

An expedient total synthesis of (-)-dactylolide and formal synthesis of (-)-zampanolide

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Supporting Information

General Procedure ^1H and ^{13}C NMR spectra were collected on a 360 MHz or 500 MHz Bruker spectrometer. Chemical shifts were reported in parts per million relative to tetramethylsilane (TMS) using deuterated chloroform (CDCl_3) as the internal reference, and coupling constants were reported in Hertz. Optical rotation measurements were performed on a Rudolph AUTOPOL IV polarimeter at Biocryst Pharmaceuticals, Inc. FTIR spectra were recorded on a BIO-RAD FTS-40 spectrometer. HRMS determination was performed in the laboratory of mass spectrometry at the University of Illinois, Urbana-Champaign. Solvents and reagents were used as purchased without further purification.

5,6-Bis-(tert-butyl-dimethyl-silanyloxy)-hex-2-ynoic acid ethyl ester (6) To a flame-dried flask under Ar, a BuLi solution (1.6 M in hexanes, 21 mL, 33.7 mmol) was added dropwise into a solution of the alkyne (7.37 g, 22.5 mmol) in THF (63 mL) at -78°C and stirred for 15 min. Ethyl chloroformate (6.45 mL, 67.5 mmol) was then added, and the solution was warmed to rt and kept stirring for 45 min before quenched with a

saturated NaHCO₃ solution (60 mL). The aqueous solution was extracted with Et₂O (3 X 60 mL). The combined organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 2% EtOAc in hexanes) afforded the alkynoate (*R*_f = 0.40, 2% EtOAc in hexanes) as colorless oil (9.5 g, 100%). ¹H NMR (360 MHz, CDCl₃) δ 4.21 (q, *J* = 7.2, 2H), 3.87 (m, 1H), 3.59 (dd, *J* = 10.2, 4.9, 1H), 3.48 (dd, *J* = 10.2, 6.9, 1H), 2.65 (dd, *J* = 17.0, 4.7, 1H), 2.43 (dd, *J* = 17.0, 6.6, 1H), 1.29 (t, *J* = 7.2, 3H), 0.89 (s, 18H), 0.12 (s, 3H), 0.08 (s, 3H), 0.06 (s, 6H). ¹³C NMR (90 MHz, CDCl₃) δ 154.9, 87.2, 74.8, 71.4, 66.7, 62.1, 35.2, 26.1, 25.0, 23.3, 18.3, 14.2, -4.3, -4.6, -5.1, -5.2. [α]_D²⁰ -6.4 (c 0.90, CH₂Cl₂). IR (CH₂Cl₂): 1710, 1471, 1115, 1082 cm⁻¹. HRMS (ESI) calcd for C₂₀H₄₁O₄Si₂ (M+H)⁺: 401.2543, found: 401.2528.

5,6-Bis-(tert-butyl-dimethyl-silanyloxy)-3-methyl-hex-2-enoic acid ethyl ester (7)

To a solution of NaOMe (61 mg, 1.1 mmol) in MeOH (54 mL), were added PhSH (2.86 mL, 28.0 mmol) and the alkynoate (9.0 g, 22.5 mmol). The solution was kept stirring for 20 h at rt, before filtered through a silica plug, which was then eluted with Et₂O to bring down the yellow band. Evaporation of solvents yielded the crude product. Flash chromatography (silica, 10% EtOAc in hexanes) afforded the alkenoate (*R*_f = 0.40, 10% EtOAc in hexanes) as pale yellow oil (10.35 g, 90%). ¹H NMR (360 MHz, CDCl₃) δ 7.51 (m, 2H), 7.35 (m, 3H), 5.94 (s, 1H), 4.21 (m, 2H), 3.63 (m, 1H), 3.33 (dd, *J* = 10.0, 5.0, 1H), 3.15 (dd, *J* = 10.0, 5.6, 1H), 1.29 (t, *J* = 7.2, 3H), 0.82 (s, 9H), 0.79 (s, 9H), -0.01 (s, 3H), -0.04 (s, 3H), -0.09 (s, 6H). ¹³C NMR (90 MHz, CDCl₃) δ 166.1, 156.9, 135.6, 131.5, 129.4, 115.9, 71.8, 67.6, 60.1, 41.8, 18.3, 15.5, 14.3, -4.2, -4.6, -5.2, -5.3.

To a flame-dried flask under Ar, a MeMgBr solution (3.0 M in Et₂O, 473 μL, 1.42 mmol) was added dropwise into a suspension of CuI (296 mg, 1.56 mmol) in THF

(4.7 mL) at -78°C . The reaction mixture was warmed to rt and then cooled back to -78°C , before a solution of the thioether (0.50g, 0.98 mmol) in THF (0.5 mL) was added. The solution was warmed to 0°C and kept stirring for 1 h. Water (0.5 mL) was then added, and the mixture was diluted with Et_2O (20 mL), dried over Na_2SO_4 . The solution was filtered through a silica plug, which was then eluted with Et_2O (10 mL). The combined organics were concentrated under reduced pressure to afford the product ($R_f = 0.55$, 10% EtOAc in hexanes) as colorless oil without further purification (395 mg, 97%). ^1H NMR (360 MHz, CDCl_3) δ 5.70 (s, 1H), 4.14 (m, 2H), 3.81 (m, 1H), 3.54 (dd, $J = 9.9, 5.0$, 1H), 3.37 (dd, $J = 9.9, 6.8$, 1H), 2.45 (dd, $J = 12.7, 3.8$, 1H), 2.18 (d, $J = 1.4$, 3H), 2.15 (dd, $J = 12.7, 7.9$, 1H), 1.26 (t, $J = 7.0$, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.05 (s, 6H), 0.03 (s, 3H), 0.0 (s, 3H). ^{13}C NMR (90 MHz, CDCl_3) δ 166.8, 156.9, 118.5, 71.8, 67.3, 59.6, 46.2, 26.2, 26.0, 25.7, 19.7, 18.5, 18.3, 15.5, 14.3, -4.2, -4.7, -5.1, -5.2. $[\alpha]_D^{20}$ -7.7 (c 2.35, CH_2Cl_2). IR (CH_2Cl_2): 1713, 1653, 1474, 1226, 1154, 1094 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{45}\text{O}_4\text{Si}_2$ ($\text{M}+\text{H}$) $^+$: 417.2856, found: 417.2860.

