SUPPORTING INFORMATION

FOR

Myriaporone 3/4 SAR Studies Reveal a Novel Pharmacophore Targeting Eukaryotic Protein Synthesis

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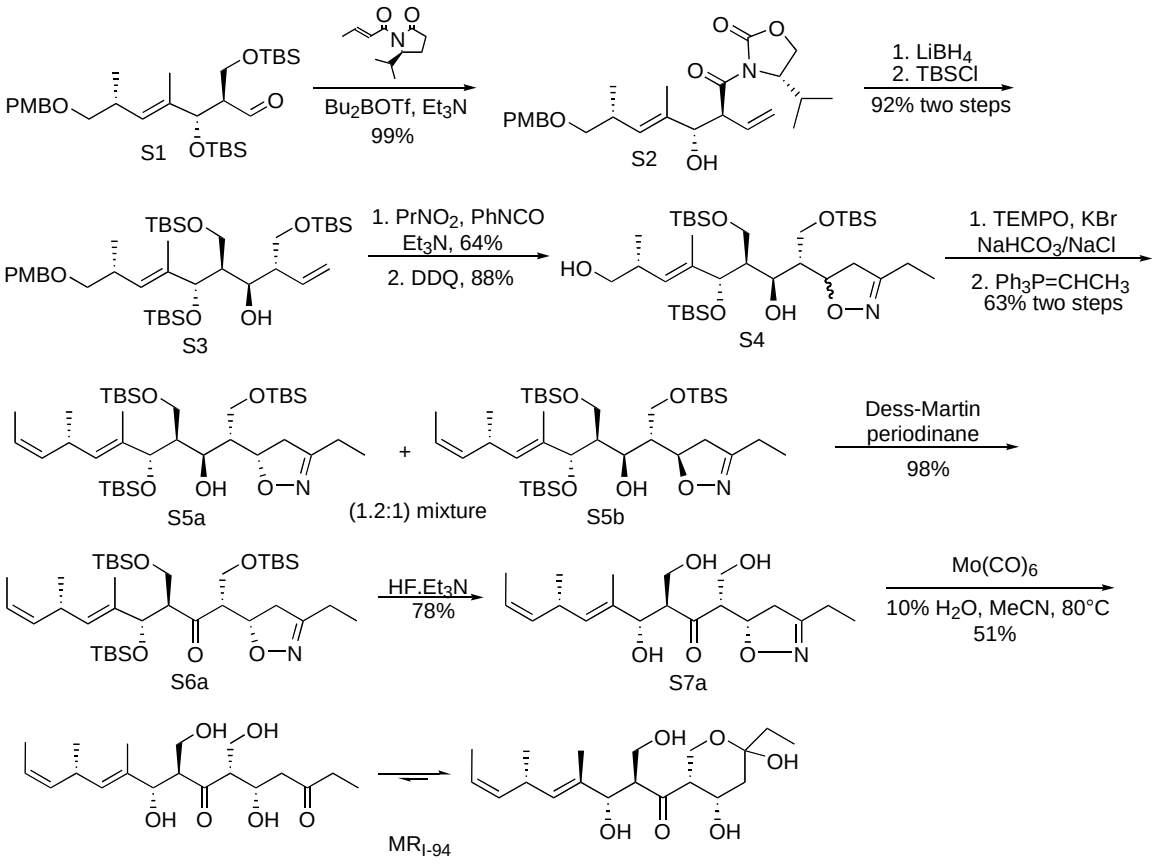
Myriaporone Analog Syntheses:

General Methods

Infrared spectra were obtained on a Perkin-Elmer FT-IR spectrometer (Paragon 1000) and absorption frequencies are reported in reciprocal centimeters (cm^{-1}). NMR spectra were obtained using either a Varian Unity Plus 300 or Varian VXR-500 spectrometer. ^{1}H NMR spectra were collected at 300 MHz or 500 MHz and ^{13}C NMR spectra were collected at 75 MHz or 126 MHz. Chemical shifts for ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) relative to either residual chloroform (7.26 ppm, 77.230 ppm) in $CDCl_3$ or residual methanol (4.87 ppm, 49.150 ppm) in CD_3OD and coupling constants are reported in hertz (Hz). Mass spectra were obtained using a JEOL AX505HA mass spectrometer employing the fast atom bombardment (FAB) ionization method.

Aldehyde **1** and myriaporones 3 and 4 were synthesized as previously reported (Fleming and Taylor 2004). Reagents were purchased commercially and used without further purification. Reactions were performed under nitrogen atmosphere. Solvents were purified by standard procedures. Column chromatography was performed using either silica gel (EM Science 60, 230-400 mesh) or Biotage prepacked silica gel flash cartridges and the Biotage Horizon Pump and Flash Collector automated system.

Figure S1. Synthetic Route to deoxymyriaporone MR-1-94



3-[5-(*tert*-Butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-3-hydroxy-9-(4-methoxy-benzyloxy)-6,8-dimethyl-2-vinyl-non-6-enoyl]-4-isopropyl-oxazolidin-2-one, S2. A solution of (*R*)-3-((*E*)-but-2-enoyl)-4-isopropyloxazolidin-2-one (0.58 g, 2.95 mmol) in CH_2Cl_2 (4 mL) was dried for 15 min over activated 4Å molecular sieves, then transferred to the reaction flask (under N_2) via cannula. The sieves were rinsed with additional CH_2Cl_2 (2.5 mL). 1.0 M dibutylboryltrifluoromethanesulfonate solution in CH_2Cl_2 (2.95 mL, 2.95 mmol) was added at –78°C and the resulting dark yellow mixture removed from the cold bath for three minutes to dissolve any frozen triflate. The flask was recooled to –78°C and triethylamine (0.5 mL, 3.55 mmol) was added, causing the dark yellow color to fade. The reaction was stirred for 50 min at -78°C and then at 0°C for 15 min (solution turned yellow). While the reaction mixture was being cooled back down to -78°C, a solution of aldehyde **S1** (1.11 g, 1.97 mmol) in

CH_2Cl_2 (4 mL) was dried over activated 4Å molecular sieves, then added to the cooled reaction mixture via cannula. The sieves were rinsed with additional CH_2Cl_2 (2 mL). The bath temperature was raised to –20°C over one hour and then maintained at this temperature for an additional hour. The temperature was slowly increased to 0°C and stirring was continued for an additional six hours, followed by quenching with pH 7 phosphate buffer solution (7 mL). 30% H_2O_2 was then added dropwise while maintaining the internal temperature below 5°C. Addition of the peroxide was continued until the internal temperature remained constant. The mixture was allowed to warm to room temperature over 45 min and then poured over sat. $NaHCO_3$ (aq) (17 mL) and the aqueous layer extracted with CH_2Cl_2 (3 x 15 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Column chromatography (EtOAc/n-hexanes, gradient of solvents) was then used to isolate the desired alcohol **S2** (1.27 g, 1.7 mmol, 86.5%).

