): δ 7.29 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.69 (t, *J* = 2.5 Hz, 1H), 5.47 (t, *J* = 2.5 Hz, 1H), 4.47 (d, *J* = 12 Hz, 1H), 4.44 (d, *J* = 11.5 Hz, 1H), 3.83 (s, 3H), 3.39 (m, 1H), 3.37 (m, 1H), 3.21 (m, 1H), 2.35 (m, 1H), 1.91 (m, 1H), 1.76 (m, 1H), 1.60 (m, 1H), 1.18 (m, 1H), 1.01-1.10 (m, 14H), 1.0 (d, *J* = 6 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.21, 153.02, 131.20, 129.31 (2C), 121.00, 113.90 (2C), 85.81, 76.03, 72.68, 55.50, 43.09, 38.99, 32.68, 30.93, 18.12, 17.64, 17.56, 17.53, 17.31, 13.98, 13.38, 13.06, 12.51; [α]_D -7.6 (*c* 0.5, CHCl₃); **IR** (thin film): 2952, 2862, 1610, 1513, 1460, 1247, 852 cm⁻¹; **HRMS** (ESI) calculated for C₂₅H₄₂O₃SiNa⁺ 441.2795, found 441.2789.

8-(4-Methoxy-benzyloxy)-3,5,7-trimethyl-oct-1-en-4-ol, **2**

To a stirred solution of siloxane **13** (183 mg, 0.42 mmol, 1.0 eq) in DMF (2.10 mL) was added TBAF·H₂O (332 mg, 1.27 mmol, 3.0 eq) and the reaction mixture was heated to 65 °C for 6h. The reaction was then cooled to room temp and diluted with H₂O (25 mL) and Et₂O (25 mL). The organic phase was dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% Et₂O/hexanes) to yield **2** (128 mg, 95%) as an oil.

¹H NMR (400 MHz, CDCl₃): δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.73 (m, 1H), 5.12 (m, 2H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 12 Hz, 1H), 3.80 (s, 3H), 3.31 (dd, *J* = 5.2, 8.8 Hz, 1H), 3.20 (dd, *J* = 6.8, 9.2 Hz, 1H), 3.18 (t, *J* = 5.2 Hz, 1H), 2.27 (m, 1H), 1.86 (m, 1H), 1.75 (m, 1H), 1.55 (m, 1H), 1.06 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.27, 142.03, 131.05, 129.36 (2C), 116.39, 113.93 (2C), 76.19, 75.91, 72.88, 55.48, 42.29, 38.57, 31.78, 30.89, 18.30, 16.78, 13.48; [α]_D +2.7 (*c* 0.5, CHCl₃); **IR** (thin film): 3425, 2958, 1690, 1513, 1251, 1038, 994, 905 cm⁻¹; **HRMS** (ESI) calculated for C₁₉H₃₀O₃Na⁺ 329.2087, found 329.2096.

3,5-Bis-(*tert*-butyl-dimethyl-silynyloxy)-2-methyl-hept-6-enoic acid **3**-(4-methoxy-benzyloxy)-2,4-dimethyl-1-(1-methyl-allyl)-pentyl ester, **14**

To a stirred solution of homoallylic alcohol **2** (125 mg, 0.408 mmol, 1.0 eq) and acid **3** (164 mg, 0.408 mmol, 1.0 eq) in toluene (40.80 mL) at -78 °C was added triethylamine (682 μL, 4.90 mmol, 12.0 eq), DMAP (1.25 g, 10.2 mmol, 25.0 eq), then 2,4,6-trichlorobenzoyl chloride (720 μL, 4.61 mmol, 11.3 eq) and the reaction mixture was allowed to warm to rt. The reaction was stirred for 8 h and was then quenched with saturated NaHCO₃ solution and extracted with EtOAc (3x). The combined organic

extracts were dried with MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% Et_2O /hexanes) to yield **14** (253 mg, 90%) as an oil.

^1H NMR (500 MHz, CDCl_3): δ 7.28 (d, J = 9 Hz, 2H), 6.90 (d, J = 6.5 Hz, 2H), 5.80 (m, 1H), 5.72 (m, 1H), 5.13 (d, J = 16.5 Hz, 1H), 4.98-5.06 (m, 3H), 4.78 (m, 1H), 4.45 (d, J = 11.5 Hz, 1H), 4.41 (d, J = 11.5 Hz, 1H), 4.24 (m, 1H), 4.19 (m, 1H), 3.83 (s, 3H), 3.34 (dd, J = 4.5, 9 Hz, 1H), 3.16 (dd, J = 7.5, 9.5 Hz, 1H), 2.70 (m, 1H), 2.48 (m, 1H), 1.88 (m, 2H), 1.78 (m, 1H), 1.55 (m, 1H), 1.37 (m, 1H), 1.13 (d, J = 7 Hz, 3H), 0.99 (d, J = 6.5 Hz, 3H), 0.98 (m, 1H), 0.97 (d, J = 6.5 Hz, 3H), 0.91-0.93 (m, 21H), 0.13 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 173.42, 159.21, 142.66, 140.79, 131.14, 129.27 (2C), 115.38, 114.34, 113.89 (2C), 79.35, 75.50, 72.76, 72.27, 70.36, 55.47, 46.30, 42.83, 40.71, 38.28, 31.91, 30.84, 26.30 (3C), 26.15 (3C), 18.67, 18.40, 18.35, 17.64, 14.98, 11.45, -3.29, -4.06, -4.08, -4.12; $[\alpha]_{\text{D}}^{25}$ +2.3; **IR** (thin film): 2956, 2930, 1733, 1249, 1091, 1040, 836, 775 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{39}\text{H}_{70}\text{O}_6\text{Si}_2\text{Na}^+$ 713.4603, found 713.4605.

4,6-Bis-(*tert*-butyl-dimethyl-silanyloxy)-10-[4-(4-methoxy-benzyloxy)-1,3-dimethyl-butyl]-3,9-dimethyl-3,4,5,6,9,10-hexahydro-oxecin-2-one, **15**

To a stirred solution of diene **14** (253 mg, 0.367 mmol, 1.0 eq) in toluene (18.35 mL) at 110 °C was added Grubbs catalyst 2nd generation (47 mg, 0.055 mmol, 0.15 eq) in 3 equal batches over 18 h. The reaction mixture was cooled to rt and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% Et_2O /hexanes) to yield **15** (192 mg, 76%) as an oil.

^1H NMR (500 MHz, CDCl_3): δ 7.25 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 9 Hz, 2H), 5.41 (t, J = 10.5 Hz, 1H), 5.15 (t, J = 9.75 Hz, 1H), 4.57-4.64 (m, 2H), 4.41 (m, 2H), 3.97 (m, 1H), 3.81 (s, 3H), 3.28 (dd, J = 6, 9.5 Hz), 3.21 (dd, J = 6, 9 Hz, 1H), 2.62-2.72 (m, 2H), 2.07 (m, 1H), 1.99 (m, 1H), 1.92 (m, 1H), 1.76 (m, 1H), 1.35 (m, 1H), 1.16 (d, J = 7 Hz, 3H), 1.02 (m, 1H), 0.99 (d, J = 6.5 Hz, 3H), 0.97 (d, J = 7 Hz, 3H), 0.92 (d, J = 6.5 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 173.07, 159.21, 134.32, 133.31, 131.13, 129.22 (2C), 113.87 (2C), 77.31, 75.92, 72.56, 71.27, 64.23, 55.47, 48.75, 43.93, 38.82, 34.26, 30.28, 30.21, 26.04 (3C), 26.02 (3C), 18.35, 18.25, 17.78, 15.88, 13.49, 8.81, -4.17, -4.19, -4.62, -4.73; $[\alpha]_{\text{D}}^{25}$ +12.3 (*c* 0.5, CHCl_3); **IR** (thin film): 2955, 2930, 1727, 1250, 1082, 1042, 836, 775 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{37}\text{H}_{66}\text{O}_6\text{Si}_2\text{Na}^+$ 685.4290, found 642.4263.

