Electronic Supplementary Information (ESI)

Protecting-group-free synthesis of haterumadienone- and puupehenone-type marine natural products

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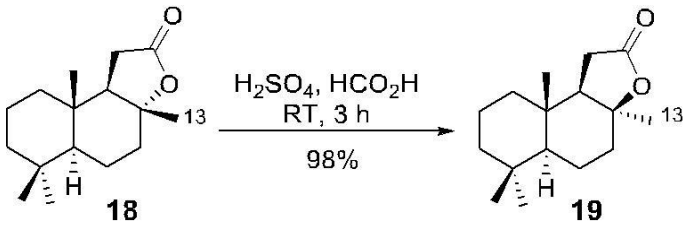
1. Table of Contents

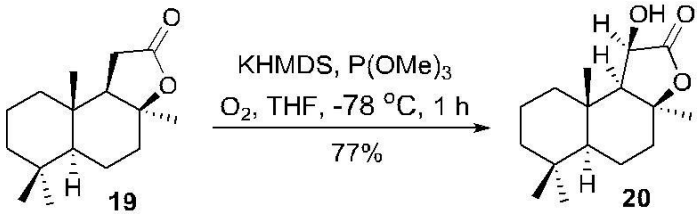
2. General Information

Common reagents and materials were purchased from commercial sources and were used without further purification. Organic solvents were routinely dried and/or distilled prior to use and stored over molecular sieves under argon. All experiments were carried out under an argon atmosphere in flame-dried glassware using standard inert techniques for introducing reagents and solvents unless otherwise noted. Organic extracts were, in general, dried over anhydrous sodium sulfate (Na_2SO_4). TLC plates were visualized by exposure to ultra violet light (UV). IR spectra were recorded by using an Electrothemal Nicolet 380 spectrometer. High-resolution mass spectra (HRMS) were recorded by using an Electrothemal LTQ-Orbitrap mass spectrometer. Melting points were measured by using a Gongyi X-5 microscopy digital melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were obtained by using a Bruker Avance III 400 MHz NMR spectrometer. Chemical shifts for protons are reported in parts per million (δ scale) and are referenced to residual protium in the NMR solvents ($CDCl_3$: δ 7.26; C_6D_6: δ 7.15; CD_3OD: δ 3.31). Chemical shifts for carbon resonances are reported in parts per million (δ scale) and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0; C_6D_6: δ 128.02; CD_3OD: δ 49.05). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hertz (Hz), and integration.

3. Experimental Procedures

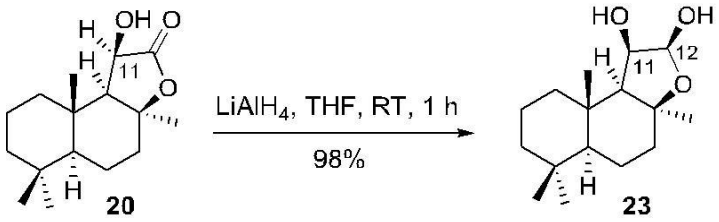


8-Episclareolide (19): [1] (+)-Sclareolide (**18**) (10.0 g, 40 mmol) was dissolved in the mixture of HCO_2H (99%, 170 mL) and concentrated H_2SO_4 (93%, 7 mL). The resulting mixture was stirred at room temperature for 3 hours, poured into ice-cold water, and extracted with Et_2O (4 × 100 mL). The combined organic layers were washed with saturated aqueous Na_2CO_3 (200 mL) and brine (200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated to afford 8-episclareolide (**19**, 9.8 g, 98%) as a white solid. M.p.: 89–91 °C; $[\alpha]^{25} = -34$ (c = 0.4 in $CHCl_3$), lit., [1] $[\alpha]^{22} = -32$ (c = 0.4 in $CHCl_3$); IR (film): ν_{max} = 2945, 1773, 1275, 1261, 764, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.70 (dd, *J* = 17.9, 7.8 Hz, 1 H), 2.35 (d, *J* = 18.0 Hz, 1 H), 2.28 (d, *J* = 14.7 Hz, 1 H), 1.74 (d, *J* = 7.7 Hz, 1 H), 1.58 (d, *J* = 9.3 Hz, 2 H), 1.51 (d, *J* = 18.0 Hz, 2 H), 1.43 (d, *J* = 15.3 Hz, 3 H), 1.30 (s, 3 H), 1.14 (t, *J* = 12.9 Hz, 1 H), 0.88 (s, 6 H), 0.84 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.6, 85.6, 54.68, 51.4, 41.6, 40.8, 36.0, 35.0, 33.5, 32.9, 32.3, 29.9, 22.1, 18.2, 18.0, 14.5 ppm; HRMS (ESI): m/z calcd. for $C_{16}H_{27}O_2$ $[M + H]^+$: 251.2006; found: 251.2012



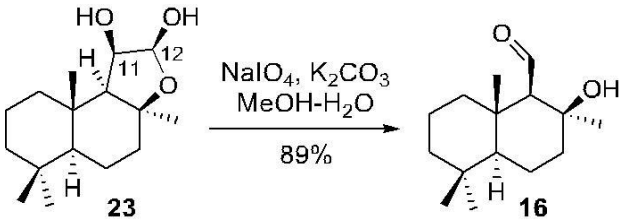
α-Hydroxy Lactone 20: To a solution of 8-episclareolide **19** (8.39 g, 33.5 mmol) in THF

(150 mL) was added KHMDS (50.25 mL, 1.0 M in THF, 50.25 mmol) at -78 °C. The mixture was stirred at -78 °C for 30 minutes, added with $P(OMe)_3$ (5.94 g, 5.65 mL, 50.25 mmol) , bubbled with O_2 (balloon pressure) for 20 minutes, stirred at -78 °C for 1 hour,[2] and quenched with aqueous 2 N HCl (100 mL). The resulting mixture was extracted with EtOAc (3 ×100 mL), and the combined organic phases were washed with brine (2 × 100 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was subjected to flash column chromatography over silica gel (100–200 mesh) for purification using EtOAc/petroleum ether (1 : 30 → 1 : 15) as eluent to give α-hydroxy lactone **20** (6.92 g, 77%) as a white solid. M.p.: 51–52 °C; IR (film): ν_{max} = 2999, 2937, 2832, 1601, 1570, 1488, 1271, 1218, 1049, 1034, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.37 (d, *J* = 3.7 Hz, 1 H), 3.44 (s, br, OH), 2.07 (td, *J* = 14.5, 7.3 Hz, 1 H), 1.80–1.72 (m, 3 H), 1.65–1.54 (m, 2 H), 1.52 (s, 3 H), 1.48–1.36 (m, 3 H), 1.24–1.17 (m, 1 H), 1.11 (dd, *J* = 17.8, 4.3 Hz, 1 H), 1.04 (dd, *J* = 11.7, 5.6 Hz, 1 H), 0.93 (s, 3 H), 0.90 (s, 3 H), 0.88 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 86.5, 71.3, 61.4, 48.8, 42.1, 41.8, 35.9, 33.2, 32.9, 31.6, 21.9, 18.2, 18.1, 16.6 ppm; HRMS (ESI): m/z calcd. for $C_{16}H_{26}O_3Na$ $[M+ Na]^+$: 289.1774; found: 256.1782.



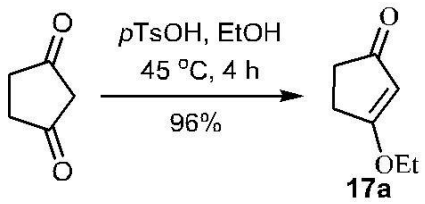
Lactol 23: To an ice-cold solution of the α-hydroxy lactone **20** (6.66 g, 25 mmol) in dry THF (150 mL) was added $LiAlH_4$ (2.85 g, 75 mmol) in portions. The mixture was allowed to warm up to room temperature and stirring was continued for 1 hour, after which time it was then slowly quenched at 0 °C with 3 mL of water, 3 mL of an aqueous 15% NaOH solution followed by 9 mL of water to afford a granular inorganic precipitate. The mixture was filtered over a pad of celite, the solid was rinsed with DCM, and the

filtrate was extracted with DCM (3 × 100 mL). The combined organic phases were washed with brine (2 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated to give lactol **23** (6.57 g, 98%) as a white solid. M.p.: 69–71 °C; IR (film): ν_{max} = 3371, 2946, 2924, 2359, 1674, 1457, 1369, 1074, 1045 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.26 (d, *J* = 4.2 Hz, 1 H), 4.21 (t, *J* = 4.7 Hz, 1 H), 3.44 (s, br, OH), 1.93–1.75 (m, 2 H), 1.61 (d, *J* = 3.4 Hz, 1 H), 1.55–1.45 (m, 5 H), 1.42 (s, 3 H), 1.29 (d, *J* = 19.1 Hz, 1 H), 1.20 (d, *J* = 13.4 Hz, 1 H), 1.12 (d, *J* = 13.5 Hz, 1 H), 1.06 (d, *J* = 9.7 Hz, 1 H), 1.01 (d, *J* = 11.0 Hz, 1 H), 0.96 (s, 3 H), 0.92 (s, 3 H), 0.88 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 96.1, 82.4, 74.4, 64.3, 48.9, 42.9, 42.1, 35.7, 34.1, 33.4, 33.2, 32.5, 22.0, 18.4, 18.2, 17.0 ppm; HRMS (ESI): m/z calcd. for $C_{16}H_{29}O_3$ $[M+H]^+$: 269.2111; found: 269.2116.



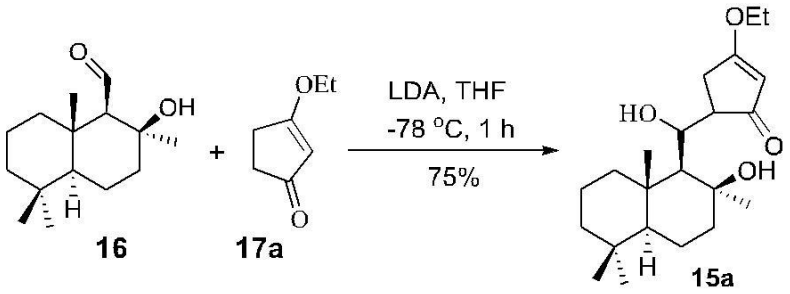
***β*-Hydroxy aldehyde 16:** To an ice-cold solution of lactol **23** (5.37 g, 20 mmol) in THF (100 mL) was added dropwise a solution of $NaIO_4$ (8.56 g, 40mmol) in water (100 mL), then warmed to room temperature. After stirring for 2 hours, the resulting precipitate was filtered and the filtrate was extracted with AcOEt (3 × 100 mL), washed with aqueous sodium thiosulfate, brine, dried over Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was subjected to flash column chromatography over silica gel (100–200 mesh) for purification using EtOAc/petroleum ether (1 : 20 → 1 : 10) as eluent to give *β*-hydroxy aldehyde **16** (4.24 g, 89%) as a white solid. M.p.: 72–74 °C; IR (film): ν_{max} = 3458, 2926, 1710, 1461, 1386, 1181, 1122, 1078, 916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 10.03 (d, *J* = 2.3 Hz, 1 H), 2.87 (s, br, OH), 2.09 (d, *J* = 2.0 Hz, 1 H), 1.77–1.69 (m, 2 H), 1.63–1.56 (m, 2 H), 1.51–1.49 (m, 2 H), 1.44–1.37 (m, 2 H), 1.18 (s,

3 H), 1.33 (dd, *J* = 13.4, 4.2 Hz, 1 H), 1.22 (d, *J* = 4.1 Hz, 1 H), 1.14 (s, 3 H), 0.91 (d, *J* = 12.1 Hz, 1 H), 0.87 (s, 3 H), 0.84 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.6, 71.3, 69.3, 55.2, 41.6, 41.5, 40.3, 39.7, 33.6, 33.3, 31.1, 21.6, 18.3, 18.0, 16.9 ppm; HRMS (ESI): m/z calcd. for $C_{15}H_{26}O_2Na$ $[M + Na]^+$ 261.1825; found 261.1829.



17a

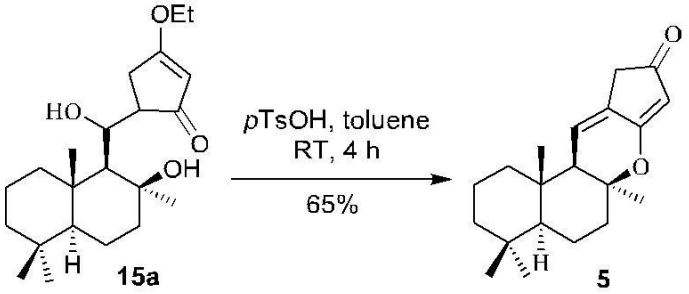
***β*-Alkoxy enone 17a**: To a solution of 1,3-cyclopendione (0.49 g, 5 mmol) in EtOH (10 mL) were added *p*TsOH (173 mg, 1 mmol) at room temperature. The resulting mixture was heated to 45 °C and stirred at that temperature for 4 hours before it was cooled to room temperature and diluted with EtOAc (20 mL). The mixture so obtained was sequentially washed with saturated aqueous Na_2CO_3 (2 × 30 mL) and brine (2 ×30 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, to give *β*-alkoxy enone **17a** (0.61 g, 96 %) as a yellow oil without further purification. IR (film): ν_{max} = 1700, 1675, 1582, 1340, 1247, 1184, 1026 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.28 (s, 1 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 2.60 (m, 2 H), 2.43 (m, 2 H), 1.40 (t, *J* = 7.1 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.8, 190.0, 104.4, 67.5, 33.7, 28.3, 13.9 ppm; HRMS (ESI): m/z calcd. for $C_7H_{10}O_2Na$ $[M + Na]^+$ 149.0573; found 149.0575.



16 **17a** **15a**

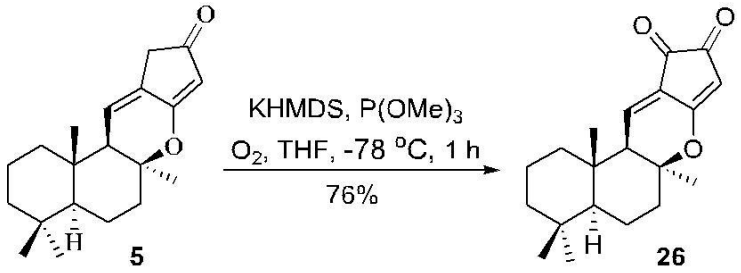
Aldol adduct 15a: To a solution of *β*-alkoxy enone **17a** (0.38 g, 3 mmol) in THF (4 mL) was added LDA (9.0 mL, 1.0 M in THF, 9.0 mmol) at -78 °C. The resulting mixture was stirred at that temperature for 30 minutes before a solution of *β*-hydroxy aldehyde **16** (0.72 g, 3 mmol) in THF (5 mL) was added. The mixture so obtained was stirred at −78 °C for 1 hour before it was quenched with saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give aldol adduct **15a** (0.82 g, 75 %) as a white solid. $[\alpha]^{25}$ = 36 (c = 0.25 in $CHCl_3$); M.p.: 60–62 °C; R (film): ν_{max} = 3492, 3345, 2926, 2844, 1669, 1588,1342, 1023, 913 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (s, 1 H), 5.24 (s, 1 H), 4.88 (s, br, 1 H), 4.23 (d, *J* = 11.2 Hz, 1 H), 4.06 (dd, *J* = 13.9,

6.9 Hz, 1 H), 3.04 (m, 1 H), 2.64 (dd, *J* = 17.5, 7.4 Hz, 1 H), 2.32 (dd, *J* = 17.6, 3.2 Hz, 1 H), 1.73–1.59 (m, 4 H), 1.44–1.41 (m, 3 H), 1.39 (s, 3 H), 1.34 (s, 2 H), 1.30–1.23 (m, 2 H), 1.18 (s, 3 H), 1.14 (s, 1 H), 0.88 (s, 1 H), 0.85 (s, 3 H), 0.82 (s, 3 H), 0.77–0.33 (m, 3 H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.7, 189.6, 103.0, 73.1, 72.2, 67.9, 58.2, 55.7, 49.0, 43.0, 41.7, 40.4, 39.0, 33.4, 33.2, 32.5, 32.2, 21.4, 18.2, 18.0, 15.4, 13.8 ppm; HRMS (ESI): m/z calcd for $C_{22}H_{36}O_4Na$ $[M + Na]^+$ 387.2506, found 387.2513.



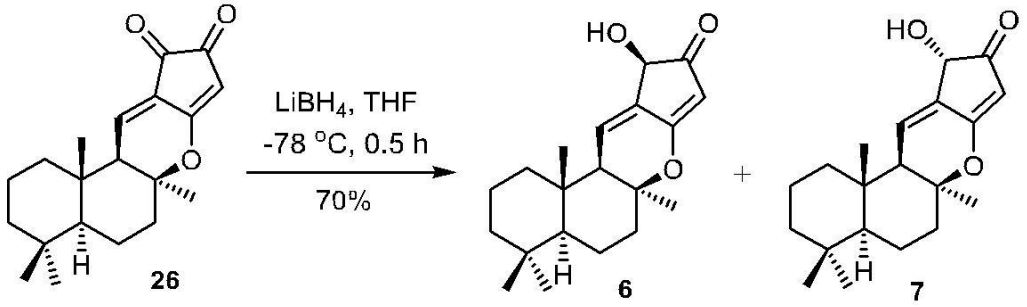
Haterumadienone (5): To a solution of aldol adduct **15a** (0.73 g, 2 mmol) in toluene (8 mL) were added *p*TsOH (0.69 g, 4 mmol) at room temperature and stirred at that temperature for 4 hours before it was cooled to room temperature and diluted with EtOAc

(20 mL). The mixture so obtained was sequentially washed with saturated aqueous Na_2CO_3 (30 mL) and brine (30 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give haterumadienone (**5**, 0.39 g, 65 %) as a yellow solid. M.p.: 102–104 °C; $[\alpha]^{25}$ = -62 (c = 0.14 in $CHCl_3$), lit.,[3] $[\alpha]^{25}$ = -57 (c = 0.14 in $CHCl_3$); IR (film): ν_{max} = 2924, 1694, 1573, 1406, 1175 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ = 5.61 (s, 1 H), 5.29 (d, *J* = 6.3 Hz, 1 H), 2.83 (d, *J* = 20.1 Hz, 1 H), 2.76 (d, *J* = 20.3 Hz, 1 H), 1.96 (d, *J* = 14.5 Hz 1 H), 1.36–1.34 (m, 1 H), 1.33–1.31 (m, 1 H), 1.31–1.28 (m, 1 H), 1.30–1.25 (m, 4 H), 1.27–1.25 (m, 1 H), 1.25–1.22 (m, 3 H), 1.14 (dd, *J* = 13.9, 5.0 Hz, 1 H), 1.03 (dd, *J* = 11.7, 4.3 Hz, 1 H), 0.96 (s, 1 H), 0.81 (s, 1 H), 0.74 (s, 1 H), 0.68 (s, 3 H), 0.68−0.65 (m, 1 H), 0.58 (d, *J* = 11.8 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 199.0, 178.0, 133.0, 121.4, 110.1, 80.3, 54.0, 53.9, 42.0, 40.0, 39.6, 39.4, 37.9, 33.7, 33.2, 28.6, 22.1, 18.6, 18.4, 14.7 ppm; HRMS (ESI): m/z calcd. for $C_{20}H_{28}O_2Na$ $[M + Na]^+$ 323.1982; found 323.1985. All spectral data match those of the natural haterumadienone.[3]



Haterumadiendione (26): To a solution of haterumadienone (**5**, 0.30 g, 1 mmol) in THF (3 mL) was added KHMDS (2 mL, 1.0 M in THF, 2 mmol) at -78 °C. The resulting mixture was stirred at that temperature for 30 minutes before $P(OMe)_3$ (0.25 g, 236 μL, 2 mmol) was added. O_2 (balloon pressure) was bubbled through the mixture for 1 minute, and stirred at that temperature for 1 hour, then quenched with saturated aq. $NaHCO_3$ (10 mL). The mixture so obtained was extracted with EtOAc (3 ×20 mL), and the combined

organic phases were washed with brine (2 × 30 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was subjected to flash column chromatography over silica gel (100–200 mesh) for purification using EtOAc/petroleum ether (1 : 20 → 1 : 10) as eluent to give haterumadiendione (**26**, 238 mg, 76%) as a yellow solid. M.p.: 76–78 °C; $[\alpha]^{25}$ = 29 (c = 0.28 in $CHCl_3$); IR (film): ν_{max} = 2925, 2851, 1749, 1709, 1658, 1541, 1406, 1161, 1128 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.89 (d, *J* = 5.9 Hz, 1 H), 6.06 (s, 1 H), 2.31 (d, *J* = 14.6 Hz, 1 H), 2.22 (d, *J* = 6.1 Hz, 1 H), 1.67 (d, *J* = 12.1 Hz, 2 H), 1.59−1.57 (m, 1 H), 1.49 (d, *J* = 13.1 Hz, 1 H), 1.42 (d, *J* = 12.0 Hz, 2 H), 1.26 (s, 3 H), 1.19−1.17 (m, 3 H), 1.02 (d, *J* = 11.6 Hz, 1 H), 0.90 (s, 3 H), 0.82 (s, 3 H), 0.76 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.3, 186.4, 181.1, 130.6, 128.9, 111.7, 83.2, 54.5, 54.1, 41.3, 41.2, 39.8, 38.8, 33.6, 33.2, 29.2, 21.8, 18.1, 17.9, 14.9 ppm; HRMS (ESI): m/z calcd. for $C_{20}H_{26}O_3Na$ $[M + Na]^+$ 337.1774; found 337.1781.

