Kulinone, a Euphane-type Triterpenoid from *Melia Azedarach,* L.

By FREDERIC C. CHANG* and CHAO-KUO CHIANG

(*Department of Pharmacognosy, University of Tennessee Medical Units, Memphis, Tennessee,* 38103)

A new triterpenoid of the euphane (20β-H)[1] series, for which the name "kulinone" is proposed, has been isolated from light petroleum extracts of the bark of *Melia azedarach*, L. (Chinese name: Ku Lien), from Taiwan.

Kulinone (Ia), $C_{30}H_{48}O_2$† (M^+ 440), crystallizes from light petroleum as crystals, m.p. 138°, $[\alpha]_D$ $-20°$, λ_{max} 2·84, 9·8, and 10·1 (–OH), 5·83 (6-ring C=O), 6·0, 11·8, and 12·1 μ (–CH=C$<$); τ 8·64—9·18 (18H, 6Me), 8·31—8·43 (6H, 2 C=C–Me), 5·95 (1H, m, $W_{\frac{1}{2}} \sim 16$ c./sec., C*H*OH), 4·9 (1H, m, –C*H*=C$<$), and 4·7 (1H, m, –C*H*=C$<$). It gives a positive tetranitromethane test, forms a dinitrophenylhydrazone, and can be acetylated under mild conditions to (Ib) ($[\alpha]_D$ $-5°$). On catalytic hydrogenation, it readily forms a dihydro-compound (Ic) which resists further hydrogenation, but still reacts with tetranitromethane. The n.m.r. spectrum of (Ic) has lost the 1-proton multiplet at τ 4·9 and the 6-proton signals in the vinyl methyl region, with concomitant gain of 6 protons in the high-field tertiary methyl region.

The foregoing properties and characteristics are compatible with a triterpenoid hydroxy-ketone with two double bonds, one of which is resistant to neutral catalytic hydrogenation. Kulinone was converted into the known compounds, butyrospermol[2] and Δ^8-euphen-3β-ol,[3] thus confirming these features, and revealing the complete structure, except for the position and configuration of the hydroxy-group.

The methanesulphonate (Id), m.p. 153°, was treated with lithium aluminium hydride to give an unsaturated alcohol (Ie), which under acidic

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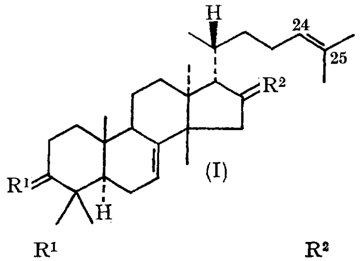
† All new compounds have been adequately characterized by elemental, and i.r. and n.m.r. spectral analysis.

catalytic hydrogenation conditions[4] (PtO_2–HOAc) yielded (II). Compounds (Ie) and (II) were shown by direct comparison with authentic specimens‡ (m.p., mixed m.p., $[\alpha]_D$, t.l.c., i.r., and n.m.r.) to be butyrospermol and Δ^8-euphen-3β-ol, respectively.



(I)

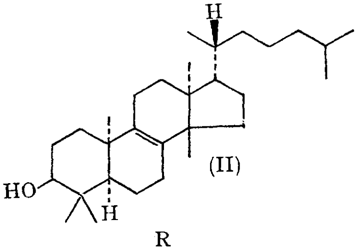
R^1	R^2
a; O	H, β-OH
b; O	H, β-OAc
c; O	H, β-OH (24, 25-dihydro)
d; O	H, β-OMs
e; H, β-OH	H, H
f; R^1R^2 = O	
g; -O-CH_2-CH_2-O-	O
h; O	H, α-OH
i; O	H, α-OAc
j; O	H, H

