Supporting information

Tris*nor*-euphane-type triterpenoid and other constituents isolated from *Euphorbia tanquahuete* Sessé & Moc. Preparation and cytotoxic evaluation of semisynthetic derivatives of euphol

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Spectroscopic Data of Isolated Compounds.

Squalene

Colorless oil, 175 mg; Rf 0.33 (*n*-hexane 100 %); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm) 5.11 (6H, *m*, vinylic hydrogens), 2.04 (20H, *m*, methylenes), 1.68 (6H, *s*, methyls), 1.60 (18H, *s*, methyls). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm) 135.25, 135.04, 131.38, 124.57, 124.46, 124.44, 39.92, 39.90, 28.44, 26.94, 26.83, 25.85, 17.83, 16.2, 16.16. Spectroscopic constants were consistent with those reported in the literature.[1]

1-Octacosanol

Flat plates (n-hexane/EtOAc), 1.15 g, mp 75 – 77 °C; Rf 0.59 (*n*-hexane/EtOAc 8:2); MS (EI, *m/z*) 409 [M^+-H], 392 [M^+-H_2O]; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm) 3.63 (2H, *t*, *J* = 6.6 Hz, CH_2-OH), 1.56 (2H, *m*, C-CH_2-C), 1.26 (50H, *bs*, C-$(CH_2)_{25}$-C), 0.88 (3H, *t*, *J* = 6.3 Hz, CH_3-C); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm) 63.12, 32.91, 31.94, 29.70, 29.63, 29.46, 29.35, 25.80, 22.68. Spectroscopic constants were consistent with those reported in the literature.[2,3]

*Euphol (**2**)*

White solid, 1.35 g, Rf 0.57 (*n*-hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 5.09 (1H, *t*, *J* = 7.2 Hz, H-24), 3.24 (1H, *dd*, *J* = 11.6 Hz, *J* = 4.8 Hz, H-3), 1.68 (3H, *s*, H-26); 1.60 (3H, *s*, H-27), 1.00 (3H, *s*, H-28), 0.95 (3H, *s*, H-19), 0.87 (3H, *s*, H-30), 0.85 (3H, *d*, *J* = 6.4 Hz, H-21), 0.80 (3H, *s*, H-29), 0.75 (3H, *s*, H-18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C (ppm) 35.4 (C1),

28.1 (C2), 79.1 (C3), 39.1 (C4), 51.1 (C5), 19.1 (C6), 27.8 (C7), 133.7 (C8), 134.1 (C9), 37.4 (C10), 21.7 (C11), 31.0 (C12), 44.2 (C13), 50.2 (C14), 29.9 (C15), 28.3 (C16), 49.8 (C17), 15.7 (C18), 20.3 (C19), 36.0 (C20), 19.1 (C21), 35.5 (C22), 24.9 (C23), 125.4 (C24), 131.1 (C25), 17.7 (C26), 25.9 (C27), 15.8 (C28), 28.2 (C29), 24.6 (C30). Spectroscopic constants were consistent with the data reported in the literature.[4,5]

*Eupha-8,23-diene-3β-25-diol (**3**)*

White amorphous solid, 6 mg; Rf 0.5 (CH_2Cl_2/Me_2CO 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 5.58 (2H, *m*, H-23 y H-24), 3.24, H-3 (1H, *dd*, *J* = 11.6 Hz, *J* = 4.4 Hz); 1.31 (6H, *s*, H-26 y H-27), 1.00 (3H, *s*, H-28); 0.95 (3H, *s*, H-19); 0.88 (3H, *s*, H-30); 0.82 (3H, *d*, *J* = 6 Hz, H-21); 0.80 (3H, *s*, H-29); 0.78 (3H, *s*, H-18); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 139.25 (C-24), 134.01 (C-8), 133.50 (C-9), 125.69 (C-23), 78.98 (C-3), 70.74 (C-25), 50.96 (C-5), 50.01 (C-14), 49.54 (C-17), 44.16 (C-13), 38.94 (C-4), 38.14 (C-22), 37.27 (C-10), 36.20 (C-20), 35.24 (C-1), 30.97 (C-12), 29.92 (C-27), 29.87 (C-26), 29.74 (C-15), 28.05 (C-28), 27.92 (C-2 y C-16), 27.67 (C-7), 24.45 (C-30), 21.48 (C-11), 20.14 (C-19), 19.05 (C-21), 18.93 (C-6), 15.77 (C-18), 15.52 (C-29). Spectroscopic data were consistent with those reported in the literature.[6,7]

*Cycloeucalenol (**4**)*

White solid, 10 mg; Rf 0.55 (*n*-hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 4.72, H-28a (*s*, 1H); 4.67, H-28b (*s*, 1H); 3.21 , H-3 (*ddd*, 1H, *J* = 10.4 Hz, *J* = 9.2 Hz, *J* = 4.8 Hz); 2.24, H-25 (*h*, 1H, *J* = 6.4 Hz); 1.03, H-26 (*d*, 3H, *J* = 6.8 Hz); 1.02, H-27 (*d*, 3H, *J* = 6.8 Hz); 0.98, H-29 (*d*, 3H, *J* = 6.8 Hz); 0.97, H-18 (*s*, 3H); 0.90, H-21 (*d*, 3H, *J* = 6.4 Hz); 0.89, H-30 (*s*, 3H); 0.39, H-19a (*d*, 1H, *J* = 4 Hz); 0.14, H-19b (*d*, 1H, *J* = 4 Hz); ^{13}C RMN (100 MHz, $CDCl_3$) δC (ppm) 157.08 (C-24), 106.08 (C-28), 76.74 (C-3), 52.37 (C-17), 49.07 (C-14), 47.03 (C-8),

45.52 (C-13), 44.77 (C-4), 43.50 (C-5), 36.29 (C-20), 35.51 (C-15), 35.18 (C-22), 34.98 (C-2), 33.98 (C-25), 33.05 (C-12), 31.48 (C-23), 30.96 (C-1), 29.70 (C-10), 28.27 (C-16), 27.40 (C-19), 27.14 (C-11), 25.33 (C-7), 24.83 (C-6), 23.72 (C-9), 22.16 (C-27), 22.03 (C-26), 19.30 (C-30), 18.50 (C-21), 17.95 (C-18), 14.56 (C-29). Spectroscopic data were consistent with those reported in the literature.[8]

*Lupeol (**5**)*

White solid, 234 mg, Rf 0.56 (n-hexane/EtOAc 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm) 4.69 (1H, *s*, H-30a); 4.57, (1H, *s*, H-30b); 3.19 (1H, *dd*, *J* = 11.1 Hz , *J* = 5.4 Hz, H-3); 2.38 (1H, *td*, *J* = 11.1 Hz, *J* = 5.7 Hz, H-19); 1.68 (3H, *s*, H-29); 1.03 (3H, *s*); 0.97 (6H, *s*); 0.94 (3H, s); 0.83 (3H, *s*); 0.79 (3H, *s*); 0.76 (3H, *s*); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C (ppm) 150.96 (C-20), 109.31 (C-30), 78.99 (C-3), 55.30 (C-5), 50.44 (C-9), 48.30 (C-19), 47.99 (C-18), 43.00 (C-17), 42.83 (C-14), 40.83 (C-8), 40.00 (C-22), 38.86 (C-4), 38.71 (C-1), 38.05 (C-13), 37.17 (C-10), 35.58 (C-16), 34.28 (C-7), 30.92, 29.85 (C-21), 27.99 (C-23), 27.42 (C-2 y C-15), 25.14 (C-12), 20.93 (C-11), 19.31 (C-29), 18.32 (C-6), 18.00 (C-28), 16.12 (C-25), 15.98 (C-26), 15.37 (C-24), 14.55 (C-27). Direct comparison with the data in the literature,[9] and with an authentic sample available in the laboratory confirmed the structure.

β-sitosterol

White needles, 125 mg; m.p. 155 – 157 °C, Rf 0.53 (*n*-hexane/EtOAc 7:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H (ppm) 5.35 (1H, *d*, *J* = 5.1 Hz, H-6), 3.52 (1H, *m*, H-3) 1.01 (3H, *s*), 0.92 (3H, *d*, *J* = 6.6 Hz), 0.84 (3H, *s*), 0.82 (3H, *s*) 0.80 (3H, *s*), 0.68 (3H, *s*). These data were in accordance with those reported in the literature,[10] and with the data of an authentic sample available in the laboratory.

Preparation of Semisynthetic Derivatives and Spectroscopic Data.

25,26,27-tris-nor-*3β-hydroxyeuphan-24-al* (**1**):

Procedure 1. It was followed the procedure reported in the literature for the oxidative cleavage of olefins.[11] To a solution of compound **2** (50 mg, 0.12 mmol) in dioxane-water (3:1, 5 mL) was added 2,6-lutidine (0.1 mL, 0.86 mmol), OsO_4 (two drops of 2.5 % solution in *t*-BuOH) and $NaIO_4$ (103 mg, 0.48 mmol). The reaction was stirred at r. t. for 20 h and then water and CH_2Cl_2 were added to the reaction. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed, and the crude residue was purified by column chromatography to afford aldehyde **1** (yield 25 %).