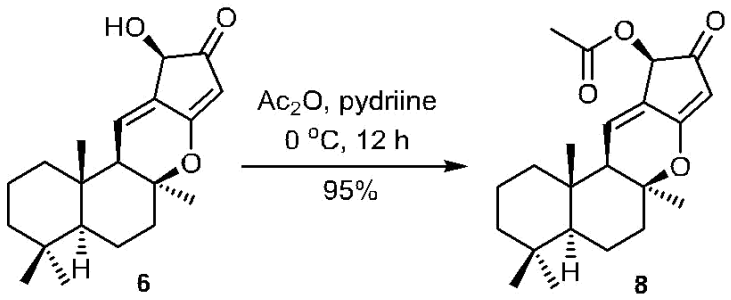


20-Hydroxyhaterumadienone (6) and 20-*epi*-hydroxyhaterumadienone (7): To a solution of haterumadiendione (**26**, 188 mg, 0.6 mmol) in THF (2.0 mL) was added $LiBH_4$ (26.1 mg, 1.2 mmol) at -78 °C. The resulting mixture was stirred at that temperature for 30 minutes before it was quenched with saturated aqueous $NaHCO_3$ (3 mL). The resulting mixture was extracted with EtOAc (3 × 10 mL), and the combined organic phases were dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether/CH_2Cl_2 (1 : 10 : 5) to give

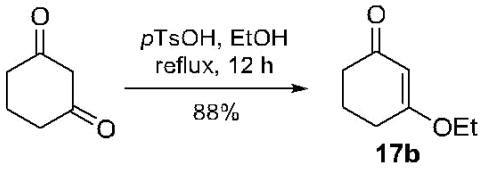
20-hydroxyhaterumadienone (**6**, 110 mg, 58 %) and 20-*epi*-hydroxyhaterumadienone (**7**, 23 mg, 12 %). The ratio is 82:18 based on the ^{1}H NMR diagram of the corresponding crude mixture.

20-Hydroxyhaterumadienone (6): IR (film): ν_{max} = 3391, 2924, 2852, 1563, 1403, 1127 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.28 (d, *J* = 5.5 Hz, 1 H), 5.35 (s, 1 H), 4.62 (s, 1 H), 3.26 (s, br, 1 H), 2.23 (d, *J* = 14.2 Hz, 1 H), 1.99 (d, *J* = 5.2 Hz, 1 H), 1.73 (d, *J* = 12.4 Hz, 1 H), 1.67–1.63 (m, 1 H), 1.55–1.52 (m, 2 H), 1.45–1.41 (m, 1 H), 1.41–1.39 (m, 2 H), 1.27 (s, 3 H), 1.16 (d, *J* = 15.1 Hz, 1 H), 1.09 (d, *J* = 13.0 Hz, 1 H), 0.96 (d, *J* = 11.0 Hz, 1 H), 0.91 (s, 3 H), 0.84 (s, 3 H), 0.80 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.3, 178.0, 135.2, 123.4, 105.1, 81.7, 70.8, 54.1, 53.7, 41.7, 40.2, 39.5, 39.3, 33.7, 33.2, 28.9, 21.9, 18.3, 18.0, 14.4 ppm; HRMS (ESI): m/z calcd. for $C_{20}H_{28}O_3Na$ $[M + Na]^+$ 339.1931; found 339.1936. All spectral data match those of natural 20-hydroxyhaterumadienone.[4]

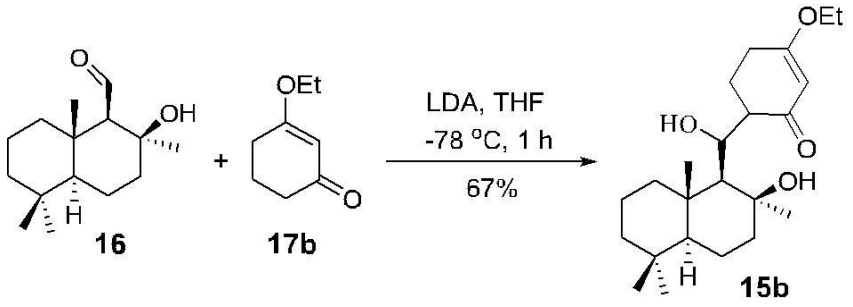
20-Epihydroxyhaterumadienone (7): IR (film): ν_{max} = 3367, 2923, 2852, 1558, 1403, 1125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.33 (d, *J* = 2.7 Hz, 1 H), 5.41 (s, 1 H), 4.54 (s, 1 H), 2.23 (d, *J* = 13.9 Hz, 1 H), 2.01 (d, *J* = 4.8 Hz, 1 H), 1.63 (d, *J* = 16.9 Hz, 1 H), 1.56–1.53 (m, 2 H), 1.49–1.46 (m, 1 H), 1.45–1.43 (m, 2 H), 1.30 (s, 3 H), 1.21–1.19 (m, 1 H), 1.14 (d, *J* = 11.8 Hz, 1 H), 0.98 (d, *J* = 11.6 Hz, 1 H), 0.92 (s, 3 H), 0.86 (s, 3 H), 0.82 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.1, 179.0, 134.4, 125.9, 106.9, 82.0, 70.0, 54.1, 54.1, 41.6, 40.1, 39.8, 39.3, 33.7, 33.2, 28.6, 22.0, 18.3, 18.1, 14.9 ppm; HRMS (ESI): m/z calcd. for $C_{20}H_{28}O_3Na$ $[M + Na]^+$ 339.1931; found 339.1937. All spectral data match those of the natural 20-epihydroxyhaterumadienone.[5]



20-Acetoxyhaterumadienone (8): To a solution of 20-hydroxyhaterumadienone (**6**, 63 mg, 0.2 mmol) in pyridine (1.0 mL) was added Ac_2O (204 mg, 189 μL, 2 mmol) at 0 °C. The reaction mixture was stirred at that temperature for 12 hours before it was quenched with saturated aqueous $NaHCO_3$ (3 mL). The resulting mixture was extracted with EtOAc (3 × 10 mL), and the combined organic phases were dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was purified by flash column chromatography over silica gel (100–200 mesh) using EtOAc/petroleum ether (1 : 20 → 1 : 10) as eluent to give 20-acetoxyhaterumadienone (**8**, 68 mg, 95 %) as a white foam. $[\alpha]^{28}$ = -38 (c = 0.10 in CCl_4); IR (film): ν_{max} = 3363, 2924, 2360, 2341, 1592, 1403, 1124 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.16 (s, 1 H), 5.67 (s, 1 H), 5.44 (s, 1 H), 2.23 (d, *J* = 15.1 Hz, 1 H), 2.19 (s, 3 H), 1.98 (d, *J* = 4.2 Hz, 1 H), 1.66 (d, *J* = 12.9 Hz, 1 H), 1.62–1.59 (m, 1 H), 1.56–1.52 (m, 2 H), 1.49–1.45 (m, 1 H), 1.45–1.42 (m, 2 H), 1.27 (s, 3 H), 1.21–1.18 (m, 1 H), 1.13 (d, *J* = 13.9 Hz, 1 H), 0.96 (d, *J* = 11.2 Hz, 1 H), 0.91 (s, 3 H), 0.85 (s, 3 H), 0.80 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 177.6, 170.8, 133.2, 124.6, 107.1, 81.6, 70.7, 54.1, 53.8, 41.6, 40.2, 39.8, 39.2, 33.7, 33.2, 28.9, 21.9, 20.8, 18.3, 18.1, 14.5 ppm; HRMS (ESI): m/z calcd. for $C_{22}H_{30}O_4Na$ $[M + Na]^+$ 381.2036; found 381.2039. All spectral data are similar to those of the natural 20-epihydroxyhaterumadienone.[6]

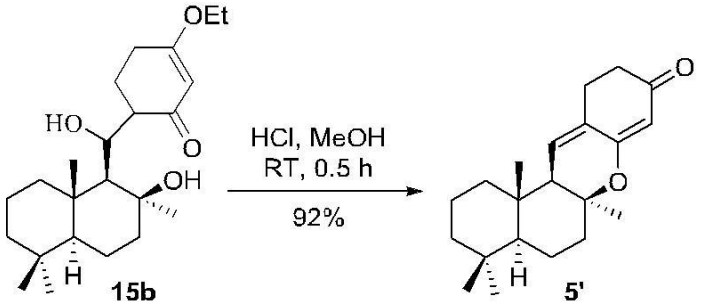


***β*-Alkoxy enone 17b**: To a solution of 1,3-cyclohexanedione (0.56 g, 5 mmol) in toluene (10 mL) were added *p*TsOH (173 mg, 1 mmol) and EtOH (0.46 g, 585 μL, 50 mmol) at room temperature. The resulting mixture was heated to reflux and stirred at that temperature for 12 hours before it was cooled to room temperature and diluted with EtOAc (20 mL). The mixture so obtained w as sequentially washed with saturated aqueous Na_2CO_3 (2 × 30 mL) and brine (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 15 → 1 : 10) to give *β*-alkoxy enone **17b** (0.62 g, 88 %) as a yellow oil. IR (film): ν_{max} = 2943, 2359, 1646, 1598, 1377, 1219, 1182, 1136, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.22 (s, 1 H), 3.78 (q, *J* = 7.0 Hz, 2 H), 2.28 (t, *J* = 6.3 Hz, 2 H), 2.22−2.20 (m, 2 H), 1.86−1.84 (m, 2 H), 1.24 (t, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.8, 189.9, 104.4, 67.5, 33.7, 28.3, 13.9 ppm; HRMS (ESI): m/z calcd. for $C_8H_{13}O_2$ $[M + H]^+$ 141.0910; found 141.0912.



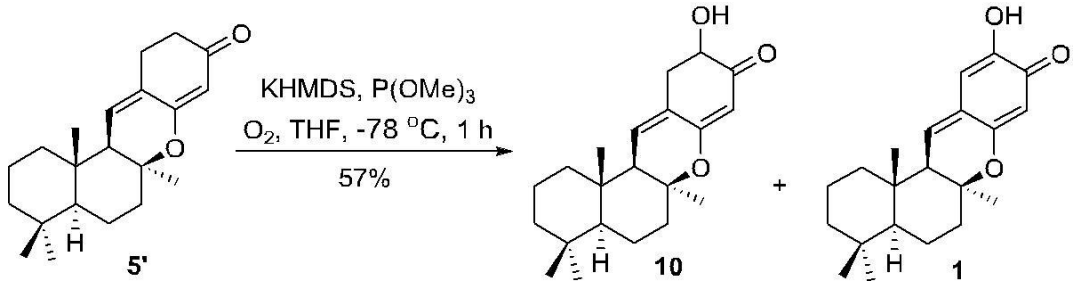
Aldol adduct 15b: To a solution of *β*-alkoxy enone **17b** (0.56 g, 4 mmol) in THF (5 mL) was added LDA (8.0 mL, 1.0 M in THF, 8.0 mmol) at -78 °C. The resulting mixture was stirred at that temperature for 30 minutes before a solution of *β*-hydroxy aldehyde **16**

(0.96 g, 4 mmol) in THF (5 mL) was added. The mixture so obtained was stirred at -78 °C for 1 hour before it was quenched with saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give aldol adduct **15b** (1.01 g, 67 %) as a white solid. M.p.: 80–82 °C; IR (film): ν_{max} = 3341, 2926, 2845, 1717, 1605, 1459, 1384, 1193, 1025, 912 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.33 (s, 1 H), 4.34 (d, *J* = 9.8 Hz, 1 H), 3.90 (td, *J* = 16.1, 8.1 Hz, 2 H), 2.60 (dd, *J* = 12.1, 10.8 Hz, 1 H), 2.46 (q, *J* = 17.2 Hz, 2 H), 2.03 (d, *J* = 15.9 Hz, 2 H), 1.69−1.67 (m, 3 H), 1.57−1.55 (m, 1 H), 1.43 (d, *J* = 12.0 Hz, 1 H), 1.37−1.35 (m, 2 H), 1.34 (s, 4 H), 1.29−1.27 (m, 1 H), 1.24−1.22 (m, 1 H), 1.19 (s, 3 H), 1.10−1.08 (m, 2 H), 0.87−0.85 (m, 1 H), 0.84 (s, 3 H), 0.82 (s, 3 H) 0.77 (d, *J* = 12.1 Hz, 1 H), 0.62 (t, *J* = 12.4 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.6, 178.4, 102.5, 73.4, 72.4, 64.8, 56.3, 55.5, 49.6, 43.2, 42.0, 40.2, 39.2, 33.6, 33.5, 32.4, 29.1, 24.9, 21.6, 18.5, 18.3, 15.7, 14.0 ppm; HRMS (ESI): m/z calcd. for $C_{23}H_{38}O_4Na$ $[M + Na]^+$ 401.2662; found 401.2668.



Enone 5': The aldol adduct **15b** (0.95 g, 2.5 mmol) was dissolved in hydrogen chloride-methanol solution (2 M, 2 mL) at room temperature and stirred for 30 minutes before it was diluted with EtOAc (10 mL). The mixture so obtained was sequentially washed with saturated aqueous Na_2CO_3 (20 mL) and brine (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under

vacuum. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give enone **27** (0.72 g, 92 %) as a white solid. $[\alpha]^{25}$ = -206 (c = 0.20 in $CHCl_3$); M.p.: 106–107 °C; IR (film): ν_{max} = 2937, 1643, 1576, 1397, 1206, 1159, 1144, 1135, 1016, 865 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.10 (d, *J* = 6.7 Hz, 1 H), 5.42 (s, 1 H), 2.66−2.64 (m, 2 H), 2.42−2.40 (m, 2 H), 2.11 (d, *J* = 12.9 Hz, 1 H), 1.81 (d, *J* = 6.9 Hz, 1 H), 1.63 (d, *J* = 12.5 Hz, 1 H), 1.50 (m, 4 H), 1.39−1.37 (m, 2 H), 1.21−1.19 (m, 1 H), 1.15 (s, 3 H), 1.08−1.06 (m, 1 H), 0.91−0.89 (m, 1 H), 0.87 (s, 3 H), 0.80 (s, 6 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 167.1, 130.2, 128.5, 107.4, 77.5, 54.2, 53.7, 41.6, 39.8, 39.6, 39.0, 36.9, 33.6, 33.0, 28.4, 28.0, 21.9, 18.3, 18.0, 14.4 ppm; HRMS (ESI): m/z calcd. for $C_{21}H_{30}O_2Na$ $[M + Na]^+$ 337.2138; found 337.2142.

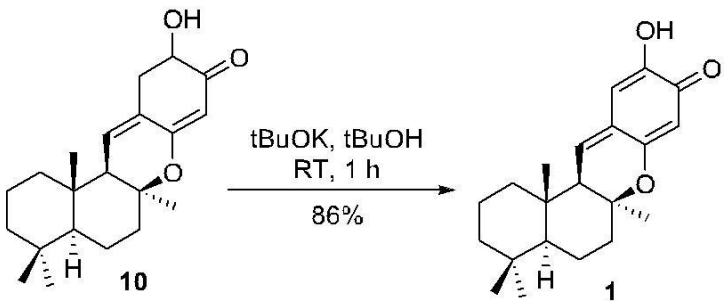


Puupehenone (1) and *α*-hydroxylated product 28: To a solution of enone **5'** (0.31 g, 1 mmol) in THF (3 mL) was added KHMDS (1.5 mL, 1.0 M in THF, 1.5 mmol) at -78 °C. The resulting mixture was stirred at that temperature for 30 minutes before $P(OMe)_3$ (0.19 g, 177 μL, 1.5 mmol) was added. O_2 (balloon pressure) was bubbled through the mixture for 1 minutes, and stirred at that temperature for 1 hour, then quenched with saturated aqueous $NaHCO_3$ (10 mL). The mixture so obtained was extracted with EtOAc (3 ×20 mL), and the combined organic phases were washed with brine (2 × 30 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was subjected to flash column chromatography over silica gel (100–200 mesh) for purification using EtOAc/petroleum ether (1 : 20 → 1 : 10) as eluent to give

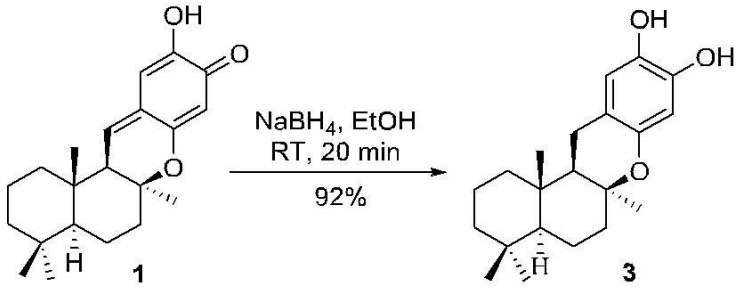
puupehenone (**1**, 125 mg, 38%) as a yellow oil and *α*-hydroxylated product **10** (62 mg, 19%) as a colorless oil.

***α*-Hydroxylated product 10**: IR (film): ν_{max} = 3344, 2923, 2358, 2341, 1642, 1570, 1457, 1404, 1159, 1135, 1102,1016, 898, 803 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.26 (d, *J* = 6.9 Hz, 1 H), 5.48 (s, 1 H), 4.14 (dd, *J* = 12.5, 6.3 Hz, 1 H), 3.95 (s, 1 H), 3.01 (dd, *J* = 13.6, 6.3 Hz, 1 H), 2.59 (t, *J* = 13.1 Hz, 1 H), 2.15 (d, *J* = 13.9 Hz, 1 H), 2.07 (s, 1 H), 1.87 (d, *J* = 7.0 Hz, 1 H), 1.67 (d, *J* = 12.2 Hz, 1 H), 1.55−1.53 (m, 2 H), 1.43−1.41 (m, 2 H), 1.26 (s, 1 H), 1.18 (s, 3 H), 1.12−1.10 (m, 1 H), 0.96−0.94 (m, 1 H), 0.90 (s, 3 H), 0.83 (s, 3 H), 0.82 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 168.0, 131.1, 128.8, 103.7, 78.1, 71.2, 53.9, 53.8, 41.7, 39.8, 39.6, 39.0, 36.9, 33.6, 33.1, 28.4, 21.9, 18.4, 18.0, 14.5 ppm; HRMS (ESI): m/z calcd. for $C_{21}H_{30}O_3Na$ $[M + Na]^+$ 353.2087; found 353.2094.

