

Supporting Information

Synthesis of (-)-Terpestacin via Catalytic, Stereoselective Fragment Coupling: Siccanol is Terpestacin, not 11-*epi*-Terpestacin

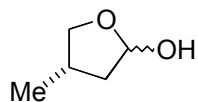
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Experimental Procedures and Data for Compounds 1-16

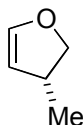
General Information. Unless otherwise noted, all reactions in exclusively organic solvents were performed under an oxygen-free atmosphere of argon with rigid exclusion of moisture from reagents and glassware. Dichloromethane was distilled from calcium hydride. Tetrahydrofuran and diethyl ether were distilled from a blue solution of sodium benzophenone ketyl. Analytical thin layer chromatography (TLC) was performed using EM Science silica gel 60 F₂₅₄ plates. The developed chromatogram was analyzed by UV lamp (254 nm), ethanolic phosphomolybdic acid, potassium permanganate (KMnO₄), or ceriumammonium molybdate (CAM). Liquid chromatography was performed using a forced flow (flash chromatography) of the indicated solvent system on Silicycle Silica Gel (230-400 mesh).¹ ¹H and ¹³C NMR spectra were recorded in CDCl₃, unless otherwise noted, on a Varian Inova 500 MHz spectrometer. Chemical shifts in ¹H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz), and integration. Chemical shifts of ¹³C NMR spectra are reported in ppm from the central peak of CDCl₃ (77.23 ppm), or C₆D₆ (128.39 ppm) on the δ scale. Infrared (IR) spectra were recorded on a Perkin-Elmer 2000 FT-IR. High resolution mass spectra (HRMS) were obtained on a Bruker Daltonics APEXII 3 Tesla Fourier Transform Mass Spectrometer by Dr. Li Li of the Massachusetts Institute of Technology Department of Chemistry Instrumentation Facility. Optical Rotations were measured on a Perkin-Elmer 241 polarimeter at 589 nm.

¹ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



4-Methyl-tetrahydrofuran-2-ol: A 100 mL round bottom flask charged with β -methallyl alcohol (16.9 mL, 200 mmol), benzene (20 mL), triethylamine (22 mL, 160 mmol), $\text{Rh}(\text{Cl})(\text{PPh}_3)_3$ (0.10 g, 0.11 mmol) and placed in a steel bomb, which was then pressurized to 1200 psi of 1:1 H_2 :CO (synthesis gas) at 80 °C. After stirring 20 h, the reaction mixture was allowed to cool, and the pressure carefully released. After concentration of the solution *in vacuo*, the product was purified by vacuum distillation (80 °C, 50 mmHg) to a clear, colorless oil (16.33 g, 81%).²

¹H NMR (500 MHz, CDCl_3): δ 5.51 (t, $J = 3.7$ Hz, 1H), 4.15 (t, $J = 13.3$ Hz, 0.6H), 3.92 (t, $J = 12.8$ Hz, 0.4H), 3.56 (t, $J = 13.7$ Hz, 0.4H), 3.37 (t, $J = 12.8$ Hz, 0.6H), 2.57 (m, 0.4H), 2.29 (m, 0.6H), 2.02 (m, 0.6H), 1.58 (m, 0.6H), 1.46 (m, 0.4H), 1.10 (d, $J = 11.0$ Hz, 0.4H), 1.04 (d, $J = 11.4$ Hz, 3H); ¹³C NMR (125 MHz, CDCl_3): δ 99.4, 98.9, 74.4, 73.6, 41.9, 41.8, 33.4, 31.5, 17.9, 17.3.

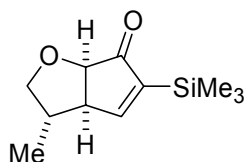


3-Methyl-2,3-dihydro-furan (7): To 4-methyl-tetrahydrofuran-2-ol (8.59 g, 85 mmol) was added a catalytic amount of *p*-toluenesulfonic acid and distilled over between 175-200 °C. Water was removed from the biphasic mixture and the organic layer dried with Na_2SO_4 . This was filtered through a plug of cotton to provide the title compound (8.06 g, 94%).

¹H NMR (500 MHz, CDCl_3): δ 6.29 (t, $J = 2.4$ Hz, 1H), 4.93 (t, $J = 2.6$ Hz, 1H), 4.37 (t, $J = 8.7$ Hz, 1H), 3.84 (dd, $J^1 = 6.7$ Hz, $J^2 = 8.7$ Hz, 1H), 3.01 (m, 1H), 1.07 (d, $J = 6.7$ Hz, 3H); ¹³C NMR (125 MHz, CDCl_3): δ 145.3, 106.6, 76.9, 36.7, 20.8.

² Botteghi, C.; Consiglio, G.; Ceccarelli, G.; Stefani, A. *J. Org. Chem.* **1972**, *37*, 1835.

Resolution of (±)-7: To (*IR*)-(+)- α -pinene (36.6 mL, 230 mmol) was added borane dimethylsulfide (10 mL, 100 mmol) and the mixture was stirred one hour. The white precipitate that had formed was diluted with THF (100 mL) and stirred an additional 3 h to ensure full hydroboration. The solvent was removed by vacuum (to remove DMS) and rediluted with THF (100 mL). After cooling to -78 °C, (±)-7 (15.1 g, 180 mmol) was added and immediately warmed to -25 °C. The white slurry was stirred 16 h and then warmed to 0 °C. At this time a 4:1 solution of 3M NaOH: 30% H₂O₂ was added *slowly* and stirred 2 h. The mixture was extracted with dichloromethane (3 x 100 mL), dried with Na₂SO₄, and filtered. Distillation afforded a solution of enriched 7 that was carried directly onto the next step.



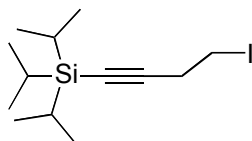
3-Methyl-5-trimethylsilyl-2,3,3a,6a-tetrahydro-cyclopenta[b]furan-6-one (6): To a solution of 7 (6.8 g, 80 mmol) in dichloromethane (250 mL) was added the dicobalthexacarbonyl complex of trimethyl acetylene (6.1 g, 16 mmol), cooled to 0 °C, and added NMO (12.1 g, 100 mmol) in a single portion. The reaction mixture was allowed to warm to room temperature, stirred 16 h and quenched with 10% HCl (200 mL). The aqueous layer was extracted with dichloromethane (2 x 200 mL) and organic layers combined. This was dried with MgSO₄, filtered, and concentrated *in vacuo* to afford a brown oil. The crude product was purified by silica gel chromatography (85:15 hexanes:ethyl acetate) to afford (-)-6 (1.71 g, 51%) in >95% ee. The enantiomeric excess was determined by HPLC (chiracel-OD : 0.5% *i*PrOH/hexanes) t_R (minor) 30.1 min, t_R (major) 32.2 min. R_f (80:20 hexane:ethyl acetate): 0.36

¹H NMR (500 MHz, CDCl₃): δ 7.63 (d, $J = 2.7$ Hz, 1H), 4.25 (d, $J = 5.5$ Hz, 1H), 3.58 (dd, $J^1 = 5.2$ Hz, $J^2 = 8.8$ Hz, 1H), 3.52 (dd, $J^1 = 2.4$ Hz, $J^2 = 8.8$ Hz, 1H), 2.98 (m, 1H), 2.11 (m, 1H), 1.97 (m, 1H), 1.08 (d, $J = 7.0$ Hz, 3H), 0.12 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 210.0, 171.2, 147.4, 80.6, 73.8, 54.1, 38.0, 19.0, -1.9

IR (thin film/NaCl): 2960, 2865, 1697, 1573, 1454, 1287, 1243, 1079, 936, 836 cm⁻¹

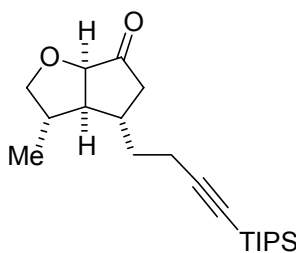
HRMS-ESI(NaI) m/z calc'd for C₁₁H₁₈O₂SiNa: 233.0968, found: 233.0966.