Procedure 2. Compound **1** was obtained from the epoxide **12**, which in turn was obtained from euphol (**2**) following the procedure reported for lanosterol[12] (see procedure below). To a solution of **12** (100 mg, 0.23 mmol) in Et_2O was added H_5IO_6 (61 mg, 0.27 mmol), and stirred at r. t. for 30 min. The reaction was washed with water and brine. The organic layer was dried over $MgSO_4$, and the solvent evaporated to yield **1** as a white solid after column chromatography eluting with *n*-hexane-EtOAc 8:2. Yield: 67 %; HRMS (ESI, *m/z*) calcd. for $H_{27}H_{45}O_2$ $[M+H]^+$ 401.34195, found: 401.34118; m. p. 128 – 130 °C (*n*-hexane); $[\alpha]_D$ = +20.9° (*c* 0.15, $CHCl_3$); Rf 0.41 (*n*-hexane/EtOAc 8:2, two developments). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.78 (1H, *t*, *J* = 1.8 Hz, H-24), 3.23 (1H, *dd*, *J* = 12, 4.8 Hz, H-3), 2.68 (1H, *dt*, *J* = 6, 2.8 Hz, H-23), 1.00 (3H, *s*, H-29), 0.95 (3H, *s*, H-19), 0.88 (3H, *s*, H-30), 0.85 (3H, *d*, *J* = 6 Hz, H-21), 0.80 (3H, *s*, H-28), 0.77 (3H, *s*, H-18). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 35.4 (C-1), 28.1 (C-2), 79.1 (C-3), 39.1 (C-4), 51.1 (C-5), 19.1 (C-6), 27.8 (C-7), 133.5 (C-8), 134.2 (C-9), 37.4 (C-10), 21.6 (C-11), 31.0 (C-12), 44.3 (C-13), 50.2 (C-14), 29.9 (C-15), 28.2 (C-16), 49.6 (C-17), 15.7 (C-18), 20.3 (C-19),

35.6 (C-20), 18.9 (C-21), 41.1 (C-22), 27.4 (C-23), 203.3 (C-24), 15.8 (C-28), 28.2 (C-29), 24.6 (C-30).

Euphyl benzoate (**6**): To a solution of **2** (50 mg, 0.12 mmol) in pyridine (1 mL) was added benzoyl chloride (1 mL, 8.6 mmol). The reaction mixture was stirred at rt for 2 h until the starting material was consumed. The reaction mixture was washed with water, extracted with EtOAc, washed with HCl 10 %, then with conc. $NaHCO_3$ solutions, and finally with brine. The organic layers were pooled and dried over $MgSO_4$, and the solvent evaporated under reduced pressure. After column chromatography (eluted with *n*-hexane/EtOAc 20:1) compound **6** was obtained as white flat plates. Yield: 79 %; $[\alpha]_D$ = +53.5° (*c* 0.29, $CHCl_3$); MS (DART+, *m/z*) $[M+H]^+$ 531 (12), 445 (16), 409 (100), 117 (77); m. p.: 151 – 153 °C (MeOH/$CHCl_3$, lit. 137-139 °C[13]), tlc Rf. 0.70 (*n*-hexane/EtOAc 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 8.05 (2H, br *d*, *J* = 9 Hz,), 7.59 – 7.52 (1H, *m*, *J* = 9 Hz), 7.470 – 7.40 (2H, *m*, *J* = 9 Hz), 5.10 (1H, t, J = 6 Hz), 4.75 (1H, *dd*, *J* = 12 Hz, *J* = 4.2 Hz), 1.69 (3H, *s*), 1.61 (3H, *s*), 1.04 (3H, *s*), 1.02 (3H, *s*), 0.96 (3H, *s*), 0.89 (3H, *s*), 0.86 (3H, *d*, *J* = 6 Hz), 0.77 (3H, *s*, H-18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C (ppm) 35.1 (C-1), 24.4 (C-2), 81.7 (C-3), 38.4 (C-4), 51.3 (C-5), 19.1 (C-6), 27.7 (C-7), 133.8 (C-8), 134.0 (C-9), 37.3 (C-10), 21.7 (C-11), 31.0 (C-12), 44.3 (C-13), 50.2 (C-14), 29.9 (C-15), 28.3 (C-16), 49.8 (C-17), 15.7 (C-18), 20.4 (C-19), 36.0 (C-20), 19.0 (C-21), 35.6 (C-22), 24.9 (C-23), 125.4 (C-24), 131.0 (C-25), 17.8 (C-26), 25.9 (C-27), 17.1 (C-28), 28.3 (C-29), 24.6 (C-30), 166.5 (C-31), 131.2 (C-32), 129.7 (C-33, C-33'), 128.5 (C-34, C-34'), 132.8 (C35). Spectroscopic data and NMR assignments were not previously reported in the literature.

3β-acetoxy euphane (**7**). Euphol (**2**, 100 mg, 0.23 mmol) was dissolved in pyridine (1 mL), then acetic anhydride (2 mL) was added to the solution. The reaction mixture was stirred for 12 h at r.

t. Then the mixture was poured into an ice bath, extracted with EtOAc then washed with 10 % HCl, and conc. $NaHCO_3$ solutions, brine, and finally the organic layer was dried over $MgSO_4$. After solvent evaporation the reaction crude was chromatographed (eluted with *n*-hexane/EtOAc 98:2) to obtain **7** as colorless needles. Yield: 89 %; mp 100 – 103 °C (MeOH/$CHCl_3$, lit. 109 °C[13]); $[\alpha]_D$ = +32.5° (*c* 0.32, $CHCl_3$); MS (DART+, *m/z*) 469 $(M+H)^+$; Rf (tlc) 0.52 (*n*-hexane/EtOAc 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 5.09 (1H, *t*, *J* = 7.2 Hz, H24), 4.50 (1H, *dd*, *J* = 11.8, 4.6 Hz), 2.05 (3H, *s*, H2'), 1.68 (3H, *s*, H26), 1.60 (3H, *s*, H27), 0.97 (3H, *s*, H19), 0.88 (3H, *s*, H30), 0.87 (6H, *s*, H28, H29), 0.85 (3H, *d*, *J* = 6 Hz, H21), 0.74 (3H, *s*, H18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C (ppm) 35.1 (C1), 24.4 (C2), 81.1 (C3), 38.0 (C4), 51.2 (C5), 18.9 (C6), 27.7 (C7), 133.8 (C8), 134.0 (C9), 37.3 (C10), 21.7 (C11), 31.0 (C12), 44.2 (C13), 50.2 (C14), 29.9 (C15), 28.3 (C16), 49.8 (C17), 15.7 (C18), 20.3 (C19), 36.0 (C20), 19.1 (C21), 35.6 (C22), 24.9 (C23), 125.3 (C24), 131.0 (C25), 17.8 (C26), 25.9 (C27), 16.8 (C28), 28.1 (C29), 24.6 (C30), 171.2 (C1'), 21.5 (C2').

Euphone (**8**): To a solution of **2** (500 mg, 1.17 mmol) in acetone, Jones' reagent was added dropwise until orange color remained and tlc indicated consumption of starting material. The excess of Jones's reagent was quenched with *i*-PrOH until the solution turned green. Celite was added to the reaction mixture and the excess solvent was evaporated under reduced pressure. The residue was purified by column chromatography to yield **8** as colorless needles. Yield: 86 %; $[\alpha]_D$ = +65.4 ° (*c* 0.35, $CHCl_3$); MS (DART+, *m/z*) $[M+H]^+$ 425 (100), 407 (24), 191 (16), 117 (16); m. p. 119 – 120 °C (*I*-PrOH, lit. 117-118 °C,[14] 119 °C[15]); Rf (tlc) 0.40 (*n*-hexane/EtOAc 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 5.09 (1H, br *t*, J = 7.0 Hz, H24), 2.50 (2H, *m*, H2), 1.68 (3H, *s*, H26), 1.61 (3H, *s*, H27), 1.10 (3H, *s*, H29), 1.05 (3H, *s*, H28), 1.05 (3H, *s*, H19), 0.90 (3H, *s*, H30), 0.86 (3H, *d*, *J* = 6.4 Hz, H21), 0.75 (3H, *s*, H18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C

(ppm) 35.7 (C1), 34.7 (C2), 218.3 (C3), 47.4 (C4), 51.6 (C5), 21.3 (C6), 27.6 (C7), 132.8 (C8), 134.9 (C9), 37.3 (C10), 21.6 (C11), 31.0 (C12), 44.3 (C13), 50.3 (C14), 29.9 (C15), 28.3 (C16), 49.8 (C17), 15.9 (C18), 20.4 (C19), 36.0 (C20), 19.0 (C21), 35.5 (C22), 24.9 (C23), 125.3 (C24), 131.1 (C25), 17.8 (C26), 25.9 (C27), 19.9 (C28), 26.9 (C29), 24.4 (C30). Spectroscopic data and NMR assignment were not previously reported in the literature.

Euphone oxime (**9**). The procedure was adapted from that reported for lanosterol.[12] To a solution of compound **8** (54 mg, 0.13 mmol) in EtOH (5 mL) was added hydroxylamine hydrochloride ($HONH_2 \cdot HCl$, 25 mg, 0.39 mmol) and NaOAc (48.6 mg, 0.59 mmol). The reaction was refluxed for 2 h and then EtOAc was added to the reaction mixture (10 mL) before washing with water, $NaHCO_3$ and brine. After removal of the solvent compound **9** was obtained quantitatively as a white solid (98 %) which upon recrystallization from methanol yielded white flat plates. $[\alpha]_D$ = - 3.43 ° (*c* 0.35, $CHCl_3$); HRMS (EI+, *m/z*) calcd. for $C_{30}H_{49}O_1N_1$: 439.3814, found: 439.3833; m. p.: 188 - 190 °C (MeOH; lit. 192 - 193 °C,[14] 194 - 195 °C[15]). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.09 (1H, *t*, *J* = 7.1 Hz, H24), 3.05 (1H, *ddd*, *J* = 15.4, 5.6, 3.7, H2), 2.34 - 2.21 (1H, *m*), 1.68 (3H, *s*, H26), 1.60 (3H, *s*, H27), 1.16 (3H, *s*), 1.08 (3H, *s*), 1.05 (3H, *s*), 0.88 (3H, *s*, H30), 0.85 (3H, *d*, *J* = 6 Hz, H21), 0.73 (3H, *s*, H18). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 35.2 (C1), 23.2 (C2), 167.3 (C3), 40.5 (C4), 51.8 (C5), 19.9 (C6), 27.6 (C7), 133.5 (C8), 134.3 (C9), 37.5 (C10), 21.7 (C11), 31.0 (C12), 44.2 (C13), 50.2 (C14), 29.9 (C15), 28.3 (C16), 49.8 (C17), 15.7 (C18), 19.9 (C19), 36.0 (C20), 19.1 (C21), 35.5 (C22), 24.9 (C23), 125.3 (C24), 131.1 (C25), 17.8 (C26), 25.9 (C27), 17.8 (C28), 27.5 (C29), 24.5 (C30). Spectroscopic data and NMR assignment were not previously reported in the literature.

