Total Synthesis of (-)- and (+)-Membrenone C

James A. Marshall and Keith C. Ellis

Department of Chemistry, University of Virginia

Charlottesville, VA 22904

jam5x@virginia.edu

Supporting Information

Experimental Procedures for all compounds.....	pp S1-S18
Selected ^1H and ^{13}C NMR spectra.....	pp S19-S38

Total Synthesis of (-)- and (+)-Membrenone C

James A. Marshall and Keith C. Ellis
Department of Chemistry, University of Virginia
Charlottesville, VA 22904
jam5x@virginia.edu

Supporting Information

(2*S*, 3*S*, 4*R*)-(+)-1-(*tert*-Butyldimethylsilyloxy)-2,4-dimethyl-

5-hexyn-3-ol (3). To a solution of (*P*)-allenylstannane (*P*)-**1** (0.733 g, 2.14 mmol) and (2*S*)-3-(*tert*-butyldimethylsilyloxy)-

2-methylpropanal **2** (0.280 g, 1.38 mmol) in CH₂Cl₂ (14 mL) at -78 °C was added BF₃•OEt₂ (0.50 mL, 4.22 mmol) dropwise over 5 min. After 1 h the reaction was quenched at -78 °C by addition of 10 mL of MeOH/NaHCO₃(sat.) (5:1, v/v) and warmed to room temperature. The layers were separated and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by gradient elution chromatography on silica gel (0% -5% EtOAc/hexanes) afforded 0.289 g (82%) of a colorless oil. *R*_f = 0.80 (25% EtOAc/hexanes); [α]_D²⁰ = +1.61 (*c* 2.1, CHCl₃); IR (film) 3490, 3310, 2965, 2365 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 3.89 (1H, dd, *J* = 2.7, 9.6 Hz), 3.72 (2H, dd, *J* = 2.7, 9.9 Hz), 3.51 (1H, br s), 2.52 (1H, qt, *J* = 2.7, 6.9 Hz), 2.16 (1H, m), 2.06 (1H, d, *J* = 2.4 Hz), 1.31 (3H, d, *J* = 6.6 Hz), 1.01 (3H, d, *J* = 7.2 Hz), 0.90 (9H, s), 0.09 (6H, d, *J* = 0.9 Hz); ¹³C NMR (75.5 MHz, CDCl₃) 86.35, 78.26, 69.88, 69.40, 36.26, 30.20, 25.83, 18.14, 17.66, 9.36, -5.71.

(2*S*, 3*S*, 4*R*)-(+)-1,3-Bis(*tert*-butyldimethylsilyloxy)-2,4-

dimethyl-5-hexyn-3-ol (4). To a solution of alcohol **3** (4.125

g, 16.1 mmol) in CH₂Cl₂ (161 mL) at 0 °C was added 2,6-lutidine (3.75 mL, 32.2 mmol) and TBSOTf (5.6 mL, 24.2 mmol). The mixture was allowed to warm to room temperature and stirred for 1.5 h. The reaction was quenched with H₂O (50 mL), and the aqueous layer was extracted with CH₂Cl₂, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (1% EtOAc/hexanes) afforded 4.04 g (87%) of a colorless oil. R_f = 0.95 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ = +7.7 (c 1.0, CHCl₃); IR (film) 3325, 2943, 2864 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 3.76 (1H, dd, J = 1.8, 7.8 Hz), 3.43 (2H, dq, J = 1.5, 8.4 Hz), 2.59 (1H, qd, J = 2.4, 6.9 Hz), 2.12 (1H, m), 2.05 (1H, d, J = 2.7 Hz), 1.20 (3H, d, J = 6.9 Hz), 0.90 (18H, s), 0.86 (3H, d, J = 6.9 Hz), 0.08 (6H, s), 0.05 (6H, d, J = 1.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃) 74.30, 69.80, 65.60, 39.34, 30.97, 26.11, 25.90, 18.42, 18.18, 10.11, -3.84, -4.16, -5.25. Anal. Calcd for C₂₀H₄₂O₂Si₂: C, 64.80; H, 11.42. Found: C, 64.53; H, 11.63.

(2*S*, 3*S*, 4*R*)-(+)-3-(*tert*-Butyldimethylsilyloxy)-2,4-dimethyl-5-hexyn-1-ol (**5**). Bis-silyl ether **4** (0.108 g, 0.29 mmol) was taken up in 95% EtOH (2.7 mL) and PPTS (8 mg, 0.03 mmol) was

added at room temperature. After the reaction was judged complete by TLC (approximately 48 to 60 h), brine (5 mL) was added and the mixture was extracted with ether, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (10% EtOAc/hexanes) afforded 0.069 g (92%) of a yellow oil. R_f = 0.72 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ = +6.8 (c 0.99, CHCl₃); IR (film) 3318, 2924, 2484 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 3.76 (1H, dd, J = 2.1, 7.5 Hz), 3.59 (1H, dd, J = 8.4, 10.5 Hz), 3.51 (1H, dd, J = 6.0, 10.5 Hz), 2.63 (1H, m), 2.19 (1H, m), 2.08 (1H, d, J = 2.4 Hz), 1.66 (1H, br s), 1.22 (3H, d, J = 6.9 Hz), 0.93 (3H, d, J = 6.9 Hz), 0.91 (9H, s), 0.10 (6H, s); ¹³C NMR (75.5 MHz, CDCl₃) 87.14, 75.48, 70.20, 65.76, 39.90, 30.38, 26.03, 18.35, 10.89, -3.84, -4.20. Anal. Calcd for C₁₄H₂₈O₂Si: C, 65.57; H, 11.00. Found: C, 65.34; H, 11.07.