IR (film, cm^{-1}) 3499, 2958, 2930, 2858, 1782, 1738, 1694; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 9.0 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 5.93 (ddd, J = 17.1, 8.6, 9.9 Hz, 1 H), 5.41 (d, J = 17.1 Hz, 1 H), 5.33 (d, J = 9.6 Hz, 1 H), 5.28 (dd, J = 9.9, 1.5 Hz, 1 H), 4.92 (dd, J = 9.2, 9.3 Hz, 1 H), 4.47 (m, 1 H), 4.46 (m, 1 H), 4.42 (m, 1 H), 4.42 (m, 1 H), 4.42 (d, J = 10.8 Hz, 1 H), 4.41 (d, J = 9.9 Hz, 1 H), 4.18 (m, 2 H), 3.80 (s, 3 H), 3.80 (m, 2 H), 3.30 (dd, J = 9.0, 6.6 Hz, 1 H), 3.24 (dd, J = 9.0, 7.2 Hz, 1 H), 2.79 (m, 1 H), 2.32 (m, 1 H), 1.55 (d, J = 0.9 Hz, 3 H), 1.03 (d, J = 6.6 Hz, 3 H), 0.894 (s, 9 H), 0.875 (s, 9 H), 0.806 (d, J = 6.9 Hz, 6 H), 0.085 (s, 3 H), 0.053 (s, 3 H), 0.001 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.1, 159.1, 153.5, 135.6, 135.4, 130.9, 129.7, 129.3, 119.9, 113.9, 76.5, 75.4, 72.8, 70.6, 62.9, 60.1, 58.2, 55.5, 51.5, 44.6, 33.1, 28.1, 26.1, 26.0, 18.3, 18.1, 17.8, 14.5, 13.4, -4.5, -5.2, -5.4, -5.4; HRMS (FAB) *m/z* $[M\text{-}C(CH3)3]^+$ calcd for $C_{36}H_{60}NO_8Si_2$, 690.3858; obsd 690.3853.

6-(*tert*-Butyl-dimethyl-silanyloxy)-3,5-bis-(*tert*-butyl-dimethyl-silanyloxymethyl)-10-(4-methoxybenzyloxy)-7,9-dimethyl-deca-1,7-dien-4-ol, S3. To a solution of oxazolidinone **S2** (1.43 g, 1.91 mmol) in ether (12.4 mL) at 0°C were added H_2O (0.7 mL, 38.2 mmol) and 2 M $LiBH_4$ solution in ether (4.8 mL, 9.55 mmol). After stirring at

0°C for one hour, the reaction mixture was warmed to room temperature and stirring was continued for one hour. The reaction was quenched with 2 N NaOH (aq) (10 mL) and diluted with ether (10 mL). After stirring for five minutes, the reaction mixture was poured over ether (20 mL) and the separated organic phase washed with sat. $NaHCO_3$ (aq.) (14 mL) and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give the crude alcohol. Without further purfication, the crude material (354 mg, 0.568mmol) was dissolved in CH_2Cl_2 (6 mL) at room temperature under N_2. Triethylamine (95 μL, 0.682 mmol), *tert*-butyldimethylsilyl chloride (103 mg, 0.682 mmol), and 4- dimethylaminopyridine (DMAP) (7 mg, 0.0568 mmol) were added to the reaction mixture sequentially and stirring was continued overnight. The reaction was quenched with H_2O (5 mL) and diluted with CH_2Cl_2 (10 mL). The separated aqueous phase was extracted with additional CH_2Cl_2 (3 x 5 mL) and the combined extracts washed with H_2O (15 mL) and sat. NH_4Cl (aq) (2 x 10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification via column chromatography (EtOAc/n-hexanes, gradient of solvents) yielded the desired product **S3** (378 mg, 0.513 mmol, 90% two steps).

IR (film, cm^{-1}) 3511, 2854, 2930, 2885, 2857, 1614; ^1H NMR (500 MHz, CDCl3) δ 7.27 (d, J = 9.0 Hz, 2 H), 6.89 (d, J = 9.0 Hz, 2 H), 5.92 (ddd, J = 17.1, 9.0, 10.5 Hz, 1 H), 5.31 (d, J = 9.0 Hz, 1 H), 5.17 (m, 1 H), 5.14 (dd, J = 10.0, 2.0 Hz, 1 H), 4.47 (d, J = 5.0 Hz, 1 H), 4.46 (d, J = 11.5 Hz, 1 H), 4.42 (d, J = 11.5 Hz, 1 H), 4.14 (m, 1 H), 3.85 (dd, J = 10.0, 6.5 Hz, 1 H), 3.83 (m, 1 H), 3.82 (s, 3 H), 3.80 (dd, J = 10.5, 4.0 Hz, 1 H), 3.64 (m, 2 H), 3.57 (d, J = 4.0 Hz, 1 H), 3.32 (dd, J = 9.0, 6.0 Hz, 1 H), 3.23 (dd, J = 8.3, 7.5 Hz, 1 H), 2.77 (m, 1 H), 2.34 (m, 1 H), 1.58 (d, J = 1.0 Hz, 3 H), 1.03 (d, J = 7.0 Hz, 3 H), 0.908 (s, 9 H), 0.889 (s, 9 H), 0.097 (s, 3H), 0.061 (s, 3H), 0.045 (s, 3H), 0.034 (s, 3H), 0.034 (s, 3H), 0.019 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 159.2, 139.0, 135.8, 130.9, 129.7, 129.3, 116.8, 113.9, 76.6, 75.3, 72.8, 69.8, 66.1, 65.2, 60.5, 55.5, 51.3, 44.9, 33.1, 26.2, 26.0, 18.6, 18.4, 18.2, 17.9, 15.5, 13.4, -4.5, -5.1 (2C), -5.2 (2C), -5.2; HRMS (FAB) *m/z* $(M\text{-}OTBS)^+$ calcd for $C_{34}H_{60}O_5Si_2$, 605.4058; obsd 605.4032.

5,9-Bis-(*tert*-butyl-dimethyl-silanyloxy)-6-(*tert*-butyl-dimethyl-silanyloxymethyl)-8-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-2,4-dimethyl-non-3-ene-1,7-diol, S4. To a solution of alkene **S3** (1.92 g, 2.61 mmol) in benzene (9 mL) at room temperature under N_2 were added 1-nitropropane (0.87 mL, 9.79 mmol) and phenyl isocyanate (1.79 mL, 16.44 mmol). A solution of triethylamine (0.27 mL, 1.96 mmol) in benzene (5 mL) was added via syringe pump over 45 min and stirring was continued overnight. The reaction mixture was filtered through a bed of Celite, rinsed with benzene (40 mL), and concentrated *in vacuo*. Column chromatography (EtOAc/n-hexanes, gradient of solvents) allowed for isolation of the desired isoxazoline as a mixture of inseparable diastereomers (1.09 g, 1.35 mmol, 52%), along with 731 mg of the unreacted started alkene **S3**. 900 mg (1.11 mmol) of the cycloaddition isoxazoline was dissolved in CH_2Cl_2 (30 mL) and cooled to 0°C. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (759 mg, 3.34 mmol) and three drops of H_2O were added and the reaction warmed to room temperature. After stirring an additional 20 min, the reaction was diluted with CH_2Cl_2 (50 mL) and washed with sat. $NaHCO_3$ (aq) (3 x 30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification via column chromatography (EtOAc/n-hexanes, gradient of solvents) provided the desired alcohol **S4** (764 mg, 1.11 mmol, quant. yield). The two diastereomers were difficult to separate completely at this stage and, therefore, normally taken on as the mixture. A small amount, however, was separated for characterization purposes providing **S4a**, the 'natural' isomer (less polar), and **S4b**, the 'unnatural' isomer (more polar), in a 1.2:1 ratio.