5,7-Bis-(*tert*-butyl-dimethyl-silanyloxy)-11-hydroxy-15-(4-methoxy-benzyloxy)-4,10,12,14-tetramethyl-pentadeca-2,8-dienoic acid ethyl ester, **16**

To a stirred solution of **15** (191 mg, 0.298 mmol) in toluene (3.67 mL) at -100 °C was added DIBAL-H (67 μ L, 0.367 mmol, 1.2 eq) in CH₂Cl₂ (300 μ L) over 30 minutes. The reaction was stirred for an additional 15 minutes, then quenched by pouring into a solution of saturated Na₂SO₄ (50 mL). EtOAc (50 mL) was then added and the resulting solution stirred for 1h, filtered through Celite, and separated. The organic phase was dried with MgSO₄, filtered, and concentrated *in vacuo*.

To a stirred solution of the intermediate hydroxy aldehyde in CH₂Cl₂ (1.835 mL) at 0 °C was added (triphenyl- λ^5 -phosphanylidene)acetic acid ethyl ester (384 mg, 1.1 mmol, 3.0 eq) and the reaction mixture was allowed to warm to rt. The reaction was stirred for 2 h and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% EtOAc/hexanes) to yield **16** (148 mg, 73% over 2 steps) as an oil.

¹H NMR (500 MHz, CDCl₃): δ 7.28 (d, J = 9 Hz, 2H), 6.95 (dd, J = 7, 16 Hz, 1H), 6.90 (d, J = 8.5 Hz, 2H), 5.84 (dd, J = 1.5, 16 Hz, 1H), 5.49 (t, J = 10 Hz, 1H), 5.20 (t, J = 11 Hz, 1H), 4.56 (td, J = 3, 9, Hz, 1H), 4.47 (d, J = 11.5 Hz, 1H), 4.43 (d, J = 12 Hz, 1H), 4.21 (q, J = 7 Hz, 2H), 3.98 (m, 1H), 3.83 (s, 3H), 3.33 (dd, J = 5.5, 9 Hz, 1H), 3.19-3.32 (m, 2H), 2.56 (m, 2H), 1.88 (m, 1H), 1.80 (m, 1H), 1.51-1.57 (m, 2H), 1.44 (m, 1H), 1.31 (t, J = 7 Hz, 3H), 1.10 (m, 1H), 1.05 (d, J = 6.5 Hz, 3H), 0.96 (d, J = 6.5 Hz, 3H), 0.88-0.93 (m, 24H), 0.13 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 166.85, 159.26, 151.09, 135.88, 132.87, 131.05, 129.35 (2C), 121.61, 113.92 (2C), 76.53, 76.04, 71.72, 66.29, 60.37, 55.49, 43.00, 42.84, 38.66, 36.73, 31.28, 30.85, 26.14 (3C), 26.04 (3C), 18.31, 18.29, 18.10, 16.93, 14.50, 13.71, 13.21, -2.98, -3.91, -4.13, -4.27; [α]_D +15.84 (*c* 0.5, CHCl₃); **IR** (thin film): 2956, 2928, 2855, 1698, 1647, 1623, 1514, 1462, 1360, 1249, 1073, 835, 773 cm⁻¹; **HRMS** (ESI) calculated for C₄₁H₇₄O₇Si₂Na⁺ 757.4865, found 757.4837.

14,18,20,24-Tetrakis-(*tert*-butyl-dimethyl-silanyloxy)-6-(4-methoxy-benzyloxy)-5,7,11,13,15,21-hexamethyl-tetracos-1,3,9,16,22-pentaen-8-one, **18**

To a stirred solution of **16** (148 mg, 0.201 mmol, 1.0 eq) in CH₂Cl₂ (2.00 mL) at -78 °C was added DIBAL-H (118 μ L, 0.644 mmol, 3.2 eq) and the reaction mixture was warmed to 0 °C for 30 min. The

reaction was quenched by pouring into a saturated solution of Na₂SO₄ (25 mL) and stirred with EtOAc (25 mL) for 45 min, filtered through Celite, and separated. The organic phase was dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude diol was used directly in the next step.

¹H NMR (500 MHz, CDCl₃): δ 7.28 (d, *J* = 9 Hz, 2H), 6.90 (d, *J* = 8 Hz, 2H), 5.55 (m, 2H), 5.53 (t, *J* = 11 Hz, 1H), 5.18 (t, *J* = 10.5 Hz, 1H), 4.57 (td, *J* = 3, 5.5 Hz, 1H), 4.45 (m, 2H), 4.08 (m, 2H), 3.91 (m, 1H), 3.83 (s, 3H), 3.32 (dd, *J* = 5.5, 9 Hz, 1H), 3.19-3.24 (m, 2H), 2.56 (m, 1H), 2.38 (m, 1H), 1.88 (m, 1H), 1.79 (m, 1H), 1.48 (m, 2H), 1.23 (d, *J* = 7 Hz, 3H), 1.00 (d, *J* = 7 Hz, 3H), 0.88-0.98 (m, 24H), 0.14 (s, 3H), 0.11 (s, 3H), 0.08 s, 6H).

To a stirred solution of the intermediate diol in CH₂Cl₂ (2.00 mL) at 0 °C was added 2,6-lutidine (94 μL, 0.804 mmol, 4.0 eq) and TBSOTf (138 μL, 0.603 mmol, 3.0 eq) and the reaction mixture was allowed to warm to rt. The reaction was stirred for 2.5 h and quenched with a saturated NaHCO₃ solution. The mixture was extracted with CH₂Cl₂ and the combined organic extracts were dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product was used directly in the next step.

¹H NMR (400 MHz, CDCl₃): δ 7.25 (d, *J* = 11 Hz, 2H), 6.86 (d, *J* = 11 Hz, 2H), 5.54 (m, 2H), 5.38 (t, *J* = 13 Hz, 1H), 5.24 (t, *J* = 10.5 Hz, 1H), 4.52 (m, 1H), 4.40 (m, 2H), 4.13 (m, 2H), 3.89 (dt, *J* = 3.5, 10.5 Hz, 1H), 3.80 (s, 3H), 3.36 (m, 1H), 3.32 (dd, *J* = 6.5, 12 Hz, 1H), 3.08 (t, *J* = 9.5 Hz, 1H), 2.56 (m, 1H), 2.37 (m, 1H), 1.86 (m, 1H), 1.73 (m, 1H), 1.61 (m, 1H), 1.51 (m, 1H), 0.96 (d, *J* = 7 Hz, 3H), 0.83-0.93 (m, 45H), 0.08 (s, 6H), 0.06 (s, 12H), 0.01 (s, 6H).

To a stirred biphasic solution of the intermediate obtained above in CH₂Cl₂ (7.73 mL) and pH=7 Buffer (2.32 mL) at 0 °C was added DDQ (54 mg, 0.241 mmol, 1.2 eq) and the reaction was allowed to warm to rt. The reaction was stirred for 1 h and the layers were then separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic extracts dried with MgSO₄, filtered through a plug of silica with EtOAc, and concentrated *in vacuo*. The crude product was used without further purification.