(2*R*, 3*S*, 4*R*)-(-)-3-(*tert*-Butyldimethylsilyloxy)-2,4-dimethyl-5-

hexynal (6). To a stirring solution of oxalyl chloride (0.25 mL, 2.9

mmol) in CH₂Cl₂ (20 mL) at -78 °C was added DMSO (0.40 mL, 5.6 mmol). After 15 min, alcohol **5** (0.484 g, 1.90 mmol) in CH₂Cl₂ (1 mL) was added. After 15 min, triethylamine (1.20 mL, 8.6 mmol) was added over 30 minutes by means of a syringe pump. The reaction mixture was stirred at -78 °C for 3 h, then warmed to -40 °C. After 10 min, the reaction was quenched with saturated NaHCO₃ (20 mL), and warmed to room temperature. The layers were separated and the aqueous layer was washed two times with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was triturated with 10% EtOAc/hexanes, filtered, and concentrated to afford 0.472 g (98%) of light yellow oil which was used without further purification. *R*_f = 0.80 (25%

EtOAc/hexanes); [α]²⁰_D = -35.2 (*c* 1.3 CHCl₃); IR (film) 3327, 2968, 2881, 1736 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 9.74 (1H, s), 4.17 (1H, dd, *J* = 2.1, 8.1 Hz), 2.91 (1H, dq, *J* = 1.8, 6.9 Hz), 2.61 (1H, m), 1.25 (3H, d, *J* = 7.2 Hz), 1.17 (3H, d, *J* = 6.9 Hz), 0.90 (1H, d, *J* = 1.2 Hz), 0.87 (9H, s), 0.10 (3H, s), -0.01 (3H, s); ¹³C NMR (75.5 MHz, CDCl₃) 86.08, 74.10, 71.02, 51.01, 31.20, 25.90, 18.24, 17.94, 7.00, -4.13, -4.12.

(3*R*, 4*R*, 5*R*, 6*S*, 7*R*)-(+)-6-(*tert*-

Butyldimethylsilyloxy)-3,5,7-trimethyl-1-

trimethylsilylnonan-1,8-diyn-4-ol (8). To a stirring

solution of aldehyde **6** (2.262 g, 8.90 mmol) in THF/HMPA (3:1, 45 mL) was added Pd(OAc)₂ (0.121 g, 0.54 mmol). The reaction was cooled to 0 °C and PPh₃ (0.142 g, 0.54 mmol) was added. Upon complete dissolution of the PPh₃, pulverized InI (3.268 g, 13.5 mmol) was added, followed by the mesylate of (*S*)-4-TMS-3-butyn-2-ol (2.83 g, 12.8 mmol). After stirring at 0 °C for 2 h, the reaction was quenched by pouring into a stirring solution of NH₄Cl (100 mL), 10% HCl (50 mL), and Et₂O (100 mL). The layers were separated and the aqueous layer was washed with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography (5% EtOAc/hexanes) afforded

3.272 g (97%) of alcohol **8** and its syn diastereomer as a 96:4 inseparable mixture. $R_f = 0.79$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = +14.1$ (c 0.9, CHCl_3); IR (film) 3580, 3326, 2977, 2857, 2173 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) 3.68 (1H, dd, $J = 3.6, 6.0$ Hz), 3.38 (1H, t, $J = 5.4$ Hz), 2.73 (2H, m), 2.06 (1H, d, $J = 2.4$ Hz), 2.03 (1H, m), 1.79 (1H, br s), 1.22 (3H, d, $J = 6.9$ Hz), 1.20 (3H, d, $J = 7.2$ Hz), 1.05 (3H, d, $J = 6.9$ Hz), 0.91 (9H, s), 0.15 (9H, s), 0.12 (3H, s), 0.07 (3H, s); ^{13}C NMR (75.5 MHz, CDCl_3) 107.39, 87.35, 76.40, 74.92, 70.12, 40.72, 32.15, 30.88, 26.07, 18.36, 17.78, 17.44, 9.67, 0.12, -3.74, -4.03. Anal. Calcd for $\text{C}_{21}\text{H}_{40}\text{O}_2\text{Si}_2$: C, 66.25; H, 10.59. Found: C, 66.29; H, 10.41.

(3R, 4R, 5R, 6S, 7R)-(-)-3,5,7-Trimethylnonan-1,8-diyne-4,6-diol (9).

To a stirring solution of alcohol **8** (0.828 g, 2.17 mmol) in THF (22 mL) at 0 °C was added TBAF (1.0M in THF, 11.0 mL, 11.0 mmol). After 3 h the reaction was judged to be complete by TLC and was quenched by the addition of saturated aqueous NH_4Cl (20 mL) and EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. Purification by column chromatography (25% EtOAc/hexanes) afforded 0.415 g (98%) of a yellow oil. $R_f = 0.25$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = -2.3$ (c 1.1, CHCl_3); IR (film) 3315, 3266, 2976, 2951, 2871 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) 3.65 (2H, dq, $J = 0.9, 9.0$ Hz), 2.68 (1H, m), 2.56 (1H, m), 2.30 (1H, m), 2.20 (1H, d, $J = 2.4$ Hz), 2.08 (1H, d, $J = 2.4$ Hz), 1.32 (3H, d, $J = 6.9$ Hz), 1.18 (3H, d, $J = 6.9$ Hz), 0.93 (3H, d, $J = 7.2$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) 86.04, 85.65, 79.79, 79.40, 71.30, 70.19, 35.76, 31.26, 30.18, 17.80, 16.76, 4.26. Anal. Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2$: C, 74.19; H, 9.34. Found: C, 74.02; H, 9.42.

(3R, 4R, 5R, 6S, 7R)-(-)-3,5,7-Trimethyl-4,6-

bis(triethylsilyloxy)nonan-1,8-diyne (10). To a stirring solution of diol **9** (0.254 g, 1.30 mmol) in CH_2Cl_2 (13 mL) was added 2,6-lutidine (0.61 mL, 5.2 mmol). The reaction

was cooled to 0 °C, and TESOTf (0.65 mL, 2.9 mmol) was subsequently added. After 2 h, the reaction was quenched by addition of NH₄Cl (20 mL) and Et₂O (10 mL). The layers were separated and the aqueous layer was washed with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography (0.5% EtOAc/hexanes) afforded 0.557 g (100%) of **10** as a yellow oil. *R*_f = 0.90 (25% EtOAc/hexanes); [α]_D²⁰ = -0.2 (*c* 2.78, CHCl₃); IR (film) 3327, 2960, 2890 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.77 (1H, dt, *J* = 1.2, 5.4 Hz), 3.57 (1H, dt, *J* = 1.2, 4.5 Hz), 2.70 (2H, m), 2.06 (3H, m), 1.19 (6H, qd, *J* = 1.5, 7.2 Hz), 0.94-1.03 (21H, m), 0.67 (12H, q, *J* = 7.5 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 87.79, 86.55, 76.16, 75.88, 70.22, 69.69, 40.30, 31.30, 30.17, 17.72, 15.71, 10.91, 7.09, 5.58. Anal. Calcd for C₂₄H₄₆O₂Si₂: C, 68.18; H, 10.97. Found: C, 68.36; H, 11.10.