5,6-Bis-(tert-butyl-dimethyl-silanyloxy)-3-methyl-hex-2-enal (8) To a flame-dried flask under Ar, a DIBAL-H solution (1.0 M in CH_2Cl_2 , 2.2 mL, 2.2 mmol) was added dropwise into a solution of the ester (416 mg, 1.0 mmol) in CH_2Cl_2 (7.8 mL) at -78°C and stirred for 2 h. The solution was then poured directly into a stirring mixture of a saturated sodium potassium tartrate aqueous solution (3 mL) and hexanes (17 mL). The aqueous layer was extracted with Et_2O (10 mL), and the combined organics were filtered through a celite plug. Evaporation of solvents afforded the alcohol ($R_f = 0.20$, 20% EtOAc in hexanes) as colorless oil without further purification (354 mg, 95%). ^1H NMR (360 MHz, CDCl_3) δ 5.45 (t, $J = 7.1$, 1H), 4.15 (m, 2H), 3.77 (m, 1H), 3.51 (dd, $J = 9.9$,

5.4, 1H), 3.39 (dd, J = 9.9, 6.3, 1H), 2.31 (dd, J = 13.3, 4.2, 1H), 2.06 (dd, J = 13.3, 7.5, 1H), 1.70 (s, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.04 (s, 9H), 0.02 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 136.8, 126.6, 72.1, 67.5, 59.7, 44.9, 26.2, 26.1, 25.9, 23.6, 18.6, 17.2, -4.1, -4.6, -5.06, -5.13. [α]_D²⁰ -4.4 (c 0.90, CH₂Cl₂). IR (CH₂Cl₂): 1473, 1226, 1154, 1094 cm⁻¹. HRMS (ESI) calcd for C₁₉H₄₃O₃Si₂ (M+H)⁺: 375.2751, found: 375.2756.

To a solution of the allylic alcohol (151 mg, 0.404 mmol) and NaOAc (27 mg, 0.324 mmol) in CH₂Cl₂ (2 mL), was added PCC (174 mg, 0.808 mmol). The reaction mixture was stirred for 1 h at rt, before diluted with Et₂O (10 mL) and then filtered through a silica plug. The plug was washed with Et₂O (4 mL). Evaporation of solvents afforded the enal (R_f = 0.50, 20% EtOAc in hexanes) as yellowish oil (141 mg, 94%, 6:1 Z:E). ¹H NMR (360 MHz, CDCl₃) δ 9.99 (d, J = 8.0, 1H), 5.92 (d, J = 8.0, 1H), 3.86 (m, 1H), 3.56 (dd, J = 9.8, 4.7, 1H), 3.37 (dd, J = 9.8, 7.2, 1H), 2.53 (dd, J = 13.3, 4.5, 1H), 2.21 (s, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.051 (s, 6H), 0.045 (s, 3H), 0.01 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 191.4, 161.6, 130.2, 72.0, 67.1, 46.0, 26.1, 14.3, -4.2, -4.6, -5.13, -5.15. [α]_D²⁰ -2.4 (c 1.83, CH₂Cl₂). IR (CH₂Cl₂): 1672, 1469, 1108 cm⁻¹. HRMS (ESI) calcd for C₁₉H₄₁O₃Si₂ (M+H)⁺: 373.2594, found: 373.2589.

8,9-Bis-(tert-butyl-dimethylsilanyloxy)-6-methyl-nona-1,5-dien-4-ol (9) To a flame-dried flask under Ar, allylmagnesium bromide (1.0 M solution in ether, 29.0 mL) was added dropwise into a solution of (-)-Ipc₂BOMe (10.0 g, 31.9 mmol) in anhydrous ether (32 mL) at 0°C. The reaction mixture was stirred at rt for 1 h before cooled to -78°C. The aldehyde (7.18 g, 19.3 mmol) was added dropwise into the borane solution and allowed to stir for 1 h and then warm slowly to rt during 1 h. An aqueous solution of NaOH (3 M, 12.8 mL) was added, followed by slow addition of a 30% H₂O₂ solution

(25.5 mL). The mixture was refluxed for 3 h. After cooled to rt, the biphasic solution was separated, and the aqueous layer was extracted with ether (3 X 50 mL). The combined organics were dried over Na₂SO₄, and rotavapped to yield the crude product. Flash chromatography (silica, 10% EtOAc in hexanes) afforded the homoallylic alcohol (R_f = 0.50, 20% EtOAc in hexanes) as colorless oil (5.70 g, 71%) along with other isomers (two diastereomers for each of the Z/E isomers, combined yield: 88%, de: 90%). ¹H NMR (360 MHz, CDCl₃) δ 5.81 (m, 1H), 5.25 (dd, J = 8.5, 1.0, 1H), 5.12 (m, 2H), 4.41 (dd, J = 14.6, 6.3, 1H), 3.77 (ddd, J = 12.2, 11.2, 5.6, 1H), 3.49 (dd, J = 10.0, 4.5, 1H), 3.41 (dd, J = 10.0, 4.4, 1H), 2.31 (dd, J = 11.4, 6.5, 1H), 2.28 (m, 2H), 2.05 (dd, J = 11.4, 6.7, 1H), 1.72 (d, J = 1.2, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.055 (s, 3H), 0.047 (s, 6H), 0.045 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 136.1, 134.7, 130.2, 118.0, 72.3, 68.0, 67.2, 44.9, 42.3, 26.2, 26.1, 18.6, 18.4, 17.6, -4.05, -4.50, -5.05, -5.11. $[\alpha]_D^{20}$ -10 (c 1.3, CH₂Cl₂). IR (CH₂Cl₂): 1471, 1120, 1092 cm⁻¹. HRMS (ESI) calcd for C₂₂H₄₆O₃Si₂Na (M+Na)⁺: 437.2883, found: 437.2885.

