Biomimetic Synthesis of Pinnatal and Sterekunthal A.

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Supporting Information

General methods. Reactions were carried out under Ar atmosphere in flame dried glassware. Tetrahydrofuran (THF) and methylene chloride (CH_2Cl_2) were purified by passage over activated alumina. Benzene (PhH) was distilled from CaH_2 immediately prior to use. Dimethylsulfoxide (DMSO) was stored over 4 Å molecular sieves. All other reagents and solvents were used without further purification from commercial sources. Organic extracts were dried over MgSO_4 . Flash column chromatography was carried out with EcoChrom ICN SiliTech 32–63 D 60 Å silica gel. Preparative reverse-phase HPLC (RP-HPLC) was performed on a Rainin instrument with an Alltech Econosil C-18 (10 μ) column. Reactions and chromatography fractions were monitored with Merck silica gel 60 F_{254} plates, visualized with ceric ammonium molybdate, *p*-anisaldehyde, and dinitrophenylhydrazine. NMR spectra were measured on a Bruker DRX spectrometer at 500 MHz for ^1H spectra and 125 MHz for ^{13}C spectra in CDCl_3 unless otherwise specified and calibrated from residual solvent signal. IR spectra were measured with a Genesis FT-IR spectrometer by thin film. Melting points were determined with an electrothermal apparatus and are uncorrected.

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8-(tert-Butyl-diphenyl-silanyloxy)-2,6-dimethyl-octa-2,6-dienoic acid ethyl ester (14). To a solution of 18-crown-6 (11.47g, 43.41 mmol) in THF (100 mL) was added 2-[bis-(2,2,2-trifluoro-ethoxy)-phosphoryl]-propionic acid ethyl ester.¹ The solution was cooled to -78°C , and KHMDs (32.0 mL, 0.5 M in toluene, 16.0 mmol) was added. After 30 min, a solution of aldehyde **13**² (5.30 g, 14.47 mmol) in THF (40 mL) was added dropwise. The reaction mixture was maintained at -78°C for 1 h, then quenched with aqueous NH_4Cl (100 mL). The mixture was extracted with Et_2O (6×100 mL). The combined organic layers were washed with brine (1×250 mL), dried, and concentrated *in vacuo*. Flash chromatography (15:1 hexanes : EtOAc) afforded unsaturated ethyl ester **14** as a colorless oil (4.94 g, 76%): R_f 0.28 (19:1 hexanes : EtOAc); IR: 1713, 2857, 2930 cm^{-1} ; ^1H NMR (500 MHz): δ 7.68–7.71 (m, 4H), 7.36–7.44 (m, 6H), 5.91 (m, 1H), 5.42 (m, 1H), 4.18–4.24 (m, 4H), 2.54 (m, 2H), 2.09 (t, $J = 7.5$ Hz, 2H), 1.90 (q, $J = 1.4$ Hz, 3H), 1.45 (s, 3H), 1.31 (t, $J = 7.0$ Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (125 MHz) δ 168.1, 142.2, 136.2, 135.6, 134.0, 129.5, 127.6, 127.3, 124.6, 61.0, 60.0, 38.9, 27.6, 26.8, 20.6, 19.1, 16.1, 14.3; HRMS (FAB+) Calcd for $\text{C}_{24}\text{H}_{29}\text{O}_3\text{Si}$ ($M - t\text{Bu}$)⁺: 393.1886, Found: 393.1893.

8-(tert-Butyl-diphenyl-silanyloxy)-2,6-dimethyl-octa-2,6-dien-1-ol. A solution of ethyl ester **14** (4.94 g, 11.0 mmol) in CH_2Cl_2 (110 mL) was cooled to -78°C . DIBAL (16.1 mL, 1.5 M in toluene, 24.1 mmol) was added dropwise, and following addition the reaction mixture was maintained at -78°C for 30 min. The reaction was quenched with aqueous Rochelle's salts (250 mL) and stirred vigorously for 12 hours at rt. The mixture was extracted with CH_2Cl_2 (3×200 mL). The combined organic phases were dried and concentrated *in vacuo*. Flash chromatography (3:1 hexanes : EtOAc) yielded the title allylic alcohol as a

