POMACERONE, A FURANOID TRITERPENE FROM PHELLINUS POMACEUS

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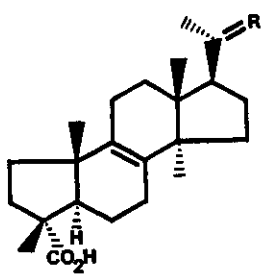
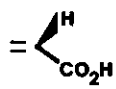
Abstract - The structure of a new furanoid triterpene was determined by a combination of chemical and physical methods as 23,26-dioxo-lanosta-8(9),23,25-trien-3,22-dione (pomacerone) (**3**).

Among the compounds isolated from Phellinus pomaceus[1,2] are ergosta-7,22-dien-3-one, ergosta-7,22-dien-3β-ol, friedelin, taraxerol and β-boswellic, ursolic, phellinic (**1**) and javeroic (**2**) acids. The same fungus, this time collected in the Los Tilos woods of La Palma (Canary Islands), has now yielded a new furanoid triterpene with a lanosterol skeleton, pomacerone (**3**), biogenetically related to **1** and **2** (Scheme 1).



(**1**) R = O

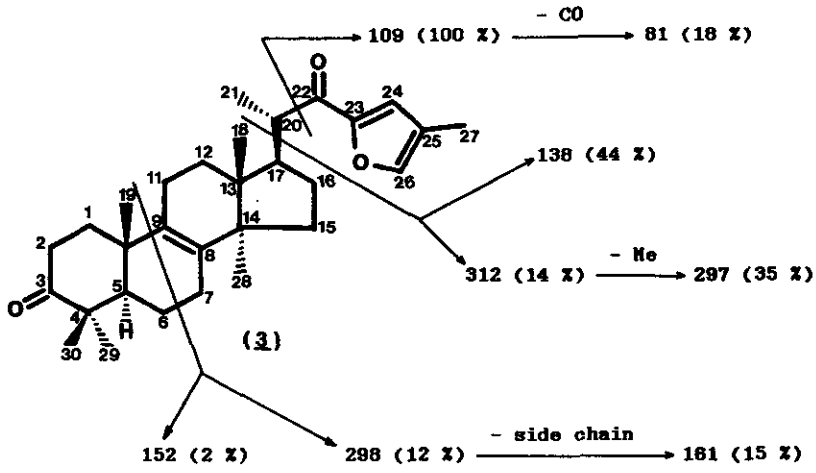
(**2**) R = 

RESULTS AND DISCUSSION

Pomacerone was isolated as a white solid, mp 216-218°, $[\alpha]_D^{20}$ +81.5° (c 7.74, $CHCl_3$). Its molecular formula, $C_{30}H_{42}O_3$, (hrms) indicated the presence of a double bond which resisted hydrogenation.[3,4] The ir spectrum had bands at 1700

(saturated ketone) and 3065, 3050, 1660, 1600, 895 and 750 cm^{-1} (conjugated furylketone). Compound **3** formed a 2,4-dinitrophenylhydrazone, mp 105°, and gave a positive Zimmermann reaction, indicating the presence of an α-methylene ketone.

In uv, there were absorption maxima at 234, 254 and 292 nm (log ∈= 3.68, 3.25 and 3.80, respectively) while ms showed fragmentation typical of lanosterol triterpene derivatives (Scheme 1). The molecular ion peak at m/z 450, the base peak at m/z 109 ($C_6H_5O_2$) and the prominent peak at m/z 138 ($C_8H_{10}O_2$) all confirmed the furylketone group.



Scheme 1

The ^1H nmr spectrum of pomacerone had the characteristic features of a lanostane derivative, namely, signals for five angular methyls, at δ 0.81, 0.92, 1.05, 1.08 and 1.11, and for one secondary methyl group as a doublet at δ 1.17 typical of the C-21H. The side chain was deduced from signals at δ 2.07 (3H, br s), 3.22 (1H, dq, J=6.8, 10.5 Hz), 7.04 (1H, br s), and 7.35 (1H, br s), assigned to C-27H, C-20H, C-24H and C-26H, respectively. Signals for the other eighteen protons appeared at between δ 2.50 and 0.90 and correspond to two methines and eight methylenes, one (δ 2.45) α to a carbonyl and two allylic at δ 1.60.