Diastereomer a: $[\alpha]^{20}$ D = +17.2° (*c.* 1.0, $CHCl_3$); IR (film, cm^{-1}) 3486, 2954, 2915; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.23 (d, J = 10 Hz, 1 H), 4.70 (ddd, J = 10.1, 10.0, 6.5 Hz, 1 H), 4.46 (d, J = 6.0 Hz, 1 H), 4.10 (m, 1 H) 3.84 (dd, J = 10.8, 6.5 Hz, 1 H), 3.79 (dd, J = 10.8, 3.5 Hz, 1 H), 3.72 (dd, J = 10.5, 3.5 Hz, 1 H), 3.67 (dd, J = 10.0, 3.0 Hz, 1 H), 3.58 (d, J = 4.5 Hz, 1 H), 3.46 (dd, J = 10.5, 6.5 Hz, 1 H), 3.39 (dd, J = 9.8, 6.5 Hz, 1 H), 3.06 (dd, J = 17.5, 10.0 Hz, 1 H), 2.99 (dd, J = 17.5, 10.5 Hz, 1 H), 2.66 (m, 1 H), 2.32 (q, J = 7.5 Hz, 2 H), 1.85 (m, 1 H), 1.85 (m, 1 H), 1.59 (d, J = 1.5 Hz, 3 H), 1.14 (t, J = 7.5 Hz, 3 H), 0.970 (d, J = 6.5 Hz, 3 H), 0.883 (s, 9 H), 0.878 (s, 9 H), 0.855 (s, 9 H), 0.079 (s, 3 H), 0.040 (s, 3 H), 0.033 (s, 3 H), 0.026 (s, 3 H), 0.023 (s, 3 H), 0.006 (s, 3 H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ (ppm) 161.9, 137.6, 129.5, 80.4, 76.8, 69.4, 68.0, 60.9, 60.6, 48.8, 43.7, 42.1, 35.5, 26.1, 26.1, 26.0, 21.7, 18.5, 18.3, 18.2, 17.1, 13.3, 11.1, -4.5, -5.1, -5.3, -5.3 (2C), -5.4; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{35}H_{73}NO_6Si_3$, 688.4824; obsd 688.4810.

Diastereomer b: $[\alpha]^{20}$ D = -19.9° (*c.* 1.0, $CHCl_3$); IR (film, cm^{-1}) 3494, 2955, 2858; ^1H NMR (500 MHz, $CDCl_3$) δ 5.20 (d, J = 9.0 Hz, 1 H), 5.03 (ddd, J = 10.5, 10.5, 5.0 Hz, 1 H), 4.47 (d, J = 8.0 Hz, 1 H), 4.20 (d, J = 9.0 Hz, 1 H), 3.88 (dd, J = 10.8, 5.5 Hz, 1 H), 3.83 (dd, J = 10.8, 3.0 Hz, 1 H), 3.71 (dd, J = 10.3, 3.0 Hz, 1 H), 3.64 (dd, J = 10.5, 3.5 Hz, 1 H), 3.46 (dd, J = 10.5, 7.0 Hz, 1 H), 3.41 (dd, J = 10.5, 7.5 Hz, 1 H), 3.13 (dd, J = 17.0, 10.5 Hz, 1 H), 2.85 (dd, J = 17.0, 11.0 Hz, 1 H, 2.66 (m, 1 H), 2.32 (qd, J = 15.5, 7.5 Hz, 2 H), 2.13 (m, 1 H), 1.84 (m, 1 H), 1.59 (d, J = 1.0 Hz, 3 H), 1.14 (t, J = 7.5 Hz, 3 H), 0.980 (d, J = 6.5 Hz, 3 H), 0.878 (s, 9 H), 0.874 (s, 9 H), 0.850 (s, 9 H), 0.086 (s, 3 H), 0.050 (s, 3 H), 0.028 (s, 3 H), 0.014 (s, 3 H), 0.001 (s, 3 H), -0.014 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 160.9, 137.8, 130.2, 80.7, 76.7, 69.7, 67.9, 61.1, 59.8, 45.8, 43.5, 38.5, 35.5, 2.61, 26.1, 26.0, 21.8, 18.4, 18.4, 18.1, 17.0, 12.5, 11.1, -4.6, -5.1, -5.4, -5.5, -5.5, -5.5; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{35}H_{74}NO_6Si_3$, 688.4824; obsd 688.4806.

1,5-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-ol, S5a. Primary alcohol **S4** (50 mg, 0.073mmol) was dissolve in methylene chloride (1 mL) and TEMPO (1.2 mg, 0.007 mmol) and KBr 2M (4 μL, 0.007 mmol) were added. The solution was then cooled to 0°C and a solution of $NaHCO_3$/NaOCl (15 mg of $NaHCO_3$ per mL of NaOCl, 0.12 mL of NaOCl, 0.08 mmol) was added slowly (only when the solution is yellow). The mixture was stired 5 more minutes at 0°C. The solution was then extracted with methylene chloride (3 x 5 mL). The combined extracts were then washed by 2N HCl, sat. $Na_2S_2O_3$ (aq.) and sat. $NaHCO_3$ (aq.) sequentially. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Without further purification, the crude material was taken on to the next step. (Ethyl)triphenylphosphonium bromide (50 mg, 0.073 mmol) was suspended in THF (1 mL) and cooled to 0°C. A 2.1 M solution of *n*-

BuLi in hexanes (0.16 mL, 0.33 mmol) was added dropwise and the reaction mixture stirred for 45 min. The reaction was cooled to –78°C, followed by dropwise addition of the crude aldehyde in THF (1 mL). The reaction mixture was allowed to warm to room temperature slowly and stirring was continued overnight. The reaction was then quenched with sat. $NaHCO_3$ (aq.) (2 mL) and the aqueous phase extracted with ethyl acetate (3 x 5 mL). The combined extracts were washed with sat. $NaHCO_3$ (aq.) (5 mL) and brine, then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The desired product was then isolated via column chromatography (EtOAc/n-hexanes, gradient of solvents) as two separate diastereomers – **S5a** (less polar) and **S5b** (more polar) -- in 1.2:1 ratio (overall: 32 mg, 0.046 mmol, 63% two steps).

$[\alpha]^{20}$ D = +36.7° (*c.* 1.0, $CHCl_3$); IR (film, cm^{-1}) 3500, 3000, 2929, 2858; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (m, 1 H), 5.29 (d, J = 7.5 Hz, 1 H), 5.23 (ddd, J = 9.0, 9.0, 1.5 Hz, 1 H), 4.71 (ddd, J = 10.0, 10.0, 7.0 Hz, 1 H), 4.42 (d, J = 7.0 Hz, 1 H), 4.13 (m, 1 H), 3.83 (dd, J = 10.5, 5.5 Hz, 1 H), 3.80 (dd, J = 10.5, 3.5 Hz, 1 H), 3.67 (m, 2 H), 3.63 (d, J = 5.5 Hz, 1 H), 3.41 (m, 1 H), 3.06 (dd, J = 17.5, 10.0 Hz, 1 H), 2.96 (dd, J = 17.5, 10.5 Hz, 1 H), 2.33 (q, J = 7.5 Hz, 2 H), 1.87 (ddd, J = 7.0, 7.0, 3.5 Hz, 1 H), 1.85 (m, 1 H), 1.62 (ddd, J = 7.0, 1.5, 1.5 Hz, 3 H), 1.56 (s, 3 H), 1.15 (t, J = 7.5 Hz, 3 H), 1.01 (d, J = 7.0 Hz, 3 H), 0.879 (s, 9 H), 0.875 (s, 9 H), 0.864 (s, 9 H), 0.069 (s, 3 H), 0.032 (s, 3 H), 0.029 (s, 3 H), 0.024 (s, 3 H), 0.015 (s, 3 H), 0.000 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 161.9, 135.4, 133.5, 132.2, 121.9, 80.5, 76.6, 69.6, 61.0, 60.9, 49.1, 43.5, 42.3, 30.6, 26.2 (2C), 26.0, 21.7, 21.5, 18.5, 18.4, 18.2, 13.2, 12.5, 11.1, -4.5, -5.1, -5.3, -5.3, -5.4, -5.4; HRMS (FAB) *m/z* $(M\text{-}OTBS)^+$ calcd for $C_{31}H_{60}NO_4Si_2$, 566.4061; obsd 566.4044.