3-O-*Methyl euphol* (**10**): To a solution of **2** (52 mg, 0.12 mmol) in THF was added NaH (70 mg, 2.92 mmol) followed by CH_3I (253 mg, 1.80 mmol). After stirring at r. t. overnight, cold water (10 mL) was added to the reaction mixture and then it was extracted with EtOAc (3x). The organic layer was washed with water and brine, and then dried over $MgSO_4$. After chromatographic purification (*n*-hexane/EtOAc 95:5) compound **4** was obtained as a white solid (68 %). Recrystallization from methanol yielded colorless prismatic needles. HRMS (ESI, *m/z*): calcd. for $C_{31}H_{52}O$ $[M+H]^+$: 441.40964, found: 441.41130; $[\alpha]_D$ = +44.7° (*c* 0.34, $CHCl_3$); m. p. 109 - 111 °C (MeOH); Rf (tlc) 0.66 (*n*-hexane/EtOAc 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 5.09 (1H, *t*, *J* = 7.0 Hz, H24), 3.36 (3H, *s*, H31), 2.68 (1H, *dd*, *J* = 11.8, 4.2 Hz, H3), 1.68 (3H, *s*, H26), 1.60 (3H, *s*, H27), 0.98 (3H, *s*, H29), 0.95 (3H, *s*, H19), 0.87 (3H, s, H30), 0.85 (3H, *d*, *J* = 6.4 Hz), 0.78 (3H, *s*, H28), 0.75 (3H, *s*, H18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C (ppm) 35.3 (C1), 22.9 (C2), 88.8 (C3), 39.0 (C4), 51.6 (C5), 19.1 (C6), 27.8 (C7), 133.6 (C8), 134.3 (C9), 37.4 (C10), 21.7 (C11), 31.0 (C12), 44.3 (C13), 50.2 (C14), 29.9 (C15), 28.3 (C16), 49.8 (C17), 15.7 (C18), 20.3 (C19), 36.0 (C20), 19.0 (C21), 35.6 (C22), 24.9 (C23), 125.4 (C24), 131.0 (C25), 17.8 (C26), 25.9 (C27), 16.4 (C28), 28.2 (C29), 24.6 (C30), 57.7 (C31). This compound was not previously reported in the literature.

3β-Hydroxy-euphan-26-al (**11**). To a solution of freshly sublimated selenium dioxide (SeO_2, 64 mg, 0.58 mmol) in EtOH (3 mL) was added to a solution of **2** (103 mg, 0.24 mmol) in EtOH (4 mL). The reaction was refluxed for 6 h. The solvent was evaporated at reduced pressure and the residue was chromatographed on Florisil using a mixture of *n*-hexane/Et_2O as eluent to yield **11** as white solid (yield: 78 %). $[\alpha]_D$ = +21.1° (*c* 0.28, $CHCl_3$); Rf (tlc) 0.53 (*n*-hexane/EtOAc 7:3). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.39 (1H, *s*, H26), 6.49 (1H, *t*, *J* = 7.3,1.3 Hz, H24), 3.23 (1H, *dd*, *J* = 11.6, 4.6 Hz, H3), 1.75 (3H, *s*, H27), 1.00 (3H, *s*, H29), 0.95 (3H, *s*, H19), 0.90 (3H,

d, *J* = 6 Hz, H21), 0.88 (3H, *s*, H30), 0.80 (3H, *s*, H28), 0.76 (3H, *s*, H18). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 35.4 (C1), 28.0 (C2), 79.1 (C3), 39.1 (C4), 51.1 (C5), 19.0 (C6), 27.8 (C7), 133.6 (C8), 134.2 (C9), 37.4 (C10), 21.6 (C11), 31.2 (C12), 44.3 (C13), 50.2 (C14), 29.8 (C15), 28.3 (C16), 49.7 (C17), 15.7 (C18), 20.3 (C19), 36.0 (C20), 19.1 (C21), 34.0 (C22), 26.0 (C23), 155.7 (C24), 139.2 (C25), 195.6 (C26), 9.4 (C27), 15.9 (C28), 28.2 (C29), 24.6 (C30). This compound was not previously reported in the literature.

3β-hydroxy-24,25-epoxy-euphane (**12**): To a solution of **2** (101 mg, 0.23 mmol) in CH_2Cl_2 was added under stirring a solid mixture of MCPBA (124 mg, 0.72 mmol) and $NaHCO_3$ (128 mg, 1.52 mmol). The first half of this mixture was added in portions at r. t. over 30 min. Then the reaction mixture was cooled to 0°C on an ice bath, and the second half of the MCPBA/$NaHCO_3$ mixture was added in portions over 30 min. The reaction was continued for 2 h at 0 °C, then it was filtered, washed with sat. solution of $NaHCO_3$ and brine. The organic layers were pooled and dried over $MgSO_4$. After evaporation of the solvent, the colorless reaction crude was chromatographed to obtain **12** as a white solid (yield: 78 %) which upon recrystallization from *n*-hexane yielded white nodules, mp 134 – 137 °C, $[\alpha]_D$ = +28.3° (*c* 0.43, $CHCl_3$); HRMS (EI, *m/z*) calcd. for $C_{30}H_{49}O_2$: 442.3811, found: 442.3817; Rf (tlc) 0.51 (*n*-hexane/EtOAc 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm) 3.23 (1H, *dd*, J = 12.4 Hz, *J* = 5.2 Hz, H3), 2.70 (1H, *t*, *J* = 6 Hz, H24), 1.31 (3H, *s*, H26), 1.26 (3H, s, H27), 1.00 (3H, *s*, H29), 0.95 (3H, *s*, H19), 0.87 (3H, s, H30), 0.85 (3H, *d*, *J* = 6 Hz, H21), 0.79 (3H, *s*, H28), 0.76 (3H, *s*, H18). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C (ppm) 35.4 (C1), 28.1 (C2), 79.1 (C3), 39.1 (C4), 51.1 (C5), 19.1 (C6), 27.8 (C7), 133.6 (C8), 134.2 (C9), 37.4 (C10), 21.7 (C11), 31.1 (C12), 44.3 (C13), 50.2 (C14), 29.9 (C15), 28.3 (C16), 49.5 (C17), 15.7 (C18), 20.3 (C19), 35.9 (C20), 19.2 (C21), 31.8 (C22), 25.4 (C23),

64.9 (C24), 58.5 (C25), 25.1 (C26), 18.9 (C27), 15.8 (C28), 28.2 (C29), 24.6 (C30). This compound was not previously reported in the literature.

Figure S1. ^{1}H NMR spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**, $CDCl_3$, 400 MHz)

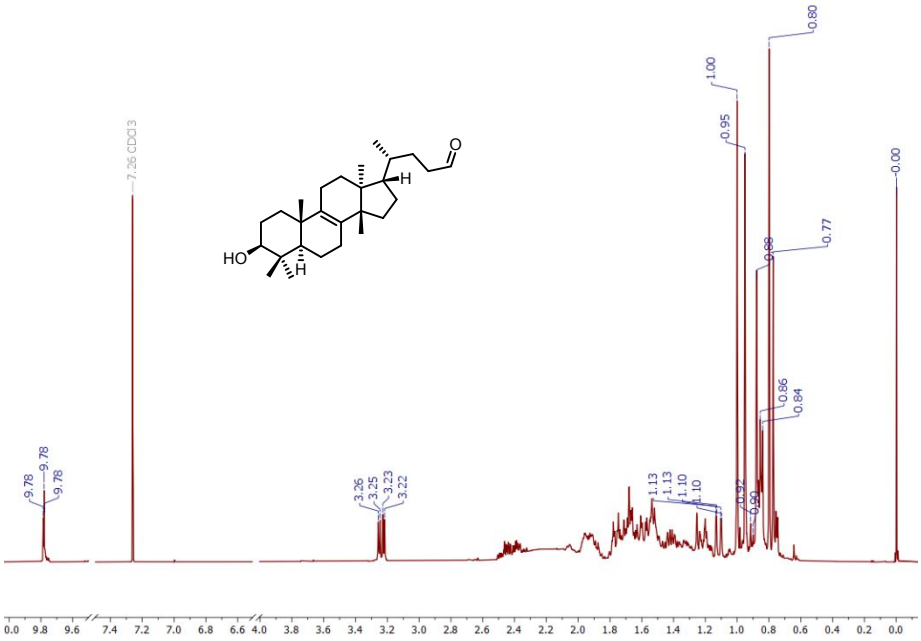


Figure S2. ^{13}C NMR spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**, $CDCl_3$, 100 MHz)