$[\alpha]_D = -56.7$ (c 1.0, EtOH)



(4-iodo-but-1-ynyl)-triisopropyl-silane (9): To a solution of triphenylphosphine (11.4 g, 43 mmol) in 3:1 diethyl ether (150 mL): acetonitrile (50 mL) was added iodine (11.0 g, 43 mmol) and stirred for 0.5 hr. After the orange precipitate had stopped forming, imidazole (3.0 g, 43 mmol) was added and the reaction mixture was stirred for an additional 5 min before addition of the alcohol (6.56 g, 29 mmol). After stirring 1 h, the stir bar was removed and the mixture was concentrated *in vacuo*. The residue was taken up in hexanes (3 x 200 mL) and then filtered through a plug of silica gel. The filtrate was concentrated *in vacuo* to afford **9** (7.0 g, 72 %).³ R_f (hexane): 0.6

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 3.25 (t, $J = 7.3$ Hz, 2H), 2.84 (t, $J = 7.3$ Hz, 2H), 1.08 (m, 21H)



3-Methyl-5-trimethylsilyl-2,3,3a,6a-tetrahydro-cyclopenta[b]furan-6-one (6a):

To a 250 mL round bottom flask equipped with CuI (0.86 g, 4.5 mmol) was added freshly distilled THF (30 mL), and dimethyl sulfide (2.2 mL, 50 mmol). After CuI had dissolved, the solution was cooled to -78 °C. In a separate flask, a solution of (4-iodo-but-1-ynyl)-triisopropyl-silane (3.0 g, 9 mmol) in diethyl ether (30 mL) was cooled to -78 °C and added *t*-butyllithium (10.6 mL, 1.7M in hexanes, 18 mmol). The resulting solution was allowed to warm to room temperature after 0.5 h. At this time, the mixture was transferred slowly to the CuI solution *via cannula* to afford a black slurry. A

³ Overman, L. E.; Brown, M. J.; McCann, S. F. *Org. Synth.* **1990**, *68*, 182.

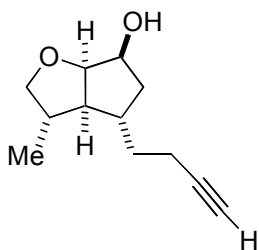
solution (–)-**6** (0.53 g, 2.5 mmol) in THF (2 mL) was added to the black slurry and stirred at –40 °C for 6 hr. The reaction mixture was quenched with 3M HCl and the biphasic mixture was allowed to stir 16 h. After the addition of diethyl ether (50 mL), the mixture was separated into two layers, and the aqueous layer was extracted twice with diethyl ether (2 x 50 mL). The organic layers were combined, washed with brine (75 mL), dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (85:15 hexanes:ethyl acetate) to afford **6a** (1.92 g, 54%). R_f (80:20 hexane:ethyl acetate): 0.41

¹H NMR (500 MHz, CDCl₃): δ 4.24 (d, *J* = 5.8 Hz, 1H), 3.89 (m, 1H), 3.51 (m, 1H), 2.55 (dd, *J*¹ = 5.5 Hz, *J*² = 16.2 Hz, 1H), 2.35 (m, 2H), 2.17 (m, 3H), 2.04 (dd, *J*¹ = 1.2 Hz, *J*² = 7.9 Hz, 1H), 1.75 (m, 1H), 1.63 (m, 1H), 1.07 (d, *J* = 6.7 Hz), 1.03 (s, 18H); ¹³C NMR (125 MHz, CDCl₃): δ 215.3, 107.5, 82.3, 81.6, 75.8, 53.9, 42.9, 40.5, 37.0, 35.5, 18.8, 18.4, 18.0, 11.4

IR (thin film/NaCl): 2941, 2865, 2170, 1754, 1463, 1381, 1062, 995, 883, 676, 661 cm⁻¹

HRMS-ESI(NaI) *m/z* calc'd for C₂₁H₃₆O₂SiNa: 371.2377, found: 371.2375.

[α]_D = –8.0, (*c* 1.0, EtOH)

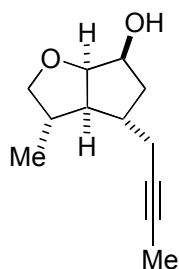


4-But-3-ynyl-3-methyl-hexahydro-cyclopenta[b]furan-6-ol (10): To a solution of **6a** (4.0 g, 11.5 mmol) in 75 mL of methanol at 0 °C was added sodium borohydride (0.44 g, 11.5 mmol) and stirred 3 h. The reaction mixture was quenched with 1M HCl (80 mL) and diluted with ethyl acetate (150 mL). After removal of the organic layer, the aqueous layer was extracted with ethyl acetate (2 x 80 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude oil was taken up in THF (75 mL) and cooled to –78 °C. TBAF (17.2 mL, 17.2 mmol, 1.0 M THF) was added and the reaction mixture was allowed to warm to room temperature over 16 h. Water (200 mL) was added and the reaction mixture was extracted with diethyl ether (3 x

150 mL). The organics were combined, dried over MgSO₄, filtered and concentrated *in vacuo*. The crude oil was purified by silica gel chromatography (75:25 hexanes:ethyl acetate) to afford (-)-**10** (1.69 g, 76% over 2 steps). R_f (80:20 hexane:ethyl acetate): 0.19
¹H NMR (500 MHz, CDCl₃): δ 4.45 (dd, *J*¹ = 5.2 Hz, *J*² = 8.2 Hz, 1H), 4.09 (m, 1H), 4.02 (dd, *J*¹ = 6.1 Hz, *J*² = 8.5 Hz, 1H), 3.53 (dd, *J*¹ = 6.1 Hz, *J*² = 8.5 Hz, 1H), 2.63 (dd, *J*¹ = 0.92 Hz, *J*² = 3.4 Hz, 1H), 2.22 (dt, *J*¹ = 2.4 Hz, *J*² = 7.3 Hz, 2H), 1.95-2.10 (m, 3H), 1.85 (m, 1H), 1.64 (m, 1H), 1.56 (m, 1H), 1.40 (m, 1H), 1.05 (d, *J* = 4.6 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 84.6, 84.0, 77.0, 72.1, 68.7, 56.6, 41.0, 40.1, 39.8, 34.6, 17.9, 17.3
 IR (thin film/NaCl): 3451, 3294, 2927, 2116, 1452, 1378, 1341, 1184, 1089, 1054, 1018, 829 cm⁻¹

HRMS-ESI(NaI) *m/z* calc'd for C₁₂H₁₈O₂Na: 217.1199, found: 217.1198.

[α]_D = -38 (*c* 1.0, EtOH)



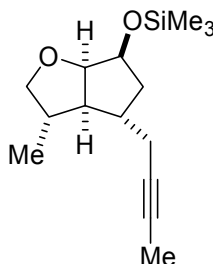
4-But-2-ynyl-3-methyl-hexahydro-cyclopenta[b]furan-6-ol (11): To a degassed solution of potassium *tert*-butoxide (1.12 g, 10 mmol) in DMSO (15 mL), was added (-)-**10** (0.69 g, 3.5 mmol) and stirred 15 min. The reaction mixture was quenched with water (15 mL) and 1 M HCl (15 mL). Diethyl ether (50 mL) was added, the organic layer was separated and the aqueous layer was extracted with ether (2 x 50 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated *in vacuo*. The crude oil was loaded on a plug of silica gel and vacuum filtered using 60:40 hexanes:ethyl acetate as an eluent. The filtered solution was concentrated *in vacuo* to afford (-)-**11** (0.65 g, 94%). R_f (80:20 hexane:ethyl acetate): 0.28

¹H NMR (500 MHz, CDCl₃): δ 4.31 (dd, *J*¹ = 5.2 Hz, *J*² = 7.6 Hz, 1H), 3.98 (m, 1H), 3.89 (dd, *J*¹ = 6.1 Hz, *J*² = 8.2 Hz, 1H), 3.40 (dd, *J*¹ = 5.8 Hz, *J*² = 8.2 Hz, 1H), 2.80 (d, *J* = 3.4 Hz, 1H), 1.77-2.10 (m, 6H), 1.66 (t, *J* = 2.7 Hz, 3H), 1.46 (m, 1H), 0.94 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 84.8, 77.4, 77.0, 76.5, 72.2, 55.6, 41.4, 41.0, 39.4, 24.1, 17.6, 3.3

IR (thin film/NaCl): 3447, 2920, 2360, 2341, 1653, 1558, 1456, 1088, 1014, 668 cm^{-1}

HRMS-EI m/z calc'd for $\text{C}_{12}\text{H}_{18}\text{O}_2$: 193.1223, found: 195.1388.

$[\alpha]_{\text{D}} = -16$ (c 1.0, EtOH)



(4-But-2-ynyl-3-methyl-hexahydro-cyclopenta[b]furan-6-yloxy)-trimethyl-silane (4):

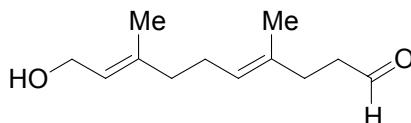
To a solution of (–)-**11** (1.39g, 7.2 mmol) in THF (50 mL) was added triethylamine (2.0 mL, 14.3 mmol) and chlorotrimethylsilane (1.4 mL, 10.7 mmol). The reaction mixture was stirred at room temperature for 1 h, quenched with water (80 mL) and extracted with diethyl ether (3X 75 mL). The organics were combined, dried with MgSO_4 , filtered and concentrated *in vacuo* to afford a yellow oil. The crude product was purified by silica gel chromatography 95:5 (hexane:ethyl acetate) to afford (–)-**4** as a clear colorless oil (1.63 g, 86%). R_f (95:5 hexane:ethyl acetate): 0.38

^1H NMR (500 MHz, CDCl_3): δ 4.21 (dd, $J^1 = 4.6$ Hz, $J^2 = 6.1$ Hz, 1H), 4.12 (m, 1H), 3.96 (dd, $J^1 = 6.1$ Hz, $J^2 = 8.2$ Hz, 1H), 3.37 (dd, $J^1 = 5.5$ Hz, $J^2 = 8.5$ Hz, 1H), 2.09 (m, 2H), 2.0 (m, 1H), 1.85 (m, 3H), 1.74 (t, $J = 2.7$ Hz, 3H), 1.52 (m, 1H), 0.99 (d, $J = 6.7$ Hz, 3H), 0.09 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 84.8, 77.9, 76.3, 76.3, 74.2, 55.2, 42.0, 41.4, 38.0, 25.3, 18.4, 3.5, 0.2.