(3*R*, 4*R*, 5*R*, 6*S*, 7*R*)-(+)-4,6,8-Trimethyl-5,7-bis(triethylsilyloxy)undecan-2,9-diyne (11**).** To a stirring solution of diyne **10** (0.557 g, 1.30 mmol) in THF (13 mL) at -78 °C was added BuLi (2.4 M in hexanes, 1.7 mL, 3.9 mmol). After 1 h, (MeO)₂SO₂ (0.37 mL, 3.9 mmol) was added. After 15 min, the reaction mixture was warmed to 0 °C for 1 h, and then warmed to room temperature overnight. The reaction was quenched with NH₄Cl (20 mL) and Et₂O (10 mL) and the layers were separated. The aqueous layers were extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography (1% EtOAc/hexanes) afforded 0.596 g (100%) of **11** as a yellow oil. *R*_f = 0.98 (25% EtOAc/hexanes); [α]_D²⁰ = +4.9 (*c* 0.81, CHCl₃); IR (film) 2968, 2925, 2881 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.72 (1H, dd, *J* = 4.2, 6.9 Hz), 3.54 (1H, t, *J* = 4.8 Hz), 2.67 (1H, m), 2.59 (1H, m), 1.93 (1H, m), 1.79 (6H, s), 1.13-1.07 (6H, m), 1.00-0.95 (18H, m), 0.94-0.89 (3H, m), 0.67 (12H, dq, *J* = 2.4, 7.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 83.29, 82.01, 77.17, 76.32, 76.08, 39.64, 31.80, 29.82, 17.72, 15.20, 10.89, 7.11, 5.56, 5.52, 3.72, 3.61.

(4*R*, 5*R*, 6*R*, 7*S*, 8*R*)-(-)-4,6,8-Trimethylundecan-2,9-diyne-5,7-diol (12**).** To a solution of the bis-TES ether **11** (2.68 g, 5.94 mmol) in THF (60 mL) at 0 °C was added TBAF (18 mL, 18 mmol). The reaction mixture was stirred for 30 minutes at 0 °C, and then warmed to room temperature for 3 h. The reaction was quenched with saturated aqueous NH₄Cl (60 mL) and extracted with ethyl acetate. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% EtOAc/hexanes) to afford 1.29g (98%) of a yellow solid. $R_f = 0.35$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = -11.89$ (c 2.00, CHCl₃); IR (film) 3441, 2969, 1466 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.56 (1H, dd, $J = 1.5, 9.3$ Hz), 3.54 (1H, dd, $J = 2.4, 8.7$ Hz), 3.01 (2H, br s), 2.61 (1H, dqq, $J = 2.4, 6.6, 6.9$ Hz), 2.48 (1H, dqq, $J = 2.4, 6.6, 6.9$ Hz), 2.24 (1H, ddq, $J = 2.1, 6.9, 7.2$), 1.82 (3H, d, $J = 2.7$ Hz), 1.77 (3H, d, $J = 2.4$ Hz), 1.24 (3H, d, $J = 6.9$), 1.12 (3H, d, $J = 6.6$ Hz), 0.89 (3H, d, $J = 6.9$ Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 80.98, 80.10, 80.05, 79.95, 79.03, 77.44, 35.80, 31.40, 30.36, 18.16, 17.23, 4.36, 3.49. Anal. Calcd for C₁₄H₂₂O₂: C, 75.63; H, 9.97. Found: C, 75.35; H, 10.05.

(4*R*, 5*R*, 6*R*, 7*S*, 8*R*)-5,7-Bis(dimethylsilyloxy)-4,6,8-trimethylundecan-2,9-diyne (13**).** A dry flask was charged with diol **12** (0.219 g, 0.99 mmol), a stir bar, and tetramethyldisilazane (3.5 mL, 19.7 mmol). The reaction mixture was stirred at room temperature until the solid diol dissolved, and then was heated to 80 °C. After 6 hr, the reaction mixture was cooled to room temperature and concentrated via rotary evaporation to remove excess silazane. The crude oil was heated to 60 °C under high vacuum (0.03 mmHg) overnight. The resulting viscous oil was used in the next step without purification. IR 2977, 2121 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.73 (1H, m), 4.69 (1H, m), 3.62 (1H, dd, $J = 4.5, 6.9$ Hz), 3.43 (1H, dd, $J = 4.5, 6.9$ Hz), 2.71 (1H, m), 2.58 (1H, m), 2.24 (1H, dq, $J = 4.2, 7.2$ Hz), 1.80 (3H, d, $J =$

2.4 Hz), 1.77 (3H, d, $J = 2.4$ Hz), 1.15 (3H, d, $J = 6.9$ Hz), 1.13 (3H, d, $J = 6.9$ Hz), 0.92 (3H, d, $J = 6.9$ Hz), 0.26 (3H, dd, $J = 2.7, 3.0$ Hz), 0.22 (3H, dd, $J = 2.7, 5.4$ Hz).

(4*R*, 5*R*, 6*R*, 7*S*, 8*R*)-Bis-Siloxane (14). The residue from the previous step was dissolved in THF (4 mL), and H_2PtCl_6 (0.05 M in THF, 0.1 mL, 4.95 μmol) was added. The yellow solution was heated to 75 $^\circ\text{C}$. After 5 h the hydrosilylation was judged complete by IR analysis (Si-H, 2121 cm^{-1}). The mixture was diluted with ether and filtered through Celite 521. The mother liquor was concentrated under reduced pressure to afford 0.323 g (97%) of **14** as a yellow oil that was used without further purification. IR 2977, 1256 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.81 (2H, m), 4.03 (1H, t, $J = 2.1$ Hz), 3.67 (2H, dd, $J = 3.9, 9.6$ Hz), 2.99 (1H, m), 2.67 (1H, q, $J = 7.2$ Hz), 1.76 (3H, d, $J = 6.6$ Hz), 1.75 (3H, d, $J = 6.3$ Hz), 1.12 (3H, d, $J = 7.5$ Hz), 0.91 (3H, d, $J = 6.6$ Hz), 0.89 (3H, d, $J = 7.2$ Hz), 0.24 (3H, d, $J = 3.0$ Hz), 0.22 (3H, s), 0.15 (3H, s), 0.07 (3H, s).