Puupehenone (1): ν_{max} = 3132, 2924, 2853, 2362, 1616, 1400, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (s, br, 1 H), 6.66 (d, *J* = 6.9 Hz, 1 H), 6.20 (s, 1 H), 5.86 (s, 1 H), 2.17 (dd, *J* = 2.4, 11.4 Hz, 1 H), 2.04 (d, *J* = 6.9 Hz, 1 H), 1.68 (d, *J* = 6.9 Hz, 1 H), 1.23 (s, 3 H), 0.91 (s, 3 H), 0.85 (s, 3 H), 0.82 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.1, 162.8, 147.5, 140.4, 129.4, 106.1, 105.1, 78.9, 54.9, 53.9, 41.7, 40.8, 40.1, 39.3, 33.7, 33.3, 28.1, 21.9, 18.5, 18.1, 15.0 ppm; HRMS (ESI): m/z calcd. for $C_{21}H_{29}O_3$ $[M + H]^+$ 329.2111; found 329.2106. All spectral data match those of authentic puupehenone.[1]

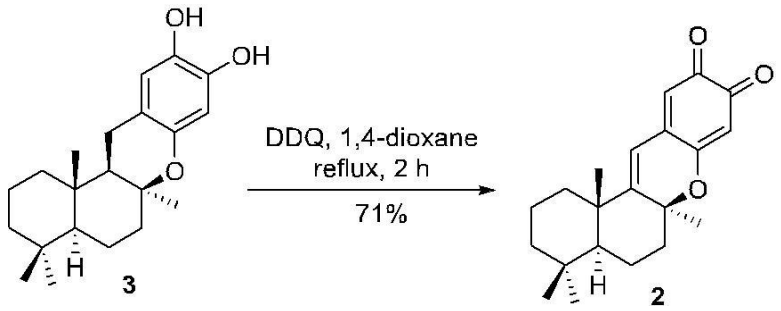


From ***α*-hydroxylated product 28** to **puupehenone (1)**: To a solution of *α*-hydroxylated product **10** (50 mg, 0.15 mmol) in ^{t}BuOH (3 mL) was added ^{t}BuOK (34 mg, 0.3 mmol) at room temperature. The resulting mixture was stirred at room temperature for 1 hour, and then quenched with aqueous 2 N HCl (5 mL). The mixture so obtained was extracted with EtOAc (3 × 10 mL), and the combined organic phases were washed with brine (2 × 10 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under vacuum, the residue was subjected to flash column chromatography over silica gel (100– 200 mesh) for purification using EtOAc/petroleum ether (1 : 20 → 1 : 10) as eluent to give puupehenone (**1**, 42 mg, 86%).



Puupehenol (3): To a solution of puupehenone (**1**, 66 mg, 0.2 mmol) in EtOH (2 mL) followed by the addition of $NaBH_4$ (15 mg, 0.4 mmol) and stirred for 20 minutes at room temperature. The reaction mixture was cooled to 0 °C and quenched by the dropwise addition of aqueous 2 N HCl until gas evolution ceased then concentrated under vacuum. The crude product was then dissolved in EtOAc (20 mL), washed with water (10 mL), brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give puupehenol (**3**, 61 mg, 92 %) as a yellow oil. IR (film): ν_{max} = 2924, 2852, 2359, 1661, 1604, 1520, 1456, 1376, 1223, 1160, 1133, 1014, 911, 734 cm^{-1}; ^{1}H NMR (400 MHz, CD_3COCD_3): δ = 7.51 (s, OH), 7.08 (s, OH), 6.46 (s, 1 H), 6.16 (s, 1 H), 2.76 (dd, *J* = 17.5, 8.1 Hz, 1 H), 2.59 (d, *J* = 17.6 Hz, 1 H), 1.09 (s, 3 H), 0.86 (s, 3 H), 0.79 (s, 3 H), 0.71 (s, 3 H) ppm; ^{13}C NMR (100 MHz, CD_3COCD_3): δ = 148.7, 144.6, 139.4, 115.4, 113.8, 104.8, 75.5, 56.1, 50.5, 42.8, 41.5, 40.9, 39.2, 34.2,

33.9, 27.5, 22.9, 22.4, 19.3, 19.2, 14.9 ppm; HRMS (ESI): m/z calcd. for $C_{21}H_{31}O_3$ [M + H]$^+$ 331.2268; found 331.2272. All spectral data match those of authentic puupehenol.[7]



Puupehedione (2): To a solution of puupehenol (**3**, 50 mg, 0.15 mmol) in 1,4-dioxane (2 mL) was added with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 170 mg, 0.75 mmol). The resulting mixture was stirred under reflux for 2 hours,[6] concentrated under reduced pressure, diluted with ether (10 mL), washed with saturated aqueous $NaHCO_3$ (3 x 10 mL) and brine (10 mL), and concentrated. The residue was purified by flash column chromatography over silica gel (100–200 mesh) with EtOAc/petroleum ether (1 : 20 → 1 : 10) to give puupehedione (**2**, 104 mg, 71%) as a red oil. IR (film): ν_{max} = 2922, 2359, 1653, 1646, 1603, 1559, 1457, 1393, 1229, 1065, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.31 (s, 1 H), 6.12 (s, 1 H), 5.95 (s, 1 H), 2.09–2.06 (m, 1 H), 2.03–2.00 (m, 1 H), 1.88 (d, *J* = 9.0 Hz, 1 H), 1.69 (d, *J* = 14.4 Hz, 1 H), 1.60 (d, *J* = 14.2 Hz, 1 H), 1.54 (s, 3 H), 1.47–1.46 (m, 1 H), 1.46–1.42 (m, 1 H), 1.32–1.29 (m, 1 H), 1.24 (s, 3 H), 1.13 (d, *J* = 12.4 Hz, 1 H), 0.96 (s, 3 H), 0.89 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.9, 179.5, 169.4, 164.5, 138.3, 122.1, 115.3, 109.1, 81.8, 43.4, 41.6, 40.8, 38.6, 33.8, 32.7, 30.8, 29.5, 25.1, 21.1, 18.7, 16.7 ppm; HRMS (ESI): m/z calcd. for $C_{21}H_{26}O_3Na$ [M + Na]$^+$349.1774; found 349.1770. All spectral data match those of the natural puupehedione.[8]

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Supplementary Table 1. Comparison of ^{1}H NMR (C_6D_6) spectroscopic data of the natural[3] and synthetic haterumadienone.

Natural δ_H [ppm, *J* (Hz), mult] 500 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
5.65 (s, 1 H)	5.61 (s, 1 H)	0.04
5.24 (d, *J* = 6.5 Hz, 1 H)	5.29 (d, *J* = 6.3 Hz, 1 H)	−0.05
2.82 (d, *J* = 20.0 Hz, 1 H)	2.83 (d, *J* = 20.1 Hz, 1 H)	−0.01
2.78 (d, *J* = 20.0 Hz, 1 H)	2.76 (d, *J* = 20.3 Hz, 1 H)	0.02
1.96 (td, *J* = 14.0, 3.0 Hz, 1 H)	1.96 (d, *J* = 14.5 Hz, 1 H)	0
1.36 (m, 1 H)	1.36−1.34 (m, 1 H)	–
1.31 (d, *J* = 6.5 Hz, 1 H)	1.33−1.31 (m, 1 H)	–
1.31 (m, 1 H)	1.31−1.28 (m, 1 H)	–
1.26 (m, 1 H)	1.27−1.25 (m, 1 H)	–
1.25 (m, 3 H)	1.25−1.22 (m, 3 H)	–
1.15 (dt, *J* = 14.0, 5.0 Hz, 1 H)	1.14 (dd, *J* = 13.9, 5.0 Hz, 1 H)	0.01
1.02 (dt, *J* = 13.5 Hz, 4.0, 1 H)	1.03 (dd, *J* = 11.7, 4.3Hz, 1 H)	−0.01
0.94 (s, 3 H)	0.96 (s, 3 H)	−0.02
0.81 (s, 3 H)	0.81 (s, 3 H)	0
0.74 (s, 3 H)	0.74 (s, 3 H)	0
0.68 (s, 3 H)	0.68 (s, 3 H)	0
0.67 (dt, *J* = 12.5, 5.5 Hz, 1 H)	0.68−0.65 (m, 1 H)	–
0.56 (dd, *J* = 11.5, 2.0 Hz, 1 H)	0.58 (d, *J* = 11.8 Hz, 1 H)	−0.02

Supplementary Table 2. Comparison of ^{1}C NMR (C_6D_6) spectroscopic data of the natural[3] and synthetic haterumadienone.

Natural δ_C ppm, 125 MHz	**Synthetic** δ_C ppm, 100 MHz	**Err** (Natural−Synthetic), $\Delta\delta_H$ (ppm)
199.2	199.0	0.02
177.9	178.0	−0.01
132.9	133.0	−0.01
121.2	121.4	−0.02
110.1	110.1	0
80.1	80.3	−0.02
53.8	54.0	−0.02
53.7	53.9	−0.02
41.8	42.0	−0.02
39.8	40.0	−0.02
39.4	39.6	−0.02
39.4	39.4	0
37.8	37.9	−0.01
33.6	33.7	−0.01
33.1	33.2	−0.01
28.5	28.6	−0.01
22.0	22.1	−0.01
18.4	18.6	−0.02
18.3	18.4	−0.01
14.5	14.7	−0.02

Supplementary Table 3. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the natural[4] and synthetic 20-hydroxyhaterumadienone.

Natural δ_H [ppm, *J* (Hz), mult] 500 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
6.26 (d, *J* = 6.5 Hz, 1 H)	6.28 (d, *J* = 5.5 Hz, 1 H)	−0.02
5.34 (br s, 1 H)	5.35 (br, s, 1 H)	−0.01
4.60 (s, 1 H)	4.62 (s, 1 H)	−0.02
	3.26 (br, s, OH)	−
2.22 (Td, *J* = 14.5, 3.0 Hz, 1 H)	2.23 (d, *J* = 14.2 Hz, 1 H)	0
1.98 (d, *J* = 6.5 Hz, 1 H)	1.99 (d, *J* = 5.2 Hz, 1 H)	−0.01
1.72 (br d, *J* = 12.5 Hz, 1 H)	1.73 (d, *J* = 12.4 Hz, 1 H),	−0.01
1.65 (dt, *J* = 14.5, 5.0 Hz, 1 H)	1.67-1.63 (m, 1 H)	−
1.54 (m, 2 H)	1.55-1.52 (m, 2 H)	−
1.42 (m, 1 H)	1.45-1.41 (m, 1 H)	−
1.40 (m, 2 H)	1.41-1.39 (m, 2 H)	−
1.26 (s, 3 H)	1.27 (s, 3 H)	−0.01
1.16 (dt, *J* = 12.5, 4.0 Hz, 1 H)	1.16 (d, *J* = 15.1 Hz, 1 H)	0
1.10 (dt, *J* = 12.5 Hz, 4.0, 1 H)	1.09 (d, *J* = 13.0 Hz, 1 H)	0.01
0.94 (dd, *J* = 12.5, 2.5 Hz, 1 H)	0.96 (d, *J* = 11.0 Hz, 1 H)	−0.02
0.89 (s, 3 H)	0.91 (s, 3 H)	−0.02
0.82 (s, 3 H)	0.84 (s, 3 H)	−0.02
0.78(s, 3 H)	0.80 (s, 3 H)	−0.02

Supplementary Table 4. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the natural[4] and synthetic 20-hydroxyhaterumadienone.

Natural δ_C ppm, 125 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
202.1	202.3	−0.02
177.8	178.0	−0.01
135.1	135.2	−0.01
123.3	123.4	−0.01
105.0	105.1	−0.01
81.6	81.7	−0.01
70.8	70.8	0
54.1	54.1	0
53.6	53.7	−0.01
41.6	41.7	−0.01
40.1	40.2	−0.01
39.5	39.5	0
39.2	39.3	−0.01
33.6	33.7	0.01
33.1	33.2	−0.01
28.9	28.9	0
21.9	21.9	0
18.3	18.3	0
18.0	18.0	0
14.3	14.4	−0.01

Supplementary Table 5. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the natural[5] and synthetic 20-epihydroxyhaterumadienone.

Natural δ_H [ppm, *J* (Hz), mult] 600 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
6.32 (dt, *J* = 6.6, 1.8 Hz, 1 H)	6.33 (d, *J* = 2.7 Hz, 1 H)	−0.01
5.41 (d, *J* = 1.8 Hz, 1 H)	5.41 (s, 1 H)	0
4.52 (ddd, *J* = 2.4, 1.8, 1.8 Hz, 1 H)	4.54 (s, 1 H)	−0.02
2.7 (d, *J* = 2.4 Hz, OH)		–
2.24 (ddd, *J* = 14.5, 3.6, 3.0 Hz, 1 H)	2.23 (d, *J* = 13.9 Hz, 1 H)	0.01
2.02 (d, *J* = 6.6 Hz, 1 H)	2.01 (d, *J* = 4.8 Hz, 1 H)	0.01
1.71(ddd, *J* = 12.6, 4.8, 3.6 Hz, 1 H)	1.70 (d, *J* = 12.4 Hz, 1 H)	0.01
1.65 (ddd, *J* = 14.5, 13.5, 4.8 Hz, 1 H)	1.63 (d, *J* = 16.9 Hz, 1 H)	0.02
1.54 (m, 2 H)	1.56−1.53 (m, 2 H)	–
1.46 (m, 1 H)	1.49−1.46 (m, 1 H)	–
1.43 (m, 2 H)	1.45−1.43 (m, 2 H)	–
1.30 (s, 3 H)	1.30 (s, 3 H)	0
1.21 (ddd, *J* = 13.2, 12.6, 4.0 Hz, 1 H)	1.20 (m, 1 H)	–
1.16 (dt, *J* = 12.6, 12.0, 3.6 Hz, 1 H)	1.14 (d, *J* = 11.8 Hz, 1 H)	0.02
0.99 (dd, *J* = 12.0, 2.4 Hz, 1 H)	0.98 (d, *J* = 11.6 Hz, 1 H)	0.01
0.92 (s, 3 H)	0.92 (s, 3 H)	0
0.86 (s, 3 H)	0.86 (s, 3 H),	0
0.82 (s, 3 H)	0.82 (s, 1 H)	0

Supplementary Table 6. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the natural[5] and synthetic 20-epihydroxyhaterumadienone.

Natural δ_C ppm, 150 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
201.9	202.1	−0.02
178.8	179.0	−0.02
134.2	134.4	−0.02
125.9	125.9	0
106.8	106.9	−0.01
81.9	82.0	−0.01
70.0	70.0	0
54.0	54.1	−0.01
54.0	54.1	−0.01
41.6	41.6	0
40.1	40.1	0
39.8	39.8	0
39.3	39.3	0
33.7	33.7	0
33.2	33.2	0
28.6	28.6	0
22.0	22.0	0
18.3	18.3	0
18.0	18.1	−0.01
14.9	14.9	0

Supplementary Table 7. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the natural[6] and synthetic 20-acetoxyhaterumadienone.

Natural δ_H [ppm, *J* (Hz), mult] 400 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
6.16 (d, *J* = 6.6 Hz, 1 H)	6.16 (s, 1 H)	0
5.65 (s, 1 H)	5.67 (s, 1 H)	−0.02
5.45 (s, 1 H)	5.44 (s, 1 H)	0.01
2.25 (dt, *J* = 14.7, 2.9 Hz, 1 H)	2.23 (d, *J* = 15.1 Hz, 1 H)	0.02
2.19 (s, 3 H)	2.19 (s, 3 H)	0
1.97 (d, *J* = 6.6 Hz, 1 H)	1.98 (d, *J* = 4.2 Hz, 1 H)	−0.01
1.66 (td, *J* = 14.0, 5.2 Hz, 1 H)	1.66 (d, *J* = 12.9 Hz, 1 H)	0
1.60 (m, 1 H)	1.62−1.59 (m, 1 H)	−
1.54 (m, 2 H)	1.56−1.52 (m, 2 H)	−
1.47 (m, 1 H)	1.49−1.45 (m, 1 H)	−
1.45 (m, 2 H)	1.45−1.42 (m, 2 H)	−
1.28 (s, 3 H)	1.27 (s, 3 H)	0.01
1.22 (m, 1 H)	1.21−1.18 (m, 1 H)	−
1.12 (dt, *J* = 12.7, 3.0 Hz, 1 H)	1.13 (d, *J* = 13.9 Hz, 1 H)	−0.01
0.97 (dd, *J* = 11.7, 2.1 Hz, 1 H)	0.96 (d, *J* = 11.2 Hz, 1 H)	0.01
0.92 (s, 3 H)	0.91 (s, 3 H)	0.01
0.85 (s, 3 H)	0.85 (s, 3 H)	0
0.80 (s, 3 H)	0.80 (s, 3 H)	0

Supplementary Table 8. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the natural[6] and synthetic 20-acetoxyhaterumadienone.

Natural δ_C ppm, 100 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
197.0	196.8	0.02
177.0	177.2	−0.02
171.0	170.8	0.02
133.2	133.2	0
124.6	124.6	0
107.1	107.1	0
80.7	81.6	0.01
70.7	70.7	0
54.0	54.1	−0.01
54.0	53.8	0.02
41.6	41.6	0
40.2	40.2	0
39.7	39.8	−0.01
39.2	39.2	0
33.7	33.7	0
33.1	33.2	−0.01
28.8	28.9	−0.01
21.9	21.9	0
21.0	20.8	−0.02
18.3	18.3	0
18.1	18.1	0

14.5	14.5	0

Supplementary Table 9. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the authentic[1] and synthetic puupehenone.

Authentic δ_H [ppm, *J* (Hz), mult] 400 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
6.88 (s, br, 1 H)	6.88 (s, br, 1 H)	0
6.66 (d, *J* = 6.8 Hz, 1 H)	6.66 (d, *J* = 6.9 Hz, 1 H)	0
6.20 (s, 1 H)	6.20 (s, 1 H)	0
5.86 (d, *J* = 1.3 Hz, 1 H)	5.86 (s, 1 H)	0
2.04 (d, *J* = 7.0 Hz, 1 H)	2.04 (d, *J* = 6.9 Hz, 1 H)	0
1.23 (s, 3 H)	1.23 (s, 3 H)	0
0.91 (s, 3 H)	0.91 (s, 3 H)	0
0.84 (s, 3 H)	0.85 (s, 3 H)	−0.01
0.81 (s, 3 H)	0.82 (s, 3 H)	−0.01

Supplementary Table 10. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the authentic[1] and synthetic puupehenone.

Authentic δ_C ppm, 125 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
182.0	182.1	−0.01
162.8	162.8	0
147.4	147.5	−0.01
140.6	140.4	0.02
129.3	129.2	0.01
106.0	106.1	−0.01
105.1	105.1	0
78.8	78.9	−0.01
54.8	54.9	−0.01
53.8	53.9,	−0.01
41.6	41.7	−0.01
40.7	40.8	−0.01
40.0	40.1	−0.01
39.2	39.3	−0.01
33.7	33.7	0
33.3	33.3	0
28.0	28.1	−0.01
21.9	21.9	0
18.4	18.5	−0.01
18.1	18.1	0
15.0	15.0	0

Supplementary Table 11. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the authentic[7] and synthetic puupehenol.