¹H NMR (400 MHz, CDCl₃): δ 5.55 (m, 2H), 5.43 (t, *J* = 12.5 Hz, 1H), 5.27 (t, *J* = 10.5 Hz, 1H), 4.53 (m, 1H), 4.14 (m, 2H), 3.91 (m, 1H), 3.54 (dd, *J* = 6.5, 12 Hz, 1H), 3.37 (t, *J* = 4 Hz, 1H), 3.32 (m, 1H), 2.58 (m, 1H), 2.37 (m, 1H), 1.65 (m, 1H), 1.64 (m, 1H), 1.43 (m, 1H), 1.33 (m, 1H), 0.97 (d, *J* = 7 Hz, 3H), 0.94 (d, *J* = 7 Hz, 3H), 0.82-0.92 (m, 42H), 0.09 (s, 6H), 0.06 (s, 6H), 0.04 (s, 6H), 0.03 (s, 6H).

To a solution of the intermediate alcohol in CH₂Cl₂ (2.00 mL) at 0 °C was added Dess-Martin periodinane (128 mg, 0.302 mmol, 1.5 eq) and the solution was allowed to warm to rt. The solution was stirred for 45 min and was then quenched with Na₂SO₃-doped saturated NaHCO₃ solution. The mixture was stirred vigorously for 30 min (until the organic layer was clear) and then the two layers were separated. The organic phase was dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% Et₂O/petroleum ether) to yield **17** (109 mg, 60% 4-steps) as an oil.

¹H NMR (500 MHz, CDCl₃): δ 9.54 (d, *J* = 2.5 Hz, 1H), 5.57 (m, 2H), 5.45 (t, *J* = 10.5 Hz, 1H), 5.30 (dd, *J* = 9, 11.5 Hz, 1H), 4.56 (m, 1H), 4.16 (m, 2H), 3.94 (m, 1H), 3.43 (t, *J* = 3.5 Hz, 1H), 2.63 (m, 1H), 2.40 (m, 1H), 1.88 (m, 1H), 1.75 (m, 1H), 1.64 (m, 1H), 1.54 (m, 1H), 1.27 (m, 2H), 1.25 (d, *J* = 7 Hz, 3H), 1.23 (d, *J* = 7.5 Hz, 3H), 0.84-1.00 (m, 42H), 0.12 (s, 6H), 0.09 (s, 6H), 0.08 (s, 6H), 0.06 (s, 6H).

A solution of phosphonate **4** (32 mg, 0.078 mmol, 1.0 eq) in dry THF (390 μ L) was added to a flask containing Ba(OH) $_2$ •8H $_2$ O (20 mg, 0.062 mmol, 0.8 eq) previously heated to 120 $^{\circ}$ C for 1.5 h then cooled to rt. The reaction was stirred for 30 min, then aldehyde **17** (50 mg, 0.062 mmol, 0.8 eq) was added as a solution in 40:1 THF:H $_2$ O (390 μ L), and the reaction was stirred for 6h. CH $_2$ Cl $_2$ (50 mL) and MgSO $_4$ were then added to the reaction and the mixture was filtered through Celite and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% Et $_2$ O/petroleum ether) to yield **18** (54 mg, 80%) as an oil.

1 H NMR (400 MHz, CDCl $_3$): δ 7.27 (d, J = 9.6 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 6.66 (dd, J = 8.4, 16 Hz, 1H), 6.39 (dt, J = 10.8, 16.8 Hz, 1H), 6.03 (d, J = 16.4 Hz, 1H), 6.01 (t, J = 9.6 Hz, 1H), 5.54 (d, J = 2.8 Hz, 2H), 5.52 (t, J = 10.4 Hz, 1H), 5.41 (t, J = 10.8 Hz, 1H), 5.24 (dd, J = 8.4, 10.8 Hz, 1H), 5.14 (dd, J = 2, 16.8 Hz, 1H), 5.00 (d, J = 10.4 Hz, 1H), 4.51-4.58 (m, 3H), 4.13 (m, 2H), 3.91 (m, 1H), 3.80 (s, 3H), 3.68 (dd, J = 3.2, 8.8 Hz, 1H), 3.35 (t, J = 3.6 Hz, 1H), 2.90 (m, 1H), 2.76 (m, 1H), 2.58 (m, 1H), 2.38 (m, 1H), 2.28 (m, 1H), 1.34-1.57 (m, 5H), 1.08 (d, J = 6.8 Hz, 3H), 1.00 (d, J = 6.4 Hz, 3H), 0.83-0.95 (m, 48H), -0.09 (s, 3H), -0.06 (s, 3H), -0.04 (s, 3H), -0.02 (s, 3H), -0.01 (s, 3H); **13 C NMR** (100 MHz, CDCl $_3$): δ 203.28, 159.37, 153.14, 134.19, 133.24, 133.06, 132.64, 131.03, 129.86, 129.61 (2C), 128.11, 117.60, 113.93 (2C), 84.45, 80.21, 75.65, 72.31, 66.64, 64.40, 55.50, 48.98, 42.38, 41.51, 39.31, 36.66, 36.10, 34.85, 34.71, 29.94, 26.40 (3C), 26.25 (3C), 26.17 (6C), 20.81, 20.03, 19.15, 18.66, 18.60, 18.36, 18.34, 15.28, 14.65, 13.13, -2.71, -3.50, -3.53, -3.97, -4.04, -4.12, -4.80, -4.84; [α] $_D$ -13.22 (*c* 0.5, CHCl $_3$); **IR** (thin film): 2956, 2927, 2856, 1720, 1513, 1463, 1249, 1180, 1089, 1038, 836, 774 cm $^{-1}$; **HRMS** (ESI) calculated for C $_{62}$ H $_{114}$ O $_7$ Si $_4$ Na $^+$ 1105.7533, found 1105.7570.

14,18,20,24-Tetrakis-(tert-butyl-dimethyl-silanyloxy)-5,7,11,13,15,21-hexamethyl-tetracos-1,3,16,22-tetraene-6,8-diol, 19

Enone **18** (23.4 mg, 0.022 mmol, 1.0 eq) was added with degassed toluene to a flask containing [Ph $_3$ P•CuH] $_6$ (21 mg, 0.011 mmol, 0.5 eq) at rt. The reaction was stirred for 8h, flushed through a plug of silica with EtOAc and concentrated *in vacuo* to yield the intermediate ketone as an oil.

1 H NMR (500 MHz, CDCl $_3$): δ 7.27 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 9 Hz, 2H), 6.44 (dt, J = 11, 16.5 Hz, 1H), 6.04 (t, J = 11 Hz, 1H), 5.52-5.56 (m, 3H), 5.40 (t, J = 10.5 Hz, 1H), 5.26 (dd, J = 8.5, 11 Hz, 1H), 5.19 (d, J = 16.5 Hz, 1H), 5.08 (d, J = 10 Hz, 1H), 4.50-4.58 (m, 3H), 4.136 (m, 2H), 3.905 (m, 1H), 3.81 (s, 3H), 3.65 (dd, J = 3, 8 Hz, 1H), 3.37 (m, 1H), 2.70-2.78 (m, 3H), 2.58 (m, 2H), 2.33-2.44 (m, 3H), 1.62-1.72 (m, 2H), 1.46 (m, 1H), 1.38 (m, 2H), 1.28 (m, 2H), 1.18 (d, J = 7 Hz, 3H), 1.11 (m, 1H), 1.09 (d, J = 7 Hz, 1H), 0.97 (d, J = 7 Hz, 3H), 0.95 (d, J = 7 Hz, 3H), 0.91 (s, 18H), 0.90 (s, 9H), 0.87-0.88 (m, 12H), 0.85 (d, J = 7 Hz, 3H), 0.80 (d, J = 6.5 Hz, 3H), 0.09 (s, 3H), 0.07 (s, 6H), 0.05 (s, 6H), 0.04 (s, 6H). **13 C NMR** (100 MHz, CDCl $_3$): δ 214.64, 159.38, 134.16, 133.31, 133.13, 132.55, 132.32, 130.97, 129.82, 129.57 (2C), 128.57, 118.03, 113.95 (2C), 84.07, 80.13, 75.59, 72.35, 66.69, 64.43, 55.50, 50.69, 42.36, 41.61, 41.40, 40.66, 36.43, 35.79, 35.26, 30.04, 29.94 (2C), 29.62, 26.48

(3C), 26.25 (6C), 26.18 (3C), 20.52, 19.78, 19.08, 18.70, 18.66, 18.35, 15.47, 14.40, 13.27, -2.74, -3.25, -3.48, -3.98, -4.06, -4.10, -4.79, -4.84; $[\alpha]_D^{25} +7.69$ (*c* 0.5, CHCl₃); **IR** (thin film): 2929, 1709, 1613, 1513, 1249, 1037 cm⁻¹; **HRMS** (ESI) calculated for C₆₂H₁₁₆O₇Si₄Na⁺ 1107.7690, found 1107.7676.