6-[4,5-Bis-(tert-butyl-dimethyl-silanyloxy)-2-methyl-pent-1-enyl]-5,6-dihydro-

pyran-2-one (11) To a flame-dried flask under Ar, acryloyl chloride (2.23 mL, 27.6 mmol) was added dropwise into a solution of the alcohol (5.70 g, 13.8 mmol), Et₃N (4.29 mL, 30.4 mmol), and DMAP (84 mg, 0.70 mmol) in CH₂Cl₂ (138 mL) at rt. The solution was stirred for 16 h, before brine (100 mL) was added. The aqueous layer was extracted with CH₂Cl₂ (2 X 50 mL), and the combined organics were washed with brine (50 mL) and then dried over Na₂SO₄. The solvents were removed under reduced pressure. Flash chromatography (silica, 2% EtOAc in hexanes) afforded the acrylate (R_f = 0.40, 10% EtOAc in hexanes) as colorless oil (5.12 g, 79%). ¹H NMR (360 MHz, CDCl₃) δ 6.37 (dd,

$J = 17.2, 1.3, 1\text{H}$), 6.07 (dd, $J = 17.2, 10.0, 1\text{H}$), 5.78 (dd, $J = 10.0, 1.3, 1\text{H}$), 5.68 (m, 2H), 5.24 (dd, $J = 9.3, 1.2, 1\text{H}$), 5.06 (m, 2H), 3.75 (ddd, $J = 12.5, 11.6, 5.6, 1\text{H}$), 3.48 (dd, $J = 10.0, 5.4, 1\text{H}$), 3.38 (dd, $J = 10.0, 6.1, 1\text{H}$), 2.40 (m, 2H), 2.31 (dd, $J = 13.9, 6.0, 1\text{H}$), 2.06 (dd, $J = 13.9, 6.5, 1\text{H}$), 1.75 (d, $J = 1.1, 3\text{H}$), 0.89 (s, 9H), 0.85 (s, 9H), 0.04 (s, 6H), 0.03 (s, 3H), 0.0 (s, 3H). ^{13}C NMR (90 MHz, CDCl_3) δ 165.7, 138.3, 133.7, 130.8, 129.5, 125.7, 118.2, 71.8, 70.7, 67.3, 45.0, 39.6, 26.2, 26.1, 18.6, 18.3, 17.7, -4.2, -4.6, -5.08, -5.13. $[\alpha]_{\text{D}}^{20}$ -8.2 (c 0.17, CH_2Cl_2). IR (CH_2Cl_2): 1715, 1409, 1201 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{48}\text{O}_4\text{Si}_2\text{Na}$ ($\text{M}+\text{Na}$) $^{+}$: 491.2989, found: 491.2995.

To a flame-dried flask under Ar, Grubbs' second generation catalyst (208 mg, 0.245 mmol) was added into a solution of the acrylate (2.29 g, 4.90 mmol) in CH_2Cl_2 (300 mL). The solution was heated under refluxing for 16 h, and then the solvent was removed under reduced pressure. Flash chromatography (silica, 20% EtOAc in hexanes) afforded the lactenone ($R_f = 0.28$, 20% EtOAc in hexanes) as colorless oil (2.06 g, 96%). ^1H NMR (360 MHz, CDCl_3) δ 6.87 (dddd, $J = 13.2, 8.5, 3.6, 1.4, 1\text{H}$), 6.03 (ddd, $J = 13.2, 1.7, 1.7, 1\text{H}$), 5.40 (dd, $J = 8.4, 0.9, 1\text{H}$), 5.15 (m, 1H), 3.77 (ddd, $J = 11.6, 5.2, 1.4, 1\text{H}$), 3.51 (dd, $J = 10.0, 5.1, 1\text{H}$), 3.39 (dd, $J = 10.0, 6.5, 1\text{H}$), 2.37 (m, 3H), 2.08 (dd, $J = 13.5, 7.0, 1\text{H}$), 1.76 (d, $J = 1.4, 1\text{H}$), 0.89 (s, 9H), 0.88 (s, 9H), 0.05 (s, 12H). ^{13}C NMR (90 MHz, CDCl_3) δ 164.6, 144.9, 140.6, 124.9, 122.0, 75.0, 72.4, 67.1, 44.6, 29.9, 26.2, 26.1, 18.5, 18.3, 18.1, -4.2, -4.5, -5.09, -5.12. $[\alpha]_{\text{D}}^{20}$ -12 (c 0.17, CH_2Cl_2). IR (CH_2Cl_2): 1719, 1424 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{45}\text{O}_4\text{Si}_2$ ($\text{M}+\text{H}$) $^{+}$: 441.2856, found: 441.2860.

6-[4,5-Bis-(tert-butyl-dimethyl-silanyloxy)-2-methyl-pent-1-enyl]-4-hydroxy-tetrahydro-pyran-2-one (12)

To a solution of the lactenone (0.600 g, 1.36 mmol) in MeOH (6.8 mL), was added an aqueous H_2O_2 solution (30%, 488 mg, 4.58 mmol).

The solution was cooled to 0°C, and an aqueous NaOH solution (6.0 M, 0.14 mL, 0.82 mmol) was added dropwise and stirred for 10 min. The reaction mixture was then warmed to rt and kept stirring for 0.5 h, before diluted with Et₂O (15 mL) and H₂O (15 mL). Concentrated aqueous HCl solution was added to adjust the pH to 4. The aqueous layer was extracted with Et₂O (2 X 15 mL), and the combined organics were washed with brine (10 mL). After dried over Na₂SO₄, the organic solution was concentrated under reduced pressure. The residue was re-dissolved in PhH (3.4 mL), and the resultant solution was refluxed for 15 min using a Dean-Stark apparatus to remove water. After evaporation of PhH, flash chromatography (silica, 20% EtOAc in hexanes) afforded the epoxide (*R*_f = 0.32, 20% EtOAc in hexanes) as colorless viscous oil (515 mg, 83%). ¹H NMR (360 MHz, CDCl₃) δ 5.22 (ddd, *J* = 18.7, 8.8, 3.0, 1H), 5.21 (d, *J* = 1.5, 1H), 3.75 (ddd, *J* = 11.8, 5.0, 1.8, 1H), 3.66 (dd, *J* = 6.8, 3.9, 1H), 3.58 (d, *J* = 4.1, 1H), 3.50 (dd, *J* = 10.0, 5.1, 1H), 3.37 (dd, *J* = 10.0, 6.6, 1H), 2.33 (m, 2H), 2.05 (m, 2H), 1.73 (d, *J* = 0.7, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.044 (s, 3H), 0.040 (s, 6H), 0.035 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 167.9, 140.5, 123.8, 72.2, 70.7, 67.1, 52.3, 49.3, 44.4, 30.1, 26.2, 26.1, 18.6, 18.3, 18.0, -4.2, -4.5, -5.08, -5.10, -5.12. [*α*]_D²⁰ +34 (c 0.37, CH₂Cl₂). IR (CH₂Cl₂): 1738, 1473, 1363, 1112, 1080, 1013 cm⁻¹. HRMS (ESI) calcd for C₂₃H₄₅O₅Si₂ (M+H)⁺: 457.2806, found: 457.2805.

