# Euferol and Melliferol: Two Novel Triterpenoids from *Euphorbia mellifera*

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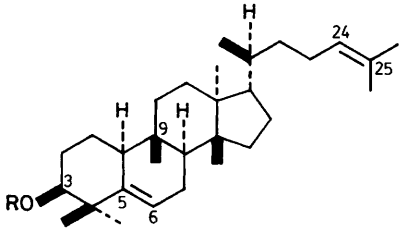
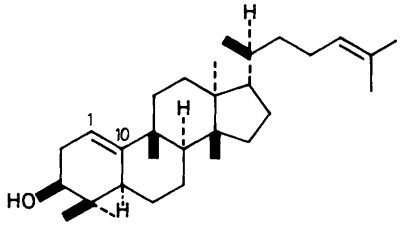
The structures and stereochemistries of two novel skeletons euferol [19(10→9)*abeo*-8α,9β,10α-tirucall-5-en-3β-ol] and melliferol [19(10→9)*abeo*-5α,8α,9β-tirucall-1(10)-en-3β-ol], found in *Euphorbia mellifera*, have been established from spectral data and single crystal *X*-ray analyses.

*Euphorbia mellifera* Ait., an Euphorbiaceae commonly encountered in the Atlantic island of Madeira, has been found to contain two triterpenes euferol (**1**) and melliferol (**2**), corresponding respectively to the new skeletons 19(10→9)*abeo*-8α,9β,10α-tirucall-5-en-3β-ol and 19(10→9)*abeo*-5α,8α,9β-tirucall-1(10)-en-3β-ol.

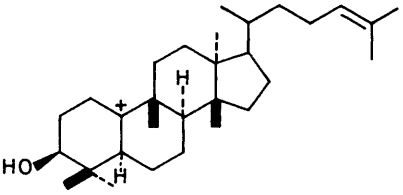
Euferol (**1**), $C_{30}H_{50}O$, by mass spectrometry, contained in its $^1H$ NMR spectrum (360 MHz, $CDCl_3$) five singlets attributed



(1) R = H
(3) R = Ac



(2)



(4)

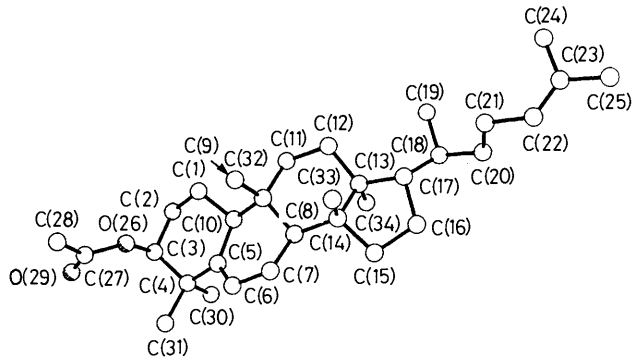


**Figure 1.** 3-D Structure of (**3**) obtained by X-ray analysis with atomic labelling. Oxygen atoms appear as shaded circles.

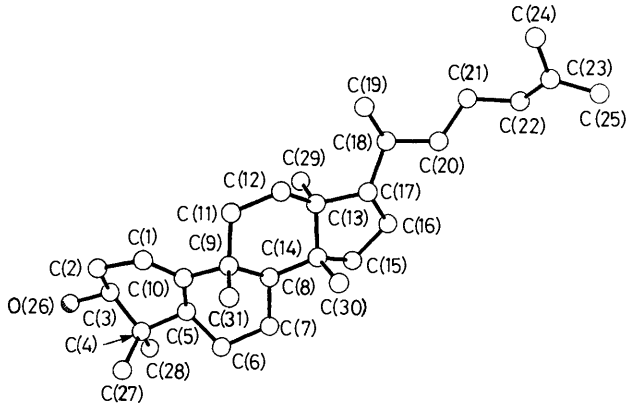


**Figure 2.** 3-D Structure of one of the pair of crystallographically independent molecules of (**2**) obtained by X-ray analysis with atomic labelling. Oxygen atoms appear as shaded circles.

to tertiary methyl groups (δ 0.81, 0.84, 0.87, 1.06, and 1.14), two methyl groups attached to an $sp^2$ carbon (δ 1.60 and 1.68), one secondary methyl group [δ 0.92 (d, *J* 6 Hz)], two olefinic protons at δ 5.11 and 5.67, and a proton attached to C(3) [δ 3.45 (t, *J* 2.5 Hz)] with features characteristic of equatorial configuration.[1] Euferol which could not be induced to crystallize yielded however a crystalline monoacetate which gave essentially the same $^1H$ NMR spectrum as (**1**), except for the proton attached to C(3) which now appeared at δ 4.72 (t, *J* 2.5 Hz). Of the two olefinic protons, the one at δ 5.11 [the same as in (**1**)] was assigned to the C(24) hydrogen and the other which had suffered a small shift to δ 5.57, in relation to (**1**), was ascribed to the olefinic proton at C(6).[1] The retro-Diels–Alder reaction involving cleavage of ring B observed in the mass spectrum of (**1**) and (**3**) further pointed towards the presence of a double bond at C(5)–C(6).[2]

Melliferol (**2**), isomeric with (**1**), had similarly to (**1**), in its $^1H$ NMR spectrum (360 MHz, $CDCl_3$) five tertiary methyl groups (δ 0.64, 0.78, 0.84, 1.01, and 1.03), two methyls attached to a $sp^2$ carbon (δ 1.60 and 1.68), one secondary methyl [δ 0.91 (d, *J* 6 Hz)], two olefinic protons at δ 5.10 and 5.36, and a proton attached to carbon linked to an oxygen function [δ 3.52 (m, $w_{\frac{1}{2}}$ 20 Hz)].