The COSY spectrum (Figure 1) showed couplings between H-24, H-26 and H-27. The H-20 was seen to be coupled with the methine H-17, and H-21. All these observations were confirmed by double resonance experiments. The H-17 signal, a symmetrical quartet which collapsed to a triplet when the H-20 was decoupled by

irradiation at δ 3.22. indicated that $J_{14,17}$ is of the same order as $J_{17,20}$ which agrees with the Karplus equation for the stereochemistry for **3** (which is also supported by biogenetical considerations).[2,5] Selective spin decoupling

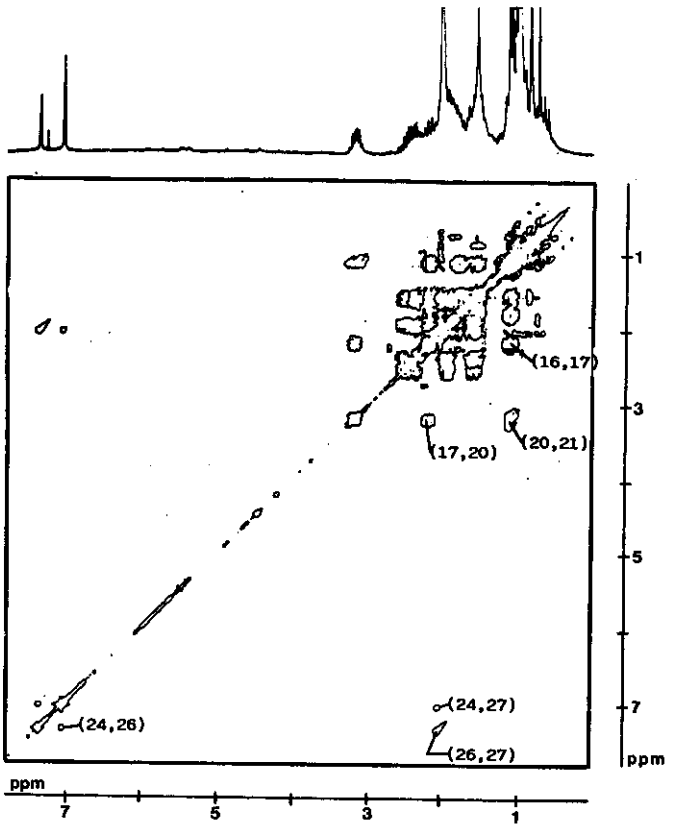
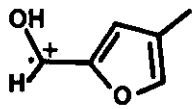


Figure 1

gave the following measurements for the coupling constants: $J_{14,17}$=10.0 Hz, $J_{17,20}$=10.5 Hz, $J_{20,21}$=6.8 Hz, $J_{24,24}$=0.9 Hz, $J_{24,27}$=1.5 Hz and $J_{24,27}$<0.5 Hz (undetermined). The new product was subjected to $LiAlH_4$ reduction (dry THF, 6 h, reflux) and yielded a diol (3,22-tetrahydropomacerone) the ^1H nmr spectrum of which showed furanic protons H-24 and H-26 at δ 6.10 and 7.15, respectively. Moreover, two new signals appeared at δ 3.20 (dd, J=6.9, 10.0Hz) and 4.72 (d, J=6.5 Hz) for one proton each, assignable to H-3 and H-22, respectively and geminal to both hydroxy groups. These signals were not seen in the $LiAlD_4$ reduction product. The carbonyl of Ring A was sited on C-3 as the double doublet is at δ 3.20 a characteristic occurrence in 3β-hydroxy-lanostanes.[6,7] Acetylation of the diol (Ac_2O, py, room temp, 24 h) afforded a diacetyl

derivative (3,22-diacetoxy-23,26-dioxolanosta-8(9),23,25-triene) in the ^{1}H nmr spectrum of which the furanic protons H-24 and H-26 were shifted to δ 6.14 and 7.15, respectively. The H-3 and H-22 signals, in this case geminal to acetoxy groups, appeared about 1 ppm downfield at δ 4.55 and 5.84, respectively. The ms cleavage was as shown in Scheme 1, while the molecular ion was seen at m/z 538, m/z 463 (M^+-HOAc-Me), m/z 403 (M^+-2HOAc-Me) and the base peak at m/z 111 ($C_6H_7O_2$) for fragment 4 (the corresponding acetate with loss of the ketene).



(4)

EXPERIMENTAL

Melting points are uncorrected. Ir spectra were recorded on a Perkin-Elmer 258 spectrophotometer, optical rotations on a Perkin-Elmer polarimeter, mod. 241, and uv spectra on a Perkin-Elmer 402 spectrophotometer. Hrms were taken on a VG Micromass ZAB-1F mass spectrometer connected to a PDP 11/34 (DEC) computer system. The ^{1}H nmr spectra were read at 200 MHz on a Bruker spectrometer, mod. WP200SY, or at 90 MHz on a Perkin-Elmer R32B spectrometer, with TMS as internal reference. Tlc was carried out on silica gel LS-254, 0.2 mm plates (Schleicher & Schüll). The two-dimensional COSY-90° experiment was made at 200 Hz with a sweep width of 2000 Hz (1K data points in W_2, 256t_1 values, zero-filled to 1K) in W_1. There was a one-second relaxation delay and eight transients were taken for each t_1.