To a stirred solution of the intermediate ketone in CH₂Cl₂ (220 μL) at 0 °C was added DDQ (6 mg, 0.026 mmol, 1.2 eq) and the solution was warmed to rt. The reaction was stirred 30 min, then quenched with pH = 7 buffer (10 mL), and the aqueous layer extracted with CH₂Cl₂ (3 x 10 mL). The combined organic extracts were dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% EtOAc/petroleum ether) to yield the intermediate hydroxyl ketone (17 mg, 82% over 2 steps) as an oil.

¹H NMR (500 MHz, CDCl₃): δ 6.54 (dt, *J* = 10.5, 17 Hz, 1H), 6.10 (t, *J* = 11 Hz, 1H), 5.52 (m, 2H), 5.37 (t, *J* = 10 Hz, 1H), 5.25 (m, 3H), 5.11 (d, *J* = 10 Hz, 1H), 4.50 (t, *J* = 8 Hz, 1H), 4.11 (m, 2H), 3.71 (t, *J* = 5 Hz, 1H), 3.34 (m, 2H), 2.73 (m, 1H), 2.65 (m, 1H), 2.55 (m, 1H), 2.35 (m, 2H), 1.65 (m, 1H), 1.38 (m, 1H), 1.30 (m, 2H), 1.23 (m, 2H), 1.15 (m, 2H), 1.10 (m, 2H), 1.14 (d, *J* = 7 Hz, 3H), 0.97 (d, *J* = 7 Hz, 3H), 0.94 (d, *J* = 7 Hz, 3H), 0.92 (d, *J* = 7 Hz, 3H), 0.88 (m, 42 H), 0.06 (s, 3H), 0.04 (s, 9H), 0.02 (s, 9H), 0.01 (s, 3H).

To a stirred solution of the intermediate hydroxy ketone (8.5 mg, 8.8 μmol, 1.0 eq) in Et₂O (150 μL) at -40 °C was added a 0.28M solution of Zn(BH₄)₂ (126 μL, 35.2 μmol, 4.0 eq) dropwise over 5 min. The solution was stirred for 30 min, then quenched with saturated NH₄Cl (10 mL), and the aqueous phase extracted with EtOAc. The organic phase was dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography (25% Et₂O/petroleum ether) to yield **19** (7 mg, 88%) as an oil.

¹H NMR (400 MHz, CDCl₃): δ 6.64 (dt, *J* = 10.4, 16 Hz, 1H), 6.20 (t, *J* = 11.2 Hz, 1H), 5.54 (d, *J* = 2.8 Hz, 2H), 5.40 (t, *J* = 10.4 Hz, 1H), 5.17-5.29 (m, 4H), 4.52 (m, 1H), 4.13 (m, 2H), 3.89 (m, 1H), 3.77 (m, 1H), 3.45 (d, *J* = 10.8 Hz, 1H), 3.36 (t, *J* = 3.6 Hz, 1H), 2.81 (m, 1H), 2.58 (m, 1H), 2.37 (m, 1H), 1.62-1.74 (m, 2H), 1.22-1.52 (m, 8H), 0.83-0.97 (m, 54H), 0.08 (s, 3H), 0.06 (s, 9H), 0.04 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 134.63, 133.33, 132.51, 132.24 (2C), 129.53, 119.29, 80.96, 80.23, 77.45, 72.36, 66.71, 64.44, 42.36, 41.65, 41.39, 37.10, 36.60, 35.74, 35.39, 32.67, 30.55, 29.94, 26.49 (3C), 26.25 (3C), 26.18 (3C), 20.75, 19.81, 18.69 (2C), 18.36 (2C), 16.88, 15.63, 13.33, 4.35, -2.75, -3.28, -3.45, -3.98, -4.09 (2C), -4.79, -4.84; $[\alpha]_D^{25} +7.7$ (*c* 0.5, CHCl₃); **IR** (thin film): 3425, 2959, 2928, 2855, 1513, 1460, 1250, 1180, 1089, 1037, 835 cm⁻¹; **HRMS** (ESI) calculated for C₅₄H₁₁₀O₆Si₄Na⁺ 989.7271, found 989.7300.

[Bis-(2,2,2-trifluoro-ethoxy)-phosphoryl]-acetic acid 3,9,13,15,19-pentakis-(*tert*-butyl-dimethyl-silanyloxy)-2,6,8,10,16-pentamethyl-1-(1-methyl-penta-2,4-dienyl)-nonadeca-11,17-dienyl ester, 20

To a stirred solution of diol **19** (7.0 mg, 7.7 μmol , 1.0 eq) in CH_2Cl_2 (150 μL) at 0 $^\circ\text{C}$ was added 2,6-lutidine (2.7 μL , 23.1 μmol , 3.0 eq) and TBSOTf (3.5 μL , 15.4 μmol , 2.0 eq). The reaction was stirred for 45 min, quenched with saturated NaHCO_3 solution (10 mL), and the aqueous phase was extracted with CH_2Cl_2 (3 x 10mL). The combined organic extracts were dried over MgSO_4 , filtered through a plug of silica with EtOAc, and concentrated *in vacuo*. The crude product was used without further purification.

^1H NMR (500 MHz, CDCl_3): δ 6.66 (dt, $J = 10.5, 17$ Hz, 1H), 6.12 (t, $J = 11$ Hz, 1H), 5.57 (m, 2H), 5.43 (m, 2H), 5.27 (dd, $J = 9, 11.5$ Hz, 1H), 5.24 (d, $J = 17.5$ Hz, 1H), 5.14 ($J = 10.5$ Hz, 1H), 4.55 (t, $J = 8.5$ Hz, 1H), 4.16 (m, 2H), 3.92 (m, 1H), 3.79 (m, 1H), 3.50 (dd, $J = 2.5, 7.5$ Hz, 1H), 3.39 (t, $J = 3$ Hz, 1H), 2.82 (m, 1H), 2.60 (m, 1H), 2.40 (m, 2H), 1.73 (m, 1H), 1.68 (m, 1H), 1.60 (m, 2H), 1.48 (m, 1H), 1.40 (m, 2H), 1.32 (m, 1H), 1.25 (m, 1H), 1.03 (m, 1H), 0.99 (d, $J = 6.5$ Hz, 3H), 0.97 (d, $J = 6.5$ Hz, 3H), 0.93 (m, 51H), 0.87 (d, $J = 6.5$ Hz, 3H), 0.86 (d, $J = 7$ Hz, 3H), 0.11 (s, 6H), 0.10 (s, 6H), 0.09 (s, 6H), 0.06 (s, 6H), 0.04 (s, 6H).