(4*R*, 5*R*, 6*R*, 7*S*, 8*R*)-Diol (15). A solution of bis-siloxane **14** (53.6 mg, 0.16 mmol) in toluene (1.5 mL) was cooled to -78 $^\circ\text{C}$ for 15 minutes. DIBAL-H (3 mL, 1.0 M in toluene, 3 mmol) was added and the reaction stirred for 1 h. The reaction mixture was poured into Rochelle's salts at 0 $^\circ\text{C}$, stirred overnight, and extracted with EtOAc. The extract was washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% EtOAc/hexanes) to afford 51.8 mg (96%) of a clear oil. ^1H NMR (300 MHz, CDCl_3) δ 5.83 (2H, m), 4.62 (2H, s), 4.03 (1H, m), 3.84 (1H, m), 2.99 (1H, m), 2.91 (1H, m), 2.65 (1H, m), 1.76 (3H, d, $J = 6.6$ Hz), 1.75 (3H, d, $J = 6.3$ Hz), 1.12 (3H, d, $J = 7.5$ Hz), 0.91 (3H, d, $J = 6.6$ Hz), 0.89 (3H, d, $J = 7.2$ Hz), 0.24 (3H, d, $J = 3.0$ Hz), 0.22 (3H, s), 0.15 (3H, s), 0.07 (3H, s).

Hydride Siloxane Cleavage Model System

Alcohol (II). To a solution of alcohol **I**¹ (300 mg, 1.40 mmol) in toluene (7 mL) at 0 °C was added DIBAL-H (14 mL, 1.0 M in toluene, 14 mmol). The reaction mixture was heated to 110 °C for 1 h, then cooled to room temperature and poured into Rochelle's salts. Stirring overnight was followed by extraction with EtOAc. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% EtOAc/hexanes) to afford 196 mg (65%) of clear oil. ¹H NMR (300 MHz, CDCl₃) _ 7.35 (5H, m), 6.19 (1H, q), 4.78 (1H, q), 4.11 (1H, m), 2.65 (2H, ddd), 1.96 (1H, br s), 1.61 (3H, d), 0.14 (6H, m).

Ester (III). To a solution of alcohol **II** (45.0 mg, 0.20 mmol) in CH₂Cl₂ was added DMAP (5 mg, 40 μmol). The reaction mixture was stirred until the DMAP dissolved and was then cooled to 0 °C. Propionic anhydride (0.05 mL, 0.40 mmol) and NEt₃ (0.08 mL, 0.60 mmol) were added and the reaction mixture stirred at 0 °C for 20 h. The reaction was quenched with saturated aqueous NH₄Cl and extracted with CH₂Cl₂. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% EtOAc/hexanes) to afford 50 mg (89%) of a clear oil. ¹H NMR (300 MHz, CDCl₃) _ 7.19 (5H, m), 6.03 (1H, q), 5.79 (1H, q), 4.01 (1H, m), 2.73 (2H, ddd), 2.38 (2H, dd), 1.61 (3H, d), 1.14 (3H, t), 0.14 (6H, m).

Diketone (IV). To silane **III** (50.0 mg, 0.20 mmol) in MeOH/THF (2:1, 3 mL) was added KF (107 mg, 2 mmol). The reaction mixture was

stirred for 15 min, then cooled to 0 °C. H₂O₂ (1.7 mL, 15 mmol) and KHCO₃ (116 mg, 1.0 mmol) were added, and the reaction was heated to 65 °C. After 2 h, the reaction was cooled to 0 °C, carefully quenched with methanolic Na₂S₂O₄ (10%), and diluted with Et₂O. Extraction with Et₂O was followed by washing with brine, drying over MgSO₄, and concentration under reduced pressure. The crude product was purified by chromatography on silica gel (10% EtOAc/hexanes) to afford 25 mg (78%) of a yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 7.35 (5H, m), 3.99 (1H, s), 3.55 (1H, s), 2.49 (2H, m), 1.15 (3H, t).

(4*S*, 5*R*, 6*S*, 7*R*, 8*S*)-5,7-Dihydroxy-4,6,8-trimethyl-

undecane-3,9-dione (16). To bis-siloxane **14** (0.252 g, 0.74 mmol) in MeOH/THF (2:1, 11.1 mL) were added KF (0.43 g,

7.4 mmol) and KHCO₃ (0.74 g, 7.4 mmol) and the reaction mixture was cooled to 0 °C for 15 minutes. H₂O₂ (11 mL, 111 mmol) was added slowly by syringe. After three hours, the reaction was carefully quenched with methanolic Na₂S₂O₄ (10%) and diluted with EtOAc. Extraction with EtOAc followed by washing with brine, drying over MgSO₄, and concentration under reduced pressure afforded 0.206 g (107%) of crude β -hydroxy diketone which was carried on without purification. ¹H NMR (300 MHz, CDCl₃) δ 4.49 (1H, t, *J* = 2.4 Hz), 3.45 (2H, t, *J* = 3.0 Hz), 2.72 (1H, m), 2.66 (1H, dq, *J* = 7.2, 17.7 Hz), 2.42 (1H, dq, *J* = 7.2, 17.7 Hz), 2.16 (1H, dq, *J* = 7.5, 14.1 Hz), 2.11 (1H, qd, *J* = 3.3, 7.5 Hz), 1.76 (1H, m), 1.70 (1H, dq, *J* = 7.5, 14.1 Hz), 1.32 (3H, d, *J* = 7.5 Hz), 1.07 (3H, t, *J* = 7.2 Hz), 1.05 (3H, d, *J* = 7.2 Hz), 0.98 (3H, d, *J* = 6.9 Hz), 0.91 (3H, t, *J* = 7.8 Hz).

(4*S*, 5*S*, 6*S*, 7*R*, 8*S*)-(+)-bis-Propionic Ester of 5,7-

Dihydroxy-4,6,8-trimethylundecane-3,9-dione (17). To a solution of β -hydroxy diketone **16** (0.206 g, 0.80 mmol) and propionic acid (0.30 mL, 4.0 mmol) in CH₂Cl₂ (8 mL) at 0 °C was added DMAP (0.109 g, 0.80 mmol) and DCC (0.83 g, 4.0

mmol). After 12 h, the reaction mixture was filtered through a plug of Celite 521 and concentrated under reduced pressure. Chromatography on silica gel (5% EtOAc/hexanes) afforded 0.126 g (46% for 2 steps) of diketo diester **17**. $R_f = 0.58$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = +70.2$ (c 0.79, CHCl_3); IR (film) 2986, 2950, 1736 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.17 (1H, dd, $J = 2.5, 9.5$ Hz), 5.14 (1H, dd, $J = 3.5, 9.0$ Hz), 3.30 (1H, dq, $J = 3.0, 7.0$ Hz), 2.99 (1H, m), 2.25-2.64 (8H, m), 2.07 (1H, m), 1.02-1.15 (15H, m), 0.99 (3H, t, $J = 7.5$ Hz), 0.91 (3H, d, $J = 6.5$ Hz); ^{13}C NMR δ (125 MHz, CDCl_3) 212.01, 73.65, 73.10, 47.56, 46.31, 35.74, 35.45, 34.26, 27.59, 27.46, 13.84, 9.55, 9.26, 9.11, 7.70, 7.54.

