Macrolactonization via Ti(IV)-Mediated Epoxy-Acid Coupling: A Total Synthesis of (-)-Dactylolide [and Zampanolide]

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Supporting Information

Spectroscopic characterization data for compounds **1-15**, **18**, **19**, and **21**.

General Information.

^1H and ^{13}C NMR spectra were recorded on a Varian VI-500, VI-300, or VXR-300 spectrometer. Proton chemical shifts are referenced to TMS (0.00 ppm) for spectra obtained in CDCl_3 . Non-first order multiplets are identified as "nfom." Carbon chemical shifts are referenced to CDCl_3 (77.00 ppm). Infrared (IR) spectra were obtained in a Prospect MIDAC FT-IR spectrometer. High resolution mass spectra were recorded either on a Finnigan FTMS 2001 or Bruker Biotof II instrument. Optical rotations were measured on a JASCO-DIP-370 polarimeter using a 3.5 mm i.d. x 50 mm l. cell. Combustion analyses were performed by M-H-W Laboratories, Phoenix, AZ.

(-)-(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-3,11-Dimethyl-19-methylene-7,13-dioxo-6,21-dioxabicyclo[15.3.1]heneicosa-2,8,10,14-tetraene-5-carboxaldehyde [(-)-Dactylolide (1**)]**

To a stirred benzene (3 mL) solution of diol **15** (4.1 mg, 0.01 mmol) was added Pb(OAc)₄ (16 mg, 0.036 mmol) at room temperature. After consumption of starting material (tlc, ~45 min), the reaction mixture was directly load onto a silica-gel column and eluted with hexane/EtOAc (6:1 to 2:1) to provide a 4:1 mixture of dactylolide [(-)-**1**] and its hydrate (3.8 mg, 90%) as a colorless oil.

¹H NMR (500 MHz, CDCl₃): δ 9.67 (s, 1H, CHO), 7.64 (dd, *J* = 14.9 and 11.6 Hz, 1H, H-3), 6.85 (ddd, *J* = 16.2, 8.6, and 6.0 Hz, 1H, H-9), 6.16 (d, *J* = 11.6 Hz, 1H, H-4), 6.01 (d, *J* = 16.2 Hz, 1H, H-2), 5.97 (d, *J* = 14.9 Hz, 1H, H-8), 5.32 (dd, *J* = 11.6 and 2.4 Hz, 1H, H-19), 5.24 (d, *J* = 8.0 Hz, 1H, H-16), 4.75 (s, 2H, H₂C=C-13), 3.97 (ddd, *J* = 11.1, 8.0, and 2.7 Hz, 1H, H-15), 3.96 (d, *J* = 14.3 Hz, 1H, H_a-6), 3.33 (dddd, *J* = 11.9, 9.6, 2.7, and 2.7 Hz, 1H, H-11), 3.23 (d, *J* = 14.3 Hz, 1H, H_b-6), 2.55 (d, *J* = 13.9 Hz, 1H, H_a-18), 2.32 (d, *J* = 14.1 Hz, 1H, H_b-18), 2.40-2.27 (m, 2H), 2.18 (app d, *J* = 13.3 Hz, 1H, H_b-18), 2.11 (app d, *J* = 12.9 Hz, 1H, H_{eq}-14), 1.96 (t, *J* = 12.4 Hz, 1H, H_{ax}-12), 1.95 (m, 1H, H), 1.86 (s, 3H, Me-C-5), and 1.72 (s, 3H, Me-C-17).

¹³C NMR (125 MHz, CDCl₃): δ 199.1, 197.4, 166.3, 146.0, 144.0, 143.5, 140.4, 131.5, 130.9, 130.5, 125.6, 119.8, 109.3, 76.5, 75.7, 75.3, 44.9, 40.8, 40.4, 39.71, 39.67, 24.1, and 16.0.

IR (neat): 3428, 2935, 2892, 1718, 1700, 1653, 1635, and 1281 cm⁻¹.

HRMS (ESI +PEG) Calcd for C₂₃H₂₈O₅Na (M+Na)⁺: 407.1829, found: 407.1831; Calcd for C₂₃H₃₀O₆Na (M+H₂O+Na)⁺: 425.1935, found: 425.1927; Calcd for C₂₄H₃₂O₆Na (M+MeOH+Na)⁺: 439.2091, found: 439.2099.

$[\alpha]_D^{23^\circ\text{C}}$ = -127.8° and 128.9°, *c* = 0.39 and 0.26, respectively, in MeOH.

(2E,5E)-7-[(1,1-Dimethylethyl)diphenylsilyl]oxy}-3-methyl-2,5-heptadienal (2)

¹H NMR (500 MHz, CDCl₃): δ 10.00 (d, *J* = 7.5 Hz, 1H, H-1), 7.68-7.66 (m, 4H, ArH), 7.45-7.36 (m, 6H, ArH), 5.89 (dq, *J* = 8.0 and 1.0 Hz, 1H, H-2), 5.71-5.62 (m, 2H, H-5 and H-6), 4.21-4.19 (nfom, 2H, H-7), 2.93-2.90 (nfom, 2H, H-4), 2.14 (d, *J* = 1.0 Hz, 3H, Me), and 1.06 (s, 9H, *t*-Bu-Si).

¹³C NMR (125 MHz, CDCl₃): δ 191.3, 162.3, 133.6, 135.5, 133.0, 129.7, 129.6, 127.7, 124.9, 64.0, 43.1, 26.8, 19.2, and 17.5.

IR (neat): 3071, 2957, 2932, 2858, 1725, 1675, and 1428 cm⁻¹.

HRMS (ESI) Calcd for C₂₄H₃₀O₂SiNa (M+Na)⁺: 401.1912, found: 401.1907.

TLC R_f = 0.4, hexanes : ethyl acetate = 6 : 1.

(-)-(3S)-{5-[(Trimethylsilyl)methyl]-3-[(trimethylsilyl)oxy]hex-5-enyl} 2,2-dimethylpropanoate (3)

¹H NMR (500 MHz, CDCl₃): δ 4.62 (ddd, *J* = 2.0, 1.0, and 1.0 Hz, 1H, H_a-6), 4.59 (ddd, *J* = 2.5, 1.0, and 1.0 Hz, 1H, H_b-6), 4.20 (ddd, *J* = 11.0, 6.0, and 5.0 Hz, 1H, H_a-1), 4.06 (ddd, *J* = 11.0, 9.0, and 5.5 Hz, 1H, H_b-1), 3.93 (dddd, *J* = 8.5, 7.5, 6.0, and 4.0 Hz, 1H, H-3), 2.19 (ddd, *J* = 13.5, 6.0, and 1.0 Hz, 1H, H_a-4), 2.07 (ddd, *J* = 14.0, 7.0, and 1.0 Hz, 1H, H_b-4), 1.88 (dddd, *J* = 14.5, 9.0, 6.0, and 3.5 Hz, 1H, H_a-2), 1.61 (dddd, *J* = 14.0, 9.0, 5.0, and 5.0 Hz, 1H, H_b-2), 1.53 (dd, *J* = 13.0 and 1.0 Hz, 1H, H_a-6'), 1.51 (dd, *J* = 13.0 and 1.0 Hz, 1H, H_b-6'), 1.20 (s, 9H, *t*-Bu-Pv), 0.12 (s, 9H, Me-OTMS), and 0.03 (s, 9H, Me-TMS).

¹³C NMR (125 MHz, CDCl₃): δ 178.4, 143.8, 110.1, 68.0, 61.3, 46.8, 38.7, 36.0, 27.2, 27.1, -0.3, and -1.4.

IR (neat): 2958, 1732, and 1481 cm⁻¹.

HRMS (ESI) Calcd for C₁₈H₃₈O₃Si₂Na (M+Na)⁺: 381.2252, found: 381.2255.

TLC R_f = 0.6, hexanes : ethyl acetate = 9 : 1.

[α]_D^{23°C} = -28.2°, *c* = 1.65, CH₂Cl₂.