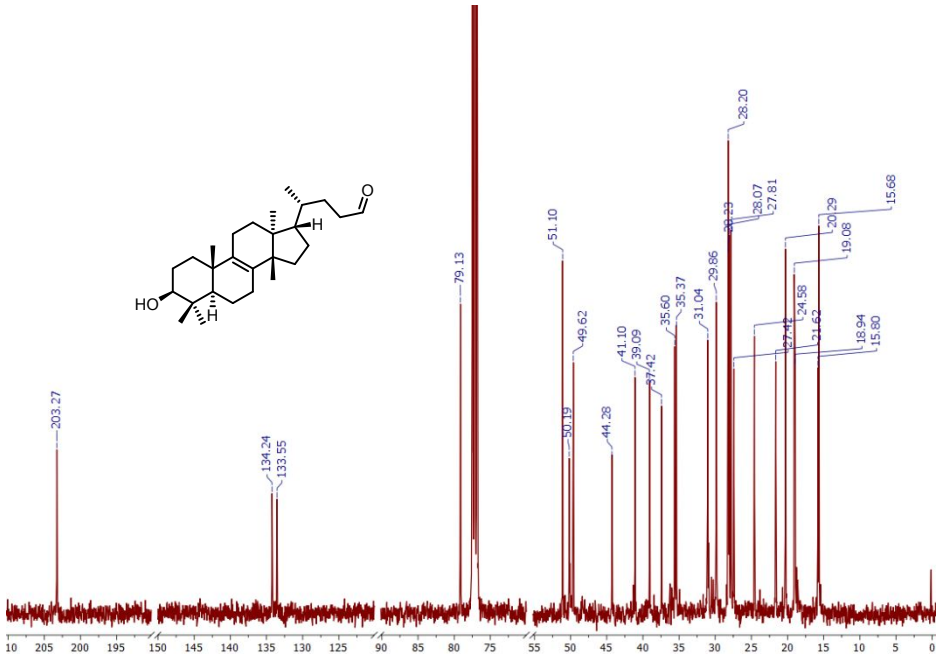


Figure S3. DEPT-90 spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**)

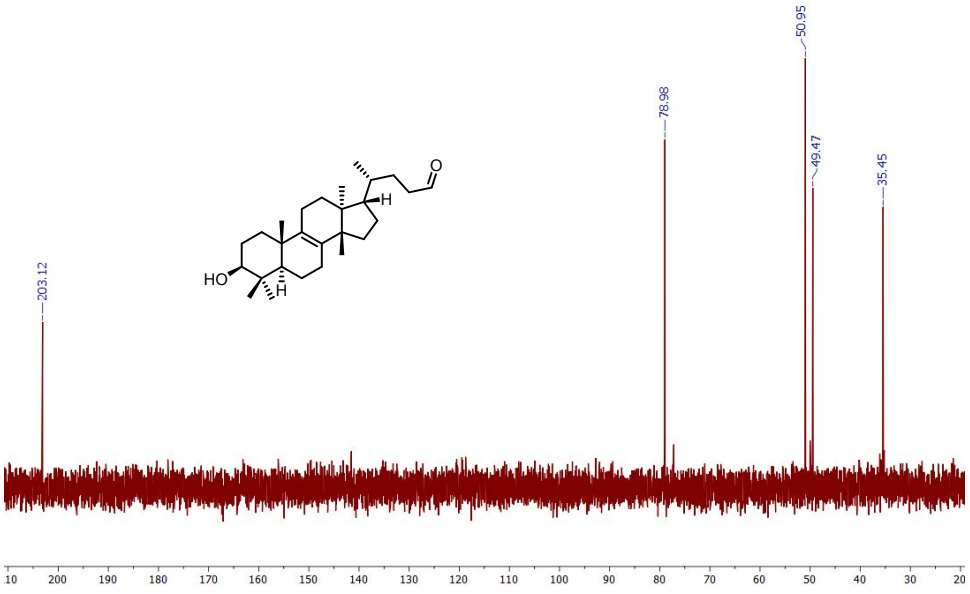


Figure S4. DEPT-135 spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**)

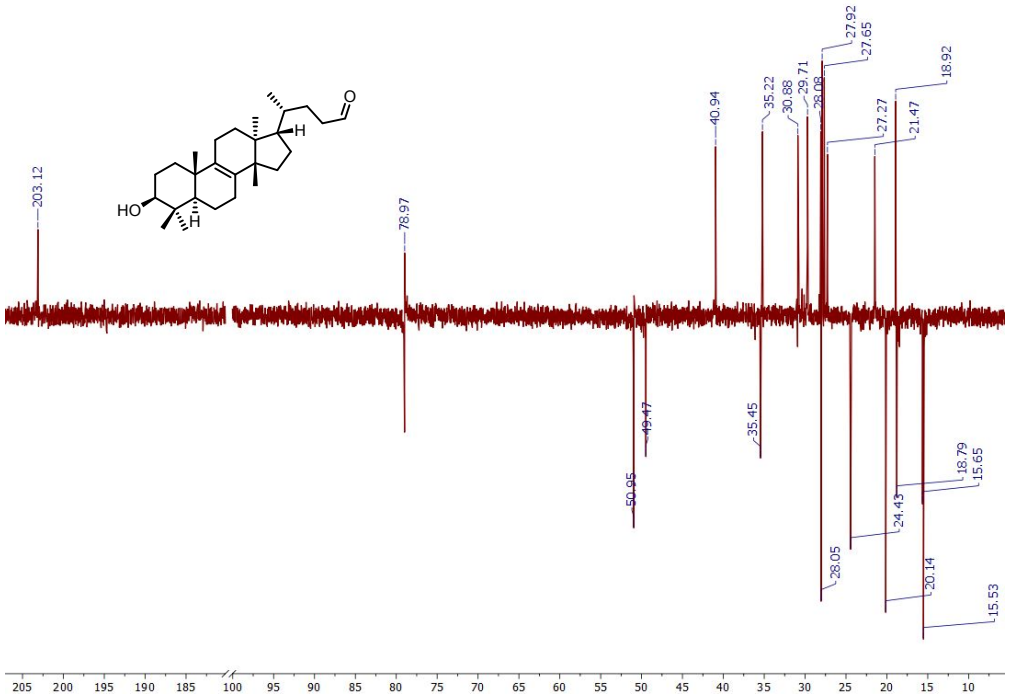


Figure S5. HMBC spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**)

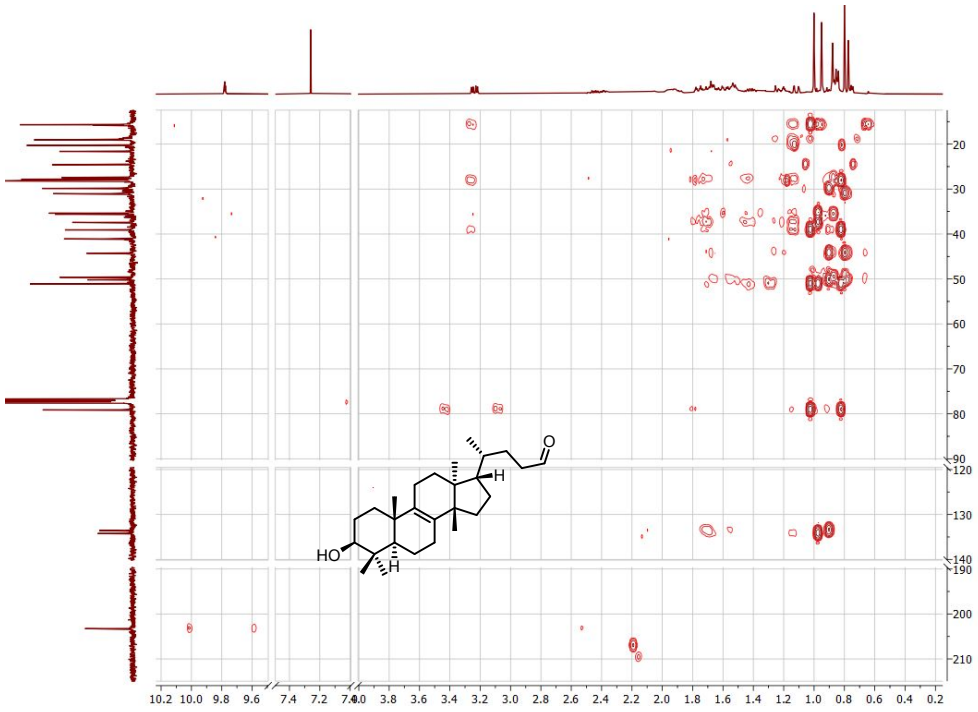


Figure S6. HSQC spectrum of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**)