To a solution of (PhSe)₂ (482 mg, 1.55 mmol) in EtOH (8.2 mL) under Ar at rt, was added NaBH₄ (118 mg, 3.09 mmol) and stirred for 5 min before cooled to 0°C. HOAc (176 μL, 3.09 mmol) was then added dropwise, and the solution was kept stirring for 5 min before a solution of the epoxide (471 mg, 1.03 mmol) in EtOH (6.2 mL) was added. The reaction mixture was stirred for 15 min, and then diluted with EtOAc (36 mL).

The organic solution was washed with half-saturated NaCl solution (9 mL). The aqueous solution was then extracted with EtOAc (2 X 9 mL) and the combined organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 1:1 EtOAc:hexanes) afforded the alcohol (*R*_f = 0.30, 1:1 EtOAc:hexanes) as pale yellow oil (368 mg, 78%). ¹H NMR (360 MHz, CDCl₃) δ 5.42 (ddd, *J* = 8.8, 8.8, 3.4, 1H), 5.28 (d, *J* = 8.6, 1H), 4.37 (ddd, *J* = 7.6, 3.9, 3.9, 1H), 3.76 (ddd, *J* = 11.6, 5.5, 5.5, 1H), 3.50 (dd, *J* = 10.1, 5.5, 1H), 3.38 (dd, *J* = 10.1, 6.4, 1H), 2.71 (dd, *J* = 17.7, 4.9, 1H), 2.61 (ddd, *J* = 17.7, 3.4, 1.3, 1H), 2.34 (dd, *J* = 13.4, 4.9, 1H), 2.07 (dd, *J* = 13.4, 7.0, 1H), 1.93 (ddd, *J* = 14.2, 3.9, 3.9, 1H), 1.82 (dd, *J* = 14.2, 3.4, 1H), 1.76 (s, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.04 (s, 12H). ¹³C NMR (90 MHz, CDCl₃) δ 170.7, 139.6, 125.3, 73.0, 72.2, 67.1, 63.0, 44.5, 38.9, 36.3, 26.2, 26.1, 18.5, 18.3, 17.9, -4.21, -4.50, -5.10, -5.12. [α]_D²⁰ -6.4 (c 0.90, CH₂Cl₂). [α]_D²⁰ +14 (c 0.20, CH₂Cl₂). IR (CH₂Cl₂): 1728, 1424 cm⁻¹. HRMS (ESI) calcd for C₂₃H₄₇O₅Si₂ (M+H)⁺: 459.2962, found: 459.2960.

2-Allyl-6-[4,5-bis-(tert-butyl-dimethyl-silanyloxy)-2-methyl-pent-1-enyl]-4-

triethylsilanyloxy-tetrahydro-pyran (13)

To a flame-dried flask under Ar, an allylMgBr solution (1.0 M in Et₂O, 0.37 mL, 0.37 mmol) was added dropwise into a solution of the lactone (57 mg, 0.12 mmol) in Et₂O (1.2 mL) at -78°C. The suspension was stirred for 0.5 h, before quenched with H₂O (1.2 mL) and then diluted with EtOAc (25 mL). The mixture was dried over Na₂SO₄, and the solvents were removed under reduced pressure to afford the hemi-ketal (*R*_f = 0.60, 1:1 EtOAc:hexanes) as colorless oil (53 mg). This material was used without further purification. To a solution of the hemi-ketal (53 mg, 0.11 mmol) in CH₂Cl₂ (1.1 mL) a flame-dried flask under Ar at -78°C, were added Et₃SiH (0.18 mL, 1.1 mmol) in one portion and TFA (41 μL, 0.55 mmol)

sequentially. The solution was then warmed to -40°C and kept stirring for 0.5 h, before quenched with a saturated NaHCO_3 solution (1.1 mL). The mixture was diluted with Et_2O (25 mL) and dried over Na_2SO_4 . The solvents were then removed under reduced pressure. Flash chromatography (silica, 5% EtOAc in hexanes) afforded the tetrahydropyran ($R_f = 0.50$, 10% EtOAc in hexanes) as pale yellow oil (55 mg, 76%). ^1H NMR (360 MHz, CDCl_3) δ 5.84 (m, 1H), 5.20 (d, $J = 7.9$, 1H), 5.07 – 4.99 (m, 2H), 4.54 (ddd, $J = 13.5$, 8.3, 5.2, 1H), 4.18 (m, 1H), 3.88 (m, 1H), 3.75 (ddd, $J = 11.8$, 11.8, 5.8, 1H), 3.52 – 3.36 (m, 2H), 2.33 – 2.25 (m, 2H), 2.13 (dd, $J = 13.3$, 6.8, 1H), 2.01 (dd, $J = 13.3$, 6.8, 1H), 1.70 (s, 3H), 1.64 – 1.19 (m, 4H), 0.96 (t, $J = 8.0$, 9H), 0.89 (s, 9H), 0.87 (s, 9H), 0.58 (q, $J = 8.0$, 6H), 0.045 (s, 3H), 0.041 (s, 3H), 0.035 (s, 6H). ^{13}C NMR (90 MHz, CDCl_3) δ 135.5, 135.3, 129.1, 116.5, 72.7, 71.3, 69.3, 67.5, 65.2, 44.9, 40.9, 39.8, 38.9, 26.2, 26.1, 18.6, 17.9, 7.1, 5.1, -4.2, -4.5, -5.06, -5.14. $[\alpha]_D^{20}$ -3.3 (c 0.30, CH_2Cl_2). IR (CH_2Cl_2): 1471, 1081 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{32}\text{H}_{67}\text{O}_4\text{Si}_3$ ($\text{M}+\text{H}$) $^+$: 599.4347, found: 599.4353.