(-)-2-[(2*R*,6*S*)-6-[(1*E*,4*E*)-6-[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2-methyl-1,4-hexadienyl]tetrahydro-4-methylene-2H-pyran-2-yl]ethyl 2,2-dimethylpropanoate (4)

¹H NMR (500 MHz, CDCl₃): δ 7.70 – 7.67 (m, 4H, ArH), 7.44 – 7.36 (m, 6H, ArH), 5.66 (dtt, *J* = 15.0, 7.0, and 1.5 Hz, 1H, H-11), 5.58 (dtt, *J* = 15.0, 5.0, and 1.0 Hz, 1H, H-12), 5.23 (dq, *J* = 7.5 and 1.5 Hz, 1H, H-8), 4.75 (t, *J* = 1.5 Hz, 2H, H₂C=C-5), 4.18 (m, 4H, H_{a,b}-13 and H_{a,b}-1), 3.98 (ddd, *J* = 11.0, 7.5, and 2.0 Hz, 1H, H-7), 3.43 (dddd, *J* = 10.5, 8.5, 5.0, and 2.5 Hz, 1H, H-3), 2.73 (m, 2H, H_{a,b}-10), 2.20 (m, 2H, H_{eq}-4 and H_{eq}-6), 2.05 (app t, *J* = 12.5 Hz, 1H, H_{ax}-6), 1.98 (app t, *J* = 12.5 Hz, 1H, H_{ax}-4), 1.90 (dddd, *J* = 14.0, 8.0, 6.0, and 6.0 Hz, 1H, H_a-2), 1.82 (dddd, *J* = 14.0, 7.0, 7.0, and 4.5 Hz, 1H, H_b-2), 1.65 (d, *J* = 1.0 Hz, 3H, Me-C-7), 1.19 (s, 9H, *t*-Bu-Pv), and 1.05 (s, 9H, *t*-Bu-Si).

¹³C NMR (125 MHz, CDCl₃): δ 178.4, 144.3, 138.7, 135.5, 133.8, 130.9, 129.5, 128.1, 127.6, 125.9, 108.7, 75.5, 75.0, 64.4, 61.1, 42.1, 40.8, 40.5, 38.6, 35.2, 27.2, 26.8, 19.2, and 16.9.

IR (neat): 2959, 2932, 2858, 1728, and 1428 cm⁻¹.

Comb. Anal.: Calcd for C₃₄H₅₀O₄Si: C, 75.22; H, 8.77%. Found: C, 74.94; H, 8.80%.

TLC R_f = 0.55, hexanes : ethyl acetate = 1 : 1.

$[\alpha]_D^{23^\circ\text{C}}$ = -9.4°, *c* = 1.34, CH₂Cl₂.

Chemical structure of compound **5**, a bicyclic enone. The structure features a six-membered ring with an oxygen atom at position 7. A double bond is located between carbons 1 and 2, with a carbonyl group (=O) at position 1. A methyl group (Me) is attached to carbon 9. A side chain at carbon 9 includes a double bond between carbons 11 and 12, and a tert-butyldimethylsilyloxy (TBDPSO) group at the end. The numbering of the carbons is as follows: 1 (carbonyl carbon), 2 (alkene carbon), 3 (ring carbon), 4 (ring carbon), 5 (ring carbon), 6 (ring carbon), 7 (oxygen), 8 (ring carbon), 9 (methyl-bearing carbon), 10 (ring carbon), 11 (alkene carbon), 12 (alkene carbon).

$$[\alpha]_D^{23^\circ\text{C}} = +11.4^\circ, n_D = 1.55, \text{CH}_2\text{Cl}_2.$$

(-)-(1,1-Dimethylethyl)diphenyl[(2*E*,5*E*)-6-[(2*S*,6*S*)-6-[(2*E*)-3-iodo-2-propenyl]-tetrahydro-4-methylene-2*H*-pyran-2-yl]-5-methyl-2,5-hexadienyl]oxy]silane (6a)

¹H NMR (500 MHz, CDCl₃): δ 7.70-7.67 (m, 4H, Ar*H*), 7.44-7.36 (m, 6H, Ar*H*), 6.57 (dt, *J* = 15.0 and 7.5 Hz, 1H, H-14), 6.36-6.29 (m, 2H, H-13 and H-14, *Z*-isomer), 6.10 (dt, *J* = 14.5 and 1.5 Hz, 1H, H-14), 5.67 (dt, *J* = 15.0, 8.0, and 1.5 Hz, 1H, H-2), 5.59 (dt, *J* = 15.0 and 5.0 Hz, 1H, H-3), 5.23 (dq, *J* = 8.0 and 1.5 Hz, 1H, H-6), 4.75 (app t, *J* = 1.5 Hz, 2H, H₂C=C-9), 4.18 (app dq, *J* = 5.0 and 1.0 Hz, 2H, H_{a,b}-1), 4.00 (ddd, *J* = 10.5, 7.5, and 2.5 Hz, 1H, H-7), 3.46 (dddd, *J* = 11.1, 6.0, 6.0, and 2.0 Hz, 1H, H-11, *Z*-isomer), 3.37 (dddd, *J* = 11.0, 6.0, 6.0, and 2.0 Hz, 1H, H-11), 2.73 (m, 2H, H_{a,b}-4), 2.41 (t, *J* = 6.0 Hz, 2H, H_{a,b}-12, *Z*-isomer), 2.36 (dddd, *J* = 15.0, 7.0, 6.5, and 1.5 Hz, 1H, H_a-12), 2.28-2.14 (m, 3H, H_{eq}-8, H_{eq}-10, and H_b-12), 2.03 (app t, *J* = 12.5 Hz, 1H, H_{ax}-8), 1.93 (app t, *J* = 12.5 Hz, 1H, H_{ax}-10), 1.66 (d, *J* = 1.5 Hz, 3H, Me-C-5), and 1.06 (s, 9H, *t*-BuSi).

¹³C NMR (125 MHz, CDCl₃): δ 144.0, 142.2, 138.4, 135.5, 133.7, 130.8, 129.5, 128.00, 127.5, 125.8, 108.9, 76.8, 76.55, 75.66, 64.3, 42.5, 42.1, 40.7, 39.8, 26.8, 19.2, and 16.98.

Distinct resonance from *cis*-isomer: 144.1, 137.5, 128.02, 125.9, 108.8, 84.3, 76.59, 75.73, 41.3, 39.9, and 16.96.

IR (neat): 3071, 2932, 2856, 1652, and 1428 cm⁻¹.

HRMS (FABMS, PEG + NaI) Calcd for C₃₂H₄₁IO₂SiNa (M+Na)⁺: 635.1818, found: 635.1866.

TLC R_f = 0.43, hexanes : ethyl acetate = 12 : 1.

$[\alpha]_D^{23^\circ\text{C}}$ = -3.1°, *c* = 1.54, CH₂Cl₂, (*E* : *Z* = 4 : 1).

(-)-(1,1-Dimethylethyl)diphenyl[(2*E*,5*E*)-6-[(2*S*,6*S*)-6-(2-propenyl)tetrahydro-4-methylene-2*H*-pyran-2-yl]-5-methyl-2,5-hexadienyl]oxy]silane (6b**)**

¹H NMR (500 MHz, CDCl₃): δ 7.69 – 7.67 (m, 4H, ArH), 7.44 – 7.36 (m, 6H, ArH), 5.85 (dddd, *J* = 17.0, 10.5, 7.5, and 6.5 Hz, 1H, H-13), 5.66 (dtt, *J* = 15.0, 7.0, and 1.5 Hz, 1H, H-3), 5.58 (dt, *J* = 15.0 and 5.0, 1H, H-2), 5.26 (dq, *J* = 7.5 and 1.0 Hz, 1H, H-6), 5.09 (dddd, *J* = 17.5, 2.0, 2.0, and 2.0 Hz, 1H, H_{cis}-14), 5.05 (dddd, *J* = 10.5, 2.5, 1.0, and 1.0 Hz, 1H, H_{trans}-14), 4.73 (app t, *J* = 2.0 Hz, 2H, H₂C=C-9), 4.17 (m, 2H, H_{a,b}-1), 4.01 (ddd, *J* = 11.0, 8.0, and 3.0 Hz, 1H, H-7), 3.37 (dddd, *J* = 11.5, 6.5, 6.5, and 2.5 Hz, 1H, H-11), 2.72 (m, 2H, H_{a,b}-4), 2.41 (dtt, *J* = 14.0, 6.0, and 1.5 Hz, 1H, H_a-12), 2.27-2.21 (m, 2H, H_b-12 and H_{eq}-10), 2.16 (ddd, *J* = 13.5, 2.5, and 1.5 Hz, 1H, H_{eq}-8), 2.04 (dddd, *J* = 13.0, 11.0, 1.5, 1.5, and 1.5 Hz, 1H, H_{ax}-8), 1.93 (dddd, *J* = 13.0, 11.0, 1.5, 1.5, and 1.5 Hz, 1H, H_{ax}-10), 1.65 (d, *J* = 1.0 Hz, 3H, Me-C-5), and 1.05 (s, 9H, *t*-Bu-Si).