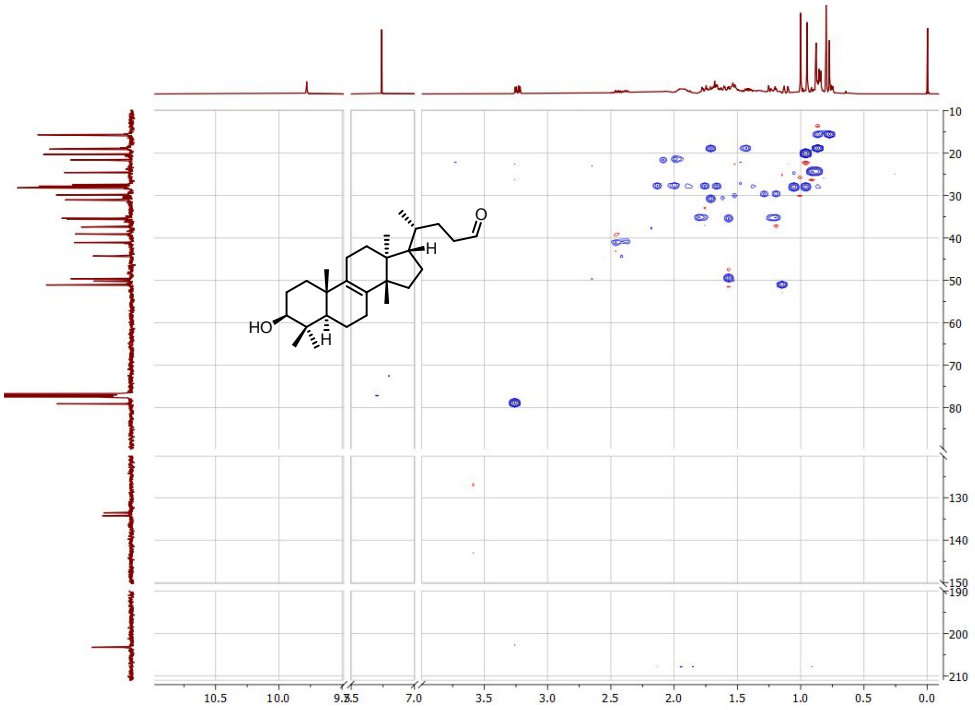
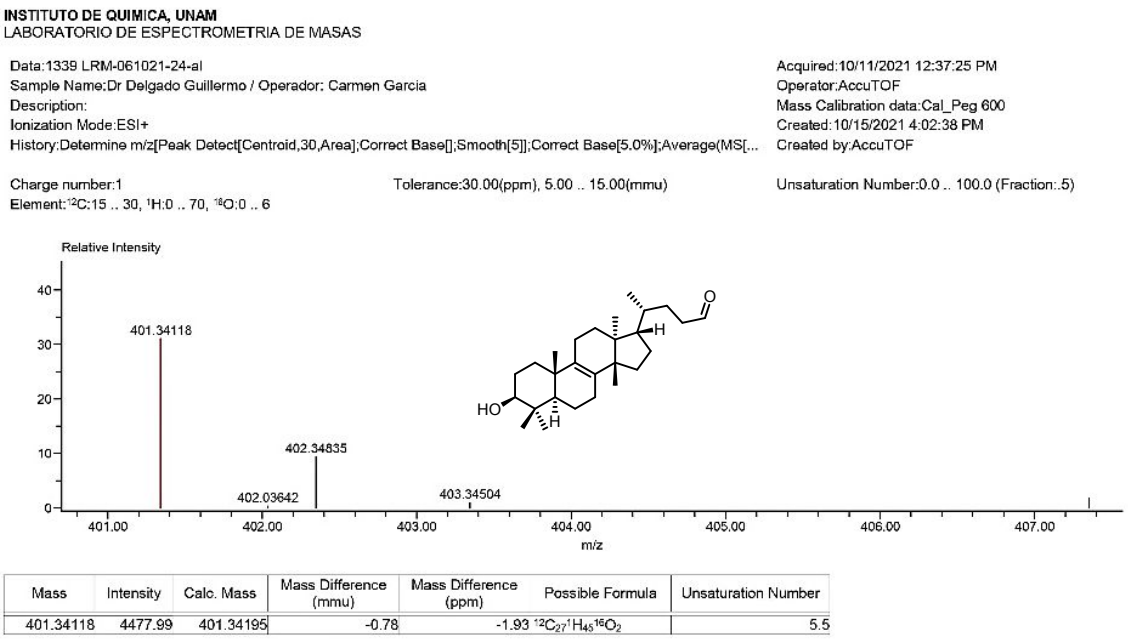


Figure S7. HRESIMS of 25,26,27-tris*nor*-3β-hydroxyeuphan-24-al (**1**)



Mass	Intensity	Calc. Mass	Mass Difference (mmu)	Mass Difference (ppm)	Possible Formula	Unsaturation Number
401.34118	4477.99	401.34195	-0.78	-1.93	$^{12}C_{27}{}^{1}H_{45}{}^{16}O_2$	5.5

Figure S8. ^{1}H NMR spectrum of euphyl benzoate (**6**, $CDCl_3$, 400 MHz)

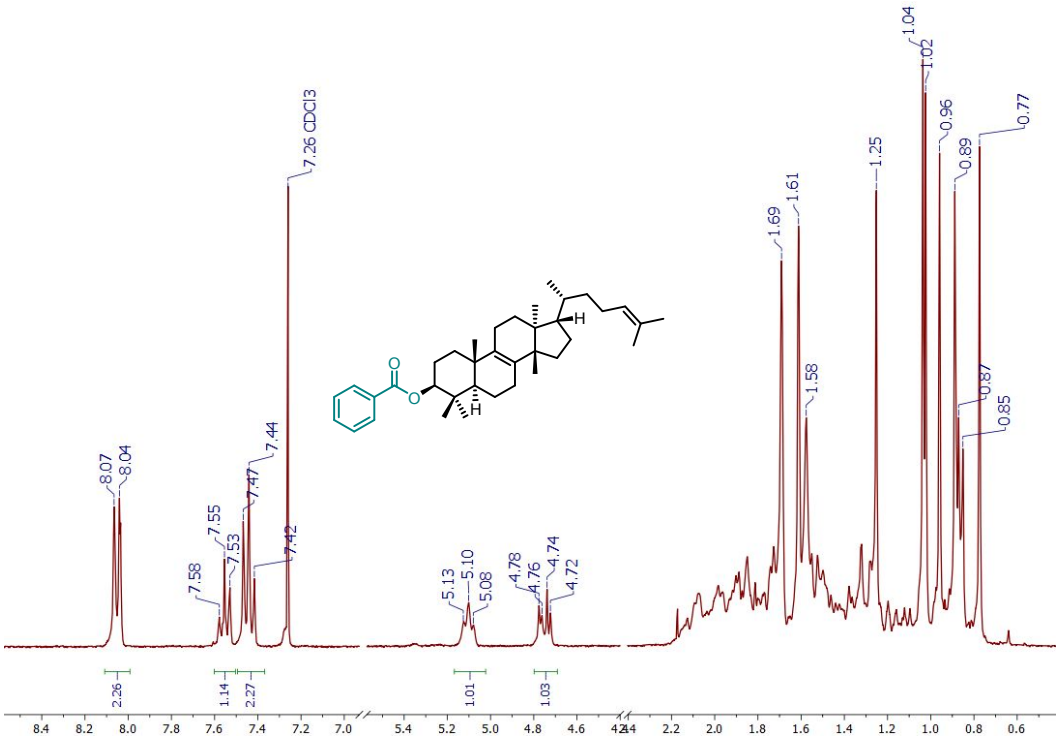


Figure S9. ^{13}C NMR spectrum of euphyl benzoate (**6**, $CDCl_3$, 100 MHz)

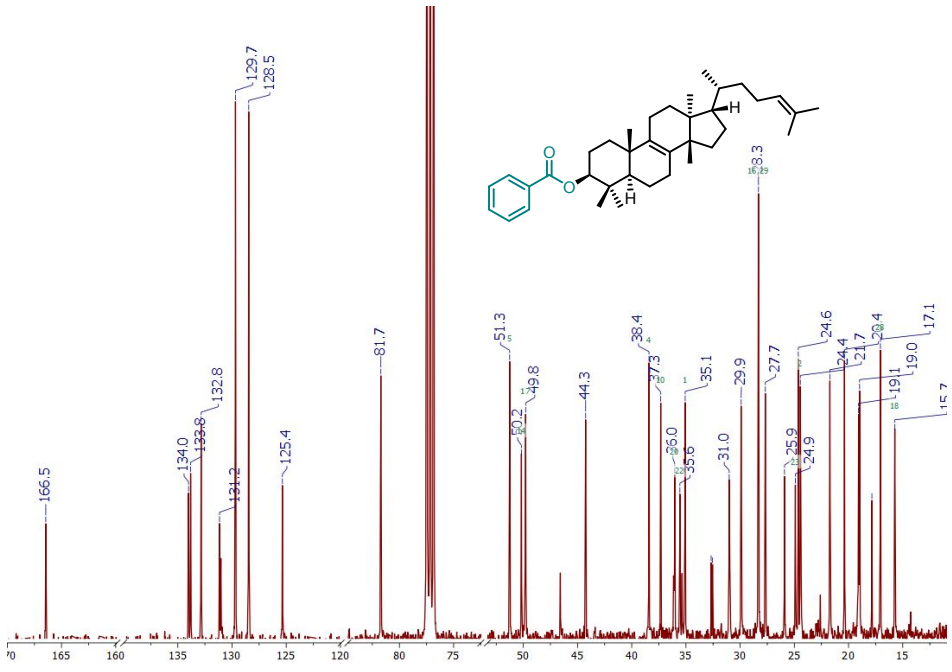


Figure S10. ^{1}H NMR spectrum of 3β-acetoxy euphane (**7**, $CDCl_3$, 400 MHz)