Authentic δ_H [ppm, *J* (Hz), mult] 400 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
	7.51 (s, OH)	−
	7.08 (s, OH)	−
6.39 (s, 1 H)	6.46 (s, 1 H)	−0.07
6.09 (s, 1 H)	6.16 (s, 1 H)	−0.07
2.65 (dd, *J* = 17.5, 8.0 Hz, 1 H)	2.76 (dd, *J* = 17.5, 8.1 Hz, 1 H)	−0.11
2.48 (d, *J* = 17.5, Hz, 1 H)	2.59 (d, *J* = 17.6 Hz, 1 H)	−0.11
0.99 (s, 3 H)	1.09 (s, 3 H)	−0.1
0.76 (s, 3 H)	0.86 (s, 3 H)	−0.1
0.68 (s, 3 H)	0.79 (s, 3 H)	−0.11
0.59 (s, 3 H)	0.71 (s, 3 H)	−0.12

Supplementary Table 12. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the authentic[7] and synthetic puupehenol.

Authentic δ_C ppm, 100 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
148.4	148.7	−0.03
144.6	144.6	0
139.4	139.4	0
115.2	115.4	−0.02
113.6	113.8	−0.02
104.7	104.8	−0.01
75.3	75.5	−0.02
55.8	56.1	−0.03
50.3	50.5	−0.02
42.6	42.8	−0.02
41.3	41.5	−0.02
40.6	40.8	−0.02
39.0	39.2	−0.02
34.0	34.2	−0.02
33.7	33.9	−0.02
27.3	27.5	−0.02
22.6	22.9	−0.03
22.2	22.4	−0.02
19.1	19.3	−0.02
19.0	19.2	−0.02
14.7	14.9	−0.02

Supplementary Table 13. Comparison of ^{1}H NMR ($CDCl_3$) spectroscopic data of the natural[8] and synthetic puupehedione.

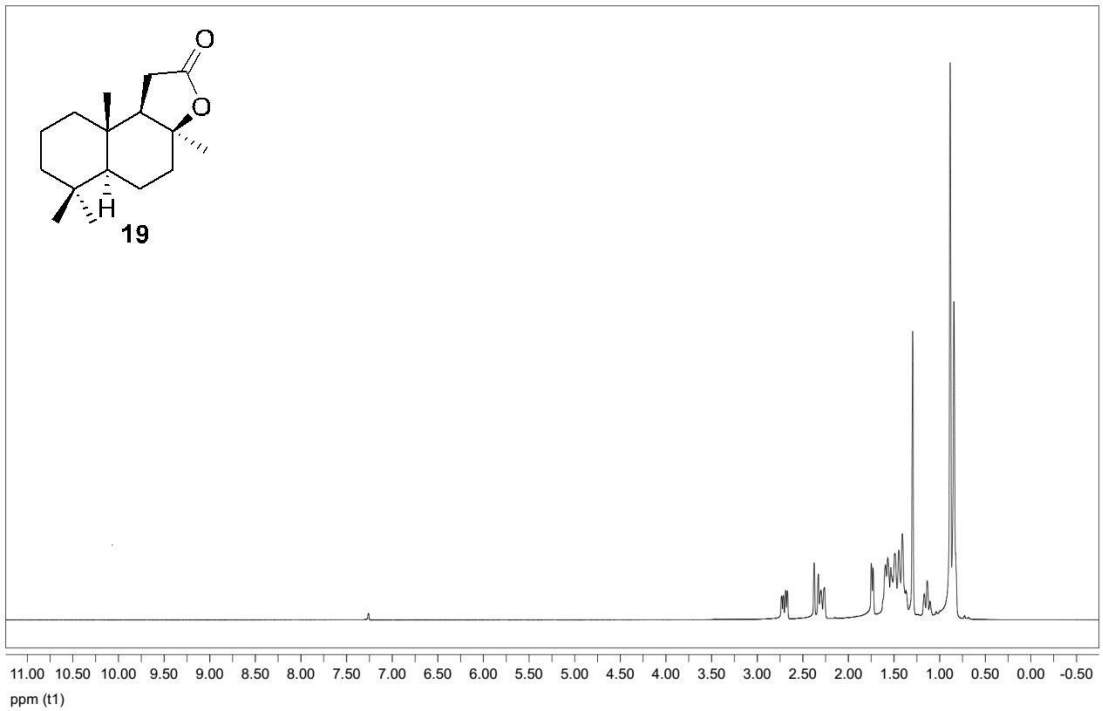
Natural δ_H [ppm, *J* (Hz), mult] 300 MHz	**Synthetic** δ_H [ppm, *J* (Hz), mult] 400 MHz	**Err** (Natural−Synthetic) $\Delta\delta_H$ (ppm)
6.30 (s, 1 H)	6.31 (s, 1 H)	−0.01
6.11 (s, 1 H)	6.12 (s, 1 H)	−0.01
5.95 (s, 1 H)	5.95 (s, 1 H)	0
2.05 (m, 1 H)	2.09−2.06 (m, 1 H)	−
2.02 (m, 1 H)	2.03−2.00 (m, 1 H)	−
1.88 (m, 1 H)	1.88 (d, *J* = 9.0 Hz, 1 H)	−
1.69 (m, 1 H)	1.69 (d, *J* = 14.4 Hz, 1 H)	−
1.57 (m, 1 H)	1.60 (d, *J* = 14.2 Hz, 1 H)	−
1.52 (s, 3 H)	1.54 (s, 3 H)	−0.02
1.46 (m, 1 H)	1.47−1.46 (m, 1 H)	−
1.45 (m, 1 H)	1.46−1.42 (m, 1 H)	−
1.29 (m, 1 H)	1.32−1.29 (m, 1 H)	−
1.23 (s, 3 H)	1.24 (s, 3 H)	−0.01
1.13 (m, 1 H)	1.13 (d, *J* = 12.4 Hz, 1 H)	0
0.94 (s, 3 H)	0.96 (s, 3 H)	−0.02
0.88 (s, 3 H)	0.89 (s, 3 H)	−0.01

Supplementary Table 14. Comparison of ^{13}C NMR ($CDCl_3$) spectroscopic data of the natural[8] and synthetic puupehenol.

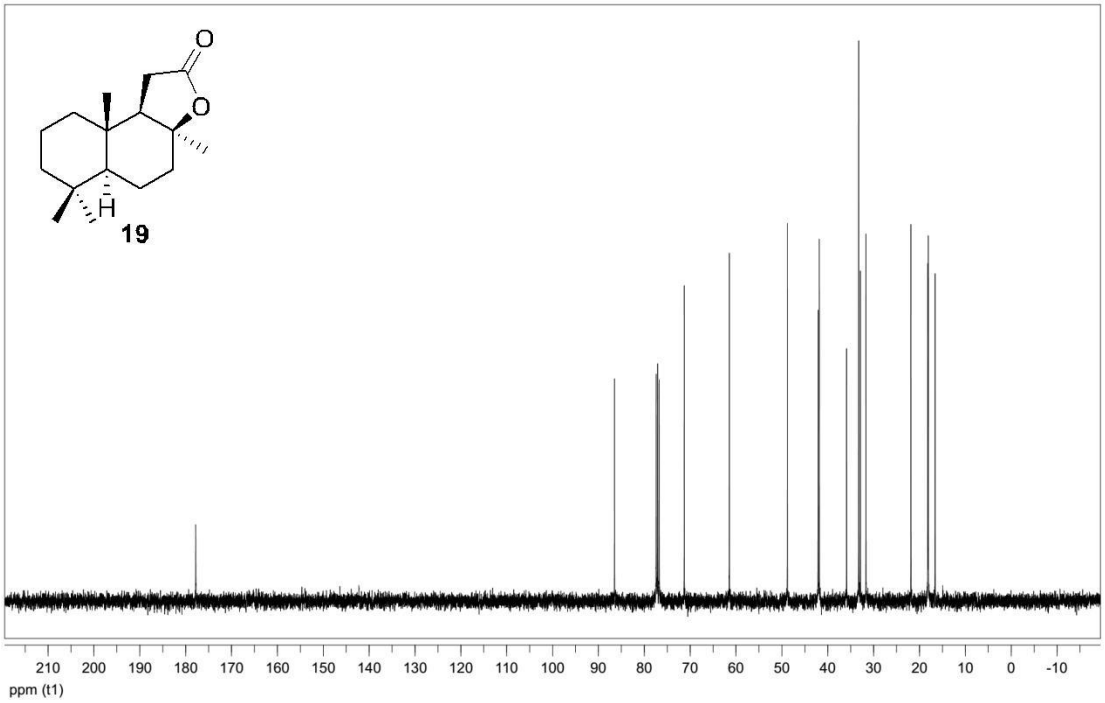
Natural δ_C ppm, 100 MHz	**Synthetic** δ_C ppm, 400 MHz	**Err** (Natural−Synthetic), $\Delta\delta_C$ (ppm)
180.9	180.9	0
179.4	179.5	−0.01
169.5	169.4	0.01
164.6	164.5	0.01
138.3	138.3	0
122.0	122.1	−0.01
115.2	115.3	−0.01
109.0	109.1	−0.01
81.8	81.8	0
43.2	43.4	−0.02
41.5	41.6	−0.01
40.8	40.8	0
38.4	38.6	−0.02
33.8	33.8	0
32.6	32.7	−0.01
30.8	30.8	0
29.4	29.5	−0.01
25.0	25.1	−0.01
21.0	21.1	−0.01
18.6	18.7	−0.01
16.6	16.7	−0.01

4 ^{1}H and ^{13}C NMR Spectra of Compounds

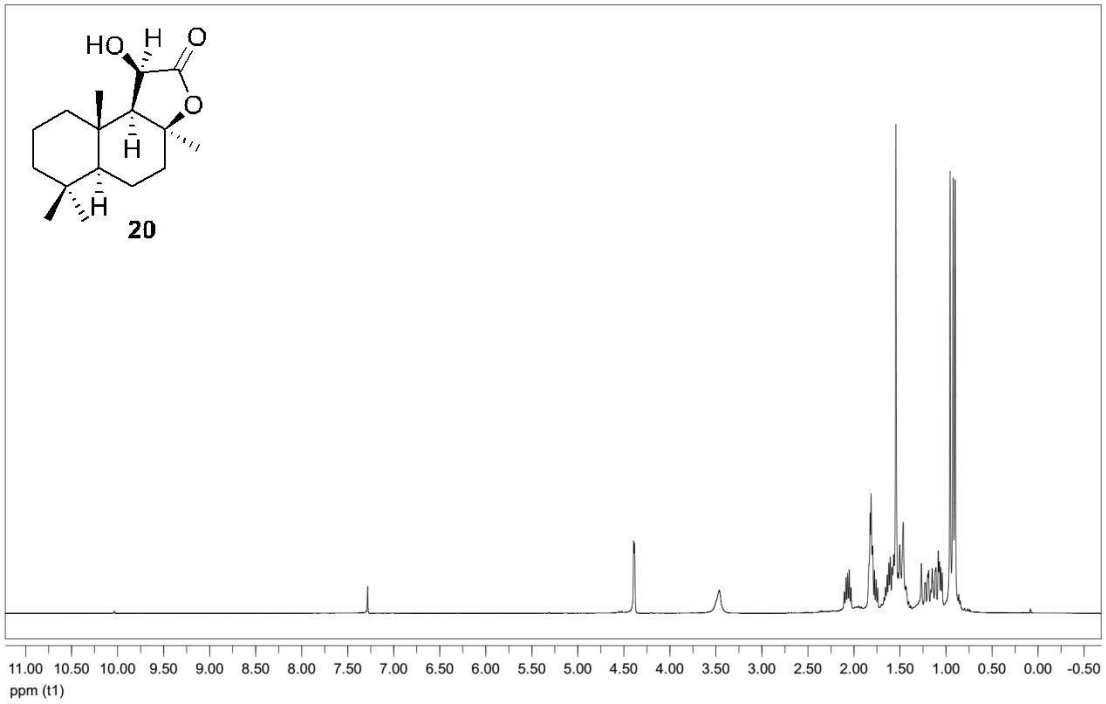
^{1}H NMR Spectrum of 8-episclareolide (19) (400 MHz, $CDCl_3$)



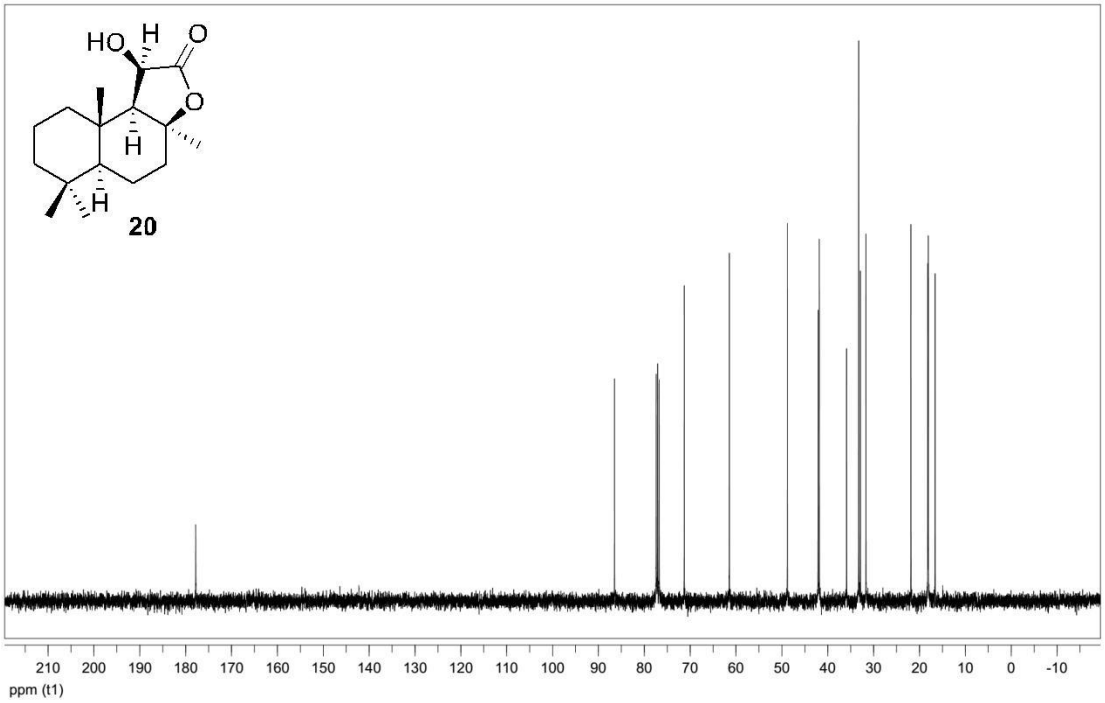
^{13}C NMR Spectrum of 8-episclareolide (19) (100 MHz, $CDCl_3$)



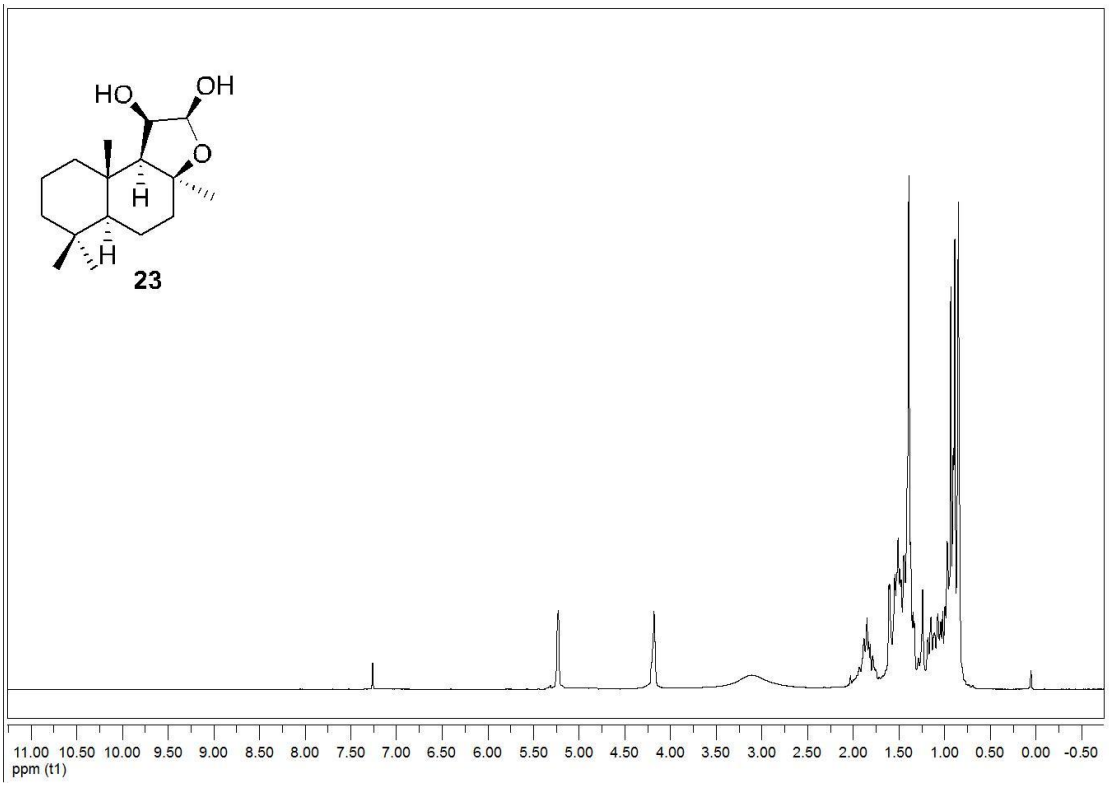
^{1}H NMR Spectrum of α-Hydroxy Lactone 20 (400 MHz, $CDCl_3$)



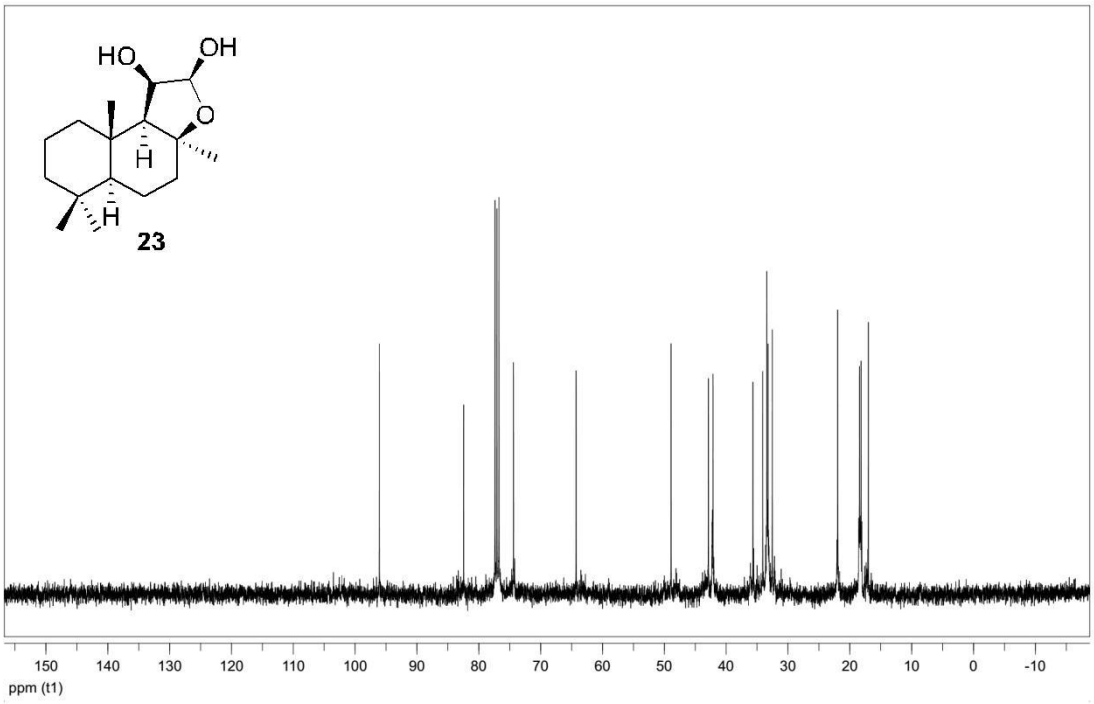
^{13}C NMR Spectrum of α-Hydroxy Lactone 20 (100 MHz, $CDCl_3$)