Isolation of Pomacerone (3) The fungus (2.5 kg) was collected in the Bosque de Los Tilos (La Palma, Canary Islands), cut into small pieces and extracted with acetone (20 l) for 1 week at room temperature and then filtered. The residue was homogenized with acetone (25 l) and left to stand for 1 week at room temperature. The homogenate was filtered, the filtrates were combined and the organic solvent was removed under reduced pressure. The residue was made alkaline (pH 9.5) by adding 5% aq. Na_2CO_3 and extracted (x 5) with $CHCl_3$ (total, 2.5 l). The $CHCl_3$ layer was washed with H_2O, dried with Na_2SO_4 and taken to dryness. The residue (36 g) was percolated through neutral aluminum oxide (600g) (Merck, 90 active, 0.063-0.200 mm) by elution with MeOH and the resulting fraction (32 g) was subjected to chromatography on silica gel (900 g, Merck 40, 0.063-0.200 mm). Elution with 10% Me_2CO in n-hexane gave Fraction A (3.5 g). This fraction was rechromatographed on a silica gel column (225 g, Merck 40, 0.063-0.200 mm) and eluted with 10% Me_2CO in n-hexane to yield four fractions (A-1, -2, -3 and -4). After evaporation of the solvent from Fraction A-2,

treatment with n-hexane-C_6H_6 afforded compound **3** as a colourless amorphous solid (1.35 g), mp 216-218°C, $[\alpha]_D^{20}$ + 81.5° (c 7.74, $CHCl_3$), R_f=0.48 [n-hexane-Me_2CO (7:3)], blue fluorescence under uv light); ir ($CHCl_3$) ν_{max} cm^{-1}: 3065, 3050, 1700, 1660, 1600, 1502, 1455, 1435, 1375, 1315, 1215, 895 and 750; uv (EtOH) λ_{max} (log ϵ) nm: 234 (3.68), 254 (3.25), 292 (3.80); hrms M^+ 450.3141 ($C_{30}H_{42}O_3$), [M-side chain-H]$^+$ 312.2445 ($C_{22}H_{32}O_2$); ms m/z (rel. int. %) 450 [M^+] (6), 435 [M-Me]$^+$ (17), 312 [M-side chain-H]$^+$ (14), 297 (35), 161 (15), 138 (44), 109 (100), 81 (18); ^1H nmr ($CDCl_3$, 200 MHz, δ ppm): 7.35 (1H, br s, fine coupling, H-26), 7.04 (1H, br s, fine coupling, H-24), 3.22 (1H, dq, J=6.8, 10.5 Hz, H-20), 2.60-2.30 (2H, m, H-2), 2.22 (1H, q, J=10.5 Hz, H-17), 2.07 (3H, br s, fine coupling, H-27), 1.17 (3H, d, J=6.8 Hz, H-21), 1.11 (3H, s), 1.08 (3H, s), 1.05 (3H, s), 0.92 (3H, s), 0.81 (3H, s), 2.03-0.90 (15H, m, H-5 + 7 methylenes).

Reduction/Acetylation of Pomacerone **3** (200 mg) was treated with $LiAlH_4$ (70 mg) in dry THF (20 ml, 6 h, reflux) and the usual work-up gave a white solid (150 mg), homogenous under tlc: ^1H nmr ($CDCl_3$, 90 MHz, δ ppm): 7.15 (1H, br s, H-26), 6.10 (1H, br s, H-24), 4.72 (1H, d, J=6.5 Hz, fine coupling, H-22), 3.20 (1H, dd, J=6.9, 10.0 Hz, H-3), 2.02 (3H, s, H-27), 2.00-1.70 (19H, m, 3 methines + 8 methylenes), 1.00-0.70 (18H, 6 methyls). Acetylation of this diol with Ac_2O (2ml)-Py (1 ml) (room temp , 24 h) gave a diacetate which was purified by prep. tlc (silica gel, 10% Me_2CO in n-hexane) to give 3,22-diacetoxy-23,26-dioxo-lanosta-8(9),23,25-triene (3,22-tetrahydropomacerone diacetate) (80 mg): ir ($CHCl_3$) ν_{max} cm^{-1}: 1730, 1450, 1370, 1240, 1035, 755; uv (EtOH) λ_{max} (log ϵ) nm: 270 (3.5); ms, m/z (rel. int. %): 538 [M]$^+$ (28), 463 [M-HOAc-Me]$^+$ (98), 403 [M-2HOAc-Me]$^+$ (17), 111 (100); ^1H nmr ($CDCl_3$, 90 MHz, δ ppm): 7.15 (1H, br s, H-26), 6.14 (1H, br s, H-24), 5.84 (1H, d, J=6.0 Hz, fine coupling, H-22), 4.55 (1H, m, H-3), 2.05 (6H, s, H-27 + H-22 OAc), 2.00 (3H, s, H-3 OAc), 2.00-1.05 (19H, m, 3 methines + 8 methylenes), 1.03-0.70 (18H, 6 methyls).

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