To a stirred solution of the intermediate alcohol and bis(2,2,2-trifluoroethyl)phosphonoacetic acid (6.0 mg, 19.3 μmol , 2.5 eq) in toluene (770 μL) at 0 $^\circ\text{C}$ was added Et_3N (6.0 μL , 43.1 μmol , 5.6 eq), DMAP (8.0 mg, 64.7 μmol , 8.4 eq), and 2,4,6-trichlorobenzoyl chloride (4.0 μL , 26.9 μmol , 3.5eq) and the reaction was allowed to warm to rt. The reaction was stirred for 8h and was then quenched with saturated NaHCO_3 solution. The mixture was extracted with EtOAc and the combined extracts dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% EtOAc/petroleum ether) to yield **20** (7.8 mg, 74% over 2 steps).

^1H NMR (500 MHz, CDCl_3): δ 6.54 (dt, $J = 10.5, 17$ Hz, 1H), 6.03 (t, $J = 11$ Hz, 1H), 5.54 (d, $J = 3$ Hz, 2H), 5.36 (t, $J = 10$ Hz, 1H), 5.21-5.38 (m, 2H), 5.15 (d, $J = 10.5$ Hz, 1H), 5.06 (dd, $J = 4.5, 8$ Hz, 1H), 4.41-4.53 (m, 5H), 4.13 (m, 2H), 3.89 (m, 1H), 3.59 (m, 1H), 3.34 (m, 1H), 3.19 (s, 1H), 3.11 (s, 1H), 3.02 (m, 1H), 2.57 (m, 1H), 2.37 (m, 1H), 1.74 (m, 1H), 1.62 (m, 1H), 1.53 (m, 1H), 1.16-1.48 (m, 9H), 0.97 (d, $J = 7$ Hz, 3H), 0.95 (d, $J = 6.5$ Hz, 3H), 0.94 (d, $J = 7$ Hz, 3H), 0.79-0.90 (m, 54H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 12H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); **^{13}C NMR** (100 MHz, CDCl_3): δ 164.66, 133.32 (2C), 132.73, 132.42, 131.87, 130.34, 129.53, 126.273 (q, $J = 270.5$ Hz, 2C), 118.72, 80.83, 79.98, 72.53 (2C), 66.69, 64.42, 62.80 (q, $J = 38.3$ Hz, 2C), 42.37, 41.89, 41.65, 38.49, 35.97, 34.88, 34.75, 34.00, 33.44, 32.39, 31.33, 30.54, 29.94, 26.49 (5C), 26.17 (5C), 26.08 (5C), 20.40, 19.48, 18.70, 18.35 (2C), 17.96, 15.25, 13.32, 9.22, -2.76, -3.06, -3.38, -3.54, -3.99, -4.06, -4.11, -4.40, -4.80; **$[\alpha]_D$** -28.4 (c 0.5, CHCl_3); **IR** (thin film): 3449, 2927, 1739, 1299, 1265, 1174, 1070 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{66}\text{H}_{129}\text{F}_6\text{O}_{10}\text{PSi}_5\text{Na}^+$ 1389.7966, found 1389.7898.

8,10,14,20-Tetrakis-(*tert*-butyl-dimethyl-silanyloxy)-7,13,15,17,21-pentamethyl-22-(1-methyl-penta-2,4-dienyl)-oxacyclodocosa-3,5,11-trien-2-one, 21

Phosphonate **20** (7.8 mg, 5.7 μ mol, 1.0 eq) was treated with a 3:1:1 AcOH:THF:H₂O solution (500 μ L) at 0 °C and the solution was slowly warmed to rt. The reaction was stirred for 24 h and was then cooled to 0 °C, diluted with EtOAc (10 mL) and quenched with saturated NaHCO₃ solution (10 mL). The layers were separated and the aqueous phase extracted with EtOAc (10 mL). The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% EtOAc/hexanes) to yield the intermediate alcohol (5.6 mg, 60%).

¹H NMR (500 MHz, CDCl₃): δ 6.57 (dt, J = 10.5, 17 Hz, 1H), 6.06 (t, J = 16.5 Hz, 1H), 5.66 (m, 2H), 5.39 (m, 2H), 5.28 (m, 1H), 5.25 (d, J = 17 Hz, 1H), 5.18 (d, J = 10.5 Hz, 1H), 5.09 (dd, J = 4.5, 7.5 Hz, 1H), 4.54 (m, 1H), 4.48 (m, 4H), 3.93 (m, 1H), 3.62 (m, 1H), 3.35 (m, 1H), 3.20 (s, 1H), 3.16 (s, 1H), 3.05 (m, 1H), 2.60 (m, 1H), 2.40 (m, 1H), 1.77 (m, 1H), 1.65 (m, 1H), 1.59 (m, 1H), 1.47 (m, 1H), 1.37 (m, 2H), 1.28 (m, 4H), 1.01 (m, 1H), 1.00 (d, J = 7 Hz, 3H), 0.98 (d, J = 7 Hz, 3H), 0.91 (m, 36H), 0.87 (d, J = 7 Hz, 3H), 0.86 (d, J = 7 Hz, 3H), 0.84 (d, J = 7 Hz, 3H), 0.83 (d, J = 6.5 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H), 0.05 (s, 3H)

To a stirred solution of the intermediate allylic alcohol (5.6 mg, 4.4 μ mol, 1.0 eq) in CH₂Cl₂ (90 μ L) at 0 °C was added Dess-Martin periodinane (3.0 mg, 6.6 μ mol, 1.5 eq) and the solution was allowed to warm to rt. The reaction was stirred for 45 min and was then quenched with Na₂SO₃-doped saturated NaHCO₃ solution. The mixture was stirred vigorously for 15 min (until the organic layer was clear) and then the two layers were separated. The organic phase was dried over MgSO₄, filtered, and concentrated *in vacuo* to yield the intermediate aldehyde which was used without purification.

¹H NMR (500 MHz, CDCl₃): δ 9.50 (d, J = 8 Hz, 1H), 6.80 (dd, J = 6.5, 15.5 Hz, 1H), 6.55 (dt, J = 10.5, 16.5 Hz, 1H), 6.13 (ddd, J = 1.5, 8, 15 Hz, 1H), 6.04 (t, J = 10.5 Hz, 1H), 5.36 (m, 2H), 5.23 (m, 2H), 5.16 (d, J = 10.5 Hz, 1H), 5.07 (dd, J = 4, 7 Hz, 1H), 4.53 (m, 1H), 4.46 (m, 4H), 4.05 (m, 1H), 3.59 (m, 1H), 3.33 (m, 1H), 3.18 (s, 1H), 3.14 (s, 1H), 3.03 (m, 1H), 2.66 (m, 1H), 2.55 (m, 1H), 1.75 (m, 2H), 1.57 (m, 2H), 1.48 (m, 1H), 1.40 (m, 1H), 1.33 (m, 2H), 1.20 (m, 3H), 1.08 (d, J = 7 Hz, 3H), 0.98 (d, J = 7 Hz, 3H), 0.89 (m, 39H), 0.81 (d, J = 7 Hz, 3H), 0.81 (d, J = 6 Hz, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H).

To a flask containing K₂CO₃ (4.0 mg, 26.4 μ mol, 6.0 eq), briefly flame-dried under vacuum, was added a solution of the intermediate aldehyde and 18-crown-6 (14.0 mg, 52.8 μ mol, 12.0eq) as a solution in toluene (4.4 mL) and the reaction was stirred for 6h. The reaction was diluted with EtOAc, washed with water, and the organic phase dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% Et₂O/hexanes) to yield **21** (3 mg, 74 % of desired diastereoisomer over 2 steps).