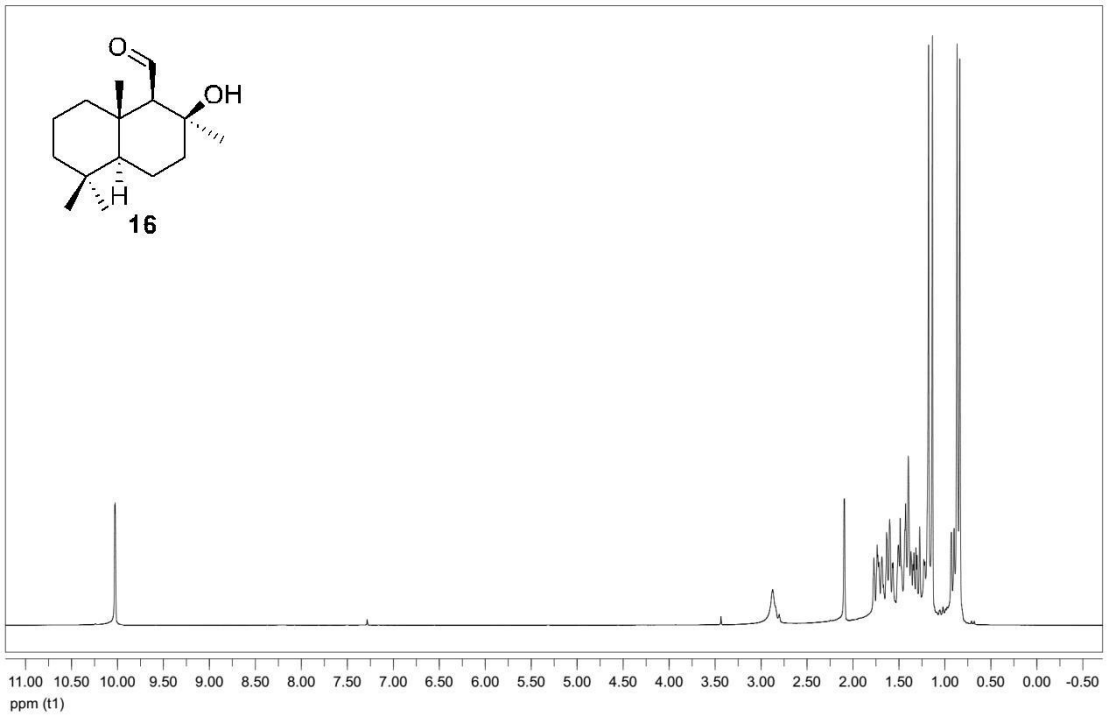
^{1}H NMR Spectrum of Lactol 23 (400 MHz, $CDCl_3$)



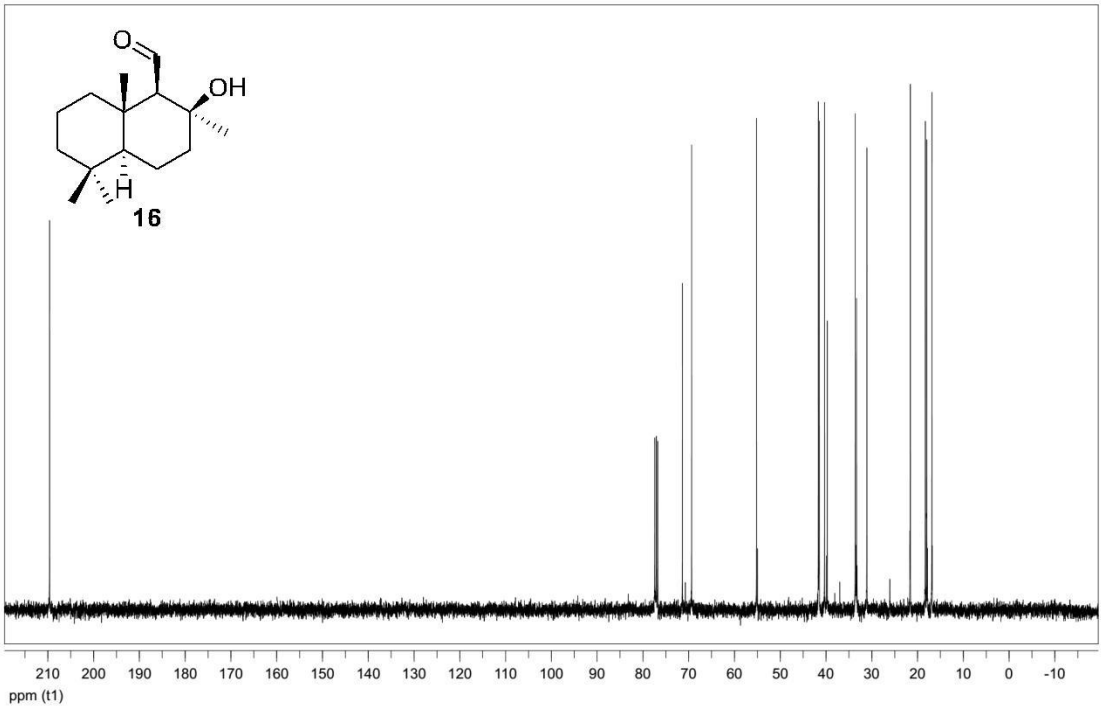
^{13}C NMR Spectrum of Lactol 23 (100 MHz, $CDCl_3$)



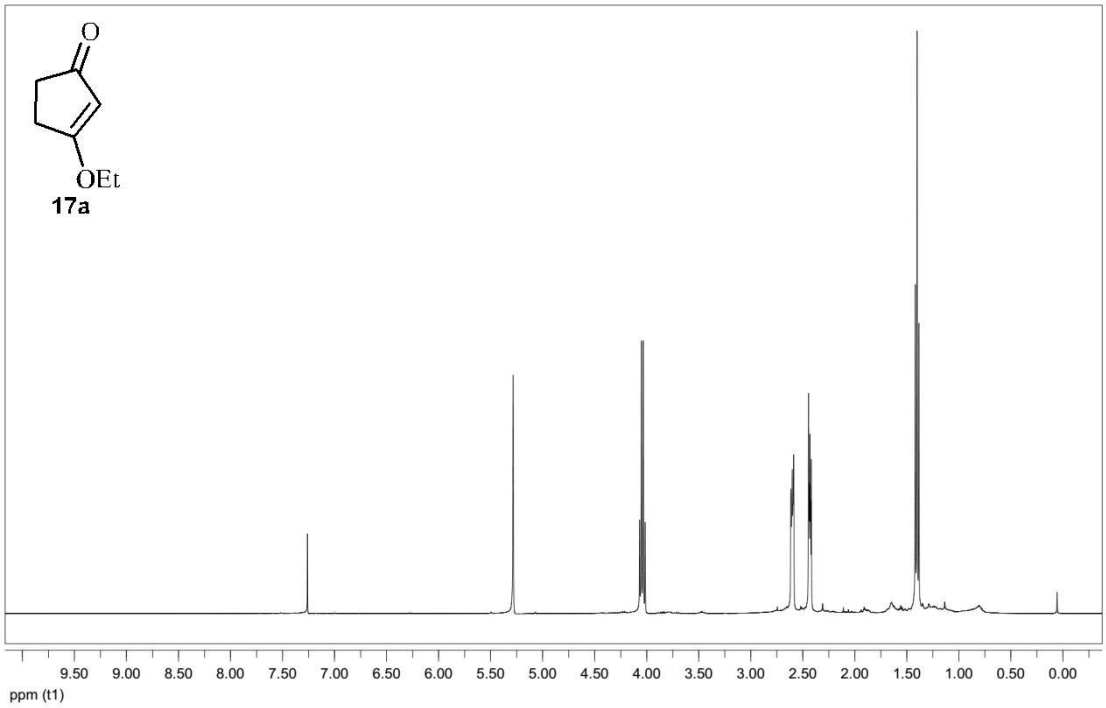
^{1}H NMR Spectrum of *β*-Hydroxy Aldehyde 16 (400 MHz, $CDCl_3$)



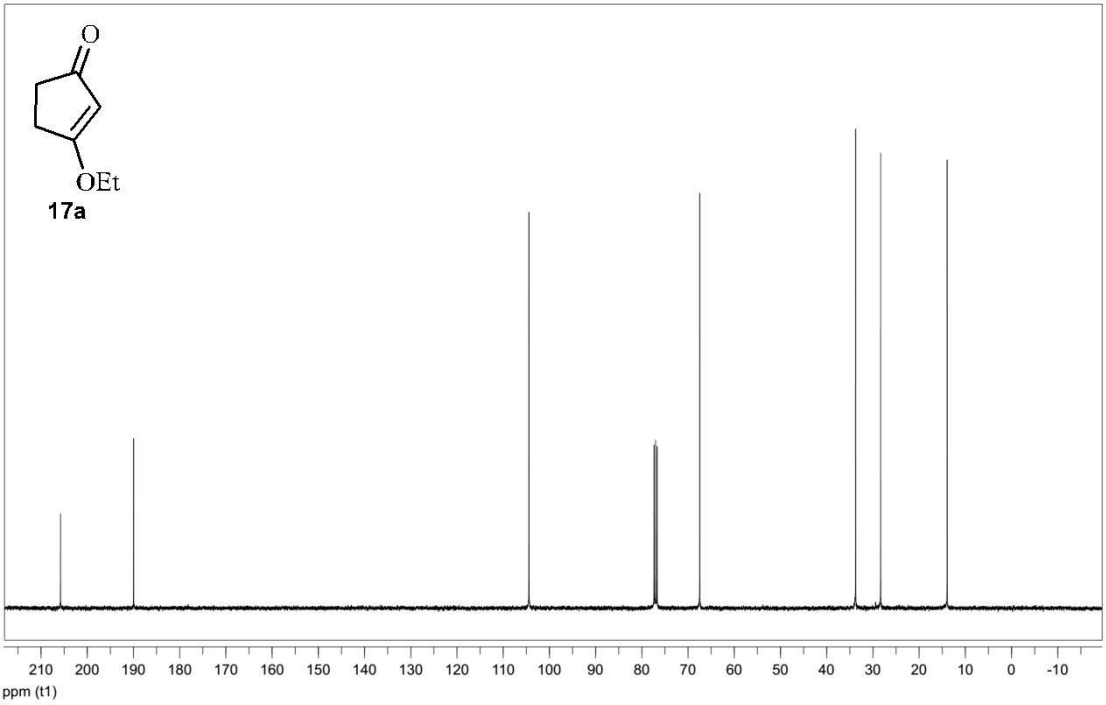
^{13}C NMR Spectrum of *β*-Hydroxy Aldehyde 16 (100 MHz, $CDCl_3$)



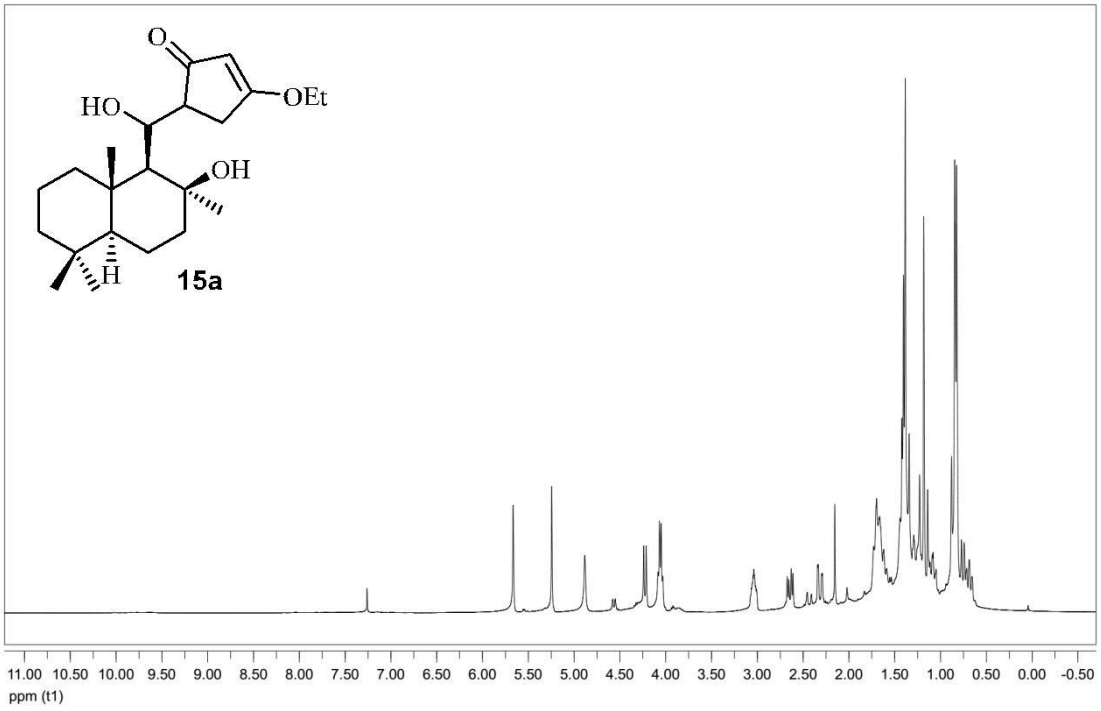
^{1}H NMR Spectrum of *β*-Alkoxy Enone 17a (400 MHz, $CDCl_3$)



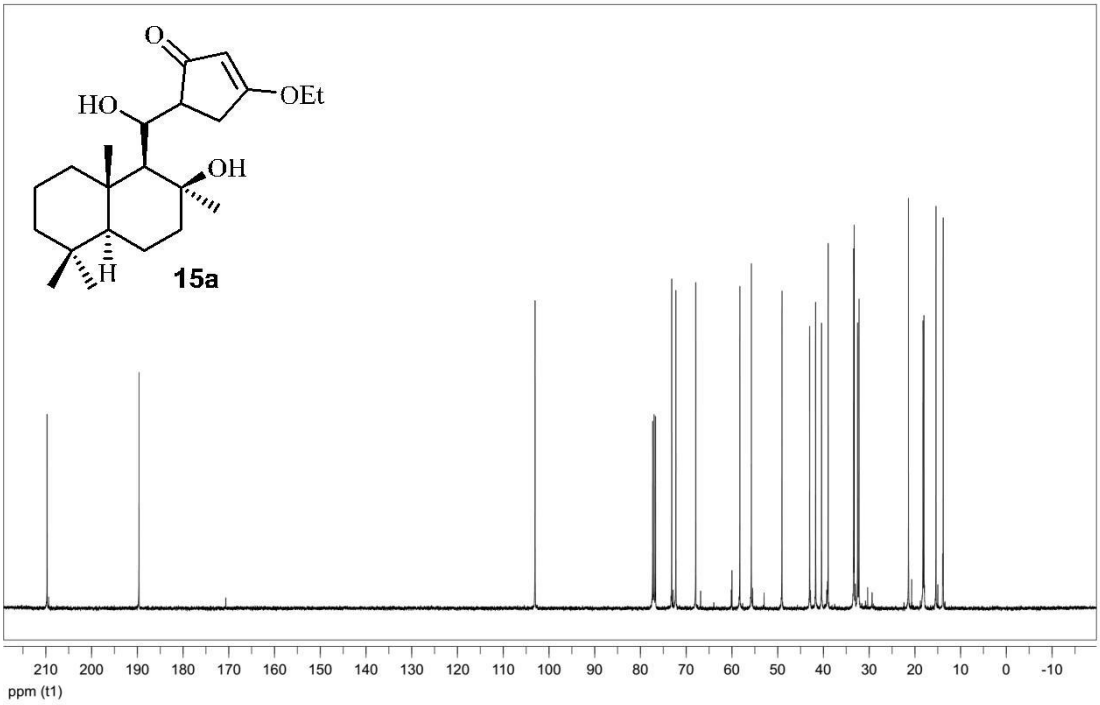
^{13}C NMR Spectrum of *β*-Alkoxy Enone 17a (100 MHz, $CDCl_3$)



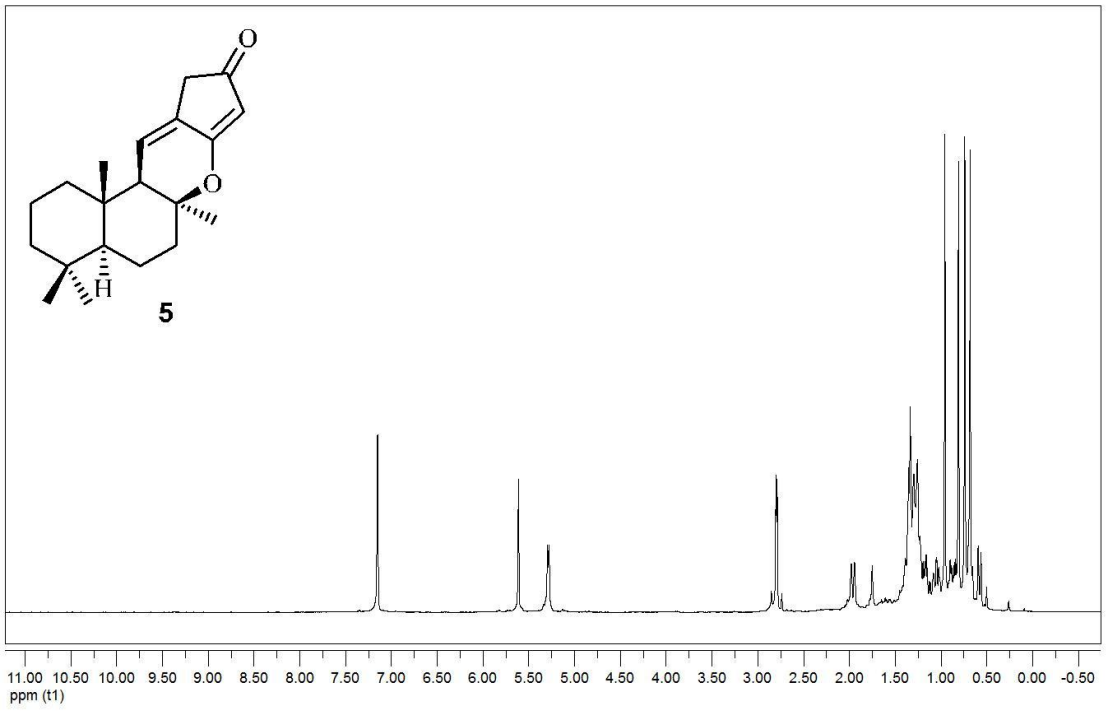
^{1}H NMR Spectrum of Aldol Adduct 15a (400 MHz, $CDCl_3$)



