Total Synthesis of (-)-Dictyostatin
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SUPPORTING INFORMATION

General Experimental Procedures.
\(^1\)H 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 \(J_{nxh} = 8.3\) Hz and \(J_{CH} = 130\) 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\(_2\)Cl\(_2\), and Et\(_2\)O 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

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{Si} & \quad \text{Pr} \\
\text{Pr} & \quad \text{Pr} \\
\end{align*}
\]

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\(_2\)O (100 mL). The organic phase was dried over MgSO\(_4\), filtered, and concentrated \(\text{in vacuo}\). The crude product was purified by flash chromatography (25% Et\(_2\)O/hexanes) to yield the intermediate silyl ether (7.40 g, 97%) as an oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta 7.36\) (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\(_3\)): \(\delta 174.77, 153.45, 139.03, 135.70, 129.71\) (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\(_4\)Cl. The organic phase was separated and then washed with water and saturated aqueous NaCl, dried over MgSO\(_4\), and concentrated \(\text{in vacuo}\). The crude product was purified

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

\[ ^1H \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3): \delta \ 5.87 \ (m, \ 1H), \ 5.24 \ (dt, \ J = 2, \ 17.2 \ Hz, \ 1H), \ 5.17 \ (dt, \ J = 1.6, \ 10.4 \ Hz, \ 1H), \ 4.52 \ (m, \ 1H), \ 3.66 \ (t, \ J = 10.8 \ Hz, \ 1H), \ 3.47 \ (m, \ 1H), \ 2.85 \ (b, \ 1H), \ 1.96 \ (m, \ 1H), \ 1.94 \ (s, \ 3H), \ 1.00 - 1.07 \ (m, \ 12H), \ 0.91 \ (m, \ 2H), \ 0.77 \ (d, \ J = 6.8 \ Hz, \ 3H); \]

\[ ^13C \text{NMR} \ (400 \text{ MHz}, \text{CDCl}_3): \delta 138.53, \ 115.46, \ 105.55, \ 79.18, \ 75.84, \ 65.16, \ 41.29, \ 17.57, \ 17.40, \ 17.34 \ (2C), \ 13.86, \ 13.17, \ 11.09, \ 4.97. \]

To a stirred solution of the intermediate alcohol (2.40 g, 8.80 mmol, 1.0 eq) in CH$_2$Cl$_2$ (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 NaHCO$_3$, the layers were separated, and the organic layer was dried over MgSO$_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (10% Et$_2$O/hexanes) to yield 6 (2.80 g, 82%) as an oil.

\[ ^1H \text{NMR} \ (500 \text{ MHz}, \text{CDCl}_3): \delta \ 7.31 \ (d, \ J = 9 \ Hz, \ 2H), \ 6.90 \ (d, \ J = 8.5 \ Hz, \ 2H), \ 5.84 \ (m, \ 1H), \ 5.22 \ (dt, \ J = 1.5, \ 17.5 \ Hz, \ 1H), \ 5.11 \ (dt, \ J = 1.8, \ 10.5 \ Hz, \ 1H), \ 4.51 \ (d, \ J = 11.5 \ Hz, \ 1H), \ 4.46 \ (m, \ 1H), \ 4.42 \ (d, \ J = 11.5 \ Hz, \ 1H), \ 3.83 \ (s, \ 3H), \ 3.61 \ (dd, \ J = 6, \ 9 \ Hz, \ 1H), \ 3.28 \ (dd, \ J = 7.5, \ 9 \ Hz, \ 1H), \ 1.96 \ (m, \ 1H), \ 1.904 \ (s, \ 1H), \ 1.0-1.1 \ (m, \ 14H), \ 0.95 \ (d, \ J = 7 \ Hz, \ 3H); \]

\[ ^13C \text{NMR} \ (100 \text{ MHz}, \text{CDCl}_3): \delta 159.24, \ 139.69, \ 131.21, \ 129.38 \ (2C), \ 114.81, \ 113.91 \ (2C), \ 104.64, \ 79.44, \ 79.54, \ 72.84, \ 72.66, \ 55.50, \ 40.30, \ 17.68, \ 17.57, \ 17.49, \ 13.89, \ 13.40, \ 12.09, \ 5.02 \ (2C); \]

\[ [\alpha]_D -17.7 \ (c 0.5, \text{CHCl}_3); \]

\[ \text{IR} \ (\text{thin film}): 2989, \ 2120, \ 1247, \ 1066, \ 985, \ 911 \ \text{cm}^{-1}; \]

\[ \text{HRMS} \ (\text{ESI}): \text{calculated for C}_{23}\text{H}_{36}\text{O}_3\text{SiNa}^+ 411.2325, \text{found 411.2323}. \]