¹H NMR (500 MHz, CDCl₃): δ 7.02 (m, 1H), 6.56-6.64 (m, 2H), 6.09 (t, J = 11 Hz, 1H), 6.06 (dd, J = 6, 15.5 Hz, 1H), 5.64 (d, J = 11.5 Hz, 1H), 5.63 (m, 1H), 5.44 (t, J = 10.5 Hz, 1H), 5.37 (t, J = 8.5 Hz, 1H), 5.24 (d, J = 10.5 Hz, 1H), 5.16 (d, J = 10.5 Hz, 1H), 5.10 (m, 1H), 4.57 (t, J = 9 Hz), 4.07 (m, 1H), 3.68 (m, 1H), 3.23 (d, J = 6.5 Hz, 1H), 3.08 (m, 1H), 2.63 (m, 1H), 2.57 (m, 2H), 1.86 (m, 1H), 1.43-1.56 (m, 5H), 1.31 (m, 4H), 1.06 (d, J = 6.5 Hz, 3H), 1.05 (d, J = 7 Hz, 3H), 1.01 (d, J = 7 Hz, 3H), 0.99 (d, J = 7 Hz, 3H), 0.88-0.96 (m, 36H), 0.82 (d, J = 6.5 Hz, 3H), 0.80 (d, J = 6.5 Hz, 3H), 0.15 (s, 3H), 0.12 (s, 3H), 0.109 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); **¹³C NMR** (100 MHz, CDCl₃): δ 166.80, 143.17, 134.28, 132.66, 131.98, 130.07, 128.57, 128.22, 118.69, 118.42, 114.12, 81.14, 79.12, 77.45, 70.47, 66.64, 43.20, 41.54, 39.18, 35.32, 34.85, 34.66, 32.16, 30.49, 29.94 (2C), 29.60 (2C), 26.45 (3C), 26.27 (3C), 26.13 (3C), 26.06 (3C), 22.93, 20.50, 19.98, 18.73, 18.50, 18.38, 16.40, 14.37, -2.45, -3.25, -3.55, -3.72, -3.91 (2C), -4.08 (2C); **[α]_D** -17.8 (c 0.1, CHCl₃); **IR** (thin film): 2955, 2929,

2857, 1716, 1640, 1474, 1225, 1045 cm^{-1} ; **HRMS** (ESI) calculated for $\text{C}_{56}\text{H}_{108}\text{O}_6\text{Si}_4\text{Na}^+$ 1011.7115, found 1011.7131.

Dictyostatin, **1**

To a solution of macro lactone **21** (3.0 mg, 3 μmol , 1.0 eq) in THF (400 μL) at 0 $^{\circ}\text{C}$ was added HF $\cdot$ pyridine (100 μL) dropwise over 2 min and the solution was allowed to slowly warm to rt. The reaction was stirred 40 h and was then cooled to 0 $^{\circ}\text{C}$, diluted with EtOAc (2 mL), and quenched with saturated NaHCO_3 solution (2mL). The layers were separated and the aqueous layer extracted with EtOAc (3 x 2mL). The combined organic extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (50 $\rightarrow$ 75 $\rightarrow$ 100% EtOAc/hexanes) to yield **1** (1.1 mg, 67%).

^1H NMR (500 MHz, CD_3OD): δ 7.18 (dd, $J = 11.5, 16$ Hz, 1H), 6.68 (dt, $J = 10.5, 16.5$ Hz, 1H), 6.62 (t, $J = 11.5$ Hz, 1H), 6.16 (dd, $J = 6.5, 15.5$ Hz, 1H), 6.03 (t, $J = 11$ Hz, 1H), 5.53 (d, $J = 11.5$ Hz, 1H), 5.52 (t, $J = 10.5$ Hz, 1H), 5.38 (dd, $J = 8.5, 11$ Hz, 1H), 5.31 (t, $J = 11$ Hz, 1H), 5.22 (d, $J = 17.5$ Hz, 1H), 5.09-5.13 (m, 2H), 4.62 (m, 1H), 4.03 (dt, $J = 3, 11$ Hz, 1H), 3.34 (m, 1H), 3.13 (dt, $J = 7, 10$ Hz, 1H), 3.07 (dd, $J = 3, 8$ Hz, 1H), 2.73 (m, 1H), 2.57 (m, 1H), 1.82 (m, 1H), 1.86 (m, 1H), 1.60 (m, 1H), 1.58 (m, 1H), 1.55 (m, 1H), 1.47 (m, 1H), 1.40 (m, 1H), 1.22 (m, 1H), 1.12 (d, $J = 7$ Hz, 3H), 1.09 (d, $J = 7$ Hz, 3H), 1.07 (m, 1H), 1.04 (d, $J = 7$ Hz, 3H), 0.98 (d, $J = 6.5$ Hz, 3H), 0.92 (d, $J = 6.5$ Hz, 3H), 0.90 (d, $J = 7$ Hz, 3H), 0.88 (m, 1H), 0.67 (m, 1H); **^{13}C NMR** (125 MHz, CD_3OD): δ 168.10, 146.24, 144.74, 134.76, 134.36, 133.28, 131.12, 130.71, 128.38, 118.33, 117.83, 80.13, 78.39, 73.49, 70.16, 65.35, 43.84, 42.01, 40.60, 40.37, 36.36, 35.53, 35.12, 32.79, 32.46, 31.09, 21.58, 19.09, 17.85, 15.69, 13.53, 10.12; $[\alpha]_{\text{D}} -22.00$ (c 0.05 MeOH); **HRMS** (ESI) calculated for $\text{C}_{32}\text{H}_{52}\text{O}_6\text{H}^+$ 533.3836, found 533.3831.

Table. Comparison of data for synthetic and natural dictyostatin

Entry	Natural (CD ₃ OD)		Synthetic (CD ₃ OD)	
	¹ H δ (mult, <i>J</i>)	¹³ C δ		¹³ C δ ³
1	-	168.10	-	168.10
2	5.52 (d, 11)	118.03	5.53 (d, 11.5)	117.83
3	6.62 (t, 11)	144.89	6.62 (t, 11.5)	144.74
4	7.17 (dd, 11, 16)	128.58	7.18 (dd, 11.5, 16)	128.68
5	6.14 (dd, 6.7, 16)	146.42	6.16 (dd, 6.5, 15.5)	146.28
6	2.57 (brm)	44.05	2.57 (m)	43.99
7	4.02 (dt, 3.1, 10.7)	70.37	4.03 (dt, 3, 11)	70.26
8	1.47 (m)	40.59	1.47 (m)	40.60
	1.38 (m)		1.40 (m)	
9	4.62 (br dd, 4.8, 8.7)	65.50	4.62 (m)	65.35
10	5.37 (br dd, 8.7, 11)	134.89	5.38 (dd, 8.5, 11)	134.76
11	5.52 (br t, 11)	131.32	5.52 (t, 10.5)	131.03
12	2.72 (brm)	35.74	2.73 (m)	35.53
13	3.06 (dd, 2.9, 8.2)	80.37	3.07 (dd, 3, 8)	80.35
14	1.58 (m)	35.32	1.60 (m)	35.31
15	1.22 (m)	42.26	1.22 (m)	42.11
	0.88 (m)		0.88 (m)	
16	1.50 (m)	31.22	1.52 (m)	31.09
17	1.56 (m)	32.74	1.58 (m)	32.73
	0.68 (m)		0.67 (m)	
18	1.82 (m)	32.50	1.82 (m)	32.46
	1.08 (m)		1.07 (m)	
19	3.33 (m)	73.72	3.34 (m)	73.55
20	1.86 (m)	40.82	1.86 (m)	40.70
21	5.10 (dd, 5, 7)	78.63	5.09-5.13 (m, 2H)	78.48
22	5.11 (brd, 11)	118.58		118.59
23	3.13 (m)	35.82	3.13 (dt (7, 10)	36.36
24	5.30 (t, 11)	134.53	5.31 (t, 11)	134.55
25	6.02 (t, 11)	131.22	6.03 (t, 11)	131.12
26	6.67 (dt, 11, 17)	133.43	6.68 (dt, 10.5, 16.5)	133.28
	5.21 (brd, 17)		5.22 (d, 17.5)	
27	1.11 (d, 7.0)	13.75	1.12 (d, 7)	13.53
28	1.09 (d, 7.1)	19.35	1.09 (d, 6.5)	19.12
29	0.92 (d, 6.4)	15.97	0.92 (d, 6.5)	15.84
30	0.89 (d, 6.5)	21.81	0.90 (d, 7)	21.58
31	1.03 (d, 6.8)	10.39	1.04 (d, 7)	10.21
32	0.98 (d, 6.7)	18.06	0.98 (d, 6.5)	17.95

³ Due to limited sample, this data was obtained by HSQC and HMBC experiments.

