6α-Hydroxypolyporenic Acid C

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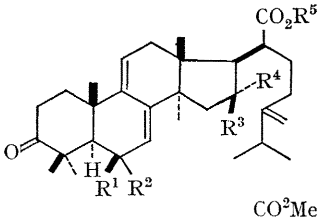
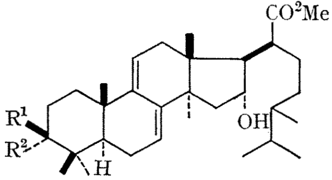
Summary Extraction of the mycelium of *Trametes feei* grown on a synthetic medium has yielded the new tetracyclic triterpene 6α-hydroxypolyporenic acid C (Ia) (6α,16α-dihydroxy-3-oxo-24-methylenelanosta-7,9(11)-dien-21-oic acid) isolated as its methyl ester.

THERE is continued interest in the search for compounds related to the tetracyclic triterpenoid antibiotics of the fusidic acid group both by modification (chemical and microbiological) of known compounds and by investigation of the metabolites of fungi related to those which produce these antibiotics.[1] Related tetracyclic triterpenes with somewhat weaker, but nevertheless appreciable pharmacological activity, are polyporenic acid A and polyporenic acid C[2] which are produced by members of the basidiomycete class of fungi. We now report the isolation of a new tetracyclic triterpene possessing the rare feature of oxygenation at C-6.

Extraction of the mycelium of the basidiomycete fungus *Trametes feei* grown on a synthetic medium has given a complex triterpenoid acid fraction which, after methylation (diazomethane) and chromatographic separation (alumina column) yielded the known methyl polyporenate C (10% of mycelial weight), methyl 3-*O*-acetyltumulosate (10%) and a mixture of at least three more polar esters (4%). The major component of this latter group was isolated by preparative layer chromatography and was homogeneous to t.l.c. analysis; its mass spectrum however, indicated the presence of about 10% of a higher molecular weight compound (*M* 556). Mild alkali treatment did not affect the major component but converted the minor constituent into a more polar product (probably by hydrolysis of an acetyl group) and this mixture was now readily separated by preparative layer chromatography. The major component had m.p. 222—223° C, $[\alpha]_D$ (CHCl$_3$) +99° and we propose the structure (Ib), methyl 6α-hydroxypolyporenate C, for this new compound based on the following evidence. The spectral and analytical data indicate the molecular formula $C_{32}H_{48}O_5$, and are in accord with (Ib); the allylic position of a hydroxy-group was evident from the u.v. spectrum of the derived ketone (Ic) which had λ_{max} 290 nm. (ϵ 10,800) with a shoulder at about 225 nm. (ϵ 4,000).[3] Catalytic hydrogenation (AcOH–Adams catalyst) of (Ib) effected hydrogenolysis of the allylic hydroxy-group with simultaneous reduction of the side-chain double bond and partial reduction of the 3-keto function to give a mixture of methyl dihydropolyporenate C (IIa) and methyl dihydrodehydrotumulosate (IIb) each identical (m.p., mixed m.p., and u.v., i.r., and n.m.r. spectra) with the corresponding authentic specimen. The location of the vinylidene double bond at the C-24 (28) position and not at the other possible position for such a group (C-25) was indicated by the absence of any signal in the n.m.r. spectrum of (Ib) that could be attributed to a methyl group attached to a double bond. These results prove that the new compound must be the methyl ester of either 6-hydroxy- or 12-hydroxypolyporenic acid C. The n.m.r. spectrum of (Ib) serves to distinguish between these two possibilities. Thus the C*H*OH signal under consideration appears as a doublet at δ 4·40 (*J* 10·0 Hz.) (unaffected by D$_2$O) coupled to an upfield proton at δ 1·68 (*J* 10·0 Hz.) as shown by spin–spin decoupling. This technique was also used to confirm that any coupling with the adjacent vinylic proton was negligible ($J < 0·5$ Hz.). This coupling with upfield proton can only occur if the secondary hydroxyl group is located at C-6 and not at C-12; further, the magnitude of the coupling constant and the absence of any coupling with the vinylic proton at C-7 constitute conclusive evidence that the C-6 hydroxy-group possesses the α-equatorial configuration.[4]



	R^1	R^2	R^3	R^4	R^5
(Ia)	H	OH	H	OH	H
(Ib)	H	OH	H	OH	Me
(Ic)	O		O		Me



(IIa) R^1R^2=O

(IIb) R^1=OH, R^2=H

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[3] L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York, 1959, p. 20.

[4] N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, 1964, p. 53.