pale yellow oil (4.20 g, 94%); R_f 0.37 (3:1 hexanes : EtOAc); IR: 2857, 2931, 3341 cm^{-1} ; ^1H NMR (500 MHz): δ 7.67-7.71 (m, 4H), 7.36-7.44 (m, 6H), 5.36 (m, 1H), 5.27 (m, 1H), 4.20 (d, J = 6.6 Hz, 2H), 4.11 (s, 2H), 2.14 (m, 2H), 2.00 (m, 2H), 1.80 (m, 3H), 1.46 (s, 3H), 1.28 (br s, 1H), 1.05 (s, 9H); ^{13}C NMR (125 MHz) δ 136.5, 135.6, 134.7, 133.9, 129.5, 127.7, 127.6, 124.5, 61.5, 61.0, 39.4, 26.8, 25.7, 21.2, 19.1, 16.3; HRMS (EI⁺) Calcd for $\text{C}_{22}\text{H}_{27}\text{O}_2\text{Si}$ ($\text{M} - t\text{Bu}$)⁺: 351.1780, Found: 351.1780.

tert-Butyl-[3,7-dimethyl-8-(tetrahydro-pyran-2-yloxy)-octa-2,6-dienyloxy]-diphenyl-silane. To a solution of the above allylic alcohol (4.20 g, 10.3 mmol) and PPTS (25.8 mg, 0.103 mmol) in CH_2Cl_2 (5 mL) was added 3,4-dihydro-2H-pyran (1.0 mL, 11.3 mmol). The reaction mixture was maintained at rt for 36 h. It was then diluted with Et_2O (75 mL) and washed with brine (3×50 mL). The organic phase was dried and concentrated *in vacuo* to afford the title THP-protected alcohol as a pale yellow oil (5.05 g, 99%); R_f 0.22 (15:1 hexanes : EtOAc); IR: 2858, 2931 cm^{-1} ; ^1H NMR (500 MHz): δ 7.66-7.71 (m, 4H), 7.35-7.44 (m, 6H), 5.36 (m, 2H), 4.59 (t, J = 3.7 Hz, 1H), 4.22 (d, J = 6.0 Hz, 2H), 4.13 (d, J = 11.4, 1H), 4.08 (d, J = 11.4, 1H), 3.89 (m, 1H), 3.52 (m, 1H), 2.15 (m, 2H), 2.00 (t, J = 7.3 Hz, 2H), 1.80-1.91 (m, 1H), 1.77 (d, J = 1.2 Hz, 3H), 1.68-1.75 (m, 1H), 1.49-1.63 (m, 4H), 1.43 (s, 3H), 1.04 (s, 9H); ^{13}C NMR (125 MHz) δ 136.5, 135.6, 134.0, 131.9, 129.5, 129.0, 127.5, 124.3, 97.5, 65.4, 62.2, 61.1, 39.6, 30.7, 26.8, 25.9, 25.5, 21.7, 19.5, 19.2, 16.3; HRMS (FAB⁺) Calcd for $\text{C}_{31}\text{H}_{44}\text{LiO}_3\text{Si}$ ($\text{M} + \text{Li}$)⁺: 499.3220, Found: 499.3229.

3,7-Dimethyl-8-(tetrahydro-pyran-2-yloxy)-octa-2,6-dien-1-ol. To a solution of the above differentially protected diol (5.05 g, 10.3 mmol) in THF (20 mL) was added TBAF (15.4 mL, 1.0 M in THF, 15.4 mmol). After 1 h, the reaction mixture was diluted with water (75 mL) and extracted with Et_2O (3×75 mL). The combined organic phases were washed with NaHCO_3 (150 mL), water (150 mL), and brine (150 mL), dried, and concentrated *in vacuo*. Flash chromatography (8:1 hexanes : EtOAc, then 3:1 hexanes : EtOAc) afforded the title allylic alcohol (2.36 g, 90%) as a pale yellow oil: R_f 0.12 (3:1 hexanes : EtOAc); IR: 2871, 2942, 3391 cm^{-1} ; ^1H NMR (500 MHz): δ 5.40 (m, 1H), 5.32 (t, J = 6.9 Hz, 1H), 4.58 (t, J = 3.2 Hz, 1H), 4.03-4.14 (m, 4H), 3.88 (m, 1H), 3.51 (m, 1H), 2.19 (q, J = 7.4 Hz, 2H), 2.04 (t, J = 7.4 Hz, 2H), 1.78-1.87 (m, 1H), 1.76 (d, J = 1.2 Hz, 3H), 1.68-1.74 (m, 1H), 1.67 (s, 3H), 1.49-1.62 (m, 4H), 1.45 (br s, 1H); ^{13}C NMR (125 MHz) δ 139.0, 132.2, 128.8, 123.9, 97.5, 65.4, 62.1, 59.3, 39.5, 30.6, 26.0, 25.5, 21.7, 19.5, 16.3; HRMS (FAB⁺) Calcd for $\text{C}_{15}\text{H}_{27}\text{O}_3$ ($\text{M} + \text{H}$)⁺: 255.1960, Found: 255.1954.