Procedure for the Synthesis of Acid 3

To a stirred solution of **22**⁴ (500 mg, 1.37 mmol, 1.0 eq) in toluene (13.7 mL) was added crotonaldehyde (560 μ L, 6.85 mmol, 5.0 eq) and Grubbs second generation catalyst (58 mg, 0.069 mmol, 0.05 eq) and the reaction was heated to 60 °C. After stirring for 3h, the reaction was cooled to rt, and the volatiles were removed *in vacuo*. The residue was dissolved in CH₂Cl₂ (13.70 mL) and cooled to -78 °C. DIBAL-H (300 μ L, 1.64 mmol, 1.2 eq), was added and the reaction was warmed to 0 °C and stirred for 15 min, before being quenched with saturated Na₂SO₄ (25 mL). The mixture was stirred with EtOAc (50 mL) for 1h, and was then filtered through Celite, and the layers were separated. The organic phase was dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% EtOAc/hexanes) to yield the allylic alcohol (460 mg, 86%) as an oil.

¹H NMR (400 MHz, CDCl₃): δ 7.25 (d, J = 9.2 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.41 (m, 2H), 4.09 (d, J = 5.6 Hz, 2H), 3.81 (s, 3H), 3.70 (m, 1H), 3.46 (dd, J = 5.6, 9.2 Hz, 1H), 3.26 (dd, J = 6.8, 8.8 Hz, 1H), 2.18 (m, 2H), 1.92 (m, 1H), 0.91 (d, J = 7.2 Hz, 3H), 0.87 (m, 9H), 0.02 (s, 6H); **¹³C NMR** (100 MHz, CDCl₃): δ 159.26, 131.37, 131.03, 130.00 (2C), 113.93 (2C), 73.55, 72.88, 72.32, 64.11, 55.51, 38.68, 36.71, 26.11 (3C), 18.34, 13.59, -4.01, -4.45.

To a stirred solution of (+)-diethyltartrate (30 μ L, 0.175 mmol, 0.15 eq) in CH₂Cl₂ (7.00 mL) over freshly activated 4Å molecular sieves (92 mg) at 0 °C was added Ti(*i*-PrO)₄ (45 μ L, 0.152 mmol, 0.13 eq) and the reaction was stirred for 5 min. The reaction was then cooled to -20 °C and a 3.3M solution of *tert*-butyl hydrogen peroxide in toluene (636 μ L, 1.8 eq) was added. The reaction was stirred for 20 min, and then the allylic alcohol (0.46 g, 1.17 mmol, 1.0 eq) was added as a solution in CH₂Cl₂ (1.75 mL). The reaction was kept at this temperature for 15h, and then H₂O (0.86 mL) was added and the solution warmed to rt. The mixture was stirred for 45 min, and then a 30 % solution of NaOH in saturated NaCl (0.17 mL) was added. The reaction was stirred for 30 min, and was then filtered through a plug of cotton and then filtered through Celite with CH₂Cl₂ and water. The layers were separated, and the organic phase was washed with saturated aqueous NaCl, dried over MgSO₄, and concentrated *in vacuo*. The product was used without further purification.

¹H NMR (500 MHz, CDCl₃): δ 7.27 (d, J = 6.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 4.43 (m, 2H), 4.01 (m, 1H), 3.95 (ddd, J = 2.5, 5.5, 17.5 Hz, 1H), 3.83 (s, 3H), 3.64 (m, 1H), 3.38 (dd, J = 7, 9.5 Hz, 1H), 3.26 (dd, J = 6.5, 9.5 Hz, 1H), 3.10 (m, 1H), 2.95 (m, 1H), 2.06 (m, 1H), 1.71 (m, 1H), 1.52 (m, 1H), 0.91 (m, 12H), 0.10 (s, 6H).

⁴ White, J. D.; Hong, J.; Robarge, L. D. *J. Org. Chem.* **1999**, *64*, 6206.

To a stirred solution of the intermediate epoxy alcohol in THF (4.00 mL) and MeCN (1.20 mL) was added PPh₃ (0.368 g, 1.40 mmol, 1.2 eq) and imidazole (0.096 g, 1.40 mmol, 1.2 eq) and the solution was cooled to 0 °C. I₂ (0.356 g, 1.40 mmol, 1.2 eq) was then added as a solution in THF (0.68 mL) and the reaction was stirred for 45 min. Activated zinc⁵ (0.459 g, 7.02 mmol, 6.0 eq) was then added and the solution heated to reflux for 30 min. The reaction was cooled to rt, water was added (0.15 mL) and the mixture was filtered through Celite and concentrated *in vacuo*. The crude product was purified by flash chromatography (10% EtOAc/hexanes) to yield the allylic alcohol as an oil.

To a solution of the allylic alcohol (0.36 g, 0.913 mmol, 1.0 eq) in CH_2Cl_2 (3.65 mL) at 0 °C was added imidazole (0.155 g, 2.28 mmol, 2.5 eq) and TBSCl (0.165 g, 1.10 mmol, 1.2 eq) and the reaction was warmed to rt. The reaction was stirred for 4h, diluted with Et_2O (25 mL), washed with aq. NH_4Cl (25 mL) and saturated aqueous NaCl (25 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo* to give **24** (464 mg, 78% over 3 steps). The intermediate silyl ether could be used without further purification.

¹**H NMR** (500 MHz, CDCl₃): δ 7.28 (d, *J* = 6.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.82 (m, 1H), 5.13 (d, *J* = 17 Hz, 1H), 5.04 (d, *J* = 10 Hz, 1H), 4.44 (m, 2H), 4.20 (m, 1H), 3.91 (m, 1H), 3.83 (s, 3H), 3.46 (dd, *J* = 6, 9.5 Hz, 1H), 3.22 (dd, *J* = 7.5, 9.5 Hz, 1H), 2.01 (m, 1H), 1.66 (m, 1H), 1.48 (m, 1H), 0.92 (d, *J* = 7 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H), 0.07 (s, 6H).

To a stirred solution of **24** (464 mg, 0.91 mmol) in CH₂Cl₂ (9 mL) at 0 °C was added DDQ (0.249 g, 1.10 mmol, 1.2 eq). The reaction was stirred for 15 min and was then quenched with pH = 7 buffer (25 mL). The mixture was extracted with CH₂Cl₂ (3 x 25 mL), and the combined organic extracts were dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% Et₂O/hexanes) to provide the intermediate alcohol.

To a stirred solution of the intermediate alcohol in CH_2Cl_2 (7 mL) at 0 °C was added Dess-Martin periodinane (0.372 g, 0.88 mmol, 1.2 eq) and the reaction was warmed to rt. The reaction was stirred for 45 min and was then quenched with Na_2SO_3 -doped saturated NaHCO_3 solution (25 mL) and EtOAc (25 mL). The mixture was stirred vigorously 30 min (until the organic layer was clear) and then the two layers were separated. The organic phase was dried over MgSO_4 , filtered, and concentrated *in vacuo* to provide the crude aldehyde, which was used immediately without further purification.