(-)-Membrenone C (18). To diester diketone **17** (25 mg, 0.06 mmol) in CH_2Cl_2 (5.4 mL) at -78°C was added Hunig's base (0.15 mL, 0.86 mmol). After 15 min at -78°C , TiCl_4 (1.0 M in CH_2Cl_2 , 0.55 mL, 0.55 mmol) was added over 1 h.

After being stirred for an additional 45 min at -78°C , the reaction mixture was warmed to -5°C for 24 h. The reaction was quenched with NH_4Cl and extracted with Et_2O . The extract was washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$) to afford 11.3 mg (51%) of a yellow solid. $R_f = 0.30$ (10% $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$); $[\alpha]_D^{20} = -22.6$ (c 0.85, CHCl_3) lit.² -28.2 (c 0.46 CHCl_3); IR (film) 2986, 2934, 2882, 1675, 1615 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.25 (1H, dd, $J = 2.5, 10.0$ Hz), 3.89 (1H, dd, $J = 2.0, 13.5$ Hz), 2.51 (1H, m), 2.22-2.46 (5H, m), 2.21 (1H, m), 1.74 (3H, s), 1.71 (3H, s), 1.19 (3H, d, $J = 7.0$ Hz), 1.18 (3H, t, $J = 8.0$ Hz), 1.10 (3H, d, $J = 7.0$ Hz), 1.07 (3H, t, $J = 7.5$ Hz), 1.02 (3H, d, $J = 7.5$ Hz); ^{13}C NMR δ (125 MHz, CDCl_3) 197.10, 194.56, 173.71, 172.48, 108.66, 107.71, 81.69, 80.94, 40.44, 39.92, 34.67, 25.42, 10.91, 10.81, 9.78, 9.32, 9.25, 9.10.

(2S, 3S, 4S)-(-)-1-(tert-Butyldimethylsilyloxy)-2,4-dimethyl-6-trimethylsilyl-5-hexyn-3-ol (19). To a stirring solution of (2S)-3-(tert-butyldimethylsilyloxy)-2-

methylpropanal **2** (1.23 g, 6.0 mmol) in THF/HMPA (3:1, 33 mL) was added Pd(OAc)₂ (0.081 g, 0.36 mmol). The reaction mixture was cooled to 0 °C and PPh₃ (0.095 g, 0.36 mmol) was added. Upon complete dissolution of the PPh₃, pulverized InI (2.02 g, 8.0 mmol) was added, followed by the mesylate of (*R*)-4-TMS-3-butyn-2-ol (1.85 g, 8.4 mmol). After stirring at 0 °C for 2 h, the reaction mixture was quenched by pouring into a stirring solution of NH₄Cl (25 mL) and Et₂O (25 mL). The layers were separated and the aqueous layer was washed with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure.

Purification by column chromatography (5% EtOAc/hexanes) afforded 1.49 g (75%) of alcohol **19**. *R*_f = 0.75 (25% EtOAc/hexanes); [α]_D²⁰ = -4.8 (*c* 1.21, CHCl₃); IR (film) 3510, 2968, 2182, 1946 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) _ 3.63 (2H, m), 3.51 (1H, s), 2.69 (1H, m), 2.33 (1H, d, *J* = 4.5 Hz), 1.78 (1H, m), 1.17 (3H, d, *J* = 7.2 Hz), 0.94 (3H, d, *J* = 6.9 Hz), 0.90 (9H, s), 0.15 (9H, s), 0.06 (6H, s); ¹³C NMR _ (75.5 MHz, CDCl₃) 108.49, 87.00, 75.26, 66.66, 38.07, 31.88, 25.87, 18.24, 17.66, 10.43, 0.14, -0.91, -5.50. Anal. Calcd for C₁₇H₃₆O₂Si₂: C, 62.13; H, 11.04. Found: C, 62.33; H, 10.92.

(2*S*, 3*S*, 4*S*)-(+)-4,6-Bis(*tert*-butyldimethylsilyloxy)-3,5-dimethyl-1-trimethylsilyl-1-hexyne (20**).** To a solution of alcohol **19** (0.77 g, 2.30 mmol) in CH₂Cl₂ (25 mL) at 0 °C was added 2,6-lutidine (0.40 mL, 5.5 mmol) and TBSOTf

(0.70 mL, 3.0 mmol). The mixture was allowed to warm to room temperature and stirred for 1.5 h. The reaction was quenched with H₂O (25 mL), and the aqueous layer was extracted with CH₂Cl₂, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (1% EtOAc/hexanes) afforded 1.00 g (97%) of a colorless oil. *R*_f = 0.93 (25% EtOAc/hexanes); [α]_D²⁰ = +2.9 (*c* 1.73, CHCl₃); IR (film) 2960, 2174, 1929 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) _ 3.76 (1H, s), 3.49 (2H, m), 2.64 (1H, m), 1.91 (1H, m), 1.17 (3H, d, *J* = 7.2 Hz), 0.92 (9H, s), 0.91 (9H, s), 0.86 (3H, d, *J* = 5.4 Hz), 0.14 (9H, s), 0.09 (6H, d, *J* = 7.5 Hz), 0.05 (6H, s); ¹³C NMR _ (75.5 MHz, CDCl₃) 110.28, 85.72, 81.49, 74.12, 65.84, 39.58, 32.80, 25.97,

18.42, 18.26, 17.88, 11.61, 0.16, -3.98, -4.18, -5.23, -5.27. Anal. Calcd for C₂₃H₅₀O₂Si₃: C, 62.37; H, 11.38. Found: C, 62.58; H, 11.44.