IR (thin film/NaCl): 2956, 2921, 1456.1438, 1370, 1249, 1101, 841, 749 cm^{-1}

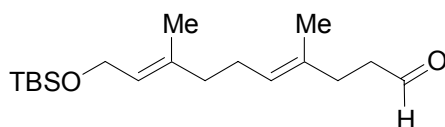
HRMS-ESI(NaI) m/z calc'd for $\text{C}_{15}\text{H}_{26}\text{O}_2\text{SiNa}$: 289.1594, found: 289.1592.

$[\alpha]_{\text{D}} = -35$ (c 1.0, EtOH)



10-Hydroxy-4,8-dimethyl-deca-4,8-dienal (5a): To a solution of acetate (**12**) (2.82 g, 9.4 mmol) in methanol (40 mL) at 0 °C was added potassium carbonate (2.61 g, 19

mmol) and allowed to warm to room temperature. The reaction mixture was stirred for 1 h and then diluted with water (80 mL) and ethyl acetate (50 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 x 80 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated *in vacuo* to afford the crude triol. The triol was taken up in methanol (40 mL) and cooled to 0 °C. An aqueous solution (40 mL) of sodium periodate (4.0 g, 19 mmol) was added *slowly*. When disappearance of the starting material was ascertained by TLC analysis, the reaction mixture was diluted with 1M HCl (20 mL) and ethyl acetate (50 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 x 80 mL). The combined organic layers were dried (MgSO₄), filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (70:30 hexane:ethyl acetate) afforded **5a** (1.34 g, 70% over 2 steps). R_f (70:30 hexane:ethyl acetate): 0.19
¹H NMR (500 MHz, CDCl₃): δ 9.70 (s, 1H), 5.36 (t, *J* = 7.0 Hz, 1H), 5.10 (m, 1H), 4.12 (d, *J* = 6.7 Hz, 2H), 2.49 (t, *J* = 5.8 Hz, 2H), 2.31 (t, *J* = 7.3 Hz, 2H), 2.00-2.12 (m, 5H), 1.63 (s, 3H), 1.60 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 203.4, 138.9, 133.3, 125.1, 124.0, 59.4, 42.0, 39.4, 32.0, 26.0, 16.3, 16.2.
 IR (thin film/NaCl): 3382, 2920, 1723, 1668, 1444, 1112, 1013 cm⁻¹
 HRMS-ESI(NaI) *m/z* calc'd for C₁₂H₂₀O₂Na: 219.1356, found: 219.1361.

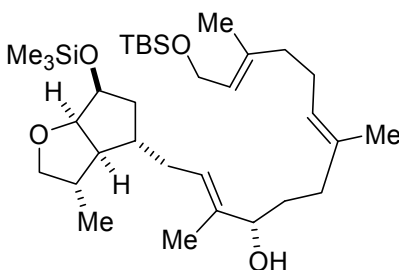


10-(*tert*-Butyl-dimethyl-silyloxy)-4,8-dimethyl-deca-4,8-dienal (5): To a solution of **5a** (6.2 g, 32 mmol) in dichloromethane (150 mL) was added 2,6-lutidine (11.0 mL, 95 mmol) and cooled to -78 °C. After 10 min, *tert*-butyldimethylsilyltrifluoromethanesulfonate (10.9 mL, 48 mmol) was slowly added and stirred at -78 °C for 2 h. The reaction mixture was diluted with water (200 mL) and the organic layer was collected. The aqueous layer was extracted with dichloromethane (2 x 100 mL) and the combined organic layers were dried (MgSO₄), filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (70:30 hexane:ethyl acetate) afforded **5** (7.5 g, 76% yield). R_f (95:5 hexane:ethyl acetate): 0.34

^1H NMR (500 MHz, CDCl_3): δ 9.76 (t, $J = 1.8$ Hz, 1H), 5.30 (t, $J = 6.4$ Hz, 1H), 5.15 (t, $J = 6.7$ Hz, 1H), 4.20 (d, $J = 6.4$ Hz, 2H), 2.52 (m, 2H), 2.32 (t, $J = 7.3$ Hz, 2H), 2.10 (m, 2H), 2.03 (m, 2H), 1.62 (s, 6H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 202.8, 136.7, 133.3, 125.3, 124.8, 60.5, 42.3, 39.5, 32.0, 26.4, 26.2, 25.9, 18.6, 16.5, 16.3, -4.8.

IR (thin film/ NaCl): 2955, 2929, 1728, 1670, 1472, 1255, 1066, 836, 776 cm^{-1}

HRMS-ESI(NaI) m/z calc'd for $\text{C}_{18}\text{H}_{34}\text{O}_2\text{SiNa}$: 333.2220, found: 333.2223.



13-(*tert*-Butyl-dimethyl-silanyloxy)-3,7,11-trimethyl-1-(3-methyl-6-trimethylsilyloxy-hexahydro-cyclopenta[*b*]furan-4-yl)-trien-4-ol (13):

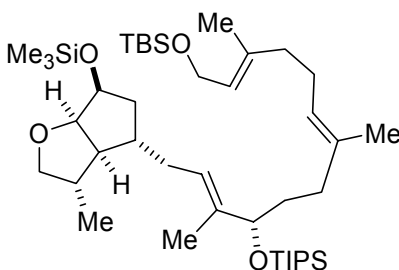
To a solution of $\text{Ni}(\text{cod})_2$ (5.5 mg, 0.02 mmol), (*R*)-*P*-ferrocenyl-*P*-(*p*-xylyl)-phenylphosphine (8.5 mg, 0.02 mmol) in ethyl acetate (1 mL) was added triethylborane (58 μL , 0.4 mmol) and stirred 5 min and cooled to 0 $^\circ\text{C}$. A mixture of alkyne (–)-(4) (53 mg, 0.2 mmol) and aldehyde (5) (125 mg, 0.4 mmol) was added to this mixture and stirred 16 h. The reaction was opened to air and then filtered through a plug of silica gel and concentrated *in vacuo*. Silica gel chromatography (92:8 hexanes:ethyl acetate) afforded the reductive coupled products (98 mg, 2.6:1 mixture of regioisomers, 2.1:1* mixture of diastereomers, 85%). R_f (80:20 hexane:ethyl acetate): 0.5. * This was determined by NMR integration after the cyclization to compound (–)-(15).

^1H NMR (500 MHz, CDCl_3): δ 5.61 (q, $J = 6.7$ Hz, 0.3H minor regioisomer), 5.35 (t, $J = 7.0$ Hz, 0.7H major regioisomer), 5.29 (m, 1H), 5.13 (m, 1H), 4.25 (m, 1H), 4.18 (d, $J = 6.1$ Hz, 2H), 4.10 (m, 1H), 3.97 (m, 2H), 3.38 (m, 1H), 1.94-2.18 (m, 10H), 1.77-1.84 (m, 3H), 1.60-1.69 (m, 11H), 1.45 (m, 1H), 1.01 (m, 3H), 0.89 (s, 9H), 0.13 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 138.6, 138.5, 136.91, 136.89, 135.0, 134.9, 125.1, 125.0, 124.7, 124.6, 121.5, 84.7, 84.54, 84.52, 77.59, 77.55, 76.30, 76.28, 76.2, 75.4, 74.33, 74.32, 60.5, 56.2, 55.89, 55.85, 42.2, 42.14, 42.10, 42.06, 41.1, 39.7, 38.2, 38.0,

36.3, 36.12, 36.11, 34.3, 34.3, 34.2, 34.1, 33.33, 33.26, 26.41, 26.37, 26.36, 26.2, 18.6, 18.53, 18.51, 16.53, 16.50, 16.2, 16.1, 13.9, 11.9, 11.8, 0.33, 0.31, -4.86, -4.87.