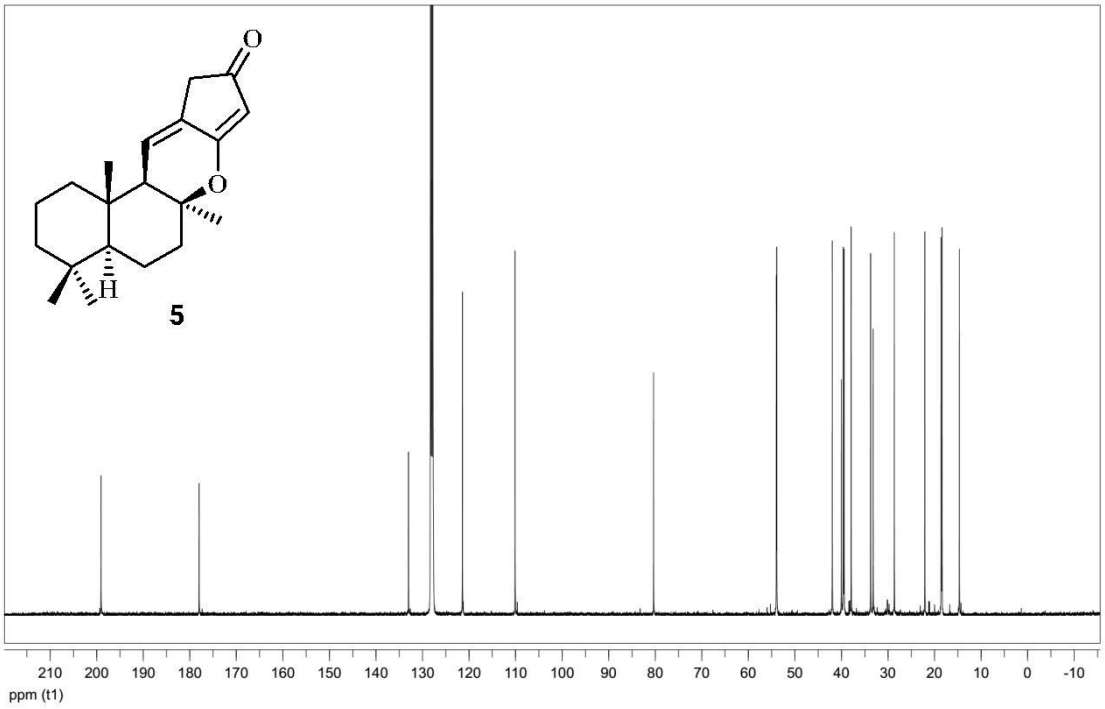
^{13}C NMR Spectrum of Aldol Adduct 15a (100 MHz, $CDCl_3$)



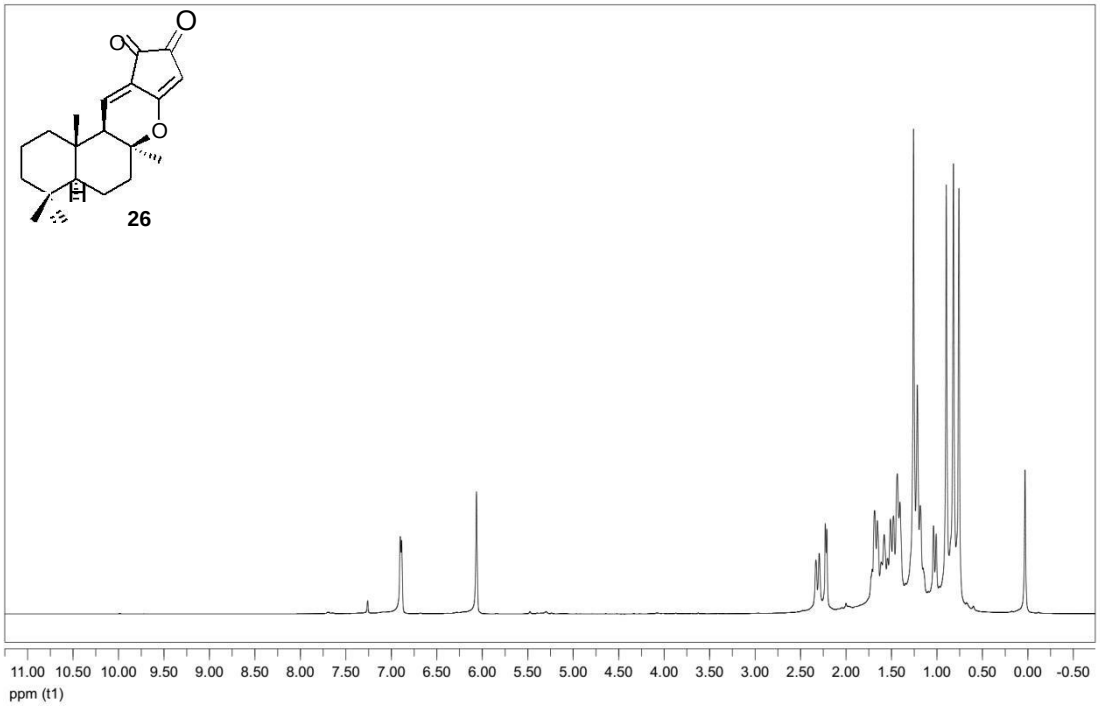
^{1}H NMR Spectrum of Haterumadienone (5) (400 MHz, C_6D_6)



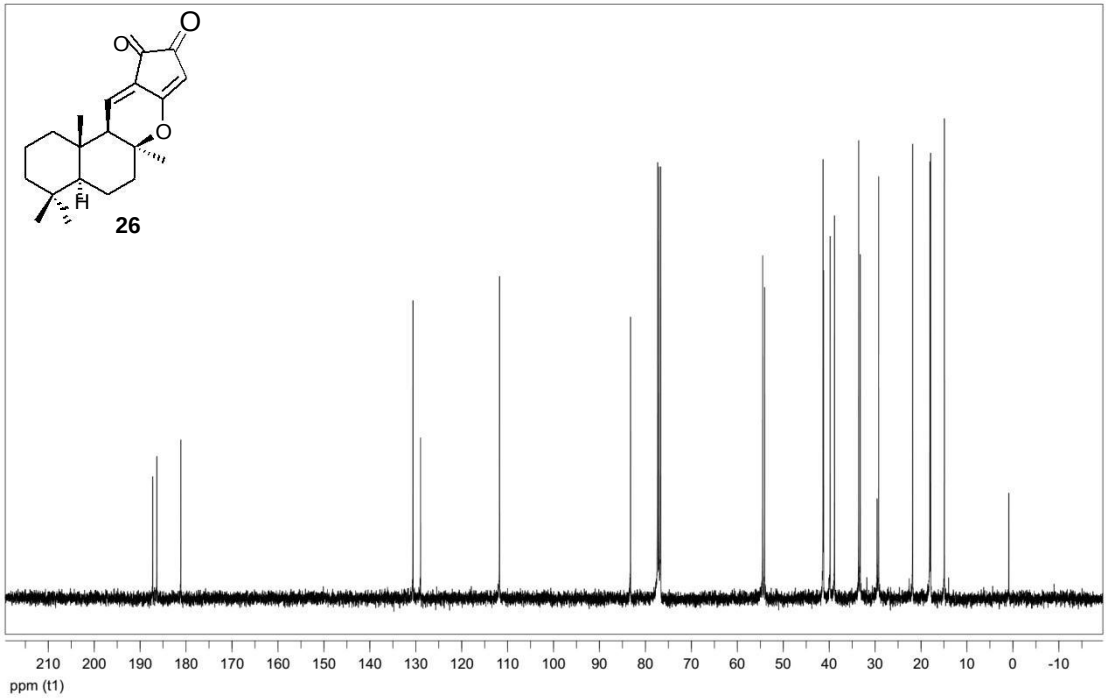
^{13}C NMR Spectrum of Haterumadienone (5) (100 MHz, C_6D_6)



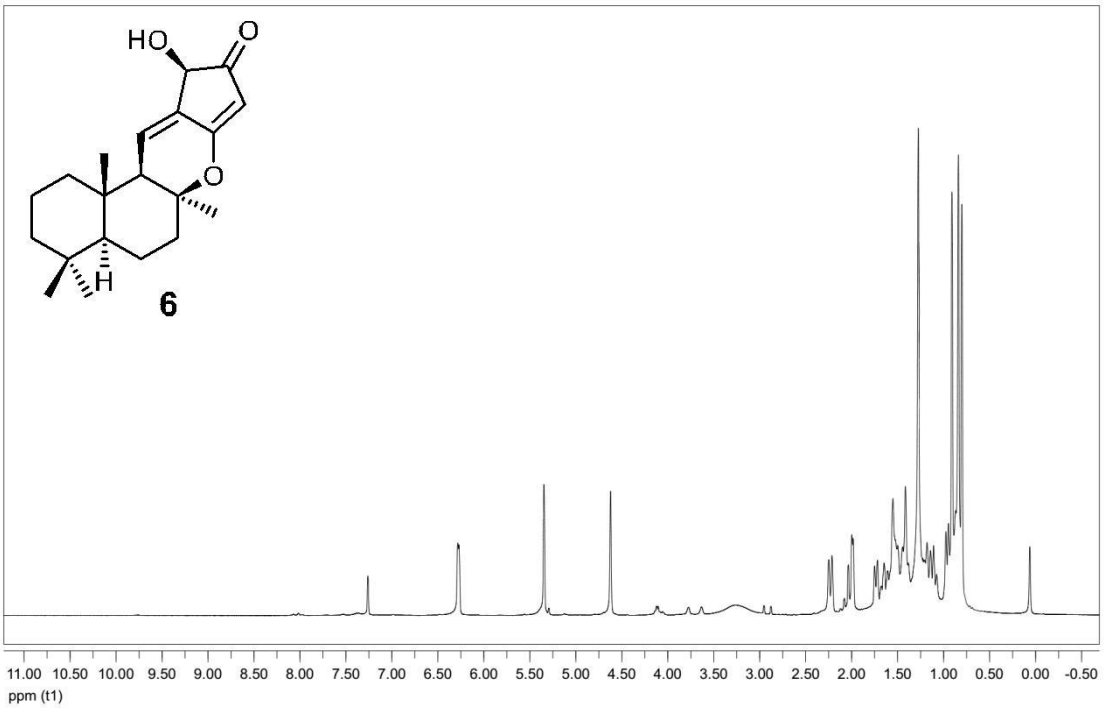
^{1}H NMR Spectrum of Haterumadiendione (26) (400 MHz, $CDCl_3$)



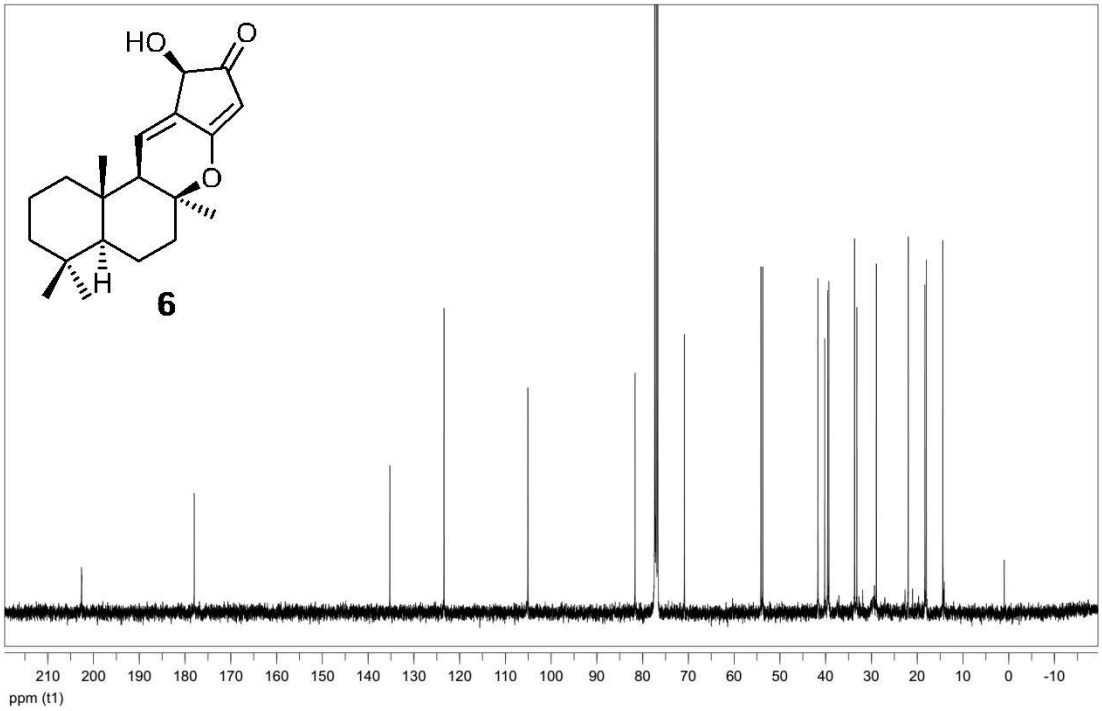
^{13}C NMR Spectrum of Haterumadiendione (26) (100 MHz, $CDCl_3$)



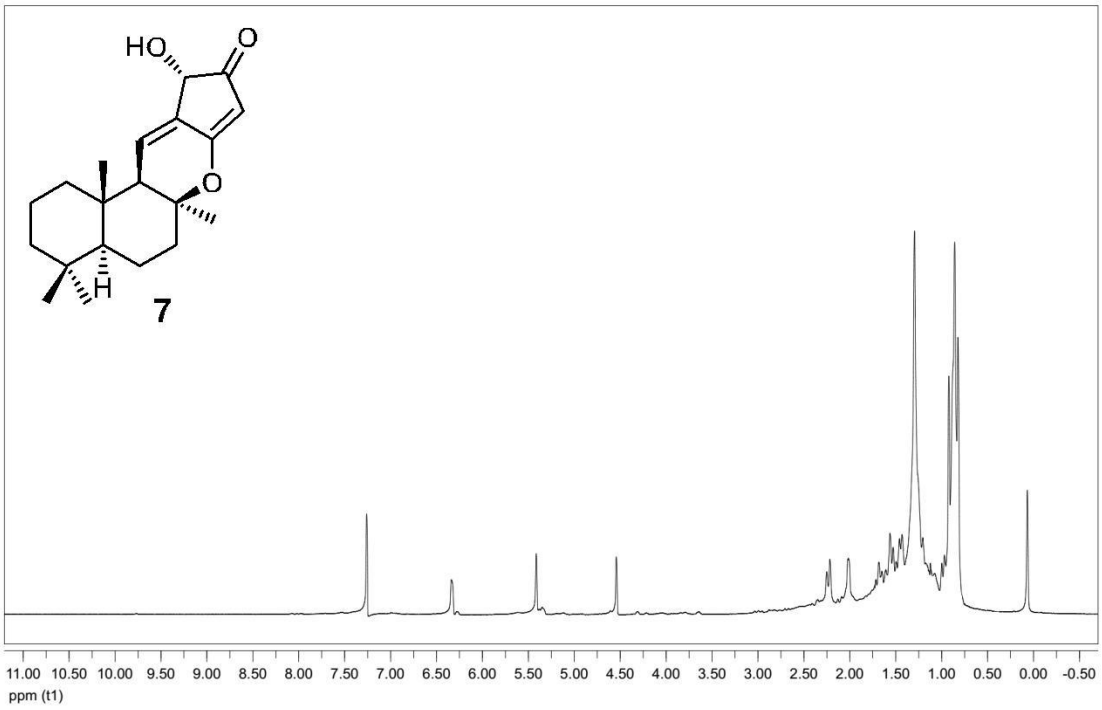
^{1}H NMR Spectrum of 20-Hydroxyhaterumadienone (6) (400 MHz, $CDCl_3$)



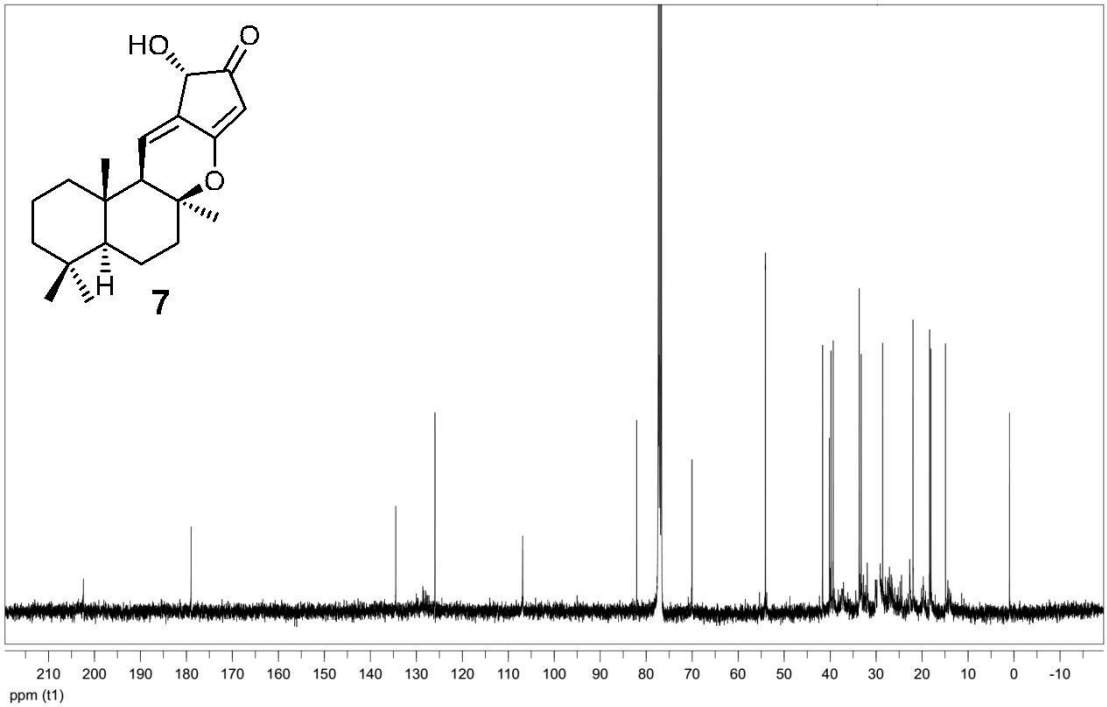
^{13}C NMR Spectrum of 20-Hydroxyhaterumadienone (6) (100 MHz, $CDCl_3$)



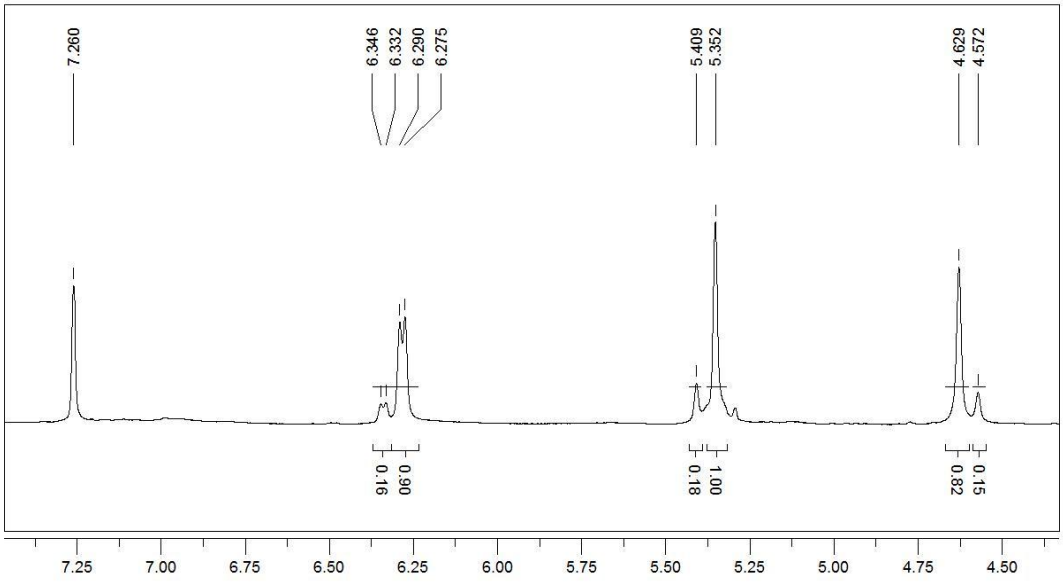
^{1}H NMR Spectrum of 20-*epi*-Hydroxyhaterumadienone (7) (400 MHz, $CDCl_3$)