¹³C NMR (125 MHz, CDCl₃): δ 144.7, 138.0, 135.5, 134.6, 133.8, 130.8, 129.5, 128.2, 127.6, 126.2, 116.9, 108.5, 77.7, 75.7, 64.4, 42.2, 40.9, 40.8, 39.9, 26.8, 19.2, and 16.9.

IR (neat): 3070, 2930, 2856, 1653, and 1428 cm⁻¹.

Comb. Anal.: Calcd for C₃₄H₄₂O₂Si: C, 78.96; H, 8.70%. Found: C, 78.71; H, 8.68%.

TLC R_f = 0.6, hexanes : ethyl acetate = 9 : 1.

$[\alpha]_D^{23} = -2.3^\circ$, *c* = 1.07, CH₂Cl₂.

(2*R*,3*R*)-3-{3-[(2*S*,6*R*)-6-[(2*E*)-3-Iodo-2-propenyl]tetrahydro-4-methylene-2H-pyran-2-yl]-2-methyl-2-propenyl]oxirane methanol (7a)

¹H NMR (500 MHz, CDCl₃): δ 6.57 (dt, *J* = 15.5 and 7.6 Hz, 1H, H-13), 6.10 (dt, *J* = 15.5 and 2.3 Hz, 1H, H-14), 5.33 (dq, *J* = 7.9 and 1.3 Hz, 1H, H-6), 4.76 (t, *J* = 1.8 Hz, 2H, H₂C=C-9), 4.02 (ddd, *J* = 11.1, 7.6, and 2.7 Hz, 1H, H-7), 3.94 (ddd, *J* = 12.7, 5.5, and 2.6 Hz, 1H, H_a-1), 3.67 (ddd, *J* = 12.7, 7.7, and 4.2 Hz, 1H, H_b-1), 3.38 (dddd, *J* = 11.3, 6.6, 5.8, and 2.1 Hz, 1H, H-11), 3.08 (ddd, *J* = 5.7, 5.7, and 2.3 Hz, 1H, H-3), 2.96 (ddd, *J* = 4.1, 2.5, and 2.5 Hz, 1H, H-2), 2.38-2.17 (m, 6H, H_{a,b}-4, H_{a,b}-12, H_{eq}-8, and H_{eq}-10), 2.05 (app t, *J* = 12.2 Hz, 1H, H_{ax}-8), 1.93 (app t, *J* = 12.2 Hz, 1H, H_{ax}-10), 1.76 (d, *J* = 1.3 Hz, 3H, Me-C-5), and 1.64 (dd, *J* = 7.4 and 5.5 Hz, 1H, OH).

¹³C NMR (125 MHz, CDCl₃): δ 143.7, 142.2, 135.3, 127.8, 109.1, 76.9, 76.6, 75.4, 61.4, 58.2, 54.4, 42.4, 41.4, 40.5, 39.7, and 17.4.

IR (neat): 3440, 2981, 2938, 2894, 1652, and 1423 cm⁻¹.

HRMS (MSFAB, PEG + NaI) Calcd for C₁₆H₂₃IO₃Na (M+Na)⁺: 413.0590, found: 413.0597.

TLC R_f = 0.38, hexanes : ethyl acetate = 1 : 1.

$[\alpha]_D^{23^\circ\text{C}} = +17.1^\circ$, *c* = 2.5, CH₂Cl₂.

(2*R*,3*R*)-3-{3-[(2*S*,6*S*)-6-(2-Propenyl)tetrahydro-4-methylene-2H-pyran-2-yl]-2-methyl-2-propenyl}oxirane methanol (7b)

¹H NMR (500 MHz, CDCl₃): δ 5.85 (dddd, *J* = 17.0, 10.5, 8.0, and 7.0 Hz, 1H, H-13), 5.35 (dq, *J* = 7.5 and 1.0 Hz, 1H, H-6), 5.10 (dddd, *J* = 17.0, 1.0, 1.0, and 1.0 Hz, 1H, H_{cis}-14), 5.06 (dddd, *J* = 10.0, 2.0, 1.0, and 1.0 Hz, 1H, H_{trans}-14), 4.74 (app t, *J* = 1.5 Hz, 2H, H₂C=C-9), 4.03 (ddd, *J* = 11.0, 8.0, and 2.5 Hz, 1H, H-7), 3.94 (ddd, *J* = 12.5, 5.5, and 3.0 Hz, 1H, H_a-1), 3.66 (ddd, *J* = 12.5, 7.5, and 4.0 Hz, 1H, H_b-1), 3.38 (dddd, *J* = 11.0, 6.0, 6.0, and 2.5 Hz, 1H, H-11), 3.08 (ddd, *J* = 5.5, 5.5, and 2.0 Hz, 1H, H-3), 2.95 (ddd, *J* = 4.0, 2.0, and 2.0 Hz, 1H, H-2), 2.41 (dddd, *J* = 14.0, 6.0, 6.0, 1.5, and 1.5 Hz, 1H, H_a-12), 2.33 (dd, *J* = 14.5 and 6.0 Hz, 1H, H_a-4), 2.29-2.16 (m, 4H), 2.06 (app t, *J* = 12.5 Hz, 1H, H_{ax}-8), 1.94 (app t, *J* = 12.5 Hz, 1H, H_{ax}-12), 1.76 (d, *J* = 1.0 Hz, 3H, Me-C-5), and 1.61 (dd, *J* = 7.5 and 5.5 Hz, 1H, OH).

¹³C NMR (125 MHz, CDCl₃): δ 144.2, 135.0, 134.4, 128.0, 116.9, 108.7, 77.7, 75.4, 61.5, 58.3, 54.5, 41.4, 40.64, 40.62, 39.8, and 17.3.

IR (neat): 3465, 3074, 2980, 2938, 2894, 1652, and 1419 cm⁻¹.

HRMS (CI, NH₃ in CH₄) Calcd for C₁₆H₂₅O₃ (M+H)⁺: 265.1804, found: 265.1794; Calcd for C₁₆H₂₉NO₃ (M+NH₄)⁺: 282.2069, found: 282.2060.

TLC R_f = 0.47, hexanes : ethyl acetate = 1 : 1.

$[\alpha]_D^{23} = +18.0^\circ$, *c* = 1.0, CH₂Cl₂.

(2*E*,4*Z*)-5-Methyl-7-oxo-2,4-heptadienyl 2,2-dimethylpropanoate (8)

¹H NMR (500 MHz, CDCl₃): δ 9.60 (t, *J* = 2.0 Hz, 1H, H-1), 6.39 (dd, *J* = 15.0 and 11.0 Hz, 1H, H-5), 6.13 (d, *J* = 10.5 Hz, 1H, H-4), 5.75 (dt, *J* = 15.0 and 6.5 Hz, 1H, H-6), 4.60 (t, *J* = 6.5 Hz, 2H, H-7), 3.27 (d, *J* = 2.0 Hz, 2H, H-2), 1.87 (s, 3H, Me-C-3), and 1.21 (s, 9H, *t*-Bu-Pv).

¹³C NMR (125 MHz, CDCl₃): δ 198.2, 178.1, 129.9, 128.65, 128.63, 127.1, 64.5, 47.6, 38.7, 27.1, and 24.7.

IR (neat): 3346, 2964, 1725, and 1480 cm⁻¹.

TLC *R_f* = 0.35, hexanes : ethyl acetate = 6 : 1.