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

\[ \text{To a solution of Ti(i-PrO)$_3$Cl (0.503 g, 1.93 mmol, 3.0 eq) in Et}_2\text{O (6.40 mL) at -40 °C was added (siloxy)enyne 6 (0.25 g, 0.64 mmol, 1.0 eq) and a 2M solution of i-PrMgCl (1.93 mL, 3.86 mmol, 6.0 eq) via syringe pump over 2h. The reaction was stirred an additional 6h, quenched with saturated NH}_4\text{Cl (25 mL), and stirred with EtOAc (50 mL) for 1h. The mixture was filtered through Celite, the layers were separated, and the organic phase dried over MgSO}_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (40% CH}_2\text{Cl}_2/hexanes) to yield siloxane 7 (0.162 g, 65%) as an oil.} \]

\[ ^1H \text{NMR} \ (500 \text{ MHz}, \text{CDCl}_3): \delta 7.30 \ (d, \ J = 8.5 \ Hz, \ 2H), \ 6.90 \ (d, \ J = 8.5 \ Hz, \ 2H), \ 6.12 \ (qd, \ J = 3, \ 6 \ Hz, \ 1H), \ 4.75 \ (m, \ 1H), \ 4.48 \ (m, \ 1H), \ 3.83 \ (s, \ 3H), \ 3.59 \ (dd, \ J = 7.5, \ 9 \ Hz, \ 1H), \ 3.55 \ (dd, \ J = 2, \ 10 \ Hz, \ 1H), \ 3.43 \ (dd, \ J = 6.5, \ 8.5 \ Hz, \ 1H), \ 2.30 \ (m, \ 1H), \ 2.00 \ (m, \ 1H), \ 1.80 \ (dd, \ J = 2.5, \ 6.5 \ Hz, \ 3H), \ 1.07-1.16 \ (m, \ 5H), \ 1.03 \ (d, \ J = 7 \ Hz, \ 6H), \ 0.99 \ (d, \ J = 6.5 \ Hz, \ 6H), \ 0.91 \ (d, \ J = 6.5 \ Hz, \ 3H); \]

\[ ^13C \text{NMR} \ (100 \text{ MHz}, \text{CDCl}_3): \delta 159.21, \ 142.83, \ 131.82, \ 131.27, \ 129.36 \ (2C), \ 113.92, \ 83.24, \ 74.30, \ 73.01, \ 55.49, \ 42.24, \ 36.37, \ 20.79, \ 18.26, \ 17.83, \ 17.74, \ 17.65, \ 14.79, \ 13.52, \ 12.95, \ 9.86; \]

\[ [\alpha]_D -21.1 \ (c 0.5, \text{CHCl}_3); \]

\[ \text{IR} \ (\text{thin film}): 2948, \ 1610, \ 1508, \ 1037, \ 832 \ \text{cm}^{-1}; \]

\[ \text{HRMS} \ (\text{ESI}): \text{calculated for C}_{23}\text{H}_{38}\text{O}_3\text{SiNa}^+ 413.2482, \text{found 413.2482}. ]}
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 (dd, J = 1.5, 8.5 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, 8.8 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); **13C NMR** (100 MHz, CDCl3): δ 166.08, 159.31, 132.91, 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 MgSO₄, filtered, and concentrated in vacuo. The crude material was used without further purification.

\[ ^1H \text{ NMR (500 MHz, CDCl}_3\]: \( \delta \) 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 NH₄Cl (25 mL). The mixture was extracted with EtOAc (3 x 25 mL), and 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 9 (0.098 g, 85% over 3 steps) as an oil.

\[ ^1H \text{ NMR (500 MHz, CDCl}_3\]: \( \delta \) 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); \[ ^13C \text{ NMR (100 MHz, CDCl}_3\]: 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, CHCl₃); \[ IR \] (thin film): 2989, 2853, 2721, 1613, 1524, 1253, 1037 cm⁻¹; \[ HRMS \] (ESI) calculated for C₁₈H₂₆O₃Na⁺ 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 CH₂Cl₂ (3.40 mL) at 0 °C 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 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 10 (73 mg, 78 %) as an oil.