2-Allyl-6-[3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2-methyl-propenyl]-tetrahydro-pyran-4-ol (14) To a solution of the silyl ether (180 mg, 0.30 mmol) in THF (4.8 mL), was added a TBAF solution (1.0 M in THF, 1.2 mL, 1.2 mmol) and stirred for 6 h. The reaction mixture was then diluted with EtOAc (20 mL) and brine (5 mL). The aqueous layer was extracted with EtOAc (2 X 10 mL). The combined organics were dried over Na_2SO_4 and concentrated under reduced pressure to give the triol ($R_f = 0.15$, EtOAc) as pale yellow oil (69 mg). To a flame-dried flask under Ar, the triol was re-dissolved in CH_2Cl_2 (3.0 mL), and dimethoxypropane (180 μL , 1.5 mmol) and $\text{TsOH}\cdot\text{H}_2\text{O}$ (6 mg, 0.03 mmol) were added. The reaction were stirred for 16 h, before quenched with a

saturated NaHCO₃ solution (3 mL) and then diluted with EtOAc (30 mL). The organic solution was separated, dried over Na₂SO₄, and concentrated under reduced pressure. Flash chromatography (silica, 40% EtOAc in hexanes) afforded the acetone (R_f = 0.40, 1:1 EtOAc: hexanes) as yellow oil (72 mg, 81%). ¹H NMR (360 MHz, CDCl₃) δ 5.78 (m, 1H), 5.20 (d, J = 8.5, 1H), 5.06 – 4.98 (m, 2H), 4.50 (m, 1H), 4.21 – 4.14 (m, 2H), 3.94 (dd, J = 8.1, 6.0, 1H), 3.84 (m, 1H), 3.49 (dd, J = 7.6, 7.6, 1H), 2.37 (dd, J = 13.7, 5.8, 1H), 2.29 (dd, J = 14.3, 7.7, 1H), 2.20 – 2.10 (m, 2H), 1.70 (s, 3H), 1.68 – 1.42 (m, 4H), 1.37 (s, 3H), 1.31 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 135.7, 134.9, 128.4, 117.0, 109.1, 74.8, 71.2, 69.4, 69.0, 64.9, 43.8, 40.8, 38.8, 37.9, 27.2, 26.0, 17.7. [α]_D²⁰ +3.6 (c 0.22, CH₂Cl₂). IR (CH₂Cl₂): 1423 cm⁻¹. HRMS (ESI) calcd for C₁₇H₂₉O₄ (M+H)⁺: 297.2066, found: 297.2072.

2-Allyl-6-[3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2-methyl-propenyl]-tetrahydro-pyran-4-one (15)

To a solution of the alcohol (72 mg, 0.24 mmol) and NaOAc (16 mg, 0.20 mmol) in CH₂Cl₂ (2.5 mL), was added PCC (108 mg, 0.50 mmol) and stirred for 1.5 h. The reaction mixture was then diluted with Et₂O (7.5 mL) and filter through a silica plug, which was washed with Et₂O (2.0 mL). The combined organics were concentrated under reduced pressure. Flash chromatography (silica, 20% EtOAc in hexanes) afforded the ketone (R_f = 0.60, 1:1 EtOAc: hexanes) as pale yellow oil (53 mg, 74%). ¹H NMR (360 MHz, CDCl₃) δ 5.79 (m, 1H), 5.30 (dd, J = 7.6, 1.3, 1H), 5.11 – 5.06 (m, 2H), 4.30 (ddd, J = 13.8, 7.9, 6.0, 1H), 4.20 (ddd, J = 12.9, 12.9, 6.5, 1H), 3.97 (dd, J = 8.0, 6.0, 1H), 3.67 (m, 1H), 3.51 (dd, J = 7.9, 7.1, 1H), 2.47 – 2.14 (m, 8H), 1.69 (s, 3H), 1.38 (s, 3H), 1.32 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 206.9, 136.8, 133.5, 126.8, 118.2, 109.2, 76.5, 74.6, 74.2, 69.3, 47.8, 47.2, 43.6, 40.7, 27.1, 25.9, 17.7. [α]_D²⁰ -12 (c 0.23, CH₂Cl₂). IR

(CH₂Cl₂): 1715, 1064 cm⁻¹. HRMS (ESI) calcd for C₁₇H₂₇O₄ (M+H)⁺: 295.1909, found: 295.1915.

2-Allyl-6-[3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2-methyl-propenyl]-4-methylene-tetrahydropyran (16)

To a flame-dried flask under Ar, ⁿBuLi (1.5 M solution in hexanes, 0.24 mL) was added dropwise into a solution of MePh₃PBr (129 mg, 0.36 mmol) in anhydrous THF (2.1 mL) at -78°C. The reaction mixture was stirred for 15 min, before warmed to 0°C and continued to stir for 20 min. A solution of the ketone (53 mg, 0.18 mmol) in THF (2.1 mL) was then added and stirred at rt for 1.5 h. The reaction was quenched with H₂O (4 mL) and the aqueous layer was extracted with ether (3 X 4 mL). The combined organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 5% EtOAc in hexanes) afforded the methylene tetrahydropyran (R_f = 0.45, 20% EtOAc in hexanes) as slightly yellow oil (41 mg, 78%). ¹H NMR (500 MHz, CDCl₃) δ 5.83 (m, 1H), 5.30 (dd, J = 7.5, 1.0, 1H), 5.06 (m, 2H), 4.73 (dd, J = 1.5, 1.5, 2H), 4.22 (ddd, J = 13.2, 6.1, 6.1, 1H), 4.01 (m, 1H), 4.00 (dd, J = 7.6, 5.7, 1H), 3.54 (dd, J = 7.5, 7.5, 1H), 3.36 (m, 1H), 2.41 (dd, J = 14.0, 6.3, 2H), 2.27-2.12 (m, 2H), 2.03 (ddd, J = 11.5, 11.5, 1.2, 1H), 1.92 (ddd, J = 11.5, 11.5, 1.2, 1H), 1.72 (d, J = 1.0, 3H), 1.41 (s, 3H), 1.35 (s, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 144.6, 135.7, 134.8, 128.4, 117.1, 109.1, 108.9, 78.0, 75.7, 74.8, 69.5, 43.8, 41.0, 40.2, 27.2, 26.0, 17.7. HRMS (EI) calcd for C₁₈H₂₈O₃ (M⁺), 292.2038, found 292.2031.