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3,7-Dimethyl-8-(tetrahydro-pyran-2-yloxy)-octa-2,6-dienal (15). A solution of the above allylic alcohol (879.1 mg, 3.456 mmol) in CH_2Cl_2 (35 mL) was cooled to 0 $^\circ\text{C}$. MnO_2 (2.90 g, 34.6 mmol) was added, and the reaction mixture was allowed to warm to rt. After 5 h, the reaction mixture was filtered through celite and concentrated *in vacuo*. Flash chromatography (3:1 hexanes : EtOAc) afforded **15** (708.0 mg, 81%) as a yellow oil: R_f 0.53 (1:1 hexanes : EtOAc); IR: 1675, 2870, 2942 cm^{-1} ; ^1H NMR (500 MHz): δ 9.99 (d, J = 8.1 Hz, 1H), 5.87 (m, 1H), 5.31 (t, J = 6.4 Hz, 1H), 4.57 (t, J = 3.2 Hz, 1H), 4.12 (d, J = 11.4 Hz, 1H), 4.04 (d, J = 11.4 Hz, 1H), 3.87 (m, 1H), 3.51 (m, 1H), 2.22-2.34 (m, 4H), 2.16 (d, J = 1.2 Hz, 3H), 1.77-1.87 (m, 1H), 1.76 (s, 3H), 1.67-1.73 (m, 1H), 1.48-1.63 (m, 4H); ^{13}C NMR (125 MHz) δ 191.3, 163.2, 133.2, 127.5, 127.3, 97.5, 65.2, 62.1, 40.7, 30.6, 25.4, 25.3, 21.2, 19.4, 17.5; HRMS (FAB⁺) Calcd for $\text{C}_{15}\text{H}_{25}\text{O}_3$ ($\text{M} + \text{H}$)⁺: 253.1804, Found: 253.1804.