\[ ^1H \text{ NMR (500 MHz, CDCl}_3\]: \( \delta \) 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); \[ ^13C \text{ NMR (100 MHz, CDCl}_3\]: 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, CHCl₃); \[ IR \] (thin film): 2955, 2927, 2853, 1721, 1613, 1524, 1358, 1253, 1037 cm⁻¹; \[ HRMS \] (ESI) calculated for C₁₈H₂₄O₃Na⁺ 311.1617, found 311.1613.
To a solution of PMP-acetal 10 (0.073 g, 0.252 mmol, 1.0 eq) in CH₂Cl₂ (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 Na₂SO₄ (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 MgSO₄, filtered, and concentrated in vacuo. The crude product was used without further purification.

**¹H NMR** (500 MHz, CDCl₃): 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 (d, J = 7 Hz, 3H), 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 CH₂Cl₂ (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 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 washed with water, dried over MgSO₄, 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, CDCl₃): δ 9.72 (d, J = 1 Hz, 1H), 7.25 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.66 (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 NH₄Cl solution. The mixture was extracted with EtOAc and the combined organic extracts dried over MgSO₄, filtered, and concentrated in vacuo to yield the intermediate β-hydroxy phosphonate. This material was dissolved in CH₂Cl₂ (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 Na₂SO₃-doped saturated NaHCO₃ 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 MgSO₄, 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, CDCl₃): 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), 3.72 (s, 3H), 2.99 (d, J = 7 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\(_3\)) \(\delta\) 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 C\(_{21}\)H\(_{31}\)O\(_6\)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\(_2\)O (150 mL) and water (150 mL). The layers were separated and the organic phase dried with MgSO\(_4\), filtered and concentrated \(\text{in vacuo}\). The crude product was purified by flash chromatography (5% Et\(_2\)O/hexanes) to yield 12 (7.35 g, 95%) as a clear oil.

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 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), 4.38 (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\(_3\)): \(\delta\) 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 C\(_{25}\)H\(_{40}\)O\(_3\)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 Ti(\(i\)-PrO)\(_3\)Cl (0.495 g, 1.8 mmol, 3.0 eq) in Et\(_2\)O (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 \(i\)-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\(_4\)Cl (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 \(\text{in vacuo}\). The crude product was purified by flash chromatography (40% CH\(_2\)Cl\(_2\)/hexanes) to yield 13 (0.183 g, 73%) as a clear oil.
**1H NMR** (500 MHz, CDCl$_3$): $\delta$ 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, CDCl$_3$): $\delta$ 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; [\(\alpha\)]$_D^2$ -7.6 (c 0.5, CHCl$_3$); **IR** (thin film): 2952, 2862, 1610, 1513, 1460, 1247, 852 cm$^{-1}$; **HRMS** (ESI) calculated for C$_{25}$H$_{42}$O$_3$SiNa$^+$ 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•H$_2$O (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 H$_2$O (25 mL) and Et$_2$O (25 mL). The organic phase was dried with MgSO$_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (25% Et$_2$O/hexanes) to yield 2 (128 mg, 95%) as an oil.

**1H NMR** (400 MHz, CDCl$_3$): $\delta$ 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, CDCl$_3$): $\delta$ 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; [\(\alpha\)]$_D$ +2.7 (c 0.5, CHCl$_3$); **IR** (thin film): 3425, 2958, 1690, 1513, 1460, 1247, 852 cm$^{-1}$; **HRMS** (ESI) calculated for C$_{19}$H$_{30}$O$_3$Na$^+$ 329.2087, found 329.2096.

3,5-Bis-((tert-butyl-dimethyl-silanyloxy)-2-methyl-hept-6-enoic acid 5-(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 NaHCO$_3$ solution and extracted with EtOAc (3x). The combined organic
extracts were dried with MgSO₄, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (10% Et₂O/hexanes) to yield 14 (253 mg, 90%) as an oil.