IR (thin film/NaCl): 3451, 2956, 1668, 1472, 1381, 1250, 1065, 838, 776 cm^{-1}

HRMS-ESI(NaI) m/z calc'd for $\text{C}_{33}\text{H}_{62}\text{O}_4\text{Si}_2\text{Na}$: 601.4079, found: 601.4073



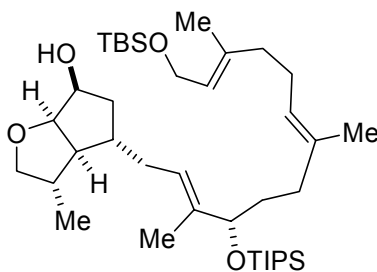
4-[13-(*tert*-Butyl-dimethyl-silanyloxy)-3,7,11-trimethyl-4-triisopropylsilanyloxy-trideca-2,7,11-trienyl]-3-methyl-6-trimethylsilanyloxy-hexahydro-

cyclopenta[*b*]furan (13a): To a solution of allylic alcohol **13** (1.6 g, 2.8 mmol) in dichloromethane (20 mL) was added 2,6-lutidine (1 mL, 8.3 mmol) and cooled to $-78\text{ }^{\circ}\text{C}$. After 10 min, triisopropylsilyltrifluoromethanesulfonate (1.1 mL, 4.1 mmol) was added slowly and stirred 2 h. The reaction mixture was quenched with water (80 mL) and diluted with dichloromethane (80 mL). The organic layer was collected and the aqueous layer was extracted further with dichloromethane (2 x 80 mL). The combined organic layers were dried (MgSO_4), filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (95:5 hexane:ethyl acetate) afforded **13a** (1.92 g, 97% yield). R_f (95:5 hexane:ethyl acetate): 0.28

^1H NMR (500 MHz, CDCl_3): δ 5.30 (t, $J = 5.5$ Hz, 1H), 5.24 (m, 1H), 5.07 (t, $J = 6.4$ Hz, 1H), 4.24 (m, 1H), 4.17 (d, $J = 6.1$ Hz, 2H), 4.07 (m, 2H), 3.96 (m, 1H), 3.40 (m, 1H), 1.70-2.10 (m, 13H), 1.60 (m, 11H), 1.03 (m, 24H), 0.89 (s, 9H), 0.12 (m, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 138.3, 138.2, 137.0, 135.2, 124.64, 124.59, 124.4, 123.9, 123.8, 84.61, 84.55, 84.4, 78.6, 78.4, 76.2, 74.4, 74.3, 60.5, 55.9, 55.7, 42.2, 42.1, 42.0, 41.3, 41.2, 39.7, 38.0, 37.7, 35.7, 35.6, 34.7, 34.6, 34.3, 34.2, 26.49, 26.46, 26.2, 25.9, 18.7, 18.61, 18.57, 18.5, 18.4, 18.31, 18.28, 18.25, 18.2, 16.5, 16.29, 16.27, 13.9, 12.61, 12.58, 12.5, 11.4, 11.3, 0.3, -4.9

IR (thin film/NaCl): 2957, 2866, 1669, 1464, 1249, 1065, 838, 775, 680 cm^{-1}

HRMS-ESI(NaI) m/z calc'd for $C_{42}H_{82}O_4Si_3Na$: 757.5414, found: 757.5418

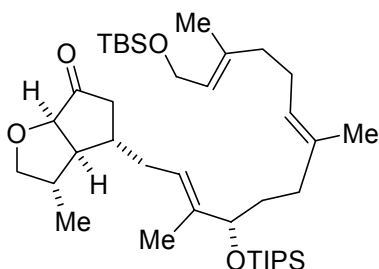


4-[13-(*tert*-Butyl-dimethyl-silanyloxy)-3,7,11-trimethyl-4-triisopropylsilanyloxy-trideca-2,7,11-trienyl]-3-methyl-hexahydro-cyclopenta[*b*]furan-6-ol (13b): To a solution of **13a** (1.9 g, 2.7 mmol) in methanol (10 mL) at 0 °C was added sodium hydroxide (0.1 g) in methanol (10 mL) and stirred 10 min. The reaction mixture was diluted in water (100 mL), extracted with ethyl acetate (3 x 75 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Silica gel chromatography (92:8 hexanes:ethyl acetate) on the crude oil afforded **13b** (1.05 g, 59%) and its regioisomer **13b'** (410 mg, 23%). R_f (85:15 hexane:ethyl acetate): 0.37 (desired) R_f (85:15 hexane:ethyl acetate): 0.39 (undesired).

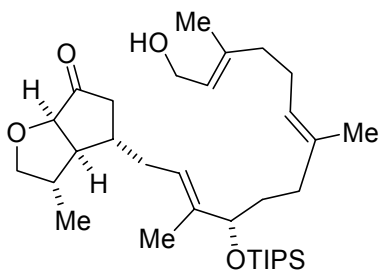
1H NMR (500 MHz, $CDCl_3$): δ 5.29 (t, $J = 5.8$ Hz, 1H), 5.25 (t, $J = 7.0$ Hz, 1H), 5.07 (t, $J = 6.7$ Hz, 1H), 4.41 (m, 1H), 4.17 (d, $J = 6.1$ Hz, 2H), 4.04 (m, 2H), 3.97 (dt, $J^1 = 6.1$ Hz, $J^2 = 2.1$ Hz, 1H), 3.49 (m, 1H), 2.68 (s, 1H), 1.75-2.16 (m, 13H), 1.60 (m, 11H), 1.03 (m, 24H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): 138.5, 138.4, 137.1, 137.0, 135.3, 124.48, 124.47, 124.2, 124.1, 123.9, 84.6, 84.5, 78.6, 78.5, 76.97, 77.00, 72.4, 60.5, 56.5, 56.4, 42.2, 41.3, 41.2, 39.9, 39.7, 35.7, 35.6, 34.74, 34.66, 33.2, 26.5, 26.2, 18.6, 18.4, 18.37, 18.33, 18.28, 18.2, 18.1, 16.5, 16.3, 12.9, 12.6, 12.5, 11.32, 11.30, -4.9

IR (thin film/ $NaCl$): 3473, 2929, 1669, 1464, 1255, 1065, 836, 775, 680 cm^{-1}

HRMS-ESI(NaI) m/z calc'd for $C_{39}H_{74}O_4Si_2Na$: 685.5018, found: 685.5000



4-[13-(*tert*-Butyl-dimethyl-silyloxy)-3,7,11-trimethyl-4-triisopropylsilyloxy-trideca-2,7,11-trienyl]-3-methyl-hexahydro-cyclopenta[*b*]furan-6-one (13c): To a solution of TPAP (56 mg, 0.16 mmol) and NMO (380 mg, 3.2 mmol) in dichloromethane (16 mL) at 0 °C was added **13b** (1.05 g, 1.6 mmol) and stirred for 2.5 h. The reaction mixture was diluted with ethyl acetate (20 mL) and filtered through a plug of silica gel and washed with an additional ethyl acetate (400 mL). The solution was concentrated *in vacuo* and silica gel chromatography of the crude mixture (90:10 hexane:ethyl acetate) afforded **13c** (0.93 g, 89%) as a clear colorless oil. R_f (85:15 hexane:ethyl acetate): 0.49 ^1H NMR (500 MHz, CDCl_3): δ 5.28 (m, 2H), 5.06 (m, 1H), 4.22 (d, $J = 7.6$ Hz, 1H), 4.17 (d, $J = 6.1$ Hz, 2H), 4.07 (t, $J = 7.0$ Hz, 1H), 3.92 (m, 1H), 3.48 (m, 1H), 2.50 (m, 1H), 1.78-2.23 (m, 12H), 1.60 (m, 11H), 1.07 (m, 3H), 1.02 (m, 21H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): 215.7, 139.98, 139.89, 137.00, 136.99, 135.15, 135.14, 124.5, 124.0, 122.5, 122.4, 82.34, 82.32, 78.3, 78.2, 76.03, 75.96, 60.4, 53.6, 53.5, 42.5, 42.3, 40.44, 40.42, 39.7, 37.9, 37.8, 35.5, 35.4, 34.7, 34.6, 34.1, 34.0, 26.5, 26.2, 18.6, 18.32, 18.25, 18.2, 17.62, 17.58, 17.4, 16.5, 16.3, 13.0, 12.6, 12.5, 11.6, 11.5, -4.9 IR (thin film/NaCl): 2941, 1754, 1669, 1464, 1255, 1065, 836, 776, 680 cm^{-1} (ESI/NaI) m/z calc'd for $\text{C}_{39}\text{H}_{72}\text{O}_4\text{Si}_2\text{Na}$: 683.4861, found: 683.4854



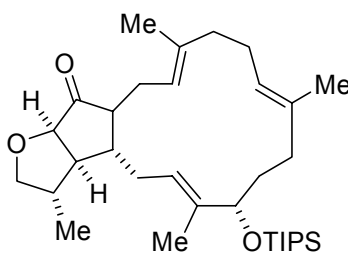
4-(13-Hydroxy-3,7,11-trimethyl-4-triisopropylsilyloxy-trideca-2,7,11-trienyl)-3-methyl-hexahydro-cyclopenta[*b*]furan-6-one (13d): To a solution of **13c** (0.93, 1.4

mmol) in THF (20 mL) was added 1 M HCl (20 mL) and stirred 8 h. The reaction mixture was diluted with ethyl acetate (60 mL) and water (60 mL). The organic layer was collected while the aqueous layer was washed with ethyl acetate (2x 60 mL). The organics were combined, washed with brine and dried with MgSO₄, filtered, and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (70:30 hexane:ethyl acetate) afforded **13d** (650 mg, 84% yield). R_f (70:30 hexane:ethyl acetate): 0.27