1,5-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-one, S6a. To a solution of alcohol **S5a** (67 mg, 0.096 mmol) in "wet" CH_2Cl_2 (0.6 mL) were added solid $NaHCO_3$ (32 mg, 0.038 mmol) and 15 wt% Dess-Martin periodinane solution (0.4 mL, 0.192 mmol) at room temperature. The reaction was stirred for seven hours, then diluted with CH_2Cl_2 (5 mL) and washed with sat. $NaHCO_3$ (aq.) (2 x 3 mL). The organic phase

was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification via column chromatography (EtOAc/n-hexanes, gradient of solvents) led to isolation of the desired ketone **S6a** (62 mg, 0.089 mmol, 99%).

$[\alpha]^{20}$ D = +75.0° (*c.* 1.0, $CHCl_3$); IR (film, cm^{-1}) 2956, 2929, 2858, 1704; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (qd, J = 7.0, 11.0 Hz, 1 H), 5.18 (m, 1 H), 5.17 (d, J = 8.5 Hz, 1 H), 4.74 (ddd, J = 9.0, 9.0, 9.0 Hz, 1 H), 4.24 (m, 1 H), 3.94 (dd, J = 10.5, 6.0 Hz, 1 H), 3.90 (dd, J = 11.0, 6.0 Hz, 1 H), 3.43 (m, 2 H), 3.43 (m, 1 H), 3.38 (m, 1 H), 3.11 (ddd, J = 6.0, 6.0, 6.0 Hz, 1 H), 3.04 (dd, J = 17.3, 10.5 Hz, 1 H), 2.77 (dd, J = 17.5, 9.0 Hz, 1 H), 2.33 (dq, J = 15.3, 7.5 Hz, 1 H), 2.26 (dq, J = 15.3, 7.5 Hz, 1 H), 1.65 (s, 3 H), 1.63 (dd, J = 7.0, 1.5 Hz, 3 H), 1.13 (t, J = 7.5 Hz, 3 H), 1.00 (d, J = 6.5 Hz, 3 H), 0.899 (s, 9 H), 0.831 (s, 9 H), 0.813 (s, 9 H), 0.076 (s, 3 H), 0.074 (s, 3 H), 0.064 (s, 3 H), -0.029 (s, 3 H), -0.032 (s, 3 H), -0.036 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 212.6, 160.6, 135.1, 133.4, 132.9, 122.0, 77.8, 63.3, 61.1, 60.4, 56.7, 41.2, 30.5, 26.1, 26.1 (2 C), 21.6, 21.1, 18.4 (2 C), 18.3, 13.2, 11.5, 11.0, 1.2, -4.5, -4.8, -5.2, -5.2, -5.5 (2 C); HRMS (FAB) *m/z* $(M-H)^+$ calcd for $C_{37}H_{72}NO_5Si_3$, 694.4718; obsd 694.4715.

2-(3-Ethyl-4,5-dihydro-isoxazol-5-yl)-1,5-dihydroxy-4-hydroxymethyl-6,8-dimethyl-undeca-6,9-dien-3-one, S7a. To a solution of **S6a** (16 mg, 0.021 mmol) in THF (0.15 mL) at room temperature in a nalgene vial was added a solution of 37 wt% HF in triethyl-amine (≈0.1 mL). After stirring at 50°C for 2 days, the reaction was diluted with ethyl acetate (2 mL) and washed with sat. $NaHCO_3$ (aq) (2 x 1 mL) and brine. The organic phase was then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification via column chromatography (EtOAc/n-hexanes, gradient of solvents) led to isolation of the desired triol **S7a** (5.8 mg, 0.016 mmol, 72%).

$[\alpha]^{20}$ D = +160.3° (*c.* 1.0, $CHCl_3$); IR (film, cm^{-1}) 3367, 2969, 1708; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.33 (qd, J = 7.0, 11.5 Hz, 1 H), 5.27 (d, J = 9.5 Hz, 1 H), 5.16 (ddd, J = 11.0, 9.0, 1.5 Hz, 1 H), 4.82 (ddd, J = 9.0, 9.0, 8.0 Hz, 1 H), 4.21 (dd, J = 9.5, 2.0 Hz, 1 H), 4.11 (ddd, J = 10.8, 4.8, 5.0 Hz, 1 H), 3.99 (ddd, J = 11.9, 6.0, 6.0 Hz, 1 H), 3.81 (t, J = 6.5 Hz, 1 H), 3.53 (dd, J = 15.8, 9.5 Hz, 1 H), 3.40 (m, 1 H), 3.39 (dd, J = 17.8, 9.5 Hz, 1 H), 3.36 (m, 1 H), 3.11 (m, 1 H), 3.06 (m, 1 H), 2.74 (dd, J = 17.5, 8.0, 1 H), 2.56 (m, 1

H), 2.29 (q, J = 7.5 Hz, 2 H), 1.67 (d, J = 1.0 Hz, 3 H), 1.62 (dd, J = 6.8, 1.5 Hz, 3 H), 1.10 (t, J = 7.5 Hz, 3 H), 0.998 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 215.8, 161.7, 135.0, 134.5, 132.5, 122.6, 78.2, 63.0, 61.9, 60.8, 56.1, 41.4, 30.5, 21.4, 21.3, 13.2, 11.0, 10.8, 1.2; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{19}H_{32}NO_5$, 354.2280; obsd 354.2257.

Deoxymyriaporone 4, deoxymyriaporone 3, $MR_{I\text{-}94}$. To a solution of triol **S7a** (33 mg, 0.0935 mmol) in acetonitrile (1.5 mL) at RT were added molybdenum hexacarbonyl (49 mg, 0.187 mmol) and H_2O (0.15 mL). The reaction was heated to reflux (80°C) and stirring was continued for one hour. The reaction mixture was then allowed to cool to RT, filtered through a short plug of silica gel, and rinsed with ethyl acetate (30 mL). After concentrating *in vacuo* and purifying via flash column chromatography (EtOAc/n-hexanes, gradient of solvents), the equilibrating mixture of **$MR_{I\text{-}94}$** (17 mg, 0.0478 mmol, 51%) was isolated.