[(2*E*,4*Z*,8*E*)-10-[(2*S*,6*S*)-[2-[(1*E*)-3-[(2*R*,3*R*)-3-[[[(1,1-Dimethylethyl)-dimethylsilyl]oxy]methyl]oxiranyl]-2-methyl-1-propenyl]tetrahydro-4-methylene-2H-pyran-6-yl]]-7-hydroxy-5-methyl-2,4,8-decatrienyl] 2,2-dimethylpropanoate (9)

¹H NMR (500 MHz, CDCl₃): δ 6.51 (dd, *J* = 15.0 and 11.0 Hz, 1H, H-3), 6.01 (d, *J* = 11.0 Hz, 1H, H-4), 5.73 (dt, *J* = 15.5 and 6.6 Hz, 1H, H-9), 5.67 (dt, *J* = 15.0 and 6.6 Hz, 1H, H-2), 5.57 (dd, *J* = 15.3 and 6.4 Hz, 1H, H-8), 5.34 (dq, *J* = 7.6 and 1.0 Hz, 1H, H-16), 4.74 (s, 2H, H₂C=C-13), 4.59 (m, 2H, H_{a,b}-1), 4.25 (m, 1H, H-7), 4.02 (ddd, *J* = 10.8, 8.6, and 2.3 Hz, 1H, H-15), 3.77 (dd, *J* = 11.8 and 3.7 Hz, 1H, H_a-21), 3.70 (dd, *J* = 11.8 and 4.7 Hz, 1H, H_b-21), 3.36 (dddd, *J* = 11.2, 6.0, 6.0, and 2.4 Hz, 1H, H-11), 2.92 (ddd, *J* = 5.8, 5.8, and 2.1 Hz, 1H, H-19), 2.87 (ddd, *J* = 4.7, 3.7, and 2.1 Hz, 1H, H-20), 2.54/2.53* (dd, *J* = 13.1 and 8.4 Hz, 1H, H_a-6), 2.42-2.15 (m, 7H), 2.04 (t, *J* = 12.5 Hz, 1H, H_{ax}-14), 1.91 (t, *J* = 12.5 Hz, 1H, H_{ax}-12), 1.85 (s, 3H, Me-C-5), 1.75 (d, *J* = 2.3 Hz, 3H, Me-C-17), 1.57 (d, *J* = 3.1 Hz, 1H, OH), 1.21 (s, 9H, *t*-Bu-Pv), 0.9 (s, 9H, *t*-Bu-Si), 0.08 (s, 3H, Me-C-Si), and 0.07 (s, 3H, Me-C-Si).

¹³C NMR (125 MHz, CDCl₃): δ 178.2, 144.3, 136.3, 135.3/135.2*, 134.7/134.6*, 129.7, 127.9, 127.57/127.53*, 127.48, 125.6, 108.8, 77.7, 75.5, 71.0, 64.9, 63.5, 58.4, 55.0, 41.7, 40.7, 40.51/40.47*, 39.9, 39.15/39.10*, 38.7, 27.2, 25.9, 24.4, 18.3, 17.4, -5.3, and -5.4.

IR (neat): 3470, 2957, 2934, 2898, 2858, 1729, 1653, and 1281 cm⁻¹.

HRMS (ESI) Calcd for C₃₅H₅₈O₆SiNa (M+Na)⁺: 625.3895, found: 625.3888.

TLC R_f = 0.45, hexanes : ethyl acetate = 1 : 1.

$[\alpha]_D^{23^\circ\text{C}}$ = +6.4°, c = 1.32, CH_2Cl_2 , (dr. = 2 : 1).

* Due to two diastereomers.

[(2*E*,4*Z*,8*E*)-10-[(2*S*,6*S*)-[2-[(1*E*)-3-[(2*R*,3*R*)-3-[[[(1,1-Dimethylethyl)-dimethylsilyl]oxy]methyl]oxiranyl]-2-methyl-1-propenyl]tetrahydro-4-methylene-2H-pyran-6-yl]]-7-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-methyl-2,4,8-dectrienyl] 2,2-dimethylpropanoate (10)

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.49 (dd, J = 15.0 and 11.0 Hz, 1H, H-3), 5.90 (d, J = 11.0 Hz, 1H, H-4), 5.63-5.55 (m, 2H, H-2 and H-9), 5.48 (dd, J = 15.0 and 6.6 Hz, 1H, H-8), 5.33 (d, J = 7.5 Hz, 1H, H-16), 4.72 (br s, 2H, $\text{H}_2\text{C}=\text{C}-13$), 4.57 (app d, J = 6.5 Hz, 2H, $\text{H}_{a,b}-1$), 4.19 (app q, J = 6.5 Hz, 1H, H-7), 4.01 (ddd, J = 10.6, 7.9, and 2.6 Hz, 1H, H-15), 3.77 (dd, J = 11.6 and 3.8 Hz, 1H, H_a-21), 3.69 (dd, J = 11.8 and 4.7 Hz, 1H, H_b-21), 3.32 (dddd, J = 12.3, 6.0, 6.0, and 2.3 Hz, 1H, H-11), 2.91 (ddd, J = 5.8, 5.8, and 2.1 Hz, 1H, H-19), 2.87 (ddd, J = 4.7, 3.7, and 2.1 Hz, 1H, H-20), 2.44/2.43* (dd, J = 12.9 and 6.6 Hz, 1H, H_a-6), 2.38-2.29 (m, 2H), 2.27-2.13 (m, 5H), 2.03 (app t, J = 12.5 Hz, 1H, $\text{H}_{ax}-14$), 1.90 (app t, J = 12.5 Hz, 1H, $\text{H}_{ax}-12$), 1.80 (s, 3H, Me-C-5), 1.75 (d, J = 1.3 Hz, 3H, Me-17), 1.20 (s, 9H, *t*-Bu-Pv), 0.9 (s, 9H, *t*-Bu-TBS-C21), 0.86/0.85* (s, 9H, *t*-Bu-TBS-C7), 0.074 (s, 3H, Me-Si), 0.065 (s, 3H, Me-Si), and 0.002/-0.004* (m, 6H, Me-Si).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 178.2, 144.4, 137.2, 135.77/135.72*, 135.1/134.9*, 130.9, 127.96/127.92*, 126.6, 125.76/125.72*, 124.3, 108.6, 77.94/77.87*, 75.4, 72.33/72.27*, 65.1, 63.5, 58.4, 55.0, 41.7, 41.6, 40.7, 39.9, 39.0, 38.7, 27.2, 25.8, 24.9, 18.3, 18.1, 17.3, -4.4, -4.9, -5.3, and -5.4.

IR (neat): 2955, 2931, 2895, 2857, 1729, and 1254 cm^{-1} .

HRMS (FABMS PEG + NaI) Calcd for $C_{41}H_{72}O_6Si_2Na$ ($M+Na$)⁺: 739.4765, found: 739.4760.

TLC R_f = 0.36, hexanes : ethyl acetate = 9 : 1.

$[\alpha]_D^{23^\circ C} = -1.3^\circ$, $c = 1.67$, CH_2Cl_2 .

* Due to two diastereomers.

(2*E*,4*Z*,8*E*)-10-[(2*S*,6*S*)-[2-[(1*E*)-3-[(2*R*,3*R*)-3-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]oxiranyl]-2-methyl-1-propenyl]tetrahydro-4-methylene-2*H*-pyran-6-yl]]-7-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-methyl-2,4,8-decatrien-1-ol (11)

1H NMR (500 MHz, $CDCl_3$): δ 6.44 (dd, $J = 15.0$ and 11.0 Hz, 1H, H-3), 5.90 (d, $J = 11.0$ Hz, 1H, H-4), 5.70 (dt, $J = 15.0$ and 6.0 Hz, 1H, H-2), 5.59 (dt, $J = 15.0$ and 7.0 Hz, 1H, H-9), 5.48 (dd, $J = 15.5$ and 6.5 Hz, 1H, H-8), 5.33 (dq, $J = 8.0$ and 1.0 Hz, 1H, H-16), 4.72 (br s, 2H, $H_2C=C-13$), 4.20 (ddd, $J = 6.5$, 6.5 , and 6.0 Hz, 1H, H-7), 4.16 (t, $J = 6.0$ Hz, 2H, $H_{a,b}-1$), 4.01 (ddd, $J = 11.0$, 8.0 , and 3.0 Hz, 1H, H-15), 3.77 (dd, $J = 12.0$ and 4.0 Hz, 1H, H_a-21), 3.69 (dd, $J = 12.0$ and 5.0 Hz, 1H, H_b-21), 3.32 (m, 1H, H-11), 2.91 (ddd, $J = 6.0$, 6.0 , and 2.0 Hz, 1H, H-19), 2.87 (ddd, $J = 4.5$, 4.0 , and 2.0 Hz, 1H, H-20), 2.43 (ddd, $J = 13.0$, 7.0 , and 6.0 Hz, 1H, H_a-6), 2.37-2.24 (m, 3H), 2.23-2.13 (m, 4H), 2.04 (t, $J = 12.5$ Hz, 1H, $H_{ax}-14$), 1.90 (t, $J = 12.5$ Hz, 1H, $H_{ax}-12$), 1.80 (s, 3H, Me-C-5), 1.75 (d, $J = 1.5$ Hz, 3H, Me-C-17), 1.30 (t, $J = 6.0$ Hz, 1H, OH), 0.90 (s, 9H, *t*-Bu-Si-C21), 0.87/0.86* (s, 9H, *t*-Bu-Si-C7), 0.074 (s, 3H, Me-Si-C21), 0.065 (s, 3H, Me-Si-C21), and 0.011/0.009/0.007* (s, 6H, Me-Si-C7).