¹H NMR (500 MHz, CDCl₃): δ 5.41 (t, *J* = 7.0 Hz, 1H), 5.28 (t, *J* = 7.0, 1H), 5.07 (m, 1H), 4.24 (d, *J* = 7.9 Hz, 1H), 4.15 (d, *J* = 6.7 Hz, 2H), 4.08 (t, *J* = 6.4 Hz, 1H), 3.95 (m, 1H), 3.50 (m, 1H), 2.50 (m, 1H), 2.01-2.25 (m, 11H), 1.80 (m, 2H), 1.67 (s, 3H), 1.62 (m, 2H), 1.58 (s, 6H), 1.08 (m, 3H), 1.03 (m, 21H); ¹³C NMR (125 MHz, CDCl₃): 216.1, 216.0, 140.0, 139.9, 139.7, 135.4, 124.4, 124.0, 123.84, 123.83, 123.6, 123.5, 122.5, 122.4, 82.41, 82.38, 82.3, 78.7, 78.3, 78.2, 76.1, 76.0, 59.5, 54.6, 53.6, 53.5, 42.9, 42.5, 42.4, 40.5, 40.4, 40.2, 39.7, 37.9, 37.8, 37.4, 35.6, 35.5, 35.3, 34.8, 34.7, 34.6, 34.1, 34.0, 33.2, 26.5, 26.4, 26.42, 26.2, 18.4, 18.30, 18.27, 17.7, 17.6, 17.5, 16.5, 16.40, 16.36, 16.3, 13.9, 12.62, 12.55, 12.6, 12.3, 11.7, 11.6

IR (thin film/NaCl): 3438, 2942, 1751, 1668, 1464, 1382, 1064, 883, 681 cm⁻¹

HRMS-ESI(NaI) *m/z* calc'd for C₃₃H₅₈O₄SiNa: 569.3997, found: 569.3988



4,8,12,17-Tetramethyl-11-triisopropylsilyloxy-19-oxa-tricyclo[13.6.0.0]henicosane-3,7,12-trien-21-one (15): To a solution of triphenylphosphine (77 mg, 0.3 mmol) in 6 mL of a 1:1 mixture of benzene:diethyl ether was added iodine (70 mg, 0.28 mmol) and imidazole (19 mg, 0.28 mmol) and stirred 5 min. A solution of **13d** in benzene (1 mL) was added and the reaction mixture was stirred for 40 min. At this stage, benzene (3 mL) was added and after 15 min, the reaction was complete by TLC. The crude mixture was

poured into saturated sodium thiosulfate (40 mL), and diluted with hexane (40 mL). The organic layer was collected and the aqueous layer was extracted further with hexanes (2 x 40 mL). After combining the organic layers, this was washed with brine, dried by MgSO₄ and filtered into a round bottom wrapped in foil. The solution was concentrated *in vacuo* to crude iodide (**13e**) and carried onto the next step without further purification.

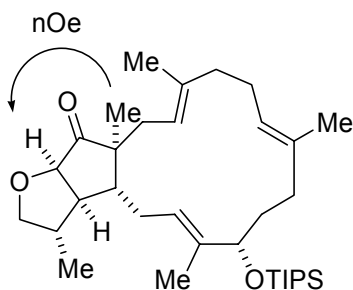
To the crude iodide (**13e**) was diluted in THF (26 mL), cooled to 0 °C and added LiHMDS (64 mg, 0.38 mmol, 4 mL THF) over 1.5 h. After addition, TLC reveals full conversion. The reaction mixture was diluted with water (50 mL) and extracted with diethyl ether (3 x 40 mL). The organics were combined, washed with brine (40 mL) and dried with MgSO₄. The solution was filtered and concentrated *in vacuo* to afford a yellow oil that was purified with silica gel chromatography (90:10 hexane:ethyl acetate) to afford a 2.1:1 mixture of diastereomers (**15**, **15a**) (32 mg, 33% over 2 steps). The desired diastereomer was then separated by silica gel chromatography (95:5 hexane:ethyl acetate). R_f (90:10 hexane:ethyl acetate): 0.31 (desired diastereomer, (–)-**15**) R_f (90:10 hexane:ethyl acetate): 0.33 (undesired diastereomer **15a**).

¹H NMR (500 MHz, C₆D₆): δ 5.48 (m, 1H), 5.16 (t, *J* = 6.4 Hz, 1H), 5.04 (m, 1H), 4.18 (d, *J* = 7.6 Hz, 1H), 4.13 (dd, *J*¹ = 4.2 Hz, *J*² = 10.7 Hz, 1H), 3.71 (dd, *J*¹ = 5.8 Hz, *J*² = 8.5 Hz, 1H), 3.34 (dd, *J*¹ = 3.7 Hz, *J*² = 8.5 Hz, 1H), 3.02 (m, 1H), 1.65-2.28 (m, 15 H), 1.64 (s, 3H), 1.58, (s, 3H), 1.49 (s, 3H), 1.13 (m, 21H), 0.79 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (125 MHz, C₆D₆): δ 213.8, 136.6, 135.8, 133.8, 126.7, 126.1, 125.7, 82.3, 78.2, 75.2, 56.4, 53.7, 47.2, 40.5, 39.7, 35.7, 34.4, 32.1, 29.9, 24.8, 18.9, 15.9, 15.4, 13.8, 13.1, 10.8

IR (thin film/NaCl): 2939, 2865, 1751, 1457, 1061, 883 cm⁻¹

HRMS-ESI(NaI) *m/z* calc'd for C₃₃H₅₆O₃SiNa: 551.3891, found: 551.3909

[α]_D = -8.4 (*c* 1.9, EtOH)



1,4,8,12,17-Pentamethyl-11-triisopropylsilyloxy-19-oxa-

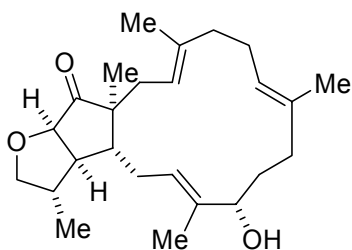
tricyclo[13.6.0.0^{16,20}]henicosa-3,7,12-trien-21-one (16): To a solution of (-)-**15** (19 mg, 0.036 mmol) in toluene (0.5 mL) was added NaH (4.3 mg, 0.11 mmol) and methyl iodide (22 μ L, 0.36 mmol) and stirred for 5 min before the addition of water (1.3 μ L, 0.072 mmol). The reaction mixture was stirred for 15 h and filtered through a plug of silica gel (40 mL of ethyl acetate). The reaction mixture was concentrated *in vacuo* to afford a yellow oil. Purification by silica gel chromatography (95:5 hexane:ethyl acetate) afforded (+)-**16** (12.1 mg, 62%) and the vinyl-methyl ether (**15c**) (2 mg, 10%). R_f (90:10 hexane:ethyl acetate): 0.34

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 5.33 (t, $J = 6.7$ Hz, 1H), 5.02 (t, $J = 7.0$ Hz, 1H), 4.83 (m, 1H), 4.51 (d, $J = 7.9$ Hz, 1H), 3.96 (dd, $J^1 = 4.0$ Hz, $J^2 = 10.4$ Hz, 1H), 3.74 (dd, $J^1 = 5.2$ Hz, $J^2 = 8.8$ Hz, 1H), 3.60 (dd, $J^1 = 2.4$ Hz, $J^2 = 8.8$ Hz, 1H), 1.65-2.35 (m, 15H), 1.57 (s, 3H), 1.55 (s, 3H), 1.53 (s, 3H), 1.11 (d, $J = 7.0$ Hz, 3H), 1.04 (m, 21H), 0.99 (s, 3H); $^{13}\text{C NMR}$ (125 MHz, C_6D_6): δ 217.4, 136.6, 136.2, 134.9, 127.5, 125.0, 122.8, 82.1, 79.7, 75.1, 53.2, 53.1, 48.2, 41.8, 39.8, 35.6, 35.5, 32.6, 29.9, 24.4, 19.9, 18.8, 18.1, 16.0, 15.3, 13.1, 10.9

IR (thin film/NaCl): 2932, 2866, 1750, 1462, 1382, 1061, 883 cm^{-1}

HRMS-ESI(NaI) m/z calc'd for $\text{C}_{33}\text{H}_{58}\text{O}_3\text{SiNa}$: 565.4047, found: 565.4047.