7-Hydroxy-5-methyl-hepta-2,4-dienoic acid ethyl ester (18) To a flame-dried flask under Ar, a LiHMDS solution (1.0 M in THF, 34.5 mL, 34.5 mmol) was added dropwise into a solution of triethyl phosphonoacetate (6.91 mL, 34.5 mmol) in THF (34 mL) and stirred for 15 min. at 0°C. A solution of the enal (3.95 g, 17.2 mmol) in THF (52 mL) was

then added. The reaction mixture was warmed to rt and stirred for 1 h, before diluted with Et₂O (100 mL) and quenched with H₂O (30 mL). The aqueous solution was extracted with Et₂O (30 mL), and the combined organics were dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 5% EtOAc in hexanes) afforded the dienoate (*R*_f = 0.40, 10% EtOAc in hexanes) as colorless oil (5.03 g, 98%). ¹H NMR (360 MHz, CDCl₃) δ 7.54 (dd, *J* = 15.3, 11.8, 1H), 6.05 (d, *J* = 11.6, 1H), 5.75 (d, *J* = 15.1, 1H), 4.19 (q, *J* = 7.5, 2H), 3.70 (t, *J* = 6.5, 2H), 2.50 (t, *J* = 6.6, 2H), 1.90 (s, 3H), 1.29 (t, *J* = 7.4, 3H), 0.87 (s, 9H), 0.04 (s, 6H). ¹³C NMR (90 MHz, CDCl₃) δ 167.7, 147.1, 141.1, 125.7, 119.5, 61.9, 60.2, 39.2, 36.7, 26.2, 25.2, 14.5, -5.1. IR (CH₂Cl₂): 1704, 1637, 1156, 1101 cm⁻¹. HRMS (ESI) calcd for C₁₆H₃₁O₃Si (M+H)⁺: 299.2042, found: 299.2047.

To a solution of the silyl ether (298 mg, 1.0 mmol) in THF (10 mL), was added a Py•HF solution (65% in Py, 0.3 mL, ~10.0 mmol) and stirred for 4 h. The reaction mixture was diluted with Et₂O (30 mL), and quenched with a saturated NaHCO₃ solution (10 mL) along with solid NaHCO₃ until no gas was evolved. The aqueous layer was extracted with EtOAc (10 mL), and the combined organics were dried over Na₂SO₄. Evaporation of solvents afforded the alcohol (*R*_f = 0.30, 1:1 EtOAc: hexanes) as pale yellow oil (169 mg, 92%) without further purification. ¹H NMR (360 MHz, CDCl₃) δ 7.54 (dd, *J* = 15.1, 11.7, 1H), 6.09 (d, *J* = 11.7, 1H), 5.77 (d, *J* = 15.5, 1H), 4.17 (q, *J* = 7.2, 2H), 3.72 (t, *J* = 6.7, 2H), 2.55 (t, *J* = 6.7, 2H), 1.90 (s, 3H), 1.27 (t, *J* = 7.2, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 167.9, 146.4, 140.5, 126.1, 119.7, 60.9, 60.4, 36.2, 24.7, 14.5. IR (CH₂Cl₂): 1704, 1637, 1154 cm⁻¹. HRMS (ESI) calcd for C₁₀H₁₇O₃ (M+H)⁺: 185.1178, found: 185.1168.

7-Hydroxy-5-methyl-nona-2,4,8-trienoic acid ethyl ester (19) A solution of Dess-Martin periodinane (15% in CH₂Cl₂, 17 mL, 8.14 mmol) was added into the alcohol (1.00 g, 5.43 mmol) at 0°C. The reaction mixture was warmed to rt and kept stirring for 1 h, before quenched with isopropanol (6 mL) and stirred for 5 more minutes. The mixture was filtered through silica, which was then eluted with EtOAc. The combined organics were concentrated under reduced pressure. Flash chromatography (silica, 30% EtOAc in hexanes) afforded the aldehyde (*R_f* = 0.35, 30% EtOAc in hexanes) as pale yellow oil (602 mg, 61%). ¹H NMR (360 MHz, CDCl₃) δ 9.59 (t, *J* = 1.8, 1H), 7.39 (dd, *J* = 15.1, 11.7, 1H), 6.21 (d, *J* = 11.7, 1H), 5.83 (d, *J* = 15.1, 1H), 4.16 (q, *J* = 7.2, 2H), 3.40 (s, 2H), 1.89 (s, 3H), 1.25 (t, *J* = 7.2, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 197.5, 167.2, 139.2, 139.0, 127.8, 121.4, 60.5, 47.9, 25.3, 14.4. IR (CH₂Cl₂): 1718, 1706, 1638, 1158 cm⁻¹. HRMS (ESI) calcd for C₁₀H₁₅O₃ (*M*+H)⁺: 183.1021, found: 183.1036.

To a flame-dried flask under Ar, a vinylMgBr solution (1.0 M in THF, 0.93 mL, 0.93 mmol) was added dropwise into a solution of the aldehyde (67 mg, 0.37 mmol) in THF (2.8 mL) at -78°C. The reaction mixture was stirred for 2 h, before quenched with a saturated NH₄Cl solution (0.9 mL), warmed to rt, and diluted with EtOAc (20 mL). The organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 30% EtOAc in hexanes) afforded the allylic alcohol (*R_f* = 0.50, 1:1 EtOAc: hexanes) as brown oil (38 mg, 49%). ¹H NMR (360 MHz, CDCl₃) δ 7.53 (dd, *J* = 15.1, 11.7, 1H), 6.11 (d, *J* = 11.7, 1H), 5.88 (m, 1H), 5.77 (d, *J* = 15.1, 1H), 5.25 (d, *J* = 17.2, 1H), 5.11 (d, *J* = 10.4, 1H), 4.17 (g, *J* = 7.1, 2H), 2.62 (dd, *J* = 13.4, 8.2, 1H), 2.41 (dd, *J* = 13.4, 5.4, 1H), 1.91 (s, 3H), 1.27 (t, *J* = 7.1, 3H). ¹³C NMR (90 MHz, CDCl₃) δ 167.7, 145.7, 140.5, 140.3, 126.7, 120.0, 115.3, 71.6, 60.3, 40.6, 25.3, 14.5. IR (CH₂Cl₂):

1707, 1640, 1632, 1157 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{19}\text{O}_3$ ($\text{M}+\text{H}$) $^{+}$: 211.1334, found: 211.1334.

7-(tert-Butyl-dimethyl-silanyloxy)-5-methyl-nona-2,4,8-trienoic acid (4) In a flame-dried flask under Ar, a solution of the allylic alcohol (195 mg, 0.93 mmol), TBSCl (280 mg, 1.86 mmol) and Im (190 mg, 2.79 mmol) in DMF (2.0 mL) was kept stirring for 20 h, before diluted with Et_2O (40 mL) and quenched with H_2O (10 mL). The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography (silica, 10% EtOAc in hexanes) afforded the TBS ether (R_f = 0.32, 10% EtOAc in hexanes) as pale yellow oil (254 mg, 85%). ^1H NMR (360 MHz, CDCl_3) δ 7.53 (dd, J = 15.1, 11.6, 1H), 6.05 (d, J = 11.6, 1H), 5.83 (dd, J = 10.4, 6.1, 1H), 5.78 (dd, J = 10.4, 6.6, 1H), 5.75 (d, J = 15.3, 1H), 5.17 (ddd, J = 17.1, 1.4, 1.4, 1H), 5.04 (ddd, J = 10.3, 1.3, 1.3, 1H), 4.22 (m, 1H), 4.19 (q, J = 7.1, 2H), 2.58 (dd, J = 13.2, 7.7, 1H), 2.34 (dd, J = 13.2, 5.4, 1H), 1.90 (s, 3H), 1.28 (t, J = 7.1, 3H), 0.86 (s, 9H), 0.01 (s, 6H). ^{13}C NMR (90 MHz, CDCl_3) δ 167.6, 146.2, 141.1, 141.0, 126.1, 119.3, 114.1, 73.0, 60.1, 41.7, 25.9, 25.7, 18.3, 14.4, -2.9, -4.4. IR (CH_2Cl_2): 1708, 1631 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{33}\text{O}_3\text{Si}$ ($\text{M}+\text{H}$) $^{+}$: 325.2199, found: 325.2205.