^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 136.41/136.37*, 135.7/135.6*, 135.2/135.1*, 129.5, 128.72/128.70*, 127.94/127.90*, 126.7, 125.74/125.69*, 108.6, 78.0/77.9*, 75.5, 72.4/72.3*,

63.81/63.79*, 63.5, 58.4, 55.0, 41.7, 41.6, 40.7, 39.94/39.89*, 39.0, 25.9, 25.8, 24.97/24.95*, 18.3, 18.2, 17.3, -4.4, -4.82/-4.84*, -5.3, and -5.4.

IR (neat): 3446, 2953, 2929, 2857, 1472, and 1254 cm^{-1} .

HRMS (ESI) Calcd for $\text{C}_{36}\text{H}_{64}\text{O}_5\text{Si}_2\text{Na}$ ($\text{M}+\text{Na}$)⁺: 655.4190, found: 655.4179.

TLC R_f = 0.17, hexanes : ethyl acetate = 5 : 1.

$[\alpha]_D^{23^\circ\text{C}}$ = -0.63°, c = 1.47, CH_2Cl_2 , (dr. = 7 : 6).

* Due to two diastereomers.

(2*E*,4*Z*,8*E*)-10-[(2*S*,6*S*)-[2-[(1*E*)-3-[(2*R*,3*R*)-(3-Hydroxymethyl)oxiranyl]-2-methyl-1-propenyl]tetrahydro-4-methylene-2H-pyran-6-yl]]-7-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-methyl-2,4,8-dectrienoic acid (12)

¹H NMR (500 MHz, CDCl₃): δ 7.60 (dd, *J* = 15.5 and 11.5 Hz, 1H, H-3), 6.07 (d, *J* = 11.5 Hz, 1H, H-4), 5.74 (d, *J* = 15.0 Hz, 1H, H-2), 5.69-5.62 (m, 1H, H-9), 5.51-5.46 (m, 1H, H-8), 5.34 (d, *J* = 7.5 Hz, 1H, H-16), 4.73 (s, 2H, H₂C=C-13), 4.22 (m, 1H, H-7), 4.02/4.01* (ddd, *J* = 11.5, 8.0, and 3.5 Hz, 1H, H-15), 3.94 (ddd, *J* = 13.0, 2.5, and 2.5 Hz, 1H, H_a-21), 3.65 (ddd, *J* = 12.5, 4.0, and 2.5 Hz, 1H, H_b-21), 3.341/3.335* (dddd, *J* = 12.0, 6.0, 6.0, and 2.5 Hz, 1H, H-11), 3.13/3.11* (ddd, *J* = 7.0, 5.0, and 2.5 Hz, 1H, H-19), 2.98 (ddd, *J* = 5.0, 2.5, and 2.5 Hz, 1H, H-20), 2.51 (ddd, *J* = 13.0, 7.5, and 6.5 Hz, 1H, H_a-6), 2.38 (ddd, *J* = 13.5, 5.0, and 5.0 Hz, 1H, H_b-6), 2.33-2.20 (m, 5H), 2.19-2.14 (m, 2H), 2.06-2.00 (m, 1H, H_{ax}-14), 1.96-1.90 (m, 1H, H_{ax}-12), 1.91 (s, 3H, Me-C-5), 1.75 (s, 3H, Me-C-17), 0.85/0.84* (s, 9H, *t*-Bu-Si), and -0.009/-0.012/-0.015/-0.017 (s, 6H, Me-Si).

¹³C NMR (75 MHz, CDCl₃): δ 171.8, 148.0/147.9*, 144.3, 142.8, 135.5/135.3*, 135.0/134.9*, 127.9, 126.5/126.4*, 125.72/125.66*, 118.5, 108.7, 77.9/77.8*, 75.4/75.3*, 73.1, 61.3/61.2*, 58.7, 54.9/54.8*, 42.1, 41.3, 40.7, 39.9/39.8*, 38.7, 26.01/25.94*, 25.8, 18.1, 17.5, -4.4, and -4.9.

IR (neat): 3410, 2952, 2931, 2893, 2856, 1685, 1635, and 1254 cm⁻¹.

HRMS (ESI) Calcd for C₃₀H₄₈O₆SiNa (M+Na)⁺: 555.3112, found: 555.3102.

TLC R_f = 0.33, hexanes : ethyl acetate = 1 : 1 with 4% MeOH.

$[\alpha]_D^{23^\circ\text{C}}$ = +23.9°, *c* = 0.65, CH₂Cl₂.

* Due to two diastereomers.

(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-5-[(1*R*)-(1,2-Dihydroxy)ethyl]-13-[[1,1-dimethylethyl)dimethylsilyl]oxy]-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]heneicosa-2,8,10,14-tetraen-7-one (13)

¹H NMR (500 MHz, CDCl₃): δ 7.58/7.45* (dd, *J* = 15.0 and 11.5 Hz, 1H, H-3), 6.03/6.01* (d, *J* = 11.0 Hz, 1H, H-4), 5.75/5.69* (d, *J* = 15.0 Hz, 1H, H-2), 5.65/5.58* (dddd, *J* = 15.5, 7.5, 6.0, and 1.5 Hz, 1H, H-9), 5.46/5.44* (dd, *J* = 15.5 and 6.5 Hz, 1H, H-8), 5.31/5.26* (d, *J* = 8.0 Hz, 1H), 5.09-5.04 (m, 1H, H-19), 4.71 (app s, 2H, H₂C=C-13), 4.31-4.24 (m, 1H, H-7), 3.92 (ddd, *J* = 10.5, 8.0, and 2.5 Hz, 1H, H-15), 3.76-3.65 (m, 2H, H_a-21 and H-20), 3.58 (ddd, *J* = 12.0, 12.0, and 5.0 Hz, 1H, H_b-21), 3.37-3.27 (m, 1H, H-11), 2.83/2.61* (dd, *J* = 13.0 and 7.5 Hz, 1H, H_a-6), 2.51-2.37 (m, 3H), 2.27 (dd, *J* = 13.0 and 6.5 Hz, 1H, H_b-6), 2.21-2.10 (m, 4H), 2.04-1.91 (m, 2H), 1.94/1.88* (s, 3H, Me-C-5), 1.74/1.68* (d, *J* = 1.5 Hz, 3H, Me-C-17), 0.89/0.87* (s, 9H, *t*-Bu-Si), and 0.040/0.036//0.024/0.006* (s, 6H, Me-Si).

¹³C NMR (75 MHz, CDCl₃): δ 167.8/167.4*, 148.4/147.5*, 144.72/144.65*, 141.8/141.4*, 133.7/133.3/132.3/129.9*, 128.0/127.8*, 125.5/125.2*, 118.5/118.3*, 108.53/108.48*, 77.8/77.6*, 75.7/75.5*, 73.0/72.4*, 72.0/71.9*, 71.2/70.9*, 62.8/62.6*, 41.4/41.2/40.8/40.62/40.56/40.53*, 39.1, 38.5, 25.9, 24.9, 18.3/18.1*, 17.5/16.9*, -4.2, -4.5, and -4.8.

IR (neat): 3391, 2952, 2928, 2893, 2855, 1709, 1694, and 1256 cm⁻¹.

HRMS (ESI) Calcd for C₃₀H₄₈O₆SiNa (M+Na)⁺: 555.3112, found: 555.3105.

TLC R_f = 0.31, hexanes : ethyl acetate = 1 : 1.

$[\alpha]_D^{23} = +13.2^\circ$, *c* = 0.49, CH₂Cl₂, (dr = 1 : 1).

* Due to two diastereomers.

(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-5-[(1*R*)-(1,2-Dihydroxy)ethyl]-13-hydroxy-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]heneicosa-2,8,10,14-tetraen-7-one (14)

Spectral data of the less polar diastereomer.