IR (film, cm^{-1}) 3391, 2968, 1705; ^{1}H NMR (500 MHz, CD_3OD), ^{13}C NMR (126 MHz, CD_3OD) δ (ppm) 217.4, 215.7, 213.0, 136.0, 135.0, 134.8, 134.7, 134.6, 134.5, 123.2, 123.1, 98.6, 79.7, 79.2, 67.0, 66.1, 63.8, 63.4, 62.8, 60.8, 58.2, 56.9, 56.5, 55.7, 55.6, 48.6, 38.7, 37.4, 35.5, 31.6, 21.6, 21.6, 13.3, 11.0, 10.9, 8.1, 8.1, 8.0; HRMS (FAB) *m/z* $(M\text{-}OH)^+$ calcd for $C_{19}H_{31}O_5$, 339.2171; obsd 339.2161.

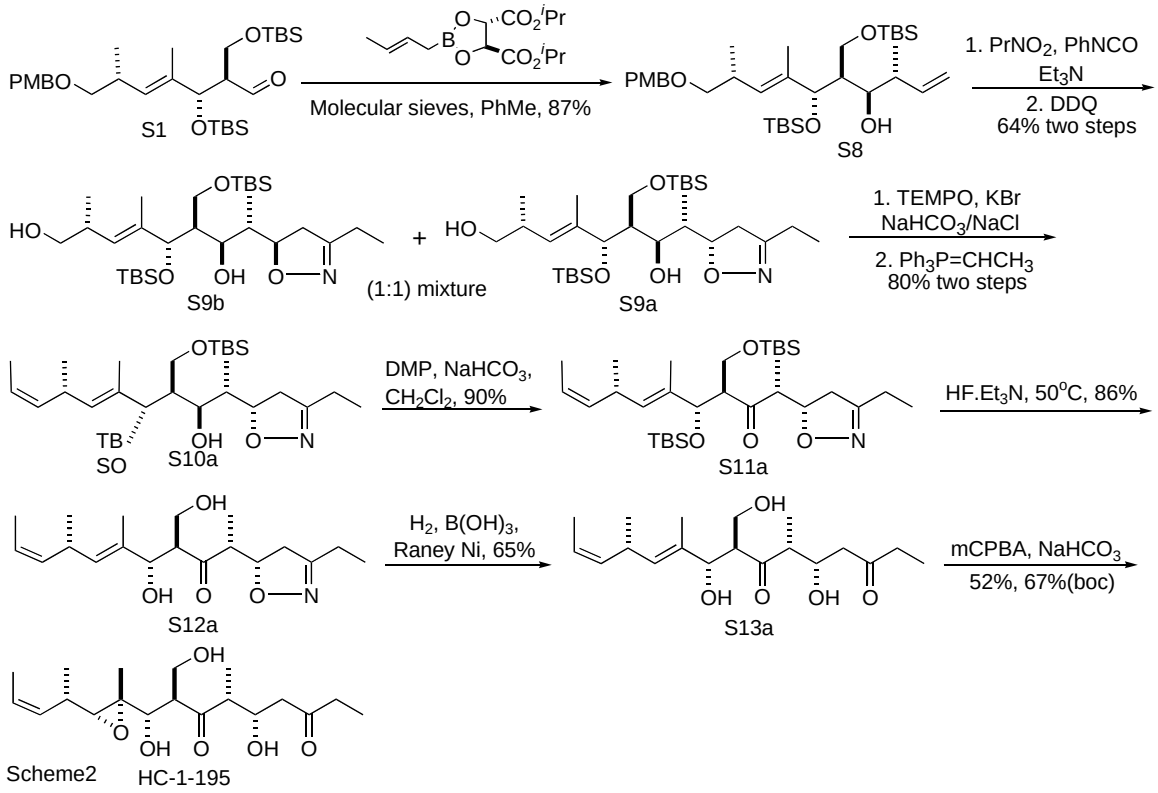
Characteristic ^{1}H NMR signals of deoxymyriaporone 4:

δ 5.33 (qd, J = 7.0, 11.5 Hz, 1 H), 5.19 (dd, J = 9.0, 1.5 Hz, 1 H), 5.18 (m, 1 H), 4.49 (ddd, J = 9.8, 7.0, 3.0 Hz, 1 H), 3.95 (d, J = 6.0 Hz, 2 H), 3.41 (m, 1 H), 3.00 (dt, J = 7.5, 5.5 Hz, 1 H), 2.70 (dd, J = 16.5, 3.0 Hz 1 H), 2.55 (dd, J = 16.5, 9.5 Hz, 1 H), 2.46 (m, 2 H), 1.69 (s, 3 H), 1.62 (dd, J = 7.0, 1.5 Hz, 3 H), 0.99 (d, J = 5.0 Hz, 3 H), 0.99 (t, J = 7.0 Hz, 3 H).

Characteristic signals of ^{1}H NMR deoxymyriaporone 3:

δ 5.33 (qd, J = 7.0, 11.5 Hz, 1 H), 5.19 (dd, J = 9.0, 1.5 Hz, 1 H), 5.18 (m, 1 H), 4.75 (m, 1 H), 4.29 (dd, J = 12.0, 12.0 Hz, 1 H), 3.71 (dd, J = 12.0, 4.5 Hz, 1 H), 3.41 (m, 1 H), 2.86 (ddd, J = 12.0, 5.0, 2.5 Hz, 1 H), 1.93 (dd, J = 14.0, 3.5 Hz, 1H), 1.74 (dd, J = 14.0, 3.5 Hz, 1 H), 1.69 (s, 3 H), 1.62 (dd, J = 7.0, 1.5 Hz, 3 H), 1.55 (qd, J = 7.0, 1.5 Hz, 2 H), 0.99 (d, J = 5.0 Hz, 3 H), 0.90 (t, J = 7.0 Hz, 3 H);

Figure S2. Synthetic Route to deoxymyriaporone HC-1-195



6-(*tert*-Butyl-dimethyl-silanyloxy)-5-(*tert*-butyl-dimethyl-silanyloxymethyl)-10-(4-methoxybenzyloxy)-3,7,9-trimethyl-deca-1,7-dien-4-ol, S8. To a solution of **S1** (111.2 mg, 0.196 mmol) in toluene (0.5 ml) at room temperature was added 4Å molecular sieves (ca. 120 mg). The suspension was cooled at -78˚C. The Roush reagent (ca. 1.0 in toluene, 0.7 ml) was added to the suspension via syringe**.** The reaction mixture was stirred overnight at -78˚C and quenched with NaOH (1N, 1 ml), warmed to 0˚C, stirred for 20 min, then filtered through Celite and the filter cake was washed with Et_2O (3 x 5 ml). The filtrate was

transferred to a separatory funnel and diluted with NaOH (1N, 10 ml), the layers were separated, and the aqueous layer extracted with Et_2O (4 x 5 ml). The organic layers were combined and washed with brine, dried over K_2CO_3, filtered, and concentrated in vacuo. Purification via flash chromatography (EtOAc/n-hexanes, gradient of solvents) provided **S8** as oil (106 mg, 87%).