To a stirred solution of the intermediate aldehyde in THF (11.68 mL) and H₂O (2.92 mL) at rt. was added a 2M solution of 2-methyl-2-butene in THF (1.53 mL, 3.07 mmol, 4.2 eq) and KH₂PO₄ (0.140 g, 0.80 mmol, 1.1 eq). The reaction was stirred for 5 min, and then NaClO₂ (0.198 g, 2.19 mmol, 3.0 eq) was added and the reaction was stirred for 2.5h. The reaction was quenched with aq. NH₄Cl (25 mL) and the mixture extracted with EtOAc (2 x 25 mL). The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (25% EtOAc/hexanes) to yield **3** (0.250 g, 64% over 3 steps) as an oil.

⁵ Activated by washing with 2% HCl, distilled water, 95% EtOH, and finally Et₂O.

¹H NMR (500 MHz, CDCl₃): δ 5.79 (m, 1H), 5.17 (d, *J* = 17 Hz, 1H), 5.10 (d, *J* = 10 Hz, 1H), 4.20 (dd, *J* = 7, 13 Hz, 1H), 4.01 (m, 1H), 2.75 (qd, *J* = 3, 7 Hz, 1H), 1.83 (m, 1H), 1.71 (dt, *J* = 6.5, 14 Hz, 1H), 1.23 (d, *J* = 7 Hz, 3H), 0.94 (s, 9H), 0.91 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H); **¹³C NMR** (400 MHz, CDCl₃): δ 177.17, 141.46, 115.18, 71.93, 71.78, 45.50, 43.92, 26.08 (3C), 25.96 (3C), 18.36, 18.18, 13.95, -3.67, -4.00, -4.43, -4.49; [**α**]_D + 28.4 (*c* 0.5 CHCl₃); **IR** (thin film): 1714, 1320, 1249, 1060, 957, 911 cm⁻¹; **HRMS** (ESI) calculated for C₂₀H₄₂O₄Si₂Na⁺ 425.2513, found 425.2503.

10	9	8	7	6	5	4	3	2	1	ppm
Relax. delay 1.500 sec	OBSERVE	H1, 500.3674242	DATA PROCESSING						Solvent: CDCl3	
Pulse 20.8 degrees			Line broadening 0.1 Hz						Ambient temperature	
Acq. time 3.000 sec			FT size 131072						File: gwo-13-096-H	
Width 7200.1 Hz			Total time 2 minutes							
28 repetitions

77.563
77.248
76.929

26.081
25.963
18.359

-4.490
-4.426
-4.001
-3.671

13.949

18.181

45.498

43.924

71.935
71.783

115.180

141.465

177.174

200 180 160 140 120 100 80 60 40 20 0 ppm

Solvent: CDCl₃
Ambient temperature
File: gwo-13-096-Cl3

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 95 minutes

Relax. delay 1.500 sec
Pulse 40.3 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
2048 repetitions

OBSERVE C13, 100.6189623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

77.583
77.265
76.950

77.566
77.247
76.933

131.815
131.269
129.355

113.920

83.241

74.298
73.005

55.489

42.239

36.366

20.787
18.255
17.826
17.743
17.652
14.786
13.523
12.951
9.857

200 180 160 140 120 100 80 60 40 20 0 ppm

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
1024 repetitions

OBSERVE C13, 100.6189623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
WALTZ-16 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 48 minutes

Solvent: CDCl₃
Ambient temperature
File: gwo-11-012-C13

77.576
77.432
77.257
76.942

129.514
130.393
130.795
132.908

126.165
129.036

113.934

73.070
72.771

55.496

39.712
35.339

18.129
17.814
11.894

166.084

159.307

200 180 160 140 120 100 80 60 40 20 0 ppm

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
704 repetitions

OBSERVE C13, 100.6185623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 33 minutes

Solvent: CDCl3
Ambient temperature
File: gwo-12-067-C13

77.564
77.447
77.246
76.927

77.564
77.451
77.246
76.931

12

77.562
77.247
76.929

Solvent: CDCl₃
Ambient temperature
File: gwo-11-014-C13

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 48 minutes

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.311 sec
Width 25000.0 Hz
1024 repetitions

Solvent: CDCl₃
Ambient temperature
File: gwo-13-022-H

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 2 minutes

OBSERVE H1, 500.3674242

Relax. delay 1.500 sec
Pulse 20.8 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
28 repetitions

15

15

18

10	9	8	7	6	5	4	3	2	1	ppm
Relax. delay 1.500 sec	OBSERVE	H1, 400.1547278	DATA PROCESSING	Line broadening 0.1 Hz						
Pulse 33.0 degrees				FT size 131072						
Acq. time 2.999 sec				Total time 2 minutes						
Width 6002.4 Hz										
32 repetitions										
										Solvent: CDCl3
										Ambient temperature
										File: gwo-12-128-H

18

[illegible]

77.564
77.451
77.246
76.927
72.361
66.706
64.435
42.363
41.646
41.392
37.095
36.602
35.737
35.388
32.665
30.545
26.487
26.248
26.176
20.753
19.809
18.690
18.356
16.877
4.351
-2.745
-3.276

134.633
133.325
133.086
132.506
132.240
129.533
119.285
80.962
80.227

-3.451
-3.978
-4.088
-4.793
-4.835

200 180 160 140 120 100 80 60 40 20 0 ppm

Solvent: CDCl₃
Ambient temperature
File: gwo-13-123-C

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 8.9 hours

Relax. delay 1.500 sec
Pulse 40.3 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
11360 repetitions
OBSERVE C13, 100.6189623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

20

[illegible]

77.560
77.447
77.242
76.927
72.353
66.687
64.423
63.001
62.618
42.366
41.885
41.650
38.494
35.972
34.880
34.747
33.996
33.435
32.388
31.326
30.541
29.942
26.491
26.237
26.169
26.081
20.397
19.479
18.701
18.345
17.962
15.243
13.320
9.220
1.256
-2.757
-3.056
-3.382

164.662
133.317
132.726
132.419
131.873
130.337
129.533
118.724
80.830
79.984

-3.542
-3.993
-4.061
-4.110
-4.402
-4.804

200 180 160 140 120 100 80 60 40 20 0 ppm

Solvent: CDCl₃
Ambient temperature
File: gwo-13-121-C3

DATA PROCESSING
Line broadening 1.2 Hz
FT size 131072
Total time 11.7 hours

Relax. delay 1.500 sec
Pulse 40.3 degrees
Acq. time 1.311 sec
Width 25007.8 Hz
14928 repetitions
OBSERVE C13, 100.6189623
DECOUPLE H1, 400.1574807
Power 38 dB
continuously on
GARP-1 modulated

10	9	8	7	6	5	4	3	2	1	ppm
Relax. delay 1.500 sec	OBSERVE	H1, 500.3674242	DATA PROCESSING	Line broadening 0.1 Hz					Solvent: CDCl ₃	
Pulse 20.8 degrees				FT size 131072					Ambient temperature	
Acq. time 3.000 sec				Total time 15 minutes					File: gwo-13-088-2	
Width 7200.1 Hz										
200 repetitions

21

10	9	8	7	6	5	4	3	2	1	ppm
Relax. delay 1.500 sec	OBSERVE	H1, 500.3693956	DATA PROCESSING	Line broadening 0.1 Hz					Solvent: CD3OD	
Pulse 20.8 degrees				FT size 131072					Ambient temperature	
Acq. time 3.000 sec				Total time 45 minutes					File: gwo-13-117-3	
Width 7200.1 Hz										
604 repetitions										