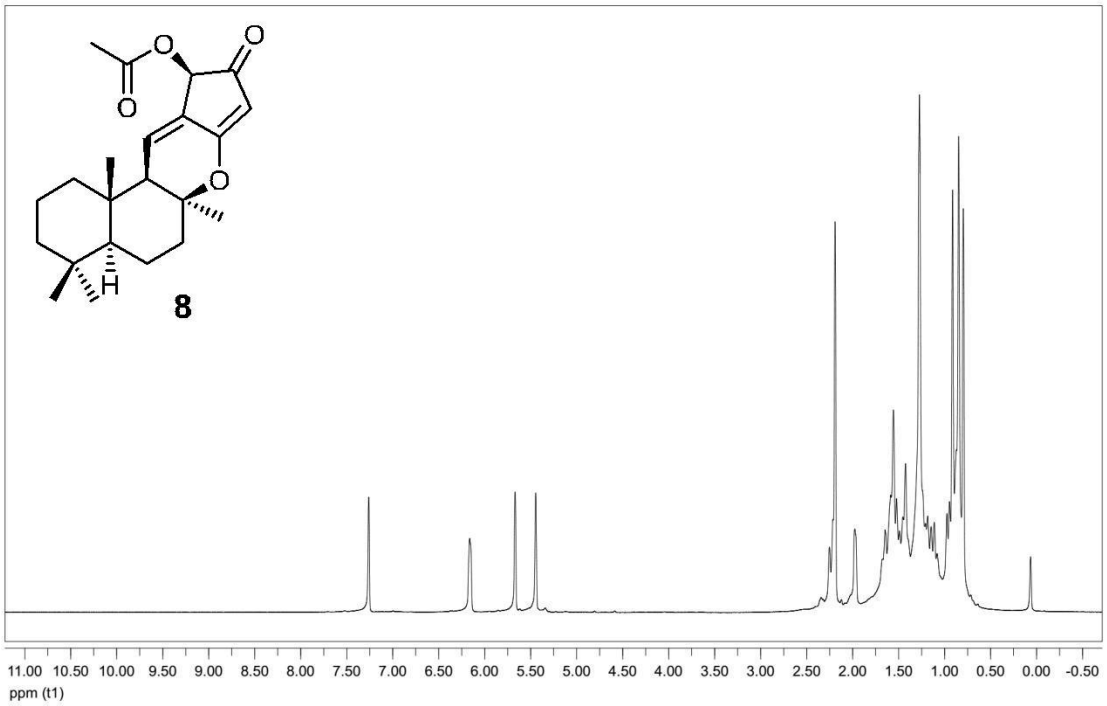
^{13}C NMR Spectrum of 20-*epi*-Hydroxyhaterumadienone (7) (100 MHz, $CDCl_3$)



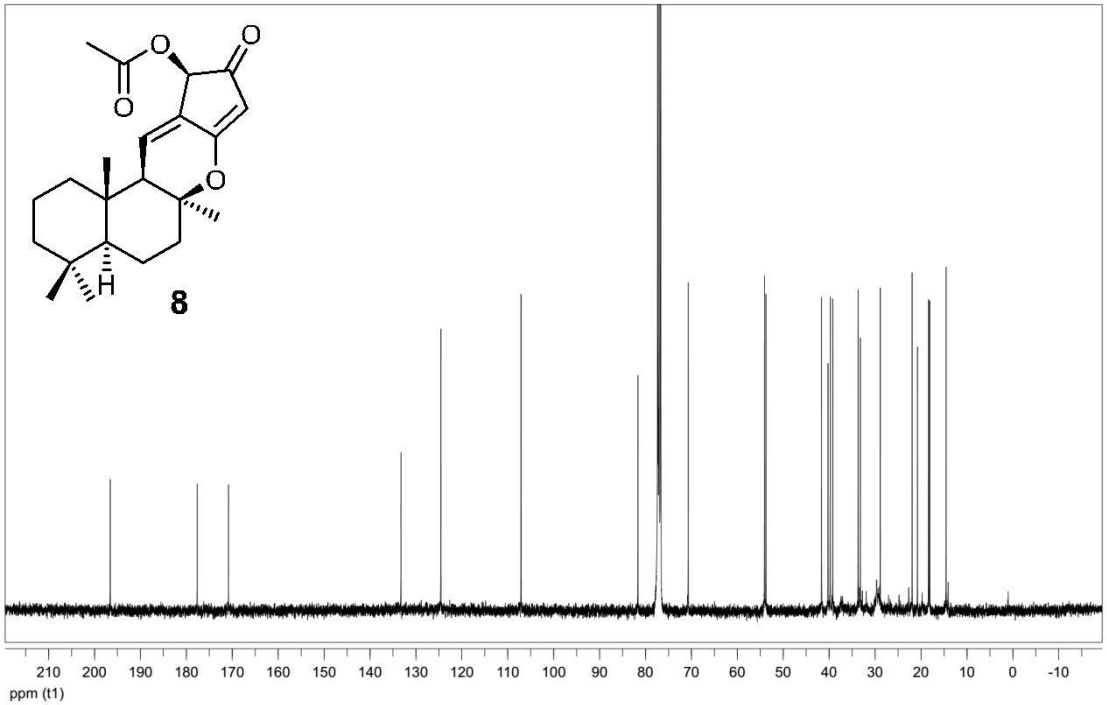
The Ratio of 6 and 7



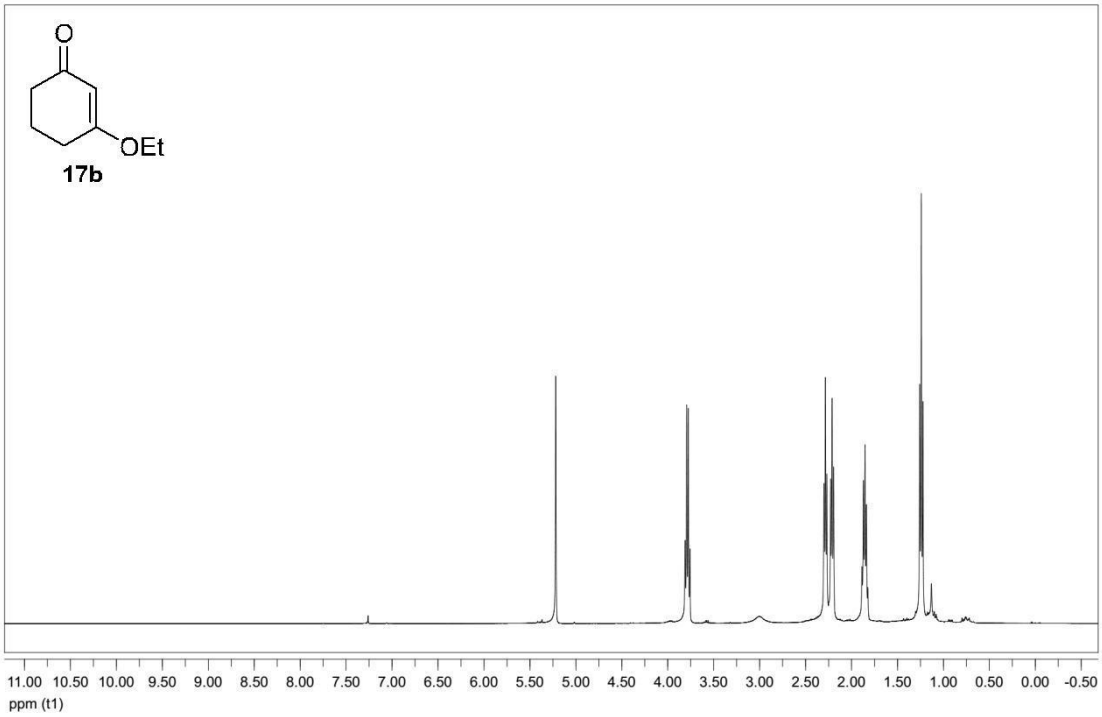
^{1}H NMR Spectrum of 20-Acetoxyhaterumadienone (8) (400 MHz, $CDCl_3$)



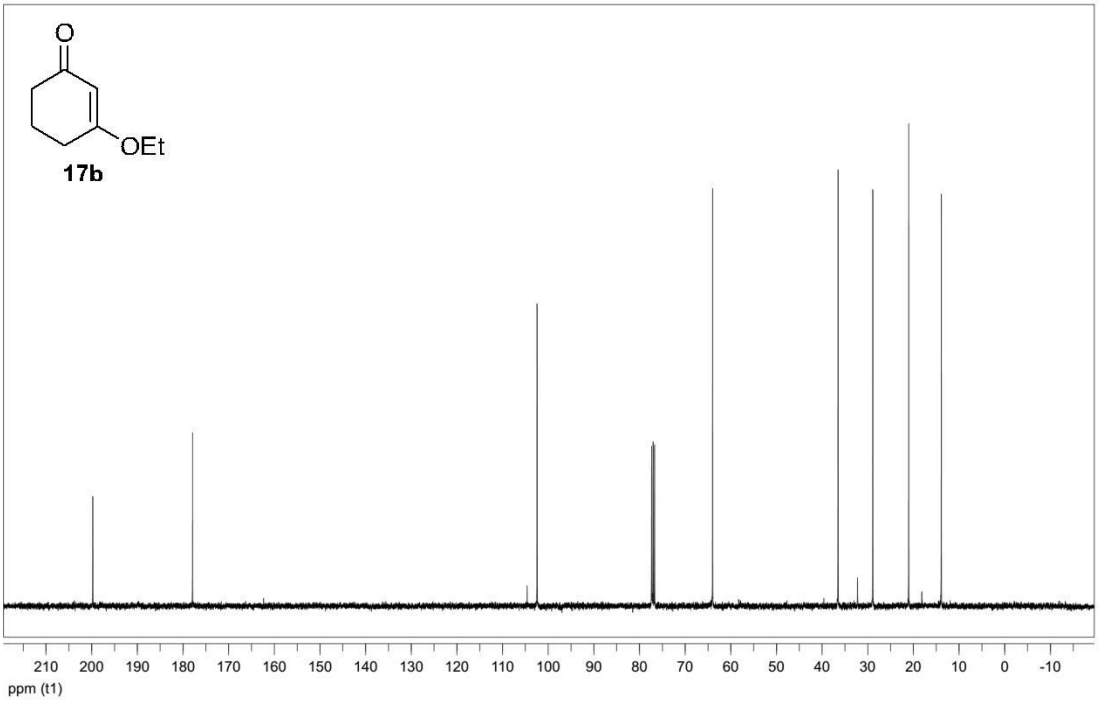
^{13}C NMR Spectrum of 20-Acetoxyhaterumadienone (8) (100 MHz, $CDCl_3$)



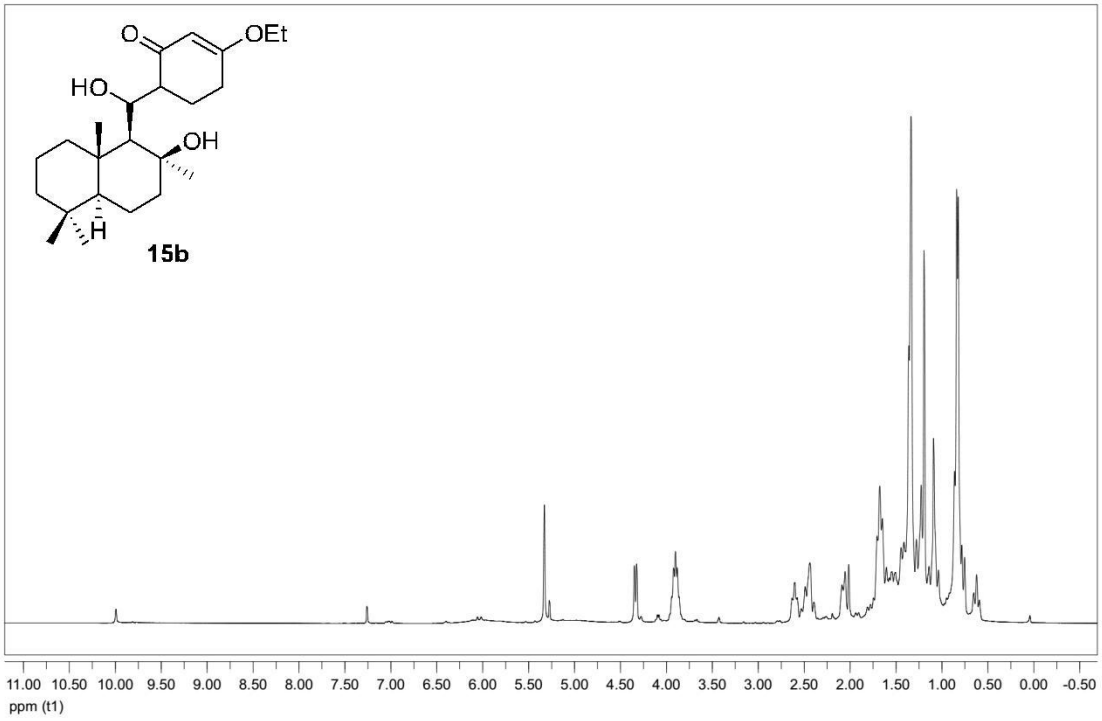
^{1}H NMR Spectrum of *β*-Alkoxy Enone 17b (400 MHz, $CDCl_3$)



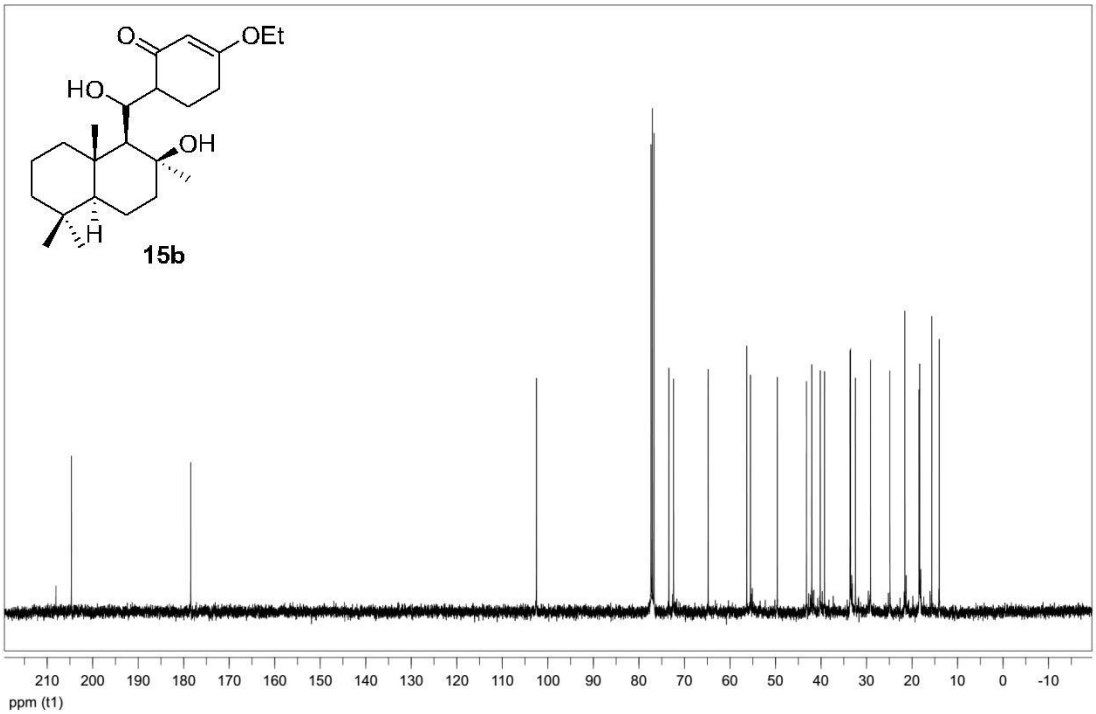
^{13}C NMR Spectrum of *β*-Alkoxy Enone 17b (100 MHz, $CDCl_3$)



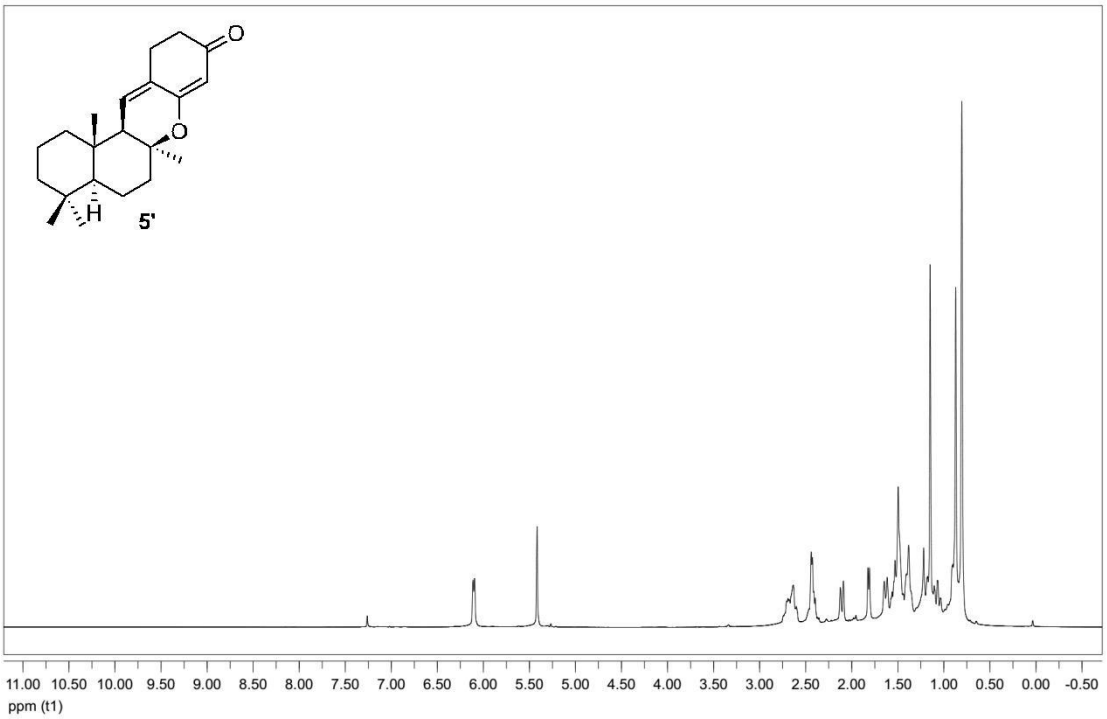
^{1}H NMR Spectrum of Aldol Adduct 15b (400 MHz, $CDCl_3$)



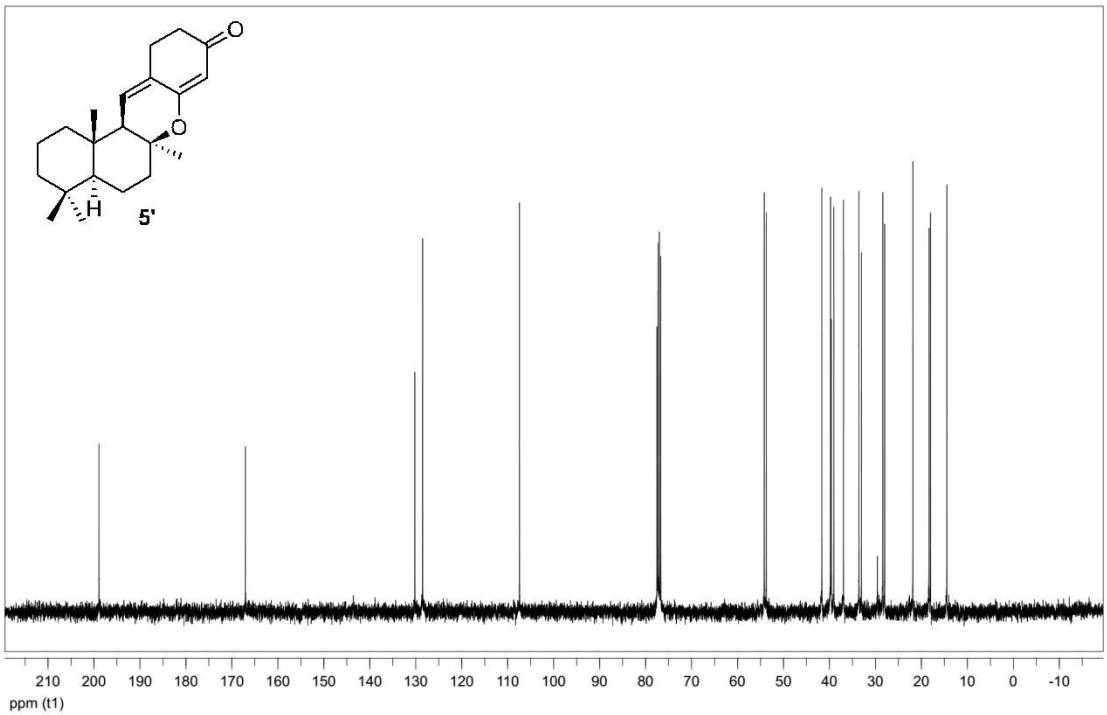
^{13}C NMR Spectrum of Aldol Adduct 15b (100 MHz, $CDCl_3$)