$[\alpha]^{20}D$ = -19.0˚ (c.0.014, CH_2Cl_2); IR(film, cm^{-1}) 3504, 2955, 2925, 2857, 1612; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) -0.05-0.15 (m, 12 H), 0.80-1.05 (m, 24H), 1.54 (s, 3H), 1.62-1.70 (m, 1H), 2.26-2.45 (m 1H), 2.70-2.88(m, 1H), 3.20-3.38(m ,2H), 3.60-3.87(m, 7H), 4.18-4.53(m, 3H), 5.00-5.15(m, 2H), 5.34(d, *J* = 9.6 Hz), 5.80-5.94(m, 2H), 6.89(d, *J* = 6.8 Hz, 2H), 7.26 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125MHz) δ (ppm) -5.23, -5.20, -4.5, 13.5, 17.4, 17.9, 18.2, 18.3, 26.0, 26.1, 33.1, 42.1, 42.2, 55.5, 59.7, 72.9, 73.6, 75.3, 76.5, 113.9, 114.3, 129.3, 129.8, 130.9, 135.4, 142.9, 159.3; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{34}H_{62}O_5Si_2Na$, 629.4034; obsd 629.4039.

5-(*tert*-butyl-dimethyl-silanyloxy)-6-(*tert*-butyl-dimethyl-silanyloxymethyl)-8-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-2,4-dimethyl-non-3-ene-1,7-diol, S9. To a solution of **S8** (54.3 mg, 0.0872 mmol), PhNCO (0.10 ml, 0.935 mmol), and Et_3N (5 µl, 0.06 mmol) in benzene (1.0 ml), a solution of nitropropane (35 µl, 0.39mmol) in benzene (1.0 ml) was added dropwise with syringe pump at room temperature in ca. 10 h. After the adddtion, another batch of PhNCO (0.10 ml, 0.935 mmol) was added, and a solution of nitropropane (35 µl, 0.39 mmol) in benzene (1.0 ml) was added in ca. 10 h. The mixture was filtered through a plug of celite and the Celite washed with EtOAc, the solvent was evaporated. Flash chromatography of the residue using Biotage gave a crude mixture (56 mg). The crude mixture was dissolved in DCM (0.9 ml) and water (50 µl) was added. DDQ (71.1 mg, 0.12 mmol) was then added to the mixture and the resulting mixture was stirred for 2.5 h. The mixture was diluted with ether (10 ml) and washed with sat. $NaHCO_3$, brine, and dried over $MgSO_4$. Removal of solvent and flash chromatography of the residue over the silica gel (EtOAc/n-hexanes, gradient of solvents) gave the 'natural' isomer (less polar) **S9a** (13mg, 27% in two steps) and the 'unnatural' isomer (more polar) **S9b** (13mg, 27% in two steps).

Diastereomer a: $[\alpha]^{20}D$ = -16.6˚ (c.0.014, CH_2Cl_2); IR(film, cm^{-1}) 3484, 2926,2855; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 0.03-0.11 (m, 12 H), 0.72(d, *J* = 6.9 Hz, 3 H), 0.87-0.91 (m, 18 H), 1.00 (d, *J* = 6.9 Hz, 3 H), 1.15 (t, *J* = 7.5 Hz, 3 H), 1.26-1.33 (m, 1 H), 1.54-1.63 (m, 4 H), 2.20-2.39 (m, 3 H), 2.56-2.87 (m, 3 H), 3.40-3.55(m, 2 H), 3.69-3.87 (m, 4 H), 4.51 (d, *J* = 5.4 Hz), 4.98-5.07 (m, 1 H), 5.28(d, *J* = 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) -5.3, -5.1, -4.5, 9.7, 11.2, 13.2, 17.2, 18.2, 18.3, 21.6, 26.01, 26.07, 35.5, 36.0, 38.8, 43.7, 59.9, 67.9, 72.1, 76.4, 81.6, 129.8, 137.2, 160.0. HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{29}H_{59}O_5Si_2Na$, 580.3830; obsd 580.3859.

Diastereomer b: $[\alpha]^{20}D$ = +45.9˚ (c.0.037, CH_2Cl_2); IR(film, cm^{-1}) 3400, 2955, 2929, 2857; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 0.00-0.15 (m, 12 H), 0.77(d, *J* = 6.9 Hz, 3 H), 0.85-0.97 (m, 18 H), 1.04 (d, *J* = 6.9 Hz, 3 H), 1.17 (t, *J* = 7.5 Hz, 3 H), 1.3-1.40 (m, 1 H), 1.58-1.82 (m, 5 H), 2.31-2.42 (m, 2 H), 2.61-2.82 (m, 2 H), 2.97-3.10 (m, 2 H), 3.36-3.54 (m, 2 H), 3.64-3.90 (m, 4 H), 4.53 (d, *J* = 5.4 Hz), 4.77-4.90 (m, 1 H), 5.32 (d, *J* = 9.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) -5.22, -5.25, -5.2, -4.5, 10.5, 11.1, 13.9, 17.2, 18.2, 18.3, 21.5, 26.0, 26.1, 35.6, 41.4, 41.8, 43.8, 59.5, 68.0, 71.3, 76.6, 80.5, 129.3, 136.8, 160.4; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{29}H_{59}O_5Si_2Na$, 580.3830; obsd 580.3828.

5-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-ol, S10b. To a solution of **S9b** (176 mg, 0.315 mmol) in CH_2Cl_2 (3 ml) was added sat. $NaHCO_3$ (3 ml) and KBr (2M, 20 μl). The mixture was cooled to 0^oC, and TEMPO (5.8 mg, 0.037 mmol) was added. The mixture was stirred vigorously, and a solution of NaOCl (0.7 M, 0.54 ml, 0.38 mmol) was added dropwise in ca.10 min. After stirring for 2 h at 0˚C, the reaction was quenched by addition of sat. $Na_2S_2O_3$ (2 ml) and sat. $NaHCO_3$ (3 ml), and the resulting mixture was extracted with Et_2O (20 ml). Organic layer was washed with brine (10 ml), dried ($MgSO_4$) and evaporated. The resultant aldehyde residue was taken to next step with further purification. To a suspension of Ph_3PEtBr (643 mg, 1.46 mmol) in THF (3 ml) at 0˚C, BuLi (2.5M, 0.50 ml, 1.25 mmol) was added dropwise in ca. 5 min. The resulting red orange

suspension was stirred at 0˚C for ca. 1h and was then cooled to -76˚C. The crude aldehyde in THF (2 ml) was cannulated into the mixture. After the mixture was stirred overnight, it was diluted with EtOAc (20 ml), and washed with sat. $NaHCO_3$ (10 ml), brine (2x20ml), dried ($MgSO_4$). The solvent was removed in vacuo and the flash chromatography of the residue using biotage system gave **S10b** (116 mg, 65%).

$[\alpha]^{20}D$ = -15.3˚ (c.0.0086, CH_2Cl_2); IR(film, cm^{-1}) 3497, 2929; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 0.01-0.08 (m, 12 H), 0.70 (d, *J* = 6.9 Hz, 3 H), 0.84-0.92 (m, 18 H), 1.02 (d, *J* = 6.6 Hz, 3 H), 1.14 (t, *J* = 7.5 Hz, 3 H), 1.56-1.64(m, 7 H), 2.25-2.38 (m, 3H), 2.59-2.68 (m, 1H), 2.76-2.86(m, 1 H), 3.39-3.47 (m, 1 H), 3.65-3.84 (m, 4 H), 4.45 (d, *J* = 6.3 Hz, 1H), 5.02-5.10 (m, 1 H), 5.21-5.37 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ (ppm) -5.54, -5.46, -5.35, -4.59, 9.5, 11.1, 12.4, 13.1, 18.0, 18.2, 21.5, 25.9, 26.0, 30.5, 35.7, 38.8, 43.4, 60.0, 72.1, 76.2, 81.4, 122.0, 132.2, 133.0, 135.1, 159.9; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{31}H_{61}O_5Si_2Na$, 590.4037; obsd 590.4073.