(120 mg, 0.50 mmol) was added at room temperature. After the reaction was judged complete by TLC (approximately 48 to 60 h), brine (25 mL) was added and the mixture was extracted with ether, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (10% EtOAc/hexanes) afforded 0.568 g (90%) of a yellow oil. *R*_f = 0.45 (25% EtOAc/hexanes); [α]_D²⁰ = +8.7 (*c* 1.77, CHCl₃); IR (film) 3362, 2960, 2165, 1945 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.64 (2H, m), 3.62 (1H, m), 2.62 (1H, dd, *J* = 3.3, 6.9 Hz), 2.49 (1H, br s), 1.91 (1H, m), 1.17 (3H, d, *J* = 7.2 Hz), 0.89 (9H, s), 0.87 (3H, d, *J* = 6.9 Hz), 0.11 (6H, s), 0.06 (6H, d, *J* = 11.7 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 109.49, 86.31, 76.56, 64.93, 39.84, 31.04, 25.87, 25.64, 18.14, 18.08, 13.04, -0.05, -0.41, -3.63, -4.22, -4.50. Anal. Calcd for C₁₇H₃₆O₂Si₂: C, 62.13; H, 11.04. Found: C, 62.07; H, 11.09.

chloride (0.10 mL, 1.10 mmol) in CH₂Cl₂ (7.6 mL) at -78 °C was added DMSO (0.16 mL, 2.3 mmol). After 15 min, alcohol **21** (0.248 g, 0.76 mmol) in CH₂Cl₂ (1 mL) was added. After 15 min, triethylamine (0.50 mL, 3.4 mmol) was added dropwise. The reaction mixture was stirred at -78 °C for 3 h, and then warmed to -40 °C. After 10 min, the reaction was quenched with saturated NaHCO₃ (20 mL), and warmed to room temperature. The layers were separated and the aqueous layer was washed two times with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude oil was triturated with 10% EtOAc/hexanes, filtered, and concentrated to afford 0.250 g (100%)

of light yellow oil which was used without further purification. $R_f = 0.88$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = -29.3$ (c 0.91 CHCl_3); IR (film) 2968, 2855, 2165, 1736 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.89 (1H, s), 4.05 (1H, t, $J = 4.8$ Hz), 2.69 (1H, m), 2.60 (1H, m), 1.20 (3H, d, $J = 7.5$ Hz), 1.12 (3H, d, $J = 7.2$ Hz), 0.91 (9H, s), 0.13 (6H, s), 0.09 (6H, d, $J = 13.8$ Hz); ^{13}C NMR δ (75.5 MHz, CDCl_3) 203.56, 74.14, 50.67, 32.06, 25.77, 18.15, 17.16, 9.69, -0.20, -4.36, -4.47.

(3S, 4S, 5S, 6R, 7S)-(+)-4-(*tert*-Butyldimethylsilyloxy)-3,5,7-trimethyl-1-trimethylsilylnonan-1,8-diyne-6-ol

(23). To a solution of (*M*)-allenylstannane (*M*)-**1** (0.342 g, 0.62 mmol) and aldehyde **22** (0.100 g, 0.31 mmol) in CH_2Cl_2 (3.1 mL) at -78°C was added $\text{BF}_3 \cdot \text{OEt}_2$ (0.15 mL, 0.93 mmol) dropwise over 5 min. After 1 h the reaction was quenched at -78°C by addition of 5 mL of $\text{MeOH}/\text{NaHCO}_3(\text{sat.})$ (5:1, v/v) and warmed to room temperature. The layers were separated and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. Purification by gradient elution chromatography on silica gel (0% - 1% EtOAc/hexanes) afforded 0.089 g (76%) of a colorless oil. $R_f = 0.73$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = +8.8$ (c 0.54, CHCl_3); IR (film) 3528, 3310, 2965, 2165 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.96 (1H, dd, $J = 1.8, 9.9$ Hz), 3.61 (1H, dd, $J = 2.4, 6.0$ Hz), 2.73 (1H, dq, $J = 2.4, 7.2$ Hz), 2.55 (1H, m), 2.30 (1H, m), 2.06 (1H, d, $J = 2.4$ Hz), 1.30 (3H, d, $J = 6.6$ Hz), 1.22 (3H, d, $J = 7.2$ Hz), 0.92 (3H, d, $J = 6.9$ Hz), 0.91 (9H, s), 0.15 (9H, s), 0.09 (6H, d, $J = 4.2$ Hz); ^{13}C NMR δ (75.5 MHz, CDCl_3) 109.52, 97.28, 86.61, 77.25, 73.05, 72.88, 70.07, 39.93, 30.71, 25.92, 18.34, 17.03, 9.36, -0.02, -4.35.

(3S, 4S, 5S, 6R, 7S)-(+)-3,5,7-Trimethylnonan-1,8-diyne-4,6-diol (ent-9).

To a stirring solution of alcohol **23** (0.895 g, 2.35 mmol) in THF (24 mL) at 0°C was added TBAF (1.0M in THF, 12.0 mL, 12.0 mmol). After 3 h the reaction was judged to be complete

by TLC and was quenched by the addition of saturated aqueous NH_4Cl (20 mL) and EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. Purification by column chromatography (15% EtOAc/hexanes) afforded 0.46 g (100%) of a yellow oil. $R_f = 0.26$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = +2.1$ (c 4.1, CHCl_3); IR (film) 3315, 3266, 2976, 2951, 2871 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.65 (2H, dq, $J = 0.9, 9.0$ Hz), 2.68 (1H, m), 2.56 (1H, m), 2.30 (1H, m), 2.20 (1H, d, $J = 2.4$ Hz), 2.08 (1H, d, $J = 2.4$ Hz), 1.32 (3H, d, $J = 6.9$ Hz), 1.18 (3H, d, $J = 6.9$ Hz), 0.93 (3H, d, $J = 7.2$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 86.04, 85.65, 79.79, 79.40, 71.30, 70.19, 35.76, 31.26, 30.18, 17.80, 16.76, 4.26.