8-Hydroxy-2-(5-hydroxy-4-methyl-pent-3-enyl)-2-methyl-2H-benzo[g]chromene-5,10-dione (19). A solution of unsaturated aldehyde **15** (708.0 mg, 2.806 mmol), naphthoquinone **16** (485.0 mg, 2.551 mmol), β -alanine (34.1 mg, 0.382 mmol), and HOAc (1 mL) in PhH (35 mL) was heated at reflux for 18 h. The reaction mixture was then concentrated *in vacuo*. Flash chromatography (2:1 hexanes : EtOAc) afforded a mixture of diastereomers **18** (537.8 mg, 50%), a red oil: ^1H NMR (500 MHz): δ 7.99 (d, J = 8.5 Hz, 1H), 7.57 (d, J = 2.6 Hz, 1H), 7.12 (dd, J = 8.5, 2.6 Hz, 1H), 6.71 (br s, 1H), 6.68 (d, J = 10.1 Hz, 1H), 5.66 (d, J = 10.1 Hz, 1H), 5.34 (q, J = 6.7 Hz, 1H), 4.57 (t, J = 3.5, 1H), 4.05 (m, 2H), 3.84 (m, 1H), 3.48 (m, 1H), 2.21 (m, 2H), 1.89-1.98 (m, 1H), 1.74-1.84 (m, 1H), 1.63-1.74, (m, 5H), 1.52-1.60 (m, 4H), 1.49 (s, 3H); A solution of **18** (537.8 mg, 1.267 mmol) and TsOH $\cdot$ H₂O (24.0 mg, 0.126 mmol) in MeOH (15 mL) was maintained at rt for 1.5 h. The reaction mixture was then diluted with NaHCO₃ (50 mL) and extracted with CH₂Cl₂ (4 $\times$ 50 mL). The combined organic phases were dried and concentrated *in vacuo*. Flash chromatography (1:1 hexanes : EtOAc) afforded allylic alcohol **19** (418.3 mg, 97%) as a red solid: mp 112-114 $^{\circ}\text{C}$; R_f 0.16 (1:1 hexanes : EtOAc); IR: 1451, 1573, 1601, 1648, 1675, 2938, 2978, 3311 cm^{-1} ; ^1H NMR (500 MHz): δ 8.80 (br s, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 2.6 Hz, 1H), 7.15 (dd, J = 8.5, 2.6 Hz, 1H), 6.68 (d, J = 10.0 Hz, 1H), 5.67 (d, J = 10.0 Hz, 1H), 5.27 (t, J = 7.3 Hz, 1H), 4.23 (d, J = 12.1 Hz, 1H), 4.11 (d, J = 12.1 Hz, 1H), 2.94 (br s, 1H), 2.26 (m, 2H), 1.84-1.92 (m, 1H), 1.76-1.83 (m, 1H), 1.75 (d, J = 1.4 Hz, 3H), 1.51 (s, 3H); ^{13}C NMR (125 MHz) δ 181.2, 180.8, 161.7, 151.9, 134.4, 133.1, 130.3, 129.1, 127.9, 124.1, 121.3, 117.8, 116.1, 112.8, 82.6, 61.4, 41.1, 27.0, 22.1, 21.4; HRMS (EI⁺) Calcd for C₂₀H₂₀O₅ (M⁺): 340.1311, Found: 340.1317.

5-(8-Hydroxy-2-methyl-5,10-dioxo-5,10-dihydro-2H-benzo[g]chromen-2-yl)-2-methyl-pent-2-enal (12). A solution of oxalyl chloride (0.30 mL, 2.0 M in CH₂Cl₂, 0.60 mmol) in CH₂Cl₂ (10 mL) was cooled to -78 $^{\circ}\text{C}$. DMSO (80.0 μL , 1.21 mmol) was added dropwise, and the mixture was stirred 30 min. A solution of **19** (100.0 mg, 0.294 mmol) in CH₂Cl₂ (1 mL) was added dropwise, and the reaction mixture was stirred 30 min. Et₃N (0.25 mL, 1.78 mmol) was added dropwise, and the reaction mixture was maintained at -78 $^{\circ}\text{C}$. After 30 min, the reaction mixture was allowed to warm to rt, diluted with aqueous NH₄Cl (25 mL), and extracted with CH₂Cl₂ (3 $\times$ 25 mL). The combined organic phases were dried and concentrated *in vacuo*. Flash chromatography (2:1 hexanes : EtOAc, then 1:1 hexanes : EtOAc) afforded unsaturated aldehyde **12** (86.3 mg, 87%): R_f 0.43 (1:1 hexanes : EtOAc); IR 1573, 1600, 1648, 1675, 2929, 3280; ^1H NMR (500 MHz): δ 10.10 (s, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.56 (d, J = 2.5 Hz, 1H), 7.15 (dd, J = 8.5, 2.5 Hz, 1H), 6.89 (br s, 1H), 6.73 (d, J = 10.0 Hz, 1H), 6.52 (t, J = 8.2 Hz, 1H), 5.67 (d, J = 10.0 Hz, 1H), 2.75 (m, 1H), 2.03-2.12 (m, 2H), 1.81-1.89 (m, 1H), 1.72 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (125 MHz) δ 191.2, 181.0, 179.8, 160.7, 152.0, 148.4, 136.3, 133.3, 129.3, 129.2, 124.6, 120.9, 117.4, 116.9, 112.8, 82.4, 41.1, 27.5, 21.8, 16.4; HRMS (FAB⁺) Calcd for C₂₀H₁₉O₅ (M + H)⁺: 339.1232, Found: 339.1240.