5-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-ol, S10a.

See procedure for **S10b**.

$[\alpha]^{20}D$ = +55.2˚ (c.0.0055, CH_2Cl_2); IR(film, cm^{-1}) 3504, 2929, 2858; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 0.01-0.11 (m, 12 H), 0.80 (d, *J* = 6.6 Hz, 3 H), 0.90-0.91(m, 18 H), 1.05 (d, *J* = 6.6 Hz, 3 H), 1.16 (t, *J* = 7.5 Hz, 3 H), 1.56-1.79 (m, 7 H), 2.30-2.38 (m, 2 H), 2.68-2.77 (m, 1 H), 3.00-3.10 (m, 1 H), 3.38-3.47 (m, 1 H), 3.68-3.82 (m, 3 H), 3.87-3.92 (m, 1 H), 4.48 (d, J = 3.9 Hz, 1 H), 4.76-4.84 (m, 1 H), 5.22-5.39 (m, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) -5.40, -5.35, -5.31, -4.55, 10.7, 11.6, 13.07, 13.14, 18.1, 18.2, 21.45, 21.54, 25.9, 26.0, 30.6, 41.6, 42.0, 43.6, 59.7, 71.5, 76.5, 80.8, 121.8, 131.8, 132.7, 135.4, 160.4; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{31}H_{61}O_5Si_2Na$, 590.4037; obsd 590.4056.

5-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-one, S11a. To a solution of **S10a** (185 mg, 0.326 mmol) in CH_2Cl_2 (3.0 ml), $NaHCO_3$ (100 mg, 1.19 mmol) and DMP

(0.4M, 1.60 ml, 0.64 mmol) were added at room temperature. After the resulting mixture was stirred at room temperature for ca. 2h, it was diluted with CH_2Cl_2 (15 ml) and quenched with addition of sat. $Na_2S_2O_3$ (15 ml) and sat. $NaHCO_3$ (15 ml). The organic layer was separated and washed with brine (20 ml), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue using biotage system gave **S11a** (156 mg, 85%).

$[\alpha]^{20}D$ = +119.0˚ (c.0.0037, CH_2Cl_2); IR(film, cm^{-1}) 2928, 1709; ^1H NMR ($CDCl_3$, 500 MHz) δ (ppm) -0.05- -0.03 (m, m, 12H), 0.78-0.88 (m, 18 H), 1.00 (d, *J* = 6.6 Hz, 3 H), 1.13 (t, *J* = 7.5 Hz, 3 H), 1.32 (d, *J* = 7.2 Hz, 3 H), 1.58-1.65 (m, 6 H), 2.25-2.35 (m, 2 H), 2.52-2.61 (m, 1 H), 2.74-2.85 (m, 1 H), 3.09-3.22 (m, 2 H), 3.29-3.48 (m, 3 H), 4.15 (d, *J* = 9.3 Hz, 1 H), 4.58-4.67 (m, 1 H), 5.12-5.20 (m, 2 H), 5.27-5.38 (m 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) -5.44, -5.40, -4.7, -4.5, 10.9, 11.0, 13.1, 13.2, 18.3, 18.5, 20.9, 21.6, 26.0, 26.1, 30.5, 42.0, 54.8, 55.7, 64.6, 77.6, 81.0, 122.1, 133.1, 133.6, 134.9, 160.6, 214.7; HRMS (FAB) *m/z* $(M-H)^+$ calcd for $C_{31}H_{58}NO_4Si_2$ 564.3904, found 564.3922.

5-(*tert*-butyl-dimethyl-silanyloxy)-4-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-(3-ethyl-4,5-dihydro-isoxazol-5-yl)-6,8-dimethyl-undeca-6,9-dien-3-one, S11b.

See procedure for **S11a.**

$[\alpha]^{20}D$ = +37.4˚ (c.0.0088, CH_2Cl_2); IR(film, cm^{-1}) 2958, 2929, 2858, 1712; ^1H NMR ($CDCl_3$, 500 MHz) δ (ppm) -0.06-0.02 (m, 12H), 0.82-0.84 (m, 18 H), 0.99-1.05 (m, 6 H), 1.14 (t, *J* = 7.5 Hz, 3 H), 1.61-1.65 (m, 6H), 2.29-2.37 (m, 2 H), 2.60-2.67 (m, 1 H), 2.81-2.91 (m, 1 H), 3.17-3.27 (m, 3 H), 3.33-3.41 (m, 1 H), 3.49-3.56 (m, 1 H), 4.06 (d, J = 9.6 Hz, 1 H), 4.94-5.01 (m, 1 H), 5.11-5.19 (m, 2 H), 5.26-5.37 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ (ppm) -5.5, -5.4, -4.8, -4.3, 8.1, 10.9, 11.2, 13.2, 18.3, 18.6, 20.9, 21.4, 26.0, 26.1, 30.5, 37.6, 52.2, 56.5, 63.6, 78.4, 78.8, 122.2, 133.1, 133.7, 134.8, 160.5, 213.5; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{31}H_{59}O_4Si_2Na$, 588.3880; obsd 588.3873.

2-(3-Ethyl-4,5-dihydro-isoxazol-5-yl)-1-hydroxy-4-hydroxymethyl-6,8-dimethyl-undeca-6,9-dien-3-one, S12a. To a solution of **S11a** (75 mg, 0.13 mmol) THF (1.5 ml) and transferred to a nalgene vial. After addition of a solution of 37 wt% HF in Et_3N (0.66 ml), the nalgene vial was put into oil bath (49˚C) and the resulting solution was stirred for

24 h. The reaction mixture was diluted with Et_2O (20 ml) and washed with sat. $NaHCO_3$ (10 ml). Aqueous layer was separated and extracted with Et_2O (10 ml). Organic layers were combined and washed with brine (20 ml), dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over silica gel (EtOAc/n-hexanes, gradient of solvents) gave **S12a** as an oil (39mg, 86%).

$[\alpha]^{20}D$ = +91.9˚ (c.0.025, CH_2Cl_2); IR(film, cm^{-1}) 3400, 2972, 1707; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.01 (d, *J* = 6.6 Hz, 3 H), 1.12-1.17 (m, 6 H), 1.63-1.65 (m, 3 H), 1.71(s, 3 H), 2.16-2.18 (m, 1 H), 2.29-2.36 (m, 3 H), 2.84-3.03 (m, 2 H), 3.13-3.21 (m, 2 H), 3.36-3.44 (m, 1 H), 3.62-3.74 (m, 2 H), 4.27-4.29(m, 1 H), 4.69-4.77 (m, 1 H), 5.17-5.24 (m, 1 H), 5.33-5.39 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 10.9, 11.7, 12.6, 13.2, 21.4, 21.5, 30.6, 39.8, 51.2, 56.2, 62.5, 77.5, 122.5, 133.0, 133.8, 134.6, 161.4, 217.2; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{19}H_{31}O_4Na$, 360.2151; obsd 360.2154.

2-(3-Ethyl-4,5-dihydro-isoxazol-5-yl)-5-hydroxy-4-hydroxymethyl-6,8-dimethyl-undeca-6,9-dien-3-one, S12b.

See procedure for **S12a**.