To a solution of the ester (241 mg, 0.74 mmol) in EtOH (3.7 mL), was added dropwise an aqueous NaOH solution (1.0 M, 1.85 mL) at 0°C . The reaction mixture was then warmed to rt and stirred for 20 h before an aqueous HCl solution was added (1.0 M, 1.85 mL). EtOAc (20 mL) was added and allowed to partition. The aqueous layer was extracted with EtOAc (2 X 5 mL) and the organics were combined, dried over Na_2SO_4 , and solvents were removed under reduced pressure. The residue was re-dissolved in toluene (4 mL) and then rotavapped to afford the acid (R_f = 0.56, EtOAc) as pale yellow

viscous oil (208 mg, 95%). This material was used without further purification. This is a known compound. {Hoye, T. R.; Hu, M. *J. Am. Chem. Soc.* **2003**, *125*, 9576.}

5-(6-Allyl-4-methylene-tetrahydro-pyran-2-yl)-1-(tert-butyl-dimethyl-silanyloxy)-4-methyl-pent-4-en-2-ol (3) To a solution of the acetonide (29 mg, 0.1 mmol) in EtOH (0.33 mL) and CH₂Cl₂ (0.33 mL) at 0°C, was added TFA (0.33 mL) dropwise and stirred for 10 min. The solvents were removed under reduced pressure, and the residue was co-evaporated with PhMe (2 X 2 mL) to remove TFA to afford the diol. To a flame-dried flask under Ar, Et₃N (56 µL, 0.4 mmol) was added dropwise into a solution of the diol, TBSCl (38 mg, 0.25 mmol), DMAP (2 mg, 16 µmol) in CH₂Cl₂ (1.0 mL) at 0°C. The reaction mixture was warmed to rt and stirred for 1.5 h, before quenched with H₂O (0.5 mL). The aqueous layer was extracted with Et₂O (2 X 5 mL), and the combined organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 20% EtOAc in hexanes) afforded the alcohol (R_f = 0.35, 20% EtOAc in hexanes) as colorless oil (35 mg, 97%). ¹H NMR (360 MHz, CDCl₃) δ 5.83 (m, 1H), 5.30 (d, J = 7.8, 1H), 5.10 – 5.03 (m, 2H), 4.73 (s, 2H), 4.01 (ddd, J = 10.8, 7.8, 2.7, 1H), 3.79 (dddd, J = 13.5, 10.6, 6.7, 3.8, 1H), 3.59 (dd, J = 10.0, 3.8, 1H), 3.44 (dd, J = 10.0, 6.6, 1H), 3.36 (m, 1H), 2.43 – 2.14 (m, 6H), 2.04 (dd, J = 11.3, 11.3, 1H), 1.92 (dd, J = 11.3, 11.3, 1H), 1.72 (d, J = 1.2, 3H), 0.90 (s, 9H), 0.06 (s, 6H). ¹³C NMR (90 MHz, CDCl₃) δ 144.6, 136.0, 134.7, 128.6, 117.3, 108.8, 77.9, 75.7, 70.1, 66.7, 43.4, 40.8, 40.1, 26.1, 18.4, 17.4, -5.2.

7-(tert-Butyl-dimethyl-silanyloxy)-5-methyl-nona-2,4,8-trienoic acid 4-(6-allyl-4-methylene-tetrahydro-pyran-2-yl)-1-(tert-butyl-dimethyl-silanyloxymethyl-3-methyl-but-3-enyl ester (20) To a flame-dried flask under Ar, trichlorobenzoyl chloride

(20 μ L, 0.13 mmol) was added dropwise into a solution of the acid (25 mg, 0.084 mmol) and Et₃N (24 μ L, 0.17 mmol) in PhMe (0.8 mL). The reaction mixture was stirred for 1 h, before was added a solution of the alcohol (14 mg, 0.038 mmol) and DMAP (6 mg, 0.046 mmol) in PhMe (0.4 mL). The resultant suspension was stirred for 1 h, and then a saturated NaHCO₃ solution (1.2 mL) was added followed by Et₂O (20 mL). The aqueous layer was extracted with Et₂O (5 mL), and the combined organic solution was dried over Na₂SO₄ and concentrated under reduced pressure. Flash chromatography (silica, 5% EtOAc in hexanes) afforded the ester (R_f = 0.50, 0.55, 20% EtOAc in hexanes) as yellow oil (28 mg, yield:100%, dr: 3:1). Major diastereomer: ¹H NMR (360 MHz, CDCl₃) δ 7.54 (dd, J = 15.7, 11.7, 1H), 6.06 (d, J = 11.7, 1H), 5.88 – 5.75 (m, 2H), 5.76 (d, J = 15.5, 1H), 5.30 (d, J = 7.9, 1H), 5.17 (d, J = 17.1, 1H), 5.10 – 5.01 (m, 4 H), 4.72 (s, 2H), 4.24 (dd, J = 12.3, 5.8, 1H), 3.98 (m, 1H), 3.66 (m, 2H), 3.34 (m, 1H), 2.36 – 1.83 (m, 10H), 1.90 (s, 3H), 1.73 (s, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.00 (s, 6H). ¹³C NMR (90 MHz, CDCl₃) The carbon spectrum is too complicated to interpret properly. $[\alpha]_D^{20}$ +28 (c 0.05, CH₂Cl₂). HRMS (ESI) calcd for C₃₇H₆₅O₅Si₂ (M+H)⁺: 645.4371, found: 645.4370.