Most possible positions for the hydroxy-group can be eliminated as the group is secondary and non-allylic (by n.m.r.). However, derivative (If), product of Jones oxidation of (Ia), proved to be a key compound in further characterization of kulinone. Compound (If) is a diketone, with its new carbonyl group absorbing at 5·73 μ; it forms a 3-monoacetal (Ig), the o.r.d. curve of which has a strong positive Cotton effect ($[\phi]_{333m\mu}$ + 11,300°). The i.r. spectral information[5] places the original hydroxy-group in the D-ring; o.r.d. places it at C-16.§ Reduction of (Ig) by lithium aluminium hydride yields a mixture of epimeric alcohols, which after hydrolysis gave kulinone and its 16-epimer, (Ih) [(Ih) : (Ia) = 60 : 40, by t.l.c. estimation]. (Ih) has m.p. 173°, $[\alpha]_D$ −47°, τ 5·54 (1H, m, $W_{\frac{1}{2}} \sim 21$ c./sec., C*H*OH), and forms an acetate (Ii) with $[\alpha]_D$ −90°.

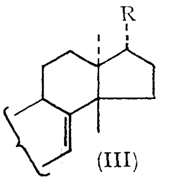
On the bases of (i) $[M]_D$ differences calculated¶ from specific rotations of (Ia), (Ib), (Ih), (Ii), and butyrospermone (Ij),[2] (ii) the estimated coupling constants[7,8] involving the C-16 proton in each of the epimers (Ia) and (Ih), which contribute towards a significant difference in band widths (at half height,[9] $W_{\frac{1}{2}}$), and (iii) an expectation that the major epimer should result from an attack of the metal hydride from the less hindered β-face of the ketone, we suggest that the hydroxy-group of kulinone has the β-configuration.

Accordingly, kulinone would be 16β-hydroxybutyrospermone (16β-hydroxyeupha-7,24-dien-3-one).

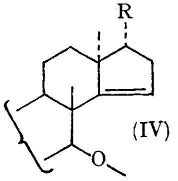
A proposed[10] biogenetic pathway to linonin-type triterpenes from euphane or tirucallane precursors has received increasingly strong support recently.[11] Particularly significant is a report[12] of the isolation from the same plant, *Melia azardirachta*, L. (a plant closely related to and often mistaken for *M. azedarach*), of three compounds corresponding to intermediate stages in the proposed biogenetic scheme [(III) → (IV) → (V) → (VI); R = C_8H_{17}]. However, the isolation of kulinone, with an oxygenated substituent at C-16 and the intact C-8 side chain (R) of butyrospermol, apparently representing an earlier stage of biogenesis, suggests



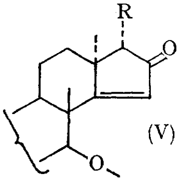
(II)



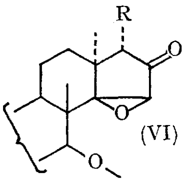
(III)



(IV)



(V)



(VI)

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§ Although no D-ring ketones of the euphane (or tirucallane) series have been reported, an intense Cotton effect of positive sign is characteristic of a 16-keto-compound of the 2-oxo-A-nor-steroid type of *trans*-hexahydroindan-2-ones. (P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry", Holden-Day, San Francisco, 1965, p. 105.)

¶ Calculated according to the principles of Klyne and Stokes (*J. Chem. Soc.*, 1954, 1979), which, however, were found not to be applicable in deducing the configuration of the 16-acetoxy-group of tetrahydrofusidic acid, which has a 8α-Me, 9β-H, 13α-H, and 14β-Me configuration (W. O. Godtfredsen, W. V. Daehne, S. Vangedal, A. Marquet, D. Arigoni, and A. Melera, *Tetrahedron*, 1965, 3505.)

that another route to (VI) might be possible. The alternative route (ignoring changes in the side-chain) would have the C-16 oxygenation step preceding the oxidative rearrangement [(III) → (Ia) → (V)] at the 7-, 8-, and, 14-centres.**

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** G. P. Cotterrell, T. G. Halsall, and M. J. Wriglesworth (*Chem. Comm.*, 1967, 1121) have recently reported a chemical model for a possible oxidative rearrangement which involves a 7α,8α-epoxide.

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