\(^1\)H NMR (500 MHz, CDCl₃): 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, CDCl₃): 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; \([\alpha]_D^0 +2.3;\) IR (thin film): 2956, 2930, 1733, 1249, 1091, 1040, 836, 775 cm\(^{-1}\); HRMS (ESI) calculated for C\(_{39}\)H\(_{70}\)O\(_6\)Si\(_2\)Na\(^+\) 713.4603, found 713.4605.

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

\[\text{14} \quad \text{OPMB} \quad \text{TBSO} \]

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% Et₂O/hexanes) to yield 14 (192 mg, 76%) as an oil.

\(^1\)H NMR (500 MHz, CDCl₃): 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, CDCl₃): 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; \([\alpha]_D^0 +12.3 (c 0.5, \text{CHCl}_3);\) IR (thin film): 2956, 2930, 1733, 1249, 1091, 1040, 836, 775 cm\(^{-1}\); HRMS (ESI) calculated for C\(_{37}\)H\(_{66}\)O\(_6\)Si\(_2\)Na\(^+\) 685.4290, found 642.4263.
5,7-Bis-(tert-butyl-dimethyl-silyloxy)-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 µL, 0.367 mmol, 1.2 eq) in CH₂Cl₂ (300 µL) 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 1 h, 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-λ⁵-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, 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-silyloxy)-6-(4-methoxy-benzyloxy)-5,7,11,13,15,21-hexamethyl-tetracosa-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 µL, 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 Na$_2$SO$_4$ (25 mL) and stirred with EtOAc (25 mL) for 45 min, filtered through Celite, and separated. The organic phase was dried with MgSO$_4$, filtered, and concentrated in vacuo. The crude diol was used directly in the next step.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 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), 0.11 (s, 3H), 0.08 s, 6H).

To a stirred solution of the intermediate diol in CH$_2$Cl$_2$ (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 NaHCO$_3$ solution. The mixture was extracted with CH$_2$Cl$_2$ and the combined organic extracts were dried with MgSO$_4$, filtered, and concentrated in vacuo. The crude product was used directly in the next step.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH$_2$Cl$_2$ (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 CH$_2$Cl$_2$ (3 x 10 mL) and the combined organic extracts dried with MgSO$_4$, filtered through a plug of silica with EtOAc, and concentrated in vacuo. The crude product was used without further purification.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 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 CH$_2$Cl$_2$ (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 Na$_2$SO$_3$-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 dried over MgSO$_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (10% Et$_2$O/petroleum ether) to yield 17 (109 mg, 60% 4-steps) as an oil.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 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 µL) was added to a flask containing Ba(OH)\(_2\)•8H\(_2\)O (20 mg, 0.062 mmol, 0.8 eq) previously heated to 120 °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 µL), and the reaction was stirred for 6 h. 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.

\[ \text{1H NMR} (400 MHz, CDCl}_3\): \(\delta\) 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, \(J = 10.8\) Hz, 1H), 5.41 (t, \(J = 10.8\) Hz, 1H), 5.24 (dd, \(J = 8.4, 10.8\) Hz, 1H), 5.14 (dd, \(J = 2, 10.8\) 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); \[ \text{13C NMR} (100 MHz, CDCl}_3\): \(\delta\) 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), 26.17 (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; \[ [\alpha]_D \] -13.22 (c 0.5, CHCl\(_3\)); \[ \text{IR} \] (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-silyloxy)-5,7,11,13,15,21-hexamethyl-tetracosa-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]\(_6\), PhH at rt. The reaction was stirred for 8 h, flushed through a plug of silica with EtOAc and concentrated in vacuo to yield the intermediate ketone as an oil.

\[ \text{1H NMR} (500 MHz, CDCl}_3\): \(\delta\) 7.27 (d, \(J = 8.5\) Hz, 2H), 6.88 (d, \(J = 9\) Hz, 2H), 6.44 (dt, \(J = 11\) 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 (m, 2H), 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); \[ \text{13C NMR} (100 MHz, CDCl}_3\): \(\delta\) 214.64, 159.38, 153.11, 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.
To a stirred solution of the intermediate ketone in CH$_2$Cl$_2$ (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 CH$_2$Cl$_2$ (3 x 10 mL). The combined organic extracts were dried with MgSO$_4$, 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.