(3*S*, 4*S*, 5*S*, 6*R*, 7*S*)-(+)-3,5,7-Trimethyl-4,6-

bis(triethylsilyloxy)nonan-1,8-diyne (ent-10). To a stirring solution of diol ent-9 (0.457 g, 2.4 mmol) in CH_2Cl_2 (24 mL) was added 2,6-lutidine (1.10 mL, 9.4 mmol). The

reaction was cooled to 0 °C, and TESOTf (1.2 mL, 5.2 mmol) was subsequently added. After 2 h, the reaction was quenched by addition of NH_4Cl (20 mL) and Et_2O (10 mL). The layers were separated and the aqueous layer was washed with Et_2O . The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. Purification by column chromatography (0.5% EtOAc/hexanes) afforded 0.806 g (81%) of ent-10 as a yellow oil. $R_f = 0.90$ (25% EtOAc/hexanes); $[\alpha]_D^{20} = +0.8$ (c 1.13, CHCl_3); IR (film) 3327, 2960, 2890 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.77 (1H, dt, $J = 1.2, 5.4$ Hz), 3.57 (1H, dt, $J = 1.2, 4.5$ Hz), 2.70 (2H, m), 2.06 (3H, m), 1.19 (6H, qd, $J = 1.5, 7.2$ Hz), 0.94-1.03 (21H, m), 0.67 (12H, q, $J = 7.5$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 87.79, 86.55, 76.16, 75.88, 70.22, 69.69, 40.30, 31.30, 30.17, 17.72, 15.71, 10.91, 7.09, 5.58.

(3*S*, 4*S*, 5*S*, 6*R*, 7*S*)-(-)-4,6,8-Trimethyl-5,7-

bis(triethylsilyloxy)undecan-2,9-diyne (ent-11). To a

stirring solution of bis-alkyne ent-**10** (0.710 g, 1.70 mmol) in THF (17 mL) at -78 °C was added BuLi (1.6 M in hexanes, 5.3 mL, 8.5 mmol). After 1 h, (MeO)₂SO₂ (1 mL, 10.2 mmol) was added. After 15 min, the reaction mixture was warmed to 0 °C for 1 h, and then warmed to room temperature overnight. The reaction was quenched with NH₄Cl (20 mL) and Et₂O (10 mL) and the layers were separated. The aqueous layers were extracted with Et₂O and the combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification by column chromatography (1% EtOAc/hexanes) afforded 0.615 g (81%) of ent-**11** as a yellow oil. R_f = 0.98 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ = -4.8 (*c* 0.90, CHCl₃); IR (film) 2968, 2925, 2881 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 3.72 (1H, dd, *J* = 4.2, 6.9 Hz), 3.54 (1H, t, *J* = 4.8 Hz), 2.67 (1H, m), 2.59 (1H, m), 1.93 (1H, m), 1.79 (6H, s), 1.13-1.07 (6H, m), 1.00-0.95 (18H, m), 0.94-0.89 (3H, m), 0.67 (12H, dq, *J* = 2.4, 7.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃) 83.29, 82.01, 77.17, 76.32, 76.08, 39.64, 31.80, 29.82, 17.72, 15.20, 10.89, 7.11, 5.56, 5.52, 3.72, 3.61.

(4*S*, 5*S*, 6*S*, 7*R*, 8*S*)-(+)-4,6,8-Trimethylundecan-2,9-diyne-5,7-diol (ent-12**).** To a solution of the bis-TES ether ent-**11** (0.615 g, 1.4 mmol) in THF (15 mL) at 0 °C was added TBAF (1.0 M in THF, 9 mL, 9 mmol). The reaction mixture was stirred for 30 minutes at 0 °C, and then warmed to room temperature for 3 h. The reaction was quenched with saturated aqueous NH₄Cl (30 mL) and extracted with ethyl acetate. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (15% EtOAc/hexanes) to afford 0.218g (72%) of a yellow solid. R_f = 0.35 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ = +12.0 (*c* 0.81, CHCl₃); IR (film) 3441, 2969, 1466 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 3.56 (1H, dd, *J* = 1.5, 9.3 Hz), 3.54 (1H, dd, *J* = 2.4, 8.7 Hz), 3.01 (2H, br s), 2.61 (1H, dq, *J* = 2.4, 6.6, 6.9 Hz), 2.48 (1H, dq, *J* = 2.4, 6.6, 6.9 Hz), 2.24 (1H, ddq, *J* = 2.1, 6.9, 7.2), 1.82 (3H, d, *J* = 2.7 Hz), 1.77 (3H, d, *J* = 2.4 Hz), 1.24 (3H, d, *J* = 6.9), 1.12 (3H, d, *J* = 6.6 Hz), 0.89 (3H, d, *J* = 6.9 Hz); ¹³C NMR (75.5

MHz, CDCl₃) 80.98, 80.10, 80.05, 79.95, 79.03, 77.44, 35.80, 31.40, 30.36, 18.16, 17.23, 4.36, 3.49.

(4*S*, 5*S*, 6*S*, 7*R*, 8*S*)-5,7-Bis(dimethylsilyloxy)-4,6,8-trimethylundecan-2,9-diyne (ent-13). A dry flask was charged with diol ent-12 (0.103 g, 0.45 mmol), a stir bar, and tetramethyldisilazane (1.6 mL, 9.0 mmol). The

reaction mixture was stirred at room temperature until the solid diol dissolved, and then was heated to 80 °C. After 6 hr, the reaction mixture was cooled to room temperature and concentrated via rotary evaporation to remove excess silazane. The crude oil was heated to 60 °C under high vacuum (0.03 mmHg) overnight. The resulting viscous oil was used in the next step without purification. IR 2977, 2121 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.73 (1H, m), 4.69 (1H, m), 3.62 (1H, dd, *J* = 4.5, 6.9 Hz), 3.43 (1H, dd, *J* = 4.5, 6.9 Hz), 2.71 (1H, m), 2.58 (1H, m), 2.24 (1H, dq, *J* = 4.2, 7.2 Hz), 1.80 (3H, d, *J* = 2.4 Hz), 1.77 (3H, d, *J* = 2.4 Hz), 1.15 (3H, d, *J* = 6.9 Hz), 1.13 (3H, d, *J* = 6.9 Hz), 0.92 (3H, d, *J* = 6.9 Hz), 0.26 (3H, dd, *J* = 2.7, 3.0 Hz), 0.22 (3H, dd, *J* = 2.7, 5.4 Hz).

(4*S*, 5*S*, 6*S*, 7*R*, 8*S*)-Bis-Siloxane (ent-14). The residue from the previous step was dissolved in THF (1.8 mL), and H₂PtCl₆ (0.05 M in THF, 0.05 mL, 2.5 μ mol) was added.