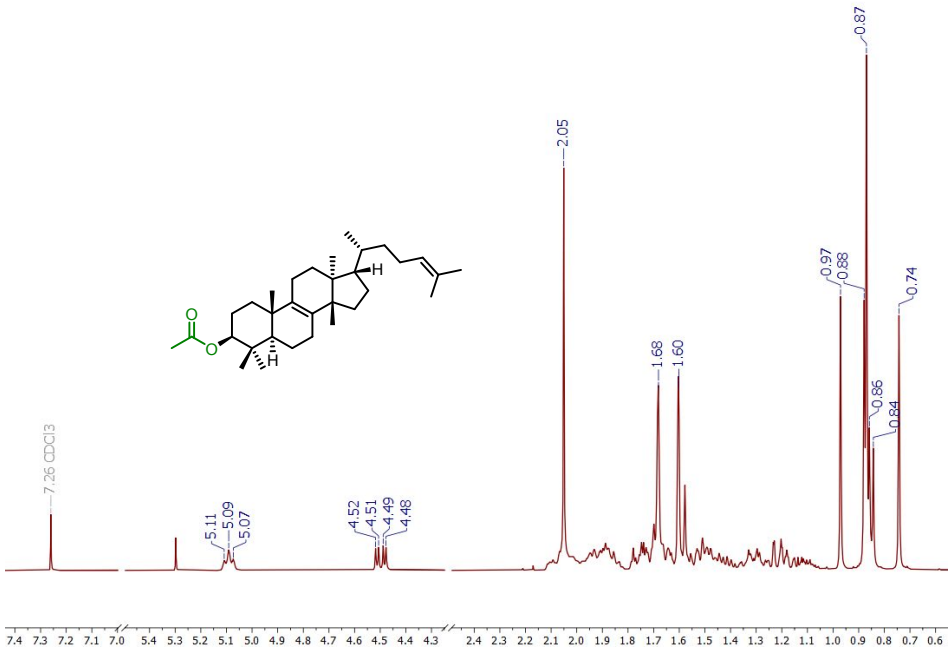


Figure S11. ^{13}C NMR spectrum of 3β-acetoxy euphane (**7**, $CDCl_3$, 100 MHz)

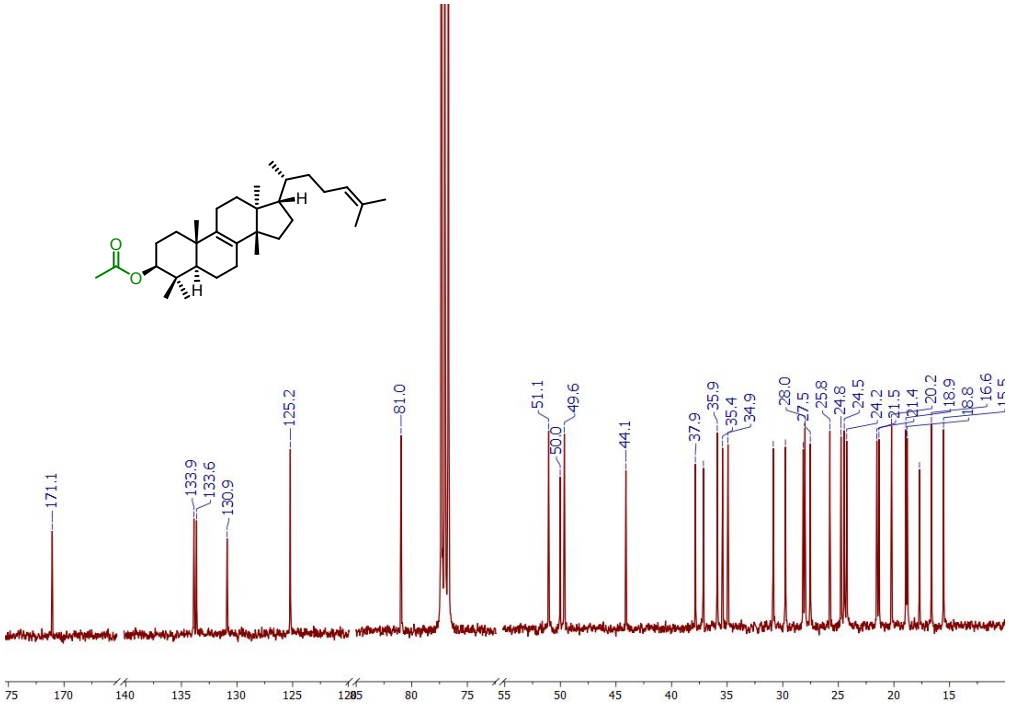


Figure S12. ^{1}H NMR spectrum of euphone (**8**, $CDCl_3$, 300 MHz)

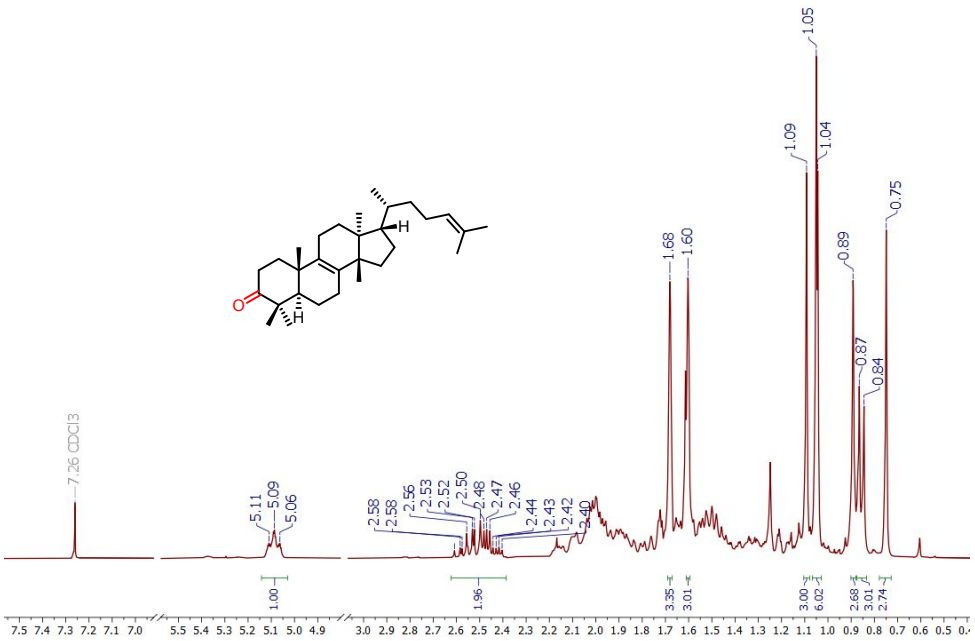


Figure S13. ^{13}C NMR spectrum of euphone (**8**, $CDCl_3$, 75 MHz)

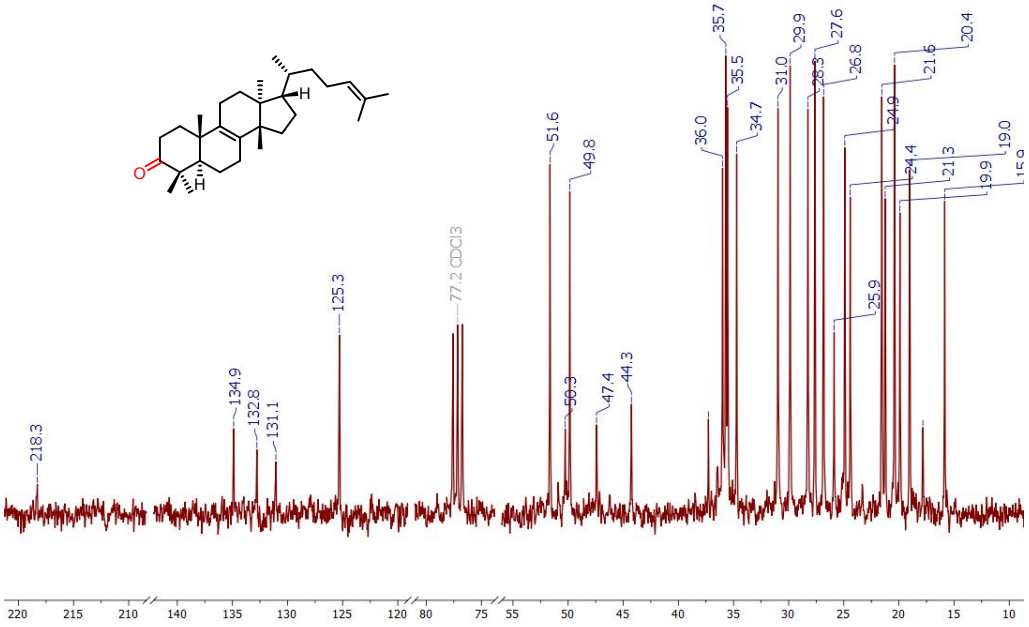


Figure S14. ^{1}H NMR spectrum of euphone oxime (**9**, $CDCl_3$, 300 MHz)

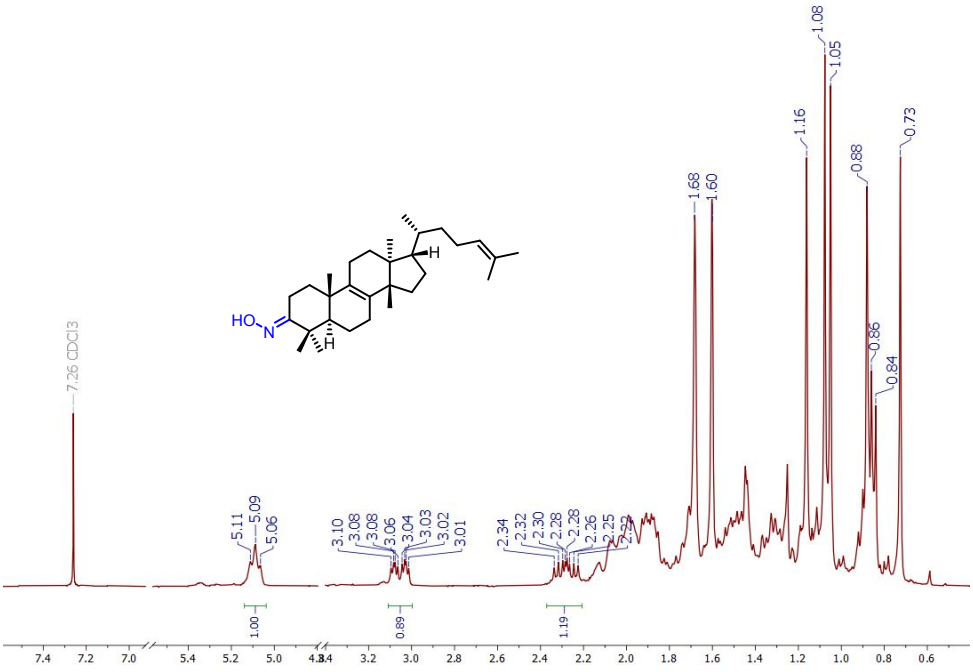


Figure S15. ^{13}C NMR spectrum of euphone oxime (**9**, $CDCl_3$, 75 MHz)