$^1$H NMR (500 MHz, CDCl$_3$): 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 Et$_2$O (150 µL) at -40 °C was added a 0.28M solution of Zn(BH$_4$)$_2$ (126 µL, 35.2 µmol, 4.0 eq) dropwise over 5 min. The solution was stirred for 30 min, then quenched with saturated NH$_4$Cl (10mL), and the aqueous phase extracted with EtOAc. The organic phase was dried with MgSO$_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography (25% Et$_2$O/petroleum ether) to yield 19 (7 mg, 88%) as an oil.

$^1$H NMR (400 MHz, CDCl$_3$): 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); $^{13}$C NMR (100 MHz, CDCl$_3$): 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; [α]$_D$ +7.7 (c 0.5, CHCl$_3$); IR (thin film): 3425, 2959, 2928, 2855, 1513, 1460, 1250, 1180, 1089, 1037, 835 cm$^{-1}$; HRMS (ESI) calculated for C$_{54}$H$_{110}$O$_6$Si$_4$Na$^+$ 989.7271, found 989.7300.
To a stirred solution of diol 19 (7.0 mg, 7.7 µmol, 1.0 eq) in CH₂Cl₂ (150 µL) at 0 °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 NaHCO₃ solution (10 mL), and the aqueous phase was extracted with CH₂Cl₂ (3 x 10mL). The combined organic extracts were dried over MgSO₄, filtered through a plug of silica with EtOAc, and concentrated in vacuo. The crude product was used without further purification.

H NMR (500 MHz, CDCl₃): 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), 0.86 (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 °C was added Et₃N (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, 3.5 eq) and the reaction was allowed to warm to rt. The reaction was stirred for 8h and was then quenched with saturated NaHCO₃ solution. The mixture was extracted with EtOAc and the combined extracts dried over MgSO₄, 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).

H NMR (500 MHz, CDCl₃): 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); ¹³C NMR (100 MHz, CDCl₃): 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, -3.06, -3.54, -3.99, -4.06, -4.11, -4.40, -4.80; [α]D -28.4 (c 0.5, CHCl₃); IR (thin film): 3449, 2927, 1739, 1299, 1265, 1174, 1070 cm⁻¹; HRMS (ESI) calculated for C₆₆H₁₂₉F₆O₁₀PSi₅Na⁺ 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 µmol, 1.0 eq) was treated with a 3:1:1 AcOH:THF:H₂O solution (500 µL) 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 µmol, 1.0 eq) in CH₂Cl₂ (90 µL) at 0 °C was added Dess-Martin periodinane (3.0 mg, 6.6 µmol, 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, 15.5 Hz, 1H), 6.55 (dd, J = 10.5, 16.5 Hz, 1H), 6.13 (dd, J = 1.5, 8 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, 36H), 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 µmol, 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 µmol, 12.0 eq) 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, 1474, 1225, 1045 cm\(^{-1}\); HRMS (ESI) calculated for C\(_{56}H_{108}O_{6}Si_{4}Na\)\(^{+}\) 1011.7115, found 1011.7131.

**Dictyostatin, 1**

To a solution of macrolactone 21 (3.0 mg, 3 \(\mu\)mol, 1.0 eq) in THF (400 \(\mu\)L) at 0 °C was added HF•pyridine (100 \(\mu\)L) 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 °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 \textit{in vacuo}. The crude product was purified by flash chromatography (50 \(\rightarrow\) 75 \(\rightarrow\) 100% EtOAc/hexanes) to yield 1 (1.1 mg, 67%).

\(^{1}H\) NMR (500 MHz, CD\(_3\)OD): \(\delta\) 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\(_3\)OD): \(\delta\) 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; [\(\alpha\)]\(D\) -22.00 (c 0.05 MeOH); HRMS (ESI) calculated for C\(_{32}H_{52}O_{6}H\)\(^{+}\) 533.3836, found 533.3831.
Table. Comparison of data for synthetic and natural dictyostatin

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</tr>
<tr>
<td>29</td>
<td>5.21 (brd, 17)</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>1.11 (d, 7.0)</td>
<td>13.75</td>
</tr>
<tr>
<td>31</td>
<td>1.09 (d, 7.1)</td>
<td>19.35</td>
</tr>
<tr>
<td>32</td>
<td>0.92 (d, 6.4)</td>
<td>15.97</td>
</tr>
<tr>
<td>33</td>
<td>0.89 (d, 6.5)</td>
<td>21.81</td>
</tr>
<tr>
<td>34</td>
<td>1.03 (d, 6.8)</td>
<td>10.39</td>
</tr>
<tr>
<td>35</td>
<td>0.98 (d, 6.7)</td>
<td>18.06</td>
</tr>
</tbody>
</table>