13-Hydroxy-5-hydroxymethyl-3,11-dimethyl-19-methylene-6,21-dioxa-

bicyclo[15.3.1]heneic osa-2,8,10,14-tetraen-7-one (21) To a solution of the bis-TBS ether (6.4 mg, 10 μ mol) in MeOH (200 μ L) and CH₂Cl₂ (50 μ L), was added an aqueous HCl solution (1.0 M, 20 μ L) and stirred for 4.5 h. A saturated NaHCO₃ solution (0.1 mL) was then added, and the aqueous solution was extracted with EtOAc (2 X 3 mL). The organics were combined, dried over Na₂SO₄, and solvents were removed under reduced pressure. Flash chromatography (silica, 1:1 EtOAc: hexanes) afforded the diol (R_f = 0.31,

1:1 EtOAc: hexanes) as a slightly yellow solid (3.3 mg, yield: 80%, dr: 3:1).major diastereomer: ^1H NMR (360 MHz, CDCl_3) δ 7.59 (m, 1H), 6.14 (d, $J = 11.7$, 1H), 5.94-5.76 (m, 3H), 5.32 (d, $J = 8.0$, 1H), 5.27 (ddd, $J = 17.1$, 1.2, 1.2, 1H), 5.16-5.02 (m, 4H), 4.72 (s, 2H), 4.29 (m, 1H), 3.98 (m, 1H), 3.74 (dd, $J = 12.1$, 3.1, 1H), 3.64 (dd, $J = 12.1$, 6.4, 1H), 3.34 (m, 1H), 2.64 (m, 1H), 2.45-1.87 (m, 9H), 1.94 (s, 3H), 1.74 (s, 3H). ^{13}C NMR (90 MHz, CDCl_3) δ 167.9, 146.4, 144.5, 141.5, 140.3, 134.7, 134.5, 129.5, 126.7, 119.5, 117.1, 115.5, 109.0, 77.9, 75.7, 73.9, 71.6, 64.6, 40.9, 40.8, 40.1, 29.9, 25.4, 17.4. $[\alpha]_D^{20} +11$ (c 0.07, CH_2Cl_2). HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{37}\text{O}_5$ ($\text{M}+\text{H}$) $^+$: 417.2641, found: 417.2644.

To a flame-dried flask under Ar, the Grubbs' second generation catalyst (0.8 mg, 1.0 μmol) was added into a stirring solution of the hexaene (4.1 mg, 10 μmol) in CH_2Cl_2 (10 mL), and kept stirring for 1 h. The solution was concentrated under reduced pressure. Flash chromatography (silica, 3:2 EtOAc: hexanes) afforded the pentaene ($R_f = 0.32$, 3:2 EtOAc: hexanes) as a colorless solid (3.6 mg, yield: 93%, dr: 1:1). ^1H NMR (360 MHz, CDCl_3) δ 7.58 (dd, $J = 15.1$, 11.6)/7.45 (dd, $J = 15.1$, 11.5, 1H)*, 6.06 (d, $J = 11.5$, 1H), 5.81 (d, $J = 15.1$)/5.76(d, $J = 15.1$, 1H)*, 5.76 – 5.56 (m, 2H), 5.29 (d, $J = 7.0$)/5.23 (d, $J = 8.0$, 1H)*, 5.18 (m, 1H), 4.73 (s)/4.71 (s, 2H)*, 4.35 (dd, $J = 12.0$, 7.1)/4.23 (dd, $J = 12.2$, 5.5, 1H)*, 3.94 (ddd, $J = 17.6$, 8.4, 2.7, 1H), 3.72 (m, 2H), 3.32 (ddd, $J = 11.1$, 11.1, 2.3, 1H), 2.82 (dd, $J = 13.4$, 8.3,)*/2.56 – 1.62 (m, 10H), 1.99 (s)/1.88 (s, 3H)*, 1.72 (s)/1.69 (s, 3H)*. *: due to diastereomers. ^{13}C NMR (90 MHz, CDCl_3) The carbon spectrum is too complicated to interpret properly. HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{33}\text{O}_5$ ($\text{M}+\text{H}$) $^+$: 389.2328, found: 389.2306.

(-)-Dactylolide (2) To a solution of the diol (3.6 mg, 9.3 μmol) in CH_2Cl_2 (100 μL), was added dropwise a Dess-Martin solution (15% in CH_2Cl_2 , 77 μL , 37.2 μmol) at 0°C and then warmed to rt. The reaction mixture was stirred for 0.5 h before diluted with CH_2Cl_2 (1.0 mL) and Et_2O (2.0 mL). Pyridine (5 μL , 91 μmol) was added and the whole solution was filter through a plug of celite. Solvents were removed under reduced pressure. Flash chromatography (silica, 1:1 EtOAc: hexanes) afforded dactylolide (R_f = 0.46, 3:2 EtOAc: hexanes) as a colorless solid (3.2 mg, 90%). ^1H NMR (500 MHz, CDCl_3) δ 9.67 (s, 1H), 7.63 (dd, J = 15.1, 11.6, 1H), 6.85 (ddd, J = 16.1, 8.6, 5.9, 1H), 6.15 (d, J = 11.6, 1H), 6.00 (d, J = 16.2, 1H), 5.96 (d, J = 15.1, 1H), 5.32 (dd, J = 11.4, 2.4, 1H), 5.24 (d, J = 8.0, 1H), 4.75 (s, 2H), 3.97 (ddd, J = 11.1, 8.1, 2.5, 1H), 3.95 (d, J = 14.3, 1H), 3.32 (dddd, J = 11.4, 9.1, 2.5, 2.5, 1H), 3.23 (d, J = 14.3, 1H), 2.54 (d, J = 14.0, 1H), 2.39-2.27 (m, 3H), 2.17 (ddd, J = 13.2, 1.6, 1.6, 1H), 2.11 (ddd, J = 13.0, 1.6, 1.6, 1H), 1.96 (m, 2H), 1.86 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (90 MHz, CDCl_3) δ 199.3, 197.6, 166.5, 146.2, 144.2, 140.6, 131.7, 131.1, 130.7, 125.8, 120.0, 109.5, 76.7, 75.9, 75.5, 45.1, 41.0, 40.6, 39.94, 39.90, 24.3, 16.3. $[\alpha]_D^{20}$ = -136 (c 1.2, MeOH). IR (CH_2Cl_2): 1722, 1703, 1668, 1638, 1283 cm^{-1} . HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{29}\text{O}_5$ ($\text{M}+\text{H}$) $^+$: 385.2015, found: 385.2023.