$[\alpha]^{20}D$ = -41.9˚ (c.0.016, CH_2Cl_2); IR(film, cm^{-1}) 3401, 2971, 1708; ^1H NMR ($CDCl_3$, 500 MHz) δ (ppm) 1.01-1.06 (m, 6 H), 1.15-1.20 (m, 3 H), 1.64 (d, J = 6.6 Hz, 3 H), 1.69 (s, 3 H), 2.14-2.24 (br, 1 H), 2.30- 2.52 (br, 3 H), 2.64-2.72 (m, 1 H), 2.96-3.19 (m, 3 H), 3.35-3.43 (m, 1 H), 3.68-3.72 (m, 2 H), 4.30 (d, *J* = 8.7 Hz, 2 H), 4.73-4.82 (m, 1 H), 5.17-5.24 (m, 1 H), 5.30-5.38 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 11.1, 11.5, 11.6, 13.1, 21.4, 21.5, 30.6, 40.1, 51.7, 57.7, 62.1, 81.8, 122.4, 133.0, 133.9, 134.7, 160.5, 216.7; HRMS (FAB) *m/z* $(M+Na)^+$ calcd for $C_{19}H_{31}O_4Na$, 360.2151; obsd 360.2144.

8-(hydroxymethyl)-5,9-dihydroxy-10,12-dimethyl-pentadeca-10,13-diene-3,7-dione, S13b. Preparation of deactivated Raney Ni: Raney 2800 Ni purchased from Aldrich was washed with water to neutral (pH paper) and then reflux in acetone for 24h.

Compound **S12b** (25.0 mg, 0.0742 mmol) was dissolved in a MeOH/H_2O (1.2 ml, 5:1) solution. Boric acid (28 mg, 0.45mmol) and a spatula tip of the deactivated Raney Ni were

added and the mixture was stirred at room temperature under balloon pressure of hydrogen for 3.5 h. The mixture was diluted with ether, filtered through a plug of celite, and washed with sat. $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated. Reverse phase chromatography of the residue, using H_2O-MeOH, gave **S13b** (15.6 mg, 62%) as an oil.

$[\alpha]^{20}D$ = +72.5˚ (c.0.015, CH_2Cl_2); IR(film, cm^{-1}) 3400, 2919, 1708; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.00-1.09 (m, 9H), 1.62-1.69 (m, 6H), 2.40-2.56 (m,4H), 2.71 (dd, 1H, *J* = 2.4, 17.4 Hz), 2.88-2.99 (m, 2H), 3.14-3.21 (m, 1H), 3.32-3.44 (m,1H), 3.52-3.64 (m, 1H), .64-3.74 (m,1H), 3.94 (br, 1H), 4.24-4.35 (m 2H), 5.16-5.23 (m, 1H), 5.29-5.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ (ppm) 7.7, 11.4, 12.7, 13.2, 21.4, 30.6, 37.1, 45.7, 52.7, 58.3, 62.7, 71.2, 77.1, 122.4, 132.8, 134.3, 134.7, 212.4, 218.3; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{19}H_{33}O_5$, 341.2328; obsd 341.2325.

8-(hydroxymethyl)-5,9-dihydroxy-10,12-dimethyl-pentadeca-10,13-diene-3,7-dione, S13a.

See procedure for **S13b**.

$[\alpha]^{20}D$ = +8.6˚ (c.0.024, CH_2Cl_2); IR(film, cm^{-1}) 3401, 2921, 1707; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.01-1.09 (m, 9H), 1.63-1.71 (m, 6H), 2.19 (d, 1H), 2.45-2.60 (m, 3H), 2.64-2.77 (m, 2H), 3.00-3.03 (m, 1H), 3.28-3.42 (m, 2H), 3.56-3.6 (m, 1H), 3.70-3.80 (m, 1H), 4.17-4.21(dd, 1H, *J* = 8.7, 3.3 Hz), 4.46-4.54 (m, 1H), 5.16-5.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 125MHz) δ (ppm) 7.7, 10.4, 11.5, 13.2, 21.4, 30.6, 37.1, 45.0, 52.2, 56.2, 62.7, 68.9, 78.0, 122.5, 133.0, 134.1, 134.7, 212.6, 217.2; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{19}H_{33}O_5$, 341.2328; obsd 341.2351.

HC-1-203. To a solution of **S13b** (15.5 mg, 0.0456 mmol) in CH_2Cl_2 (0.25 ml), $NaHCO_3$ (14.5 mg, 0.173 mmol) and a solution of mCPBA in CH_2Cl_2 (0.5 ml) were added at -50˚C. The resulting mixture was stirred at -50˚C for 15h. The reaction was quenched with a solution of sat. $Na_2S_2O_3$ and sat. $NaHCO_3$ (8 ml, 1:1), then extracted with ether (20 + 5 ml). Ether layers were combined and washed with sat. $NaHCO_3$, brine, dried ($MgSO_4$), and

evaporated. Reverse phase chromatography of the residue, using H_2O-MeOH, gave some unreacted starting material **S13b** (3.4 mg) and **HC-1-203** (8.5 mg, 52%, 67% BOC).
$[\alpha]^{20}D$ = -14.5˚ (c.0.017, CH_2Cl_2); IR(film, cm^{-1}) 35002919, 1710; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.02-1.14 (m, 9H), 1.34 (s, 3H), 1.62 (d, 1H, *J* = 1.5 Hz), 2.41-2.59 (m, 5H), 2.69-2.77 (m 2H), 3.47-3.54 (m, 1H), 3.67-3.80 (m, 2H), 3.88 (br, 1H), 4.26-4.32 (m, 1H), 5.24-5.32 (m, 1H), 5.47-5.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 125MHz) δ (ppm) 7.7, 11.6, 12.8, 13.5, 18.8, 31.6, 37.1, 45.7, 52.7, 57.6, 61.1, 63.0, 67.0, 71.3, 76.3, 125.0, 130.4, 212.5, 217.5; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{19}H_{33}O_6$, 357.2277; obsd 357.2293.

HC-1-195.

See procedure for **HC-1-203**.
$[\alpha]^{20}D$ = -8.8˚ (c.0.0010, CH_2Cl_2); IR(film, cm^{-1}) 3411, 2922, 1709; ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.04-1.14 (m, 9H), 1.35 (s, 3H), 1.62 (d, *J* = 1.8 Hz), 2.42-2.53 (m, 4H), 2.65-2.78 (m, 4H), 3.04-3.12 (m, 1H), 3.20-3.27 (m, 1H), 3.46 (dd, J = 2.7, 9 Hz), 3.59 (br, 1H), 3.75 (br, 2H), 4.46-4.54 (m, 1H), 5.23-5.31 (m, 1H), 5.47-5.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 75MHz) δ (ppm) 7.3, 0.4, 11.9, 13.5, 18.8, 31.6, 37.1, 44.8, 52.3, 55.1, 61.4, 63.1, 66.9, 68.9, 77.1, 125.9, 130.4, 212.6, 217.2; HRMS (FAB) *m/z* $(M+H)^+$ calcd for $C_{19}H_{33}O_6$, 357.2277; obsd 357.2288.

Reference

Fleming, K. N. and Taylor, R. E. (2004) “Total Synthesis and Stereochemical Assignment of Myriaporones 1, 3, and 4“ Angewandte Chemie, International Edition, **43**: 1728-1730.