Pinnatal (1). Aldehyde **12** (26.8 mg, 0.0792 mmol) was left standing at rt for 7 d. The reaction mixture was passed over a short plug of silica (1:1 hexanes : EtOAc), then purification by reverse-phase HPLC (3:2 MeOH : H₂O) afforded **1** (24.4 mg, 91%).

Lit. ¹ H NMR data ³	Found ¹ H NMR data	Lit. ¹³ C NMR data ^{3,4} (acetone- <i>d</i> ₆)	Found ¹³ C NMR data (acetone- <i>d</i> ₆)
0.70 (s, 3H)	0.71 (s, 3H)	18.49	19.0
1.18 (s, 3H)	1.18 (s, 3H)	23.93	24.5
1.73 (m, 1H)	-	25.76	26.3
1.84-2.04 (3H, m)	1.82-2.09 (4H, m)	37.73	38.3
2.26 (ddd, <i>J</i> = 6, 8, 14 Hz, 1H)	2.21-2.29 (m, 1H)	47.10	47.6
2.94 (dd, <i>J</i> = 4, 7 Hz, 1H)	2.94 (dd, <i>J</i> = 3.8, 7.1 Hz, 1H)	50.27	50.8
7.28 (dd, <i>J</i> = 2.5, 8.5 Hz, 1H)	7.29 (dd, <i>J</i> = 2.6, 8.7 Hz, 1H)	56.40	56.9
-	7.47 (br s, 1H)	78.67	79.1
7.54 (d, <i>J</i> = 2.5 Hz, 1H)	7.56 (d, <i>J</i> = 2.6 Hz, 1H)	84.87	85.4
7.83 (d, <i>J</i> = 7 Hz, 1H)	7.83 (d, <i>J</i> = 7.1 Hz, 1H)	112.64	113.1
8.22 (d, <i>J</i> = 8.5 Hz, 1H)	8.24 (d, <i>J</i> = 8.7 Hz, 1H)	123.33	123.9
10.26 (s, 1H)	10.27 (s, 1H)	128.10	128.6
		130.67	131.3
		137.66	138.1
		140.26	140.7
		142.03	142.7
		163.25	163.8
		177.40	177.9
		193.45	194.0
		203.56	204.2

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Sterekunthal A (4). A solution of **1** (20.2 mg, 0.0587 mmol) in PhH (5 mL) was heated to 160 °C in a sealed tube. The reaction mixture was passed over a short plug of silica (1:1 hexanes : EtOAc), then purification by reverse-phase HPLC (3:2 MeOH : H₂O) afforded **4** (18.6 mg, 92%).

Lit. ¹ H NMR data ³	Found ¹ H NMR data	Lit. ¹³ C NMR data ³	Found ¹³ C NMR data
1.29 (s, 3H)	1.31 (s, 3H)	18	18.4
1.85 (m, 2H)	1.75-1.91 (m, 2H)	24	23.6
2.13 (s, 3H)	2.11 (s, 3H)	31	31.9
2.49 (m, 3H)	2.40-2.55 (m, 3H)	42	40.5
6.44 (dd, <i>J</i> = 6.0, 9.5 Hz, 1H)	6.45 (dd, <i>J</i> = 6.0, 9.8 Hz, 1H)	44	43.6
6.95 (d, <i>J</i> = 9.5 Hz, 1H)	6.96 (d, <i>J</i> = 9.8 Hz, 1H)	49	49.1
7.16 (dd, <i>J</i> = 2.5, 8.5 Hz, 1H)	7.20 (dd, <i>J</i> = 2.6, 8.7 Hz, 1H)	113	112.5
-	7.38 (br s, 1H)	120	119.5
7.49 (d, <i>J</i> = 2.5 Hz, 1H)	7.53 (d, <i>J</i> = 2.6 Hz, 1H)	122	121.8
7.99 (d, <i>J</i> = 8.5 Hz, 1H)	8.06 (d, <i>J</i> = 8.7 Hz, 1H)	125	124.7
9.95 (s, 1H)	9.97 (s, 1H)	130	129.7
		135	134.2
		138	137.7
		139	138.1
		140	140.1
		163	161.6
		182	181.7
		185	184.0
		204	204.6
		208	207.4

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