¹H NMR (500 MHz, CDCl₃): δ 7.56 (dd, *J* = 15.0 and 11.6 Hz, 1H, H-3), 6.06 (d, *J* = 11.3 Hz, 1H, H-4), 5.80 (d, *J* = 15.0 Hz, 1H, H-2), 5.73 (dddd, *J* = 15.7, 7.1, 5.9, and 1.3 Hz, 1H, H-9), 5.59 (dddd, *J* = 15.8, 4.9, 1.3, and 1.3 Hz, 1H, H-8), 5.26 (d, *J* = 8.0 Hz, 1H, H-16), 5.08 (ddd, *J* = 9.5, 7.0, and 2.7 Hz, 1H, H-19), 4.72 (br s, 2H, H₂C=C-13), 4.34 (app t, dddd, *J* = 6.3, 6.3, 6.3, and 6.3 Hz, 1H, H-7), 3.95 (ddd, *J* = 10.8, 7.8, and 2.5 Hz, 1H, H-15), 3.73-3.67 (m, 2H, H_a-21 and H-20), 3.60 (m, 1H, H_b-21), 3.32 (dddd, *J* = 11.3, 9.6, 2.2, and 2.2 Hz, 1H, H-11), 2.81 (dd, *J* = 13.4 and 7.9 Hz, 1H, H_a-6), 2.55 (d, *J* = 7.4 Hz, 1H, OH-20), 2.45-2.41 (m, 2H), 2.35 (dd, *J* = 13.8 and 9.3 Hz, 1H, H_b-6), 2.25-2.10 (m, 5H), 2.01-1.93 (m, 2H), 1.89 (s, 3H, Me-C-5), 1.71 (d, *J* = 1.3 Hz, 3H, Me-C-17), and 1.43 (d, *J* = 5.9 Hz, 1H, OH-7).

¹³C NMR (125 MHz, CDCl₃): δ 167.5, 146.7, 144.4, 141.1, 133.0, 131.9, 129.9, 128.6, 125.5, 118.9, 108.6, 77.6, 75.9, 72.5, 71.2, 69.8, 62.8, 41.05, 41.00, 40.6, 40.1, 39.2, 24.1, and 16.9.

TLC *R*_f = 0.32, hexanes : ethyl acetate = 1 : 2, with 4% MeOH.

$[\alpha]_D^{23^\circ\text{C}}$ = +6.0°, *c* = 0.51, CH₂Cl₂.

Spectral data of the more polar diastereomer.

¹H NMR (500 MHz, CDCl₃): δ 7.44 (dd, *J* = 15.3 and 11.6 Hz, 1H, H-3), 6.06 (d, *J* = 11.4 Hz, 1H, H-4), 5.76 (d, *J* = 15.4 Hz, 1H, H-2), 5.67 (ddd, *J* = 15.4, 7.4, and 5.9 Hz, 1H, H-9), 5.61 (dd, *J* = 15.4 and 6.4 Hz, 1H, H-8), 5.32 (d, *J* = 8.0 Hz, 1H, H-16), 5.05 (ddd, *J* = 9.5, 7.0, and 2.7 Hz, 1H, H-19), 4.73 (br s, 2H, H₂C=C-13), 4.25 (dddd, *J* = 8.5, 6.8, 4.2, and 3.7 Hz, 1H, H-7), 3.92 (ddd, *J* = 10.4, 7.9, and 2.5 Hz, 1H, H-15), 3.68-3.62 (m, 2H, H_a-21 and H-20), 3.58-3.53 (m, 1H, H_b-21), 3.33 (dddd, *J* = 11.4, 9.1, 2.5, and 2.5 Hz, 1H, H-11), 2.60-2.51 (m, 4H), 2.44 (dd, *J* = 14.2 and 9.5 Hz, 1H, H_a-18), 2.40 (dd, *J* = 8.8 and 4.7 Hz, 1H, OH-21), 2.27-2.23 (m,

^1H , 2.19-2.12 (m, 3H), 2.04-2.00 (m, 2H), 1.99 (s, 3H, Me-C-5), 1.67 (s, 3H, Me-C-17), and 1.52 (d, $J = 3.8$ Hz, 1H, OH-7).

^{13}C NMR (75 MHz, CDCl_3): δ 167.8, 148.1, 144.5, 141.2, 133.2, 133.1, 129.9, 129.1, 125.6, 118.9, 108.7, 75.6, 72.7, 72.4, 71.1, 71.0, 62.5, 40.7, 40.6, 40.5, 40.3, 38.4, 25.5, and 16.6.

IR (neat): 3396, 2930, 1699, and 1278 cm^{-1} .

HRMS (FAB, NaI) Calcd for $\text{C}_{24}\text{H}_{34}\text{O}_6\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 441.2253, found: 441.2278.

TLC $R_f = 0.30$, hexanes : ethyl acetate = 1 : 2, with 4% MeOH.

$[\alpha]_D^{23^\circ\text{C}} = +32.8^\circ$, $c = 0.39$, CH_2Cl_2 .

(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-5-[(1*R*)-(1,2-Dihydroxy)ethyl]-3,11-dimethyl-19-methylene-6,21-dioxabicyclo[15.3.1]heneicosa-2,8,10,14-tetraen-7,13-dione (15)

^1H NMR (500 MHz, CDCl_3): δ 7.63 (dd, $J = 15.0$ and 11.5 Hz, 1H, H-3), 6.83 (ddd, $J = 16.0$, 9.0 , and 4.5 Hz, 1H, H-9), 6.12 (d, $J = 12.0$ Hz, 1H, H-4), 5.95 (d, $J = 15.5$ Hz, 1H, H-8), 5.92 (d, $J = 15.0$ Hz, 1H, H-2), 5.20 (d, $J = 8.0$ Hz, 1H, H-16), 5.13 (ddd, $J = 11.0$, 7.0 , and 2.0 Hz, 1H, H-19), 4.74 (app q, $J = 1.5$ Hz, 2H, $\text{H}_2\text{C}=\text{C}-13$), 4.10 (d, $J = 14.0$ Hz, 1H, H_a-6), 3.97 (ddd, $J = 11.0$, 8.0 , and 2.5 Hz, 1H, H-15), 3.76-3.63 (m, 3H), 3.30 (dddd, $J = 12.0$, 10.0 , 2.0 , and 2.0 Hz, 1H, H-11), 3.06 (d, $J = 14.0$ Hz, 1H, H_b-6), 2.48-2.44 (m, 2H), 2.37 (dddd, $J = 15.0$, 10.0 , 5.0 , and 2.0 Hz, 1H, H_a-12), 2.29-1.91 (m, 7H), 1.81 (s, 3H, Me-C-5), and 1.71 (d, $J = 1.0$ Hz, 3H, Me-C-17).

^{13}C NMR (125 MHz, CDCl_3): δ 197.9, 167.0, 146.3, 143.63, 143.57, 140.0, 132.6, 131.3, 129.6, 125.3, 120.4, 109.1, 76.4, 75.9, 72.8, 70.9, 62.8, 45.1, 41.6, 40.9, 40.6, 40.1, 23.6, and 16.6.

IR (neat): 3410, 2935, 2899, 1700, 1685, 1635, and 1281 cm^{-1} .

HRMS (FABMS + NaI) Calcd for $\text{C}_{24}\text{H}_{32}\text{O}_6\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 439.2097, found: 439.2081.

TLC $R_f = 0.37$, hexanes : ethyl acetate = 1 : 2 with 2% MeOH.

$[\alpha]_D^{23^\circ\text{C}} = -76.8^\circ$, $c = 0.57$, CH_2Cl_2 .

(±)-(2*E*,4*Z*)-7-[(2,2-Dimethylethyl)dimethylsilyl]oxy-5-methyl-2,4,8-nontrienoic acid (18)

¹H NMR (500 MHz, CDCl₃): δ 7.65 (dd, *J* = 15.0 and 11.5 Hz, 1H, H-3), 6.11 (d, *J* = 11.5 Hz, 1H, H-4), 5.81 (ddd, *J* = 17.5, 10.5, and 6.5 Hz, 1H, H-8), 5.77 (d, *J* = 15.0, 1H, H-2), 5.19 (ddd, *J* = 17.0, 2.0, and 1.0 Hz, 1H, H_{cis}-9), 5.06 (ddd, *J* = 10.5, 2.0, and 1.0 Hz, 1H, H_{trans}-9), 4.25 (dddd, *J* = 8.0, 6.5, 5.5, 1.5, and 1.5 Hz, 1H, H-7), 2.60 (dd, *J* = 13.0 and 7.5 Hz, 1H, H_a-6), 2.36 (dd, *J* = 13.5 and 4.8 Hz, 1H, H_b-6), 1.93 (s, 3H, Me-C-5), 0.86 (s, 9H, *t*-Bu-Si), 0.014 (s, 3H, Me-Si), and 0.008 (s, 3H, Me-Si).