The isomeric relationship between (**1**) and (**2**) became evident from a study of their respective $^{13}C$ NMR spectra. Thus signals in both spectra at δ 125.3 and 130.9 were attributed to the olefinic carbons at C(24) and C(25) respectively, and δ *ca.* 76 to the carbon bearing the alcohol function [C(3)]. Whereas the $\Delta^{5,6}$ carbons[3] of (**1**) resonated at δ 142.1 and 121.9, the spectrum of (**2**) possessed a pair of signals, at δ 152.9 and 114.8 respectively, indicating that the olefinic bond is positioned differently in the triterpenoid nucleus. That it occupies the $\Delta^{1(10)}$ position (a very rare example) was suggested by the presence in its mass spectrum of two fragments *m/z* 354 and 72, resulting from a retro-Diels–Alder reaction, involving the cleavage of ring A.

The structure and stereochemistry of (**2**) and (**3**) were established unambiguously by X-ray analysis (Figures 1 and 2).* These studies confirmed the C(1)–C(10) position for the double bond in (**2**) and its C(5)–C(6) siting in (**3**). Also as deduced from the $^1H$ NMR data the C(3) proton in (**3**) is equatorial. In (**2**) this proton is axial.

It is interesting to speculate that if the carbocation (**4**) is indeed the biogenetic precursor of these two natural products,

* *Crystal data.—For* (**2**). $C_{30}H_{50}O$, $M$ = 426.7, monoclinic, $a$ = 18.331(11), $b$ = 7.393(6), $c$ = 22.801(23) Å, β = 111.47(6)°, $U$ = 2 876 Å$^3$, space group $P2_1$, $Z$ = 4 (2 crystallographically independent molecules), $D_c$ = 0.99 g cm$^{-3}$, μ(Cu-$K_\alpha$) = 4 cm$^{-1}$. For (**3**). $C_{32}H_{52}O_2$, $M$ = 468.8, monoclinic, $a$ = 12.391(4), $b$ = 7.452(2), $c$ = 15.626(6) Å, β = 93.46(3)°, $U$ = 1 440 Å$^3$, space group $P2_1$, $Z$ = 2, $D_c$ = 1.08 g cm$^{-3}$, μ(Cu-$K_\alpha$) = 5 cm$^{-1}$. Data for both structures were measured on a Nicolet R3m diffractometer with Cu-$K_\alpha$ radiation (graphite monochromator) using ω-scans. Both structures were solved by direct methods, (**2**) was refined isotropically to give $R$ = 0.158, $R_w$ = 0.158 for 2 316 independent observed reflections [$|F_o| \geq 3\rho(|F_o|)$, $8 \leq 58°$]; (**3**) was refined anisotropically to give $R$ = 0.047, $R_w$ = 0.051 for 1 900 reflections. Isotropic only of (**2**) was performed because of the very poor quality and exceptionally small crystals available, and the consequently very limited data set. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See 'Notice to Authors', *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue No. 1.

then their absolute stereochemistries would be depicted as in (**1**) and (**2**).

## Experimental

*Euferol* (**1**) *and Melliferol* (**2**).—The oily fraction obtained from extraction of the aerial parts (3.2 kg) of *Euphorbia mellifera* with acetone and hexane followed by saponification (10% KOH, EtOH, 24 h, room temp.) was purified by argented column chromatography [$SiO_2$, 20% $AgNO_3$, eluting with hexane–EtOAc (95:5)] to yield a pure fraction of euferol (**1**) (350 mg) as a homogeneous colourless glass; *m/z* (%) 426 ($M^+$, 2), 274 (11), 259 (19), 231 (5), 219 (4), 207 (29), 163 (15), 152 (1), and 134 (27). Acetylation of (**1**) ($Ac_2O$, py, 24 h, room temp.) gave white crystals of the monoacetate (**3**), m.p. 123–124 °C ($Me_2CO$); $[\alpha]_D^{25}$ +25.7 (*c* 1.20, $CHCl_3$). Further elution yielded melliferol (**2**) (100 mg), m.p. 132–134 °C ($Me_2CO$), $[\alpha]_D^{25}$ −38.8 °C (*c* 0.75, $CHCl_3$); *m/z* (%) 426 ($M^+$, 5), 354 (1), 259 (2), 241 (3), 231 (2), 219 (4), 207 (22), and 72 (50).

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