The yellow solution was heated to 75 °C. After 5 h the hydrosilylation was judged complete by IR analysis (Si-H, 2121 cm⁻¹). The mixture was diluted with ether and filtered through Celite 521. The mother liquor was concentrated under reduced pressure to afford 0.133 g (85%) of ent-14 as a yellow oil that was used without further purification. IR 2977, 1256 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.81 (2H, m), 4.03 (1H, t, *J* = 2.1 Hz), 3.67 (2H, dd, *J* = 3.9, 9.6 Hz), 2.99 (1H, m), 2.67 (1H, q, *J* = 7.2 Hz), 1.76 (3H, d, *J* = 6.6 Hz), 1.75 (3H, d, *J* = 6.3 Hz), 1.12 (3H, d, *J* = 7.5 Hz), 0.91 (3H, d, *J* = 6.6 Hz), 0.89 (3H, d, *J* = 7.2 Hz), 0.24 (3H, d, *J* = 3.0 Hz), 0.22 (3H, s), 0.15 (3H, s), 0.07 (3H, s).

(4*R*, 5*S*, 6*R*, 7*S*, 8*R*)-5,7-Dihydroxy-4,6,8-trimethyl-

undecane-3,9-dione (ent-16). To bis-siloxane ent-14 (0.133 g,

0.40 mmol) in MeOH/THF (2:1, 6.8 mL) were added KF (0.28

g, 4.0 mmol) and KHCO₃ (0.45 g, 4.0 mmol) and the reaction mixture was cooled to 0 °C

for 15 minutes. H₂O₂ (7.7 mL, 67.5 mmol) was added slowly by syringe. After three

hours, the reaction was carefully quenched with methanolic Na₂S₂O₄ (10%) and diluted

with EtOAc. Extraction with EtOAc followed by washing with brine, drying over

MgSO₄, and concentration under reduced pressure afforded a yellow oil which was

carried on without purification. ¹H NMR (300 MHz, CDCl₃) _ 4.49 (1H, t, *J* = 2.4 Hz),

3.45 (2H, t, *J* = 3.0 Hz), 2.72 (1H, m), 2.66 (1H, dq, *J* = 7.2, 17.7 Hz), 2.42 (1H, dq, *J* =

7.2, 17.7 Hz), 2.16 (1H, dq, *J* = 7.5, 14.1 Hz), 2.11 (1H, qd, *J* = 3.3, 7.5 Hz), 1.76 (1H,

m), 1.70 (1H, dq, *J* = 7.5, 14.1 Hz), 1.32 (3H, d, *J* = 7.5 Hz), 1.07 (3H, t, *J* = 7.2 Hz),

1.05 (3H, d, *J* = 7.2 Hz), 0.98 (3H, d, *J* = 6.9 Hz), 0.91 (3H, t, *J* = 7.8 Hz). ■

(4*R*, 5*S*, 6*R*, 7*S*, 8*R*)-(-)-bis-Propionic Ester of 5,7-

Dihydroxy-4,6,8-trimethylundecane-3,9-dione (ent-17).

To a solution of β-hydroxy diketone ent-16 from the previous

step and propionic acid (0.17 mL, 2.3 mmol) in CH₂Cl₂ (4.5

mL) at 0 °C was added DMAP (0.055 g, 0.4 mmol) and DCC

(0.464 g, 2.25 mmol). After 12 h, the reaction mixture was filtered through a plug of

Celite 521 and concentrated under reduced pressure. Chromatography on silica gel (5%

EtOAc/hexanes) afforded 0.063 g (43% for 2 steps) of diketo diester ent-17. *R*_f = 0.58

(25% EtOAc/hexanes); [α]_D²⁰ = -67.8 (*c* 0.55, CHCl₃); IR (film) 2986, 2950, 1736 cm⁻¹;

¹H NMR (500 MHz, CDCl₃) _ 5.17 (1H, dd, *J* = 2.5, 9.5 Hz), 5.14 (1H, dd, *J* = 3.5, 9.0

Hz), 3.30 (1H, dq, *J* = 3.0, 7.0 Hz), 2.99 (1H, m), 2.25-2.64 (8H, m), 2.07 (1H, m), 1.02-

1.15 (15H, m), 0.99 (3H, t, *J* = 7.5 Hz), 0.91 (3H, d, *J* = 6.5 Hz); ¹³C NMR _ (125 MHz,

CDCl₃) 212.01, 73.65, 73.10, 47.56, 46.31, 35.74, 35.45, 34.26, 27.59, 27.46, 13.84,

9.55, 9.26, 9.11, 7.70, 7.54. ■

(+)-Membrenone C (ent-18). To diester diketone ent-17 (25 mg, 0.06 mmol) in CH₂Cl₂ (5.4 mL) at -78 °C was added Hunig's base (0.15 mL, 0.86 mmol). After 15 min at -78 °C, TiCl₄ (1.0 M in CH₂Cl₂, 0.54 mL, 0.54 mmol) was added

over 1 h. After being stirred for an additional 45 min at -78 °C, the reaction mixture was warmed to -5 °C for 24 h. The reaction was quenched with NH₄Cl and extracted with Et₂O. The extract was washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel (10% Et₂O/CH₂Cl₂) to afford 10.5 mg (47%) of a yellow solid. *R*_f = 0.30 (10% Et₂O/CH₂Cl₂); [α]_D²⁰ = +23.5 (*c* 0.63, CHCl₃); IR (film) 2986, 2934, 2882, 1675, 1615 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.25 (1H, dd, *J* = 2.5, 10.0 Hz), 3.89 (1H, dd, *J* = 2.0, 13.5 Hz), 2.51 (1H, m), 2.22-2.46 (5H, m), 2.21 (1H, m), 1.74 (3H, s), 1.71 (3H, s), 1.19 (3H, d, *J* = 7.0 Hz), 1.18 (3H, t, *J* = 8.0 Hz), 1.10 (3H, d, *J* = 7.0 Hz), 1.07 (3H, t, *J* = 7.5 Hz), 1.02 (3H, d, *J* = 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 197.10, 194.56, 173.71, 172.48, 108.66, 107.71, 81.69, 80.94, 40.44, 39.92, 34.67, 25.42, 10.91, 10.81, 9.78, 9.32, 9.25, 9.10.

References

1. Marshall, J. A.; Yanik, M. M. *Org. Lett.* **2000**, 2, 2173.
2. Perkins, M. V.; Sampson, R. A. *Org. Lett.* **2001**, 3, 123.