(500 MHz, DMSO-*d*₆): δ 12.03 (br s, 1H, COOH), 7.39 (dd, *J* = 15.0 and 11.5 Hz, 1H, H-3), 6.14 (d, *J* = 11.5 Hz, 1H, H-4), 5.86 (ddd, *J* = 16.0, 10.5, and 5.5 Hz, 1H, H-8), 5.74 (d, *J* = 15.0, 1H, H-2), 5.22 (d, *J* = 17.0 Hz, 1H, H_{cis}-9), 5.06 (d, *J* = 10.5 Hz, 1H, H_{trans}-9), 4.30 (m, 1H, H-7), 2.53 (dd, *J* = 13.0 and 8.5 Hz, 1H, H_a-6), 2.25 (dd, *J* = 13.5 and 4.5 Hz, 1H, H_b-6), 1.89 (s, 3H, Me-C-5), 0.82 (s, 9H, *t*-Bu-Si), -0.012 (s, 3H, Me-Si), and -0.022 (s, 3H, Me-Si).

¹³C NMR (125 MHz, CDCl₃): δ 173.1, 147.8, 143.4, 140.9, 126.0, 118.3, 114.3, 72.80, 41.78, 25.8, 25.7, 18.1, -4.6, and -5.0.

IR (neat): 2959, 2932, 2858, 1728, and 1428 cm⁻¹.

HRMS (CI, NH₃ in CH₄) Calcd for C₁₆H₂₉O₃Si (M+H)⁺: 297.1886, found: 297.1882; Calcd for C₁₆H₃₂NO₃Si (M+NH₄)⁺: 314.2151, found 314.2146.

TLC R_f = 0.25, hexanes : ethyl acetate = 6 : 1.

(2*R*,3*S*,5*E*)-6-[(2*S*,6*S*)-6-(2-Propenyl)tetrahydro-4-methylene-2*H*-pyran-2-yl]-1,2,3-triol-5-methyl-5-hexen-3-yl (2*E*,4*Z*)-7-[(2,2-dimethylethyl)dimethylsilyl]-oxy-5-methyl-2,4,8-nontrienoate (19)

¹H NMR (500 MHz, CDCl₃): δ 7.61/7.58* (dd, *J* = 15.5 and 12.0 Hz, 1H, H-3), 6.08 (d, *J* = 12.0 Hz, 1H, H-4), 5.86-5.74 (m, 3H, H-2, H-8, and H-13'), 5.31 (d, *J* = 8.0 Hz, 1H, H-6'), 5.19 (dt, *J* = 17.0 and 1.5 Hz, 1H), 5.09-4.98 (m, 4H), 4.75 (br s, 2H, H₂C=C-9'), 4.24 (m, 1H, H-7), 3.97 (ddd, *J* = 11.0, 7.5, and 2.5 Hz, 1H, H-7'), 3.67-3.52 (m, 3H, H_{a,b}-1 and H-2), 3.33/3.32* (dddd, *J* = 11.0, 6.5, 6.5, and 1.5 Hz, 1H, H-11'), 2.66-2.52 (m, 4H), 2.39-2.31 (m, 3H), 2.23-2.10 (m, 3H), 2.04-1.87 (m, 2H), 1.92 (s, 3H, Me-C-5), 1.72 (t, *J* = 1.5 Hz, 3H, Me-C-5'), 0.86 (s, 9H, *t*-Bu-TBS), and 0.009/0.008/-0.002/-0.004* (s, 6H, Me-TBS).

¹³C NMR (125 MHz, CDCl₃): δ 168.3, 147.6, 144.4, 142.93/142.85*, 140.9, 134.8, 134.6, 128.8, 126.0, 117.97/117.91*, 116.8, 114.3, 108.6, 77.6, 75.4, 72.97/72.96*, 72.63, 72.59, 62.1, 41.83/41.79*, 40.74, 40.71, 40.6, 39.9, 25.80/25.79*, 25.60/25.56*, 18.1, 17.4, -4.6, and -4.9.

IR (neat): 3428, 2928, 2856, 1711, 1637, and 1278 cm⁻¹.

HRMS (FAB, NaI) Calcd for C₃₂H₅₂O₆SiNa (M+Na)⁺: 583.3431, found: 583.3477.

TLC R_f = 0.22, hexanes : ethyl acetate = 2 : 1.

[α]_D^{23°C} = -29.8°, *c* = 1.06, CH₂Cl₂.

* Due to two diastereomers.

(2Z,4E)-N-[(1S)-[(1S,2E,5S,8E,10Z,14E,17S)-3,11-Dimethyl-19-methylene-7,13-dioxo-6,21-dioxabicyclo-[15.3.1]-heneicosa-2,8,10,14-tetraen-5-yl]hydroxymethyl] 2,4-hexadienamide (21)

21 Zampanolide

To a stirred solution of amidoalane **20** [prepared by addition of DIBAL-H (15 μ L, 1 M in hexanes) to a THF (0.4 mL) solution of 2Z,4E-dienylamide (**9**, 2 mg, 0.02 mmol) at room temperature and stirring for 30 min] was added dactylolide (1 mg, 2.6 μ mol in 0.4 mL of THF). The resulting solution was stirred for 60 min at room temperature and tlc indicated consumption of starting material. Reaction was quenched by addition of aqueous Rochelle's salt (1 mL) and vigorously stirred until both layers became clear. After partition between CH_2Cl_2 and H_2O , the combined organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. The crude product was purified by HPLC (SiO_2 , hexane:EtOAc = 1:1) to provide, in order of elution, zampanolide (**21**) and C(20)-*epi*-zampanolide (*epi*-**21**).

^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ 8.31 (d, J = 8.9 Hz, 1H, NH), 7.52 (dd, J = 14.9 and 11.5 Hz, 1H, H-3), 7.48-7.42 (m, 1H, H-4'), 6.74 (ddd, J = 16.0, 8.5, and 5.6 Hz, 1H, H-9), 6.37 (t, J = 11.5 Hz, 1H, H-3'), 6.20 (d, J = 11.9 Hz, 1H, H-4), 6.13 (d, J = 5.2 Hz, 1H, OH), 6.03-5.92 (m, 1H, H-5'), 5.95 (d, J = 16.4 Hz, 1H, H-8), 5.93 (d, J = 15.0 Hz, 1H, H-2), 5.65 (d, J = 11.6 Hz, 1H, H-2'), 5.32 (ddd, J = 9.0, 6.2, and 4.9 Hz, 1H, H-20), 5.10 (d, J = 7.8 Hz, 1H, H-16), 4.96 (ddd, J = 10.1, 6.1, and 1.8 Hz, 1H, H-19), 4.73 (br s, 2H, $\text{CH}_2=\text{C}-13$), 4.13 (d, J = 14.2 Hz, 1H, H_a-6), 3.86 (ddd, J = 11.1, 7.8, and 2.5 Hz, 1H, H-15), 3.00 (d, J = 14.3 Hz, 1H, H_b-6), 2.37-2.25 (m, 3H), 2.17 (app d, J = 12.6 Hz, 1H, $\text{H}_{eq}-14$), 2.12-2.03 (m, 2H), 1.90-1.81 (m, 2H), 1.79 (dd, J = 6.7 and 1.3 Hz, 3H, Me-C-5'), 1.74 (s, 3H, Me-C-5), and 1.61 (s, 3H, Me-C-17). [The resonance for H-11 is apparently under the residual $\text{CD}_3\text{SOCHD}_2$ peak.]