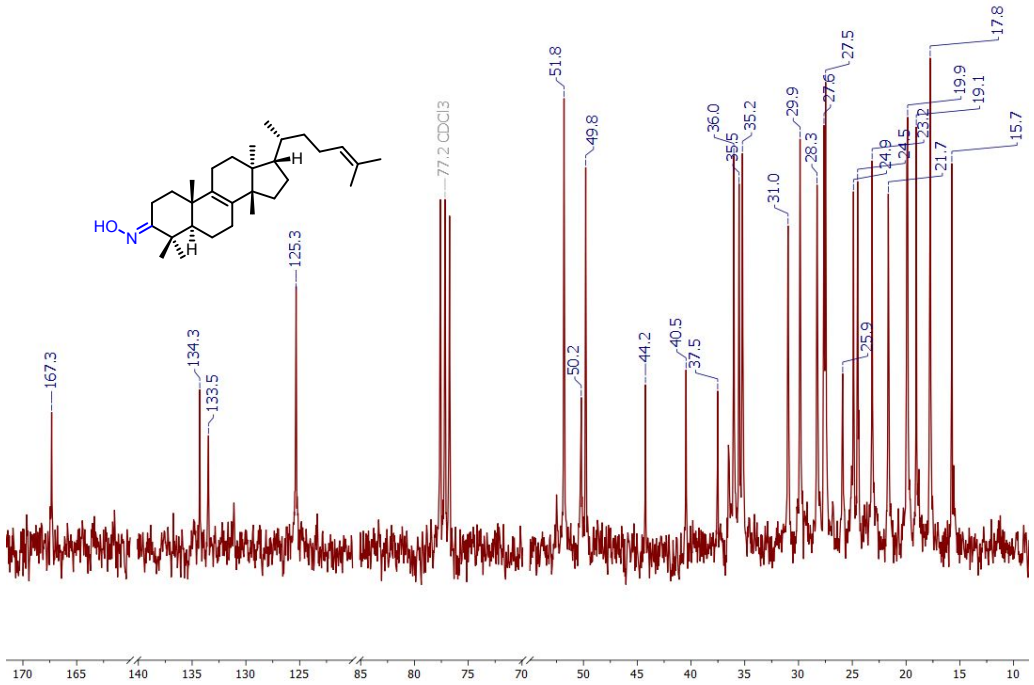


Figure S16. ^{1}H NMR spectrum of 3-*O*-methyl euphol (**10**, $CDCl_3$, 400 MHz)

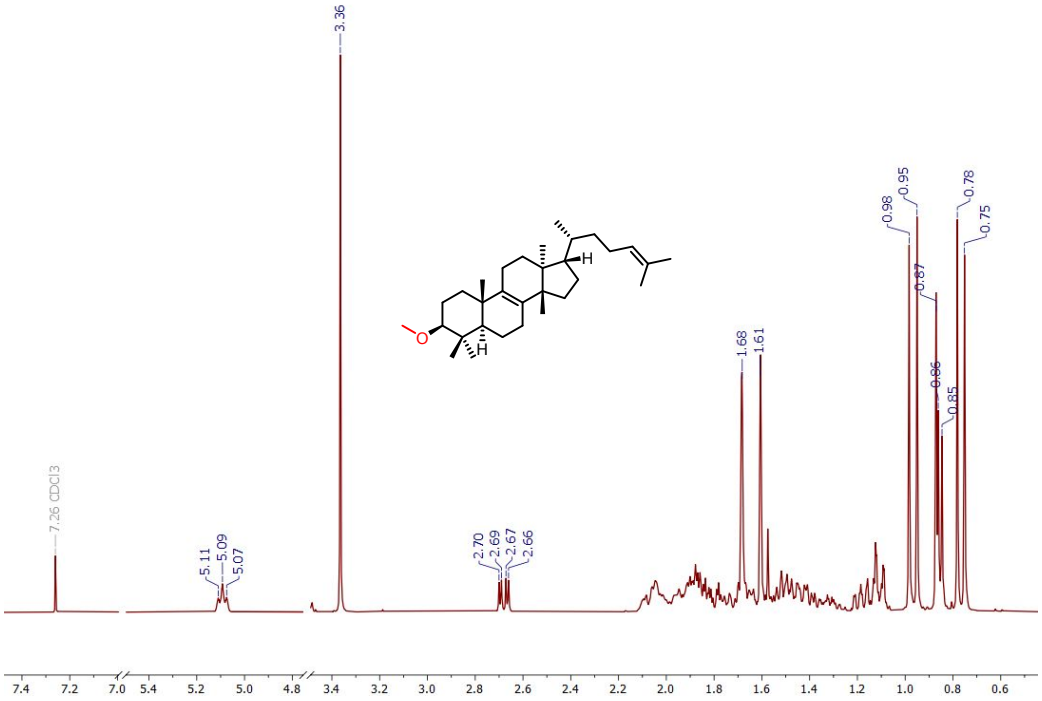


Figure S17. ^{13}C NMR spectrum of 3-*O*-methyl euphol (**10**, $CDCl_3$, 100 MHz)

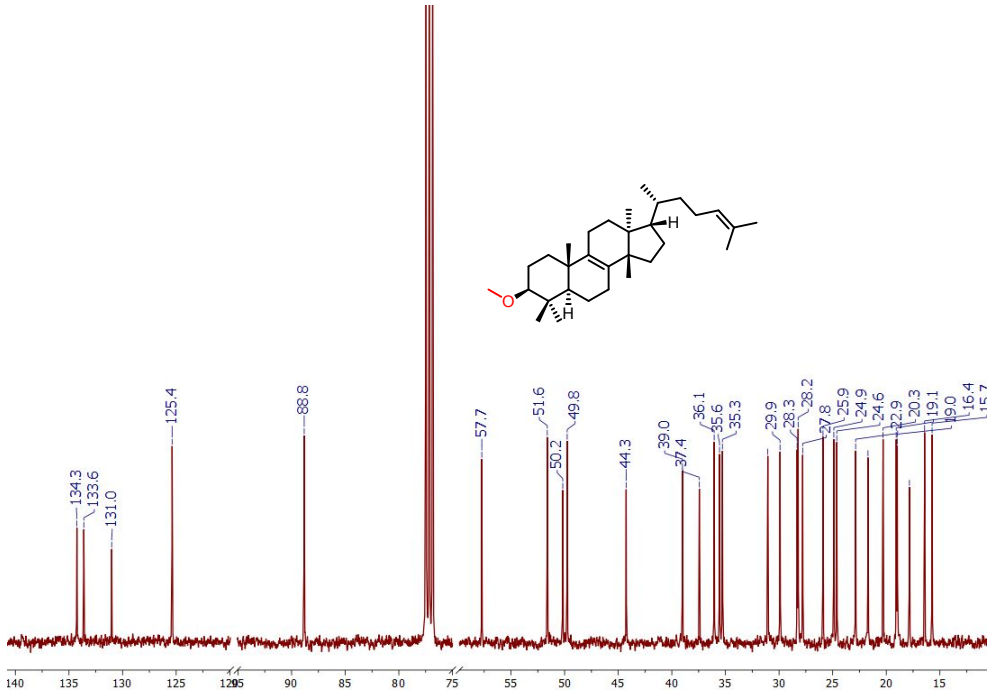


Figure S18. ^{1}H NMR spectrum of 3β-hydroxy-euphan-26-al (**11**, $CDCl_3$, 400 MHz)

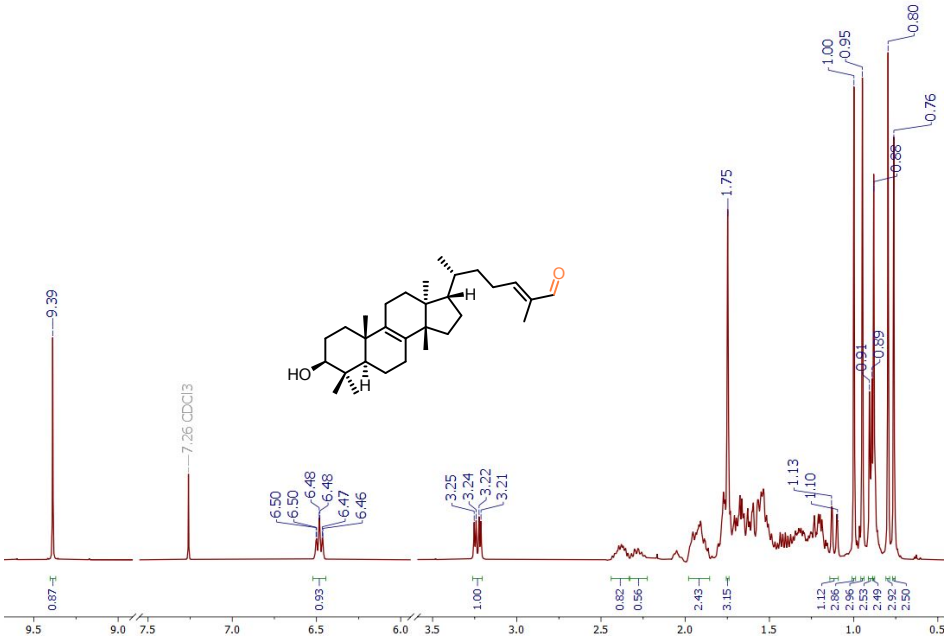


Figure S19. ^{13}C NMR spectrum of 3β-hydroxy-euphan-26-al (**11**, $CDCl_3$, 100 MHz)