$[\alpha]_D = +5.0$, (c 0.8, EtOH)



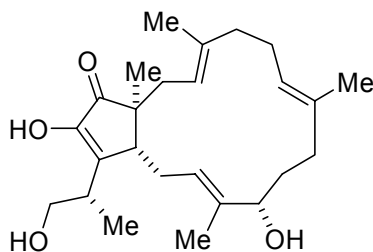
11-Hydroxy-1,4,8,12,17-pentamethyl-19-oxa-tricyclo[13.6.0.0]^{16,20}henicosa-3,7,12-trien-21-one (3a): To a solution of (+)-**16** (10 mg, 0.0184 mmol) in THF (0.2 mL) was added TBAF (32 μ L, 1.0 M THF) and stirred 3 h. The reaction mixture was diluted with water (2 mL) and extracted with diethyl ether (3 x 3 mL). The organics were combined, dried with MgSO₄, filtered through a plug of silica gel, and concentrated *in vacuo* to afford a clear and colorless oil. Purification by silica gel chromatography (85:15 hexane:ethyl acetate) afforded (+)-**3a** (5 mg, 72%) as a clear colorless oil. R_f (70:30 hexane:ethyl acetate): 0.19

¹H NMR (500 MHz, CDCl₃): δ 5.46 (t, $J = 7.0$ Hz, 1H), 4.92 (t, $J = 4.9$ Hz, 2H), 4.50 (d, $J = 7.9$ Hz, 1H), 4.01 (dd, $J^1 = 4.0$ Hz, $J^2 = 8.8$ Hz, 1H), 3.79 (dd, $J^1 = 5.5$ Hz, $J^2 = 8.5$ Hz, 1H), 3.62 (dd, $J^1 = 2.4$ Hz, $J^2 = 8.5$ Hz, 1H), 1.65-2.42 (m, 16 H), 1.62 (s, 3H), 1.57 (s, 3H), 1.54 (s, 3H), 1.14 (d, $J = 7.0$ Hz, 3H), 0.97 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 219.3, 136.4, 136.2, 135.8, 126.3, 124.6, 122.3, 81.6, 78.3, 75.3, 53.2, 52.4, 46.1, 41.3, 39.0, 34.5, 34.1, 30.0, 29.1, 23.8, 19.8, 18.7, 15.8, 15.0, 12.0.

IR (thin film/NaCl): 3461, 2930, 1748, 1663, 1456, 1381, 1096, 1005, 914, 735 cm⁻¹

HRMS-ESI(NaI) m/z calc'd for C₂₅H₃₈O₃Na: 409.2713, found: 409.2721.

$[\alpha]_D = +27.7$, (c 0.83, EtOH)



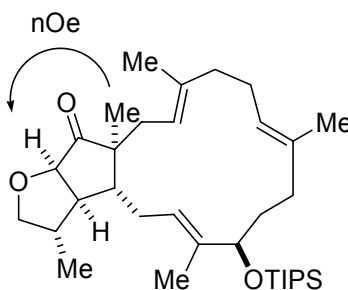
(-)-Terpestacin (1a): To a solution of potassium bis(trimethylsilyl)amide (8 mg, 0.039 mmol dissolved in 0.25 mL THF) at -78 °C was added (+)-**3a** (5 mg, 0.013 mmol in 0.15 mL THF) and stirred for 1 hour. During the addition, the solution progressively turned

orange. Triethylphosphite (4 μ L, 0.023 mmol) was then added and oxygen was bubbled through the reaction mixture for 45 min whereby the solution becomes colorless. To this colorless solution was added water (4 mL) and extracted with ethyl acetate (3 x 4 mL). The organics were combined, dried with NaSO₄, filtered through celite, and concentrated *in vacuo* to afford a clear and colorless oil. The crude hemi-ketal (**17**) was taken up in MeOH (1 mL), added potassium carbonate (9 mg, 0.065 mmol) and stirred at room temperature for 2 h. The reaction mixture was transferred to water (4 mL) and extracted with ethyl acetate (3 x 4 mL). The organics were combined dried with NaSO₄, filtered through celite, and *conc in vacuo* to afford a clear and colorless oil. Preparative silica gel chromatography (1:2 ethyl acetate:hexane, 0.5% HOAc) afforded (-)-**1a** (2.5 mg, 48% over 2 steps). R_f (1:2 hexane:ethyl acetate, 0.5% HOAc): 0.28

¹H NMR (500 MHz, CDCl₃): δ 5.79 (s, 1H), 5.41 (m, 1H), 5.25 (dd, $J^1 = 5.2$ Hz, $J^2 = 10.1$ Hz, 1H), 5.14 (m, 1H), 4.07 (dd, $J^1 = 4.0$ Hz, $J^2 = 10.1$ Hz, 1H), 3.90 (dd, $J^1 = 7.0$ Hz, $J^2 = 10.4$ Hz, 1H), 3.83 (dd, $J^1 = 5.5$ Hz, $J^2 = 10.4$ Hz, 1H), 2.72 (dd, $J^1 = 2.1$ Hz, $J^2 = 11.3$ Hz, 1H), 2.68 (m, 1H), 2.45 (d, $J = 17.4$ Hz, 1H), 2.40 (dd, $J^1 = 10.4$ Hz, $J^2 = 13.7$ Hz, 1H), 2.22-2.30 (m, 2H), 2.09-2.12 (m, 2H), 1.90-2.04 (m, 2H), 1.68-1.80 (m, 3H), 1.65 (s, 3H), 1.64 (s, 3H), 1.58 (s, 3H), 1.30 (d, $J = 7.3$ Hz, 3H), 1.01 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 208.0, 149.0, 146.8, 138.3, 136.7, 133.1, 129.1, 124.5, 121.7, 76.7, 66.3, 49.8, 49.1, 40.5, 39.5, 37.3, 35.1, 30.0, 29.0, 24.0, 16.4, 15.8, 15.5, 14.6, 10.7. IR (thin film/NaCl): 3366, 2925, 1699, 1653 cm⁻¹

HRMS-ESI(NaI) *m/z* calc'd for C₂₅H₃₈O₄Na: 425.2662, found: 425.2682

$[\alpha]_D = -18$, (*c* 0.1, MeOH)



1,4,8,12,17-Pentamethyl-11-triisopropylsilyloxy-19-oxatricyclo[13.6.0.0^{16,20}]henicosa-3,7,12-trien-21-one (11-*epi*-16): To a solution of C11-*epi*-15 (40 mg, 0.076 mmol) in toluene (1 mL) was added NaH (9.0 mg, 0.23 mmol) and

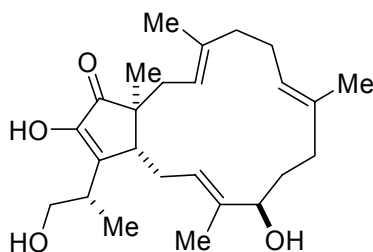
methyl iodide (50 μL , 0.76 mmol) and stirred for 5 min before the addition of water (3 μL , 0.15 mmol). The reaction mixture was stirred for 6 h and filtered through a plug of silica gel (80 mL of ethyl acetate). The reaction mixture was concentrated *in vacuo* to afford a yellow oil. Purification by silica gel chromatography (95:5 hexane:ethyl acetate) afforded **(+)-11-*epi*-16** (15.1 mg, 37%). R_f (90:10 hexane:ethyl acetate): 0.34

^1H NMR (500 MHz, C_6D_6): δ 5.35 (t, $J = 6.7$ Hz, 1H), 5.22 (t, $J = 6.7$ Hz, 1H), 4.95 (m, 1H), 4.27 (d, $J = 7.9$ Hz, 1H), 4.12 (dd, $J^1 = 2.7$ Hz, $J^2 = 11$ Hz, 1H), 3.66 (dd, $J^1 = 5.8$ Hz, $J^2 = 8.9$ Hz, 1H), 3.36 (dd, $J^1 = 3.4$ Hz, $J^2 = 8.9$ Hz, 1H), 2.90 (dd, $J^1 = 5.5$ Hz, $J^2 = 13.1$ Hz, 1H), 1.67-2.20 (m, 15H), 1.66 (s, 3H), 1.57 (s, 3H), 1.46 (s, 3H), 1.10 (m, 21H), 0.83 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6): δ 213.9, 138.0, 136.5, 133.4, 127.1, 124.4, 123.8, 82.2, 78.1, 75.3, 52.7, 51.6, 45.2, 40.1, 39.9, 36.1, 31.8, 30.1, 27.8, 24.8, 19.5, 18.7, 15.3, 15.1, 13.8, 13.0, 10.5

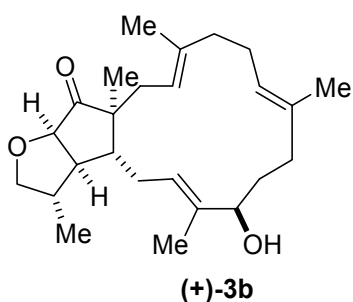
IR (thin film/NaCl): 2940, 1750, 1457, 1064, 883 cm^{-1}

(ESI/NaI) m/z calc'd for $\text{C}_{33}\text{H}_{56}\text{O}_3\text{SiNa}$: 551.3891, found: 551.3895

$[\alpha]_D = +72.8$, (c 1.5, EtOH)

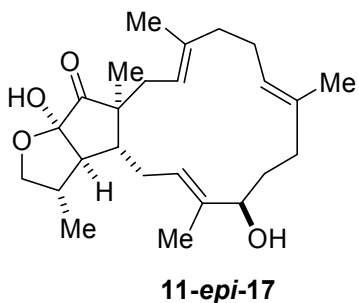


(+)-11-*epi*-terpestacin (1b): To a solution of potassium bis(trimethylsilyl)amide (8 mg, 0.039 mmol dissolved in 0.25 mL THF) at -78 $^{\circ}\text{C}$ was added **(+)-3b** (5 mg, 0.013 mmol



in 0.15 mL THF) and stirred for 1.5 h. During the addition, the solution progressively turns orange. Triethyl phosphite (4 μL , 0.023 mmol) was then added and oxygen was bubbled through the reaction mixture for 30 min whereby the solution becomes colorless. To this colorless solution was added water (4 mL) and extracted with diethyl ether (2 x 8 mL).