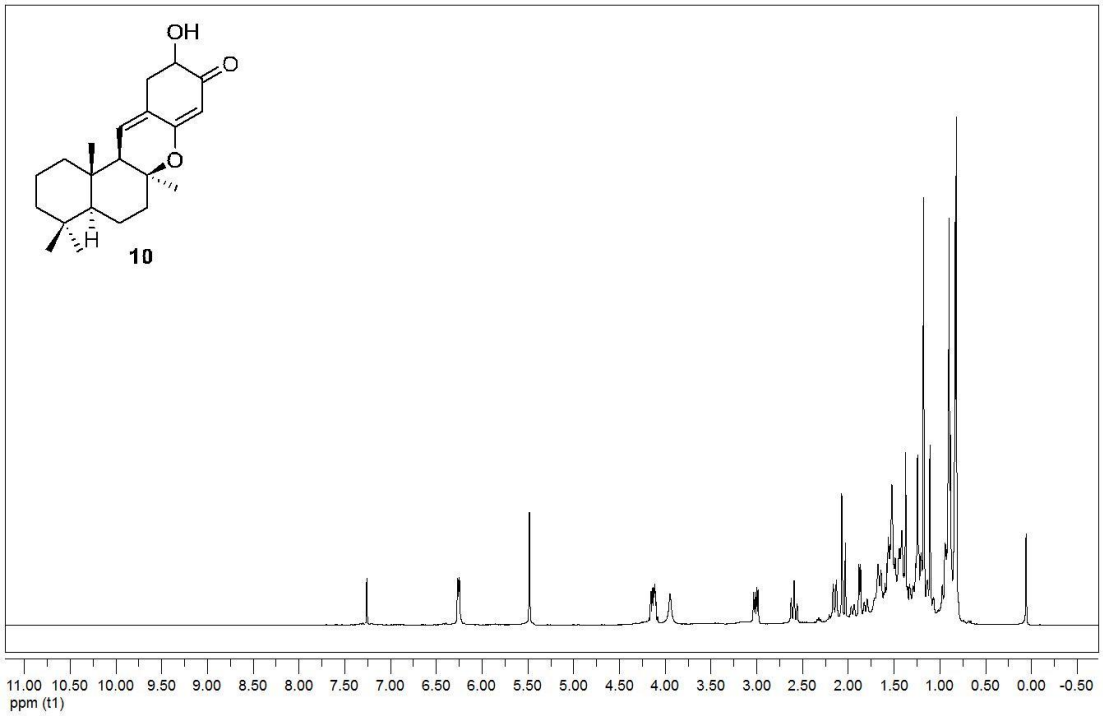
^{1}H NMR Spectrum of Enone 5' (400 MHz, $CDCl_3$)



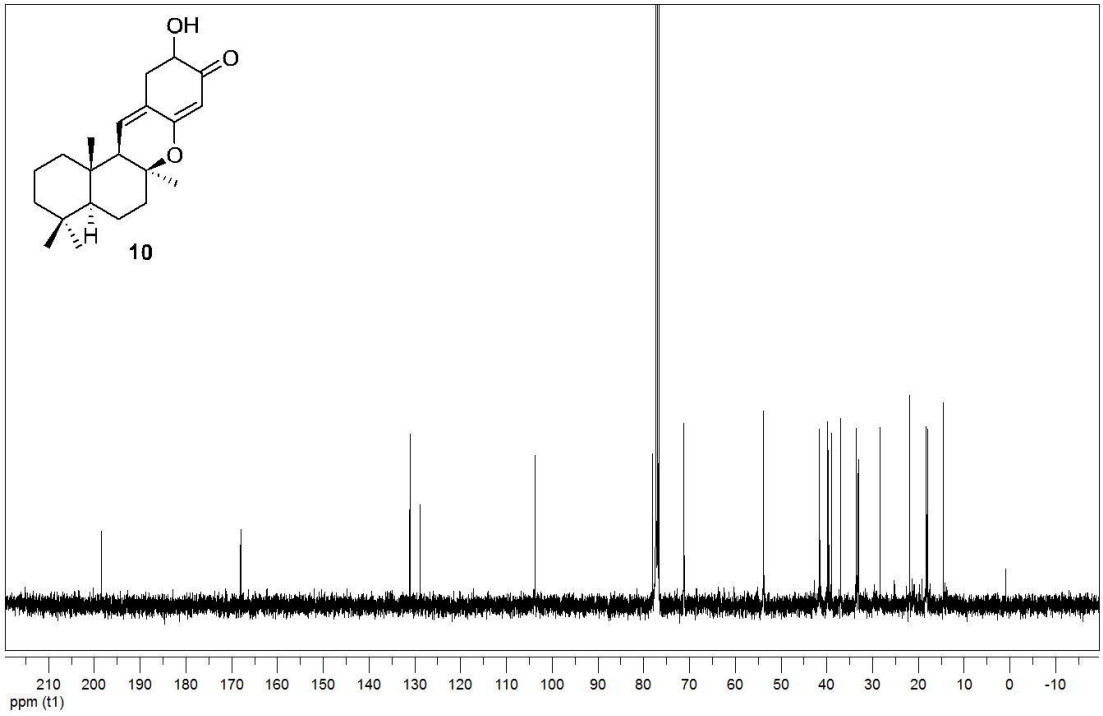
^{13}C NMR Spectrum of Enone 5' (100 MHz, $CDCl_3$)



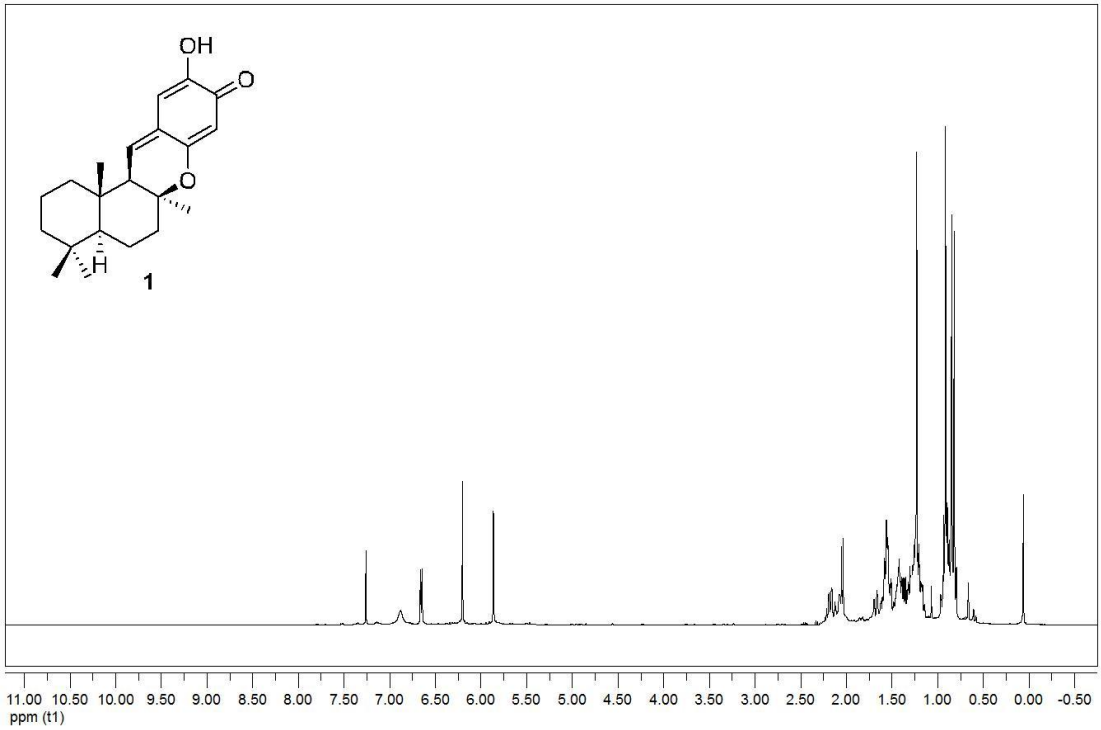
^{1}H NMR Spectrum of *α*-Hydroxylated Product 10 (400 MHz, $CDCl_3$)



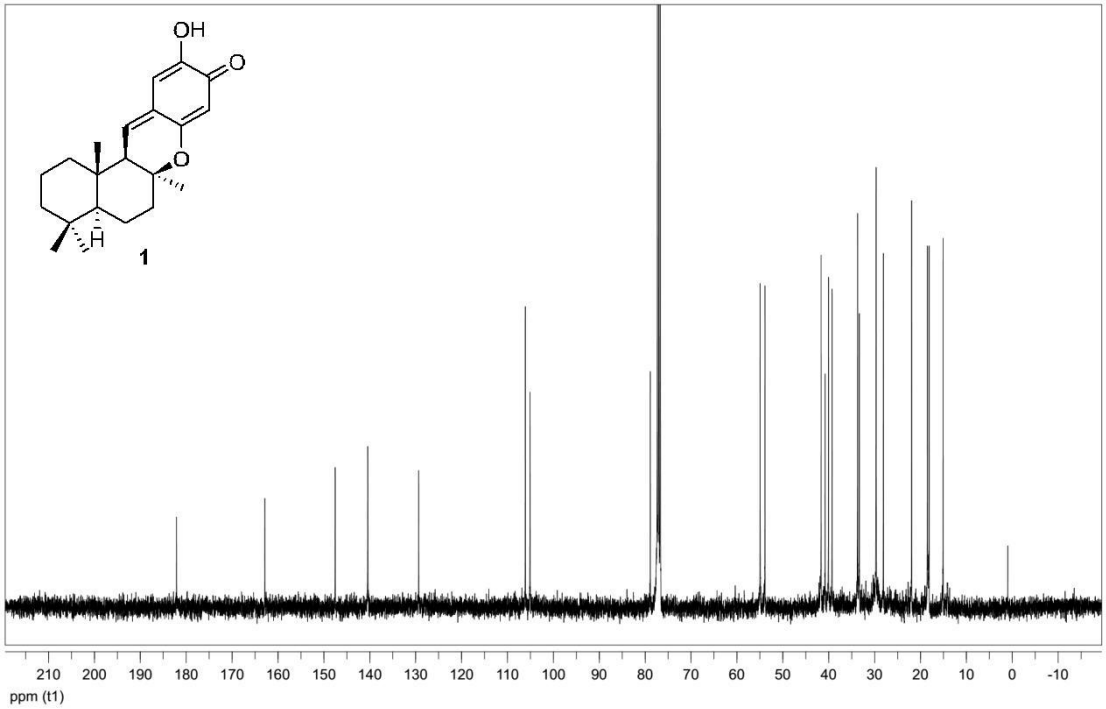
^{13}C NMR Spectrum of *α*-Hydroxylated Product 10 (100 MHz, $CDCl_3$)



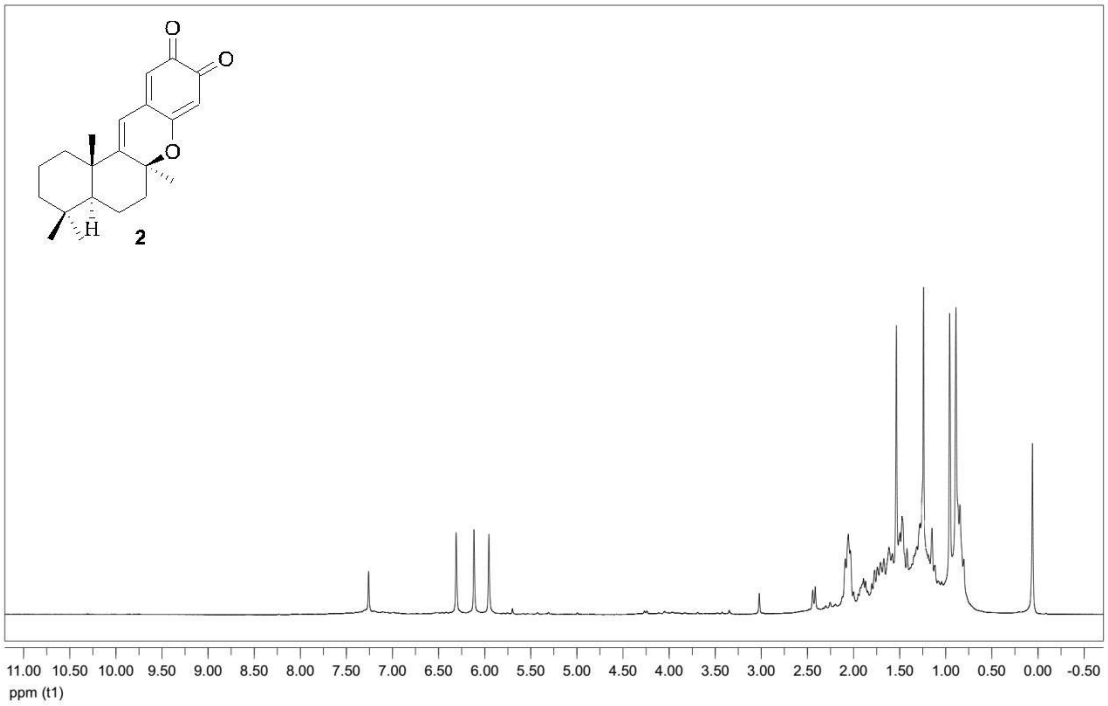
^{1}H NMR Spectrum of Puupehenone (1) (400 MHz, $CDCl_3$)



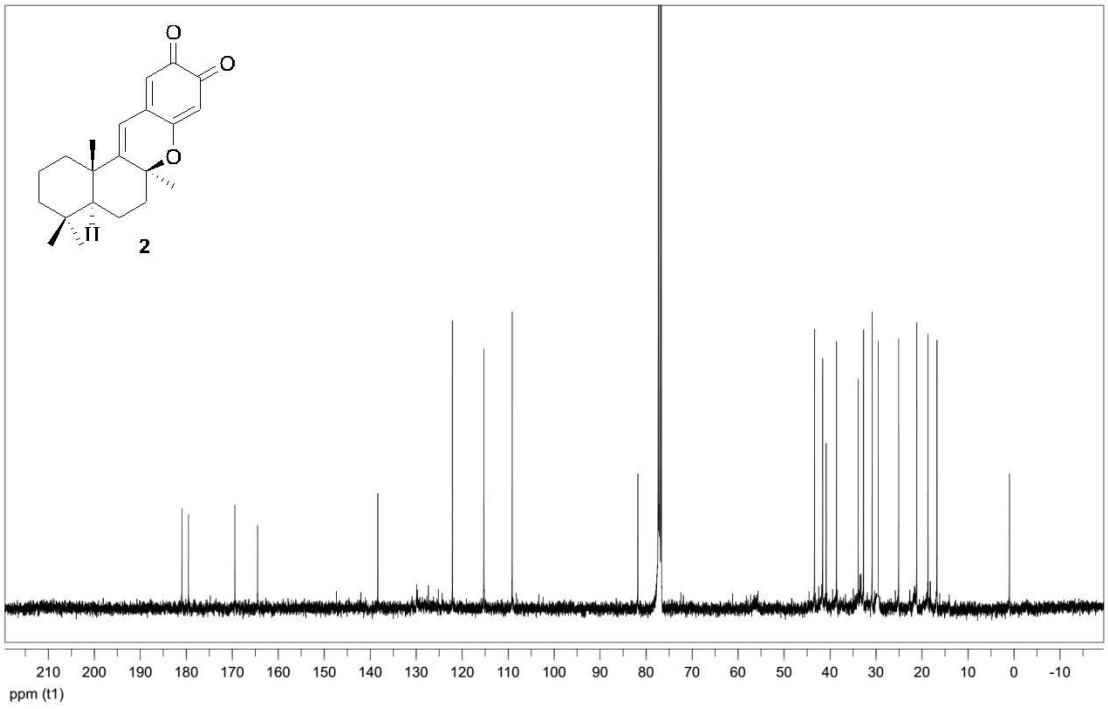
^{13}C NMR Spectrum of Puupehenone (1) (100 MHz, $CDCl_3$)



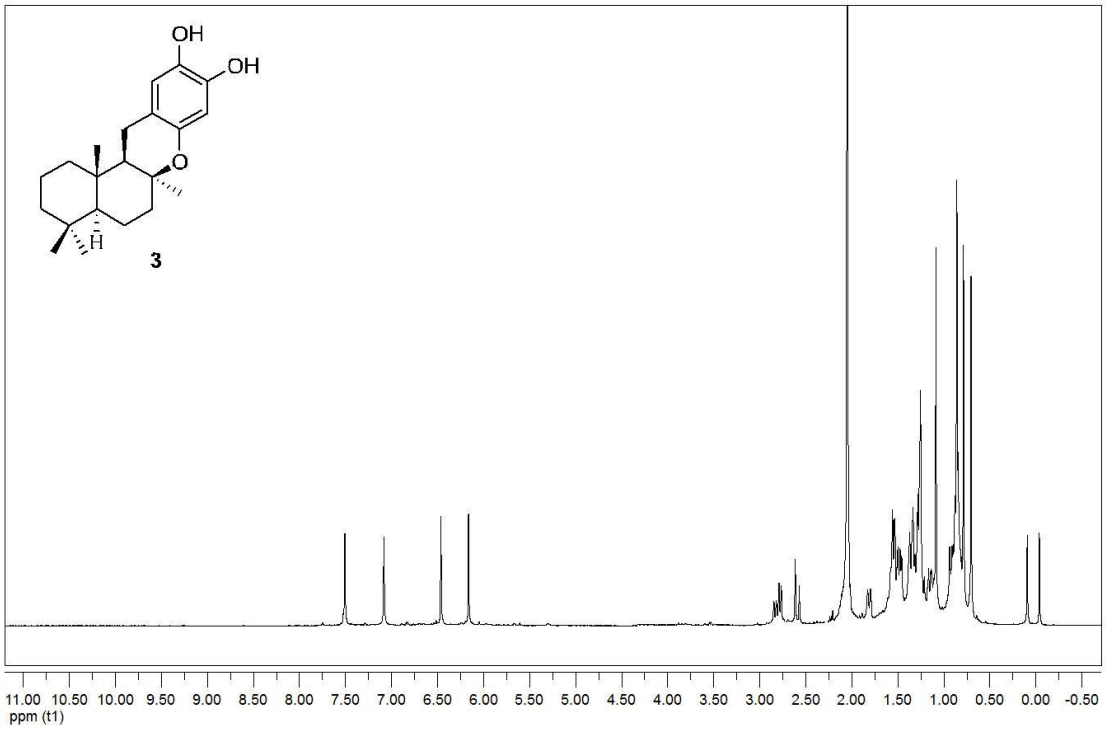
^{1}H NMR Spectrum of Puupehedione (2) (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of Puupehedione (2) (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of Puupehenol (3) (400 MHz, CD_3COCD_3)



^{13}C NMR Spectrum of Puupehenol (3) (100 MHz, CD_3COCD_3)