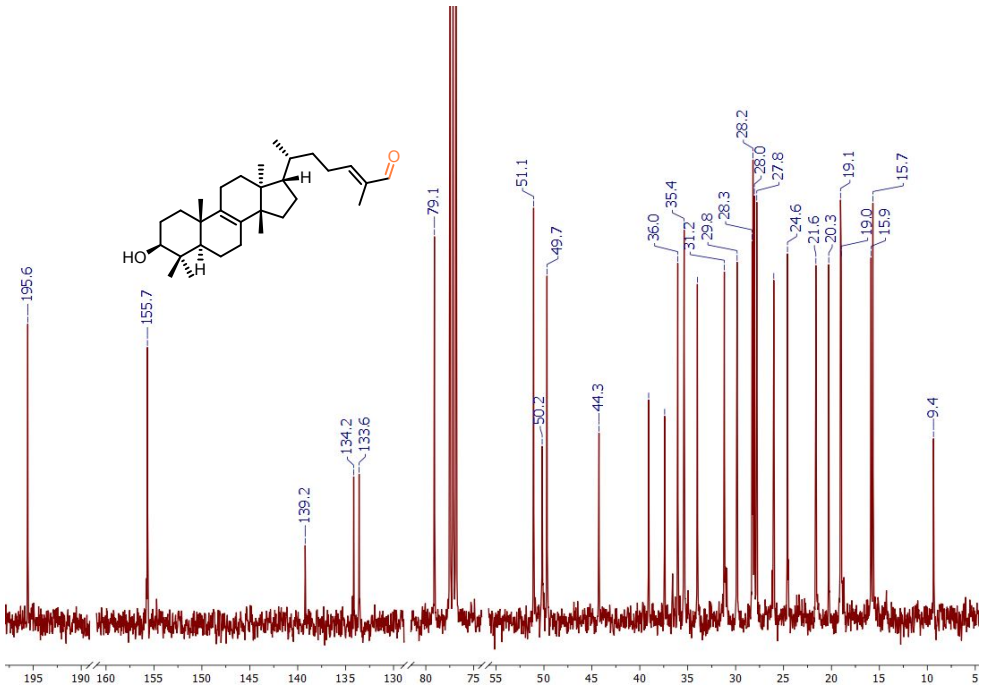


Figure S20. ^{1}H NMR spectrum of 3β-hydroxy-euphan-24,25-epoxy (**12**, $CDCl_3$, 400 MHz)

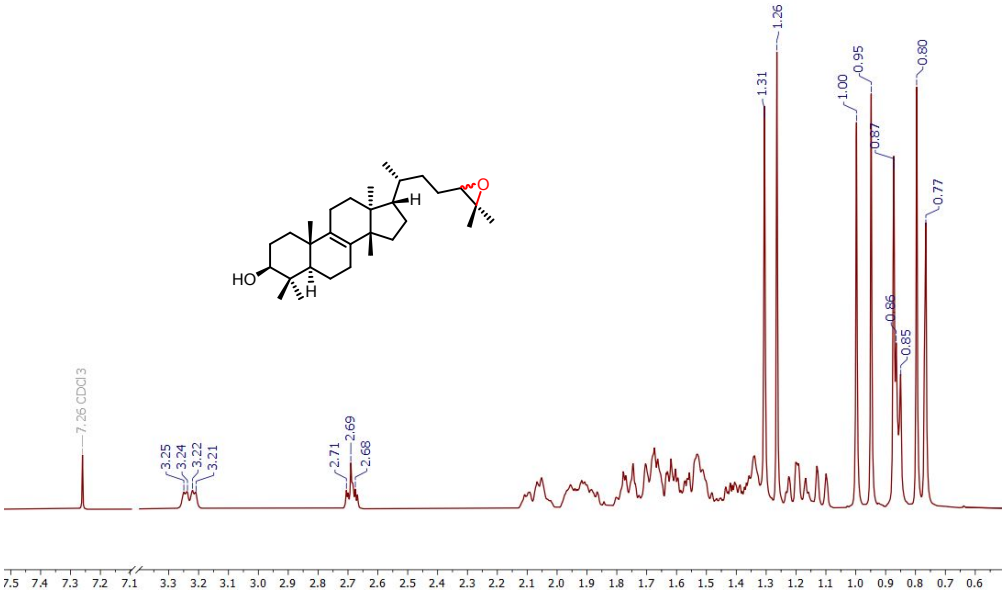
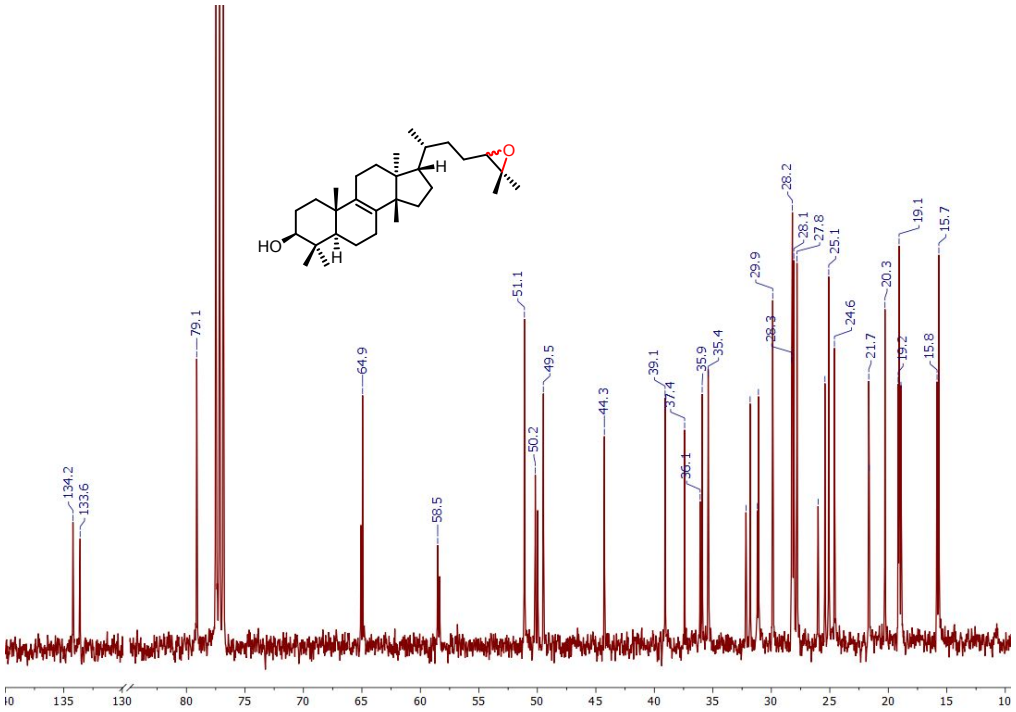


Figure S21. ^{13}C NMR spectrum of 3β-hydroxy-euphan-26-al (**12**, $CDCl_3$, 100 MHz)



Crystal Data and Structure Refinement of Euphone (8).

Identification code	118dlg22	
Empirical formula	C_{30} H_{48} O	
Formula weight	424.68	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 12.6173(3) Å	α= 90°.
	b = 16.2243(3) Å	β= 111.5050(10)°.
	c = 13.3964(3) Å	γ = 90°.
Volume	2551.43(10) $Å^3$	
Z	4	
Density (calculated)	1.106 Mg/m^3	
Absorption coefficient	0.475 mm^{-1}	
F(000)	944	
Crystal size	0.628 x 0.501 x 0.437 mm^3	

Theta range for data collection	3.546 to 68.344°.
Index ranges	-15<=h<=15, -19<=k<=19, -16<=l<=16
Reflections collected	44614
Independent reflections	9273 [R(int) = 0.0366]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7531 and 0.6659
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9273 / 115 / 613
Goodness-of-fit on F^2	0.806
Final R indices [I>2sigma(I)]	R1 = 0.0360, wR2 = 0.0921
R indices (all data)	R1 = 0.0362, wR2 = 0.0923
Absolute structure parameter	0.09(6)
Largest diff. peak and hole	0.404 and -0.195 e.Å^{-3}

Crystal Data and Structure Refinement of 3-*O*-Methyl Euphol (10).

Identification code	142DLG22	
Empirical formula	C_{31} H_{52} O	
Formula weight	440.72	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 7.2976(5) Å	α= 90°.
	b = 16.0249(10) Å	β= 95.494(3)°.
	c = 11.5631(7) Å	γ = 90°.
Volume	1346.01(15) Å^3	
Z	2	
Density (calculated)	1.087 Mg/m^3	
Absorption coefficient	0.464 mm^{-1}	
F(000)	492	
Crystal size	0.356 x 0.170 x 0.143 mm^3	

Theta range for data collection	3.840 to 68.332°.
Index ranges	-7<=h<=8, -19<=k<=19, -13<=l<=13
Reflections collected	26907
Independent reflections	4829 [R(int) = 0.0209]
Completeness to theta = 67.679°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7531 and 0.6834
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4829 / 1 / 298
Goodness-of-fit on F^2	1.058
Final R indices [I>2sigma(I)]	R1 = 0.0298, wR2 = 0.0774
R indices (all data)	R1 = 0.0300, wR2 = 0.0776
Absolute structure parameter	0.09(4)
Largest diff. peak and hole	0.174 and -0.165 e.$Å^{-3}$

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