^1H NMR (500 MHz, CDCl_3): δ 7.65 (dd, J = 15.2 and 11.7 Hz, 1H, H-3), 7.42 (m, 1H, H-4'), 6.82 (ddd, J = 15.8, 9.3, and 4.2 Hz, 1H, H-9), 6.46 (t, J = 11.5 Hz, 1H, H-3'), 6.31 (d, J = 7.8 Hz, 1H, NH), 6.11 (d, J = 11.6 Hz, 1H, H-4), 6.06 (dq, J = 15.2 and 6.7 Hz, 1H, H-5'), 5.95 (d, J = 15.0 Hz, 1H, H-2), 5.94 (d, J = 16.5 Hz, 1H, H-8), 5.46-5.43 (m, 1H, H-20), 5.44 (d, J = 11.4

Hz, 1H, H-2'), 5.30 (ddd, $J = 11.1, 5.8,$ and 1.9 Hz, 1H, H-19), 5.20 (d, $J = 7.8$ Hz, 1H, H-16), 4.73 (br s, 2H, $\text{CH}_2=\text{C}-13$), 4.13 (d, $J = 13.7$ Hz, 1H, H_a-6), 3.96 (ddd, $J = 10.9, 8.1,$ and 2.5 Hz, 1H, H-15), 3.56 (d, $J = 3.9$ Hz, 1H, OH), 3.29 (m, 1H, H-11), 3.04 (d, $J = 13.7$ Hz, 1H, H_b-6), 2.42 (d, $J = 13.7$ Hz, 1H, H_a-18), 2.37 (dddd, $J = 14.7, 9.7, 4.6,$ and 1.6 Hz, 1H, H_a-10), 2.24 (app dd, $J = 14.9$ and 10.1 Hz, 1H, H_b-10), 2.21 (dd, $J = 13.7$ and 11.0 Hz, 1H, H_b-18), 2.14 (app d, $J = 13.1$ Hz, 1H, $\text{H}_{eq}-14$), 2.09 (app d, $J = 13.1$ Hz, $\text{H}_{eq}-12$), 1.97-1.90 (m, 2H, $\text{H}_{ax}-12$ and $\text{H}_{ax}-14$), 1.87 (dd, $J = 6.9$ and 1.8 Hz, 3H, Me-C-5'), 1.81 (s, 3H, Me-C-5), and 1.72 (s, 3H, Me-C-17).

HRMS (ESI) Calcd for $\text{C}_{29}\text{H}_{37}\text{NO}_6\text{Na}$ ($\text{M}+\text{Na}$)⁺: 518.2519, found: 518.2538.

TLC $R_f = 0.47$, hexanes : ethyl acetate = 1 : 1, with 2% MeOH.

(2Z,4E)-N-[(1R)-[(1S,2E,5S,8E,10Z,14E,17S)-3,11-Dimethyl-19-methylene-7,13-dioxo-6,21-dioxabicyclo-[15.3.1]-heneicosa-2,8,10,14-tetraen-5-yl]hydroxymethyl] 2,4-hexadienamide C(20)-*epi*-Zampanolide (21)

21-*epi* C(20)-*epi*-Zampanolide

¹H NMR (500 MHz, DMSO-*d*₆): δ 8.41 (d, *J* = 9.0 Hz, 1H, NH), 7.50 (dd, *J* = 14.8 and 11.6 Hz, 1H, H-3), 7.50-7.44 (m, 1H, H-4'), 6.74 (ddd, *J* = 16.3, 8.4, and 5.6 Hz, 1H, H-9), 6.42 (t, *J* = 11.3 Hz, 1H, H-3'), 6.24 (d, *J* = 11.7 Hz, 1H, H-4), 6.03 (d, *J* = 4.9 Hz, 1H, OH), 6.02-5.97 (m, 1H, H-5'), 6.00 (d, *J* = 15.0 Hz, 1H, H-2), 5.93 (d, *J* = 16.2 Hz, 1H, H-8), 5.66 (d, *J* = 11.3 Hz, 1H, H-2'), 5.34 (ddd, *J* = 9.1, 5.9, and 4.9 Hz, 1H, H-20), 5.08 (d, *J* = 7.8 Hz, 1H, H-16), 5.03 (ddd, *J* = 9.8, 5.9, and 2.6 Hz, 1H, H-19), 4.73 (br s, 2H, CH₂=C-13), 4.19 (d, *J* = 14.0 Hz, 1H, H_a-6), 3.88 (ddd, *J* = 10.5, 7.8, and 2.2 Hz, 1H, H-15), 2.90 (d, *J* = 14.1 Hz, 1H, H_b-6), 2.33-2.26 (m, 2H), 2.19-2.04 (m, 4H), 1.88-1.79 (m, 2H), 1.81 (dd, *J* = 6.9 and 1.9 Hz, 3H, Me-C-5'), 1.75 (s, 3H, Me-C-5), and 1.63 (s, 3H, Me-C-17). [The resonance for H-11 is apparently under the residual CD₃SOCHD₂ peak.]

¹H NMR (500 MHz, CDCl₃): δ 7.67 (dd, *J* = 15.0 and 11.5 Hz, 1H, H-3), 7.42 (m, 1H, H-4'), 6.83 (ddd, *J* = 16.4, 9.4, and 4.9 Hz, 1H, H-9), 6.46 (t, *J* = 11.5 Hz, 1H, H-3'), 6.34 (d, *J* = 7.9 Hz, 1H, NH), 6.13 (d, *J* = 11.4 Hz, 1H, H-4), 6.06 (dq, *J* = 14.3 and 7.0 Hz, 1H, H-5'), 6.00 (d, *J* = 15.0 Hz, 1H, H-2), 5.94 (d, *J* = 16.3 Hz, 1H, H-8), 5.53 (ddd, *J* = 7.7, 4.6, and 3.4 Hz, 1H, H-20), 5.45 (d, *J* = 11.2 Hz, 1H, H-2'), 5.27 (m, 1H, H-19), 5.25 (d, *J* = 8.5 Hz, 1H, H-16), 4.74 (br s, 2H, CH₂=C-13), 4.12 (d, *J* = 13.8 Hz, 1H, H_a-6), 3.96 (ddd, *J* = 11.0, 8.0, and 2.8 Hz, 1H, H-15), 3.52 (d, *J* = 4.9 Hz, 1H, OH), 3.29 (m, 1H, H-11), 3.06 (d, *J* = 13.7 Hz, 1H, H_b-6), 2.52 (d, *J* = 13.9 and 11.0 Hz, 1H, H_a-18), 2.37 (dddd, *J* = 14.9, 10.0, 4.9, and 2.2 Hz, 1H, H_a-10), 2.26 (d, *J* = 13.8 Hz, 1H, H_b-18), 2.26-2.22 (m, 1H, H_b-10), 2.15 (app d, *J* = 13.3 Hz, 1H, H_{eq}-14), 2.10 (app d, *J* = 13.4 Hz, 1H, H_{eq}-12), 1.99-1.91 (m, 2H, H_{ax}-12 and H_{ax}-14), 1.88 (dd, *J* = 6.8 and 1.5 Hz, 3H, Me-C-5'), 1.82 (s, 3H, Me-C-5), and 1.72 (s, 3H, Me-C-17).

Copies of NMR Spectra

	SI page
¹ H NMR (CDCl ₃) Synthetic Dactylolide (1)	24
¹³ C NMR (CDCl ₃) Synthetic Dactylolide (1)	25
¹ H NMR (DMSO-d ₆) Synthetic Zampanolide (21)	26
¹ H NMR (DMSO-d ₆) Natural Zampanolide	27
(taken from Supporting Information for Smith, A. B., III; Safonov, I. G.; Corbett, R. M. <i>J. Am. Chem. Soc.</i> 2001, <i>123</i> , 12426-12427.)	
¹ H NMR (CDCl ₃) Synthetic Zampanolide (21)	28
¹ H NMR (CDCl ₃) Synthetic <i>epi</i> -Zampanolide (<i>epi</i> - 21)	29

Dactylolide (-)-1
CDCl₃ 500 MHz
[Hoye/Hu synthetic]

zampanolide (**21**)
DMSO-d₆ 500 MHz
[Hoye/Hu synthetic]

zampanolide (21)
CDCl₃ 500 MHz
[Hoye/Hu synthetic]

JT-45-53-3

12-JUL-1995 19:15:46.75

DFILE : ALPHA
SFILE : JT45533H

COMNT : JT-45-53-3
EXMOD : SINGL
IRMOD : NON
POINT : 32768
FREQU : 10000.00 Hz
SCANS : 54
DUMMY : 0
ACQTM : 3.2768 sec
PD : 1.0000 sec
RGAIN : 18

PW1 : 5.65 usec

OBNUC : ^1H
OBFRQ : 500.00 MHz
OBSET : 162410.00 Hz

IRNUC : ^1H
IRFRQ : 500.00 MHz
IRSET : 162410.00 Hz
IRATN : 511
IRAPW : 52.0 usec
IRBP1 : 25
IRBP2 : 6
IRANS : 0

ADBIT : 16
CTEMP : 26.8 c
CSPED : 14 Hz
SLVNT : DMSO

RESOL : 0.31 Hz
BF : 0.10 Hz
T1 : 0.00 %
T2 : 0.00 %
T3 : 90.00 %
T4 : 100.00 %
REFVL : 0.00 ppm
XE : 5001.22 Hz
XS : 45.47 Hz

operator