Due to limited sample, this data was obtained by HSQC and HMBC experiments.
Procedure for the Synthesis of Acid 3

![Chemical Structure]

To a stirred solution of 22 (500 mg, 1.37 mmol, 1.0 eq) in toluene (13.7 mL) was added crotonaldehyde (560 µL, 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 µL, 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 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), 3.70 (m, 1H), 3.64 (dd, J = 5.6, 9.2 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 µl, 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 µl, 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 µl, 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).

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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 zinc (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 CH₂Cl₂ (3.65 mL) at 0 °C was added imidazole (0.155 g, 2.28 mmol, 2.5 eq) and TBSCI (0.165 g, 1.10 mmol, 1.2 eq) and the reaction was warmed to rt. The reaction was stirred for 4h, diluted with Et₂O (25 mL), washed with aq. NH₄Cl (25 mL), and saturated aqueous NaCl (25 mL), dried over MgSO₄, filtered, and concentrated in vacuo to give 24 (464 mg, 78% over 3 steps). The intermediate silyl ether could be used without further purification.

**1H 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 then was 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 CH₂Cl₂ (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 Na₂SO₃-doped saturated NaHCO₃ 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 MgSO₄, 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.

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4. Activated by washing with 2% HCl, distilled water, 95% EtOH, and finally Et₂O.
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 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); $^{13}$C NMR (400 MHz, CDCl$_3$): $\delta$ 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; $[\alpha]_D + 28.4$ (c 0.5 CHCl$_3$); IR (thin film): 1714, 1320, 1249, 1060, 957, 911 cm$^{-1}$; HRMS (ESI) calculated for C$_{20}$H$_{42}$O$_4$Si$_2$Na$^+$ 425.2513, found 425.2503.
Data Acquired: Dec 28 2005

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

Observe H1, 500.3674242

Data Processing
Line broadening 0.1 Hz
FT size 131072
Total time 2 minutes

Solvent: CDCl3
Ambient temperature
File: gwo-13-096-H
Data Acquired: Dec 26 2005

University of Colorado at Boulder NMR

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

0 ppm

10 9 8 7 6 5 4 3 2 1 ppm

DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 1 minutes

Solvent: CDCl3
Ambient temperature
File: gwo-ketophosphonate-H
Data Acquired: Aug 31 2005

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
60 repetitions

Observe H1, 500.3674242

Data Processing
Line broadening 0.1 Hz
FT size 131072
Total time 4 minutes

Solvent: CDCl3
Ambient temperature
File: gwo-12-073-1
Data Acquired: Dec 26 2005

10 9 8 7 6 5 4 3 2 1 ppm

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

Observe H1, 500.3674242

Data Processing
Line broadening 0.1 Hz
FT size 131072
Total time 2 minutes

Solvent: CDC13
Ambient temperature
File: gwo-11-062-H
Data Acquired: May 12 2005

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7199.4 Hz
76 repetitions

OBSERVE H1, 500.3674242
DATA PROCESSING
Line broadening 0.1 Hz
FT size 131072
Total time 5 minutes

Solvent: CDC13
Ambient temperature
File: gwo-11-014-2

University of Colorado at Boulder NMR
Data Acquired: Oct 15 2005

Relax. delay 1.500 sec
Pulse 19.7 degrees
Acq. time 3.000 sec
Width 7200.1 Hz
20 repetitions

Observe H1, 500.3674242

Data Processing
Line broadening 0.1 Hz
FT size 131072
Total time 1 minutes

Solvent: CDCl3
Ambient temperature
File: gwo-12-129-H
Data Acquired: Jan 13 2006

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 H2, 400.1574807
Power 38 dB continuously on
GARP-1 modulated

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

Solvent: CDCl3
Ambient temperature
File: gwo-l3-123-C

University of Colorado at Boulder NMR
Data Acquired: Dec 22 2005

University of Colorado at Boulder NMR

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

Observe H1, 500.3674242

Data Processing
Line broadening 0.1 Hz
FT size 131072
Total time 15 minutes

Solvent: CDC13
Ambient temperature
File: gwo-13-088-2