The organic layers were combined and washed with water (2 x 8 mL), dried with NaSO₄, filtered through celite, and concentrated *in vacuo* to afford a clear and colorless oil. The crude hemi-ketal (**11-*epi*-17**) was taken up in MeOH (1 mL), added potassium carbonate



(9 mg, 0.065 mmol) and stirred at room temperature 2.5 h.

The reaction mixture was transferred to water (4 mL), extracted with diethyl ether (2 x 8 mL) and washed with water (5 x 8 mL). The organic layers were combined, dried with NaSO₄, and concentrated *in vacuo*. Silica gel chromatography (2:1 hexane:ethyl acetate, 0.25% HOAc) afforded (+)-**11-*epi*-terpestacin** (3.0 mg, 58 %). R_f (1:2

hexane:ethyl acetate, 0.5% HOAc): 0.6.

¹H NMR (500 MHz, CDCl₃): δ 5.50 (dt, *J*¹ = 0.9 Hz, *J*² = 4.9 Hz, 1H), 5.34 (t, *J* = 7.3 Hz, 1H), 5.13 (m, 1H), 4.06 (dd, *J*¹ = 3.7 Hz, *J*² = 9.2 Hz, 1H), 3.89 (dd, *J*¹ = 6.7 Hz, *J*² = 10.4 Hz, 1H), 3.83 (dd, *J*¹ = 5.5 Hz, *J*² = 10.4 Hz, 1H), 2.71 (m, 1H), 2.57 (dd, *J*¹ = 2.1 Hz, *J*² = 11.9 Hz, 1H), 2.50 (dd, *J*¹ = 6.1 Hz, *J*² = 17.4 Hz, 1H), 2.05-2.27 (m, 6H), 1.98 (dd, *J*¹ = 9.1 Hz, *J*² = 14.0 Hz, 1H), 1.70-1.88 (m, 4H), 1.68 (s, 3H), 1.60 (s, 3H), 1.56 (s, 3H), 1.30 (d, *J* = 7.3 Hz, 3H), 1.13 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 207.6, 148.9, 146.4, 137.7, 135.9, 134.4, 127.0, 125.6, 121.9, 76.7, 66.4, 48.8, 48.7, 40.3, 38.9, 37.2, 35.5, 29.5, 28.6, 24.3, 16.7, 15.3, 15.2, 14.5, 11.4.

IR (thin film/NaCl): 3344, 2932, 1649, 1651 cm⁻¹

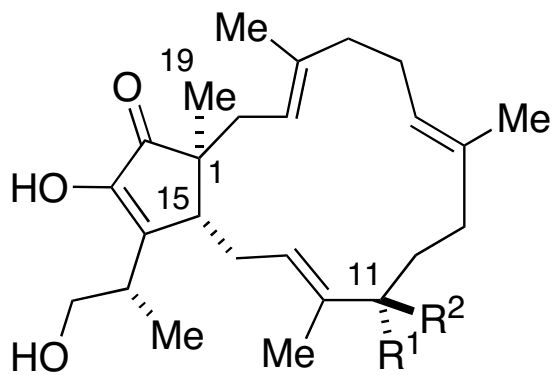
HRMS-ESI *m/z* calc'd for C₂₅H₃₉O₄: 403.2843, found: 403.2845

[α]_D = +36, (*c* 0.50, MeOH)

Selected ¹H NMR data for terpestacin (**1a**), 11-*epi*-terpestacin (**1b**), and "siccanol"

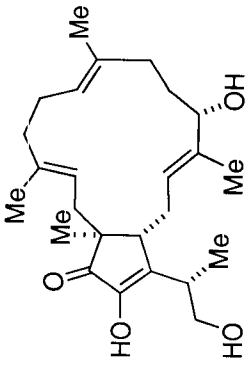
(all data obtained using CDCl₃ solvent, ppm)

Carbon number	terpestacin (1a) <i>natural</i> Oka, 1993 (ref. 2b)	terpestacin (1a) <i>synthetic</i> Myers, 2002 (ref. 4)	terpestacin (1a) <i>synthetic</i> (this work)	"siccanol" <i>natural</i> Miyagawa, 2002 (ref. 6)	"siccanol" <i>natural</i> from Prof. Miyagawa (analyzed at MIT)	11- <i>epi</i> -terpestacin (1b) <i>synthetic</i> (this work)
2	1.72, 2.39	1.67-1.79, 2.39	1.68-1.80, 2.40	1.75, 2.36	1.68-1.82, 2.40	2.05-2.27
3	5.24	5.24	5.25	5.25	5.25	<u>5.34</u>
9	1.81, 2.08	1.67-1.79, 2.08-2.13	1.68-1.80, 2.09-2.12	1.78, 2.18	1.68-1.82, 2.09-2.12	1.70-1.88, 2.05-2.27
10	1.62, 1.81	1.67-1.79	1.68-1.80	1.70, 1.75	1.68-1.82	1.70-1.88
11	4.05	4.06	4.06	4.07	4.06	4.06
13	5.41	5.40	5.41	5.38	5.41	<u>5.50</u>
14	1.92, 2.44	1.89-2.02, 2.44	1.90-2.04, 2.45	1.92, 2.44	1.90-2.05, 2.45	<u>1.70-1.88, 2.50</u>
15	2.71	2.71	2.72	2.72	2.71	<u>2.57</u>
19	1.00	1.00	1.01	0.99	1.00	<u>1.13</u>

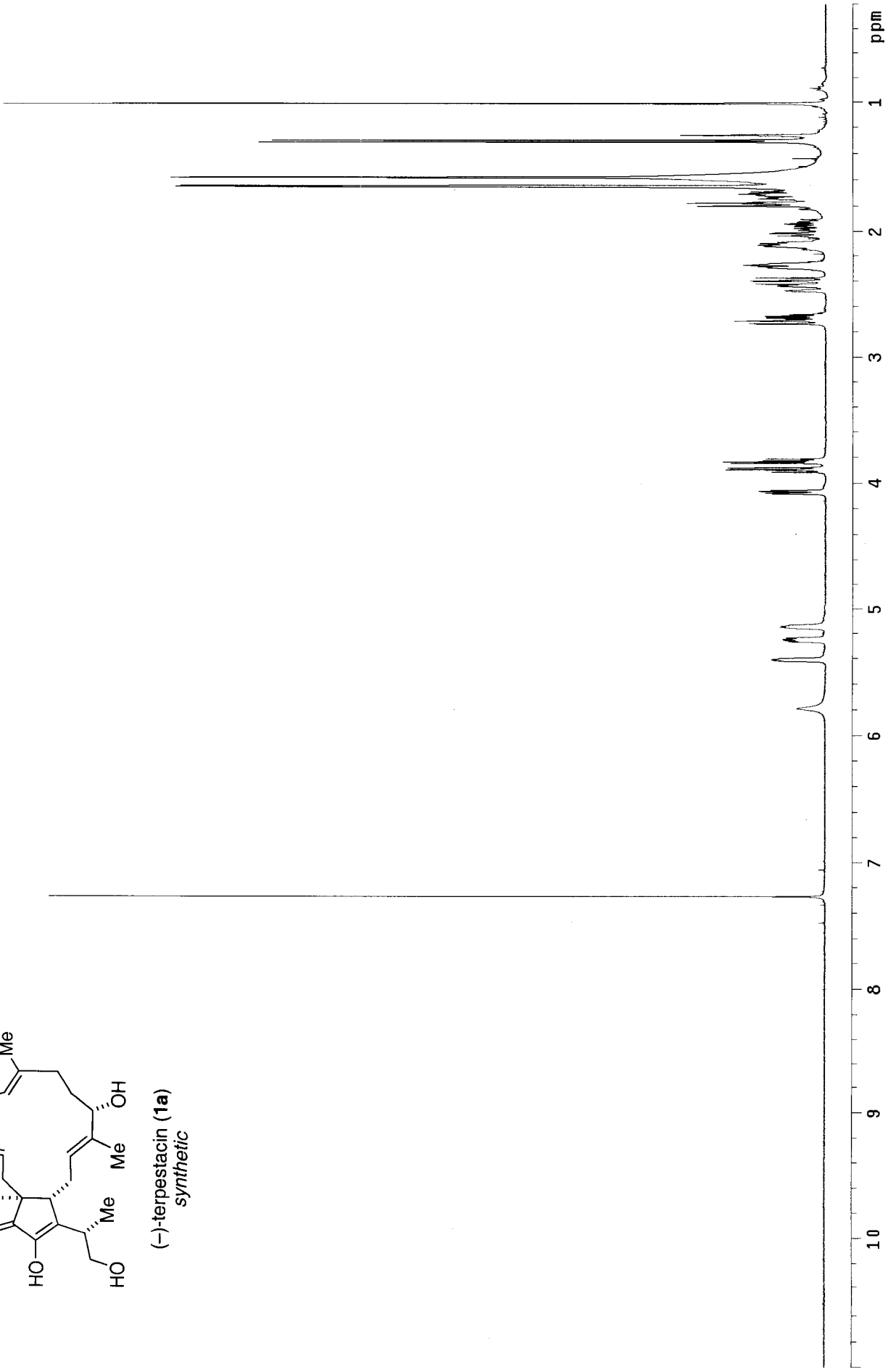


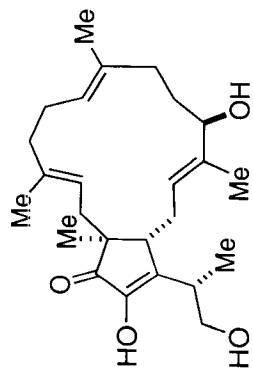
1a (R¹ = OH; R² = H; terpestacin)

1b (R¹ = H; R² = OH; 11-*epi*-terpestacin)

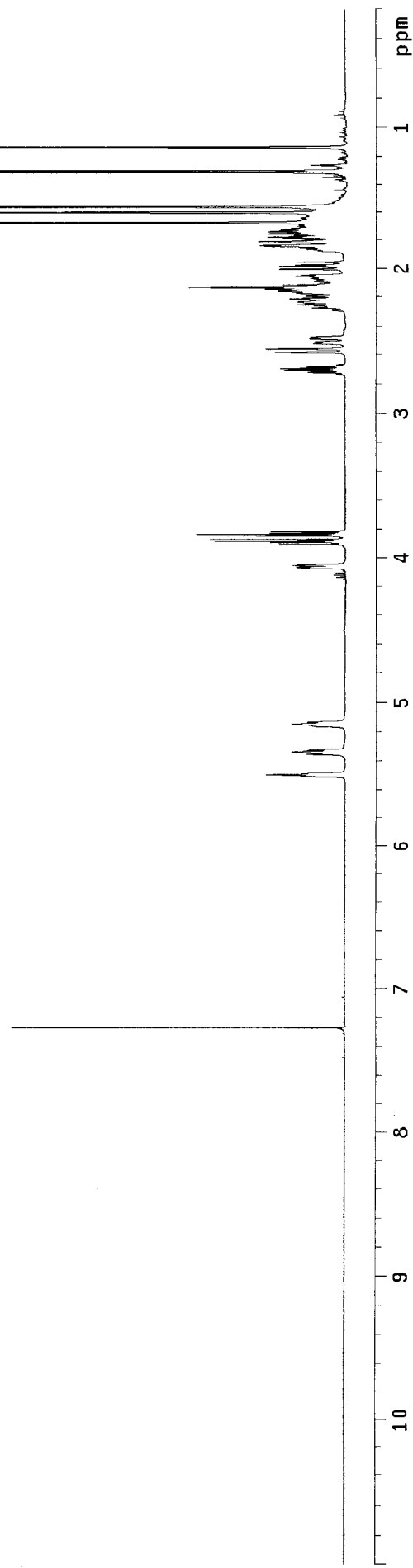


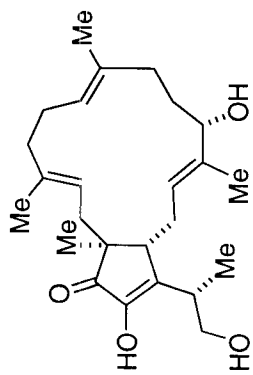
(-)-terpestacin (**1a**)
synthetic



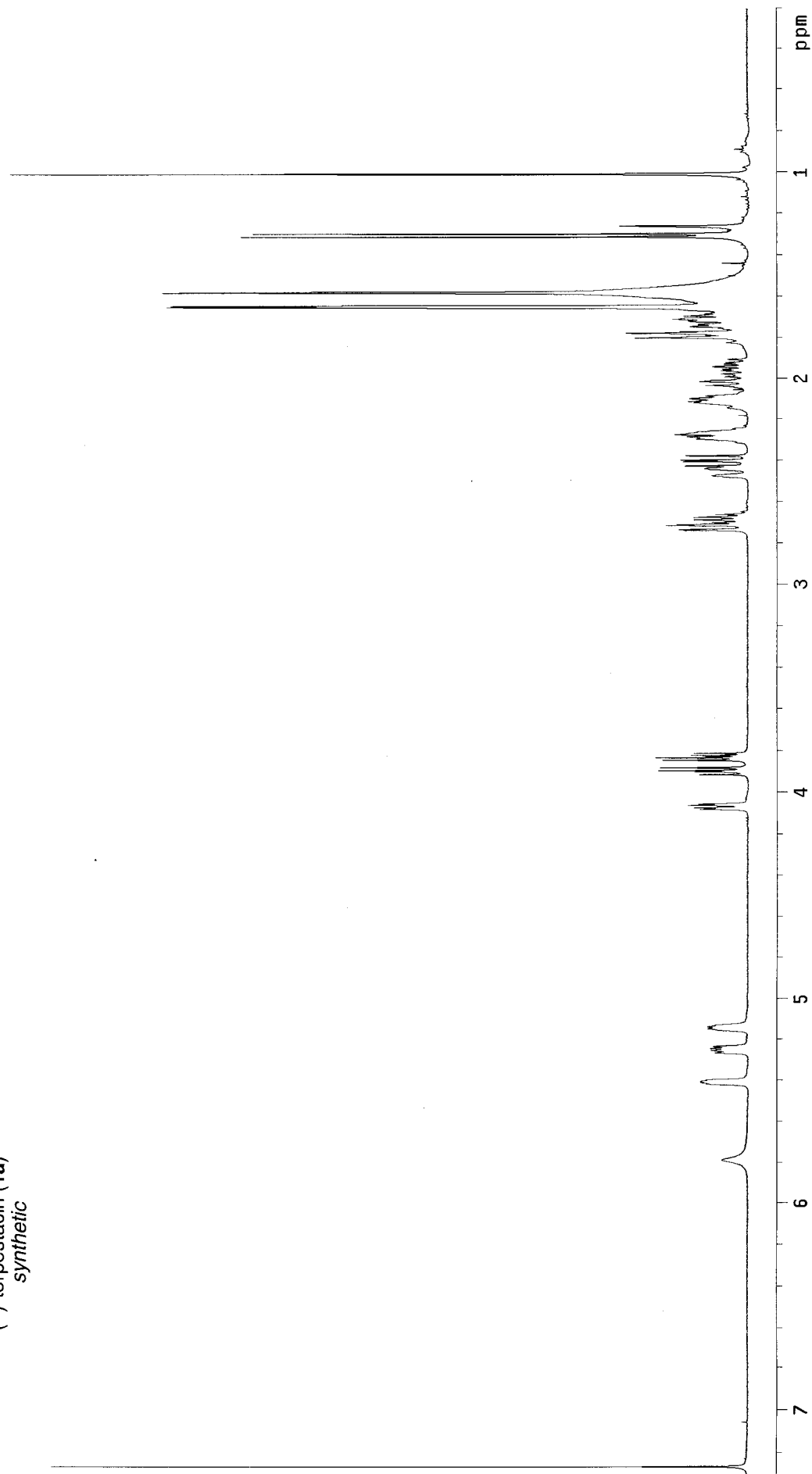


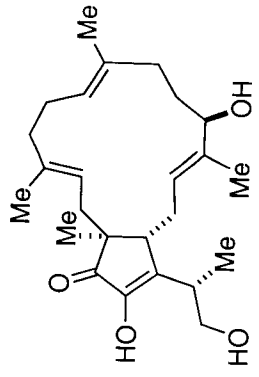
(+)-11-epi-terpestacin (**1b**)
synthetic





(-)-terpestacin (1a)
synthetic





(+)-11-epi-terpestacin (**1b**)
synthetic

